

# Paths of analysis\*

L11

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.

**Strategies:** none selected

**FGI Coeff:** 0

**Tunnels Coeff:** 0

**JSON Parameters:** {}

## 2 Paths

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

### 2.1 Path 1

**Score:** 358.72

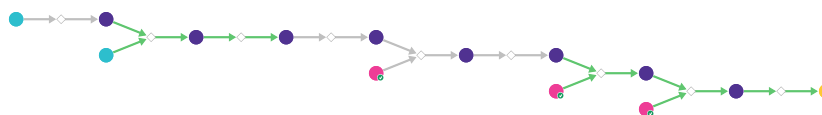
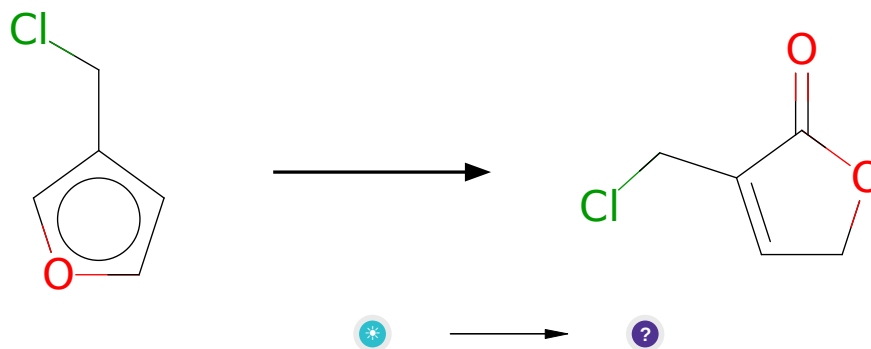


Figure 1: Outline of path 1

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



**Substrates:**

1. 3-chloromethyl-furan

**Products:**

1. O=C1OCC=C1CCl

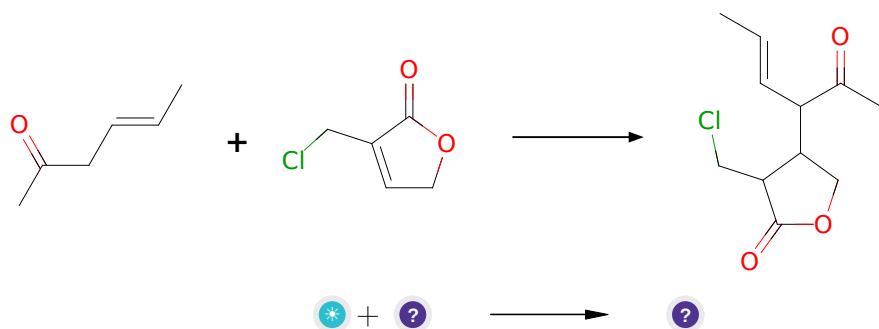
**Typical conditions:** NBS.MW.MeOH

**Protections:** none

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

**Retrosynthesis ID:** 49766

### 2.1.2 Michael addition



**Substrates:**

1. hex-4t-en-2-one
2. O=C1OCC=C1CCl

**Products:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1CCl

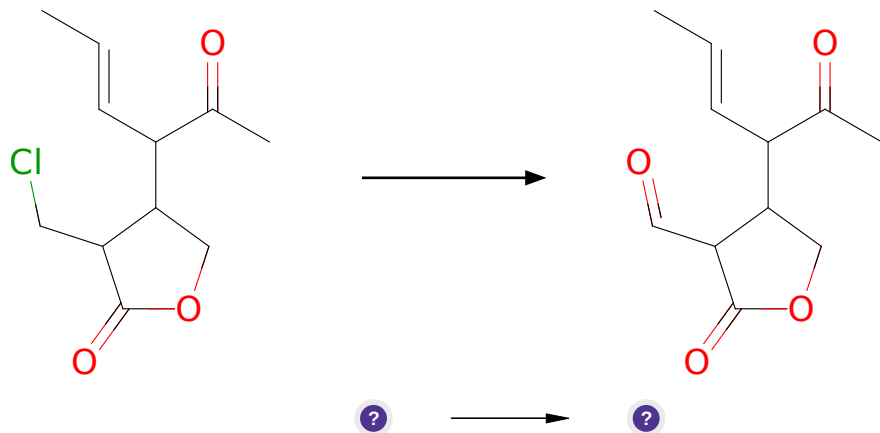
**Typical conditions:** EtONa or other base

