Paths of analysis*

PG2A

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselecitve reactions, 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: `137.29`

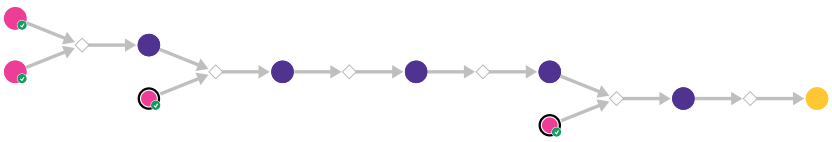
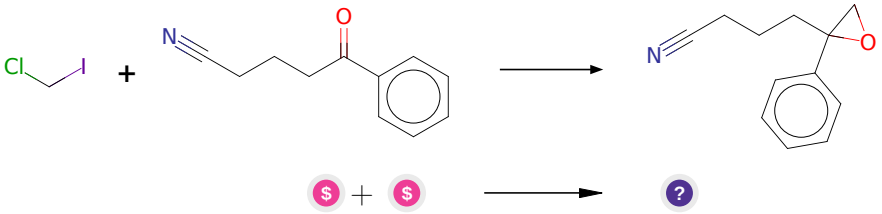


Figure 1: Outline of path 1

2.1.1 Synthesis of epoxides under Simmons-Smith conditions



Substrates:

1. 5-Oxo-5-phenylvaleronitrile - *available at Sigma-Aldrich*
2. Chloroiodomethane - *available at Sigma-Aldrich*

Products:

1. N#CCCCC1(c2ccccc2)CO1

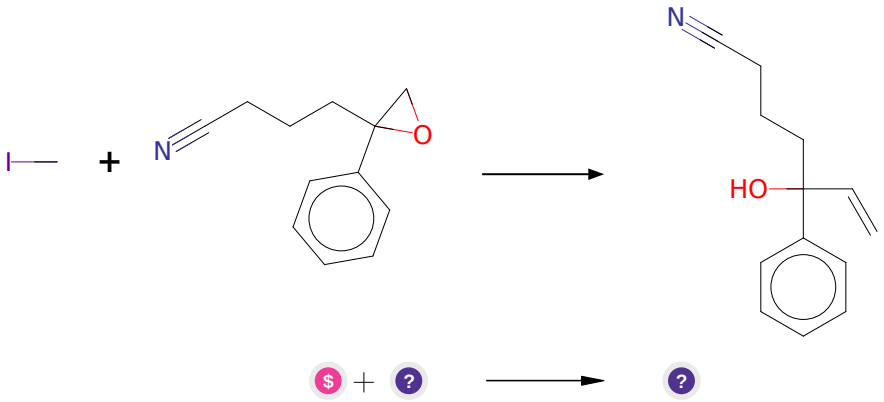
Typical conditions: Et2Zn.tetrahydrothiophene or MeLi.LiBr.Et2O.-78 deg C

Protections: none

Reference: *10.1016/S0040-4039(00)84103-9* and *10.1016/S0040-4039(97)10675-X* and *10.1246/bcsj.70.707* and *10.1021/jo971773h*

Retrosynthesis ID: 31019397

2.1.2 Synthesis of allylic alcohols from epoxides



Substrates:

1. Iodomethane - *available at Sigma-Aldrich*
2. N#CCCCC1(c2ccccc2)CO1

Products:

1. C=CC(O)(CCCC#N)c1ccccc1

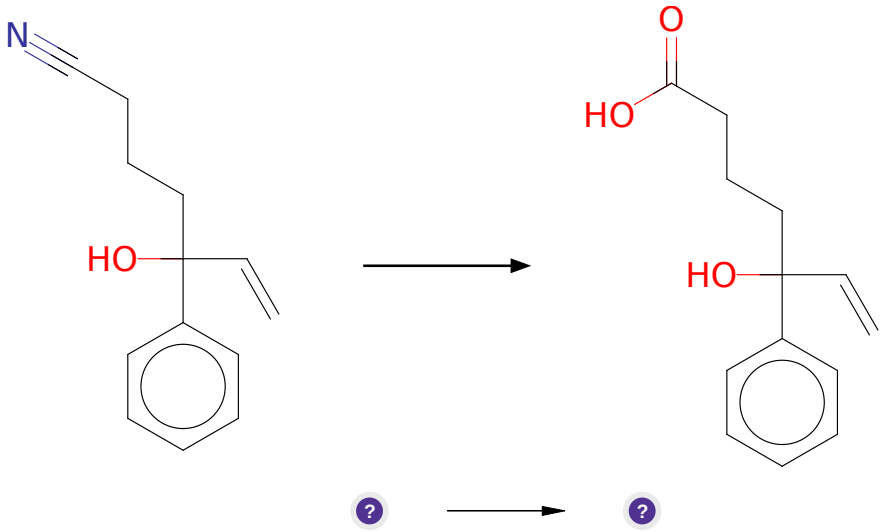
Typical conditions: 1.DMS.2.nBuLi.THF.3.epoxide

Protections: none

Reference: *10.1016/S0040-4039(00)73522-2* and *10.1016/j.tetasy.2011.06.015* and *10.1016/j.tetlet.2016.10.068*

Retrosynthesis ID: 10012631

2.1.3 Base hydrolysis of nitriles to carboxylic acids



Substrates:

1. C=CC(O)(CCCC#N)c1ccccc1

Products:

1. C=CC(O)(CCCC(=O)O)c1ccccc1

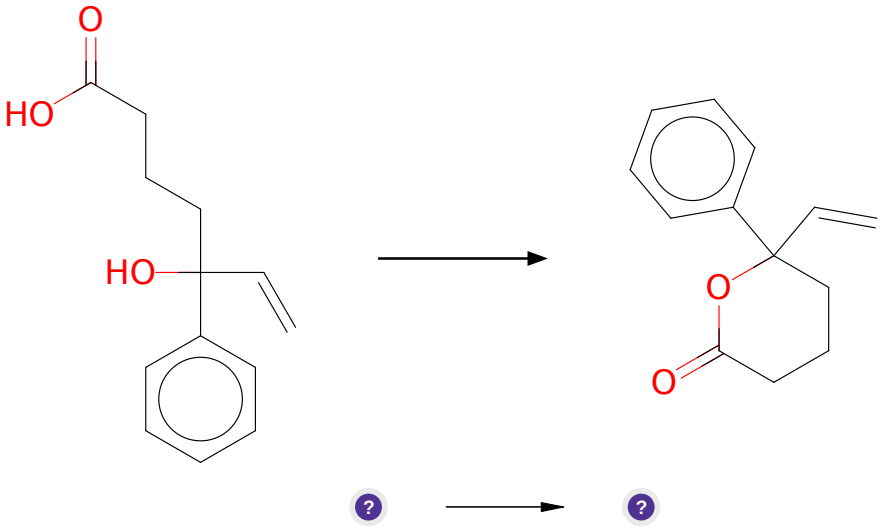
Typical conditions: NaOH.heating.H2O

Protections: none

Reference: *10.1002/1099-0690(200111)2001:22<4207::AID-EJOC4207>3.0.CO;2-3* and *10.1021/acs.jmedchem.5b00702* and *10.1016/j.bmc.2011.07.045*

Retrosynthesis ID: 15107

2.1.4 Intramolecular Nucleophilic Acyl Addition



Substrates:

1. C=CC(O)(CCCC(=O)O)c1ccccc1

Products:

1. C=CC1(c2ccccc2)CCCC(=O)O1

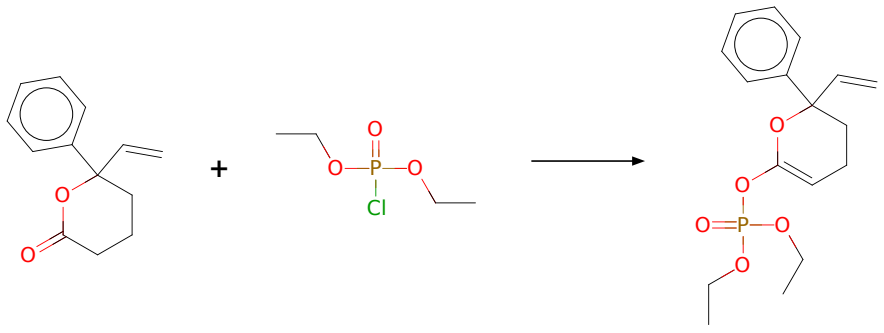
Typical conditions: DCC.4-PPY.DCM or HCl.THF

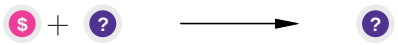
Protections: none

Reference: *10.1016/S0040-4020(01)85848-8* p. 613, 615 and *10.1021/jm00046a007* p. 3243, 3244

Retrosynthesis ID: 10161

2.1.5 Fosforylation of ketones





Substrates:

1. Diethyl chlorophosphate - *available at Sigma-Aldrich*
2. C=CC1(c2ccccc2)CCCC(=O)O1

Products:

1. C=CC1(c2ccccc2)CCC=C(OP(=O)(OCC)OCC)O1

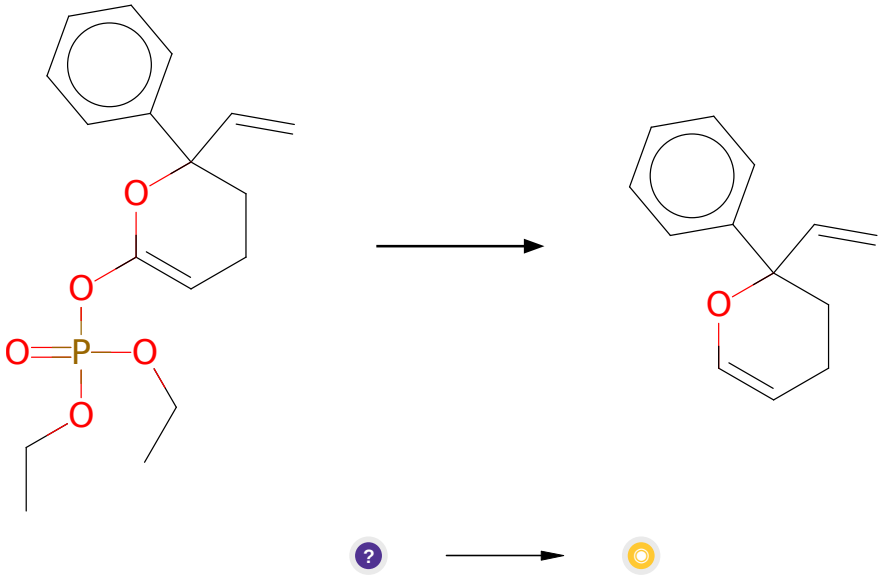
Typical conditions: KHMDS.HMPA.THF.cooling

Protections: none

Reference: *10.1021/ja970619+*

Retrosynthesis ID: 23009

2.1.6 Reduction of enol phosphonates



Substrates:

1. C=CC1(c2ccccc2)CCC=C(OP(=O)(OCC)OCC)O1

Products:

1. C=CC1(c2ccccc2)CCC=CO1

Typical conditions: Et3Al.Pd(PPh3)4

Protections: none

Reference: *10.1021/jo00387a038* AND *10.1021/jo00292a049* AND *10.1039/C1CS15100B*

