Paths of analysis*

L10

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+1000000*(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

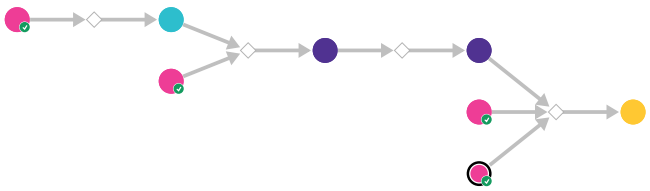
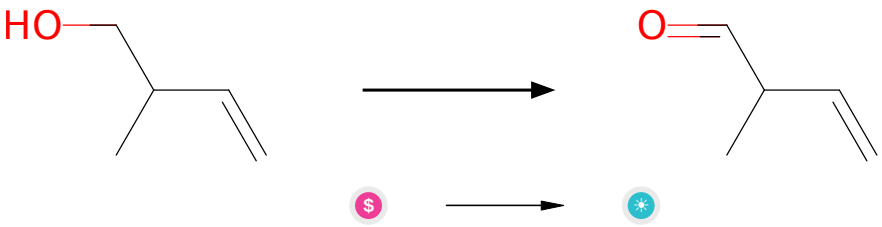


Figure 1: Outline of path 1

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

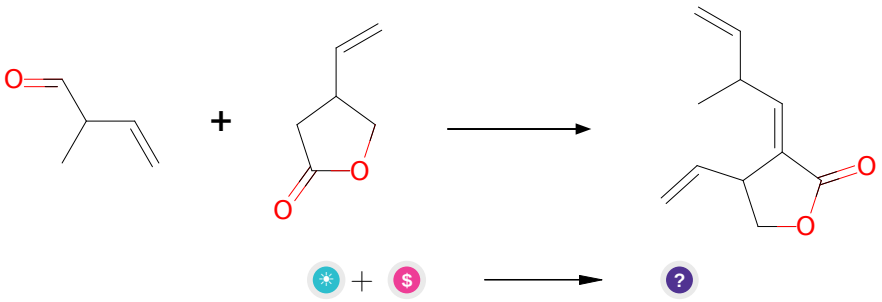
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

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

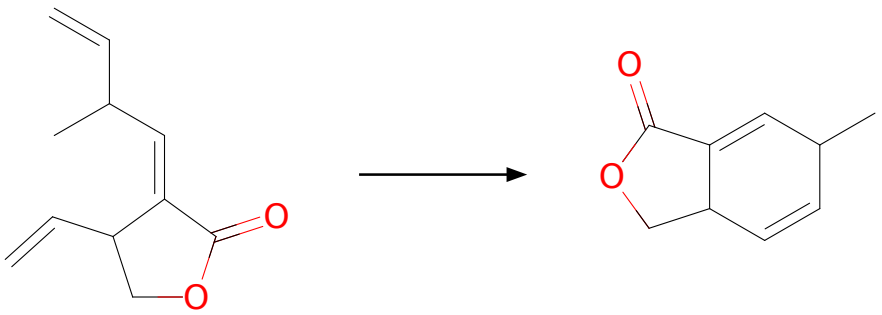
Typical conditions: 1.LDA.2RCHO

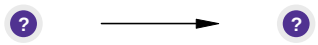
Protections: none

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

2.1.3 Ring-Closing Metathesis





Substrates:

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

Products:

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

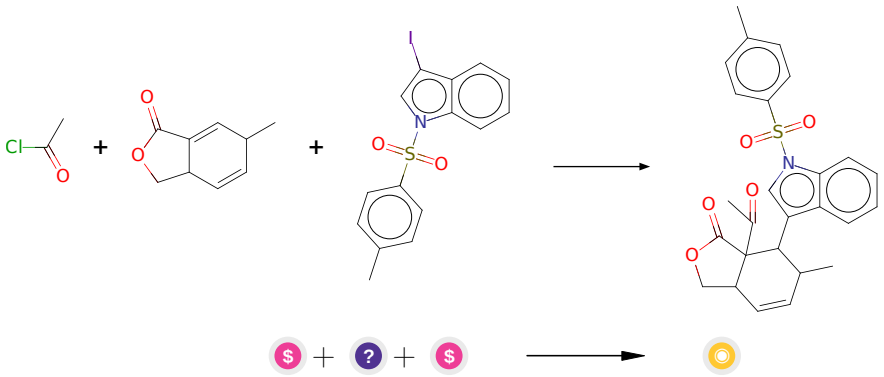
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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. 3-Iodo-1-tosyl-1H-indole - *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)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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

