Paths of analysis*

L9_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: `84.06`

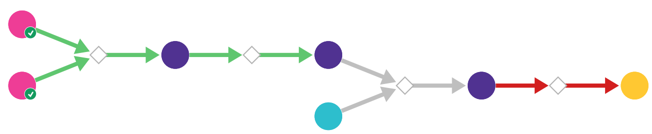
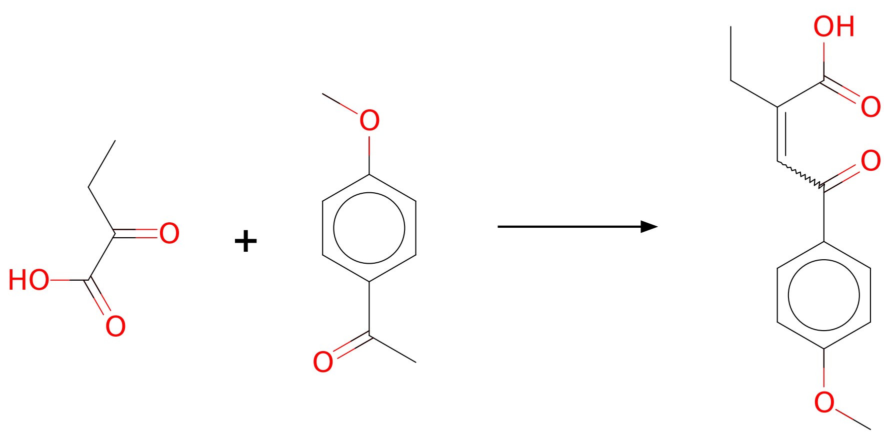
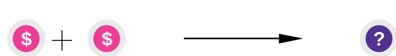


Figure 1: Outline of path 1

2.1.1 Aldol Condensation





Substrates:

1. Ketobutyric acid - *available at Sigma-Aldrich*
2. Acetanisole - *available at Sigma-Aldrich*

Products:

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

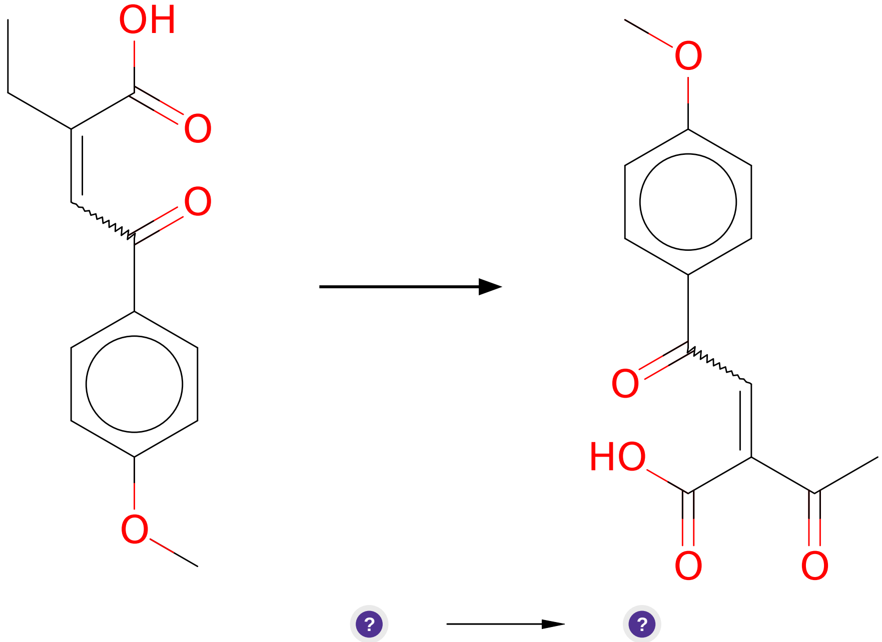
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10898

2.1.2 Allylic Oxidation of Alkenes



Substrates:

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

Products:

1. COc1ccc(C(=O)C=C(C(C)=O)C(=O)O)cc1

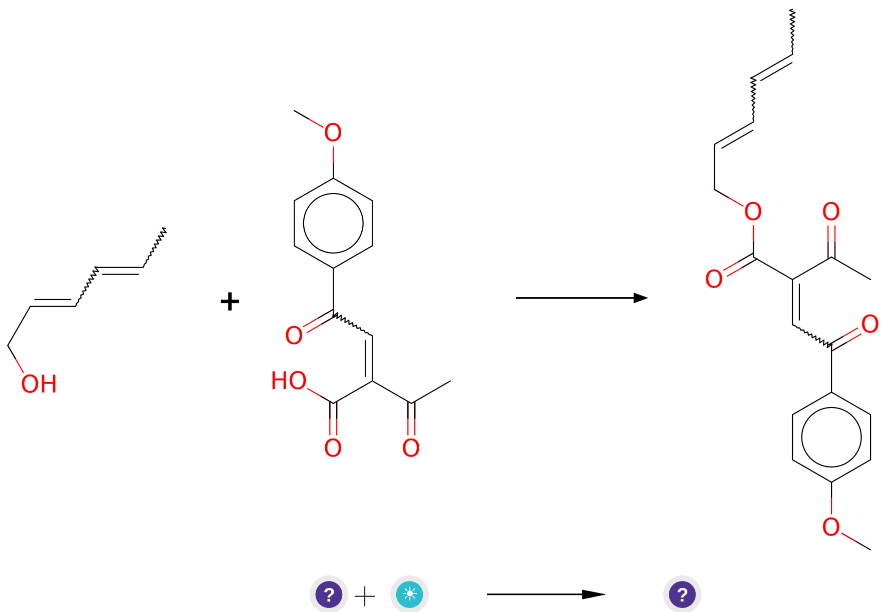
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.1.3 Steglich Esterification



