Paths of analysis*

Y5A

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: 2000051.25

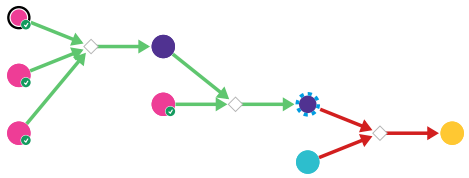
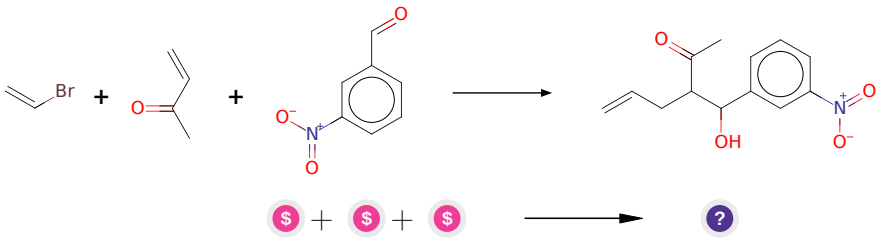


Figure 1: Outline of path 1

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

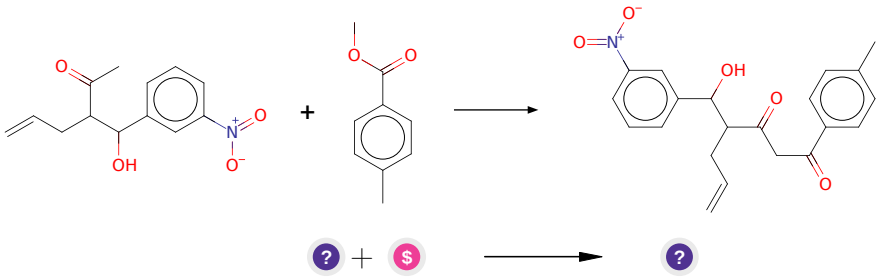
Typical conditions: 1.RCuLi.2.RCHO

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

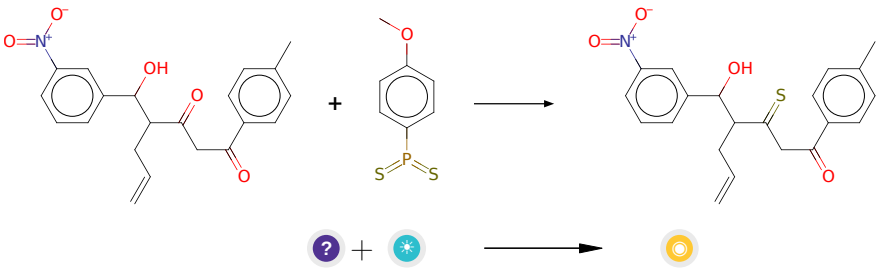
Typical conditions: NaOMe.MeOH

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 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes
		1.3-Dioxolanes
		1.3-Dithianes
		1.3-Dithiolanes
		Dimethyl Acetals and Ketals
		N,N-Dimethylhydrazones

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 11476

2.2 Path 2

Score: 2000076.25

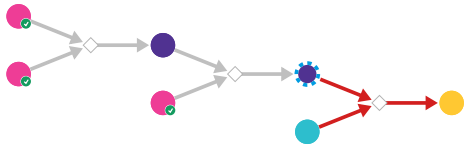
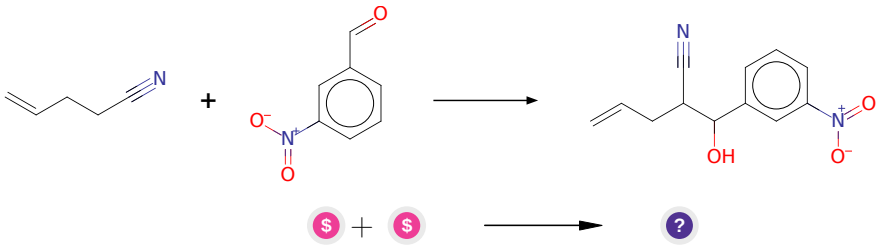