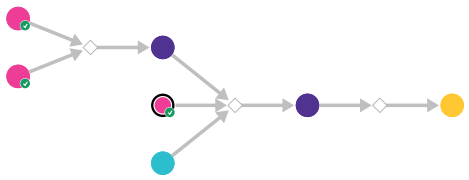
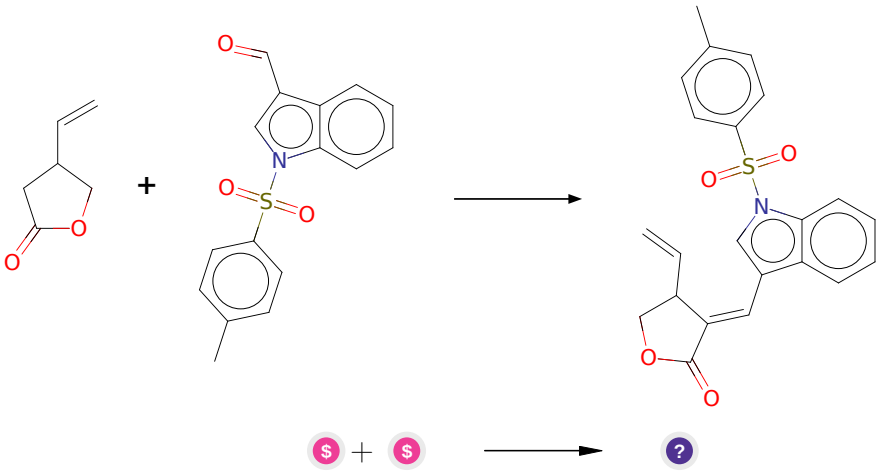


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes



Substrates:

1. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)/C1=C/c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

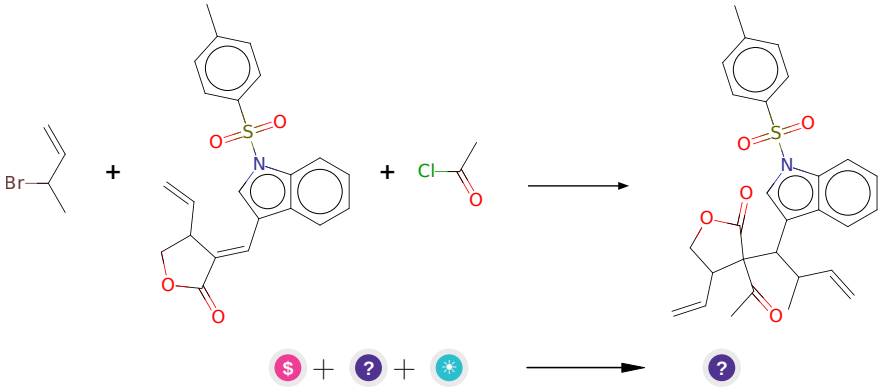
Typical conditions: 1.LDA.2RCHO

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. Acetyl chloride - *available at Sigma-Aldrich*
2. C=CC1COC(=O)/C1=C/c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12
3. 3-brom-but-1-en

