Paths of analysis*

Y1A

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

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: `1000164.14`

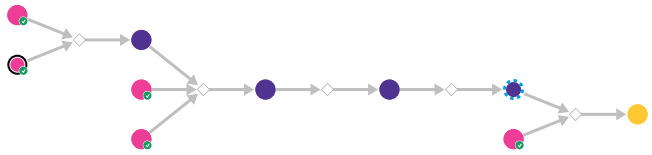
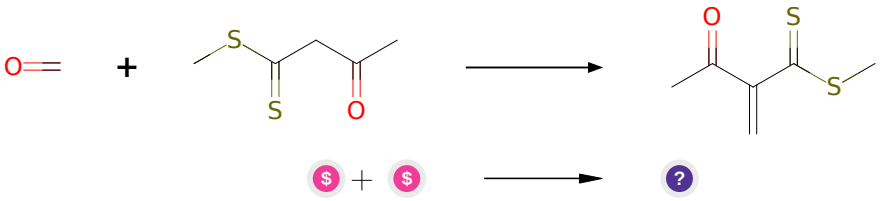


Figure 1: Outline of path 1

2.1.1 Eschenmoser methenylation



Substrates:

1. 4-(methylsulfanyl)-4-sulfanylidenebutan-2-one - *available at Sigma-Aldrich*
2. Formalin - *available at Sigma-Aldrich*

Products:

1. C=C(C(C)=O)C(=S)SC

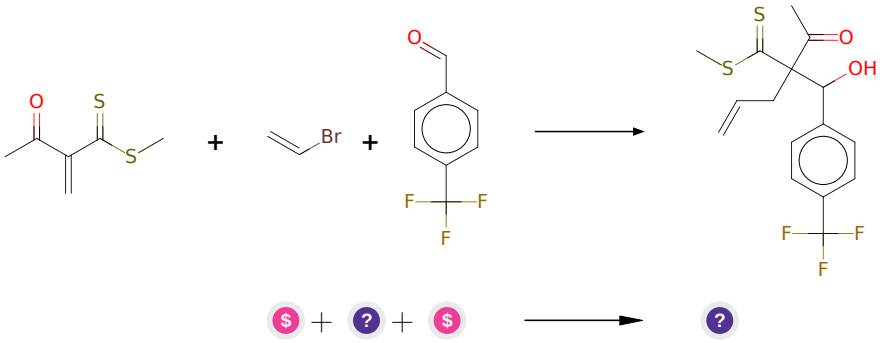
Typical conditions: iPr2NH.TFA.HCHO.or.organocatalyst

Protections: none

Reference: DOI:*10.1016/S0040-4039(00)82176-0* AND DOI:*10.1021/jo052529q* AND DOI:*10.1039/b924577d*

Retrosynthesis ID: 7270

2.1.2 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

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

Products:

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

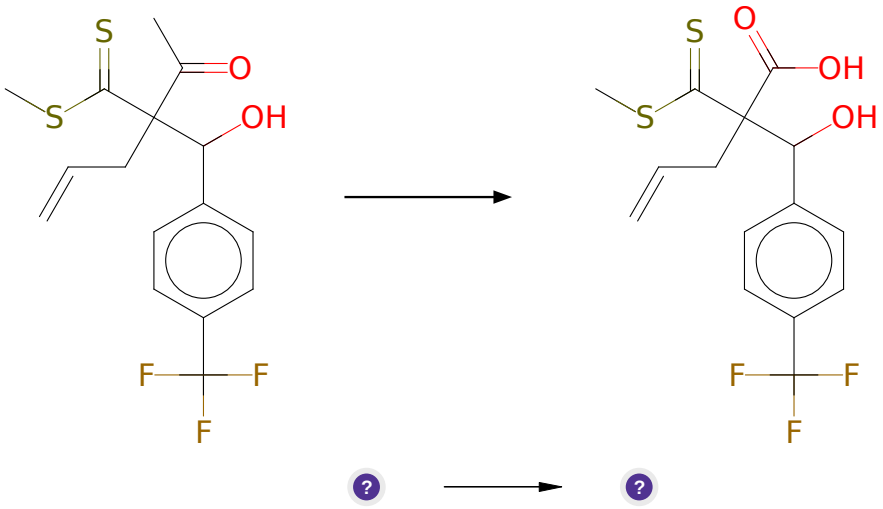
Typical conditions: 1.RCuLi.2.RCHO

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

2.1.3 Synthesis of Carboxylic Acids via Haloform Reaction



Substrates:

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

Products:

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

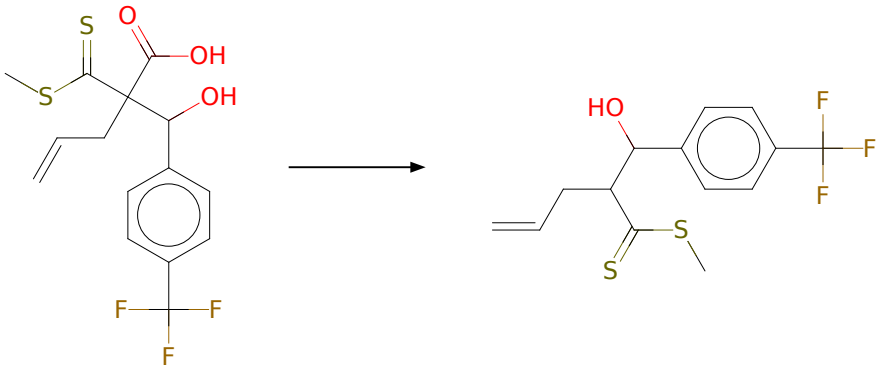
Typical conditions: I2.KI.KOH.H2O.dioxane

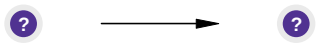
Protections: none

Reference: *10.1021/jacs.8b12242* SI p. S25 and *10.1021/ol5025025* SI p. S27

Retrosynthesis ID: 10366

2.1.4 Decarboxylation of tertiary carboxylic acids





Substrates:

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

Products:

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

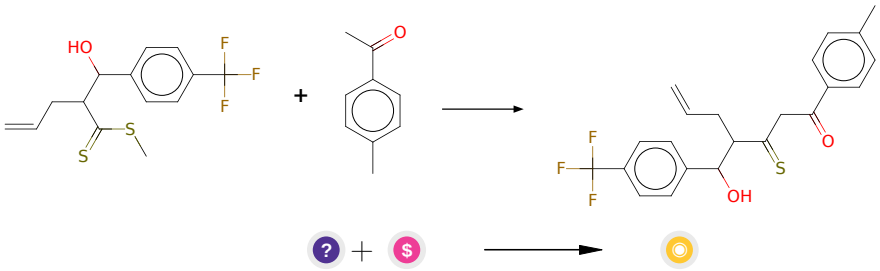
Typical conditions: DMSO.135C

Protections: none

Reference: DOI: *10.1021/jm990630f* AND *10.1016/S0040-4039(99)02191-7*

Retrosynthesis ID: 7791

2.1.5 Condensation of ketones with dithioesters



Substrates:

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

Products:

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

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.2 Path 2

Score: `1000164.14`

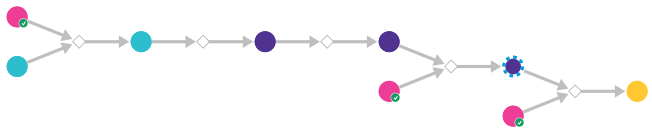
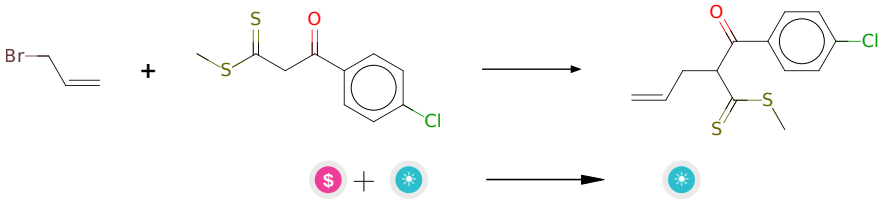


Figure 2: Outline of path 2

2.2.1 Alkylation of ketones



Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*
2. p-chlor-benzoyl-dithioessigsaeure-methylester

Products:

1. a-allyl-a-(p-chlorobenzoyl)dithioacetate

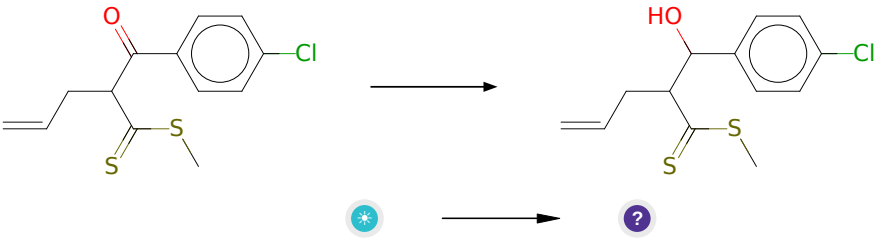
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: *10.1021/jo1019738* OR DOI: *10.1021/jm00114a016*

