Paths of analysis*

L9_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: `125.08`

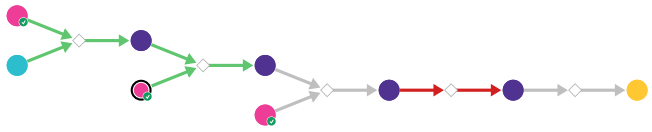
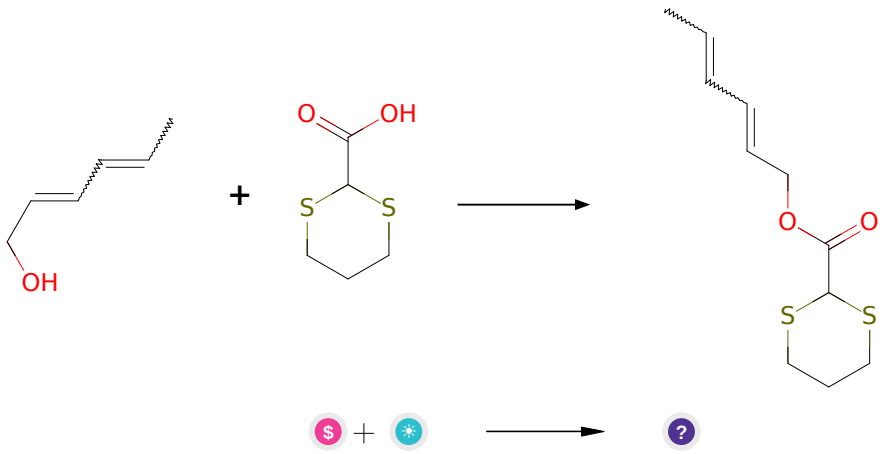


Figure 1: Outline of path 1

2.1.1 Steglich Esterification



Substrates:

1. 1,3-dithiane-2-carboxylic acid - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C1SCCCS1

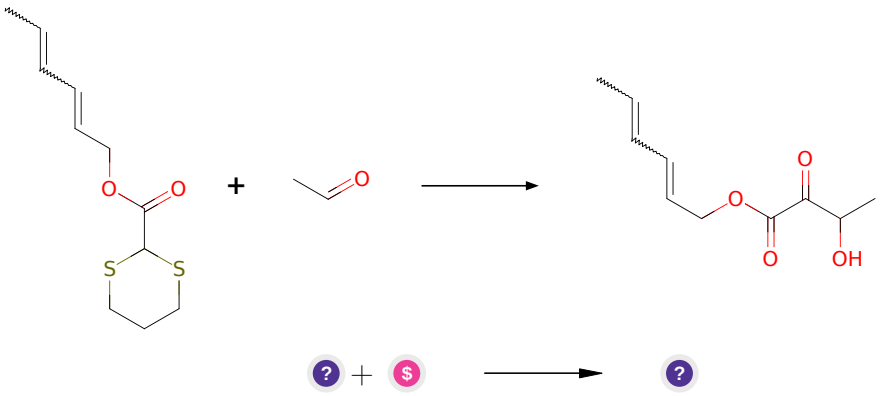
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.1.2 Corey-Seebach



Substrates:

1. CC=CC=CCOC(=O)C1SCCCS1
2. Ethanal - *available at Sigma-Aldrich*

Products:

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

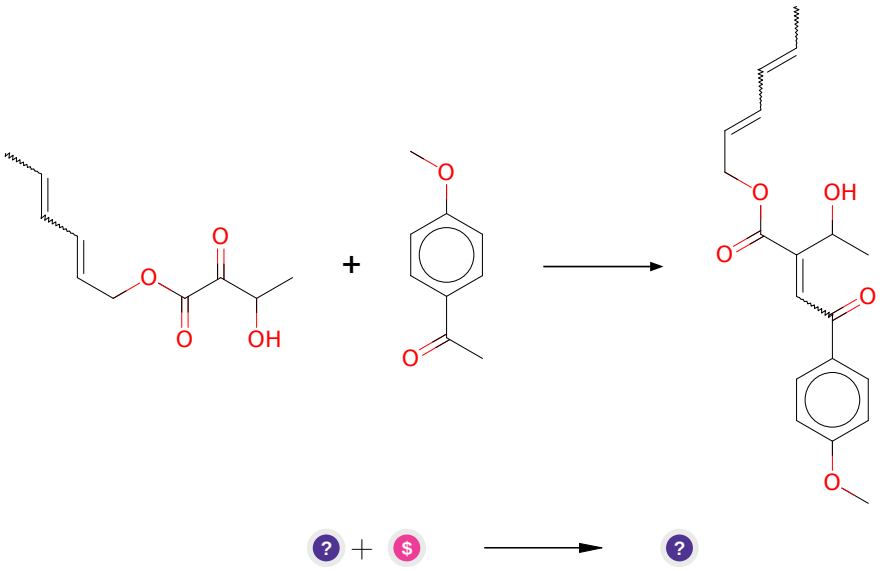
Typical conditions: BuLi.THF.-30C.HgO.H2O.THF

Protections: none

Reference: *10.1055/s-1977-24412*

Retrosynthesis ID: 11200

2.1.3 Aldol Condensation



Substrates:

1. CC=CC=CCOC(=O)C(=O)C(C)O
2. Acetanisole - *available at Sigma-Aldrich*

Products:

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

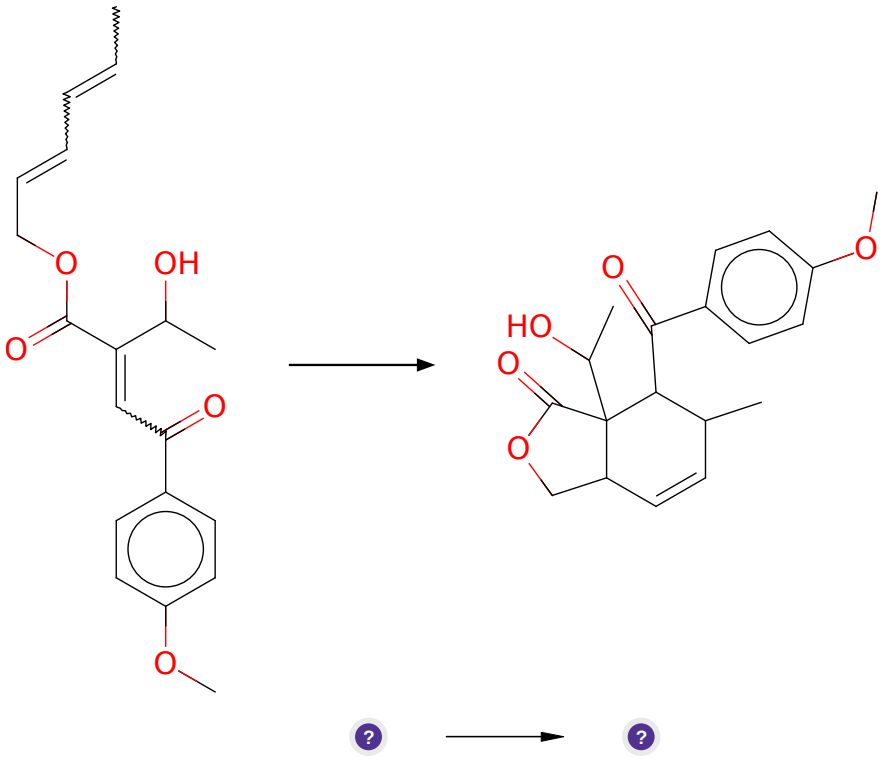
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10898

