Paths of analysis*

Y7

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselecitve reactions, Tunnels, FGI, FGI with protections

Max. paths returned: 50

Max. iterations: 2000

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1500 $/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 5

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

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Strategies: none selected

FGI Coeff: 0

Tunnels Coeff: 0

JSON Parameters: {}

2 Paths

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

2.1 Path 1

Score: 2250115.31

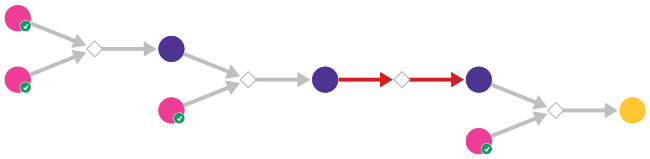
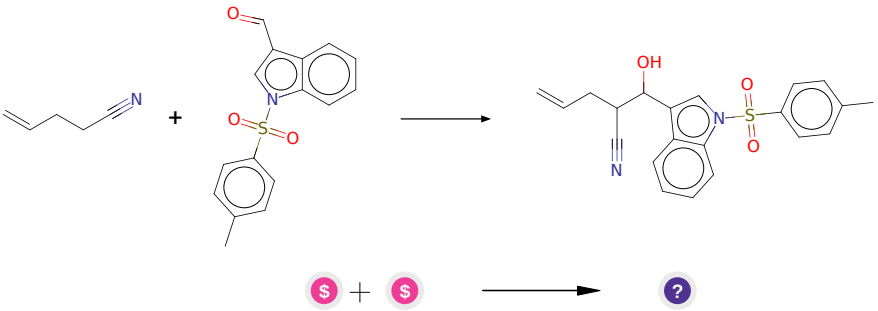


Figure 1: Outline of path 1

2.1.1 Aldol-like condensation with nitriles



Substrates:

1. 4-Pentenenitrile - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(C#N)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

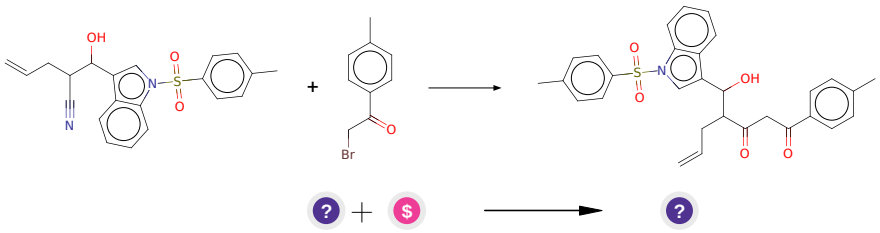
Typical conditions: LDA.THF.cooling

Protections: none

Reference: *10.1039/B800634B* and *10.1002/anie.201302613* and *10.1021/jm701319c* and *10.1016/S0040-4020(98)00122-7* and *10.1021/jo025872t*

Retrosynthesis ID: 23727

2.1.2 Blaise Reaction



Substrates:

1. C=CCC(C#N)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12
2. 2-Bromo-4'-methylacetophenone - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

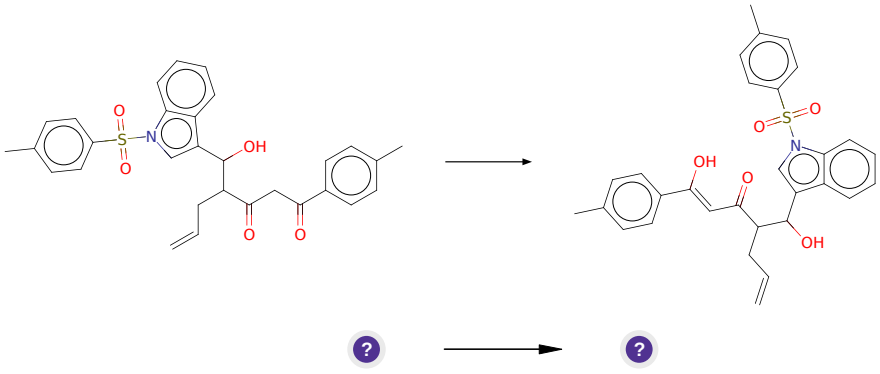
Typical conditions: Zn.TMSCl.THF then HCl

Protections: none

Reference: *10.1002/ejoc.201403402*

Retrosynthesis ID: 10000153

2.1.3 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

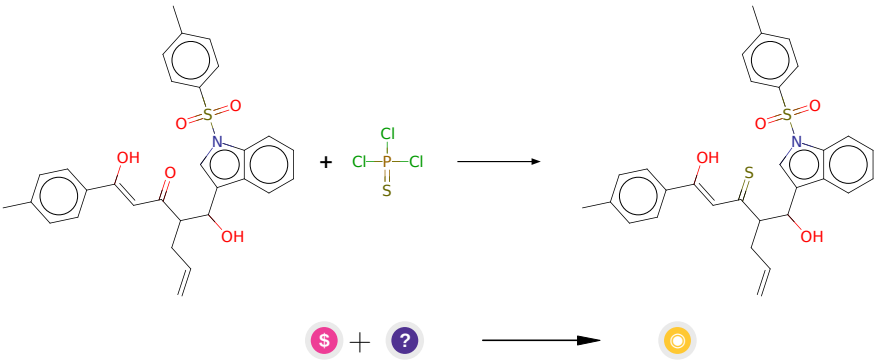
Typical conditions: solvent

Protections: none

Reference: *10.1021/ja01065a003* AND *10.1021/jo8012385*

Retrosynthesis ID: 7781

2.1.4 Thionation of Carbonyl Compounds using PSCl3



Substrates:

1. Phosphorus thiochloride - *available at Sigma-Aldrich*
2. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: NEt3.H2O.microwave.70-100C

Protections: none

Reference: DOI: *10.1021/jo7022069*

Retrosynthesis ID: 11555

2.2 Path 2

Score: 2250115.31

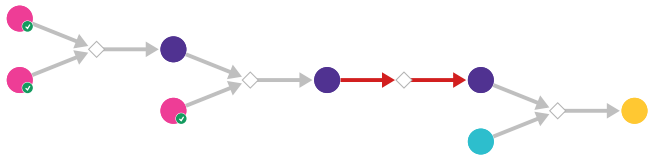
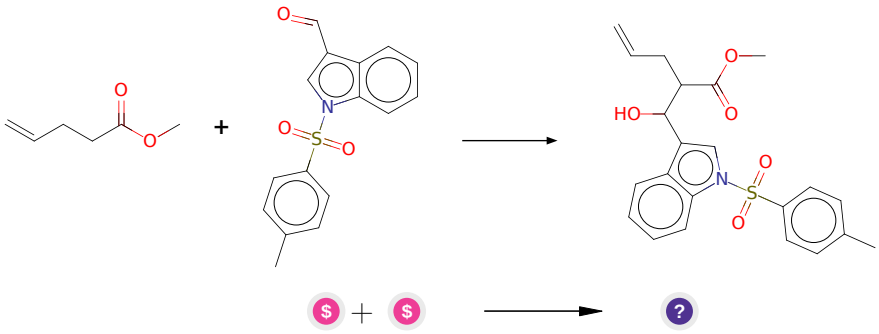


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes



Substrates:

1. Methyl 4-pentenoate - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)OC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

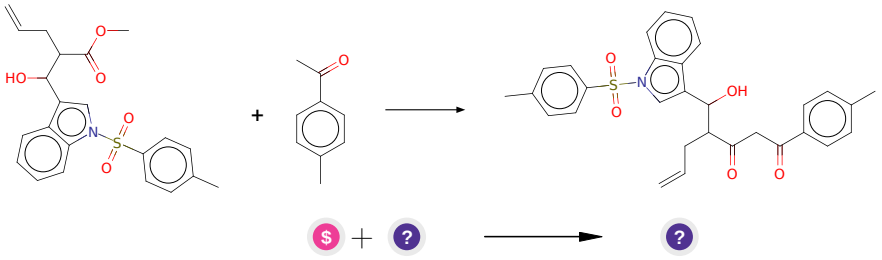
Typical conditions: LDA.THF

Protections: none

Reference: *10.1016/j.bmcl.2005.02.066* and *10.3762/bjoc.9.175* and *10.1021/ol1016178*

Retrosynthesis ID: 4788

2.2.2 Condensation of methyl ketones with esters



Substrates:

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC(C(=O)OC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

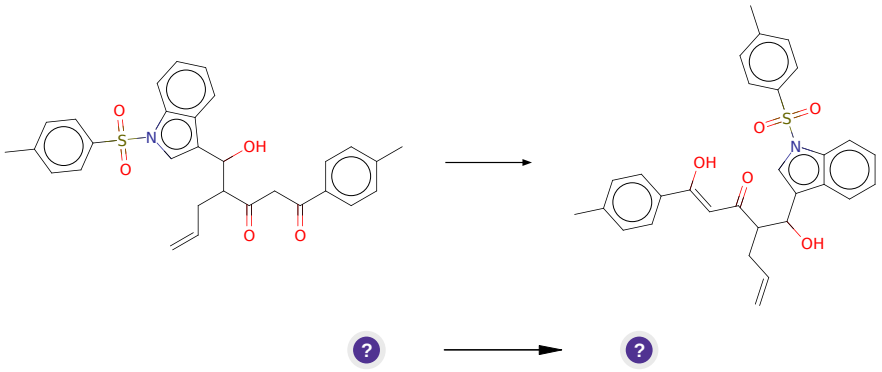
Typical conditions: NaOMe.MeOH

Protections: none

Reference: *10.1016/j.tetlet.2007.10.010* and *10.1016/j.tetlet.2013.09.025* and *10.1016/j.ejmech.2013.10.072* and *10.1002/ange.19921040631*

