Paths of analysis*

C25

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: 277.20

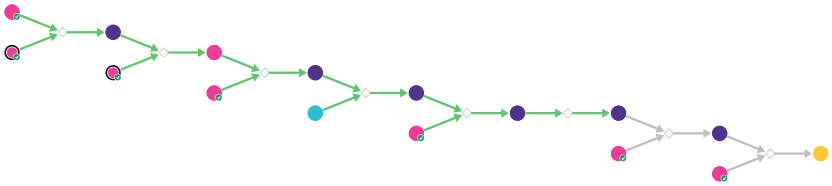
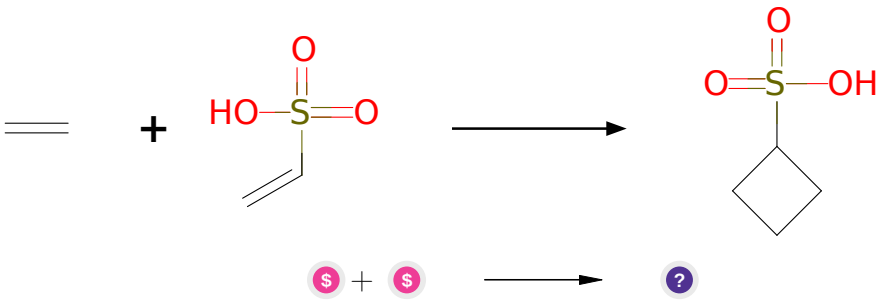


Figure 1: Outline of path 1

2.1.1 [2+2] photocycloaddition



Substrates:

1. Sodium vinylsulfonate solution - *available at Sigma-Aldrich*
2. Ethene - *available at Sigma-Aldrich*

Products:

1. O=S(=O)(O)C1CCC1

Typical conditions: light

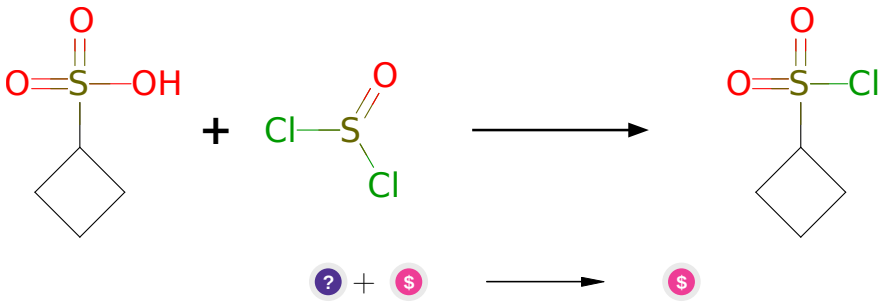
Protections: none

Yield: moderate

Reference: *10.1002/0471264180.or044.02* and *10.1021/acs.chemrev.5b00723* and *10.1007/s11426-015-5516-5* and *10.1016/S0957-4166(00)80211-6* and CN107805197A, p.0009 and *10.1039/c2sc20658g*

Retrosynthesis ID: 1225

2.1.2 Synthesis sulfonyl chlorides from sulfonic acids



Substrates:

1. O=S(=O)(O)C1CCC1
2. Thionyl chloride - *available at Sigma-Aldrich*

Products:

1. Cyclobutanesulfonyl chloride - *AstaTech*

Typical conditions: SOCl2.DMF.20C

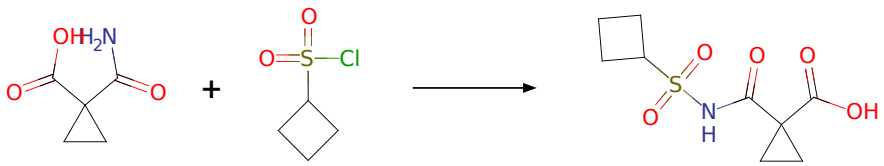
Protections: none

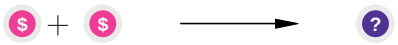
Yield: good

Reference: Patent: WO2003106445 A1, 2003

Retrosynthesis ID: 2000

2.1.3 Sulfonylation of amides





Substrates:

