Paths of analysis*

L7

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

*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.

Strategies: none selected

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: 76.25

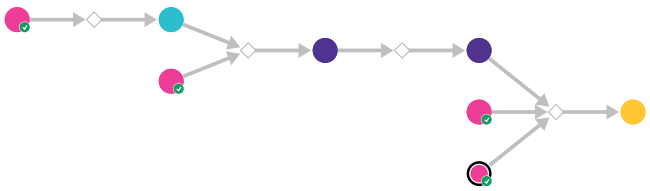
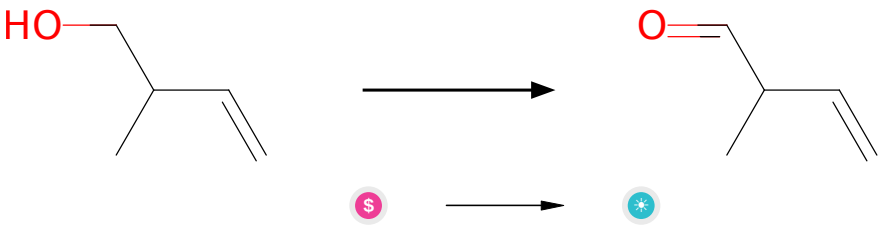


Figure 1: Outline of path 1

2.1.1 Oxidation of primary alcohols with DMP



Substrates:

1. 2-Methyl-3-buten-1-ol - *available at Sigma-Aldrich*

Products:

1. 2-methyl-but-3-enal

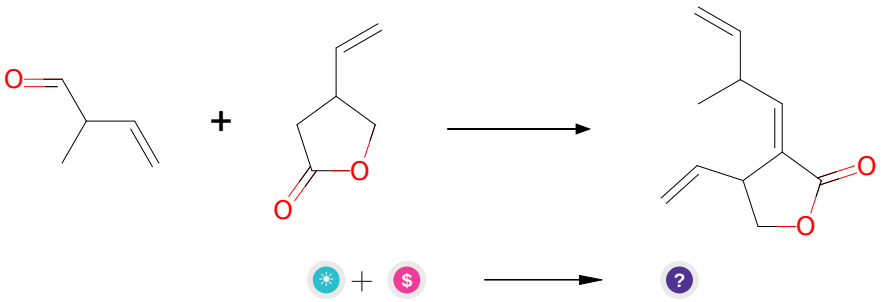
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.1.2 Condensation of esters with aldehydes



Substrates:

1. 2-methyl-but-3-enal
2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

Products:

1. C=CC(C)/C=C1/C(=O)OCC1C=C

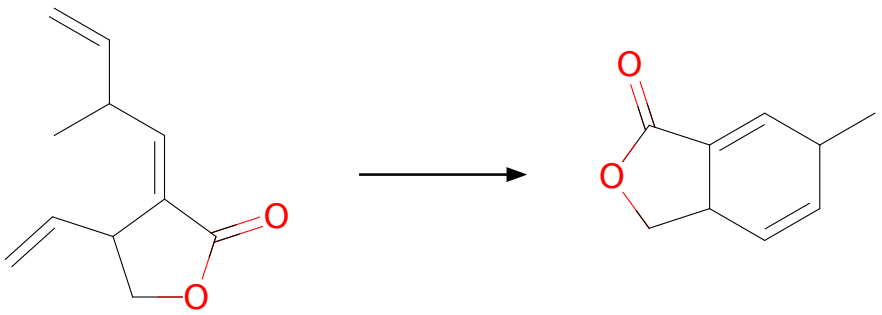
Typical conditions: 1.LDA.2RCHO

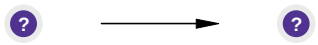
Protections: none

Reference: *10.1021/jo970387x* AND *10.1021/jo00076a051* AND *10.1016/S0040-4039(97)10827-9* AND *10.1055/s-2002-25767* AND *10.1039/P19920003277*

Retrosynthesis ID: 14981

2.1.3 Ring-Closing Metathesis





Substrates:

1. C=CC(C)/C=C1/C(=O)OCC1C=C

Products:

1. CC1C=CC2COC(=O)C2=C1

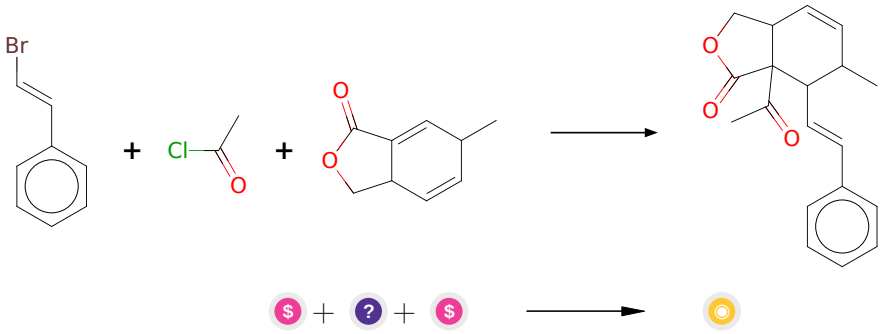
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.1.4 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. b-Bromostyrene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13033

2.2 Path 2

Score: 106.04

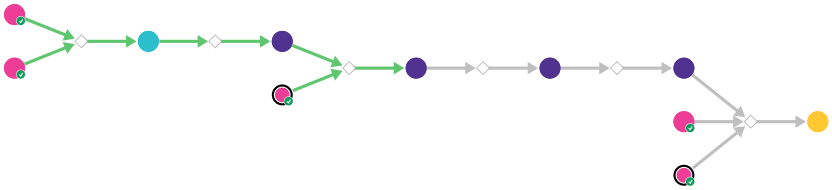
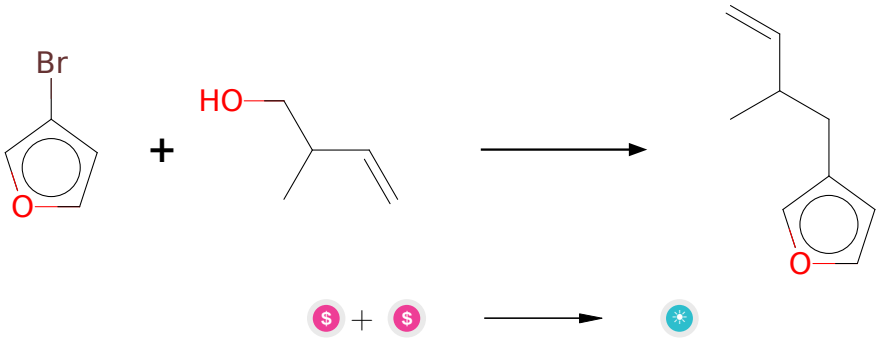


Figure 2: Outline of path 2

2.2.1 Double decarboxylative coupling or aryl halides with alcohols as latent nucleophiles



Substrates:

1. 2-Methyl-3-buten-1-ol - *available at Sigma-Aldrich*
2. 3-Bromofuran - *available at Sigma-Aldrich*

Products:

1. 3-(2-methyl-but-3-enyl)-furan

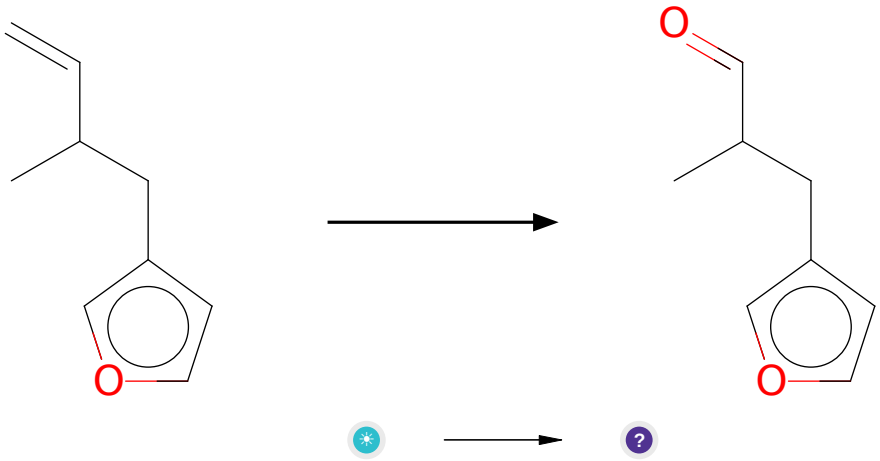
Typical conditions: 1.Oxalyl chloride 2.[Ir]-catalyst.[Ni]-catalyst.blue.light.dioxane.DMSO.DMF.CsHCO3.70 deg C

Protections: none

Reference: *10.1021/jacs.6b09533*

Retrosynthesis ID: 10032259

2.2.2 Ozonolysis



Substrates:

1. 3-(2-methyl-but-3-enyl)-furan

Products:

1. CC(C=O)Cc1ccoc1

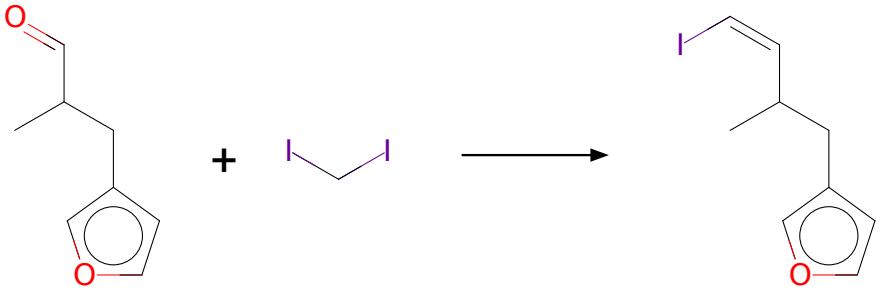
Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

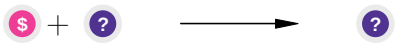
Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5074

2.2.3 Iodoolefination of aldehydes





Substrates:

1. Diiodomethane - *available at Sigma-Aldrich*
2. CC(C=O)Cc1ccoc1

Products:

1. CC(/C=C\I)Cc1ccoc1

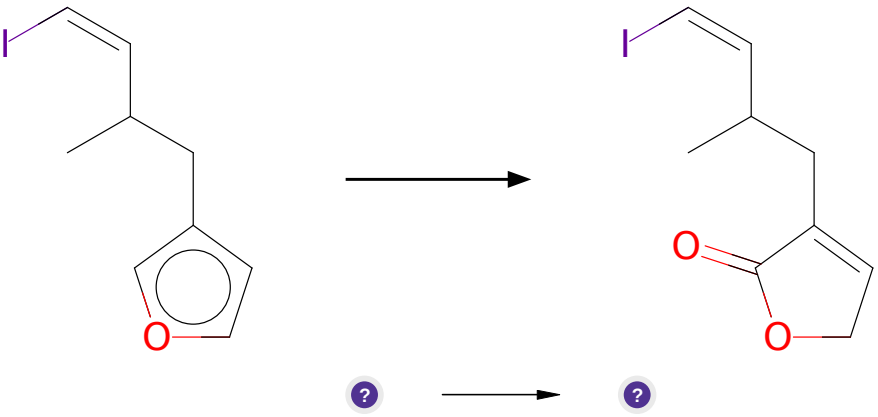
Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

Protections: none

Reference: *10.1021/ja00171a035* and *10.1039/C0OB00977F* and WO2009033499 (p.25)

Retrosynthesis ID: 10001773

2.2.4 NBS-promoted oxidation of furans to lactones



Substrates:

1. CC(/C=C\I)Cc1ccoc1

Products:

1. CC(/C=C\I)CC1=CCOC1=O

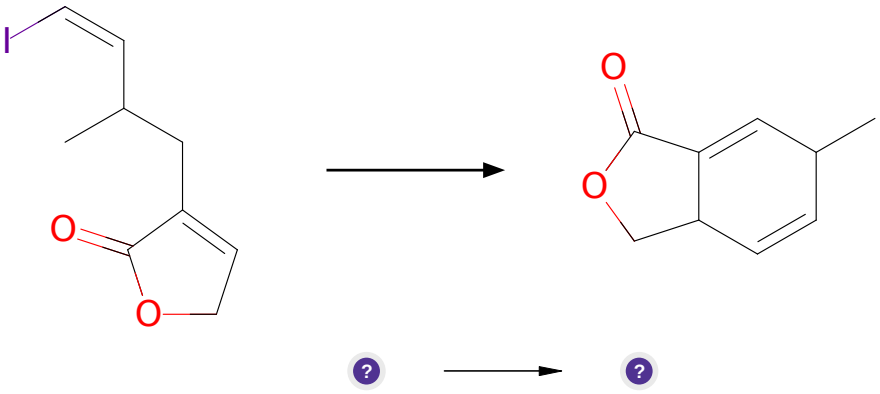
Typical conditions: NBS.MW.MeOH

Protections: none

Reference: DOI: *10.1016/S0040-4039(01)01261-8*

Retrosynthesis ID: 49766

2.2.5 Heck Reaction



Substrates:

1. CC(/C=C\I)CC1=CCOC1=O

Products:

1. CC1C=CC2COC(=O)C2=C1

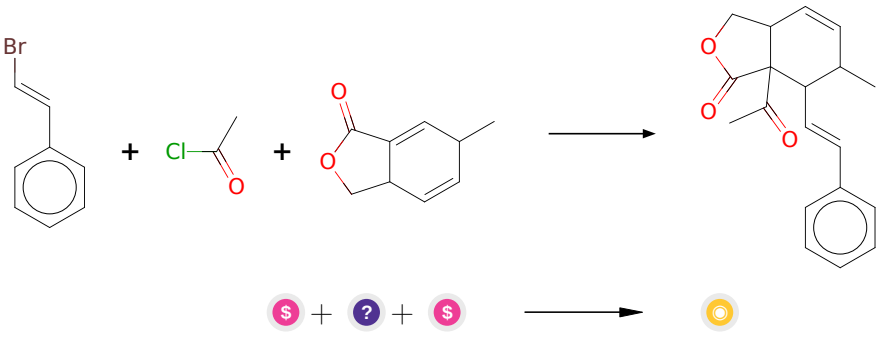
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

Protections: none

Reference: DOI: *10.1021/jo00270a011* or DOI: *10.1021/ar00049a001* or DOI: *10.1021/ja00206a034* or DOI: *10.1021/cr020039h* or DOI: *10.1039/C1CS15101K* or DOI: *10.1002/9780470716076*

Retrosynthesis ID: 8584

2.2.6 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. b-Bromostyrene - *available at Sigma-Aldrich*

2. CC1C=CC2COC(=O)C2=C1

3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13033

2.3 Path 3

Score: 106.04

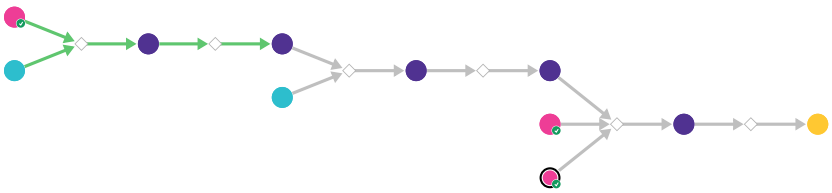
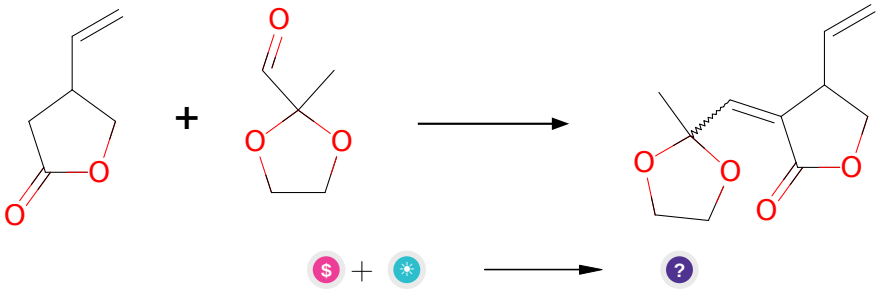


Figure 3: Outline of path 3

2.3.1 Condensation of esters with aldehydes/ketones



Substrates:

1. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*
2. 2-methyl-[1,3]dioxolane-2-carbaldehyde

Products:

1. C=CC1COC(=O)C1=CC1(C)OCCO1

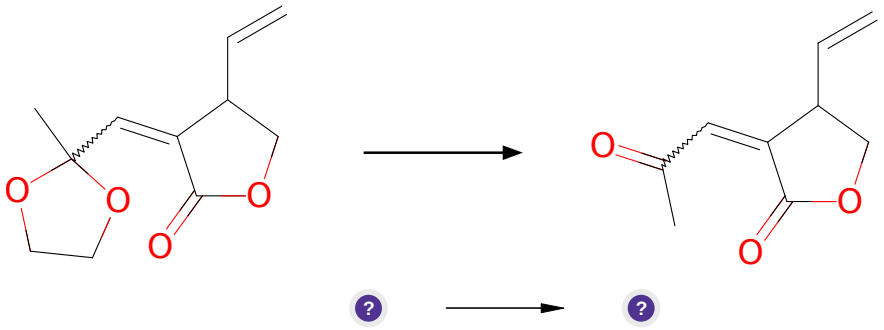
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.3.2 Hydrolysis of ketals



Substrates:

1. C=CC1COC(=O)C1=CC1(C)OCCO1

Products:

1. C=CC1COC(=O)C1=CC(C)=O

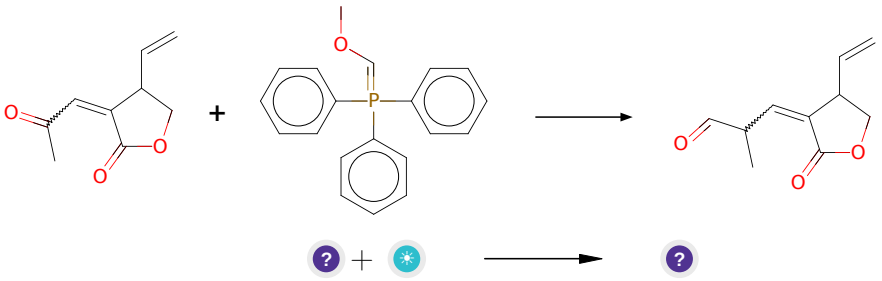
Typical conditions: H2O.HCl

Protections: none

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

Retrosynthesis ID: 31013139

2.3.3 Olefination of ketones followed by hydrolysis



Substrates:

1. C=CC1COC(=O)C1=CC(C)=O
2. triphenylphosphonium methoxymethylide

Products:

1. C=CC1COC(=O)C1=CC(C)C=O

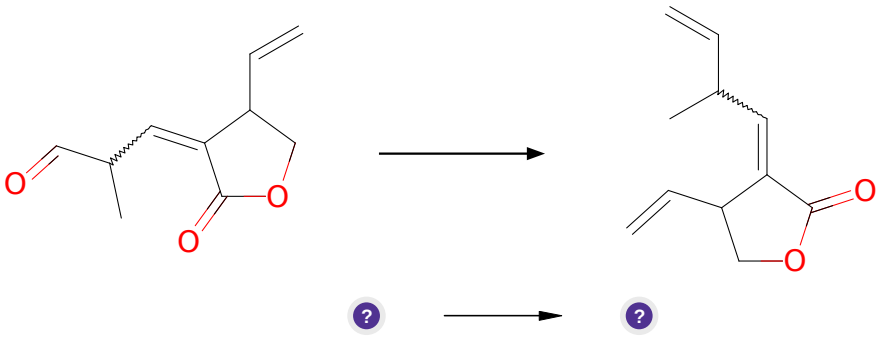
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014861

2.3.4 Tebbe Olefination



Substrates:

1. C=CC1COC(=O)C1=CC(C)C=O

Products:

1. C=CC(C)C=C1C(=O)OCC1C=C

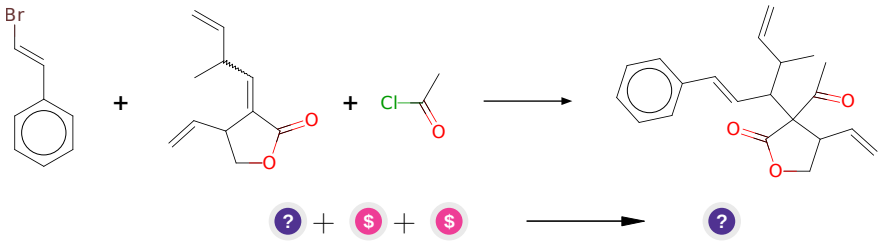
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

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

Retrosynthesis ID: 11714

2.3.5 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. C=CC(C)C=C1C(=O)OCC1C=C
2. b-Bromostyrene - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(/C=C/c1ccccc1)C1(C(C)=O)C(=O)OCC1C=C

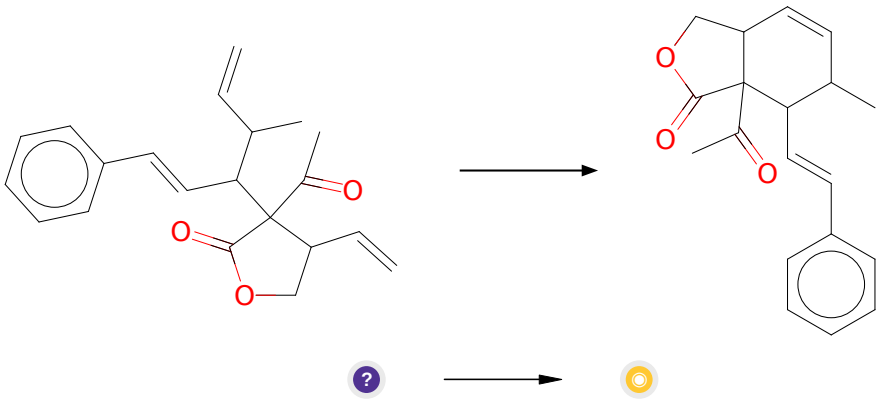
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3* AND *10.1021/ja0320018* AND *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815*

