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

FGI Coeff: 0

Tunnels Coeff: 0

JSON Parameters: {}

2 Paths

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

2.1 Path 1

Score: `176.35`

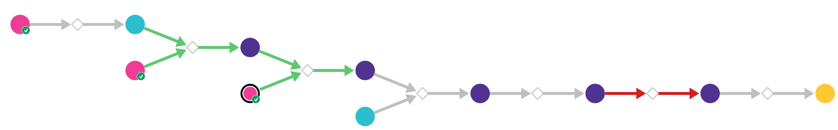
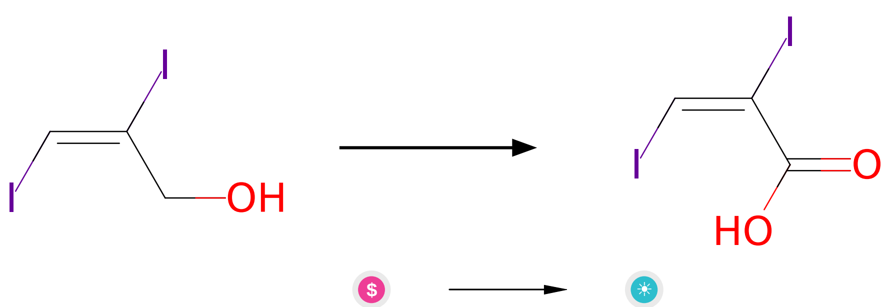


Figure 1: Outline of path 1

2.1.1 Jones Oxidation



Substrates:

1. (e)-a,b-diiodoallyl alcohol - *available at Sigma-Aldrich*

Products:

1. 2,3-diiodo-acrylic acid

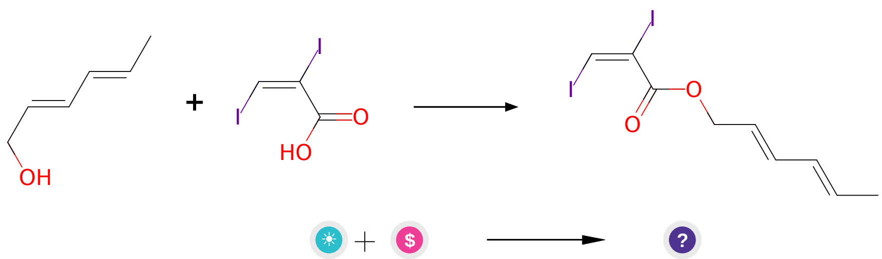
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

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

Retrosynthesis ID: 11160

2.1.2 Steglich Esterification



Substrates:

1. 2,3-diiodo-acrylic acid
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

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

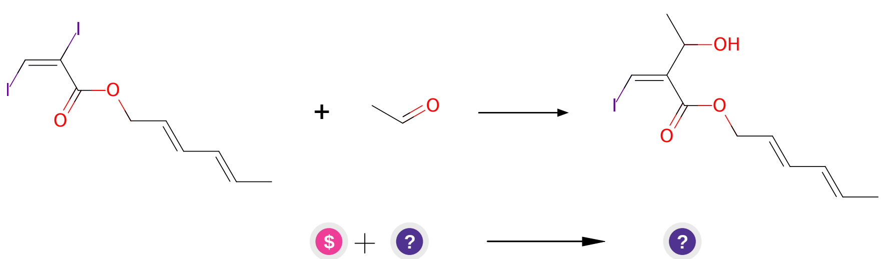
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.1.3 Reformatsky Reaction



Substrates:

1. Ethanal - *available at Sigma-Aldrich*
2. C/C=C/C=C/COC(=O)/C(I)=C\I

Products:

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

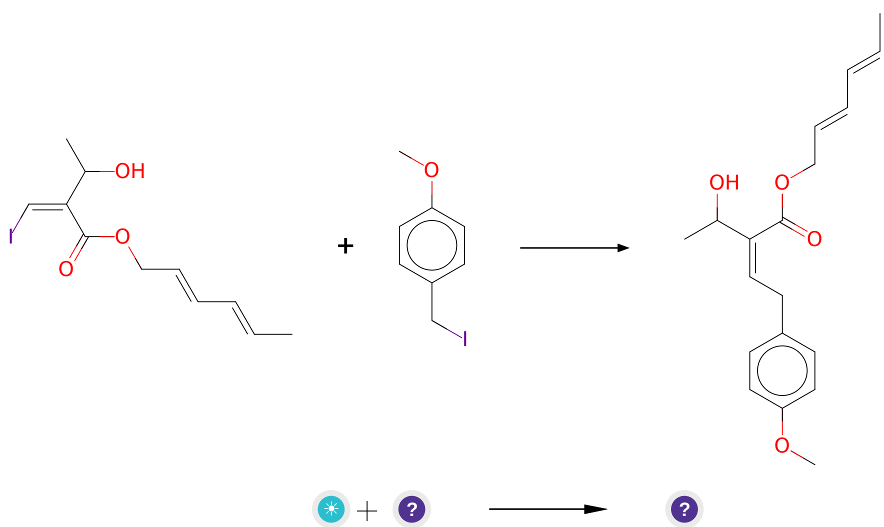
Typical conditions: Zn.THF

Protections: none

Reference: *10.1016/j.bmc.2016.07.052* p. 4521, 4520 and *10.1016/j.ejmech.2013.07.047* p. 214, 218

Retrosynthesis ID: 11539

2.1.4 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. p-methoxybenzyl iodide
2. C/C=C/C=C/COC(=O)/C(=C\I)C(C)O

Products:

1. C/C=C/C=C/COC(=O)/C(=C\Cc1ccc(OC)cc1)C(C)O

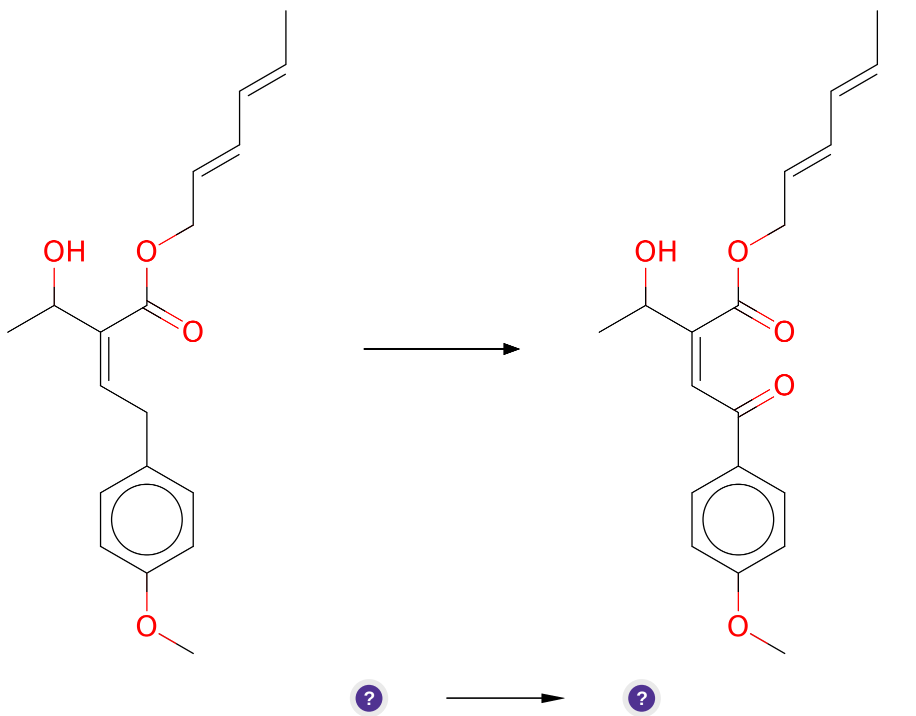
Typical conditions: [Pd].catalyst

Protections: none

Reference: *10.1016/j.bmcl.2005.12.066* and *10.1021/ol052070m* and *10.1021/ol5023195* and *10.1002/anie.200703134* and *10.1016/j.bmcl.2005.09.084* and *10.1021/ol0344873*

Retrosynthesis ID: 25165

2.1.5 Allylic Oxidation of Alkenes



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\Cc1ccc(OC)cc1)C(C)O

Products:

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

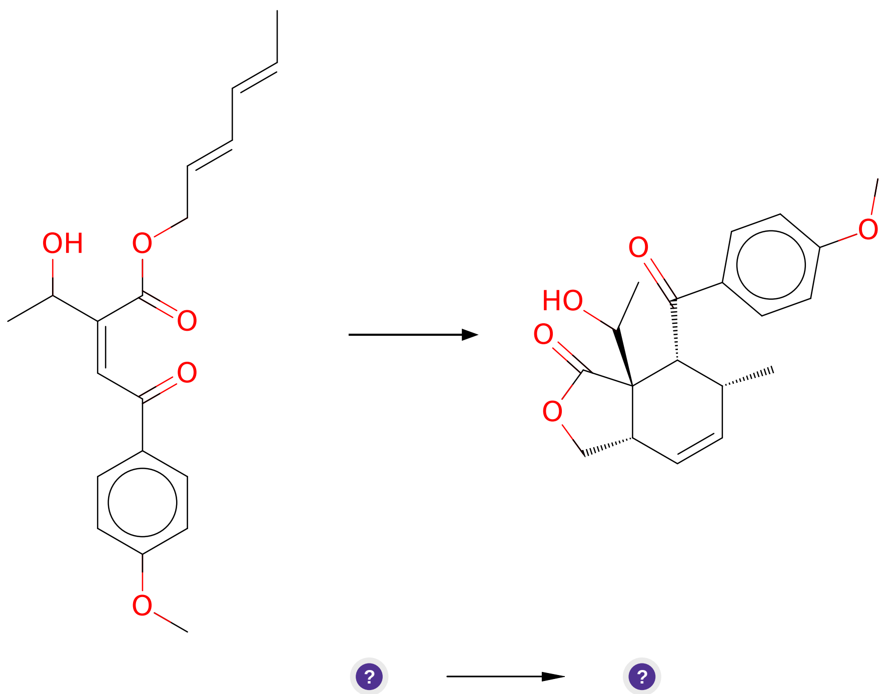
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.1.6 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

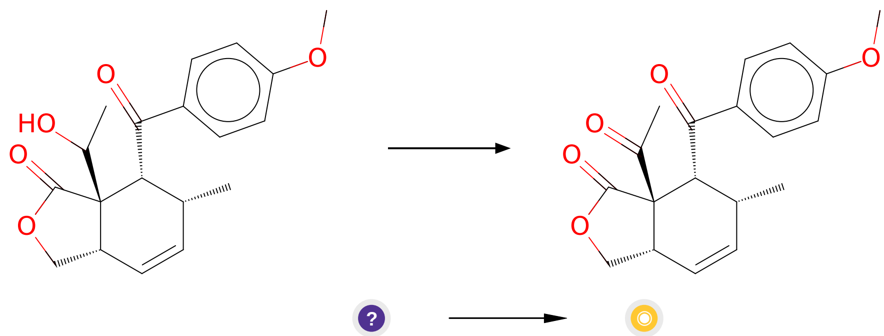
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.1.7 Swern Oxidation



Substrates:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C(C)O)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: oxalyl chloride.DMSO.DCM.NMe3.-40C

