Paths of analysis*
L3

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselecitve 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: 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

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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.*
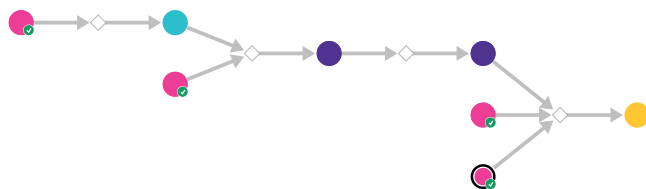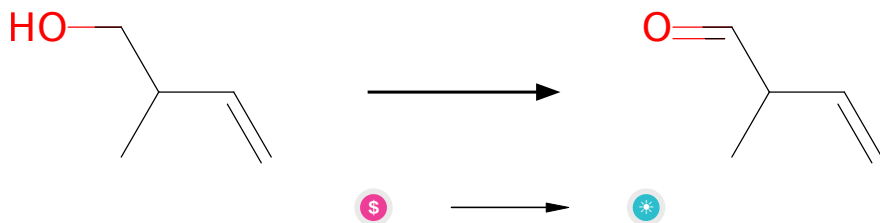
2.1 Path 1

Score: 76.25

Figure 1: Outline of path 1

2.1.1 Oxidation of primary alcohols with DMP

Substrates:

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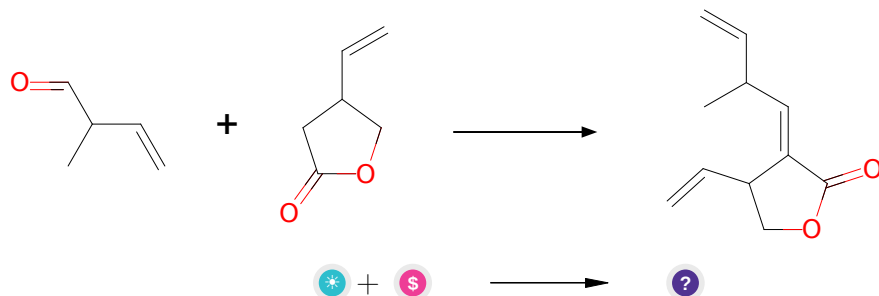
Products:

1. 2-methyl-but-3-enal

Typical conditions: DMP.DCM.0-25 C

Protections: none

Retrosynthesis ID: 50426

2.1.2 Condensation of esters with aldehydes

Substrates:

1. 2-methyl-but-3-enal

2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*
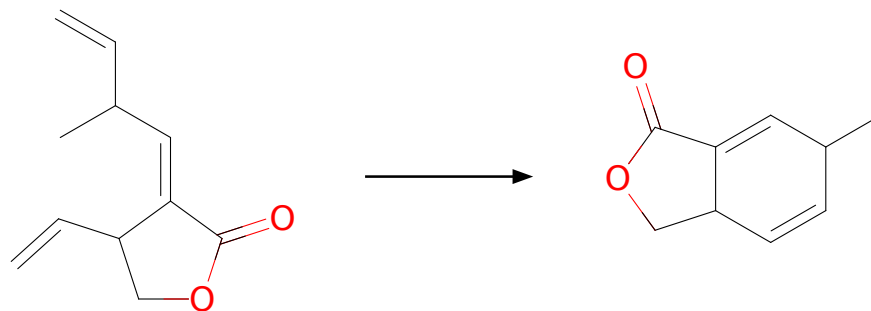
Products:

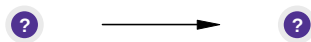1. C=CC(C)/C=C1/C(=O)OCC1C=C

Typical conditions: 1.LDA.2RCHO

Protections: none

Retrosynthesis ID: 14981

2.1.3 Ring-Closing Metathesis

Substrates:

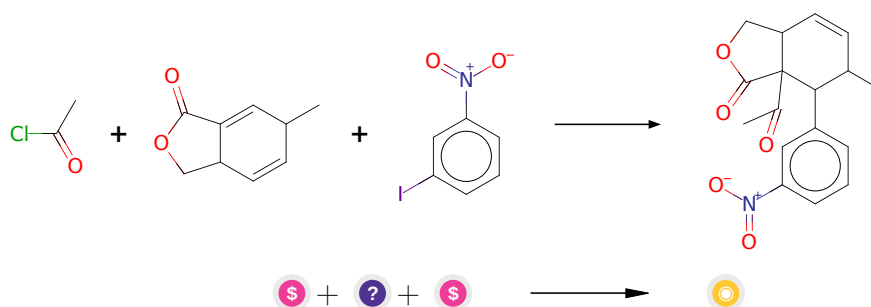1. C=CC(C)/C=C1/C(=O)OCC1C=C

Products:

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

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

2.1.4 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
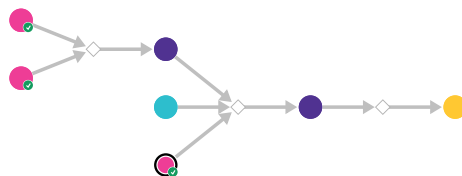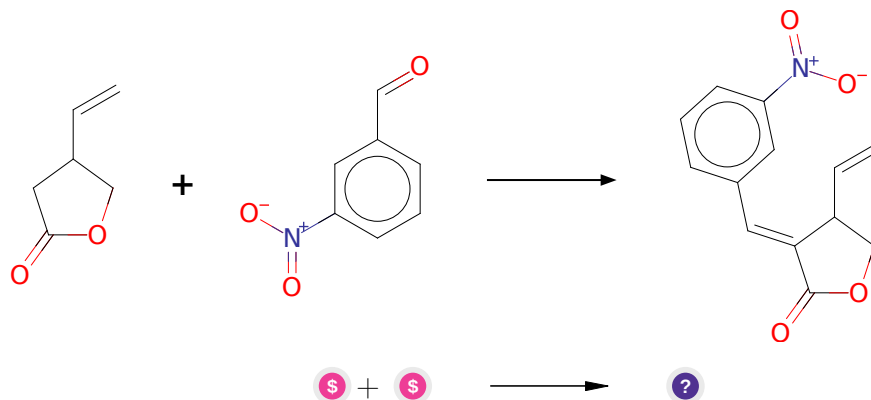
2.2 Path 2

Score: 76.25

Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes

Substrates:

1. 4-ethenyloxolan-2-one -   *available at Sigma-Aldrich*

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

Products:
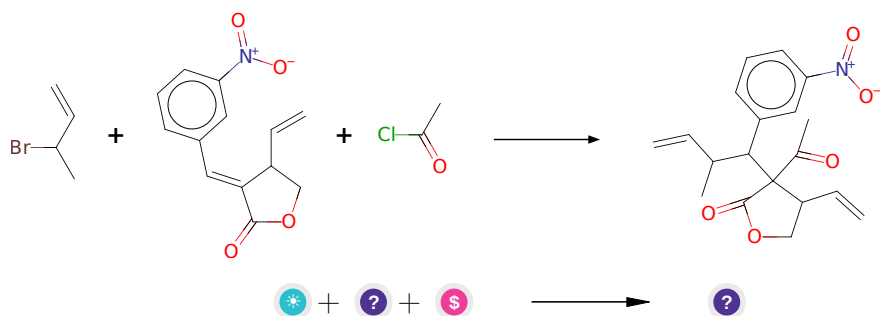
1. C=CC1COC(=O)/C1=C/c1cccc([N+](=O)[O-])c1

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

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

Substrates:

1. 3-brom-but-1-en

2. C=CC1COC(=O)/C1=C/c1cccc([N+](=O)[O-])c1

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

Products:
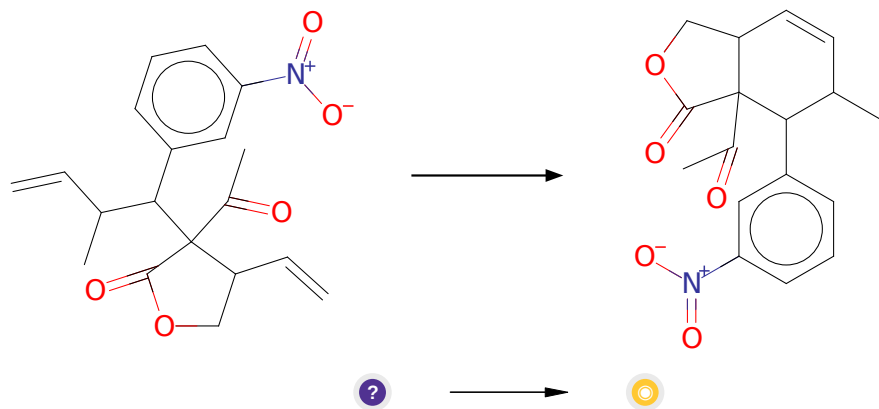
1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

