Paths of analysis*

L4_DIA

Synthia

October 11, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: 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

*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.

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: `51.25`

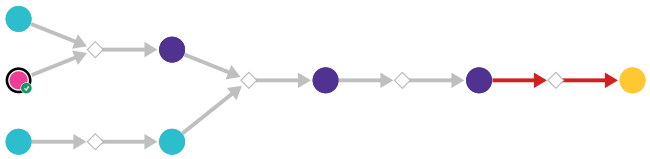
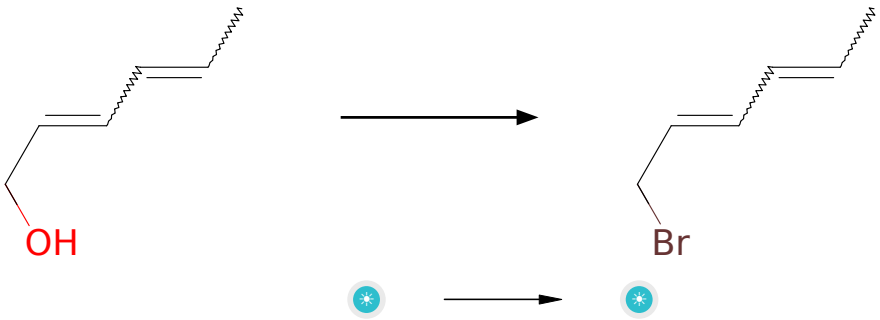


Figure 1: Outline of path 1

2.1.1 Appel Reaction



Substrates:

1. sorbic alcohol

Products:

1. 1-brom-hexa-2,4-dien

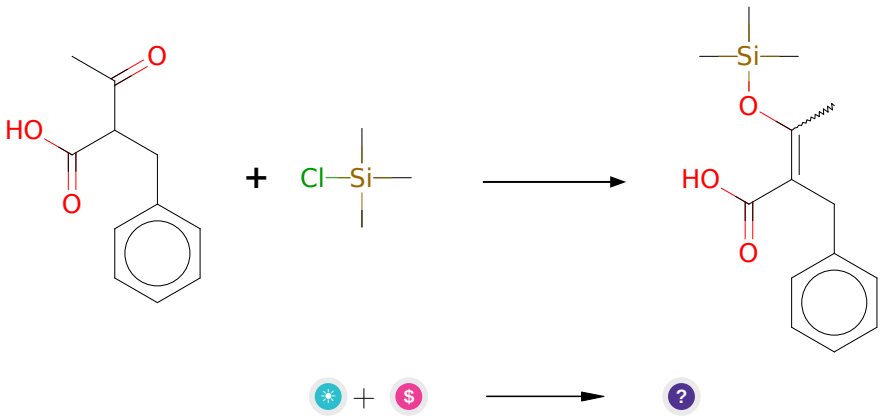
Typical conditions: PPh3.CBr4

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 Enol esters and ethers synthesis



Substrates:

1. 2-benzyl-acetoacetic acid
2. TMSCl - *available at Sigma-Aldrich*

Products:

1. CC(O[Si](C)(C)C)=C(Cc1ccccc1)C(=O)O

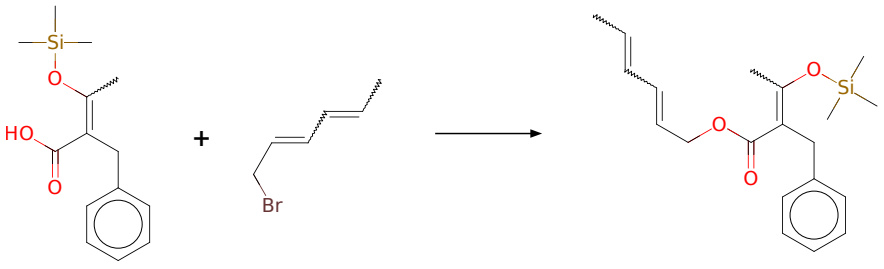
Typical conditions: 1. Et3N.Electrophile

