Paths of analysis*

Y6A

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`

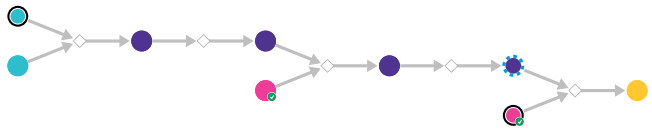
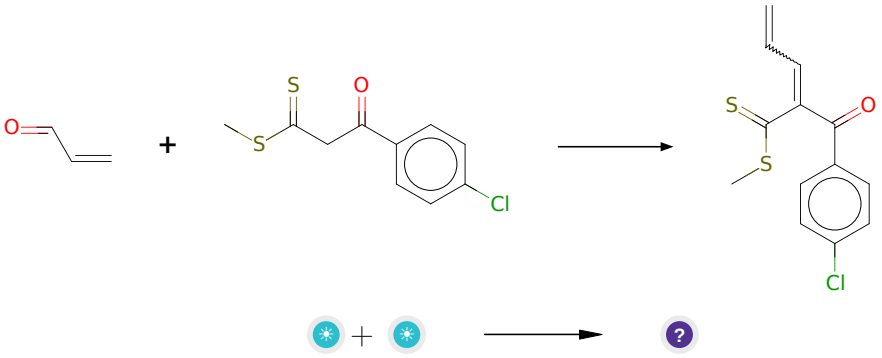


Figure 1: Outline of path 1

2.1.1 Aldol Condensation



Substrates:

1. Acrolein
2. p-chlor-benzoyl-dithioessigsaeure-methylester

Products:

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

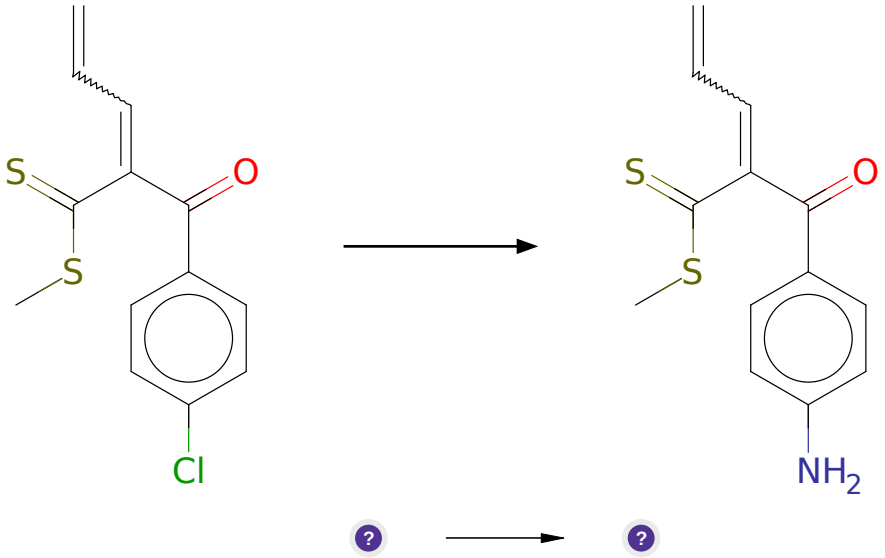
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.1.2 Amination of aryl chlorides



Substrates:

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

Products:

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

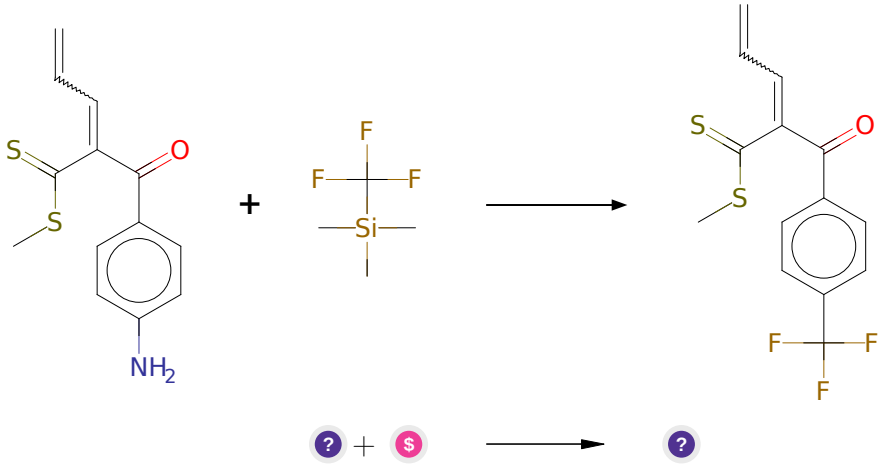
Typical conditions: [Pd].Ligand.base

Protections: none

Reference: *10.1021/ja903049z* and *10.1021/jo060945k* and *10.1021/jo060190h* and *10.1021/ja8055358* and *10.1021/ja068926f* and *10.1002/anie.200601612* and *10.1021/acscatal.0c04280*

Retrosynthesis ID: 28545

2.1.3 One-Pot Sandmeyer Trifluoromethylation



Substrates:

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

Products:

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

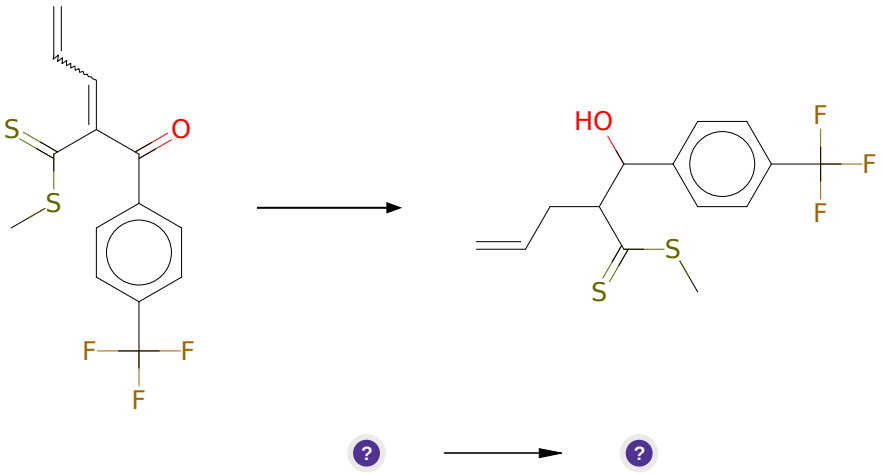
Typical conditions: 1.pTSA.tBuONO.2.TMSCF3.CuSCN.Cs2CO3.MeCN.rt or AgCF3

Protections: none

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

Retrosynthesis ID: 10000381

2.1.4 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

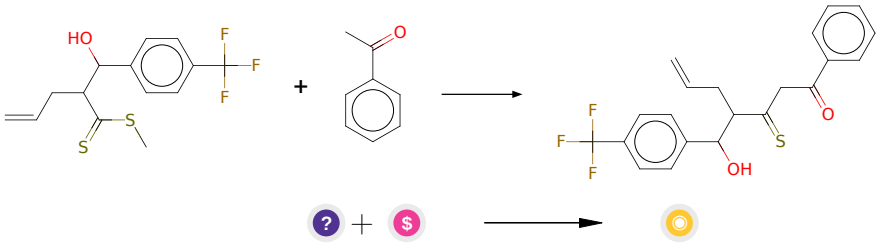
Typical conditions: NaBH4.transition.metal.salt.(eg.Pd(OAc)2.or.CeCl3)

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

2.1.5 Condensation of ketones with dithioesters



Substrates:

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

2. Acetophenone - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=S)CC(=O)c1ccccc1)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`

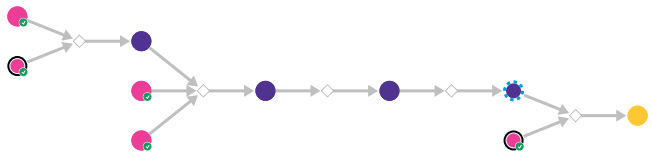
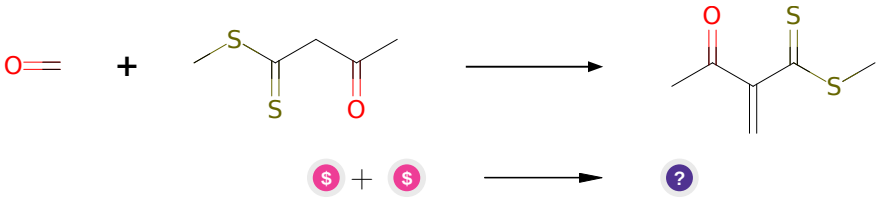