Substrates:

1. COc1ccc(C(=O)C=C(C(C)=O)C(=O)O)cc1
2. sorbic alcohol

Products:

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

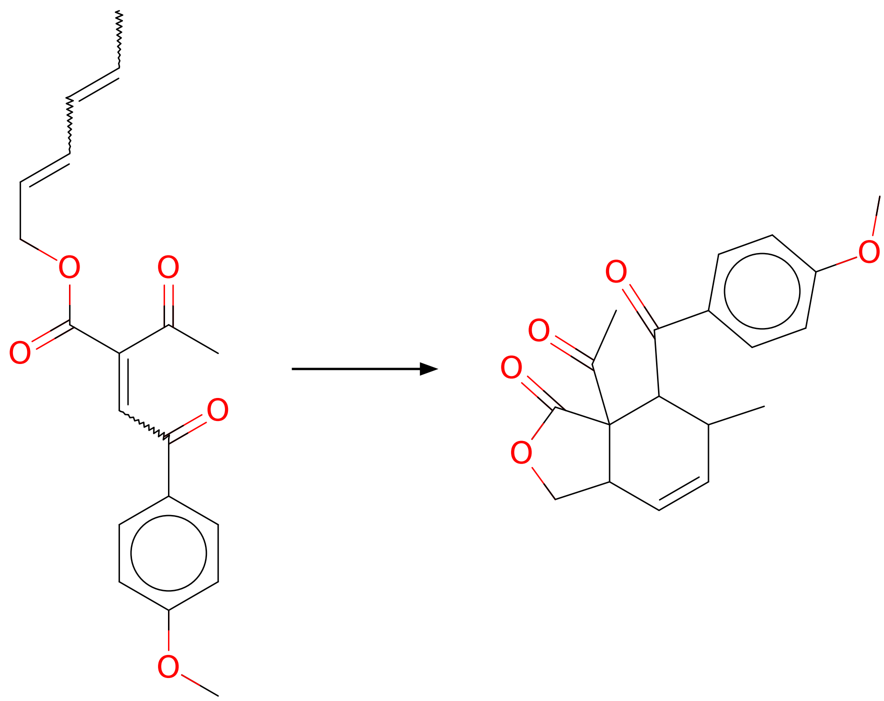
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

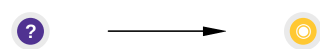
Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.1.4 Diels-Alder





Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)cc1

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: 90.31

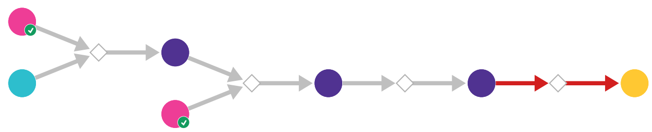
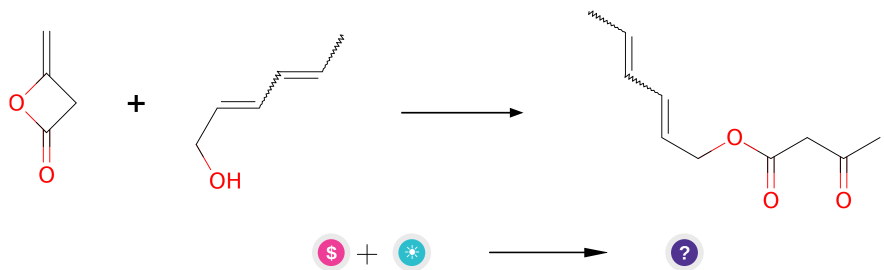


Figure 2: Outline of path 2

2.2.1 Reaction of alcohols with diketene



Substrates:

1. diketene - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

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

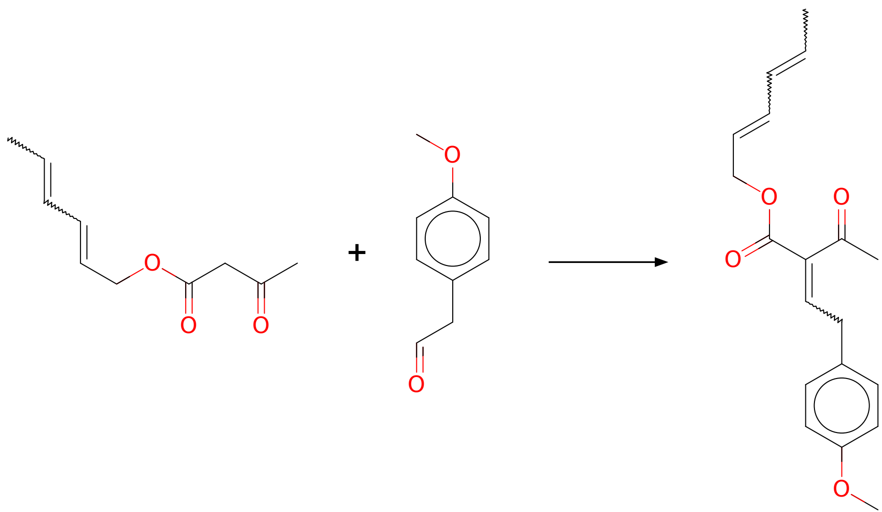
Typical conditions: DCM.heat

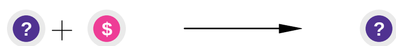
Protections: none

Reference: WO2012/31028 A2 (p.39) AND *10.1021/ol051945u* AND *10.1021/ol0069756* AND *10.1002/adsc.200800532*

