Paths of analysis*

L11

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

3 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: 358.72

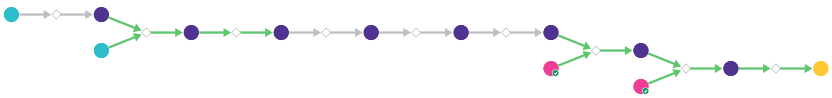
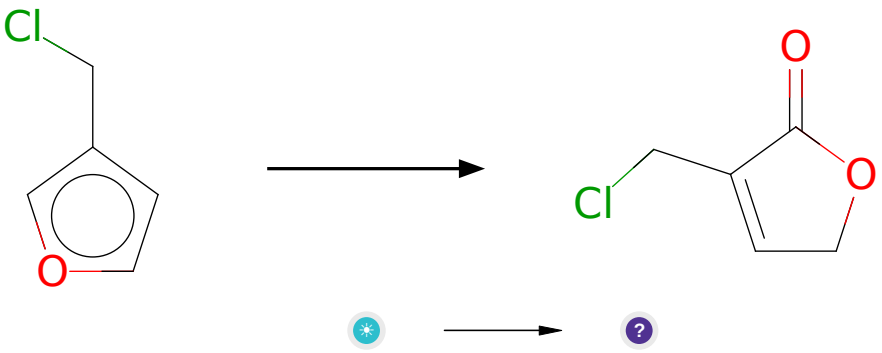


Figure 1: Outline of path 1

2.1.1 NBS-promoted oxidation of furans to lactones



Substrates:

1. 3-chlormethyl-furan

Products:

1. O=C1OCC=C1CCl

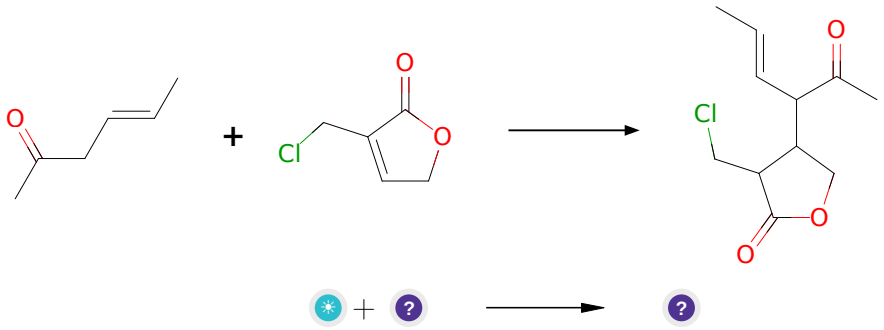
Typical conditions: NBS.MW.MeOH

Protections: none

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

Retrosynthesis ID: 49766

2.1.2 Michael addition



Substrates:

1. hex-4t-en-2-one
2. O=C1OCC=C1CCl

Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1CCl

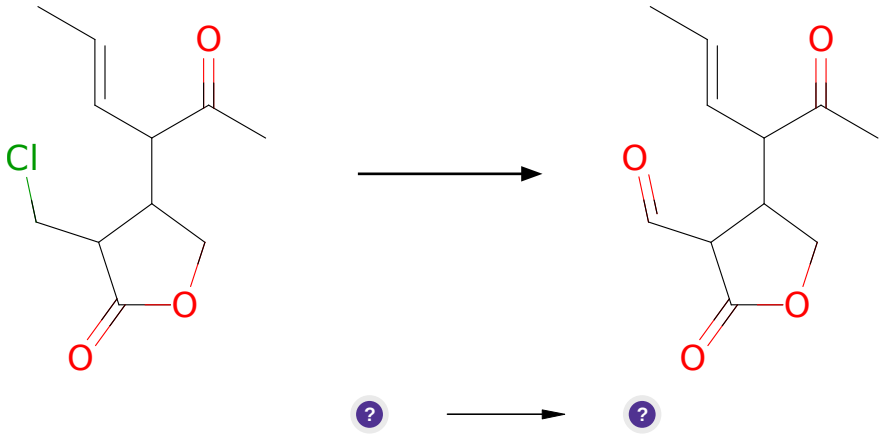
Typical conditions: EtONa or other base

Protections: none

Reference: *10.1016/j.tetlet.2011.02.073* AND *10.1016/j.molstruc.2010.12.005* AND *10.1016/S0040-4039(97)00695-3* AND *10.1021/ol016401g* AND *10.1002/ejoc.200500330*

Retrosynthesis ID: 15774

2.1.3 Kornblum Oxidation



Substrates:

1. C/C=C/C(C(C)=O)C1COC(=O)C1CCl

Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

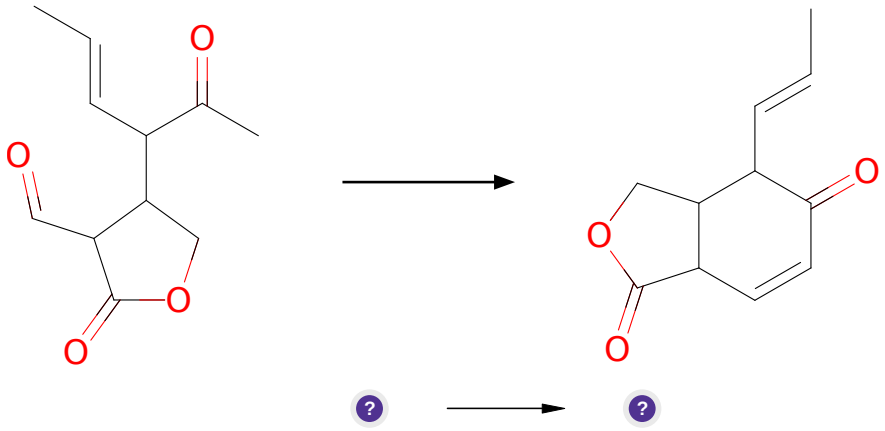
Typical conditions: DMSO.NEt3

Protections: none

Reference: *10.1080/00397918608056381* and *10.1002/9780470638859.conrr373*

Retrosynthesis ID: 11658

2.1.4 Aldol Condensation



Substrates:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

Products:

1. C/C=C/C1C(=O)C=CC2C(=O)OCC21

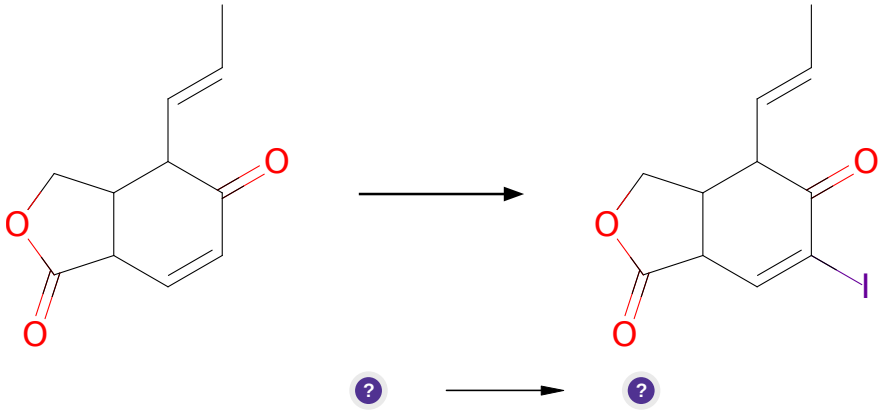
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10896

2.1.5 Alpha-iodination of alpha-beta-unsaturated carbonyl compounds



Substrates:

1. C/C=C/C1C(=O)C=CC2C(=O)OCC21

Products:

1. C/C=C/C1C(=O)C(I)=CC2C(=O)OCC21

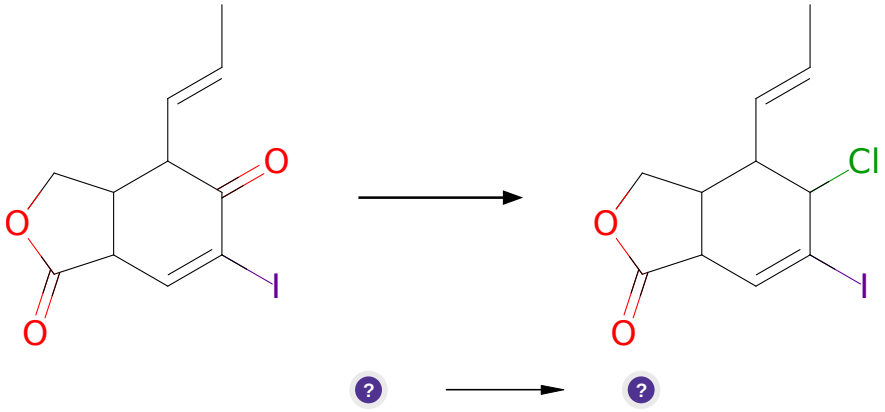
Typical conditions: DMAP.K2CO3.H2O.THF

Protections: none

Reference: DOI: *10.1055/s-2005-868495*

Retrosynthesis ID: 786

2.1.6 Synthesis of alkyl chlorides from ketones



Substrates:

1. C/C=C/C1C(=O)C(I)=CC2C(=O)OCC21

Products:

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21

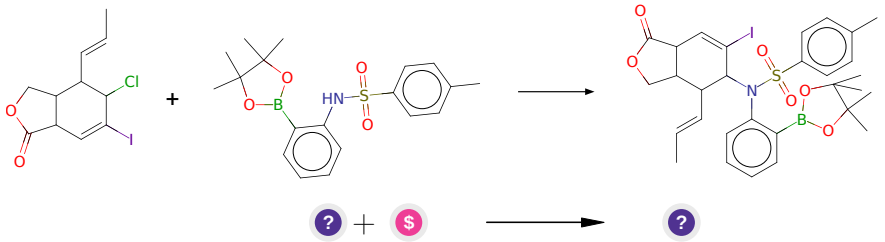
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11620

