Paths of analysis*

L5

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: `84.06`

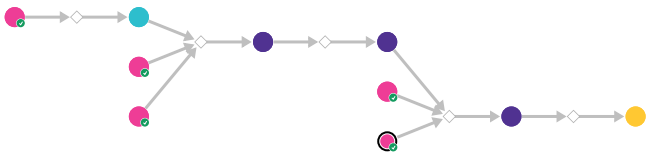
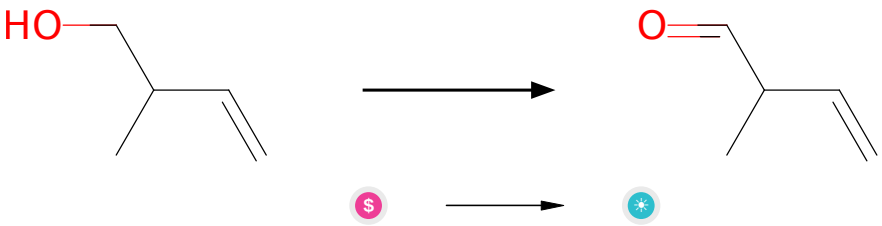


Figure 1: Outline of path 1

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

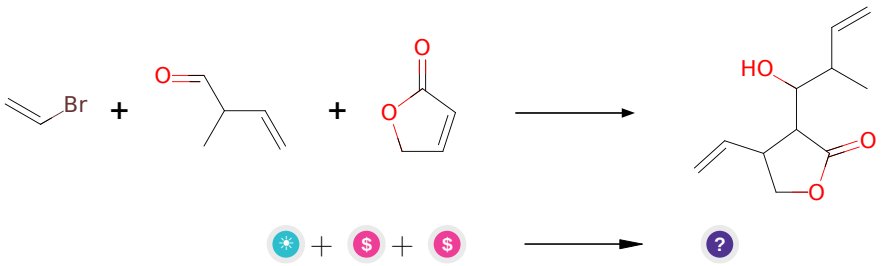
Typical conditions: DMP.DCM.0-25 C

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 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

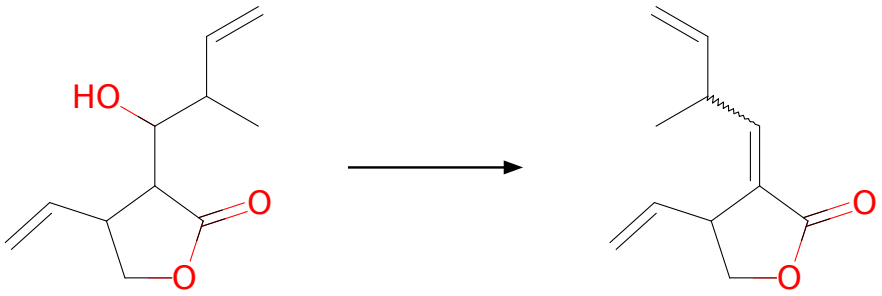
Typical conditions: 1.RCuLi.2.RCHO

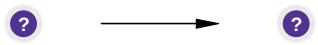
Protections: none

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

2.1.3 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

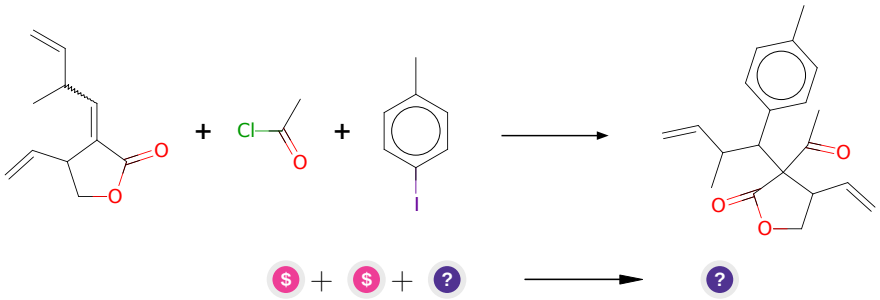
Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7731

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



Substrates:

1. 4-Iodotoluene - *available at Sigma-Aldrich*
2. Acetyl chloride - *available at Sigma-Aldrich*
3. C=CC(C)C=C1C(=O)OCC1C=C

Products:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)=O)C(=O)OCC1C=C

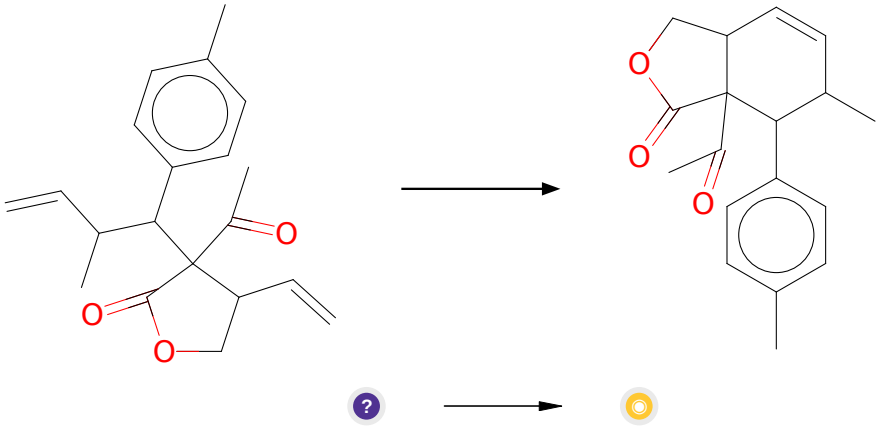
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20528

2.1.5 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C)cc1

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: `84.06`

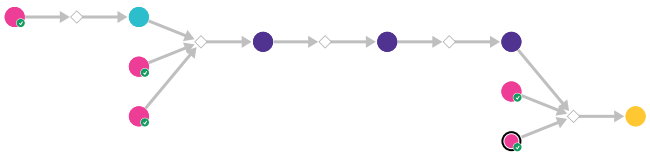
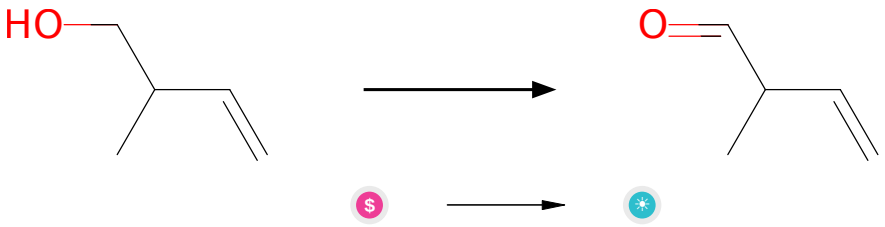


Figure 2: Outline of path 2

2.2.1 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

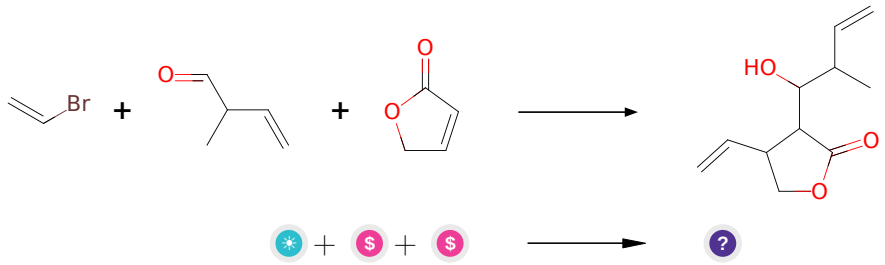
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.2.2 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

