

# Paths of analysis\*

O4

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

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

### 2.1 Path 1

**Score:** 20.00

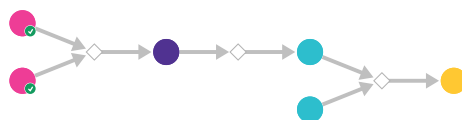
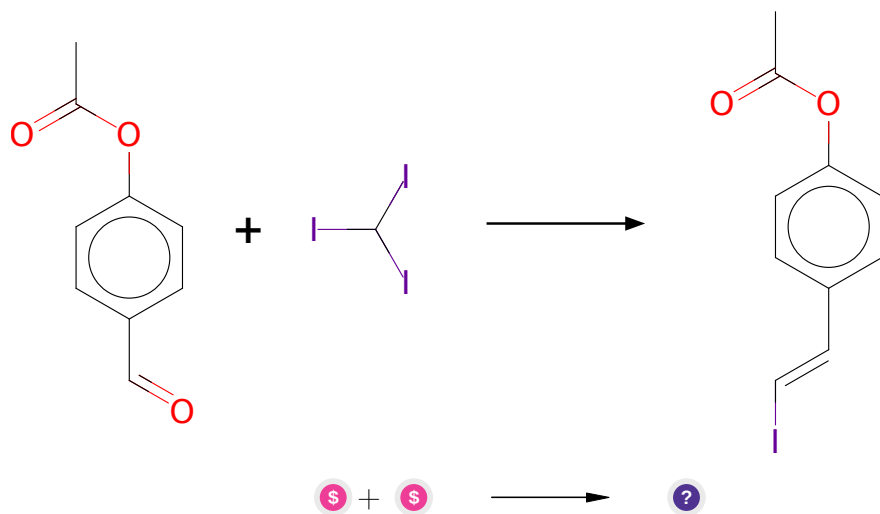


Figure 1: Outline of path 1

#### 2.1.1 Takai olefination



**Substrates:**

1. Iodoform - *available at Sigma-Aldrich*

2. 4-Acetoxybenzaldehyde - *available at Sigma-Aldrich*

**Products:**

1. CC(=O)Oc1ccc(/C=C/I)cc1

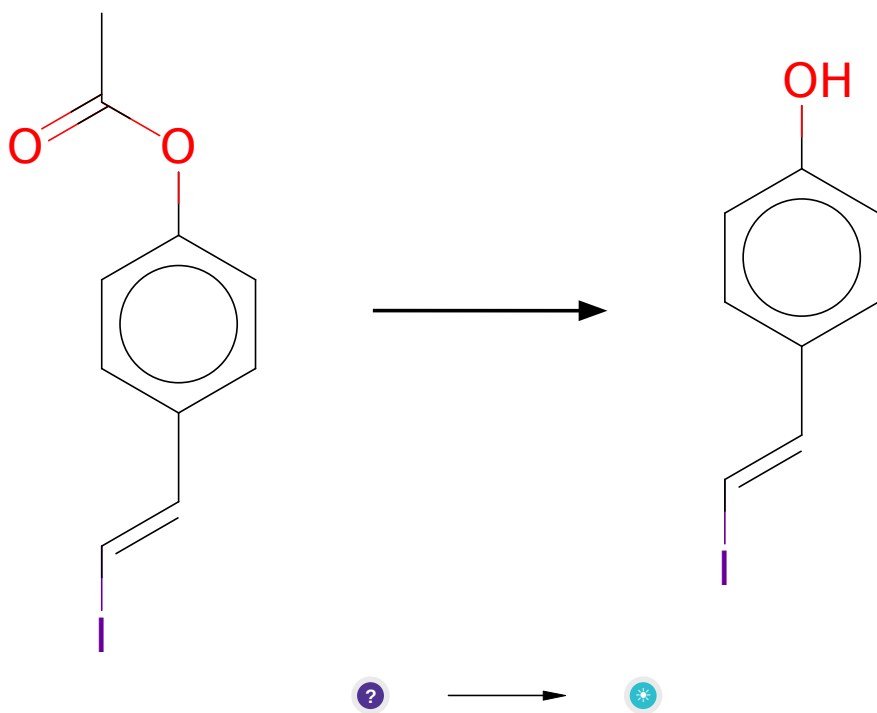
**Typical conditions:** CrCl<sub>2</sub>.THF

