

Paths of analysis*

Y4

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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 100000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

Min. search width: 400

Max. reactions per product: 60

*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: 2250125.08

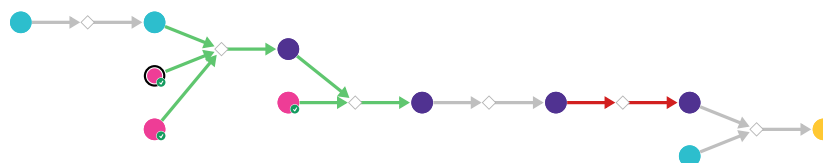
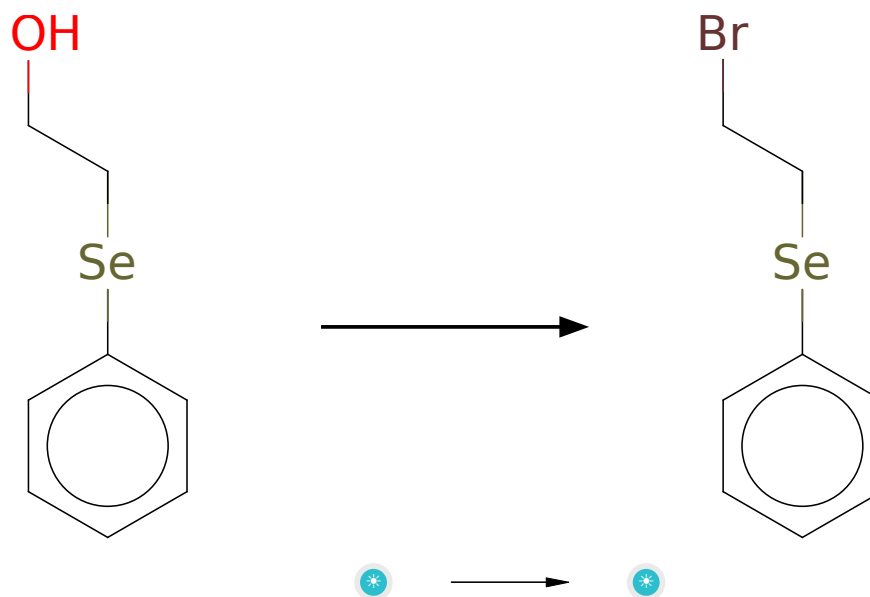


Figure 1: Outline of path 1

2.1.1 Appel Reaction

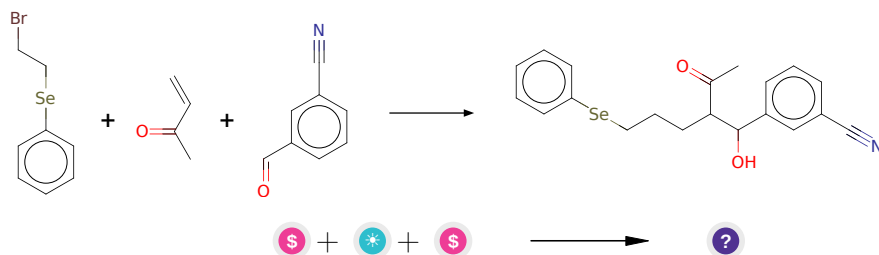


Substrates:

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](#) (experimental)**Retrosynthesis ID:** 9990037**2.1.2 Conjugated addition of cuprate-aldol sequence****Substrates:**

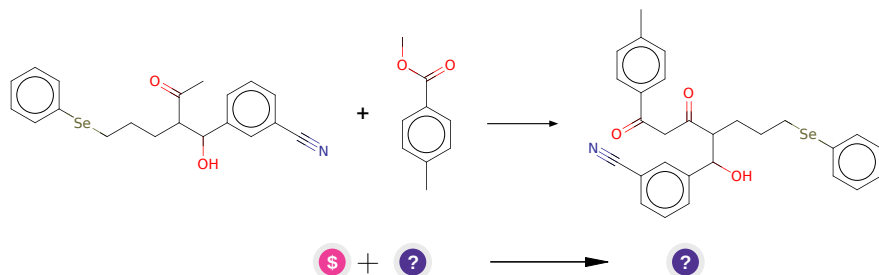
1. 3-Buten-2-one - [available at Sigma-Aldrich](#)
2. 2-bromaethylphenylselenid
3. 3-Cyanobenzaldehyde - [available at Sigma-Aldrich](#)

Products:

1. CC(=O)C(CCC[Se]c1ccccc1)C(O)c1ccc(C#N)c1

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)c1

Products:

