

# Paths of analysis\*

L8

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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\*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.

**JSON Parameters:**  $\{\}$

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

**Score:** 125.08

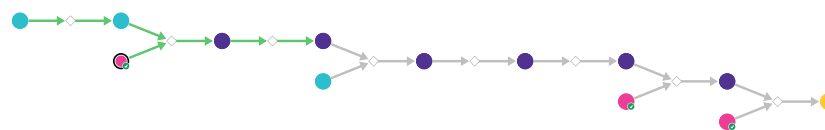
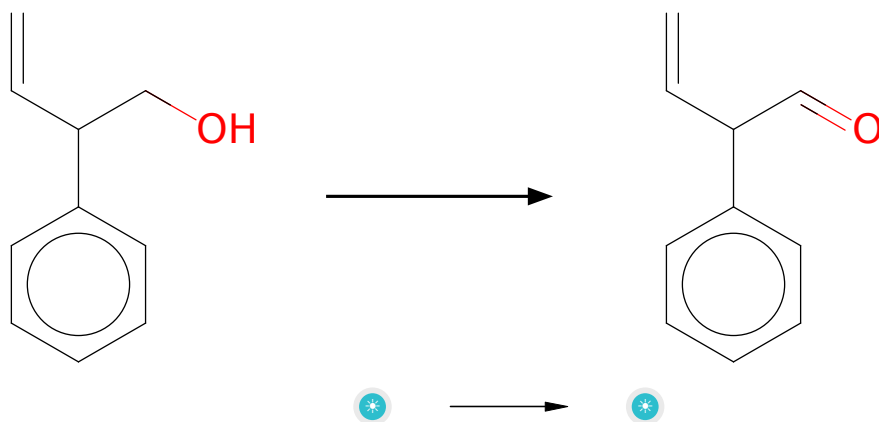


Figure 1: Outline of path 1

### 2.1.1 Oxidation of primary alcohols with DMP



1. 2-phenylbut-3-en-1-ol

1. 2-phenyl-but-3-enal

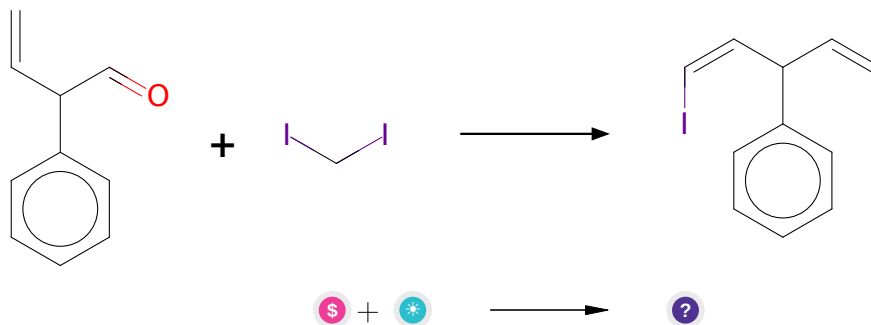
**Typical conditions:** DMP.DCM.0-25 C

**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

### 2.1.2 Iodoolefination of aldehydes



#### Substrates:

1. Diiodomethane - [available at Sigma-Aldrich](#)
2. 2-phenyl-but-3-enal

#### Products:

1. C=CC(/C=C\I)c1ccccc1

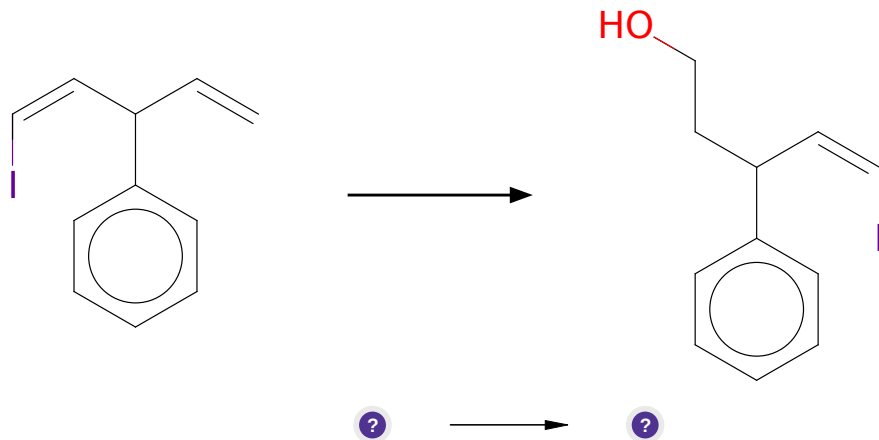
**Typical conditions:** 1.PPh<sub>3</sub>.2.NaN(TMS)2.HMPA.THF

**Protections:** none

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

**Retrosynthesis ID:** 10001773

### 2.1.3 Rh(I) catalyzed hydroboration



**Substrates:**

1. C=CC(/C=C\I)c1ccccc1

**Products:**

1. OCCC(/C=C\I)c1ccccc1

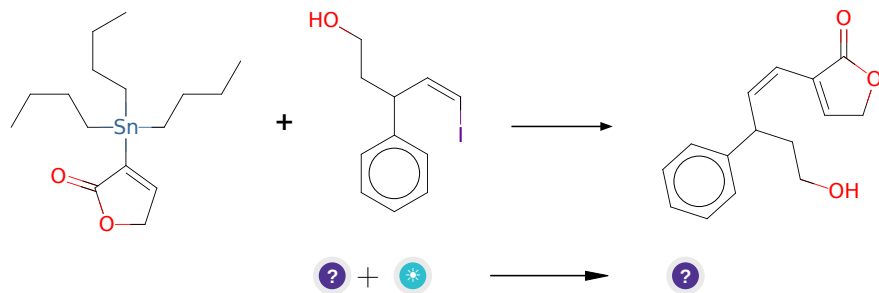
**Typical conditions:** Wilkinson's catalyst.catecholborane.THF.MeOH.NaOH.H2O2

