Paths of analysis*

L3

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: `125.08`

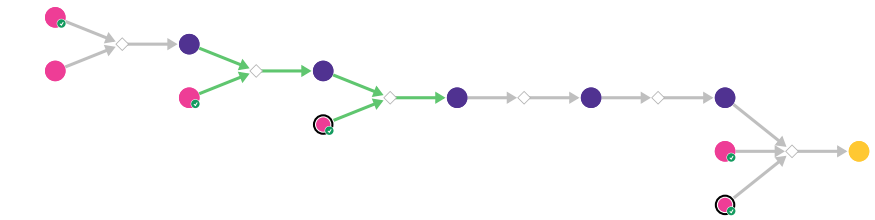
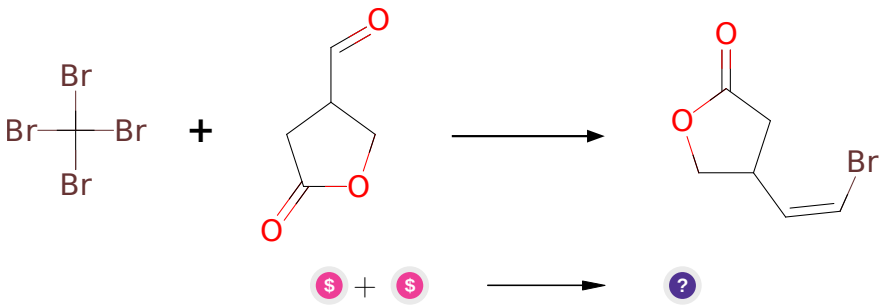


Figure 1: Outline of path 1

2.1.1 Synthesis of Z-bromoalkenes



Substrates:

1. Tetrabromomethane - *available at Sigma-Aldrich*
2. 5-oxotetrahydrofuran-3-carbaldehyde - *A1BioChemLabs*

Products:

1. O=C1CC(/C=C\Br)CO1

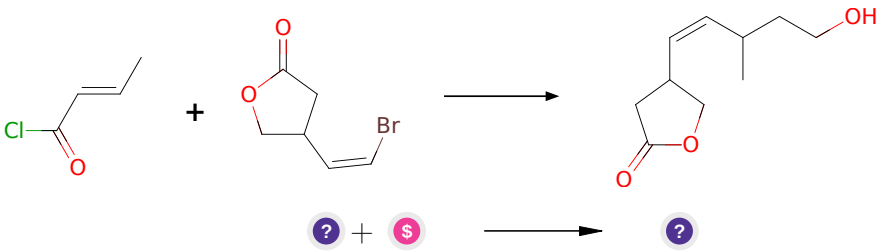
Typical conditions: 1.CBr4.Ph3P.TEA.THF.cooling to rt.2. nBu3SnH.Pd(PPh3)4.toluene.rt

Protections: none

Reference: *10.1002/chem.201101630* (SI p.13) and *10.1021/jo0498157* and *10.1016/j.tetlet.2004.01.151* and *10.1021/ol035127i*

Retrosynthesis ID: 10001762

2.1.2 Chriral auxiliary directed enantioselective Micheal addition



Substrates:

1. O=C1CC(/C=C\Br)CO1
2. Crotonoyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(/C=C\C1COC(=O)C1)CCO

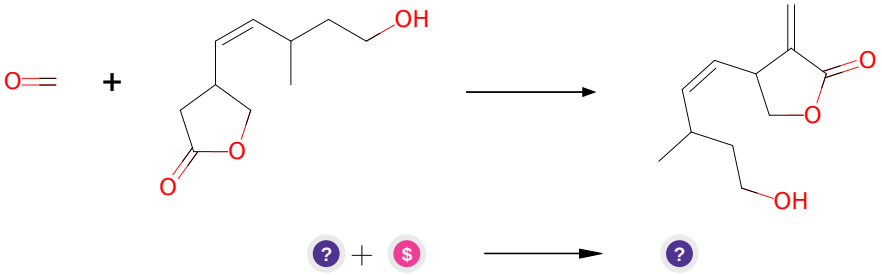
Typical conditions: 1.Chiral auxiliary(Oppolzer's,Evans' or Seebach's).or.ephedrine.2.RMgX.3.LAH

Protections: none

Reference: *10.1016/j.tetlet.2010.11.083* AND *10.1039/B404205K* AND *10.1021/ol006410+* AND *10.1002/anie.199702741* AND *10.1016/j.tet.2015.05.023* AND *10.1021/jm9005302* AND *10.1016/j.tet.2011.12.046*

Retrosynthesis ID: 15874

2.1.3 Eschenmoser methenylation



Substrates:

1. CC(/C=C\C1COC(=O)C1)CCO
2. Formalin - *available at Sigma-Aldrich*

Products:

