Paths of analysis*

L1

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

*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.

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`

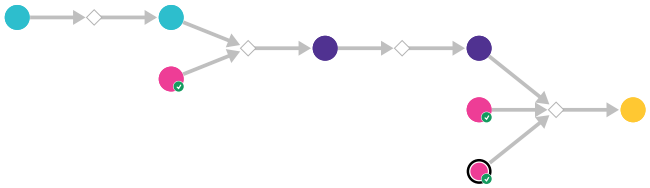
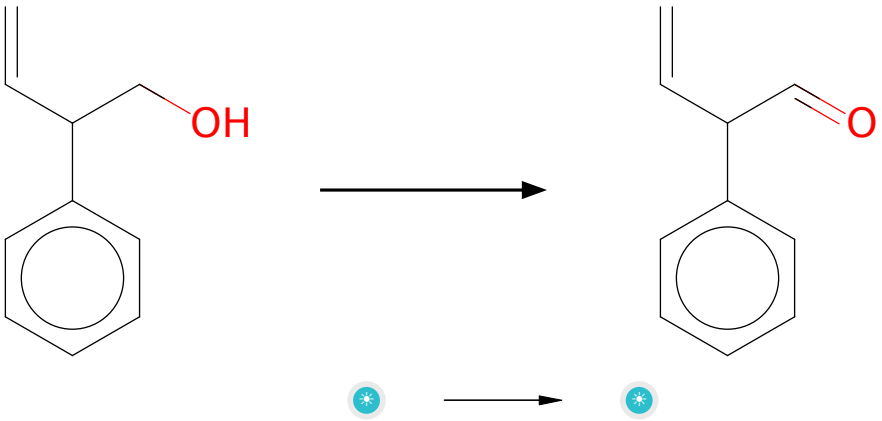


Figure 1: Outline of path 1

2.1.1 Oxidation of primary alcohols with DMP



Substrates:

1. 2-phenylbut-3-en-1-ol

Products:

1. 2-phenyl-but-3-enal

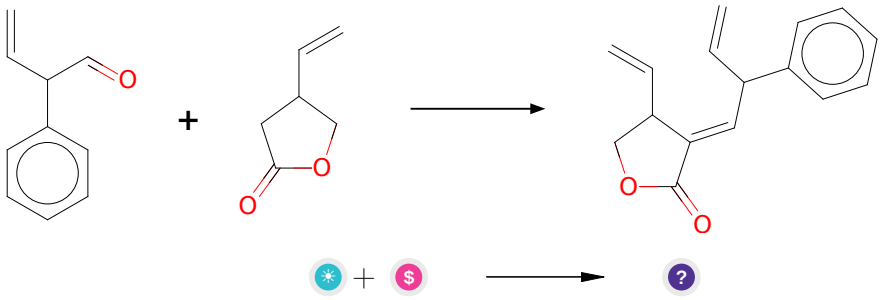
Typical conditions: DMP.DCM.0-25 C

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-phenyl-but-3-enal
2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)/C1=C/C(C=C)c1ccccc1

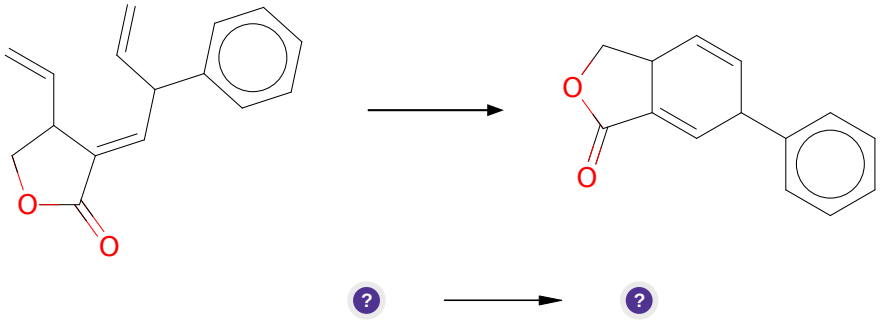
Typical conditions: 1.LDA.2RCHO

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=CC1COC(=O)/C1=C/C(C=C)c1ccccc1

Products:

1. O=C1OCC2C=CC(c3ccccc3)C=C12

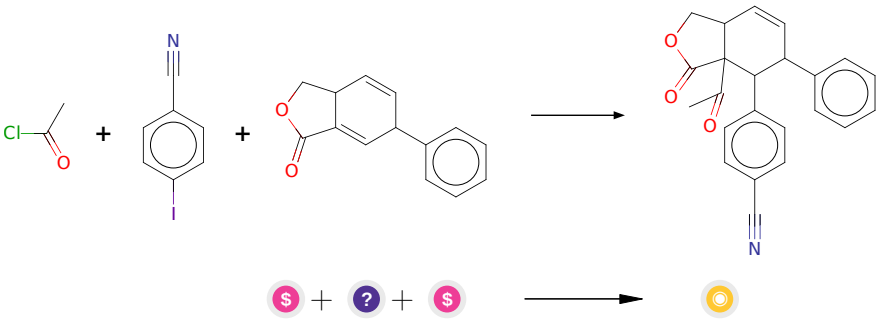
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

