

# Paths of analysis\*

Y1

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

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

### 2.1 Path 1

**Score:** 2250132.89

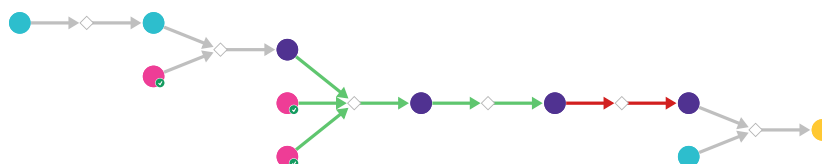
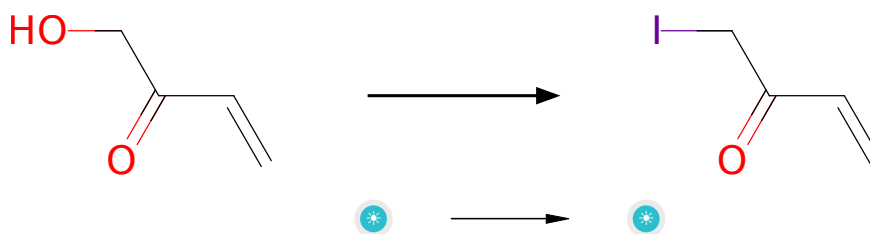


Figure 1: Outline of path 1

#### 2.1.1 Synthesis Of Alkyl Iodides Via Appel Reaction



**Substrates:**

1. 1-hydroxy-but-3-en-2-one

**Products:**

1. 1-iodo-but-3-en-2-one

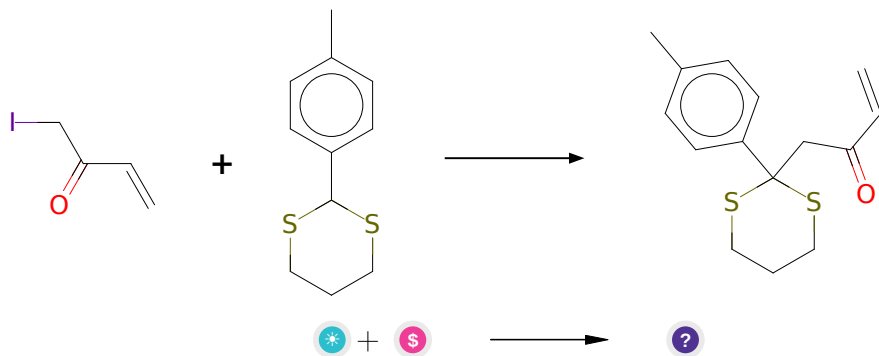
**Typical conditions:** Imidazole.PPh3.I2

**Protections:** none

**Reference:** [10.1002/1099-0690\(200102\)2001:3<493::AID-EJOC493>3.0.CO2-B](#) (compound 20) and [10.1016/j.tet.2014.09.030](#)

**Retrosynthesis ID:** 9990040

### 2.1.2 Alkylation of dithianes



**Substrates:**

1. 1-iodo-but-3-en-2-one
2. 2-p-tolyl-[1,3]dithiane - [available at Sigma-Aldrich](#)

**Products:**

1. C=CC(=O)CC1(c2ccc(C)cc2)SCCSC1

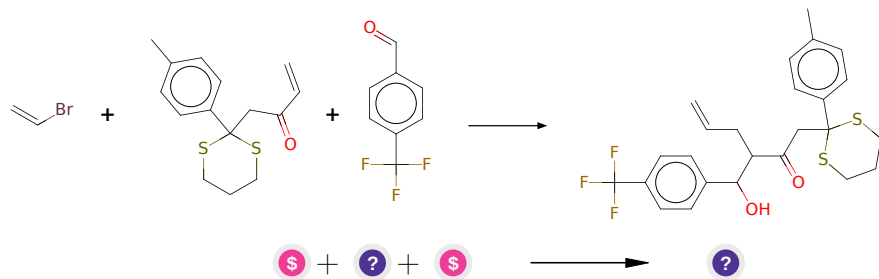
**Typical conditions:** LDA.THF

**Protections:** none

**Reference:** [10.1021/ja055740s](#) (SI) and [10.1016/S0008-6215\(99\)00275-X](#) and [10.1021/ja0618954](#)

**Retrosynthesis ID:** 34220

### 2.1.3 Alkenylation-Aldol reaction of enones and enoate esters



**Substrates:**

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=CC(=O)CC1(c2ccc(C)cc2)SCCCS1
3. Bromoethylene - *available at Sigma-Aldrich*