Retrosynthesis ID: 14881

2.2.2 Knoevenagel Condensation





Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. 2-(4-Methoxyphenyl)acetaldehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=CCc1ccc(OC)cc1)C(C)=O

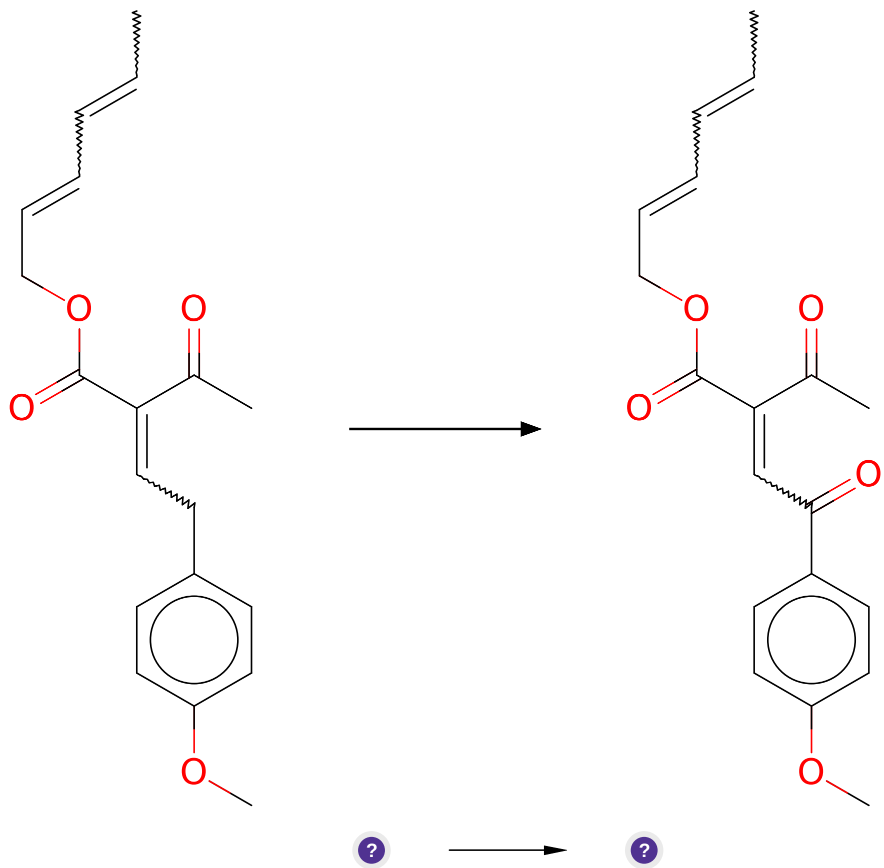
Typical conditions: base e.g.piperidine. solvent

Protections: none

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

Retrosynthesis ID: 252

2.2.3 Allylic Oxidation of Alkenes



Substrates:

1. CC=CC=CCOC(=O)C(=CCc1ccc(OC)cc1)C(C)=O

Products:

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

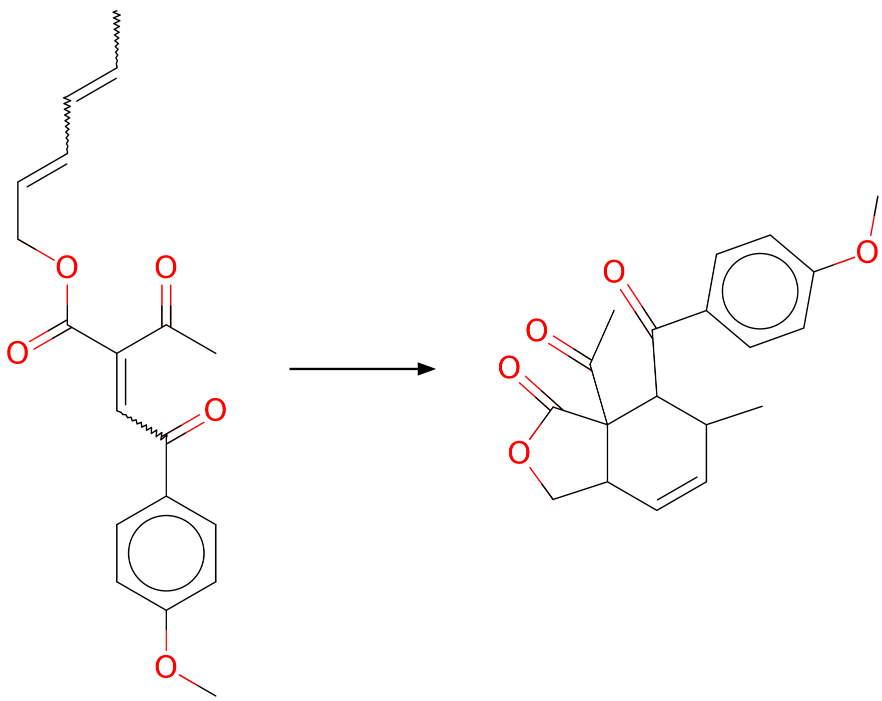
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

