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(54) **PHARMACEUTICAL COMPOSITION FOR TREATING ALZHEIMER'S DISEASE**

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USPC **514/227.2**; 514/211.01; 514/370; 514/275; 544/54; 544/330; 548/199; 540/544

(58) **Field of Classification Search**

USPC 514/227.2, 211.01, 370, 275; 544/54, 544/330; 548/199; 540/544

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,115,494	A	12/1963	Joseph et al.	
3,227,713	A	1/1966	Behner et al.	
3,235,551	A	2/1966	Schubert et al.	
3,636,116	A	1/1972	Trepanier	
3,719,674	A	3/1973	Trepanier	
3,775,409	A	11/1973	Harsanyi et al.	
4,311,840	A	1/1982	Condon	
4,895,841	A	1/1990	Sugimoto et al.	
4,906,626	A	3/1990	Amrein et al.	
5,100,901	A	3/1992	Sugimoto et al.	
5,236,942	A	8/1993	Miller	
5,328,915	A	7/1994	Long et al.	
5,880,147	A	3/1999	Yoshida et al.	
5,952,374	A	9/1999	Clarkson, Jr. et al.	
6,096,753	A	8/2000	Spohr et al.	
6,590,123	B2	7/2003	Bekesi et al.	
6,713,276	B2	3/2004	Cordell et al.	
7,183,070	B2	2/2007	Cordell et al.	
7,309,706	B2 *	12/2007	Rupp et al.	514/269
7,326,792	B2 *	2/2008	Shum et al.	548/331.5
7,414,050	B2 *	8/2008	Illig et al.	514/222.5
7,763,609	B2 *	7/2010	Zhu et al.	514/229.2
7,902,238	B2 *	3/2011	Galley et al.	514/374
8,173,642	B2 *	5/2012	Kobayashi et al.	514/227.2

(Continued)

FOREIGN PATENT DOCUMENTS

DE	140144	2/1980
EP	0798 292	10/1995

(Continued)

OTHER PUBLICATIONS

Co-pending U.S. Appl. No. 13/260,103, entitled Isothiourea Derivatives or Isourea Derivatives Having BACEI Inhibitory Activity, filed Sep. 23, 2011.

(Continued)

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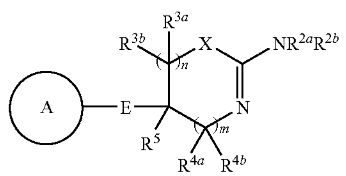
(57) **ABSTRACT**

A pharmaceutical composition for treating Alzheimer's disease containing a compound represented by the general formula (I);

(I)



wherein ring A is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;
E is lower alkylene, etc.;
X is S, O, or NR^1;
R^1 is a hydrogen atom or lower alkyl;
R^{2a}, R^{2b}, R^{3a}, R^{3b}, R^{4a} and R^{4b} are each independently a hydrogen atom, halogen, hydroxy, etc.;
n and m are each independently an integer of 0 to 3;
n+m is an integer of 1 to 3; and
R^5 is a hydrogen atom, optionally substituted lower alkyl, etc.;
its pharmaceutically acceptable salt, or a solvate thereof as an active ingredient.

9 Claims, No Drawings

(56) **References Cited**

U.S. PATENT DOCUMENTS

2002/0019427	A1	2/2002	Carry et al.	
2005/0165080	A1	7/2005	Rupp et al.	
2006/0173006	A1	8/2006	Sun et al.	
2006/0183790	A1	8/2006	Cole et al.	
2006/0183792	A1	8/2006	Fobare et al.	
2006/0183943	A1	8/2006	Hu et al.	
2007/0004730	A1	1/2007	Zhou et al.	
2007/0004786	A1	1/2007	Malamas et al.	
2007/0027199	A1	2/2007	Malamas et al.	
2007/0224656	A1	9/2007	Cordell et al.	
2008/0200445	A1	8/2008	Zhu et al.	
2009/0023729	A1	1/2009	Nakamuta et al.	
2009/0082560	A1	3/2009	Kobayashi et al.	
2010/0075957	A1	3/2010	Tamura et al.	
2010/0093999	A1	4/2010	Motoki et al.	
2010/0125087	A1	5/2010	Holenz et al.	
2010/0234365	A1 *	9/2010	Liu et al.	514/227.8
2010/0261727	A1	10/2010	Chi et al.	
2011/0009395	A1	1/2011	Audia et al.	
2011/0046122	A1	2/2011	Andreini et al.	
2011/0065695	A1	3/2011	Beauchamp et al.	
2011/0190279	A1	8/2011	Hori et al.	
2011/0237576	A1	9/2011	Yonezawa et al.	
2012/0015961	A1	1/2012	Tamura et al.	
2012/0016116	A1	1/2012	Kobayashi et al.	
2012/0022249	A1	1/2012	Kobayashi et al.	
2012/0172355	A1	7/2012	Tamura et al.	
2012/0238548	A1	9/2012	Gabellieri et al.	
2012/0238557	A1	9/2012	Masui et al.	
2012/0245154	A1	9/2012	Anan et al.	
2012/0245155	A1	9/2012	Yoshida et al.	
2012/0245157	A1	9/2012	Masui et al.	
2012/0253035	A1	10/2012	Narquizian et al.	
2012/0258962	A1	10/2012	Hilpert et al.	
2012/0295900	A1	11/2012	Hilpert et al.	
2013/0158260	A1	6/2013	Kobayashi et al.	

FOREIGN PATENT DOCUMENTS

EP	0713704	5/1996
EP	0717040	6/1996
EP	0718294	6/1996
EP	1043312	10/2000
EP	1283039	2/2003
EP	1 577 294	9/2005
EP	1 942 105	7/2008
EP	1942105	7/2008
EP	2147914	1/2010
EP	2151435	2/2010
EP	2 233 474	9/2010
EP	2305672	4/2011
EP	2332943	6/2011
EP	2 360 155	8/2011
EP	2415756	2/2012
GB	1001093	8/1965
JP	62-120374	6/1987
JP	8-231521	9/1996
JP	09-067355	3/1997
JP	10-505862	12/1999
JP	11/349572	12/1999
JP	2005-509651	4/2004
JP	2004-149429	5/2004
JP	2005-517634	6/2005
JP	2005-526005	9/2005
JP	2005-531520	10/2005
JP	2006-519758	8/2006
JP	2009-051828	3/2009
JP	2009-520685	5/2009
WO	94/012165	6/1994
WO	95/09619	4/1995
WO	96/09286	3/1996
WO	96/14842	5/1996
WO	96/18608	6/1996
WO	97/07098	2/1997
WO	97/14686	4/1997
WO	97/38977	10/1997
WO	99/18960	4/1999
WO	00/00200	1/2000
WO	01/19788	3/2001
WO	01/078709	10/2001
WO	WO 01/87293	11/2001
WO	2002/062766	8/2002
WO	02/088101	11/2002
WO	02/096897	12/2002
WO	03/039446	5/2003
WO	03/040096	5/2003
WO	03/040115	5/2003
WO	03/040142	5/2003
WO	03/082191	10/2003
WO	2004/009549	1/2004
WO	2004/014843	2/2004
WO	2004/031154	4/2004
WO	2004/039404	5/2004
WO	2004/043916	5/2004
WO	2004/096795	11/2004
WO	2005/014555	2/2005
WO	2005/032493	4/2005
WO	2005/058311	6/2005
WO	2005/097767	10/2005
WO	WO2005/111031 A2	11/2005
WO	2005/121100	12/2005
WO	2006/009655	1/2006
WO	2006/023750	3/2006
WO	2006/029850	3/2006
WO	2006/041404	4/2006
WO	2006/041405	4/2006
WO	2006/065204	6/2006
WO	2006/065277	6/2006
WO	2006/076284	7/2006
WO	2006/099379	9/2006
WO	2006/138265	12/2006
WO	2006/138304	12/2006
WO	WO 2006/138192	12/2006
WO	WO 2006/138217	12/2006
WO	2007/002220	1/2007
WO	WO 2007/005366	1/2007
WO	WO 2007/005404	1/2007
WO	WO 2007/016012	2/2007
WO	WO 2007/038271	4/2007
WO	2007/049532	5/2007
WO	2007/058580	5/2007
WO	WO 2007/058582	5/2007
WO	WO 2007/058583	5/2007
WO	WO 2007/058601	5/2007
WO	WO 2007/058602	5/2007
WO	2007/073284	6/2007
WO	WO 2007/078813	7/2007
WO	2007/092846	8/2007
WO	2007/092854	8/2007
WO	2007/114771	10/2007
WO	2007/120096	10/2007
WO	2007/146225	12/2007
WO	2008/011560	1/2008
WO	2008/022024	2/2008
WO	2008/073365	6/2008
WO	WO 2008/073370	6/2008
WO	2008/103351	8/2008
WO	WO 2008/133273	11/2008
WO	WO2008/133274 A1	11/2008
WO	2009/010454	1/2009
WO	2009/064418	5/2009
WO	2009/097278	8/2009
WO	2009/097401	8/2009
WO	2009/097578	8/2009
WO	2009/103626	8/2009
WO	2009/131974	10/2009
WO	2009/131975	10/2009
WO	WO 2009/134617	11/2009
WO	2009/151098	12/2009
WO	2010/019392	2/2010
WO	2010/019393	2/2010
WO	WO 2010/013302	2/2010
WO	WO 2010/013794	2/2010

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

WO	2010/047372	4/2010
WO	2010/056194	5/2010
WO	2010/056195	5/2010
WO	2010/056196	5/2010
WO	2010/113848	10/2010
WO	2010/128058	11/2010
WO	2010/129864	11/2010
WO	2011/005738	1/2011
WO	2011/009897	1/2011
WO	2011/009898	1/2011
WO	2011/009943	1/2011
WO	2011/020806	2/2011
WO	2011/029803	3/2011
WO	2011/044181	4/2011
WO	2011/044184	4/2011
WO	2011/044185	4/2011
WO	2011/044187	4/2011
WO	2011/058763	5/2011
WO	2011/060207	5/2011
WO	2011/069934	6/2011
WO	2011/070029	6/2011
WO	2011/070781	6/2011
WO	2011/071057	6/2011
WO	2011/071109	6/2011
WO	2011/071135	6/2011
WO	2011/077726	6/2011
WO	2011/080176	7/2011
WO	2011/138293	11/2011
WO	2011/154374	12/2011
WO	2011/154431	12/2011
WO	2012/000933	1/2012
WO	2012/006953	1/2012
WO	2012/019966	2/2012
WO	2012/038438	3/2012
WO	2012/057247	5/2012
WO	2012/057248	5/2012
WO	2012/085038	6/2012
WO	2012/093148	7/2012
WO	2012/095469	7/2012
WO	2012/095521	7/2012
WO	2012/098064	7/2012
WO	2012/098213	7/2012
WO	2012/098461	7/2012
WO	2012/104263	8/2012
WO	2012/107371	8/2012
WO	2012/110440	8/2012
WO	2012/110441	8/2012
WO	2012/110459	8/2012
WO	2012/117027	9/2012
WO	2012/119883	9/2012
WO	2012/120023	9/2012
WO	2012/126791	9/2012
WO	2012/136603	10/2012
WO	2012/139993	10/2012
WO	2012/147762	11/2012
WO	2012/147763	11/2012
WO	2012/156284	11/2012
WO	2012/162330	11/2012
WO	2012/162334	11/2012
WO	2012/163790	12/2012
WO	2012/168164	12/2012
WO	2012/168175	12/2012

OTHER PUBLICATIONS

Kondrat'eva et al., "Noncyclic dimer of 4-methyl-2-dimethlaminooxazole," Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 7, Jul. 1977, pp. 1680-1682 (with English translation).

Clark, et al., "Antitumor Imidazotetrazines, 32,1 Synthesis of Novel Imidazotetrazinones and Related Bicyclic Heterocycles to Probe the Mode of Action of the Antitumor Drug Temozolomide", J. Med. Chem., vol. 38, 1995, pp. 1493-1504.

Congreve, et al., "Application of Fragment Screening by X-ray Crystallography to the Discovery of Aminopyridines as Inhibitors of β-Secretase§", J. Med. Chem., vol. 50, 2007, pp. 1124-1132.

Huang, et al., "Progress in the Development of Nonpeptidomimetic BACE 1 Inhibitors for Alzheimer's Disease", Current Medicinal Chemistry, vol. 16, 2009, pp. 1806-1820.

Goodyer et al., "Synthesis of N-benzyl- and N-phenyl-2-amino-4,5-dihydrothiazoles and thioureas and evaluation as modulators of the isoforms of nitric oxide synthase," Bioorganic & Medicinal Chemistry, 2003, vol. 11, pp. 4189-4206.

Siddiqui et al., "Some extensions of Von Bruan (BrCN) reaction on organic bases," Proc. Pakistan Acad. Sci., 1988, vol. 25, No. 3, pp. 231-240.

Ozawa et al., Pharmacological actions of 2-Aminoethylisothiuronium (AET) derivatives. I1), Yakugaku Zasshi, 1968, vol. 88, No. 2, pp. 156-162 (with English language abstract).

Curtis et al., The byozynsethis of Phenols. Part VIII. The synthesis of (2-carboxy-3,5-dihydroxyphynyl)propan-2-one (C-acetyl-o-orsellinic acid). Journal of the Chemical Society, 1964, pp. 5382-5385.

Burton et al., "Addition reactions of quinones. Part I. The reaction of cysteine and thiourea and its derivatives with some quinones," Journal of the Chemical Society, 1952, pp. 2193-2196.

Matsui, "Yomo bochuzai no kenkyu (the 6th report) Kagaku kozo to yomo shokugai boshi koka tono kankei (III)," Journal of Synthetic Organic Chemistry, Japan, 1950, vol. 8, No. 10, pp. Ho61-Ho65(and International Search Report issued in PCT/JP2010/055528, which corresponds to co-pending U.S. Appl. No. 13/260,103).

Desai et al., "The condensation of thiocarbamides with monochloroacetic acide and the conversion of arylformamidinethiolacetic acids into pseudothiohydantoin derivatives," Recuil des Travaux Chimiques des Pays-Bas et de la Belgique, 1935, pp. 118-121.

Cole et al., "Acylguanidines as small-molecule beta-secretase inhibitors," J. Med. Chem., 2006, pp. 6158-6161.

Co-pending U.S. Appl. No. 13/417,786, entitled Aminodihydrothiazine Derivatives Substituted With a Cyclic Group, filed Mar. 12, 2012.

Hünig et al., "Azofarbstoffe Durch Oxydative Kupplung, XVII[1)]Synthese von 3-substituierten Thiazolon-(2)-hydrazonen und Thiazolon-(2)-benzolsulfonylhydrazonen", 1961, vol. 647, pp. 66-76 (with English abstract).

Koriyama et al., "Reversal of diastereofacial selectivity in the nucleophilic addition reaction to chiral *N*-sulfinimine and application to the synthesis of indrizidine 223AB," Tetrahedron, vol. 58, 2002, pp. 9621-9628.

Fujisawa et al., "Switchover of diastereofacial selectivity in the condensation reaction of optically active *N*-sulfinimine with ester enolate," Tetrahedron Letters, vol. 37, No. 22, 1996, pp. 3881-3884.

Vilaivan et al., "Recent Advances in Catalytic Asymmetric Addition to Imines and Related C=N Systems," Current Organic Chemistry, vol. 9, 2005, pp. 1315-1392.

Hua et al., "*N*-Alkylidenesulfinamides," Sulfur Reports, vol. 21, 1999, pp. 211-239.

Vippagunta et al. "Crystalline Solids". Advanced Drug Delivery Reviews, vol. 48, 2001, pp. 3-26.

Gavezzotti. "Are Crystal Structures Predictable". Accounts of Chemical Research, vol. 27, 1994, pp. 309-314.

Savoca et al., "1,5-Diazabicyclo[4.3.0]non-5-ene[1]," Encyclopedia of Reagents for Organic Synthesis, 2006, 10 pages total.

Creeke et al., "Synthesis and elaboration of heterocycles via iodocyclisation of unsaturated thioureas," Tetrahedron Letters, 1989, vol. 30, No. 33, pp. 4435-4438.

Mellor et al.,"A general route to spirocycles by radical additions to exocyclic unsaturated sulphides and related compounds," Tetrahedron Letters, 1991, vol. 32, No. 48, pp. 7111-7114.

Murai et al., "Indo-cyclization of *N*-homoallyl thioamides leading to 2,4-diaryl-5,6-dihydro-4*H*-1,3-thiazines," Chemistry Letters, 2004, vol. 33, No. 5, pp. 508-509.

Singh et al., "Synthesis of heterocyclic compounds via enamines. Part 8.[1] Acid-catalysed transformations in a 4,4,6-trimethyl-1,4-dihydropyrimidine-2(3*H*)-thione derivatives and related compounds," J. Chem. Soc., Perkin Trans. 1, 1980, pp. 1013-1018.

(56) **References Cited**

OTHER PUBLICATIONS

International Search Report for PCT/JP2006/321015.
Specification for co-pending U.S. Appl. No. 12/997,802 entitled Sulfur-Containing Heterocyclic Derivative Having Beta Secretase Inhibitory Activity.
Database Registry [Online], Chemical Abstracts Service, Columbus, Ohio, US; May 29, 2007, "2H-Indol-2-ome,4-(-2-amino-5,6-dihydro-4-methyl-4H-1,3-thiazin-4-yl)-1,3-dihydro-", XP002646872, Database accession No. 935998-84-8.
Schubert et al., "Neue synthesen von 2-Amino-5,6-dihydro-4H-1,3-thiazinen," Archiv der Pharmazie, 1968, vol. 301, No. 10, pp. 750-762.
Huang et al., "Pharmacophore model construction of βsecretase inhibitors," 2008, Acta Chimica Sinica, vol. 66, No. 16, pp. 1889-1897 (English language abstract provided).
Specification for co-pending U.S. Appl. No. 12/997,802, filed Dec. 13, 2010 entitled Sulfur-Containing Heterocyclic Derivative Having Beta Secretase Inhibitory Activity.
Co-pending U.S. Appl. No. 13/518,285, entitled 4-Amino-1,3-Thiazine or Oxazine Derivative, filed Jun. 21, 2012.
Bol'but et al., Heterocyclizations of Functionalized Heterocumulenes with C,N- and C,O-Dinucleophiles: III. Cyclization of *N*-(1-Aryl-1-chloro-2,2,2-trifluoroethyl)-*N'*-arylcarbodiimides with 3-Substituted 1-Phenylpyrazol-5-ones, Russian Journal of Organic Chemistry, 2003, vol. 29, No. 2, pp. 1789-1791.
Trepanier et al,, "Synthesis and screening for antidepressant activity of some aminoindanooxazolines, aminoindanooxazines, and aminoacenaphthoxazolines," Journal of Medicinal Chemistry, 1970, vol. 13, No. 4, pp. 729-733.
Sayed et al., "α-Enones in heterocyclic synthesis of indazole, thiazine, chromene and quinolone derivatives with their antimicrobial activities," Journal of Chemical Research, 2009, vol. 12, pp. 726-728.
Database Caplus [Online] Chemical Abstracts Service, Columbus, Ohio, US; Xu, Yungen et al: "Preparation of benzimidazolyl and benzothiazolyl isothiourea derivatives as nitric oxide synthase inhibitors", XP002679913, retrieved from STN Database accession No. 2005:46620 abstract Accessed Jul. 13, 2012.
Bol'but et al., "Synthesis of 4-imino-2-trifluoromethyl-3,4-dihydro-2h-Benzo-[1,3]Thiazines," Chemistry of Heterocyclic Compounds, 2001, vol. 37, No. 4, pp. 522-523.
Vovk et al., "Intramolecular thermal cyclization of N-(1-Aryl-1-aryloxy-2,2,2-trifluoroethyl)-N'-arylcarbodiimides," Russian Journal of Organic Chemistry, 2000, vol. 36, No. 12, pp. 1739-1742.
Vovk et al., "Regioselective cyclization of 1-chloroalkylcarbodiimides with 1,1- and 1,2-bifunctional nucleophilic reagents," Russian Journal of Organic Chemistry, 1997, vol. 22, No. 1, pp. 96-102.
Potts et al., "N-Acyl-β-enamino Ketones: Versatile Heterocyclic Synthons," J. Org. Chem., 1983, 48, pp. 625-626.
Rivkin et al., "Piperazinyl pyrimidine derivatives as potent γ-secretase modulators," Bioorganic & Medicinal Chemistry Letters, 2010, 20, pp. 1269-1271.
Rivkin et al., "Purine derivatives as potent γ-secretase modulators," Bioorganic & Medicinal Chemistry Letters, 2010, 20, pp. 2279-2282.
Edwards et al. "Application of Fragment-Based Lead Generation to the Discovery of Novel, Cyclic Amidine β-Secretase Inhibitors with Nanomolar Potency, Cellular Activity, and High Ligand Efficiency", Journal of Medicinal Chemistry, vol. 50, No. 24, 2007, pp. 5912-5925.
Cohen et al., "Synthesis of 2-Amino-5,6-dihydro-4*H*-1,3-thiazines and Related Compounds by Acid Catalyzed Cyclization of Allylic Isothiuronium Salts", J. Heterocyclic Chem., vol. 14, Aug. 1977, pp. 717-723.
Kuo et al., "A Synthesis of Estrone via Novel Intermediates. Mechanism of the Coupling Reaction of a Vinyl Carbinol with a β Diketone", The Journal of Organic Chemistry, vol. 33, No. 8, Aug. 1968, pp. 3126-3132.
Liebscher et al., "2-arylimino-3-thiazolines—Formation of Unusual Tautomers of 2-arylamino-thiazolines—A Revision", Tetrahedron Letters, vol. 26, No. 35, 1985, pp. 4179-4180.
Garcia et al., "Syntheses and Spectral Properties of β-lodoureas and 2-Amino-4,4-diphenyl-2-oxazolines", J. Heterocyclic Chem., vol. 28, 1991, pp. 777-780.
Schaumann et al. "Cycloadditionsreaktionen von Heterokumulenen, XIII[1)]Stickstoffhaltige Fünfring-Heterocyclen aus Carbodiimiden oder Keteniminen mit 3-Dimethylamino-2*H*-azirinen", Liebigs Ann. Chem, 1981, pp. 290-305 (with English language abstract).
Fernandez et al., "Syntheses of β-iodourea derivatives of carbohydrates and glycosylamino-oxazolines", Carbohydrate Research, vol. 216, 1991, pp. 21-32.
Cambie et al., "vic-lodothiocyanates and lodoisothiocyanates. Part 2.[1,2] New Syntheses of Thiazolidin-2-ones and 2-Amino-2-thiazolines", J.C.S. Perkin I, 1979, pp. 765-770.
Hünig et al., "Azofarbstoffe Durch Oxydative Kupplung, XVIII[1)] Synthese von 3-substituierten Thiazolon-(2)-hydrazonen and Thiazolon-(2)-benzolsulfonylhydrazonen", 1961, vol. 647, pp. 66-76.
STN a the Web, RN 79005-45-1, 1964.
Zhu et al., Two novel Diastereoselective Three-Component Reactions of Alkenes or 3,4-Dihydro-(2*H*)-pyran with Urea/Thiourea-Aldehyde Mixtures: [4+2] Cycloaddition vs Biginelli-Type Reaction, Organic Letters, 2006, vol. 8, No. 12, pp. 2599-2602.
Calabrese et al. "NO Synthase and NO-Dependent Signal Pathways in Brain Aging and Neurodegenerative Disorders: The Role of Oxidant/Antioxidant Balance". Neurochemical Balance, vol. 25, No. 9/10, pp. 1315-1341 (2000).
Kavya et al. "Nitric oxide synthase regulation and diversity: Implications in Parkinson's Disease", Nitric Oxide: Biology and Chemistry, vol. 15, No. 4, pp. 280-294 (2006).
Chiou et al. "Review: Effects of Nitric Oxide on Eye Diseases and Their Treatment". Journal of Ocular Pharmacology and Therapeutics, vol. 17, No. 2, pp. 189-198 (2001).
Ishii et al. "Subacute NO generation induced by Alzheimer's β-amyloid in the living brain: reversal by inhibition of the inducible NO synthase". The Federation of American Societies for Experimental Biology Journal, vol. 14, pp. 1485-1489 (2000).
Pak et al. "Morphine via nitric oxide modulates β-amyloid metabolism: a novel protective mechanism for Alzheimer's disease", Medical Science Monitor, vol. 11, No. 10, pp. BR357-BR366 (2005).
Kiselyov et al., "Design and chemical synthesis of [1,2,4]triazol[1,5-c]pyrimidin-5-y1 amines, a novel class of VEGFR-2 kinase inhibitors," 2009, Tetrahedron Letters, vol. 50, pp. 3809-3812.
Mulcahy et al., "A stereoselective synthesis of (+)-Gonyautoxin 3," Journal of the American Chemical Society, 2008, vol. 130, pp. 12630-12631.
"Diphenyl Cyanocarbonimidate," e-EROS Encyclopedia of Reagents for Organic Synthesis, 2001, 2 pages total.
Shafik et al., "Synthesis of novel 2-[2-(substituted amino)phenethyl]-1H-benzimidazoles; 3,4-dihydro and 1,2,3,4-tetrahydropyrimido[1,6-a]-benzimidazoles as potential antiulcer agents," 2004, Pharmazie, vol. 59, No. 12, pp. 899-905.
Pohl et al., "Synthesis of partially saturated condensed triazoles by reaction of ω-Aminoalkyl-1,2,4-triazoles with electrophiles," Journal fuer Praktische Chemie Chemiker-Zeitung, 1992, vol. 334, pp. 630-636.
Buschauer et al., "Isohistamine and Homologe als Bausteine von H_2-Antagonisten,"Arzneimittel-Forschung, 1985, vol. 35, pp. 1025-1029 (English language abstract provided).
Buschauer et al., "7,8-Dihydroimidazo[1,2-c]pyrimidin-5(6H)-one, -5(6H)-thione and -5(6H1)-ylidencyanamide," Chemische Berichte, 1984, vol. 117, pp. 2597-2614.
Borchers et al., "H_2-Antihystaminika, 19. Mitt, [1]) Syntheses and H_2-antihistaminische Wirkung N^{α}-substituierter Histamine," Archie der Pharmazie (Weinheim, Germany), 1984, vo1.317, pp. 455-459.
Cheong et al., "Pharmacophore elucidation for a new series of 2-aryl-pyrazolo-triazolo-pyrimidines as potent human A_3 adenosine receptor antagonists," Bioorganic & Medicinal Chemistry Letters, 2011, vol. 21, pp. 2898-2905.

(56) **References Cited**

OTHER PUBLICATIONS

Xu et al., "Copper-catalyzed cascade synthesis of benzimidazoquinazoline derivatives under mild condition," Chemical Communications, 2011, vo1,47, pp. 5596-5598.
Kishore et al., "QSAR of adenosine receptor antagonists: exploring physicochemical requirements for binding of pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine derivatives with human adenosine A3 receptor subtype," Bioorganic & Medicinal Chemistry Letters, 2011, vol. 21, No. 2, pp. 818-823.
Dolzhenko et al., "8-methyl-2-[4-(trifluoromethyl)pheny1]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]-pyrimidin-5-amine methanol disolvate," Acta Crystallographica, Section E: Structure Reports Online, 2010, E66(7), 12 pages total.
Beaton et al., "3,4-dihydro-l-isoquinolinamines: a novel class of nitric oxide synthase inhibitors with a range of isoform selectivity and potency," Bioorganic & Medicinal Chemistry Letters, 2001, vo1. 11, pp. 1023-1026.
Beaton et al., "The synthesis of 1-aminodihydroisoquinolines by an imine addition cyclisation reaction," 1998, Tetrahedron Letters, vol. 39, pp. 1227-1230.
Tian et al., "Radiosynthesis of 8-Fluoro-3-(4-[^{18}F]Fluoropheny1)-3,4-Dihydro-1-Isoquinolinamine ([^{1}8F]FFDI), a potential PET radiotracer for the inducible nitric oxide synthase," 2008, Current Radiopharmaceuticals, vol. I, pp. 49-53.
Weinhardt et al, "Synthesis and antidepressant profiles of phenyl-substituted 2-amino- and 2-((alkoxycarbonyl)amino)11,4,5,6-tetrahydropyrimidines," Journal of Medicinal Chemistry, vol. 28, No. 6, 1985, pp. 694-698.
Meschino et al., "2-Amino-5,6-dihydro-1,3-oxazines. The reduction of carboxylic esters with sodium borohydride," J. Org. Chem., vol. 28, 1963, pp. 3129-3134.
Poos et al., "2-amino-5-aryl-2-oxazolines. Potent new anorectic agent," J. Med, Chem., vol. 6, 1963, pp. 266-272.
Sandin et al., "A fast and parallel route to cyclic isothioureas and guanidines with use of microwave-assisted chemistry," J. Org. Chem., vol. 69, 2004, pp. 1571-1580.
Weinhardt et al., "Synthesis and central nervous system propreties of 2-[(Alkoxycarbony)amino]-4(5)-pheny1-2-imidazolines," Journal of Medicinal Chemistry, vol. 27, No. 5, 1984, pp. 616-627.
Woodgate et al., "A new synthesis of 2-amino-2-thiazolines," Heterocycles, vol. 7, No. 1, 1977, pp. 109-112.
Co-pending U.S.Appl. No. 13/881,112, entitled Fused Aminodihydropyrimidine Derivative, filed Apr. 23, 2013.
Co-pending U.S. Appl. No. 13/881,250, entitled Naphthyridine Derivative, filed Apr. 24, 2013.
Co-pending U.S. Appl. No. 13/877,745, entitled Aminodihydrothiazine Derivtives Substituted with a Cycle Group, filed May 6, 2013.
Co-pending U.S. Appl. No. 13/941,082, entitled Aminodihydrothiazine Derivatives, filed Jul. 12, 2013.
Co-pending U.S. Appl. No. 13/952,073, entitled Sulfur-Containing Heterocyclic Derivative Having Beta Secretase Inhibitory Activity, filed Jul. 26, 2013.
Dörwald, "Side reactions in organic synthesis: a guide to successful synthesis design" 2005 Wiley-VCH Verlag GmbH & Co., KGaA, Wienheim, chapter 1, 32 pages total.
Wermuth; Practice of Medicinal Chemistry, Third Ed., 2008, Elsevier, chapter 15, 54 pages total.
Co-pending U.S. Appl. No. 14/112,400, entitled Pyridine Derivatives and a Pharmaceutical Composition for Inhibiting BACE1 Containing Them, filed Oct. 17, 2013.
Co-pending U.S. Appl. No. 14/113,327, entitled Oxazine Derivatives and a Pharmaceutical Composition for Inhibiting BACE1 Containing Them, filed Oct. 22, 2013.
Co-pending U.S. Appl. No. 14/070,202, entitled A Pharmaceutical Composition for Treating Alzheimer's Disease, filed Nov. 1, 2013.

* cited by examiner

PHARMACEUTICAL COMPOSITION FOR TREATING ALZHEIMER'S DISEASE

TECHNICAL FIELD

The present invention relates to a pharmaceutical composition which has reducing effect to produce amyloid β protein and is useful as an agent for treating disease induced by production, secretion and/or deposition of amyloid β protein, especially Alzheimer's disease.

BACKGROUND ART

In the brain of Alzheimer's patient, the peptide composed of about 40 amino acids residue as is called amyloid β protein, that accumulates to form insoluble specks (senile specks) outside nerve cells is widely observed. It is concerned that this senile specks kill nerve cells to cause Alzheimer's disease. The therapeutic agents for Alzheimer's disease, such as decomposition agents of amyloid β protein and amyloid β vaccine, are under investigation.

Secretase is an enzyme which cleaves amyloid βprecursor protein (APP) in cell and produce amyloid β protein. The enzyme which controls the production of N terminus of amyloid β protein is called as BACE 1 (beta-site APP-cleaving enzyme 1, β-secretase). It is thought that inhibition of this enzyme leads to reduction of producing amyloid β protein and that the therapeutic agent for Alzheimer's disease will be created by the inhibition.

Patent Literature 1 describes the compounds which are similar to those of the compounds contained in the pharmaceutical composition of the present invention, and the compounds have NO synthase enzyme inhibitory activity and are useful for dementia.

Patent. Literature 2 to 10 describes the compounds which are known as BACE 1 inhibitor, however, have different structures from the compounds contained in the pharmaceutical composition of the present invention.

[Patent Literature 1] International Patent Application Publication WO96/014842

[Patent Literature 2] International Patent Application Publication WO02/96897

[Patent Literature 3] International Patent Application Publication WO04/043916

[Patent Literature 4] International Patent Application Publication WO2005/058311

[Patent Literature 5] international Patent Application Publication WO2005/097767

[Patent Literature 6] International Patent Application Publication WO2006/041404

[Patent Literature 7] International Patent Application Publication WO2006/041405

[Patent Literature 8] US Patent Application Publication US2007/0004786

[Patent Literature 9] US Patent Application Publication US2007/0004730

[Patent Literature 10] US Patent Application Publication US2007/27199

[Patent Literature 11] International Patent Application Publication WO2007/049532

DISCLOSURE OF INVENTION

Problems to be Solved by the Invention

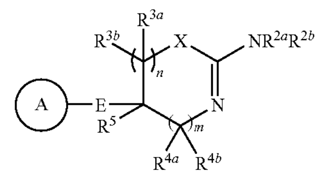
The present invention provides pharmaceutical compositions which have reducing effects to produce amyloid β protein, especially BACE 1 inhibitory activity, and which are useful as an agent for treating disease induced by production, secretion and/or deposition of amyloid β protein.

Means to Solve the Problems

The present invention provides:

(a) a pharmaceutical composition for treating Alzheimer's disease containing a compound represented by the general formula (I):

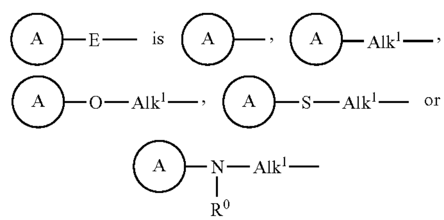
[Chemical formula 1]



(I)

wherein ring A is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

[Chemical formula 2]



wherein Alk^1 is lower alkylene or lower alkenylene;

R^0 is a hydrogen atom, lower alkyl or acyl;

X is S, O, or NR^1;

R^1 is a hydrogen atom or lower alkyl;

R^{2a} and R^{2b} are each independently a hydrogen atom, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino, optionally substituted amidino, optionally substituted acyl, optionally substituted carbamoyl, optionally substituted carbamoylcarbonyl, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

R^{3a}, R^{4a} and R^{4b} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted acyl, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted amino, optionally substituted carbamoyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

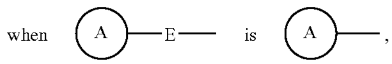
n and m are each independently an integer of 0 to 3;

n+m is an integer of 1 to 3;

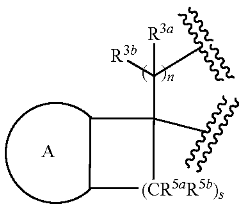
each R^{3a}, each R^{3b}, each R^{4a}, and each R^{4b} may be independently different;

R^5 is a hydrogen atom, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

[Chemical formula 3]



R^5 and ring A can be taken together to form



wherein R^{5a} and R^{5b} are each independently a hydrogen atom or lower alkyl;

s is an integer of 1 to 4;

each R^{5a} and each R^{5b} may be different;

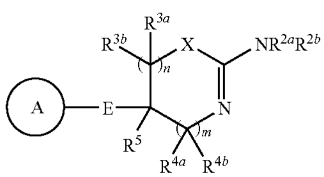
with the proviso that the compound wherein n+m is 2; R^5 is a hydrogen atom; and

ring A is non-substituted phenyl is excluded,

its pharmaceutically acceptable salt, or a solvate thereof as an active ingredient,

(a1) a pharmaceutical composition for treating Alzheimer's disease containing a compound represented by the general formula (I):

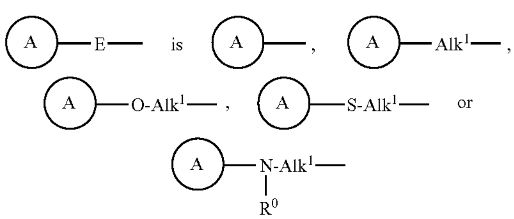
[Chemical formula 4]



(I)

wherein ring A is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

[Chemical formula 5]



wherein Alk^1 is lower alkylene;

R^0 is a hydrogen atom, lower alkyl or acyl;

X is S, O, or NR^1;

R^1 is a hydrogen atom or lower alkyl;

R^{2a} and R^{2b} are each independently a hydrogen atom, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino, optionally substituted amidino, optionally substituted acyl, optionally substituted carbamoyl, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

R^{3a}, R^{3b}, R^{4a}, and R^{4b} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted acyl, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted amino, optionally substituted carbamoyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

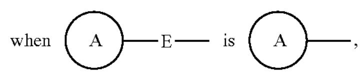
n and m are each independently an integer of 0 to 3;

n+m is an integer of 1 to 3;

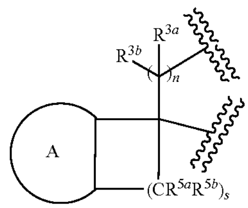
each R^{3a}, each R^{3b}, each R^{4a}, and each R^{4b} may be independently different;

R^5 is a hydrogen atom, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

[Chemical formula 6]



R^5 and ring A can be taken together to form



wherein R^{5a} and R^{5b} are each independently a hydrogen atom or lower alkyl;

s is an integer of 1 to 4;

each R^{5a} and each R^{5b} may be different;

with the proviso that the compound wherein n+m is 2; R^3 is a hydrogen atom; and

ring A is non-substituted phenyl is excluded,

its pharmaceutically acceptable salt, or a solvate thereof as an active ingredient,

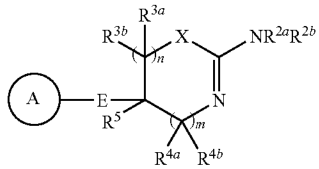
(b) the pharmaceutical composition for treating Alzheimer's disease according to (a), wherein X is S,

(c) the pharmaceutical composition for treating Alzheimer's disease according to (a), wherein n is 2, and m is 0,

(d) the pharmaceutical composition for treating Alzheimer's disease according to (a), wherein E is a bond,

(e) a pharmaceutical composition for treating Alzheimer's disease containing a compound represented by the general formula (I):

[Chemical formula 7]


(I)

wherein each symbols are the same as described in (a), with the proviso that the compounds as shown below;

i) wherein n+m is 2, R^3 is a hydrogen atom, and ring A is non-substituted phenyl;

ii) wherein n is 2, m is 0, R^{2a} is a hydrogen atom, R^{2b} is a hydrogen atom or acetyl, R^5 is methyl, and ring A is phenyl or 4-methoxyphenyl;

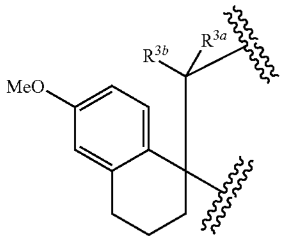
iii) wherein n is 2, m is 0, R^{2a} is a hydrogen atom, R^{2b} is a hydrogen atom or acetyl,

R^5 is ethyl, and ring A is 3,4-dimethoxyphenyl;

iv) wherein n is 2, in is 0, R^{2a} is a hydrogen atom, R^{2b} is a hydrogen atom or acetyl, and R^5 and ring A is phenyl;

v) wherein n is 2, m is 0, R^{2a} and R^{2b} is a hydrogen atom, R^5 and ring A are taken together to form

[Chemical formula 8]



wherein Me is methyl, and each symbols are the same as described above; and

vi) wherein n+m is 2,

R^5 is a hydrogen atom, and

ring A is phenyl substituted with one or two substituent(s) selected from the group of hydroxy, halogen, lower alkyl, lower alkoxy, nitro, amino, lower alkylcarbonylamino, mercapto, lower alkylthio, and carbamoyl, non-substituted phenyl,

or non-substituted naphthyl; are excluded,

its pharmaceutically acceptable salt, or a solvate thereof as an active ingredient,

(f) the pharmaceutical composition for treating Alzheimer's disease according to (e), wherein X is S,

(g) the pharmaceutical composition for treating Alzheimer's disease according to (e) or (f), wherein n is 2, and m is 0,

(h) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (g), wherein R^5 is optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group,

(i) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (h), wherein R^{1a} is a hydrogen atom; R^{2b} is a hydrogen atom, optionally substituted lower alkyl, optionally substituted acyl, optionally substituted lower alkylsulfonyl, or optionally substituted amidino,

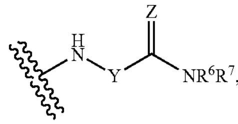
(j) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (h), wherein $NR^{2a}R^{2b}$ is represented by the formula:

[Chemical formula 9]

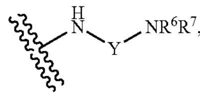
(a)

$—NH_2$,

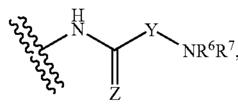
(b)



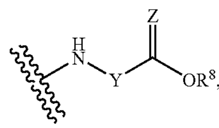
(c)



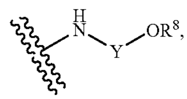
(d)



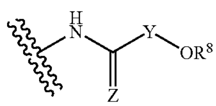
(e)



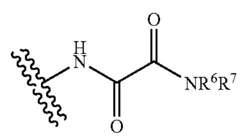
(f)



(g)


or

(h)



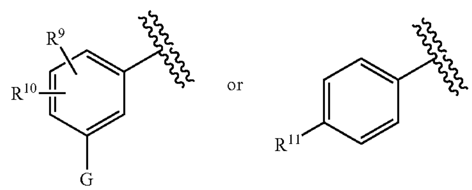
wherein R^6, R^7, and R^8 are each independently a hydrogen atom, lower alkyl or acyl, Y is optionally substituted lower alkylene, optionally substituted lower alkenylene or optionally substituted lower alkynylene;

Z is O or S;

(k) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (j), wherein ring A is substituted phenyl,

(l) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (j), wherein ring A is represented by the formula:

[Chemical formula 10]



wherein R^9, R^{10} and R^{11} are hydrogen atom or G;

G is halogen, hydroxy, cyano, nitro, mercapto, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted acyl, optionally substituted acyloxy, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted lower alkoxycarbonyloxy, optionally substituted aryloxycarbonyloxy, optionally substituted amino, optionally substituted carbamoyl, optionally substituted carbamoyloxy, optionally substituted lower alkylthio, optionally substituted arylthio, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, optionally substituted lower alkylsulfinyl, optionally substituted arylsulfinyl, optionally substituted lower alkylsulfonyloxy, optionally substituted arylsulfonyloxy, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy, an optionally substituted heterocyclic group or optionally substituted heterocyclicoxy;

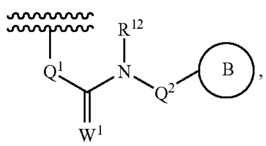
each G may be independently different,

(m) the pharmaceutical composition for treating Alzheimer's disease according to (l),

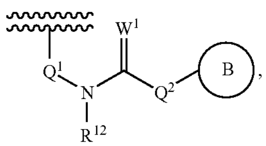
wherein G is represented by the formula:

[Chemical formula 11]

(i)



(ii)



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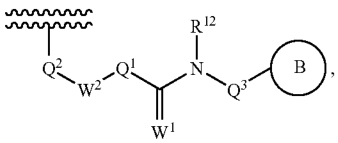

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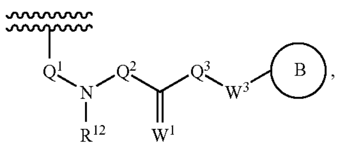

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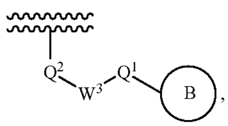

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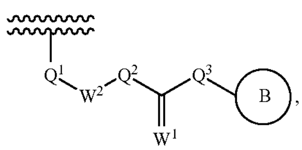

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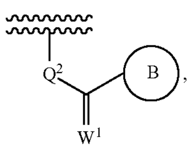

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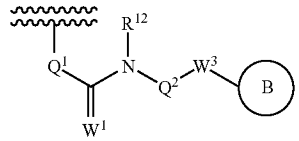
(viii)



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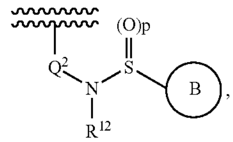

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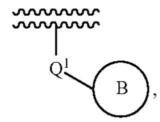

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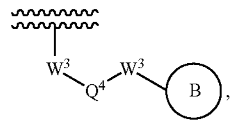

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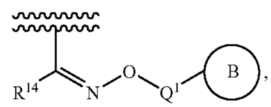

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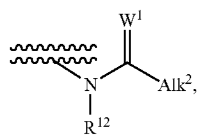
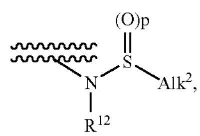
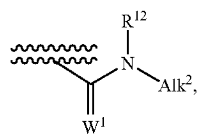


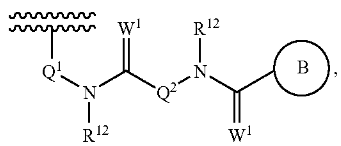
(xiv)



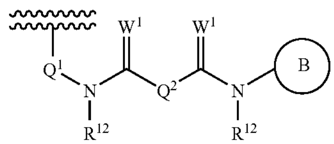
(xv)



(xvi)

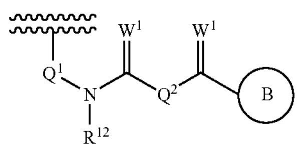


(xvii)



or

(xviii)



wherein Q^1, Q^2, and Q^3 are each independently a bond, optionally substituted lower alkylene, or optionally substituted lower alkenylene;

Q^4 is optionally substituted lower alkylene or optionally substituted lower alkenylene;

W^1 and W^2 are each independently O or S;

W^3 is O, S or NR^{12};

R^{12} is a hydrogen atom, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, lower alkoxycarbonyl lower alkyl, carbocyclic lower alkyl or acyl;

R^{14} is a hydrogen atom or lower alkyl;

ring B is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

Alk^2 is optionally substituted lower alkyl;

p is 1 or 2;

if there are multiple W^1, multiple W^3, and multiple R^{12}, each may be independently different;

in (xii), the position of an oxygen atom may be cis or trans to a substituent R^{14},

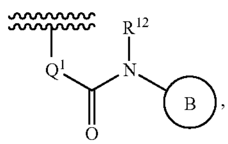
(n) the pharmaceutical composition for treating Alzheimer's disease according to (m), wherein ring B is aryl optionally substituted with one or more substituents selected from the group of halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, cyano, optionally substituted carbamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy and an optionally substituted heterocyclic group, or

heteroaryl optionally substituted with one or more substituents selected from the group of halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, cyano, optionally substituted carbamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy and an optionally substituted heterocyclic group,

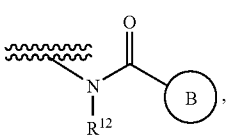
(o) the pharmaceutical composition for treating Alzheimer's disease according to (m), wherein G is represented by the formula:

[Chemical formula 12]

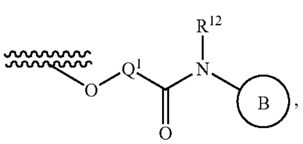
(i')



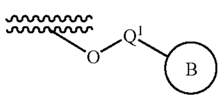
(ii')



(iii')

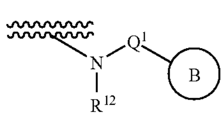


(v')



or

(v'')



wherein, each symbols are the same as described above,

(p) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (o), wherein R^5 is C1 to C3 alkyl,

(q) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (o), wherein R^5 is methyl,

(r) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (q), wherein

R^{3a} and R^{3b} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower a optionally substituted lower alkoxy or optionally substituted aryl,

(s) the pharmaceutical composition for treating Alzheimer's disease according to any one of (e) to (q), wherein

R^{3a} and R^{3b} are both hydrogen atoms,

(t) the pharmaceutical composition according to any one of (a) to (d) which is the composition for reducing amyloid β production,

its pharmaceutically acceptable salt, or a solvate thereof as an active ingredient,

(u) the pharmaceutical composition according to any one of (a) to (d) or (d) which is the composition for treating disease induced by production, secretion and/or deposition of amyloid β protein,

(v) a method for treating disease induced by production, secretion and/or deposition of amyloid β protein (for example, Alzheimer's disease) comprising administering the compound as defined in any one of formula (I) in above (a),

its pharmaceutically acceptable salt, or a solvate thereof,

(w) use of the compound as defined in any one of formula (I) in above (a), its pharmaceutically acceptable salt, or a solvate thereof, in the manufacture of a medicament for the treatment of disease induced by production, secretion and/or deposition of amyloid β protein (for example, Alzheimer's disease),

(x) a method for treating Alzheimer's disease characterizing in administering the compound as defined in any one of formula (I) in above (a),

its pharmaceutically acceptable salt, or a solvate thereof,

(y) use of the compound as defined in any one of formula (I) in above (a),

its pharmaceutically acceptable salt, or a solvate thereof, in the manufacture of a medicament for the treatment of Alzheimer's disease.

Effect of the Invention

The composition of the present invention is useful as an agent for treating disease such as Alzheimer's disease induced by production, secretion and/or deposition of amyloid β protein.

Additionally, because the pharmaceutical composition of the present invention comprises the compound which has the characteristics: it has high inhibitory activity against BACE-1, it has high selectivity against other enzymes, and the like; as an active ingredient, it can be a medicament whose side effects are reduced. The pharmaceutical composition of the present invention can be a medicament which possess a great safety margin in side effect by comprising an optical active compound which has a suitable conformation as an active ingredient. The pharmaceutical composition of the present invention can be an excellent medicament because it comprises the compound which has the following characteristics as an active ingredient: high metabolic stability, high dissolubility, high oral absorbability, high bioavailability, preferable clearance, high transfer to brain, long half-life, high proteinunbound fraction, low inhibitory activity to hERG channel, low inhibitory activity to CYPs, and/or negative activity in Ames assay.

BEST MODE FOR CARRYING OUT THE INVENTION

As used herein, the "halogen" includes fluorine, chlorine, bromine, and iodine. A halogeno part of the "halogeno lower alkyl", the "halogeno lower alkoxy", the "halogeno acyl", the "halogeno lower alkylthio" and the "halogeno lower alkoxycarbonyl" is the same.

The "lower alkyl" includes a straight or branched alkyl of a carbon number of 1 to 15, preferably a carbon number of 1 to 10, further preferably a carbon number of 1 to 6, and more further preferably a carbon number of 1 to 3, and examples include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, hexyl, isohexyl, n-heptyl, isoheptyl, n-octyl, isooctyl, n-nonyl, and n-decyl.

A lower alkyl part of the "carbocyclic lower alkyl", the "lower alkoxy", the "halogeno lower alkyl", the "halogeno lower alkoxy", the "halogeno lower alkylthio", the "hydroxy lower alkyl", the "lower alkoxycarbonyl", the "halogeno lower alkoxycarbonyl", the "lower alkoxycarbonyl lower alkyl", the "lower alkoxycarbonyloxy", the "lower alkylamino", the "lower alkylcarbonylamino", the "lower alkoxycarbonylamino", the "lower alkoxy lower alkyl", the "lower alkylcarbamoyl", the "hydroxy lower alkylcarbamoyl", the "amino lower alkyl", the "hydroxy imino lower alkyl", the "lower alkoxy imino lower alkyl", the "lower alkylthio", the "lower alkylsulfonyl", the "lower alkyl sulfamoyl", the "lower alkylsulfinyl", the "lower alkylsulfonyloxy", the "lower alkoxycarbonyl lower alkynyl", the "lower alkylthio lower alkyl", the "aryl lower alkyl", the "aryl lower alkylamino", the "aryl lower alkoxycarbonyl", the "aryl lower alkylcarbamoyl", the "heterocyclic group lower alkylamino" and the "heterocyclic group lower alkylcarbamoyl" is the same as that of the aforementioned "lower alkyl".

The example of the "optionally substituted lower alkyl" as a substituent of ring A is lower alkyl optionally substituted with one or more substituents selected from the "substituent group α", "hydroxyimino" and "lower alkoxyimino"; the group defined as above (i), (iv), (vi), (x) (wherein each Q^1 is optionally substituted lower alkylene); the group defined as (v), (vii), (ix) (wherein Q^2 is optionally substituted lower alkylene); and the group (xii).

In other "optionally substituted lower alkyl" is optionally substituted with one or more substituents selected from the "substituent group α".

The "substituent group α" is selected from the group of halogen, hydroxy, lower alkoxy, hydroxy lower alkoxy, lower alkoxy lower alkoxy, acyl, acyloxy, carboxy, lower alkoxycarbonyl, amino, acylamino, lower alkylamino, lower alkylthio, carbamoyl, lower alkylcarbamoyl, hydroxy lower alkylcarbamoyl, sulfamoyl, lower alkylsulfamoyl, lower alkylsulfinyl, cyano, nitro, aryl, and heterocyclic group.

Especially as a substituent of the "optionally substituted lower alkyl" in Alk^2, halogen, hydroxy, lower alkoxy, lower alkoxy lower alkoxy, lower alkoxycarbonyl, amino, acylamino, lower alkylamino and/or lower alkylthio are preferable.

The example of the "optionally substituted lower alkoxy" as a substituent of ring A is lower alkoxy optionally substituted with one or more substituents selected from the above "substituent group α"; above (iii) wherein Q^1 is optionally substituted lower alkylene. Q^2 is a bond, W^2 is O; above (v) wherein Q^1 is optionally substituted lower alkylene, Q^2 is a bond. W^3 is O; above (vi) wherein Q^1 is a bond, Q^2 is optionally substituted lower alkylene, W^2 is O; or above (xi) wherein Q^4 is optionally substituted lower alkylene, W^2 is O.

In other case, the substituents of the "optionally substituted lower alkoxy", the "optionally substituted lower alkoxycarbonyl", the "optionally substituted lower alkoxycarbonyloxy", the "optionally substituted lower alkylsulfonyl", the "optionally substituted lower alkylsulfinyl", the "optionally substituted lower alkylsulfonyloxy" and the "optionally substituted lower alkylthio" are one or more substituents selected from the "substituent group α".

The "lower alkenyl" includes a straight or branched alkenyl of a carbon number of 2 to 15, preferably a carbon number of 2 to 10, further preferably a carbon number of 2 to 6 and more further preferably a carbon number of 2 to 4 having one or more double bonds at an arbitrary position. Specifically examples include vinyl, allyl, propenyl, isopropenyl, butenyl, isobutenyl, prenyl, butadienyl, pentenyl, isopentenyl, hexenyl, isohexenyl, hexadienyl, heptenyl, octenyl, nonenyl, decenyl, undecenyl, dodenyl, tridecenyl, tetradecenyl, and pentadecenyl.

The "lower alkynyl" includes a straight or branched alkynyl of a carbon number of 2 to 10, preferably a carbon number of 2 to 8, further preferably a carbon number of 3 to 6, having one or more triple bonds at an arbitrary position. Specifically, examples include ethynyl, propenyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, and decynyl. These may further have a double bond at an arbitrary position.

A lower alkynyl part of the "lower alkoxycarbonyl lower alkynyl" is the same as that of above "lower alkynyl".

The example of the "optionally substituted lower alkenyl" as a substituent of ring A is lower alkenyl optionally substituted with one or more substituents selected from the above "substituent group α"; above (i), (ii), (iv), (vi), (viii) or (x), wherein Q^1 is optionally substituted lower alkenylene; (v), (vii) or (ix), wherein $Q^2$is optionally substituted lower alkenylene.

In other case, the substituents of the "optionally substituted lower alkenyl" and the "optionally substituted lower alkynyl" are one or more substituents selected from the "substituent group α".

The example of the "optionally substituted lower amino" as a substituent of ring A is amino optionally substituted with one or more substituents selected from the group of lower alkyl, acyl, hydroxy, lower alkoxy, lower alkoxyl carbonyl, a carbocyclic group and a heterocyclic group; (ii), wherein Q^1 is a bond; (iv), wherein Q^1 is a bond; (v), wherein Q^2 is a bond, W^3 is NR^{12}; (ix), wherein $Q^2$is a bond; (xiii); or (xiv).

The example of the "optionally substituted carbamoyl" as a substituent of ring A is carbamoyl optionally substituted with one or more substituents selected from the group of lower alkyl, acyl, hydroxy, lower alkoxy, lower alkoxycarbonyl, a carbocyclic group and a heterocyclic group; (i), (viii), wherein each Q^1 is bond; or (xv).

In other case, the substituents of the "optionally substituted amino", the "optionally substituted amidino", the "optionally substituted carbamoyl", the "optionally substituted carbamoylcarbonyl", and the "optionally substituted carbamoyloxy" are one or two substituents selected from the group of lower alkyl, acyl, hydroxy, lower alkoxy, lower alkoxycarbonyl, a carbocyclic group and a heterocyclic group, and the like.

The "acyl" includes aliphatic acyl of a carbon number of 1 to 10, carbocyclic carbonyl and heterocyclic carbonyl. Specifically, formyl, acetyl, propyonyl, butylyl, isobutylyl, valeryl, pivaloyl, hexanoyl, acryloyl, propioloyl, methacryloyl, crotonoyl, benzoyl, cyclohexanecarbonyl, pyridinecarbonyl, furancarbonyl, thiophenecarbonyl, benzothiazolcarbonyl, pyradinecarbonyl, piperidinecarbonyl, thiomorpholinocarbonyl, and the like.

The part of the acyl of the "halogenoacyl", the "acylamino" and the "acyloxy" is the same as the aforementioned "acyl".

The substituent of the "optionally substituted acyl" and "optionally substituted acyloxyl" is one or more substituents selected from the group of the "substituent group α". The ring part of the "carbocyclic carbonyl" and the "heterocyclic carbonyl" is optionally substituted with one or more substituents selected from the group of "lower alkyl"; the "substituent group α"; and "lower alkyl substituted with one or more substituents selected from the group of the substituent α".

The "carbocyclic group" includes cycloalkyl, cycloalkenyl, aryl and non-aromatic fused carbocyclic group.

The "cycloalkyl" includes a carbocyclic group of a carbon number of 3 to 10, preferably a carbon number of 3 to 8, further preferably a carbon number of 4 to 8, and examples include, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, and cyclodecyl, and the like.

The "cycloalkenyl" includes cycloalkenyl having one or more double bonds at an arbitrary position in a ring of the aforementioned cycloalkyl, and examples include cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptynyl, cyclooctynyl, and cyclohexadienyl, and the like.

The "aryl" includes phenyl, naphthyl, anthryl, and phenanthryl, and the like, and phenyl is particularly preferable.

The "non-aromatic fused a carbocyclic group" includes group fused with two or more ring groups selected from the group of the above "cycloalkyl", the "cycloalkenyl" and the "aryl". Specifically, examples include indanyl, indenyl, tetrahydronaphthyl, and fluorenyl, and the like.

The carbocyclic part of the "carbocyclicoxy", and the "carbocyclic lower alkyl" is the same as the aforementioned "carbocyclic group".

The aryl part of the "aryl lower alkyl", the "aryloxy", the "aryloxycarbonyl", the "aryloxycarbonyloxy", the "aryl lower alkoxycarbonyl", the "arylthio", the "arylamino", the "aryl lower alkylamino", the "arylsulfonyl", the "arylsulfonyloxy", the "arylsulfinyl", the "arylsulfamoyl", the "arylcarbamoyl" and the "aryl lower alkylcarbamoyl" is the same as the aforementioned "aryl".

The "heterocyclic group" includes a heterocyclic group having one or more heteroatoms arbitrary selected from O, S, and N in a ring, specifically includes a 5- to 6-membered heteroaryl such as pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazolyl, triazinyl, tetrazolyl, isoxazolyl, oxazolyl, oxadiazolyl, isothiazolyl, thiazolyl, thiadiazolyl, isothiazolyl, furyl and thienyl; a bicyclic fused heterocyclic group such as indolyl, isoindolyl, indazolyl, indolidinyl, indolinyl, isoindolinyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, purinyl, pteridinyl, benzopyranyl, benzimidazolyl, benzioxazolyl, benzoxazolyl, benzoxadiazolyl, benzisothiazolyl, benzothiazolyl, benzothiadiazolyl, benzofuryl, isobenzofuryl, benzothienyl, benzotriazolyl, imidazopyridyl, pyrazolopyridyl, triazolopyridyl, itnidazothiazolyl, pyrazinopyridazinyl, quinazolinyl, quinolyl, isoquinolyl, naphthyridinyl, dihydrobenzofuryl, tetrahydroquinolyl, tetrahydroisoquinolyl, dihydrobenzoxazine, tetrahydrobenzothienyl; a tricyclic fused heterocyclic group such as carbazolyl, acridinyl, xanthenyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, dibenzofuryl, and imidazoquinolyl; a non-aromatic heterocyclic group such as dioxanyl, thiiranyl, oxyranyl, oxathioranyl, azethidinyl, thianyl, pyrrolidinyl, pyrrolinyi, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, morpholinyl, morpholino, thiomorpholinyl, thiomorpholino, dihydropyridyl, dihydrobenzoimidazolyl, tetrahydropyridyl, tetrahydrofuryl, tetrahydropyranyl, tetrahydrothiazolyl, tetrahydroisothiazolyl, dihydroxadinyl, hexahydroazepinyl, tetrahydroazepyinyl. Preferable is a 5- to 6-membered heteroaryl, or a non-aromatic heterocyclic group.

The heterocyclic part of the "heterocyclicoxy", the "heterocyclic thio", the "heterocyclic carbonyl", the "heterocyclic amino", the "heterocyclic carbonylamino", the "heterocyclic sulfamoyl", the "heterocyclic sulfonyl", the "heterocyclic carbamoyl", the "heterocyclicoxycarbonyl", the "heterocyclic lower alkylamino" and the "heterocyclic lower alkyl carbamoyl" is the same as the aforementioned "heterocyclic group".

The example of the substituent of the "optionally substituted carbocyclic group" and the "optionally substituted heterocyclic group" in ring A is;

the substituent α, wherein preferable is for example, halogen, hydroxy, acyl, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, amino, lower alkylamino, lower alkylthio; lower alkyl optionally substituted with one or more substituents selected from the group of substituent α, wherein preferable is halogen, hydroxy, lower alkoxy, lower alkoxycarbonyl, and the like;

amino lower alkyl substituted with one or more substituents selected from the group of substituent α, wherein preferable is acyl, lower alkyl and for lower alkoxy, and the like; hydroxyimino lower alkyl; lower alkoxyimino lower alkyl;

lower alkenyl optionally substituted with one or more substituents selected from the group of substituent α, wherein preferable is lower alkoxycarbonyl, halogen and /or halogeno lower alkoxycarbonyl, and the like;

lower alkynyl optionally substituted with one or more substituents selected from the group of substituent α, wherein preferable is for example, lower alkoxycarbonyl,

lower alkoxy optionally substituted with one or more substituents selected from the group of substituent α, wherein preferable is for example, lower alkyl carbamoyl and for hydroxy lower alkyl carbamoyl,

lower alkylthio optionally substituted with one or more substituents selected from the group of substituent α,

lower alkylamino substituted with one or more substituents selected from the group of substituent α,

lower alkylsulfonyl optionally substituted with one or more substituents selected from the group of substituent α,

aryl lower alkoxycarbonyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

acyl substituted with one or more substituents selected from the group of substituent α,

cycloalkyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

lower alkylsulfinyl optionally substituted with one or more substituents selected from the group of substituent α, sulfamoyl,

aryl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclic optionally group substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

aryloxy optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl, heterocyclicoxy optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

arylthio optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclicthio optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl, arylamino optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclicamino optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl, aryl lower alkylamino optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclic lower alkylamino optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

lower alkyl sulfamoyl optionally substituted with one or more substituents selected from the group of substituent α,

aryl sulfamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclic sulfamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

arylsulfonyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclic sulfomyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

aryl carbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclic carbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

aryl lower alkylcarbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclic lower alkylcarbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

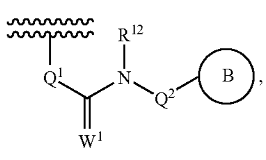
aryloxycarbonyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

heterocyclicoxycarbonyl optionally substituted with one or more substituents selected from the group of substituent α, azido, and lower alkyl,

lower alkylenedioxy optionally substituted with halogen; oxo; azido;

[Chemical formula 13]

(i)



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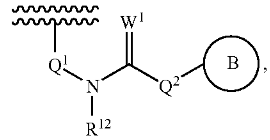
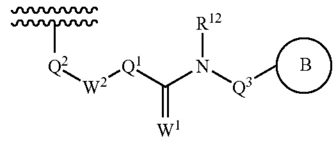
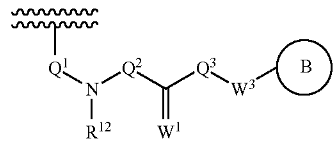
(ii)



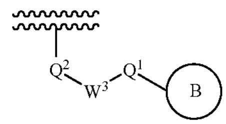
(iii)



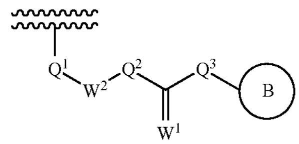
(iv)



(v)



(vi)



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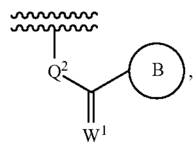
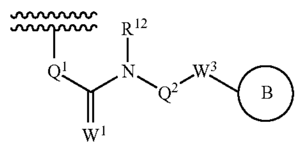
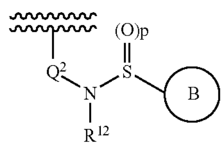


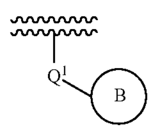
(viii)



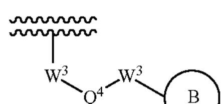
(ix)



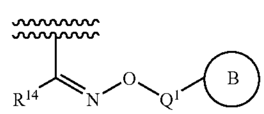
(x)



(xi)



(xii)



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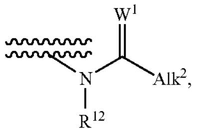
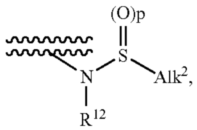
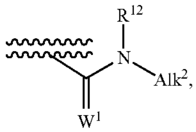
(xiii)



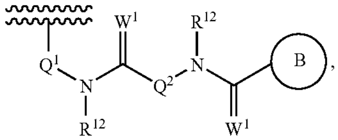
(xiv)



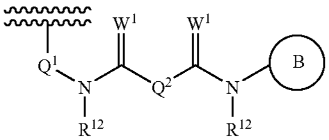
(xv)



(xvi)

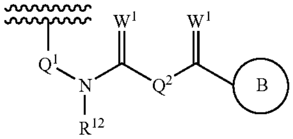


(xvii)



or

(xviii)



wherein Q^1, Q^2 and Q^3 are each independently a bond, optionally substituted lower alkylene or optionally substituted lower alkenylene;

Q^4 is optionally substituted lower alkylene or optionally substituted lower alkenylene;

W^1 and W^2 are each independently O or S;

W^3 is O, S or NR^{12};

R^{12} is a hydrogen atom, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, lower alkoxycarbonyl lower alkyl, carbocyclic group lower alkyl or acyl;

R^{14} is a hydrogen atom or lower alkyl;

ring B is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

Alk^2 is optionally substituted lower alkyl;

and the ring A is optionally substituted with one or more substituents selected from these groups.

If there are multiple W^1, multiple W^3, and multiple R^{12}, each may be independently different.

In addition, an oxygen atom in (xii) may be cis or trans position to the substituent R^{14}.

The substituent of the "substituted phenyl" is, in the same way, phenyl substituted with one or two substituents selected preferably from the group of the substituent α or (i) to (xv).

The substituent of the "optionally substituted carbocyclic group" or the "optionally substituted heterocyclic group" in ring B is optionally substituted with one or more substituents selected from the following group of, for example;

the substituent α, wherein preferable is halogen, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, acyl, amino, lower alkylamino, acylamino, carbamoyl, lower alkylcarbamoyl, cyano, and nitro, and the like;

lower alkyl optionally substituted with one or more substituents selected from the group of the substituent α, wherein preferable is halogen, hydroxy, and lower alkoxy, and the like; amino lower alkyl substituted with one or more substituents selected from the group of substituent α,

hydroxyimino lower alkyl;

lower alkoxyimino lower alkyl;

lower alkenyl optionally substituted with one or more substituents selected from the group of substituent α;

lower alkynyl optionally substituted with one or more substituents selected from the group of substituent α;

lower alkoxy optionally substituted with one or more substituents selected from the group of substituent α, wherein preferable is halogen, hydroxy, and the like;

lower alkylthio optionally substituted with one or more substituents selected from the group of substituent α, wherein preferable is halogen;

lower alkylamino substituted with one or more substituents selected from the group of substituent α, wherein preferable is amino;

lower alkylsulfonyl optionally substituted with one or more substituents selected from the group of substituent α;

aryl lower alkoxycarbonyl optionally substituted with one or more substituents selected from the group of substituent α and lower alkyl;

acyl substituted with one or more substituents selected from the group of substituent α, wherein preferable is halogen;

lower alkylsulfonyl optionally substituted with one or more substituents selected from the group of substituent α;

sulfamoyl;

lower alkyl sulfamoyl optionally substituted with one or more substituents selected from the group of substituent α;

cycloalkyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

aryl optionally substituted with one or more substituents selected from the group of substituent αazido and lower alkyl;

heterocyclic group optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl, wherein preferable is halogen, lower alkyl, and the like; aryloxy optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

heterocyclicoxy optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

arylthio optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl, wherein preferable is halogen, hydroxy, lower alkoxy, acyl, and the like;

heterocyclic thio optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

arylamino optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl, wherein preferable is halogen, hydroxy, lower alkoxy, acyl;

heterocyclic amino optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

aryl lower alkylamino optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl, wherein preferable is halogen, hydroxy, lower alkoxy, acyl;

heterocyclic lower alkylamino optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

arylsulfamoyl optionally substituted with one or more substituents selected from the group of substituent αazido and lower alkyl;

heterocyclic sulfamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

arylsulfonyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

heterocyclic sulfonyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

arylcarbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

heterocyclic carbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

aryl lower alkylcarbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

heterocyclic lower alkylcarbamoyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

aryloxy carbonyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

heterocyclicoxycarbonyl optionally substituted with one or more substituents selected from the group of substituent α, azido and lower alkyl;

lower alkylenedioxy optionally substituted with halogen; oxo; and the like.

In other case, the substituent of the "optionally substituted carbocyclic group", the "optionally substituted heterocyclic group", the "optionally substituted carbocyclicoxy", the "optionally substituted arylsulfonyl", the "optionally substituted aryloxycarbonyloxy", the "optionally substituted heterocyclicoxy", the "optionally substituted arylsulfinyl", the "optionally substituted arylsulfonyloxy", the "optionally substituted arylthio" is one or more substituents selected from the group of "lower alkyl" and the "substituent α".

"heteroaryl" include aromatic ring group in the aforementioned "heterocyclic group".

The substituent of the "optionally substituted 5- to 6-membered heteroaryl" is the same as the substituent of the "optionally substituted heterocyclic group" in the aforementioned "ring B". Preferable is one or more substituent selected from lower alkyl and a substituent α.

The "lower alkylene" includes a straight or branched bivalent carbon chain of a carbon number of 1 to 10, preferably a carbon number of 1 to 6, further preferably a carbon number of 1 to 3, Specifically, examples include methylene, dimethylene, trimethylene, tetramethylene, and methyltrimethylene, and the like.

The part of lower alkylene of the "lower alkylenedioxy" is the same as the aforementioned "lower alkylene".

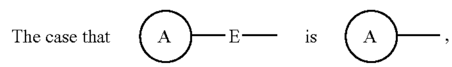
The "lower alkenylene" includes a straight or branched bivalent carbon chain of a carbon number of 2 to 10, preferably a carbon number of 2 to 6, further preferably a carbon number of 2 to 4 having double bond at an arbitrary position. Specifically, examples include vinylene, propenylene, butenylene, butadienylene, methylpropenylene, pentenylene, and hexenylene, and the like.

The "lower alkynylene" includes a straight or branched bivalent carbon chain of a carbon number of 2 to 10, preferably a carbon number of 2 to 6, further preferably a carbon number of 2 to 4 having triple bond at an arbitrary position. Specifically, examples include ethynylene, propynylene, butynylene, pentynylene, and hexynylene, and the like.

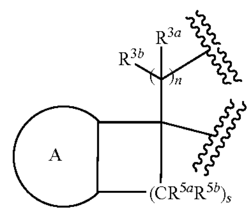
The substituent of the "optionally substituted lower alkylene", the "optionally substituted lower alkenylene", the "optionally substituted lower alkynylene" is the substituent α, preferable is halogen, hydroxy and the like.

The "each R^{3a}, each R^{3b}, each R^{4a}, and each R^{4b} may be independently different" means when n is 2 or 3, two or three R^{3a} may be independently different, and two or three R^{3b} may be independently different. In the same way, when in is 2 or 3, two or three R^{4a} may be independently different, and two or three R^{4b} may be independently different.

[Chemical formula 14]

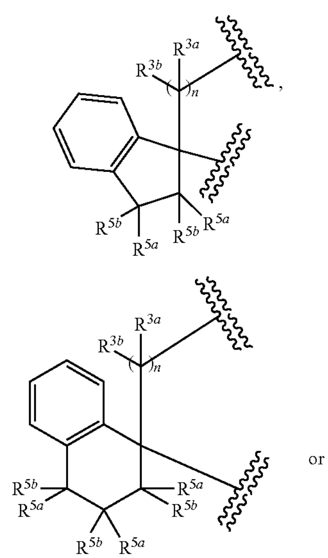


R^5 and ring A can be taken together to form



means for example, include the following structures.

[Chemical formula 15]



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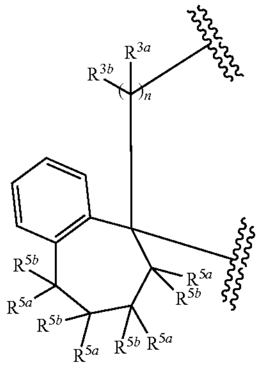


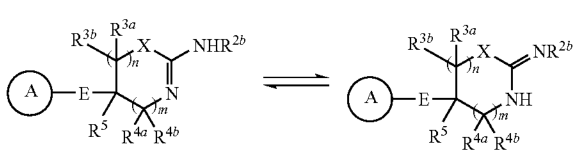
wherein each symbols are the same as described above; preferably, R^{5a} and R^{5b} are all hydrogen atoms.

In this description, "solvate" includes, for example, a solvate with an organic solvent and a hydrate, and the like. When hydrate is formed, arbitrary number of water molecules may be coordinated.

The compound (I) includes a pharmaceutically acceptable salt. Examples include salts with alkali metals (lithium, sodium or potassium, and the like), alkaline earth metals (magnesium or calcium, and the like), ammonium, organic bases or amino acids, and salts with inorganic acids (hydrochloric acid, sulfuric acid, nitric acid, hydrobromic acid, phosphoric acid or hydroiodic acid, and the like), and organic acid (acetic acid, trifluoroacetic acid, citric acid, lactic acid, tartaric acid, oxalic acid, maleic acid, fumaric acid, manderic acid, glutaric acid, malic acid, benzoic acid, phthalic acid, benzenesulfonic acid, p-toluenesulfonic acid, methanesulfonic acid, or ethanesulfonic acid, and the like). Particularly, hydrochloric acid, phosphoric acid, tartaric acid, or methanesulfonic acid is preferable. These salts can be formed by a conventional method.

In addition, the compound (I) is not limited to a specific isomer, but includes all possible isomers (keto-enol isomer, imine-enamine isomer, diastereo isomer, optical isomer, and rotational isomer, and the like) and racemates. For example, the compound (I), wherein R^{2a} is a hydrogen atom, includes following tautomer.

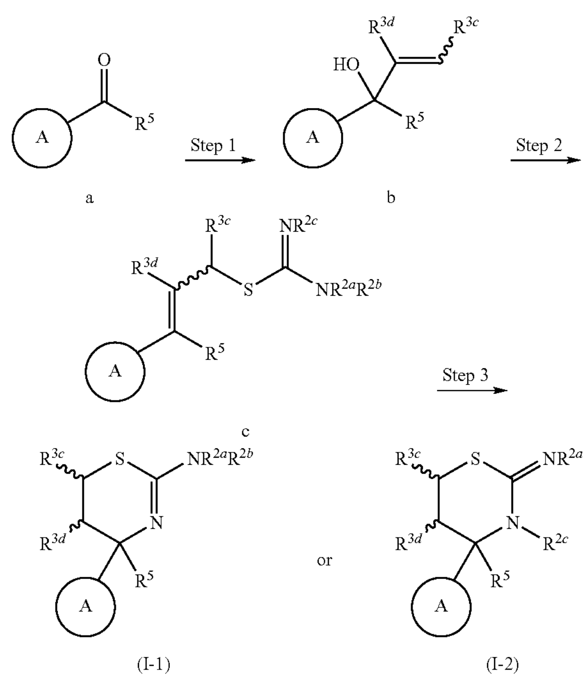
[Chemical formula 16]



The compound (I) in this invention can be prepared by the process described in, for example Non-patent Document 1 or following process.

The synthesis of aminodihydrothiazine ring; Method A

[Chemical formula 17]



In formula, at least either R^{2b} or R^{2c} is a hydrogen atom, either R^{3c} or R^{3d} is each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted acyl, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted amino, optionally substituted carbamoyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group. Other symbols are the same as described above.

(Step 1)

To a solution of compound (a), which is commercially available or prepared by known method, in appropriate solvent or mixture of solvents, such as ether, tetrahydrofuran, and the like is added the Grignard reagent having substituent corresponds to the target compound; for example vinylmagnesium chloride, vinylmagnesium bromide, or propenylmagnesium bromide, and the like; at −100° C. to 50° C., preferably −80° C. to 0° C. The mixture is reacted for 0.2 to 24 hours, preferably 0.5 to 5 hours, to obtain compound (b).

(Step 2)

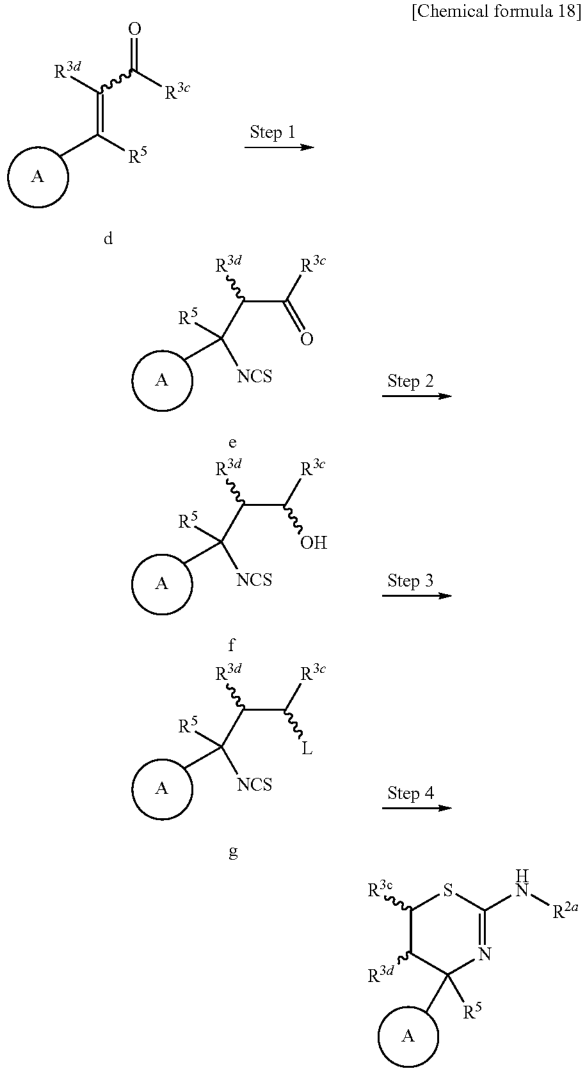
The compound (b) in solvent, such as toluene or absence of solvent is treated with thiourea derivatives having substituent corresponds to the target compound, such as thiourea, N-methylthiourea, N,N'-dimethylthiourea, and the like in the presence of an acid or mixture of acids, such as acetic acid, trifluoroacetic acid, hydrochloric acid, or sulfuric acid, and the like. The mixture is reacted at −20° C. to 100° C., preferably 0° C. to 50° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (c).

(Step 3)

The compound (c) in solvent, such as toluene or absence of solvent is treated with an acid or mixture of acids, such as trifluoroacetic acid, methanesulfonic acid, trifluoromethanesulfonic acid, and the like. The mixture is reacted at −20° C. to 100° C., preferably 0° C. to 50° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (I-2), wherein R^{2b} is a hydrogen atom, or the compound (I-1), wherein R^{2c} is a hydrogen atom.

The synthesis of aminodihydrothiazine ring; Method B

[Chemical formula 18]



(I-3)

In formula, L is leaving group such as halogen or sulfonyloxy, and the like. Other symbols are the same as described above.

(Step 1)

The compound (d) which is commercially available or prepared by known method is reacted with thiocyanic acid; for example, sodium thiocyanic acid, ammonium thiocyanic acid, and the like; in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; in the presence of acid; for example, water, hydrochloric acid, sulfuric acid, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 24 hours, preferably 1 to 12 hours, to obtain the compound (e),

(Step 2)

To the compound (e) in solvent or mixture of solvents; for example, tetrahydrofuran, methanol, ethanol, water, and the like; in the presence or the absence of buffer like sodium dihydorgen phosphate, and the like; reducing agent; for example sodium borohydride, and the like; is added and the mixture is reacted at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, to obtain the compound (f).

(Step 3)

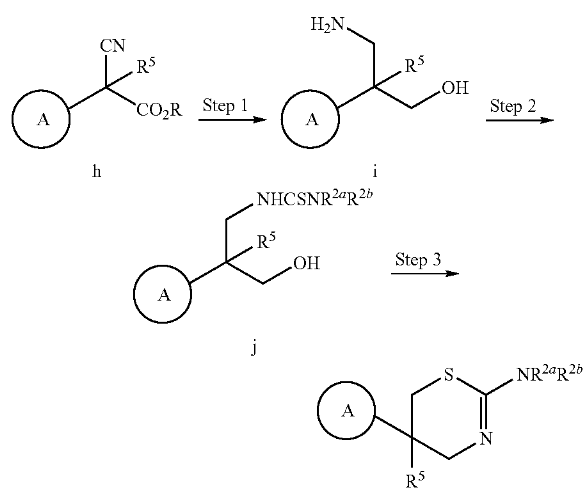
The compound (f) in the presence or the absence of solvent; for example, toluene, dichloromethane, and the like; is reacted with halogenating agent; for example thionyl chloride, phosphorus oxychloride, carbon tetrabromide-triphenylphosphine, and the like; at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, to obtain the compound (g). Alternatively, the compound (f) in the presence or the absence of solvent; for example, toluene, dichloromethane, and the like; under base; for example triethylamine, and the like; is reacted with sulfonating agent; for example, methanesulfonyl chloride, p-toluenesulfonylchloride, and the like; at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, to obtain the compound (g).

(Step 4)

To the compound (g) in solvent or mixture of solvents, for example methanol, ethanol, water, and the like; is reacted with primary amine; for example, ammonia or methylamine, and the like; at −20° C. to 80° C., preferably 0° C. to 40° C. for 0.5 to 48 hours, preferably 1 to 24 hours, to obtain the compound (I-3).

The synthesis of aminodihydrothiazine ring; Method C

[Chemical formula 19]



(I-4)

In formula, R is a hydrogen atom or protective groups of carboxyl group. Other symbols are the same as described above.

(Step 1)

The compound (h) which is commercially available or prepared by known method is reacted with reducing agent; for example, lithium aluminium hydride, diisobutyl aluminium hydride, and the like; in solvent; for example tetrahydrofuran, ether, and the like; at −80° C. to 150° C., preferably 25° C. to 100° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, to obtain the compound (i).

(Step 2)

The compound (i) in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; in the presence or the absence of base; for example, diisopropylethylamine, triethylamine, pyridine, sodium hydroxide, and the like; is reacted with corresponding isothiocyanate; for example, 4-methoxybenzylisothiocyanate, t-butylisothiocyanate, and the like; or corresponding thiocarbamoylhalide; for example, N,N-dimethylthiocarbamoylchloride, N,N-diethylthiocarbamoylchloride, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (j).

(Step 3)

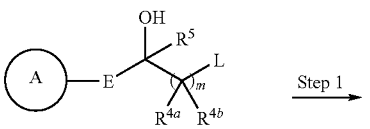
The compound (j) in solvent; for example, acetonitrile, toluene, dichloromethane, and the like; is reacted with halogenating agent; for example thionyl chloride, phosphorus oxychloride, carbon tetrabromide-triphenylphosphine, and the like; at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, or alternatively, the compound (j) in solvent; for example, toluene, dichloromethane, and the like; in the presence of base; for example triethylamine, and the like; is reacted with sulfonating agent; for example, methanesulfonyl chloride, p-toluenesulfonylchloride, and the like; at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours. The obtained halogenated compound or sulfonylated compound is reacted with base; for example, diisopropylamine, potassium carbonate, sodium hydrogencarbonate, sodium hydride, sodium hydroxide, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (I-4).

The synthesis of aminodihydrothiazine ring; Method D

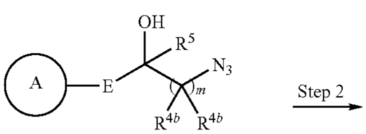
The synthesis of aminothiazoline ring; Method A

The synthesis of tetrahydrothiazepine ring; Method A

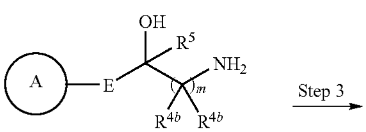
[Chemical formula 20]



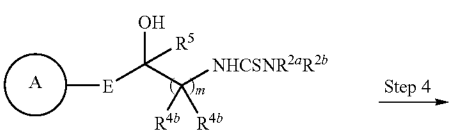
k



l



m



n

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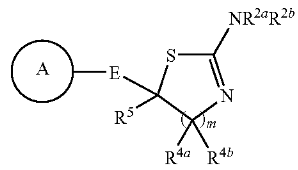


(I-5)

In formula, L is leaving group such as halogen or sulfonyloxy, and the like; m is an integer of 1 to 3; and the other symbols are the same as described above.

(Step 1)

The compound (k) which is commercially available or prepared by known method is reacted with azide reagent; for example, sodium azide, and, the like; in solvent; for example N,N-dimethylformamide, tetrahydrofuran, and the like; at 0° C. to 200° C., preferably 40° C. to 150° C. for 0.5 to 24 hours, preferably 1 to 12 hours, to obtain the compound (l).

(Step 2)

The compound 0) is reacted with reducing agent; for example, lithium aluminium hydride, diisobutyl aluminium hydride, and the like; in solvent; for example tetrahydrofuran, ether, and the like; at −80° C. to 150° C., preferably 25° C. to 100° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, to obtain the compound (m).

(Step 3)

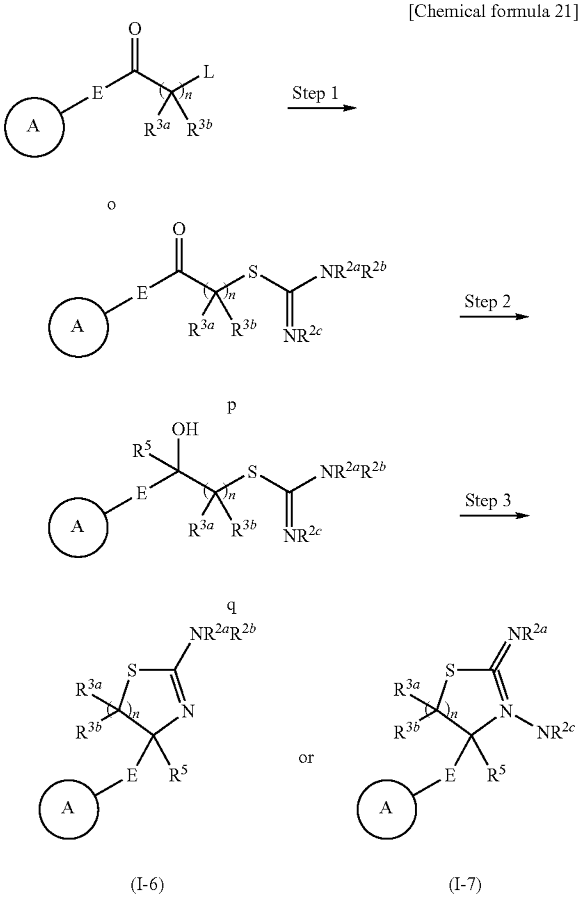
The compound (m) in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; is reacted with corresponding isothiocyanate; for example, methylisothiocyanate, ethylisothiocyanate, and the like; or corresponding thiocarbamoylhalide; for example, N,N-dimethylthiocarbamoylchloride, N,N-diethylthiocarbamoylchloride, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (n).

(Step 4)

The compound (n) in solvent; for example, acetonitrile, toluene, dichloromethane and the like; is reacted with halogenating agent; for example thionyl chloride, phosphorus oxychloride, carbon tetrabromide-triphenylphosphine, and the like; at −80° C. to 50° C., preferably −20° C. to 20° C. for 0,1 to 24 hours, preferably 0.5 to 12 hours, or alternatively, the compound (n) in solvent; for example, toluene, dichloromethane, and the like; in the presence of base; for example diisopropylethylamine, triethylamine, and the like; is reacted with sulfonating agent; for example, methanesulfonyl chloride, p-toluenesulfonylchloride, and the like; at −80° C. to 50° C., preferably -20° C. to 20° C. for 0,1 to 24 hours, preferably 0.5 to 12 hours. The obtained halogenated compound or sulfonylated compound is reacted with base; for example, diisopropylamine, potassium carbonate, sodium hydrogencarbonate, sodium hydride, sodium hydroxide, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (I-5).

The synthesis of aminodihydrothiazine ring; Method E
The synthesis of aminothiazoline ring; Method B
The synthesis of tetrahydrothiazepine ring; Method B

[Chemical formula 21]



In formula, at lease one of R^{2b}) and R^{2c} is a hydrogen atom, n is an integer of 1 to 3, and the other symbols are the same as described above.

(Step 1)

The compound (o) which is commercially available or prepared by known method is reacted with substituted thiourea; for example, thiourea, N-methylthiourea, N,N,-dimethylthiourea, N,N'-dimethylthiourea, and the like; in solvent; for example, ethanol, methanol, tetrahydrofuran, toluene, and the like; at −20° C. to 200° C., preferably 0° C. to 150° C. for 0.5 to 200 hours, preferably 1 to 120 hours, to obtain the compound (p).

(Step 2)

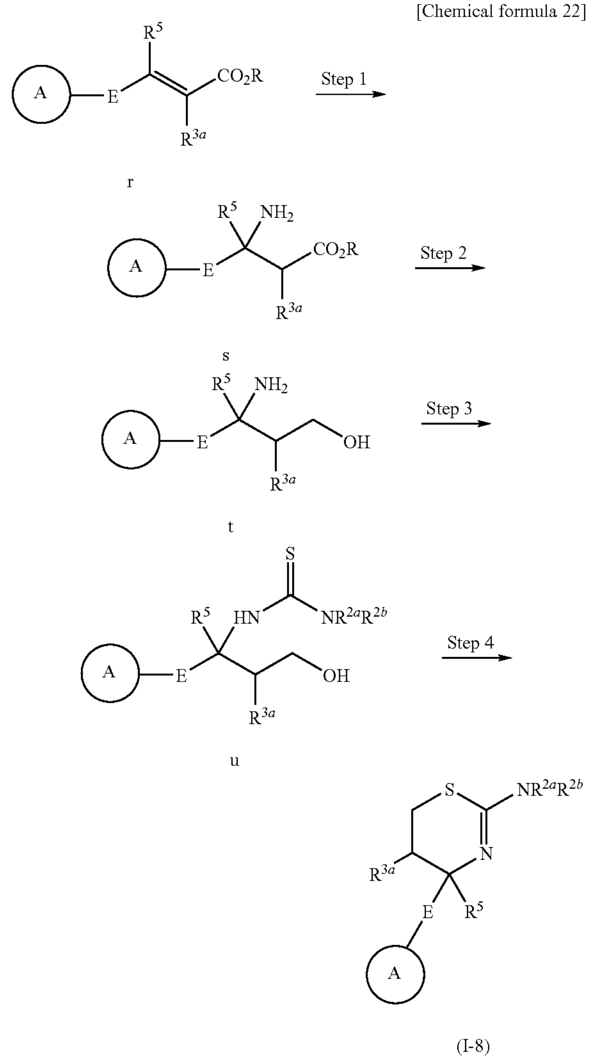
To the compound (p) in solvent or mixture of solvents; for example, ether, tetrahydrofuran, and the like; the Grignard reagent having substituent corresponding to target compound; for example methylmagnesium chloride, ethylmagnesium bromide, or benzylmagnesium bromide, and the like; is added at −100° C. to 50° C., preferably −80° C. to 30° C., and the mixture is reacted for 0.2 to 24 hours, preferably 0.5 to 5 hours, to obtain the compound (q).

(Step 3)

To the compound (q) in the presence or the absence of solvent; for example, toluene, and the like; acid or mixture of acids, such as trifluoroacetic acid, methanesulfonic acid, trifluoromethanesulfonic acid, and the Like; is added and the mixture is reacted at −20° C. to 100° C., preferably 0° C. to 50° C. for 0.5 to 200 hours, preferably 1 to 150 hours, to obtain the compound (I-6)(wherein R^{2c} is H), or the compound (I-7)(wherein R^{2b} is H).

The synthesis of aminodihydrothiazine ring; Method F

[Chemical formula 22]



In formula, each symbols are the same as described above.

(Step 1)

The compound (r) which is commercially available or prepared by known method is reacted with ammonium chloride in solvent; for example, acetic acid, and the like; at 0° C. to 200° C., preferably 10° C. to 100° C. for 0.1 to 100 hours, preferably 0.5 to 24 hours, to obtain the compound (s).

(Step 2)

The compound (s) is reacted with reducing agent; for example, lithium aluminium hydride, diisobutyl aluminium hydride, and the like; in solvent; for example tetrahydrofuran, ether, and the like; at −80° C. to 150° C., preferably 0° C. to 100° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours, to obtain the compound (t).

(Step 3)

The compound (t) in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; in the presence or the absence of base; for example, diisopropylethylamine, triethylamine, pyridine, sodium hydroxide, and the like; is reacted with corresponding isothiocyanate; for example, 4-methoxybenzylisothiocyanate, t-butylisothiocyanate, and the like; or corresponding carbamoylhalide; for example, N,N-dimethylthiocarbamoylchloride, N,N-diethylthiocarbamoylchloride, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (u).

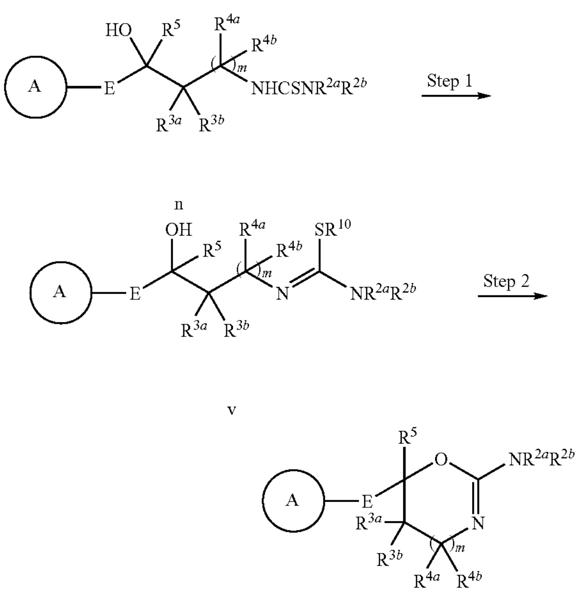
(Step 4)

The compound (u) in solvent; for example, acetonitrile, toluene, dichloromethane, and the like; is reacted with halogenating agent; for example thionyl chloride, phosphorus oxychloride, carbon tetrabromide-triphenylphosphine, and the like; at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hour preferably 0.5 to 12 hours, or alternatively, the compound (u) in solvent; for example, toluene, dichloromethane, and the like; in the presence of base; for example triethylamine, and the like; is reacted with sulfonating agent; for example, methanesulfonyl chloride, p-toluenesulfonylchloride, and the like; at −80° C. to 50° C. preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours. The obtained halogenated compound or sulfonylated compound is reacted with base; for example, diisopropylamine, potassium carbonate, sodium hydrogencarbonate, sodium hydride, sodium hydroxide, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (I-8).

The synthesis of aminodihydrooxazine ring; Method A

The synthesis of aminotetrahydrooxazepine ring; Method A

[Chemical formula 23]



n

v

(I-9)

In formula, each symbols are the same as described above.

(Step 1)

The compound (n) which is obtained by Step 3(the compound (m) to the compound (n)) of "The synthesis of aminodihydrothiazine ring; Method D", in solvent; for example, methanol, ethanol, N,N-dimethylformamide, tetrahydrofuran, and the like; in the presence or the absence of base; for example, diisopropylethylamine, triethylamine, pyridine, sodium hydroxide, and the like; is reacted with alkylating agent; for example, methyl iodide, dimethyl sulfate, benzyl bromide, and the like; at 0° C. to 200° C., preferably 40° C. to 150° C. for 0.1 to 48 hours, preferably 0.5 to 24 hours, to obtain the compound (v).

(Step 2)

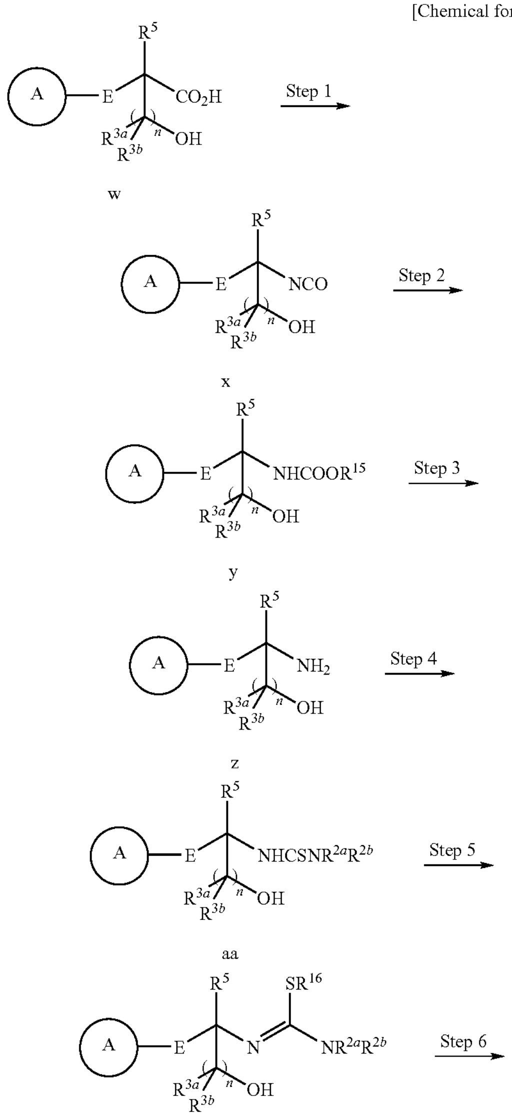
The compound (v) in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, dichloromethane, and the like; in the presence or the absence of base; for example, diisopropylethylamine, triethylamine, pyridine, sodium hydroxide, and the like; is reacted with metallic oxide; for example, silver oxide, mercury oxide, manganese dioxide, and the like; at 0° C. to 200° C., preferably 10° C. to 150° C. for 1 to 120 hours, preferably 0.5 to 100 hours, to obtain the compound (I-9).

The synthesis of aminodihydrooxazine ring; Method B

The synthesis of aminoxazoline ring

The synthesis of aminotetrahydrooxazepine ring; Method B

[Chemical formula 24]



w

x

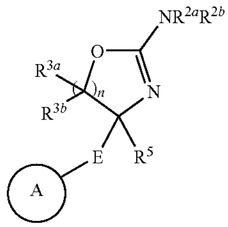
y

z

aa

ab

-continued



(I-10)

In formula, R^{15} is optionally substituted lower alkyl; for example, t-butyl, benzyl, and the like; R^{16} is hydrogen atom or lower alkyl; n is an integer of 1 to 3, and the other symbols are the same as described above.

(Step 1)

The compound (w) which is commercially available or prepared by known method in solvent; for example, toluene, t-butylalcohol, tetrahydrofuran, and the like; in the presence of base; for example, diisopropylethylamine, triethylamine, pyridine, and the like; is reacted with azide reagent; for example, diphenyl phosphoryl azide, and the like; at 0° C. to 200° C., preferably 40° C. to 150° C. for 1 to 48 hours, preferably 0.5 to 24 hours, to obtain the compound (x).

(Step 2)

The compound (x) in solvent; for example, toluene, xylene, N,N-dimethylformamide, tetrahydrofuran, and the like; is reacted with alcohol; for example, t-butylalcohol, 3,4-dimethoxybenzylalcohol, 4-methoxybenzylalcohol, and the like; at 0° C. to 300° C., preferably 50° C. to 200° C. for 1 to 800 hours, preferably 5 to 500 hours, to obtain the compound (y).

(Step 3)

The compound (y) in the presence or the absence of solvent; for example, water, toluene, dichloromethane, methanol, 1,4-dioxane, acetic acid, ethyl acetate, and the like; in the presence of acid; for example, hydrochloric acid, sulfuric acid, hydrobromic acid, trifluoroacetic acid, and the like; at 0° C. to 200° C., preferably 25° C. to 150° C. for 0.1 to 48 hours, preferably 0.5 to 24 hours, to obtain the compound (z).

(Step 4)

The compound (z) in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; in the presence of base; for example, diisopropylethylamine, triethylamine, pyridine, and the like; is reacted with corresponding isothiocyanate, or thiocarbamoylhalide corresponding to target compound; for example, N,N-dimethylthiocarbamoylchloride, N,N-diethylthiocarbamoylchloride, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (aa).

(Step 5)

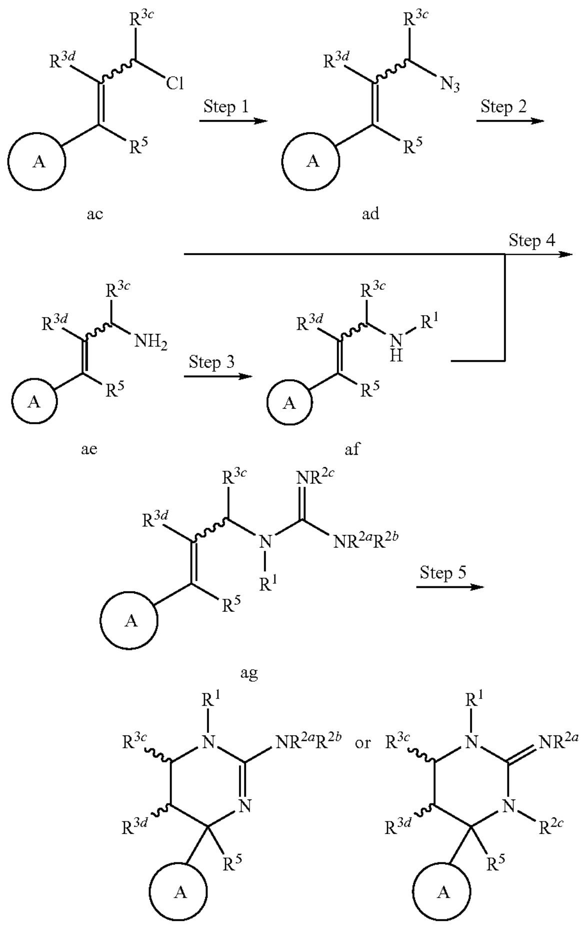
The compound (aa) in solvent; for example, methanol, ethanol, N,N-dimethylformamide, tetrahydrofuran, and the like; in the presence or the absence of base; for example, diisopropylethylamine, triethylamine, pyridine, sodium hydroxide, and the like; is reacted with alkylating agent; for example, methyl iodide, dimethyl sulfate, benzyl bromide, and the like; at 0° C. to 200° C., preferably 40° C. to 150° C. for 1 to 48 hours, preferably 0.5 to 24 hours, to obtain the compound (ab).

(Step 6)

The compound (ab) in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, dichloromethane, and the like; in the presence of base; for example, diisopropylethylamine, triethylamine, pyridine, sodium hydroxide, and the like; is reacted with metallic oxide; for example, silver oxide, mercury oxide, manganese dioxide, and the like; at 0° C. to 200° C., preferably 10° C. to 150° C. for 1 to 120 hours, preferably 0.5 to 100 hours, to obtain the compound (O-10).

The synthesis of aminotetrahydropyrimidine ring

[Chemical formula 25]



In formula, each symbols are the same as described above.

(Step 1)

To the compound (ac) prepared by known method in solvent; for example, N,N-dimethylformamide, methanol, and the like; is reacted with azide reagent; for example, sodium azide, lithium azide, and the like; at 20° C. to 150° C., preferably 50° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (ad).

(Step 2)

To the suspension of lithium aluminium hydride in solvent; for example, tetrahydrofuran, or ether, and the like; the compound (ad) dissolved in solvent; for example, tetrahydrofuran, or diethyl ether, and the like; is added under nitrogen atmosphere, at −80° C. to 20° C., preferably −30° C. to 0° C., and the mixture is reacted for 1 minute to 10 hours, preferably 10 minutes to 1 hour, or alternatively to the compound (ad) in solvent; for example, ethanol, isopropanol, or n-butanol, and the like; Raney-Nickel is added at 10° C. to 110° C., preferably 50° C. to 80° C., and reacted for 1 minute to 10 hours, preferably 10 minutes to 1 hour, to obtain the compound (ae).

(Step 3)

The compound (ae) in solvent; for example, tetrahydrofuran, dichloromethane, and the like; in the presence of acid; for example, acetic acid, or propionic acid, and the like; is reacted with reducing agent; for example, sodium cyanoborohydride, sodium triacetoxyborohydride, and the like; at −50° C. to 100° C., preferably 0° C. to 50° C., for 0.1 to 48 hours, preferably 0.5 to 24 hours, or the compound (ae) in solvent; for example, tetrahydrofuran, N,N-dimethylformamide, and the like; in the presence of dehydrating agent; for example, 1-ehthyl-3-(3-dimethylaminopropyl)carbodiimide-N-hydroxybenzotriazole, carbonyldiimidazole, and the like; or in the presence of base; for example, triethylamine, potassium carbonate, and the like; is reacted with carboxylic acid; for example, formic acid, acetic acid, and the like; at −50° C. to 100° C., preferably 0° C. to 50° C. for 0.1 to 48 hours, preferably 0.5 to 16 hours, to obtain the compound (af). And next, to the suspension of lithium aluminium hydride in solvent; for example, tetrahydrofuran, or diethyl ether, and the like; the aforementioned amide compound dissolved in solvent; for example, tetrahydrofuran, or ether, and the like; is added at −50° C. to 60° C., preferably 0° C. to 50° C., and the mixture is reacted for 1 minute to 48 hours, preferably 10 minutes to 10 hours, to obtain the compound (af).

(Step 4)

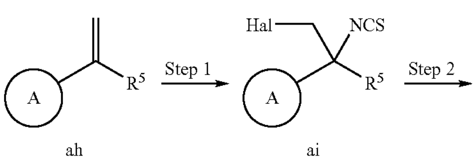
The compound (ae) or the compound (af) in solvent; for example, acetonitrile, tetrahydrofuran, N,N-dimethylformamide, and the like; is reacted with 3,5-dimethylpyrazole-1-carboxyamidine or S-methylthiourea at 0° C. to 150° C., preferably 20° C. to 100° C., and the mixture is reacted for 0.5 to 120 hours, preferably 1 to 24 hours, to obtain the compound (ag).

(Step 5)

To the compound (ag) (wherein at least either R^{2b} or R^{2c} is a hydrogen atom) in the presence or the absence of solvent; for example, toluene, and the like; acid; for example, trifluoroacetic acid, methanesulfonic acid, trifluoromethanesulfonic acid, and the like, or the mixture thereof; is added and the mixture is reacted at −20° C. to 100° C., preferably 0° C. to 50° C., and the mixture is reacted for 0.5 to 120 hours, preferably 1 to 72 hours, to obtain the compound (I-2) (wherein R^{2b} is a hydrogen atom) or the compound (I-1) (wherein R^{2c} is a hydrogen atom) respectively, Proviso, if R^{2a}, R^{2b}, and R^{2c} have fragile structure under acidic condition; for example, t-butyloxycarbonyl, and the like; R^{2a}, R^{2b}, and R^{2c} in the compound (I-1) or the compound (I-2) may be transformed into a hydrogen atom.

The synthesis of aminothiazoline ring; Method C

[Chemical formula 26]



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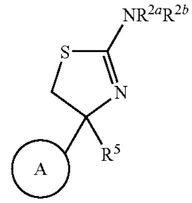


(I-11)

In formula, Hal is halogen, and other symbols are the same as described above.

(Step 1)

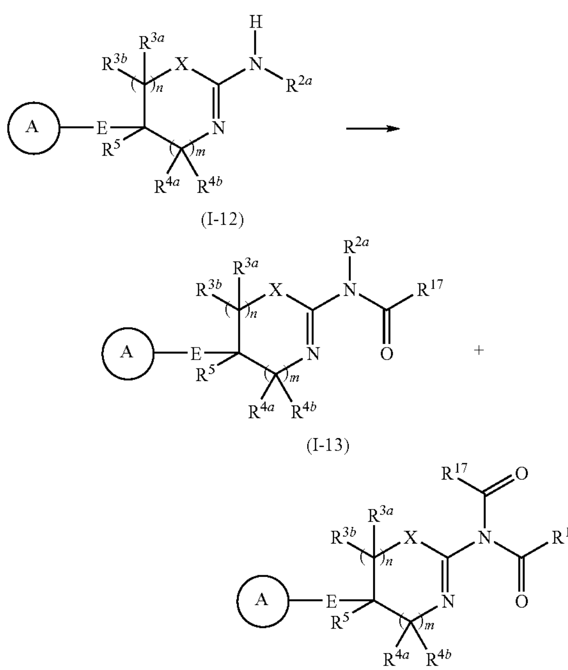
The compound (ah) which is commercially available or prepared by known method in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; or in mixed-solvent; for example, chloroform-water, and the like; is reacted with halogen; for example, including iodine, bromine, chorine; phase transfer catalyst; for example, sodium thiocyanic acid, ammonium thiocyanic acid, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C., for 0.5 to 48 hours, preferably 1 to 24 hours, to obtain the compound (ai).

(Step 2)

The compound (ai) in solvent; for example, toluene, chloroform, tetrahydrofuran, and the like; is reacted with amine having substituent corresponding to target compound; for example ammonia, methylamine, diethylamine, and the like; at 0° C. to 150° C., preferably 20° C. to 100° C., for 0.5 to 48 hours, preferably 1 to 24 hours, to obtain the compound (I-11).

The aminoacyl derivative-1

[Chemical formula 27]

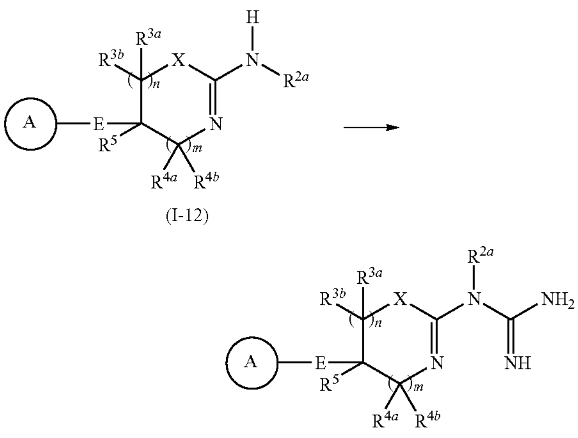


In formula, R^{17} is optionally substituted lower alkyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group, and the other symbols are the same as described above.

The compound (I-12) wherein R^{2b} is a hydrogen atom in the presence or the absence of solvent; for example, tetrahydrofuran, dichloromethane, and the like; in the presence of base; for example, pyridine, triethylamine, and the like; is reacted with acylating agent having substituent corresponding to target compound; for example, benzoyl chloride, 2-furoyl chloride, acetic anhydride, and the like; at −80° C. to 100° C., preferably −20° C. to 40° C., for 0.1 to 24 hours, preferably 1 to 12 hours, or alternatively, the compound (I-12) in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, dichloromethane, and the like; in the presence of dehydrating agent; for example, dicyclohexylcarbodiimide, carbonyldiimidazole, and the like; is reacted with carboxylic acid having substituent corresponding to target compound; for example, amino acid, glycolic acid, and the like; at −80° C. to 100° C., preferably −20° C. to 40° C., for 0.1 to 24 hours, preferably 1 to 12 hours, to obtain the compound (I-13) and/or the compound (I-14) (wherein R^{2a} is a hydrogen atom).

The guanidino derivatives

[Chemical formula 28]


(I-12)

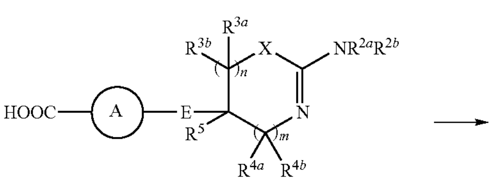
(I-15)

In formula, each symbols are the same as described above,

The compound (I-12) wherein R^{2b} is a hydrogen atom in solvent; for example, acetonitrile, tetrahydrofuran. N,N-dimethylformamide, and the like; in the presence or the absence of base; for example, triethylamine, sodium hydrogencarbonate, and the like; is reacted with 3,5-dimethylpyrazole-1-carboxyamidine, or S-methylisothiourea etc. at 0° C. to 150° C., preferably 20° C. to 100° C., for 0.5 to 120 hours, preferably 1 to 24 hours, to obtain the compound (I-15).

The carbamoyl derivatives

[Chemical formula 29]


(I-16)

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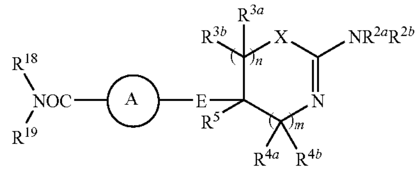
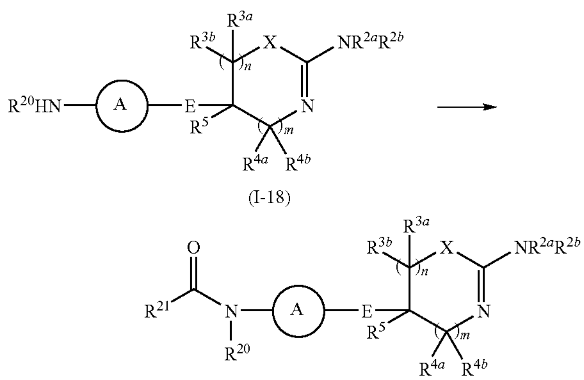

(I-17)

In formula, $CONR^{18}R^{19}$ is optionally substituted carbamoyl, and the other symbols are the same as described above.

The compound (I-16) having a carboxyl group as substituent of ring A in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, dichloromethane, and the like; in the presence of dehydrating agent; for example, dicyclohexylcarbodiimide, carbonyldiimidazole, dicyclohexylcarbodiimide-N-hydroxybenzotriazole, and the like; is reacted with primary amine or secondary amine (aniline, 2-aminopyridine, dimethylamine etc.) at −80° C. to 100° C., preferably −20° C. to 40° C., for 0.1 to 24 hours, preferably 1 to 12 hours, to obtain the compound (I-17).

The acylamino derivative-2

[Chemical formula 30]


(I-18)

(I-19)

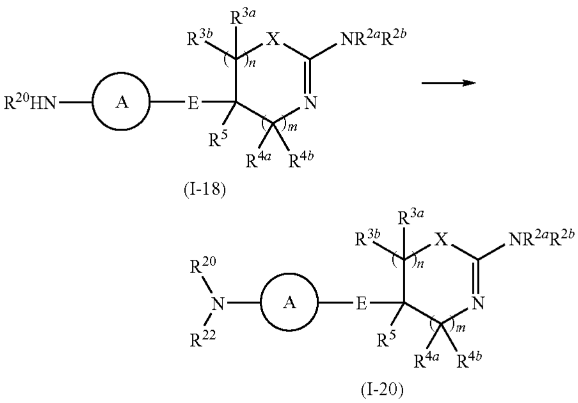
In formula, NHR^{20} is optionally substituted amino; $NR^{20}COR^{21}$ is optionally substituted acyl amino, optionally substituted ureido, carboxy amino having substituent on oxygen atom, and the other symbols are the same as described above.

The compound (I-18) having an optionally substituted amino group on ring A in the presence or the absence of solvent; for example, tetrahydrofuran, dichloromethane, and the like; in the presence or the absence of base; for example, pyridine, triethylamine, and the like; is reacted with reagent including acid chloride, acid anhydride, chloroformate ester derivatives, isocyanate derivatives (benzoyl chloride, 2-furoyl chloride, acetic anhydride, benzyl chloroformate, di-t-butyl dicarbonate, phenyl isocyanate etc.), at −80° C. to 100° C., preferably −20° C. to 40° C., for 0.1 to 24 hours, preferably 1 to 12 hours. Or alternatively, the compound (I-18) having an optionally substituted amino group on ring A in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, dichloromethane, and the like; in the presence of dehydrating agent; for example, dicyclohexylcarbodiimide, carbonyldiimidazole, dicyclohexylcarbodiimide-N-hydroxybenzotriazole, and the like; is reacted with carboxylic acid having substituent corresponding to target compound;

for example, benzoic acid, 2-pyridinecarboxylic acid, and the like; at 80° C. to 100° C., preferably −20° C. to 40° C., for 0.1 to 24 hours, preferably 1 to 12 hours, to obtain the compound (I-19).

The alkylamino derivatives

[Chemical formula 31]

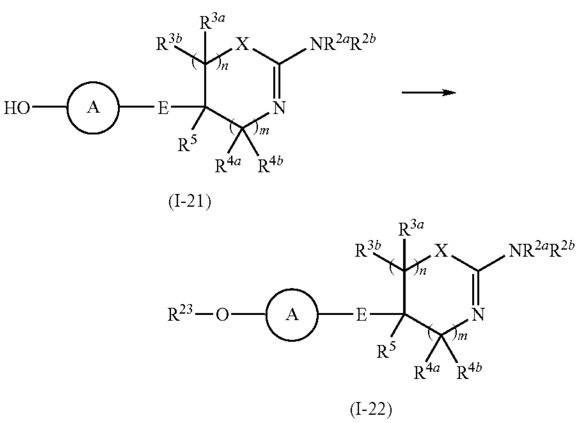


In formula, NHR^{20} is optionally substituted amino, R^{22} is lower alkyl.

The compound(I-18) having an amino group on ring A in solvent; for example, dichloromethane, tetrahydrofuran, and the like; in the presence or the absence of acid; for example, acetic acid, and the like; is reacted with aldehyde having substituent corresponding to target compound; for example, benzaldehyde, pyridine-2-carboaldehyde, and the like; and reducing agent; for example, sodium borohydride, sodium triacetoxyborohydride, and the like; at −80° C. to 100° C., preferably 0° C. to 40° C., for 0.5 to 150 hours, preferably 1 to 24 hours, to obtain the compound (I-20).

The substituted alkoxy derivatives

[Chemical formula 32]

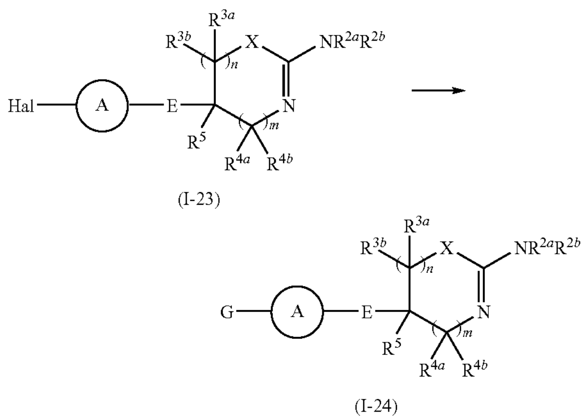


In formula, R^{23} is optionally substituted lower alkyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group, etc., and the other symbols are the same as described above.

The compound (I-21) having a hydroxy group as substituent of A ring in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, and the like; in the presence of base; for example potassium carbonate, sodium hydroxide, sodium hydride, and the like; is reacted with alkylating agent having substituent corresponding to target compound; for example, benzylchloride, methyl iodide, and the like; at −80° C. to 100° C., preferably 0° C. to 40° C., for 0.5 to 150 hours, preferably 1 to 24 hours, or alternatively, the compound (I-18) in solvent; for example, N,N-dimethylformamide, tetrahydrofuran, and the like; under Mitsunobu reagent; for example triphenylphosphine-azodicarboxylic acid ethyl ester, and the like; is reacted with alcohol; for example, 2-aminoethanol, and the like; at −80° C. to 100° C., preferably 0° C. to 40° C., for 0.5 to 72 hours, preferably 1 to 24 hours, to obtain the compound (I-22).

The introduction of substituent with palladium coupling reaction

[Chemical formula 33]

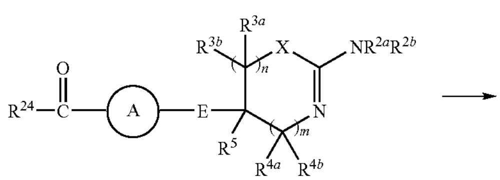


In formula, Hal is halogen, G is optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted lower alkoxycarbonyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group etc., and the other symbols are the same as described above.

The compound (I-23) having halogen as substituent of A ring in solvent; for example, tetrahydrofuran, N,N-dimethylformamide, 1,2dimethoxyethane, methanol, and the like; in the presence of base; for example, triethylamine, sodium carbonate, and the like; palladium catalyst; for example, palladium acetate, palladium chloride, and the like; and ligand; for example triphenylphosphine, and the like; is reacted with compound having substituent corresponding to target compound(styrene, propargyl alcohol, aryl boronic acid, carbon monoxide), with or without microwave irradiation, at −80° C. to 150° C., preferably 0° C. to 100° C., for 0.5 to 72 hours, preferably 1 to 24 hours, to obtain the compound (I-24).

The oxime derivatives

[Chemical formula 34]



(I-25)

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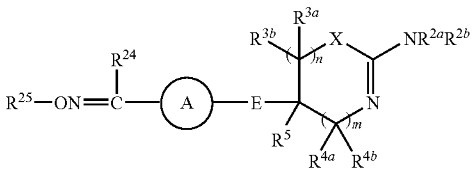


(I-26)

In formula, in R^{24} is a hydrogen atom or optionally substituted lower alkyl etc., R^{25} is a hydrogen atom, optionally substituted lower alkyl, optionally substituted lower alkenyl or an optionally substituted carbocyclic group or an optionally substituted heterocyclic group etc., and the other symbols are the same as described above.

The compound (I-25) having an acyl group as substituent of A ring in solvent; for example, methanol, ethanol, and the like; in the presence or the absence of additives; for example, potassium acetate, and the like; is reacted with hydroxylamine having substituent corresponding to target compound (hydroxylamine, methoxylamine, O-benzylhydroxylamine, etc.) or the salt thereof, at 0° C. to 100° C., preferably 0° C. to 40° C., for 0.5 to 150 hours, preferably 1 to 72 hours, to obtain the compound (I-26).

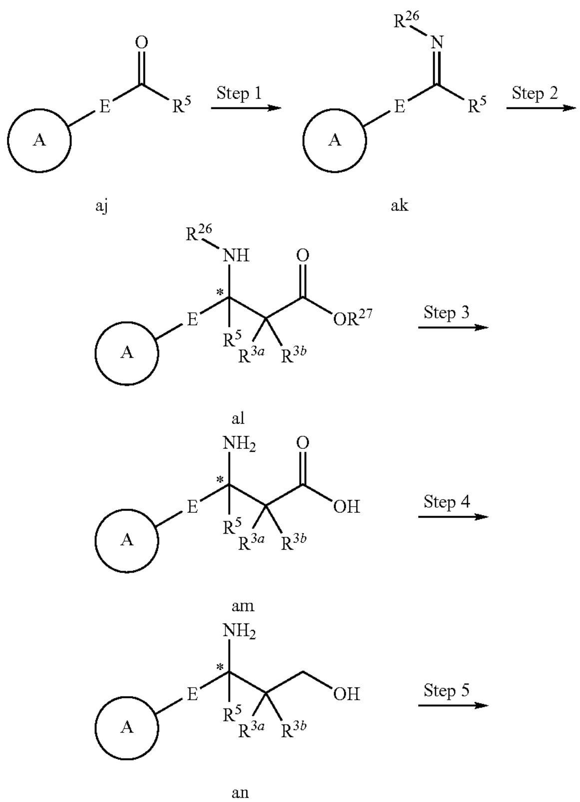
Production of optical active compounds

For example, Optical active compound aq, one embodiment of the pharmaceutical composition of the present invention can be synthesized in the following method.

1) n=2

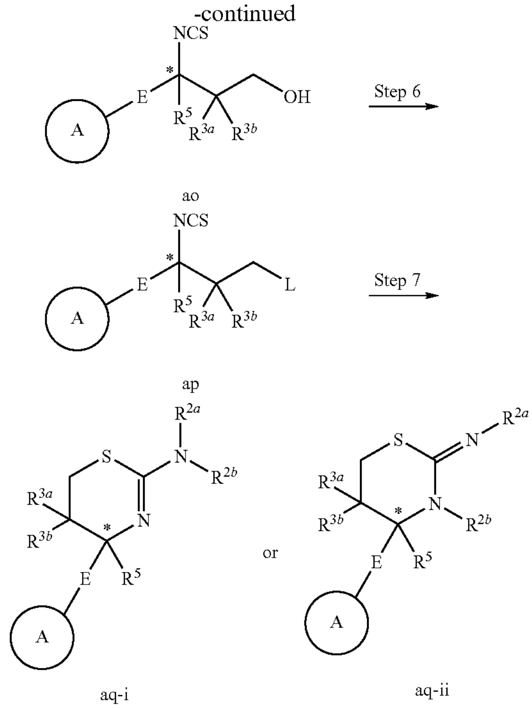
1-1) X=S

[Chemical formula 35]



aj, ak, al, am, an

-continued



ao, ap, aq-i, aq-ii

wherein R^5 is hydrogen, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, lower alkoxycarbonyl, optionally substituted carbamoyl, an optionally substituted cabocyclic group or an optionally substituted heterocyclic group, R^{25} is a chiral sulfoxide having optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted carbocyclic group or optionally substituted heterercyclic group, R^{3a} and R^{3b} are each independently hydrogen, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkoxycarbonyl, optionally substituted carbamoyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group, optionally substituted acyl, carboxy or optionally substituted amino, R^{27} is optionally substituted lower alkyl, optionally substituted lower alkenyl, R^{2a} and R^{2b} are each independently hydrogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino, optionally substituted amidino, optionally substituted acyl, optionally substituted carbamoyl, optionally substituted carbamoylcarbonyl, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group, L is an leaving group such as halogen, methanesulfonyloxy, trifluoromethylsulfonyloxy and the like, and other symbols are the same as described above.