**Protections:** none

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

**Retrosynthesis ID:** 15774

### 2.1.3 Kornblum Oxidation



**Substrates:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1CCl

**Products:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

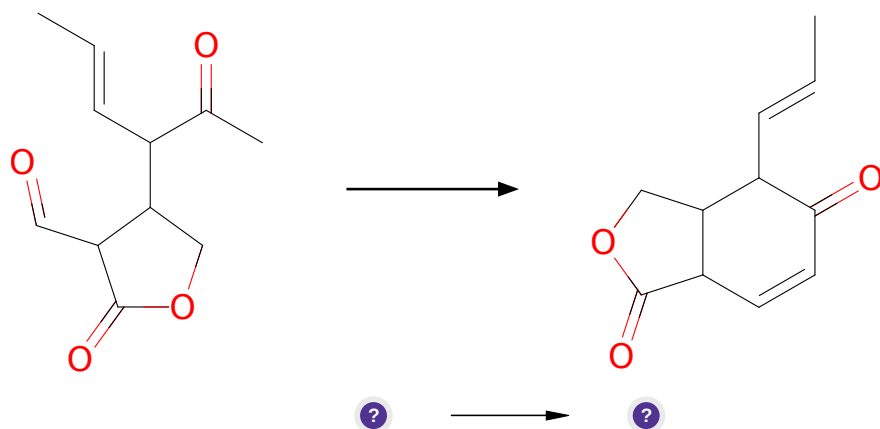
**Typical conditions:** DMSO.NEt<sub>3</sub>

**Protections:** none

**Reference:** [10.1080/00397918608056381](https://doi.org/10.1080/00397918608056381) and [10.1002/9780470638859.conrr373](https://doi.org/10.1002/9780470638859.conrr373)

**Retrosynthesis ID:** 11658

### 2.1.4 Aldol Condensation



**Substrates:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

**Products:**

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

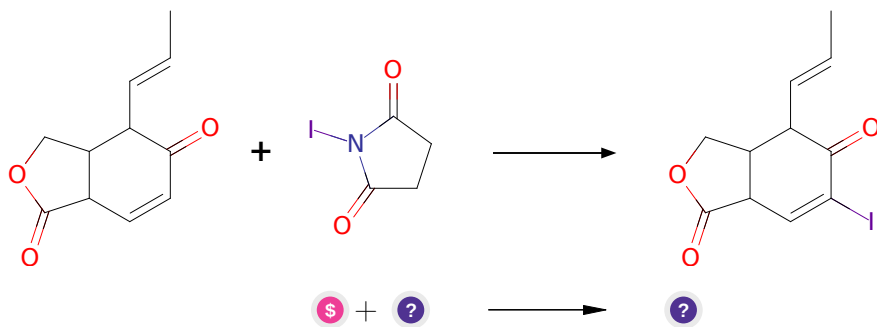
**Typical conditions:** NaOEt.base

**Protections:** none

**Reference:** [10.1080/00397911.2016.1206938](https://doi.org/10.1080/00397911.2016.1206938)

**Retrosynthesis ID:** 10896

#### 2.1.5 Alpha-halogenation of alpha-beta-unsaturated ketones



**Substrates:**

1. N-Iodosuccinimide - [available at Sigma-Aldrich](#)

2. C/C=C/C1C(=O)C=CC2C(=O)OCC21

**Products:**

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

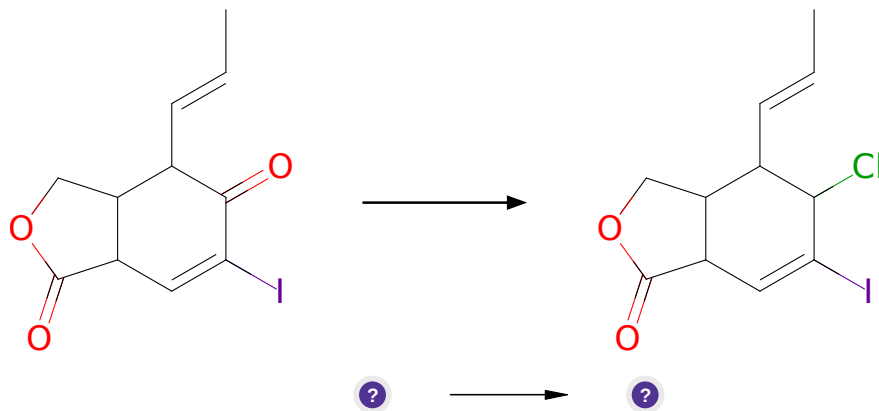
**Typical conditions:** NCS or NBS or NIS.CH<sub>3</sub>CN.rt

**Protections:** none

**Reference:** DOI: [10.1002/anie.200353037](https://doi.org/10.1002/anie.200353037)

**Retrosynthesis ID:** 792

### 2.1.6 Synthesis of alkyl chlorides from ketones



**Substrates:**

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

**Products:**

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21

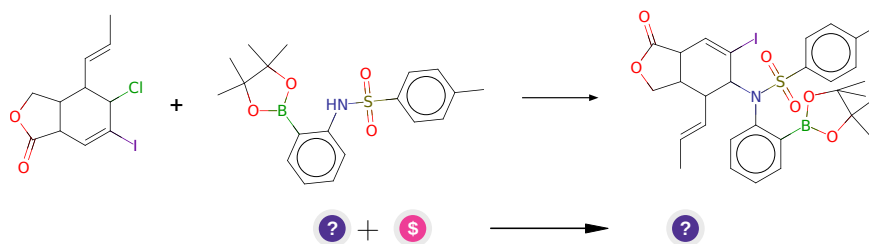
**Typical conditions:** InO<sub>3</sub>.chloroform.SiMe<sub>2</sub>Cl