Retrosynthesis ID: 23046

2.2 Path 2

Score: 137.29

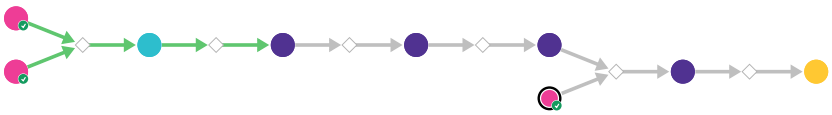
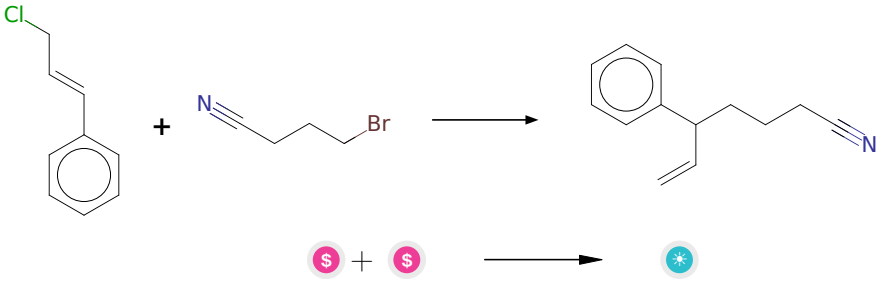


Figure 2: Outline of path 2

2.2.1 Asymmetric allylic alkylation



Substrates:

1. 4-Bromobutyronitrile - *available at Sigma-Aldrich*
2. Cinnamyl chloride - *available at Sigma-Aldrich*

Products:

1. 5-phenyl-6-heptenenitrile

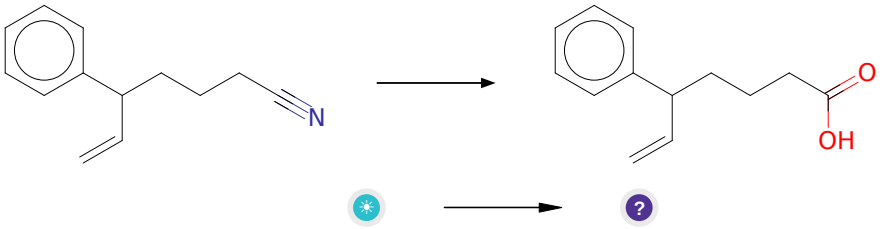
Typical conditions: 1.Mg.2.Chiral.[Cu].catalyst.

Protections: none

Reference: *10.1351/pac200880051025*

Retrosynthesis ID: 7454

2.2.2 Base hydrolysis of nitriles to carboxylic acids



Substrates:

1. 5-phenyl-6-heptenenitrile

Products:

1. C=CC(CCCC(=O)O)c1ccccc1

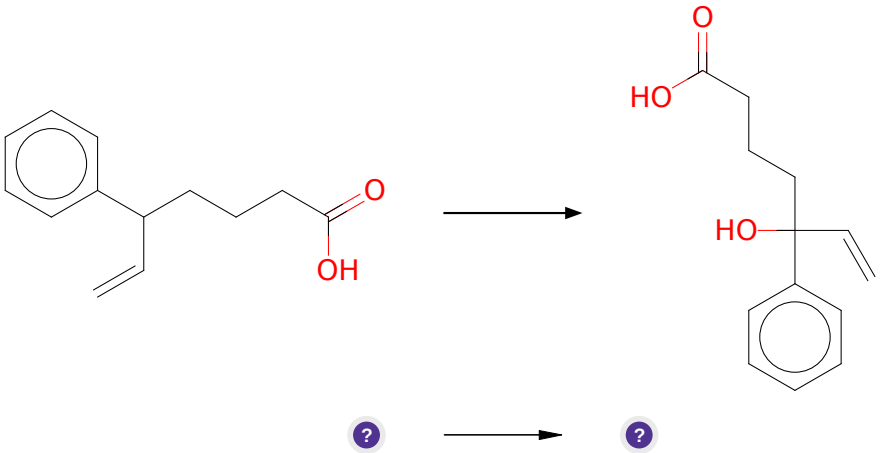
Typical conditions: NaOH.heating.H2O

Protections: none

Reference: *10.1002/1099-0690(200111)2001:22<4207::AID-EJOC4207>3.0.CO;2-3* and *10.1021/acs.jmedchem.5b00702* and *10.1016/j.bmc.2011.07.045*

Retrosynthesis ID: 15107

2.2.3 Allylic oxidation to alcohol



Substrates:

1. C=CC(CCCC(=O)O)c1ccccc1

Products:

1. C=CC(O)(CCCC(=O)O)c1ccccc1

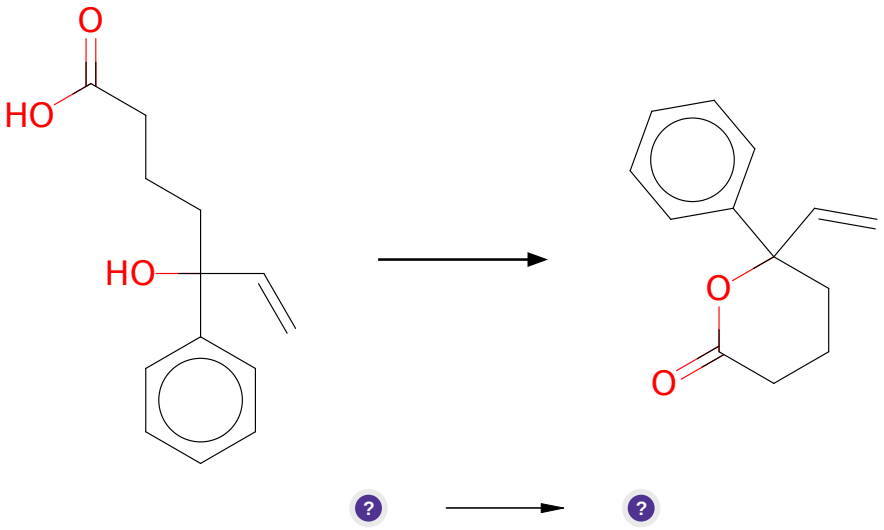
Typical conditions: ArCOOOH or t-BuOOOH

Protections: none

Reference: DOI: *10.1021/ja00458a072* AND *10.1016/j.tetlet.2013.03.046* AND *10.1039/b612423b*