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. 4-Iodobenzonitrile - *available at Sigma-Aldrich*
2. O=C1OCC2C=CC(c3ccccc3)C=C12

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

Products:

1. CC(=O)C12C(=O)OCC1C=CC(c1ccccc1)C2c1ccc(C#N)cc1

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: 106.04

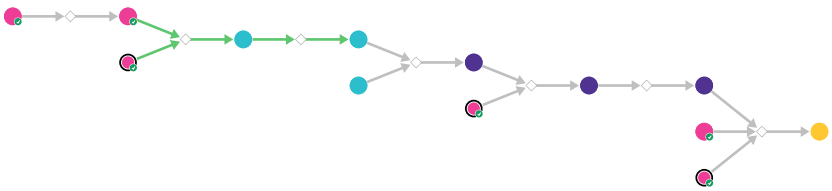
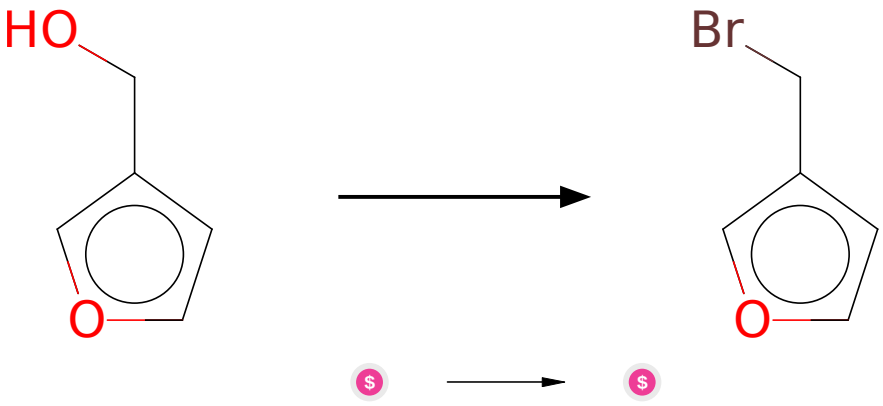


Figure 2: Outline of path 2

2.2.1 Appel Reaction



Substrates:

1. Furan-3-methanol - *available at Sigma-Aldrich*

Products:

1. 3-(bromomethyl)furan - *available at Sigma-Aldrich*

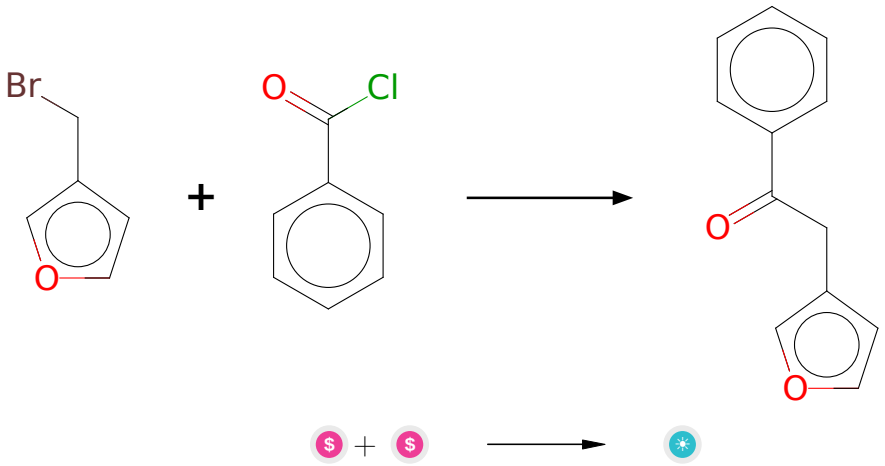
Typical conditions: PPh3.CBr4

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

2.2.2 Grignard reaction with acyl chlorides



Substrates:

1. 3-(bromomethyl)furan - *available at Sigma-Aldrich*
2. Benzoyl chloride - *available at Sigma-Aldrich*

Products:

1. C12H10O2

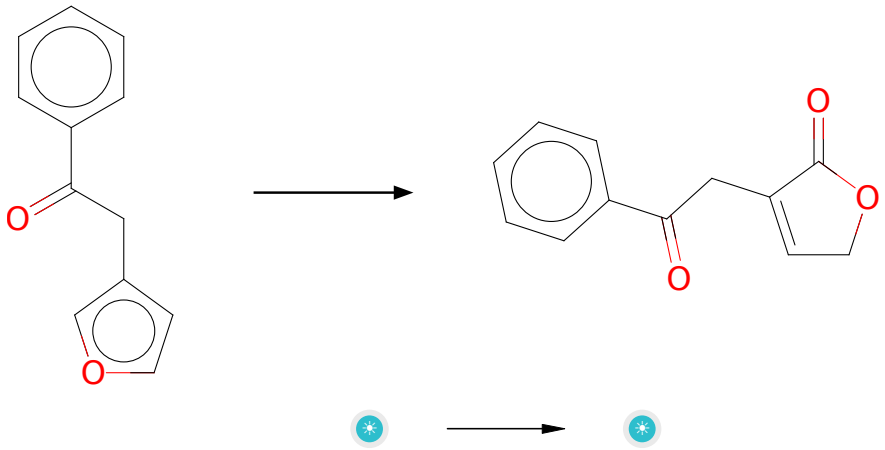
Typical conditions: 1.i-PrMgCl.LiCl 2.ZnCl2 3. CuCl

