

Paths of analysis*

Y2

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselective 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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

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

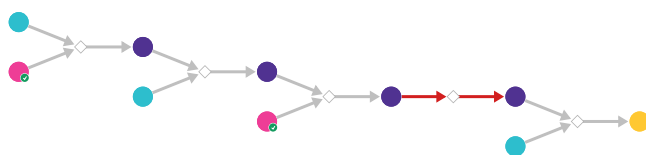
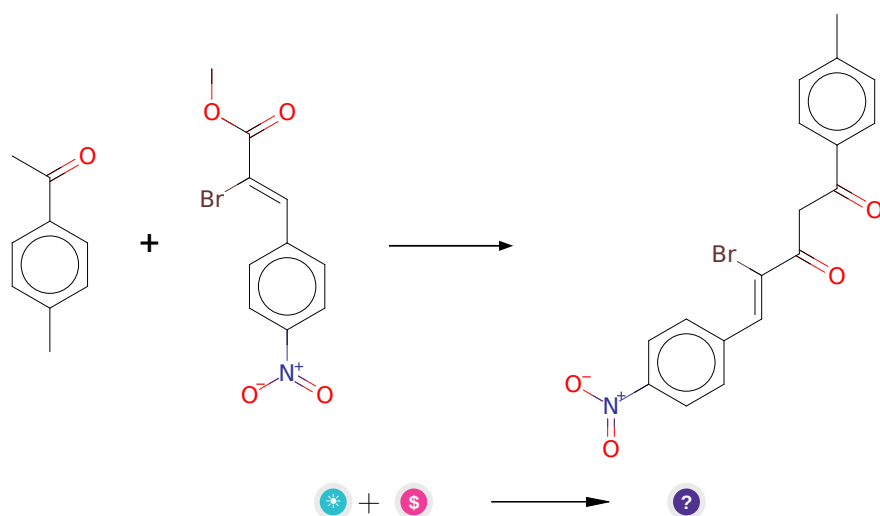


Figure 1: Outline of path 1

2.1.1 Condensation of methyl ketones with esters



Substrates:

1. a-bromo-4-nitro-trans-cinnamic acid methyl ester
2. Methyl p-tolyl ketone - *available at Sigma-Aldrich*

Products:

1. Cc1ccc(C(=O)CC(=O)/C(Br)=C/c2ccc([N+](=O)[O-])cc2)cc1

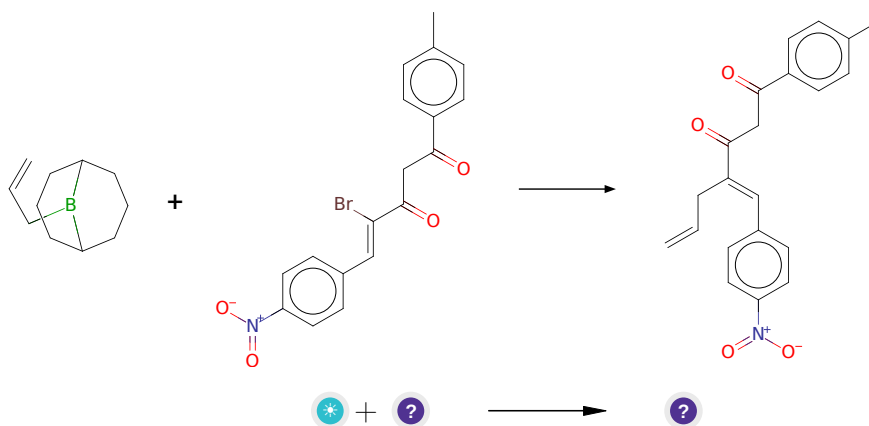
Typical conditions: NaOMe.MeOH

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

2.1.2 Suzuki coupling of alkyl-9-BBNs with vinyl bromides



Substrates:

1. 9-allyl-9-bora-bicyclo[3.3.1]nonane
2. Cc1ccc(C(=O)CC(=O)/C(Br)=C/c2ccc([N+](=O)[O-])cc2)cc1

Products:

