Paths of analysis*

L8_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

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

2.1 Path 1

Score: `100.08`

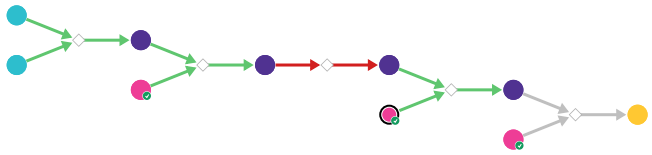
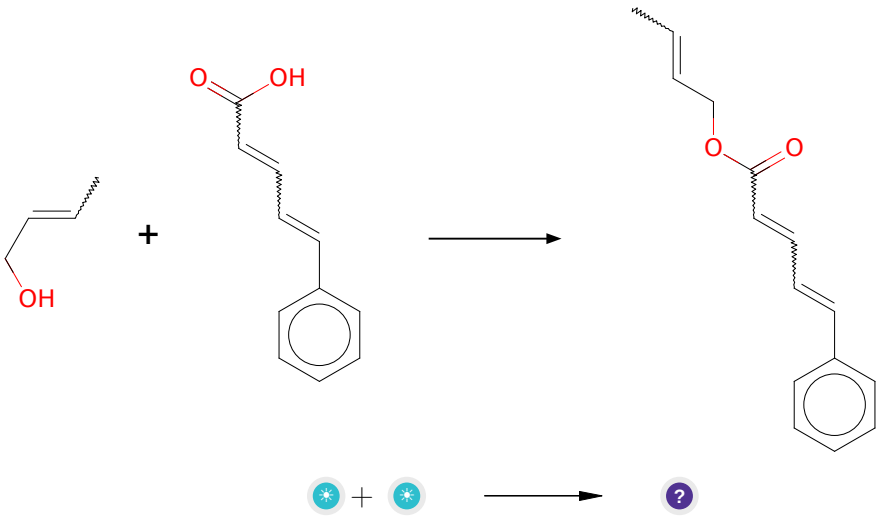


Figure 1: Outline of path 1

2.1.1 Steglich Esterification



Substrates:

1. crotonalkohol

2. 5-phenyl-penta-2,4-dienoic acid

Products:

1. CC=CCOC(=O)C=CC=Cc1ccccc1

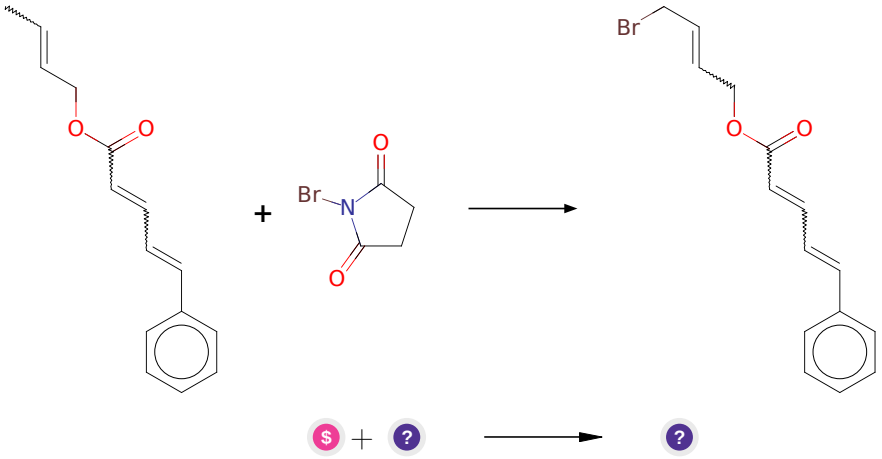
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.1.2 Wohl-Ziegler Bromination



Substrates:

1. N-Bromosuccinimide - *available at Sigma-Aldrich*
2. CC=CCOC(=O)C=CC=Cc1ccccc1

Products:

1. O=C(C=CC=Cc1ccccc1)OCC=CCBr

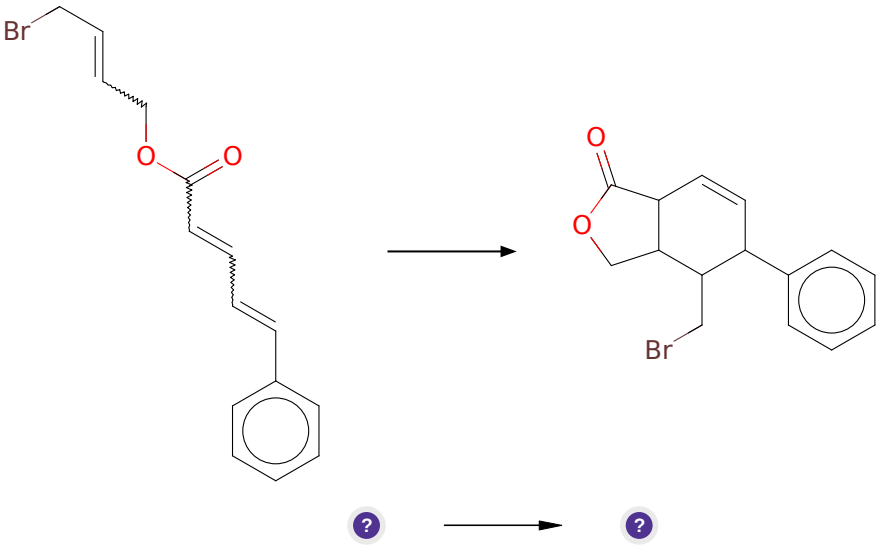
Typical conditions: NBS.AIBN or (BzO)2 or heat

