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

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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: 388.50

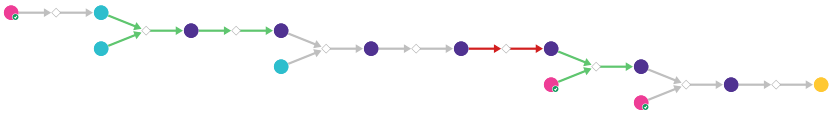
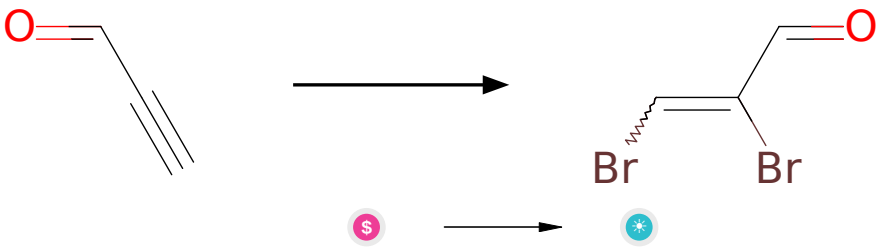


Figure 1: Outline of path 1

2.1.1 Bromination of Alkynes



Substrates:

1. propynal - *available at Sigma-Aldrich*

Products:

1. 2,3-dibromo-propenal

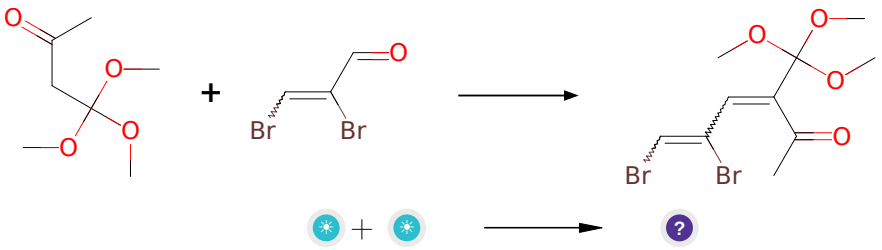
Typical conditions: NBS. THF. 80C

Protections: none

Reference: DOI: *10.1016/j.tetlet.2011.06.047* or DOI: *10.1055/s-2006-941558* or DOI: *10.1021/jo011016q*

Retrosynthesis ID: 8354

2.1.2 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

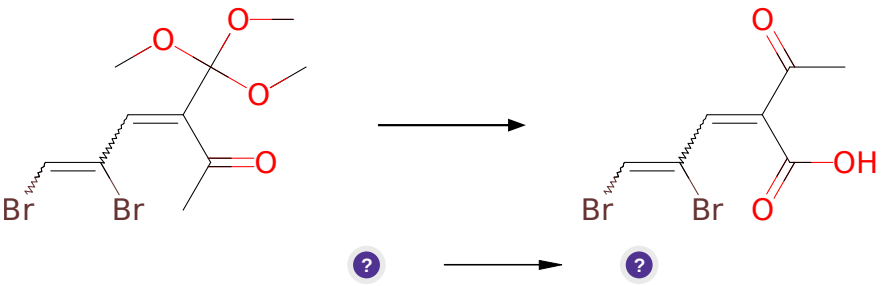
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.1.3 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

