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: `360.85`

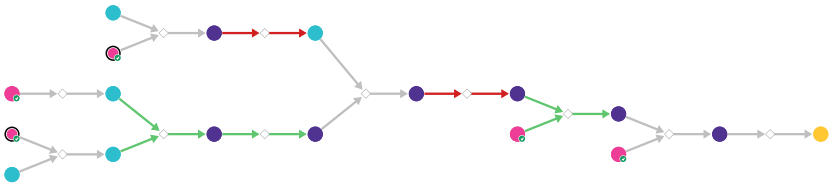
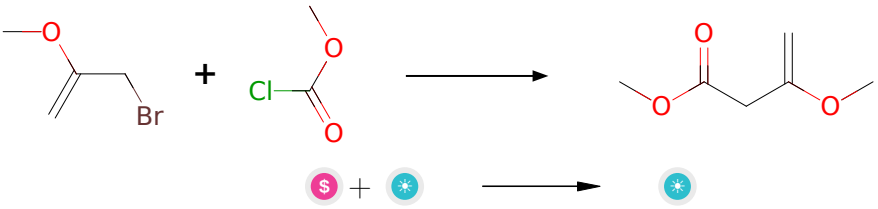


Figure 1: Outline of path 1

2.1.1 Grignard reaction with acyl chlorides



Substrates:

1. Methyl chloroformate - *available at Sigma-Aldrich*
2. 3-bromo-2-methoxy-propene

Products:

1. methyl 3-methoxy-3-butenoate

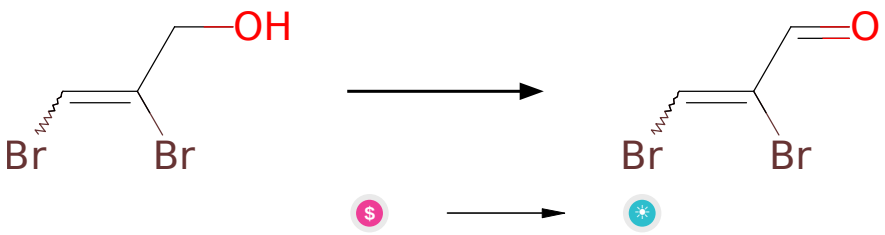
Typical conditions: 1.i-PrMgCl.LiCl 2.ZnCl2 3. CuCl

Protections: none

Reference: *10.1016/0040-4039(94)85361-4* and *10.1016/0040-4039(96)00258-4* and *10.1021/jo3005556* AND *10.1016/0040-4039(96)00689-2*

Retrosynthesis ID: 2530

2.1.2 Oxidation of primary alcohols with DMP



Substrates:

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

Products:

1. 2,3-dibromo-propenal

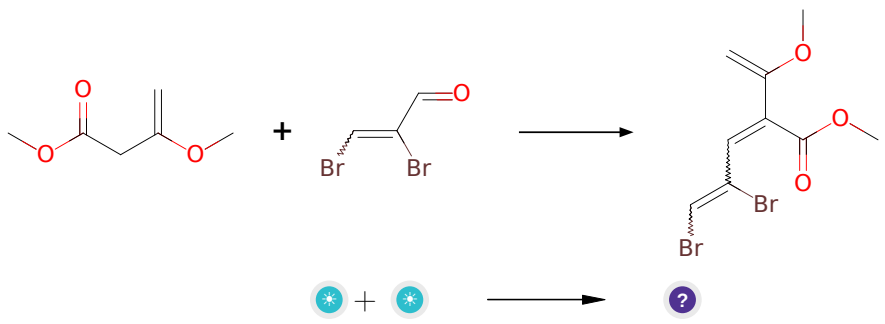
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.1.3 Condensation of esters with aldehydes/ketones



Substrates:

1. methyl 3-methoxy-3-butenoate
2. 2,3-dibromo-propenal

Products:

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

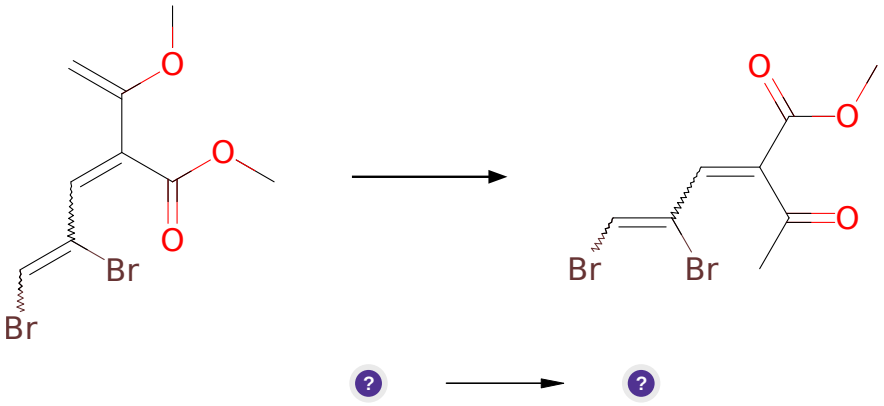
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.1.4 Synthesis of ketones and aldehydes from enol ethers



Substrates:

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

Products:

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

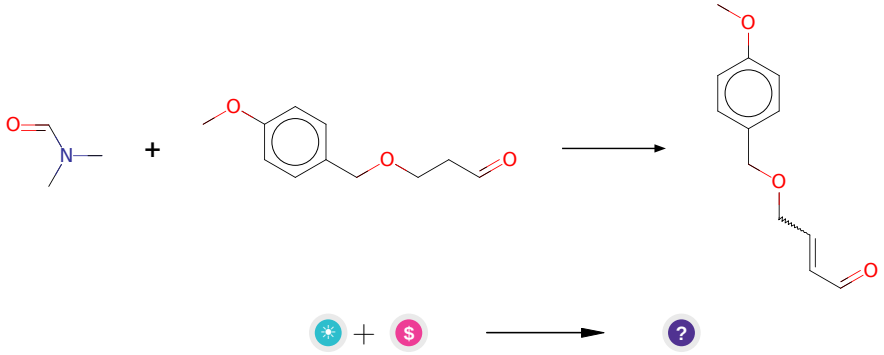
Typical conditions: [H+].THF

Protections: none

Reference: *10.1081/SCC-120023437* AND *10.1016/j.bmcl.2007.11.020* AND *10.1016/j.tet.2011.03.084* AND *10.1021/ja00270a023* AND *10.1055/s-1994-25424* AND

Retrosynthesis ID: 14844

2.1.5 Shapiro reaction followed by DMF addition



Substrates:

1. 3-(p-methoxybenzyloxy)propanal
2. Dimethylformamide - *available at Sigma-Aldrich*

Products:

1. COc1ccc(COCC=CC=O)cc1

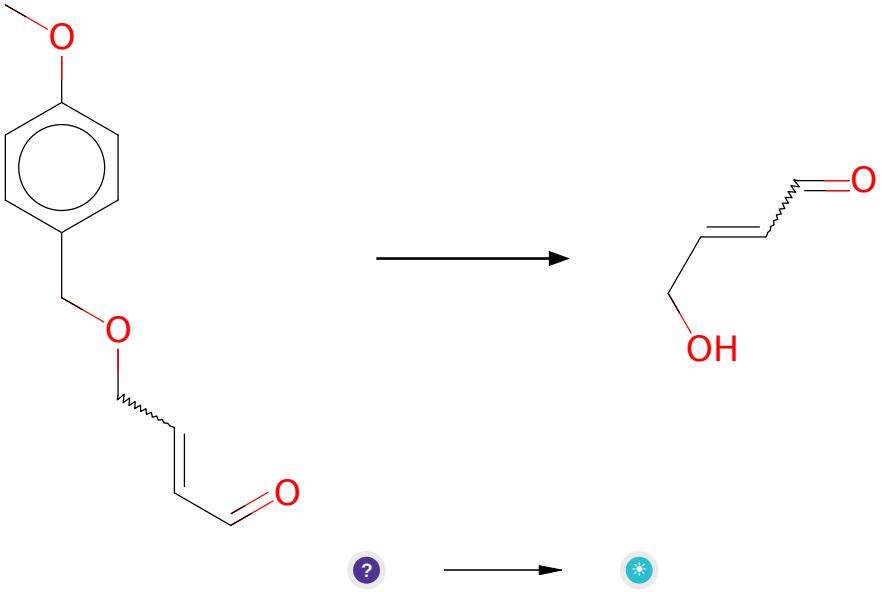
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then DMF.3.NaBH4