**Products:**

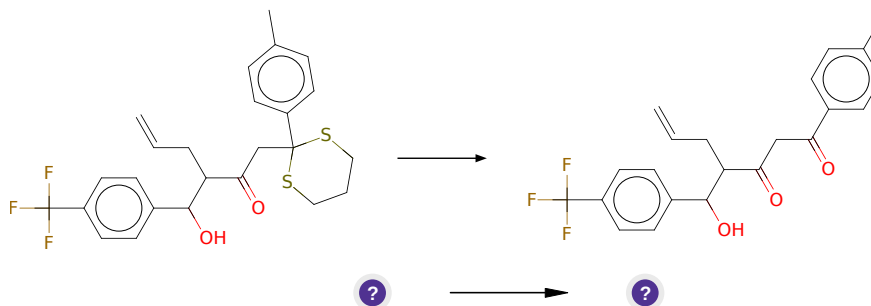
1. C=CCC(C(=O)CC1(c2ccc(C)cc2)SCCCS1)C(O)c1ccc(C(F)(F)F)cc1

**Typical conditions:** 1.RCuLi.2.RCHO

**Protections:** none

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

**Retrosynthesis ID:** 20547

**2.1.4 Synthesis of ketones from dithianes****Substrates:**

1. C=CCC(C(=O)CC1(c2ccc(C)cc2)SCCCS1)C(O)c1ccc(C(F)(F)F)cc1

**Products:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

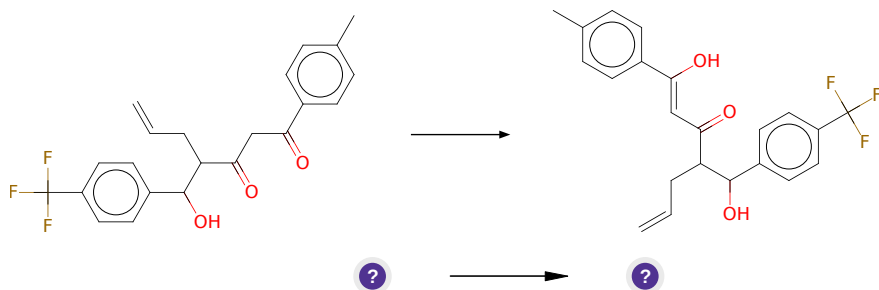
**Typical conditions:** MeI.CaCO<sub>3</sub>

**Protections:** none

**Reference:** [10.1016/j.tet.2013.09.075](#) and [10.1021/jo00007a015](#) and [10.1021/jo0610412](#) and [10.1021/ol901024t](#) and [10.1021/ol500553x](#) and [10.1021/jo0626459](#)

**Retrosynthesis ID:** 31724

### 2.1.5 Keto-enol Tautomerism



**Substrates:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Products:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

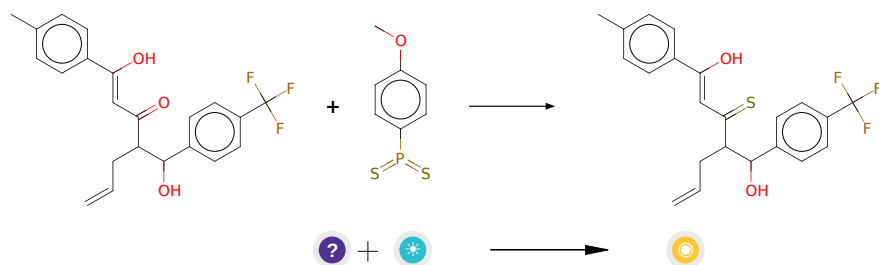
**Typical conditions:** solvent

**Protections:** none

**Reference:** [10.1021/ja01065a003](https://doi.org/10.1021/ja01065a003) AND [10.1021/jo8012385](https://doi.org/10.1021/jo8012385)