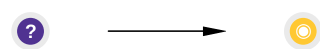
Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.2.4 Diels-Alder





Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)cc1

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: `90.31`

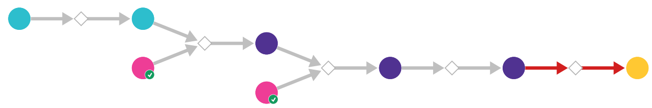
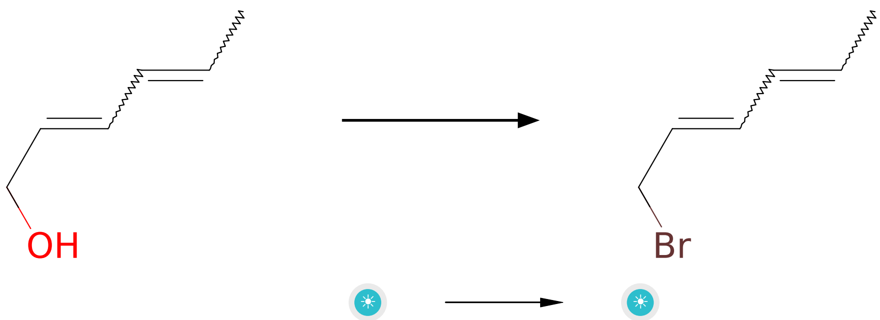


Figure 3: Outline of path 3

2.3.1 Appel Reaction



Substrates:

1. sorbic alcohol

Products:

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

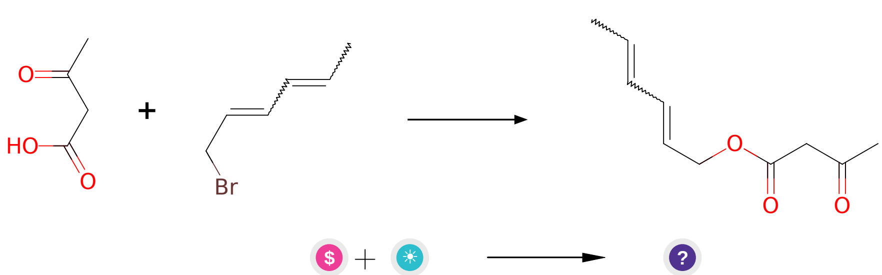
Typical conditions: PPh3.CBr4

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

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



Substrates:

1. Lithium acetoacetate - *available at Sigma-Aldrich*
2. 1-brom-hexa-2,4-dien

Products:

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

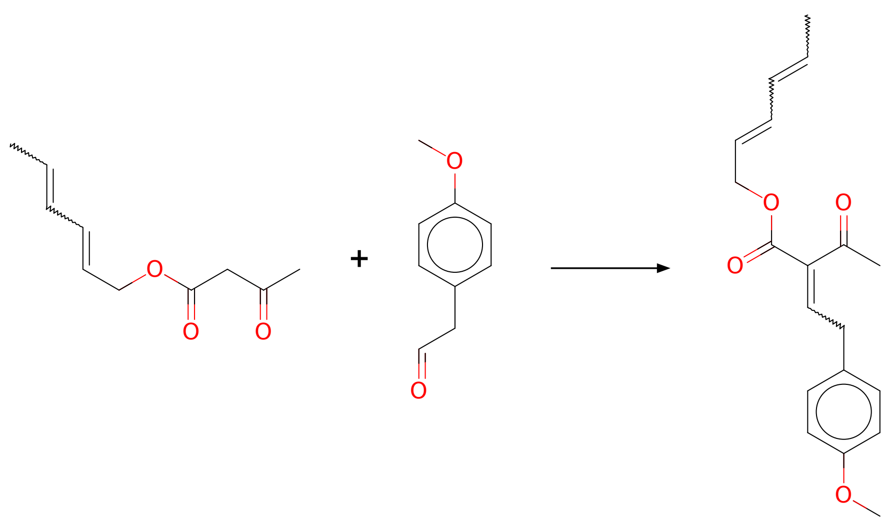
Typical conditions: K2CO3.DMF

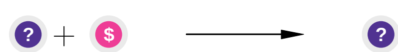
Protections: none

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

2.3.3 Knoevenagel Condensation





Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. 2-(4-Methoxyphenyl)acetaldehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=CCc1ccc(OC)cc1)C(C)=O

