Paths of analysis*

L9_STEREO

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: `84.06`

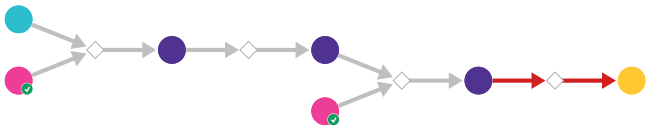
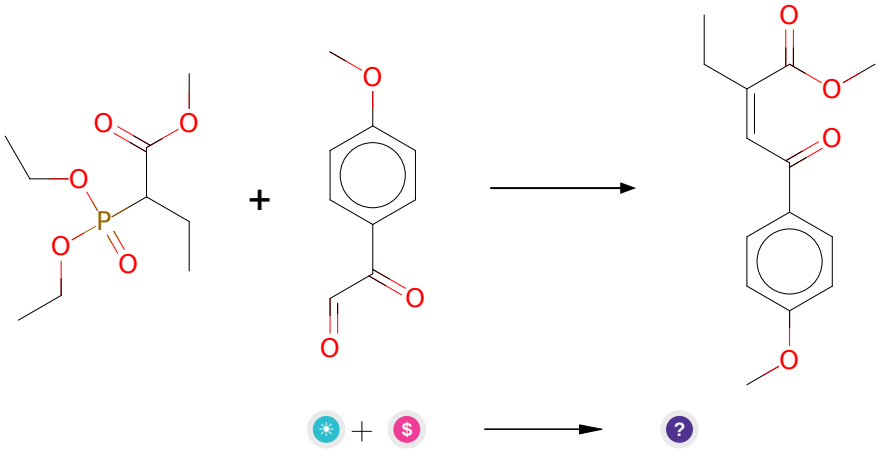


Figure 1: Outline of path 1

2.1.1 HWE olefination



Substrates:

1. diethylphosphono-2 butanoate de methyle
2. 4-Methoxyphenylglyoxal hydrate - *available at Sigma-Aldrich*

Products:

1. CC/C(=C/C(=O)c1ccc(OC)cc1)C(=O)OC

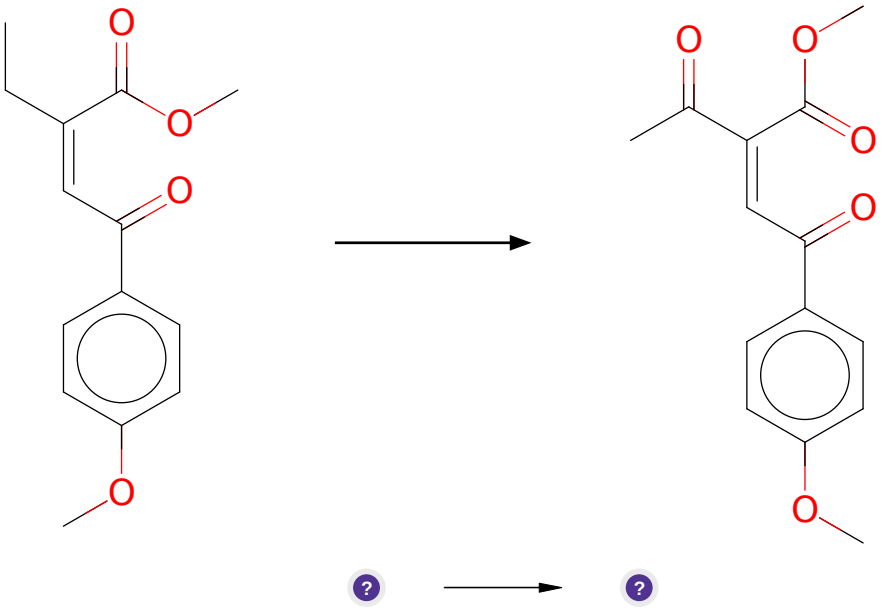
Typical conditions: 1.Base 2.RCHO

Protections: none

Reference: *10.3109/1061186X.2014.928718* and *10.1016/S0968-0896(03)00373-0* and *10.1016/j.bmcl.2011.04.076* and *10.1016/j.tetlet.2012.04.044* and *10.1021/ja0581604*

Retrosynthesis ID: 14764

2.1.2 Allylic Oxidation of Alkenes



Substrates:

1. CC/C(=C/C(=O)c1ccc(OC)cc1)C(=O)OC

Products:

1. COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

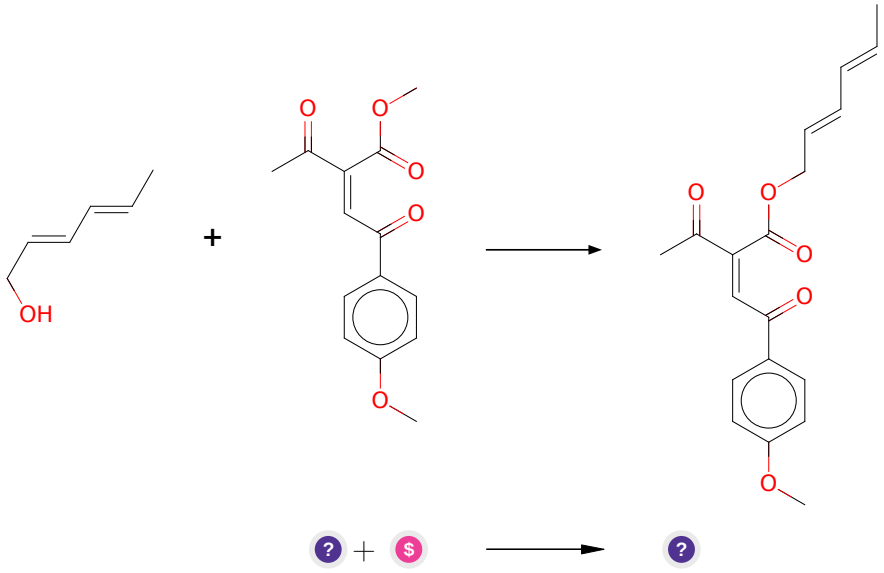
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.1.3 Acid catalyzed transesterification



Substrates:

1. COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

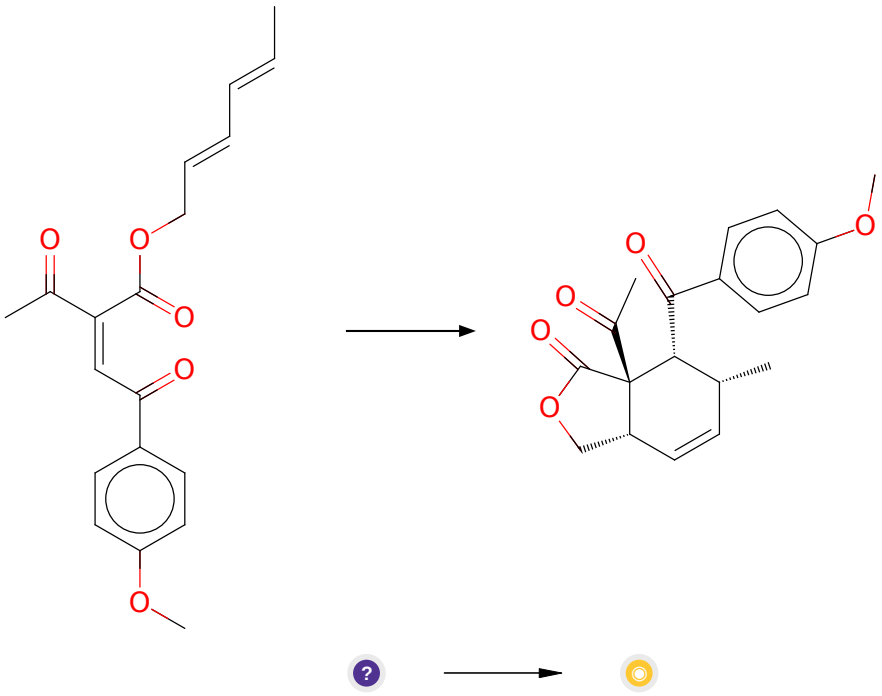
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.1.4 Diels-Alder



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C(C)=O)cc1

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 Path 2

Score: 106.04

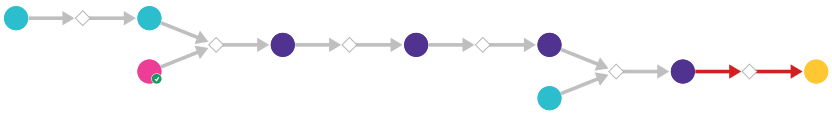
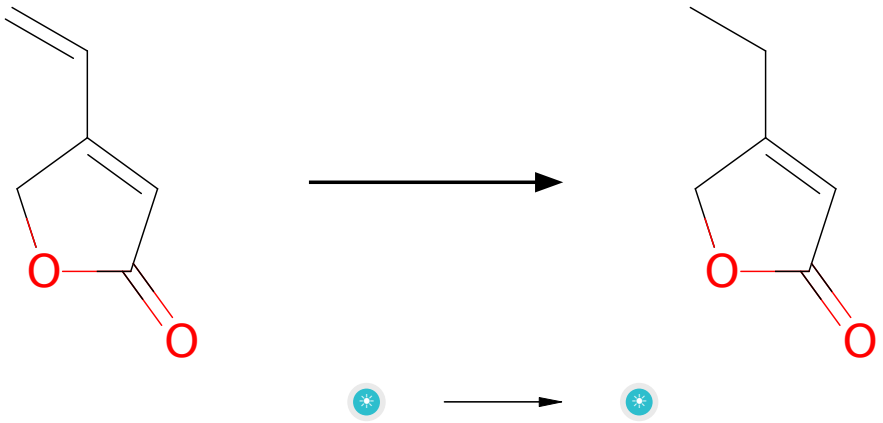


Figure 2: Outline of path 2

2.2.1 Homogenous Reduction of C=C Double Bond



Substrates:

1. 4-vinyl-5h-furan-2-one

Products:

1. 4-ethyl-5h-furan-2-one

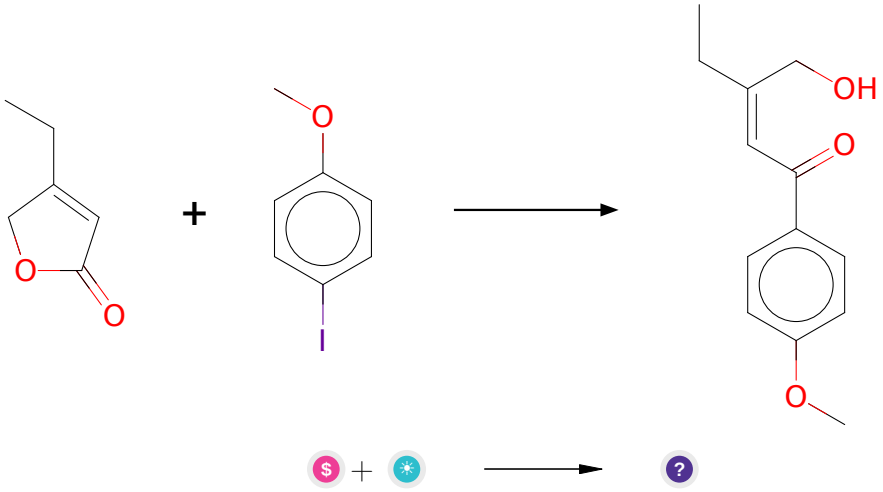
Typical conditions: H2.Pd/C or Pd(OH)2/C

Protections: none

Reference: DOI: *10.1021/ja044280k* and *10.1021/jo980128n* and *10.1021/ja00213a006*

Retrosynthesis ID: 9995777

2.2.2 Ring opening of lactones with organolithium reagents



Substrates:

1. 4-Iodoanisole - *available at Sigma-Aldrich*
2. 4-ethyl-5h-furan-2-one

Products:

1. CC/C(=C/C(=O)c1ccc(OC)cc1)CO

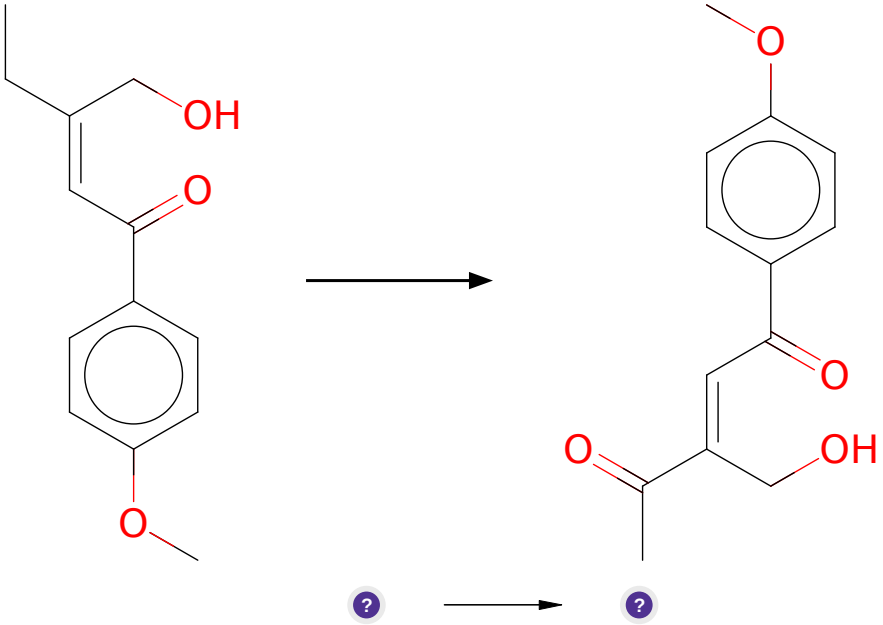
Typical conditions: BuLi.ether.-78C

Protections: none

Reference: *10.1002/jhet.233* and *10.1021/ol070572p* and *10.1002/ejoc.200801000* and *10.1021/ja905843e* (SI) and *10.1016/j.tet.2009.05.007*

