

# Paths of analysis\*

PG1A

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

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

### 2.1 Path 1

**Score:** 20.00

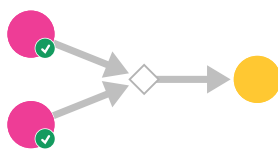
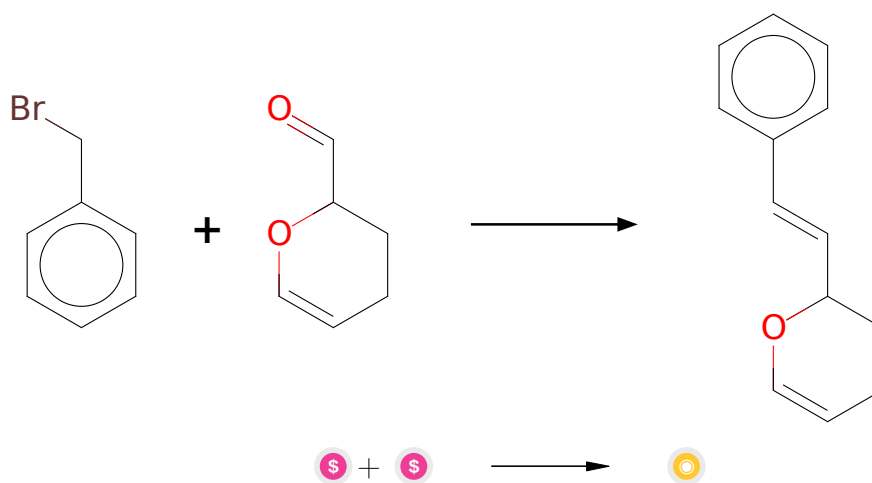


Figure 1: Outline of path 1

#### 2.1.1 Wittig-Schlosser olefination



**Substrates:**

1.  $\alpha$ -Bromotoluene - *available at Sigma-Aldrich*

2. 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*

**Products:**

1. 2-styryl-3,4-dihydro-2h-pyran

**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

## 2.2 Path 2

**Score:** 20.00

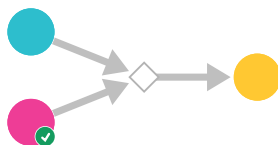
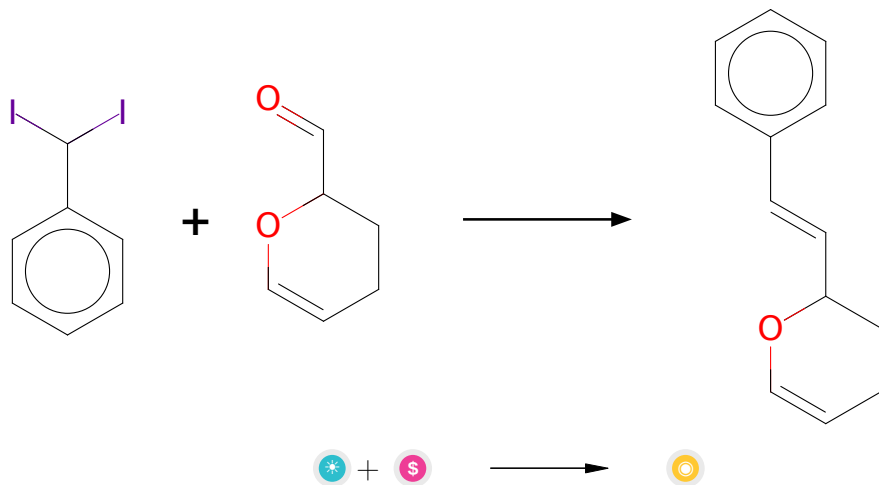


Figure 2: Outline of path 2

### 2.2.1 Takai olefination



**Substrates:**

1.  $\alpha,\alpha$ -diiodotoluene
2. 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*