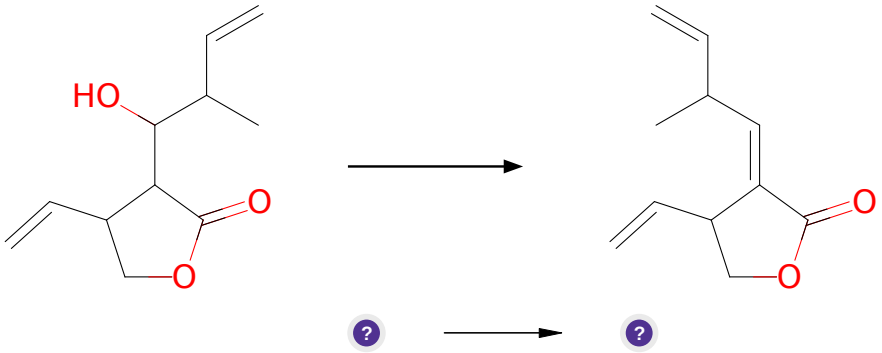
Typical conditions: 1.RCuLi.2.RCHO

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

2.2.3 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

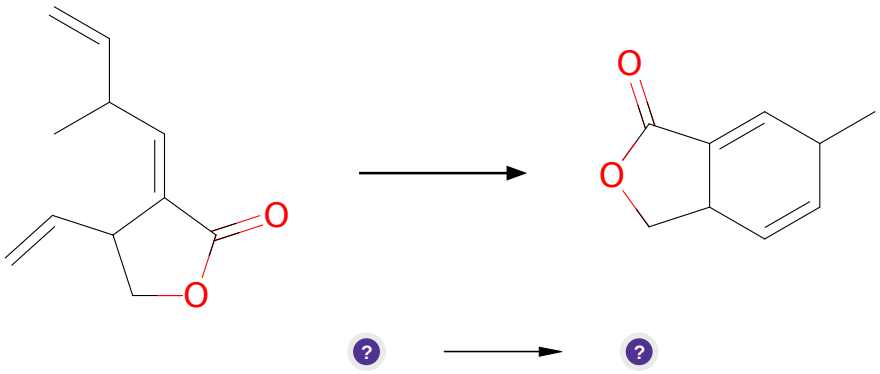
Typical conditions: TsOH

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

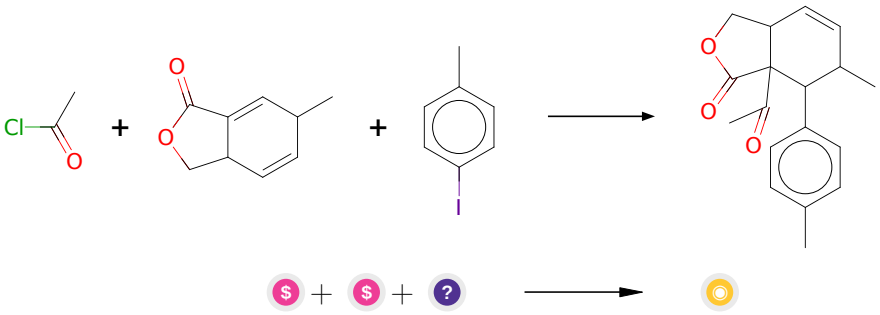
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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. 4-Iodotoluene - *available at Sigma-Aldrich*
2. Acetyl chloride - *available at Sigma-Aldrich*

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

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C)cc1

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: 115.31

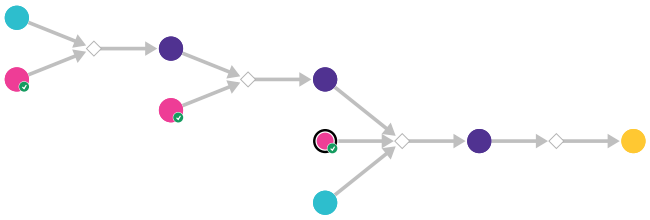
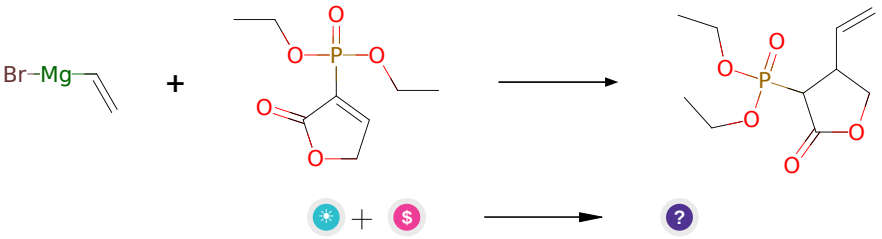