1. C=C1C(=O)OCC1/C=C\C(C)CCO

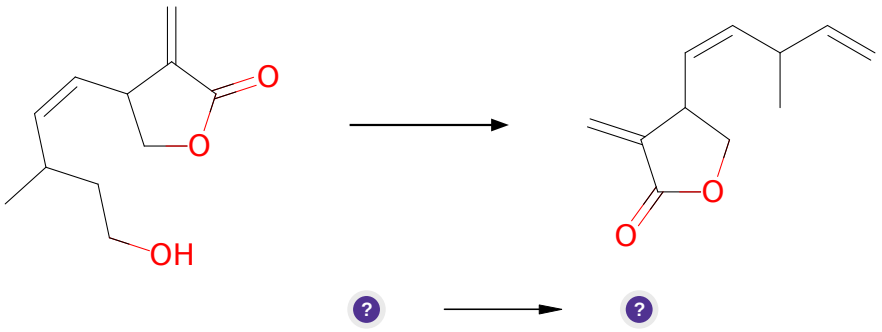
Typical conditions: iPr2NH.TFA.HCHO.or.organocatalyst

Protections: none

Reference: DOI:*10.1016/S0040-4039(00)82176-0* AND DOI:*10.1021/jo052529q* AND DOI:*10.1039/b924577d*

Retrosynthesis ID: 7270

2.1.4 Synthesis of alkenes from alcohols



Substrates:

1. C=C1C(=O)OCC1/C=C\C(C)CCO

Products:

1. C=CC(C)/C=C\C1COC(=O)C1=C

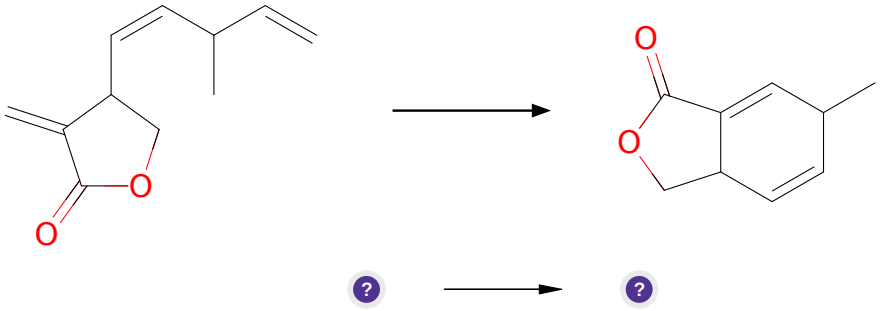
Typical conditions: PhSeCN.PBu3.THF then H2O2.THF.H2O

Protections: none

Reference: *10.1016/j.tet.2011.05.034* and *10.1055/s-0036-1588104* and *10.1002/anie.200501760* and *10.1002/anie.200700854* and *10.1002/asia.201301248* and *10.1021/ol501095w*

Retrosynthesis ID: 31010457

2.1.5 Ring-Closing Metathesis



Substrates:

1. C=CC(C)/C=C\C1COC(=O)C1=C

Products:

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

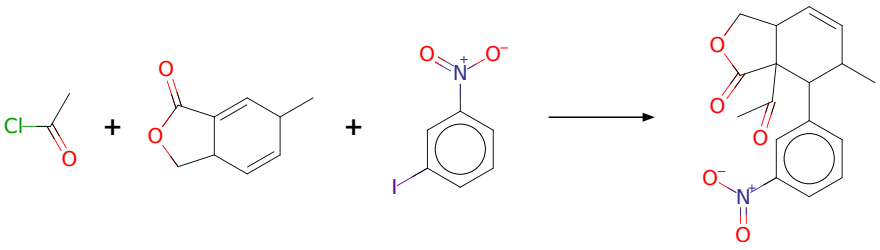
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

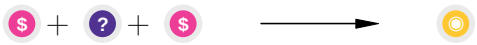
Protections: none

Reference: DOI: *10.1021/jo202073n* and *10.1021/jm060486f* and *10.1039/B801206G* and *10.1021/ol052856k*

Retrosynthesis ID: 31014201

2.1.6 Conjugated addition of organocuprate-acylation of enones and enoate esters





Substrates:

1. 1-Iodo-3-nitrobenzene - *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)C2c1cccc([N+](=O)[O-])c1

