Paths of analysis*
Y6

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.*
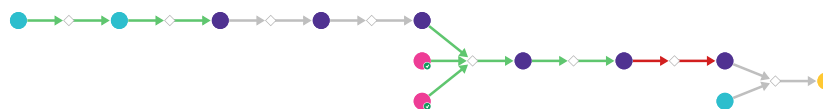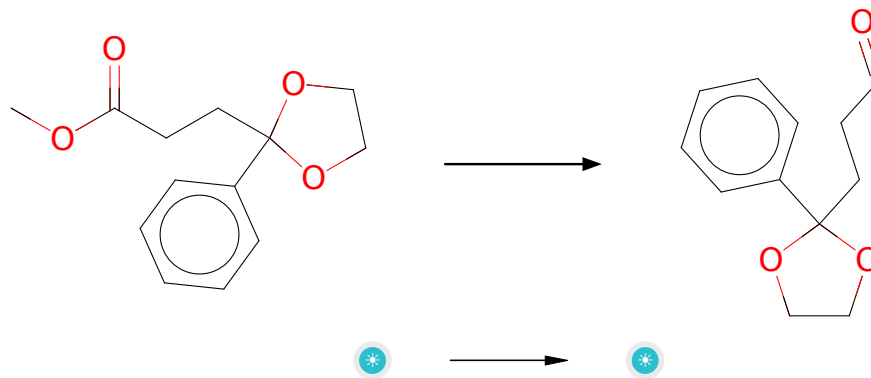
2.1 Path 1

Score: 2250084.06

Figure 1: Outline of path 1

2.1.1 Aldehyde Formation

Substrates:

1. 2-[2-(methoxycarbonyl)ethyl]-2-phenyl-1,3-dioxolane

Products:

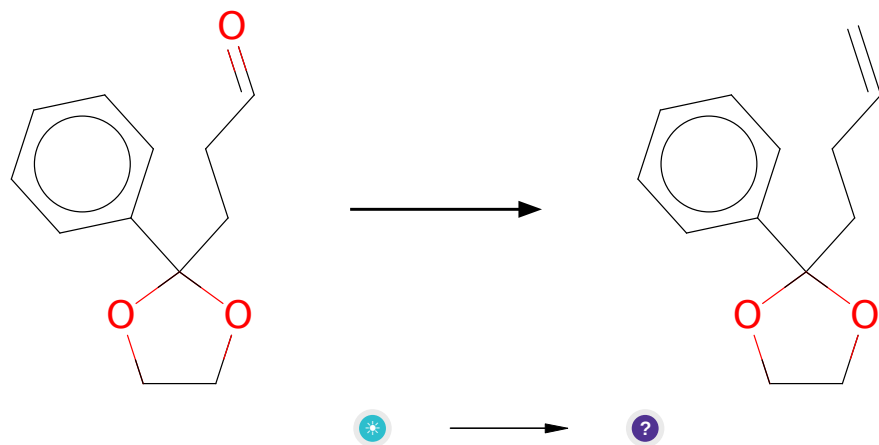1. 3-(2-phenyl-[1,3]dioxolan-2-yl)-propionaldehyde

Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Retrosynthesis ID: 28551

2.1.2 Tebbe Olefination

Substrates:

1. 3-(2-phenyl-[1,3]dioxolan-2-yl)-propionaldehyde

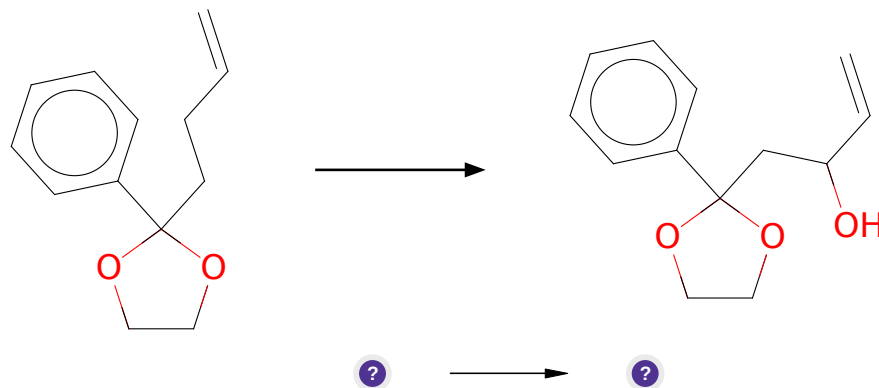**Products:**

1. C=CCCC1(c2ccccc2)OCCO1

Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Retrosynthesis ID: 11714

2.1.3 Allylic oxidation to alcohol

Substrates:

1. C=CCCC1(c2ccccc2)OCCO1
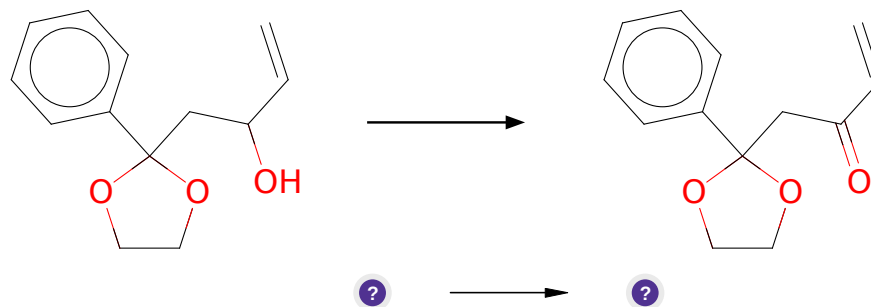
Products:

1. C=CC(O)CC1(c2ccccc2)OCCO1

Typical conditions: ArCOOOH or t-BuOOOH

Protections: none

Reference: DOI: *10.1021/ja00458a072* AND *10.1016/j.tetlet.2013.03.046* AND *10.1039/b612423b*

Retrosynthesis ID: 7603

2.1.4 Swern Oxidation

Substrates:

1. C=CC(O)CC1(c2ccccc2)OCCO1

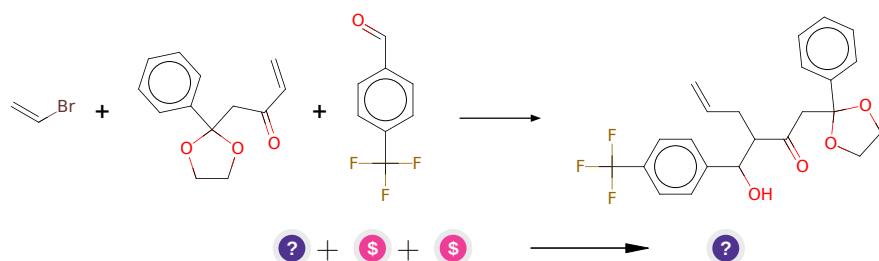**Products:**

1. C=CC(=O)CC1(c2ccccc2)OCCO1

Typical conditions: oxalyl chloride.DMSO.DCM.NMe3.-40C

Protections: none

Reference: *10.1055/s-1990-27036*

Retrosynthesis ID: 11163

2.1.5 Alkenylation-Aldol reaction of enones and enoate esters

Substrates:

1. C=CC(=O)CC1(c2ccccc2)OCCO1

2. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

3. Bromoethylene - *available at Sigma-Aldrich*

Products:

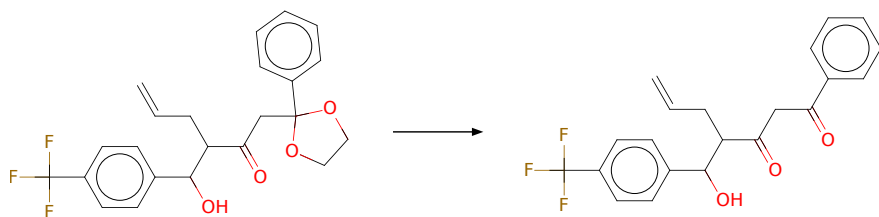1. C=CCC(C(=O)CC1(c2ccccc2)OCCO1)C(O)c1ccc(C(F)(F)F)cc1
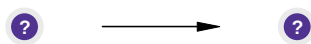
Typical conditions: 1.RCuLi.2.RCHO

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

2.1.6 Hydrolysis of ketals

Substrates:

    1. C=CCC(C(=O)CC1(c2ccccc2)OCCO1)C(O)c1ccc(C(F)(F)F)cc1

Products:

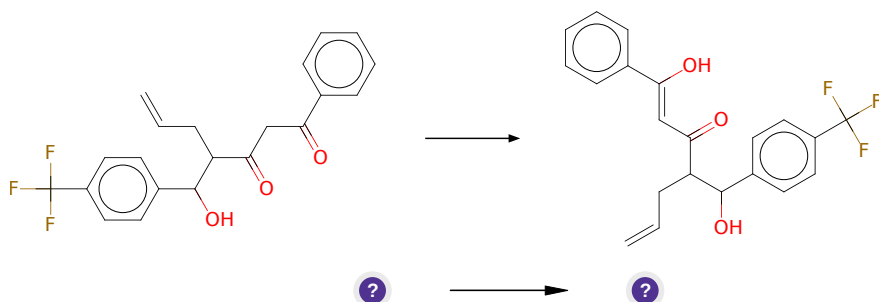   1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: H2O.HCl

Protections: none

Reference: *10.1021/jo0159035* and *10.1021/jo00194a003* and

Retrosynthesis ID: 31013139

2.1.7   Keto-enol Tautomerism

Substrates:

    1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Products:
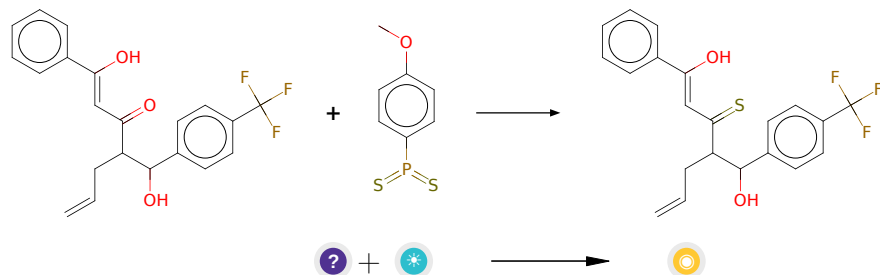
    1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.1.8 Synthesis of Thioketones using Lawesson's Reagent

Substrates:

1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798
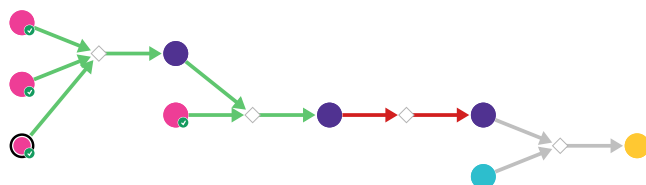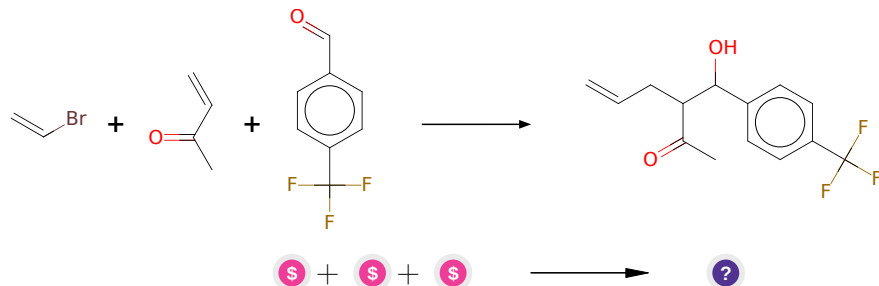
2.2 Path 2

Score: 2250084.06

Figure 2: Outline of path 2

2.2.1 Alkenylation-Aldol reaction of enones and enoate esters

Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

2. Bromoethylene - *available at Sigma-Aldrich*

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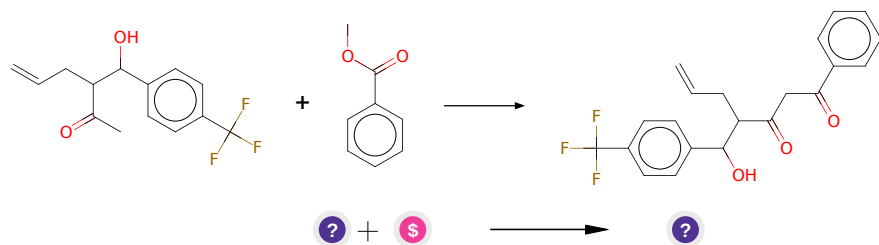
Products:

1. C=CCC(C(C)=O)C(O)c1ccc(C(F)(F)F)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

2.2.2 Condensation of methyl ketones with esters

Substrates:

1. C=CCC(C(C)=O)C(O)c1ccc(C(F)(F)F)cc1

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

Products:
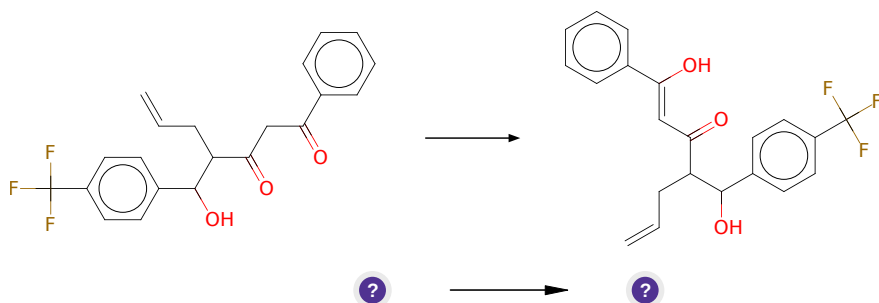
1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

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

2.2.3   Keto-enol Tautomerism

Substrates:

1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Products:

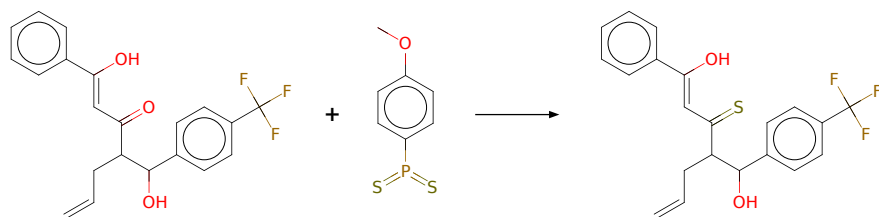1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1
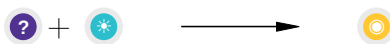
Typical conditions: solvent

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)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

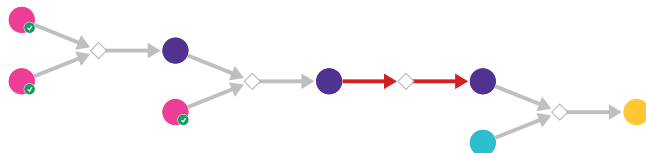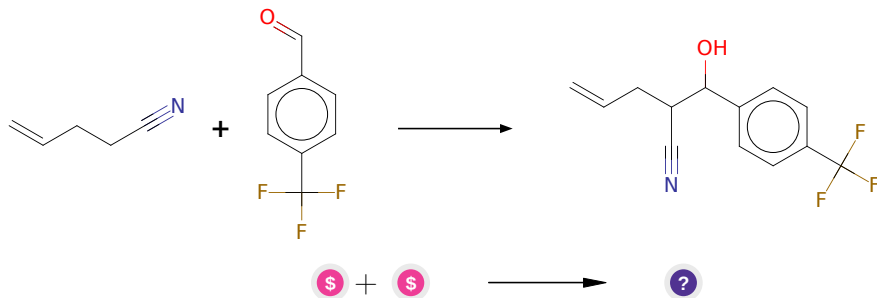## 2.3   Path 3

Score: 2250115.31

Figure 3: Outline of path 3

2.3.1   Aldol-like condensation with nitriles

Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

2. 4-Pentenenitrile - *available at Sigma-Aldrich*
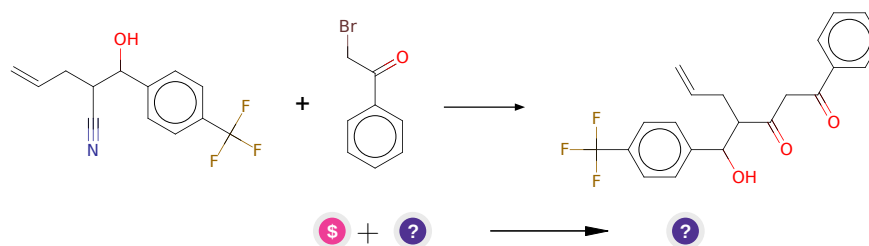
Products:

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

Typical conditions: LDA.THF.cooling

Protections: none

Reference: *10.1039/B800634B* and *10.1002/anie.201302613* and *10.1021/jm701319c* and *10.1016/S0040-4020(98)00122-7* and *10.1021/jo025872t*

Retrosynthesis ID: 23727

2.3.2 Blaise Reaction

Substrates:

1. Phenacyl bromide - *available at Sigma-Aldrich*

2. C=CCC(C#N)C(O)c1ccc(C(F)(F)F)cc1

Products:
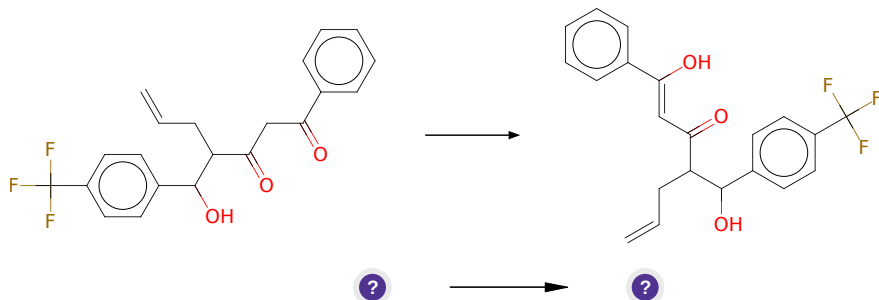
1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: Zn.TMSCl.THF then HCl

Protections: none

Reference: *10.1002/ejoc.201403402*

Retrosynthesis ID: 10000153

2.3.3 Keto-enol Tautomerism

Substrates:

1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Products:

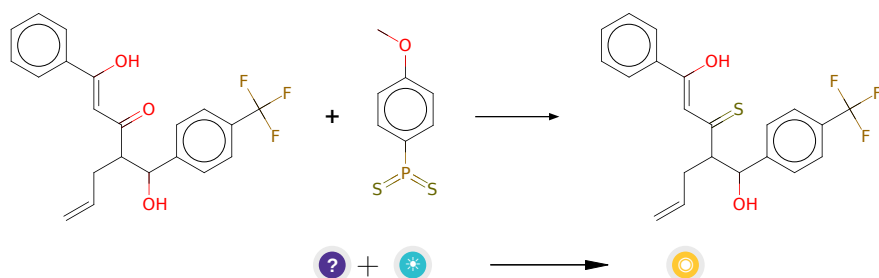1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

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)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798
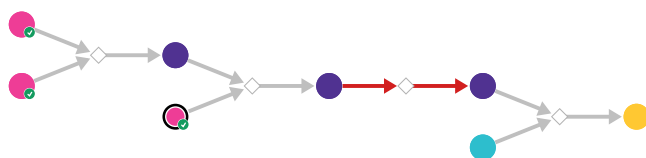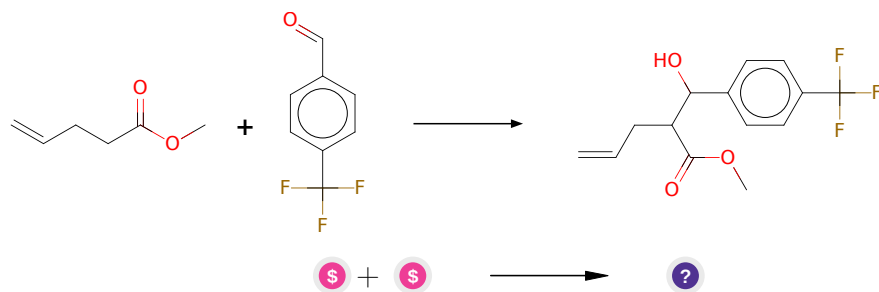
2.4 Path 4