Protections: none

Reference: *10.1016/0040-4039(94)85361-4* and *10.1016/0040-4039(96)00258-4* and *10.1021/jo3005556* AND *10.1016/0040-4039(96)00689-2*

Retrosynthesis ID: 2530

2.2.3 Oxidation furans to 2-(5H)-furanones



Substrates:

1. C12H10O2

Products:

1. 2-phenacyl-2-buten-4-olide

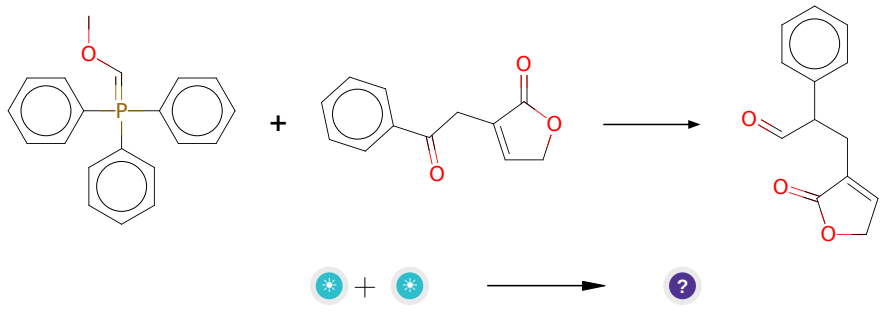
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

Reference: DOI: *10.1055/s-2005-869865*

Retrosynthesis ID: 50717

2.2.4 Olefination of ketones followed by hydrolysis



Substrates:

1. 2-phenacyl-2-buten-4-olide

2. triphenylphosphonium methoxymethylide

Products:

1. O=CC(CC1=CCOC1=O)c1ccccc1

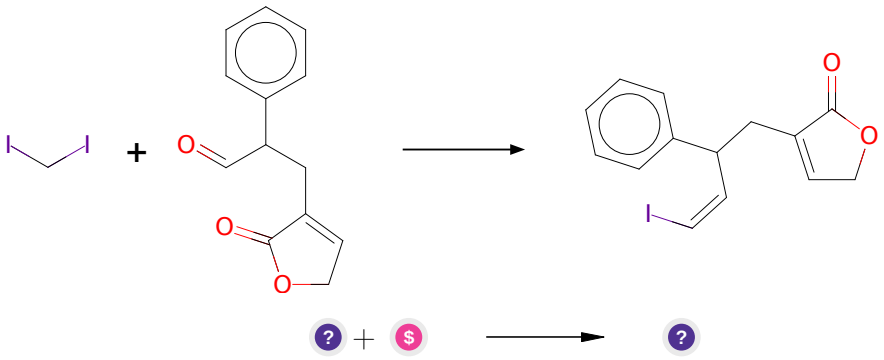
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

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

2.2.5 Iodoolefination of aldehydes



Substrates:

1. O=CC(CC1=CCOC1=O)c1ccccc1
2. Diiodomethane - *available at Sigma-Aldrich*

Products:

1. O=C1OCC=C1CC(/C=C\I)c1ccccc1

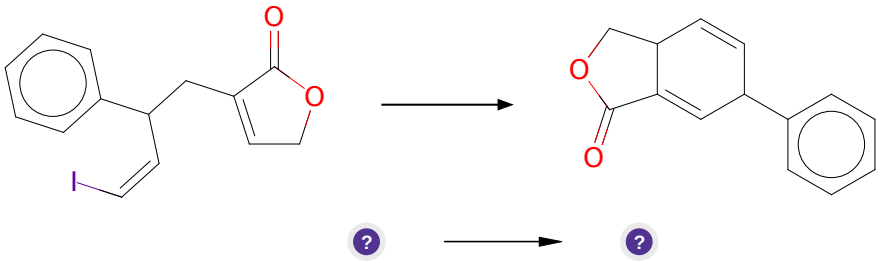
Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

Protections: none

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

Retrosynthesis ID: 10001773

2.2.6 Heck Reaction



Substrates:

1. O=C1OCC=C1CC(/C=C\I)c1ccccc1

Products:

1. O=C1OCC2C=CC(c3ccccc3)C=C12

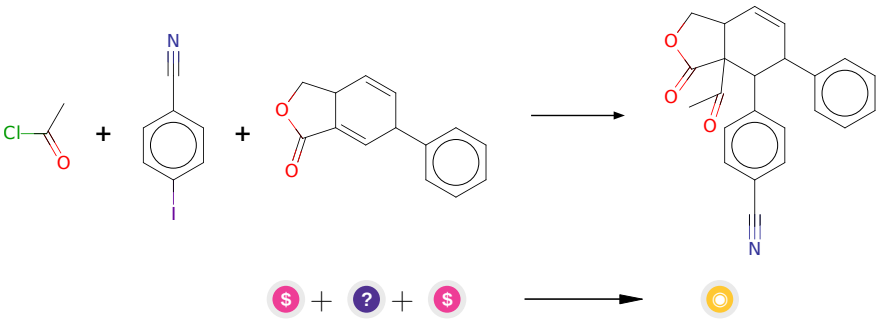
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

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

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



Substrates:

1. 4-Iodobenzonitrile - *available at Sigma-Aldrich*
2. O=C1OCC2C=CC(c3ccccc3)C=C12
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(c1ccccc1)C2c1ccc(C#N)cc1

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

2.3 Path 3

Score: 106.04

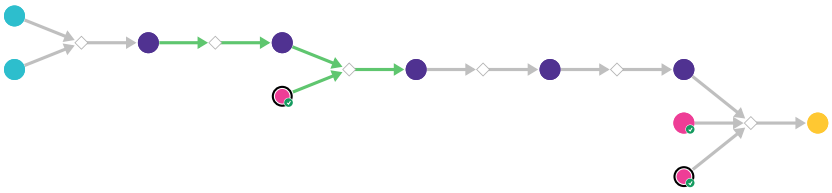
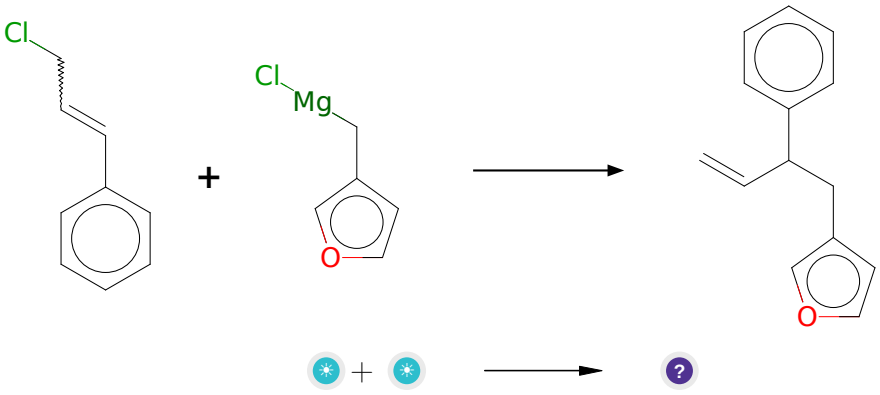


Figure 3: Outline of path 3

2.3.1 NHC-catalyzed Grignard allylic substitution



Substrates:

1. cinnamyl chloride

2. (furan-3-ylmethyl)magnesium chloride

Products:

1. C=CC(Cc1ccoc1)c1ccccc1

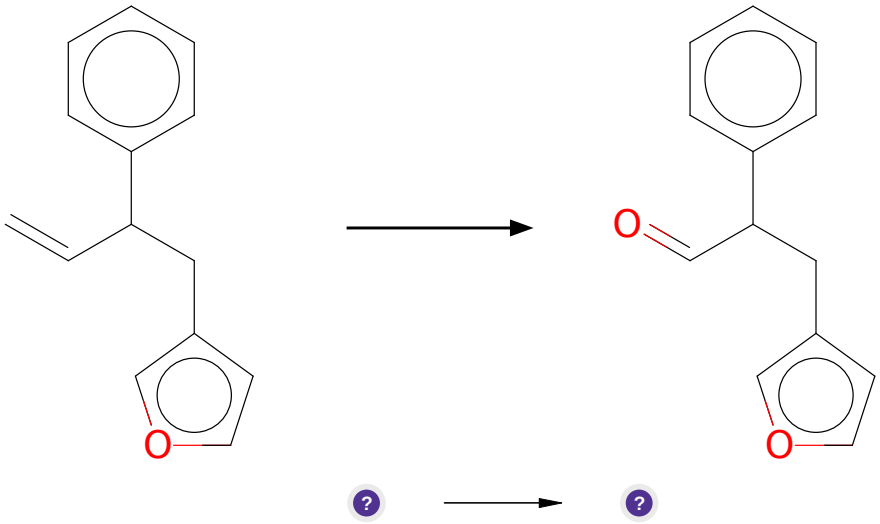
Typical conditions: RMgCl.THF.NHC-complex

Protections: none

Reference: *10.1016/j.tetlet.2012.12.124*

Retrosynthesis ID: 1171

2.3.2 Ozonolysis



Substrates:

1. C=CC(Cc1ccoc1)c1ccccc1

Products:

1. O=CC(Cc1ccoc1)c1ccccc1

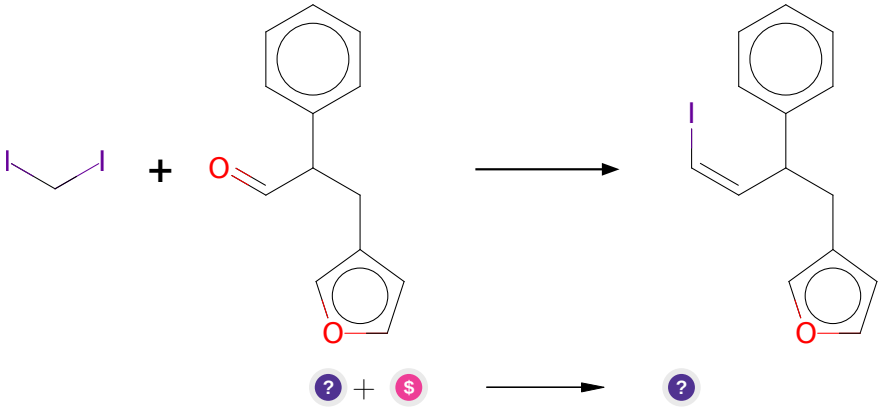
Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5074

2.3.3 Iodoolefination of aldehydes



Substrates:

1. O=CC(Cc1ccoc1)c1ccccc1
2. Diiodomethane - *available at Sigma-Aldrich*

Products:

1. I/C=C\C(Cc1ccoc1)c1ccccc1

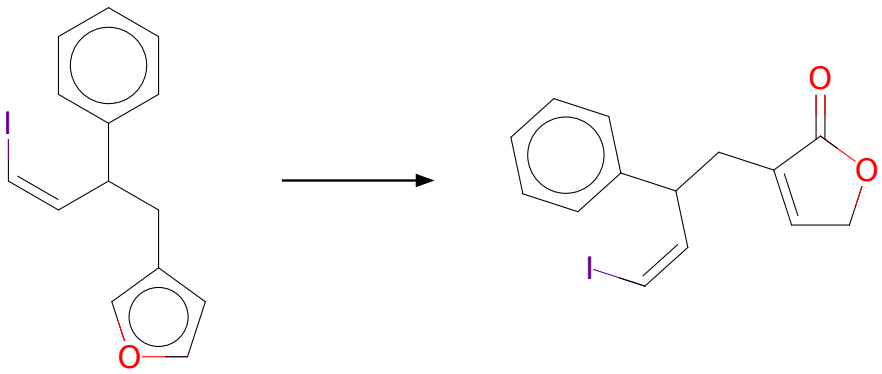
Typical conditions: 1.PPh3.2.NaN(TMS)2.HMPA.THF

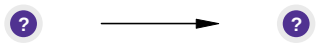
Protections: none

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. I/C=C\C(Cc1ccoc1)c1ccccc1

Products:

1. O=C1OCC=C1CC(/C=C\I)c1ccccc1

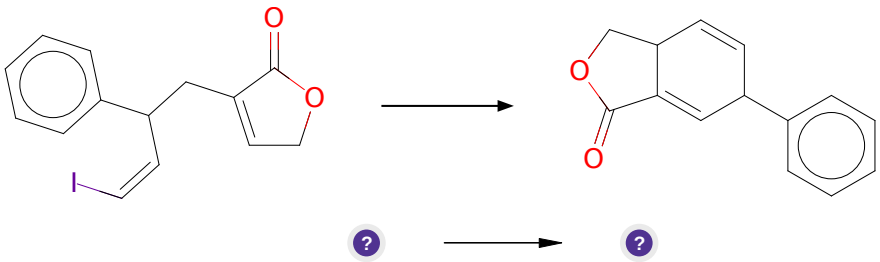
Typical conditions: NBS.MW.MeOH

Protections: none

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

Retrosynthesis ID: 49766

2.3.5 Heck Reaction



Substrates:

1. O=C1OCC=C1CC(/C=C\I)c1ccccc1

Products:

1. O=C1OCC2C=CC(c3ccccc3)C=C12

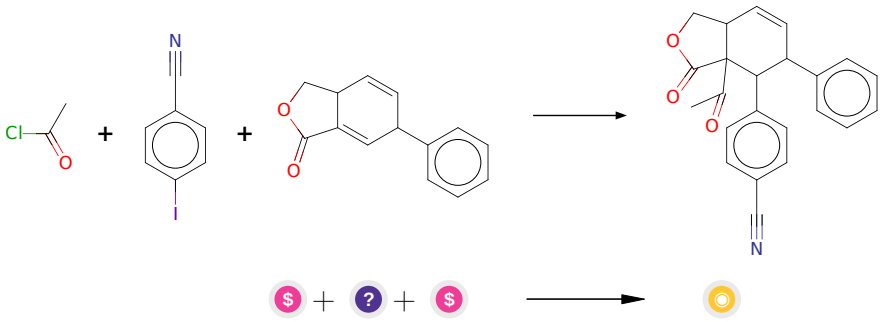
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

