

# Paths of analysis\* O2

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:** 20.00

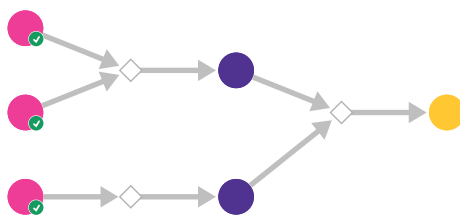
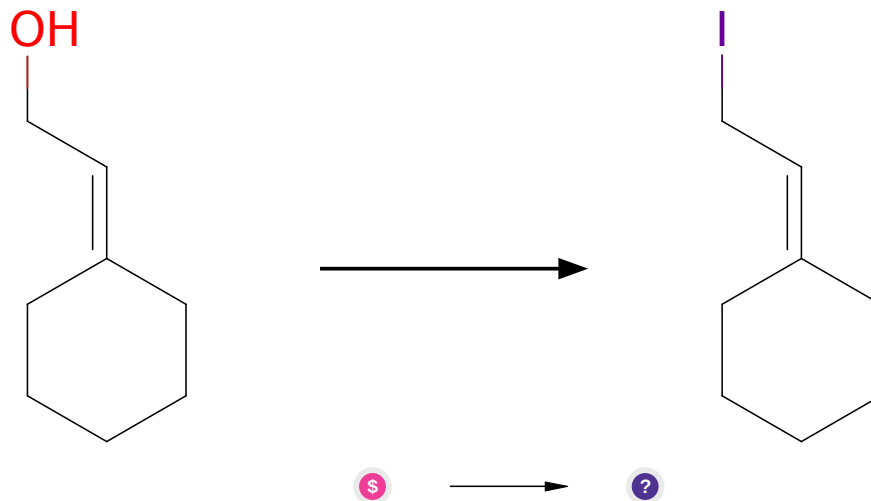


Figure 1: Outline of path 1

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



**Substrates:**

1. 2-cyclohexylideneethan-1-ol - *available at Sigma-Aldrich*

**Products:**

1. ICC=C1CCCCC1

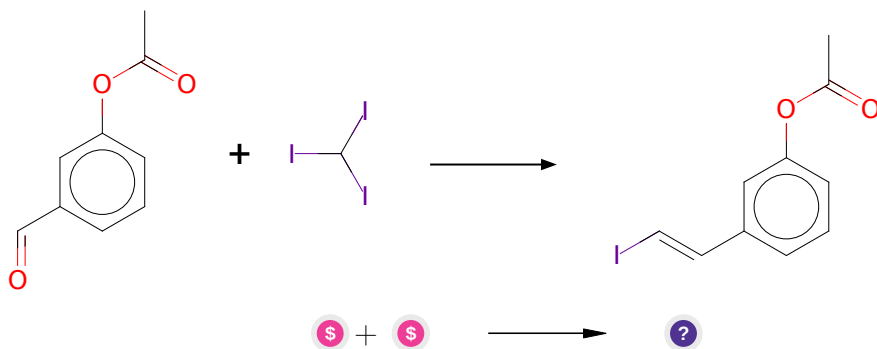
**Typical conditions:** Imidazole.PPh3.I2

**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 Takai olefination**



**Substrates:**

1. 3-Formylphenyl acetate - *available at Sigma-Aldrich*
2. Iodoform - *available at Sigma-Aldrich*

**Products:**

1. CC(=O)Oc1ccc(/C=C/I)c1

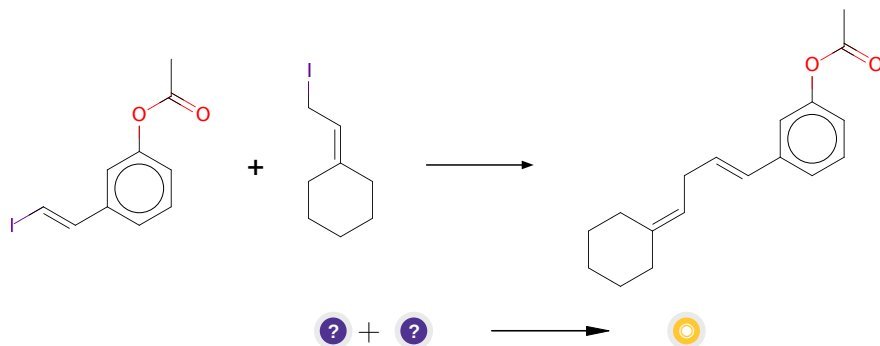
**Typical conditions:** CrCl<sub>2</sub>.THF

**Protections:** none

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

**Retrosynthesis ID:** 10497

### 2.1.3 Palladium catalysed alkylation of vinyl iodides



**Substrates:**

1. ICC=C1CCCCC1
2. CC(=O)Oc1cccc(/C=C/I)c1

**Products:**

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

**Typical conditions:** [Pd].catalyst

**Protections:** none

**Reference:** [10.1016/j.bmcl.2005.12.066](#) and [10.1021/ol052070m](#) and [10.1021/ol5023195](#) and [10.1002/anie.200703134](#) and [10.1016/j.bmcl.2005.09.084](#) and [10.1021/ol0344873](#)

