Paths of analysis*

L9

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

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

2.1 Path 1

Score: `193.93`

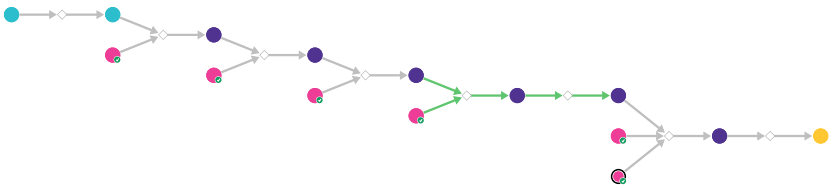
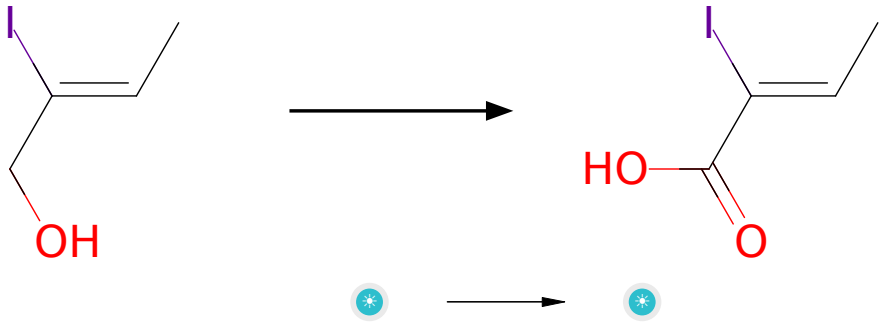


Figure 1: Outline of path 1

2.1.1 Jones Oxidation



Substrates:

1. (z)-2-iodo-2-buten-1-ol

Products:

1. 2-iodo-crotonic acid

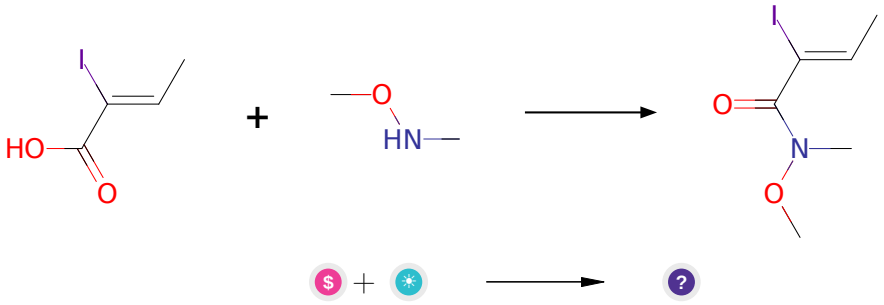
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

Reference: *10.1002/9780470638859.conrr349* and *10.1021/jm00270a004*

Retrosynthesis ID: 11160

2.1.2 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. n-methoxymethylamine - *available at Sigma-Aldrich*
2. 2-iodo-crotonic acid

Products:

1. C/C=C(\I)C(=O)N(C)OC

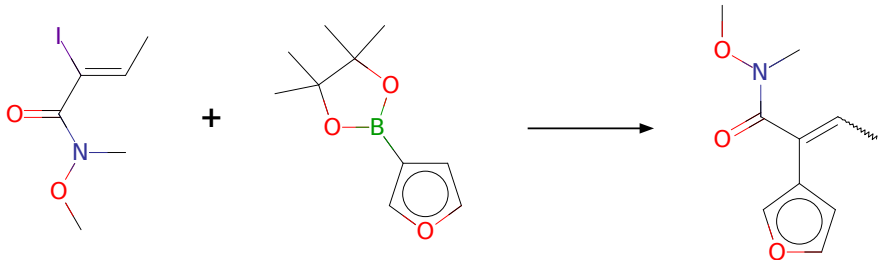
Typical conditions: DCC.DMAP or CDI.TEA.DCM

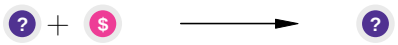
Protections: none

Reference: Patent: WO2007/67333A2, 2007 & *10.1016/j.bmcl.2008.09.100*

Retrosynthesis ID: 1152

2.1.3 Suzuki coupling of arylboronic pinacol esters with vinyl iodides





Substrates:

1. C/C=C(\I)C(=O)N(C)OC
2. 3-Furanboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. CC=C(C(=O)N(C)OC)c1ccoc1

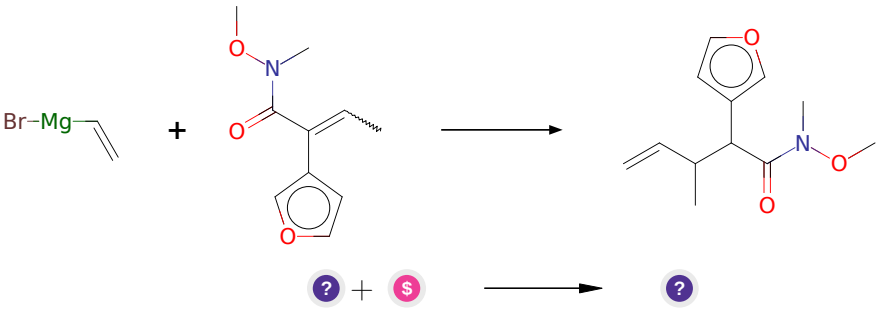
Typical conditions: Pd catalyst.base.solvent

