

Paths of analysis*

L6

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselective 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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

Min. search width: 400

Max. reactions per product: 60

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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

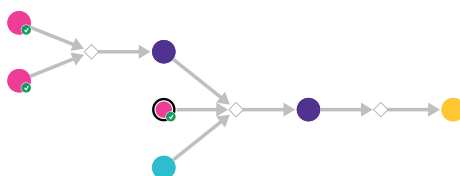
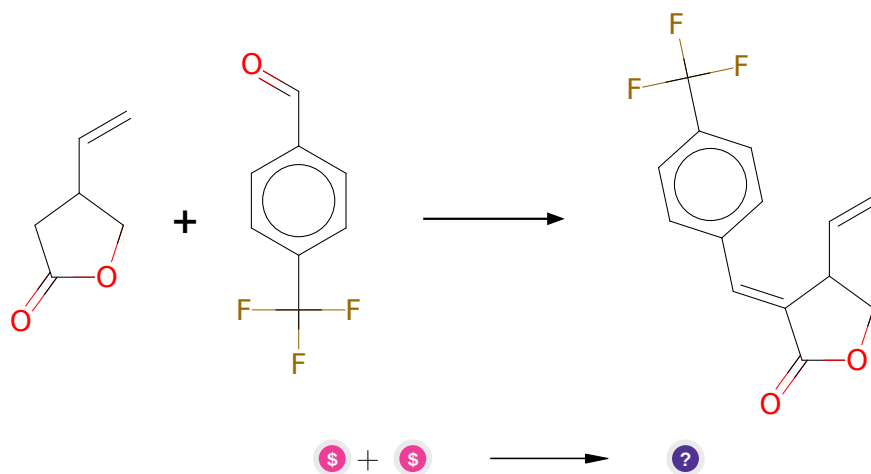


Figure 1: Outline of path 1

2.1.1 Condensation of esters with aldehydes



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

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

Products:

1. C=CC1COC(=O)/C1=C/c1ccc(C(F)(F)F)cc1

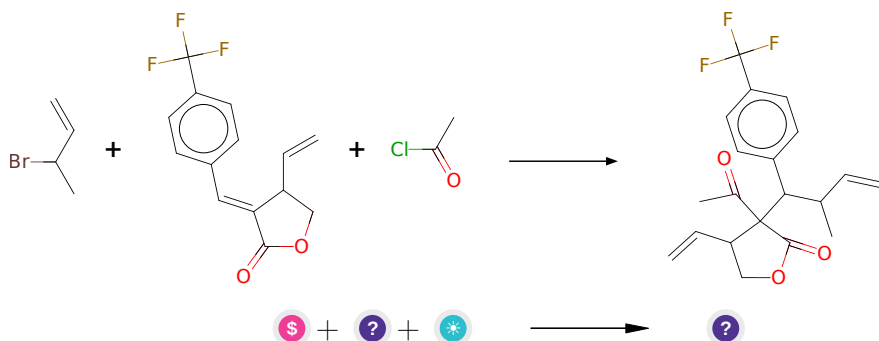
Typical conditions: 1.LDA.2RCHO

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

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. C=CC1COC(=O)/C1=C/c1ccc(C(F)(F)F)cc1
3. 3-brom-but-1-en

Products:

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

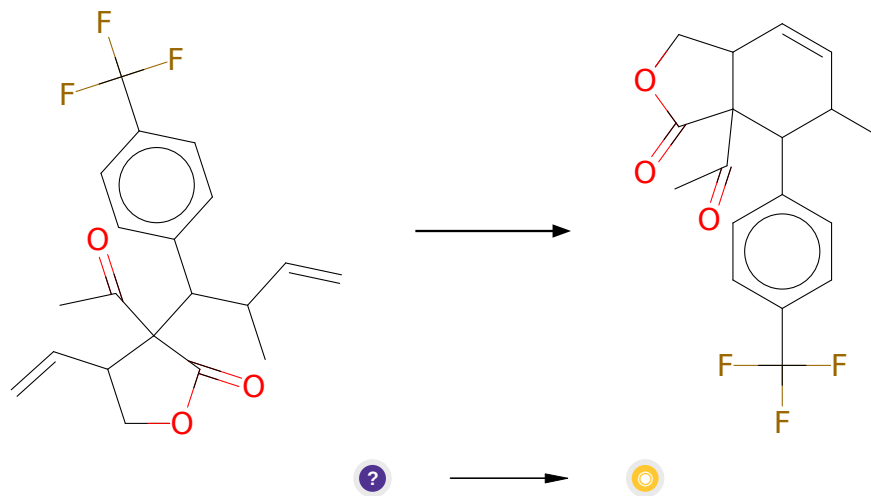
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: [10.3987/COM-99-S143](#) AND [10.1021/ja00148a023](#) AND [10.1016/S0040-4039\(01\)80891-1](#)