Products:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

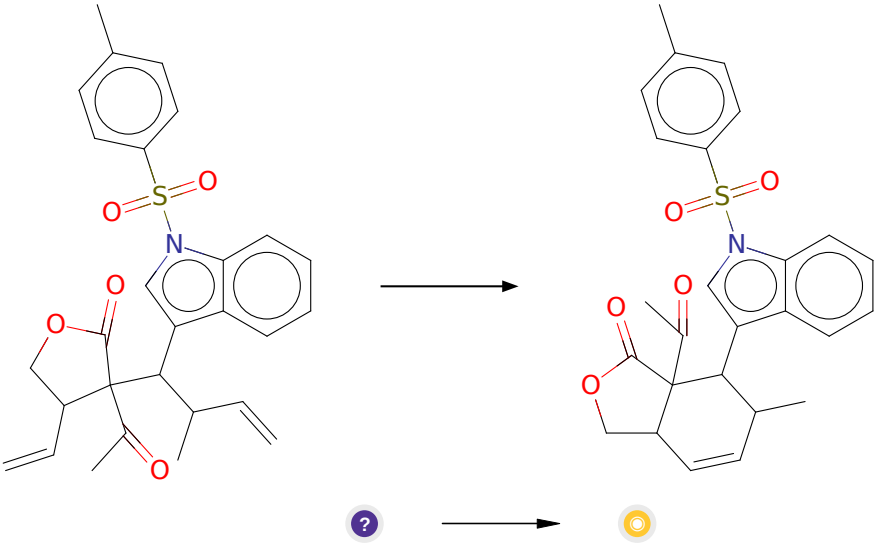
Typical conditions: 1.RCuLi.2.AcCl.HMPA

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(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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

2.3 Path 3

Score: `106.04`

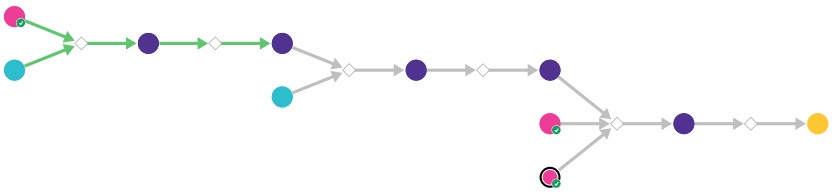
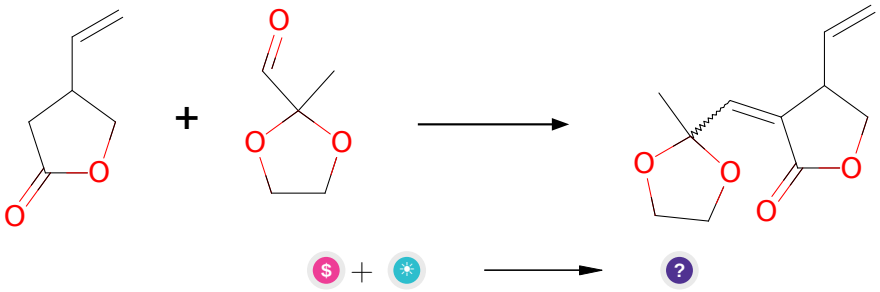


Figure 3: Outline of path 3

2.3.1 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

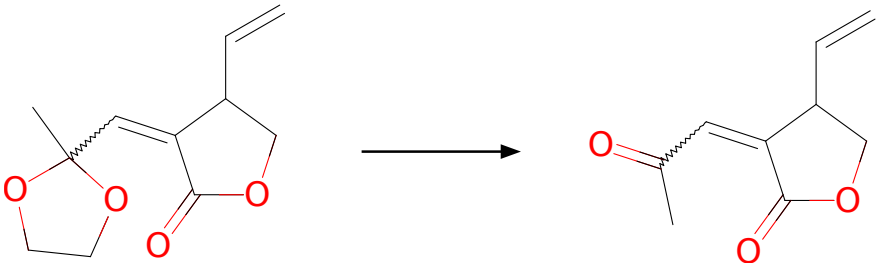
Typical conditions: LDA.THF

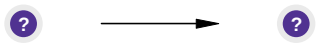
Protections: none

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

Retrosynthesis ID: 14983

2.3.2 Hydrolysis of ketals





Substrates:

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

Products:

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

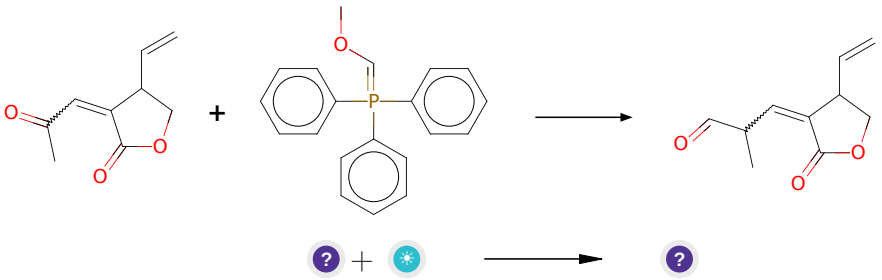
Typical conditions: H2O.HCl

Protections: none

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

Retrosynthesis ID: 31013139

2.3.3 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

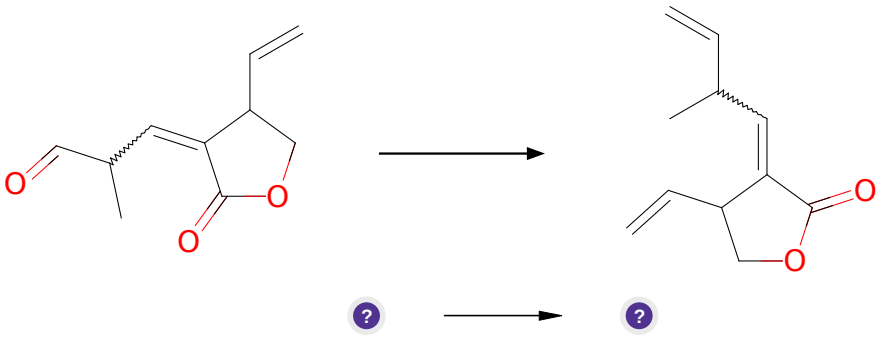
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

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

2.3.4 Tebbe Olefination



Substrates:

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

Products:

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

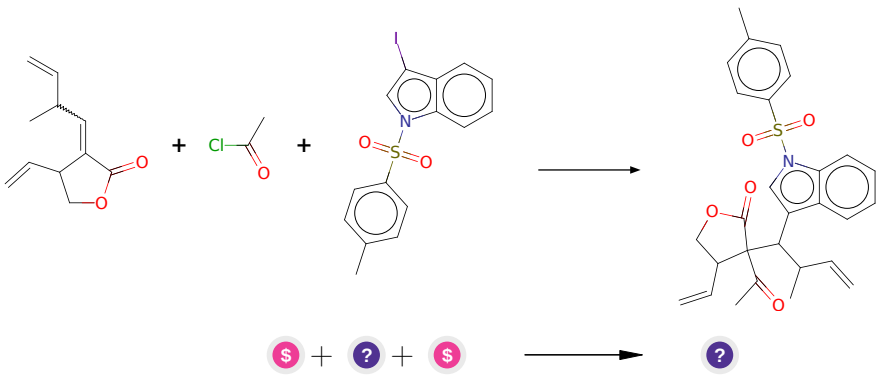
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

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

Retrosynthesis ID: 11714

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *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(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

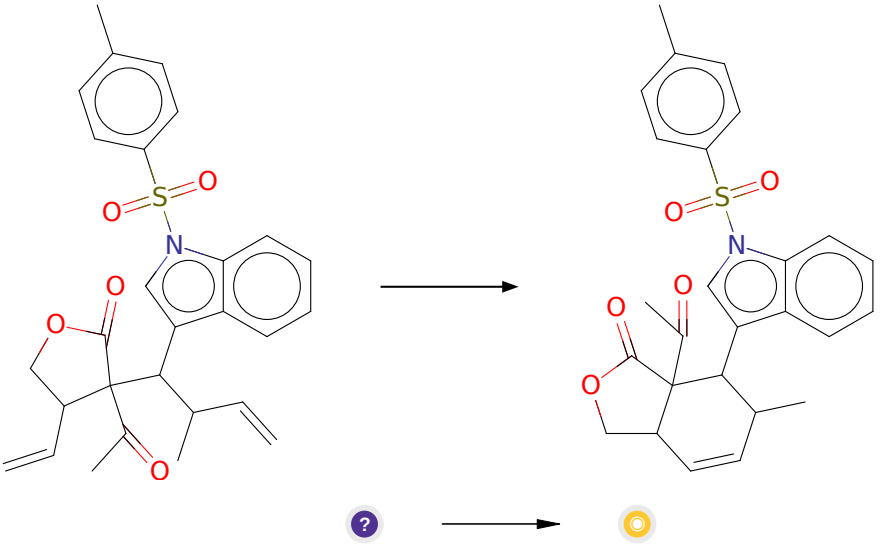
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20528