2.1.7 Alkylation of sulfonamides with alkyl chlorides



Substrates:

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21
2. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

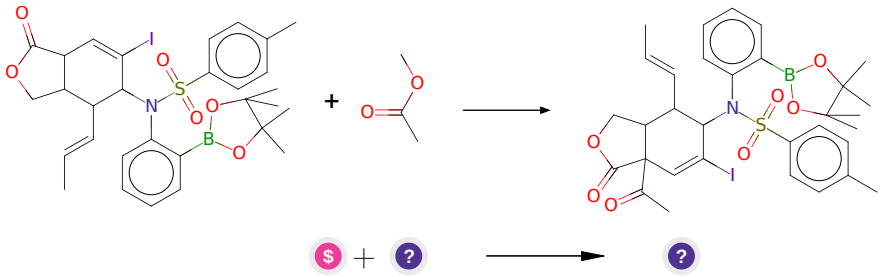
Typical conditions: LDA

Protections: none

Reference: *10.1002/1099-0690(200101)2001:2<323::AID-EJOC323>3.0.CO;2-A*

Retrosynthesis ID: 7727

2.1.8 Claisen Condensation



Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)C

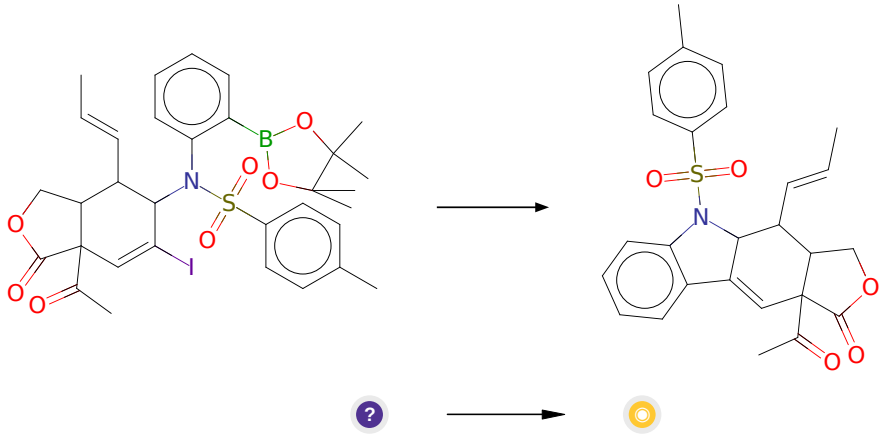
Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.1.9 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)C

Products:

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10176

2.2 Path 2

Score: 358.72

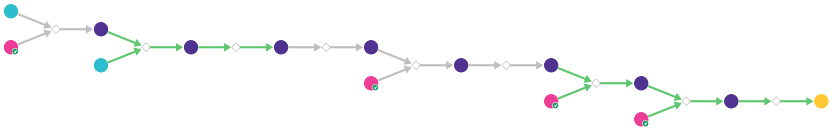
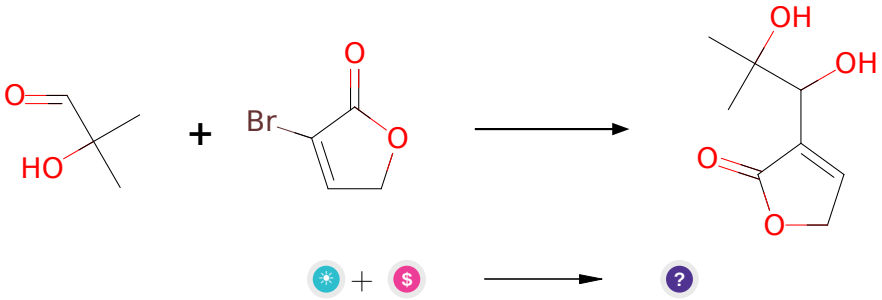


Figure 2: Outline of path 2

2.2.1 Reformatsky Reaction



Substrates:

1. a-hydroxy-isobutyraldehyd
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

Products:

1. CC(C)(O)C(O)C1=CCOC1=O

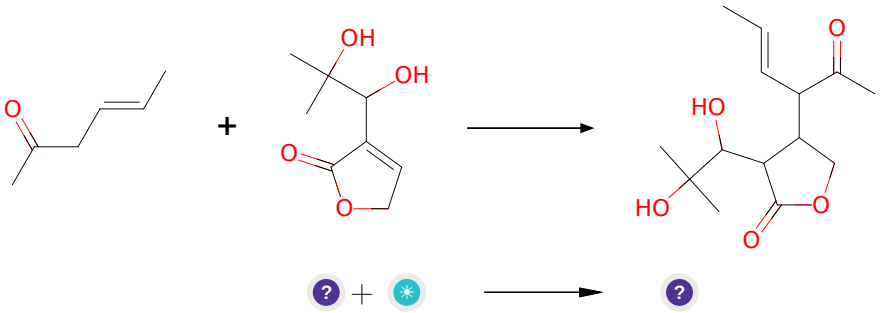
Typical conditions: Me2Zn.B(OMe)3.toluene.Et2O

Protections: none

Reference: *10.1021/jo200774e* p. 6373 and *10.1021/jo00163a019* p. 2522, 2525

Retrosynthesis ID: 11164

2.2.2 Michael addition



Substrates:

1. CC(C)(O)C(O)C1=CCOC1=O
2. hex-4t-en-2-one

Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C(O)C(C)(C)O

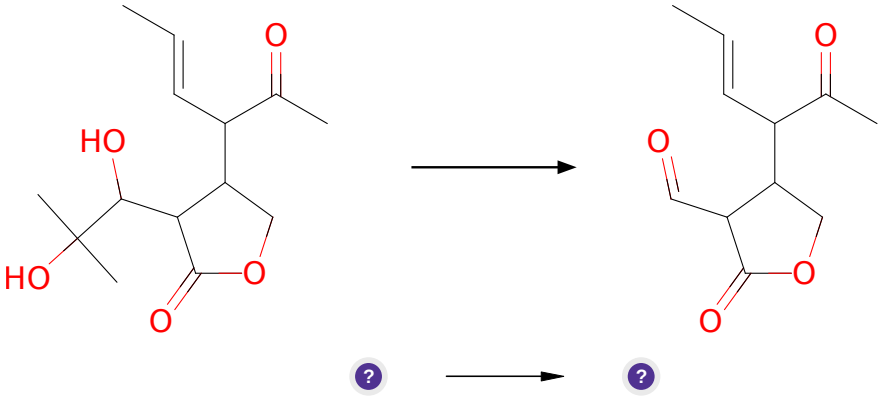
Typical conditions: EtONa or other base

Protections: none

Reference: *10.1016/j.tetlet.2011.02.073* AND *10.1016/j.molstruc.2010.12.005* AND *10.1016/S0040-4039(97)00695-3* AND *10.1021/ol016401g* AND *10.1002/ejoc.200500330*

Retrosynthesis ID: 15774

2.2.3 Cleavage of 1,2-diols with NaIO4



Substrates:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C(O)C(C)(C)O

Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

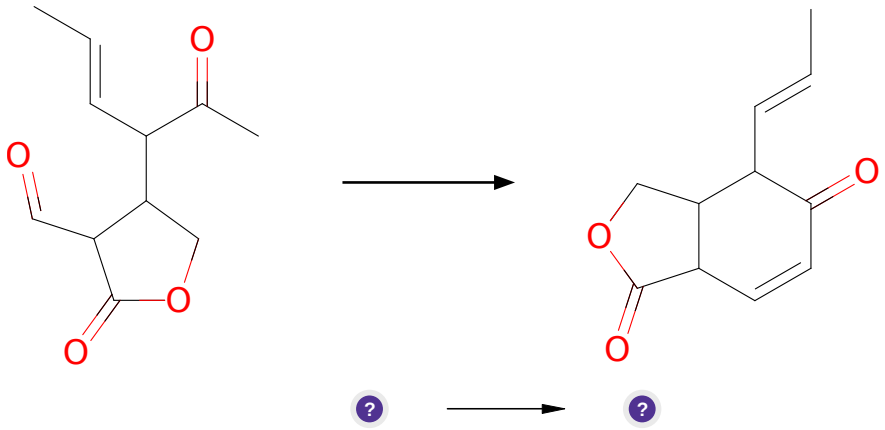
Typical conditions: NaIO4.solvent

Protections: none

Reference: *10.1039/C5OB00238A* and *10.1002/chem.201301371* and *10.1021/ol052106a*

Retrosynthesis ID: 31017509

2.2.4 Aldol Condensation



Substrates:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

Products:

1. C/C=C/C1C(=O)C=CC2C(=O)OCC21

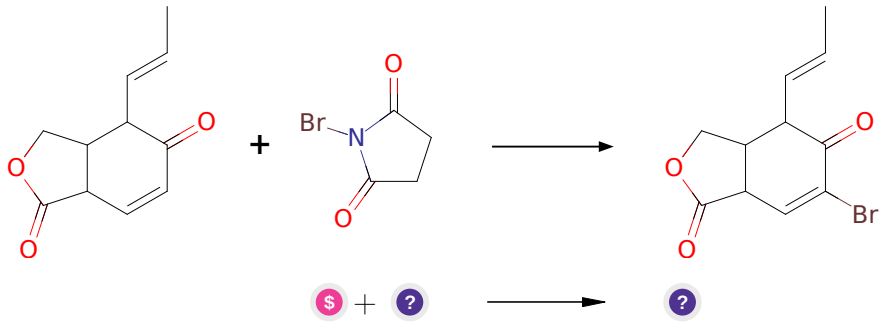
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10896

