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: `112.89`

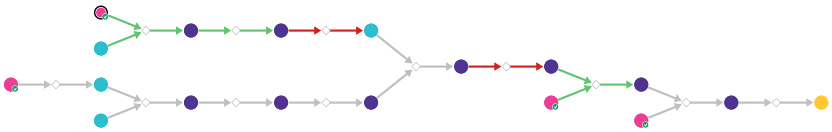
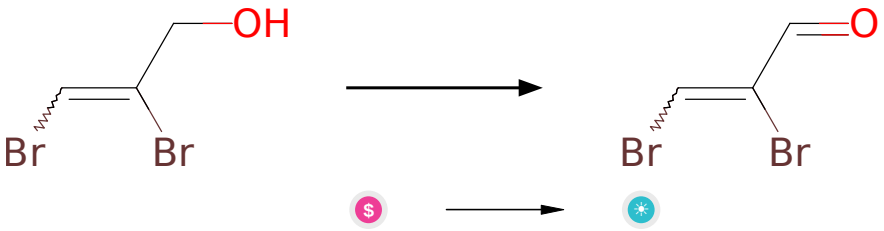


Figure 1: Outline of path 1

2.1.1 Oxidation of primary alcohols with DMP



Substrates:

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

Products:

1. 2,3-dibromo-propenal

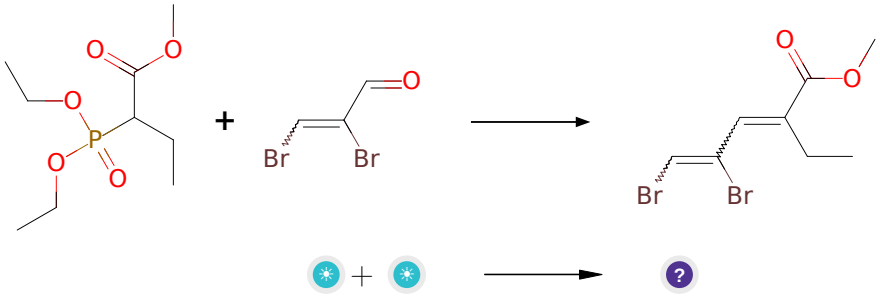
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.1.2 Wittig-Horner Reaction



Substrates:

1. 2,3-dibromo-propenal
2. diethylphosphono-2 butanoate de methyle

Products:

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

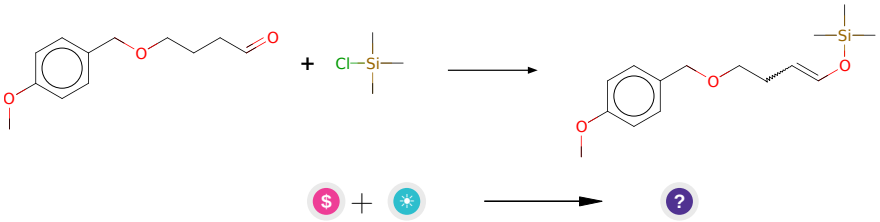
Typical conditions: NaH.THF.0 C or NaH.DMF.0-50 C

Protections: none

Reference: *10.1021/acs.jmedchem.5b01239* p. 63, 71 and *10.1021/jm950725r* p. 3150, 3153

Retrosynthesis ID: 11549

2.1.3 Enol esters and ethers synthesis



Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. 4-(4-methoxybenzyl)oxy-1-butanal

Products:

1. COc1ccc(COCCC=CO[Si](C)(C)C)cc1

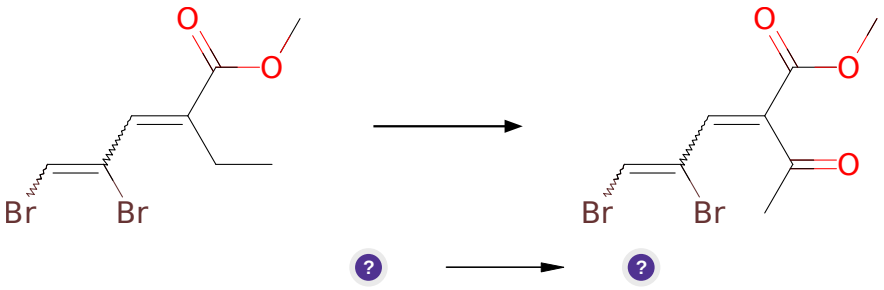
Typical conditions: 1.LDA.2.Electrophile

