# Paths of analysis*

Y3

Synthia

October 10, 2022

## 1 Analysis parameters

**Analysis type:** Automatic Retrosynthesis

**Rules:** none selected

**Filters:** Exclude Diastereoselecitve 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:** 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

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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:** 2250125.08

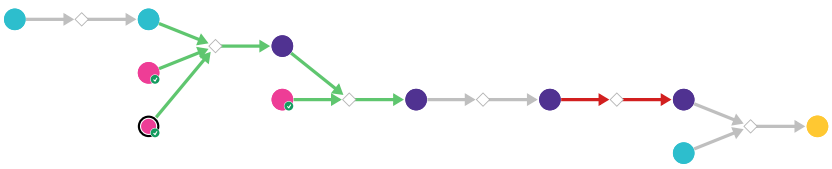
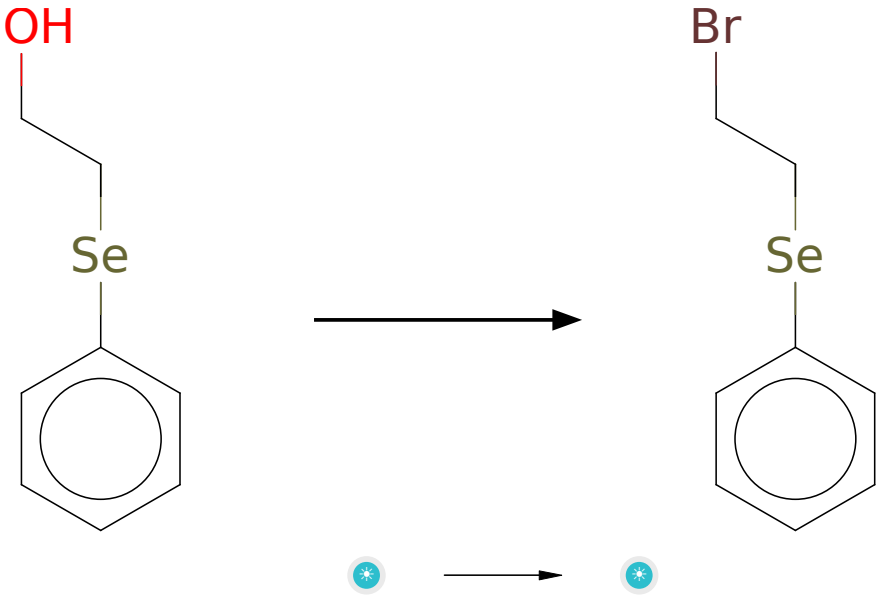


Figure 1: Outline of path 1

### 2.1.1 Appel Reaction



**Substrates:**

1. 2-phenylselanyl-ethanol

**Products:**

1. 2-bromaethylphenylselenid

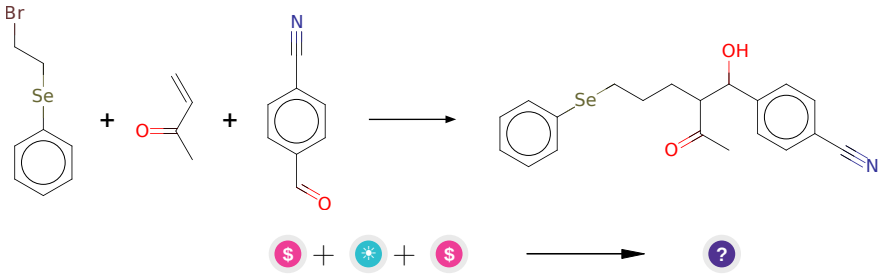
**Typical conditions:** PPh3.CBr4

**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

### 2.1.2 Conjugated addition of cuprate-aldol sequence




**Substrates:**

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*
2. 2-bromaethylphenylselenid
3. 3-Buten-2-one - *available at Sigma-Aldrich*

**Products:**

1. CC(=O)C(CCC[Se]c1ccccc1)C(O)c1ccc(C#N)cc1

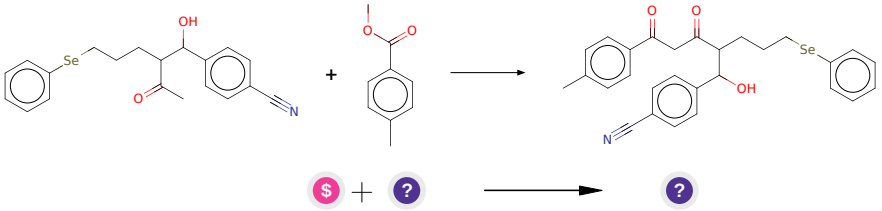
**Typical conditions:** 1.RCuLi.2.RCHO

**Protections:** none

**Reference:** *10.1021/jo9905672* AND *10.1021/ja0320018* AND *10.1021/ja015900+* AND *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1* AND *10.1271/bbb.69.391* AND *10.1039/b612593j*

