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

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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: `2250164.14`

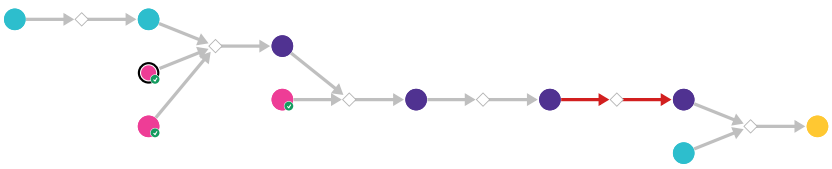
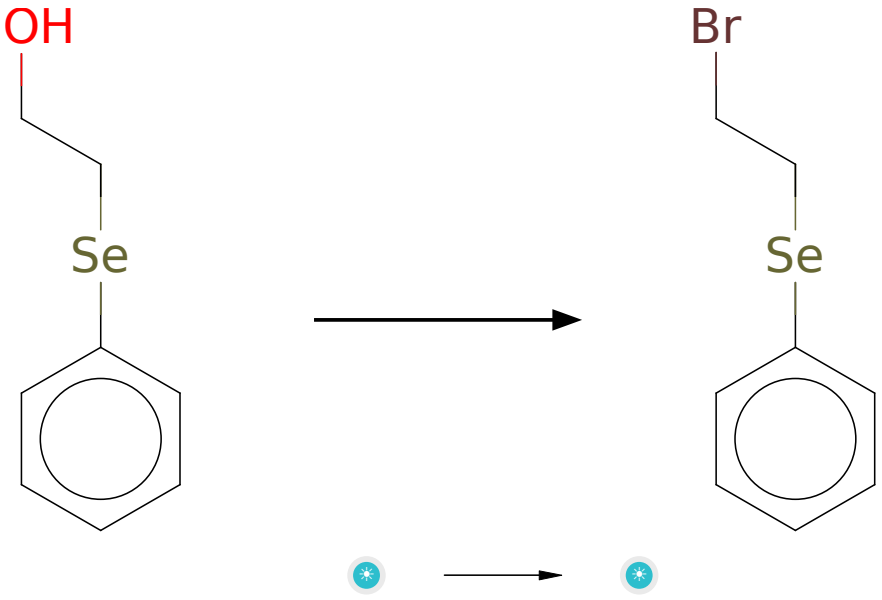


Figure 1: Outline of path 1

2.1.1 Appel Reaction



Substrates:

1. 2-phenylselanyl-ethanol

Products:

1. 2-bromaethylphenylselenid

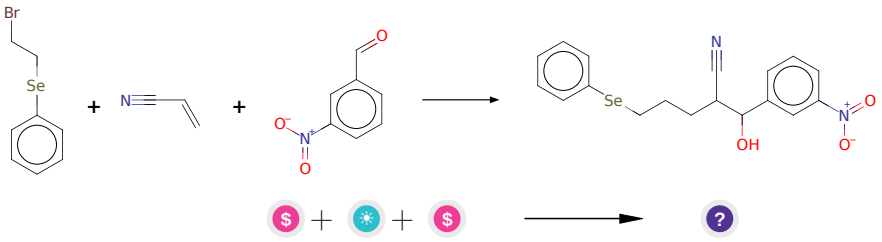
Typical conditions: PPh3.CBr4

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. Vinyl cyanide - *available at Sigma-Aldrich*
2. 2-bromaethylphenylselenid
3. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. N#CC(CCC[Se]c1ccccc1)C(O)c1cccc([N+](=O)[O-])c1

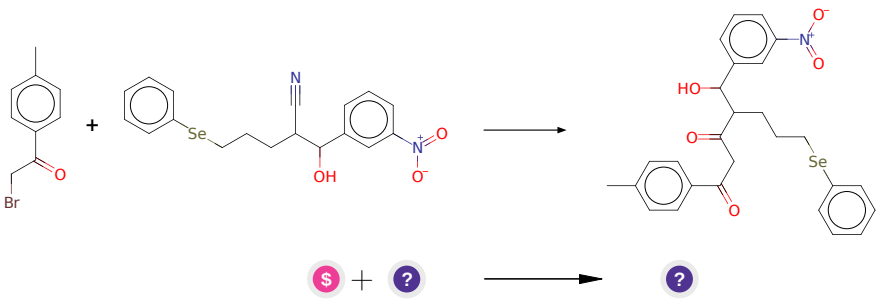
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo034174l* AND *10.1021/ol070011y* AND *10.1021/jo902164z* AND *10.1016/S0968-0896(98)80016-3* AND *10.1016/S0040-4020(98)00122-7*

Retrosynthesis ID: 20513

2.1.3 Blaise Reaction



Substrates:

1. 2-Bromo-4'-methylacetophenone - *available at Sigma-Aldrich*
2. N#CC(CCC[Se]c1ccccc1)C(O)c1cccc([N+](=O)[O-])c1

Products:

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2cccc([N+](=O)[O-])c2)cc1

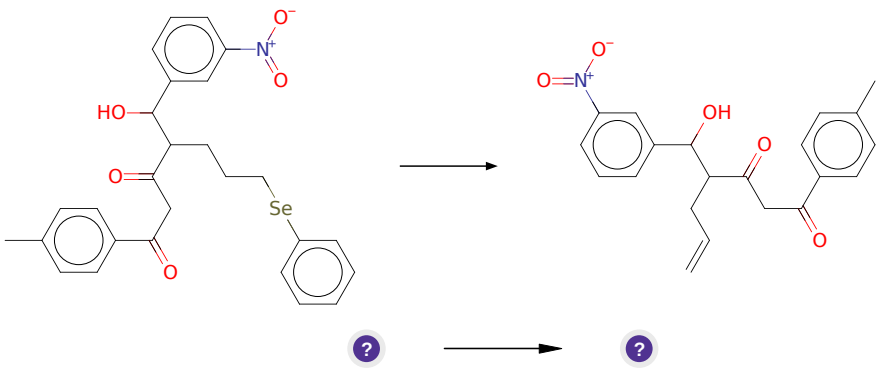
Typical conditions: Zn.TMSCl.THF then HCl

Protections: none

Reference: *10.1002/ejoc.201403402*

Retrosynthesis ID: 10000153

2.1.4 Selenoxide Elimination



Substrates:

1. Cc1ccc(C(=O)CC(=O)C(CCC[Se]c2ccccc2)C(O)c2cccc([N+](=O)[O-])c2)cc1

Products:

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

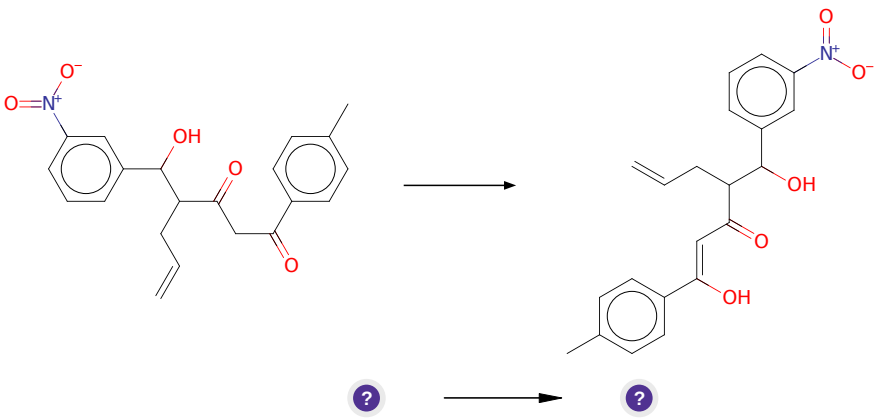
Typical conditions: 1) O3 or H2O2 or NaIO4. low temperature. 2) pyridine or Et3N

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)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

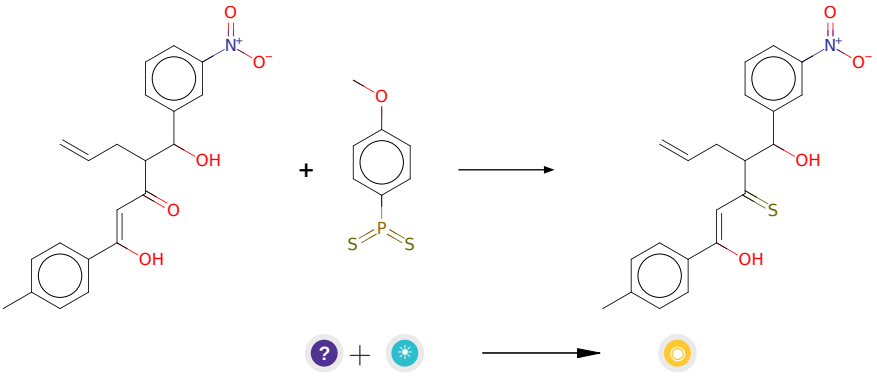
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.1.6 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

