

# 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:**  $\text{TUNNEL\_COEF} * \text{FGI\_COEF} * \text{STEP} * 20 + 1000000 * (\text{CONFLICT} + \text{NON\_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

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

**Min. search width:** 400

**Max. reactions per product:** 60

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\*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:** 106.04

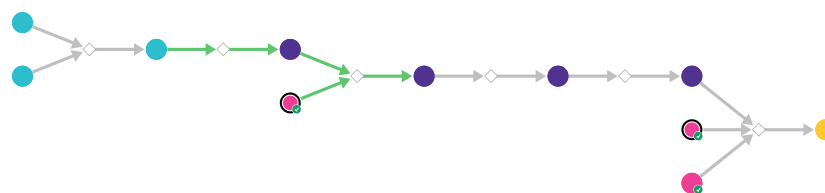
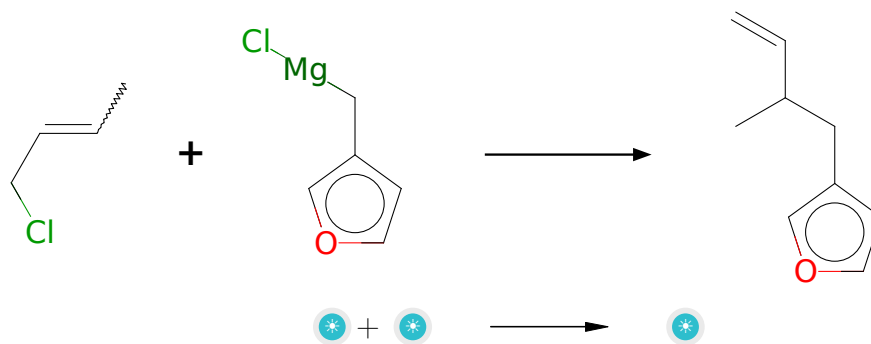


Figure 1: Outline of path 1

#### 2.1.1 NHC-catalyzed Grignard allylic substitution



**Substrates:**

1. crotyl chloride
2. (furan-3-ylmethyl)magnesium chloride

**Products:**

1. 3-(2-methyl-but-3-enyl)-furan

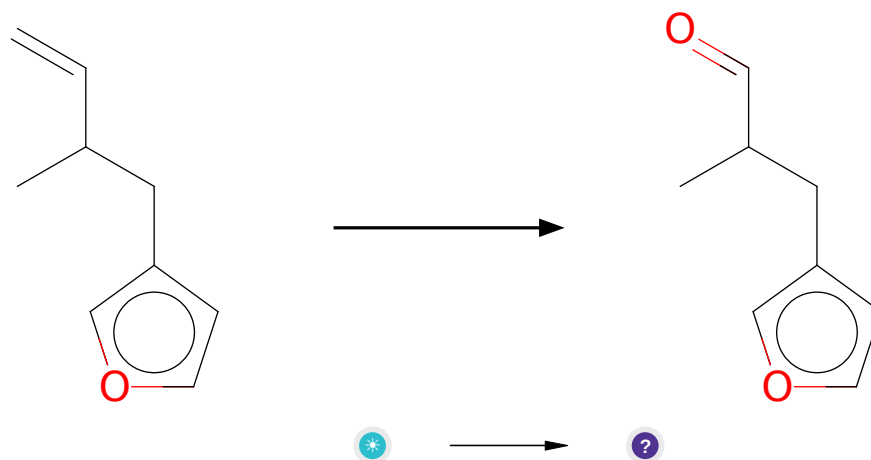
**Typical conditions:** RMgCl.THF.NHC-complex

**Protections:** none

**Reference:** [10.1016/j.tetlet.2012.12.124](https://doi.org/10.1016/j.tetlet.2012.12.124)

**Retrosynthesis ID:** 1171

### 2.1.2 Ozonolysis



**Substrates:**

1. 3-(2-methyl-but-3-enyl)-furan

**Products:**

1. CC(C=O)Cc1ccoc1

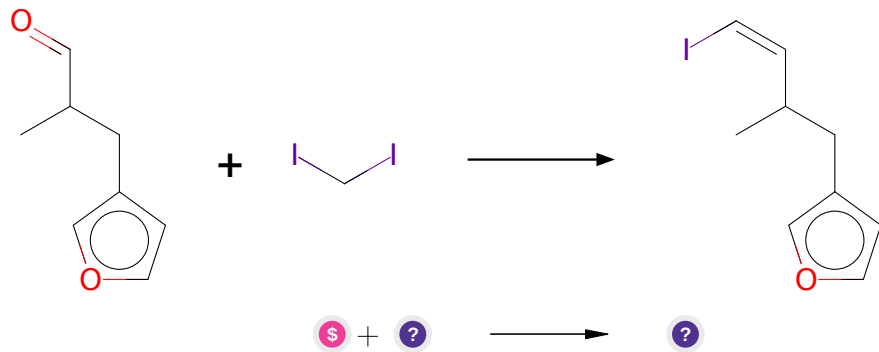
**Typical conditions:** O<sub>3</sub>.MeOH.CH<sub>2</sub>Cl<sub>2</sub>.PPh<sub>3</sub> or Me<sub>2</sub>S.low temperature