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2ccc(C#N)c2)cc1

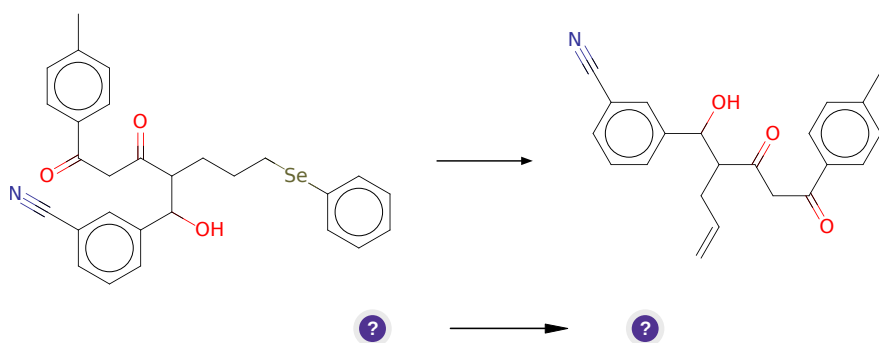
Typical conditions: NaOMe.MeOH

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)c2)cc1

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

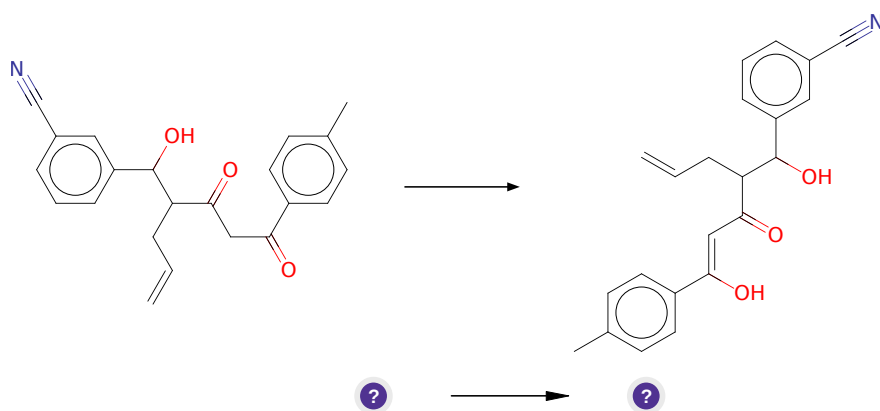
Typical conditions: 1) O₃ or H₂O₂ or NaIO₄. low temperature. 2) pyridine or Et₃N

Protections: none

Reference: DOI: [10.1021/ja00852a019](https://doi.org/10.1021/ja00852a019) or DOI: [10.1021/ja00258a056](https://doi.org/10.1021/ja00258a056) or DOI: [10.1039/B716256A](https://doi.org/10.1039/B716256A) or DOI: [10.1055/s-1998-1970](https://doi.org/10.1055/s-1998-1970) or DOI: [10.1016/S0040-4039\(00\)76646-9](https://doi.org/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)c1cccc(C#N)c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

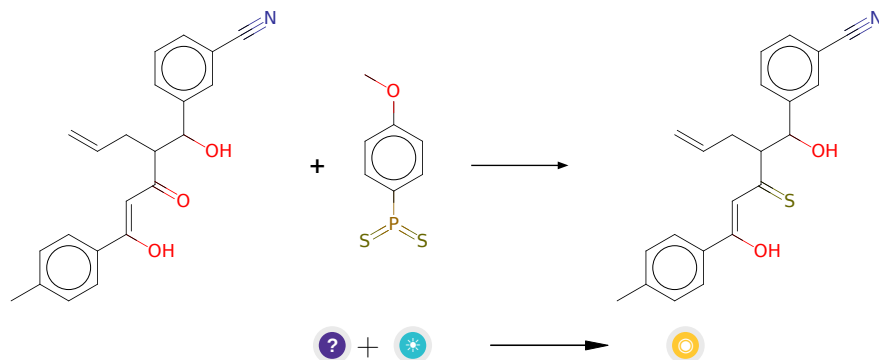
Typical conditions: solvent

Protections: none

Reference: [10.1021/ja01065a003](https://doi.org/10.1021/ja01065a003) AND [10.1021/jo8012385](https://doi.org/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)c1cccc(C#N)c1
2. 4-methoxyphenyl-dithiophosphonaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

