Paths of analysis*

L7_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

5 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: 76.25

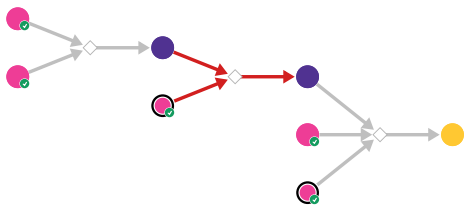
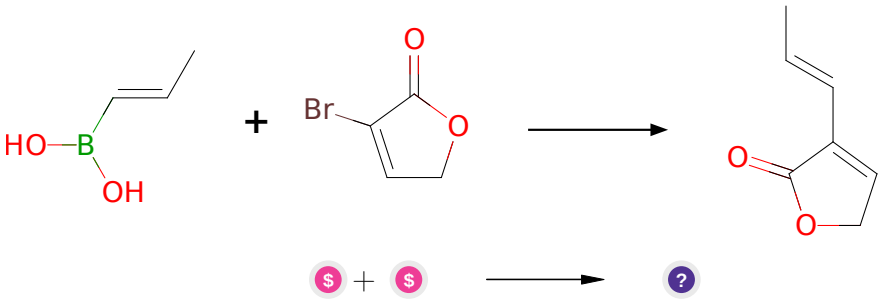


Figure 1: Outline of path 1

2.1.1 Suzuki coupling of vinyl bromides with alkenyl boronic acids



Substrates:

1. trans-Propenylboronic acid - *available at Sigma-Aldrich*
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1=CCOC1=O

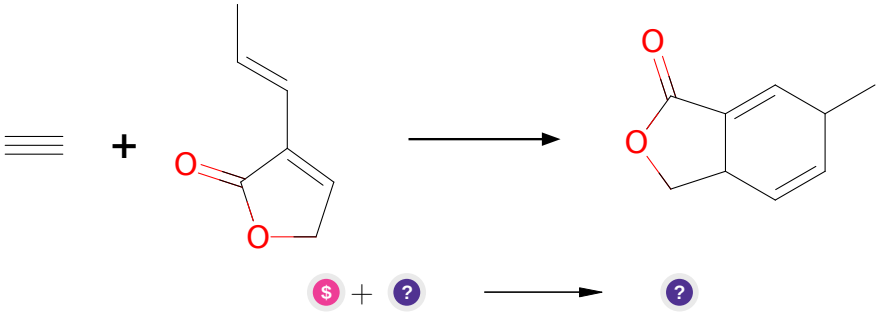
Typical conditions: Pd catalyst.base.solvent

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: 24937

2.1.2 Diels-Alder



Substrates:

1. Calcium carbide - *available at Sigma-Aldrich*
2. C/C=C/C1=CCOC1=O

Products:

1. CC1C=CC2COC(=O)C2=C1

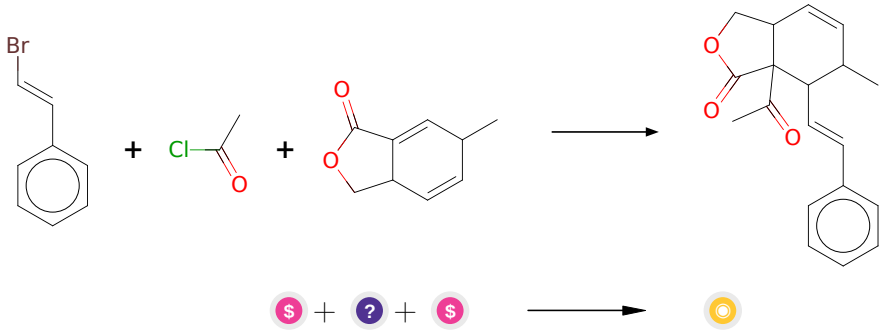
Typical conditions: H2O.MeOH.EtOH.isooctane

Protections: none

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

Retrosynthesis ID: 10557

2.1.3 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. b-Bromostyrene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

