

Paths of analysis*

L2

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselective 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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

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

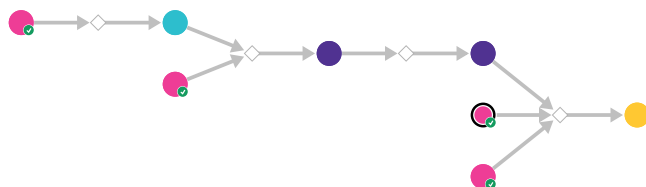
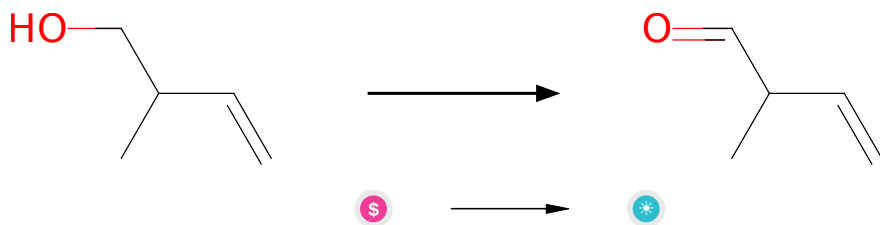


Figure 1: Outline of path 1

2.1.1 Oxidation of primary alcohols with DMP



Substrates:

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

Products:

1. 2-methyl-but-3-enal

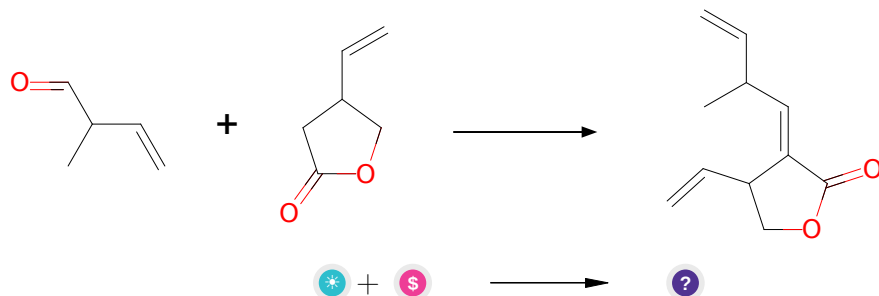
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: [10.1016/j.bmc.2020.115469](https://doi.org/10.1016/j.bmc.2020.115469) p. 3, 9 and [10.1021/acs.jmedchem.8b01878](https://doi.org/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

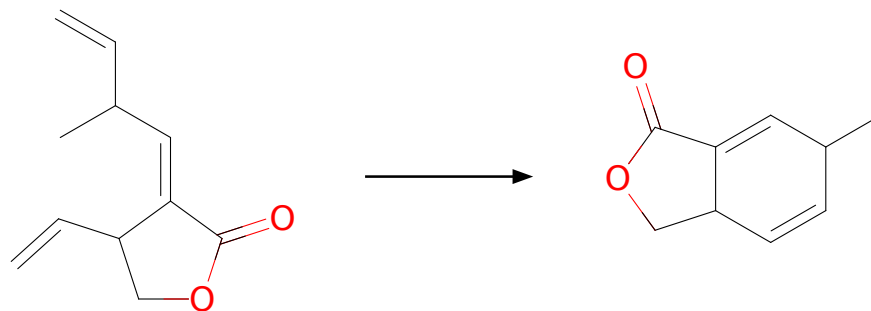
Typical conditions: 1.LDA.2RCHO

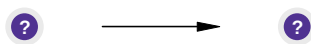
Protections: none

Reference: [10.1021/jo970387x](https://doi.org/10.1021/jo970387x) AND [10.1021/jo00076a051](https://doi.org/10.1021/jo00076a051) AND [10.1016/S0040-4039\(97\)10827-9](https://doi.org/10.1016/S0040-4039(97)10827-9) AND [10.1055/s-2002-25767](https://doi.org/10.1055/s-2002-25767) AND [10.1039/P19920003277](https://doi.org/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

