# Paths of analysis*

L11_DIA

Synthia

October 11, 2022

## 1 Analysis parameters

**Analysis type:** Automatic Retrosynthesis

**Rules:** none selected

**Filters:** 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:** TUNNEL_COEF*FGI_COEF*STEP*20+1000000*(CONFLICT+NON_SELECTIVITY+FILTERS+PROTECT)

**Chemical scoring formula:** SMALLER^ 3,SMALLER^ 1.5

**Min. search width:** 400

**Max. reactions per product:** 60

**Strategies:** none selected

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**FGI Coeff:** 0

**Tunnels Coeff:** 0

**JSON Parameters:** {}

# 2 Paths

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

## 2.1 Path 1

**Score:** 281.47

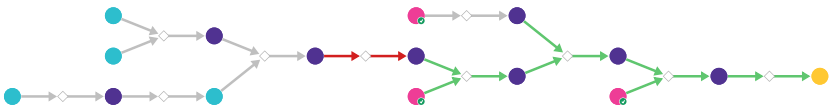
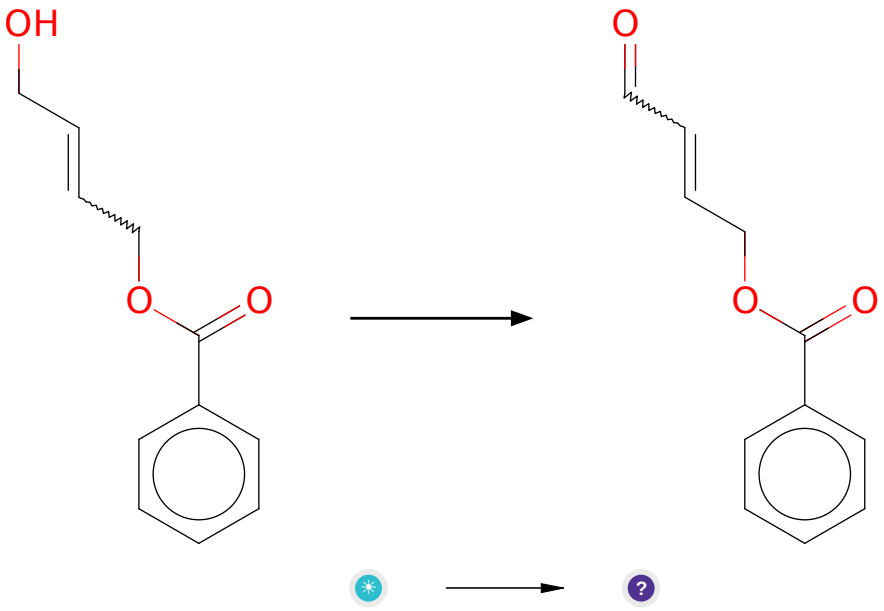