**Retrosynthesis ID:** 20515

### 2.1.3 Condensation of methyl ketones with esters



**Substrates:**

1. Methyl p-toluate - *available at Sigma-Aldrich*
2. CC(=O)C(CCC[Se]c1ccccc1)C(O)c1ccc(C#N)cc1

**Products:**

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2ccc(C#N)cc2)cc1

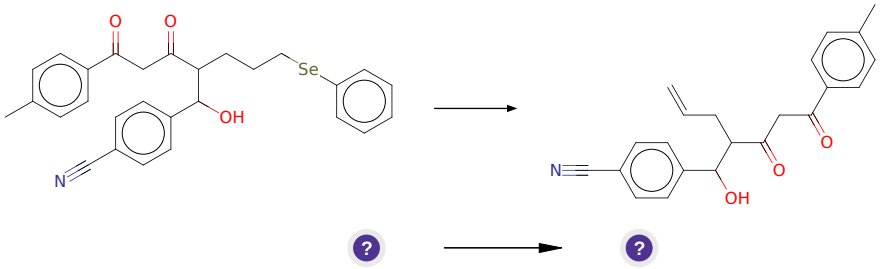
**Typical conditions:** NaOMe.MeOH

**Protections:** none

**Reference:** *10.1016/j.tetlet.2007.10.010* and *10.1016/j.tetlet.2013.09.025* and *10.1016/j.ejmech.2013.10.072* and *10.1002/ange.19921040631*

**Retrosynthesis ID:** 4792

### 2.1.4 Selenoxide Elimination



**Substrates:**

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2ccc(C#N)cc2)cc1

**Products:**

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

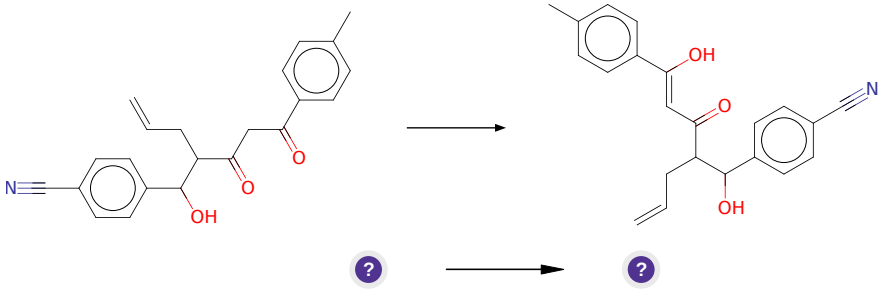
**Typical conditions:** 1) O3 or H2O2 or NaIO4. low temperature. 2) pyridine or Et3N

**Protections:** none

**Reference:** DOI: *10.1021/ja00852a019* or DOI: *10.1021/ja00258a056* or DOI: *10.1039/B716256A* or DOI: *10.1055/s-1998-1970* or DOI: *10.1016/S0040-4039(00)76646-9*

**Retrosynthesis ID:** 8381

### 2.1.5 Keto-enol Tautomerism




**Substrates:**

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

**Products:**

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

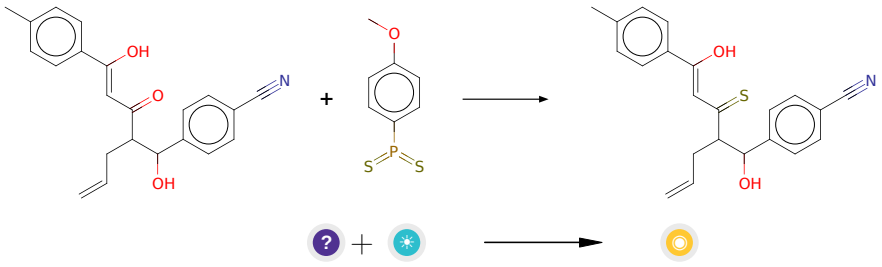
**Typical conditions:** solvent

**Protections:** none

**Reference:** *10.1021/ja01065a003* AND *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#N)cc1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

**Products:**

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

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

**Protections:** none

**Reference:** DOI: *10.1021/ol990629a*

**Retrosynthesis ID:** 10798

## 2.2 Path 2

**Score:** 2250164.14

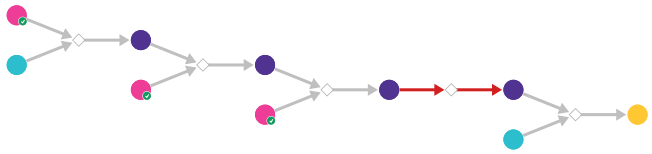
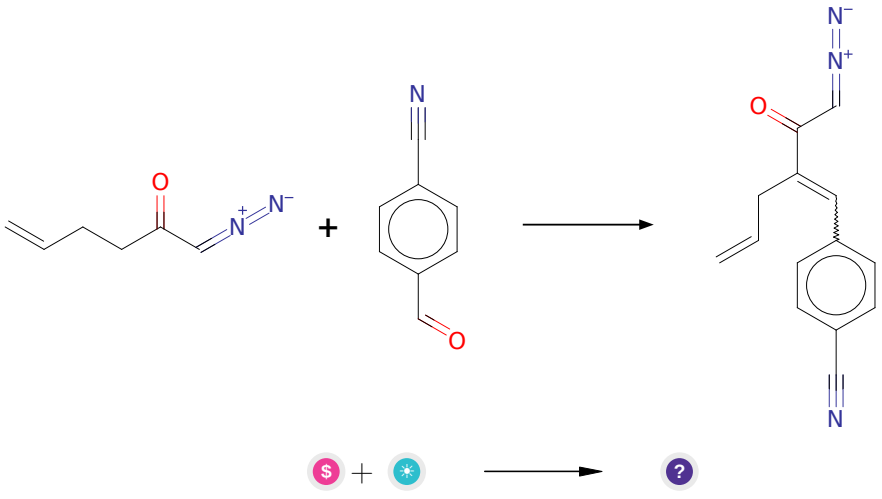


