Paths of analysis*

C27

Synthia

March 3, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: FGI, FGI with protections

Max. paths returned: 5

Max. iterations: 300

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1000 $/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 10

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

Strategies: none selected

*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.

FGI 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: 625.04

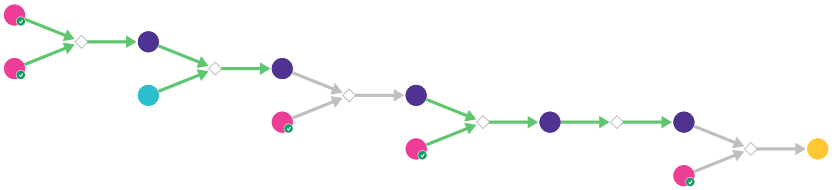
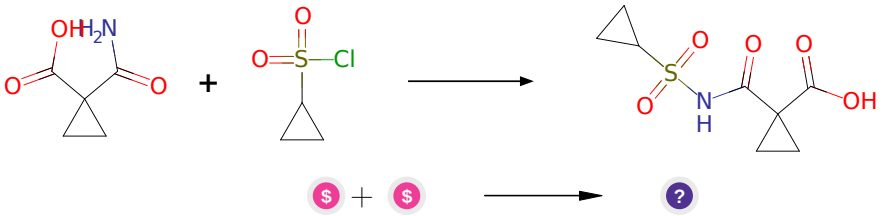


Figure 1: Outline of path 1

2.1.1 Sulfonylation of amides



Substrates:

1. 1-(Aminocarbonyl)-1-cyclopropanecarboxylic acid - *available at Sigma-Aldrich*
2. Cyclopropanesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: Py.RSO2Cl

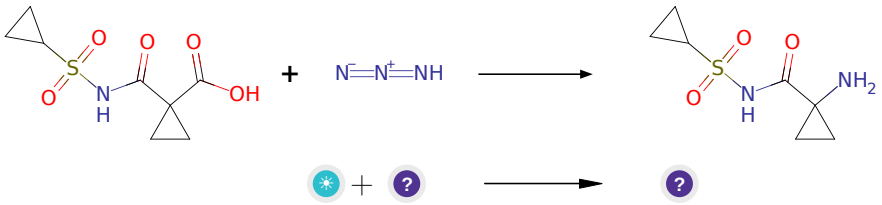
Protections: none

Yield: good

Reference: *10.1021/ja9945313* AND *10.1016/j.ejmech.2013.04.028* AND *10.1039/c5ra14001c* AND *10.1016/j.bmcl.2013.12.043* AND *10.1016/j.tetasy.2012.08.013*

Retrosynthesis ID: 14787

2.1.2 Schmidt Reaction



Substrates:

1. hydrazoic acid
2. O=C(O)C1(C(=O)NS(=O)(=O)C2CC2)CC1

Products:

1. NC1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: azide.H+.40C

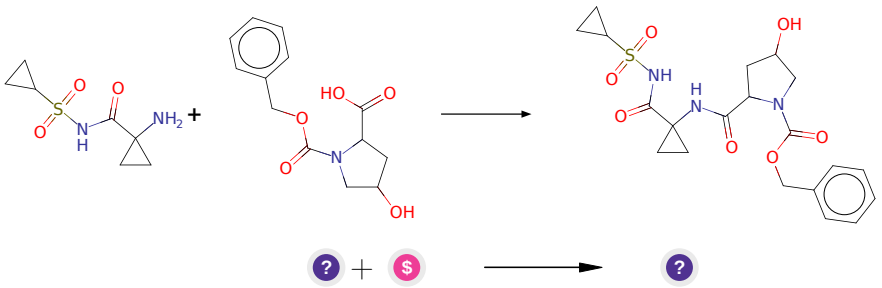
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.1.3 Amide coupling



Substrates:

1. NC1(C(=O)NS(=O)(=O)C2CC2)CC1
2. Z-Hyp-OH - *available at Sigma-Aldrich*

Products:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

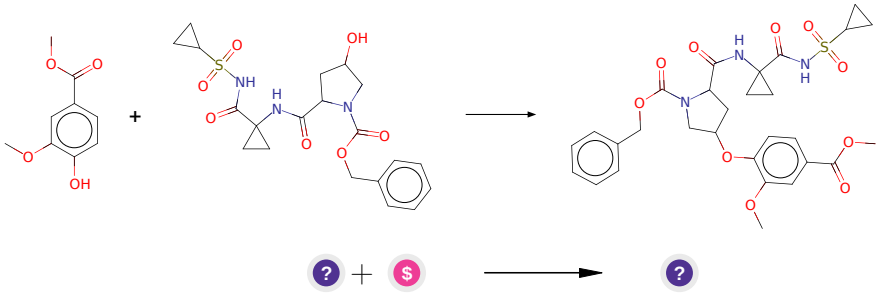
Protections: none

Yield: good

Reference: *10.1021/cr100048w* and *10.1039/B701677H* and *10.1039/C5RA24527C* and *10.3727/000000006783981206* and *10.1021/np060007f* and *10.1021/jo00012a058* and *10.1016/j.bmcl.2007.08.037* and *10.1039/C0OB00355G* and *10.1021/jm500031w* (p.3056) and *10.1016/j.tet.2011.03.046*

Retrosynthesis ID: 10087

2.1.4 Mitsunobu reaction



Substrates:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1
2. Methyl vanillate - *available at Sigma-Aldrich*

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)N(C(=O)OCc3ccccc3)C2)c(OC)

Typical conditions: DEAD.or.DCAD.or.DIAD.PPh3

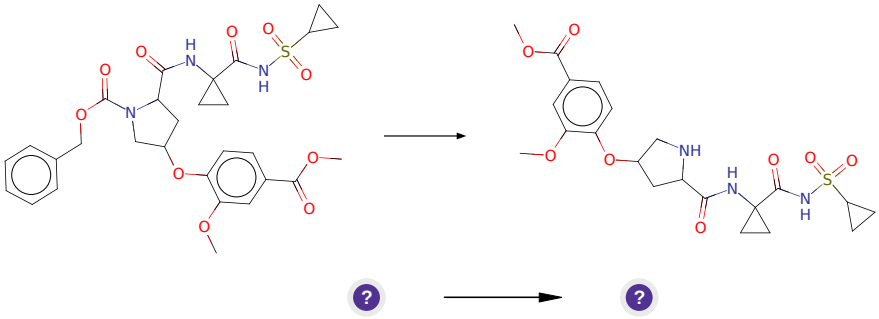
Protections: none

Yield: good

Reference: DOI: *10.1021/jo0345751* AND *10.1021/ol0618757*

Retrosynthesis ID: 7562

2.1.5 Cleavage of benzyloxycarbamates



Substrates:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)N(C(=O)OCc3ccccc3)C2)c(OC)

Products:

1. COC(=O)c1ccc(OC2CNC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)C2)c(OC)c1

Typical conditions: H2.Pd/C

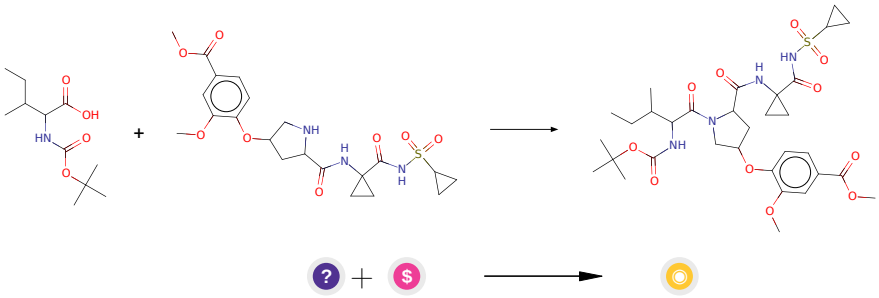
Protections: none

Yield: good

Reference: *10.1021/jm070755h* and *10.1021/jm2016057* and *10.1055/s-0033-1340215* and *10.1016/S0040-4039(03)01181-X*