Figure 2: Outline of path 2

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

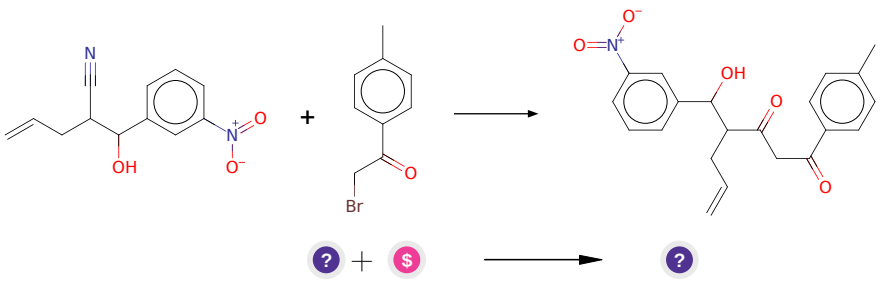
Typical conditions: LDA.THF.cooling

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

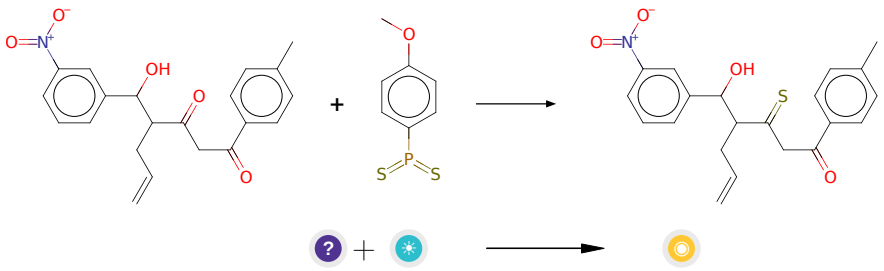
Typical conditions: Zn.TMSCl.THF then HCl

Protections: none

Reference: *10.1002/ejoc.201403402*

Retrosynthesis ID: 10000153

2.2.3 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes 1.3-Dioxolanes 1.3-Dithianes 1.3-Dithiolanes Dimethyl Acetals and Ketals N,N-Dimethylhydrazones

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 11476

2.3 Path 3

Score: 2000076.25

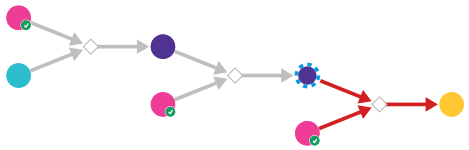
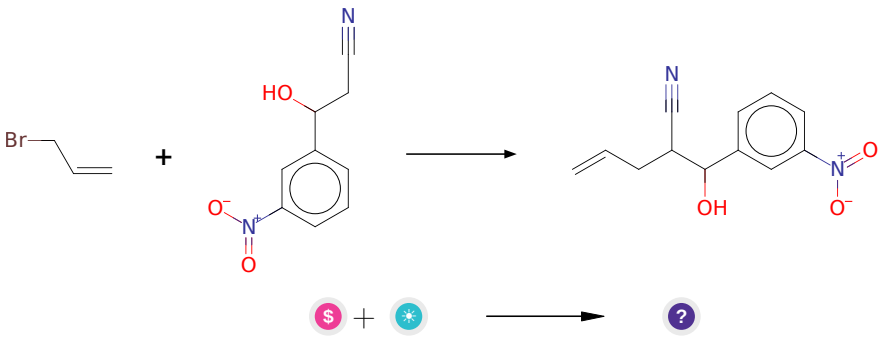


Figure 3: Outline of path 3

2.3.1 Alkylation of Nitriles



Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*
2. C9H8N2O3

Products:

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

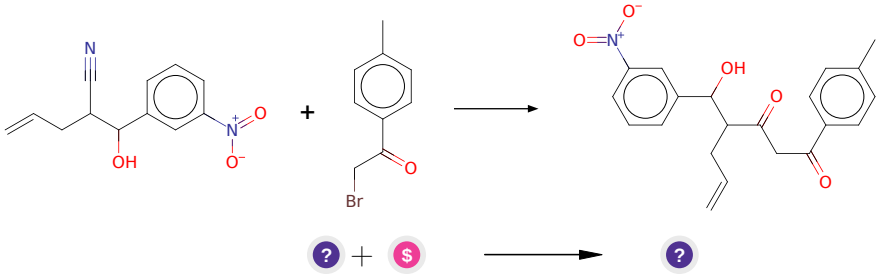
Typical conditions: base e.g. BuLi.THF

Protections: none

Reference: *10.1021/jm701319c* and WO2017/59191A1 p.0210 and US2011/237556A1 p.7 and *10.1021/ja058303m* and *10.1021/acs.orglett.9b03078* and *10.1016/S0040-4020(01)80336-7*