Protections: none

Reference: *10.1021/jo901926z* and *10.1002/chem.201303586* (SI p.7) and *10.1021/jo015699l*

Retrosynthesis ID: 9990428

2.1.6 Deprotection of PMB ethers



Substrates:

1. COc1ccc(COCC=CC=O)cc1

Products:

1. 4-hydroxy-but-2-enal

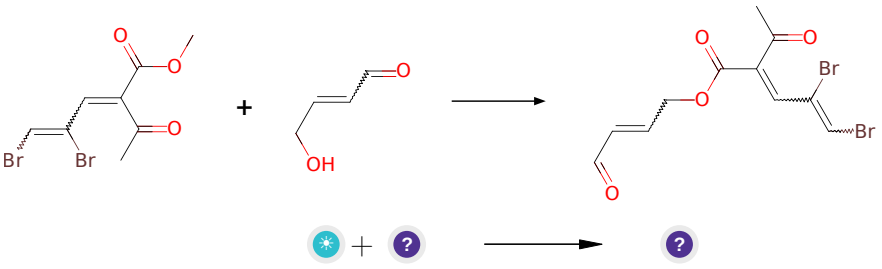
Typical conditions: DDQ.H2O.DCM or CAN.H2O.ACN

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

2.1.7 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

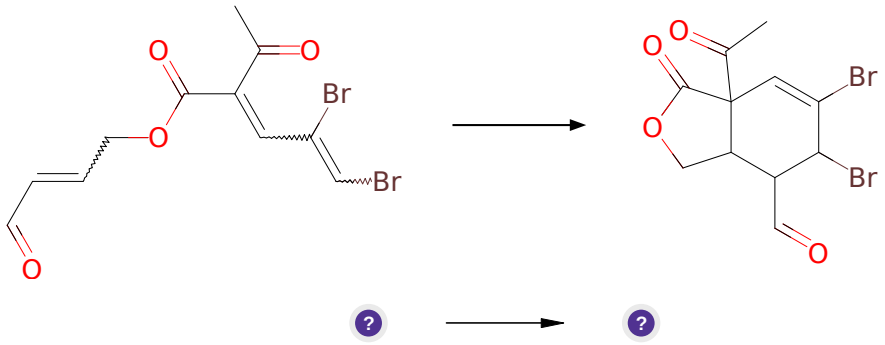
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.1.8 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

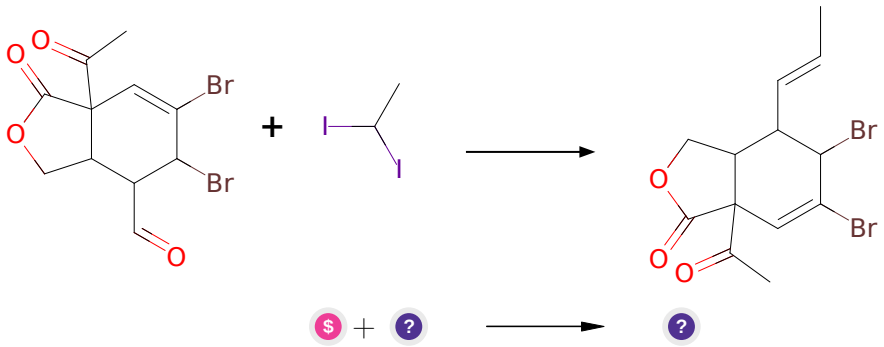
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.1.9 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

