Paths of analysis*

C26

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

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

2.1 Path 1

Score: 347.27

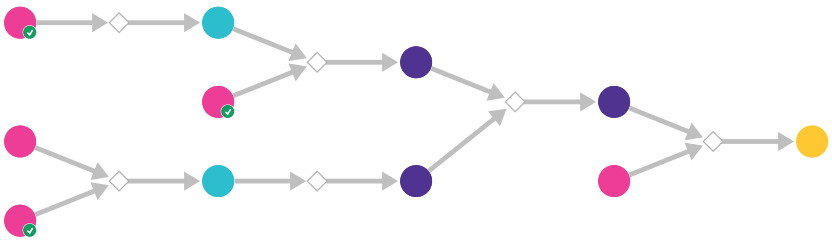
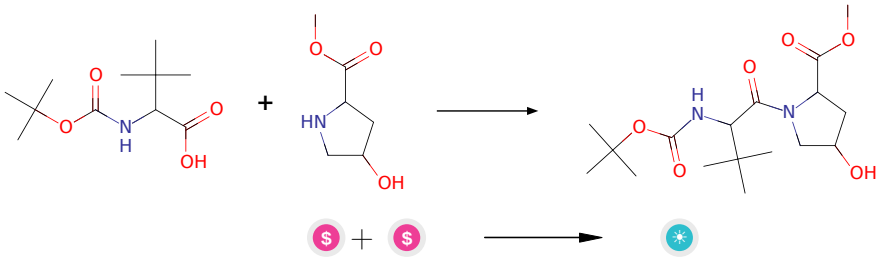


Figure 1: Outline of path 1

2.1.1 Amide coupling



Substrates:

1. 2-[(tert-butoxy)carbonyl]amino-3,3-dimethylbutanoic acid - *Enamine*
2. Methyl 4-hydroxypyrrolidine-2-carboxylate - *available at Sigma-Aldrich*

Products:

1. 1-(2-tert-butoxycarbonylamino-3,3-dimethyl-butyryl)-4-hydroxy-pyrrolidine-2-carboxylic acid methyl ester

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

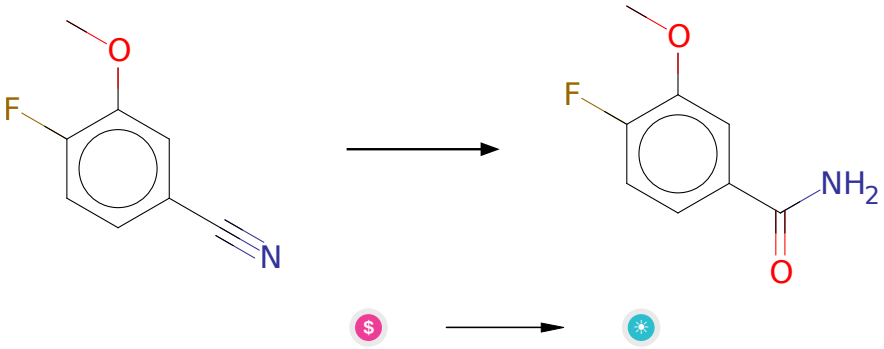
Protections: none

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 Hydrolysis of nitriles to amides



Substrates:

1. 4-Fluoro-3-methoxybenzonitrile - *available at Sigma-Aldrich*

Products:

1. 4-fluoro-3-methoxybenzamide

Typical conditions: H2SO4.DCM.rt

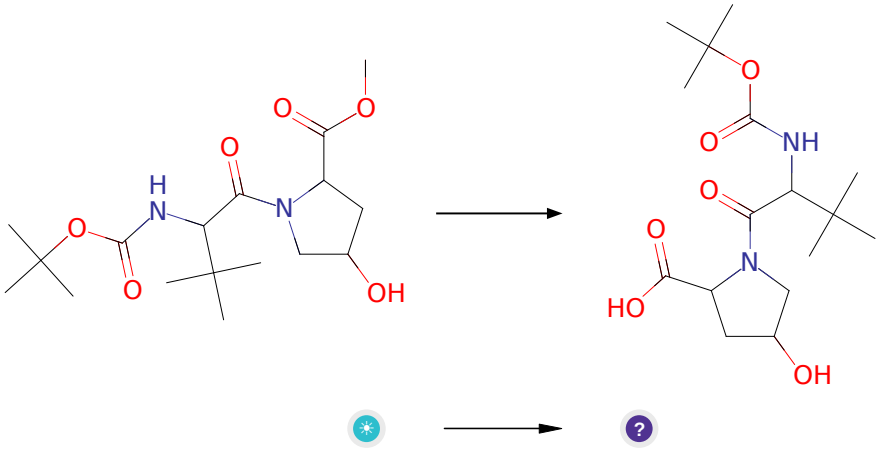
Protections: none

Yield: moderate

Reference: *10.1021/jo00040a061* and *10.1016/0223-5234(90)90132-M* and *10.1016/j.tetlet.2011.09.012*

