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

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

2.1 Path 1

Score: `125.08`

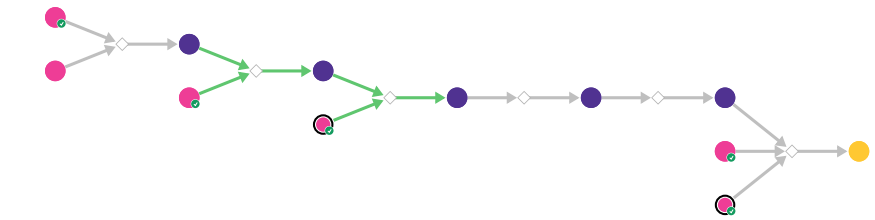
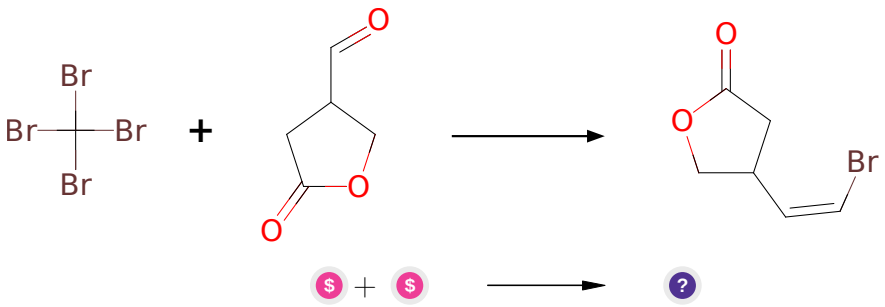


Figure 1: Outline of path 1

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

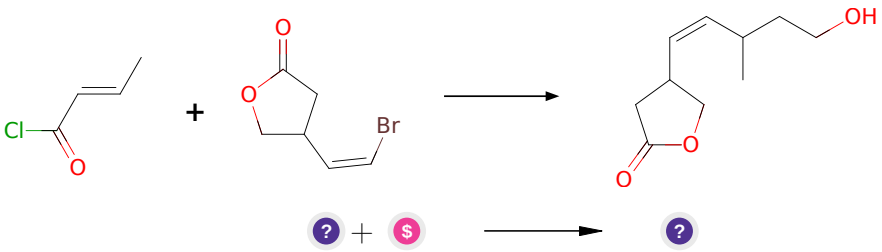
Typical conditions: 1.CBr4.Ph3P.TEA.THF.cooling to rt.2. nBu3SnH.Pd(PPh3)4.toluene.rt

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

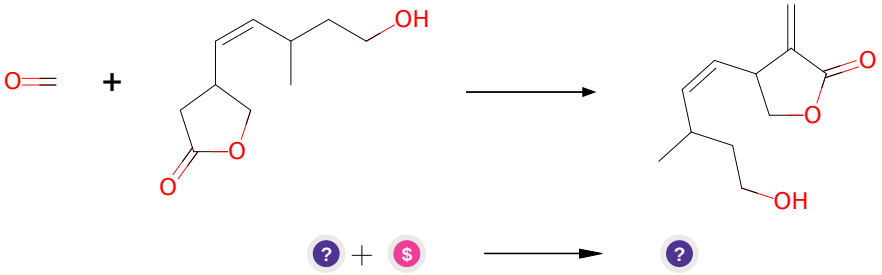
Typical conditions: 1.Chiral auxiliary(Oppolzer's,Evans' or Seebach's).or.ephedrine.2.RMgX.3.LAH

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

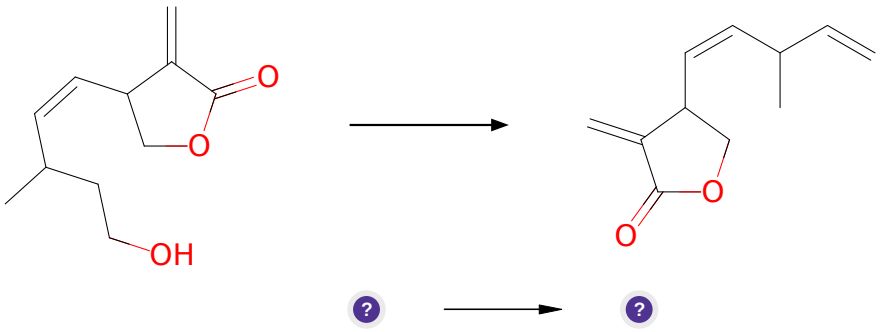
Typical conditions: iPr2NH.TFA.HCHO.or.organocatalyst