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: 10321

2.1.4 Conjugate addition of organocuprate



Substrates:

1. CC=C(C(=O)N(C)OC)c1ccoc1
2. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(C(=O)N(C)OC)c1ccoc1

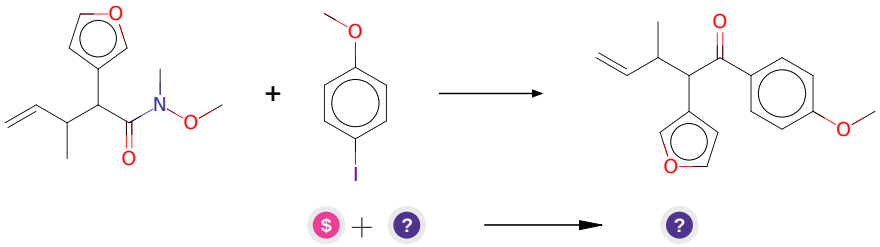
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

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

2.1.5 Synthesis of ketones from Weinreb amides



Substrates:

1. 4-Iodoanisole - *available at Sigma-Aldrich*
2. C=CC(C)C(C(=O)N(C)OC)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

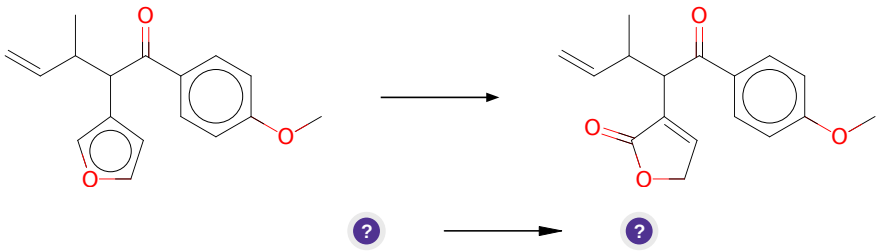
Typical conditions: 1.RmgBr.THF 2.TFA.DCM

Protections: none

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 5060

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



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O

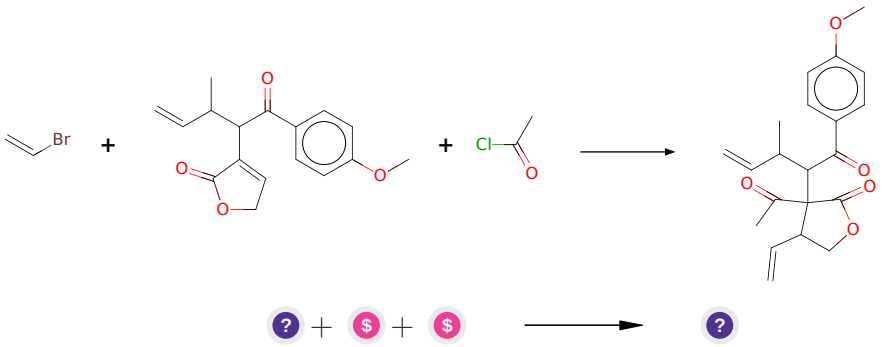
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

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

Retrosynthesis ID: 50717

2.1.7 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O
2. Bromoethylene - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

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

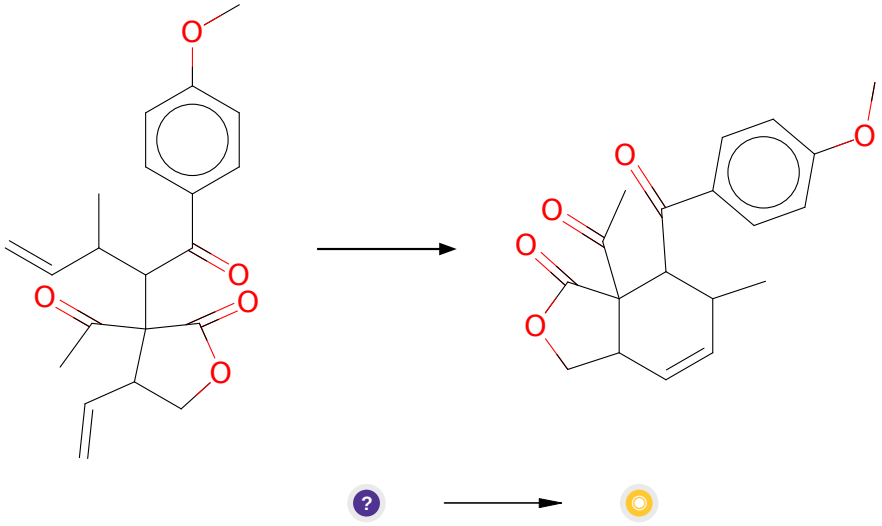
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13032