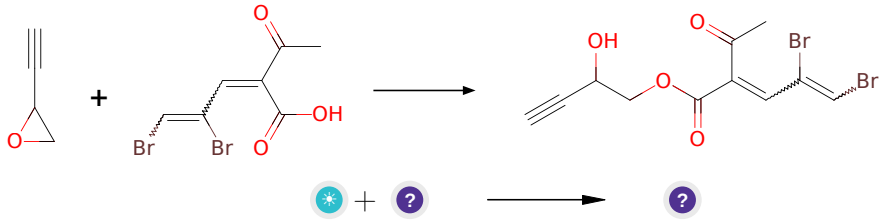
Typical conditions: HCl.H2O

Protections: none

Reference: *10.1016/j.tetasy.2010.12.014*

Retrosynthesis ID: 25207

2.1.4 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

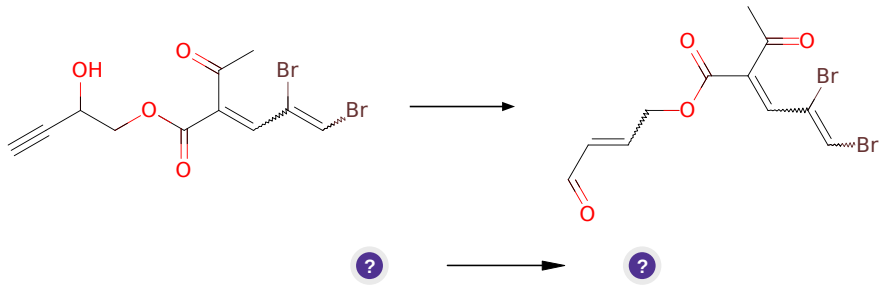
Typical conditions: RCOOH.catalyst

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

2.1.5 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

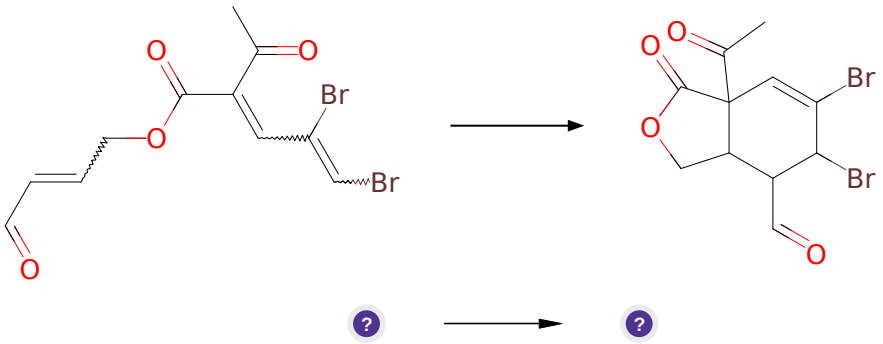
Typical conditions: H+

Protections: none

Reference: *10.1021/cr60273a001*

Retrosynthesis ID: 10143

2.1.6 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

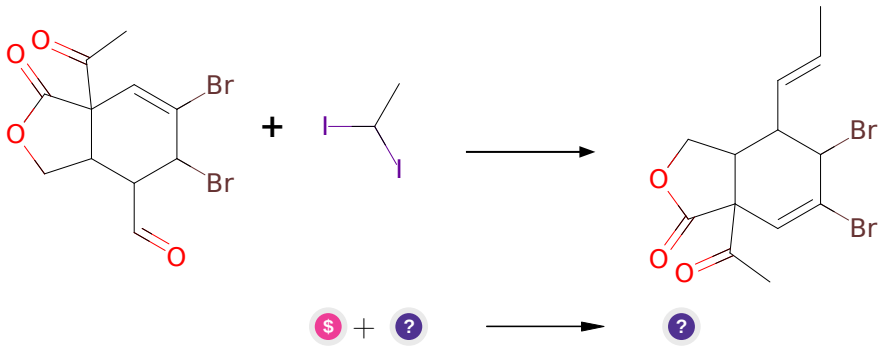
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.1.7 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

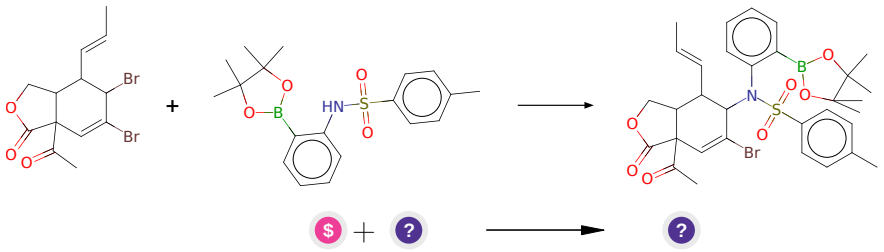
Typical conditions: CrCl2.THF.DMF

Protections: none

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

Retrosynthesis ID: 10942

2.1.8 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

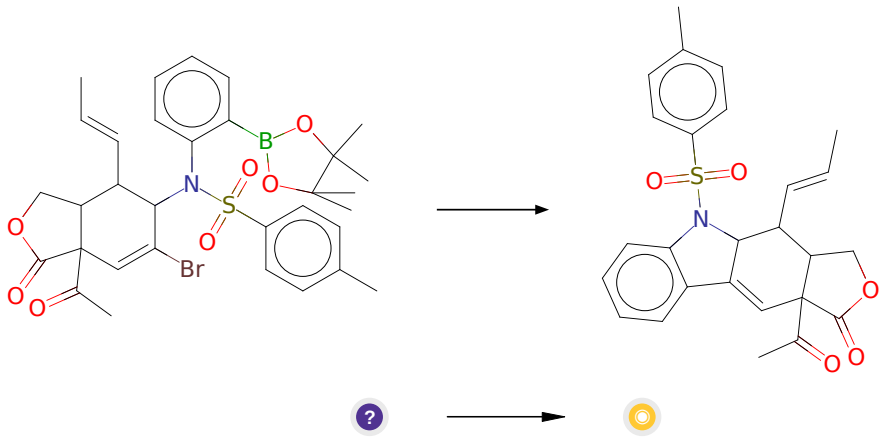
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.1.9 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