Retrosynthesis ID: 4792

2.2.3 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

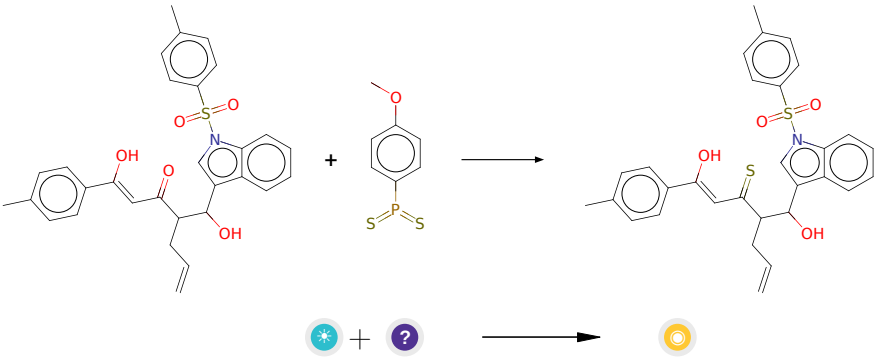
Typical conditions: solvent

Protections: none

Reference: *10.1021/ja01065a003* AND *10.1021/jo8012385*

Retrosynthesis ID: 7781

2.2.4 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

1. 4-methoxyphenyl-dithiophosphonsaeureanhydrid
2. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.3 Path 3

Score: 2250125.08

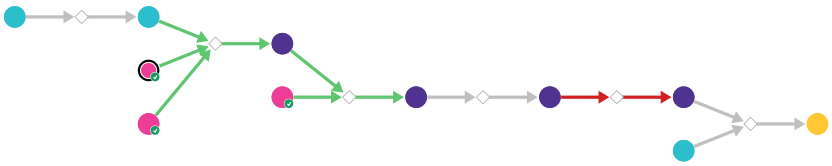
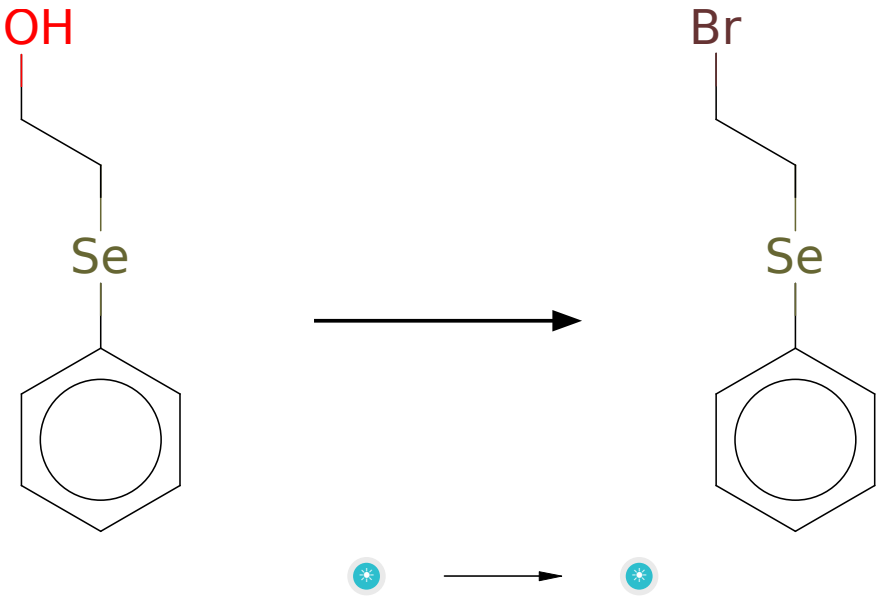


Figure 3: Outline of path 3

2.3.1 Appel Reaction



Substrates:

1. 2-phenylselanyl-ethanol

Products:

1. 2-bromaethylphenylselenid

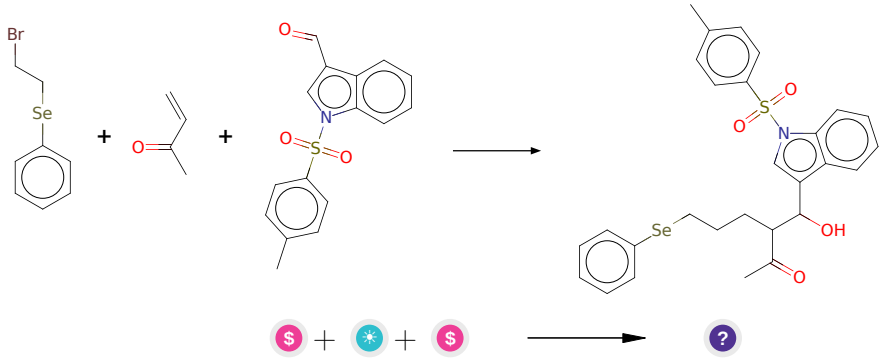
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.3.2 Conjugated addition of cuprate-aldol sequence



Substrates:

1. 3-Buten-2-one - *available at Sigma-Aldrich*
2. 2-bromaethylphenylselenid
3. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. CC(=O)C(CCC[Se]c1ccccc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