Retrosynthesis ID: 7603

2.2.4 Intramolecular Nucleophilic Acyl Addition



Substrates:

1. C=CC(O)(CCCC(=O)O)c1ccccc1

Products:

1. C=CC1(c2ccccc2)CCCC(=O)O1

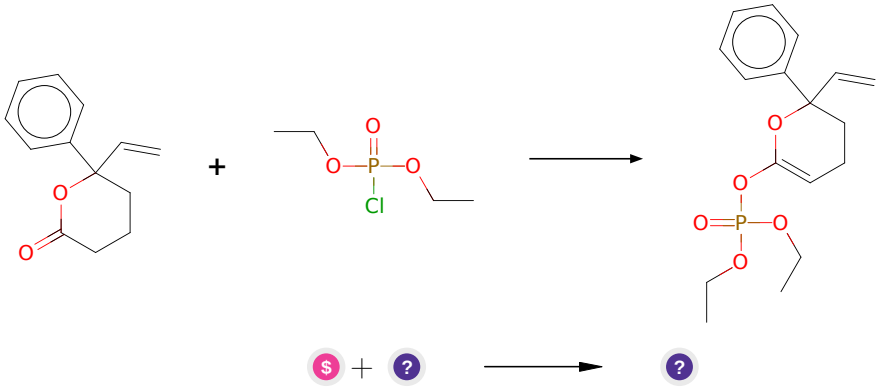
Typical conditions: DCC.4-PPY.DCM or HCl.THF

Protections: none

Reference: *10.1016/S0040-4020(01)85848-8* p. 613, 615 and *10.1021/jm00046a007* p. 3243, 3244

Retrosynthesis ID: 10161

2.2.5 Fosforylation of ketones



Substrates:

1. Diethyl chlorophosphate - *available at Sigma-Aldrich*
2. C=CC1(c2ccccc2)CCCC(=O)O1

Products:

1. C=CC1(c2ccccc2)CCC=C(OP(=O)(OCC)OCC)O1

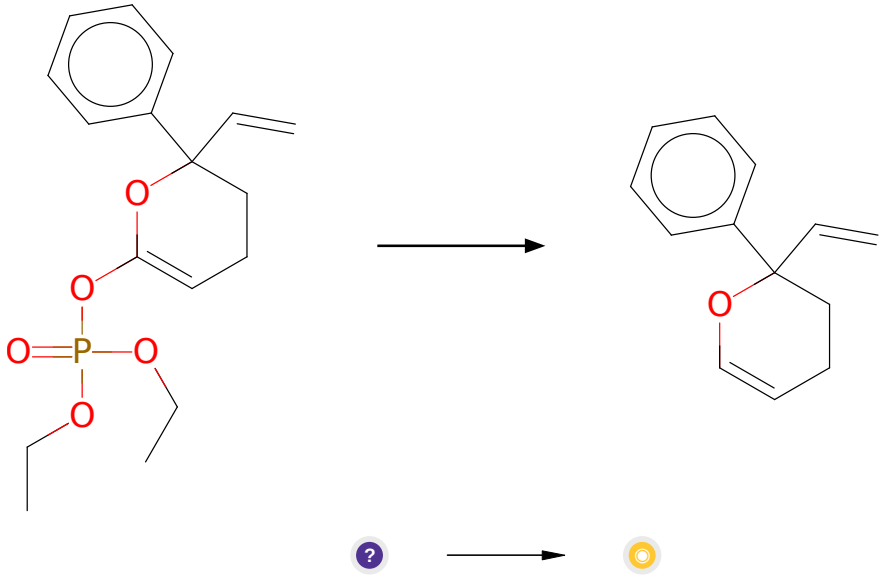
Typical conditions: KHMDS.HMPA.THF.cooling

Protections: none

Reference: *10.1021/ja970619+*

Retrosynthesis ID: 23009

2.2.6 Reduction of enol phosphonates



Substrates:

1. C=CC1(c2ccccc2)CCC=C(OP(=O)(OCC)OCC)O1

Products:

1. C=CC1(c2ccccc2)CCC=CO1

Typical conditions: Et3Al.Pd(PPh3)4

Protections: none

Reference: *10.1021/jo00387a038* AND *10.1021/jo00292a049* AND *10.1039/C1CS15100B*

Retrosynthesis ID: 23046

2.3 Path 3

Score: `164.14`

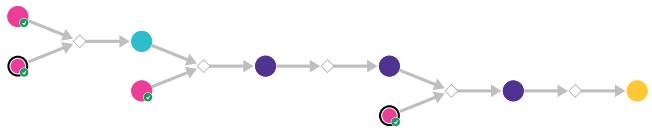
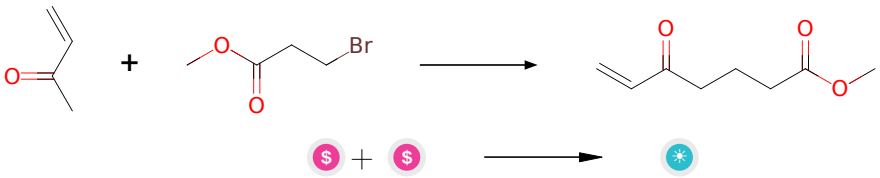


Figure 3: Outline of path 3

2.3.1 Alkylation of ketones



Substrates:

1. Methyl 3-bromopropionate - *available at Sigma-Aldrich*
2. 3-Buten-2-one - *available at Sigma-Aldrich*

Products:

1. 5-oxo-hept-6-enoic acid methyl ester

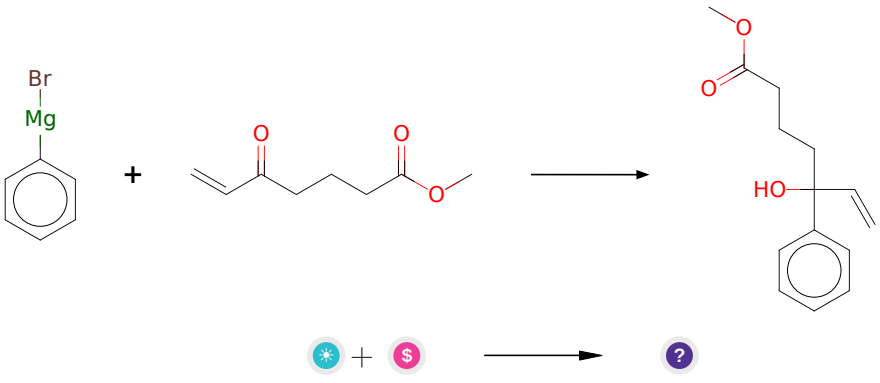
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: *10.1021/jo1019738* OR DOI: *10.1021/jm00114a016*

Retrosynthesis ID: 1866

2.3.2 Grignard-Type Reaction



Substrates:

1. 5-oxo-hept-6-enoic acid methyl ester
2. Phenylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CC(O)(CCCC(=O)OC)c1ccccc1

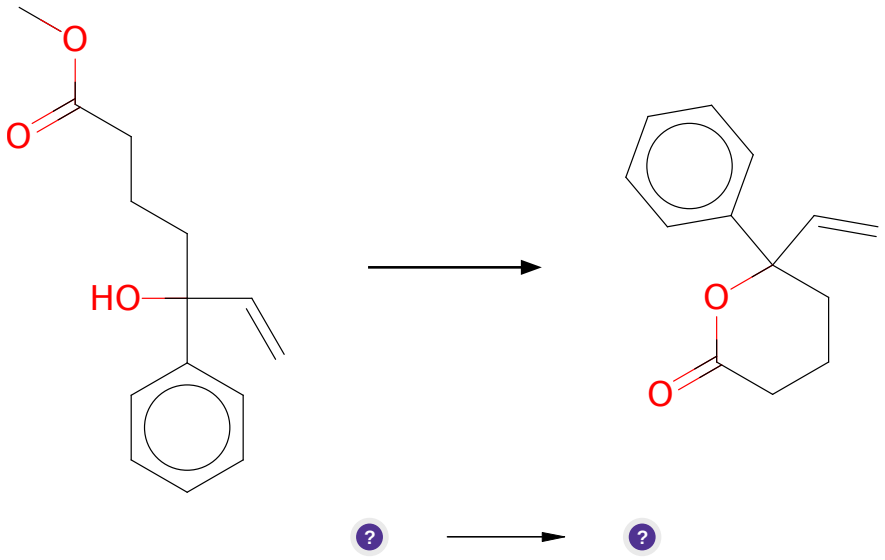
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.3.3 Acid catalyzed transesterification



Substrates:

1. C=CC(O)(CCCC(=O)OC)c1ccccc1

Products:

1. C=CC1(c2ccccc2)CCCC(=O)O1

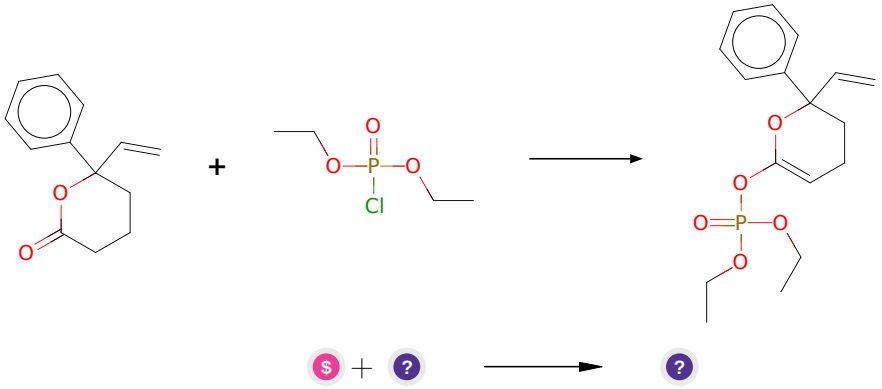
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.3.4 Fosforylation of ketones



Substrates:

1. Diethyl chlorophosphate - *available at Sigma-Aldrich*
2. C=CC1(c2ccccc2)CCCC(=O)O1

Products:

1. C=CC1(c2ccccc2)CCC=C(OP(=O)(OCC)OCC)O1

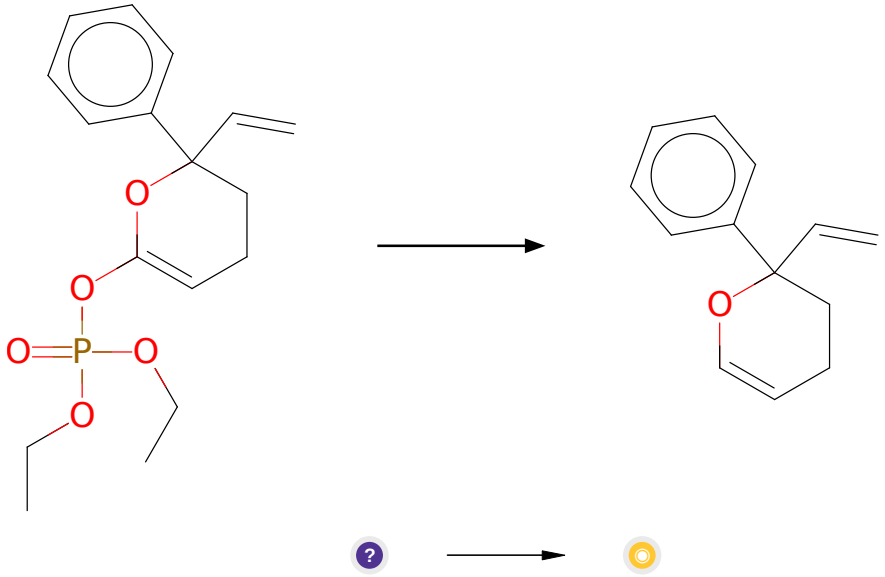
Typical conditions: KHMDS.HMPA.THF.cooling

