Paths of analysis*

BMK4

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

*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.

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: `84.06`

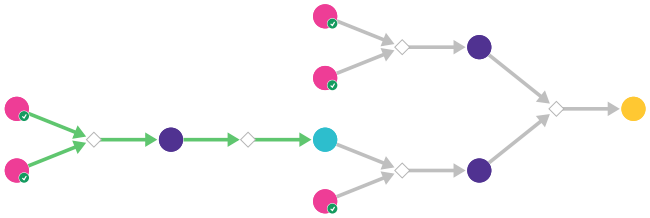
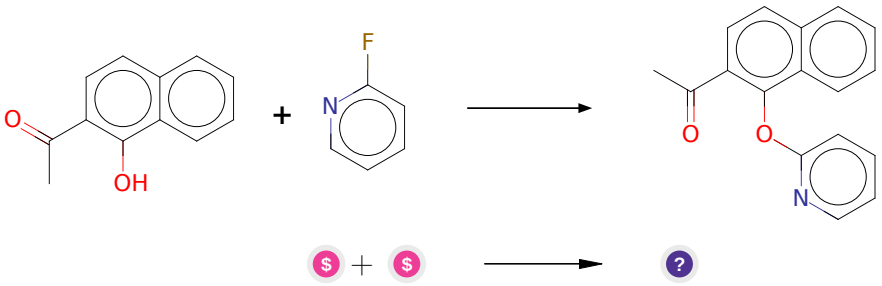


Figure 1: Outline of path 1

2.1.1 Nucleophilic aromatic substitution



Substrates:

1. 2-Fluoropyridine - *available at Sigma-Aldrich*
2. 2-Acetyl-1-naphthol - *available at Sigma-Aldrich*

Products:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

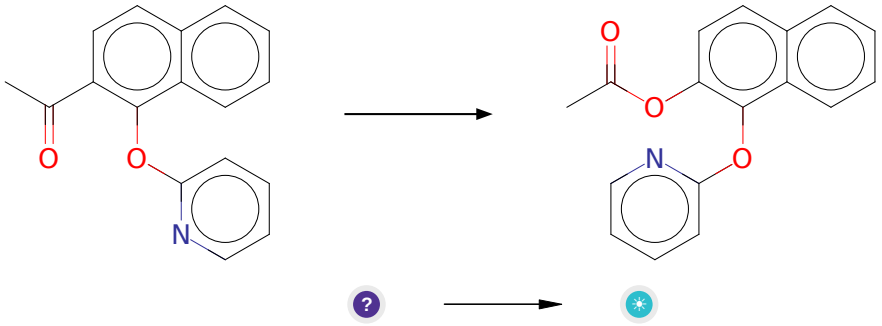
Typical conditions: NaH.THF.0-80 C or K2CO3.DMF.110 C

Protections: none

Reference: *10.1016/j.tetlet.2015.10.008* p. 6479, 6483 and *10.1016/j.ejmech.2016.06.056* p. 82, 85

Retrosynthesis ID: 49475

2.1.2 Bayer-Villiger oxidation



Substrates:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

Products:

1. C17H13NO3

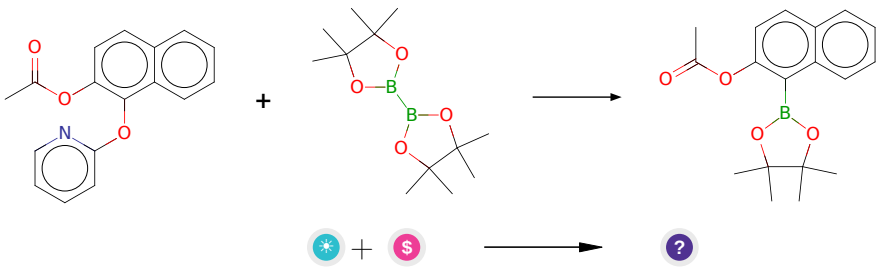
Typical conditions: mCPBA.NaHCO3.DCM

Protections: none

Reference: *10.1021/ol702571c* and *10.1021/ja00272a051* and *10.1080/00397910801997835*

Retrosynthesis ID: 4811

2.1.3 Rh-catalyzed borylation of aryl pyridyl ethers



Substrates:

