Paths of analysis*

C35

Synthia

March 3, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: FGI, FGI with protections

Max. paths returned: 5

Max. iterations: 300

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1000 $/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 10

My Stockroom:

1. Max. molecular weight - 1000 g/mol

Reaction scoring formula: TUNNEL_COEF*FGI_COEF*STEP*20+1000000*(CONFLICT+NON_SELECTIVITY+FILTERS+PROTECT)

Chemical scoring formula: SMALLER^ 3,SMALLER^ 1.5

Min. search width: 400

Max. reactions per product: 60

Strategies: none selected

*The results stated herein were generated using the proprietary platform owned and maintained by Grzybowski Scientific Inventions, Inc., a subsidiary of Merck KGaA, Darmstadt Germany. The results are provided on an as is basis, and shall be used solely in connection with the rights afforded in the license agreement and for no other purpose.

FGI Coeff: 0

JSON Parameters: {}

2 Paths

2 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: 397.04

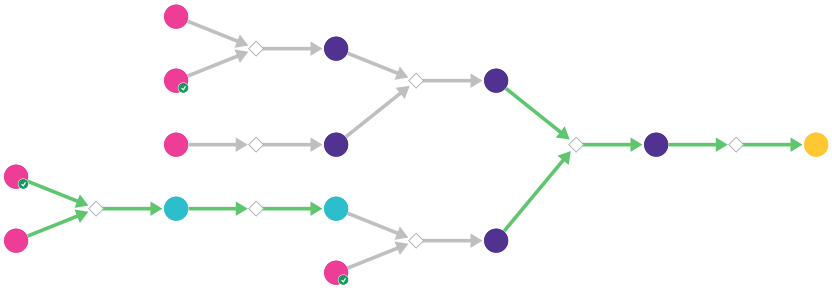
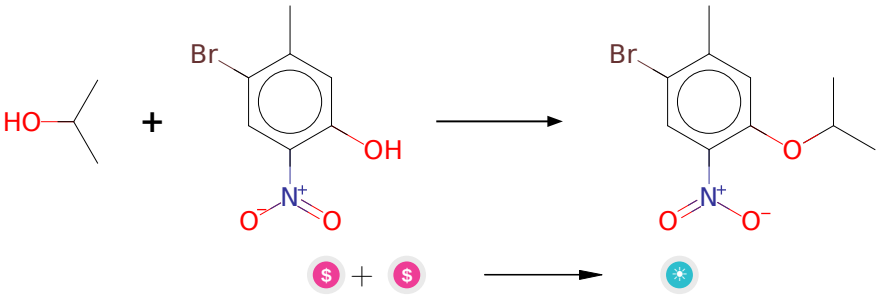


Figure 1: Outline of path 1

2.1.1 Mitsunobu reaction



Substrates:

1. 2-Propanol - *available at Sigma-Aldrich*
2. 4-Bromo-5-methyl-2-nitrophenol - *Combi-Blocks*

Products:

1. C10H12BrNO3

Typical conditions: DEAD.or.DCAD.or.DIAD.PPh3

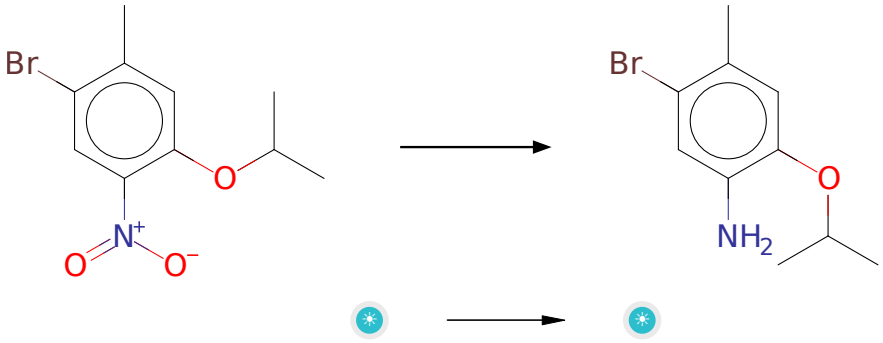
Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo0345751* AND *10.1021/ol0618757*