Retrosynthesis ID: 24103

2.2.3 Allylic Oxidation of Alkenes



Substrates:

1. CC/C(=C/C(=O)c1ccc(OC)cc1)CO

Products:

1. COc1ccc(C(=O)/C=C(\CO)C(C)=O)cc1

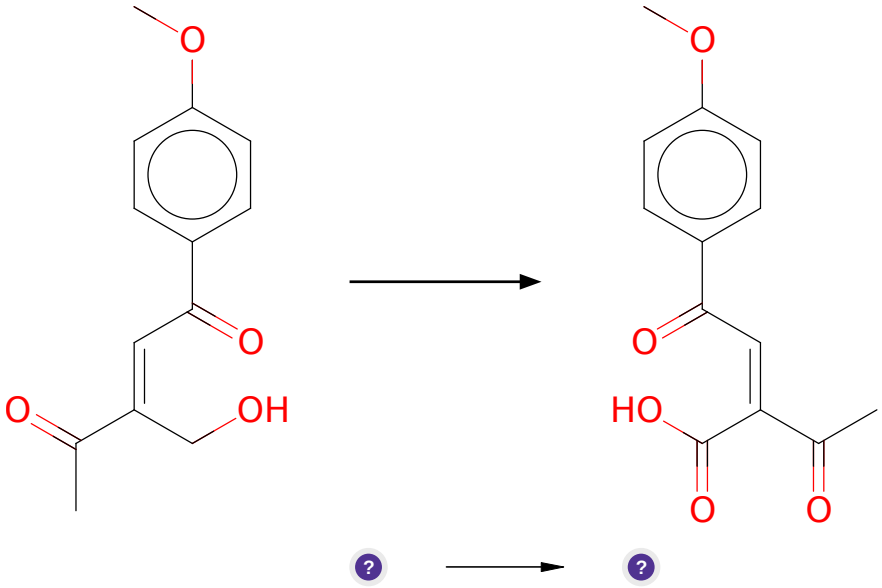
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.2.4 Jones Oxidation



Substrates:

1. COc1ccc(C(=O)/C=C(\CO)C(C)=O)cc1

Products:

1. COc1ccc(C(=O)/C=C(/C(C)=O)C(=O)O)cc1

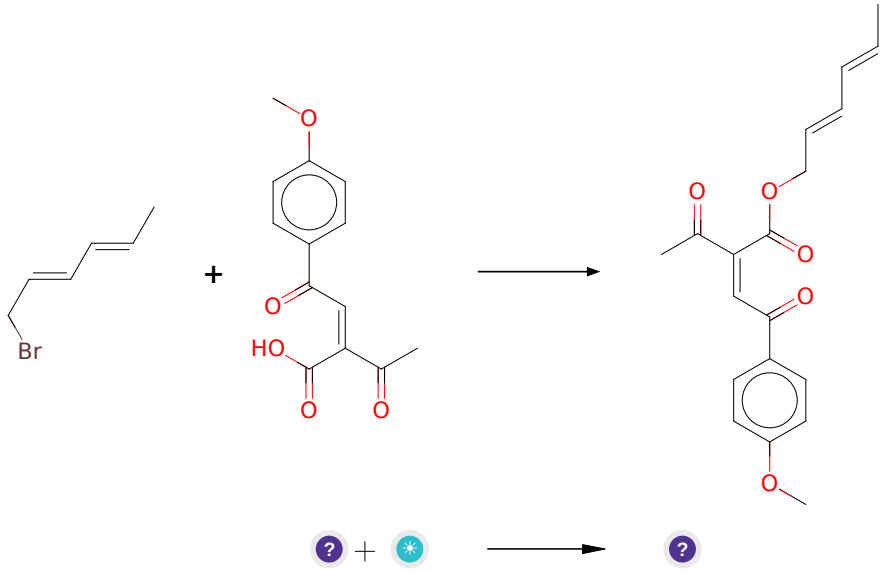
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

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

Retrosynthesis ID: 11160

2.2.5 Synthesis of esters from alkyl chlorides and carboxylic acids or thioacids



Substrates:

1. COc1ccc(C(=O)/C=C(/C(C)=O)C(=O)O)cc1
2. 2,4-hexadienyl bromide

Products:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

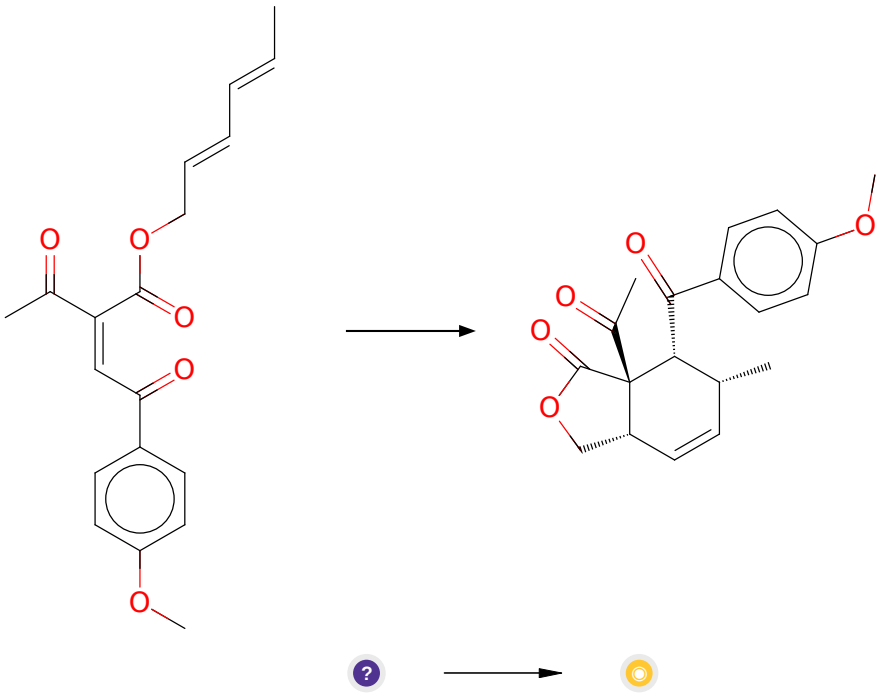
Typical conditions: K2CO3.DMF

Protections: none

Reference: *10.1016/j.bmcl.2005.08.026* AND *10.1021/ol034655r* (SI) AND *10.1039/C3RA41967C* AND *10.1016/j.bmcl.2012.03.093*