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

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 12521

2.2 Path 2

Score: 132.89

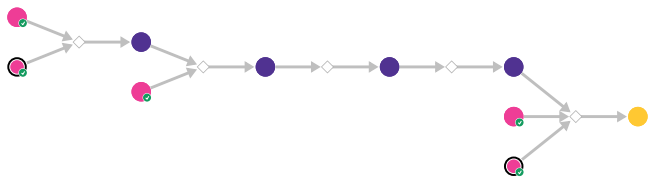
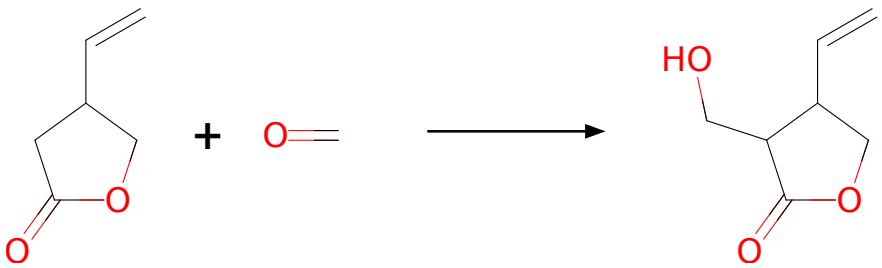
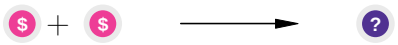


Figure 2: Outline of path 2

2.2.1 Hydroxymethylation of esters/amides





Substrates:

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

Products:

1. C=CC1COC(=O)C1CO

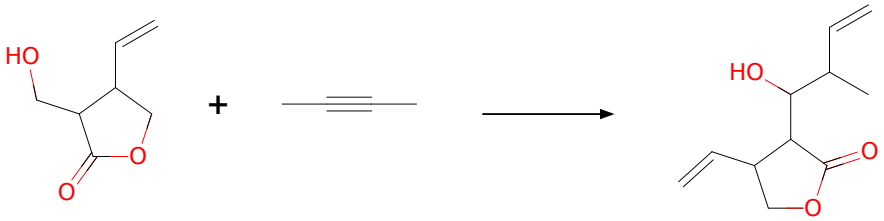
Typical conditions: LDA.THF

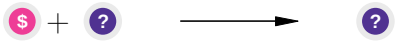
Protections: none

Reference: *10.1021/ja806021y* and *10.1016/S0040-4039(00)01464-7* and *10.1021/ja045752y* and

Retrosynthesis ID: 4787

2.2.2 Coupling of alkynes and alcohols





Substrates:

1. 2-Butyne - *available at Sigma-Aldrich*
2. C=CC1COC(=O)C1CO

Products:

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

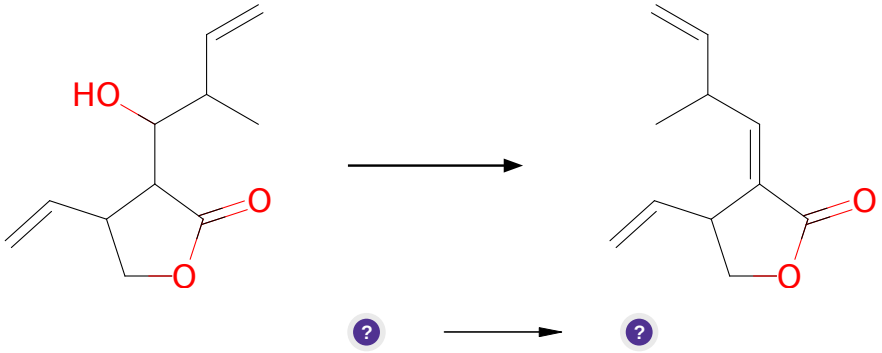
Typical conditions: H2Ru(CO)(PPh3)3.2,4,6-(iPr)3PhSO3H.SL-J009-1.TBAI.IPA.THF.95C

Protections: none

Reference: DOI: *10.1021/jacs.5b00747*

Retrosynthesis ID: 9894

2.2.3 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

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

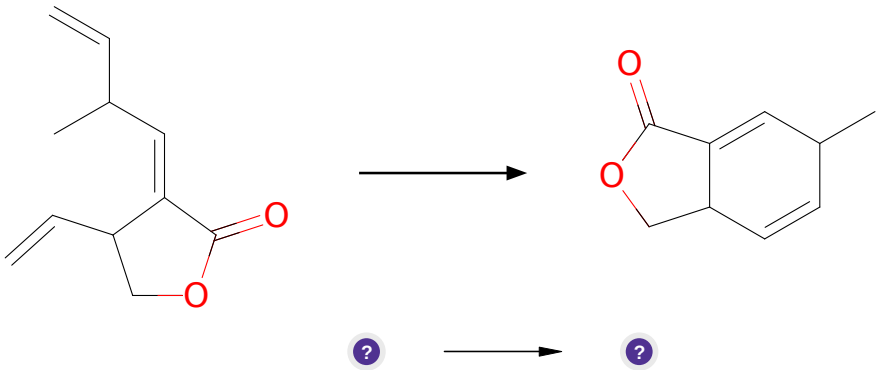
Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732

2.2.4 Ring-Closing Metathesis



Substrates:

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

Products:

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

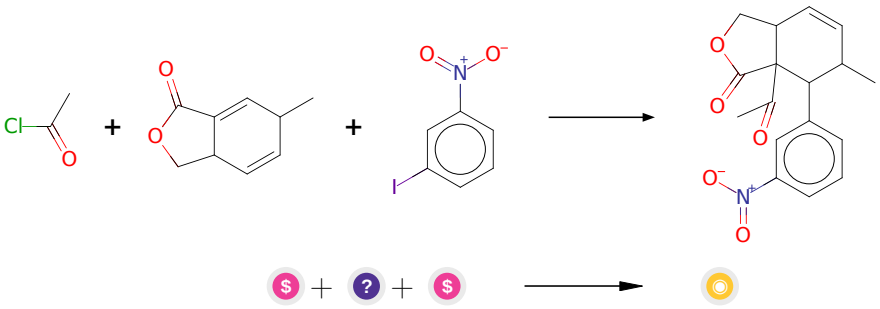
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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

2.2.5 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. 1-Iodo-3-nitrobenzene - *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)C2c1cccc([N+](=O)[O-])c1

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

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 12521

2.3 Path 3

Score: 132.89

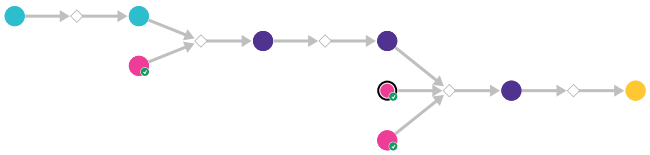
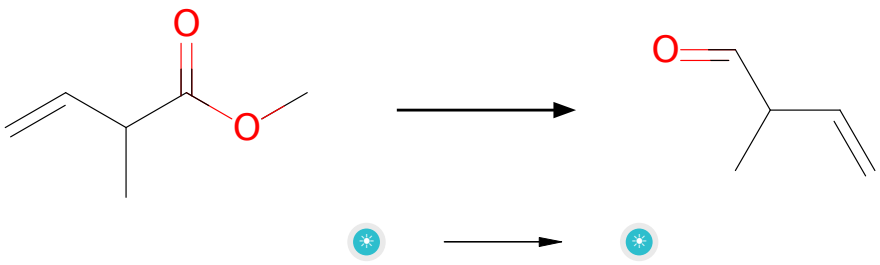


Figure 3: Outline of path 3

2.3.1 Aldehyde Formation



Substrates:

1. 2-methylbut-3-ensaeuremethylester

Products:

1. 2-methyl-but-3-enal

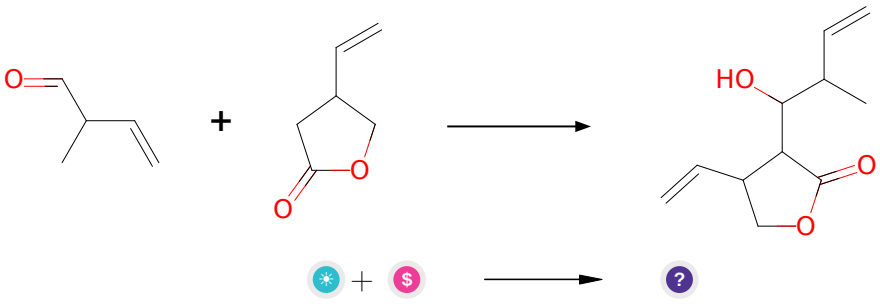
Typical conditions: DIBAL.solvent e.g. DCM

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

2.3.2 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(O)C1C(=O)OCC1C=C

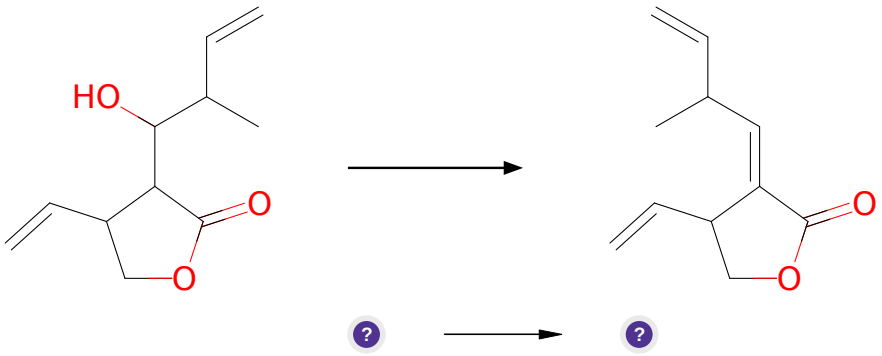
Typical conditions: LDA.THF

Protections: none

Reference: *10.1016/j.bmcl.2005.02.066* and *10.3762/bjoc.9.175* and *10.1021/ol1016178*