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. 4-Iodobenzonitrile - *available at Sigma-Aldrich*
2. O=C1OCC2C=CC(c3ccccc3)C=C12
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(c1ccccc1)C2c1ccc(C#N)cc1

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

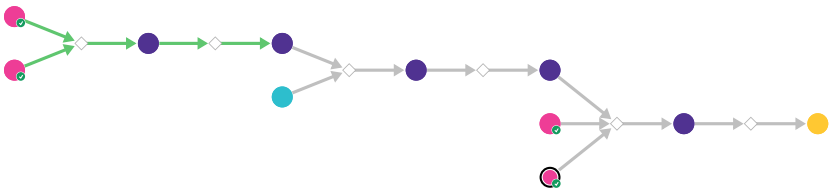
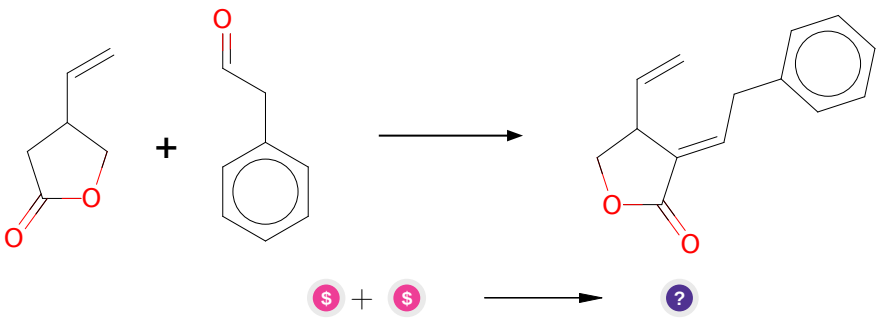


Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes



Substrates:

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

Products:

1. C=CC1COC(=O)/C1=C/Cc1ccccc1

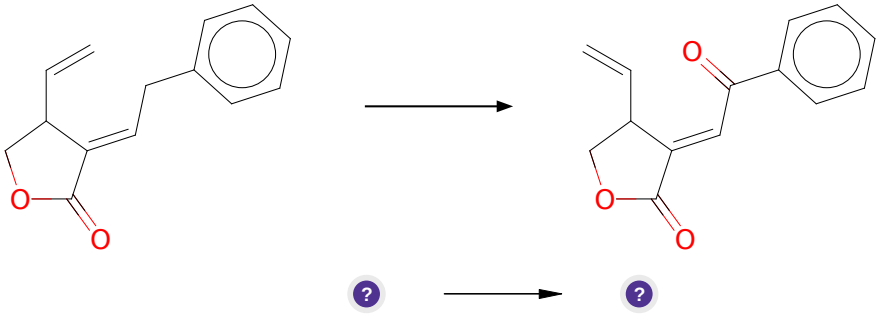
Typical conditions: 1.LDA.2RCHO

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

2.4.2 Allylic Oxidation of Alkenes



Substrates:

1. C=CC1COC(=O)/C1=C/Cc1ccccc1

Products:

1. C=CC1COC(=O)/C1=C/C(=O)c1ccccc1

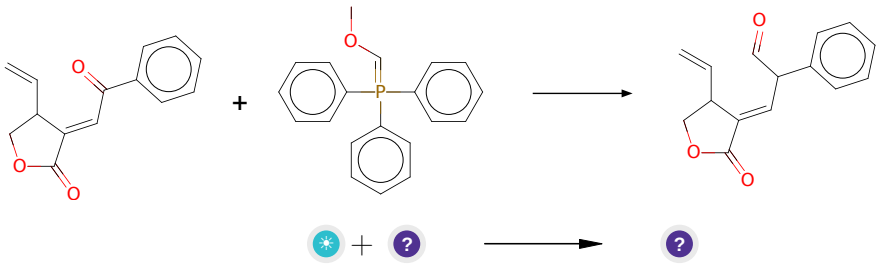
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.4.3 Olefination of ketones followed by hydrolysis



Substrates:

1. triphenylphosphonium methoxymethylide
2. C=CC1COC(=O)/C1=C/C(=O)c1ccccc1

Products:

1. C=CC1COC(=O)/C1=C/C(C=O)c1ccccc1

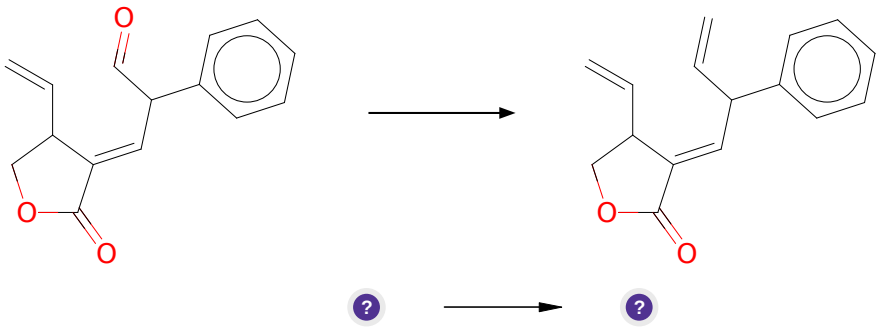
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