Retrosynthesis ID: 14685

2.2.6 Diels-Alder



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C(C)=O)cc1

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 Path 3

Score: `146.61`

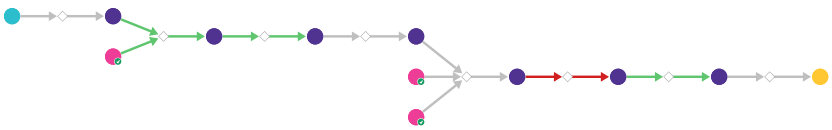
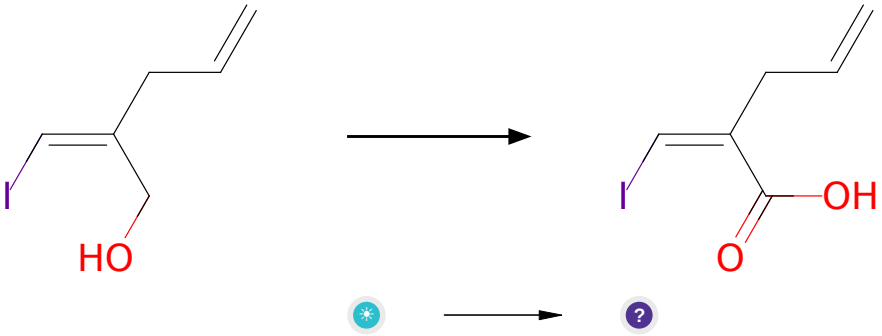


Figure 3: Outline of path 3

2.3.1 Jones Oxidation



Substrates:

1. (z)-2-iodomethylene-pent-4-en-1-ol

Products:

1. C=CC/C(=C/I)C(=O)O

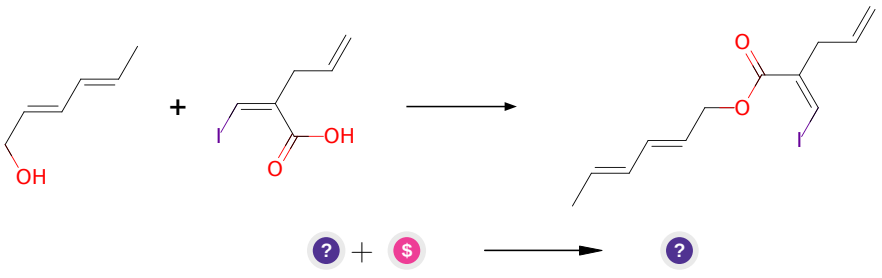
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

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

Retrosynthesis ID: 11160

2.3.2 Steglich Esterification



Substrates:

1. C=CC/C(=C/I)C(=O)O
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

1. C=CC/C(=C/I)C(=O)OC/C=C/C=C/C

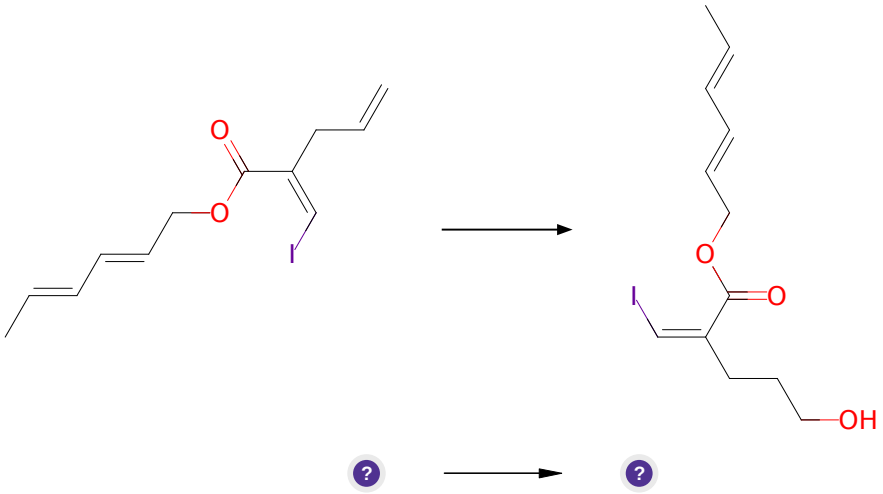
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.3.3 Rh(I) catalyzed hydroboration



Substrates:

1. C=CC/C(=C/I)C(=O)OC/C=C/C=C/C

Products:

1. C/C=C/C=C/COC(=O)/C(=C\I)CCCO

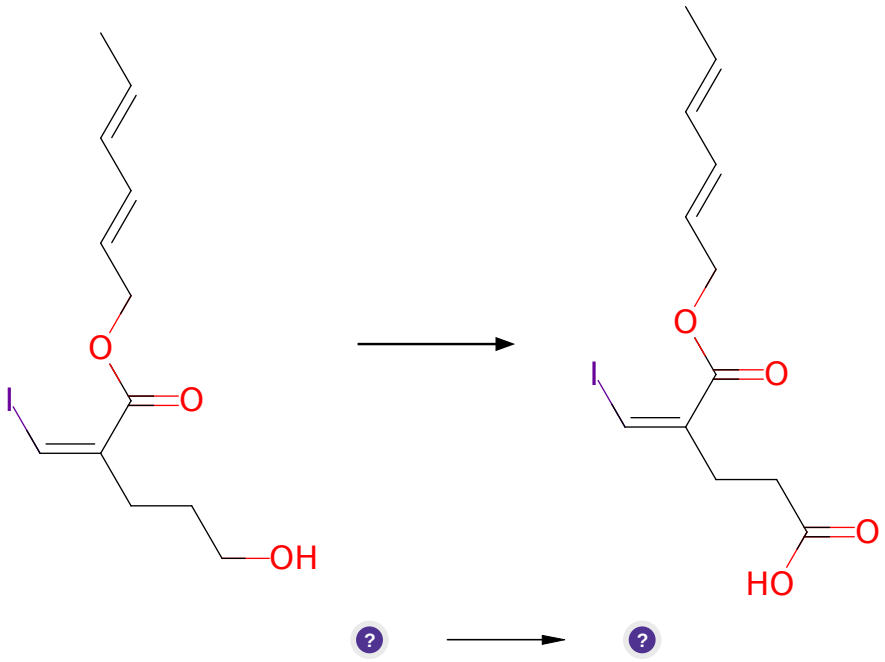
Typical conditions: Wilkinson's catalyst.cateholborane.THF.MeOH.NaOH.H2O2

Protections: none

Reference: DOI: *10.1021/ja00043a009*

Retrosynthesis ID: 9910000

2.3.4 Jones Oxidation



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\I)CCCO

Products:

1. C/C=C/C=C/COC(=O)/C(=C\I)CCC(=O)O

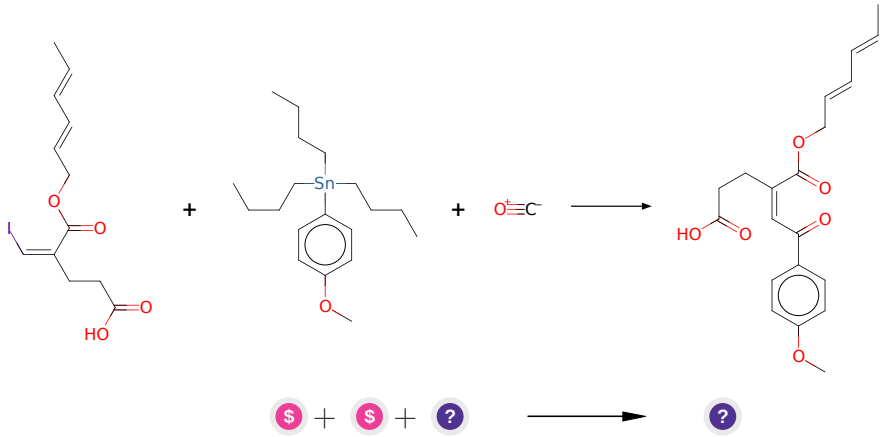
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