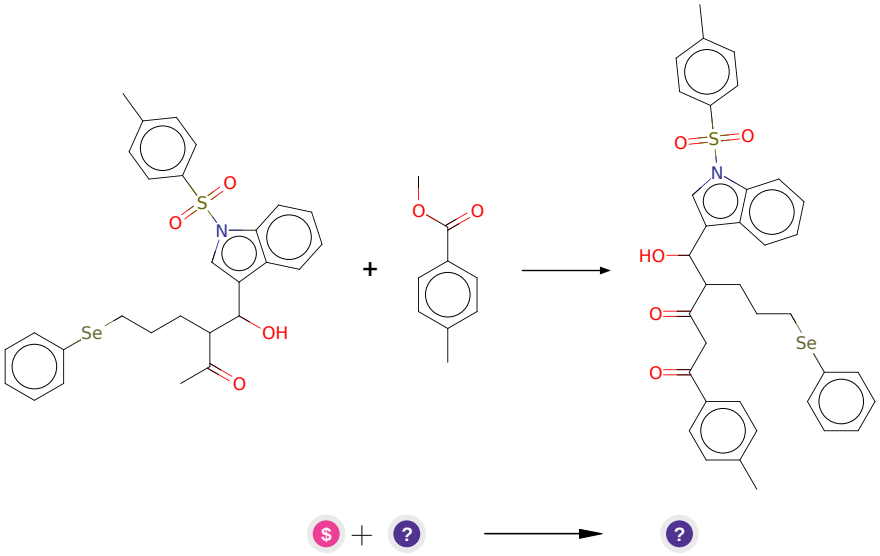
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo9905672* AND *10.1021/ja0320018* AND *10.1021/ja015900+* AND *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1* AND *10.1271/bbb.69.391* AND *10.1039/b612593j*

Retrosynthesis ID: 20515

2.3.3 Condensation of methyl ketones with esters



Substrates:

1. Methyl p-toluate - *available at Sigma-Aldrich*
2. CC(=O)C(CCC[Se]c1ccccc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2cn(S(=O)(=O)c3ccc(C)cc3)c3ccccc23)cc1

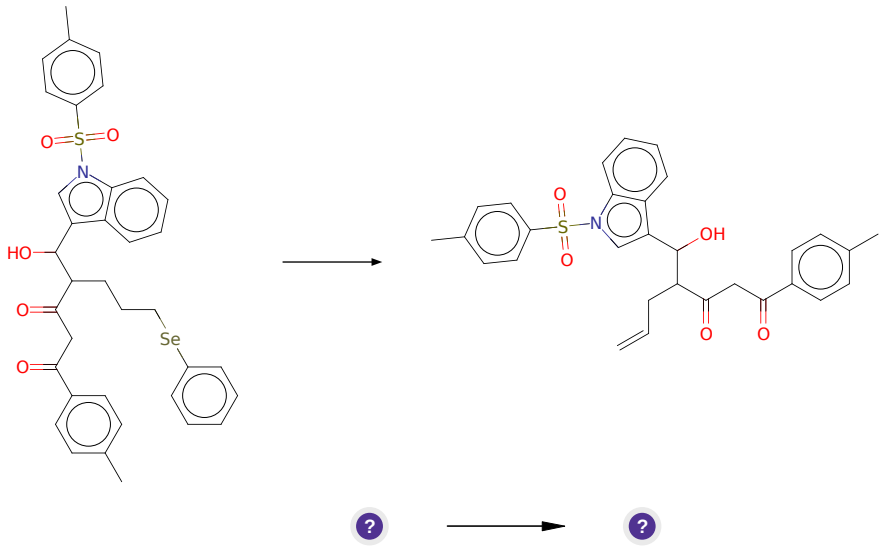
Typical conditions: NaOMe.MeOH

Protections: none

Reference: *10.1016/j.tetlet.2007.10.010* and *10.1016/j.tetlet.2013.09.025* and *10.1016/j.ejmech.2013.10.072* and *10.1002/ange.19921040631*

Retrosynthesis ID: 4792

2.3.4 Selenoxide Elimination



Substrates:

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2cn(S(=O)(=O)c3ccc(C)cc3)c3ccccc23)cc1

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

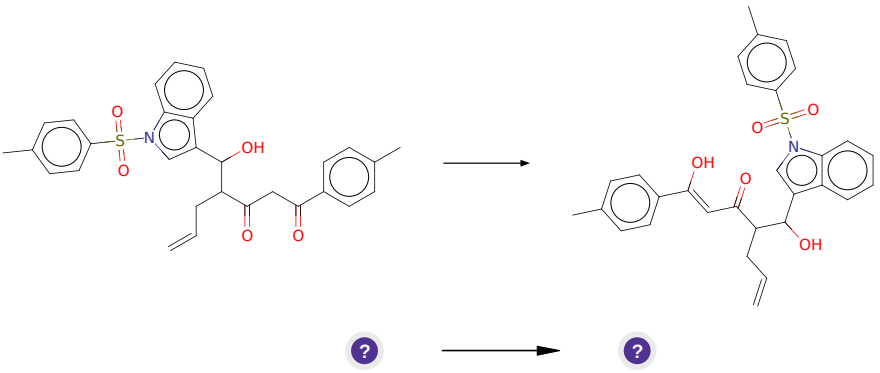
Typical conditions: 1) O3 or H2O2 or NaIO4. low temperature. 2) pyridine or Et3N