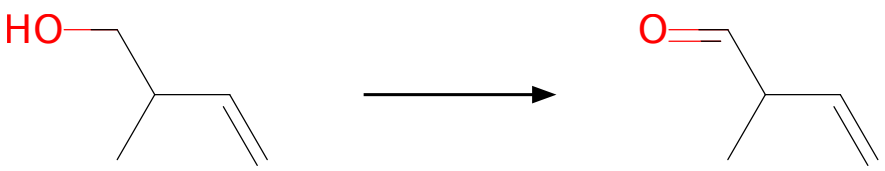
Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13033

2.2 Path 2

Score: 76.25

2.2.1 Oxidation of primary alcohols with DMP



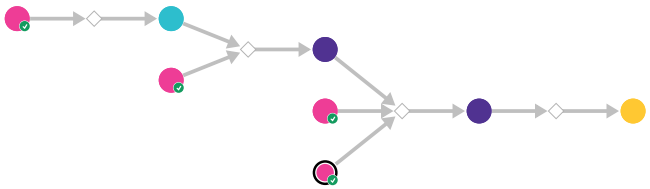
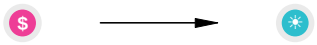


Figure 2: Outline of path 2



Substrates:

1. 2-Methyl-3-buten-1-ol - *available at Sigma-Aldrich*

Products:

1. 2-methyl-but-3-enal

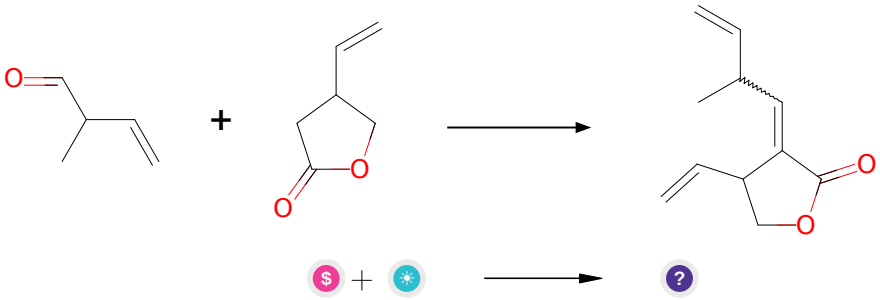
Typical conditions: DMP.DCM.0-25 C

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 Condensation of esters with aldehydes/ketones



Substrates:

1. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*
2. 2-methyl-but-3-enal

Products:

1. C=CC(C)C=C1C(=O)OCC1C=C

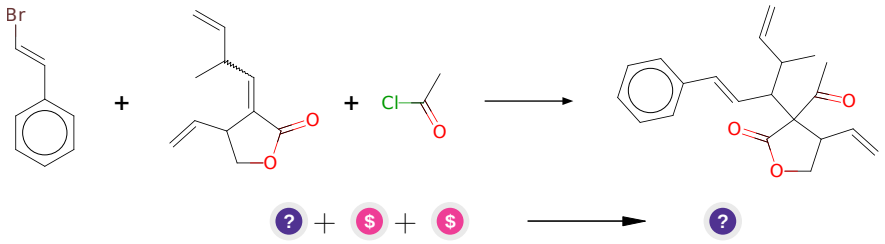
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.2.3 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. C=CC(C)C=C1C(=O)OCC1C=C
2. b-Bromostyrene - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(/C=C/c1ccccc1)C1(C(C)=O)C(=O)OCC1C=C

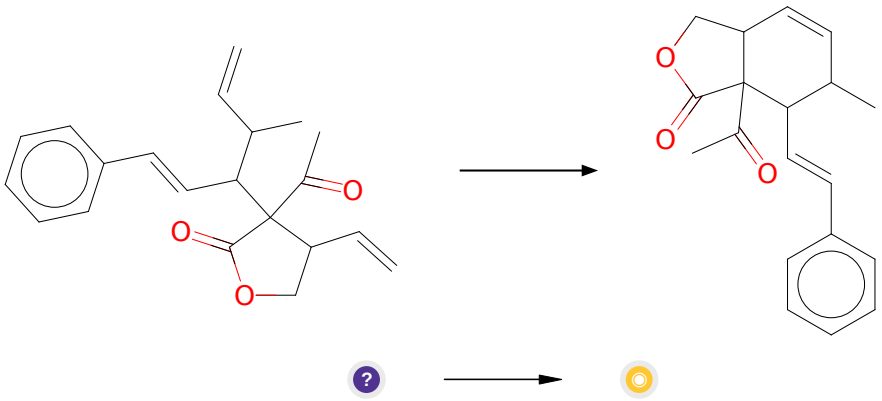
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3* AND *10.1021/ja0320018* AND *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815*