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

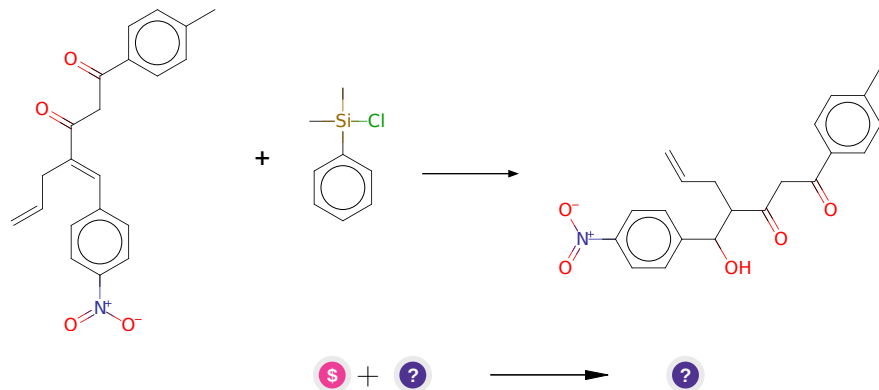
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: [10.1021/ja00183a048](#) and [10.1039/b707338k](#) and [10.1016/j.tet.2015.05.039](#) and [10.1021/jo991064z](#) and [10.1021/ol060290+](#) and [10.1246/bcsj.65.2863](#)

Retrosynthesis ID: 25176

2.1.3 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

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

Products:

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

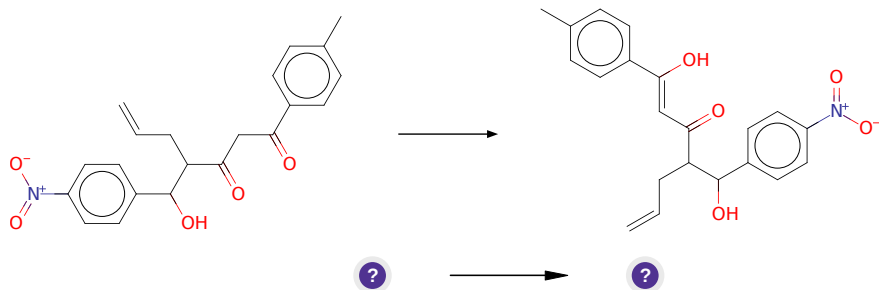
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

Reference: [10.1021/ja058370g](#) AND (Oxidation) [10.1021/jo9905672](#) or [10.1021/ol300832f](#)

Retrosynthesis ID: 20295

2.1.4 Keto-enol Tautomerism



Substrates:

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

Products:

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

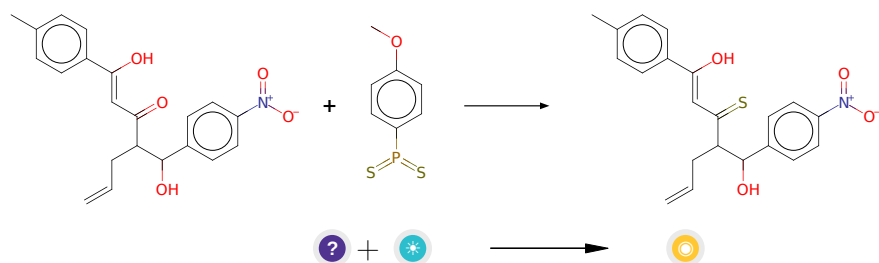
Typical conditions: solvent

Protections: none

Reference: [10.1021/ja01065a003](#) AND [10.1021/jo8012385](#)

Retrosynthesis ID: 7781

2.1.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](#)

Retrosynthesis ID: 10798

2.2 Path 2

Score: 2250164.14

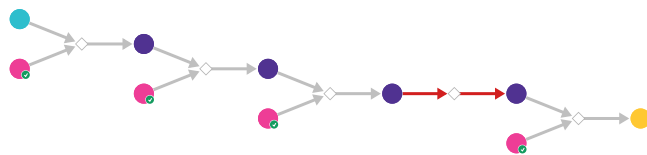
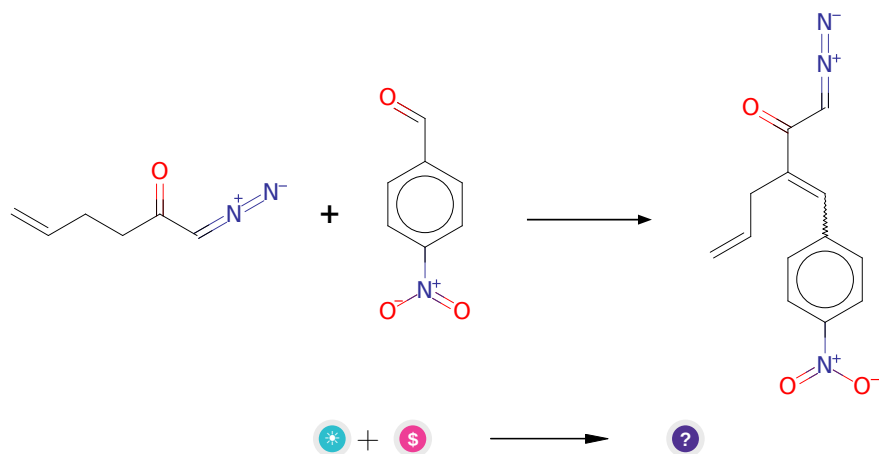


