Paths of analysis*

Analysis 10

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

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

2.1 Path 1

Score: 139.31

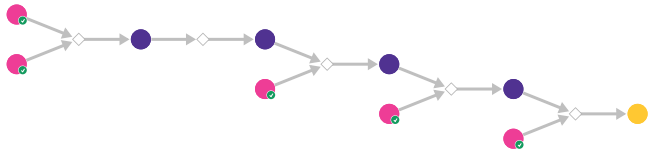
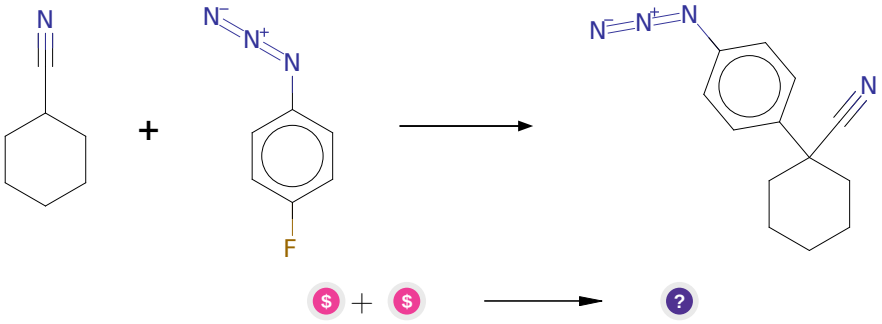


Figure 1: Outline of path 1

2.1.1 Nucleophilic aromatic substitution



Substrates:

1. Cyclohexanecarbonitrile - *available at Sigma-Aldrich*
2. 4-Fluorophenyl azide solution - *available at Sigma-Aldrich*

Products:

1. N#CC1(c2ccc(N=[N+]=[N-])cc2)CCCCC1

Typical conditions: KHMDS.Toluene.THF.RT

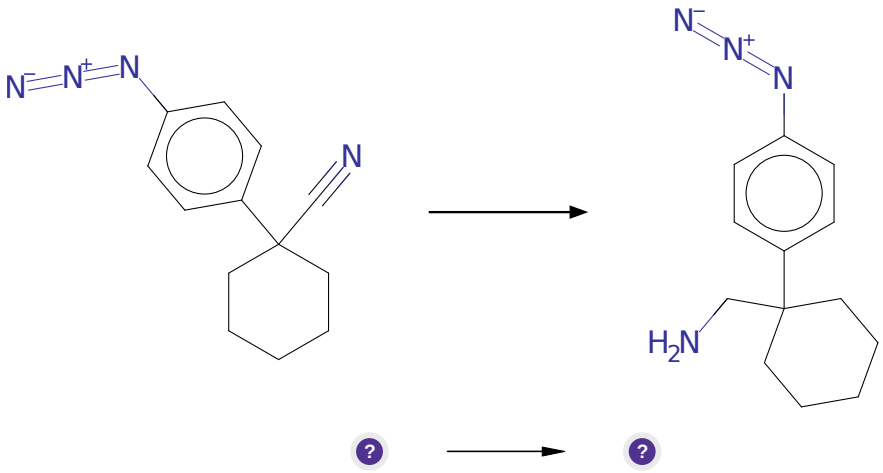
Protections: none

Yield: good

Reference: *10.1016/j.tet.2006.08.018* and *10.1021/jo051737f*

Retrosynthesis ID: 31010741

2.1.2 Reduction of cyanides to amines



Substrates:

1. N#CC1(c2ccc(N=[N+]=[N-])cc2)CCCCC1

Products:

1. [N-]=[N+]=Nc1ccc(C2(CN)CCCCC2)cc1

Typical conditions: CoCl2.NaBH4

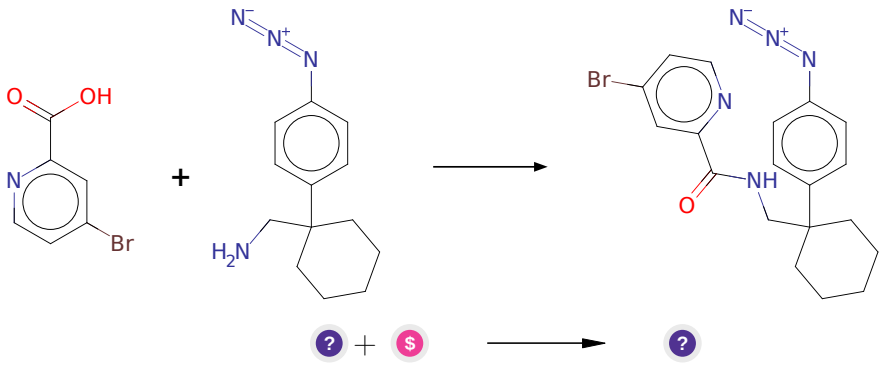
Protections: none

Yield: good

Reference: *10.1021/ol202535f*

Retrosynthesis ID: 9900034

2.1.3 Amide coupling



Substrates:

1. [N-]=[N+]=Nc1ccc(C2(CN)CCCCC2)cc1
2. 4-Bromopyridine-2-carboxylic acid - *available at Sigma-Aldrich*

Products:

1. [N-]=[N+]=Nc1ccc(C2(CNC(=O)c3cc(Br)ccn3)CCCCC2)cc1

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

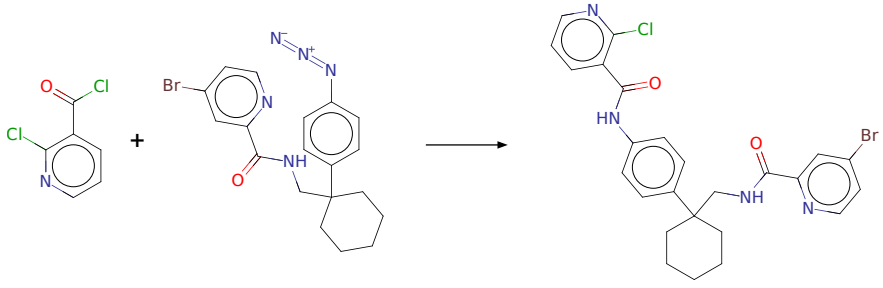
Protections: none

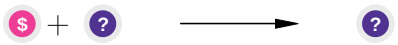
Yield: good

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 Synthesis of amides from azides





Substrates:

1. 2-Chloronicotinoyl chloride - *available at Sigma-Aldrich*
2. [N-]=[N+]=Nc1ccc(C2(CNC(=O)c3cc(Br)ccn3)CCCCC2)cc1

Products:

1. O=C(NCC1(c2ccc(NC(=O)c3cccnc3Cl)cc2)CCCCC1)c1cc(Br)ccn1

Typical conditions: PPh3.DCM

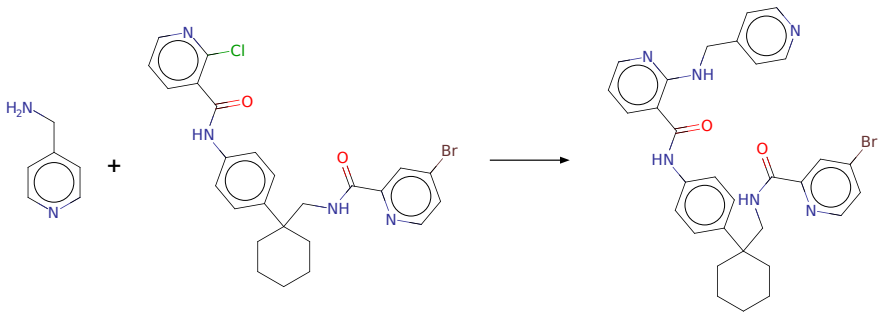
Protections: none

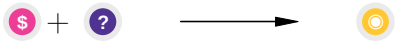
Yield: moderate

Reference: *10.1021/jo026687i* AND *10.1002/cbic.200900617* AND *10.1016/j.carres.2013.03.028*

Retrosynthesis ID: 15318

2.1.5 Nucleophilic aromatic substitution





Substrates:

1. 4-Picolylamine - *available at Sigma-Aldrich*
2. O=C(NCC1(c2ccc(NC(=O)c3cccnc3Cl)cc2)CCCCC1)c1cc(Br)ccn1

Products:

1. O=C(NCC1(c2ccc(NC(=O)c3cccnc3NCc3ccncc3)cc2)CCCCC1)c1cc(Br)ccn1

Typical conditions: solvent. Heating or pressure

Protections: none

Yield: good

Reference: *10.1021/jm00040a009* or *10.1111/bph.12233* or *10.1246/cl.1987.1187*