Protections: none

Reference: *10.1016/j.steroids.2018.10.005* (Scheme 1) and *10.1016/j.bmc.2010.06.075* (Scheme 2) and *10.1021/acs.orglett.9b03865* (p. SI 6)

Retrosynthesis ID: 245554

2.1.3 Diels-Alder



Substrates:

1. O=C(C=CC=Cc1ccccc1)OCC=CCBr

Products:

1. O=C1OCC2C1C=CC(c1ccccc1)C2CBr

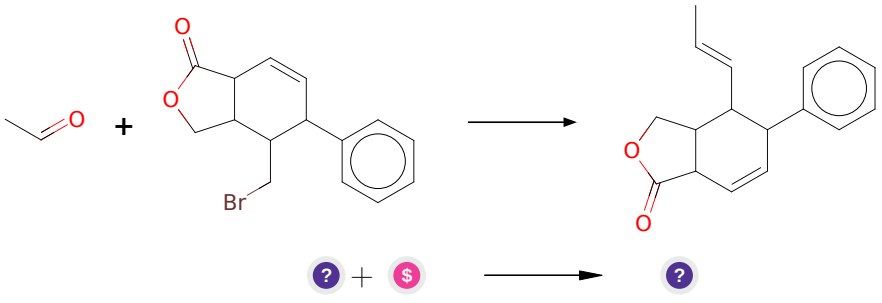
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.1.4 Wittig-Schlosser olefination



Substrates:

1. O=C1OCC2C1C=CC(c1ccccc1)C2CBr
2. Ethanal - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1C(c2ccccc2)C=CC2C(=O)OCC21

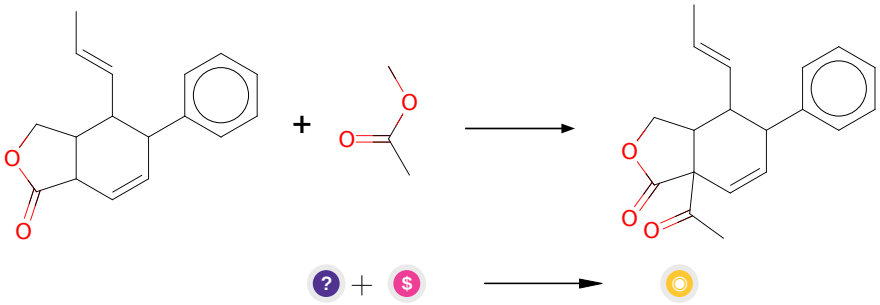
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde.3.base

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

2.1.5 Claisen Condensation



Substrates:

1. C/C=C/C1C(c2ccccc2)C=CC2C(=O)OCC21
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.2 Path 2

Score: 105.08

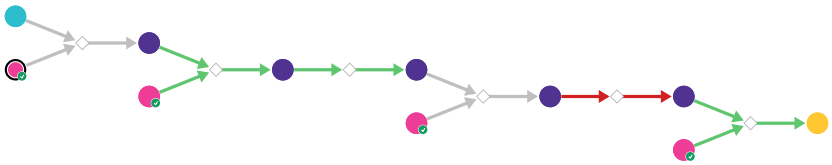
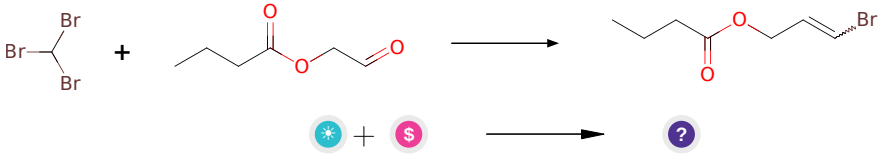


Figure 2: Outline of path 2

2.2.1 Takai olefination



Substrates:

1. butyryloxy-acetaldehyde
2. Bromoform - *available at Sigma-Aldrich*

Products:

1. CCCC(=O)OCC=CBr

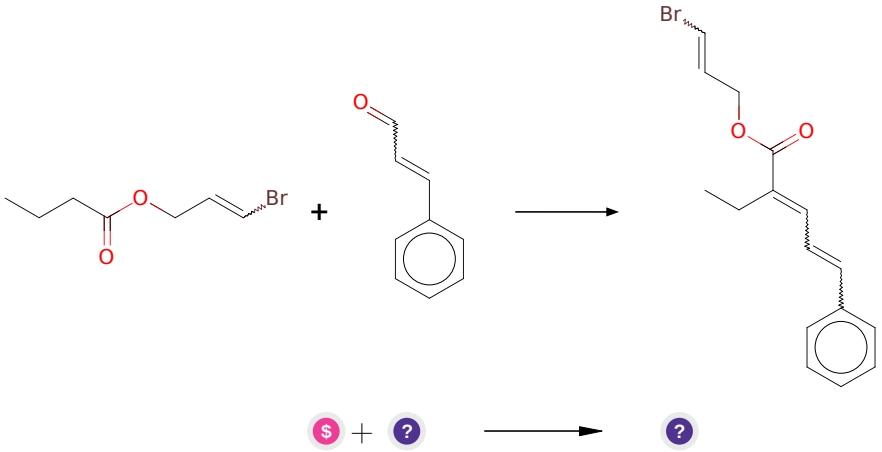
Typical conditions: CrCl2.THF

Protections: none

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

Retrosynthesis ID: 11463

2.2.2 Condensation of esters with aldehydes/ketones



Substrates:

1. zimtaldehyd - *available at Sigma-Aldrich*
2. CCCC(=O)OCC=CBr

Products:

1. CCC(=CC=Cc1ccccc1)C(=O)OCC=CBr

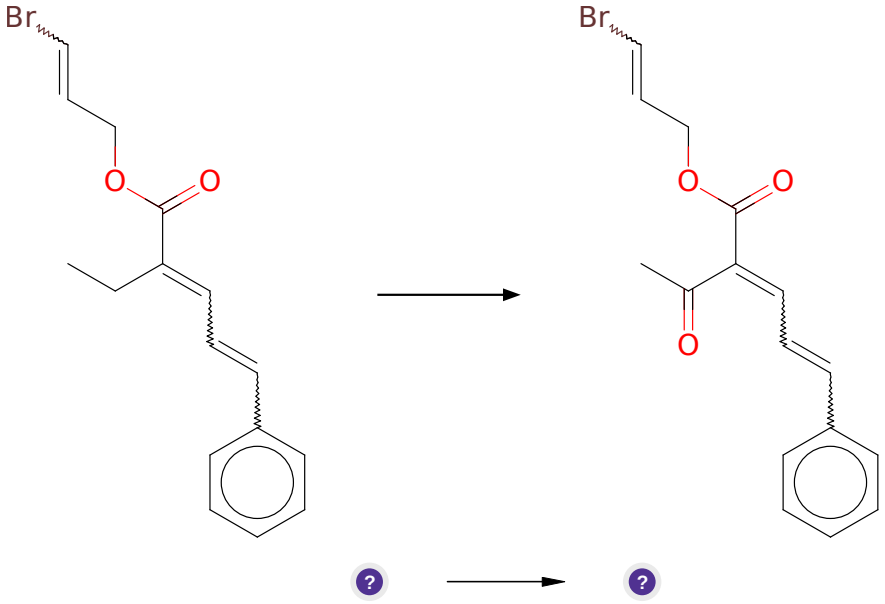
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.2.3 Allylic Oxidation of Alkenes



Substrates:

1. CCC(=CC=Cc1ccccc1)C(=O)OCC=CBr

Products:

1. CC(=O)C(=CC=Cc1ccccc1)C(=O)OCC=CBr

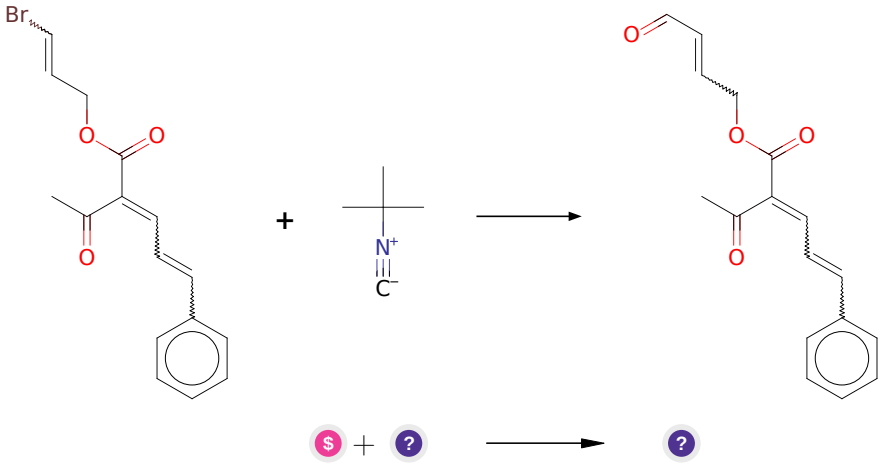
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

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 Pd-catalyzed formylation of vinyl halides



Substrates:

1. tert-Butyl isocyanide - *available at Sigma-Aldrich*
2. CC(=O)C(=CC=Cc1ccccc1)C(=O)OCC=CBr

Products:

1. CC(=O)C(=CC=Cc1ccccc1)C(=O)OCC=CC=O

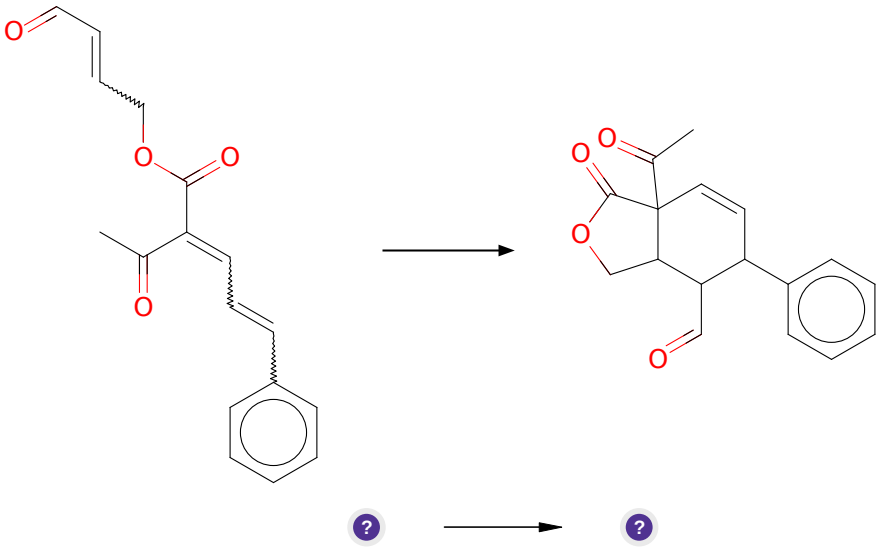
Typical conditions: Pd(OAc)2.JohnPhos.Na2CO3.H2O.Et3SiH.DMF.65C

