Paths of analysis*

(re)C21

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: `191.10`

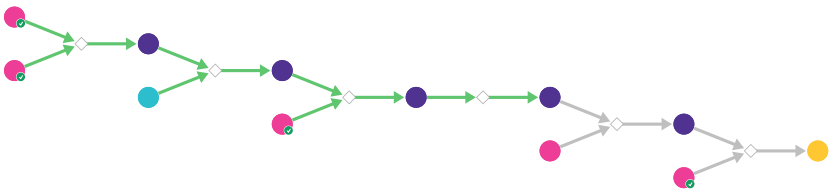
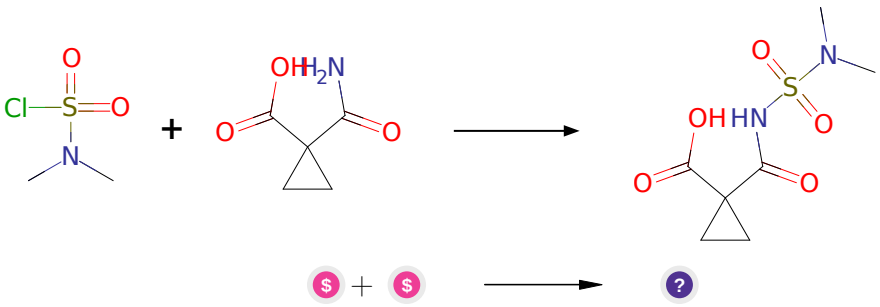


Figure 1: Outline of path 1

2.1.1 Sulfonylation of amides



Substrates:

1. 1-(Aminocarbonyl)-1-cyclopropanecarboxylic acid - *available at Sigma-Aldrich*
2. N,N-Dimethylsulfamoyl chloride - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(C(=O)O)CC1

Typical conditions: Py.RSO2Cl

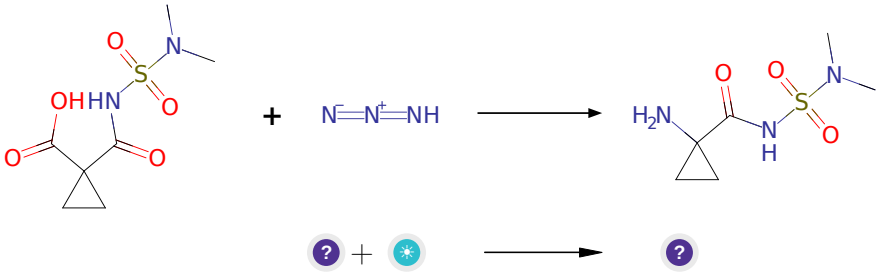
Protections: none

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. CN(C)S(=O)(=O)NC(=O)C1(C(=O)O)CC1
2. hydrazoic acid

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(N)CC1

Typical conditions: azide.H+.40C

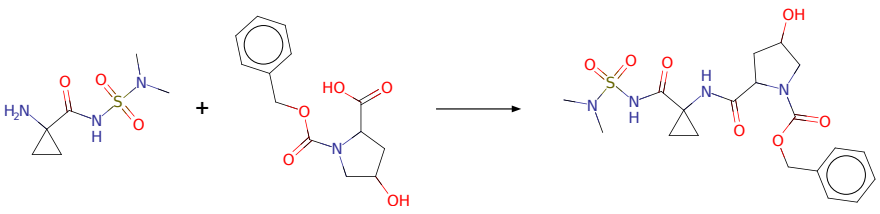
Protections: none

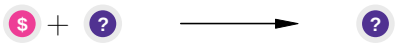
Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.1.3 Amide coupling





Substrates:

1. Z-Hyp-OH - *available at Sigma-Aldrich*
2. CN(C)S(=O)(=O)NC(=O)C1(N)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