Retrosynthesis ID: 9990024

2.1.6 Amide coupling



Substrates:

1. COC(=O)c1ccc(OC2CNC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)C2)c(OC)c1
2. 2-[(tert-butoxy)carbonyl]amino-3-methylpentanoic acid - *available at Sigma-Aldrich*

Products:

1. CCC(C)C(NC(=O)OC(C)(C)C)C(=O)N1CC(Oc2ccc(C(=O)OC)cc2OC)CC1C(=O)NC1(C(=O)NS(=O

Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

Protections: none

Yield: good

Reference: *10.1021/ol400686f* and *10.1021/jo00200a057* and *10.1021/cr100048w* and *10.1039/B701677H* and *10.1039/C5RA24527C* and *10.3727/000000006783981206* and *10.1021/np060007f* and *10.1021/jo00012a058* and *10.1016/j.bmcl.2007.08.037* and *10.1039/C0OB00355G* and *10.1021/jm500031w* (p.3056) and *10.1016/j.tet.2011.03.046*

Retrosynthesis ID: 9147

2.2 Path 2

Score: 627.67

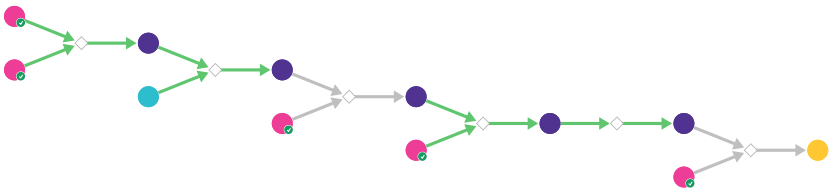
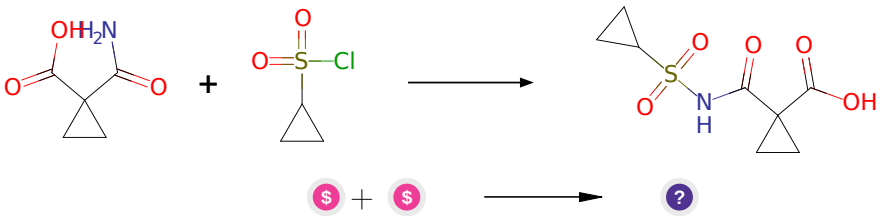


Figure 2: Outline of path 2

2.2.1 Sulfonylation of amides



Substrates:

1. 1-(Aminocarbonyl)-1-cyclopropanecarboxylic acid - *available at Sigma-Aldrich*

2. Cyclopropanesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: Py.RSO2Cl

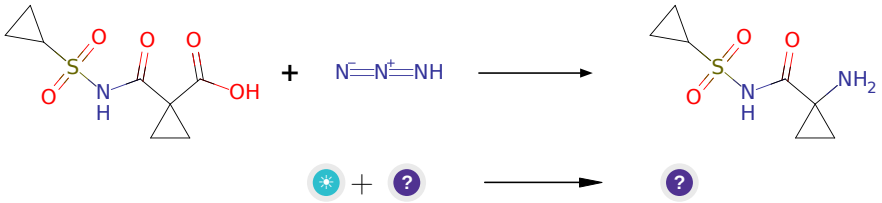
Protections: none

Yield: good

Reference: *10.1021/ja9945313* AND *10.1016/j.ejmech.2013.04.028* AND *10.1039/c5ra14001c* AND *10.1016/j.bmcl.2013.12.043* AND *10.1016/j.tetasy.2012.08.013*

Retrosynthesis ID: 14787

2.2.2 Schmidt Reaction



Substrates:

1. hydrazoic acid
2. O=C(O)C1(C(=O)NS(=O)(=O)C2CC2)CC1

Products:

1. NC1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: azide.H+.40C

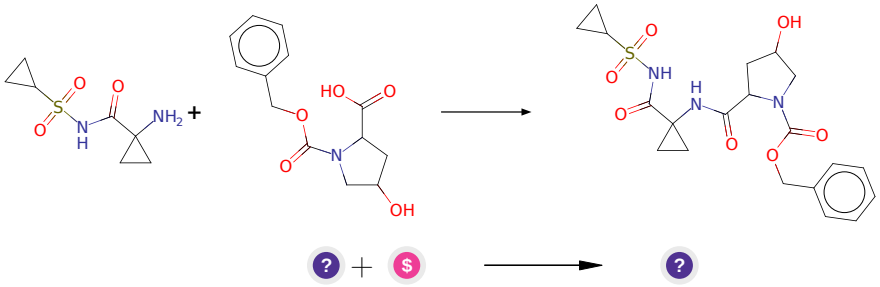
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.2.3 Amide coupling



Substrates:

1. NC1(C(=O)NS(=O)(=O)C2CC2)CC1
2. Z-Hyp-OH - *available at Sigma-Aldrich*

Products:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

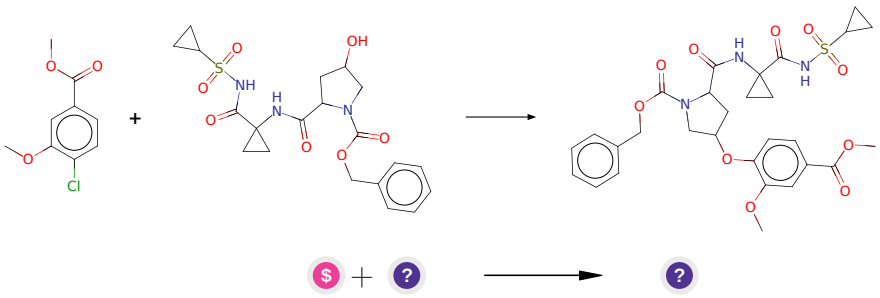
Protections: none

Yield: good

Reference: *10.1021/cr100048w* and *10.1039/B701677H* and *10.1039/C5RA24527C* and *10.3727/000000006783981206* and *10.1021/np060007f* and *10.1021/jo00012a058* and *10.1016/j.bmcl.2007.08.037* and *10.1039/C0OB00355G* and *10.1021/jm500031w* (p.3056) and *10.1016/j.tet.2011.03.046*

Retrosynthesis ID: 10087

2.2.4 Buchwald-Hartwig Reaction



Substrates:

1. Methyl 4-chloro-3-methoxybenzoate - *available at Sigma-Aldrich*
2. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)N(C(=O)OCc3ccccc3)C2)c(OC)

Typical conditions: Pd(OAc)2.ligand.Cs2CO3.solvent.heat

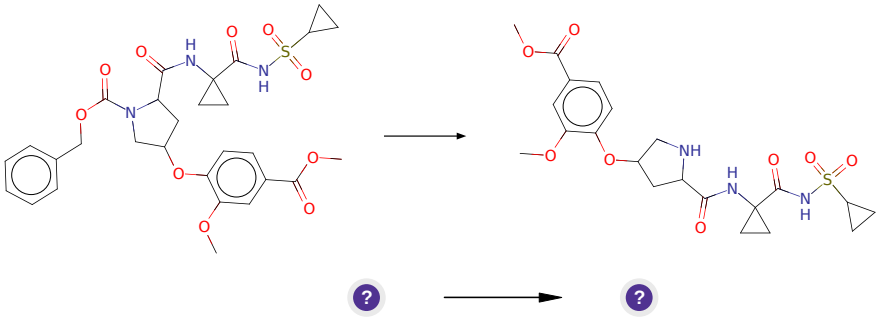
Protections: none

Yield: good

Reference: *10.1021/ja016863p* and *10.1021/ja016863p* and *10.1021/ja103248d* and *10.1021/jo025732j* and *10.1021/ja002543e* and *10.1002/jhet.4158*