Retrosynthesis ID: 20532

2.3.6 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(/C=C/c1ccccc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.4 Path 4

Score: `115.31`

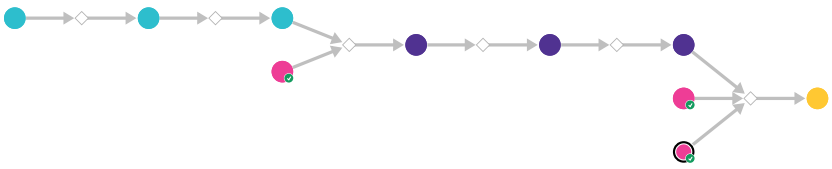
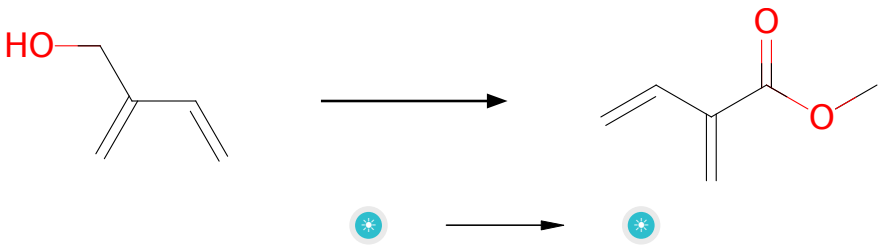


Figure 4: Outline of path 4

2.4.1 Tandem oxidation-esterification



Substrates:

1. 2-methylene-but-3-en-1-ol

Products:

1. 2-methylene-but-3-enoic acid methyl ester

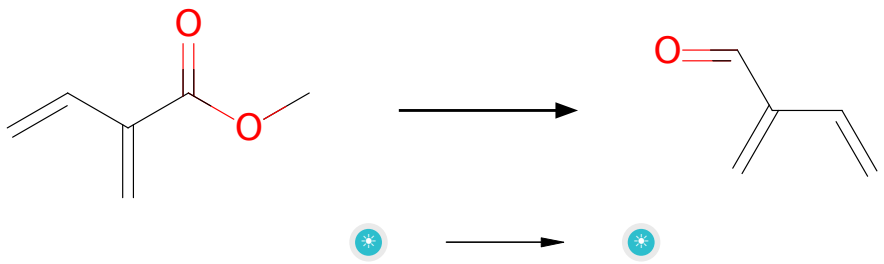
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

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

2.4.2 Aldehyde Formation



Substrates:

1. 2-methylene-but-3-enoic acid methyl ester

Products:

1. isoprenal

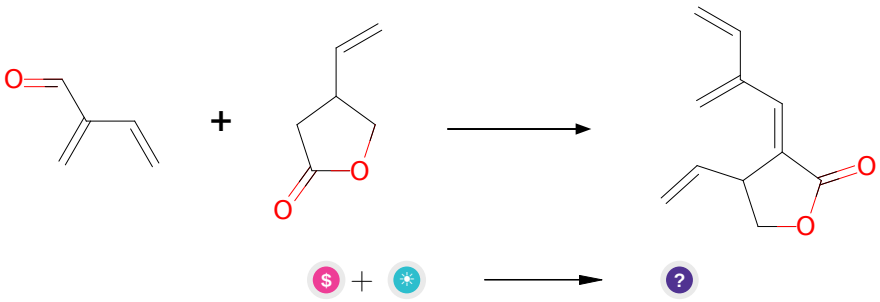
Typical conditions: DIBAL.solvent e.g. DCM

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

2.4.3 Condensation of esters with aldehydes



Substrates:

1. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*
2. isoprenal

Products:

1. C=CC(=C)/C=C1/C(=O)OCC1C=C

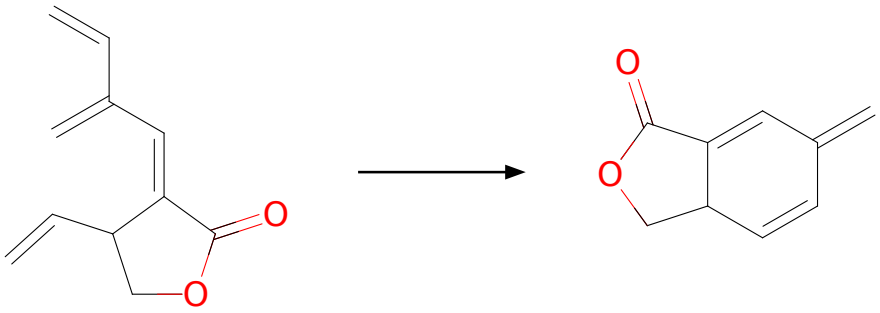
Typical conditions: 1.LDA.2RCHO

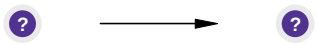
Protections: none

Reference: *10.1021/jo970387x* AND *10.1021/jo00076a051* AND *10.1016/S0040-4039(97)10827-9* AND *10.1055/s-2002-25767* AND *10.1039/P19920003277*

Retrosynthesis ID: 14981

2.4.4 Ring-Closing Metathesis





Substrates:

1. C=CC(=C)/C=C1/C(=O)OCC1C=C

Products:

1. C=C1C=CC2COC(=O)C2=C1

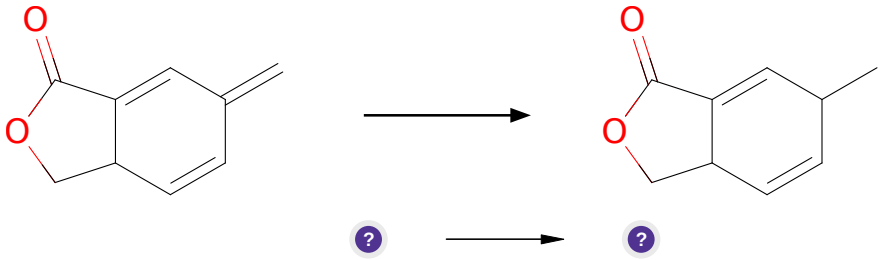
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.4.5 Heterogeneous Reduction of C=C Double Bond



Substrates:

1. C=C1C=CC2COC(=O)C2=C1

Products:

1. CC1C=CC2COC(=O)C2=C1

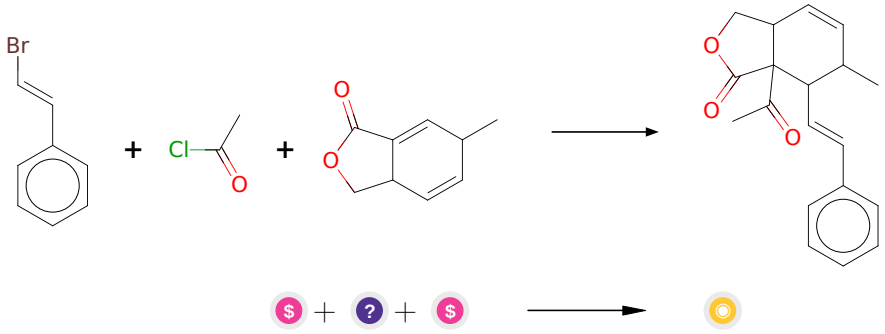
Typical conditions: H2.Wilkinson's Catalyst or other catalyst e.g. Crabtree's

Protections: none

Reference: DOI: *10.1021/jo00052a031* and *10.1021/jo050669u* and *10.1016/j.tetlet.2010.11.078* and *10.1002/anie.198701901* and Patent: US2005/119242 A1, 2005 (page 39) and *10.1021/ja412342g*

Retrosynthesis ID: 9995785

2.4.6 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. b-Bromostyrene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

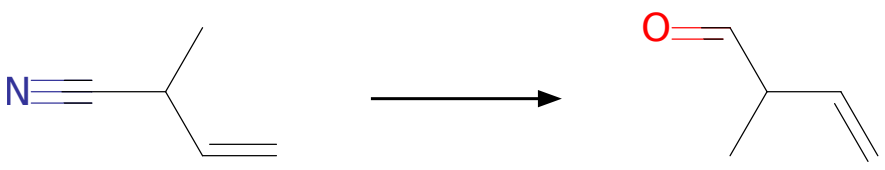
Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13033

