Paths of analysis*

L6_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

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: 76.25

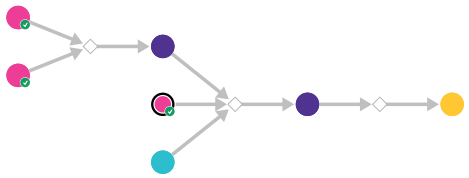
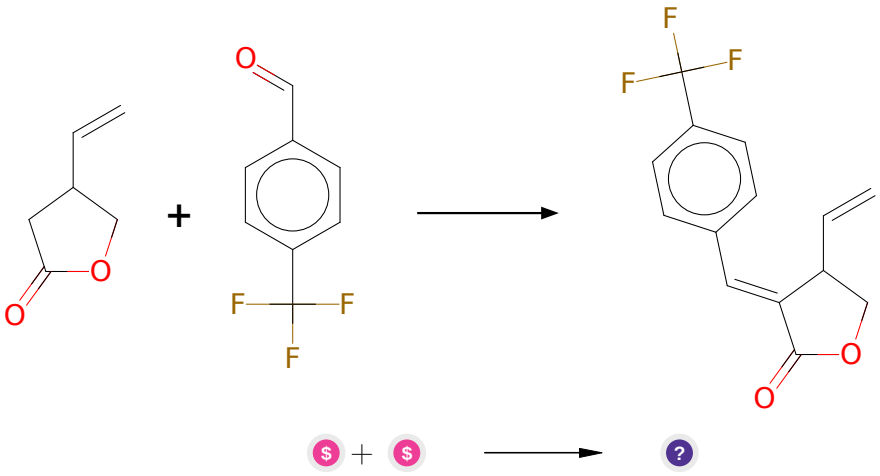


Figure 1: Outline of path 1

2.1.1 Condensation of esters with aldehydes



Substrates:

1. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*
2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)/C1=C/c1ccc(C(F)(F)F)cc1

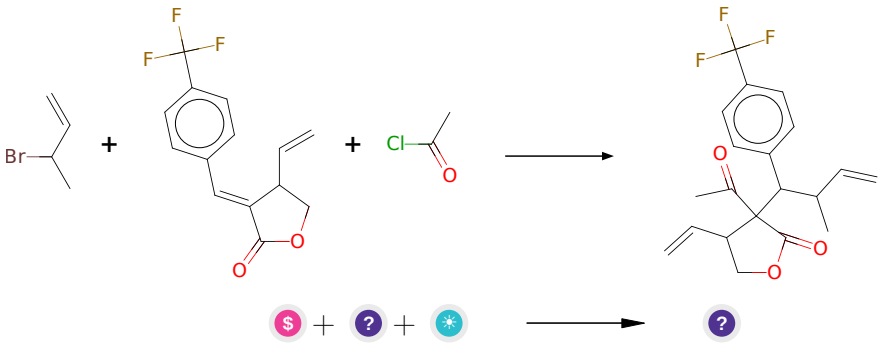
Typical conditions: 1.LDA.2RCHO

Protections: none

Reference: *10.1021/jo970387x* AND *10.1021/jo00076a051* AND *10.1016/S0040-4039(97)10827-9* AND *10.1055/s-2002-25767* AND *10.1039/P19920003277*

Retrosynthesis ID: 14981

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. C=CC1COC(=O)/C1=C/c1ccc(C(F)(F)F)cc1
3. 3-brom-but-1-en

Products:

1. C=CC(C)C(c1ccc(C(F)(F)F)cc1)C1(C(C)=O)C(=O)OCC1C=C

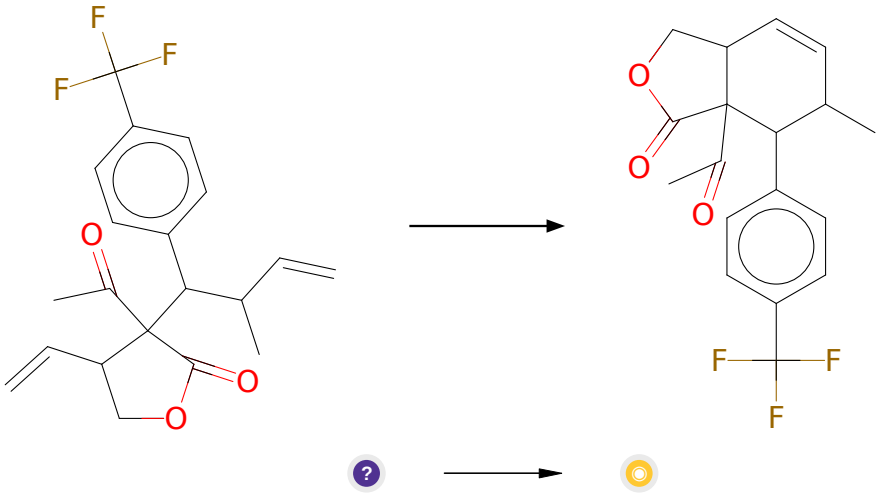
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20523