Figure 2: Outline of path 2

2.2.1 Aldol Condensation



Substrates:

1. 1-diazo-hex-5-en-2-one
2. 4-Nitrobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CCC(=Cc1ccc([N+](=O)[O-])cc1)C(=O)C=[N+]=[N-]

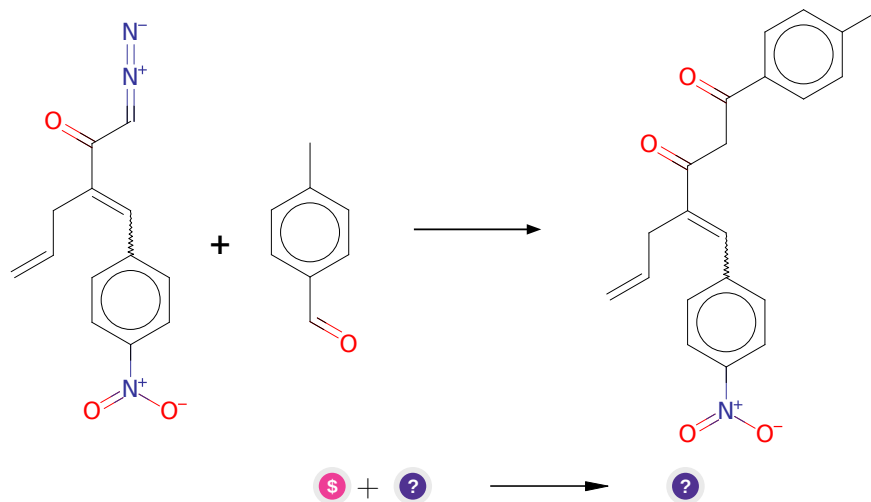
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.2.2 Homologation of aldehydes to ketones with diazoalkanes



Substrates:

1. p-Tolualdehyde - *available at Sigma-Aldrich*
2. C=CCC(=Cc1ccc([N+](=O)[O-])cc1)C(=O)C=[N+]=[N-]

Products:

1. C=CCC(=Cc1ccc([N+](=O)[O-])cc1)C(=O)CC(=O)c1ccc(C)cc1

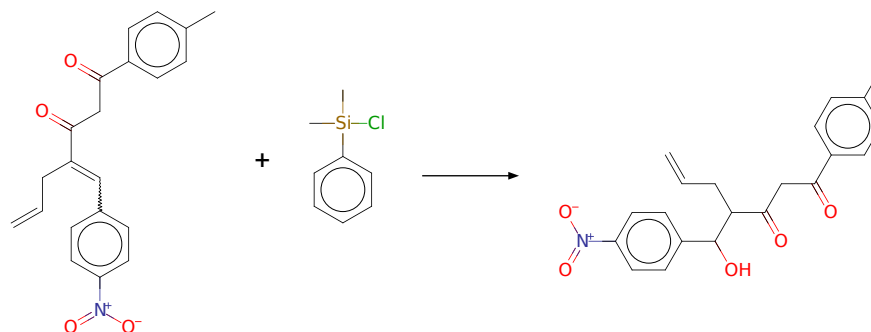
Typical conditions: Lewis.acid

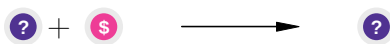
Protections: none

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

2.2.3 Addition of silanes to Michael acceptors followed by oxidation





Substrates:

1. C=CCC(=Cc1ccc([N+](=O)[O-])cc1)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)c1ccc([N+](=O)[O-])cc1

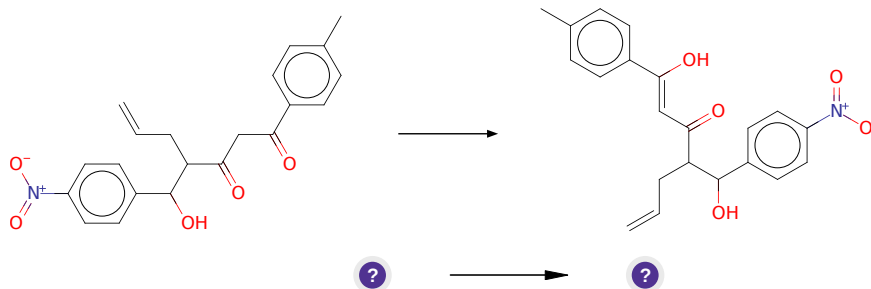
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