1. C17H13NO3
2. Bis(pinacolato)diboron - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1

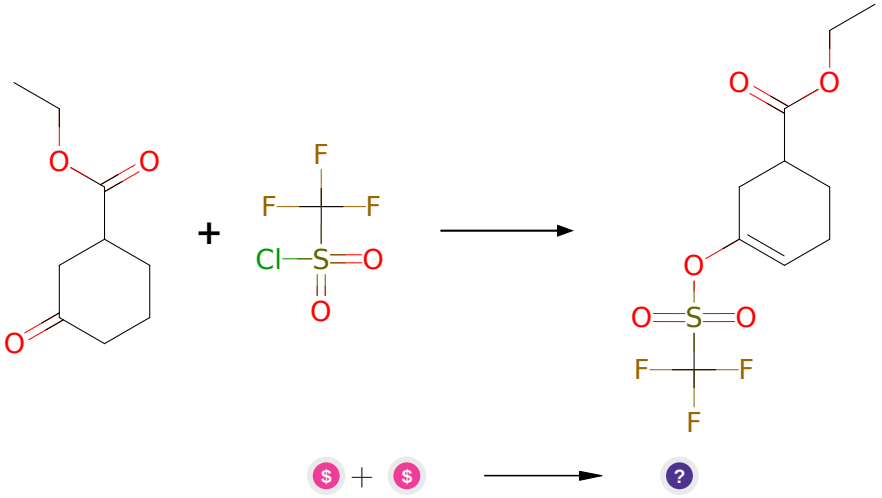
Typical conditions: [RhCl(cod)]2.PCy3.100C

Protections: none

Reference: DOI: *10.1021/ja511622e*

Retrosynthesis ID: 9950

2.1.4 Synthesis of enol sulfonates



Substrates:

1. Triflyl chloride - *available at Sigma-Aldrich*
2. Ethyl 3-oxocyclohexane-1-carboxylate - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

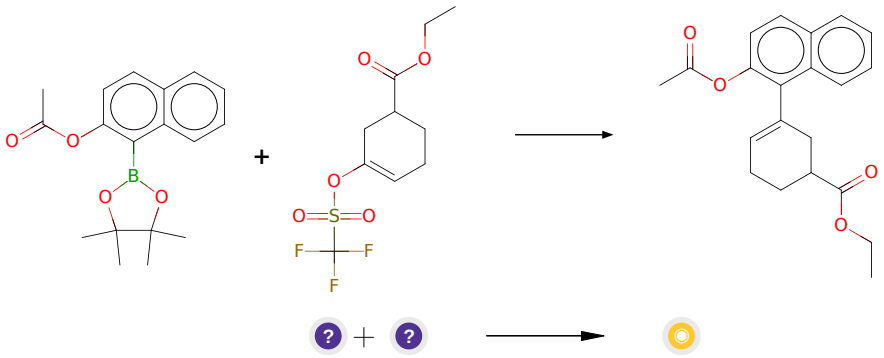
Typical conditions: base.electrophile.THF

Protections: none

Reference: *10.1021/jm960394y* and *10.1021/ja068826+* and *10.1002/anie.201500112* and *10.1021/jacs.6b08608*

Retrosynthesis ID: 10004758

2.1.5 Suzuki coupling of arylboronic pinacol esters with vinyl triflates



Substrates:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1
2. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

Products:

1. CCOC(=O)C1CCC=C(c2c(OC(C)=O)ccc3ccccc23)C1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10841

2.2 Path 2

Score: `84.06`

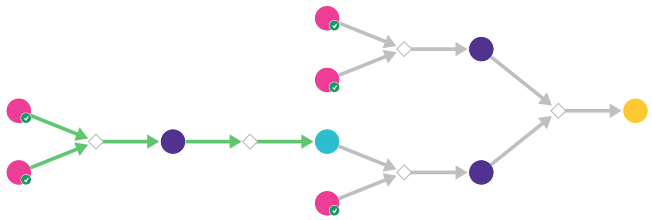
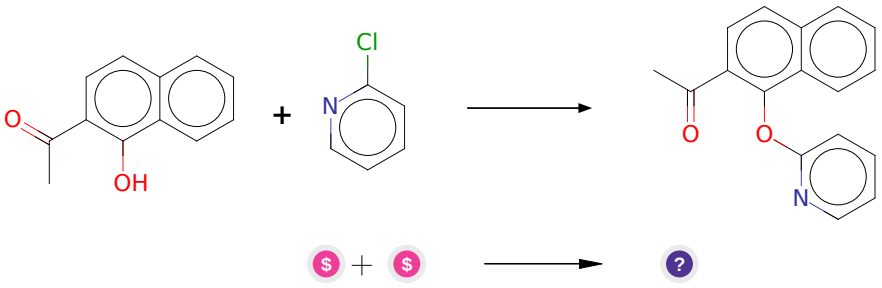


Figure 2: Outline of path 2

2.2.1 Nucleophilic aromatic substitution



Substrates:

1. 2-Chloropyridine - *available at Sigma-Aldrich*
2. 2-Acetyl-1-naphthol - *available at Sigma-Aldrich*