2.1.3 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1ccc(C(F)(F)F)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C(F)(F)F)cc1

Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.2 Path 2

Score: 76.25

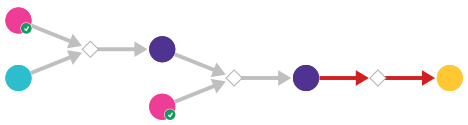
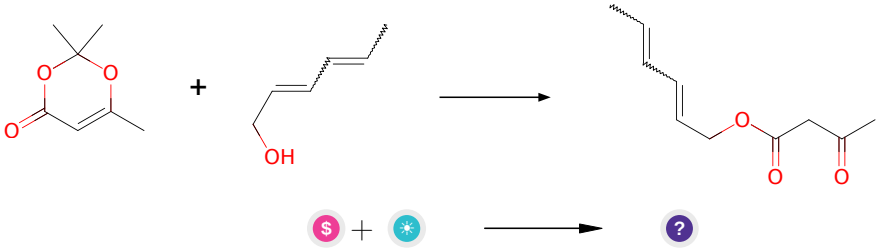


Figure 2: Outline of path 2

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

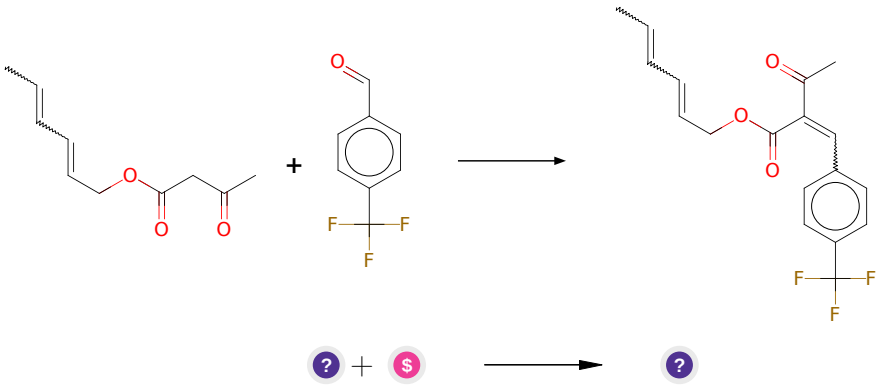
Typical conditions: alcohol

Protections: none

Reference: DOI: *10.1021/ja00154a049*

Retrosynthesis ID: 12398

2.2.2 Knoevenagel Condensation



Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C(F)(F)F)cc1)C(C)=O

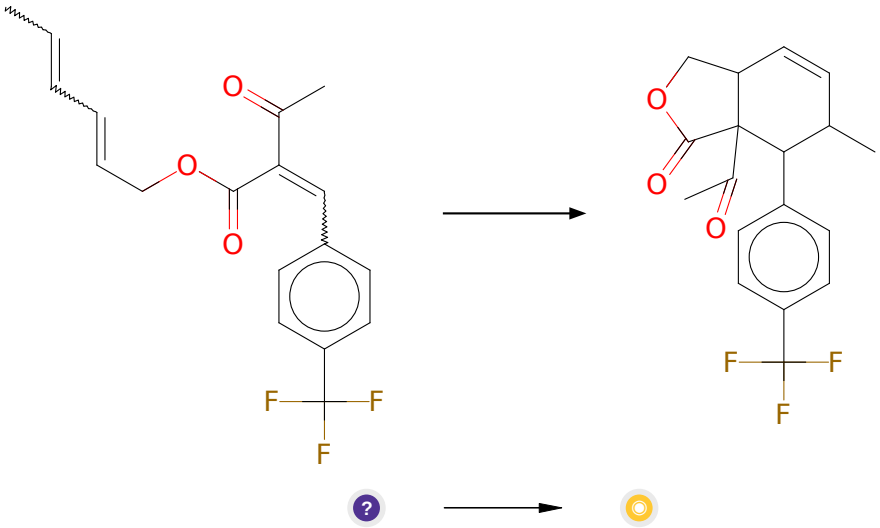
Typical conditions: base e.g.piperidine. solvent