Retrosynthesis ID: 1866

2.2.2 Reduction of ketones with NaBH4



Substrates:

1. a-allyl-a-(p-chlorobenzoyl)dithioacetate

Products:

1. C=CCC(C(=S)SC)C(O)c1ccc(Cl)cc1

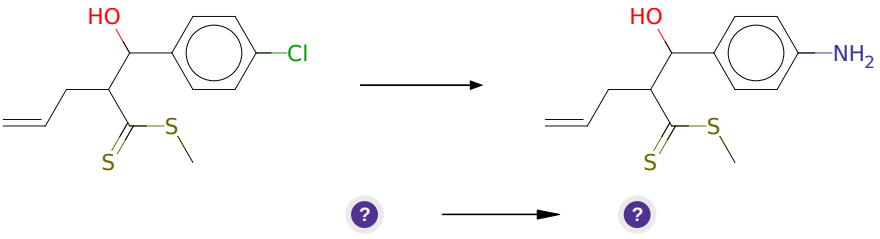
Typical conditions: NaBH4.EtOH.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112360* p. 3, 8 and *10.1016/j.ejmech.2010.10.012* p. 434, 436

Retrosynthesis ID: 50432

2.2.3 Coupling of Ammonia with Aryl Halides



Substrates:

1. C=CCC(C(=S)SC)C(O)c1ccc(Cl)cc1

Products:

1. C=CCC(C(=S)SC)C(O)c1ccc(N)cc1

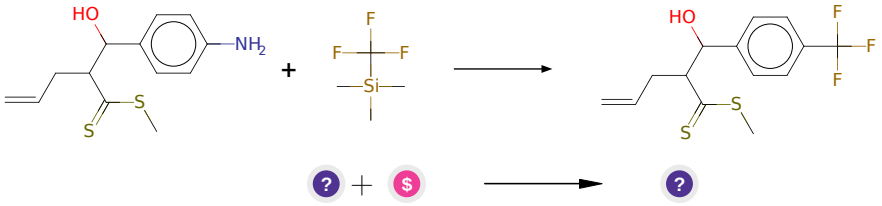
Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

Protections: none

Reference: *10.1021/ja903049z* and *10.1021/ol027119s* and *10.1021/jo9006738*

Retrosynthesis ID: 10142

2.2.4 One-Pot Sandmeyer Trifluoromethylation



Substrates:

1. C=CCC(C(=S)SC)C(O)c1ccc(N)cc1
2. TFMTMS - *available at Sigma-Aldrich*

Products:

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

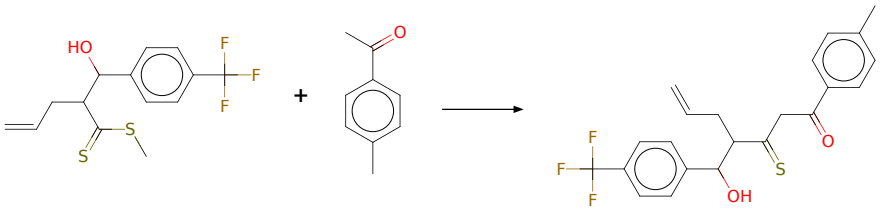
Typical conditions: 1.pTSA.tBuONO.2.TMSCF3.CuSCN.Cs2CO3.MeCN.rt or AgCF3

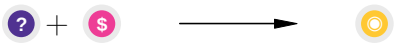
Protections: none

Reference: *10.1002/adsc.201400340* and *10.1021/ja4056239*

Retrosynthesis ID: 10000381

2.2.5 Condensation of ketones with dithioesters





Substrates:

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

Products:

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

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

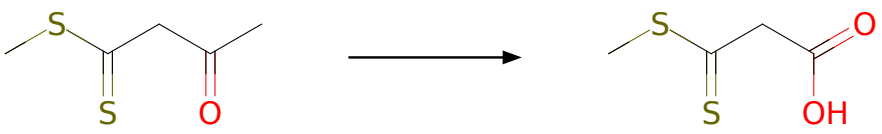
Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.3 Path 3

Score: `1000176.35`

2.3.1 Synthesis of Carboxylic Acids via Haloform Reaction



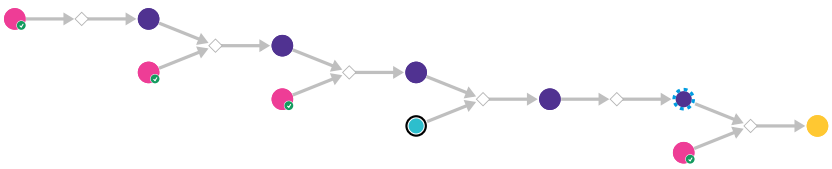
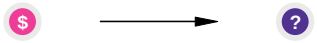