Protections: none

Reference: DOI: *10.1021/ja00852a019* or DOI: *10.1021/ja00258a056* or DOI: *10.1039/B716256A* or DOI: *10.1055/s-1998-1970* or DOI: *10.1016/S0040-4039(00)76646-9*

Retrosynthesis ID: 8381

2.3.5 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

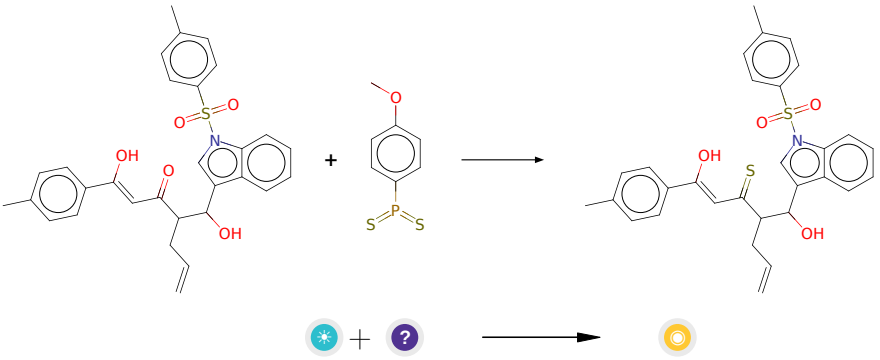
Typical conditions: solvent

Protections: none

Reference: *10.1021/ja01065a003* AND *10.1021/jo8012385*

Retrosynthesis ID: 7781

2.3.6 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

1. 4-methoxyphenyl-dithiophosphonsaeureanhydrid
2. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.4 Path 4

Score: 2250125.08

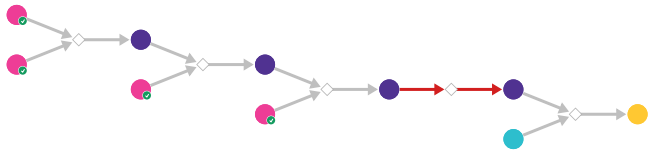
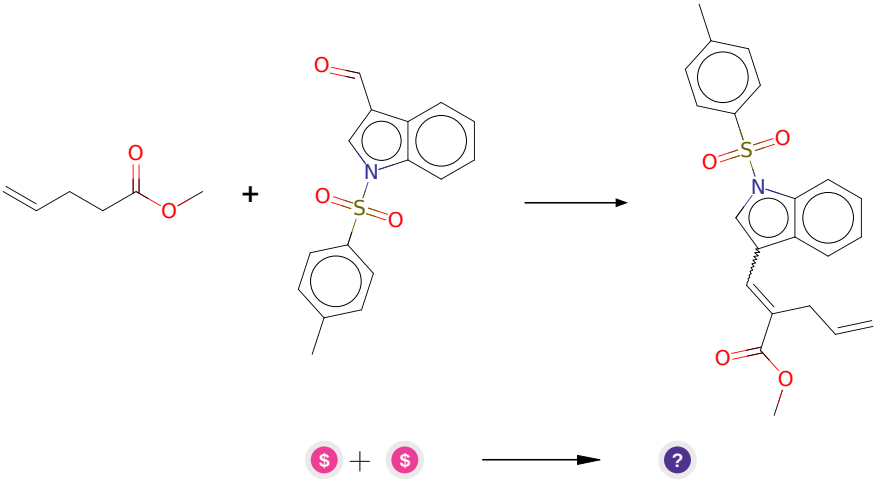


Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes/ketones



Substrates:

1. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

2. Methyl 4-pentenoate - *available at Sigma-Aldrich*

Products:

1. C=CCC(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)OC

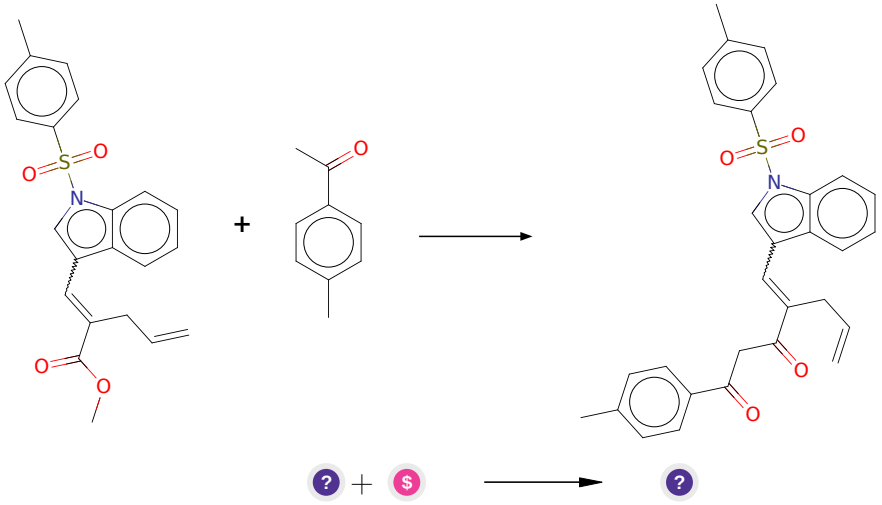
Typical conditions: LDA.THF

Protections: none

Reference: *10.1021/op040006z* AND *10.1016/j.bmcl.2005.10.104* AND

Retrosynthesis ID: 14983

2.4.2 Condensation of methyl ketones with esters



Substrates:

1. C=CCC(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)OC
2. Methyl p-tolyl ketone - *available at Sigma-Aldrich*

Products:

1. C=CCC(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)CC(=O)c1ccc(C)cc1

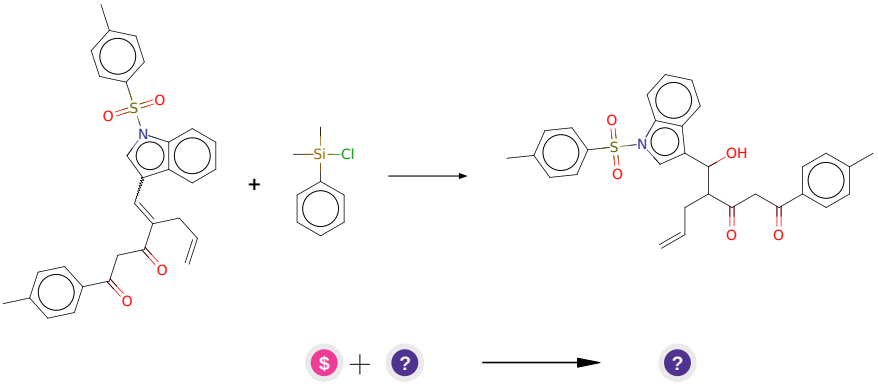
Typical conditions: NaOMe.MeOH

Protections: none

Reference: *10.1016/j.tetlet.2007.10.010* and *10.1016/j.tetlet.2013.09.025* and *10.1016/j.ejmech.2013.10.072* and *10.1002/ange.19921040631*

Retrosynthesis ID: 4792

2.4.3 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

1. DMPSCl - *available at Sigma-Aldrich*
2. C=CCC(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)CC(=O)c1ccc(C)cc1

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

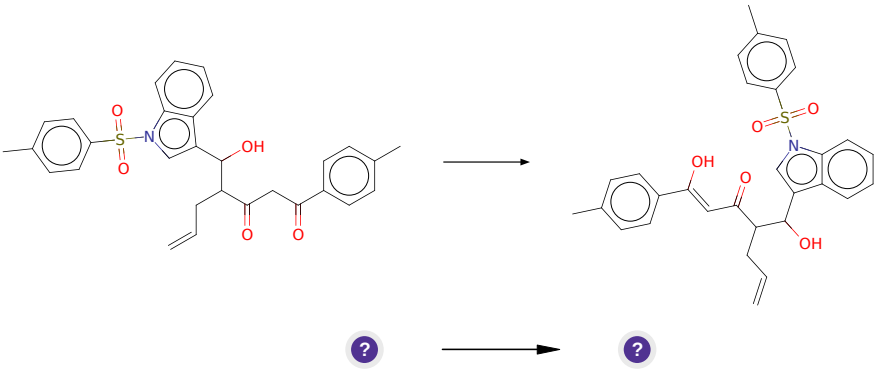
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

Reference: *10.1021/ja058370g* AND (Oxidation) *10.1021/jo9905672* or *10.1021/ol300832f*

Retrosynthesis ID: 20301

2.4.4 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

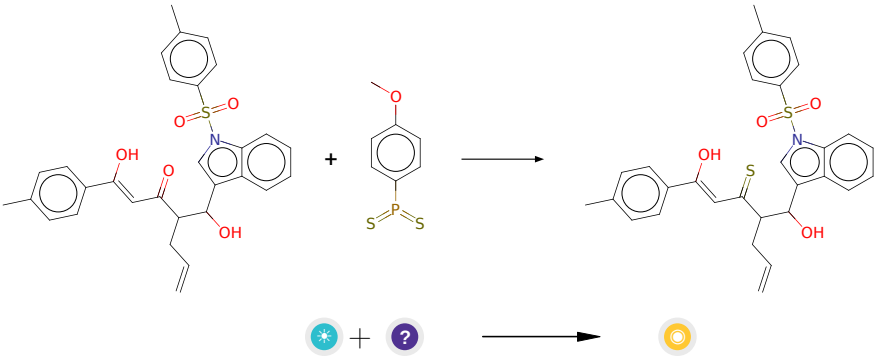
Typical conditions: solvent

Protections: none

Reference: *10.1021/ja01065a003* AND *10.1021/jo8012385*

Retrosynthesis ID: 7781

2.4.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

1. 4-methoxyphenyl-dithiophosphonsaeureanhydrid
2. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.5 Path 5