Protections: none

Reference: DOI: *10.1021/ol5014262*

Retrosynthesis ID: 3104

2.2.5 Diels-Alder



Substrates:

1. CC(=O)C(=CC=Cc1ccccc1)C(=O)OCC=CC=O

Products:

1. CC(=O)C12C=CC(c3ccccc3)C(C=O)C1COC2=O

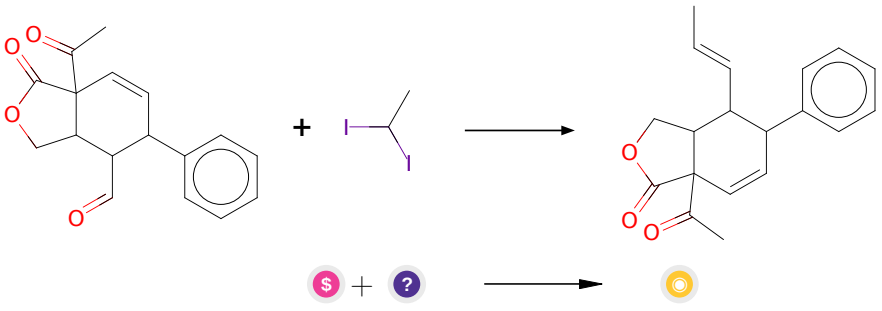
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.2.6 Takai olefination



Substrates:

1. 1,1-Diiodoethane - *available at Sigma-Aldrich*
2. CC(=O)C12C=CC(c3ccccc3)C(C=O)C1COC2=O

Products:

1. C/C=C/C1C(c2ccccc2)C=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

2.3 Path 3

Score: 120.37

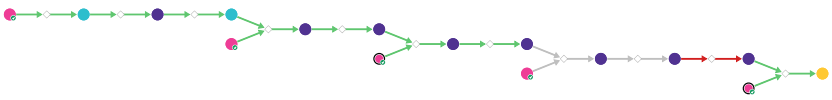
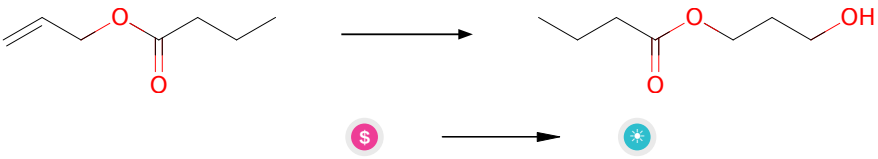


Figure 3: Outline of path 3

2.3.1 Brown Hydroboration of Alkenes



Substrates:

1. Allyl butyrate - *available at Sigma-Aldrich*

Products:

1. butyric acid 3-hydroxy-propyl ester

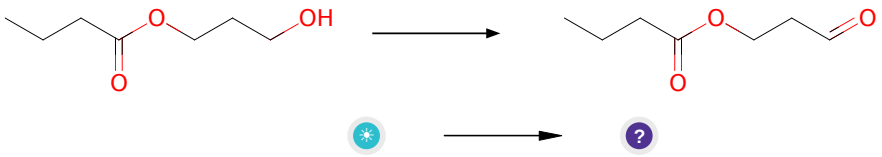
Typical conditions: B2H6.H2O2.THF.NaOH

Protections: none

Reference: *10.1002/9780470638859.conrr118*

Retrosynthesis ID: 4772

2.3.2 Oxidation of primary alcohols with DMP



Substrates:

1. butyric acid 3-hydroxy-propyl ester

Products:

1. CCCC(=O)OCCC=O

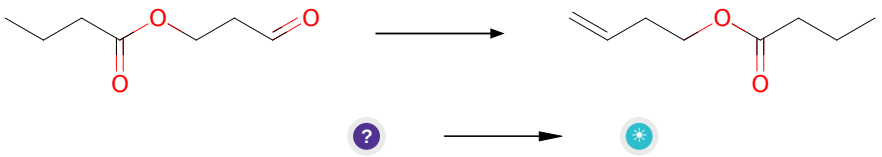
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.3.3 Tebbe Olefination



Substrates:

1. CCCC(=O)OCCC=O

Products:

1. 3-butenyl butyrate

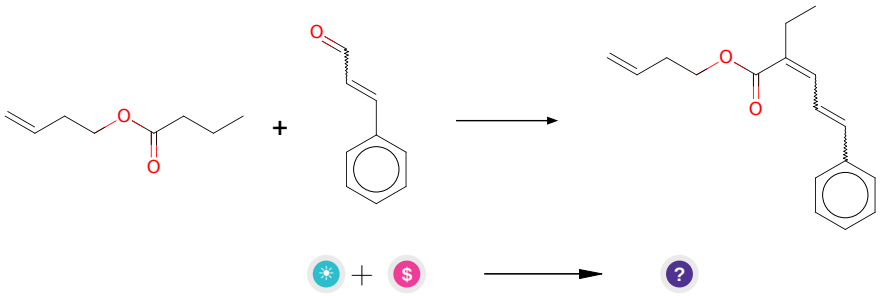
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Reference: *10.1016/j.tet.2007.03.015* and *10.1002/9780470638859.conrr617*

Retrosynthesis ID: 11714

2.3.4 Condensation of esters with aldehydes/ketones



Substrates:

1. 3-butenyl butyrate
2. zimtaldehyd - *available at Sigma-Aldrich*

Products:

1. C=CCCOC(=O)C(=CC=Cc1ccccc1)CC

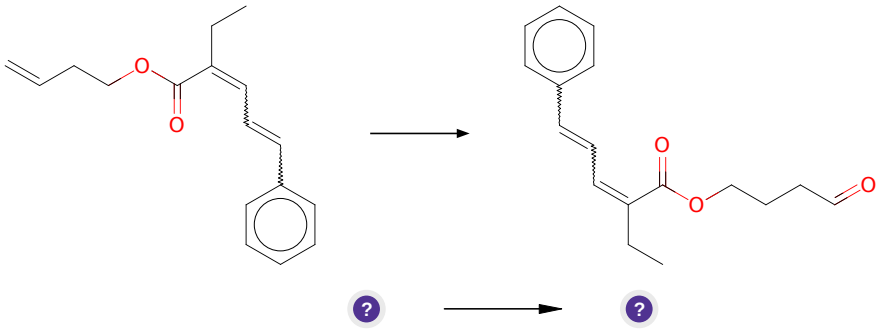
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.3.5 Tsuji-Wacker Oxidation of alkenes



Substrates:

1. C=CCCOC(=O)C(=CC=Cc1ccccc1)CC

Products:

1. CCC(=CC=Cc1ccccc1)C(=O)OCCCC=O

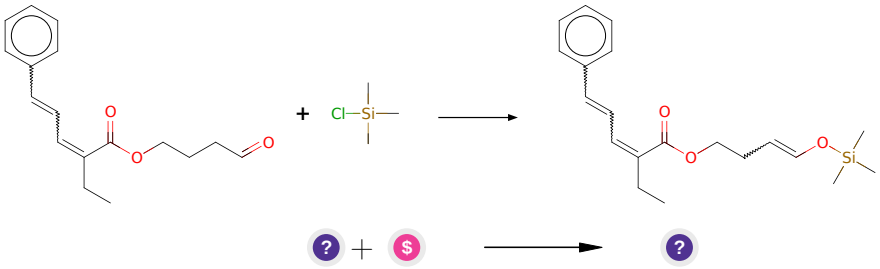
Typical conditions: PdCl2(PhCn)2.CuCl2.AgNO2.O2.tBuOH.MeNO2.rt

Protections: none

Reference: *10.1021/jacs.6b08788* and *10.1021/ja411749k*and *10.1002/anie.201306756* and *10.1016/S0040-4039(03)01709-X* and *10.1021/acs.orglett.6b01165*

Retrosynthesis ID: 28273

2.3.6 Enol esters and ethers synthesis



Substrates:

1. CCC(=CC=Cc1ccccc1)C(=O)OCCCC=O
2. TMSCl - *available at Sigma-Aldrich*

Products:

1. CCC(=CC=Cc1ccccc1)C(=O)OCCC=CO[Si](C)(C)C

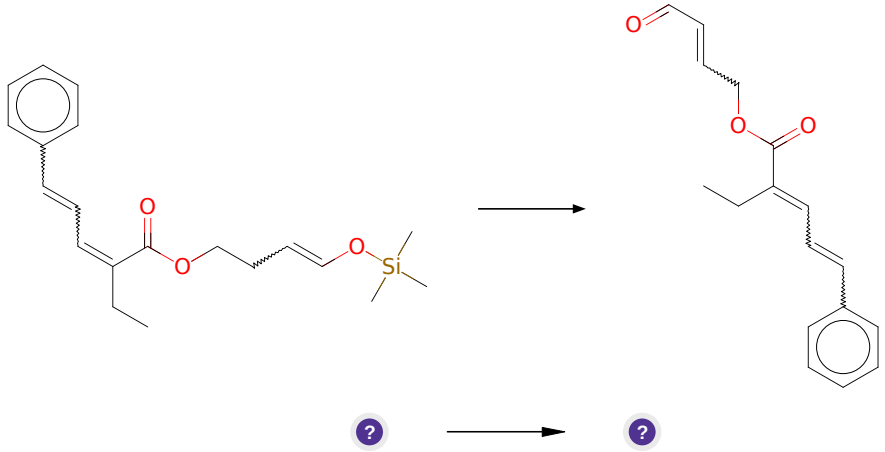
Typical conditions: 1.LDA.2.Electrophile

Protections: none

Reference: US2467095A AND WO2014169833a1 AND *10.1016/j.steroids.2011.03.014* AND *10.1021/ol200875m* (SI) AND *10.1021/ja00531a034*

Retrosynthesis ID: 7797

2.3.7 Dehydrogenation of silyl enol ethers



Substrates:

1. CCC(=CC=Cc1ccccc1)C(=O)OCCC=CO[Si](C)(C)C

Products:

1. CCC(=CC=Cc1ccccc1)C(=O)OCC=CC=O

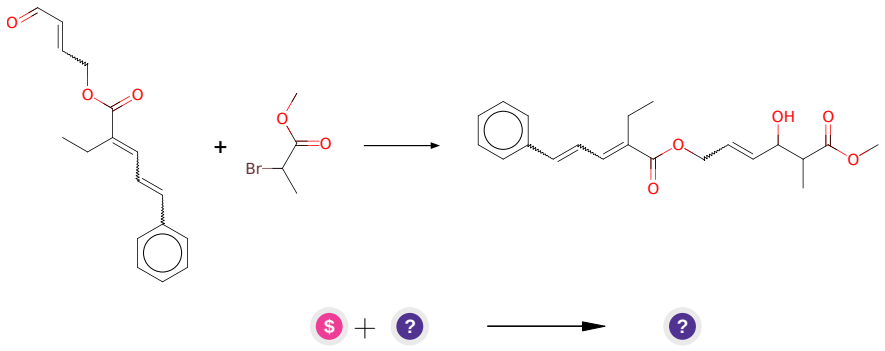
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

Protections: none

Reference: *10.1271/bbb.60.405* and *10.1039/C3CC46778C* and US2015284405 p.40 and *10.1016/S0040-4039(01)81518-5* and US2010204477 p. 15-16 and *10.1016/0040-4039(95)00694-8* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999877

2.3.8 Reformatsky Reaction



Substrates:

1. Methyl 2-bromopropionate - *available at Sigma-Aldrich*
2. CCC(=CC=Cc1ccccc1)C(=O)OCC=CC=O

Products:

1. CCC(=CC=Cc1ccccc1)C(=O)OCC=CC(O)C(C)C(=O)OC

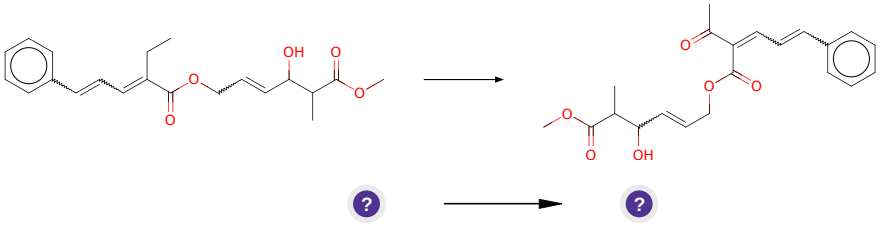
Typical conditions: Me2Zn.B(OMe)3.toluene.Et2O

Protections: none

Reference: *10.1021/jo200774e* p. 6373 and *10.1021/jo00163a019* p. 2522, 2525

Retrosynthesis ID: 11164

2.3.9 Allylic Oxidation of Alkenes



Substrates:

1. CCC(=CC=Cc1ccccc1)C(=O)OCC=CC(O)C(C)C(=O)OC

Products:

1. COC(=O)C(C)C(O)C=CCOC(=O)C(=CC=Cc1ccccc1)C(C)=O

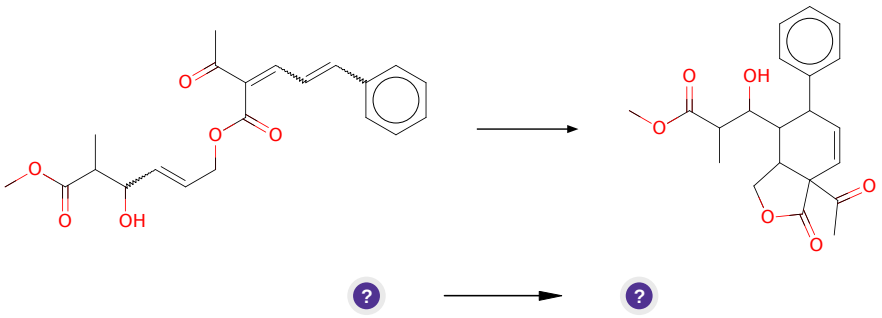
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.3.10 Diels-Alder



Substrates:

1. COC(=O)C(C)C(O)C=CCOC(=O)C(=CC=Cc1ccccc1)C(C)=O

Products:

1. COC(=O)C(C)C(O)C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

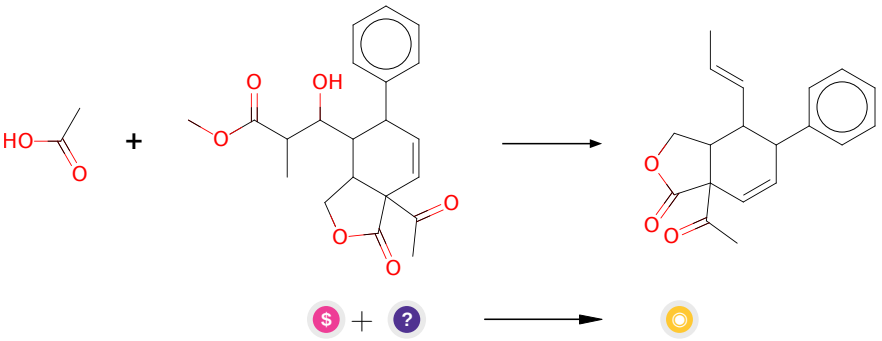
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.3.11 Tandem Krapcho decarboxylation and elimination



