Paths of analysis*

L11_DIA

Synthia

October 11, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: 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

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

Tunnels 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: 250.22

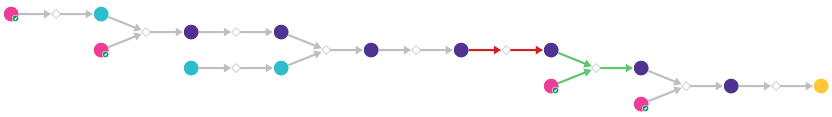
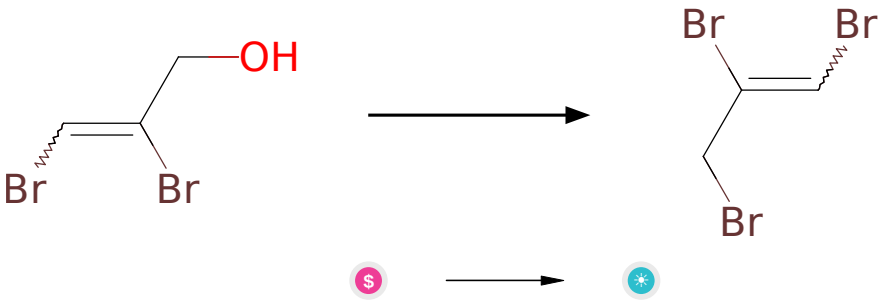


Figure 1: Outline of path 1

2.1.1 Appel Reaction



Substrates:

1. 2,3-Dibromoallyl alcohol - *available at Sigma-Aldrich*

Products:

1. 1,2,3-tribrom-propen

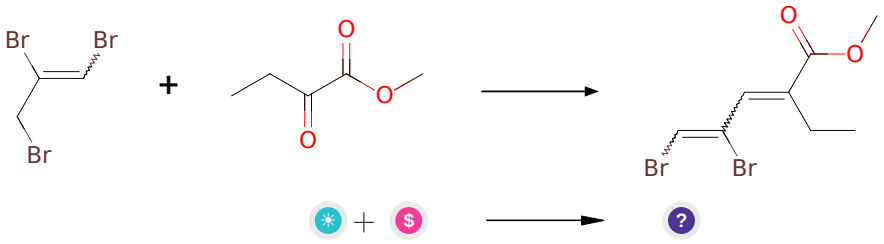
Typical conditions: PPh3.CBr4

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

2.1.2 HWE/Wittig Olefination



Substrates:

1. 1,2,3-tribrom-propen
2. Methyl 2-ketobutyrate - *available at Sigma-Aldrich*

Products:

1. CCC(=CC(Br)=CBr)C(=O)OC

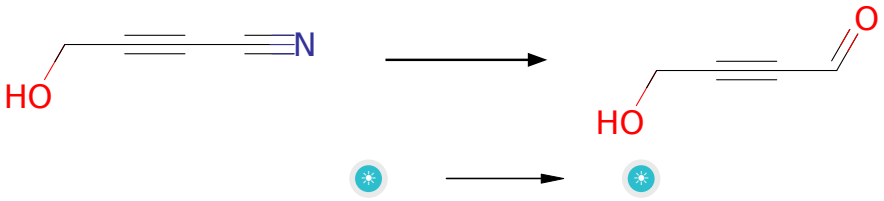
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1002/anie.200705005* and *10.1021/ol052106a* and *10.1021/jo00075a064* and *10.1021/ol3027297*

Retrosynthesis ID: 24425

2.1.3 Reduction of nitriles to aldehydes



Substrates:

1. g-hydroxybut-2-ynenitrile

Products:

1. 4-hydroxy-but-2-ynal

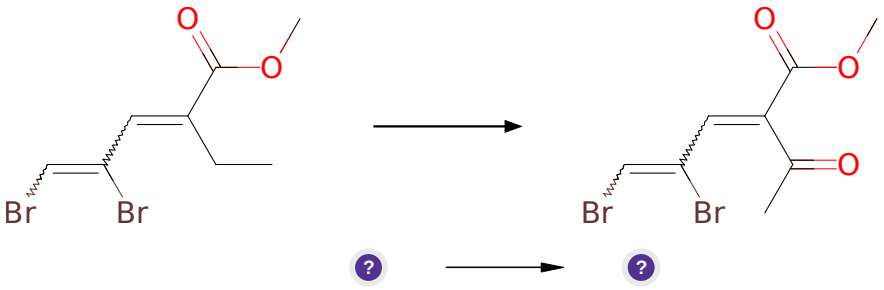
Typical conditions: DIBALH.DCM

Protections: none

Reference: *10.1016/j.bmc.2006.01.061* and *10.1016/j.tet.2012.07.022* and *10.1016/j.bmcl.2009.01.075* and *10.1016/j.bmcl.2007.09.081* and *10.1021/jo000502v*

Retrosynthesis ID: 31406

2.1.4 Allylic Oxidation of Alkenes



Substrates:

1. CCC(=CC(Br)=CBr)C(=O)OC

Products:

1. COC(=O)C(=CC(Br)=CBr)C(C)=O

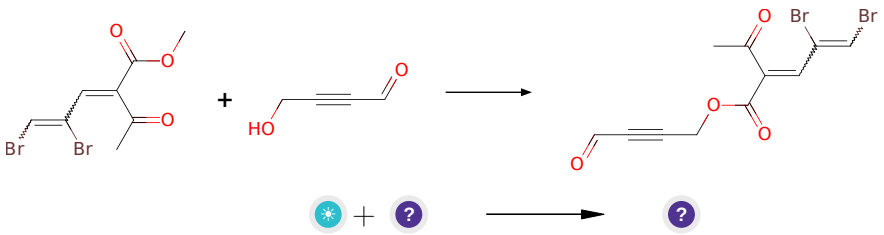
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.1.5 Acid catalyzed transesterification



Substrates:

1. 4-hydroxy-but-2-ynal
2. COC(=O)C(=CC(Br)=CBr)C(C)=O

Products:

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC#CC=O

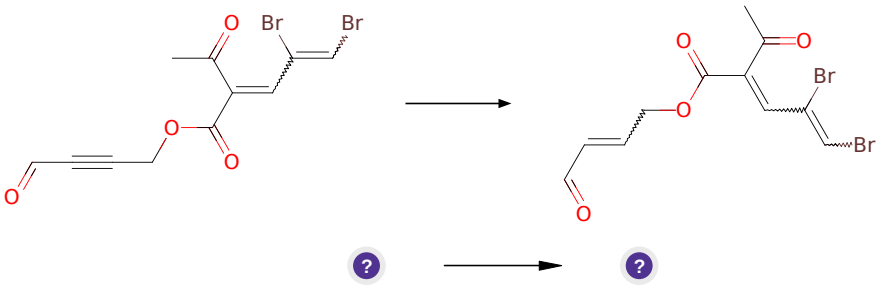
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.1.6 Reduction of alkynes to alkenes



Substrates:

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC#CC=O

Products:

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC=CC=O

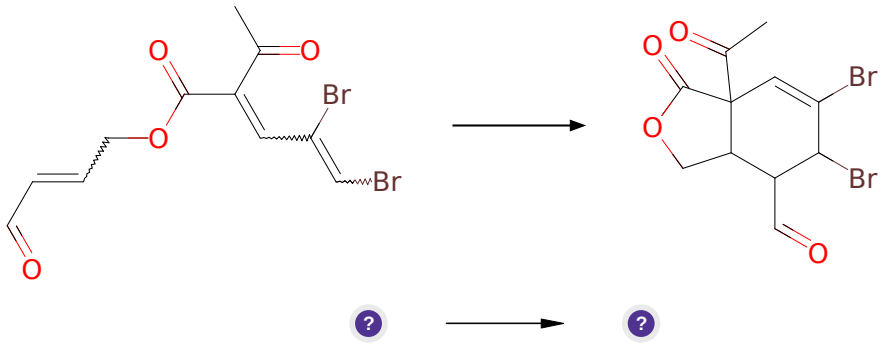
Typical conditions: H2.Lindlar's catalyst