Figure 3: Outline of path 3

2.3.1 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

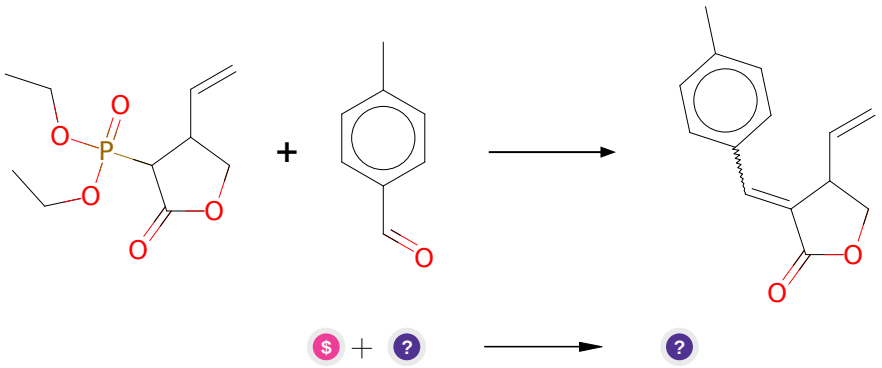
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

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

2.3.2 Wittig-Horner Reaction



Substrates:

1. p-Tolualdehyde - *available at Sigma-Aldrich*
2. C=CC1COC(=O)C1P(=O)(OCC)OCC

Products:

1. C=CC1COC(=O)C1=Cc1ccc(C)cc1

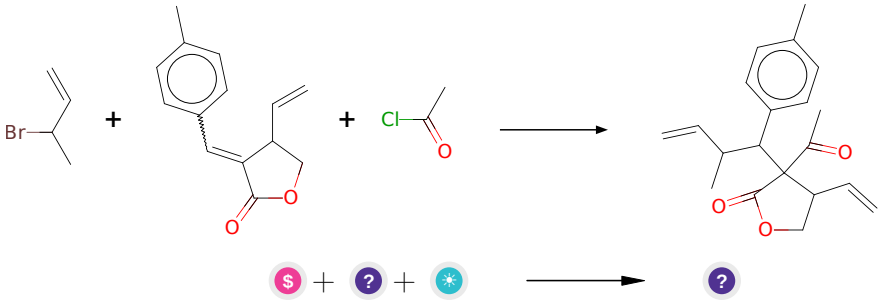
Typical conditions: NaH.THF.0 C or NaH.DMF.0-50 C

Protections: none

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

Retrosynthesis ID: 11549

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. C=CC1COC(=O)C1=Cc1ccc(C)cc1
3. 3-brom-but-1-en

Products:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)=O)C(=O)OCC1C=C

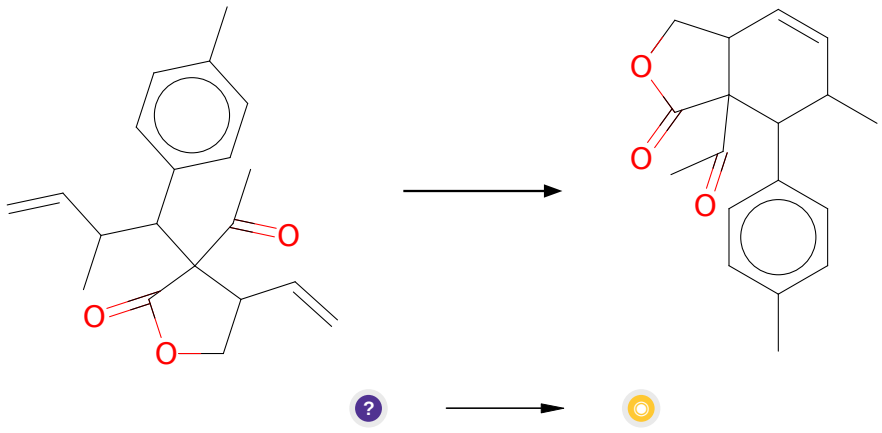
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20527