**Products:**

1. 2-styryl-3,4-dihydro-2h-pyran

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

**Protections:** none

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

**Retrosynthesis ID:** 10942

## 2.3 Path 3

Score: 20.00

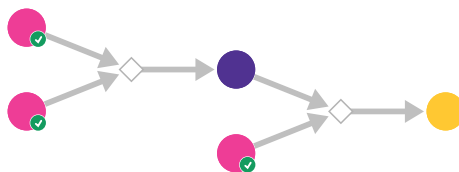
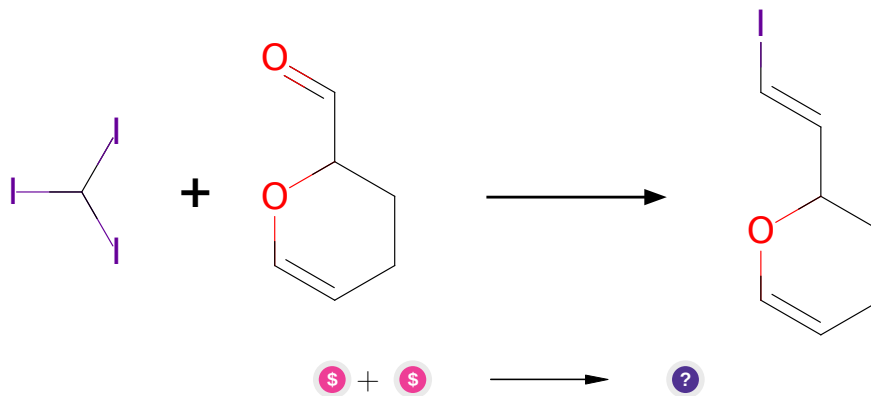


Figure 3: Outline of path 3

### 2.3.1 Takai olefination



**Substrates:**

1. Iodoform - *available at Sigma-Aldrich*
2. 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*

**Products:**

1. I/C=C/C1CCC=CO1

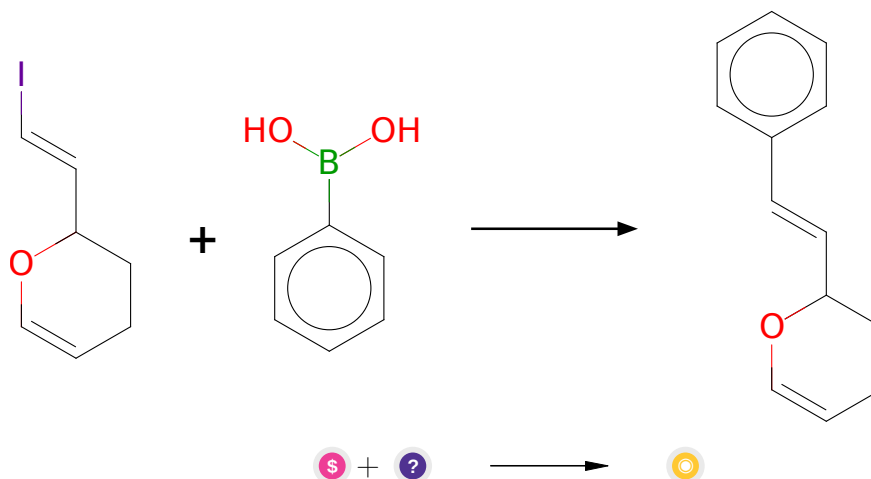
**Typical conditions:** CrCl<sub>2</sub>.THF