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

Retrosynthesis ID: 11160

2.3.5 Stille Carbonylative Cross-Coupling



Substrates:

1. Tributyl(4-methoxyphenyl)stannane - *available at Sigma-Aldrich*
2. CORM-2 - *available at Sigma-Aldrich*
3. C/C=C/C=C/COC(=O)/C(=C\I)CCC(=O)O

Products:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)CCC(=O)O

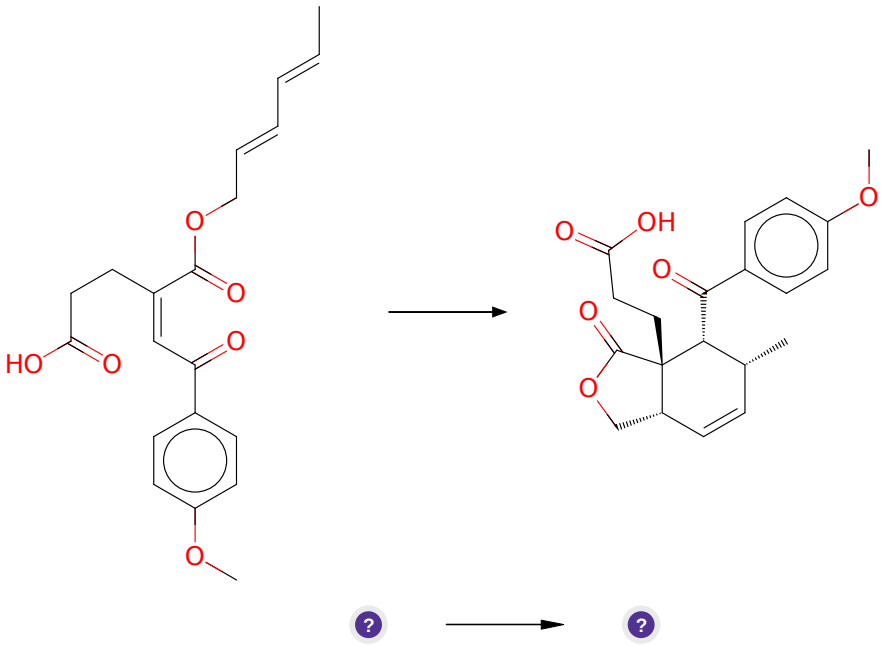
Typical conditions: Pd(0) complex

Protections: none

Reference: DOI: *10.1002/anie.198605081*

Retrosynthesis ID: 245571

2.3.6 Diels-Alder



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)CCC(=O)O

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32CCC(=O)O)cc1

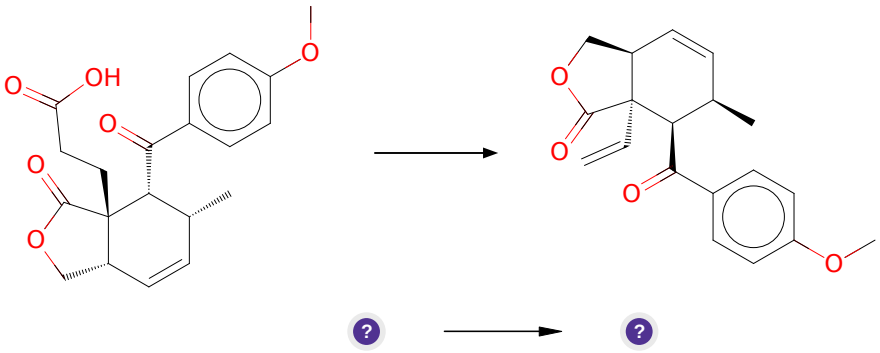
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.3.7 Catalytic dehydrogenative decarboxyolefination of carboxylic acids



Substrates:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32CCC(=O)O)cc1

Products:

1. C=C[C@]12C(=O)OC[C@H]1C=C[C@@H](C)[C@H]2C(=O)c1ccc(OC)cc1

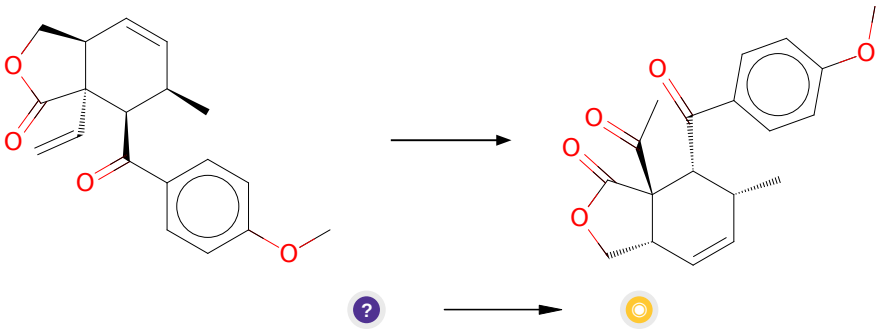
Typical conditions: [Ir]-photocatalyst.[Co]-catalyst.Cs2CO3.DME/H2O.blue.light.rt

Protections: none

Reference: *10.1038/s41557-018-0142-4* and *10.1021/acscatal.8b03282* and *10.1021/acs.joc.9b00167*

Retrosynthesis ID: 10032311

2.3.8 Wacker-Tsuji Olefin oxidation



Substrates:

1. C=C[C@]12C(=O)OC[C@H]1C=C[C@@H](C)[C@H]2C(=O)c1ccc(OC)cc1

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C(C)=O)cc1

Typical conditions: PdCl2.CuCl2.H2O.DMSO.O2

Protections: none

Reference: *10.1021/ja043203m* and *10.1002/anie.200502886* and *10.1021/acs.joc.6b00137* and *10.1016/j.tet.2013.07.048* and *10.1002/1521-3773(20011001)40:19<3675::AID-ANIE3675>3.0.CO;2-G* and *10.1002/cctc.201500241* and *10.1016/j.tetlet.2013.01.082*

Retrosynthesis ID: 26291

2.4 Path 4

Score: `164.14`

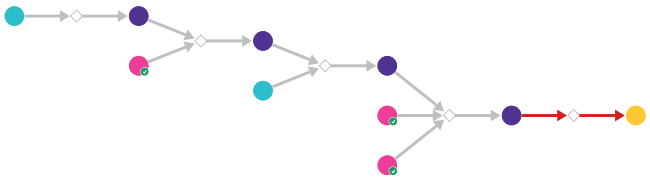
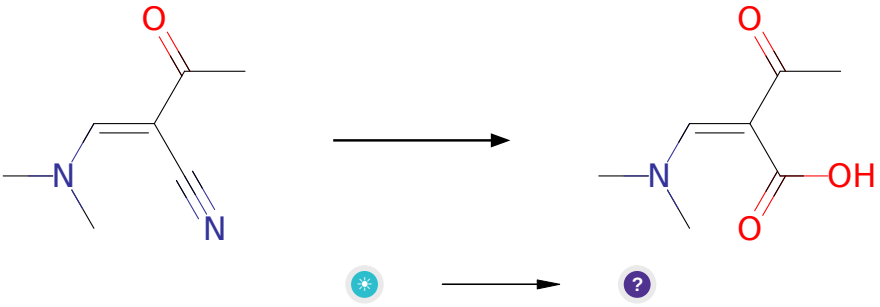