Retrosynthesis ID: 4788

2.3.3 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

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

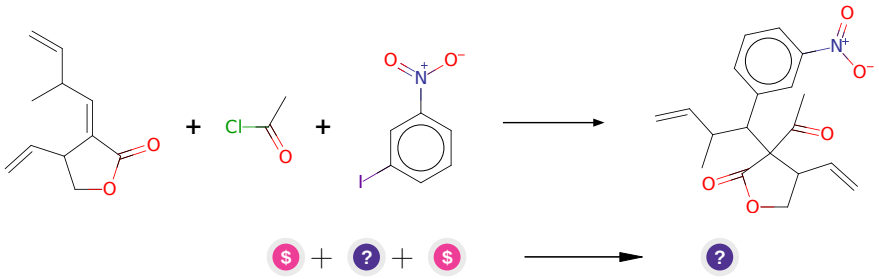
Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732

2.3.4 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. C=CC(C)/C=C1/C(=O)OCC1C=C
3. 1-Iodo-3-nitrobenzene - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

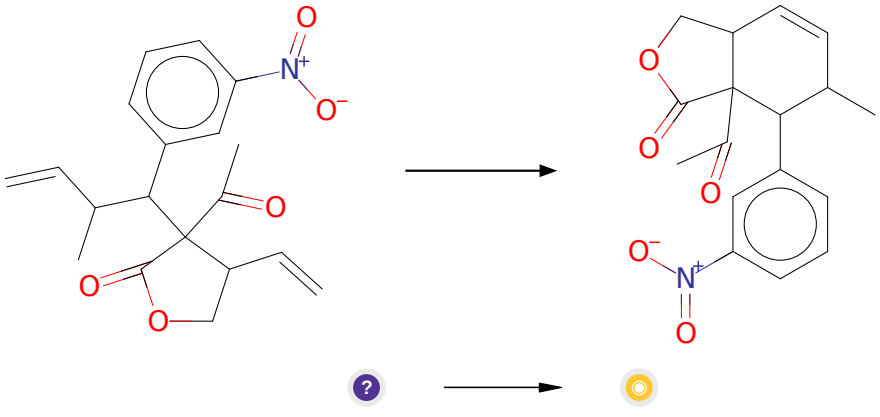
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 20524

2.3.5 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cccc([N+](=O)[O-])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 Path 4

Score: `156.35`

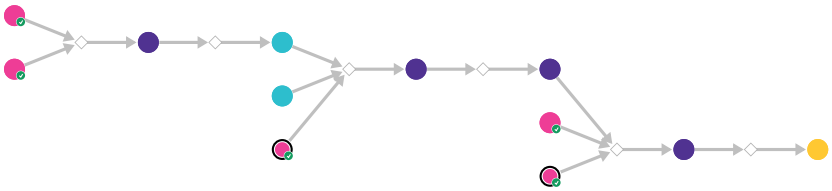
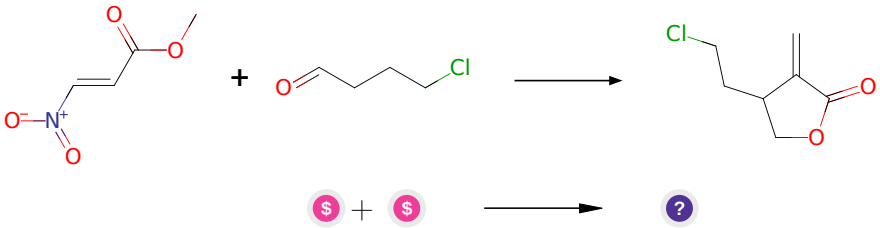


Figure 4: Outline of path 4

2.4.1 Stereoselective condensation of aldehydes with nitroalkenes followed by reduction/elimination



Substrates:

1. methyl (2E)-3-nitroprop-2-enoate - *available at Sigma-Aldrich*
2. 4-Chlorobutanal - *available at Sigma-Aldrich*

Products:

1. C=C1C(=O)OCC1CCCl

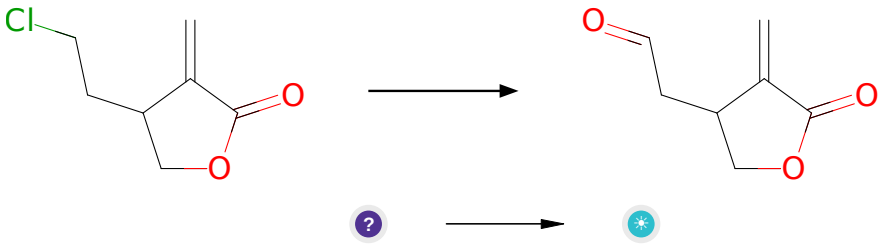
Typical conditions: organocatalyst.chloroform then NaBH4.MeOH then DBU

Protections: none

Reference: *10.1021/acs.orglett.7b00254*

Retrosynthesis ID: 10007505

2.4.2 Kornblum Oxidation



Substrates:

1. C=C1C(=O)OCC1CCCl

Products:

1. C7H8O3

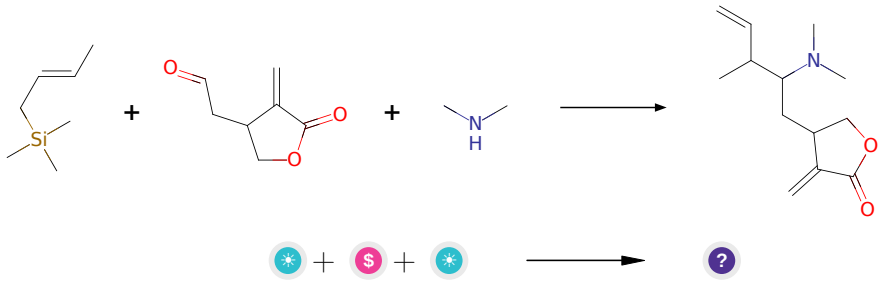
Typical conditions: DMSO.NEt3

Protections: none

Reference: *10.1080/00397918608056381* and *10.1002/9780470638859.conrr373*

Retrosynthesis ID: 11658

2.4.3 Aza-Hosomi-Sakurai Reaction



Substrates:

1. 2-butenyltrimethylsilane
2. Dimethylamine - *available at Sigma-Aldrich*
3. C7H8O3

Products:

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

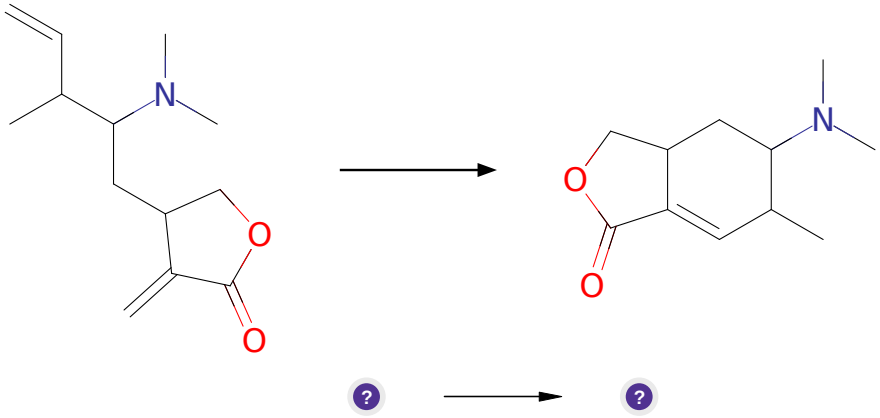
Typical conditions: Lewis.Acid.or.TBAF.THF

Protections: none

Reference: *10.1021/ja306362m* AND *10.1021/ja0262582*

Retrosynthesis ID: 5684

2.4.4 Ring-Closing Metathesis



Substrates:

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

Products:

1. CC1C=C2C(=O)OCC2CC1N(C)C

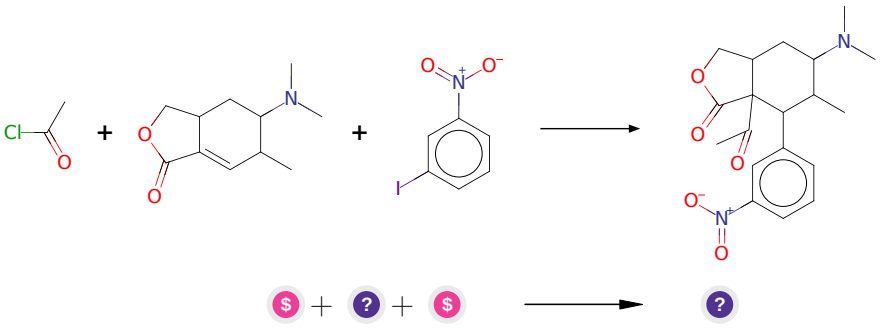
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1021/jo202073n* and *10.1021/jm060486f* and *10.1039/B801206G* and *10.1021/ol052856k*

Retrosynthesis ID: 31014201

2.4.5 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. 1-Iodo-3-nitrobenzene - *available at Sigma-Aldrich*
2. CC1C=C2C(=O)OCC2CC1N(C)C
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1CC(N(C)C)C(C)C2c1cccc([N+](=O)[O-])c1