2.1.8 Ring-Closing Metathesis



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)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

2.2 Path 2

Score: `193.93`

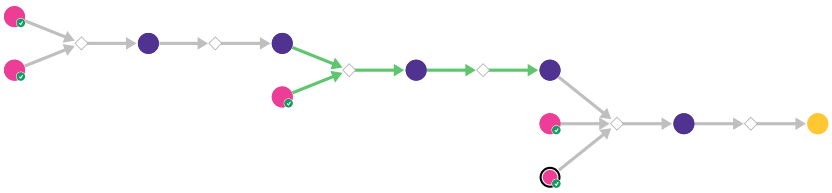
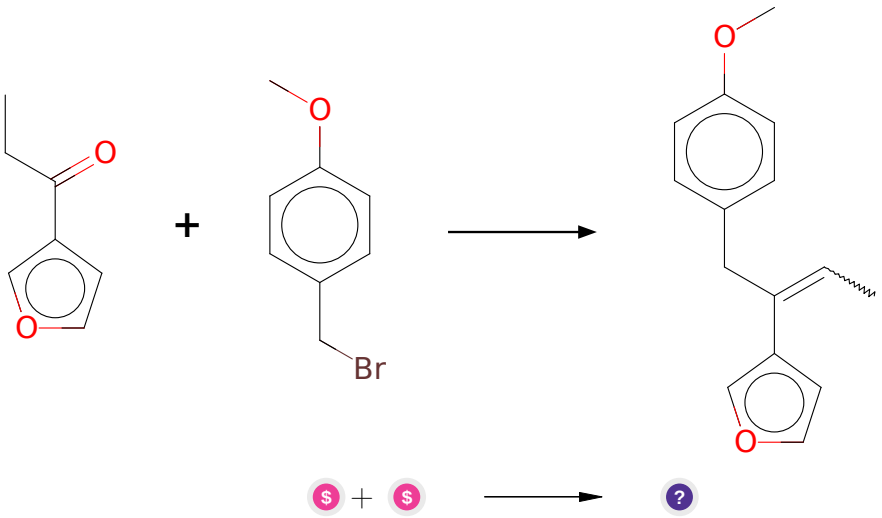


Figure 2: Outline of path 2

2.2.1 Shapiro reaction followed by alkyl bromide addition



Substrates:

1. 4-Methoxybenzyl bromide - *available at Sigma-Aldrich*
2. 1-(furan-3-yl)propan-1-one - *available at Sigma-Aldrich*

Products:

1. CC=C(Cc1ccc(OC)cc1)c1ccoc1

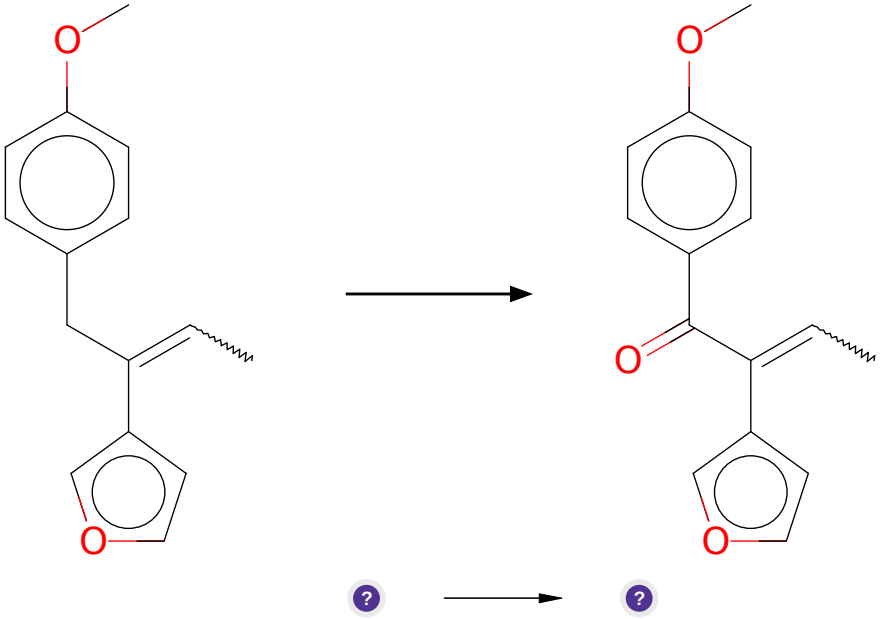
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then alkyl bromide.cooling