**Protections:** none

**Reference:** *10.1021/ja00283a046* and *10.1021/ja00237a081*

**Retrosynthesis ID:** 10497

**2.1.2 Hydrolysis of acetates**



**Substrates:**

1. CC(=O)Oc1ccc(/C=C/I)cc1

**Products:**

1. C<sub>8</sub>H<sub>7</sub>IO

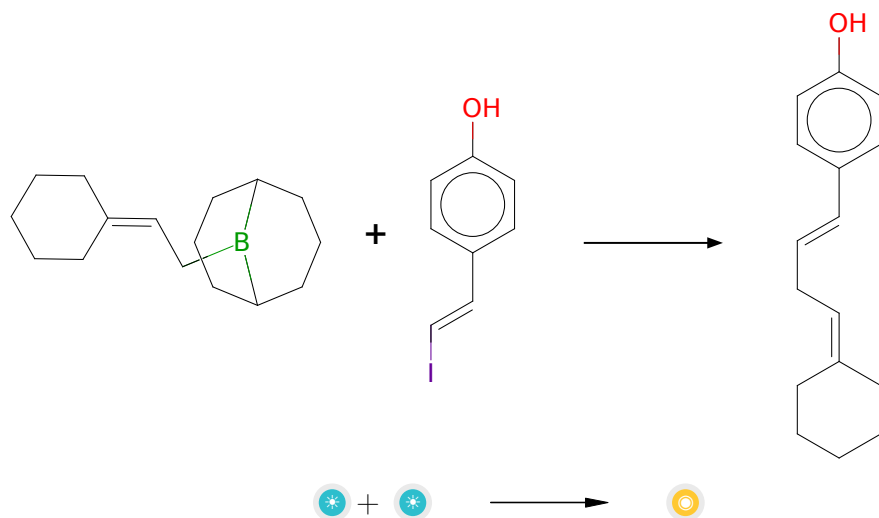
**Typical conditions:** KOH.MeOH

**Protections:** none

**Reference:** [10.3762/bjoc.10.40](#) and [10.1016/j.bmc.2009.11.035](#) and [10.1016/S0040-4020\(02\)01584-3](#)

**Retrosynthesis ID:** 32805

### 2.1.3 Suzuki coupling of alkyl-9-BBNs with vinyl iodides



**Substrates:**

- 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane
- C<sub>8</sub>H<sub>7</sub>IO

**Products:**

- Oc1ccc(/C=C/CC=C2CCCCC2)cc1

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

**Protections:** none

**Reference:** [10.1021/jo015995y](#) and [10.1016/j.tetlet.2010.11.139](#) And [10.1021/ol0600741](#) and [10.1055/s-2002-32602](#) and [10.1002/anie.200501760](#)

**Retrosynthesis ID:** 25168

## 2.2 Path 2

**Score:** 25.00

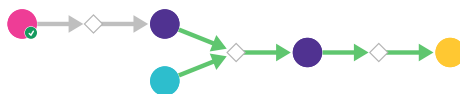
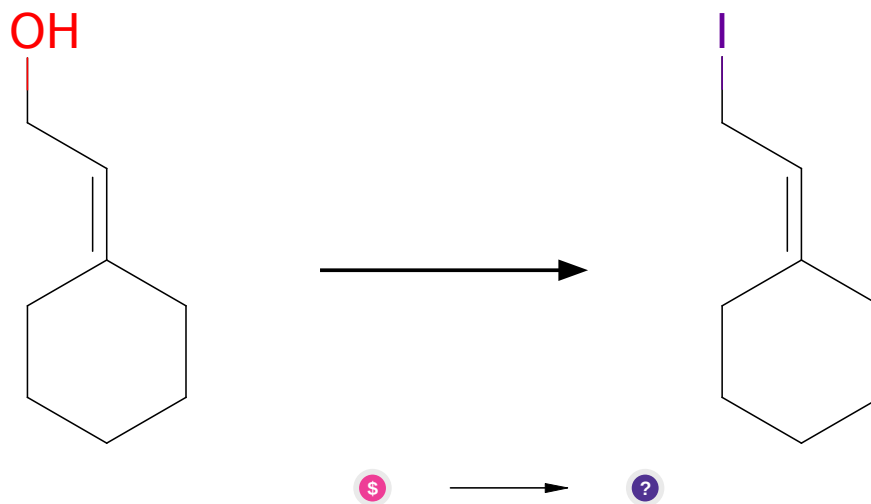


Figure 2: Outline of path 2

### 2.2.1 Synthesis Of Alkyl Iodides Via Appel Reaction



**Substrates:**

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

**Products:**

1. ICC=C1CCCCC1

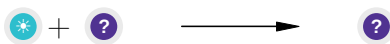
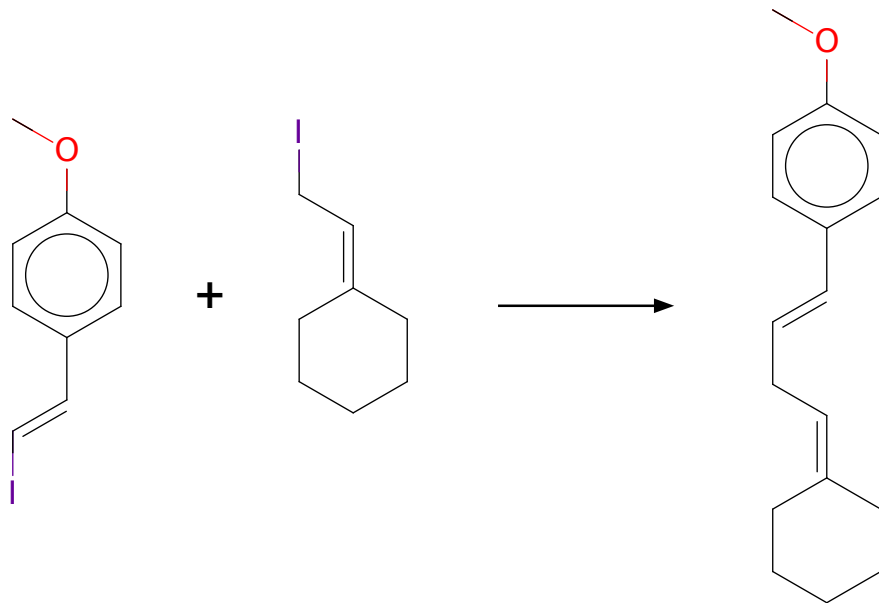
**Typical conditions:** Imidazole.PPh<sub>3</sub>.I<sub>2</sub>

