

Paths of analysis*

Analysis 1

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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

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

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

2.1 Path 1

Score: 313.73

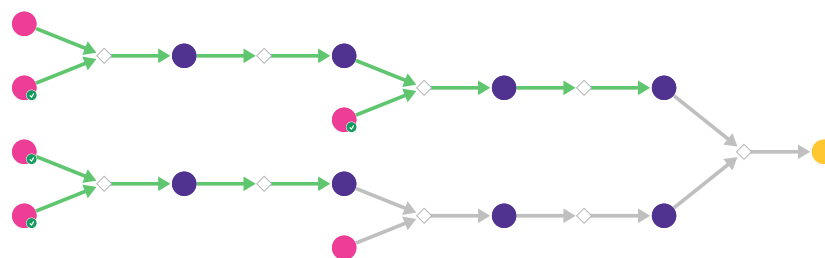
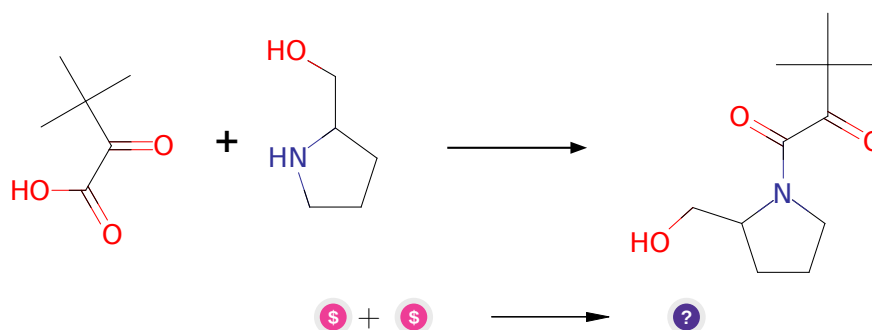


Figure 1: Outline of path 1

2.1.1 Amide coupling



Substrates:

1. Pyrrolidin-2-ylmethanol - *Combi-Blocks*
2. Trimethylpyruvic acid - *available at Sigma-Aldrich*

Products:

1. CC(C)(C)C(=O)C(=O)N1CCCC1CO

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

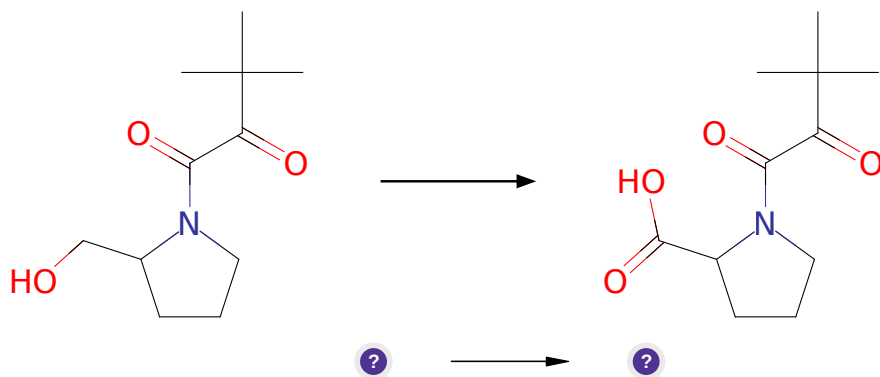
Protections: none

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

2.1.2 Jones Oxidation



Substrates:

1. CC(C)(C)C(=O)C(=O)N1CCCC1CO

Products:

1. CC(C)(C)C(=O)C(=O)N1CCCC1C(=O)O

Typical conditions: cromate.sulfate.H₂O.acetone

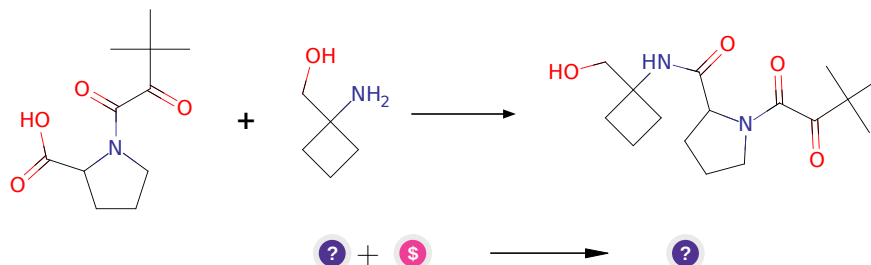
Protections: none

Yield: moderate

Reference: [10.1002/9780470638859.conrr349](#) and [10.1021/jm00270a004](#)

Retrosynthesis ID: 11160

2.1.3 Amide coupling



Substrates:

- CC(C)(C)C(=O)C(=O)N1CCCC1C(=O)O
- (1-Amino-cyclobutyl)-methanol - *available at Sigma-Aldrich*