Retrosynthesis ID: 7562

2.1.2 Reduction of nitro group



Substrates:

1. C10H12BrNO3

Products:

1. C10H14BrNO

Typical conditions: Zn. aq NH4. EtOH //Zn.Hcl

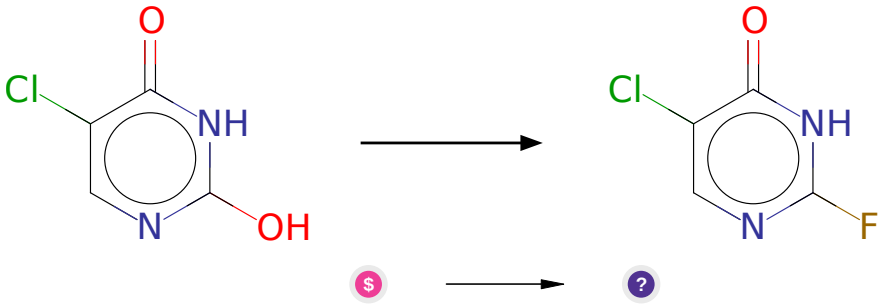
Protections: none

Yield: good

Reference: DOI: *10.1002/anie.201512005* and *10.1002/anie.201104681* and *10.3390/molecules17055497* and *10.3390/molecules19022655* and *10.1021/ol5033464* (SI,page 3) and *10.5012/bkcs.2013.34.4.1275*

Retrosynthesis ID: 6145

2.1.3 Synthesis of haloarenes via triflates



Substrates:

1. 5-chloro-uracil - *Combi-Blocks*

Products:

1. O=c1[nH]c(F)ncc1Cl

Typical conditions: 1.Tf2O 2. [Pd].MX

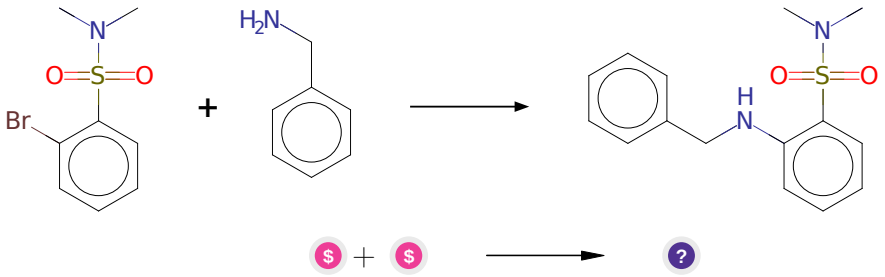
Protections: none

Yield: moderate

Reference: *10.1016/j.tetasy.2012.04.008* and WO2007/136577 (p46) and *10.1021/ol202098h* and *10.1021/ol402859k* and *10.1021/jacs.5b09308*

Retrosynthesis ID: 23940

2.1.4 Amination of aryl bromides



Substrates:

1. 2-Bromo-N,N-dimethylbenzenesulphonamide 1g pack - *Combi-Blocks*
2. Benzylamine - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)c1ccccc1NCc1ccccc1

