Paths of analysis*

L10

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: `115.31`

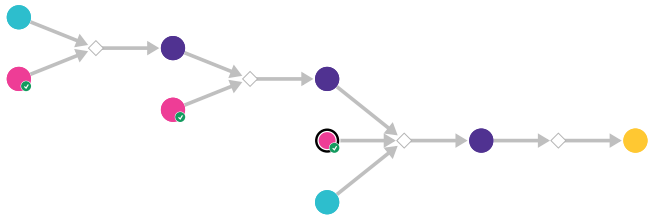
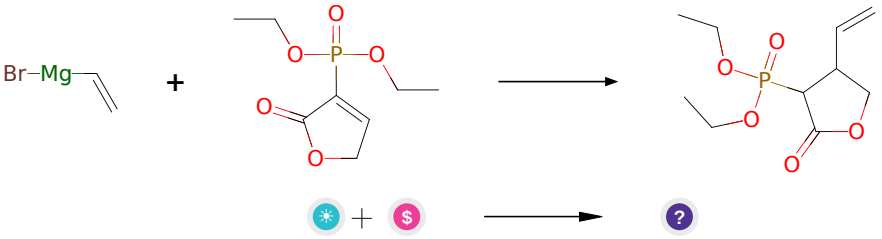


Figure 1: Outline of path 1

2.1.1 Conjugate addition of organocuprate



Substrates:

1. a-diethoxyphosphinyl-da,b-butenolide
2. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)C1P(=O)(OCC)OCC

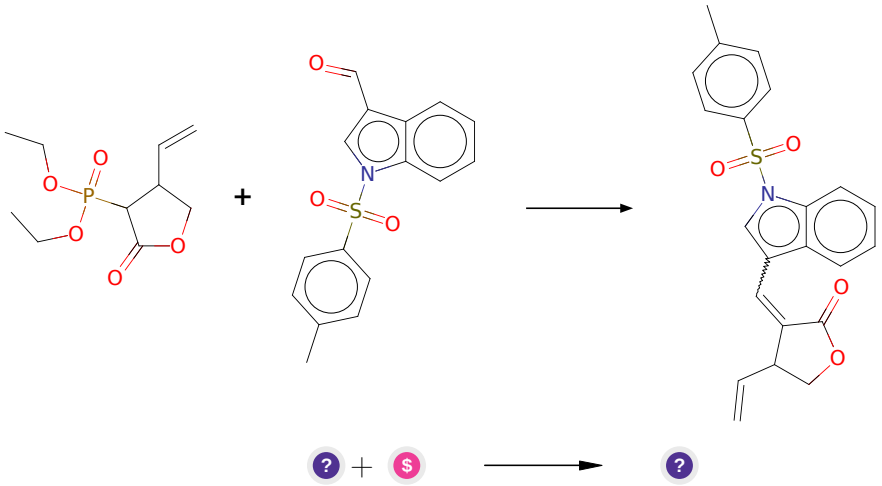
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

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: 10003577

2.1.2 Wittig-Horner Reaction



Substrates:

1. C=CC1COC(=O)C1P(=O)(OCC)OCC
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)C1=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

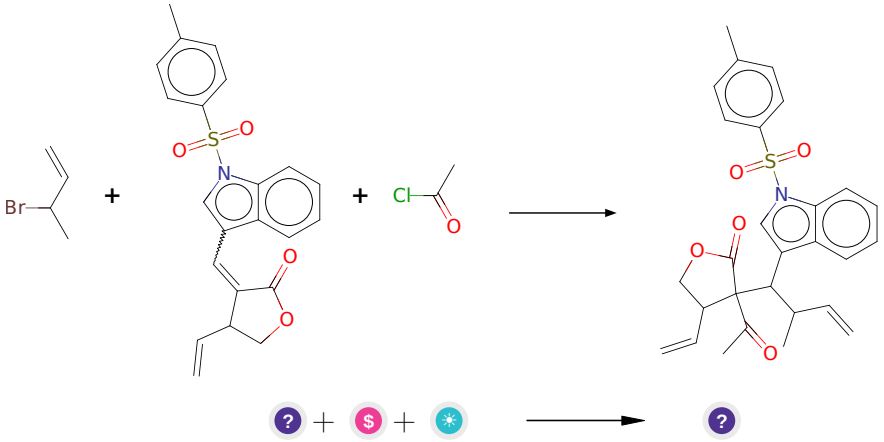
Typical conditions: NaH.THF.0 C or NaH.DMF.0-50 C