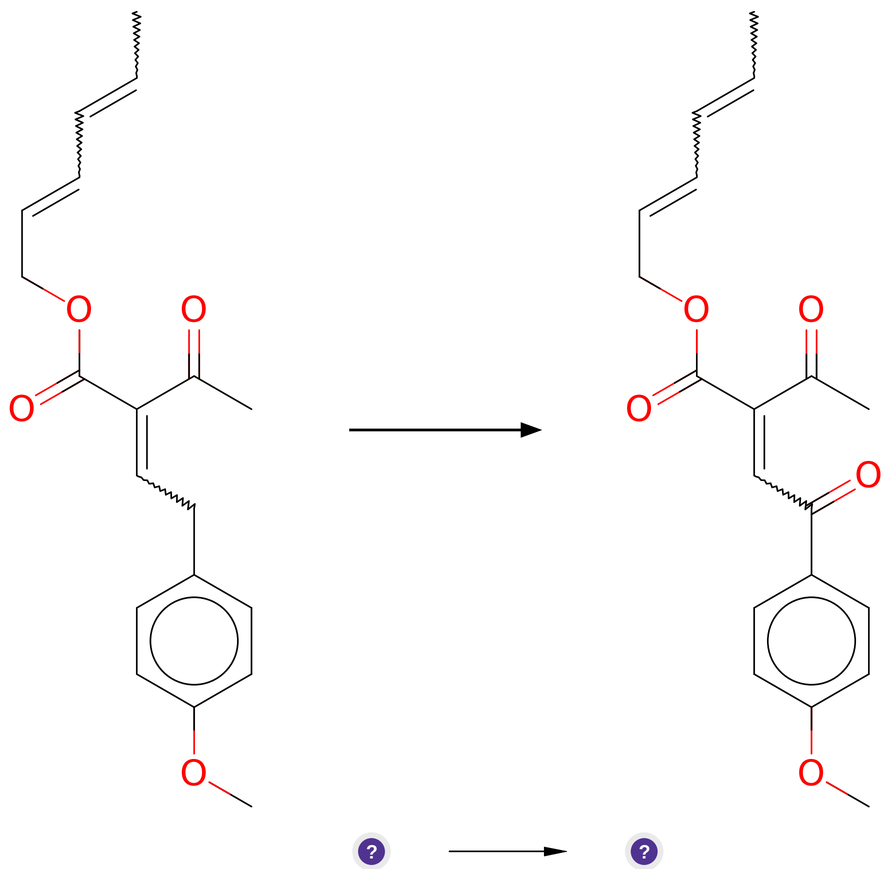
Typical conditions: base e.g.piperidine. solvent

Protections: none

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

Retrosynthesis ID: 252

2.3.4 Allylic Oxidation of Alkenes



Substrates:

1. CC=CC=CCOC(=O)C(=CCc1ccc(OC)cc1)C(C)=O

Products:

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

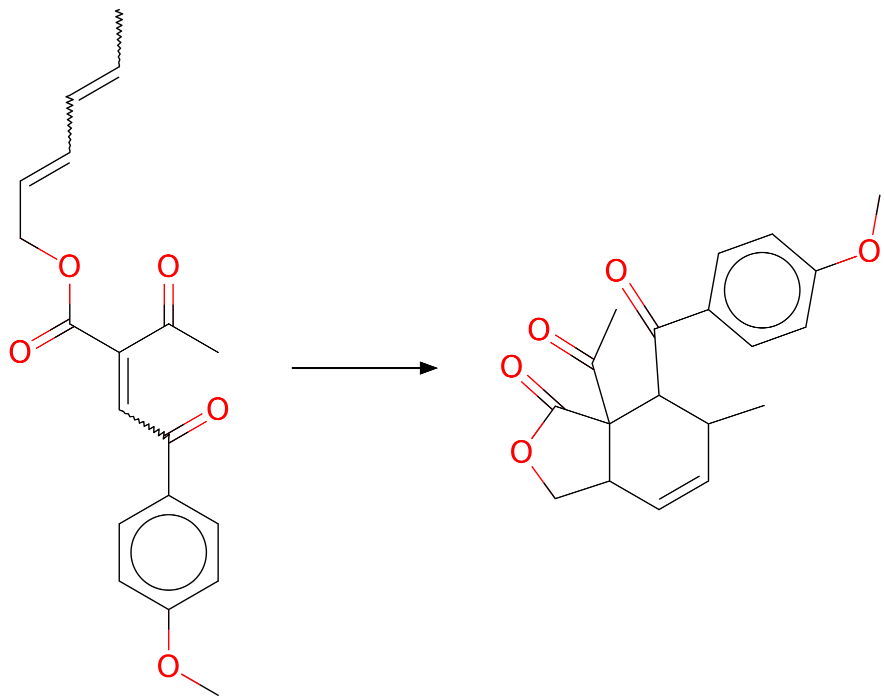
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

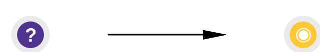
Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.3.5 Diels-Alder





Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)cc1

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 Path 4

Score: `90.31`

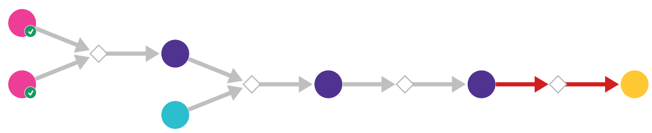
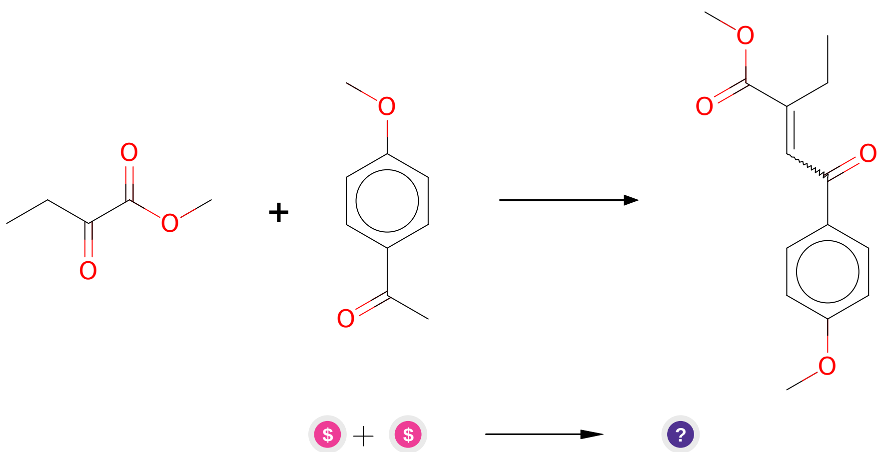


Figure 4: Outline of path 4

2.4.1 Aldol Condensation



Substrates:

1. Acetanisole - *available at Sigma-Aldrich*
2. Methyl 2-ketobutyrate - *available at Sigma-Aldrich*

Products:

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

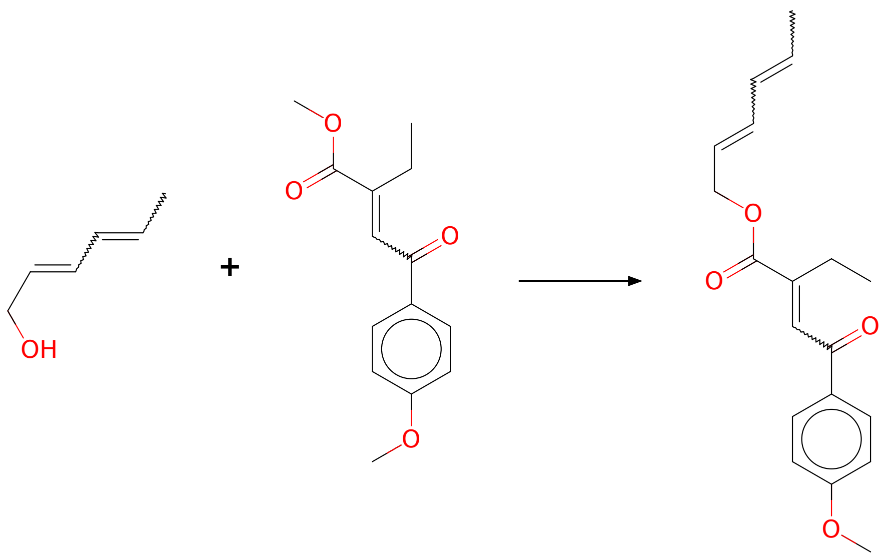
Typical conditions: NaOEt.base

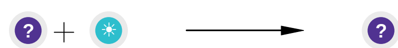
Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10898

2.4.2 Acid catalyzed transesterification





Substrates:

1. CCC(=CC(=O)c1ccc(OC)cc1)C(=O)OC
2. sorbic alcohol

Products:

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

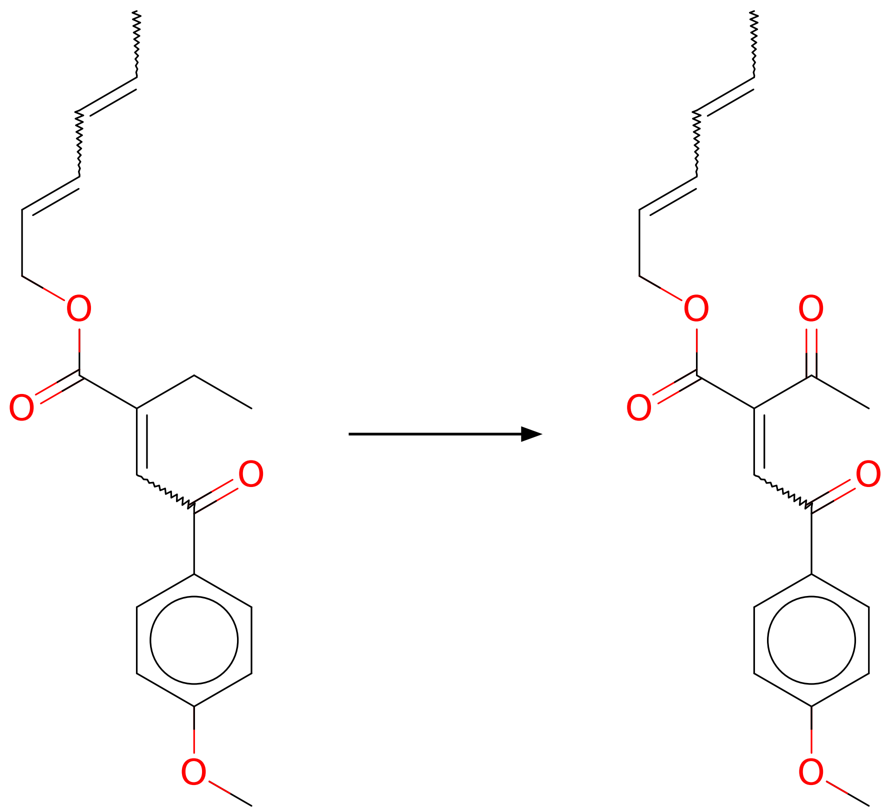
Typical conditions: H+

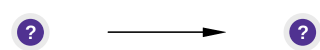
Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.4.3 Allylic Oxidation of Alkenes