**Protections:** none

**Reference:** [10.1016/j.tet.2017.03.039](https://doi.org/10.1016/j.tet.2017.03.039)

**Retrosynthesis ID:** 5074

### 2.1.3 Iodoolefination of aldehydes



#### Substrates:

1. Diiodomethane - *available at Sigma-Aldrich*
2. CC(C=O)Cc1ccoc1

#### Products:

1. CC(/C=C\I)Cc1ccoc1

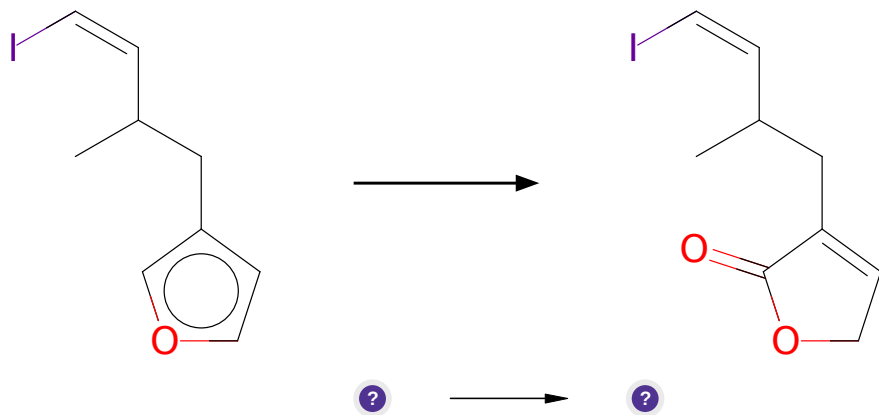
**Typical conditions:** 1.PPh<sub>3</sub>.2.Na<sup>+</sup>N<sup>-</sup>(TMS)<sup>-</sup>.2.HMPA.THF

**Protections:** none

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

**Retrosynthesis ID:** 10001773

### 2.1.4 NBS-promoted oxidation of furans to lactones



#### Substrates:

1. CC(/C=C\I)Cc1ccoc1

**Products:**

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

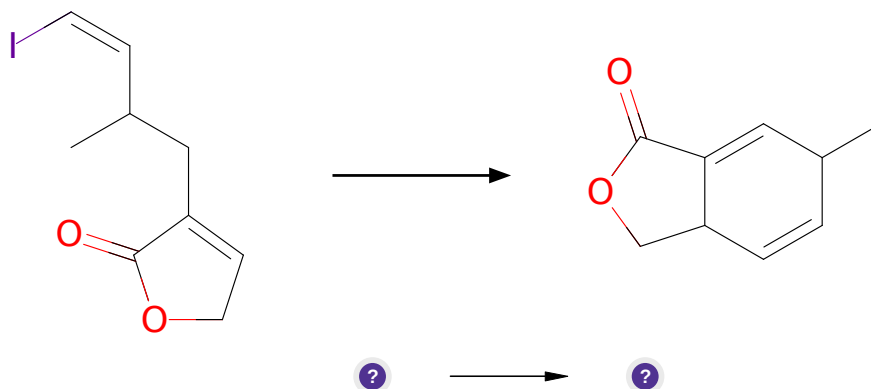
**Typical conditions:** NBS.MW.MeOH

**Protections:** none

**Reference:** DOI: [10.1016/S0040-4039\(01\)01261-8](https://doi.org/10.1016/S0040-4039(01)01261-8)

**Retrosynthesis ID:** 49766

### 2.1.5 Heck Reaction



**Substrates:**

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

**Products:**

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

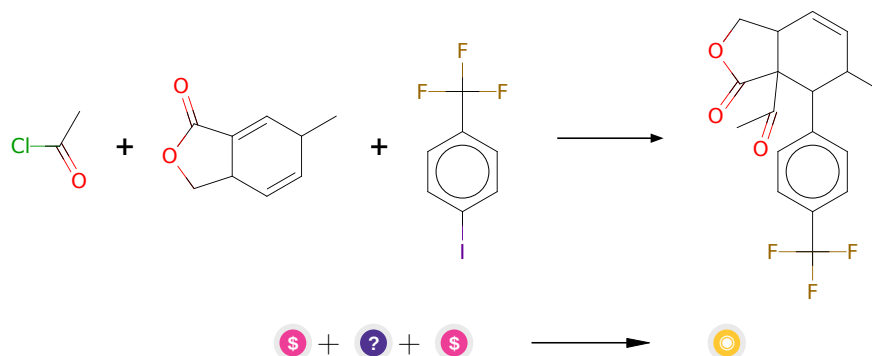
**Typical conditions:** Pd (cat). ligand. base e.g DIPEA.solvent

**Protections:** none

**Reference:** DOI: [10.1021/jo00270a011](https://doi.org/10.1021/jo00270a011) or DOI: [10.1021/ar00049a001](https://doi.org/10.1021/ar00049a001) or DOI: [10.1021/ja00206a034](https://doi.org/10.1021/ja00206a034) or DOI: [10.1021/cr020039h](https://doi.org/10.1021/cr020039h) or DOI: [10.1039/C1CS15101K](https://doi.org/10.1039/C1CS15101K) or DOI: [10.1002/9780470716076](https://doi.org/10.1002/9780470716076)