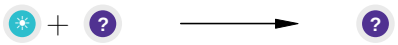
Protections: none

Reference: *10.1016/S0040-4020(03)00977-3* AND *10.1021/ja00056a002*

Retrosynthesis ID: 7799

2.1.3 Synthesis of esters from alkyl chlorides and carboxylic acids or thioacids





Substrates:

1. 1-brom-hexa-2,4-dien
2. CC(O[Si](C)(C)C)=C(Cc1ccccc1)C(=O)O

Products:

1. CC=CC=CCOC(=O)C(Cc1ccccc1)=C(C)O[Si](C)(C)C

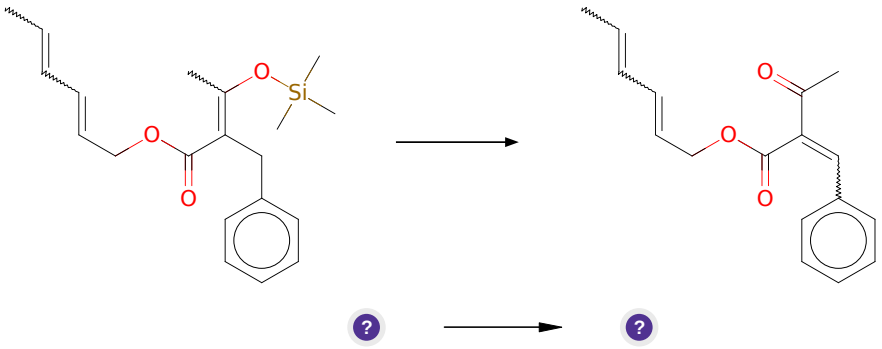
Typical conditions: K2CO3.DMF

Protections: none

Reference: *10.1016/j.bmcl.2005.08.026* AND *10.1021/ol034655r* (SI) AND *10.1039/C3RA41967C* AND *10.1016/j.bmcl.2012.03.093*

Retrosynthesis ID: 14685

2.1.4 Dehydrogenation of silyl enol ethers



Substrates:

1. CC=CC=CCOC(=O)C(Cc1ccccc1)=C(C)O[Si](C)(C)C

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccccc1)C(C)=O

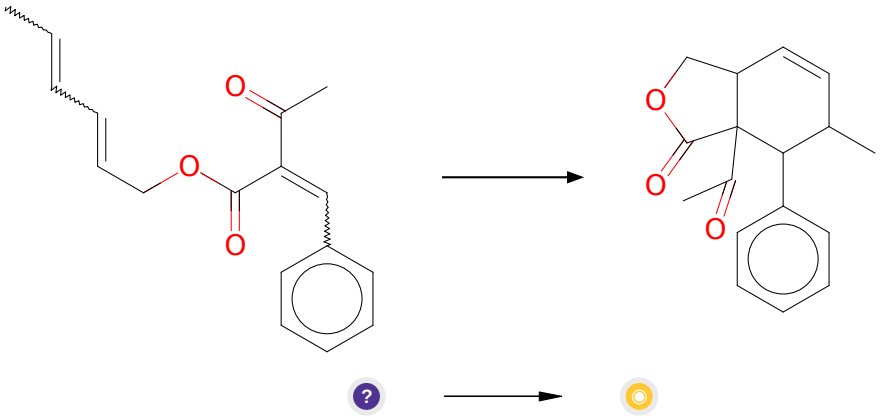
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

Protections: none

Reference: *10.1271/bbb.60.405* and *10.1039/C3CC46778C* and US2015284405 p.40 and *10.1016/S0040-4039(01)81518-5* and US2010204477 p. 15-16 and *10.1016/0040-4039(95)00694-8* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999877

2.1.5 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccccc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccccc1

Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.2 Path 2

Score: 76.25

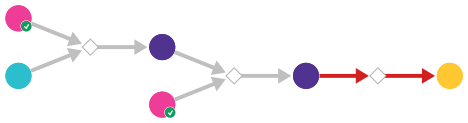
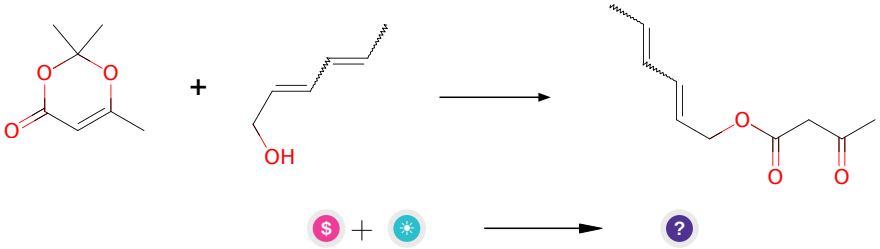