**Protections:** none

**Reference:** DOI: [10.1021/ja0283246](https://doi.org/10.1021/ja0283246)

**Retrosynthesis ID:** 11620

### 2.1.7 Alkylation of sulfonamides with alkyl chlorides



**Substrates:**

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21
2. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

**Products:**

1. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

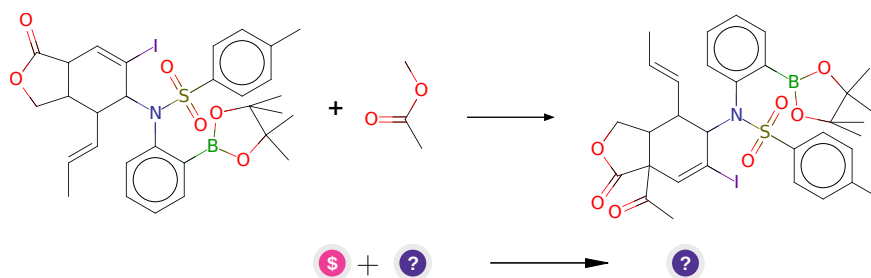
**Typical conditions:** LDA

**Protections:** none

**Reference:** [10.1002/1099-0690\(200101\)2001:2<323::AID-EJOC323>3.0.CO;2-A](#)

**Retrosynthesis ID:** 7727

### 2.1.8 Claisen Condensation



**Substrates:**

1. Methyl acetate - [available at Sigma-Aldrich](#)
2. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

**Products:**

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)O2

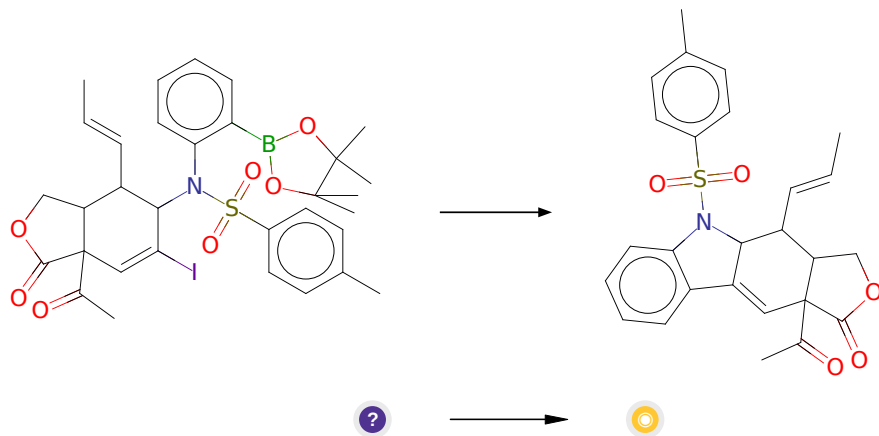
**Typical conditions:** Base.Solvent

**Protections:** none

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

**Retrosynthesis ID:** 5015

## 2.1.9 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



**Substrates:**

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)OCC13

**Products:**

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

**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:** 10176

## 2.2 Path 2

**Score:** 358.72

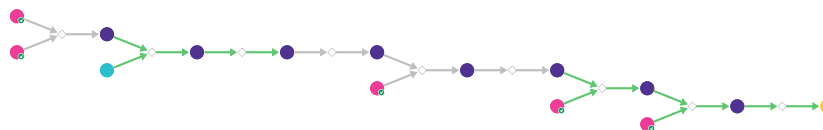
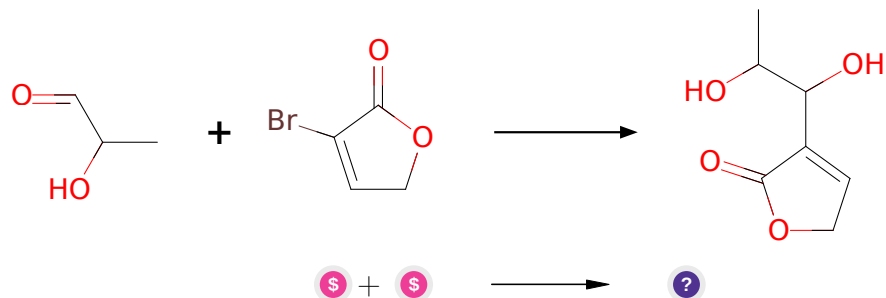


