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+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

4 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: 2250125.08

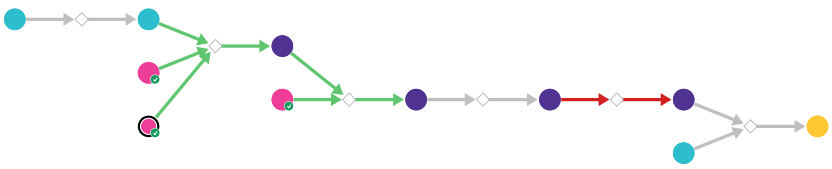
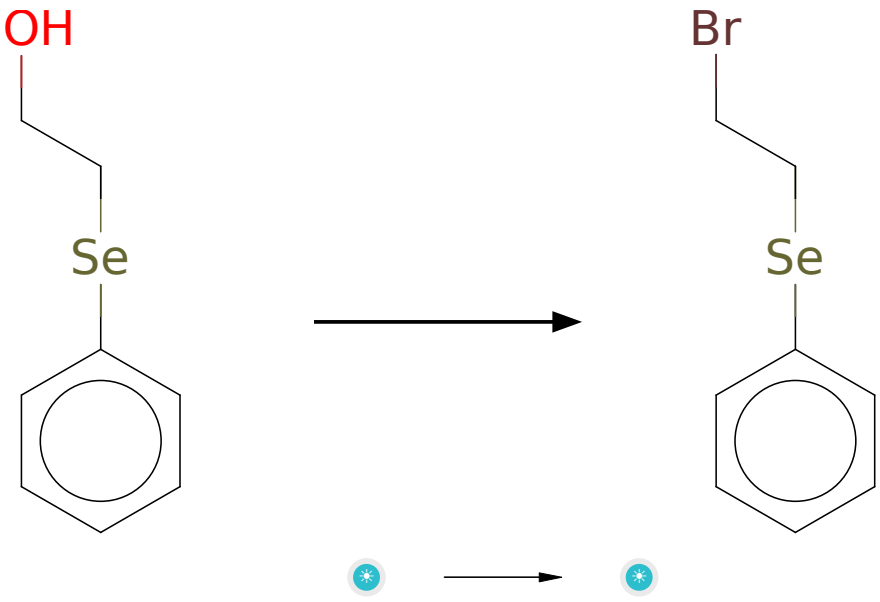


Figure 1: Outline of path 1

2.1.1 Appel Reaction



Substrates:

1. 2-phenylselanyl-ethanol

Products:

1. 2-bromaethylphenylselenid

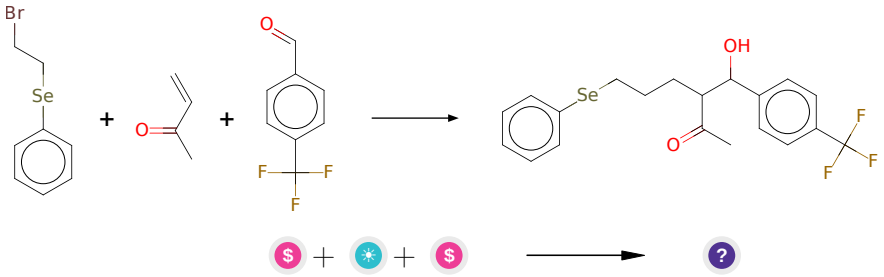
Typical conditions: PPh3.CBr4

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. a,a,a-Trifluoro-p-tolualdehyde - *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(F)(F)F)cc1

