Paths of analysis*

Y1

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

*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: 2250084.06

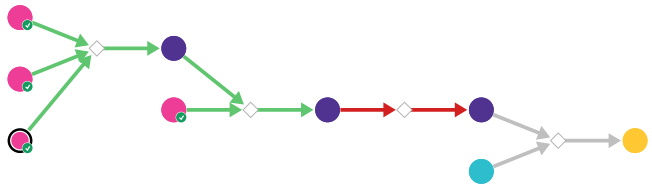
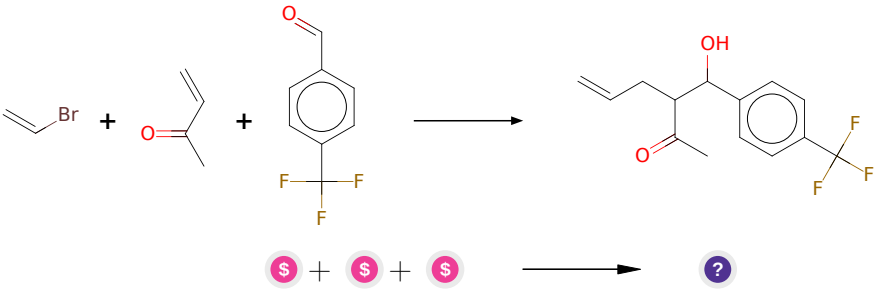


Figure 1: Outline of path 1

2.1.1 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

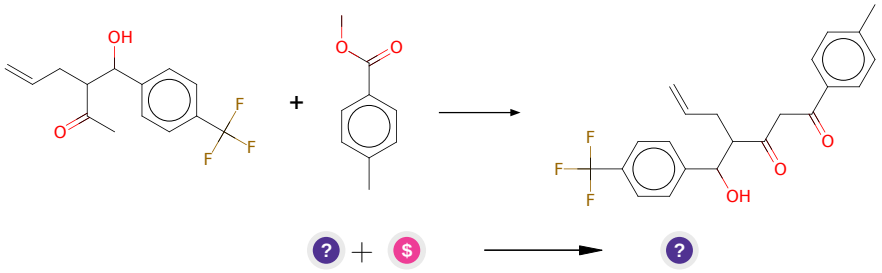
Typical conditions: 1.RCuLi.2.RCHO

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

2.1.2 Condensation of methyl ketones with esters



Substrates:

1. C=CCC(C(C)=O)C(O)c1ccc(C(F)(F)F)cc1
2. Methyl p-toluate - *available at Sigma-Aldrich*

Products:

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

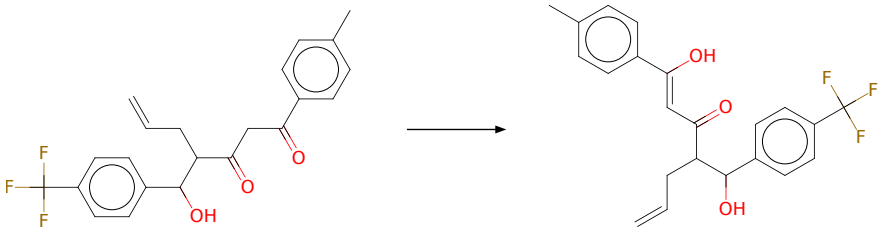
Typical conditions: NaOMe.MeOH

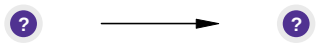
Protections: none

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

2.1.3 Keto-enol Tautomerism





Substrates:

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

Products:

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

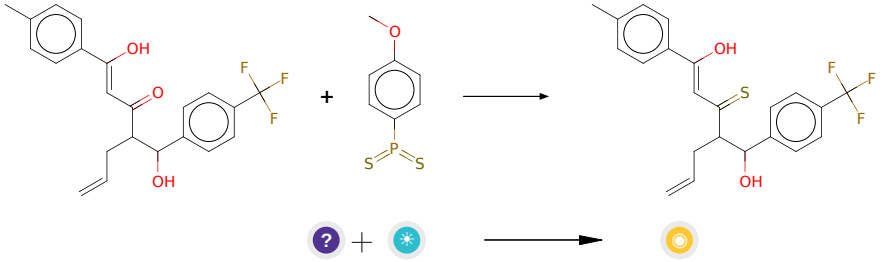
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.1.4 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)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: 2250115.31