Retrosynthesis ID: 20532

2.2.4 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(/C=C/c1ccccc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.3 Path 3

Score: `90.31`

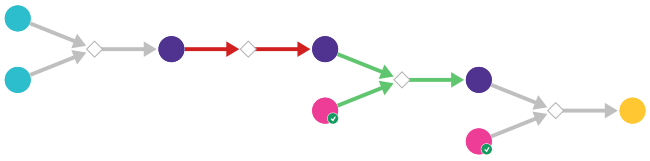
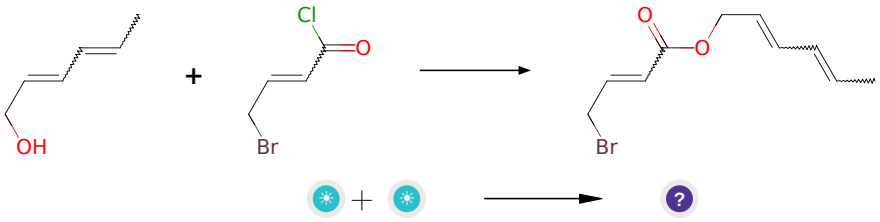


Figure 3: Outline of path 3

2.3.1 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. 4-bromcrotonsaeurechlorid
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C=CCBr

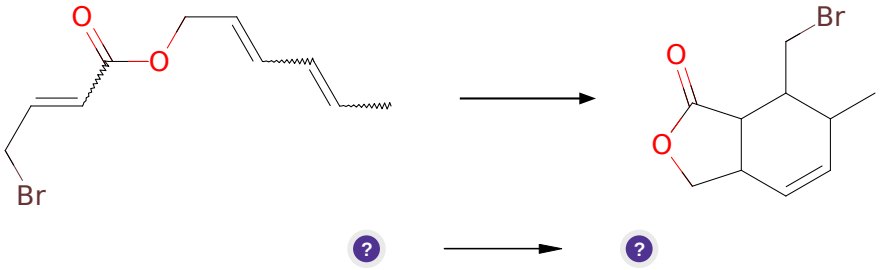
Typical conditions: base.DCM

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

2.3.2 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C=CCBr

Products:

1. CC1C=CC2COC(=O)C2C1CBr

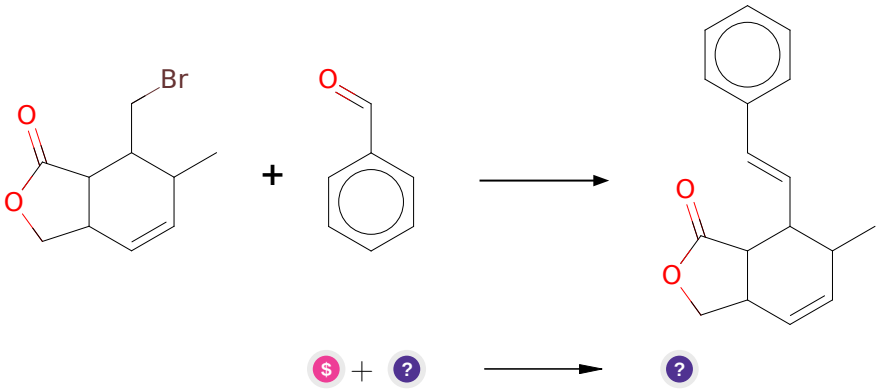
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.3.3 Wittig-Schlosser olefination



Substrates:

1. Benzaldehyde - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2C1CBr

Products:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1

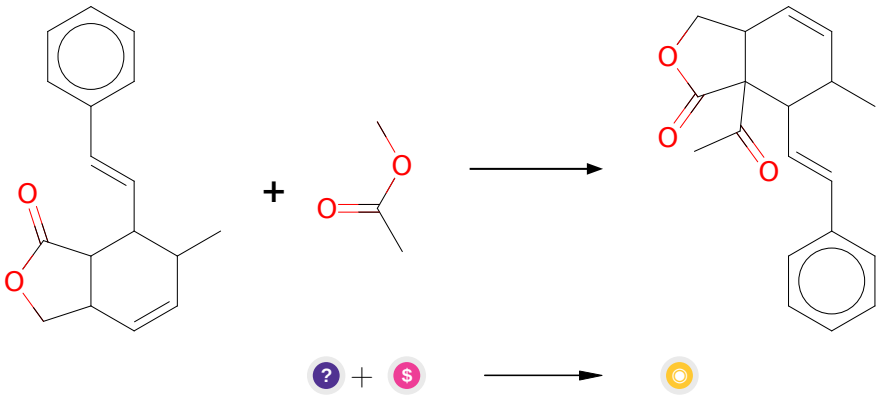
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde.3.base

Protections: none

Reference: *10.1021/ol049701h* and *10.1021/ja00535a063* and Kurti and Czako; Strategic Applications of Named Reactions in Organic Synthesis. 1st edn., 488-489.

Retrosynthesis ID: 9546

2.3.4 Claisen Condensation



Substrates:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: Base.Solvent

Protections: none

Reference: *10.1021/cr020703u* and *10.1021/cr60088a002*

Retrosynthesis ID: 5015

2.4 Path 4

Score: `90.31`

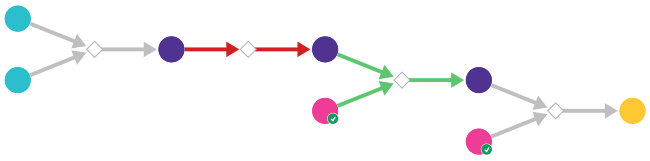
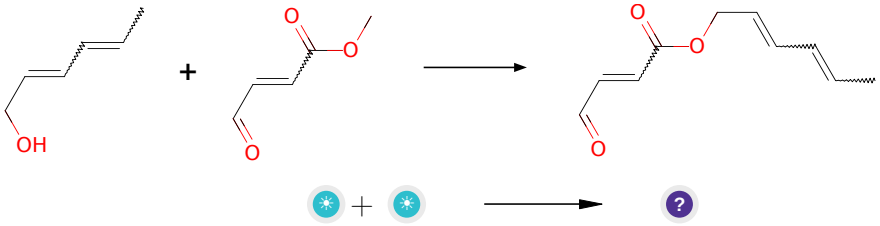


Figure 4: Outline of path 4

2.4.1 Acid catalyzed transesterification



Substrates:

1. sorbic alcohol
2. 4-oxobutenoate methyl ester

Products:

1. CC=CC=CCOC(=O)C=CC=O

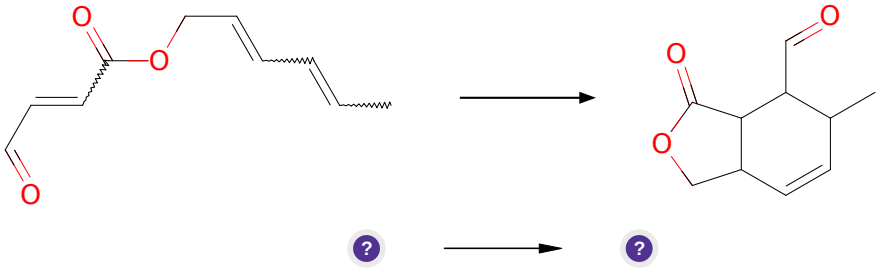
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.4.2 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C=CC=O

Products:

1. CC1C=CC2COC(=O)C2C1C=O

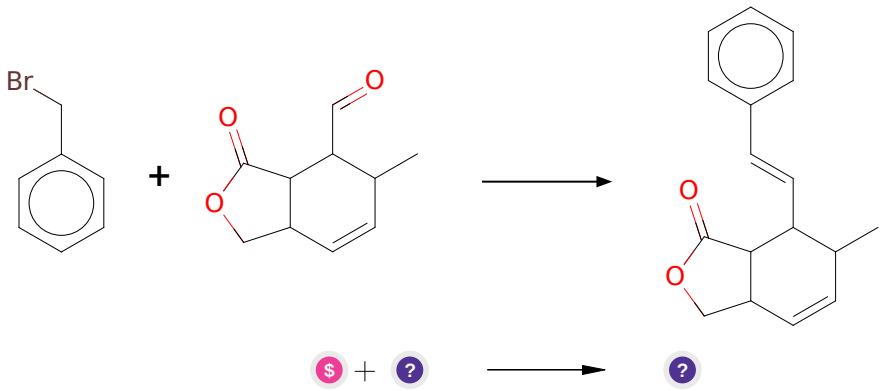
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.4.3 Wittig-Schlosser olefination