**Protections:** none

**Reference:** DOI: [10.1021/ja00043a009](https://doi.org/10.1021/ja00043a009)

**Retrosynthesis ID:** 9910000

### 2.1.4 Stille Reaction of Vinyl Iodides with Alkenyl Stannanes



**Substrates:**

1. OCCC(/C=C\I)c1ccccc1
2. 3-tributylstannyl-2(5h)-furanone

**Products:**

1. O=C1OCC=C1/C=C\C(CCO)c1ccccc1

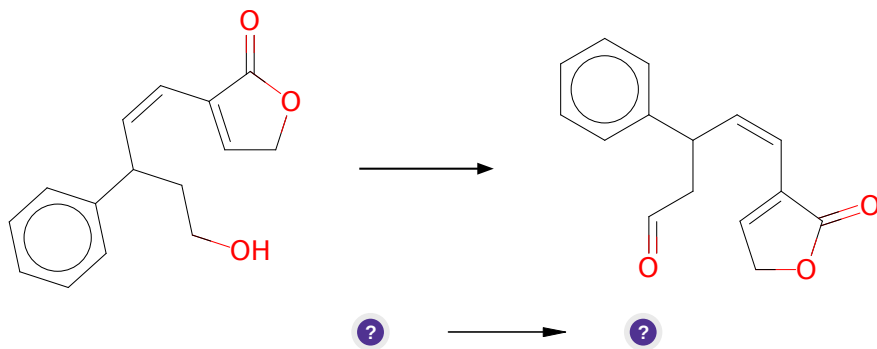
**Typical conditions:** Pd (cat). Ligand. CuCl. THF. AsPh3. Heating

**Protections:** none

**Reference:** DOI: [10.1021/jo047732k](https://doi.org/10.1021/jo047732k) or [10.1021/ja062524q](https://doi.org/10.1021/ja062524q) (SI, page S35) or [10.1021/ja1009579](https://doi.org/10.1021/ja1009579) (SI, page S-15) or [10.1055/s-0034-1378360](https://doi.org/10.1055/s-0034-1378360) or [10.1021/ja028726d](https://doi.org/10.1021/ja028726d) or [10.1016/j.tetlet.2015.10.087](https://doi.org/10.1016/j.tetlet.2015.10.087)

**Retrosynthesis ID:** 9991429

**2.1.5 Oxidation of primary alcohols with DMP**



**Substrates:**

1. O=C1OCC=C1/C=C\C(CCO)c1ccccc1

**Products:**

1. O=CCC(/C=C\C1=CCOC1=O)c1ccccc1

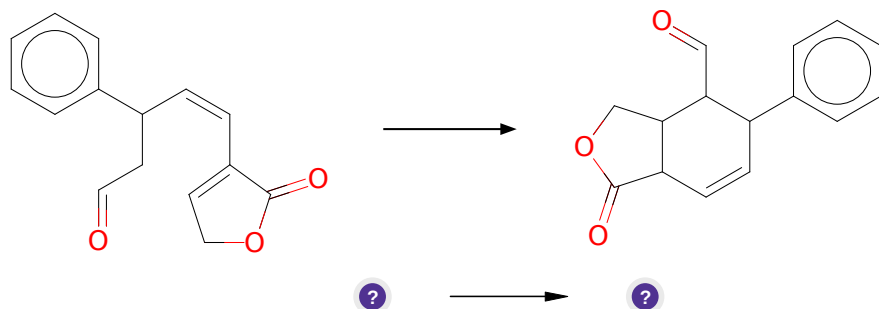
**Typical conditions:** DMP.DCM.0-25 C

**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

### 2.1.6 Michael addition



**Substrates:**

1. O=CCC(/C=C\C1=CCOC1=O)c1ccccc1

**Products:**

1. O=CC1C(c2ccccc2)C=CC2C(=O)OCC21

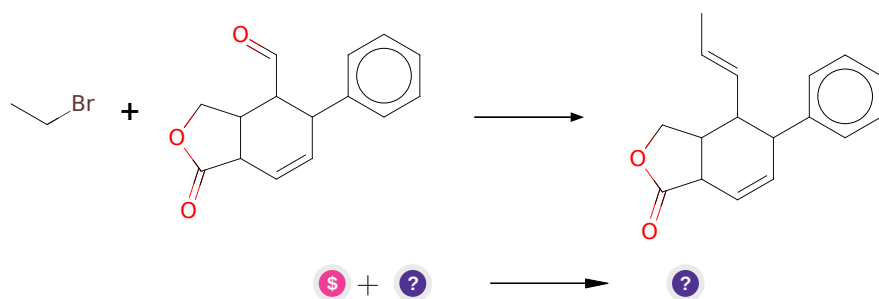
**Typical conditions:** EtONa or other base

**Protections:** none

**Reference:** [10.1016/j.tetlet.2011.02.073](#) AND [10.1016/j.molstruc.2010.12.005](#)  
AND [10.1016/S0040-4039\(97\)00695-3](#) AND [10.1021/ol016401g](#) AND  
[10.1002/ejoc.200500330](#)

**Retrosynthesis ID:** 15774

### 2.1.7 Wittig-Schlosser olefination



**Substrates:**

1. Bromoethane - *available at Sigma-Aldrich*
2. O=CC1C(c2ccccc2)C=CC2C(=O)OCC21

**Products:**

1. C/C=C/C1C(c2ccccc2)C=CC2C(=O)OCC21

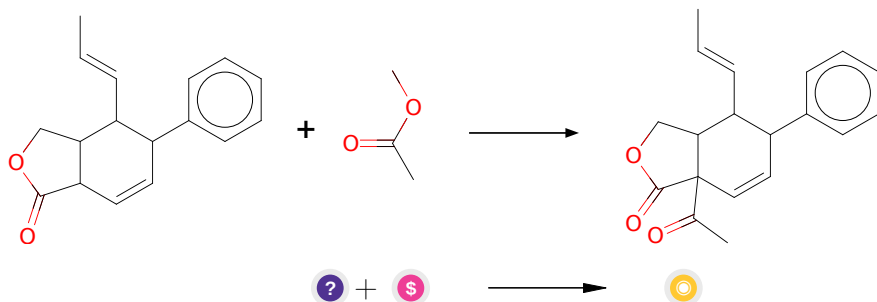
**Typical conditions:** 1.PPh<sub>3</sub> or trialkylphosphite.2.base.aldehyde.3.base

**Protections:** none

**Reference:** [10.1021/ol049701h](#) and [10.1021/ja00535a063](#) and Kurti and Czako; Strategic Applications of Named Reactions in Organic Synthesis. 1st edn., 488-489.