**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

### 2.2.2 Palladium catalysed alkylation of vinyl iodides



#### Substrates:

1. (E)-2-(4-methoxyphenyl)-1-iodo-1-ethene
2. ICC=C1CCCCC1

#### Products:

1. COc1ccc(/C=C/CC=C2CCCCC2)cc1

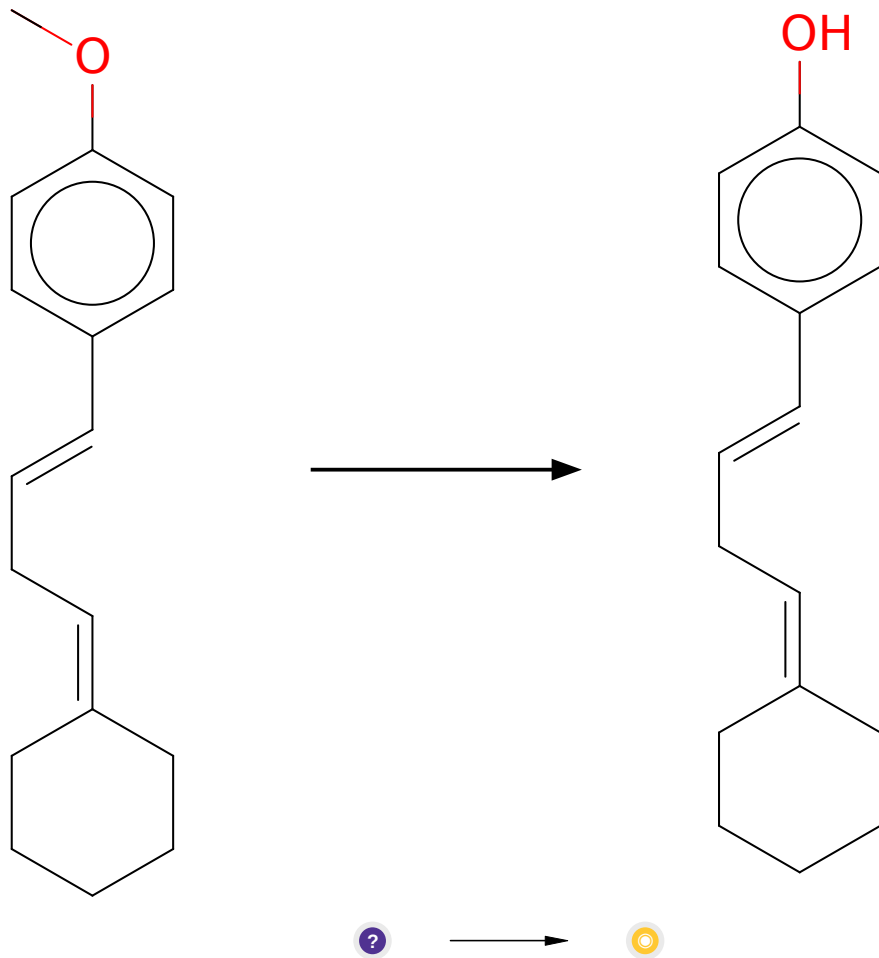
**Typical conditions:** [Pd].catalyst

**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

### 2.2.3 Demethylation of Phenols



#### Substrates:

1. COc1ccc(/C=C/CC=C2CCCCC2)cc1

#### Products:

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

**Typical conditions:** BBr<sub>3</sub>.CH<sub>2</sub>Cl<sub>2</sub>

**Protections:** none

**Reference:** DOI: [10.1021/ja00105a021](https://doi.org/10.1021/ja00105a021) and [10.1021/jm00176a011](https://doi.org/10.1021/jm00176a011) and [10.1021/jm970277i](https://doi.org/10.1021/jm970277i) and [10.1021/ja0106164](https://doi.org/10.1021/ja0106164) and Patent: US2010/16298, 2010, A1, page 185

Retrosynthesis ID: 10011837

## 2.3 Path 3

Score: 25.00

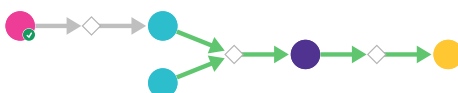
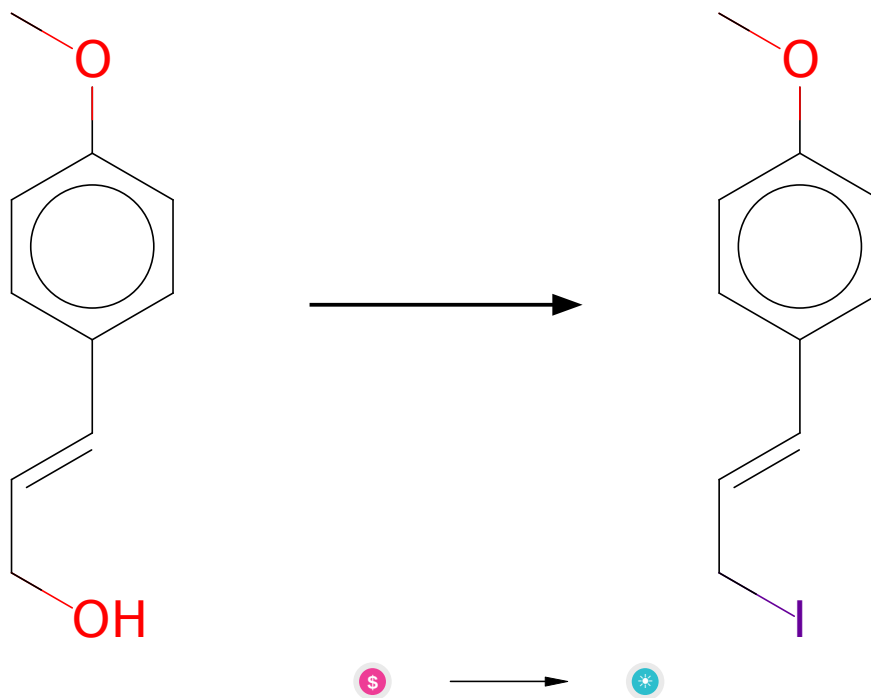