2.3.4 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C)cc1

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`

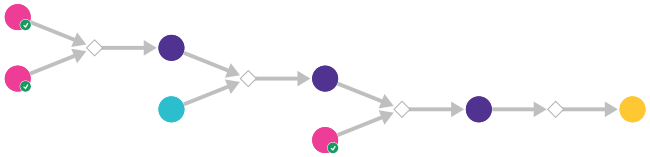
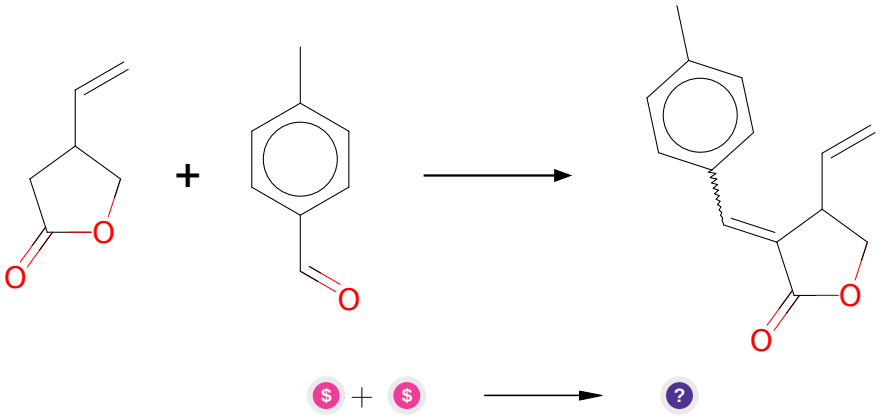


Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes/ketones



Substrates:

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

Products:

1. C=CC1COC(=O)C1=Cc1ccc(C)cc1

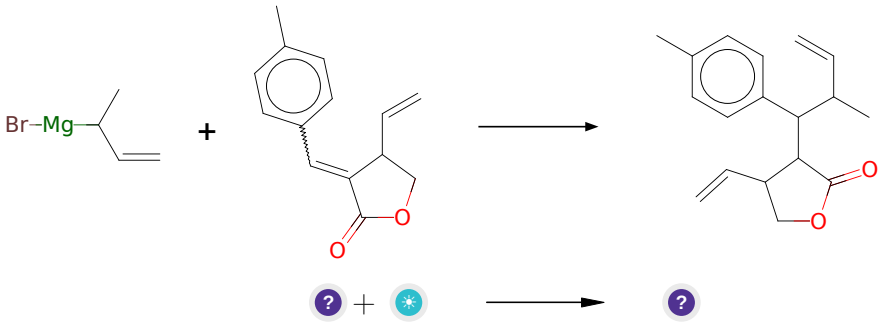
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.4.2 Conjugate addition of organocuprate



Substrates:

1. C=CC1COC(=O)C1=Cc1ccc(C)cc1
2. 3-butenylmagnesium bromide

Products:

1. C=CC(C)C(c1ccc(C)cc1)C1C(=O)OCC1C=C

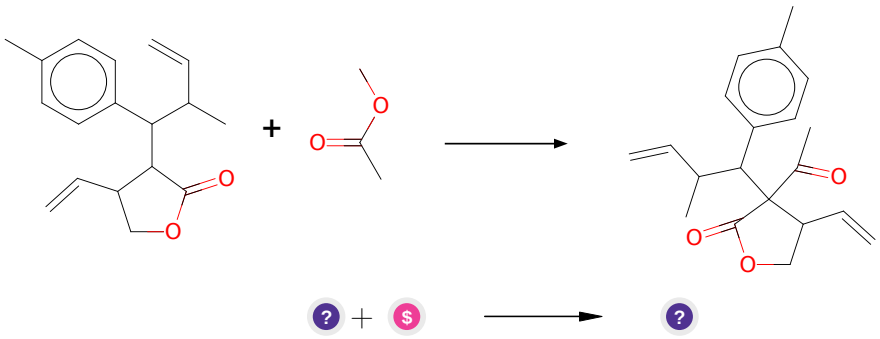
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

Protections: none

Reference: *10.3891/acta.chem.scand.24-3490* AND *10.1016/S0040-4020(01)92354-3* AND AND *10.1016/j.tet.2011.12.046* AND *10.1016/S0040-4039(02)01713-6*