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

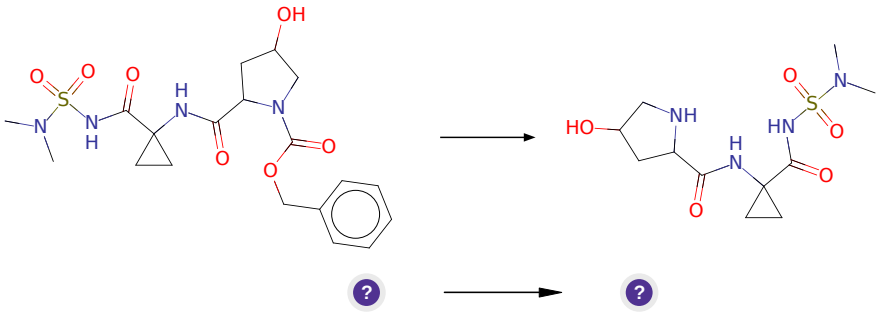
Protections: none

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 Cleavage of benzyloxycarbamates



Substrates:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2)CC1

Typical conditions: H2.Pd/C

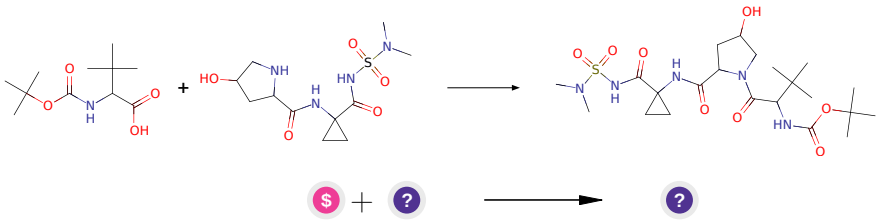
Protections: none

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

2.1.5 Amide coupling



Substrates:

1. 2-[(tert-butoxy)carbonyl]amino-3,3-dimethylbutanoic acid - *Enamine*
2. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)CC1

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

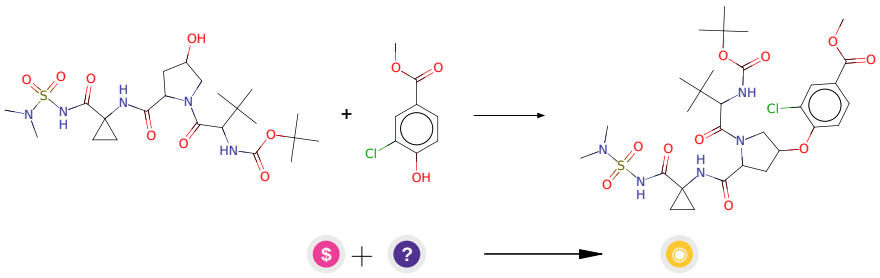
Protections: none

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

2.1.6 Mitsunobu reaction



Substrates:

1. Methyl 3-chloro-4-hydroxybenzoate - *available at Sigma-Aldrich*
2. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)CC1

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)N(C)C)CC3)N(C(=O)C(NC(=O)OC(C)(C)C

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

Protections: none

Yield: good

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

Retrosynthesis ID: 7562

2.2 Path 2

Score: 225.96

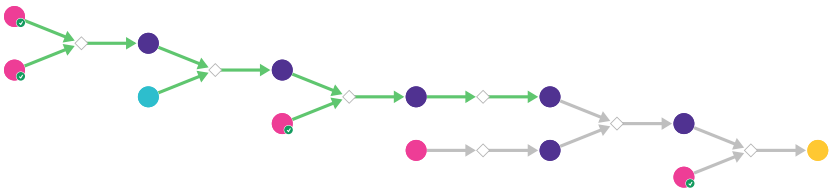
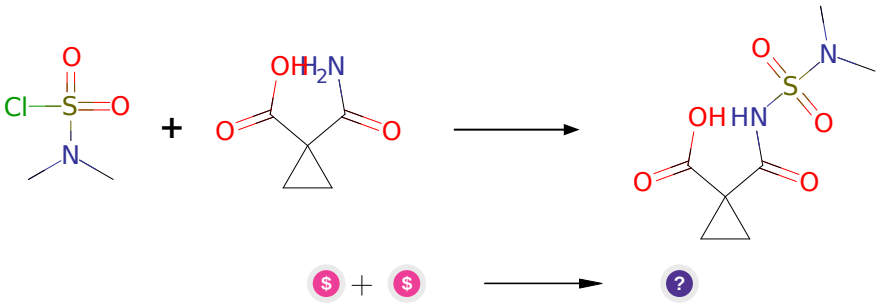