Protections: none

Reference: *10.1021/ja970619+*

Retrosynthesis ID: 23009

2.3.5 Reduction of enol phosphonates



Substrates:

1. C=CC1(c2ccccc2)CCC=C(OP(=O)(OCC)OCC)O1

Products:

1. C=CC1(c2ccccc2)CCC=CO1

Typical conditions: Et3Al.Pd(PPh3)4

Protections: none

Reference: *10.1021/jo00387a038* AND *10.1021/jo00292a049* AND *10.1039/C1CS15100B*

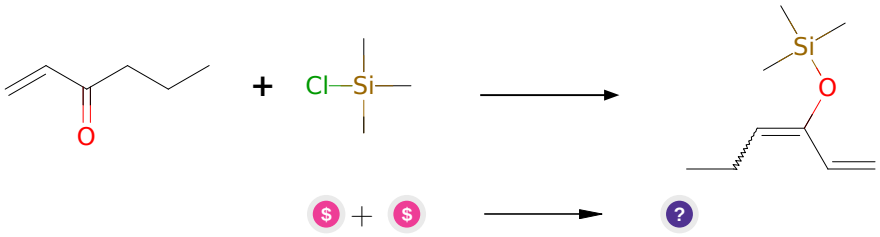
Retrosynthesis ID: 23046

2.4 Path 4

Score: `170.12`

Figure 4: Outline of path 4

2.4.1 Enol esters and ethers synthesis



Substrates:

1. 1-Hexen-3-one - *available at Sigma-Aldrich*
2. TMSCl - *available at Sigma-Aldrich*

Products:

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

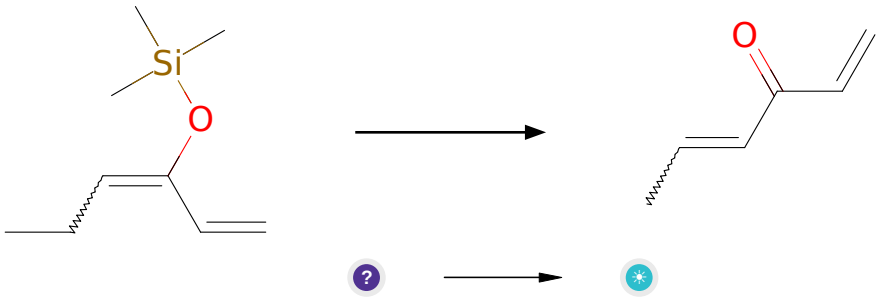
Typical conditions: 1.LDA.2.Electrophile

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=CC(=CCC)O[Si](C)(C)C

Products:

1. hexa-1,4-dien-3-one

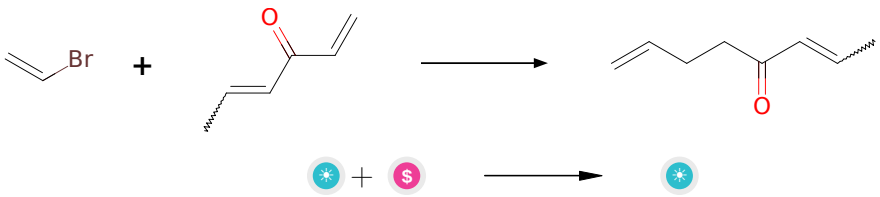
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

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 Suzuki alkyl-vinyl coupling



Substrates:

1. hexa-1,4-dien-3-one
2. Bromoethylene - *available at Sigma-Aldrich*

Products:

1. octa-2,7-dien-4-one

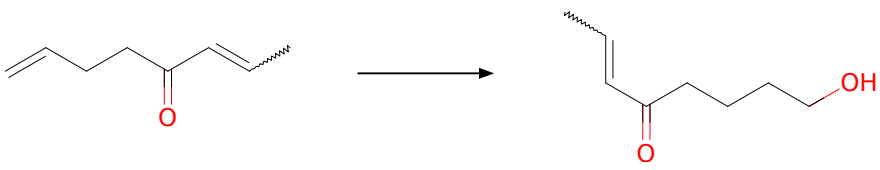
Typical conditions: 1. 9BBN-H. or. PinB-Bpin. Cu. 2. [Pd]. Ligand. Base

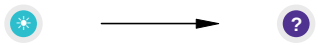
Protections: none

Reference: *10.1002/1521-3773(20011217)40:24<4544::AID-ANIE4544>3.0.CO;2-N* and *10.1021/ol300575d*

Retrosynthesis ID: 10034488

2.4.4 Rh(I) catalyzed hydroboration





Substrates:

1. octa-2,7-dien-4-one

Products:

1. CC=CC(=O)CCCCO

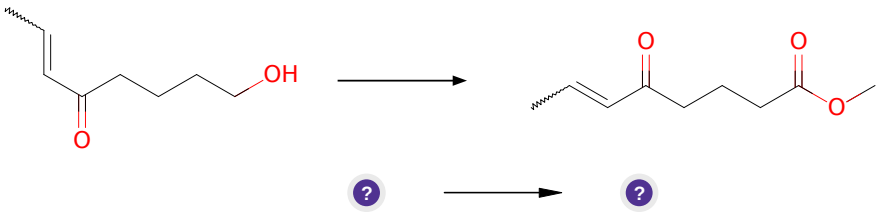
Typical conditions: Wilkinson's catalyst.cateholborane.THF.MeOH.NaOH.H2O2

Protections: none

Reference: DOI: *10.1021/ja00043a009*

Retrosynthesis ID: 9910000

2.4.5 Tandem oxidation-esterification



Substrates:

1. CC=CC(=O)CCCCO

Products:

1. CC=CC(=O)CCCC(=O)OC

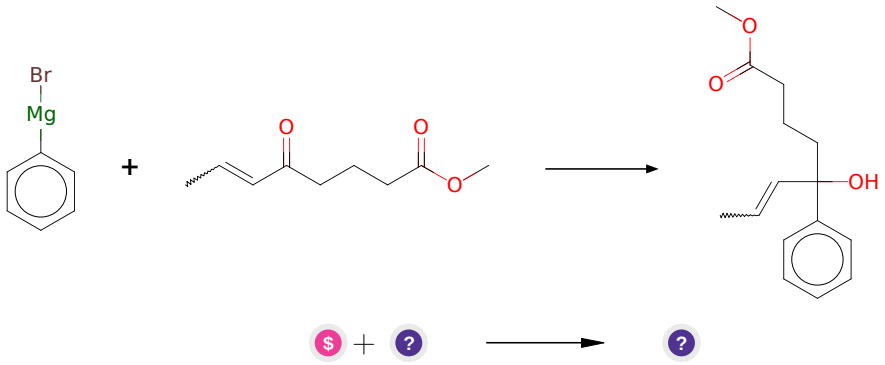
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

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

2.4.6 Grignard-Type Reaction



Substrates:

1. Phenylmagnesium bromide solution - *available at Sigma-Aldrich*
2. CC=CC(=O)CCCC(=O)OC

Products:

1. CC=CC(O)(CCCC(=O)OC)c1ccccc1

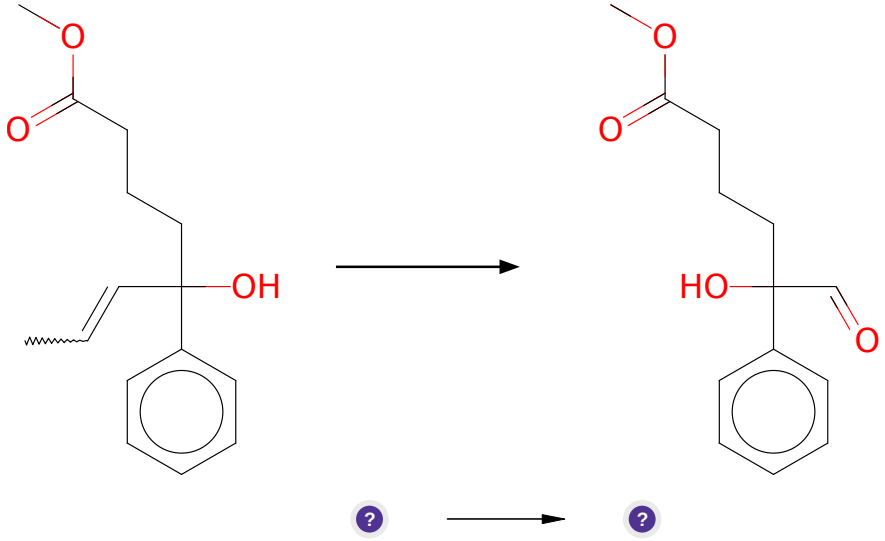
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.4.7 Ozonolysis



Substrates:

1. CC=CC(O)(CCCC(=O)OC)c1ccccc1

Products:

1. COC(=O)CCCC(O)(C=O)c1ccccc1

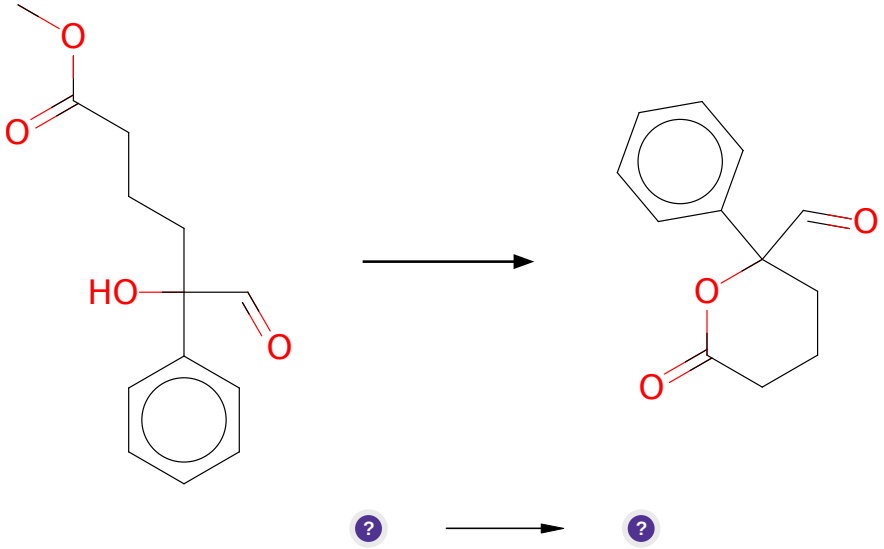
Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5075

2.4.8 Acid catalyzed transesterification



Substrates:

1. COC(=O)CCCC(O)(C=O)c1ccccc1

Products:

1. O=CC1(c2ccccc2)CCCC(=O)O1

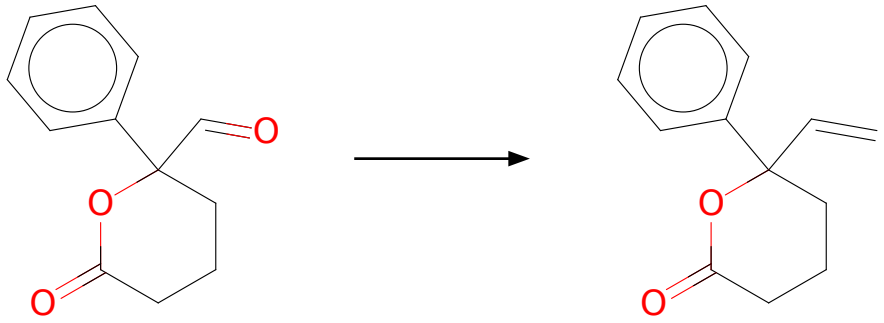
Typical conditions: H+

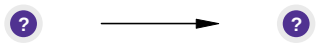
Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.4.9 Tebbe Olefination