Products:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

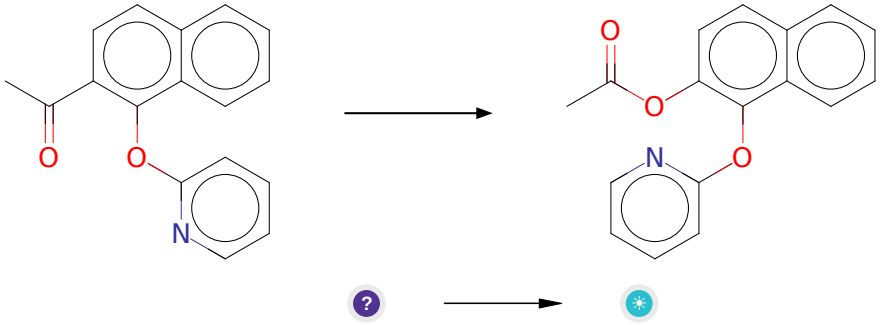
Typical conditions: K2CO3.DMAc

Protections: none

Reference: *10.1021/jm400463q* and *10.1016/j.bmc.2015.06.048* and *10.1007/s00044-013-0839-2* and *10.1021/jm2013453*

Retrosynthesis ID: 29655

2.2.2 Bayer-Villiger oxidation



Substrates:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

Products:

1. C17H13NO3

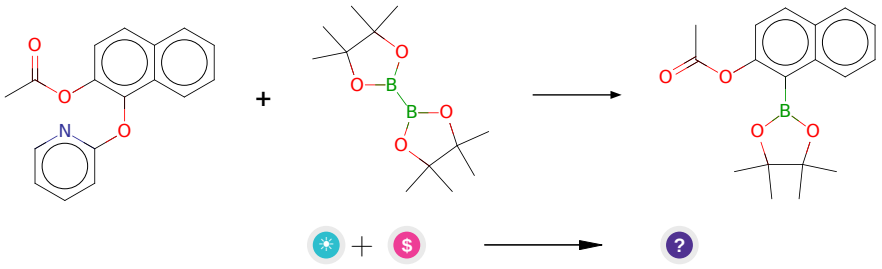
Typical conditions: mCPBA.NaHCO3.DCM

Protections: none

Reference: *10.1021/ol702571c* and *10.1021/ja00272a051* and *10.1080/00397910801997835*

Retrosynthesis ID: 4811

2.2.3 Rh-catalyzed borylation of aryl pyridyl ethers



Substrates:

1. C17H13NO3
2. Bis(pinacolato)diboron - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1

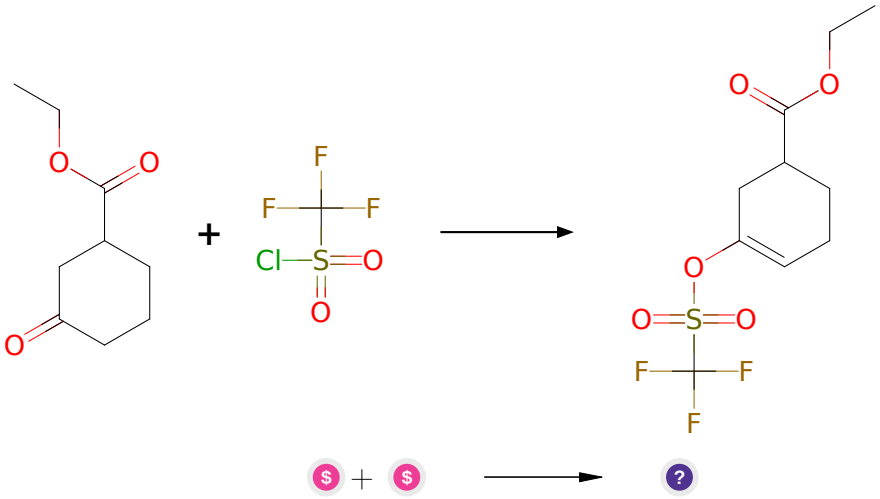
Typical conditions: [RhCl(cod)]2.PCy3.100C

Protections: none

Reference: DOI: *10.1021/ja511622e*

Retrosynthesis ID: 9950

2.2.4 Synthesis of enol sulfonates



Substrates:

1. Triflyl chloride - *available at Sigma-Aldrich*
2. Ethyl 3-oxocyclohexane-1-carboxylate - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

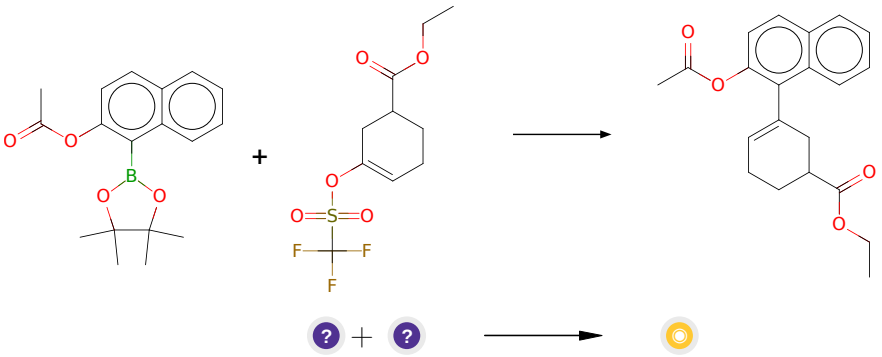
Typical conditions: base.electrophile.THF