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

2.2.3 Ring-Closing Metathesis

Substrates:

1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

Products:

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

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

Protections: none

Retrosynthesis ID: 31014187

2.3 Path 3
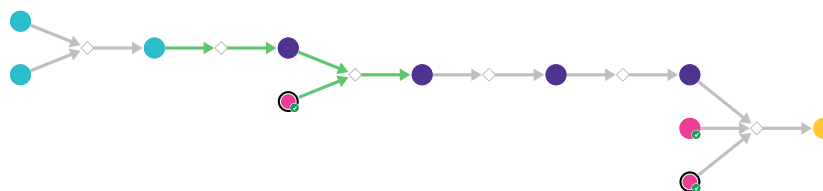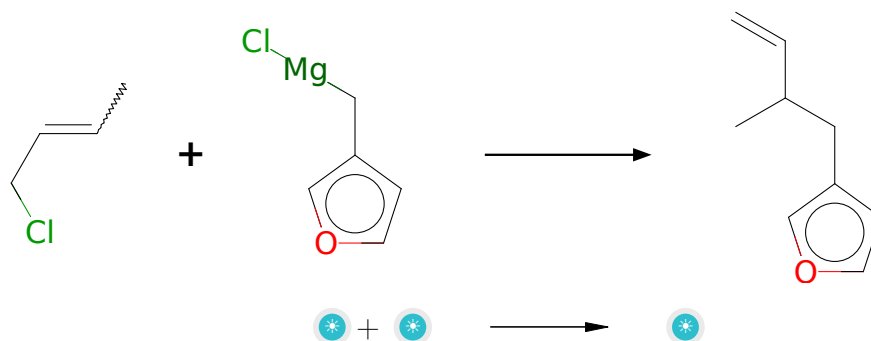
Score: 106.04

Figure 3: Outline of path 3

2.3.1 NHC-catalyzed Grignard allylic substitution

Substrates:

1. crotyl chloride

    2. (furan-3-ylmethyl)magnesium chloride
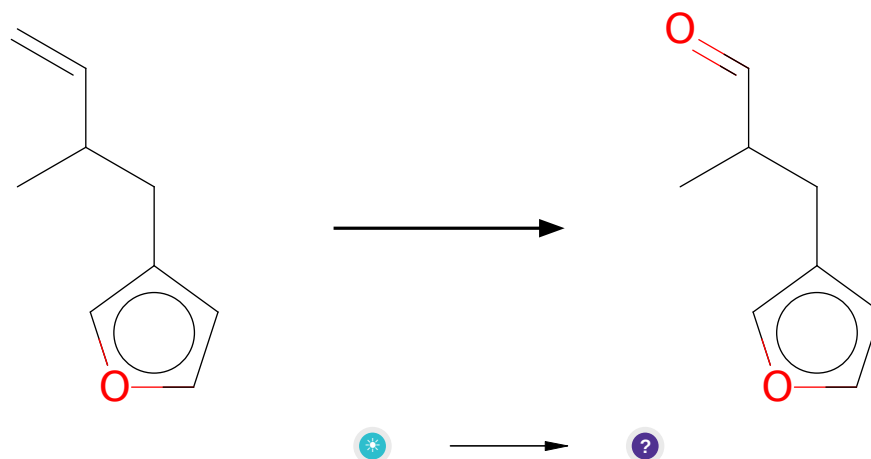
Products:

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

Typical conditions: RMgCl.THF.NHC-complex

Protections: none

Reference: *10.1016/j.tetlet.2012.12.124*

Retrosynthesis ID: 1171

2.3.2 Ozonolysis

Substrates:

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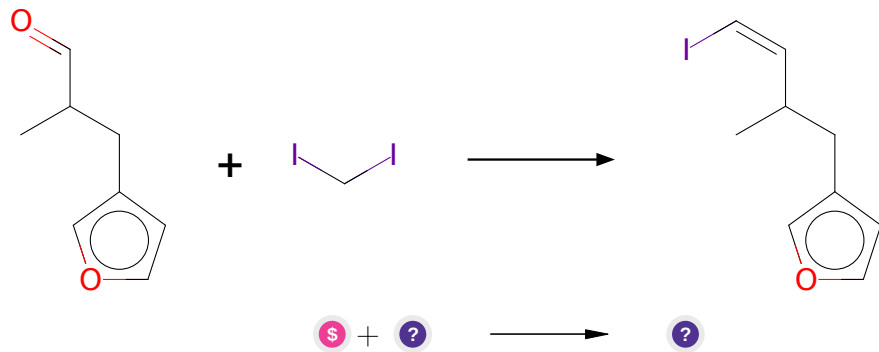
Products:

    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

2.3.3 Iodoolefination of aldehydes

Substrates:

1. Diiodomethane -   *available at Sigma-Aldrich*

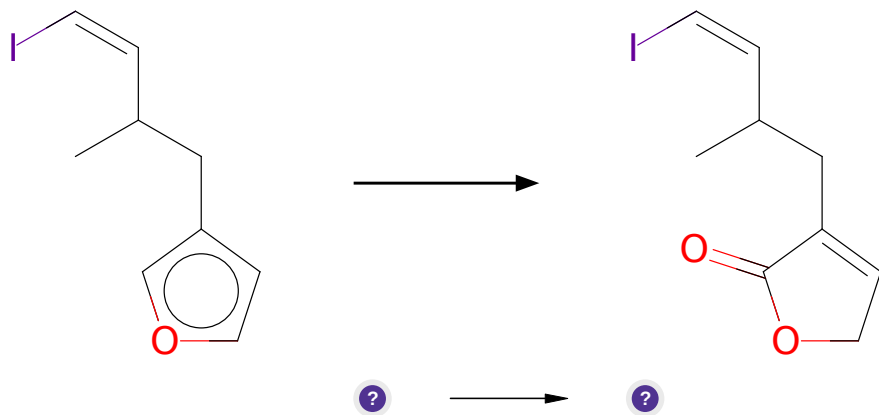2. CC(C=O)Cc1ccoc1

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

2.3.4 NBS-promoted oxidation of furans to lactones

Substrates:

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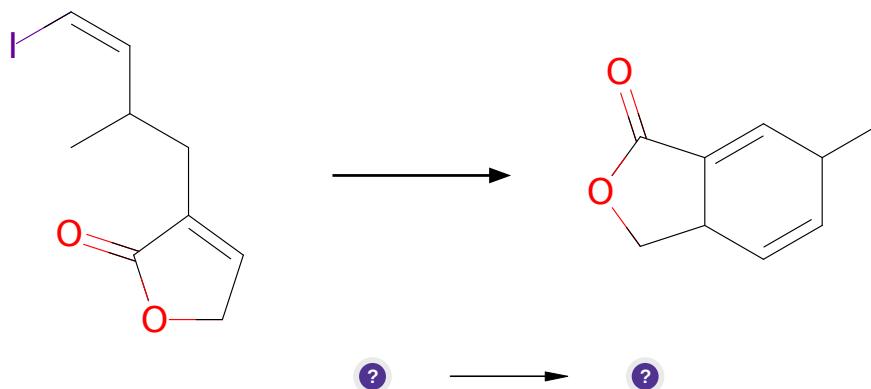
Products:

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

2.3.5 Heck Reaction

Substrates:

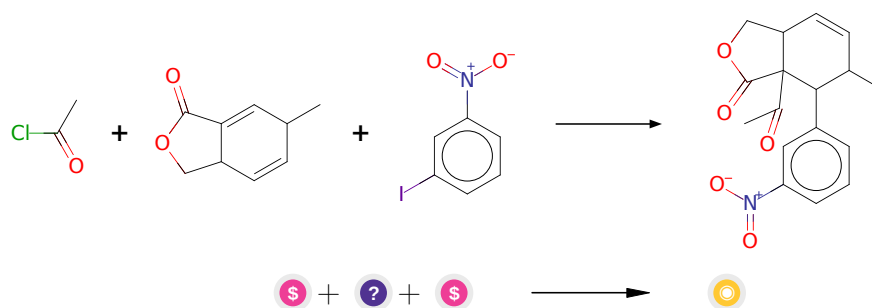1. CC(/C=C\I)CC1=CCOC1=O

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

2.3.6 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
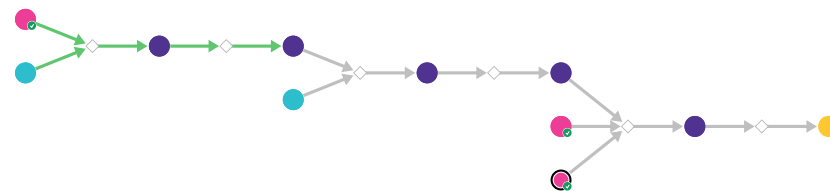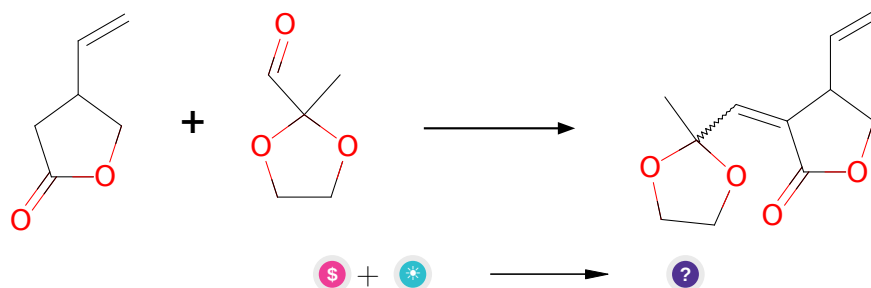
2.4 Path 4

Score: 106.04

Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes/ketones

Substrates:

1. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

2. 2-methyl-[1,3]dioxolane-2-carbaldehyde
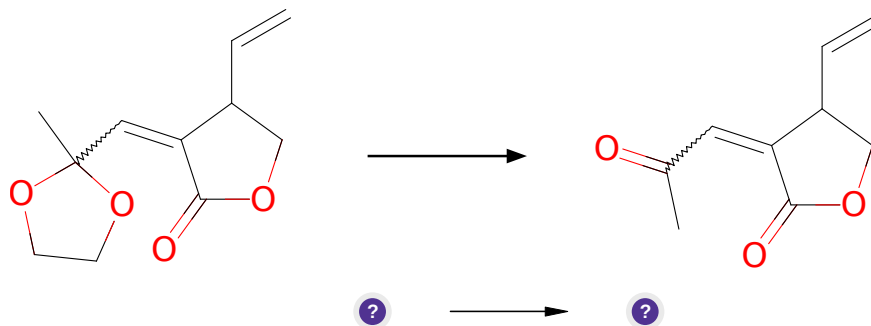
Products:

1. C=CC1COC(=O)C1=CC1(C)OCCO1

Typical conditions: LDA.THF

Protections: none

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

Retrosynthesis ID: 14983

2.4.2 Hydrolysis of ketals

Substrates:

1. C=CC1COC(=O)C1=CC1(C)OCCO1

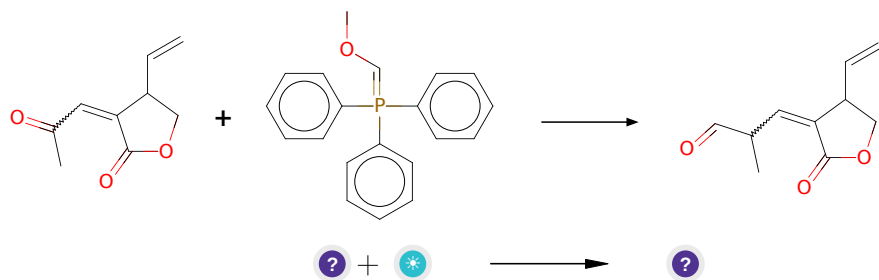**Products:**

1. C=CC1COC(=O)C1=CC(C)=O

Typical conditions: H2O.HCl

Protections: none

Reference: *10.1021/jo0159035* and *10.1021/jo00194a003* and

Retrosynthesis ID: 31013139

2.4.3 Olefination of ketones followed by hydrolysis

Substrates:

1. C=CC1COC(=O)C1=CC(C)=O

2. triphenylphosphonium methoxymethylide
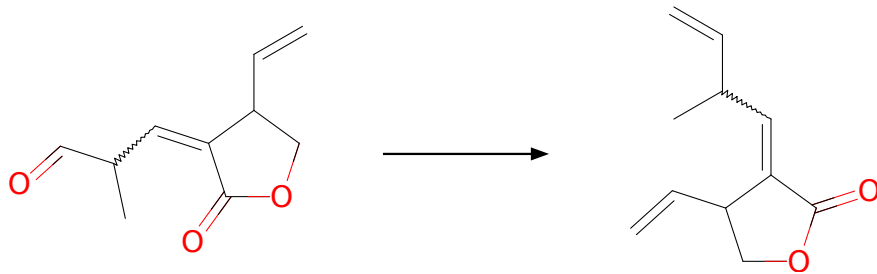
Products:

1. C=CC1COC(=O)C1=CC(C)C=O

Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone
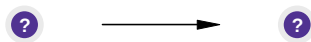
Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014861

2.4.4 Tebbe Olefination

Substrates:

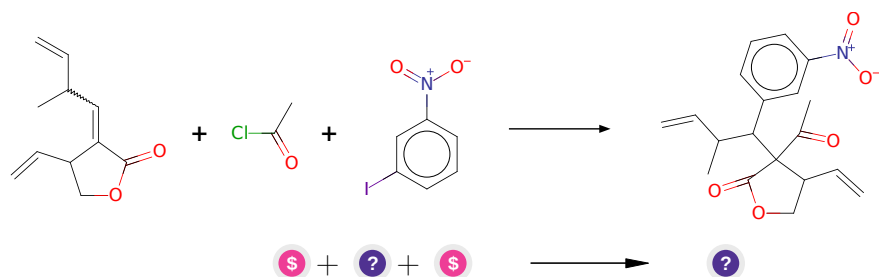1. C=CC1COC(=O)C1=CC(C)C=O

Products:

1. C=CC(C)C=C1C(=O)OCC1C=C

Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Reference: *10.1016/j.tet.2007.03.015* and *10.1002/9780470638859.conrr617*

Retrosynthesis ID: 11714

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

Substrates:

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

2. C=CC(C)C=C1C(=O)OCC1C=C

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

Products:

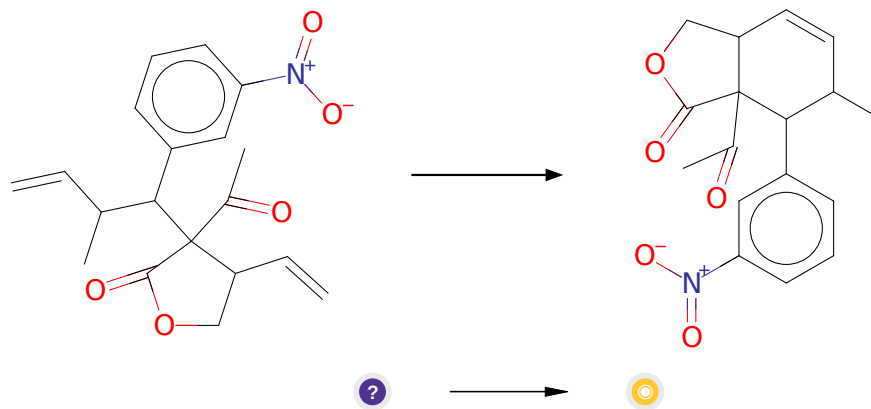1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

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: 20528

2.4.6 Ring-Closing Metathesis

Substrates:

1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

Products:

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

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
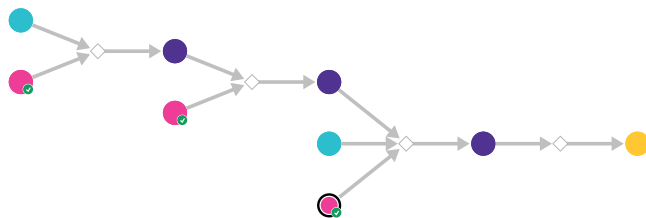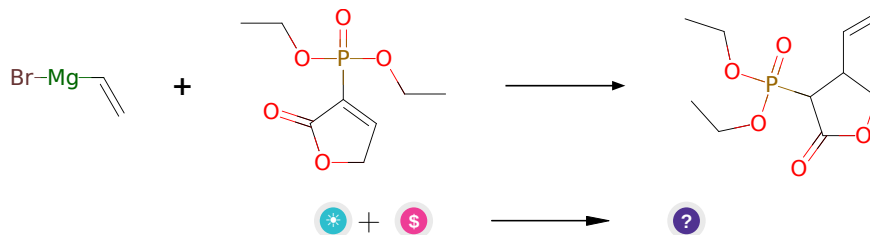
2.5 Path 5