Protections: none

Reference: *10.1021/acs.jmedchem.5b01239* p. 63, 71 and *10.1021/jm950725r* p. 3150, 3153

Retrosynthesis ID: 11549

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



Substrates:

1. C=CC1COC(=O)C1=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12
2. Acetyl chloride - *available at Sigma-Aldrich*
3. 3-brom-but-1-en

Products:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

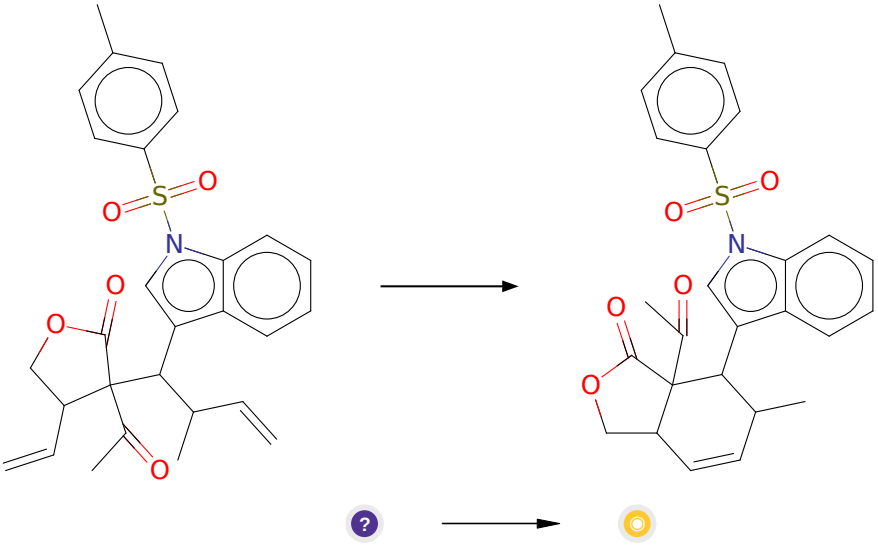
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20527

2.1.4 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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 Path 2

Score: `132.89`

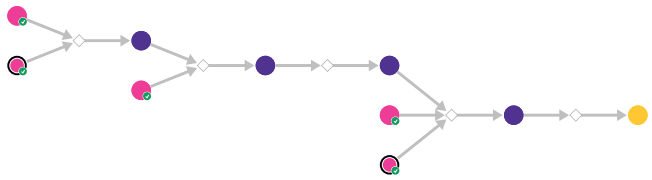
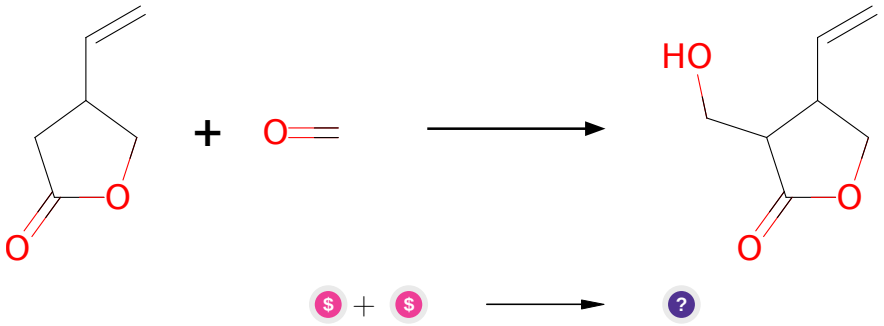