**Retrosynthesis ID:** 8584

### 2.1.6 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

## 2.2 Path 2

Score: 106.04

### 2.2.1 Alkylation of Esters



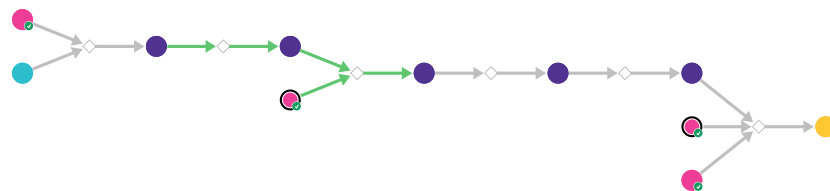
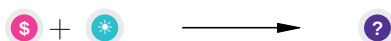


Figure 2: Outline of path 2



**Substrates:**

1. Methyl propionate - *available at Sigma-Aldrich*
2. 3-chlormethyl-furan

**Products:**

1. COC(=O)C(C)Cc1ccoc1

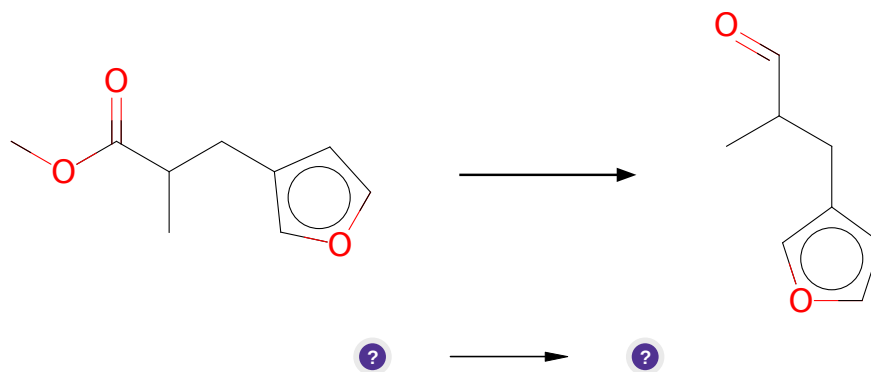
**Typical conditions:** base e.g. BuLi.THF

**Protections:** none

**Reference:** [10.1021/ja065404r](https://doi.org/10.1021/ja065404r) and [10.1016/S0040-4020\(01\)88337-X](https://doi.org/10.1016/S0040-4020(01)88337-X)  
and [10.1016/0040-4039\(95\)00562-Q](https://doi.org/10.1016/0040-4039(95)00562-Q) and [10.1021/acs.orglett.6b01901](https://doi.org/10.1021/acs.orglett.6b01901) and  
[10.1021/jo00073a034](https://doi.org/10.1021/jo00073a034) and [10.1021/ol2023278](https://doi.org/10.1021/ol2023278)

**Retrosynthesis ID:** 31017152

**2.2.2 Aldehyde Formation**



**Substrates:**

1. COC(=O)C(C)Cc1ccoc1

**Products:**

1. CC(C=O)Cc1ccoc1

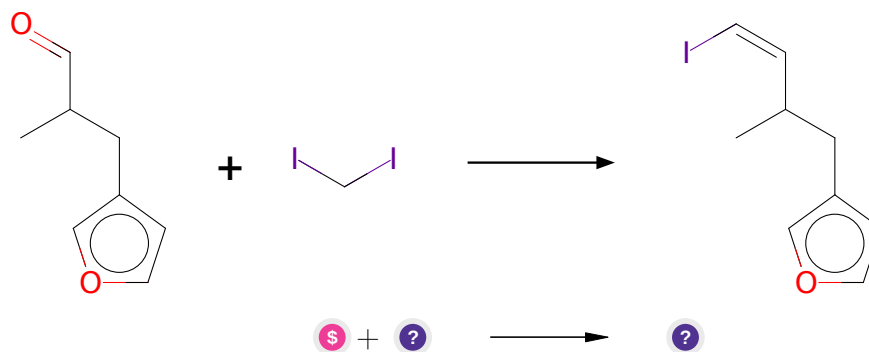
**Typical conditions:** DIBAL.solvent e.g. DCM