**Protections:** none

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

**Retrosynthesis ID:** 10497

### 2.3.2 Suzuki coupling of arylboronic acids with vinyl iodides



**Substrates:**

1. Phenylboric acid - *available at Sigma-Aldrich*
2. I/C=C/C1CCC=CO1

**Products:**

1. 2-styryl-3,4-dihydro-2h-pyran

**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:** 11208

## 2.4 Path 4

Score: 20.00

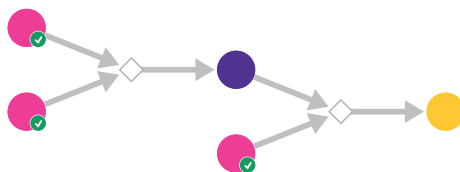
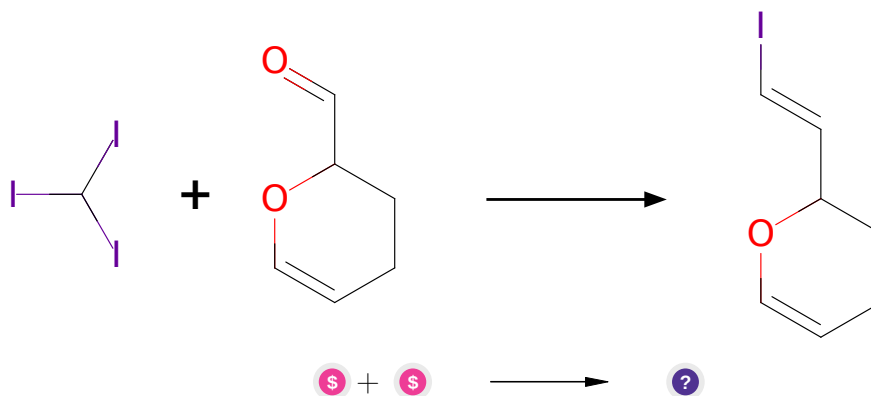


Figure 4: Outline of path 4

### 2.4.1 Takai olefination



**Substrates:**

1. Iodoform - *available at Sigma-Aldrich*
2. 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*

**Products:**

1. I/C=C/C1CCC=CO1

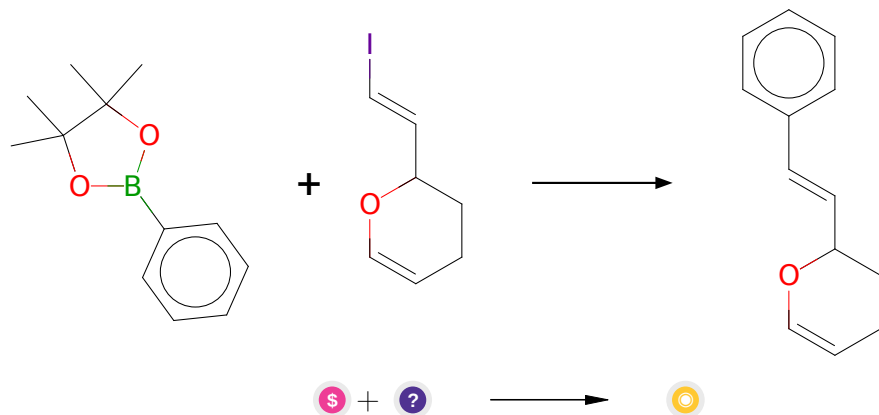
**Typical conditions:** CrCl2.THF

**Protections:** none

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

**Retrosynthesis ID:** 10497

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



#### Substrates:

1. (Pinacolboryl)benzene - *available at Sigma-Aldrich*
2. I/C=C/C1CCC=CO1

#### Products:

1. 2-styryl-3,4-dihydro-2h-pyran

**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

## 2.5 Path 5

**Score:** 45.00

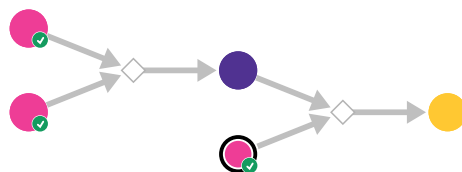
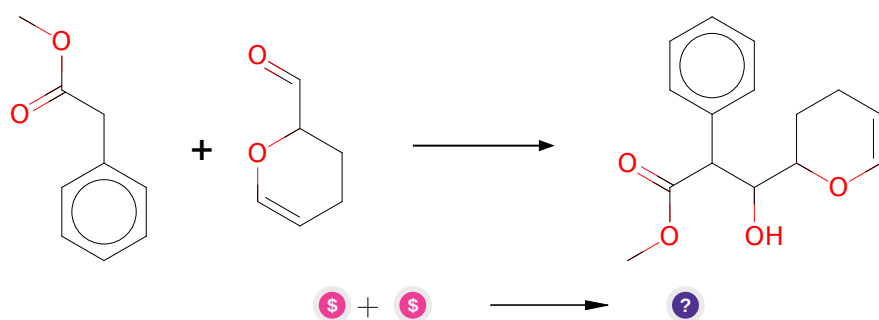