Protections: none

Reference: *10.1016/S0040-4039(00)75263-4* and *10.1021/ol300652k* and *10.1016/j.bmc.2009.08.038*

Retrosynthesis ID: 9990467

2.2.2 Allylic Oxidation of Alkenes



Substrates:

1. CC=C(Cc1ccc(OC)cc1)c1ccoc1

Products:

1. CC=C(C(=O)c1ccc(OC)cc1)c1ccoc1

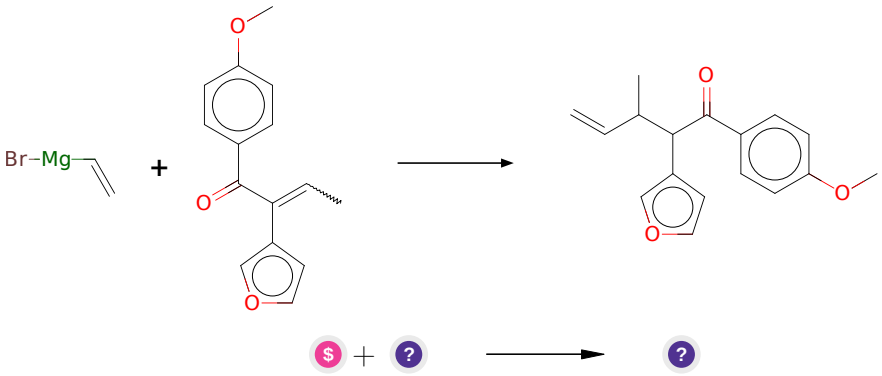
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

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

Retrosynthesis ID: 2583

2.2.3 Conjugate addition of organocuprate



Substrates:

1. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*
2. CC=C(C(=O)c1ccc(OC)cc1)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

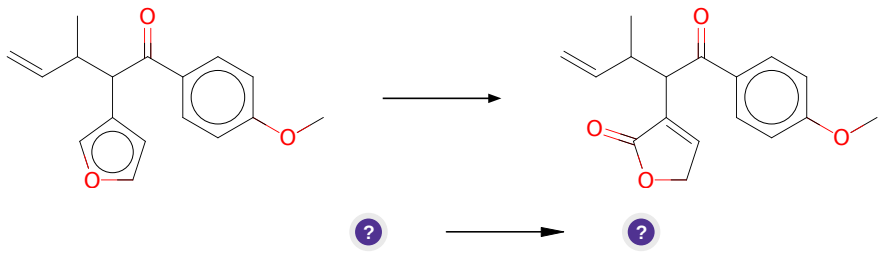
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

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

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



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O

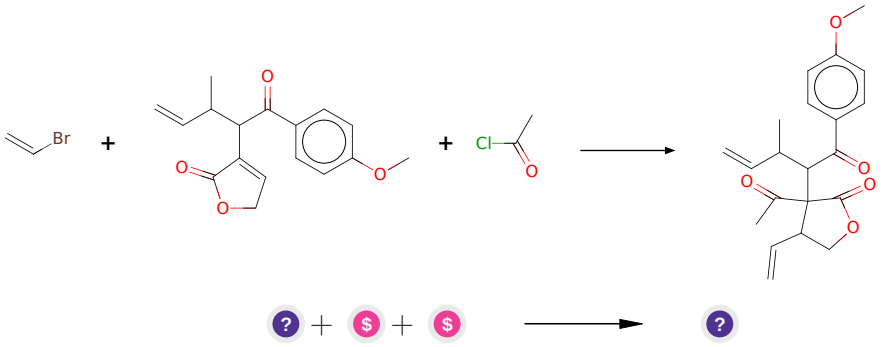
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

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

Retrosynthesis ID: 50717

2.2.5 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O
2. Bromoethylene - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

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

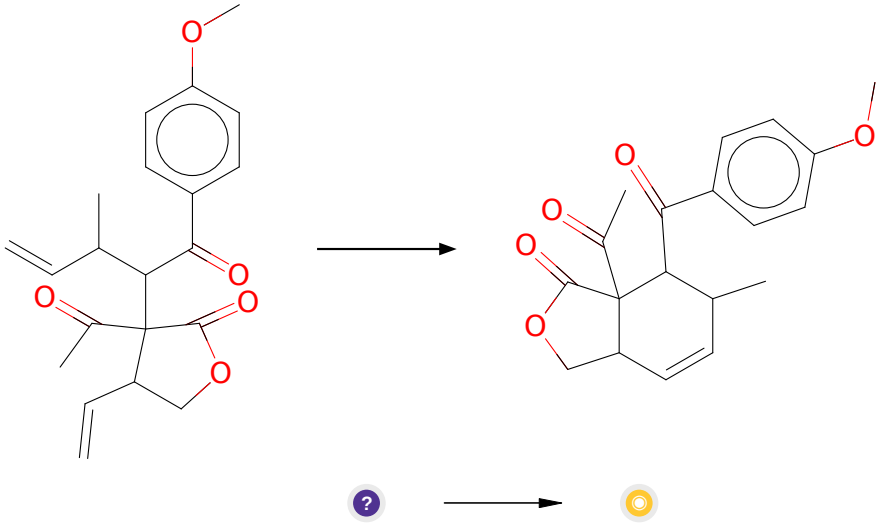
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13032