**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

**2.2.3 Iodoolefination of aldehydes**



**Substrates:**

1. Diiodomethane - *available at Sigma-Aldrich*
2. CC(C=O)Cc1ccoc1

**Products:**

1. CC(/C=C\I)Cc1ccoc1

**Typical conditions:** 1.PPh<sub>3</sub>.2.Na<sup>+</sup>N<sup>-</sup>(TMS)<sup>-</sup>.3.HMPA.THF

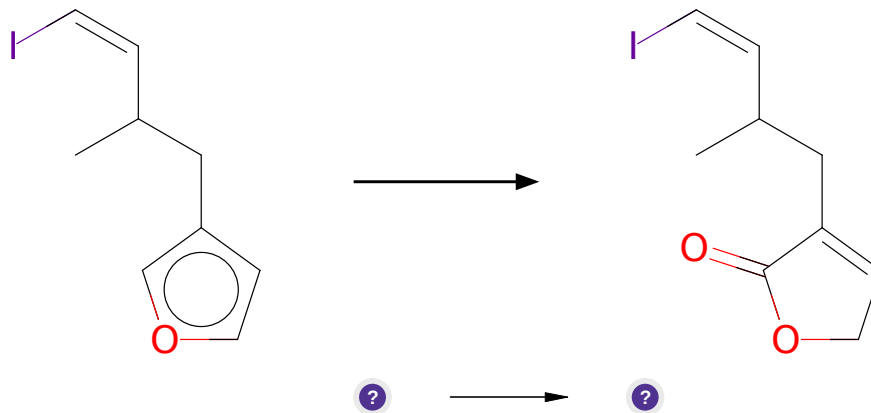
**Protections:** none

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

**Retrosynthesis ID:** 10001773



### 2.2.4 NBS-promoted oxidation of furans to lactones



**Substrates:**

1. CC(/C=C\I)Cc1ccoc1

**Products:**

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

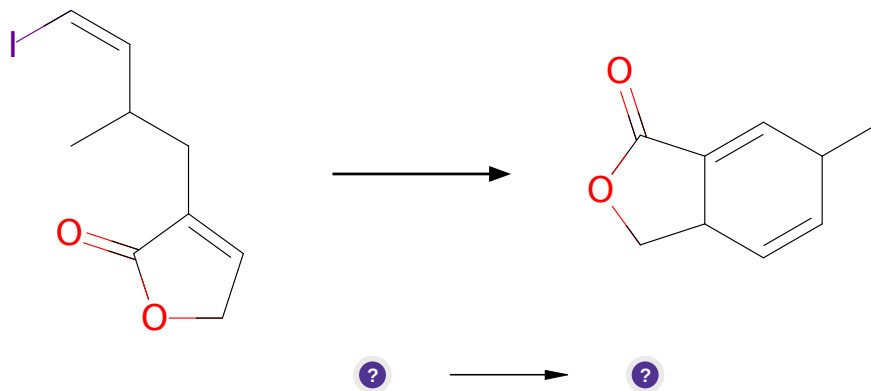
**Typical conditions:** NBS.MW.MeOH

**Protections:** none

**Reference:** DOI: [10.1016/S0040-4039\(01\)01261-8](https://doi.org/10.1016/S0040-4039(01)01261-8)

**Retrosynthesis ID:** 49766

### 2.2.5 Heck Reaction



**Substrates:**

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

**Products:**

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

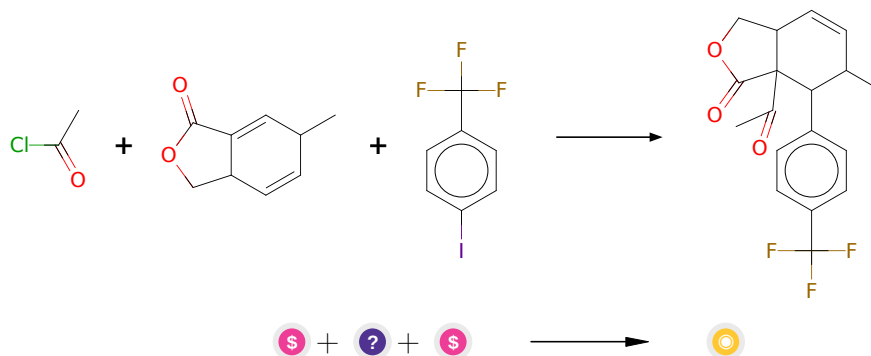
**Typical conditions:** Pd (cat). ligand. base e.g DIPEA.solvent

**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

**2.2.6 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

## 2.3 Path 3

Score: 106.04

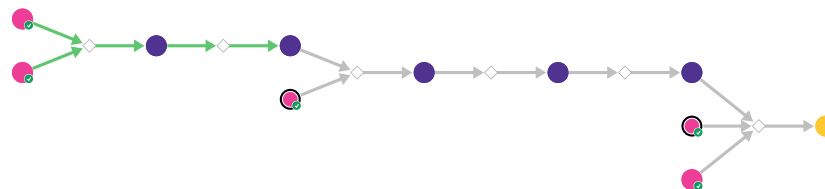
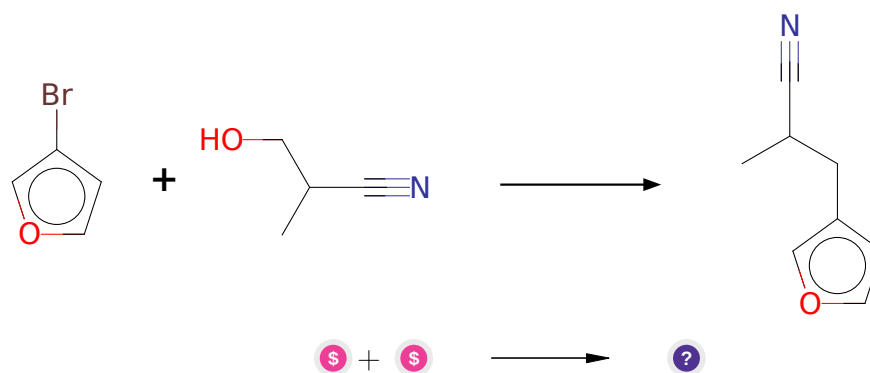


Figure 3: Outline of path 3

### 2.3.1 Double decarboxylative coupling or aryl halides with alcohols as latent nucleophiles



#### Substrates:

1. 3-Bromofuran - *available at Sigma-Aldrich*
2. 3-hydroxy-2-methylpropanenitrile - *available at Sigma-Aldrich*