Score: 2250115.31

Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes

Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

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

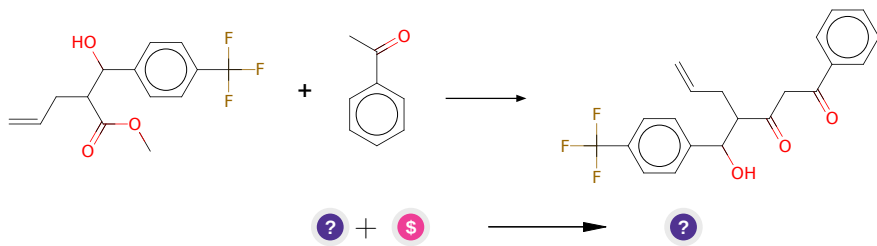**Products:**

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

Typical conditions: LDA.THF

Protections: none

Retrosynthesis ID: 4788

2.4.2 Condensation of methyl ketones with esters

Substrates:

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

2. Acetophenone - *available at Sigma-Aldrich*

Products:
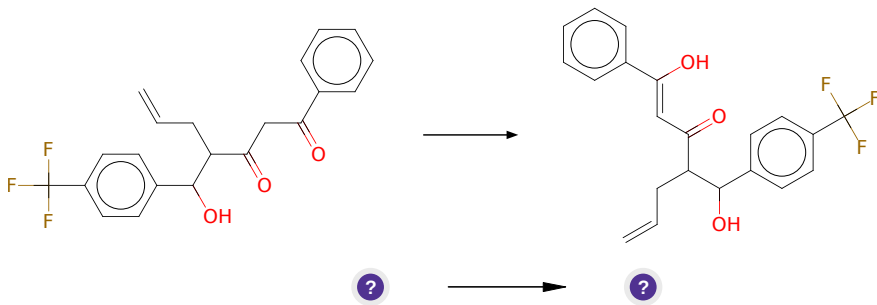
1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: NaOMe.MeOH

Protections: none

Retrosynthesis ID: 4792

2.4.3 Keto-enol Tautomerism

Substrates:

1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Products:

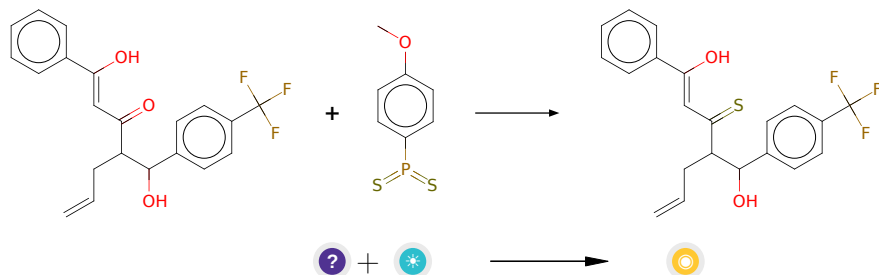1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

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)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798
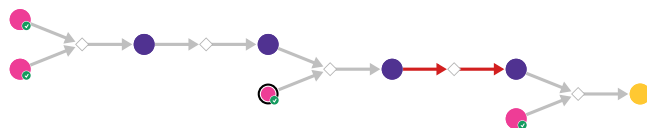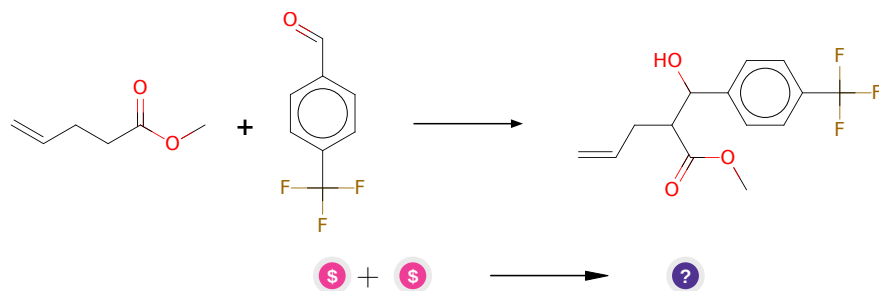
2.5   Path 5

