Paths of analysis*
L3_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+1000 000*(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.*
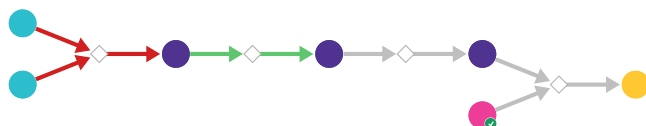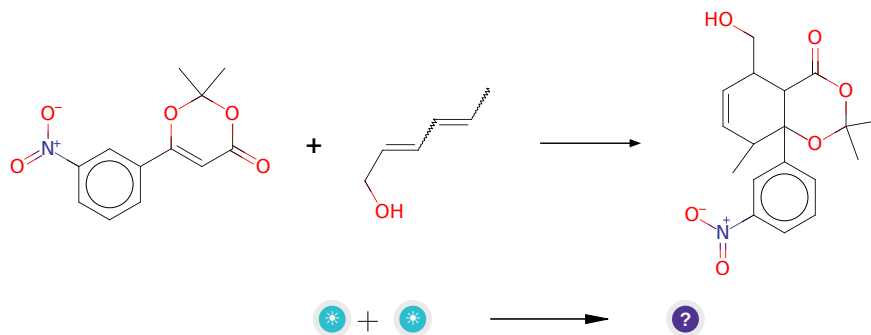
2.1 Path 1

Score: 84.06

Figure 1: Outline of path 1

2.1.1 Diels-Alder

Substrates:

1. C12H11NO5

2. sorbic alcohol

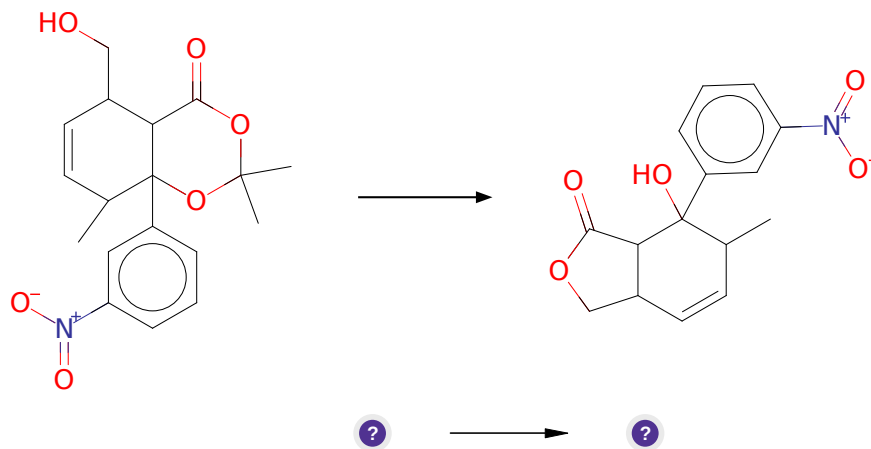**Products:**

1. CC1C=CC(CO)C2C(=O)OC(C)(C)OC12c1cccc([N+](=O)[O-])c1

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

Protections: none

Retrosynthesis ID: 18116

2.1.2 Hydrolysis of acetals

Substrates:

1. CC1C=CC(CO)C2C(=O)OC(C)(C)OC12c1cccc([N+](=O)[O-])c1

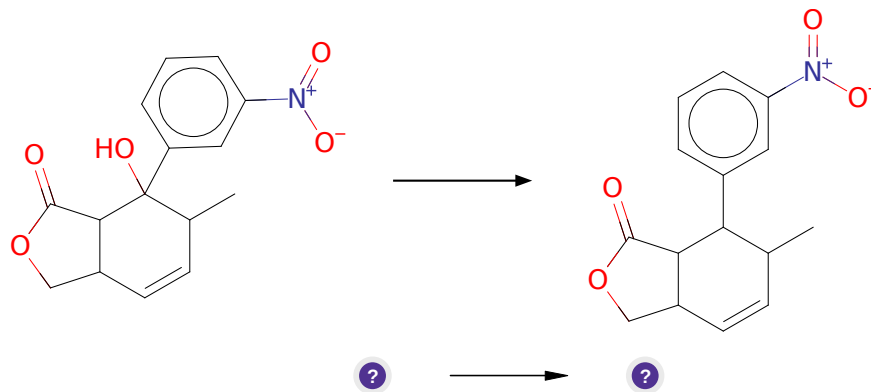**Products:**

1. CC1C=CC2COC(=O)C2C1(O)c1cccc([N+](=O)[O-])c1

Typical conditions: NaOH.MeOH/H2O.rt

Protections: none

Retrosynthesis ID: 23615

2.1.3 Deoxygenation of alcohols with silanes

Substrates:

1. CC1C=CC2COC(=O)C2C1(O)c1cccc([N+](=O)[O-])c1
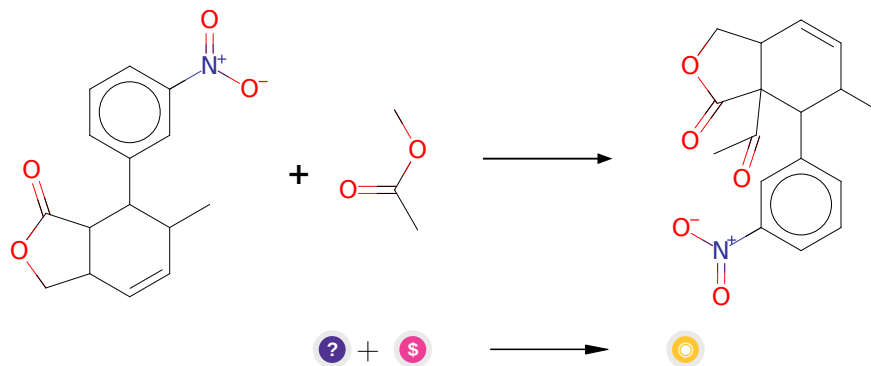
Products:

1. CC1C=CC2COC(=O)C2C1c1cccc([N+](=O)[O-])c1

Typical conditions: Et3SiH.Lewis.or.Bronsted.Acid

Protections: none

Reference: *10.1021/jo0158534* AND *10.1021/ol3020144*

Retrosynthesis ID: 8163

2.1.4 Claisen Condensation

Substrates:

1. CC1C=CC2COC(=O)C2C1c1cccc([N+](=O)[O-])c1

2. Methyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cccc([N+](=O)[O-])c1

Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015
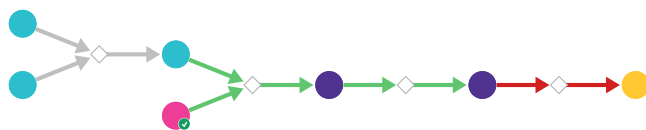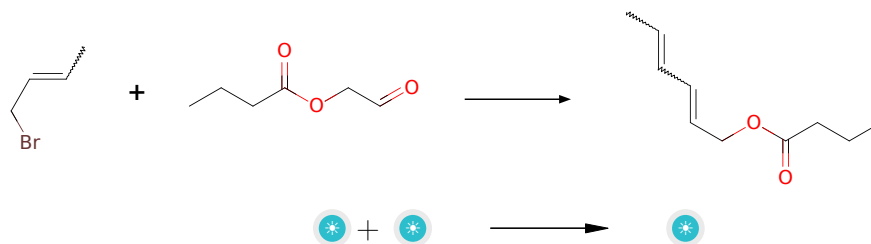
2.2   Path 2

Score: 90.31

Figure 2: Outline of path 2

2.2.1   Wittig olefination

Substrates:

1. butyryloxy-acetaldehyde

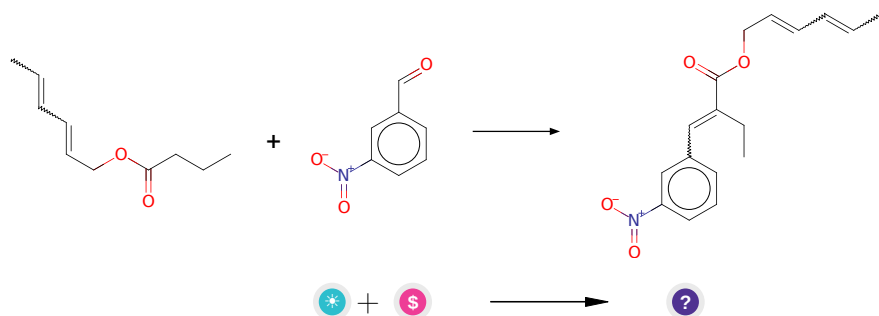2. crotyl bromide

Products:

1. butyric acid hexa-2,4-dienyl ester

Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1021/ja0015287* and *10.1021/ja404673s* and *10.1021/ol901979x*

Retrosynthesis ID: 9545

2.2.2 Condensation of esters with aldehydes/ketones

Substrates:

1. butyric acid hexa-2,4-dienyl ester

2. 3-Nitrobenzaldehyde - *available at Sigma-Aldrich*

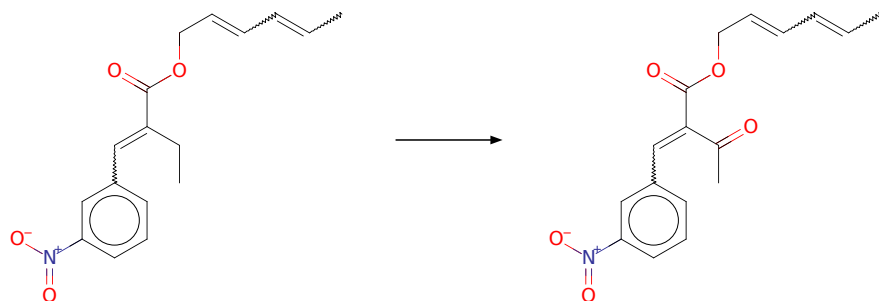**Products:**

1. CC=CC=CCOC(=O)C(=Cc1cccc([N+](=O)[O-])c1)CC
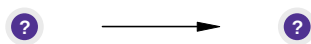
Typical conditions: LDA.THF

Protections: none

Reference: *10.1021/op040006z* AND *10.1016/j.bmcl.2005.10.104* AND

Retrosynthesis ID: 14983

2.2.3 Allylic Oxidation of Alkenes

Substrates:

1. CC=CC=CCOC(=O)C(=Cc1cccc([N+](=O)[O-])c1)CC

Products:

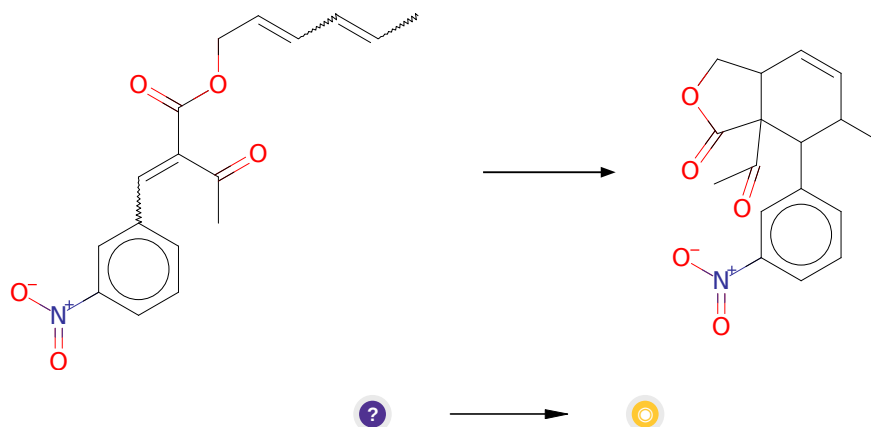1. CC=CC=CCOC(=O)C(=Cc1cccc([N+](=O)[O-])c1)C(C)=O

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(=Cc1cccc([N+](=O)[O-])c1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cccc([N+](=O)[O-])c1

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
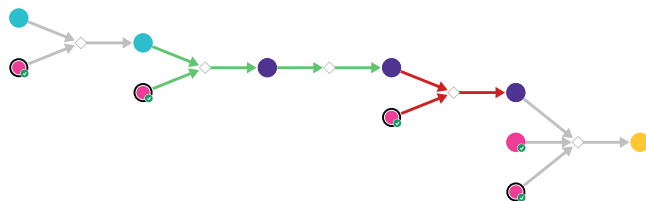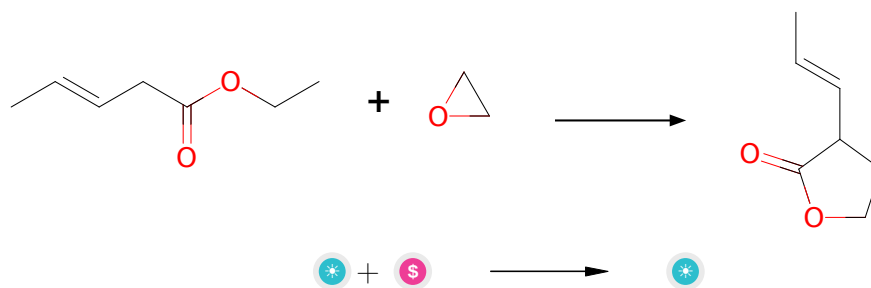
2.3 Path 3