Figure 3: Outline of path 3

### 2.3.1 Synthesis Of Alkyl Iodides Via Appel Reaction



**Substrates:**

1. 3-(4-Methoxyphenyl)prop-2-en-1-ol - *available at Sigma-Aldrich*

**Products:**

1. 1-(3-iodo-propenyl)-4-methoxy-benzene



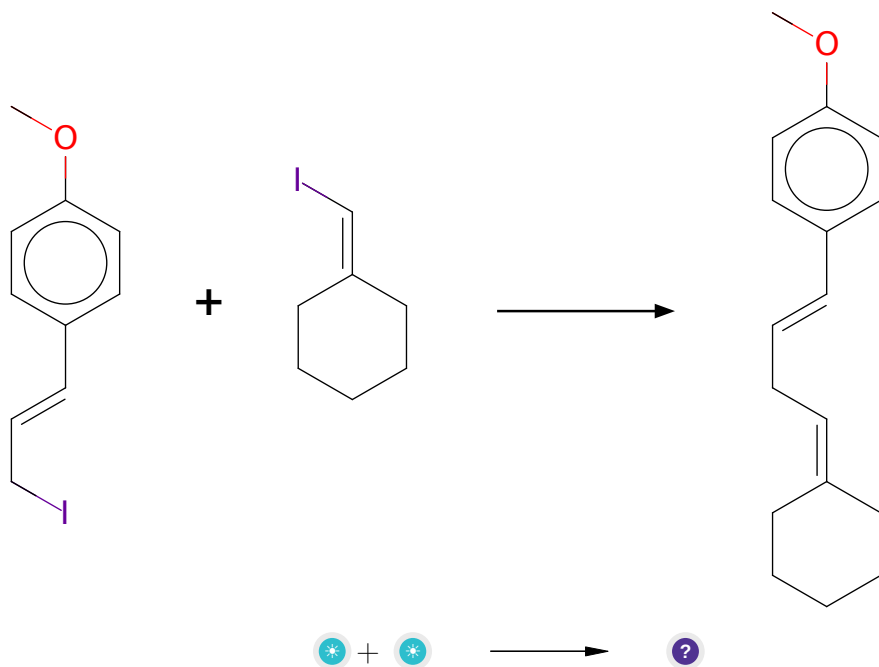
**Typical conditions:** Imidazole.PPh<sub>3</sub>.I<sub>2</sub>

**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

### 2.3.2 Palladium catalysed alkylation of vinyl iodides



**Substrates:**

1. iodomethylene cyclohexane
2. 1-(3-iodo-propenyl)-4-methoxy-benzene

**Products:**

1. COc1ccc(/C=C/CC=C2CCCCC2)cc1

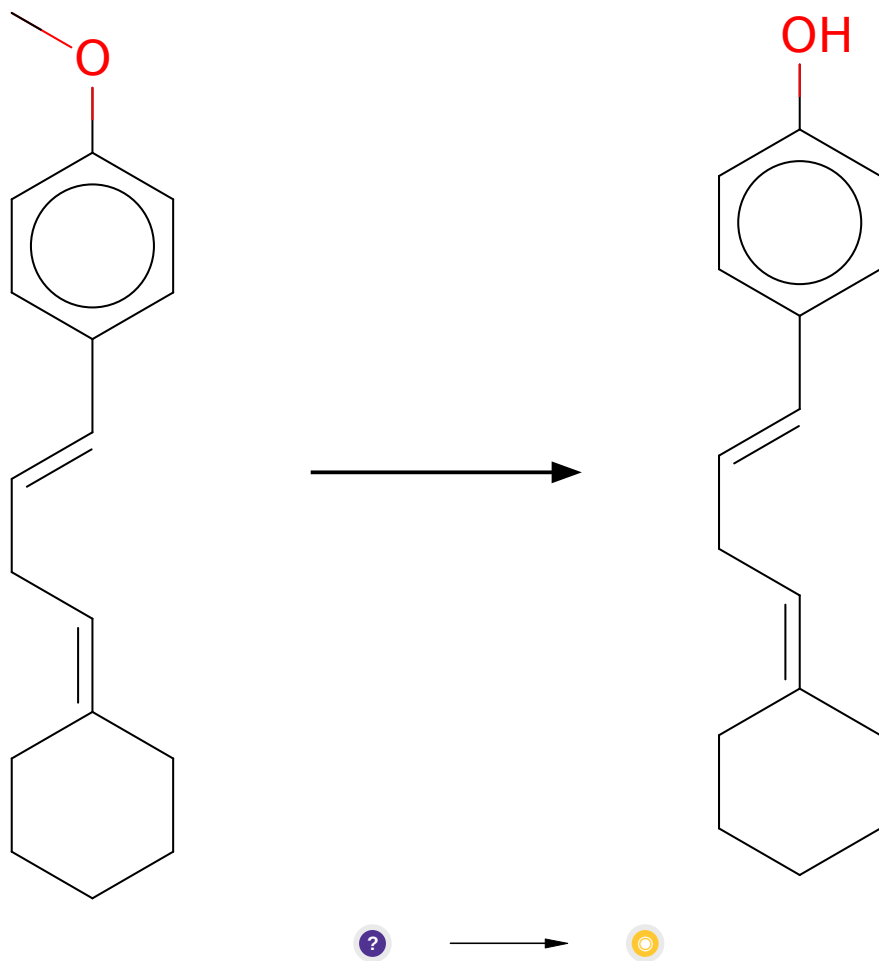
**Typical conditions:** [Pd].catalyst

**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: 25165

### 2.3.3 Demethylation of Phenols



**Substrates:**

1. COc1ccc(/C=C/CC=C2CCCCC2)cc1

**Products:**

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

**Typical conditions:** BBr<sub>3</sub>.CH<sub>2</sub>Cl<sub>2</sub>

**Protections:** none

**Reference:** DOI: [10.1021/ja00105a021](https://doi.org/10.1021/ja00105a021) and [10.1021/jm00176a011](https://doi.org/10.1021/jm00176a011) and [10.1021/jm970277i](https://doi.org/10.1021/jm970277i) and [10.1021/ja0106164](https://doi.org/10.1021/ja0106164) and Patent: US2010/16298, 2010, A1, page 185