#### Products:

1. CC(C#N)Cc1ccoc1

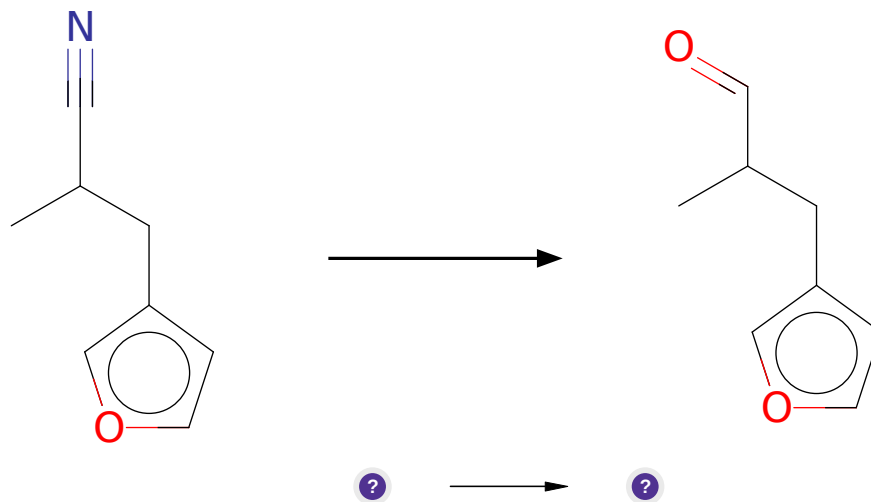
**Typical conditions:** 1.Oxalyl chloride 2.[Ir]-catalyst.[Ni]-catalyst.blue.light.dioxane.DMSO.DMF.CsHCO<sub>3</sub>.70 deg C

**Protections:** none

**Reference:** *10.1021/jacs.6b09533*

**Retrosynthesis ID:** 10032259

### 2.3.2 Reduction of nitriles to aldehydes



**Substrates:**

1. CC(C#N)Cc1ccoc1

**Products:**

1. CC(C=O)Cc1ccoc1

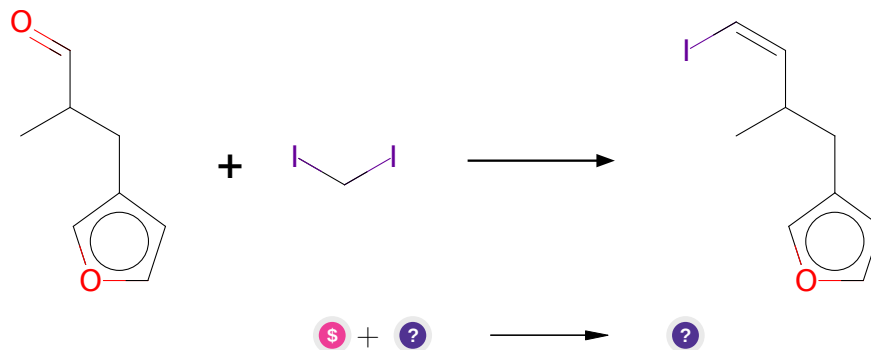
**Typical conditions:** DIBALH.DCM

**Protections:** none

**Reference:** [10.1016/j.bmc.2006.01.061](https://doi.org/10.1016/j.bmc.2006.01.061) and [10.1016/j.tet.2012.07.022](https://doi.org/10.1016/j.tet.2012.07.022) and [10.1016/j.bmcl.2009.01.075](https://doi.org/10.1016/j.bmcl.2009.01.075) and [10.1016/j.bmcl.2007.09.081](https://doi.org/10.1016/j.bmcl.2007.09.081) and [10.1021/jo000502v](https://doi.org/10.1021/jo000502v)

**Retrosynthesis ID:** 31406

### 2.3.3 Iodoolefination of aldehydes



**Substrates:**

1. Diiodomethane - *available at Sigma-Aldrich*
2. CC(C=O)Cc1ccoc1

**Products:**

1. CC(/C=C\I)Cc1ccoc1

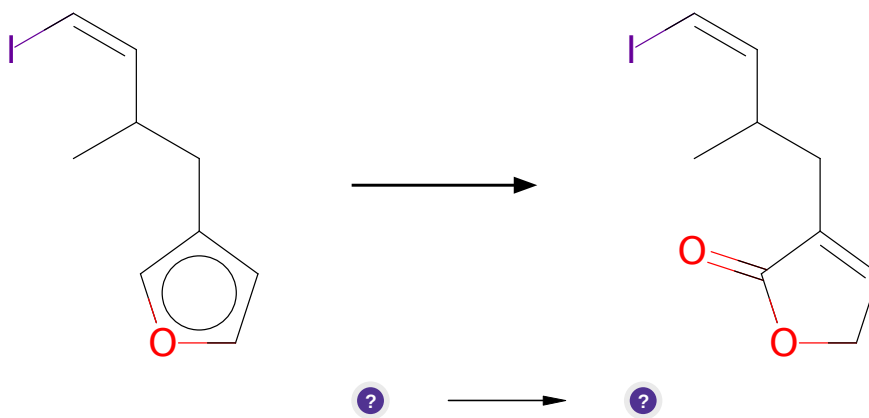
**Typical conditions:** 1.PPh<sub>3</sub>.2.Na<sup>+</sup>N<sup>-</sup>(TMS)<sup>-</sup>.2.HMPA.THF