Figure 2: Outline of path 2



### 2.2.1 Reformatsky Reaction



#### Substrates:

1. DL-Lactaldehyde solution - *available at Sigma-Aldrich*
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

#### Products:

1. CC(O)C(O)C1=CCOC1=O

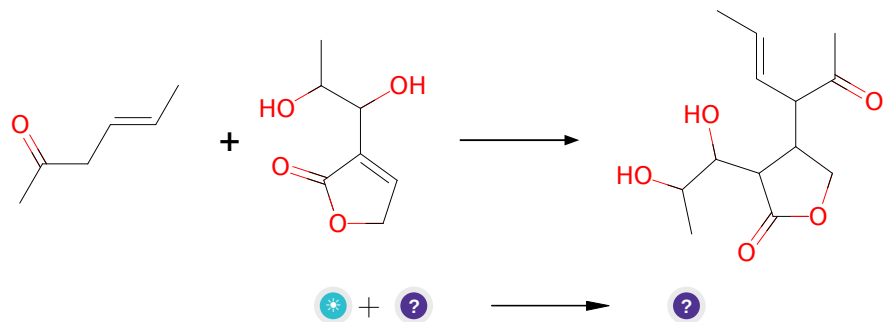
**Typical conditions:** Me2Zn.B(OMe)3.toluene.Et2O

**Protections:** none

**Reference:** [10.1021/jo200774e](#) p. 6373 and [10.1021/jo00163a019](#) p. 2522, 2525

**Retrosynthesis ID:** 11164

### 2.2.2 Michael addition



#### Substrates:

1. hex-4t-en-2-one
2. CC(O)C(O)C1=CCOC1=O

#### Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C(O)C(C)O

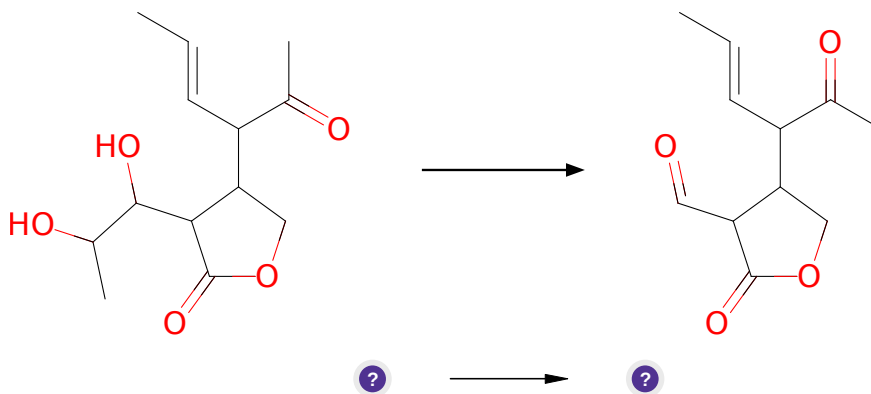
**Typical conditions:** EtONa or other base

**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

### 2.2.3 Cleavage of 1,2-diols with NaIO<sub>4</sub>



**Substrates:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C(O)C(C)O

**Products:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

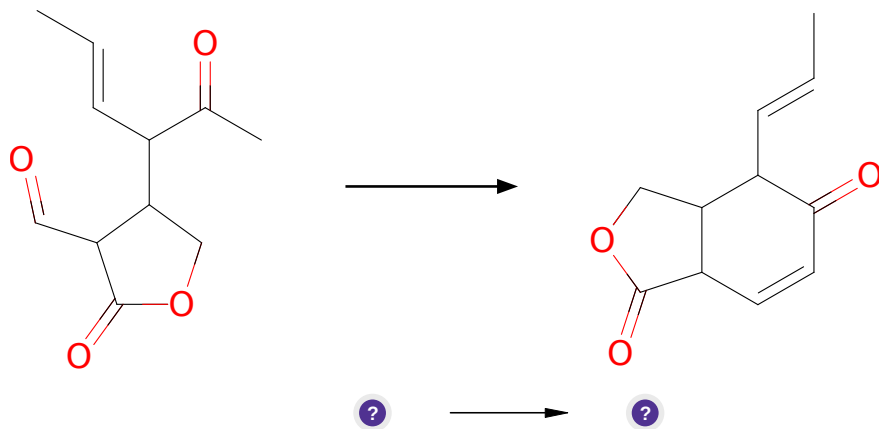
**Typical conditions:** NaIO<sub>4</sub>.solvent