**Retrosynthesis ID:** 25162

## 2.2 Path 2

**Score:** 20.00

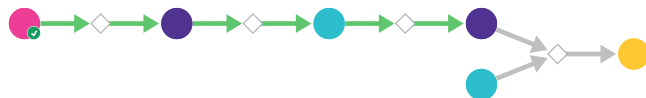
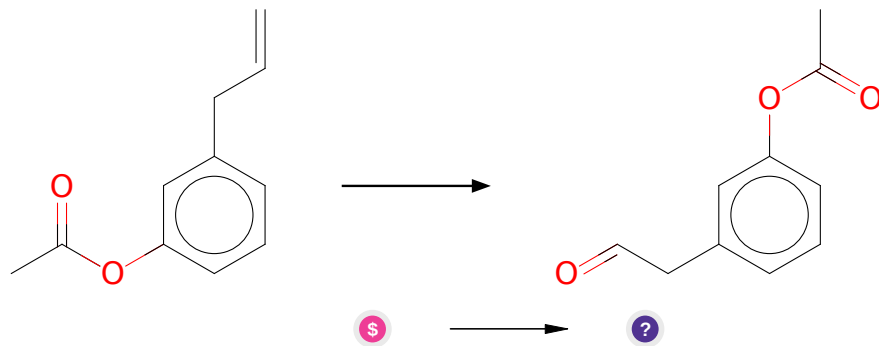


Figure 2: Outline of path 2

### 2.2.1 Ozonolysis



#### Substrates:

1. 3-(3-Acetoxyphenyl)-1-propene - *available at Sigma-Aldrich*

#### Products:

1. CC(=O)Oc1cccc(CC=O)c1

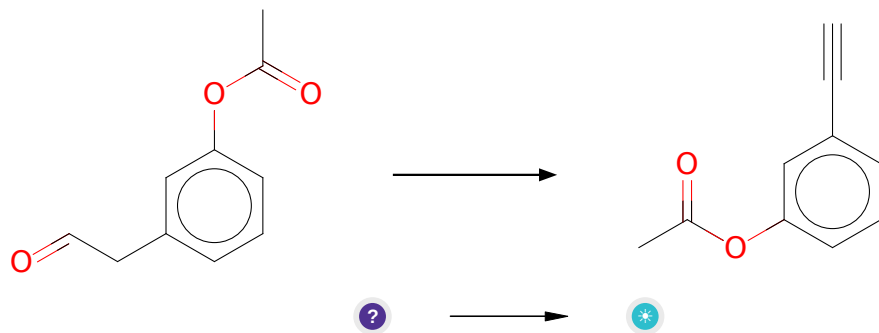
**Typical conditions:** O<sub>3</sub>.MeOH.CH<sub>2</sub>Cl<sub>2</sub>.PPh<sub>3</sub> or Me<sub>2</sub>S.low temperature

**Protections:** none

**Reference:** *10.1016/j.tet.2017.03.039*

**Retrosynthesis ID:** 5074

### 2.2.2 Synthesis of alkynes from aldehydes



#### Substrates:

1. CC(=O)Oc1cccc(CC=O)c1

#### Products:

1. 3-acetoxy-phenylacetylen

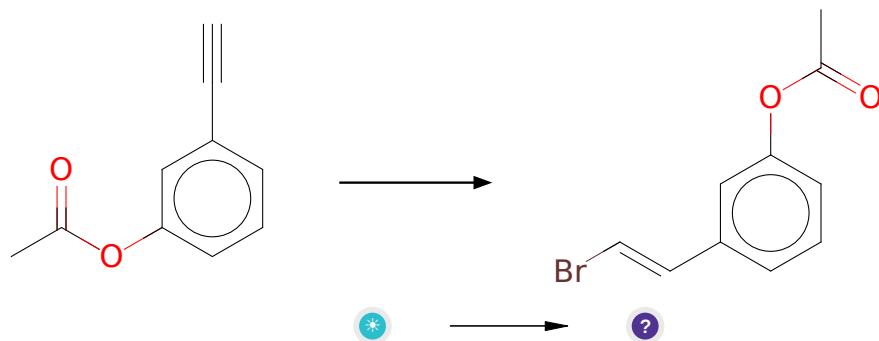
**Typical conditions:** P1-base.DMF

**Protections:** none

**Reference:** [10.1055/s-0028-1087919](https://doi.org/10.1055/s-0028-1087919)

**Retrosynthesis ID:** 15028

### 2.2.3 Bromination of vinylalanes



**Substrates:**

1. 3-acetoxy-phenylacetylen

**Products:**

1. CC(=O)Oc1cccc(/C=C/Br)c1

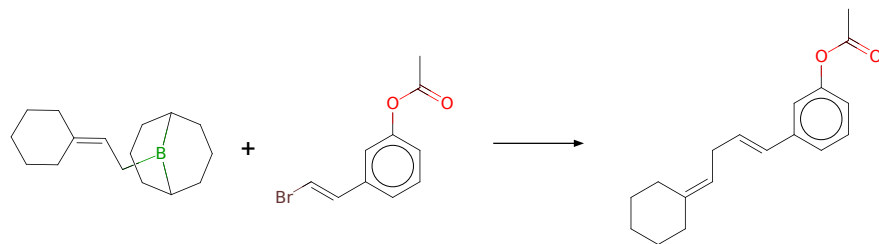
**Typical conditions:** Schwartz's reagent.then.Br<sub>2</sub>