Substrates:

1. glacial - *available at Sigma-Aldrich*
2. COC(=O)C(C)C(O)C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

Products:

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

Typical conditions: 1. Ac2O.py 2. DMSO.H2O.NaCl.170C

Protections: none

Reference: DOI: *10.1021/jo00263a005* and *10.1021/jo00386a011* and *10.1021/ol006085q*

Retrosynthesis ID: 9605

2.4 Path 4

Score: 129.38

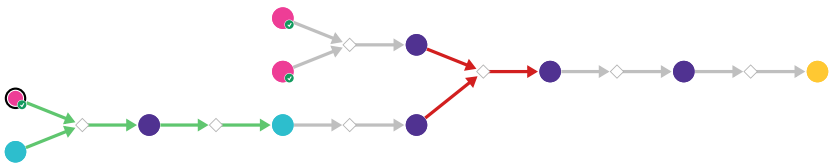
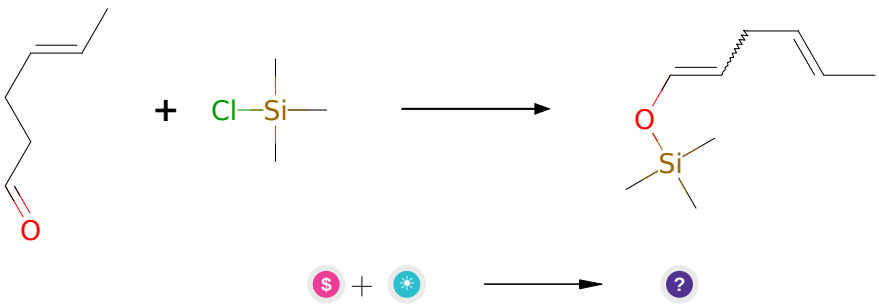


Figure 4: Outline of path 4

2.4.1 Enol esters and ethers synthesis



Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. hex-4t-enal

Products:

1. C/C=C/CC=CO[Si](C)(C)C

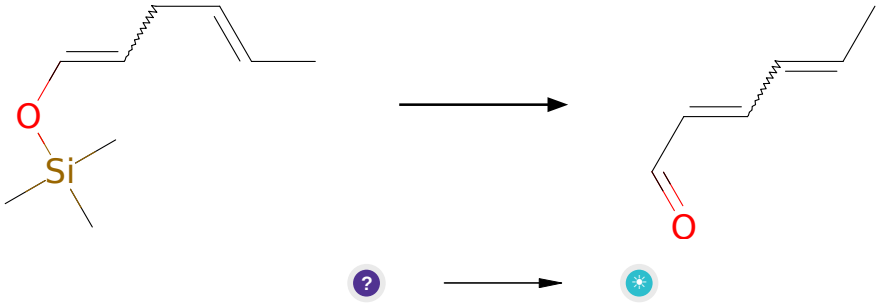
Typical conditions: 1.LDA.2.Electrophile

Protections: none

Reference: US2467095A AND WO2014169833a1 AND *10.1016/j.steroids.2011.03.014* AND *10.1021/ol200875m* (SI) AND *10.1021/ja00531a034*

Retrosynthesis ID: 7797

2.4.2 Dehydrogenation of silyl enol ethers



Substrates:

1. C/C=C/CC=CO[Si](C)(C)C

Products:

1. 2,4-hexadienal

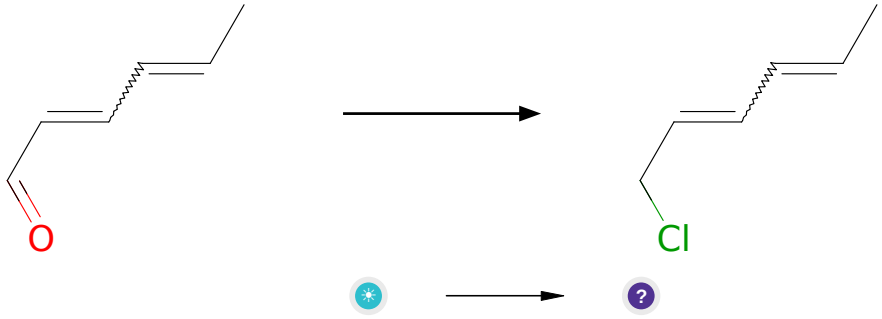
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

Protections: none

Reference: *10.1271/bbb.60.405* and *10.1039/C3CC46778C* and US2015284405 p.40 and *10.1016/S0040-4039(01)81518-5* and US2010204477 p. 15-16 and *10.1016/0040-4039(95)00694-8* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999877

2.4.3 Synthesis of alkyl chlorides from aldehydes



Substrates:

1. 2,4-hexadienal

Products:

1. C/C=C/C=CCCl

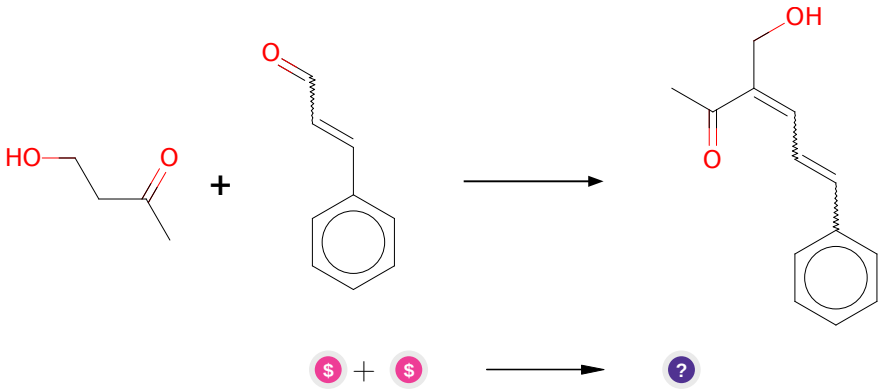
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11621

2.4.4 Aldol Condensation



Substrates:

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

Products:

1. CC(=O)C(=CC=Cc1ccccc1)CO

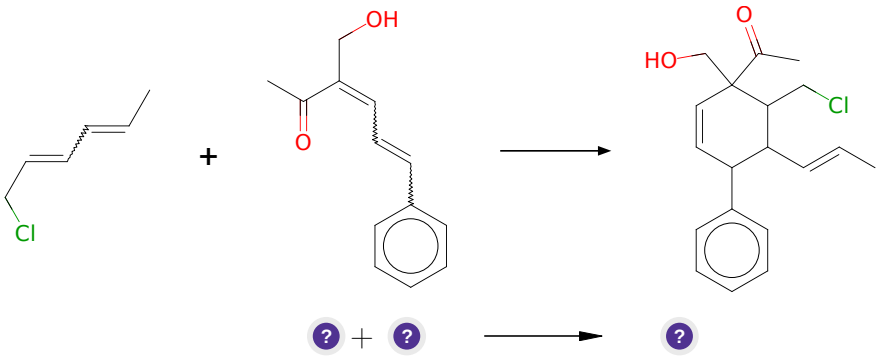
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.4.5 Diels-Alder



Substrates:

1. C/C=C/C=CCCl
2. CC(=O)C(=CC=Cc1ccccc1)CO

Products:

1. C/C=C/C1C(c2ccccc2)C=CC(CO)(C(C)=O)C1CCl

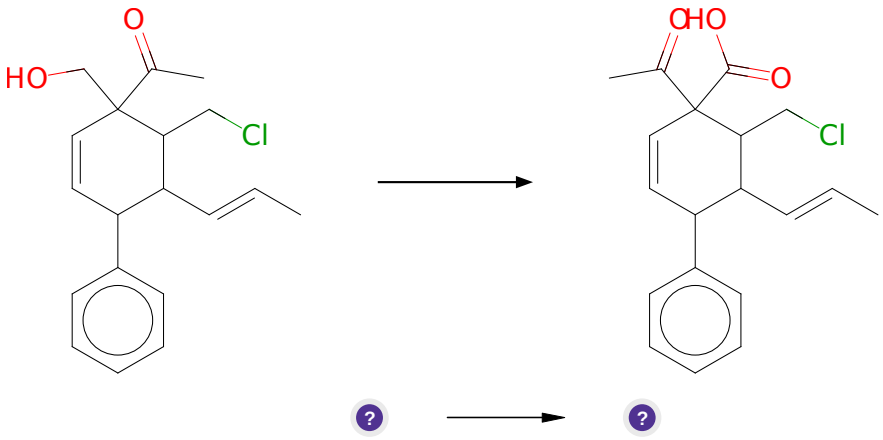
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.4.6 Jones Oxidation



Substrates:

1. C/C=C/C1C(c2ccccc2)C=CC(CO)(C(C)=O)C1CCl

Products:

1. C/C=C/C1C(c2ccccc2)C=CC(C(C)=O)(C(=O)O)C1CCl

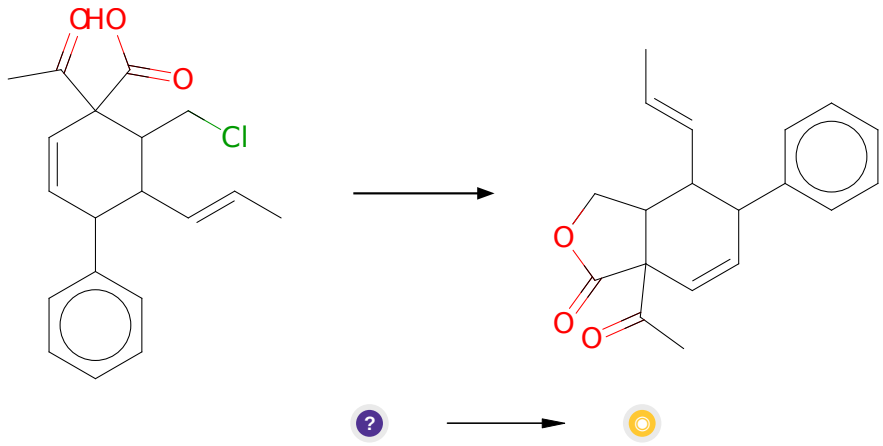
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

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

Retrosynthesis ID: 11160

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



Substrates:

1. C/C=C/C1C(c2ccccc2)C=CC(C(C)=O)(C(=O)O)C1CCl

Products:

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

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: 14684