Retrosynthesis ID: 20523

2.1.3 Ring-Closing Metathesis



Substrates:

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

Products:

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

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

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.2 Path 2

Score: 76.25

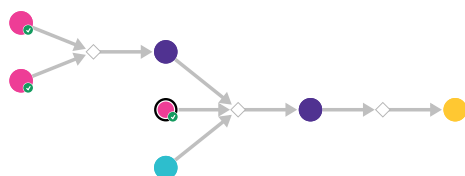
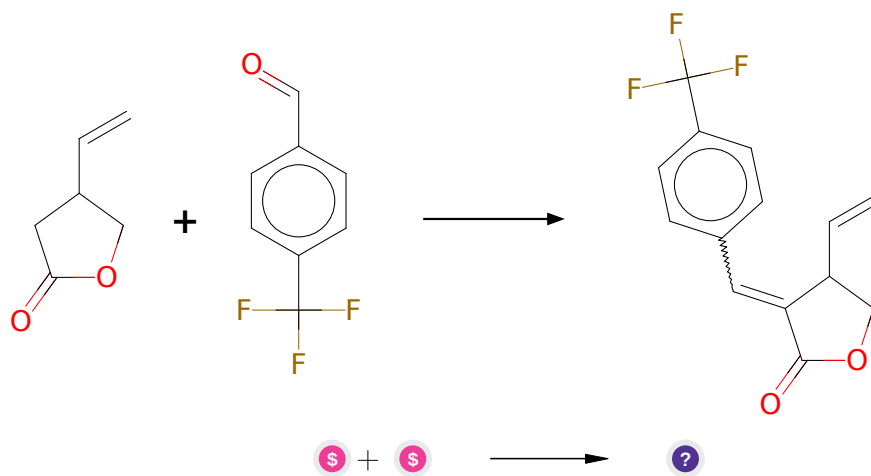


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes/ketones



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

Products:

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

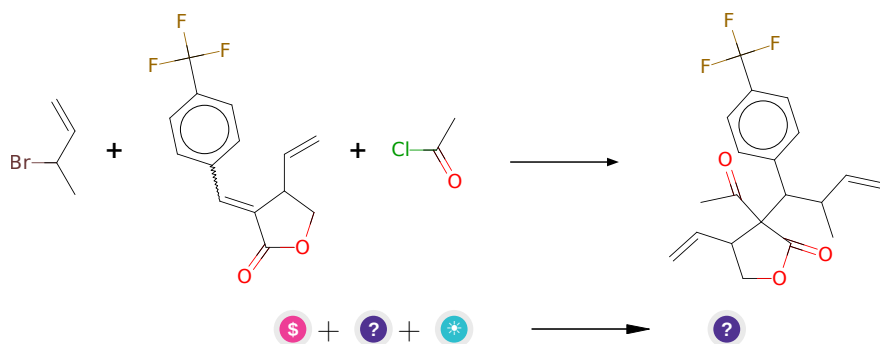
Typical conditions: LDA.THF

Protections: none

Reference: [10.1021/op040006z](#) AND [10.1016/j.bmcl.2005.10.104](#) AND

Retrosynthesis ID: 14983

2.2.2 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(F)(F)F)cc1
3. 3-brom-but-1-en

Products:

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

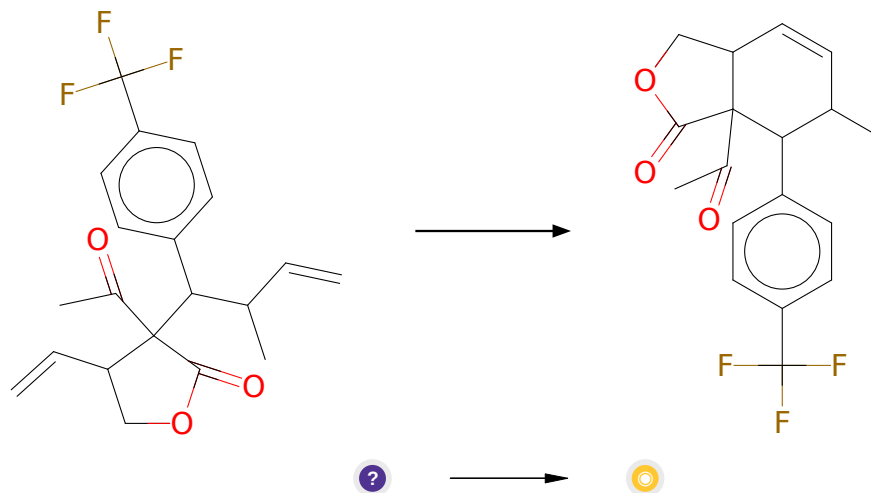
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20527

2.2.3 Ring-Closing Metathesis



Substrates:

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

Products:

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

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

Protections: none

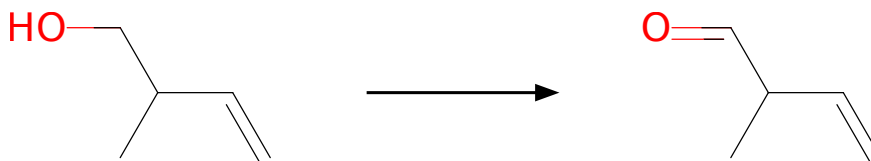
Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.3 Path 3

Score: 76.25

2.3.1 Oxidation of primary alcohols with DMP



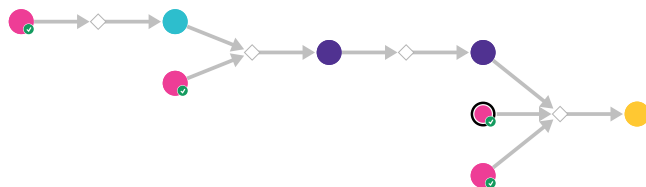
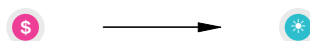


Figure 3: Outline of path 3



Substrates:

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

Products:

1. 2-methyl-but-3-enal

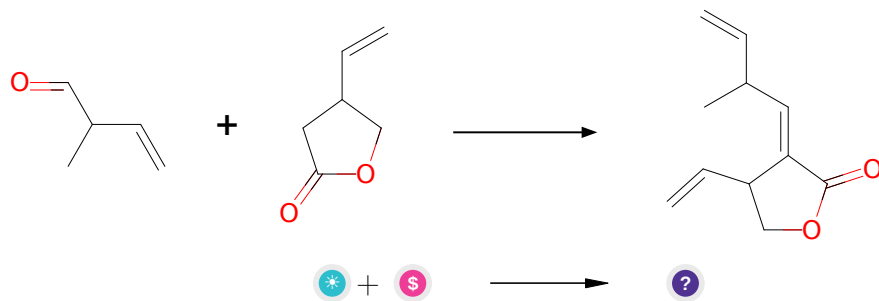
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: [10.1016/j.bmc.2020.115469](https://doi.org/10.1016/j.bmc.2020.115469) p. 3, 9 and [10.1021/acs.jmedchem.8b01878](https://doi.org/10.1021/acs.jmedchem.8b01878) SI p. S43

Retrosynthesis ID: 50426

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=C1/C(=O)OCC1C=C

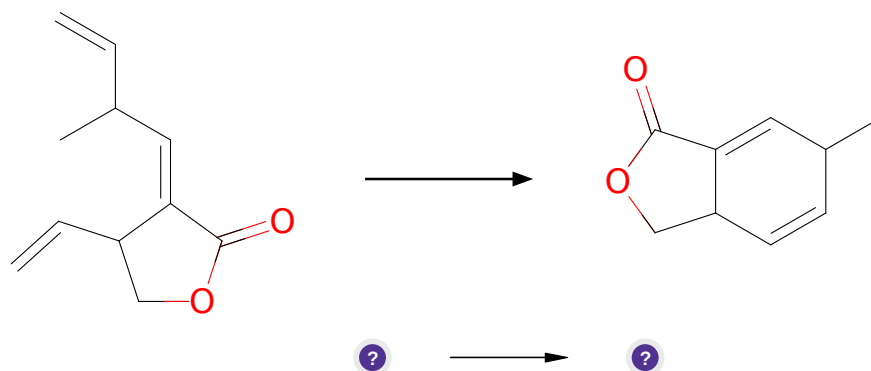
Typical conditions: 1.LDA.2RCHO

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

2.3.3 Ring-Closing Metathesis



Substrates:

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

Products:

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

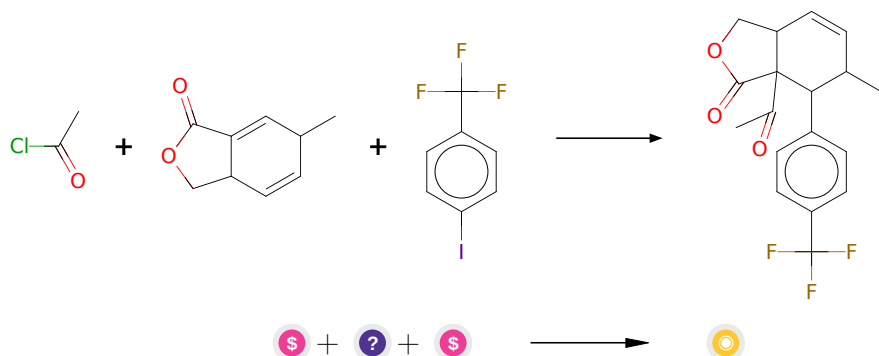
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH₂Cl₂

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

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. 4-Iodobenzotrifluoride - *available at Sigma-Aldrich*

Products:

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

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

Protections: none

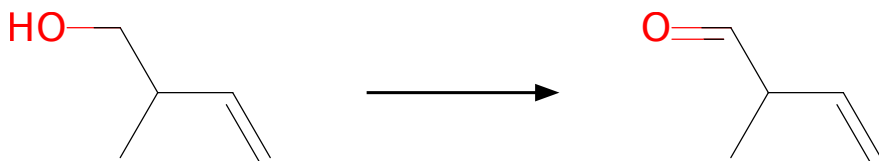
Reference: [10.3987/COM-99-S143](#) AND [10.1021/ja00148a023](#) AND [10.1016/S0040-4039\(01\)80891-1](#)

Retrosynthesis ID: 12521

2.4 Path 4

Score: 76.25

2.4.1 Oxidation of primary alcohols with DMP



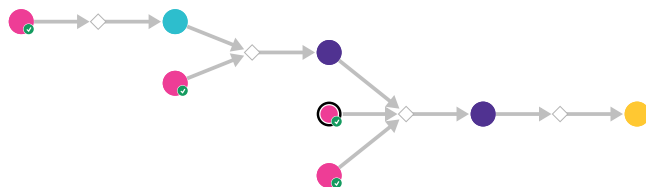
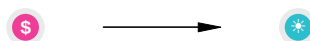


Figure 4: Outline of path 4



Substrates:

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

Products:

1. 2-methyl-but-3-enal

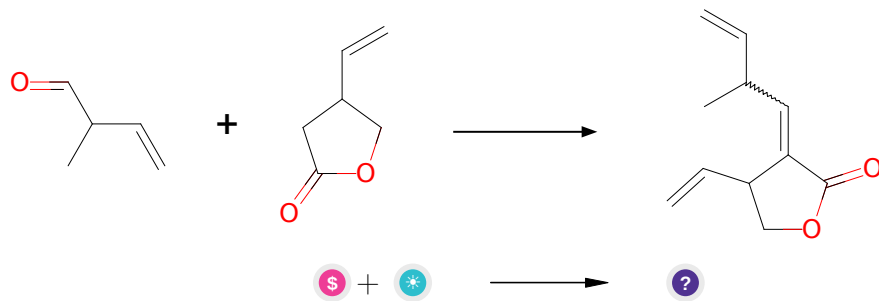
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: [10.1016/j.bmc.2020.115469](https://doi.org/10.1016/j.bmc.2020.115469) p. 3, 9 and [10.1021/acs.jmedchem.8b01878](https://doi.org/10.1021/acs.jmedchem.8b01878) SI p. S43