Products:

- CC(C)(C)C(=O)C(=O)N1CCCC1C(=O)NC1(CO)CCC1

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

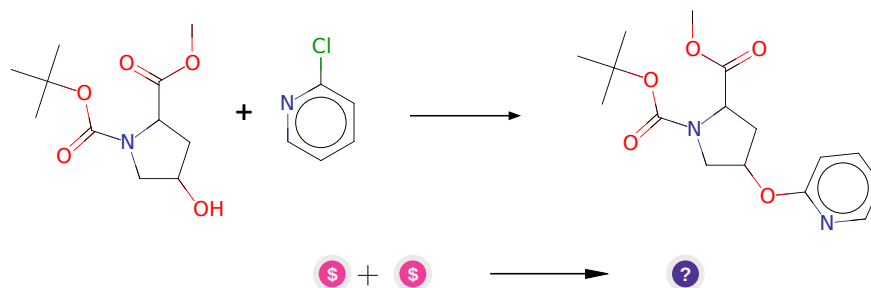
Protections: none

Yield: moderate

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 Buchwald-Hartwig Reaction



Substrates:

- 2-Chloropyridine - *available at Sigma-Aldrich*

2. 1-tert-butyl 2-methyl 4-hydroxypyrrolidine-1,2-dicarboxylate - *available at Sigma-Aldrich*

Products:

1. COC(=O)C1CC(Oc2ccccc2)CN1C(=O)OC(C)(C)C

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

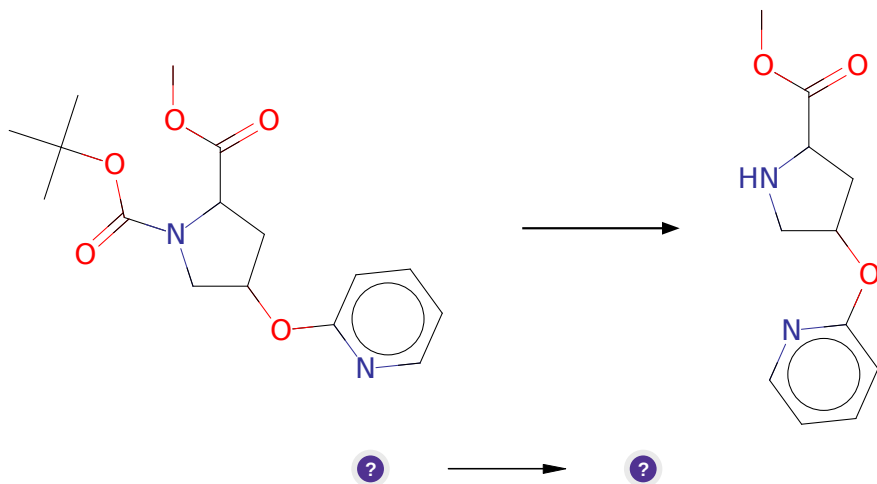
Protections: none

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

2.1.5 Boc removal



Substrates:

1. COC(=O)C1CC(Oc2ccccc2)CN1C(=O)OC(C)(C)C

Products:

1. COC(=O)C1CC(Oc2ccccc2)CN1

Typical conditions: TFA.DCM or HCl.EtOH

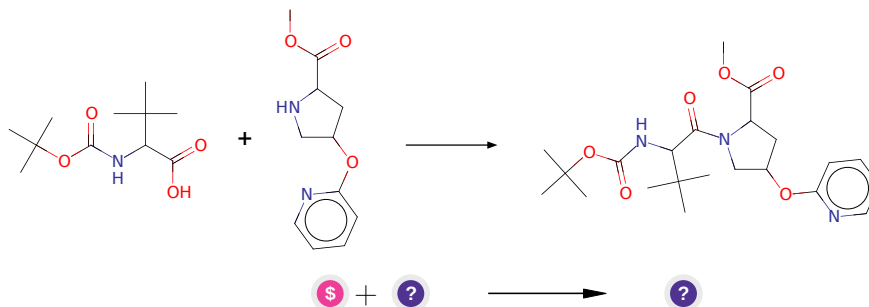
Protections: none

Yield: good

Reference: [10.1021/jm070794t](#) and [10.1021/jm020598g](#) and [10.1021/acs.oprd.5b00144](#) and [10.1016/j.bmc.2003.08.022](#)

Retrosynthesis ID: 10025810

2.1.6 Amide coupling



Substrates:

1. 2-[(tert-butoxy)carbonyl]amino-3,3-dimethylbutanoic acid - *Enamine*
2. COC(=O)C1CC(Oc2ccccc2)CN1

Products:

1. COC(=O)C1CC(Oc2ccccc2)CN1C(=O)C(NC(=O)OC(C)(C)C(C)(C)C(C)(C)C

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

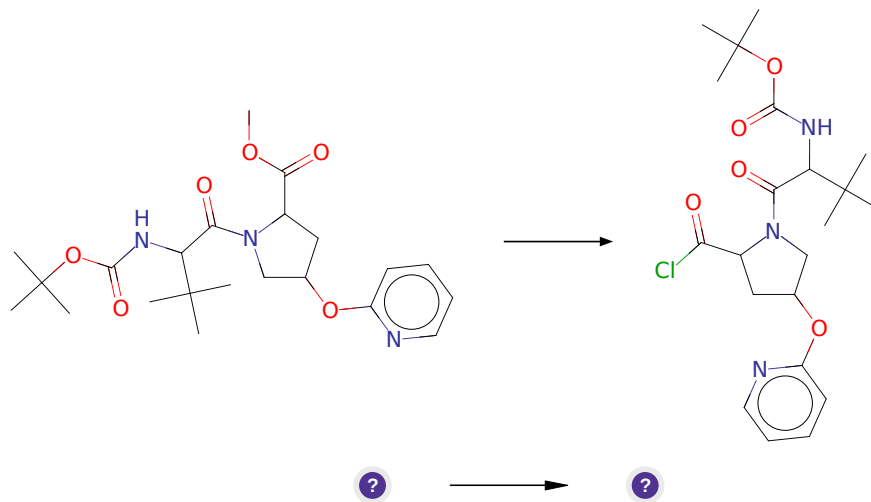
Protections: none

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

2.1.7 Synthesis of acid chlorides from esters



Substrates:

1. COC(=O)C1CC(Oc2ccccc2)CN1C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C

Products:

1. CC(C)(C)OC(=O)NC(C(=O)N1CC(Oc2ccccc2)CC1C(=O)Cl)C(C)(C)C

Typical conditions: 1. LiOH.H₂O.THF. 2. evapo-
rate.3.SOCl₂.or.oxalyl.chloride

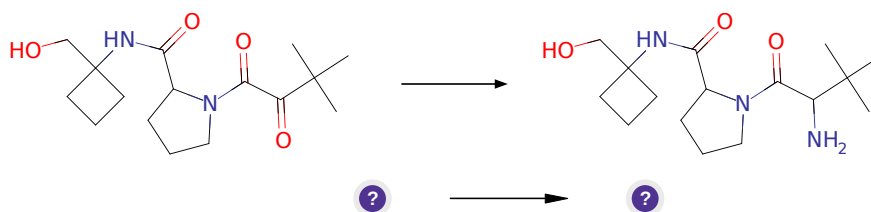
Protections: none

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

2.1.8 Chemoselective reductive alkylation of ammonia with carbonyl compounds



Substrates:

1. CC(C)(C)C(=O)C(=O)N1CCCC1C(=O)NC1(CO)CCC1

Products:

1. CC(C)(C)C(N)C(=O)N1CCCC1C(=O)NC1(CO)CCC1

Typical conditions: titanium isopropoxide.NaBH₄.EtOH.RT

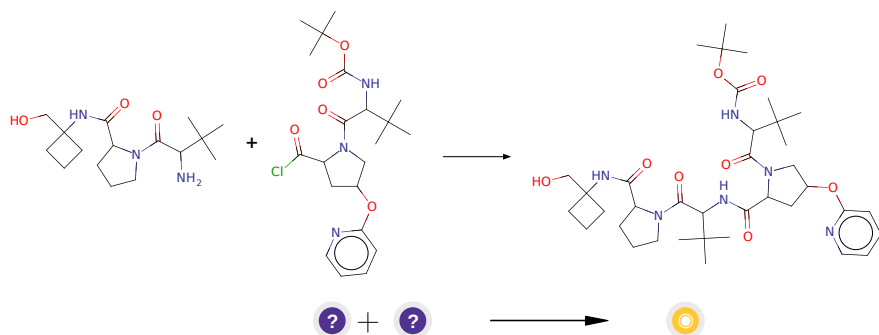
Protections: none

Yield: good

Reference: [10.1016/j.tet.2003.12.024](#) and [10.1016/j.bmc.2011.01.008](#)

Retrosynthesis ID: 10537

2.1.9 Reaction of acyl chlorides with amines



Substrates:

1. CC(C)(C)OC(=O)NC(C(=O)N1CC(Oc2cccn2)CC1C(=O)Cl)C(C)(C)C

2. CC(C)(C)C(N)C(=O)N1CCCC1C(=O)NC1(CO)CCC1

Products:

1. CC(C)(C)OC(=O)NC(C(=O)N1CC(Oc2cccn2)CC1C(=O)NC(C(=O)N1CCCC1C(=O)NC1(CO)CCC1

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