2.2.6 Ring-Closing Metathesis



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)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

2.3 Path 3

Score: 193.93

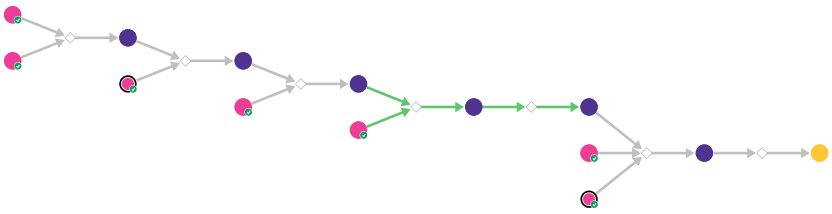
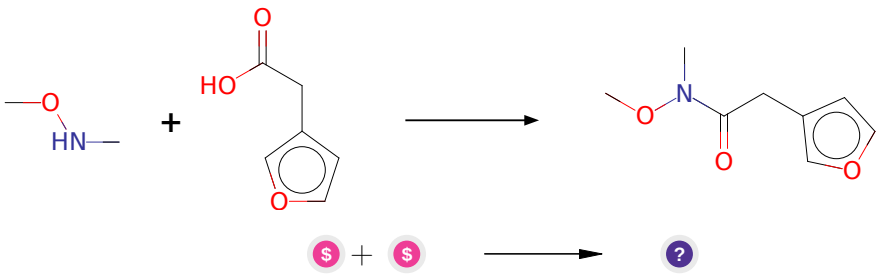


Figure 3: Outline of path 3

2.3.1 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. 2-(Furan-3-yl)acetic acid - *available at Sigma-Aldrich*
2. n-methoxymethylamine - *available at Sigma-Aldrich*

Products:

1. CON(C)C(=O)Cc1ccoc1

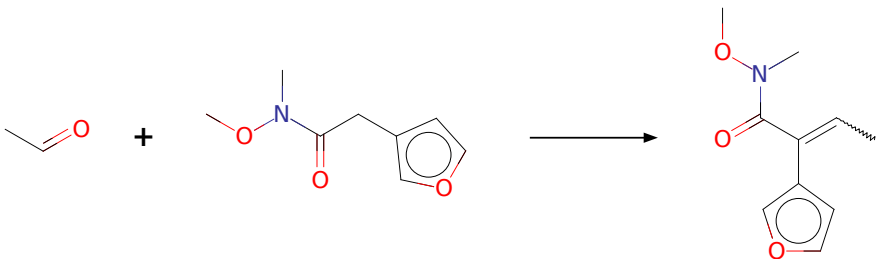
Typical conditions: DCC.DMAP or CDI.TEA.DCM

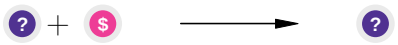
Protections: none

Reference: Patent: WO2007/67333A2, 2007 & *10.1016/j.bmcl.2008.09.100*

Retrosynthesis ID: 1152

2.3.2 Condensation of amides with aldehydes





Substrates:

1. CON(C)C(=O)Cc1ccoc1
2. Ethanal - *available at Sigma-Aldrich*

Products:

1. CC=C(C(=O)N(C)OC)c1ccoc1

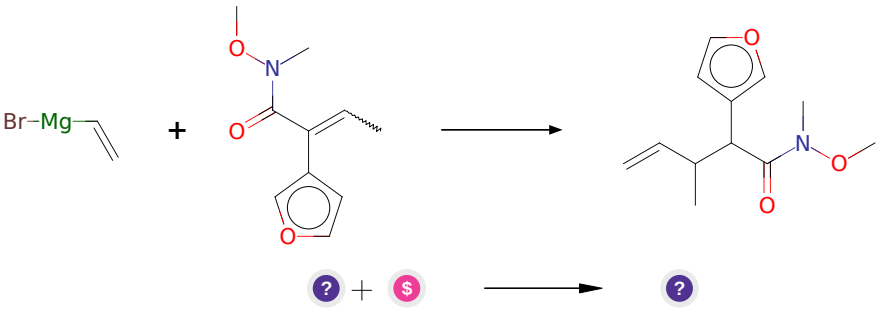
Typical conditions: piperidine.EtOH

Protections: none

Reference: *10.1021/ja075335w* (Si) AND *10.1016/j.bmcl.2012.10.016* AND *10.1016/j.tetlet.2013.12.097* AND *10.1021/ol303097j*