Protections: none

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

Retrosynthesis ID: 252

2.2.3 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C(F)(F)F)cc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C(F)(F)F)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: 76.25

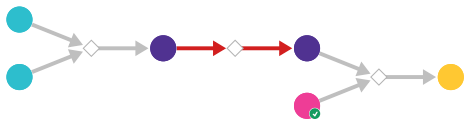
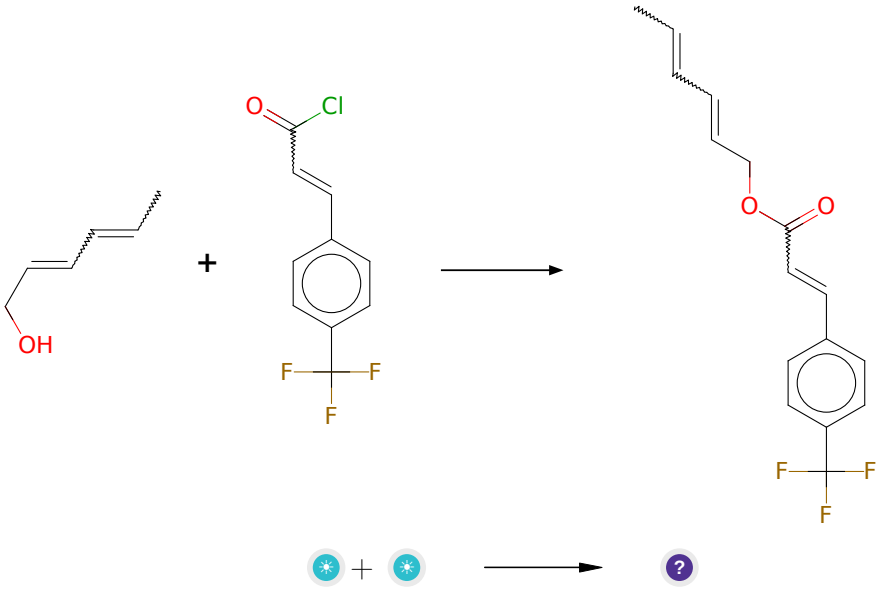


Figure 3: Outline of path 3

2.3.1 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. 3-(4-trifluoromethyl-phenyl)-acryloyl chloride
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C=Cc1ccc(C(F)(F)F)cc1