Substrates:

1. a-Bromotoluene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2C1C=O

Products:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1

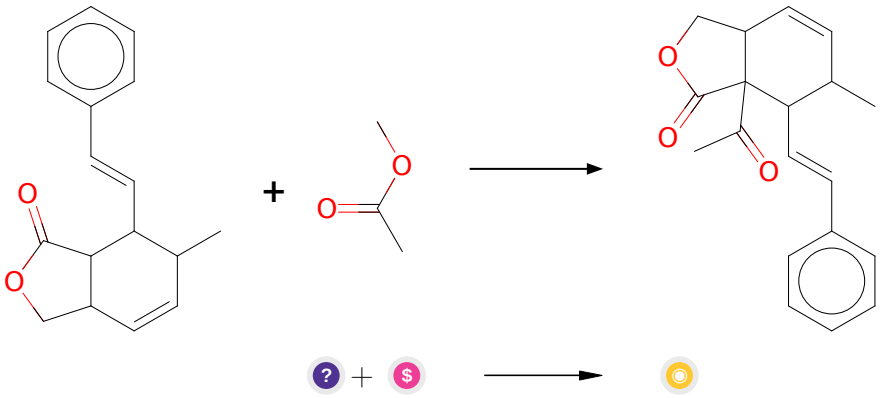
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde.3.base

Protections: none

Reference: *10.1021/ol049701h* and *10.1021/ja00535a063* and Kurti and Czako; Strategic Applications of Named Reactions in Organic Synthesis. 1st edn., 488-489.

Retrosynthesis ID: 9546

2.4.4 Claisen Condensation



Substrates:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: Base.Solvent

Protections: none

Reference: *10.1021/cr020703u* and *10.1021/cr60088a002*

Retrosynthesis ID: 5015

2.5 Path 5

Score: `90.31`

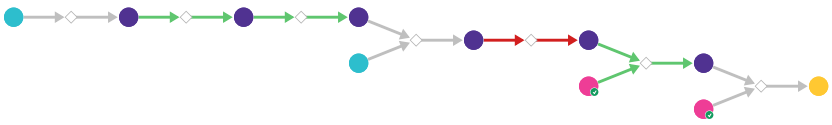
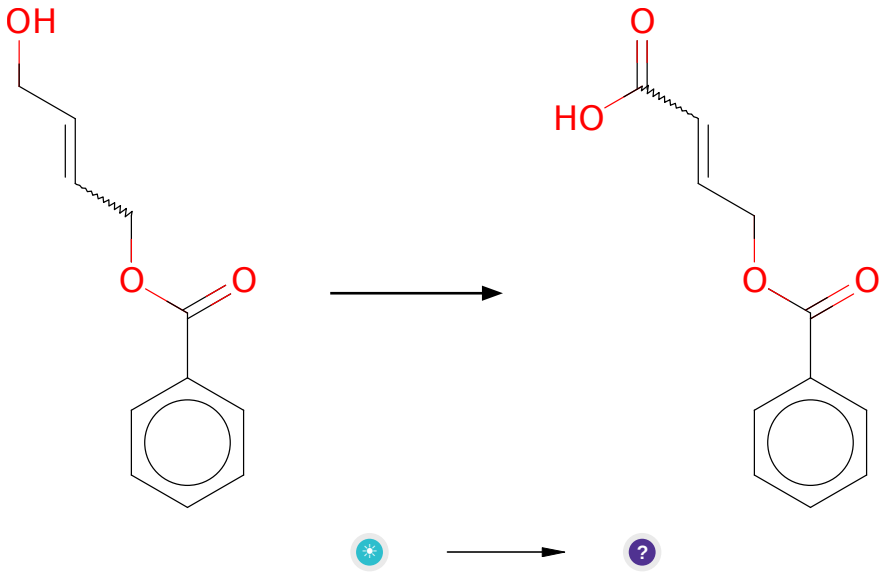