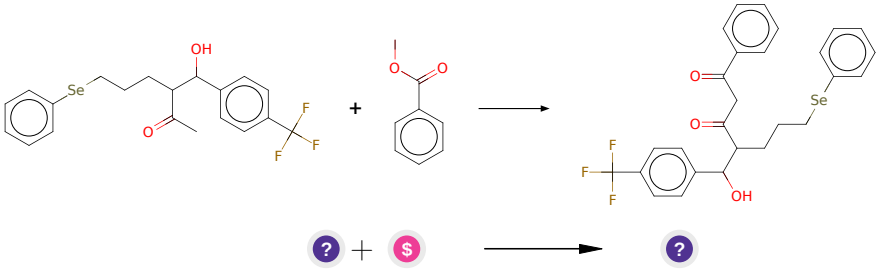
Typical conditions: 1.RCuLi.2.RCHO

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. CC(=O)C(CCC[Se]c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1
2. Methyl benzoate - *available at Sigma-Aldrich*

Products:

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

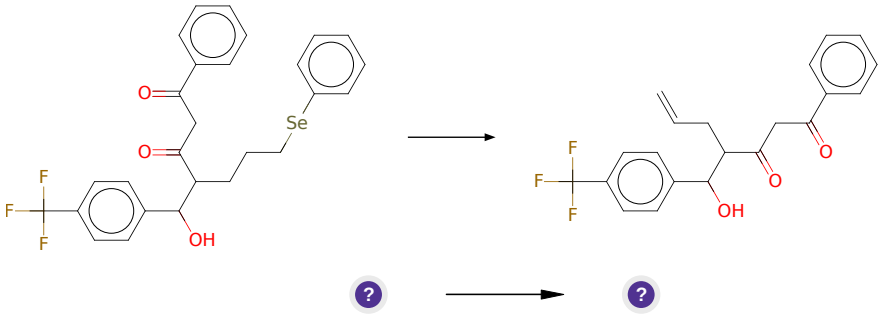
Typical conditions: NaOMe.MeOH

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. O=C(CC(=O)C(CCC[Se]c1ccccc1)C(O)c1ccc(C(F)(F)F)cc1)c1ccccc1

Products:

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

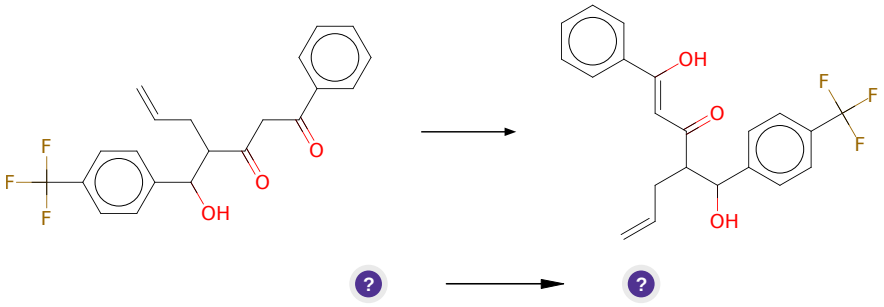
Typical conditions: 1) O3 or H2O2 or NaIO4. low temperature. 2) pyridine or Et3N

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)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

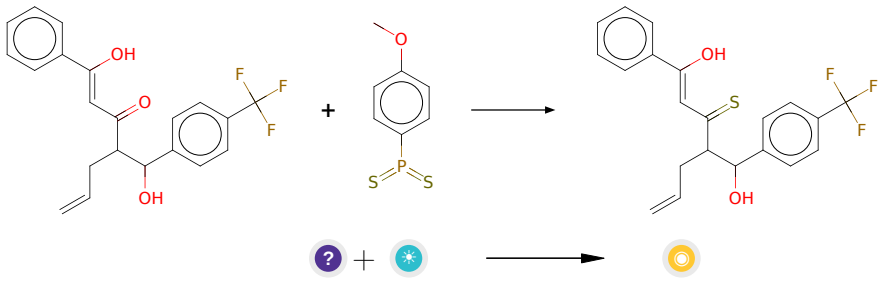
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.1.6 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: 2250125.08