Figure 2: Outline of path 2

2.2.1 Synthesis of 1,3-dicarbonyl compounds from 1,3-dioxinones



Substrates:

1. Diketene acetone adduct - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)CC(C)=O

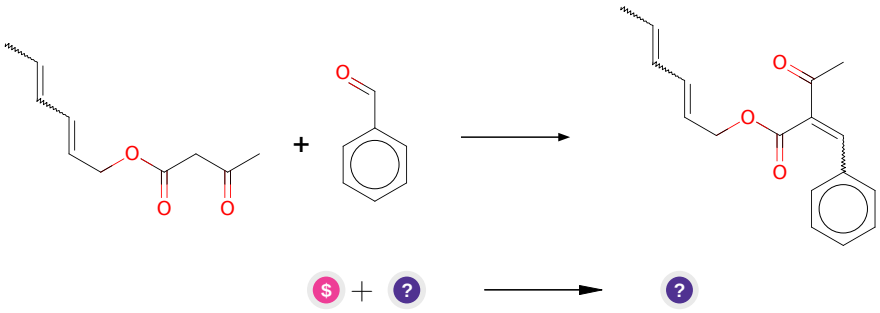
Typical conditions: alcohol

Protections: none

Reference: DOI: *10.1021/ja00154a049*

Retrosynthesis ID: 12398

2.2.2 Knoevenagel Condensation



Substrates:

1. Benzaldehyde - *available at Sigma-Aldrich*
2. CC=CC=CCOC(=O)CC(C)=O

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccccc1)C(C)=O

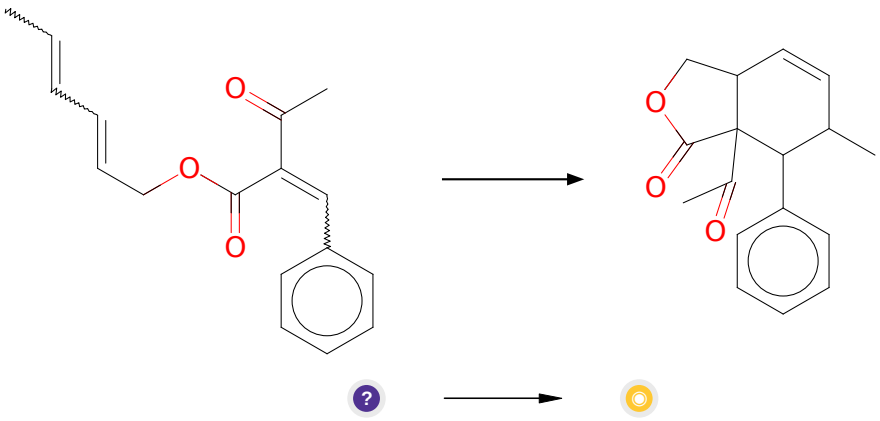
Typical conditions: base e.g.piperidine. solvent

Protections: none

Reference: *10.1002/0471264180.or015.02* and *10.13005/ojc/350154*

Retrosynthesis ID: 252

2.2.3 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccccc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccccc1

Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.3 Path 3

Score: 76.25

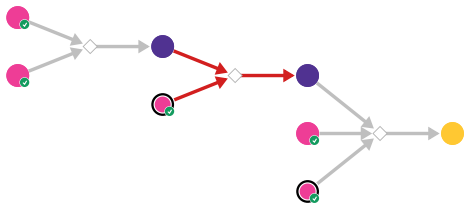
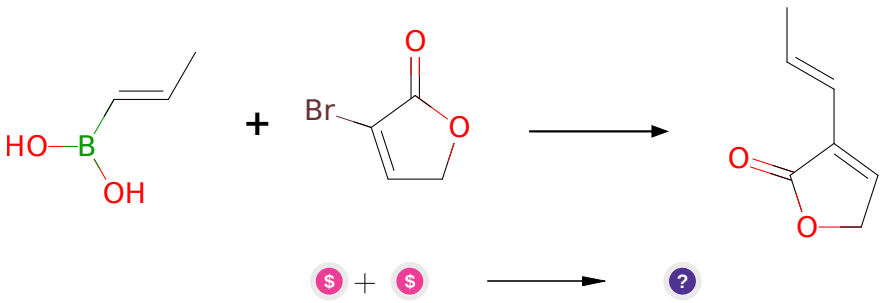


Figure 3: Outline of path 3

2.3.1 Suzuki coupling of vinyl bromides with alkenyl boronic acids



Substrates:

1. trans-Propenylboronic acid - *available at Sigma-Aldrich*
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1=CCOC1=O

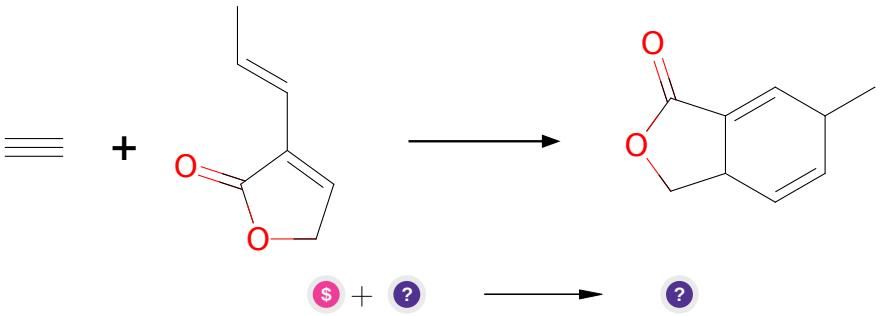
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 24937

2.3.2 Diels-Alder



Substrates:

1. Calcium carbide - *available at Sigma-Aldrich*
2. C/C=C/C1=CCOC1=O

Products:

1. CC1C=CC2COC(=O)C2=C1

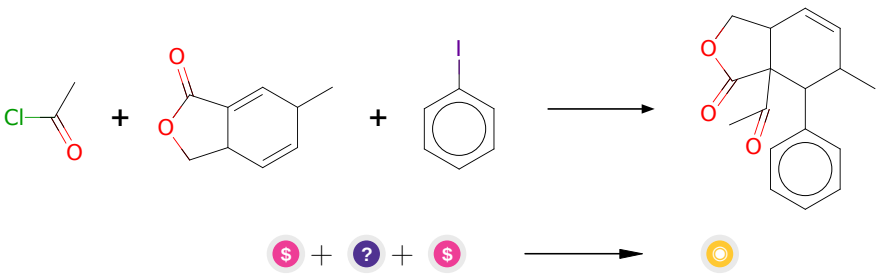
Typical conditions: H2O.MeOH.EtOH.isooctane

Protections: none

Reference: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z*

Retrosynthesis ID: 10557

2.3.3 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. Iodobenzene - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccccc1

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

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 12521

2.4 Path 4

Score: 76.25

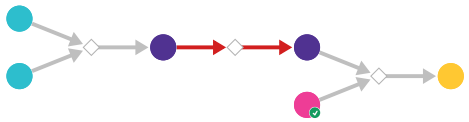
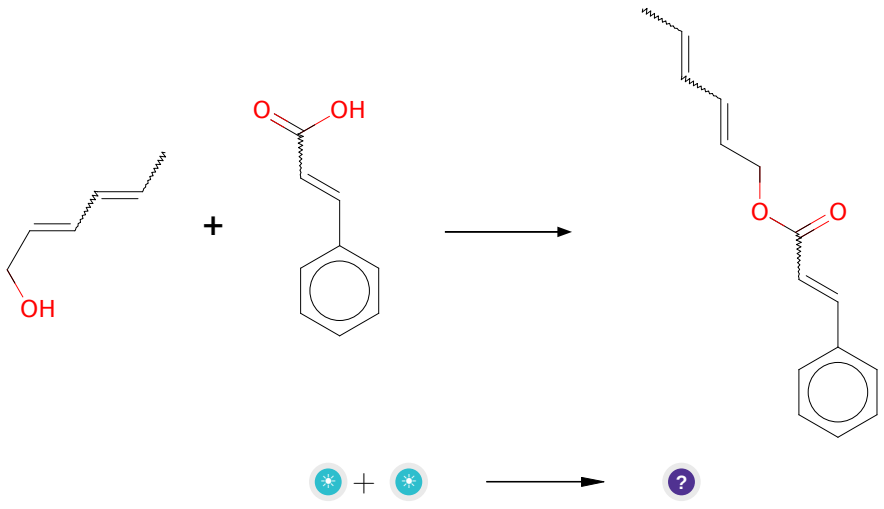