Score: 2250160.36

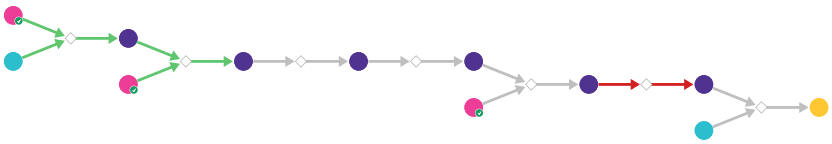
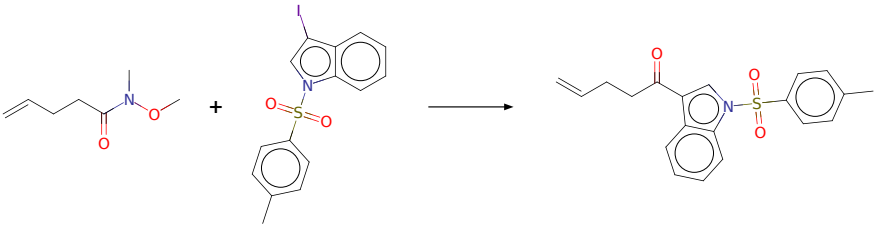


Figure 5: Outline of path 5

2.5.1 Synthesis of ketones from Weinreb amides



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *available at Sigma-Aldrich*
2. n-methoxy-n-methyl-4-pentenamide

Products:

1. C=CCCC(=O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

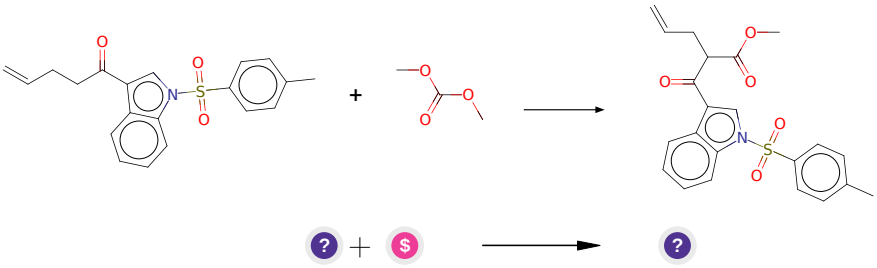
Typical conditions: 1.RmgBr.THF 2.TFA.DCM

Protections: none

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 5060

2.5.2 Carboethoxylation of enolates - Claisen condensation



Substrates:

1. C=CCCC(=O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12
2. dimethyl ester - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)OC)C(=O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

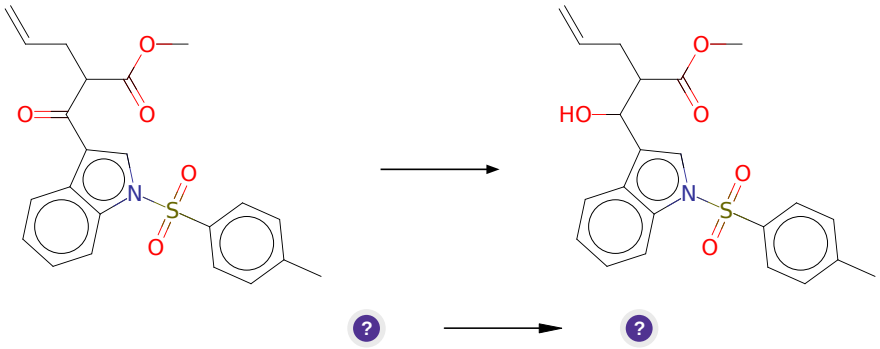
Typical conditions: NaH.THF

Protections: none

Reference: *10.1016/j.bmc.2011.06.055* AND *10.1021/ja01036a055* AND WO2010/48014 (amides,p.32) AND *10.1016/S0040-4020(02)00350-2* AND *10.1021/ol201243u* (Supporting information)

Retrosynthesis ID: 8167

2.5.3 Reduction of ketones with NaBH4



Substrates:

1. C=CCC(C(=O)OC)C(=O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)OC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