Figure 1: Outline of path 1

### 2.1.1 Oxidation of primary alcohols with DMP




**Substrates:**

1. 4-hydroxy-2-butenyl-benzoat

**Products:**

1. O=CC=CCOC(=O)c1ccccc1

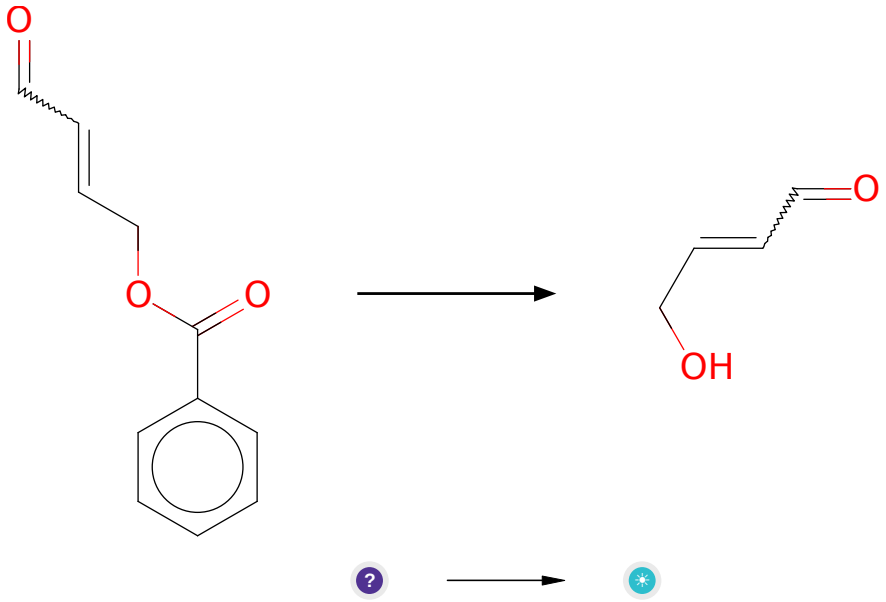
**Typical conditions:** DMP.DCM.0-25 C

**Protections:** none

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

**Retrosynthesis ID:** 50426

### 2.1.2 Hydrolysis of benzoates




**Substrates:**

1. O=CC=CCOC(=O)c1ccccc1

**Products:**

1. 4-hydroxy-but-2-enal

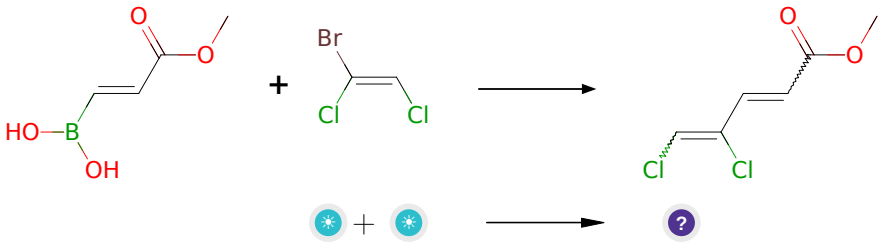
**Typical conditions:** LiOH/K2CO3/NH3.MeOH.H2O.THF

**Protections:** none

**Reference:** *10.1021/jm0502788* and *10.1016/j.tetlet.2008.09.165* and *10.1021/jm034098e* and *10.1021/jo049277y* and *10.1055/s-0033-1338657*

**Retrosynthesis ID:** 25136

### 2.1.3 Suzuki coupling of vinyl bromides with alkenyl boronic acids




**Substrates:**

1. (e)-2-(methoxycarbonyl)ethyl-1-enylboronic acid
2. 1-bromo-1,2-dichloro-ethene

**Products:**

1. COC(=O)C=CC(Cl)=CCl

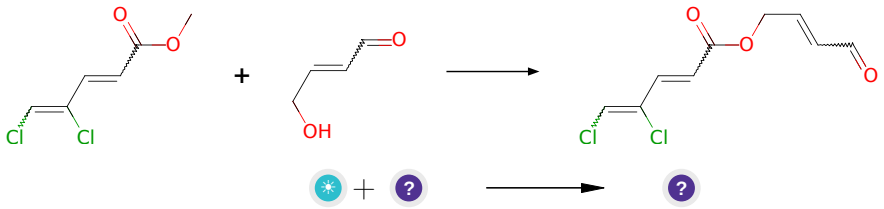
**Typical conditions:** Pd catalyst.base.solvent