Figure 5: Outline of path 5

2.5.1 Jones Oxidation



Substrates:

1. 4-hydroxy-2-butenyl-benzoat

Products:

1. O=C(O)C=CCOC(=O)c1ccccc1

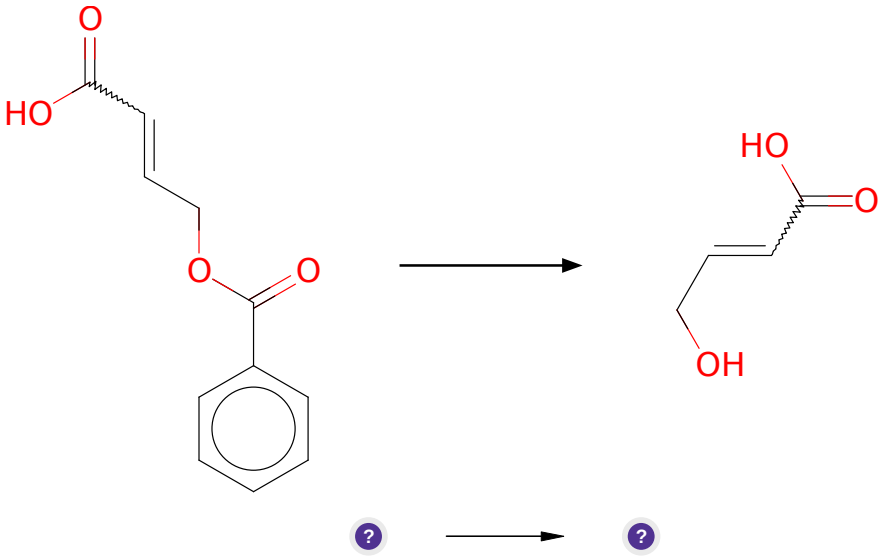
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

Reference: *10.1002/9780470638859.conrr349* and *10.1021/jm00270a004*

Retrosynthesis ID: 11160

2.5.2 Hydrolysis of benzoates



Substrates:

1. O=C(O)C=CCOC(=O)c1ccccc1

Products:

1. O=C(O)C=CCO

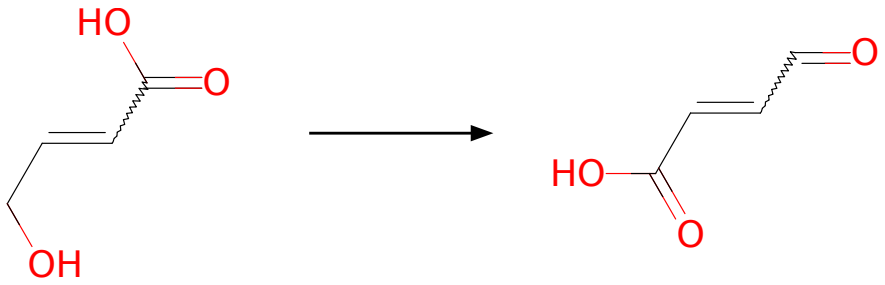
Typical conditions: LiOH/K2CO3/NH3.MeOH.H2O.THF

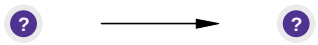
Protections: none

Reference: *10.1021/jm0502788* and *10.1016/j.tetlet.2008.09.165* and *10.1021/jm034098e* and *10.1021/jo049277y* and *10.1055/s-0033-1338657*

Retrosynthesis ID: 25136

2.5.3 Oxidation of primary alcohols with DMP





Substrates:

1. O=C(O)C=CCO

Products:

1. O=CC=CC(=O)O

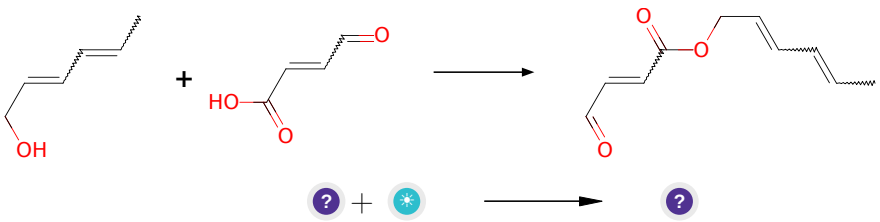
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.5.4 Steglich Esterification