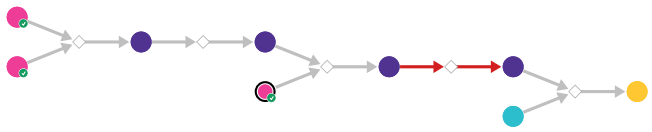
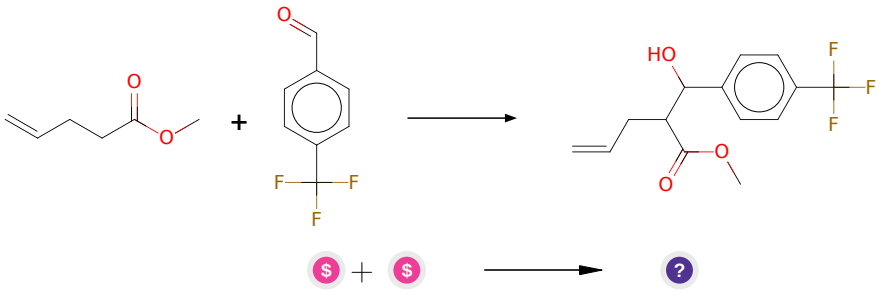


Figure 2: Outline of path 2

2.2.1 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

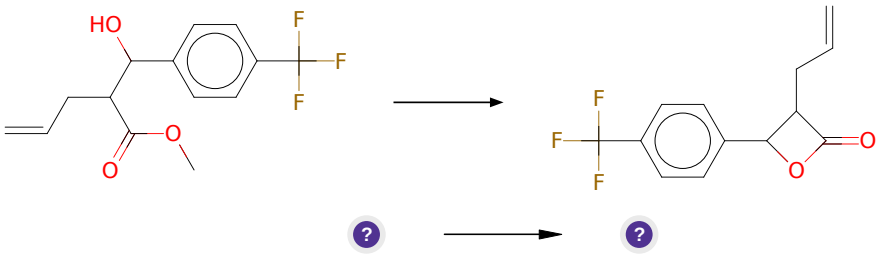
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 4788

2.2.2 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

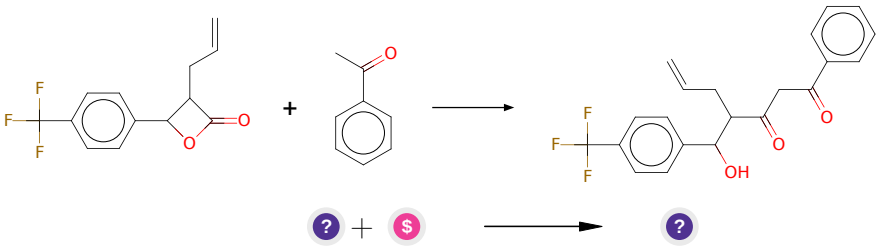
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.2.3 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