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

Products:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: Py.RSO2Cl

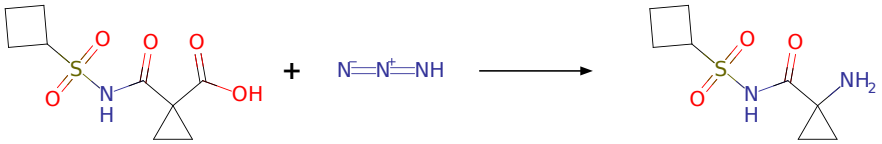
Protections: none

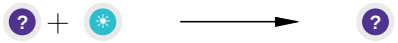
Yield: good

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

2.1.4 Schmidt Reaction





Substrates:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. hydrazoic acid

Products:

1. NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: azide.H+.40C

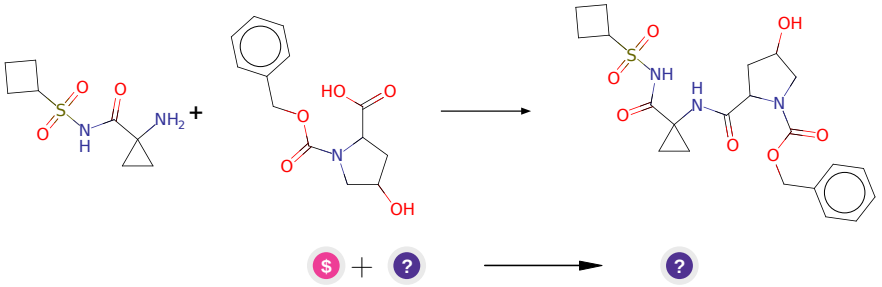
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.1.5 Amide coupling



Substrates:

1. Z-Hyp-OH - *available at Sigma-Aldrich*
2. NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

Products:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CCC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

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

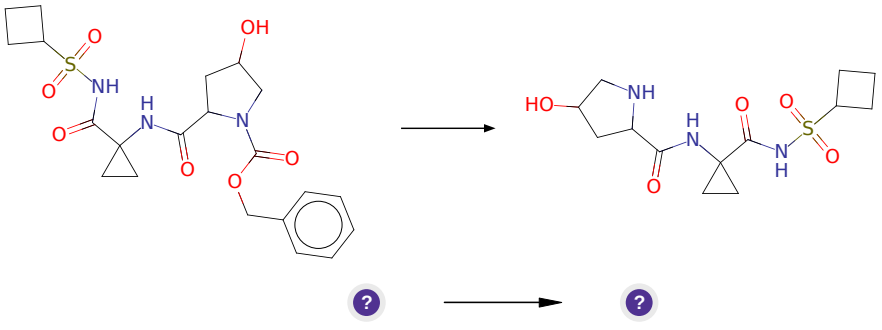
Protections: none

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

2.1.6 Cleavage of benzyloxycarbamates



Substrates:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CCC2)CC1)C1CC(O)CN1C(=O)OCc1ccccc1

Products:

1. O=C(NC1(C(=O)NS(=O)(=O)C2CCC2)CC1)C1CC(O)CN1

Typical conditions: H2.Pd/C

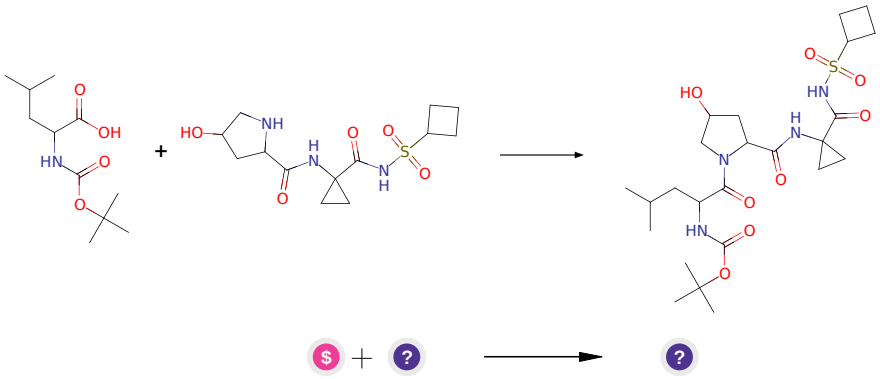
Protections: none

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

2.1.7 Amide coupling



Substrates:

1. 2-[(tert-butoxy)carbonyl]amino-4-methylpentanoic acid - *available at Sigma-Aldrich*
2. O=C(NC1(C(=O)NS(=O)(=O)C2CCC2)CC1)C1CC(O)CN1

Products:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

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

Protections: none

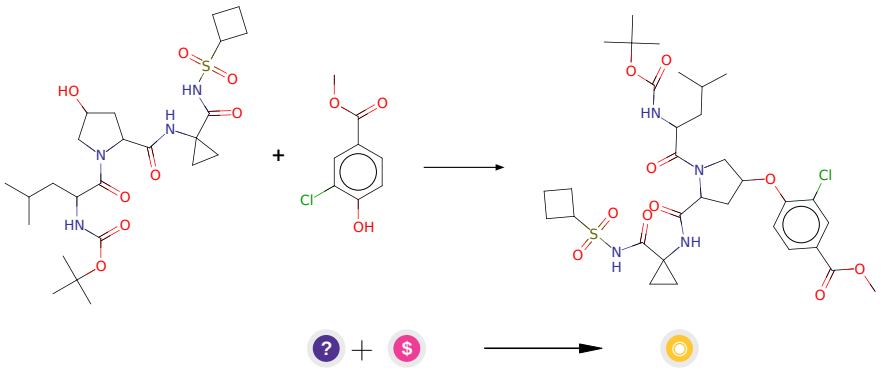
Yield: good

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

2.1.8 Mitsunobu reaction



Substrates:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. Methyl 3-chloro-4-hydroxybenzoate - *available at Sigma-Aldrich*

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CCC4)CC3)N(C(=O)C(CC(C)C)NC(=O)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: 393.79

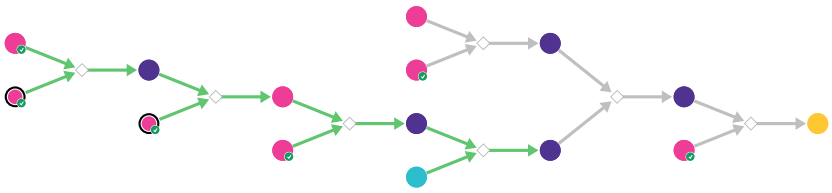
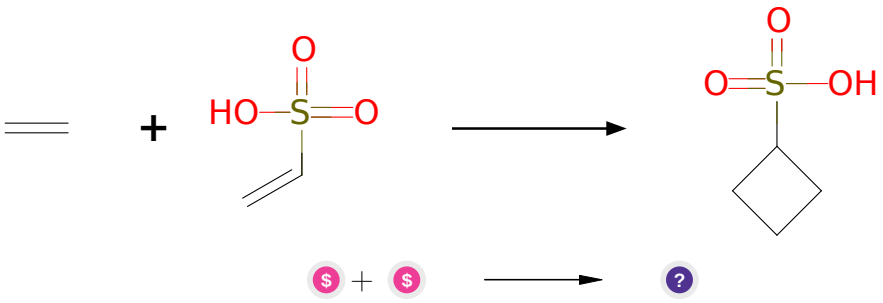


Figure 2: Outline of path 2

2.2.1 [2+2] photocycloaddition



Substrates:

1. Sodium vinylsulfonate solution - *available at Sigma-Aldrich*
2. Ethene - *available at Sigma-Aldrich*

Products:

1. O=S(=O)(O)C1CCC1

Typical conditions: light

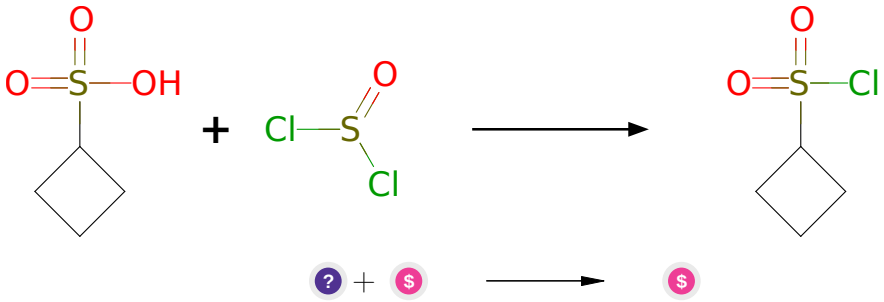
Protections: none

Yield: moderate

Reference: *10.1002/0471264180.or044.02* and *10.1021/acs.chemrev.5b00723* and *10.1007/s11426-015-5516-5* and *10.1016/S0957-4166(00)80211-6* and CN107805197A, p.0009 and *10.1039/c2sc20658g*

Retrosynthesis ID: 1225

2.2.2 Synthesis sulfonyl chlorides from sulfonic acids



Substrates:

1. O=S(=O)(O)C1CCC1
2. Thionyl chloride - *available at Sigma-Aldrich*

Products:

1. Cyclobutanesulfonyl chloride - *AstaTech*

Typical conditions: SOCl2.DMF.20C

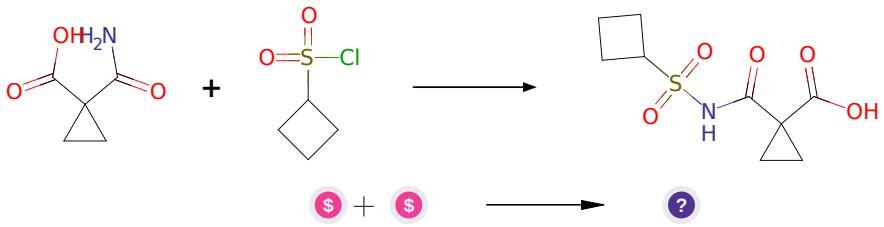
Protections: none

Yield: good

Reference: Patent: WO2003106445 A1, 2003

Retrosynthesis ID: 2000

2.2.3 Sulfonylation of amides



Substrates:

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

Products:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: Py.RSO2Cl

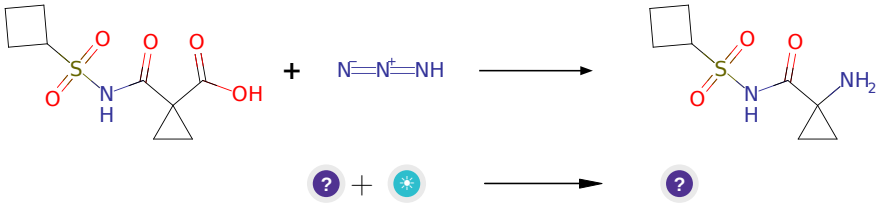
Protections: none

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

2.2.4 Schmidt Reaction



Substrates:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. hydrazoic acid

Products:

1. NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: azide.H+.40C

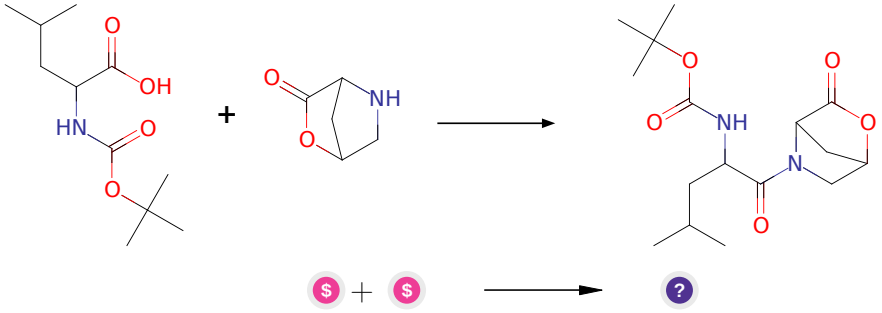
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.2.5 Amide coupling



Substrates:

1. cis-4-hydroxy-proline lactone - *Enamine*
2. 2-[(tert-butoxy)carbonyl]amino-4-methylpentanoic acid - *available at Sigma-Aldrich*

Products:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC2CC1C(=O)O2

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

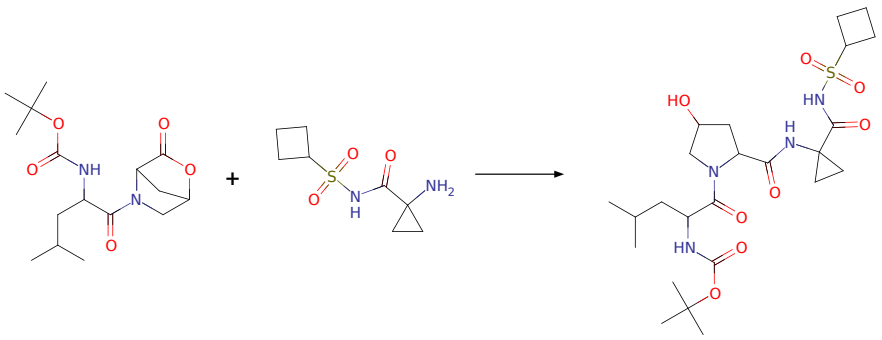
Protections: none

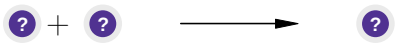
Yield: good

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

2.2.6 Intramolecular amidation of esters





Substrates:

1. NC1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC2CC1C(=O)O2

Products:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: DABAL-(Me)3.THF.cooling

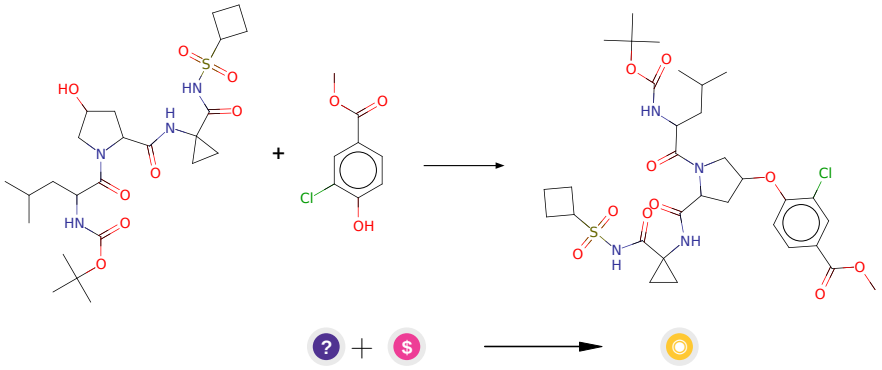
Protections: none

Yield: good

Reference: *10.1016/j.tetlet.2006.06.004* and *10.1246/cl.1987.803* and *10.1016/j.polymer.2013.01.040* and *10.1016/j.tetasy.2003.11.026* and *10.1021/ol050773y*

Retrosynthesis ID: 5035

2.2.7 Mitsunobu reaction



Substrates:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. Methyl 3-chloro-4-hydroxybenzoate - *available at Sigma-Aldrich*

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CCC4)CC3)N(C(=O)C(CC(C)C)NC(=O)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: `435.11`