**Retrosynthesis ID:** 7781

### 2.1.6 Synthesis of Thioketones using Lawesson's Reagent



**Substrates:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

**Products:**

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Typical conditions:** Lawesson's Reagent.neat.microwave

**Protections:** none

**Reference:** DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

**Retrosynthesis ID:** 10798

## 2.2 Path 2

Score: 2250164.14

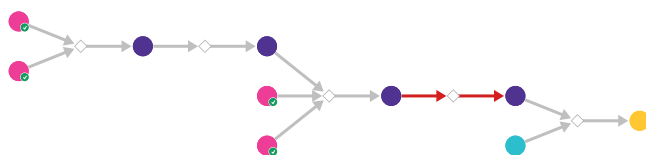
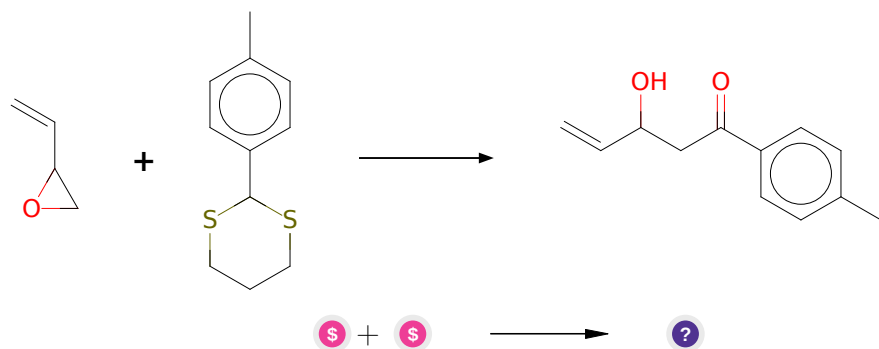


Figure 2: Outline of path 2

### 2.2.1 Corey-Seebach



**Substrates:**

1. 2-p-tolyl-[1,3]dithiane - [available at Sigma-Aldrich](#)
2. 2-Vinyloxirane - [available at Sigma-Aldrich](#)

**Products:**

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

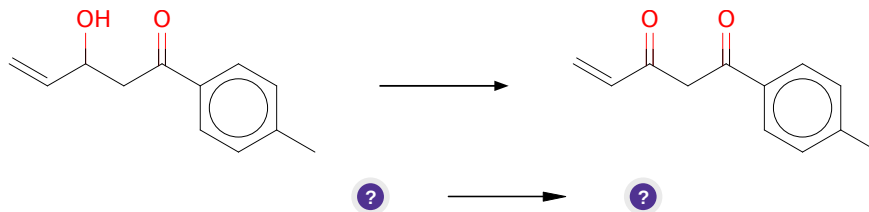
**Typical conditions:** BuLi.THF.-30C.HgO.H2O.THF

**Protections:** none

**Reference:** [10.1055/s-1977-24412](#)

**Retrosynthesis ID:** 11197

### 2.2.2 Swern Oxidation



**Substrates:**

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

**Products:**

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

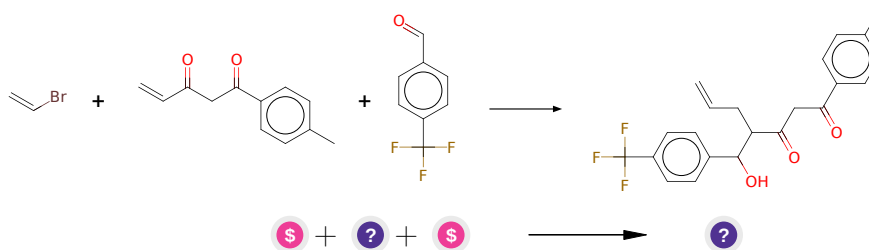
**Typical conditions:** oxalyl chloride.DMSO.DCM.NMe3.-40C

**Protections:** none

**Reference:** [10.1055/s-1990-27036](#)

**Retrosynthesis ID:** 11163

### 2.2.3 Alkenylation-Aldol reaction of enones and enoate esters



**Substrates:**

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=CC(=O)CC(=O)c1ccc(C)cc1
3. Bromoethylene - *available at Sigma-Aldrich*