Figure 4: Outline of path 4

2.4.1 Acid hydrolysis of nitriles to carboxylic acids



Substrates:

1. 3-dimethylamino-2-acetyl propenenitrile

Products:

1. CC(=O)/C(=C/N(C)C)C(=O)O

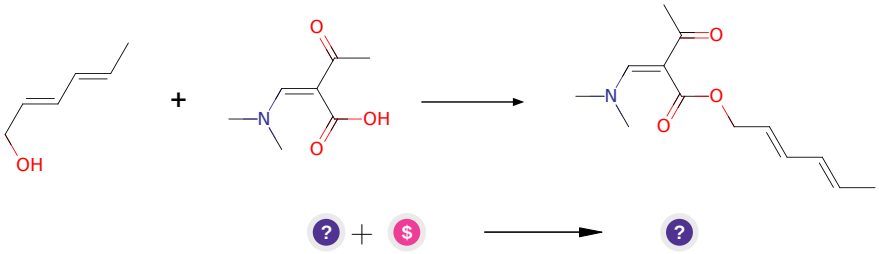
Typical conditions: Hcl.heating.H2O

Protections: none

Reference: *10.1021/jm301796k* and *10.1016/j.bmcl.2007.06.054* and *10.1021/jm801532e*

Retrosynthesis ID: 16027

2.4.2 Steglich Esterification



Substrates:

1. CC(=O)/C(=C/N(C)C)C(=O)O
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

1. C/C=C/C=C/COC(=O)/C(=C\N(C)C)C(C)=O

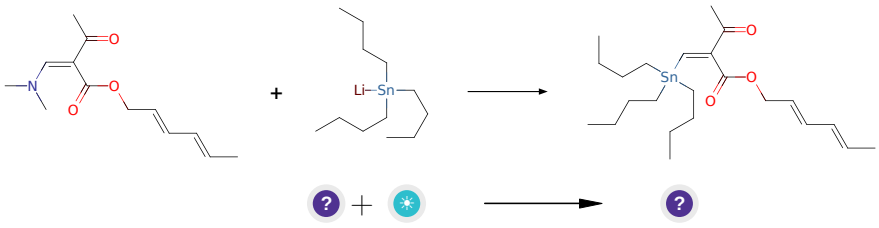
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.4.3 Stannylation of enamines



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\N(C)C)C(C)=O
2. C12H27LiSn

Products:

1. C/C=C/C=C/COC(=O)/C(=C\[Sn](CCCC)(CCCC)CCCC)C(C)=O

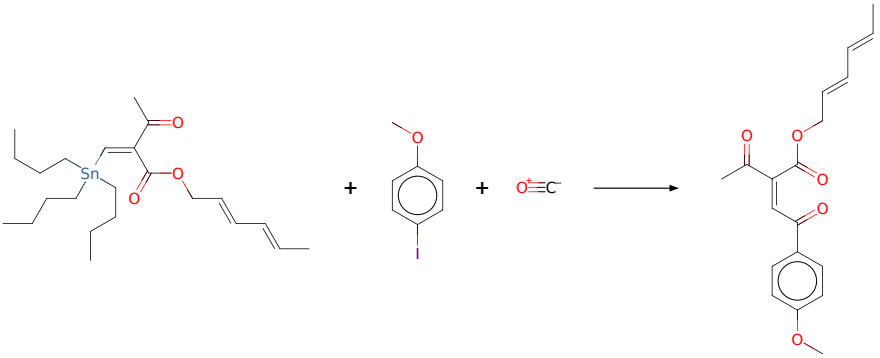
Typical conditions: Bu3SnLi.THF.MeI

Protections: none

Reference: DOI: *10.1021/ol8020435*

Retrosynthesis ID: 1780

2.4.4 Stille Carbonylative Cross-Coupling



Substrates:

1. CORM-2 - *available at Sigma-Aldrich*
2. 4-Iodoanisole - *available at Sigma-Aldrich*
3. C/C=C/C=C/COC(=O)/C(=C\[Sn](CCCC)(CCCC)CCCC)C(C)=O