Retrosynthesis ID: 10798

2.2 Path 2

Score: 2250164.14

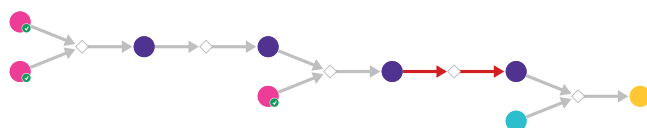
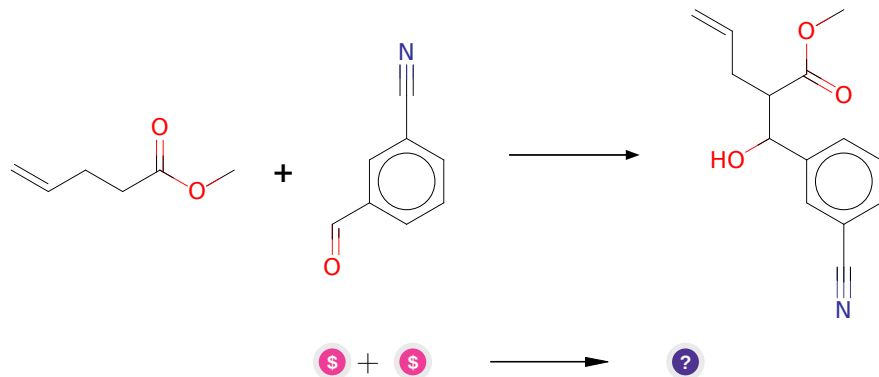


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes



Substrates:

1. Methyl 4-pentenoate - *available at Sigma-Aldrich*
2. 3-Cyanobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)OC)C(O)c1cccc(C#N)c1

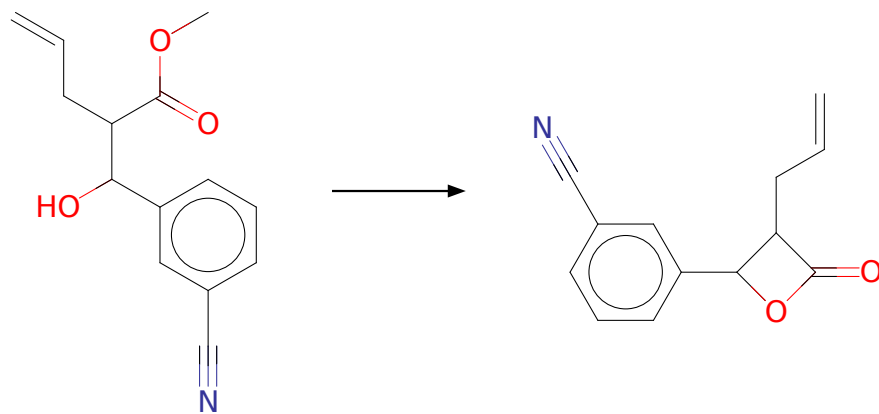
Typical conditions: LDA.THF

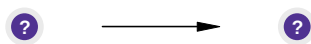
Protections: none

Reference: [10.1016/j.bmcl.2005.02.066](#) and [10.3762/bjoc.9.175](#) and [10.1021/ol1016178](#)

Retrosynthesis ID: 4788

2.2.2 Acid catalyzed transesterification





Substrates:

1. C=CCC(C(=O)OC)C(O)c1cccc(C#N)c1

Products:

1. C=CCC1C(=O)OC1c1cccc(C#N)c1

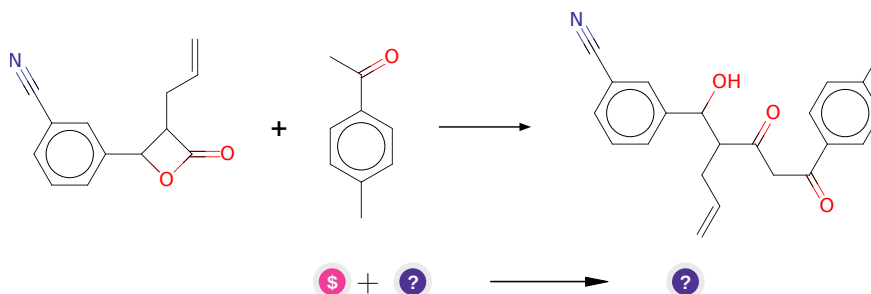
Typical conditions: H+

Protections: none

Reference: [10.1021/cr00020a004](#)

Retrosynthesis ID: 50438

2.2.3 Ring opening of lactones with enolates



Substrates:

1. Methyl p-tolyl ketone - [available at Sigma-Aldrich](#)
2. C=CCC1C(=O)OC1c1cccc(C#N)c1

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

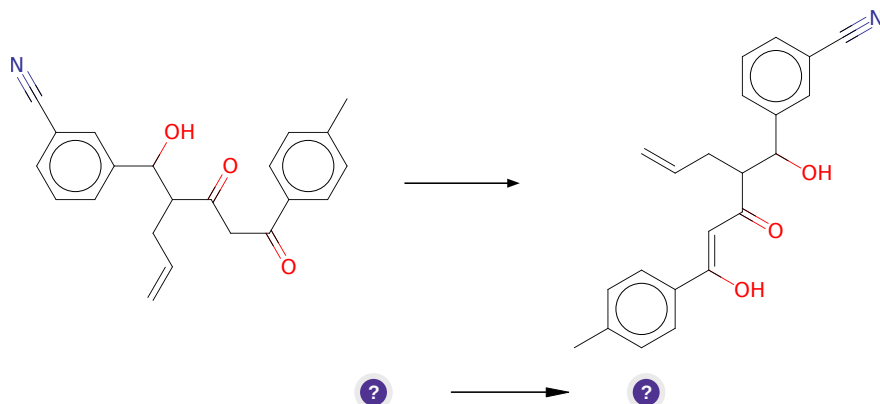
Typical conditions: LiHMDS.THF

Protections: none

Reference: [10.1021/ol801493w](#) and [10.1021/ol403423r](#) and [10.1021/ja061938g](#) and [10.1021/ja036521e](#)

Retrosynthesis ID: 24105

2.2.4 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

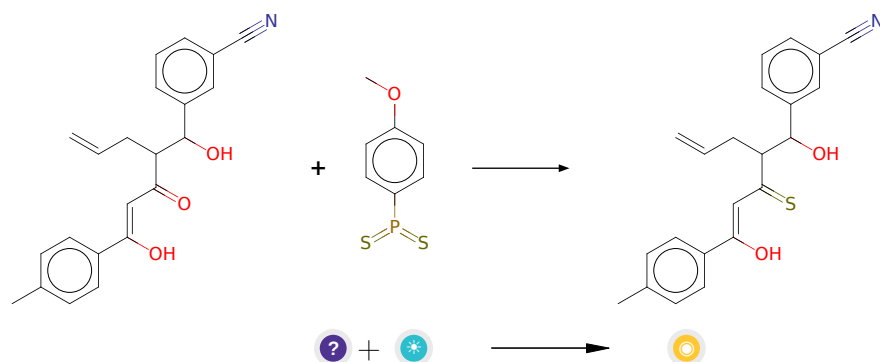
Typical conditions: solvent

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)c1cccc(C#N)c1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

Retrosynthesis ID: 10798

2.3 Path 3

Score: 2250164.14

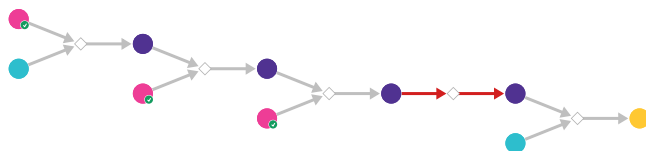
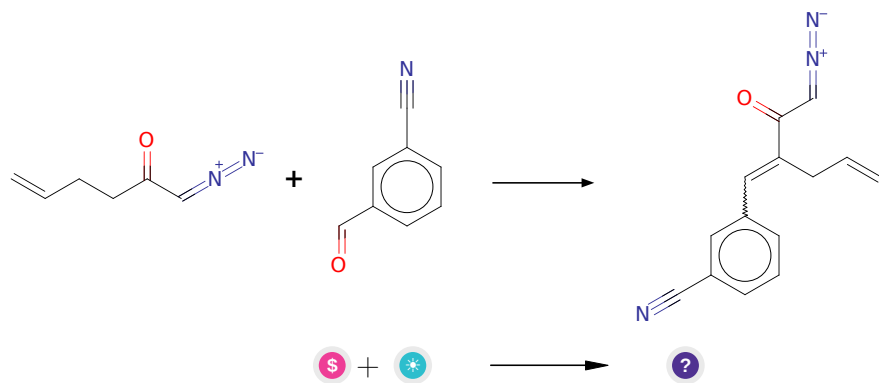


Figure 3: Outline of path 3

2.3.1 Aldol Condensation



Substrates:

1. 3-Cyanobenzaldehyde - *available at Sigma-Aldrich*
2. 1-diazo-hex-5-en-2-one

Products:

1. C=CCC(=Cc1cccc(C#N)c1)C(=O)C=[N+]=[N-]

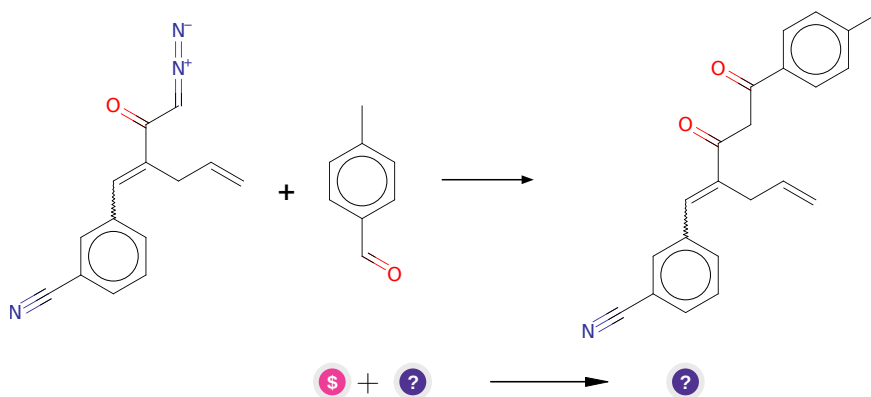
Typical conditions: NaOEt.base

Protections: none

Reference: [10.1080/00397911.2016.1206938](#)