Score: 93.83

Figure 3: Outline of path 3

2.3.1 Synthesis of lactones from epoxides

Substrates:

1. pent-3t()-enoic acid ethyl ester

2. Oxirane - *available at Sigma-Aldrich*

Products:

1. 3-(1-propenyl)-tetrahydro-2-furanone

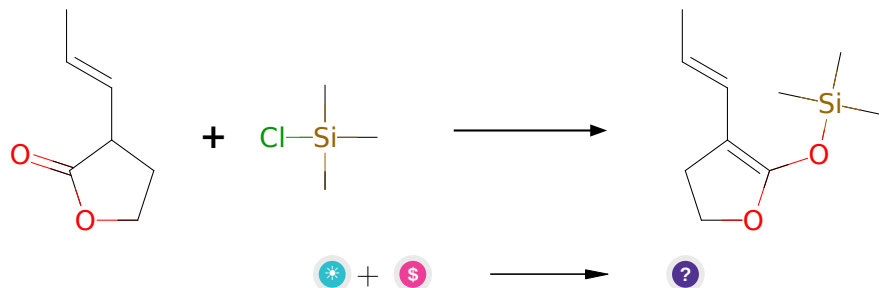**Typical conditions:** EtONa.EtOH.rt

Protections: none

Reference: *10.1021/ja9049959* and *10.1016/j.tetlet.2014.12.024* and *10.1021/jo00077a012* and *10.1016/0040-4039(96)00494-7* and *10.1002/chem.201403294*

Retrosynthesis ID: 21258

2.3.2 Enol esters and ethers synthesis

Substrates:

1. 3-(1-propenyl)-tetrahydro-2-furanone

2. TMSCl - *available at Sigma-Aldrich*
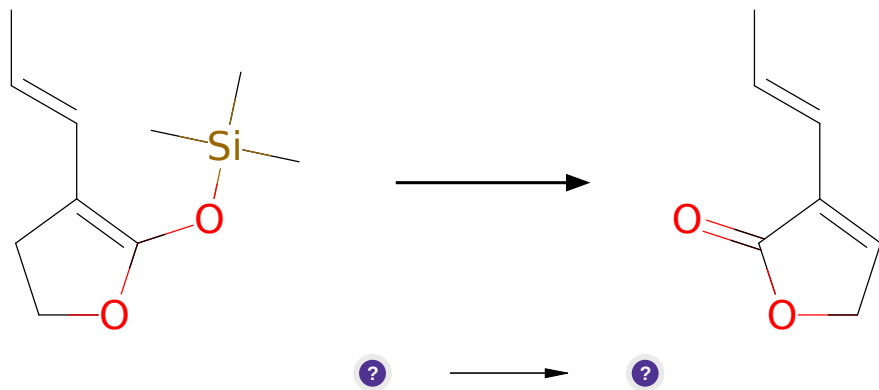
Products:

1. C/C=C/C1=C(O[Si](C)(C)C)OCC1

Typical conditions: 1. Et3N.Electrophile

Protections: none

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

Retrosynthesis ID: 7799

2.3.3 Dehydrogenation of silyl enol ethers

Substrates:

1. C/C=C/C1=C(O[Si](C)(C)C)OCC1

Products:

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

2.3.4 Diels-Alder
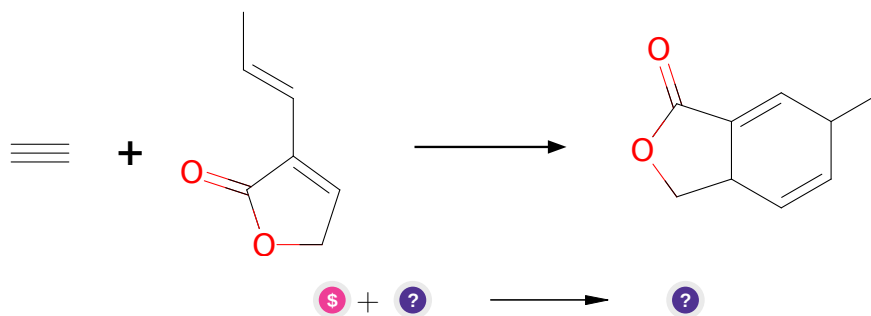
Substrates:

1. Calcium carbide - *available at Sigma-Aldrich*

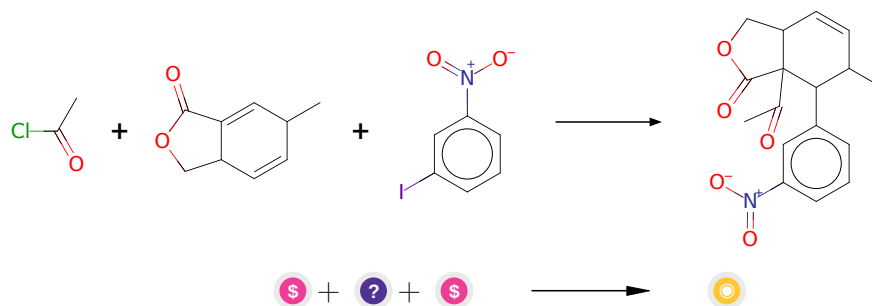2. C/C=C/C1=CCOC1=O

Products:

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

Typical conditions: H2O.MeOH.EtOH.isooctane

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

Retrosynthesis ID: 10557

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

Substrates:

1. 1-Iodo-3-nitrobenzene -   *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)C2c1cccc([N+](=O)[O-])c1

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
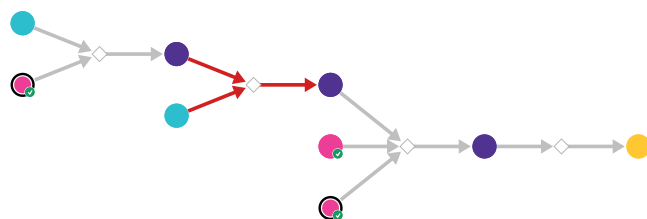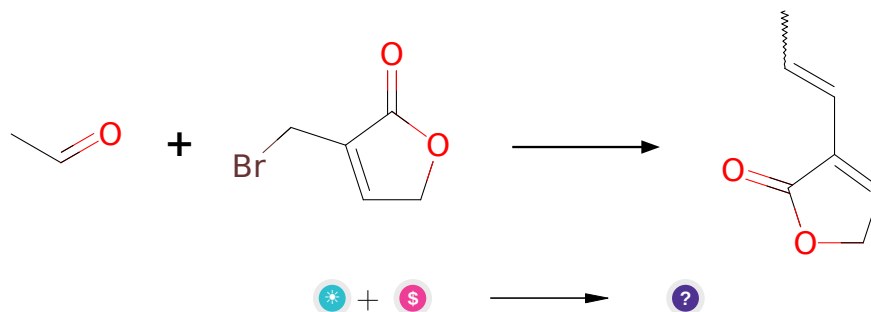
2.4   Path 4

Score: 95.31

Figure 4: Outline of path 4

2.4.1 Wittig olefination

Substrates:

1. 3-bromomethyl-5h-furan-2-one

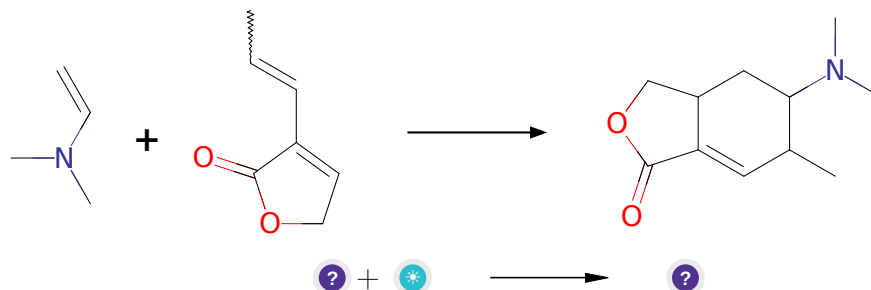2. Ethanal - *available at Sigma-Aldrich*

Products:

1. CC=CC1=CCOC1=O

Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1021/ja0015287* and *10.1021/ja404673s* and *10.1021/ol901979x*