2.2 Path 2

Score: 399.23

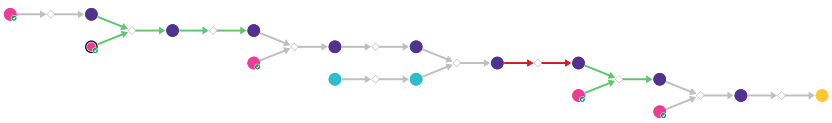
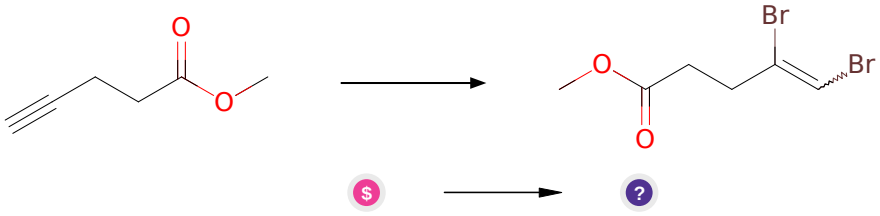


Figure 2: Outline of path 2

2.2.1 Bromination of Alkynes



Substrates:

1. Methyl pent-4-ynoate - *available at Sigma-Aldrich*

Products:

1. COC(=O)CCC(Br)=CBr

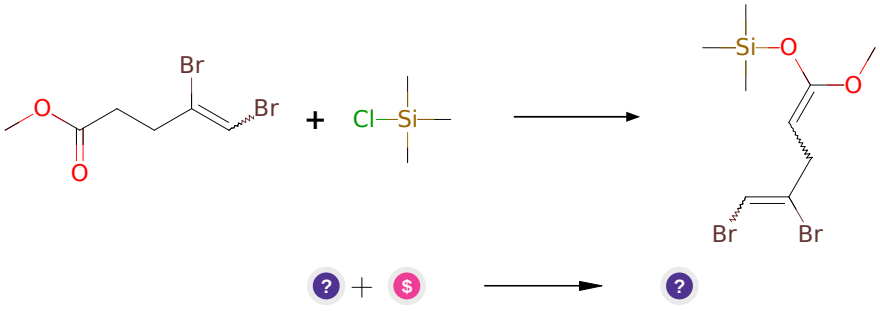
Typical conditions: NBS. THF. 80C

Protections: none

Reference: DOI: *10.1016/j.tetlet.2011.06.047* or DOI: *10.1055/s-2006-941558* or DOI: *10.1021/jo011016q*

Retrosynthesis ID: 8354

2.2.2 Enol esters and ethers synthesis



Substrates:

1. COC(=O)CCC(Br)=CBr

2. TMSCl - *available at Sigma-Aldrich*

Products:

1. COC(=CCC(Br)=CBr)O[Si](C)(C)C

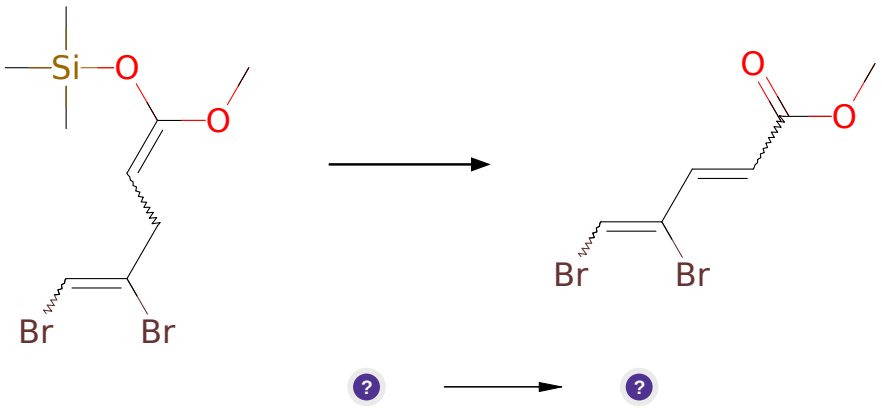
Typical conditions: 1.LDA.2.Electrophile