Typical conditions: base.DCM

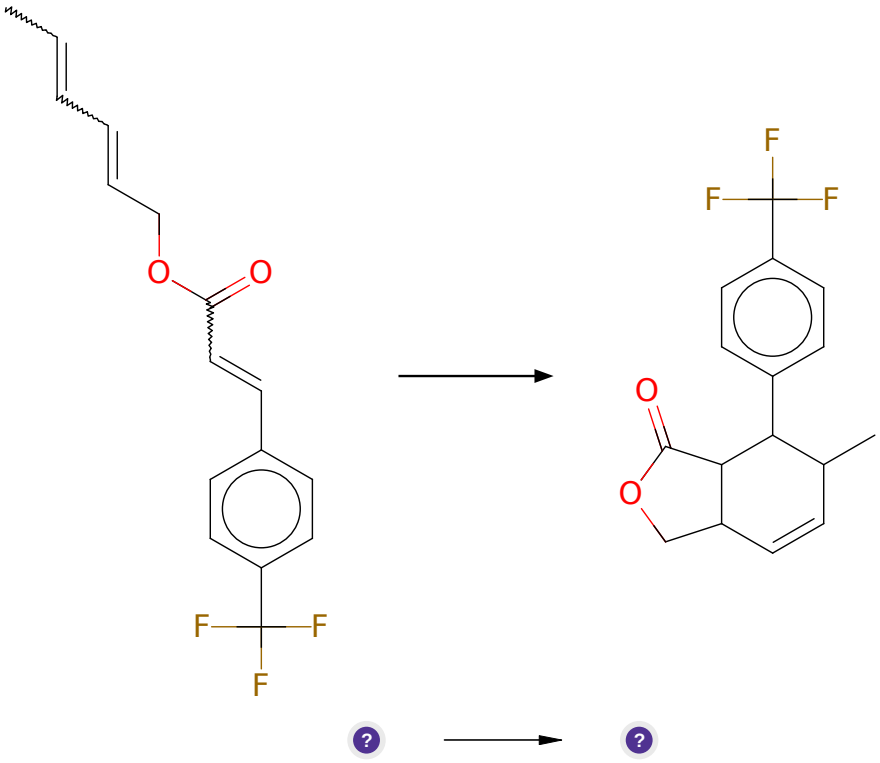
Protections: none

Reference: *10.1016/j.bmcl.2012.03.021* AND *10.1021/ja026266i* (SI, hydroperoxides) AND *10.1016/j.tetasy.2004.07.044* AND *10.1021/jm1006929*

(SI) AND *10.1016/j.tet.2011.05.017* AND *10.1016/j.tetasy.2012.09.002* AND *10.1021/ol016268s* (SI) AND *10.1021/jo801116n* AND *10.1021/jo00279a041* AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549

2.3.2 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C=Cc1ccc(C(F)(F)F)cc1

Products:

1. CC1C=CC2COC(=O)C2C1c1ccc(C(F)(F)F)cc1

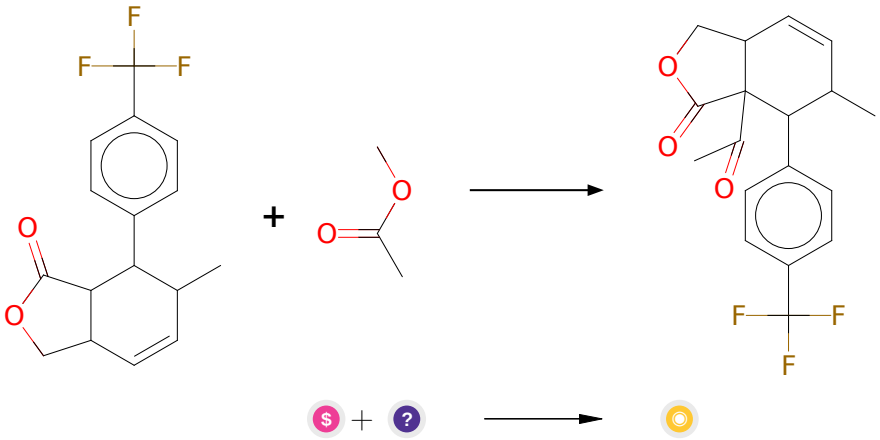
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.3.3 Claisen Condensation



Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2C1c1ccc(C(F)(F)F)cc1

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C(F)(F)F)cc1

Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.4 Path 4

Score: `76.25`

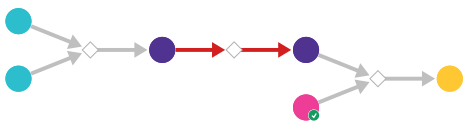
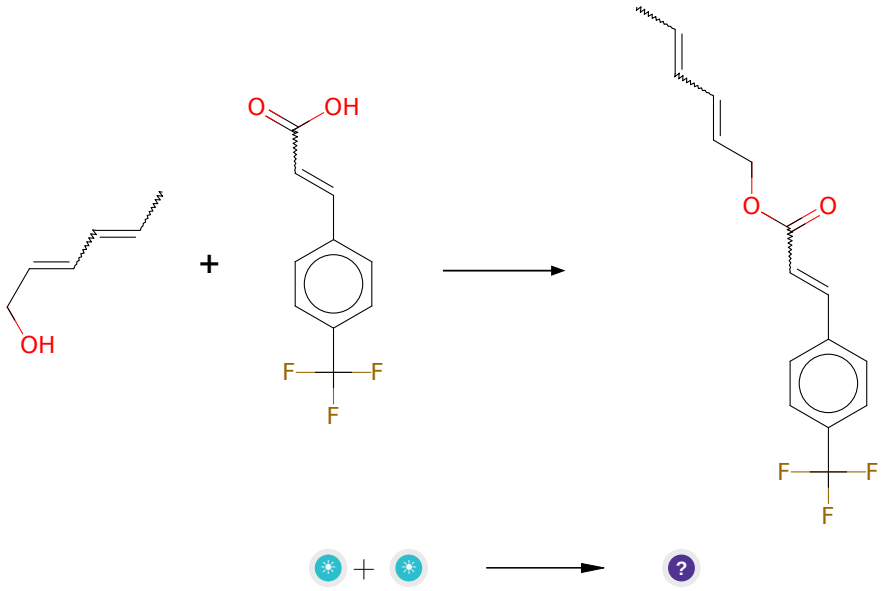