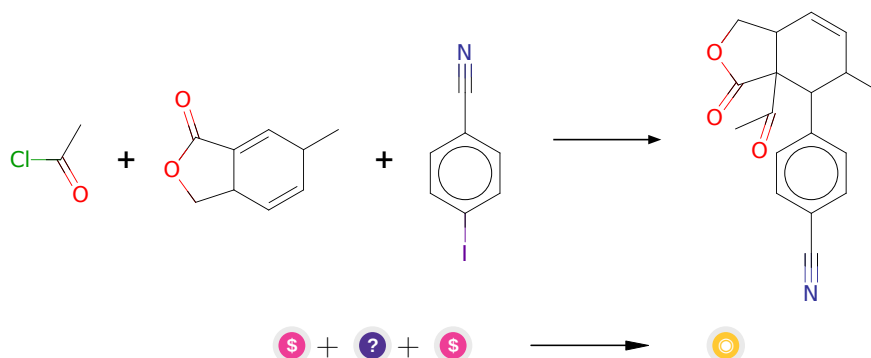
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. 4-Iodobenzonitrile - *available at Sigma-Aldrich*

Products:

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

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

Protections: none

Reference: [10.3987/COM-99-S143](https://doi.org/10.3987/COM-99-S143) AND [10.1021/ja00148a023](https://doi.org/10.1021/ja00148a023) AND [10.1016/S0040-4039\(01\)80891-1](https://doi.org/10.1016/S0040-4039(01)80891-1)

Retrosynthesis ID: 12521

2.2 Path 2

Score: 76.25

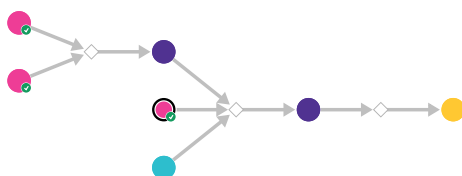
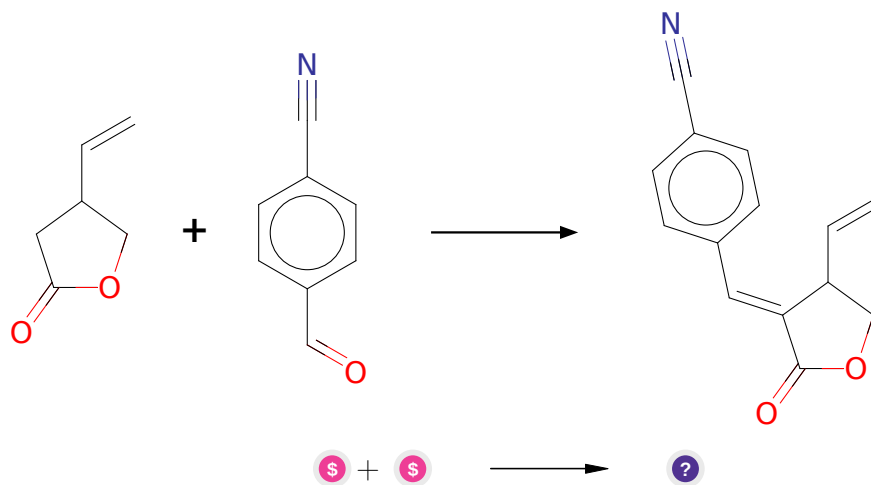


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes



Substrates:

1. 4-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

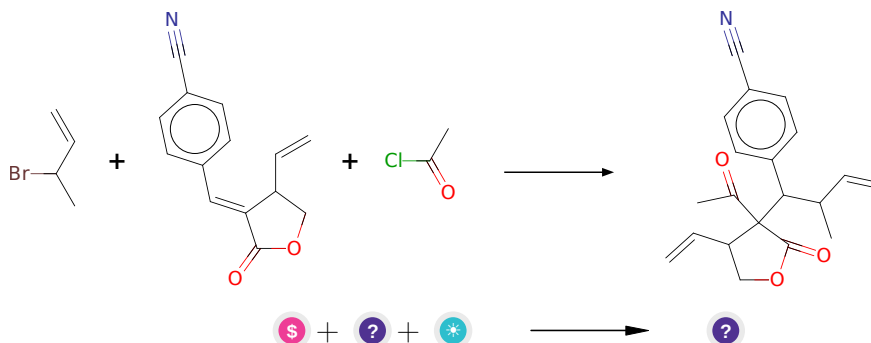
Typical conditions: 1.LDA.2RCHO

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

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



Substrates:

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

Products:

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

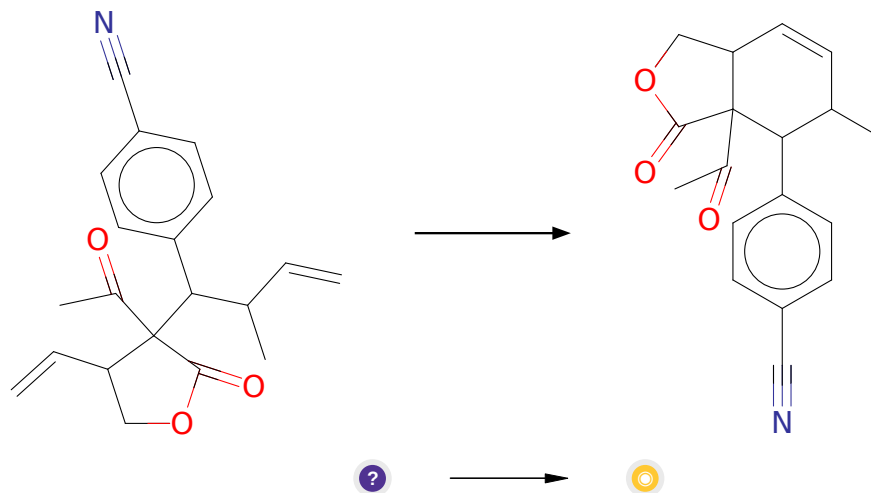
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: [10.3987/COM-99-S143](#) AND [10.1021/ja00148a023](#) AND [10.1016/S0040-4039\(01\)80891-1](#)

Retrosynthesis ID: 20523

2.2.3 Ring-Closing Metathesis



Substrates:

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

Products:

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

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

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.3 Path 3

Score: 106.04

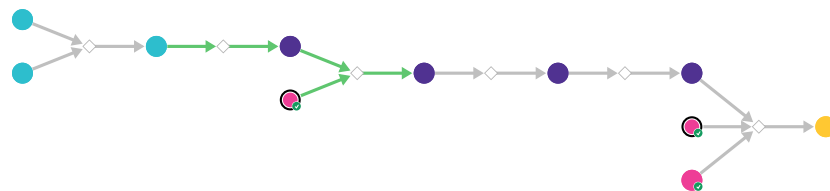
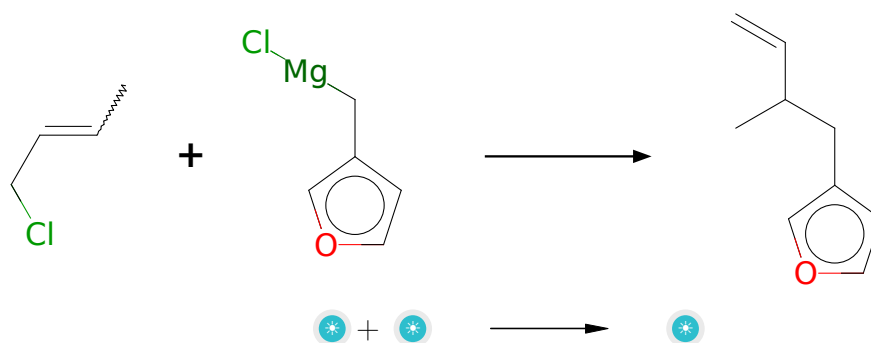


Figure 3: Outline of path 3

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

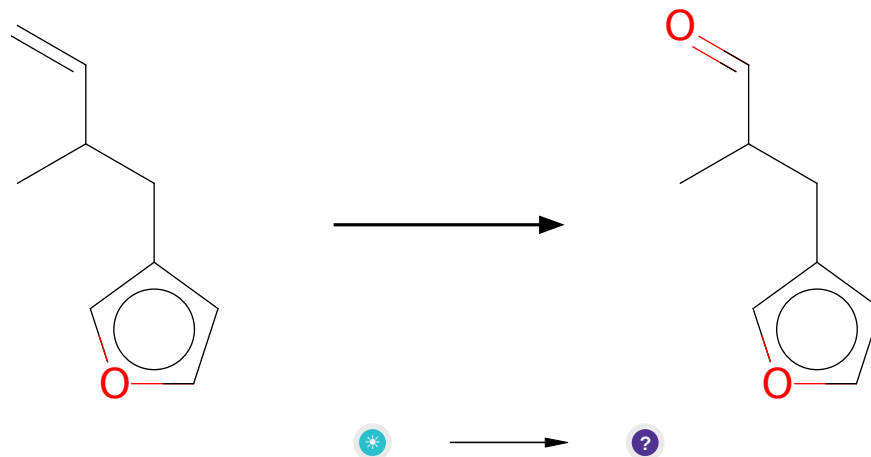
Typical conditions: RMgCl.THF.NHC-complex

Protections: none

Reference: [10.1016/j.tetlet.2012.12.124](https://doi.org/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