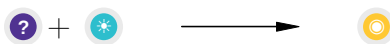
**Protections:** none

**Reference:** DOI: [10.1039/C2CC36604E](https://doi.org/10.1039/C2CC36604E) (SI, page S18) AND DOI: [10.1080/00397910008087318](https://doi.org/10.1080/00397910008087318)

**Retrosynthesis ID:** 7405

### 2.2.4 Suzuki coupling of alkyl-9-BBNs with vinyl bromides





**Substrates:**

1. CC(=O)Oc1cccc(/C=C/Br)c1
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane

**Products:**

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

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

**Protections:** none

**Reference:** [10.1021/ja00183a048](#) and [10.1039/b707338k](#) and [10.1016/j.tet.2015.05.039](#) and [10.1021/jo991064z](#) and [10.1021/ol060290+](#) and [10.1246/bcsj.65.2863](#)

**Retrosynthesis ID:** 25174

## 2.3 Path 3

**Score:** 25.00

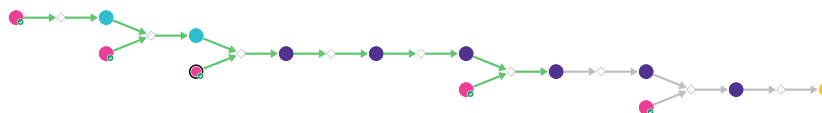
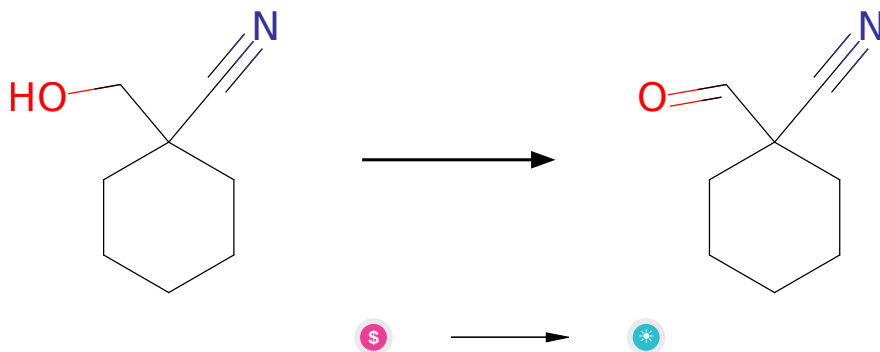


Figure 3: Outline of path 3

### 2.3.1 Oxidation of primary alcohols with DMP



**Substrates:**

1. 1-(hydroxymethyl)cyclohexane-1-carbonitrile - *available at Sigma-Aldrich*

**Products:**

1. 1-formylcyclohexanecarbonitrile

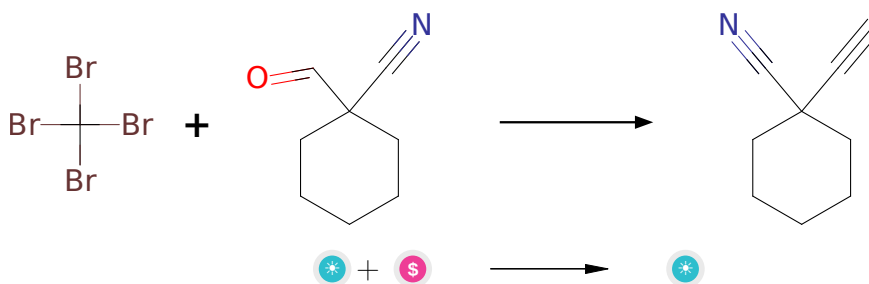
**Typical conditions:** DMP.DCM.0-25 C

**Protections:** none

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

**Retrosynthesis ID:** 50426

**2.3.2 Corey-Fuchs reaction**



**Substrates:**

1. 1-formylcyclohexanecarbonitrile
2. Tetrabromomethane - *available at Sigma-Aldrich*