**Protections:** none

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

**Retrosynthesis ID:** 10001773

**2.3.4 NBS-promoted oxidation of furans to lactones**



**Substrates:**

1. CC(/C=C\I)Cc1ccoc1

**Products:**

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

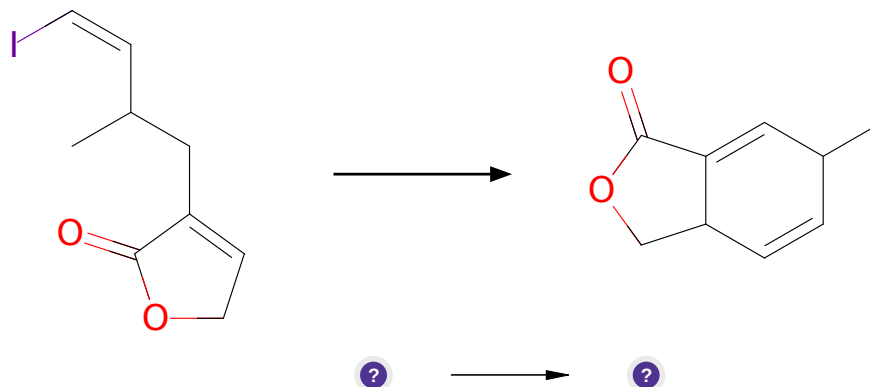
**Typical conditions:** NBS.MW.MeOH

**Protections:** none

**Reference:** DOI: [10.1016/S0040-4039\(01\)01261-8](#)

**Retrosynthesis ID:** 49766

### 2.3.5 Heck Reaction



**Substrates:**

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

**Products:**

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

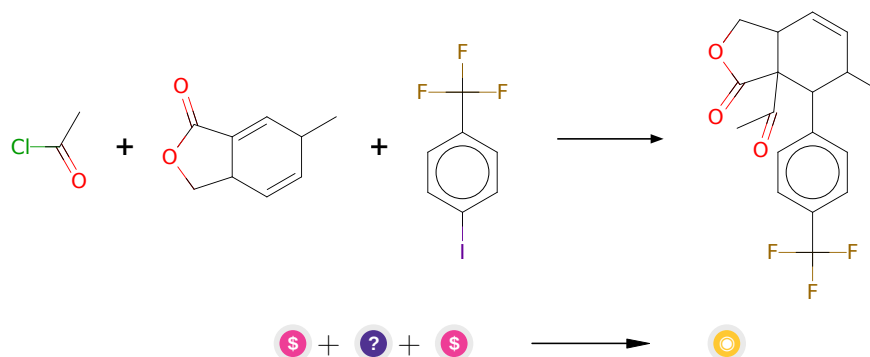
**Typical conditions:** Pd (cat). ligand. base e.g DIPEA.solvent

**Protections:** none

**Reference:** DOI: [10.1021/jo00270a011](https://doi.org/10.1021/jo00270a011) or DOI: [10.1021/ar00049a001](https://doi.org/10.1021/ar00049a001) or DOI: [10.1021/ja00206a034](https://doi.org/10.1021/ja00206a034) or DOI: [10.1021/cr020039h](https://doi.org/10.1021/cr020039h) or DOI: [10.1039/C1CS15101K](https://doi.org/10.1039/C1CS15101K) or DOI: [10.1002/9780470716076](https://doi.org/10.1002/9780470716076)

**Retrosynthesis ID:** 8584

### 2.3.6 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: 115.31

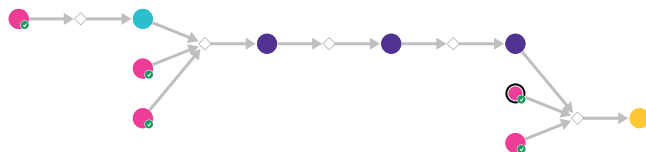
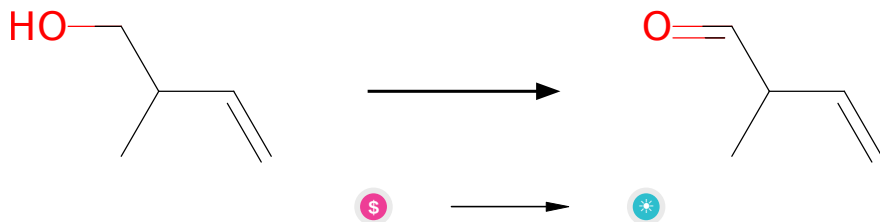


Figure 4: Outline of path 4

### 2.4.1 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

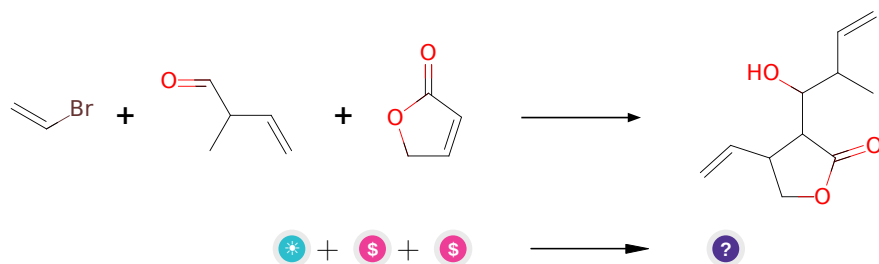
**Typical conditions:** DMP.DCM.0-25 C

**Protections:** none

**Reference:** [10.1016/j.bmc.2020.115469](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 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