Retrosynthesis ID: 14975

2.3.3 Conjugate addition of organocuprate



Substrates:

1. CC=C(C(=O)N(C)OC)c1ccoc1
2. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CC(C)C(C(=O)N(C)OC)c1ccoc1

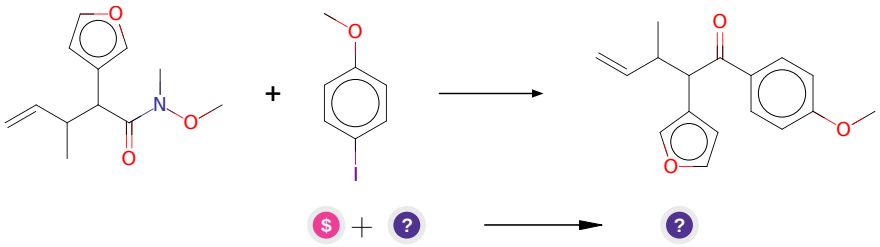
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

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

2.3.4 Synthesis of ketones from Weinreb amides



Substrates:

1. 4-Iodoanisole - *available at Sigma-Aldrich*
2. C=CC(C)C(C(=O)N(C)OC)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

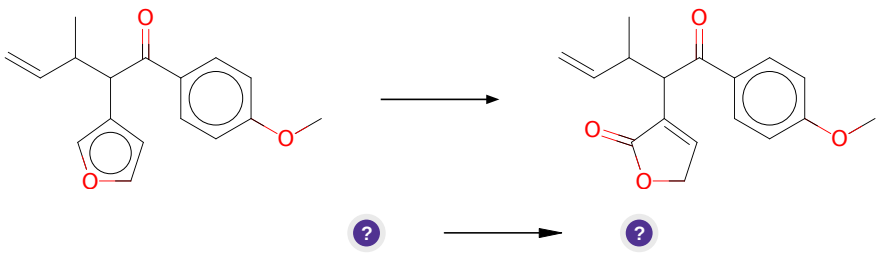
Typical conditions: 1.RmgBr.THF 2.TFA.DCM

Protections: none

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 5060

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



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O

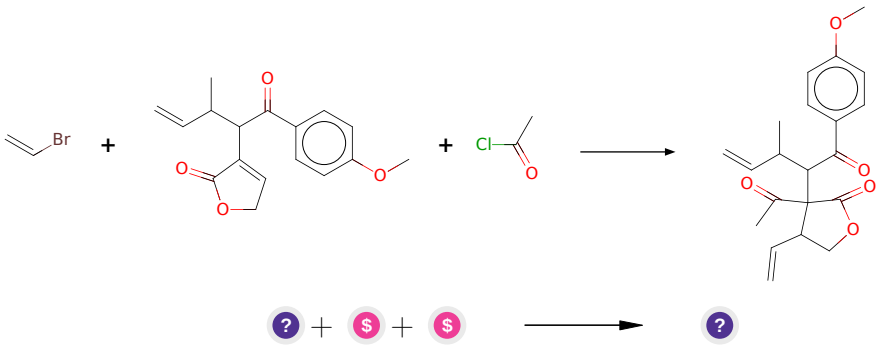
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

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

Retrosynthesis ID: 50717

2.3.6 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O
2. Bromoethylene - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

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

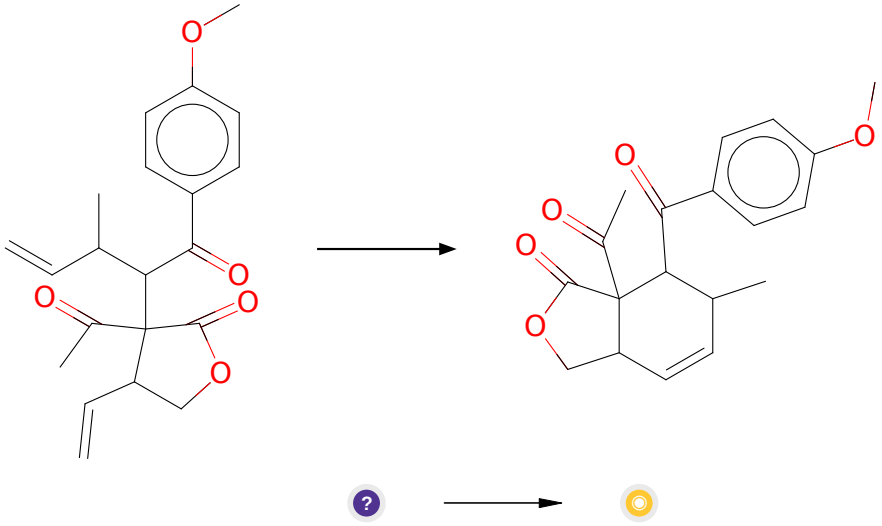
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13032

2.3.7 Ring-Closing Metathesis



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)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

