Paths of analysis*

Y5

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

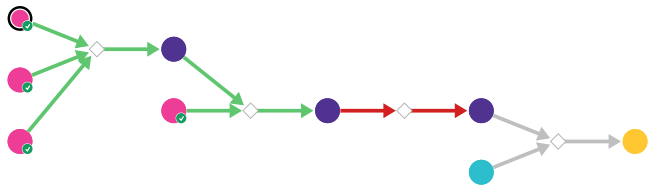
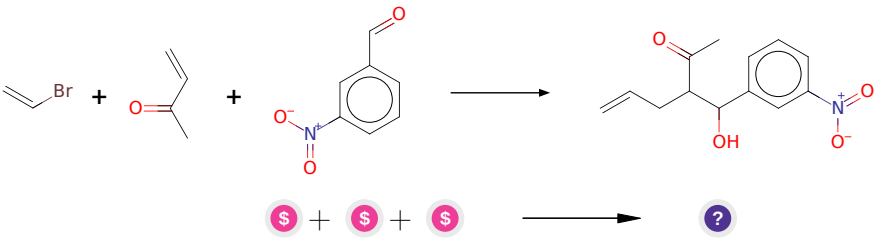


Figure 1: Outline of path 1

2.1.1 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. 3-Buten-2-one - *available at Sigma-Aldrich*
2. Bromoethylene - *available at Sigma-Aldrich*
3. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(C)=O)C(O)c1cccc([N+](=O)[O-])c1

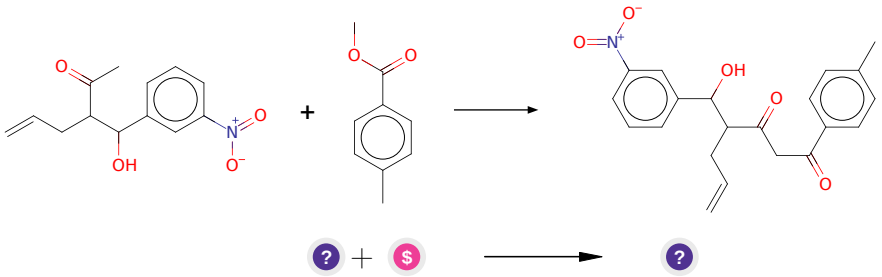
Typical conditions: 1.RCuLi.2.RCHO

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)c1cccc([N+](=O)[O-])c1
2. Methyl p-toluate - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

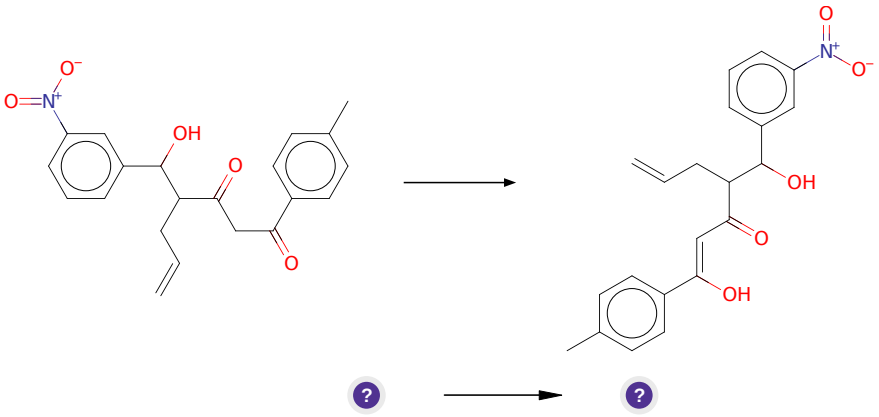
Typical conditions: NaOMe.MeOH

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)c1cccc([N+](=O)[O-])c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

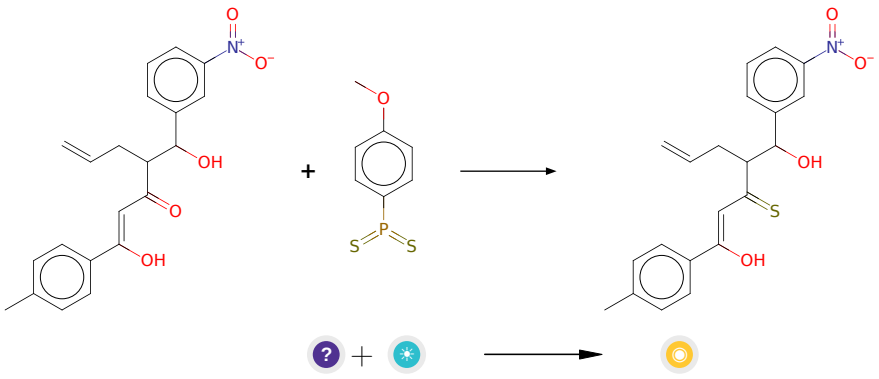
Typical conditions: solvent

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)c1cccc([N+](=O)[O-])c1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.2 Path 2