Figure 2: Outline of path 2

2.2.1 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

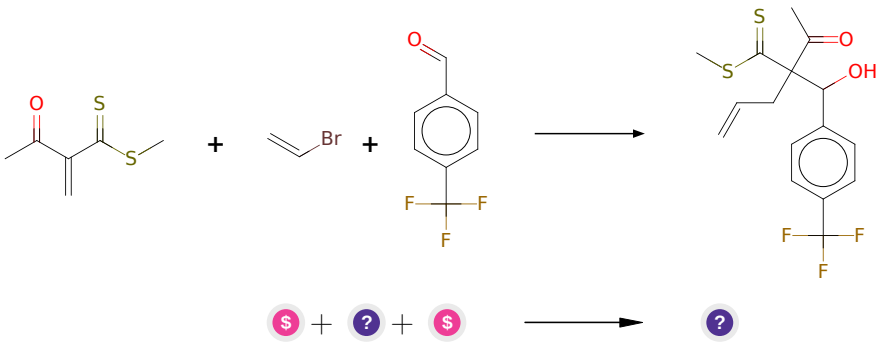
Typical conditions: iPr2NH.TFA.HCHO.or.organocatalyst

Protections: none

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

Retrosynthesis ID: 7270

2.2.2 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

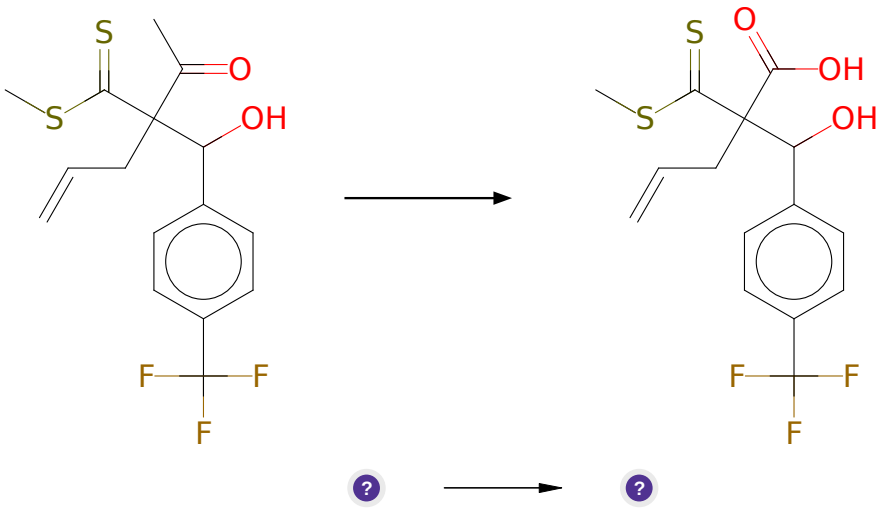
Typical conditions: 1.RCuLi.2.RCHO

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

2.2.3 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

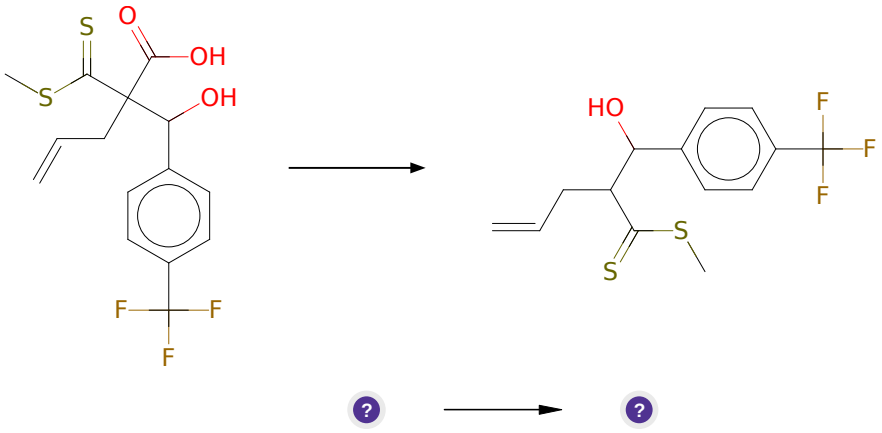
Typical conditions: I2.KI.KOH.H2O.dioxane