**Products:**

1. 1-ethynylcyclohexylcyanide

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

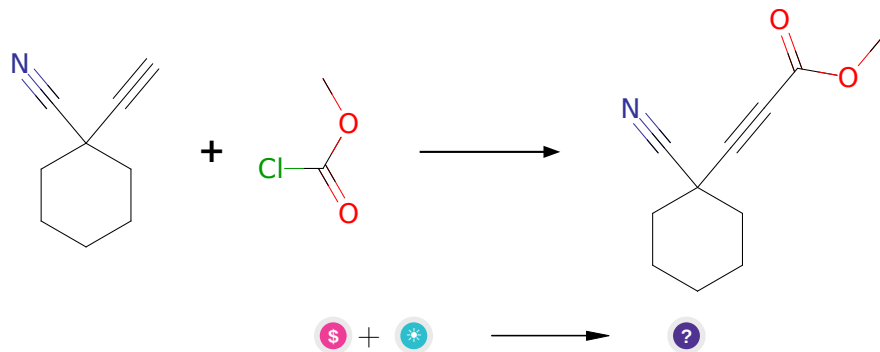
**Protections:** none

**Reference:** [10.1002/ejoc.200601137](#) and [10.1016/S0040-4039\(01\)94157-7](#)

**Retrosynthesis ID:** 10912



### 2.3.3 Chloroformate Addition To Terminal Alkynes



#### Substrates:

1. Methyl chloroformate - *available at Sigma-Aldrich*
2. 1-ethynylcyclohexylcyanid

#### Products:

1. COC(=O)C#CC1(C#N)CCCCC1

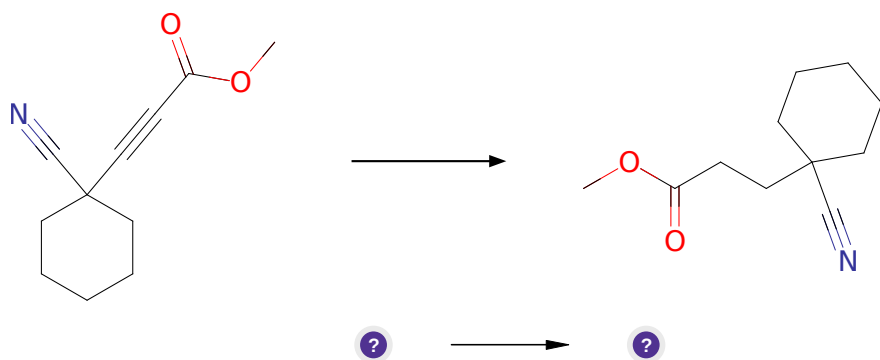
**Typical conditions:** 1)n-BuLi.solvent.2) chloroformate

**Protections:** none

**Reference:** DOI: [10.1021/jo00092a015](https://doi.org/10.1021/jo00092a015)

**Retrosynthesis ID:** 2049

### 2.3.4 Reduction of alkyne to alkane



#### Substrates:

1. COC(=O)C#CC1(C#N)CCCCC1

**Products:**

1. COC(=O)CCC1(C#N)CCCC1

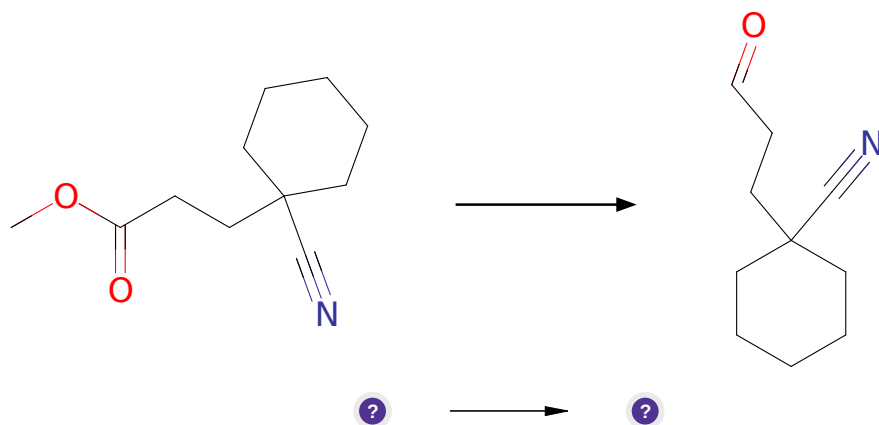
**Typical conditions:** H<sub>2</sub>.Pd/C

**Protections:** none

**Reference:** [10.1016/j.bmc.2011.05.030](#) AND [10.1021/ol048591b](#) AND [10.1021/jo020486x](#)

**Retrosynthesis ID:** 14626

**2.3.5 Aldehyde Formation**



**Substrates:**

1. COC(=O)CCC1(C#N)CCCC1

**Products:**

1. N#CC1(CCC=O)CCCC1

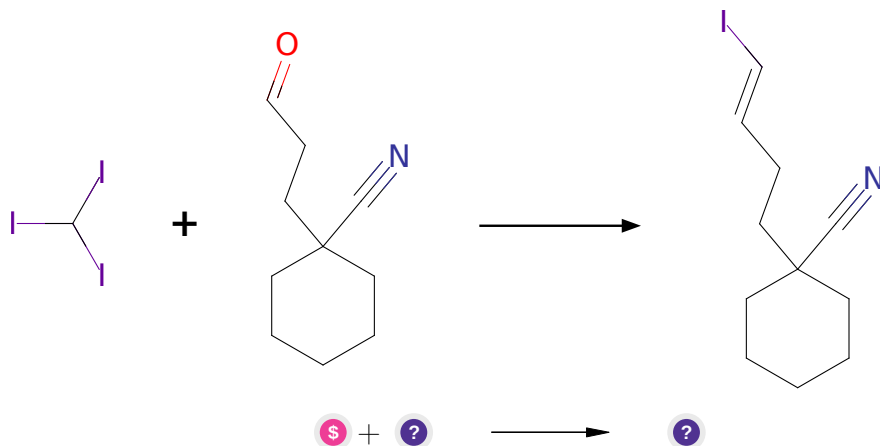
**Typical conditions:** DIBAL.solvent e.g. DCM