Reference: [10.1021/ja058370g](#) AND (Oxidation) [10.1021/jo9905672](#) or [10.1021/ol300832f](#)

Retrosynthesis ID: 20301

2.2.4 Keto-enol Tautomerism



Substrates:

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

Products:

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

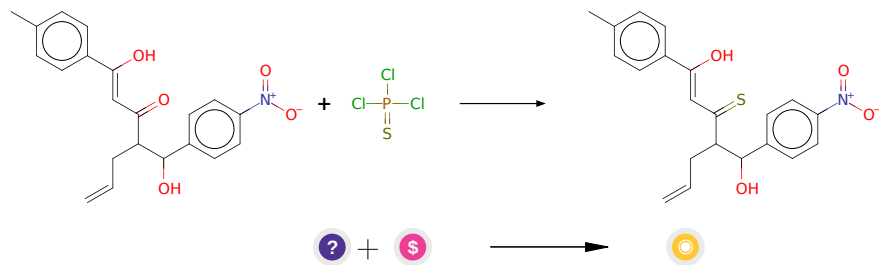
Typical conditions: solvent

Protections: none

Reference: [10.1021/ja01065a003](#) AND [10.1021/jo8012385](#)

Retrosynthesis ID: 7781

2.2.5 Thionation of Carbonyl Compounds using PSCl3



Substrates:

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

Products:

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

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

Protections: none

Reference: DOI: [10.1021/jo7022069](https://doi.org/10.1021/jo7022069)

Retrosynthesis ID: 11555

2.3 Path 3

Score: 2250164.14

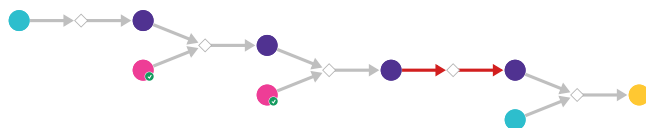
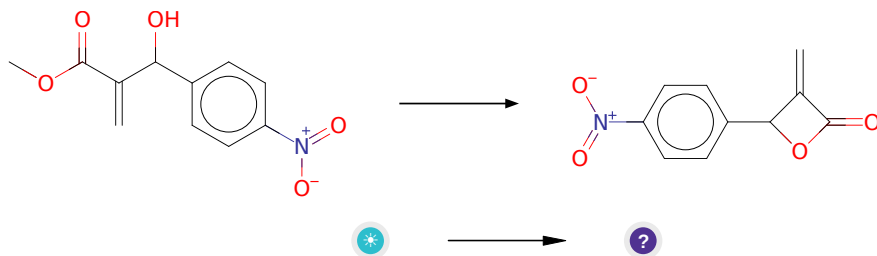


Figure 3: Outline of path 3

2.3.1 Acid catalyzed transesterification



Substrates:

1. 3-hydroxy-2-methylene-3-(4-nitrophenyl)propanoic acid methyl ester

Products:

1. C=C1C(=O)OC1c1ccc([N+](=O)[O-])cc1

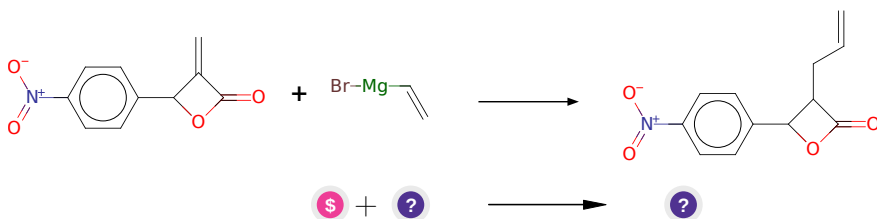
Typical conditions: H⁺

Protections: none

Reference: [10.1021/cr00020a004](#)

Retrosynthesis ID: 50438

2.3.2 Conjugate addition of organocuprate



Substrates:

1. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*
2. C=C1C(=O)OC1c1ccc([N+](=O)[O-])cc1

Products:

1. C=CCC1C(=O)OC1c1ccc([N+](=O)[O-])cc1

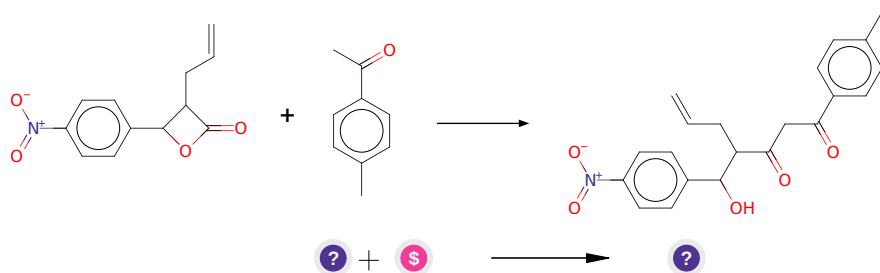
Typical conditions: 1. CuCN.LiCl. 2. Electrophile. 3. NH₄Cl

Protections: none

Reference: [10.1021/ol036071v](#) AND [10.1016/j.tet.2011.12.046](#) AND [10.1002/anie.201007644](#) AND [10.1002/anie.201007644](#) AND [10.1055/s-1997-1371](#)

Retrosynthesis ID: 10003577

2.3.3 Ring opening of lactones with enolates



Substrates:

1. C=CCC1C(=O)OC1c1ccc([N+](=O)[O-])cc1
2. Methyl p-tolyl ketone - [available at Sigma-Aldrich](#)

Products:

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

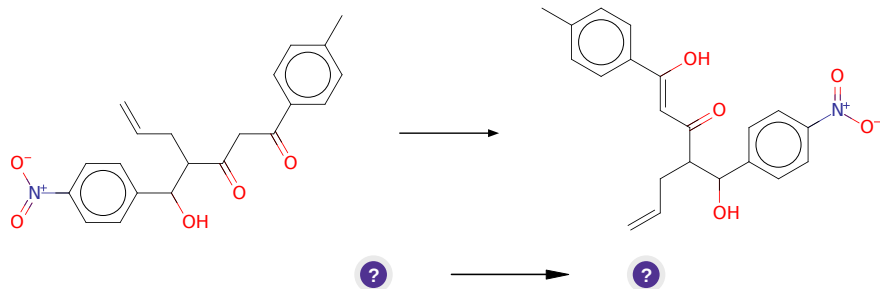
Typical conditions: LiHMDS.THF

Protections: none

Reference: [10.1021/ol801493w](#) and [10.1021/ol403423r](#) and [10.1021/ja061938g](#) and [10.1021/ja036521e](#)

Retrosynthesis ID: 24105

2.3.4 Keto-enol Tautomerism



Substrates:

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

Products:

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

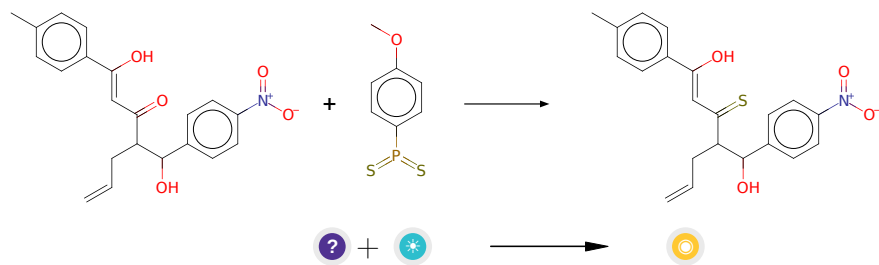
Typical conditions: solvent

Protections: none

Reference: [10.1021/ja01065a003](https://doi.org/10.1021/ja01065a003) AND [10.1021/jo8012385](https://doi.org/10.1021/jo8012385)

Retrosynthesis ID: 7781

2.3.5 Synthesis of Thioketones using Lawesson's Reagent



Substrates:

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](https://doi.org/10.1021/ol990629a)