**Protections:** none

**Reference:** [10.1039/C5OB00238A](#) and [10.1002/chem.201301371](#) and  
[10.1021/ol052106a](#)

**Retrosynthesis ID:** 31017508

### 2.2.4 Aldol Condensation



**Substrates:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

**Products:**

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

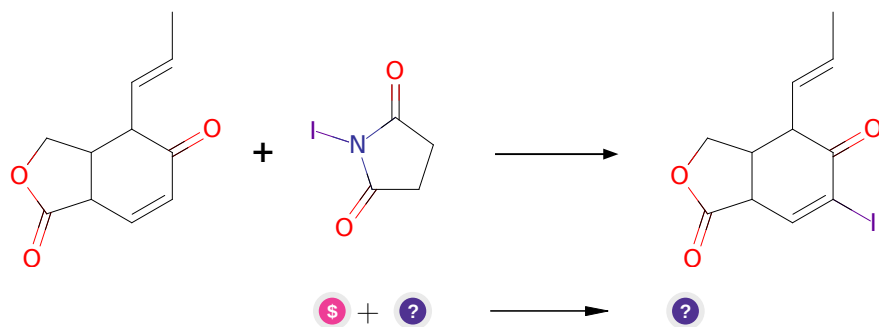
**Typical conditions:** NaOEt.base

**Protections:** none

**Reference:** [10.1080/00397911.2016.1206938](https://doi.org/10.1080/00397911.2016.1206938)

**Retrosynthesis ID:** 10896

### 2.2.5 Alpha-halogenation of alpha-beta-unsaturated ketones



**Substrates:**

1. N-Iodosuccinimide - *available at Sigma-Aldrich*

2. C/C=C/C1C(=O)C=CC2C(=O)OCC21

**Products:**

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

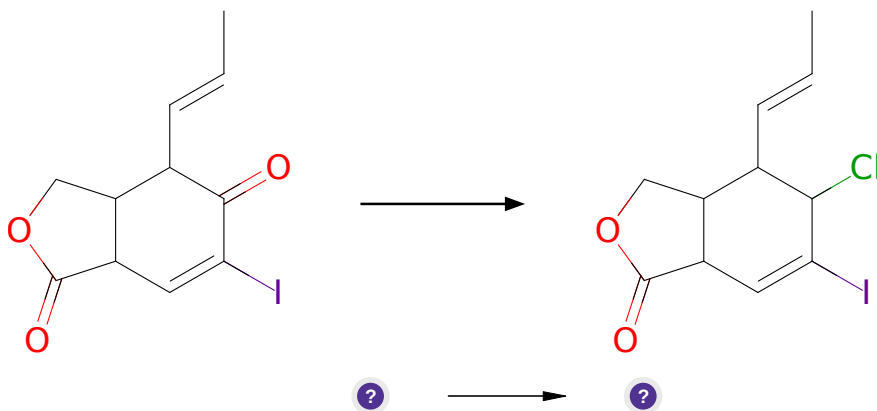
**Typical conditions:** NCS or NBS or NIS.CH<sub>3</sub>CN.rt

**Protections:** none

**Reference:** DOI: [10.1002/anie.200353037](https://doi.org/10.1002/anie.200353037)

**Retrosynthesis ID:** 792

#### 2.2.6 Synthesis of alkyl chlorides from ketones



**Substrates:**

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

**Products:**

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21

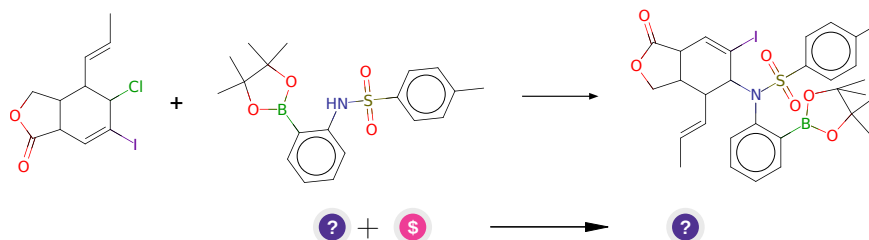
**Typical conditions:** InO<sub>3</sub>.chloroform.SiMe<sub>2</sub>Cl

**Protections:** none

**Reference:** DOI: [10.1021/ja0283246](https://doi.org/10.1021/ja0283246)

**Retrosynthesis ID:** 11620

### 2.2.7 Alkylation of sulfonamides with alkyl chlorides



#### Substrates:

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21
2. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

#### Products:

1. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

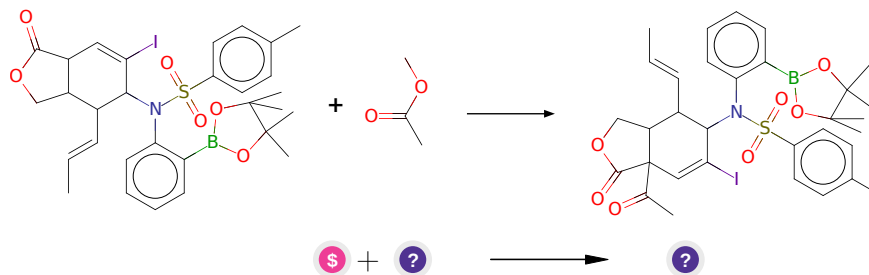
Typical conditions: LDA

Protections: none

Reference: [10.1002/1099-0690\(200101\)2001:2<323::AID-EJOC323>3.0.CO;2-A](#)