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

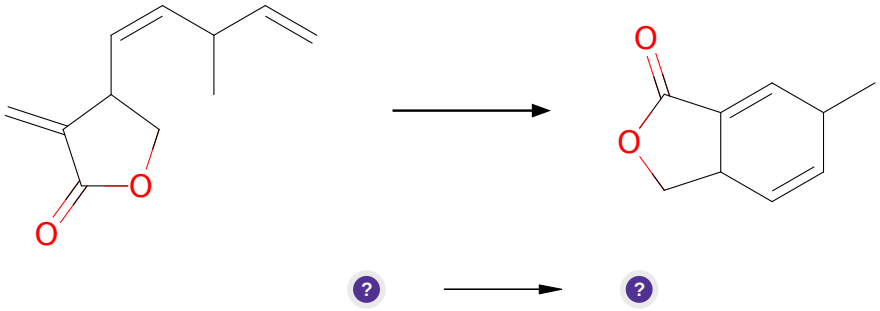
Typical conditions: PhSeCN.PBu3.THF then H2O2.THF.H2O

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

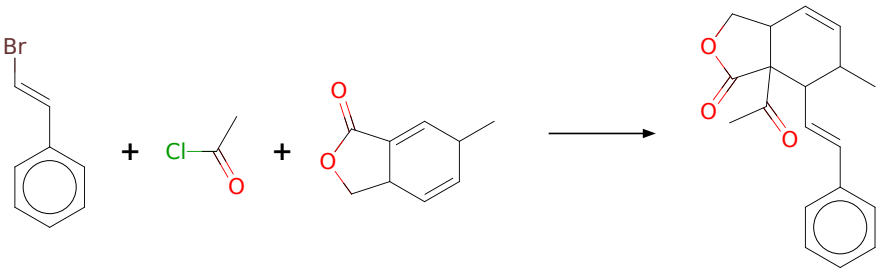
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

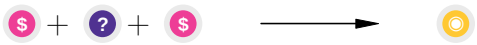
Protections: none

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

Retrosynthesis ID: 31014201

2.1.6 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: 132.89

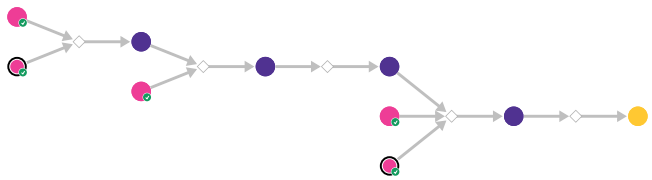
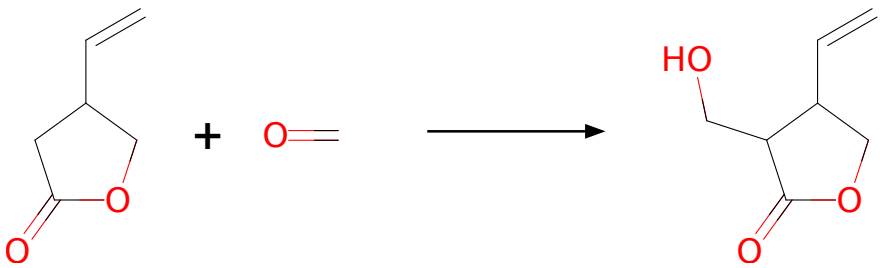
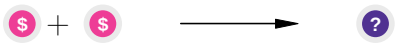