Substrates:

1. O=CC1(c2ccccc2)CCCC(=O)O1

Products:

1. C=CC1(c2ccccc2)CCCC(=O)O1

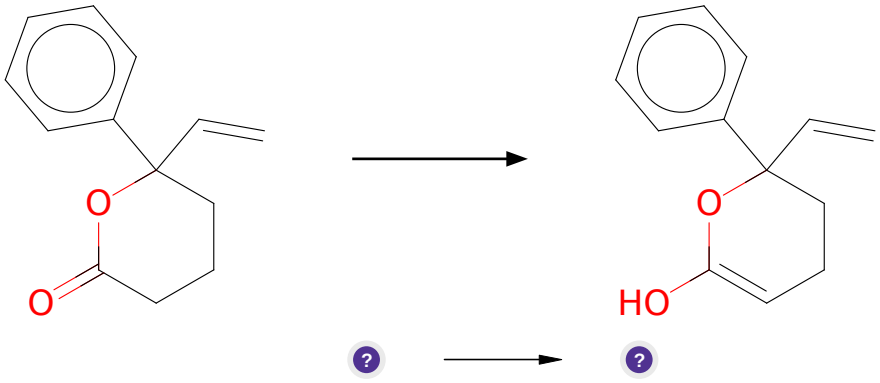
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

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

Retrosynthesis ID: 11714

2.4.10 Keto-Enol Tautomerism



Substrates:

1. C=CC1(c2ccccc2)CCCC(=O)O1

Products:

1. C=CC1(c2ccccc2)CCC=C(O)O1

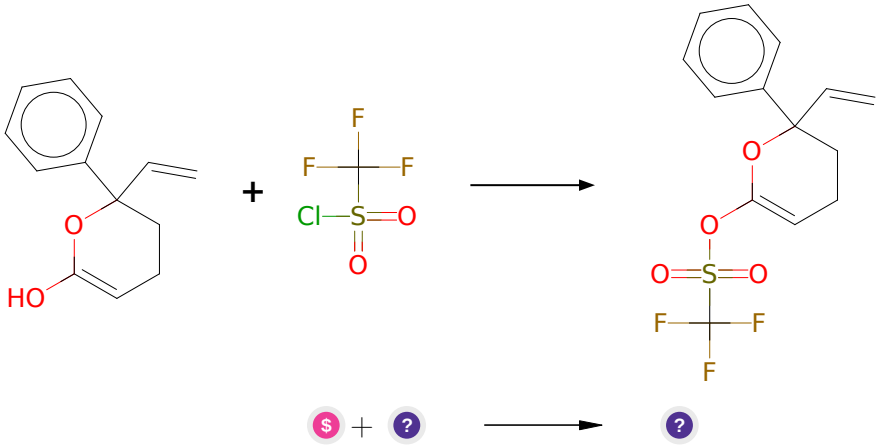
Typical conditions: solvent

Protections: none

Reference: *10.1021/jo8012385* *10.1021/ja01065a003*

Retrosynthesis ID: 8720

2.4.11 Sulfonylation of hydroxyl group



Substrates:

1. Triflyl chloride - *available at Sigma-Aldrich*
2. C=CC1(c2ccccc2)CCC=C(O)O1

Products:

1. C=CC1(c2ccccc2)CCC=C(OS(=O)(=O)C(F)(F)F)O1

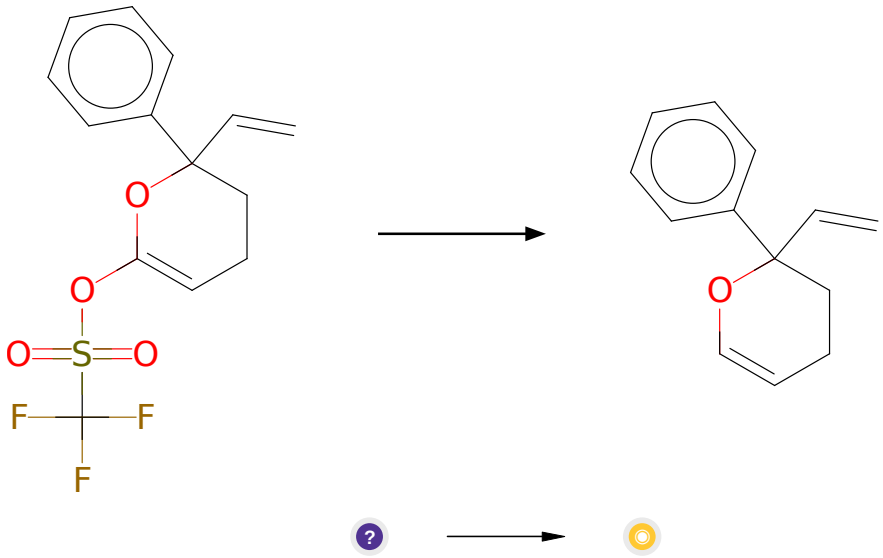
Typical conditions: TEA.THF.0 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112889* p. 4, 11 and *10.1016/j.bmc.2019.04.031* p. 2743, 2750

Retrosynthesis ID: 50428

2.4.12 Reduction of enol sulfonates



Substrates:

1. C=CC1(c2ccccc2)CCC=C(OS(=O)(=O)C(F)(F)F)O1

Products:

1. C=CC1(c2ccccc2)CCC=CO1

Typical conditions: Et3Al.Pd(PPh3)4 or Bu3SnH.LiCl.Pd(PPh3)4

Protections: none

Reference: *10.1021/ol060233g* and *10.1021/ja055220x* and *10.1021/ja029382u* and *10.1021/ja9925958* and *10.1021/jacs.6b03373* and *10.1016/j.tet.2016.03.101*

Retrosynthesis ID: 31014801