Figure 3: Outline of path 3



Substrates:

1. 4-(methylsulfanyl)-4-sulfanylidenebutan-2-one - *available at Sigma-Aldrich*

Products:

1. CSC(=S)CC(=O)O

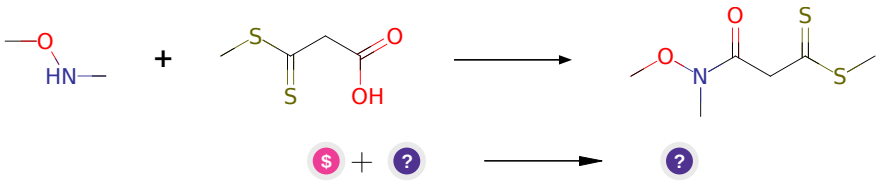
Typical conditions: I2.KI.KOH.H2O.dioxane

Protections: none

Reference: *10.1021/jacs.8b12242* SI p. S25 and *10.1021/ol5025025* SI p. S27

Retrosynthesis ID: 10366

2.3.2 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. n-methoxymethylamine - *available at Sigma-Aldrich*
2. CSC(=S)CC(=O)O

Products:

1. CON(C)C(=O)CC(=S)SC

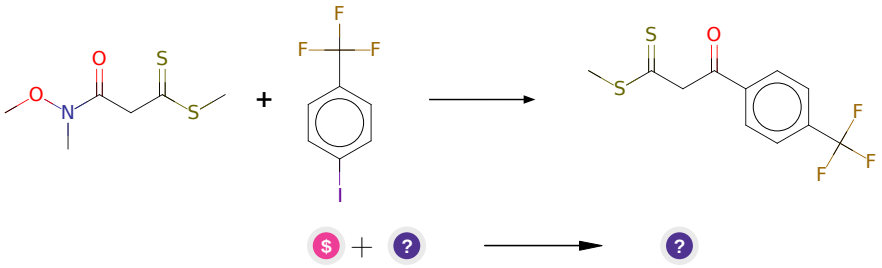
Typical conditions: DCC.DMAP or CDI.TEA.DCM

Protections: none

Reference: Patent: WO2007/67333A2, 2007 & *10.1016/j.bmcl.2008.09.100*

Retrosynthesis ID: 1152

2.3.3 Synthesis of ketones from Weinreb amides



Substrates:

1. 4-Iodobenzotrifluoride - *available at Sigma-Aldrich*
2. CON(C)C(=O)CC(=S)SC

Products:

1. CSC(=S)CC(=O)c1ccc(C(F)(F)F)cc1

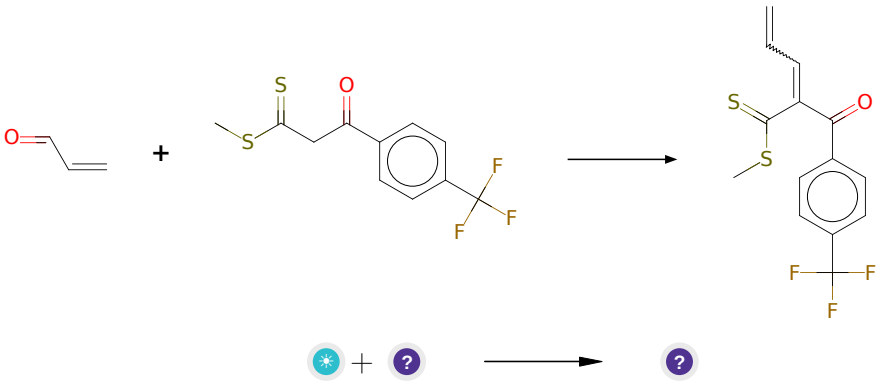
Typical conditions: 1.RmgBr.THF 2.TFA.DCM

Protections: none

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 5060

2.3.4 Aldol Condensation



Substrates:

1. Acrolein
2. CSC(=S)CC(=O)c1ccc(C(F)(F)F)cc1

Products:

1. C=CC=C(C(=O)c1ccc(C(F)(F)F)cc1)C(=S)SC

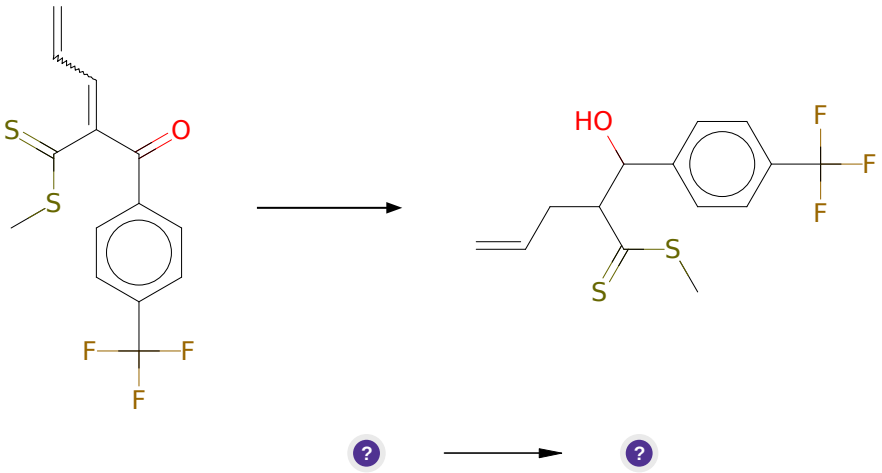
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.3.5 Reduction of enones to saturated alcohols



Substrates:

1. C=CC=C(C(=O)c1ccc(C(F)(F)F)cc1)C(=S)SC

Products:

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

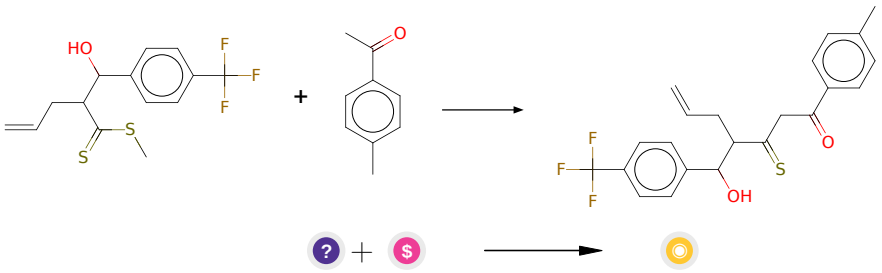
Typical conditions: NaBH4.transition.metal.salt.(eg.Pd(OAc)2.or.CeCl3)

Protections: none

Reference: *10.1080/00397910902788117* AND *10.1021/jo00235a009* AND *10.1016/0040-4020(95)00125-R* AND *10.1021/ja01327a041* AND *10.1021/jo00302a056* AND *10.1002/adsc.200900628*

Retrosynthesis ID: 15304

2.3.6 Condensation of ketones with dithioesters



Substrates:

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

Products:

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

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.4 Path 4

Score: 1000176.35

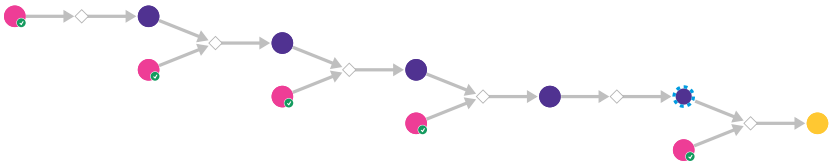
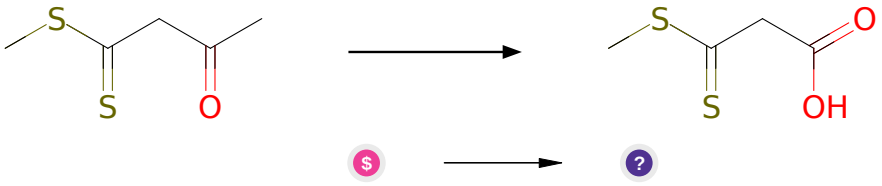


Figure 4: Outline of path 4

2.4.1 Synthesis of Carboxylic Acids via Haloform Reaction



Substrates:

1. 4-(methylsulfanyl)-4-sulfanylidenebutan-2-one - *available at Sigma-Aldrich*

Products:

1. CSC(=S)CC(=O)O

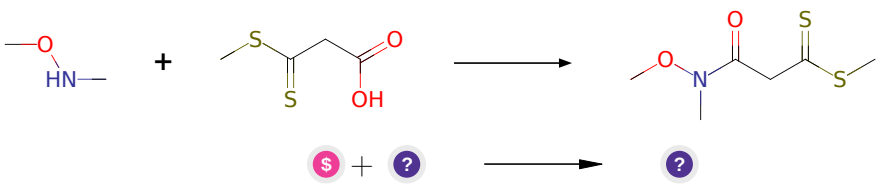
Typical conditions: I2.KI.KOH.H2O.dioxane