Figure 4: Outline of path 4

2.4.1 Steglich Esterification



Substrates:

1. sorbic alcohol
2. 4-trifluormethyl-zimtsaeure

Products:

1. CC=CC=CCOC(=O)C=Cc1ccc(C(F)(F)F)cc1

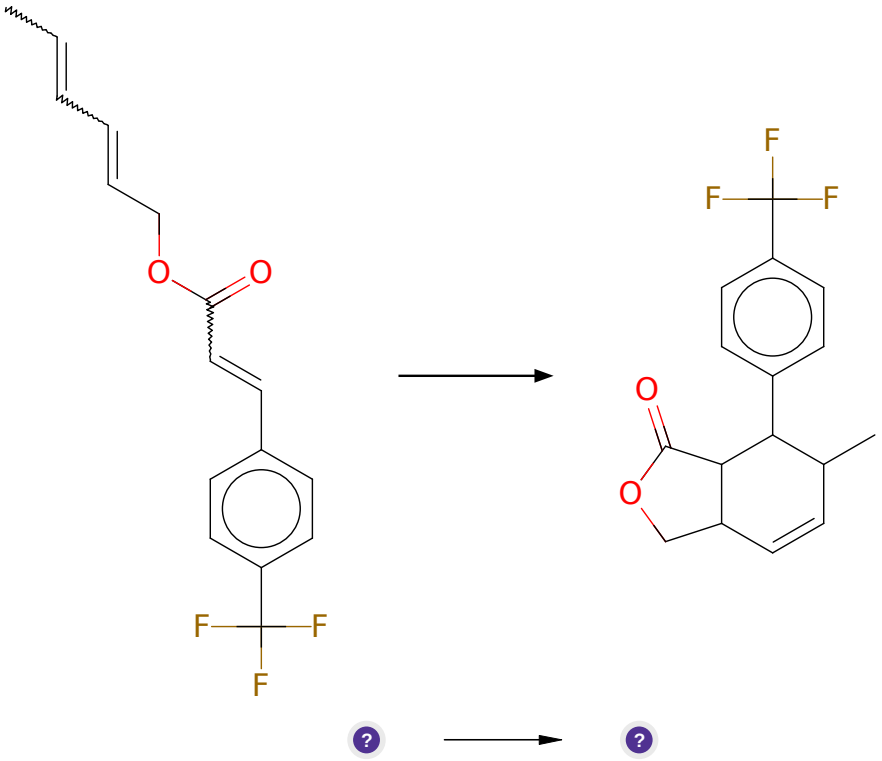
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.4.2 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C=Cc1ccc(C(F)(F)F)cc1

Products:

1. CC1C=CC2COC(=O)C2C1c1ccc(C(F)(F)F)cc1

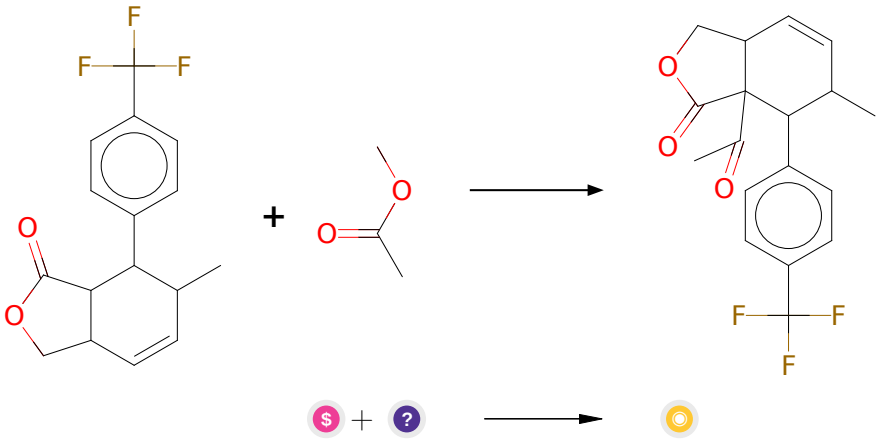
Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