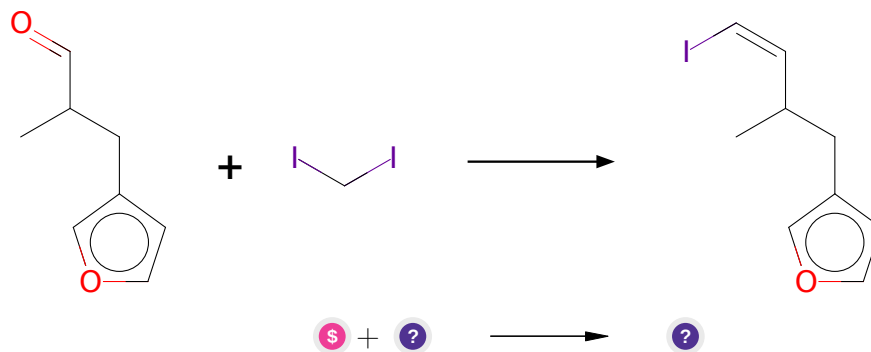
Typical conditions: O₃.MeOH.CH₂Cl₂.PPh₃ or Me₂S.low temperature

Protections: none

Reference: [10.1016/j.tet.2017.03.039](https://doi.org/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

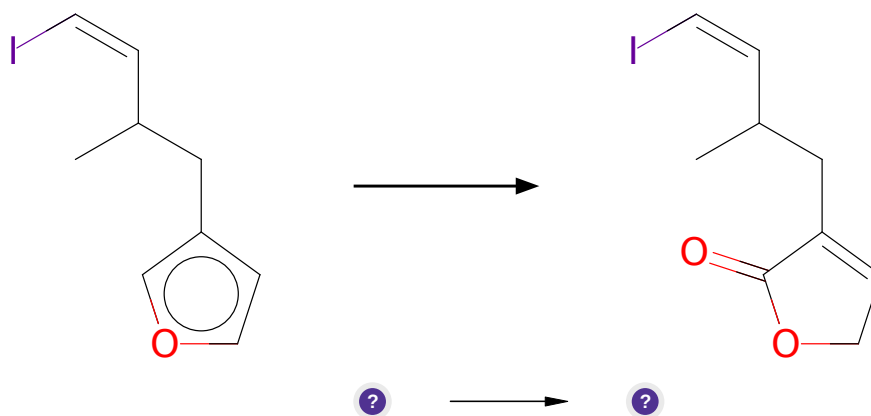
Typical conditions: 1.PPh₃.2.Na⁺N⁻(TMS)⁻.2.HMPA.THF

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

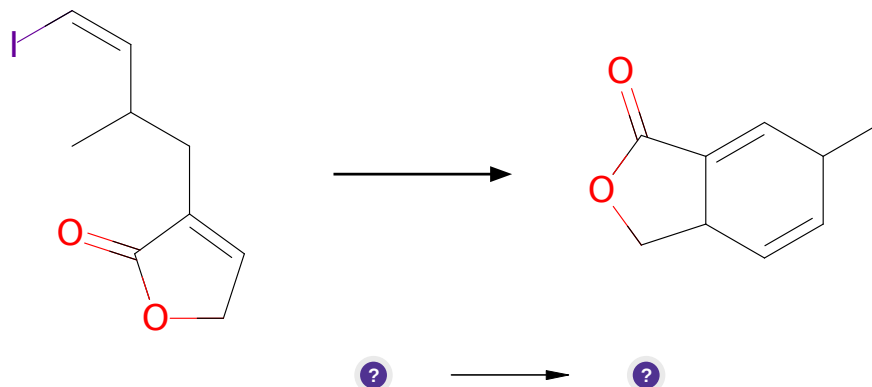
Typical conditions: NBS.MW.MeOH

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

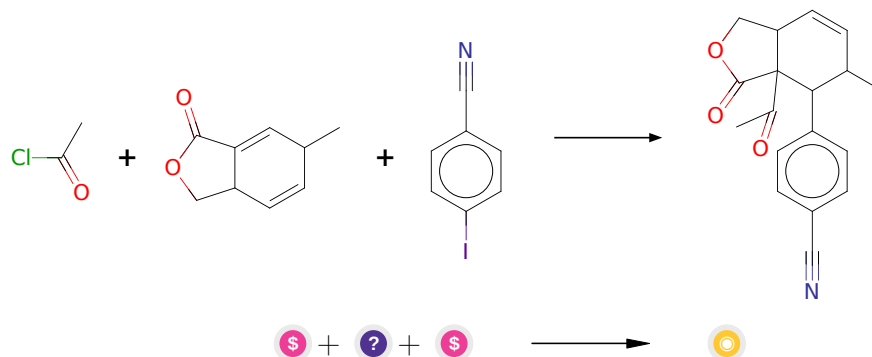
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