Retrosynthesis ID: 10049

2.3.2 Homologation of aldehydes to ketones with diazoalkanes



Substrates:

1. p-Tolualdehyde - [available at Sigma-Aldrich](#)
2. C=CCC(=Cc1cccc(C#N)c1)C(=O)C=[N+]=[N-]

Products:

1. C=CCC(=Cc1cccc(C#N)c1)C(=O)CC(=O)c1ccc(C)cc1

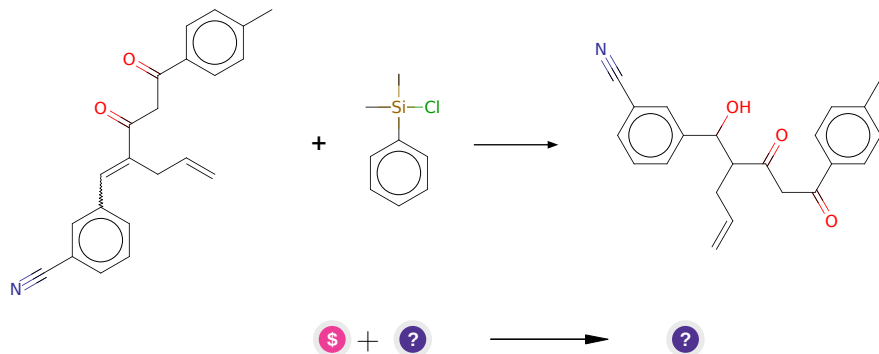
Typical conditions: Lewis.acid

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

2.3.3 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

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

Products:

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

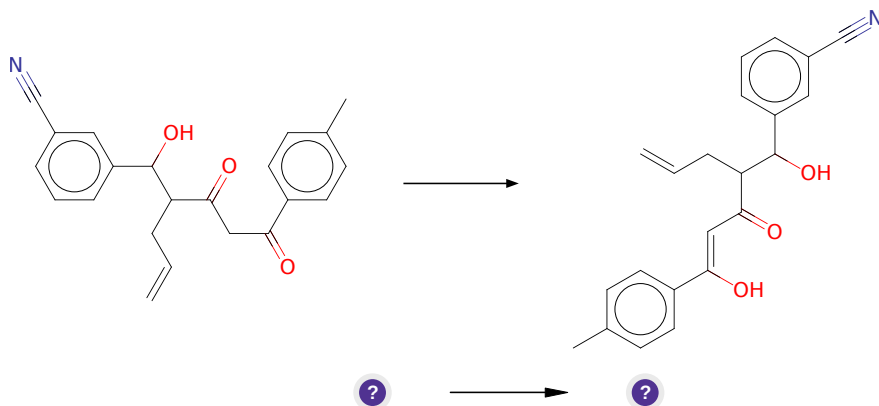
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H₂O₂

Protections: none

Reference: [10.1021/ja058370g](#) AND (Oxidation) [10.1021/jo9905672](#) or [10.1021/ol300832f](#)

Retrosynthesis ID: 20301

2.3.4 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

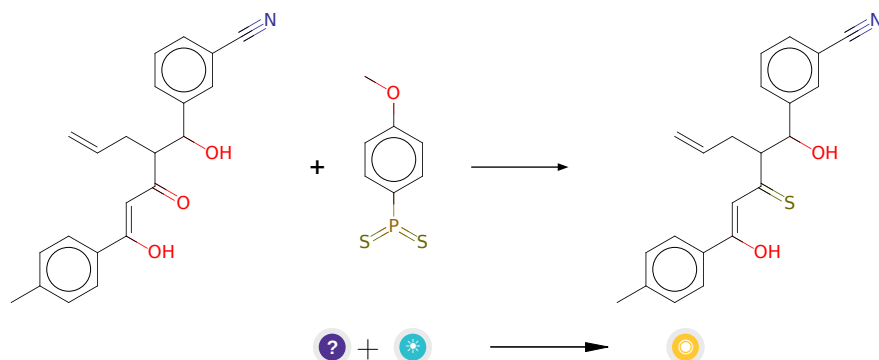
Typical conditions: solvent

Protections: none

Reference: [10.1021/ja01065a003](https://doi.org/10.1021/ja01065a003) AND [10.1021/jo8012385](https://doi.org/10.1021/jo8012385)