Protections: none

Reference: *10.1021/jacs.8b12242* SI p. S25 and *10.1021/ol5025025* SI p. S27

Retrosynthesis ID: 10366

2.4.2 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. n-methoxymethylamine - *available at Sigma-Aldrich*
2. CSC(=S)CC(=O)O

Products:

1. CON(C)C(=O)CC(=S)SC

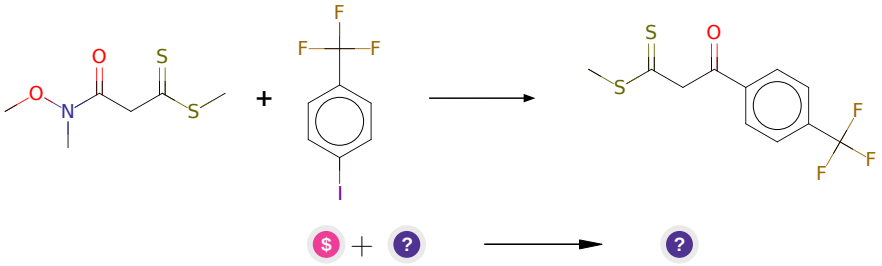
Typical conditions: DCC.DMAP or CDI.TEA.DCM

Protections: none

Reference: Patent: WO2007/67333A2, 2007 & *10.1016/j.bmcl.2008.09.100*

Retrosynthesis ID: 1152

2.4.3 Synthesis of ketones from Weinreb amides



Substrates:

1. 4-Iodobenzotrifluoride - *available at Sigma-Aldrich*
2. CON(C)C(=O)CC(=S)SC

Products:

1. CSC(=S)CC(=O)c1ccc(C(F)(F)F)cc1

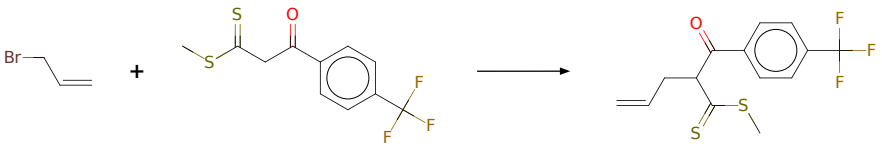
Typical conditions: 1.RmgBr.THF 2.TFA.DCM

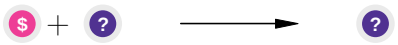
Protections: none

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 5060

2.4.4 Alkylation of ketones





Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*
2. CSC(=S)CC(=O)c1ccc(C(F)(F)F)cc1

Products:

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

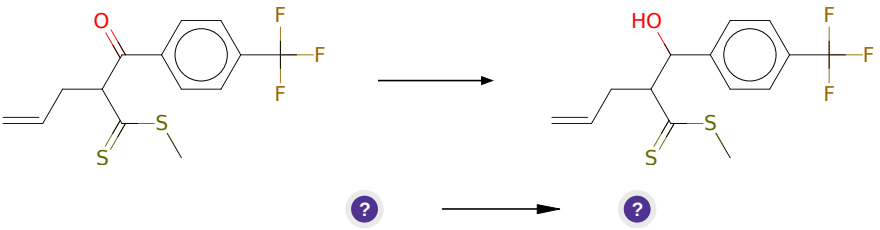
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: *10.1021/jo1019738* OR DOI: *10.1021/jm00114a016*

Retrosynthesis ID: 1866

2.4.5 Reduction of ketones with NaBH4



Substrates:

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

Products:

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

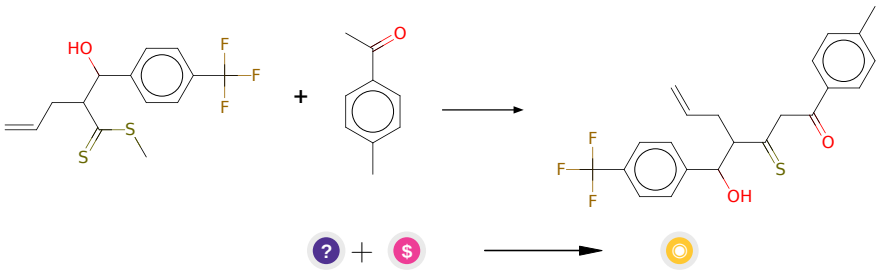
Typical conditions: NaBH4.EtOH.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112360* p. 3, 8 and *10.1016/j.ejmech.2010.10.012* p. 434, 436

Retrosynthesis ID: 50432

2.4.6 Condensation of ketones with dithioesters



Substrates:

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

Products:

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

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.5 Path 5

Score: 1000176.35

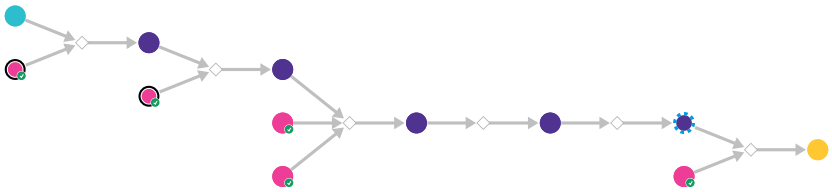
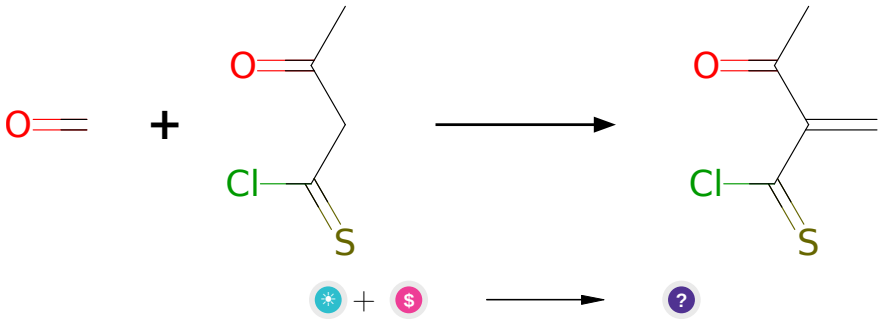


Figure 5: Outline of path 5

2.5.1 Eschenmoser methenylation



Substrates:

1. C4H5ClOS
2. Formalin - *available at Sigma-Aldrich*

Products:

1. C=C(C(C)=O)C(=S)Cl

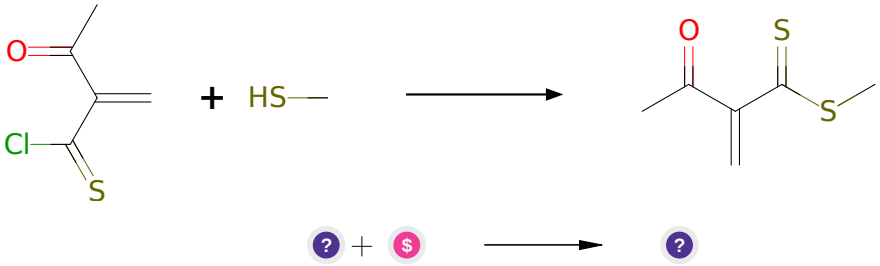
Typical conditions: iPr2NH.TFA.HCHO.or.organocatalyst

Protections: none

Reference: DOI:*10.1016/S0040-4039(00)82176-0* AND DOI:*10.1021/jo052529q* AND DOI:*10.1039/b924577d*

Retrosynthesis ID: 7270

2.5.2 Reaction of acyl chlorides with thiols and thiophenols



Substrates:

1. C=C(C(C)=O)C(=S)Cl
2. Methanethiol - *available at Sigma-Aldrich*

Products:

1. C=C(C(C)=O)C(=S)SC

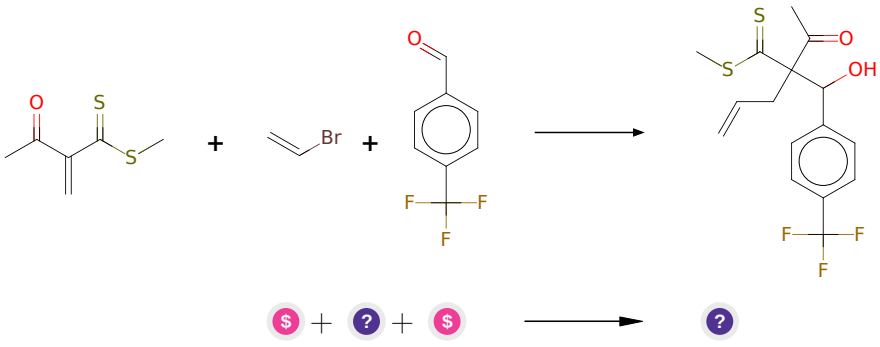
Typical conditions: NEt3.solvent

Protections: none

Reference: *10.3891/acta.chem.scand.53-0594* AND *10.1016/j.bmc.2004.10.021* AND *10.1016/j.tetlet.2011.05.115* AND *10.1016/j.tetlet.2010.09.066* AND *10.1021/jo00095a047* AND *10.1021/ja8033763* AND *10.1021/ol0266828*