2.2 Path 2

Score: 2250164.14

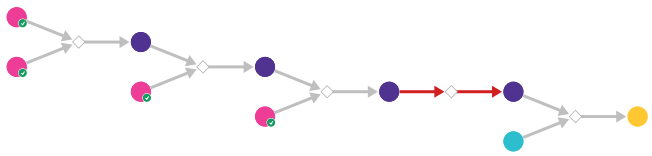
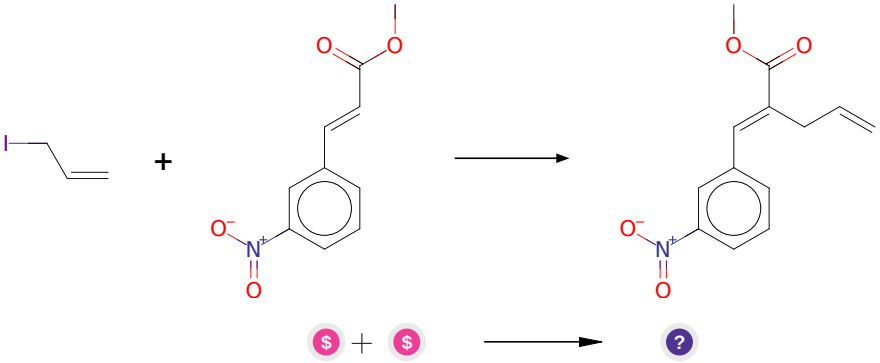


Figure 2: Outline of path 2

2.2.1 Alkylation of vinyl esters



Substrates:

1. Allyl iodide - *available at Sigma-Aldrich*
2. (E)-Methyl 3-(3-nitrophenyl)acrylate - *available at Sigma-Aldrich*

Products:

1. C=CC/C(=C\c1cccc([N+](=O)[O-])c1)C(=O)OC

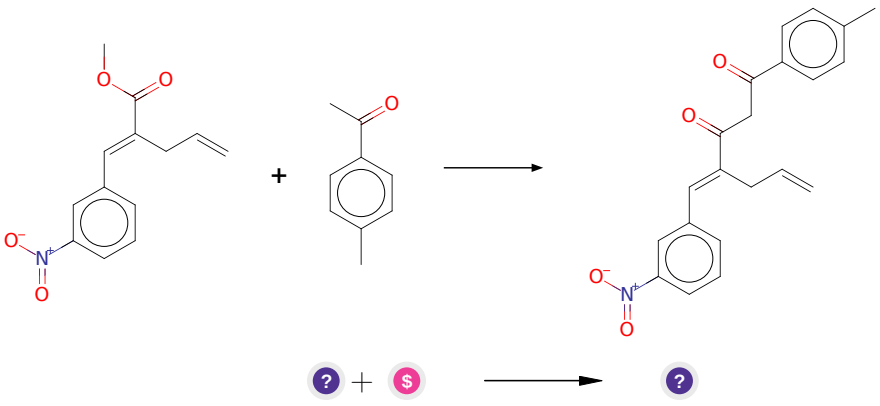
Typical conditions: LDA.THF

Protections: none

Reference: DOI: *10.1039/C39870001410*

Retrosynthesis ID: 886

2.2.2 Condensation of methyl ketones with esters



Substrates:

1. C=CC/C(=C\c1cccc([N+](=O)[O-])c1)C(=O)OC
2. Methyl p-tolyl ketone - *available at Sigma-Aldrich*

Products:

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

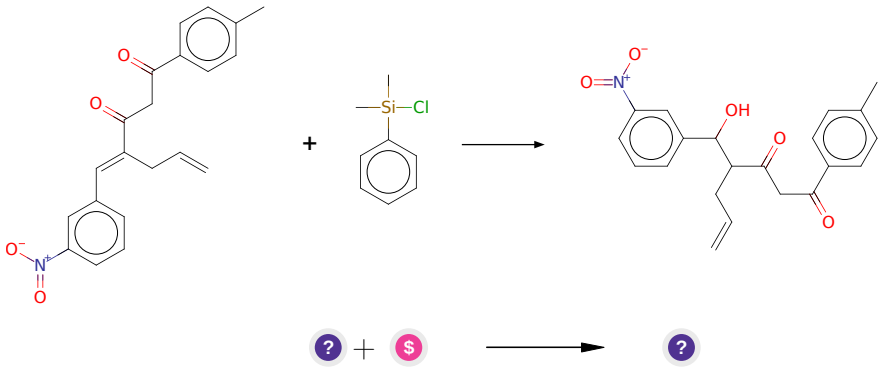
Typical conditions: NaOMe.MeOH

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

2.2.3 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

1. C=CC/C(=C\c1cccc([N+](=O)[O-])c1)C(=O)CC(=O)c1ccc(C)cc1
2. DMPSCl - *available at Sigma-Aldrich*

Products:

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

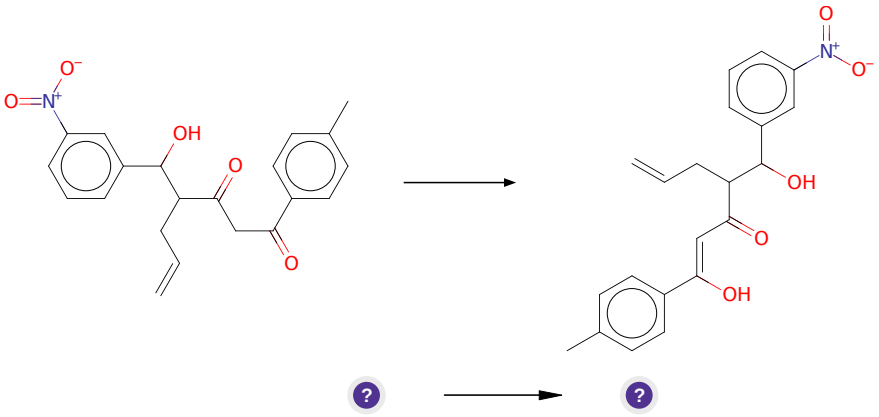
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

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

Retrosynthesis ID: 20295

2.2.4 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

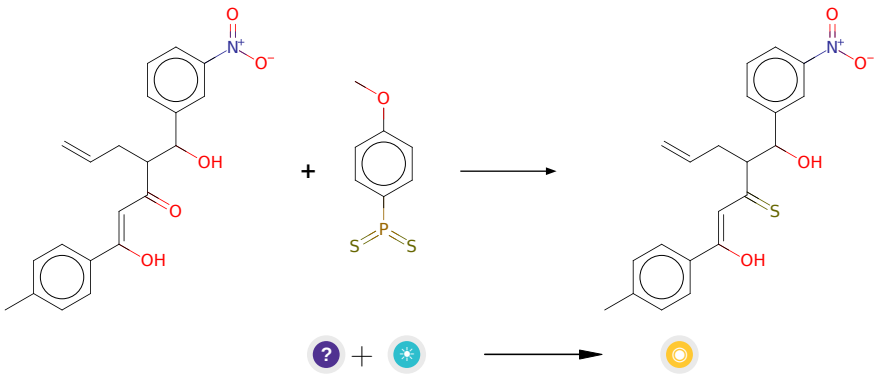
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.2.5 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

2.3 Path 3

Score: 2250164.14

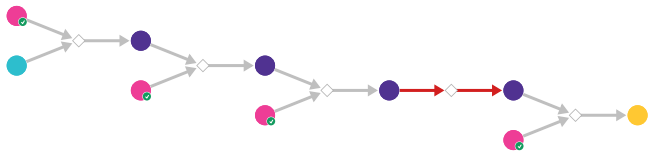
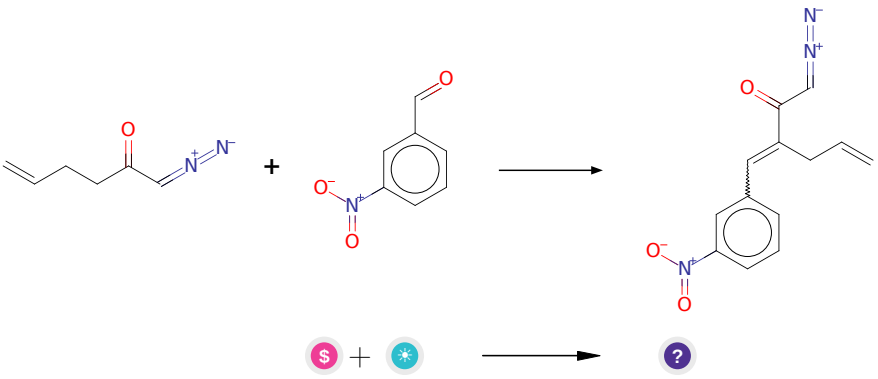


Figure 3: Outline of path 3

2.3.1 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-]

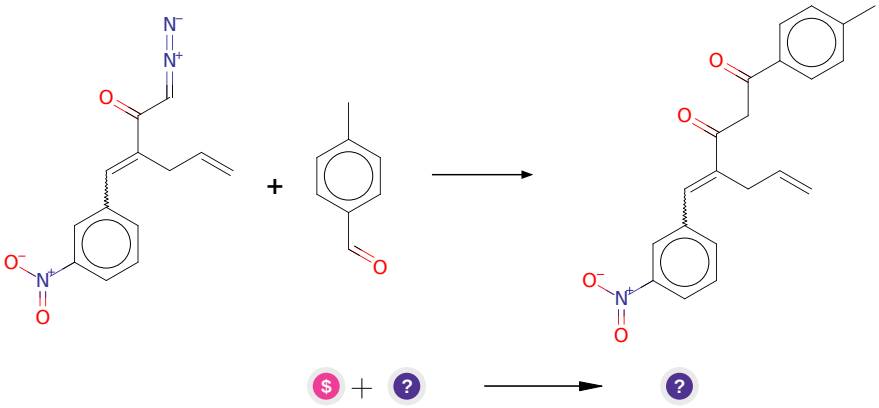
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.3.2 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