2.3.6 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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

2.4 Path 4

Score: 106.04

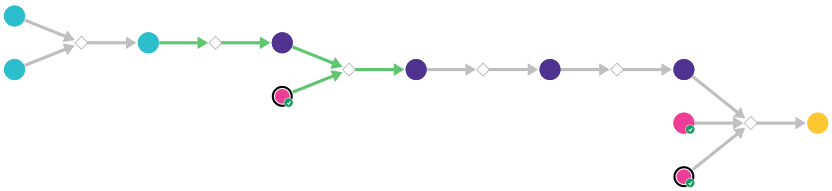
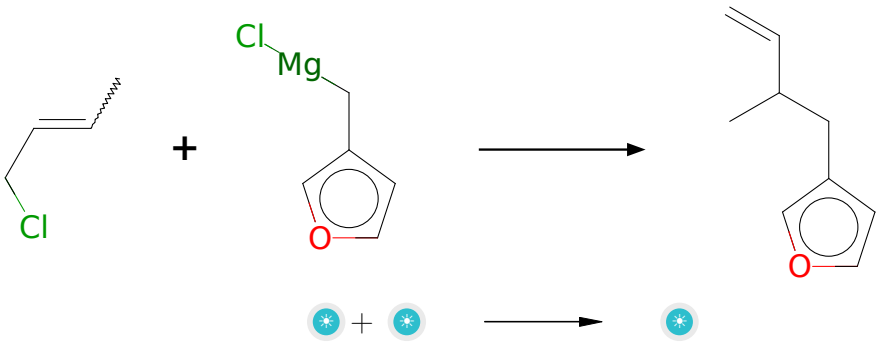


Figure 4: Outline of path 4

2.4.1 NHC-catalyzed Grignard allylic substitution



Substrates:

1. crotyl chloride
2. (furan-3-ylmethyl)magnesium chloride

Products:

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

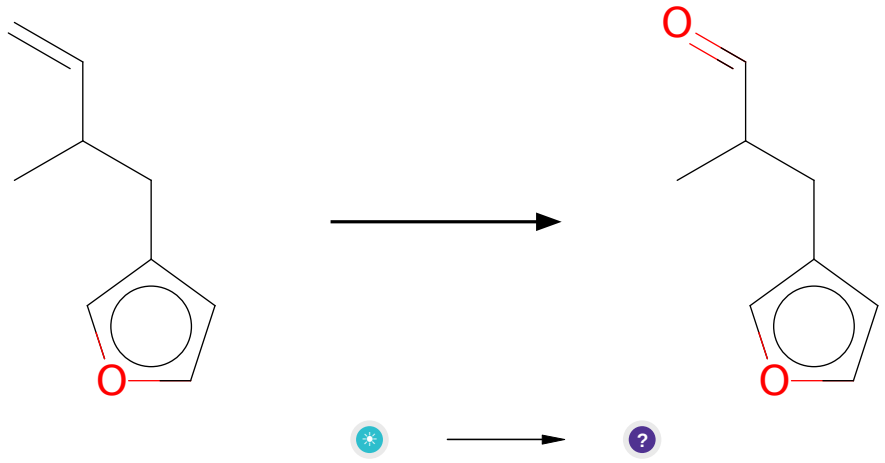
Typical conditions: RMgCl.THF.NHC-complex

Protections: none

Reference: *10.1016/j.tetlet.2012.12.124*

Retrosynthesis ID: 1171

2.4.2 Ozonolysis



Substrates:

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

Products:

1. CC(C=O)Cc1ccoc1

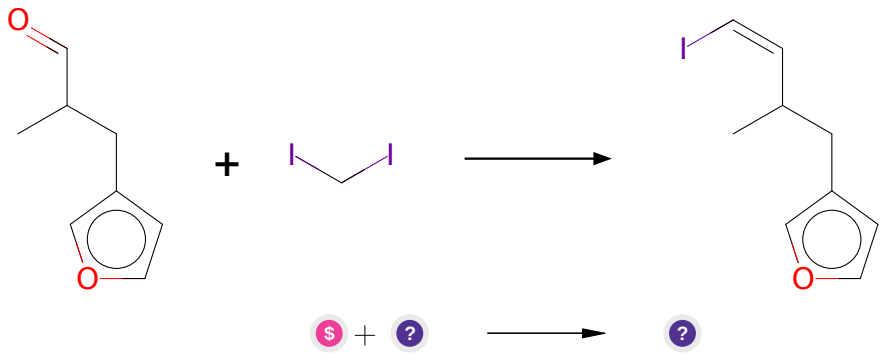
Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5074

2.4.3 Iodoolefination of aldehydes



Substrates:

1. Diiodomethane - *available at Sigma-Aldrich*
2. CC(C=O)Cc1ccoc1

Products:

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

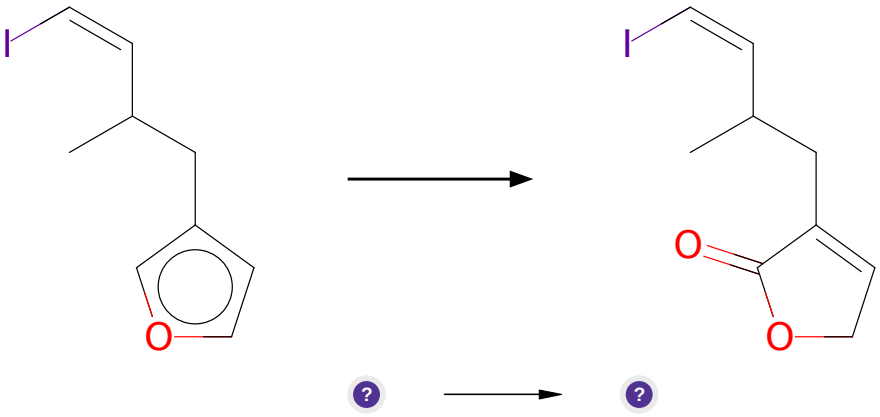
Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

Protections: none

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

Retrosynthesis ID: 10001773

2.4.4 NBS-promoted oxidation of furans to lactones



Substrates:

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

Products:

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

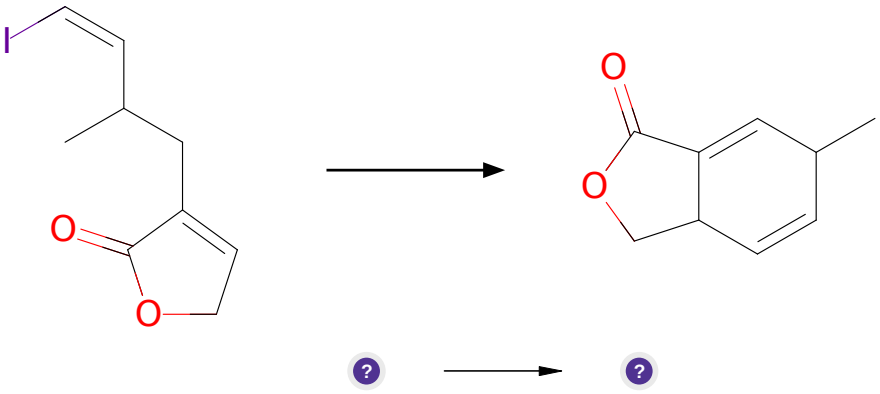
Typical conditions: NBS.MW.MeOH

Protections: none

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

Retrosynthesis ID: 49766

2.4.5 Heck Reaction



Substrates:

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

Products:

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

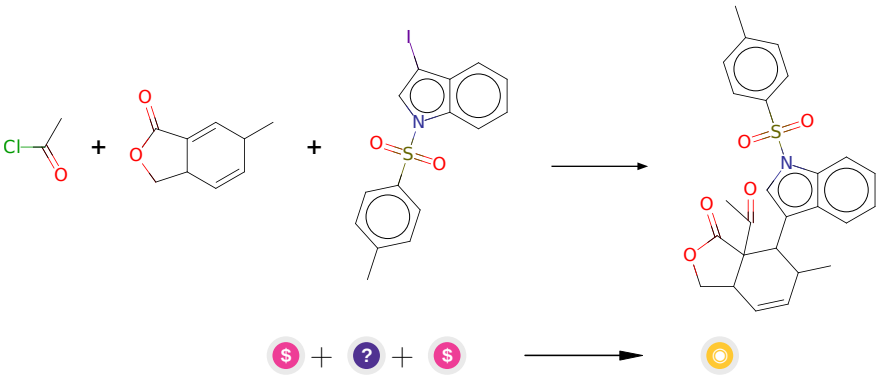
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

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

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *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)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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

2.5 Path 5

Score: `115.31`

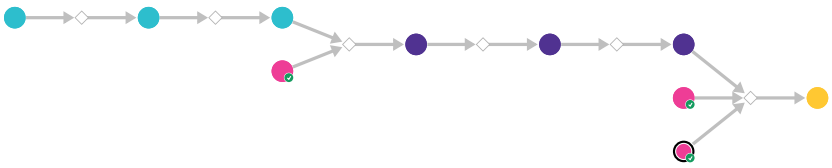
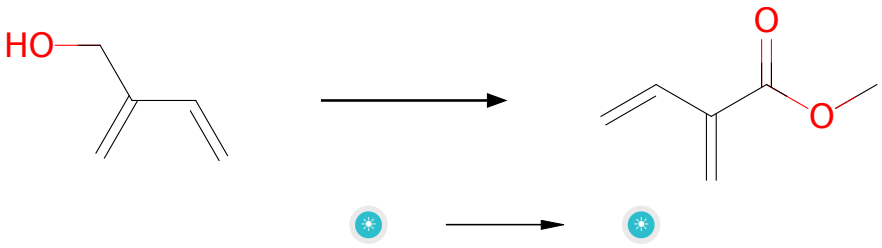


Figure 5: Outline of path 5

2.5.1 Tandem oxidation-esterification



Substrates:

1. 2-methylene-but-3-en-1-ol

Products:

1. 2-methylene-but-3-enoic acid methyl ester

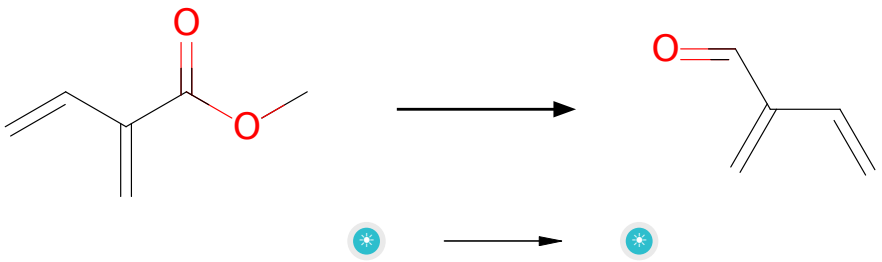
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

Protections: none

Reference: *10.1016/S0040-4039(00)73550-7* and *10.1016/j.tet.2005.03.097* and *10.1021/ol062940f*

Retrosynthesis ID: 25234

2.5.2 Aldehyde Formation



Substrates:

1. 2-methylene-but-3-enoic acid methyl ester

Products:

1. isoprenal

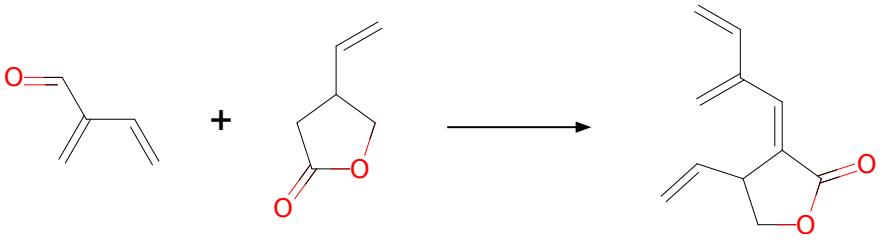
Typical conditions: DIBAL.solvent e.g. DCM