**Retrosynthesis ID:** 9546

### 2.1.8 Claisen Condensation



**Substrates:**

1. C/C=C/C1C(c2ccccc2)C=CC2C(=O)OCC21

2. Methyl acetate - [available at Sigma-Aldrich](#)

**Products:**

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

**Typical conditions:** Base.Solvent

**Protections:** none

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

**Retrosynthesis ID:** 5015

## 2.2 Path 2

**Score:** 146.56

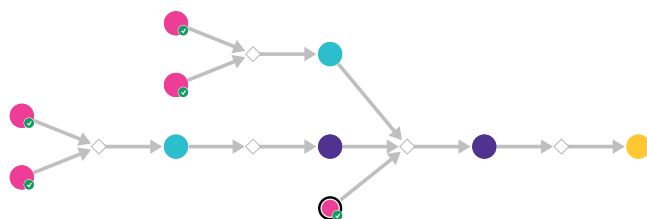
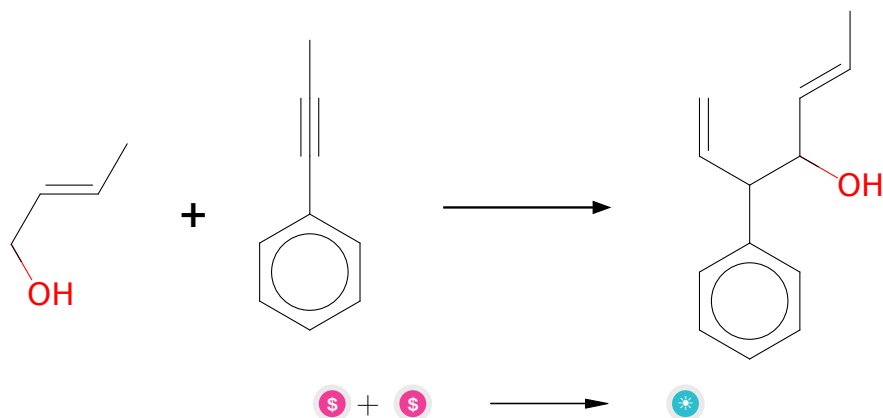


Figure 2: Outline of path 2

### 2.2.1 Coupling of alkynes and alcohols



#### Substrates:

1. 2-Buten-1-ol - *available at Sigma-Aldrich*
2. 1-Phenyl-1-propyne - *available at Sigma-Aldrich*

#### Products:

1. C<sub>13</sub>H<sub>16</sub>O

**Typical conditions:** H<sub>2</sub>Ru(CO)(PPh<sub>3</sub>)<sub>3</sub>.2,4,6-(iPr)<sub>3</sub>PhSO<sub>3</sub>H.SL-J009-1.TBAL.IPA.THF.95C

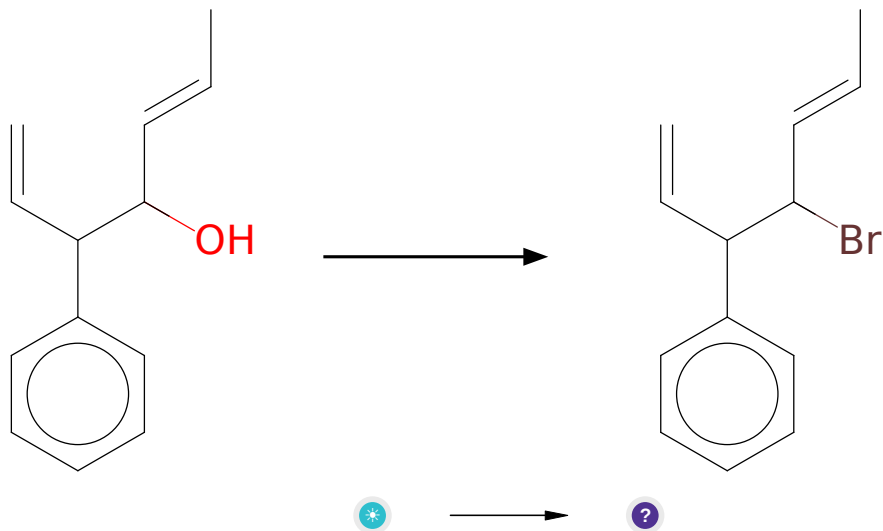
**Protections:** none

**Reference:** DOI: [10.1021/jacs.5b00747](https://doi.org/10.1021/jacs.5b00747)

**Retrosynthesis ID:** 9895



### 2.2.2 Appel Reaction



**Substrates:**

1. C<sub>13</sub>H<sub>16</sub>O

**Products:**

1. C=CC(c1ccccc1)C(Br)/C=C/C

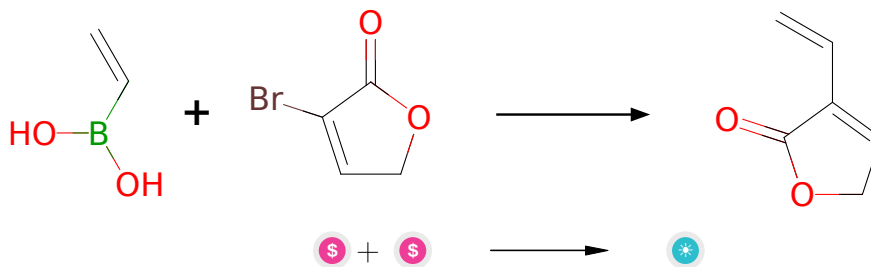
**Typical conditions:** PPh<sub>3</sub>.CBr<sub>4</sub>

**Protections:** none

**Reference:** [10.1016/j.jfluchem.2015.03.009](https://doi.org/10.1016/j.jfluchem.2015.03.009) and [10.1016/j.tet.2005.12.006](https://doi.org/10.1016/j.tet.2005.12.006) and [10.1021/jm00161a029](https://doi.org/10.1021/jm00161a029) and [10.1055/s-1995-5215](https://doi.org/10.1055/s-1995-5215)