Score: 115.31

Figure 5: Outline of path 5

2.5.1 Conjugate addition of organocuprate

Substrates:

1. a-diethoxyphosphinyl-da,b-butenolide

2. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*
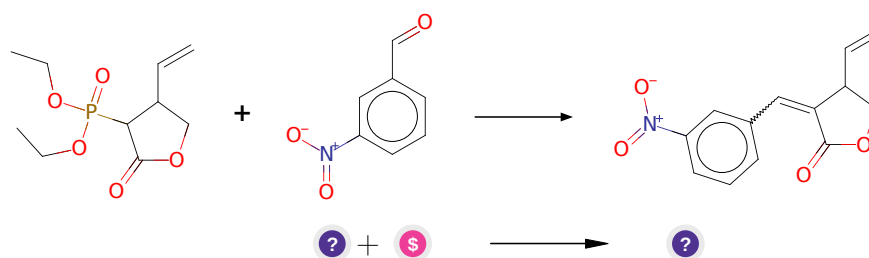
Products:

1. C=CC1COC(=O)C1P(=O)(OCC)OCC

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

2.5.2 Wittig-Horner Reaction

Substrates:

1. C=CC1COC(=O)C1P(=O)(OCC)OCC

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

Products:

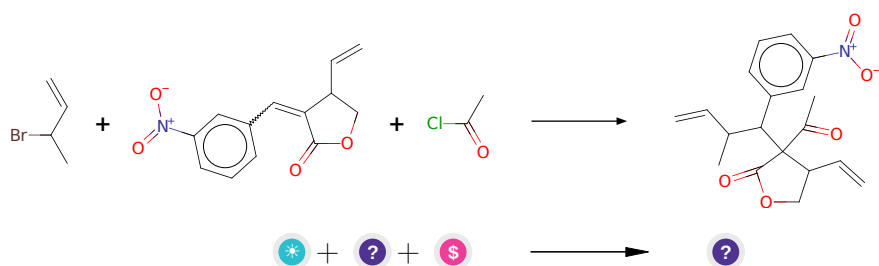1. C=CC1COC(=O)C1=Cc1cccc([N+](=O)[O-])c1

Typical conditions: NaH.THF.0 C or NaH.DMF.0-50 C

Protections: none

Reference: *10.1021/acs.jmedchem.5b01239* p. 63, 71 and *10.1021/jm950725r* p. 3150, 3153

Retrosynthesis ID: 11549

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

Substrates:

1. 3-brom-but-1-en

2. C=CC1COC(=O)C1=Cc1cccc([N+](=O)[O-])c1

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

Products:

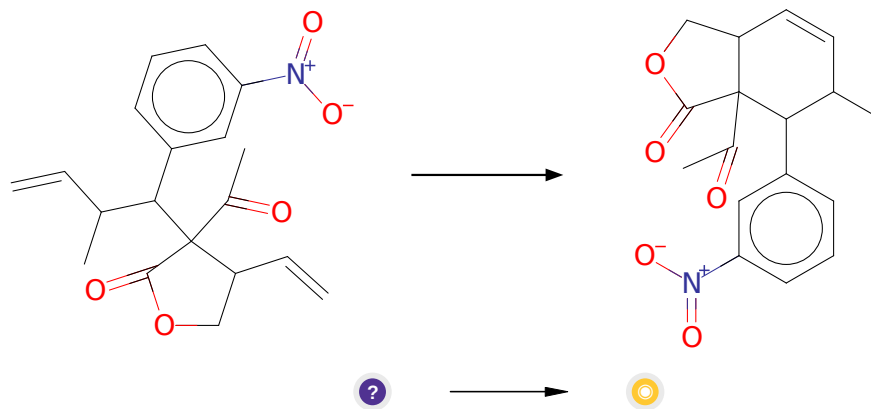1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

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: 20527

2.5.4 Ring-Closing Metathesis

Substrates:

1. C=CC(C)C(c1cccc([N+](=O)[O-])c1)C1(C(C)=O)C(=O)OCC1C=C

Products:

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

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