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

2.1.4 Allylic Oxidation of Alkenes



Substrates:

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

Products:

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

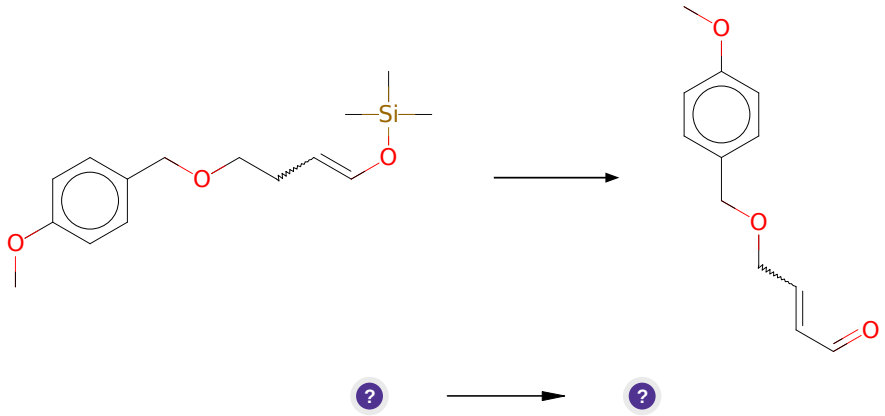
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

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 Dehydrogenation of silyl enol ethers



Substrates:

1. COc1ccc(COCCC=CO[Si](C)(C)C)cc1

Products:

1. COc1ccc(COCC=CC=O)cc1

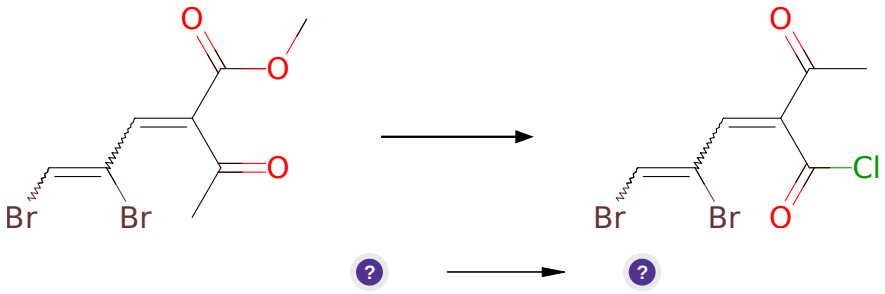
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

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

2.1.6 Synthesis of acid chlorides from esters



Substrates:

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

Products:

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

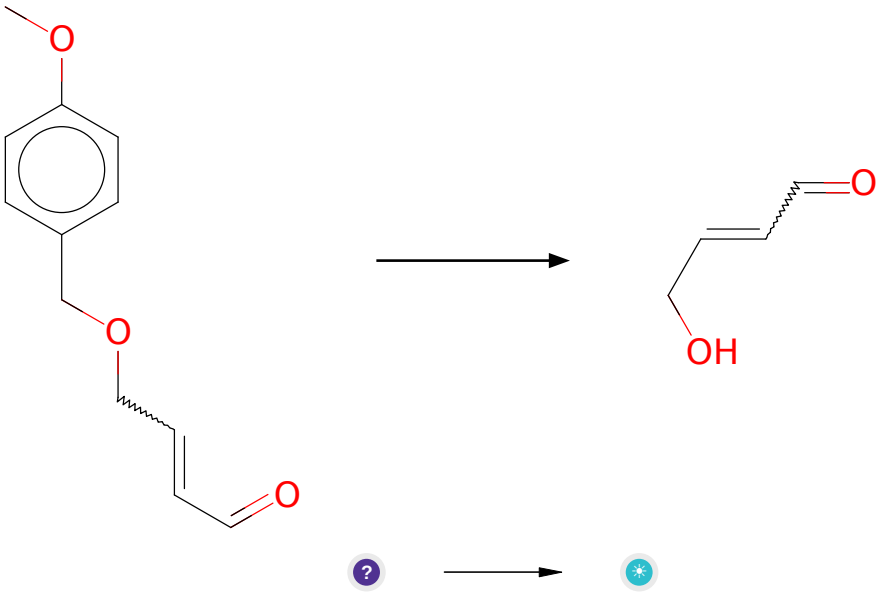
Typical conditions: 1. LiOH.H2O.THF.2. evaporate.3.SOCl2.or.oxalyl.chloride