Figure 2: Outline of path 2

### 2.2.1 Aldol Condensation




**Substrates:**

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*
2. 1-diazo-hex-5-en-2-one

**Products:**

1. C=CCC(=Cc1ccc(C#N)cc1)C(=O)C=[N+]=[N-]

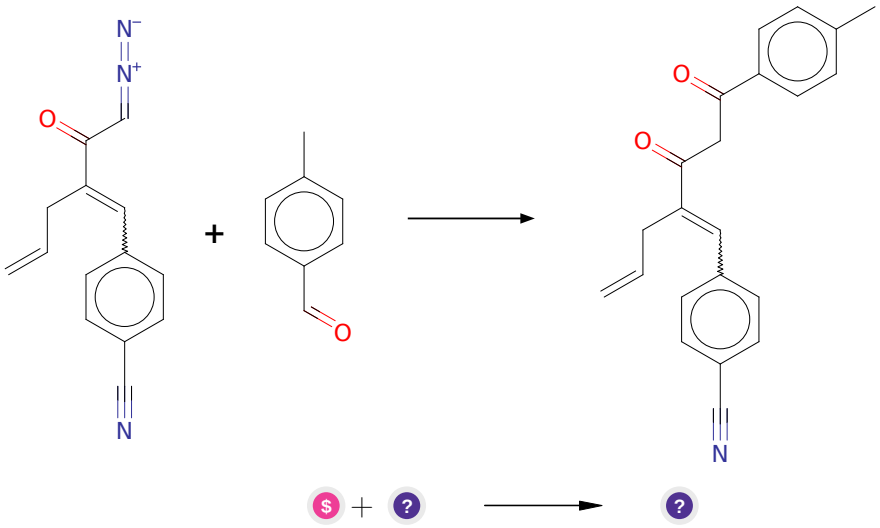
**Typical conditions:** NaOEt.base

**Protections:** none

**Reference:** *10.1080/00397911.2016.1206938*

**Retrosynthesis ID:** 10049

### 2.2.2 Homologation of aldehydes to ketones with diazoalkanes




**Substrates:**

1. p-Tolualdehyde - *available at Sigma-Aldrich*
2. C=CCC(=Cc1ccc(C#N)cc1)C(=O)C=[N+]=[N-]

**Products:**

1. C=CCC(=Cc1ccc(C#N)cc1)C(=O)CC(=O)c1ccc(C)cc1

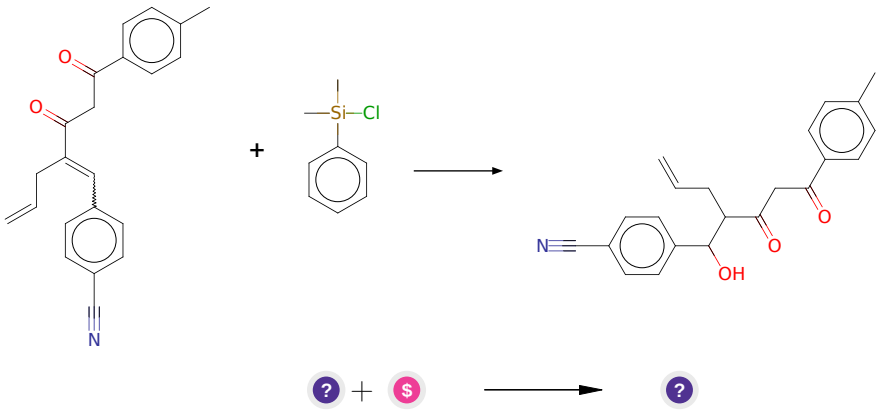
**Typical conditions:** Lewis.acid

**Protections:** none

**Reference:** *10.1021/jo00275a006* AND *10.1016/j.tet.2014.05.107* AND *10.1016/j.tet.2014.11.059* AND *10.1021/ol9010932*