Figure 5: Outline of path 5

### 2.5.1 Condensation of esters with aldehydes



#### Substrates:

1. Methyl phenylacetate - *available at Sigma-Aldrich*
2. 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*

#### Products:

1. COC(=O)C(c1ccccc1)C(O)C1CCC=CO1

**Typical conditions:** LDA.THF

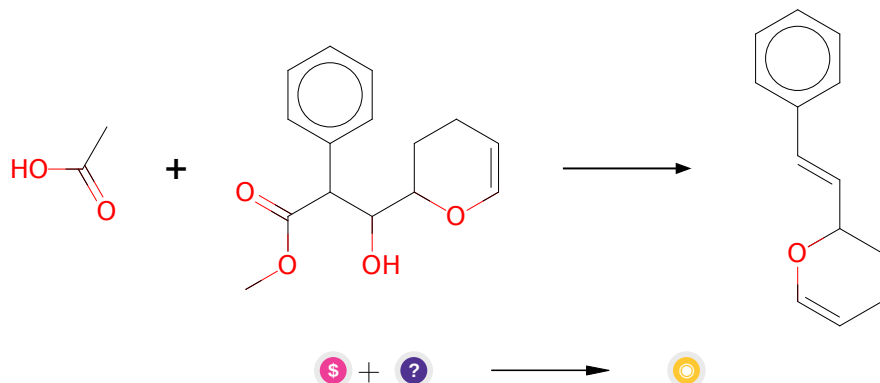
**Protections:** none

**Reference:** [10.1016/j.bmcl.2005.02.066](https://doi.org/10.1016/j.bmcl.2005.02.066) and [10.3762/bjoc.9.175](https://doi.org/10.3762/bjoc.9.175) and [10.1021/ol1016178](https://doi.org/10.1021/ol1016178)

**Retrosynthesis ID:** 4788



### 2.5.2 Tandem Krapcho decarboxylation and elimination



#### Substrates:

1. glacial - *available at Sigma-Aldrich*
2. COC(=O)C(c1ccccc1)C(O)C1CCC=CO1

#### Products:

1. 2-styryl-3,4-dihydro-2h-pyran

**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](https://doi.org/10.1021/jo00263a005) and [10.1021/jo00386a011](https://doi.org/10.1021/jo00386a011) and [10.1021/ol006085q](https://doi.org/10.1021/ol006085q)

**Retrosynthesis ID:** 9605

## 2.6 Path 6

**Score:** 45.00

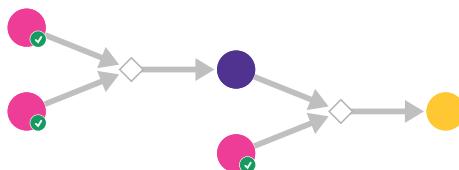
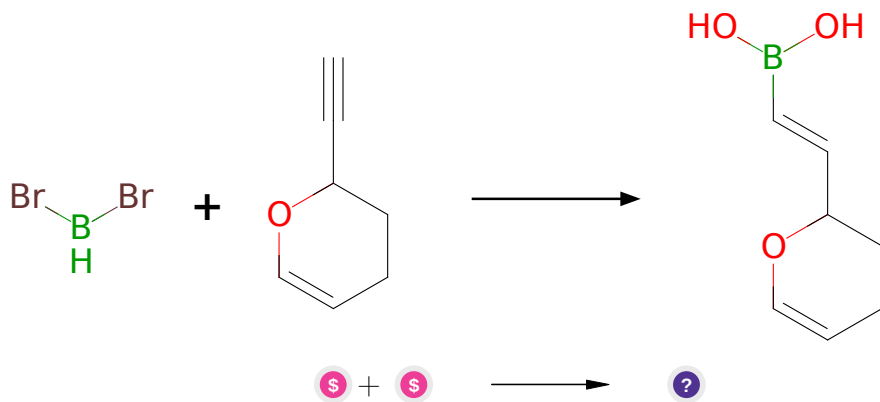


Figure 6: Outline of path 6

### 2.6.1 Synthesis of vinylboronic acids



#### Substrates:

1. 2-ethynyl-3,4-dihydro-2H-pyran - *available at Sigma-Aldrich*
2. Dibromoborane dimethyl sulfide - *available at Sigma-Aldrich*