Protections: none

Reference: *10.1021/jm960394y* and *10.1021/ja068826+* and *10.1002/anie.201500112* and *10.1021/jacs.6b08608*

Retrosynthesis ID: 10004758

2.2.5 Suzuki coupling of arylboronic pinacol esters with vinyl triflates



Substrates:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1
2. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

Products:

1. CCOC(=O)C1CCC=C(c2c(OC(C)=O)ccc3ccccc23)C1

Typical conditions: Pd catalyst.base.solvent

Protections: none

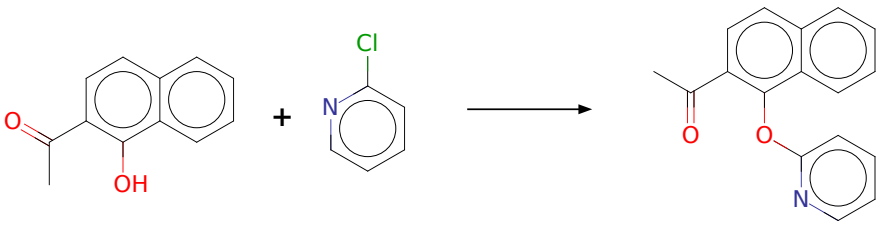
Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10841

2.3 Path 3

Score: 84.06

2.3.1 Nucleophilic aromatic substitution



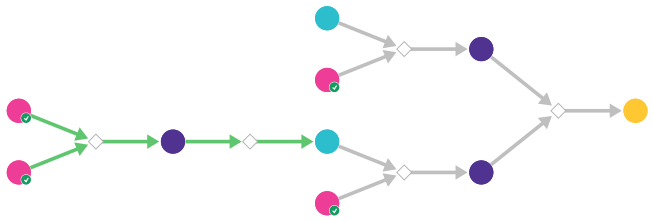
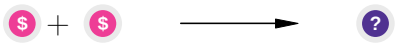


Figure 3: Outline of path 3



Substrates:

1. 2-Chloropyridine - *available at Sigma-Aldrich*
2. 2-Acetyl-1-naphthol - *available at Sigma-Aldrich*

Products:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

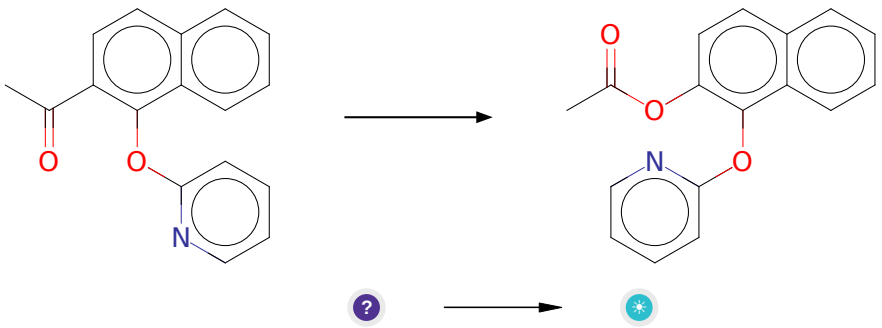
Typical conditions: K2CO3.DMAc

Protections: none

Reference: *10.1021/jm400463q* and *10.1016/j.bmc.2015.06.048* and *10.1007/s00044-013-0839-2* and *10.1021/jm2013453*

Retrosynthesis ID: 29655

2.3.2 Bayer-Villiger oxidation



Substrates:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

Products:

1. C17H13NO3

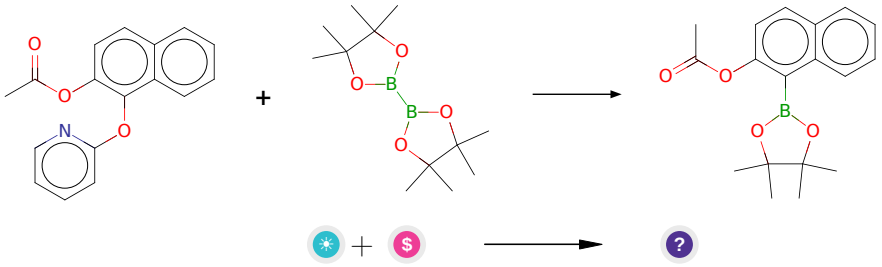
Typical conditions: mCPBA.NaHCO3.DCM

Protections: none

Reference: *10.1021/ol702571c* and *10.1021/ja00272a051* and *10.1080/00397910801997835*