**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

### 2.3.6 Takai olefination



#### Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. N#CC1(CCC=O)CCCCC1

#### Products:

1. N#CC1(CC/C=C/I)CCCCC1

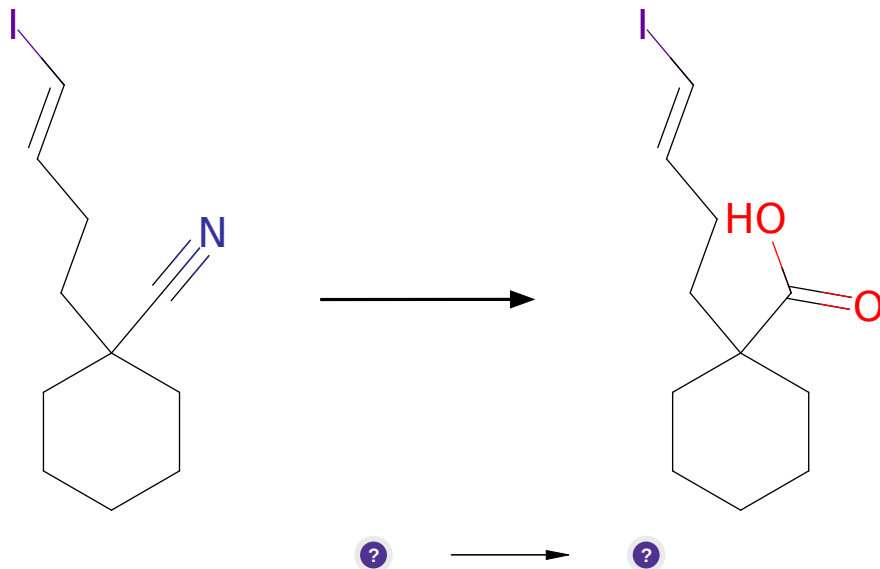
**Typical conditions:** CrCl2.THF

**Protections:** none

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

**Retrosynthesis ID:** 10497

### 2.3.7 Base hydrolysis of nitriles to carboxylic acids



**Substrates:**

1. N#CC1(CC/C=C/I)CCCCC1

**Products:**

1. O=C(O)C1(CC/C=C/I)CCCCC1

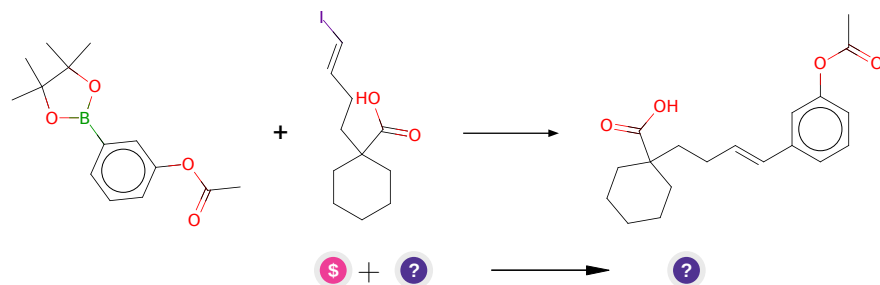
**Typical conditions:** NaOH.heating.H2O

**Protections:** none

**Reference:** [10.1002/1099-0690\(200111\)2001:22<4207::AID-EJOC4207>3.0.CO;2-3](#) and [10.1021/acs.jmedchem.5b00702](#) and [10.1016/j.bmc.2011.07.045](#)

**Retrosynthesis ID:** 15107

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



**Substrates:**

1. 3-Acetoxyphenylboronic acid pinacol ester - *available at Sigma-Aldrich*
2. O=C(O)C1(CC/C=C/I)CCCCC1

**Products:**

1. CC(=O)Oc1cccc(/C=C/CCC2(C(=O)O)CCCCC2)c1

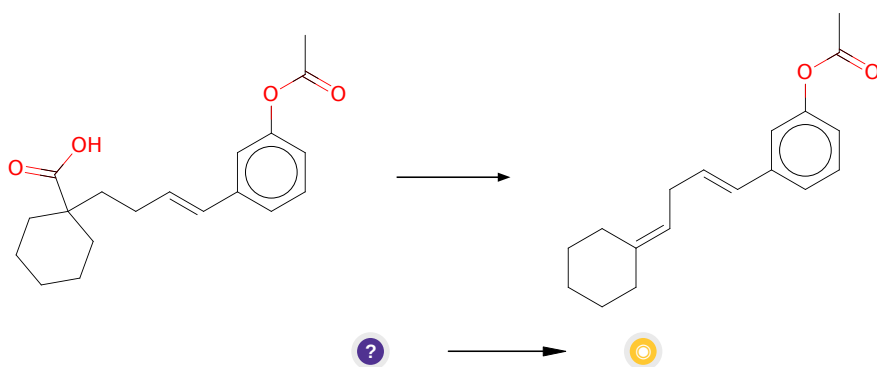
**Typical conditions:** Pd catalyst.base.solvent