Protections: none

Reference: *10.1021/ja073476s* and *10.1016/j.tet.2007.04.043* and *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24406

2.1.7 Deprotection of PMB ethers



Substrates:

1. COc1ccc(COCC=CC=O)cc1

Products:

1. 4-hydroxy-but-2-enal

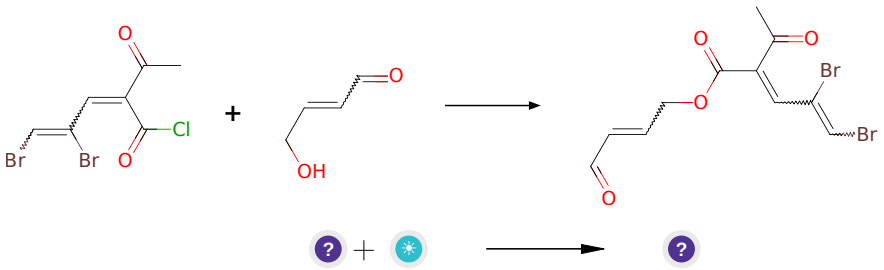
Typical conditions: DDQ.H2O.DCM or CAN.H2O.ACN

Protections: none

Reference: *10.1080/00397911.2019.1639757* and *10.1039/C9OB01504C* and *10.1080/00397911.2019.1660900* and *10.1039/C9OB00556K*

Retrosynthesis ID: 31010150

2.1.8 Reaction of acyl chlorides with alcohols and phenols



Substrates:

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

Products:

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

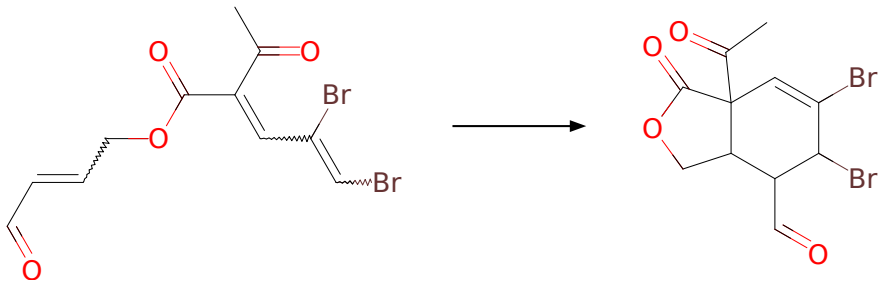
Typical conditions: base.DCM

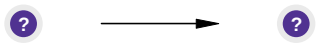
Protections: none

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

2.1.9 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

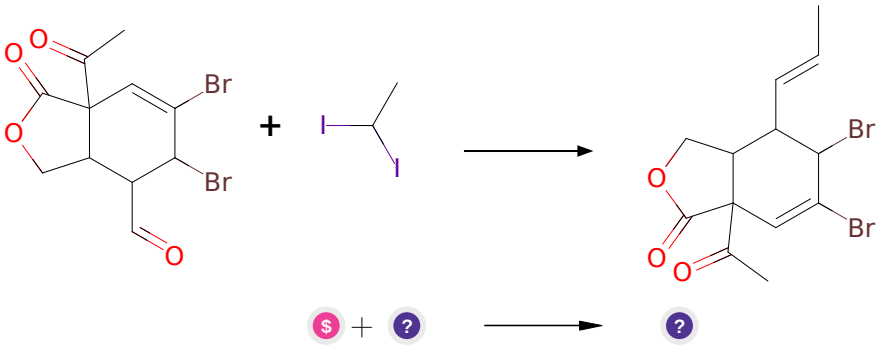
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.1.10 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