**Retrosynthesis ID:** 9990042

### 2.2.3 Suzuki coupling of vinyl bromides with alkenyl boronic acids



**Substrates:**

1. Vinylboronic acid - *available at Sigma-Aldrich*
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

**Products:**

1. 3-vinyl-2(5h)-furanone

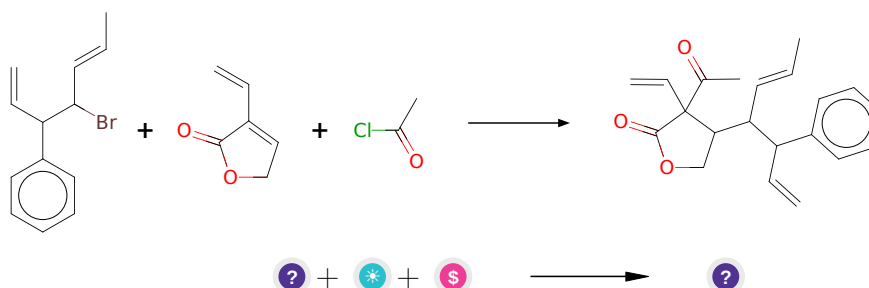
**Typical conditions:** Pd catalyst.base.solvent

**Protections:** none

**Reference:** [10.1021/cr00039a007](#) and [10.1007/3418\\_2012\\_32](#) and [10.1021/cr0505268](#) and [10.1016/j.jfluchem.2016.01.018](#) and [10.1039/C3CS60197H](#)

**Retrosynthesis ID:** 24926

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



**Substrates:**

1. C=CC(c1ccccc1)C(Br)/C=C/C
2. 3-vinyl-2(5h)-furanone
3. Acetyl chloride - *available at Sigma-Aldrich*

**Products:**

1. C=CC(c1ccccc1)C(/C=C/C)C1COC(=O)C1(C=C)C(C)=O

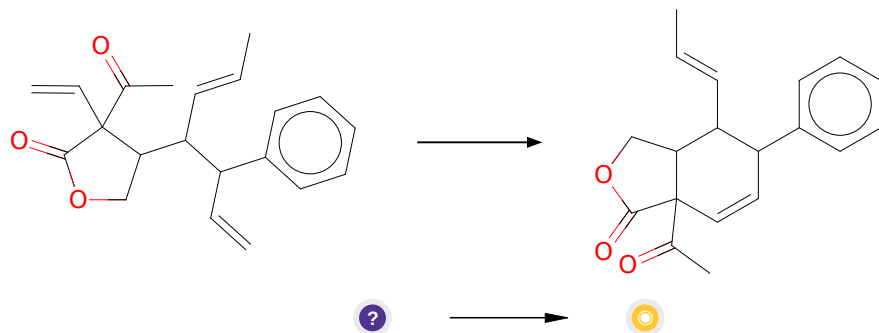
**Typical conditions:** 1.RCuLi.2.AcCl.HMPA

**Protections:** none

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

**Retrosynthesis ID:** 20523

### 2.2.5 Ring-Closing Metathesis



**Substrates:**

1. C=CC(c1ccccc1)C(/C=C/C)C1COC(=O)C1(C=C)C(C)=O

**Products:**

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

**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](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:** 161.11

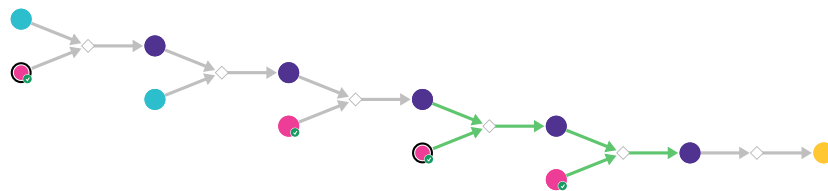
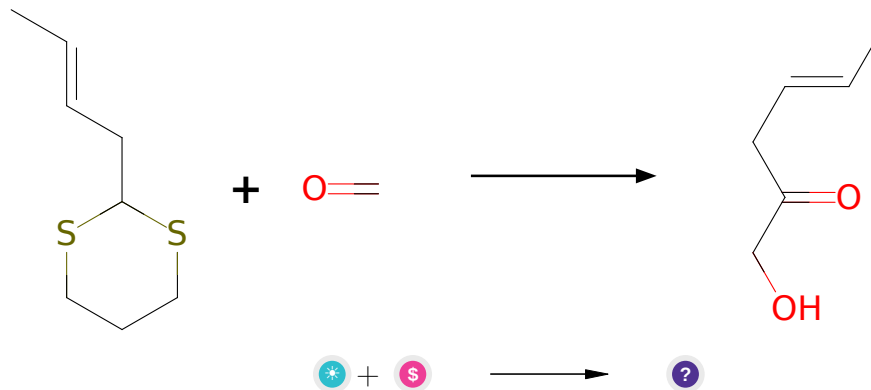


Figure 3: Outline of path 3

### 2.3.1 Corey-Seebach



#### Substrates:

1. (E)-1-(1,3-dithian-2-yl)but-2-ene
2. Formalin - *available at Sigma-Aldrich*

#### Products:

1. C/C=C/CC(=O)CO

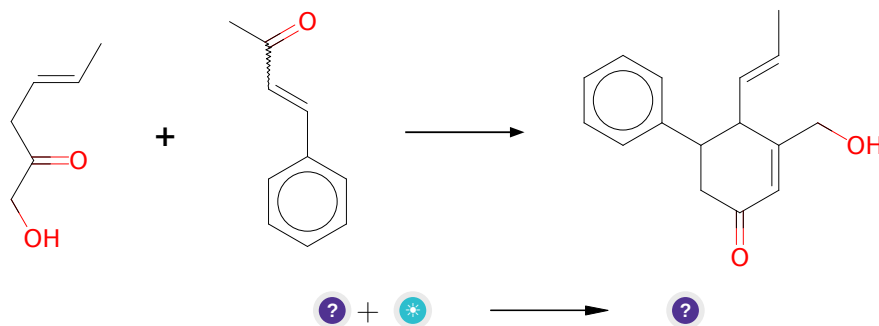
**Typical conditions:** BuLi.THF.-30C.HgO.H2O.THF