Score: `2250115.31`

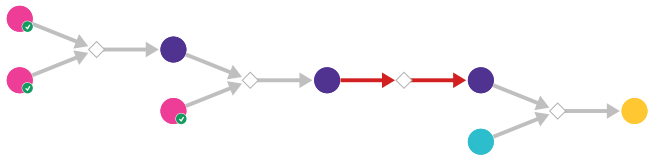
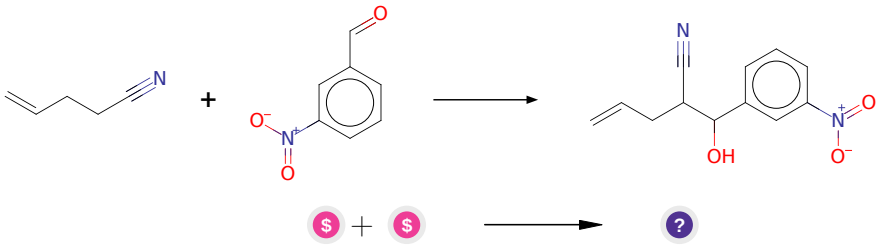


Figure 2: Outline of path 2

2.2.1 Aldol-like condensation with nitriles



Substrates:

1. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*
2. 4-Pentenenitrile - *available at Sigma-Aldrich*

Products:

1. C=CCC(C#N)C(O)c1cccc([N+](=O)[O-])c1

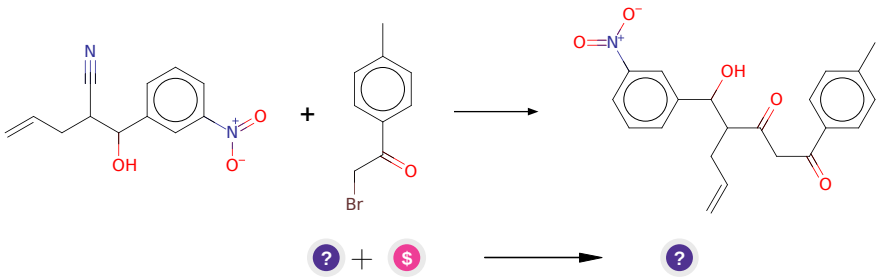
Typical conditions: LDA.THF.cooling

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)c1cccc([N+](=O)[O-])c1
2. 2-Bromo-4'-methylacetophenone - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

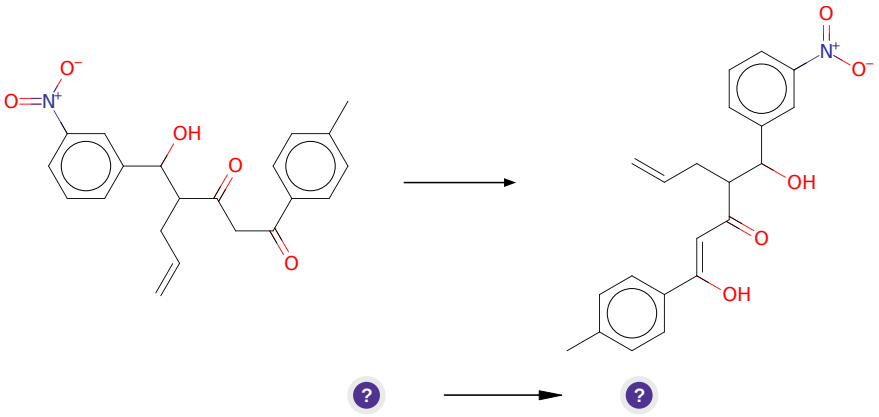
Typical conditions: Zn.TMSCl.THF then HCl

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)c1cccc([N+](=O)[O-])c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