Protections: none

Reference: *10.1021/ja054487t* (SI) AND *10.1021/jm9810912*

Retrosynthesis ID: 14627

2.1.7 Diels-Alder



Substrates:

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC=CC=O

Products:

1. CC(=O)C12C=C(Br)C(Br)C(C=O)C1COC2=O

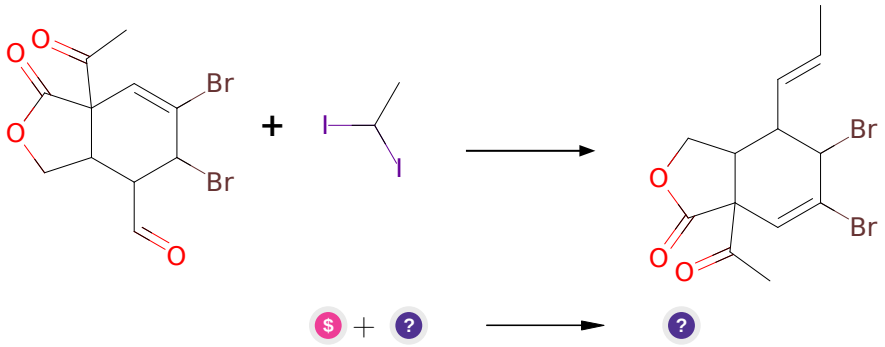
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.1.8 Takai olefination



Substrates:

1. 1,1-Diiodoethane - *available at Sigma-Aldrich*
2. CC(=O)C12C=C(Br)C(Br)C(C=O)C1COC2=O

Products:

1. C/C=C/C1C(Br)C(Br)=CC2(C(C)=O)C(=O)OCC12

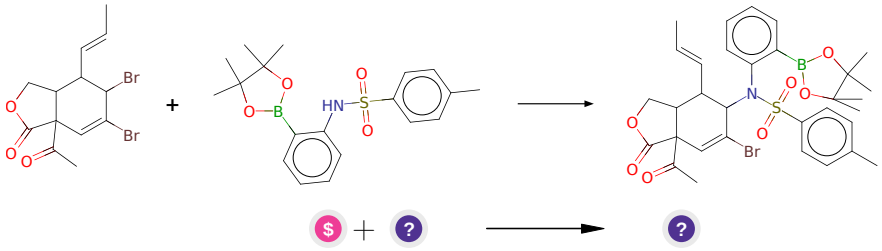
Typical conditions: CrCl2.THF.DMF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10942

2.1.9 Alkylation of amines with alkyl bromides



Substrates:

1. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*
2. C/C=C/C1C(Br)C(Br)=CC2(C(C)=O)C(=O)OCC12

Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O

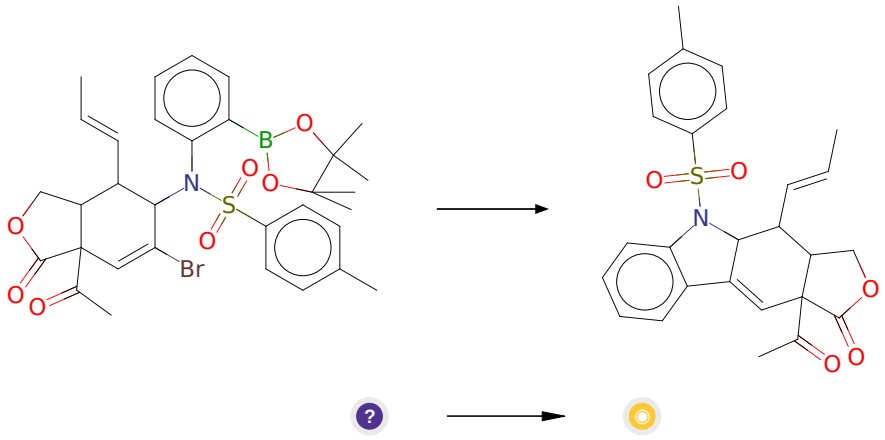
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.1.10 Suzuki coupling of arylboronic pinacol esters with vinyl Bromides