2.2.5 Alpha-halogenation of alpha-beta-unsaturated ketones



Substrates:

1. N-Bromosuccinimide - *available at Sigma-Aldrich*
2. C/C=C/C1C(=O)C=CC2C(=O)OCC21

Products:

1. C/C=C/C1C(=O)C(Br)=CC2C(=O)OCC21

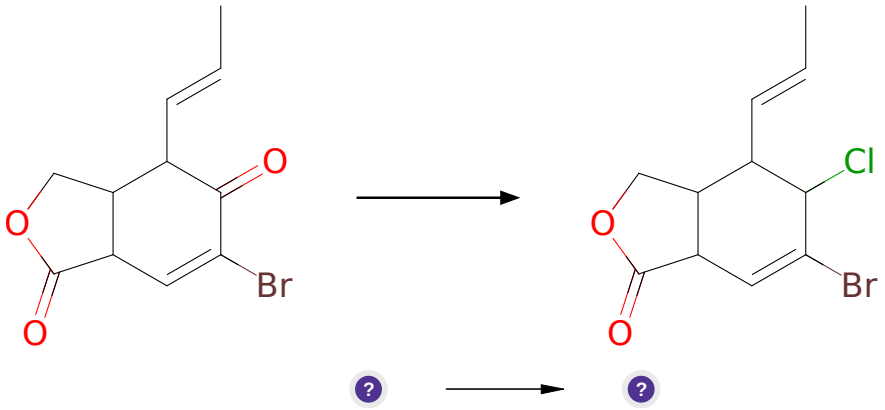
Typical conditions: NCS or NBS or NIS.CH3CN.rt

Protections: none

Reference: DOI: *10.1002/anie.200353037*

Retrosynthesis ID: 792

2.2.6 Synthesis of alkyl chlorides from ketones



Substrates:

1. C/C=C/C1C(=O)C(Br)=CC2C(=O)OCC21

Products:

1. C/C=C/C1C(Cl)C(Br)=CC2C(=O)OCC21

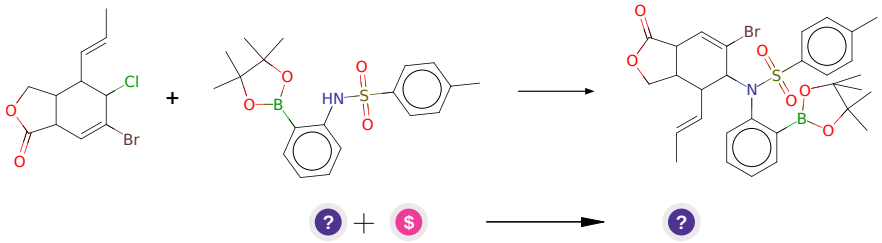
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11620

2.2.7 Alkylation of sulfonamides with alkyl chlorides



Substrates:

1. C/C=C/C1C(Cl)C(Br)=CC2C(=O)OCC21
2. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1C2COC(=O)C2C=C(Br)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

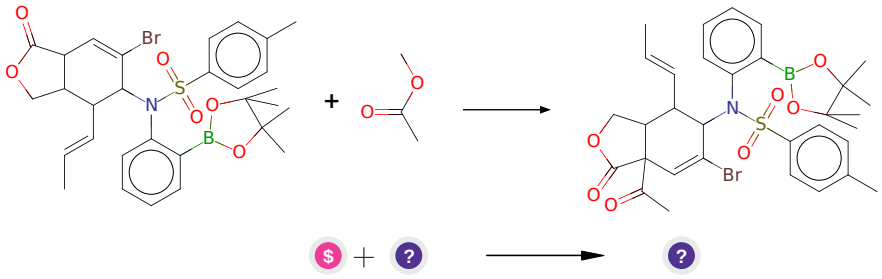
Typical conditions: LDA

Protections: none

Reference: *10.1002/1099-0690(200101)2001:2<323::AID-EJOC323>3.0.CO;2-A*

Retrosynthesis ID: 7727

2.2.8 Claisen Condensation



Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. C/C=C/C1C2COC(=O)C2C=C(Br)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O