Retrosynthesis ID: 10003575

2.4.3 Claisen Condensation



Substrates:

1. C=CC(C)C(c1ccc(C)cc1)C1C(=O)OCC1C=C
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)=O)C(=O)OCC1C=C

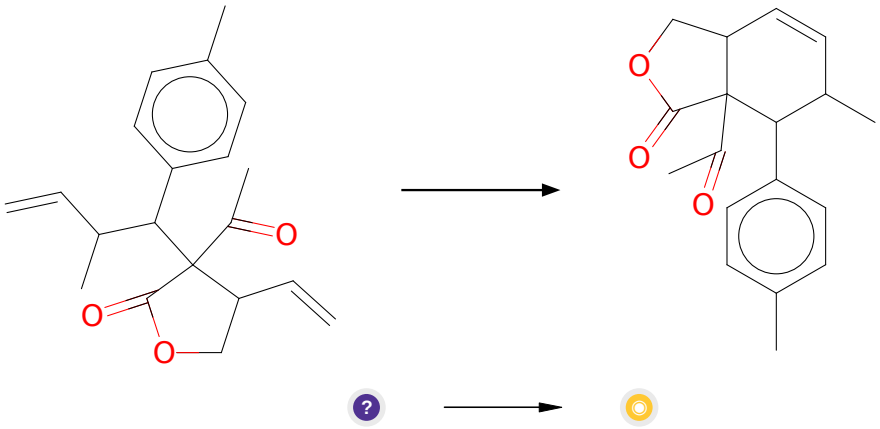
Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.4.4 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C)cc1

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 Path 5

Score: `115.31`

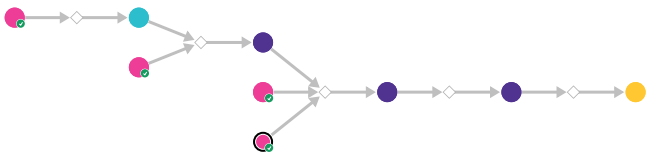
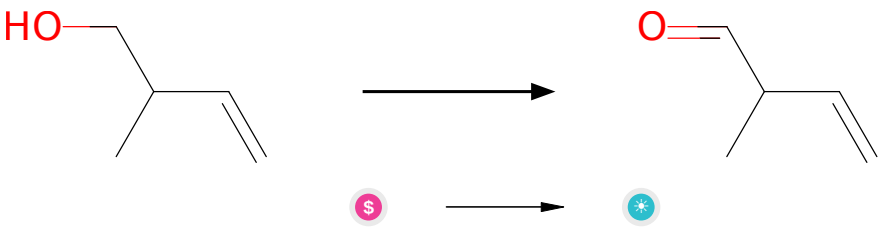


Figure 5: Outline of path 5

2.5.1 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

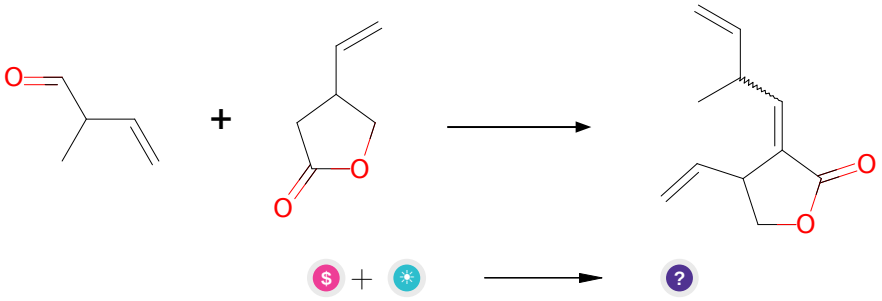
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.5.2 Condensation of esters with aldehydes/ketones



Substrates:

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

Products:

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

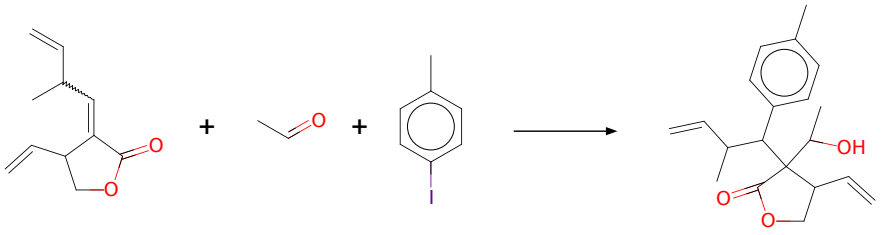
Typical conditions: LDA.THF

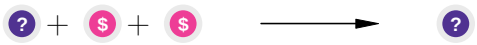
Protections: none

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

Retrosynthesis ID: 14983

2.5.3 Conjugated addition of cuprate-aldol sequence





Substrates:

1. C=CC(C)C=C1C(=O)OCC1C=C
2. 4-Iodotoluene - *available at Sigma-Aldrich*
3. Ethanal - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)O)C(=O)OCC1C=C

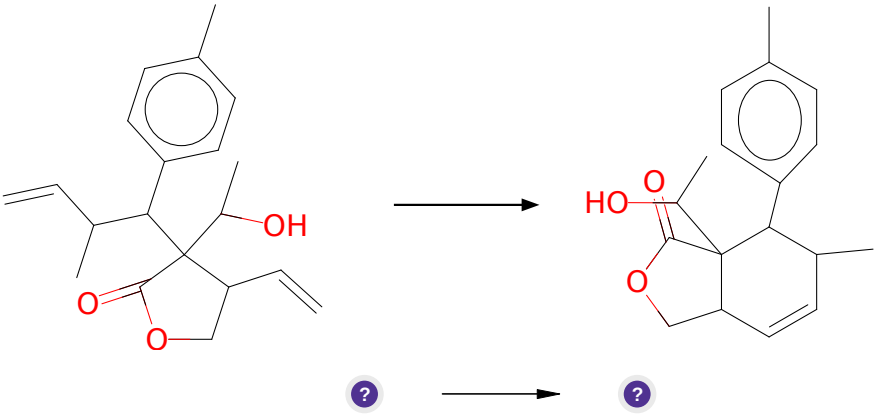
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo9905672* AND *10.1021/ja0320018* AND *10.1021/ja015900+* AND *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1* AND *10.1271/bbb.69.391* AND *10.1039/b612593j*

Retrosynthesis ID: 20516

2.5.4 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1ccc(C)cc1)C1(C(C)O)C(=O)OCC1C=C

Products:

1. Cc1ccc(C2C(C)C=CC3COC(=O)C32C(C)O)cc1

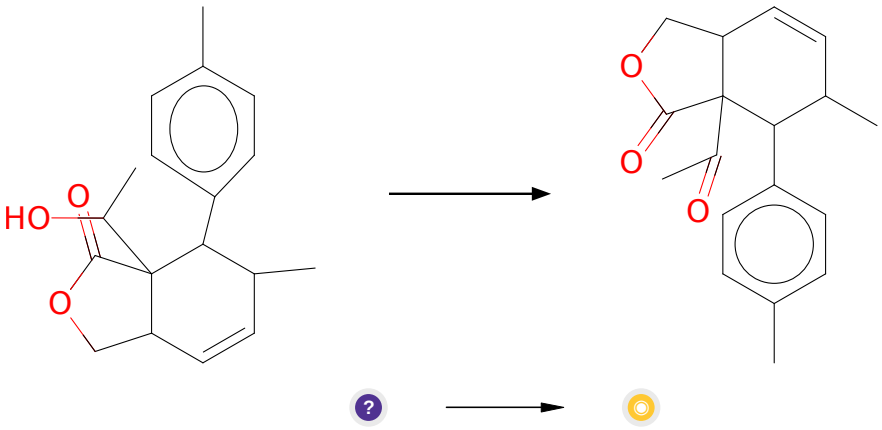
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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 Swern Oxidation



Substrates:

1. Cc1ccc(C2C(C)C=CC3COC(=O)C32C(C)O)cc1

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C)cc1

Typical conditions: oxalyl chloride.DMSO.DCM.NMe3.-40C

Protections: none

Reference: *10.1055/s-1990-27036*

Retrosynthesis ID: 11163