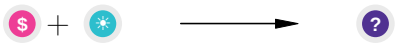
Protections: none

Reference: *10.1039/C39940000483* and *10.1039/C3CC47867J* and *10.1021/jo00222a054* and *10.1021/ja9934908* and *10.1021/jo902426z*

Retrosynthesis ID: 28551

2.5.3 Condensation of esters with aldehydes





Substrates:

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

Products:

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

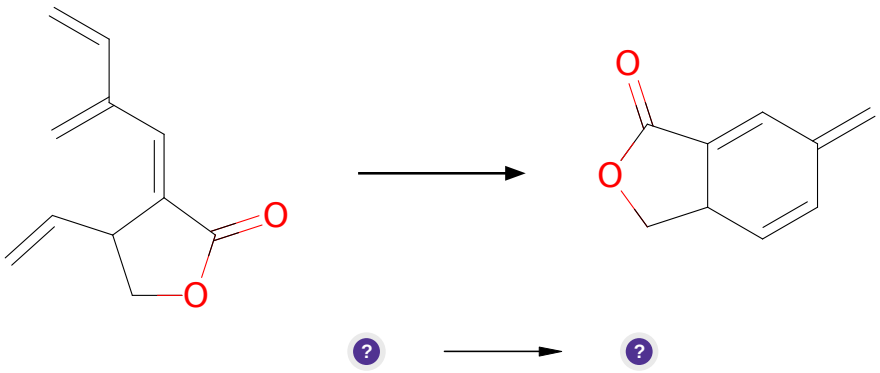
Typical conditions: 1.LDA.2RCHO

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

2.5.4 Ring-Closing Metathesis



Substrates:

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

Products:

1. C=C1C=CC2COC(=O)C2=C1

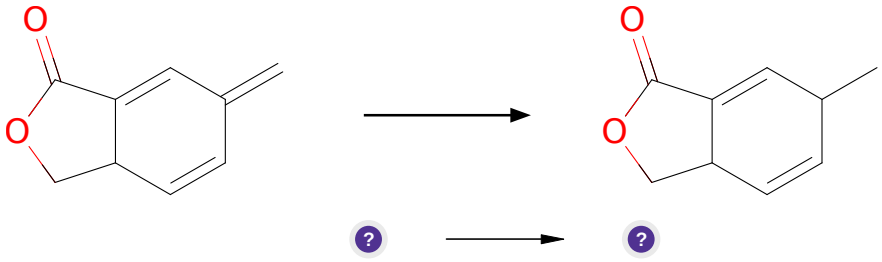
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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

2.5.5 Heterogeneous Reduction of C=C Double Bond



Substrates:

1. C=C1C=CC2COC(=O)C2=C1

Products:

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

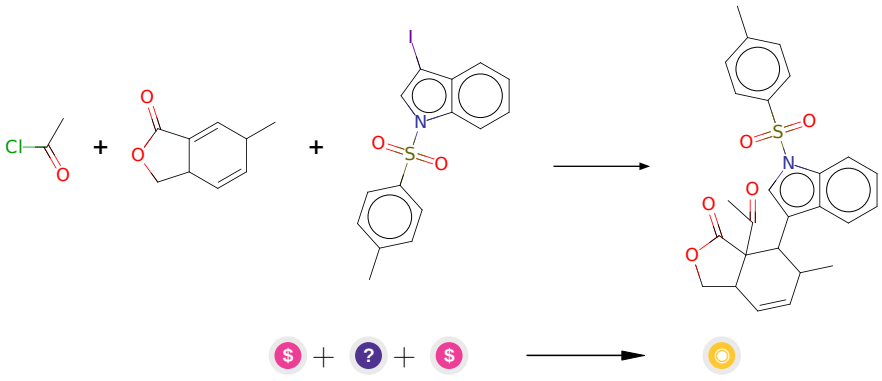
Typical conditions: H2.Wilkinson's Catalyst or other catalyst e.g. Crabtree's

Protections: none

Reference: DOI: *10.1021/jo00052a031* and *10.1021/jo050669u* and *10.1016/j.tetlet.2010.11.078* and *10.1002/anie.198701901* and Patent: US2005/119242 A1, 2005 (page 39) and *10.1021/ja412342g*

Retrosynthesis ID: 9995785

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *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)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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