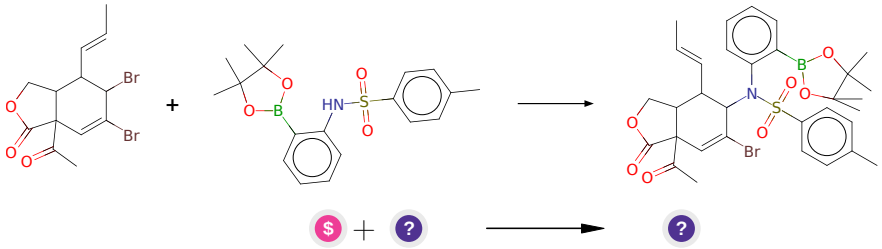
Typical conditions: CrCl2.THF.DMF

Protections: none

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

Retrosynthesis ID: 10942

2.1.11 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

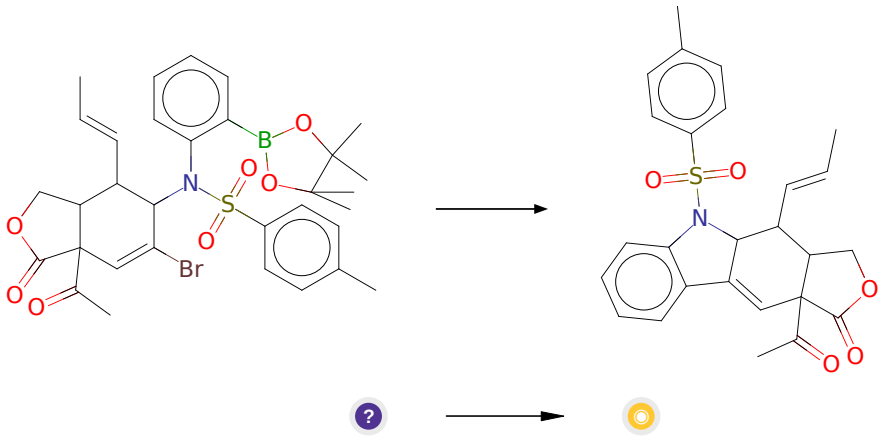
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.1.12 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: 250.22

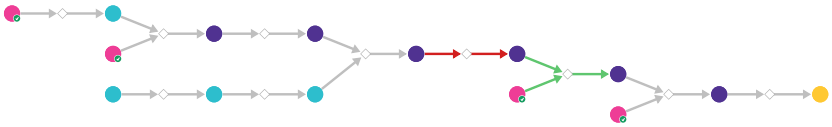
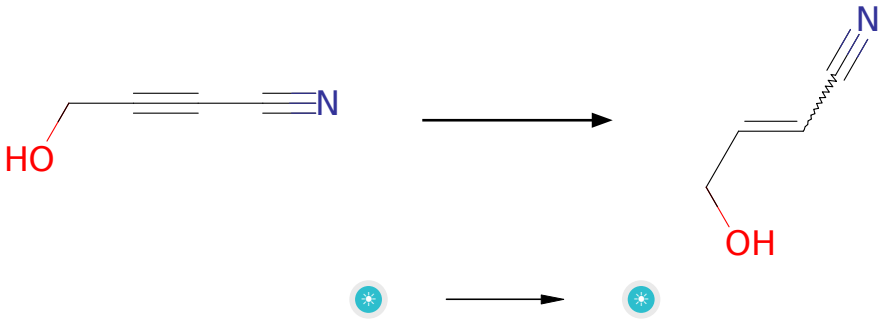


Figure 2: Outline of path 2

2.2.1 Reduction of alkynes to alkenes



Substrates:

1. g-hydroxybut-2-ynenitrile

Products:

1. 4-hydroxycrotonitril

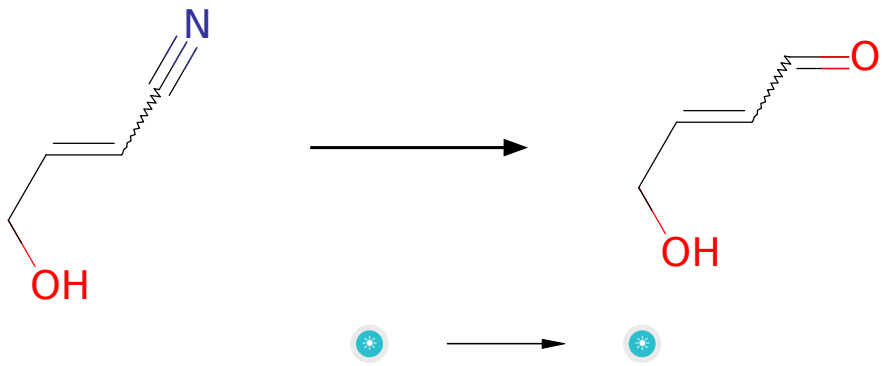
Typical conditions: H2.Lindlar's catalyst