Protections: none

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

Retrosynthesis ID: 10366

2.2.4 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

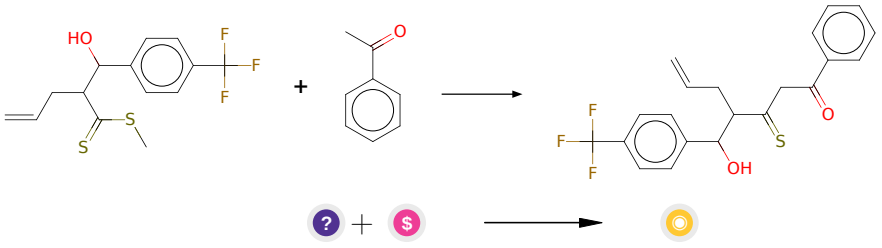
Typical conditions: DMSO.135C

Protections: none

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

Retrosynthesis ID: 7791

2.2.5 Condensation of ketones with dithioesters



Substrates:

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

Products:

1. C=CCC(C(=S)CC(=O)c1ccccc1)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 (TB-DMS) Methyl Ether

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

Retrosynthesis ID: 9996413

2.3 Path 3

Score: `1000164.14`

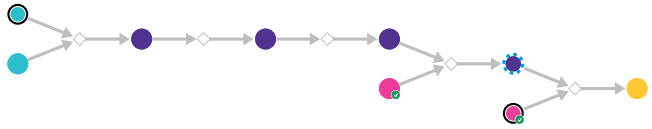
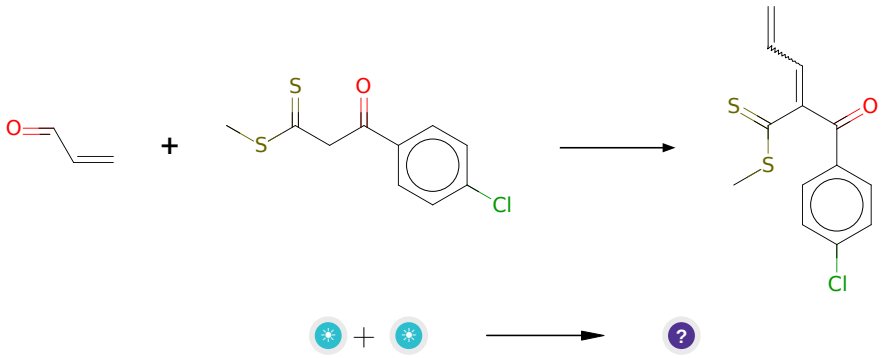


Figure 3: Outline of path 3

2.3.1 Aldol Condensation



Substrates:

1. Acrolein
2. p-chlor-benzoyl-dithioessigsaeure-methylester

Products:

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

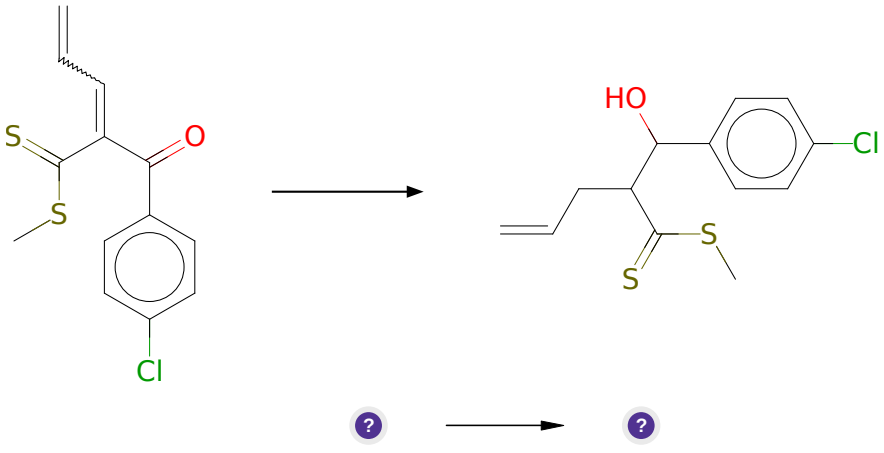
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.3.2 Reduction of enones to saturated alcohols