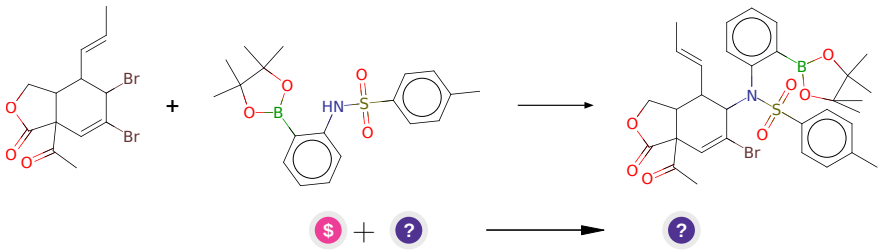
Typical conditions: CrCl2.THF.DMF

Protections: none

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

Retrosynthesis ID: 10942

2.1.10 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

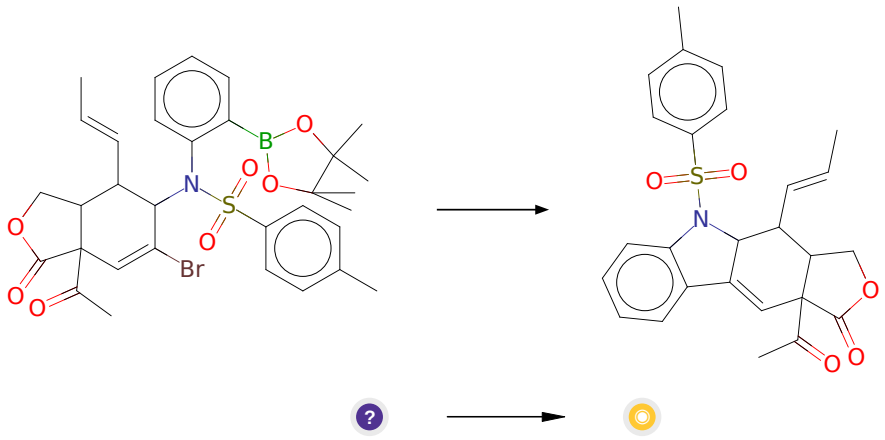
Typical conditions: K2CO3 or other base

Protections: none

Reference: *10.1016/j.tetlet.2007.09.110*

Retrosynthesis ID: 7668

2.1.11 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

2.2 Path 2

Score: 369.43

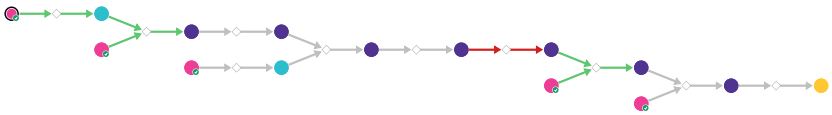
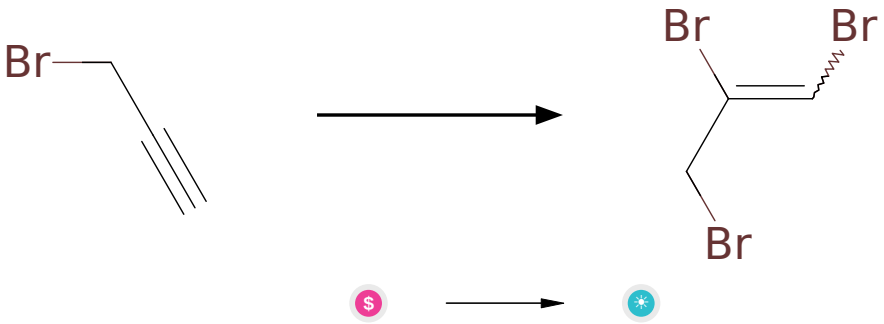


Figure 2: Outline of path 2

2.2.1 Bromination of Alkynes



Substrates:

1. 3-Bromo-1-propyne - *available at Sigma-Aldrich*

Products:

1. 1,2,3-tribrom-propen

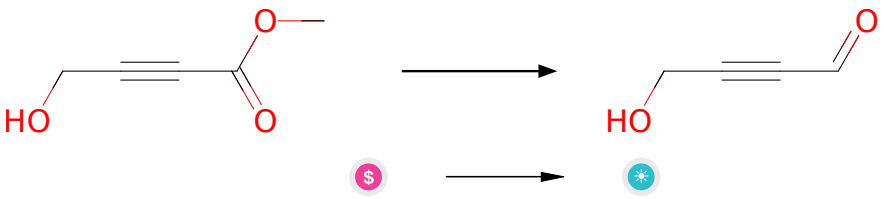
Typical conditions: NBS. THF. 80C

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 Aldehyde Formation



Substrates:

1. methyl 4-hydroxybut-2-ynoate - *available at Sigma-Aldrich*

Products:

1. 4-hydroxy-but-2-ynal

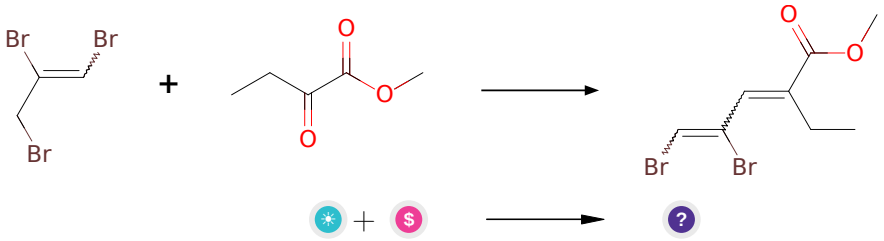
Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Reference: *10.1039/C39940000483* and *10.1039/C3CC47867J* and *10.1021/jo00222a054* and *10.1021/ja9934908* and *10.1021/jo902426z*

Retrosynthesis ID: 28551

2.2.3 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

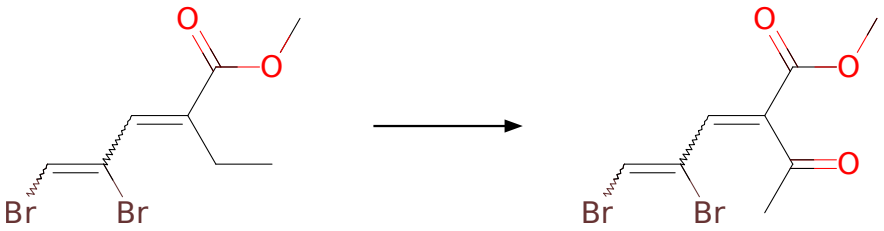
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

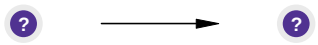
Protections: none

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

Retrosynthesis ID: 24425

2.2.4 Allylic Oxidation of Alkenes





Substrates:

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

Products:

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

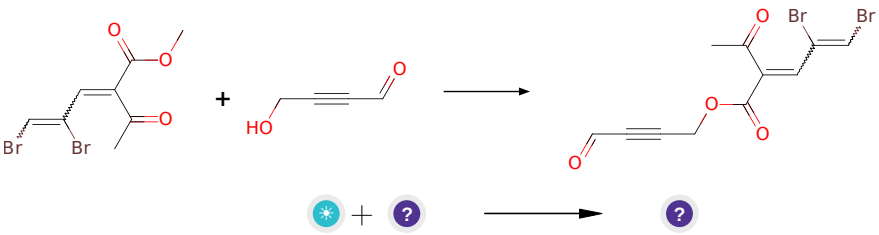
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.2.5 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

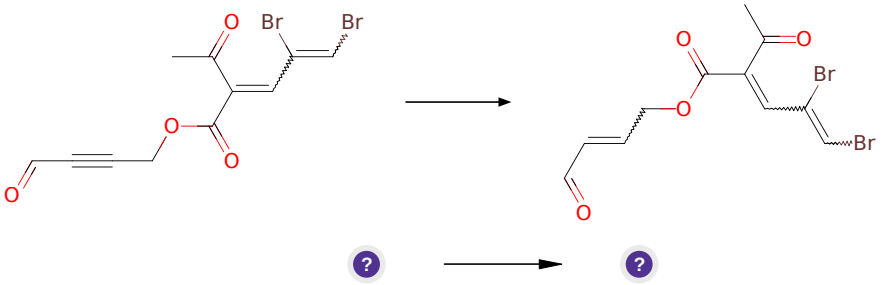
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.2.6 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