Protections: none

Reference: US2467095A AND WO2014169833a1 AND *10.1016/j.steroids.2011.03.014* AND *10.1021/ol200875m* (SI) AND *10.1021/ja00531a034*

Retrosynthesis ID: 7797

2.2.3 Dehydrogenation of silyl enol ethers



Substrates:

1. COC(=CCC(Br)=CBr)O[Si](C)(C)C

Products:

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

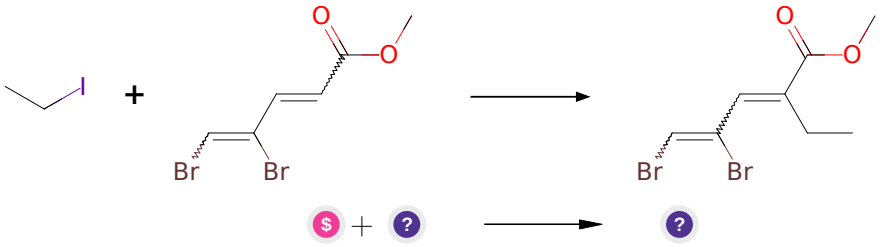
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

Protections: none

Reference: *10.1271/bbb.60.405* and *10.1039/C3CC46778C* and US2015284405 p.40 and *10.1016/S0040-4039(01)81518-5* and US2010204477 p. 15-16 and *10.1016/0040-4039(95)00694-8* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999877

2.2.4 Alkylation of vinyl esters



Substrates:

1. Iodoethane - *available at Sigma-Aldrich*
2. COC(=O)C=CC(Br)=CBr

Products:

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

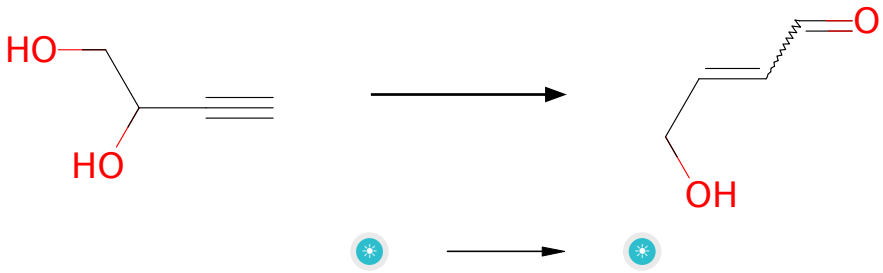
Typical conditions: LDA.THF

Protections: none

Reference: DOI: *10.1039/C39870001410*

Retrosynthesis ID: 886

2.2.5 Meyer-Schuster Rearrangement



Substrates:

1. but-3-in-1,2-diol

Products:

1. 4-hydroxy-but-2-enal

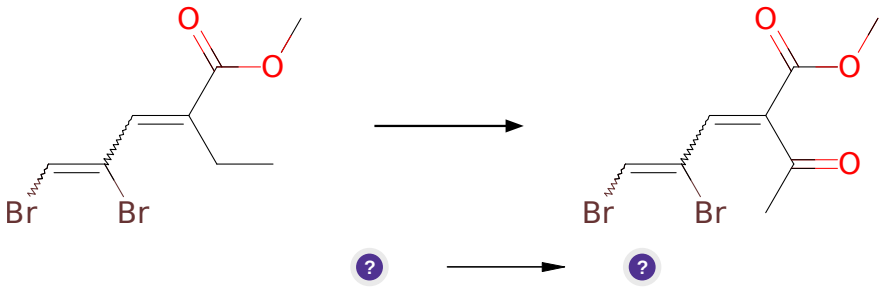
Typical conditions: H+

Protections: none

Reference: *10.1021/cr60273a001*

Retrosynthesis ID: 10143

2.2.6 Allylic Oxidation of Alkenes



Substrates:

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

Products:

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

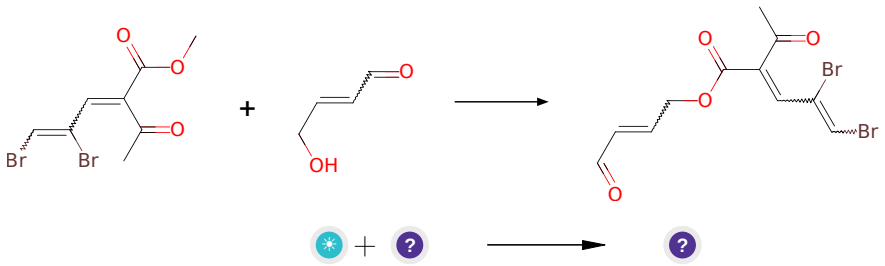
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.2.7 Acid catalyzed transesterification