Retrosynthesis ID: 7727

### 2.2.8 Claisen Condensation



#### Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

#### Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)OCC21

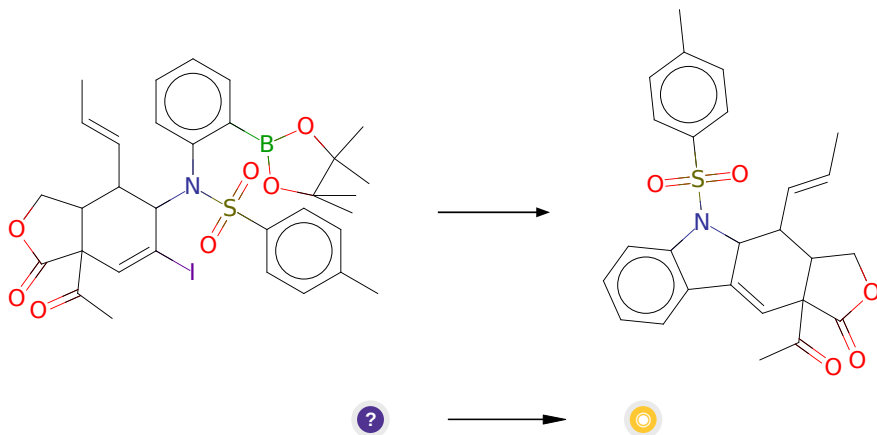
**Typical conditions:** Base.Solvent

**Protections:** none

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

**Retrosynthesis ID:** 5015

### 2.2.9 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



**Substrates:**

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)O2

**Products:**

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

**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:** 10176

## 2.3 Path 3

**Score:** 358.72

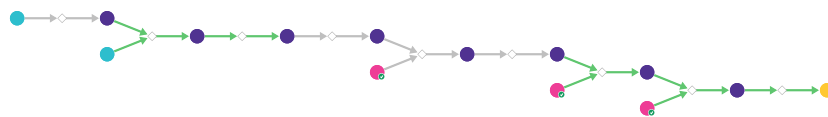
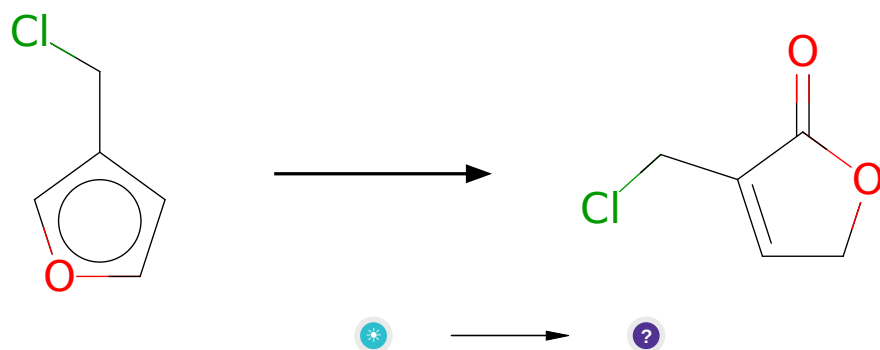