**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:** 5045

### 2.3.9 Catalytic dehydrogenative decarboxyolefination of carboxylic acids

**Substrates:**

1. CC(=O)Oc1cccc(/C=C/CCC2(C(=O)O)CCCCC2)c1

**Products:**

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

**Typical conditions:** [Ir]-photocatalyst.[Co]-catalyst.Cs<sub>2</sub>CO<sub>3</sub>.DME/H<sub>2</sub>O.blue.light.rt

**Protections:** none

**Reference:** [10.1038/s41557-018-0142-4](#) and [10.1021/acscatal.8b03282](#) and [10.1021/acs.joc.9b00167](#)

**Retrosynthesis ID:** 10032330

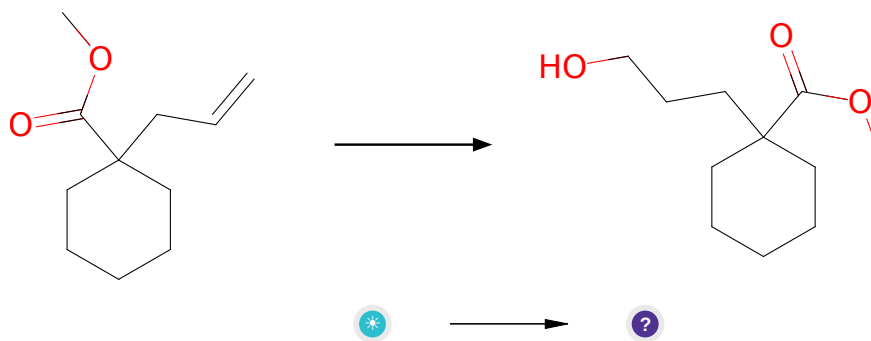
## 2.4 Path 4

Score: 25.00



Figure 4: Outline of path 4

### 2.4.1 Brown Hydroboration of Alkenes



**Substrates:**

1. 1-allyl-cyclohexanecarboxylic acid methyl ester

**Products:**

1. COC(=O)C1(CCCO)CCCCC1

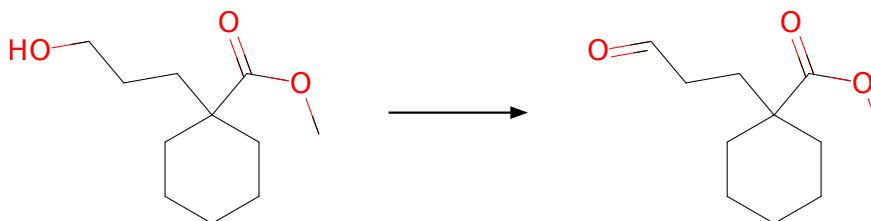
**Typical conditions:** B<sub>2</sub>H<sub>6</sub>.H<sub>2</sub>O<sub>2</sub>.THF.NaOH

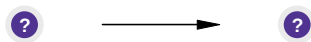
**Protections:** none

**Reference:** [10.1002/9780470638859.conrr118](https://doi.org/10.1002/9780470638859.conrr118)

**Retrosynthesis ID:** 4772

### 2.4.2 Oxidation of primary alcohols with DMP





**Substrates:**

1. COC(=O)C1(CCCO)CCCCC1

**Products:**

1. COC(=O)C1(CCC=O)CCCCC1

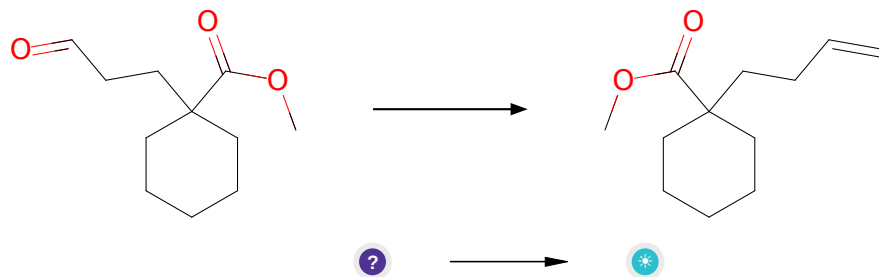
**Typical conditions:** DMP.DCM.0-25 C

**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

### 2.4.3 Tebbe Olefination



**Substrates:**

1. COC(=O)C1(CCC=O)CCCCC1

**Products:**

1. 1-but-3-enyl-cyclohexanecarboxylic acid methyl ester

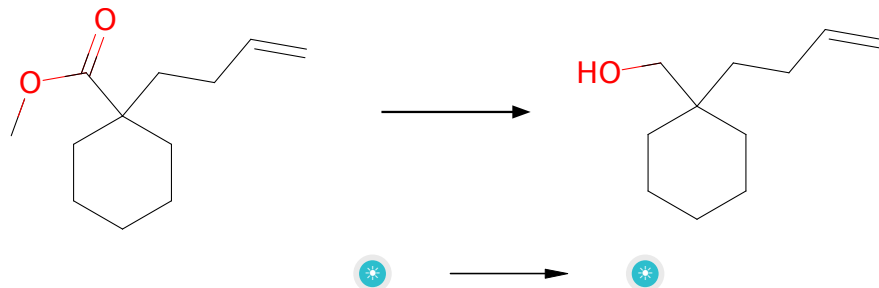
**Typical conditions:** Cp<sub>2</sub>TiCl<sub>2</sub>.AlMe<sub>3</sub>.toluene