**Retrosynthesis ID:** 10011837

## 2.4 Path 4

Score: 25.00

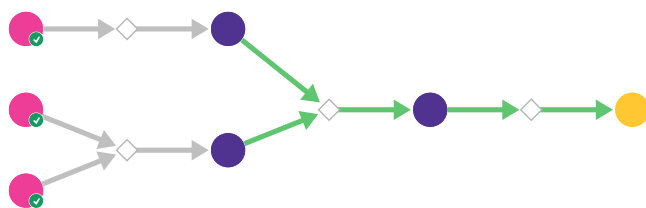
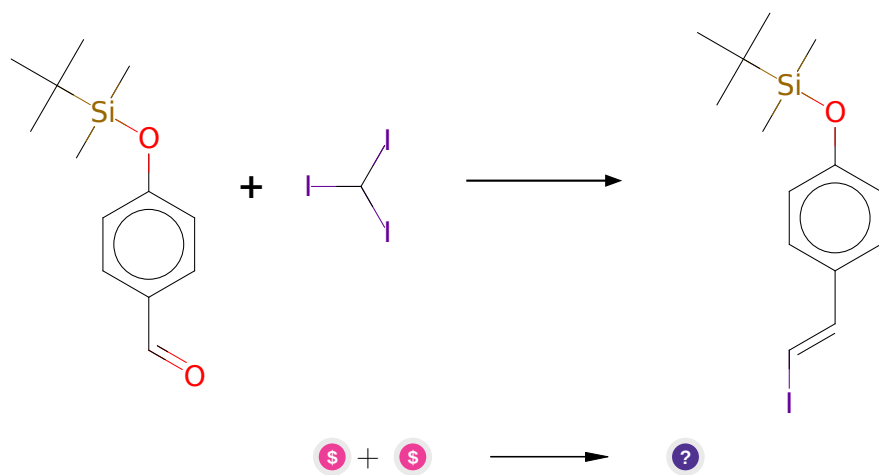


Figure 4: Outline of path 4

### 2.4.1 Takai olefination



**Substrates:**

1. 4-[(tert-Butyldimethylsilyl)oxy]benzaldehyde - *available at Sigma-Aldrich*
2. Iodoform - *available at Sigma-Aldrich*

**Products:**

1. CC(C)(C)[Si](C)(C)Oc1ccc(/C=C/I)cc1

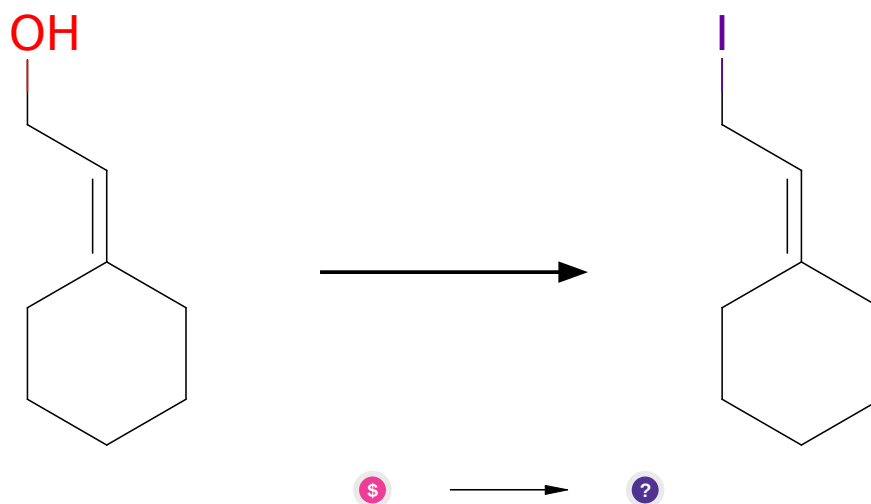
**Typical conditions:** CrCl<sub>2</sub>.THF

**Protections:** none

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

**Retrosynthesis ID:** 10497

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



**Substrates:**

1. 2-cyclohexylideneethan-1-ol - [available at Sigma-Aldrich](#)