**Products:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

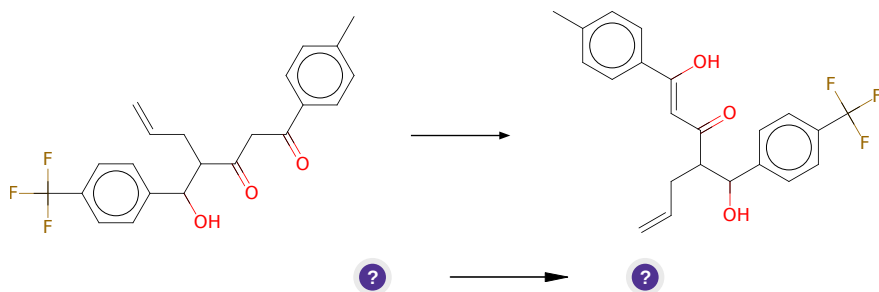
**Typical conditions:** 1.RCuLi.2.RCHO

**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

#### 2.2.4 Keto-enol Tautomerism



**Substrates:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Products:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

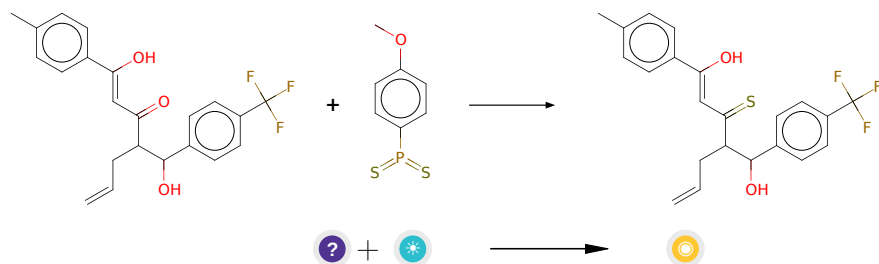
**Typical conditions:** solvent

**Protections:** none

**Reference:** [10.1021/ja01065a003](#) AND [10.1021/jo8012385](#)

**Retrosynthesis ID:** 7781

#### 2.2.5 Synthesis of Thioketones using Lawesson's Reagent





**Substrates:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

**Products:**

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Typical conditions:** Lawesson's Reagent.neat.microwave

**Protections:** none

**Reference:** DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

**Retrosynthesis ID:** 10798

## 2.3 Path 3

Score: 2250164.14

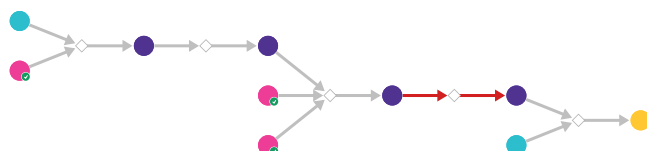
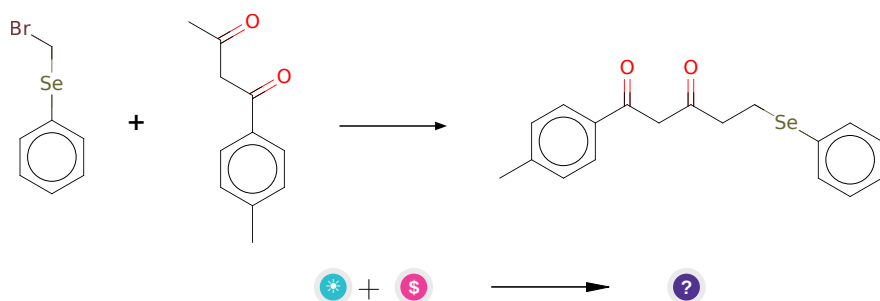


Figure 3: Outline of path 3

### 2.3.1 Alkylation of ketones



**Substrates:**

1. bromo-phenylselenomethane

2. 1-p-tolyl-butane-1,3-dione - *available at Sigma-Aldrich*

**Products:**

1. Cc1ccc(C(=O)CC(=O)CC[Se]c2ccccc2)cc1

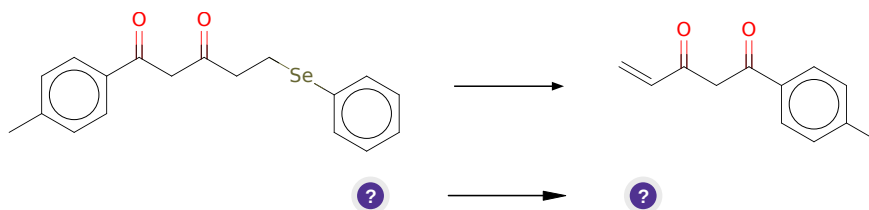
**Typical conditions:** LDA or other base.THF.-78C