Figure 2: Outline of path 2

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

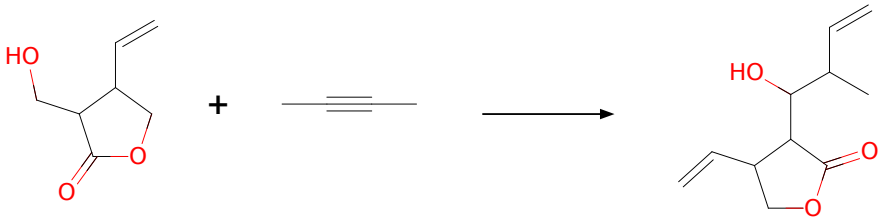
Typical conditions: LDA.THF

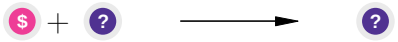
Protections: none

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

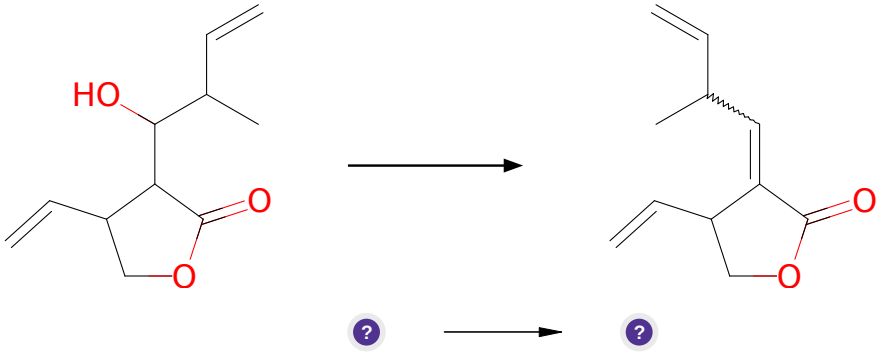
Typical conditions: H2Ru(CO)(PPh3)3.2,4,6-(iPr)3PhSO3H.SL-J009-1.TBAI.IPA.THF.95C

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=C1C(=O)OCC1C=C

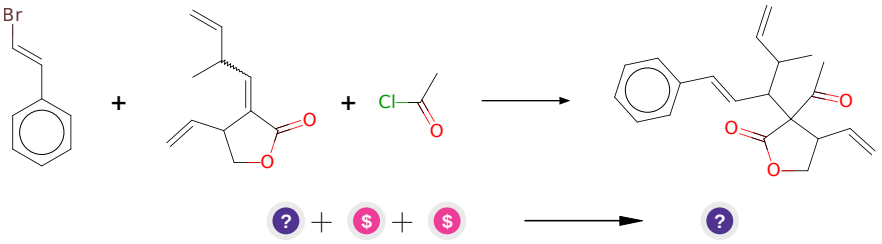
Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7731

2.2.4 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

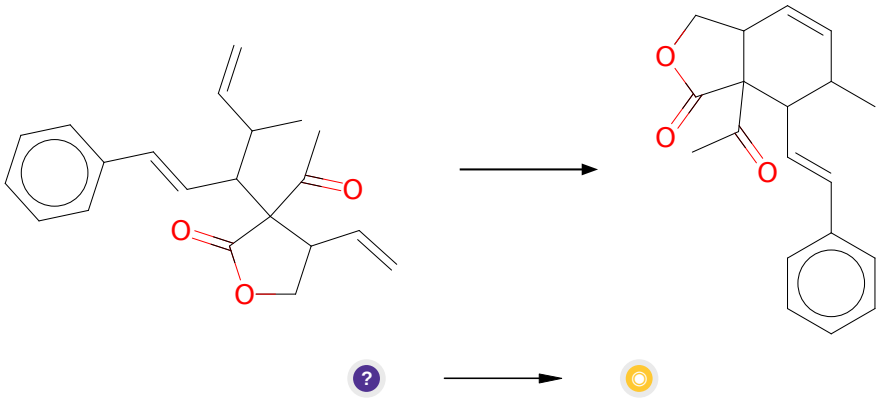
Typical conditions: 1.RCuLi.2.AcCl.HMPA

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

2.2.5 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

2.3 Path 3

Score: 137.29

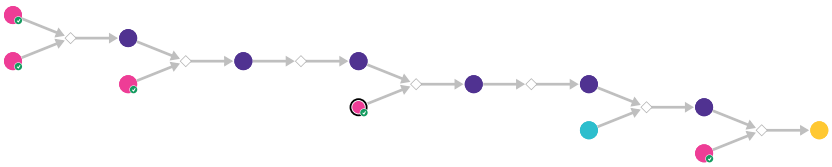
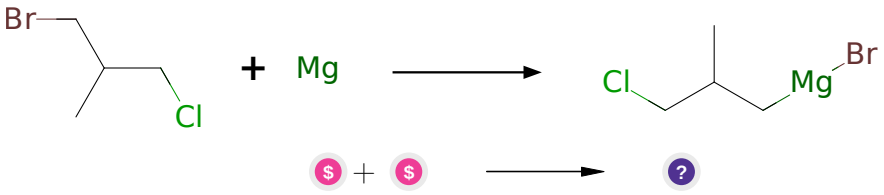