**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:** 24937

### 2.1.4 Acid catalyzed transesterification




**Substrates:**

1. 4-hydroxy-but-2-enal
2. COC(=O)C=CC(Cl)=CCl

**Products:**

1. O=CC=CCOC(=O)C=CC(Cl)=CCl

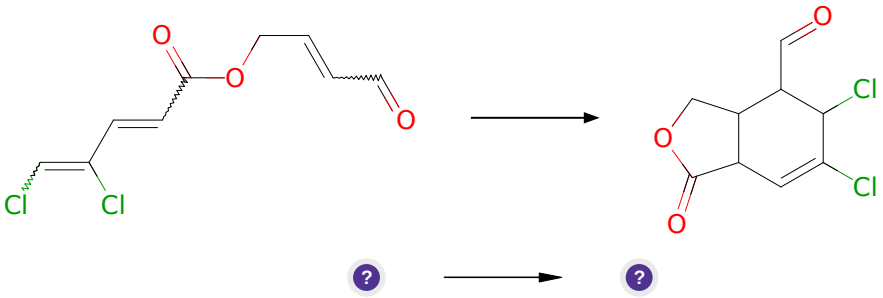
**Typical conditions:** H+

**Protections:** none

**Reference:** *10.1021/cr00020a004*

**Retrosynthesis ID:** 50438

### 2.1.5 Diels-Alder




**Substrates:**

1. O=CC=CCOC(=O)C=CC(Cl)=CCl

**Products:**

1. O=CC1C(Cl)C(Cl)=CC2C(=O)OCC21

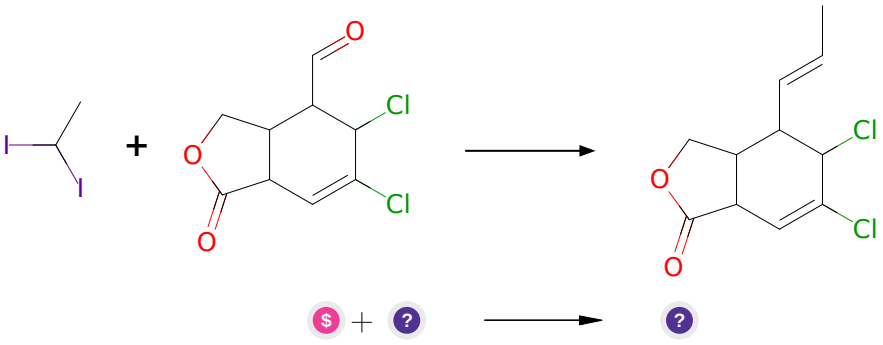
**Typical conditions:** Lewis acid or chiral Lewis acid. Solvent.

**Protections:** none

**Reference:** DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

**Retrosynthesis ID:** 18116

### 2.1.6 Takai olefination



**Substrates:**

1. 1,1-Diiodoethane - *available at Sigma-Aldrich*
2. O=CC1C(Cl)C(Cl)=CC2C(=O)OCC21