The above compounds ak and al can be synthesized according to the method described in (1)T, Fujisawa et al., Tetrahedron Lett., 37, 3881-3884 (1996), (2)D. H. Hua et al, Sulfur Reports, vol. 21, pp. 211-239 (1999), (3)Y. Koriyama et al., Tetrahedron, 58, 9621-9628 (2002), (4)T. Vilavan et al, Cuuent Organic Chemistry, 9, 1315-1392 (2005) and the like, or by optical resolution of each intermediate or final compound, or by the method described below. Examples of methods for optical resolution are separation of optical isomers using an optically active column, kinetic resolution by an enzyme reaction or the like, crystallization of diastereomers by salt formulation using a chiral acid or a chiral base, and a preferential crystallization etc.

Step 1

Compound ak can be obtained by reacting Compound aj, which is commercially available or can be prepared by a known method, with a chiral reagent having a substituent corresponding to the target compound such as para-toluene, tert-butylsulfine amide or the like at 60° C. to 120° C., preferably 80° C. to 100° C. in a solvent such as ether, tetrahydrofuran, toluene, benzene or the like or a mixed solvent such as ether-tetrahydrofuran or the like for 0.5 to 24 hours, preferably 0.5 to 5 hours in the presence of moleculer sieves or magnesium sulfate or the like, under continuous evaporation by Dean-Stark apparatus, or in the presence of a chiral reagent having a substituent corresponding to the target compound such as para-toluene, tert-butylsulfine amide ane the like according to the method described in the above literatures.

Step 2

Compound al can be diastereoselectively obtained by reacting compound ak with a metal, which is lithium, aluminum, zinc, titanium or the like, enolate of acetate ester or the like possessing a substituent corresponding to the target compound which is commercially available or prepared by a known method, at −100° C. to 0° C., preferably −80° C. to −50° C. for 0.5 to 24 hours, preferably 0.5 hours in a solvent such as ether, tetrahydrofuran, toluene, methylene chloride or a mixed solvent of ethertetrahydrofuran or the like, or obtained according to the method described in the above literature (1) or (3). Alternatively, ketenesilyl acetate of acetate ester which is prepared from ester acetate or the like possessing a substituent corresponding to the target compound can be used.

Step 3

Compound am can be obtained by reacting Compound al in a solvent such as methanol, ethanol ether, tetrahydrofuran, 1,4-dioxane, methylene chloride, ethyl acetate or the like, which contains hydrogen chloride, trifluoroacetic acid or the like, or in trifluoroacetcic acid without a solvent, or at −30° C. to 100° C., preferably −10° C. to 90° C. for 0.5 to 12 hours, preferably 0.5 to 5 hours.

Step 4

To a solution of Compound am in a solvent such as ether, tetrahydrofuran, toluene or the like or a mixed solvent such as ether-tetrahydrofuran is added a reductant such as a borantetrahydrofuran complex, a boran-dimethylsulfide complex, a boran-triethylamine complex, a boran-pyridine complex or the like, or ether of tetrahydrofuran solution of them at −30° C. to 30° C., preferably −10° C. to 20° C. and the mixture is reacted for 0.5 to 12 hours, preferably 0.5 to 5 hours to obtain Compound an.

Step 5

To a solution of Compound an in a solvent such as methylene chloride, toluene or the like or a mixed solvent of methylene chloride-water or the like is added calcium carbonate, potassium carbonate or the like, and added thiophosgene at −30° C. to 50° C., preferably −10° C. to 25° C., followed by reacting for 0.5 to 12 hours, preferably 0.5 to 5 hours to obtain Compound ao.

Step 6

To a solution of Compound ao in a solvent such as methylene chloride, tetrahydrofuran, toluene or the like are added oxalyl chloride, thionyl chloride or the like and a catalytic amount of N,N-dimethylformamide at −30° C. to 50° C., preferably −10° C. to 20° C. The mixture is reacted at 0° C. to 100° C., preferably 20° C. to 90° C. for 0.5 to 12 hours, preferably 0.5 to 5 hours to obtain Compound ap. Alternatively, Compound ap can be obtained by halogenation according to the method described in Comprehensive Organic Transformations, Richard C Larock (Mcgraw-Hill) or by reacting Compound ao with a sulfonylation reagent such as methanesulfonyl chloride, p-toluene sulfonyl chloride or the like in the presence of a base such as diisopropylethylamine, triethylamine or the like in a solvent such as toluene, dichloromethane or the like at −80° C. to 50° C., preferably −20° C. to 20° C. for 0.1 to 24 hours, preferably 0.5 to 12 hours.

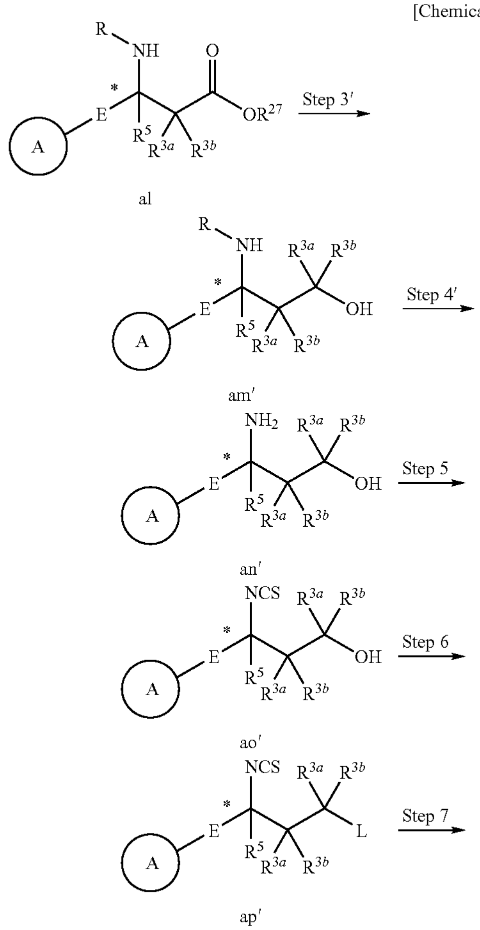
Step 7

To a solution of Compound ap in a solvent such as ethyl acetate, methylene chloride, tetrahydrofuran, toluene or the like is added 15 to 30% aqueous ammonia or a reagent having a substituent corresponding to the target compound such as tert-butyl amine at −30° C. to 50° C., preferably −10° C. to 30° C. The mixture is reacted at −10° C. to 30° C., preferably 0° C. to 30° C. for 0.5 to 72 hours to obtain Compound aq-i or Compound aq-ii.

In the case that thus-obtained Compound aq-i or Compound aq-ii is a compound wherein R^{2a} and/or R^{2b} is hydrogen, the target substituent R^{2a} or R^{2b} can be introduced by the usual method, if necessary.

1-2) Introduction of R^{3a} and R^{3b}

[Chemical formula 36]



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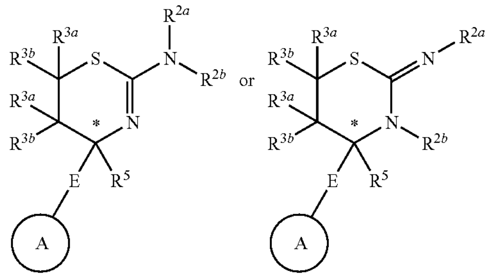


aq-iii   aq-iv

wherein each symbols are the same as described above.

To obtain Compound aq-iii or aq-iv wherein R^{3a} and R^{3b} are substituted at the carbon atom neighboring to X, R^{3a} and R^{3b} may be introduced by conducting Step 3' and Step 4' instead of Step 3 and Step4.

Step 3'

To a solution of Compound al in a solvent such as ether, tetrahydrofuran or the like or a mixed solvent such as ether-tetrahydrofuran or the like is added a Grignard reagent having a substituent corresponding to the target compound such as methyl magnesium chloride, ethyl magnesium bromide or the like at −100° C. to 50° C., preferably −80° C. to 30° C. to obtain Compound am'. Alternatively, after conversion of Compound al to Weinreb amide thereof, the compound is reacted sequentially with a Grignard reagent having a substituent corresponding to the target compound such as $R^{3\ a}$ MgBr, $R^{3\ b}$ MgBr or the like to obtain Compound am', The reaction may be conducted for 0.2 to 24 hours, preferably 0.2 to 5 hours.

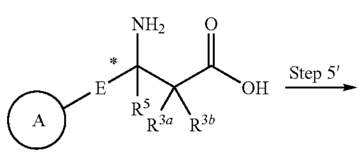
Step 4'

Compound an' can be synthesized according to the above-mentioned Step 3. Compound an can be obtained by reacting Compound am' in a solvent such as methanol, ethanol, ether, tetrahydrofuran, 1,4-dioxane, methylene chloride, ethyl acetate or the like which includes hydrogen chloride, trifluoroacetic acid or the like, without a solvent, or in trifluoroacetic acid without a solvent at −30° C. to 100° C., preferably −10° C. to 90° C. for 0.5 to 12 hours, preferably 0.5 to 5 hours.

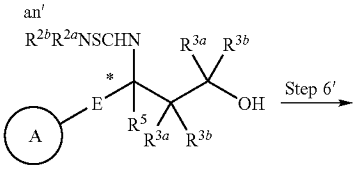
Then, the target Compound aq-iii or aq-iv can be obtained by conducting the similar methods to Steps 5 to 7 mentioned in the above 1-1),

1-3) X═O

[Chemical formula 37]

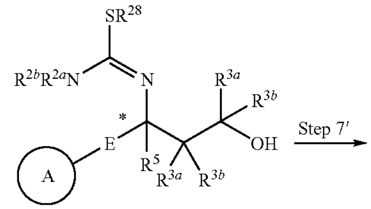


an'

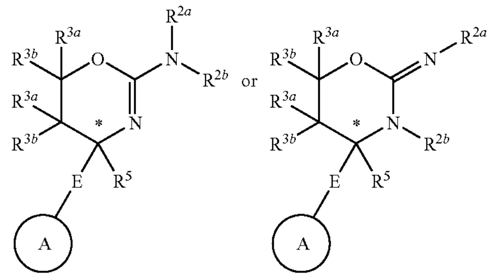


ao'

-continued



ap''



aq-v   aq-vi

wherein R^{28} is alkyl or optionally substituted alkylsulfonyl, optionally substituted carbocyclic sulfonyl or optionally substituted heterocyclic sulfonyl and other symbols are the same as described above.

The target compound can be obtained by conducting the following steps instead of Steps 5 to 7 described in the above 1-1).

Step 5'

Compound ao' can be obtained by reacting Compound an' with an isothiocyanate having the substituent corresponding to the target compound such as ally isothiocyanate, tert-butylisothiocyanate or the like or a thiocarbamoyl halide having the substituent corresponding to the target compound such as N,N-dimethylthiocarbamoyl chloride, N,N-diethylthiocarbamoyl chloride or the like in a solvent such as toluene, chloroform, tetrahydrofuran or the like at 0° C. to 150° C., preferably 20° C. to 100° C. for 0.5 to 120 hours, preferably 1 to 72 hours.

Step 6'

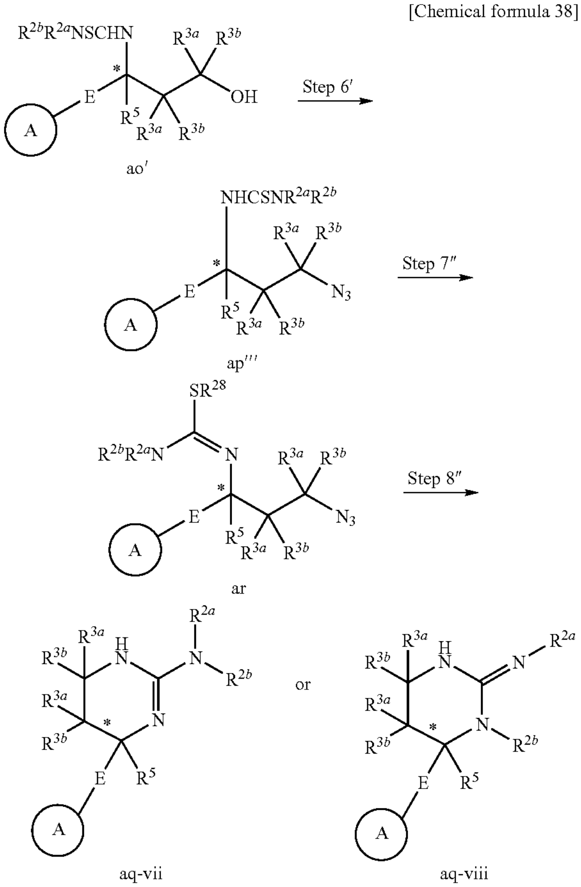
Compound ap'' can be obtained by reacting Compound ao' with an alkylating agent such as methyl iodide, diethyl sulfate, benzylbromide or the like or a sulfonating agent such as p-toluensulfonyl chloride in the presence or absence of a base such as diisopropylethylamine, triethylamine, pyridine, sodium hydroxide or the like in a solvent such as methanol, ethanol, dimethylformamide, tetrahydrofuran or the like at 0° C. to 200° C., preferably 40° C. to 150° C. for 0.1 to 48 hours, preferably 0.5 to 24 hours.

Step 7

Compound aq-v or aq-vi can be obtained by reacting Compound ap' in the presence or absence of a base such as diisopropylethylamine, triethylamine, pyridine, sodium hydroxide or the like, in the presence or absence of a metallic oxide such as silver oxide, mercury oxide, manganese dioxide or the like, in a solvent such as dimethylformamide, tetrahydrofuran, dichloromethane or the like at 0° C. to 200° C., preferably 10° C. to 150° C. for 1 to 120 hours, preferably 0.5 to 100 hours.

1-4) X=N

[Chemical formula 38]



wherein each symbols are the same as described above.

Step 6"

Compound ap''' can be obtained by reacting Compound ao' with an azidation agent such as sodium azide, trimethylsillylazide or the like in the presence or absence of an acid such as trifluoroacetic acid or the like in a solvent such as chloroform, tetrahydrofuran or the like at −10° C. to 200° C., preferably 0° C. to 100° C. for 0.1 to 48 hours, preferably 0.5 to 24 hours.

Step 7'

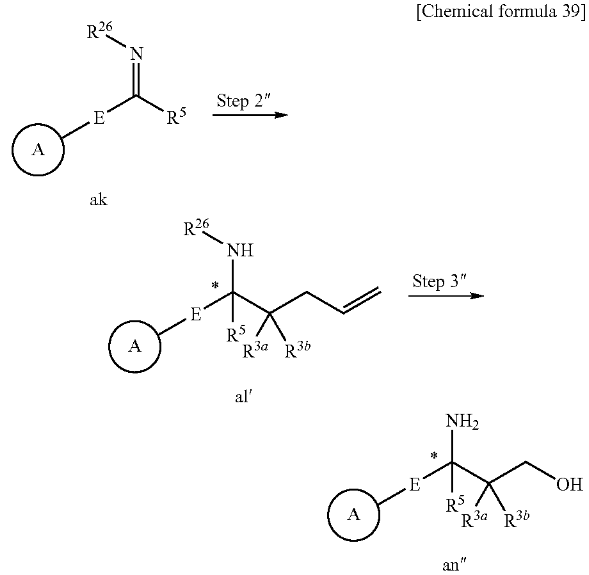
Compound ar can be obtained by reacting Compound ap''' with an alkylating agent such as methyl iodide, diethyl sulfate, benzylbromide or the like or a sulfonating agent such as p-toluensulfonyl chloride in the presence or absence of a base such as diisopropylethylamine, triethylamine, pyridine, sodium hydroxide or the like in a solvent such as methanol, ethanol, dimethylformamide, tetrahydrofuran or the like at 0° C. to 200° C., preferably 40° C. to 150° C. for 0.1 to 48 hours, preferably 0.5 to 24 hours.

Step 8"

To a solution of Compound ar in a solvent such as tetrahydrofuran, ethyl acetate, methanol or the like is added a catalytic reduction catalyst such as 10% Pd/C, and the mixture is reacted under hydrogen atmosphere at normal pressures to 5 atm, preferably at normal pressure to 2 atm at 10° C. to 100° C., preferably 20° C. to 80° C. for 0.5 to 48 hours, preferably 6 to 20 hours to obtain Cyclized Compound aq-vii or aq-viii. Alternatively, Cyclized Compound aq-vii or aq-viii can be obtained by reducing a azide group of Compound or by the method described in "Comprehensive Organic Transformations, Richard C Larock (Mcgraw-Hill)". If necessary, the compound obtained by reduction may be treated with a base such as triethylamine, sodium hydroxide or the like to obtain Compound aq-vii or aq-viii.

2) n=3

[Chemical formula 39]



wherein the each symbols are the same as defined above.

Step 2"

Compound al' can be obtained by reacting Compound ak with a Grignard reagent having a substituent corresponding to the target compound such as an allyl Grignard reagent in a solvent such as ether, tetrahydrofuran, toluene or the like or a mixed solvent such as ether-tetrahydrofuran at −80° C. to 50° C., preferably −40° C. to 30° C. for 0.5 to 12 hours, preferably 0.5 to 8 hours.

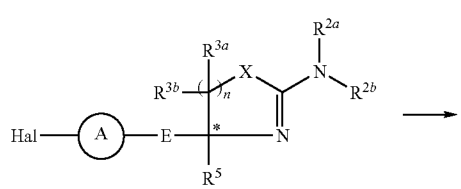
Step 3"

Compound an" can be obtained by hydroboration, wherein Compound al' is reacted with a reductant such as a boran-tetrahydrofuran complex, a boran-dimethylsulfide complex, a boran-triethylamine complex, a boran-pyridine complex or the like or an ether or tetrahydrofuran solution of them in a solvent such as ether, tetrahydrofuran, toluene or the like or a mixed solvent such as ether-tetrahydrofuran or the like at −30° C. to 30° C., preferably −15° C. to 20° C. for 0.5 to 12 hours, preferably 0.5 to 5 hours.

Substituents R^{3a} and R^{3b} can be introduced into thus-obtained Compound an" by the method according to the above-mentioned 1-2).

3) Conversion of Substituents (1)

[Chemical formula 40]



aq-1

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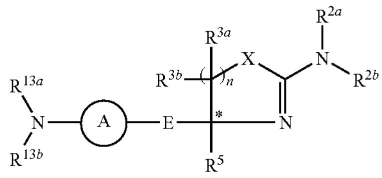


as-1

wherein R^{13a} and R^{13b} are amino-protecting groups and the other symbols are the same as defined above.

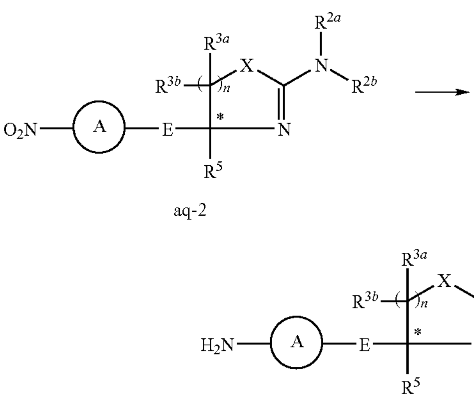
Synthesis of Compound as-1

To a solution of Compound aq-1 in a solvent such as tetrahydrofuran, toluene, xylene or the like are added tris-dibenzyliden acetone dipalladium, palladium acetate or palladium(0) prepared in situ and a phosphine ligand such as tri-tert-butylphosphine, dicyclohexylbiphenyl phosphine or the like, and further added a reagent having the substituent corresponding to the target compound such as lithium hexamethyl disilazide at −10° C. to 30° C., followed by reacting at 30° C. to 120° C., preferably 50° C. to 100° C. for 0.5 to 48 hours, preferably 3 to 20 hours to obtain Compound as-1.

An amino protecting group may be a group which is deprotected by the method described in "Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons)" etc. and the examples are lower alkoxy-carbonyl, lower alkenyloxycarbonyl, trialkylsillyl, acyl, methansulfonyl, trifiuoroethansulfonyl, toluensulfonyl and the like.

4) Conversion of Substituent (2)

[Chemical formula 41]



aq-2

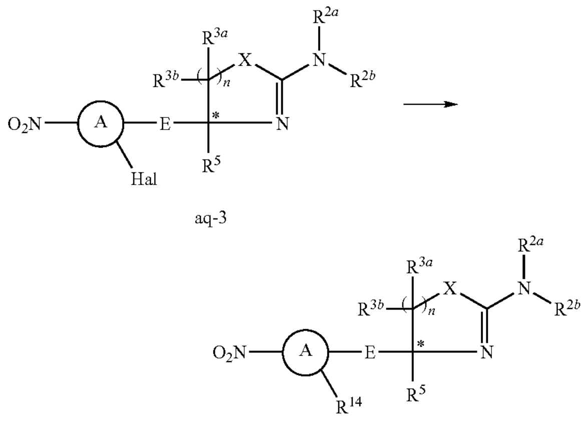
as-2

Synthesis of Compound as-2

To a solution of aq-2 in a solvent such as tetrahydrofuran, ethyl acetate, methanol or the like is added a catalytic reduction catalyst such as 10% Pd/C, and then the mixture is reacted at normal pressure to 5 atm, preferably normal pressure to 2 atm under hydrogen atmosphere for 0.5 to 48 hours, preferably 6 to 20 hours to obtain Compound as-2. Alternatively. Compound as-2 can be obtained by the method described in "Comprehensive Organic Transformations, Richard C Larock (McGraw-Hill)".

5) Conversion of Substituent (3)

[Chemical formula 42]



aq-3

as-3

wherein R^{14} is hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkylthio, optionally substituted lower amino, optionally substituted aromatic carbocyclicoxy or heterocyclic oxy, optionally substituted aromatic carbocyclicamino or heterocyclic amino, optionally substituted aromatic carbocyclicthio or heterocyclicthio, cyano, azide, optionally substituted carbocyclic group, optionally substituted heterocyclic group, optionally substituted carbamoyl or the like and the other symbols are the same as defined above.

Synthesis of Compound as-3

To a solution of Compound aq-3 in a solvent such as tetrahydrofuran, ethanol or the like is added a reagent having the substituent corresponding to the target compound such as ethanol, methanethiol, dimethyl amine or the like at −10° C. to 30° C. and the mixture is reacted for 0.5 to 12 hours, preferably 1 to 8 hours to obtain Compound as-3.

Then, the similar reaction described in the above "4) Conversion of substituent (2)" may be conducted, and further a coupling reaction may be conducted according to the above-mentioned method for producing Compound (I-19), if necessary.

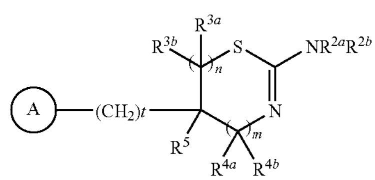
In all of above mentioned steps, if a compound having substituent which interrupts the reaction; (for example, hydroxy, mercapto, amino, formyl, carbonyl, carboxyl, etc.), the substituent of the compound is protected by methods described in Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons) beforehand, and is deprotected at preferable step.

The compound (I) in this invention presented below; in particular, X is S, and E is a bond or methylene; is preferable.

1) A Compound represented by the general formula (I'),

[Chemical formula 43]

(I')



wherein, t is 0 or 1, the other symbols are the same as above (a), with the proviso that the compounds represented below;

i) wherein n+m is 2, R^5 is a hydrogen atom, and ring A is non-substituted phenyl;

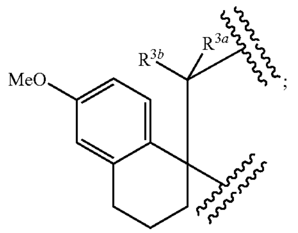
ii) wherein n is 2, no is 0, R^{2a} is a hydrogen atom, R^{2b} is a hydrogen atom or acetyl, R^5 is methyl, and ring A is phenyl or 4-methoxyphenyl;

iii) wherein n is 2, m is 0, R^{2a} is a hydrogen atom, R^{2b} is a hydrogen atom or acetyl, R^5 is ethyl, and ring A is 3,4-dimethoxyphenyl;

iv) wherein n is 2, m is 0, R^{2a} is a hydrogen atom, R^{2b} is a hydrogen atom or acetyl, and R^5 and ring A are phenyl;

v) wherein n is 2, m is 0, R^{2a} and R^{2b} are a hydrogen atom, R^5 and ring A are taken together to form

[Chemical formula 44]



and

vi) wherein n+m is 1 or 2; R^5 is a hydrogen atom; and ring A is phenyl substituted by one or two substituent selected from hydroxy, halogen, lower alkyl, lower alkoxy, nitro, amino, lower alkyl carbonylamino, mercapto, lower alkylthio, carbamoyl, lower alkylamino, lower alkyl carbamoyl and lower alkoxycarbonyl; non-substituted phenyl, or non-substituted naphthyl; are excluded.

In addition, in formula (I'), preferable is the compound represented below.

2) The compound, wherein n is 1 and m is 0 (this compound is represented by nm-1),

3) the compound, wherein n is 2 and m is 0 (this compound is represented by nm-2),

4) the compound, wherein n is 3 and m is 0 (this compound is represented by nm-3),

5) the compound, wherein R^{2a} is a hydrogen atom: R^{2b} is a hydrogen atom, optionally substituted lower alkyl, optionally substituted acyl, optionally substituted lower alkylsulfonyl, or optionally substituted amidino (this compound is represented by R2-1),

6) the compound, wherein R^{2a} is a hydrogen atom; R^{2b} is a hydrogen atom, optionally substituted lower alkyl or optionally substituted acyl (this compound is represented by R2-2),

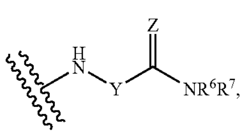
7) the compound, wherein $NR^{2a}R^{2b}$ is represented by the following formula:

[Chemical formula 45]

(a)

$-NH_2$,

(b)



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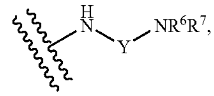
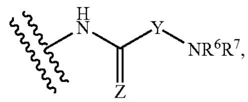
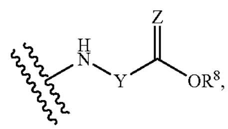
(c)



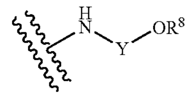
(d)



(e)

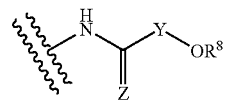


(f)



or

(g)



wherein each symbols are the same as described above,

R^6, R^7 and R^8 are each independently a hydrogen atom, lower alkyl or acyl,

Y is optionally substituted lower alkylene, optionally substituted lower alkenylene or optionally substituted lower alkynylene,

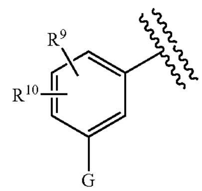
Z is O or S (this compound is represented by R2-3),

8) the compound, wherein $NR^{2a}R^{2b}$ is NH_2 (this compound is represented by R2-4),

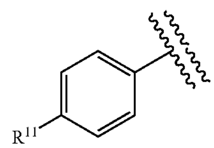
9) the compound, wherein ring A is substituted phenyl or substituted pyridyl (this compound is represented by A-1),

10) the compound, wherein ring A is represented by the following formula:

[Chemical formula 46]



or

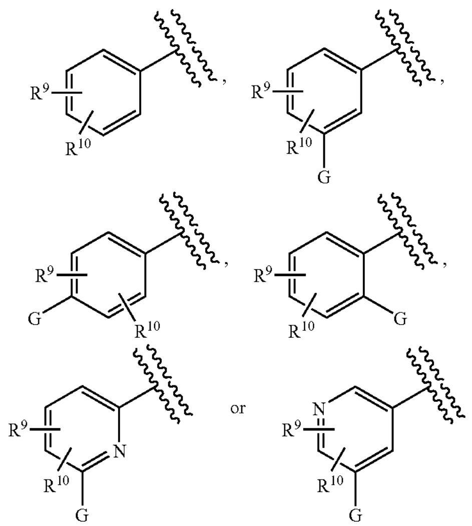


wherein R^9, R^{10} and R^{11} is a hydrogen atom or G,

G is halogen, hydroxy, cyano, nitro, mercapto, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted acyl, optionally substituted acyloxy, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted lower alkoxycarbonyloxy; optionally substituted aryloxycarbonyloxy, optionally substituted amino, optionally substituted carbamoyl, optionally substituted carbamoyloxy, optionally substituted lower alkylthio, optionally substituted arylthio, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, optionally substituted lower alkylsulfinyl, optionally substituted arylsulfinyl, optionally substituted lower alkylsulfonyloxy, optionally substituted arylsulfonyloxy, optionally substituted sulfamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy, an optionally substituted heterocyclic group or optionally substituted heterocyclicoxy, each G may be different (this compound is represented by A-2),

11) the compound, wherein ring A is represented by the following formula:

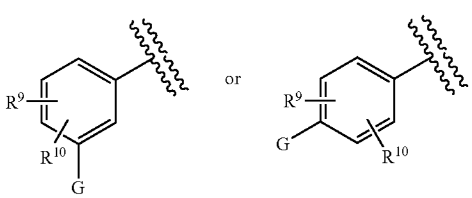
[Chemical formula 47]



wherein R^9 and R^{10} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, cyano, nitro, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, optionally substituted carbamoyl, optionally substituted carbamoyloxy, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, optionally substituted lower alkylsulfonyloxy, optionally substituted arylsulfonyloxy, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy, an optionally substituted heterocyclic group or optionally substituted heterocyclicoxy, G is the same as described above 10) (this compound is represented by A-3),

12) the compound, wherein ring A is represented by the following formula:

[Chemical formula 48]



wherein R^9 and R^{10} is the same as described in 11), G is the same as described in 10) (this compound is represented by A-4),

13) the compound, wherein ring A, R^9, and R^{10} are defined in 11), G is optionally substituted amino (this compound is represented by A-5),

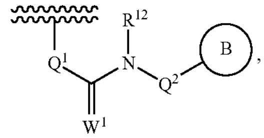
14) the compound, wherein ring A, R^9 and R^{10} are defined in 11), G is optionally substituted arylcarbonylamino or optionally substituted heterocyclic carbonylamino,

15) the compound, wherein ring A, R^9 and R^{10} are defined in 11), G is optionally substituted heterocyclic carbonylamino (this compound is represented by A-6),

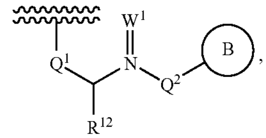
16) the compound, wherein ring A is defined in 11), G is represented by the following formula:

[Chemical formula 49]

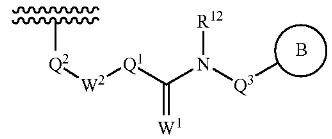
(i)



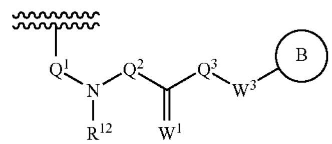
(ii)



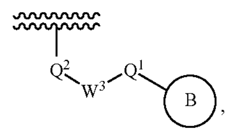
(iii)



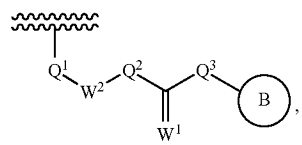
(iv)



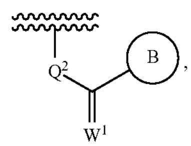
(v)



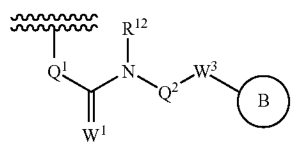
(vi)



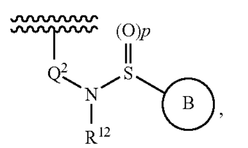
(vii)



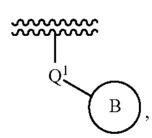
(viii)



(ix)

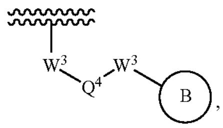


(x)

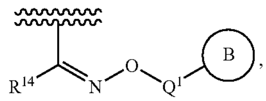


-continued

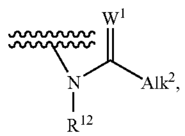
(xi)



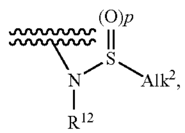
(xii)



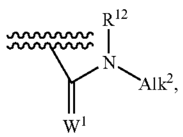
(xiii)



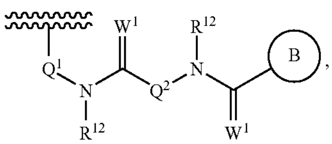
(xiv)



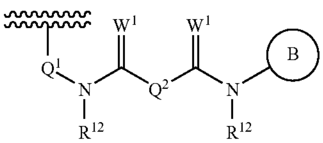
(xv)



(xvi)

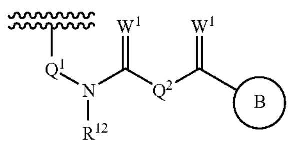


(xvii)



or

(xviii)



wherein Q^1, Q^2 and Q^3 are each independently a bond, optionally substituted lower alkylene or optionally substituted lower alkenylene:

Q^4 is optionally substituted lower alkylene or optionally substituted lower alkenylene;

W^1 and W^2 are each independently O or S;

W^3 is O, S or NR^{12};

R^{12} is a hydrogen atom, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, lower alkoxycarbonyl lower alkyl, carbocyclic lower alkyl or acyl;

R^{14} is a hydrogen atom or lower alkyl;

ring B is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group;

Alk^2 is optionally substituted lower alkyl; and

R^9 and R^{10} are the same as described in 11) (this compound is represented by A-7),

17) the compound, wherein ring A, R^9 and R^{10} are the group defined in 11); G is the group defined in 16); ring B is aryl optionally substituted with one or more substituents selected from halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, cyano, optionally substituted carbamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy or an optionally substituted heterocyclic group or

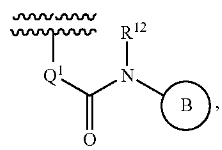
heteroaryl optionally substituted with one or more substituents selected from halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, cyano, optionally substituted carbamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy or an optionally substituted heterocyclic group;

and the other symbols are the same as described in 16) (this compound is represented by A-8),

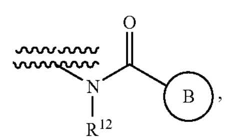
18) the compound, wherein ring A, R^9 and R^{10} are defined in 11), G is represented by the following formula;

[Chemical formula 50]

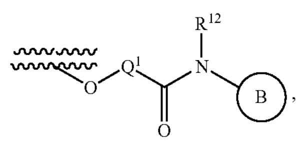
(i')



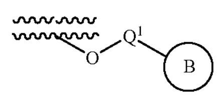
(ii')



(iii')

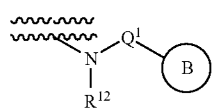


(v')



or

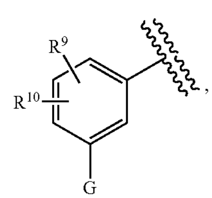
(v'')



wherein each symbols are the same as described in 16) (this compound is represented by A-9),

19) the compound, wherein ring A is represented by the following formula:

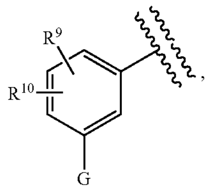
[Chemical formula 51]



wherein G is defined in 16), ring B is optionally substituted aryl or optionally substituted heteroaryl, either R^9 or R^{10} is a hydrogen atom; and the other is a hydrogen atom, halogen, optionally substituted lower alkyl, cyano, nitro, optionally substituted lower alkoxy, optionally substituted amino, optionally substituted carbamoyl, optionally substituted lower alkylsulfonyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group (this compound is represented by A-10),

20) the compound, wherein ring A is represented by the following formula:

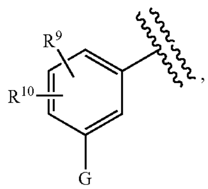
[Chemical formula 52]



wherein G is defined in 18), the other symbols are the same as described in 19) (this compound is represented by A-11),

21) the compound, wherein ring A is represented by the following formula:

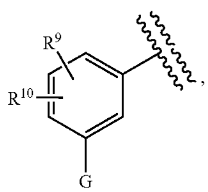
[Chemical formula 53]



wherein G is defined in 16), ring B is optionally substituted phenyl, optionally substituted 5- to 6-membered heteroaryl, optionally substituted benzothiazolyl or optionally substituted benzothienyl, and R^9 and R^{10} are the same as described in 19) (this compound is represented by A-12),

22) the compound, wherein ring A is represented by the following formula:

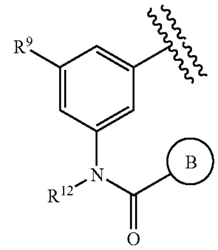
[Chemical formula 54]



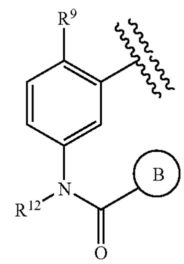
wherein G is defined in 18), ring B is defined in 21), R^9 and R^{10} are the same as described in 19) (this compound is represented by A-13),

23) the compound, wherein ring A is represented by the following formula:

[Chemical formula 55]



or



wherein R^9 is a hydrogen atom, halogen, optionally substituted lower alkyl, cyano, nitro, optionally substituted lower alkoxy, optionally substituted amino, optionally substituted carbamoyl, optionally substituted lower alkylsulfonyl, an optionally substituted carbocyclic group or an optionally substituted heterocyclic group, ring B is the same as described in 21): and R^{12} is a hydrogen atom or lower alkyl (this compound is represented by A-14),

24) the compound, wherein R^5 is a hydrogen atom or C1 to C3 alkyl (this compound is represented by R5-1),

25) the compound, wherein R^5 is C1 to C3 alkyl (this compound is represented by R5-2),

26) the compound, wherein R^5 is methyl (this compound is represented by R5-3),

27) the compound, wherein R^{3a} and R^{3b} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy or optionally substituted aryl (this compound is represented by R3-1),

28) the compound wherein, R^{3a} is a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy or optionally substituted aryl, R^{3b} is a hydrogen atom, one R^3 is a hydrogen atom when n is 2, one or two R^{2a} is (are) a hydrogen atom(s) when n is 3 (this compound is represented by R3-2),

29) the compound, wherein R^{3a} and R^{3b} are all hydrogen atoms (this compound is represented by R3-3), and

in a compound represented by the general formula (I'), a compound, wherein the combination of n, m, R^{2a}, R^{2b}, ring A, R^{3a}, and R^{3b} (nm, R^2, A, R^5, R^3) is the following compound.

(nm, R^2, A, R^5 R^3)=(nm-1,R2-1,A-1,R5-1,R3-1),(nm-1,R2-1,A-1,R5-1,R3-2),(nm-1,R2-1,A-1,R5-2,R3-1),(nm-1,R2-1,A-1,R5-2,R3-2),(nm-1,R2-1,A-1,R5-3,R3-1),(nm-1,R2-1,A-1,R5-3,R3-2),(nm -1,R2-1,A-2,R5-1,R3-1),(nm-1,R2-1,A-2,R5-1,R3-2),(nm-1,R2-1,A-2,R5-2,R3-1),(nm-1,R2-1,A-2,R5-2,R3-2),(nm-1,R2-1,A-2,R5-3,R3-1),(nm-1,R2-1,A-2,R5-3,R3-2),(nm-1,R 2-1,A-3,R5-1,R3-1),(nm-1,R2-1,A-3,R5-1,R3-2),(nm-1,R2-1,A-3,R5-2,R3-1),(nm-1,R2-1,A-3,R5-2,R3-2),(nm-1,R2-1,A-3,R5-3,R3-1),(nm-1,R2-1,A-3,R5-3,R3-2),(nm-1,R2-1,A-4,R5-1,R3-1),(nm-1,R2-1,A-4,R5-1,R3-2),(nm-1,R2-1,A-4,R5-2,R3-1),(nm-1,R2-1,A-4,R5-2,R3-2),(nm-1,R2-1,A-4,R5-3,R3-1),(nm-1,R2-1,A-4,R5-3,R3-2),(nm-1,R2-1,A-5,R5-1,R3-1),(nm-1,R2-1,A-5,R5-1,R3-2),(nm-1,R2-1,A-5,R5-2,R3-1),(nm-1,R2-1,A5,R 5-2,R3-2),(nm-1,R2-1,A-5,R5-3,R3-1),(nm-1,R2-1,A-5,R5-3,R3-2),(nm1,R2-1,A-6,R5-1,R3-1),(nm-1,R2-1,A-6,R5-1,R3-2),(nm-1,R2-1,A-6,R5-2,R3-1,),(nm-1,R2-1,A-6,R5-2,R3-2),(nm-1,R2-1,A-6,R5-3,R3-1),(nm-1,R2-1,A-6,R5-3,R3-2),(nm-1,R2-1,A-7,R5-1,R3-1),(nm-1,R2-1,A-7,R5-1,R3-2),(nm-1,R2-1,A-7,R5-2,R3-1),(nm-1,R2-1,A-7,R5-2,R3-2),(nm-1,R2-1,A-7,R5-3,R3-1),(nm-1,R2-1, A-7,R5-3,R3-2),(nm-1,R2-1,A-8,R5-1,R3-1), (nm-1,R2-1,A-8,R5-1,R3-2),(nm-1,R2-1,A-8,R5-2,R3-1),(nm-1,R2-1,A-8,R5-2,R3-2),(nm-1,R2-1,A-8,R5-3,R3-1),(nm-1,R2-1,A-8,R5-3,R3-2),(nm-1,R2-1,A-9,R5-1,R3-1),(nm-1,R2-1,A-10,R5-1,R3-2),(nm-1,R2-1,A-10,R5-2,R3-1),(nm-1,R2-1,A-10,R5-2,R3-2),nm -1,R2-1,A-9,R5-3,R3-1(nm-1,R2-1,A-9,R5-3,R3-2),(nm-1,R2-1,A-10,R5-1,R3-1),(nm-1,R2-1,A-10,R5-1,R3-2),(nm-1,R2-1,A-10,R5-2,R3-1),(nm-1,R2-1,A-10,R5-2,R3-2),(nm-1,R2-1,A-10,R5-3,R3-1),(nm-1,R2-1,A-10,R5-2,R3-1),(nm-1,R2-1,A-10,R5-1,R3-1),(nm-1,R2-1,A-11,R5-1,R3-2),(nm-1,R2-1,A-11,R5-2,R3-1),(nm-1,R2-1,A-11,R5-2,R3-2), (nm-1,R2-1,A-11,R5-3,R3-1),(nm-1,R2-1,A-10,R5-3,R3-2),(nm-1,R2-1,A-12,R5-1,R3-1),(nm-1,R2-1,A-12,R5-1,R3-2),(nm-1,R2-1,A-12,R5-2,R3-1),(nm-1,R2-1,A-12,R5-2,R3-2),(nm-1,R2-1,A-12,R5-3,R3-1),(nm-1,R2-1,A-12,R5-3,R3-2),(nm-1,R2-1,A-13,R5-1,R3-1),(nm-1,R2-1,A-13,R5-1,R3-2),(nm-1,R2-1,A-13,R5-2,R3-1),(nm-1,R2-1,A-13,R5-2,R 3-2),(nm-1,R2-1,A-13,R5-3,R3-1),(nm-1,R2-1,A-13,R5-3,R3-2),(nm-1,R2-1,A-14,R5-1,R3-1),(nm-1,R2-1,A-14,R5-1,R3-2),(nm-1,R2-1,A-14,R5-2,R3-1),(nm-1,R2-1,A-14,R5-2,R3-2),(nm-1,R2-1,A-14,R5-3,R3-1),(nm-1,R2-1,A-14,R5-3,R3-2),(nm-1,R2-2,A-1,R5-1,R3-1),(nm-1,R2-2,A-1,R5-1,R3-2),(nm-1,R2-2,A-1,R5-2,R3-1),(nm-1,R2-2,A-1,R5-2,R3-2),(nm-1,R2-2,A-1,R5-3,R3-1),(nm-1,R2-2,A-1,R5-3,R3-2),(nm-1,R2-2,A-2,R5-1,R3-1),(nm-1,R2-2,A-2,R5-1,R3-2),(nm-1,R2-2,A-2,R5-2,R3-1),(nm-1,R2-2,A-2,R5-2,R3-2),(nm-1,R2-2,A-2,R5-3,R3-1),(nm-1,R2-2,A-2,R5-3,R3-2),(nm-1,R2-2,A-3,R5-1,R3-1),(nm-1,R2-2,A-3,R5-1,R3-2),(nm-1,R2-2,A-3,R5-2,R3-1),(nm-1,R2-2,A-3,R5-2,R3-2),(nm-1,R2-2,A-3,R5-3,R3-1),(nm-1,R2-2,A-3,R5-3,R3-2),(nm-1,R2-2,A-4,R5-1,R3-1),(nm-1,R2-2,A-4,R5-3,R3-1),(nm-1,R2-2,A-4,R5-3,R3-2),(nm-1,R2-2,A-5,R5-1,R3-1),(nm-1,R2-2,A-5,R5-1,R3-2),(nm-1,R2-2,A-5,R5-2,R3-1),(nm-1,R2-2,A-5,R5-2,R3-2),(nm-1,R2-2,A-5,R5-1,R3-2),(nm-1,R2-2,A-5,R5-2,R3-1),(nm-1,R2-2,A-5,R5-2,R3-2),(nm 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(nm-2,R2-1,A-11,R5-3,R3-1),(nm-2,R2-1,A-11,R5-3,R3-2),(nm-2,R2-1,A-12,R5-1,R3-1),(nm-2,R2-1,A-12,R5-1,R3-2),(nm-2,R2-1,A-12,R5-2),(R3-1),(nm-2,R2-1,A-12,R5-2,R3-2),(nm-2,R2-1,A-12,R5-3,R3-1),(nm-2,R2-1,A-12,R5-3,R3-2),(nm-2,R2-1,A-13,R5-1,R3-1),(nm-2,R2-1,A-13,R5-1,R3-2),(nm-2,R2-1,A-13,R5-2,R3-1),(nm-2,R2-1,A-13,R5-2,R3-2),(nm-2,R2-1,A-13,R5-3,R3-1),(nm-2,R2-1,A-13,R5-3,R3-2),(nm-2,R2-1,A-14,R5-1,R3-1),(nm-2,R2-1,A-14,R5-1,R3-2),(nm-2,R2-1,A-14,R5-2,R3-1),(nm-2,R2-1,A-14,R5-2,R3-2),(nm-2,R2-1,A-14,R5-3,R3-1),(nm-2,R2-1,A-14,R5-3,R3-2),(nm-2,R2-2,A-1,R5-1,R3-1),(nm-2,R2-2,A-1,R5-1,R3-2),(nm-2,R2-2,A-1,R5-2,R3-1),(nm-2,R2-2,A-1,R5-2,R3-2),(nm-2,R2-2,A-1,R5-3,R3-1),(nm-2,R2-2,A-1,R5-3,R3-2),(nm-2,R2-2,A-2,R5-1,R3-1),(nm-2,R2-2,A-2,R5-1,R3-2),(nm-2,R2-2,A-2,R5-2,R3-1),(nm-2,R2-2,A-2,R5-2,R3-2),(nm-2,R2-2,A-2,R5-3,R3-1),(nm-2,R2-2,A-2,R5-3,R3-2),(nm-2,R2-2,A-3,R5-1,R3-1),(nm-2,R2-2,A-3,R5-1,R3-2),(nm-2,R2-2,A-3,R5-2,R3-1),(nm-2,R2-2,A-3,R5-2,R3-2),(nm-2,R2-2,A-3,R5-3,R3-1),(nm-2,R2-2,A-3,R5-3,R3-2),(nm-2,R2-2,A-4,R5-1,R3-1), (nm-2,R2-2,A-4,R5-1,R3-2),(nm-2,R2-2,A-4,R5-2,R3-1),(nm-2,R2-2,A-4,R5-2,R3-2),(nm-2,R2-2,A-4,R5-3,R3-1),(nm-2,R2-2,A-4,R5-3,R3-2),(nm-2,R2-2,A-5,R5-1,R3-1),(nm-2,R2-2,A-5,R5-1,R3-2),(nm-2,R2-2,A-5,R5-2,R3-1),(nm-2,R2-2,A-5,R5-2,R3-2),(nm 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-11,R5-3,R3-1),(nm-2,R2-2,A-11,R5-3,R3-2),(nm-2,R2-2,A-12,R5-1,R3-1),(nm-2,R2-2,A-12,R5-1,R3-2),(nm-2,R2-2,A-12,R5-2,R3-1),(nm-2,R2-2,A-12,R5-2R3-2),(nm-2,R2-2,A-12,R5-3,R3-1),(nm-2,R2-2A-12,R5-3,R3-2),(nm-2,R2-2,A-13,R5-1,R3-1),(nm-2,R2-2,A-13,R5-1,R3-2),(nm-2,R2-2,A-13,R5-2,R3-1),(nm-2,R2-2,A-13,R5-2,R3-2),(nm-2,R2-2,A-13,R5-3,R3-1),(nm-2,R2-2,A-13,R5-3,R3-2),(nm-2,R2-2,A-14,B5-1,R3-1),(nm-2,R2-2,A-14,R5-1,R3-2),(nm-2,R2-2,A-14,R5-2,R3-1),(nm-2,R2-2,A-14,R5-2,R3-2),(nm-2,R2-2,A-14,R5-3,R3-1),(nm-2,R2-2,A-14,R5-3,R3-2),(nm-2,R2-3,A-1,R5-1,R3-1),(nm-2,R2-3,A-1,R5-1,R3-2),(nm-2,R2-3,A-1,R5-2,R3-1),(nm-2,R2-3,A-1,R5-2,R3-2),(nm-2,R2-3,A-1,R5-3,R3-1),(nm-2,R2-3,A-1,R5-3,R3-2),(nm-2,R2-3,A-2,R5,-1,R3-1),(nm 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(nm-2,R2-3,A-8,R5-2,R3-1),(nm-2,R2-3,A-8,R5-2,R3-2),(nm-2,R2-3,A-8,R5-3,R3-1),(nm-2,R2-3,A-8,R5-3,R3-2),(nm-2,R2-3,A-9,R5-1,R3-1),(nm-2,R2-3,A-9,R5-1,R3-2),(nm-2,R2-3,A-9,R5-2,R3-1),(nm-2,R2-3,A-9,R5-2,R3-2),(nm-2,R2-3,A-9,R5-3,R3-1),(nm -2,R2-3,A-9,R5-3,R3-2),(nm-2,R2-3,A-10,R5-1,R3-1),(nm-2,R2-3,A-10,R5-1,R3-2),(nm-2,R2-3,A-10,R5-2,R3-1),(nm-2,R2-3,A-10,R5-2,R3-2),(nm-2,R2-3,A-10,R5-3,R3-1),(nm-2,R2-3,A-10,R5-3,R3-2),(nm-2,R2-3,A-11,R5-1,R3-1),(nm-2,R2-3,A-11,R5-1,R3-2), 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(nm-3,R2-1,A-8,R5-1,R3-2),(nm-3,R2-1,A-8,R5-2,R3-1),(nm-3,R2-1,A-8,R5-2,R3-2),(nm-3,R2-1,A-8,R5-3,R3-1),(nm-3,R2-1,A-8,R5-3,R3-2),(nm-3,R2-1,A-9,R5-1,R3-1),(n m-3,R2-1,A-9,R5-1,R3-2),(nm-3,R2-1,A-9,R5-2,R3-1),(nm-3,R2-1,A-9,R5-2,R3-2),(nm -3,R2-1,A-9,R5-3,R3-1),(nm-3,R2-1,A-9,R5-3,R3-2),(nm-3,R2-1,A-10,R5-1,R3-1),(nm-3,R2-1,A-10,R5-1,R3-2),(nm-3,R2-1,A-10,R5-2,R3-1),(nm-3,R2-1,A-10,R5-2,R3-2),(nm-3,R2-1,A-10,R5-3,R3-1),(nm-3,R2-1,A-10,R5-3,R3-2),(nm-3,R2-1,A-11,R5-1,A-11,R5-1,R3-1),(nm3,R2-1,A-11,R5-1,R3-2),(nm-3,R2-1,A-11,R5-2,R3-1),(nm-3,R2-1,A-11,R5-2,R3-2), (nm-3,R2-1,A-11,R5-3,R3-1),(nm-3,R2-1,A-11,R5-3,R3-2),(nm-3,R2-1,A-12,R5-1,R3-1),(nm-3,R2-1,A-12,R5-1,R3-2),(nm-3,R2-1,A-12,R5-2,R3-1),(nm-3,R2-1,A-12,R5-2,R3-2),(nm-3,R2-1,A-12,R5-3,R3-1),(nm-3,R2-1,A-12,R5-3,R3-2),(nm-3,R2-1,A-13,R5-1,R3-1),(nm-3,R2-1,A-13,R5-1,R3-2),(nm-3,R2-1,A-13,R5-2,R3-1),(nm-3,R2-1,A-13,R5-2,R3-2),(nm-3,R2-1,A-13,R5-3,R3-1),(nm-3,R2-1,A-13,R5-3,R3-2),(nm-3,R2-1,A-14,R5-1,R3-1),(nm-3,R2-1,A-14,R5-1,R3-2),(nm-3,R2-1,A-14,R5-2,R3-1),(nm-3,R2-1,A-14,R5-2,R3-2),(nm-3,R2-1,A-14,R5-3,R3-1),(nm-3,R2-1,A-14,R5-3,R3-2),(nm-3,R2-2,A-1,R5-1,R3-1),(nm-3,R2-2,A-1,R5-1,R3-2),(nm-3,R2-2,A-1,R5-2,R3-1),(nm-3,R2-2,A-1,R5-2,R3-2),(nm-3,R2-2,A-1,R5-3,R3-1),(nm-3,R2-2,A-1,R5-3,R3-2),(nm-3,R2-2,A-2,R5-1,R3-1),(nm-3,R2-2,A-2,R5-1,R3-2),(nm-3,R2-2,A-2,R5-2,R3-1),(nm-3,R2-2,A-2,R5-2,R3-2),(nm-3,R2-2,A-2,R5-3,R3-1),(nm-3,R2-2,A-2,R5-3,R3-2),(nm-3,R2-2,A-3,R5-1,R3-1),(nm-3,R2-2,A-3,R5-1,R3-2),(nm-3,R2-2,A-3,R5-2,R3-1),(nm-3,R2-2,A-3,R5-2,R3-2),(nm-3,R2-2,A-3,R5-3,R3-1),(nm-3,R2-2,A-3,R5-3,R3-2),(nm-3,R2-2,A-4,R5-1,R3-1), (nm-3,R2-2,A-4,R5-1,R3-2),(nm-3,R2-2,A-4,R5-2,R3-1),(nm-3,R2-2,A-4,R5-2,R3-2),(nm-3,R2-2,A-4,R5-3,R3-1),(nm-3,R2-2,A-4,R5-3,R3-2),(nm-3,R2-2,A-5,R5-1,R3-1),(nm-3,R2-2,A-5,R5-1,R3-2),(nm-3,R2-2,A-5,R5-2,R3-1),(nm-3,R2-2,A-5,R5-2,R3-2),(nm -3,R2-2,A-5,R5-3,R3-1),(nm-3,R2-2,A-5,R5-3,R3-2),(nm-3,R2-2,A-6,R5-1,R3-1),(nm-3,R2-2,A-6,R5-1,R3-2),(nm-3,R2-2,A-6,R5-2,R3-1),(nm-3,R2-2,A-6,R5-2,R3-2),(nm-3,R2-2,A-6,R5-3,R3-1),(nm-3,R2-2,A-6,R5-3,R3-2),(nm-3,R2-2,A-7,R5-1,R3-1),(nm-3,R2-2,A-7,R5-1,R3-2),(nm-3,R2-2,A-

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(nm-3,R3-3,A-11,R5-2,R3-1),(nm-3,R2-3,A-11,R5-2,R3-2),(nm-3,R2-3,A-11,R5-3,R3-1),(nm-3,R2-3,A-11,R5-3,R3-2),(nm-3,R2-3,A-12,R5-1,R3-1),(nm-3,R2-3,A-12,R5-1,R3-2),(nm-3,R2-3,A-12,R5-2,R3-1),(nm-3,R2-3,A-12,R5-2,R3-2),(nm-3,R2-3,A-12,R5-3,R3-1),(nm-3,R2-3,A-12,R5-3,R3-2),(nm-3,R2-3,A-13,R5-1,R3-1),(nm-3,R2-3,A-13,R5-1,R3-2),(nm-3,R2-3,A-13,R5-2,R3-1),(nm-3,R2-3,A-13,R5-2,R3-2),(nm-3,R2-3,A-13,R5-3,R3-1),(nm-3,R2-3,A-13,R5-3,R3-2),(nm-3,R2-3,A-14,R5-1,R3-1),(nm-3,R2-3,A-14,R5-1,R3-2),(nm-3,R2-3,A-14,R5-2,R3-1),(nm-3,R2-3,A-14,R5-2,R3-2),(nm-3,R2-3,A-1 4,R5-3,R3-1),(nm-3,R2-3,A-14,R5-3,R3-2),(nm-3,R2-4,A-1,R5-1,R3-1),(nm-3,R2-4,A-1,R5-1,R3-2),(nm-3,R2-4,A-1,R5-2,R3-1),(nm-3,R2-4,A-1,R5-2,R3-2),(nm-3,R2-4,A-1,R5-3,R3-1),(nm-3,R2-4,A-1,R5-3,R3-2),(nm-3,R2-4,A-2,R5-1,R3-1),(nm-3,R2-4,A-2,R5-1,R3-2),(nm-3,R2-4A-2,R5-2,R3-1),(nm-3,R2-4,A-2,R5-2,R3-2),(nm-3,R2-4,A-2,R5-3,R3-1),(nm-3,R2-4,A-2,R5-3,R3-2),(nm-3,R2-4,A-3,R5-1,R3-1),(nm-3,R2-4,A-3,R5-1,R3-2),(nm-3,R2-4,A-3,R5-2,R3-1),(nm-3,R2-4,A-3,R5-2,R3-2),(nm-3,R2-4,A-3,R5-3,R3-1),(nm-3,R2-4,A-3,R5-3,R3-2),(nm-3,R2-4,A-4,R5-1,R3-1),(nm-3,R2-4,A-4,R5-1,R3-2),(nm-3,R2-4,A-4,R5-2,R3-1),(nm-3,R2-4,A-4,R5-2),(nm-3,R2-4,A-4,R5-3,R3-1), (nm-3,R2-4,A-4,R5-3,R3-2),(nm-3,R2-4,A-5,R5-1,R3-1),(nm-3,R2-4,A-5,R5-1,R3-2),(nm-3,R2-4,A-5,R5-2,R3-1),(nm-3,R2-4,A-5,R5-2,R3-2),(nm-3,R2-4,A-5,R5-3,R3-1),(nm-3,R2-4,A-5,R5-3,R3-2),(nm-3,R2-4,A-6,R5-1,R3-1),(nm-3,R2-4,A-6,R5-1,R3-2),(nm -3,R2-4,A-6,R5-2,R3-1),(nm-3,R2-4,A-6,R5-2,R3-2),(nm-3,R2-4,A-6,R5-3,R3-1),(nm-3,R2-4,A-6,R5-3,R3-2),(nm-3,R2-4,A-7,R5-1,R3-1),(nm-3,R2-4,A-7,R5-1,R3-2),(nm-3,R2-4,A-7,R5-2,R3-1),(nm-3,R2-4,A-7,R5-2,R3-2),(nm-3,R2-4,A-7,R5-3,R3-1),(nm-3,R2-4,A-7,R5-3,R3-2),(nm-3,R2-4,A-8R5-1,R3-1),(nm-3,R2-4,A-8,R5-1,R3-2),(nm-3,R2-4,A-8,R5-2,R3-1),(nm-3,R2-4,A-8,R5-2,R3-2),(nm-3,R2-4,A-8,R5-3,R3-1),(nm-3,R2-4,A-8,R5-3,R3-2),(nm-3,R2-4,A-9,R5-1,R3-1),(nm-3,R2-4,A-9,R5-1,R3-2),(nm-3,R2-4,A-9,R5-2,R3-1),(nm-3,R2-4,A-9,R5-2,R3-2),(nm-3,R2-4,A-9,R5-3,R3-1),(nm-3,R2-4,A-9,R5-3,R3-2),(nm-3,R2-4,A-10,R5-1,R3-1),(nm-3,R2-4,A-10,R5-1,R3-2),(nm-3,R2-4,A-10,R5-2,R3-1),(nm-3,R2-4,A-10,R5-2,R3-2),(nm-3,R2-4,A-10,R5-3,R3-1),(nm-3,R2-4,A-1 0,R5-3,R3-2),(nm-3,R2-4,A-11,R5-1,R3-1),(nm-3,R2-4,A-11,R5-1,R3-2),(nm-3,R2-4,A -11,R5-2,R3-1),(nm-3,R2-4,A-11,R5-2,R3-2),(nm-3,R2-4,A-11,R5-3,R3-1),(nm-3,R2-4,A-11,R5-3,R3-2),(nm-3,R2-4,A-12,R5-1,R3-1),(nm-3,R2-4,A-12,R5-1,R3-2),(nm-3,R2-4,A-12,R5-2,R3-1),(nm-3,R2-4,A-12,R5-2,R3-2),(nm-3,R2-4,A-12,R5-3,R3-1),(nm-3,R2-4,A-12,R5-3,R3-2),(nm-3,R2-4,A-13,R5-1,R3-1),(nm-3,R2-4,A-13,R5-1,R3-2),(nm-3,R2-4,A-13,R5-2,R3-1),(nm-3,R2-4,A-13,R5-2,R3-2),(nm-3,R2-4,A-13,R5-3,R3-1),(nm-3,R2-4,A-13,R5-3,R3-2),(nm-3,R2-4,A-14,R5-1,R3-1),(nm-3,R2-4,A-14,R5-1,R3-2),(nm-3,R2-4,A-14,R5-2,R3-1),(nm-3,R2-4,A-14,R5-2,R3-2),(nm-3,R2-4,A-14,R5-3,R3-1),(nm-3,R2-4,A-14,R5-3,R3-2), and (nm-3,R2-4,A-14,R5-3,R3-3).

In the compound represented by the general formula (I'), a compound, wherein the combination of n, m, R^{2a}, R^{2b}, ring A, R^5, R^{3a}, and R^{3b} (nm, R^2, A, R^5, R^3) is one of the above compound, and E is a bond.

The compounds of the invention can be employed in the treatment and/or prevention of disease associated with the generation, secretion or deposition of β-amyloid protein, such as dementia of the Alzheimer's type (Alzheimer's disease, senile dementia of Alzheimer type), Down's syndrome, memory impairment, prion disease (Creutzfeldt-Jakob disease), mild cognitive impairment (MCI), Dutch type of hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, other type of degenerative dementia, mixed dementia with Alzheimer's and vascular type, dementia with Parkinson's Disease, dementia with progressive supranuclear palsy, dementia with Cortico-basal degeneration, Alzheimer's disease with diffuse Lewy body disease, age-related macular degeneration, Parkinson's Disease, amyloid angiopathy and so on.

The compounds of the invention can be administrated in combination with other pharmaceutical agents such as other therapeutic drugs for Alzheimer's disease, acetylcholinesterase inhibitors and so on. The compounds of the invention can be treated with concomitantly with the anti-dementia agents such as Donepezil Hydrochloride, Tacrine, Galantamine, Rivastigmine, Zanapezil, Memantine, Vinpocetine.

When the present compound is administered to a human, it can be administered orally as powders, granules, tablets, capsules, pills, solutions, or the like, or parenterally as injectables, suppositories, transdermal absorbable agents, absorbable agents, or the like. In addition, the present compound can be formulated into pharmaceutical preparations by adding pharmaceutical additives such as excipients, binders, wetting agents, disintegrating agents, lubricants and the like, which are suitable for formulations and an effective amount of the present compound,

A dose is different depending on state of disease, an administration route, and an age and a weight of a patient, and is usually 0.1 μg to 1 g/day, preferably 0.01 to 200 mg/day when orally administered to an adult, and is usually 0.1 μg to 10 g/day, preferably 0.1 to 2 g/day when parenterally administered,

Following examples and test examples illustrate the present invention in more detail, but the present invention is not limited by these examples,

In example, the meaning of each abbreviation is following.

Me methyl

Et ethyl

iPr or Pr^i isopropyl

Ph phenyl

Bn benzyl

Boc t-butoxycarbonyl

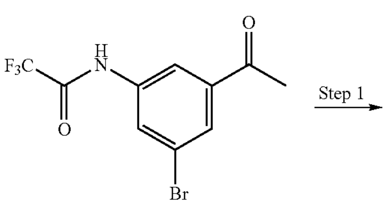
TBDPS t-butyldiphenylsilyl

EXAMPLE

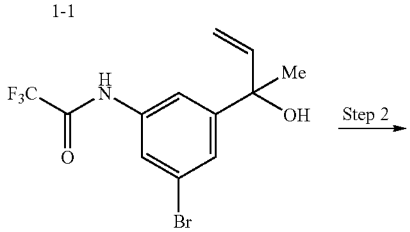
Reference Example 1

The Synthesis of Compound 588

[Chemical formula 56]



1-1



1-2

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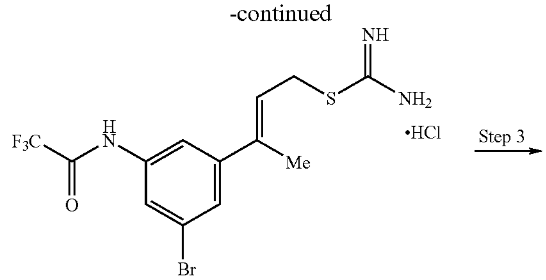

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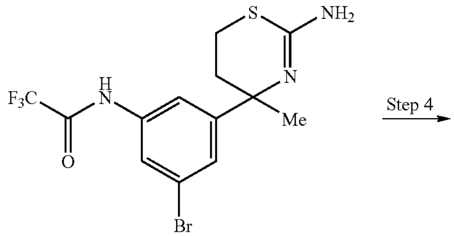

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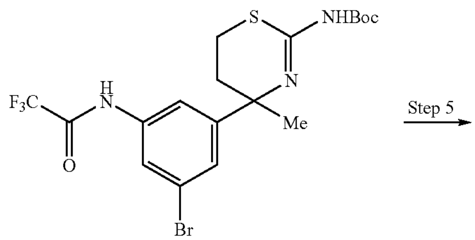

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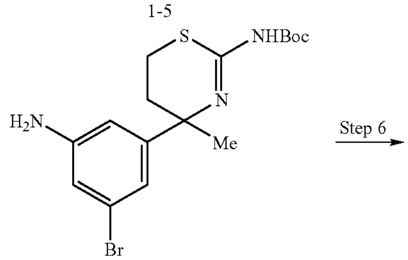
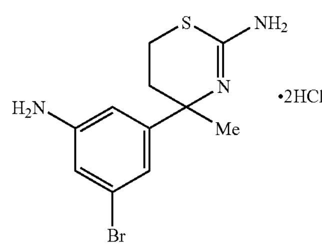


1-6



588

Step 1

Under nitrogen atmosphere, the compound (1-1)(7.98 g) was dissolved into diethyl ether (330 ml)-tetrahydrofuran (36 ml), vinylmagnesium chloride in tetrahydrofuran solution (1.32 mol/L, 44.8 ml) was added under cooling with dry ice-acetone bath, and stirred for 20 min. Then, the reaction solution was stirred for 30 min under cooling with ice-water bath and stirred for 35 min at room temperature. And then, saturated ammonium chloride solution was added to the mixture, the mixture was extracted with ethyl acetate, and organic layer was washed with saturated ammonium chloride solution, saturated sodium hydrogencarbonate solution, and brine, and dried over anhydrous magnesium sulfate, and the solvent was evaporated. Then, the residue was purified by silica gel column chromatography to afford the compound (1-2)(6.00 g).

^{1}H-NMR($CDCl_3$): 1.63(3H, s), 2.08(1H, br), 5.20(1H, dd, J=10.6, 1.6 Hz), 5.31(1H, dd, J=17.1, 1.6 Hz), 6.09(1H, m), 7.46(1H, m), 7.52(1H, dd, J=3,4, 2.6 Hz), 7.80(1H, dd, J=3.9, 2.6 Hz), 8,06(1H, br)

Step 2

The compound (1-2)(6.36 g) was dissolved into acetic acid (30 ml), and added thiourea (1.50 g), 1 mol/L hydrochloride-acetic acid solution (20.7 ml). The reaction mixture was stirred at room temperature for 3 hours, then stirred at 40° C. for 3 hours, then stirred at room temperature for 66 hours, and at 40° C. for 19 hours. Thiourea (0.450 g), and 1 mol/L hydrochloric acid-acetic acid solution (7.53 ml) was added, and stirred at 40° C. for 23 hours. After the consumption of the compound (1-2), the solvent was evaporated under reduced pressure, then the obtained residue was crystallized from methanol-diethyl ether to afford the compound (1-3)(5.23 g) as crystal. On the other hand, filtrate was evaporated under reduced pressure, and the compound (1-3)(3,00 g) was obtained as a crude solid product.

^{1}H-NMR(DMSO-d_6): 2.09(3H, s), 4.10(2H, d, J=7.3 Hz), 5.94(1H, t, J=7.7 Hz), 7.50(1H, s), 7.75(1H, s), 7.87(1H, s), 9.17(3H, br), 11.46(1H, s)

Step 3

The compound (1-3)(5.23 g) dissolved in trifluoroacetic acid (25 ml) was added methanesulfonic acid (2.14 ml) drop-wise under cooling with ice-water bath. After addition, the reaction mixture was stirred at room temperature for 3.5 hours. After the consumption of the compound (1-3), the solvent was evaporated under reduced pressure. To the residue obtained was added water and sodium carbonate and then extracted with ethyl acetate. The organic layer was washed with saturated sodium hydrogencarbonate solution, and was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure to afford the compound (1-4)(4.90 g) as a crude product.

^{1}H-NMR(CDCl3): 1.53(3H, s), 1.90(1H, m), 2.09(1H, m), 2.74(1H, m), 2.97(1H, m), 4.32(2H, br), 7.34(1H, t, J=1.6 Hz), 7.37(1H, t, J=1.8 Hz), 7.86(1H, t, J=1.8 Hz)

Step 4

Under nitrogen atmosphere, the compound (1-4)(4.90 g) dissolved in tetrahydrofuran was added di-t-butyl-dicarbonate (2.97 g) and triethylamine (1.89 ml) under cooling with ice-water bath and then stirred for 2 hours. The reaction mixture was stirred at room temperature for 3 hours. The reaction mixture was added water, and then extracted with ethyl acetate. The organic layer was washed with water, and dried over anhydrous magnesium sulfate, then the solvent was evaporated under reduced pressure. Then the obtained residue was crystallized from ethyl acetate-diethyl ether to afford the compound (1-5)(4.62 g) as crystal.

^{1}H-NMR($CDCl_3$): 1.36(9H, s), 1.72(3H, s), 2.10(1H, m), 2.41(1H, m),2.62(1H, m), 2.75(1H, m), 7.22(1H, s), 7.48(1H, s), 8.29(1H, s)

Step 5

The compound (1-5)(1.00 g) was dissolved into tetrahydrofuran (8.7 ml), and 1 mol/L lithium hydroxide (4.43 ml) was added and stirred at 50° C. for 4 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and the organic layer was washed with water, brine successively, and dried over anhydrous magnesium sulfate, and the solution was evaporated under reduced pressure. The obtained residue was purified by medium-pressured silica gel column chromatography to afford the compound (1-6)(0.668 g).

^{1}H-NMR($CDCl_3$): 1.51(9H, s), 1.63(3H, s), 2.06(1H, m), 2.40(1H, m), 2.68-2.74(2H, m), 3.83(2H, br), 6.51(1H, t, J=1.8 Hz), 6.72-6.74(2H, m)

Step 6

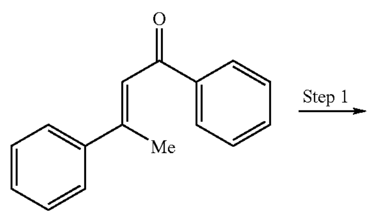
The compound (1-6)(20.0 mg) was dissolved into 4 mol/L hydrochloric acid in 1,4-dioxane, and the mixture was stirred for 16 hours. The reaction solvent was evaporated under reduced pressure and the obtained residue was crystallized from methanol-diethyl ether to afford the compound (588) (14.7 mg).

^{1}H-NMR(DMSO-d_6): 1.59(3H, s), 2.09-2.76(4H, m), 6.44 (1H, t, J=1.6 Hz), 6.60(1H, t J=1.9 Hz), 6.71(1H, t, J=2.0 Hz), 10.4(1H, s)

Reference Example 2

The Synthesis of Compound 835

[Chemical formula 57]



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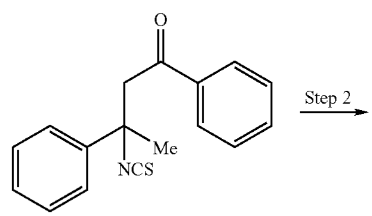

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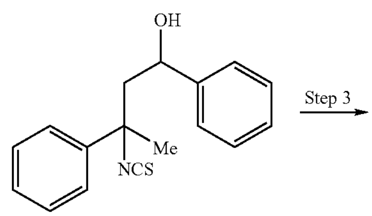

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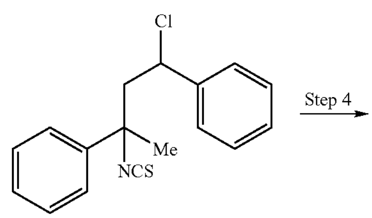

2-4

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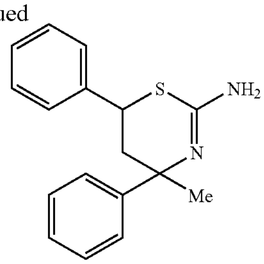


835

Step 1

The compound (2-1)(2020 mg) was dissolved into chloroform (20 ml), then water(4 ml) and sodium thiocyanate (1470 mg) were added at room temperature with stirring, and then sulfuric acid (1.94 ml) was added dropwise under cooling with ice-water bath. After an addition was complete, the reaction mixture was warmed to room temperature and then stirred for 345 minutes, then stirred at 60 ° C. overnight. Because the compound (2-1) was remained(checked by TLC), the reaction mixture was cooled to room temperature, then sodium thiocyanate (1470 mg), water (5 ml) and sulfuric acid (1.94 ml) were added successively. After the reaction mixture was warmed to 60° C., the mixture was stirred for 1 day. Saturated sodium bicarbonate solution was added to the reaction mixture to be basic condition under cooling with ice-water bath, and then the reaction mixture was extracted with ethyl acetate. The organic layer was washed with brine, then dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography to afford the compound (2-2) (968 mg).

^{1}H-NMR($CDCl_3$, 270 MHz): 1.99 (3H, s), 3.55 (1H, d, J=16.1 Hz), 3.69(1H, d, J=16.1 Hz), 7.12-7.64 (8H, m), 7.82-7.95 (2H, m)

Step 2

The compound (2-2)(842 mg) was dissolved into ethano (8.4 ml), sodium dihydrogen phosphate and an aqueous solution of sodium borohydride (113.2 mg) in water (2.8 ml) were added successively under cooling with ice-water bath with stirring, and the mixture was stirred for 30 minutes. After the consumption of the compound (2-2)(checked by TLC), ethyl acetate and water were added to the reaction mixture under cooling with ice-water bath, and then stirred for a few minutes. The reaction mixture was extracted with ethyl acetate. The organic layer was washed with water, brine successively, and dried over anhydrous magnesium sulfate. The solvent was evaporated to afford the compound (2-3)(904.8 mg) as a crude product.

Step 3

To a solution of compound (23)(900 mg) in toluene (10 ml) was added a solution of thionyl chloride (0.7 ml) in toluene (5 ml) under cooling with ice-water bath with stirring, and then stirred for 1 hour at the same temperature. After the consumption of the compound (2-3)(checked by TLC), the reaction solvent was evaporated under reduced pressure to afford the compound (2-4)(1076.8 mg) as a crude product.

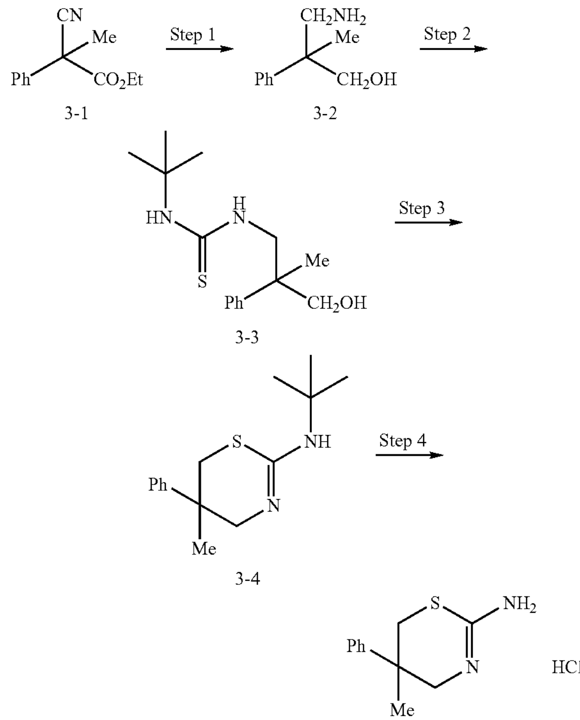
Step 4

The compound. (2-4)(1070 mg) was dissolved into about 7 mol/L ammonia in methanol (20 ml) at room temperature, then the mixture was stirred for 1 day. After the consumption of the compound (2-4)(checked by TLC), the reaction solvent was evaporated under reduced pressure to afford the compound (835)(2633 mg) as a crude product.

Reference Example 3

The Synthesis of Compound 561

[Chemical formula 58]



561

Step 1

To tetrahydrofuran (30 ml) under cooling with ice-water bath with stirring, lithium aluminum hydride (0.63 g) was added portionwise, then a solution of compound (3-1)(1.94 g) in tetrahydrofuran (40 ml) was added dropwise. The reaction mixture was reacted for 20 minutes at room temperature, then reacted for 3 hours under reflux. Then ice was added in small portions under cooling, and then stirred for 1 day at room temperature. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography to afford the compound (3-2)(0.90 g).

^{1}H-NMR($CDCl_3$): 1.22(3H, s), 3.08(1H, d, J=12.5 Hz), 3.34(1H, d, J=12.5 Hz), 3.85(1H, d, J=11.0 Hz), 4.11(1H, d, J=11.0 Hz), 7.21-7.25(1H, m), 7.34-7.40(2H, m), 7.46-7.50 (2H, m).

Step 2

The compound (3-2)(0.90 g) was dissolved into tetrahydrofuran (15 ml), t-butylisothiocyanate (0.69 g) in tetrahydrofuran (5 ml) was added under cooling with ice-water bath with stirring. The reaction mixture was stirred for 3 days at room temperature, water was added and extracted with dichloromethane. The organic layer,was dried over anhydrous magnesium sulfate, then the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography to afford the compound (3-3)(1.33 g).

^{1}H-NMR(CDCl$_3$): 1.12(9H, s), 1.34(3H, s), 3.15(1H, br), 3.76(1H, d, J=11.2 Hz), 3.87(1H, dd, J=14.2, 4.6 Hz), 4.13 (1H, d, J=11.2 Hz), 4.23(1H, dd, J=14,2, 6.6 Hz), 5.18(1H ,br), 6.01(1H, br), 7.23-7.28(1H, m), 7.34-7.41(4H, m).

Step 3

The compound (3-3)(315 mg) was dissolved into acetonitrile (3 ml), triphenylphosphine (440 mg), and carbon tetrachloride (520 mg) in acetonitrile 3 ml) were added under cooling with ice-water bath with stirring. The reaction mixture was stirred for 1 hour at room temperature, and then potassium carbonate (460 mg) was added and stirred for 2 days at room temperature. Then water was added to the reaction mixture and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography to afford the compound (3-4)(0.23 g).

^{1}H-NMR(CDCl3): 1.30(9H, s), 1.36(3H, s), 3.13(1H, d, J=12.2 Hz), 3.24(1H, dd, J=12.2, 2.3 Hz), 3.51(1H, br), 3.53 (1H, d, J=15.2 Hz), 3.99(1H, dd, J=15.2, 2.3 Hz), 7.20-7.25 (1H, m), 7.30-7.36(2H, m), 7.39-7.43(2H, m).

Step 4

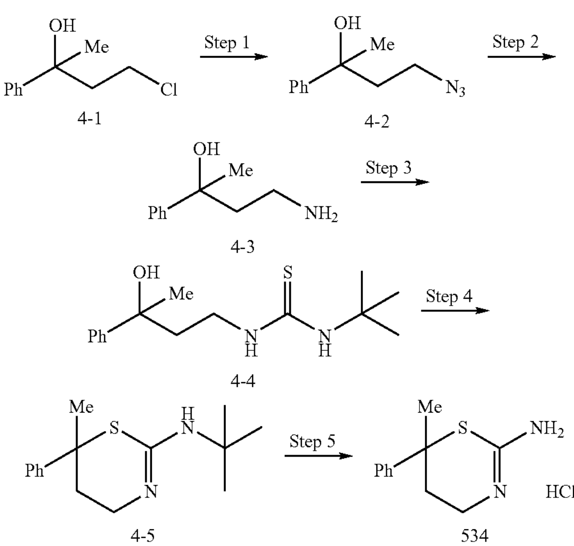
To the compound (3-4)(0.22 g), conc. hydrochloric acid (4.5 ml) was added, then stirred for 2 hours under reflux, and then the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol-diethyl ether to afford the compound (561)(0.16 g).

^{1}H-NMR,(DMSO-d$_6$): 1.33(3H, s), 3.33-3.49(2H, m), 3.65-3.96(2H, m), 7.29(1H, t, J=7.6 Hz), 7.40(2H, t, J=7.6 Hz), 7.48(2H, t, J=7.6 Hz).

Reference Example 4

The Synthesis of Compound 534

[Chemical formula 59]



Step 1

The compound (4-1)(0.72 g) was dissolved into N,N-dimethylformamide (15 ml), then sodium azide (0.31 g) was added. The reaction mixture was stirred at 100° C. for 13 hours, then water was added and the mixture was extracted with diethyl ether, the organic layer was dried over anhydrous magnesium sulfate to afford the compound (4-2)(0.71 g) as a crude product.

Step 2

To a solution of the compound (4-2)(0.71 g) in tetrahydrofuran (10 ml), lithium aluminum hydride (0.14 g) was added portionwise under cooling with ice-water bath with stirring, then stirred for 2 hours at room temperature. After the consumption of the starting material, ice was added in small portions, then stirred for 18 hours at room temperature. The reaction mixture was filtered then filtrate was evaporated under reduced pressure to afford the compound (4-3)(0.89 g) as a crude product.

Step 3

The compound (4-3)(0.89 g) was dissolved into tetrahydrofuran (10 ml), then t-butylisothiocyanate (0.56 g) in tetrahydrofuran (5 ml) was added under cooling with ice-water bath with stirring. The reaction mixture was stirred for 4 hours at room temperature, and water was added, and then extracted with dichloromethane, and the organic layer was dried over anhydrous magnesium sulfate. Then the residue was purified by silica gel column chromatography to afford the compound (4-4)(0.72 g).

^{1}H-NMR(CDCl$_3$): 1.39(9H, s), 2.08(3H, s), 2.09-2.15(2H, m), 3.37-3.44(1H, m), 3.80-3.87(1H, m), 5.97(1H, br.), 6.86 (1H, br.), 7.28-7.43(5H, m).

Step 4

The compound (4-4)(120 mg) was dissolved into acetonitrile (2 ml), triphenylphosphine (170 mg), and carbon tetrachloride (200 mg) in acetonitrile (1 ml) were added under cooling with ice-water bath with stirring. The reaction mixture was stirred for 5 hours at room temperature, and then potassium carbonate (177 mg) was added and stirred for 5 days at room temperature. Then water was added to the reaction mixture and the mixture was extracted with dichloromethane, the organic layer was dried over anhydrous magnesium sulfate, then the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography to afford the compound (4-5)(0.06 g),

^{1}H-NMR(CDCl$_3$): 1.35(9H, s), 1.59(3H, s), 1.91(1H, ddd, J=13.5, 8.8, 5.0 Hz), 2.06(1H, dt, J=13.5, 5.0 Hz), 3.00(1H, ddd, J=15.1, 8.8, 5.0 Hz), 3.30(1H, dt, J=15.1, 5.0 Hz), 7.24-7.38(5H, m).

Step 5

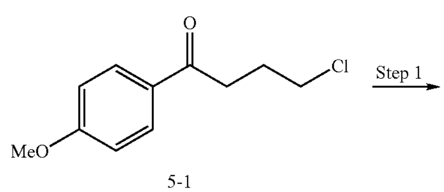
To the compound (4-5)(0.06 g), conc. hydrochloric acid (3 ml) was added, then the mixture was stirred for 1 hour under reflux, and the solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol-water to afford the compound (534)(0.02 g).

^{1}H-NMR(DMSO-d$_6$): 1.43(3H, s), 1.77(1H, dt. J=8.4, 3.4 Hz), 2.11(1H, d, J=9.2 Hz), 2.48-2.50(1H, m), 2.83-2.99 (1H,), 6.12(1H, br), 6,65(1H, br), 7.21-7.24(1H, m), 7.31-7, 37(4H, m).

Reference Example 5

The Synthesis of Compound 1008

[Chemical formula 60]



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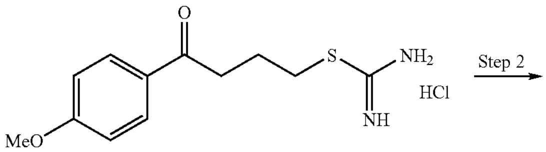
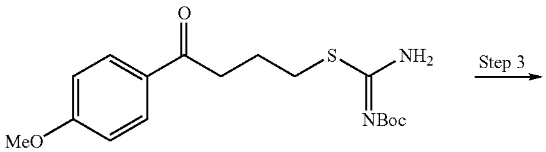
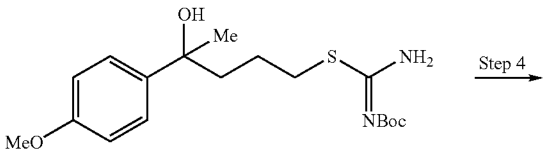


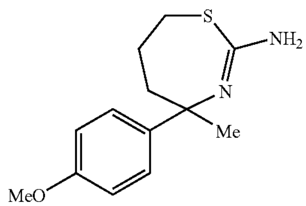
5-2



5-3



5-4



1008

Step 1

The compound (5-1)(3.00 g) was dissolved into ethanol (30 ml), and thiourea (1.13 g) was added, and then the mixture was refluxed for 26 hours, and the solvent was evaporated under reduced pressure. The obtained residue was crystallized from ethyl acetate/hexane to afford the compound (5-2) (4.03 g).

^{1}H-NMR(DMSO-d_6): 1.95(2H, quint, J=6.8 Hz), 3.13(2H, t, J=6.8 Hz), 3.21(2H, t, J=6.8 Hz), 3.85(3H, s), 7.06(2H, d, J=8.8 Hz), 7.95(2H, d, J=8.8 Hz), 9.18(4H, br).

Step 2

The compound (5-2)(1.00 g) was dissolved into tetrahydrofuran (25 ml), then di-t-butyl-dicarbonate (1.74 g), and triethylamine (0.88 g) were added, and then the mixture was stirred for 3 hours at room temperature. Water was added to the reaction mixture, and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was evaporated, under reduced pressure. The residue was purified by silica gel column chromatography to afford the compound (5-3)(1.24 g).

^{1}H-NMR($CDCl_3$): 1.50(9H, 5), 2.07-2.17(2H, m), 2.98 (2H, t, J=7.8 Hz), 3.09(2H, t, J=6.3 Hz), 6.95(2H, d, J=8.9 Hz), 7.95(2H, d, J=8.9 Hz),

Step 3

The compound (5-3)(1.18 g) was dissolved into tetrahydrofuran (12 ml), then 0.9 mol/L methylmagnesium bromide in tetrahydrofuran solution (10.1 ml) was added under cooling with acetonitrile-dry ice bath with stirring, and then reaction mixture was stirred for 1 hour, then stirred for 30 minutes at room temperature. After the reaction, saturated ammonium chloride solution was added under cooling with ice-water bath with stirring, then the mixture was extracted with diethyl ether, and the organic layer was dried over anhydrous magnesium sulfate, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (5-4) (0.39 g),

^{1}H-NMR($CDCl_3$): 1.51(9H, s), 1.63(3H, s), 1.55-1.65(2H, m), 1.87-1.91(2H, m), 2.96-3.12(2H, m), 6.86(2H, d, J=8.9 Hz), 7.36(2H, d, J=8.9 Hz).

Step 4

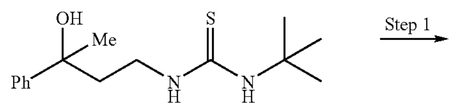
The compound (5-4)(0.24 g) was dissolved into trifluoroacetic acid (6 ml), and stirred for 20 hours at room temperature, then the reaction solvent was evaporated under reduced pressure. To the residue, water and saturated sodium hydrogencarbonate was added, and then extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography to afford the compound (1008)(0.06 g).

^{1}H-NMR($CDCl_3$): 1.54(3H, s), 1.77-1.87(1H, m), 1.90-1.97(1H, m), 2.20-2.36(2H, m), 2.67-2.79(2H, m), 3.81(3H, s), 5.30(2H, br), 6.87(2H, d, J=9.0 Hz), 7.33(2H, d, J=9.0 Hz).

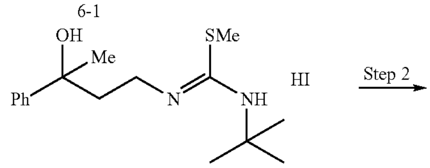
Reference Example 6

The Synthesis of Compound 783

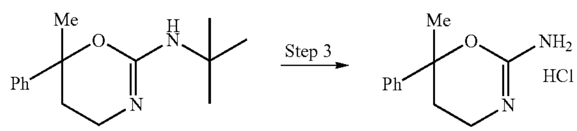
[Chemical formula 61]



6-1



6-2



6-3 783

Step 1

The compound (6-1)(0.55 g) was dissolved into methanol (7 ml), and methyl iodide (0.36 g) was added at room temperature with stirring. The mixture was stirred at room temperature for 18 hours, then the reaction solvent was evaporated under reduced pressure to afford the compound (6-2) (0.92 g) as a crude product.

Step 2

The compound (6-2)(0.92 g) was dissolved into tetrahydrofuran (7 ml), then triethylamine (0.24 g) and silver oxide (1.1 g) was added. The mixture was stirred at room temperature for 3 days, then the insolubles was removed by filtration, then the filtrate was evaporated under reduced pressure, and then the obtained residue was purified by silica gel column chromatography to afford the compound (6-3)(0.31 g).

^{1}H-NMR($CDCl_3$): 1.35(9H, s), 1.60(3H, s), 1.92(1H, ddd, J=9.2, 5.8, 3.4 Hz), 2,07(1H, dt, J=9.2, 3.4 Hz), 3.00(1H, ddd, J=9.2, 5.8, 3.4 Hz), 3.30(1H, dt, J=9.2, 3.4 Hz), 7.24-7.38(5H, m).

Step 3

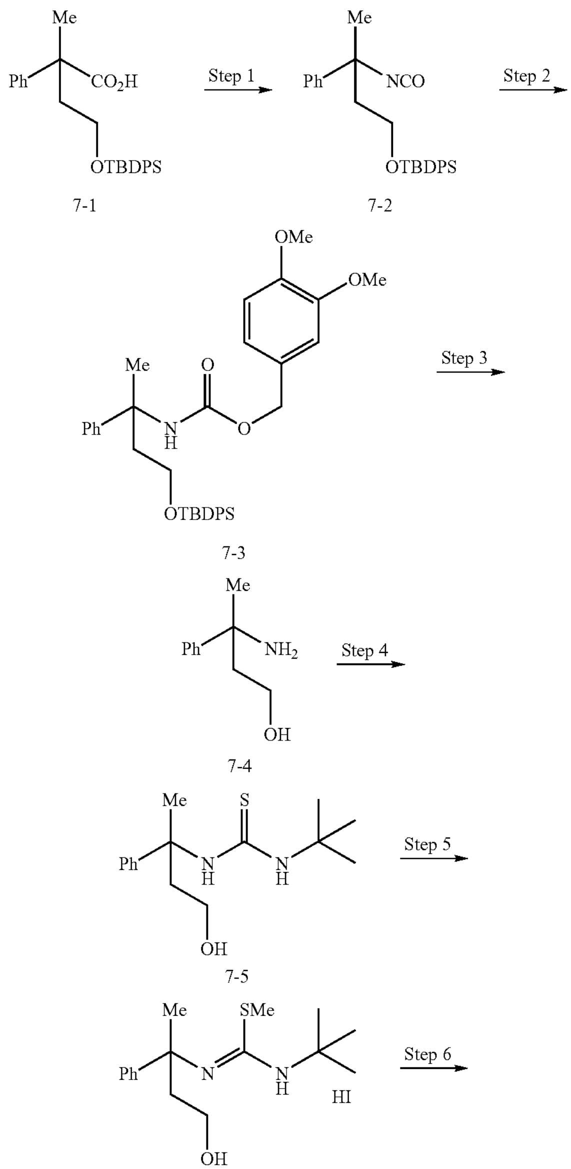
To the compound (6-3)(0.22 g), conc. hydrochloric acid (3 ml) was added, then the mixture was stirred for 1 hour under reflux, and then the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from water to afford the compound (783)(0.13 g).

^{1}H-NMR(DMSO-d_6): 1.44(3H, s), 1.78(1H, dt, J=12.4, 4.2 Hz), 2.12(1H, d, J=8.9 Hz), 2.51-2.52(1H, m), 2.96(1H, d, J=4.2 Hz), 6.12(1H, br), 6.66(1H, br), 7.21-7.24(1H, m), 7.32-7.37(4H, m).

Reference Example 7

The Synthesis of Compound 69

[Chemical formula 62]



7-1, 7-2, 7-3, 7-4, 7-5, 7-6

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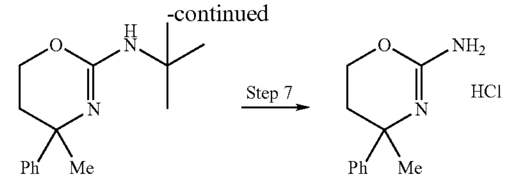


7-7 69

Step 1

A solution of the compound (7-1)(1.93 g), diphenylphosphoryl azide (1.60 g), and triethylamine (0.59 g) in toluene (20 ml) was stirred at 80° C. for 3 hours, and water was added, and then the mixture was extracted with diethyl ether. The organic layer was dried over anhydrous sodium sulfate, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (7-2)(1.69 g).

^{1}H-NMR($CDCl_3$): 1.00(9H, s), 1.72(3H, s), 2.17-2.22(2H, m), 3.49-3.58(1H, m), 3.70-3.80(1H, m), 7.20-7.42(10H, m), 7.58-7.63(5H, m).

Step 2

The compound (7-2)(1.68 g) was dissolved into toluene (9 ml), and 3,4-dimethoxybenzylalcohol (0.79 g) was added, the mixture was refluxed for 8 hours. To the reaction mixture, water was added, then the mixture was extracted with dichloromethane, and the organic layer was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (7-3)(2.09 g).

^{1}H-NMR($CDCl_3$): 1.03(9H, s), 1.87(3H, s), 2.04(2H, m), 3.48(1H, m), 3.51(1H, m), 3.62(3H, s), 3.65(3H, s), 4.95(1H, d, J=12.2 Hz), 5.03(1H, d, J=12.2 Hz), 6.80-7.09(3H, m), 7.22-7.42(10H, m), 7.56-7.64(5H, m).

Step 3

The compound (7-3)(2.09 g) was dissolved into 1,4-dioxane (15 ml), and 4 mol/L hydrochloric acid-1,4-dioxane (15 ml) solution was added, then stirred at room temperature for 24 hours. To the reaction mixture, water and 1 mol/L—sodium hydroxide solution were added and extracted with dichloromethane, then the organic layer was dried over anhydrous sodium sulfate, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (7-4)(0.45 g).

^{1}H-NMR($CDCl_3$): 1.57(3H, s), 1.07-1.98(2H,), 3.48-3.56 (1H, 3.72-3.86(1H, m), 7.23-7.45(15H, m).

Step 4

The compound (7-4)(0.44 g) was dissolved into tetrahydrofuran (15 ml), t-butylisothiocyanate (0.41 g) and diisopropylethylamine (0.46 g) were added. After the mixture was stirred at room temperature for 3 days, water was added, and extracted with dichloromethane, then the organic layer was dried over anhydrous sodium sulfate, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (7-5)(0.17 g).

^{1}H-NM($CDCl_3$): 1.79(3H, s), 1.82-2.20(2H, 3.71-3.81 (2H, m), 5.09(1H, br), 7.30-7.52(5H, m).

Step 5

The compound (7-5)(0.17 g) was dissolved into tetrahydrofuran (3.4 ml), then methyl iodide (0.11 g) was added at room temperature with stirring. The mixture was stirred for

23 hours, the reaction solvent was evaporated under reduced pressure to afford the compound (7-6)(0.28 g) as a crude product.

Step 6

The compound (7-6)(0.28 g) was dissolved into tetrahydrofuran (5 ml), then triethylamine (74 mg) and silver oxide (0.34 g) were added. The mixture was stirred at room temperature for 20 hours, then insolubles were removed by filtration, and then the filtrate was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (7-7)(0.14 g).

^{1}H-NMR(CDCl$_3$): 1.36(9H, s), 1.49(3H, s), 1.96-2.09(2H, m), 2.77-3.83(1H, m), 4.05-4.10(1H, m), 7.19(1H, t, J=7.3 Hz), 7.31(2H, t, J=7.3 Hz), 7.44(2H, d, J=7.3 Hz).

Step 7

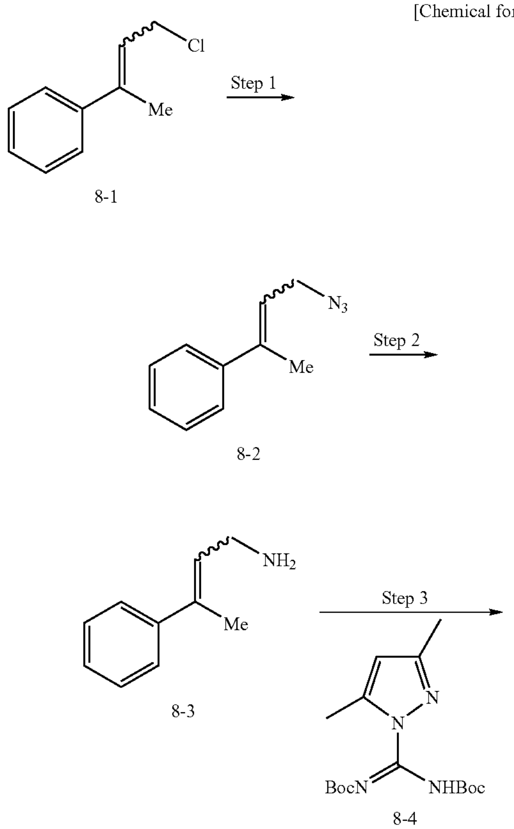
To the compound (7-7)(0.12 g) conc. hydrochloric acid (9 ml) was added, then stirred for 1 hour under reflux, and then the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol-water to afford the compound (69)(0.10 g).

^{1}H-NMR(DMSO-d$_6$): 1.65(3H, s), 2.28-2.35(1H, m), 2.39-2.44(1H, m), 3.97(1H, dt, J=7.8, 3.0 Hz), 4.53(1H, dt, J=7.8, 3.0 Hz), 7.32-7.44(5H, m), 8.44(2H, br), 10.33(1H, s).

Reference Example 8

The Synthesis of Compound 256

[Chemical formula 63]



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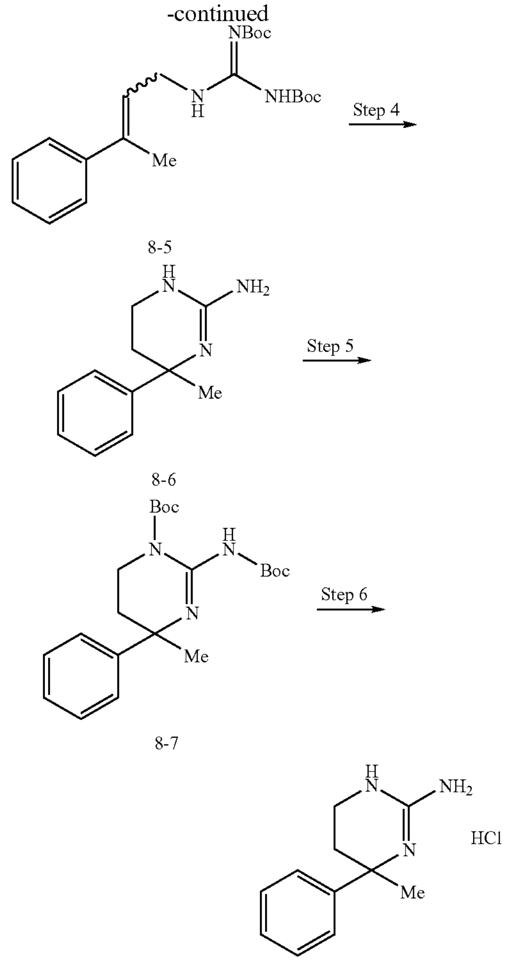


256

Step 1

The compound (8-1)(4890 mg) was dissolved into N,N-dimethylformamide (100 ml), then sodium azide (5720 mg) was added at room temperature with stirring, and the solution was warmed to 80° C., and stirred for 12 hours. After the consumption of the compound (8-1)(checked by TLC), the reaction mixture was cooled to room temperature, then diethyl ether and water were added, and then the mixture was extracted with diethyl ether. The organic layer was washed with brine, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure to afford the compound (8-2)(4940 mg) as a crude product.

Step 2

To the suspension of lithium aluminum hydride (1080 mg) in tetrahydrofuran (90 ml) under nitrogen atmosphere under cooling with ice-water bath, the compound (8-2)(4940 mg) in tetrahydrofuran (15 ml) solution was added, the reaction mixture was stirred for 30 minutes. After the consumption of the compound (8-2)(checked by TLC), 1 mol/L sodium hydroxide solution was added under cooling with ice-water bath, then stirred for a while. The generated gel was removed with filtration, and the filtrate was extracted with diethyl ether. The organic layer was washed with brine, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure to afford the compound (8-3)(4219.1 mg) as a crude product.

Step 3

The compound (8-3)(800 mg) was dissolved into acetonitrile (16 ml), the compound (8-4)(1840 mg) was added with stirring at room temperature, and stirred for 13 hours. After the consumption of the compound (8-3)(checked by TLC), the reaction solvent was evaporated under reduced pressure, the obtained residue was purified by silica gel column chromatography to afford the compound (8-5)(1550.7 mg).

8-5-(Z): ^{1}H-NMR($CDCl_3$, 270 MHz): 1.49 (18H, s), 2.06 (3H, d, J=1.4 Hz), 3.91-4.00 (2H, m), 5.54 (1H, td, 7.1, 1.4 Hz), 7.12-7.41 (5H, m), 8.17-8.25 (1H, m), 11.47 (1H, s)

8-5-(E): ^{1}H-NMR($CDCl_3$, 270 MHz): 1.49 (9H, s), 1.52 (9H,s), 2.09 (3H, d, J=1.5 Hz), 4.24 (2H, dd, J=6.6, 5.3 Hz), 5.80 (1H, td, J=6.6, 1.5 Hz), 7.21-7.48 (5H, m), 8.28-8.38 (1H, m), 11.51 (1H, s)

Step 4

The compound (8-5)(474.1 mg) was dissolved into trifluoroacetic acid (4.5 ml) under cooling with ice-water bath, then warmed to room temperature, and stirred for 4 hours. After the consumption of the compound (8-5)(checked by NMR), the reaction mixture was poured into floating ice—1 mol/L sodium hydroxide solution to be neutralized, then the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure to afford the compound (8-6)(326.4 mg) as a crude product,

Step 5

The compound (8-6)(326.4 mg) was dissolved into 1,4-dioxane (2.4 ml), sodium hydroxide (195 mg) and water (1.2 ml) were added successively, then di-t-butyl dicarbonate (0.84 ml) was added under cooling with ice-water bath. The reaction mixture was warmed to room temperature, and stirred for 15 hours, then the consumption of the compound (8-6) was checked by LC-MS. After added water to the reaction mixture, the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure, and the obtained residue was purified by silica gel column chromatography to afford the compound (8-7)(113.6 mg).

^{1}H-NMR($CDCl_3$, 400 MHz): 1.46 (9H, s), 1.51 (9H, s), 1.64 (3H, s), 2.06 (1H, ddd, J=13.4, 11.4, 5.0 Hz), 2.27 (1H, dt, J=13.4, 4.6 Hz), 3.15 (1H, ddd, J=12.9, 11.3, 4.6 Hz), 3,70 (1H, dt, J=12.9, 4.7 Hz), 7.23-7.29 (1H, m), 7.33-7.38 (4H, m)

Step 6

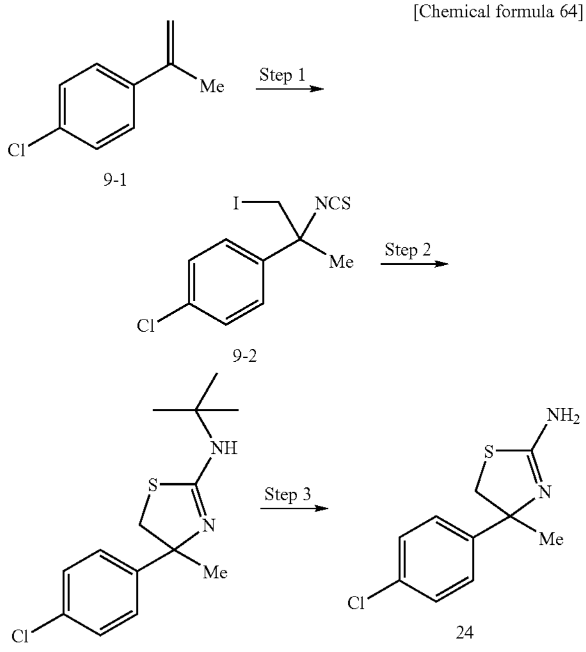
The compound (8-7)(110 mg) was dissolved into 4 mol/L hydrochloric acid-1,4-dioxane solution (1 ml) under cooling ice-water bath, the mixture was warmed to room temperature, and stirred for 2 days, then the consumption of the compound (8-7) was checked by LC-MS, and diethyl ether and water were added at room temperature. After separation of diethyl ether layer, water layer was evaporated under reduced pressure. To the obtained residue, methanol was added, then the generated crystal was filtered. The methanol in the filtrate was evaporated under reduced pressure to afford the compound (256)(69 mg).

^{1}H-NMR(DMSO-d_6, 400 MHz): 1.57 (3H, s), 1.87-1.96 (1H, m), 2.30 (1H, dt, J=13.6, 3.8 Hz), 2.60 (1H, td, J=12.0, 3.7 Hz), 3.25 (1H, ddd, J=12.8, 8.2, 4.4 Hz), 6.93 (2H,s), 7.27-7.44 (5H, m), 7.94 (1H, s), 8.63 (1H,s)

Reference Example 9

The Synthesis of Compound 24

[Chemical formula 64]



Step 1

The compound (9-1)(0.39 g) was dissolved into chloroform (20 ml), iodine (1.53 g), potassium thiocyanate (1.25 g), catalytic amount of tetrabutylammonium chloride, and water (1 ml) were added at room temperature, then stirred for 15 hours. To the reaction mixture, 10% thiosodium sulfate solution and water were added, and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (9-2) (0.56 g).

^{1}H-NMR($CDCl_3$): 1.95(3H, s), 3.62(2H, s), 7.30-7.40(4H, m).

Step 2

To a solution of the compound (9-2)(0.56 g) in tetrahydrofuran (10 ml), t-butylamine (0.24 g) was added and stirred at room temperature for 18 hours. The reaction solvent was evaporated under reduced pressure, then the obtained residue was purified by silica gel column chromatography to afford the compound (9-3)(190 mg).

^{1}H-NMR(CDCl3): 1.43(9H, s), 1.56(3H, s), 3.27(1H, d, J=10.6 Hz), 3.36(1H, d, J=10.6 Hz), 7.28(2H, d, J=8.2 Hz), 7.43(2H, d, J=8.2 Hz).

Step 3

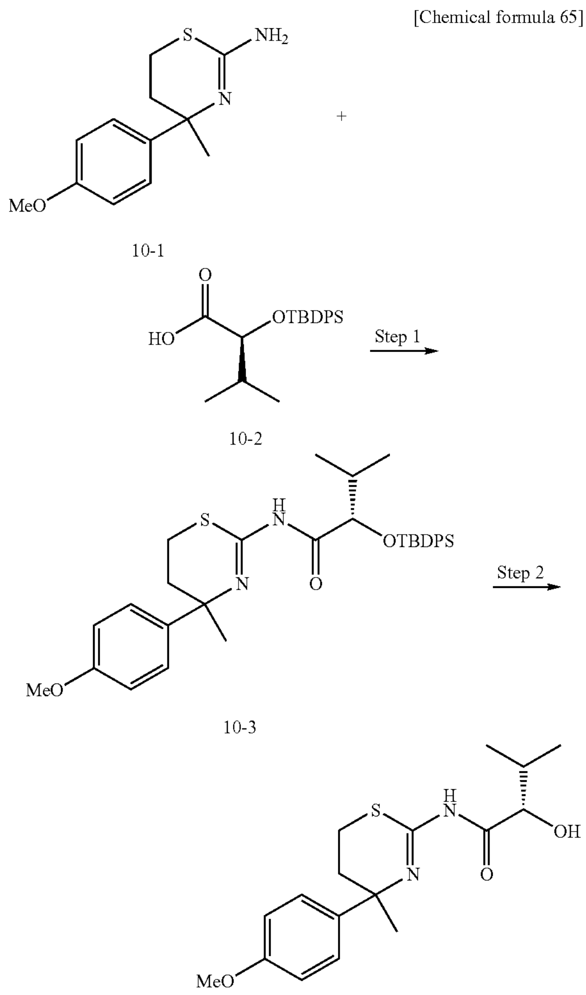
To the compound (9-3)(190 mg), conc. hydrochloric acid (3 ml) was added, then stirred at 100° C. for 3 hours. To the reaction mixture, 6 mol/L sodium hydroxide was added to neutralize, the mixture was extracted with dichloromethane. The organic layer was dried with anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography, then crystallized from dichloromethane/n-hexane to afford the compound (24)(110 mg).

^{1}H-NMR($CDCl_3$): 1.62(3H, s), 3.47(1H, d, J=10.6 Hz), 3.52(1H, d, J=10.6 Hz), 4.59(2H, br), 7.29(2H, d, J=8.6 Hz), 7.39(2H, d, J=8.6 Hz).

Reference Example 10

The Synthesis of Compound 48

[Chemical formula 65]



10-1

10-2

10-3

48

Step 1

The compound (10-1)(79.6 mg) and (10-2)(120 mg) were dissolved into N,N-dimethylformamide (3 ml), then 1-hydroxybenzotriazole (54.6 mg) and N,N'-diisopropylcarbodiimide (0.063 ml) were added, then the reaction mixture was stirred overnight at room temperature. Then after the consumption of the compound (10-1), water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate, and the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (10-3)(110.2 mg) as a crude product of diastereomer.

^{1}H-NMR($CDCl_3$): 0.78-1.00 (6H, m), 1.14 (9/2H, s), 1.16 (9/2H, s) 1.52 (3/2H, s), 1.54 (3/2H, s) 1.86-2.28 (3H, m), 2.56-2.89 (2H, m), 3.80 (3/2H, s), 3.81 (3/2H, s) 4.04-4.14 (1H, m), 6.80-6.91 (2H, 7.08-7.22 (2H, m), 7.30-7.51 (6H, m), 7.61-7.76 (4H, m)

Step 2

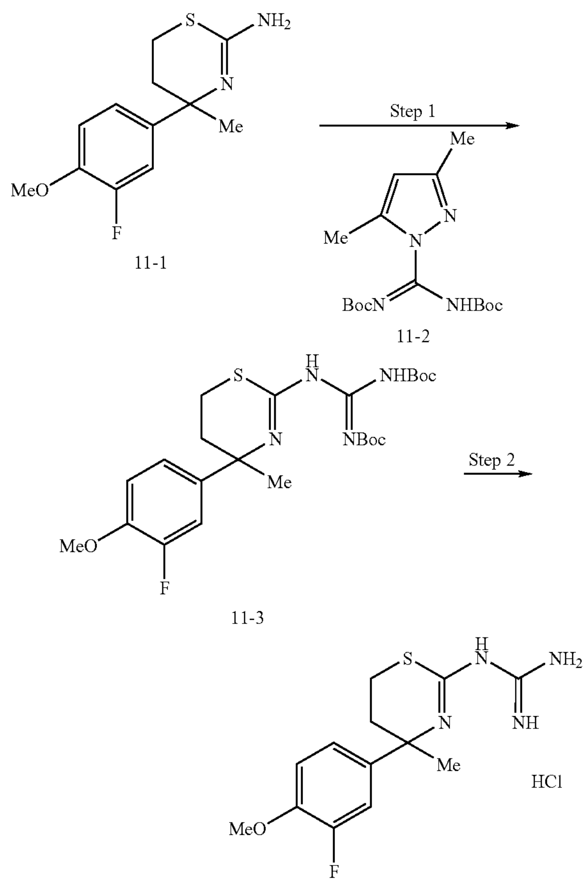
The compound (10-3)(100 mg) was dissolved into tetrahydrofuran (3 ml) under nitrogen atmosphere, then 1 mol/L tetrabutylammonium fluoride in tetrahydrofuran (0.18 ml) was added at 0° C. with stirring, then the reaction mixture was stirred at 0° C. for 5 minutes. After the consumption of the compound (10-3), water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate, then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (48)(40.7 mg) as a mixture of diastereomers.

^{1}H-NMR($CDCl_3$): 0.80-0.90 (3H, m) 1.01-1.12(3H, m) 1.70 (3H, m), 2.02-2.31(2H, m) 2.39--2.55 (1H, m), 2.61-2.90 (2H,) 3.53-3.70 (1H, m) 3.81 (3H, m), 3.96-4.08(1H, m) 6.87-6.96 (2H, m), 7.13-7.22 (2H, m)

Reference Example 11

The Synthesis of Compound 707

[Chemical formula 66]



11-1

11-2

11-3

707

Step 1

The compound (11-1)(150 mg) was dissolved into acetonitrile (5 ml), then the compound (11-2)(219.6 mg) was added at room temperature with stirring, and then the reaction mixture was warmed to 60° C., and stirred for 25 hours. The compound (11-1) was remained (checked by TLC). The reaction solvent was evaporated under reduced pressure, then the obtained residue was purified by silica gel column chromatography to afford the compound (11-1)(211.4 mg). ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.46 (9H, s), 1.50 (9H, s), 1.57 (3H, s), 1.90 (1H, ddd, J=13.7, 10.0, 3.8 Hz) 2.11 (1H, ddd, J=13.7, 6.5, 3.7 Hz) 2.68-2.76 (1H, m), 2.86-2.93 (1H, m), 3.88 (3H, s), 6.91 (1H, t, J=8.6 Hz) 6.99-7.03 (1H,), 7.06 (1H, dd, J=13.0, 2.2 Hz), 10.14 (1H, s), 13.93 (1H, s)

Step 2

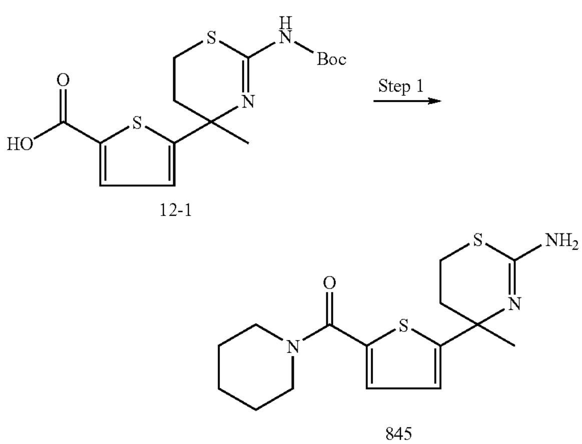
The compound (11-3)(210 mg) was dissolved into 4 mol/L hydrochloric acid in 1,4-dioxane (4 ml) under cooling with ice-water bath, then the mixture was warmed to room temperature and stirred for 67 hours. After the consumption of the compound (11-3)(checked by LC/MS), the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol-diethyl ether, and crystal was collected by filtration and washed with diethyl ether to afford compound (707)(140.2 mg).

^{1}H-NMR(DMSO-d_6, 400 MHz): 1.56 (3H, s), 1.90-2.01 (1H, m), 2.43-2.62 (2H, m), 2.95-3.03 (1H,), 3.84 (3H, s), 7.10-7.27 (3H, m), 7.76 (3H, br s), 8.26 (1H, br s), 9.42 (1H, s)

Reference Example 12

The Synthesis of Compound 845

[Chemical formula 67]



Step 1

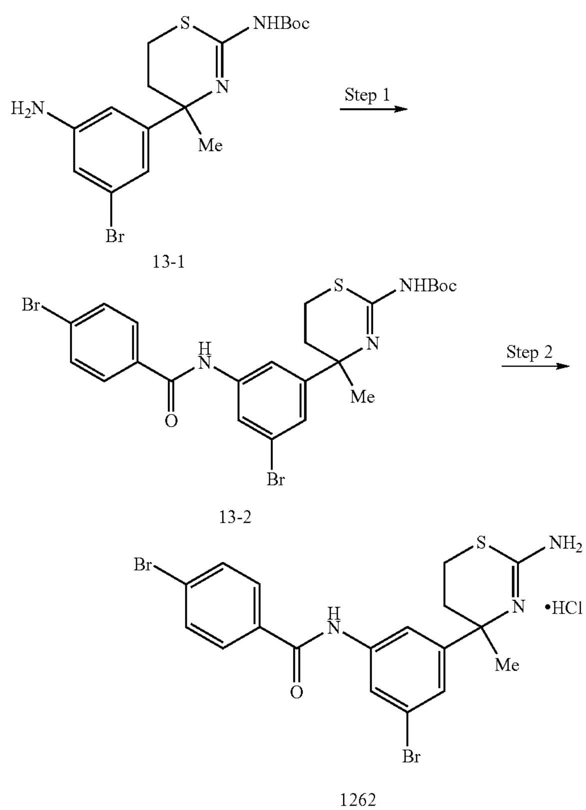
The compound (12-1)(50 mg) and piperidine (17,9 mg) were dissolved into N,N-dimethylformamide (2 ml), then O-(7-azahenzotriazo-1-yl)-1,1,3,3-tetramethyluronium-hexafluorophosphate (79.8 mg) was added, and then the mixture was stirred at room temperature for 40 hours. After the consumption of the compound (12-1), the solvent was evaporated under reduced pressure with heating. To the obtained residue, saturated sodium hydrogencarbonate solution was added, and extracted with ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate, then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (845)(30.7 mg).

^{1}H-NMR($CDCl_3$): 1.60 (3H, s), 1.51-1.82 (6H, m), 1.87-1.98 (1H, m), 2.09-2.19(1H, m), 2.91-2.97 (2H, m), 3.64-3.68 (4H,), 6.73 (1H, d, J=4.05 Hz), 7.14(1H, d, J=4.05 Hz)

Reference Example 13

The Synthesis of Compound 1262

[Chemical formula 68]



Step 1

The compound (13-1)(50.0 mg) was dissolved into tetrahydrofuran (1 ml) under nitrogen atmosphere, then triethylamine (19 μl), and 4-bromobenzoyl chloride (30.1 mg) were added under cooling with ice-water bath, and stirred for 40 minutes. The reaction solvent was evaporated under reduced pressure, and then the obtained residue was dissolved into ethyl acetate. The solution was washed with saturated sodium hydrogencarbonate solution, and dried over magnesium sulfate, and then the solvent was evaporated under reduced pressure. The generated crystal was collected by filtration to afford the compound (13-2)(57.2 mg).

^{1}H-NMR($CDCl_3$): 1.48(9H, s), 1.68(3H, s), 2.08(1H, m), 2.44(1H, m), 2.65(1H, m), 2.76(1H, m), 7.18(1H, s), 7.32 (1H, s), 7.64(2H, d, J=8.2 Hz), 7.78(2H, d, J=8.2 Hz), 8.15 (1H, s), 8.25(1H, br)

Step 2

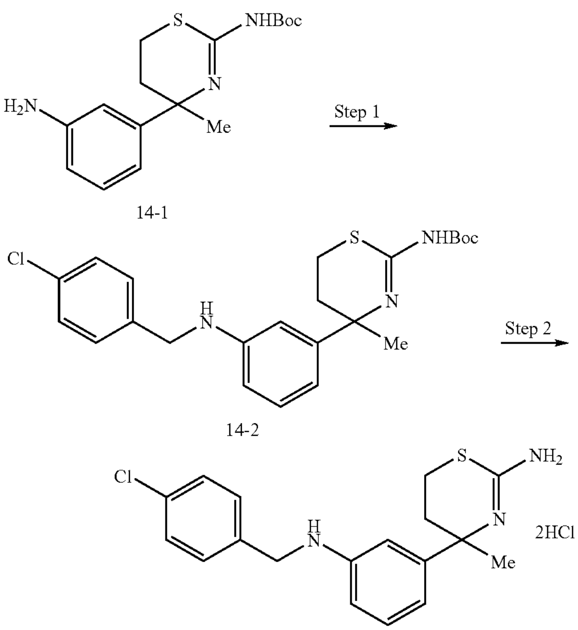
The compound (13-2)(62.3 mg) was dissolved into 4 mol/L hydrochloric acid-1,4-dioxane and stirred for 24 hours. The reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol/diethyl ether to afford the compound (1262)(44.7 mg).

^{1}H-NMR(DMSO-d_6): 1.67(3H, s), 2.10(1H, m), 2.50-2.61 (3H, m), 7.33(1H, s), 7.74(1H, s), 7.77(2H, d, J=8,6 Hz), 7.91(2H, d, J=8.6 Hz), 8.08(1H, s), 10.6(1H, s)

Reference Example 14

The Synthesis of Compound 753

[Chemical formula 69]



753

Step 1

The compound (14-1)(46 mg) was dissolved into dichloromethane (2 ml), then 4-chlorobenzaldehyde (20 mg) and acetic acid (17 mg) was added at room temperature, and then stirred for 20 minutes, and then sodium triacetoxyborohydride (45 mg) was added under cooling with ice-water bath. The mixture was stirred at room temperature for 14 hours, and then water was added and extracted with dichloromethane. The organic layer was dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (14-2)(52 mg).

^{1}H-NMR($CDCl_3$): 1.50(9H, s), 1.64(3H, s), 2.02-2.10(1H, m), 2.40(1H, dt, J=14.0 4.1 Hz), 2.62-2.74(2H, m), 4.30(2H, s), 6.49(1H, ddd, J=7.8, 2.0, 0.8 Hz), 6.52(1H, t, J=2.0 Hz), 6.60(1H, ddd, J=7.8, 2.0, 0.8 Hz), 7.16(1H, t, J=7.8 Hz), 7.18-7.33(4H, m).

Step 2

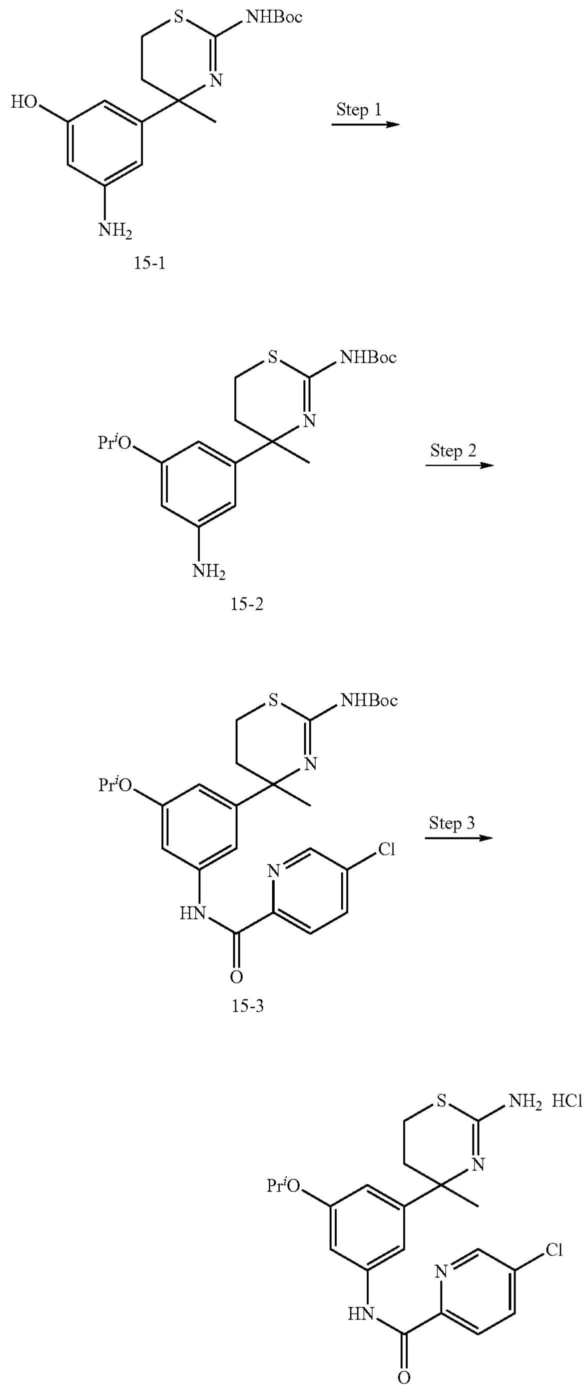
To the compound (14-2)(52 mg), 4 mol/L hydrochloric acid in 1,4-dioxane solution (4 ml) was added, then the mixture was stirred at room temperature for 4 days, and then the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol/diethyl ether to afford the compound (753)(42 mg),

^{1}H-NMR(DMSO-d_6): 1.58(3H, s), 2.00(1H, ddd, J=14.3, 11.3, 3.3 Hz),2.49-2.57(2H, m), 3.07(1H, dt, J=12.7, 3.3 Hz), 4.27(2H, s), 6.47(1H, d, J=8.2 Hz), 6.51-6.53(2H, m), 7.08 (1H, t, J=8.2 Hz), 7.37(4H, s), 8.80(2H, br).

Reference Example 15

The Synthesis of Compound 1135

[Chemical formula 70]



1135

Step 1

To a solution of the compound (15-1)(101 mg), 2-propanol (56 μl), and triphenylphosphine (189 mg) in tetrahydrofuran (2 ml), diethyl azodicarboxylate (2.2 mol/L) in toluene (328 μl) was added dropwise, then stirred for 1 hour at room temperature. After the consumption of the compound (15-1), the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (15-2)(280 mg) as a mixture of triphenylphosphine oxide and diethyl hydrazodicarboxylate.

Step 2

To the suspension of 5-chloropyridine-2-carboxylic acid (47 mg) in toluene (1 ml), N,N-dimethylformamide (1 drop) and thionylchloride (91 μl) were added and stirred at. 100° C. for 1 hour. The solvent was evaporated under reduced pressure, then the obtained residue was dissolved into tetrahydrofuran (1 ml), and then the mixture of the compound (15-2) (280 mg), and pyridine (194 μl) in tetrahydrofuran (0.5 ml) were added dropwise at 0° C. and stirred for 10 minutes. After the consumption of the compound (15-2), water was added and the mixture was extracted with ethyl acetate. The organic layer, was washed with water, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (15-3)(68 mg) as a mixture of diethyl hydrazodicarboxylate.