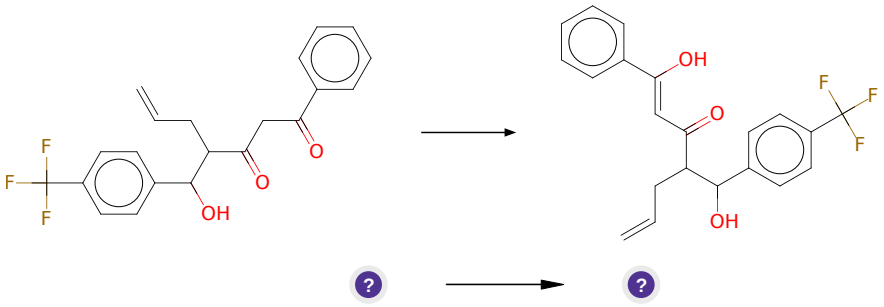
Typical conditions: LiHMDS.THF

Protections: none

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

Retrosynthesis ID: 24105

2.2.4 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

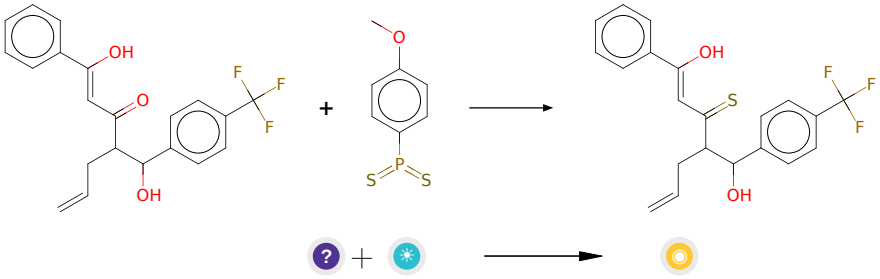
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.2.5 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: 2250132.89

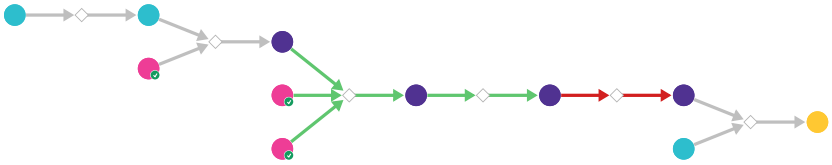
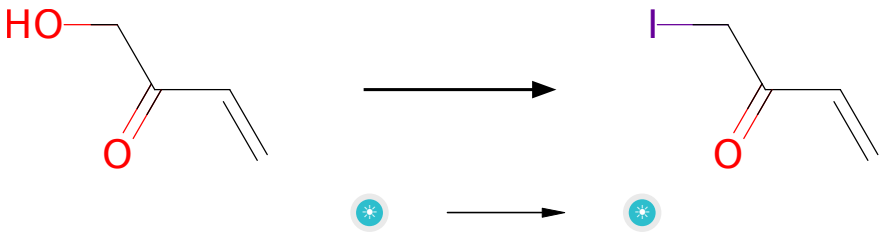


Figure 3: Outline of path 3

2.3.1 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

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

Products:

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

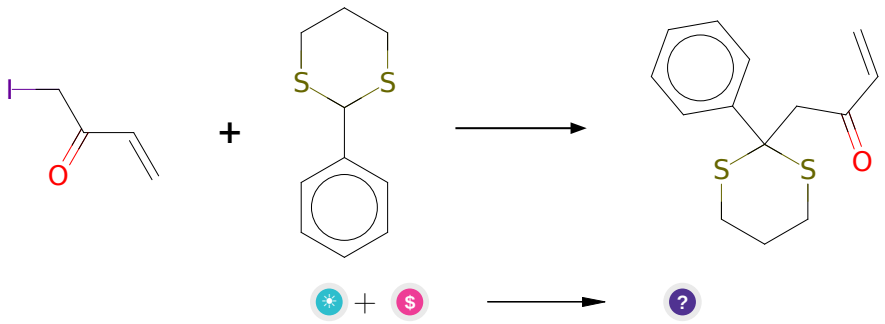
Typical conditions: Imidazole.PPh3.I2

Protections: none

Reference: *10.1002/1099-0690(200102)2001:3<493::AID-EJOC493>3.0.CO2-B* (compound 20) and *10.1016/j.tet.2014.09.030*

Retrosynthesis ID: 9990040

2.3.2 Alkylation of dithianes



Substrates:

1. 1-iodo-but-3-en-2-one
2. 2-Phenyl-1,3-dithiane - *available at Sigma-Aldrich*

Products:

1. C=CC(=O)CC1(c2ccccc2)SCCCS1

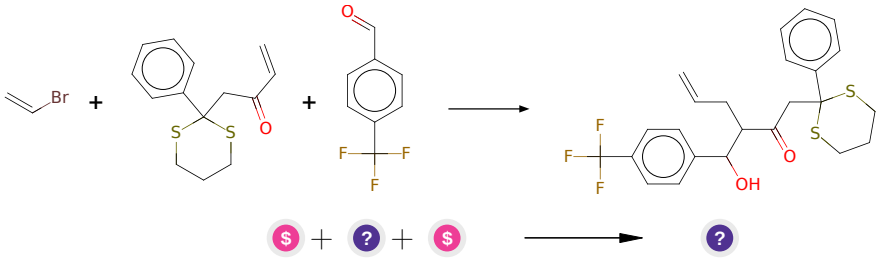
Typical conditions: LDA.THF

Protections: none

Reference: *10.1021/ja055740s* (SI) and *10.1016/S0008-6215(99)00275-X* and *10.1021/ja0618954*

Retrosynthesis ID: 34220

2.3.3 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=CC(=O)CC1(c2ccccc2)SCCCS1
3. Bromoethylene - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC1(c2ccccc2)SCCCS1)C(O)c1ccc(C(F)(F)F)cc1

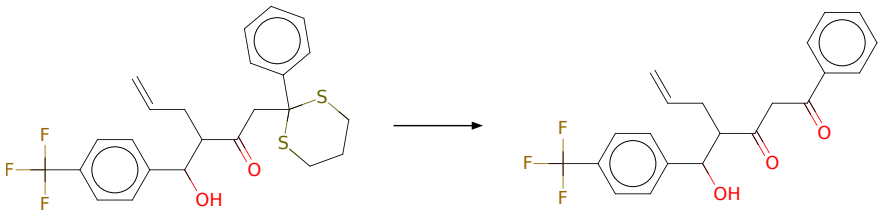
Typical conditions: 1.RCuLi.2.RCHO

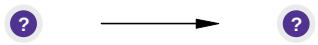
Protections: none

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

2.3.4 Synthesis of ketones from dithianes





Substrates:

1. C=CCC(C(=O)CC1(c2ccccc2)SCCCS1)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

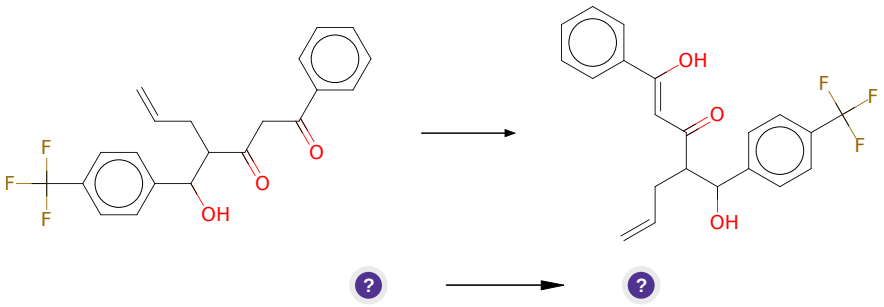
Typical conditions: MeI.CaCO3

Protections: none

Reference: *10.1016/j.tet.2013.09.075* and *10.1021/jo00007a015* and *10.1021/jo0610412* and *10.1021/ol901024t* and *10.1021/ol500553x* and *10.1021/jo0626459*

Retrosynthesis ID: 31724

2.3.5 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

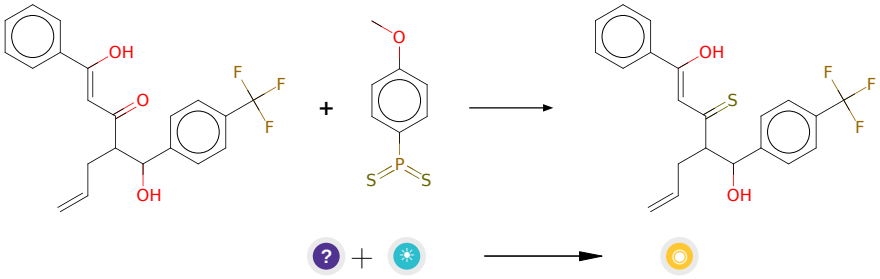
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.3.6 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: `2250145.10`