**Products:**

1. ICC=C1CCCCC1

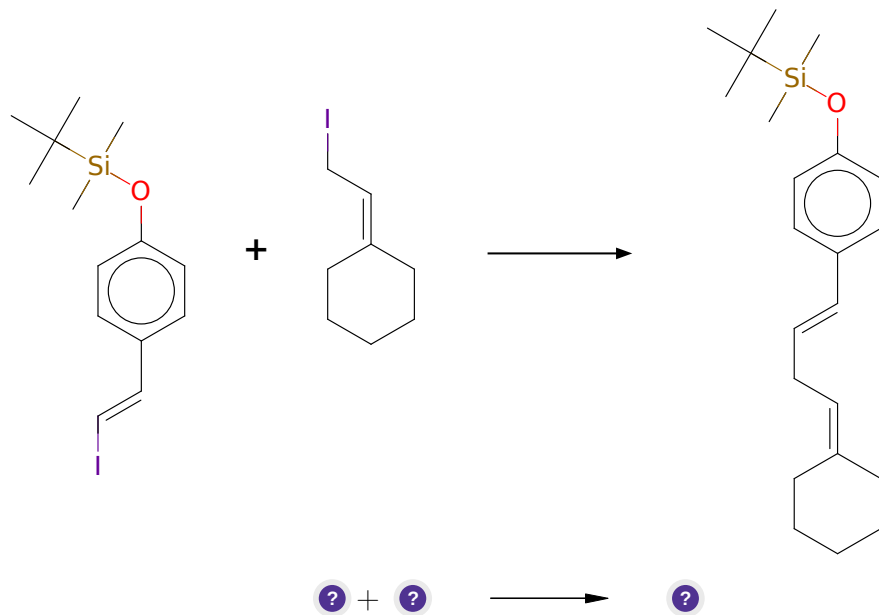
**Typical conditions:** Imidazole.PPh<sub>3</sub>.I<sub>2</sub>

**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

### 2.4.3 Palladium catalysed alkylation of vinyl iodides



**Substrates:**

1. CC(C)(C)[Si](C)(C)Oc1ccc(/C=C/I)cc1
2. ICC=C1CCCCC1

**Products:**

1. CC(C)(C)[Si](C)(C)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

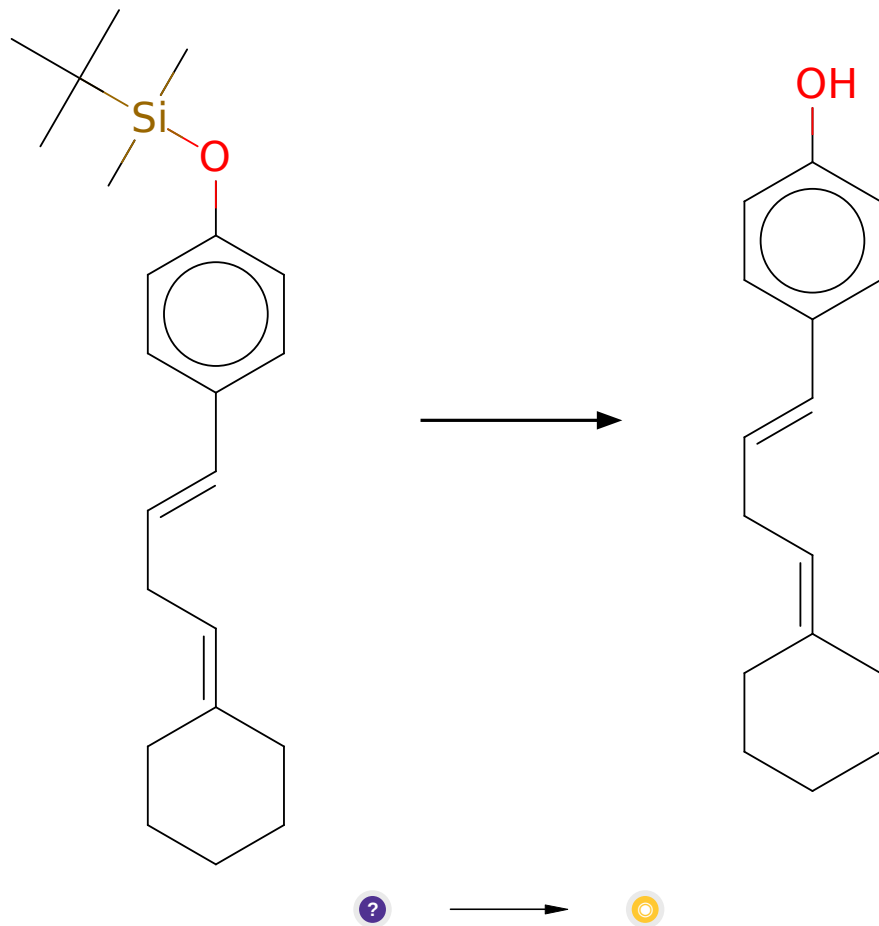
**Typical conditions:** [Pd].catalyst

**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

#### 2.4.4 Deprotection of TBS aryl ethers



**Substrates:**

1. CC(C)(C)[Si](C)(C)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

**Products:**

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

**Typical conditions:** TBAF.THF

**Protections:** none

**Reference:** [10.1016/j.tet.2013.01.017](#) and [10.1016/j.tet.2004.04.042](#)

**Retrosynthesis ID:** 31011409

## 2.5 Path 5

Score: 25.00

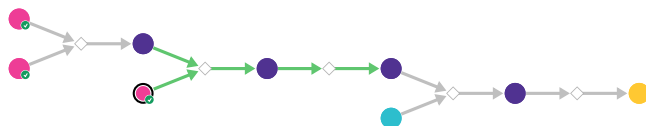
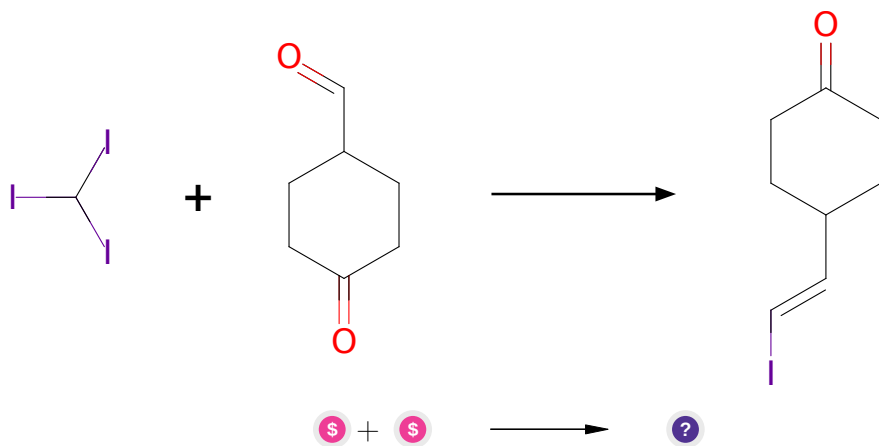