2.5 Path 5

Score: 115.31

2.5.1 Reduction of nitriles to aldehydes



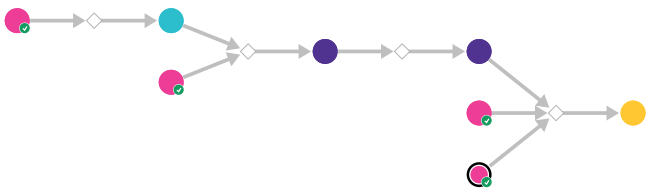
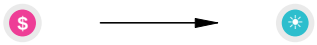


Figure 5: Outline of path 5



Substrates:

1. 2-Methyl-3-butenenitrile - *available at Sigma-Aldrich*

Products:

1. 2-methyl-but-3-enal

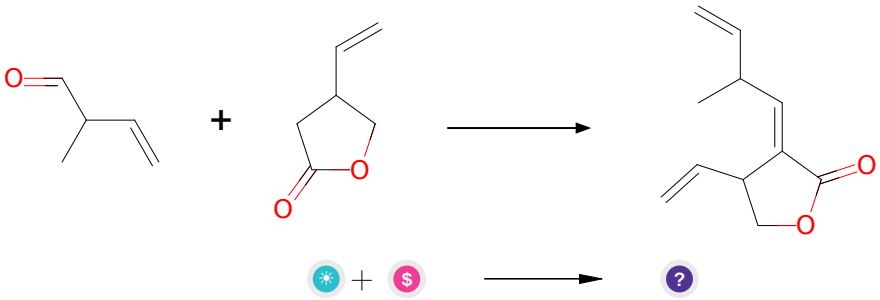
Typical conditions: DIBALH.DCM

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

2.5.2 Condensation of esters with aldehydes



Substrates:

1. 2-methyl-but-3-enal
2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

Products:

1. C=CC(C)/C=C1/C(=O)OCC1C=C

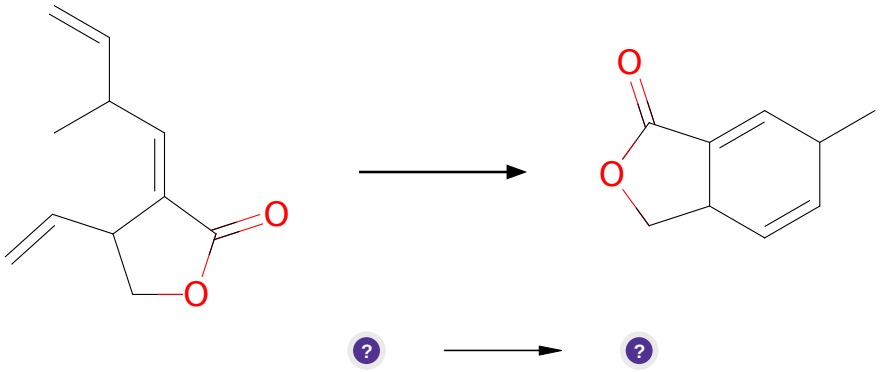
Typical conditions: 1.LDA.2RCHO

Protections: none

Reference: *10.1021/jo970387x* AND *10.1021/jo00076a051* AND *10.1016/S0040-4039(97)10827-9* AND *10.1055/s-2002-25767* AND *10.1039/P19920003277*

Retrosynthesis ID: 14981

2.5.3 Ring-Closing Metathesis



Substrates:

1. C=CC(C)/C=C1/C(=O)OCC1C=C

Products:

1. CC1C=CC2COC(=O)C2=C1

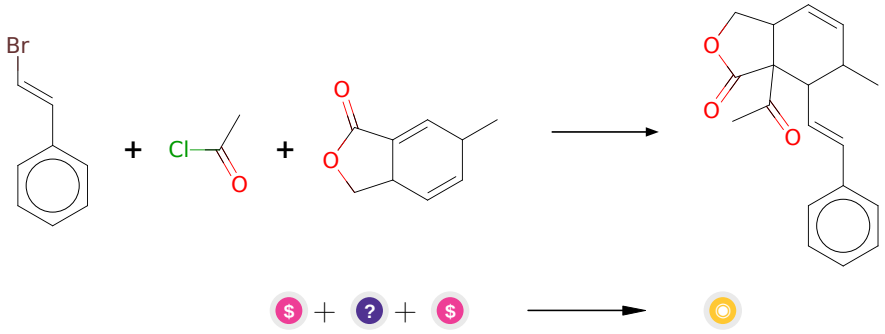
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.5.4 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. b-Bromostyrene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2/C=C/c1ccccc1

Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13033