#### Products:

1. OB(O)/C=C/C1CCC=CO1

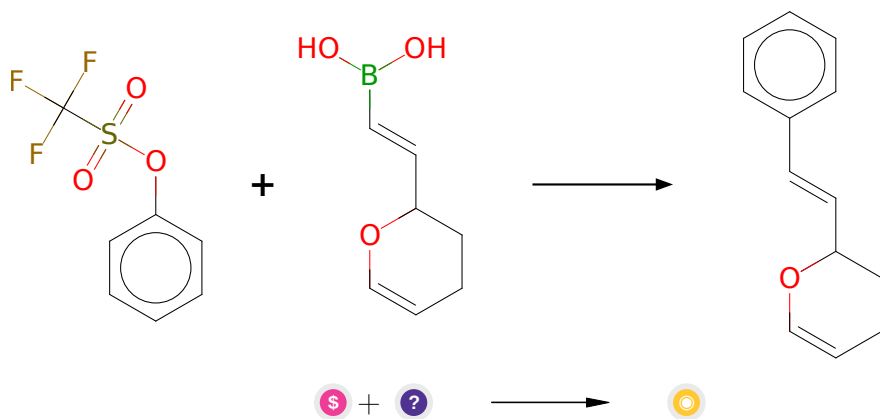
**Typical conditions:** HBr2xMe2S.THF

**Protections:** none

**Reference:** [10.1021/ol501309e](#) AND [10.1021/jacs.5b09773](#)

**Retrosynthesis ID:** 4763

### 2.6.2 Suzuki coupling of aryl triflates with alkenyl boronic acids



#### Substrates:

1. Phenyl triflate - *available at Sigma-Aldrich*

2. OB(O)/C=C/C1CCC=CO1

**Products:**

1. 2-styryl-3,4-dihydro-2H-pyran

**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:** 24874

## 2.7 Path 7

Score: 45.00

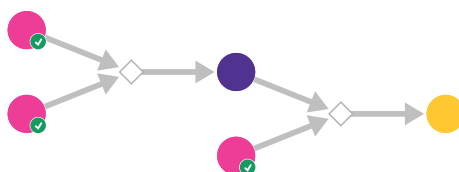
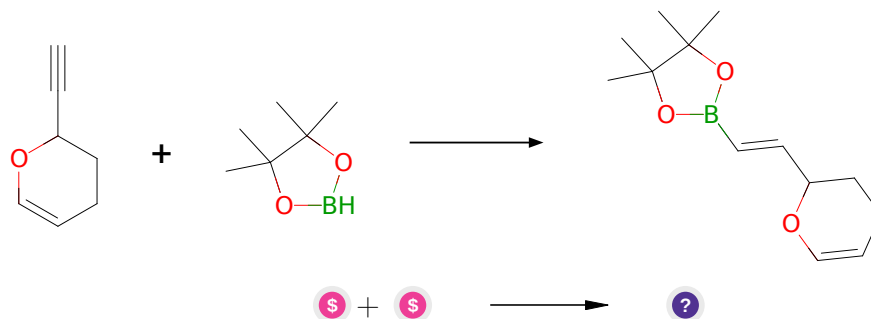


Figure 7: Outline of path 7

### 2.7.1 Synthesis of bis-borylated derivatives from boronate derivatives



**Substrates:**

1. 2-ethynyl-3,4-dihydro-2H-pyran - *available at Sigma-Aldrich*
2. HBpin - *available at Sigma-Aldrich*