Retrosynthesis ID: 4811

2.3.3 Rh-catalyzed borylation of aryl pyridyl ethers



Substrates:

1. C17H13NO3
2. Bis(pinacolato)diboron - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1

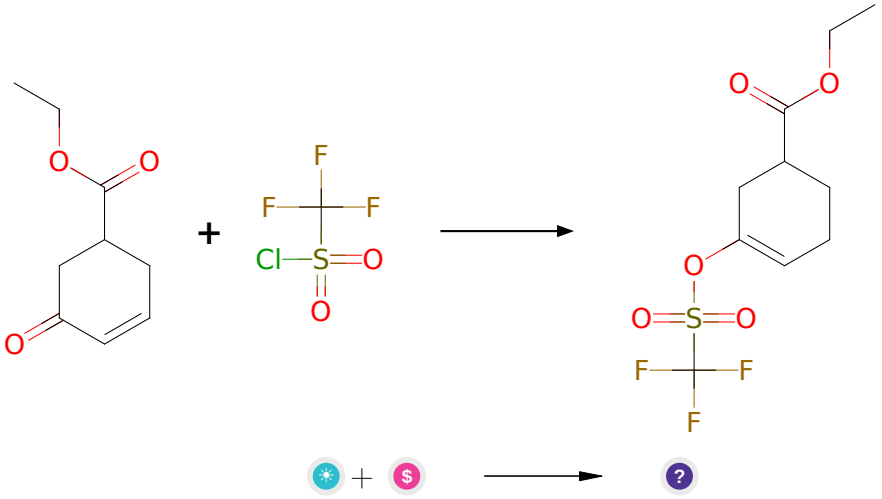
Typical conditions: [RhCl(cod)]2.PCy3.100C

Protections: none

Reference: DOI: *10.1021/ja511622e*

Retrosynthesis ID: 9950

2.3.4 Luche reduction of enones followed by enolate sulfonylation



Substrates:

1. C9H12O3
2. Triflyl chloride - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

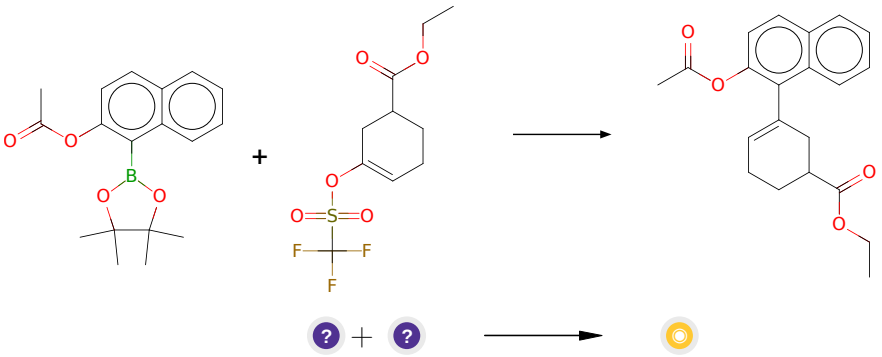
Typical conditions: L-selectridereg.THF

Protections: none

Reference: *10.1055/s-1985-31204* and *10.1021/ja00073a057* and *10.1021/ja057640s* and *10.1021/ol049780x* and *10.1021/ol1023954* and *10.1021/jo062423a*

Retrosynthesis ID: 25238

2.3.5 Suzuki coupling of arylboronic pinacol esters with vinyl triflates



Substrates:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1
2. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

Products:

1. CCOC(=O)C1CCC=C(c2c(OC(C)=O)ccc3ccccc23)C1

Typical conditions: Pd catalyst.base.solvent

Protections: none

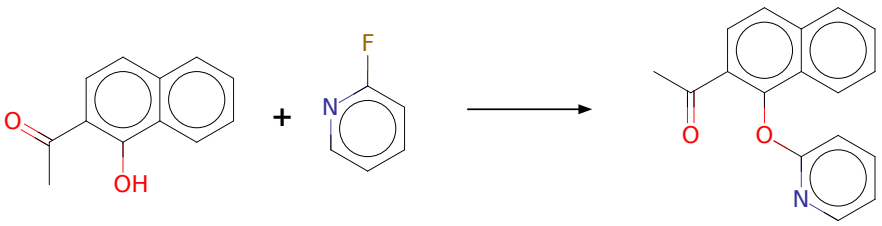
Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10841