**Products:**

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

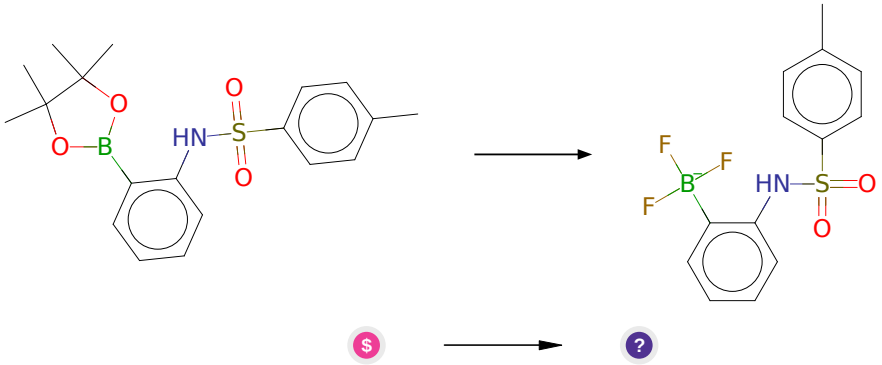
**Typical conditions:** CrCl2.THF.DMF

**Protections:** none

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

**Retrosynthesis ID:** 10942

### 2.1.7 Synthesis of organotrifluoroborate salts in mild conditions




**Substrates:**

1. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

**Products:**

1. Cc1ccc(S(=O)(=O)Nc2ccccc2[B-](F)(F)F)cc1

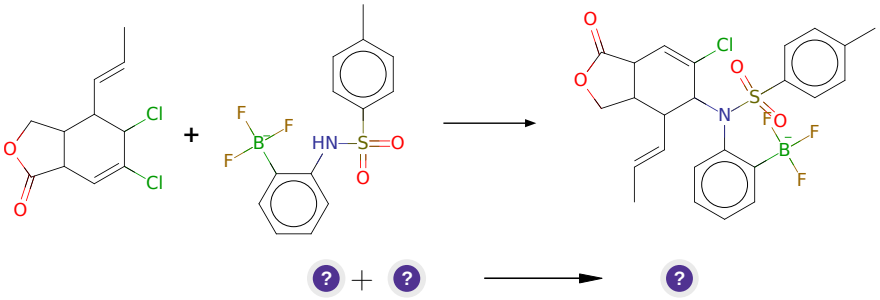
**Typical conditions:** KF.tartaric acid.CH3CN.THF.H2O.rt

**Protections:** none

**Reference:** DOI: *10.1002/anie.201203930*

**Retrosynthesis ID:** 6072

### 2.1.8 Alkylation of sulfonamides with alkyl chlorides



**Substrates:**

1. Cc1ccc(S(=O)(=O)Nc2ccccc2[B-](F)(F)F)cc1
2. C/C=C/C1C(Cl)C(Cl)=CC2C(=O)OCC21

**Products:**

1. C/C=C/C1C2COC(=O)C2C=C(Cl)C1N(c1ccccc1[B-](F)(F)F)S(=O)(=O)c1ccc(C)cc1

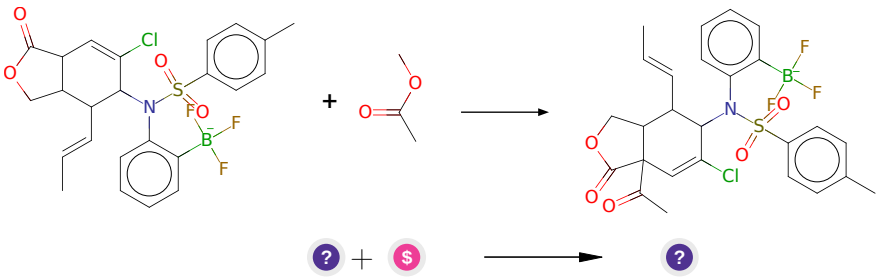
**Typical conditions:** LDA

**Protections:** none

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

**Retrosynthesis ID:** 7727

### 2.1.9 Claisen Condensation



**Substrates:**

1. C/C=C/C1C2COC(=O)C2C=C(Cl)C1N(c1ccccc1[B-](F)(F)F)S(=O)(=O)c1ccc(C)cc1
2. Methyl acetate - *available at Sigma-Aldrich*