Figure 4: Outline of path 4

2.4.1 Steglich Esterification



Substrates:

1. cinnamic acid
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C=Cc1ccccc1

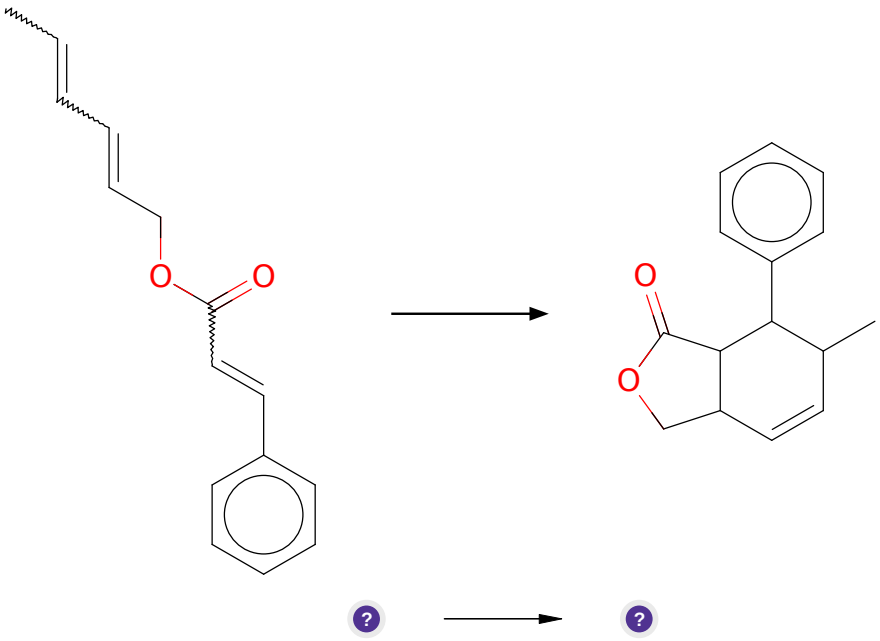
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.4.2 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C=Cc1ccccc1

Products:

1. CC1C=CC2COC(=O)C2C1c1ccccc1

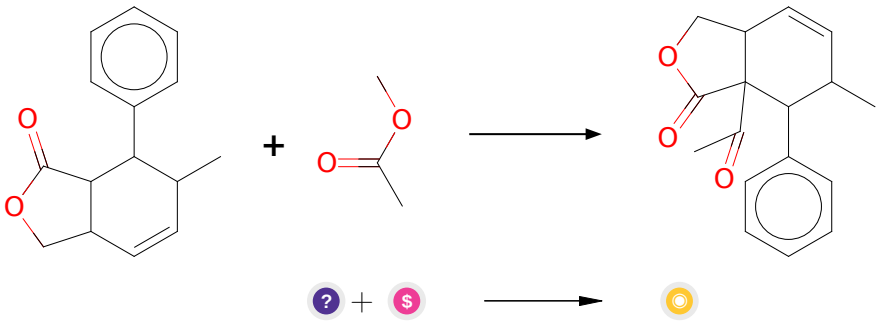
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.4.3 Claisen Condensation



Substrates:

1. CC1C=CC2COC(=O)C2C1c1ccccc1
2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccccc1

Typical conditions: Base.Solvent

Protections: none

Reference: *10.1021/cr020703u* and *10.1021/cr60088a002*

Retrosynthesis ID: 5015

2.5 Path 5

Score: 76.25

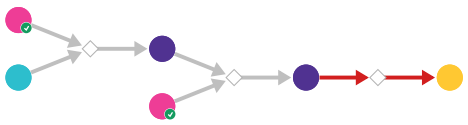
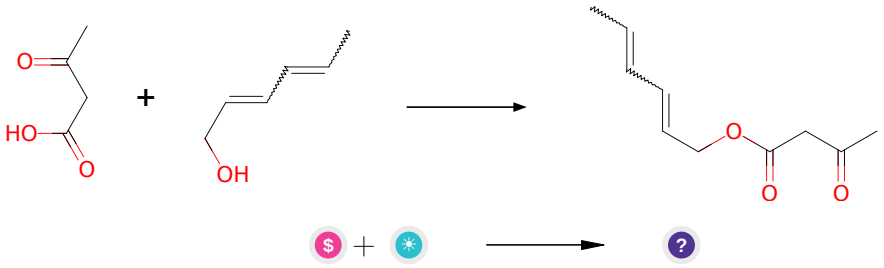


Figure 5: Outline of path 5

2.5.1 Steglich Esterification



Substrates:

1. Lithium acetoacetate - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)CC(C)=O

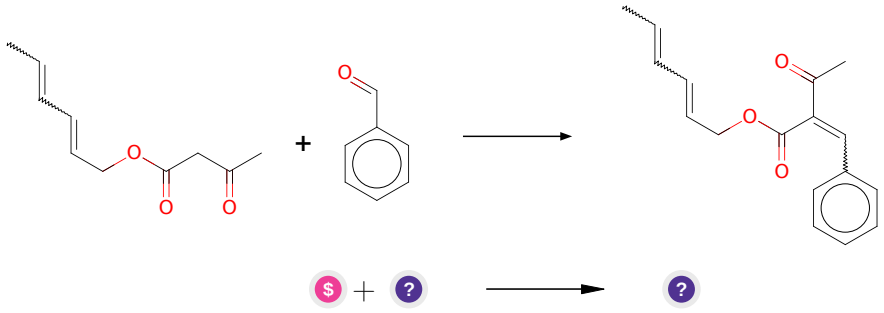
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.5.2 Knoevenagel Condensation



Substrates:

1. Benzaldehyde - *available at Sigma-Aldrich*
2. CC=CC=CCOC(=O)CC(C)=O

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccccc1)C(C)=O

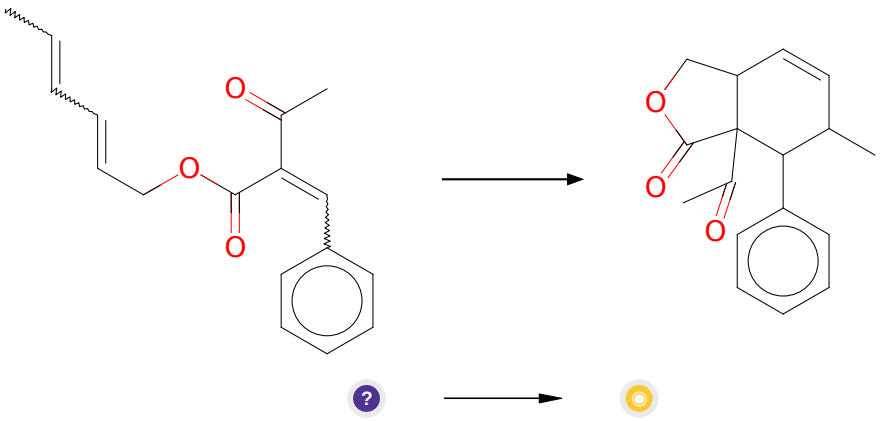
Typical conditions: base e.g.piperidine. solvent

Protections: none

Reference: *10.1002/0471264180.or015.02* and *10.13005/ojc/350154*

Retrosynthesis ID: 252

2.5.3 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccccc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccccc1

Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116