**Protections:** none

**Reference:** DOI: [10.1021/ja0123554](https://doi.org/10.1021/ja0123554) or DOI: [10.1016/j.tet.2011.09.114](https://doi.org/10.1016/j.tet.2011.09.114)

**Retrosynthesis ID:** 1867

### 2.3.2 Selenoxide Elimination



**Substrates:**

1. Cc1ccc(C(=O)CC(=O)CC[Se]c2ccccc2)cc1

**Products:**

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

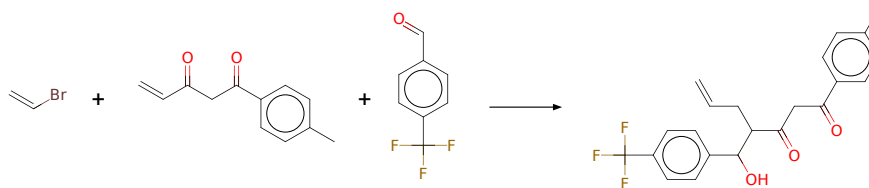
**Typical conditions:** 1) O<sub>3</sub> or H<sub>2</sub>O<sub>2</sub> or NaIO<sub>4</sub>. low temperature. 2) pyridine or Et<sub>3</sub>N

**Protections:** none

**Reference:** DOI: [10.1021/ja00852a019](https://doi.org/10.1021/ja00852a019) or DOI: [10.1021/ja00258a056](https://doi.org/10.1021/ja00258a056) or DOI: [10.1039/B716256A](https://doi.org/10.1039/B716256A) or DOI: [10.1055/s-1998-1970](https://doi.org/10.1055/s-1998-1970) or DOI: [10.1016/S0040-4039\(00\)76646-9](https://doi.org/10.1016/S0040-4039(00)76646-9)

**Retrosynthesis ID:** 8381

### 2.3.3 Alkenylation-Aldol reaction of enones and enoate esters





**Substrates:**

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=CC(=O)CC(=O)c1ccc(C)cc1
3. Bromoethylene - *available at Sigma-Aldrich*

**Products:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

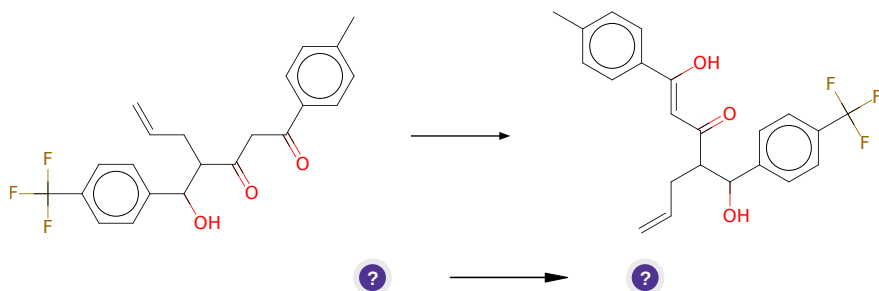
**Typical conditions:** 1.RCuLi.2.RCHO

**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

**2.3.4 Keto-enol Tautomerism**



**Substrates:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Products:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

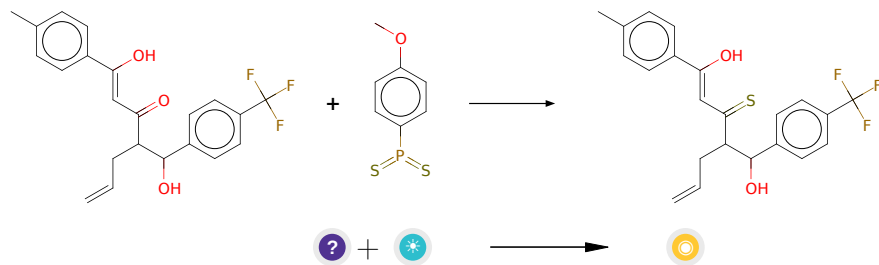
**Typical conditions:** solvent

**Protections:** none

**Reference:** [10.1021/ja01065a003](#) AND [10.1021/jo8012385](#)

**Retrosynthesis ID:** 7781

### 2.3.5 Synthesis of Thioketones using Lawesson's Reagent



#### Substrates:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

#### Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Typical conditions:** Lawesson's Reagent.neat.microwave