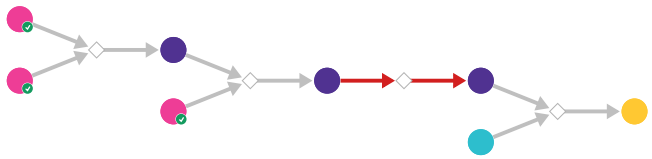
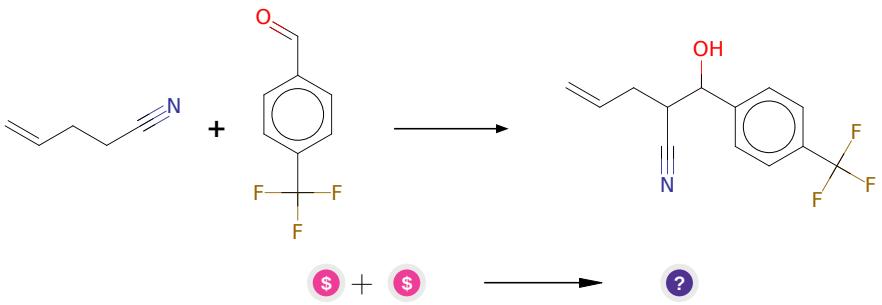


Figure 2: Outline of path 2

2.2.1 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

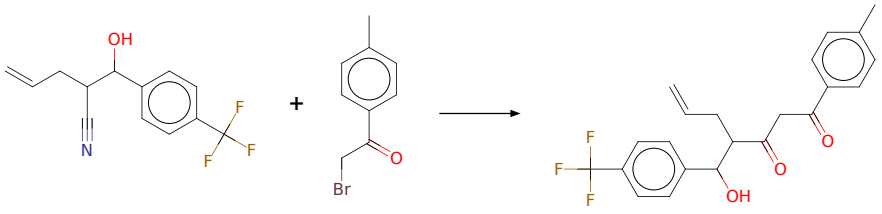
Typical conditions: LDA.THF.cooling

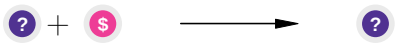
Protections: none

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

2.2.2 Blaise Reaction





Substrates:

1. C=CCC(C#N)C(O)c1ccc(C(F)(F)F)cc1
2. 2-Bromo-4'-methylacetophenone - *available at Sigma-Aldrich*

Products:

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

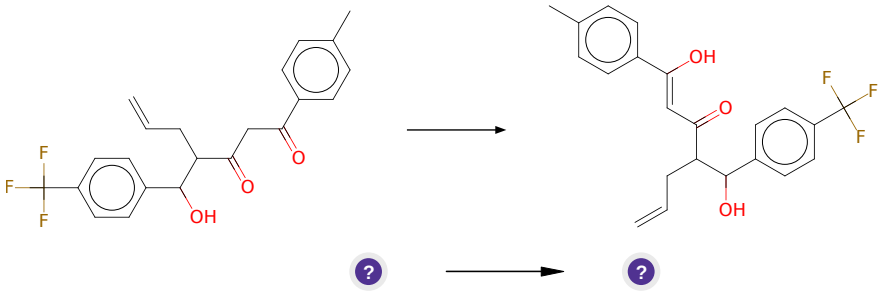
Typical conditions: Zn.TMSCl.THF then HCl

Protections: none

Reference: *10.1002/ejoc.201403402*

Retrosynthesis ID: 10000153

2.2.3 Keto-enol Tautomerism



Substrates:

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

Products:

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

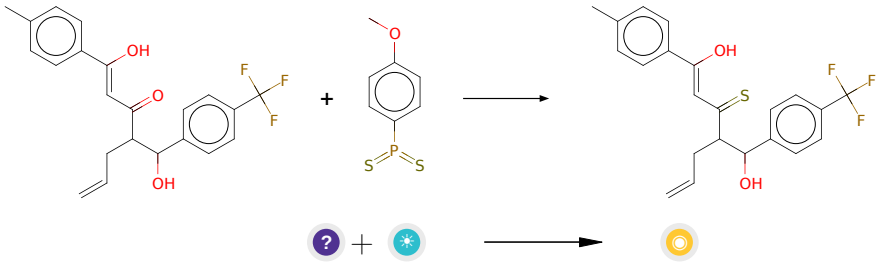
Typical conditions: solvent

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)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

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

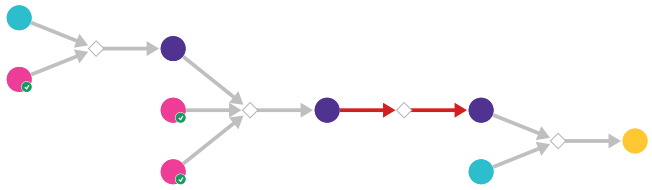
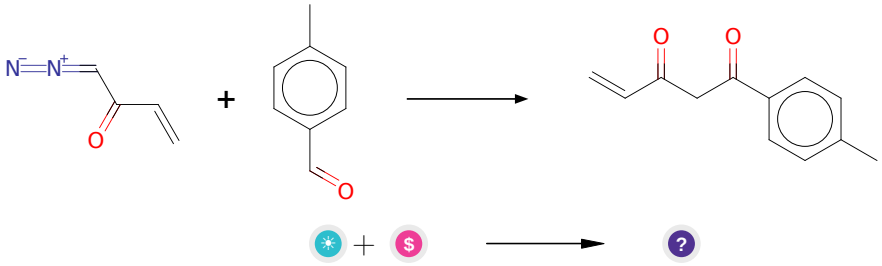


Figure 3: Outline of path 3

2.3.1 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

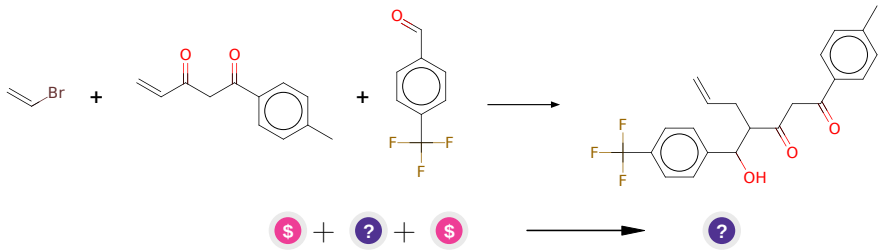
Typical conditions: Lewis.acid

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

2.3.2 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=CC(=O)CC(=O)c1ccc(C)cc1
3. Bromoethylene - *available at Sigma-Aldrich*

Products:

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

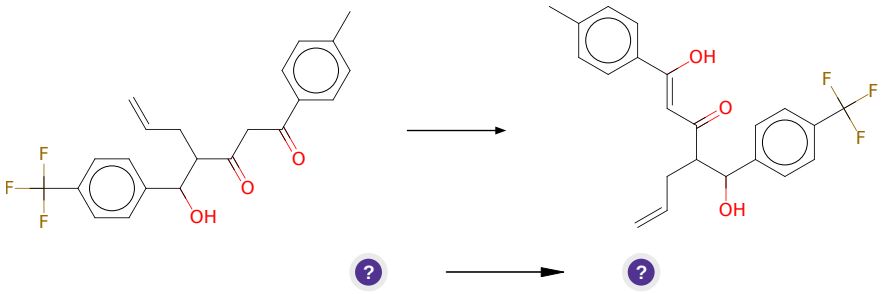
Typical conditions: 1.RCuLi.2.RCHO

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(F)(F)F)cc1

Products:

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

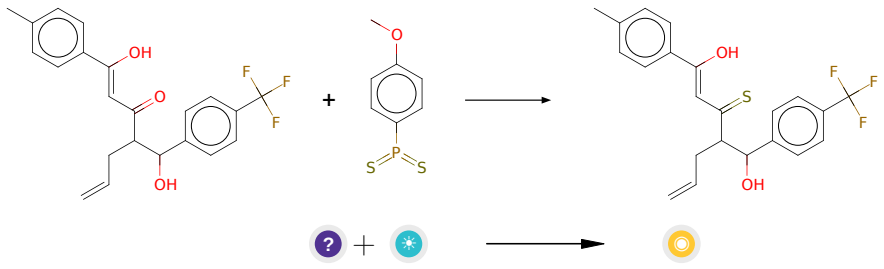
Typical conditions: solvent

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)c1ccc(C)cc1)C(O)c1ccc(C(F)(F)F)cc1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)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: 2250125.08

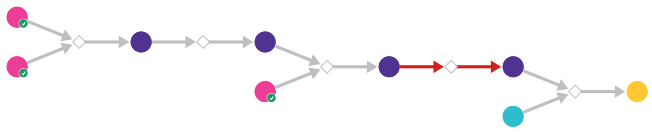
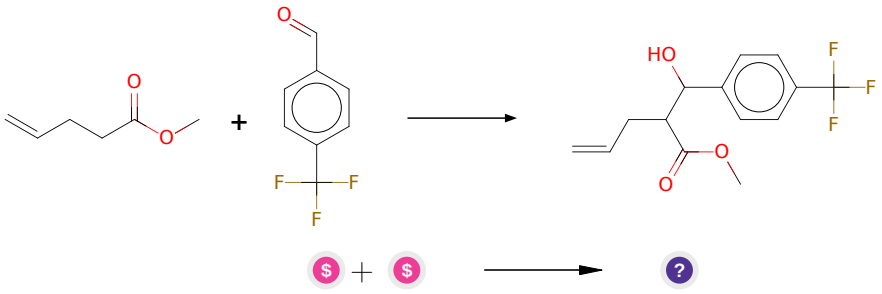


Figure 4: Outline of path 4

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

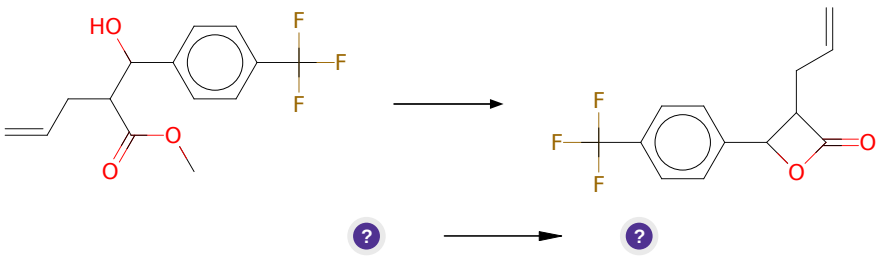
Typical conditions: LDA.THF

Protections: none

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(F)(F)F)cc1

Products:

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

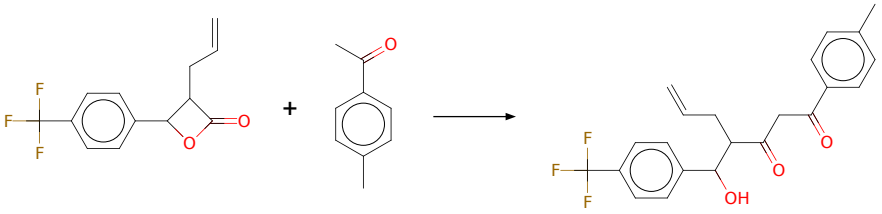
Typical conditions: H+

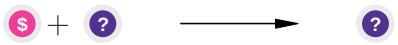
Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.4.3 Ring opening of lactones with enolates





Substrates:

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

Products:

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

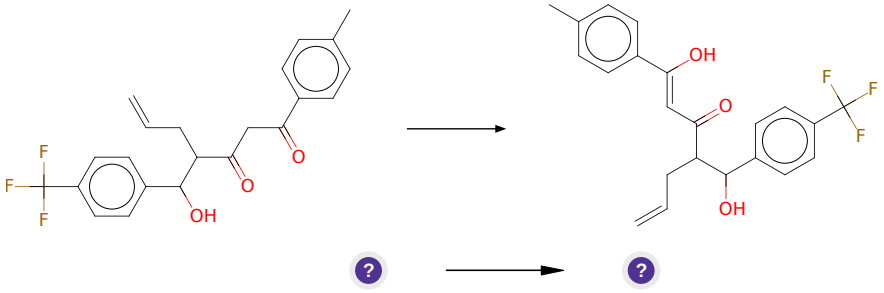
Typical conditions: LiHMDS.THF

Protections: none

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

Retrosynthesis ID: 24105

2.4.4 Keto-enol Tautomerism



Substrates:

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

Products:

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

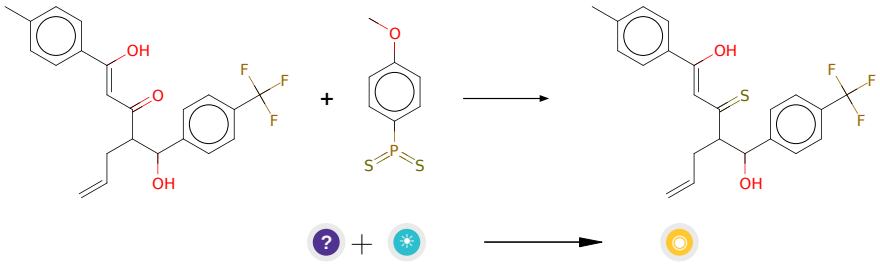
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.4.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

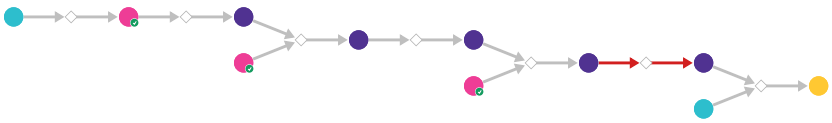
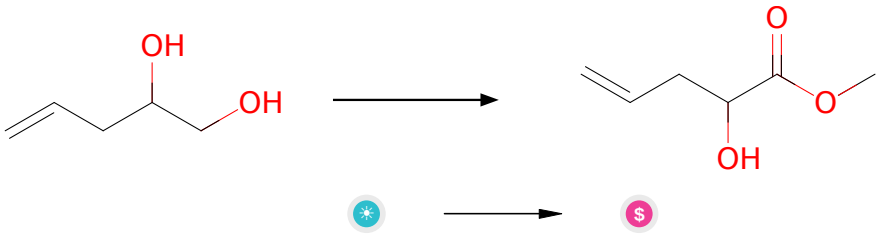


Figure 5: Outline of path 5

2.5.1 Tandem oxidation-esterification



Substrates:

1. 4-penten-1,2-diol

Products:

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

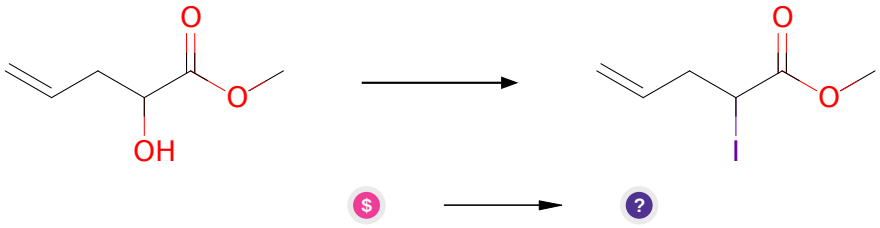
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

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

2.5.2 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

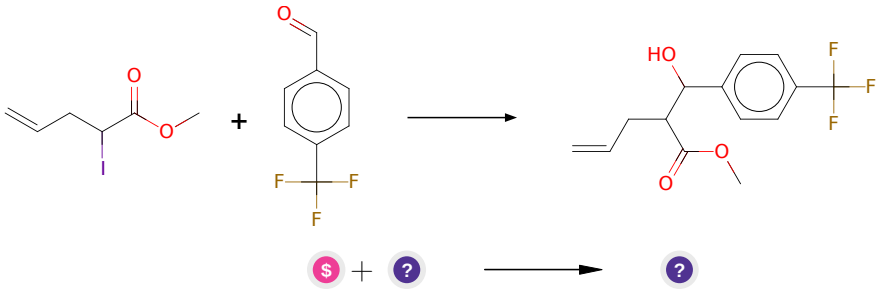
Typical conditions: Imidazole.PPh3.I2

Protections: none

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

Retrosynthesis ID: 9990043

2.5.3 Reformatsky Reaction



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=CCC(I)C(=O)OC

Products:

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

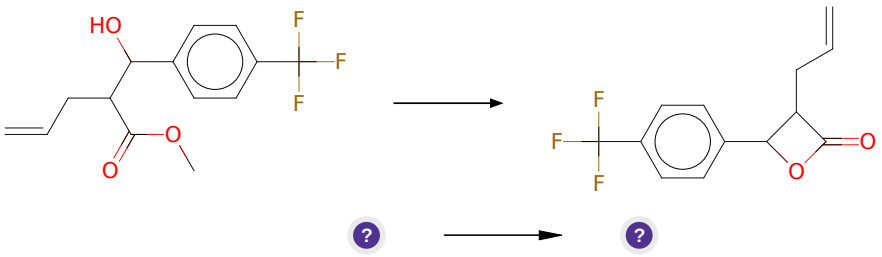
Typical conditions: Zn.THF

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

2.5.4 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

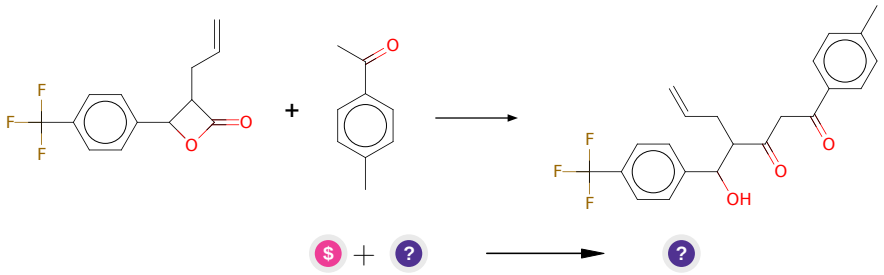
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.5.5 Ring opening of lactones with enolates



Substrates:

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

Products:

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

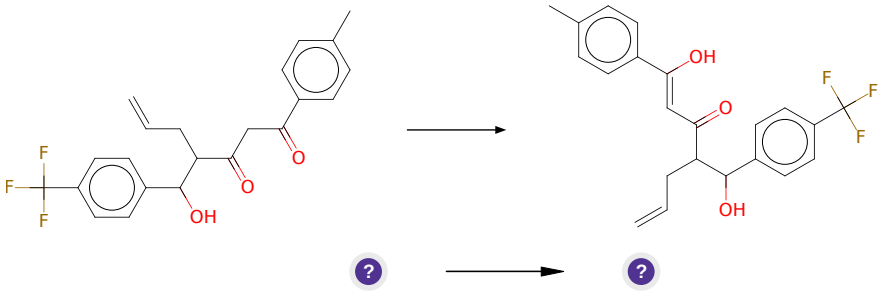
Typical conditions: LiHMDS.THF

Protections: none

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

Retrosynthesis ID: 24105

2.5.6 Keto-enol Tautomerism



Substrates:

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

Products:

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

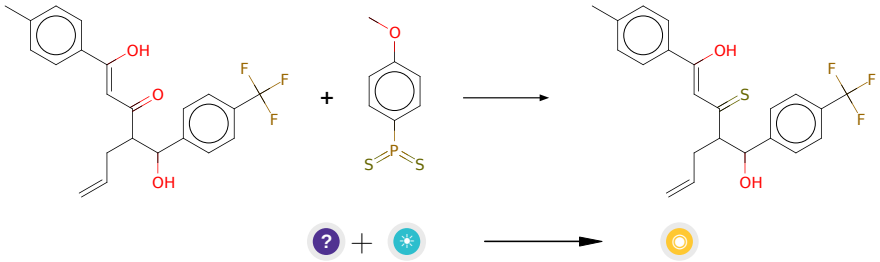
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.5.7 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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