Retrosynthesis ID: 11358

2.1.3 Synthesis of Carboxylic Acids via Ester Hydrolysis



Substrates:

1. 1-(2-tert-butoxycarbonylamino-3,3-dimethyl-butyryl)-4-hydroxy-pyrrolidine-2-carboxylic acid methyl ester

Products:

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

Typical conditions: water.base

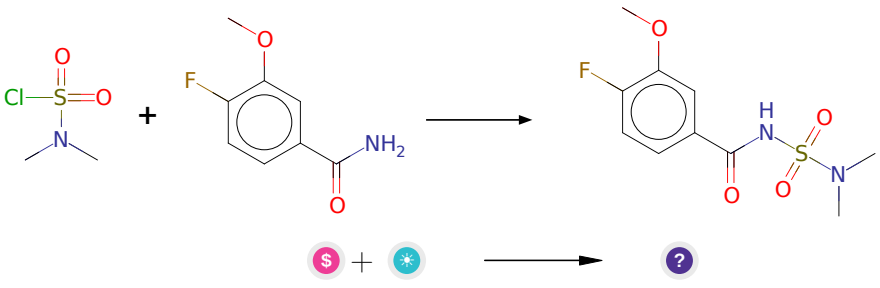
Protections: none

Yield: moderate

Reference: DOI: *10.1016/j.phytochem.2012.08.001* and *10.1021/jm900803q* and *10.1002/anie.201303108* (SI page S14) and *10.1016/j.ejmech.2010.09.003*

Retrosynthesis ID: 9224

2.1.4 Sulfonylation of amides



Substrates:

1. N,N-Dimethylsulfamoyl chloride - *available at Sigma-Aldrich*
2. 4-fluoro-3-methoxybenzamide

Products:

1. COc1cc(C(=O)NS(=O)(=O)N(C)C)ccc1F

Typical conditions: Py.RSO2Cl

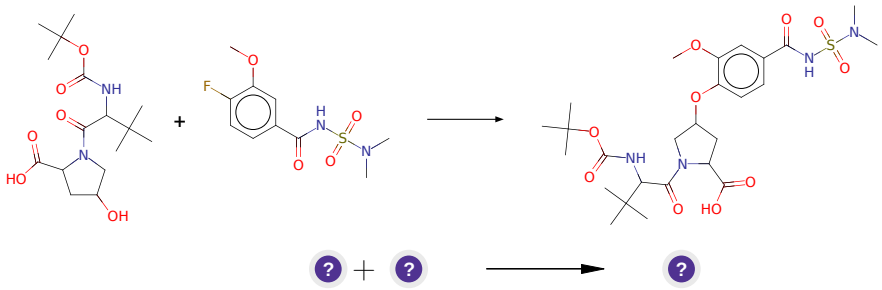
Protections: none

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

2.1.5 Nucleophilic aromatic substitution



Substrates:

1. CC(C)(C)OC(=O)NC(C(=O)N1CC(O)CC1C(=O)O)C(C)(C)C
2. COc1cc(C(=O)NS(=O)(=O)N(C)C)ccc1F

Products:

1. COc1cc(C(=O)NS(=O)(=O)N(C)C)ccc1OC1CC(C(=O)O)N(C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)

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

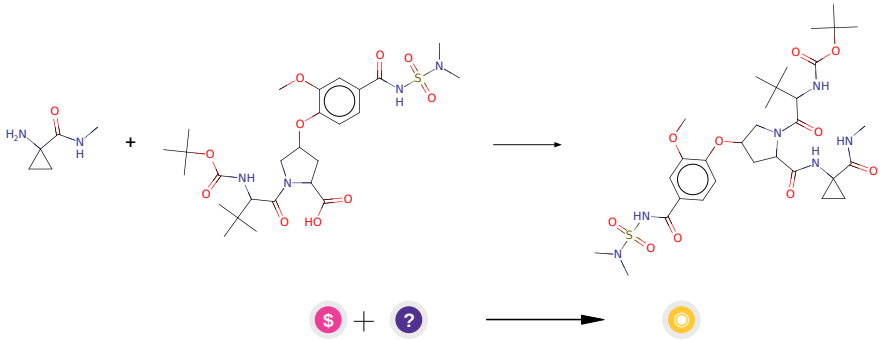
Protections: none

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

2.1.6 Amide coupling



Substrates:

1. 1-amino-N-methylcyclopropanecarboxamide - *A1BioChemLabs*
2. COc1cc(C(=O)NS(=O)(=O)N(C)C)ccc1OC1CC(C(=O)O)N(C(=O)C(NC(=O)OC(C)(C)C)C(C)(C)C)

Products:

1. CNC(=O)C1(NC(=O)C2CC(Oc3ccc(C(=O)NS(=O)(=O)N(C)C)cc3OC)CN2C(=O)C(NC(=O)OC(C)(

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