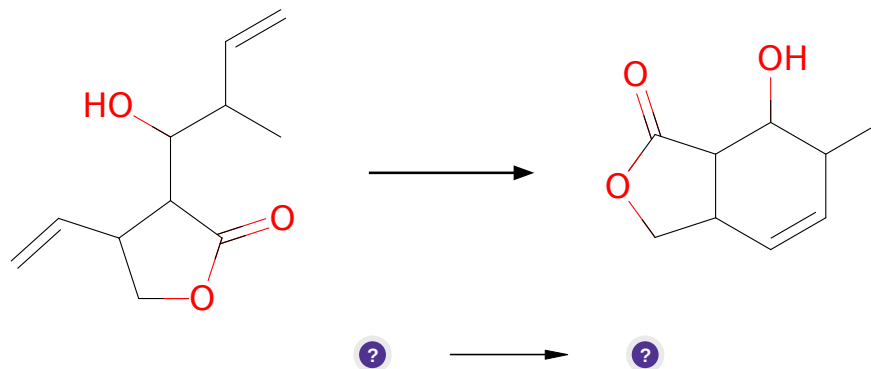
**Protections:** none

**Reference:** [10.1021/jo2010186](https://doi.org/10.1021/jo2010186) AND [10.1021/jo101439h](https://doi.org/10.1021/jo101439h) AND [10.1021/ja906241w](https://doi.org/10.1021/ja906241w) AND [10.1016/S0040-4039\(01\)80891-1](https://doi.org/10.1016/S0040-4039(01)80891-1) AND [10.1016/S0040-4020\(01\)82115-3](https://doi.org/10.1016/S0040-4020(01)82115-3)

**Retrosynthesis ID:** 13048



### 2.4.3 Ring-Closing Metathesis



**Substrates:**

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

**Products:**

1. CC1C=CC2COC(=O)C2C1O

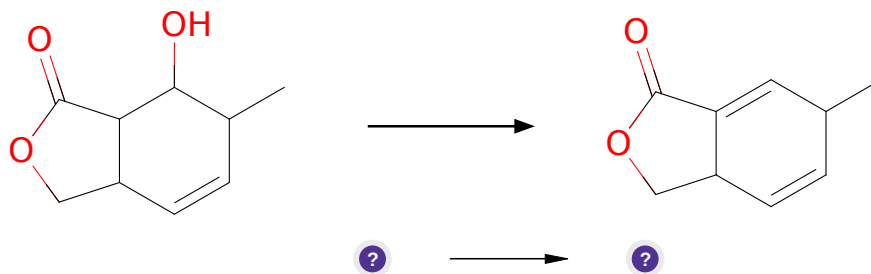
**Typical conditions:** catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

**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

### 2.4.4 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. CC1C=CC2COC(=O)C2C1O

**Products:**

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

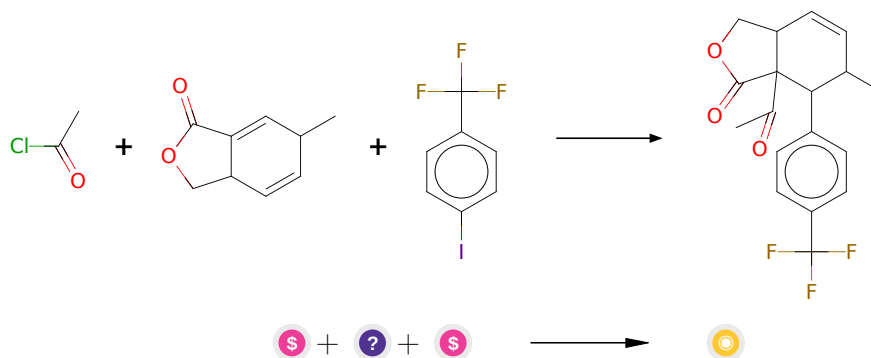
**Typical conditions:** TsOH

**Protections:** none

**Reference:** DOI: [10.1002/anie.201204977](https://doi.org/10.1002/anie.201204977) AND [10.1021/ol062777o](https://doi.org/10.1021/ol062777o)

**Retrosynthesis ID:** 7731

#### 2.4.5 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](https://doi.org/10.3987/COM-99-S143) AND [10.1021/ja00148a023](https://doi.org/10.1021/ja00148a023) AND [10.1016/S0040-4039\(01\)80891-1](https://doi.org/10.1016/S0040-4039(01)80891-1)