**Products:**

1. CC1(C)OB(/C=C/C2CCC=CO2)OC1(C)C

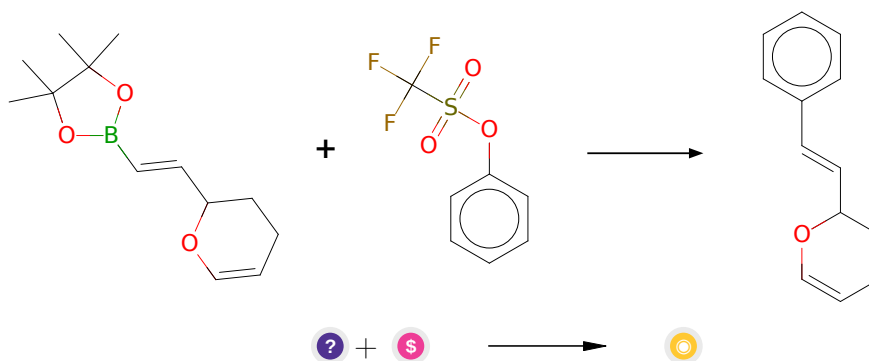
**Typical conditions:** Cy2BH.THF.85C

**Protections:** none

**Reference:** DOI: [10.1016/j.tet.2010.04.020](https://doi.org/10.1016/j.tet.2010.04.020)

**Retrosynthesis ID:** 307

### 2.7.2 Suzuki coupling of aryl triflates with alkenyl boronic acids pinacol esters



**Substrates:**

1. CC1(C)OB(/C=C/C2CCC=CO2)OC1(C)C
2. Phenyl triflate - *available at Sigma-Aldrich*

**Products:**

1. 2-styryl-3,4-dihydro-2h-pyran

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

**Protections:** none

**Reference:** [10.1021/cr00039a007](https://doi.org/10.1021/cr00039a007) and [10.1007/3418\\_2012\\_32](https://doi.org/10.1007/3418_2012_32) and [10.1021/cr0505268](https://doi.org/10.1021/cr0505268) and [10.1016/j.jfluchem.2016.01.018](https://doi.org/10.1016/j.jfluchem.2016.01.018) and [10.1039/C3CS60197H](https://doi.org/10.1039/C3CS60197H)

**Retrosynthesis ID:** 10985

## 2.8 Path 8

Score: 45.00

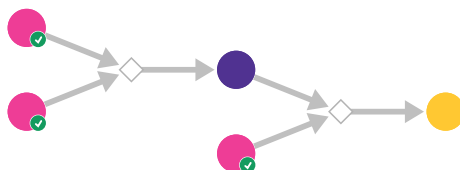
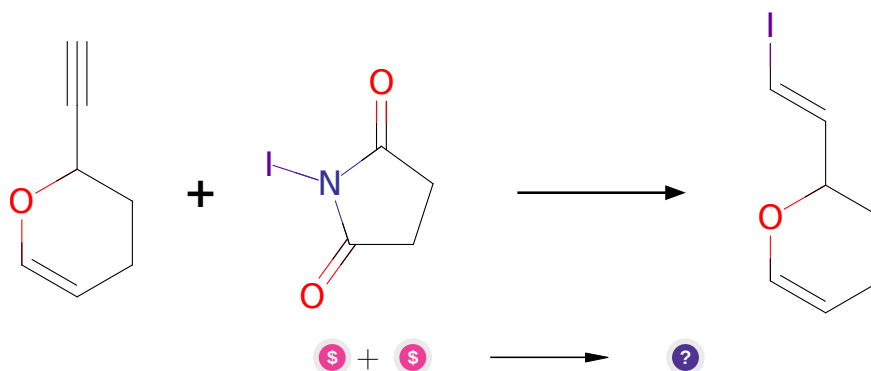


Figure 8: Outline of path 8

### 2.8.1 Synthesis of vinyl iodides from terminal alkynes



**Substrates:**

1. 2-ethynyl-3,4-dihydro-2H-pyran - *available at Sigma-Aldrich*
2. N-Iodosuccinimide - *available at Sigma-Aldrich*

**Products:**

1. I/C=C/C1CCC=CO1

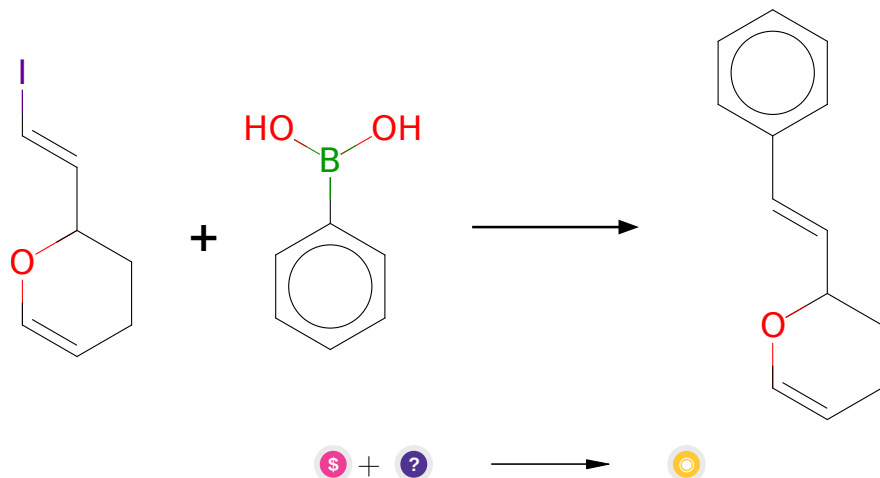
**Typical conditions:** NiCl2(PPh3)2.DIBAL-H.NIS or I2