Substrates:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O

Products:

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

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: 10695

2.2 Path 2

Score: 269.29

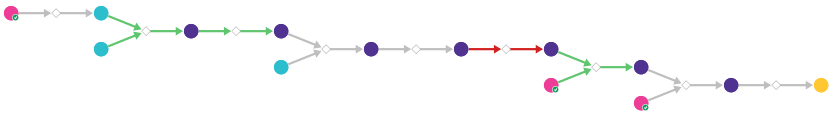
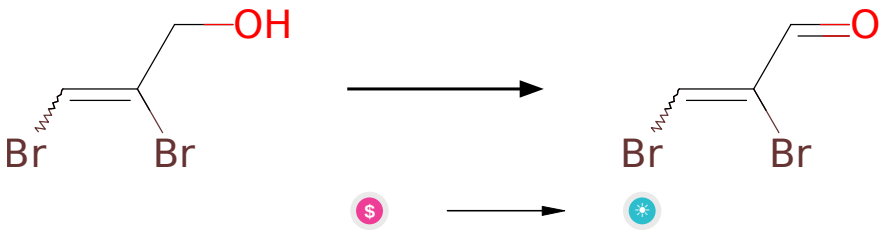


Figure 2: Outline of path 2

2.2.1 Oxidation of primary alcohols with DMP



Substrates:

1. 2,3-Dibromoallyl alcohol - *available at Sigma-Aldrich*

Products:

1. 2,3-dibromo-propenal

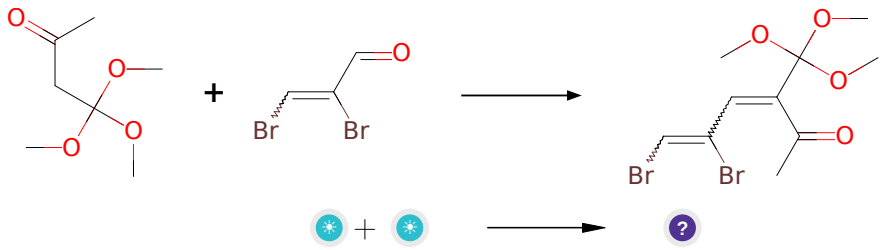
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

Retrosynthesis ID: 50426

2.2.2 Aldol Condensation



Substrates:

1. 3,3,3-trimethoxybutan-2-one
2. 2,3-dibromo-propenal

Products:

1. COC(OC)(OC)C(=CC(Br)=CBr)C(C)=O

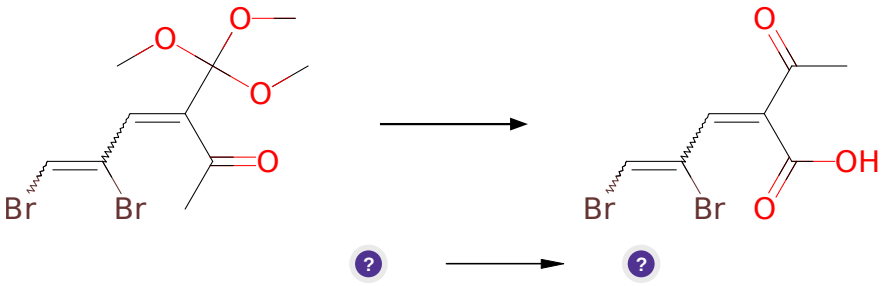
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.2.3 Synthesis of carboxylic acids from acetals