Substrates:

1. O=CC=CC(=O)O
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C=CC=O

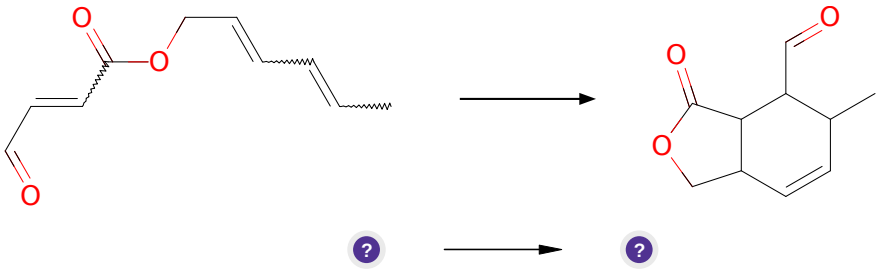
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.5.5 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C=CC=O

Products:

1. CC1C=CC2COC(=O)C2C1C=O

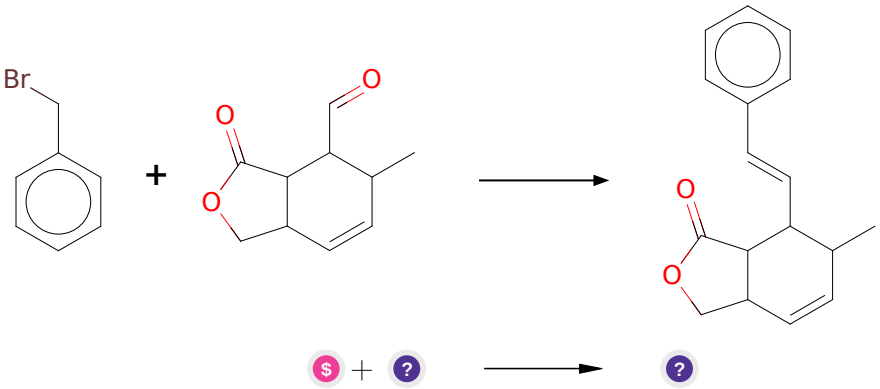
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.5.6 Wittig-Schlosser olefination



Substrates:

1. a-Bromotoluene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2C1C=O

Products:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1

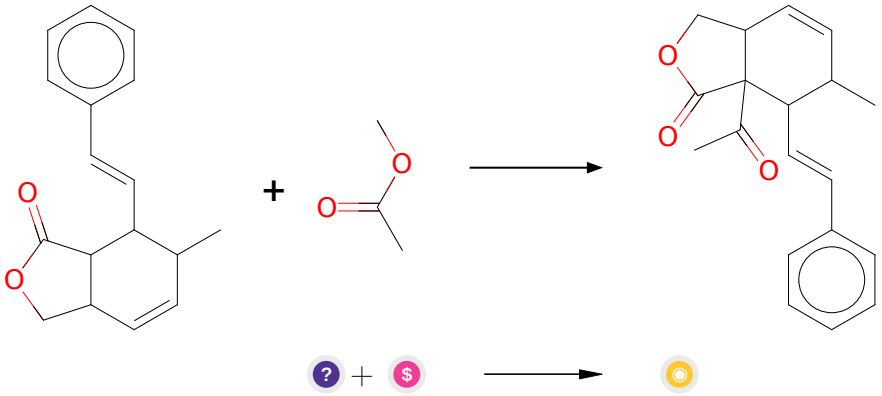
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde.3.base

Protections: none

Reference: *10.1021/ol049701h* and *10.1021/ja00535a063* and Kurti and Czako; Strategic Applications of Named Reactions in Organic Synthesis. 1st edn., 488-489.

Retrosynthesis ID: 9546

2.5.7 Claisen Condensation



Substrates:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: Base.Solvent

Protections: none

Reference: *10.1021/cr020703u* and *10.1021/cr60088a002*

Retrosynthesis ID: 5015