**Retrosynthesis ID:** 15017

### 2.2.3 Addition of silanes to Michael acceptors followed by oxidation




**Substrates:**

1. C=CCC(=Cc1ccc(C#N)cc1)C(=O)CC(=O)c1ccc(C)cc1
2. DMPSCl - *available at Sigma-Aldrich*

**Products:**

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

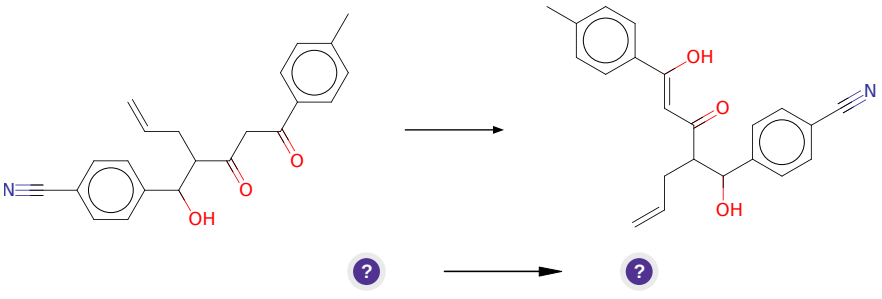
**Typical conditions:** 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

**Protections:** none

**Reference:** *10.1021/ja058370g* AND (Oxidation) *10.1021/jo9905672* or *10.1021/ol300832f*

**Retrosynthesis ID:** 20301

### 2.2.4 Keto-enol Tautomerism




**Substrates:**

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

**Products:**

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

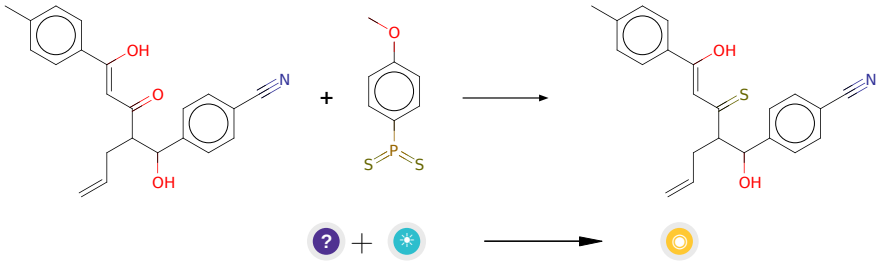
**Typical conditions:** solvent

**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#N)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

**Products:**

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

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

**Protections:** none

**Reference:** DOI: *10.1021/ol990629a*

**Retrosynthesis ID:** 10798

## 2.3 Path 3

**Score:** `2250164.14`

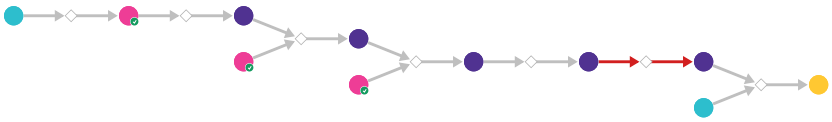
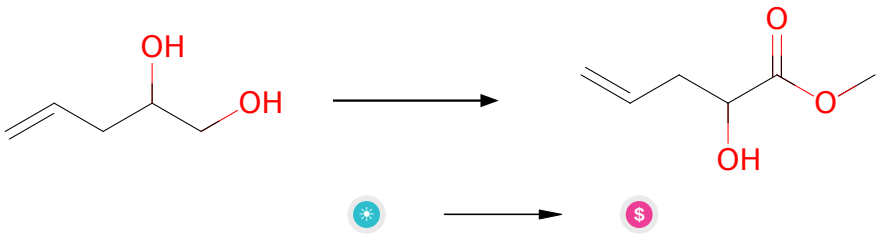


Figure 3: Outline of path 3

### 2.3.1 Tandem oxidation-esterification




**Substrates:**

1. 4-penten-1,2-diol

**Products:**

1. methyl 2-hydroxypent-4-enoate - *available at Sigma-Aldrich*

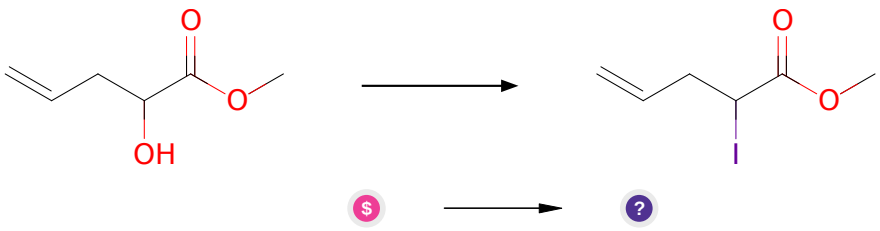
**Typical conditions:** Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

**Protections:** none

**Reference:** *10.1016/S0040-4039(00)73550-7* and *10.1016/j.tet.2005.03.097* and *10.1021/ol062940f*

**Retrosynthesis ID:** 25234

### 2.3.2 Synthesis Of Alkyl Iodides Via Appel Reaction




**Substrates:**

1. methyl 2-hydroxypent-4-enoate - *available at Sigma-Aldrich*

**Products:**

1. C=CCC(I)C(=O)OC

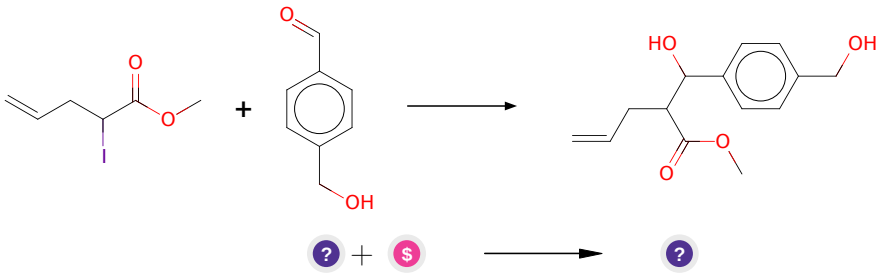
**Typical conditions:** Imidazole.PPh3.I2