**Protections:** none

**Reference:** [10.1016/j.tet.2007.03.015](https://doi.org/10.1016/j.tet.2007.03.015) and [10.1002/9780470638859.conrr617](https://doi.org/10.1002/9780470638859.conrr617)

**Retrosynthesis ID:** 11714

#### 2.4.4 Esters reduction with LAH



##### Substrates:

1. 1-but-3-enyl-cyclohexanecarboxylic acid methyl ester

##### Products:

1. (1-but-3-enyl-cyclohexyl)-methanol

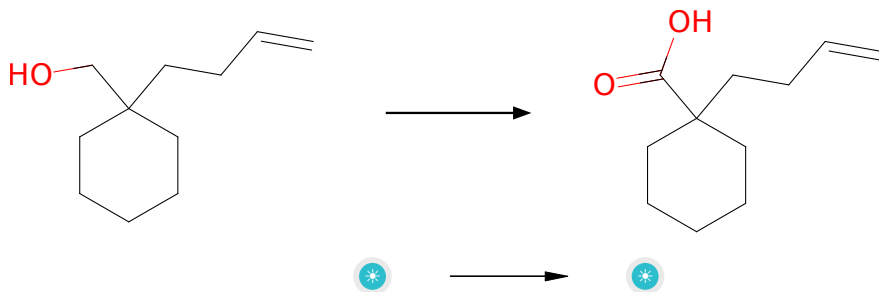
**Typical conditions:** LiAlH<sub>4</sub>.THF.0-20 C

**Protections:** none

**Reference:** [10.1016/j.ejmech.2019.112011](https://doi.org/10.1016/j.ejmech.2019.112011) p. 5, 10 and [10.1016/j.ejmech.2020.112910](https://doi.org/10.1016/j.ejmech.2020.112910) p. 3, 7

**Retrosynthesis ID:** 9910006

#### 2.4.5 Jones Oxidation



##### Substrates:

1. (1-but-3-enyl-cyclohexyl)-methanol

##### Products:

1. acide 1-(but-3-enyl)cyclohexanecarboxylique



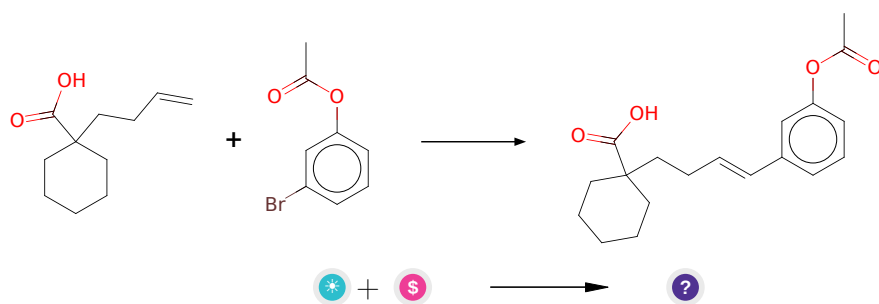
**Typical conditions:** cromate.sulfate.H2O.acetone

**Protections:** none

**Reference:** [10.1002/9780470638859.conrr349](https://doi.org/10.1002/9780470638859.conrr349) and [10.1021/jm00270a004](https://doi.org/10.1021/jm00270a004)

**Retrosynthesis ID:** 11160

#### 2.4.6 Heck Reaction



**Substrates:**

1. acide 1-(but-3-enyl)cyclohexanecarboxylique
2. 3-Bromophenyl acetate - *available at Sigma-Aldrich*

**Products:**

1. CC(=O)Oc1cccc(/C=C/CCC2(C(=O)O)CCCCC2)c1

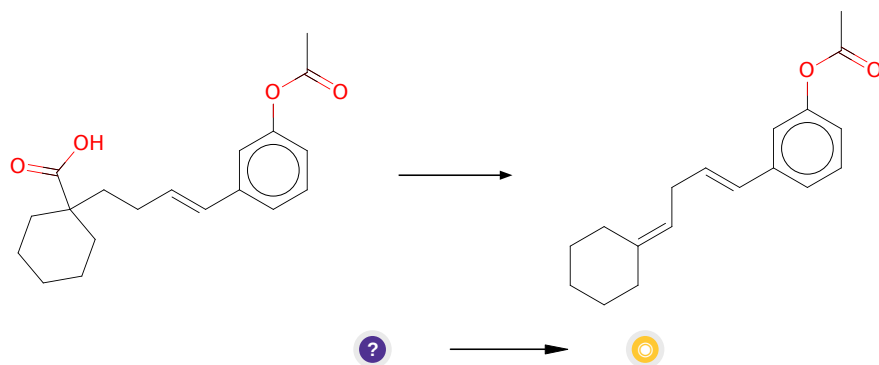
**Typical conditions:** Pd (cat). Ligand e.g. TXPTS. Base. Temp