Step 3

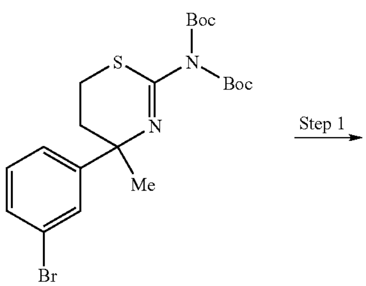
To the compound (15-3)(68 mg) as a mixture of diethyl hydrazodicarboxylate, 4 mol/L in hydrochloric acid in 1,4-dioxane solution (1 ml) was added, then the mixture was stirred at room temperature for 16 hours. After the consumption of the compound (44), the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from 2-propanol/diethyl ether to afford the compound (1135)(36 mg).

^{1}H-NMR(DMSO-d$_6$): 1.30(3H, d, J=6.4 Hz), 1.31(3H, d, J=6.4 Hz), 1.65(3H, s), 2.04-2.11(1H, m), 2.50-2.64(2H, m), 3.12-3.16(1H, m), 4.61(1H, sep, J=6.4 Hz), 6.66(1H, t, J=2.0 Hz), 7.48(1H, t, J=2.0 Hz), 7.60(1H, t, J=2.0 Hz), 8.16 (1H, dd, J=8.4, 0.8 Hz), 8.22(1H, dd, J=8.4, 2.4 Hz), 8.79(1H, dd, J=2.4, 0.8 Hz), 10.33(1H, s), 10.72(1H, s).

Reference Example 16

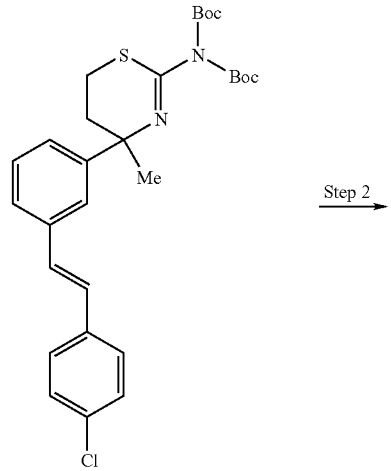
The Synthesis of Compound 161

[Chemical formula 71]

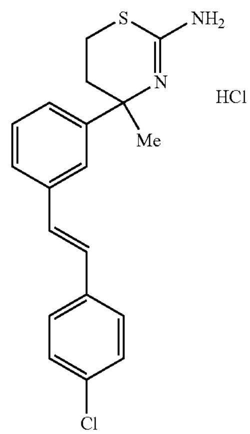


16-1

-continued



16-2



161

Step 1

The compound (16-1)(200 mg), palladium acetate (4.7 mg), and tri-(o-tolyl)phosphine (12.5 mg), were dissolved into N,N-dimethylformamide (2 ml) under nitrogen atmosphere, then n-butylamine (0.196 ml), and p-chlorostyrene (0.074 ml) were added at room temperature with stirring, then the solution was warmed to 80° C., and stirred for 3 hours. After the consumption of the compound (16-1)(checked by TLC), the reaction mixture was cooled to room temperature, and saturated ammonium chloride solution was added to the mixture. The mixture was extracted with ethyl acetate, the organic layer was washed with water and brine, and dried over magnesium sulfate, and then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (16-2)(213.1 mg).

^{1}H-NMR(CDCl$_3$, 400 MHz): 1.54 (18H, s), 1.64 (3H, s), 1.96 (1H, ddd, J=13.7, 9.1, 4.0 Hz) 2.10 (1H, ddd, J=13.7, 8.1, 3.4 Hz) 2.86 (1H, ddd, J=12.3, 9.1, 3.4 Hz), 3.03 (1H, ddd, J=12.3, 8.1, 4.0 Hz), 7.08 (1H, d, J=16.4 Hz) 7.15 (1H, d, J=16.4 Hz), 7.27-7.40 (5H, m) 7.44 (2H, d, J=8.8 Hz), 7.58 (1H, s)

Step 2

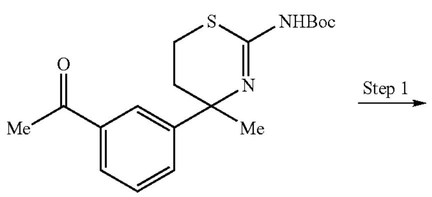
The compound (16-2)(213 mg) was dissolved into 4 mol/L, hydrochloric acid in 1,4-dioxane (5 ml) under cooling with ice-water bath, then the mixture was warmed to room temperature and stirred for 63 hours. After the consumption of the compound (16-2)(checked by LC/MS), the reaction mixture was diluted with diethyl ether. The generated crystal was collected by filtration, and washed with diethyl ether to afford the compound (161)(108.6 mg).

[1]H-NMR(DMSO-d_6, 400 MHz): 1.69 (3H, s), 2.08-2.18 (1H, m), 2.56-2.70 (2H, m), 3.13-3.20 (1H, m), 7.23 (1H, d, J=8.0 Hz), 7.31 (1H, d, J=17.0 Hz), 7.35 (1H, d, J=17.0 Hz), 7.45 (2H, d, J=8.6 Hz), 7.46 (1H, t, 7.6 Hz), 7.59 (1H, d, J=2.0 Hz), 7.61-7.64 (1H, m), 7.64 (2H, d, J=8.6 Hz), 8.53-9.50 (2H, br), 10.67 (1H, br s)

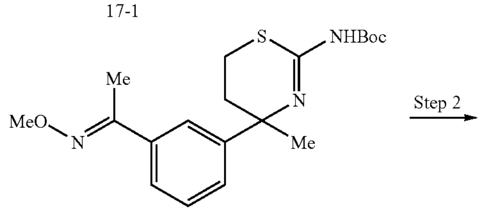
Reference Example 17

The Synthesis of Compound 597

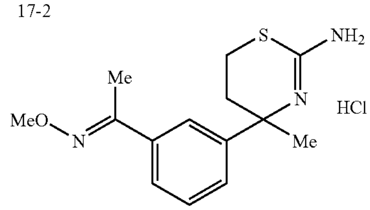
[Chemical formula 72]



17-1



17-2



597

Step 1

The solution of compound (17-1)(135 mg), O-metbxylhydroxylamine hydrochloride (39 mg), and potassium acetate (27 mg) in methanol (3 ml) was stirred at room temperature for 16 hours, then water was added. The mixture was extracted with dichloromethane, the organic layer was dried over anhydrous sodium sulfate, then the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography to afford the compound (17-2)(110 mg).

[1]H-NMR($CDCl_3$): 1.51(9H, s), 1.70(3H, s), 2.14(1H, ddd, J=14.4, 11.4, 3.4 Hz), 2.22(3H, s), 2.48(1H, m), 2.65(1H, dt, J=12.6, 11.4 Hz), 2.78(1H, ddd, J=12.6, 5.6, 3.4 Hz), 4.00 (3H, s), 7.30(1H, d, J=7.8 Hz), 7.38(1H, d, J=7.8 Hz), 7.54-7.57(2H, m).

Step 2

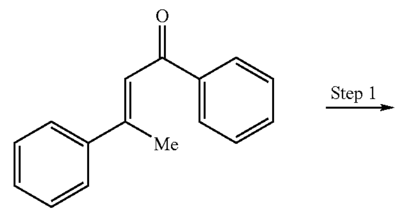
To the compound (17-2)(110 mg), 4 mol/L hydrochloric acid in 1,4-dioxane (4.5 ml) solution was added and stirred for 4 days at room temperature, then the reaction solvent was evaporated under reduced pressure. The obtained residue was crystallized from methanol/diethyl ether to afford compound (597)(65 mg).

[1]H-NMR(DMSO-d_6): 1.67(3H, s), 2.08-2.15(1H, m), 2.20 (3H, s), 2.56-2.64(2H, m), 3.14-3.17(1H, m), 3.92(3H, s), 7.37(1H, d, J=8.0 Hz), 7.48(1H, d, J=8.0 Hz), 7.56(1H, s), 7.62(1H, d, J=8.0 Hz).

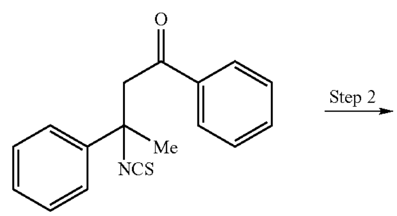
Reference Example 18

The Synthesis of Compounds 134 and 135

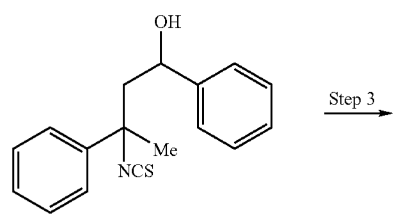
[Chemical formula 73]



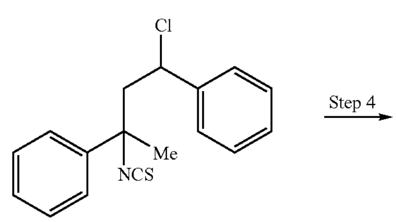
18-1



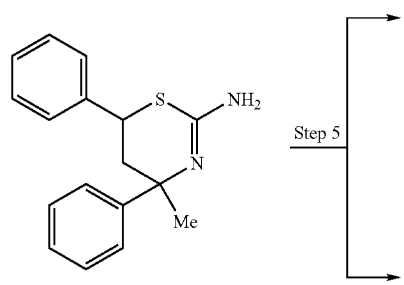
18-2



18-3

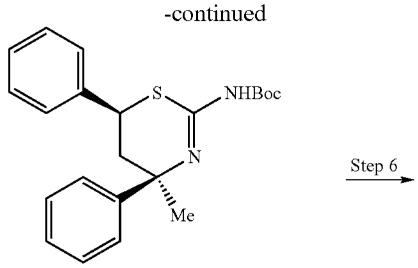


18-4



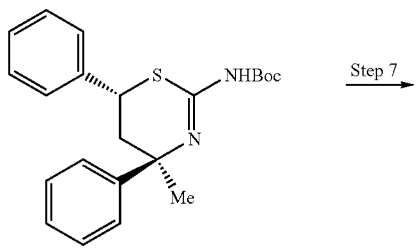
18-5

-continued

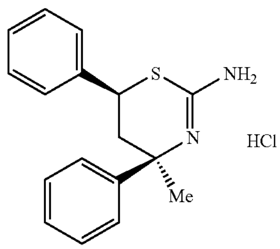


18-6a (racemate)

+

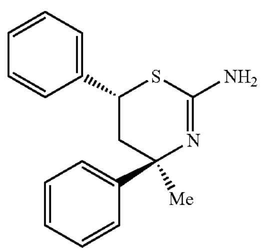


18-6b (racemate)



441 (racemate)

+



835 (racemate)

Step 1

The compound (18-1) (2020 mg) was dissolved into chloroform (20 ml), and water (4 ml) and sodium thiocyanate (1470 mg) were added to the solution with stirring at room temperature. Sulfuric acid (1.94 ml) was added dropwise to the reaction mixture under cooling with ice-water bath. After the addition was completed, the reaction mixture was warmed to room temperature and then stirred for 345 minutes, then stirred at 60° C. for overnight. Because the compound (18-1) was remained (checked by TLC), the reaction mixture was cooled to room temperature, then sodium thiocyanate (1470 mg), water (5 ml) and sulfuric acid (1.94 ml) were added successively. After the reaction mixture was warmed to 60° C., the mixture was stirred for 1 day. A saturated sodium bicarbohydrate solution was added to the reaction mixture to be basic condition under cooling with ice-water bath, and then the reaction mixture was extracted with ethyl acetate. The organic layer was washed with brine, then dried over

anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was subjected to silica gel chromatography to afford the compound (18-2) (968 mg).

^{1}H-NMR($CDCl_3$, 270 MHz): 1.99 (3H, s), 3.55 (1H, d, J=16.1 Hz), 3.69 (1H, d, J=16.1 Hz), 7.12-7.64 m), 7.82-7.95 (2H, m)

Step 2

The compound (18-2) (842 mg) was dissolved into ethanol (8.4 ml). Sodium dihydrogen phosphate(1600 mg) and sodium borohydride (113.2 mg) in water (2.8 ml) were added to the solution successively under cooling with ice-water bath with stirring, and the mixture was stirred for 30 minutes at the same temperature. After the consumption of the compound (18-2) (checked by TLC), ethyl acetate and water were added to the mixture under cooling with ice-water bath, and then stirred for a few minutes. The reaction mixture was extracted with ethyl acetate. The organic layer was washed with water and brine successively, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to afford the compound (18-3) (904.8 mg) as a crude product.

Step 3

To a stirring solution of the compound (18-3) (900 mg) in toluene (10 ml) was added a solution of thionyl chloride (0.7 ml) in toluene (5 ml) under cooling with ice-water bath, and stirred for 1 hour at the same temperature. After the consumption of the compound (18-3)(checked by TLC), the reaction solution was concentrated under reduced pressure to afford the compound (18-4)(1076.8 mg) as a crude product.

Step 4

The compound (18-4) (1070 mg) was dissolved into ca. 7 mol/L ammonia in methanol (20 ml) at room temperature, then the mixture was stirred for 1 day. After the consumption of the compound (18-4)(checked by TLC), the reaction solution was concentrated under reduced pressure to afford the compound (18-5) (2633 mg) as a crude product.

Step 5

The compound (18-5)(2633 mg) was dissolved into tetrahydrofuran (10 ml), and 4-dimethylaminopyridine (43.2 mg) and di-t-butyl dicarbonate (0.976 ml) were added to the solution successively under cooling with ice-water bath with stirring. The reaction mixture was warmed to room temperature and then stirred for 260 minutes. Because the compound (18-5) was remained (checked by TLC) in the reaction solution, di-t-butyl dicarbonate (0.488 ml) was added to the reaction mixture at room temperature and then stirred at the same temperature for overnight. After, addition of water, the reaction mixture was extracted with ethyl acetate. The organic layer was washed with brine, then dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was subjected to silica gel column chromatography to afford the compound (18-6a) (99.6 mg) and the compound (18-6b) (183.2 mg).

18-6a: ^{1}H-NMR($CDCl_3$, 400 MHz): 1.49 (9H, s), 1.80 (3H, s), 2.22 (1H, t, J=13.6 Hz), 2.36 (1H, dd, J=14.2, 3.4 Hz), 4.63 (1H, dd, J=12.6, 3.4 Hz), 7.27-7.47 (10H, m)

18-6b: ^{1}H-NMR($CDCl_3$, 400 MHz): 1.53 (9H, s), 1.72 (3H, s), 2.34 (1H, t, J=13.0 Hz), 2.66 (1H, dd, J=14.0, 2.5 Hz), 3.86 (1H, dd, J=12.4, 2.5 Hz), 7.20-7.45 (10H, m)

Step 6

The compound (18-6a) (99.6 mg) was dissolved into a 4 mol/L hydrogen chloride in 1,4-dioxane solution (4 ml) on ice bath, and the mixture was warmed to room temperature and then stirred for 6 days. After the consumption of the compound (18-6a) (checked by LC-MS), the reaction mixture was concentrated under reduced pressure. The obtained residue was crystallized from dichloromethane-ethyl acetate, and the crystals were collected by filtration and washed with ethyl acetate to afford the compound (441) (52.4 mg).

^{1}H-NMR(DMSO-d_6, 400 MHz): 1.83 (3H, s), 2.43 (1H, t, J=13.2 Hz), 2.55 (1H, dd, J=14.0, 2.8 Hz), 5.10 (1H, dd, J=12.4, 2.8 Hz), 7.34-7.48 (6H, m), 7.53-7.57 (4H,

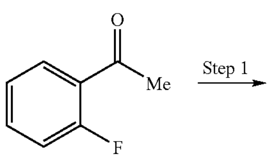
Step 7

The compound (18-6b) (183 mg) was dissolved into a 4 mol/L of hydrogen chloride in 1,4-dioxane solution (8 ml) on ice bath, and the mixture was warmed to room temperature and then stirred for 6 days. Because the compound (18-6b) was remained. (checked by LC-MS), 4 mol/L of hydrogen chloride in 1,4-dioxanesolution (2 ml) was added to the reaction mixture at room temperature, and then the mixture was stirred at 40° C. for overnight. The reaction mixture was concentrated under reduced pressure, a saturated sodium bicarbonate aqueous solution was added to be basic condition, and the reaction mixture was extracted with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. After the solvent was evaporated under reduced pressure, the obtained residue was subjected to silica gel column chromatography and crystallized from dichloromethane-diisopropyl ether. The crystals were collected by filtration and washed with diisopropyl ether to afford the compound (835) (32,2. mg).

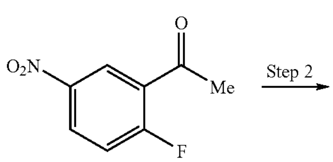
^{1}H-NMR($CDCl_3$, 400 MHz): 1.64 (3H, s), 1.95 (1H, t, J=13.2 Hz), 2.52 (1H, dd, J=13.8, 3.0 Hz), 3.84 (1H, dd, J=12.6, 3.0 Hz), 4.16-4.76 (2H, br), 7.20-7.39 (10H, m)

Reference Example 19

[Chemical formula 74]



19-1



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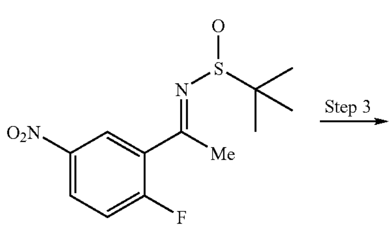

19-3

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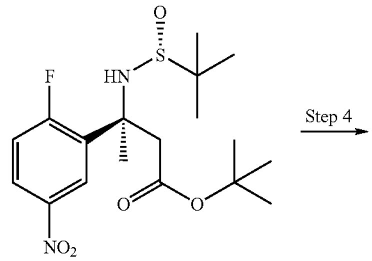
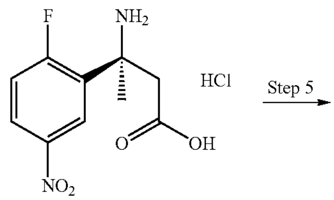


19-4



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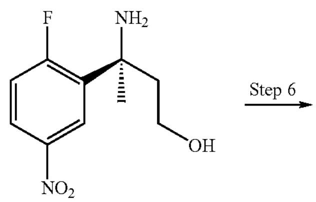
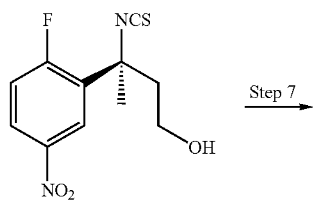
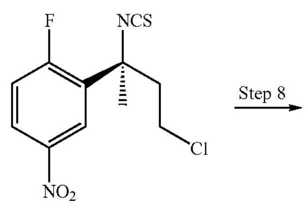


19-6



19-7



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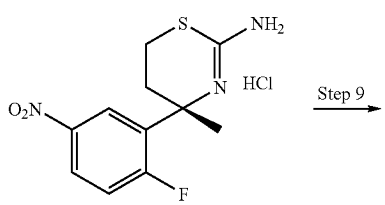
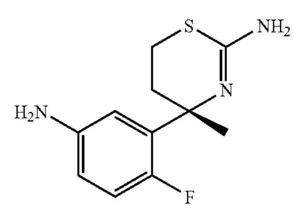


19-9



19-10

Step 1

After the compound (19-1) was added dropwise to sulfuric acid (279 ml) under cooling on acetonitrile/dry ice bath with stirring, the mixture of fuming nitric acid (42 ml) and sulfuric acid (98 ml) was added dropwise to the mixture. After stirred for 16 minutes, the reaction mixture was gradually added into ice. The precipitated crystals were collected by filtration and dried to afford the compound (19-2) (77.79 g).

^{1}H-NMR ($CDCl_3$) δ: 2.71 (3H, d, J=4.9 Hz), 7.34 (1H, t, J=9.3 Hz), 8.40 (1H, ddd, J=9.3, 6.2, 3.0 Hz), 8.78 (1H, dd, J=6.2, 3.0 Hz).

Step 2

After the mixed solution of the compound (19-2) (73.94 g), (R)-(+)-2-methyl-2-propane sulfinamide (53.82 g) and tetraethyl orthotitanate (230.20 g) in tetrahydrofuran (500 ml) was heated and refluxed for 2.5 hours. The reaction mixture was gradually poured into ice and the precipitated insoluble was removed by filtration. The filtrate was extracted with ethyl acetate, and the organic layer was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was crystallized from ethyl acetate/ n-hexane to afford the compound (19-3) (85.44 g).

^{1}H-NMR. ($CDCl_3$) δ: 1.34 (9H, s), 2.81 (3H, d, J=3.5 Hz), 7.29 (1H, t, J=8.9 Hz), 8.31 (1H, dt, J=8.9, 2.9 Hz), 8.55 (1H, dd, J=6.3, 2.9 Hz).

Step 3

A solution of t-butyl acetate (6.08 g) in tetrahydrofuran (10 ml) was added dropwise to a solution of 2M lithium diisopropylamide in tetrahydrofuran/n-heptane/ethyl benzene (27.9 ml) under cooling on acetone/dry ice bath with stirring. After stirred for 20 minutes, a solution of chlorotitanium triisopropoxide (17.5 ml) in tetrahydrofuran (30 ml) was added dropwise to the mixture. The mixture was stirred for 1 hour and a solution of the compound (19-3) (5.00 g) in tetrahydrofuran (10 ml) was added dropwise to the mixture. After reacted for 1 hour, the mixture was gradually poured into an aqueous solution of ammonium chloride under cooling on ice-water bath with stirring, and the precipitated insoluble was removed by filtration. The filtrate was extracted with ethyl acetate, and the organic layer was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to silica gel chromatography to afford the compound (19-4) (5.49 g).

^{1}H-NMR ($CDCl_3$) δ: 1.30 (9H, s), 1.35 (9H, s), 1.86 (3H, s), 3.11 (1H, dd, J=16.2, 2.1 Hz), 3.26 (1H, dd, J=16.2, 2.1 Hz), 5.55 (1H, s), 7.18 (1H, dd, J=11.1, 8.9 Hz), 8.18 (1H, ddd, J=8.9, 4.0, 2.9 Hz), 8.53 (1H, dd, J=7.0, 2.9 Hz).

Ration of diastereomers: S:R97/3, HPLC Column: AS-RH, Detection: 254 nm: Column temp.: 25° C., Mobile phase: 40% MeCNaq., Flow rate: 0.5 ml/min.

It is known that stereochemistry of the obtained compound (19-4) is preferentially afforded (S) isomer as described in Literature A, and each of diastereomers can be arbitrarily synthesized by using appropriate metal species or reaction conditions.

Literature A

(1) T. Fujisawa et al., Tetrahedron Lett., 37, 3881-3884 (1996), (2) D. H. Hua et al, Sulfur Reports, vol. 21., pp. 211-239 (1999), (3) Y. Kori ouzo et al., Tetrahedron, 58, 9621-9628 (2002), (4) Yong Qin et al., J. Org. Chem., 71, 1588-1591 (2006)

Step 4

To the compound (19-4) (12.74 g) was added a solution of 4M hydrochloric acid in 1,4-dioxane (50 ml). After the mixture was stirred at 80° C. for 1 hour, diethyl ether (50 ml) was added to the mixture. The precipitated crystals were collected by filtration, and dried to afford the compound (19-5) (7.67 g),

^{1}H-NMR (DMSO-d_6) δ: 1.76 (3H, s), 3.25 (2H, s), 7.62 (1H, dd, J=11.4, 9.4 Hz),

Step 5

To a stirred solution of the compound (19-5) (141.32 g) in tetrahydrofuran (707 ml) was added dropwise a solution of 1M boran tetrahydrofuran complex in tetrahydrofuran (2029 ml) under cooling on ice-water bath. After reacted for 3 hours 6 minutes, the mixture was added into the mixture of sodium bicarbonate (511 g), ice (1500 g) and ethyl acetate (3000 ml) at room temperature with stirring. The mixture was extracted with ethyl acetate, and the organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure to afford the compound (19-6) (115.46 g) as a crude product.

Step 6

To the compound (19-6) (3.76 g) obtained in Step 5 was added toluene (25 ml) and water (12.5 ml), Potassium carbonate (7.97 g) and thiophosgene (2.85 g) was added to the stirring mixture subsequently under cooling on ice-water bath After reacted for 3 hours, water was added to the mixture and extracted with toluene, and the organic layer was dried over anhydrous magnesium sulfate, and a part of the solvent was removed under reduced pressure to afford the compound (19-7) as a crude product.

Step 7

To a stirred solution of the compound (19-7) obtained in Step 6 in toluene (17.4 ml) was added thionyl chloride (6.67 g) and N,N-dimethylformamide (0.128 ml) at room temperature. After stirred for 2 hours at 80° C., water was added to the mixture and extracted with toluene. Solvent was evaporated under reduced pressure to afford the compound (19-8) (4.03 g).

Step 8

To a stirred solution of the compound (19-8) (4.03 g) from Step 7 in tetrahydrofuran (23.8 ml) was added,28% aqueous ammonia (23.8 ml) on ice bath, and the mixture was stirred at room temperature for 3 days. The solvent of the reaction mixture was evaporated under reduced pressure, and then ethyl acetate was added. Hydrochloric acid (6 ml) was added to the stirred mixture under cooling with ice-water bath, and the precipitated crystals were washed with ethyl acetate and water, then dried to afford the compound (19-9) (2.14 g).

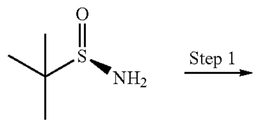
^{1}H-NMR. (DMSO-d_6) δ: 1.76 (3H, s), 2.13-2.24 (1H, m), 2.68-2.74 (2H, m), 3.19-3.25 (1H, m), 7.63 (1H, dd, 11.4, 8.9 Hz), 8.07 (1H, dd, J=7.0, 3.5 Hz), 8.36 (1H, dt, J=8.9, 3.5 Hz), 11.22 (1H, s).

Step 9

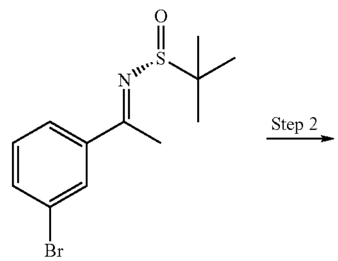
The compound (19-9) (100 mg) was dissolved into methanol (2 ml), 10% palladium carbon powder (50 mg) was added and then stirred at room temperature for 18 hours. The insoluble was removed by filtration, the solvent of the filtrate was removed under reduced pressure. Sodium carbonate and water were added to the mixture. The mixture was extracted with ethyl acetate, and the organic layer was dried over anhydrous sodium sulfate, and a solvent was evaporated under reduced pressure to afford the compound (19-10) (68 mg).

Reference Example 20

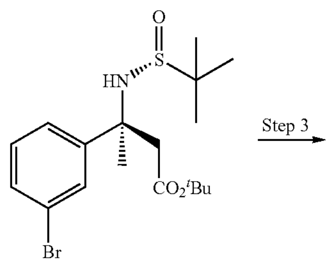
[Chemical formula 75]



20-1



20-2



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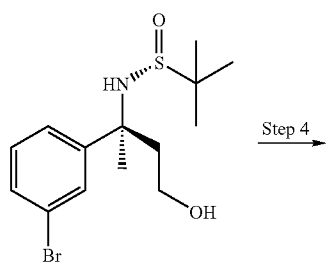

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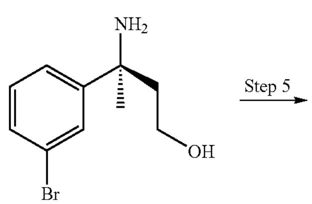
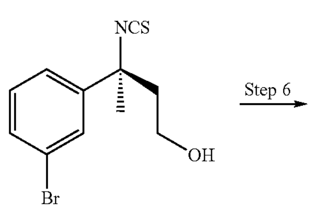


20-5



20-6

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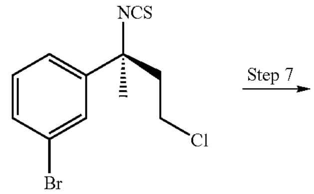

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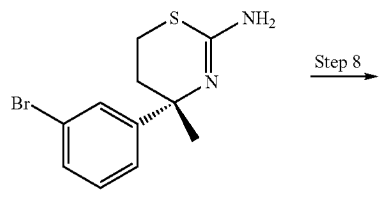
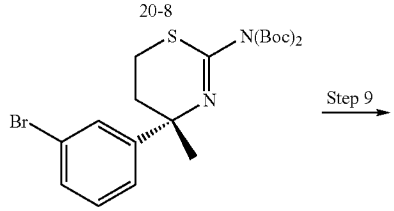
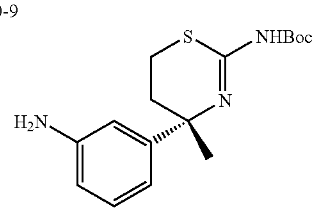


20-8



20-9



20-10

Step 1

The compound (20-1) (9.13 g) and 3'-bromoacetopherione (15.0 g) were dissolved into tetrahydrofuran (250 ml), and tetraethoxy titanium (39.5 ml) was added to the solution at room temperature with stirring and then stirred at 75° C. for 5 hours. After the consumption of the compound (20-1), brine was added to the mixture. The precipitated titanium oxide was removed by filtration, and the filtrate was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography to afford the compound (20-2) (20.1 g).

^{1}H-NMR($CDCl_3$): 1.33 (9H, s), 2.75 (3H, s), 7.30 (1H, t. J=7.8) 7.59-7.63 (1H, m), 7.79 (1H, d, J=7.8) 8.0 (1H, s).

Step 2

To a solution of diisopropylamine (42.1 ml) tetrahydrofuran (100 ml) was added dropwise n-butyl lithium in hexane solution (2.64 M, 79.5 ml) at −78° C. under nitrogen atmosphere. After stirred at. 0° C. for 30 minutes, the mixture was cooled to −78° C. again and a solution of t-butyl acetate (26.9 ml) in tetrahydrofuran (100 ml) was added dropwise to the mixture. After stirred −78° C. for 30 minutes, chloro(triisopropoxy)titanium in tetrahydrofuran (150 ml) was added dropwise to the mixture. The mixture was stirred at the same temperature for 70 minutes, the compound (2) (20.1 g) in tetrahydrofuran (100 ml) was added dropwise to the mixture and stirred at −78° C. for 3 hours. After the consumption of the compound (20-2), an aqueous solution of ammonium chloride was added. The precipitated titanium oxide was removed by filtration and the filtrate was extracted with ethyl acetate. The organic layer was washed with brine, then dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to afford the compound (20-3) as a crude product (26.4 g).

Step 3

The crude product of the compound (20-3) (26.4 g) was dissolved into toluene (80 ml) and added dropwise to a 1.0 M diisobuty aluminum hydride in toluene (253 ml) with stirring at 0° C. The reaction mixture was stirred at room temperature for 1.5 hours. After the consumption of the compound (20-3), a 1M hydrochloric acid aqueous solution was added. The mixture was extracted with ethyl acetate, the organic layer was washed with brine, then dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by crystallization to afford the compound (20-4) (18.1 g),

^{1}H-NMR($CDCl_3$):1.28(9H,s,),1.71(3H,s),2.19-2.24(2H, m),3.27-3.32(1H,m),3.54-3.66(1H, m), 3.87-3.97 (1H, m), 5.10-5.11(1H, m), 7.22 (1H, t, 7.32-7.41 (2H, m), 7.56-7.58 (1H, m)

Step 4

The compound (20-4) (18.1 g) was dissolved into methanol (130 ml) and a 10% hydrochloric acid-methanol solution (130 ml) was added to the solution with stirring at room temperature. Then, the reaction mixture was stirred at room temperature for 4 hours. After consumption of the compound (20-4), a 1M hydrochloric acid aqueous solution was added. The mixture was washed with ethyl acetate, the aqueous layer was neutralized with a 2M sodium hydroxide aqueous solution and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure to afford the crude product of the compound (20-5) (14.1 g).

Step 5

The crude product of the compound (20-5) (32.8 g) and potassium carbonate (37.1 g) were dissolved into a mixed solvent of toluene (450 ml) and water (225 ml), and thiophosgene (15.3 ml) was added dropwise to the mixture with stirring at 0° C. The reaction mixture was stirred at 0° C. for 1 hour. After consumption of the compound (20-5), water was added. After the mixture was extracted with ethyl acetate, the organic layer was washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to afford the crude product of the compound (20-6) (38.4 g).

Step 6

The crude product of the compound (20-6) (38.4 g) was dissolved into toluene (384 ml), and thionyl chloride (29.4 ml) and N,N-dimethylformamide (1.04 ml) were added dropwise to the solution with stirring at 0° C. The reaction mixture was stirred at 80° C. for 5 hours. After consumption of the compound (6), the solvent was evaporated under reduced pressure to afford the crude product of the compound (20-7) (40.9 g).

Step 7

The crude product of the compound (20-7) (40.9 g) was dissolved into tetrahydrofuran (250 ml), and 25% aqueous ammonia (250 ml) was added dropwise to the solution at 0° C. The reaction mixture was stirred at room temperature for 16 hours. After consumption of the compound (6), a saturated solution of sodium hydrogencarbonate was added. The organic layer was separated and the aqueous solution was extracted with dichloromethane. The combined organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure to afford the crude product of the compound (20-8) (38.3 g).

Step 8

The crude product of the compound (20-8) (38.3 g) was dissolved into tetrahydrofuran (383 ml), and di-t-butyl dicarbonate (61.5 g) and N,N-dimethylaminopyridine (1.64 g) were added to the solution, and the mixture was stirred at room temperature for 72 hours. After consumption of the compound (20-8), the solvent was evaporated under reduced pressure and the residue was subjected to silica gel chromatography to afford the compound (20-9) (45.3 g).

^{1}H-NMR($CDCl_3$): 1.54 (9H, s,), 1.57 (3H, s), 1.96 (2H, t, 2.80-2.92(1H, m), 3.00-3.13 (1H, m), 7.21 (1H, t, J=8.1) 7.28-7.41 (2H, m), 7.52-7.55 (1H, m).

Step 9

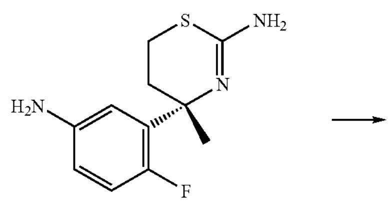
The compound (20-9) (12.1 g), tris dibenzylidene acetone dipalladium (1.14 g) and dicyclohexyl biphenyl phosphine (0.88 g) were dissolved into toluene (125 ml) under nitrogen atmosphere, and a solution of 1.6M lithium hexamethyl disilazide in tetrahydrofuran (46.9 ml) was added with stirring at room temperature. The reaction mixture was warmed to 80° C. and then stirred for 16 hours. After consumption of the compound (20-9), the mixture was cooled to 0° C. and diethyl ether and a 1M hydrochloric acid aqueous solution were added. After stirring at 0° C. for 10 minutes, the mixture was neutralized by the addition of a saturated aqueous solution of sodium carbonate. The mixture was extracted with ethyl acetate, the organic layer was washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was subjected to silica gel chromatography to afford the compound (20-10) (6.84 g).

^{1}H-NMR($CDCl_3$): 1.51 (9H, s,), 1.69 (3H, s), 2.01-2.12 (1H, m), 2.40-2.51(1H, m), 2.67-2.76 (2H, m), 6.55-6.67 (3H, m), 7.15 (1H, t, J=8.1)

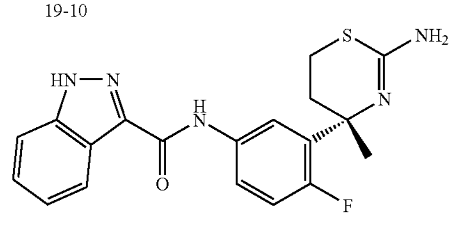
Reference Example

The Synthesis of Compound 241

[Chemical formula 76]



19-10



241

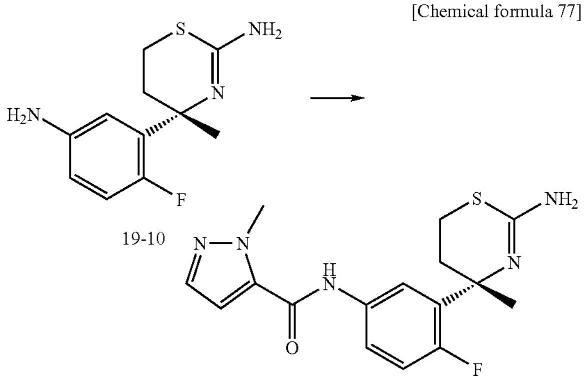
Indazole-3-carboxylic acid (71 mg) and the compound (19-10) (100 mg) were dissolved into methanol (5 ml), and 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylnmorpholinium chloride (173 mg) was added to the mixture with stirring at room temperature. The mixture was stirred for 5 hours. The reaction was quenched by the addition of brine, and the reaction mixture was extracted with ethyl acetate, dried over anhydrous magnesium sulfate and then concentrated. The crude product was purified by silica gel chromatography (NH_2-silica gel, 2-8% MeOH/$CHCl_3$) to afford the compound (241) (66 mg).

^{1}H-NMR (DMSO-d6) δ: 1.49 (3H, s), 1.78-1.86 (1H, m), 2.13-2.21 (1H, m), 2.59-2.67 (1H, m), 2.96-3.02 (1H, m), 7.11 (1H, t, J=10.7 Hz), 7.29 (1H, t, J=7.8 Hz), 7.45 (1H, t, J=7.5 Hz), 7.66 (1H, d, J=8.8 Hz), 7.74-7.78 (1H, m), 7.80-7.83 (1H, m), 8.21 (1H, d, J=8.6 Hz), 10.25 (1H, s).

Reference Example 22

The Synthesis of Compound 702

[Chemical formula 77]



19-10

702

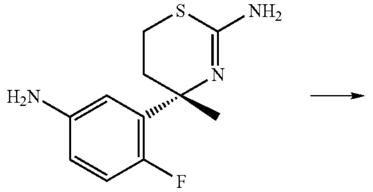
1-methylpyrazole-5-carboxylic acid (80 mg) and the compound (19-10) (145 mg) were dissolved into methanol (3 ml), and 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylmorpholinium chloride (251 mg) was added to the mixture with stirring at room temperature, and the mixture was stirred for 5 hours. The reaction was quenched by addition of brine, and the mixture was extracted with ethyl acetate, dried over anhydrous magnesium sulfate and concentrated. The crude product was purified by silica gel chromatography (NH_2-silica gel, 0-4% MeOH/$CHCl_3$) to afford the compound (702) (146 mg).

^{1}H-NMR ($CDCl_3$) δ: 1.65 (3H, s), 1.91-1.98 (1H, m), 2.57-2.62 (1H, m), 2.68-2.75 (1H, m), 2.92-2.97 (1H, m), 4.18 (3H, s), 6.82 (1H, br s), 7.02-7.08 (1H, m), 7.28-7.32 (1H, m), 7.44 (1H, s), 7.92-7.96 (1H, m).

Reference Example 23

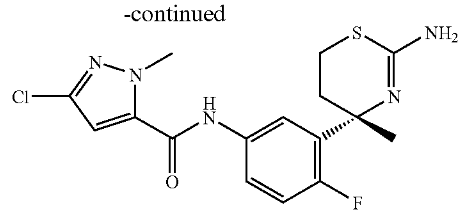
The Synthesis of the Compound 737

[Chemical formula 78]



19-10

-continued



737

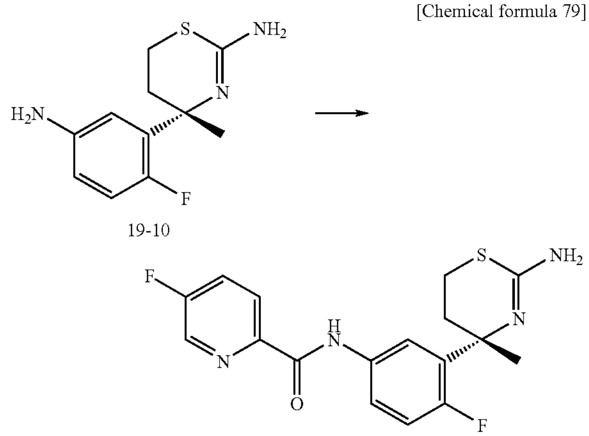
3-chloro-1-methylpyrazole-5-carboxylic acid (102 mg) and the compound (19-10) (145 mg) were dissolved into methanol (3 ml), and 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylmorpholinium chloride (251 mg) was added to the mixture with stirring at room temperature, and the mixture was stirred for 5 hours. The reaction was quenched by addition of brine, and the mixture was extracted with ethyl acetate, dried over anhydrous magnesium sulfate and concentrated to afford crude product. The crude product was purified by silica gel chromatography (NH_2-silica gel, 33-78% AcOEt/Hexane) to afford the compound (737) (51 mg).

^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s), 1.87-1.94 (1H, m), 2.47-2.53 (1H, m), 2.67-2.73 (1H, m), 2.93-2.99 (1H, m), 4.10 (3H, s), 6.62 (1H, s), 7.04 (1H, t, J=10.2 Hz), 7.33 (1H, d, J=4.3 Hz), 7.85 (1H, s).

Reference Example 24

The Synthesis of the Compound 949

[Chemical formula 79]



19-10

949

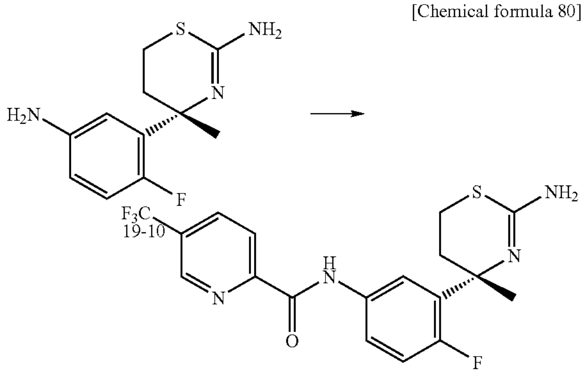
5-fluoro-2-pyridine carboxylic acid (70.7 mg) was dissolved into methanol (2 ml), and 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylmorpholinium chloride (180.1 mg) was added to the mixture with stirring at room temperature. The mixture was stirred for 5 minutes and a solution of the compound (19-10) (119.9 mg) in methanol (2 ml) was added to the reaction solution with stirring under cooling with ice-water bath. After stirred for 3 hours, a 0.5M aqueous solution of sodium hydroxide was added to the mixture with stirring under cooling with ice-water bath, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was subjected to silica gel chromatography to afford the compound (949) (149.4 mg).

^{1}H-NMR ($CDCl_3$) δ: 1.63 (3H, s), 1.82-2.00 (1H, m), 2.43-2.58 (1H, m), 2.72-2.82 (1H, m), 2.95-3.02 (1H, m), 7.06 (1H, dd, J=11,7, 9.0 Hz), 7.43-7.48 (1H, m), 7.97-8.03 (1H, m), 8.15-8.18 (1H, m), 8.42 (1H, d, J=8.1 Hz),8.72 (1H, s), 9.91 (1H, br s)

Reference Example 25

The Synthesis of the Compound 943

[Chemical formula 80]



943

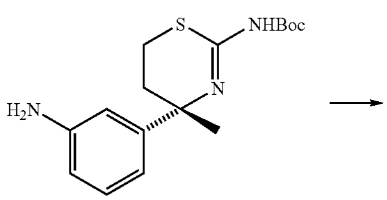
5-trifluoromethyl-2-pyridine carboxylic acid (95.7 mg) was dissolved into methanol (2 ml), and 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylmorpholinium chloride (180.1 mg) was added to the solution with stirring at room temperature. After stirring for 5 minutes, a solution of the compound (19-10) (119.9 mg) in methanol (2 ml) was added to the reaction mixture with stirring under cooling with ice-water bath. After stirring for 3 hours, a 0.5N aqueous solution of sodium hydroxide was added with stirring under cooling with ice-water bath, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure, and the obtained residue was subjected to silica gel chromatography to afford the compound (943) (174.5 mg).

^{1}H-NMR ($CDCl_3$) δ: 1.63 (3H, s), 1.82-2.00 (1H, m), 2.36-2.52 (1H, m), 2.72-2.82 (1H, m), 2.95-3.02 (1H, m), 7.07 (1H, dd, J=11.7, 8.1 Hz), 7.39-7.42 (1H, m), 7.55-7.63 (1H, m), 7.96-8.02 (1H,), 8.33 (1H, dd, J=4.8, 9.0 Hz),8.45 (1H, d, J=2.4 Hz), 9.78 (1H, s).

Reference Example 26

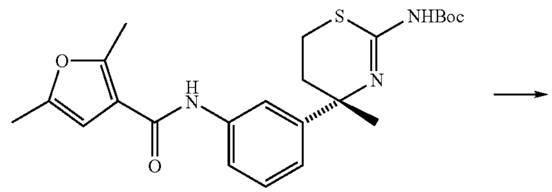
The Synthesis of the Compound 578

[Chemical formula 81]

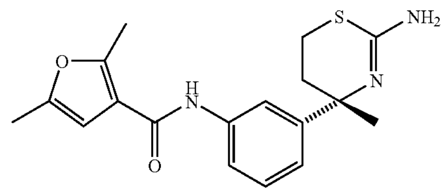


20-10

-continued



26-1



578

Step 1

To a stirred solution of 2,5-dimethylfuran carboxylic acid (115 mg) and the compound (20-10) (290 mg) in methanol (2 ml) was added 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylmorpholinium chloride (273 mg) at room temperature. After stirring for 2 hours, the reaction was quenched by addition of a saturated aqueous solution of sodium hydrogencarbonate, and the mixture was extracted with ethyl acetate. The mixture was washed with water and brine successively, dried and concentrated to afford crude product (300 mg). The crude product was purified by silica gel chromatography (silica gel, 50-66% AcOEt/hexane) to afford the compound (26-1) (221 mg).

^{1}H-NMR ($CDCl_3$) δ: 7.64-7.60 (1.0H, m), 7.43-7.41 (2.0H, m), 7.35 (1.0H, t, J=7.93 Hz), 7.04-7.02 (1.0H, m), 6.17 (1.0H, s), 2.80-2.61 (2.0H, m), 2.59(3.0H, s), 2.56-2.52 (1.0H, m), 2.30 (3.0H, s), 2.19-2.06 (1.0H, m), 1.71 (3.0H, s), 1.52 (9.0H, s).

Step 2

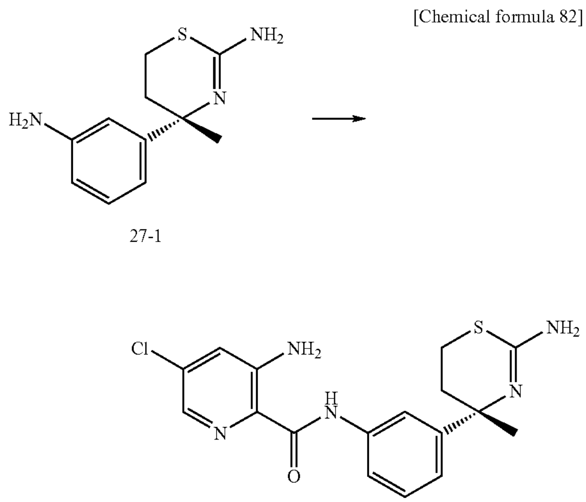
The compound (26-1) (221 mg) was dissolved into dichloroethane (1 ml) and trifluoroacetic acid (1 ml) was added to the solution with stirring at room temperature. After stirring for 1 hour 10 minutes, the solvent was evaporated. Ethyl acetate and an aqueous solution of sodium carbonate were added to the residue and the mixture was stirred for 1 hour. The mixture was extracted with ethyl acetate and washed with an aqueous solution of sodium carbonate, water and brine successively. The organic layer was dried, and concentrated to afford crude product (154 mg). The crude product was purified by recrystallization (hexane/AcOEt) to afford the compound (578) (24 mg).

(1H-NMR ($CDCl_3$) δ: 7.79 (1.0H, br s), 7.65-7.64 (1.0H, m), 7.48-7.41 (1.0H, m), 7.31 (1.0H, t, J=8.01 Hz), 7.04-7.01 (1.0H, m), 6.23 (1.0H, br s), 2.93-2.65 (2.0H, m), 2.57 (3.0H, br s), 2.40 (1.0H, ddd, J=14.11, 5.34, 3.43 Hz), 2.27 (3.0H, br s), 2.09-1.92 (1.0H, m), 1.67 (3.01H, s).

Reference Example 27

The Synthesis of the Compound 472

[Chemical formula 82]



27-1

472

The compound (27-1) (256 mg) and 3-amino-5-chloropicolinic acid hydrochloride (266 mg) were suspended in methanol (2.6 ml), and N-methylmorpholine (153 μl) was added to the suspension, and the mixture was stirred at room temperature. After stirred for 6 minutes, 4-(4,6-dimethoxy-1,3,5-triazine-2-yl)-4-methylmorpholinium chloride (385 mg) was added to the mixture, and stirred for 1 hour 10 minutes, and left to stand for 13 hours 20 minutes additionally. The solvent was evaporated, and ethyl acetate, methanol and an aqueous solution of sodium carbonate were added to the residue and stirred for 40 minutes. The aqueous layer was removed, the organic layer was washed with a saturated aqueous solution of sodium hydrogencarbonate and brine, and dried over magnesium sulfate. The magnesium sulfate was removed by filtration, the filtrate was concentrated under reduced pressure, and the obtained residue was purified by silica gel chromatography (Yamazen HI-FLASH column NH2-40W-M, ethyl acetate:hexane=1:1). The obtained fraction was concentrated and the residue was crystallized from ethyl acetate. The crystals were collected by filtration, washed with diethyl ether and dried to afford the compound (472) (82.0 mg).

^{1}H-NMR (DMSO-d_6) δ: 1.41 (3H, s), 1.72 (1H, ddd, J=13.7, 10.2, 3.6 Hz), 2.02 (1H, m), 2.58 (1H, m), 2.90 (1H, ddd, J=11.9, 6,6, 3.6 Hz), 5.77 (2H, brs), 7.09 (1H, dt, J=7.9, 1.3 Hz), 7.13 (2H, brs), 7.27 (1H, t, J=8.0 Hz), 7.33 (1H, d, J=2.2 Hz), 7.68-7.72 (2H, m), 7.85 (1H, d, J=2.0 Hz), 10.23 (1H, s).

The other compounds were synthesized in the same way. The structural formulas and physical constants are shown below.

TABLE 1

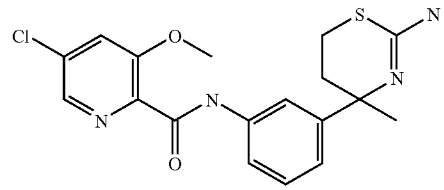
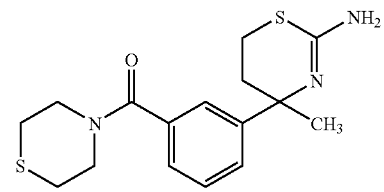
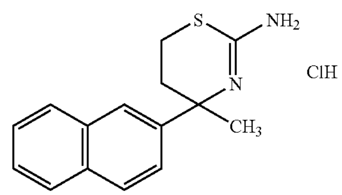
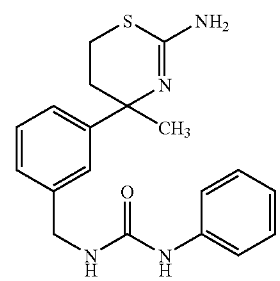
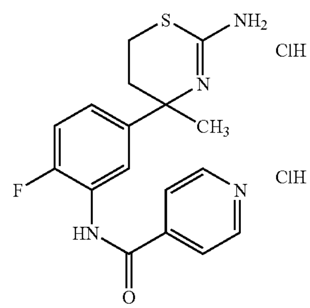
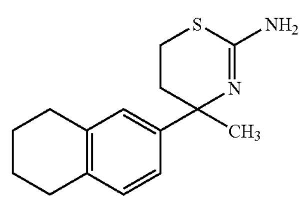
No.	Structure
1	
2	
3	
4	
5	
6	

TABLE 1-continued

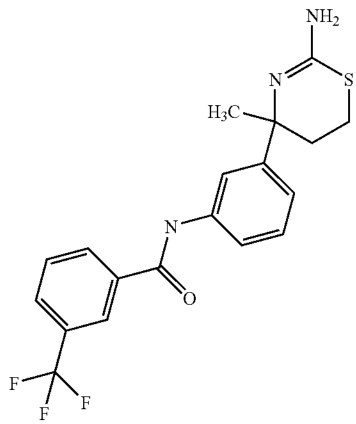
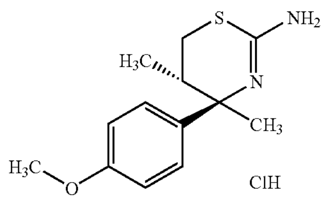
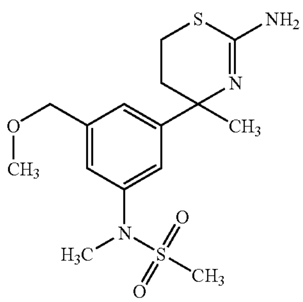
No.	Structure
7	
8	
9	

TABLE 2

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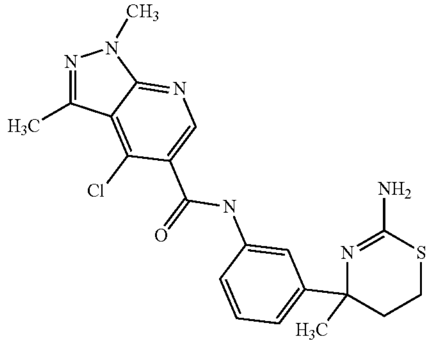
10	

TABLE 2-continued

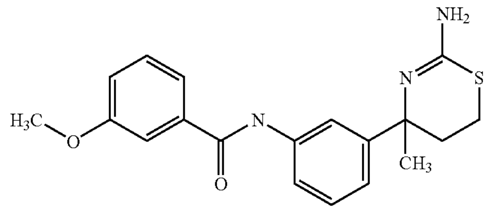
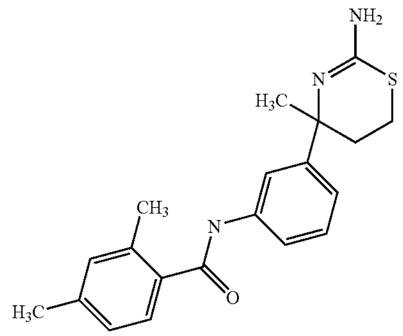
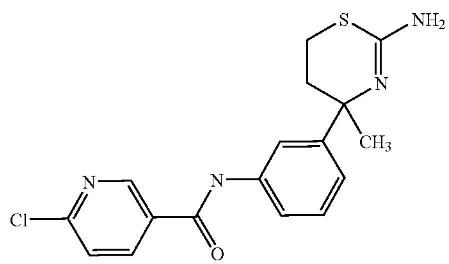
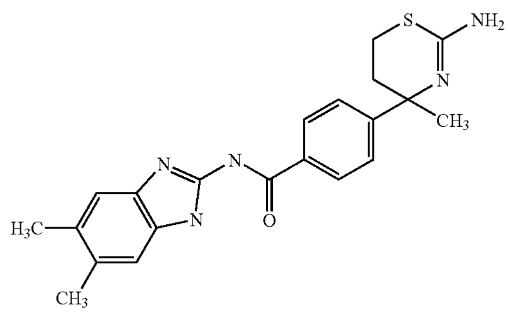
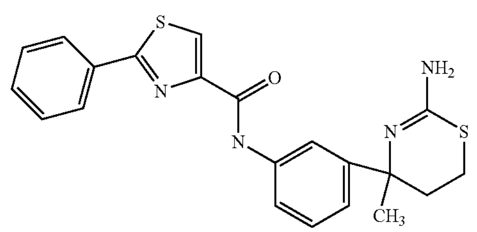
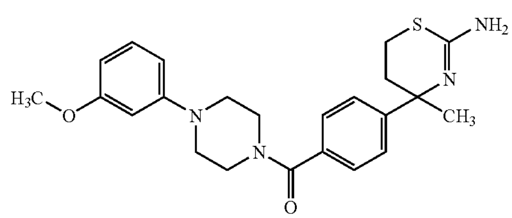
No.	Structure
11	
12	
13	
14	
15	
16	

TABLE 2-continued

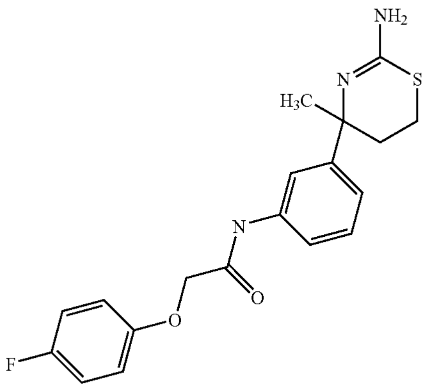
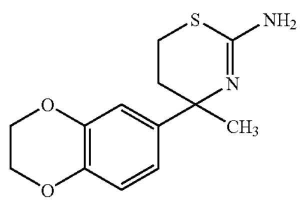
No.	Structure
17	
18	

TABLE 3

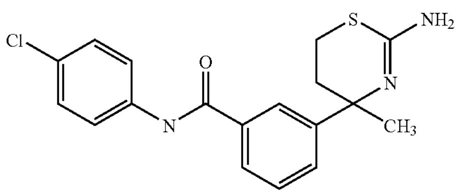
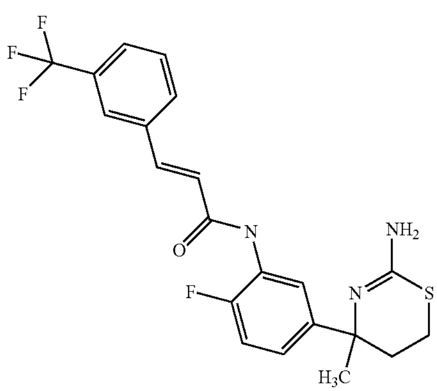
No.	Structure
19	
20	

TABLE 3-continued

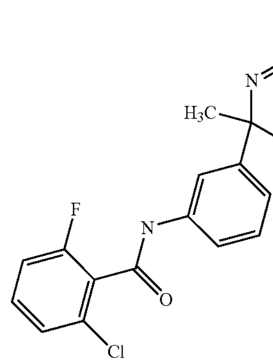
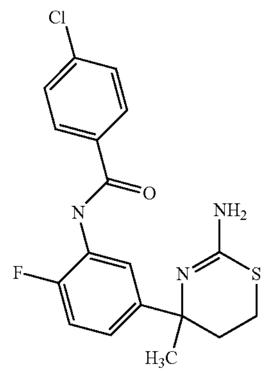
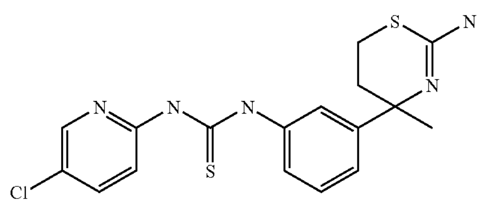
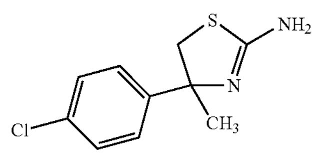
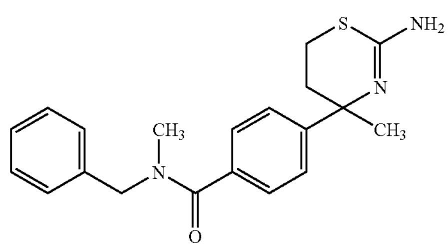
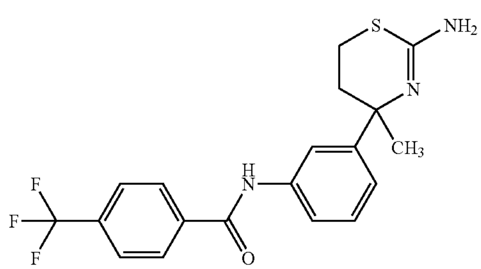
No.	Structure
21	
22	
23	
24	
25	
26	

TABLE 3-continued

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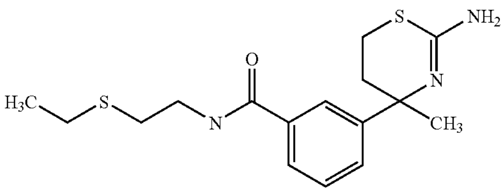
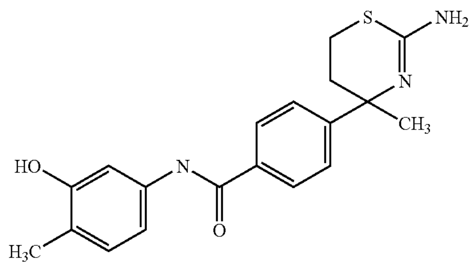
27	
28	

TABLE 4

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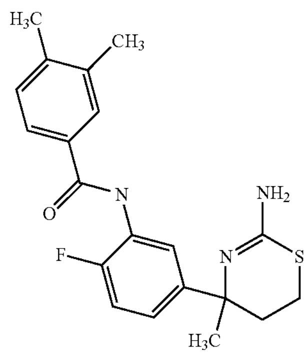
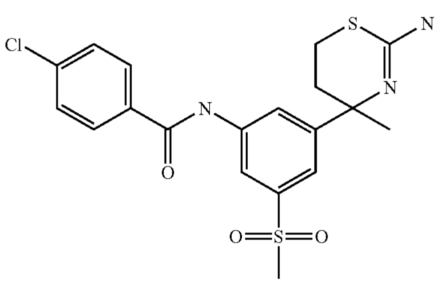
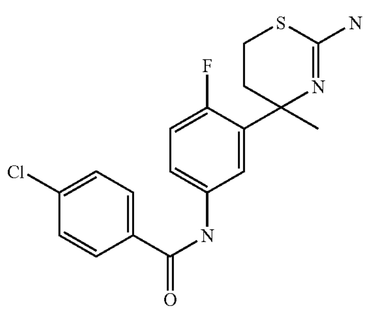
29	
30	
31	

TABLE 4-continued

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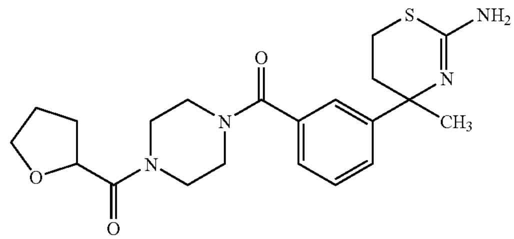
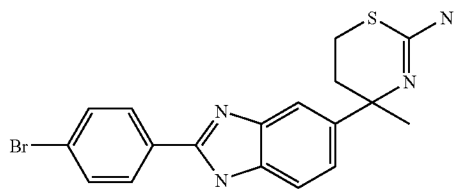
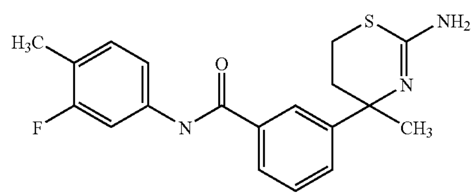
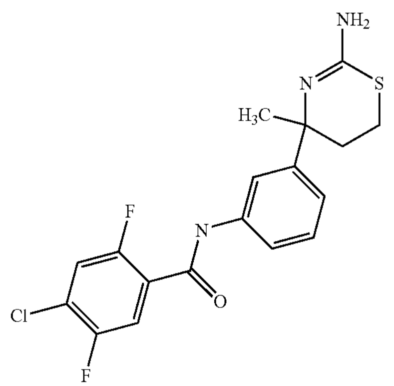
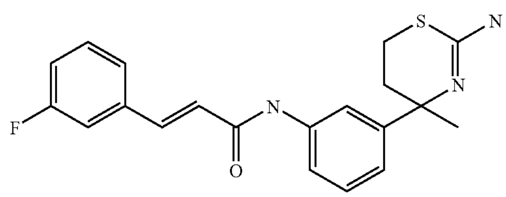
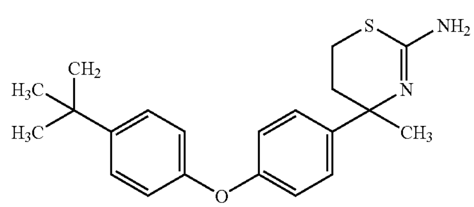
32	
33	
34	
35	
36	
37	

TABLE 4-continued

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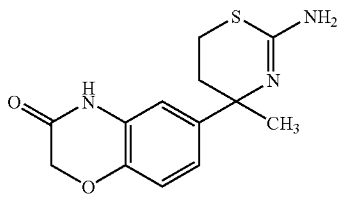
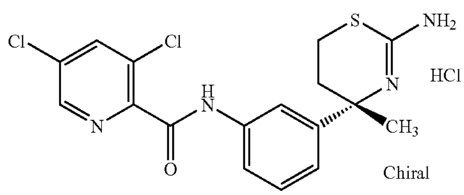
38	
39	

TABLE 5

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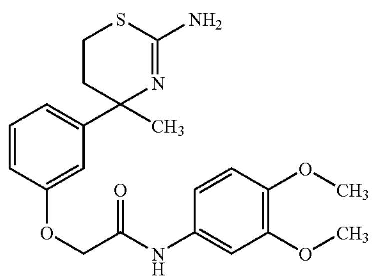
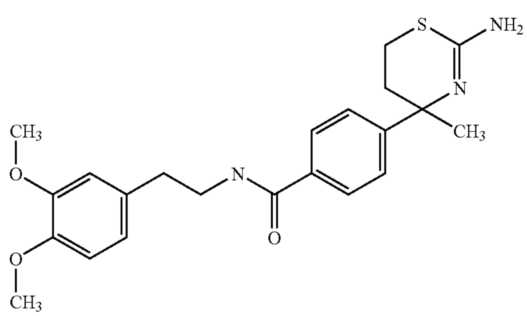
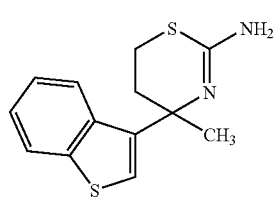
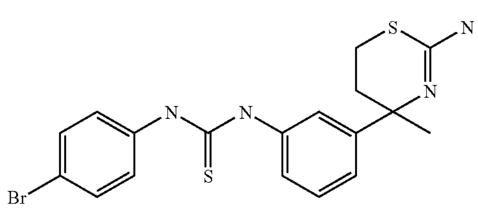
40	
41	
42	
43	

TABLE 5-continued

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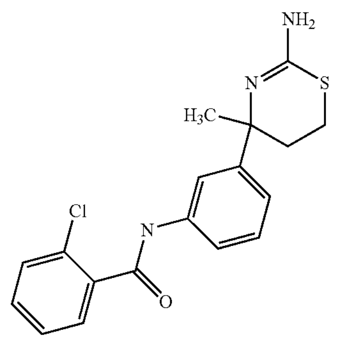
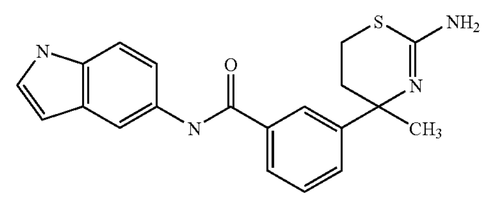
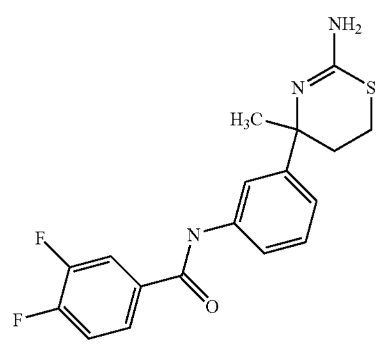
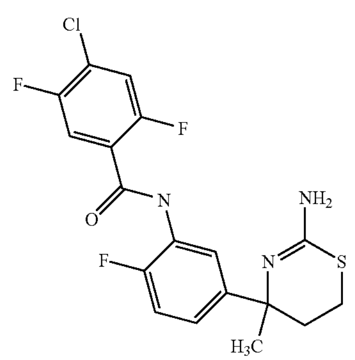
44	
45	
46	
47	

TABLE 6

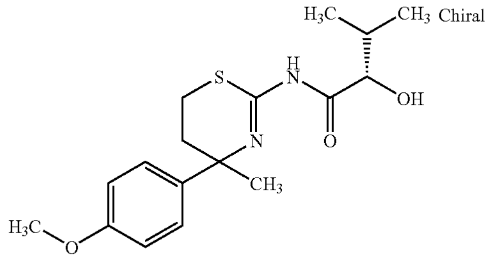
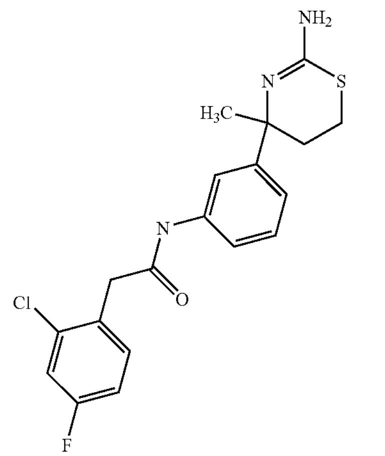
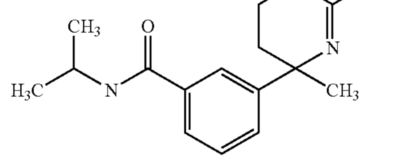
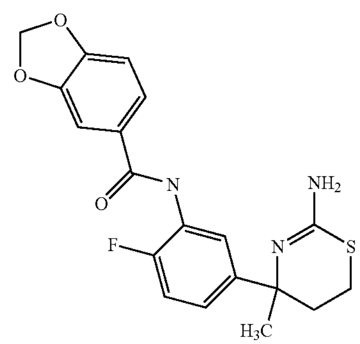
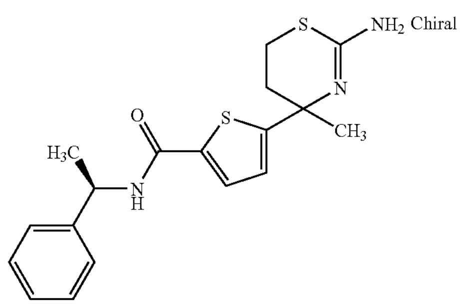
No.	Structure
48	
49	
50	
51	
52	

TABLE 6-continued

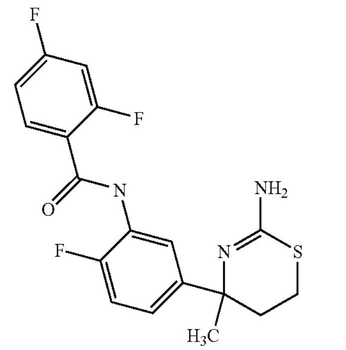
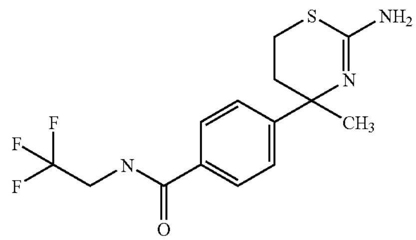
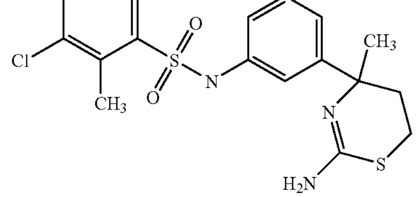
No.	Structure
53	
54	
55	

TABLE 7

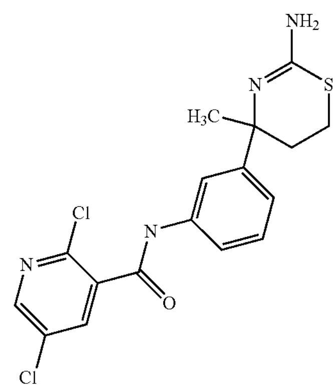
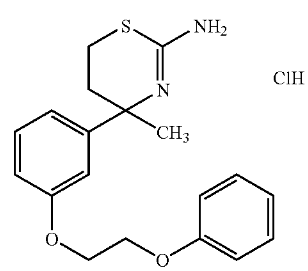
No.	Structure
56	
57	

TABLE 7-continued

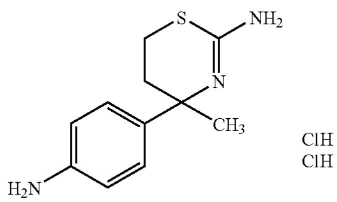
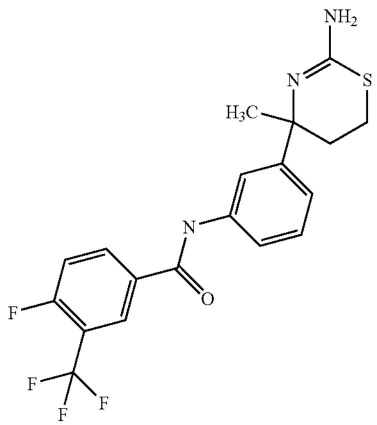
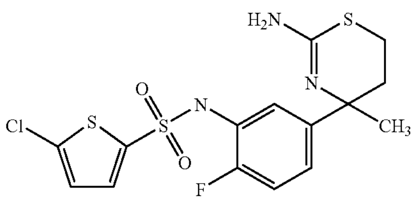
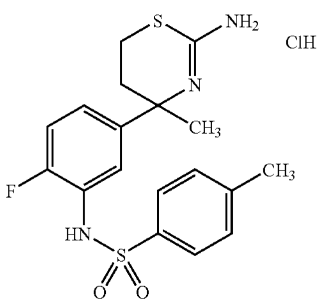
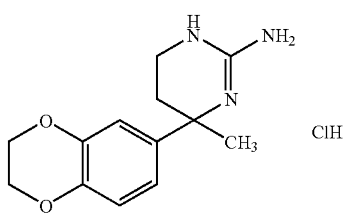
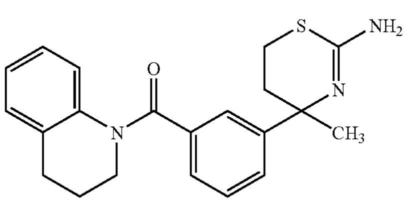
No.	Structure
58	
59	
60	
61	
62	
63	

TABLE 7-continued

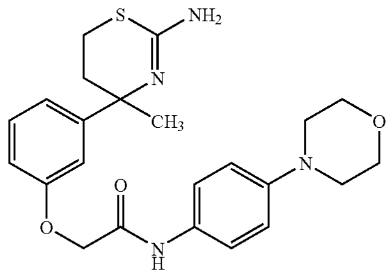
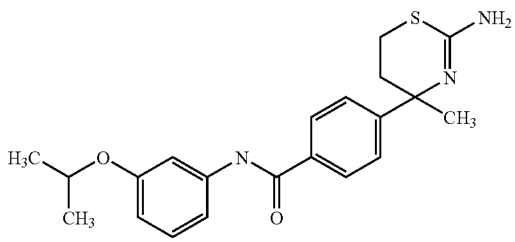
No.	Structure
64	
65	

TABLE 8

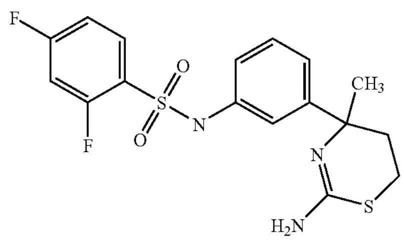
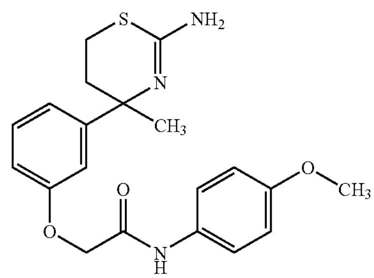
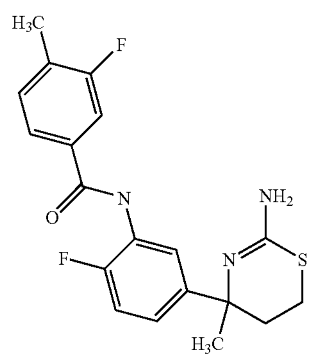
No.	Structure
66	
67	
68	

TABLE 8-continued

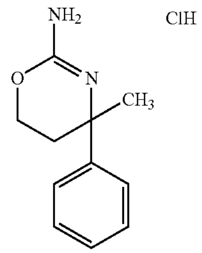
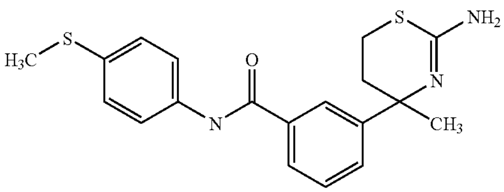
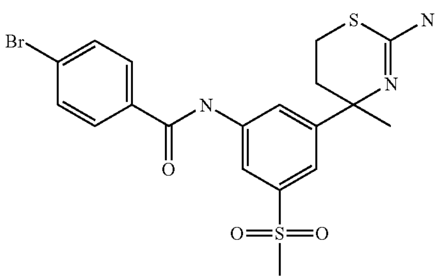
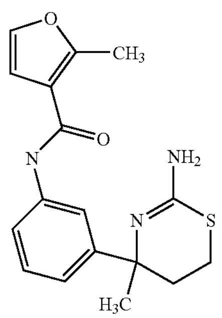
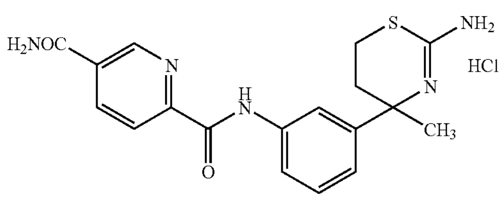
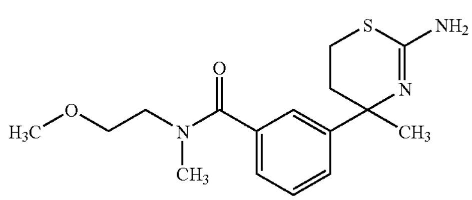
No.	Structure
69	
70	
71	
72	
73	
74	

TABLE 9

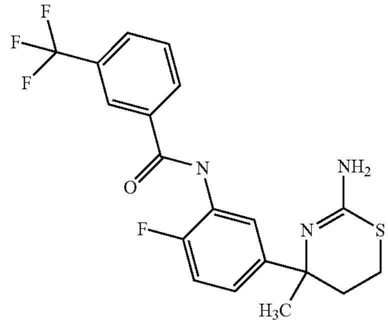
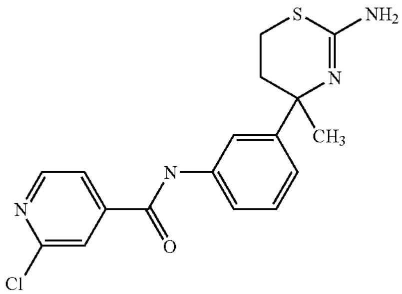
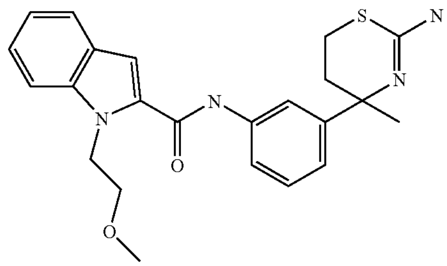
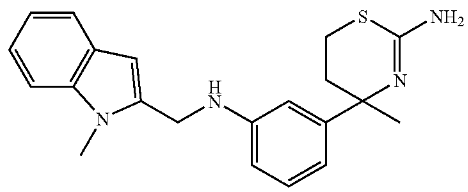
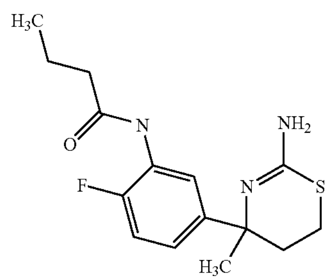
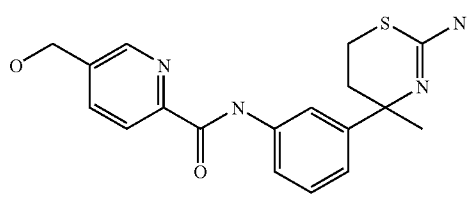
No.	Structure
75	
76	
77	
78	
79	
80	

TABLE 9-continued

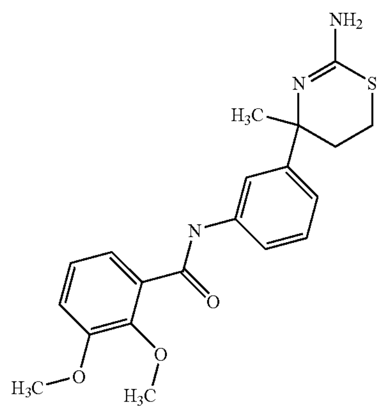
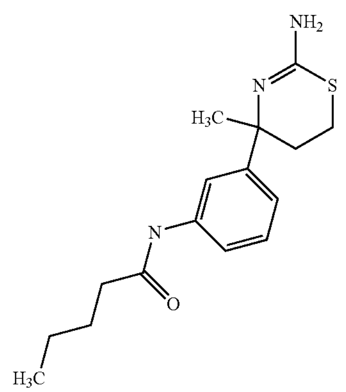
No.	Structure
81	
82	

TABLE 10

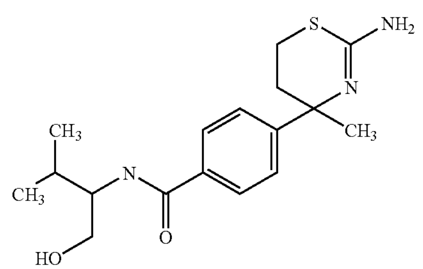
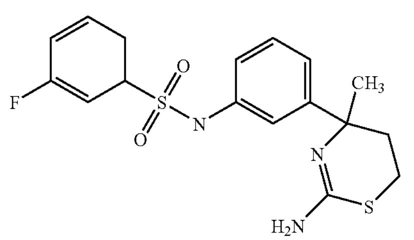
No.	Structure
83	
84	

TABLE 10-continued

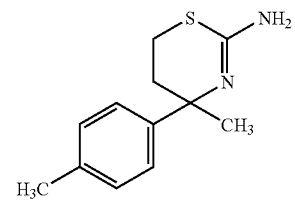
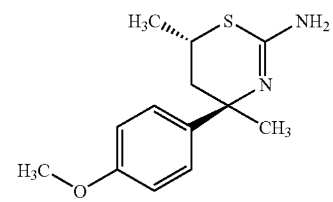
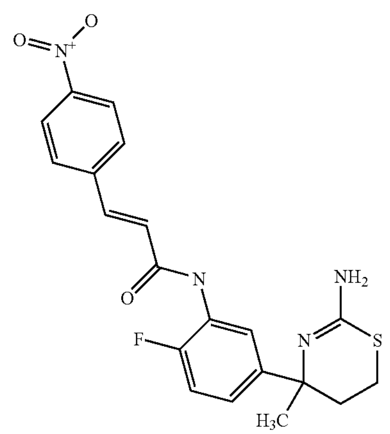
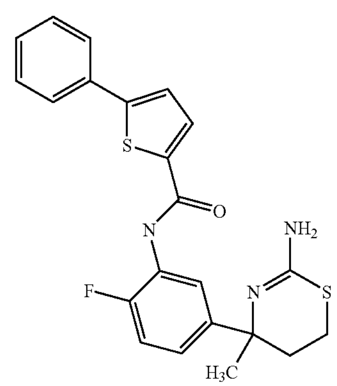
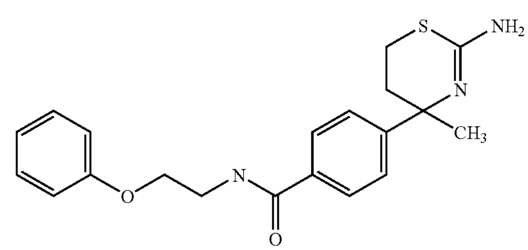
No.	Structure
85	
86	
87	
88	
89	

TABLE 10-continued

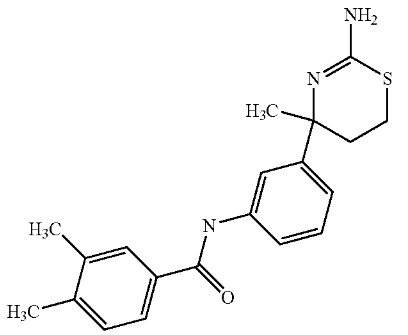
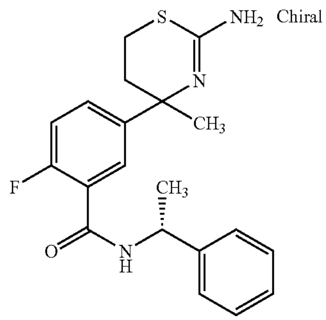
No.	Structure
90	
91	

TABLE 11

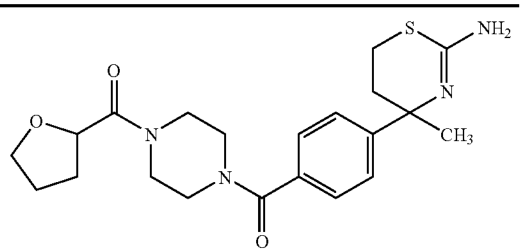
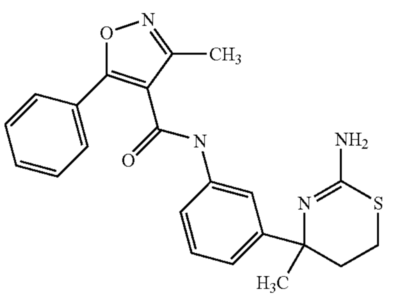
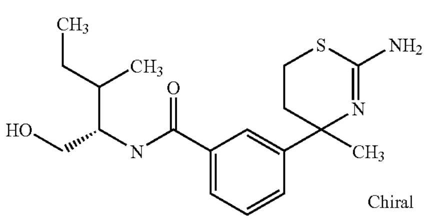
No.	Structure
92	
93	
94	

TABLE 11-continued

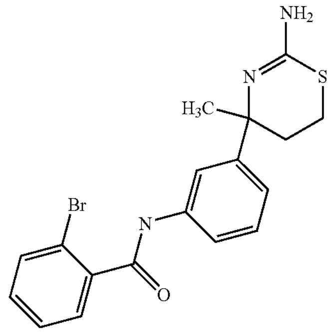
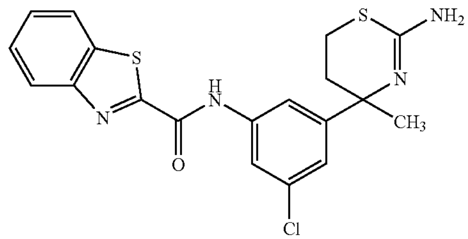
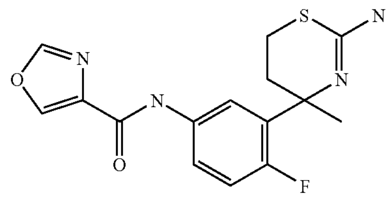
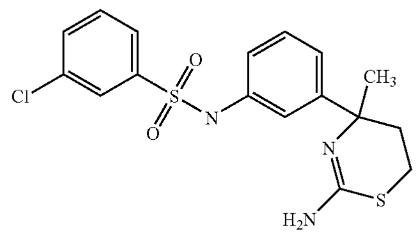
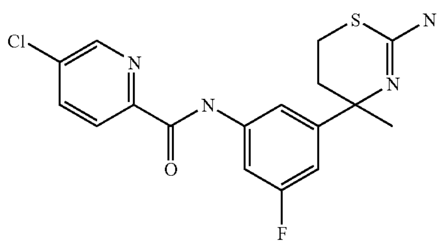
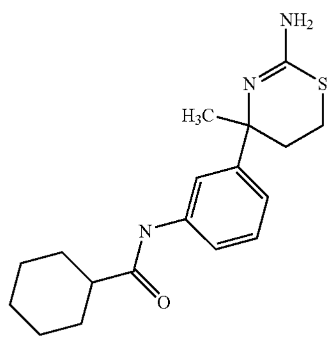
No.	Structure
95	
96	
97	
98	
99	
100	

TABLE 11-continued

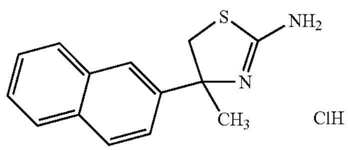
No.	Structure
101	

TABLE 12

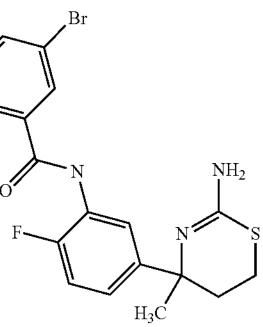
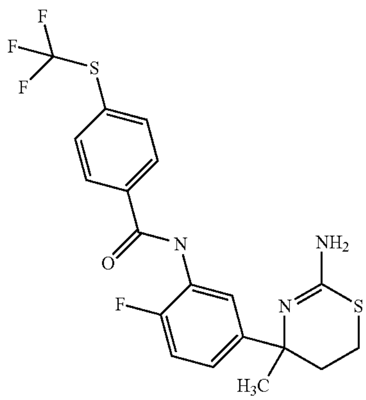
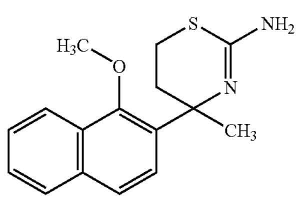
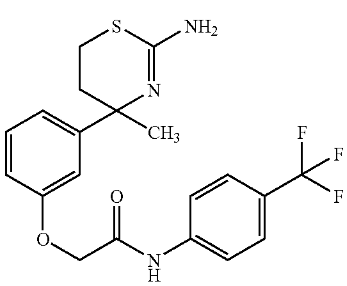
No.	Structure
102	
103	
104	
105	

TABLE 12-continued

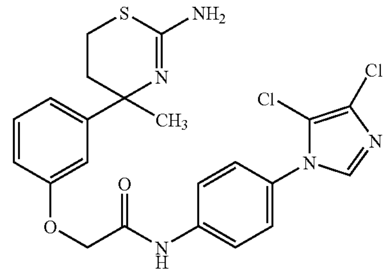
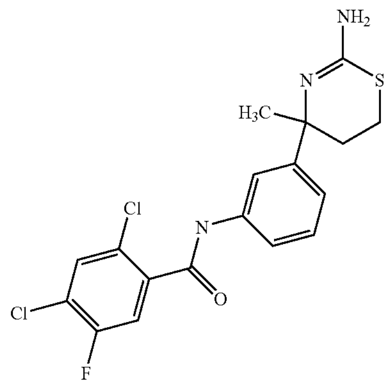
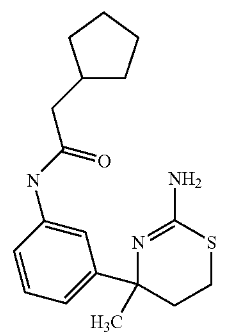
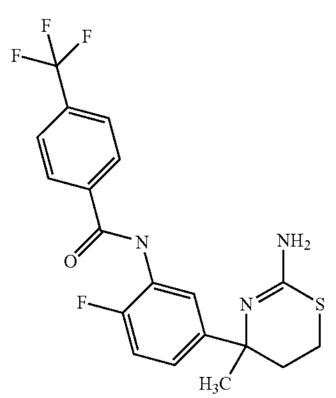
No.	Structure
106	
107	
108	
109	

TABLE 13

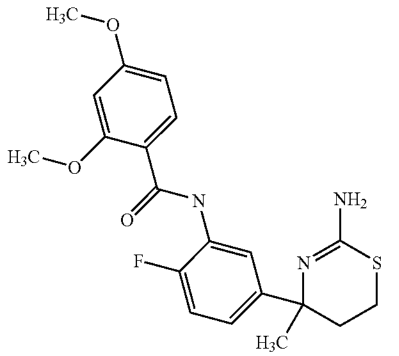
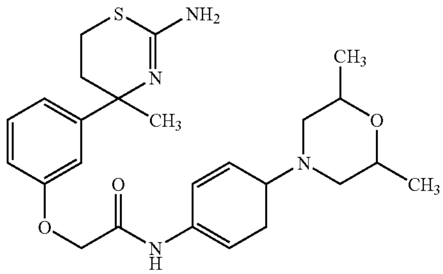
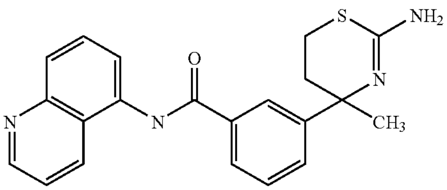
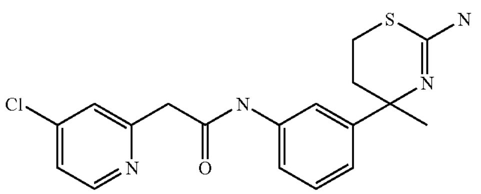
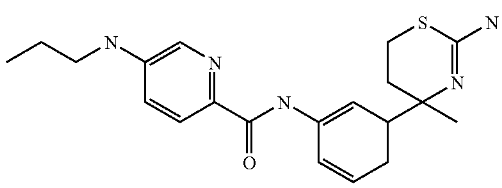
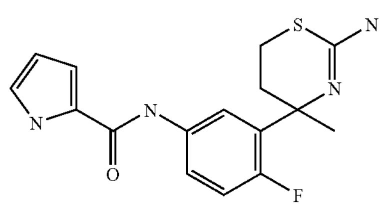
No.	Structure
110	
111	
112	
113	
114	
115	

TABLE 13-continued

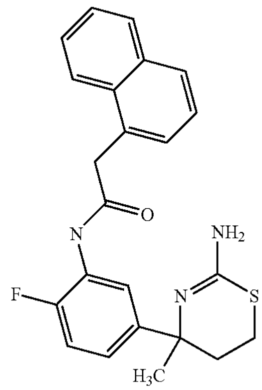
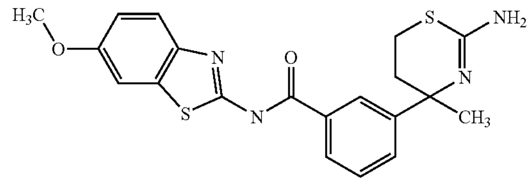
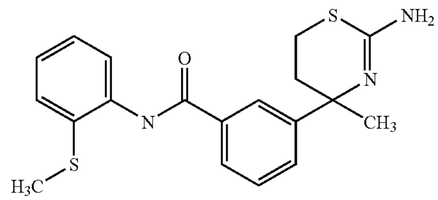
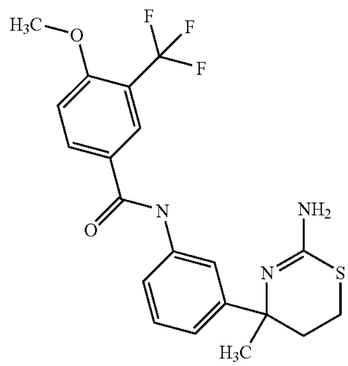
No.	Structure
116	
117	
118	
119	

TABLE 14

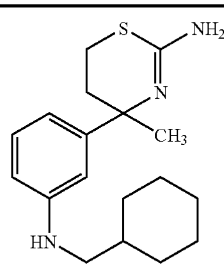
No.	Structure
120	

TABLE 14-continued

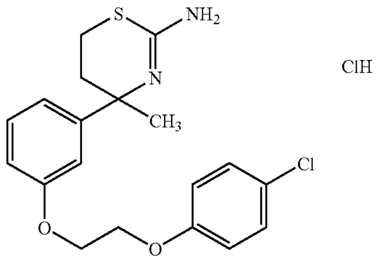
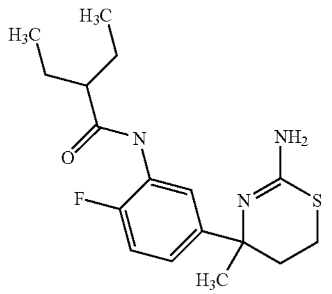
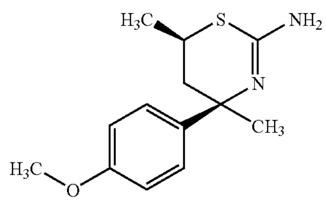
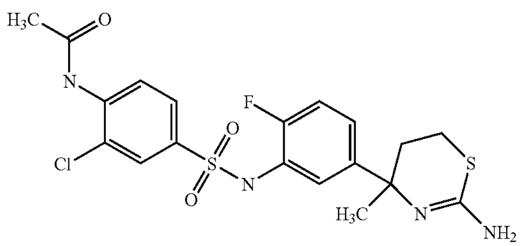
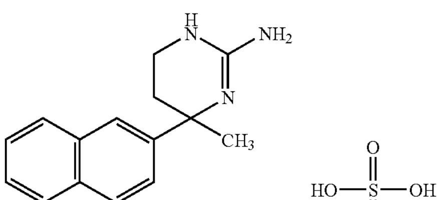
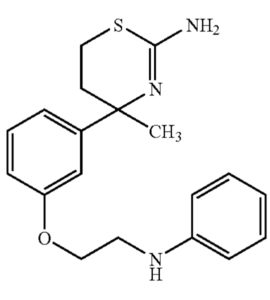
No.	Structure
121	
122	
123	
124	
125	
126	

TABLE 14-continued

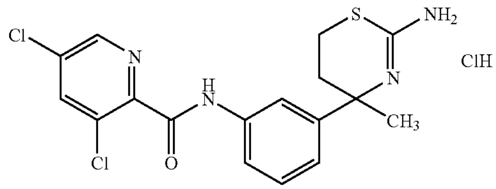
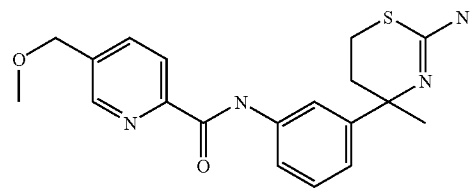
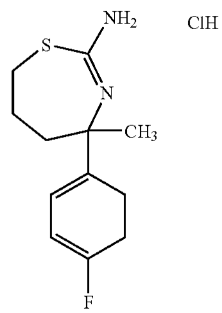
No.	Structure
127	
128	
129	

TABLE 15

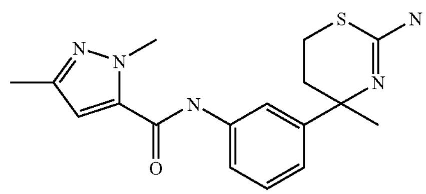
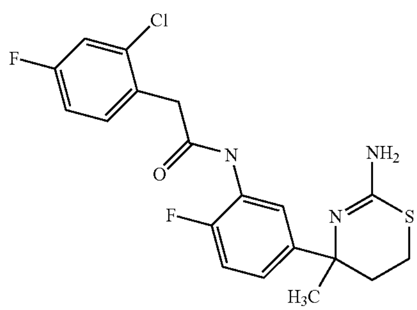
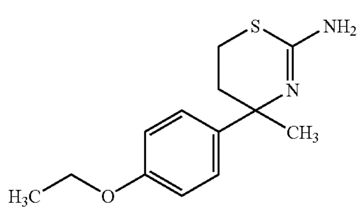
No.	Structure
130	
131	
132	

TABLE 15-continued

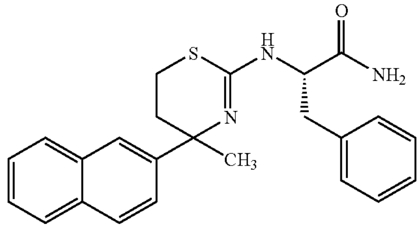
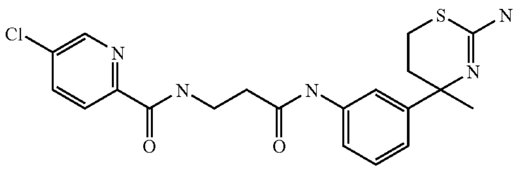
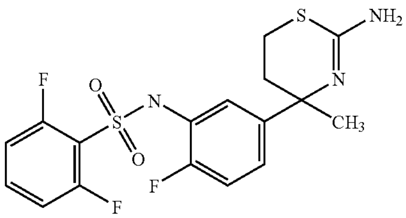
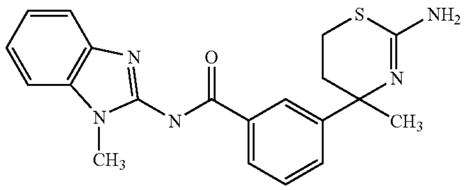
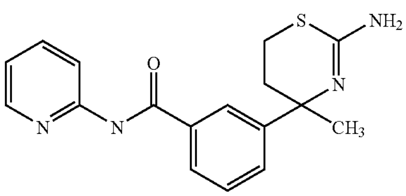
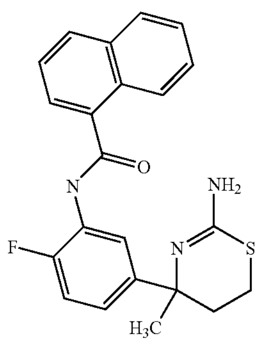
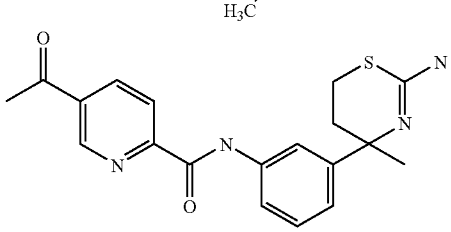
No.	Structure
133	 Chiral
134	
135	
136	
137	
138	
139	

TABLE 16

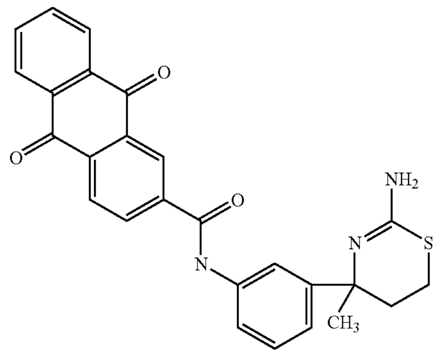
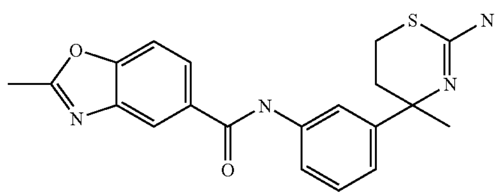
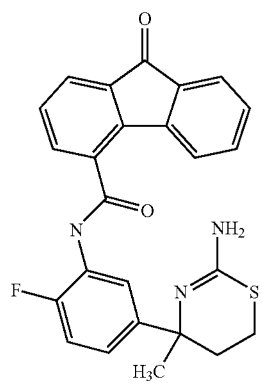
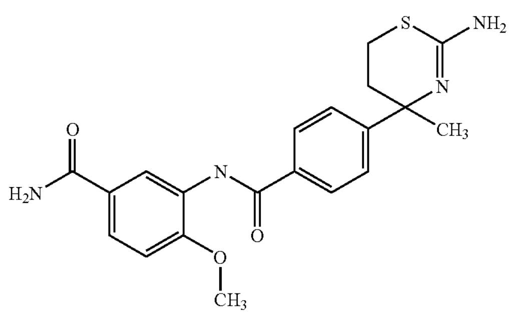
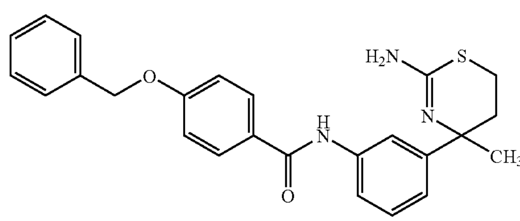
No.	Structure
140	
141	
142	
143	
144	

TABLE 16-continued

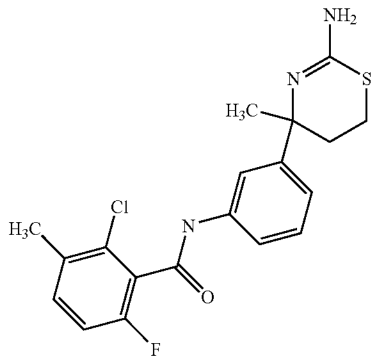
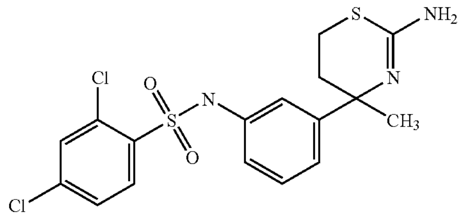
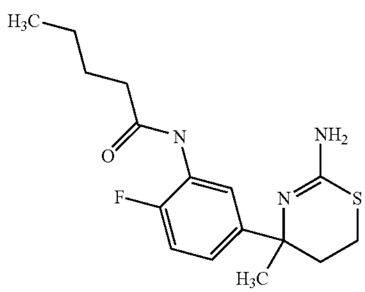
No.	Structure
145	
146	
147	

TABLE 17

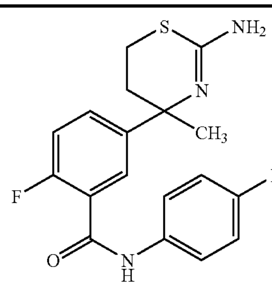
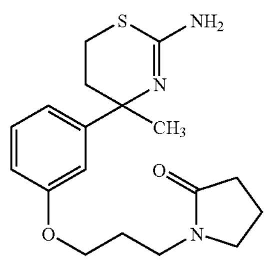
No.	Structure
148	
149	

TABLE 17-continued

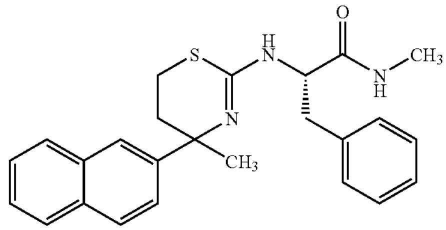
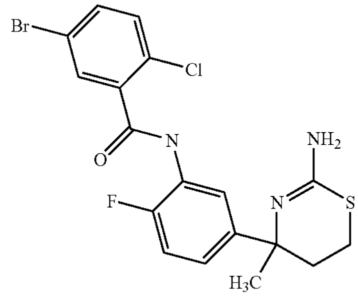
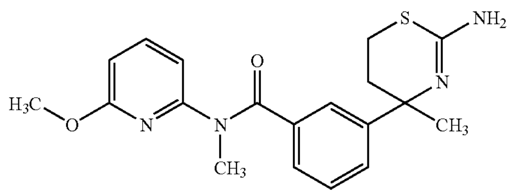
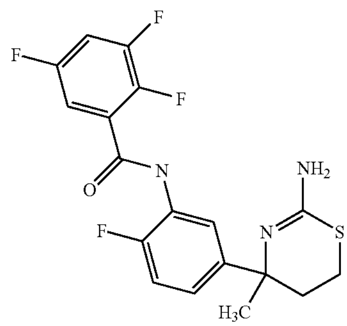
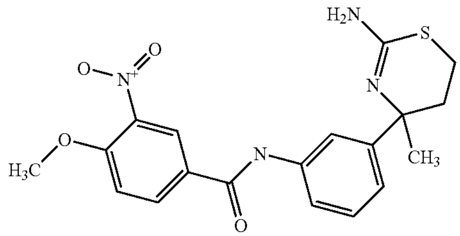
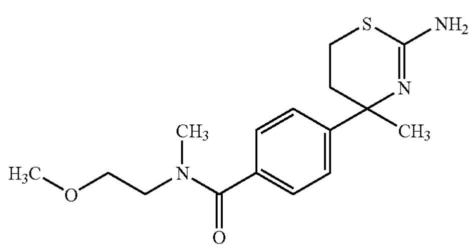
No.	Structure
150	 Chiral
151	
152	
153	
154	
155	

TABLE 17-continued

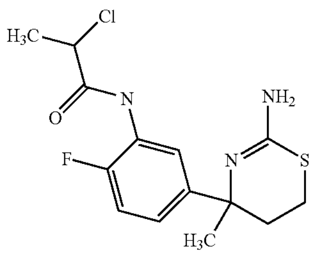
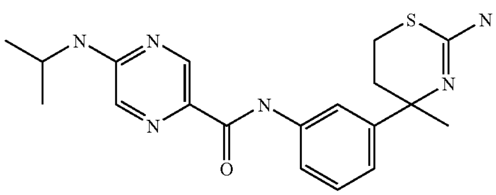
No.	Structure
156	
157	

TABLE 18

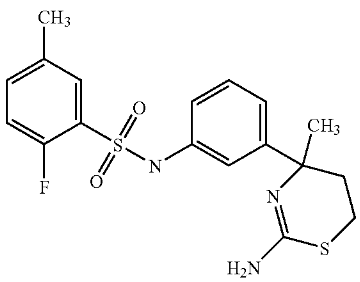
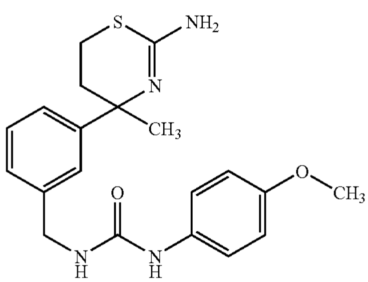
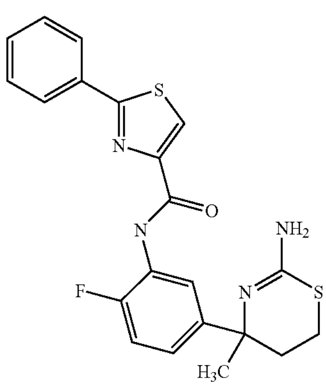
No.	Structure
158	
159	
160	

TABLE 18-continued

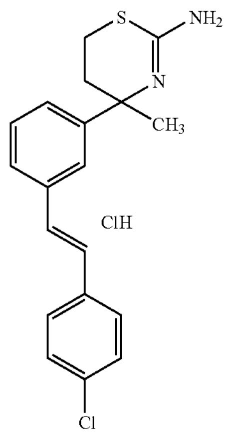
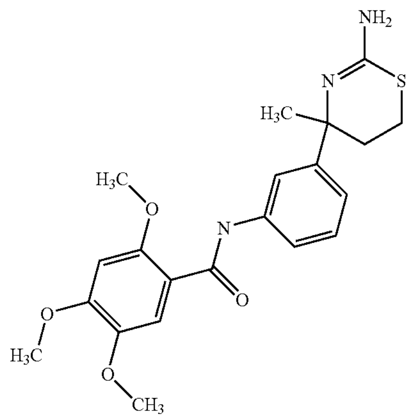
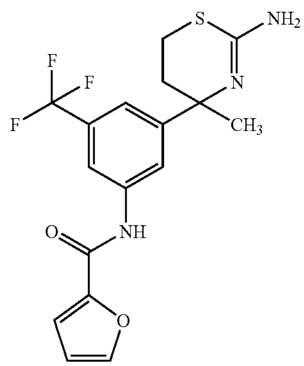
No.	Structure
161	
162	
163	

TABLE 19

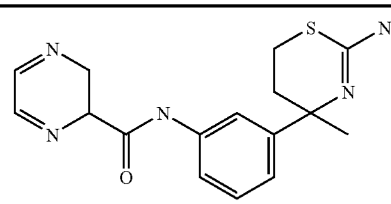
No.	Structure
164	

TABLE 19-continued

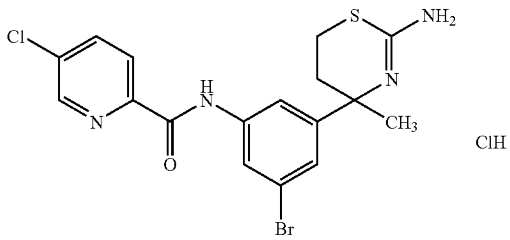
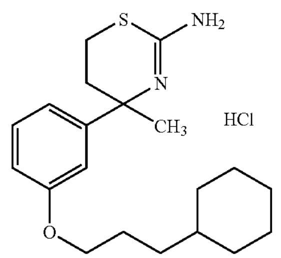
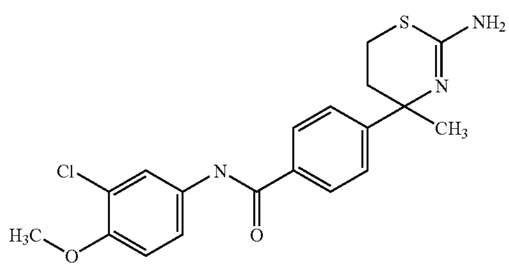
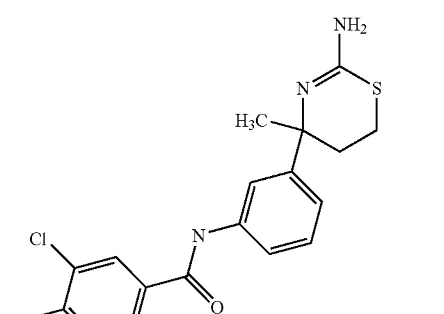
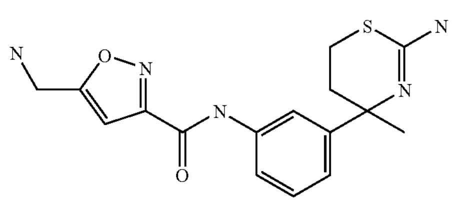
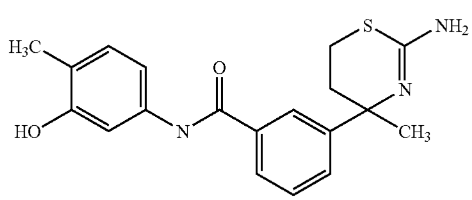
No.	Structure
165	
166	
167	
168	
169	
170	

TABLE 19-continued

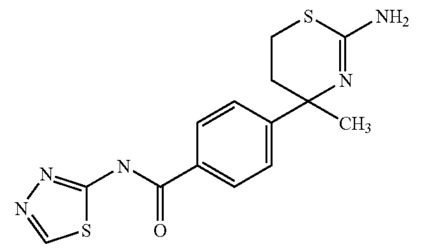
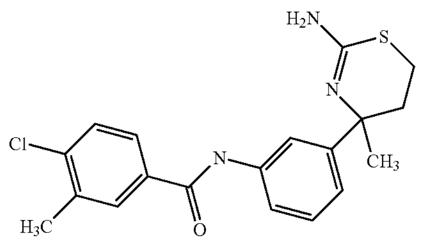
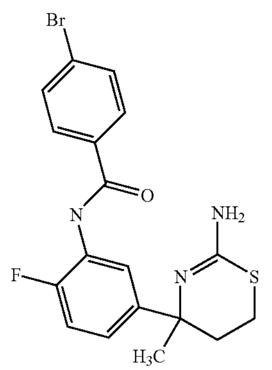
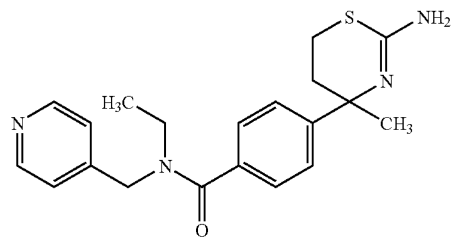
No.	Structure
171	
172	
173	
174	

TABLE 20

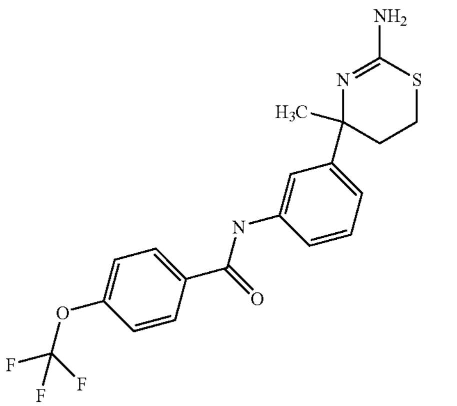
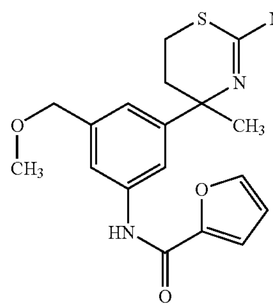
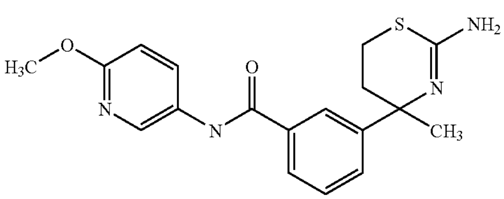
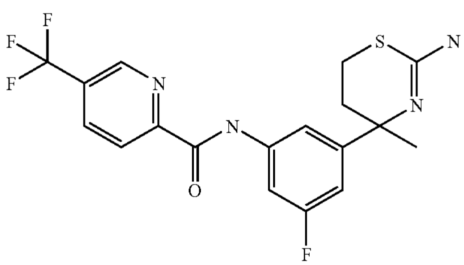
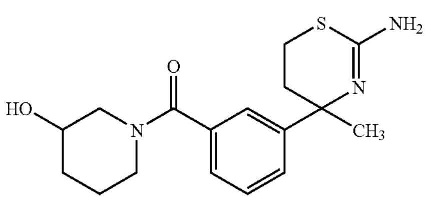
No.	Structure
175	
176	
177	
178	
179	

TABLE 20-continued

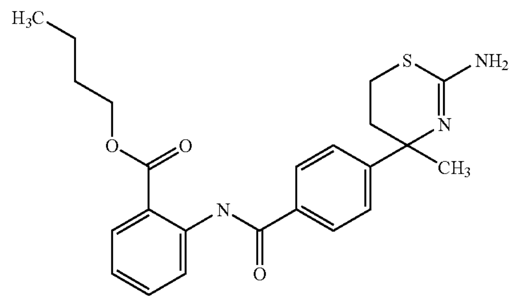
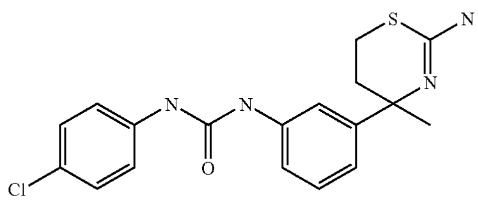
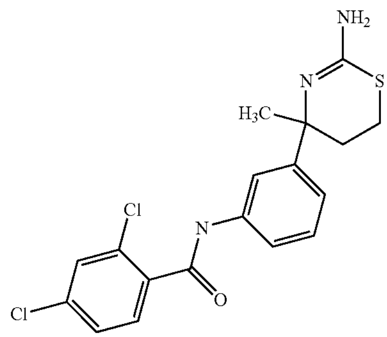
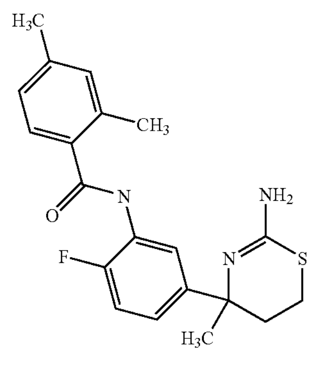
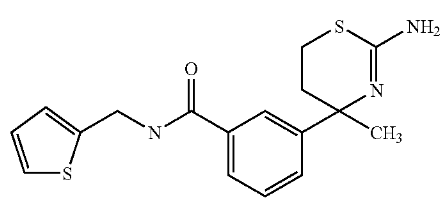
No.	Structure
180	
181	
182	
183	
184	

TABLE 20-continued

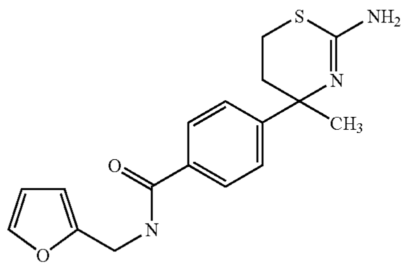
No.	Structure
185	

TABLE 21

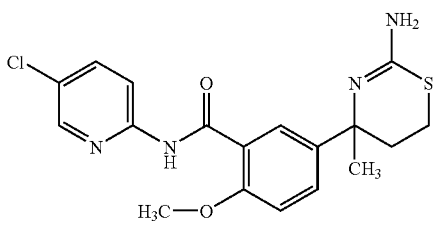
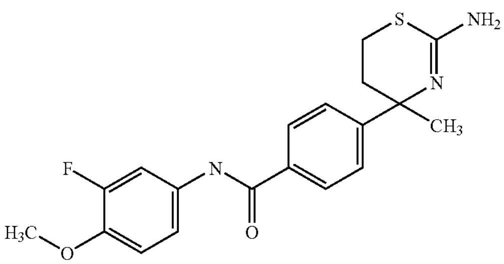
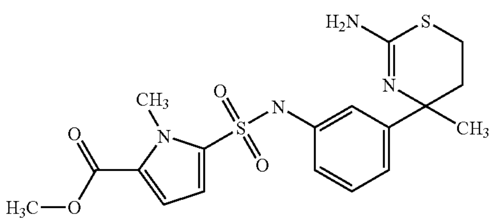
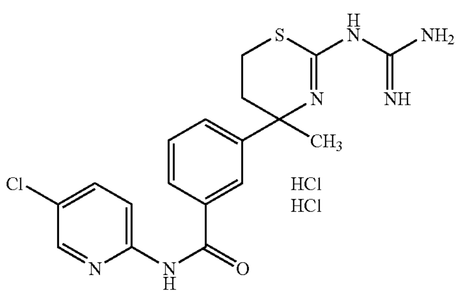
No.	Structure
186	
187	
188	
189	

TABLE 21-continued

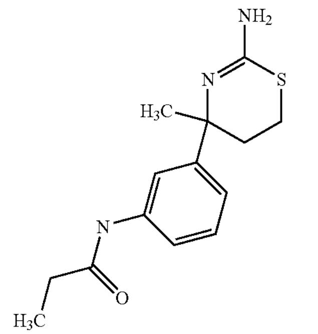
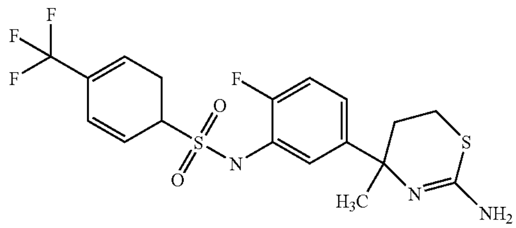
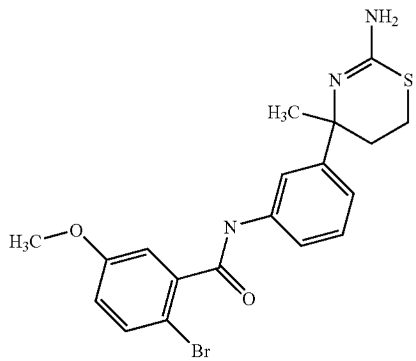
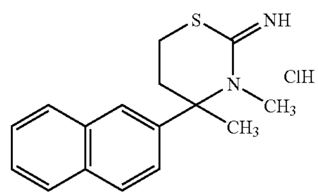
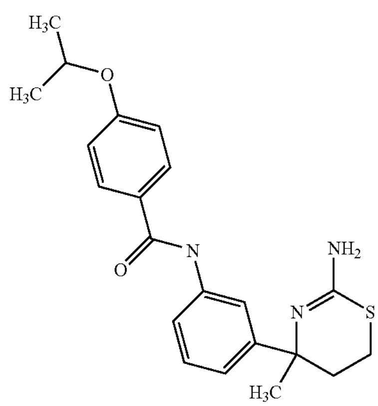
No.	Structure
190	
191	
192	
193	
194	

TABLE 22

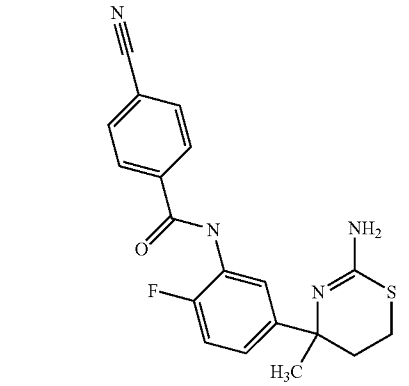
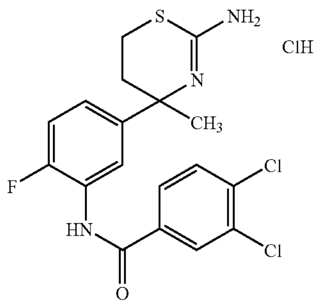
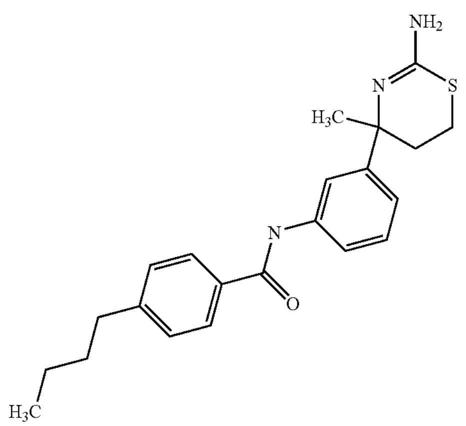
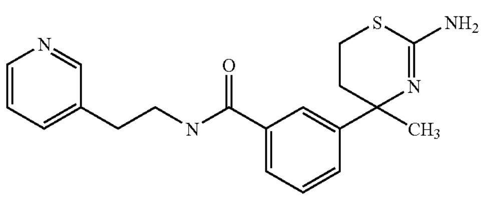
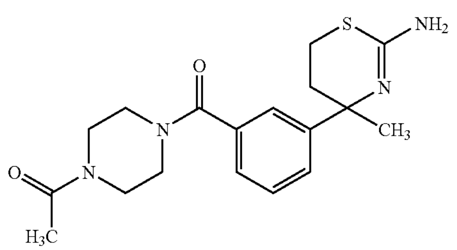
No.	Structure
195	
196	
197	
198	
199	

TABLE 22-continued

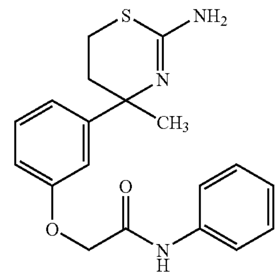
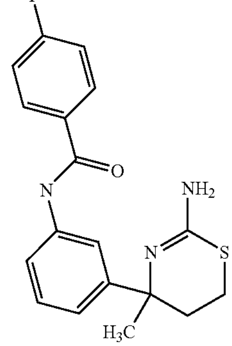
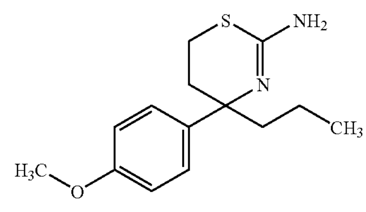
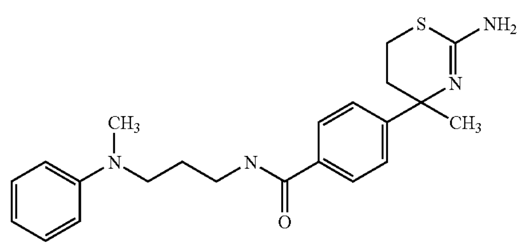
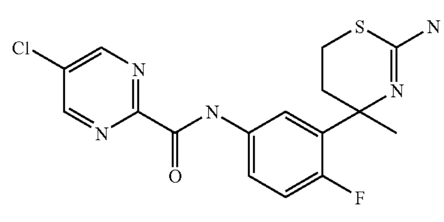
No.	Structure
200	
201	
202	
203	
204	