**Protections:** none

**Reference:** DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

**Retrosynthesis ID:** 10798

### 2.4 Path 4

Score: 2250164.14

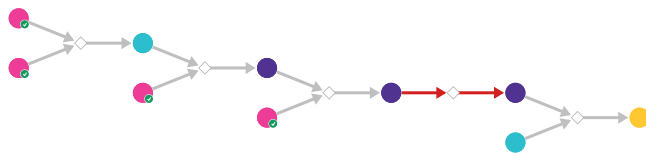
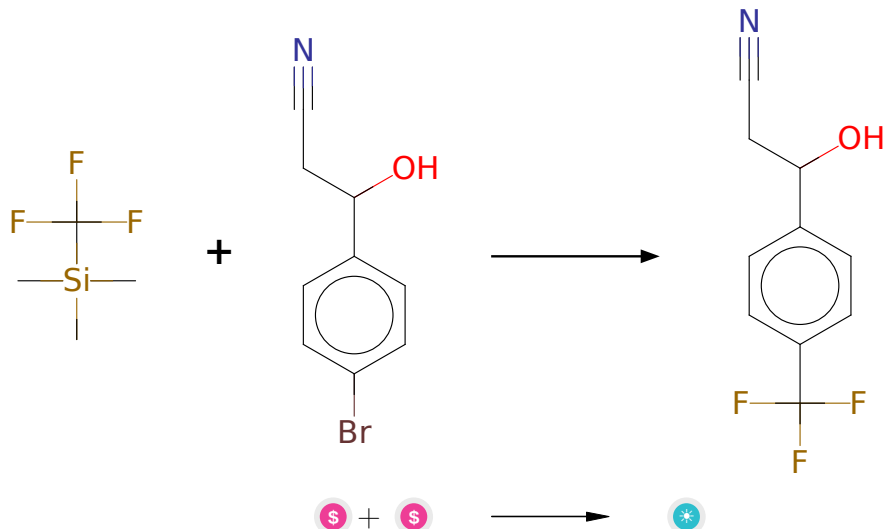


Figure 4: Outline of path 4

### 2.4.1 Trifluoromethylation of aryl bromides



#### Substrates:

1. TFMSTMS - *available at Sigma-Aldrich*
2. 3-(4-bromophenyl)-3-hydroxypropanenitrile - *available at Sigma-Aldrich*

#### Products:

1. C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>NO

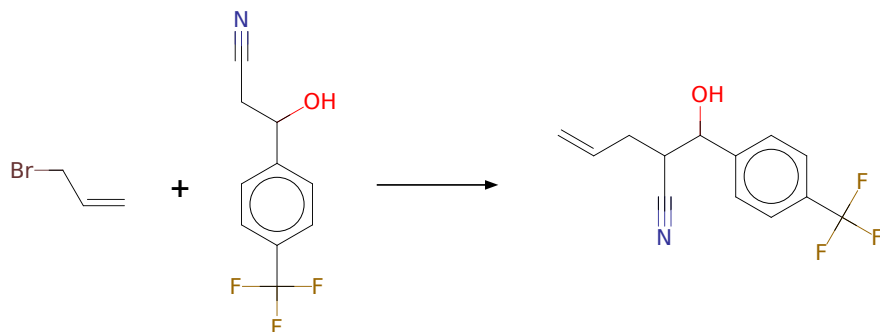
**Typical conditions:** [(phen)CuCF<sub>3</sub>].DMF.rt