**Protections:** none

**Reference:** DOI: [10.1002/anie.201408022](https://doi.org/10.1002/anie.201408022) and [10.1021/ol048363h](https://doi.org/10.1021/ol048363h) (supporting info)

**Retrosynthesis ID:** 6973

### 2.8.2 Suzuki coupling of arylboronic acids with vinyl iodides



#### Substrates:

1. Phenylboric acid - *available at Sigma-Aldrich*
2. I/C=C/C1CCCC=CO1

#### Products:

1. 2-styryl-3,4-dihydro-2h-pyran

**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:** 11208

## 2.9 Path 9

**Score:** 45.00

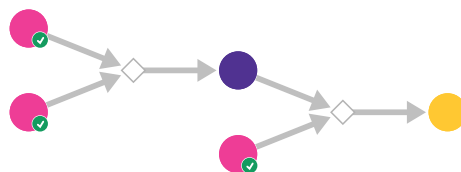
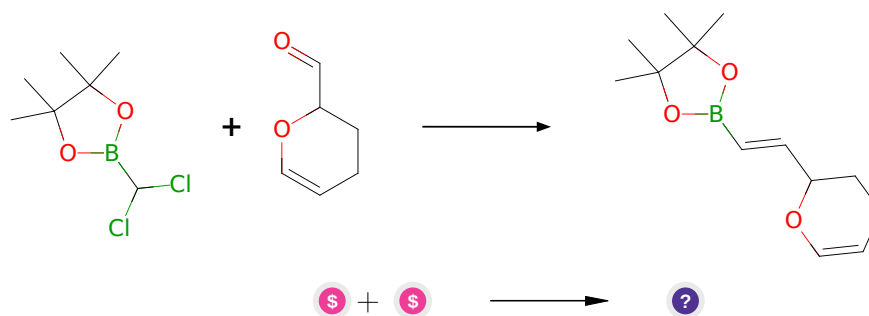


Figure 9: Outline of path 9

### 2.9.1 Addition of dichloromethylboranes to aldehydes



#### Substrates:

- 1,3,2-Dioxaborolane - *available at Sigma-Aldrich*
- 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*

#### Products:

- CC1(C)OB(/C=C/C2CCC=CO2)OC1(C)C

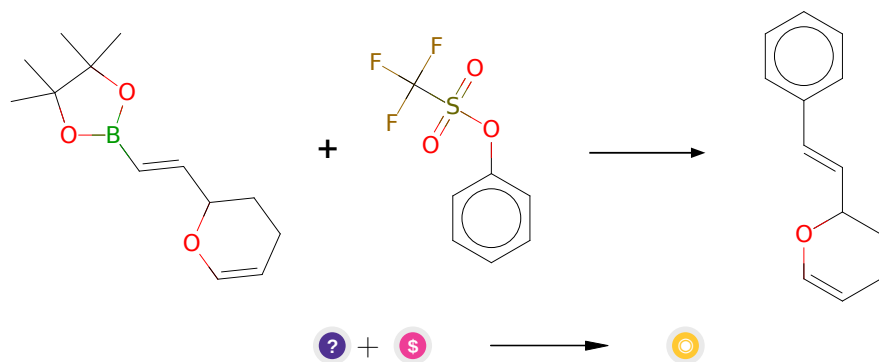
**Typical conditions:** CrCl<sub>2</sub>.LiI.THF