Typical conditions: Pd.ligand.base or CuI.ligand.base

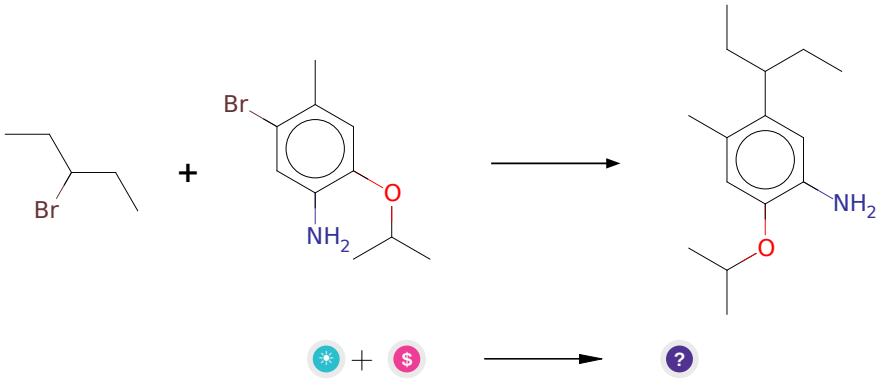
Protections: none

Yield: good

Reference: *10.1021/ja903049z* and *10.1021/jo060945k* and *10.1021/jo060190h* and *10.1039/B923255A* and *10.1021/jm8003625* and *10.1021/jo9006738*

Retrosynthesis ID: 28544

2.1.5 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. C10H14BrNO
2. 3-Bromopentane - *available at Sigma-Aldrich*

Products:

1. CCC(CC)c1cc(N)c(OC(C)C)cc1C

Typical conditions: [Ir]-photocat.[Ni]-cat.TTMSS.base.blue light

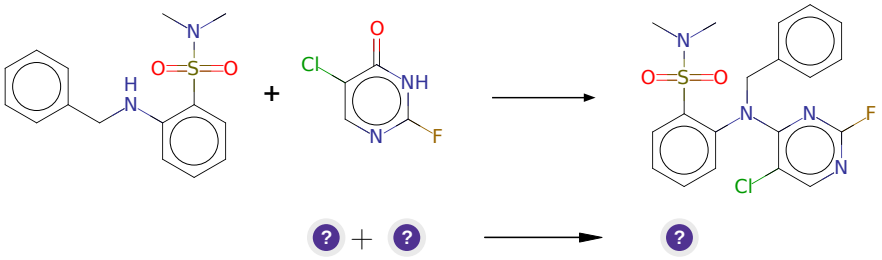
Protections: none

Yield: moderate

Reference: *10.1021/jacs.6b04818* and *10.1016/j.bbrc.2020.04.028* and *10.1021/acsmedchemlett.8b00183*

Retrosynthesis ID: 31016940

2.1.6 Amination of pyridones



Substrates:

1. CN(C)S(=O)(=O)c1ccccc1NCc1ccccc1
2. O=c1[nH]c(F)ncc1Cl

Products:

1. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(F)ncc1Cl

Typical conditions: 1.PCl5.2.amine

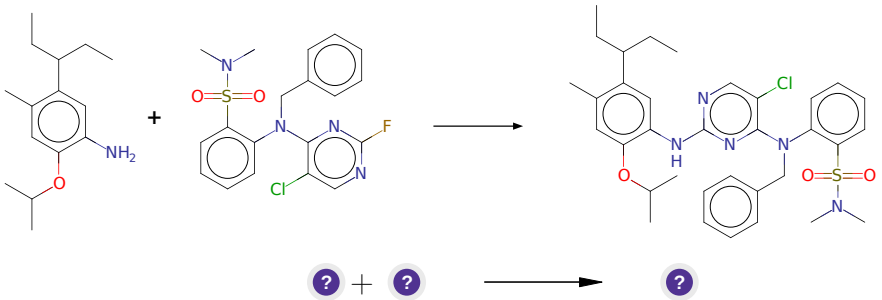
Protections: none

Yield: moderate

Reference: *10.1021/jm300780p* AND *10.3390/molecules170910902* AND *10.1021/jm00392a017*

Retrosynthesis ID: 14895

2.1.7 Nucleophilic aromatic substitution



Substrates:

1. CCC(CC)c1cc(N)c(OC(C)C)cc1C
2. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(F)ncc1Cl

Products:

1. CCC(CC)c1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: Solvent

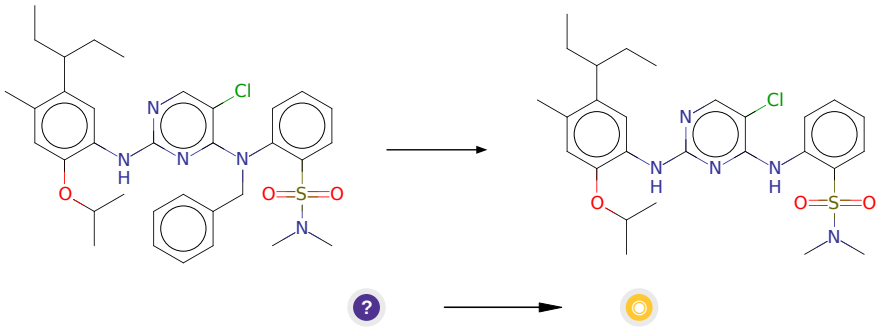
Protections: none

Yield: good

Reference: *10.1002/9781118093559.ch4*

Retrosynthesis ID: 49476

2.1.8 Debenzylation



Substrates:

1. CCC(CC)c1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Products:

1. CCC(CC)c1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: H2. Pd/C or Pd(OH)2

Protections: none

Yield: good

Reference: DOI: *10.1002/1521-3773(20020603)41:11<1895::AID-ANIE1895>3.0.CO;2-3* and *10.1021/jo400589j* and *10.1021/jm8012932* (SI,page S6) and *10.1080/00397911.2016.1261164*

Retrosynthesis ID: 9995661

2.2 Path 2

Score: 450.50

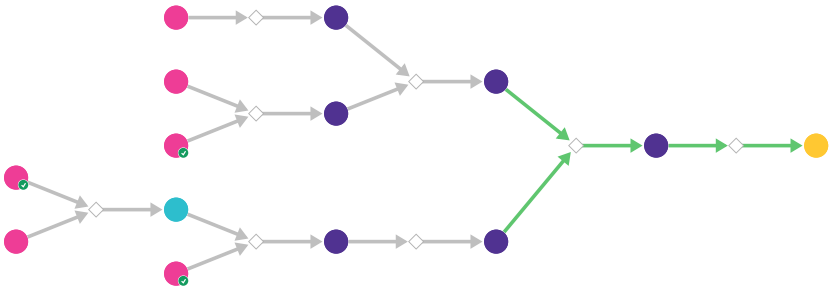
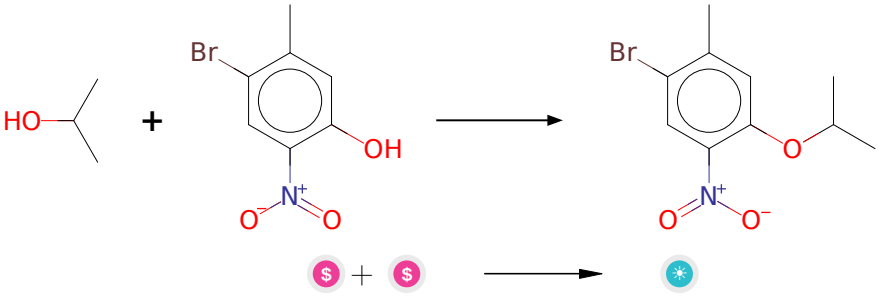


Figure 2: Outline of path 2

2.2.1 Mitsunobu reaction



Substrates:

1. 2-Propanol - *available at Sigma-Aldrich*
2. 4-Bromo-5-methyl-2-nitrophenol - *Combi-Blocks*

Products:

1. C10H12BrNO3

Typical conditions: DEAD.or.DCAD.or.DIAD.PPh3

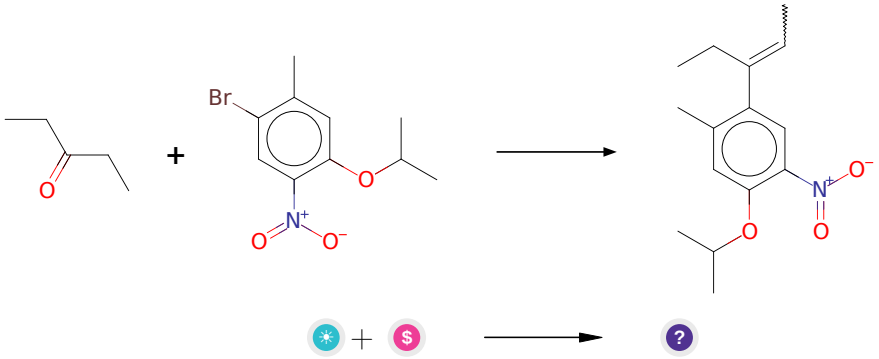
Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo0345751* AND *10.1021/ol0618757*

Retrosynthesis ID: 7562

2.2.2 Arylation of hydrazones with bromoarene



Substrates:

1. C10H12BrNO3
2. 3-Pentanone - *available at Sigma-Aldrich*

Products:

1. CC=C(CC)c1cc([N+](=O)[O-])c(OC(C)C)cc1C

Typical conditions: 1.TsNH2NH2.2.PdCl2(MeCN)2/Xphos.tBuOLi.ArX.dioxane.heating

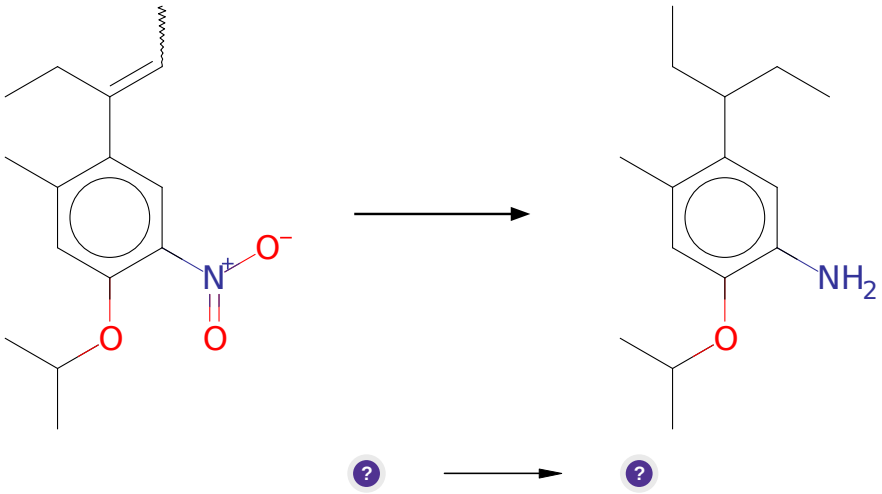
Protections: none

Yield: good

Reference: *10.1021/jo301987c* and *10.1021/acs.oprd.5b00211* and *10.1002/anie.201003450*

Retrosynthesis ID: 9990491

2.2.3 Tandem alkene/nitro reduction



Substrates:

1. CC=C(CC)c1cc([N+](=O)[O-])c(OC(C)C)cc1C

Products:

1. CCC(CC)c1cc(N)c(OC(C)C)cc1C

Typical conditions: H2.Pd/C

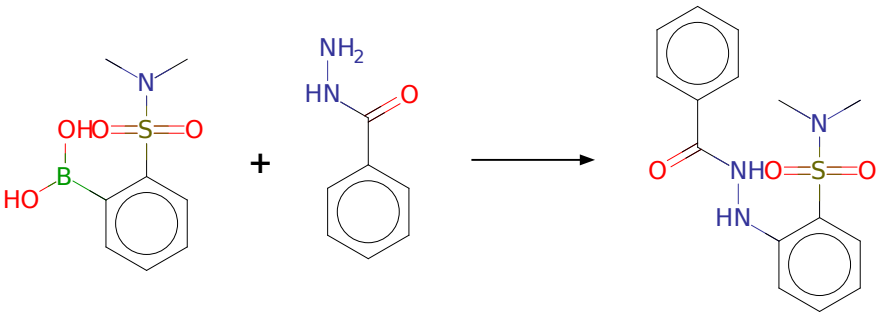
Protections: none

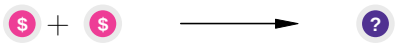
Yield: moderate

Reference: *10.1016/j.bmc.2009.05.066* and *10.1016/j.cclet.2015.05.003* and *10.1016/j.bmc.2012.12.025*

Retrosynthesis ID: 31351

2.2.4 Chan-Lam Coupling





Substrates:

1. 2-(N,N-DIMETHYLSULPHAMOYL)BENZENEBORONIC ACID - *Combi-Blocks*
2. Benzhydrazide - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)c1ccccc1NNC(=O)c1ccccc1

Typical conditions: Cu(Oac)2.dioxane

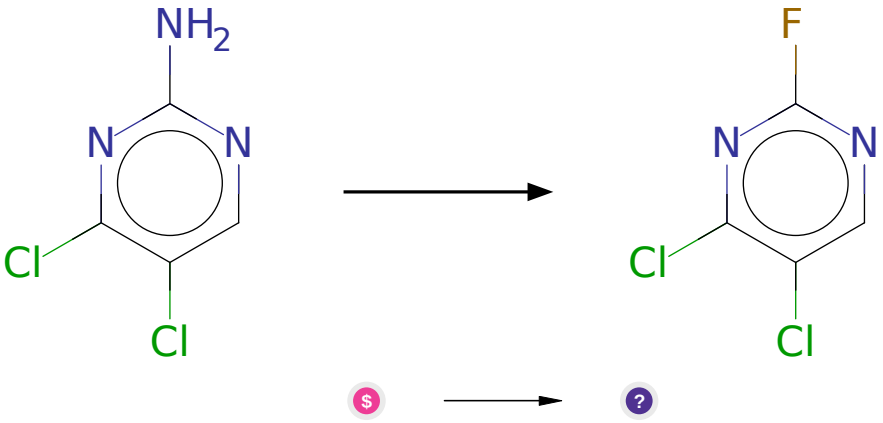
Protections: none

Yield: good

Reference: *10.1039/C4OB02343A*

Retrosynthesis ID: 31015967

2.2.5 Balz-Schiemann Reaction



Substrates:

1. 4,5-Dichloropyrimidin-2-amine - *Combi-Blocks*

Products:

1. Fc1ncc(Cl)c(Cl)n1

Typical conditions: NaNO2.HF-pyridine.-25 to 0C

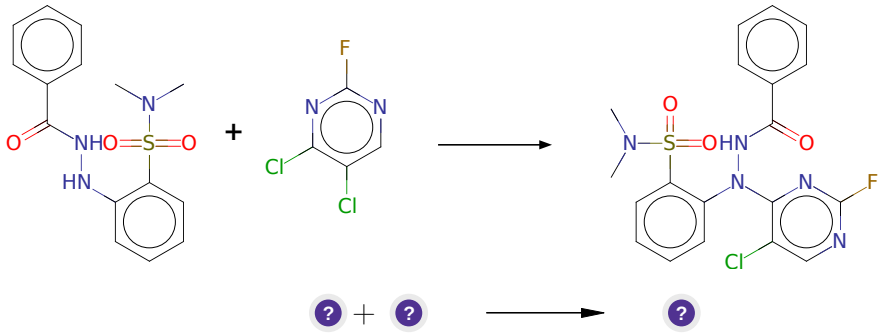
Protections: none

Yield: moderate

Reference: *10.1021/jm100432w* and *10.1021/jm5008177* and *10.1021/ol401540k* and *10.1021/jm401551n* (main text and SI, page S8) and *10.1515/chempap-2016-0033* and *10.1021/jm0311442* and *10.1016/j.jfluchem.2007.03.012* and *10.1021/jo00185a023*