**Retrosynthesis ID:** 12521

## 2.5 Path 5

**Score:** 115.31

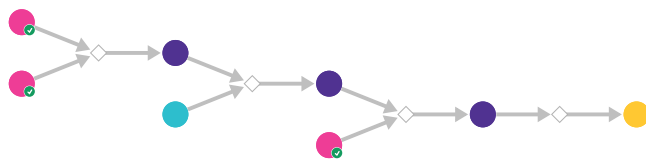
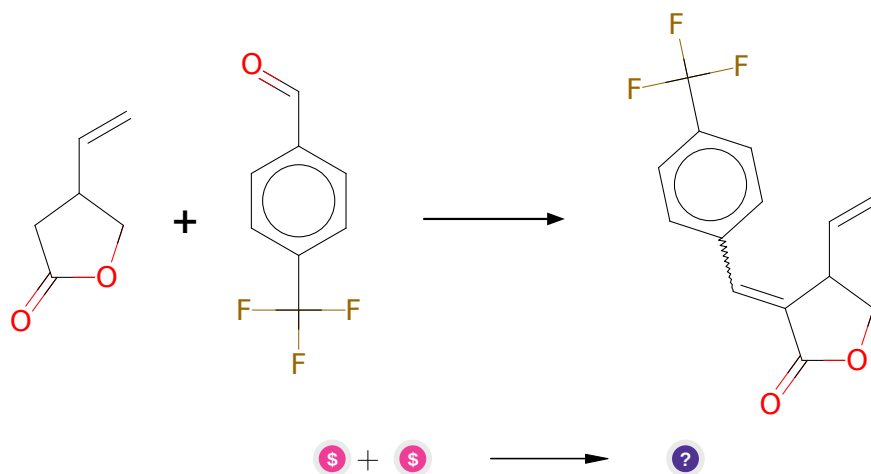


Figure 5: Outline of path 5

### 2.5.1 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

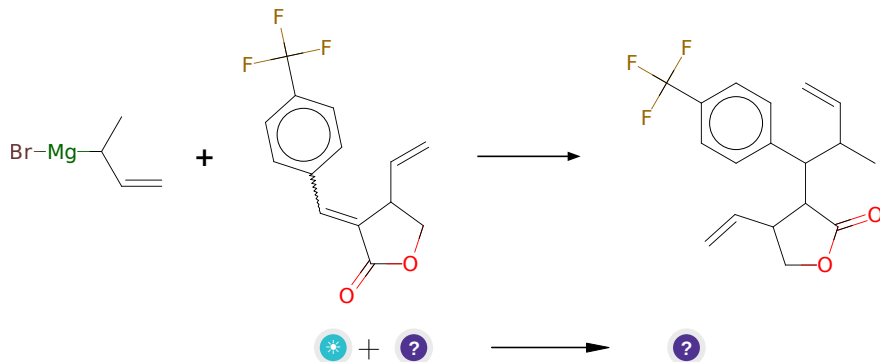
**Typical conditions:** LDA.THF

**Protections:** none

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

**Retrosynthesis ID:** 14983

### 2.5.2 Conjugate addition of organocuprate



#### Substrates:

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

#### Products:

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

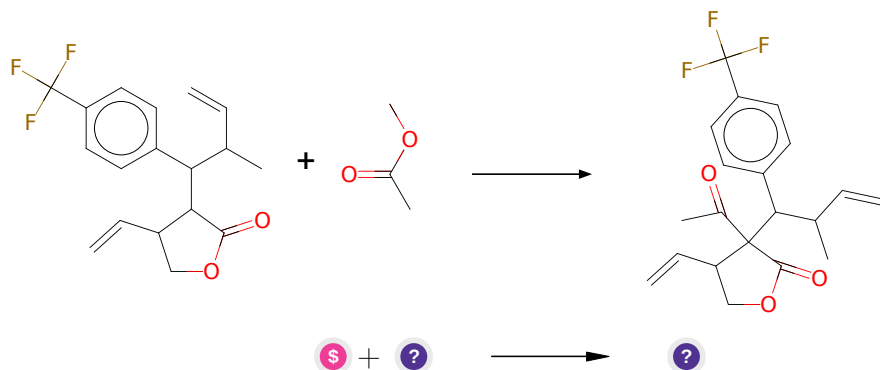
**Typical conditions:** 1. CuCN.LiCl. 2. Electrophile. 3. NH<sub>4</sub>Cl

**Protections:** none

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

**Retrosynthesis ID:** 10003575

### 2.5.3 Claisen Condensation



#### Substrates:

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

**Products:**

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

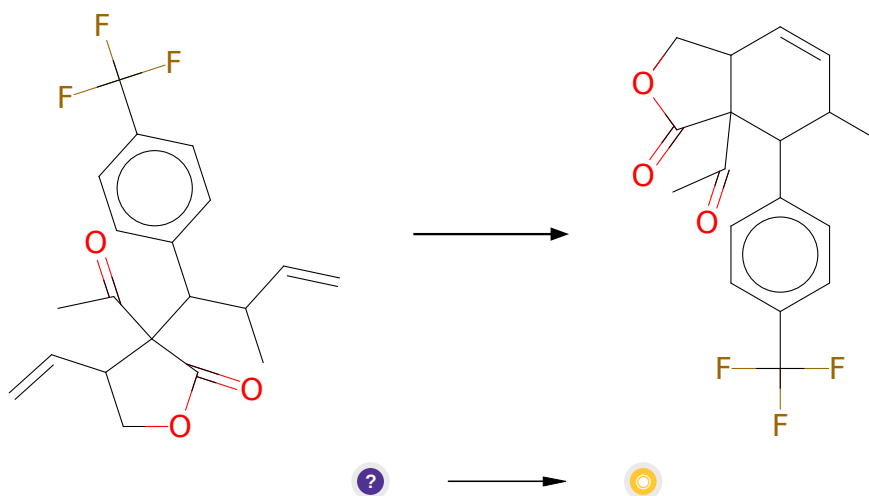
**Typical conditions:** Base.Solvent

**Protections:** none

**Reference:** [10.1021/cr020703u](#) and [10.1021/cr60088a002](#)

**Retrosynthesis ID:** 5015

#### 2.5.4 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. CH<sub>2</sub>Cl<sub>2</sub>

**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