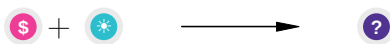
**Protections:** none

**Reference:** DOI: *10.1002/anie.201100633*

**Retrosynthesis ID:** 2269

### 2.4.2 Alkylation of Nitriles





**Substrates:**

1. Allyl bromide - *available at Sigma-Aldrich*
2. C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>NO

**Products:**

1. C=CCC(C#N)C(O)c1ccc(C(F)(F)F)cc1

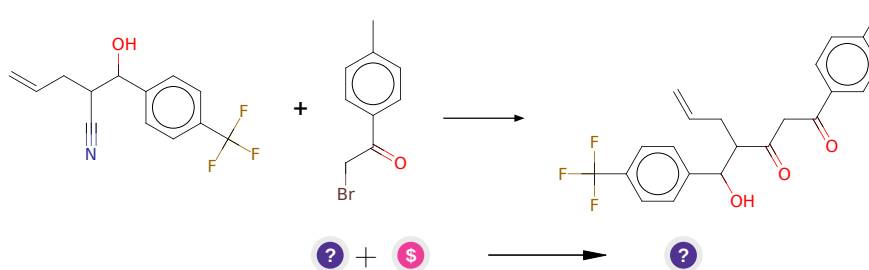
**Typical conditions:** base e.g. BuLi.THF

**Protections:** none

**Reference:** [10.1021/jm701319c](#) and WO2017/59191A1 p.0210 and US2011/237556A1 p.7 and [10.1021/ja058303m](#) and [10.1021/acs.orglett.9b03078](#) and [10.1016/S0040-4020\(01\)80336-7](#)

**Retrosynthesis ID:** 31017106

### 2.4.3 Blaise Reaction



**Substrates:**

1. C=CCC(C#N)C(O)c1ccc(C(F)(F)F)cc1
2. 2-Bromo-4'-methylacetophenone - *available at Sigma-Aldrich*

**Products:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

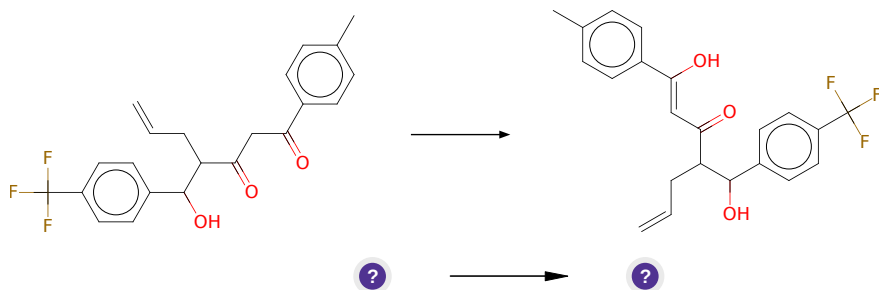
**Typical conditions:** Zn.TMSCl.THF then HCl

**Protections:** none

**Reference:** [10.1002/ejoc.201403402](#)

**Retrosynthesis ID:** 10000153

#### 2.4.4 Keto-enol Tautomerism



**Substrates:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Products:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

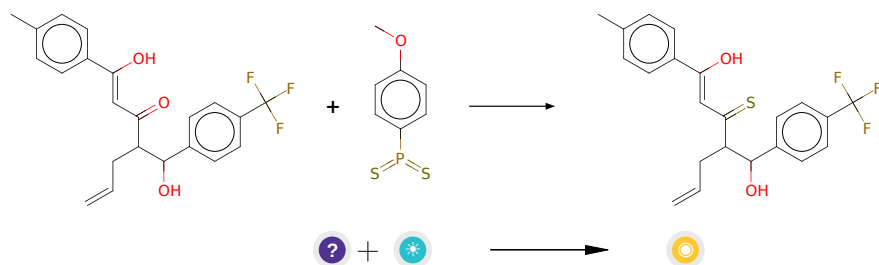
**Typical conditions:** solvent

**Protections:** none

**Reference:** [10.1021/ja01065a003](https://doi.org/10.1021/ja01065a003) AND [10.1021/jo8012385](https://doi.org/10.1021/jo8012385)

**Retrosynthesis ID:** 7781

#### 2.4.5 Synthesis of Thioketones using Lawesson's Reagent



**Substrates:**

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

**Products:**

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1

**Typical conditions:** Lawesson's Reagent.neat.microwave

**Protections:** none

**Reference:** DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

**Retrosynthesis ID:** 10798