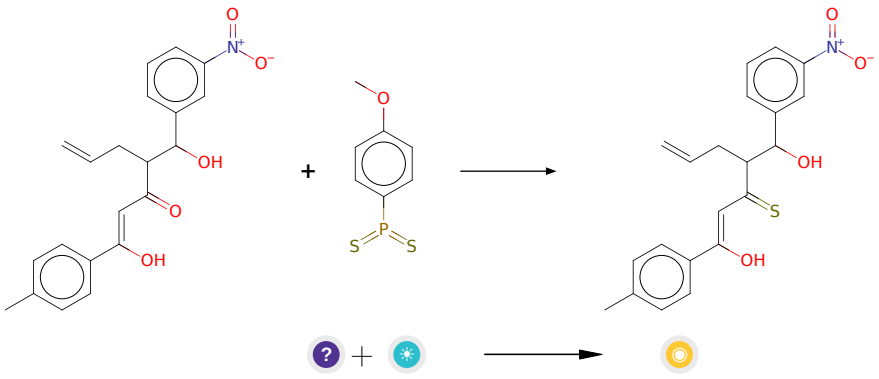
Typical conditions: solvent

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)c1cccc([N+](=O)[O-])c1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.3 Path 3

Score: `2250115.31`

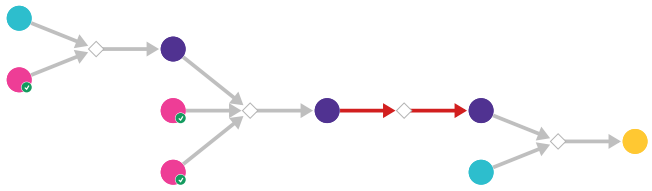
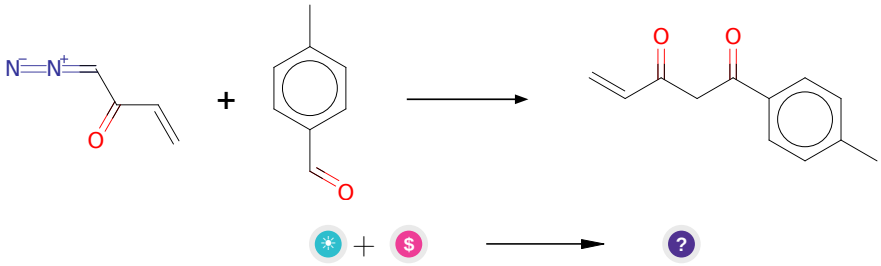


Figure 3: Outline of path 3

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

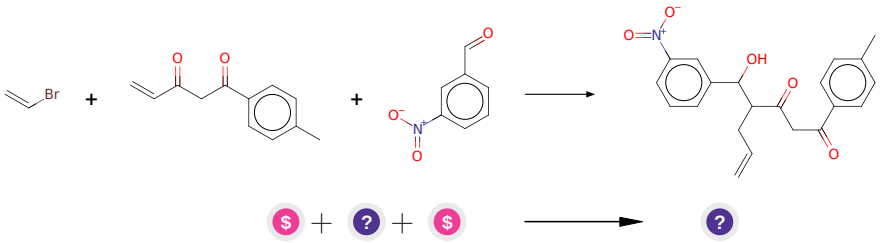
Typical conditions: Lewis.acid

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. Bromoethylene - *available at Sigma-Aldrich*
2. C=CC(=O)CC(=O)c1ccc(C)cc1
3. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

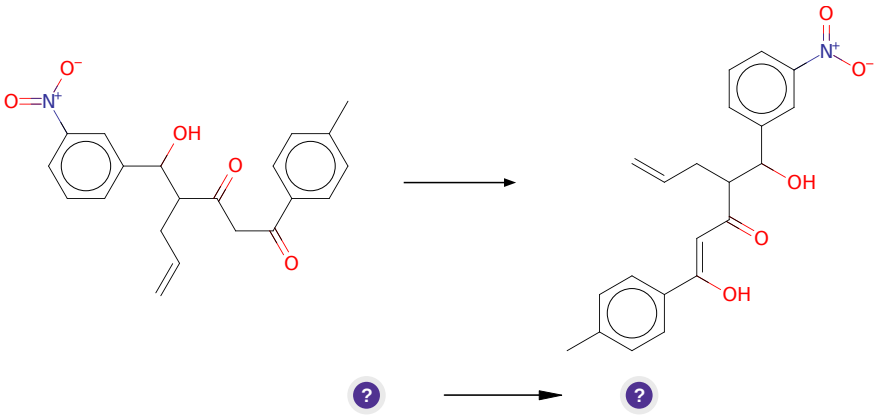
Typical conditions: 1.RCuLi.2.RCHO

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)c1cccc([N+](=O)[O-])c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