Substrates:

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

Products:

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

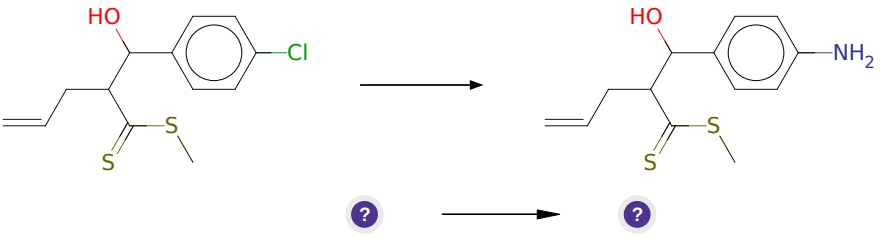
Typical conditions: NaBH4.transition.metal.salt.(eg.Pd(OAc)2.or.CeCl3)

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

2.3.3 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

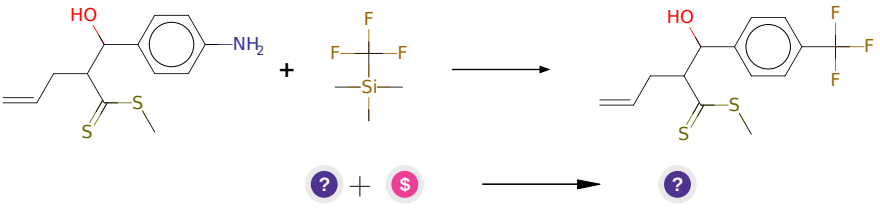
Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

Protections: none

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

Retrosynthesis ID: 10142

2.3.4 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

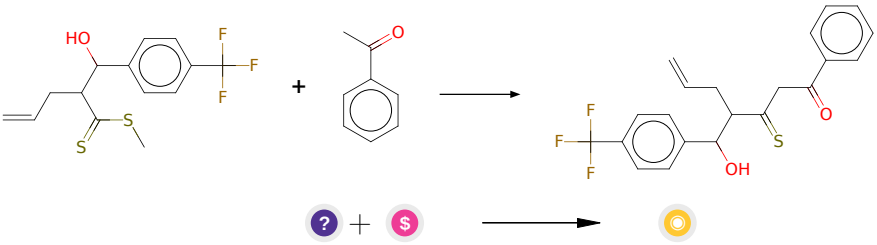
Typical conditions: 1.pTSA.tBuONO.2.TMSCF3.CuSCN.Cs2CO3.MeCN.rt or AgCF3

Protections: none

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

Retrosynthesis ID: 10000381

2.3.5 Condensation of ketones with dithioesters



Substrates:

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

Products:

1. C=CCC(C(=S)CC(=O)c1ccccc1)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: `1000164.14`

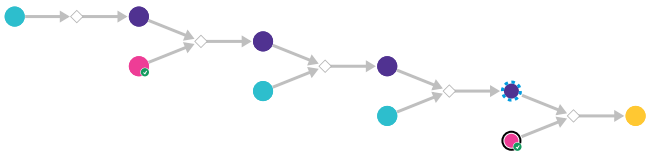
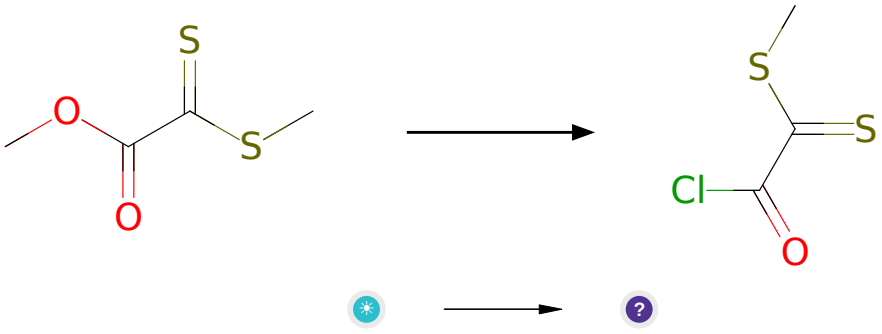