Retrosynthesis ID: 50426

2.4.2 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

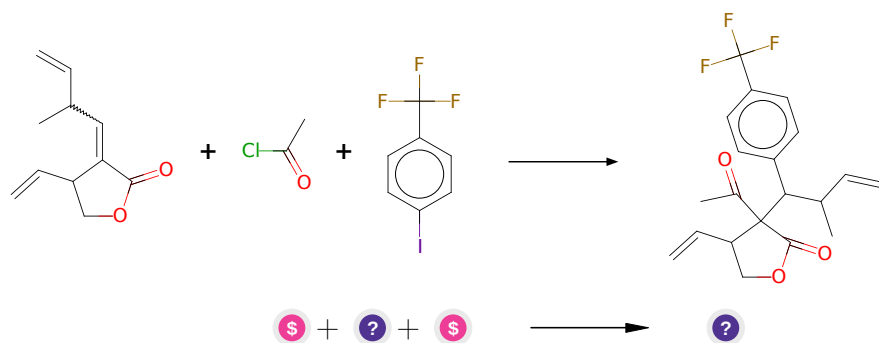
Typical conditions: LDA.THF

Protections: none

Reference: [10.1021/op040006z](#) AND [10.1016/j.bmcl.2005.10.104](#) AND

Retrosynthesis ID: 14983

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



Substrates:

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

Products:

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

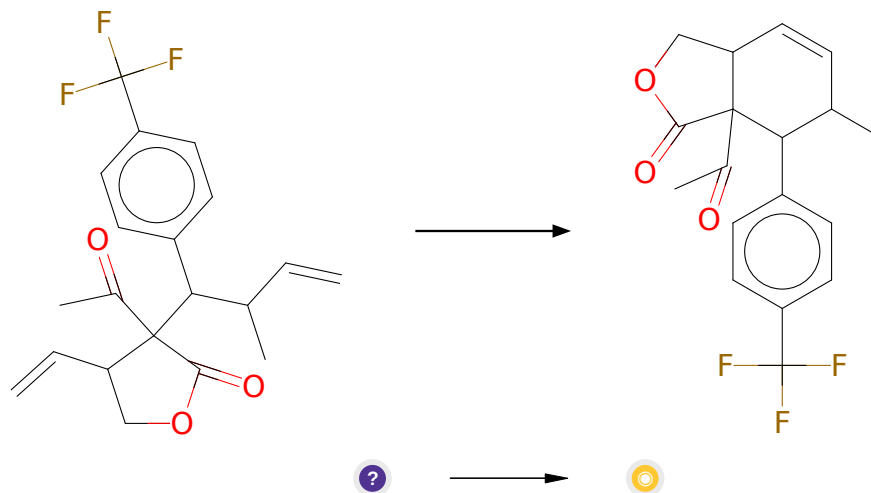
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: [10.3987/COM-99-S143](#) AND [10.1021/ja00148a023](#) AND [10.1016/S0040-4039\(01\)80891-1](#)

Retrosynthesis ID: 20528

2.4.4 Ring-Closing Metathesis



Substrates:

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

Products:

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

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

Protections: none

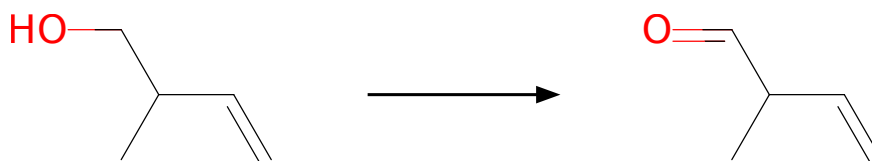
Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.5 Path 5

Score: 84.06

2.5.1 Oxidation of primary alcohols with DMP



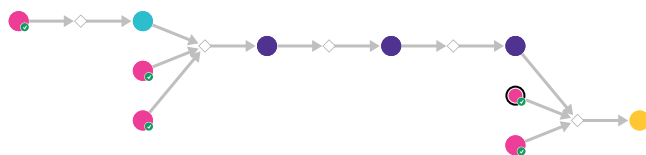
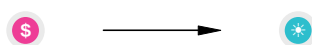


Figure 5: Outline of path 5



Substrates:

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

Products:

1. 2-methyl-but-3-enal

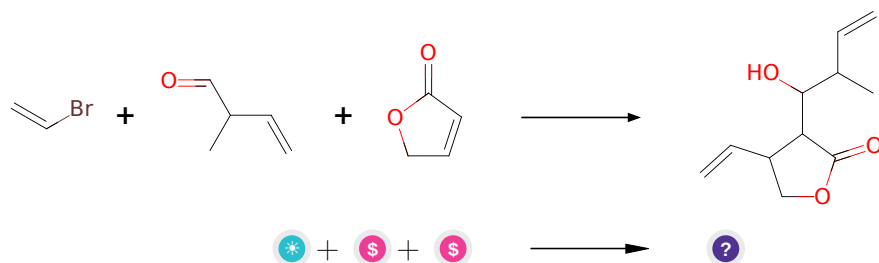
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: [10.1016/j.bmc.2020.115469](https://doi.org/10.1016/j.bmc.2020.115469) p. 3, 9 and [10.1021/acs.jmedchem.8b01878](https://doi.org/10.1021/acs.jmedchem.8b01878) SI p. S43

Retrosynthesis ID: 50426

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

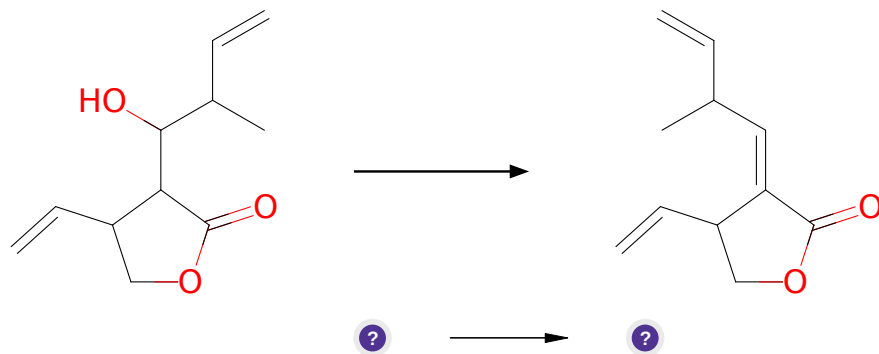
Typical conditions: 1.RCuLi.2.RCHO

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

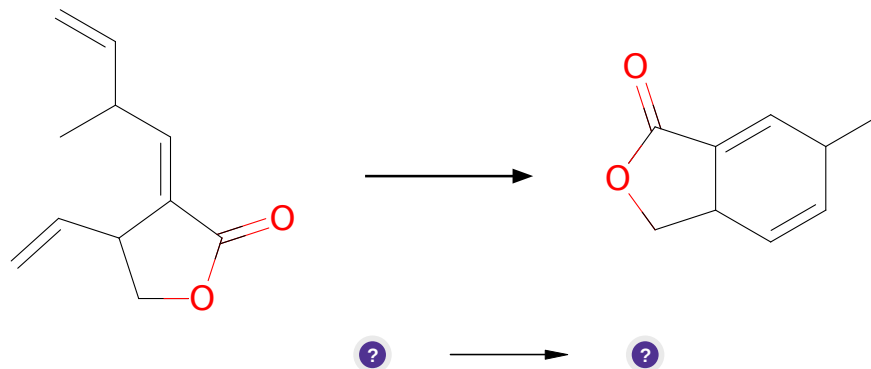
Typical conditions: TsOH

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

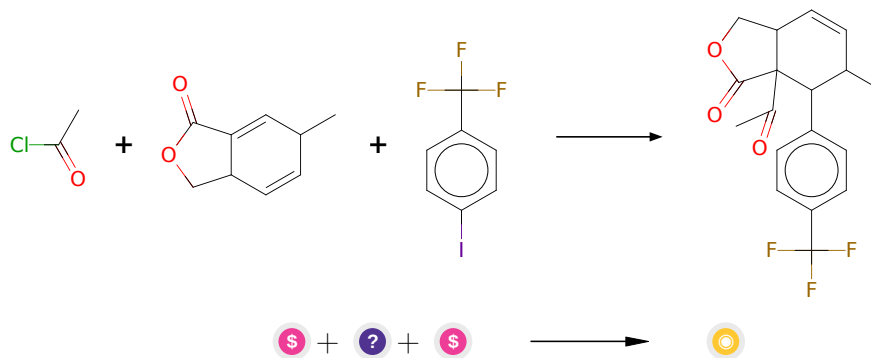
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH₂Cl₂

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

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



Substrates:

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

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

3. 4-Iodobenzotrifluoride - *available at Sigma-Aldrich*

Products:

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