**Protections:** none

**Reference:** *10.1055/s-1977-24412*

**Retrosynthesis ID:** 11019

### 2.3.2 Robinson annulation



#### Substrates:

1. C/C=C/CC(=O)CO

2. 4-phenylbutenone

**Products:**

1. C/C=C/C1C(CO)=CC(=O)CC1c1ccccc1

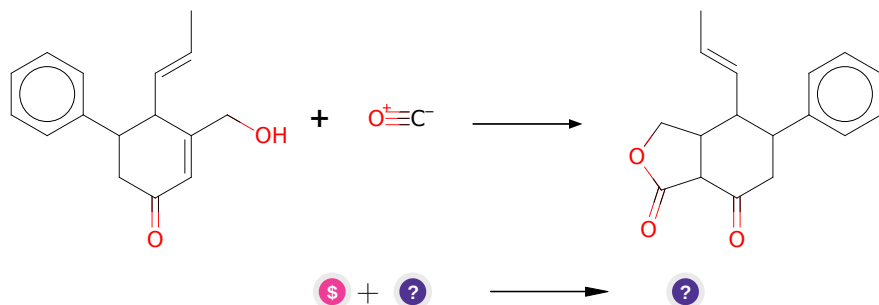
**Typical conditions:** KOH.MeOH

**Protections:** none

**Reference:** DOI: [10.1021/ja9602509](https://doi.org/10.1021/ja9602509) (SI) AND DOI: [10.1021/ja00735a059](https://doi.org/10.1021/ja00735a059) AND [10.1021/ol1011955](https://doi.org/10.1021/ol1011955)

**Retrosynthesis ID:** 7595

**2.3.3 Lactonization of allylic alcohols**



**Substrates:**

1. CORM-2 - [available at Sigma-Aldrich](#)
2. C/C=C/C1C(CO)=CC(=O)CC1c1ccccc1

**Products:**

1. C/C=C/C1C(c2ccccc2)CC(=O)C2C(=O)OCC21

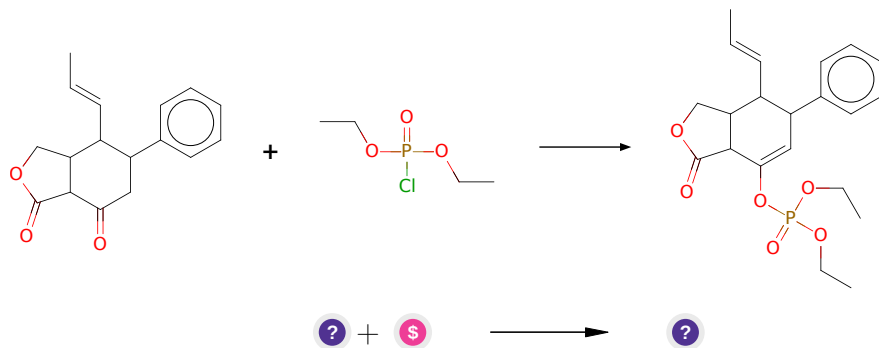
**Typical conditions:** O<sub>2</sub>.PdCl<sub>2</sub>.CuCl<sub>2</sub>.HCl.THF.rt

**Protections:** none

**Reference:** DOI: [10.1016/S0040-4039\(01\)80907-2](https://doi.org/10.1016/S0040-4039(01)80907-2) and [10.1021/jo9702709](https://doi.org/10.1021/jo9702709)

**Retrosynthesis ID:** 7676

### 2.3.4 Synthesis of enol phosphonates



#### Substrates:

1. C/C=C/C1C(c2ccccc2)CC(=O)C2C(=O)OCC21
2. Diethyl chlorophosphate - *available at Sigma-Aldrich*

#### Products:

1. C/C=C/C1C(c2ccccc2)C=C(OP(=O)(OCC)OCC)C2C(=O)OCC21

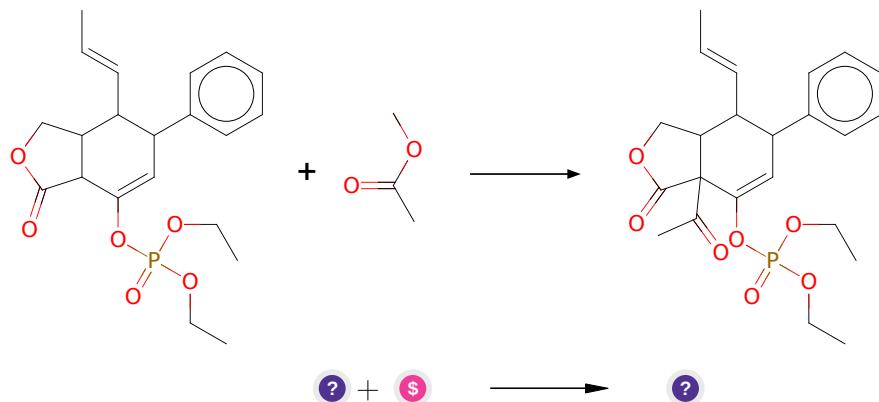
Typical conditions: 1. LDA. 2. ClP(=O)(OR)2

Protections: none

Reference: DOI: [10.1016/j.tetasy.2012.09.012](https://doi.org/10.1016/j.tetasy.2012.09.012)