Figure 4: Outline of path 4

2.4.1 Synthesis of acid chlorides from esters



Substrates:

1. dimethyl-1,1-dithiooxalat

Products:

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

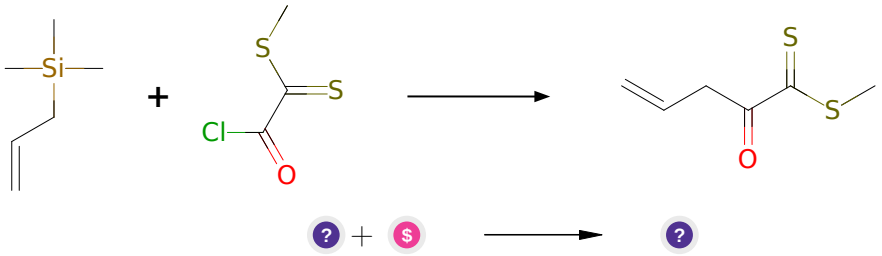
Typical conditions: 1. LiOH.H2O.THF.2. evaporate.3.SOCl2.or.oxalyl.chloride

Protections: none

Reference: *10.1021/ja073476s* and *10.1016/j.tet.2007.04.043* and *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24406

2.4.2 Hosomi-Sakurai Reaction



Substrates:

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

Products:

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

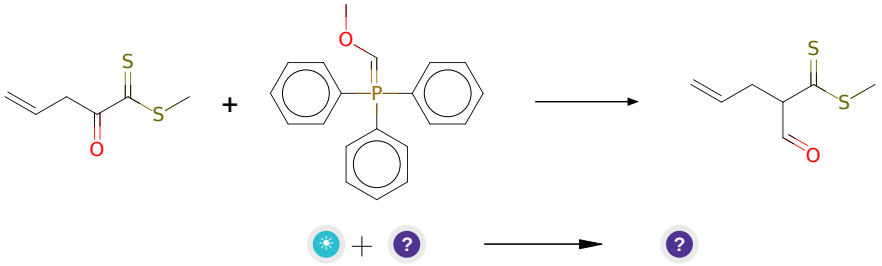
Typical conditions: CuBr.TMS.OTf.TiCl3.acetonitrile.THF.-78 C to rt

Protections: none

Reference: *10.1016/S0040-4039(00)78044-0* and *10.1021/jo0105641* and *10.1246/cl.1976.941* and *10.1021/ar00149a004*

Retrosynthesis ID: 11036

2.4.3 Olefination of ketones followed by hydrolysis



Substrates:

1. triphenylphosphonium methoxymethylide
2. C=CCC(=O)C(=S)SC

Products:

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

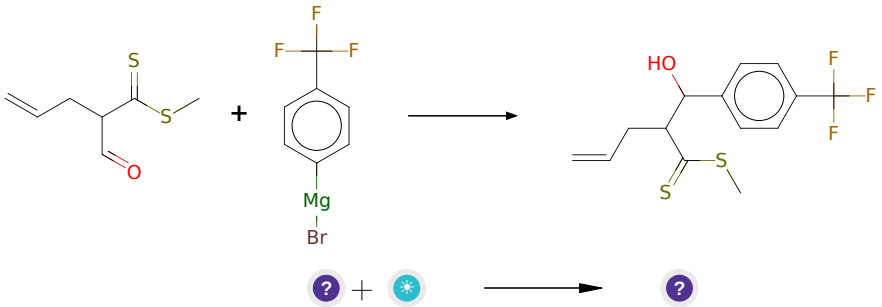
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014861

2.4.4 Grignard-Type Reaction



Substrates:

1. C=CCC(C=O)C(=S)SC
2. (4-trifluormethyl-phenyl)-magensium-bromid

Products:

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

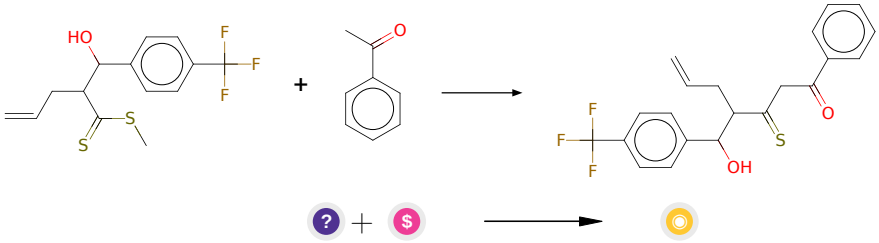
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1055/s-0030-1260809* or *10.1021/jm061429p* or *10.1021/jo0621423* or *10.1021/ja00373a036* or *10.1016/S0040-4020(01)00457-4*

Retrosynthesis ID: 25123

2.4.5 Condensation of ketones with dithioesters



Substrates:

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

Products:

1. C=CCC(C(=S)CC(=O)c1ccccc1)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

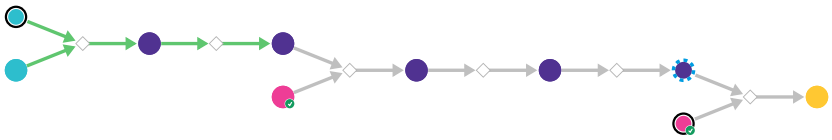
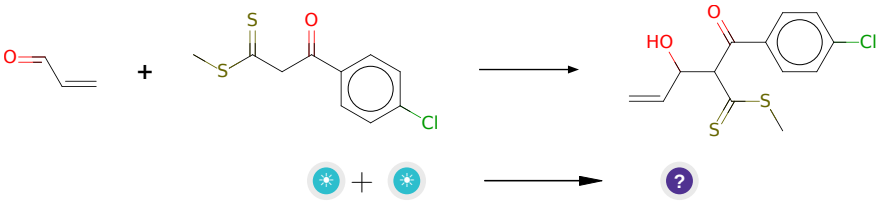


Figure 5: Outline of path 5

2.5.1 Aldol Addition



Substrates:

1. Acrolein
2. p-chlor-benzoyl-dithioessigsaeure-methylester

Products:

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

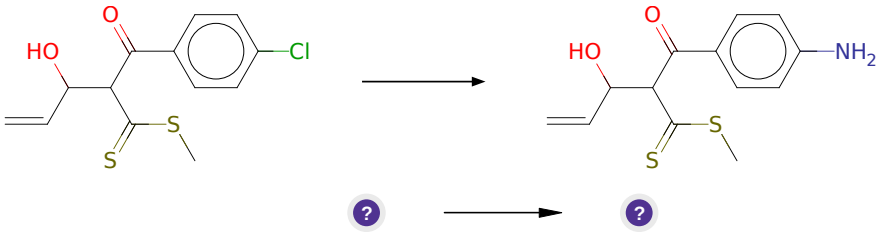
Typical conditions: LDA.THF

Protections: none

Reference: *10.1021/ja991507g* and *10.1002/anie.200906662* and *10.1007/s10593-011-0669-4* and *10.1021/ol0606435*

Retrosynthesis ID: 14924

2.5.2 Nucleophilic aromatic substitution



Substrates:

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

Products:

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

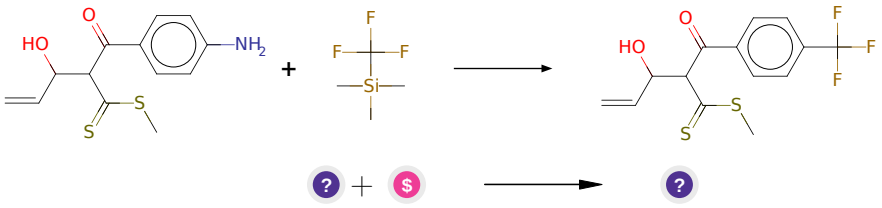
Typical conditions: solvent. Heating or pressure