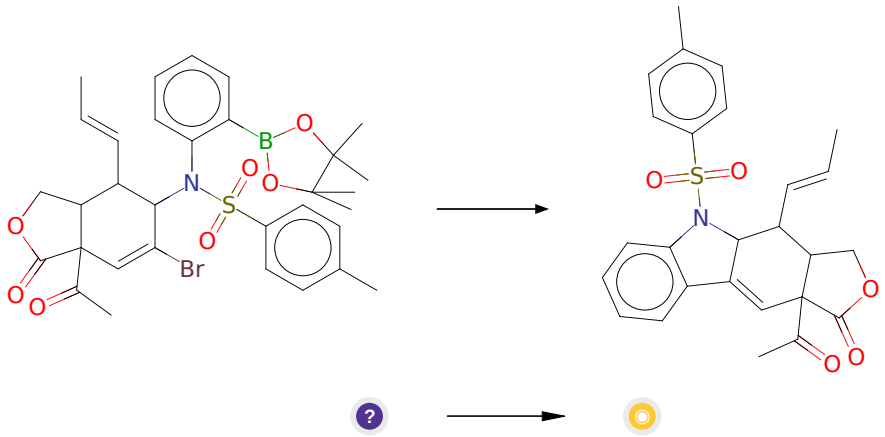
Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.2.9 Suzuki coupling of arylboronic pinacol esters with vinyl Bromides



Substrates:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(Br)=CC2(C(C)=O)C(=O

Products:

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10695

2.3 Path 3

Score: 358.72

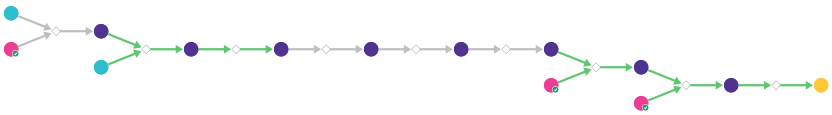
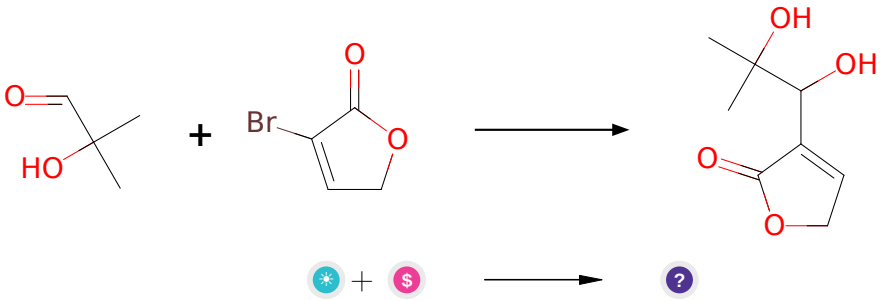


Figure 3: Outline of path 3

2.3.1 Reformatsky Reaction



Substrates:

1. a-hydroxy-isobutyraldehyd
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

Products:

1. CC(C)(O)C(O)C1=CCOC1=O

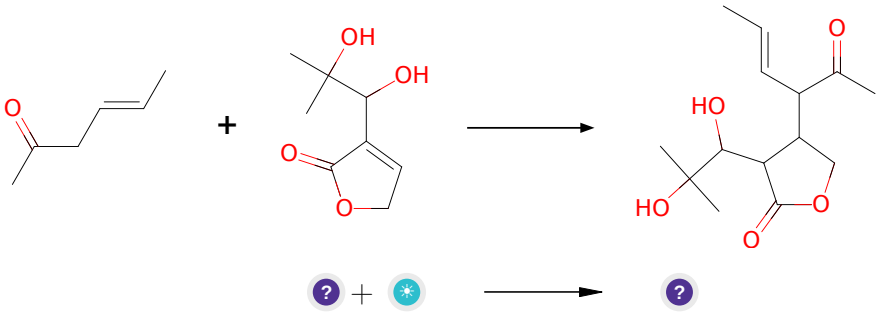
Typical conditions: Me2Zn.B(OMe)3.toluene.Et2O

Protections: none

Reference: *10.1021/jo200774e* p. 6373 and *10.1021/jo00163a019* p. 2522, 2525

Retrosynthesis ID: 11164

2.3.2 Michael addition



Substrates:

1. CC(C)(O)C(O)C1=CCOC1=O
2. hex-4t-en-2-one

Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C(O)C(C)(C)O

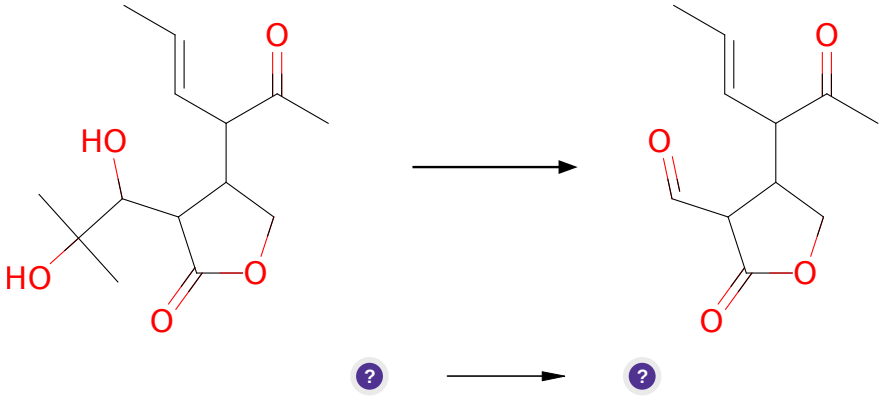
Typical conditions: EtONa or other base

Protections: none

Reference: *10.1016/j.tetlet.2011.02.073* AND *10.1016/j.molstruc.2010.12.005* AND *10.1016/S0040-4039(97)00695-3* AND *10.1021/ol016401g* AND *10.1002/ejoc.200500330*