Figure 5: Outline of path 5

### 2.5.1 Takai olefination



**Substrates:**

1. 4-Oxocyclohexanecarbaldehyde - *available at Sigma-Aldrich*
2. Iodoform - *available at Sigma-Aldrich*

**Products:**

1. O=C1CCC(/C=C/I)CC1

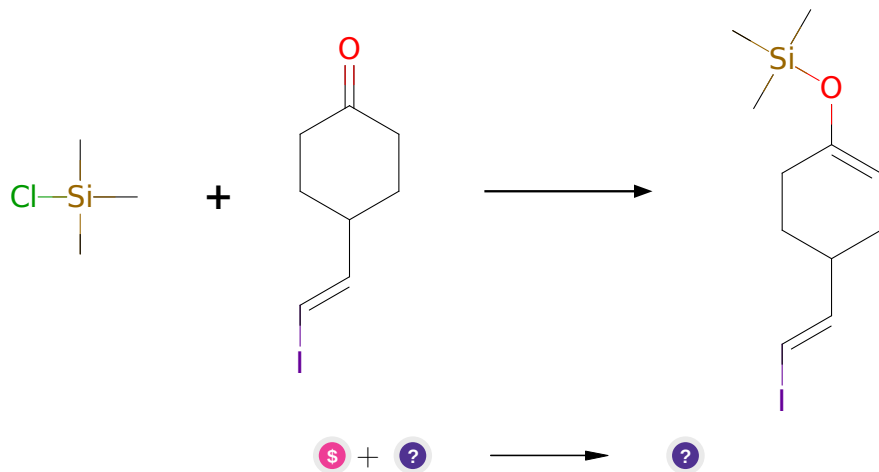
**Typical conditions:** CrCl<sub>2</sub>.THF

**Protections:** none

**Reference:** [10.1021/ja00283a046](https://doi.org/10.1021/ja00283a046) and [10.1021/ja00237a081](https://doi.org/10.1021/ja00237a081)

**Retrosynthesis ID:** 10497

## 2.5.2 Enol esters and ethers synthesis



### Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. O=C1CCC(/C=C/I)CC1

### Products:

1. C[Si](C)(C)OC1=CCC(/C=C/I)CC1

**Typical conditions:** 1.LDA.2.Electrophile

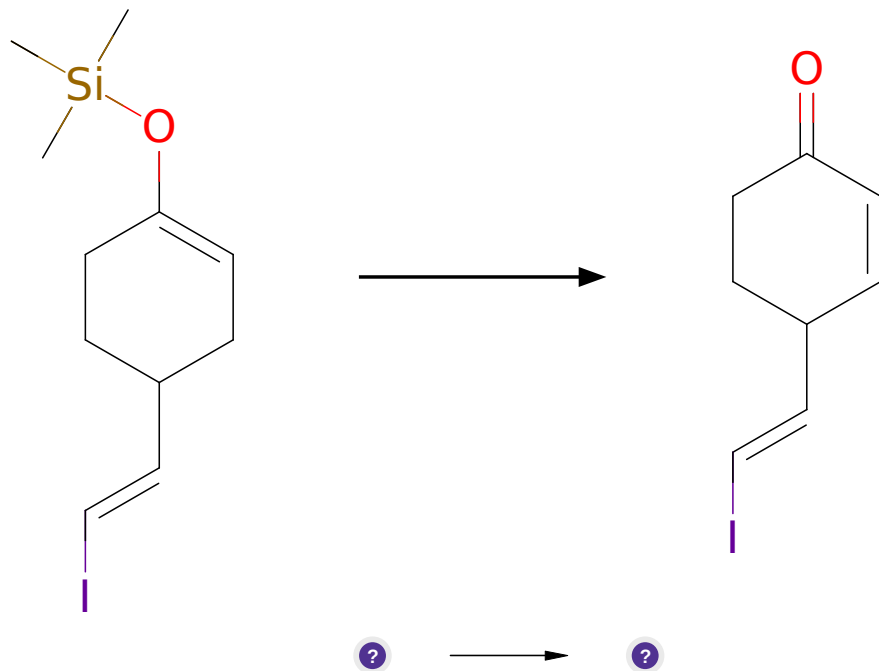
**Protections:** none

**Reference:** US2467095A AND WO2014169833a1 AND  
[10.1016/j.steroids.2011.03.014](#) AND [10.1021/ol200875m](#) (SI) AND  
[10.1021/ja00531a034](#)