Protections: none

Reference: *10.1055/s-1990-27036*

Retrosynthesis ID: 11163

2.2 Path 2

Score: `181.37`

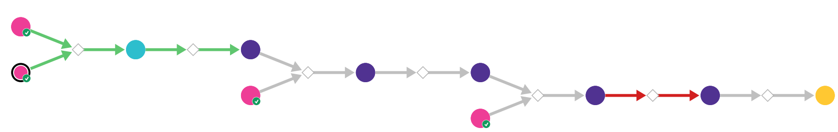
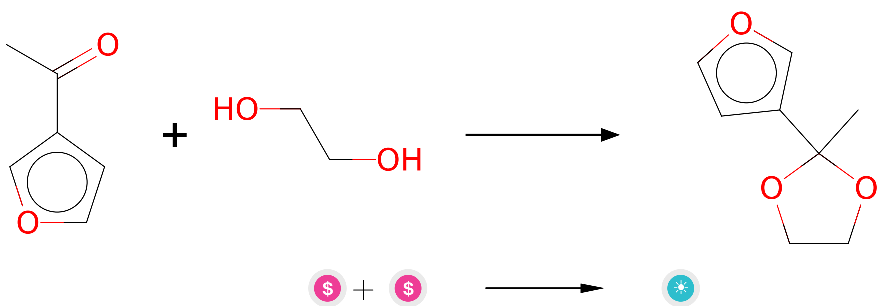


Figure 2: Outline of path 2

2.2.1 Synthesis of cyclic N,S,O/N,O -acetals



Substrates:

1. 1-(3-Furyl)-1-ethanone - *available at Sigma-Aldrich*
2. 1 - *available at Sigma-Aldrich*

Products:

1. 2-furan-3-yl-2-methyl-[1,3]dioxolane

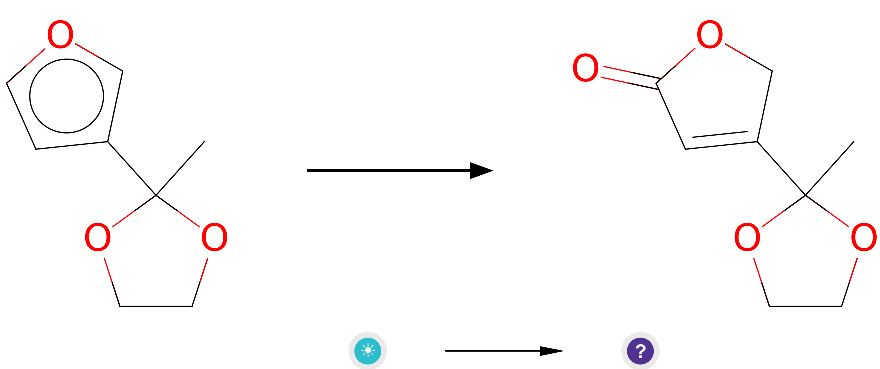
Typical conditions: heat or pTsOH

Protections: none

Reference: *10.1039/P19880000817* AND *10.1016/j.tetlet.2012.07.052* AND *10.1021/ol9009859* AND *10.1039/C0CC00110D* AND *10.1002/1521-3765(20010504)7:9<2007::AID-CHEM2007>3.0.CO;2-7* AND *10.1021/jo000510b*

Retrosynthesis ID: 9530

2.2.2 Oxidation furans to 2-(5H)-furanones



Substrates:

1. 2-furan-3-yl-2-methyl-[1,3]dioxolane

Products:

1. CC1(C2=CC(=O)OC2)OCCO1

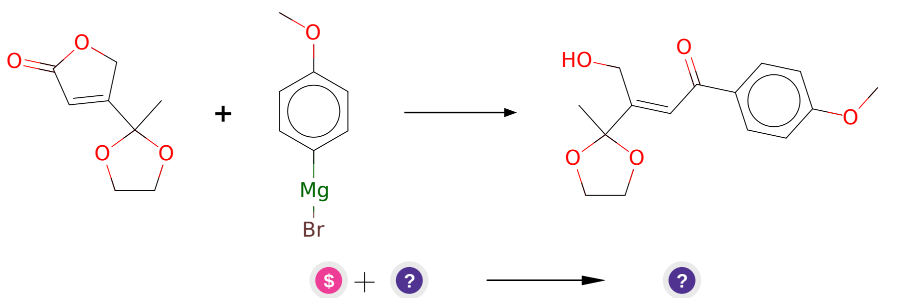
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

Reference: DOI: *10.1055/s-2005-869865*

Retrosynthesis ID: 50716

2.2.3 Ring opening of lactones with organometallic reagents



Substrates:

1. 4-Methoxyphenylmagnesium bromide solution - *available at Sigma-Aldrich*
2. CC1(C2=CC(=O)OC2)OCCO1

Products:

1. COc1ccc(C(=O)/C=C(\CO)C2(C)OCCO2)cc1

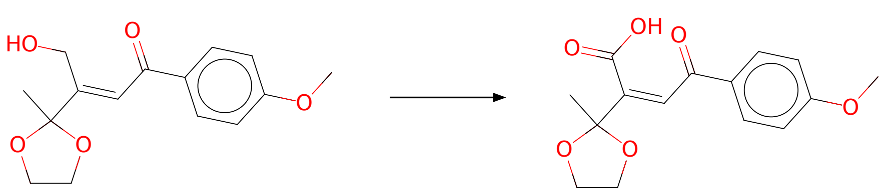
Typical conditions: ether.-78C

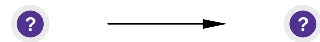
Protections: none

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

Retrosynthesis ID: 9990232

2.2.4 Jones Oxidation





Substrates:

1. COc1ccc(C(=O)/C=C(\CO)C2(C)OCCO2)cc1

Products:

1. COc1ccc(C(=O)/C=C(\C(=O)O)C2(C)OCCO2)cc1

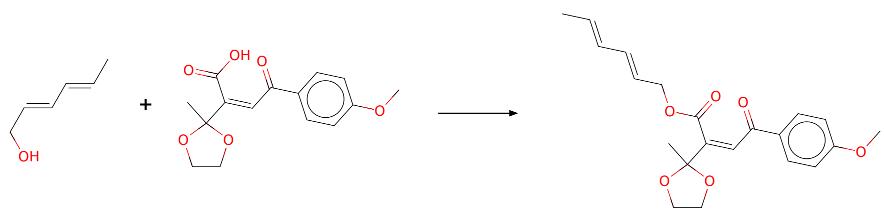
Typical conditions: cromate.sulfate.H2O.acetone

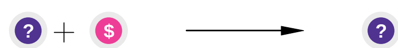
Protections: none

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

Retrosynthesis ID: 11160

2.2.5 Steglich Esterification





Substrates:

1. COc1ccc(C(=O)/C=C(\C(=O)O)C2(C)OCCO2)cc1
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C1(C)OCCO1

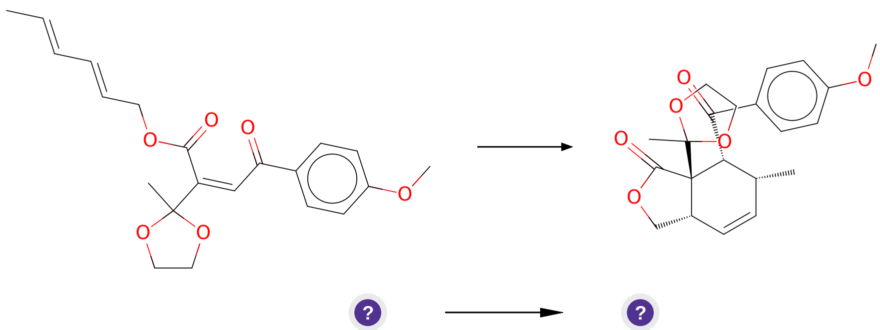
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.2.6 Diels-Alder



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\C(=O)c1ccc(OC)cc1)C1(C)OCCO1

Products:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C2(C)OCCO2)cc1

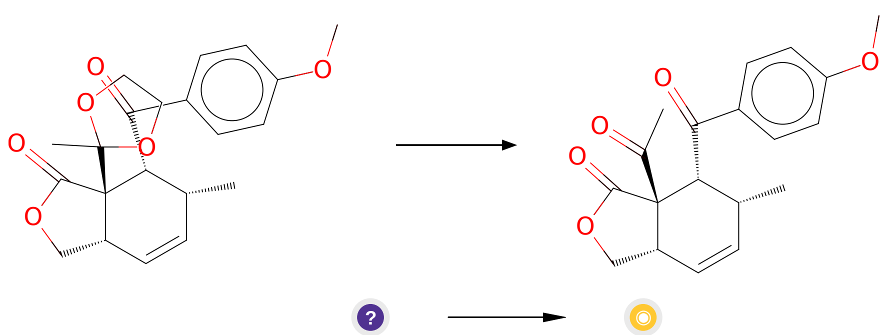
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.2.7 Hydrolysis of ketals



Substrates:

1. COc1ccc(C(=O)[C@@H]2[C@H](C)C=C[C@@H]3COC(=O)[C@@]32C2(C)OCCO2)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: H2O.HCl

Protections: none

Reference: *10.1021/jo0159035* and *10.1021/jo00194a003* and

Retrosynthesis ID: 31013139

2.3 Path 3

Score: `181.72`

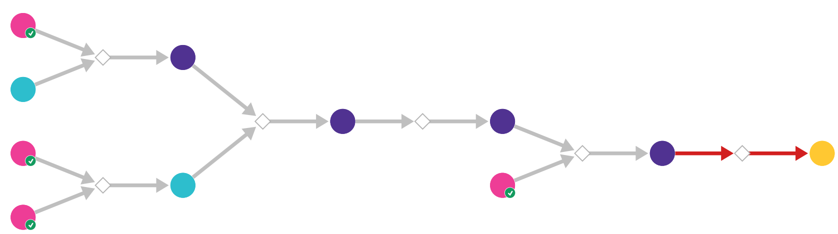
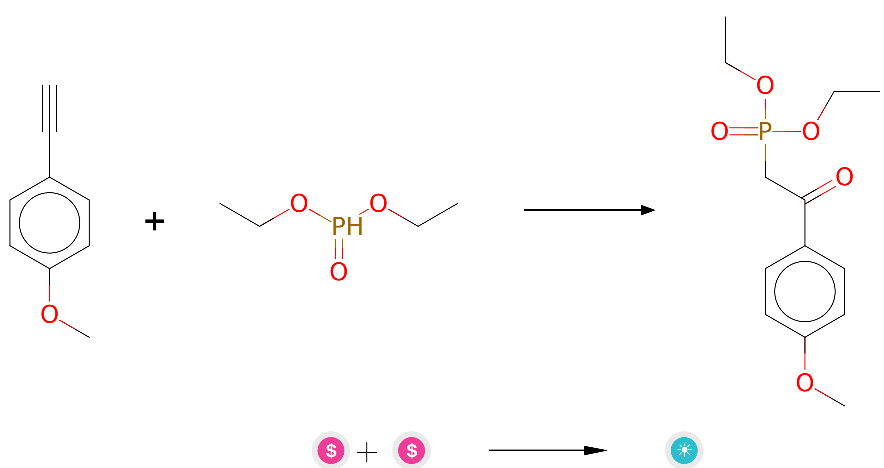


Figure 3: Outline of path 3

2.3.1 Aerobic oxyphosphorylation of terminal alkynes



Substrates:

1. Diethyl phosphite - *available at Sigma-Aldrich*
2. 4-Ethynylanisole - *available at Sigma-Aldrich*

Products:

1. 4-methoxy-phenacylphosphonsaeure-diaethylester

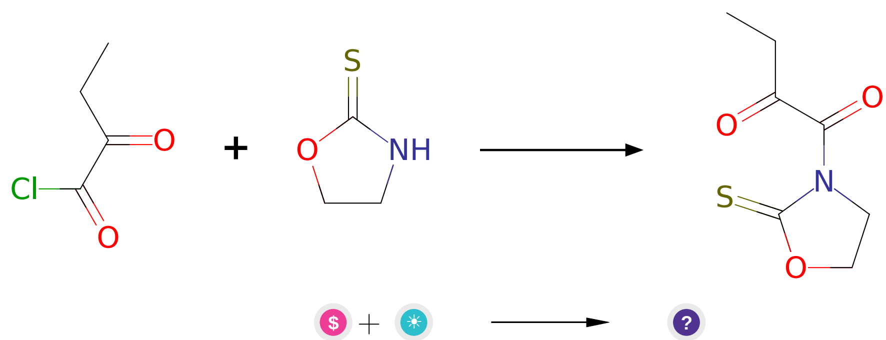
Typical conditions: Cu(acac)2.FeCl3.TEA.DMSO.O2.80C

Protections: none

Reference: DOI: *10.1021/acs.joc.5b00408*

Retrosynthesis ID: 9600

2.3.2 Acylation of amides



Substrates:

1. 1,3-oxazolidine-2-thione - *available at Sigma-Aldrich*
2. a-keto-buttersaeurechlorid

Products:

1. CCC(=O)C(=O)N1CCOC1=S

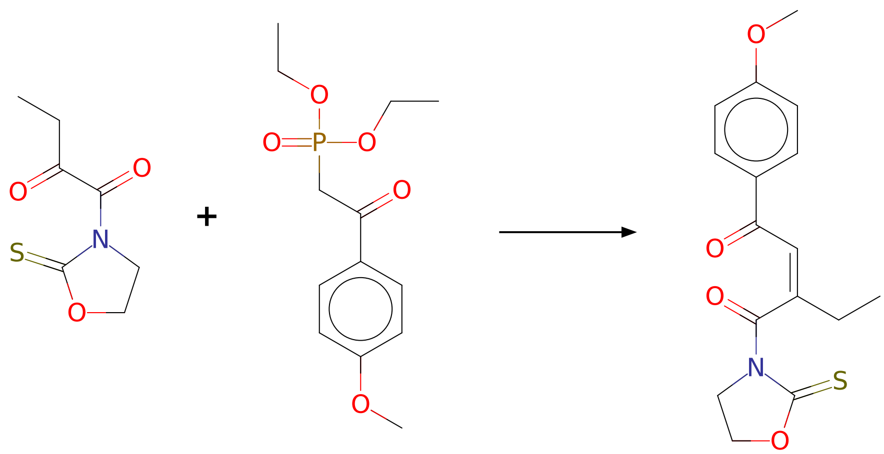
Typical conditions: LiHMDS.THF

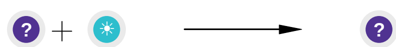
Protections: none

Reference: *10.1021/ol052943c* AND *10.1016/j.tetlet.2013.08.110* AND *10.1016/j.tet.2012.06.037* AND *10.1021/jo049759+* AND *10.1016/j.ejmech.2014.09.065* AND *10.1016/j.ejmech.2014.09.065*

Retrosynthesis ID: 14791

2.3.3 HWE olefination





Substrates:

1. CCC(=O)C(=O)N1CCOC1=S
2. 4-methoxy-phenacylphosphonsaeure-diaethylester

Products:

1. CC/C(=C/C(=O)c1ccc(OC)cc1)C(=O)N1CCOC1=S

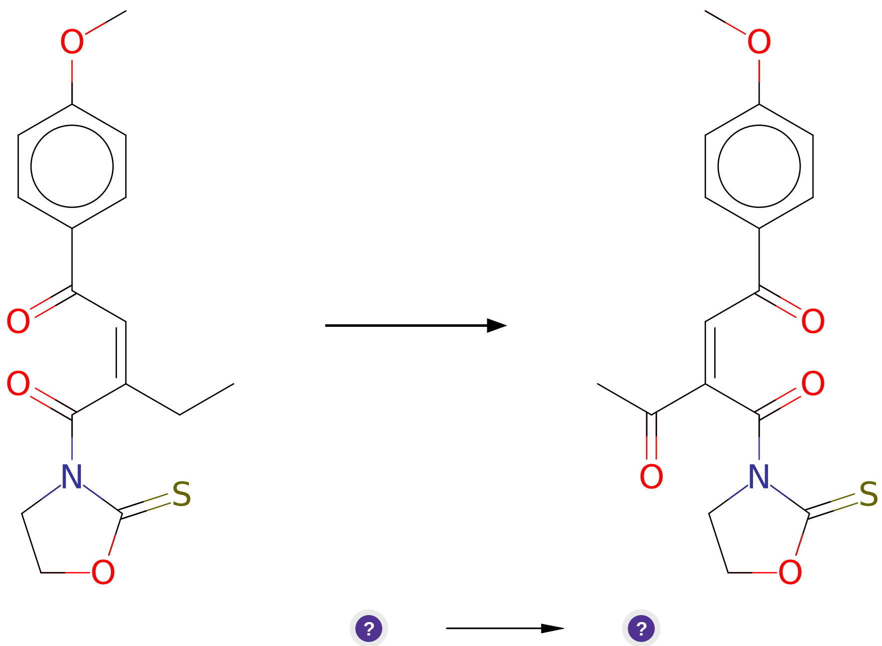
Typical conditions: 1.Base 2.RCHO

Protections: none

Reference: *10.1002/jlcr.464* 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: 14765

2.3.4 Allylic Oxidation of Alkenes



Substrates:

1. CC/C(=C/C(=O)c1ccc(OC)cc1)C(=O)N1CCOC1=S

Products:

1. COc1ccc(C(=O)/C=C(/C(C)=O)C(=O)N2CCOC2=S)cc1

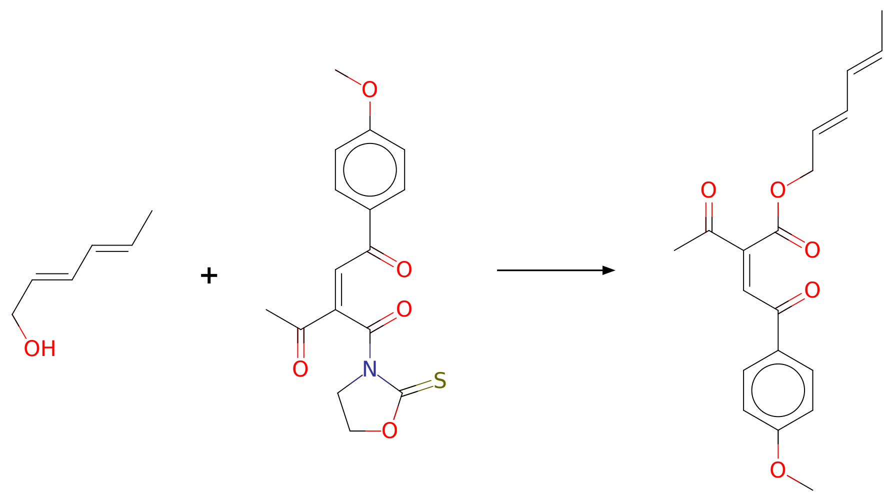
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

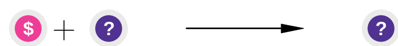
Protections: none

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

Retrosynthesis ID: 2583

2.3.5 Deprotection of N-Acyloxazolidinethiones in Esters





Substrates:

1. Sorbic alcohol - *available at Sigma-Aldrich*
2. COc1ccc(C(=O)/C=C(/C(C)=O)C(=O)N2CCOC2=S)cc1

Products:

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

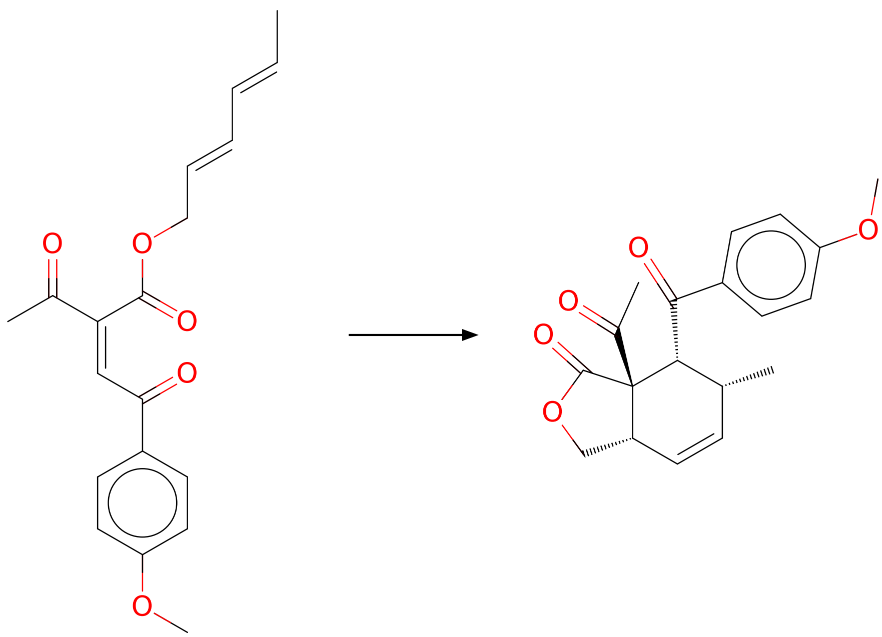
Typical conditions: MeOH.imidazole.0C

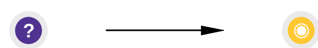
Protections: none

Reference: DOI:*10.1021/jo001387r*

Retrosynthesis ID: 10492

2.3.6 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

2.4 Path 4

Score: `186.11`

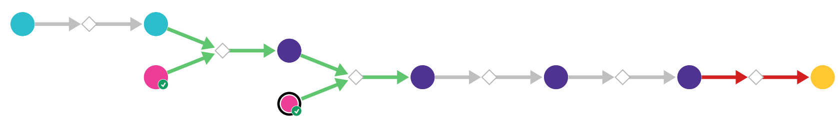
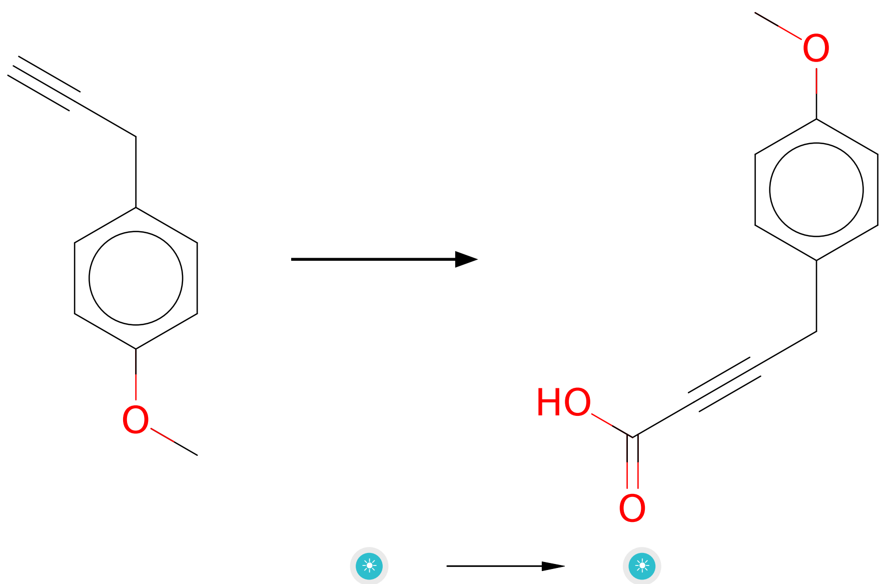