Retrosynthesis ID: 31017106

2.3.2 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

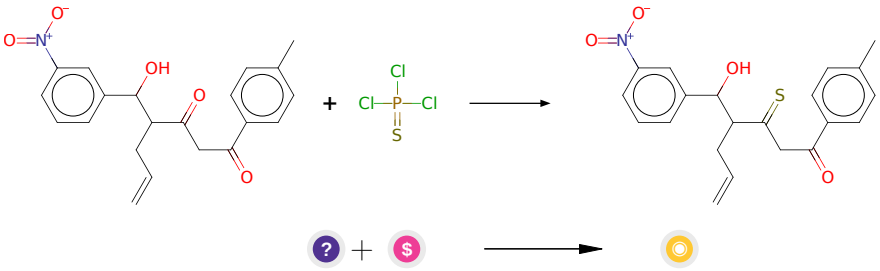
Typical conditions: Zn.TMSCl.THF then HCl

Protections: none

Reference: *10.1002/ejoc.201403402*

Retrosynthesis ID: 10000153

2.3.3 Thionation of Carbonyl Compounds using PSCl3



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(O)c1cccc([N+](=O)[O-])c1
2. Phosphorus thiochloride - *available at Sigma-Aldrich*

Products:

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

Typical conditions: NEt3.H2O.microwave.70-100C

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes 1.3-Dioxolanes 1.3-Dithianes 1.3-Dithiolanes Dimethyl Acetals and Ketals N,N-Dimethylhydrazones

Reference: DOI: *10.1021/jo7022069*

Retrosynthesis ID: 11555

2.4 Path 4

Score: 2000090.31

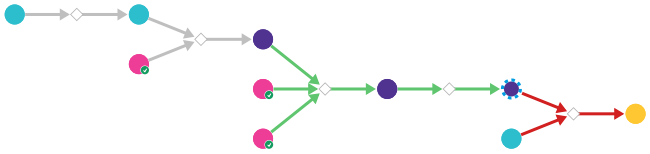
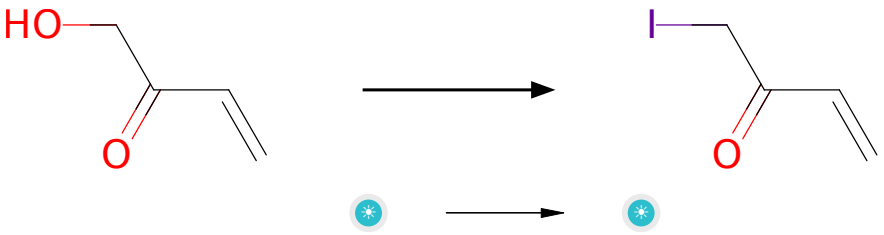