Retrosynthesis ID: 14596

2.5.3 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. C=C(C(C)=O)C(=S)SC

3. Bromoethylene - *available at Sigma-Aldrich*

Products:

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

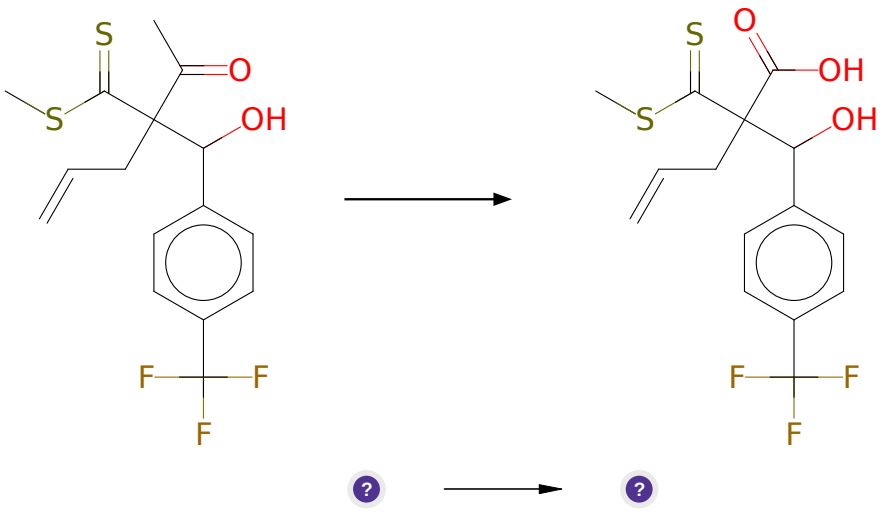
Typical conditions: 1.RCuLi.2.RCHO

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

2.5.4 Synthesis of Carboxylic Acids via Haloform Reaction



Substrates:

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

Products:

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

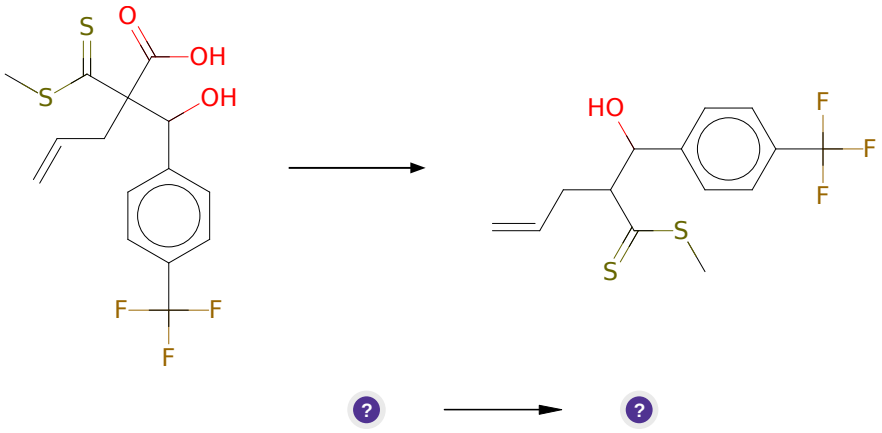
Typical conditions: I2.KI.KOH.H2O.dioxane

Protections: none

Reference: *10.1021/jacs.8b12242* SI p. S25 and *10.1021/ol5025025* SI p. S27

Retrosynthesis ID: 10366

2.5.5 Decarboxylation of tertiary carboxylic acids



Substrates:

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

Products:

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

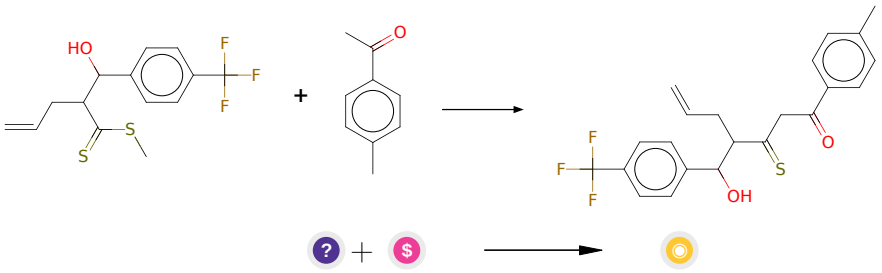
Typical conditions: DMSO.135C

Protections: none

Reference: DOI: *10.1021/jm990630f* AND *10.1016/S0040-4039(99)02191-7*

Retrosynthesis ID: 7791

2.5.6 Condensation of ketones with dithioesters



Substrates:

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

Products:

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

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413