Score: 2250125.08

Figure 5: Outline of path 5

2.5.1 Condensation of esters with aldehydes

Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

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

Products:
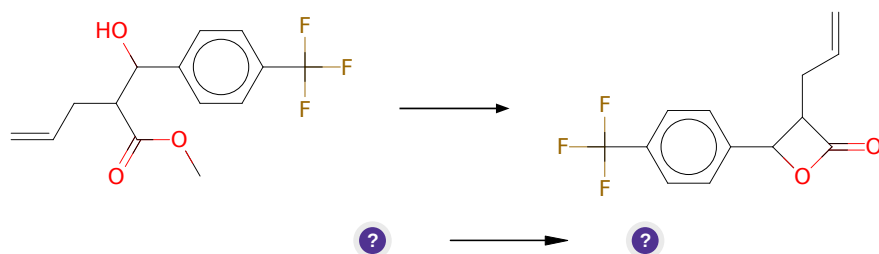
1. C=CCC(C(=O)OC)C(O)c1ccc(C(F)(F)F)cc1

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

2.5.2 Acid catalyzed transesterification

Substrates:

1. C=CCC(C(=O)OC)C(O)c1ccc(C(F)(F)F)cc1
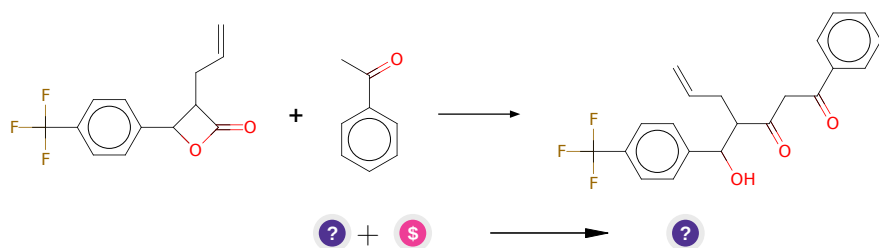
Products:

1. C=CCC1C(=O)OC1c1ccc(C(F)(F)F)cc1

Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.5.3 Ring opening of lactones with enolates

Substrates:

1. C=CCC1C(=O)OC1c1ccc(C(F)(F)F)cc1

2. Acetophenone -   *available at Sigma-Aldrich*

Products:
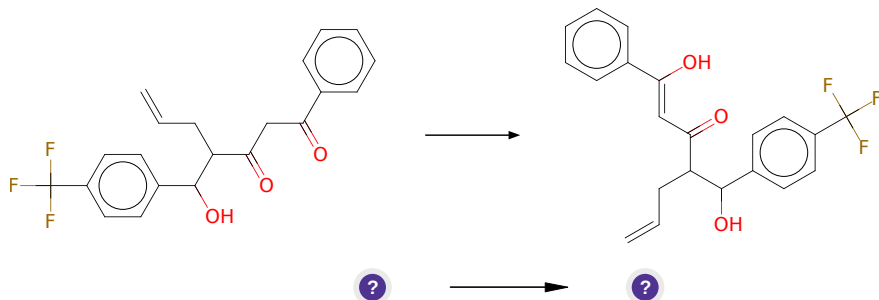
1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

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

2.5.4   Keto-enol Tautomerism

Substrates:

1. C=CCC(C(=O)CC(=O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Products:

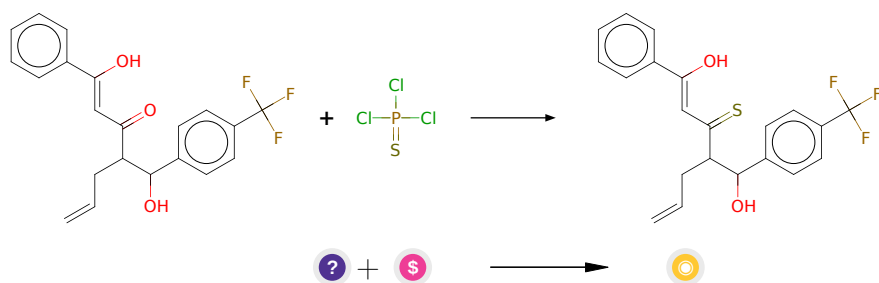1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.5.5   Thionation of Carbonyl Compounds using PSCl3

Substrates:

1. C=CCC(C(=O)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

2. Phosphorus thiochloride - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1

Typical conditions: NEt3.H2O.microwave.70-100C

Protections: none

Retrosynthesis ID: 11555