Substrates:

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

Products:

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

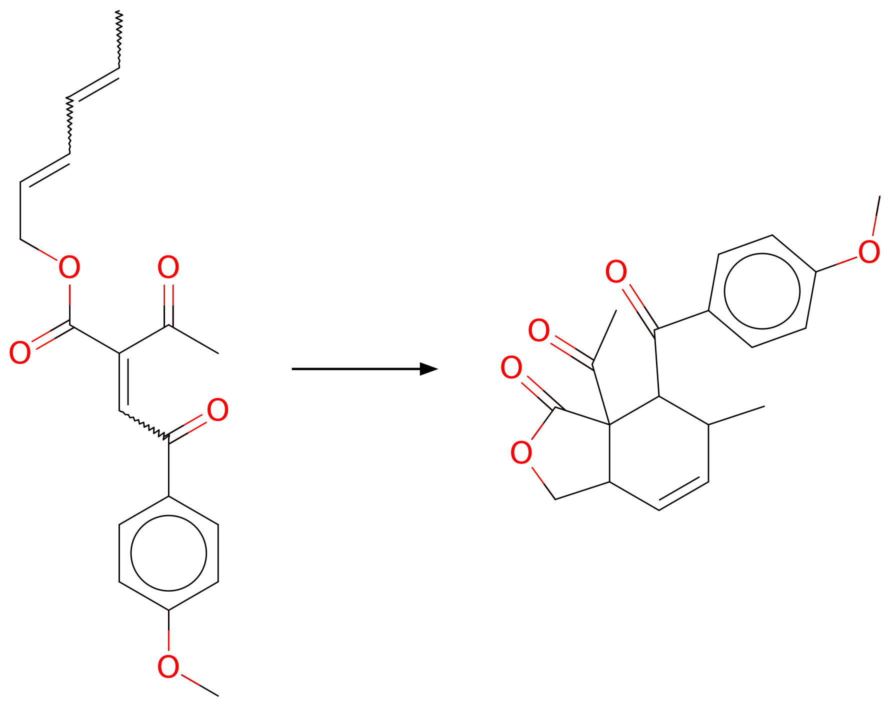
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

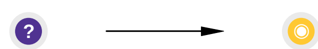
Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.4.4 Diels-Alder





Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)cc1

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

2.5 Path 5

Score: 90.31

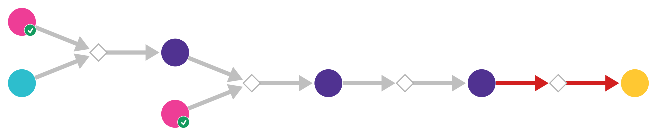
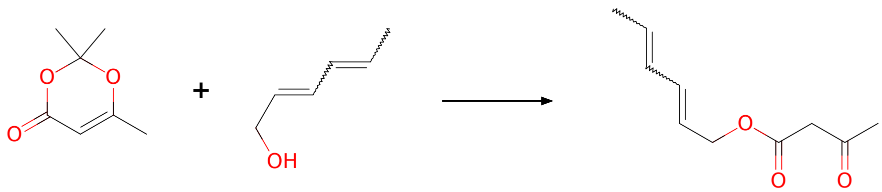
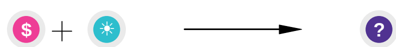


Figure 5: Outline of path 5

2.5.1 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

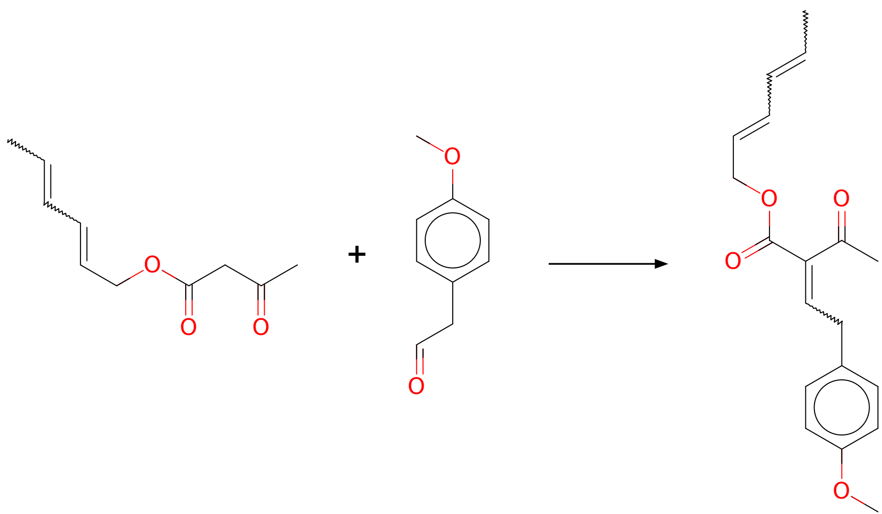
Typical conditions: alcohol

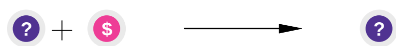
Protections: none

Reference: DOI: *10.1021/ja00154a049*

Retrosynthesis ID: 12398

2.5.2 Knoevenagel Condensation





Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. 2-(4-Methoxyphenyl)acetaldehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=CCc1ccc(OC)cc1)C(C)=O