**Protections:** none

**Reference:** DOI: [10.1039/C3GC40493E](https://doi.org/10.1039/C3GC40493E) DOI: [10.1021/ol0360288](https://doi.org/10.1021/ol0360288) or DOI: [10.1021/ol702755g](https://doi.org/10.1021/ol702755g) or DOI: [10.1055/s-0033-1340319](https://doi.org/10.1055/s-0033-1340319) or DOI: [10.1016/j.tet.2004.10.049](https://doi.org/10.1016/j.tet.2004.10.049)

**Retrosynthesis ID:** 9180

## 2.4.7 Catalytic dehydrogenative decarboxyolefination of carboxylic acids



### Substrates:

- CC(=O)Oc1cccc(/C=C/CCC2(C(=O)O)CCCCC2)c1

### Products:

- CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

**Typical conditions:** [Ir]-photocatalyst, [Co]-catalyst, Cs<sub>2</sub>CO<sub>3</sub>, DME/H<sub>2</sub>O, blue light, rt

**Protections:** none

**Reference:** [10.1038/s41557-018-0142-4](https://doi.org/10.1038/s41557-018-0142-4) and [10.1021/acscatal.8b03282](https://doi.org/10.1021/acscatal.8b03282) and [10.1021/acs.joc.9b00167](https://doi.org/10.1021/acs.joc.9b00167)

**Retrosynthesis ID:** 10032330

## 2.5 Path 5

**Score:** 45.00

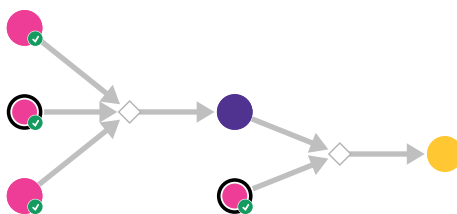
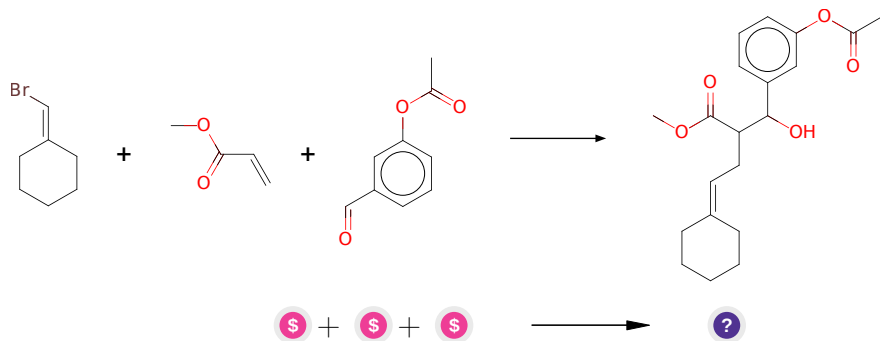


Figure 5: Outline of path 5

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



#### Substrates:

1. 3-Formylphenyl acetate - *available at Sigma-Aldrich*
2. Methyl acrylate - *available at Sigma-Aldrich*
3. Bromomethylenecyclohexane - *available at Sigma-Aldrich*

#### Products:

1. COC(=O)C(CC=C1CCCCC1)C(O)c1cccc(OC(C)=O)c1

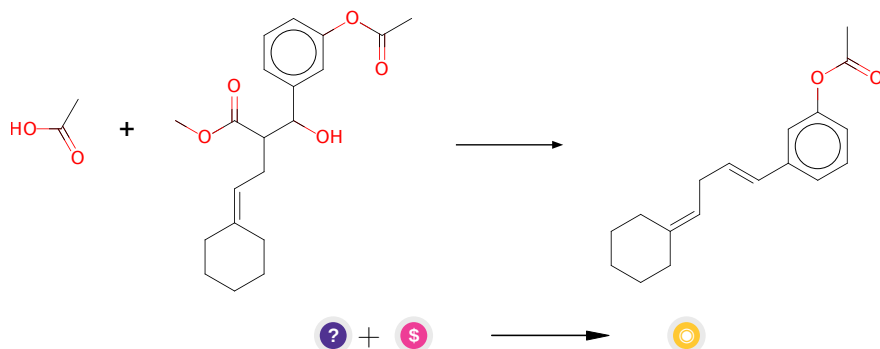
**Typical conditions:** 1.RCuLi.2.RCHO

**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:** 13051

### 2.5.2 Tandem Krapcho decarboxylation and elimination



#### Substrates:

1. COC(=O)C(CC=C1CCCCC1)C(O)c1cccc(OC(C)=O)c1

2. glacial - *available at Sigma-Aldrich*

**Products:**

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

**Typical conditions:** 1. Ac<sub>2</sub>O.py 2. DMSO.H<sub>2</sub>O.NaCl.170C

**Protections:** none

**Reference:** DOI: *10.1021/jo00263a005* and *10.1021/jo00386a011* and *10.1021/ol006085q*

**Retrosynthesis ID:** 9605