Products:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

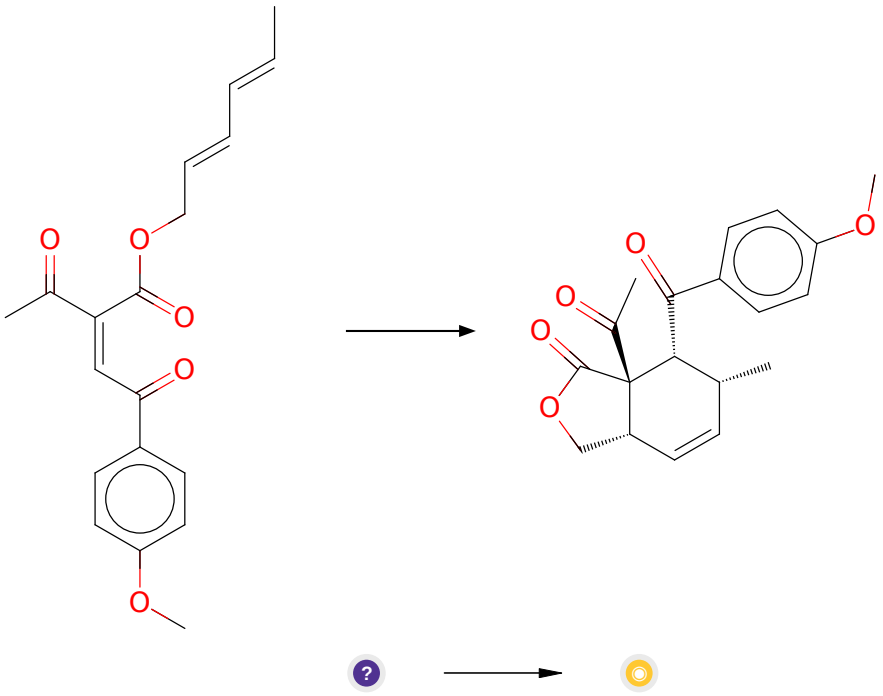
Typical conditions: Pd(0) complex

Protections: none

Reference: DOI: *10.1002/anie.198605081*

Retrosynthesis ID: 245572

2.4.5 Diels-Alder



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C(C)=O

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C(C)=O)cc1

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 Path 5

Score: `166.61`

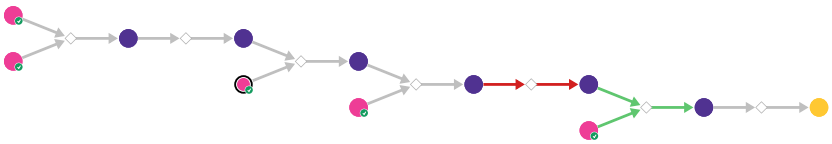
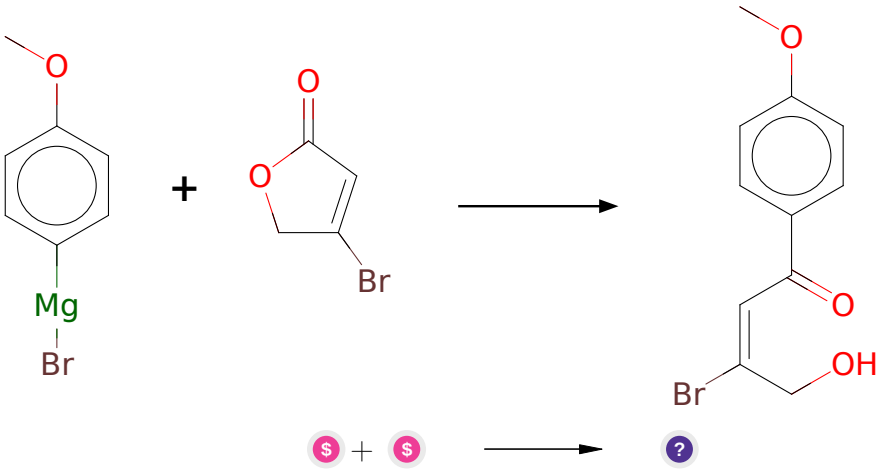


Figure 5: Outline of path 5

2.5.1 Ring opening of lactones with organometallic reagents



Substrates:

1. 4-Methoxyphenylmagnesium bromide solution - *available at Sigma-Aldrich*
2. 4-Bromofuran-2-one - *available at Sigma-Aldrich*

Products:

1. COc1ccc(C(=O)/C=C(/Br)CO)cc1

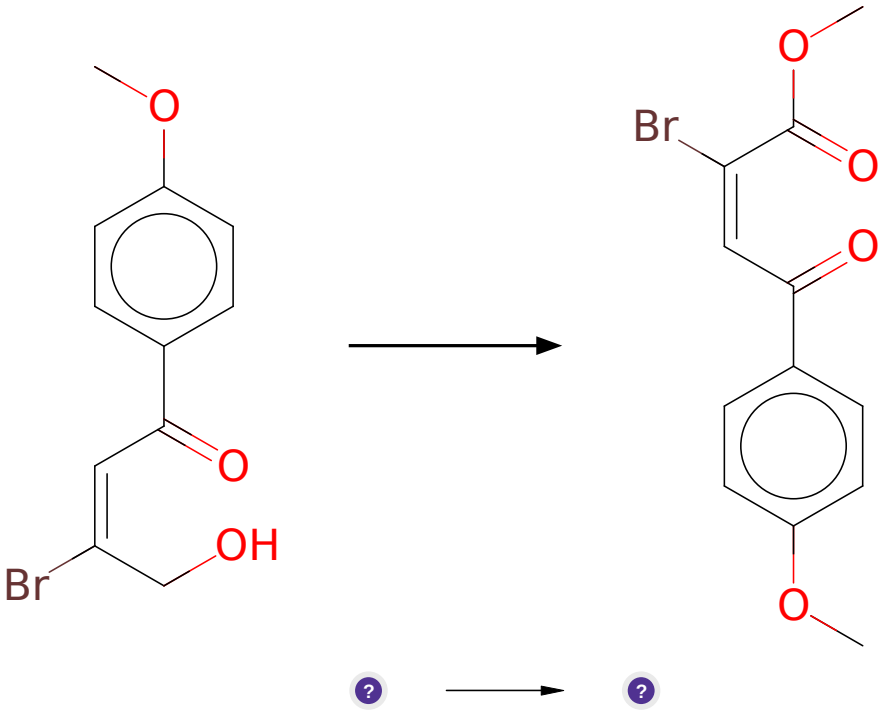
Typical conditions: ether.-78C

Protections: none

Reference: *10.1002/jhet.233* and *10.1002/ejoc.200801000* and *10.1271/bbb.67.1744*

Retrosynthesis ID: 9990232

2.5.2 Tandem oxidation-esterification



Substrates:

1. COc1ccc(C(=O)/C=C(/Br)CO)cc1

Products:

1. COC(=O)/C(Br)=C\C(=O)c1ccc(OC)cc1

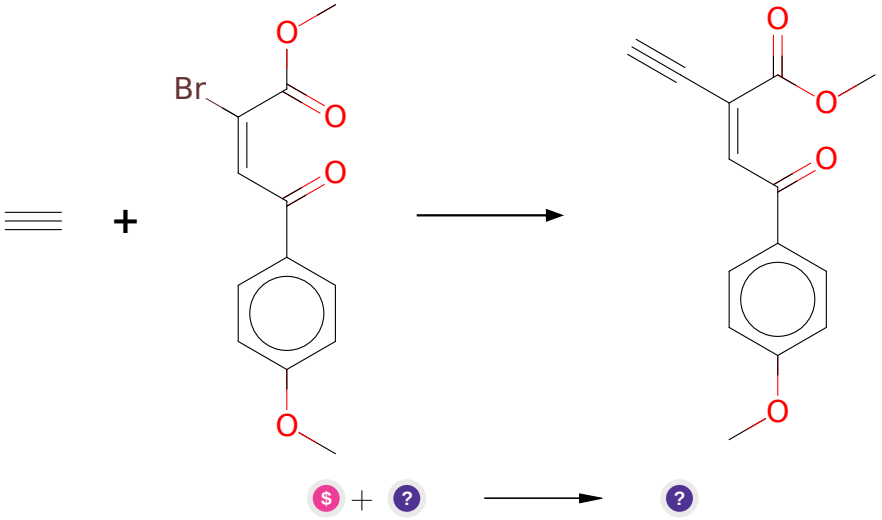
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

Protections: none

Reference: *10.1016/S0040-4039(00)73550-7* and *10.1016/j.tet.2005.03.097* and *10.1021/ol062940f*

Retrosynthesis ID: 25234

2.5.3 Sonogashira-type coupling of alkynes with vinyl Bromides



Substrates:

1. Calcium carbide - *available at Sigma-Aldrich*
2. COC(=O)/C(Br)=C\C(=O)c1ccc(OC)cc1

Products:

1. C#C/C(=C/C(=O)c1ccc(OC)cc1)C(=O)OC

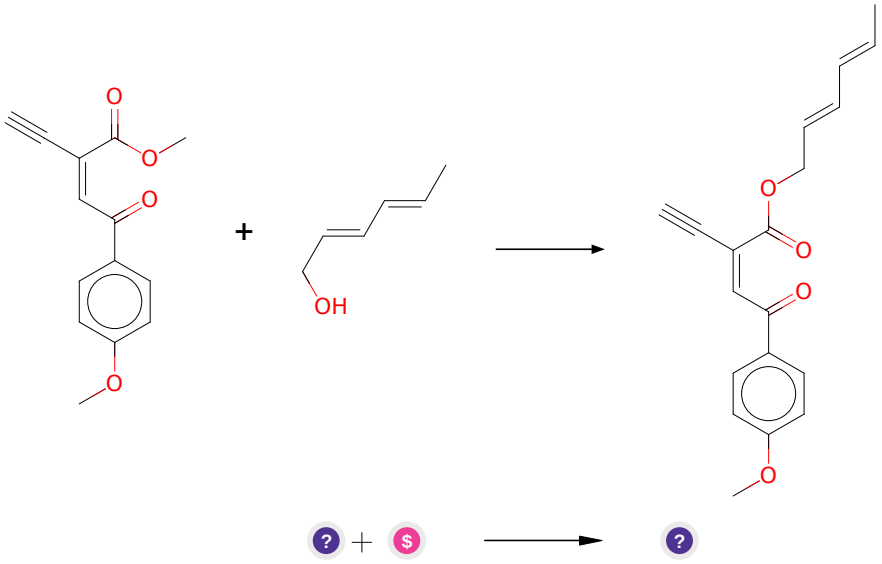
Typical conditions: Pd catalyst.CuI.base.solvent

Protections: none

Reference: US2003/236423 and *10.1055/s-0031-1290502* and *10.1021/ja510635k* (SI) and *10.1021/ol0508173* and *10.1021/ol0508173* and *10.1021/ja044744e* (SI)

Retrosynthesis ID: 25103

2.5.4 Acid catalyzed transesterification



Substrates:

1. C#C/C(=C/C(=O)c1ccc(OC)cc1)C(=O)OC
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

1. C#C/C(=C/C(=O)c1ccc(OC)cc1)C(=O)OC/C=C/C=C/C

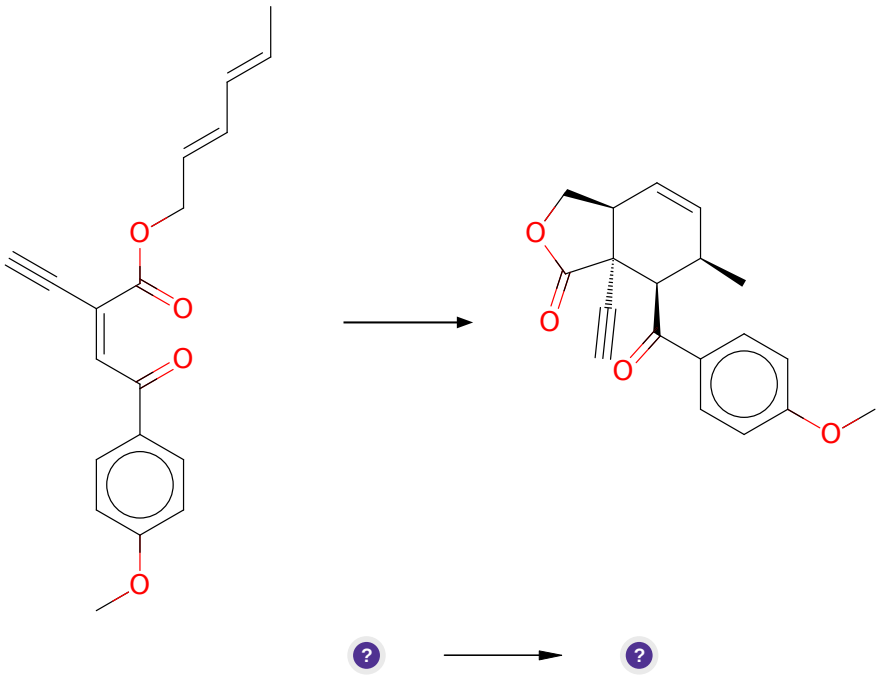
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.5.5 Diels-Alder



Substrates:

1. C#C/C(=C/C(=O)c1ccc(OC)cc1)C(=O)OC/C=C/C=C/C

Products:

1. C#C[C@]12C(=O)OC[C@H]1C=C[C@@H](C)[C@H]2C(=O)c1ccc(OC)cc1

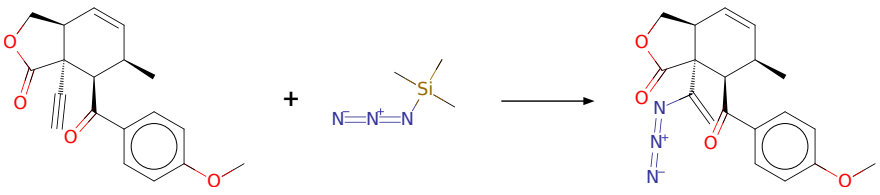
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

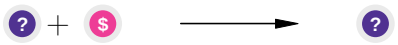
Protections: none

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 Silver-catalyzed hydroazidation of terminal alkynes





Substrates:

1. C#C[C@]12C(=O)OC[C@H]1C=C[C@@H](C)[C@H]2C(=O)c1ccc(OC)cc1
2. Trimethylsilyl azide - *available at Sigma-Aldrich*

Products:

1. C=C(N=[N+]=[N-])[C@]12C(=O)OC[C@H]1C=C[C@@H](C)[C@H]2C(=O)c1ccc(OC)cc1

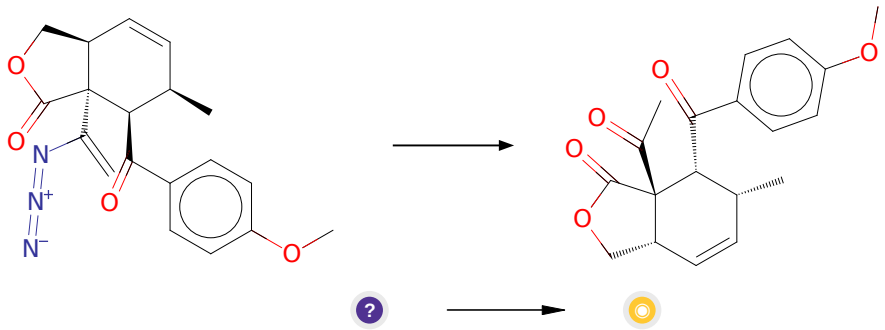
Typical conditions: Ag2CO3. H2O. DMSO. 80C

Protections: none

Reference: DOI: *10.1021/ol501661k*

Retrosynthesis ID: 1409

2.5.7 Synthesis of alpha - amino ketones from 2 - azidoallyl amines



Substrates:

1. C=C(N=[N+]=[N-])[C@]12C(=O)OC[C@H]1C=C[C@@H](C)[C@H]2C(=O)c1ccc(OC)cc1

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C(C)=O)cc1

Typical conditions: BF3 * Et2O. Ch2Cl2. rt

Protections: none

Reference: DOI: *10.1021/ol501661k*

Retrosynthesis ID: 1412