Substrates:

1. COC(OC)(OC)C(=CC(Br)=CBr)C(C)=O

Products:

1. CC(=O)C(=CC(Br)=CBr)C(=O)O

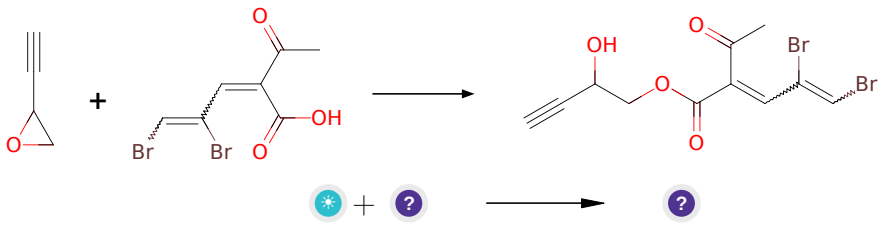
Typical conditions: HCl.H2O

Protections: none

Reference: *10.1016/j.tetasy.2010.12.014*

Retrosynthesis ID: 25207

2.2.4 Opening of epoxides with carboxylic acids



Substrates:

1. ethynyl-oxirane
2. CC(=O)C(=CC(Br)=CBr)C(=O)O

Products:

1. C#CC(O)COC(=O)C(=CC(Br)=CBr)C(C)=O

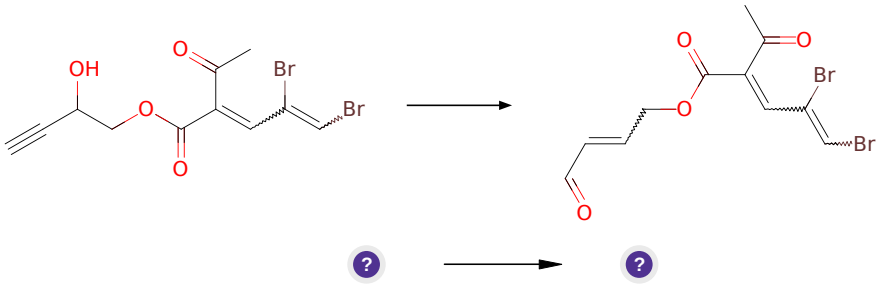
Typical conditions: RCOOH.catalyst

Protections: none

Reference: *10.1021/ol051051+* AND *10.1016/j.tet.2005.05.050* and US2011/86912 A1 (P.13) and *10.1055/s-2003-42416* and *10.5012/bkcs.2013.34.8.2286*

Retrosynthesis ID: 15151

2.2.5 Meyer-Schuster Rearrangement



Substrates:

1. C#CC(O)COC(=O)C(=CC(Br)=CBr)C(C)=O

Products:

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC=CC=O

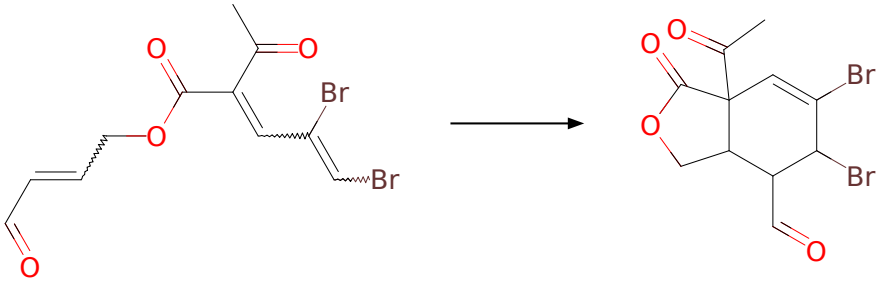
Typical conditions: H+

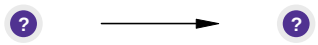
Protections: none

Reference: *10.1021/cr60273a001*

Retrosynthesis ID: 10143

2.2.6 Diels-Alder





Substrates:

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC=CC=O

Products:

1. CC(=O)C12C=C(Br)C(Br)C(C=O)C1COC2=O

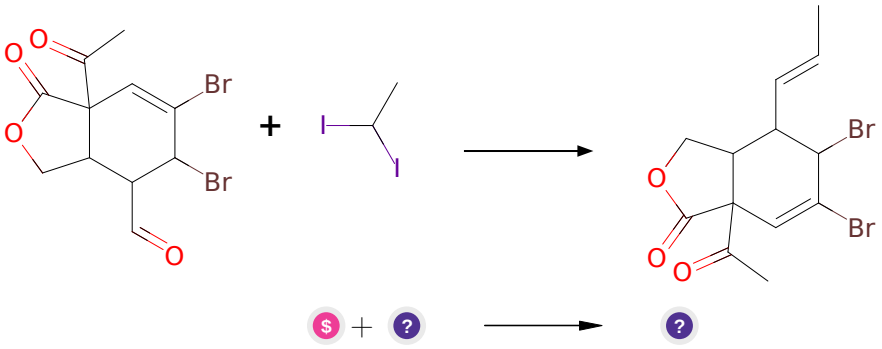
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.2.7 Takai olefination



Substrates:

1. 1,1-Diiodoethane - *available at Sigma-Aldrich*
2. CC(=O)C12C=C(Br)C(Br)C(C=O)C1COC2=O

Products:

1. C/C=C/C1C(Br)C(Br)=CC2(C(C)=O)C(=O)OCC12

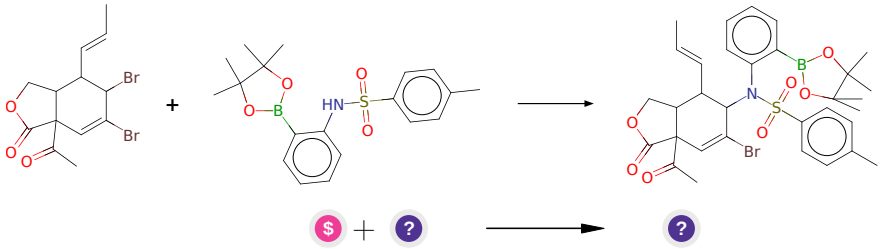
Typical conditions: CrCl2.THF.DMF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10942

2.2.8 Alkylation of amines with alkyl bromides



Substrates:

1. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*
2. C/C=C/C1C(Br)C(Br)=CC2(C(C)=O)C(=O)OCC12

Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O

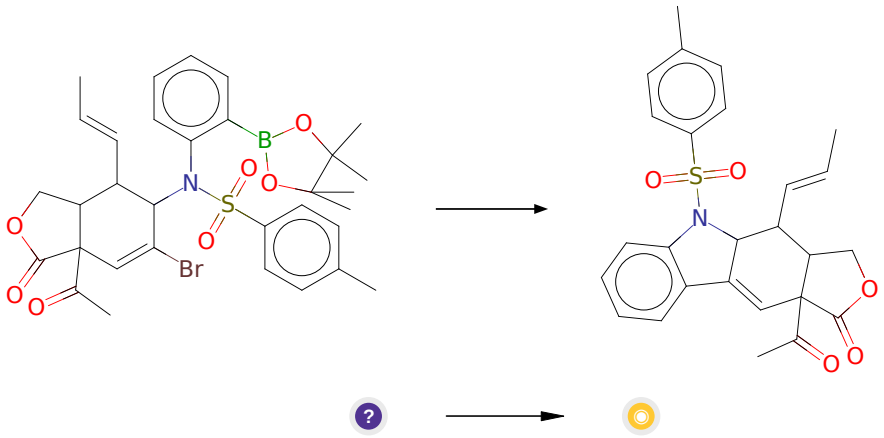
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.2.9 Suzuki coupling of arylboronic pinacol esters with vinyl Bromides



Substrates:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O

Products:

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

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: 10695