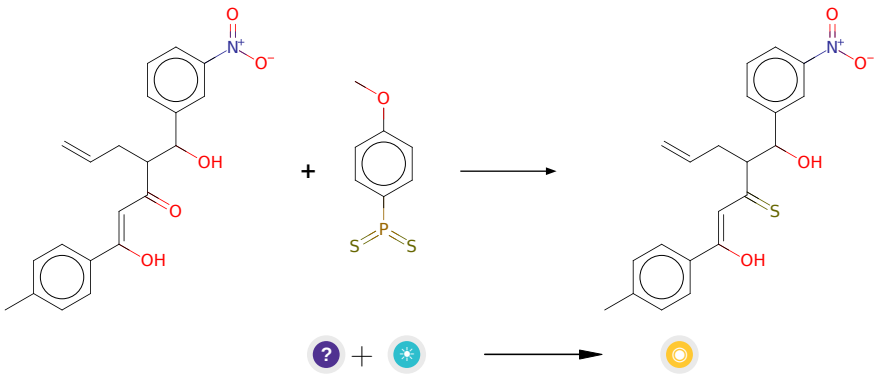
Typical conditions: solvent

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)c1cccc([N+](=O)[O-])c1

2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.4 Path 4

Score: 2250132.89

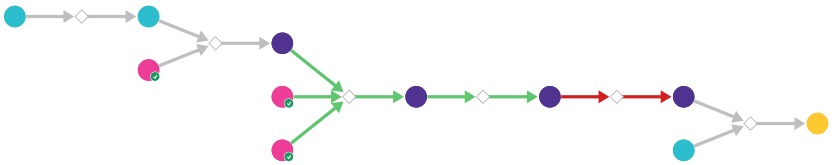
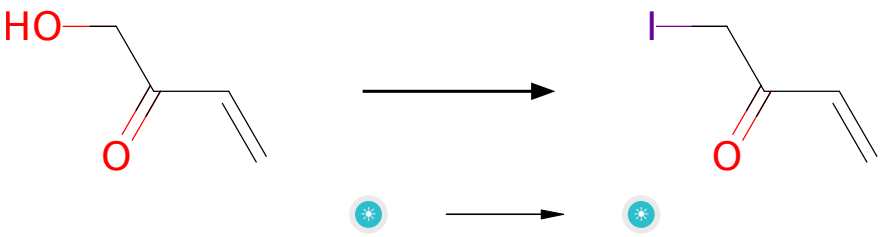


Figure 4: Outline of path 4

2.4.1 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

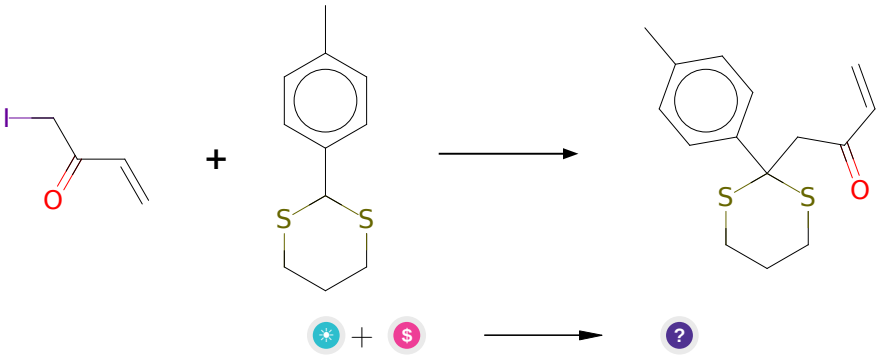
Typical conditions: Imidazole.PPh3.I2

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

2.4.2 Alkylation of dithianes



Substrates:

1. 1-iodo-but-3-en-2-one
2. 2-p-tolyl-[1,3]dithiane - *available at Sigma-Aldrich*

Products:

1. C=CC(=O)CC1(c2ccc(C)cc2)SCCCS1

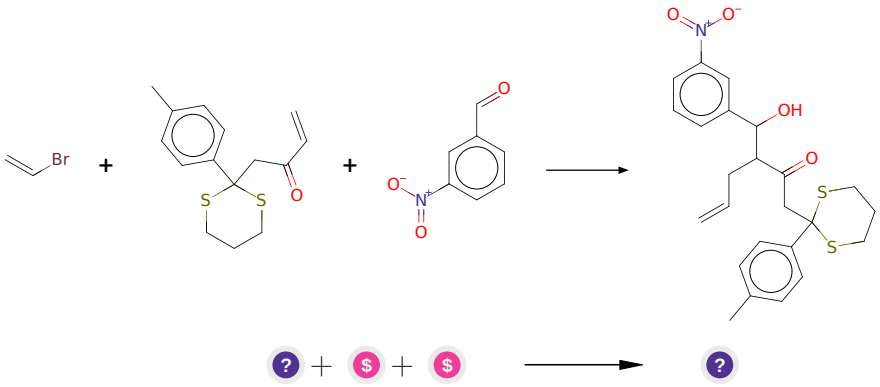
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 34220

2.4.3 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. C=CC(=O)CC1(c2ccc(C)cc2)SCCCS1
2. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*
3. Bromoethylene - *available at Sigma-Aldrich*

Products:

1. C=CCC(C(=O)CC1(c2ccc(C)cc2)SCCCS1)C(O)c1cccc([N+](=O)[O-])c1

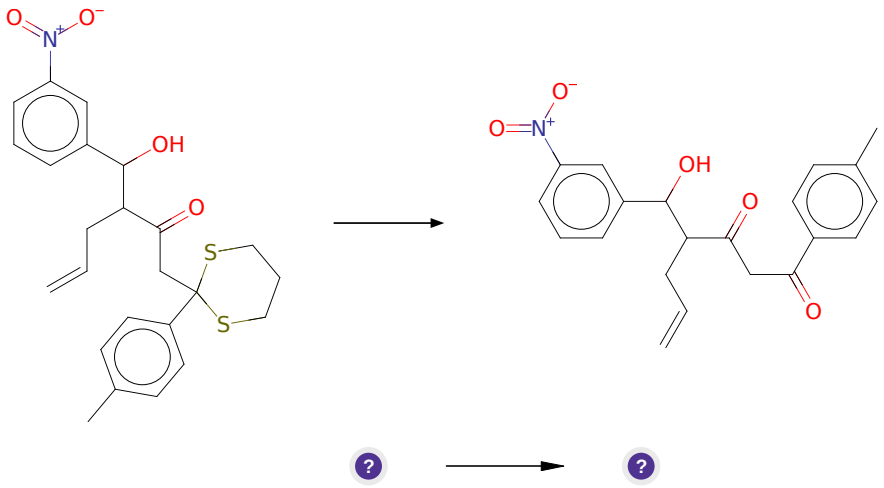
Typical conditions: 1.RCuLi.2.RCHO

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

2.4.4 Synthesis of ketones from dithianes



Substrates:

1. C=CCC(C(=O)CC1(c2ccc(C)cc2)SCCCS1)C(O)c1cccc([N+](=O)[O-])c1

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

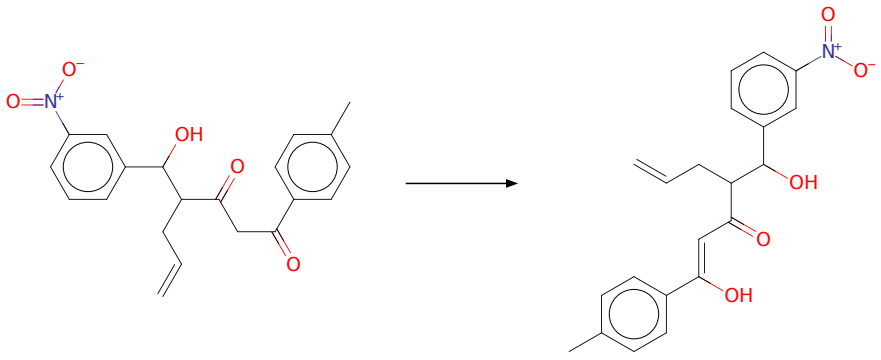
Typical conditions: MeI.CaCO3

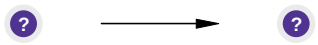
Protections: none

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

2.4.5 Keto-enol Tautomerism





Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

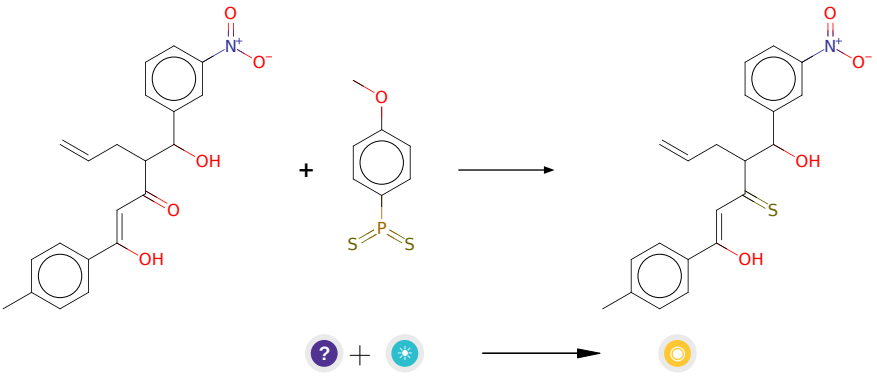
Typical conditions: solvent

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)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798

2.5 Path 5

Score: 2250164.14

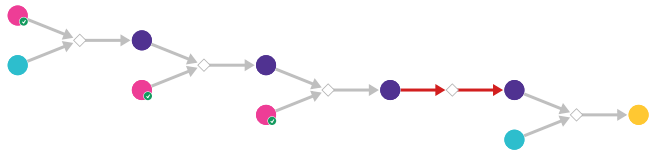
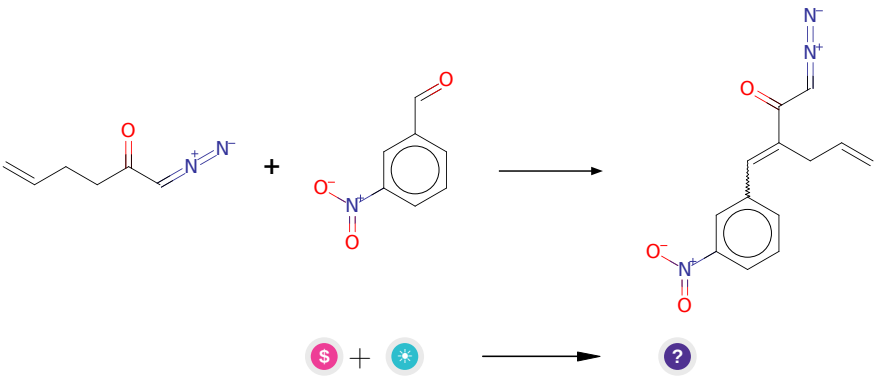


Figure 5: Outline of path 5

2.5.1 Aldol Condensation



Substrates:

1. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*
2. 1-diazo-hex-5-en-2-one

Products:

1. C=CCC(=Cc1cccc([N+](=O)[O-])c1)C(=O)C=[N+]=[N-]

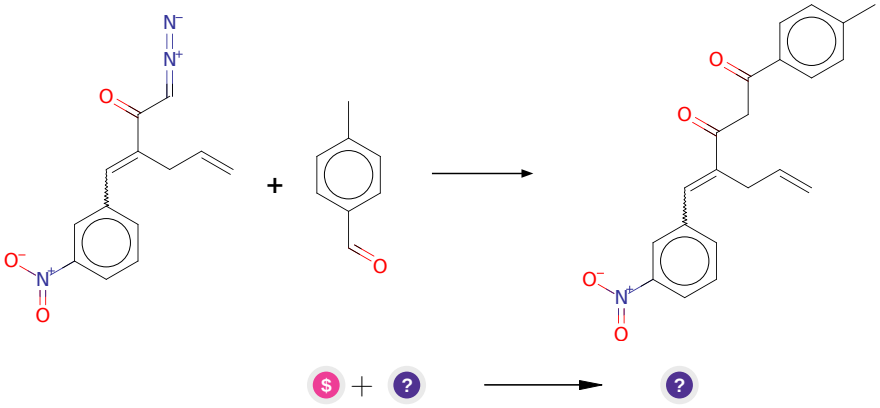
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.5.2 Homologation of aldehydes to ketones with diazoalkanes



Substrates:

1. p-Tolualdehyde - *available at Sigma-Aldrich*
2. C=CCC(=Cc1cccc([N+](=O)[O-])c1)C(=O)C=[N+]=[N-]