Retrosynthesis ID: 10798

2.4 Path 4

Score: 2250164.14

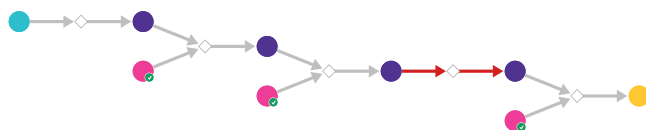
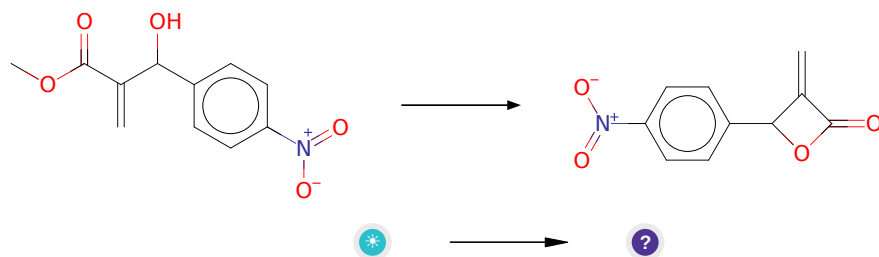


Figure 4: Outline of path 4

2.4.1 Acid catalyzed transesterification



Substrates:

1. 3-hydroxy-2-methylene-3-(4-nitrophenyl)propanoic acid methyl ester

Products:

1. C=C1C(=O)OC1c1ccc([N+](=O)[O-])cc1

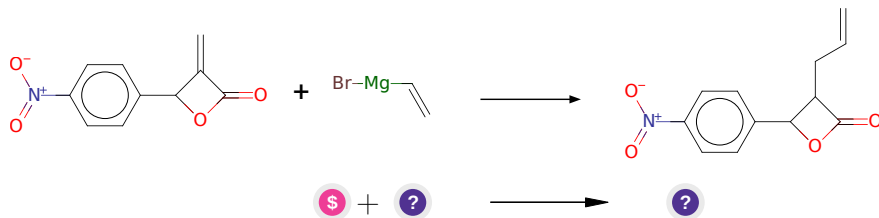
Typical conditions: H⁺

Protections: none

Reference: [10.1021/cr00020a004](https://doi.org/10.1021/cr00020a004)

Retrosynthesis ID: 50438

2.4.2 Conjugate addition of organocuprate



Substrates:

1. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*
2. C=C1C(=O)OC1c1ccc([N+](=O)[O-])cc1

Products:

1. C=CCC1C(=O)OC1c1ccc([N+](=O)[O-])cc1

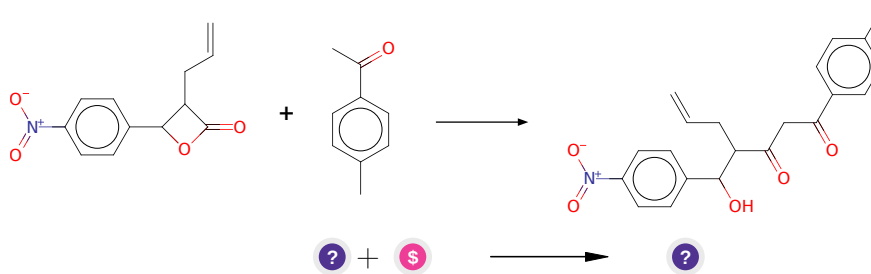
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

Protections: none

Reference: [10.1021/ol036071v](#) AND [10.1016/j.tet.2011.12.046](#) AND [10.1002/anie.201007644](#) AND [10.1002/anie.201007644](#) AND [10.1055/s-1997-1371](#)

Retrosynthesis ID: 10003577

2.4.3 Ring opening of lactones with enolates



Substrates:

1. C=CCC1C(=O)OC1c1ccc([N+](=O)[O-])cc1
2. Methyl p-tolyl ketone - [available at Sigma-Aldrich](#)

Products:

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

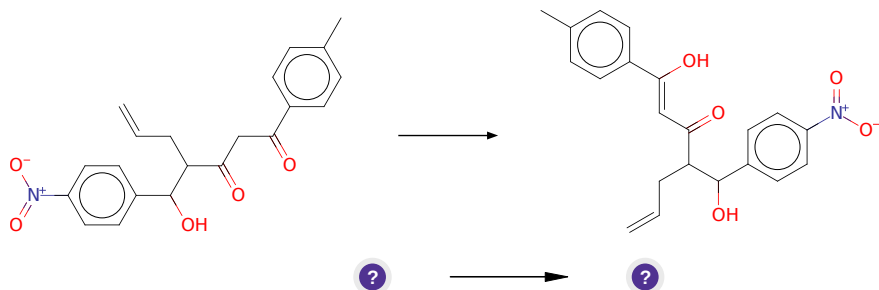
Typical conditions: LiHMDS.THF

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)c1ccc([N+](=O)[O-])cc1

Products:

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

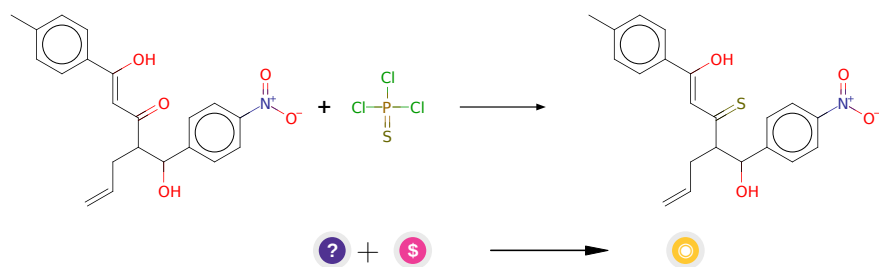
Typical conditions: solvent

Protections: none

Reference: [10.1021/ja01065a003](#) AND [10.1021/jo8012385](#)

Retrosynthesis ID: 7781

2.4.5 Thionation of Carbonyl Compounds using PSCl3



Substrates:

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

Products:

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

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

Protections: none

Reference: DOI: [10.1021/jo7022069](https://doi.org/10.1021/jo7022069)

Retrosynthesis ID: 11555

2.5 Path 5

Score: 2250164.14

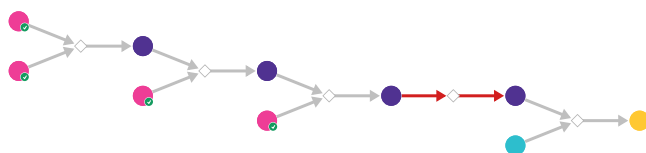
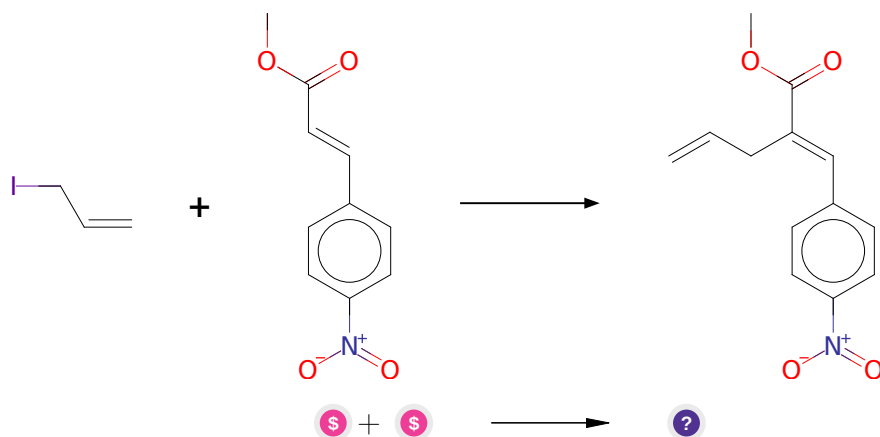


Figure 5: Outline of path 5

2.5.1 Alkylation of vinyl esters



Substrates:

1. Allyl iodide - *available at Sigma-Aldrich*
2. methyl (E)-3-(4-nitrophenyl)acrylate - *available at Sigma-Aldrich*

Products:

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

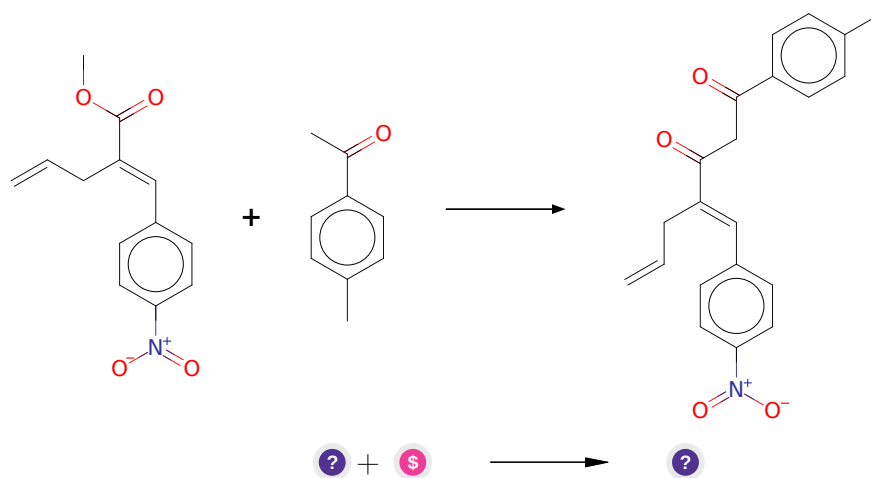
Typical conditions: LDA.THF

Protections: none

Reference: DOI: [10.1039/C39870001410](https://doi.org/10.1039/C39870001410)