2.4 Path 4

Score: 84.06

2.4.1 Nucleophilic aromatic substitution



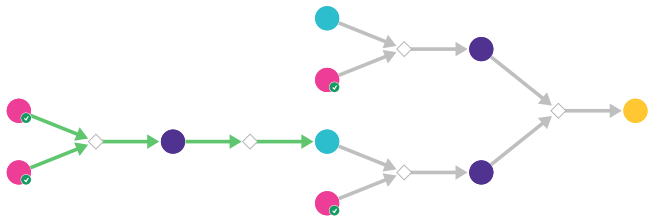
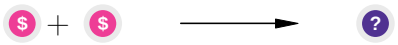


Figure 4: Outline of path 4



Substrates:

1. 2-Fluoropyridine - *available at Sigma-Aldrich*
2. 2-Acetyl-1-naphthol - *available at Sigma-Aldrich*

Products:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

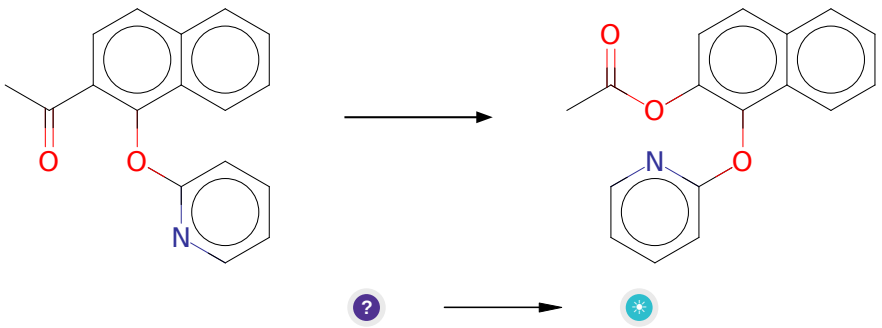
Typical conditions: NaH.THF.0-80 C or K2CO3.DMF.110 C

Protections: none

Reference: *10.1016/j.tetlet.2015.10.008* p. 6479, 6483 and *10.1016/j.ejmech.2016.06.056* p. 82, 85

Retrosynthesis ID: 49475

2.4.2 Bayer-Villiger oxidation



Substrates:

1. CC(=O)c1ccc2ccccc2c1Oc1ccccn1

Products:

1. C17H13NO3

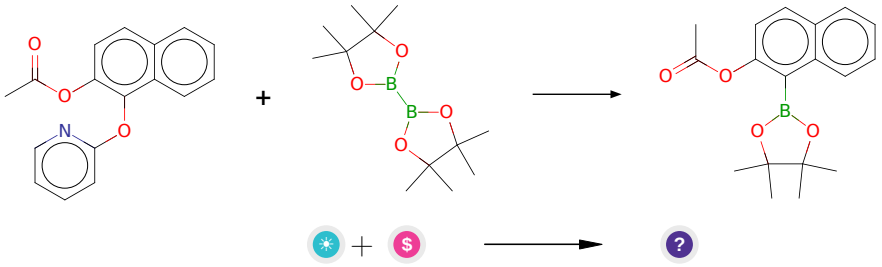
Typical conditions: mCPBA.NaHCO3.DCM

Protections: none

Reference: *10.1021/ol702571c* and *10.1021/ja00272a051* and *10.1080/00397910801997835*

Retrosynthesis ID: 4811

2.4.3 Rh-catalyzed borylation of aryl pyridyl ethers



Substrates:

1. C17H13NO3
2. Bis(pinacolato)diboron - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1

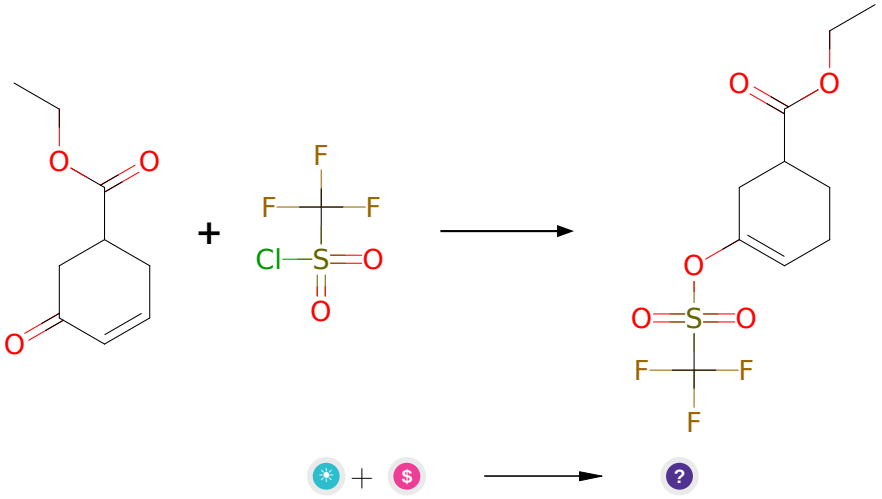
Typical conditions: [RhCl(cod)]2.PCy3.100C