Substrates:

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

Products:

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

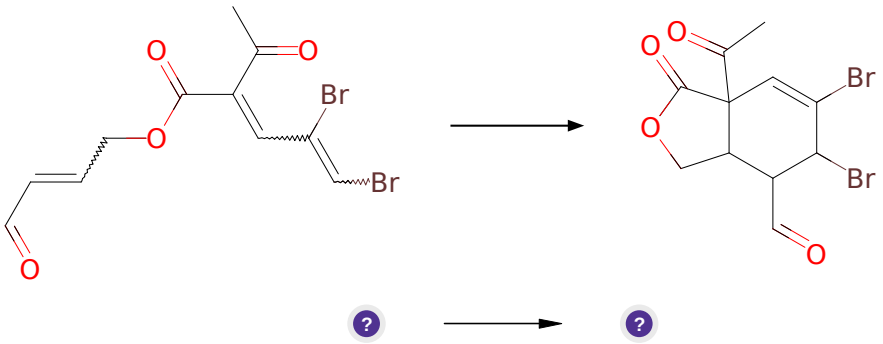
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.2.8 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

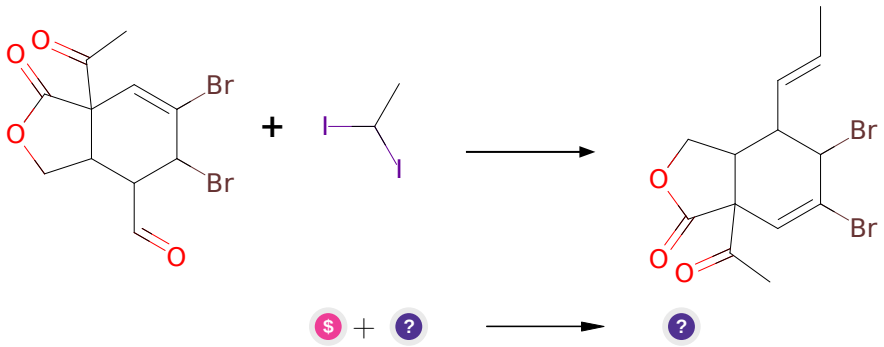
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.2.9 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

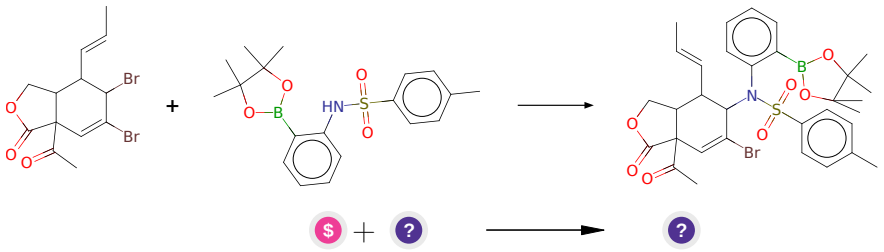
Typical conditions: CrCl2.THF.DMF

Protections: none

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

Retrosynthesis ID: 10942

2.2.10 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

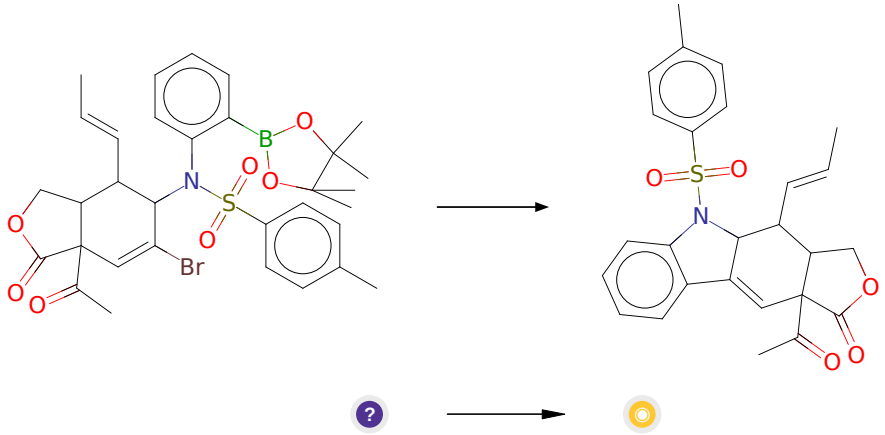
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.2.11 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