**Products:**

1. C/C=C/C1C(N(c2ccccc2[B-](F)(F)F)S(=O)(=O)c2ccc(C)cc2)C(Cl)=CC2(C(C)=O)C(=O)OCC12

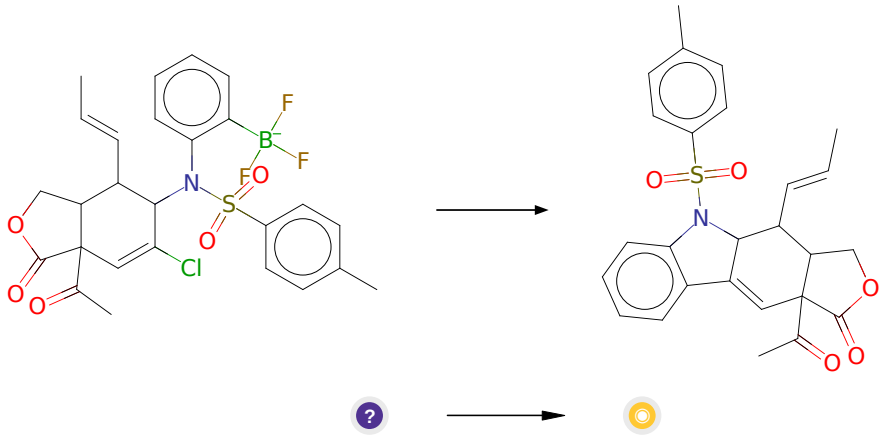
**Typical conditions:** Base.Solvent

**Protections:** none

**Reference:** *10.1021/cr020703u* and *10.1021/cr60088a002*

**Retrosynthesis ID:** 5015

### 2.1.10 Suzuki Coupling of aryltrifluoroborates with alkenyl chlorides



**Substrates:**

1. C/C=C/C1C(N(c2ccccc2[B-](F)(F)F)S(=O)(=O)c2ccc(C)cc2)C(Cl)=CC2(C(C)=O)C(=O)OCC12

**Products:**

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

**Typical conditions:** PdCl2(dppf).K2CO3.toluene.reflux

**Protections:** none

**Reference:** *10.1002/chem.200900425* and *10.1016/j.tetlet.2014.10.078*

**Retrosynthesis ID:** 10034105

## 2.2 Path 2

**Score:** 322.94

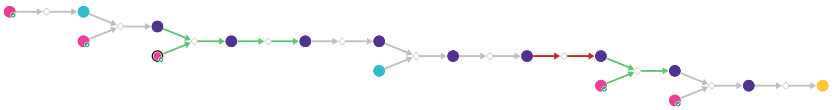
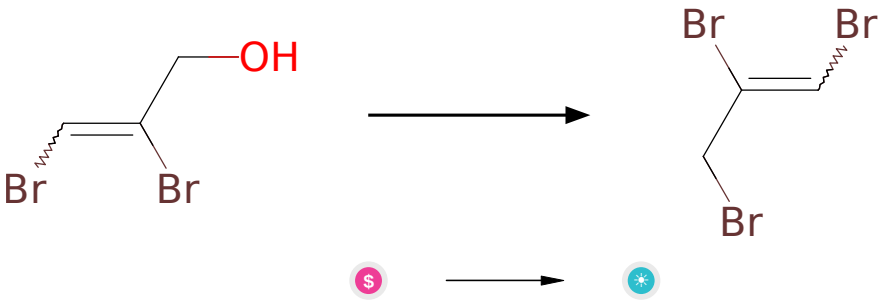


Figure 2: Outline of path 2

### 2.2.1 Appel Reaction




**Substrates:**

1. 2,3-Dibromoallyl alcohol - *available at Sigma-Aldrich*

**Products:**

1. 1,2,3-tribrom-propen

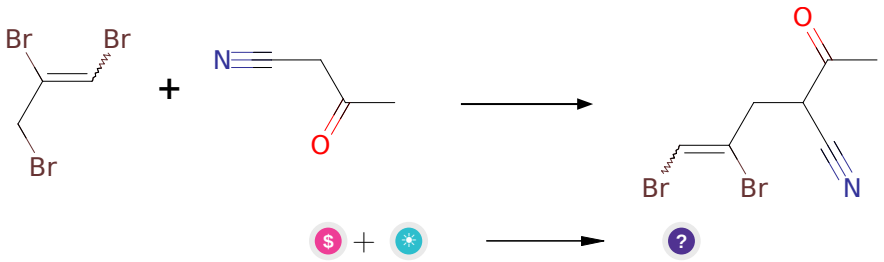
**Typical conditions:** PPh3.CBr4

**Protections:** none

**Reference:** *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

**Retrosynthesis ID:** 9990037

### 2.2.2 Alkylation of 1,3 activated CH acids




**Substrates:**

1. 3-Oxobutanenitrile - *available at Sigma-Aldrich*
2. 1,2,3-tribrom-propen

**Products:**

1. CC(=O)C(C#N)CC(Br)=CBr

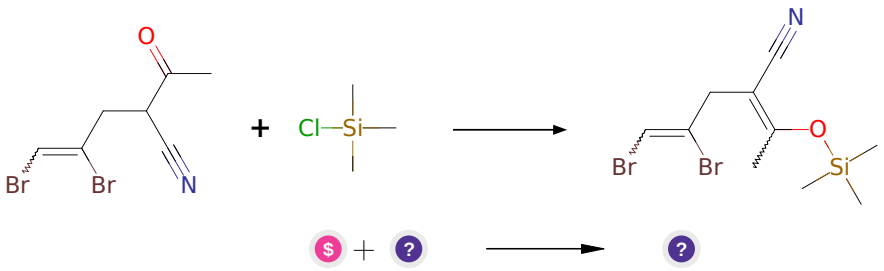
**Typical conditions:** base e.g. NaH.DMF