Figure 2: Outline of path 2

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

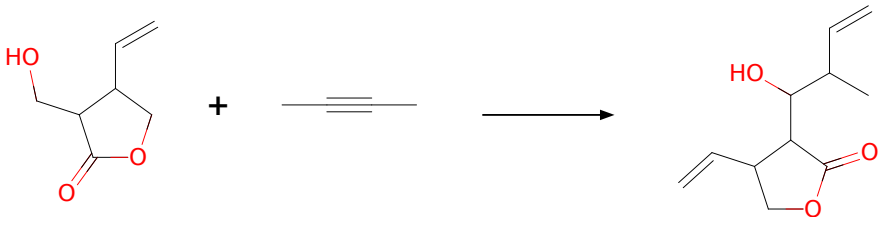
Typical conditions: LDA.THF

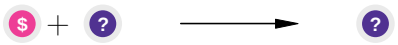
Protections: none

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

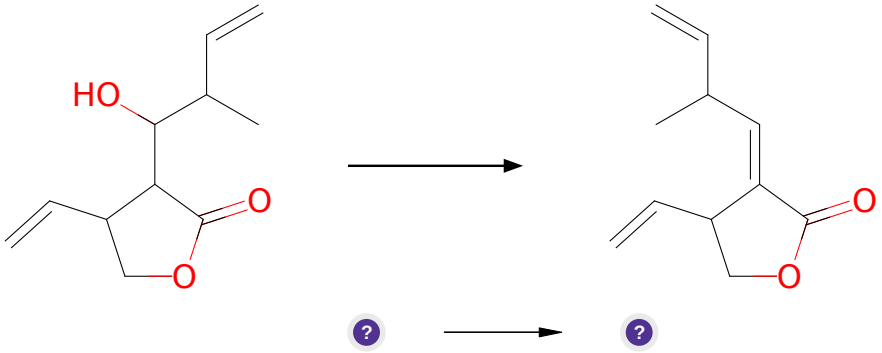
Typical conditions: H2Ru(CO)(PPh3)3.2,4,6-(iPr)3PhSO3H.SL-J009-1.TBAI.IPA.THF.95C

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

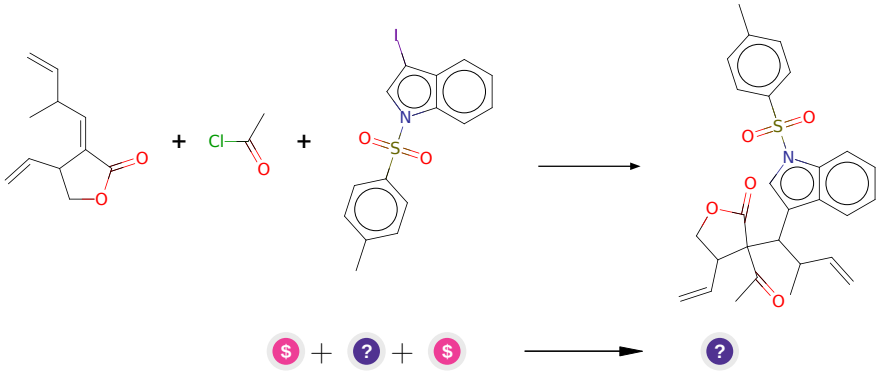
Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

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



Substrates:

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

Products:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

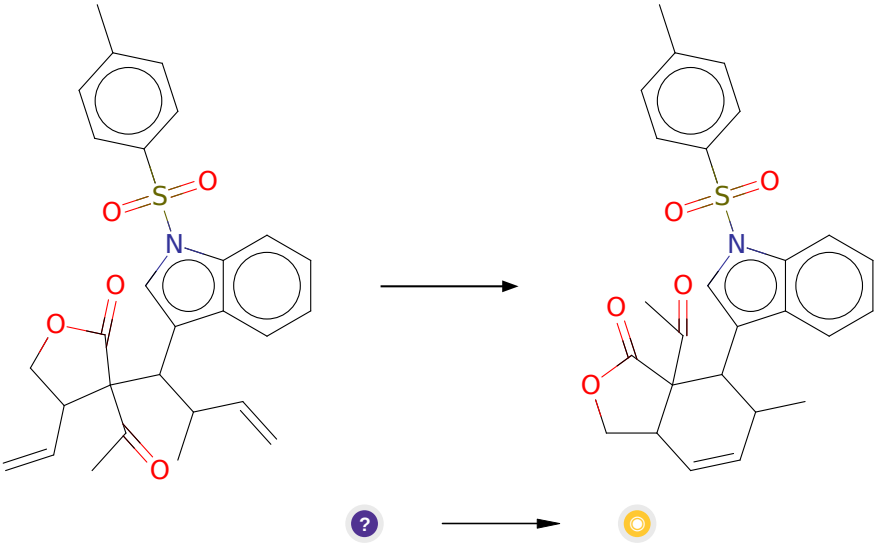
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20524

2.2.5 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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: `132.89`