Retrosynthesis ID: 7573

### 2.3.5 Claisen Condensation



#### Substrates:

1. C/C=C/C1C(c2ccccc2)C=C(OP(=O)(OCC)OCC)C2C(=O)OCC21
2. Methyl acetate - *available at Sigma-Aldrich*

**Products:**

1. C/C=C/C1C(c2ccccc2)C=C(OP(=O)(OCC)OCC)C2(C(C)=O)C(=O)OCC12

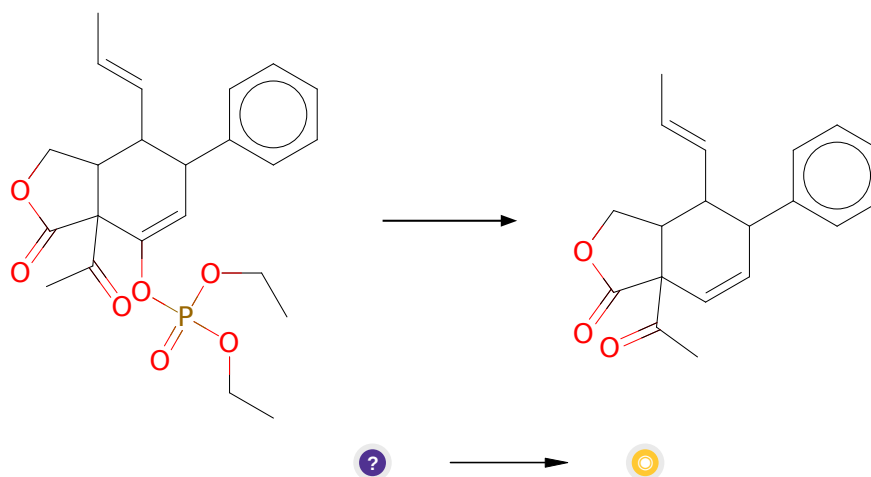
**Typical conditions:** Base.Solvent

**Protections:** none

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

**Retrosynthesis ID:** 5015

### 2.3.6 Reduction of enol phosphonates



**Substrates:**

1. C/C=C/C1C(c2ccccc2)C=C(OP(=O)(OCC)OCC)C2(C(C)=O)C(=O)OCC12

**Products:**

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

**Typical conditions:** Et<sub>3</sub>Al.Pd(PPh<sub>3</sub>)<sub>4</sub>

**Protections:** none

**Reference:** [10.1021/jo00387a038](#) AND [10.1021/jo00292a049](#) AND [10.1039/C1CS15100B](#)

**Retrosynthesis ID:** 23046

## 2.4 Path 4

Score: 164.14

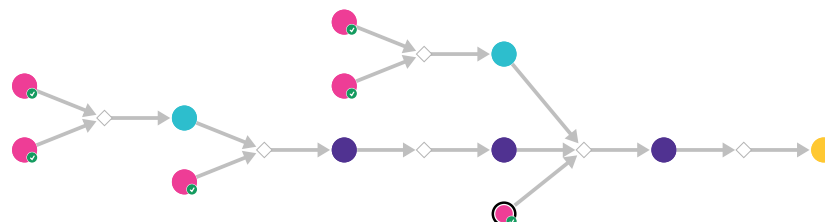
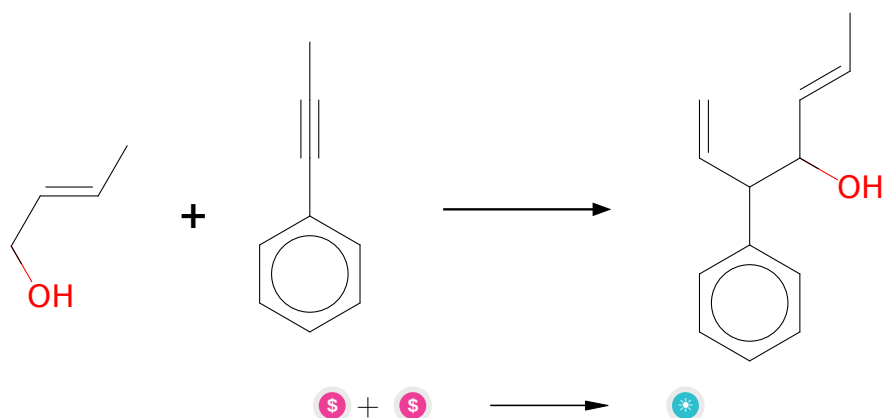


Figure 4: Outline of path 4

### 2.4.1 Coupling of alkynes and alcohols



#### Substrates:

1. 2-Buten-1-ol - *available at Sigma-Aldrich*
2. 1-Phenyl-1-propyne - *available at Sigma-Aldrich*

#### Products:

1. C<sub>13</sub>H<sub>16</sub>O

**Typical conditions:** H<sub>2</sub>Ru(CO)(PPh<sub>3</sub>)<sub>3</sub>.2,4,6-(iPr)<sub>3</sub>PhSO<sub>3</sub>H.SL-J009-1.TBAI.IPA.THF.95C

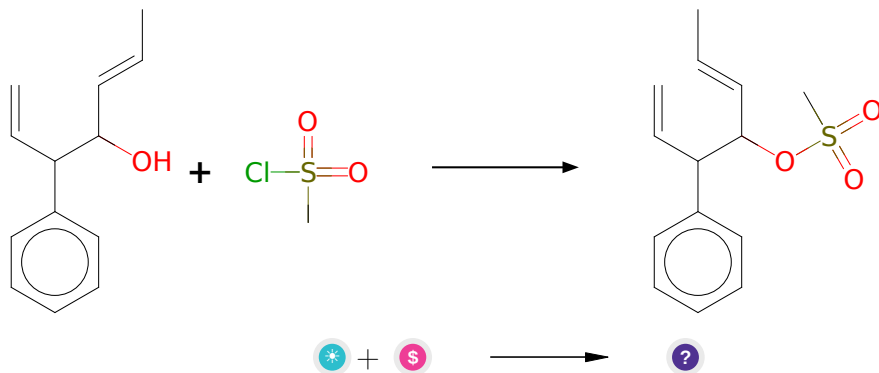
**Protections:** none

**Reference:** DOI: [10.1021/jacs.5b00747](https://doi.org/10.1021/jacs.5b00747)

**Retrosynthesis ID:** 9895



### 2.4.2 Sulfonation of secondary alcohols



#### Substrates:

1. C<sub>13</sub>H<sub>16</sub>O
2. Mesyl chloride - *available at Sigma-Aldrich*

#### Products:

1. C=CC(c1ccccc1)C(/C=C/C)OS(C)(=O)=O

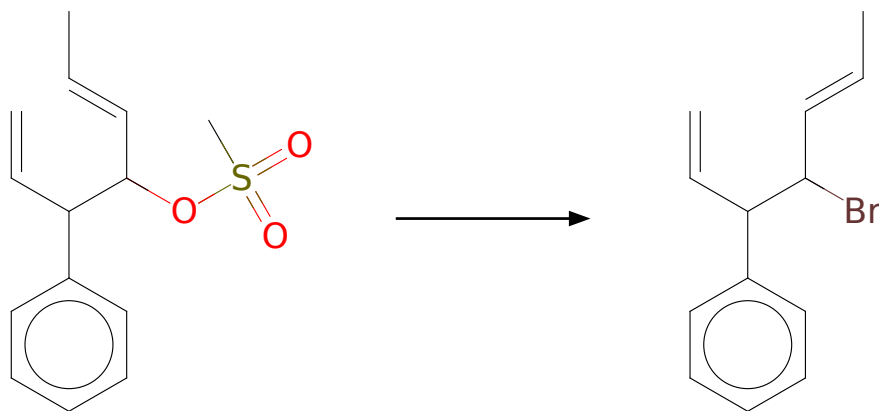
Typical conditions: Et<sub>3</sub>N.DMAP.DCM