**Protections:** none

**Reference:** *10.1002/ejic.201403224* and *10.1016/j.bmcl.2005.11.008* and *10.1021/ja058303m* and *10.1021/acs.orglett.9b03078* and *10.1016/S0040-4020(01)80336-7*

**Retrosynthesis ID:** 31017076

### 2.2.3 Enol esters and ethers synthesis




**Substrates:**

1. TMSCl - *available at Sigma-Aldrich*
2. CC(=O)C(C#N)CC(Br)=CBr

**Products:**

1. CC(O[Si](C)(C)C)=C(C#N)CC(Br)=CBr

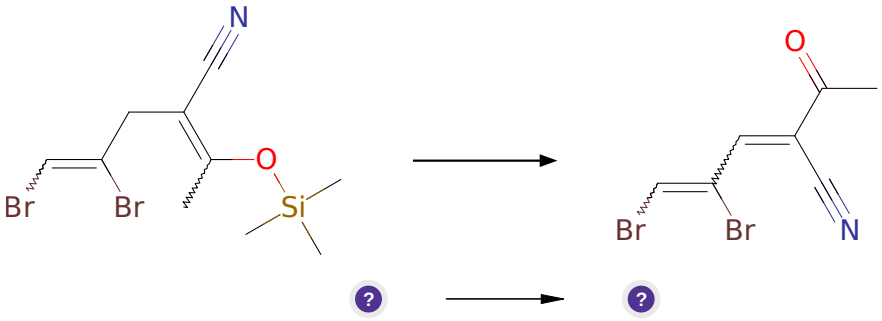
**Typical conditions:** 1. Et3N.Electrophile

**Protections:** none

**Reference:** *10.1016/S0040-4020(03)00977-3* AND *10.1021/ja00056a002*

**Retrosynthesis ID:** 7799

### 2.2.4 Dehydrogenation of silyl enol ethers




**Substrates:**

1. CC(O[Si](C)(C)C)=C(C#N)CC(Br)=CBr

**Products:**

1. CC(=O)C(C#N)=CC(Br)=CBr

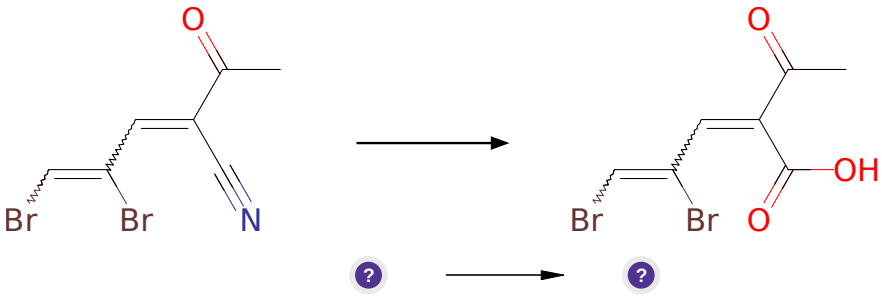
**Typical conditions:** Pd(OAc)2.Cu(OAc)2.O2.MeCN