**Protections:** none

**Reference:** *10.1002/anie.201311323* (SI) AND *10.1080/00397919008052864* and *10.1016/j.steroids.2015.02.018*

**Retrosynthesis ID:** 9990043

### 2.3.3 Reformatsky Reaction




**Substrates:**

1. C=CCC(I)C(=O)OC
2. 4-(Hydroxymethyl)benzaldehyde - *available at Sigma-Aldrich*

**Products:**

1. C=CCC(C(=O)OC)C(O)c1ccc(CO)cc1

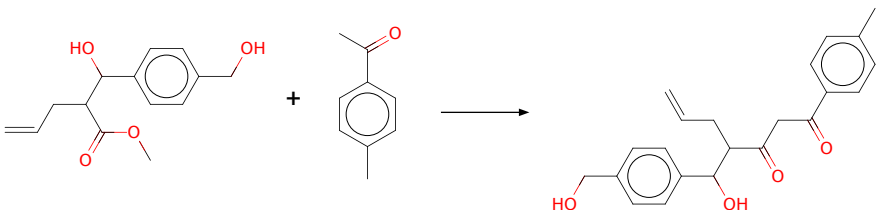
**Typical conditions:** Zn.THF

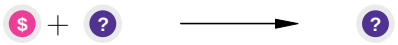
**Protections:** none

**Reference:** *10.1016/j.bmc.2016.07.052* p. 4521, 4520 and *10.1016/j.ejmech.2013.07.047* p. 214, 218

**Retrosynthesis ID:** 11539

### 2.3.4 Condensation of methyl ketones with esters





**Substrates:**

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC(C(=O)OC)C(O)c1ccc(CO)cc1

**Products:**

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

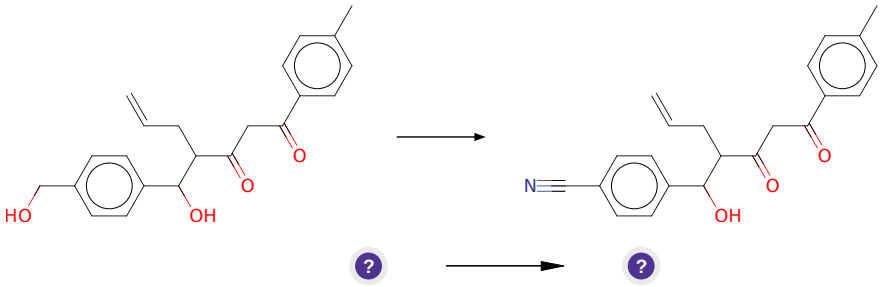
**Typical conditions:** NaOMe.MeOH

**Protections:** none

**Reference:** *10.1016/j.tetlet.2007.10.010* and *10.1016/j.tetlet.2013.09.025* and *10.1016/j.ejmech.2013.10.072* and *10.1002/ange.19921040631*