Retrosynthesis ID: 9545

2.4.2 Diels-Alder

Substrates:

1. CC=CC1=CCOC1=O

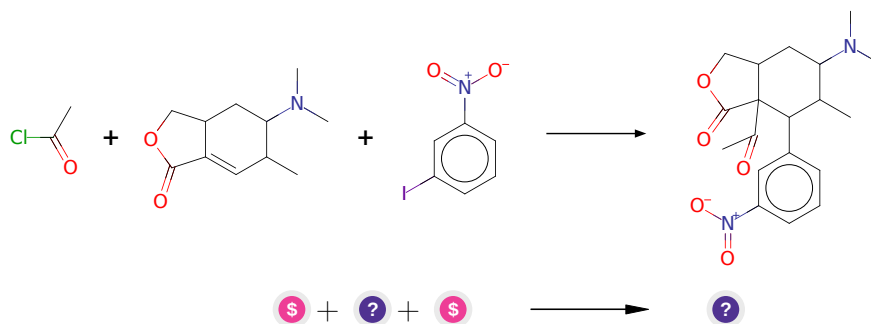2. dimethyl-vinyl-amine

Products:

1. CC1C=C2C(=O)OCC2CC1N(C)C

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

Protections: none

Retrosynthesis ID: 18116

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

Substrates:

1. 1-Iodo-3-nitrobenzene - *available at Sigma-Aldrich*

2. CC1C=C2C(=O)OCC2CC1N(C)C

3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

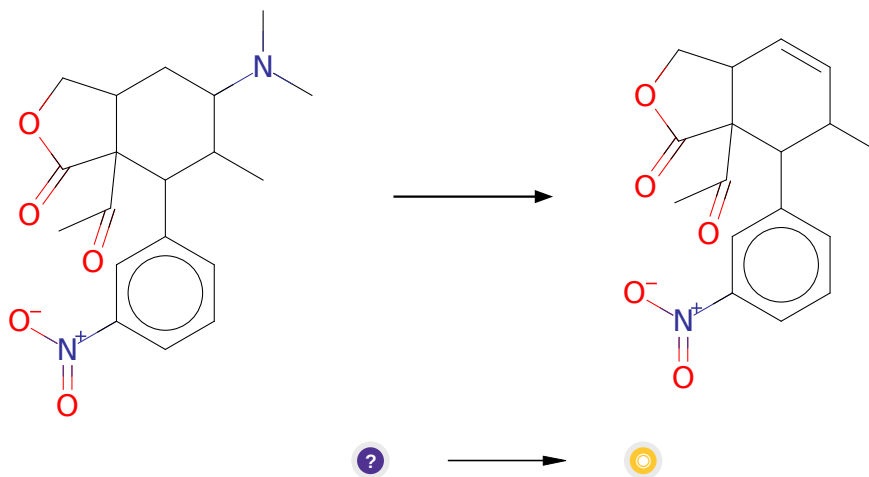1. CC(=O)C12C(=O)OCC1CC(N(C)C)C(C)C2c1cccc([N+](=O)[O-])c1

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

2.4.4 Hofmann Elimination

Substrates:

1. CC(=O)C12C(=O)OCC1CC(N(C)C)C(C)C2c1cccc([N+](=O)[O-])c1

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cccc([N+](=O)[O-])c1

Typical conditions: 1. MeI 2. Ag2O or NaOMe.heat

Protections: none

Reference: *10.1021/ja00023a034* and *10.1021/jo00301a036* and *10.1021/ja00716a066*

Retrosynthesis ID: 31010847
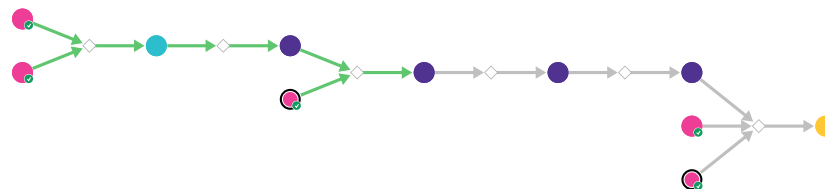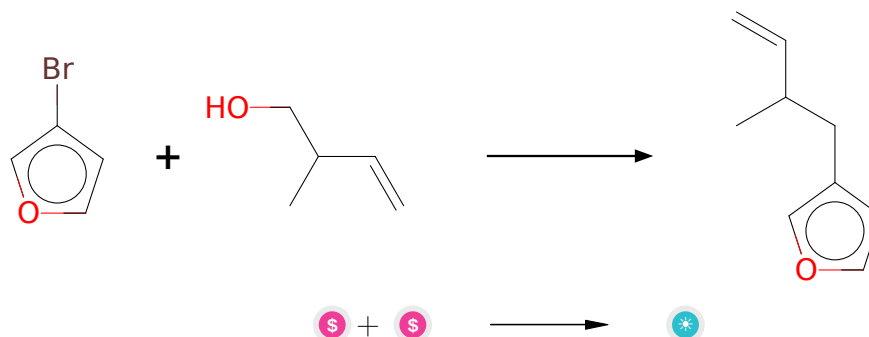
2.5 Path 5