**Retrosynthesis ID:** 7797



### 2.5.3 Dehydrogenation of silyl enol ethers



**Substrates:**

1. C[Si](C)(C)OC1=CCC(/C=C/I)CC1

**Products:**

1. O=C1C=CC(/C=C/I)CC1

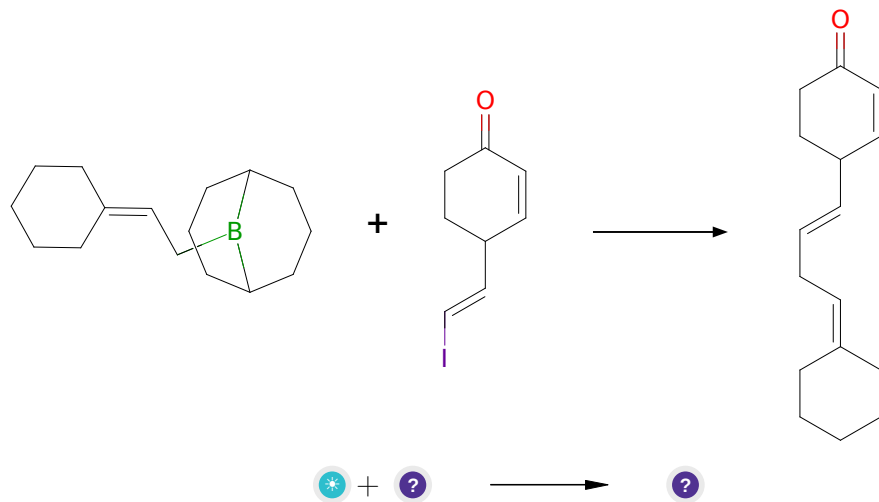
**Typical conditions:** Pd(OAc)<sub>2</sub>.Cu(OAc)<sub>2</sub>.O<sub>2</sub>.MeCN

**Protections:** none

**Reference:** [10.1271/bbb.60.405](#) and [10.1039/C3CC46778C](#) and US2015284405 p.40 and [10.1016/S0040-4039\(01\)81518-5](#) and US2010204477 p. 15-16 and [10.1016/0040-4039\(95\)00694-8](#) and [10.1021/jo00089a034](#) and [10.1016/S0040-4020\(01\)90587-3](#) and [10.1080/00397919008052802](#) and [10.1021/ja00218a060](#)

**Retrosynthesis ID:** 9999877

#### 2.5.4 Suzuki coupling of alkyl-9-BBNs with vinyl iodides



##### Substrates:

1. 9-(3,3-pentamethyleneallyl)-9-borabicyclo[3.3.1]nonane
2. O=C1C=CC(/C=C/I)CC1

##### Products:

1. O=C1C=CC(/C=C/CC=C2CCCCC2)CC1

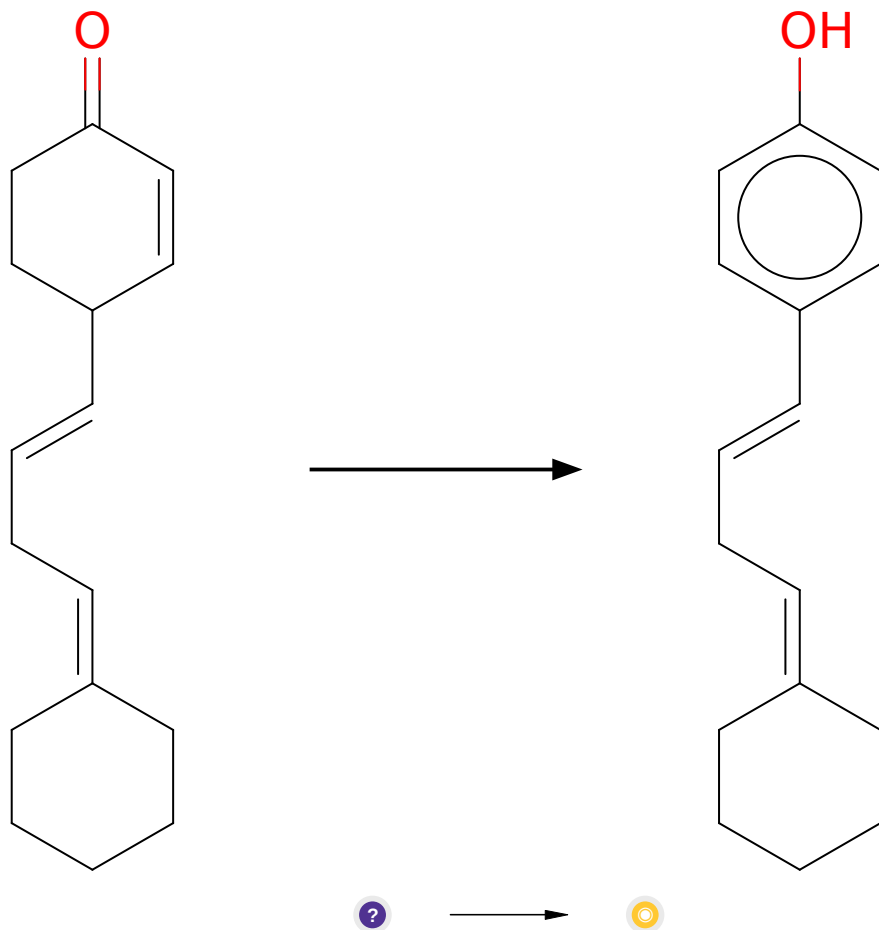
**Typical conditions:** Pd catalyst.base.solvent

**Protections:** none

**Reference:** [10.1021/jo015995y](#) and [10.1016/j.tetlet.2010.11.139](#) And [10.1021/ol0600741](#) and [10.1055/s-2002-32602](#) and [10.1002/anie.200501760](#)

**Retrosynthesis ID:** 25168

### 2.5.5 DDQ mediated aromatization



**Substrates:**

1. O=C1C=CC(/C=C/CC=C2CCCCC2)CC1

**Products:**

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

**Typical conditions:** DDQ

**Protections:** none

**Reference:** [10.1021/ja054872i](#) and [10.1021/ja00311a085](#) and [10.1021/ja00122a011](#)

**Retrosynthesis ID:** 9999983