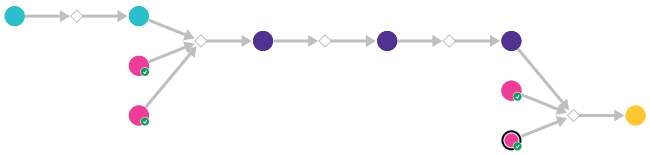
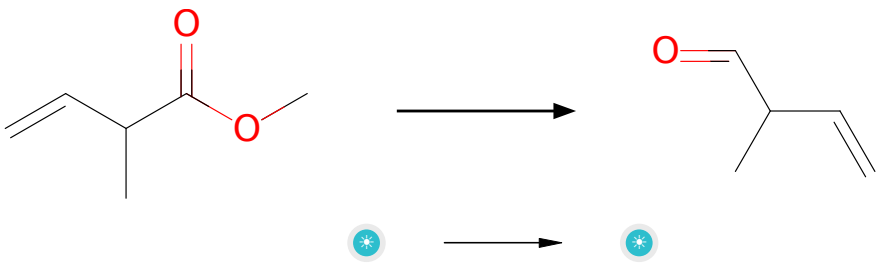


Figure 3: Outline of path 3

2.3.1 Aldehyde Formation



Substrates:

1. 2-methylbut-3-ensaeuremethylester

Products:

1. 2-methyl-but-3-enal

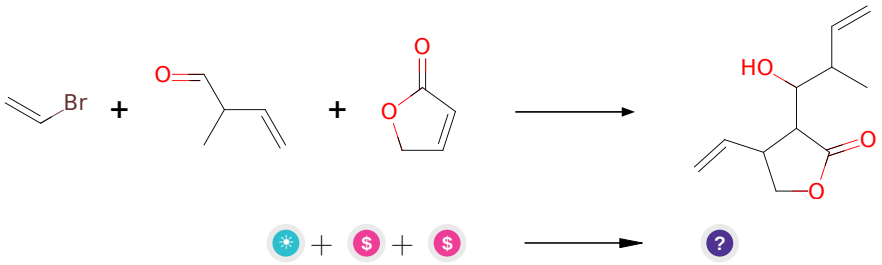
Typical conditions: DIBAL.solvent e.g. DCM

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 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. 2-methyl-but-3-enal
2. 2(5H)-Furanone - *available at Sigma-Aldrich*
3. Bromoethylene - *available at Sigma-Aldrich*

Products:

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

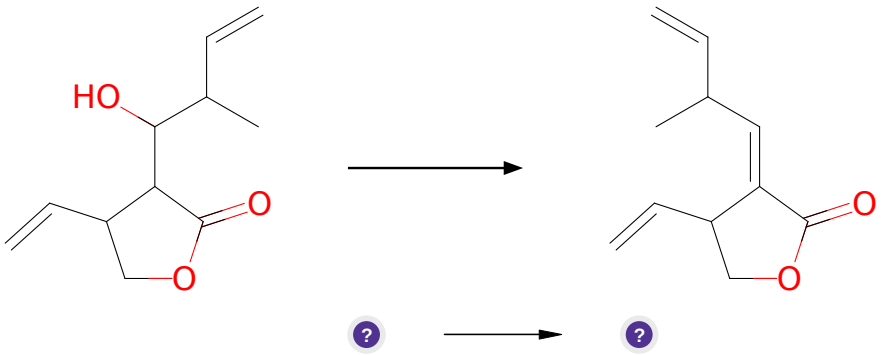
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13048

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

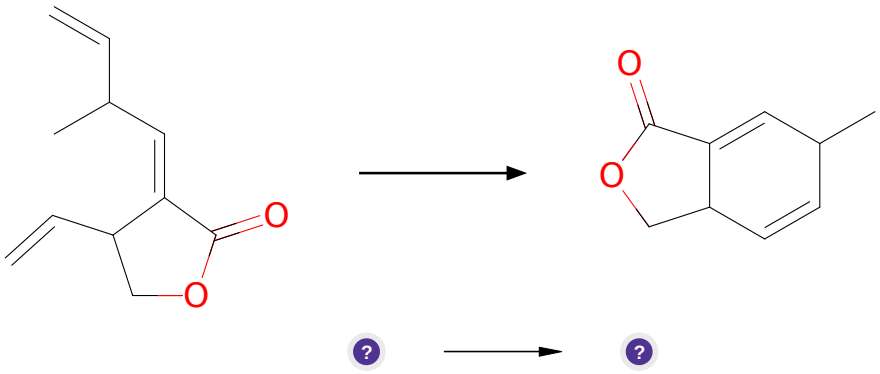
Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.3.4 Ring-Closing Metathesis



Substrates:

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

Products:

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

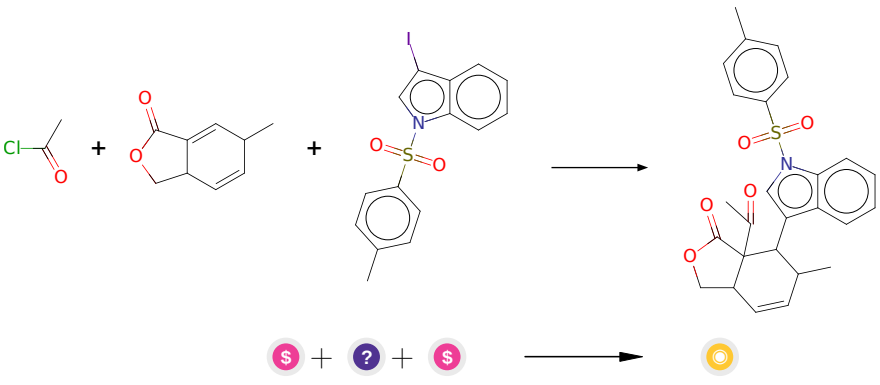
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *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)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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 Path 4

Score: 132.89

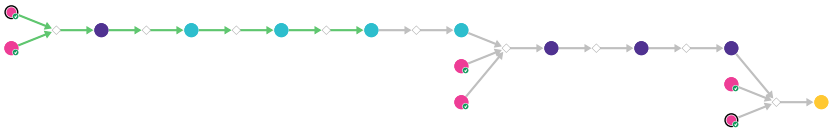
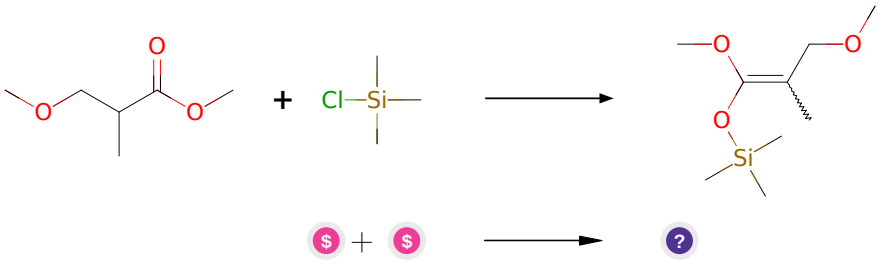


Figure 4: Outline of path 4

2.4.1 Enol esters and ethers synthesis



Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. methyl 3-methoxyisobutyrate - *available at Sigma-Aldrich*

Products:

1. COCC(C)=C(OC)O[Si](C)(C)C

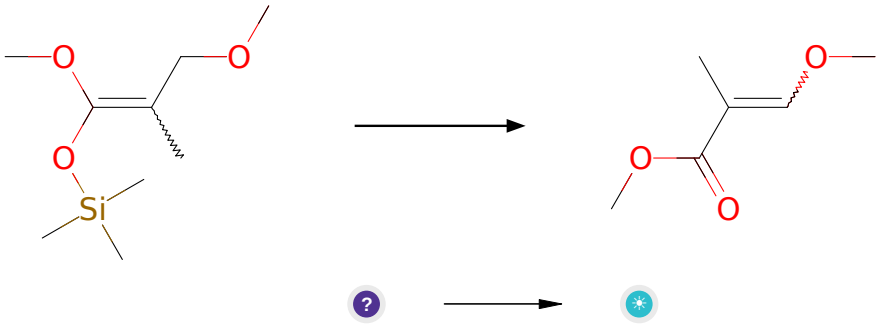
Typical conditions: 1. Et3N.Electrophile

Protections: none

Reference: *10.1016/S0040-4020(03)00977-3* AND *10.1021/ja00056a002*

Retrosynthesis ID: 7799

2.4.2 Dehydrogenation of silyl enol ethers



Substrates:

1. COCC(C)=C(OC)O[Si](C)(C)C

Products:

1. 3-methoxy-2-methyl-acrylsaeure-methylester

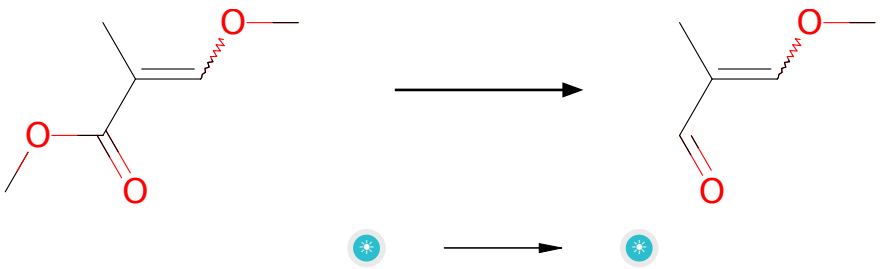
Typical conditions: CAN

Protections: none

Reference: *10.1016/0040-4039(95)00694-8* and *10.1021/jo961325u* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999878

