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+1000 000*(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

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.*
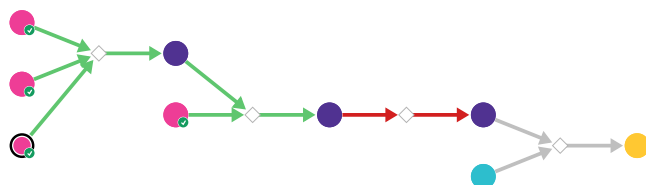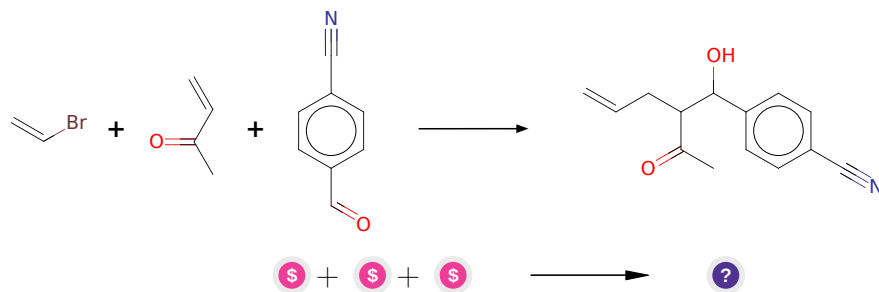
2.1 Path 1

Score: `2250084.06`

Figure 1: Outline of path 1

2.1.1 Alkenylation-Aldol reaction of enones and enoate esters

Substrates:

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*

2. Bromoethylene - *available at Sigma-Aldrich*

3. 3-Buten-2-one - *available at Sigma-Aldrich*

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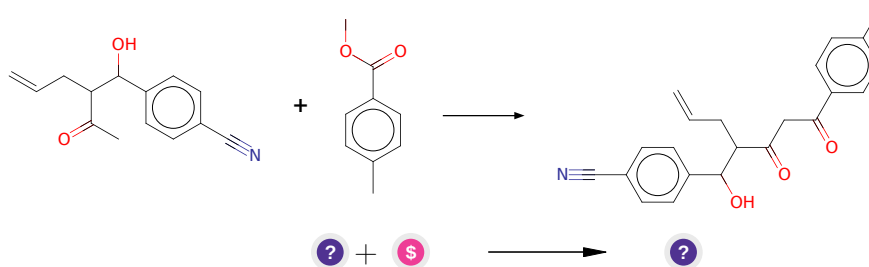
1. C=CCC(C(C)=O)C(O)c1ccc(C#N)cc1

Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3* AND *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w*

Retrosynthesis ID: 20547

2.1.2   Condensation of methyl ketones with esters

Substrates:

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

2. Methyl p-toluate -   *available at Sigma-Aldrich*

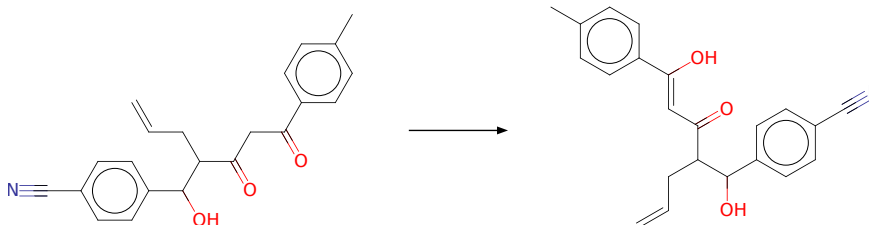**Products:**

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1
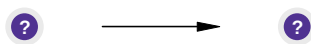
Typical conditions: NaOMe.MeOH

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

2.1.3   Keto-enol Tautomerism

Substrates:

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

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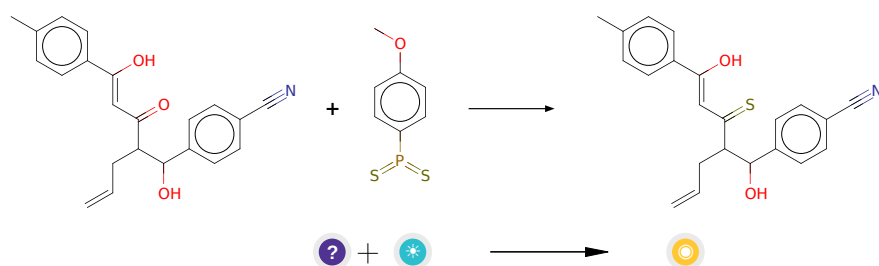
1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1

Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.1.4   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
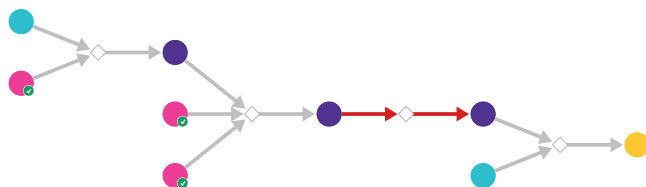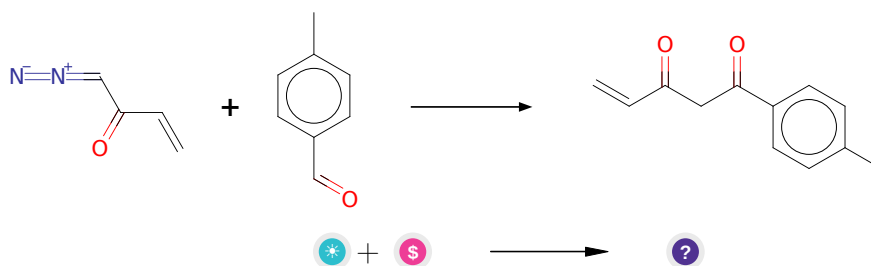
2.2   Path 2

Score: 2250115.31

Figure 2: Outline of path 2

2.2.1 Homologation of aldehydes to ketones with diazoalkanes

Substrates:

1. 1-diazo-but-3-en-2-one

2. p-Tolualdehyde - *available at Sigma-Aldrich*
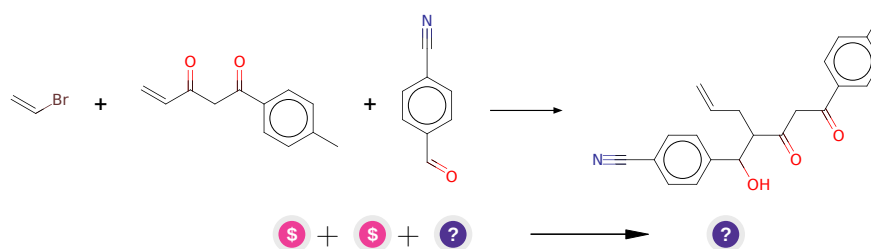
Products:

1. C=CC(=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

2.2.2 Alkenylation-Aldol reaction of enones and enoate esters

Substrates:

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*

2. Bromoethylene - *available at Sigma-Aldrich*

3. C=CC(=O)CC(=O)c1ccc(C)cc1

Products:

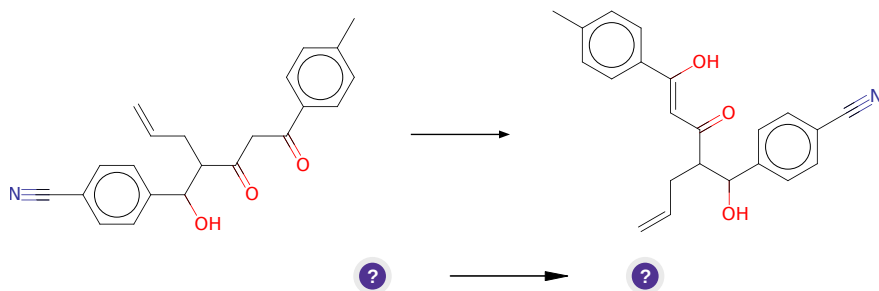1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1

Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13048

2.2.3 Keto-enol Tautomerism

Substrates:

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

Products:

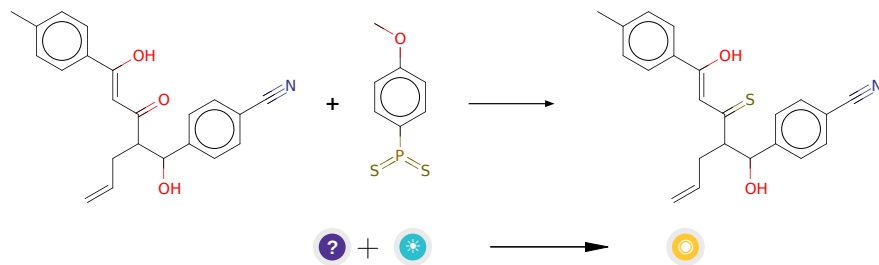1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1

Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.2.4 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
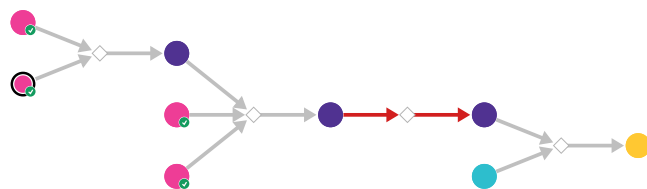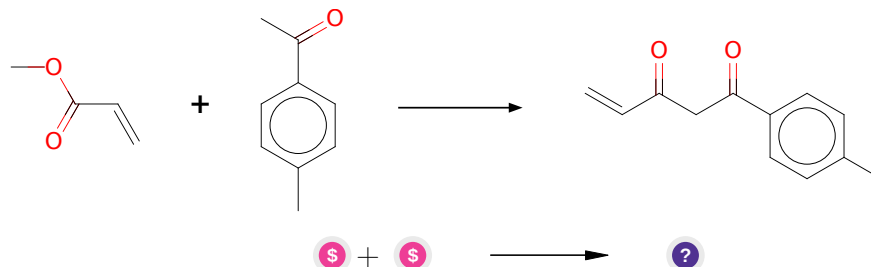
Score: 2250115.31

Figure 3: Outline of path 3

2.3.1 Condensation of methyl ketones with esters

Substrates:

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

2. Methyl acrylate - *available at Sigma-Aldrich*
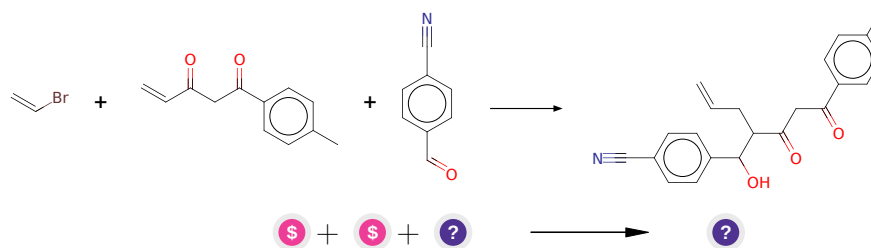
Products:

1. C=CC(=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

2.3.2 Alkenylation-Aldol reaction of enones and enoate esters

Substrates:

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*

2. Bromoethylene - *available at Sigma-Aldrich*

3. C=CC(=O)CC(=O)c1ccc(C)cc1

Products:

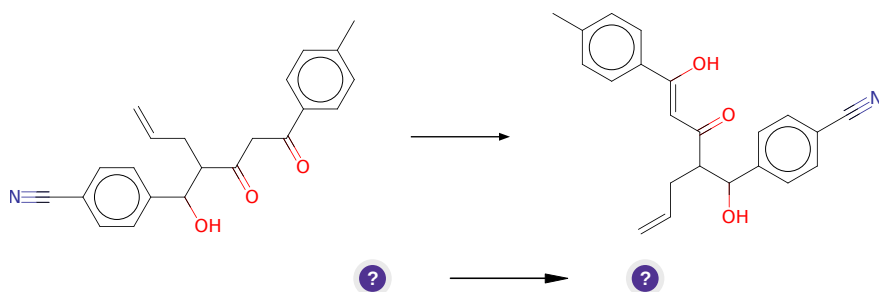1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1

Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13048

2.3.3 Keto-enol Tautomerism

Substrates:

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

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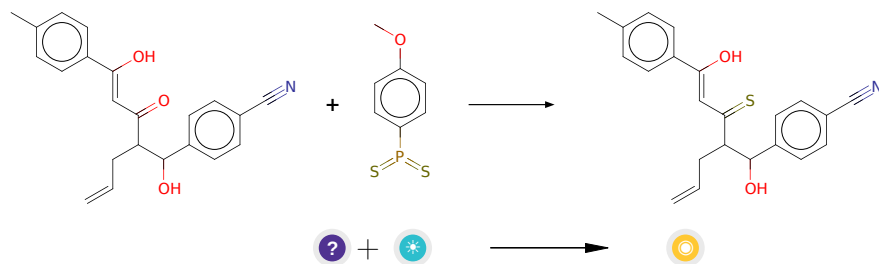
1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1

Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.3.4 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
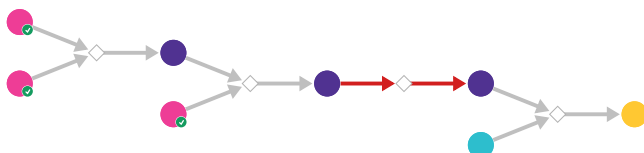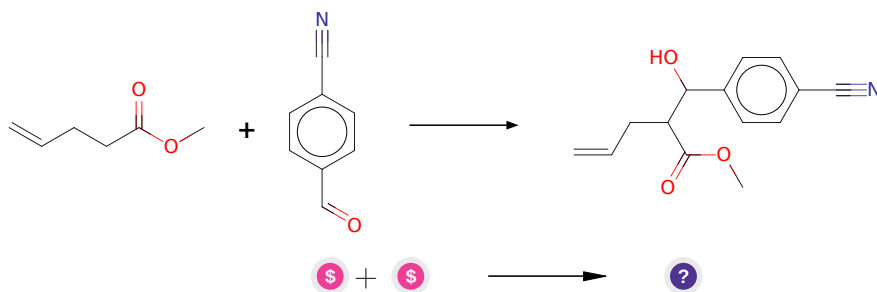
Score: 2250115.31

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*
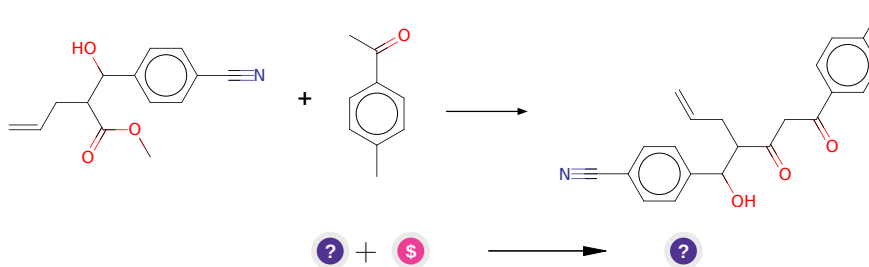
Products:

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 Condensation of methyl ketones with esters

Substrates:

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

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

Products:

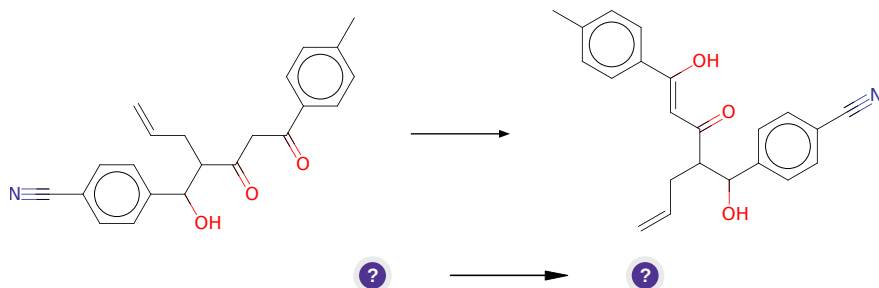1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1ccc(C#N)cc1

Typical conditions: 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

2.4.3 Keto-enol Tautomerism

Substrates:

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

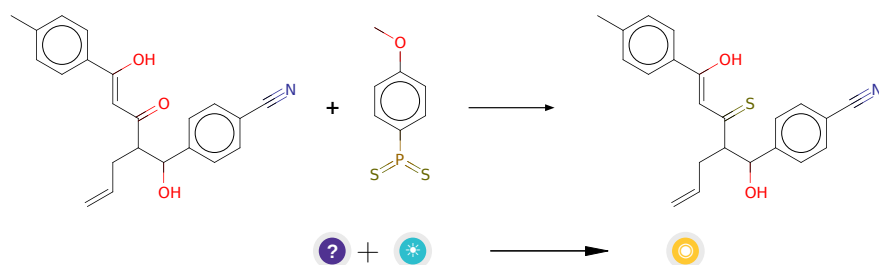**Products:**

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

2.4.4 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

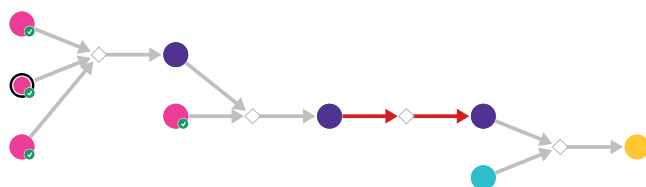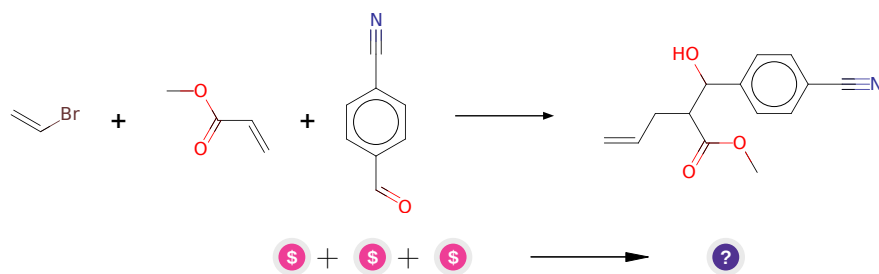**Score:** 2250115.31

Figure 5: Outline of path 5

2.5.1 Alkenylation-Aldol reaction of enones and enoate esters

Substrates:

1. 4-Cyanobenzaldehyde -   *available at Sigma-Aldrich*

2. Methyl acrylate -   *available at Sigma-Aldrich*

3. Bromoethylene -   *available at Sigma-Aldrich*
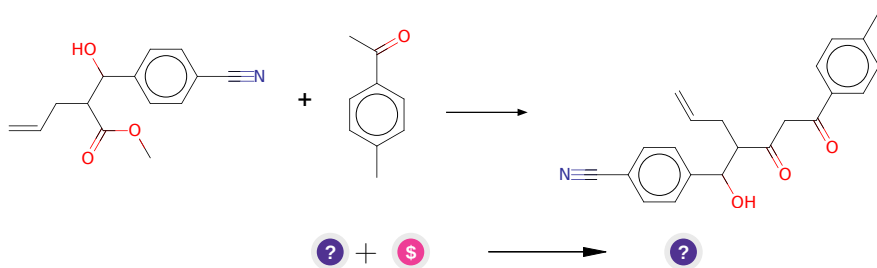
Products:

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

Typical conditions: 1.RCuLi.2.RCHO

Retrosynthesis ID: 13048

2.5.2 Condensation of methyl ketones with esters

Substrates:

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

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

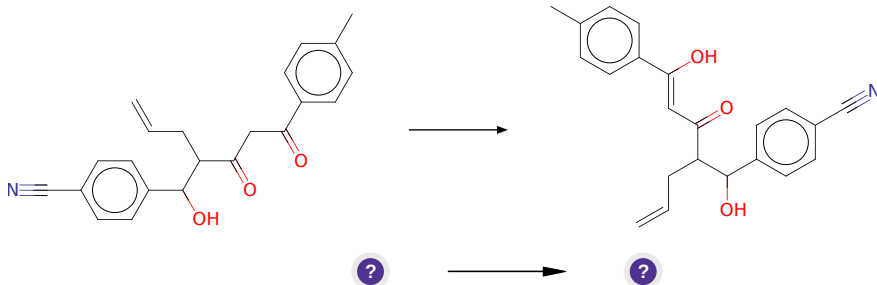**Products:**

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

Typical conditions: NaOMe.MeOH

Protections: none

Retrosynthesis ID: 4792

2.5.3 Keto-enol Tautomerism

Substrates:

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

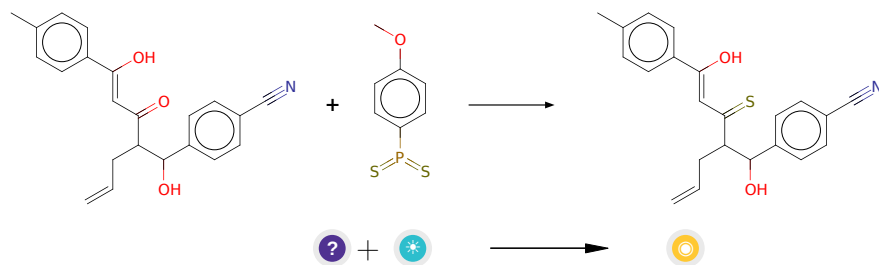**Products:**

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

2.5.4 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