2.4 Path 4

Score: `193.93`

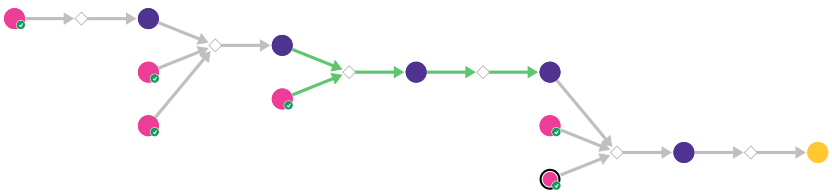
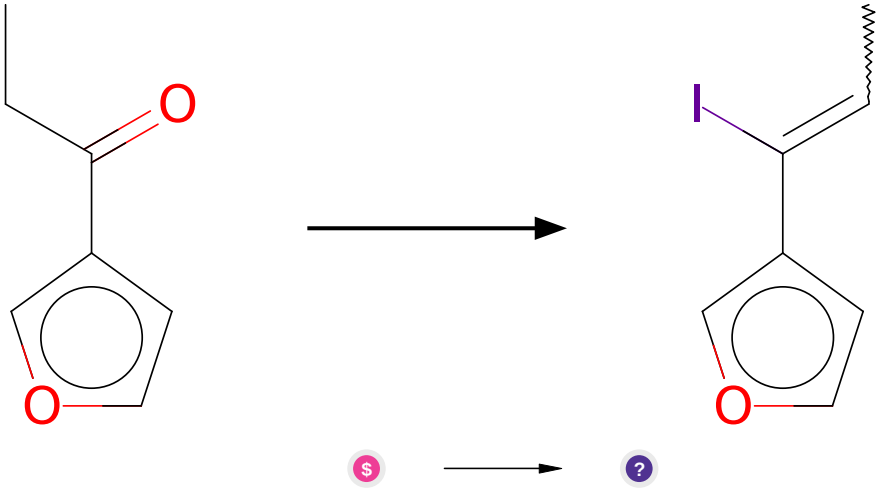


Figure 4: Outline of path 4

2.4.1 Shapiro reaction followed by halogen addition



Substrates:

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

Products:

1. CC=C(I)c1ccoc1

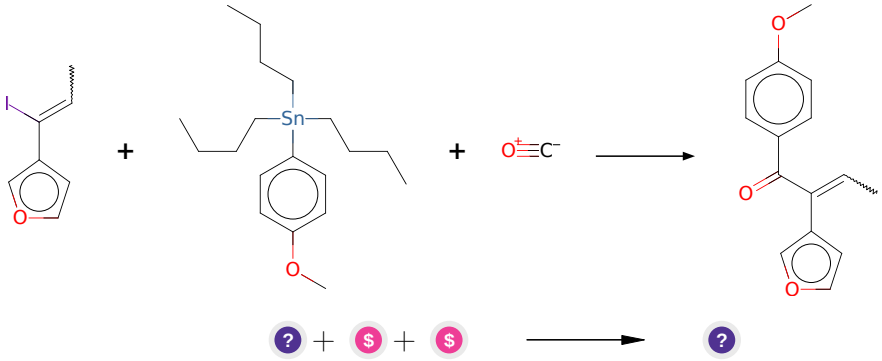
Typical conditions: 1.TsNH2NH2 2.NBS/NCS/NIS.base

Protections: none

Reference: *10.1055/s-1998-1683* and *10.1016/j.tet.2008.02.073* and *10.1021/ol503114n* and *10.1021/ja049694s*

Retrosynthesis ID: 9990471

2.4.2 Stille Carbonylative Cross-Coupling



Substrates:

1. CC=C(I)c1ccoc1
2. Tributyl(4-methoxyphenyl)stannane - *available at Sigma-Aldrich*
3. CORM-2 - *available at Sigma-Aldrich*

Products:

1. CC=C(C(=O)c1ccc(OC)cc1)c1ccoc1

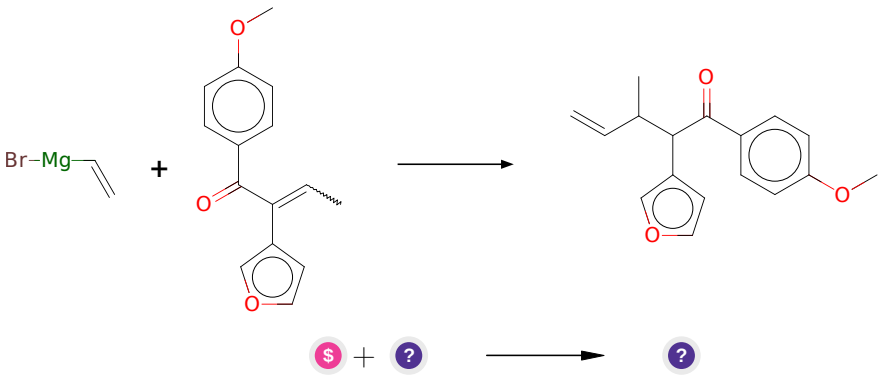
Typical conditions: Pd(0) complex

Protections: none

Reference: DOI: *10.1002/anie.198605081*

Retrosynthesis ID: 245571

2.4.3 Conjugate addition of organocuprate



Substrates:

1. Vinylmagnesium bromide solution - *available at Sigma-Aldrich*
2. CC=C(C(=O)c1ccc(OC)cc1)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

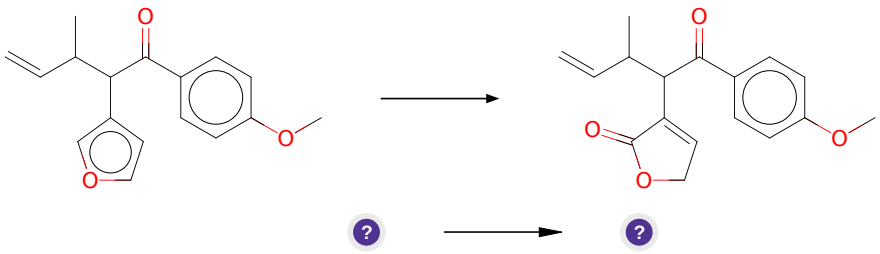
Typical conditions: 1.CuCN.LiCl.2.Eletrophile.3.NH4Cl

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

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



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)c1ccoc1

Products:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O

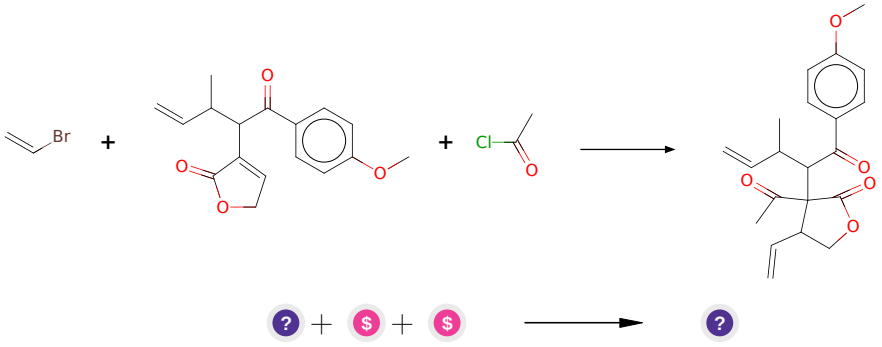
Typical conditions: 1. NBS.CHCl3.EtOH.rt 2. HCl.acetone.H2O.rt

Protections: none

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

Retrosynthesis ID: 50717

2.4.5 Alkenylation-Acylation of enones and enoate esters



Substrates:

1. C=CC(C)C(C(=O)c1ccc(OC)cc1)C1=CCOC1=O
2. Bromoethylene - *available at Sigma-Aldrich*
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

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

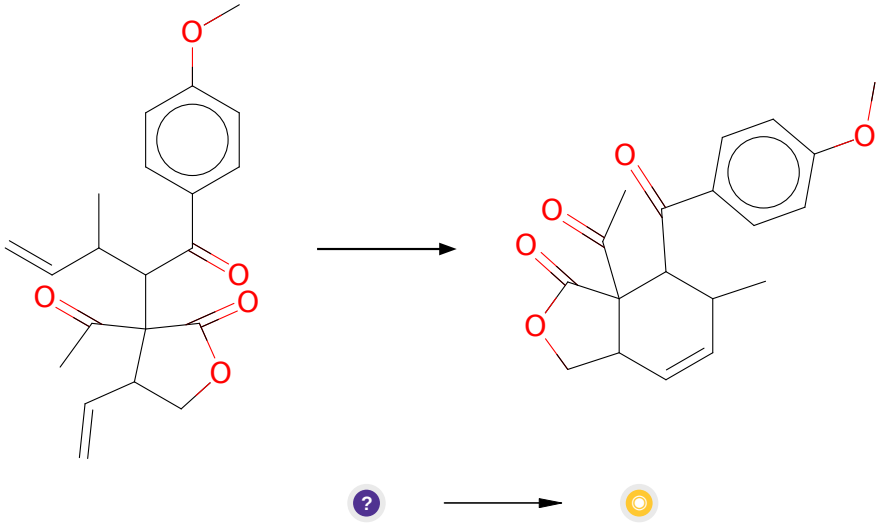
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.1246/cl.1989.1063* AND *10.1248/cpb.33.1815* AND *10.1021/ja0320018* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13032

2.4.6 Ring-Closing Metathesis



Substrates:

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

Products:

1. COc1ccc(C(=O)C2C(C)C=CC3COC(=O)C32C(C)=O)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