Figure 2: Outline of path 2

2.2.1 Sulfonylation of amides



Substrates:

1. 1-(Aminocarbonyl)-1-cyclopropanecarboxylic acid - *available at Sigma-Aldrich*
2. N,N-Dimethylsulfamoyl chloride - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(C(=O)O)CC1

Typical conditions: Py.RSO2Cl

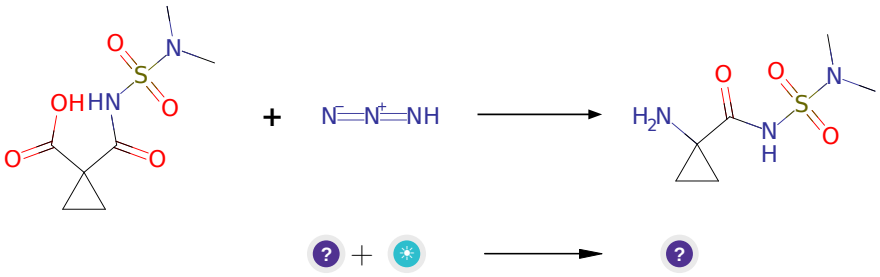
Protections: none

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. CN(C)S(=O)(=O)NC(=O)C1(C(=O)O)CC1
2. hydrazoic acid

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(N)CC1

Typical conditions: azide.H+.40C

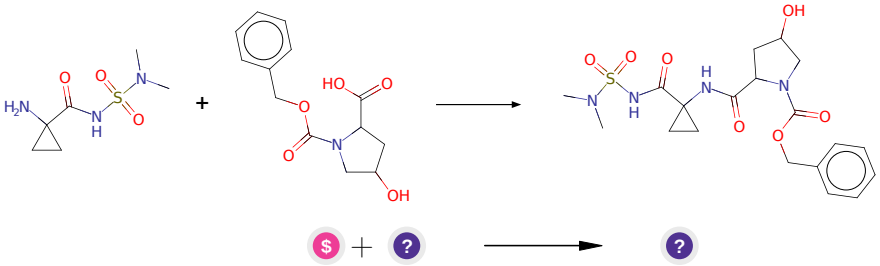
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.2.3 Amide coupling



Substrates:

1. Z-Hyp-OH - *available at Sigma-Aldrich*
2. CN(C)S(=O)(=O)NC(=O)C1(N)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

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

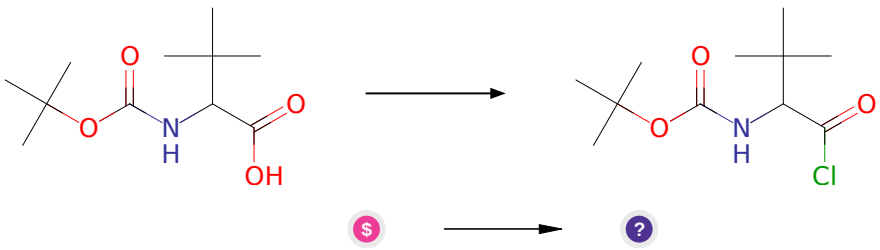
Protections: none

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 Synthesis of acid chlorides from carboxylic acids



Substrates:

1. 2-[(tert-butoxy)carbonyl]amino-3,3-dimethylbutanoic acid - *Enamine*

Products:

1. CC(C)(C)OC(=O)NC(C(=O)Cl)C(C)(C)C

Typical conditions: oxalyl.chloride.or.SOCl2

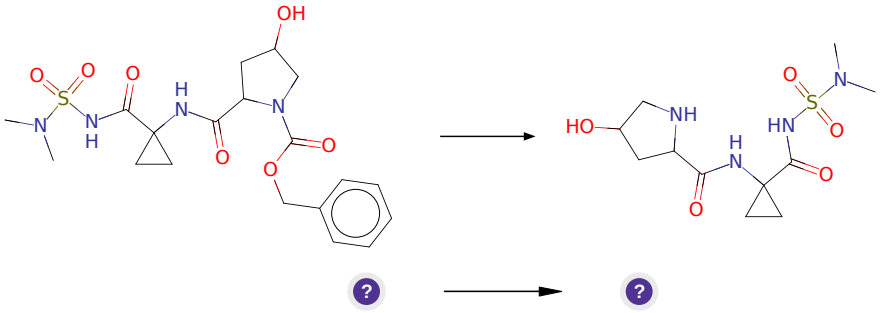
Protections: none

Yield: good

Reference: *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24405

2.2.5 Cleavage of benzyloxycarbamates



Substrates:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2)CC1

Typical conditions: H2.Pd/C

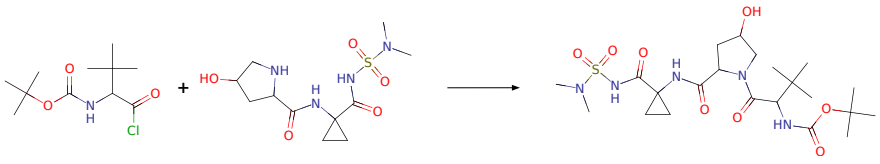
Protections: none

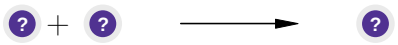
Yield: good

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

2.2.6 Reaction of acyl chlorides with amines





Substrates:

1. CC(C)(C)OC(=O)NC(C(=O)Cl)C(C)(C)C
2. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)CC1

Typical conditions: Net3 or pyridine.DCM

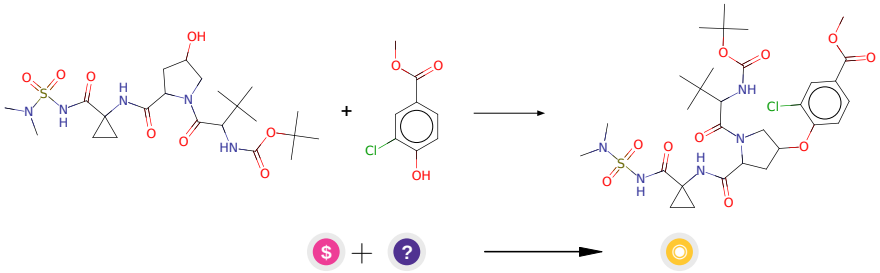
Protections: none

Yield: good

Reference: *10.1016/j.ejmech.2016.03.047* AND *10.1016/j.bmcl.2008.08.004* AND *10.1016/j.bmc.2011.03.002* AND *10.1021/ja077463q* (SI) AND *10.1016/j.tetlet.2014.10.006* (SI) AND *10.1016/j.bmcl.2008.04.018* AND *10.1021/jm980712o* AND *10.1021/jo9906173* AND *10.1021/jf9607371* AND

Retrosynthesis ID: 28547

2.2.7 Mitsunobu reaction



Substrates:

1. Methyl 3-chloro-4-hydroxybenzoate - *available at Sigma-Aldrich*
2. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)CC1

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)N(C)C)CC3)N(C(=O)C(NC(=O)OC(C)(C)C

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

Protections: none

Yield: good

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

Retrosynthesis ID: 7562

2.3 Path 3

Score: 256.66

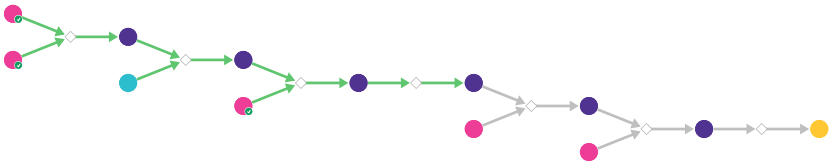
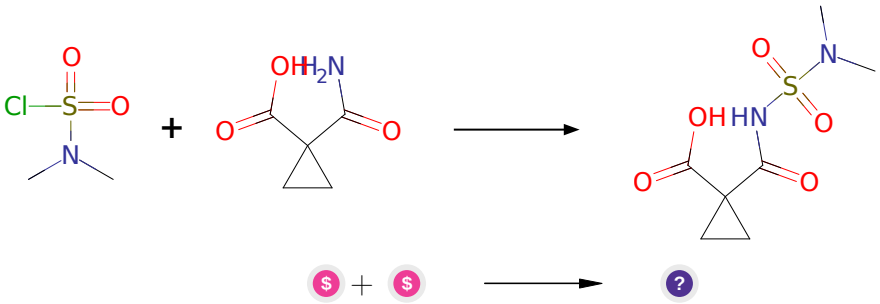