**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

### 2.2.5 Acid hydrolysis of nitriles to carboxylic acids




**Substrates:**

1. CC(=O)C(C#N)=CC(Br)=CBr

**Products:**

1. CC(=O)C(=CC(Br)=CBr)C(=O)O

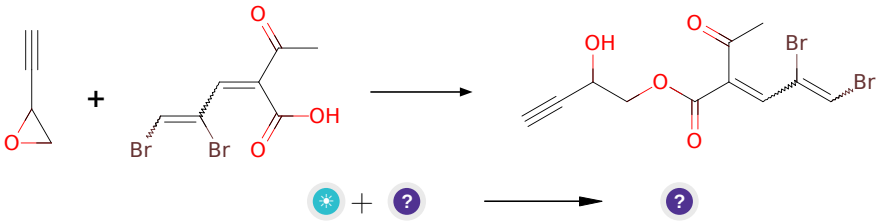
**Typical conditions:** Hcl.heating.H2O

**Protections:** none

**Reference:** *10.1021/jm301796k* and *10.1016/j.bmcl.2007.06.054* and *10.1021/jm801532e*

**Retrosynthesis ID:** 16027

### 2.2.6 Opening of epoxides with carboxylic acids




**Substrates:**

1. ethynyl-oxirane
2. CC(=O)C(=CC(Br)=CBr)C(=O)O

**Products:**

1. C#CC(O)COC(=O)C(=CC(Br)=CBr)C(C)=O

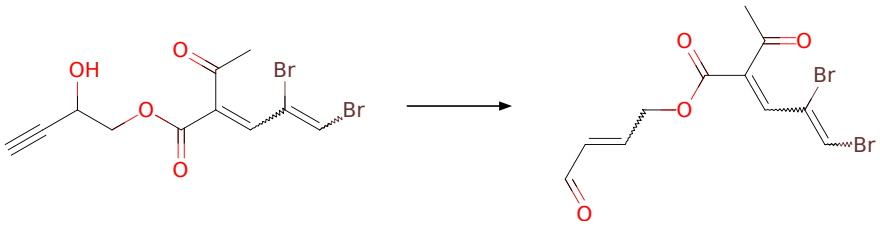
**Typical conditions:** RCOOH.catalyst

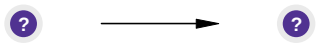
**Protections:** none

**Reference:** *10.1021/ol051051+* AND *10.1016/j.tet.2005.05.050* and US2011/86912 A1 (P.13) and *10.1055/s-2003-42416* and *10.5012/bkcs.2013.34.8.2286*