TABLE 23

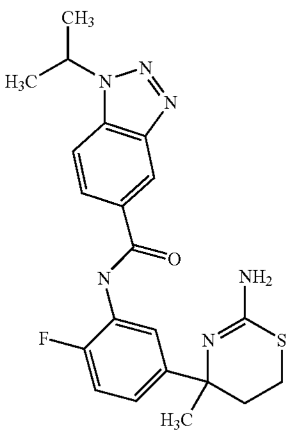
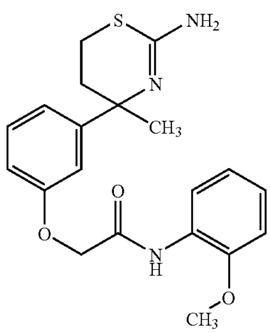
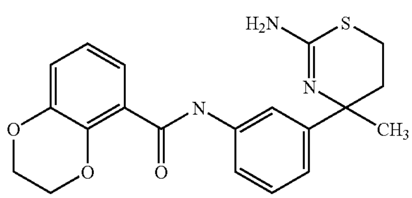
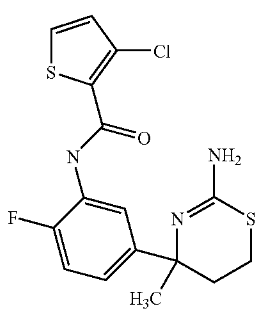
No.	Structure
205	
206	
207	
208	

TABLE 23-continued

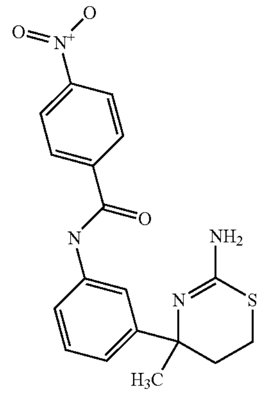
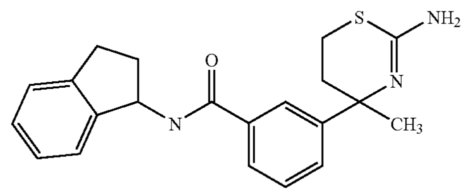
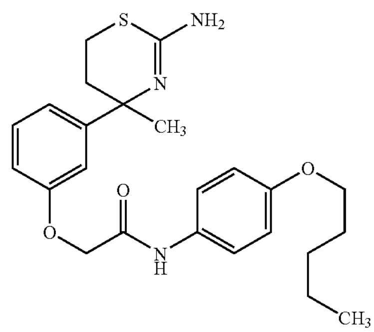
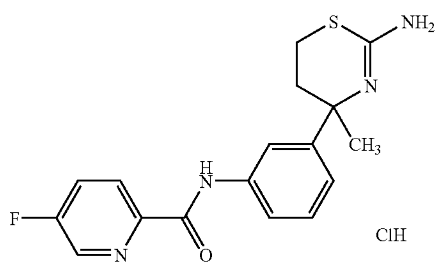
No.	Structure
209	
210	
211	
212	

TABLE 24

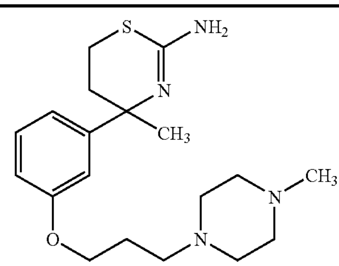
No.	Structure
213	

TABLE 24-continued

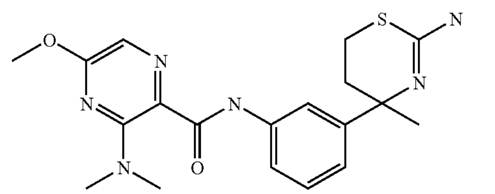
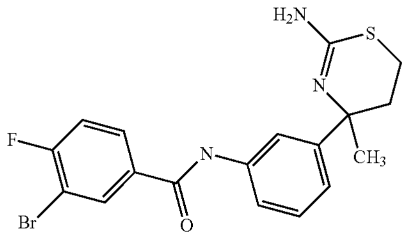
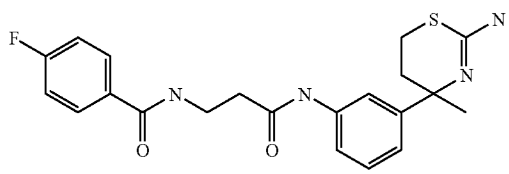
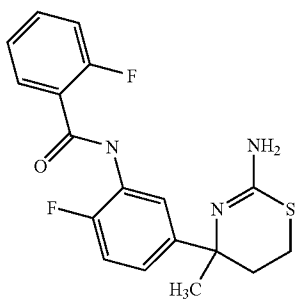
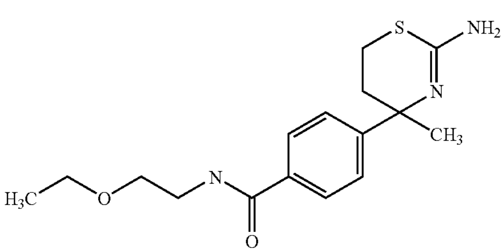
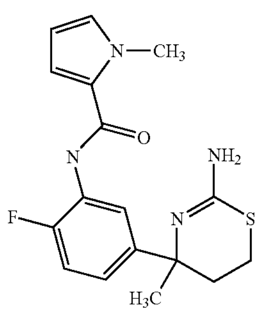
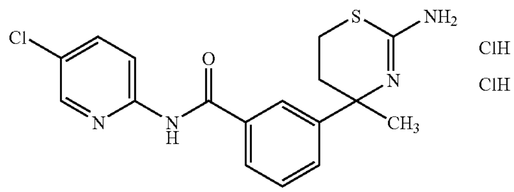
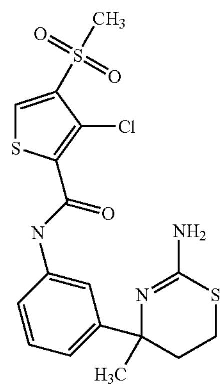
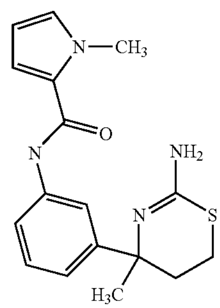
No.	Structure
214	
215	
216	
217	
218	
219	
220	
221	
222	

TABLE 25

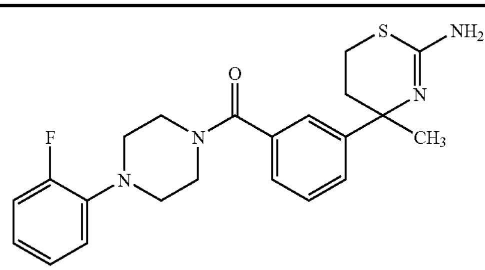
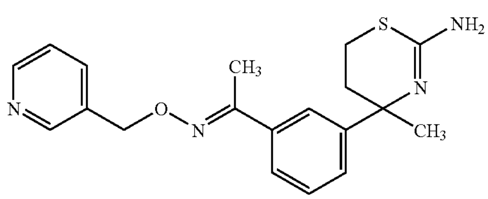
No.	Structure
223	
224	

TABLE 25-continued

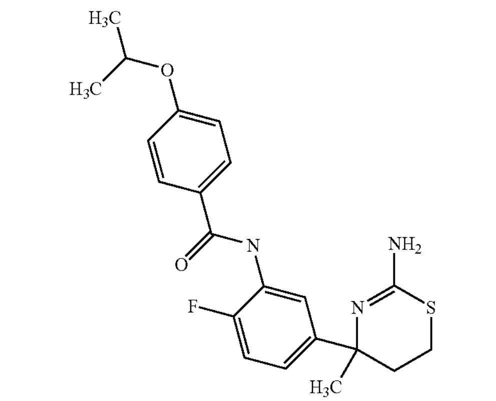
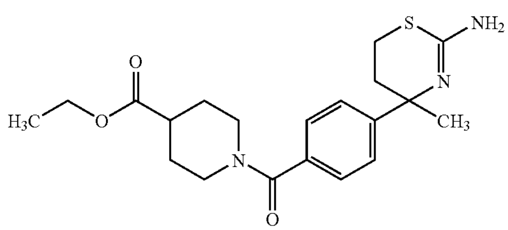
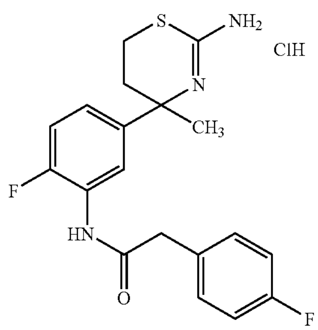
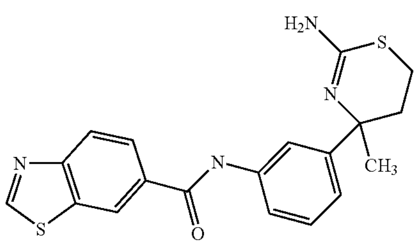
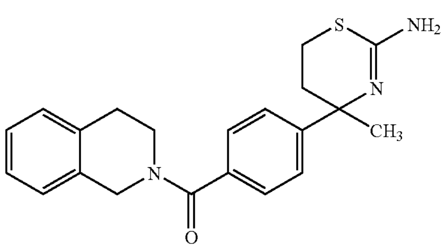
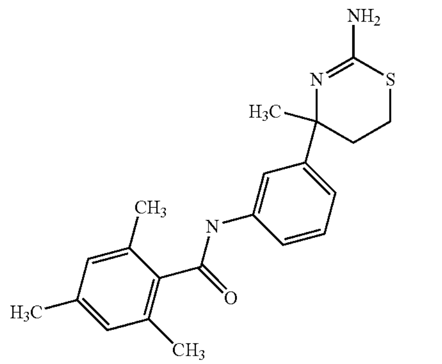
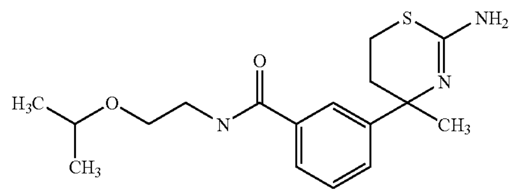
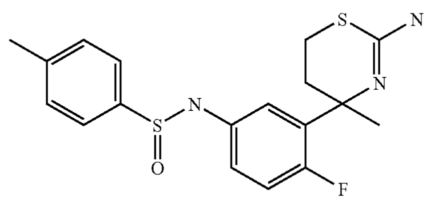
No.	Structure
225	
226	
227	
228	
229	
230	
231	
232	

TABLE 26

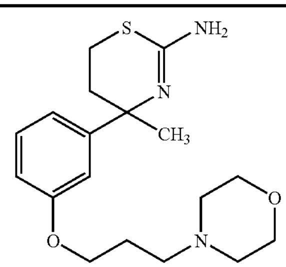
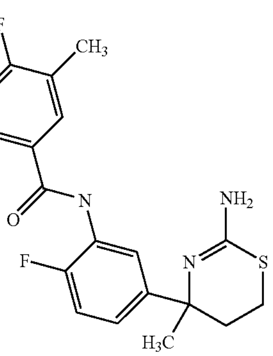
No.	Structure
233	
234	

TABLE 26-continued

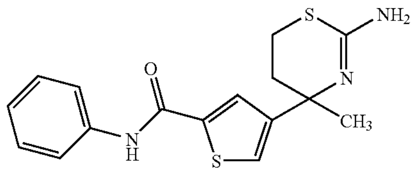
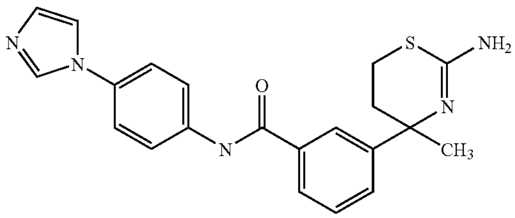
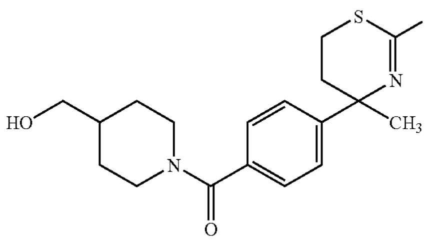
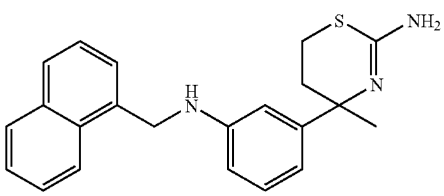
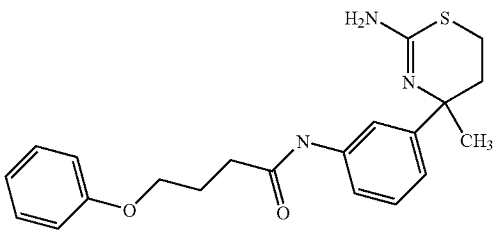
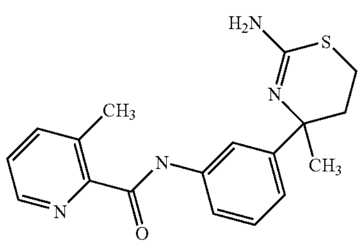
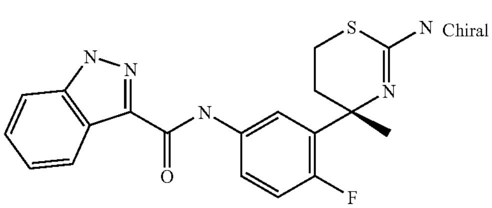
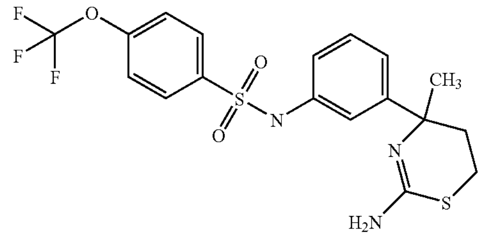
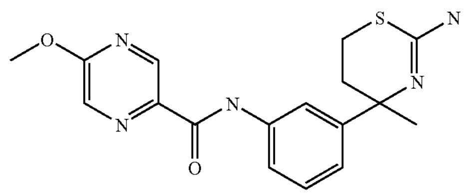
No.	Structure
235	
236	
237	
238	
239	
240	
241	
242	
243	

TABLE 27

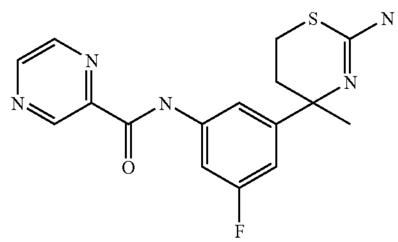
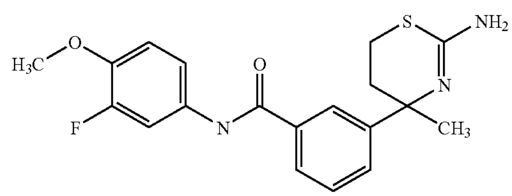
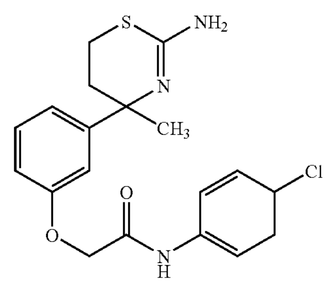
No.	Structure
244	
245	
246	

TABLE 27-continued

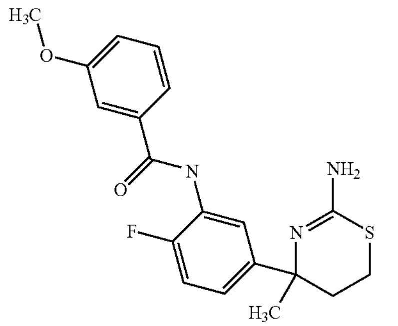
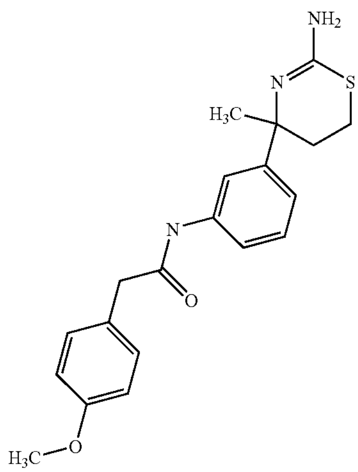
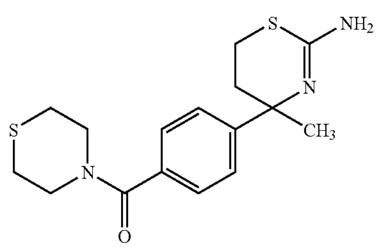
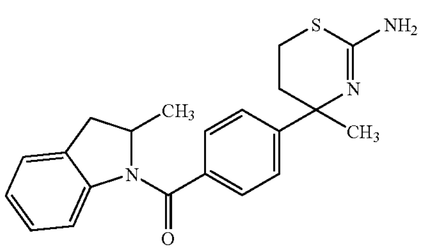
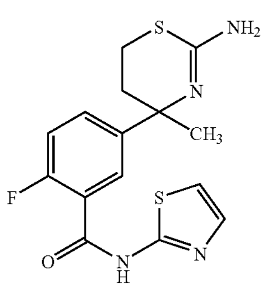
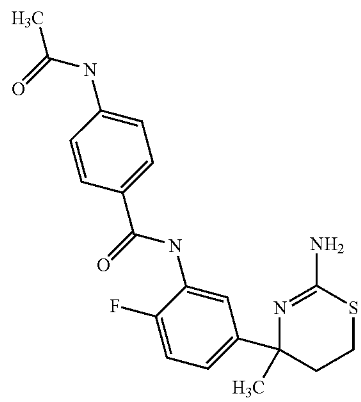
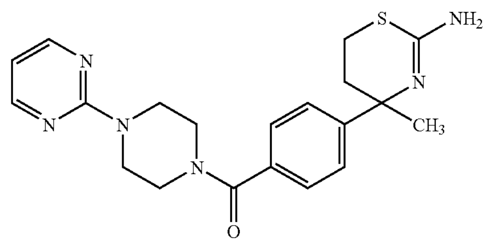
No.	Structure
247	
248	
249	
250	
251	
252	
253	

TABLE 28

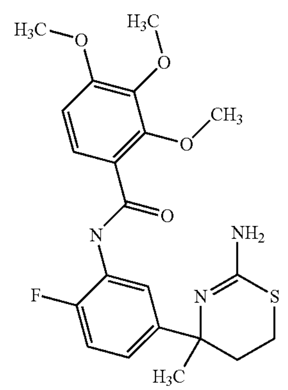
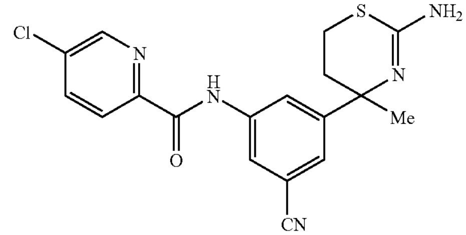
No.	Structure
254	
255	

TABLE 28-continued

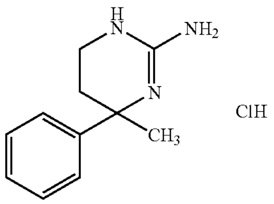
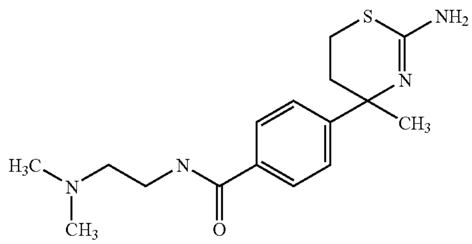
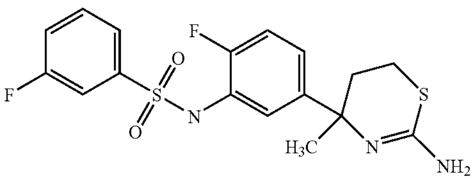
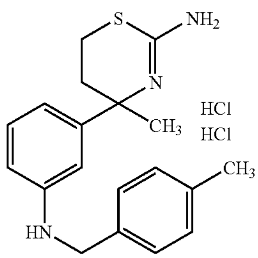
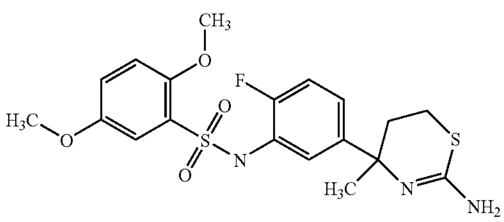
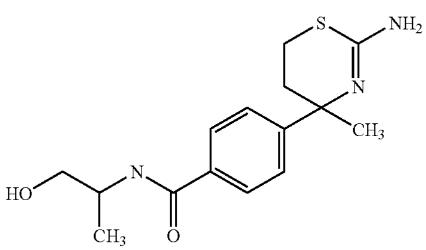
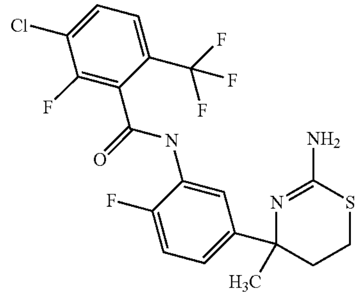
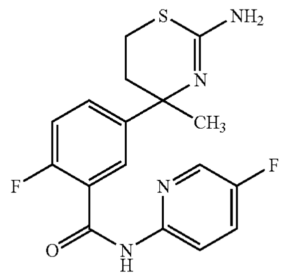
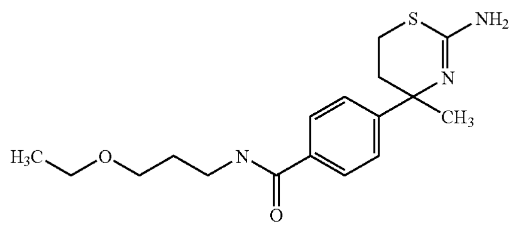
No.	Structure
256	
257	
258	
259	
260	
261	
262	
263	
264	

TABLE 29

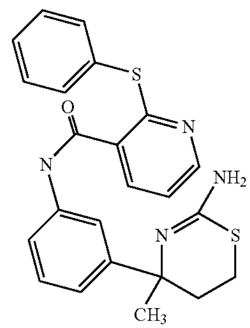
No.	Structure
265	

TABLE 29-continued

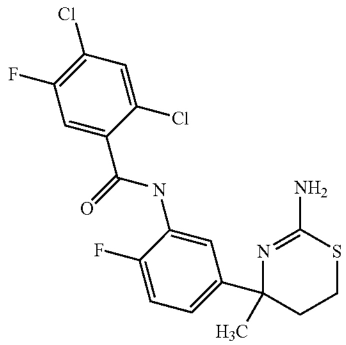
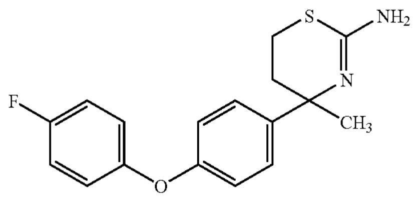
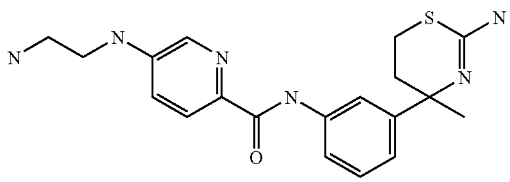
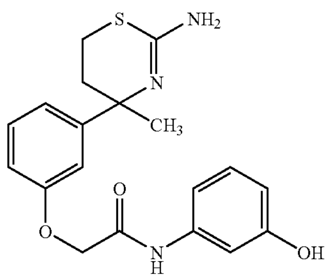
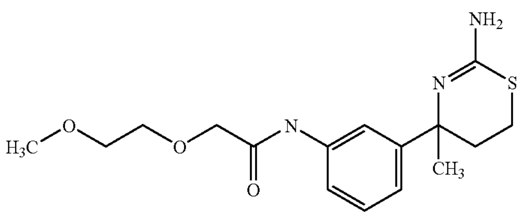
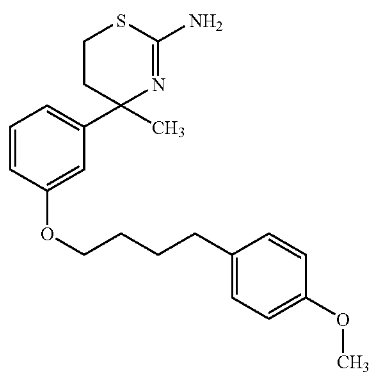
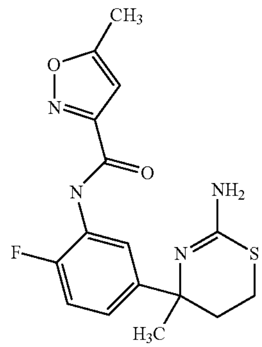
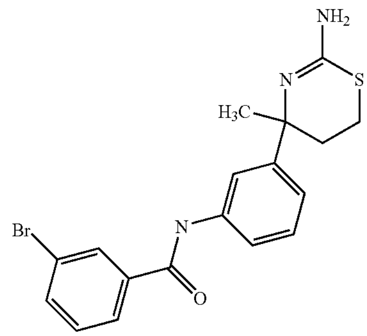
No.	Structure
266	
267	
268	
269	
270	
271	
272	
273	

TABLE 30

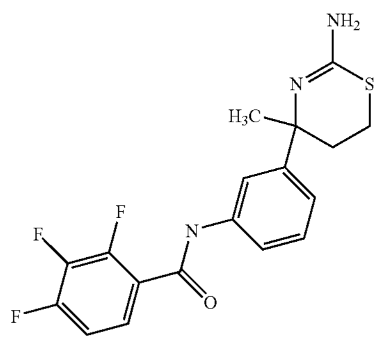
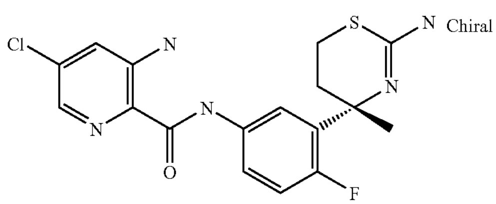
No.	Structure
274	
275	

TABLE 30-continued

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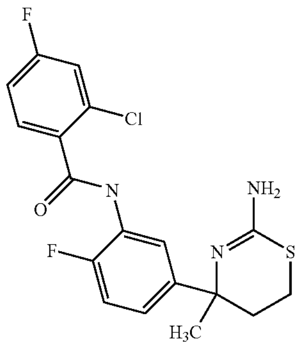
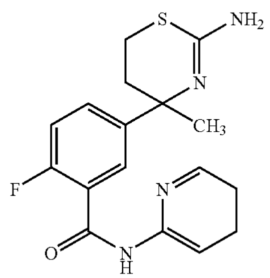
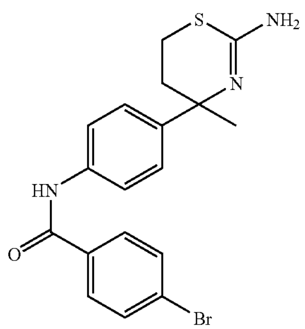
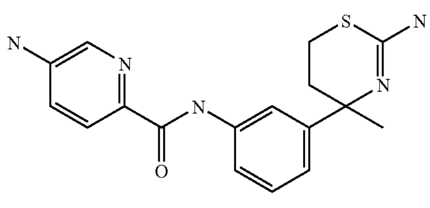
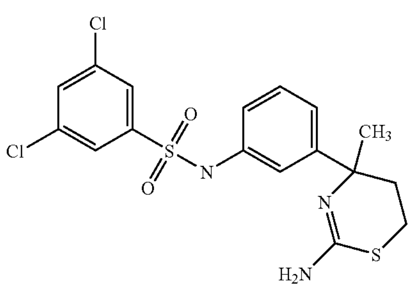
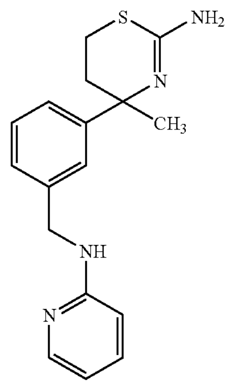
276	
277	
278	
279	
280	
281	

TABLE 31

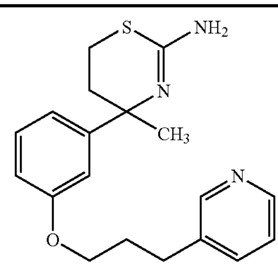
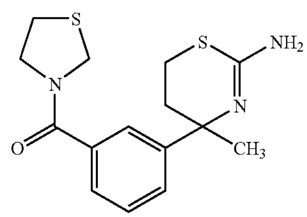
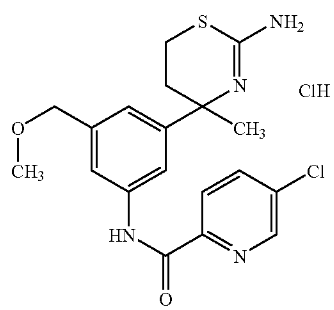
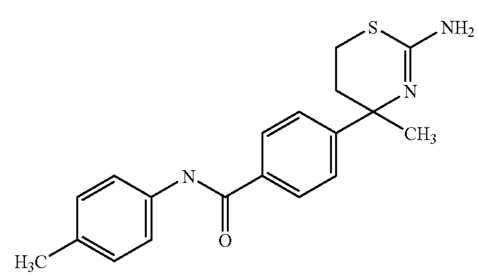
No.	Structure
282	
283	
284	
285	

TABLE 31-continued

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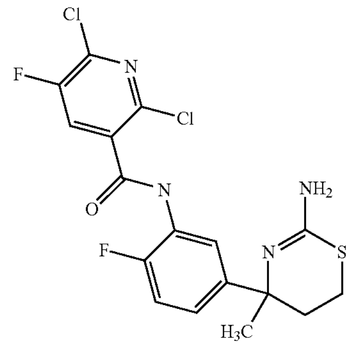
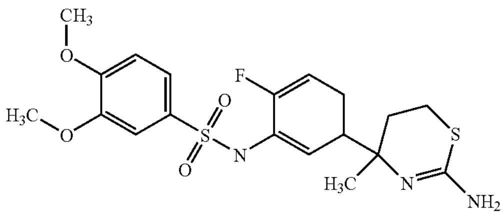
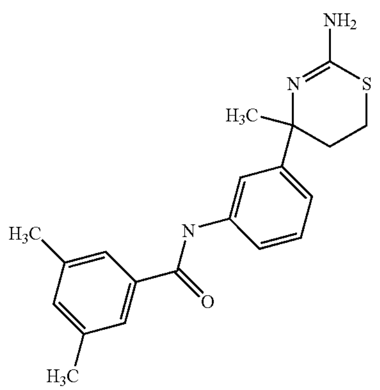
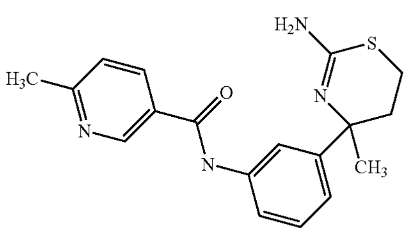
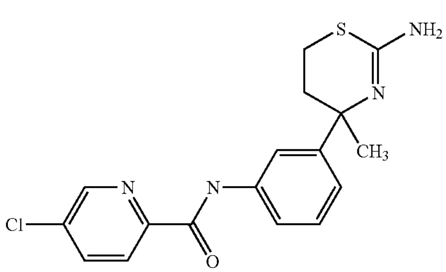
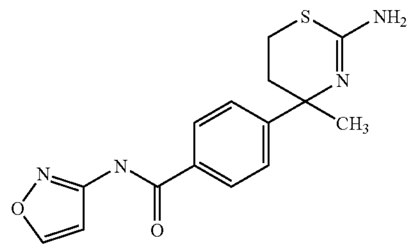
286	
287	
288	
289	
290	
291	

TABLE 32

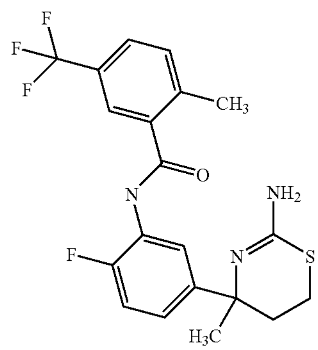
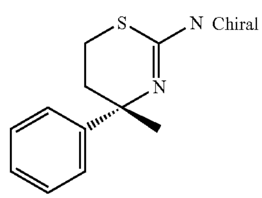
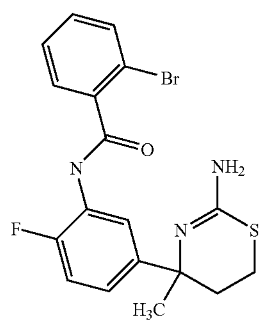
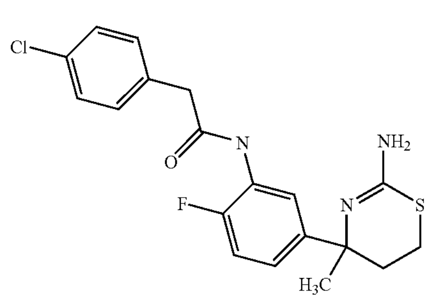
No.	Structure
292	
293	
294	
295	

TABLE 32-continued

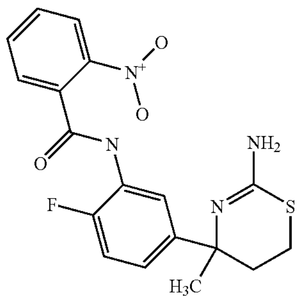
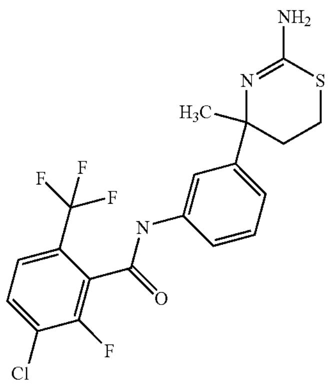
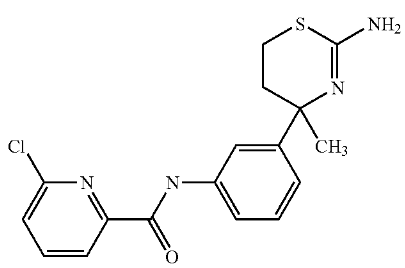
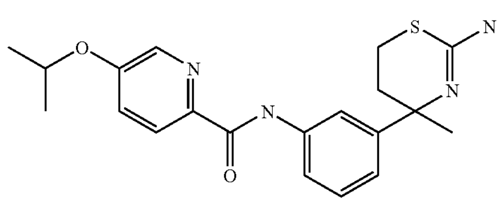
No.	Structure
296	
297	
298	
299	

TABLE 33

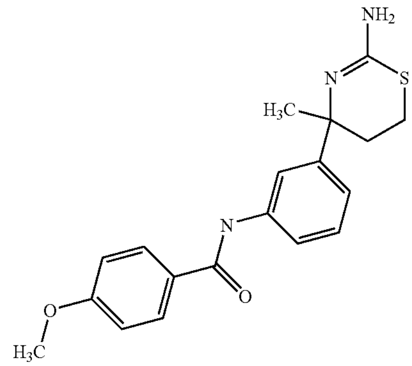
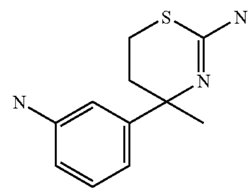
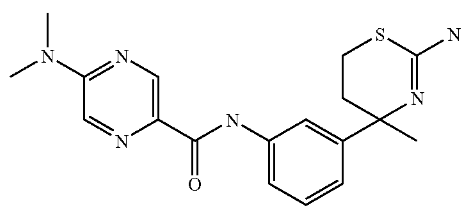
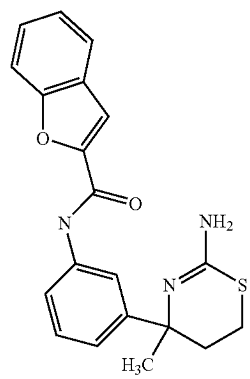
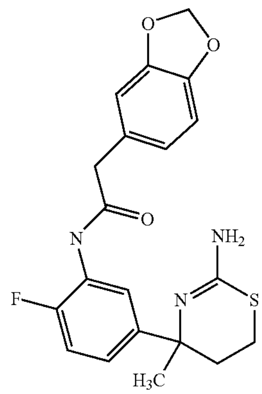
No.	Structure
300	
301	
302	
303	
304	

TABLE 33-continued

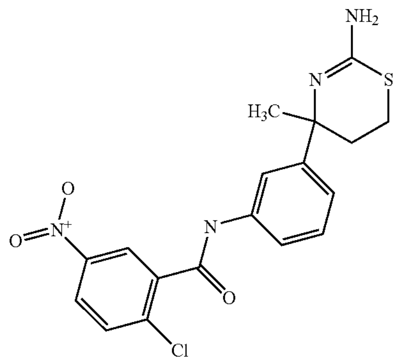
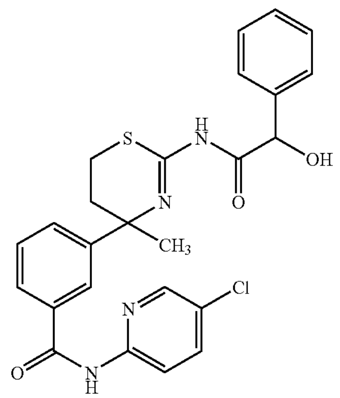
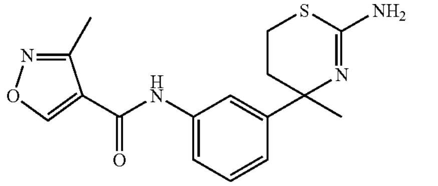
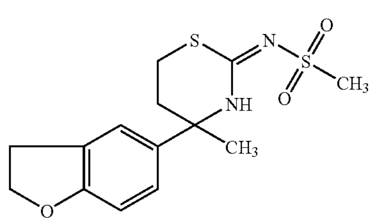
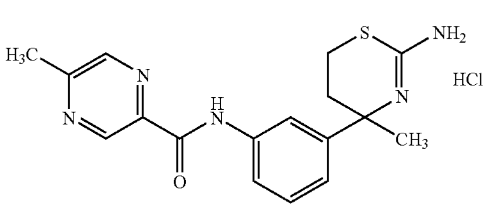
No.	Structure
305	
306	
307	
308	
309	

TABLE 34

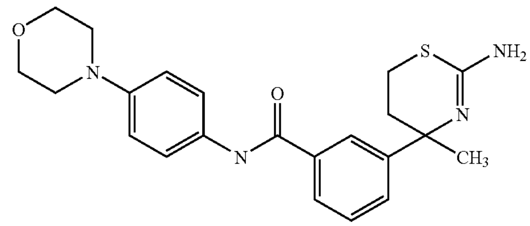
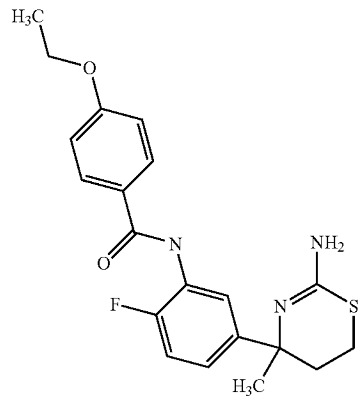
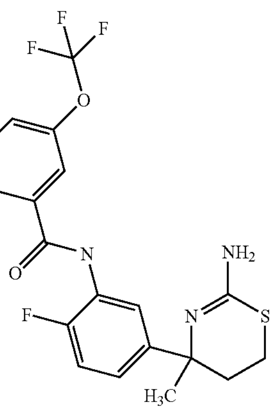
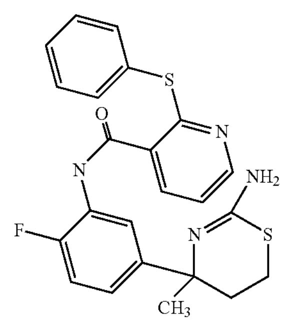
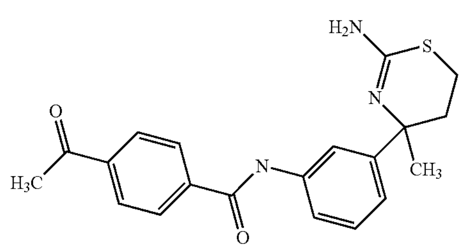
No.	Structure
310	
311	
312	
313	
314	

TABLE 34-continued

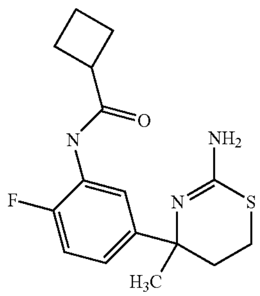
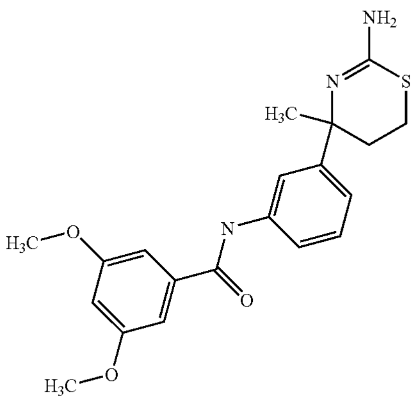
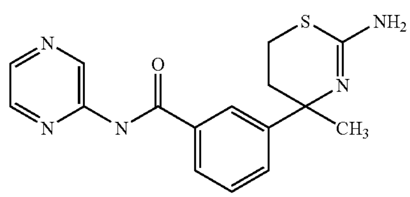
No.	Structure
315	
316	
317	

TABLE 35

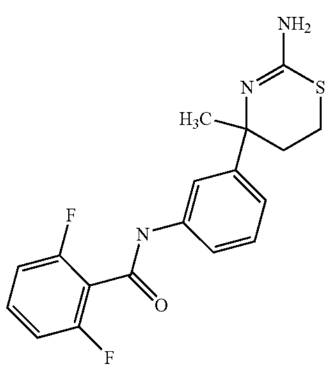
No.	Structure
318	

TABLE 35-continued

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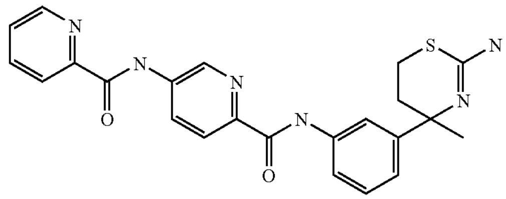
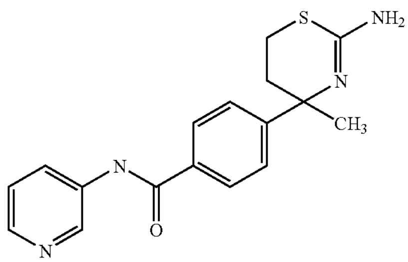
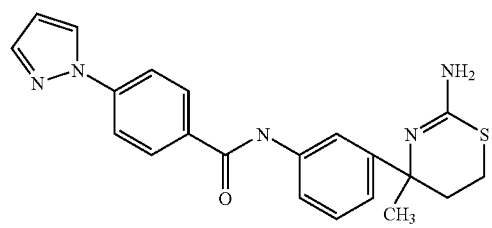
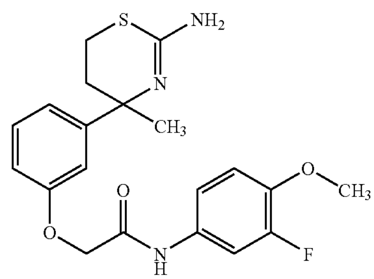
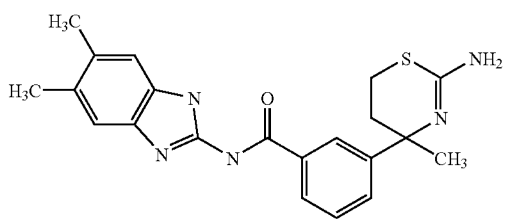
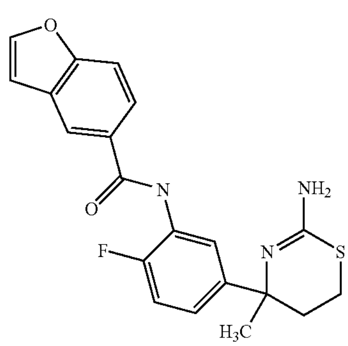
319	
320	
321	
322	
323	
324	

TABLE 35-continued

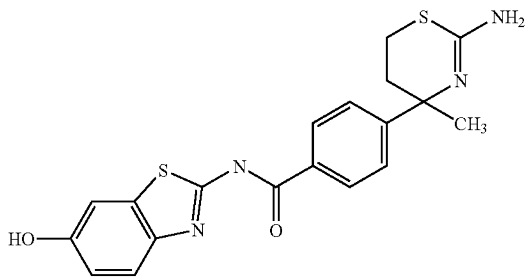
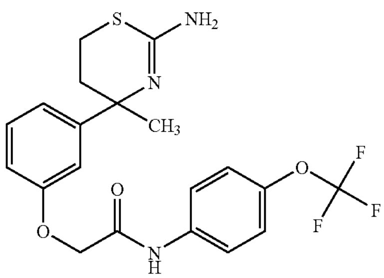
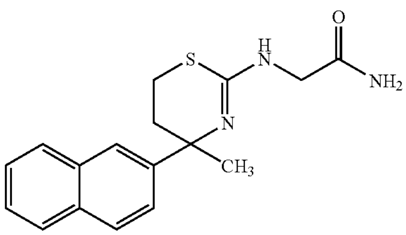
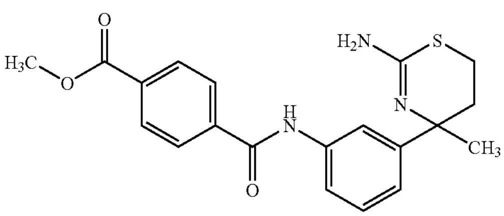
No.	Structure
325	
326	
327	
328	

TABLE 36

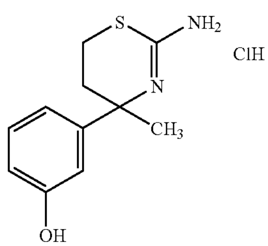
No.	Structure
329	

TABLE 36-continued

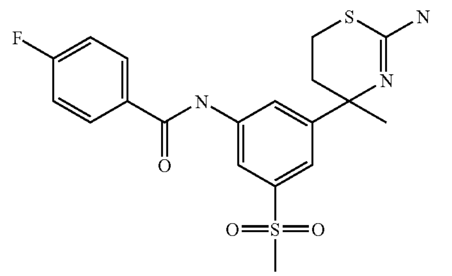
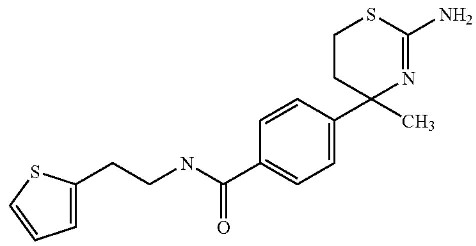
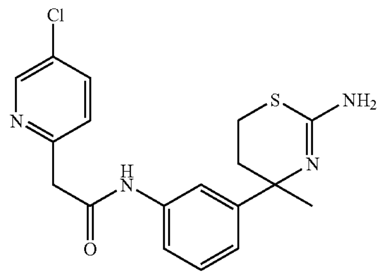
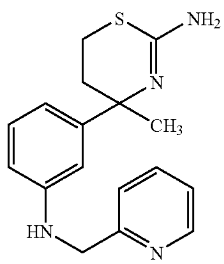
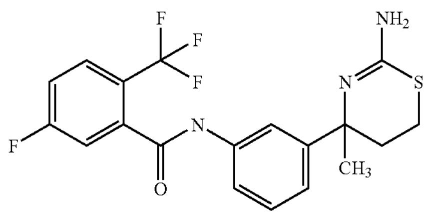
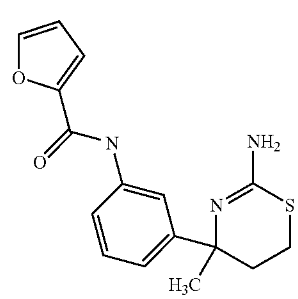
No.	Structure
330	
331	
332	
333	
334	
335	

TABLE 36-continued

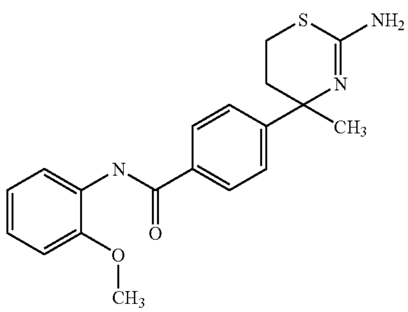
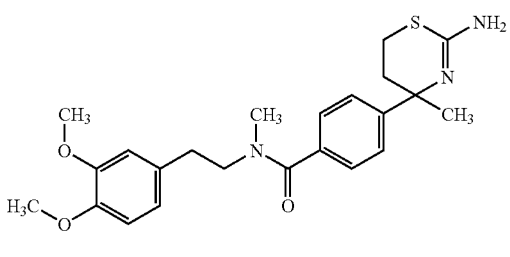
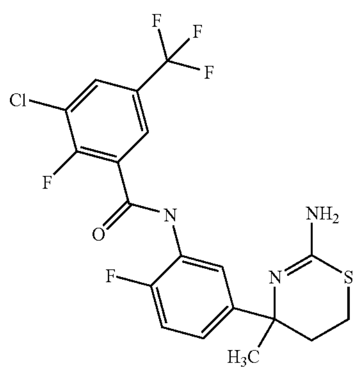
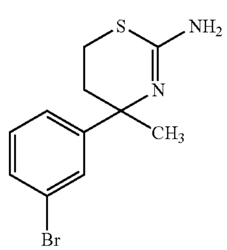
No.	Structure
336	
337	
338	
339	

TABLE 37

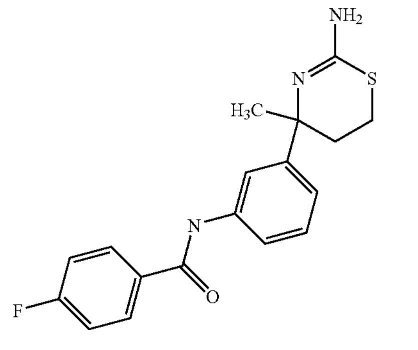
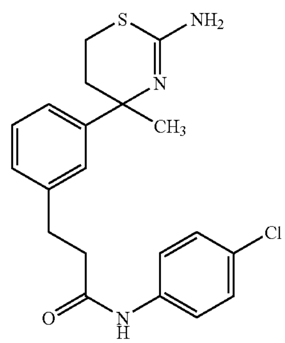
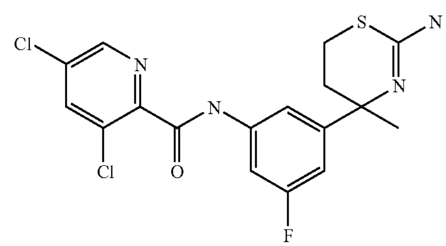
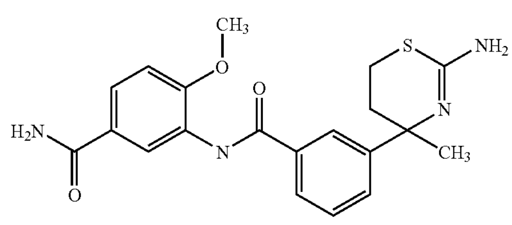
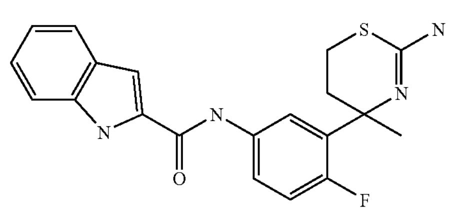
No.	Structure
340	
341	
342	
343	
344	

TABLE 37-continued

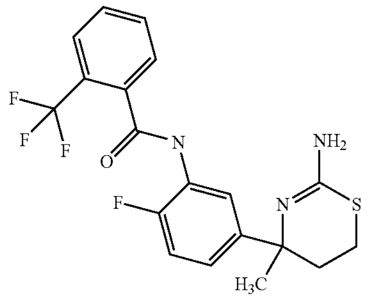
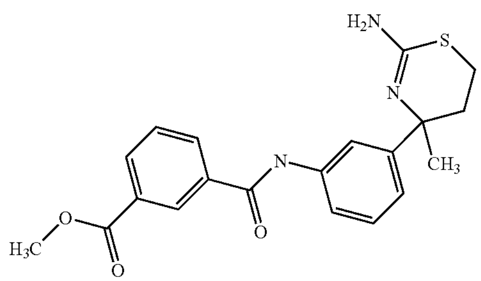
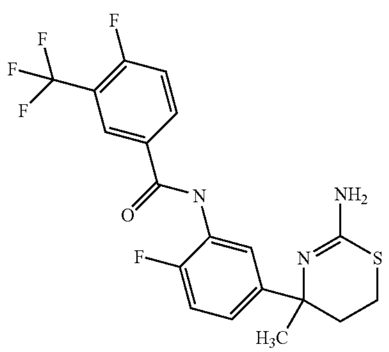
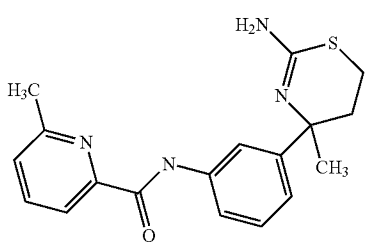
No.	Structure
345	
346	
347	
348	

TABLE 38

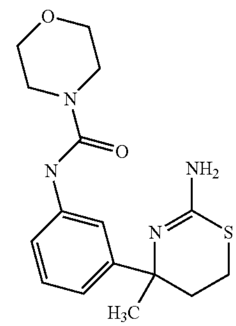
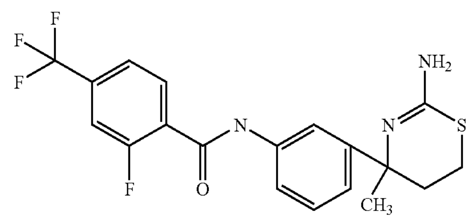
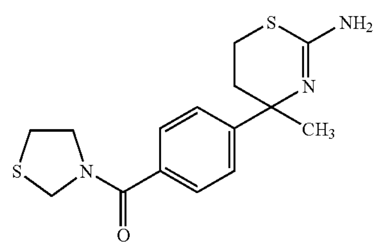
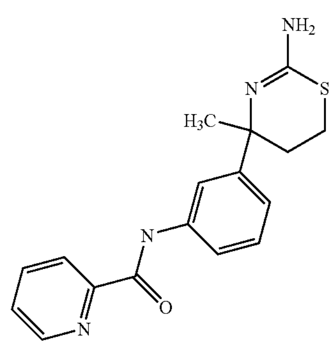
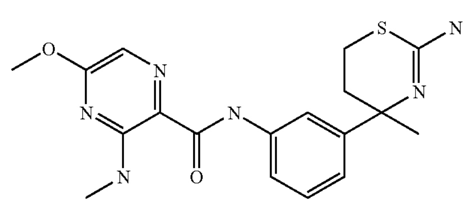
No.	Structure
349	
350	
351	
352	
353	

TABLE 38-continued

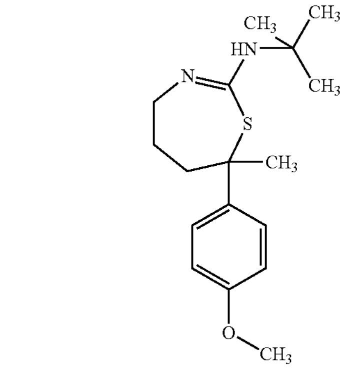
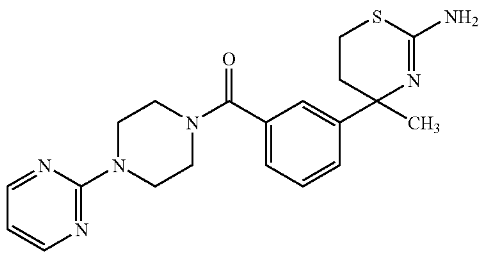
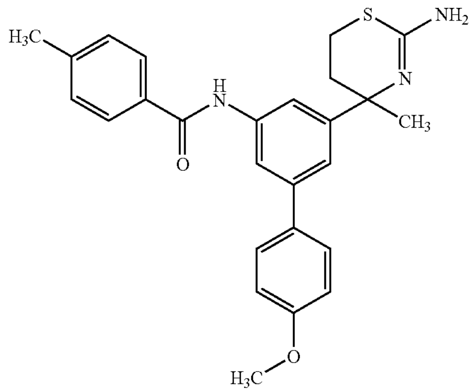
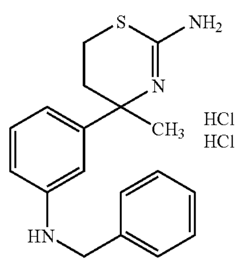
No.	Structure
354	
355	
356	
357	

TABLE 39

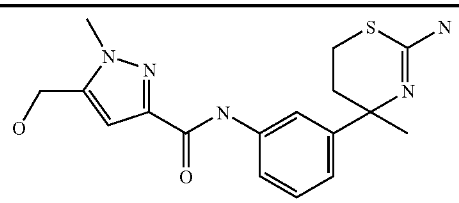
No.	Structure
358	

TABLE 39-continued

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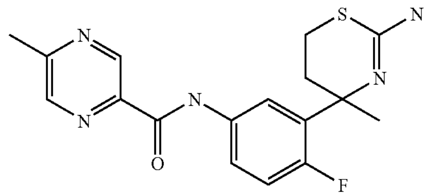
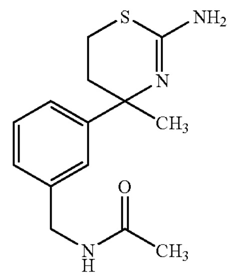
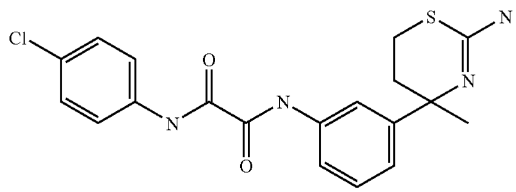
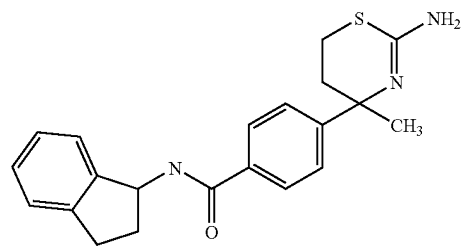
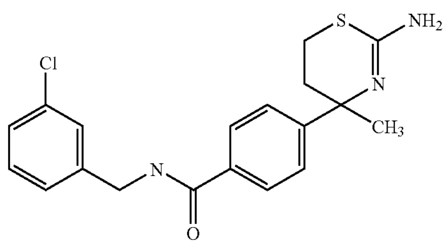
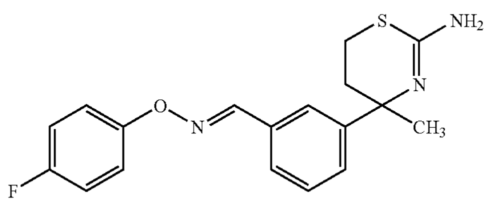
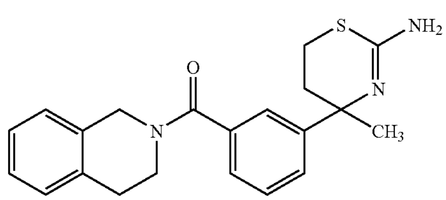
359	
360	
361	
362	
363	
364	
365	

TABLE 39-continued

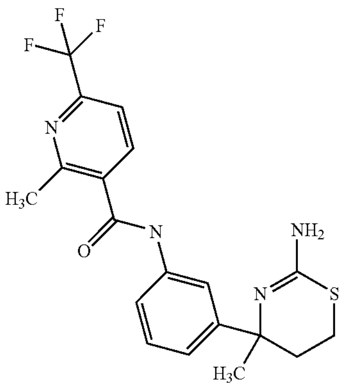
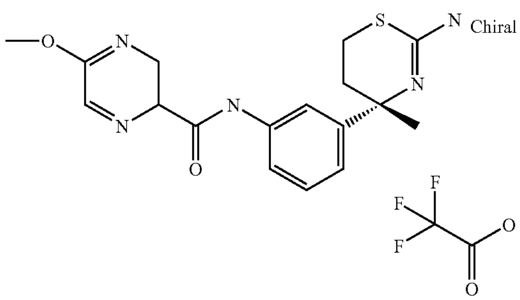
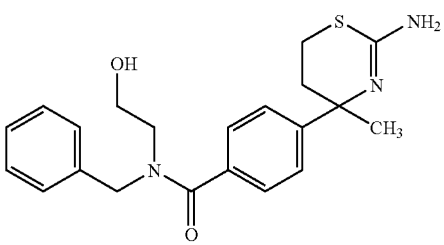
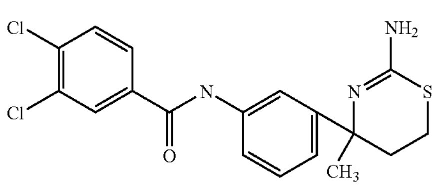
No.	Structure
366	
367	
368	
369	

TABLE 40

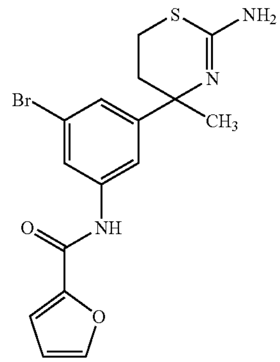
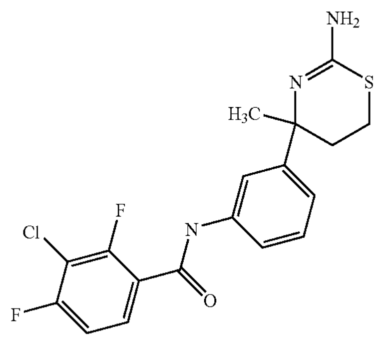
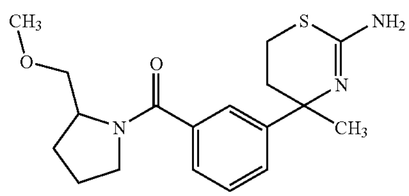
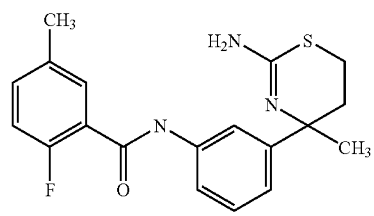
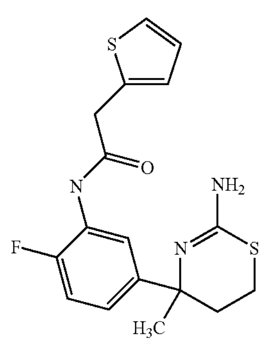
No.	Structure
370	
371	
372	
373	
374	

TABLE 40-continued

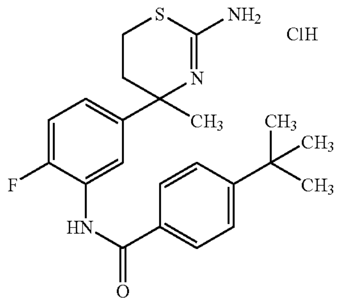
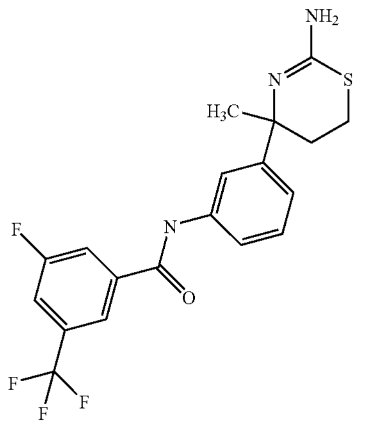
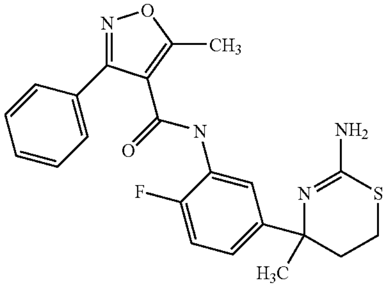
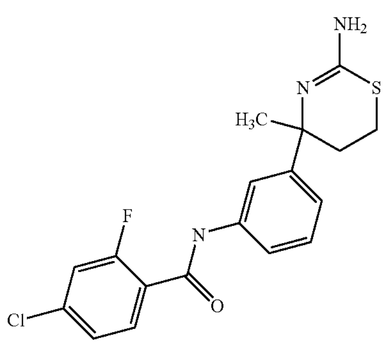
No.	Structure
375	
376	
377	
378	

TABLE 41

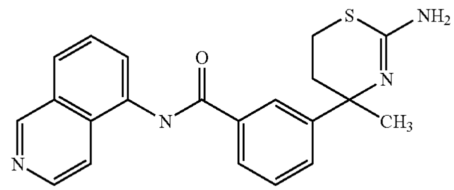
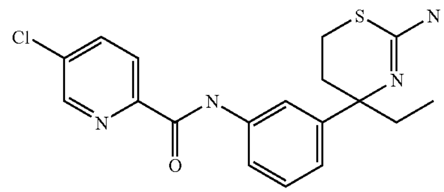
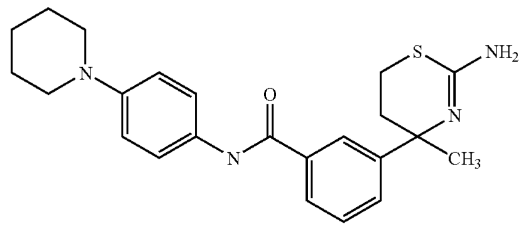
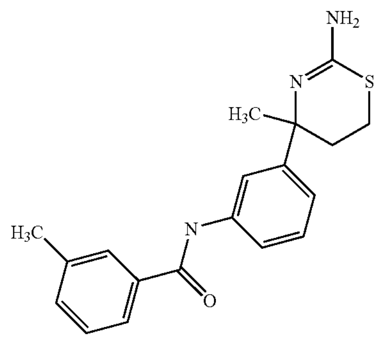
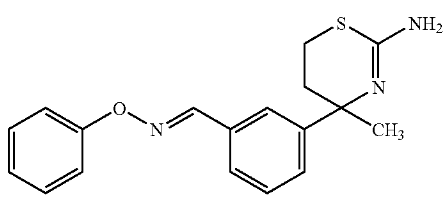
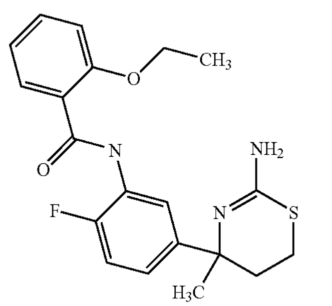
No.	Structure
379	
380	
381	
382	
383	
384	

TABLE 41-continued

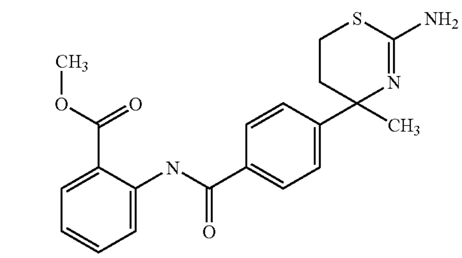
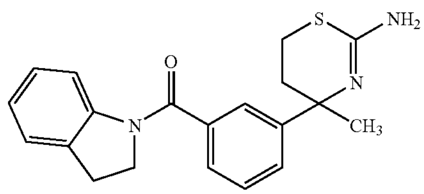
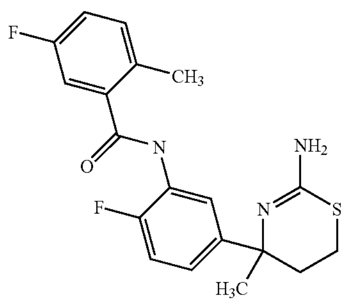
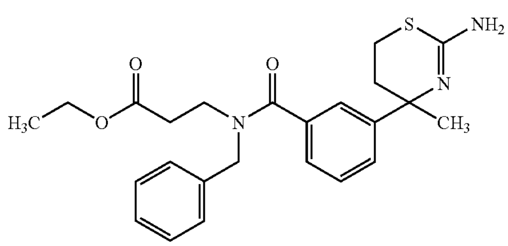
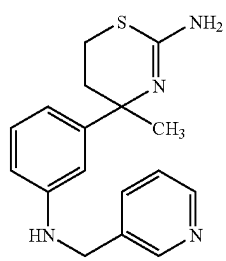
No.	Structure
385	
386	
387	
388	
389	

TABLE 42

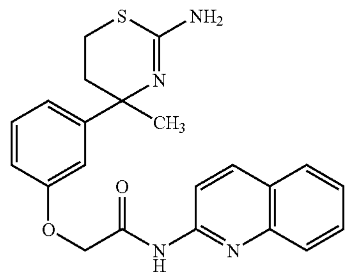
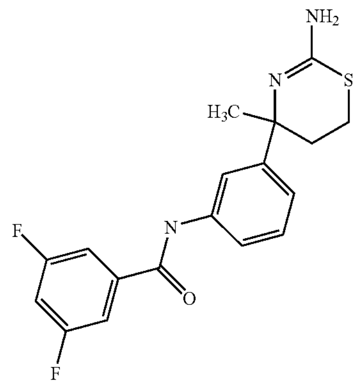
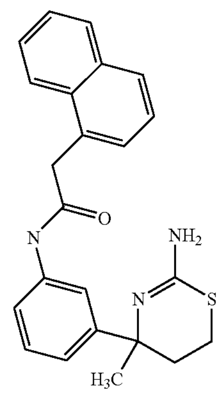
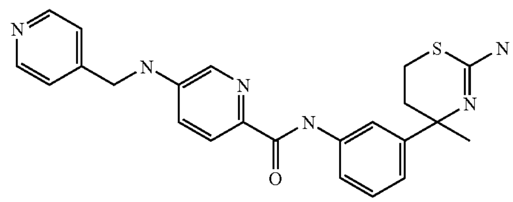
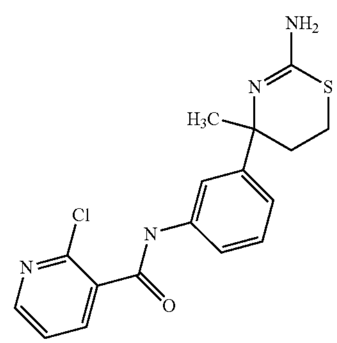
No.	Structure
390	
391	
392	
393	
394	

TABLE 42-continued

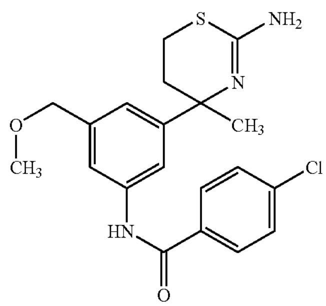
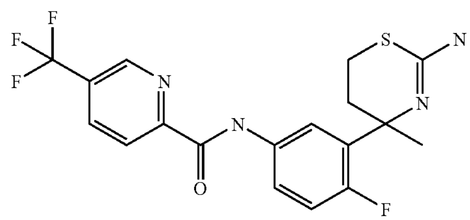
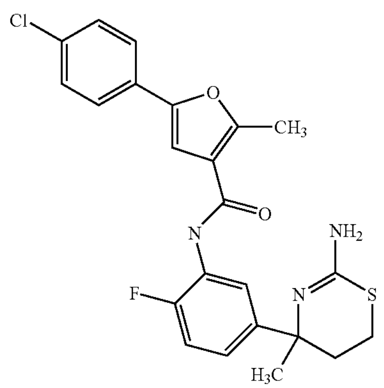
No.	Structure
395	
396	
397	

TABLE 43

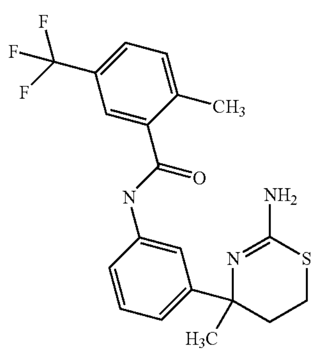
No.	Structure
398	

TABLE 43-continued

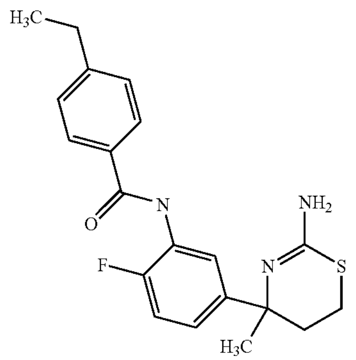
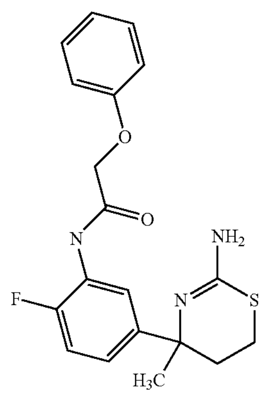
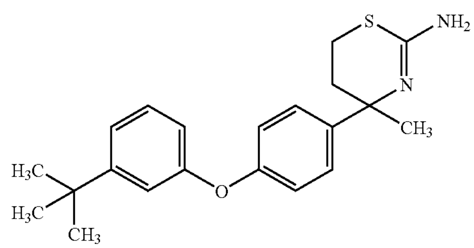
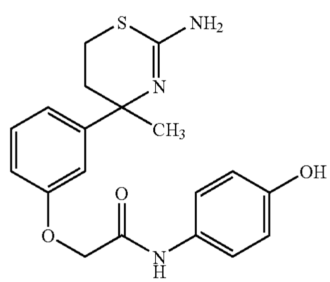
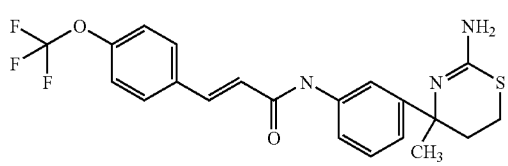
No.	Structure
399	
400	
401	
402	
403	

TABLE 43-continued

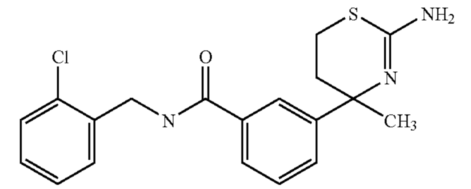
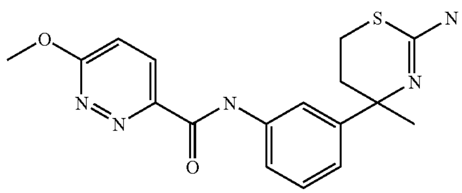
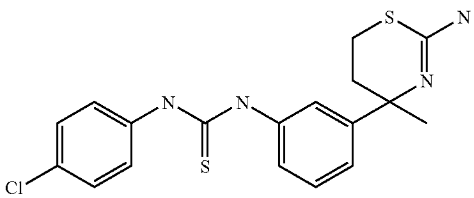
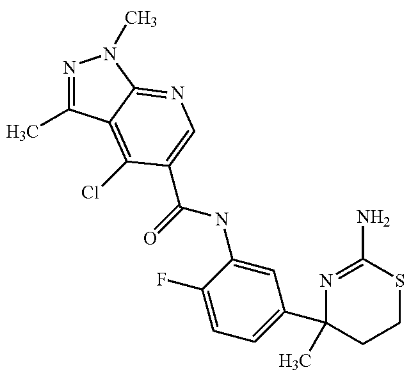
No.	Structure
404	
405	
406	
407	

TABLE 44

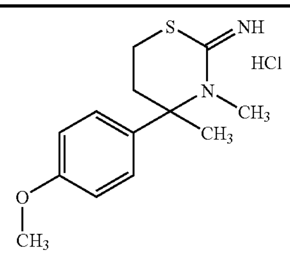
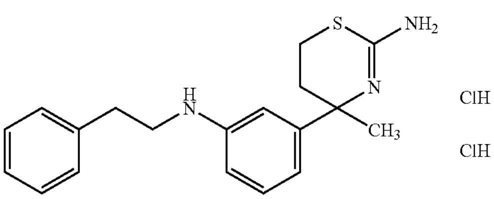
No.	Structure
408	
409	

TABLE 44-continued

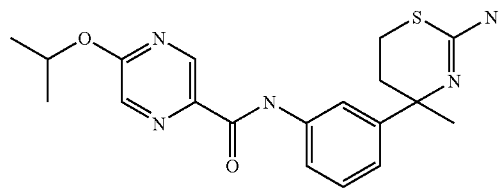
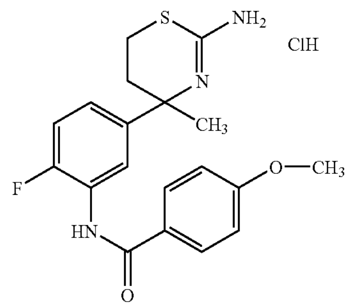
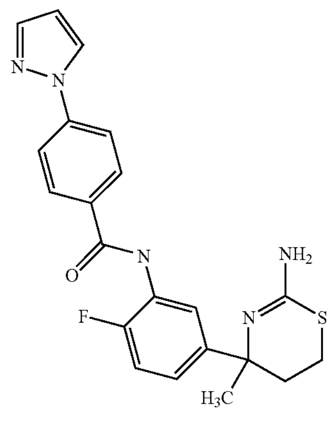
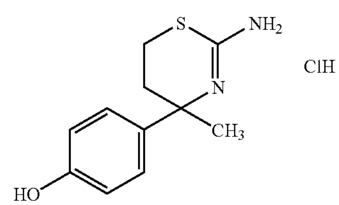
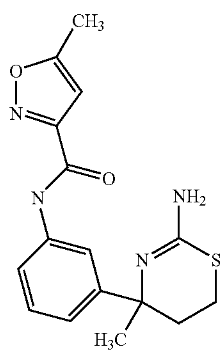
No.	Structure
410	
411	
412	
413	
414	

TABLE 44-continued

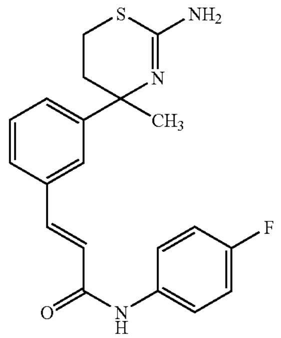
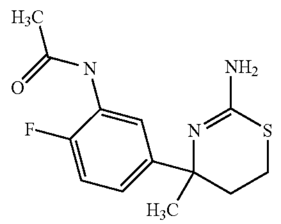
No.	Structure
415	
416	

TABLE 45

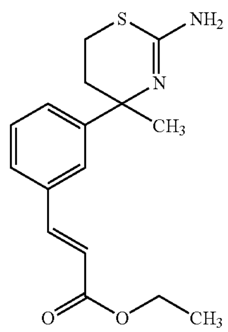
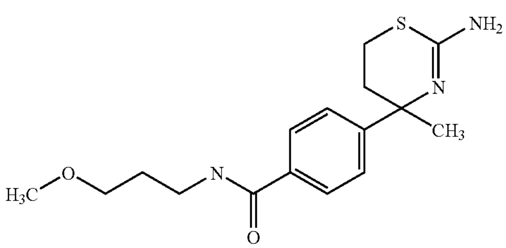
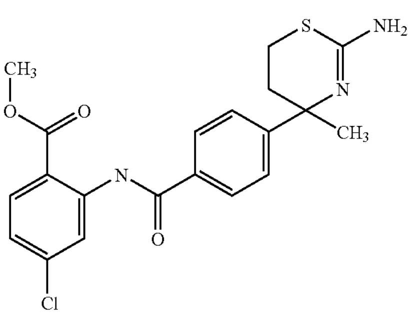
No.	Structure
417	
418	
419	

TABLE 45-continued

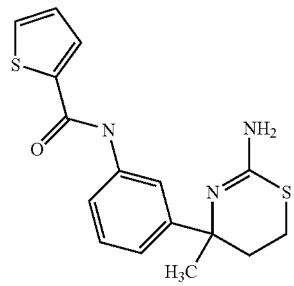
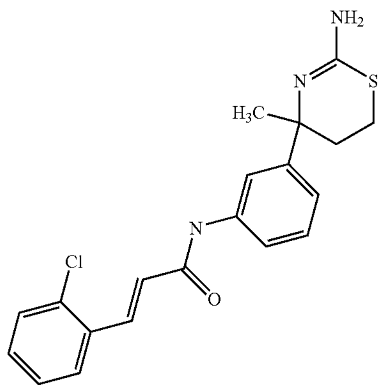
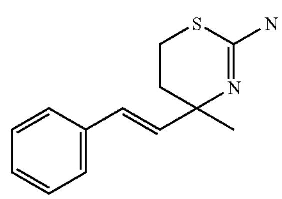
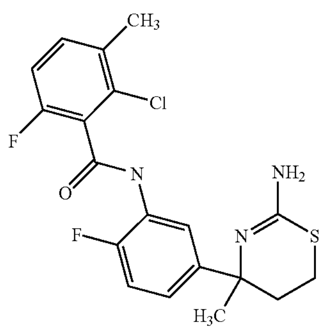
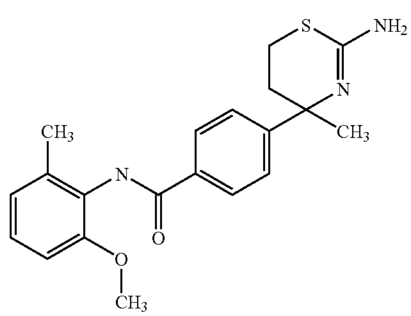
No.	Structure
420	
421	
422	
423	
424	

TABLE 46

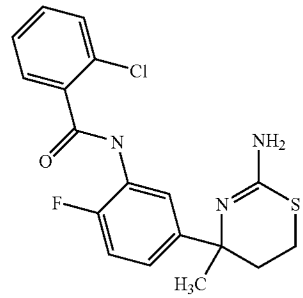
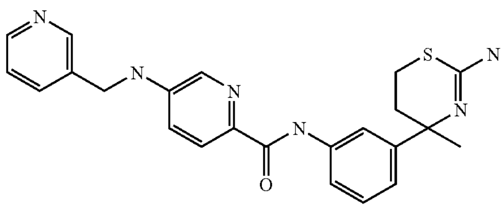
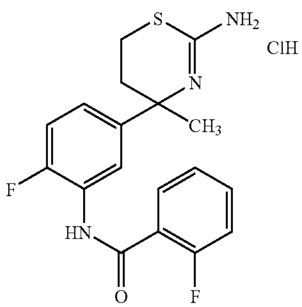
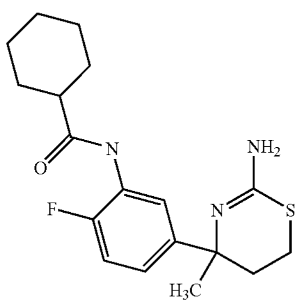
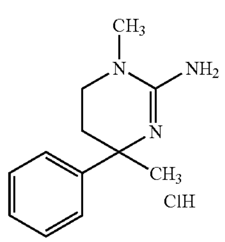
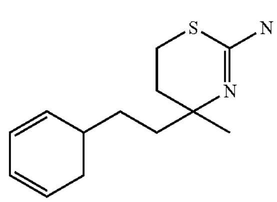
No.	Structure
425	
426	
427	
428	
429	
430	

TABLE 46-continued

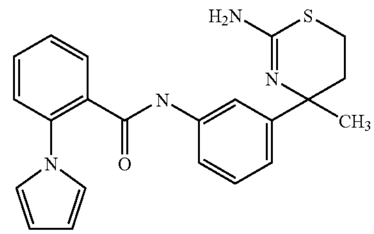
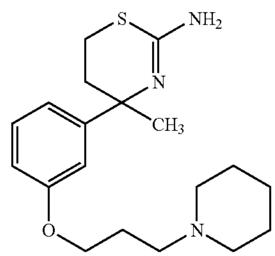
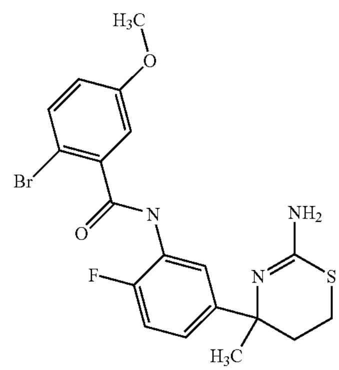
No.	Structure
431	
432	
433	

TABLE 47

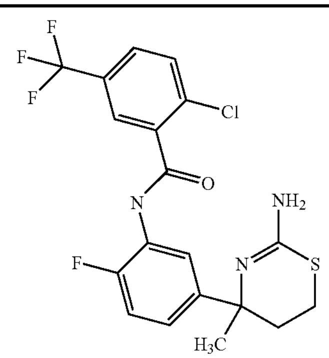
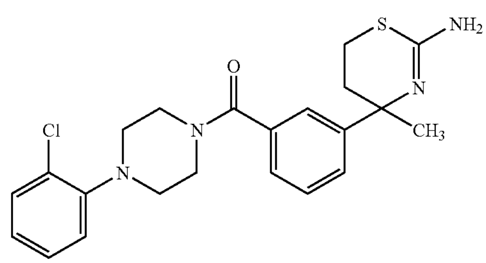
No.	Structure
434	
435	

TABLE 47-continued

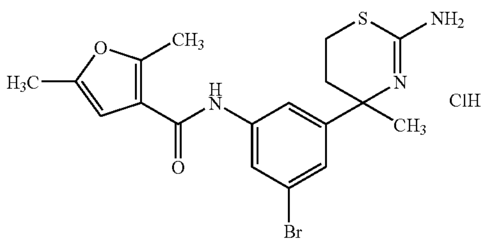
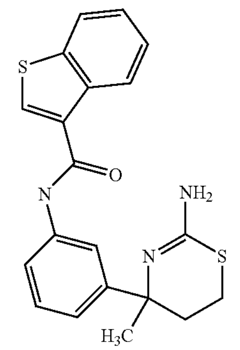
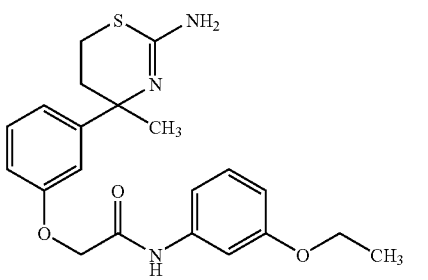
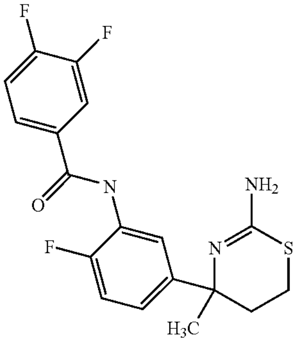
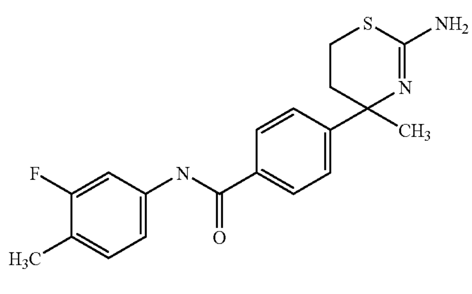
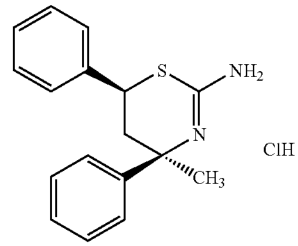
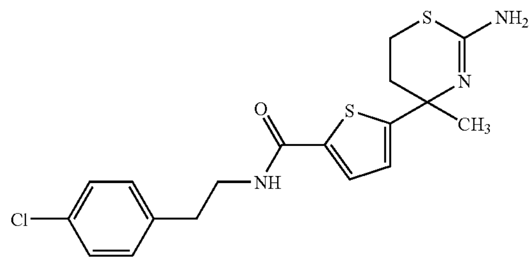
No.	Structure
436	
437	
438	
439	
440	
441 (racemate)	
442	

TABLE 48

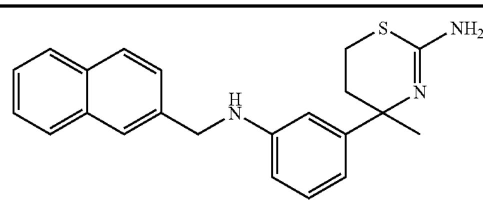
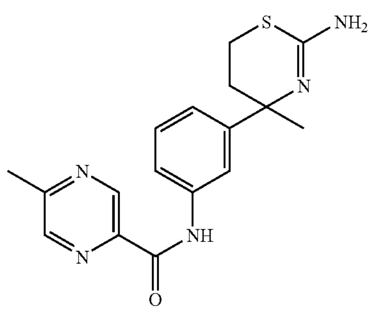
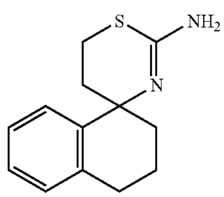
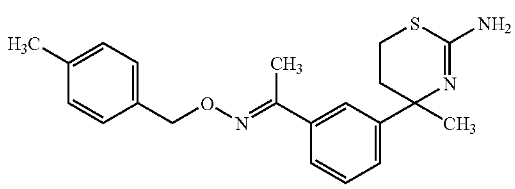
No.	Structure
443	
444	
445	
446	

TABLE 48-continued

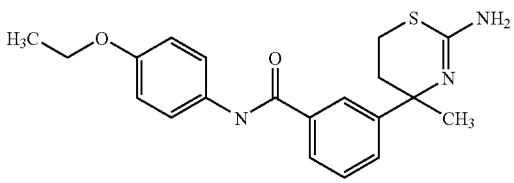
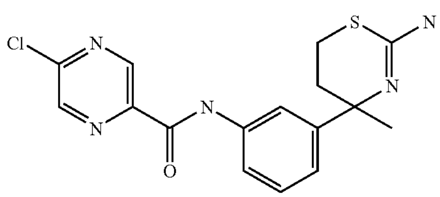
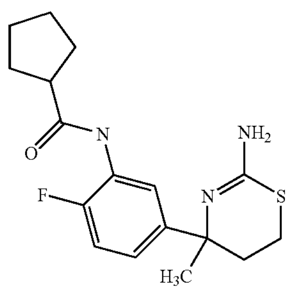
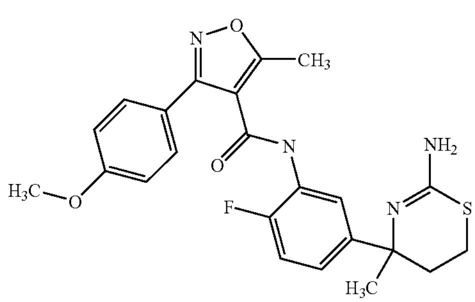
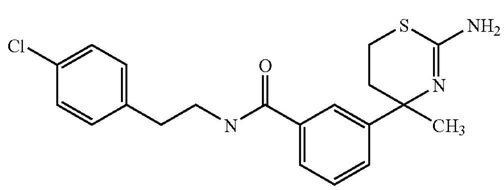
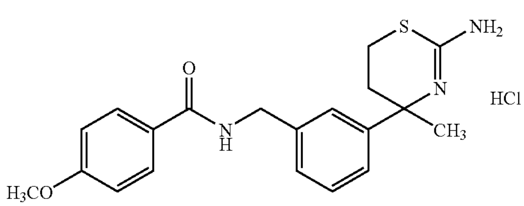
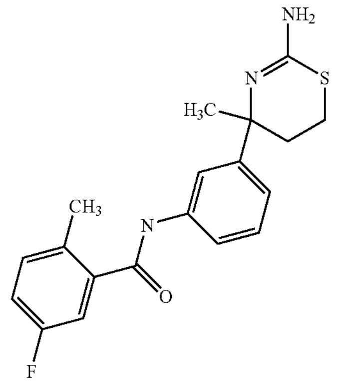
No.	Structure
447	
448	
449	
450	
451	
452	
453	

TABLE 49

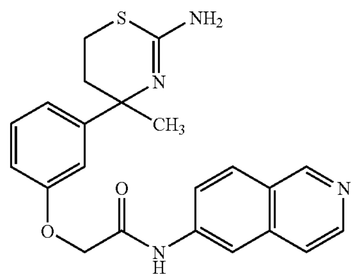
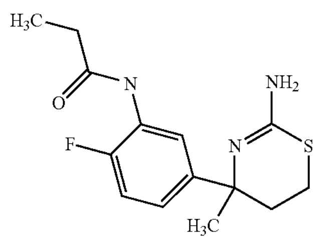
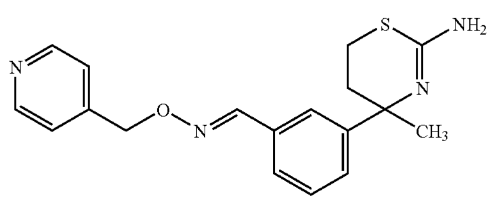
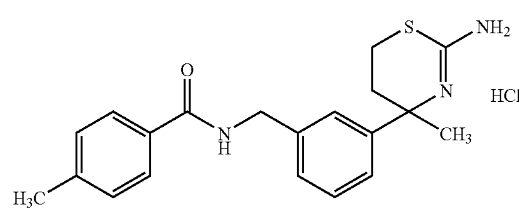
No.	Structure
454	
455	
456	
457	

TABLE 49-continued

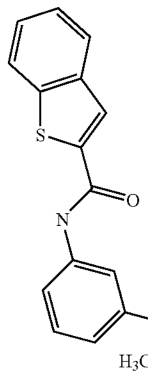
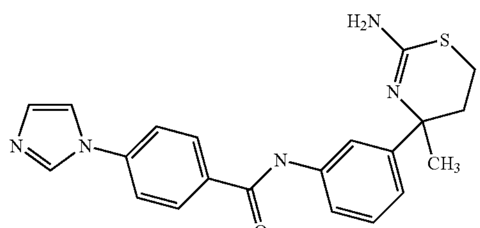
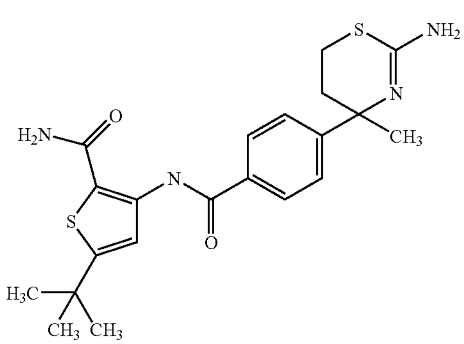
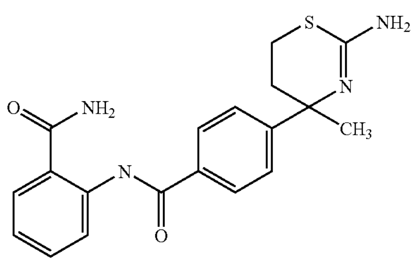
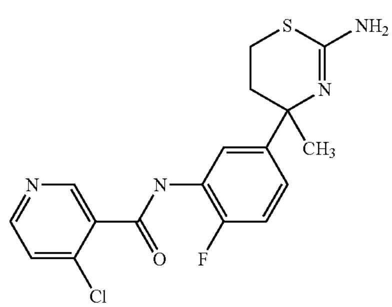
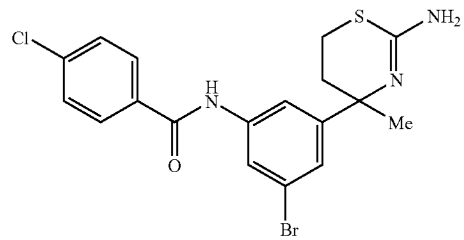
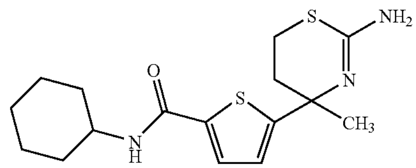
No.	Structure
458	
459	
460	
461	
462	
463	
464	

TABLE 50

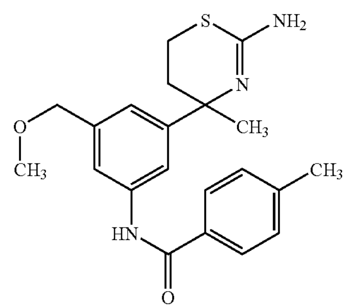
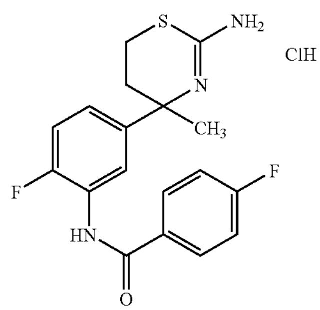
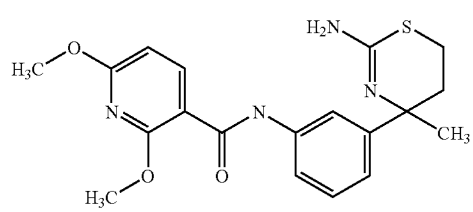
No.	Structure
465	
466	
467	

TABLE 50-continued

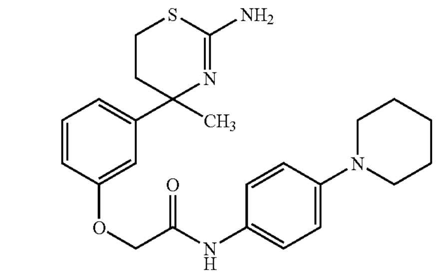
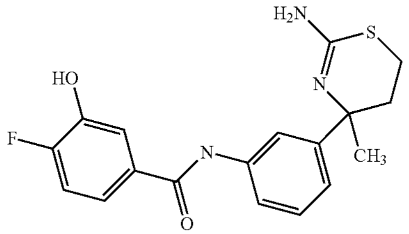
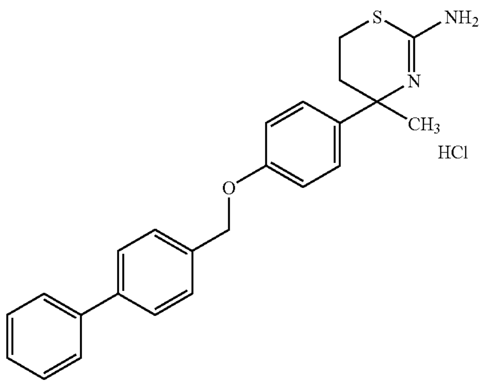
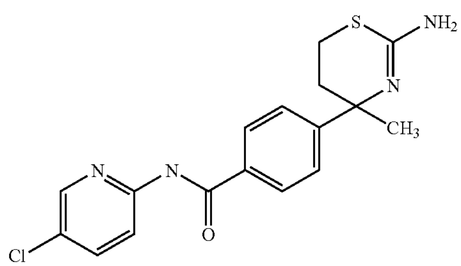
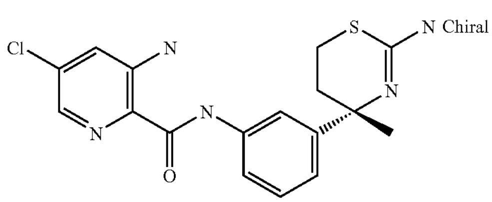
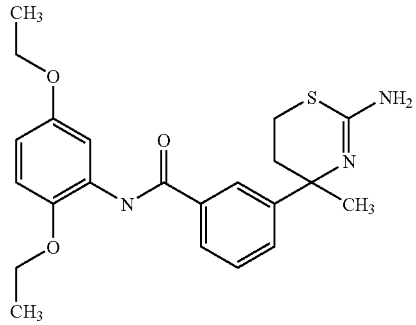
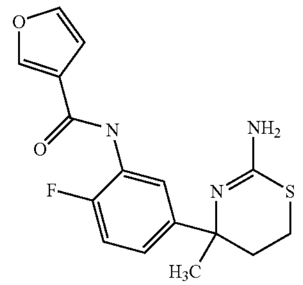
No.	Structure
468	
469	
470	
471	
472	
473	
474	

TABLE 51

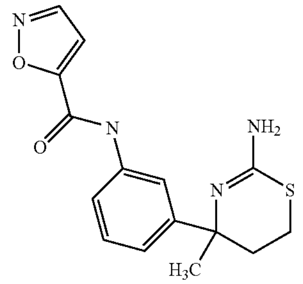
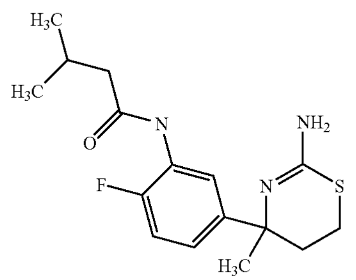
No.	Structure
475	
476	

TABLE 51-continued

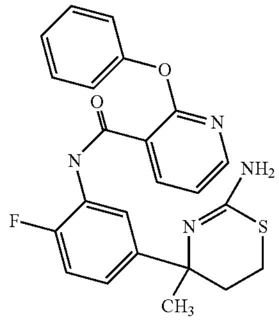
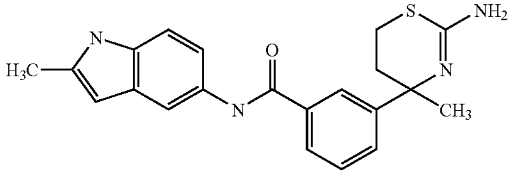
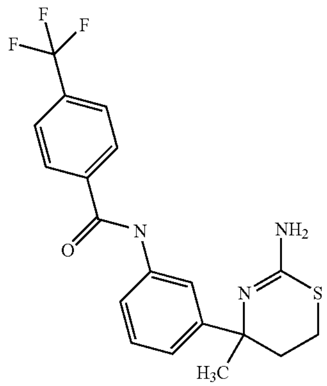
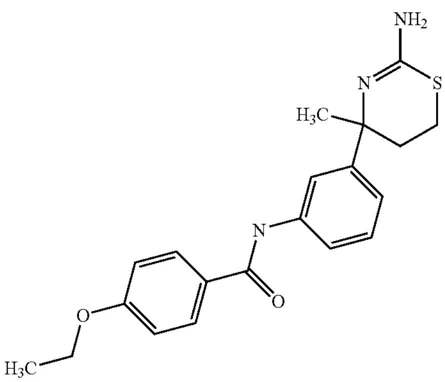
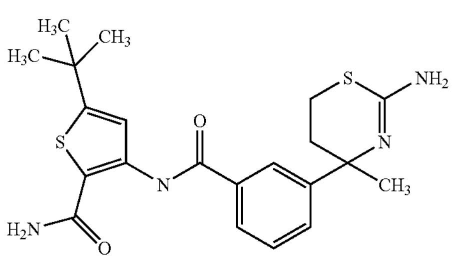
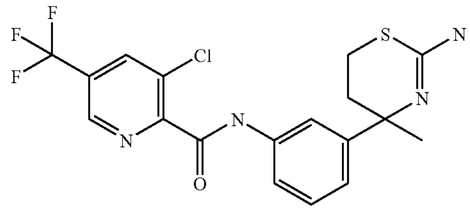
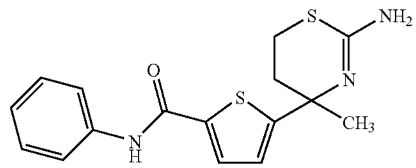
No.	Structure
477	
478	
479	
480	
481	
482	
483	

TABLE 52

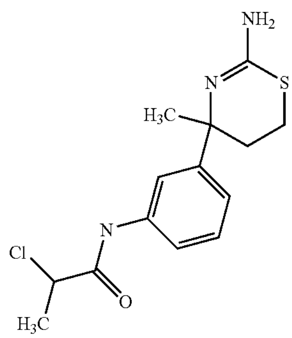
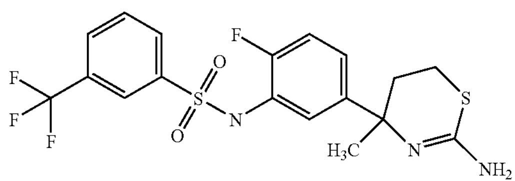
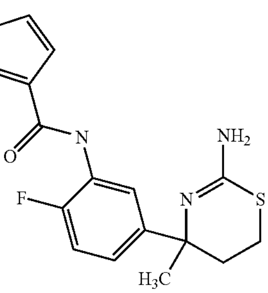
No.	Structure
484	
485	
486	

TABLE 52-continued

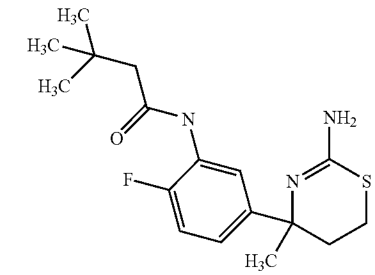
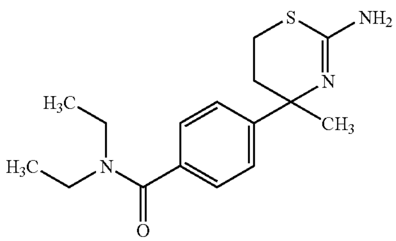
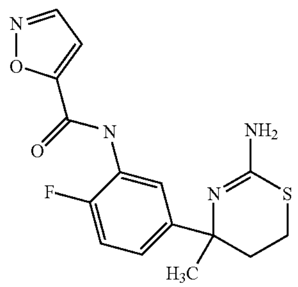
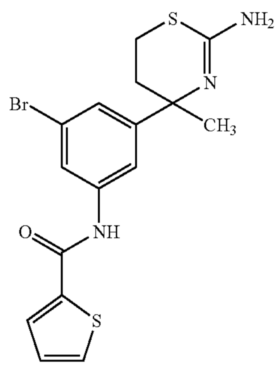
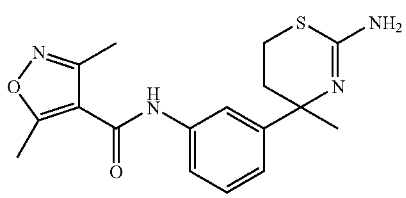
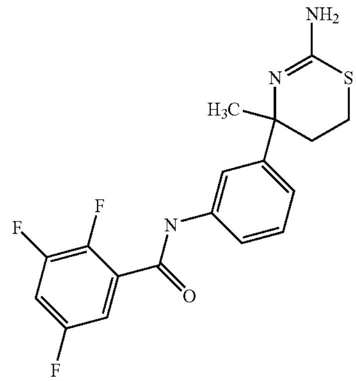
No.	Structure
487	
488	
489	
490	
491	
492	

TABLE 53

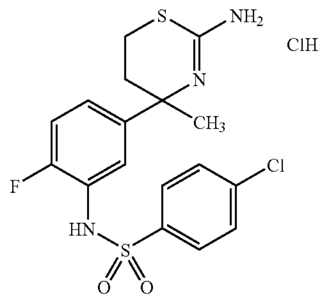
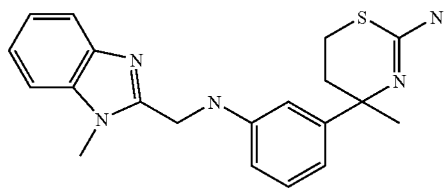
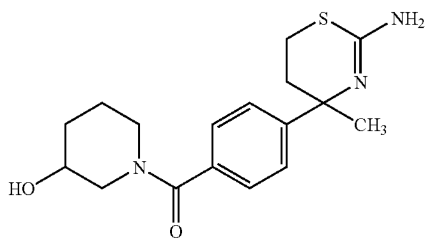
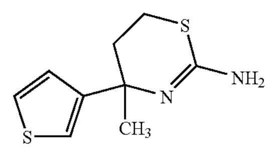
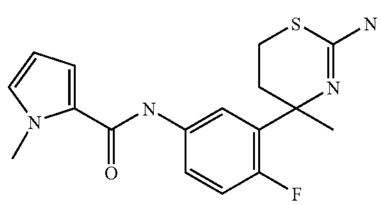
No.	Structure
493	
494	
495	
496	
497	

TABLE 53-continued

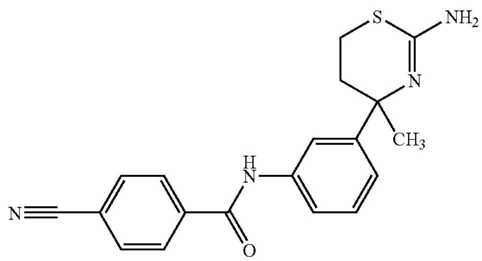
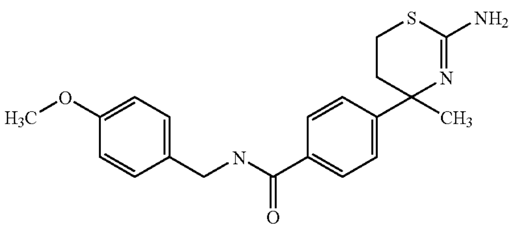
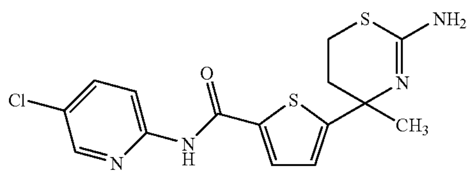
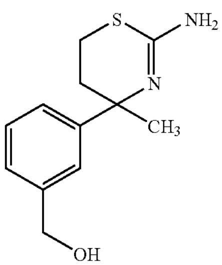
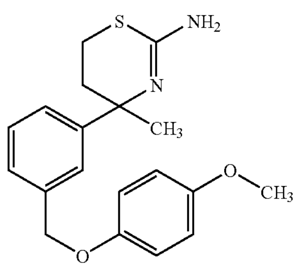
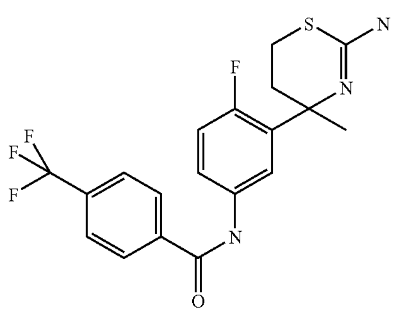
No.	Structure
498	
499	
500	
501	
502	
503	

TABLE 54

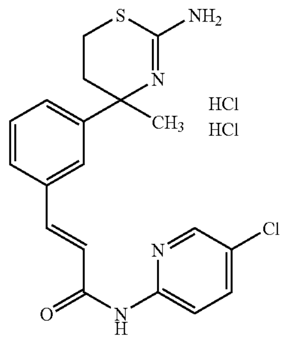
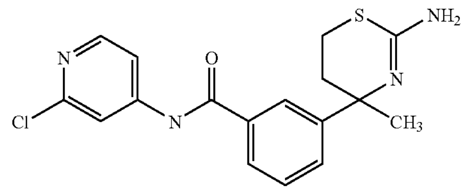
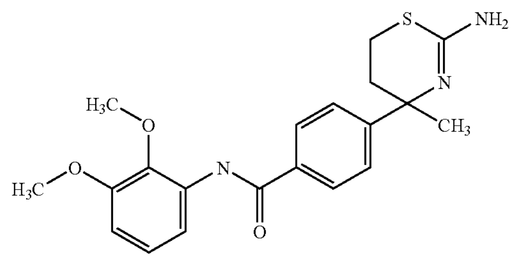
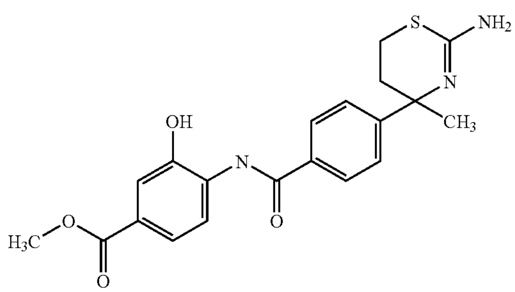
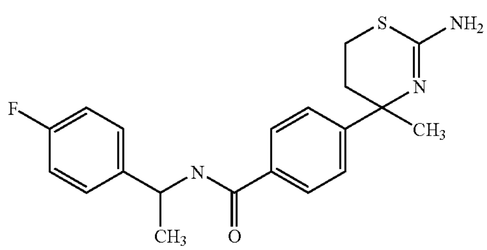
No.	Structure
504	
505	
506	
507	
508	

TABLE 54-continued

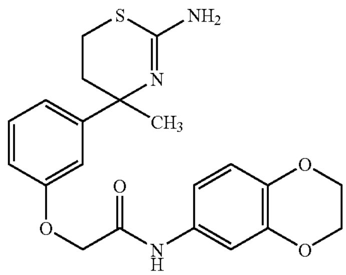
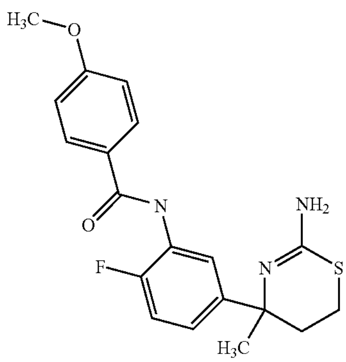
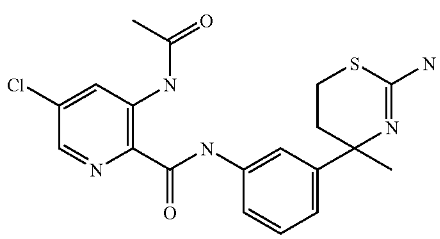
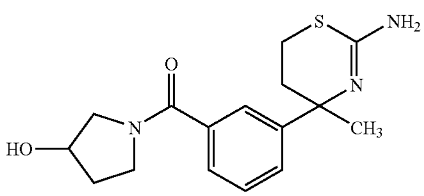
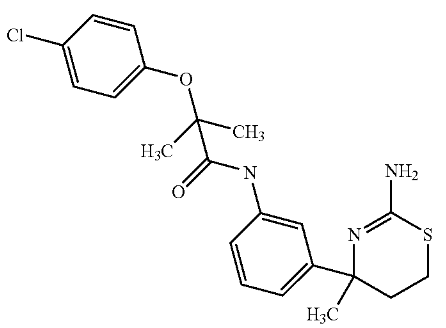
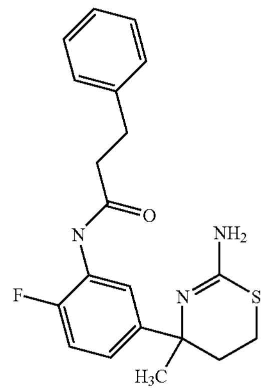
No.	Structure
509	
510	
511	
512	
513	
514	

TABLE 55

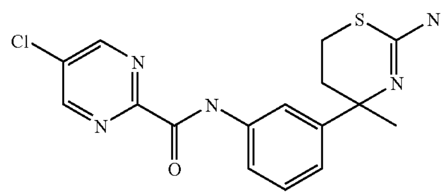
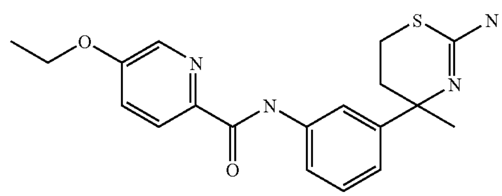
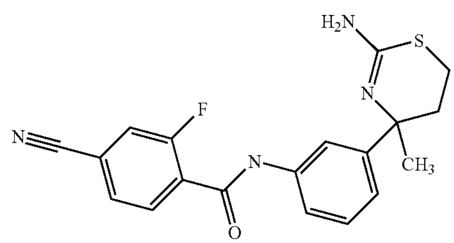
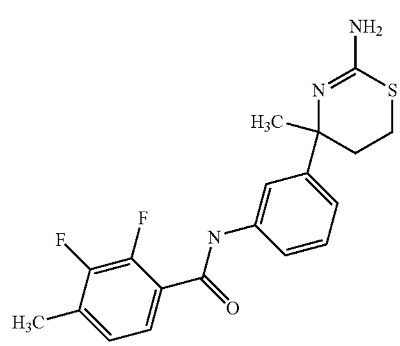
No.	Structure
515	
516	
517	
518	

TABLE 55-continued

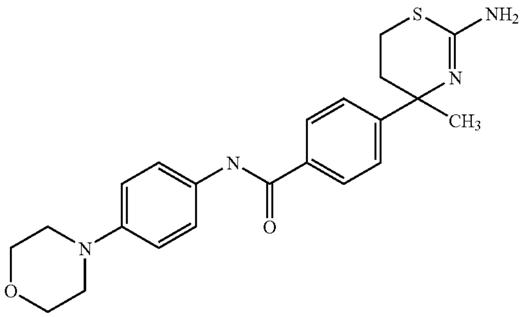
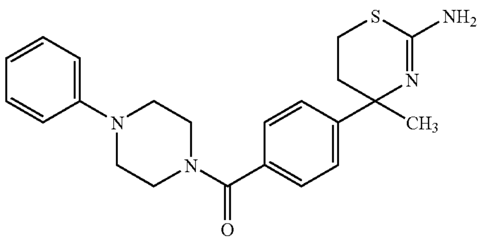
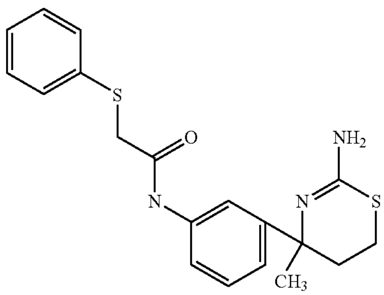
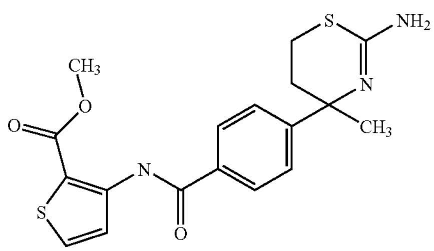
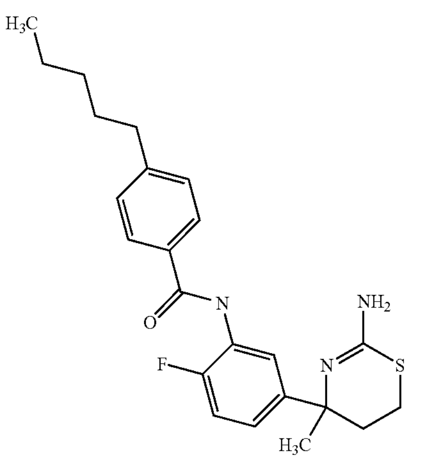
No.	Structure
519	
520	
521	
522	
523	

TABLE 55-continued

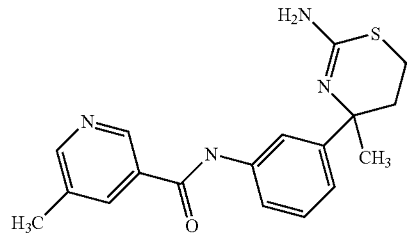
No.	Structure
524	

TABLE 56

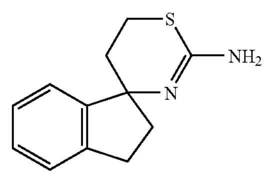
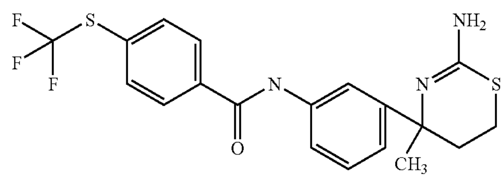
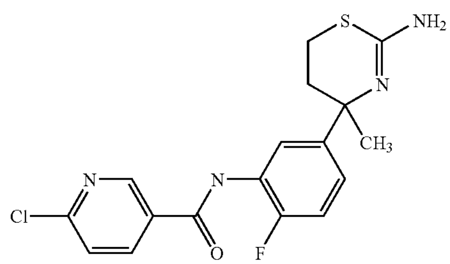
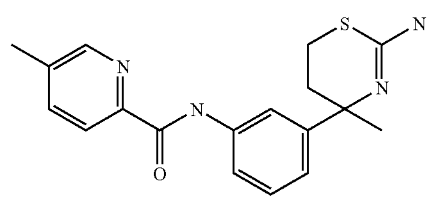
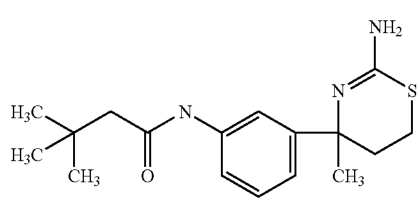
No.	Structure
525	
526	
527	
528	
529	

TABLE 56-continued

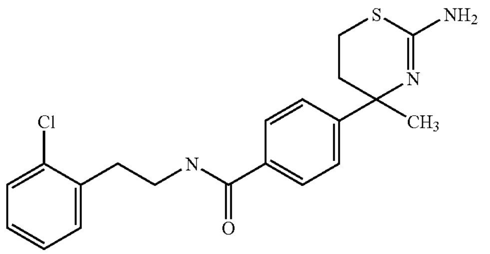
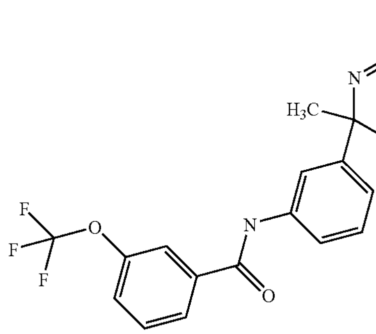
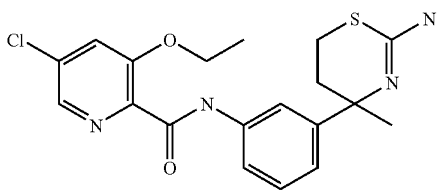
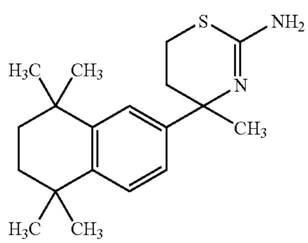
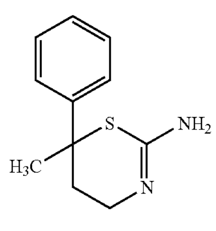
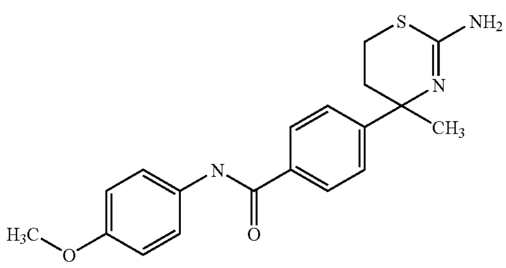
No.	Structure
530	
531	
532	
533	
534	
535	

TABLE 57

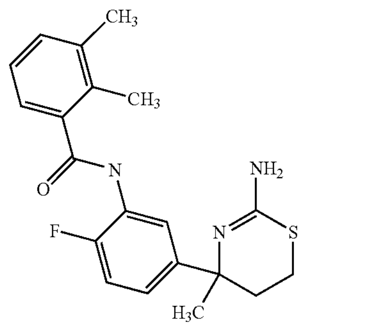
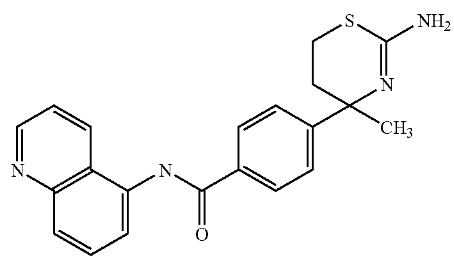
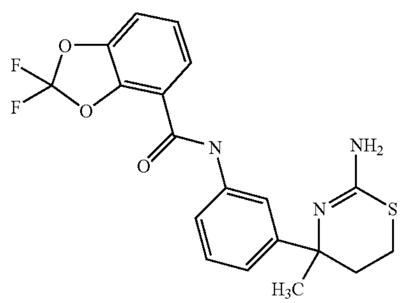
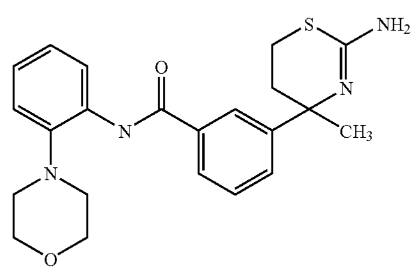
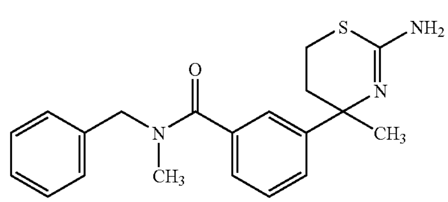
No.	Structure
536	
537	
538	
539	
540	

TABLE 57-continued

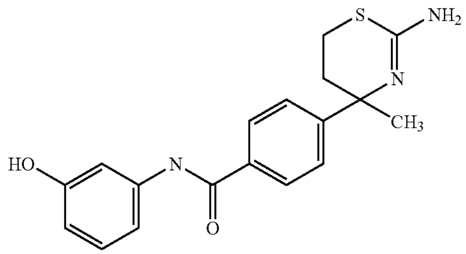
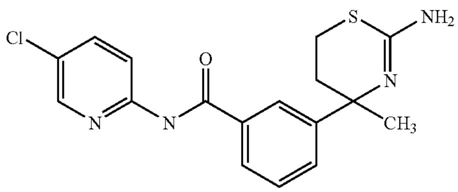
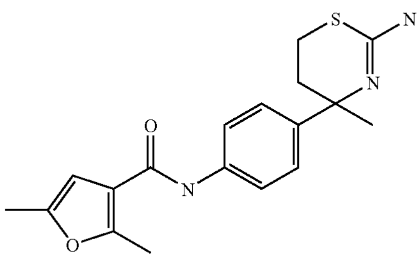
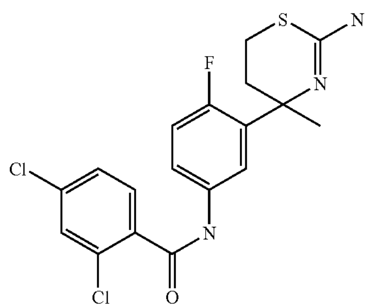
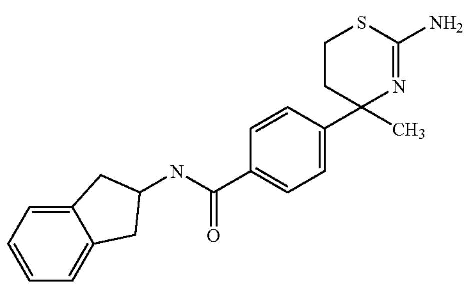
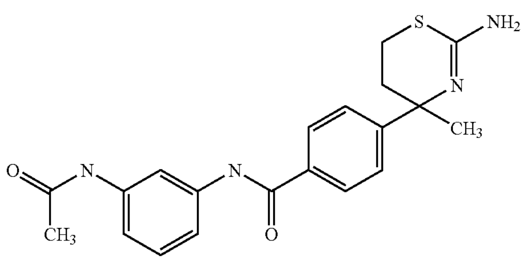
No.	Structure
541	
542	
543	
544	
545	
546	

TABLE 58

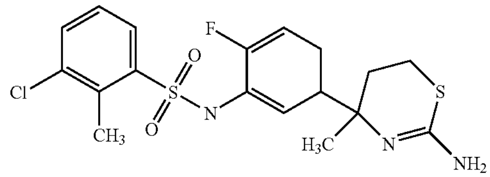
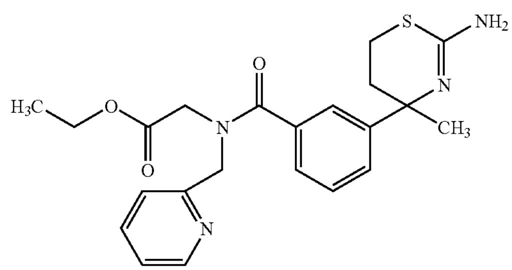
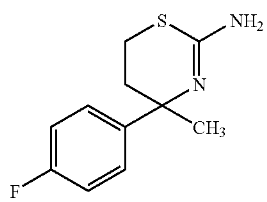
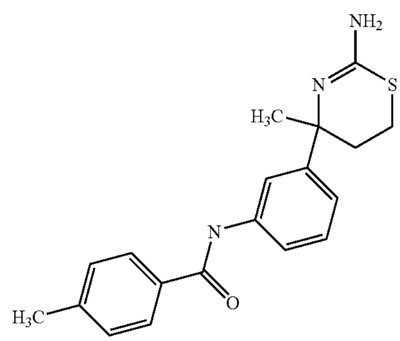
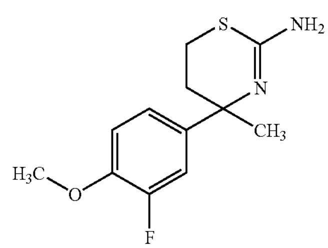
No.	Structure
547	
548	
549	
550	
551	