Figure 3: Outline of path 3

2.3.1 Sulfonylation of amides



Substrates:

1. 1-(Aminocarbonyl)-1-cyclopropanecarboxylic acid - *available at Sigma-Aldrich*
2. N,N-Dimethylsulfamoyl chloride - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(C(=O)O)CC1

Typical conditions: Py.RSO2Cl

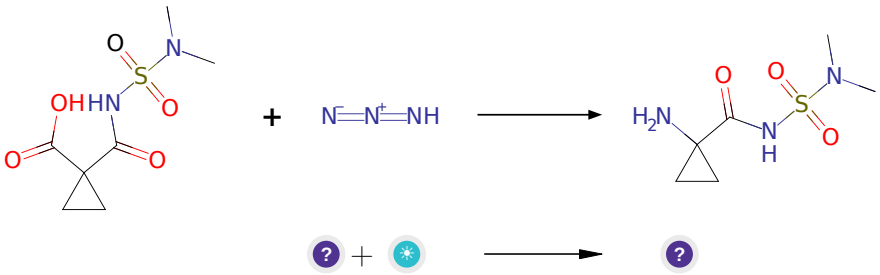
Protections: none

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. CN(C)S(=O)(=O)NC(=O)C1(C(=O)O)CC1
2. hydrazoic acid

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(N)CC1

Typical conditions: azide.H+.40C

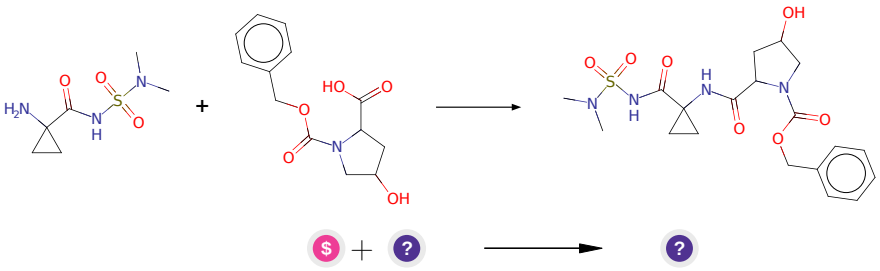
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.3.3 Amide coupling



Substrates:

1. Z-Hyp-OH - *available at Sigma-Aldrich*
2. CN(C)S(=O)(=O)NC(=O)C1(N)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

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

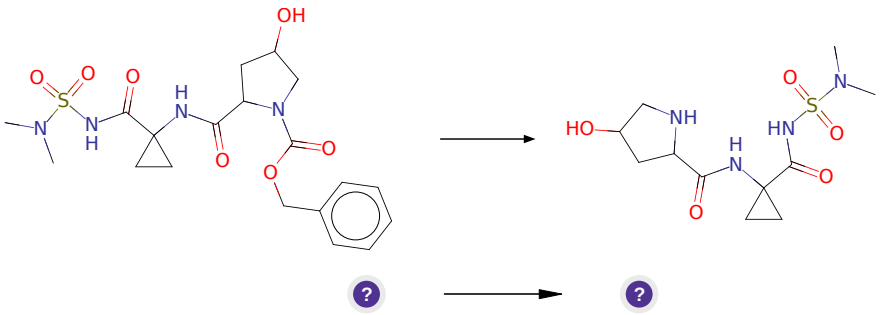
Protections: none

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. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2)CC1