Protections: none

Reference: DOI: *10.1021/ja511622e*

Retrosynthesis ID: 9950

2.4.4 Luche reduction of enones followed by enolate sulfonylation



Substrates:

1. C9H12O3
2. Triflyl chloride - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

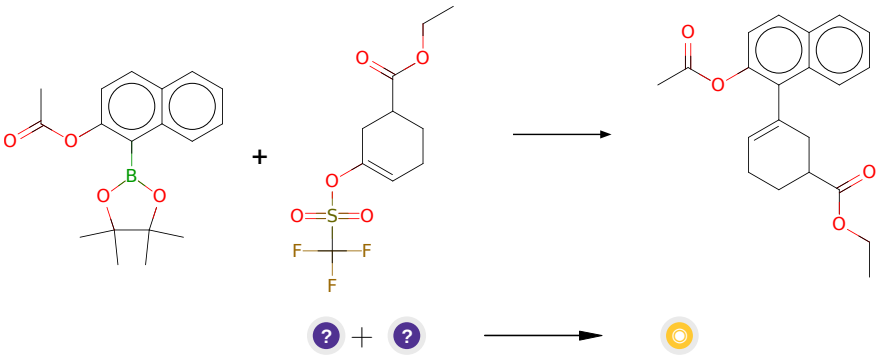
Typical conditions: L-selectridereg.THF

Protections: none

Reference: *10.1055/s-1985-31204* and *10.1021/ja00073a057* and *10.1021/ja057640s* and *10.1021/ol049780x* and *10.1021/ol1023954* and *10.1021/jo062423a*

Retrosynthesis ID: 25238

2.4.5 Suzuki coupling of arylboronic pinacol esters with vinyl triflates



Substrates:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1
2. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

Products:

1. CCOC(=O)C1CCC=C(c2c(OC(C)=O)ccc3ccccc23)C1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10841

2.5 Path 5

Score: 90.31

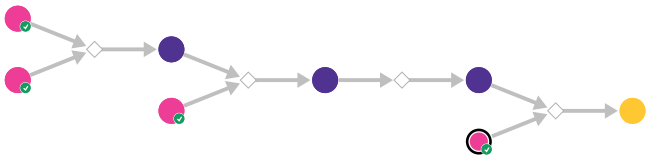
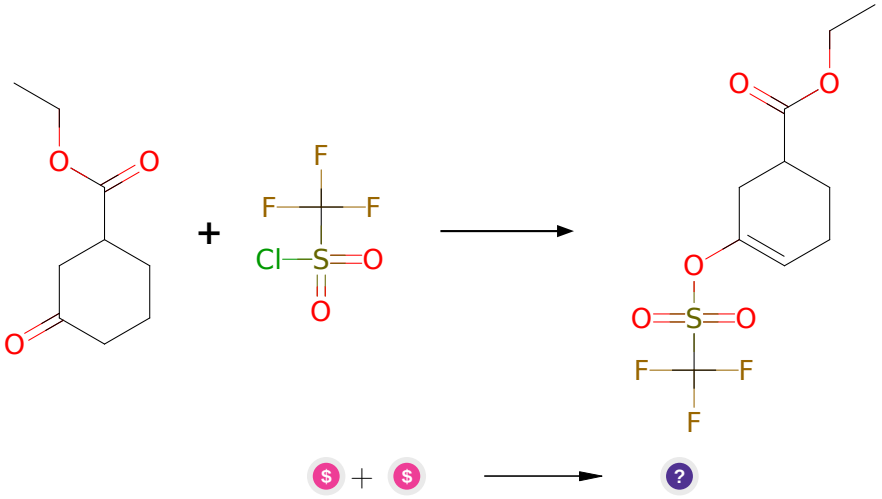


Figure 5: Outline of path 5

2.5.1 Synthesis of enol sulfonates



Substrates:

1. Triflyl chloride - *available at Sigma-Aldrich*
2. Ethyl 3-oxocyclohexane-1-carboxylate - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1

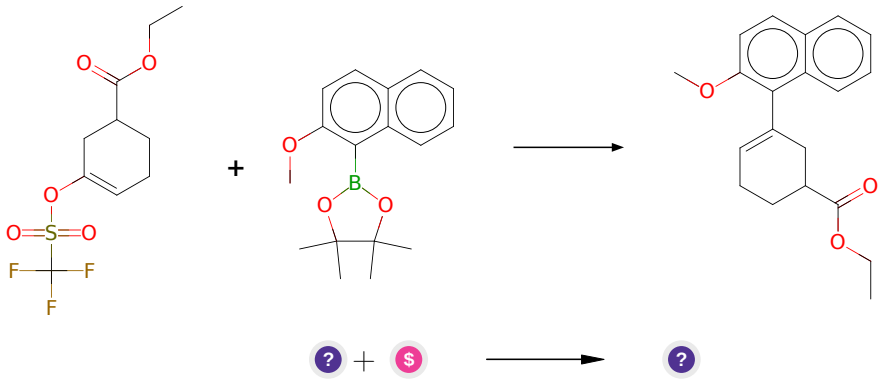
Typical conditions: base.electrophile.THF