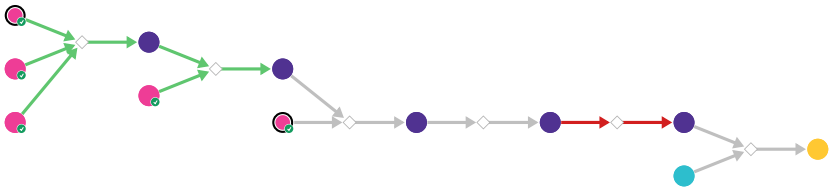
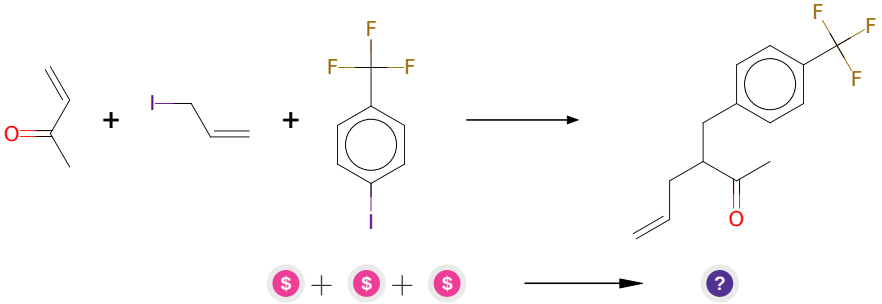


Figure 4: Outline of path 4

2.4.1 Arylation-alkylation of enones and enoate esters



Substrates:

1. 3-Buten-2-one - *available at Sigma-Aldrich*
2. Allyl iodide - *available at Sigma-Aldrich*
3. 4-Iodobenzotrifluoride - *available at Sigma-Aldrich*

Products:

1. C=CCC(Cc1ccc(C(F)(F)F)cc1)C(C)=O

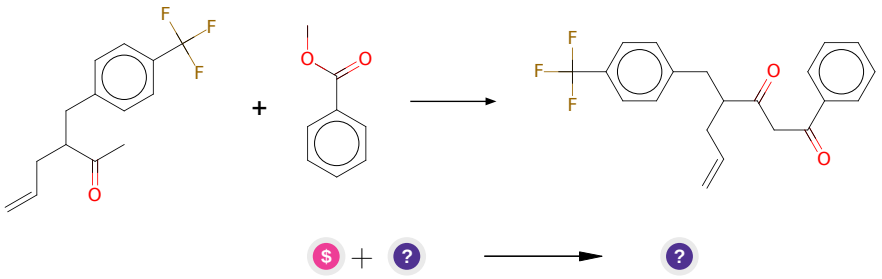
Typical conditions: 1.RCuLi.2.RI.HMPA

Protections: none

Reference: *10.1021/ja003119g* AND *10.1021/ja00093a010* AND *10.1016/S0040-4039(97)01263-X*

Retrosynthesis ID: 12523

2.4.2 Condensation of methyl ketones with esters



Substrates:

1. Methyl benzoate - *available at Sigma-Aldrich*
2. C=CCC(Cc1ccc(C(F)(F)F)cc1)C(C)=O

Products:

1. C=CCC(Cc1ccc(C(F)(F)F)cc1)C(=O)CC(=O)c1ccccc1

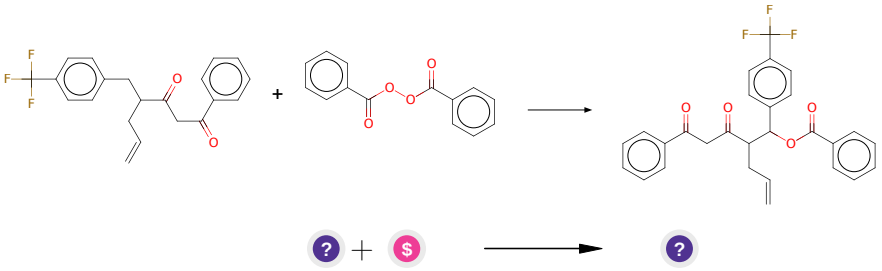
Typical conditions: NaOMe.MeOH

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 Free-radicals synthesis of benzoyl esters



