Paths of analysis*

Analysis 6

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

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FGI Coeff: 0

JSON Parameters: {}

2 Paths

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

2.1 Path 1

Score: 360.09

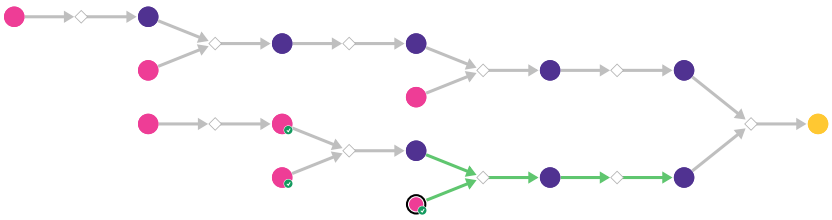
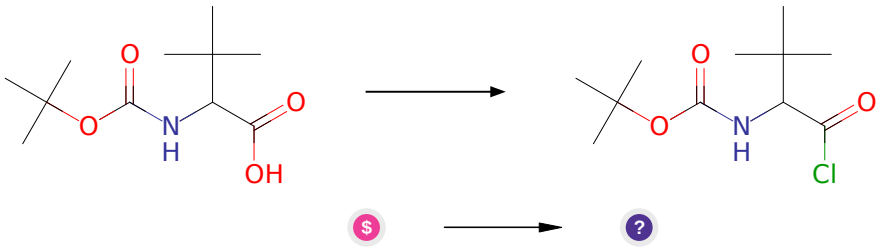


Figure 1: Outline of path 1

2.1.1 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

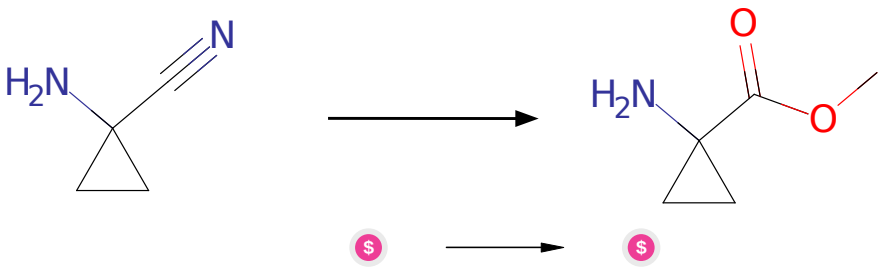
Protections: none

Yield: good

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

Retrosynthesis ID: 24405

2.1.2 Alcoholysis of nitriles to esters



Substrates:

1. 1-Amino-cyclopropanecarbonitrile - *Combi-Blocks*

Products:

1. Methyl 1-aminocyclopropanecarboxylate hydrochloride - *available at Sigma-Aldrich*

Typical conditions: HCl.alcohol.70C or H2SO4.alcohol.reflux

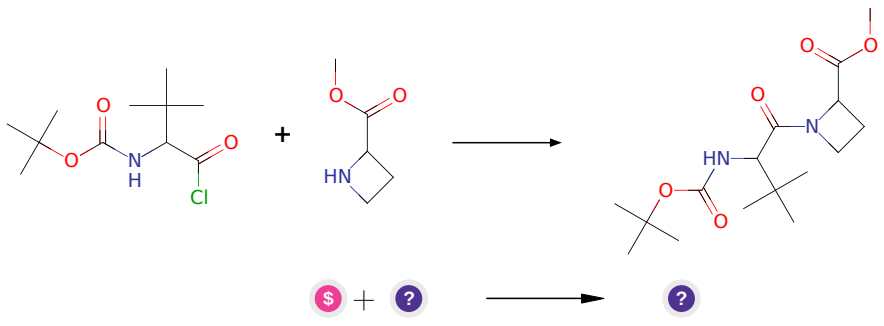
Protections: none

Yield: moderate

Reference: CN104151345 p.79 and *10.1021/jo00391a009* and WO2005058301 p.190 and WO2003084918 and CN105924353 p.37 and *10.1021/acs.jmedchem.6b01261* and *10.1080/00397919508011832*

Retrosynthesis ID: 31009685

2.1.3 Synthesis of tertiary amides from acid chlorides



Substrates:

1. azetidine-2-carboxylic acid methyl ester - *JWPharmlab*
2. CC(C)(C)OC(=O)NC(C(=O)Cl)C(C)(C)C

Products:

1. COC(=O)C1CCN1C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C

Typical conditions: TEA.DCM.rt

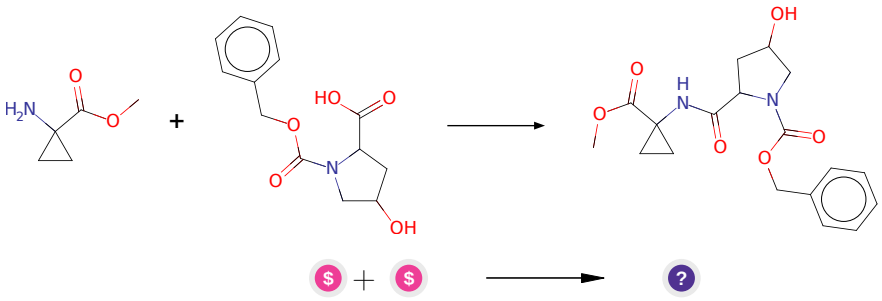
Protections: none

Yield: good

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

Retrosynthesis ID: 9146

2.1.4 Amide coupling



Substrates:

1. Z-Hyp-OH - *available at Sigma-Aldrich*
2. Methyl 1-aminocyclopropanecarboxylate hydrochloride - *available at Sigma-Aldrich*

Products:

1. COC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

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

Protections: none

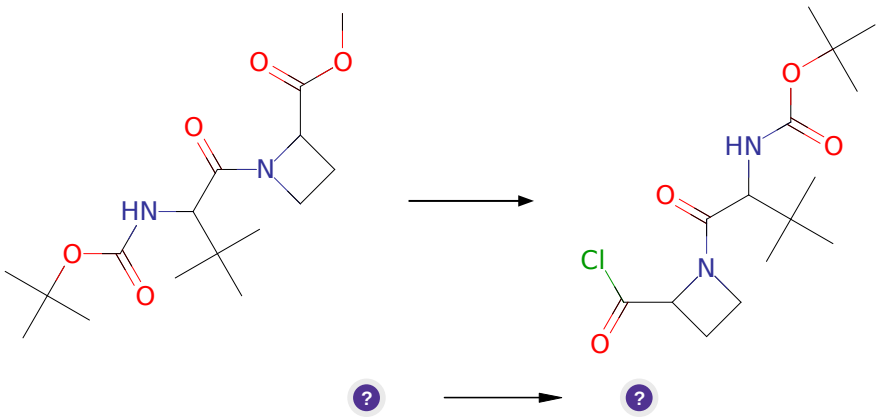
Yield: good

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

2.1.5 Synthesis of acid chlorides from esters



Substrates:

1. COC(=O)C1CCN1C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C

Products:

1. CC(C)(C)OC(=O)NC(C(=O)N1CCC1C(=O)Cl)C(C)(C)C

Typical conditions: 1. LiOH.H2O.THF.2. evaporate.3.SOCl2.or.oxalyl.chloride

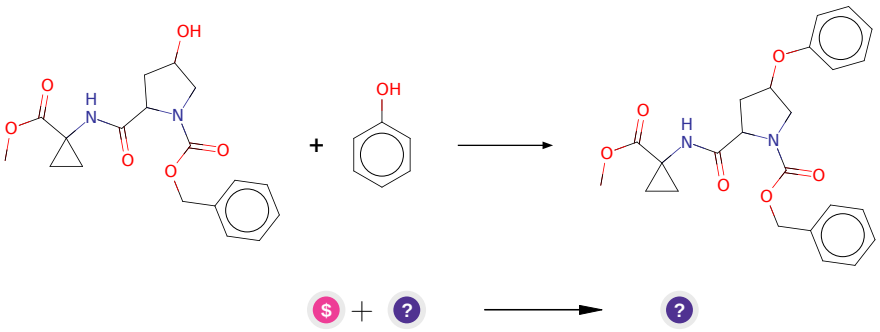
Protections: none

Yield: moderate

Reference: *10.1021/ja073476s* and *10.1016/j.tet.2007.04.043* and *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24406

2.1.6 Mitsunobu reaction



Substrates:

1. C6H6O - *available at Sigma-Aldrich*
2. COC(=O)C1(NC(=O)C2CC(O)CN2C(=O)OCc2ccccc2)CC1

Products:

1. COC(=O)C1(NC(=O)C2CC(Oc3ccccc3)CN2C(=O)OCc2ccccc2)CC1

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

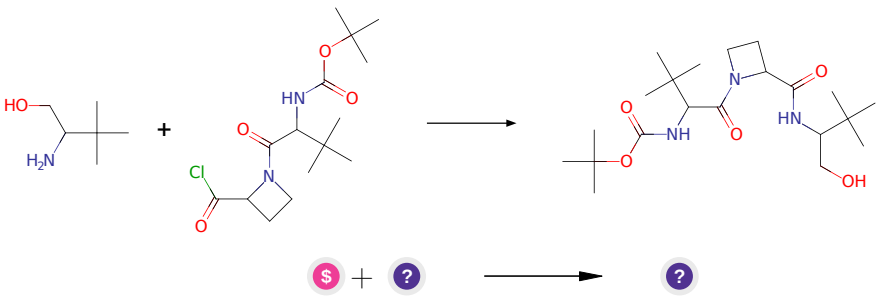
Protections: none

Yield: good

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

Retrosynthesis ID: 7562

2.1.7 Reaction of acyl chlorides with amines



Substrates:

1. 2-Amino-3,3-dimethyl-butan-1-ol - *Enamine*
2. CC(C)(C)OC(=O)NC(C(=O)N1CCC1C(=O)Cl)C(C)(C)C

Products:

1. CC(C)(C)OC(=O)NC(C(=O)N1CCC1C(=O)NC(CO)C(C)(C)C)C(C)(C)C

Typical conditions: Net3 or pyridine.DCM

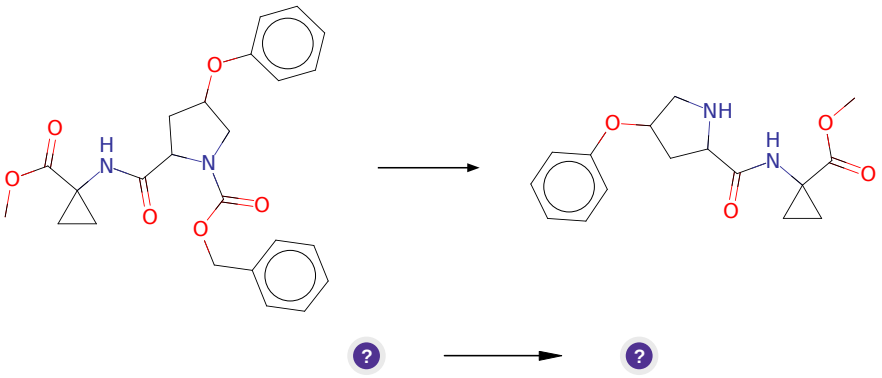
Protections: none

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

2.1.8 Cleavage of benzyloxycarbamates



Substrates:

1. COC(=O)C1(NC(=O)C2CC(Oc3ccccc3)CN2C(=O)OCc2ccccc2)CC1

Products:

1. COC(=O)C1(NC(=O)C2CC(Oc3ccccc3)CN2)CC1

Typical conditions: H2.Pd/C

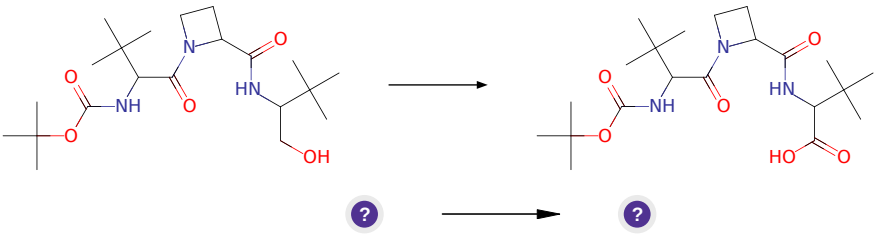
Protections: none

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

2.1.9 Jones Oxidation



Substrates:

1. CC(C)(C)OC(=O)NC(C(=O)N1CCC1C(=O)NC(CO)C(C)(C)C)C(C)(C)C

Products:

1. CC(C)(C)OC(=O)NC(C(=O)N1CCC1C(=O)NC(C(=O)O)C(C)(C)C)C(C)(C)C

Typical conditions: cromate.sulfate.H2O.acetone

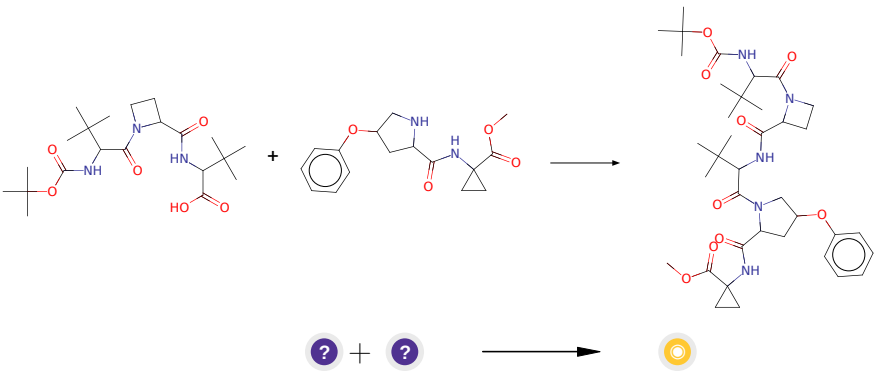
Protections: none

Yield: moderate

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

Retrosynthesis ID: 11160

2.1.10 Amide coupling



Substrates:

1. COC(=O)C1(NC(=O)C2CC(Oc3ccccc3)CN2)CC1
2. CC(C)(C)OC(=O)NC(C(=O)N1CCC1C(=O)NC(C(=O)O)C(C)(C)C)C(C)(C)C

Products:

1. COC(=O)C1(NC(=O)C2CC(Oc3ccccc3)CN2C(=O)C(NC(=O)C2CCN2C(=O)C(NC(=O)OC(C)(C)C)C

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