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=C/C(C=O)c1ccccc1

Products:

1. C=CC1COC(=O)/C1=C/C(C=C)c1ccccc1

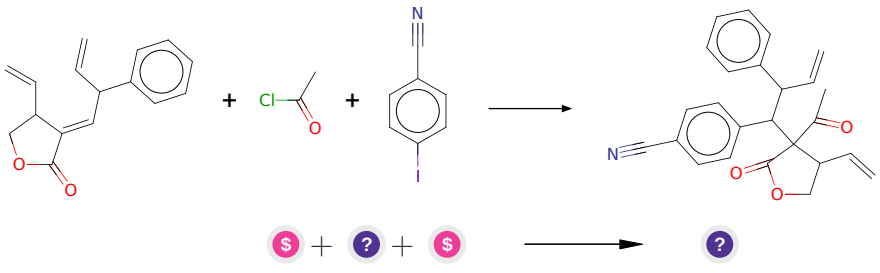
Typical conditions: Cp2TiCl2.AlMe3.toluene

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. 4-Iodobenzonitrile - *available at Sigma-Aldrich*
2. C=CC1COC(=O)/C1=C/C(C=C)c1ccccc1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. C=CC(c1ccccc1)C(c1ccc(C#N)cc1)C1(C(C)=O)C(=O)OCC1C=C

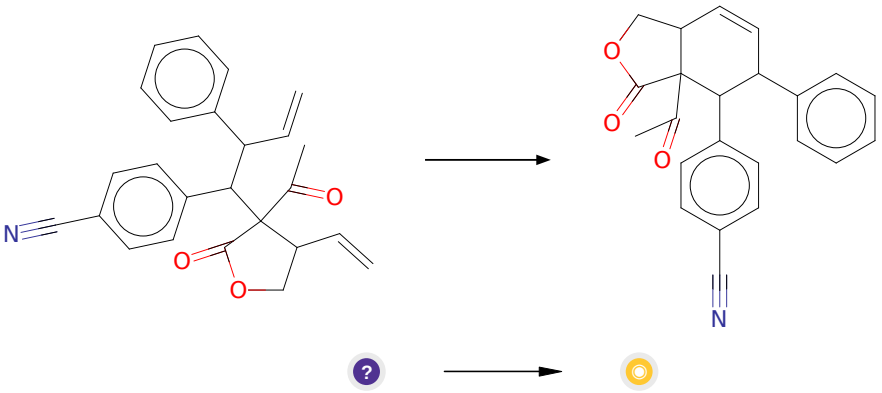
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20524

2.4.6 Ring-Closing Metathesis



Substrates:

1. C=CC(c1ccccc1)C(c1ccc(C#N)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(c1ccccc1)C2c1ccc(C#N)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

2.5 Path 5

Score: 107.50

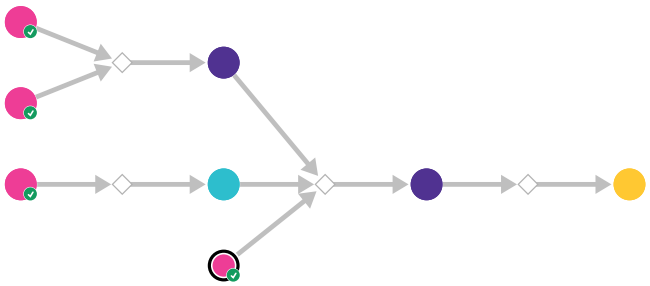
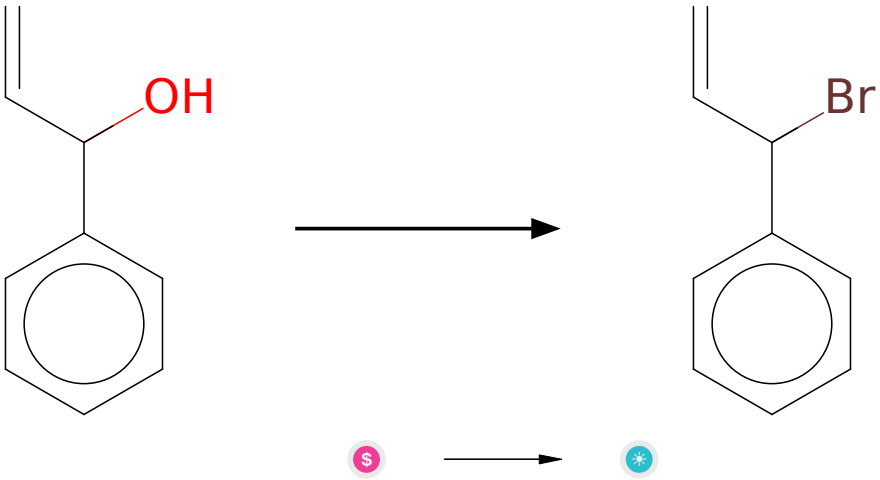