2.4.3 Aldehyde Formation



Substrates:

1. 3-methoxy-2-methyl-acrylsaeure-methylester

Products:

1. 3-methoxy-2-methyl-propenal

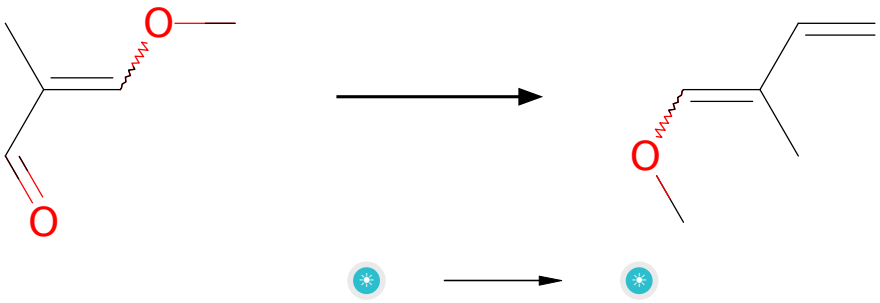
Typical conditions: DIBAL.solvent e.g. DCM

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

2.4.4 Tebbe Olefination



Substrates:

1. 3-methoxy-2-methyl-propenal

Products:

1. 1-methoxy-2-methyl-buta-1,3-diene

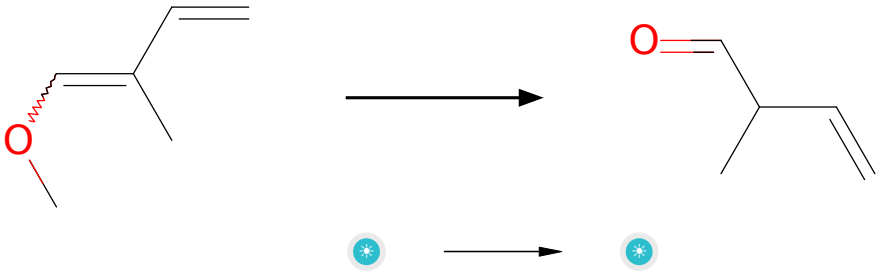
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

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

Retrosynthesis ID: 11714

2.4.5 Synthesis of ketones and aldehydes from enol ethers



Substrates:

1. 1-methoxy-2-methyl-buta-1,3-diene

Products:

1. 2-methyl-but-3-enal

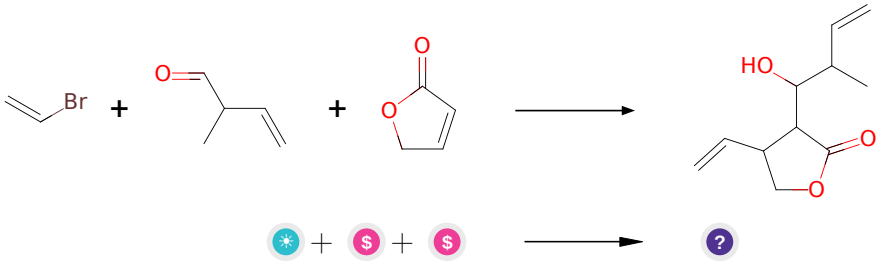
Typical conditions: [H+].THF

Protections: none

Reference: *10.1081/SCC-120023437* AND *10.1016/j.bmcl.2007.11.020* AND *10.1016/j.tet.2011.03.084* AND *10.1021/ja00270a023* AND *10.1055/s-1994-25424* AND

Retrosynthesis ID: 14842

2.4.6 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. 2-methyl-but-3-enal

2. 2(5H)-Furanone - *available at Sigma-Aldrich*

3. Bromoethylene - *available at Sigma-Aldrich*

Products:

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

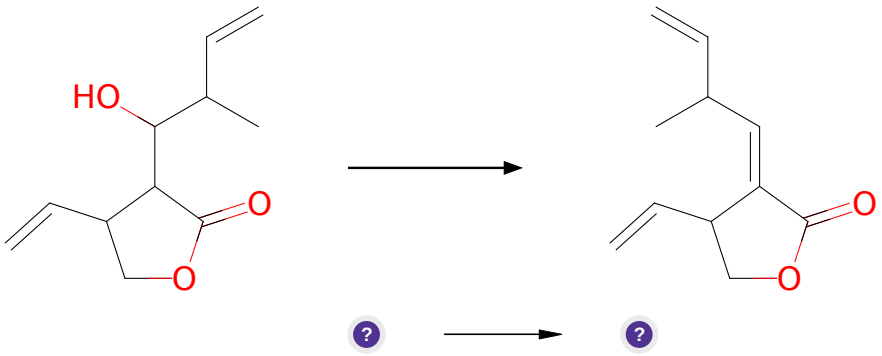
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13048

2.4.7 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

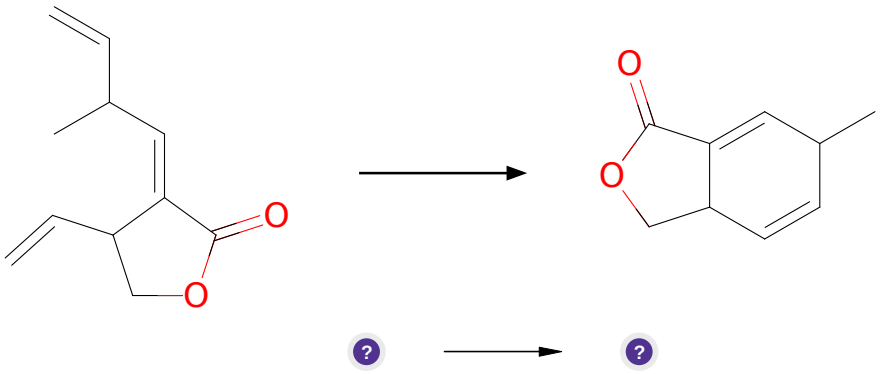
Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.4.8 Ring-Closing Metathesis



Substrates:

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

Products:

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

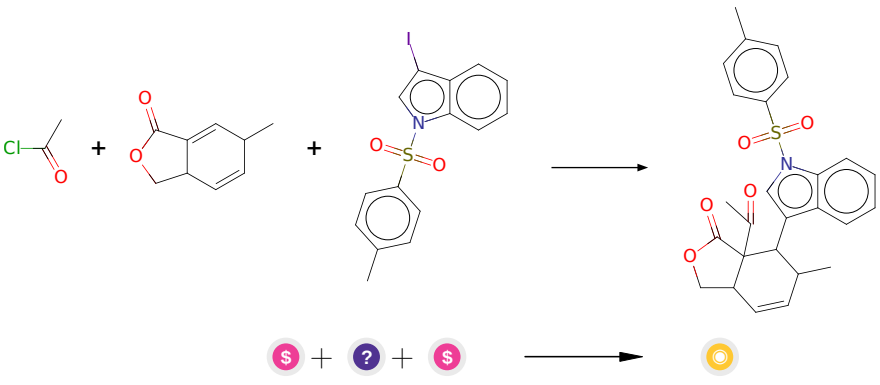
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *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)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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

2.5 Path 5

Score: 132.89

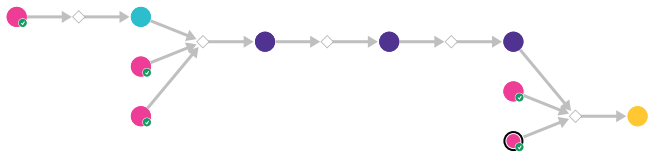
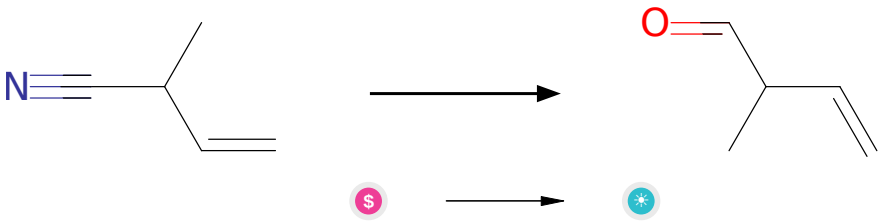


Figure 5: Outline of path 5

2.5.1 Reduction of nitriles to aldehydes



Substrates:

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

Products:

1. 2-methyl-but-3-enal

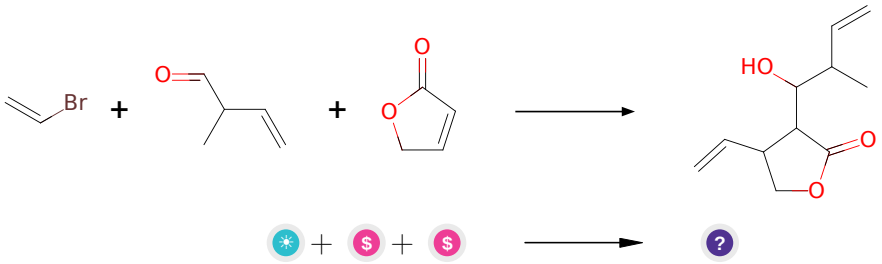
Typical conditions: DIBALH.DCM

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 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. 2-methyl-but-3-enal
2. 2(5H)-Furanone - *available at Sigma-Aldrich*
3. Bromoethylene - *available at Sigma-Aldrich*

Products:

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

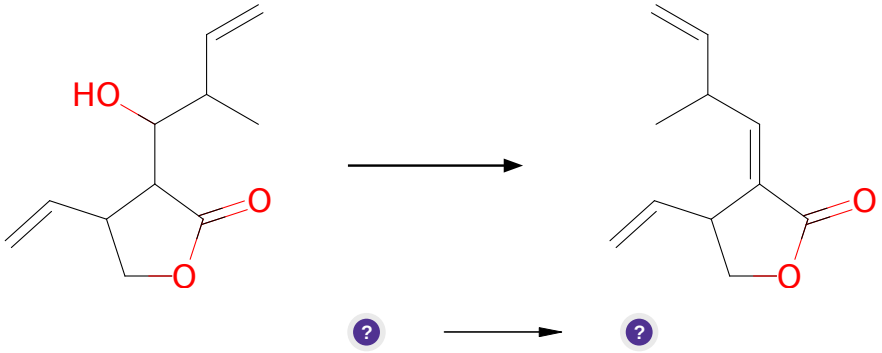
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13048

2.5.3 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

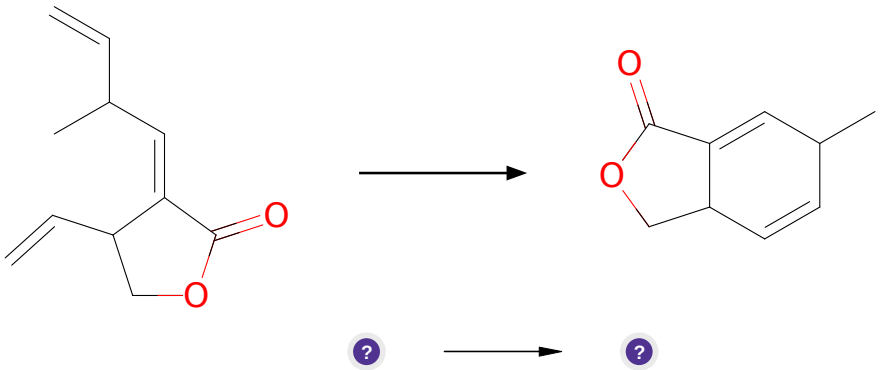
Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.5.4 Ring-Closing Metathesis



Substrates:

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

Products:

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

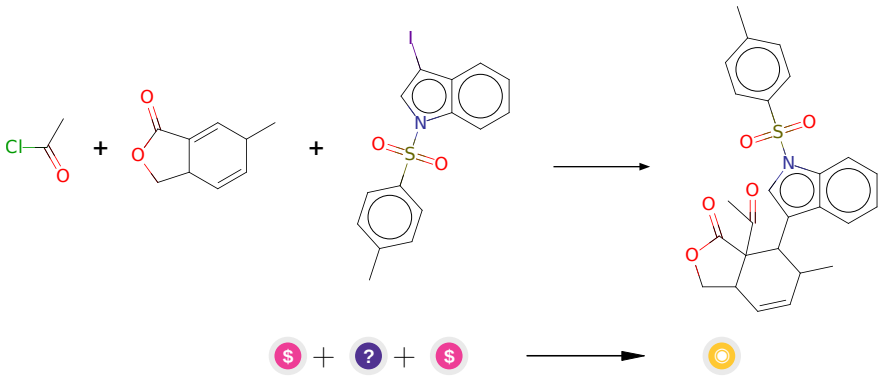
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *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)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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