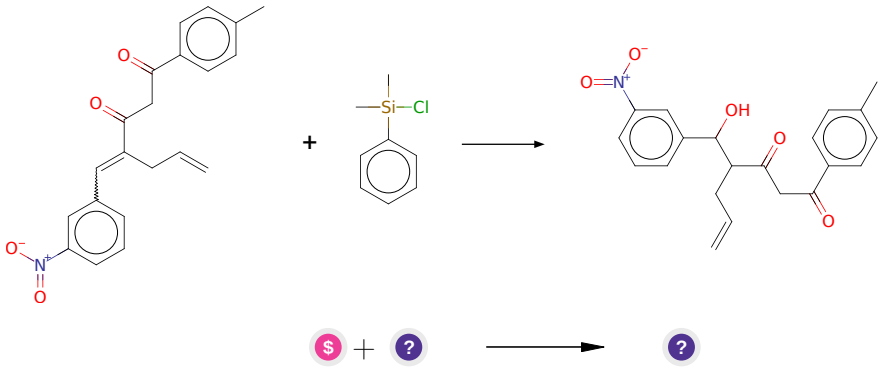
Typical conditions: Lewis.acid

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

2.3.3 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

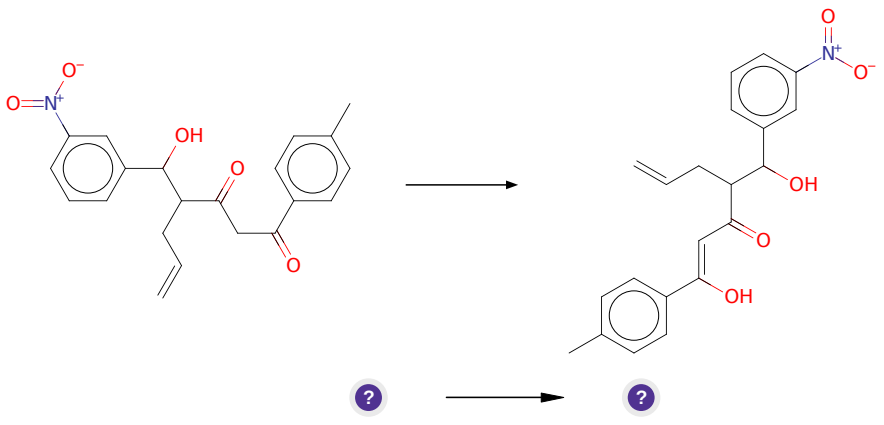
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

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

Retrosynthesis ID: 20301

2.3.4 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

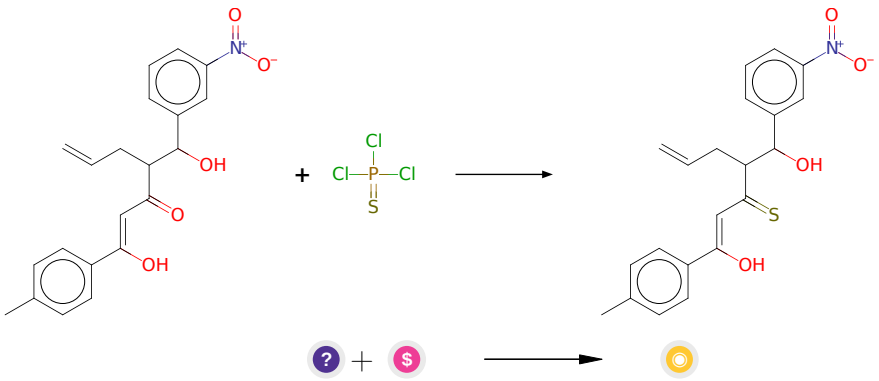
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.3.5 Thionation of Carbonyl Compounds using PSCl3



Substrates:

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

Products:

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

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

Protections: none

Reference: DOI: *10.1021/jo7022069*

Retrosynthesis ID: 11555

2.4 Path 4

Score: 2250164.14

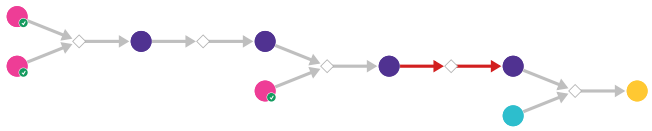
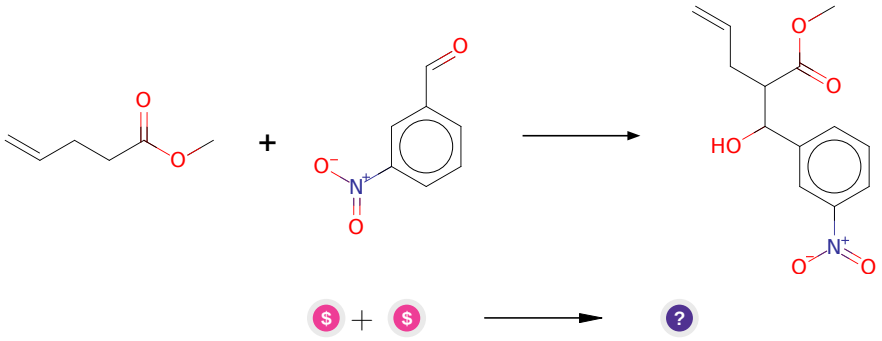


Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes



Substrates:

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

Products:

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

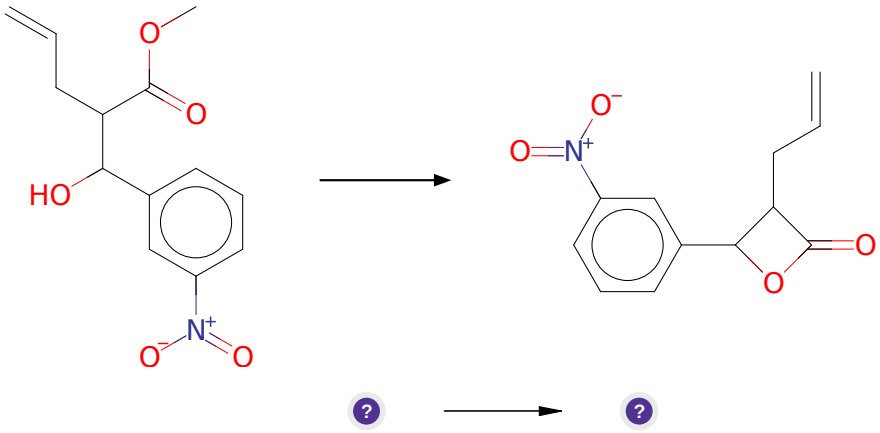
Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 4788

2.4.2 Acid catalyzed transesterification



Substrates:

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

Products:

1. C=CCC1C(=O)OC1c1cccc([N+](=O)[O-])c1

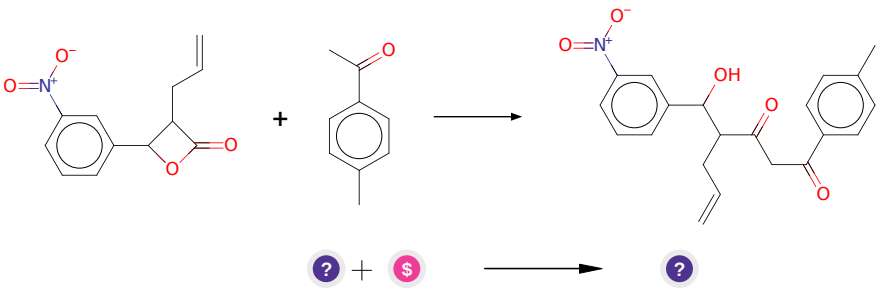
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.4.3 Ring opening of lactones with enolates



Substrates:

1. C=CCC1C(=O)OC1c1cccc([N+](=O)[O-])c1
2. Methyl p-tolyl ketone - *available at Sigma-Aldrich*

Products:

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

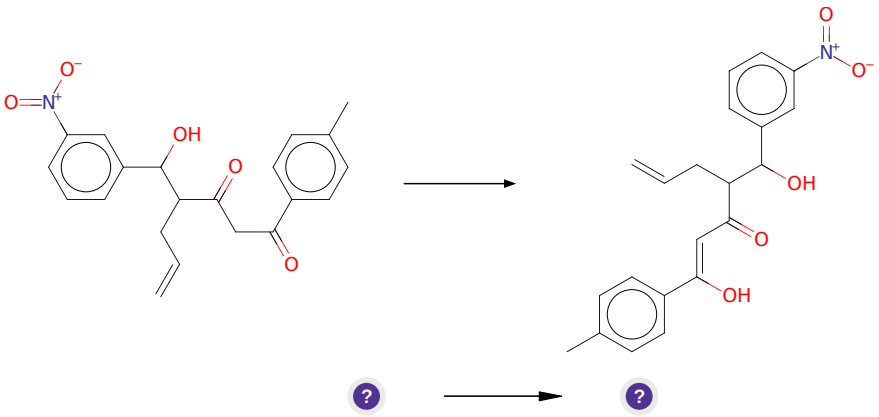
Typical conditions: LiHMDS.THF

Protections: none

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

Retrosynthesis ID: 24105

2.4.4 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

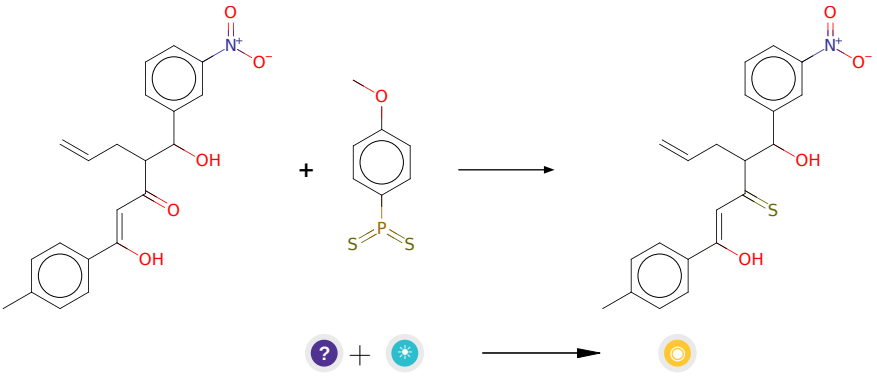
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.4.5 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

2.5 Path 5

Score: 2250176.35

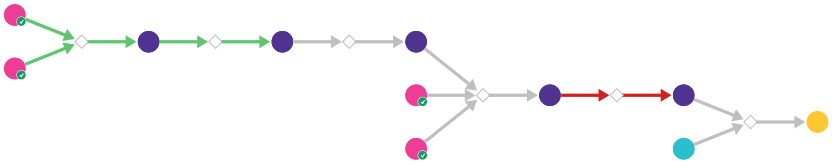
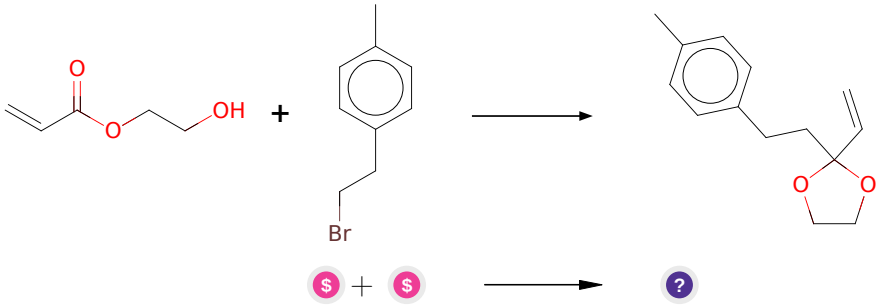


Figure 5: Outline of path 5

2.5.1 Addition of Grignard reagents to lactones



Substrates:

1. 4-(2-Bromoethyl)toluene - *available at Sigma-Aldrich*
2. 2-Hydroxyethyl acrylate - *available at Sigma-Aldrich*

Products:

1. C=CC1(CCc2ccc(C)cc2)OCCO1

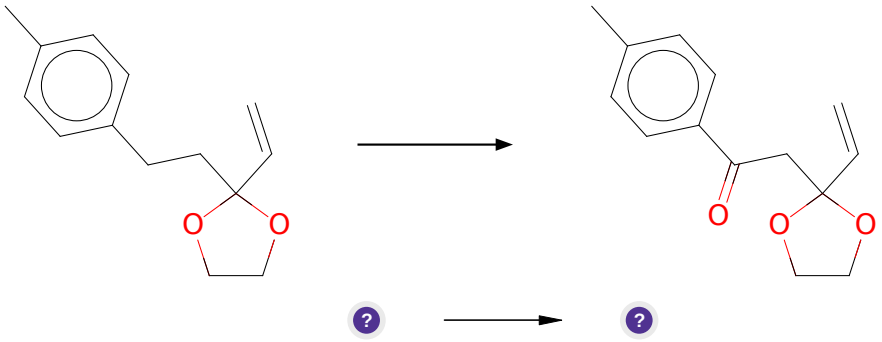
Typical conditions: 1.iPrMgCl.cooling.2.MsOH.MeOH

Protections: none

Reference: *10.1021/ja011604l* and *10.1021/ol060437x*

Retrosynthesis ID: 23155

2.5.2 Benzylic oxidation



Substrates:

1. C=CC1(CCc2ccc(C)cc2)OCCO1

Products:

1. C=CC1(CC(=O)c2ccc(C)cc2)OCCO1

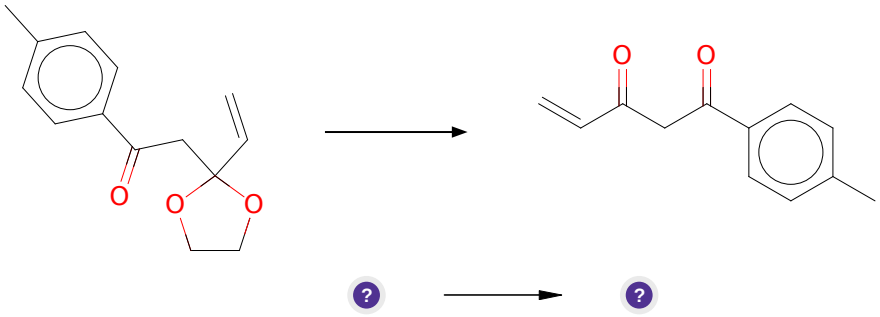
Typical conditions: DDQ.toluene.heat or CrO3.AcOH or PhP(O)HOAlkyl.O2 or CAN.THF.AcOH.H2O

Protections: none

Reference: *10.3987/COM-10-S(E)11* and *10.1038/s41467-019-10414-7* and *10.1002/ejoc.201402486* and *10.1021/acssuschemeng.9b00002*

Retrosynthesis ID: 31008180

2.5.3 Hydrolysis of ketals



Substrates:

1. C=CC1(CC(=O)c2ccc(C)cc2)OCCO1

Products:

1. C=CC(=O)CC(=O)c1ccc(C)cc1

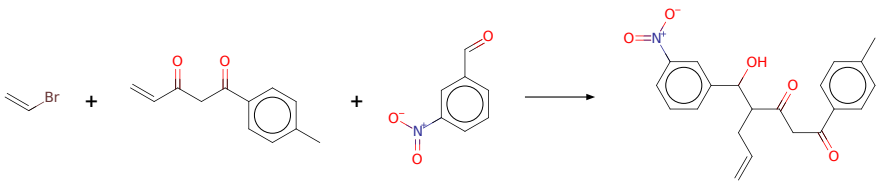
Typical conditions: H2O.HCl

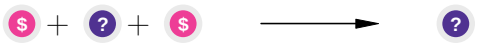
Protections: none

Reference: *10.1021/jo0159035* and *10.1021/jo00194a003* and

Retrosynthesis ID: 31013139

2.5.4 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

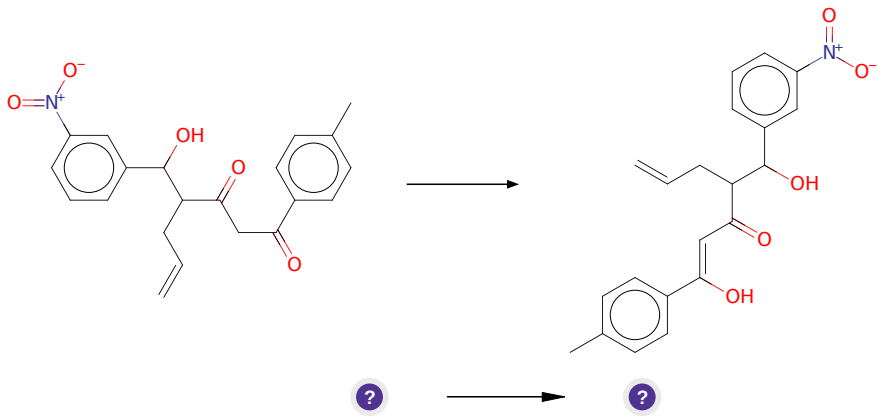
Typical conditions: 1.RCuLi.2.RCHO

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

2.5.5 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

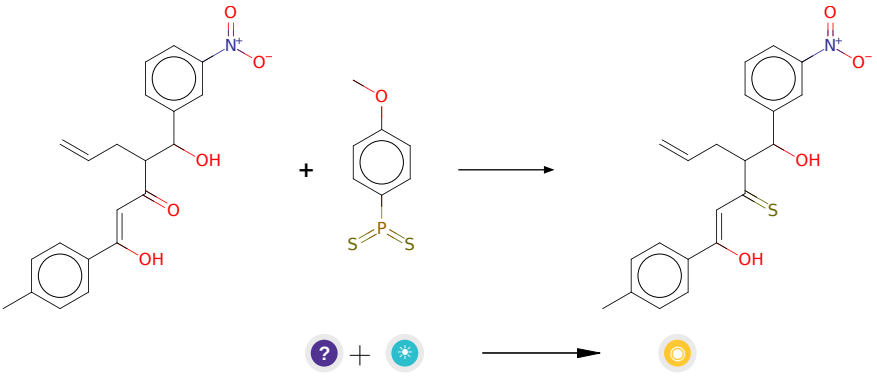
Typical conditions: solvent

Protections: none

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

Retrosynthesis ID: 7781

2.5.6 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