Figure 3: Outline of path 3

2.3.1 Synthesis of alkyl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. 1-bromo-3-chloro-2-methylpropane - *available at Sigma-Aldrich*

Products:

1. CC(CCl)C[Mg]Br

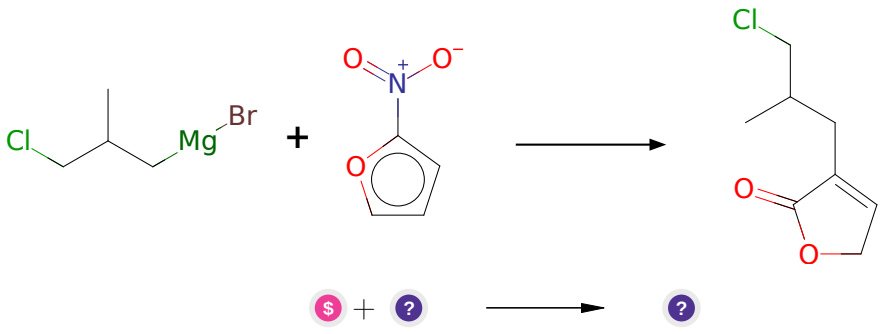
Typical conditions: Mg.THF or iPrMgBr

Protections: none

Reference: DOI: *10.1021/jo00002a039* and *10.1021/jo047877r* and *10.1021/ol006618v*

Retrosynthesis ID: 10011828

2.3.2 Reaction of nitrofurans with Grignard reagent



Substrates:

1. 2-Nitrofuran - *available at Sigma-Aldrich*
2. CC(CCl)C[Mg]Br

Products:

1. CC(CCl)CC1=CCOC1=O

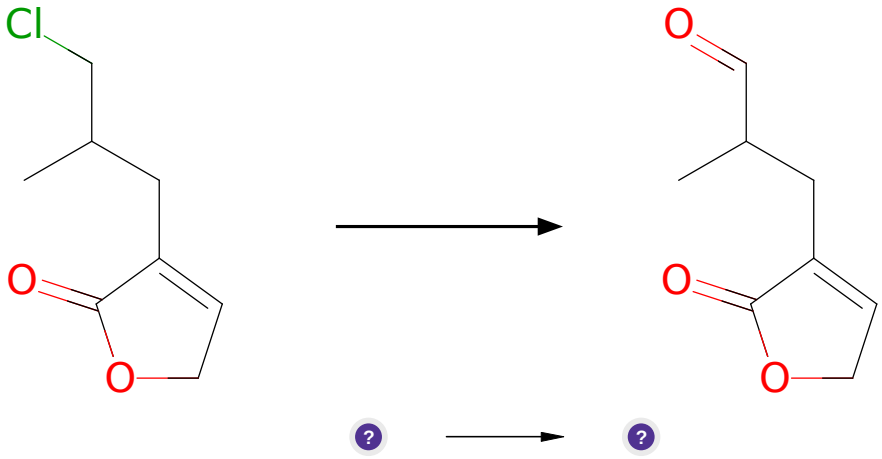
Typical conditions: Et2O.-90C

Protections: none

Reference: *10.1016/S0040-4020(01)89063-3*

Retrosynthesis ID: 49680

2.3.3 Kornblum Oxidation



Substrates:

1. CC(CCl)CC1=CCOC1=O

Products:

1. CC(C=O)CC1=CCOC1=O

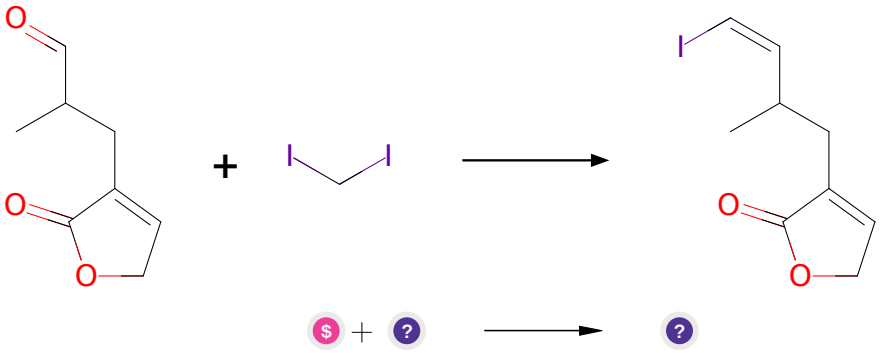
Typical conditions: DMSO.NEt3

Protections: none

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

Retrosynthesis ID: 11658

2.3.4 Iodoolefination of aldehydes



Substrates:

1. Diiodomethane - *available at Sigma-Aldrich*
2. CC(C=O)CC1=CCOC1=O

Products:

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

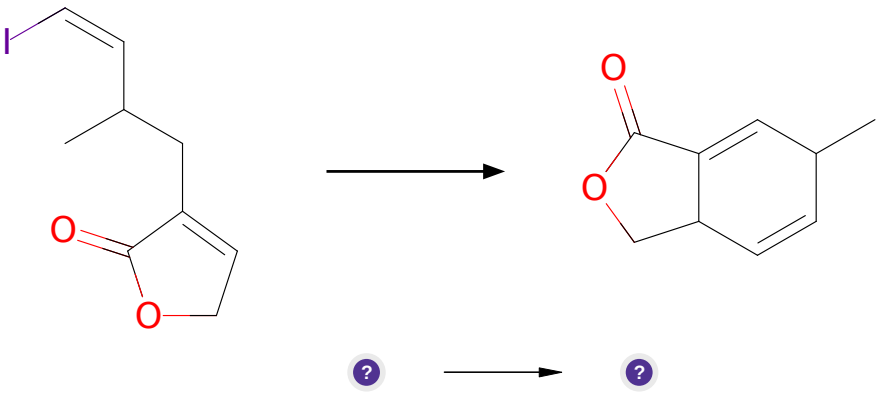
Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

Protections: none

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

Retrosynthesis ID: 10001773

2.3.5 Heck Reaction



Substrates:

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

Products:

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

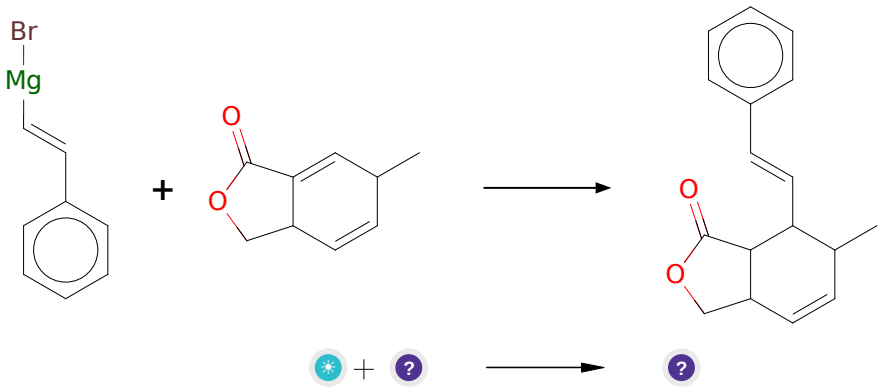
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

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

2.3.6 Conjugate addition of organocuprate



Substrates:

1. styrylmagnesium bromide
2. CC1C=CC2COC(=O)C2=C1

Products:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1

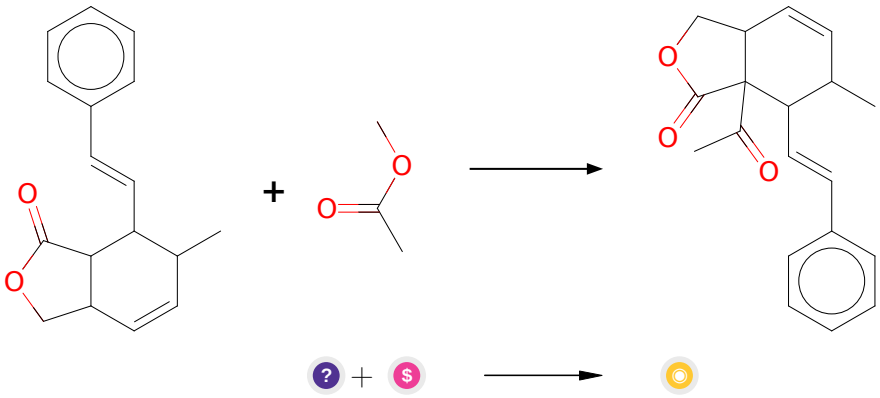
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