Figure 5: Outline of path 5

2.5.1 Appel Reaction



Substrates:

1. a-Vinylbenzyl alcohol - *available at Sigma-Aldrich*

Products:

1. 3-bromo-3-phenyl-propene

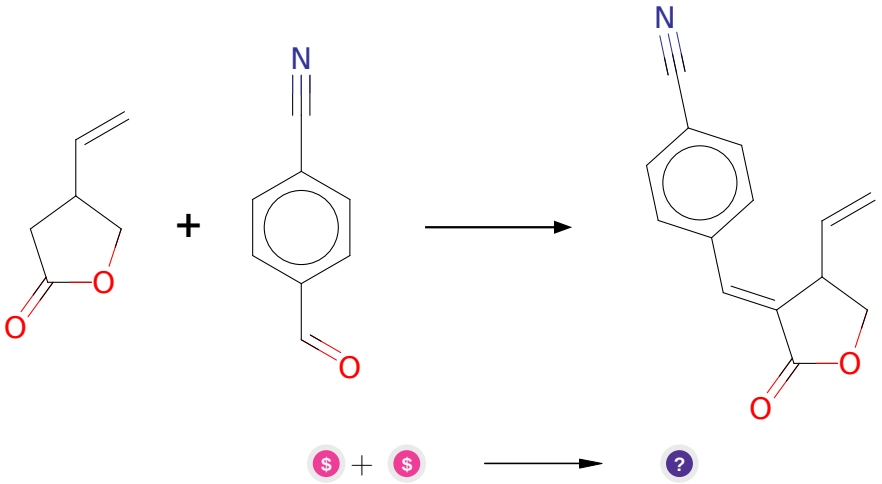
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1016/j.jfluchem.2015.03.009* and *10.1016/j.tet.2005.12.006* and *10.1021/jm00161a029* and *10.1055/s-1995-5215*

Retrosynthesis ID: 9990042

2.5.2 Condensation of esters with aldehydes



Substrates:

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

Products:

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

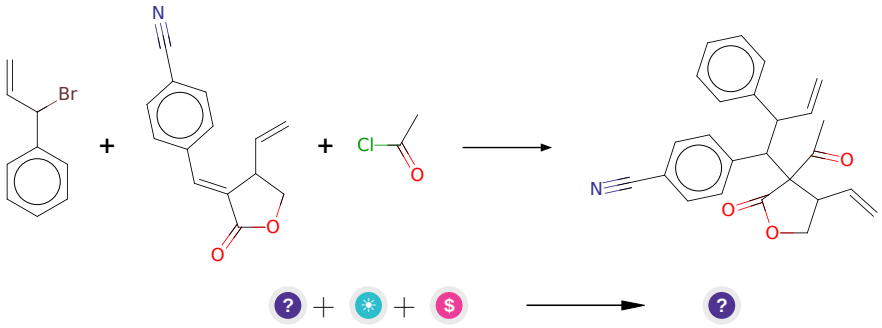
Typical conditions: 1.LDA.2RCHO

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

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



Substrates:

1. C=CC1COC(=O)/C1=C/c1ccc(C#N)cc1
2. 3-bromo-3-phenyl-propene
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. C=CC(c1ccccc1)C(c1ccc(C#N)cc1)C1(C(C)=O)C(=O)OCC1C=C

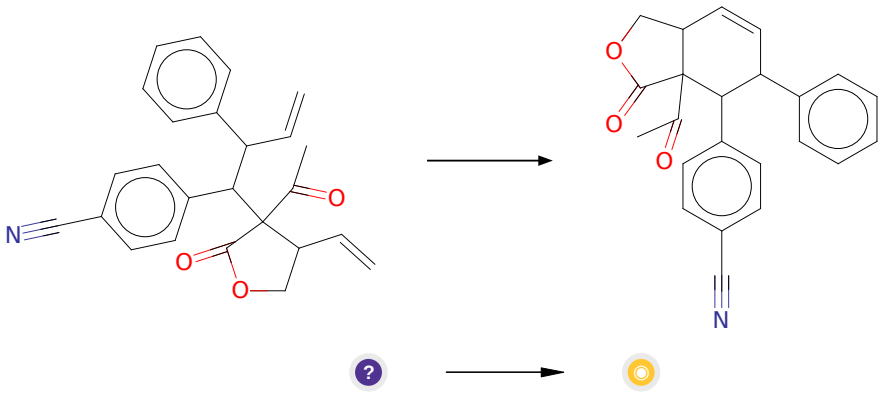
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

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

Retrosynthesis ID: 20523

2.5.4 Ring-Closing Metathesis



Substrates:

1. C=CC(c1ccccc1)C(c1ccc(C#N)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(c1ccccc1)C2c1ccc(C#N)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