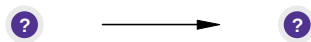
Protections: none

Reference: [10.1021/jo048289g](#) and [10.1021/ja9617808](#) and [10.1016/j.steroids.2005.10.004](#)

Retrosynthesis ID: 24386

### 2.4.3 Substitution of secondary mesyl group with bromide





**Substrates:**

1. C=CC(c1ccccc1)C(/C=C/C)OS(C)(=O)=O

**Products:**

1. C=CC(c1ccccc1)C(Br)/C=C/C

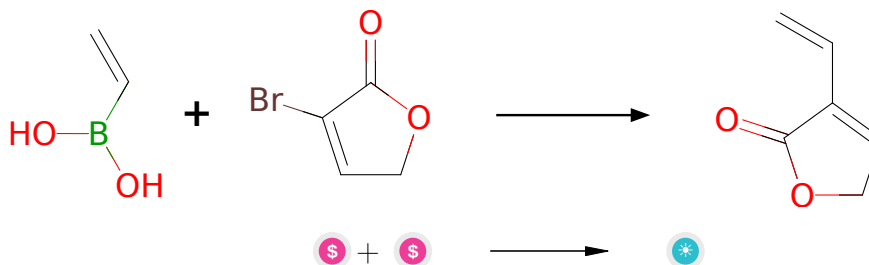
**Typical conditions:** LiBr.DMF

**Protections:** none

**Reference:** [10.1021/jo00068a037](#) and [10.1016/S0040-4020\(03\)00140-6](#)

**Retrosynthesis ID:** 29713

#### 2.4.4 Suzuki coupling of vinyl bromides with alkenyl boronic acids



**Substrates:**

1. Vinylboronic acid - [available at Sigma-Aldrich](#)
2. 3-bromo-2,5-dihydrofuran-2-one - [available at Sigma-Aldrich](#)

**Products:**

1. 3-vinyl-2(5h)-furanone

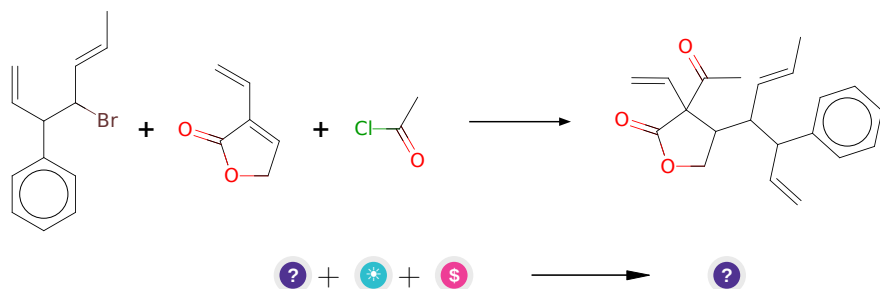
**Typical conditions:** Pd catalyst.base.solvent

**Protections:** none

**Reference:** [10.1021/cr00039a007](#) and [10.1007/3418\\_2012\\_32](#) and [10.1021/cr0505268](#) and [10.1016/j.jfluchem.2016.01.018](#) and [10.1039/C3CS60197H](#)

**Retrosynthesis ID:** 24926

### 2.4.5 Conjugated addition of organocuprate-acylation of enones and enoate esters



#### Substrates:

1. C=CC(c1ccccc1)C(Br)/C=C/C
2. 3-vinyl-2(5h)-furanone
3. Acetyl chloride - *available at Sigma-Aldrich*

#### Products:

1. C=CC(c1ccccc1)C(/C=C/C)C1COC(=O)C1(C=C)C(C)=O

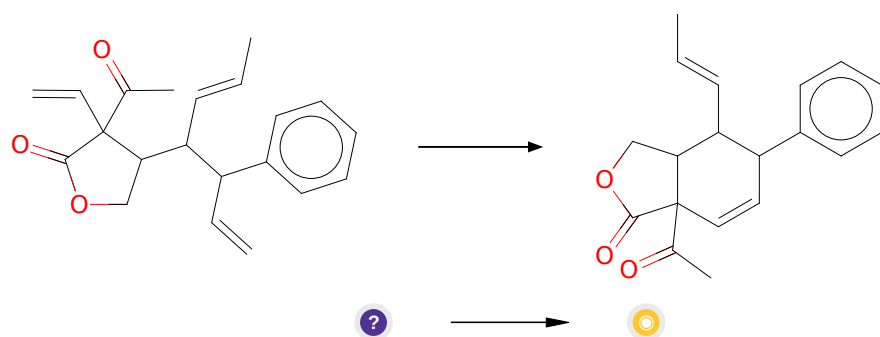
**Typical conditions:** 1.RCuLi.2.AcCl.HMPA

**Protections:** none

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

**Retrosynthesis ID:** 20523

### 2.4.6 Ring-Closing Metathesis



#### Substrates:

1. C=CC(c1ccccc1)C(/C=C/C)C1COC(=O)C1(C=C)C(C)=O

**Products:**

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

**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](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: 164.14

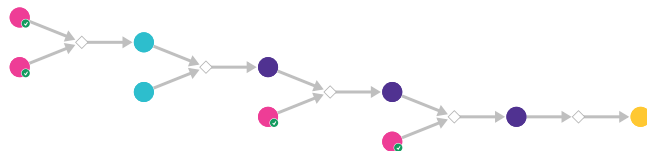
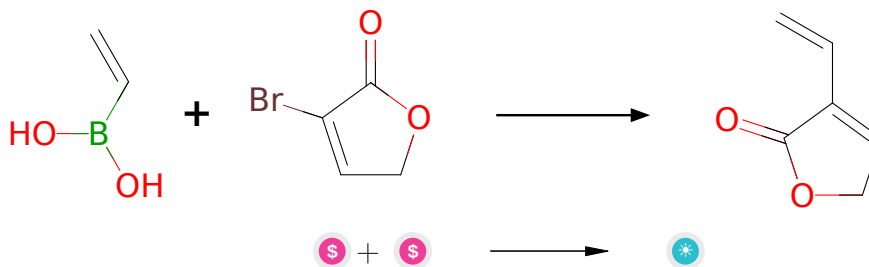