Figure 3: Outline of path 3

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



**Substrates:**

1. 3-chloromethyl-furan

**Products:**

1. O=C1OCC=C1CCl

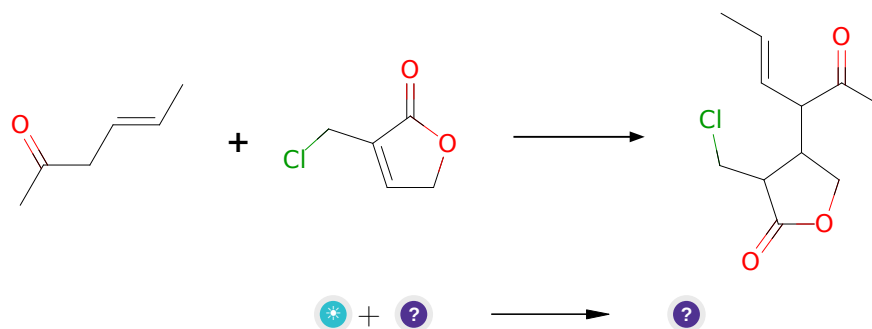
**Typical conditions:** NBS.MW.MeOH

**Protections:** none

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

**Retrosynthesis ID:** 49766

### 2.3.2 Michael addition



**Substrates:**

1. hex-4t-en-2-one
2. O=C1OCC=C1CCl

**Products:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1CCl

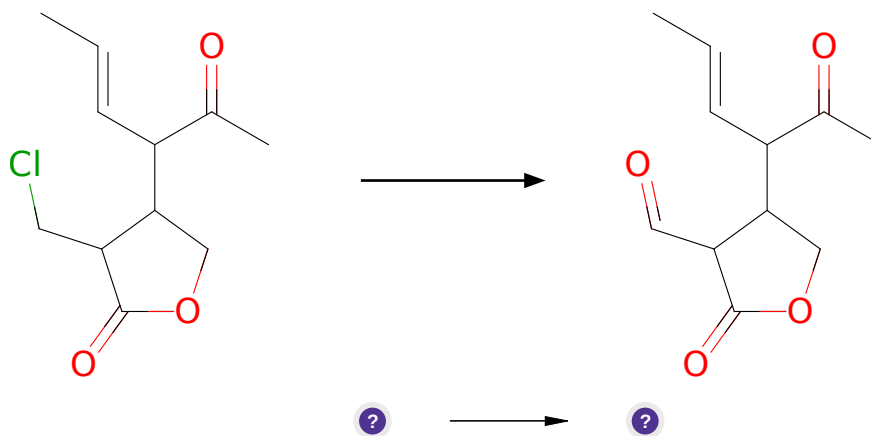
**Typical conditions:** EtONa or other base

**Protections:** none

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

**Retrosynthesis ID:** 15774

**2.3.3 Kornblum Oxidation**



**Substrates:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1CCl

**Products:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

**Typical conditions:** DMSO.NEt3

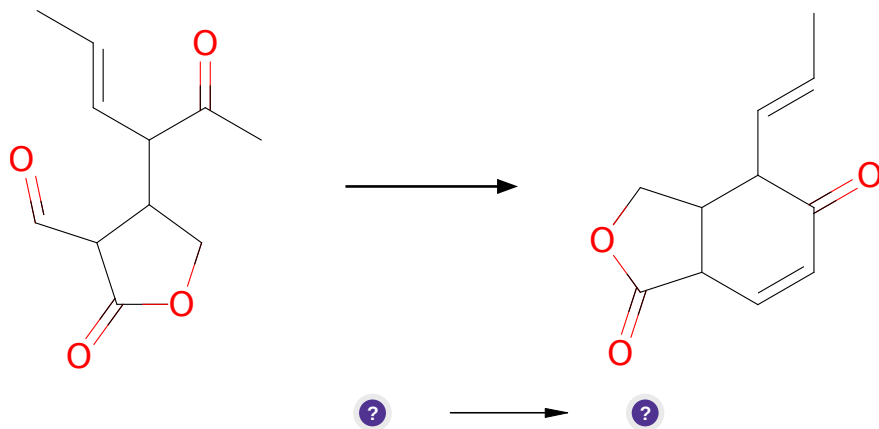
**Protections:** none

**Reference:** [10.1080/00397918608056381](https://doi.org/10.1080/00397918608056381) and [10.1002/9780470638859.conrr373](https://doi.org/10.1002/9780470638859.conrr373)

**Retrosynthesis ID:** 11658



### 2.3.4 Aldol Condensation



**Substrates:**

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

**Products:**

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

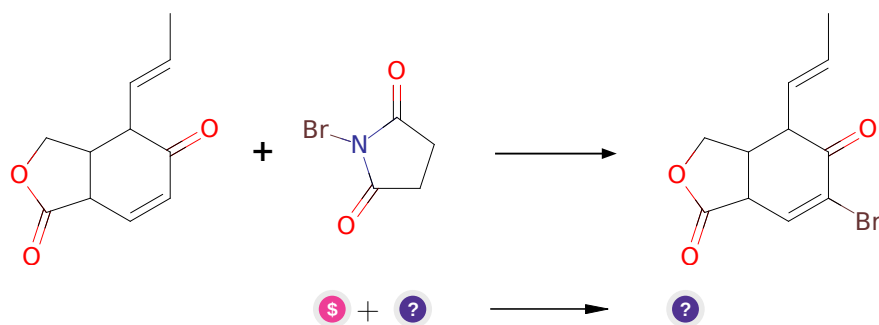
**Typical conditions:** NaOEt.base

**Protections:** none

**Reference:** [10.1080/00397911.2016.1206938](#)

**Retrosynthesis ID:** 10896

### 2.3.5 Alpha-halogenation of alpha-beta-unsaturated ketones



**Substrates:**

1. N-Bromosuccinimide - [available at Sigma-Aldrich](#)
2. C/C=C/C1C(=O)C=CC2C(=O)OCC21

**Products:**

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

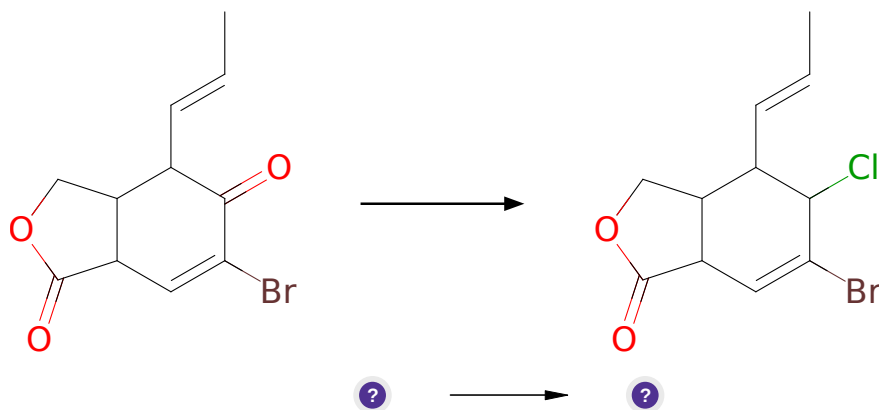
**Typical conditions:** NCS or NBS or NIS.CH<sub>3</sub>CN.rt