Protections: none

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

Retrosynthesis ID: 14627

2.2.2 Reduction of nitriles to aldehydes



Substrates:

1. 4-hydroxycrotonitril

Products:

1. 4-hydroxy-but-2-enal

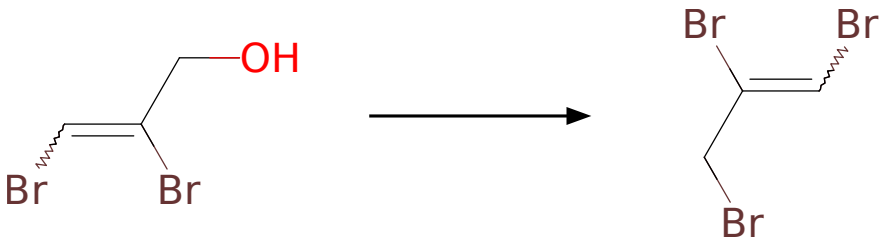
Typical conditions: DIBALH.DCM

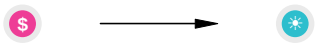
Protections: none

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

2.2.3 Appel Reaction





Substrates:

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

Products:

1. 1,2,3-tribrom-propen

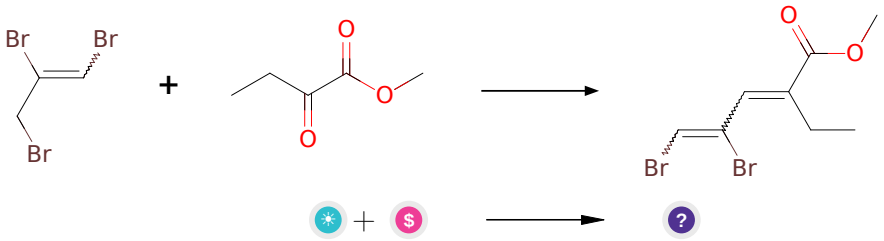
Typical conditions: PPh3.CBr4

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

2.2.4 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

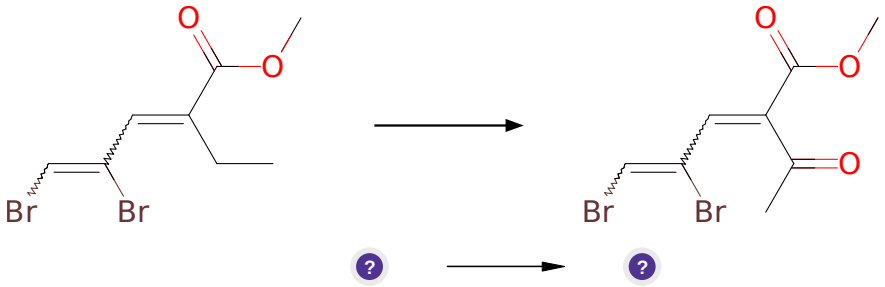
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.2.5 Allylic Oxidation of Alkenes



Substrates:

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

Products:

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

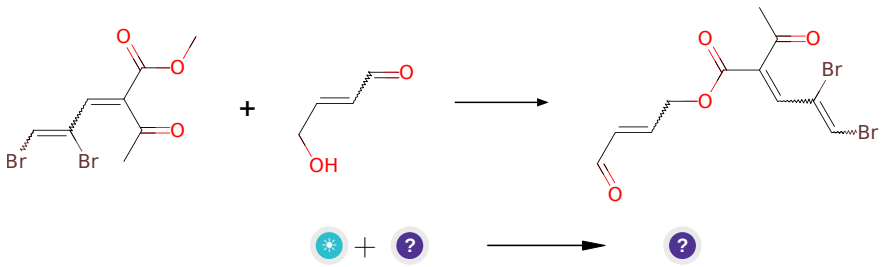
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.2.6 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