Protections: none

Reference: DOI: [10.1021/jo00270a011](https://doi.org/10.1021/jo00270a011) or DOI: [10.1021/ar00049a001](https://doi.org/10.1021/ar00049a001) or DOI: [10.1021/ja00206a034](https://doi.org/10.1021/ja00206a034) or DOI: [10.1021/cr020039h](https://doi.org/10.1021/cr020039h) or DOI: [10.1039/C1CS15101K](https://doi.org/10.1039/C1CS15101K) or DOI: [10.1002/9780470716076](https://doi.org/10.1002/9780470716076)

Retrosynthesis ID: 8584

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. 4-Iodobenzonitrile - *available at Sigma-Aldrich*

Products:

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

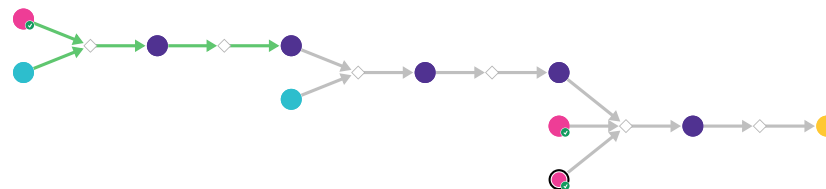
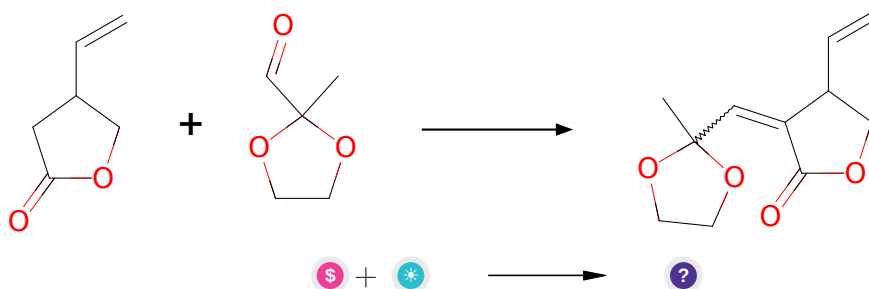