Score: 106.04

Figure 5: Outline of path 5

2.5.1 Double decarboxylative coupling or aryl halides with alcohols as latent nucleophiles

Substrates:

1. 2-Methyl-3-buten-1-ol - *available at Sigma-Aldrich*

2. 3-Bromofuran - *available at Sigma-Aldrich*

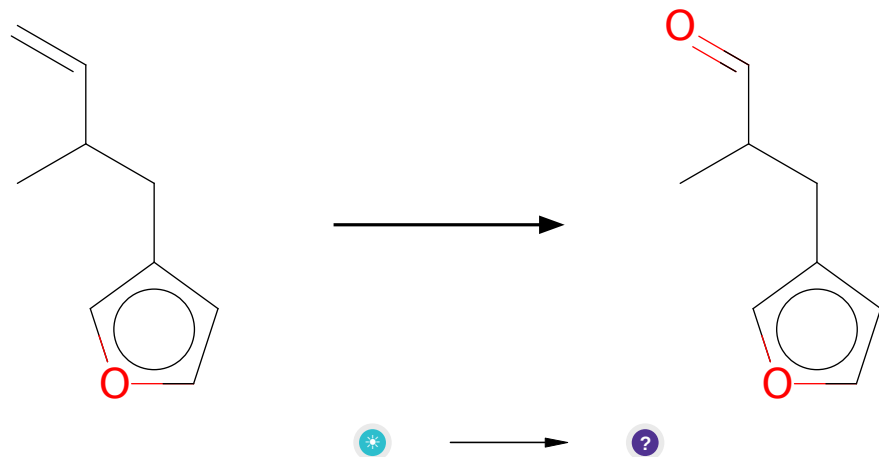**Products:**

1. 3-(2-methyl-but-3-enyl)-furan

Typical conditions: 1.Oxalyl chloride 2.[Ir]-catalyst.[Ni]-catalyst.blue.light.dioxane.DMSO.DMF.CsHCO3.70 deg C

Protections: none

Reference: *10.1021/jacs.6b09533*

Retrosynthesis ID: 10032259

2.5.2 Ozonolysis

Substrates:

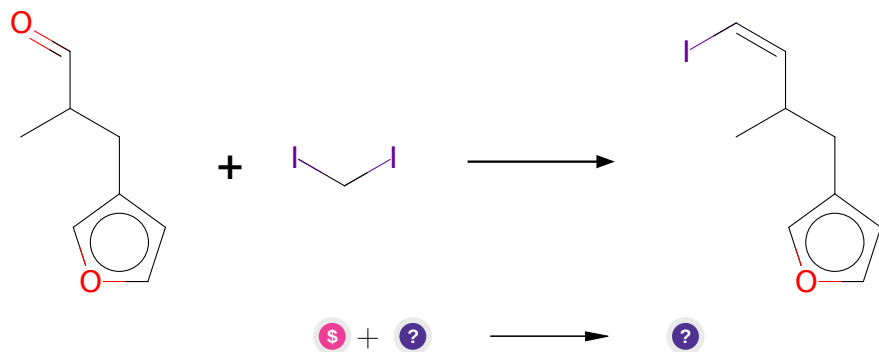1. 3-(2-methyl-but-3-enyl)-furan

Products:

1. CC(C=O)Cc1ccoc1

Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5074

2.5.3 Iodoolefination of aldehydes

Substrates:

1. Diiodomethane - *available at Sigma-Aldrich*

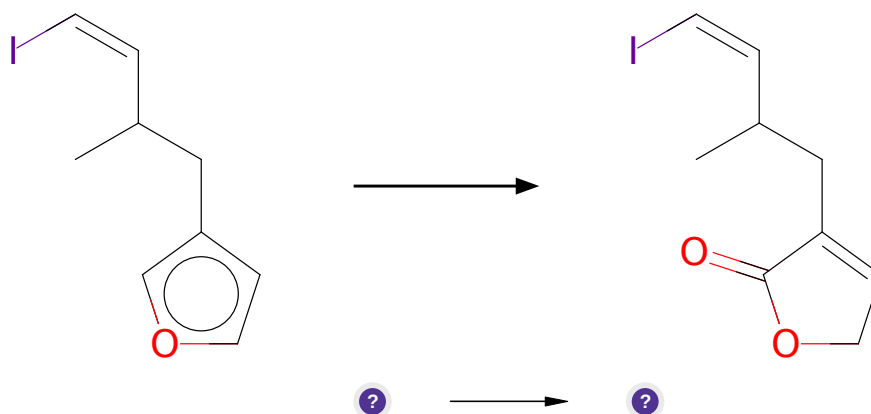2. CC(C=O)Cc1ccoc1

Products:

1. CC(/C=C\I)Cc1ccoc1

Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

Protections: none

Reference: *10.1021/ja00171a035* and *10.1039/C0OB00977F* and WO2009033499
(p.25)

Retrosynthesis ID: 10001773

2.5.4   NBS-promoted oxidation of furans to lactones

Substrates:

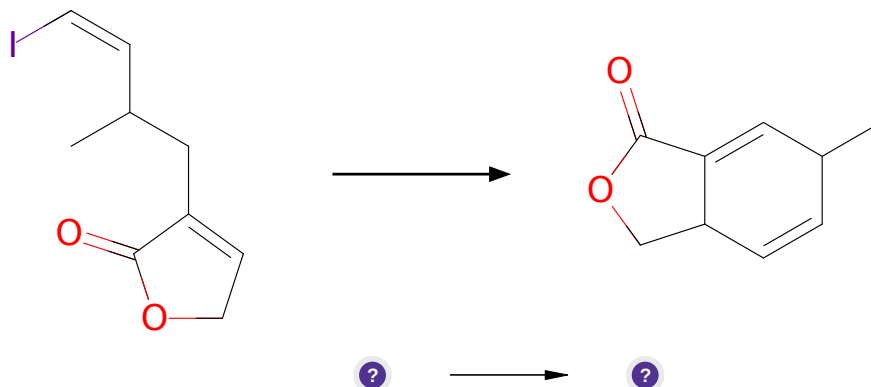1. CC(/C=C\I)Cc1ccoc1

Products:

1. CC(/C=C\I)CC1=CCOC1=O

Typical conditions: NBS.MW.MeOH

Protections: none

Reference: DOI: *10.1016/S0040-4039(01)01261-8*

Retrosynthesis ID: 49766

2.5.5 Heck Reaction

Substrates:

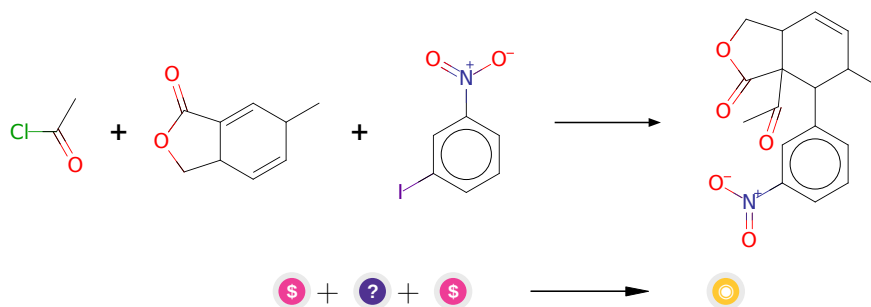1. CC(/C=C\I)CC1=CCOC1=O

Products:

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

Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

Protections: none

Reference: DOI: *10.1021/jo00270a011* or DOI: *10.1021/ar00049a001* or DOI: *10.1021/ja00206a034* or DOI: *10.1021/cr020039h* or DOI: *10.1039/C1CS15101K* or DOI: *10.1002/9780470716076*

Retrosynthesis ID: 8584

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

Substrates:

1. 1-Iodo-3-nitrobenzene - *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)C2c1cccc([N+](=O)[O-])c1

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