**Protections:** none

**Reference:** [10.1021/ja710487q](https://doi.org/10.1021/ja710487q) and [10.1016/j.bmc.2016.03.038](https://doi.org/10.1016/j.bmc.2016.03.038) and [10.1021/ja078129x](https://doi.org/10.1021/ja078129x) and [10.1016/j.bmc.2015.01.030](https://doi.org/10.1016/j.bmc.2015.01.030)

**Retrosynthesis ID:** 29414

## 2.9.2 Suzuki coupling of aryl triflates with alkenyl boronic acids pinacol esters



### Substrates:

1. CC1(C)OB(/C=C/C2CCC=CO2)OC1(C)C
2. Phenyl triflate - *available at Sigma-Aldrich*

### Products:

1. 2-styryl-3,4-dihydro-2h-pyran

**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:** 10985

## 2.10 Path 10

**Score:** 45.00

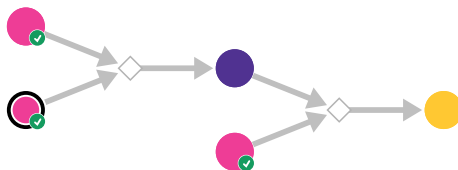
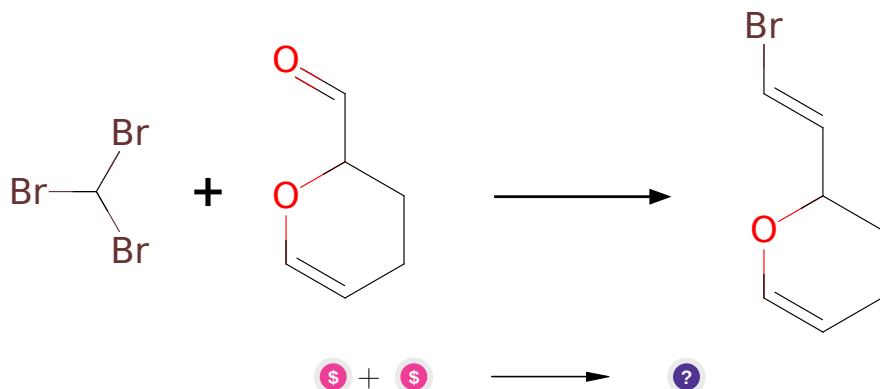


Figure 10: Outline of path 10



### 2.10.1 Takai olefination



#### Substrates:

1. 3,4-Dihydro-2H-Pyran-2-carboxaldehyde - *available at Sigma-Aldrich*
2. Bromoform - *available at Sigma-Aldrich*

#### Products:

1. Br/C=C/C1CCC=CO1

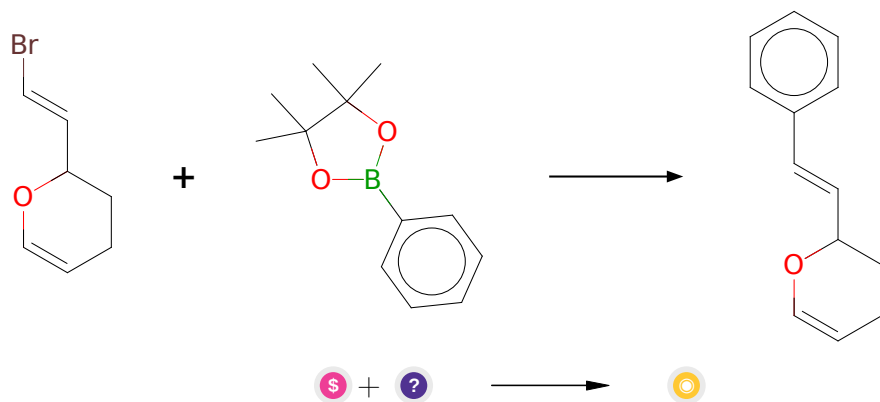
**Typical conditions:** CrCl<sub>2</sub>.THF

**Protections:** none

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

**Retrosynthesis ID:** 10292

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



#### Substrates:

1. (Pinacolboryl)benzene - *available at Sigma-Aldrich*

2. Br/C=C/C1CCC=CO1

**Products:**

1. 2-styryl-3,4-dihydro-2h-pyran

**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:** 10355