Retrosynthesis ID: 886

2.5.2 Condensation of methyl ketones with esters



Substrates:

1. C=CC/C(=C\c1ccc([N+](=O)[O-])cc1)C(=O)OC
2. Methyl p-tolyl ketone - [available at Sigma-Aldrich](#)

Products:

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

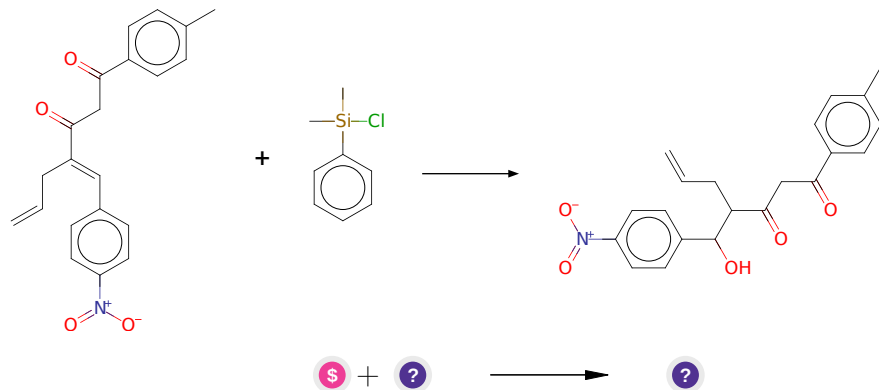
Typical conditions: NaOMe.MeOH

Protections: none

Reference: [10.1016/j.tetlet.2007.10.010](https://doi.org/10.1016/j.tetlet.2007.10.010) and [10.1016/j.tetlet.2013.09.025](https://doi.org/10.1016/j.tetlet.2013.09.025) and [10.1016/j.ejmech.2013.10.072](https://doi.org/10.1016/j.ejmech.2013.10.072) and [10.1002/ange.19921040631](https://doi.org/10.1002/ange.19921040631)

Retrosynthesis ID: 4792

2.5.3 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

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

Products:

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

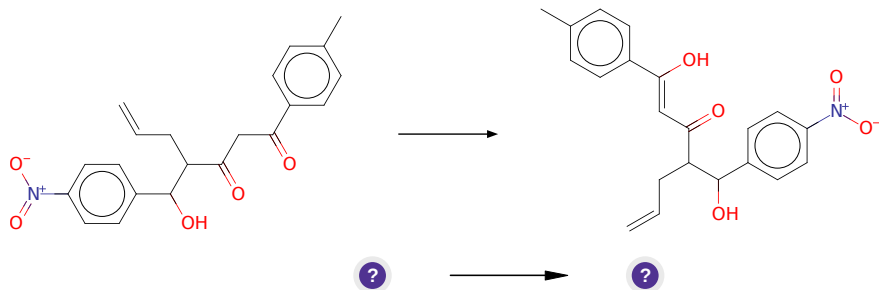
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

Reference: [10.1021/ja058370g](#) AND (Oxidation) [10.1021/jo9905672](#) or [10.1021/ol300832f](#)

Retrosynthesis ID: 20295

2.5.4 Keto-enol Tautomerism



Substrates:

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

Products:

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

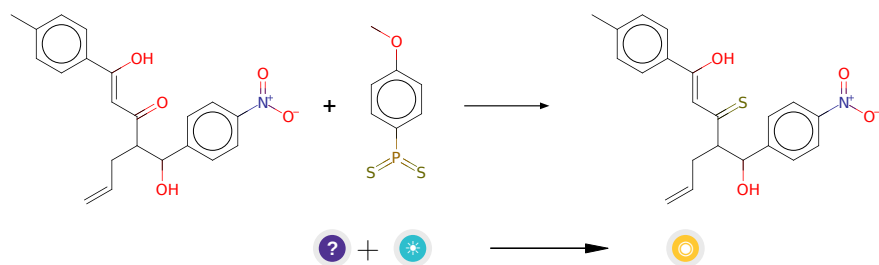
Typical conditions: solvent

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

Products:

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

Typical conditions: Lawesson's Reagent.neat.microwave

Protections: none

Reference: DOI: [10.1021/ol990629a](#)

Retrosynthesis ID: 10798