**Retrosynthesis ID:** 15151

### 2.2.7 Meyer-Schuster Rearrangement





**Substrates:**

1. C#CC(O)COC(=O)C(=CC(Br)=CBr)C(C)=O

**Products:**

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC=CC=O

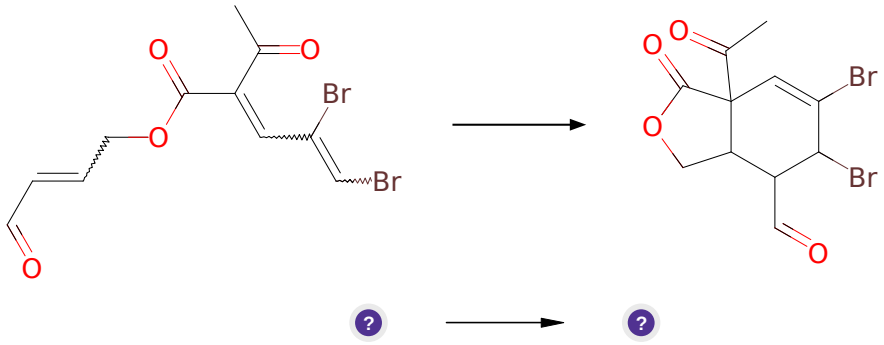
**Typical conditions:** H+

**Protections:** none

**Reference:** *10.1021/cr60273a001*

**Retrosynthesis ID:** 10143

### 2.2.8 Diels-Alder




**Substrates:**

1. CC(=O)C(=CC(Br)=CBr)C(=O)OCC=CC=O

**Products:**

1. CC(=O)C12C=C(Br)C(Br)C(C=O)C1COC2=O

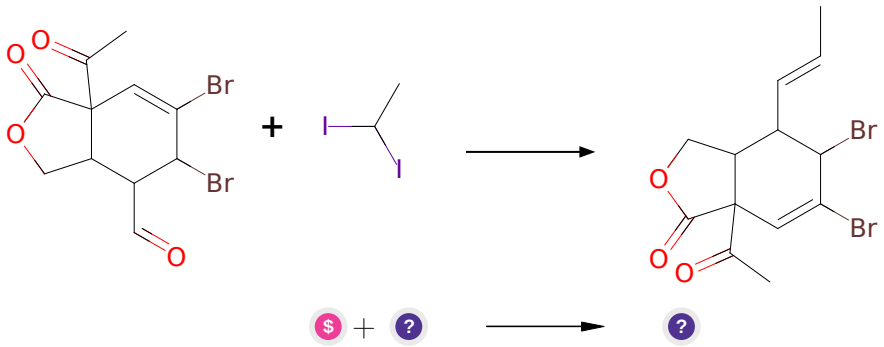
**Typical conditions:** Lewis acid or chiral Lewis acid. Solvent.

**Protections:** none

**Reference:** DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

**Retrosynthesis ID:** 18116

### 2.2.9 Takai olefination



**Substrates:**

1. 1,1-Diiodoethane - *available at Sigma-Aldrich*
2. CC(=O)C12C=C(Br)C(Br)C(C=O)C1COC2=O

**Products:**

1. C/C=C/C1C(Br)C(Br)=CC2(C(C)=O)C(=O)OCC12

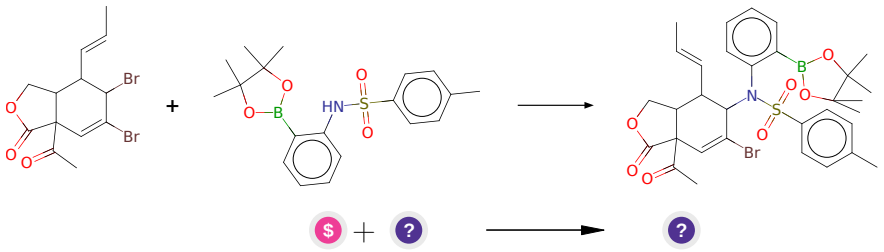
**Typical conditions:** CrCl2.THF.DMF

**Protections:** none

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

**Retrosynthesis ID:** 10942

### 2.2.10 Alkylation of amines with alkyl bromides



**Substrates:**

1. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*
2. C/C=C/C1C(Br)C(Br)=CC2(C(C)=O)C(=O)OCC12

**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

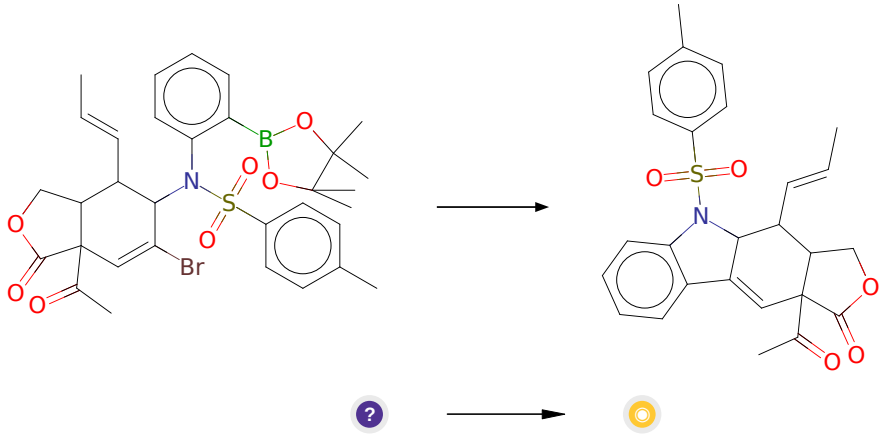
**Typical conditions:** K2CO3 or other base

**Protections:** none

**Reference:** *10.1016/j.tetlet.2007.09.110*

**Retrosynthesis ID:** 7668

### 2.2.11 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

**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