Retrosynthesis ID: 7781

2.3.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

Retrosynthesis ID: 10798

2.4 Path 4

Score: 2250164.14

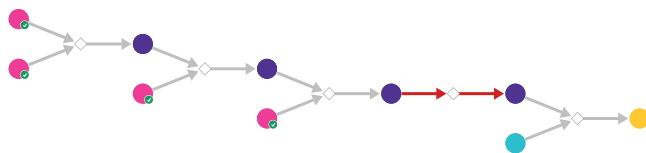
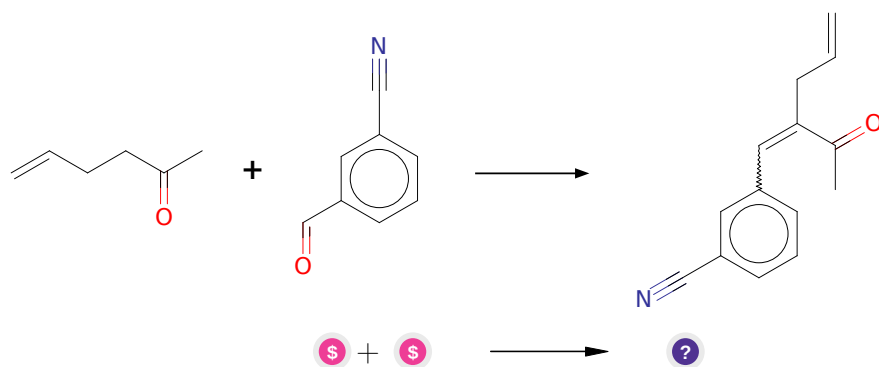


Figure 4: Outline of path 4

2.4.1 Aldol Condensation



Substrates:

1. Allylacetone - *available at Sigma-Aldrich*
2. 3-Cyanobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(=Cc1cccc(C#N)c1)C(C)=O

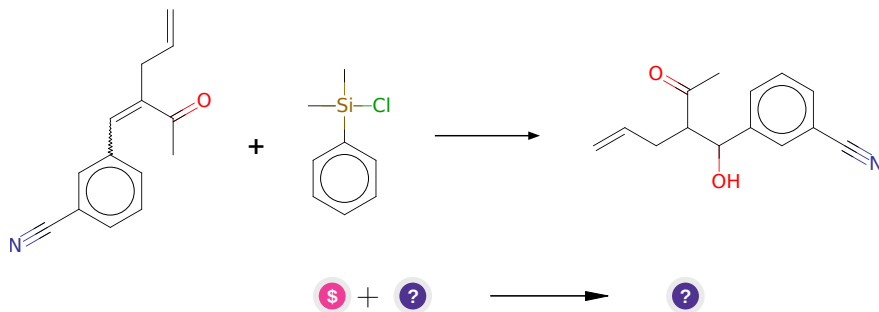
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.4.2 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

1. DMPSCl - *available at Sigma-Aldrich*
2. C=CCC(=Cc1cccc(C#N)c1)C(C)=O

Products:

1. C=CCC(C(C)=O)C(O)c1cccc(C#N)c1

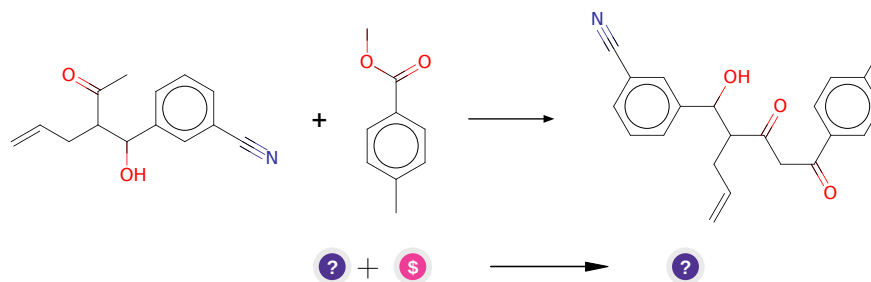
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H₂O₂

Protections: none

Reference: [10.1021/ja058370g](#) AND (Oxidation) [10.1021/jo9905672](#) or [10.1021/ol300832f](#)

Retrosynthesis ID: 20301

2.4.3 Condensation of methyl ketones with esters



Substrates:

1. C=CCC(C(C)=O)C(O)c1cccc(C#N)c1
2. Methyl p-toluate - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

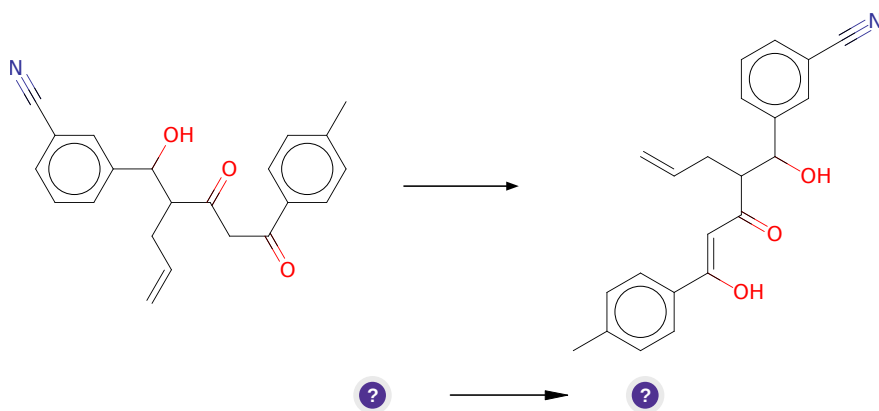
Typical conditions: NaOMe.MeOH

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

2.4.4 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

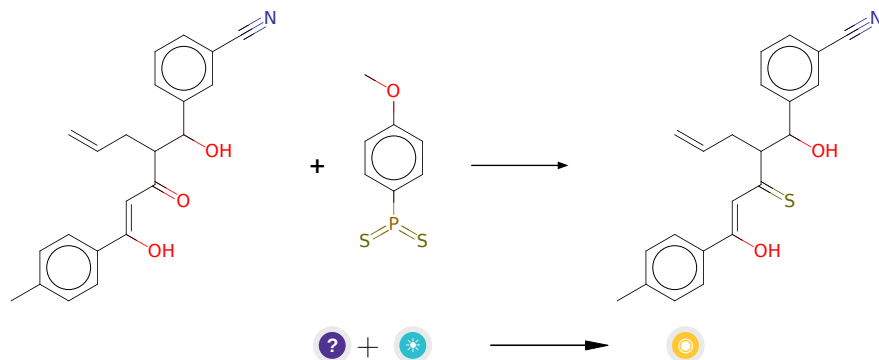
Typical conditions: solvent

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)c1cccc(C#N)c1
2. 4-methoxyphenyl-dithiophosphonaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

Retrosynthesis ID: 10798

2.5 Path 5

Score: 2250164.14

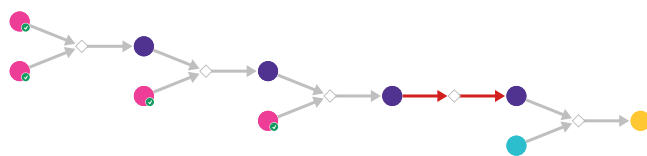
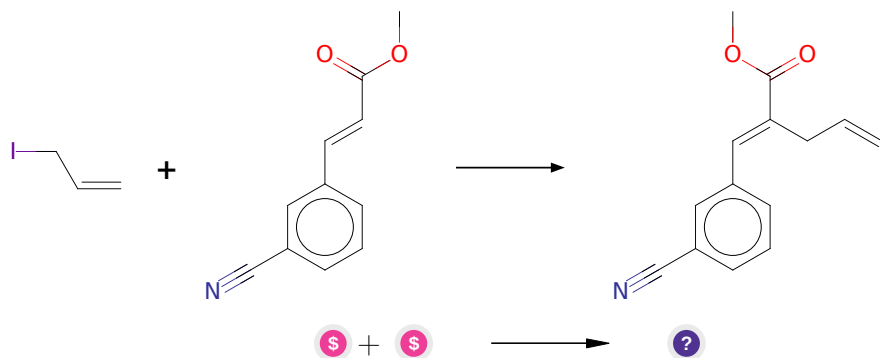


Figure 5: Outline of path 5

2.5.1 Alkylation of vinyl esters



Substrates:

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

Products:

1. C=CC/C(=C\c1cccc(C#N)c1)C(=O)OC

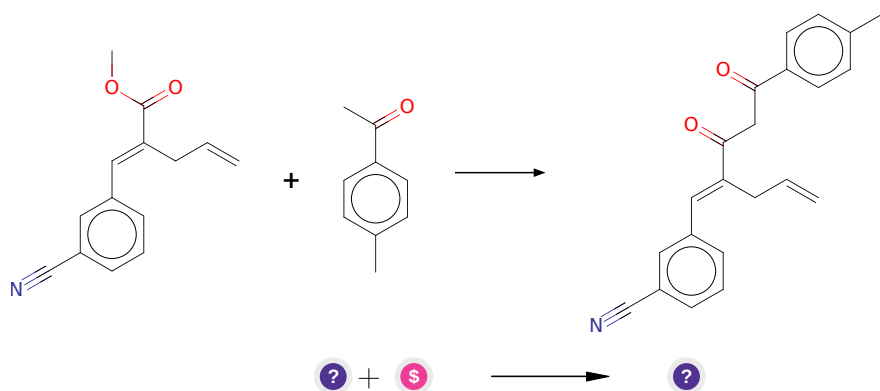
Typical conditions: LDA.THF

Protections: none

Reference: DOI: [10.1039/C39870001410](https://doi.org/10.1039/C39870001410)