Protections: none

Reference: *10.1021/ol036071v* AND *10.1016/j.tet.2011.12.046* AND *10.1002/anie.201007644* AND *10.1002/anie.201007644* AND *10.1055/s-1997-1371*

Retrosynthesis ID: 10003578

2.3.7 Claisen Condensation



Substrates:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

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

Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.4 Path 4

Score: `152.54`

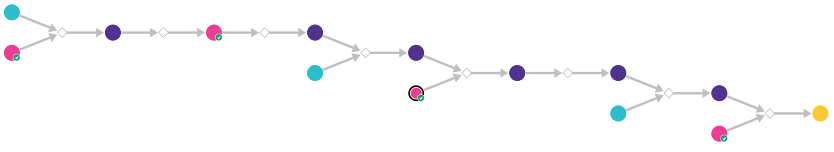
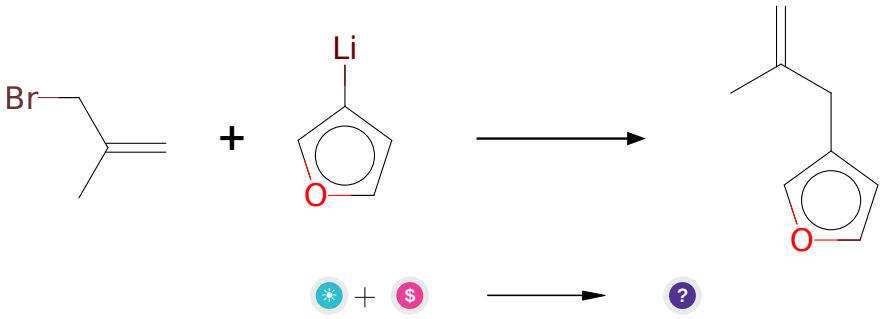


Figure 4: Outline of path 4

2.4.1 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. 3-lithiofuran
2. Methallyl bromide - *available at Sigma-Aldrich*

Products:

1. C=C(C)Cc1ccoc1

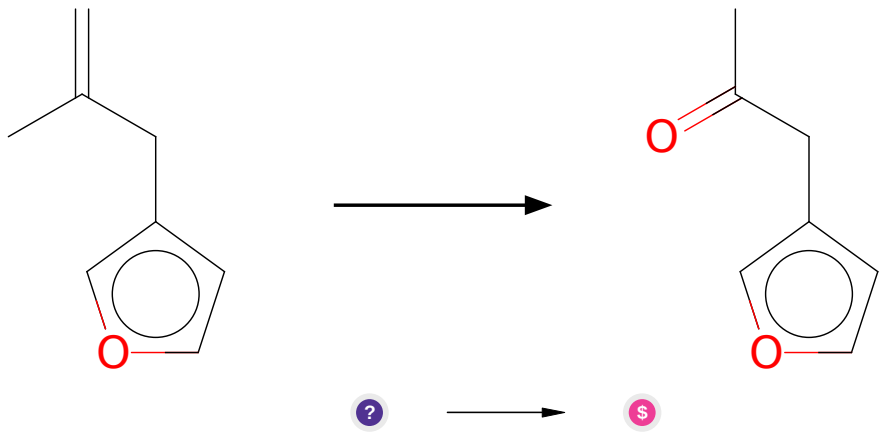
Typical conditions: CuCNxLiCl.THF

Protections: none

Reference: *10.1021/jo500347a* and *10.1016/j.bmcl.2010.10.006* and *10.1002/chem.200901432* and *10.1016/j.tet.2010.05.051* and *10.1016/j.ejmech.2011.09.012* and *10.1021/ja5102739*

Retrosynthesis ID: 10019533

2.4.2 Ozonolysis



Substrates:

1. C=C(C)Cc1ccoc1

Products:

1. 1-(furan-3-yl)propan-2-one - *available at Sigma-Aldrich*

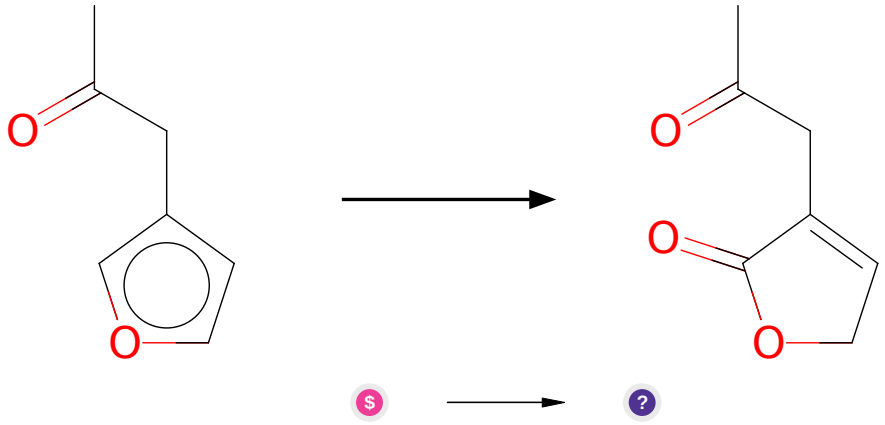
Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5077

2.4.3 Oxidation furans to 2-(5H)-furanones



Substrates:

1. 1-(furan-3-yl)propan-2-one - *available at Sigma-Aldrich*

Products:

1. CC(=O)CC1=CCOC1=O

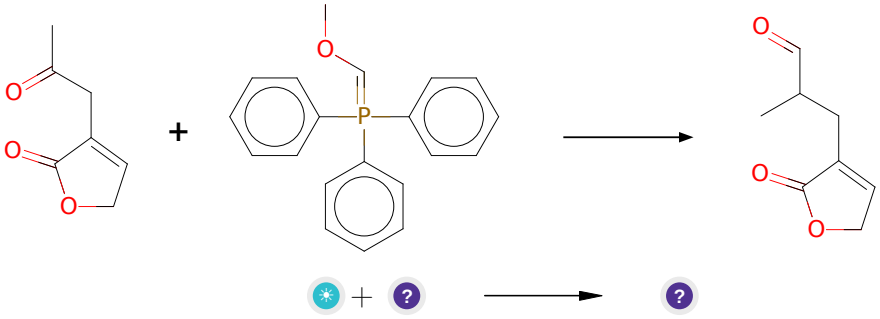
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

Reference: DOI: *10.1055/s-2005-869865*

Retrosynthesis ID: 50717

2.4.4 Olefination of ketones followed by hydrolysis



Substrates:

1. triphenylphosphonium methoxymethylide
2. CC(=O)CC1=CCOC1=O

Products:

1. CC(C=O)CC1=CCOC1=O

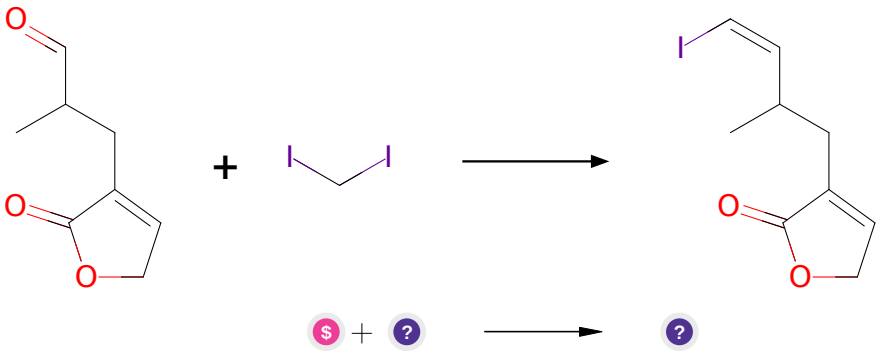
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

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

2.4.5 Iodoolefination of aldehydes



Substrates:

1. Diiodomethane - *available at Sigma-Aldrich*

2. CC(C=O)CC1=CCOC1=O

Products:

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

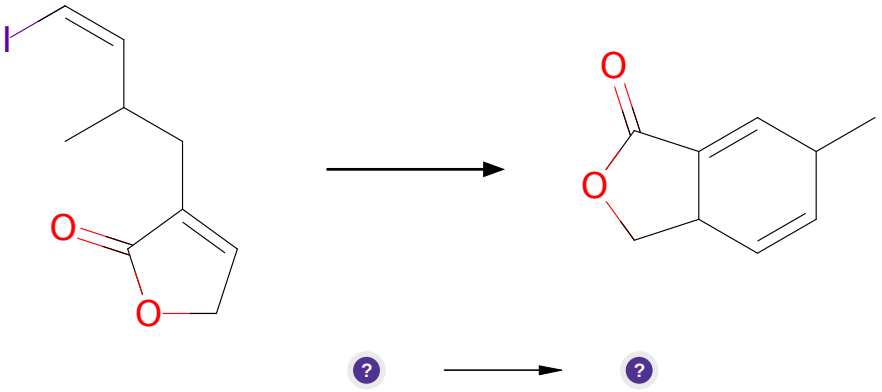
Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

Protections: none

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

Retrosynthesis ID: 10001773

2.4.6 Heck Reaction



Substrates:

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

Products:

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

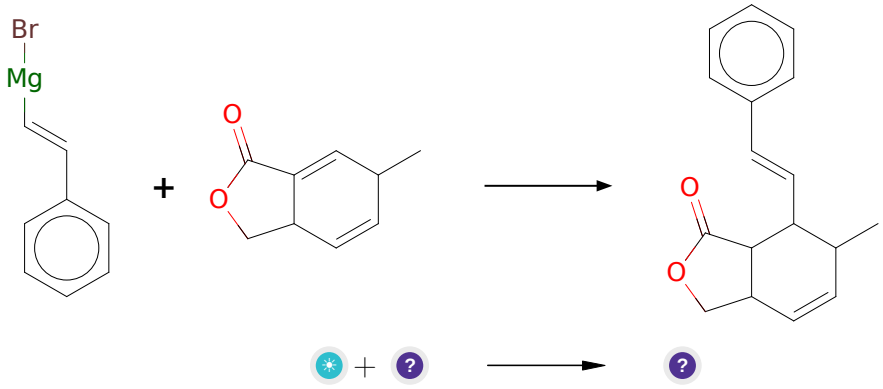
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

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

2.4.7 Conjugate addition of organocuprate



Substrates:

1. styrylmagnesium bromide
2. CC1C=CC2COC(=O)C2=C1

Products:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1

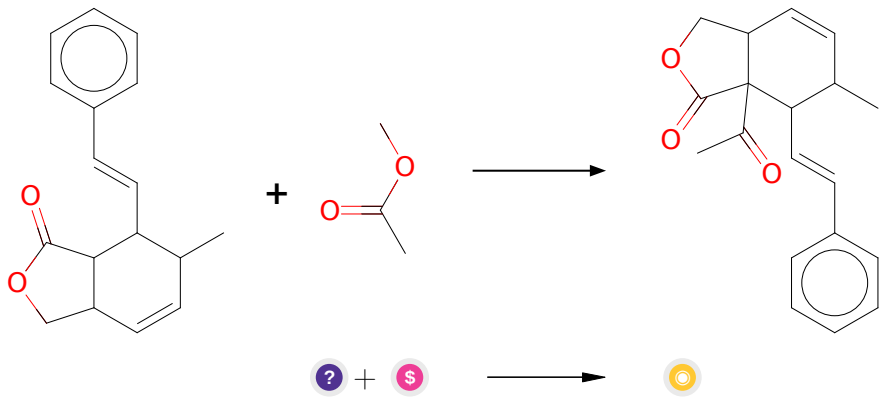
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

Protections: none

Reference: *10.1021/ol036071v* AND *10.1016/j.tet.2011.12.046* AND *10.1002/anie.201007644* AND *10.1002/anie.201007644* AND *10.1055/s-1997-1371*

Retrosynthesis ID: 10003578

2.4.8 Claisen Condensation



Substrates:

1. CC1C=CC2COC(=O)C2C1/C=C/c1ccccc1
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

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

Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015