Figure 5: Outline of path 5

### 2.5.1 Suzuki coupling of vinyl bromides with alkenyl boronic acids



**Substrates:**

1. Vinylboronic acid - *available at Sigma-Aldrich*
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

**Products:**

1. 3-vinyl-2(5h)-furanone

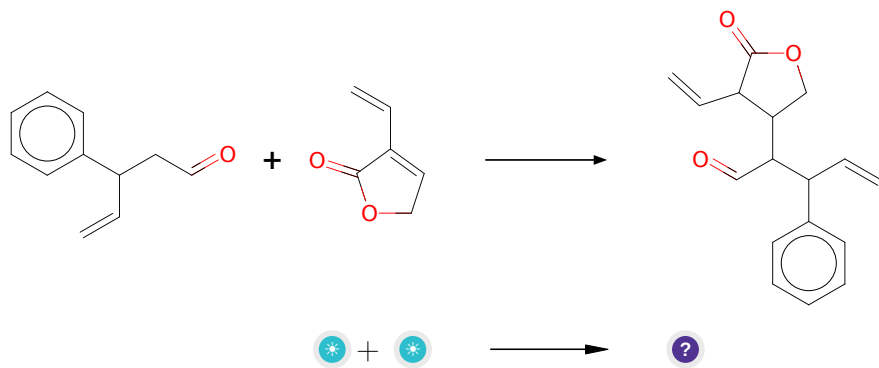
**Typical conditions:** Pd catalyst.base.solvent

**Protections:** none

**Reference:** [10.1021/cr00039a007](#) and [10.1007/3418\\_2012\\_32](#) and [10.1021/cr0505268](#) and [10.1016/j.jfluchem.2016.01.018](#) and [10.1039/C3CS60197H](#)

**Retrosynthesis ID:** 24926

### 2.5.2 Michael addition



**Substrates:**

1. 3-vinyl-2(5h)-furanone
2. 3-phenyl-4-pentenal

**Products:**

1. C=CC1C(=O)OCC1C(C=O)C(C=C)c1cccc1

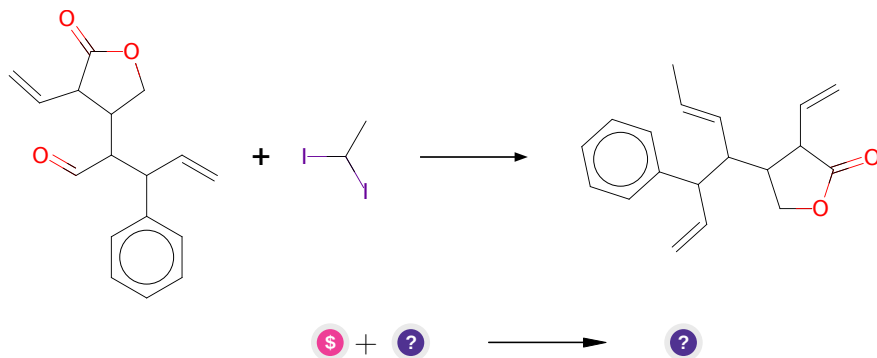
**Typical conditions:** EtONa or other base

**Protections:** none

**Reference:** [10.1016/j.tetlet.2011.02.073](#) AND [10.1016/j.molstruc.2010.12.005](#)  
AND [10.1016/S0040-4039\(97\)00695-3](#) AND [10.1021/ol016401g](#) AND [10.1002/ejoc.200500330](#)

**Retrosynthesis ID:** 15774

### 2.5.3 Takai olefination



#### Substrates:

- 1,1-Diiodoethane - *available at Sigma-Aldrich*
- C=CC1C(=O)OCC1C(C=O)C(C=C)c1ccccc1

#### Products:

- C=CC1C(=O)OCC1C(/C=C/C)C(C=C)c1ccccc1

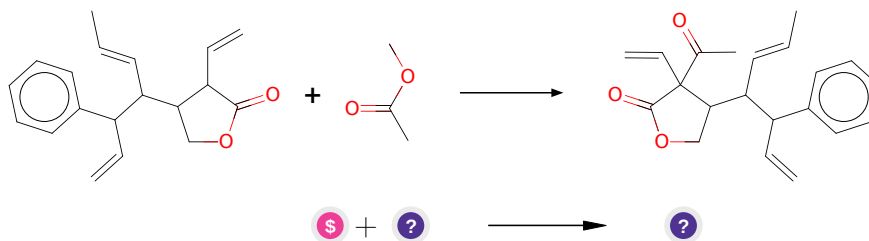
**Typical conditions:** CrCl<sub>2</sub>.THF.DMF

**Protections:** none

**Reference:** [10.1021/ja00283a046](#) and [10.1021/ja00237a081](#)

**Retrosynthesis ID:** 10942

### 2.5.4 Claisen Condensation



#### Substrates:

- Methyl acetate - *available at Sigma-Aldrich*
- C=CC1C(=O)OCC1C(/C=C/C)C(C=C)c1ccccc1

#### Products:

- C=CC(c1ccccc1)C(/C=C/C)C1COC(=O)C1(C=C)C(C)=O

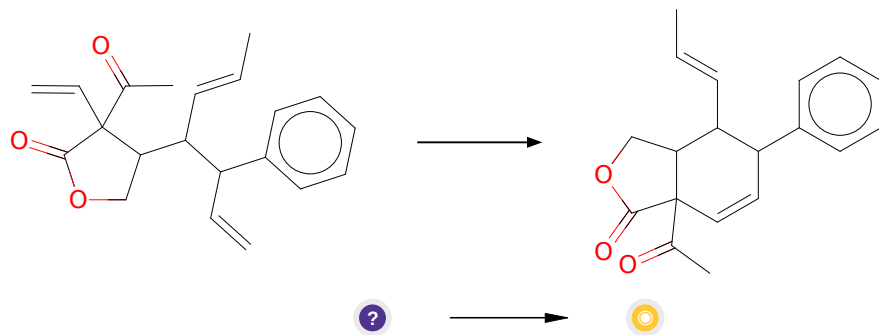
**Typical conditions:** Base.Solvent

**Protections:** none

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

**Retrosynthesis ID:** 5015

### 2.5.5 Ring-Closing Metathesis



**Substrates:**

1. C=CC(c1ccccc1)C(/C=C/C)C1COC(=O)C1(C=C)C(C)=O

**Products:**

1. C/C=C/C1C(c2ccccc2)C=CC2(C(C)=O)C(=O)OCC12

**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