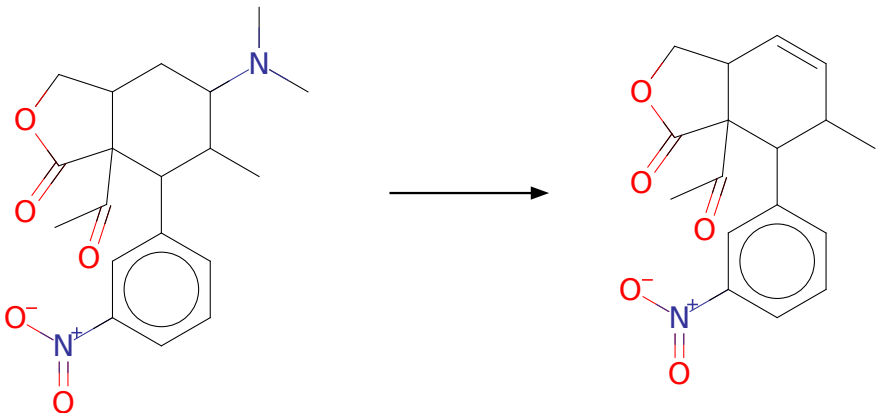
Typical conditions: 1.RCuLi.2.AcCl.HMPA

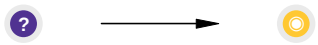
Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 12521

2.4.6 Hofmann Elimination





Substrates:

1. CC(=O)C12C(=O)OCC1CC(N(C)C)C(C)C2c1cccc([N+](=O)[O-])c1

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cccc([N+](=O)[O-])c1

Typical conditions: 1. MeI 2. Ag2O or NaOMe.heat

Protections: none

Reference: *10.1021/ja00023a034* and *10.1021/jo00301a036* and *10.1021/ja00716a066*

Retrosynthesis ID: 31010847

2.5 Path 5

Score: `164.14`

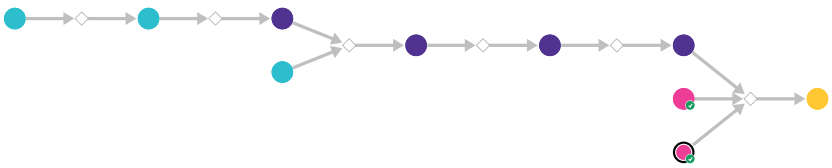
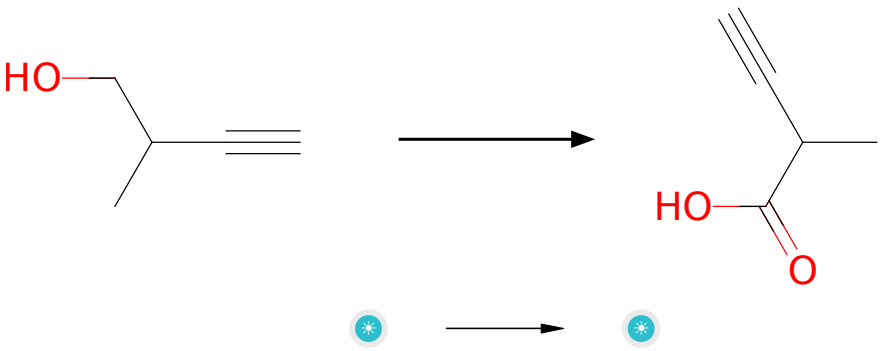


Figure 5: Outline of path 5

2.5.1 Jones Oxidation



Substrates:

1. 2-methyl-3-butyn-1-ol

Products:

1. 2-methyl-but-3-ynoic acid

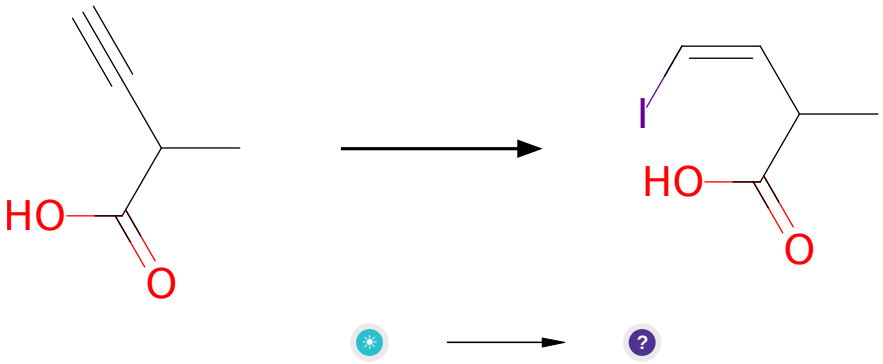
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

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

Retrosynthesis ID: 11160

2.5.2 Synthesis of Z-vinyl iodides



Substrates:

1. 2-methyl-but-3-ynoic acid

Products:

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

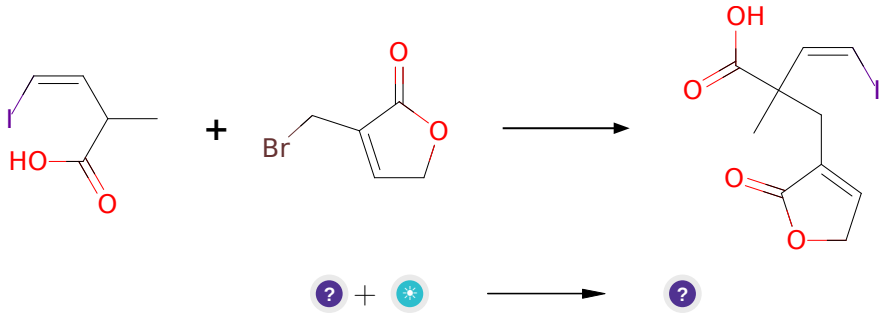
Typical conditions: InCl3.DIBALH.Et3B then I2