TABLE 58-continued

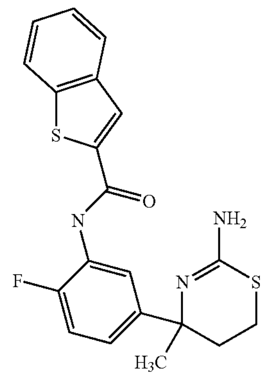
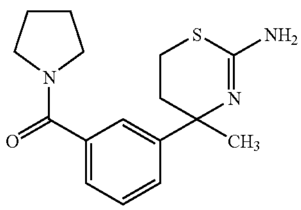
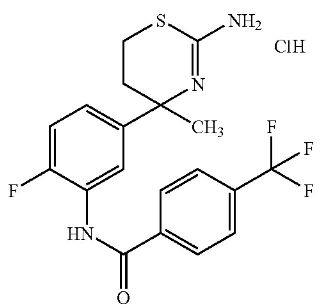
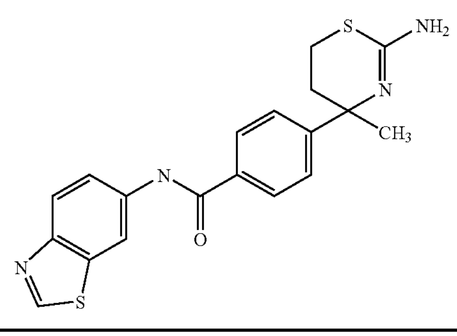
No.	Structure
552	
553	
554	
555	

TABLE 59

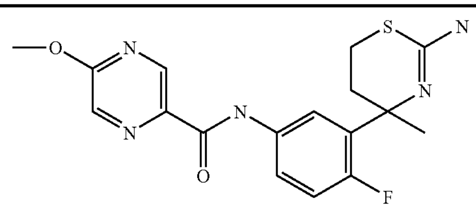
No.	Structure
556	

TABLE 59-continued

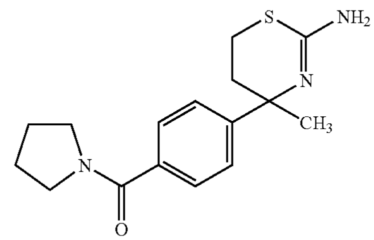
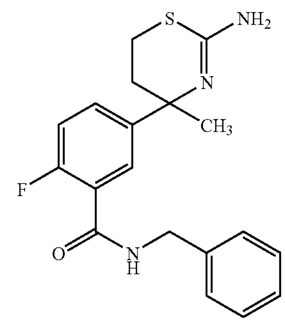
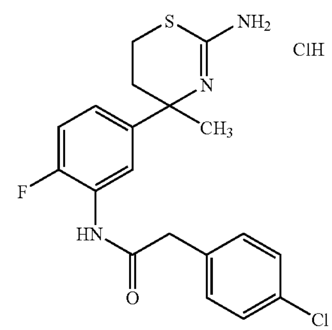
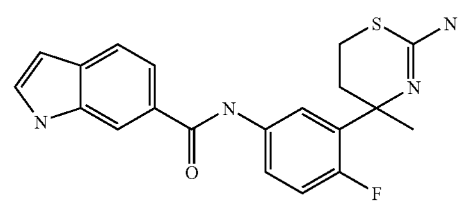
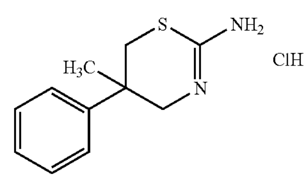
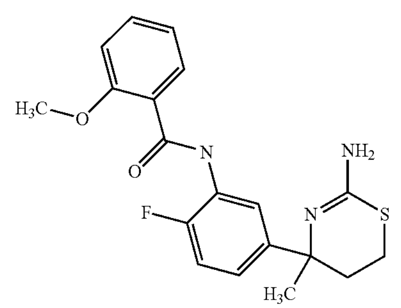
No.	Structure
557	
558	
559	
560	
561	
562	

TABLE 59-continued

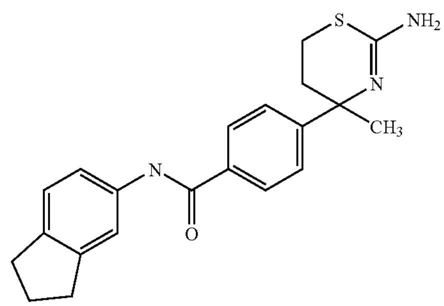
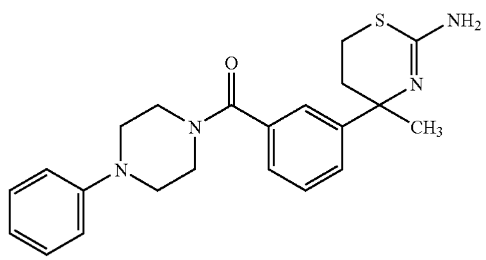
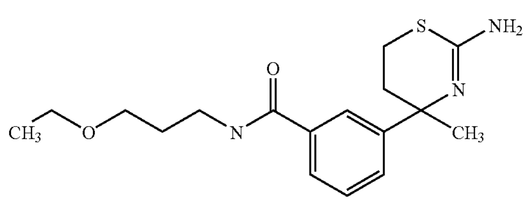
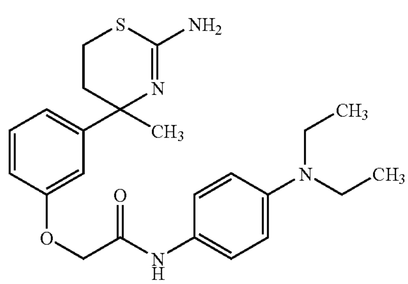
No.	Structure
563	
564	
565	
566	

TABLE 60

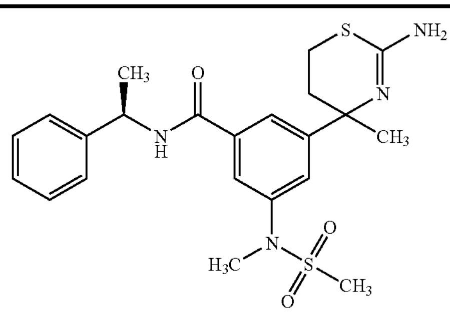
No.	Structure
567	

TABLE 60-continued

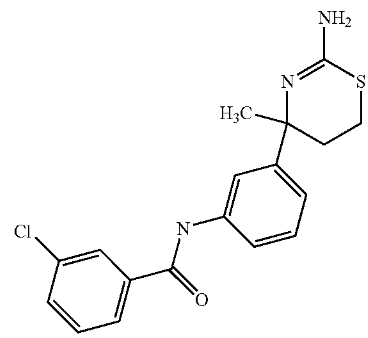
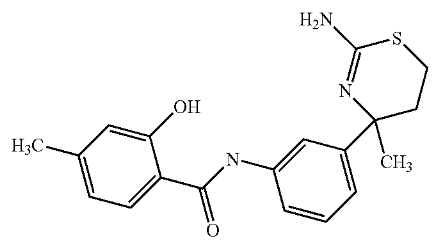
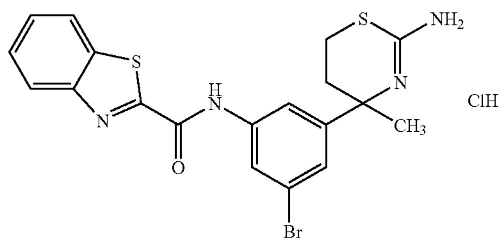
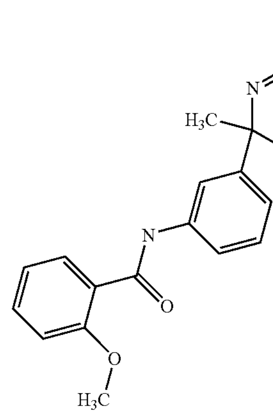
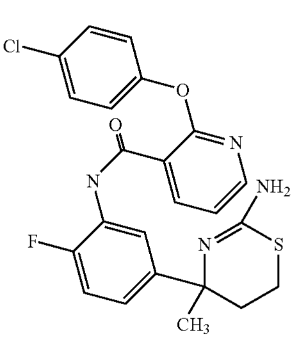
No.	Structure
568	
569	
570	
571	
572	

TABLE 60-continued

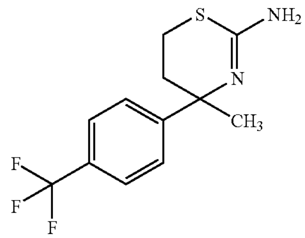
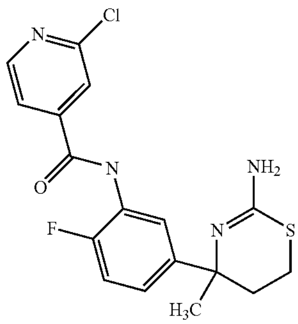
No.	Structure
573	
574	

TABLE 61

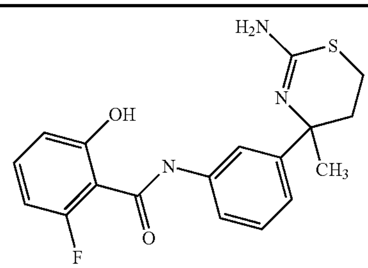
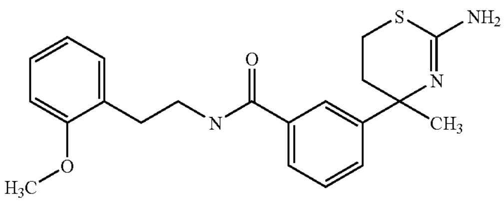
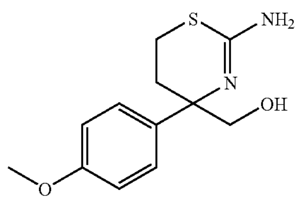
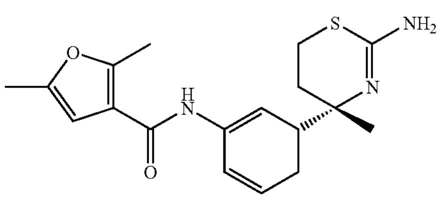
No.	Structure
575	
576	
577	
578	

TABLE 61-continued

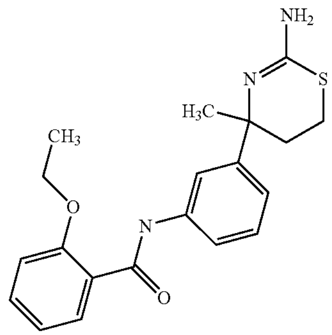
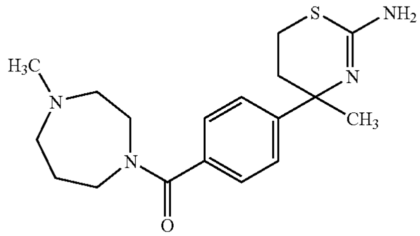
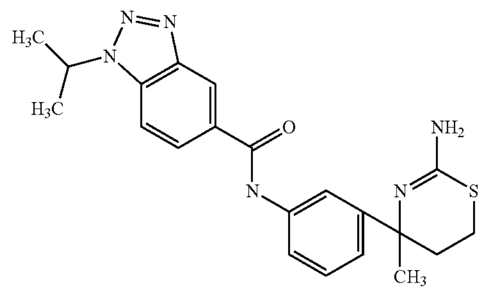
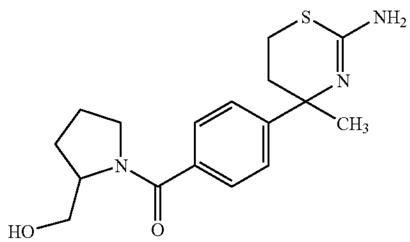
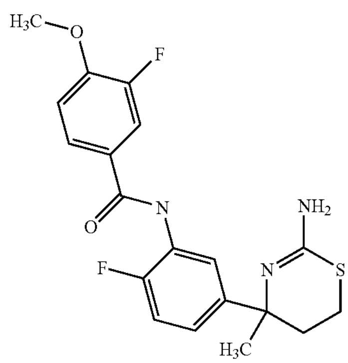
No.	Structure
579	
580	
581	
582	
583	

TABLE 61-continued

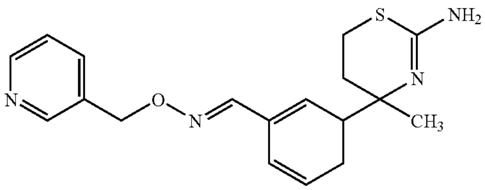
No.	Structure
584	

TABLE 62

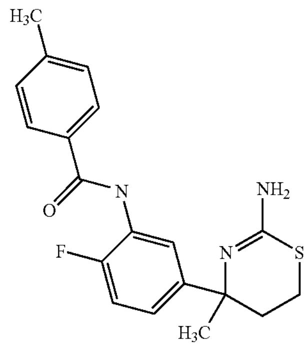
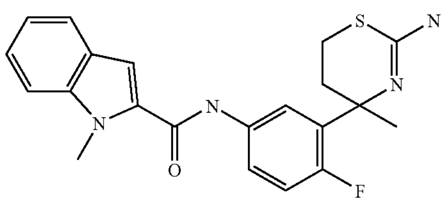
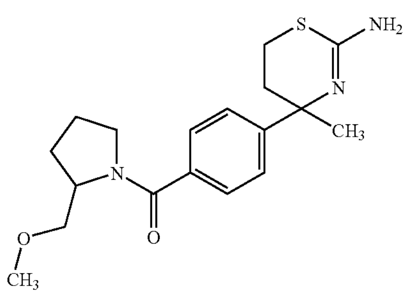
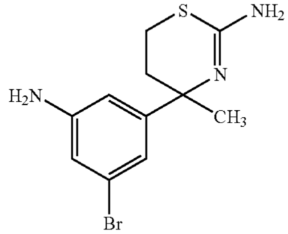
No.	Structure
585	
586	
587	
588	

TABLE 62-continued

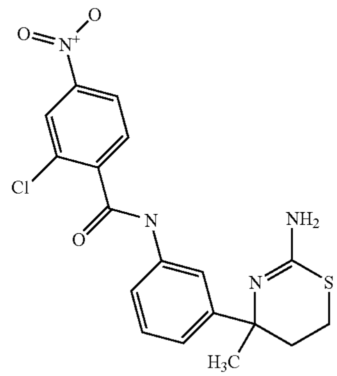
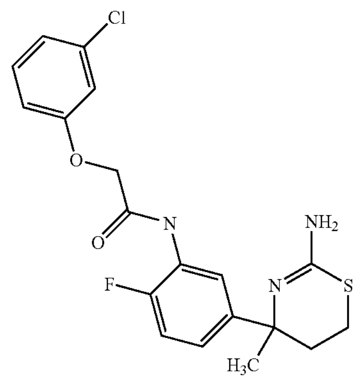
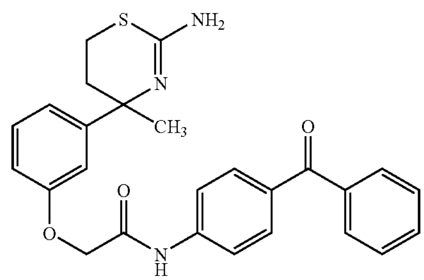
No.	Structure
589	
590	
591	

TABLE 63

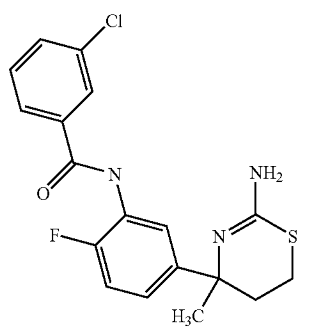
No.	Structure
592	

TABLE 63-continued

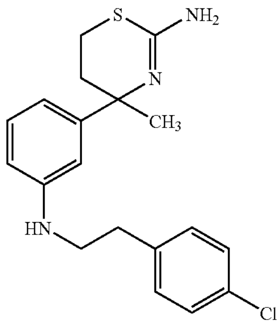
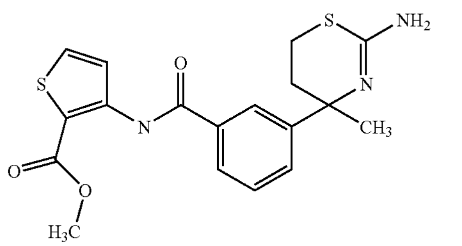
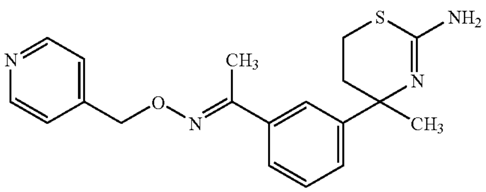
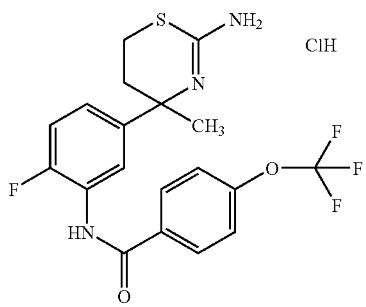
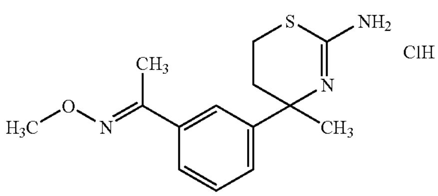
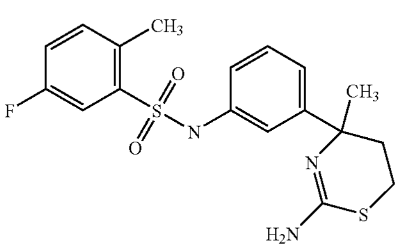
No.	Structure
593	
594	
595	
596	
597	
598	

TABLE 63-continued

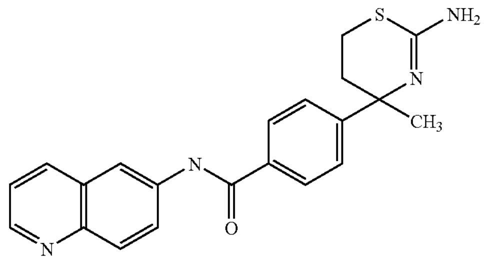
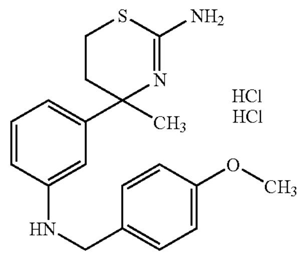
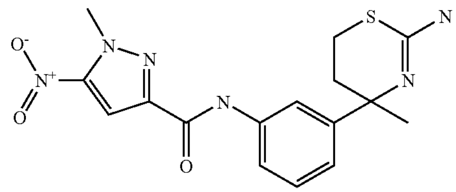
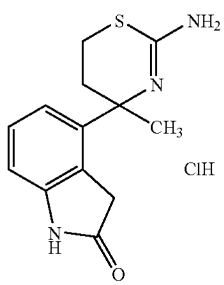
No.	Structure
599	
600	
601	
602	

TABLE 64

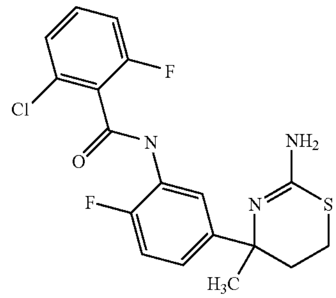
No.	Structure
603	

TABLE 64-continued

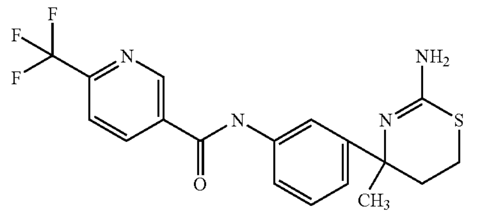
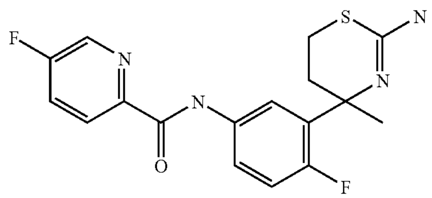
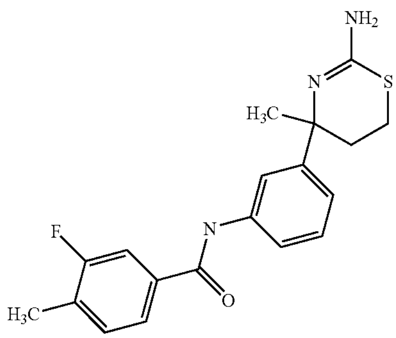
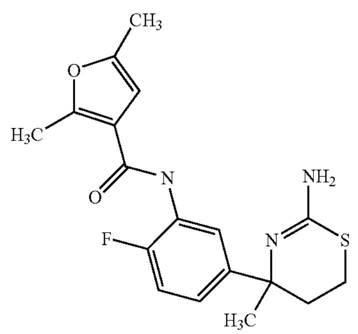
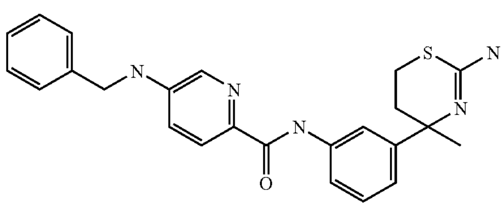
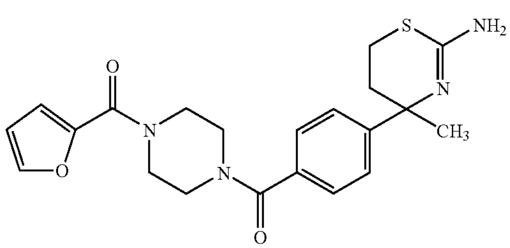
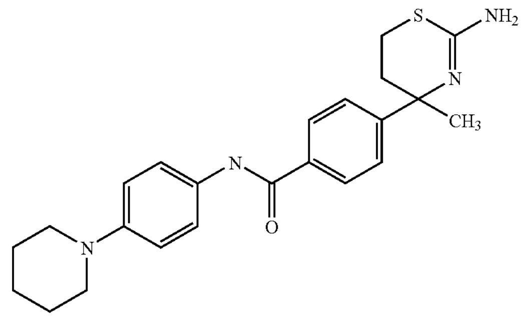
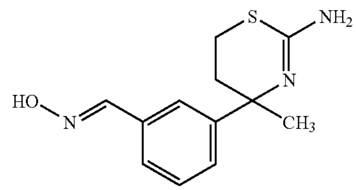
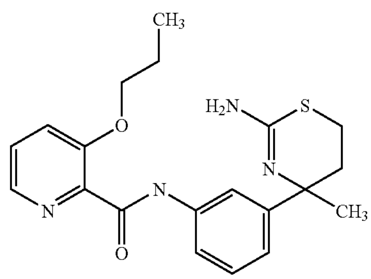
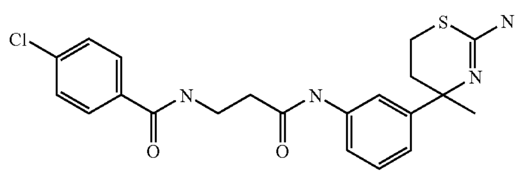
No.	Structure
604	
605	
606	
607	
608	
609	
610	
611	
612	
613	

TABLE 65

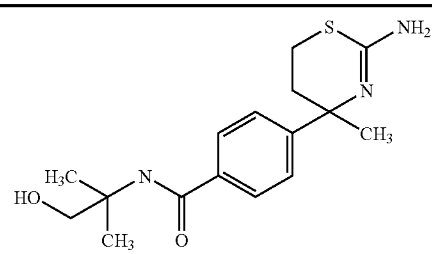
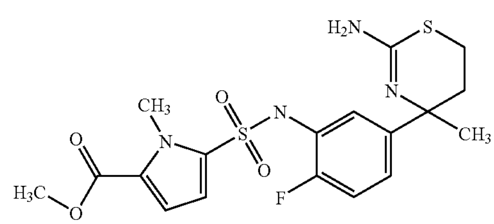
No.	Structure
614	
615	

TABLE 65-continued

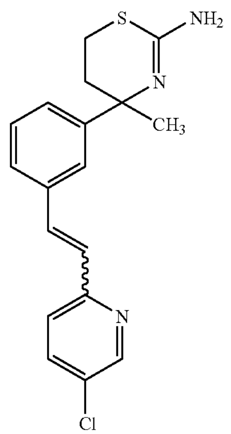
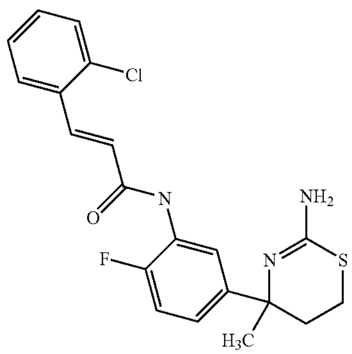
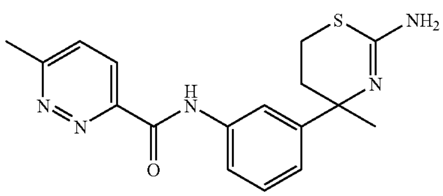
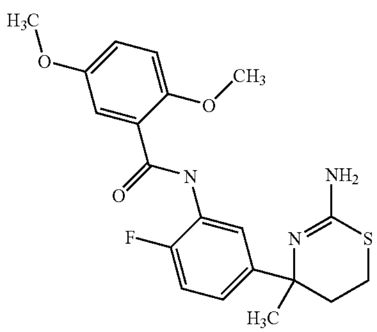
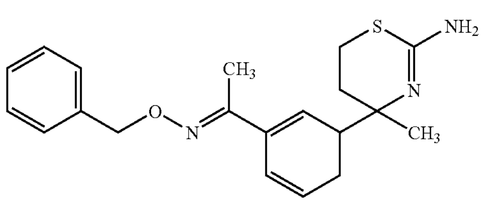
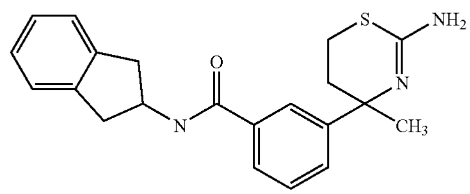
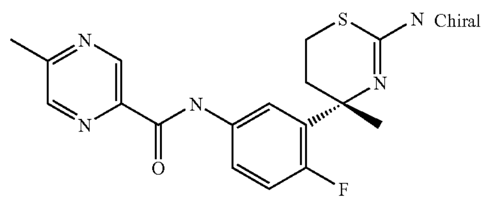
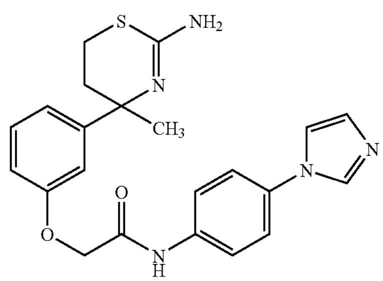
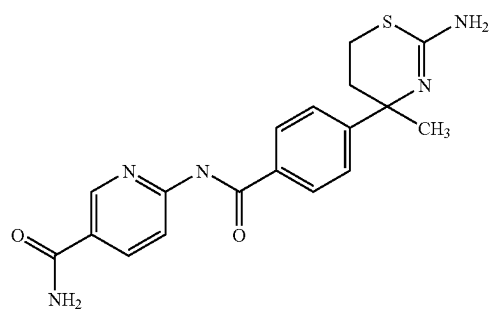
No.	Structure
616	
617	
618	
619	
620	
621	
622	
623	
624	

TABLE 66

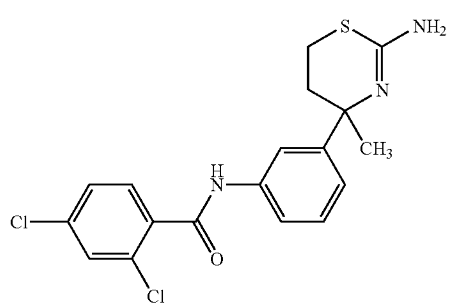
No.	Structure
625	

TABLE 66-continued

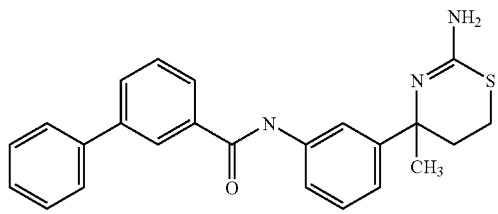
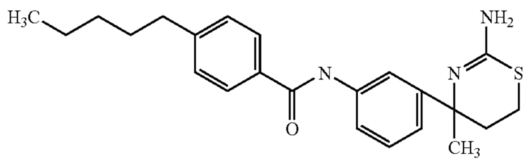
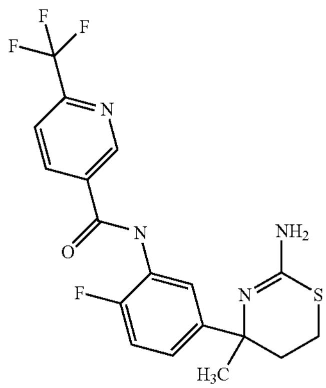
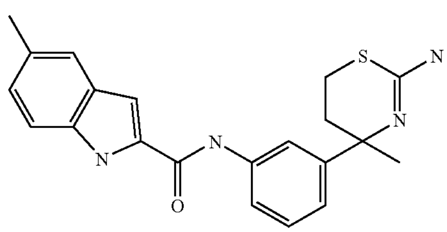
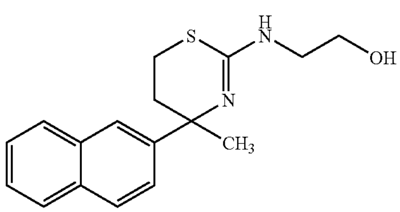
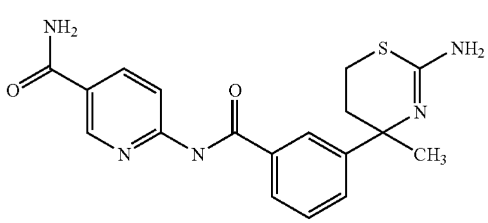
No.	Structure
626	
627	
628	
629	
630	
631	

TABLE 66-continued

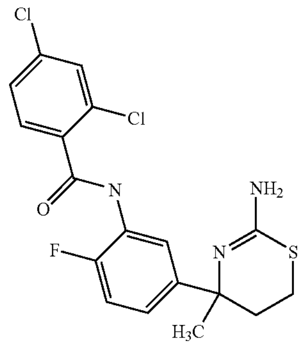
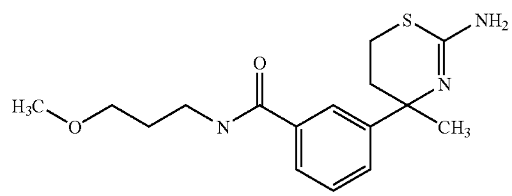
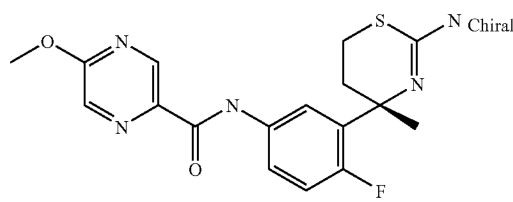
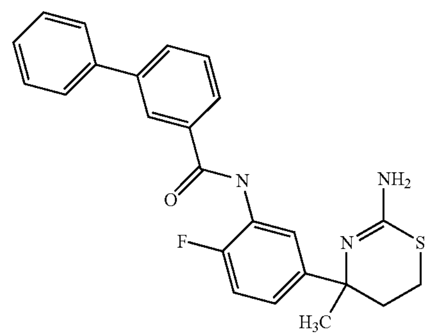
No.	Structure
632	
633	
634	
635	

TABLE 67

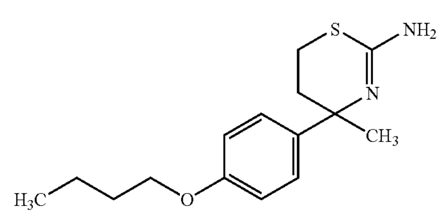
No.	Structure
636	

TABLE 67-continued

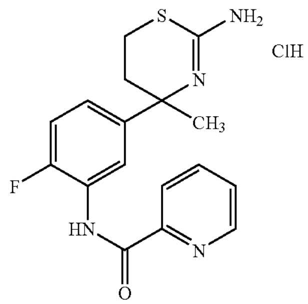
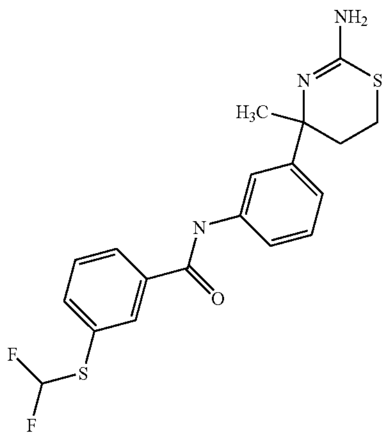
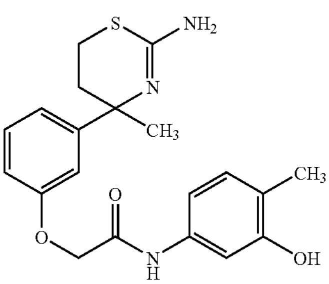
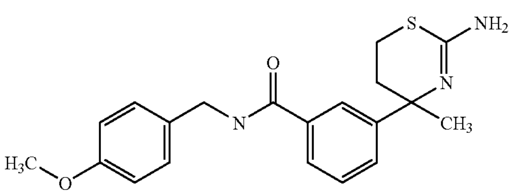
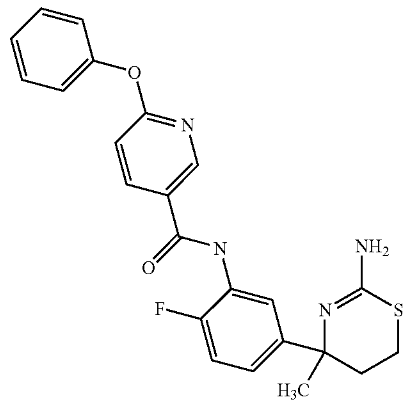
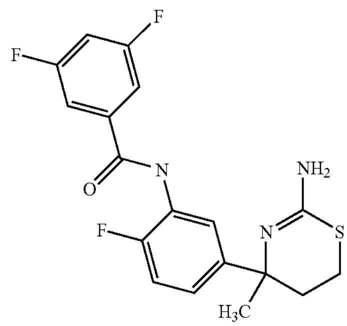
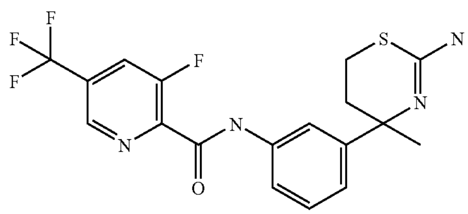
No.	Structure
637	
638	
639	
640	
641	
642	
643	

TABLE 68

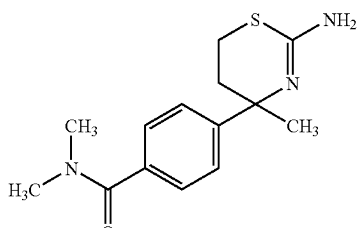
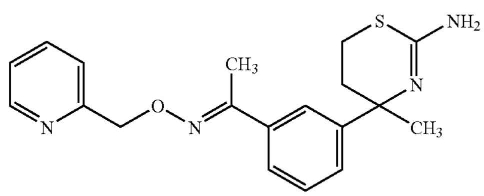
No.	Structure
644	
645	

TABLE 68-continued

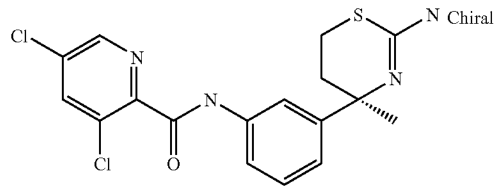
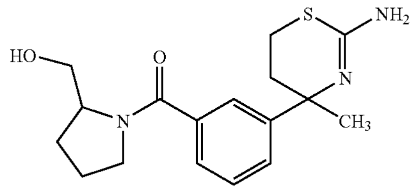
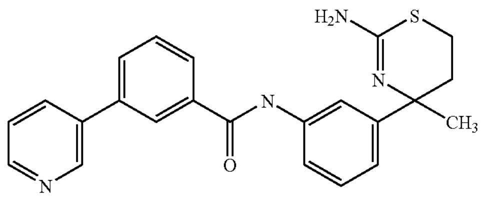
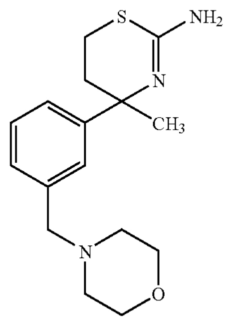
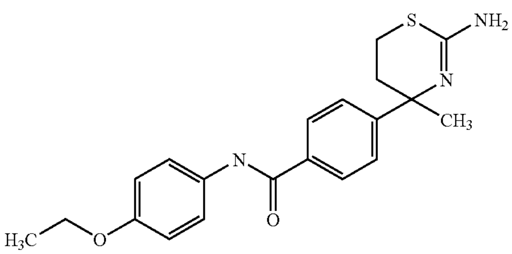
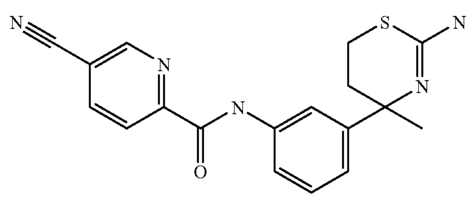
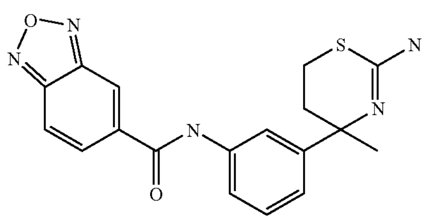
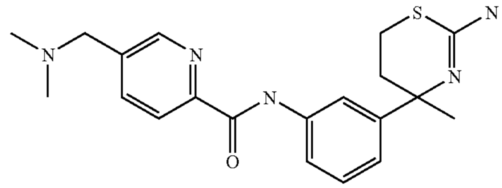
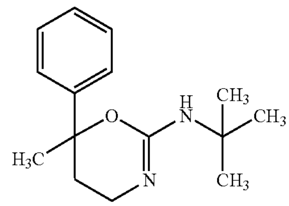
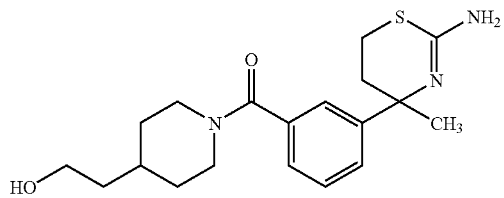
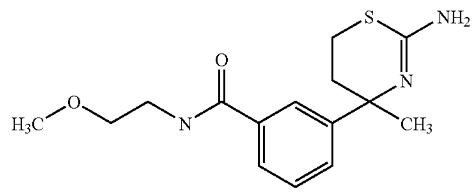
No.	Structure
646	
647	
648	
649	
650	
651	
652	
653	
654	
655	
656	

TABLE 69

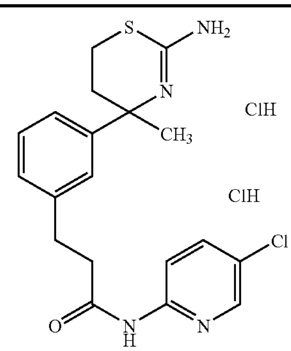
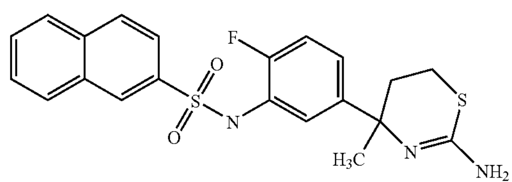
No.	Structure
657	
658	

TABLE 69-continued

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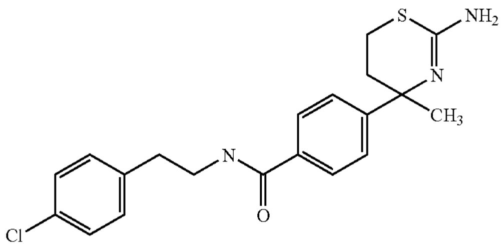
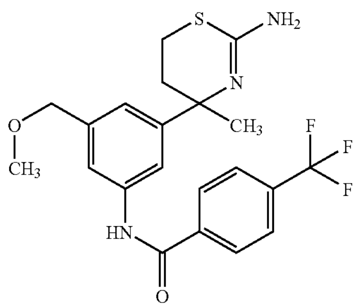
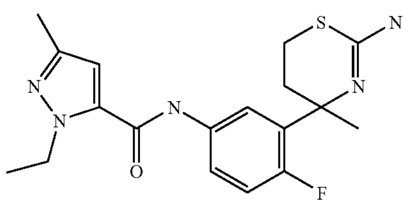
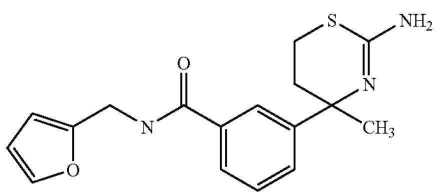
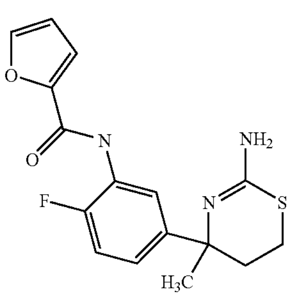
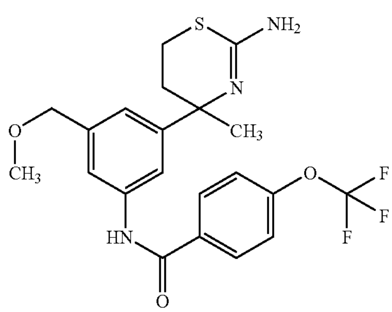
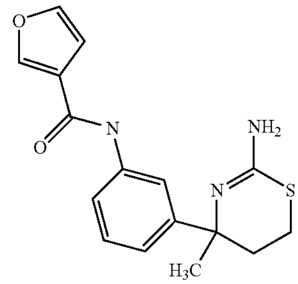
659	
660	
661	
662	
663	
664	
665	

TABLE 70

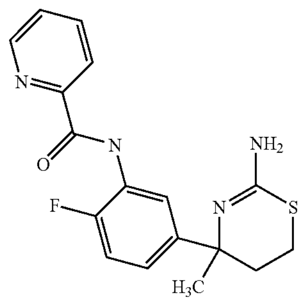
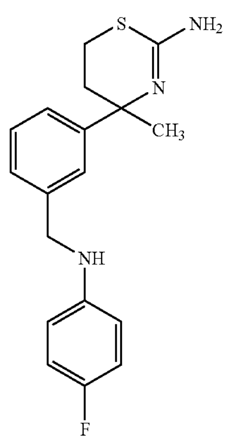
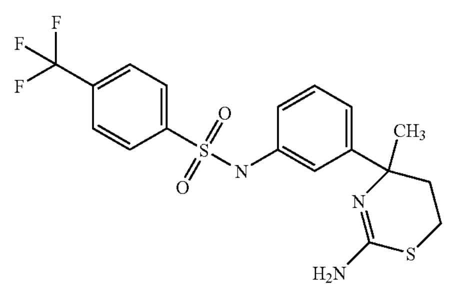
No.	Structure
666	
667	
668	

TABLE 70-continued

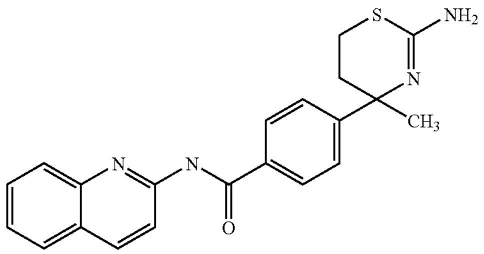
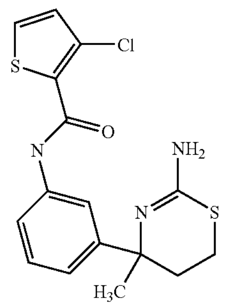
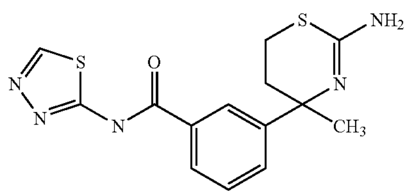
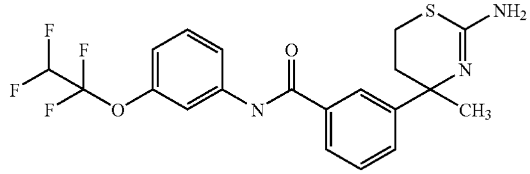
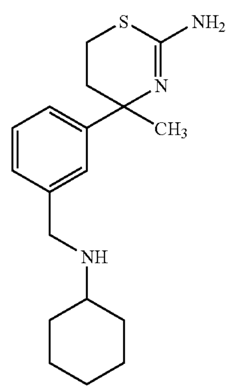
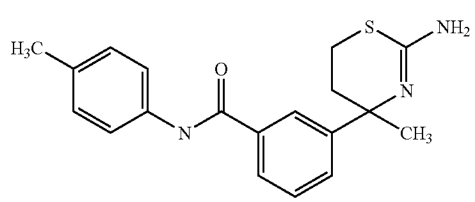
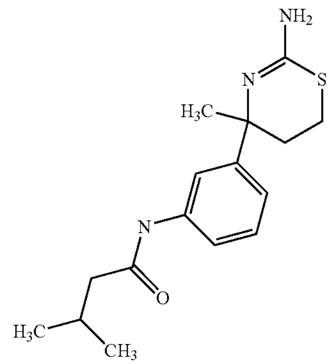
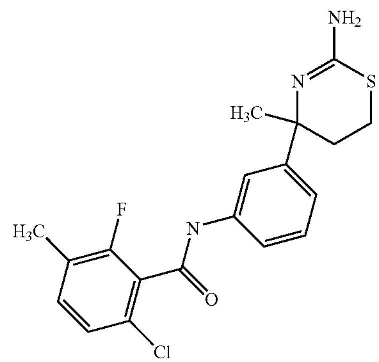
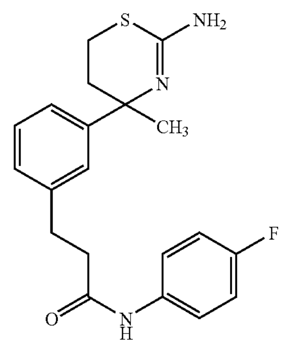
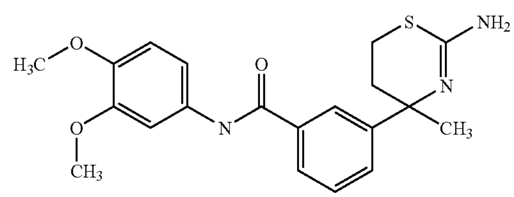
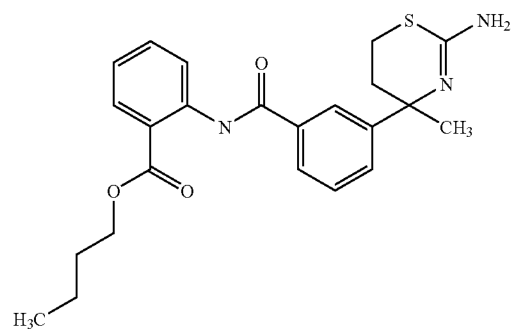
No.	Structure
669	
670	
671	
672	
673	
674	

TABLE 71

No.	Structure
675	
676	
677	
678	
679	

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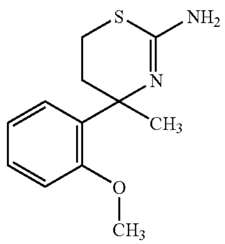
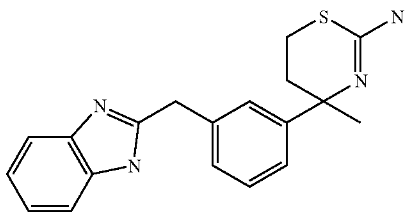
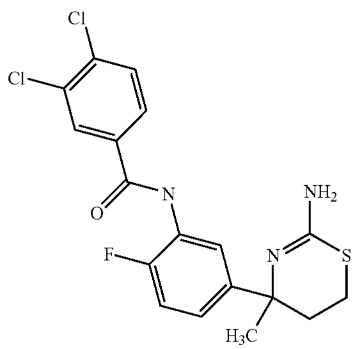
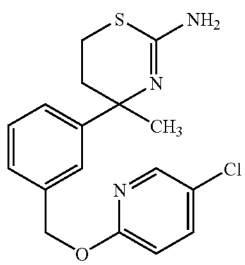
680	
681	
682	
683	

TABLE 72

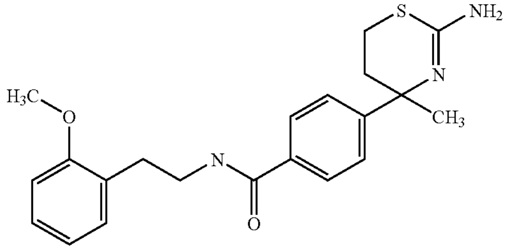
No.	Structure
684	

TABLE 72-continued

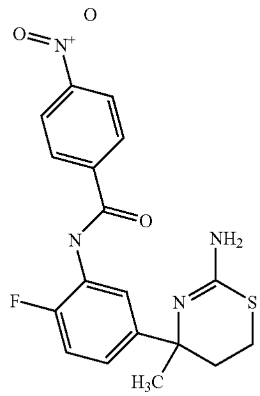
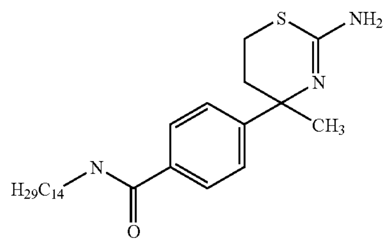
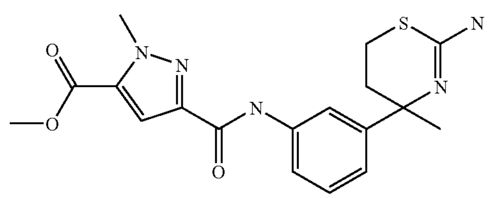
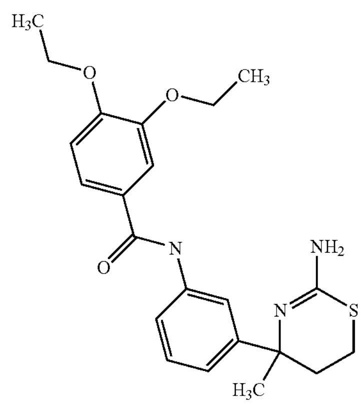
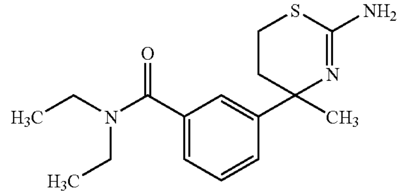
No.	Structure
685	
686	
687	
688	
689	

TABLE 72-continued

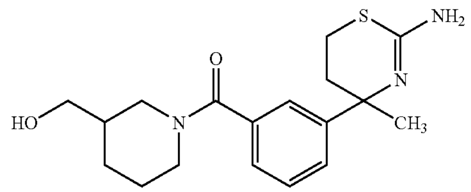
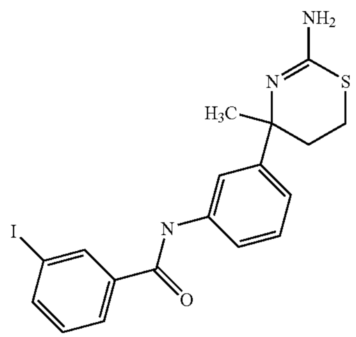
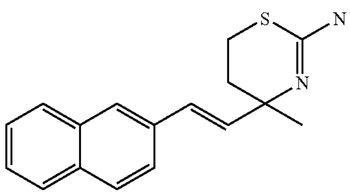
No.	Structure
690	
691	
692	

TABLE 73

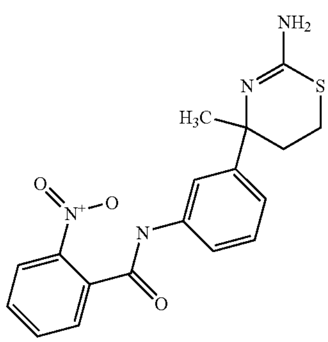
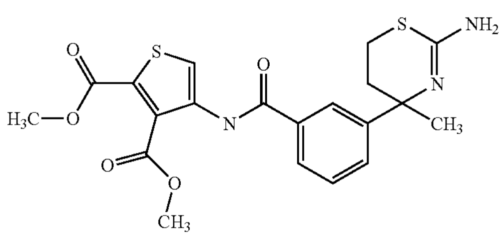
No.	Structure
693	
694	

TABLE 73-continued

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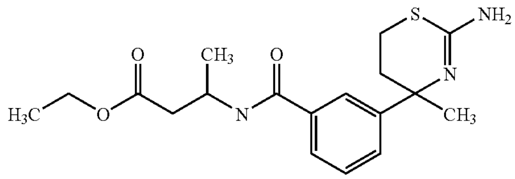
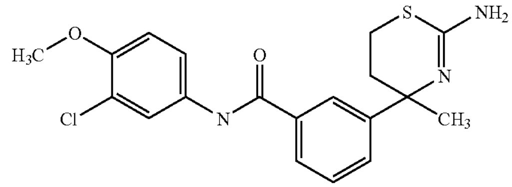
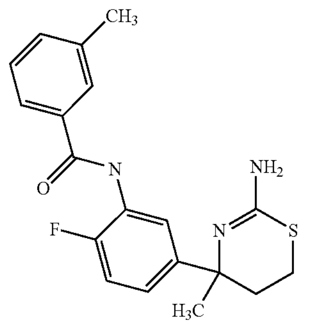
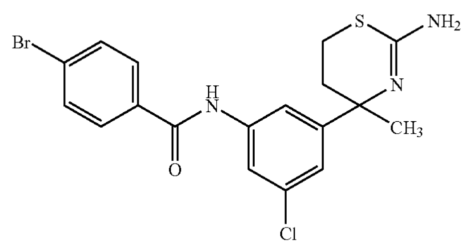
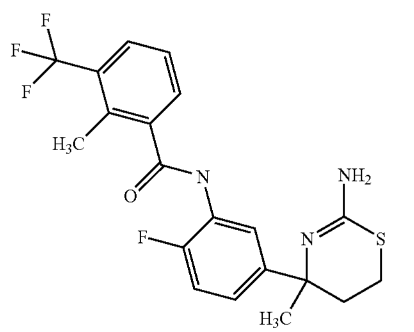
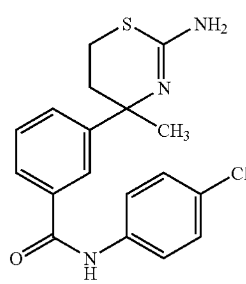
695	
696	
697	
698	
699	
700	

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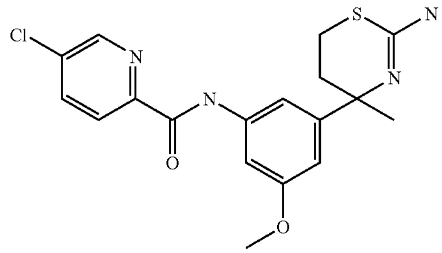
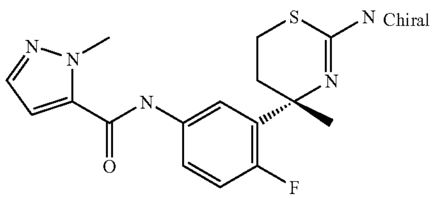
No.	Structure
701	
702	

TABLE 74

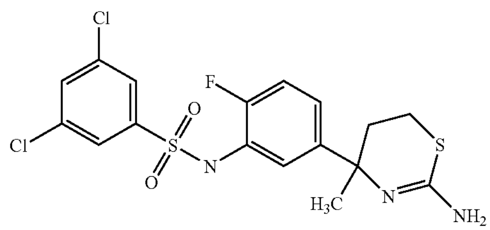
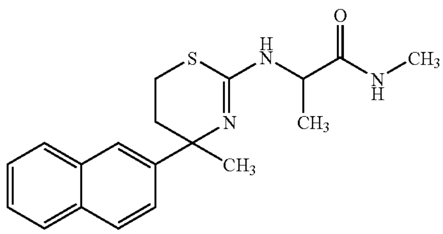
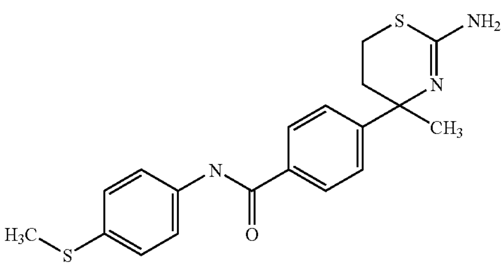
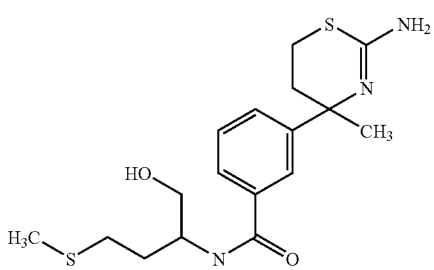
No.	Structure
703	
704	
705	
706	

TABLE 74-continued

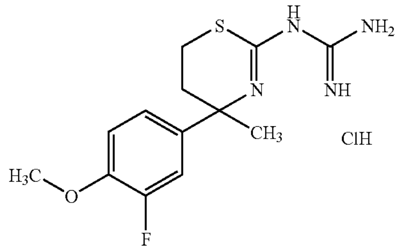
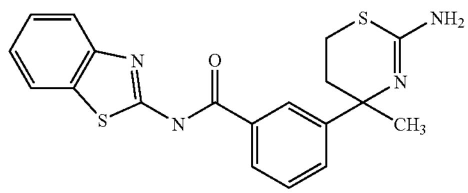
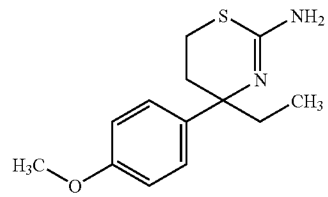
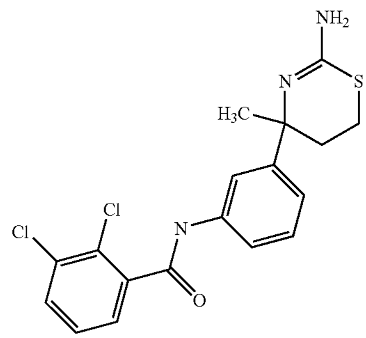
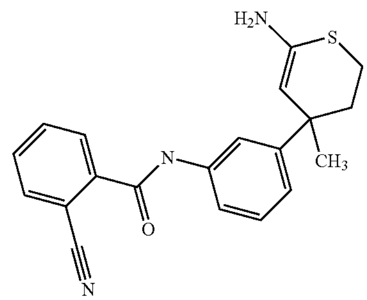
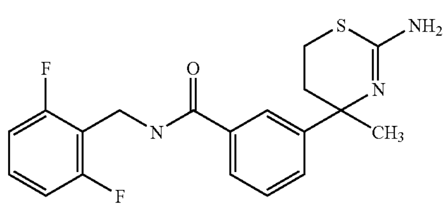
No.	Structure
707	
708	
709	
710	
711	
712	

TABLE 75

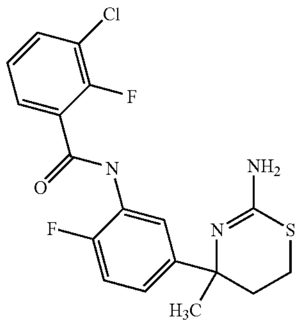
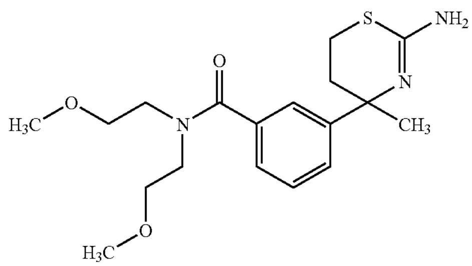
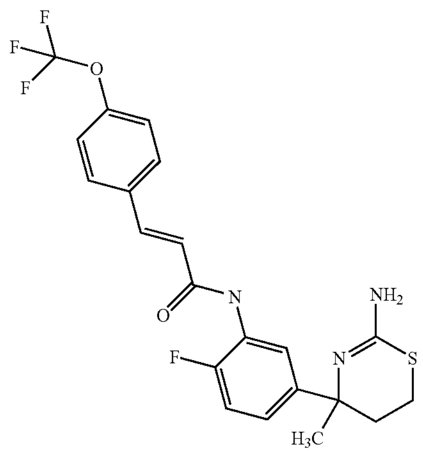
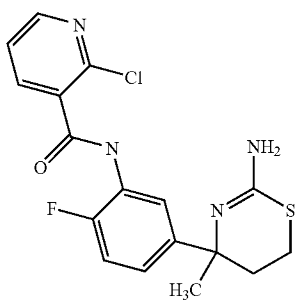
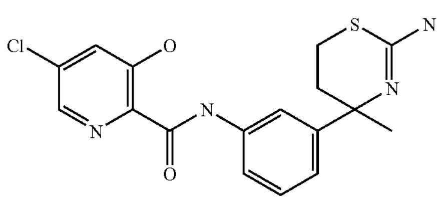
No.	Structure
713	
714	
715	
716	
717	

TABLE 75-continued

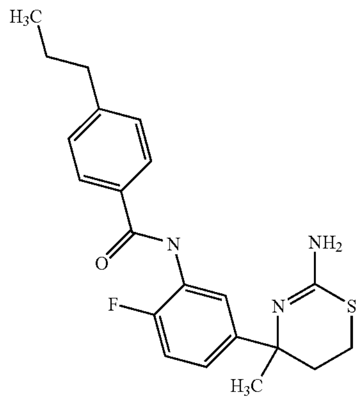
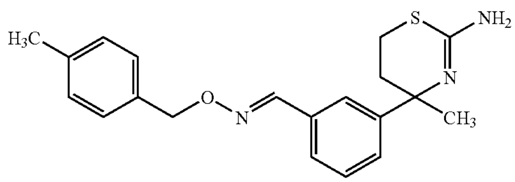
No.	Structure
718	
719	

TABLE 76

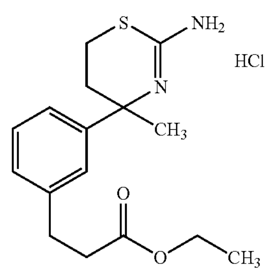
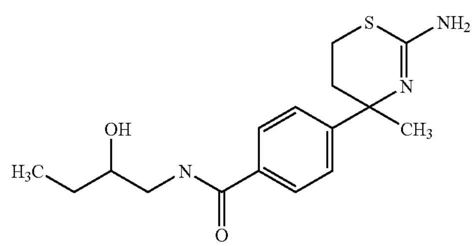
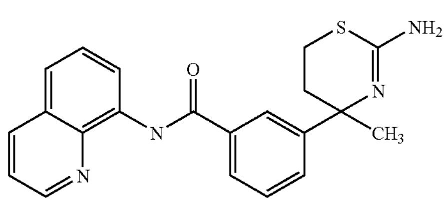
No.	Structure
720	
721	
722	

TABLE 76-continued

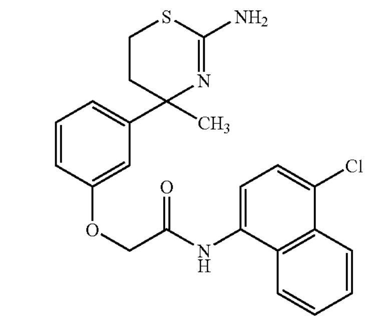
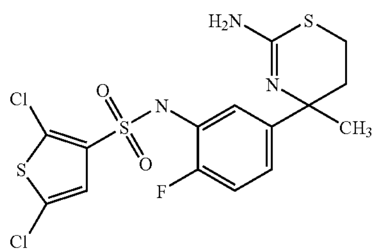
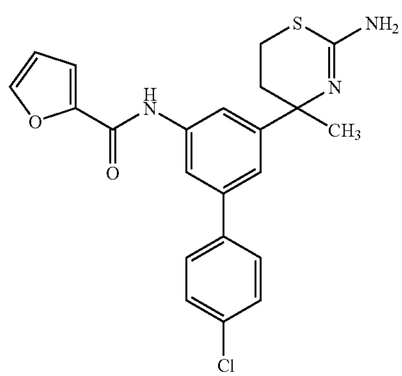
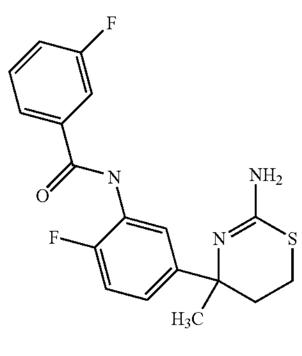
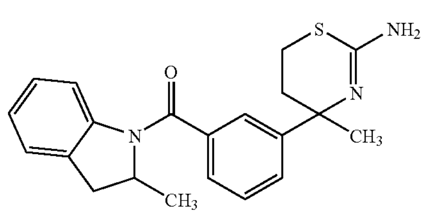
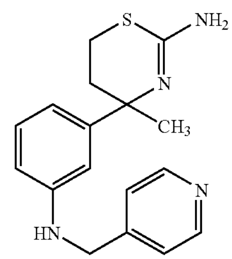
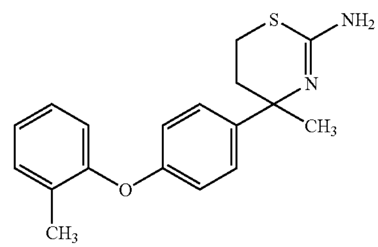
No.	Structure
723	
724	
725	
726	
727	
728	
729	

TABLE 77

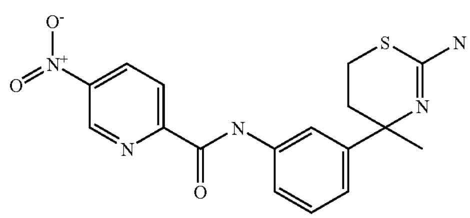
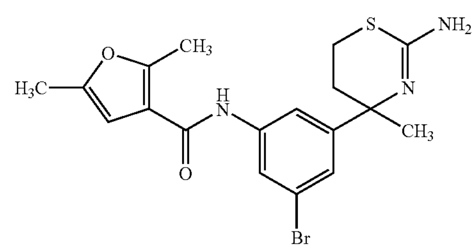
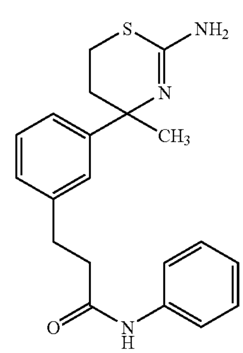
No.	Structure
730	
731	
732	

TABLE 77-continued

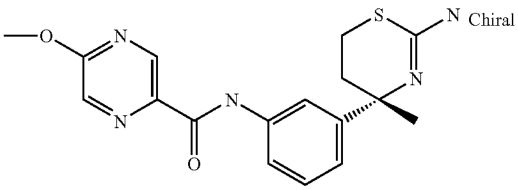
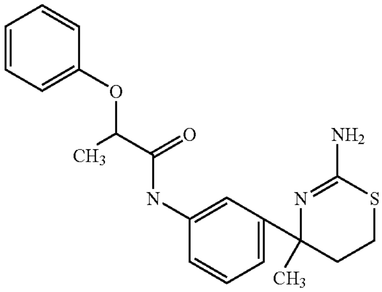
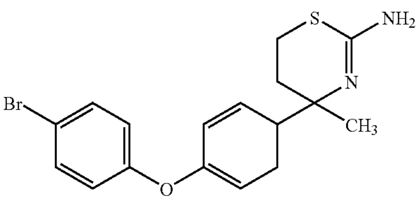
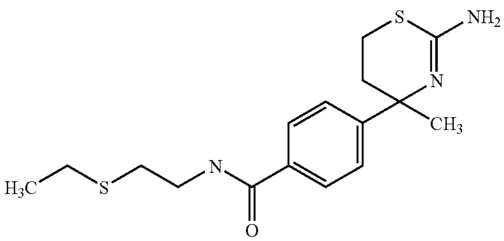
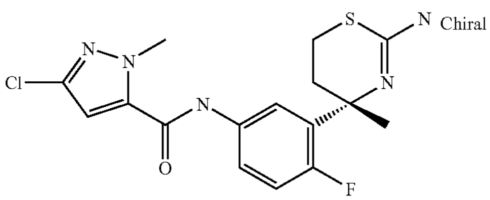
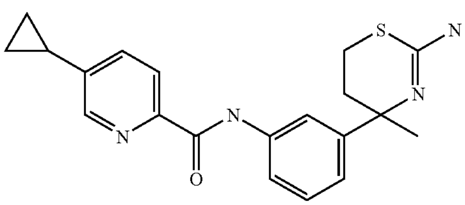
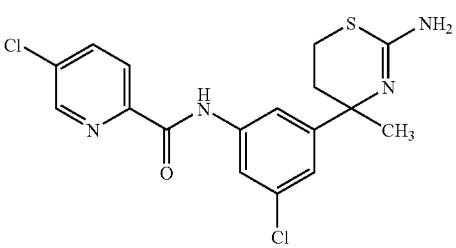
No.	Structure
733	
734	
735	
736	
737	
738	
739	

TABLE 77-continued

No.	Structure

TABLE 78

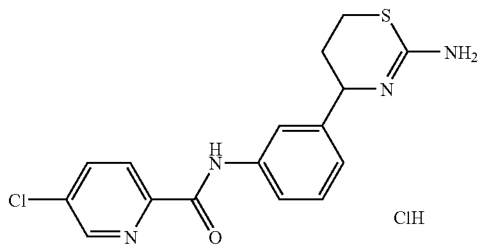
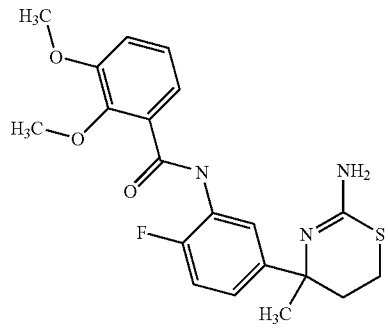
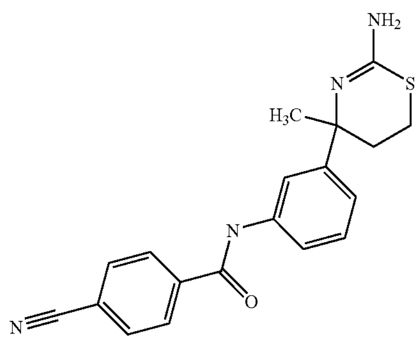
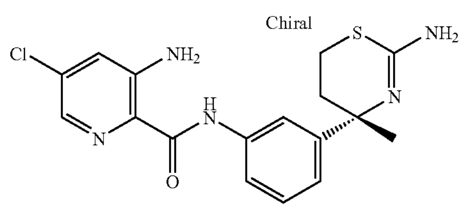
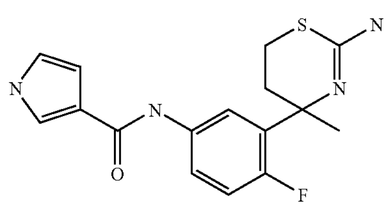
No.	Structure
740	
741	
742	
743	
744	

TABLE 78-continued

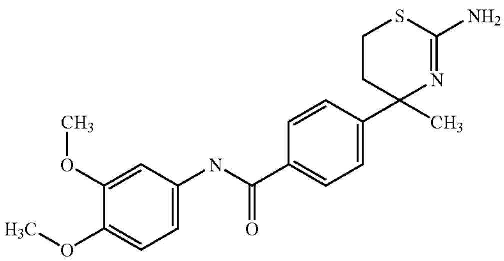
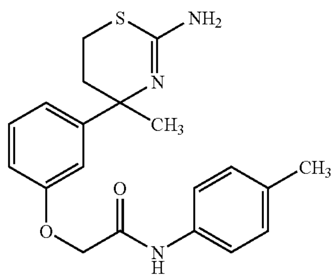
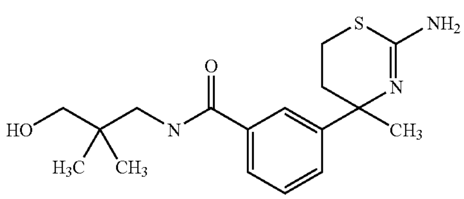
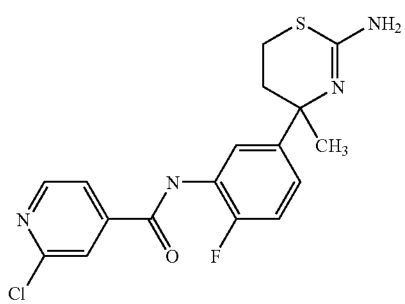
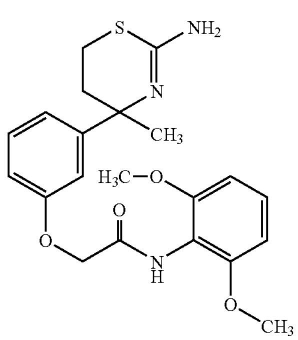
No.	Structure
745	
746	
747	
748	
749	

TABLE 79

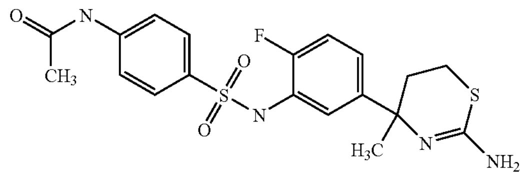
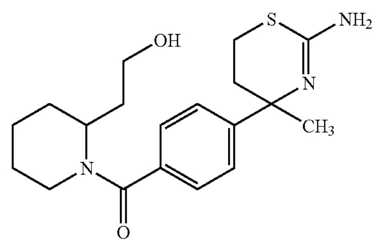
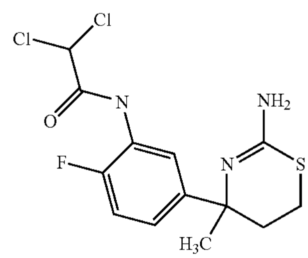
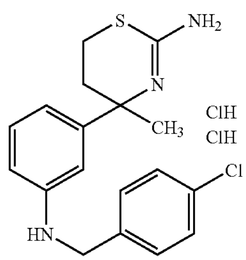
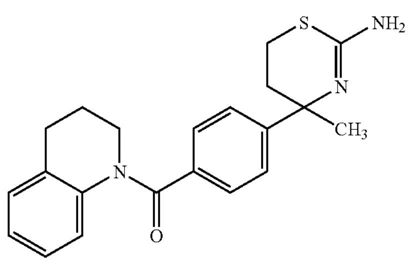
No.	Structure
750	
751	
752	
753	
754	

TABLE 79-continued

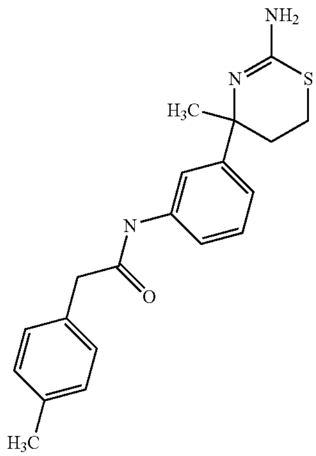
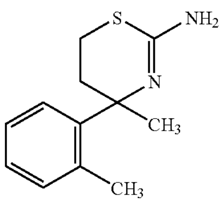
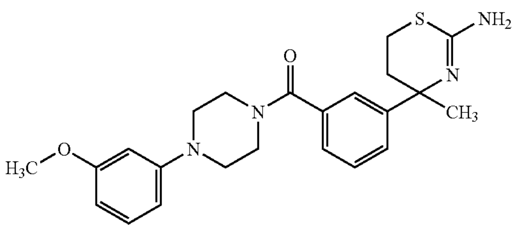
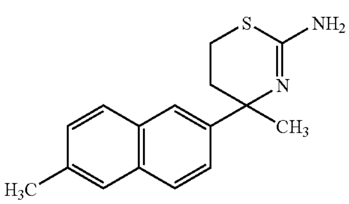
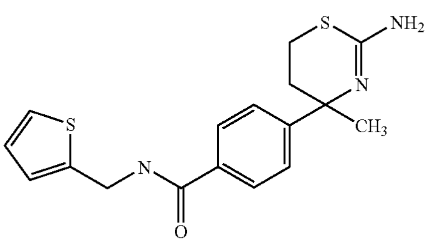
No.	Structure
755	
756	
757	
758	
759	

TABLE 80

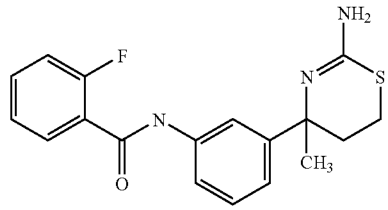
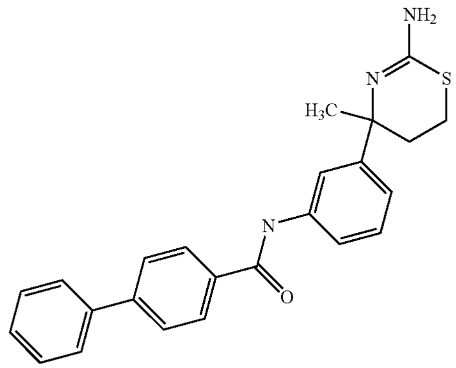
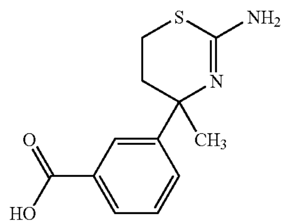
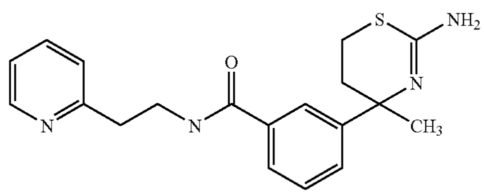
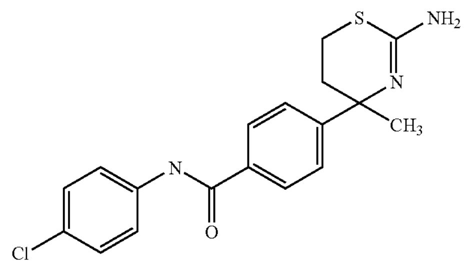
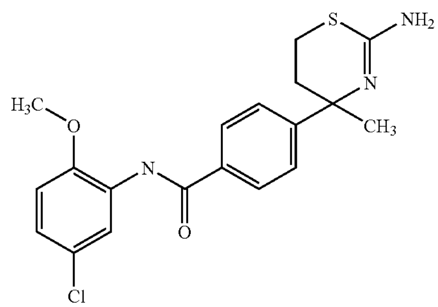
No.	Structure
760	
761	
762	
763	
764	
765	

TABLE 80-continued

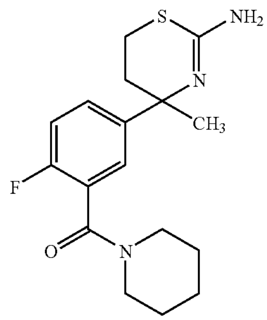
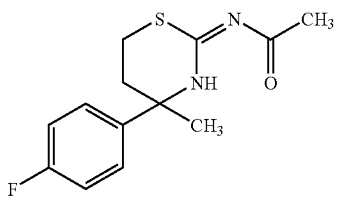
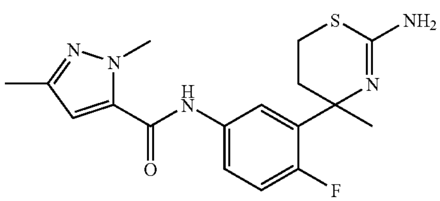
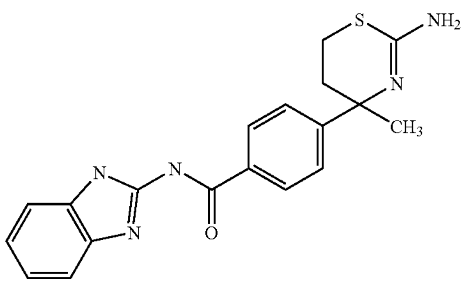
No.	Structure
766	
767	
768	
769	

TABLE 81

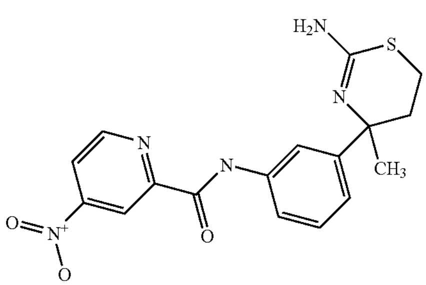
No.	Structure
770	

TABLE 81-continued

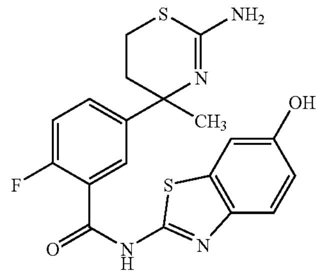
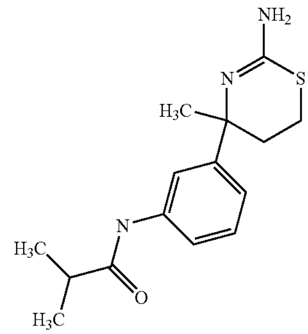
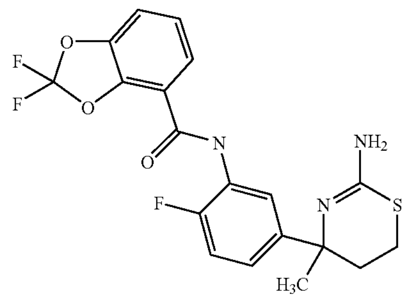
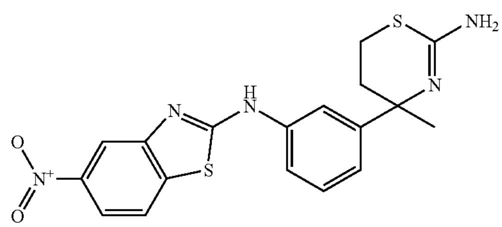
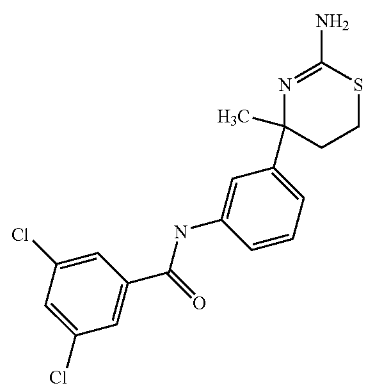
No.	Structure
771	
772	
773	
774	
775	

TABLE 81-continued

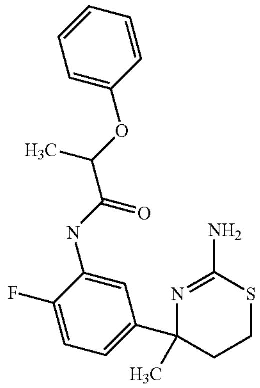
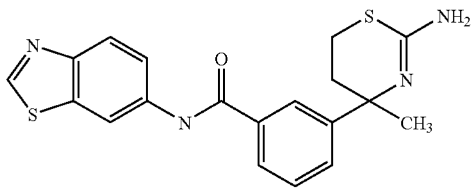
No.	Structure
776	
777	

TABLE 82

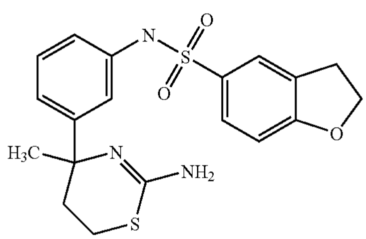
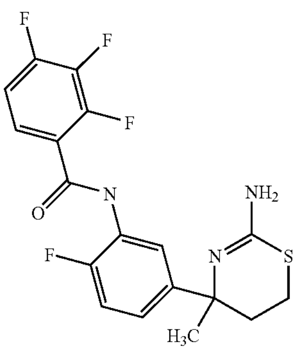
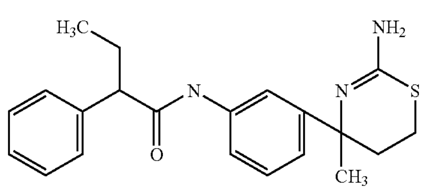
No.	Structure
778	
779	
780	

TABLE 82-continued

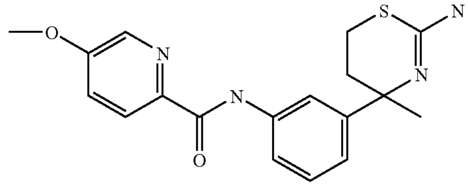
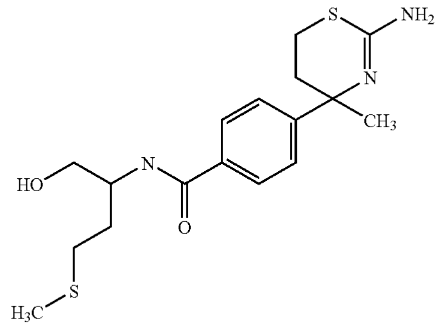
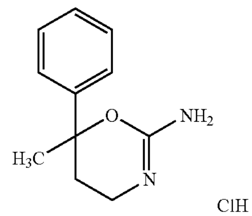
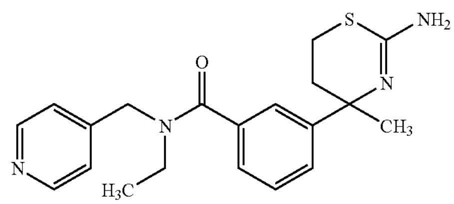
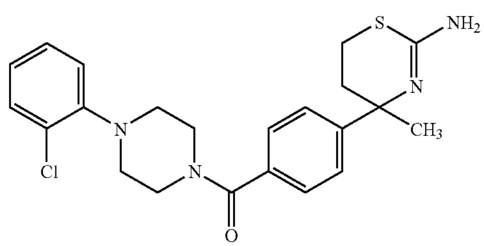
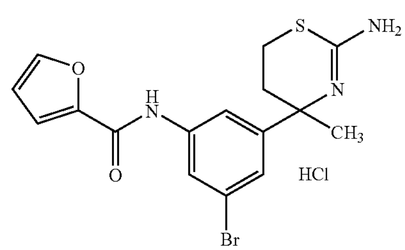
No.	Structure
781	
782	
783	
784	
785	
786	

TABLE 82-continued

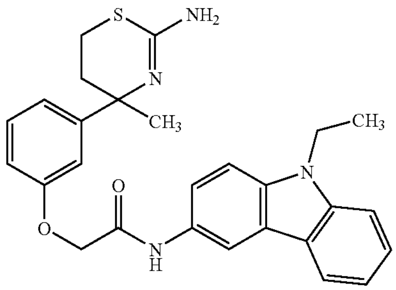
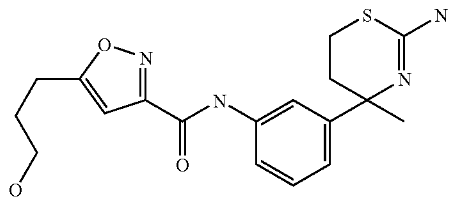
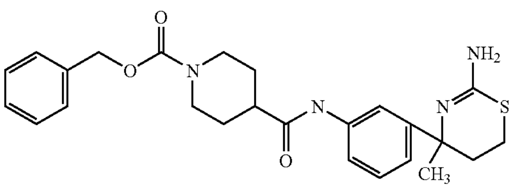
No.	Structure
787	
788	
789	

TABLE 83

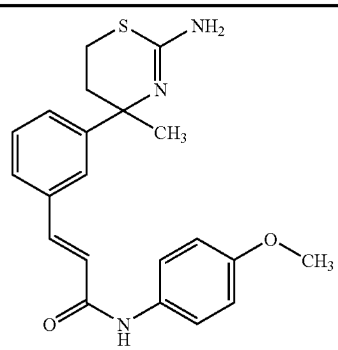
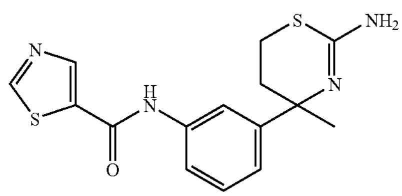
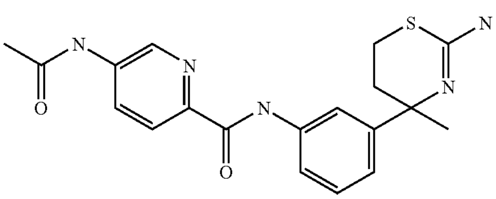
No.	Structure
790	
791	
792	

TABLE 83-continued

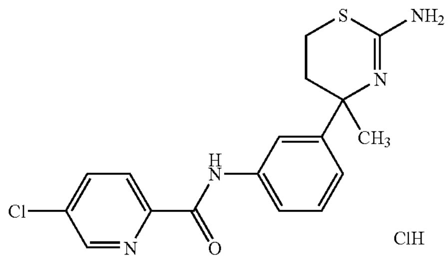
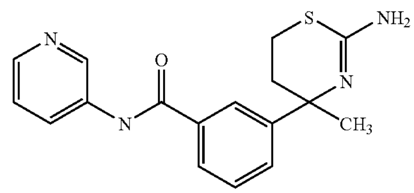
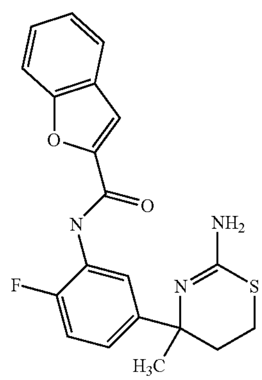
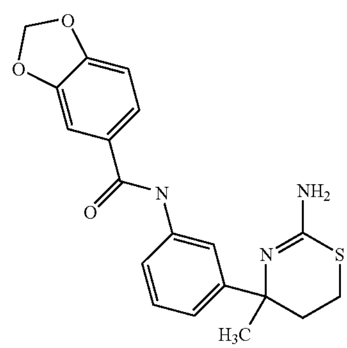
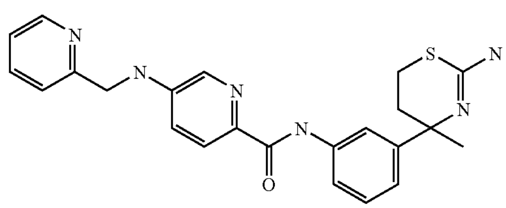
No.	Structure
793	
794	
795	
796	
797	

TABLE 83-continued

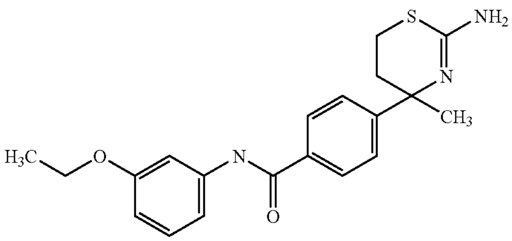
No.	Structure
798	

TABLE 84

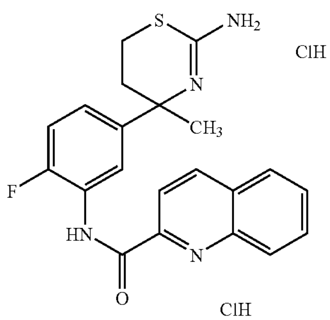
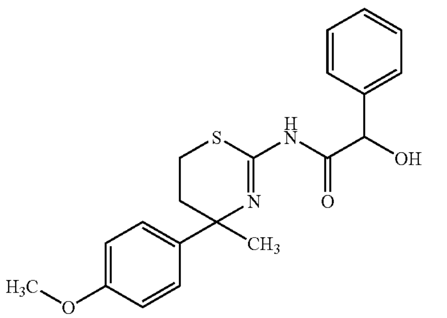
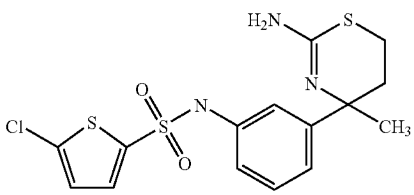
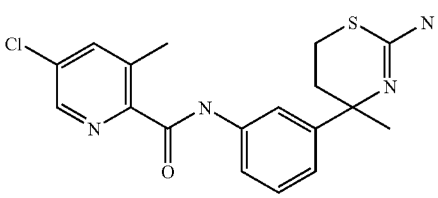
No.	Structure
799	
800	
801	
802	

TABLE 84-continued

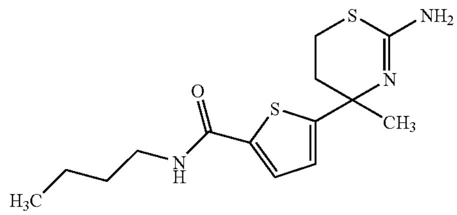
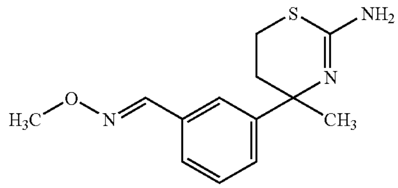
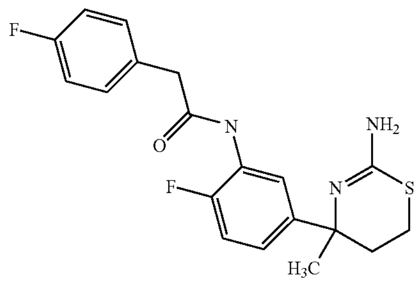
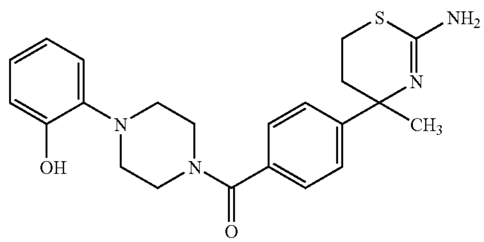
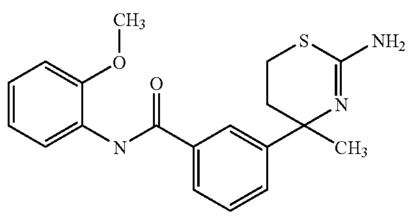
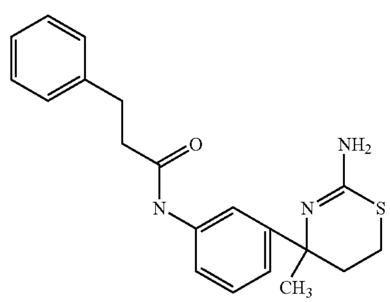
No.	Structure
803	
804	
805	
806	
807	
808	

TABLE 84-continued

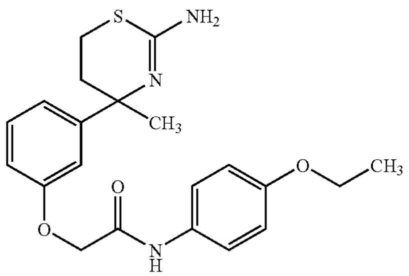
No.	Structure
809	

TABLE 85

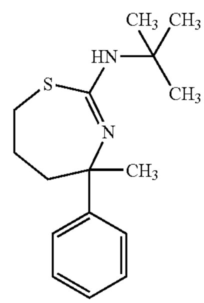
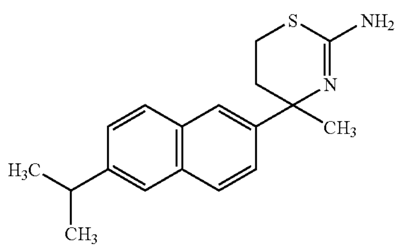
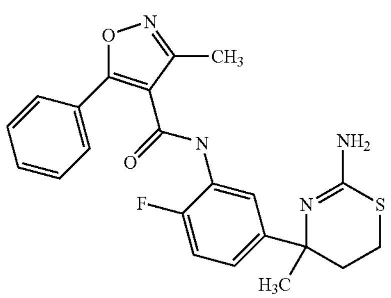
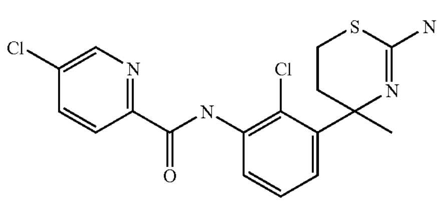
No.	Structure
810	
811	
812	
813	

TABLE 85-continued

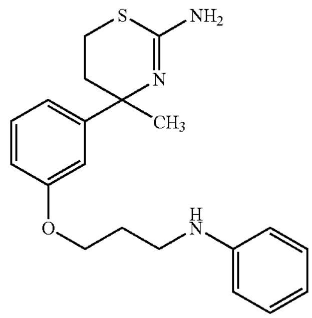
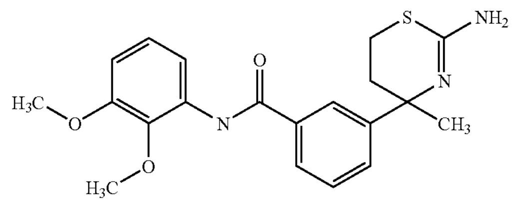
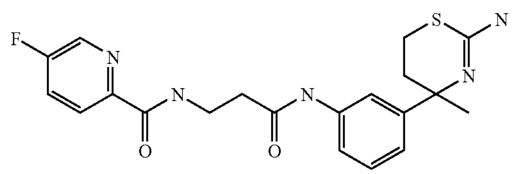
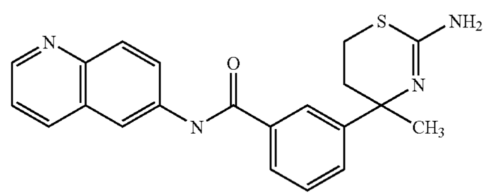
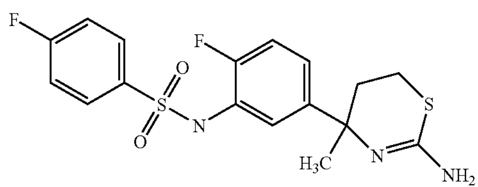
No.	Structure
814	
815	
816	
817	
818	

TABLE 86

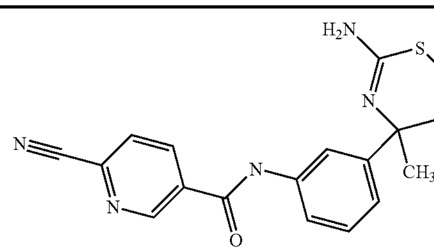
No.	Structure
819	

TABLE 86-continued

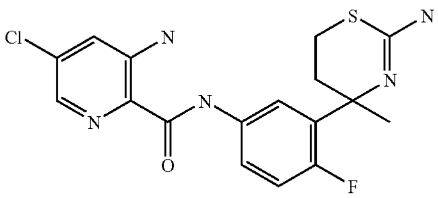
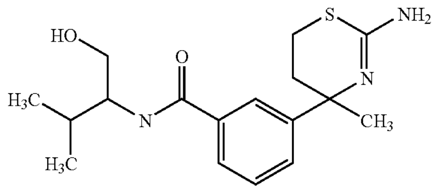
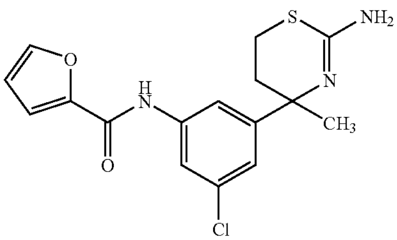
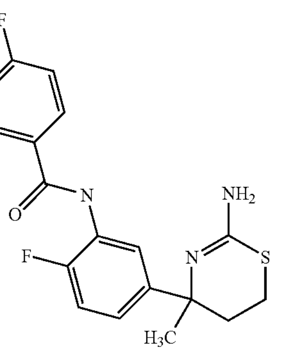
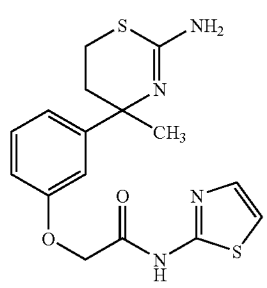
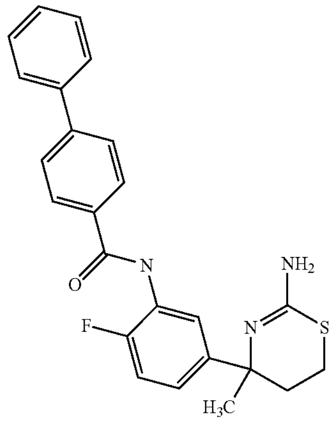
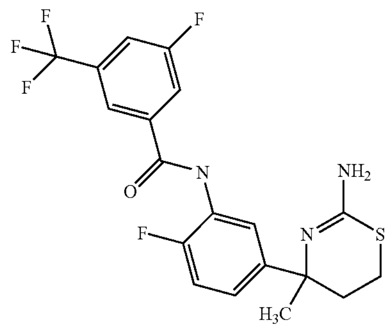
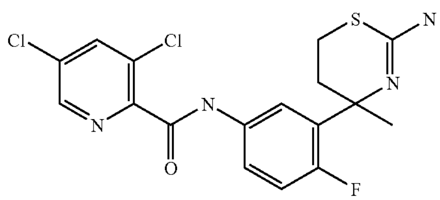
No.	Structure
820	
821	
822	
823	
824	
825	
826	
827	

TABLE 87

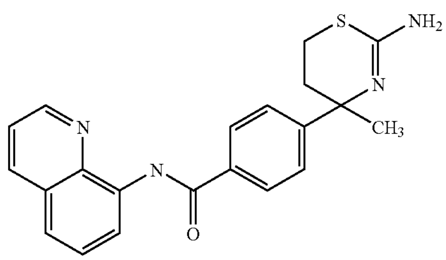
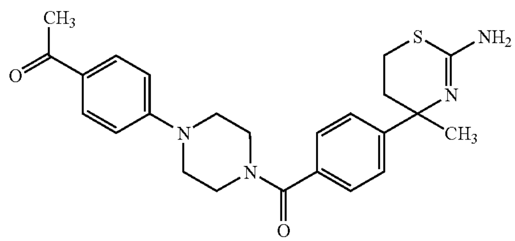
No.	Structure
828	
829	

TABLE 87-continued

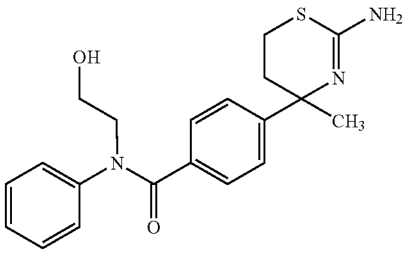
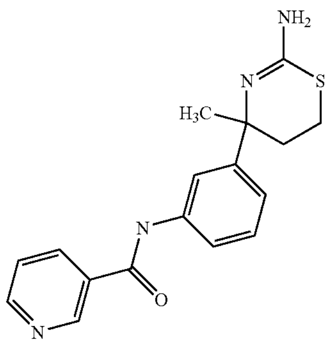
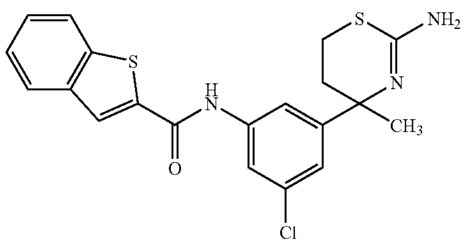
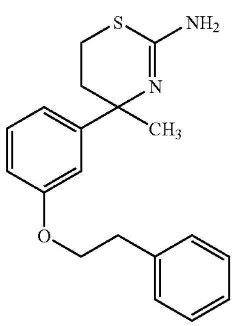
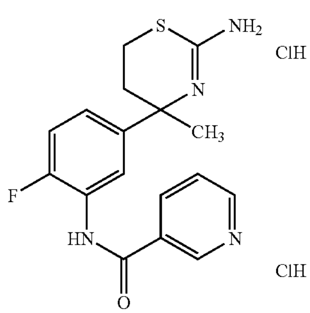
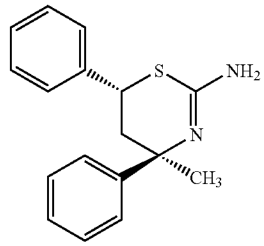
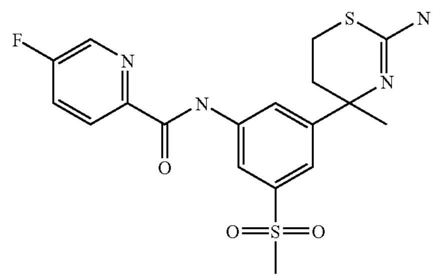
No.	Structure
830	
831	
832	
833	
834	
835 (race mate)	
836	

TABLE 88

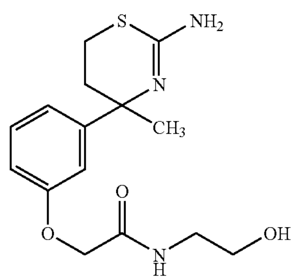
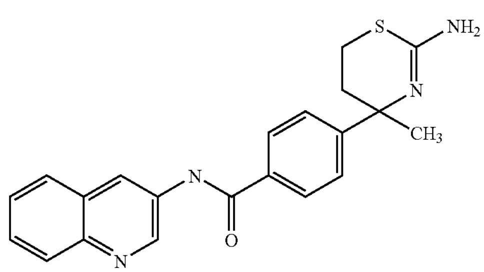
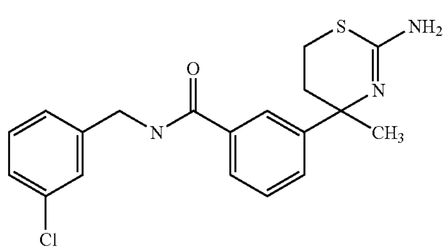
No.	Structure
837	
838	
839	

TABLE 88-continued

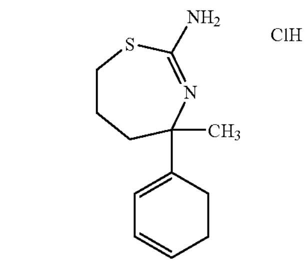
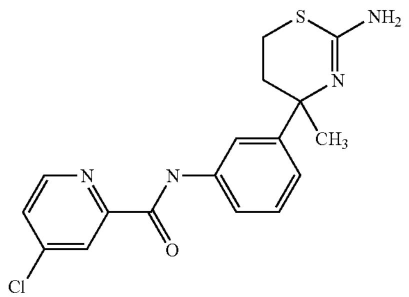
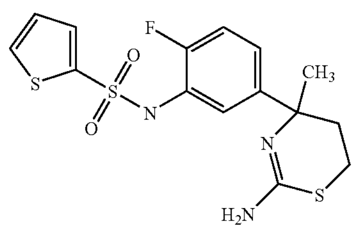
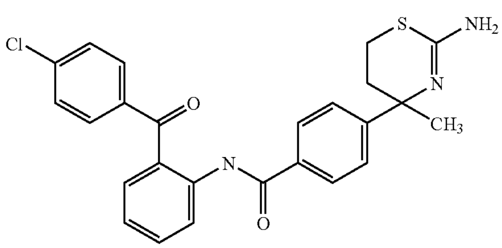
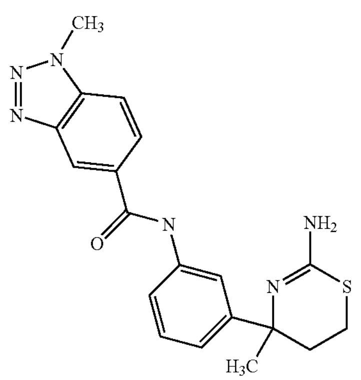
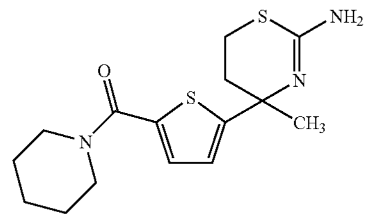
No.	Structure
840	
841	
842	
843	
844	
845	

TABLE 89

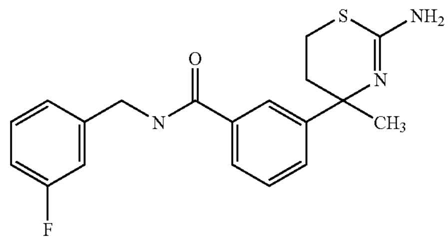
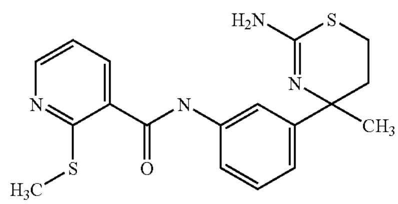
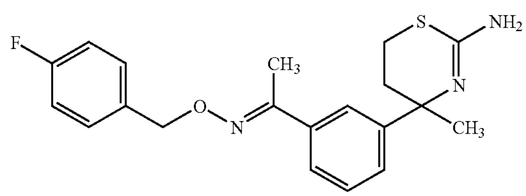
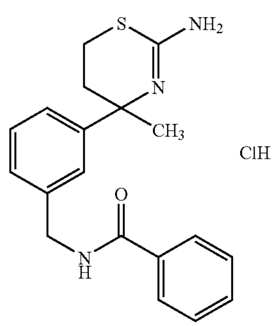
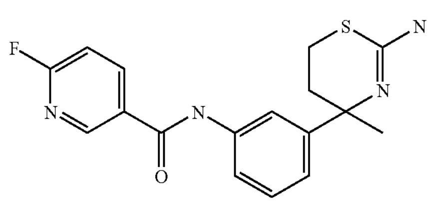
No.	Structure
846	
847	
848	
849	
850	

TABLE 89-continued

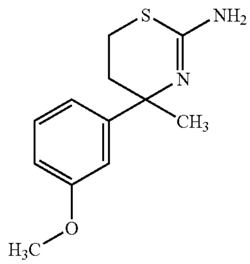
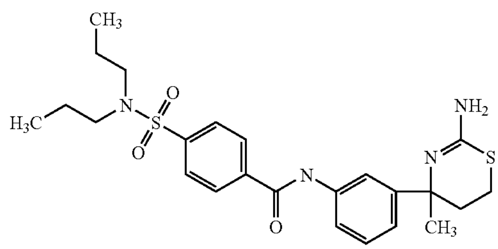
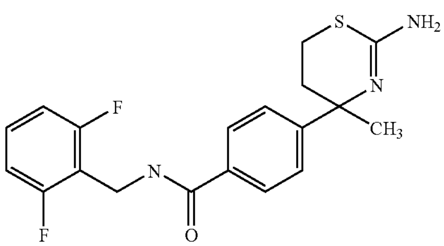
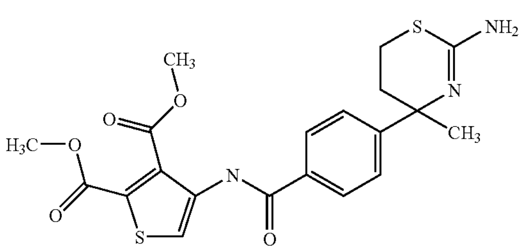
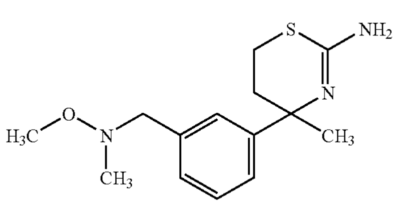
No.	Structure
851	
852	
853	
854	
855	

TABLE 90

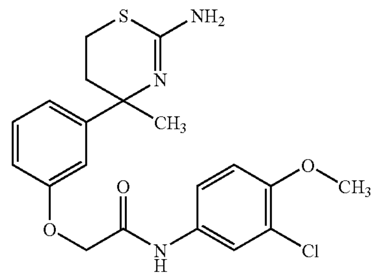
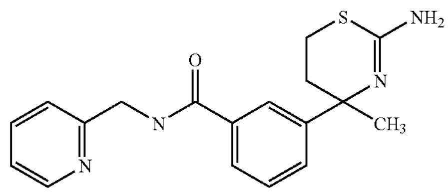
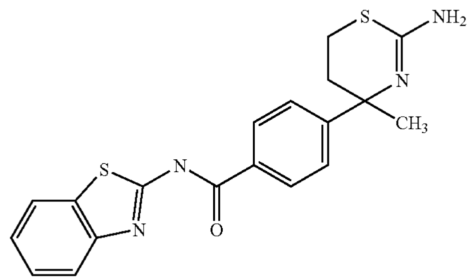
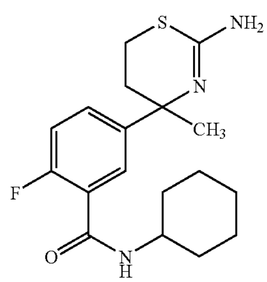
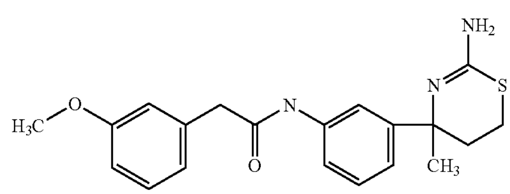
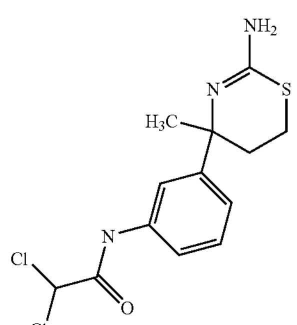
No.	Structure
856	
857	
858	
859	
860	
861	

TABLE 90-continued

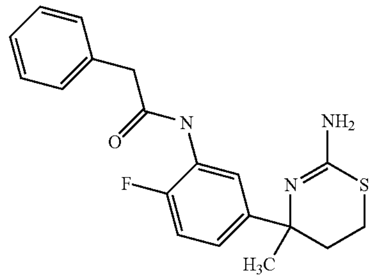
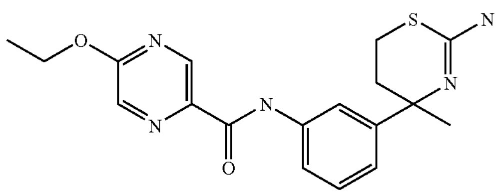
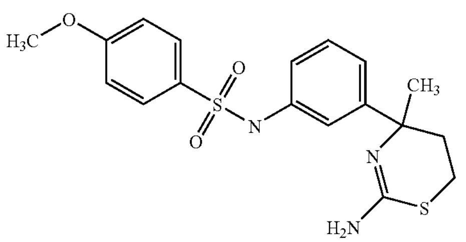
No.	Structure
862	
863	
864	

TABLE 91

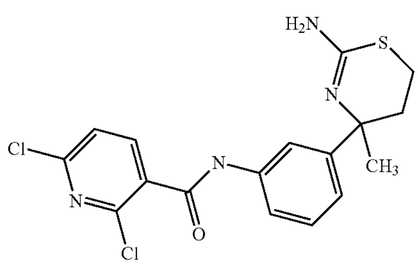
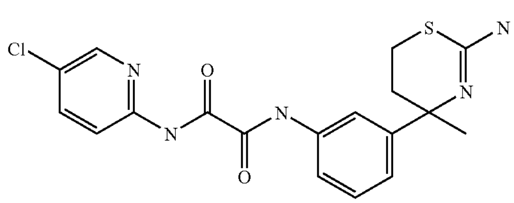
No.	Structure
865	
866	

TABLE 91-continued

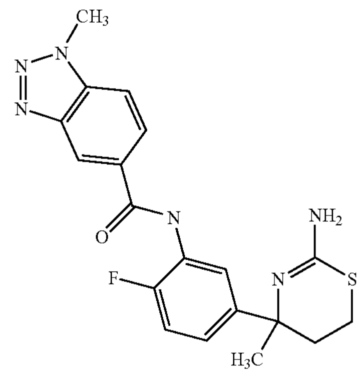
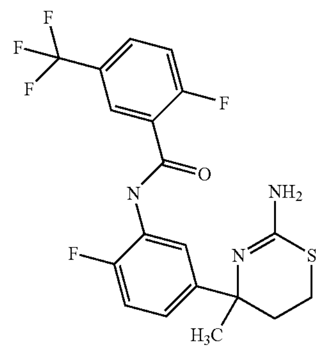
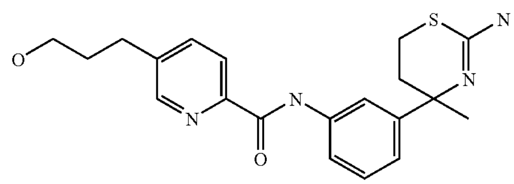
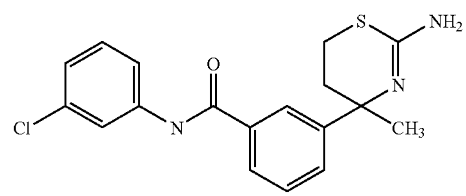
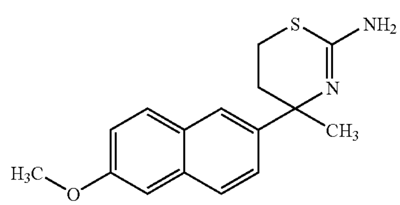
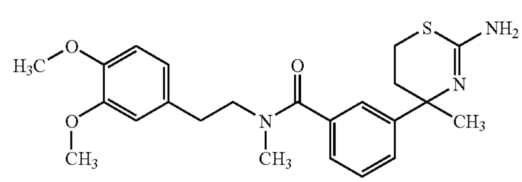
No.	Structure
867	
868	
869	
870	
871	
872	

TABLE 91-continued

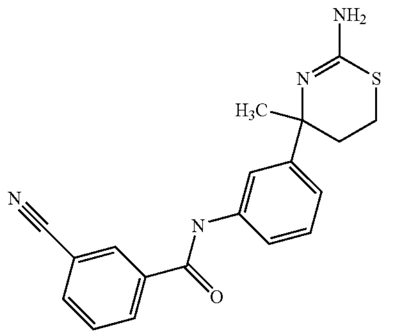
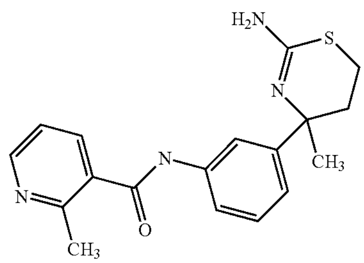
No.	Structure
873	
874	

TABLE 92

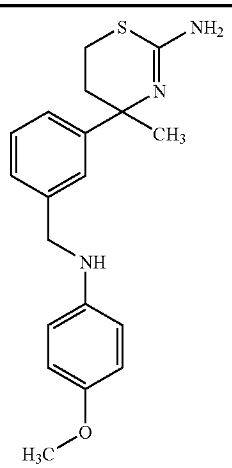
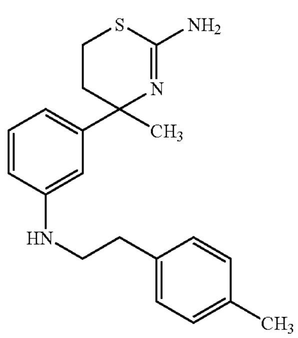
No.	Structure
875	
876	

TABLE 92-continued

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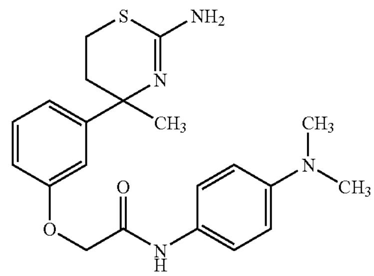
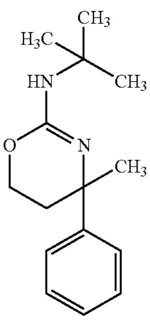
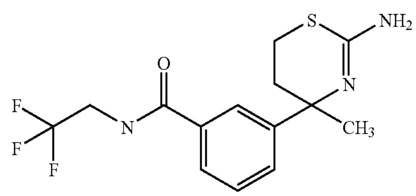
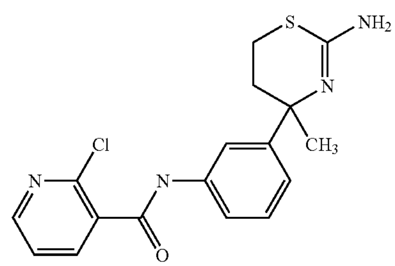
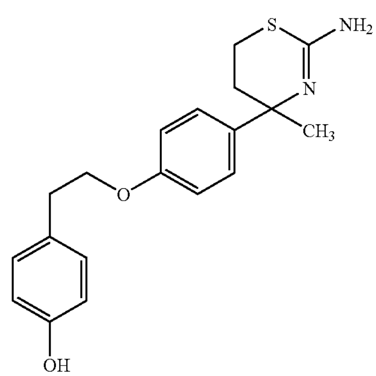
877	
878	
879	
880	
881	

TABLE 92-continued

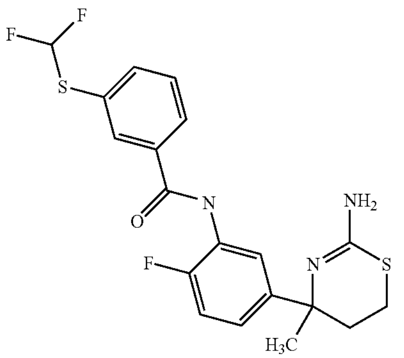
No.	Structure
882	

TABLE 93

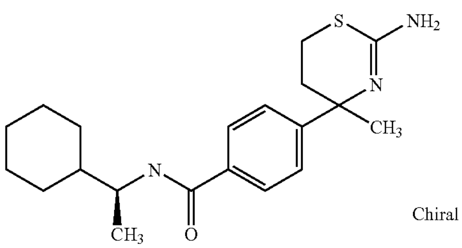
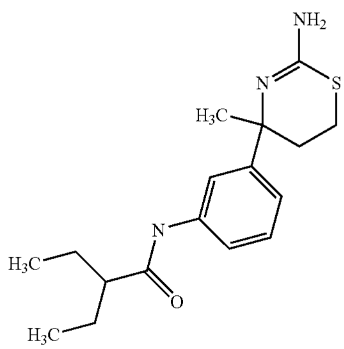
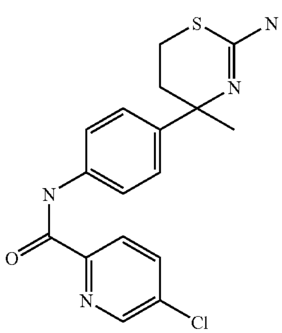
No.	Structure
883	 Chiral
884	
885	

TABLE 93-continued

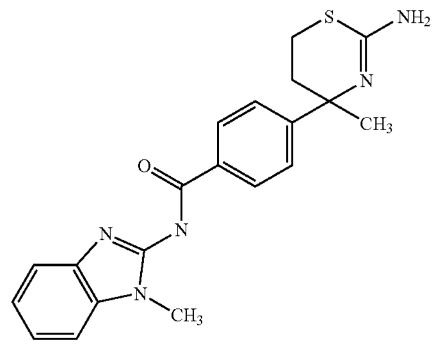
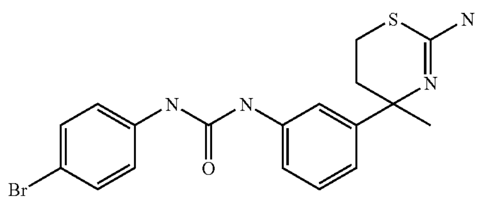
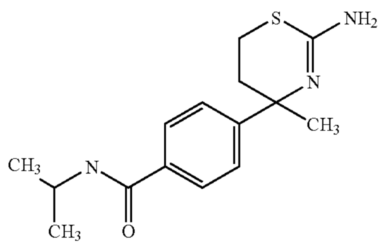
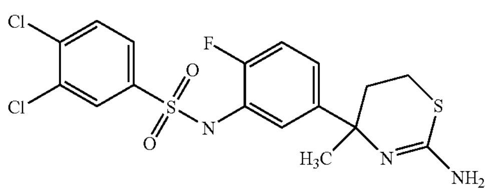
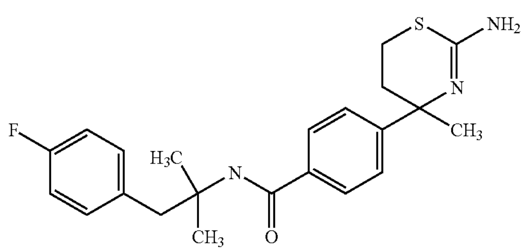
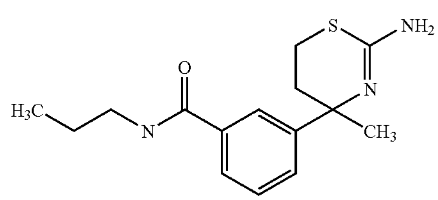
No.	Structure
886	
887	
888	
889	
890	
891	

TABLE 94

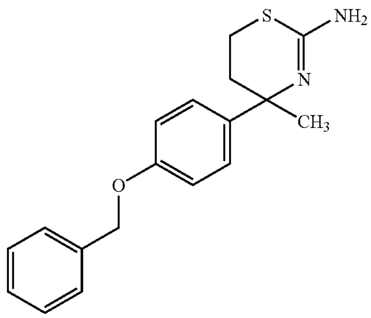
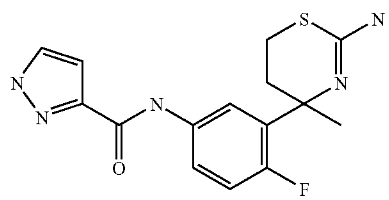
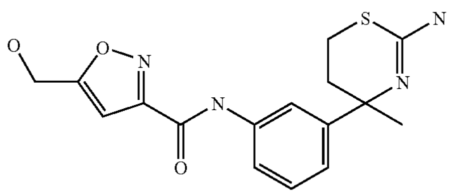
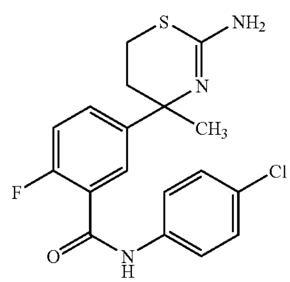
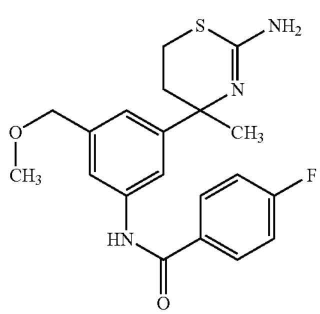
No.	Structure
892	
893	
894	
895	
896	