Figure 4: Outline of path 4

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

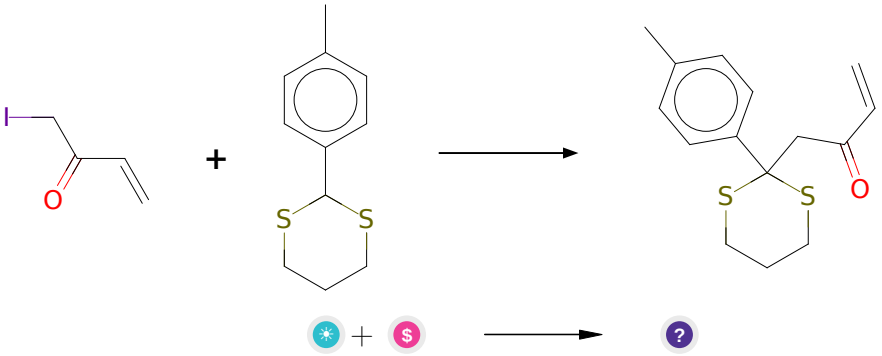
Typical conditions: Imidazole.PPh3.I2

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

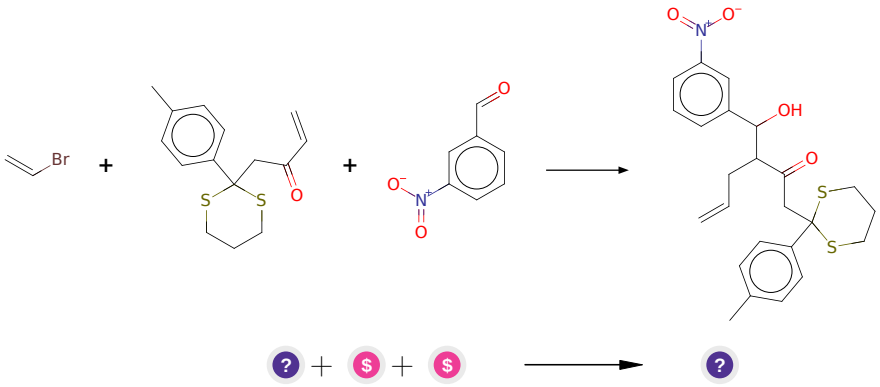
Typical conditions: LDA.THF

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

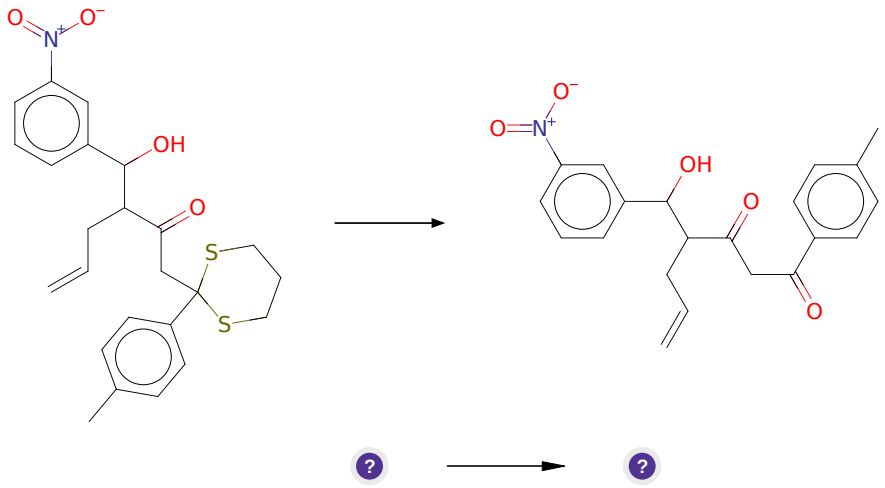
Typical conditions: 1.RCuLi.2.RCHO

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

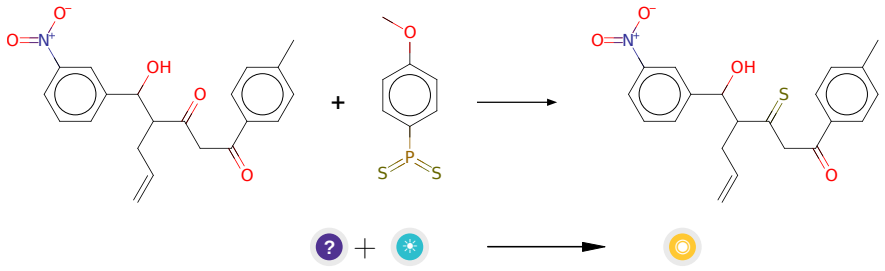
Typical conditions: MeI.CaCO3

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 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes
		1.3-Dioxolanes
		1.3-Dithianes
		1.3-Dithiolanes
		Dimethyl Acetals and Ketals
		N,N-Dimethylhydrazones

Reference: DOI: *10.1021/ol990629a*

Retrosynthesis ID: 11476

2.5 Path 5

Score: `2000100.08`

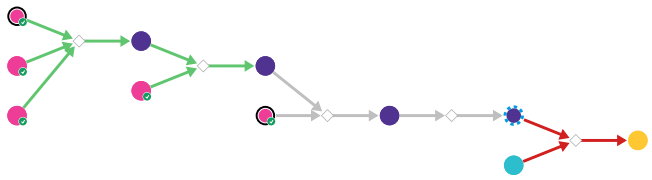
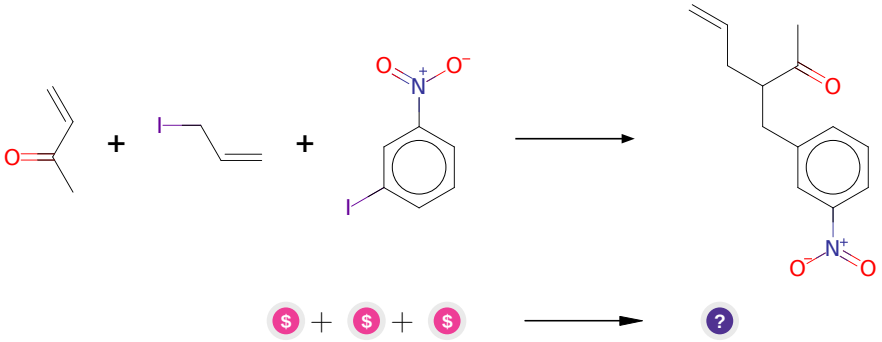


Figure 5: Outline of path 5

2.5.1 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. 1-Iodo-3-nitrobenzene - *available at Sigma-Aldrich*

Products:

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

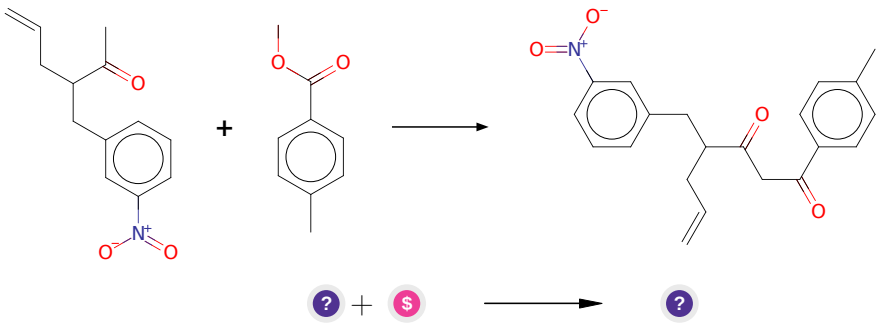
Typical conditions: 1.RCuLi.2.RI.HMPA

Protections: none

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

Retrosynthesis ID: 12523

2.5.2 Condensation of methyl ketones with esters



Substrates:

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

Products:

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

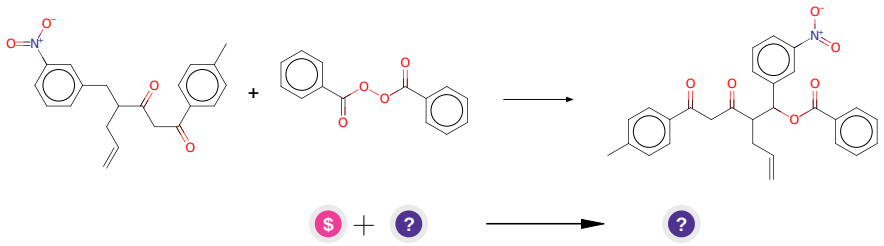
Typical conditions: NaOMe.MeOH

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

2.5.3 Free-radicals synthesis of benzoyl esters



Substrates:

1. Luperox(r) A98 - *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(OC(=O)c1ccccc1)c1cccc([N+](=O)[O-])c1

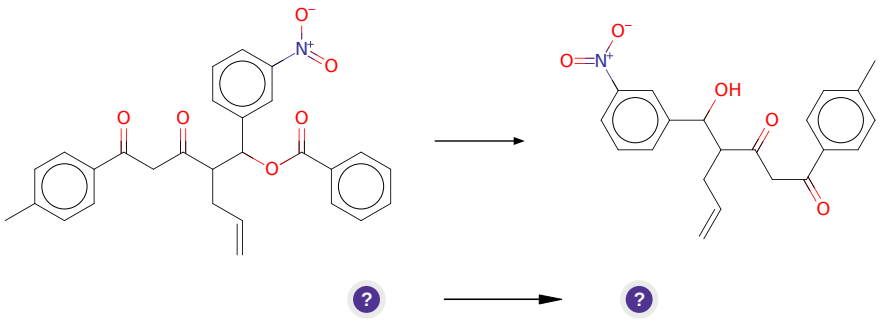
Typical conditions: CuBr

Protections: none

Reference: DOI: *10.1021/jo01265a066*

Retrosynthesis ID: 332

2.5.4 Hydrolysis of benzoates



Substrates:

1. C=CCC(C(=O)CC(=O)c1ccc(C)cc1)C(OC(=O)c1ccccc1)c1cccc([N+](=O)[O-])c1

Products:

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

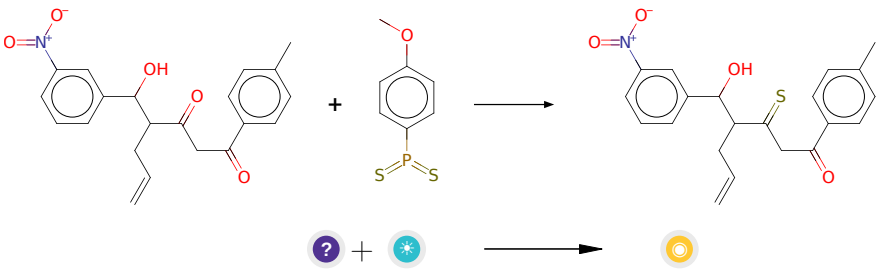
Typical conditions: LiOH/K2CO3/NH3.MeOH.H2O.THF

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

2.5.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes
		1.3-Dioxolanes
		1.3-Dithianes
		1.3-Dithiolanes
		Dimethyl Acetals and Ketals
		N,N-Dimethylhydrazones

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