**Protections:** none

**Reference:** DOI: [10.1002/anie.200353037](https://doi.org/10.1002/anie.200353037)

**Retrosynthesis ID:** 792

**2.3.6 Synthesis of alkyl chlorides from ketones**



**Substrates:**

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

**Products:**

1. C/C=C/C1C(Cl)C(Br)=CC2C(=O)OCC21

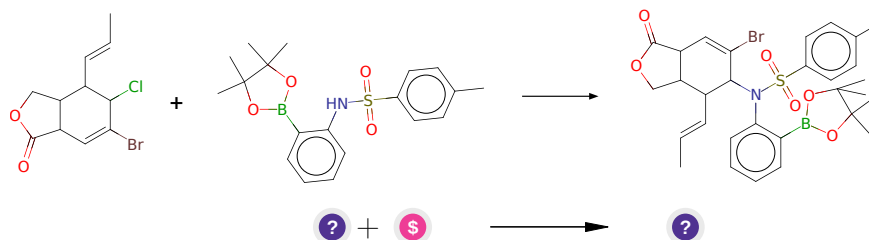
**Typical conditions:** InO<sub>3</sub>.chloroform.SiMe<sub>2</sub>Cl

**Protections:** none

**Reference:** DOI: [10.1021/ja0283246](https://doi.org/10.1021/ja0283246)

**Retrosynthesis ID:** 11620

### 2.3.7 Alkylation of sulfonamides with alkyl chlorides



#### Substrates:

1. C/C=C/C1C(Cl)C(Br)=CC2C(=O)OCC21
2. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

#### Products:

1. C/C=C/C1C2COC(=O)C2C=C(Br)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

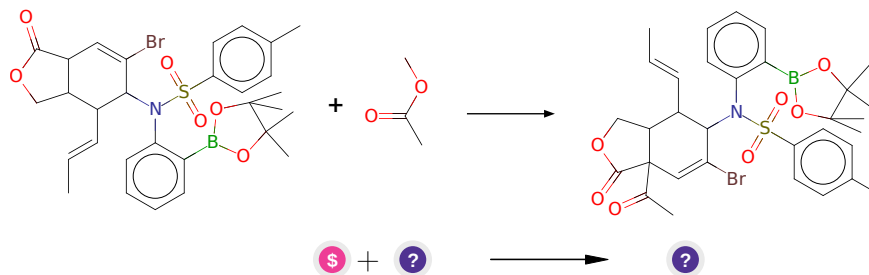
Typical conditions: LDA

Protections: none

Reference: [10.1002/1099-0690\(200101\)2001:2<323::AID-EJOC323>3.0.CO;2-A](#)

Retrosynthesis ID: 7727

### 2.3.8 Claisen Condensation



#### Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. C/C=C/C1C2COC(=O)C2C=C(Br)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

#### Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O)C21

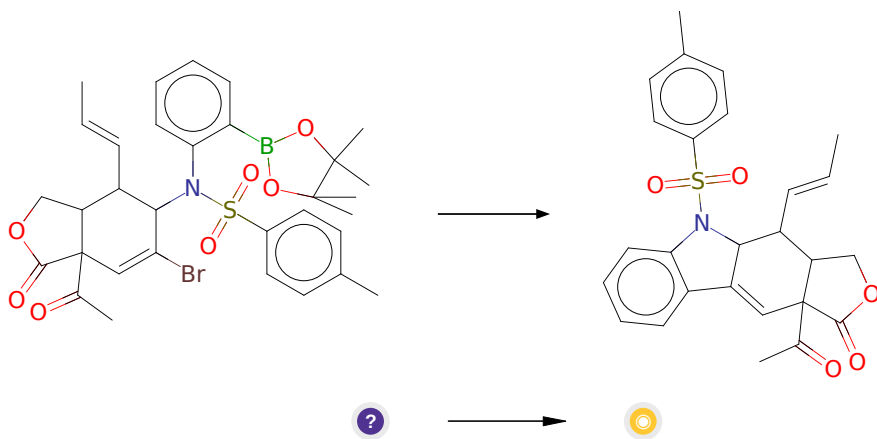
**Typical conditions:** Base.Solvent

**Protections:** none

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

**Retrosynthesis ID:** 5015

### 2.3.9 Suzuki coupling of arylboronic pinacol esters with vinyl Bromides



**Substrates:**

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O)OCC13

**Products:**

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

**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:** 10695