Products:

1. C=CCC(=Cc1cccc([N+](=O)[O-])c1)C(=O)CC(=O)c1ccc(C)cc1

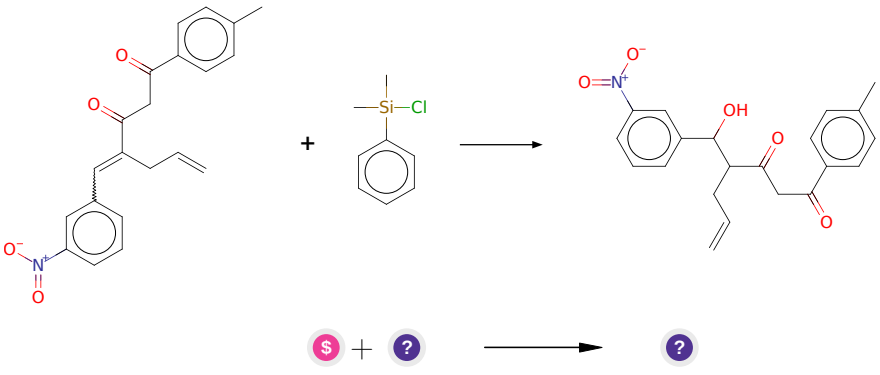
Typical conditions: Lewis.acid

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

2.5.3 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

1. DMPSCl - *available at Sigma-Aldrich*
2. C=CCC(=Cc1cccc([N+](=O)[O-])c1)C(=O)CC(=O)c1ccc(C)cc1

Products:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

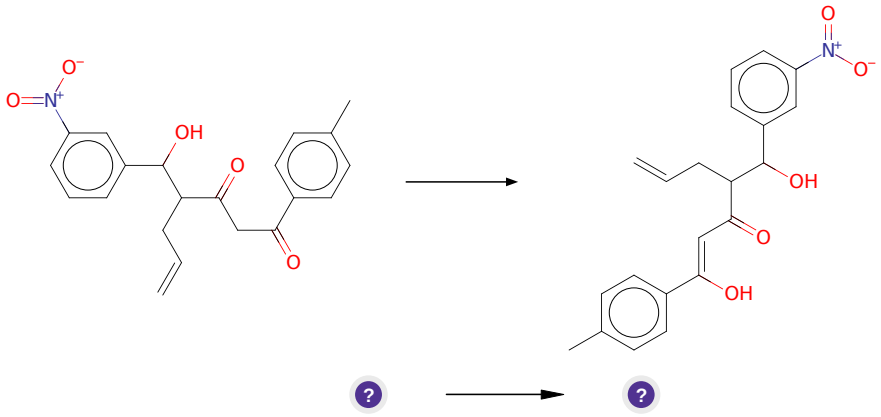
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

Reference: *10.1021/ja058370g* AND (Oxidation) *10.1021/jo9905672* or *10.1021/ol300832f*

Retrosynthesis ID: 20301

2.5.4 Keto-enol Tautomerism



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Products:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

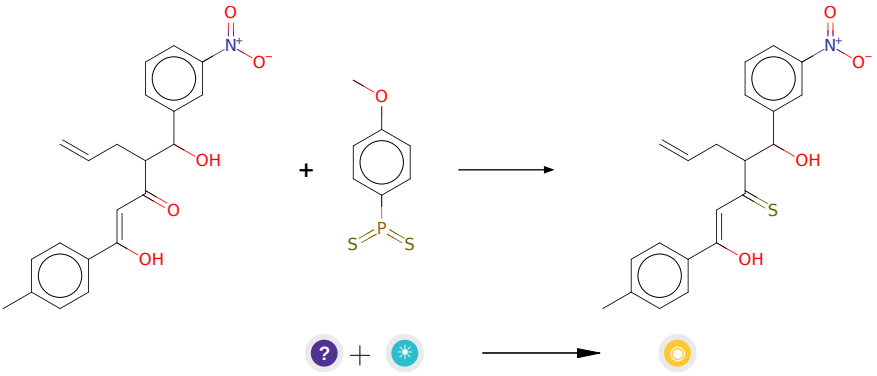
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.5.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

1. C=CCC(C(=O)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1
2. 4-methoxyphenyl-dithiophosphonsaeureanhydrid

Products:

1. C=CCC(C(=S)/C=C(\O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 10798