Retrosynthesis ID: 27014

2.2.5 Cleavage of benzyloxycarbamates



Substrates:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)N(C(=O)OCc3ccccc3)C2)c(OC)

Products:

1. COC(=O)c1ccc(OC2CNC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)C2)c(OC)c1

Typical conditions: TMSI.ACN or HBr.AcOH

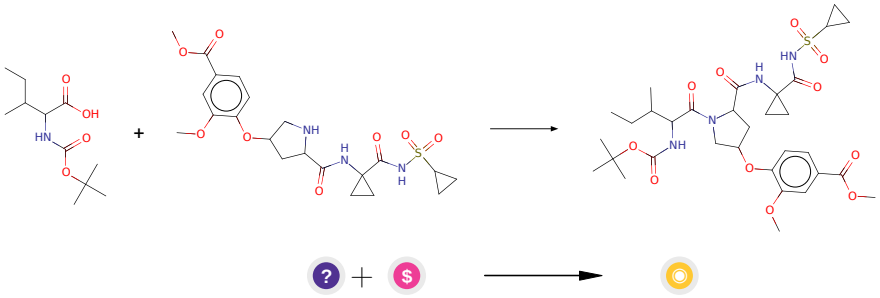
Protections: none

Yield: good

Reference: *10.1021/jo00377a016* and *10.1016/j.tet.2009.05.009* and *10.1021/ol0700761* and *10.1016/j.tetlet.2005.06.148*

Retrosynthesis ID: 9990045

2.2.6 Amide coupling



Substrates:

1. COC(=O)c1ccc(OC2CNC(C(=O)NC3(C(=O)NS(=O)(=O)C4CC4)CC3)C2)c(OC)c1
2. 2-[(tert-butoxy)carbonyl]amino-3-methylpentanoic acid - *available at Sigma-Aldrich*

Products:

1. CCC(C)C(NC(=O)OC(C)(C)C)C(=O)N1CC(Oc2ccc(C(=O)OC)cc2OC)CC1C(=O)NC1(C(=O)NS(=O

Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

Protections: none

Yield: good

Reference: *10.1021/ol400686f* and *10.1021/jo00200a057* and *10.1021/cr100048w* and *10.1039/B701677H* and *10.1039/C5RA24527C* and *10.3727/000000006783981206* and *10.1021/np060007f* and *10.1021/jo00012a058* and *10.1016/j.bmcl.2007.08.037* and *10.1039/C0OB00355G* and *10.1021/jm500031w* (p.3056) and *10.1016/j.tet.2011.03.046*

Retrosynthesis ID: 9147

2.3 Path 3

Score: 658.34

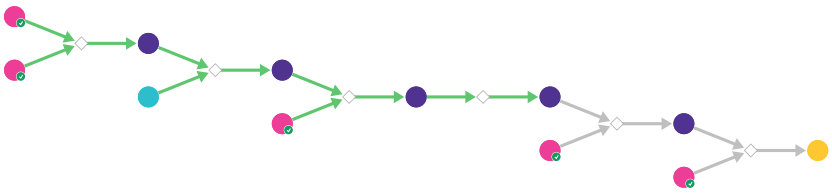
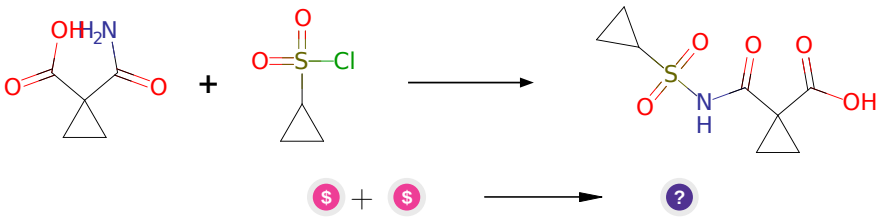


Figure 3: Outline of path 3

2.3.1 Sulfonylation of amides



Substrates:

1. 1-(Aminocarbonyl)-1-cyclopropanecarboxylic acid - *available at Sigma-Aldrich*
2. Cyclopropanesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: Py.RSO2Cl

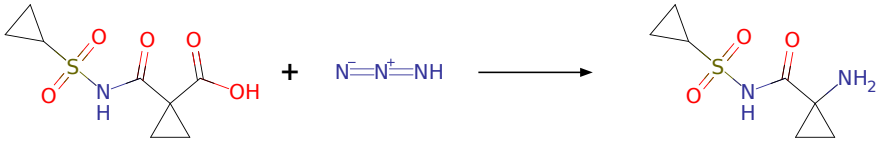
Protections: none

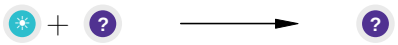
Yield: good

Reference: *10.1021/ja9945313* AND *10.1016/j.ejmech.2013.04.028* AND *10.1039/c5ra14001c* AND *10.1016/j.bmcl.2013.12.043* AND *10.1016/j.tetasy.2012.08.013*

Retrosynthesis ID: 14787

2.3.2 Schmidt Reaction





Substrates:

1. hydrazoic acid
2. O=C(O)C1(C(=O)NS(=O)(=O)C2CC2)CC1

Products:

1. NC1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: azide.H+.40C

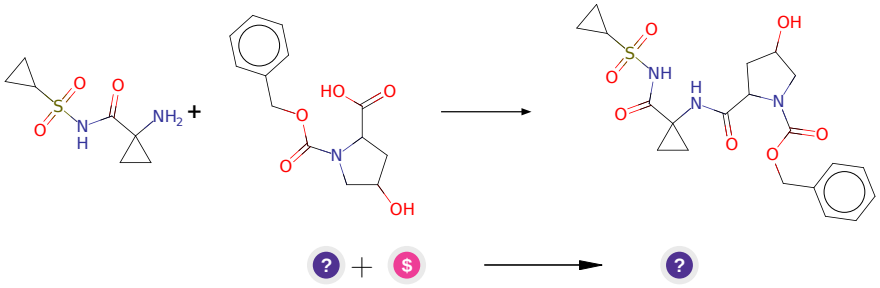
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.3.3 Amide coupling



Substrates:

1. NC1(C(=O)NS(=O)(=O)C2CC2)CC1
2. Z-Hyp-OH - *available at Sigma-Aldrich*

Products:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

Protections: none

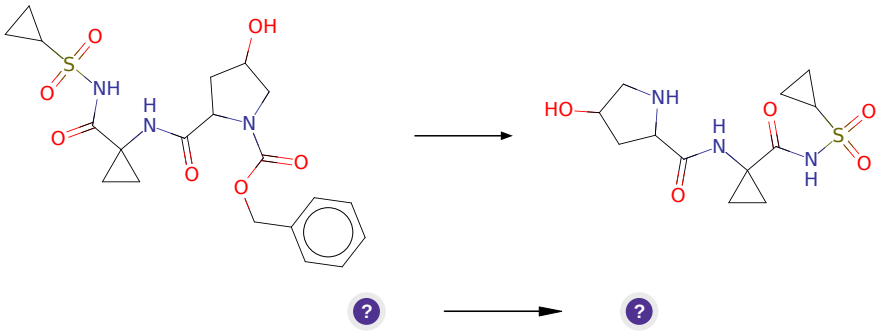
Yield: good

Reference: *10.1021/cr100048w* and *10.1039/B701677H* and *10.1039/C5RA24527C* and *10.3727/000000006783981206* and

10.1021/np060007f and *10.1021/jo00012a058* and *10.1016/j.bmcl.2007.08.037* and *10.1039/C0OB00355G* and *10.1021/jm500031w* (p.3056) and *10.1016/j.tet.2011.03.046*