Figure 4: Outline of path 4

2.4.1 Condensation of esters with aldehydes/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

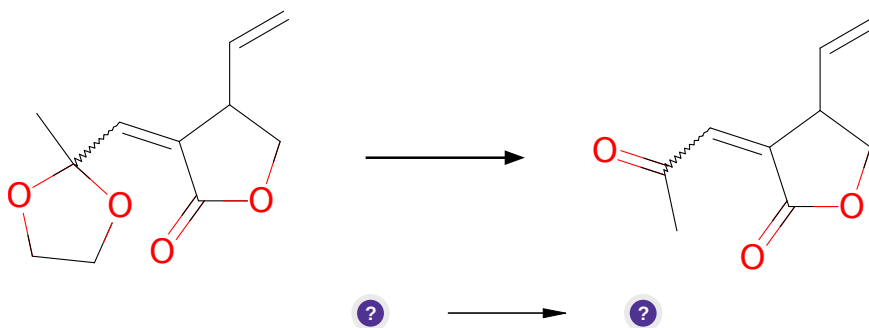
Typical conditions: LDA.THF

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

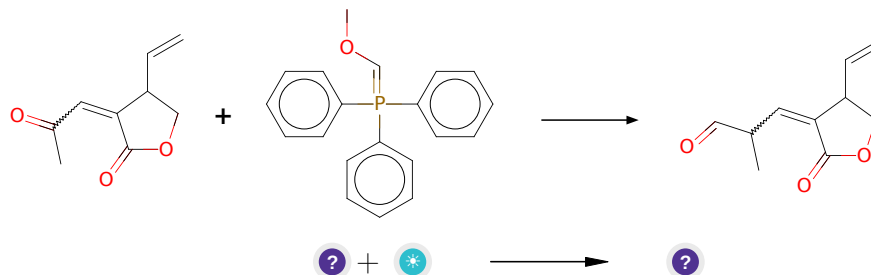
Typical conditions: H₂O.HCl

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

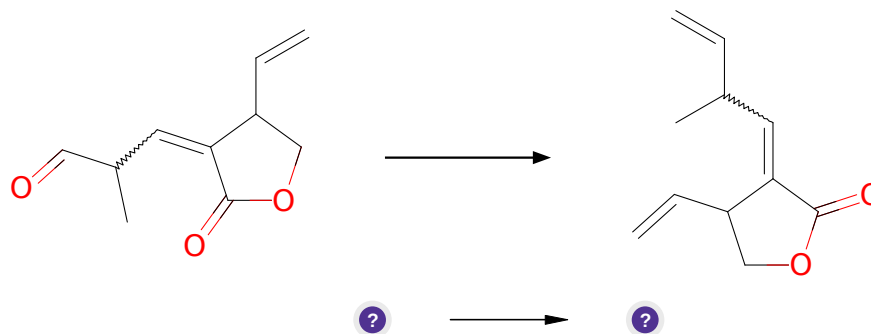
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

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

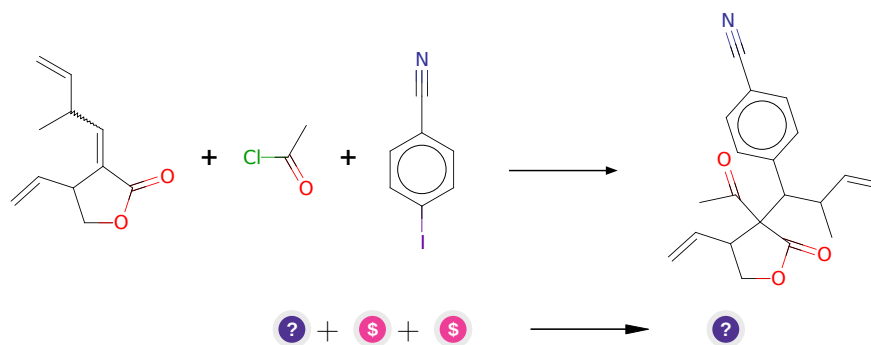
Typical conditions: Cp₂TiCl₂.AlMe₃.toluene

Protections: none

Reference: [10.1016/j.tet.2007.03.015](#) and [10.1002/9780470638859.conrrr617](#)

Retrosynthesis ID: 11714

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



Substrates:

1. C=CC(C)C=C1C(=O)OCC1C=C
2. 4-Iodobenzonitrile - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

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

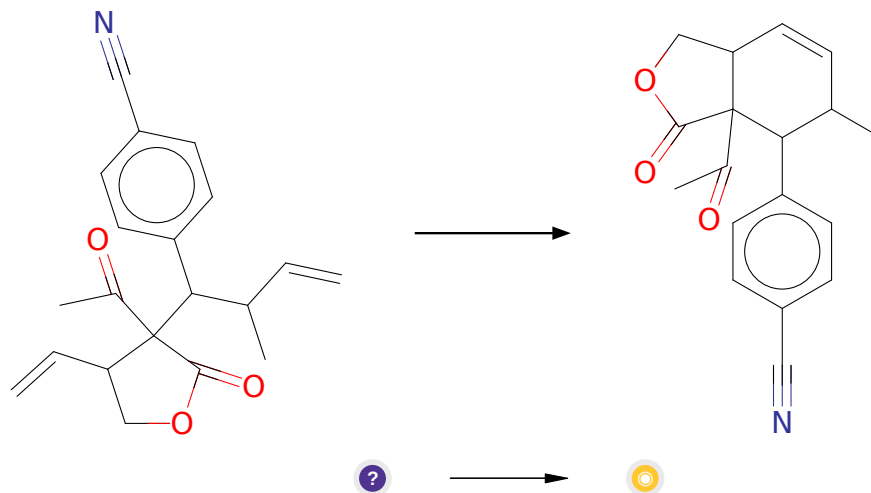
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: [10.3987/COM-99-S143](#) AND [10.1021/ja00148a023](#) AND [10.1016/S0040-4039\(01\)80891-1](#)

Retrosynthesis ID: 20528

2.4.6 Ring-Closing Metathesis



Substrates:

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

Products:

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

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

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.5 Path 5

Score: 106.04

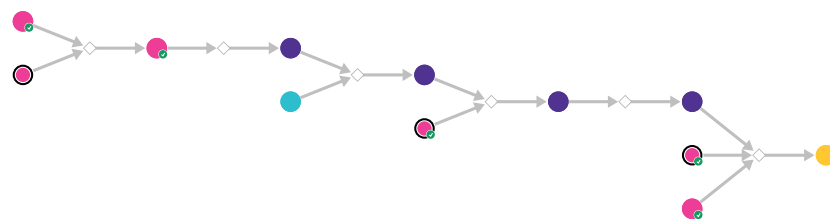
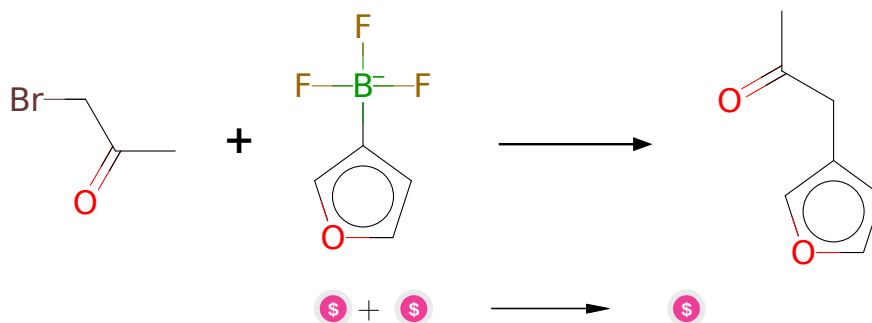


Figure 5: Outline of path 5

2.5.1 Suzuki Coupling of aryltrifluoroborates with alkyl bromides



Substrates:

1. potassium trifluoro(3-furyl)borate(1-) - *available at Sigma-Aldrich*
2. brom-aceton - *AstaTech*

Products:

1. 1-(furan-3-yl)propan-2-one - *available at Sigma-Aldrich*

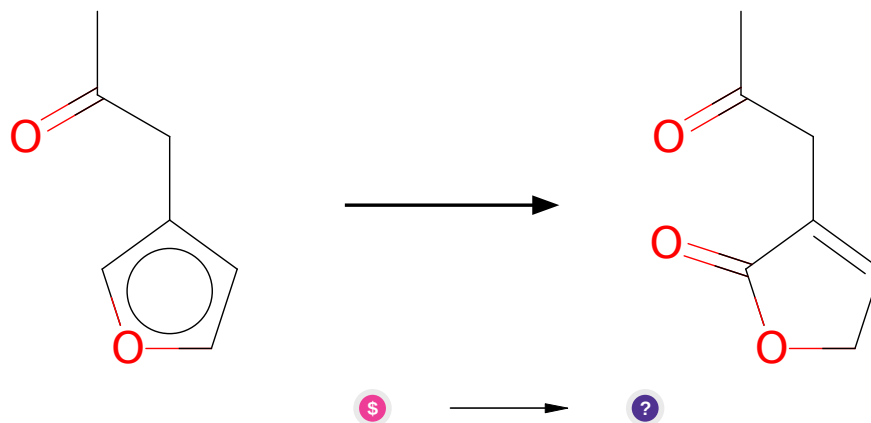
Typical conditions: NiBr₂.glyme.Bphen.LiHMDS.sBuOH.60C

Protections: none

Reference: [10.1021/ol102717x](#) and [10.1021/jo061699f](#) and [10.1016/j.tetlet.2016.09.040](#) and [10.1016/j.catcom.2017.06.052](#)

Retrosynthesis ID: 10034082

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



Substrates:

1. 1-(furan-3-yl)propan-2-one - *available at Sigma-Aldrich*

Products:

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

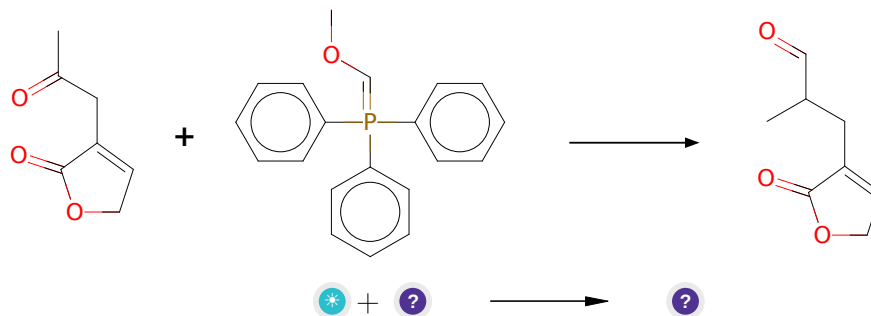
Typical conditions: 1. NBS.CHCl₃.EtOH.rt 2. HCl.acetone.H₂O.rt

Protections: none

Reference: DOI: [10.1055/s-2005-869865](https://doi.org/10.1055/s-2005-869865)

Retrosynthesis ID: 50717

2.5.3 Olefination of ketones followed by hydrolysis



Substrates:

1. triphenylphosphonium methoxymethylide
2. CC(=O)CC1=CCOC1=O

Products:

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

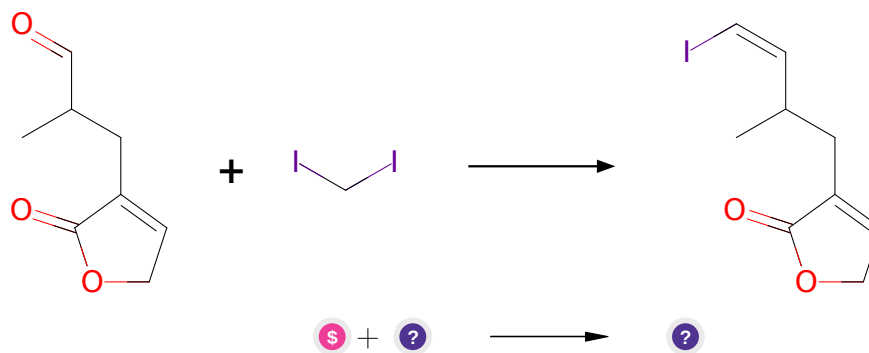
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

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

2.5.4 Iodoolefination of aldehydes



Substrates:

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

Products:

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

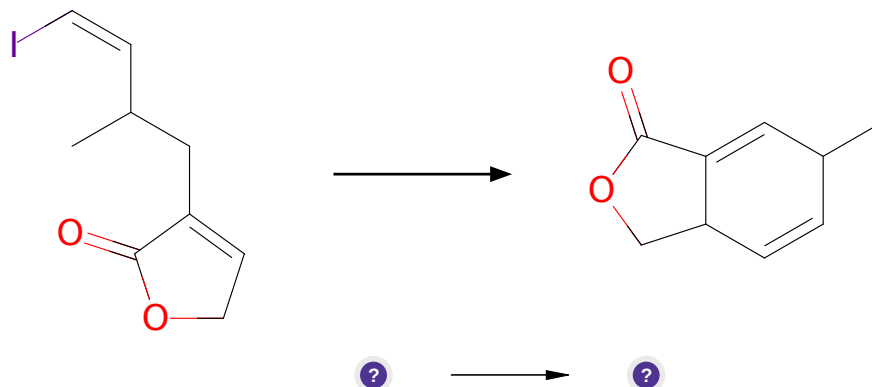
Typical conditions: 1.PPh₃.2.Na⁺N⁻(TMS)₂.HMPA.THF

Protections: none

Reference: [10.1021/ja00171a035](#) and [10.1039/C0OB00977F](#) and WO2009033499 (p.25)

Retrosynthesis ID: 10001773

2.5.5 Heck Reaction



Substrates:

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

Products:

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

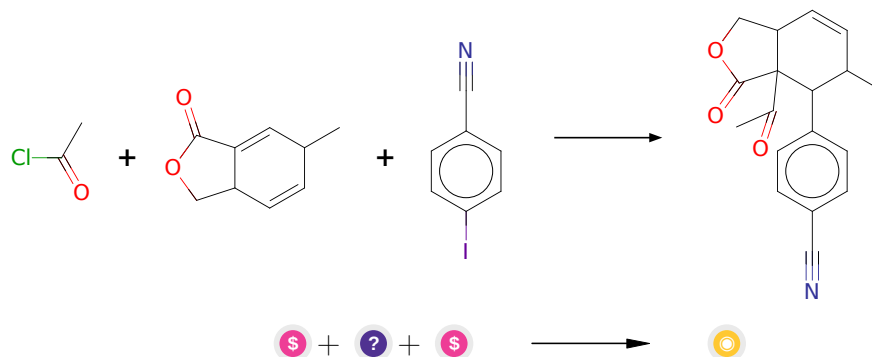
Typical conditions: Pd (cat). ligand. base e.g DIPEA.solvent

Protections: none

Reference: DOI: [10.1021/jo00270a011](https://doi.org/10.1021/jo00270a011) or DOI: [10.1021/ar00049a001](https://doi.org/10.1021/ar00049a001) or DOI: [10.1021/ja00206a034](https://doi.org/10.1021/ja00206a034) or DOI: [10.1021/cr020039h](https://doi.org/10.1021/cr020039h) or DOI: [10.1039/C1CS15101K](https://doi.org/10.1039/C1CS15101K) or DOI: [10.1002/9780470716076](https://doi.org/10.1002/9780470716076)

Retrosynthesis ID: 8584

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



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. 4-Iodobenzonitrile - *available at Sigma-Aldrich*

Products:

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

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