Substrates:

1. C=CCC(Cc1ccc(C(F)(F)F)cc1)C(=O)CC(=O)c1ccccc1
2. Luperox(r) A98 - *available at Sigma-Aldrich*

Products:

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

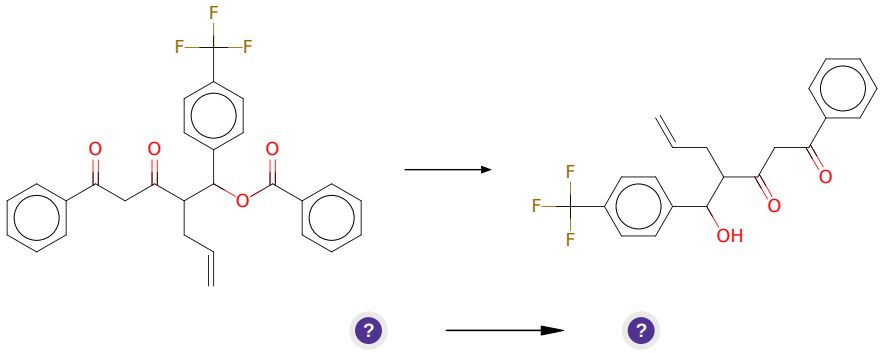
Typical conditions: CuBr

Protections: none

Reference: DOI: *10.1021/jo01265a066*

Retrosynthesis ID: 332

2.4.4 Hydrolysis of benzoates



Substrates:

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

Products:

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

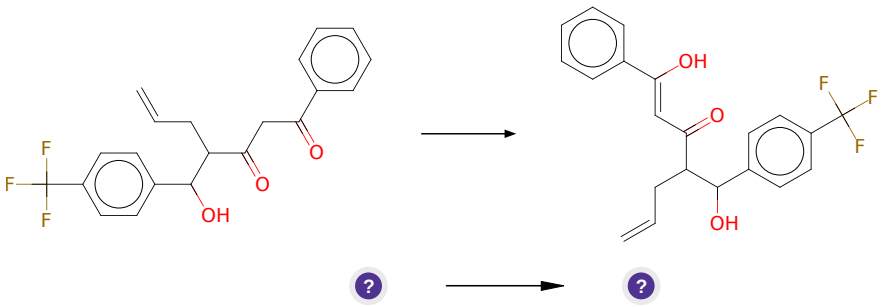
Typical conditions: LiOH/K2CO3/NH3.MeOH.H2O.THF

Protections: none

Reference: *10.1021/jm0502788* and *10.1016/j.tetlet.2008.09.165* and *10.1021/jm034098e* and *10.1021/jo049277y* and *10.1055/s-0033-1338657*

Retrosynthesis ID: 25136

2.4.5 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

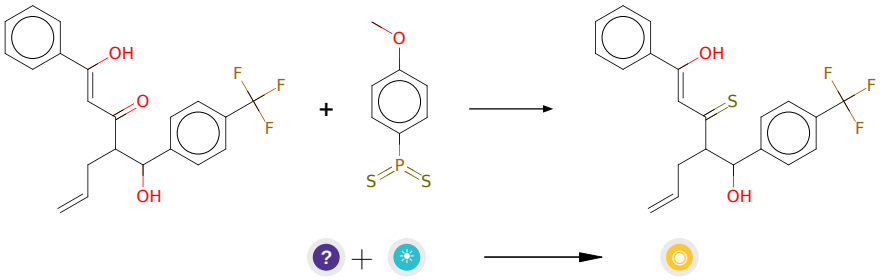
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.4.6 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