Protections: none

Reference: *10.1021/jm00040a009* or *10.1111/bph.12233* or *10.1246/cl.1987.1187*

Retrosynthesis ID: 5003

2.5.3 One-Pot Sandmeyer Trifluoromethylation



Substrates:

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

Products:

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

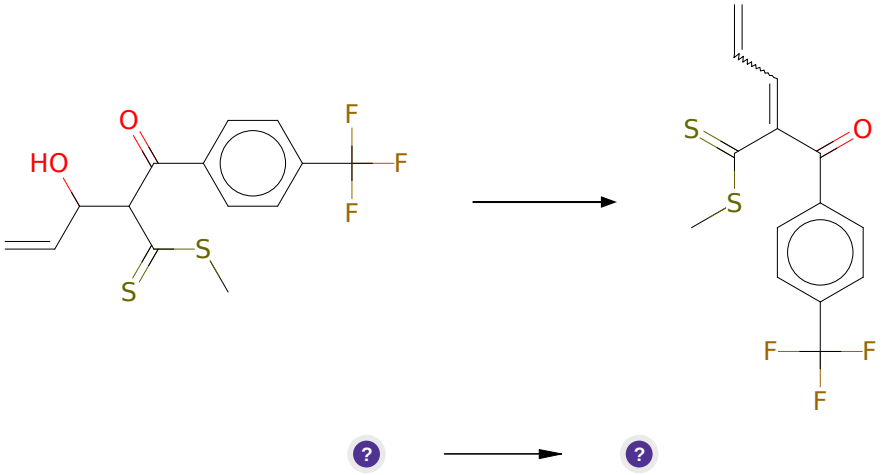
Typical conditions: 1.pTSA.tBuONO.2.TMSCF3.CuSCN.Cs2CO3.MeCN.rt or AgCF3

Protections: none

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

Retrosynthesis ID: 10000381

2.5.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

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

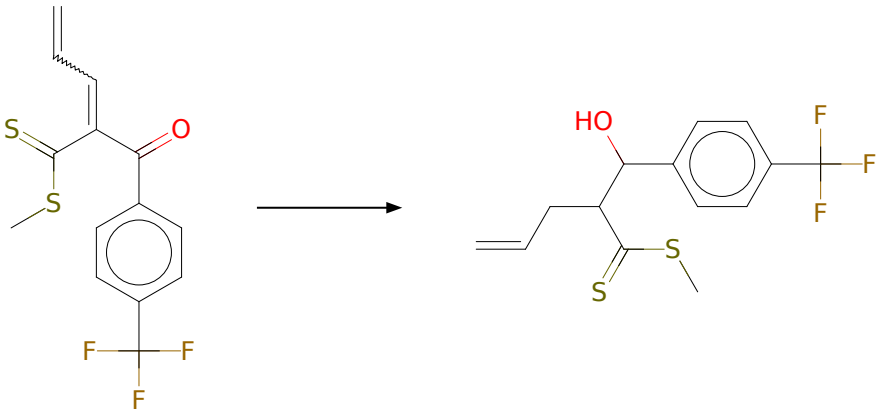
Typical conditions: TsOH

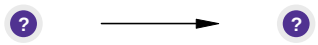
Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7731

2.5.5 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

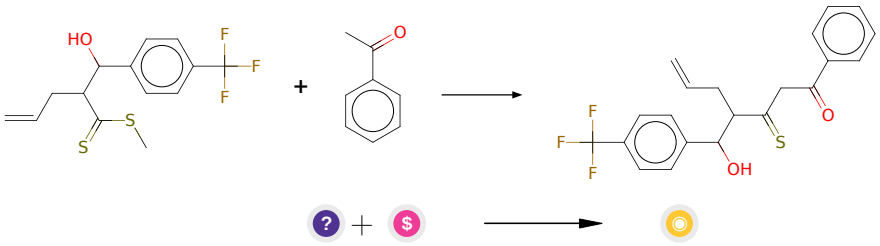
Typical conditions: NaBH4.transition.metal.salt.(eg.Pd(OAc)2.or.CeCl3)

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

2.5.6 Condensation of ketones with dithioesters



Substrates:

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

Products:

1. C=CCC(C(=S)CC(=O)c1ccccc1)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