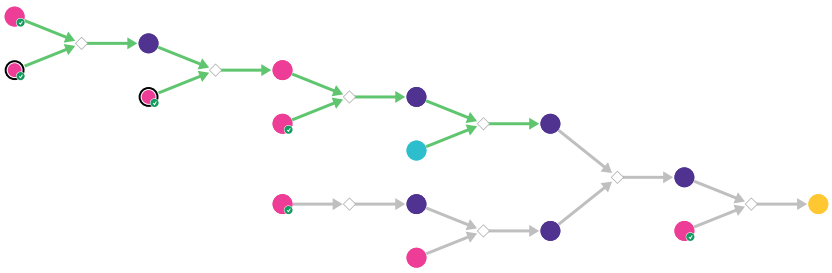
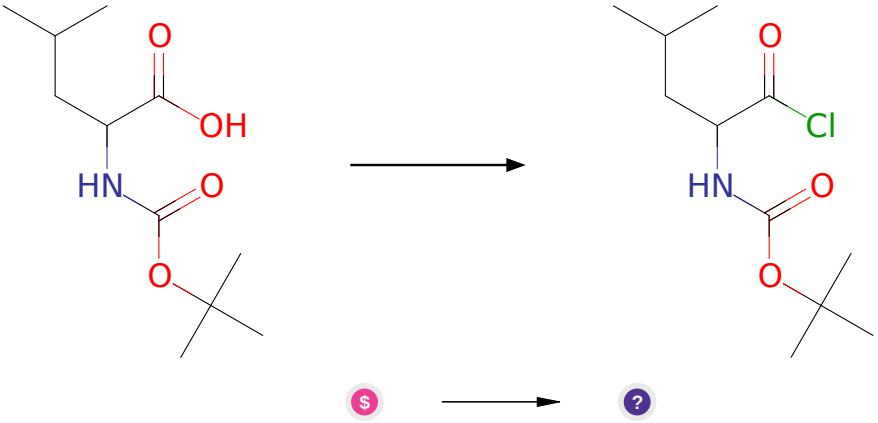


Figure 3: Outline of path 3

2.3.1 Synthesis of acid chlorides from carboxylic acids



Substrates:

1. 2-[(tert-butoxy)carbonyl]amino-4-methylpentanoic acid - *available at Sigma-Aldrich*

Products:

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

Typical conditions: oxalyl.chloride.or.SOCl2

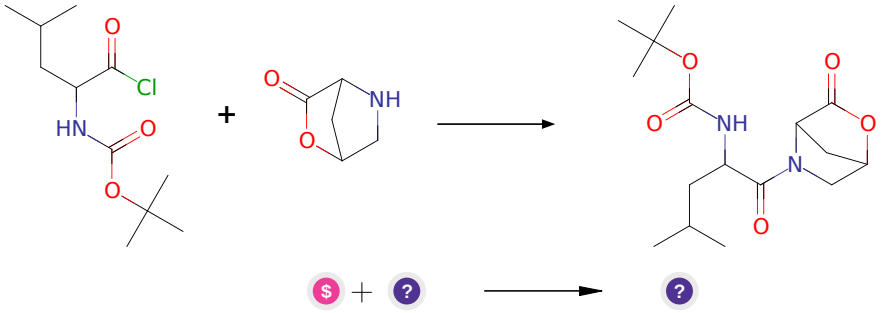
Protections: none

Yield: good

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

Retrosynthesis ID: 24405

2.3.2 Synthesis of tertiary amides from acid chlorides



Substrates:

1. cis-4-hydroxy-proline lactone - *Enamine*
2. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)Cl