Protections: none

Reference: *10.1021/jm960394y* and *10.1021/ja068826+* and *10.1002/anie.201500112* and *10.1021/jacs.6b08608*

Retrosynthesis ID: 10004758

2.5.2 Suzuki coupling of arylboronic pinacol esters with vinyl triflates



Substrates:

1. CCOC(=O)C1CCC=C(OS(=O)(=O)C(F)(F)F)C1
2. 2-Methoxy-1-naphthaleneboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(c2c(OC)ccc3ccccc23)C1

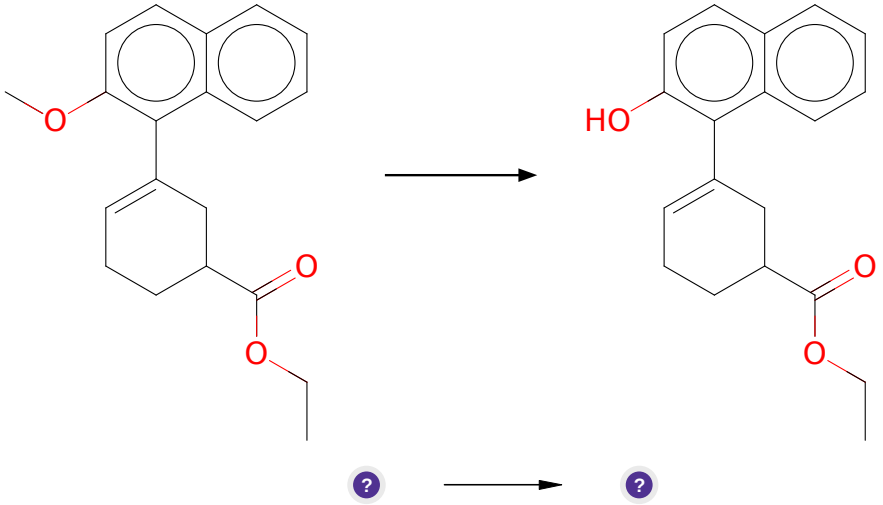
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10841

2.5.3 Demethylation of Phenols



Substrates:

1. CCOC(=O)C1CCC=C(c2c(OC)ccc3ccccc23)C1

Products:

1. CCOC(=O)C1CCC=C(c2c(O)ccc3ccccc23)C1

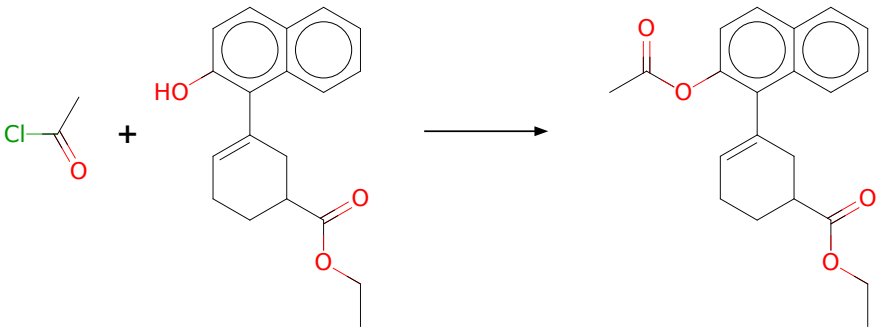
Typical conditions: BBr3.CH2Cl2

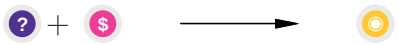
Protections: none

Reference: DOI: *10.1021/ja00105a021* and *10.1021/jm00176a011* and *10.1021/jm970277i* and *10.1021/ja0106164* and Patent: US2010/16298, 2010, A1, page 185

Retrosynthesis ID: 10011837

2.5.4 Reaction of acyl chlorides with alcohols and phenols





Substrates:

1. CCOC(=O)C1CCC=C(c2c(O)ccc3ccccc23)C1
2. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CCOC(=O)C1CCC=C(c2c(OC(C)=O)ccc3ccccc23)C1

Typical conditions: base.DCM

Protections: none

Reference: *10.1016/j.bmcl.2012.03.021* AND *10.1021/ja026266i* (SI, hydroperoxides) AND *10.1016/j.tetasy.2004.07.044* AND *10.1021/jm1006929* (SI) AND *10.1016/j.tet.2011.05.017* AND *10.1016/j.tetasy.2012.09.002* AND *10.1021/ol016268s* (SI) AND *10.1021/jo801116n* AND *10.1021/jo00279a041* AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549