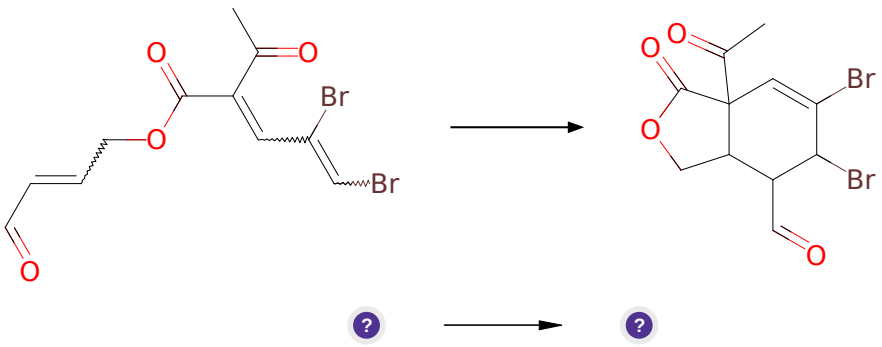
Typical conditions: H2.Lindlar's catalyst

Protections: none

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

Retrosynthesis ID: 14627

2.2.7 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

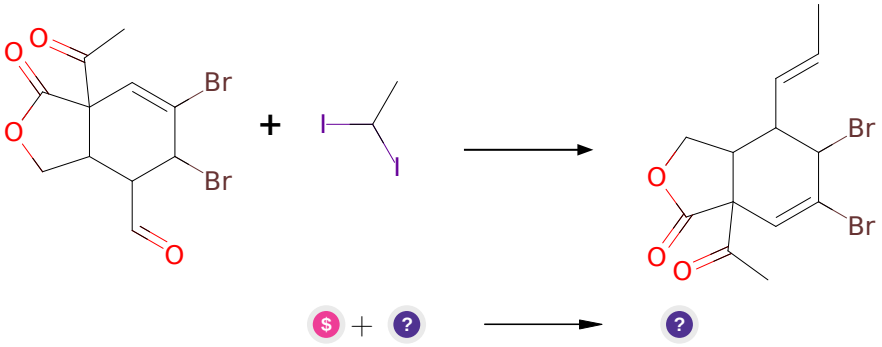
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

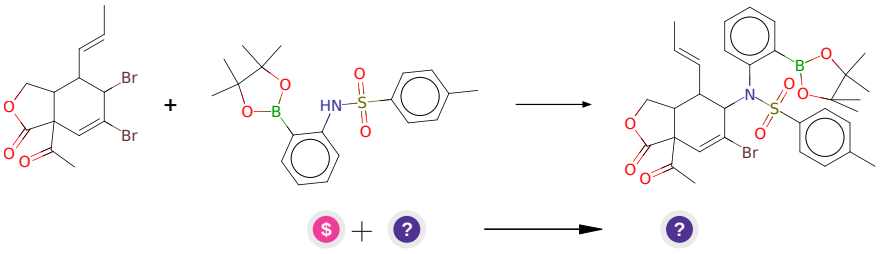
Typical conditions: CrCl2.THF.DMF

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

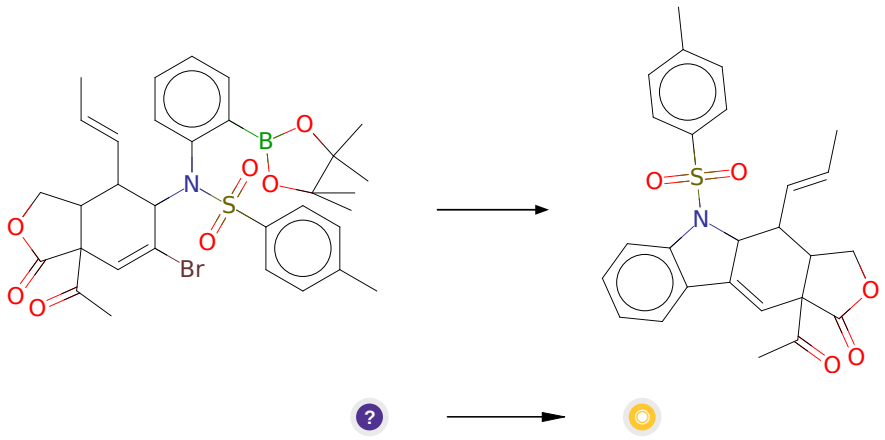
Typical conditions: K2CO3 or other base

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