Typical conditions: H2.Pd/C

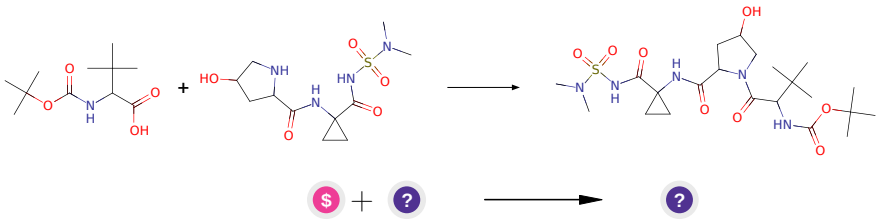
Protections: none

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. 2-[(tert-butoxy)carbonyl]amino-3,3-dimethylbutanoic acid - *Enamine*
2. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2)CC1

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)CC1

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

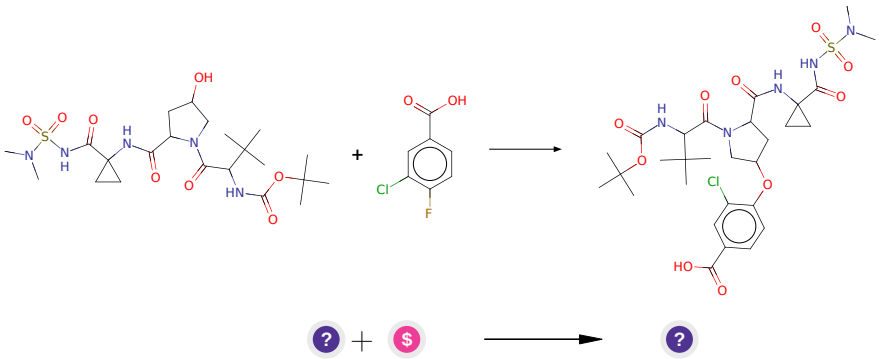
Protections: none

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 Nucleophilic aromatic substitution



Substrates:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(O)CN2C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)CC1
2. 3-Chloro-4-fluorobenzoic acid - *Combi-Blocks*

Products:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(Oc3ccc(C(=O)O)cc3Cl)CN2C(=O)C(NC(=O)OC(C)(C)

Typical conditions: NaH.THF.0-80 C or K2CO3.DMF.110 C

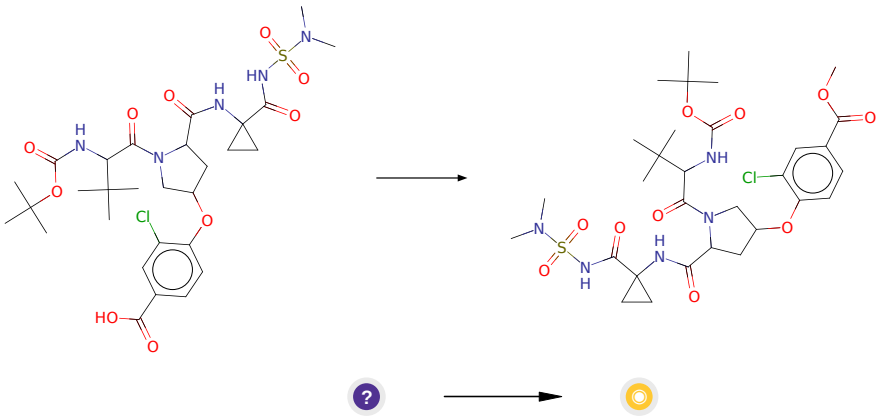
Protections: none

Yield: good

Reference: *10.1016/j.tetlet.2015.10.008* p. 6479, 6483 and *10.1016/j.ejmech.2016.06.056* p. 82, 85

Retrosynthesis ID: 49475

2.3.7 Steglich Esterification



Substrates:

1. CN(C)S(=O)(=O)NC(=O)C1(NC(=O)C2CC(Oc3ccc(C(=O)O)cc3Cl)CN2C(=O)C(NC(=O)OC(C)(C)

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)N(C)C)CC3)N(C(=O)C(NC(=O)OC(C)(C)C

Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Yield: good

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 11088