2.1.4 Diels-Alder



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)O)cc1

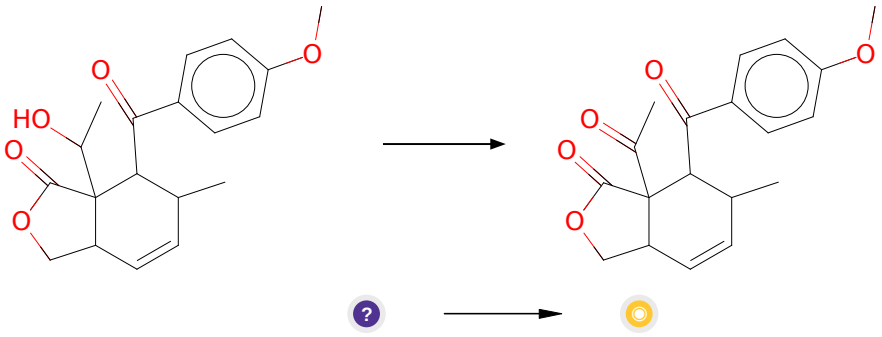
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.1.5 Swern Oxidation



Substrates:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)O)cc1

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(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: `145.10`

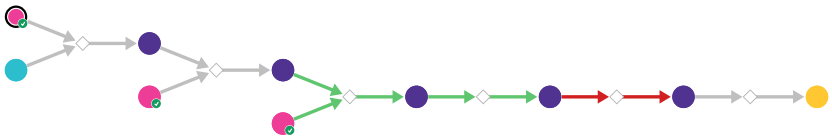
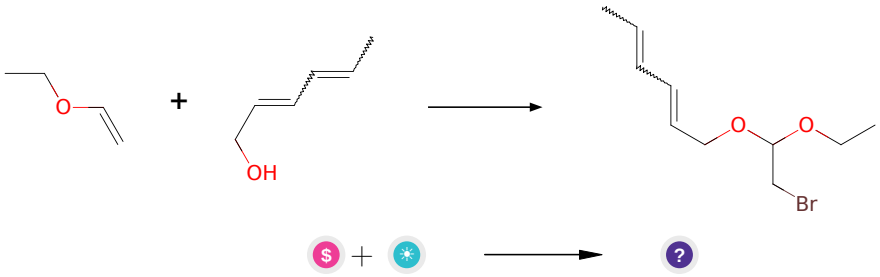


Figure 2: Outline of path 2

2.2.1 Synthesis of haloacetals



Substrates:

1. Ethoxyethylene - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

1. CC=CC=CCOC(CBr)OCC

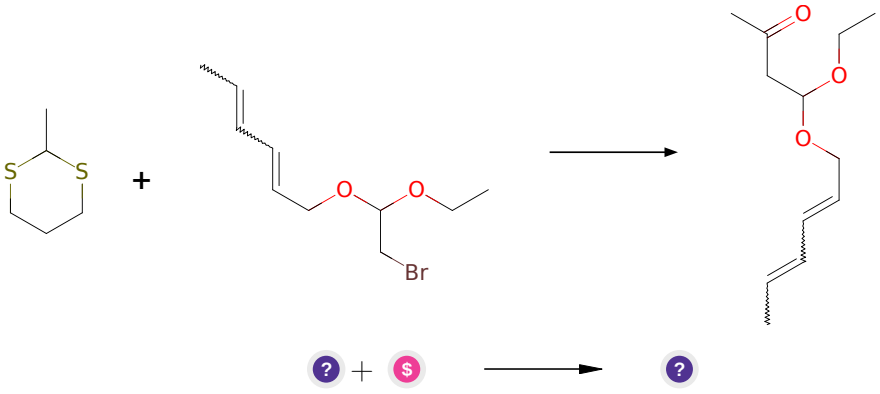
Typical conditions: NIS/NBS.DCM or MeCN

Protections: none

Reference: *10.1021/jo00073a032* and *10.1016/j.tet.2016.08.039* and *10.1055/s-0036-1588440* and *10.1055/s-0037-1611810* and *10.1016/0040-4039(94)02412-5* and *10.1016/S0040-4020(97)00658-3*

Retrosynthesis ID: 31013574

2.2.2 Corey-Seebach



Substrates:

1. CC=CC=CCOC(CBr)OCC

2. 2-Methyl-1,3-dithiane - *available at Sigma-Aldrich*

Products:

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

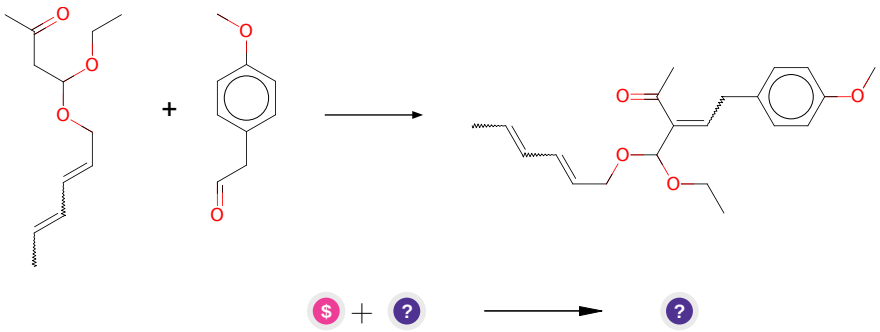
Typical conditions: 1.BuLi.TMEDA.2.TCCA

Protections: none

Reference: *10.1039/P19860000183* AND *10.1016/S0040-4020(01)85646-5* AND *10.1039/c5ob00638d* deprotection: *10.1016/j.tetlet.2006.06.131*

Retrosynthesis ID: 15272

2.2.3 Aldol Condensation



Substrates:

1. 2-(4-Methoxyphenyl)acetaldehyde - *available at Sigma-Aldrich*
2. CC=CC=CCOC(CC(C)=O)OCC

Products:

1. CC=CC=CCOC(OCC)C(=CCc1ccc(OC)cc1)C(C)=O

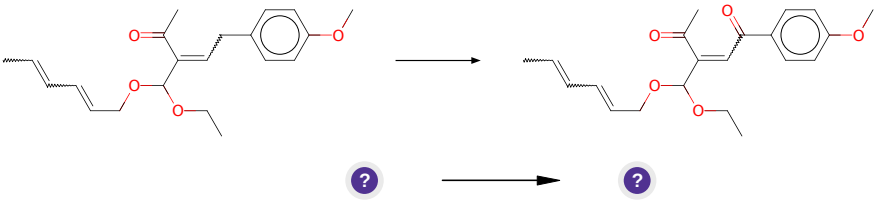
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.2.4 Allylic Oxidation of Alkenes



Substrates:

1. CC=CC=CCOC(OCC)C(=CCc1ccc(OC)cc1)C(C)=O

Products:

1. CC=CC=CCOC(OCC)C(=CC(=O)c1ccc(OC)cc1)C(C)=O

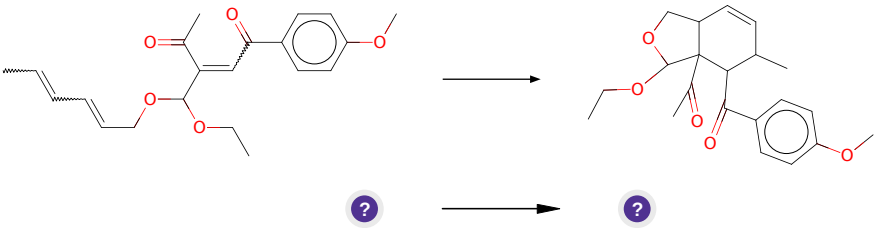
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.2.5 Diels-Alder



Substrates:

1. CC=CC=CCOC(OCC)C(=CC(=O)c1ccc(OC)cc1)C(C)=O

Products:

1. CCOC1OCC2C=CC(C)C(C(=O)c3ccc(OC)cc3)C21C(C)=O

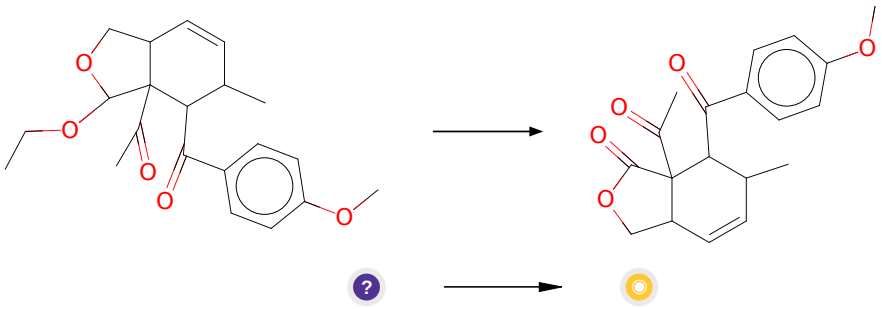
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.2.6 Oxidation of acetals to lactones



Substrates:

1. CCOC1OCC2C=CC(C)C(C(=O)c3ccc(OC)cc3)C21C(C)=O

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)cc1

Typical conditions: CrO3.H2SO4.acetone.H2O.rt

Protections: none

Reference: DOI: *10.1021/ja108642s*

Retrosynthesis ID: 14516

2.3 Path 3

Score: `154.86`

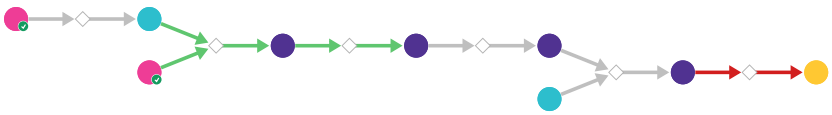
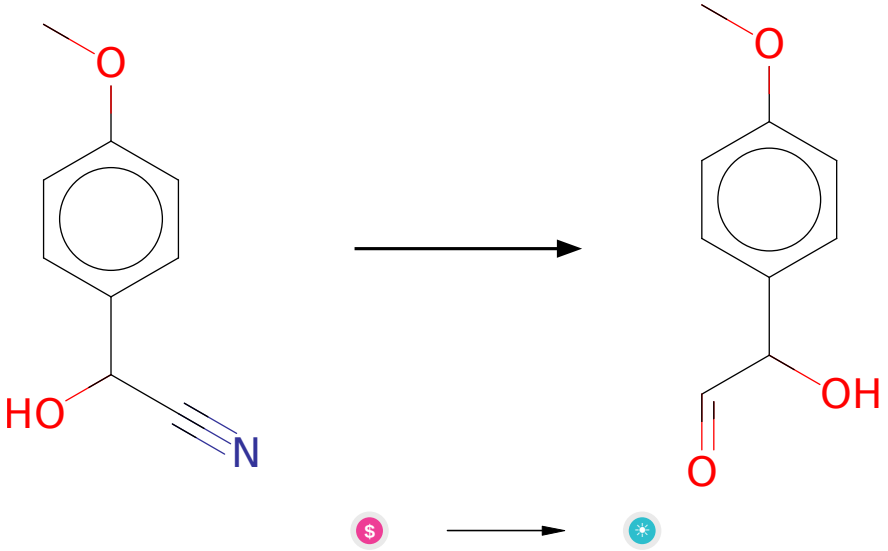


Figure 3: Outline of path 3

2.3.1 Reduction of nitriles to aldehydes



Substrates:

1. 2-hydroxy-2-(4-methoxyphenyl)acetonitrile - *available at Sigma-Aldrich*

Products:

1. p-methoxymandelaldehyd

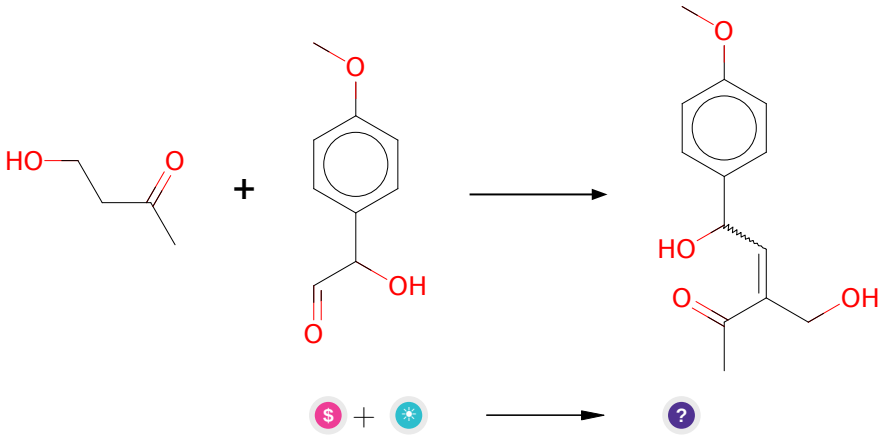
Typical conditions: DIBALH.DCM

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

2.3.2 Aldol Condensation



Substrates:

1. 4-Hydroxy-2-butanone - *available at Sigma-Aldrich*
2. p-methoxymandelaldehyd

Products:

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

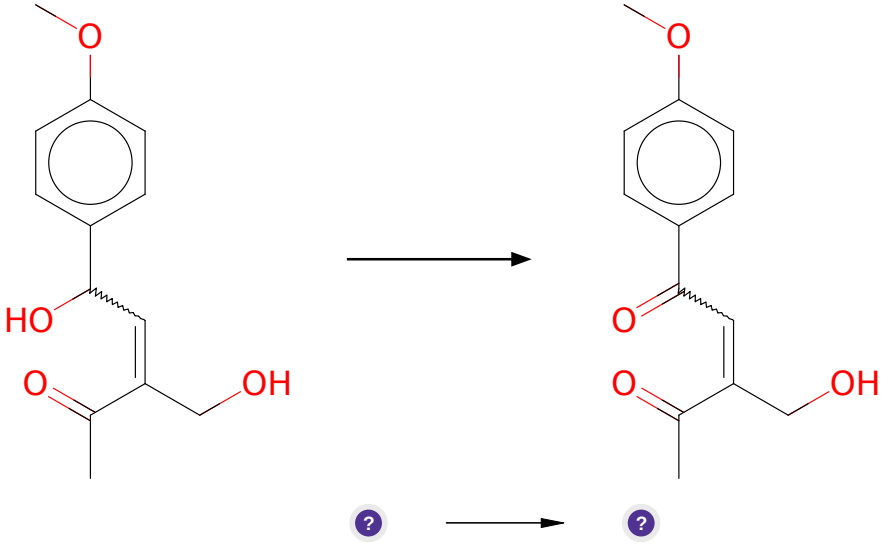
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.3.3 Oxidation of allylic alcohols



Substrates:

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

Products:

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

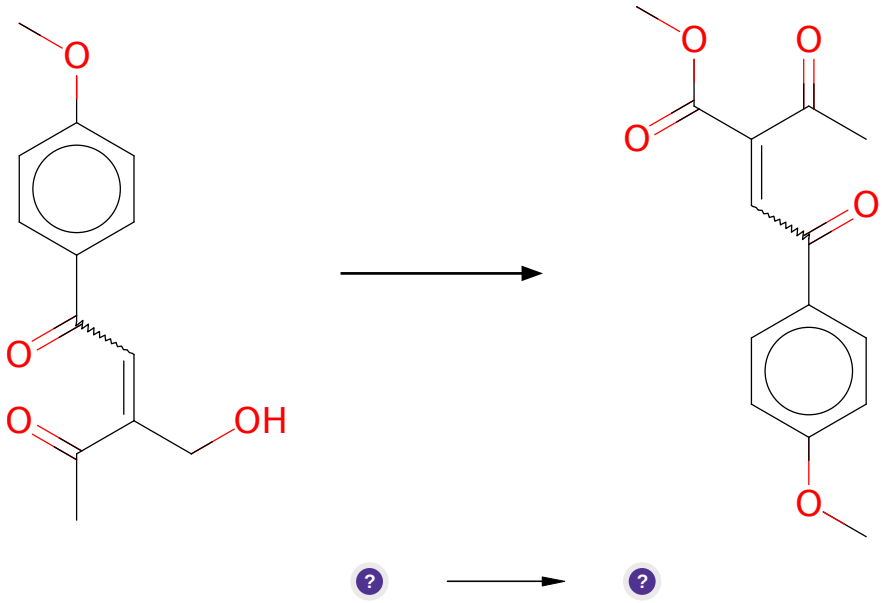
Typical conditions: MnO2.DCM

Protections: none

Reference: *10.1016/j.ejmech.2017.01.036* p. 196, 199 and *10.1016/j.ejmech.2011.03.002* p. 2218, SI p. S-4

Retrosynthesis ID: 9910003

2.3.4 Tandem oxidation-esterification



Substrates:

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

Products:

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

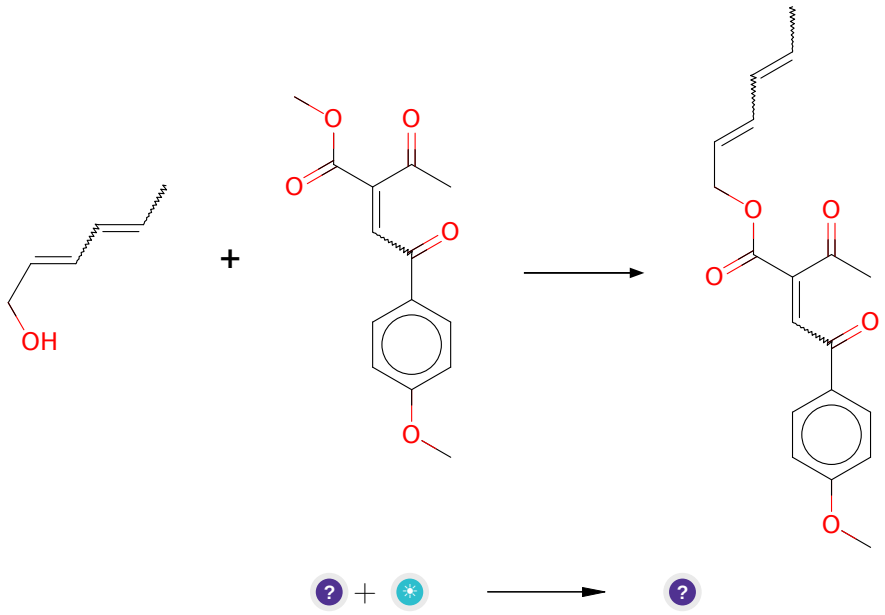
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

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

2.3.5 Acid catalyzed transesterification



Substrates:

1. COC(=O)C(=CC(=O)c1ccc(OC)cc1)C(C)=O
2. sorbic alcohol

Products:

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

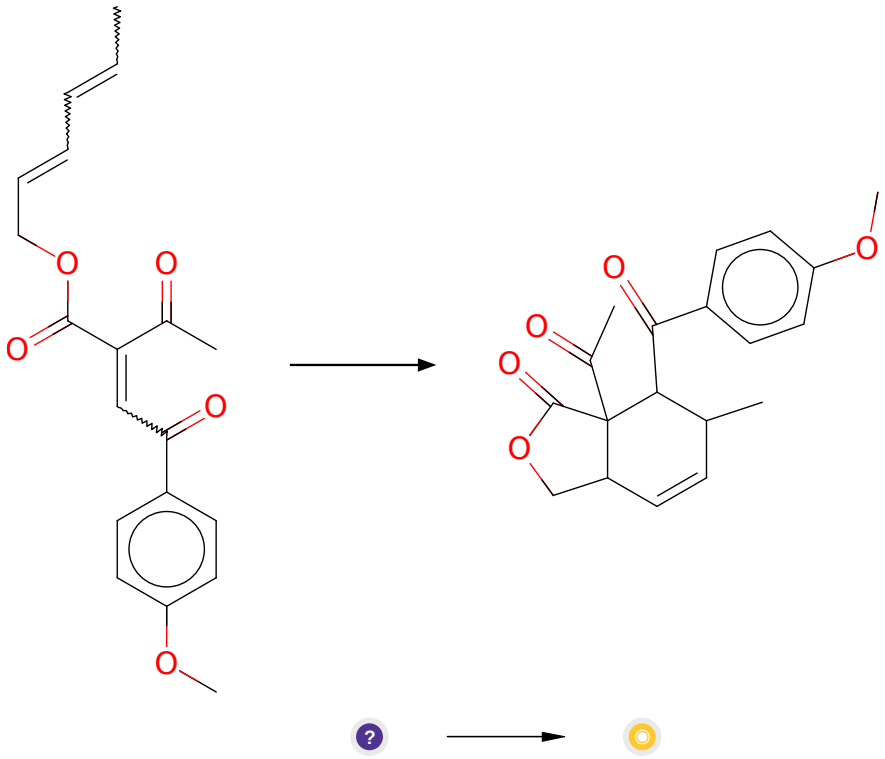
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.3.6 Diels-Alder



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(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: 156.72

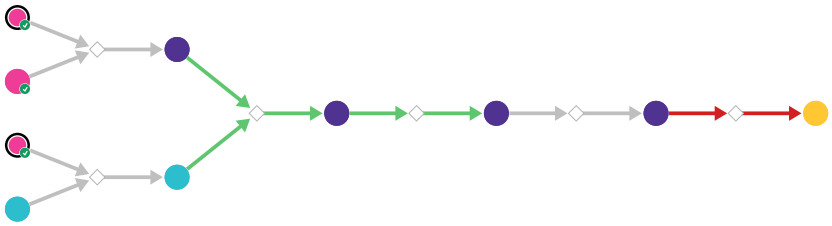
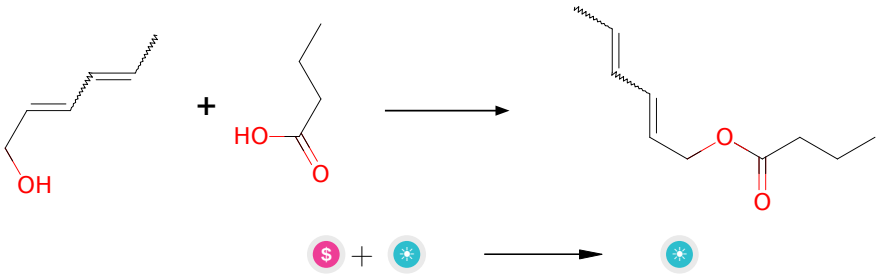


Figure 4: Outline of path 4

2.4.1 Steglich Esterification



Substrates:

1. Na - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

1. butyric acid hexa-2,4-dienyl ester

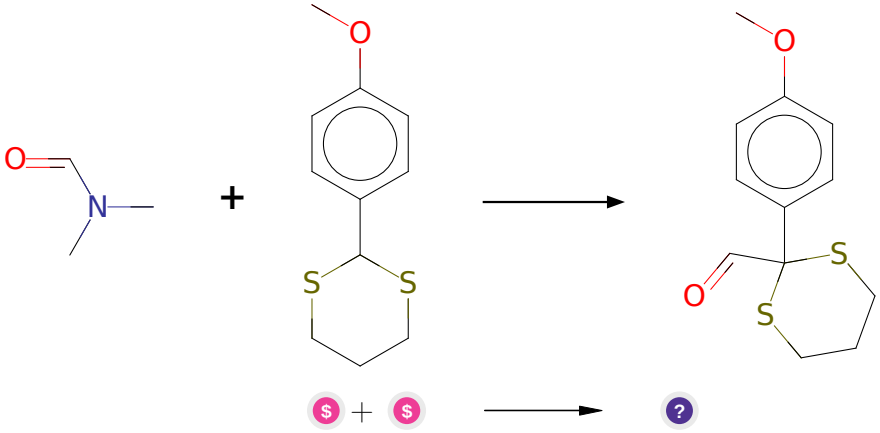
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.4.2 Formylation of dithianes



Substrates:

1. Dimethylformamide - *available at Sigma-Aldrich*
2. 2-(4-methoxyphenyl)-1,3-dithiane - *available at Sigma-Aldrich*

Products:

1. COc1ccc(C2(C=O)SCCCS2)cc1

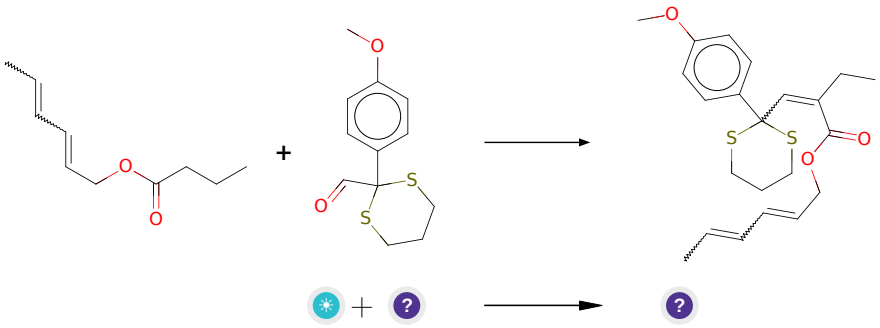
Typical conditions: LDA.DMF

Protections: none

Reference: *10.1055/s-2006-950359* and *10.3987/COM-12-S(N)85* and *10.1021/acs.orglett.5b02662*

Retrosynthesis ID: 34225

2.4.3 Condensation of esters with aldehydes/ketones



Substrates:

1. butyric acid hexa-2,4-dienyl ester
2. COc1ccc(C2(C=O)SCCCS2)cc1

Products:

1. CC=CC=CCOC(=O)C(=CC1(c2ccc(OC)cc2)SCCCS1)CC

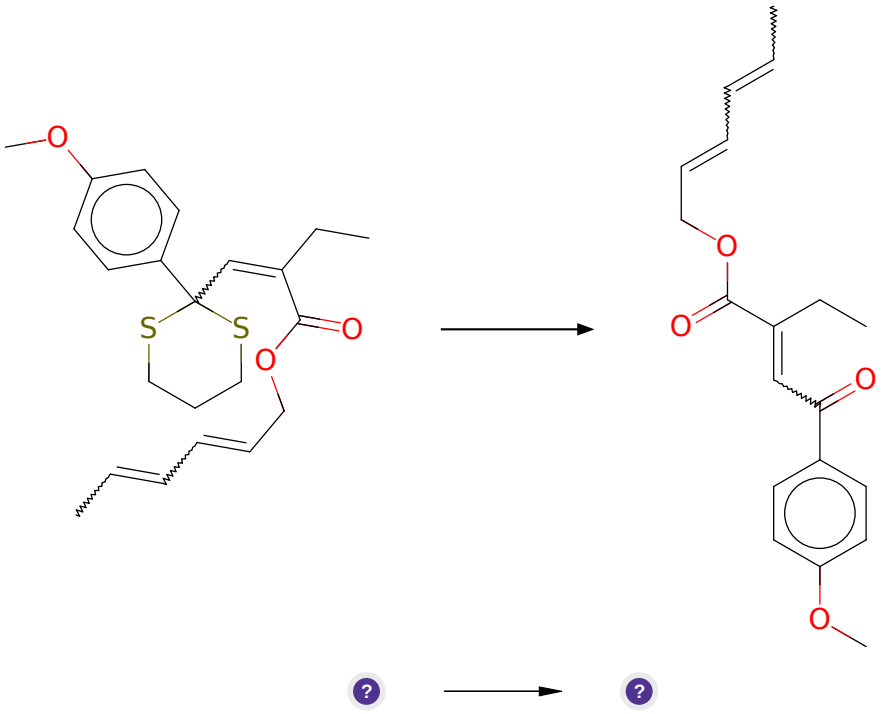
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.4.4 Synthesis of ketones from dithianes



Substrates:

1. CC=CC=CCOC(=O)C(=CC1(c2ccc(OC)cc2)SCCCS1)CC

Products:

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

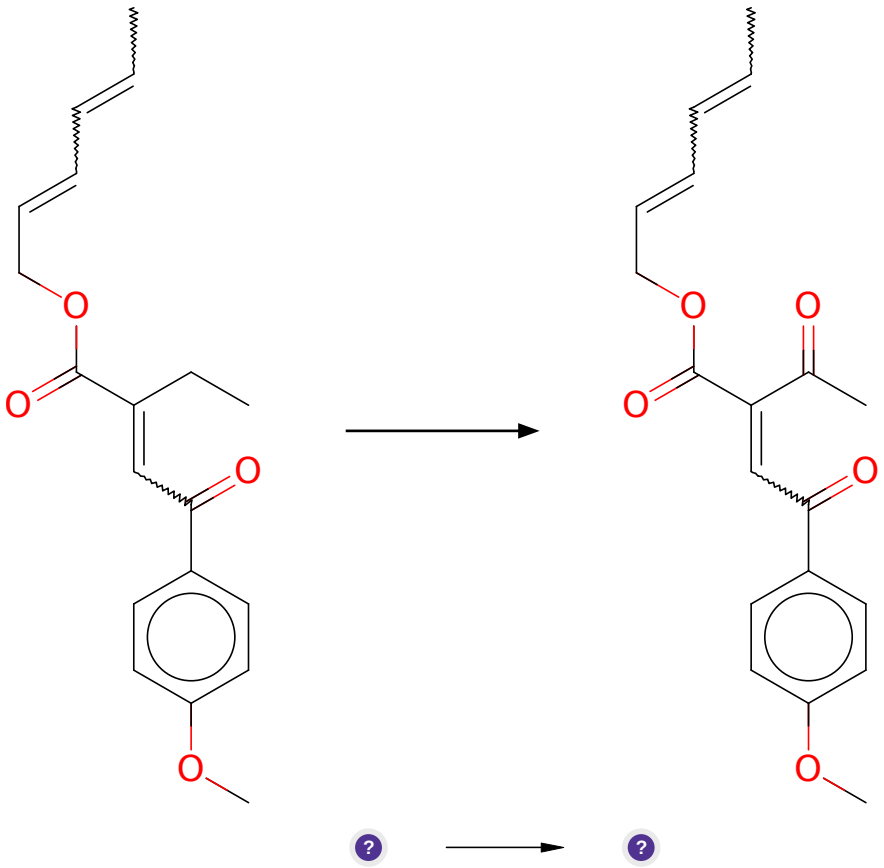
Typical conditions: MeI.CaCO3

Protections: none

Reference: *10.1016/j.tet.2013.09.075* and *10.1021/jo00007a015* and *10.1021/jo0610412* and *10.1021/ol901024t* and *10.1021/ol500553x* and *10.1021/jo0626459*

Retrosynthesis ID: 31724

2.4.5 Allylic Oxidation of Alkenes



Substrates:

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

Products:

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

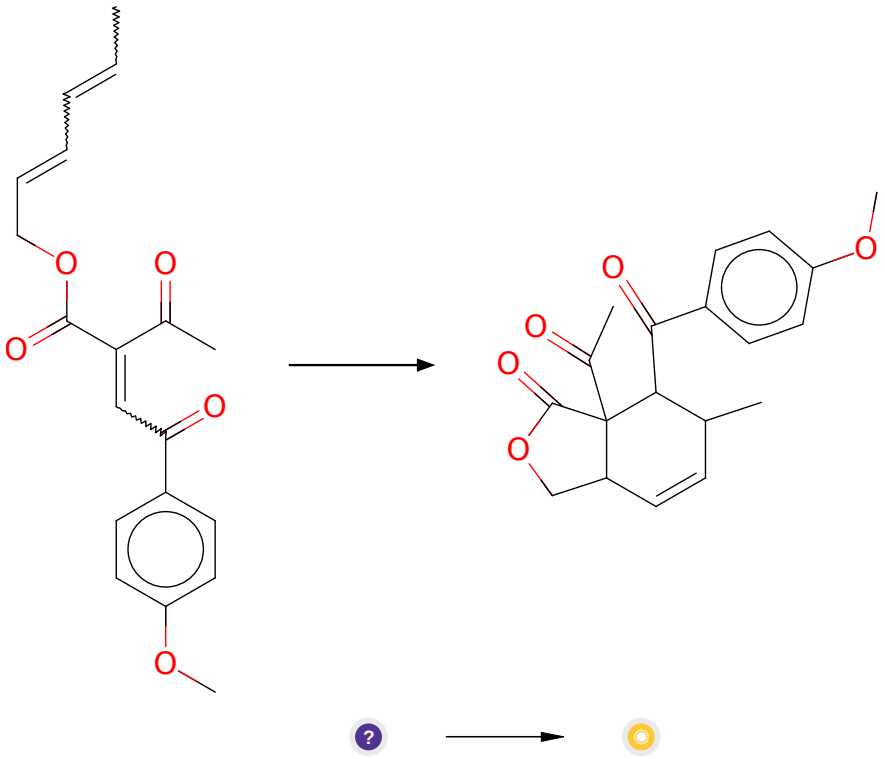
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.4.6 Diels-Alder