Products:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC2CC1C(=O)O2

Typical conditions: TEA.DCM.rt

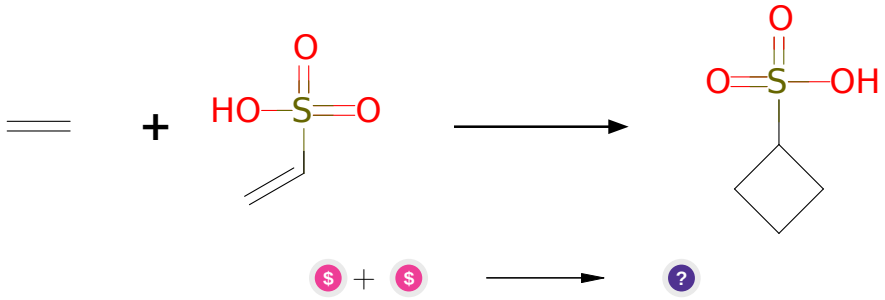
Protections: none

Yield: moderate

Reference: DOI: *10.1016/j.bmcl.2008.08.004* and *10.1016/j.tetlet.2008.05.010*

Retrosynthesis ID: 9146

2.3.3 [2+2] photocycloaddition



Substrates:

1. Sodium vinylsulfonate solution - *available at Sigma-Aldrich*
2. Ethene - *available at Sigma-Aldrich*

Products:

1. O=S(=O)(O)C1CCC1

Typical conditions: light

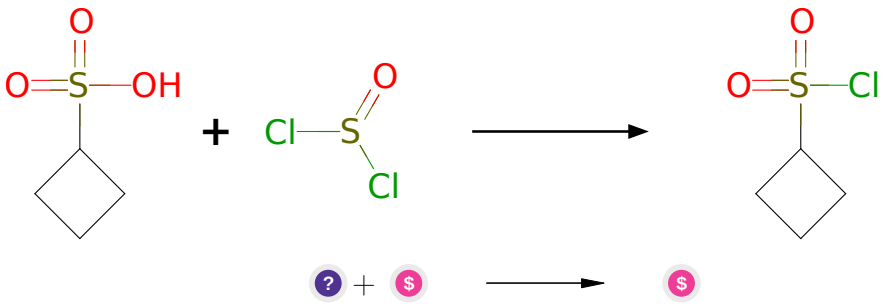
Protections: none

Yield: moderate

Reference: *10.1002/0471264180.or044.02* and *10.1021/acs.chemrev.5b00723* and *10.1007/s11426-015-5516-5* and *10.1016/S0957-4166(00)80211-6* and CN107805197A, p.0009 and *10.1039/c2sc20658g*

Retrosynthesis ID: 1225

2.3.4 Synthesis sulfonyl chlorides from sulfonic acids



Substrates:

1. O=S(=O)(O)C1CCC1

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

Products:

1. Cyclobutanesulfonyl chloride - *AstaTech*

Typical conditions: SOCl2.DMF.20C

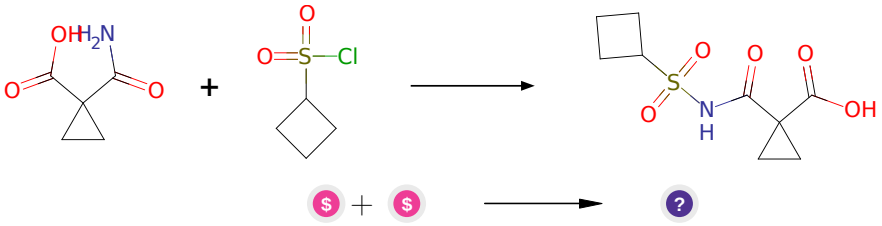
Protections: none

Yield: good

Reference: Patent: WO2003106445 A1, 2003

Retrosynthesis ID: 2000

2.3.5 Sulfonylation of amides



Substrates:

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

Products:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: Py.RSO2Cl

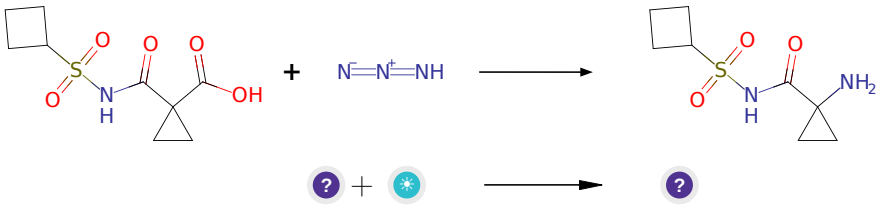
Protections: none

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

2.3.6 Schmidt Reaction



Substrates:

1. O=C(O)C1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. hydrazoic acid

Products:

1. NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: azide.H+.40C

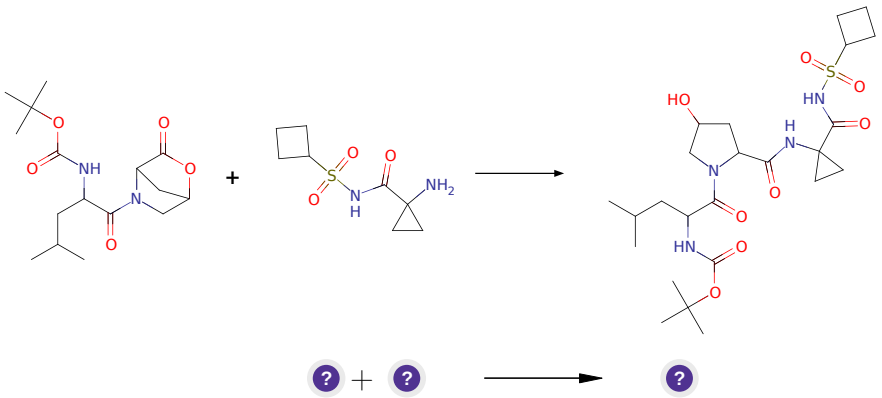
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 11704

2.3.7 Intramolecular amidation of esters



Substrates:

1. NC1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC2CC1C(=O)O2

Products:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CCC2)CC1

Typical conditions: DABAL-(Me)3.THF.cooling

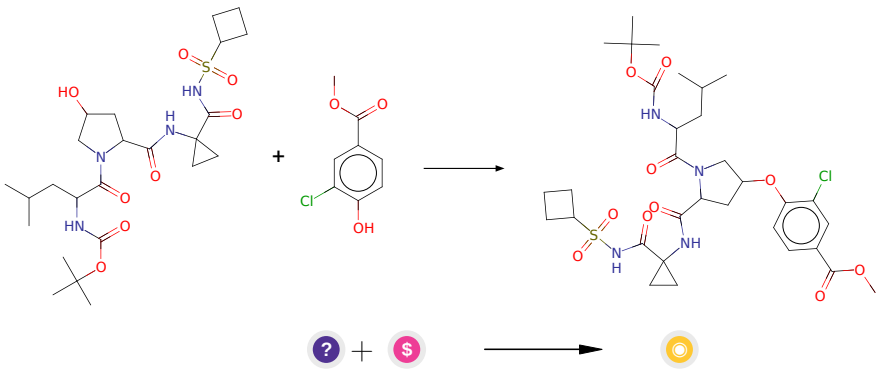
Protections: none

Yield: good

Reference: *10.1016/j.tetlet.2006.06.004* and *10.1246/cl.1987.803* and *10.1016/j.polymer.2013.01.040* and *10.1016/j.tetasy.2003.11.026* and *10.1021/ol050773y*

Retrosynthesis ID: 5035

2.3.8 Mitsunobu reaction



Substrates:

1. CC(C)CC(NC(=O)OC(C)(C)C)C(=O)N1CC(O)CC1C(=O)NC1(C(=O)NS(=O)(=O)C2CCC2)CC1
2. Methyl 3-chloro-4-hydroxybenzoate - *available at Sigma-Aldrich*

Products:

1. COC(=O)c1ccc(OC2CC(C(=O)NC3(C(=O)NS(=O)(=O)C4CCC4)CC3)N(C(=O)C(CC(C)C)NC(=O)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