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

2.4.3 Claisen Condensation



Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2C1c1ccc(C(F)(F)F)cc1

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C(F)(F)F)cc1

Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.5 Path 5

Score: `76.25`

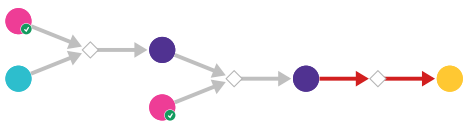
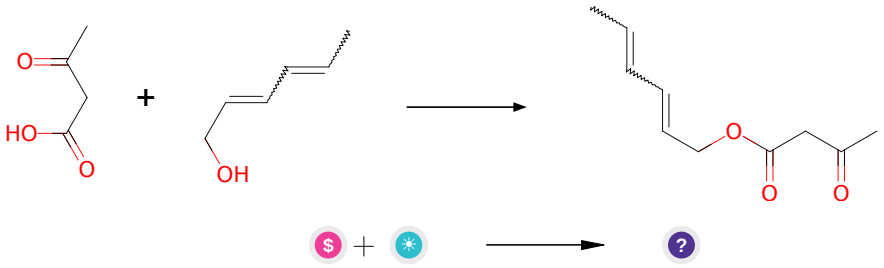


Figure 5: Outline of path 5

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

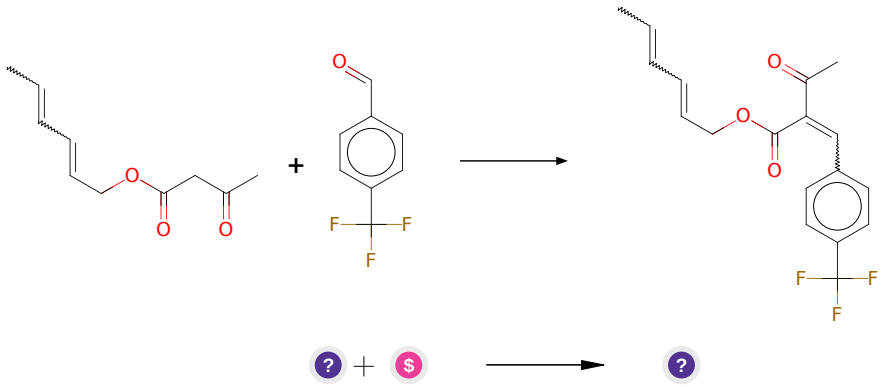
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.5.2 Knoevenagel Condensation



Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. a,a,a-Trifluoro-p-tolualdehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C(F)(F)F)cc1)C(C)=O

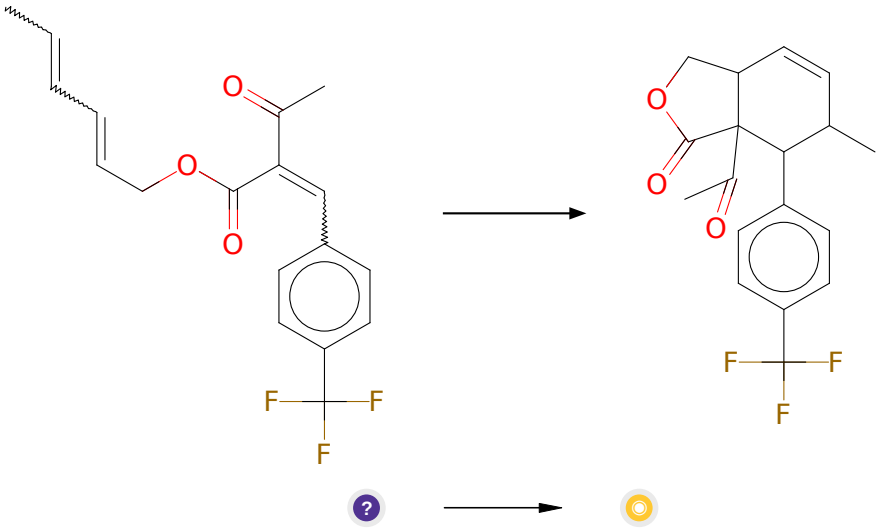
Typical conditions: base e.g.piperidine. solvent

Protections: none

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

Retrosynthesis ID: 252

2.5.3 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C(F)(F)F)cc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C(F)(F)F)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