Retrosynthesis ID: 15774

2.3.3 Cleavage of 1,2-diols with NaIO4



Substrates:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C(O)C(C)(C)O

Products:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

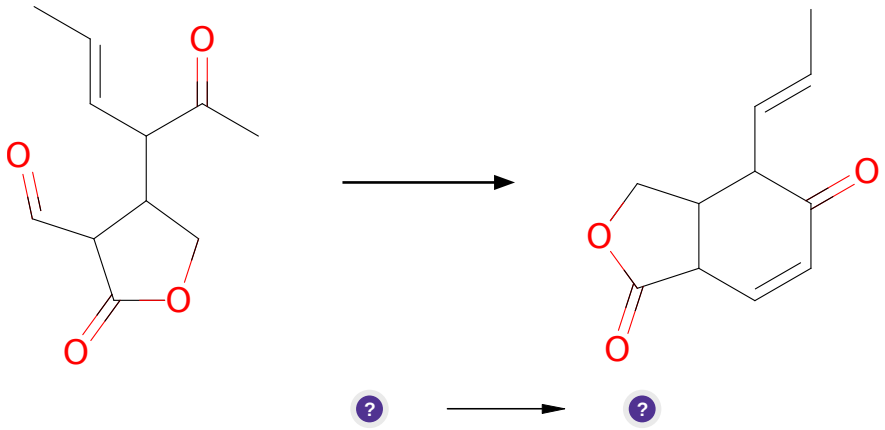
Typical conditions: NaIO4.solvent

Protections: none

Reference: *10.1039/C5OB00238A* and *10.1002/chem.201301371* and *10.1021/ol052106a*

Retrosynthesis ID: 31017509

2.3.4 Aldol Condensation



Substrates:

1. C/C=C/C(C(C)=O)C1COC(=O)C1C=O

Products:

1. C/C=C/C1C(=O)C=CC2C(=O)OCC21

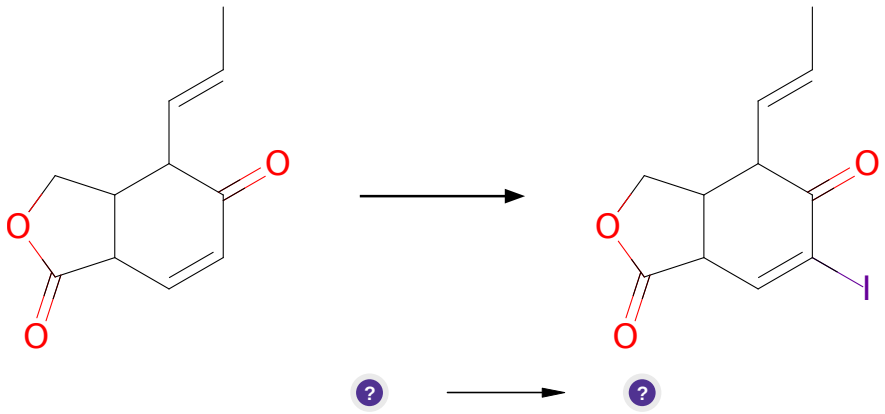
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10896

2.3.5 Alpha-iodination of alpha-beta-unsaturated carbonyl compounds



Substrates:

1. C/C=C/C1C(=O)C=CC2C(=O)OCC21

Products:

1. C/C=C/C1C(=O)C(I)=CC2C(=O)OCC21

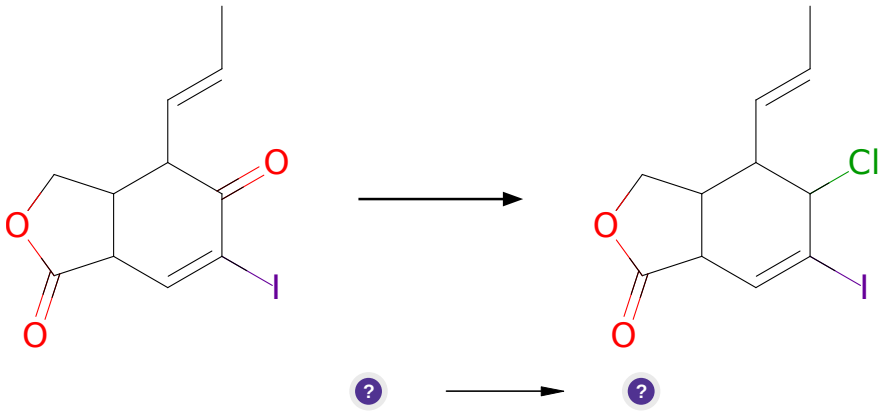
Typical conditions: DMAP.K2CO3.H2O.THF

Protections: none

Reference: DOI: *10.1055/s-2005-868495*

Retrosynthesis ID: 786

2.3.6 Synthesis of alkyl chlorides from ketones



Substrates:

1. C/C=C/C1C(=O)C(I)=CC2C(=O)OCC21

Products:

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21

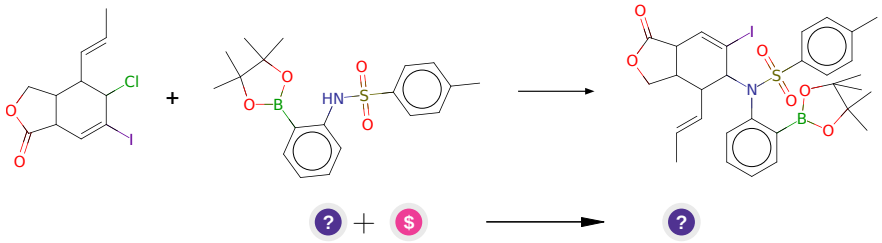
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11620

2.3.7 Alkylation of sulfonamides with alkyl chlorides



Substrates:

1. C/C=C/C1C(Cl)C(I)=CC2C(=O)OCC21
2. 2-(p-Toluenesulfonylamino)phenylboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

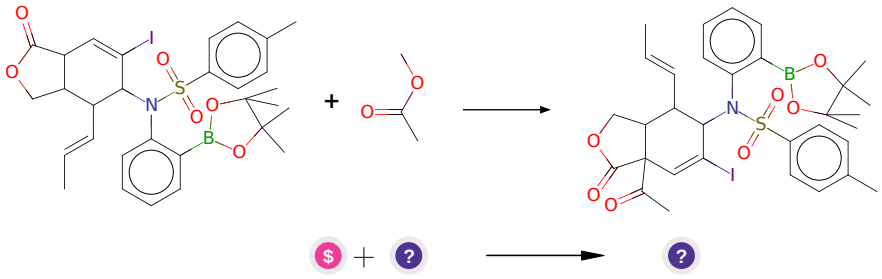
Typical conditions: LDA

Protections: none

Reference: *10.1002/1099-0690(200101)2001:2<323::AID-EJOC323>3.0.CO;2-A*

Retrosynthesis ID: 7727

2.3.8 Claisen Condensation



Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. C/C=C/C1C2COC(=O)C2C=C(I)C1N(c1ccccc1B1OC(C)(C)C(C)(C)O1)S(=O)(=O)c1ccc(C)cc1

Products:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)C

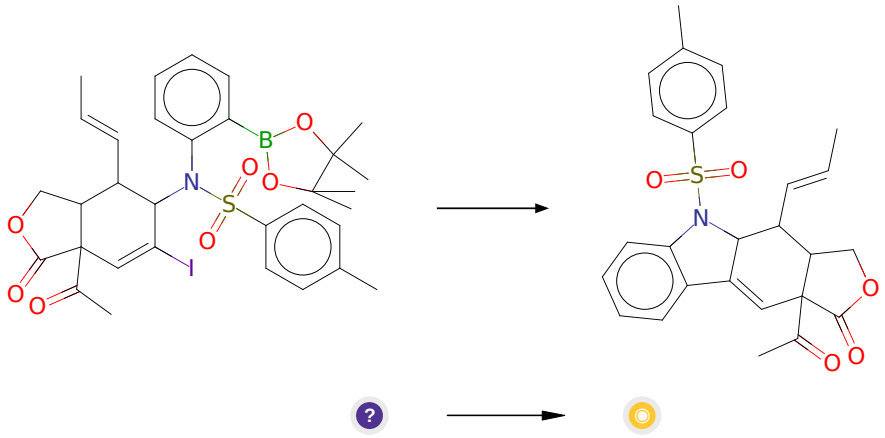
Typical conditions: Base.Solvent

Protections: none

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

Retrosynthesis ID: 5015

2.3.9 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

1. C/C=C/C1C(N(c2ccccc2B2OC(C)(C)C(C)(C)O2)S(=O)(=O)c2ccc(C)cc2)C(I)=CC2(C(C)=O)C(=O)C

Products:

1. C/C=C/C1C2C(=CC3(C(C)=O)C(=O)OCC13)c1ccccc1N2S(=O)(=O)c1ccc(C)cc1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10176