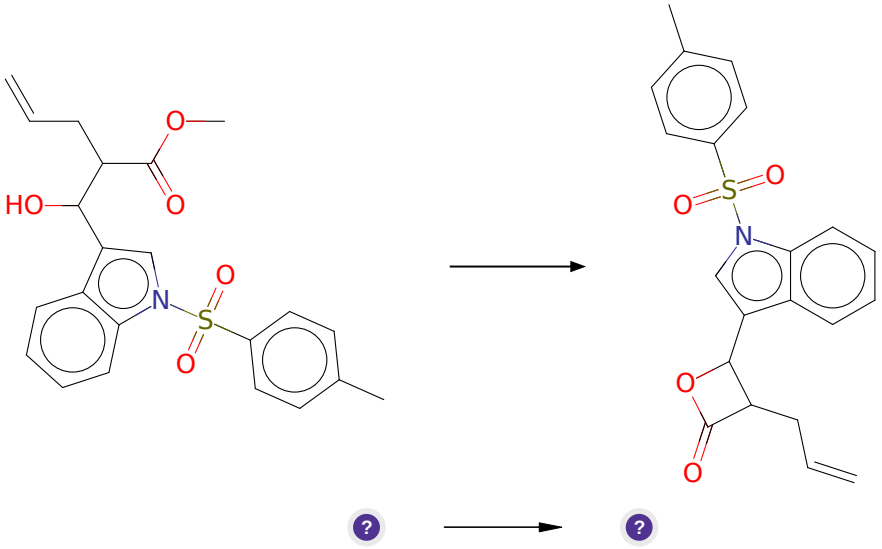
Typical conditions: NaBH4.EtOH.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112360* p. 3, 8 and *10.1016/j.ejmech.2010.10.012* p. 434, 436

Retrosynthesis ID: 50432

2.5.4 Acid catalyzed transesterification



Substrates:

1. C=CCC(C(=O)OC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC1C(=O)OC1c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

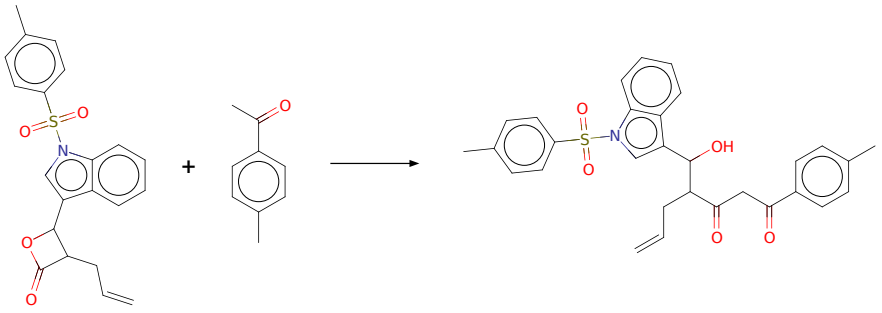
Typical conditions: H+

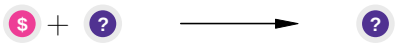
Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.5.5 Ring opening of lactones with enolates





Substrates:

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC1C(=O)OC1c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

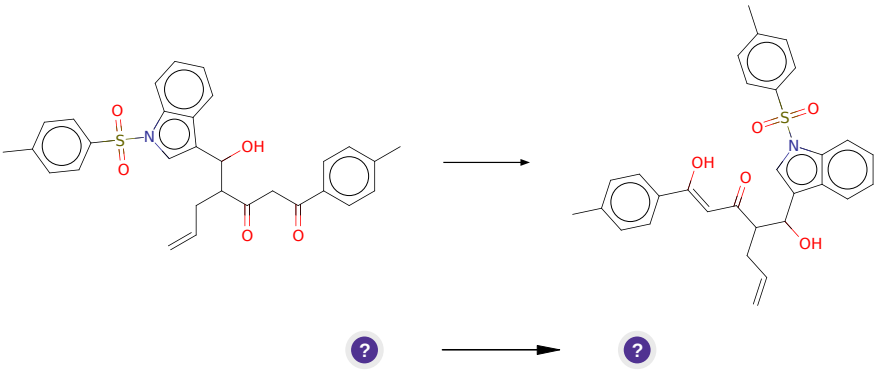
Typical conditions: LiHMDS.THF

Protections: none

Reference: *10.1021/ol801493w* and *10.1021/ol403423r* and *10.1021/ja061938g* and *10.1021/ja036521e*

Retrosynthesis ID: 24105

2.5.6 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

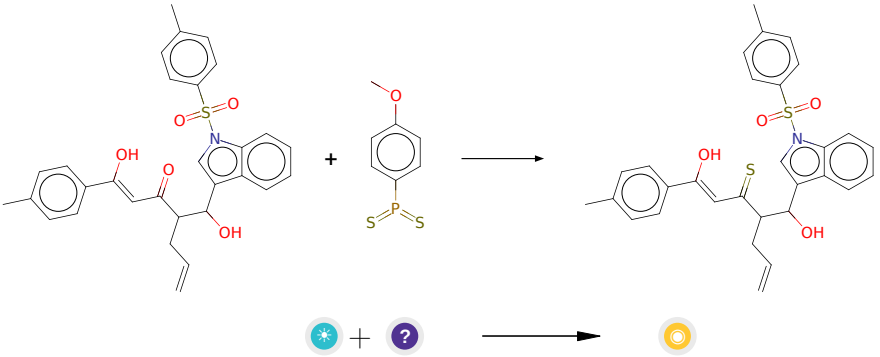
Typical conditions: solvent

Protections: none

Reference: *10.1021/ja01065a003* AND *10.1021/jo8012385*

Retrosynthesis ID: 7781

2.5.7 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

1. 4-methoxyphenyl-dithiophosphonsaeureanhydrid
2. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798