**Retrosynthesis ID:** 4792

### 2.3.5 Conversion of Alcohols into Nitriles




**Substrates:**

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

**Products:**

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

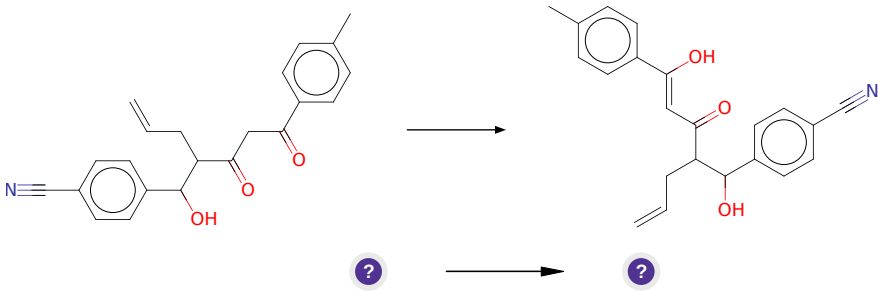
**Typical conditions:** I2.RT

**Protections:** none

**Reference:** DOI:*10.1021/jo0625352*

**Retrosynthesis ID:** 10973

### 2.3.6 Keto-enol Tautomerism




**Substrates:**

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

**Products:**

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

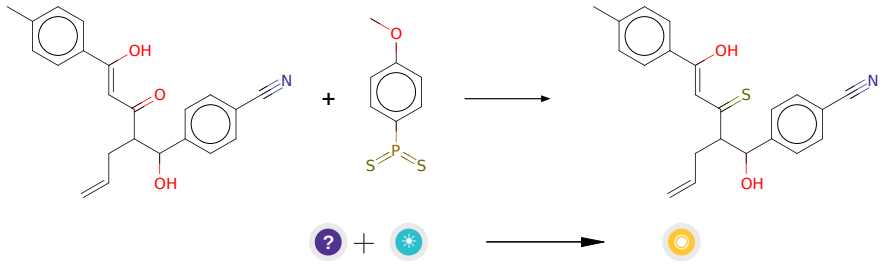
**Typical conditions:** solvent

**Protections:** none

**Reference:** *10.1021/ja01065a003* AND *10.1021/jo8012385*

**Retrosynthesis ID:** 7781

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




**Substrates:**

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

**Products:**

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

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

**Protections:** none

**Reference:** DOI: *10.1021/ol990629a*

**Retrosynthesis ID:** 10798

## 2.4 Path 4

**Score:** 2250164.14

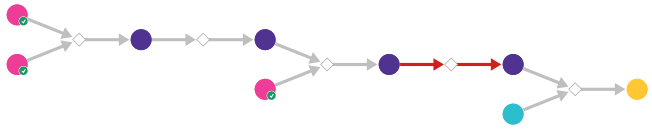
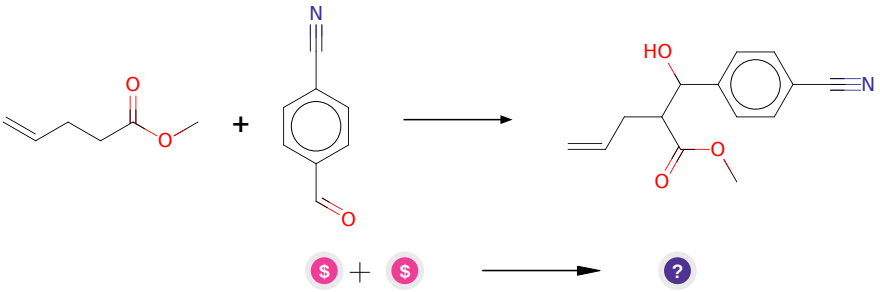


Figure 4: Outline of path 4

### 2.4.1 Condensation of esters with aldehydes




**Substrates:**

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*
2. Methyl 4-pentenoate - *available at Sigma-Aldrich*