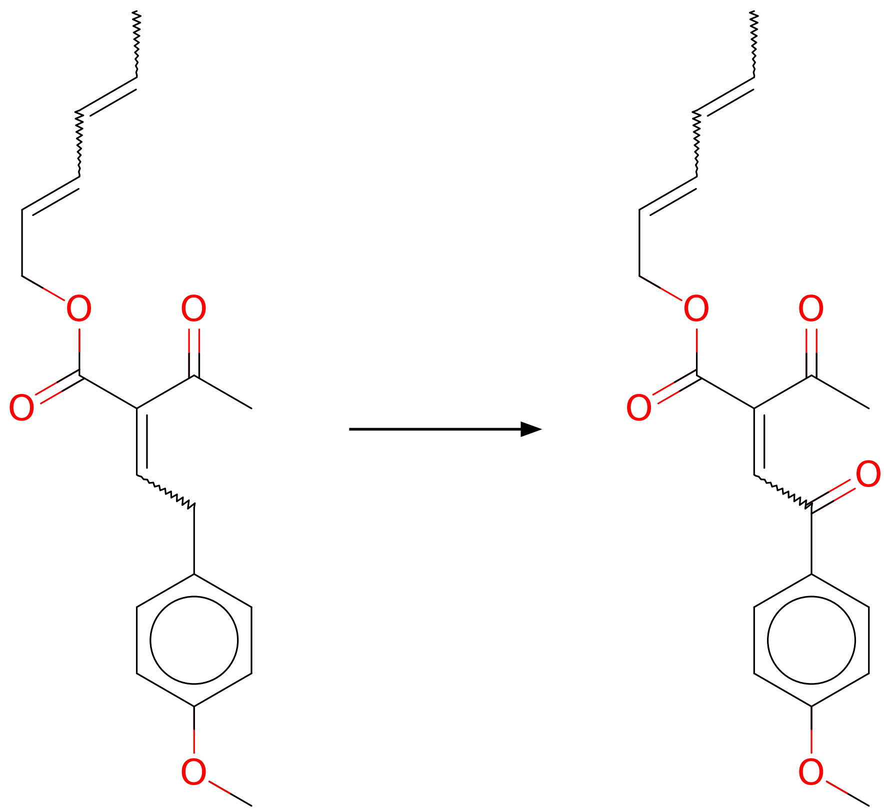
Typical conditions: base e.g.piperidine. solvent

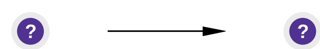
Protections: none

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

Retrosynthesis ID: 252

2.5.3 Allylic Oxidation of Alkenes





Substrates:

1. CC=CC=CCOC(=O)C(=CCc1ccc(OC)cc1)C(C)=O

Products:

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

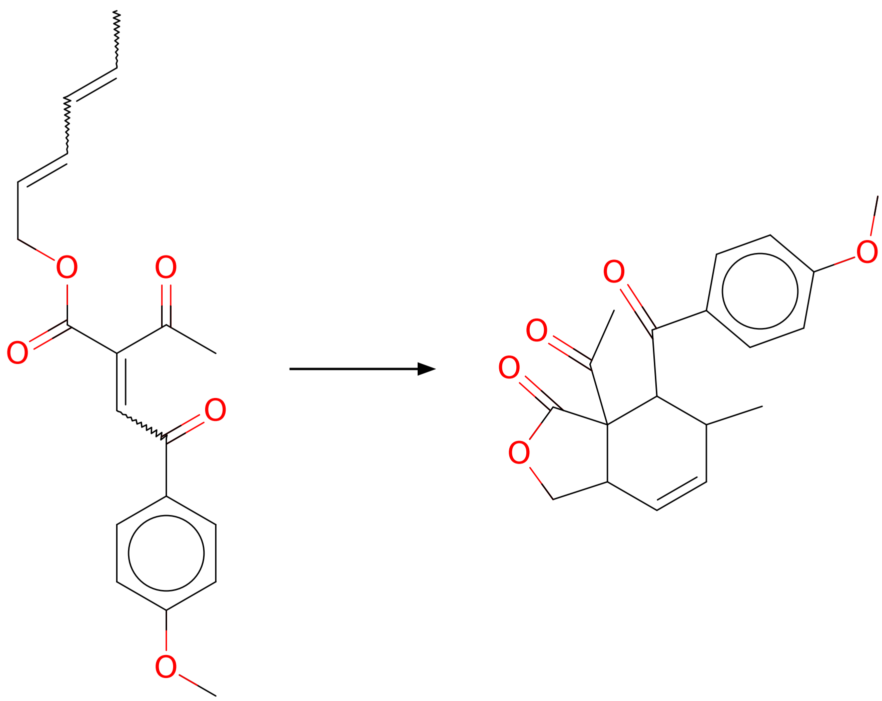
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.5.4 Diels-Alder



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)cc1

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