TABLE 94-continued

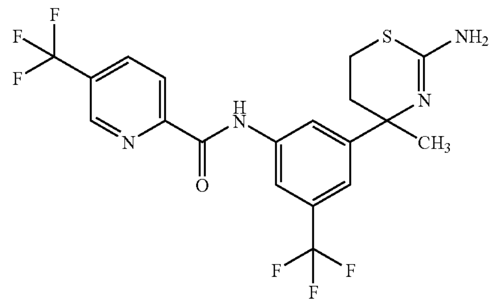
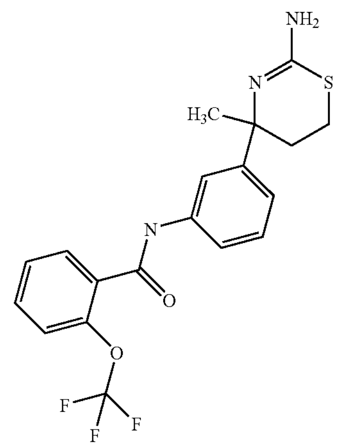
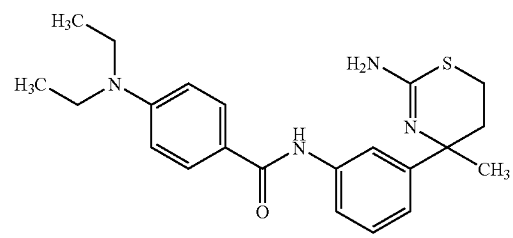
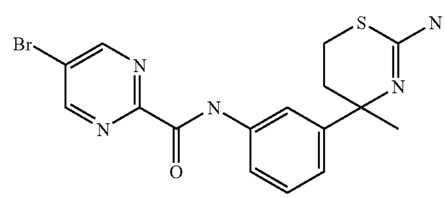
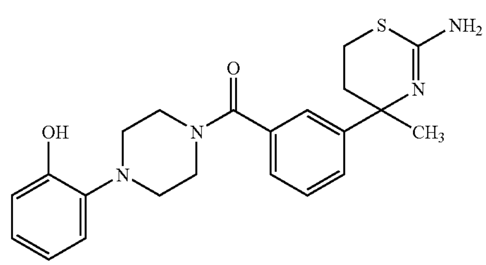
No.	Structure
897	
898	
899	
900	
901	

TABLE 95

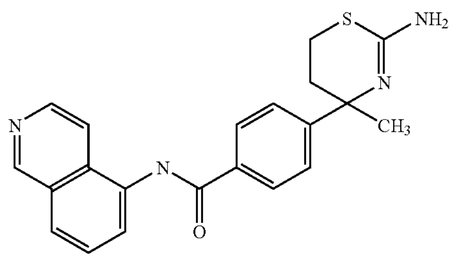
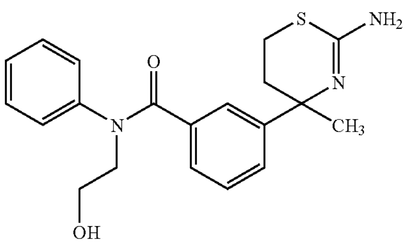
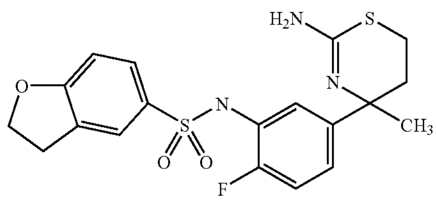
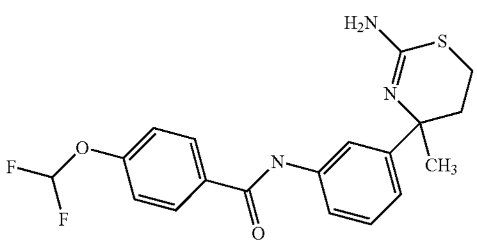
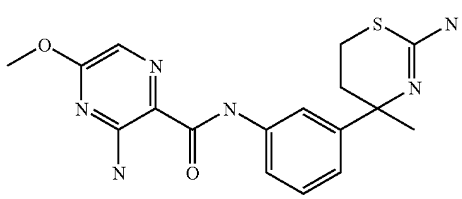
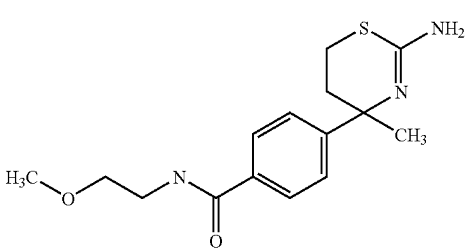
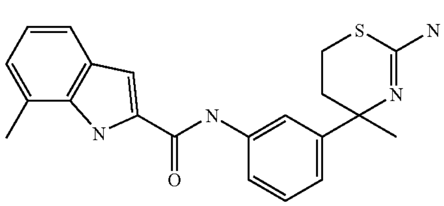
No.	Structure
902	
903	
904	
905	
906	
907	
908	

TABLE 95-continued

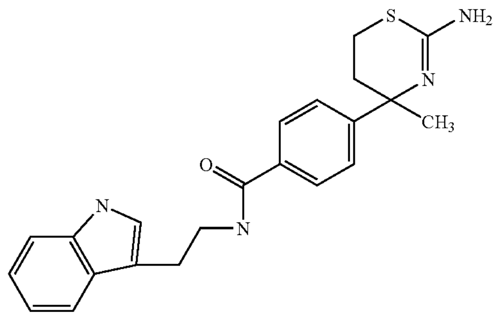
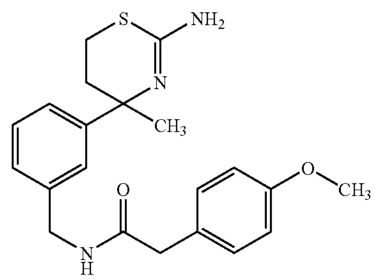
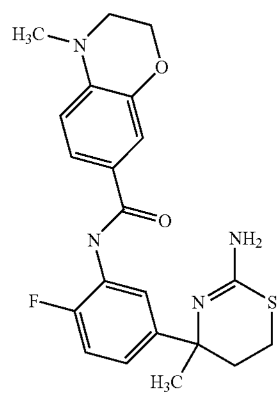
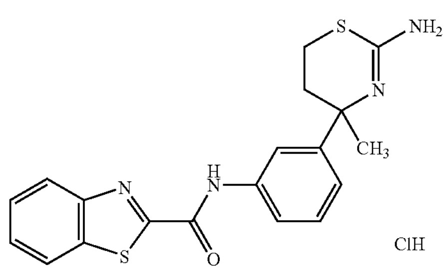
No.	Structure
909	
910	
911	
912	

TABLE 96

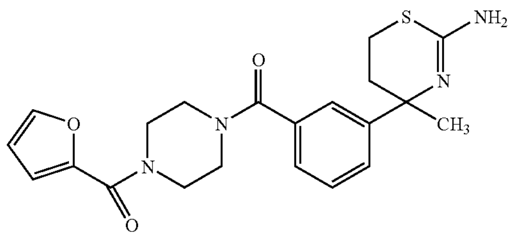
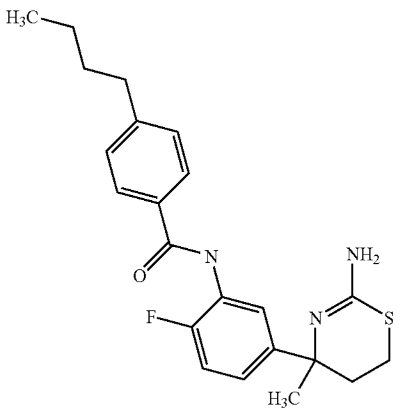
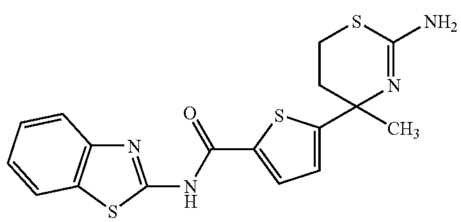
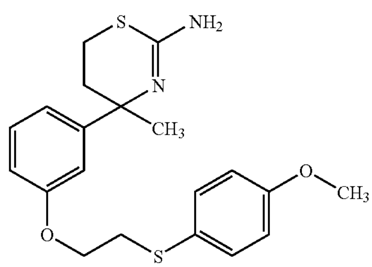
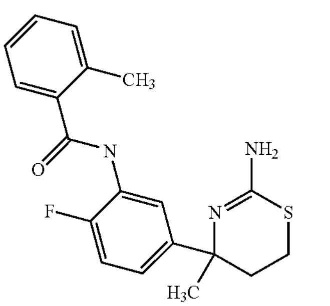
No.	Structure
913	
914	
915	
916	
917	

TABLE 96-continued

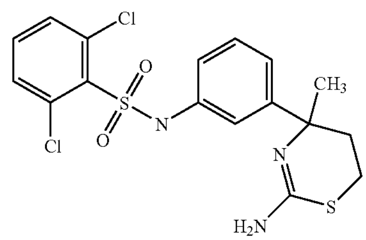
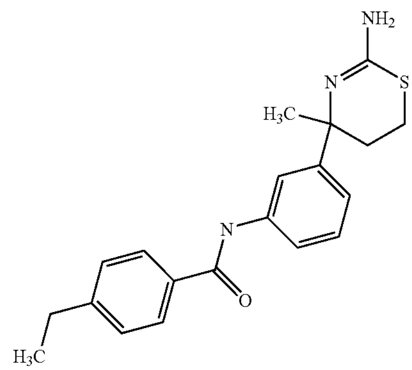
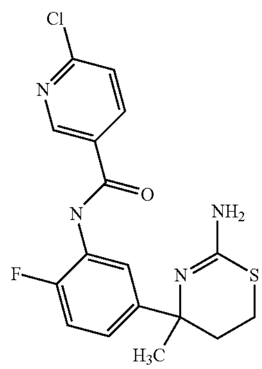
No.	Structure
918	
919	
920	

TABLE 97

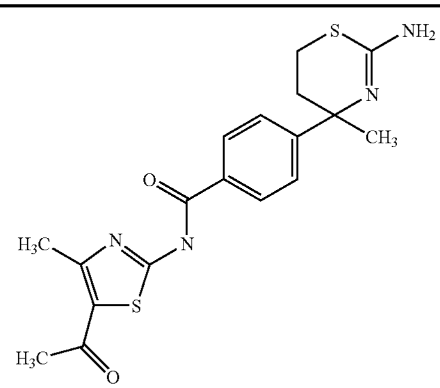
No.	Structure
921	

TABLE 97-continued

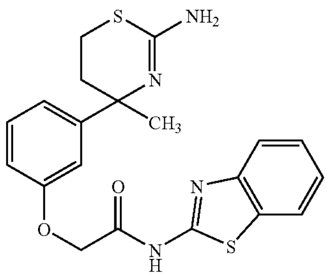
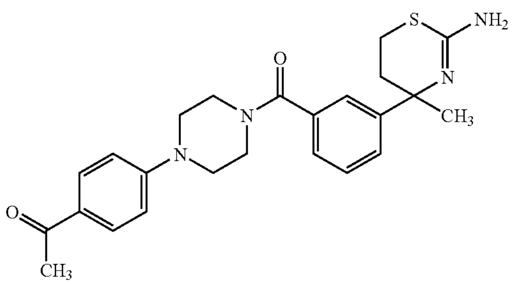
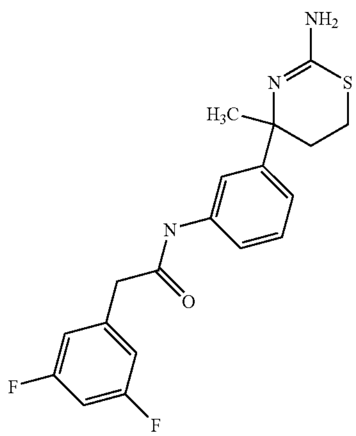
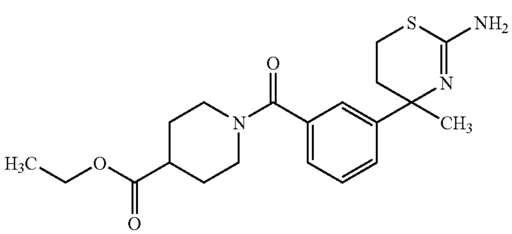
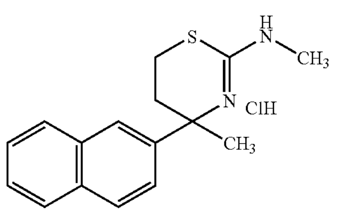
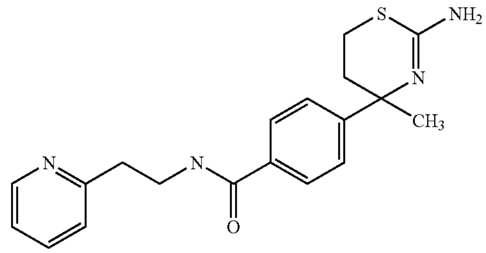
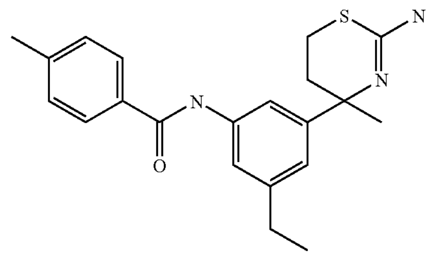
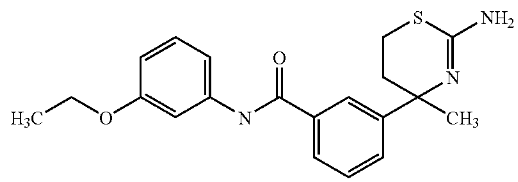
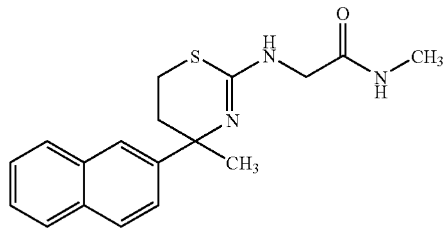
No.	Structure
922	
923	
924	
925	
926	
927	
928	
929	
930	

TABLE 98

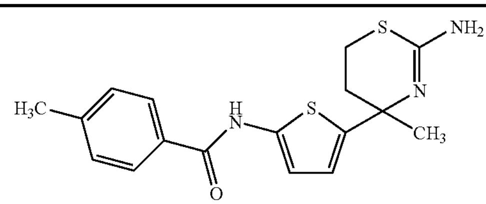
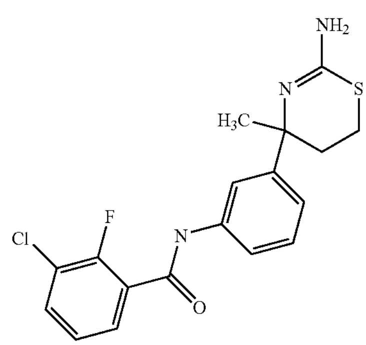
No.	Structure
931	
932	

TABLE 98-continued

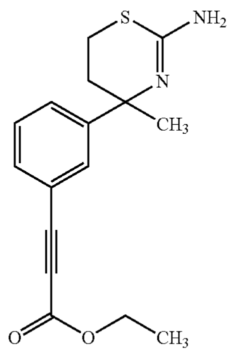
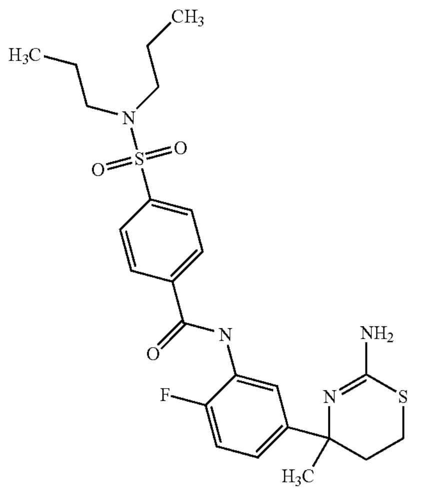
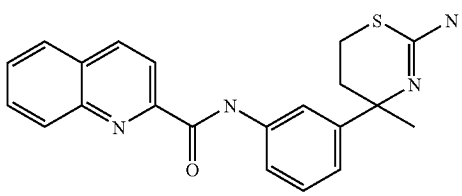
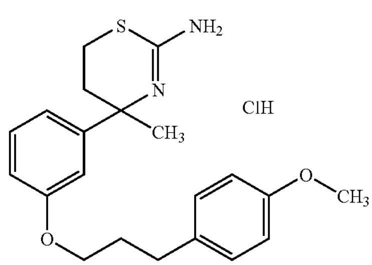
No.	Structure
933	
934	
935	
936	

TABLE 98-continued

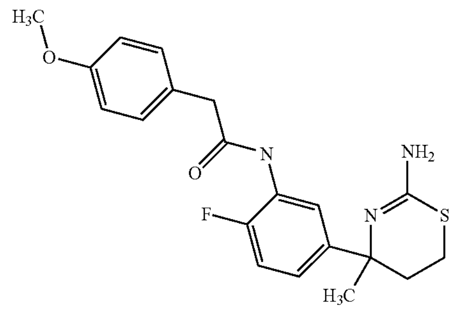
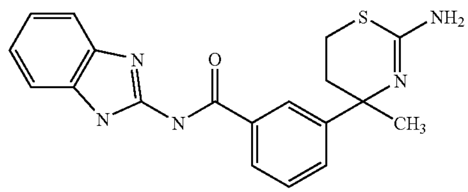
No.	Structure
937	
938	

TABLE 99

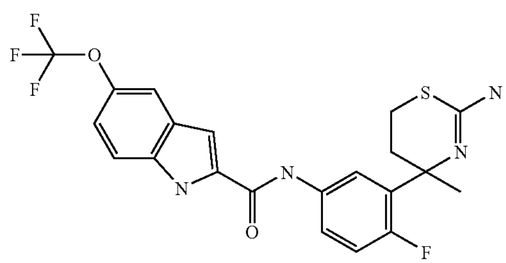
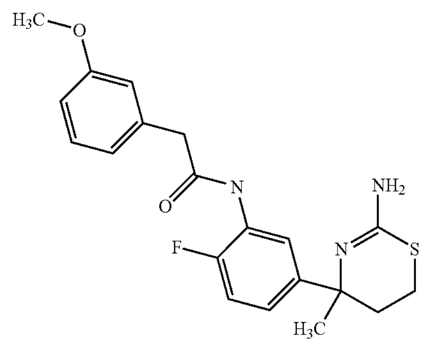
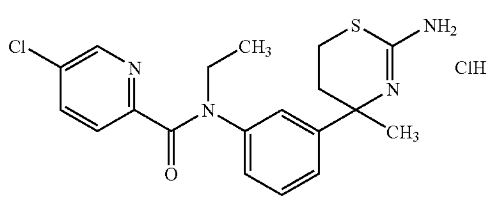
No.	Structure
939	
940	
941	

TABLE 99-continued

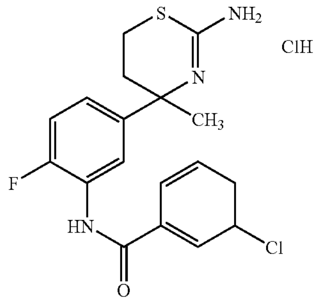
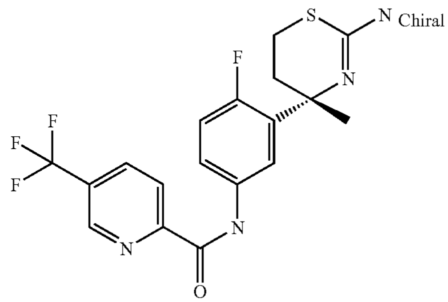
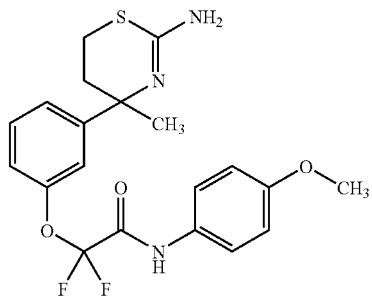
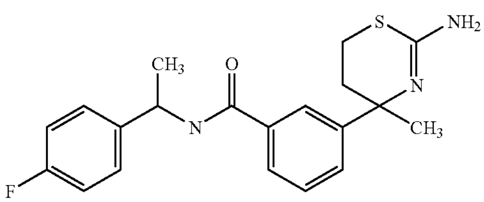
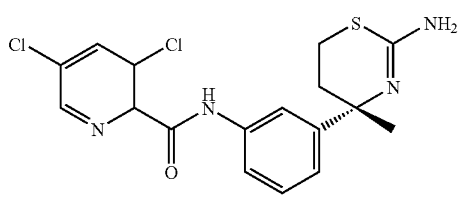
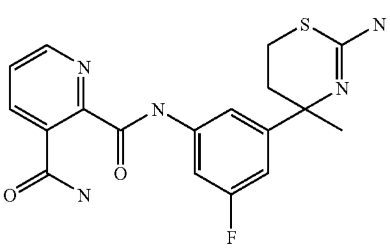
No.	Structure
942	
943	
944	
945	
946	
947	

TABLE 100

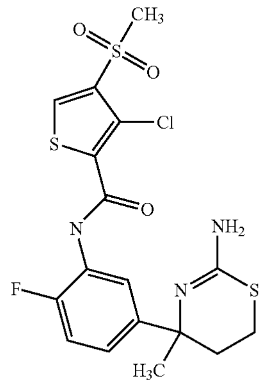
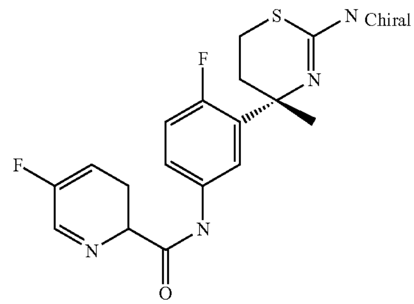
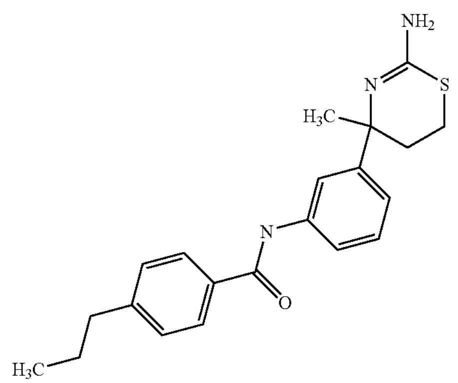
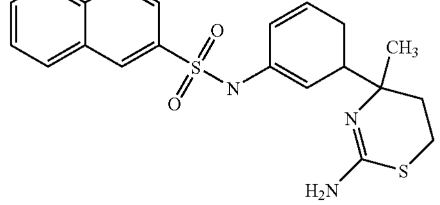
No.	Structure
948	
949	
950	
951	

TABLE 100-continued

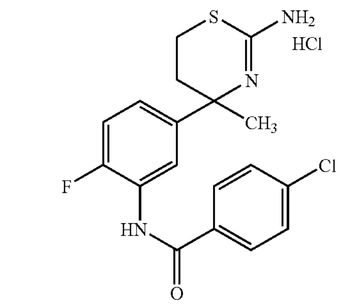
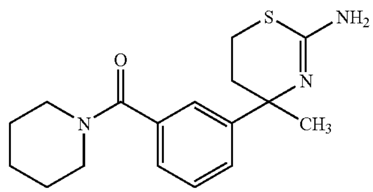
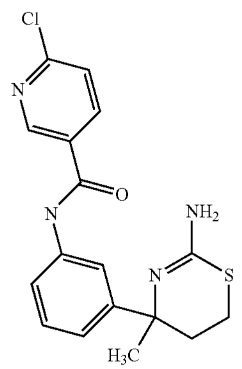
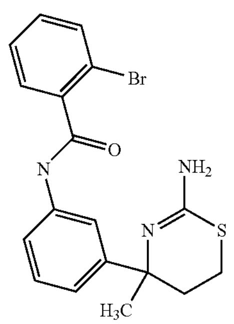
No.	Structure
952	
953	
954	
955	

TABLE 101

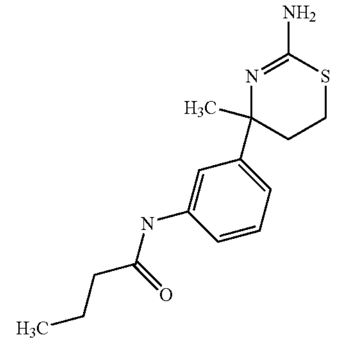
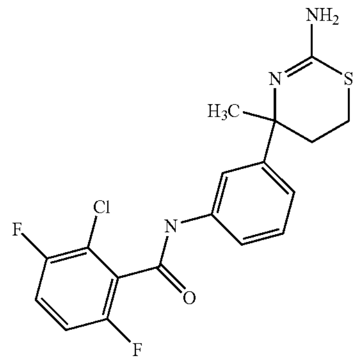
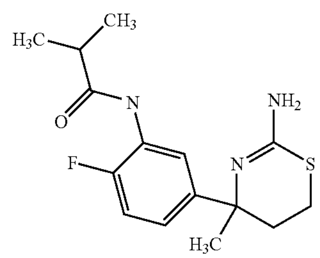
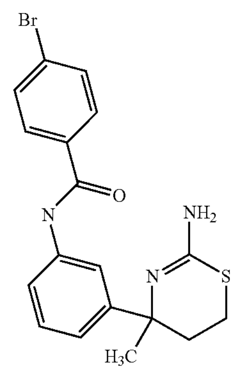
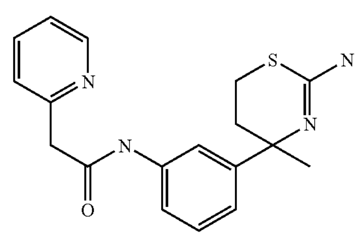
No.	Structure
956	
957	
958	
959	
960	

TABLE 101-continued

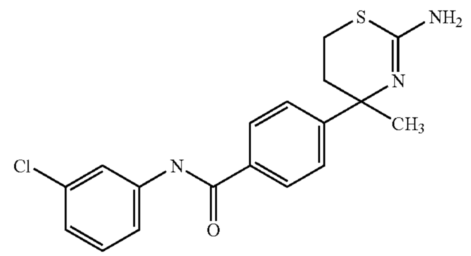
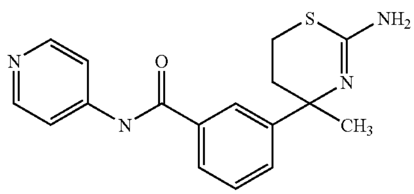
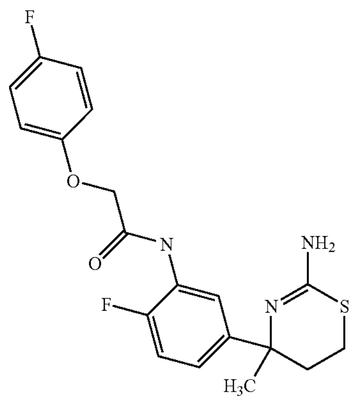
No.	Structure
961	
962	
963	

TABLE 102

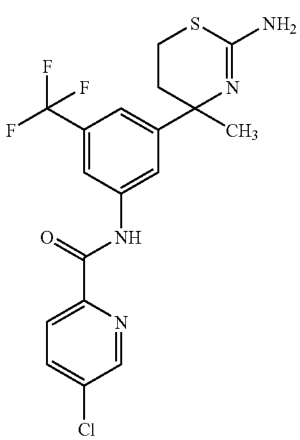
No.	Structure
964	

TABLE 102-continued

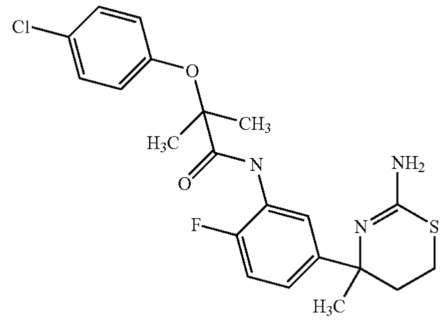
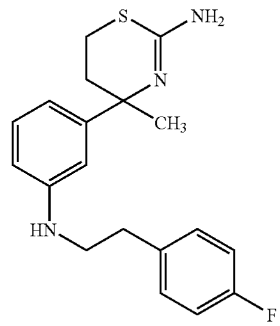
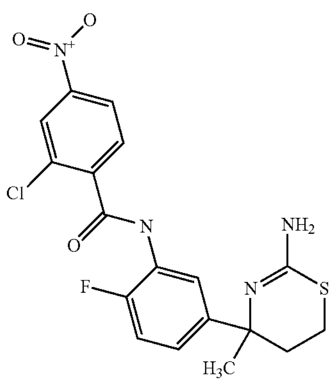
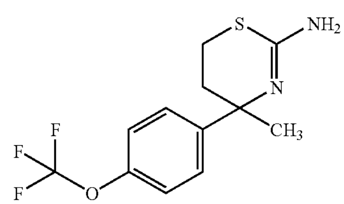
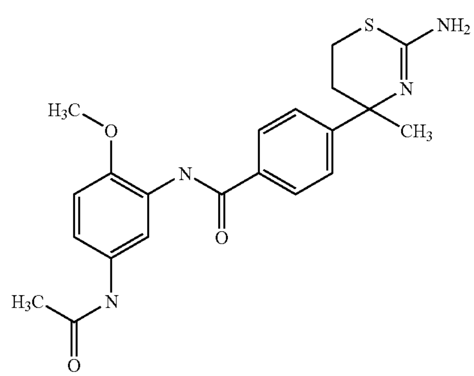
No.	Structure
965	
966	
967	
968	
969	

TABLE 102-continued

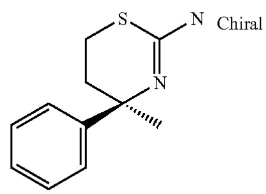
No.	Structure
970	

TABLE 103

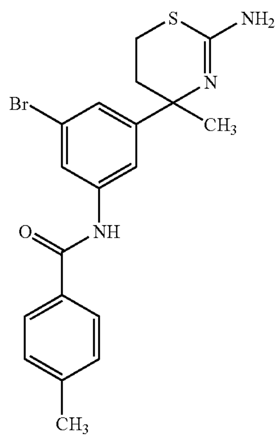
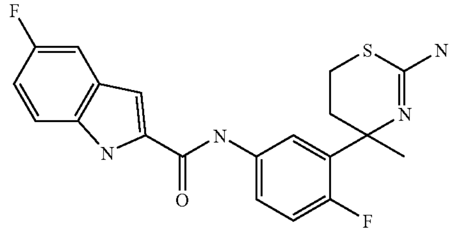
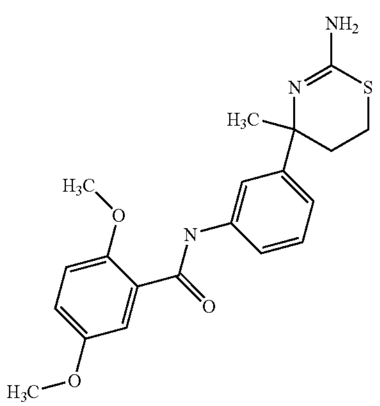
No.	Structure
971	
972	
973	

TABLE 103-continued

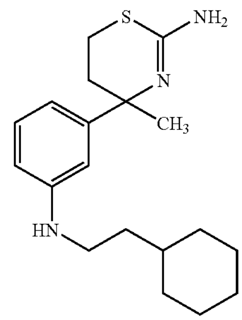
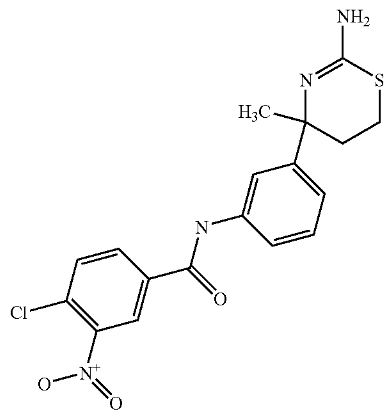
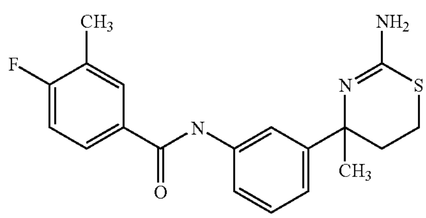
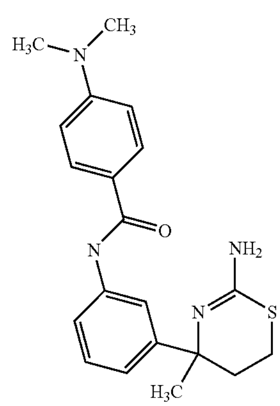
No.	Structure
974	
975	
976	
977	

TABLE 104

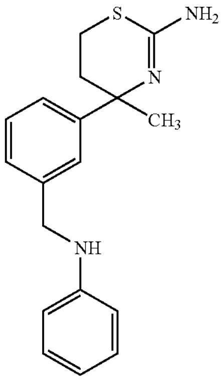
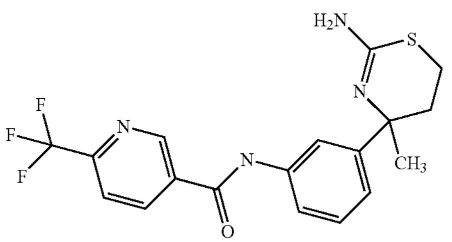
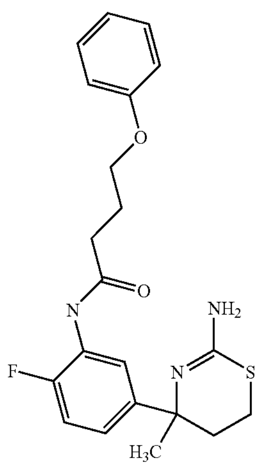
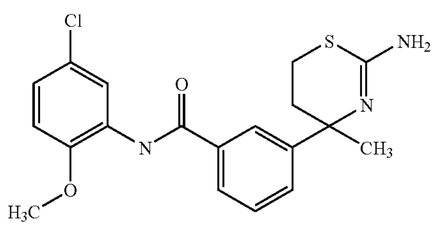
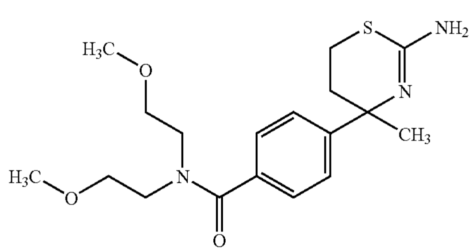
No.	Structure
978	
979	
980	
981	
982	

TABLE 104-continued

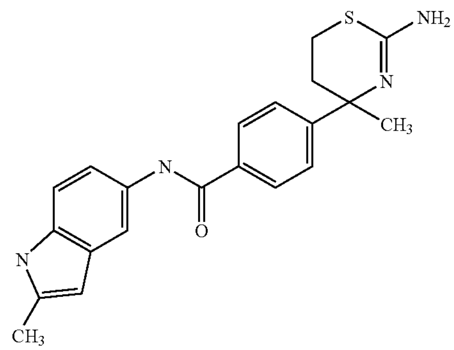
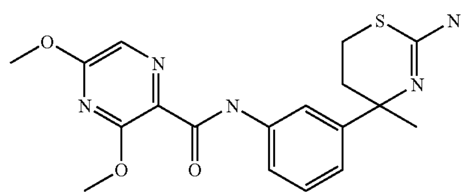
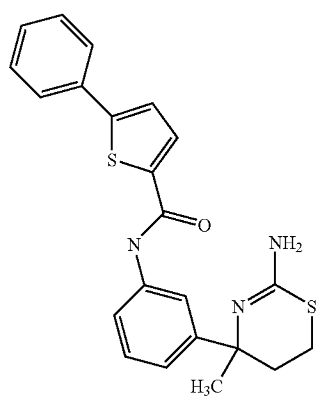
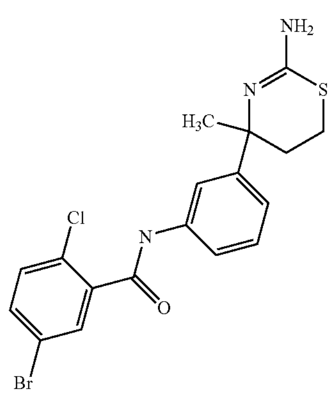
No.	Structure
983	
984	
985	
986	

TABLE 105

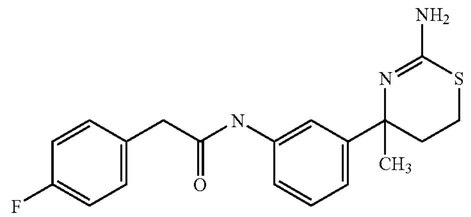
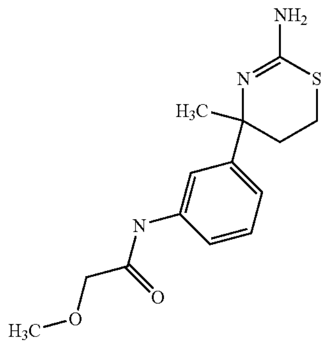
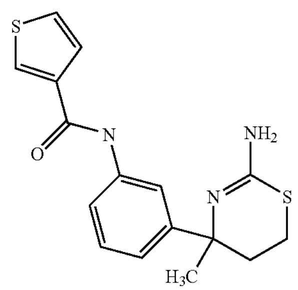
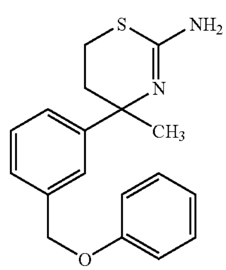
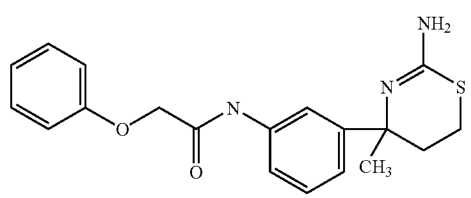
No.	Structure
987	
988	
989	
990	
991	

TABLE 105-continued

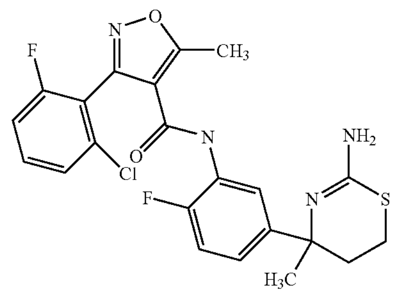
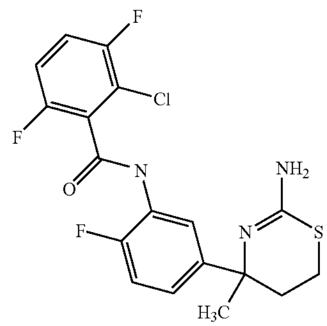
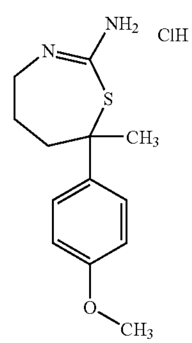
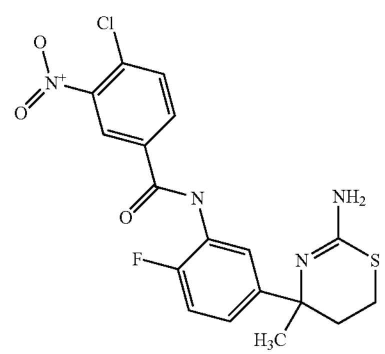
No.	Structure
992	
993	
994	
995	

TABLE 106

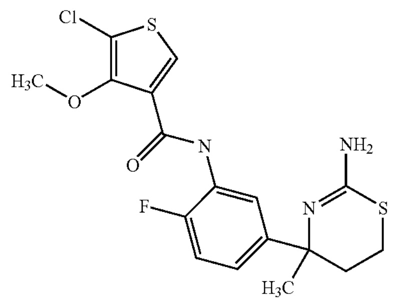
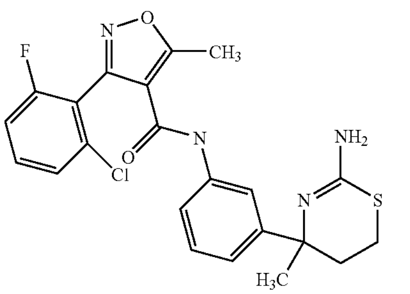
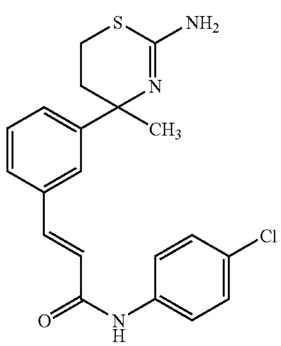
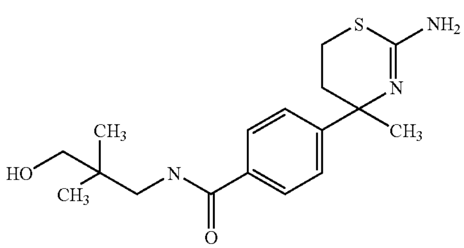
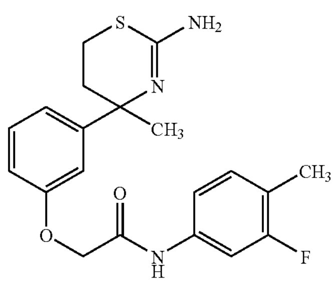
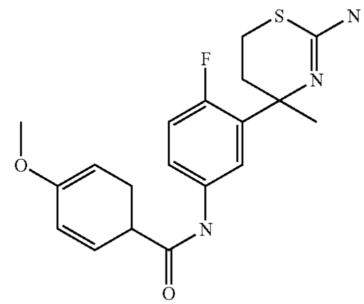
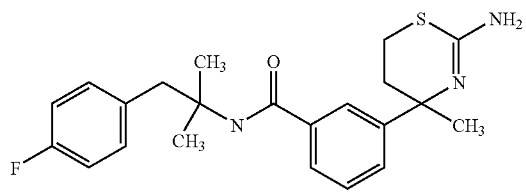
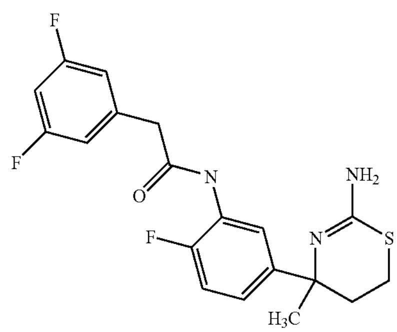
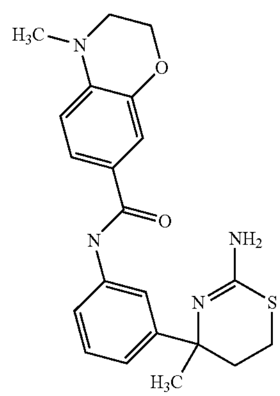
No.	Structure
996	
997	
998	
999	
1000	
1001	
1002	
1003	
1004	

TABLE 107

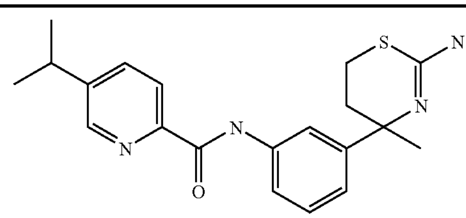
No.	Structure
1005	

TABLE 107-continued

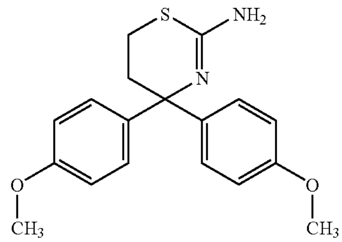
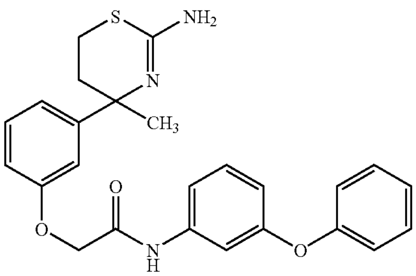
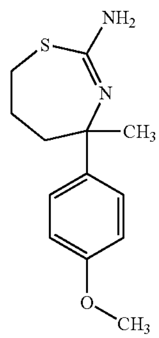
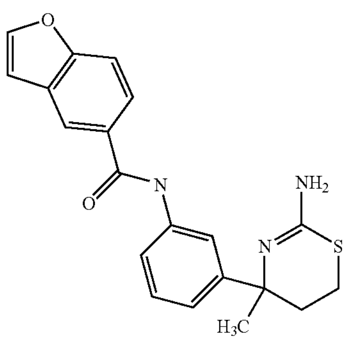
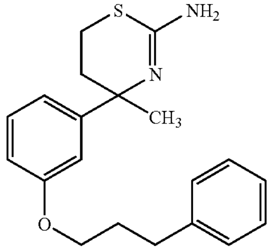
No.	Structure
1006	
1007	
1008	
1009	
1010	

TABLE 107-continued

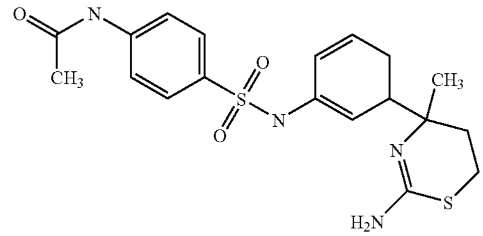
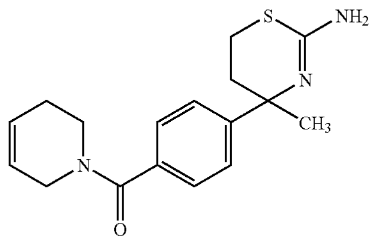
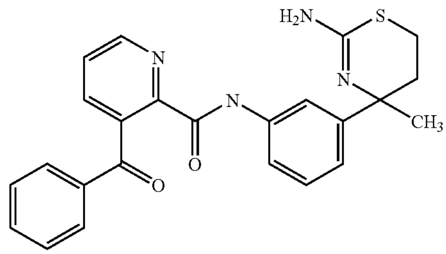
No.	Structure
1011	
1012	
1013	

TABLE 108

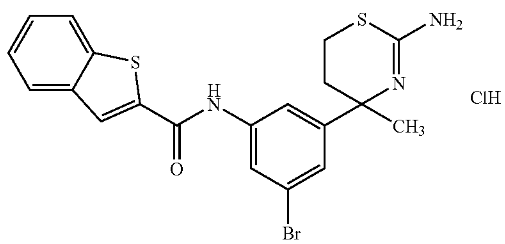
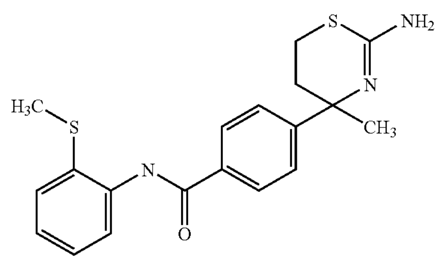
No.	Structure
1014	
1015	

TABLE 108-continued

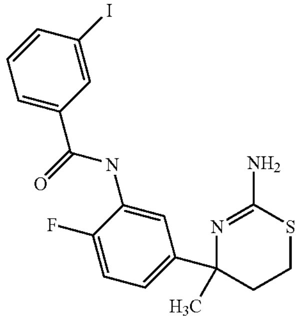
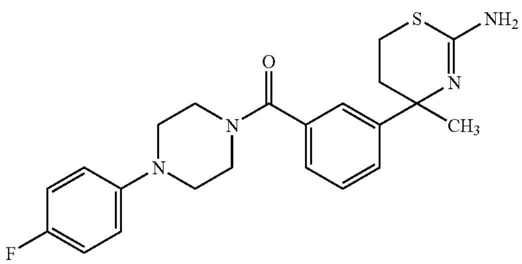
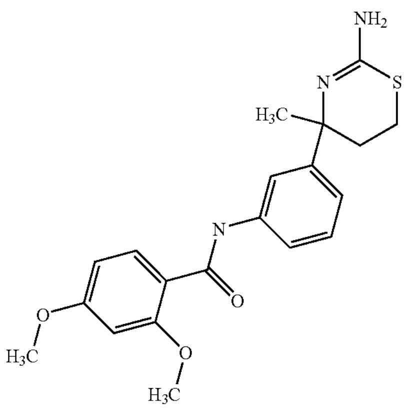
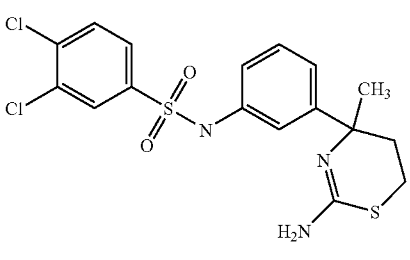
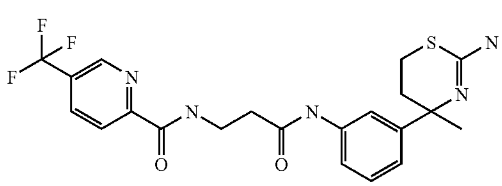
No.	Structure
1016	
1017	
1018	
1019	
1020	

TABLE 108-continued

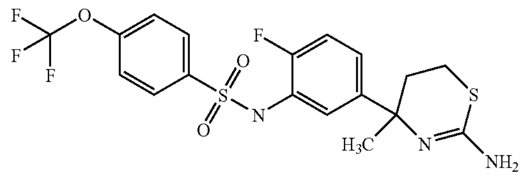
No.	Structure
1021	

TABLE 109

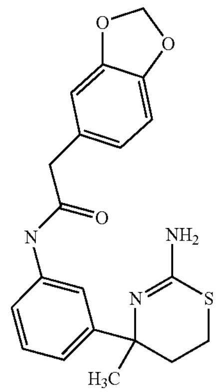
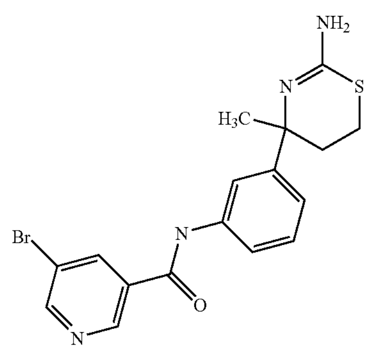
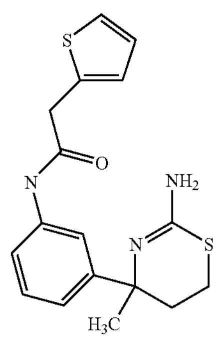
No.	Structure
1022	
1023	
1024	

TABLE 109-continued

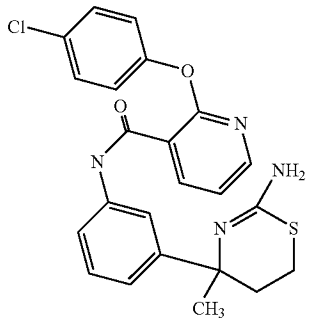
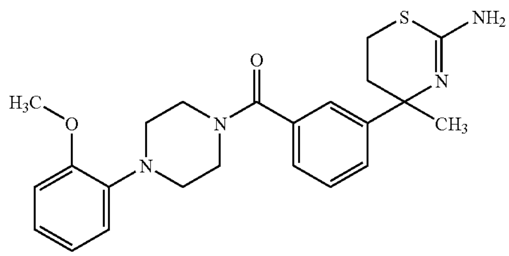
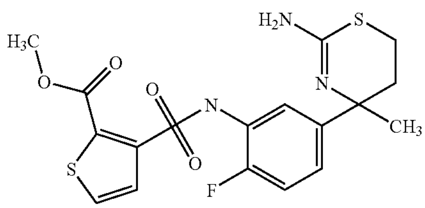
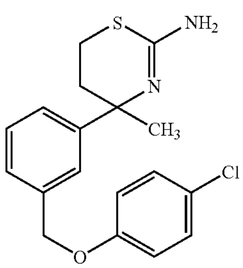
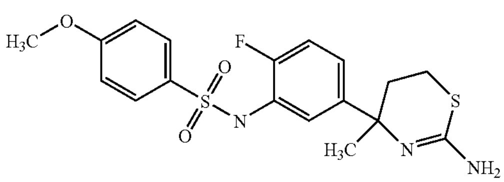
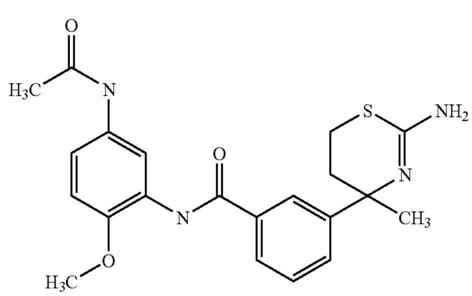
No.	Structure
1025	
1026	
1027	
1028	
1029	
1030	

TABLE 110

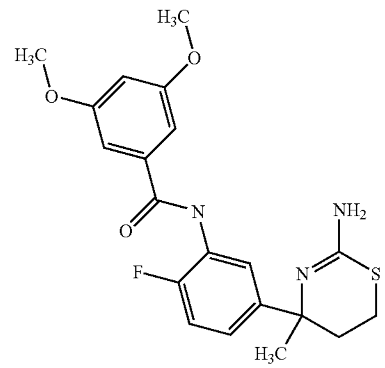
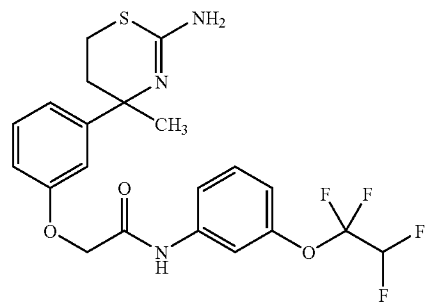
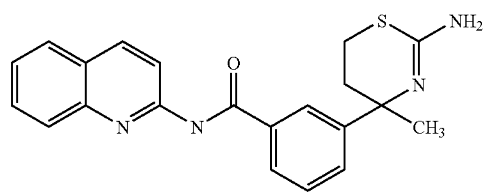
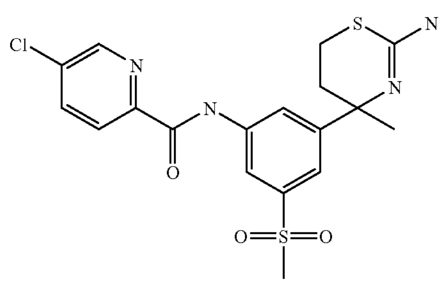
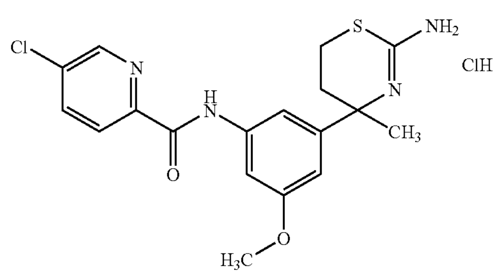
No.	Structure
1031	
1032	
1033	
1034	
1035	

TABLE 110-continued

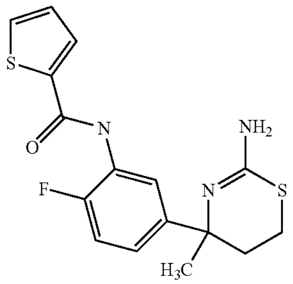
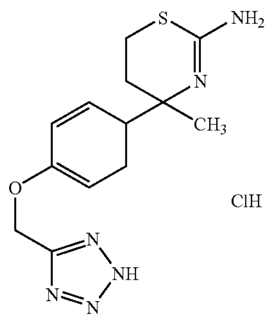
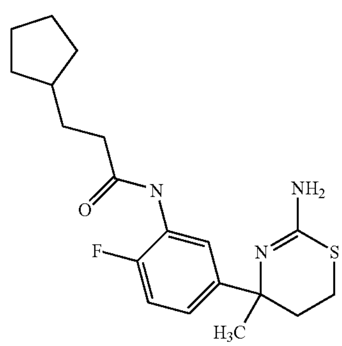
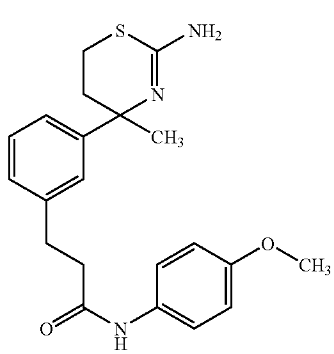
No.	Structure
1036	
1037	
1038	
1039	

TABLE 111

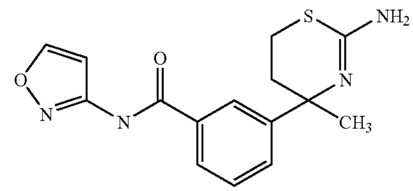
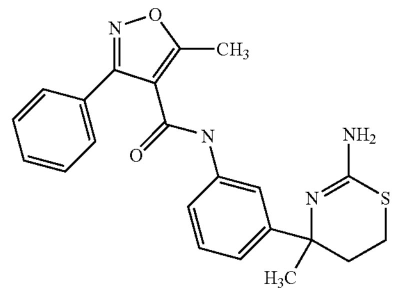
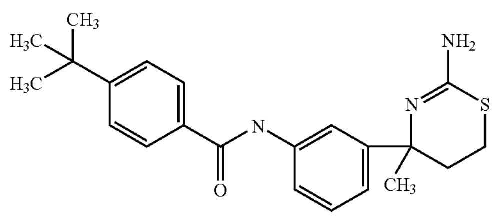
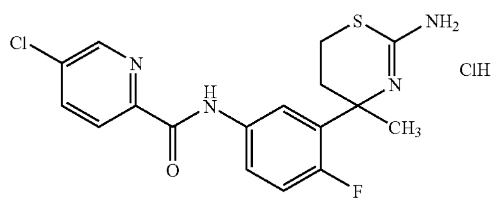
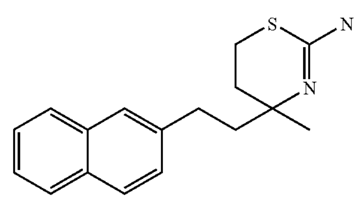
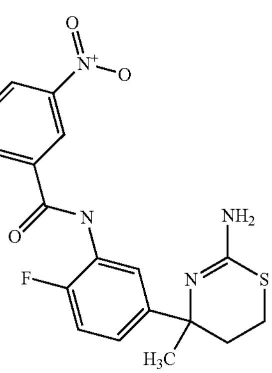
No.	Structure
1040	
1041	
1042	
1043	
1044	
1045	

TABLE 111-continued

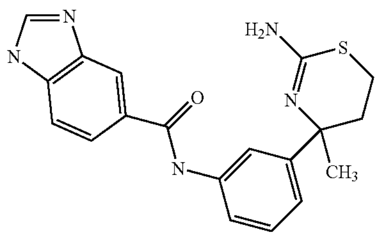
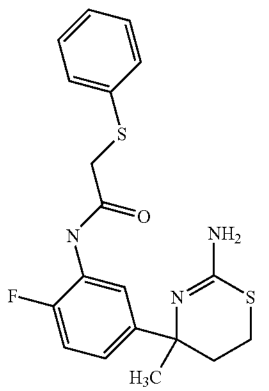
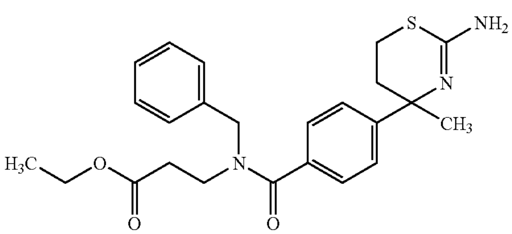
No.	Structure
1046	
1047	
1048	

TABLE 112

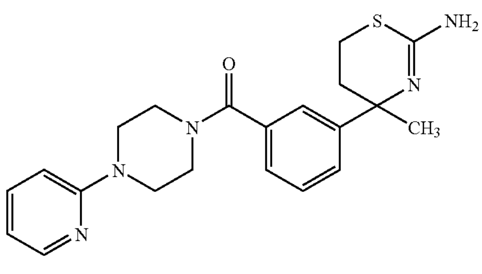
No.	Structure
1049	

TABLE 112-continued

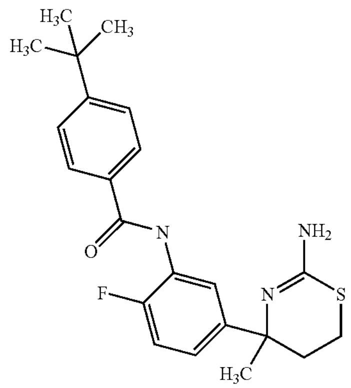
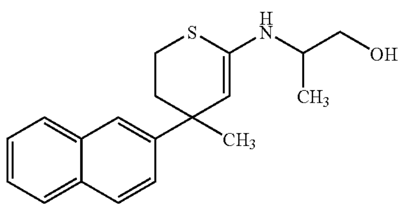
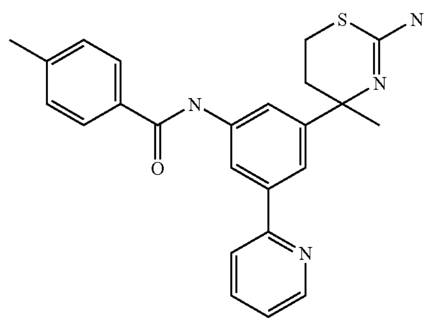
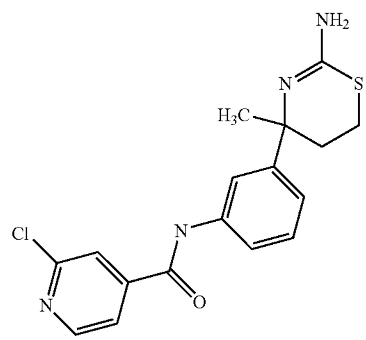
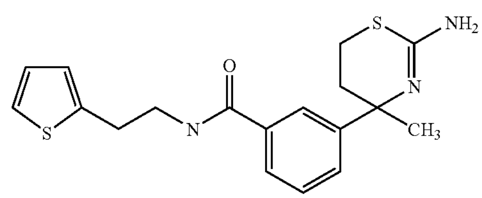
No.	Structure
1050	
1051	
1052	
1053	
1054	

TABLE 112-continued

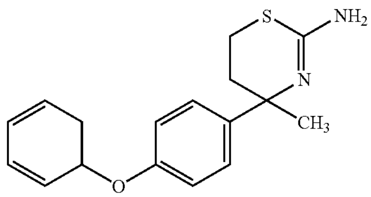
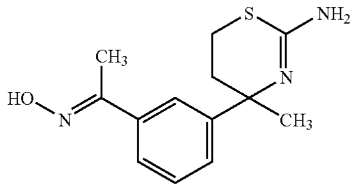
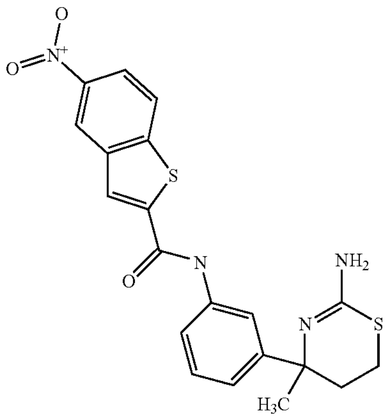
No.	Structure
1055	
1056	
1057	

TABLE 113

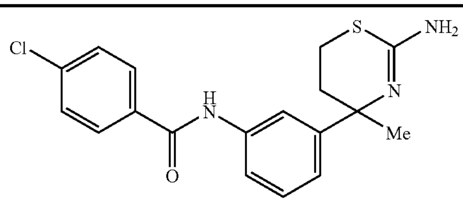
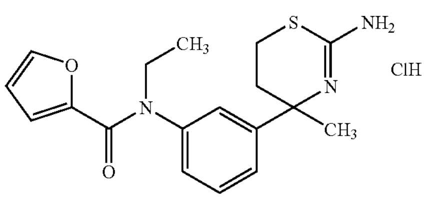
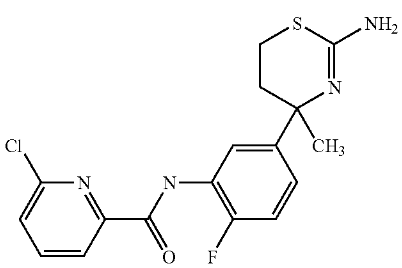
No.	Structure
1058	
1059	
1060	

TABLE 113-continued

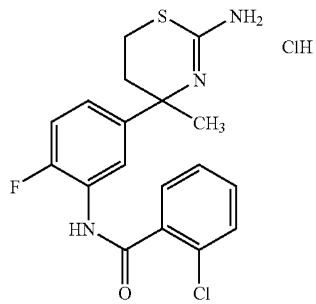
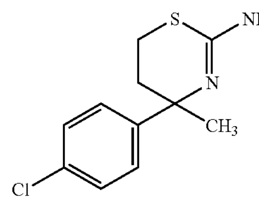
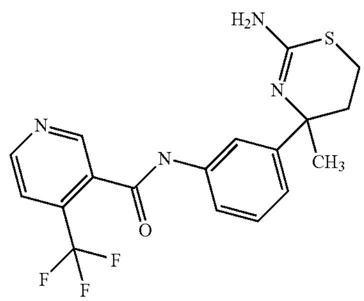
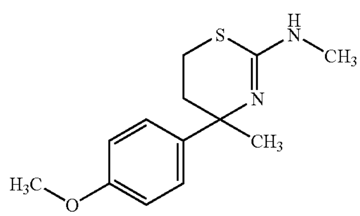
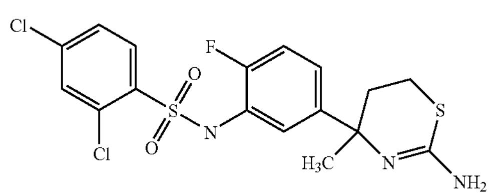
No.	Structure
1061	
1062	
1063	
1064	
1065	

TABLE 113-continued

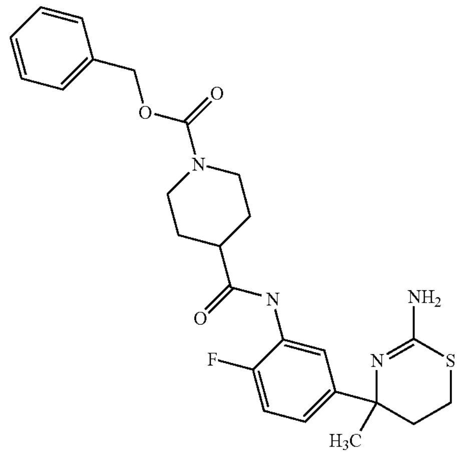
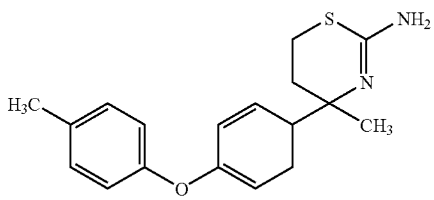
No.	Structure
1066	
1067	

TABLE 114

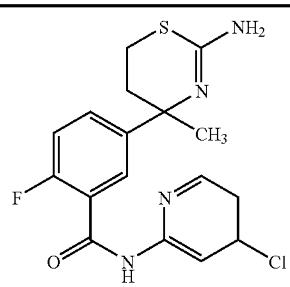
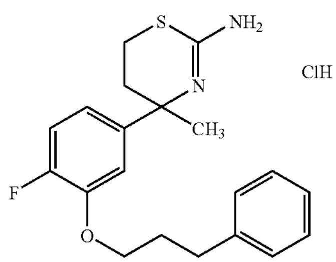
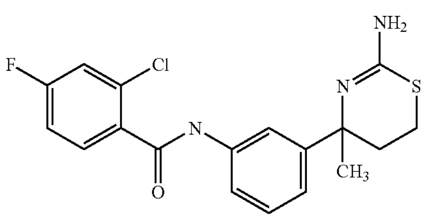
No.	Structure
1068	
1069	
1070	

TABLE 114-continued

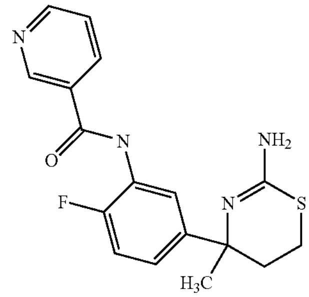
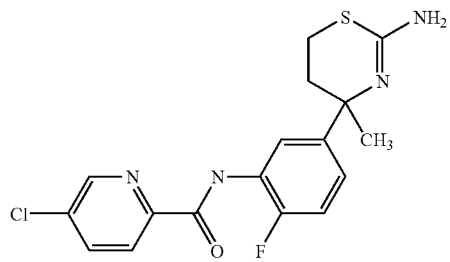
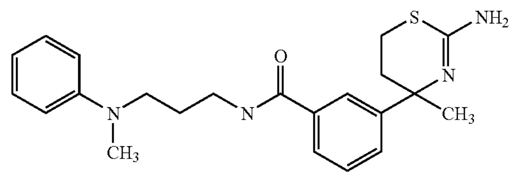
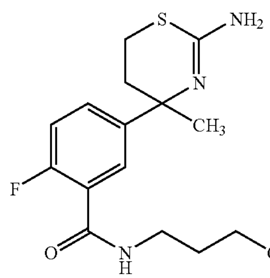
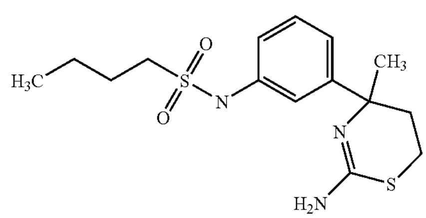
No.	Structure
1071	
1072	
1073	
1074	
1075	

TABLE 115

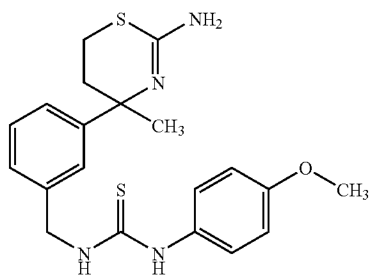
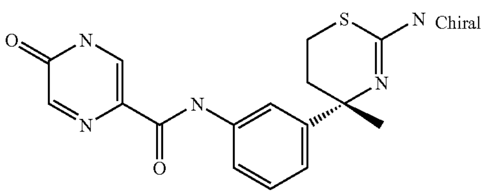
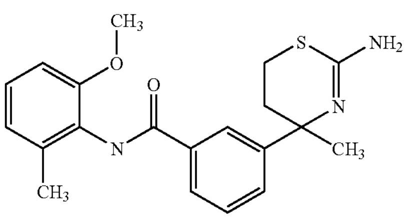
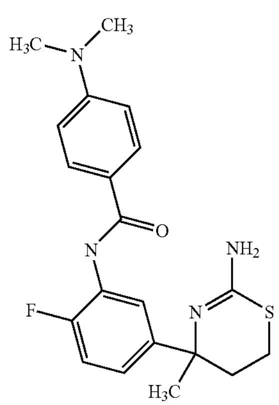
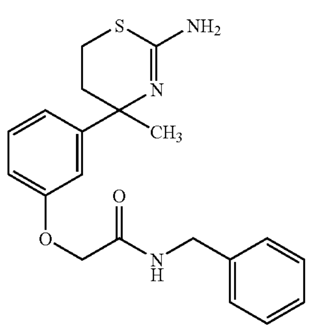
No.	Structure
1076	
1077	
1078	
1079	
1080	

TABLE 115-continued

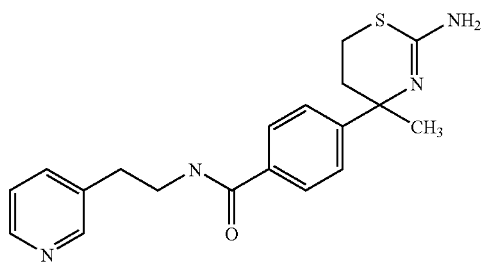
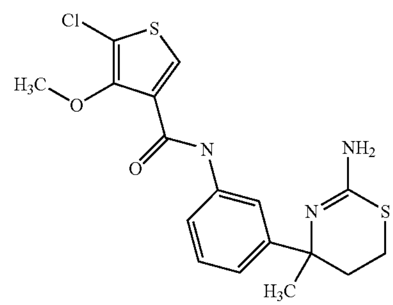
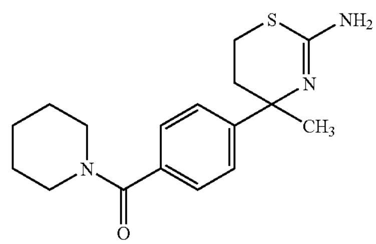
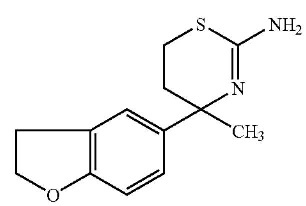
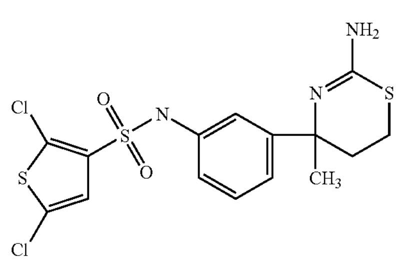
No.	Structure
1081	
1082	
1083	
1084	
1085	

TABLE 116

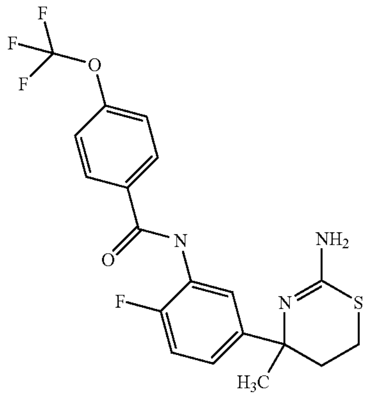
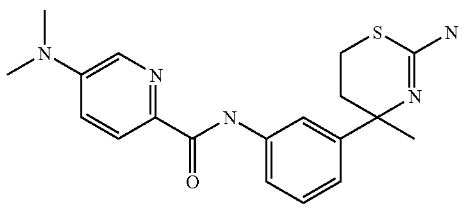
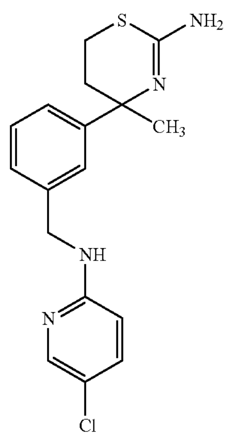
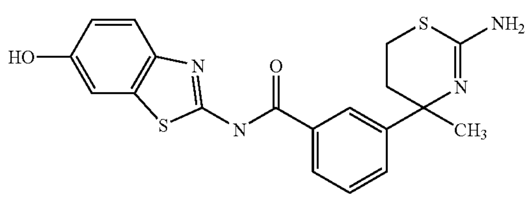
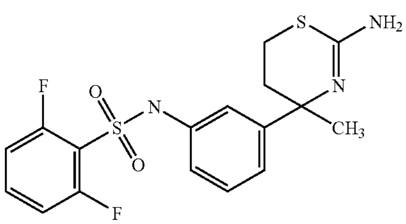
No.	Structure
1086	
1087	
1088	
1089	
1090	

TABLE 116-continued

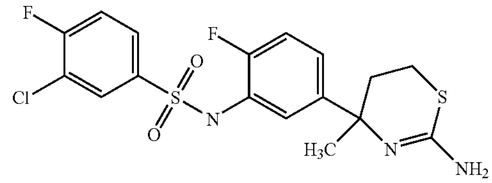
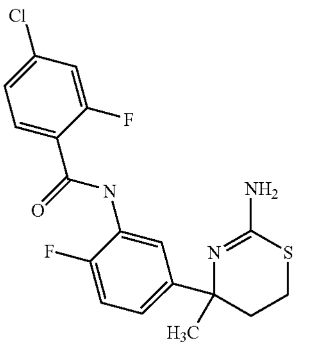
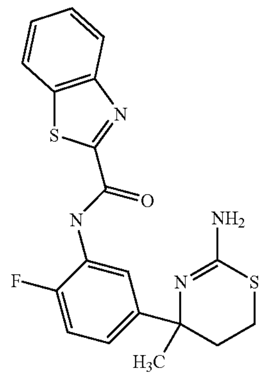
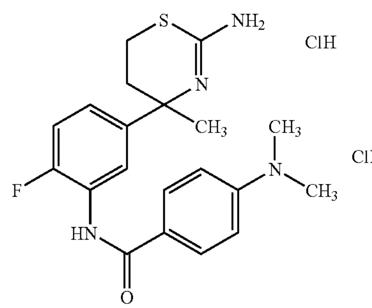
No.	Structure
1091	
1092	
1093	
1094	

TABLE 117

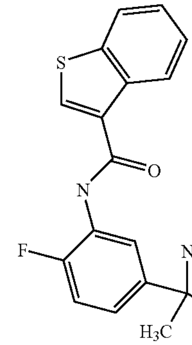
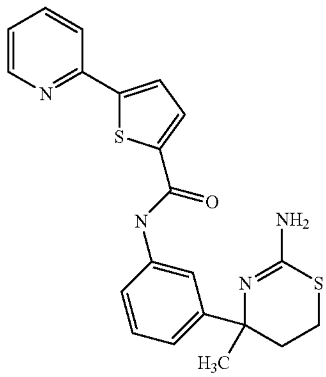
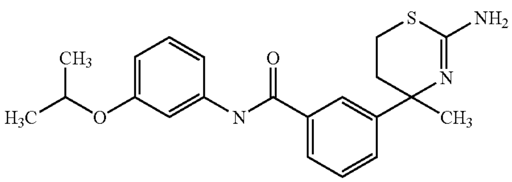
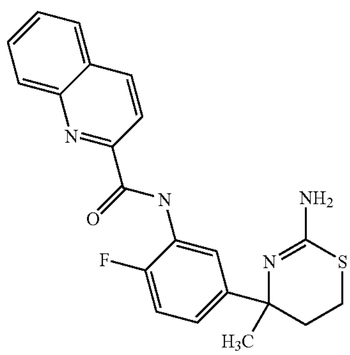
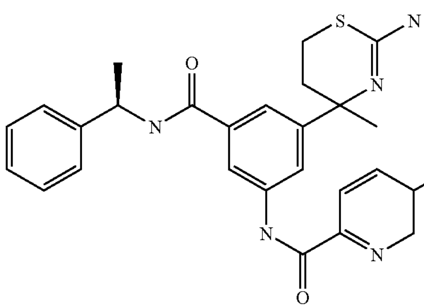
No.	Structure
1095	
1096	
1097	
1098	
1099	 Chiral

TABLE 117-continued

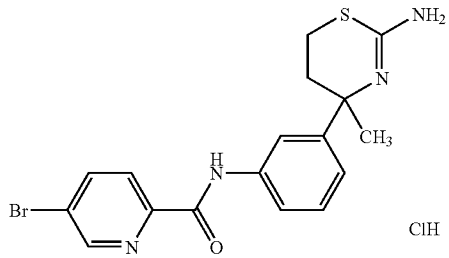
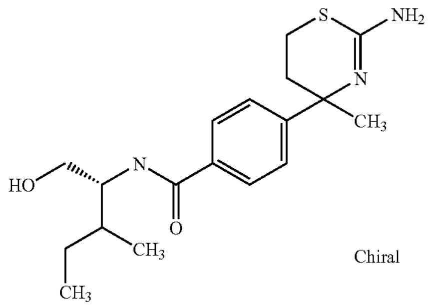
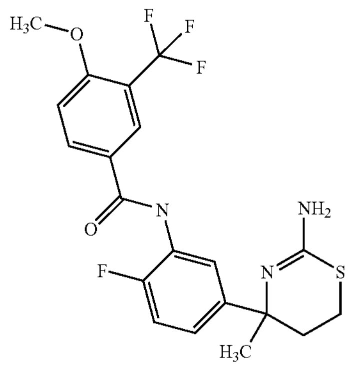
No.	Structure
1100	 ClH
1101	 Chiral
1102	

TABLE 118

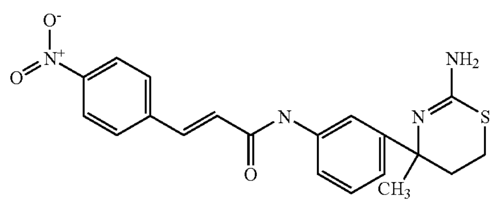
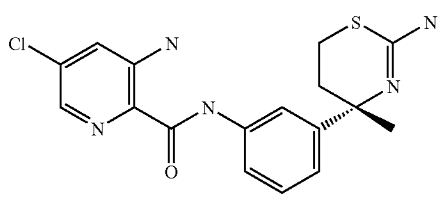
No.	Structure
1103	
1104	 Chiral

TABLE 118-continued

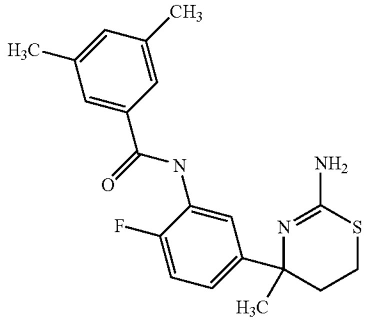
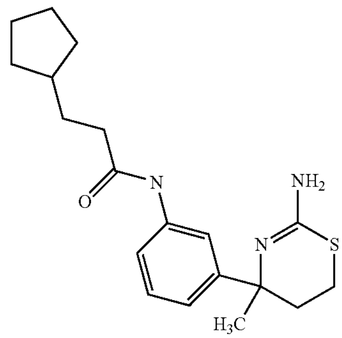
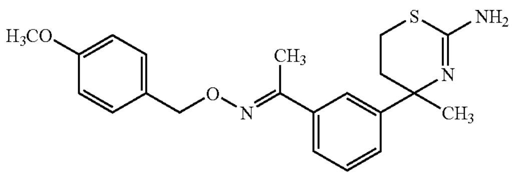
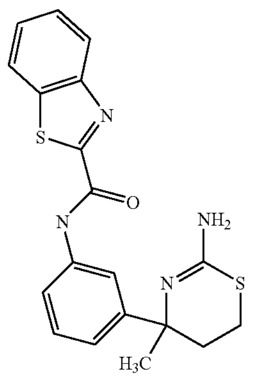
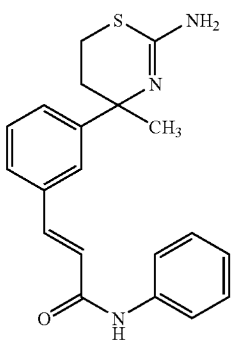
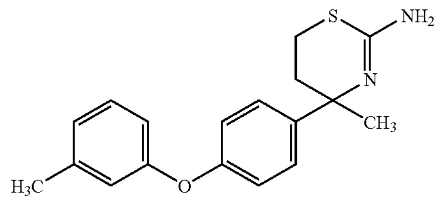
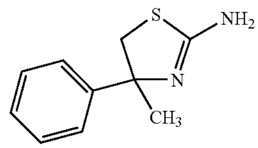
No.	Structure
1105	
1106	
1107	
1108	
1109	
1110	
1111	

TABLE 119

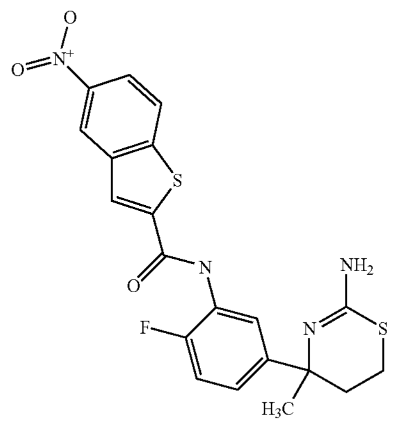
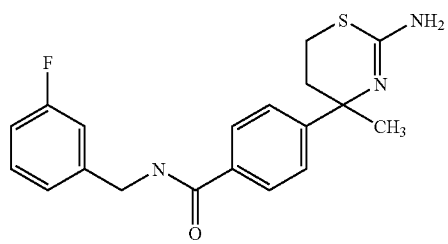
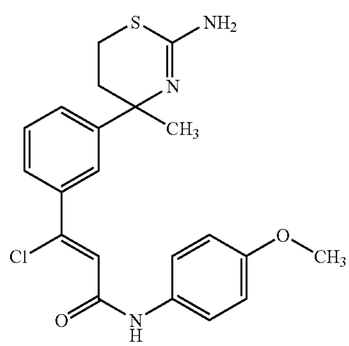
No.	Structure
1112	
1113	
1114	

TABLE 119-continued

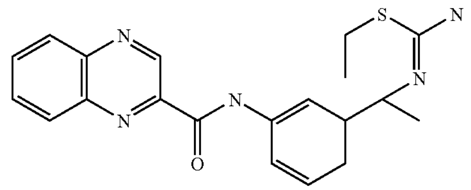
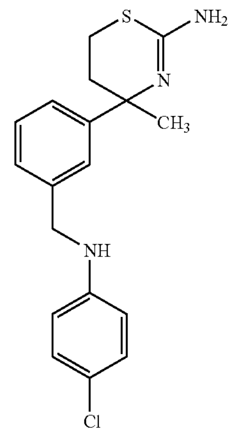
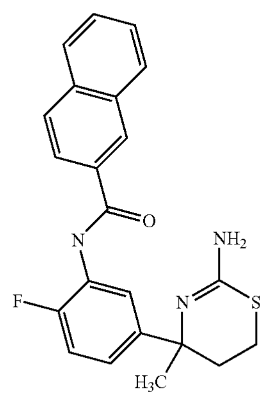
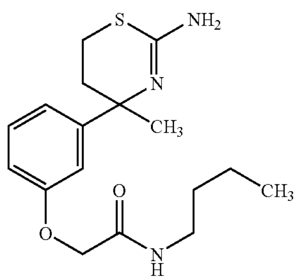
No.	Structure
1115	
1116	
1117	
1118	

TABLE 120

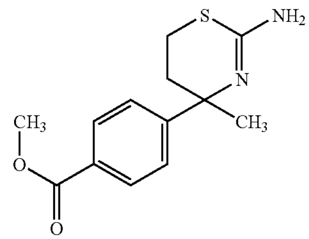
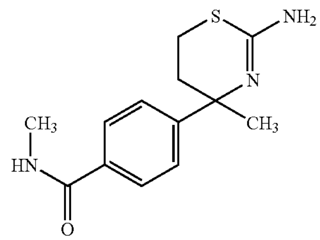
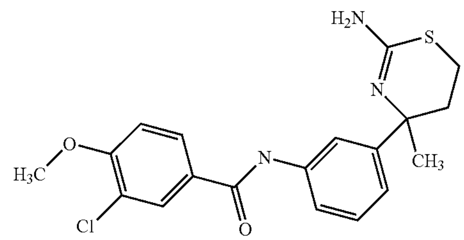
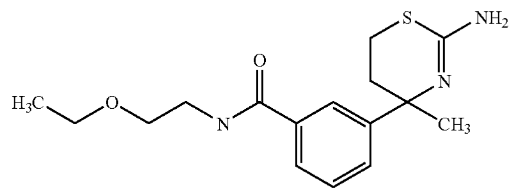
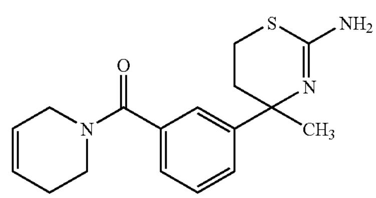
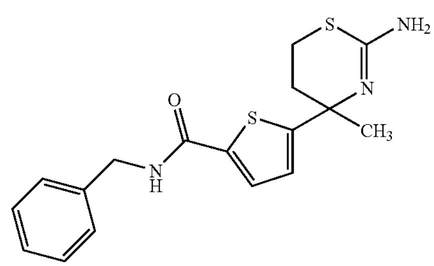
No.	Structure
1119	
1120	
1121	
1122	
1123	
1124	

TABLE 120-continued

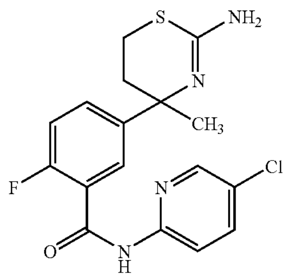
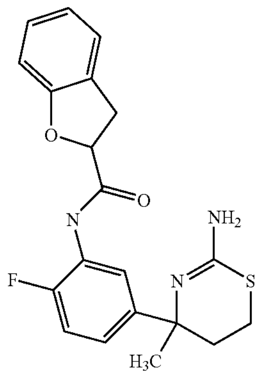
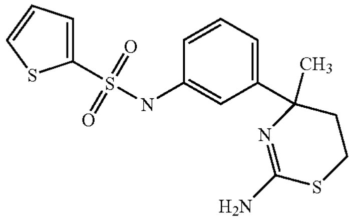
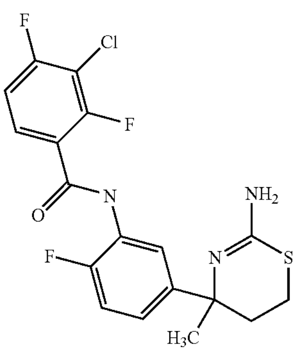
No.	Structure
1125	
1126	
1127	
1128	

TABLE 121

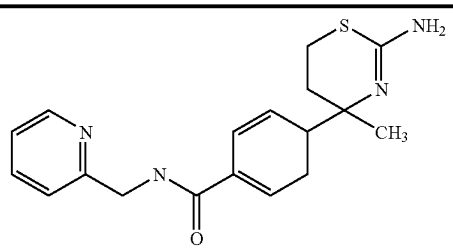
No.	Structure
1129	

TABLE 121-continued

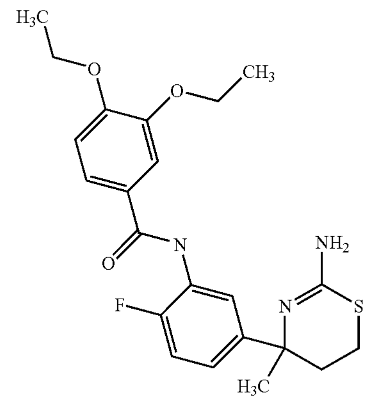
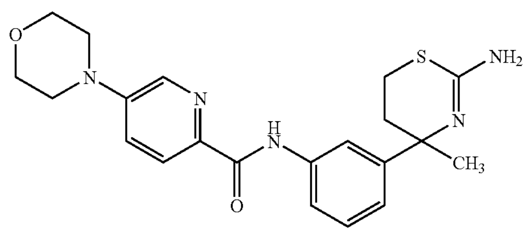
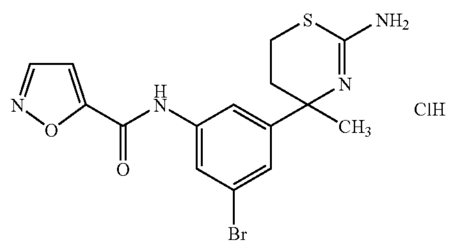
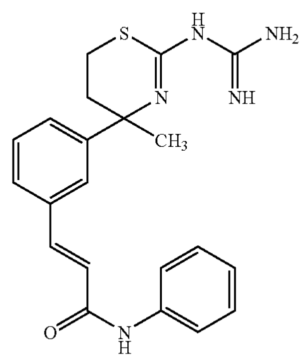
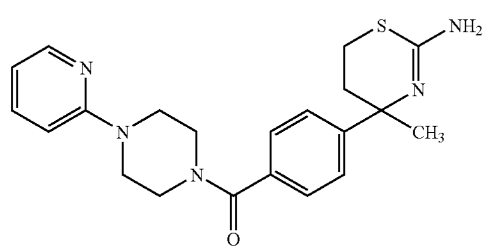
No.	Structure
1130	
1131	
1132	
1133	
1134	

TABLE 121-continued

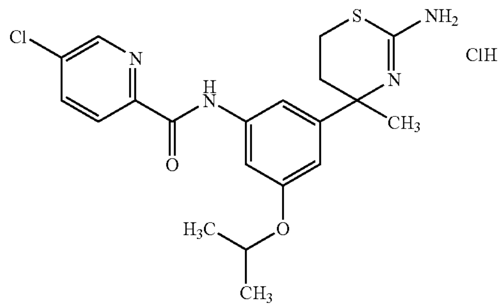
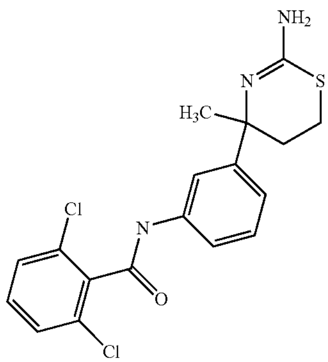
No.	Structure
1135	
1136	

TABLE 122

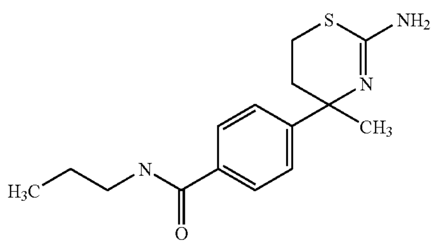
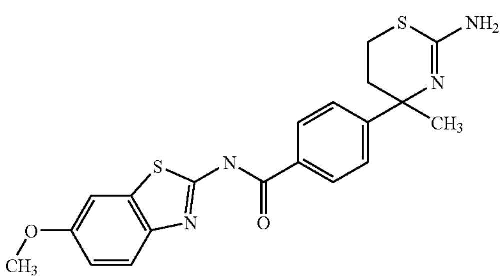
No.	Structure
1137	
1138	

TABLE 122-continued

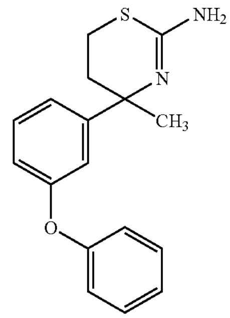
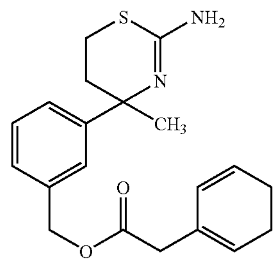
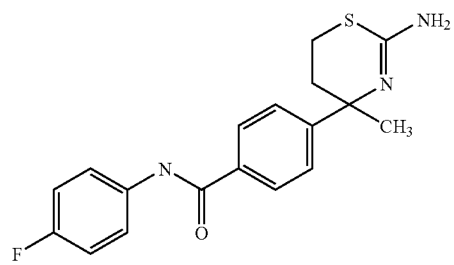
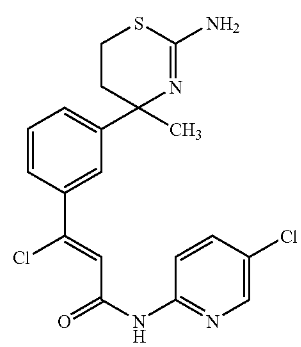
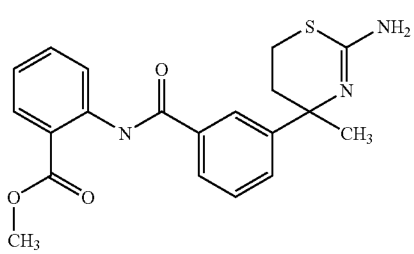
No.	Structure
1139	
1140	
1141	
1142	
1143	

TABLE 122-continued

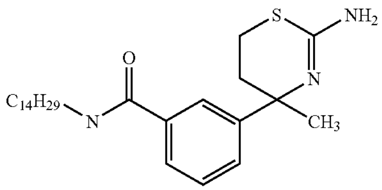
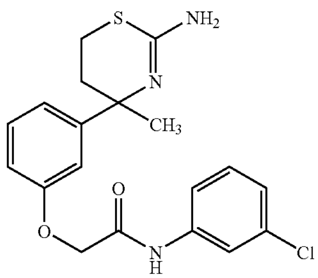
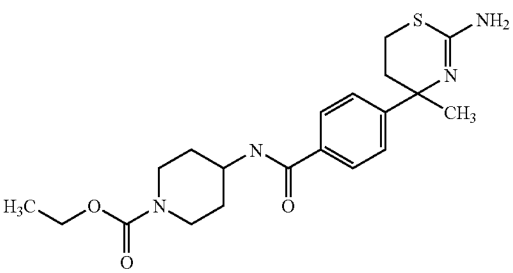
No.	Structure
1144	
1145	
1146	

TABLE 123

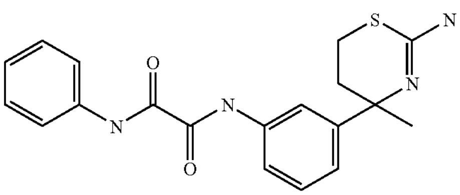
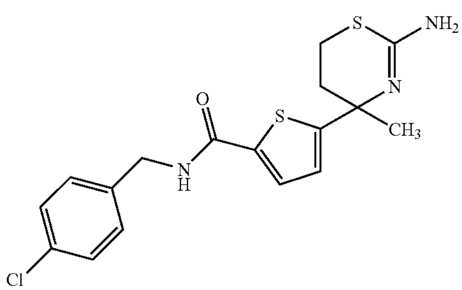
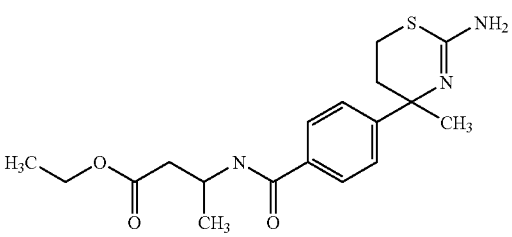
No.	Structure
1147	
1148	
1149	

TABLE 123-continued

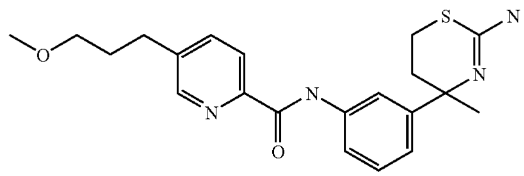
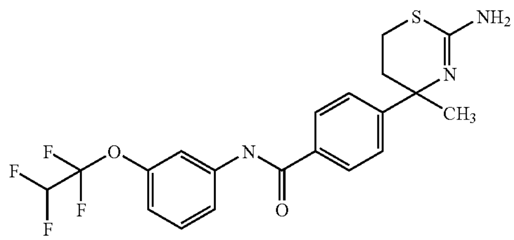
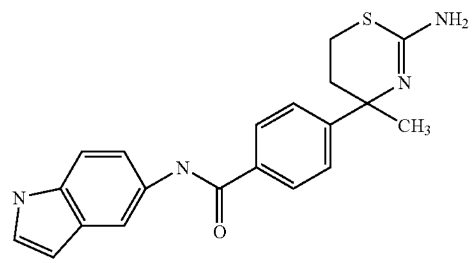
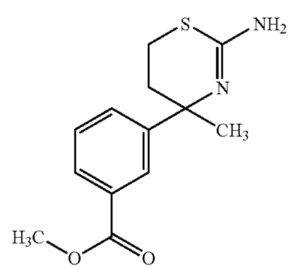
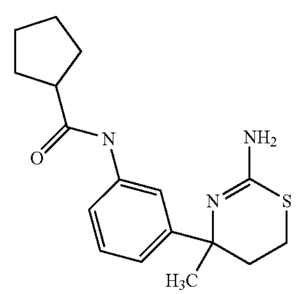
No.	Structure
1150	
1151	
1152	
1153	
1154	

TABLE 123-continued

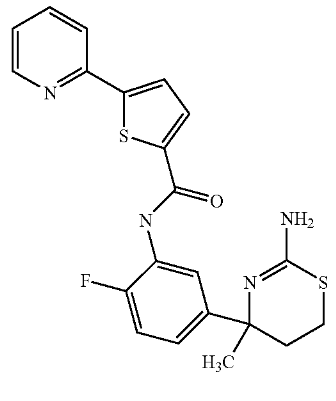
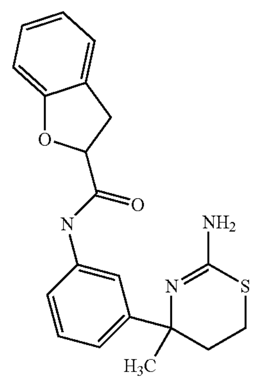
No.	Structure
1155	
1156	

TABLE 124

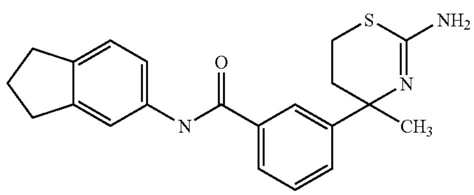
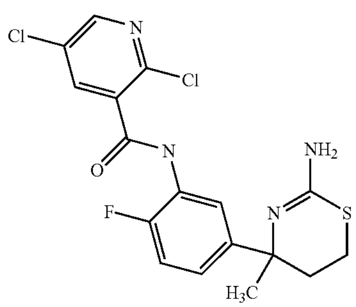
No.	Structure
1157	
1158	

TABLE 124-continued

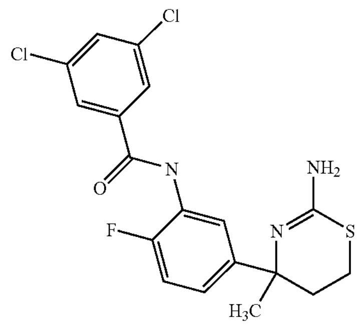
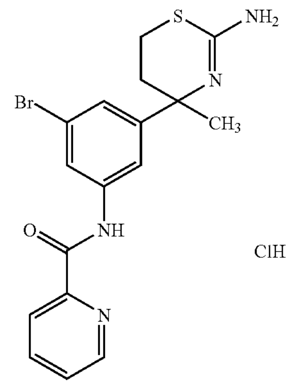
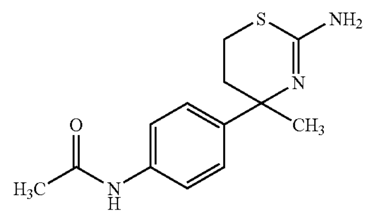
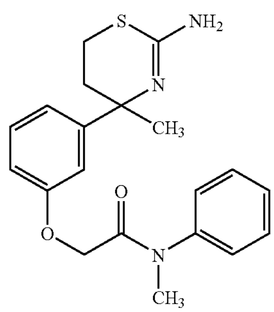
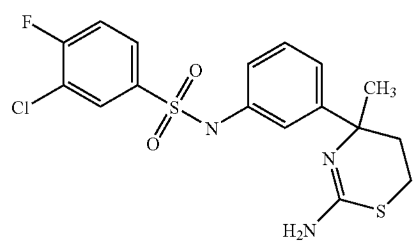
No.	Structure
1159	
1160	
1161	
1162	
1163	

TABLE 124-continued

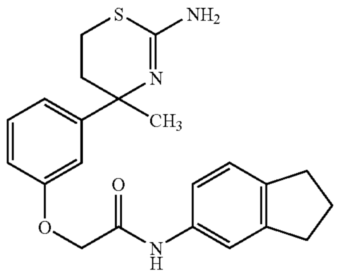
No.	Structure
1164	

TABLE 125

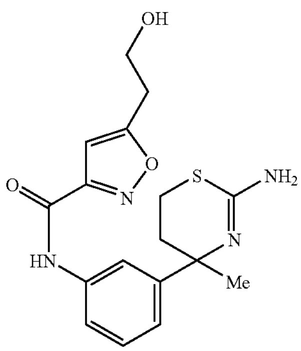
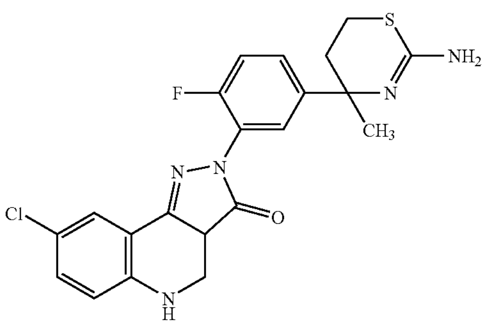
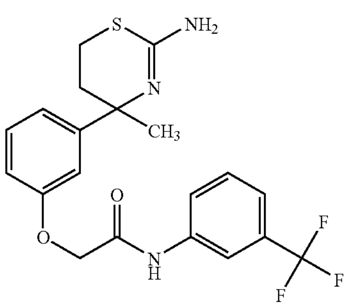
No.	Structure
1165	
1166	
1167	

TABLE 125-continued

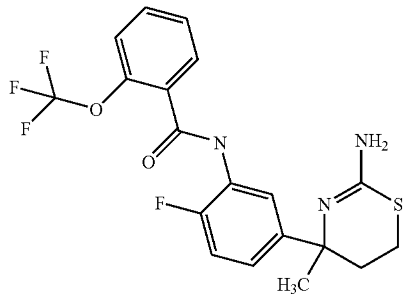
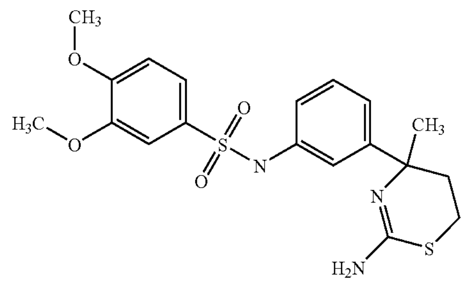
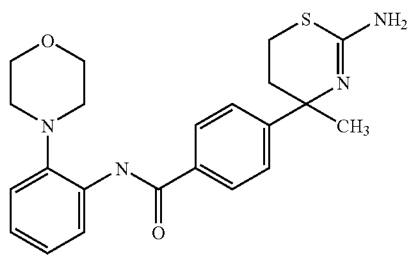
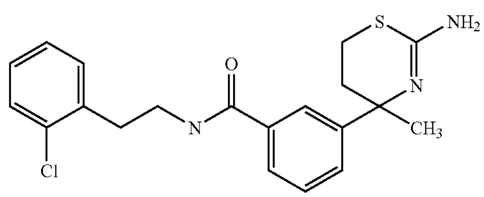
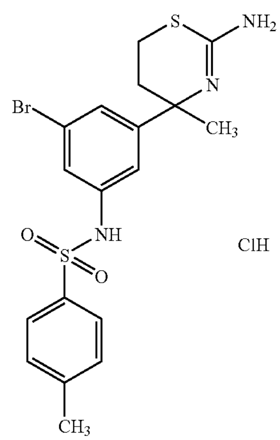
No.	Structure
1168	
1169	
1170	
1171	
1172	

TABLE 125-continued

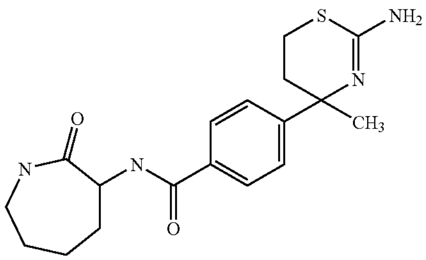
No.	Structure
1173	

TABLE 126

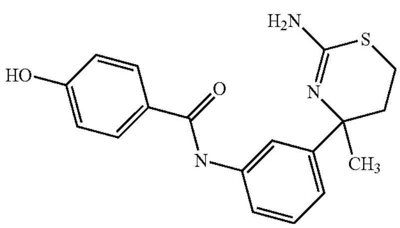
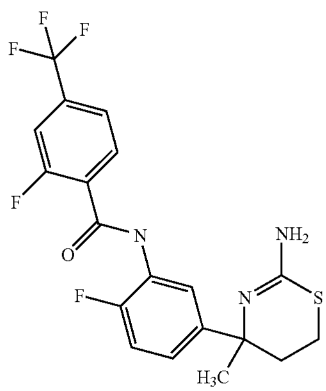
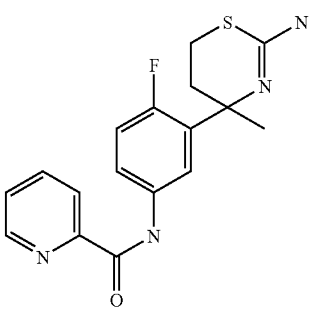
No.	Structure
1174	
1175	
1176	

TABLE 126-continued

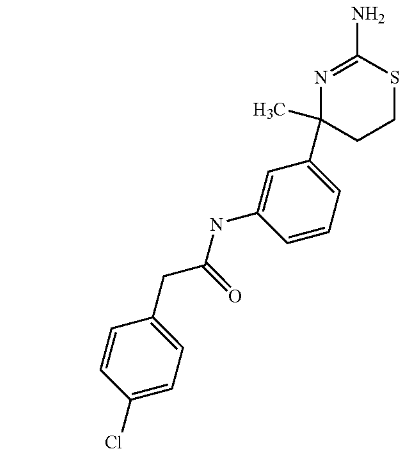
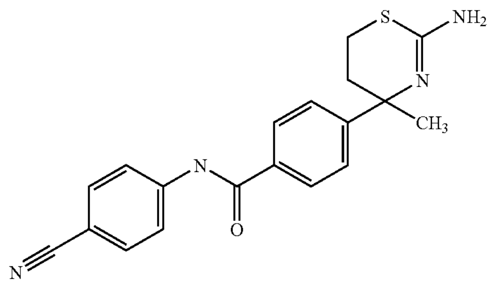
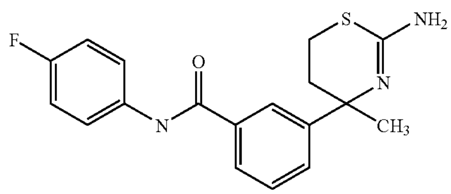
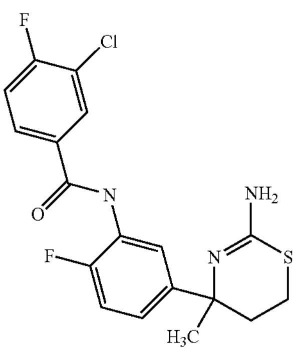
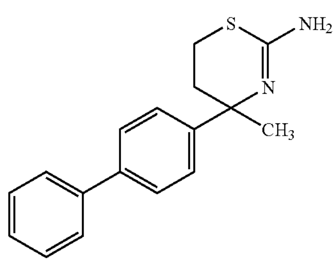
No.	Structure
1177	
1178	
1179	
1180	
1181	

TABLE 126-continued

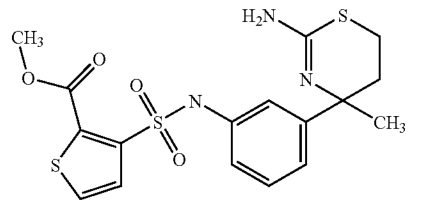
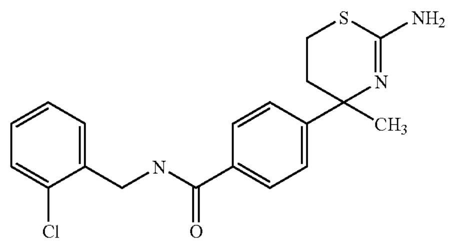
No.	Structure
1182	
1183	

TABLE 127

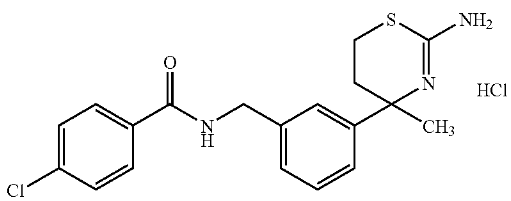
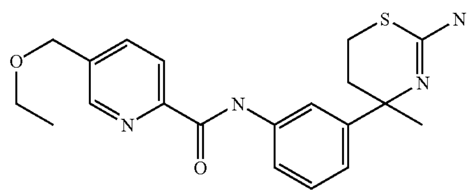
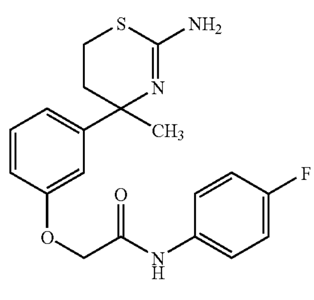
No.	Structure
1184	
1185	
1186	

TABLE 127-continued

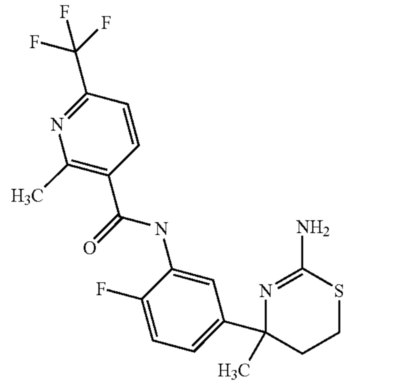
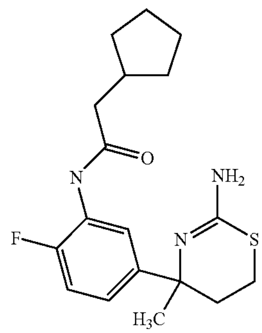
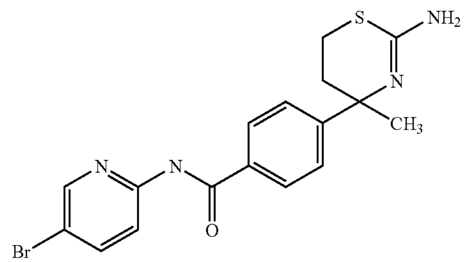
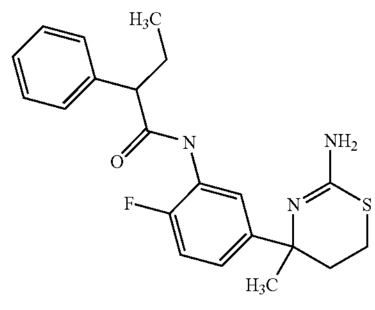
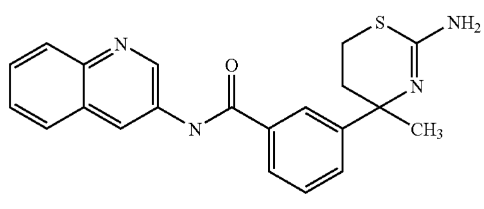
No.	Structure
1187	
1188	
1189	
1190	
1191	

TABLE 127-continued

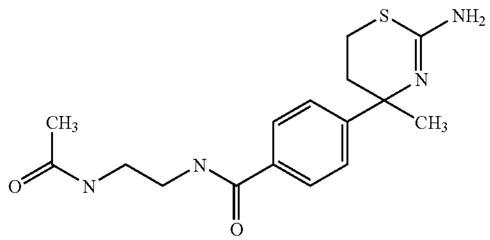
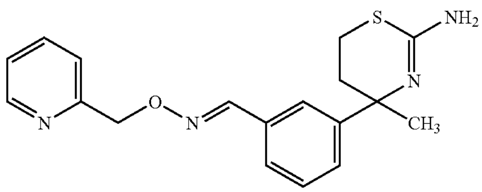
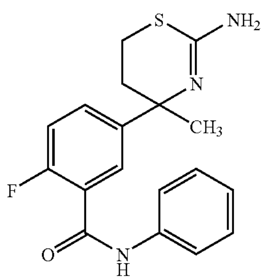
No.	Structure
1192	
1193	
1194	

TABLE 128

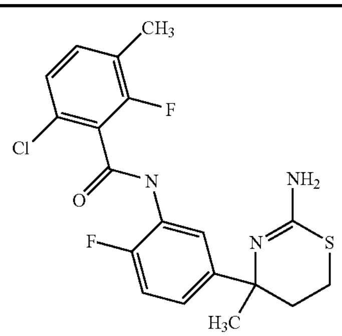
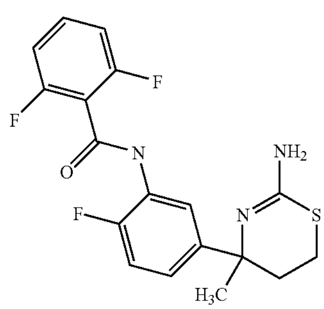
No.	Structure
1195	
1196	

TABLE 128-continued

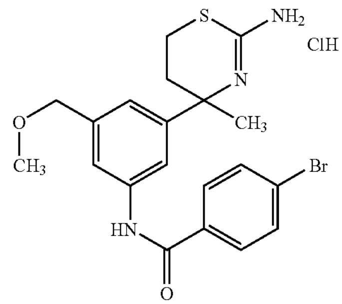
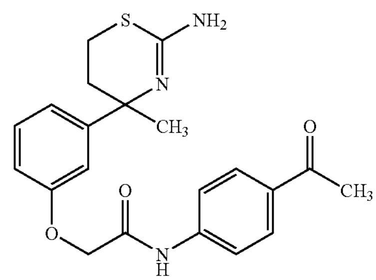
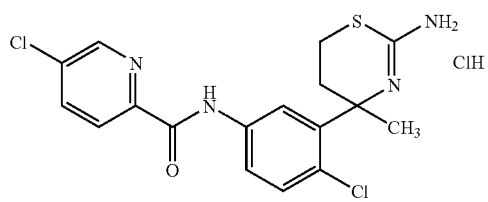
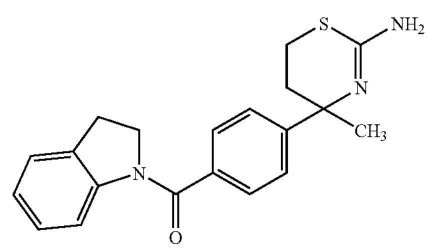
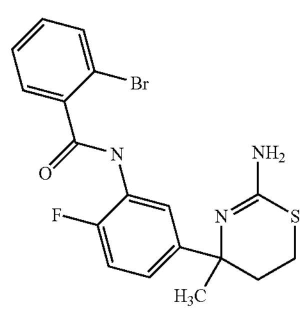
No.	Structure
1197	
1198	
1199	
1200	
1201	

TABLE 128-continued

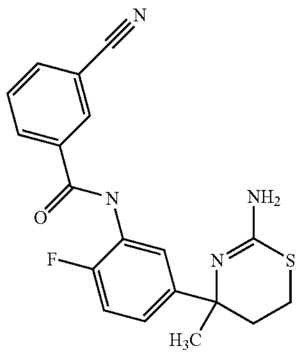
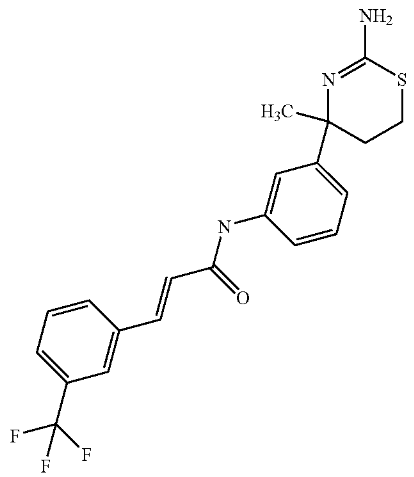
No.	Structure
1202	
1203	

TABLE 129

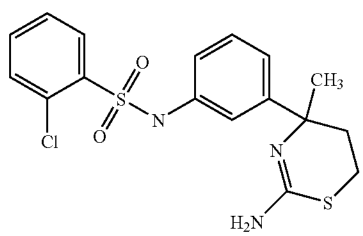
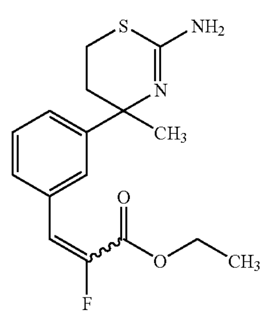
No.	Structure
1204	
1205	

TABLE 129-continued

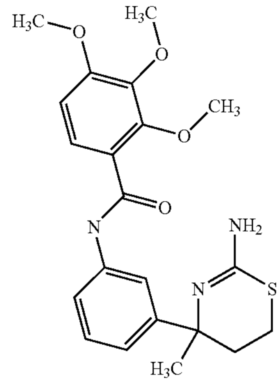
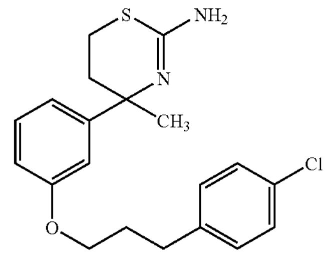
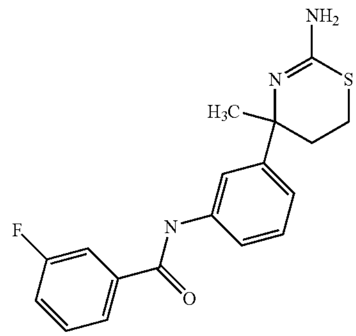
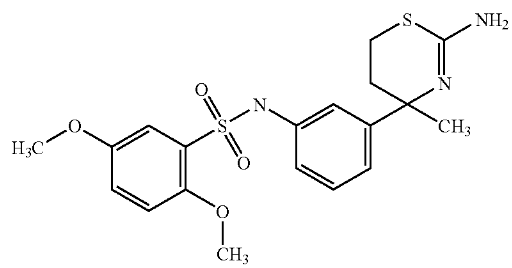
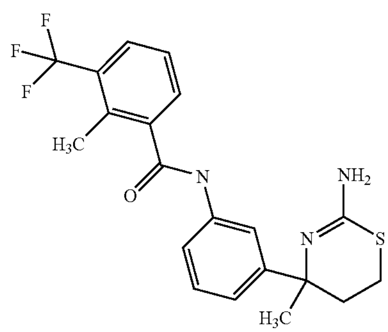
No.	Structure
1206	
1207	
1208	
1209	
1210	

TABLE 129-continued

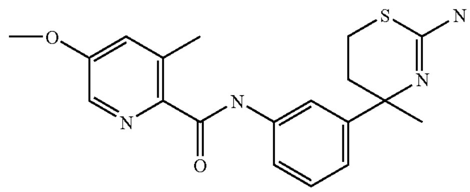
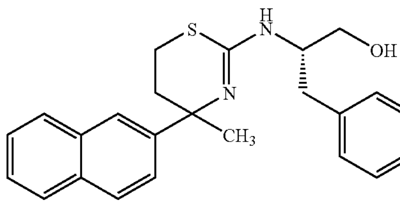
No.	Structure
1211	
1212	Chiral 

TABLE 130

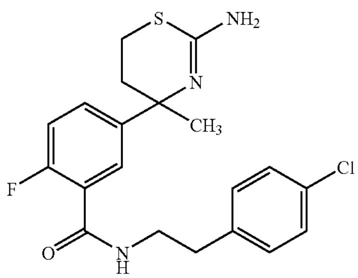
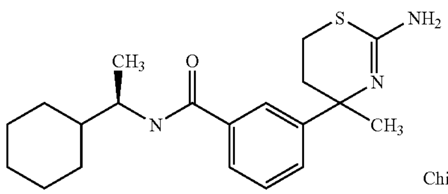
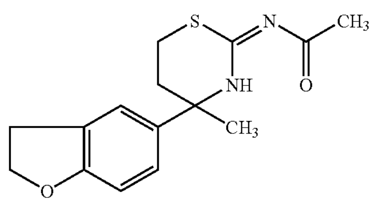
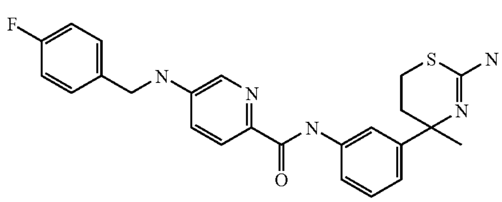
No.	Structure
1213	
1214	 Chiral
1215	
1216	

TABLE 130-continued

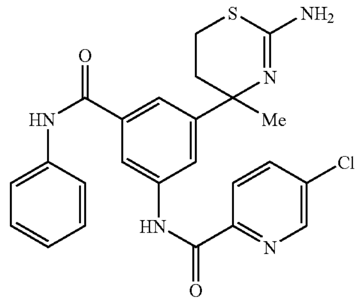
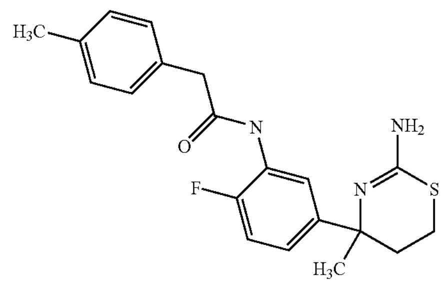
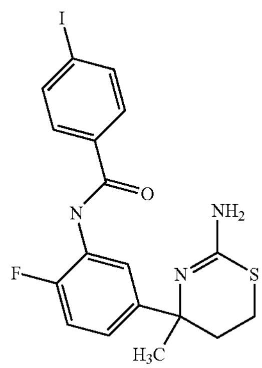
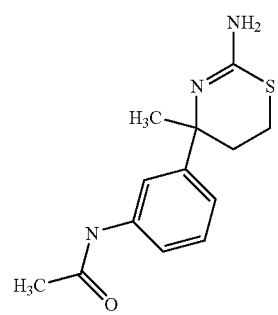
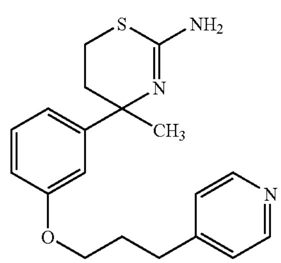
No.	Structure
1217	
1218	
1219	
1220	
1221	

TABLE 131

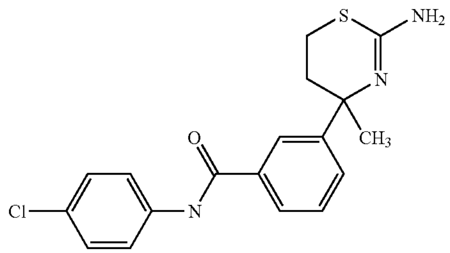
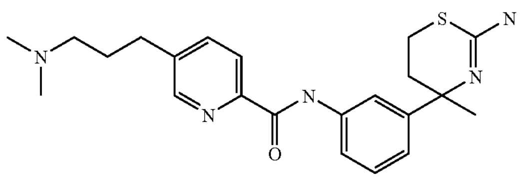
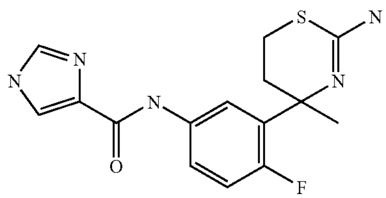
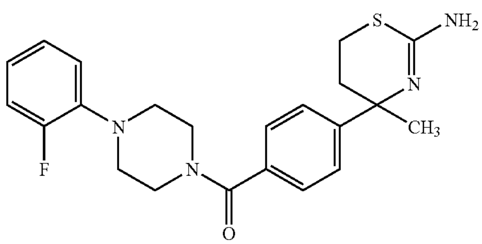
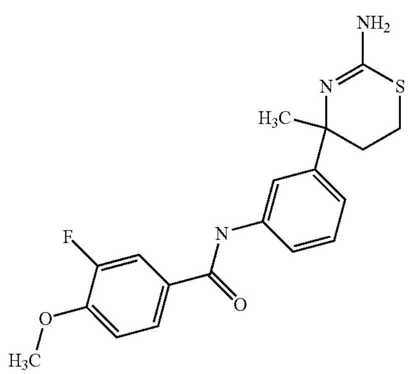
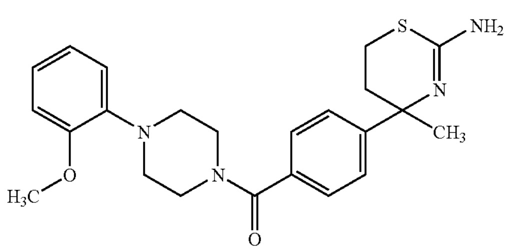
No.	Structure
1222	
1223	
1224	
1225	
1226	
1227	

TABLE 131-continued

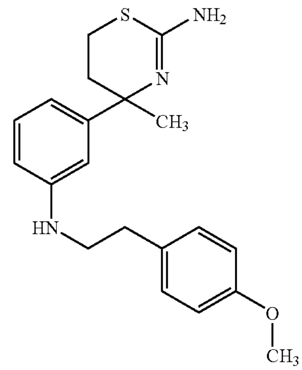
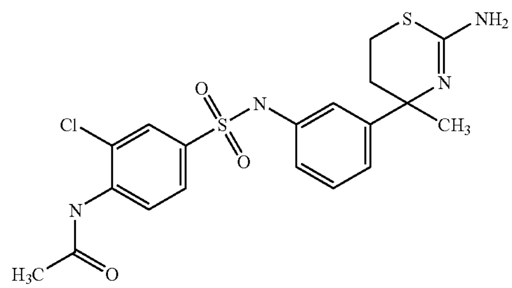
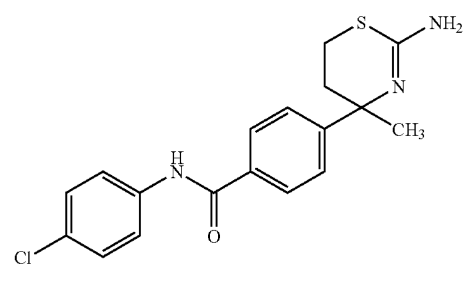
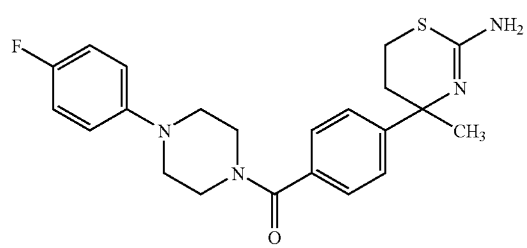
No.	Structure
1228	
1229	
1230	
1231	