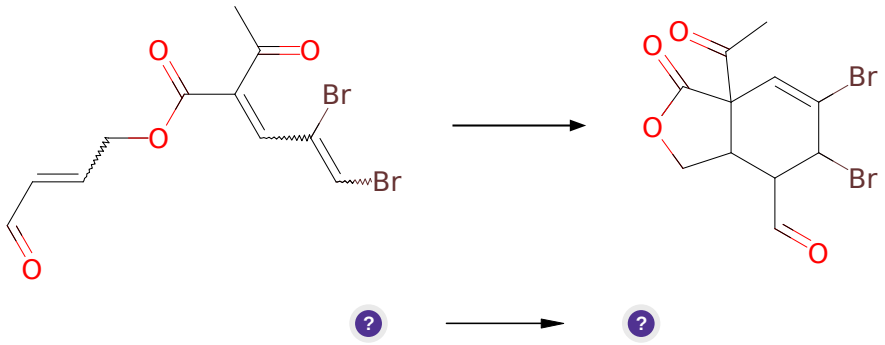
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.2.7 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

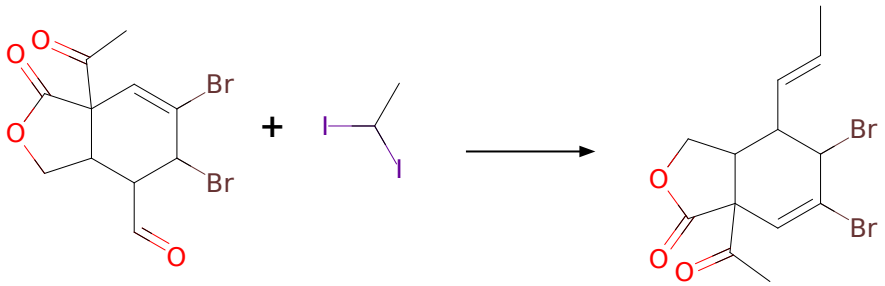
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

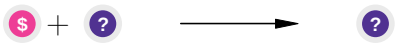
Protections: none

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

Retrosynthesis ID: 18116

2.2.8 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

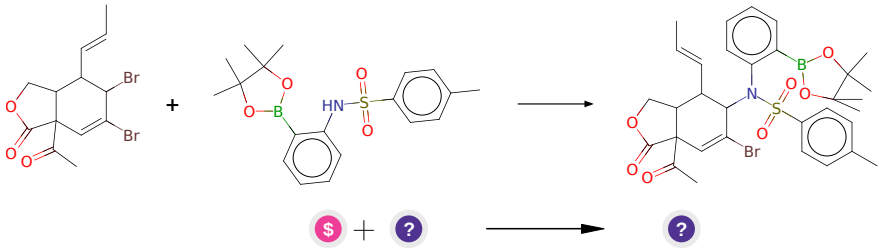
Typical conditions: CrCl2.THF.DMF

Protections: none

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

Retrosynthesis ID: 10942

2.2.9 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

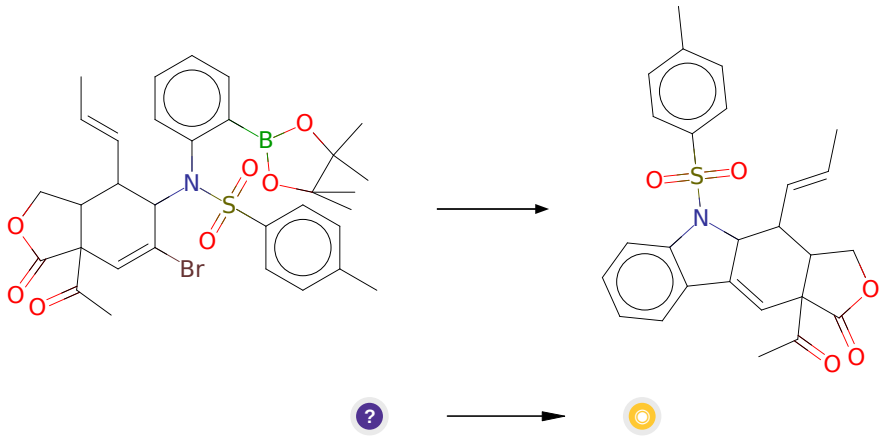
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.2.10 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