Protections: none

Reference: *10.1021/jo0344790* and *10.1021/ol026401w* and *10.1021/ol4014574* and *10.1021/ol203162s* and *10.1002/anie.201100718*

Retrosynthesis ID: 26288

2.5.3 Alkylation of carboxylic acids



Substrates:

1. CC(/C=C\I)C(=O)O
2. 3-bromomethyl-5h-furan-2-one

Products:

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

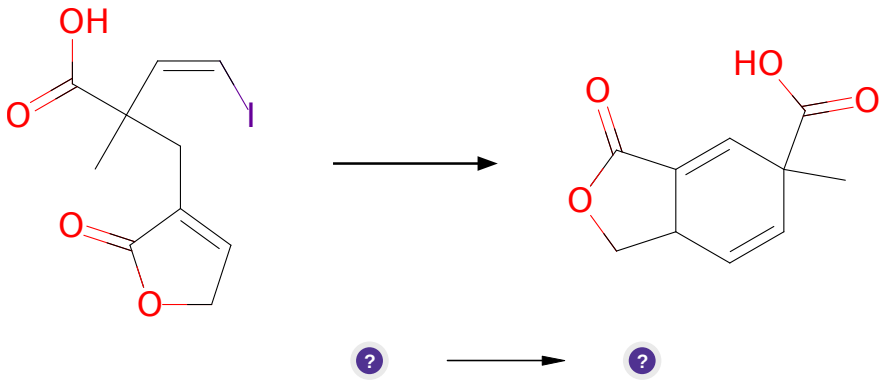
Typical conditions: nBuLi.THF.DIPEA

Protections: none

Reference: *10.1080/15257770.2013.820833* AND *10.1021/jm00078a017* AND *10.1016/j.bmc.2003.12.039* AND *10.1021/ml500411h*(SI,page 11) AND *10.1016/j.tet.2010.12.020* AND *10.1016/j.bmcl.2015.07.101*

Retrosynthesis ID: 28537

2.5.4 Heck Reaction



Substrates:

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

Products:

1. CC1(C(=O)O)C=CC2COC(=O)C2=C1

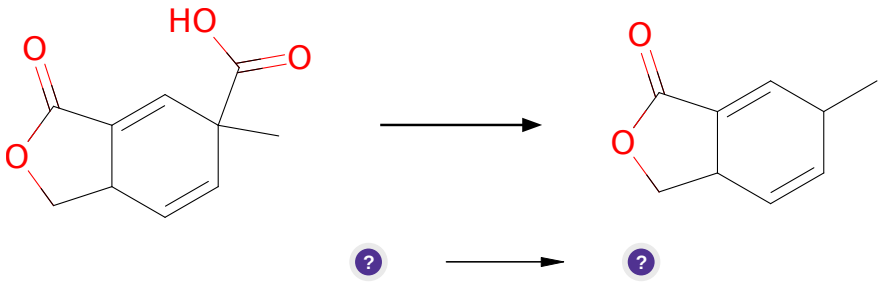
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

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

2.5.5 Decarboxylation of tertiary carboxylic acids



Substrates:

1. CC1(C(=O)O)C=CC2COC(=O)C2=C1

Products:

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

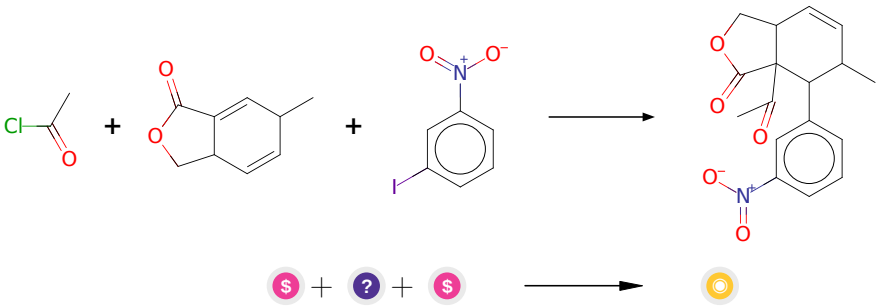
Typical conditions: DMSO.135C

Protections: none

Reference: DOI: *10.1021/jm990630f* AND *10.1016/S0040-4039(99)02191-7*

Retrosynthesis ID: 7791

2.5.6 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. 1-Iodo-3-nitrobenzene - *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)C2c1cccc([N+](=O)[O-])c1

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

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 12521