TABLE 132

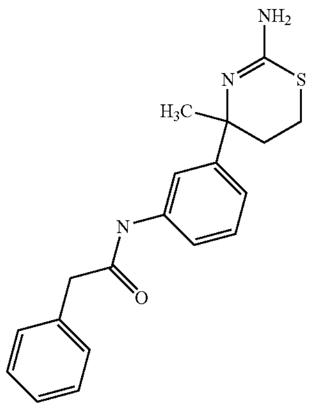
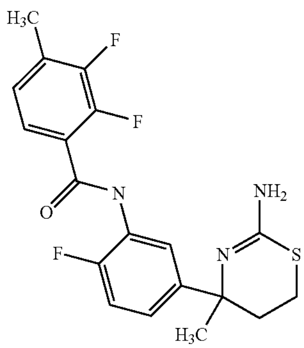
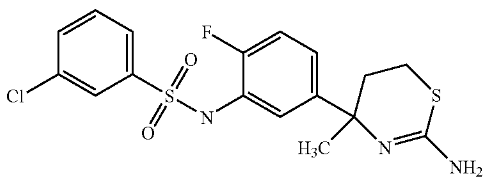
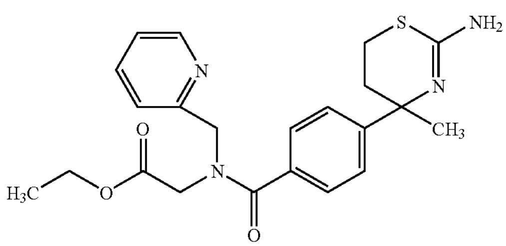
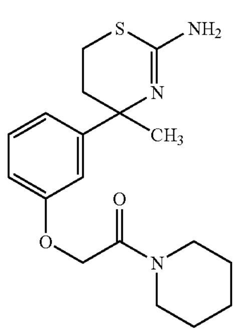
No.	Structure
1232	
1233	
1234	
1235	
1236	

TABLE 132-continued

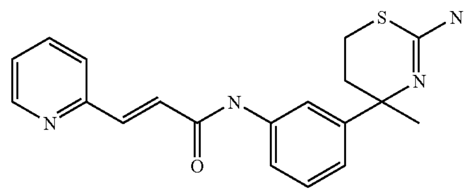
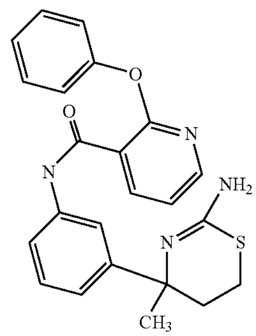
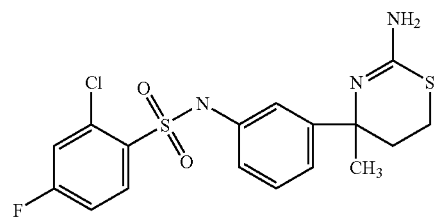
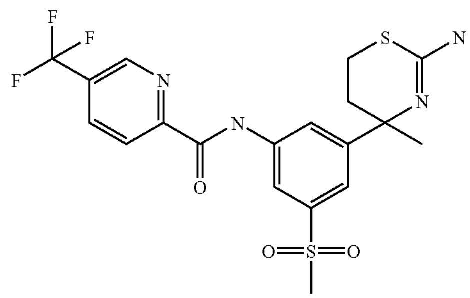
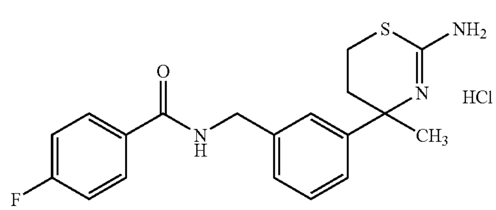
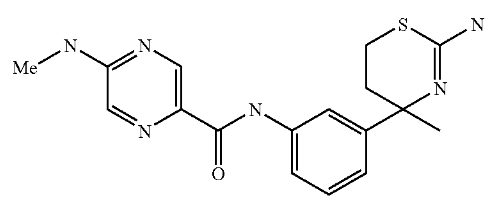
No.	Structure
1237	
1238	
1239	
1240	
1241	
1242	

TABLE 133

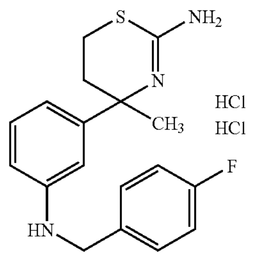
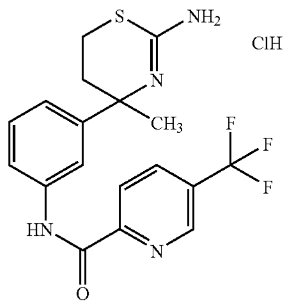
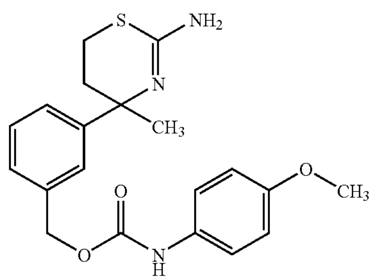
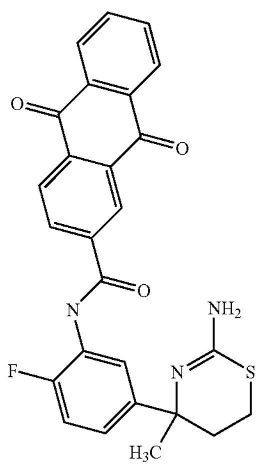
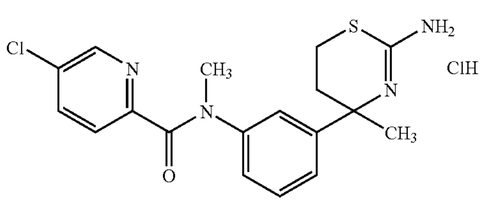
No.	Structure
1243	
1244	
1245	
1246	
1247	

TABLE 133-continued

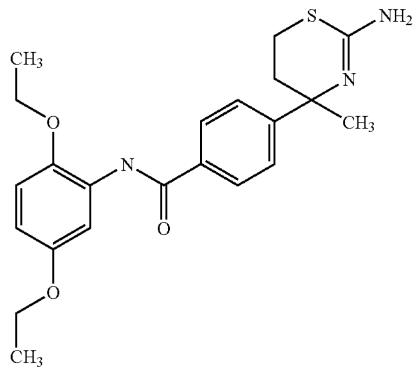
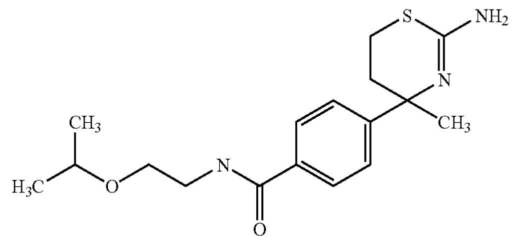
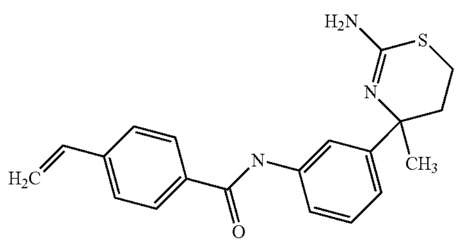
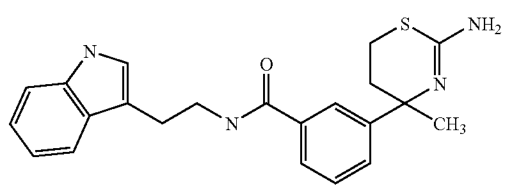
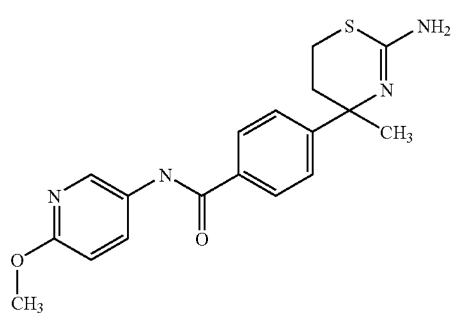
No.	Structure
1248	
1249	
1250	
1251	
1252	

TABLE 134

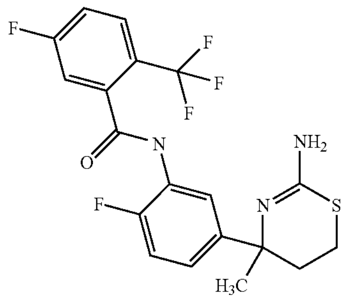
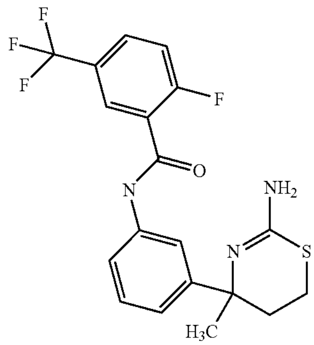
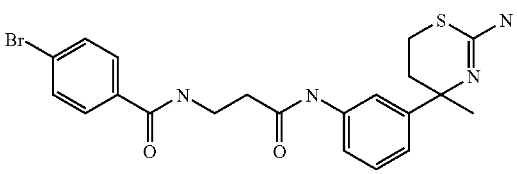
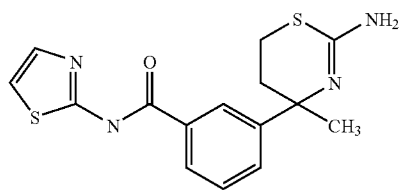
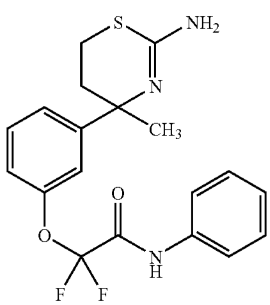
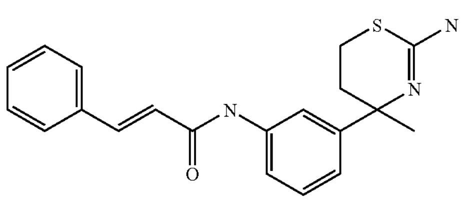
No.	Structure
1253	
1254	
1255	
1256	
1257	
1258	

TABLE 134-continued

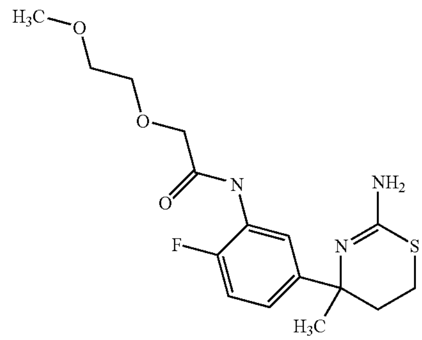
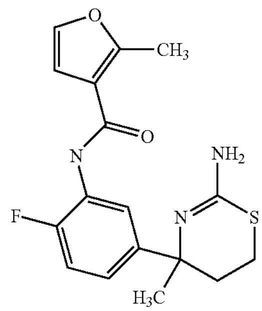
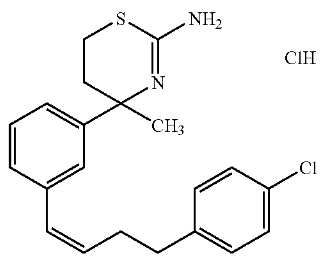
No.	Structure
1259	
1260	
1261	

TABLE 135

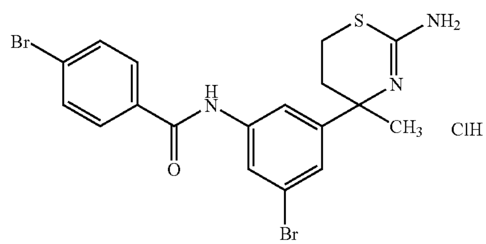
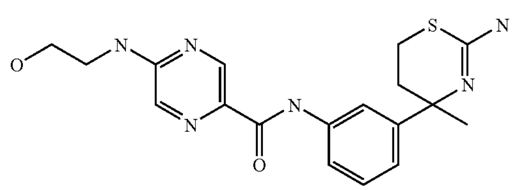
No.	Structure
1262	
1263	

TABLE 135-continued

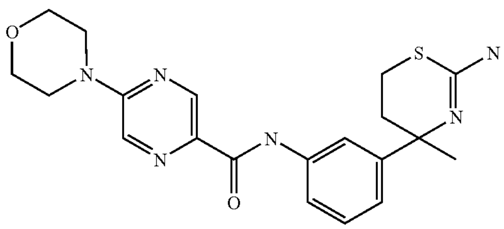
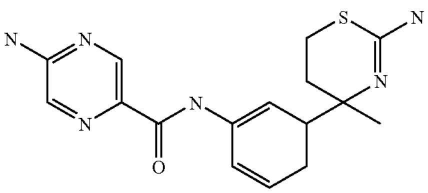
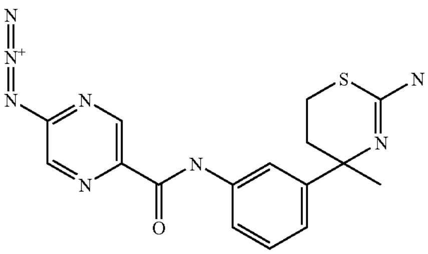
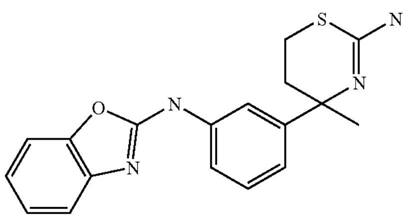
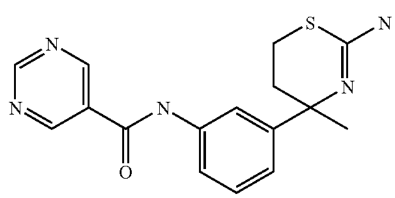
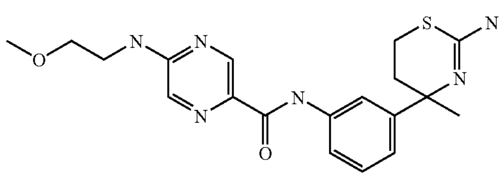
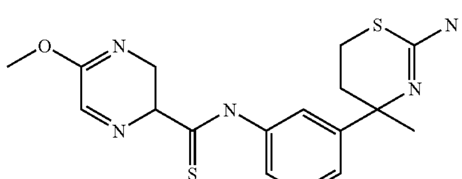
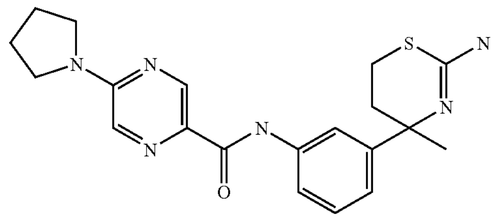
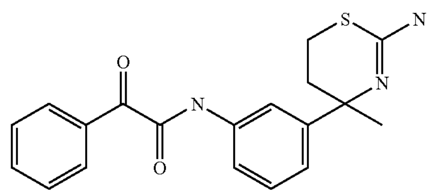
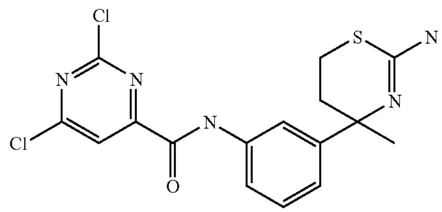
No.	Structure
1264	
1265	
1266	
1267	
1268	
1269	
1270	
1271	
1272	
1273	

TABLE 136

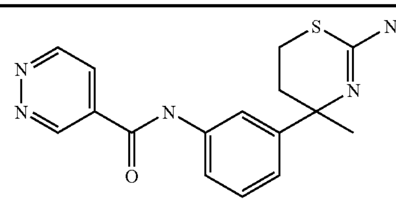
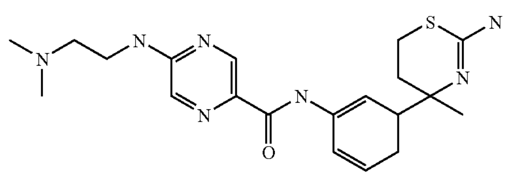
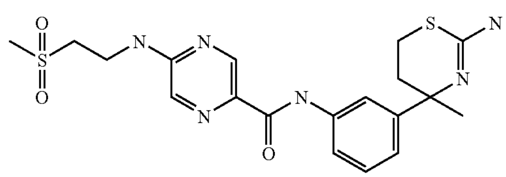
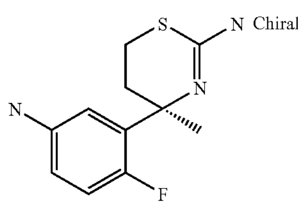
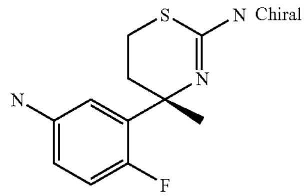
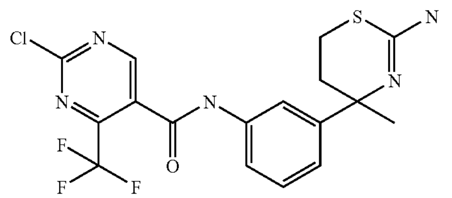
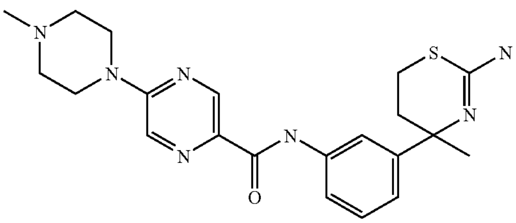
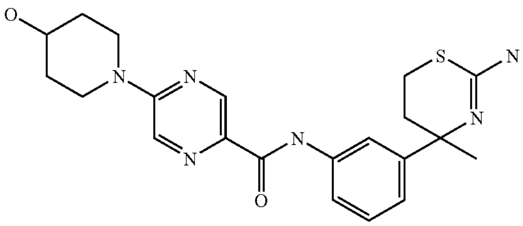
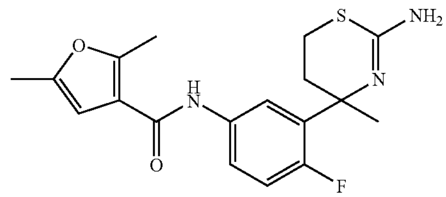
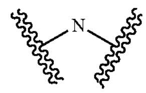
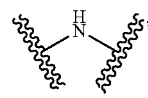
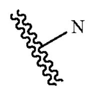
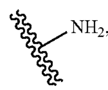
No.	Structure
1274	
1275	
1276	
1277	

TABLE 136-continued

No.	Structure
1278	
1279	
1280	
1281	
1282	

[Chemical formula 83]

in formula,  means ,

 means , and

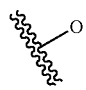
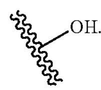
 means .

TABLE 137

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1				213.4 305.3
3	285 (dec.)			
4	amorphous			219
5				215, 262
6	147-148			
8	214-217			
9	oil			220
18	181-183			
23				213.4 272.2 305.3
24	116-117			
26	182-184			
30				267.4
33				253.3 305.3
37	amorphous			219, 275
38	240-244 (dec.)			
39				285.2
42	187-188			
43				218.1 275.7
48				230 275
57	197-198			
58	234-240			
62	198-201			

TABLE 137-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
69	194-195			
71				216.9 268.6
73	266-269			
77		δ in d20-DMSO: 1.67 (3H, s), 2.13-2.06 (1H, m), 2.63-2.55 (2H, m), 3.16-3.13 (4H, m), 3.65-3.63 (2H, m), 4.76-4.73 (2H, m), 7.15-7.08 (2H, m), 7.30 (1H, t, J = 8.0 Hz), 7.35 (1H, s), 7.42 (1H, t, J = 8.0 Hz), 7.60 (1H, d, J = 8.0 Hz), 7.69 (1H, d, J = 8.0 Hz), 7.73 (1H, brs), 7.86 (1H, d, J = 8.0 Hz), 10.52 (1H, s)		422.543
78		^{1}H-NMR ($CDCl_3$) δ: 1.76 (3H, s), 2.02 (1H, s), 2.58 (1H, d, J = 14.1 Hz), 2.78 (2H, d, J = 6.9 Hz), 3.80 (3H, d, J = 13.1 Hz), 4.54 (2H, s), 6.45 (1H, s), 6.55-6.57 (2H, m), 6.66 (1H, d, J = 8.7 Hz), 7.10 (1H, t, J = 7.0 Hz), 7.22 (2H, td, J = 7.7, 1.4 Hz), 7.34 (1H, d, J = 9.1 Hz), 7.56 (1H, d, J = 7.7 Hz).	365[M + 1]	
80				220.4 280.4

TABLE 138

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
85	147-148	1.54(3H, s), 1.75-1.86(1H, m), 2.08-2.18(1H, m), 2.33(3H, s), 2.63-2.74(1H, m), 2.81-2.90(1H, m), 4.36(2H, br), 7.13(2H, d, J = 8.6 Hz), 7.20(2H, d, J = 8.6 Hz)(solvent: CDCl3)		
86	141-142			
91			372[M + 1] 298	201 206 216
96				309
97		δ in d13-DMSO: 1.64(3H, s), 2.03-1.97(1H, m), 2.63-2.57(2H, m), 3.28-3.25(1H, m), 7.22(1H, q, J = 12.4, 9.0 Hz), 7.82-7.77(2H, m), 8.60(1H, s), 8.79(1H, s), 10.37(1H, s)		
99	221-224			
101	264-265			
104	amorphous			229, 280
113		1.58 (s, 3H), 1.88 (ddd, J = 14.1, 10.9, 3.7 Hz, 1H), 2.24 (ddd, J = 14.1, 5.9, 3.5 Hz, 1H), 2.73 (ddd, J = 12.3, 10.9, 3.5 Hz, 1H), 2.88 (ddd, J = 12.3, 5.9, 3.7 Hz, 1H), 3.83 (d, J = 15.4 Hz, 1H), 3.87 (d, J = 15.4 Hz, 1H), 7.02-7.04 (m, 1H), 7.25-7.31 (m, 2H), 7.36 (d, J = 2.0 Hz, 1H), 7.45-7.50 (m, 2H), 8.52 (d, J = 5.2 Hz, 1H), 9.43 (s, 1H) (solvent: CDCl3)		
114				214.5 306.5
115		δ in d6-DMSO: 1.47(3H, s), 1.80-1.74(1H, m, 2.22-2.18(1H, m), 2.60-2.55(1H, m), 2.96-2.93(1H, m), 6.14(1H, s), 6.93(1H, s), 7.09-7.04(2H, m), 7.63-7.61(1H, m), 7.68-7.66(1H, m), 9.85(1H, s), 11.63(1H, brs)		
120	amorphous			213
121	166-167			
125	>300			
126	amorphous			229, 271
127	280-285			
128	159-163			
129	219-222			
130	128-131	1.56 (3H, s), 1.83-1.93 (1H, m), 2.16 (1H, dq, J = 13.85, 3.41 Hz), 2.29 (3H, s), 2.72-2.77 (1H, m), 2.90-2.94 (1H, m), 4.13 (3H, s), 6.42 (1H, s), 7.10-7.14 (1H, m), 7.32 (1H, d, J = 7.91 Hz), 7.37-7.38 (1H, m), 7.60-7.63 (1H, m), (solvent: CDCl3)	344[M + 1]	
132	147-150			
134				228.5

TABLE 139

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
139	287-290	1.77 (s, 3H), 2.10 (ddd, J = 14.0, 10.8, 3.6 Hz, 1H), 2.64-2.70 (4H, m), 2.76 (td, J = 12.8, 3.6 Hz, 1H), 2.90 (dt, J = 12.8, 3.6 Hz, 1H), 7.05 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.69-7.72 (m, 2H), 8.32 (dd, J = 8.0, 0.8 Hz, 1H), 8.40 (dd, J = 8.0, 2.0 Hz, 1H), 9.14 (dd, J = 2.0, 0.8 Hz, 1H) (solvent: CDCl3 + CD3OD)		
141		δ in d17-DMSO: 1.41(3H, s), 1.75-1.70(1H, m), 2.03-1.99(1H, m), 2.62-2.56(1H, m), 2.94-2.89(1H, m), 3.89(3H, s), 6.88(1H, d, J = 8.8 Hz), 7.05(1H, d, J = 7.6 Hz), 7.24(1H, t, J = 8.0 Hz), 7.66-7.63(3H, m), 8.45-8.44(1H, m), 9.90(1H, s)		
148			362[M + 1] 286	200 208 212 218 262
149	143-145			
157		δ in d6-DMSO: 1.20(6H, d, J = 6.6 Hz), 1.41(3H, s), 1.65-1.77(1H, m), 1.96-2.07(1H, m), 2.55-2.63(1H, m), 2.85-2.95(1H, m), 4.04-4.16(1H, m), 5.79(2H, bs), 7.07(1H, d, J = 8.1 Hz), 7.25(1H, t, J = 8.1 Hz), 7.72-7.78(3H, m), 7.93(1H, s), 8.64(1H, s), 9.96(1H, s).		
159	amorphous			285
161	247-251			
163	amorphous			
164	91-96	1.68(s, 3H), 2.07-2.15(m, 1H), 3.13-3.20(m, 1H), 7.12(d, J = 7.6 Hz, 1H), 7.46(t, J = 7.6 Hz, 1H), 7.90-7.94(m, 2H), 8.83(br s, 1H), 8.96(br s, 1H), 9.31(br s, 1H), 10.36(s, 1H), 10.86(s, 1H)		
165	246-248			
166	amorphous			220, 275
176	amorphous			217, 278
178	224-225			
181				261.5
189				259
193	266-268			
196				212
202	117-118	0.85(3H, t, J = 7.3 Hz), 1.02-1.19(1H, m), 1.34-1.54(1H, m), 1.72-1.89(3H, m), 2.04-2.15(1H, m), 2.61-2.82(2H, m), 3.80(3H, s), 4.32(2H, br), 6.85(2H, d, J = 8.9 Hz), 7.18(2H, d, J = 8.9 Hz) (solvent: CDCl3)		

TABLE 140

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
204	205-208	1.64 (d, J = 1.2 Hz, 3H), 1.95 (ddd, J = 14.0, 10.8, 3.6 Hz, 1H), 2.45 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.75 (ddd, J = 12.4, 10.8, 3.6 Hz, 1H), 2.99 (ddd, J = 12.4, 6.4, 3.6 Hz, 1H), 7.09 (dd, J = 11.6, 8.8 Hz, 1H), 7.47 (dd, J = 7.2, 2.8 Hz, 1H), 8.03 (ddd, J = 8.8, 4.4, 2.8 Hz, 1H), 8.89 (s, 2H), 9.75 (s, 1H) (solvent: CDCl3)		
213	oil			216, 272
214				212.2 292.3 356.5
216				242.7
220	191-193		363[M + 3] 361[M + 1] 287 285	
224	oil	1.58(3H, s), 1.87(1H, ddd, J = 13.9, 10.5, 3.7), 2.13(1H, ddd, J = 13.9, 6.3, 3.7), 2.25(3H, s), 2.68(1H, ddd, J = 12.1, 10.5, 6.2), 2.89(1H, ddd, J = 12.1, 6.3, 3.7), 5.23(2H, s), 7.28-7.48(4H, m), 7.60(1H, s), 7.75(1H, d, J = 8.0), 8.56(1H, dd, J = 5.0, 1.4), 8.70(1H, d, J = 1.4) (solvent: CDCl3)		222
227				213

TABLE 140-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
232		1H-NMR (CDCl3) δ: 1.59 (3H, s), 1.83-1.90 (1H, m), 2.35-2.47 (4H, m), 2.60-2.67 (1H, m), 2.87-2.92 (1H, m), 4.70 (2H, br s), 6.87-6.98 (2H, m), 7.16 (1H, d, J = 6.6 Hz), 7.27 (2H, d, J = 7.8 Hz), 7.61 (2H, d, J = 8.1 Hz).	378[M + 1]	
233	oil			224, 272
235	196-200			
238		^{1}H-NMR ($CDCl_3$) δ: 1.68 (3H, s), 1.97-2.00 (1H, m), 2.53 (1H, dt, J = 14.4, 3.7 Hz), 2.63-2.79 (2H, m), 4.52 (2H, s), 6.56-6.66 (3H, m), 7.17 (1H, t, J = 8.0 Hz), 7.43-7.52 (3H, m), 7.81 (4H, dd, J = 11.6, 5.7 Hz).	362[M + 1]	
241	187-190	1H-NMR (DMSO-d6) δ: 1.49 (3H, s), 1.78-1.86 (1H, m), 2.13-2.21 (1H, m), 2.59-2.67 (1H, m), 2.96-3.02 (1H, m), 7.11 (1H, t, J = 10.7 Hz), 7.29 (1H, t, J = 7.8 Hz), 7.45 (1H, t, J = 7.5 Hz), 7.66 (1H, d, J = 8.8 Hz), 7.74-7.78 (1H, m), 7.80-7.83 (1H, m), 8.21 (1H, d, J = 8.6 Hz), 10.25 (1H, s).		
243	182-184	1.46(s, 3H), 1.75-1.83(m, 1H), 2.08-2.16(m, 1H), 2.55-2.63(m, 1H), 2.92-2.98(m, 1H), 4.02(s, 3H), 7.11(d, J = 8.0 Hz, 1H), 7.31(t, J = 8.0 Hz, 1H), 7.77(d, J = 8.0 Hz, 1H), 7.82(br s, 1H), 8.41(d, J = 1.2 Hz, 1H), 8.90(d, J = 1.2 Hz, 1H), 10.38(s, 1H) (solvent: CDCl3)		

TABLE 141

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
244	222-224			
251			351[M + 1] 311 275	200 204 215 285
255	238-239			
256	oil			215, 257
259	amorphous	1.58(3H, s), 2.01(1H, ddd, J = 15.2, 12.2, 3.4), 2.46-2.56(2H, m), 3.07(1H, ddd, J = 13.3, 5.7, 3.5), 4.24(2H, s) 6.53(1H, d, J = 7.6), 6.59-6.61(2H, m), 7.09-7.12(1H, m), 7.11(2H, d, J = 7.6), 7.24(2H, d, J = 7.6), 8.82(2H, br) (solvent: DMSO-d6)		229 298
263			383[M + 1] 287	200 284
267	114-115			
268				214.5 298.2
271	oil			229, 276
275		(CDCl3) 1.66(3H, d, J = 1.2 Hz), 1.98(1H, ddd, J = 14.0, 10.4, 3.7 Hz), 2.47(1H, ddd, J = 14.0, 6.7, 3.5 Hz), 2.79(1H, ddd, J = 12.0, 10.4, 3.5 Hz), 3.02(1H, ddd, J = 12.0, 6.7, 3.7 Hz), 4.45(2H, br), 6.16(2H, br), 7.04-7.11(2H, m), 7.38(1H, dd, J = 7.2, 2.9 Hz), 7.88(1H, d, J = 2.0 Hz), 7.96(1H, ddd, J = 8.9, 4.2, 2.9 Hz), 9.88(1H, s)		
277				216 228 281
279				214.5 292.3
281	amorphous	1.55(3H, s), 1.83(1H, ddd, J = 13.9, 10.6, 3.9), 2.10(1H, ddd, J = 13.9, 6.5, 3.6), 2.67(1H, ddd, J = 12.2, 10.6, 3.6), 2.87(1H, ddd, J = 12.2, 6.5, 3.9), 4.49(2H, d, J = 5.6), 4.85(1H, br), 6.38(1H, dt, J = 8.5, 0.9), 6.59(1H, ddd, J = 7.2, 5.2, 0.9), 7.21-7.24(2H, m), 7.28-7.32(2H, m), 7.40(1H, ddd, J = 8.5, 7.2, 1.8), 8.11(1H, ddd, J = 5.2, 1.8, 0.8) (solvent: CDCl3)		233 301
282	146-147			
284	181.5			

TABLE 141-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
293		1.57 (s, 3H), 1.78-1.89 (m, 1H), 2.10-2.19 (m, 1H), 2.69 (ddd, J = 11.9, 10.8, 3.5 Hz, 1H), 2.83-2.91 (m, 1H), 7.15-7.35 (m, 5H) (solvent: CDCl3)		
299				293.5

TABLE 142

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
301		(CDCl3) 1.53(3H, s), 1.80(1H, ddd, J = 14.0, 10.4, 3.6 Hz), 2.12(1H, ddd, J = 14.0, 6.0, 3.6 Hz), 2.75(1H, ddd, J = 12.0, 10.4, 3.6 Hz), 2.85(1H, ddd, J = 12.0, 6.0, 3.6 Hz), 3.64(2H, s), 4.32(2H, br), 6.55(1H, ddd, J = 8.0, 2.0, 0.8 Hz), 6.66(1H, t, J = 2.0 Hz), 6.70(1H, ddd, J = 8.0, 2.0, 0.8 Hz), 7.11(1H, t, J = 8.0 Hz)		
302	122-126	1.41(s, 3H), 1.67-1.76(m, 1H), 1.98-2.06(m, 1H), 2.55-2.63(m, 1H), 2.86-2.94(m, 1H), 3.19(s, 6H), 5.75(s, 2H), 7.08(d, J = 8.0 Hz, 1H), 7.26(t, J = 8.0 Hz, 1H), 7.73(d, J = 8.0 Hz, 1H), 7.76(br s, 1H), 8.16(s, 1H), 8.73(s, 1H), 10.00(s, 1H) (solvent: CDCl3)		
306				231, 258, 289
307		1.83 (ddd, J = 13.9, 10.3, 3.6 Hz, 1H), 2.13 (ddd, J = 13.6, 6.2, 3.5 Hz, 1H), 2.53 (s, 3H), 2.66-2.75 (m, 1H), 2.90 (ddd, J = 12.2, 6.3, 3.8 Hz, 1H), 7.09 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.37 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 8.79 (s, 1H) (solvent: CDCl3)		
308	167-188			
309	241-244			
319				308.9
329	238-239			
330				213.4 263.9
332				212.2
333	154-158			
339	217-218			
341	amorphous			216 249
342	184-187			
344		(DMSO) 1.49(3H, s), 1.73-1.85(1H, m), 2.15-2.28(1H, m), 2.54-2.66(1H, m), 2.92-3.04(1H, m), 5.86(2H, s), 7.03-7.25(3H, m), 7.40-7.48(2H, m), 7.64-7.78(3H, m), 10.31(1H, s), 11.74(1H, s)		
353				279.3 364.5
354	102-103			
356	amorphous	1.73 (s, 3H), 2.09-2.17 (m, 1H), 2.40(s, 3H), 2.65-2.73 (m, 2H), 3.15-3.23 (m, 1H), 3.81(s, 3H), 7.07 (d, J = 7.2 Hz, 2H), 7.29 (br s, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.78 (br s, 1H), 7.90 (d, J = 7.2 Hz, 2H), 8.00 (br s, 1H), 10.32 (s, 1H) (solvent: DMSO-d6)		267
357	amorphous			224, 298

TABLE 143

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
358		1.57 (3H, s), 1.80-1.91 (1H, m), 2.15-2.18 (1H, m), 2.70-2.94 (2H, m), 3.94 (3H, s), 4.67 (2H, s), 6.75 (1H, s), 7.05-7.08 (1H, m), 7.31 (1H, t, J = 7.91 Hz), 7.53 (1H, t, J = 1.98 Hz), 7.64-7.67 (1H, m), 8.64 (1H, s). (solvent: CDCl3)	360[M + 1]	
359	212-214	1.46(s, 3H), 1.73-1.83(m, 1H), 2.13-2.20(m, 1H), 2.54-2.61(m, 1H), 2.62(s, 3H), 2.93-3.00(m, 1H), 5.84(br s, 2H), 7.12(dd, J = 12.0, 8.8 Hz, 1H), 7.73-7.78(m, 1H), 7.81(dd, J = 7.2, 2.4 Hz, 1H), 8.68 (s, 1H), 9.13(s, 1H), 10.59(s, 1H)(solvent: CDCl3)		
360	amorphous			222

TABLE 143-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
361				280.4
364	oil		344[M + 1]	227, 271
367		(CDCl3) 1.78(3H, s), 2.07(1H, ddd, J = 14.0, 12.4, 3.6 Hz), 2.61(1H, br d, J = 14.0 Hz), 2.84(1H, td, J = 12.4, 3.2 Hz), 2.94(1H, td, J = 12.4, 3.6 Hz), 4.08(3H, s), 7.07(1H, ddd, J = 8.0, 2.0, 0.8 Hz), 7.40(1H, t, J = 8.0 Hz), 7.63(1H, ddd, J = 8.0, 2.0, 0.8 Hz), 7.74(1H, t, J = 2.0 Hz), 8.18(1H, d, J = 1.2 Hz), 9.02(1H, d, J = 1.2 Hz), 9.56(1H, s)		
375				217
380	181-182	0.86 (t, J = 7.2 Hz, 3H), 1.82-1.98 (m, 3H), 2.24 (br, 1H), 2.74 (td, J = 12.0, 3.6 Hz, 1H), 2.84 (dt, J = 12.0, 4.0 Hz, 1H), 7.08 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.58 (t, J = 2.0 Hz, 2H), 7.76 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.88 (dd, J = 8.4, 2.4 Hz, 1H), 8.25 (dd, J = 8.4, 0.8 Hz, 1H), 8.57 (dd, J = 2.4, 0.8 Hz, 1H), 9.84 (s, 1H) (solvent: CDCl3)		
383	oil			225, 269, 288
389	amorphous			292
393				213.4 316.0
395	amorphous			217, 269
396	211-213	1.64 (s, 3H), 1.96 (ddd, J = 14.0, 10.4, 4.0 Hz, 1H), 2.44 (ddd, J = 14.0, 6.8, 3.6 Hz, 1H), 2.75 (ddd, J = 12.4, 10.4, 3.6 Hz, 1H),, 2.99 (ddd, J = 12.4, 6.8, 4.0 Hz, 1H), 4.50 (2H, br), 7.08 (dd, J = 11.6, 8.8 Hz, 1H), 7.45 (dd, J = 6.8, 2.8 Hz, 1H), 8.01 (ddd, J = 8.8, 4.4, 2.8 Hz, 1H), 8.16 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H), 8.89 (dd, J = 2.0, 0.8 Hz, 1H), 9.91 (s, 1H) (solvent: CDCl3)		
401	106-107			

TABLE 144

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
405	192-194	1.41(s, 3H), 1.68-1.77(m, 1H), 1.96-2.05(m, 1H), 2.55-2.63(m, 1H), 2.88-2.95(m, 1H), 4.15(s, 3H), 5.74(s, 2H), 7.13(d, J = 8.0 Hz, 1H), 7.29(t, J = 8.0 Hz, 1H), 7.44(d, J = 8.8 Hz, 1H), 7.75(d, J = 8.0 Hz, 1H), 7.86(br s, 1H), 8.20(d, J = 8.8 Hz, 1H), 10.73(s, 1H) (solvent: CDCl3)		
406				276.9
408	221-224	1.74(3H, s), 2.28(2H, m), 2.67(2H, m), 2.91(3H, s), 3.82(3H, s), 6.90(2H, d, J = 9.0), 7.19(2H, d, J = 9.0) (solvent: CDCl3)		
409	oil			215
410	178-182	1.37(d, J = 6.0 Hz, 6H), 1.42(s, 3H), 1.70-1.78(m, 1H), 2.00-2.08(m, 1H), 2.53-2.61(m, 1H), 2.88-2.95(m, 1H), 5.36(quintet, J = 6.0 Hz, 1H), 7.11(d, J = 8.0 Hz, 1H), 7.29(t, J = 8.0 Hz, 1H), 7.75(d, J = 8.0 Hz, 1H), 7.80(br s, 1H), 8.32(d, J = 1.2 Hz, 1H), 8.87(d, J = 1.2 Hz, 1H), 10.32(s, 1H) (solvent: CDCl3)		
411				218, 264
413	251-254			
415	amorphous			226, 290
417	137-139			
422		(CDCl3) 1.45(3H, s), 1.70-1.84(1H, m), 1.96-2.04(1H, m), 2.88-2.96(1H, m), 3.04-3.14(1H, m), 6.86(1H, d, J = 15.9 Hz), 6.42(1H, d, J = 15.9 Hz), 7.22-7.41(5H, m)		
426				211.0 312.4
427				216
429	oil			211 259
430		(DMSO) 1.07(3H, s), 1.53-1.66(4H, m), 2.50-2.70(2H, m), 2.92-3.10(2H, m), 5.48(1H, s), 7.11-7.21(3H, m), 7.23-7.29(2H, m)		

TABLE 144-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
432	oil			216, 272
436	254-256			
441	181-165			
443		^{1}H-NMR ($CDCl_3$) δ: 1.55 (4H, s), 1.74-1.80 (1H, m), 2.13-2.17 (1H, m), 2.68-2.73 (2H, m), 4.33 (1H, br s), 4.48 (2H, d, J = 4.0 Hz), 4.76 (2H, t, J = 20.1 Hz), 6.52 (1H, dd, J = 7.9, 1.8 Hz), 6.63-6.65 (2H, m), 7.13 (1H, t, J = 7.8 Hz), 7.45-7.51 (2H, m), 7.79-7.82 (4H, m).	362[M + 1]	

TABLE 145

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
444	214-215	1.41(s, 3H), 1.66-1.76(m, 1H), 1.97-2.05(m, 1H), 2.53-2.62(m, 1H), 2.62(s, 3H), 2.86-2.93(m, 1H), 5.79(br s, 2H), 7.12(d, J = 8.0 Hz, 1H), 7.28(t, J = 8.0 Hz, 1H), 7.74(d, J = 8.0 Hz, 1H), 7.81(br s, 1H), 8.68(s, 1H), 9.14(s, 1H), 10.52(s, 1H) (solvent: CDCl3)		
445	92-93			
446	oil	1.57(3H, s), 1.86(1H, ddd, J = 13.9, 10.4, 3.7), 2.13(1H, ddd, J = 13.9, 6.5, 3.6), 2.25(3H, s), 2.35(3H, s), 2.70(1H, ddd, J = 12.2, 10.4, 3.6), 2.89(1H, ddd, J = 12.2, 6.5, 3.7), 4.35(2H, br), 5.19(2H, s), 7.17(2H, d, J = 8.0), 7.31-7.34(4H, m), 7.50(1H, ddd, J = 5.8, 3.0, 1.8), 7.55-7.60(1H, m) (solvent: CDCl3)		219 252
448		δ in d6-DMSO: 1.41(3H, s), 1.67-1.75(1H, m), 1.98-2.05(1H, m), 2.52-2.61(1H, m), 2.86-2.94(1H, m), 5.79(2H, bs), 7.14(1H, d, J = 7.8 Hz), 7.30(1H, t, J = 7.8 Hz), 7.73(1H, bd, J = 7.8 Hz), 7.81(1H, t, J = 1.8 Hz), 8.94(1H, m), 9.11(1H, m), 10.63(1H, bs).		
452	132-134			
456	147-149			
457	153-155			
465	194.6			
466				211
470	281 (dec.)			
482		1.60 (s, 3H), 1.91 (ddd, J = 14.0, 10.8, 4.0 Hz, 1H), 2.23 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.77 (ddd, J = 12.0, 10.8, 3.6 Hz, 1H), 2.93 (ddd, J = 12.0, 6.4, 4.0 Hz, 1H), 7.16 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.61 (t, J = 2.0 Hz, 1H), 7.75 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.14 (d, J = 1.6 Hz, 1H), 8.80 (d, J = 1.6 Hz, 1H), 9.79 (s, 1H) (solvent: CDCl3)		
483	224-227			211, 289
490		1.64 (3H, s) 2.03-2.12 (1H, m) 2.49-2.62 (m) 3.12-3.16 (1H m) 7.22 (1H, dd, J = 4.2 Hz) 7.27 (1H, bs) 7.75 (1H bs) 7.87 (1H, dd, J = 4.2 Hz) 8.04 (1H, s) 8.12 (1H, dd, J = 4.2 Hz) 10.64 (1H, s) 10.72 (1H, s) (solvent: DMSO-d6)		
491		1.58 (s, 3H), 1.85-1.96 (m, 1H), 2.15-2.24 (m, 1H), 2.50 (s, 3H), 2.67 (s, 3H), 2.71-2.81 (m, 1H), 2.90-2.98 (m, 1H), 7.13 (d, J = 6.2 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.40 (s, 1H), 7.55 (d, J = 7.6 Hz, 1H) (solvent: CDCl3)		
493				216

TABLE 146

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
494		δ in d6-DMSO: 1.37(3H, s), 1.62-1.70(1H, m), 2.0-2.12(1H, m), 2.40-2.50(1H, m), 2.79-2.83(1H, m), 3.82(3H, s), 4.52(2H, d, J = 5.4 Hz), 6.19(1H, m), 6.54(1H, d, J = 7.8 Hz), 6.62(1H, d, J = 8.1 Hz), 6.75(1H, s), 7.01(1H, t, J = 8.1 Hz), 7.14-7.25(2H, m), 7.51(1H, d, J = 8.1 Hz), 7.60(1H, d, J = 7.5 Hz).	366[M + 1]	
496	152-154			
497		δ in d6-DMSO: 1.48(3H, s), 1.83-1.77(1H, m), 2.61-2.56(1H, m), 2.99-2.95(1H, m), 3.86(3H, s), 6.07(1H, s), 6.95(1H, s), 7.03-7.02(1H, m), 7.09-7.06(1H, m), 7.58-7.57(1H, m), 7.64-7.62(1H, m), 9.83(1H, s)		
498	122-125			
500	181-184			
501	155-156			
502	137-138			
504	209-219			
511	211-214	1.58 (s, 3H), 1.90 (ddd, J = 14.0, 10.0, 3.6 Hz, 1H), 2.15 (ddd, J = 14.0, 6.8, 3.6 Hz, 1H), 2.77 (ddd, J = 12.4, 10.0, 3.6 Hz, 1H), 2.94 (ddd, J = 12.4, 6.8, 3.6 Hz, 1H), 4.34 (2H, br), 7.17 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.50 (d, J = 2.0 Hz, 1H), 7.56 (td, J = 2.0 Hz, 1H), 7.70 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.08 (d, J = 1.6 Hz), 9.70 (s, 1H) (solvent: CDCl3)		
515	204-206	1.61 (s, 3H), 1.90 (ddd, J = 14.0, 10.8, 3.6 Hz, 1H), 2.22 (ddd, J = 14.0, 6.0, 3.6 Hz, 1H), 2.77 (ddd, J = 12.4, 10.8, 3.6 Hz, 1H), 2.93 (ddd, J = 12.4, 60, 3.6 Hz, 1H), 7.15 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.65 (t, J = 2.0 Hz, 1H), 7.80 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.89 (s, 2H), 9.77 (s, 1H) (solvent: CDCl3)		
516				292.3
525	105-106			
528	173-174	1.60 (s, 3H), 1.89 (ddd, J = 14.0, 10.8, 3.6 Hz, 1H), 2.22 (ddd, J = 14.0, 6.4, 3.2 Hz, 1H), 2.44 (s, 3H), 2.77 (ddd, J = 12.4, 10.8, 3.2 Hz, 1H), 2.91 (ddd, J = 12.4, 6.4, 3.6 Hz, 1H), 4.50 (br, 2H), 7.11 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.67-7.71 (m, 2H), 7.74 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.44(d, J = 1.6 Hz, 1H), 9.98 (s, 1H) (solvent: CDCl3)		
532				305.3
533	180-181			
534	201-204			
549	100-101			
551	139-141			
554				216

TABLE 147

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
556		(CDCl3) 1.67(3H, d, J = 1.2 Hz), 1.98(1H, ddd, J = 14.0, 10.4, 3.7 Hz), 2.47(1H, ddd, J = 14.0, 6.7, 3.5 Hz), 2.79(1H, ddd, J = 12.0, 10.4, 3.5 Hz), 3.02(1H, ddd, J = 12.0, 6.7, 3.7 Hz), 4.11(3H, s), 4.45(2H, br), 7.10(1H, dd, J = 11.7, 8.8 Hz), 7.41(1H, dd, J = 6.9, 2.8 Hz), 8.04(1H, ddd, J = 8.8, 4.0, 2.8 Hz), 8.20(1H, d, J = 1.4 Hz), 9.06(1H, d, J = 1.4 Hz), 9.51(1H, s)		
558			358[M + 1] 282	200
559				224
560		δ in d10-DMSO: 1.72(3H, s), 2.12-2.05(1H, m), 2.71-2.61(2H, m), 3.22-3.19(1H, m), 6.52(1H, s), 7.26(1H, q, J = 11.6, 9.2 Hz), 7.55(1H, s), 7.66-7.62(2H, m), 7.79-7.77(1H, m), 7.90-7.88(1H, m), 8.07(1H, s), 10.42(1H, s), 11.55(1H, s)		
561	235-240			
567	oil			212
570	186-187			
573	112-114			

TABLE 147-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
577		δ in d19-DMSO: 2.14-2.07(1H, m), 2.88-2.70(3H, m), 3.07, 3.26(2H, abq, J = 12.0 Hz), 3.73(3H, s), 5.40(2H, s), 6.51(1H, s), 6.85(1H, d, J = 12.0 Hz), 7.34(1H, d, J = 8.0 Hz)		
584	152-153			
586		δ in d7-DMSO: 1.71(3H, s), 2.10-2.04(1H, m), 2.69-2.59(2H, m), 3.20-3.17(1H, m), 4.00(3H, s), 7.13(1H, d, J = 7.4 Hz), 7.33-7.23(3H, m), 7.55(1H, d, J = 8.4 Hz), 7.72-7.68(1H, m), 7.92-7.90(1H, m), 10.60(1H, s)		
588	155-156			
593	oil			226
595	oil	1.56(3H, s), 1.86(1H, ddd, J = 13.9, 10.1, 3.7), 2.11(1H, ddd, J = 13.9, 6.6, 3.6), 2.32(3H, s), 2.70(1H, ddd, J = 12.3, 10.1, 3.6), 2.90(1H, ddd, J = 12.3, 6.6, 3.7), 5.25(2H, s), 7.29-7.35(4H, m), 7.47(1H, dt, J = 6.8, 2.0), 7.56-7.58(1H, m), 8.59(2H, d, J = 6.0) (solvent: CDCl3)		220
596				215
597	192-194			
600	178-180			
601	181-192	1.59 (3H, s), 1.85-1.95 (1H, m), 2.15-2.22 (1H, m), 2.72-2.78 (1H, m), 2.88-2.96 (1H, m), 4.31 (3H, s), 7.13 (1H, d, J = 7.25 Hz), 7.33 (1H, t, J = 7.91 Hz), 7.59 (1H, s), 7.68 (1H, d, J = 7.91 Hz), 7.75 (1H, s), (solvent: CDCl3)	375[M + 1]	
602	272-285 (dec.)			

TABLE 148

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
605	230-233	1.63 (s, 3H), 1.94 (ddd, J = 14.0, 10.4, 3.6 Hz, 1H), 2.44 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.75 (ddd, J = 12.4, 10.4, 3.6 Hz, 1H),, 2.98 (ddd, J = 12.4, 6.4, 3.6 Hz, 1H), 4.50 (2H, br), 7.06 (dd, J = 11.6, 8.8 Hz, 1H), 7.40 (dd, J = 7.2, 2.8 Hz, 1H), 7.59 (ddd, J = 8.8, 8.0, 2.8 Hz, 1H), 7.99 (ddd, J = 8.8, 4.4, 2.8 Hz, 1H), 8.33 (dd, J = 8.8, 4.4 Hz, 1H), 8.45 (d, J = 2.8 Hz, 1H), 9.78 (s, 1H) (solvent: CDCl3)		
608				213.4 304.1
611	200-202			
613				238
618		1.74(s, 3H), 1.97-2.07(m, 1H), 2.45-2.55(m, 1H), 2.77-2.85(m, 1H), 2.84(s, 3H), 2.90-2.96(m, 1H), 7.11(d, J = 8.0 Hz, 1H), 7.42(t, J = 8.0 Hz, 1H), 7.57(d, J = 8.8 Hz, 1H), 7.70(d, J = 8.0 Hz, 1H), 7.74(br s, 1H), 8.29(d, J = 8.8 Hz, 1H), 10.12(s, 1H) (solvent: CDCl3)		
620				212, 253
625	107-109			
629		δ in d14-DMSO: 1.66(3H, s), 2.11-2.05(1H, m), 2.37(3H, s), 2.63-2.53(2H, m), 3.14-3.11(1H, m), 7.08-7.04(2H, t, J = 7.0 Hz), 7.43-7.35(4H, m), 7.83-7.80(2H, m), 10.39(1H, s), 11.69(1H, s)		
630		1.28 (3H, t, J = 7.7 Hz), 1.96 (1H, ddd, J = 3.8, 9.9, 13.7 Hz), 2.19 (1H, ddd, J = 3.5, 7.0, 13.7 Hz), 2.74 (1H, ddd, J = 3.6, 9.9, 12.2 Hz), 2.93 (1H, ddd, J = 3.8, 7.0, 12.1 Hz), 4.05-4.49 (4H, m), 7.40-7.50 (3H, m), 7.77-7.86 (1H, m) (solvent: CDCl3)	301[M + 1]	
634		(CDCl3) 1.67(3H, d, J = 1.2 Hz), 1.98(1H, ddd, J = 14.0, 10.4, 3.7 Hz), 2.47(1H, ddd, J = 14.0, 6.7, 3.5 Hz), 2.79(1H, ddd, J = 12.0, 10.4, 3.5 Hz), 3.02(1H, ddd, J = 12.0, 6.7, 3.7 Hz), 4.11(3H, s), 4.45(2H, br), 7.10(1H, dd, J = 11.7, 8.8 Hz), 7.41(1H, dd, J = 6.9, 2.8 Hz), 8.04(1H, ddd, J = 8.8, 4.0, 2.8 Hz), 8.20(1H, d, J = 1.4 Hz), 9.06(1H, d, J = 1.4 Hz), 9.51(1H, s)		
636	118-119			
637				229, 275
643	155-157	1.60 (s, 3H), 1.90 (ddd, J = 14.0, 10.4, 3.6 Hz, 1H), 2.20 (ddd, J = 14.0, 6.8, 3.6 Hz, 1H), 2.77 (ddd, J =		

TABLE 148-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
		12.0, 10.4, 3.6 Hz, 1H),, 2.93 (ddd, J = 12.0, 6.8, 3.6 Hz, 1H), 4.59 (brs, 1H), 7.16 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.67 (t, J = 2.0 Hz, 1H), 7.71 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.87 (dd, J = 10.0, 1.2 Hz, 1H), 8.73 (d, J = 1.2 Hz, 1H), 9.74 (s, 1H) (solvent: CDCl3)		
644	201-203			

TABLE 149

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
645	oil	1.58(3H, s), 1.87(1H, ddd, J = 14.0, 10.4, 3.6), 2.16(1H, ddd, J = 14.0, 6.3, 3.5), 2.34(3H, s), 2.70(1H, ddd, J = 12.3, 10.4, 3.5), 2.90(1H, ddd, J = 12.3, 6.3, 3.6), 5.38(2H, s), 7.18-7.33(3H, m), 7.43(1H, d, J = 8.0), 7.49-7.60(2H, m), 7.69(1H, dt, J = 7.7, 1.9), 8.59(1H, ddd, J = 4.9, 1.9, 1.1) (solvent: CDCl3)		222
649	161-162			
651	193-196	1.59 (s, 3H), 1.90 (ddd, J = 14.0, 10.4, 3.6 Hz, 1H), 2.18 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.76 (ddd, J = 12.4, 10.4, 3.6 Hz, 1H),, 2.93 (ddd, J = 12.4, 6.4, 3.6 Hz, 1H), 4.42 (br, 2 H), 7.17 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.64 (t, J = 2.0 Hz, 1H), 7.77 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.20 (dd, J = 8.0, 2.0 Hz, 1H), 8.44 (dd, J = 8.0, 0.8 Hz, 1H), 8.91 (dd, J = 2.0, 0.8 Hz, 1H), 9.87 (s, 1H) (solvent: CDCl3)		
652		δ in d21-DMSO: 1.67(3H, s), 2.14-2.07(1H, m), 2.62-2.57(2H, m), 3.17-3.14(1H, m), 5.74(1H, s), 7.14(1H, d, J = 8.0 Hz), 7.44(1H, t, J = 8.0 Hz), 7.85-7.81(2H, m), 8.01(1H, d, J = 12.0 Hz), 8.16(1H, d, J = 8.0 Hz), 8.77(1H, s), 10.95(1H, s)		
653	193-194			
654	oil			257
657	199-203			
660	amorphous			223, 266
661		δ in d9-DMSO: 1.30(3H, t, J = 7.0 Hz), 1.69(3H, s), 2.10-2.04(1H, m), 2.20(3H, s), 2.67-2.62(2H, m), 3.20-3.17(1H, m), 4.40(2H, q, J = 14.0, 7.0 Hz), 6.83(1H, s), 7.25(1H, q, J = 12.0, 9.0 Hz), 7.62-7.61(1H, m), 7.85-7.83(1H, m), 10.42(1H, s)		
664	amorphous			225, 267
667	amorphous			226
673	oil			224
677	amorphous			216
680	159-160	1.63(3H, s), 1.65-1.80(1H, m), 2.53-2.64(1H, m), 2.75-2.88(2H, m), 3.83(3H, s), 4.32(2H, br), 6.87-6.96(2H, m), 7.19-7.33(2H, m) (solvent: CDCl3)		
681		δ in d6-DMSO: 1.43(3H, s), 1.66-1.74(1H, m), 2.02-2.07(1H, m), 2.56-2.63(1H, m), 2.85-2.90(1H, m), 5.80(2H, bs), 6.91 (1H, d, J = 7.8 Hz), 6.96-6.98(2H, m), 7.25(1H, t, J = 7.8 Hz), 7.2-7.36(2H, m), 7.40(1H, m), 7.89-7.92(1H, m), 9.42(1H, bs), 10.78(1H, bs).	338[M + 1]	
683	166-168			

TABLE 150

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
687	164-167	1.60 (3H, s), 1.84-1.95 (1H, m), 2.21-2.26 (1H, m), 2.73-2.94 (2H, m), 3.92 (3H, s), 4.25 (3H, s), 7.10 (1H, d, J = 7.58 Hz), 7.34 (1H, t, J = 7.91 Hz), 7.40 (1H, s), 7.57 (1H, br s), 7.66 (1H, d, J = 7.91 Hz), 8.67 (1H, s), (solvent: CDCl3)	388[M + 1]	
692		(CDCl3) 1.50(3H, s), 1.75-1.88(1H, m), 2.00-2.10(1H, m), 2.91-2.99(1H, m), 3.08-3.18(1H, m), 6.21(1H, d, J = 15.9 Hz), 6.59(1H, d, J = 15.9 Hz), 7.42-		

TABLE 150-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
		7.47(3H, m), 7.59(1H, dd, J = 8.6, 2.0 Hz), 7.74-7.83(4H, m)		
698				269
700	177-178			
701		1.61(s, 3H), 1.90(m, 1H), 2.25(m, 1H), 2.81(m, 1H), 2.92(m, 1H), 3.86(s, 3H), 6.71(t-like, J = 1.8 Hz, 1H), 7.12(t-like, J = 1.8 Hz, 1H), 7.53(t-like, J = 1.8 Hz, 1H), 7.89(dd, J = 8.3 Hz, 2.4 Hz, 1H), 8.24(d, J = 8.3 Hz, 1H), 8.58(d, J = 2.4 Hz, 1H), 9.85(br, 1H) (solvent: CDCl3)		
702		1H-NMR(CDCl3) δ: 1.65 (3H, s), 1.91-1.98 (1H, m), 2.57-2.62 (1H, m), 2.68-2.75 (1H, m), 2.92-2.97 (1H, m), 4.18 (3H, s), 6.82 (1H, br s), 7.02-7.08 (1H, m), 7.28-7.32 (1H, m), 7.44 (1H, s), 7.92-7.96 (1H, m).		
707	167-174			
709	99-100	0.82(3H, t, J = 7.3 Hz), 1.72-1.90(3H, m). 2.06-2.15(1H, m), 2.61-2.82(2H, m), 3.80(3H, s), 4.36(2H, br), 6.86(2H, d, J = 8.9 Hz), 7.17(2H, d, J = 8.9 Hz) (solvent: CDCl3)		
717	157-162	1.58 (s, 3H), 1.90 (ddd, J = 14.0, 10.4, 3.6 Hz, 1H), 2.15 (ddd, J = 14.0, 6.8, 3.6 Hz, 1H), 2.76 (ddd, J = 12.4, 10.4, 3.6 Hz, 1H), 2.94 (ddd, J = 12.4, 6.8, 3.6 Hz, 1H), 3.49 (1H, S), 3.76 (2H, br), 7.17 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.38 (d, J = 1.6 Hz, 1H), 7.50 (t, J = 2.0 Hz, 1H), 7.73 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.22 (d, J = 2.4 Hz), 9.26 (d, J = 2.4 Hz, 1H), 10.12 (s, 1H) (solvent: CDCl3)		
719	oil			226 254
720	133-138			
725	amorphous	1.62 (s, 3H), 1.96-2.03(m, 1H), 2.38-2.49 (m, 1H), 2.63-2.71 (m, 1H), 3.05-3.12 (m, 1H), 6.73 (dd, J = 3.2, 1.6 Hz, 2H), 7.35(d, J = 3.2 Hz, 1H), 7.37 (br s, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.77 (br s, 1H), 7.96(br s, 1H), 8.01(br s, 1H), 10.35 (s, 1H) (solvent: DMSO-d6)		265
728	179-182			
729	187-169			

TABLE 151

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
730				211.0 289.9
731	91-94			
732	amorphous			211
735	166-168			
737		1H-NMR (CDCl3) δ: 1.59 (3H, s), 1.87-1.94 (1H, m), 2.47-2.53 (1H, m), 2.67-2.73 (1H, m), 2.93-2.99 (1H, m), 4.10 (3H, s), 6.62 (1H, s), 7.04 (1H, t, J = 10.2 Hz), 7.33 (1H, d, J = 4.3 Hz), 7.85 (1H, br s).		
738	181-183			
739				285
740	250 (dec.)			
743	148-150	1.60 (s, 3H), 179-2.93 (m, 4H), 4.46 (2H, br), 7.09 (d, J = 2.0 Hz, 1H), 7.12 (ddd, J = 7.6, 2.0, 0.8 Hz, 1H), 7.18 (t, J = 2.0 Hz, 1H), 7.36 (d, J = 7.6, 2.0, 0.8 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 8.21 (d, J = 2.0 Hz) (solvent: CDCl3)		
744		δ in d8-DMSO: 1.47(3H, s), 1.82-1.78(1H, m), 2.22-2.18(1H, m), 2.62-2.56(1H, m), 3.00-2.96(1H, m), 6.79(1H, s), 6.63(1H, s), 7.08-7.03(1H, m), 7.51(1H, s), 7.64-7.57(2H, m), 9.57(1H, s), 11.25(1H, s)		
753	amorphous			225, 299
756	110-111	1.55(3H, s), 1.76-1.87(1H, m), 2.08-2.17(1H, m), 2.35(3H, s), 2.65-2.76(1H, m), 2.82-2.92(1H, m), 4.35(2H, br), 7.01-7.25(4H, m) (solvent: CDCl3)		
758	156-157			

TABLE 151-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
766			336[M + 1] 260	203 212
767	98-100			
768		1.60 (3H, d, J = 1.3 Hz), 1.89-1.99 (1H, m), 2.29 (3H, s), 2.37-2.42 (1H, m), 2.70-2.75 (1H, m), 2.96-3.00 (1H, m), 4.12 (3H, s), 6.39 (1H, s), 7.04 (1H, dd, J = 11.5, 8.9 Hz), 7.18 (1H, dd, J = 6.9, 2.6 Hz), 7.60 (1H, s), 7.82-7.86 (1H, m), (solvent: CDCl3)	362[M + 1]	213 263
771			417[M + 1] 341	201
774		^{1}H-NMR ($CDCl_3$) δ: 1.77 (3H, s), 2.11-2.21 (1H, m), 2.71-2.80 (1H, m), 2.87-2.99 (2H, m), 6.91 (1H, d, J = 6.9 Hz), 7.28 (2H, s), 7.47 (1H, t, J = 8.1 Hz), 7.75 (1H, t, J = 8.6 Hz), 8.04 (1H, dd, J = 8.6, 2.3 Hz), 8.29 (1H, d, J = 8.2 Hz), 8.46 (1H, d, J = 2.2 Hz).	400[M + 1]	

TABLE 151

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
781		1.63 (s, 3H), 1.92 (ddd, J = 14.0, 10.8, 4.0 Hz, 1H), 2.29 (m, 1H), 2.78 (ddd, J = 12.4, 10.8, 3.6 Hz, 1H),, 2.91 (ddd, J = 12.4, 6.4, 4.0 Hz, 1H), 3.94 (3H, s), 7.09 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.34 (dd, J = 8.8, 2.8 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.68 (t, J = 2.0 Hz, 1H), 7.71 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.24 (d, J = 8.8 Hz, 1H), 8.28 (d, J = 2.8 Hz, 1H), 9.86 (s, 1H) (solvent: CDCl3)		
783	205-206			
786		1.66(3H, s), 2.10(1H, m), 2.57-2.64(2H, m), 3.16(1H, m), 6.74(1H, s), 7.30(1H, s), 7.36(1H, s), 7.74(1H, s), 7.98(1H, s), 8.06(1H, s), 10.33(1H, s), 10.47(1H, s) (solvent: DMSO-d6)		
790	amorphous			223, 290
791		δ in d18-DMSO: 1.41(3H, s), 1.76-1.69(1H, m), 2.02-1.98(1H, m), 2.62-2.55(1H, m), 2.92-2.89(1H, m), 7.13(1H, d, J = 7.6 Hz), 7.29(1H, t, J = 7.6 Hz), 7.62-7.59(2H, m), 8.71(1H, s), 9.28(1H, s), 10.46(1H, brs)		
792				299.4
793	269 (dec.)			
797				213.4 312.4
799				215, 240
800				225, 275
802		1.63 (s, 3H), 1.92 (ddd, J = 14.0, 11.2, 3.6 Hz, 1H), 2.28 (br, 1H), 2.78 (ddd, J = 12.4, 11.2, 3.6 Hz, 1H), 2.81 (s, 3H), 2.92 (ddd, J = 12.4, 6.4, 4.0 Hz, 1H), 7.10 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.56 (t, J = 2.0 Hz, 1H), 7.65 (d, J = 2.4 Hz, 1H), 7.74 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.41 (d, J = 2.4 Hz, 1H), 10.03 (s, 1H) (solvent: CDCl3)		
803				271
804	135-136			
810	47-48			
811	138-139			
813	204-205	182 (s, 3H), 1.89-1.94 (m, 1H), 2.78 (ddd, J = 12.4, 6.4, 3.6 Hz, 1H), 4.50 (2H, br), 7.06 (dd, J = 11.6, 8.8 Hz, 1H), 7.40 (dd, J = 7.2, 2.8 Hz, 1H), 7.59 (ddd, J = 8.8, 8.0, 2.8 Hz, 1H), 7.99 (ddd, J = 8.8, 4.4, 2.8 Hz, 1H), 8.33 (dd, J = 8.8, 4.4 Hz, 1H), 8.45 (d, J = 2.8 Hz, 1H), 9.78 (s, 1H)(solvent: CDCl3)		
814	oil			218, 272
816				214.5

TABLE 152

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
820		(CDCl3) 1.66(3H, d, J = 1.2 Hz), 1.98(1H, ddd, J = 14.0, 10.4, 3.7 Hz), 2.47(1H, ddd, J = 14.0, 6.7, 3.5 Hz),		

TABLE 152-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
		2.79(1H, ddd, J = 12.0, 10.4, 3.5 Hz), 3.02(1H, ddd, J = 12.0, 6.7, 3.7 Hz), 4.45(2H, br), 6.16(2H, br), 7.04-7.11(2H, m), 7.38(1H, dd, J = 7.2, 2.9 Hz), 7.88(1H, d, J = 2.0 Hz), 7.96(1H, ddd, J = 8.9, 4.2, 2.9 Hz), 9.88(1H, s)		
822				279
827	134-137			214.5 284.0
832				212, 299
833	oil			212, 273
834				217, 287
835	139-140			
836				221.6 279.3
840	223-225			
848	oil			223, 254
849	143-145			
850		δ in d16-DMSO: 1.41(3H, s), 1.75-1.70(1H, m), 2.02-1.99(1H, m), 2.61-2.56(1H, m), 2.93-2.88(1H, m), 7.13(1H, d, J = 8.0), 7.29(1H, t, J = 7.8 Hz), 7.35(1H, q, J = 8.4, 2.4 Hz), 7.66-7.63(2H, m), 8.52-8.47(1H, m), 8.81 (1H, s), 10.44(1H, s)		
851	82-83	1.55(3H, s), 1.76-1.88(1H, m), 2.10-2.18(1H, m), 2.66-2.77(1H, m), 2.82-2.91(1H, m), 3.81(3H, s), 6.73-6.78(1H, m), 6.88-6.92(2H, m), 7.21-7.29(1H, m) (solvent: CDCl3)		
855	oil			219
859			350[M + 1] 274	200 208 254
863	192-194	1.39(t, J = 7.2 Hz, 3H), 1.42(s, 3H), 1.71-1.79(m, 1H), 2.02-2.10(m, 1H), 2.55-2.62(m, 1H), 2.88-2.96(m, 1H), 4.47(q, J = 7.2 Hz, 2H), 5.70-6.20(br s, 2H), 7.11(d, J = 8.0 Hz, 1H), 7.29(t, J = 8.0 Hz, 1H), 7.75(d, J = 8.0 Hz, 1H), 7.80(br s, 1H), 8.38(d, J = 1.2 Hz, 1H), 8.87(d, J = 1.2 Hz, 1H), 10.34(s, 1H) (solvent: CDCl3)		
866				293.5
869		1.65 (s, 3H), 1.90-2.01 (m, 3H), 2.32 (br, 1H), 2.80 (td, J = 12.0, 3.6 Hz, 1H), 2.85 (t, J = 8.0 Hz, 2H), 2.92 (ddd, J = 12.0, 5.6, 3.6, 1H), 3.75 (t, J = 8.0 Hz, 2H), 7.11 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.70 (t, J = 2.0 Hz, 1H), 7.73-7.76 (m, 2H), 8.22 (d, J = 7.6 Hz, 1H), 8.48 (d, J = 2.0 Hz, 1H), 10.00 (s, 1H) (solvent: CDCl3)		
871	212-213			

TABLE 153

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
875	oil			222, 271
876	oil			222
878	oil			211
881	141-144			
887				262.7
892	251 (dec.)			
893		δ in d12-DMSO: 1.70(3H, s), 2.10-2.04(1H, m), 2.69-2.59(2H, m), 3.20-3.17(1H, m), 6.80(1H, brs), 7.26-7.20(1H, m), 7.88-7.81(3H, m), 10.35(1H, s)13.53(1H, brs)		
895			378[M + 1] 302	202 208 216 221 265
896	amorphous			219, 264
897	212-214			
900	205-207	1.61 (s, 3H), 1.91 (ddd, J = 14.0, 10.8, 4.0 Hz, 1H), 2.23 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.77 (ddd, J = 12.4, 10.8, 3.6 Hz, 1H), 2.92 (ddd, J = 12.4, 6.4, 4.0 Hz, 1H), 7.15 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.65 (t, J = 2.0 Hz, 1H), 7.79 (ddd,		

TABLE 153-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
		J = 8.0, 2.0, 0.8 Hz, 1H), 8.99 (s, 2H), 9.78 (s, 1H) (solvent: CDCl3)		
906				212.2 273.4 350.5
908		δ in d15-DMSO: 1.66(3H, s), 2.11-2.05(1H, m), 2.37(3H, s), 2.63-2.54(2H, m), 3.16-3.11(1H, m), 3.16(3H, s), 7.08-6.96(3H, m), 7.49-7.41(3H, m), 7.85-7.81(2H, m), 10.52(1H, s)11.69(1H, s)		
910	oil			211, 276
916	131-132			
926		1.89(3H, s), 2.15(1H, m), 2.71-2.82(2H, m), 2.96(1H, m), 3.04(3H, d, J = 4.9), 7.35(1H, dd, J = 8.7, 1.8), 7.50-7.55(2H, m), 7.74(1H, s), 7.82-7.90(3H, s), 10.40(1H, br), 11.36(1H, Br) (solvent: $CDCl_3$)		
928		1.20(t, J = 7.6 Hz, 3H), 1.53(br s, 3H), 1.82-1.97(m, 1H), 2.39(s, 3H), 2.61(q, J = 7.6 Hz, 2H), 2.99-3.07(m, 1H), 6.93(br s, 1H), 7.33(d, J = 8.4 Hz, 2H), 7.54-7.58(m, 2H), 7.87(d, J = 8.4 Hz, 2H), 10.13(s, 1H) (solvent: CDCl3)		
930	132.1-134.4		328[M + 1]	
931				299
933	amorphous			212, 259

TABLE 154

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
935	161-165	1.62 (s, 3H), 1.91 (ddd, J = 14.0, 10.4, 4.0 Hz, 1H), 2.24 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.80 (ddd, J = 12.0, 10.4, 3.6 Hz, 1H), 2.93 (ddd, J = 12.0, 6.4, 4.0 Hz, 1H), 7.15 (ddd, J = 8.0, 2.0, 1.2 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.66 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 7.75 (t, J = 2.0 Hz, 1H), 7.80-7.84 (m, 2H), 7.93 (ddd, J = 8.0, 2.0, 1.2 Hz), 8.21 (d, J = 8.4 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 8.41 (d, J = 8.0 Hz, 1H), 10.25 (s, 1H) (solvent: CDCl3)		
936	169-170			
939		δ in d6-DMSO: 1.72(3H, s), 2.11-2.05(1H, m), 2.70-2.60(2H, m), 3.21-3.18(1H, m), 7.20(1H, d, J = 9.2 Hz), 7.28(1H, q, J = 11.6, 9.2 Hz), 8.56-7.54(2H, m), 7.69(1H, s), 7.90-7.85(2H, m), 10.69(1H, s), 12.17(1H, brs)		
941				220
944	amorphous			219, 256
946		1.61 (s, 3H), 1.91 (ddd, J = 14.0, 10.8, 3.6 Hz, 1H), 2.26 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.77 (ddd, J = 12.4, 10.8, 3.6 Hz, 1H),, 2.92 (ddd, J = 12.4, 6.4, 3.6 Hz, 1H), 7.13 (ddd, J = 8.0, 2.0, 1.2 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.61 (t, J = 2.0 Hz, 1H), 7.72 (ddd, J = 8.0, 2.0, 1.2 Hz, 1H), 7.91 (d, J = 2.4 Hz, 1H), 8.49 (d, J = 2.4 Hz, 1H), 9.75 (s, 1H)(solvent: CDCl3)		
947				215.7 276.9
960				261.5
964	185-187			
966	oil			216
968	107-109			
970		1.57 (s, 3H), 1.78-1.89 (m, 1H), 2.10-2.19 (m, 1H), 2.69 (ddd, J = 11.9, 10.8, 3.5 Hz, 1H), 2.83-2.91 (m, 1H), 7.15-7.35 (m, 5H) (solvent: CDCl3)		
971		(DMSO) 1.49(3H, s), 1.73-1.86(1H, m), 2.16-2.30(1H, m), 2.54-2.65(1H, m), 2.92-3.03(1H, m), 5.86(2H, s), 7.04-7.18(2H, m), 7.38-7.50(3H, m), 7.66-7.78(2H, m), 10.35(1H, s), 11.84(1H, s)		
972		1.51 (3H, s) 1.91-1.95 (1H, m) 2.37 (3H, s) 3.00-3.05 (1H, m) 7.24 (1H s) 7.33 (2H, d J = 9.0 Hz) 7.66 (1H, s) 7.85 (2H, d J = 9.0 Hz) 8.03 (1H, s) 10.37 (1H, s) (solvent: DMSO-d6)		
974	amorphous			219
978	oil			222

TABLE 154-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
984				255.7 318.4
990	126-129			
994	130-131			

TABLE 155

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
998	amorphous			229, 290
1005	191-193			
1006	88-90	2.42-2.47(2H, m), 2.80-2.86(2H, m), 7.78(6H, s), 6.83(4H, d, J = 8.9 Hz), 7.22(4H, d, J = 8.9 Hz) (solvent: CDCl3)		
1008	125-126			
1010	90-91			
1014	206-210			
1020				216.9 245.1
1028	105-106			
1034				212.2 286.4
1035	247-251 (dec.)			
1037	amorphous			224, 272
1039	amorphous			217 249
1043	277-281			
1044		(DMSO) 1.12(3H, s), 1.60(2H, d, J = 6.2 Hz), 1.73(2H, d, J = 8.6 Hz), 2.65-2.90(2H, m), 2.93-3.13(2H, m), 5.55(1H, s), 7.34-7.52(3H, m), 7.68(1H, s), 7.79-7.90(3H, m)		
1052		1.75(s, 3H), 2.12-2.21(m, 1H), 2.40(s, 3H), 2.65-2.73(m, 2H), 3.17-3.23(m, 1H), 7.37(d, J = 8.4 Hz, 2H), 7.40-7.44(m, 1H), 7.77(br s, 1H), 7.92-7.99(m, 5H), 8.47(br s, 1H), 8.70(d, J = 4.8 Hz, 1H), 10.37(s, 1H), 10.41(s, 1H) (solvent: CDCl3)		
1055	169-170	1.56(3H, s), 1.78-1.89(1H, m), 2.04-2.15(1H, m), 2.68-2.79(1H, m), 2.86-2.95(1H, m), 4.32(2H, br), 6.94-7.02(4H, m), 7.05-7.12(1H, m), 7.25-7.37(4H, m)(solvent: CDCl3)		
1056				219
1059	262-287			
1061				216
1062	136-137	1.53(3H, s), 1.76-1.88(1H, m), 2.03-2.13(1H, m), 2.63-2.73(1H, m), 2.85-2.94(1H, m), 4.35(2H, br), 7.23-7.32(4H, m) (solvent: CDCl3)		
1064	84-85	1.52(3H, s), 1.73-1.89(1H, m), 1.97-2.07(1H, m), 2.64-2.81(1H, m), 2.82-2.91(1H, m),2.87(3H, s), 3.77(3H, s), 4.10(1H, brs), 6.84(2H, d, J = 8.9 Hz), 7.28(2H, d, J = 8.6 Hz) (solvent: CDCl3)		
1067	162-165			
1068	132-134			230
1069	194-196			
1074			324[M + 1] 248	200 207
1076	amorphous			217

TABLE 156

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1084	146-149			
1087				311.2
1088	amorphous	1.55(3H, s), 1.83(1H, ddd, J = 13.9, 10.5, 3.7), 2.09(1H, ddd, J = 13.9, 6.6, 3.6), 2.67(1H, ddd, J = 12.3, 10.5, 3.6), 2.88(1H, ddd, J = 12.3, 6.6, 3.7), 4.48(2H, d, J = 6.0), 4.91(1H, br), 6.33(1H, dd, J = 8.8, 0.8), 7.19(1H, d, J = 7.3, 7.23-7.30(2H, m),		229 318

TABLE 156-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
		7.35(1H, dd, J = 8.8, 2.8), 8.05(1H, dd, J = 2.8, 0.8) (solvent: CDCl3)		
1094				216, 322
1100	278 (dec.)			
1107	oil	1.58(3H, s), 1.90(1H, ddd, J = 13.9, 10.1, 3.7), 2.14(1H, ddd, J = 13.9, 6.8, 3.6), 2.69(1H, ddd, J = 12.2, 10.1, 3.6), 2.94(1H, ddd, J = 12.2, 6.8, 3.7), 3.81(3H, s), 4.62(2H, s), 6.90(2H, d, J = 8.8), 7.30(2H, d, J = 8.8), 7.43(1H, t, J = 7.4), 7.57(1H, ddd, J = 7,4, 1.6, 1.2), 7.81 (1H, ddd, J = 7.6, 1.6, 1.2), 7.95(1H, t, J = 1.6) (solvent : CDCl3)		226 284
1109	134-140			
1110	109-110			
1111	118-119			
1114	121-124			
1115	187-170	1.63 (s, 3H), 1.93 (ddd, J = 14.0, 10.4, 4.0 Hz, 1H), 2.24 (ddd, J = 14.0, 6.4, 3.6 Hz, 1H), 2.81 (ddd, J = 12.4, 10.4, 3.6 Hz, 1H), 2.96 (ddd, J = 12.4, 6.4, 4.0 Hz, 1H), 4.49 (br, 2 H), 7.19 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.74 (t, J = 2.0 Hz, 1H), 7.84 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.88-7.95 (m, 2H), 8.22-8.26 (m, 2H), 9.80 (s, 1H), 9.89 (s, 1H) (solvent: CDCl3)		
1116	oil			220, 255, 307
1119	153-157			
1120	213-214			
1124	169-172			225
1125	195-198			222 256 289
1131	189-191			
1132	175-180 (dec)			
1133	amorphous			219, 292
1135	255-260 (dec.)			
1139	140-141			
1140	oil			218
1142	182-186 (dec.)			

TABLE 157

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1147				214.5 275.7
1150				221.6 279.3
1153	156-159			
1160		1.64 (3H, s) 2.02-2.12 (1H, m) 2.54-2.63 (1H, m) 3.11-3.16 (1H, m) 7.28 (1H, s) 7.70 (1H, dd J = 8.1 Hz) 7.85 (1H, s) 8.04-8.17 (2H, m) 8.28 (1H s) 8.74 (1H d J = 5.1 Hz) 10.81 (1H, s) 10.96 (1H, s) (solvent: DMSO-d6)		
1161	192-193			
1166	290-295		444[M + 3] 442[M + 1] 368 366	
1172		1.55 (3H, s) 1.94-2.03 (1H, m) 2.18-2.27 (1H, m) 2.32 (3H, s) 3.03-3.07 (1H, m) 7.05 (1H, s) 7.09 (1H, s) 7.14 (1H, s) 7.37 (2H, d J = 9.0 Hz) 7.66 (2H, d, J = 9.0 Hz) 10.65 (1H, s) 10.70 (1H, s) (solvent: DMSO-d6)		
1181	194-195	1.60(3H, s), 1.81-1.93(1H, m), 2.13-2.22(1H, m), 2.70-2.81(1H, m), 2.86-2.96(1H, m), 4.36(2H, br), 7.29-7.46(5H, m), 7.53-7.61(4H, m) (solvent: CDCl3)		
1184	149-150			
1185				225.1 280.4

TABLE 157-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1193	182-183			
1194			344[M + 1] 268	209 214 261
1197	250-255 (dec.)			
1199	274-283			
1205	oil			E 213, 273 Z 219, 275
1207	106-108			
1211		1.77 (s, 3H), 1.98-2.54 (m, 2H), 2.81 (s, 3H), 2.81-2.94 (m, 2H), 3.93 (s, 3H), 7.03 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.08 (d, J = 2.4 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.63 (t, J = 2.0 Hz, 1H), 7.69 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.14 (d, J = 2.4 Hz, 1H), 10.13 (s, 1H) (solvent: CDCl3)		
1213			406[M + 1] 330	20 209 213

TABLE 158

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1215	amorphous	1.64 (s, 3H), 2.07 (ddd, J = 14.1, 11.5, 3.8 Hz, 1H), 2.17 (s, 3H), 2.39 (ddd, J = 14.1, 5.3, 3.5 Hz, 1H), 2.72 (ddd, J = 12.6, 11.5, 3.5 Hz, 1H), 2.80 (ddd, J = 12.6, 5.3, 3.8 Hz, 1H), 3.21 (t, J = 8.9 Hz, 2H), 4.58 (t, J = 8.9 Hz, 2H), 6.76 (d, J = 8.4 Hz, 1H), 6.97-7.02 (m, 1H), 7.08-7.11 (m, 1H) (solvent: CDCl3)		
1216				305.3
1217	263-266			
1221	amorphous			220, 253
1223				226.3 280.4
1224		δ in d11-DMSO: 1.46(3H, s), 1.83-1.77(1H, m), 2.18-2.15(1H, m), 2.61-2.56(1H, m), 2.99-2.95(1H, m), 7.08(1H, q, J = 12.0, 8.4 Hz), 7.72-7.66(2H, m), 7.79(2H, d, J = 9.2)9.67(1H, s)		
1228	oil			224
1230	232-234			
1240				216.9 285.2
1241	194-195			
1242		δ in d21-DMSO: 1.41(3H, m), 1.75-1.68(1H, m), 2.04-1.99(1H, m), 2.61-2.56(1H, m), 2.89(4H, s), 5.75(2H, brs), 7.07(1H, d, J = 4.0 Hz), 7.25(1H, t, J = 8.0 Hz), 7.72(1H, d, J = 8.0 Hz), 7.75(1H, s), 7.83(1H, brs), 7.96(1H, s), 8.67(1H, s), 9.96(1H, s)		
1243	amorphous	1.58(3H, s), 2.00(1H, ddd, J = 14.3, 11.5, 3.1), 2.53(1H, m), 2.56(1H, m), 3.07(1H, dt, J = 12.5, 3.1), 4.26(2H, s), 6.47-6.56(3H, m), 7.07-7.15(1H, m), 7.12(2H, t, J = 8.8), 7.39(2H, dd, J = 8.8, 5.6), 8.76(2H, br) (solvent: DMSO-d6)		223 299
1244	268-288	1.68 (s, 3H), 2.11 (ddd, J = 15.2, 12.0, 4.0 Hz, 1H), 2.57-2.64 (m, 2H), 3.16 (dt, J = 12.0, 4.0 Hz, 1H), 7.13 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.89 (t, J = 2.0 Hz, 1H), 7.97 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.52 (dd, J = 8.0, 2.4 Hz, 1H), 9.12 (d, J = 2.4 Hz, 1H), 10.68 (s, 1H), 10.92 (s, 1H) (solvent: DMSO-d6)		219 288
1245	oil			286
1247				211
1255				242.7
1257	amorphous			211
1258			352[M + 1]	228 276 301
1261	179-180			
1262	278-281			

TABLE 159

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1263		1H-NMR(δ in d6-DMSO): 1.41(3H, s), 1.65-1.77(1H, m), 1.95-2.07(1H, m), 2.54-2.63(1H, m), 2.84-2.94(1H, m), 3.39-3.46(2H, m), 3.53-3.61(2H, m), 4.83(1H, t, J = 5.4 Hz), 5.79(2H, bs), 7.07(1H, d, J = 7.5 Hz), 7.25(1H, t, J = 7.8 Hz), 7.73(1H, d, J = 7.8 Hz), 7.76(1H, m), 7.87-7.93(1H, m), 8.02(1H, d, J = 1.2 Hz), 8.63(1H, d, J = 1.2 Hz), 9.97(1H, s).	387[M + 1]	
1264		1H-NMR(δ in d6-DMSO): 1.41(3H, s), 1.65-1.77(1H, m), 1.95-2.07(1H, m), 2.53-2.63(1H, m), 2.84-2.95(1H, m), 3.73(8H, s), 5.79(2H, bs), 7.09(1H, d, J = 7.8 Hz), 7.26(1H, t, J = 7.8 Hz), 7.72(1H, d, J = 7.8 Hz), 7.75-7.78(1H, m), 8.34(1H, d, J = 1.2 Hz), 8.76(1H, d, J = 1.2 Hz), 10.08(1H, bs).	413[M + 1]	
1265		1H-NMR (DMSO-d6) δ: 1.42 (3H, s), 1.70-1.76 (1H, m), 2.02-2.05 (1H, m), 2.56-2.59 (1H, m), 2.87-2.93 (2H, m), 7.07 (1H, d, J = 7.6 Hz), 7.23-7.26 (3H, m), 7.72-7.74 (2H, m), 7.93 (1H, s), 8.60 (1H, s), 9.99 (1H, s).		
1266		1H-NMR(δ in d6-DMSO): 1.43(3H, s), 1.70-1.81(1H, m), 1.97-2.10(1H, m), 2.55-2.64(1H, m), 2.89-2.95(1H, m), 5.84(2H, bs), 7.17(1H, d, J = 7.8 Hz), 7.33(1H, t, J = 7.8 Hz), 9.98(1H, d, J = 1.2 Hz), 10.01(1H, d, J = 1.2 Hz), 10.74(1H, bs).	369[M + 1]	
1267		1H-NMR (CDCl3) δ: 1.82-1.91 (1H, m), 2.04 (3H, s), 2.22 (1H, ddd, J = 13.8, 5.2, 3.6 Hz), 2.67 (1H, dt, J = 16.7, 5.8 Hz), 2.80 (1H, dt, J = 12.4, 4.7 Hz), 6.95 (2H, d, J = 8.1 Hz), 7.06 (2H, td, J = 7.8, 1.2 Hz), 7.18 (1H, td, J = 7.6, 1.1 Hz), 7.27 (1H, d, J = 1.7 Hz), 7.32 (1H, d, J = 7.9 Hz), 7.42-7.44 (2H, m), 7.80 (1H, dd, J = 8.0, 1.9 Hz).	338[M + 1]	
1268		1H-NMR (CDCl3) δ: 1.62 (3H, s), 1.89 (1H, t, J = 12.3 Hz), 2.27-2.30 (1H, m), 2.69-2.76 (1H, m), 2.85-2.88 (1H, m), 7.11 (1H, dd, J = 11.4, 7.7 Hz), 7.30-7.53 (2H, m), 7.63 (1H, s), 7.71 (1H, d, J = 6.9 Hz).	327[M + 1]	
1269		1H-NMR (DMSO-d6) δ: 1.40 (3H, s), 1.70-1.73 (1H, m), 1.99-2.02 (1H, m), 2.57-2.60 (1H, m), 2.88-2.90 (1H, m), 3.29 (3H, s), 3.52 (4H, s), 5.75 (2H, br s), 7.07 (1H, d, J = 7.6 Hz), 7.25 (1H, t, J = 7.7 Hz), 7.72 (1H, d, J = 8.3 Hz), 7.75 (1H, s), 7.92 (1H, br s), 8.03 (1H, s), 8.64 (1H, s), 9.96 (1H, s).		
1271		1H-NMR(δ in d6-DMSO): 1.41(3H, s), 1.65-1.75(1H, m), 1.99-2.06(5H, m), 2.52-2.61(1H, m), 2.85-2.93(1H, m), 3.55(4H, t, J = 6.6 Hz), 5.79(2H, bs), 7.05(1H, d, J = 7.8 Hz), 7.25(1H, t, J = 7.8 Hz), 7.70-7.75(1H, m), 7.73-7.77(1H, m), 7.97(1H, d, J = 1.2 Hz), 8.72(1H, d, J = 1.2 Hz), 10.00(1H, s).	397[M + 1]	

TABLE 160

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1272		(CDCl3) 1.61(3H, s), 1.85-1.96(1H, m), 2.17-2.27(1H, m), 2.69-2.79(1H, m), 2.87-2.97(1H, m), 7.17 (1H, d, J = 8.1 Hz), 7.38 (1H, t, J = 8.1 Hz), 7.48-7.74(5H, m), 8.40(2H, d, J = 7.5 Hz)		
1273		1H-NMR (CDCl3) δ: 1.58 (3H, s), 1.89 (1H, t, J = 11.2 Hz), 2.27 (1H, s), 2.75-2.82 (2H, m), 6.61 (1H, dd, J = 20.3, 8.4 Hz), 7.10 (1H, d, J = 7.2 Hz), 7.37 (1H, dd, J = 15.0, 8.8 Hz), 7.90 (1H, d, J = 7.6 Hz), 8.10 (1H, d, J = 3.2 Hz), 9.37 (1H, d, J = 4.9 Hz), 9.69 (1H, s).	395[M + 1]	
1274		1H-NMR (CDCl3) δ: 1.61 (3H, s), 1.84-1.93 (1H, m), 2.30 (1H, t, J = 13.1 Hz), 2.77-2.86 (2H, m), 6.64 (1H, dd, J = 20.6, 8.6 Hz), 7.13 (1H, d, J = 7.9 Hz), 7.38-7.43 (1H, m), 7.93 (1H, d, J = 8.1 Hz), 8.13 (1H, s), 9.40 (1H, d, J = 4.9 Hz), 9.72 (1H, s).	327[M + 1]	
1275		1H-NMR (DMSO-d6) δ: 1.40 (3H, s), 1.70-1.72 (1H, m), 2.01-2.04 (1H, m), 2.18 (6H, s), 2.44 (2H, t, J = 6.3 Hz), 2.56-2.59 (1H, m), 2.86-2.92 (1H, m), 7.06 (1H, d, J = 7.6 Hz), 7.25 (1H, t, J = 7.7 Hz), 7.71-7.73 (3H, m), 8.02 (1H, s), 8.64 (1H, s), 9.95 (1H, s).		

TABLE 160-continued

No.	mp (° C.)	1H-NMR(δ)	MS (m/z)	UV (λ max: nm)
1276		1H-NMR (DMSO-d6) δ: 1.70-1.73 (1H, m), 1.99-2.02 (1H, m), 2.57-2.60 (1H, m), 2.88-2.91 (1H, m), 3.04 (3H, s), 3.43 (3H, t, J = 6.3 Hz), 3.79-3.81 (2H, m), 5.75 (3H, br s), 7.08 (1H, d, J = 7.3 Hz), 7.26 (1H, t, J = 7.8 Hz), 7.72 (1H, d, J = 7.8 Hz), 7.76 (1H, s), 8.04 (1H, s), 8.09 (1H, br s), 8.70 (1H, s), 10.01 (1H, s).		
1279		1H-NMR (CDCl3) δ: 1.73 (3H, s), 2.04 (1H, dt, J = 18.2, 6.5 Hz), 2.45 (1H, d, J = 13.6 Hz), 2.78 (2H, t, J = 11.8 Hz), 2.89 (2H, t, J = 11.5 Hz), 6.60 (1H, s), 6.99 (1H, d, J = 8.2 Hz), 7.34 (1H, t, J = 8.0 Hz), 7.48 (1H, s), 7.70 (1H, d, J = 8.2 Hz).	328[M + 1]	
1280		1H-NMR(δ in d6-DMSO): 1.42(3H, s), 1.68-1.82(1H, m), 2.02-2.09(1H, m), 2.23(3H, s), 2.43(4H, t, J = 5.1 Hz), 2.53-2.61(1H, m), 2.87-2.95(1H, m), 3.73(4H, t, J = 5.1 Hz), 6.01 (2H, bs), 7.07(1H, d, J = 7.8 Hz), 7.26(1H, t, J = 7.8 Hz), 7.73(1H, d, J = 7.8 Hz), 7.73-7.78(1H, m), 8.33(1H, d, J = 1.2 Hz), 8.72(1H, d, J = 1.2 Hz), 10.06(1H, s).	426[M + 1]	
1281		1H-NMR(δ in d6-DMSO): 1.40(3H, s), 1.30-1.50(2H, m), 1.69-1.76(1H, m), 1.82-1.88(2H, m), 2.01-2.07(1H, m), 2.52-2.61(1H, m), 2.86-2.94(1H, m), 3.76-3.83(1H, m), 4.10-4.18(2H, m), 4.82(1H, d, J = 4.2 Hz), 5.91(2H, bs), 7.07(1H, d, J = 7.8 Hz), 7.26(1H, t, J = 7.8 Hz), 7.70-7.77(2H, m), 8.33(1H, d, J = 1.2 Hz), 8.70(1H, d, J = 1.2 Hz), 10.02(1H, s).	427[M + 1]	

TABLE 161

化合物番号	MS(m/z)
2	336[M + 1]
7	394[M + 1]
10	431[M + 3]
	429[M + 1]
11	356[M + 1]
12	354[M + 1]
13	363[M + 3]
	361[M + 1]
14	394[M + 1]
15	409[M + 1]
16	425[M + 1]
17	374[M + 1]
19	362[M + 3]
	360[M + 1]
20	438[M + 1]
21	380[M + 3]
	378[M + 1]
22	380[M + 3]
	378[M + 1]
25	354[M + 1]
27	338[M + 1]
28	356[M + 1]
29	372[M + 1]
31	378[M + 1]
32	417[M + 1]
34	358[M + 1]
35	398[M + 3]
	396[M + 1]
36	370[M + 1]
40	416[M + 1]
	340
41	414[M + 1]
44	362[M + 3]
	360[M + 1]
45	365[M + 1]
46	362[M + 1]
47	416[M + 3]
	414[M + 1]
49	394[M + 3]
	392[M + 1]
50	292[M + 1]
51	388[M + 1]
52	360[M + 1]

TABLE 161-continued

化合物番号	MS(m/z)
	284
53	380[M + 1]
54	332[M + 1]
55	412[M + 3]
	410[M + 1]
56	397[M + 1]
	395[M + 1]
59	412[M + 1]
60	422[M + 1]
	420[M + 1]
61	394[M + 1]
63	366[M + 1]
64	441[M + 1]
	365
65	384[M + 1]
66	398[M + 1]
67	386[M + 1]
	310
68	376[M + 1]
70	372[M + 1]
72	330[M + 1]
74	322[M + 1]
75	412[M + 1]
76	363[M + 3]
	361[M + 1]
79	310[M + 1]
81	386[M + 1]
82	306[M + 1]
83	336[M + 1]
84	380[M + 1]
87	415[M + 1]
88	426[M + 1]
89	370[M + 1]
90	354[M + 1]
92	417[M + 1]
93	407[M + 1]
94	350[M + 1]
95	406[M + 3]
	404[M + 1]
98	398[M + 3]
	396[M + 1]
100	332[M + 1]
102	424[M + 3]

TABLE 161-continued

化合物番号	MS(m/z)
	422[M + 1]
103	444[M + 1]
105	424[M + 1]
	348
106	490[M + 1]
	414
107	414[M + 3]
	412[M + 1]
108	332[M + 1]
109	412[M + 1]
110	404[M + 1]
111	469[M + 1]
	393
112	377[M + 1]
116	408[M + 1]
117	413[M + 1]
118	372[M + 1]
119	424[M + 1]
122	338[M + 1]
124	471[M + 1]
131	412[M + 3]
	410[M + 1]
133	404[M + 1]
135	416[M + 1]
136	380[M + 1]
137	327[M + 1]
138	394[M + 1]
140	456[M + 1]
142	446[M + 1]
143	399[M + 1]
144	432[M + 1]
145	394[M + 3]
	392[M + 1]
146	433[M + 3]
	431[M + 1]
147	324[M + 1]
150	418[M + 1]
151	458[M + 3]
	456[M + 1]
152	371[M + 1]
153	398[M + 1]
154	401[M + 1]
155	322[M + 1]
156	332[M + 3]
	330[M + 1]
158	394[M + 1]

TABLE 162

160	427[M + 1]
162	416[M + 3]
	414[M + 1]
167	392[M + 3]
	390[M + 1]
168	380[M + 3]
	378[M + 1]
169	346[M + 1]
170	356[M + 1]
171	334[M + 1]
172	376[M + 3]
	374[M + 1]
173	424[M + 3]
	422[M + 1]
174	369[M + 1]
175	410[M + 1]
177	357[M + 1]
179	334[M + 1]
180	426[M + 1]
182	396[M + 3]
	394[M + 1]
183	372[M + 1]
184	346[M + 1]
185	330[M + 1]
186	393[M + 3]
	391[M + 1]

TABLE 162-continued

187	374[M + 1]
188	423[M + 1]
190	278[M + 1]
191	448[M + 1]
192	436[M + 3]
	434[M + 1]
194	384[M + 1]
195	369[M + 1]
197	382[M + 1]
198	355[M + 1]
199	361[M + 1]
200	356[M + 1]
	280
201	452[M + 1]
203	397[M + 1]
205	427[M + 1]
206	386[M + 1]
	310
207	384[M + 1]
208	386[M + 3]
	384[M + 1]
209	371[M + 1]
210	366[M + 1]
211	442[M + 1]
	366
212	345[M + 1]
215	425[M + 3]
	423[M + 1]
217	362[M + 1]
218	322[M + 1]
219	347[M + 1]
221	444[M + 1]
222	329[M + 1]
223	413[M + 1]
225	402[M + 1]
226	390[M + 1]
228	383[M + 1]
229	366[M + 1]
230	368[M + 1]
231	336[M + 1]
234	378[M + 1]
236	392[M + 1]
237	348[M + 1]
239	384[M + 1]
240	341[M + 1]
242	446[M + 1]
245	374[M + 1]
246	390[M + 1]
	314
247	374[M + 1]
248	370[M + 1]
249	336[M + 1]
250	366[M + 1]
252	401[M + 1]
253	397[M + 1]
254	434[M + 1]
257	321[M + 1]
258	398[M + 1]
260	440[M + 1]
261	308[M + 1]
262	466[M + 3]
	464[M + 1]
264	336[M + 1]
265	435[M + 1]
266	432[M + 1]
	430[M + 1]
269	372[M + 1]
	296
270	338[M + 1]
272	349[M + 1]
273	406[M + 3]
	404[M + 1]
274	380[M + 1]
276	398[M + 3]
	396[M + 1]
278	404[M + 1]
280	433[M + 3]
	431[M + 1]
283	322[M + 1]
285	340[M + 1]

TABLE 162-continued

286	433[M + 3]
	431[M + 1]
287	440[M + 1]
288	354[M + 1]
289	341[M + 1]
290	363[M + 3]
	361[M + 1]
291	317[M + 1]
292	426[M + 1]
294	424[M + 3]
	422[M + 1]
295	394[M + 3]
	392[M + 1]
296	389[M + 1]
297	448[M + 3]
	446[M + 1]
298	363[M + 3]
	361[M + 1]
300	356[M + 1]
303	366[M + 1]
304	402[M + 1]
305	407[M + 3]
	405[M + 1]
310	411[M + 1]

TABLE 163

311	388[M + 1]
312	428[M + 1]
313	453[M + 1]
314	368[M + 1]
315	322[M + 1]
316	386[M + 1]
317	328[M + 1]
318	362[M + 1]
320	327[M + 1]
321	392[M + 1]
322	404[M + 1]
	328
323	394[M + 1]
324	384[M + 1]
325	399[M + 1]
326	440[M + 1]
	364
327	314[M + 1]
328	384[M + 1]
331	360[M + 1]
334	412[M + 1]
335	316[M + 1]
336	356[M + 1]
337	428[M + 1]
338	466[M + 3]
	464[M + 1]
340	344[M + 1]
343	399[M + 1]
345	412[M + 1]
346	384[M + 1]
347	430[M + 1]
348	341[M + 1]
349	335[M + 1]
350	412[M + 1]
351	322[M + 1]
352	327[M + 1]
355	397[M + 1]
362	366[M + 1]
363	376[M + 3]
	374[M + 1]
365	366[M + 1]
366	409[M + 1]
368	384[M + 1]
369	396[M + 3]
	394[M + 1]
371	398[M + 3]
	396[M + 1]
372	348[M + 1]
373	358[M + 1]
374	364[M + 1]

TABLE 163-continued

376	412[M + 1]
377	425[M + 1]
378	380[M + 3]
	378[M + 1]
379	377[M + 1]
381	409[M + 1]
382	340[M + 1]
384	388[M + 1]
385	384[M + 1]
386	352[M + 1]
387	376[M + 1]
388	440[M + 1]
390	407[M + 1]
	331
391	362[M + 1]
392	390[M + 1]
394	363[M + 3]
	361[M + 1]
397	460[M + 3]
	458[M + 1]
398	408[M + 1]
399	372[M + 1]
400	374[M + 1]
402	372[M + 1]
	296
403	436[M + 1]
404	376[M + 3]
	374[M + 1]
407	449[M + 3]
	447[M + 1]
412	410[M + 1]
414	331[M + 1]
416	282[M + 1]
418	322[M + 1]
419	420[M + 3]
	418[M + 1]
420	332[M + 1]
421	388[M + 3]
	386[M + 1]
423	412[M + 3]
	410[M + 1]
424	370[M + 1]
425	380[M + 3]
	378[M + 1]
428	350[M + 1]
431	391[M + 1]
433	454[M + 3]
	452[M + 1]
434	448[M + 3]
	446[M + 1]
435	431[M + 3]
	429[M + 1]
437	382[M + 1]
438	400[M + 1]
	324
439	380[M + 1]
440	358[M + 1]
442	394[M + 1]
	318
447	370[M + 1]
449	336[M + 1]
450	455[M + 1]
451	390[M + 3]
	388[M + 1]
453	358[M + 1]
454	407[M + 1]
	331
455	296[M + 1]
458	382[M + 1]
459	392[M + 1]
460	431[M + 1]
461	369[M + 1]
462	381[M + 3]
	379[M + 1]
463	440[M + 3]
	438[M + 1]
464	338[M + 1]
	262
467	387[M + 1]
468	439[M + 1]

TABLE 163-continued

	363
469	360[M + 1]
471	363[M + 3]
	361[M + 1]

TABLE 164

472	376[M + 1]
473	414[M + 1]
474	334[M + 1]
475	317[M + 1]
476	324[M + 1]
477	437[M + 1]
478	379[M + 1]
479	394[M + 1]
480	370[M + 1]
481	431[M + 1]
484	314[M + 3]
	312[M + 1]
485	448[M + 1]
486	350[M + 1]
487	338[M + 1]
488	306[M + 1]
489	335[M + 1]
492	380[M + 1]
495	334[M + 1]
499	370[M + 1]
503	412[M + 1]
505	363[M + 3]
	361[M + 1]
506	386[M + 1]
507	400[M + 1]
508	372[M + 1]
509	414[M + 1]
	338
510	374[M + 1]
512	320[M + 1]
513	420[M + 3]
	418[M + 1]
514	372[M + 1]
517	369[M + 1]
518	376[M + 1]
519	411[M + 1]
520	395[M + 1]
521	372[M + 1]
522	390[M + 1]
523	414[M + 1]
524	341[M + 1]
526	426[M + 1]
527	381[M + 3]
	379[M + 1]
529	320[M + 1]
530	390[M + 3]
	388[M + 1]
531	410[M + 1]
535	356[M + 1]
536	372[M + 1]
537	377[M + 1]
538	406[M + 1]
539	411[M + 1]
540	354[M + 1]
541	342[M + 1]
542	361[M + 1]
543	344[M + 1]
544	412[M + 1]
545	366[M + 1]
546	383[M + 1]
547	430[M + 1]
	428[M + 1]
548	427[M + 1]
550	340[M + 1]
552	400[M + 1]
553	304[M + 1]
555	383[M + 1]
557	304[M + 1]
562	374[M + 1]
563	366[M + 1]

TABLE 164-continued

564	395[M + 1]
565	336[M + 1]
566	427[M + 1]
	351
568	362[M + 3]
	360[M + 1]
569	356[M + 1]
571	356[M + 1]
572	473[M + 3]
	471[M + 1]
574	381[M + 3]
	379[M + 1]
575	360[M + 1]
576	384[M + 1]
578	344[M + 1]
579	370[M + 1]
580	347[M + 1]
581	409[M + 1]
582	334[M + 1]
583	392[M + 1]
585	358[M + 1]
587	348[M + 1]
589	407[M + 3]
	405[M + 3]
590	410[M + 3]
	408[M + 1]
591	460[M + 1]
	384
592	380[M + 3]
	378[M + 1]
594	390[M + 1]
598	394[M + 1]
599	377[M + 1]
603	398[M + 3]
	396[M + 1]
604	395[M + 1]
606	358[M + 1]
607	362[M + 1]
609	413[M + 1]
610	409[M + 1]
612	385[M + 1]
614	322[M + 1]
615	441[M + 1]
616	346[M + 3]
	344[M + 1]
	270
	268
617	406[M + 3]
	404[M + 1]
619	404[M + 1]
621	366[M + 1]
623	422[M + 1]
	346
624	370[M + 1]
626	402[M + 1]
627	398[M + 3]
	396[M + 1]
628	413[M + 1]
631	370[M + 1]
632	414[M + 3]
	412[M + 1]

TABLE 165

633	322[M + 1]
635	420[M + 1]
638	408[M + 1]
639	386[M + 1]
	310
640	370[M + 1]
641	437[M + 1]
642	380[M + 1]
646	395[M + 1]
647	334[M + 1]
648	403[M + 1]
650	370[M + 1]
655	362[M + 1]

TABLE 165-continued

656	308[M + 1]
658	430[M + 1]
659	340[M + 3]
	388[M + 1]
662	330[M + 1]
663	334[M + 1]
665	316[M + 1]
666	345[M + 1]
668	430[M + 1]
669	377[M + 1]
670	368[M + 3]
	366[M + 1]
671	334[M + 1]
672	442[M + 1]
674	340[M + 1]
675	306[M + 1]
676	392[M + 1]
678	386[M + 1]
679	426[M + 1]
682	414[M + 3]
	412[M + 1]
684	384[M + 1]
685	389[M + 1]
686	446[M + 1]
688	414[M + 1]
689	306[M + 1]
690	348[M + 1]
691	452[M + 1]
693	371[M + 1]
694	448[M + 1]
695	364[M + 1]
696	392[M + 3]
	390[M + 1]
697	358[M + 1]
699	426[M + 1]
703	451[M + 3]
	449[M + 1]
704	342[M + 1]
705	372[M + 1]
706	368[M + 1]
708	383[M + 1]
710	396[M + 3]
	394[M + 1]
711	351[M + 1]
712	376[M + 1]
713	398[M + 3]
	396[M + 1]
714	366[M + 1]
715	454[M + 1]
716	381[M + 3]
	379[M + 1]
718	386[M + 1]
721	322[M + 1]
722	377[M + 1]
723	440[M + 1]
	364
724	457[M + 3]
	455[M + 1]
726	362[M + 1]
727	366[M + 1]
734	370[M + 1]
736	338[M + 1]
741	404[M + 1]
742	351[M + 1]
745	386[M + 1]
746	370[M + 1]
	294
747	336[M + 1]
748	381[M + 3]
	379[M + 1]
749	416[M + 1]
	340
750	437[M + 1]
751	362[M + 1]
752	352[M + 3]
	350[M + 1]
754	366[M + 1]
755	354[M + 1]
757	425[M + 1]
759	346[M + 1]

TABLE 165-continued

760	344[M + 1]
761	402[M + 1]
762	251[M + 1]
763	355[M + 1]
764	362[M + 3]
	360[M + 1]
765	392[M + 3]
	390[M + 1]
769	366[M + 1]
770	372[M + 1]
772	292[M + 1]
773	424[M + 1]
775	396[M + 3]
	394[M + 1]
776	388[M + 1]
777	383[M + 1]
778	404[M + 1]
779	398[M + 1]
780	368[M + 1]
782	368[M + 1]
784	369[M + 1]
785	431[M + 3]
	429[M + 1]
787	473[M + 1]
	397
788	375[M + 1]
789	467[M + 1]
794	327[M + 1]
795	384[M + 1]
796	370[M + 1]
798	370[M + 1]
801	404[M + 3]
	402[M + 1]
805	376[M + 1]
806	411[M + 1]
807	356[M + 1]

TABLE 166

808	354[M + 1]
809	400[M + 1]
	324
812	425[M + 1]
815	386[M + 1]
817	377[M + 1]
818	398[M + 1]
819	352[M + 1]
821	336[M + 1]
823	362[M + 1]
824	363[M + 1]
	287
825	420[M + 1]
826	430[M + 1]
828	377[M + 1]
829	437[M + 1]
830	370[M + 1]
831	327[M + 1]
837	324[M + 1]
	248
838	377[M + 1]
839	376[M + 3]
	374[M + 1]
841	363[M + 3]
	361[M + 1]
842	386[M + 1]
843	466[M + 3]
	464[M + 1]
844	381[M + 1]
845	324[M + 1]
	248
846	358[M + 1]
847	373[M + 1]
852	489[M + 1]
853	376[M + 1]
854	448[M + 1]
856	420[M + 1]
	344

TABLE 166-continued

857	341[M + 1]
858	383[M + 1]
860	370[M + 1]
861	334[M + 3]
	332[M + 1]
862	358[M + 1]
864	392[M + 1]
865	398[M + 3]
	396[M + 1]
867	399[M + 1]
868	430[M + 1]
870	362[M + 3]
	360[M + 1]
872	428[M + 1]
873	351[M + 1]
874	341[M + 1]
877	399[M + 1]
	323
879	332[M + 1]
880	363[M + 3]
	361[M + 1]
882	426[M + 1]
883	360[M + 1]
884	320[M + 1]
885	361[M + 1]
886	380[M + 1]
888	292[M + 1]
889	451[M + 1]
	449[M + 1]
890	400[M + 1]
891	292[M + 1]
894	347[M + 1]
898	412[M + 3]
	410[M + 1]
899	397[M + 1]
901	411[M + 1]
902	377[M + 1]
903	370[M + 1]
904	422[M + 1]
905	392[M + 1]
907	308[M + 1]
909	393[M + 1]
911	415[M + 1]
912	383[M + 1]
913	413[M + 1]
914	400[M + 1]
915	389[M + 1]
	313
917	358[M + 1]
918	433[M + 3]
	431[M + 1]
919	354[M + 1]
920	381[M + 3]
	379[M + 1]
921	389[M + 1]
922	413[M + 1]
	337
923	437[M + 1]
924	376[M + 1]
925	390[M + 1]
927	355[M + 1]
929	370[M + 1]
932	380[M + 3]
	378[M + 1]
934	507[M + 1]
937	388[M + 1]
938	366[M + 1]
940	388[M + 1]
942	378[M + 1]
943	413[M + 1]
945	372[M + 1]
948	462[M + 1]
949	363[M + 1]
950	368[M + 1]
951	412[M + 1]
952	378[M + 1]
953	318[M + 1]
954	363[M + 3]
	361[M + 1]

TABLE 166-continued

955	406[M + 3]
	404[M + 1]
956	292[M + 1]
957	398[M + 3]
	396[M + 1]
958	310[M + 1]
959	406[M + 3]
	404[M + 1]
961	362[M + 3]
	360[M + 1]
962	327[M + 1]
963	392[M + 1]

TABLE 167

965	438[M + 3]
	436[M + 1]
967	425[M + 3]
	423[M + 1]
969	413[M + 1]
973	386[M + 1]
975	407[M + 3]
	405[M + 1]
976	358[M + 1]
977	369[M + 1]
979	395[M + 1]
980	402[M + 1]
981	392[M + 3]
	390[M + 1]
982	366[M + 1]
983	379[M + 1]
985	408[M + 1]
986	440[M + 3]
	438[M + 1]
987	358[M + 1]
988	294[M + 1]
989	332[M + 1]
991	356[M + 1]
992	477[M + 1]
993	416[M + 3]
	414[M + 1]
995	425[M + 3]
	423[M + 1]
996	416[M + 3]
	414[M + 1]
997	363[M + 3]
	361[M + 1]
999	336[M + 1]
1000	388[M + 1]
	312
1001	374[M + 1]
1002	400[M + 1]
1003	394[M + 1]
1004	397[M + 1]
1007	448[M + 1]
	372
1009	366[M + 1]
1011	419[M + 1]
1012	316[M + 1]
1013	431[M + 1]
1015	372[M + 1]
1016	470[M + 1]
1017	413[M + 1]
1018	386[M + 1]
1019	433[M + 3]
	431[M + 1]
1021	464[M + 1]
1022	384[M + 1]
1023	407[M + 3]
	405[M + 1]
1024	346[M + 1]
1025	455[M + 3]
	453[M + 1]
1026	425[M + 1]
1027	444[M + 1]
1029	410[M + 1]
1030	413[M + 1]

TABLE 167-continued

1031	404[M + 1]
1032	472[M + 1]
	396
1033	377[M + 1]
1036	350[M + 1]
1038	364[M + 1]
1040	317[M + 1]
1041	407[M + 1]
1042	382[M + 1]
1045	425[M + 3]
	423[M + 1]
1046	366[M + 1]
1047	390[M + 1]
1048	440[M + 1]
1049	396[M + 1]
1050	400[M + 1]
1051	315[M + 1]
1053	363[M + 3]
	361[M + 1]
1054	360[M + 1]
1057	427[M + 1]
1058	360[M + 1]
1060	381[M + 3]
	379[M + 1]
1063	395[M + 1]
1065	451[M + 1]
	449[M + 1]
1066	485[M + 1]
1070	380[M + 3]
	378[M + 1]
1071	345[M + 1]
1072	381[M + 3]
	379[M + 1]
1073	397[M + 1]
1075	342[M + 1]
1077	344[M + 1]
1078	370[M + 1]
1079	387[M + 1]
1080	370[M + 1]
	294
1081	355[M + 1]
1082	398[M + 3]
	396[M + 1]
1083	318[M + 1]
1085	439[M + 3]
	437[M + 1]
1086	428[M + 1]
1089	399[M + 1]
1090	398[M + 1]
1091	434[M + 3]
	432[M + 1]
1092	398[M + 3]
	396[M + 1]
1093	401[M + 1]
1095	400[M + 1]
1096	409[M + 1]
1097	384[M + 1]
1098	395[M + 1]
1099	511[M + 4]
	510[M + 3]
	509[M + 2]
	508[M + 1]
1101	350[M + 1]
1102	442[M + 1]
1103	397[M + 1]
1105	372[M + 1]
1106	346[M + 1]
1108	383[M + 1]
1112	445[M + 1]

TABLE 168

1113	358[M + 1]
1117	394[M + 1]
1118	336[M + 1]
	260

TABLE 168-continued

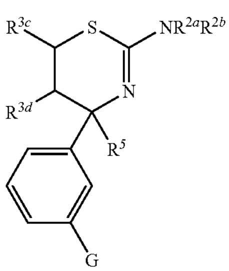
1121	392[M + 3]
	390[M + 1]
1122	322[M + 1]
1123	316[M + 1]
1126	386[M + 1]
1127	368[M + 1]
1128	416[M + 3]
	414[M + 1]
1129	341[M + 1]
1130	432[M + 1]
1134	396[M + 1]
1136	396[M + 3]
	394[M + 1]
1137	292[M + 1]
1138	413[M + 1]
1141	344[M + 1]
1143	384[M + 1]
1144	446[M + 1]
1145	390[M + 1]
	314
1146	405[M + 1]
1148	380[M + 1]
	304
1149	364[M + 1]
1151	442[M + 1]
1152	365[M + 1]
1154	318[M + 1]
1155	427[M + 1]
1156	368[M + 1]
1157	366[M + 1]
1158	415[M + 3]
	413[M + 1]
1159	414[M + 3]
	412[M + 1]
1162	370[M + 1]
	294
1163	416[M + 3]
	414[M + 1]
1164	396[M + 1]
	320
1165	361[M + 1]
1167	424[M + 1]
	348
1168	428[M + 1]
1169	422[M + 1]
1170	411[M + 1]
1171	390[M + 3]
	388[M + 1]
1173	361[M + 1]
1174	342[M + 1]
1175	430[M + 1]
1176	345[M + 1]
1177	376[M + 3]
	374[M + 1]
1178	351[M + 1]
1179	344[M + 1]
1180	398[M + 3]
	396[M + 1]
1182	426[M + 1]
1183	376[M + 3]
	374[M + 1]
1186	374[M + 1]
	298
1187	427[M + 1]
1188	350[M + 1]
1189	408[M + 3]
	406[M + 1]
1190	386[M + 1]
1191	377[M + 1]
1192	335[M + 1]
1195	412[M + 3]
	410[M + 1]
1196	380[M + 1]
1198	398[M + 1]
	322
1200	352[M + 1]
1201	424[M + 3]
	422[M + 1]
1202	369[M + 1]
1203	420[M + 1]

TABLE 168-continued

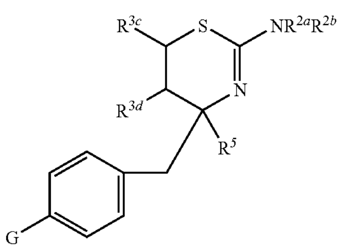
1204	398[M + 3]
	396[M + 1]
1206	416[M + 1]
1208	344[M + 1]
1209	422[M + 1]
1210	408[M + 1]
1212	391[M + 1]
1214	360[M + 1]
1218	372[M + 1]
1219	470[M + 1]
1220	264[M + 1]
1222	362[M + 3]
	360[M + 1]
1225	413[M + 1]
1226	374[M + 1]
1227	425[M + 1]
1229	455[M + 3]
	453[M + 1]
1231	413[M + 1]
1232	340[M + 1]
1233	394[M + 1]
1234	416[M + 3]
	414[M + 1]
1235	427[M + 1]
1236	348[M + 1]
	272
1237	353[M + 1]
1238	419[M + 1]
1239	416[M + 3]
	414[M + 1]
1246	474[M + 1]
1248	414[M + 1]
1249	336[M + 1]
1250	352[M + 1]
1251	393[M + 1]
1252	357[M + 1]
1253	430[M + 1]
1254	412[M + 1]
1256	333[M + 1]
1259	356[M + 1]
1260	348[M + 1]
1270	374[M + 1]
1282	362[M + 1]

[Chemical formula 84]

(Ia)

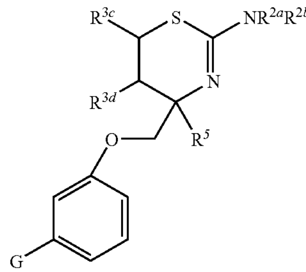


(Ib)

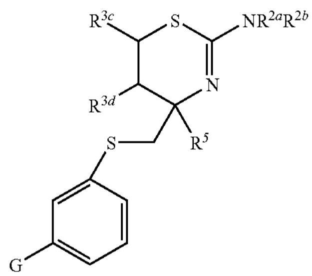


-continued

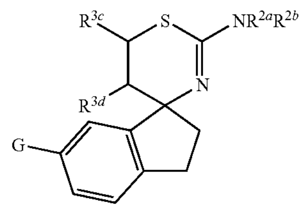
(Ic)



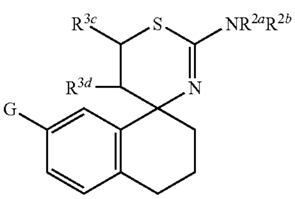
(Id)



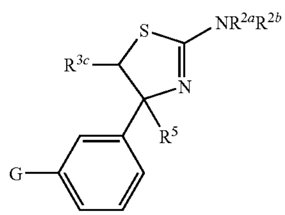
(Ie)



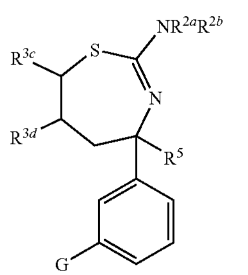
(If)



(Ig)



(Ih)



In above structural formula (Ia) to (Ih), the combination of $NR^{2a}R^{2b}$, R^{3c}, R^{3d}, R^5 and G ($NR^{2a}R^{2b}$, R^{3c}, R^{3d}, R^5, G) are the following compounds.