**Products:**

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

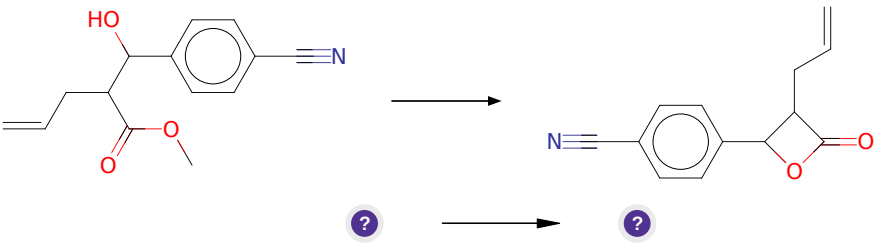
**Typical conditions:** LDA.THF

**Protections:** none

**Reference:** *10.1016/j.bmcl.2005.02.066* and *10.3762/bjoc.9.175* and *10.1021/ol1016178*

**Retrosynthesis ID:** 4788

### 2.4.2 Acid catalyzed transesterification




**Substrates:**

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

**Products:**

1. C=CCC1C(=O)OC1c1ccc(C#N)cc1

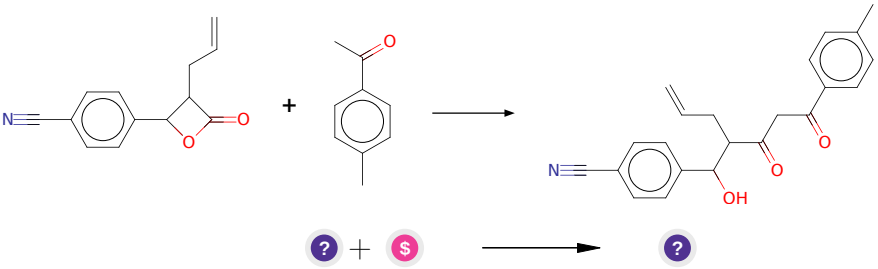
**Typical conditions:** H+

**Protections:** none

**Reference:** *10.1021/cr00020a004*

**Retrosynthesis ID:** 50438

### 2.4.3 Ring opening of lactones with enolates




**Substrates:**

1. C=CCC1C(=O)OC1c1ccc(C#N)cc1
2. Methyl p-tolyl ketone - *available at Sigma-Aldrich*

**Products:**

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

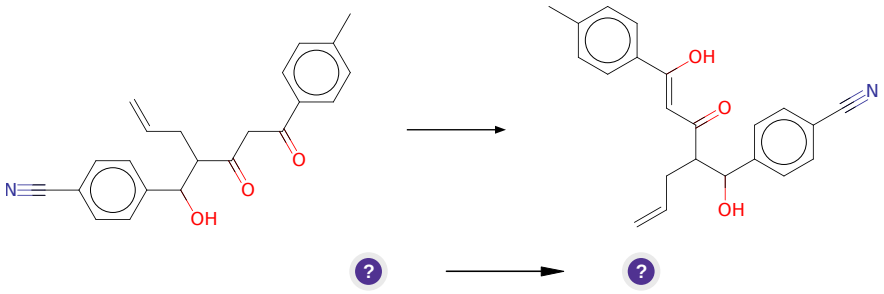
**Typical conditions:** LiHMDS.THF

**Protections:** none

**Reference:** *10.1021/ol801493w* and *10.1021/ol403423r* and *10.1021/ja061938g* and *10.1021/ja036521e*

**Retrosynthesis ID:** 24105

### 2.4.4 Keto-enol Tautomerism




**Substrates:**

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

**Products:**

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

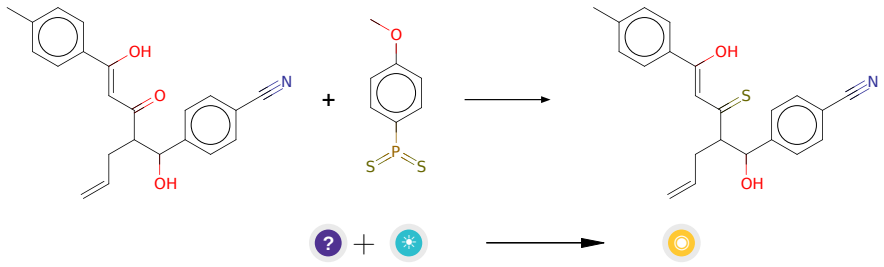
**Typical conditions:** solvent

**Protections:** none

**Reference:** *10.1021/ja01065a003* AND *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#N)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

**Products:**

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

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

**Protections:** none

**Reference:** DOI: *10.1021/ol990629a*

**Retrosynthesis ID:** 10798

## 2.5 Path 5

**Score:** 2250164.14

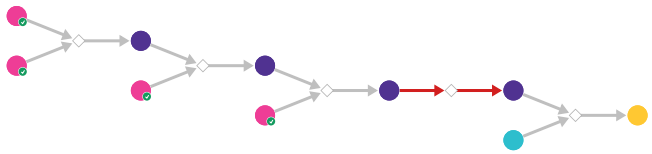
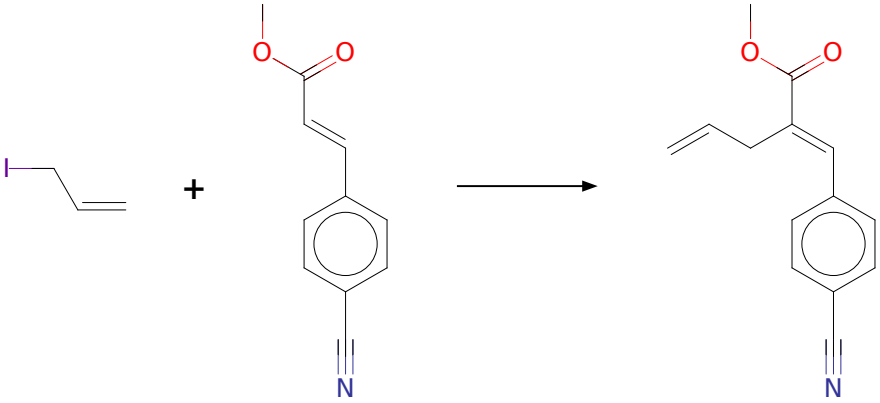
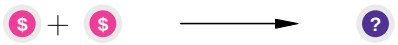