Retrosynthesis ID: 10087

2.3.4 Cleavage of benzyloxycarbamates



Substrates:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

Products:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1

Typical conditions: H2.Pd/C

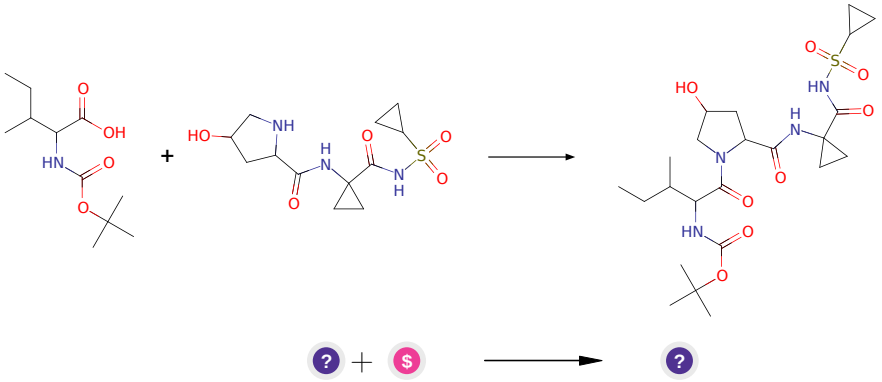
Protections: none

Yield: good

Reference: *10.1021/jm070755h* and *10.1021/jm2016057* and *10.1055/s-0033-1340215* and *10.1016/S0040-4039(03)01181-X*

Retrosynthesis ID: 9990024

2.3.5 Amide coupling



Substrates:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CC2)CC1)C1CC(O)CN1
2. 2-[(tert-butoxy)carbonyl]amino-3-methylpentanoic acid - *available at Sigma-Aldrich*

Products:

1. CCC(C)C(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CC2)CC1

Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

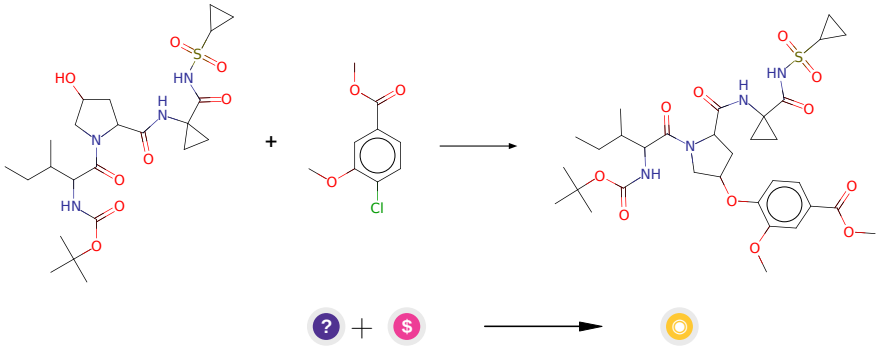
Protections: none

Yield: good

Reference: *10.1021/ol400686f* and *10.1021/jo00200a057* and *10.1021/cr100048w* and *10.1039/B701677H* and *10.1039/C5RA24527C* and *10.3727/000000006783981206* and *10.1021/np060007f* and *10.1021/jo00012a058* and *10.1016/j.bmcl.2007.08.037* and *10.1039/C0OB00355G* and *10.1021/jm500031w* (p.3056) and *10.1016/j.tet.2011.03.046*

Retrosynthesis ID: 9147

2.3.6 Buchwald-Hartwig Reaction



Substrates:

1. CCC(C)C(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CC2)CC1
2. Methyl 4-chloro-3-methoxybenzoate - *available at Sigma-Aldrich*

Products:

1. CCC(C)C(NC(=O)OC(C)(C)C)C(=O)N1CC(Oc2ccc(C(=O)OC)cc2OC)CC1C(=O)NC1(C(=O)NS(=O

Typical conditions: Pd(OAc)2.ligand.Cs2CO3.solvent.heat

Protections: none

Yield: good

Reference: *10.1021/ja016863p* and *10.1021/ja016863p* and *10.1021/ja103248d* and *10.1021/jo025732j* and *10.1021/ja002543e* and *10.1002/jhet.4158*

Retrosynthesis ID: 27014