(NHMe,H,H,Me,CONHPh),(NHMe,H,H,Me,CONH-3-pyridyl),(NHMe,H,H,Me,NHCOPh),(NHMe,H,H,Me,NHCO-2-furyl),(NHMe,H,H,Me,NHCONHPh),(NHMe,H,H,Me,NHCOCONHPh),(NHMe,H,H,Et,CONHPh),(NHMe,H,H,Et,CONH-3-pyridyl),(NHMe,H,H,Et, NHCOPh),(NHMe,H,H,Et,NHCO-2-furyl),(NHMe,H,H,Et,NHCONHPh),(NHMe,H,H,Et,NHCOCONHPh),(NHMe,H,H,CH2OH,CONHPh),(NHMe,H,H,CH2OH,CONH-3-pyridyl),(NHMe,H,H,CH2OH,NHCOPh),(NHMe,H,H,CH2OH,NHCO-2-furyl),(NHMe,H,H,CH2OH,NHCONHPh),(NHMe,H,H,CH2OH,NHCOCONHPh),(NHMe,H,Me,Me,CONHPh),(NHMe,H,Me,Me,CONH-3-pyridyl),(NHMe,H,Me,Me,NHCOPh),(NHMe,H,Me,Me,NHCO-2furyl),(NHMe,H,Me,Me,NHCONHPh),(NHMe,H,Me,Me,NHCOCONHPh),(NHMe,H,Me,Et,CONHPh),(NHMe,H,Me,Et,CONH-3-pyridyl),(NHMe,H,Me,Et,NHCOPh),(NHMe,H,Me,Et,NHCO-2-furyl),(NHMe,H,Me,Et,NHCONHPh),(NHMe,H,Me,Et,NHCOCONHPh),(NHMe,H,Me,CH2OH,CONHPh),(NHMe,H,Me,H,Me,CH2OH,CONH-3-pyridyl),(NHMe,H,Me,CH2OH,NHCOPh),(NHMe,H,Me,CH2OH,NHCO-2-furyl),(NHMe,H,Me,CH2OH,NHCONHPh),(NHMe,H,Me,CH2OH,NHCOCONHPh),(NHMe,H,Ph,Me,CONHPh),(NHMe,H,Ph,Me,CONH-3-pyridyl),(NHMe,H,Ph,Me,NHCOPh),(NHMe,H,Ph,Me,NHCO-2furyl),(NHMe,H,Ph,Me,NHCONHPh),(NHMe,H,Ph,Me,NHCOCONHPh),(NHMe,H,Ph,Et,CONHPh),(NHMe,H,Ph,Et,CONH-3-pyridyl),(NHMe,H,Ph,Et,NHCOPh),(NHMe,H,Ph,Et,NHCO-2-furyl),(NHMe,H,Ph,Et,NHCONHPh),(NHMe,H,Ph,Et,NHCOCONHPh),(NHMe,H,Ph,CH2OH,CONHPh),(NHMe,H,Ph,CH2OH,CONH-3-pyridyl),(NHMe,H,Ph,CH2OH,NHCOPh),(NHMe,H,Ph,CH2OH,NHCO-2-furyl),(NHMe,H,Ph,CH2OH,NHCONHPh),(NHMe,H,Ph,CH2OH,NHCOCONHPh),(NHMe,H,OH,Me,CONHPh),(NHMe,H,OH,Me,CONH-3-pyridyl),(NHMe,H,OH,Me,NHCOPh),(NHMe,H,OH,Me,NHCO-2-furyl),(NHMe,H,OH,Me,NHCONHPh),(NHMe,H,OH,Me,NHCOCONHPh),(NHMe,H,OH,Et,CONHPh),(NHMe,H,OH,Et,CONH-3-pyridyl),(NHMe,H,OH,Et,NHCOPh),(NHMe,H,OH,Et,NHCO-2-furyl),(NHMe,H,OH,Et,NHCONHPh),(NHMe,H,OH,Et,NHCOCONHPh),(NHMe,H,OH,CH2OH,CONHPh),(NHMe,H,OH,CH2OH,CONH-3-pyridyl),(NHMe,H,OH,CH2OH,NHCOPh),(NHMe,H,OH,CH2OH,NHCO-2-furyl),(NHMe,H,OH,CH2OH,NHCONHPh),(NHMe,H,OH,CH2OH,NHCOCONHPh),(NHMe,Me,H,Me,CONHPh),(NHMe,Me,H,Me,CONH-3-pyridyl),(NHMe,Me,H,Me,NHCOPh),(NHMe,Me,H,Me,NHCO-2-furyl),(NHMe,Me,H,Me,NHCONHPh),(NHMe,Me,H,Me,NHCOCONHPh),(NHMe,Me,H,Et,CONHPh),(NHMe,Me,H,Et,CONH-3-pyridyl),(NHMe,Me,H,Et,NHCOPh),(NHMe,Me,H,Et,NHCO-2-furyl),(NHMe,Me,H,Et,NHCONHPh),(NHMe,Me,H,Et,NHCOCONHPh),(NHMe,Me,H,CH2OH,CONHPh),(NHMe,Me,H,CH2OH,CONH-3-pyridyl),(NHMe,Me,H,CH2OH,NHCOPh),(NHMe,Me,H,CH2OH,NHCO-2-furyl),(NHMe,Me,H,CH2OH,NHCONHPh),(NHMe,Me,H,CH2OH,NHCOCONHPh),(NHMe,Me,Me,Me,CONHPh),(NHMe,Me,Me,Me,CONH-3-pyridyl),(NHMe,Me,Me,Me,NHCOPh),(NHMe,Me,Me,Me,NHCO-2-furyl),(NHMe,Me,Me,Me,NHCONHPh),(NHMe,Me,Me,Me,NHCOCONHPh),(NHMe,Me,Me,Et,CONHPh),(NHMe,Me,Me,Et,CONH-3-pyridyl),(NHMe,Me,Me,Et,NHCOPh),(NHMe,Me,Me,Et,NHCO-2-furyl),(NHMe,Me,Me,Et,NHCONHPh),(NHMe,Me,Me,Et,NHCOCONHPh),(NHMe,Me,Me,CH2OH,CONHPh),(NHMe,Me,Me,CH2OH,CONH-3-pyridyl),(NHMe,Me,Me,CH2OH,NHCOPh),(NHMe,Me,Me,CH2OH,NHCO-2-furyl),(NHMe,Me,Me,CH2OH,NHCONHPh),(NHMe,Me,Me,CH2OH,

NHCOCONHPh),(NHMe,Me,Ph,Me,CONHPh),(NHMe,Me,Ph,Me,CONH-3-pyridyl),(NHMe,Me,Ph,Me,NH-COPh),(NHMe,Me,Ph,Me,NHCO-2-furyl),(NHMe,Me,Ph,Me,NHCONHPh),(NHMe,Me,Ph,Me,NHCOCONHPh),(NHMe,Me,Ph,Et,CONHPh),(NHMe,Me,Ph,Et,CONH-3-pyridyl),(NHMe,Me,Ph,Et,NHCOPh),(NHMe,Me,Ph,Et,NHCO-2-furyl),(NHMe,Me,Ph,Et,NHCONHPh),(NHMe,Me,Ph,Et,NHCOCONHPh),(NHMe,Me,Ph,CH2OH,CONHPh),(NHMe,Me,Ph,CH2OH,CONH-3-pyridyl),(NHMe,Me,Ph,CH2OH,NHCOPh),(NHMe,Me,Ph,CH2OH,NHCO-2-furyl),(NHMe,Me,Ph,CH2OH,NHCONHPh),(NHMe,Me,Ph,CH2OH,NHCOCONHPh),(NHMe,Me,OH,Me,CONHPh),(NHMe,Me,OH,Me,CONH-3-pyridyl),(NHMe,Me,OH,Me,NHCOPh),(NHMe,Me,OH,Me,NHCO-2-furyl),(NHMe,Me,OH,Me,NHCONHPh),(NHMe,Me,OH,Me,NHCOCONHPh),(NHMe,Me,OH,Et,CONHPh),(NHMe,Me,OH,Et,CONH-3-pyridyl),(NHMe,Me,OH,Et,NHCOPh),(NHMe,Me,OH,Et,NHCO-2-furyl),(NHMe,Me,OH,Et,NHCONHPh),(NHMe,Me,OH,Et,NHCOCONHPh),(NHMe,Me,OH,CH2OH,CONHPh),(NHMe,Me,OH,CH2OH,CONH-3-pyridyl),(NHMe,Me,OH,CH2OH,NHCOPh),(NHMe,Me,OH,CH2OH,NHCO-2-furyl),(NHMe,Me,OH,CH2OH,NHCONHPh),(NHMe,Me,OH,CH2OH,NHCOCONHPh),(NHMe,Ph,H,Me,CONHPh),(NHMe,Ph,H,Me,CONH-3-pyridyl),(NHMe,Ph,H,Me,NHCOPh),(NHMe,Ph,H,Me,NHCO-2-furyl),(NHMe,Ph,H,Me,NHCONPh),(NHMe,Ph,H,Me,NHCOCONHPh),(NHMe,Ph,H,Et,CONHPh),(NHMe,Ph,H,Et,CONH-3-pyridyl),(NHMe,Ph,H,Et,NHCOPh),(NHMe,Ph,H,Et,NHCO-2-furyl),(NHMe,Ph,H,Et,NHCONHPh),(NHMe,Ph,H,Et,NHCOCONHPh),(NHMe,Ph,H,CH2OH,CONHPh),(NHMe,Ph,H,CH2OH,CONH-3-pyridyl),(NHMe,Ph,H,CH2OH,NHCOPh),(NHMe,Ph,H,CH2OH,NHCO-2-furyl),(NHMe,Ph,H,CH2OH,NHCONHPh),(NHMe,Ph,H,CH2OH,NHCOCONHPh),(NHMe,Ph,Me,Me,CONHPh),(NHMe,Ph,Me,Me,CONH-3-pyridyl),(NHMe,Ph,Me,Me,NHCOPh),(NHMe,Ph,Me,Me,NHCO-2-furyl),(NHMe,Ph,Me,Me,NHCONHPh),(NHMe,Ph,Me,Me,NHCOCONHPh),(NHMe,Ph,Me,Et,CONHPh),(NHMe,Ph,Me,Et,CONH-3-pyridyl),(NHMe,Ph,Me,Et,NHCOPh),(NHMe,Ph,Me,Et,NHCO-2-furyl),(NHMe,Ph,Me,Et,NHCONHPh),(NHMe,Ph,Me,Et,NHCOCONHPh),(NHMe,Ph,Me,CH2OH,CONHPh),(NHMe,Ph,Me,CH2OH,CONH-3-pyridyl),(NHMe,Ph,Me,CH2OH,NHCOPh),(NHMe,Ph,Me,CH2OH,NHCO-2-furyl),(NHMe,Ph,Me,CH2OH,NHCONHPh),(NHMe,Ph,Me,CH2OH,NHCOCONHPh),(NHMe,Ph,Ph,Me,CONHPh),(NHMe,Ph,Ph,Me,CONH-3-pyridyl),(NHMe,Ph,Ph,Me,NHCOPh),(NHMe,Ph,Ph,Me,NHCO-2-furyl),(NHMe,Ph,Ph,Me,NHCONHPh),(NHMe,Ph,Ph,Me,NHCOCONHPh),(NHMe,Ph,Ph,Et,CONHPh),(NHMe,Ph,Ph,Et,CONH-3-pyridyl),(NHMe,Ph,Ph,Et,NHCOPh),(NHMe,Ph,Ph,Et,NHCO-2-furyl),(NHMe,Ph,Ph,Et,NHCONHPh),(NHMe,Ph,Ph,Et,NHCOCONHPh),(NHMe,Ph,Ph,CH2OH,CONHPh),(NHMe,Ph,Ph,CH2OH,CONH-3-pyridyl),(NHMe,Ph,Ph,CH2OH,NHCOPh),(NHMe,Ph,Ph,CH2OH,NHCO-2-furyl),(NHMe,Ph,Ph,CH2OH,NHCONHPh),(NHMe,Ph,Ph,CH2OH,NHCOCONHPh),(NHMe,Ph,OH,Me,CONHPh),(NHMe,Ph,OH,Me,CONH-3-pyridyl),(NHMe,Ph,OH,Me,NHCOPh),(NHMe,Ph,OH,Me,NHCO-2-furyl),(NHMe,Ph,OH,Me,NHCONHPh),(NHMe,Ph,OH,Me,NHCOCONHPh),(NHMe,Ph,OH,Et,CONHPh),(NHMe,Ph,OH,Et,CONH-3-pyridyl),(NHMe,Ph,OH,Et,NHCOPh),(NHMe,Ph,OH,Et,NHCO-2-furyl), (NHMe,Ph,OH,Et,NHCONHPh),(NHMe,Ph,OH,Et, NHCOCONHPh),(NHMe,Ph,OH,CH2OH,CONHPh), (NHMe,Ph,OH,CH2OH,CONH-3-pyridyl),(NHMe,Ph, OH,CH2OH,NHCOPh),(NHMe,Ph,OH,CH2OH,NHCO-2-furyl),(NHMe,Ph,OH,CH2OH,NHCONHPh),(NHMe, Ph,OH,CH2OH,NHCOCONHPh), (NHCH2CH2OH,H,H,Me,CONHPh),(NHCH2CH2OH,H, H,Me,CONH-3-pyridyl),(NHCH2CH2OH,H,Me,NH-COPh),(NHCH2CH2OH,H,H,Me,NHCO-2-furyl), (NHCH2CH2OH,H,H,Me,NHCONHPh), (NHCH2CH2OH,H,H,Me,NHCOCONHPh), (NHCH2CH2OH,H,H,Et,CONHPh),(NHCH2CH2OH, H,H,Et,CONH-3-pyridyl),(NHCH2CH2OH,H,H,Et, NHCOPh),(NHCH2CH2OH,H,H,Et,NHCO-2-furyl), (NHCH2CH2OH,H,H,Et,NHCONHPh), (NHCH2CH2OH,H,H,Et,NHCOCONHPh), (NHCH2CH2OH,H,H,CH2OH,CONHPh), (NHCH2CH2OH,H,H,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,H,H,CH2OH,NHCOPh), (NHCH2CH2OH,H,H,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,H,H,CH2OH,NHCONHPh), (NHCH2CH2OH,H,H,CH2OH,NHCOCONHPh), (NHCH2CH2OH,H,Me,Me,CONHPh), (NHCH2CH2OH,H,Me,Me,CONH-3-pyridyl), (NHCH2CH2OH,H,Me,Me,NHCOPh), (NHCH2CH2OH,H,Me,Me,NHCO-2-furyl), (NHCH2CH2OH,H,Me,Me,NHCONHPh), 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(NHCH2CH2OH,H,Ph,CH2OH,NHCOCONHPh), (NHCH2CH2OH,H,OH,Me,CONHPh), (NHCH2CH2OH,H,OH,Me,CONH-3-pyridyl), (NHCH2CH2OH,H,OH,Me,NHCOPh), (NHCH2CH2OH,H,OH,Me,NHCO-2-furyl), (NHCH2CH2OH,H,OH,Me,NHCONHPh), (NHCH2CH2OH,H,OH,Me,NHCOCONHPh), (NHCH2CH2OH,H,OH,Et,CONHPh),(NHCH2CH2OH, H,OH,Et,CONH-3-pyridyl),(NHCH2CH2OH,H,OH,Et, NHCOPh),(NHCH2CH2OH,H,OH,Et,NHCO-2-furyl), (NHCH2CH2OH,H,OH,Et,NHCONHPh), (NHCH2CH2OH,H,OH,Et,NHCOCONHPh), (NHCH2CH2OH,H,OH,CH2OH,CONHPh), (NHCH2CH2OH,H,OH,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,H,OH,CH2OH,NHCOPh), (NHCH2CH2OH,H,OH,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,H,OH,CH2OH,NHCONHPh), (NHCH2CH2OH,H,OH,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Me,H,Me,CONHPh), (NHCH2CH2OH,Me,H,Me,CONH-3-pyridyl), (NHCH2CH2OH,Me,H,Me,NHCOPh), (NHCH2CH2OH,Me,H,Me,NHCO-2-furyl), (NHCH2CH2OH,Me,H,Me,NHCONHPh), (NHCH2CH2OH,Me,H,Me,NHCOCONHPh), (NHCH2CH2OH,Me,H,Et,CONHPh),(NHCH2CH2OH, Me,H,Et,CONH-3-pyridyl),(NHCH2CH2OH,Me,H,Et, NHCOPh),(NHCH2CH2OH,Me,H,Et,NHCO-2-furyl), (NHCH2CH2OH,Me,H,Et,NHCONHPh), (NHCH2CH2OH,Me,H,Et,NHCOCONHPh), (NHCH2CH2OH,Me,H,CH2OH,CONHPh), (NHCH2CH2OH,Me,H,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Me,H,CH2OH,NHCOPh), (NHCH2CH2OH,Me,H,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Me,H,CH2OH,NHCONHPh), (NHCH2CH2OH,Me,H,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Me,Me,Me,CONHPh), (NHCH2CH2OH,Me,Me,Me,CONH-3-pyridyl), (NHCH2CH2OH,Me,Me,Me,NHCOPh), (NHCH2CH2OH,Me,Me,Me,NHCO-2-furyl), (NHCH2CH2OH,Me,Me,Me,NHCONHPh), (NHCH2CH2OH,Me,Me,Me,NHCOCONHPh), (NHCH2CH2OH,Me,Me,Et,CONHPh), (NHCH2CH2OH,Me,Me,Et,CONH-3-pyridyl), (NHCH2CH2OH,Me,Me,Et,NHCOPh), (NHCH2CH2OH,Me,Me,Et,NHCO-2-furyl), (NHCH2CH2OH,Me,Me,Et,NHCONHPh), (NHCH2CH2OH,Me,Me,Et,NHCOCONHPh), (NHCH2CH2OH,Me,Me,CH2OH,CONHPh), (NHCH2CH2OH,Me,Me,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Me,Me,CH2OH,NHCOPh),CH2OH, NHCO-2-furyl),(NHCH2CH2OH,Me,Me,CH2OH, NHCONHPh),(NHCH2CH2OH,Me,Me,CH2OH, NHCOCONHPh),(NHCH2CH2OH,Me,Ph,Me, CONHPh),(NHCH2CH2OH,Me,Ph,Me,CONH-3-pyridyl),(NHCH2CH2OH,Me,Ph,Me,NRCOPh), (NHCH2CH2OH,Me,Ph,Me,NHCO-2-furyl), (NHCH2CH2OH,Me,Ph,Me,NHCONHPh), (NHCH2CH2OH,Me,Ph,Me,NHCOCONHPh), (NHCH2CH2OH,Me,Ph,Et,CONHPh),(NHCH2CH2OH, Me,Ph,Et,CONH-3-pyridyl),(NHCH2CH2OH,Me,Ph,Et, NHCOPh),(NHCH2CH2OH,Me,Ph,Et,NHCO-2-furyl), (NHCH2CH2OH,Me,Ph,Et,NHCONHPh), (NRCH2CH2OH,Me,Ph,Et,NHCOCONHPh), (NHCH2CH2OH,Me,Ph,CH2OH,CONHPh), (NHCH2CH2OH,Me,Ph,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Me,Ph,CH2OH,NHCOPh), (NHCH2CH2OH,Me,Ph,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Me,Ph,CH2OH,NHCONHPh), (NHCH2CH2OH,Me,Ph,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Me,OH,Me,CONHPh), (NHCH2CH2OH,Me,OH,Me,CONH-3-pyridyl), (NHCH2CH2OH,Me,OH,Me,NHCOPh), (NHCH2CH2OH,Me,OH,Me,NHCO-2-furyl), (NHCH2CH2OH,Me,OH,Me,NHCONHPh), (NHCH2CH2OH,Me,OH,Me,NHCOCONHPh), (NHCH2CH2OH,Me,OH,Et,CONHPh), (NHCH2CH2OH,Me,OH,Et,CONH-3-pyridyl), (NHCH2CH2OH,Me,OH,Et,NHCOPh), (NHCH2CH2OH,Me,OH,Et,NHCO-2-furyl), (NHCH2CH2OH,Me,OH,Et,NHCONHPh), (NHCH2CH2OH,Me,OH,Et,NHCOCONHPh), (NHCH2CH2OH,Me,OH,CH2OH,CONHPh), (NHCH2CH2OH,Me,OH,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Me,OH,CH2OH,NHCOPh), (NHCH2CH2OH,Me,OH,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Me,OH,CH2OH,NHCONHPh), (NHCH2CH2OH,Me,OH,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Ph,H,Me,CONHPh),(NHCH2CH2OH, Ph,H,Me,CONH-3-pyridyl),(NHCH2CH2OH,Ph,H,Me, NHCOPh),(NHCH2CH2OH,Ph,H,Me,NHCO-2-furyl), (NHCH2CH2OH,Ph,H,Me,NHCONHPh), (NHCH2CH2OH,Ph,H,Me,NHCOCONHPh), (NHCH2CH2OH,Ph,H,Et,CONHPh),(NHCH2CH2OH, Ph,H,Et,CONH-3-pyridyl),(NHCH2CH2OH,Ph,H,Et, NHCOPh),(NHCH2CH2OH,Ph,H,Et,NHCO-2-furyl), (NHCH2CH2OH,Ph,H,Et,NHCONHPh), (NHCH2CH2OH,Ph,H,Et,NHCOCONHPh), (NHCH2CH2OH,Ph,H,CH2OH,CONHPh), (NHCH2CH2OH,Ph,H,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Ph,H,CH2OH,NHCOPh), (NHCH2CH2OH,Ph,H,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Ph,H,CH2OH,NHCONHPh), (NHCH2CH2OH,Ph,H,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Ph,Me,Me,CONHPh), (NHCH2CH2OH,Ph,Me,Me,CONH-3-pyridyl), (NHCH2CH2OH,Ph,Me,Me,NHCOPh), (NHCH2CH2OH,Ph,Me,Me,NHCO-2-furyl), (NHCH2CH2OH,Ph,Me,Me,NHCONHPh), (NHCH2CH2OH,Ph,Me,Me,NHCOCONHPh), (NHCH2CH2OH,Ph,Me,Et,CONHPh),(NHCH2CH2OH, Ph,Me,Et,CONH-3-pyridyl),(NHCH2CH2OH,Ph,Me,Et, NHCOPh),(NHCH2CH2OH,Ph,Me,Et,NHCO-2-furyl), (NHCH2CH2OH,Ph,Me,Et,NHCONHPh), (NHCH2CH2OH,Ph,Me,Et,NHCOCONHPh), (NHCH2CH2OH,Ph,Me,CH2OH,CONHPh), (NHCH2CH2OH,Ph,Me,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Ph,Me,CH2OH,NHCOPh), (NHCH2CH2OH,Ph,Me,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Ph,Me,CH2OH,NHCONHPh), (NHCH2CH2OH,Ph,Me,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Ph,Ph,Me,CONHPh), (NHCH2CH2OH,Ph,Ph,Me,CONH-3-pyridyl), (NHCH2CH2OH,Ph,Ph,Me,NHCOPh), (NHCH2CH2OH,Ph,Ph,Me,NHCO-2-furyl), (NHCH2CH2OH,Ph,Ph,Me,NHCONHPh), (NHCH2CH2OH,Ph,Ph,Me,NHCOCONHPh), (NHCH2CH2OH,Ph,Ph,Et,CONHPh),(NHCH2CH2OH, Ph,Ph,Et,CONH-3-pyridyl),(NHCH2CH2OH,Ph Ph,Et, NHCOPh),(NHCH2CH2OH,Ph,Ph,Et,NHCO-2-furyl), (NHCH2CH2OH,Ph,Ph,Et,NHCONHPh), (NHCH2CH2OH,Ph,Ph,Et,NHCOCONHPh), (NHCH2CH2OH,Ph,Ph,CH2OH,CONHPh), (NHCH2CH2OH,Ph,Ph,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Ph,Ph,CH2OH,NHCOPh), (NHCH2CH2OH,Ph,Ph,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Ph,Ph,CH2OH,NHCONHPh), (NHCH2CH2OH,Ph,Ph,CH2OH,NHCOCONHPh), (NHCH2CH2OH,Ph,OH,Me,CONHPh), (NHCH2CH2OH,Ph,OH,Me,CONH-3-pyridyl), (NHCH2CH2OH,Ph,OH,Me,NHCOPh), (NHCH2CH2OH,Ph,OH,Me,NHCO-2-furyl), (NHCH2CH2OH,Ph,OH,Me,NHCONHPh), (NHCH2CH2OH,Ph,OH,Me,NHCOCONHPh), (NHCH2CH2OH,Ph,OH,Et,CONHPh), (NHCH2CH2OH,Ph,OH,Et,CONH-3-pyridyl), (NHCH2CH2OH,Ph,OH,Et,NHCOPh), (NHCH2CH2OH,Ph,OH,Et,NHCO-2-furyl), (NHCH2CH2OH,Ph,OH,Et,NHCONHPh), (NHCH2CH2OH,Ph,OH,Et,NHCOCONHPh), (NHCH2CH2OH,Ph,OH,CH2OH,CONHPh), (NHCH2CH2OH,Ph,OH,CH2OH,CONH-3-pyridyl), (NHCH2CH2OH,Ph,OH,CH2OH,NHCOPh), (NHCH2CH2OH,Ph,OH,CH2OH,NHCO-2-furyl), (NHCH2CH2OH,Ph,OH,CH2OH,NHCONHPh), (NHCH2CH2OH,Ph,OH,CH2OH,NHCOCONHPh), (NHCH2CONH2,H,H,Me,CONHPh),(NHCH2CONH2,H, H,Me,CONH-3-pyridyl),(NHCH2CONH2,H,H,Me,NH-COPh),(NHCH2CONH2,H,H,Me,NHCO-2-furyl), (NHCH2CONH2,H,H,Me,NHCONHPh), (NHCH2CONH2,H,H,Me,NHCOCONHPh), (NHCH2CONH2,H,H,Et,CONHPh),(NHCH2CONH2, H,H,Et,CONH-3-pyridyl),(NHCH2CONH2,H,H,Et, NHCOPh),(NHCH2CONH2,H,H,Et,NHCO-2-furyl), (NHCH2CONH2,H,H,Et,NHCONHPh), (NHCH2CONH2,H,H,Et,NHCOCONHPh), (NHCH2CONH2,H,H,CH2OH,CONHPh), 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(NHCH2CONH2,Ph,H,CH2OH,NHCONHPh), (NHCH2CONH2,Ph,H,CH2OH,NHCOCONHPh), (NHCH2CONH2,Ph,Me,Me,CONHPh), (NHCH2CONH2,Ph,Me,Me,CONH-3-pyridyl), (NHCH2CONH2,Ph,Me,Me,NHCOPh), (NHCH2CONH2,Ph,Me,Me,NHCO-2-furyl), (NHCH2CONH2,Ph,Me,Me,NHCONHPh), (NHCH2CONH2,Ph,Me,Me,NHCOCONHPh), (NHCH2CONH2,Ph,Me,Et,CONHPh),(NHCH2CONH2, Ph,Me,Et,CONH-3-pyridyl),(NHCH2CONH2,Ph,Me,Et, NHCOPh),(NHCH2CONH2,Ph,Me,Et,NHCO-2-furyl), (NHCH2CONH2,Ph,Me,Et,NHCONHPh), (NHCH2CONH2,Ph,Me,Et,NHCOCONHPh), (NHCH2CONH2,Ph,Me,CH2OH,CONHPh), (NHCH2CONH2,Ph,Me,CH2OH,CONH-3-pyridyl), (NHCH2CONH2,Ph,Me,CH2OH,NHCOPh), (NHCH2CONH2,Ph,Me,CH2OH,NHCO-2-furyl), (NHCH2CONH2,Ph,Me,CH2OH,NHCONHPh), (NHCH2CONH2,Ph,Me,CH2OH,NHCOCONHPh), (NHCH2CONH2,Ph,Ph,Me,CONHPh), (NHCH2CONH2,Ph,Ph,Me,CONH-3-pyridyl), (NHCH2CONH2,Ph,Ph,Me,NHCOPh), (NHCH2CONH2,Ph,Ph,Me,NHCO-2-furyl), (NHCH2CONH2,Ph,Ph,Me,NHCONHPh), (NHCH2CONH2,Ph,Ph,Me,NHCOCONHPh), (NHCH2CONH2,Ph,Ph,Et,CONHPh),(NHCH2CONH2, Ph,Ph,Et,CONH-3-pyridyl),(NHCH2CONH2,Ph,Ph,Et, NHCOPh),(NHCH2CONH2,Ph,Ph,Et,NHCO-2-furyl), (NHCH2CONH2,Ph,Ph,Et,NHCONHPh), (NHCH2CONH2,Ph,Ph,Et,NHCOCONHPh), (NHCH2CONH2,Ph,Ph,CH2OH,CONHPh), (NHCH2CONH2,Ph,Ph,CH2OH,CONH-3-pyridyl), (NHCH2CONH2,Ph,Ph,CH2OH,NHCOPh), (NHCH2CONH2,Ph,Ph,CH2OH,NHCO-2-furyl), (NHCH2CONH2,Ph,Ph,CH2OH,NHCONHPh), (NHCH2CONH2,Ph,Ph,CH2OH,NHCOCONHPh), (NHCH2CONH2,Ph,OH,Me,CONHPh), (NHCH2CONH2,Ph,OH,Me,CONH-3-pyridyl), (NHCH2CONH2,Ph,OH,Me,NHCOPh), (NHCH2CONH2,Ph,OH,Me,NHCO-2-furyl), (NHCH2CONH2,Ph,OH,Me,NHCONHPh), (NHCH2CONH2,Ph,OH,Me,NHCOCONHPh), (NHCH2CONH2,Ph,OH,Et,CONHPh), (NHCH2CONH2,Ph,OH,Et,CONH-3-pyridyl), (NHCH2CONH2,Ph,OH,Et,NHCOPh), (NHCH2CONH2,Ph,OH,Et,NHCO-2-furyl), (NHCH2CONH2,Ph,OH,Et,NHCONHPh), (NHCH2CONH2,Ph,OH,Et,NHCOCONHPh), (NHCH2CONH2,Ph,OH,CH2OH,CONHPh), (NHCH2CONH2,Ph,OH,CH2OH,CONH-3-pyridyl), (NHCH2CONH2,Ph,OH,CH2OH,NHCOPh), (NHCH2CONH2,Ph,OH,CH2OH,NHCO-2-furyl), (NHCH2CONH2,Ph,OH,CH2OH,NHCONHPh), (NHCH2CONH2,Ph,OH,CH2OH,NHCOCONHPh), (NHCH(Bn)CONH2,H,H,Me,CONHPh),(NHCH(Bn)CONH2,H,H,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,H,Me,NHCOPh),(NHCH(Bn)CONH2,H,H,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,H,H,Me,NHCONHPh),(NHCH(Bn)CONH2,H,H,Me,NHCOCONHPh),(NHCH(Bn)CONH2,H,H,Et,CONHPh),(NHCH(Bn)CONH2,H,H,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,H,Et,NHCOPh),(NHCH(Bn)CONH2,H,H,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,H,H,Et,NHCONHPh),(NHCH(Bn)CONH2,H,H,Et,NHCOCONHPh),(NHCH(Bn)CONH2,H,H,CH2OH,CONHPh),(NHCH(Bn)CONH2,H,H,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,H,CH2OH,NHCOPh),(NHCH(Bn)CONH2,H,H,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,H,H,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,H,H,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,H,Me,Me,CONHPh),(NHCH(Bn)CONH2,H,Me,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,Me,Me,NHCOPh),(NHCH(Bn)CONH2,H,Me,Me,NHCO-2-furyl,(NHCH(Bn)CONH2,H,Me,Me,NHCONHPh),(NHCH(Bn)CONH2,H,Me,Me,NHCOCONHPh),(NHCH(Bn)CONH2,H,Me,Et,CONHPh),(NHCH(Bn)CONH2,H,Me,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,Me,Et,NHCOPh),(NHCH(Bn)CONH2,H,Me,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,H,Me,Et,NHCONHPh),(NHCH(Bn)CONH2,H,Me,Et,NHCOCONHPh),(NHCH(Bn)CONH2,H,Me,CH2OH,CONHPh),(NHCH(Bn)CONH2,H,Me,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,Me,CH2OH,NHCOPh),(NHCH(Bn)CONH2,H,Me,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,H,Me,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,H,Me,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,H,Ph,Me,CONHPh),(NHCH(Bn)CONH2,H,Ph,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,Ph,Me,NHCOPh),(NHCH(Bn)CONH2,H,Ph,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,H,Ph,Me,NHCONHPh),(NHCH(Bn)CONH2,H,Ph,Me,NHCOCONHPh),(NHCH(Bn)CONH2,H,Ph,Et,CONHPh),(NHCH(Bn)CONH2,H,Ph,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,Ph,Et,NHCOPh),(NHCH(Bn)CONH2,H,Ph,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,H,Ph,Et,NHCONHPh),(NHCH(Bn)CONH2,H,Ph,Et,NHCOCONHPh),(NHCH(Bn)CONH2,H,Ph,CH2OH,CONHPh),(NHCH(Bn)CONH2,H,Ph,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,Ph,CH2OH,NHCOPh),(NHCH(Bn)CONH2,H,Ph,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,H,Ph,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,H,Ph,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,H,OH,Me,CONHPh),(NHCH(Bn)CONH2,H,OH,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,OH,Me,NHCOPh),(NHCH(Bn)CONH2,H,OH,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,H,OH,Me,NHCONHPh),(NHCH(Bn)CONH2,H,OH,Me,NHCOCONHPh),(NHCH(Bn)CONH2,H,OH,Et,CONHPh),(NHCH(Bn)CONH2,H,OH,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,OH,Et,NHCOPh),(NHCH(Bn)CONH2,H,OH,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,H,OH,Et,NHCONHPh),(NHCH(Bn)CONH2,H,OH,Et,NHCOCONHPh),(NHCH(Bn)CONH2,H,OH,CH2OH,CONHPh),(NHCH(Bn)CONH2,H,OH,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,H,OH,CH2OH,NHCOPh),(NHCH(Bn)CONH2,H,OH,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,H,OH,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,H,OH,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Me,H,Me,CONHPh),(NHCH(Bn)CONH2,Me,H,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,H,Me,NHCOPh),(NHCH(Bn)CONH2,Me,H,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,H,Me,NHCONHPh),(NHCH(Bn)CONH2,Me,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Me,H,Et,CONHPh),(NHCH(Bn)CONH2,Me,H,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,H,Et,NHCOPh),(NHCH(Bn)CONH2,Me,H,Et,NHCO-2-furyl,(NHCH(Bn)CONH2,Me,H,Et,NHCONHPh),(NHCH(Bn)CONH2,Me,H,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Me,H,CH2OH,CONHPh),(NHCH(Bn)CONH2,Me,H,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,H,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Me,H,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,H,CH2OH,NHCONHPh),(NHCH(Br)CONH2,Me,H,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Me,Me,Me,CONHPh),(NHCH(Bn)CONH2,Me,Me,Me,CONH-3-pyridyn,(NHCH(Bn)CONH2,Me,Me,Me,NHCOPh),(NHCH(Bn)CONH2,Me,Me,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,Me,Me,NHCONHPh),(NHCH(Bn)CONH2,Me,Me,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Me,Me,Et,CONHPh),(NHCH(Bn)CONH2,Me,Me,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,Me,Et,NHCOPh),(NHCH(Br)CONH2,Me,Me,Et,NHCO-2-furyl),(NRCH(Bn)CONH2,Me,Me,Et,NHCONHPh),(NHCH(Bn)CONH2,Me,Me,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Me,Me,CH2OH,CONHPh),(NHCH(Bn)CONH2,Me,Me,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,Me,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Me,Me,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,Me,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Me,Me,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Me,Ph,Me,CONHPh),(NHCH(Bn)CONH2,Me,Ph,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,Ph,Me,NHCOPh),(NHCH(Bn)CONH2,Me,Ph,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,Ph,Me,NHCONHPh),(NHCH(Bn)CONH2,Me,Ph,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Me,Ph,Et,CONHPh),(NHCH(Bn)CONH2,Me,Ph,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,Ph,Et,NHCOPh),(NHCH(Bn)CONH2,Me,Ph,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,Ph,Et,NHCONHPh),(NHCH(Bn)CONH2,Me,Ph,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Me,Ph,CH2OH,CONHPh),(NHCH(Bn)CONH2,Me,Ph,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,Ph,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Me,Ph,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,Ph,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Me,Ph,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Me,OH,Me,CONHPh),(NHCH(Bn)CONH2,Me,OH,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,OH,Me,NHCOPh),(NHCH(Bn)CONH2,Me,OH,Me,NHCO-2-furyl,(NHCH(Bn)CONH2,Me,OH,NHCONHPh),(NHCH(Bn)CONH2,Me,OH,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Me,OH,Et,CONHPh),(NHCH(Bn)CONH2,Me,OH,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,OH,Et,NHCOPh),(NHCH(Bn)CONH2,Me,OH,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,OH,Et,NHCONHPh),(NHCH(Bn)

CONH2,Me,OH,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Me,OH,CH2OH,CONHPh),(NHCH(Bn)CONH2,Me,OH,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Me,OH,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Me,OH,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Me,OH,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Me,OH,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,H,Me,CONHPh),(NHCH(Bn)CONH2,Ph,H,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,H,Me,NHCOPh),(NHCH(Bn)CONH2,Ph,H,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,H,Me,NHCONHPh),(NHCH(Bn)CONH2,Ph,H,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,H,Et,CONHPh),(NHCH(Bn)CONH2,Ph,H,Et,CONH-3-pyridyl,(NHCH(Bn)CONH2,Ph,H,Et,NHCOPh),(NHCH(Bn)CONH2,Ph,H,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,H,Et,NHCONHPh),(NHCH(Bn)CONH2,Ph,H,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,H,CH2OH,CONHPh),(NHCH(Bn)CONH2,Ph,H,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,H,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Ph,H,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,H,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Ph,H,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,Me,Me,CONHPh),(NHCH(Bn)CONH2,Ph,Me,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,Me,Me,NHCOPh),(NHCH(Bn)CONH2,Ph,Me,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,Me,Me,NHCONHPh),(NHCH(Bn)CONH2,Ph,Me,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,Me,Et,CONHPh),(NHCH(Bn)CONH2,Ph,Me,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,Me,Et,NHCOPh),(NHCH(Bn)CONH2,Ph,Me,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,Me,Et,NHCONHPh),(NHCH(Bn)CONH2,Ph,Me,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,Me,CH2OH,CONHPh),(NHCH(Bn)CONH2,Ph,Me,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,Me,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Ph,Me,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,Me,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Ph,Me,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,Ph,Me,CONHPh),(NHCH(Bn)CONH2,Ph,Ph,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,Ph,Me,NHCOPh),(NHCH(Bn)CONH2,Ph,Ph,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,Ph,Me,NHCONHPh),(NHCH(Bn)CONH2,Ph,Ph,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,Ph,Et,CONHPh),(NHCH(Bn)CONH2,Ph,Ph,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,Ph,Et,NHCOPh),(NHCH(Bn)CONH2,Ph,Ph,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,Ph,Et,NHCONHPh),(NHCH(Bn)CONH2,Ph,Ph,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,Ph,CH2OH,CONHPh),(NHCH(Bn)CONH2,Ph,Ph,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,Ph,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Ph,Ph,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,Ph,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Ph,Ph,CH2OH,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,OH,Me,CONHPh),(NHCH(Bn)CONH2,Ph,OH,Me,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,OH,Me,NHCOPh),(NHCH(Br)CONH2,Ph,OH,Me,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,OH,Me,NHCONHPh),(NHCH(Bn)CONH2,Ph,OH,Me,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,OH,Et,CONHPh),(NHCH(Bn)CONH2,Ph,OH,Et,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,OH,Et,NHCOPh),(NHCH(Bn)CONH2,Ph,OH,Et,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,OH,Et,NHCONHPh),(NHCH(Bn)CONH2,Ph,OH,Et,NHCOCONHPh),(NHCH(Bn)CONH2,Ph,OH,CH2OH,CONHPh),(NHCH(Bn)CONH2,Ph,OH,CH2OH,CONH-3-pyridyl),(NHCH(Bn)CONH2,Ph,OH,CH2OH,NHCOPh),(NHCH(Bn)CONH2,Ph,OH,CH2OH,NHCO-2-furyl),(NHCH(Bn)CONH2,Ph,OH,CH2OH,NHCONHPh),(NHCH(Bn)CONH2,Ph,OH,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,H,H,Me,CONHPh),(NHCH(Me)CH2OH,H,H,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,H,Me,NHCOPh),(NHCH(Me)CH2OH,H,H,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,H,H,Me,NHCONHPh),(NHCH(Me)CH2OH,H,H,Me,NHCOCONHPh),(NHCH(Me)CH2OH,H,H,Et,CONHPh),(NHCH(Me)CH2OH,H,H,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,H,Et,NHCOPh),(NHCH(Me)CH2OH,H,H,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,H,H,Et,NHCONHPh),(NHCH(Me)CH2OH,H,H,Et,NHCOCONHPh),(NHCH(Me)CH2OH,H,H,CH2OH,CONHPh),(NHCH(Me)CH2OH,H,H,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,H,CH2OH,NHCOPh),(NHCH(Me)CH2OH,H,H,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,H,H,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,H,H,CH2OH,NHCOCONHPh,(NHCH(Me)CH2OH,H,Me,Me,CONHPh),(NHCH(Me)CH2OH,Me,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,Me,Me,NHCOPh),(NHCH(Me)CH2OH,H,Me,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,H,Me,Me,NHCONHPh),(NHCH(Me)CH2OH,H,Me,Me,NHCOCONHPh),(NHCH(Me)CH2OH,H,Me,Et,CONHPh),(NHCH(Me)CH2OH,H,Me,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,Me,Et,NHCOPh),(NHCH(Me)CH2OH,H,Me,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,Et,NHCONHPh),(NHCH(Me)CH2OH,H,Me,Et,NHCOCONHPh),(NHCH(Me)CH2OH,H,Me,CH2OH,CONHPh),(NHCH(Me)CH2OH,H,Me,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,Me,CH2OH,NHCOPh),(NHCH(Me)CH2OH,H,Me,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,H,Me,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,H,Ph,Me,CONHPh),(NHCH(Me)CH2OH,H,Ph,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,Ph,Me,NHCOPh),(NHCH(Me)CH2OH,H,Ph,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,H,Ph,Me,NHCONHPh),(NHCH(Me)CH2OH,H,Ph,Me,NHCOCONHPh),(NHCH(Me)CH2OH,H,Ph,Et,CONHPh),(NHCH(Me)CH2OH,H,Ph,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,Ph,Et,NHCOPh),(NHCH(Me)CH2OH,H,Ph,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Et,NHCONHPh),(NHCH(Me)CH2OH,H,Ph,Et,NHCOCONHPh),(NHCH(Me)CH2OH,H,Ph,CH2OH,CONHPh,(NHCH(Me)CH2OH,H,Ph,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,Ph,CH2OH,NHCOPh),(NHCH(Me)CH2OH,H,Ph,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,H,Ph,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,H,Ph,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,H,OH,Me,CONHPh),(NHCH(Me)CH2OH,H,OH,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,OH,Me,NHCOPh),(NHCH(Me)CH2OH,H,OH,Me,NHCO-2-furyl),NHCH(Me)CH2OH,H,OH,Me,NHCONHPh),(NHCH(Me)CH2OH,H,OH,Me,NHCOCONHPh),(NHCH(Me)CH2OH,H,OH,Et,CONHPh),(NHCH(Me)CH2OH,H,OH,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,OH,Et,NHCOPh),(NHCH(Me)CH2OH,H,OH,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,H,OH,Et,NHCONHPh),(NHCH(Me)CH2OH,H,OH,Et,NHCOCONHPh),(NHCH(Me)CH2OH,H,OH,CH2OH,CONHPh),(NHCH(Me)CH2OH,H,OH,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,H,OH,CH2OH,NHCOPh),(NHCH(Me)

CH2OH,H,OH,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,H,OH,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,H,OH,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Me,H,Me,CONHPh),(NHCH(Me)CH2OH,Me,H,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,H,Me,NHCOPh),(NHCH(Me)CH2OH,Me,H,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,H,Me,NHCONHPh),(NHCH(Me)CH2OH,Me,H,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Me,H,Et,CONHPh),(NHCH(Me)CH2OH,Me,H,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,H,Et,NHCOPh),(NHCH(Me)CH2OH,Me,H,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,H,Et,NHCONHPh),(NHCH(Me)CH2OH,Me,H,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Me,H,CH2OH,CONHPh),(NHCH(Me)CH2OH,Me,H,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,H,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Me,H,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,H,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Me,H,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Me,Me,Me,CONHPh),(NHCH(Me)CH2OH,Me,Me,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,Me,Me,NH COPh),(NHCH(Me)CH2OH,Me,Me,Me,NHCO-2-furyl,(NHCH(Me)CH2OH,Me,Me,Me,NHCONHPh),(NHCH(Me)CH2OH,Me,Me,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Me,Me,Et,CONHPh),(NHCH(Me)CH2OH,Me,Me,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,Me,Et,NHCOPh),(NHCH(Me)CH2OH,Me,Me,Et,NHCO-2-furyl,(NHCH(Me)CH2OH,Me,Me,Et,NHCONHPh),(NHCH(Me)CH2OH,Me,Me,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Me,Me,CH2OH,CONHPh),(NHCH(Me)CH2OH,Me,Me,CH2OH,CONH-3-pyridyl,(NHCH(Me)CH2OH,Me,Me,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Me,Me,CH2OH,NHCO-2-furyl,(NHCH(Me)CH2OH,Me,Me,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Me,Me,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Me,Ph,Me,CONHPh),(NHCH(Me)CH2OH,Me,Ph,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,Ph,Me,NHCOPh),(NHCH(Me)CH2OH,Me,Ph,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,Ph,Me,NHCONHPh),(NHCH(Me)CH2OH,Me,Ph,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Me,Ph,Et,CONHPh),(NHCH(Me)CH2OH,Me,Ph,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,Ph,Et,NHCOPh),(NHCH(Me)CH2OH,Me,Ph,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,Ph,Et,NHCONHPh),(NHCH(Me)CH2OH,Me,Ph,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Me,Ph,CH2OH,CONHPh),(NHCH(Me)CH2OH,Me,Ph,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,Ph,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Me,Ph,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,Ph,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Me,Ph,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Me,OH,Me,CONHPh),(NHCH(Me)CH2OH,Me,OH,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,OH,Me,NHCOPh),(NHCH(Me)CH2OH,Me,OH,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,OH,Me,NHCONHPh),(NHCH(Me)CH2OH,Me,OH,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Me,OH,Et,CONHPh),(NHCH(Me)CH2OH,Me,OH,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,OH,Et,NHCOPh),(NHCH(Me)CH2OH,Me,OH,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,OH,Et,NHCONHPh),(NHCH(Me)CH2OH,Me,OH,NHCOCONHPh),(NHCH(Me)CH2OH,Me,OH,CH2OH,CONHPh),(NHCH(Me)CH2OH,Me,OH,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Me,OH,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Me,OH,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,Me,OH,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Me,OH,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,H,Me,CONHPh),(NHCH(Me)CH2OH,Ph,H,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,H,Me,NHCOPh),(NHCH(Me)CH2OH,Ph,H,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,H,Me,NHCONHPh),(NHCH(Me)CH2OH,Ph,H,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,H,Et,CONHPh),(NHCH(Me)CH2OH,Ph,H,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,H,Et,NHCOPh),(NHCH(Me)CH2OH,Ph,H,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,H,Et,NHCONHPh),(NHCH(Me)OCH2OH,Ph,B,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,H,CH2OH,CONHPh),(NHCH(Me)CH2OH,Ph,H,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,H,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Ph,H,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,H,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Ph,H,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,Me,Me,CONHPh),(NHCH(Me)CH2OH,Ph,Me,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,Me,Me,NHCOPh),(NHCH(Me)CH2OH,Ph,Me,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Me,Me,NHCONHPh),(NHCH(Me)CH2OH,Ph,Me,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,Me,Et,CONHPh),(NHCH(Me)CH2OH,Ph,Me,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,Me,Et,NHCOPh),(NHCH(Me)CH2OH,Ph,Me,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Me,Et,NHCONHPh),(NHCH(Me)CH2OH,Ph,Me,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,Me,CH2OH,CONHPh),(NHCH(Me)CH2OH,Ph,Me,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,Me,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Ph,Me,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Me,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Ph,Me,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,Ph,Me,CONHPh),(NHCH(Me)CH2OH,Ph,Ph,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,Ph,Me,NHCOPh),NHCH(Me)CH2OH,Ph,Ph,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Ph,Me,NHCONHPh),(NHCH(Me)CH2OH,Ph,Ph,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,Ph,Et,CONHPh),(NHCH(Me)CH2OH,Ph,Ph,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,Ph,Et,NHCOPh),(NHCH(Me)CH2OH,Ph,Ph,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Ph,Et,NHCONHPh),(NHCH(Me)CH2OH,Ph,Ph,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,Ph,CH2OH,CONHPh),(NHCH(Me)CH2OH,Ph,Ph,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,Ph,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Ph,Ph,CH2OH,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,Ph,CH2OH,NHCONHPh),(NHCH(Me)CH2OH,Ph,Ph,CH2OH,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,OH,Me,CONHPh),(NHCH(Me)CH2OH,Ph,OH,Me,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,OH,Me,NHCOPh),(NHCH(Me)CH2OH,Ph,OH,Me,NHCO-2-furyl),(NHCH(Me)CH2OH,OH,Me,NHCONHPh),(NHCH(Me)CH2OH,Ph,OH,Me,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,OH,Et,CONHPh),(NHCH(Me)CH2OH,Ph,OH,Et,CONH-3-pyridyl),(NHCH(Me)CH2OH)Ph,OH,Et,NHCOPh),(NHCH(Me)CH2OH,Ph,OH,Et,NHCO-2-furyl),(NHCH(Me)CH2OH,Ph,OH,Et,NHCONHPh),(NHCH(Me)CH2OH,Ph,OH,Et,NHCOCONHPh),(NHCH(Me)CH2OH,Ph,OH,CH2OH,CONHPh),(NHCH(Me)CH2OH,Ph,OH,CH2OH,CONH-3-pyridyl),(NHCH(Me)CH2OH,Ph,OH,CH2OH,NHCOPh),(NHCH(Me)CH2OH,Ph,OH,CH2OH,NHCO-2-furyl),(NHCH(Me)

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(Me)CONHMe,Ph,Me,Me,NHCOPh),(NHCH(Me) CONHMe,Ph,Me,Me,NHCO-2-furyl),(NHCH(Me) CONHMe,Ph,Me,Me,NHCONHPh),(NHCH(Me) CONHMe,Ph,Me,Me,NHCOCONHPh),(NHCH(Me) CONHMe,Ph,Me,Et,CONHPh),(NHCH(Me)CONHMe, Ph,Me,Et,CONH-3-pyridyl),(NHCH(Me)CONHMe,Ph, Me,Et,NHCOPh),(NHCH(Me)CONHMe,Ph,Me,Et, NHCO-2-furyl),(NHCH(Me)CONHMe,Ph,Me,Et, NHCONHPh),(NHCH(Me)CONHMe,Ph,Me,Et, NHCOCONHPh),(NHCH(Me)CONHMe,Ph,Me, CH2OH,CONHPh),(NHCH(Me)CONHMe,Ph,Me, CH2OH,CONH-3-pyridyl),(NHCH(Me)CONHMe,Ph, Me,CH2OH,NHCOPh),(NHCH(Me)CONHMe,Ph,Me, CH2OH,NHCO-2-furyl),(NHCH(Me)CONHMe,Ph,Me, CH2OH,NHCONHPh),(NHCH(Me)CONHMe,Ph,Me, CH2OH,NHCOCONHPh),(NHCH(Me)CONHMe,Ph, Ph,Me,CONHPh),(NHCH(Me)CONHMe,Ph,Ph,Me, CONH-3-pyridyl),(NHCH(Me)CONHMe,Ph,Ph,Me, NHCOPh),(NHCH(Me)CONHMe,Ph,Ph,Me,NHCO-2-furyl),(NHCH(Me)CONHMe,Ph,Ph,Me,NHCONHPh), (NHCH(Me)CONHMe,Ph,Ph,Me,NHCOCONHPh), (NHCH(Me)CONHMe,Ph,Ph,Et,CO NHPh),(NHCH (Me)CONHMe,Ph,Ph,Et,CONH-3-pyridyl),(NHCH(Me) CONHMe,Ph,Ph,Et,NHCOPh),(NHCH(Me)CONHMe, Ph,Ph,Et,NHCO-2-furyl),(NHCH(Me)CONHMe,Ph,Ph, Et,NHCONHPh),(NHCH(Me)CONHMe,Ph,Ph,Et, NHCOCONHPh),(NHCH(Me)CONHMe,Ph,Ph, CH2OH,CONHPh),(NHCH(Me)CONHMe,Ph,Ph, CH2OH,CONH-3-pyridyl),(NHCH(Me)CONHMe,Ph, Ph,CH2OH,NHCOPh),(NHCH(Me)CONHMe,Ph,Ph, CH2OH,NHCO-2-furyl),(NHCH(Me)CONHMe,Ph,Ph, CH2OH,NHCONHPh),(NHCH(Me)CONHMe,Ph,Ph, CH2OH,NHCOCONHPh),(NHCH(Me)CONHMe,Ph, OH,Me,CONHPh),(NHCH(Me)CONHMe,Ph,OH,Me, CONH-3-pyridyl),(NHCH(Me)CONHMe,Ph,OH,Me, NHCOPh),(NHCH(Me)CONHMe,Ph,OH,Me,NHCO-2-furyl),(NHCH(Me)CONHMe,Ph,OH,Me,NHCONHPh), (NHCH(Me)CONHMe,Ph,OH,Me,NHCOCONHPh), (NHCH(Me)CONHMe,Ph,OH,Et,CONHPh),(NHCH (Me)CONHMe,Ph,OH,Et,CONH-3-pyridyl),(NHCH (Me)CONHMe,Ph,OH,Et,NHCOPh),(NHCH(Me) CONHMe,Ph,OH,Et,NHCO-2-furyl),(NHCH(Me) CONHMe,Ph,OH,Et,NHCONHPh),(NHCH(Me) CONHMe,Ph,OH,Et,NHCOCONHPh),(NHCH(Me) CONHMe,Ph,OH,CH2OH,CONHPh),(NHCH(Me) CONHMe,Ph,OH,CH2OH,CONH-3-pyridyl),(NHCH (Me)CONHMe,Ph,OH,CH2OH,NHCOPh),(NHCH(Me) CONHMe,Ph,OH,CH2OH,NHCO-2-furyl),(NHCH(Me) CONHMe,Ph,OH,CH2OH,NHCONHPh),(NHCH(Me) CONHMe,Ph,OH,CH2OH,NHCOCONHPh), (NHCOCH(iPr)OH,H,H,Me,CONHPh),(NHCOCH(iPr) OH,H,H,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,H,H, Me,NHCOPh),(NHCOCH(iPr)OH,H,H,Me,NHCO-2-furyl),(NHCOCH(iPr)OH,H,H,Me,NHCONHPh), (NHCOCH(iPr)OH,H,H,Me,NHCOCONHPh), (NHCOCH(iPr)OH,H,H,Et,CONHPh),(NHCOCH(iPr) OH,H,H,Et,CONH-3-pyridyl),(NHCOCH(iPr)OH,H,Et, NHCOPh),(NHCOCH(iPr)OH,H,H,Et,NHCO-2-furyl), (NHCOCH(iPr)OH,H,H,Et,NHCONHPh),(NHCOCH (iPr)OH,H,H,Et,NHCOCONHPh),(NHCOCH(iPr)OH,H, H,CH2OH,CONHPh),(NHCOCH(iPr)OH,H,H,CH2OH, CONH-3-pyridyl),(NHCOCH(iPr)OH,H,H,CH2OH, NHCOPh),(NHCOCH(iPr)OH,H,H,CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,H,H,CH2OH,NHCONHPh), (NHCOCH(iPr)OH,H,H,CH2OH,NHCOCONHPh), (NHCOCH(iPr)OH,H,Me,Me,CONHPh),(NHCOCH (iPr)OH,H,H,Me,Me,CONH-3-pyridyl),(NHCOCH(iPr) OH,H,Me,Me,NHCOPh),(NHCOCH(iPr)OH,H,Me,Me, NHCO-2-furyl),(NHCOCH(iPr)OH,H,Me,Me, NHCONHPh),(NHCOCH(iPr)OH,H,Me,Me, NHCOCONHPh),(NHCOCH(iPr)OH,H,Me,Et, CONHPh),(NHCOCH(iPr)OH,H,Me,Et,CONH-3-pyridyl),(NHCOCH(iPr)OH,H,Me,Et,NHCOPh), (NHCOCH(iPr)OH,H,Me,Et,NHCO-2-furyl),(NHCOCH (iPr)OH,H,H,Me,Et,NHCONHPh),(NHCOCH(iPr)OH, H,Me,Et,NHCOCONHPh),(NHCOCH(iPr)OH,H,Me, CH2OH,CONHPh),(NHCOCH(iPr)OH,H,Me,CH2OH, CONH-3-pyridyl),(NHCOCH(iPr)OH,H,Me,CH2OH, NHCOPh),(NHCOCH(iPr)OH,Me,CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,H,Me,CH2OH,NHCONHPh), (NHCOCH(iPr)OH,H,Me,CH2OH,NHCOCONHPh), (NHCOCH(iPr)OH,H,Ph,Me,CONHPh),(NHCOCH(iPr) OH,H,Ph,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,H, Ph,Me,NHCOPh),(NHCOCH(iPr)OH,H,Ph,Me,NHCO-2-furyl),(NHCOCH(iPr)OH,H,Ph,Me,NHCONHPh), (NHCOCH(iPr)OH,H,Ph,Me,NHCOCONHPh), (NHCOCH(iPr)OH,H,Ph,Et,CONHPh),(NHCOCH(iPr) OH,H,Ph,Et,CONH-3-pyridyl,(NHCOCH(iPr)OH,H,Ph, Et,NHCOPh),(NHCOCH(iPr)OH,H,Ph,Et,NHCO-2-furyl),(NHCOCH(iPr)OH,H,Ph,Et,NHCONHPh), (NHCOCH(iPr)OH,H,Ph,Et,NHCOCONHPh), (NHCOCH(iPr)OH,Ph,CH2OH,CONHPh),(NHCOCH (iPr)OH,Ph,CH2OH,CONH-3-pyridyl),(NHCOCH(iPr) OH,H,Ph,CH2OH,NHCOPh),(NHCOCH(iPr)OH,H,Ph, CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,H,Ph, CH2OH,NHCONHPh),(NHCOCH(iPr)OH,H,Ph, CH2OH,NHCOCONHPh),(NHCOCH(iPr)OH,H,OH, Me,CONHPh),(NHCOCH(iPr)OH,H,OH,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,H,OH,Me,NHCOPh), (NHCOCH(iPr)OH,H,OH,Me,NHCO-2-furyl), (NHCOCH(iPr)OH,H,OH,Me,NHCONHPh),(NHCOCH (iPr)OH,H,OH,Me,NHCOCONHPh),(NHCOCH(iPr) OH,H,OH,Et,CONHPh),(NHCOCH(iPr)OH,H,OH,Et, CONH-3-pyridyl),(NHCOCH(iPr)OH,H,OH,Et, NHCOPh),(NHCOCH(iPr)OH,H,OH,Et,NHCO-2-furyl), (NHCOCH(iPr)OH,H,OH,Et,NHCONHPh),(NHCOCH (iPr)OH,H,OH,Et,NHCOCONHPh),(NHCOCH(iPr)OH, H,OH,CH2OH,CONHPh),(NHCOCH(iPr)OH,H,OH, CH2OH,CONH-3-pyridyl),(NHCOCH(iPr)OH,H,OH, CH2OH,NHCOPh),(NHCOCH(iPr)OH,H,OH,CH2OH, NHCO-2-furyl),(NHCOCH(iPr)OH,H,OH,CH2OH, NHCONHPh),(NHCOCH(iPr)OH,H,OH,CH2OH, NHCOCONHPh),(NHCOCH(iPr)OH,Me,H,Me, CONHPh),(NHCOCH(iPr)OH,Me,H,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,H,Me,NHCOPh), (NHCOCH(iPr)OH,Me,H,Me,NHCO-2-furyl), (NHCOCH(iPr)OH,Me,H,Me,NHCONHPh),(NHCOCH (iPr)OH,Me,H,Me,NHCOCONHPh),(NHCOCH(iPr) OH,Me,H,Et,CONHPh),(NHCOCH(iPr)OH,Me,H,Et, CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,H,Et, NHCOPh),(NHCOCH(iPr),OH,Me,H,Et,NHCO-2-furyl),(NHCOCH(iPr)OH,Me,H,Et,NHCONHPh), (NHCOCH(iPr)OH,Me,H,Et,NHCOCONHPh), (NHCOCH(iPr)OH,Me,H,CH2OH,CONHPh), (NHCOCH(iPr)OH,Me,H,CH2OH,CONH-3-pyridyl), (NHCOCH(iPr)OH,Me,H,CH2OH,NHCOPh), (NHCOCH(iPr)OH,Me,H,CH2OH,NHCO-2-furyl), (NHCOCH(iPr)OH,Me,H,CH2OH,NHCONHPh), (NHCOCH(iPr)OH,Me,H,CH2OH,NHCOCONHPh), (NHCOCH(iPr)OH,Me,Me,Me,CONHPh),(NHCOCH (iPr)OH,Me,Me,Me,CONH-3-pyridyl),(NHCOCH(iPr) OH,Me,Me,Me,NHCOPh),(NHCOH(iPr)OH,Me,Me, Me,NHCO-2-furyl),(NHCOCH(iPr)OH,Me,Me,Me, NHCONHPh),(NHCOCH(iPr)OH,Me,Me,Me, NHCOCONHPh),(NHCOCH(iPr)OH,Me,Me,Et, CONHPh),(NHCOCH(iPr)OOH,Me,Me,Et,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,Me,Et,NHCOPh), (NHCOCH(iPr)OH,Me,Me,Et,NHCO-2-furyl), (NHCOCH(iPr)OH,Me,Me,Et,NHCONHPh),(NHCOCH (iPr)OH,Me,Me,Et,NHCOCONHPh),(NHCOCH(iPr) OH,Me,Me,CH2OH,CONHPh),(NHCOCH(iPr)OH,Me, Me,CH2OH,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me, Me,CH2OH,NHCOPh),(NHCOCH(iPr)OH,Me,Me, CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,Me,Me, CH2OH,NHCONHPh),(NHCOC(iPr)OH,Me,Me, CH2OH,NHCOCONHPh),(NHCOCH(iPr)OH,Me,Ph, Me,CONHPh),(NHCOCH(iPr)OH,Me,Ph,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,Ph,Me,NHCOPh), (NHCO(iPr)OH,Me,Ph,Me,NHCO-2-furyl),(NHCOCH (iPr)OH,Me,Ph,Me,NHCONHPh),(NHCOCH(iPr)OH, Me,Ph,Me,NHCOCONHPh),(NHCOCH(iPr)OH,Me,Ph, Et,CONHPh),(NHCOCH(iPr)OH,Me,Ph,Et,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,Ph,Et,NHCOPh), (NHCOCH(iPr)OH,Me,Ph,Et,NHCO-2-furyl), (NHCOCH(iPr)OH,Me,Ph,Et,NHCONHPh),(NHCOCH (iPr)OH,Me,Ph,Et,NHCOCONHPh),(NHCOCH(iPr)OH, Me,Ph,CH2OH,CONHPh),(NHCOCH(iPr)OH,Me,Ph, CH2OH,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,Ph, CH2OH,NHCOPh),(NHCOCH(iPr)OH,Me,Ph,CH2OH, NHCO-2-furyl),(NHCOCH(iPr)OH,Me,Ph,CH2OH, NHCONHPh),(NHCOCH(iPr)OH,Me,Ph,CH2OH, NHCOCONHPh),(NHCOCH(iPr)OH,Me,OH,Me, CONHPh),(NHCOCH(iPr)OH,Me,OH,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,OH,Me,NHCOPh), (NHCOCH(iPr)OH,Me,OH,Me,NHCO-2-furyl), (NHCOCH(iPr)OH,Me,OH,Me,NHCONHPh), (NHCOCH(iPr)OH,Me,OH,Me,NHCOCONHPh), (NHCOCH(iPr)OH,Me,OH,Et,CONHPh),(NHCOCH (iPr)OH,Me,OH,Et,CONH-3-pyridyl),(NHCOCH(iPr) OH,Me,OH,Et,NHCOPh),(NHCOCH(iPr)OH,Me,OH, Et,NHCO-2-furyl),(NHCOCH(iPr)OH,Me,OH,Et, NHCONHPh),(NHCOCH(iPr)OH,Me,OH,Et, NHCOCONHPh),(NHCOCH(iPr)OH,Me,OH,CH2OH, CONHPh),(NHCOCH(iPr)OH,Me,OH,CH2OH,CONH-3-pyridyl),(NHCOCH(iPr)OH,Me,OH,CH2OH, NHCOPh),(NHCOCH(iPr)OH,Me,OH,CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,Me,OH,CH2OH,

NHCONHPh),(NHCOCH(iPr)OH,Me,OH,CH2OH, NHCOCONHPh),(NHCOCH(iPr)OH,Ph,H,Me, CONHPh),(NHCOCH(iPr)OH,Ph,H,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,H,Me,NHCOPh), (NHCOCH(iPr)OH,Ph,H,Me,NHCO-2-furyl), (NHCOCH(iPr)OH,Ph,H,Me,NHCONHPh),(NHCOCH (iPr)OH,Ph,H,Me,NHCOCONHPh),(NHCOCH(iPr)OH, Ph,H,Et,CONHPh),(NHCOCH(iPr)OH,Ph,H,Et,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,H,Et,NHCOPh), (NHCOCH(iPr)OH,Ph,H,Et,NHCO-2-furyl),(NHCOCH (iPr)OH,Ph,H,Et,NHCONHPh),(NHCOCH(iPr)OH,Ph, H,Et,NHCOCONHPh),(NHCOCH(iPr)OH,Ph,H, CH2OH,CONHPh),(NHCOCH(iPr)OH,Ph,H,CH2OH, CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,H,CH2OH, NHCOPh),(NHCOCH(iPr)OH,Ph,CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,Ph,H,CH2OH,NHCONHPh), (NHCOCH(iPr)OH,Ph,H,CH2OH,NHCOCONHPh), (NHCOCH(iPr)OH,Ph,Me,Me,CONHPh),(NHCOCH (iPr)OH,Ph,Me,Me,CONH-3-pyridyl),(NHCOCH(iPr) OH,Ph,Me,Me,NHCOPh),(NHCOCH(iPr)OH,Ph,Me, Me,NHCO-2-furyl),(NHCOCH(iPr)OH,Ph,Me,Me, NHCONHPh),(NHCOCH(iPr)OH,Ph,Me,Me, NHCOCONHPh),(NHCOCH(iPr)OH,Ph,Me,Et, CONHPh),(NHCOCH(iPr)OH,Ph,Me,Et,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,Me,Et,NHCOPh), (NHCOCH(iPr)OH,Ph,Me,Et,NHCO-2-furyl), (NHCOCH(iPr)OH,Ph,Me,Et,NHCONHPh),(NHCOCH (iPr)OH,Ph,Me,Et,NHCOCONHPh),(NHCOCH(iPr)OH, Ph,Me,CH2OH,CONHPh),(NHCOCH(iPr)OH,Ph,Me, CH2OH,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,Me, CH2OH,NHCOPh),(NHCOCH(iPr)OH,Ph,Me,CH2OH, NHCO-2-furyl),(NHCOCH(iPr)OH,Ph,Me,CH2OH, NHCONHPh),(NHCOCH(iPr)OH,Ph,Me,CH2OH, NHCOCONHPh),(NHCOCH(iPr)OH,Ph,Ph,Me, CONHPh),(NHCOCH(iPr)OH,Ph,Ph,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,Ph,Me,NHCOPh), (NHCOCH(iPr)OH,Ph,Ph,Me,NHCO-2-furyl), (NHCOCH(iPr)OH,Ph,Ph,Me,NHCONHPh),(NHCOCH (iPr)OH,Ph,Ph,Me,NHCOCONHPh),(NHCOCH(iPr) OH,Ph,Ph,Et,CONHPh),(NHCOCH(iPr)OH,Ph,Ph,Et, CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,Ph,Et, NHCOPh),(NHCOCH(iPr)OH,Ph,Ph,Et,NHCO-2-furyl), (NHCOCH(iPr)OH,Ph,Ph,Et,NHCONHPh),(NHCOCH (iPr)OH,Ph,Ph,Et,NHCOCONHPh),(NHCOCH(iPr)OH, Ph,Ph,CH2OH,CONHPh),(NHCOCH(iPr)OH,Ph,Ph, CH2OH,CONH-3-pyridyl),(NHCOCH(iPr),OH,Ph,Ph, CH2OH,NHCOPh),(NHCOCH(iPr)OH,Ph,Ph,CH2OH, NHCO-2-furyl),(NHCOCH(iPr)OH,Ph,Ph,CH2OH, NHCONHPh),(NHCOCH,(iPr)OH,Ph,Ph,CH2OH, NHCOCONHPh),(NHCOCH(iPr)OH,Ph,OH,Me, CONHPh),(NHCOCH(iPr)OH,Ph,OH,Me,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,OH,Me,NHCOPh), (NHCOCH(iPr)OH,Ph,OH,Me,NHCO-2-furyl), (NHCOCH(iPr)OH,Ph,OH,Me,NHCONHPh), (NHCOCH(iPr)OH,Ph,OH,Me,NHCOCONHPh), (NHCOCH(iPr)OH,Ph,OH,Et,CONHPh),(NHCOCH (iPr)OH,Ph,OH,Et,CONH-3-pyridyl),(NHCOCH(iPr) OH,Ph,OH,Et,NHCOPh),(NHCOCH(iPr)OH,Ph,OH,Et, NHCO-2-furyl),(NHCOCH(iPr)OH,Ph,OH,Et, NHCONHPh),(NHCOCH(iPr)OH,Ph,OH,Et, NHCOCONHPh,(NHCOCH(iPr)OH,Ph,OH,CH2OH, CONHPh),(NHCOCH(iPr)OH,Ph,OH,CH2OH,CONH-3-pyridyl),(NHCOCH(iPr)OH,Ph,OH,CH2OH, NHCOPh),(NHCOCH(iPr)OH,Ph,OH,CH2OH,NHCO-2-furyl),(NHCOCH(iPr)OH,Ph,OH,CH2OH, NHCONHPh),(NHCOCH(iPr)OH,Ph,OH,CH2OH, NHCOCONHPh), (NHSO2Me,H,H,Me,CONHPh),(NHSO2Me,H,H,Me,CONH-3-pyridyl),(NHSO2Me,H,H,Me,NHCOPh),(NHSO2Me,H,H,Me,NHCO-2-furyl),(NHSO2Me,H,H,Me,NHCONHPh),(NHSO2Me,H,H,Me,NHCOCONHPh),(NHSO2Me,H,H,Et,CONHPh),(NHSO2Me,H,H,Et,CONH-3-pyridyl),(NHSO2Me,H,H,Et,NHCOPh),(NHSO2Me,H,H,Et,NHCO-2-furyl),(NHSO2Me,H,H,Et,NHCONHPh),(NHSO2Me,H,H,Et,NHCOCONHPh),(NHSO2Me,H,H,CH2OH,CONHPh),(NHSO2Me,H,H,CH2OH,CONH-3-pyridyl),(NHSO2Me,H,H,CH2OH,NHCOPh),(NHSO2Me,H,H,CH2OH,NHCO-2-furyl),(NHSO2Me,H,H,CH2OH,NHCONHPh),(NHSO2Me,H,H,CH2OH,NHCOCONHPh),(NHSO2Me,H,Me,Me,CONHPh),(NHSO2Me,H,Me,Me,CONH-3-pyridyl),(NHSO2Me,H,Me,Me,NHCOPh),(NHSO2Me,H,Me,Me,NHCO-2-furyl),(NHSO2Me,H,Me,Me,NH,CONHPh),(NHS2Me,H,Me,Me,NHCOCONHPh),(NHSO2Me,H,Me,Et,CONHPh),(NHSO2Me,H,Me,Et,CONH-3-pyridyl),(NHSO2Me,H,Me,Et,NHCOPh),(NHSO2Me,H,Me,Et,NHCO-2-furyl),(NHSO2Me,H,Me,Et,NHCONHPh),(NHSO2Me,H,Me,Et,NHCOCONHPh),(NHSO2Me,H,Me,CH2OH,CONHPh),(NHSO2Me,H,Me,CH2OH,CONH-3-pyridyl),(NHSO2Me,H,Me,CH2OH,NHCOPh),(NHSO2Me,H,Me,CH2OH,NHCO-2-furyl),(NHSO2Me,H,Me,CH2OH,NHCONHPh),(NHSO2Me,H,Me,CH2OH,NHCOCONHPh),(NHSO2Me,H,Ph,Me,CONHPh),(NHSO2Me,H,Ph,Me,CONH-3-pyridyl),(NHSO2Me,H,Ph,Me,NHCOPh),(NHSO2Me,H,Ph,Me,NHCO-2-furyl),(NHSO2Me,H,Ph,Me,NHCONHPh),(NHSO2Me,H,Ph,Me,NHCOCONHPh),(NHSO2Me,H,Ph,Et,CONHPh),(NHSO2Me,H,Ph,Et,CONH-3-pyridyl),(NHSO2Me,H,Ph,Et,NHCOPh),(NHSO2Me,H,Ph,Et,NHCO-2-furyl),(NHSO2Me,H,Ph,Et,NHCONHPh),(NHSO2Me,H,Ph,Et,NHCOCONHPh),(NHSO2Me,H,Ph,CH2OH,CONHPh),(NHSO2Me,H,Ph,CH2OH,CONH-3-pyridyl),(NHSO2Me,H,Ph,CH2OH,NHCOPh),(NHSO2Me,H,Ph,CH2OH,NHCO-2-furyl),(NHSO2Me,H,Ph,CH2OH,NHCONHPh),(NHSO2Me,H,Ph,CH2OH,NHCOCONHPh),(NHSO2Me,H,OH,Me,CONHPh),(NHSO2Me,H,OH,Me,CONH-3-pyridyl),(NHSO2Me,H,OH,Me,NHCOPh),(NHSO2Me,H,OH,Me,NHCO-2-furyl),(NHSO2Me,H,OH,Me,NHCONHPh),(NHSO2Me,H,OH,Me,NHCOCONHPh),(NHSO2Me,H,OH,Et,CONHPh),(NHSO2Me,H,OH,Et,CONH-3-pyridyl),(NHSO2Me,H,OH,Et,NHCOPh),(NHSO2Me,H,OH,Et,NHCO-2-furyl),(NHSO2Me,H,OH,Et,NHCONHPh),(NHSO2Me,H,OH,Et,NHCOCONHPh),(NHSO2Me,H,OH,CH2OH,CONHPh),(NHSO2Me,H,OH,CH2H,CONH-3-pyridyl),(NHSO2Me,H,OH,CH2OH,NHCOPh),(NHSO2Me,H,OH,CH2OH,NHCO-2-furyl),(NHSO2Me,H,OH,CH2OH,NHCONHPh),(NHSO2Me,H,OH,CH2OH,NHCOCONHPh),(NHSO2Me,Me,H,Me,CONHPh),(NHSO2Me,Me,H,Me,CONH-3-pyridyl),(NHSO2Me,Me,H,Me,NHCOPh),(NHSO2Me,Me,H,Me,NHCO-2-furyl),(NHSO2Me,Me,H,Me,NHCONHPh),(NHSO2Me,Me,H,Me,NHCOCONHPh),(NHSO2Me,Me,H,Et,CONHPh),(NHSO2Me,Me,H,Et,CONH-3-pyridyl),(NHSO2Me,Me,H,Et,NHCOPh),(NHSO2Me,Me,H,Et,NHCO-2-furyl),(NHSO2Me,Me,H,Et,NHCONHPh),(NHSO2Me,Me,H,Et,NHCOCONHPh),(NHSO2Me,Me,H,CH2OH,CONHPh),(NHSO2Me,Me,H,CH2OH,CONH-3-pyridyl),(NHSO2Me,Me,H,CH2OH,NHCOPh),(NHSO2Me,Me,H,CH2OH,NHCO-2-furyl),(NHSO2Me,Me,H,CH2OH,NHCONHPh),(NHSO2Me,Me,H,CH2OH,NHCOCONHPh),(NHSO2Me,Me,Me,Me,CONHPh),(NHSO2Me,Me,Me,Me,CONH-3-pyridyl),(NHSO2Me,Me,Me,Me,NHCOPh),(NHSO2Me,Me,Me,Me,NHCO-2-furyl),(NHSO2Me,Me,Me,Me,NHCONHPh),(NHSO2Me,Me,Me,Me,NHCOCONHPh),(NHSO2Me,Me,Me,Et,CONHPh),(NHSO2Me,Me,Me,Et,CONH-3-pyridyl),(NHSO2Me,Me,Me,Et,NHCOPh),(NHSO2Me,Me,Me,Et,NHCO-2-furyl),(NHSO2Me,Me,Me,Et,NHCONHPh),(NHSO2Me,Me,Me,Et,NHCOCONHPh),(NHSO2Me,Me,Me,CH2OH,CONHPh),(NHSO2Me,Me,Me,CH2OH,CONH-3-pyridyl),(NHSO2Me,Me,Me,CH2OH,NHCOPh),(NHSO2Me,Me,Me,CH2OH,NHCO-2-furyl),(NHSO2Me,Me,Me,CH2OH,NHCONHPh),(NHSO2Me,Me,Me,CH2OH,NHCOCONHPh),(NHSO2Me,Me,Ph,Me,CONHPh),(NHSO2Me,Me,Ph,Me,CONH-3-pyridyl),(NHSO2Me,Me,Ph,Me,NHCOPh),(NHSO2Me,Me,Ph,Me,NHCO-2-furyl),(NHSO2Me,Me,Ph,Me,NHCONHPh),(NHSO2Me,Me,Ph,Me,NHCOCONHPh),(NHSO2Me,Me,Ph,Et,CONHPh),(NHSO2Me,Me,Ph,Et,CONH-3-pyridyl),(NHSO2Me,Me,Ph,Et,NHCOPh),(NHSO2Me,Me,Ph,Et,NHCO-2-furyl),(NHSO2Me,Me,Ph,Et,NHCONHPh),(NHSO2Me,Me,Ph,Et,NHCOCONHPh),(NHSO2Me,Me,Ph,CH2OH,CONHPh),(NHSO2Me,Me,Ph,CH2OH,CONH-3-pyridyl),(NHSO2Me,Me,Ph,CH2OH,NHCOPh),(NHSO2Me,Me,Ph,CH2OH,NHCO-2-furyl),(NHSO2Me,Me,Ph,CH2OH,NHCONHPh),(NHSO2Me,Me,Ph,CH2OH,NHCOCONHPh),(NHSO2Me,Me,OH,Me,CONHPh),(NHSO2Me,Me,OH,Me,CONH-3-pyridyl),(NHSO2Me,Me,OH,Me,NHCOPh),(NHSO2Me,Me,OH,Me,NHCO-2-furyl),(NHSO2Me,Me,OH,Me,NHCONHPh),(NHSO2Me,Me,OH,Me,NHCOCONHPh),(NHSO2Me,Me,OH,Et,CONHPh),(NHSO2Me,Me,OH,Et,CONH-3-pyridyl),(NHSO2Me,Me,OH,Et,NHCOPh),(NHSO2Me,Me,OH,Et,NHCO-2-furyl),(NHSO2Me,Me,OH,Et,NHCONHPh),(NHSO2Me,Me,OH,Et,NHCOCONHPh),(NHSO2Me,Me,OH,CH2OH,CONHPh),(NHSO2Me,Me,OH,CH2OH,CONH-3-pyridyl),(NHSO2Me,Me,OH,CH2OH,NHCOPh),(NHSO2Me,Me,OH,CH2OH,NHCO-2-furyl),(NHSO2Me,Me,OH,CH2OH,NHCONHPh),(NHSO2Me,Me,OH,CH2OH,NHCOCONHPh),(NHSO2Me,Ph,H,Me,CONHPh),(NHSO2Me,Ph,H,Me,CONH-3-pyridyl),(NHSO2Me,Ph,H,Me,NHCOPh),(NHSO2Me,Ph,H,Me,NHCO-2-furyl),(NHSO2Me,Ph,H,Me,NHCONHPh),(NHSO2Me,Ph,H,Me,NHCOCONHPh),(NHSO2Me,Ph,H,Et,CONHPh),(NHSO2Me,Ph,H,Et,CONH-3-pyridyl),(NHSO2Me,Ph,H,Et,NHCOPh),(NHSO2Me,Ph,H,Et,NHCO-2-furyl),(NHSO2Me,Ph,H,Et,NHCONHPh),(NHSO2Me,Ph,H,Et,NHCOCONHPh),(NHSO2Me,Ph,H,CH2OH,CONHPh),(NHSO2Me,Ph,H,CH2OH,CONH-3-pyridyl),(NHSO2Me,Ph,H,CH2OH,NHCOPh),(NHSO2Me,Ph,H,CH2OH,NHCO-2-furyl),(NHSO2Me,Ph,H,CH2OH,NHCONHPh),(NHSO2Me,Ph,H,CH2OH,NHCOCONHPh),(NHSO2Me,Ph,Me,Me,CONHPh),(NHSO2Me,Ph,Me,Me,CONH-3-pyridyl),(NHSO2Me,Ph,Me,Me,NHCOPh),(NHSO2Me,Ph,Me,Me,NHCO-2-furyl),(NHSO2Me,Ph,Me,Me,NHCONHPh),(NHSO2Me,Ph,Me,Me,NHCOCONHPh),(NHSO2Me,Ph,Me,Et,CONHPh),(NHSO2Me,Ph,Me,Et,CONH-3-pyridyl),(NHSO2Me,Ph,Me,Et,NHCOPh),(NHSO2Me,Ph,Me,Et,NHCO-2-furyl),(NHSO2Me,Ph,Me,Et,NHCONHPh),(NHSO2Me,Ph,Me,Et,NHCOCONHPh),(NHSO2Me,Ph,Me,CH2OH,CONHPh),(NHSO2Me,Ph,Me,CH2OH,CONH-3-pyridyl),(NHSO2Me,Ph,Me,CH2OH,NHCOPh),(NHSO2Me,Ph,Me,CH2OH,NHCO-

2-furyl),(NHSO2Me,Ph,Me,CH2OH,NHCONHPh), (NHSO2Me,Ph,Me,CH2OH,NHCOCONHPh), (NHSO2Me,Ph,Ph,Me,CONHPh),(NHSO2Me,Ph,Ph, Me,CONH-3-pyridyl),(NHSO2Me,Ph,Ph,Me,NHCOPh), (NHSO2Me,Ph,Ph,Me,NHCO-2-furyl),(NHSO2Me,Ph, Ph,Me,NHCONHPh),(NHSO2Me,Ph,Ph,Me, NHCOCONHPh),(NHSO2Me,Ph,Ph,Et,CONHPh), (NHSO2Me,Ph,Ph,Et,CONH-3-pyridyl),(NHSO2Me,Ph, Ph,Et,NHCOPh),(NHSO2Me,Ph,Ph,Et,NHCO-2-furyl), (NHSO2Me,Ph,Ph,Et,NHCONHPh),(NHSO2Me,Ph,Ph, Et,NHCOCONHPh),(NHSO2Me,Ph,Ph,CH2OH, CONHPh),(NHSO2Me,Ph,Ph,CH2OH,CONH-3- pyridyl),(NHSO2Me,Ph,Ph,CH2OH,NHCOPh), (NHSO2Me,Ph,Ph,CH2OH,NHCO-2-furyl),(NHSO2Me, Ph,Ph,CH2OH,NHCONHPh),(NHSO2Me,Ph,Ph, CH2OH,NHCOCONHPh),(NHSO2Me,Ph,OH,Me, CONHPh),(NHSO2Me,Ph,OH,Me,CONH-3-pyridyl), (NHSO2Me,Ph,OH,Me,NHCOPh),(NHSO2Me,Ph,OH, Me,NHCO-2-furyl),(NHSO2Me,Ph,OH,Me, NHCONHPh),(NHSO2Me,Ph,OH,Me,NHCOCONHPh), (NHSO2Me,Ph,OH,Et,CONHPh),(NHSO2Me,Ph,OH, Et,CONH-3-pyridyl),(NHSO2Me,Ph,OH,Et,NHCOPh), (NHSO2Me,Ph,OH,Et,NHCO-2-furyl),(NHSO2Me,Ph, OH,Et,NHCONHPh),(NHSO2Me,Ph,OH,Et, NHCOCONHPh),(NHSO2Me,Ph,OH,CH2OH, CONHPh),(NHSO2Me,Ph,OH,CH2OH,CONH-3- pyridyl),(NHSO2Me,Ph,OH,CH2OH,NHCOPh), (NHSO2Me,Ph,OH,CH2OH,NHCO-2-furyl), (NHSO2Me,Ph,OH,CH2OH,NHCONHPh),(NHSO2Me, Ph,OH,CH2OH,NHCOCONHPh),

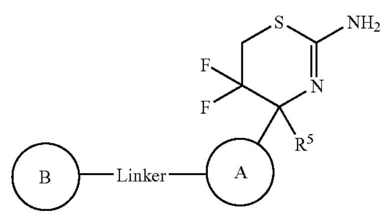
(NH2,H,H,Me,CONHPh),(NH2,H,H,Me,CONH-3-pyridyl),(NH2,H,H,Me,NHCOPh),(NH2,H,H,Me,NHCO-2-furyl),(NH2,H,H,Me,NHCONHPh),(NH2,H,H,Me, NHCOCONHPh),(NH2,H,H,Et,CONHPh),(NH2,H,H,Et, CONH-3-pyridyl),(NH2,H,H,Et,NHCOPh),(NH2,H,H, Et,NHCO-2-furyl),(NH2,H,H,Et,NHCONHPh),(NH2,H, H,Et,NHCOCONHPh),(NH2,H,H,CH2OH,CONHPh), (NH2,H,H,CH2OH,CONH-3-pyridyl),(NH2,H,H, CH2OH,NHCONHPh),(NH2,H,H,CH2OH, NHCOCONHPh),(NH2,H,Me,Me,CONHPh),(NH2,H, Me,Me,CONH-3-pyridyl),(NH2,H,Me,Me, NHCONHPh),(NH2,H,Me,Me,NHCOCONHPh),(NH2, H,Me,Et,CONHPh),(NH2,H,Me,Et,CONH-3-pyridyl), (NH2,H,Me,Et,NHCOPh),(NH2,H,Me,Et,NHCO-2- furyl),(NH2,H,Me,Et,NHCONHPh),(NH2,H,Me,Et, NHCOCONHPh),(NH2,H,Me,CH2OH,CONHPh),(NH2, H,Me,CH2OH,CONH-3-pyridyl),(NH2,H,Me,CH2OH, NHCONHPR(NH2,H,Me,CH2OH,NHCOCONHPh), (NH2,H,Ph,Me,CONHPh),(NH2,H,Ph,Me,CONH-3- pyridyl),(NH2,H,Ph,Me,NHCONHPh),(NH2,H,Ph,Me, NHCOCONHPh),(NH2,H,Ph,Et,CONHPh),(NH2,H,Ph, Et,CONH-3-pyridyl),(NH2,H,Ph,Et,NHCOPh),(NH2,H, Ph,Et,NHCO-2-furyl),(NH2,H,Ph,Et,NHCONHPh), (NH2,H,Ph,Et,NHCOCONHPh),(NH2,H,Ph,CH2OH, CONHPh),(NH2,H,Ph,CH2OH,CONH-3-pyridyl),(NH2, H,Ph,CH2OH,NHCONHPh),(NH2,H,Ph,CH2OH, NHCOCONHPh),(NH2,H,OH,Me,CONHPh),(NH2,H, OH,Me,CONH-3-pyridyl),(NH2,H,OH,Me, NHCONHPh),(NH2,H,OH,Me,NHCOCONHPh),(NH2, H,OH,Et,CONHPh),(NH2,H,OH,Et,CONH-3-pyridyl), (NH2,H,OH,Et,NHCOPh),(NH2,H,OH,Et,NHCO-2- furyl),(NH2,H,OH,Et,NHCONHPh),(NH2,H,OH,Et, NHCOCONHPh),(NH2,H,OH,CH2OH,CONHPh), (NH2,H,OH,CH2OH,CONH-3-pyridyl),(NH2,H,OH, CH2OH,NHCONHPh),(NH2,H,OH,CH2OH, NHCOCONHPh),(NH2,Me,H,Me,CONHPh),(NH2,Me, H,Me,CONH-3-pyridyl),(NH2,Me,H,Me,NHCONHPh),

(NH2Me,H,Me,NHCOCONHPh),(NH2,Me,H,Et, CONHPh),(NH2,Me,H,Et,CONH-3-pyridyl),(NH2,Me, H,Et,NHCOPh),(NH2,Me,H,Et,NHCO-2-furyl),(NH2, Me,H,Et,NHCONHPh),(NH2,Me,H,Et, NHCOCONHPh),(NH2,Me,H,CH2OH,CONHPh),(NH2, Me,H,CH2OH,CONH-3-pyridyl),(NH2,Me,H,CH2OH, NHCONHPh),(NH2,Me,H,CH2OH,NHCOCONHPh), (NH2,Me,Me,Me,CONHPh),(NH2,Me,Me,Me,CONH- 3-pyridyl),(NH2,Me,Me,Me,NHCONHPh),(NH2,Me, Me,Me,NHCOCONHPh),(NH2,Me,Me,Et,CONHPh), (NH2,Me,Me,Et,CONH-3-pyridyl),(NH2,Me,Me,Et, NHCOPh),(NH2,Me,Me,Et,NHCO-2-furyl),(NH2,Me, Me,Et,NHCONHPh),(NH2,Me,Me,Et,NHCOCONHPh), (NH2,Me,Me,CH2OH,CONHPh),(NH2,Me,Me, CH2OH,CONH-3-pyridyl),(NH2,Me,Me,CH2OH, NHCONHPh),(NH2,Me,Me,CH2OH,NHCOCONHPh), (NH2,Me,Ph,Me,CONHPh),(NH2,Me,Ph,Me,CONH-3- pyridyl),(NH2,Me,Ph,Me,NHCOPh),(NH2,Me,Ph,Me, NHCO-2-furyl),(NH2,Me,Ph,Me,NHCONHPh),(NH2, Me,Ph,Me,NHCOCONHPh),(NH2,Me,Ph,Et,CONHPh), (NH2,Me,Ph,Et,CONH-3-pyridyl),(NH2,Me,Ph,Et, NHCOPh),(NH2,Me,Ph,Et,NHCO-2-furyl),(NH2,Me,Ph, Et,NHCONHPh),(NH2,Me,Ph,Et,NHCOCONHPh), (NH2,Me,Ph,CH2OH,CONHPh),(NH2,Me,Ph,CH2OH, CONH-3-pyridyl),(NH2,Me,Ph,CH2OH,NHCONHPh), (NH2,Me,Ph,CH2OH,NHCOCONHPh),(NH2,Me,OH, Me,CONHPh),(NH2,Me,OH,Me,CONH-3-pyridyl), (NH2,Me,OH,Me,NHCONHPh),(NH2,Me,OH,Me, NHCOCONHPh),(NH2,Me,OH,Et,CONHPh),(NH2,Me, OH,Et,CONH-3-pyridyl),(NH2,Me,OH,Et,NHCOPh), (NH2,Me,OH,Et,NHCO-2-furyl),(NH2,Me,OH,Et, NHCONHPh),(NH2,Me,OH,Et,NHCOCONHPh),(NH2, Me,OH,CH2OH,CONHPh),(NH2,Me,OH,CH2OH, CONH-3-pyridyl),(NH2,Me,OH,CH2OH,NHCONHPh), (NH2,Me,OH,CH2OH,NHCOCONHPh),(NH2,Ph,H, Me,CONHPh),(NH2,Ph,H,Me,CONH-3-pyridyl),(NH2, Ph,H,Me,NHCONHPh),(NH2,Ph,H,Me, NHCOCONHPh),(NH2,Ph,H,Et,CONHPh),(NH2,Ph,H, Et,CONH-3-pyridyl),(NH2,Ph,H,Et,NHCOPh),(NH2,Ph, H,Et,NHCO-2-furyl),(NH2,Ph,H,Et,NHCONHPh), (NH2,Ph,H,Et,NHCOCONHPh),(NH2,Ph,H,CH2OH, CONHPh),(NH2,Ph,H,CH2OH,CONH-3-pyridyl),(NH2, Ph,H,(H2OH,NHCONHPh),(NH2,Ph,H,CH2OH, NHCOCONHPh),(NH2,Ph,Me,Me,CONHPh),(NH2,Ph, Me,Me,CONH-3-pyridyl),(NH2,Ph,Me,Me, NHCONHPh),(NH2,Ph,Me,Me,NHCOCONHPh),(NH2, Ph,Me,Et,CONHPh),(NH2,Ph,Me,Et,CONH-3-pyridyl), (NH2,Ph,Me,Et,NHCOPh),(NH2,Ph,Me,Et,NHCO-2- furyl),(NH2,Ph,Me,Et,NHCONHPh),(NH2,Ph,Me,Et, NHCOCONHPh),(NH2,Ph,Me,CH2OH,CONHPh), (NH2,Ph,Me,CH2OH,CONH-3-pyridyl),(NH2,Ph,Me, CH2OH,NHCONHPh),(NH2,Ph,Me,CH2OH, NHCOCONHPh),(NH2,Ph,Ph,Me,CONHPh),(NH2,Ph, Ph,Me,CONH-3-pyridyl),(NH2,Ph,Ph,Me,NHCOPh), (NH2,Ph,Ph,Me,NHCO-2-furyl),(NH2,Ph,Ph,Me, NHCONHPh),(NH2,Ph,Ph,Me,NHCOCONHPh),(NH2, Ph,Ph,Et,CONHPh),(NH2,Ph,Ph,CONH-3-pyridyl), (NH2,Ph,Ph,Et,NHCOPh),(NH2,Ph,Ph,Et,NHCO-2- furyl),(NH2,Ph,Ph,Et,NHCONHPh),(NH2,Ph,Ph,Et, NHCOCONHPh),(NH2,Ph,Ph,CH2OH,CONHPh), (NH2,Ph,Ph,CH2OH,CONH-3-pyridyl),(NH2,Ph,Ph, CH2OH,NHCOPh),(NH2,Ph,Ph,CH2OH,NHCO-2- furyl),(NH2,Ph,Ph,CH2OH,NHCONHPh),(NH2,Ph,Ph, CH2OH,NHCOCONHPh),(NH2,Ph,OH,Me,CONHPh), (NH2,Ph,OH,Me,CONH-3-pyridyl),(NH2,Ph,OH,Me, NHCONHPh),(NH2,Ph,OH,Me,NHCOCONHPh),(NH2, Ph,OH,Et,CONHPh),(NH2,Ph,OH,Et,CONH-3-pyridyl),

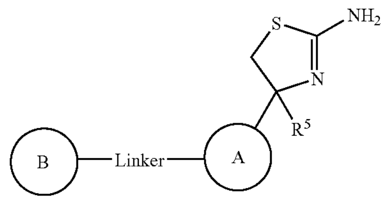
(NH2,Ph,OH,Et,NHCOPh),(NH2,Ph,OH,Et,NHCO-2-furyl),(NH2,Ph,OH,Et,NHCONHPh),(NH2,Ph,OH,Et,NHCOCONHPh),(NH2,Ph,OH,CH2OH,CONHPh),(NH2,Ph,OH,CH2OH,CONH-3-pyridyl),(NH2,Ph,OH,CH2OH,NHCOPh),(NH2,Ph,OH,CH2OH,NHCO-2-furyl),(NH2,Ph,OH,CH2OH,NHCONHPh),(NH2,Ph,OH,CH2OH,NHCOCONHPh),
(NHCH2CH(OH)CH2OH,H,H,Me,CONHPh),(NHCH2CH(OH)CH2OH,H,H,Me,CONH-3-pyridyl),(NHCH2CH(OH)CH2OH,H,H,Me,NHCOPh),(NHCH2CH(OH)CH2OH,H,H,Me,NHCO-2-furyl),(NHCH2CH(OH)CH2OH,H,H,Me,NHCONHPh),(NHCH2CH(OH)CH2OH,H,H,Me,NHCOCONHPh),(NHCH2CH(OH)CH2OMe,H,H,Me,CONHPh),(NHCH2CH(OH)CH2OMe,H,H,Me,CONH-3-pyridyl),(NHCH2CH(OH)CH2OMe,H,H,Me,NHCOPh),(NHCH2CH(OH)CH2OMe,H,H,Me,NHCO-2-furyl),(NHCH2CH(OH)CH2OMe,H,H,Me,NHCONHPh),(NHCH2CH(OH)CH2OMe,H,H,Me,NHCOCONHPh),(NHCH2CH(OH)CH2NH2,H,H,Me,CONHPh),(NHCH2CH(OH)CH2NH2,H,H,Me,CONH-3-pyridyl),(NHCH2CH(OH)CH2NH2,H,H,Me,NHCOPh),(NHCH2CH(OH)CH2NH2,H,H,Me,NHCO-2-furyl),(NHCH2CH(OH)CH2NH2,H,H,Me,NHCONHPh),(NHCH2CH(OH)CH2NH2,H,H,Me,NHCOCONHPh),(NHCH2CH(OH)CH2NHMe,H,H,Me,CONHPh),(NHCH2CH(OH)CH2NHMe,H,H,Me,CONH-3-pyridyl),(NHCH2CH(OH)CH2NHMe,H,Me,NHCOPh),(NHCH2CH(OH)CH2NHMe,H,H,Me,NHCO-2-furyl),(NHCH2CH(OH)CH2NHMe,H,H,Me,NHCONHPh),(NHCH2CH(OH)CH2NHMe,H,H,Me,NHCOCONHPh),(NHCH2CH(OH)CH2NHCOMe,H,H,Me,CONHPh),(NHCH2CH(OH)CH2NHCOMe,H,H,Me,CONH-3-pyridyl),(NHCH2CH(OH)CH2NHCOMe,H,H,Me,NHCOPh),(NHCH2CH(OH)CH2NHCOMe,H,H,Me,NHCO-2-furyl),
(NHCH2CH(OH)CH2NHCOMe,H,H,Me,NHCONHPh),
(NHCH2CH(OH)CH2NHCOMe,H,H,Me,NHCOCONHPh),(NHCH2CH(OH)CH2N(Me)Me,H,H,Me,CONHPh),(NHCH2CH(OH)CH2N(Me)Me,H,H,Me,CONH-3-pyridyl),(NHCH2CH(OH)CH2N(Me)Me,H,H,Me,NHCOPh),(NHCH2CH(OH)CH2N(Me)Me,H,H,Me,NHCO-2-furyl),(NHCH2CH(OH)CH2N(Me)Me,H,H,Me,NHCONHPh),(NHCH2CH(OH)CH2N(Me)Me,H,H,Me,NHCOCONHPh),(NHC(O)C(O)NH2,H,H,Me,CONHPh),(NHC(O)C(O)NH2,H,H,Me,CONH-3-pyridyl),(NHC(O)C(O)NH2,H,Me,NHCOPh),(NHC(O)C(O)NH2,H,H,Me,NHCO-2-furyl),(NHC(O)C(O)NH2,H,H,Me,NHCONHPh),(NHC(O)C(O)NH2,H,H,Me,NHCOCONHPh),(NHC(O)C(O)NHMe,H,H,Me,CONHPh),(NHC(O)C(O)NHMe,H,H,Me,CONH-3-pyridyl),(NHC(O)C(O)NHMe,H,H,Me,NHCOPh),(NHC(O)C(O)NHMe,H,H,Me,NHCO-2-furyl),(NHC(O)C(O)NHMe,H,H,Me,NHCONHPh),(NHC(O)C(O)NHMe,H,H,Me,NHCOCONHPh),(NHC(O)C(O)N(Me)Me,H,H,Me,CONHPh),(NHC(O)C(O)N(Me)Me,H,H,Me,CONH-3-pyridyl),(NHC(O)C(O)N(Me)Me,H,H,Me,NHCOPh),(NHC(O)C(O)N(Me)Me,H,H,Me,NHCO-2-furyl),(NHC(O)C(O)N(Me)Me,H,H,Me,NHCONHPh),(NHC(O)C(O)N(Me)Me,H,H,Me,NHCOCONHPh),

[Chemical formula 85]

(Ii)



(Ij)



In above structural formula (Ii) or (Ij), the combination of B, Linker, A, R^5 (B, Linker, A, R^5) are the following compounds.

TABLE 169

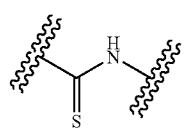
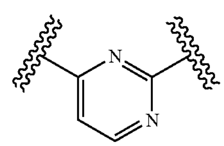
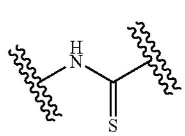
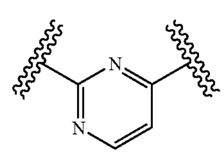
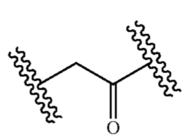
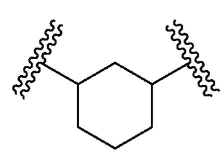
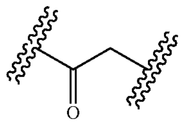
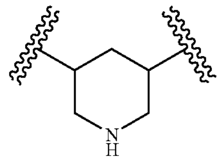
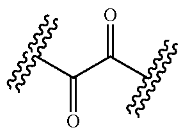
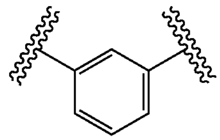
	B		Linker		A		R5
B1	Ph-	L1		A1		R51	—CN
B2	2-pyridyl-	L2		A2		R52	—C≡CH
B3	4-Me-Ph-	L3		A3		R53	—C≡CMe

TABLE 169-continued

B		Linker		A		R5	
B4	cHex-	L4		A4		R54	—CF3
B5	cHex-CH2—	L5		A5		R55	—CH2Cl
						R56	CHCl2

(B, Linker, A, R^5)=(B1,L1,A1,R51),(B1,L1,A1,R52),(B1,L1,A1,R53),(B1,L1,A1,R54),(B1,L1,A1,R55),(B1,L1,A1,R56),(B1,L1,A2,R51),(B1,L1,A2,R52),(B1,L1,A2,R53),(B1,L1,A2,R54),(B1,L1,A2,R55),(B1,L1,A2,R56),(B1,L1,A3,R51),(B1,L1,A3,R52),(B1,L1,A3,R53),(B1,L1,A3,R54),(B1,L1,A3,R55),(B1,L1,A3,R56),(B1,L1,A4,R51),(B1,L1,A4,R52),(B1,L1,A4,R53),(B1,L1,A4,R54),(B1,L1,A4,R55),(B1,L1,A4,R56),(B1,L1,A5,R51),(B1,L1,A5,R52),(B1,L1,A5,R53),(B1,L1,A5,R54),(B1,L1,A5,R55),(B1,L1,A5,R56),(B1,L2,A1,R51),(B1,L2,A 1,R52),(B1,L2,A 1,R53),(B1,L2,A1,R54),(B1,L2,A1,R55),(B1,L2,A1,R56),(B1,L2,A2,R51),(B1,L2,A2,R52),(B1,L2,A2,R53),(B1,L2,A2,R54),(B1,L2,A2,R55),(B1,L2,A2,R56),(B1,L2,A3,R51),(B1,L2,A3,R52),(B1,L2,A3,R53),(B1,L2,A3,R54),(B1,L2,A3,R55),(B1,L2,A3,R56),(B1,L2,A4,R51),(B1,L2,A4,R52),(B1,L2,A4,R53),(B1,L2,A4,R54),(B1,L2,A4,R55),(B1,L2,A4,R56),(B1,L2,A5,R51),(B1,L2,A5,R52),(B1,L2,A5,R53),(B1,L2,A5,R54),(B1,L2,A5,R55),(B1,L2,A5,R56),(B1,L3,A1,R51),(B1,L3,A1,R52),(B1,L3,A1,R53),(B1,L3,A1,R54),(B1,L3,A1,R55),(B1,L3,A1,R56),(B1,L3,A2,R51),(B1,L3,A2,R52),(B1,L3,A2,R53),(B1,L3,A2,R54),(B1,L3,A2,R55),(B1,L3,A2,R56),(B1,L3,A3,R51),(B1,L3,A3,R52),(B1,L3,A3,R53),(B1,L3,A3,R54),(B1,L3,A3,R55),(B1,L3,A3,R56),(B1,L3,A4,R51),(B1,L3,A4,R52),(B1,L3,A4,R53),(B1,L3,A4,R54),(B1,L3,A4,R55),(B1,L3,A4,R56),(B1,L3,A5,R51),(B1,L3,A5,R52),(B1,L3,A5,R53),(B1,L3,A5,R54),(B1,L3,A5,R55),(B1,L3,A5,R56),(B1,L4,A 1,R51),(B1,L4,A1,R52),(B1,L4,A1,R53),(B1,L4,A1,R54),(B1,L4,A1,R55),(B1,L4,A1,R56),(B1,L4,A2,R51),(B1,L4,A2,R52),(B1,L4,A2,R53),(B53),(B1,L4,A2,R54),(B1,L4,A2,R55),(B1,L4,A2,R56),(B1,L4,A3,R51),(B1,L4,A3,R52),(B1,L4,A3,R53),(B1,L4,A3,R54),(B1,L4,A3,R55),(B1,L4,A3,R56),(B1,L4,A4,R51),(B1,L4,A4,R52),(B1,L4,A4,R53),(B1,L4,A4,R54),(B1,L4,A4,R55),(B1,L4,A4,R56),(B1,L4,A5,R51),(B1,L4,A5,R52),(B1,L4,A5,R53),(B1,L4,A5,R54),(B1,L4,A5,R55),(B1,L4,A5,R56),(B1,L5,A1,R51),(B1,L5,A1,R52),(B1,L5,A1,R53),(B1,L5,A1,R54),(B1,L5,A1,R55),(B1,L5,A1,R56),(B1,L5,A2,R51),(B1,L5,A2,R52),(B1,L5,A2,R53),(B1,L5,A2,R54),(B1,L5,A2,R55),(B1,L5,A2,R56),(B1,L5,A3,R51),(B1,L5,A3,R52),(B1,L5A3,R53),(B1,L5,A3,R54),(B1,L5,A3,R55),(B1,L5,A3,R56),(B1,L5,A4,R51),(B1,,L5,A4,R52),(B1,L5,A4,R53),(B1,L5,A4,R54),(B1,L5,A4,R55),(B1,L5,A4,R56),(B1,L5,A5,R51),(B1,L5,A5,R52),(B1,L5,A5,R53),(B1,L5,A5,R54),(B1,L5,A5,R55),(B1,L5,A5,R56),(B2,L1,A1,R51),(B2,L1,A1,R52),(B2,L1,A1,R53),(B2,L1,A1,R54),(B2,L1,A1,R55),(B2,L1,A1,R56),(B2,L1,A2,R51),(B2,L1,A2,R52),(B2,L1,A2,R53),(B2,L1,A2,R54),(B2,L1,A2,R55),(B2,L1,A2,R56),(B2,L1,A3,R51),(B2,L1,A3,R52),(B2,L1,A3,R53),(B2,L1,A3,R54),(B2,L1,A3,R55),(B2,L1,A3,R56),(B2,L1,A4,R51),(B2,L1,A4,R52),(B2,L1,A4,R53),(B2,L1,A4,R54),(B2,L1,A4,R55),(B2,L1,A4,R56),(B2,L1,A5,R51),(B2,L1,A5,R52),(B2,L1,A5,R53),(B2,L1,A5,R54),(B2,L1,A5,R55),(B2,L1,A5,R56),(B2,L2,A1,R51),(B2,L2,A1,R52),(B2,L2,A1,R53),(B2,L2,A1,R54),(B2,L2,A1,R55),(B2,L2,A1,R56),(B2,L2,A2,R51),(B2,L2,A2,R52),(B2,L2,A2,R53),(B2,L2,A2,R54),(B2,L2,A2,R55),(B2,L2,A2,R56),(B2,L2,A3,R51),(B2,L2,A3,R52),(B2,L2,A3,R53),(B2,L2,A3,R54),(B2,L2,A3,R55),(B2,L2,A3,R56),(B2,L2,A4,R51),(B2,L2,A4,R52),(B2,L2,A4,R53),(B2,L2,A4,R54),(B2,L2,A4,R55),(B2,L2,A4,R56),(B2,L2,A5,R51),(B2,L2,A5,R52),(B2,L2,A5,R53),(B2,L2,A5,R54),(B2,L2,A5,R55),(B2,L2,A5,R56),(B2,L3,A1,R51),(B2,L3,A1,R52),(B2,L3,A1,R53),(B2,L3,A1,R54),(B2,L3,A1,R55),(B2,L3,R56),(B2,L3,A2,R51),(B2,L3,A2,R52),(B2,L3,A2,R53),(B2,L3,A2,R54),(B2,L3,A2,R55),(B2,L3,A2,R56),(B2,L3,A3,R51),(B2,L3,A3,R52),(B2,L3,A3,R53),(B2,L3,A3,R54),(B2,L3,A3R55),(B2,L3,A3,R56),(B2,L3,A4,R51),(B2,L3,A4,R52),(B2,L3,A4,R53),(B2,L3,A4,R54),(B2,L3,A4,R55),(B2,L3,A4,R56),(B2,L3,A5,R51),(B2,L3,A5,R52),(B2,L3,A5,R53),(B2,L3,A5,R54),(B2,L3,A5,R55),(B2,L3,A5,R56),(B2,L4,A1,R51),(B2,L4,A1,R52),(B2,L4,A1,R53),(B2,L4,A1,R54),(B2,L4,A1,R55),(B2,L4,A1,R56),(B2,L4,A2,R51),(B2,L4,A2,R52),(B2,L4,A2,R53),(B2,L4,A2,R54),(B2,L4,A2,R55),(B2,L4,A2,R56),(B2,L4,A3,R51),(B2,L4,A3,R52),(B2,L4,A3,R53),(B2,L4,A3,R54),(B2,L4,A3,R55),(B2,L4,A3,R56),(B2,L4,A4,R51),(B2,L4,A4,R52),(B2,L4,A4,R53),(B2,L4,A4,R54),(B2,L4,A4,R55),(B2,L4,A4,R56),(B2,L4,A5,R51),(B2,L4,A5,R52),(B2,L4,A5,R53),(B2,L4,A5,R54),(B2,L4,A5,R55),(B2,L4,A5,R56),(B2,L5,A1,R51),(B2,L5,A1,R52),(B2,L5,A1,R53),(B2,L5,A1,R54),(B2,L5,A1,R55),(B2,L5,A1,R56),(B2,L5,A2,R51),(B2,L5A2,R52),(B2,L5,A2,R53),(B2,L5,A2,R54),(B2,L5,A2,R55),(B2,L5,A2,R56),(B2,L5,A3,R51),(B2,L5,A3,R52),(B2,L5,A3,R53),(B2,L5,A3,R54),(B2,L5,A3,R55),(B2,L5,A3,R56),(B2,L5,A4,R51),(B2,L5,A4,R52),(B2,L5,A4,R53),(B2,L5,A4,R54),(B2,L5,A4,R55),(B2,L5,A4,R56),(B2,L5,A5,R51),(B2,L5,A5,R52),(B2,L5,A5,R53),(B2,L5,A5,R54),(B2,L5,A5,R55),(B2,L5,A5,R56),(B3,L1,A1,R51),(B3,L1,A1,R52),(B3,L1,A1,R53),(B3,L1,A1,R54),(B3,

L1,A1,R55),(B3,L1,A1,R56),(B3,L1,A2,R51),(B3,L1,A2,R52),(B3,L1,A2,R53),(B3,L1,A2,R54),(B3,L1,A2,R55),(B3,L1,A2,R56),(B3,L1,A3,R51),(B3,L1,A3,R52),(B3,L1,A3,R53),(B3,L1,A3,R54),(B3,L1,A3,R55),(B3,L1,A3,R56),(B3,L1,A4,R51),(B3,L1,A4,R52),(B3,L1,A4,R53),(B3,L1,A4,R54),(B3,L1,A4,R55),(B3,L1,A4,R56),(B3,L1,A5,R51),(B3,L1,A5,R52),(B3,L1,A5,R53),(B3,L1,A5,R54),(B3,L1,A5,R55),(B3,L1,A5,R56),(B3,L2,A1,R51),(B3,L2,A1,R52),(B3,L2,A1,R53),(B3,L2,A1,R54),(B3,L2,A1,R55),(B3,L2,A1,R56),(B3,L2,A2,R51),(B3,L2,A2,R52),(B3,L2,A2,R53),(B3,L2,A2,R54),(B3,L2,A2,R55),(B3,L2,A2,R56),(B3,L2,A3,R51),(B3,L2,A3,R52),(B3,L2,A3,R53),(B3,L2,A3,R54),(B3,L2,A3,R55),(B3,L2,A3,R56),(B3,L2,A4,R51),(B3,L2,A4,R52),(B3,L2,A4,R53),(B3,L2,A4,R54),(B3,L2,A4,R55),(B3,L2,A4,R56),(B3,L2,A5,R51),(B3,L2,A5,R52),(B3,L2,A5,R53),(B3,L2,A5,R54),(B3,L2,A5,R55),(B3,L2,A5,R56),(B3,L3,A1,R51),(B3,L3,A1,R52),(B3,L3,A1,R53),(B3,L3,A1,R54),(B3,L3,A1,R55),(B3,L3,A1,R56),(B3,L3,A2,R51),(B3,L3,A2,R52),(B3,L3,A2,R53),(B3,L3,A2,R54),(B3,L3,A2,R55),(B3,L3,A2,R56),(B3,L3,A3,R51),(B3,1,3,A3,R52),(B3,L3,A3,R53),(B3,L3,A3,R54),(B3,L3,A3,R55),(B3,L3,A3,R56),(B3,L3,A4,R51),(B3,L3,A4,R52),(B3,L3,A4,R53),(B3,L3,A4,R54),(B3,L3,A4,R55),(B3,L3,A4,R56),(B3,L3,A5,R51),(B3,L3,A5,R52),(B3,L3,A5,R53),(B3,L3,A5,R54),(B3,L3,A5,R55),(B3,L3,A5,R56),(B3,L4,A1,R51),(B3,L4,A1,R52),(B3,L4,A1,R53),(B3,L4,A1,R54),(B3,L4,A1,R55),(B3,L4,A1,R56),(B3,L4,A2,R51),(B3,L4,A2,R52),(B3,L4,A2,R53),(B3,L4,A2,R54),(B3,L4,A2,R55),(B3,L4,A2,R56),(B3,L4,A3,R51),(B3,L4,A3,R52),(B3,L4,A3,R53),(B3,L4,A3,R54),(B3,L4,A3,R55),(B3,L4,A3,R56),(B3,L4,A4,R51),(B3,L4,A4,R52),(B3,L4,A4,R53),(B3,L4,A4,R54),(B3,L4,A4,R55),(B3,L4,A4,R56),(B3,L4,A5,R51),(B3,L4,A5,R52),(B3,L4,A5,R53),(B3,L4,A5,R54),(B3,L4,A5,R55),(B3,L4,A5,R56),(B3,L5,A1,R51),(B3,L5,A1,R52),(B3,L5,A1,R53),(B3,L5,A1,R54),(B3,L5,A1,R55),(B3,L5,A1,R56),(B3,L5,A2,R51),(B3,L5,A2,R52),(B3,L5,A2,R53),(B3,L5,A2,R54),(B3,L5,A2,R55),(B3,L5,A2,R56),(B3,L5,A3,R51),(B3,L5,A3,R52),(B3,L5,A3,R53),(B3,L5,A3,R54),(B3,L5,A3,R55),(B3,L5,A3,R56),(B3,L5,A4,R51),(B3,L5,A4,R52),(B3,L5,A4,R53),(B3,L5,A4,R54),(B3,L5,A4,R55),(B3,L5,A4,R56),(B3,L5,A5,R51),(B3,L5,A5,R52),(B3,L5,A5,R53),(B3,L5,A5,R54),(B3,L5,A5,R55),(B3,L5,A5,R56),(B4,L1,A1,R51),(B4,L1,A1,R52),(B4,L1,A1,R53),(B4,L1,A1,R54),(B4,L1,A1,R55),(B4,L1,A1,R56),(B4,L1,A2,R51),(B4,L1,A2,R52),(B4,L1,A2,R53),(B4,L1,A2,R54),(B4,L1,A2,R55),(B4,L1,A2,R56),(B4,L1,A3,R51),(B4,L1,A3,R52),(B4,L1,A3,R53),(B4,L1,A3,R54),(B4,L1,A3,R55),(B4,L1,A3,R56),(B4,L1,A4,R51),(B4,L1,A4,R52),(B4,L1,A4,R53),(B4,L1,A4,R54),(B4,L1,A4,R55),(B4,L1,A4,R56),(B4,L1,A5,R51),(B4,L1,A5,R52),(B4,L1,A5,R53),(B4,L1,A5,R54),(B4,L1,A5,R55),(B4,L1,A5,R56),(B4,L2,A1,R51),(B4,L2,A1,R52),(B4,L2,A1,R53),(B4,L2,A1,R54),(B4,L2,A 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1,R55),(B5,L1,A1,R56),(B5,L1,A2,R51),(B5,L1,A2,R52),(B5,L1,A2,R53),(B5,L1,A2,R54),(B5,L1,A2,R55),(B5,L1,A2,R56),(B5,L1,A3,R51),(B5,L1,A3,R52),(B5,L1,A3,R53),(B5,L1,A3,R54),(B5,L1,A3,R55),(B5,L1,A3,R56),(B5,L1,A4,R51),(B5,L1,A4,R52),(B5,L1,A4,R53),(B5,L1,A4,R54),(B5,L1,A4,R55),(B5,L1,A4,R56),(B5,L1,A5,R51),(B5,L1,A5,R52),(B5,L1,A5,R53),(B5,L1,A5,R54),(B5,L1,A5,R55),(B5,L1,A5,R56),(B5,L2,A1,R51),(B5,L2,A1,R52),(B5,L2,A1,R53),(B5,L2,A1,R54),(B5,L2,A1,R55),(B5,L2,A1,R56),(B5,L2,A2,R51),(B5,L2,A2,R52),(B5,L2,A2,R53),(B5,L2,A2,R54),(B5,L2,A2,R55),(B5,L2,A2,R56),(B5,L2,A3,R51),(B5,L2,A3,R52),(B5,L2,A3,R53),(B5,L2,A3,R54),(B5,L2,A3,R55),(B5,L2,A3,R56),(B5,L2,A4,R51),(B5,L2,A4,R52),(B5,L2,A4,R53),(B5,L2,A4,R54),(B5,L2,A4,R55),(B5,L2,A4,R56),(B5,L2,A5,R51),(B5,L2,A5,R52),(B5,L2,A5,R53),(B5,L2,A5,R54),(B5,L2,A5,R55),(B5,L2,A5,R56),(B5,L3,A1,R51),(B5,L3,A1,R52),(B5,L3,A1,R53),(B5,L3,A1,R54),(B5,L3,A1,R55),(B5,L3,A1,R56),(B5,L3,A2,R51),(B5,L3,A2,R52),(B5,L3,A2,R53),(B5,L3,A2,R54),(B5,L3,A2,R55),(B5,L3,A2,R56),(B5,L3,A3,R51),(B5,L3,A3,R52),(B5,L3,A3,R53),(B5,L3,A3,R54),(B5,L3,A3,R55),(B5,L3,A3,R56),(B5,L3,A4,R51),(B5,L3,A4,R52),(B5,L3,A4,R53),(B5,L3,A4,R54),(B5,L3,A4,R55),(B5,L3,A4,R56),(B5,L3,A5,R51),(B5,L3,A5,R52),(B5,L3,A5,R53),(B5,L3,A5,R54),(B5,L3,A5,R55),(B5,L3,A5,R56),(B5,L4,A1,R51),(B5,L4,A1,R52),(B5,L4,A1,R53),(B5,L4,A1,R54),(B5,L4,A1,R55),(B5,L4,A1,R56),(B5,L4,A2,R51),(B5,L4,A2,R52),(B5,L4,A2,R53),(B5,L4,A2,R54),(B5,L4,A2,R55),(B5,L4,A2,R56),(B5,L4,A3,R51),(B5,L4,A3,R52),(B5,L4,A3,R53),(B5,L4,A3,R54),(B5,L4,A3,R55),(B5,L4,A3,R56),(B5,L4,A4,R51),(B5,L4,A4,R52),(B5,L4,A4,R53),(B5,L4,A4,R54),(B5,L4,A4,R55),(B5,L4,A4,R56),(B5,L4,A5,R51),(B5,L4,A5,R52),(B5,L4,A5,R53),(B5,L4,A5,R54),(B5,L4,A5,R55),(B5,L4,A5,R56),(B5,L5,A1,R51),(B5,L5,A1,R52),(B5,L5,A1,R53),(B5,L5,A1,R54),(B5,L5,A1,R55),(B5,L5,A1,R56),(B5,L5,A2,R51),(B5,L5,A2,R52),(B5,L5,A2,R53),(B5,L5,A2,R54),(B5,L5,A2,R55),(B5,L5,A2,R56),(B5,L5,A3,R51),(B5,L5,A3,R52),(B5,L5,A3,R53),(B5,L5,A3,R54),(B5,L5,A3,R55),(B5,L5,A3,R56),(B5,L5,A4,R51),(B5,L5,A4,

R52),(B5,L5,A4,R53),(B5,L5,A4,R54),(B5,L5,A4,R55),(B5,L5,A4,R56),(B5,L5,A5,R51),(B5,L5,A5,R52),(B5,L5,A5,R53),(B5,L5,A5,R54),(B5,L5,A5,R55),(B5,L5,A5,R56).

Test Example 1

Lowering Effect on Brain β Amyloid in Rats

A test compound was suspended in 0.5% methylcellulose, the final concentration was adjusted to 2 mg/mL, and this was orally administered to male Crg:SD rat (7 to 9 week old) at 10 mg/kg. In a vehicle control group, only 0.5% methylcellulose was administered, and an administration test was performed at 3 to 8 animals per group. A brain was isolated 3 hours after administration, a cerebral hemisphere was isolated, a weight thereof was measured, the hemisphere was rapidly frozen in liquid nitrogen, and stored at −80° C. until the day for extraction. The frozen cerebral hemisphere was transferred to a homogenizer manufactured by Teflon (registered trade mark) under ice cooling, a 5-fold volume of a weight of an extraction buffer (containing 1% CHAPS ({3-[(3-chloroamidopropyl) dimethylammonio]-1-propanesulfonate}), 20 mM Tris-HCl (pH 8.0), 150 mM NaCl, Complete (Roche) protease inhibitor) was added, up and down movement was repeated, and this was homogenized to solubilize for 2 minutes. The suspension was transferred to a centrifugation tube, allowed to stand on an ice for 3 hours or more and, thereafter centrifuged at 100,000×g and 4° C. for 20 minutes. After centrifugation, the supernatant was transferred to an ELISA plate (product No. 27730, Immuno-Biological Laboratories) for measuring β amyloid 1-40. ELISA measurement was performed according to the attached instruction. The lowering effect was calculated as a ratio compared to the brain b amyloid 1-40 level of vehicle control group.

TABLE 170

Compound No.	% of vehicle control group
634	21.1
622	50.1

Compound No. 733, 359, 39, 212, 793, 204, 243, 482 and 1282 also lowered the brain β amyloid 1-40 with approximately 60 to 90% reduction compared to those of a vehicle control group.

Therefore, it is shown that Compound (I) lowers the brain β amyloid 1-40 in rats.

Test Example 2

Lowering Effect on Brain β Amyloid in Mice

A test compound was suspended in 0.5% methylcellulose, the final concentration was adjusted to 10 mg/mL, and this was subcutaneously administered to back of male Crlj:CD-1 (ICR) mouse (7 to 8 week old) at 100 mg/kg. In a vehicle control group, only 0.5% methylcellulose was administered. A test was performed at 4 to 8 animals per group. A brain was isolated 3 hours after administration. The subsequent operations were the same as in the above test in rat.

TABLE 171

Compound No.	% of vehicle control group
1199	14.1
1043	15.0
1100	20.2
127	25.2
605	36.5
396	38.4
1244	50.1
651*	52.3

(*3 hours after 30 mg/kg of subcutaneous administration)

Compounds 309, 165, 739, 1266, 900, 220, 964, 1262 and 1014 also lowered the brain β amyloid 1-40 with approximately 60 to 90% reduction compared to those of vehicle control group.

Therefore, it is shown that Compound (I) lowers the brain β amyloid 1-40 in mice.

Formulation Example 1

A granule containing the following ingredients is prepared.

Ingredient	Compound represented by formula (I)	10 mg
	Lactose	700 mg
	Corn starch	274 mg
	HPC-L	16 mg
		1000 mg

The compound represented by the formula (I) and lactose are passed through a 60 mesh sieve. Corn starch is passed through a 120 mesh sieve. These are mixed with a V-type mixer, to a mixed powder is added a HPC-L (lower viscosity hydroxypropylcellulose) aqueous solution, the materials are kneaded, granulated (extrusion granulation, pore diameter 0.5 to 1 mm), and dried. The resulting dry granule is passed through a sieve using a vibration sieve (12/60 mesh) to obtain a granule.

Formulation Example 2

A granule for filling into a capsule containing the following ingredients is prepared.

Ingredient	Compound represented by formula (I)	15 mg
	Lactose	90 mg
	Corn starch	42 mg
	HPC-L	3 mg
		150 mg

The compound represented by the formula (I) and lactose are passed through a 60 mesh sieve. Corn starch is passed through a 120 mesh sieve. These are mixed, to a mixed powder is added a HPC-L solution, the materials are kneaded, granulated., and dried. The resulting dry granule is size-adjusted, 150 mg of which is filled into a No. 4 hard gelatin capsule.

Formulation Example 3

A tablet containing the Mowing ingredients is prepared.

Ingredient	Compound represented by the formula (I)	10 mg
	Lactose	90 mg
	Microcrystalline cellulose	30 mg
	CMC-Na	15 mg
	Magnesium stearate	5 mg
		150 mg

The compound represented by the formula (I), lactose, microcrystalline cellulose, CMC-Na (carboxymethylcellulose sodium salt) are passed through a 60 mesh sieve, and mixed. Into a mixed powder is mixed magnesium stearate to obtain a mixed powder for tabletting. The present mixed powder is compressed to obtain 150 mg of a tablet.

Formulation Example 4

The following ingredients are warmed, mixed, and sterilized to obtain an injectable.

Ingredient	Compound represented by the formula (I)	3 mg
	Nonionic surfactant	15 mg
	Purified water for injection	1 ml

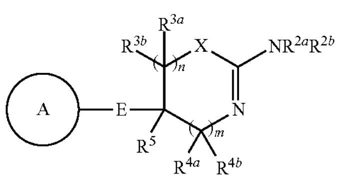
INDUSTRIAL APPLICABILITY

The pharmaceutical composition of the present invention can be a useful medicament for treating disease induced by production, secretion and/or deposition o β amyloid, especially Alzheimer's disease.

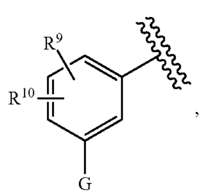
The invention claimed is:

1. A method for treating Alzheimer's disease, comprising: administering a composition in an amount effective for treating Alzheimer's disease to a subject in need thereof, wherein the composition contains a compound represented by the general formula (I):

(I)



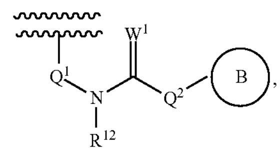
wherein ring A is



R^9 and R^{10} are each independently a hydrogen atom, halogen, hydroxy, cyano, nitro, mercapto, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted acyl, optionally substituted acyloxy, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted lower alkoxycarbonyloxy, optionally substituted lower aryloxycarbonyloxy, optionally substituted amino, optionally substituted carbamoyl, optionally substituted carbamoyloxy, optionally substituted lower alkylthio, optionally substituted arylthio, optionally substituted lower alkylsulfonyl, optionally substituted arylsulfonyl, optionally substituted lower alkyl sulfinyl, optionally substituted arylsulfinyl, optionally substituted lower alkylsulfonyloxy, optionally substituted arylsulfonyloxy, optionally substituted sulfamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy, an optionally substituted heterocyclic group, or optionally substituted heterocyclicoxy;

G is

(ii)

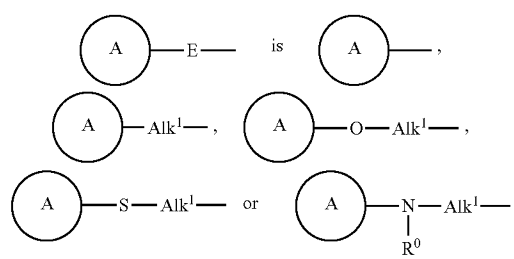


wherein Q^1 and Q^2 are each independently a bond, optionally substituted lower alkylene, or optionally substituted lower alkenylene;

W^1 is O or S;

R^{12} is a hydrogen atom, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, lower alkoxycarbonyl lower alkyl, carbocyclic lower alkyl, or acyl;

ring B is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group,



wherein Alk^1 is lower alkylene or lower alkenylene;

R^0 is a hydrogen atom, lower alkyl, or acyl;

X is S, O, or NR^1;

R^1 is a hydrogen atom or lower alkyl;

each of R^{2a} and R^{2b} is a hydrogen atom,

R^{3a}, R^{3b}, R^{4a}, and R^{4b} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted acyl, carboxy, optionally substituted lower alkoxycarbonyl, optionally substituted amino, optionally substituted carbamoyl, an optionally substituted carbocyclic group, or an optionally substituted heterocyclic group;

n is 2 and m is 0;

each R^{3a}, each R^{3b}, each R^{4a}, and each R^{4b} may be independently different;

R^5 is optionally substituted lower alkyl;

its pharmaceutically acceptable salt, or a solvate thereof as an active ingredient.

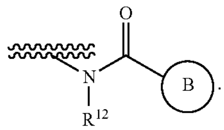
2. The method for treating Alzheimer's disease according to claim **1**, wherein X is S.

3. The method for treating Alzheimer's disease according to claim **1**, wherein E is a bond.

4. The method for treating Alzheimer's disease according to claim **1**, wherein ring B is aryl optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, cyano, optionally substituted carbamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy, and an optionally substituted heterocyclic group or heteroaryl optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyl, optionally substituted amino, cyano, optionally substituted carbamoyl, an optionally substituted carbocyclic group, optionally substituted carbocyclicoxy, and an optionally substituted heterocyclic group.

5. The method for treating Alzheimer's disease according to claim **1**, wherein G is represented by the formula:

(ii')



6. The method for treating Alzheimer's disease according to claim **1**, wherein R^5 is C1 to C3 alkyl.

7. The method for treating Alzheimer's disease according to claim **1**, wherein R^5 is methyl.

8. The method for treating Alzheimer's disease according to claim **1**, wherein R^{3a} and R^{3b} are each independently a hydrogen atom, halogen, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, or optionally substituted aryl.

9. The method for treating Alzheimer's disease according to claim **1**, wherein all of R^{3a} and all of R^{3b} are hydrogen atoms.

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