Retrosynthesis ID: 29906

2.2.6 Nucleophilic aromatic substitution



Substrates:

1. Fc1ncc(Cl)c(Cl)n1
2. CN(C)S(=O)(=O)c1ccccc1NNC(=O)c1ccccc1

Products:

1. CN(C)S(=O)(=O)c1ccccc1N(NC(=O)c1ccccc1)c1nc(F)ncc1Cl

Typical conditions: EtOH.Heat or DMF.K2CO3

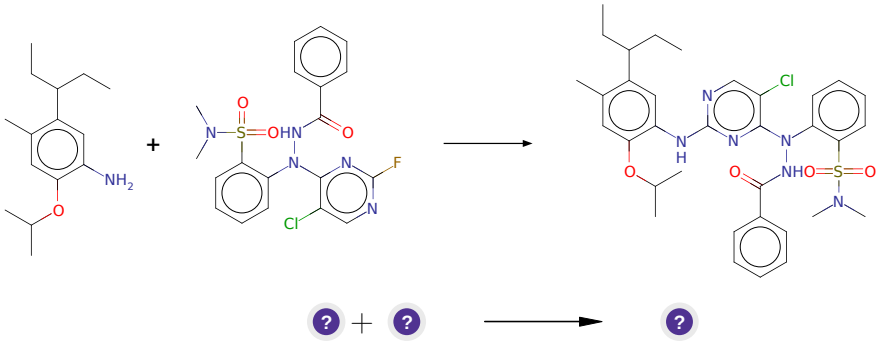
Protections: none

Yield: good

Reference: *10.1016/0040-4020(95)00966-3* and *10.1002/jhet.5570220420* and *10.1021/jo402481t*

Retrosynthesis ID: 29647

2.2.7 Nucleophilic aromatic substitution



Substrates:

1. CCC(CC)c1cc(N)c(OC(C)C)cc1C
2. CN(C)S(=O)(=O)c1ccccc1N(NC(=O)c1ccccc1)c1nc(F)ncc1Cl

Products:

1. CCC(CC)c1cc(Nc2ncc(Cl)c(N(NC(=O)c3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: Solvent

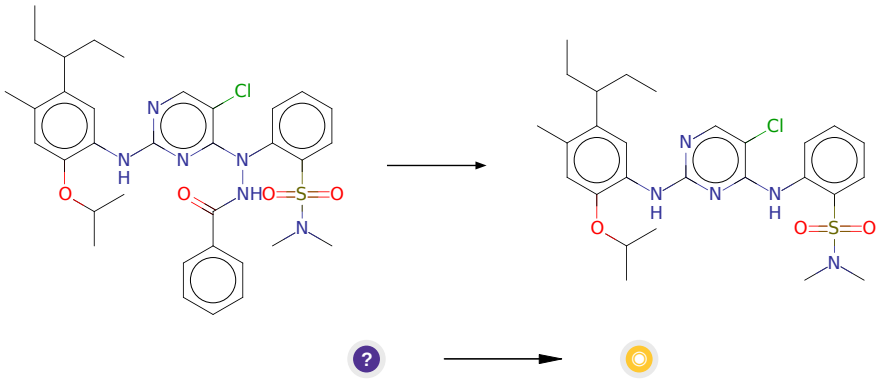
Protections: none

Yield: good

Reference: *10.1002/9781118093559.ch4*

Retrosynthesis ID: 49476

2.2.8 Reduction of phenylhydrazines



Substrates:

1. CCC(CC)c1cc(Nc2ncc(Cl)c(N(NC(=O)c3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Products:

1. CCC(CC)c1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: RaNi.H2.MeOH

Protections: none

Yield: moderate

Reference: DOI: *10.1021/ol501424f*

Retrosynthesis ID: 1808