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(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: 168.93

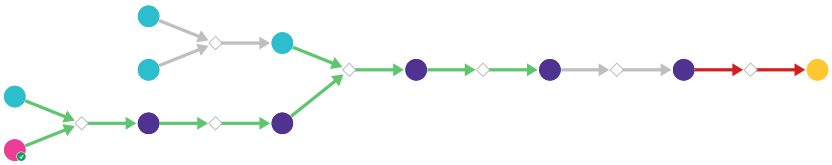
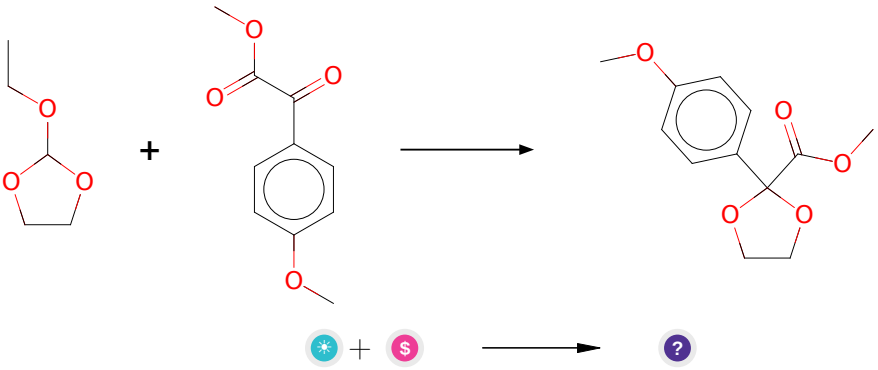


Figure 5: Outline of path 5

2.5.1 Acetalization of Carbonyl Compounds Catalyzed by Indium Triflate



Substrates:

1. 2-ethoxy-[1,3]dioxolane
2. 4-Methoxy-oxo-benzeneacetic acid Methyl ester - *available at Sigma-Aldrich*

Products:

1. COC(=O)C1(c2ccc(OC)cc2)OCCO1

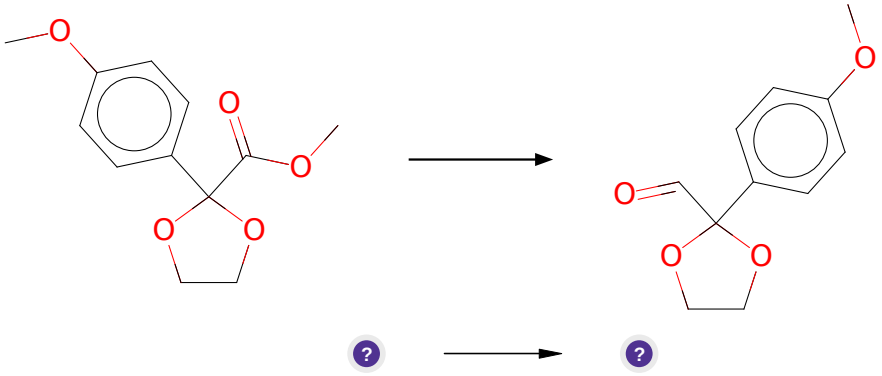
Typical conditions: indium triflate. MeOH. CH2Cl2. 20C

Protections: none

Reference: DOI: *10.1016/j.tetlet.2006.10.111* or DOI: *10.1002/cber.19620950803*

Retrosynthesis ID: 9318

2.5.2 Aldehyde Formation



Substrates:

1. COC(=O)C1(c2ccc(OC)cc2)OCCO1

Products:

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

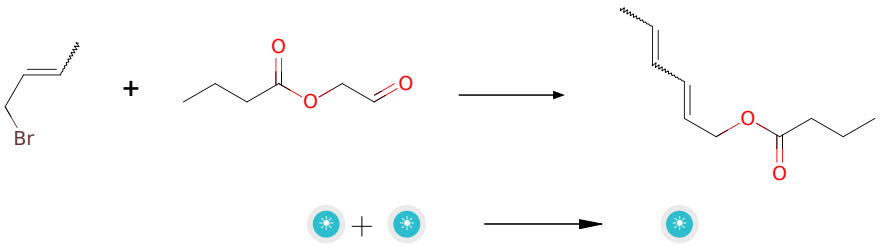
Typical conditions: DIBAL.solvent e.g. DCM

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

2.5.3 Wittig olefination



Substrates:

1. butyryloxy-acetaldehyde
2. crotyl bromide

Products:

1. butyric acid hexa-2,4-dienyl ester

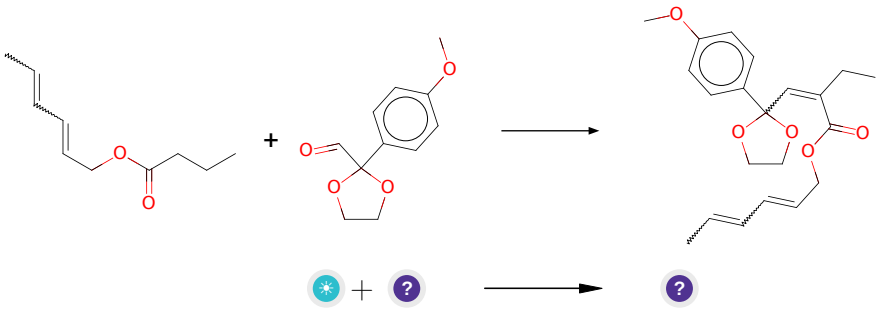
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1021/ja0015287* and *10.1021/ja404673s* and *10.1021/ol901979x*

Retrosynthesis ID: 9545

2.5.4 Condensation of esters with aldehydes/ketones



Substrates:

1. butyric acid hexa-2,4-dienyl ester
2. COc1ccc(C2(C=O)OCCO2)cc1

Products:

1. CC=CC=CCOC(=O)C(=CC1(c2ccc(OC)cc2)OCCO1)CC

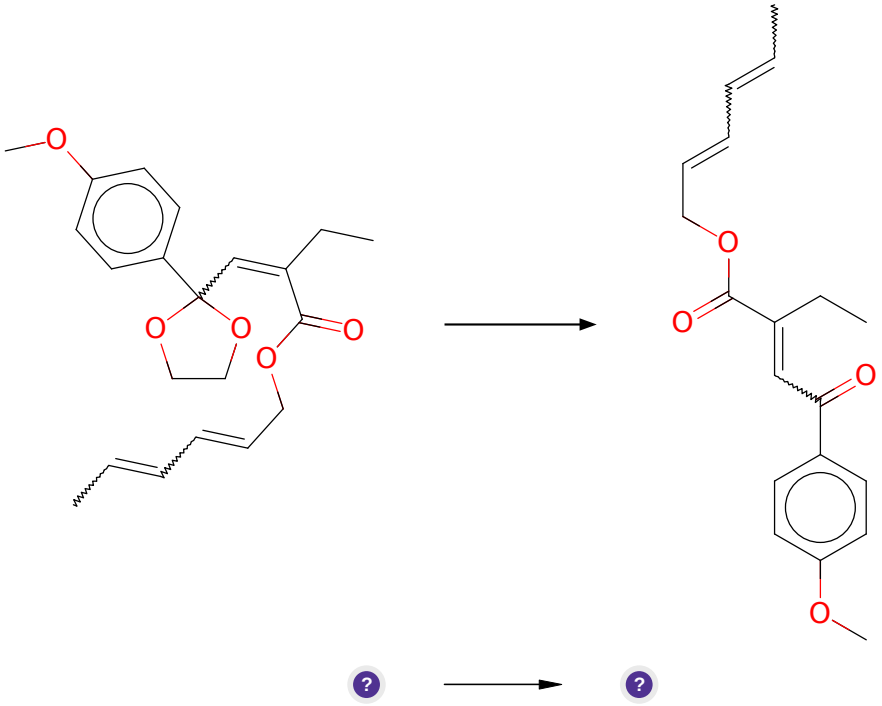
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.5.5 Hydrolysis of ketals



Substrates:

1. CC=CC=CCOC(=O)C(=CC1(c2ccc(OC)cc2)OCCO1)CC

Products:

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

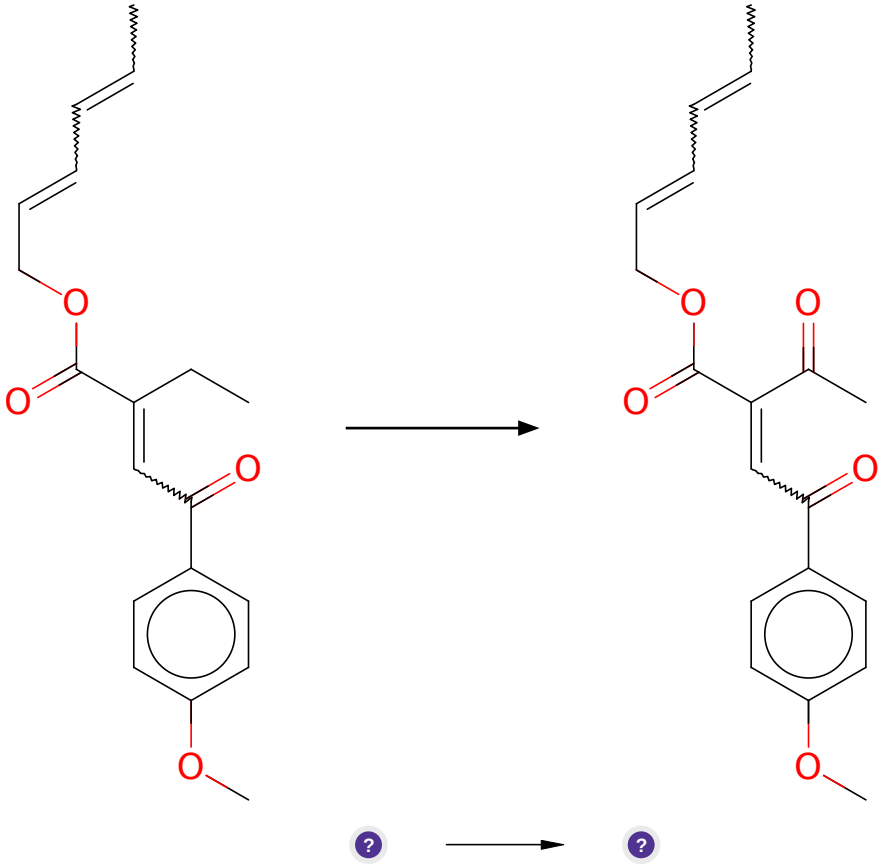
Typical conditions: H2O.HCl

Protections: none

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

Retrosynthesis ID: 31013139

2.5.6 Allylic Oxidation of Alkenes



Substrates:

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

Products:

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

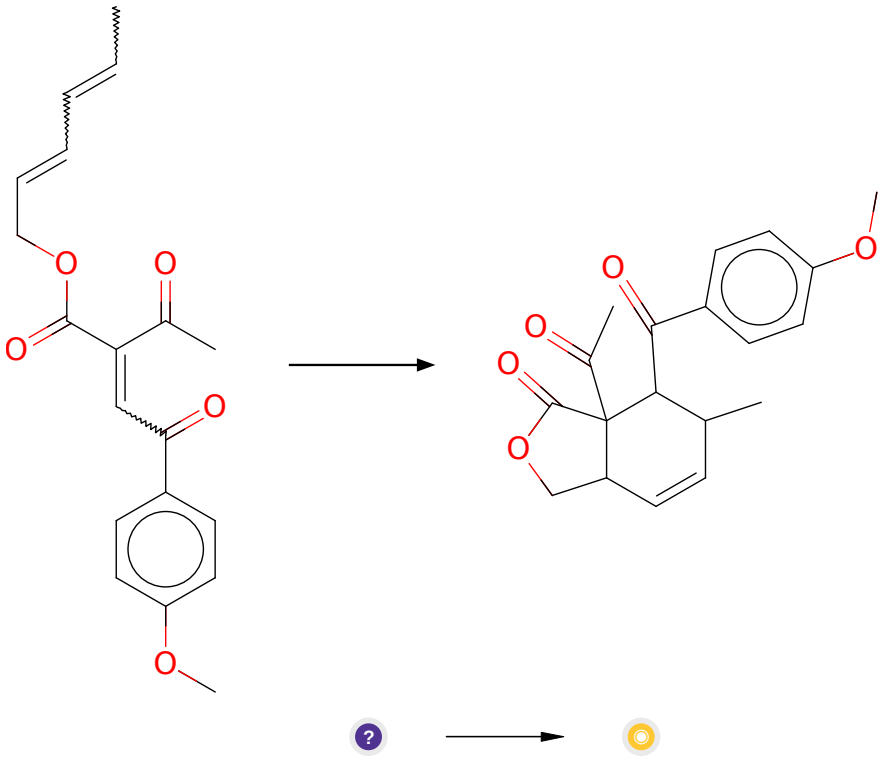
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.5.7 Diels-Alder



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(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