Figure 5: Outline of path 5

### 2.5.1 Alkylation of vinyl esters





**Substrates:**

1. Methyl 3-(4-cyanophenyl)acrylate - *available at Sigma-Aldrich*
2. Allyl iodide - *available at Sigma-Aldrich*

**Products:**

1. C=CC/C(=C\c1ccc(C#N)cc1)C(=O)OC

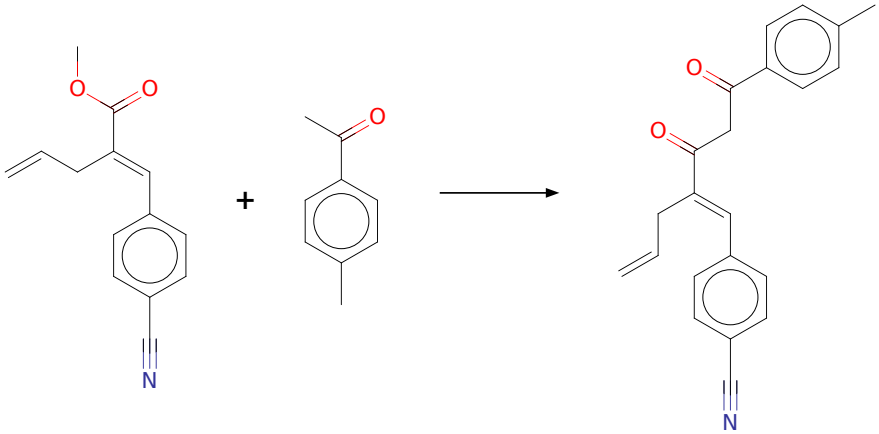
**Typical conditions:** LDA.THF

**Protections:** none

**Reference:** DOI: *10.1039/C39870001410*

**Retrosynthesis ID:** 886

### 2.5.2 Condensation of methyl ketones with esters




**Substrates:**

1. C=CC/C(=C\c1ccc(C#N)cc1)C(=O)OC
2. Methyl p-tolyl ketone - *available at Sigma-Aldrich*

**Products:**

1. C=CC/C(=C\c1ccc(C#N)cc1)C(=O)CC(=O)c1ccc(C)cc1

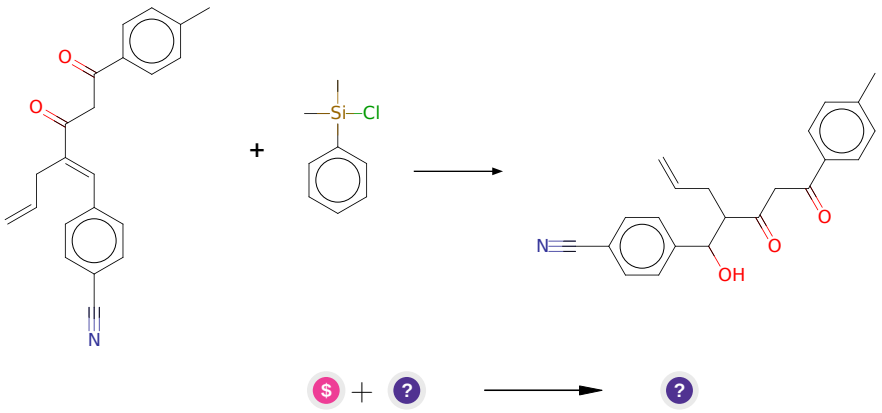
**Typical conditions:** NaOMe.MeOH

**Protections:** none

**Reference:** *10.1016/j.tetlet.2007.10.010* and *10.1016/j.tetlet.2013.09.025* and *10.1016/j.ejmech.2013.10.072* and *10.1002/ange.19921040631*

**Retrosynthesis ID:** 4792

### 2.5.3 Addition of silanes to Michael acceptors followed by oxidation




**Substrates:**

1. DMPSCl - *available at Sigma-Aldrich*
2. C=CC/C(=C\c1ccc(C#N)cc1)C(=O)CC(=O)c1ccc(C)cc1

**Products:**

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

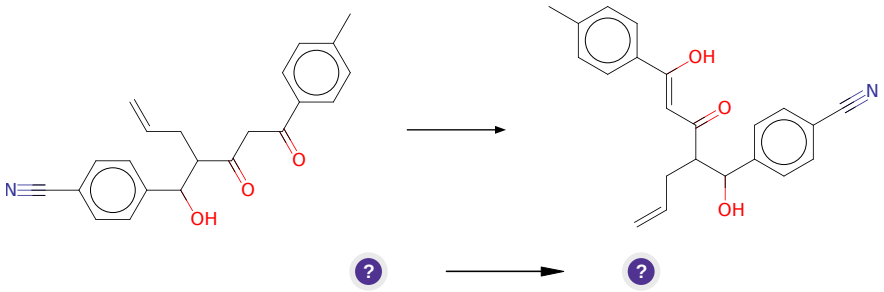
**Typical conditions:** 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

**Protections:** none

**Reference:** *10.1021/ja058370g* AND (Oxidation) *10.1021/jo9905672* or *10.1021/ol300832f*

**Retrosynthesis ID:** 20295

### 2.5.4 Keto-enol Tautomerism




**Substrates:**

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

**Products:**

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

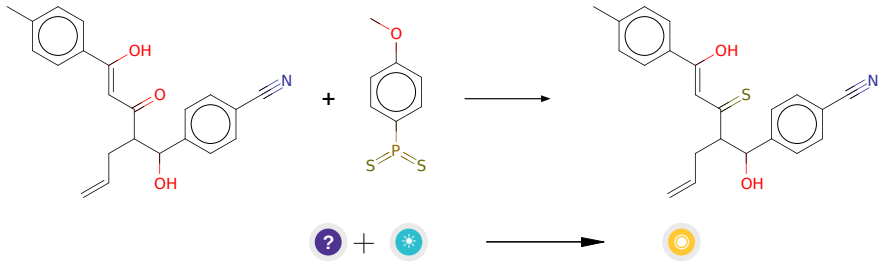
**Typical conditions:** solvent

**Protections:** none

**Reference:** *10.1021/ja01065a003* AND *10.1021/jo8012385*

**Retrosynthesis ID:** 7781

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




**Substrates:**

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

**Products:**

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

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

**Protections:** none

**Reference:** DOI: *10.1021/ol990629a*

**Retrosynthesis ID:** 10798