Figure 4: Outline of path 4

2.4.1 Carboxylation of terminal alkynes



Substrates:

1. 3-(4-methoxyphenyl)-1-propyne

Products:

1. 1-p-anisyl-but-2-in-saeure

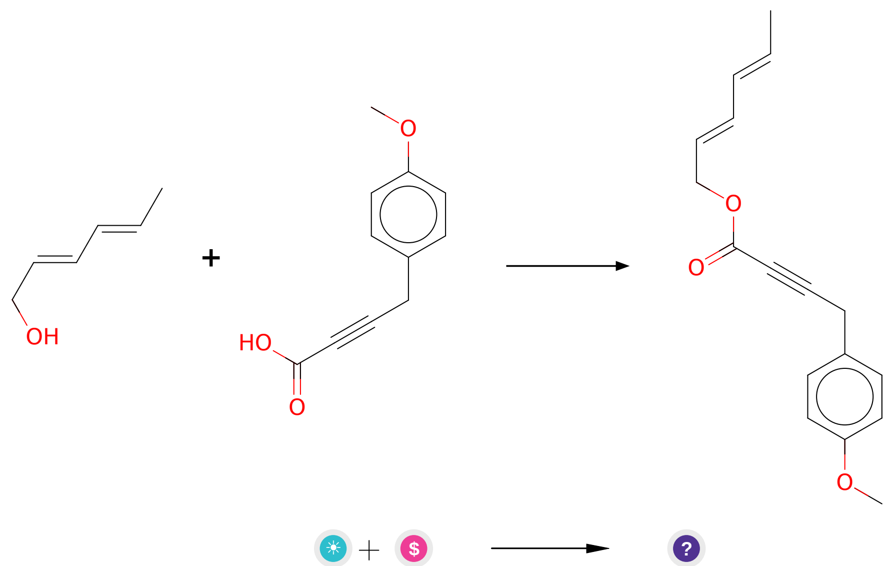
Typical conditions: 1.nBuLi or LDA.2.CO2

Protections: none

Reference: *10.1002/anie.201412468* AND *10.1016/j.tet.2008.10.107* AND *10.1002/anie.200902760* AND *10.1021/ol800583r* AND *10.1002/hlca.200800446*

Retrosynthesis ID: 15024

2.4.2 Steglich Esterification



Substrates:

1. 1-p-anisyl-but-2-in-saeure
2. Sorbic alcohol - *available at Sigma-Aldrich*

Products:

1. C/C=C/C=C/COC(=O)C#CCc1ccc(OC)cc1

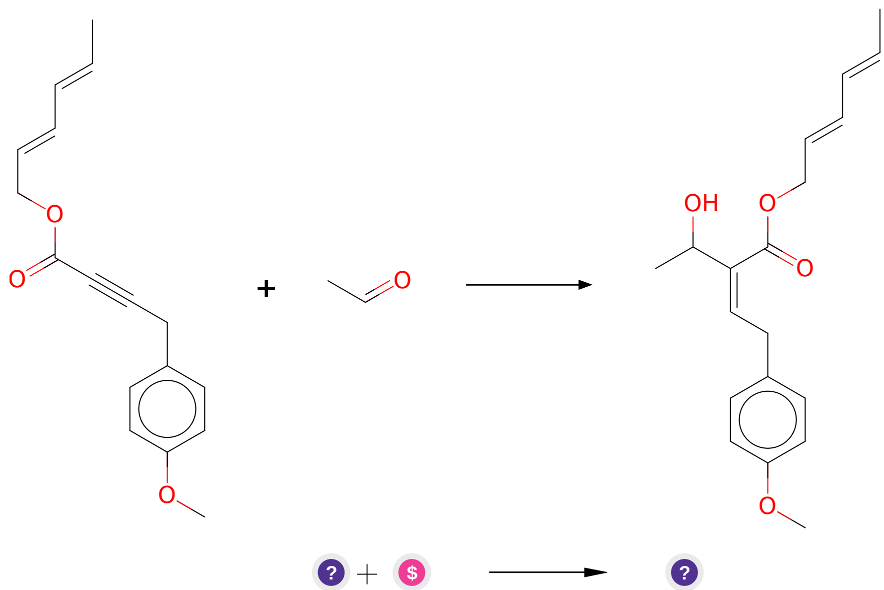
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.4.3 Stereospecific synthesis of Baylis-Hillman adducts



Substrates:

1. C/C=C/C=C/COC(=O)C#CCc1ccc(OC)cc1
2. Ethanal - *available at Sigma-Aldrich*

Products:

1. C/C=C/C=C/COC(=O)/C(=C\Cc1ccc(OC)cc1)C(C)O

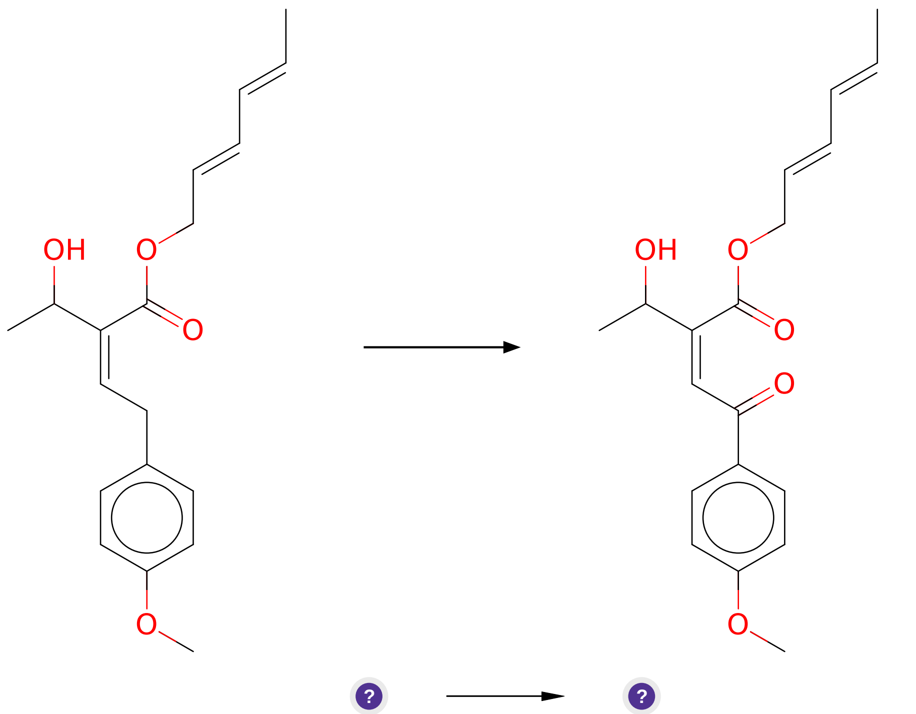
Typical conditions: 1)DIBAH/HMPA.THF.25C 2)n-Bu2BOTf(cat.).-78C

Protections: none

Reference: DOI: *10.1016/S0040-4039(98)00850-8*

Retrosynthesis ID: 406

2.4.4 Allylic Oxidation of Alkenes



Substrates:

1. C/C=C/C=C/COC(=O)/C(=C\Cc1ccc(OC)cc1)C(C)O

Products:

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

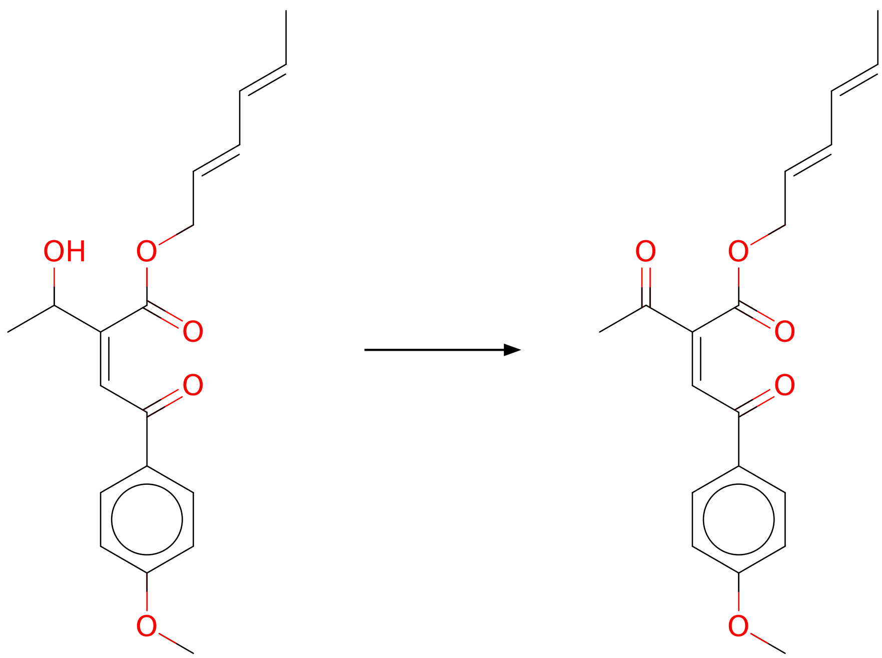
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

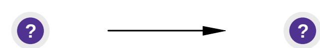
Protections: none

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

Retrosynthesis ID: 2583

2.4.5 Swern Oxidation





Substrates:

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

Products:

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

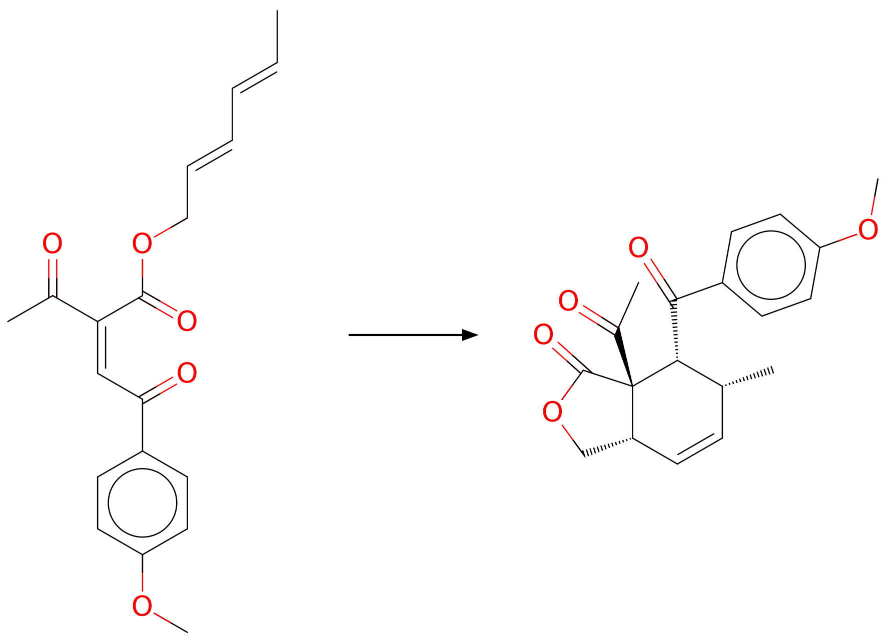
Typical conditions: oxalyl chloride.DMSO.DCM.NMe3.-40C

Protections: none

Reference: *10.1055/s-1990-27036*

Retrosynthesis ID: 11163

2.4.6 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