Retrosynthesis ID: 886

2.5.2 Condensation of methyl ketones with esters



Substrates:

1. C=CC/C(=C\c1cccc(C#N)c1)C(=O)OC

- Methyl p-tolyl ketone - *available at Sigma-Aldrich*

Products:

- C=CC/C(=C\c1cccc(C#N)c1)C(=O)CC(=O)c1ccc(C)cc1

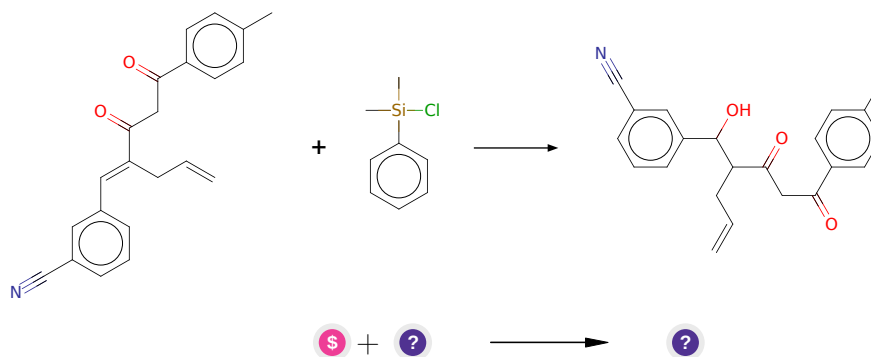
Typical conditions: NaOMe.MeOH

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:

- DMPSCl - *available at Sigma-Aldrich*
- C=CC/C(=C\c1cccc(C#N)c1)C(=O)CC(=O)c1ccc(C)cc1

Products:

- C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

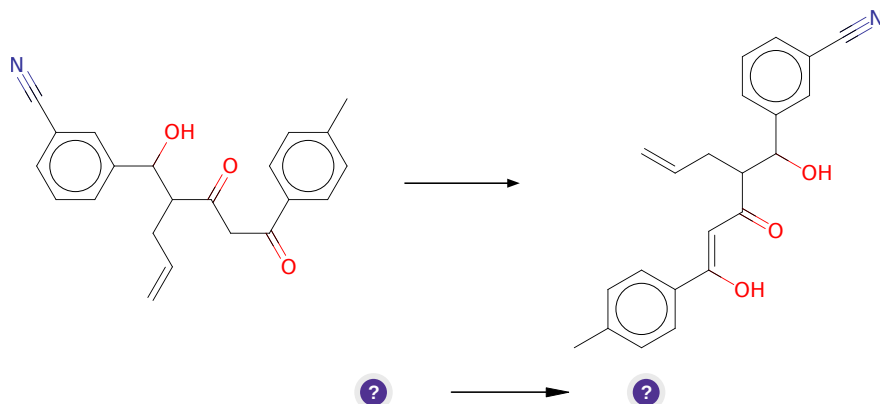
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

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)c1cccc(C#N)c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

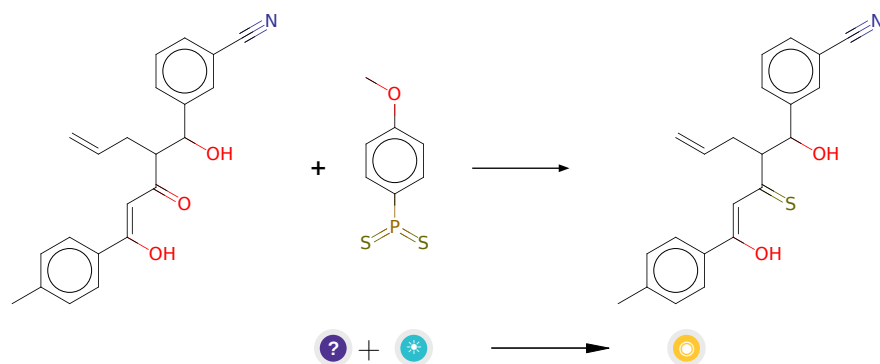
Typical conditions: solvent

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)c1cccc(C#N)c1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc(C#N)c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

Retrosynthesis ID: 10798