Retrosynthesis ID: 5003

2.2 Path 2

Score: `173.62`

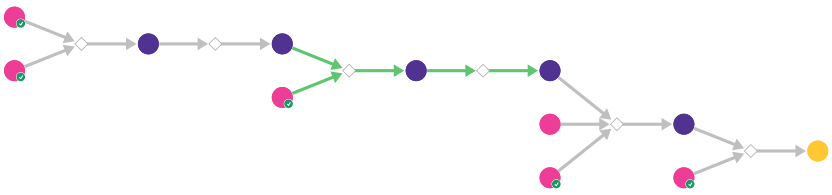
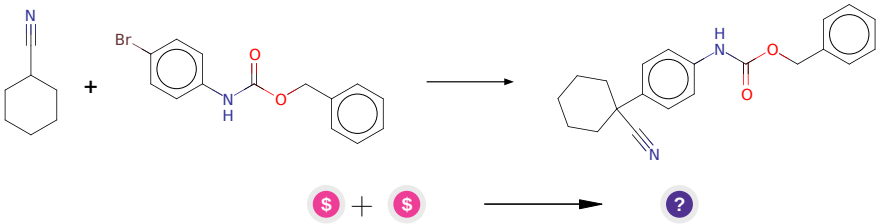


Figure 2: Outline of path 2

2.2.1 Arylation of nitriles with aryl bromides



Substrates:

1. Cyclohexanecarbonitrile - *available at Sigma-Aldrich*
2. benzyl 4-bromophenylcarbamate - *available at Sigma-Aldrich*

Products:

1. N#CC1(c2ccc(NC(=O)OCc3ccccc3)cc2)CCCCC1

Typical conditions: [Pd].catalyst.phosphine.base.heat

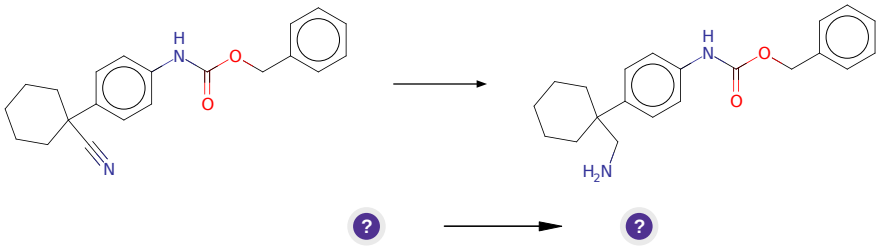
Protections: none

Yield: good

Reference: *10.1021/jo034779h* and *10.1002/ejoc.201402466* and *10.1021/ol503213z* and *10.1021/ja026584h* and *10.1021/ja0157402*

Retrosynthesis ID: 10017389

2.2.2 Reduction of cyanides to amines



Substrates:

1. N#CC1(c2ccc(NC(=O)OCc3ccccc3)cc2)CCCCC1

Products:

1. NCC1(c2ccc(NC(=O)OCc3ccccc3)cc2)CCCCC1

Typical conditions: CoCl2.NaBH4

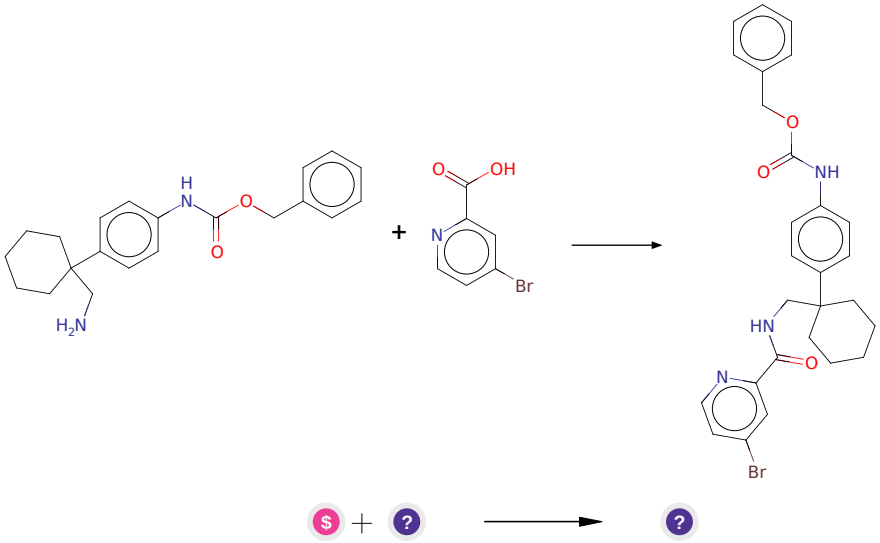
Protections: none

Yield: good

Reference: *10.1021/ol202535f*

Retrosynthesis ID: 9900034

2.2.3 Amide coupling



Substrates:

1. 4-Bromopyridine-2-carboxylic acid - *available at Sigma-Aldrich*
2. NCC1(c2ccc(NC(=O)OCc3ccccc3)cc2)CCCCC1

Products:

1. O=C(Nc1ccc(C2(CNC(=O)c3cc(Br)ccn3)CCCCC2)cc1)OCc1ccccc1

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

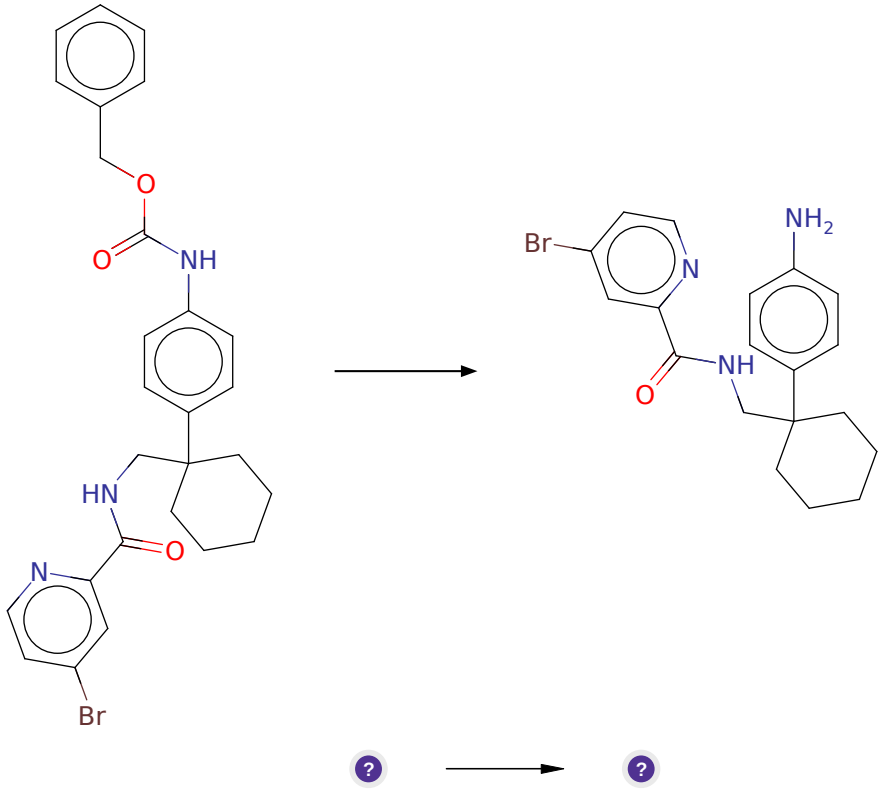
Protections: none

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

2.2.4 Cleavage of benzyloxycarbamates



Substrates:

1. O=C(Nc1ccc(C2(CNC(=O)c3cc(Br)ccn3)CCCCC2)cc1)OCc1ccccc1

Products:

1. Nc1ccc(C2(CNC(=O)c3cc(Br)ccn3)CCCCC2)cc1

Typical conditions: H2.Pd/C

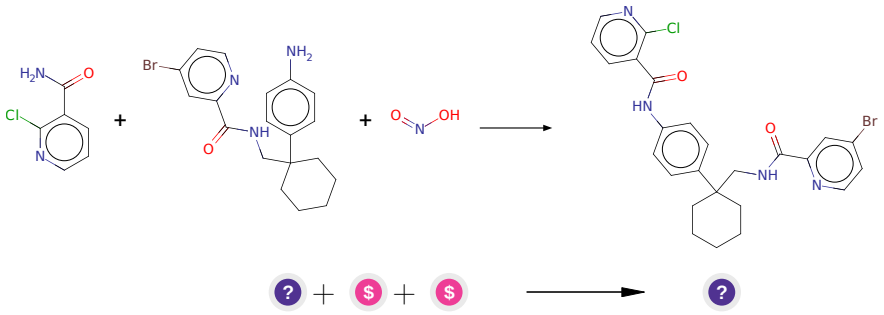
Protections: none

Yield: moderate

Reference: *10.1016/j.bmcl.2010.04.042* and *10.1016/j.tet.2011.07.090* and *10.1021/jacs.5b04988* and *10.1021/ja00062a020*

Retrosynthesis ID: 9990021

2.2.5 Synthesis of N-arylamides from arenediazonium salts



Substrates:

1. Nc1ccc(C2(CNC(=O)c3cc(Br)ccn3)CCCCC2)cc1
2. 2-Chloronicotinamide - *Combi-Blocks*
3. Calcium nitrite solution - *available at Sigma-Aldrich*

Products:

1. O=C(NCC1(c2ccc(NC(=O)c3cccnc3Cl)cc2)CCCCC1)c1cc(Br)ccn1

Typical conditions: 1) HCl.NaNO2 2) CuI.TBAI.N,N'-dimethylethane-1,2-diamine.K2CO3.DMSO.110C

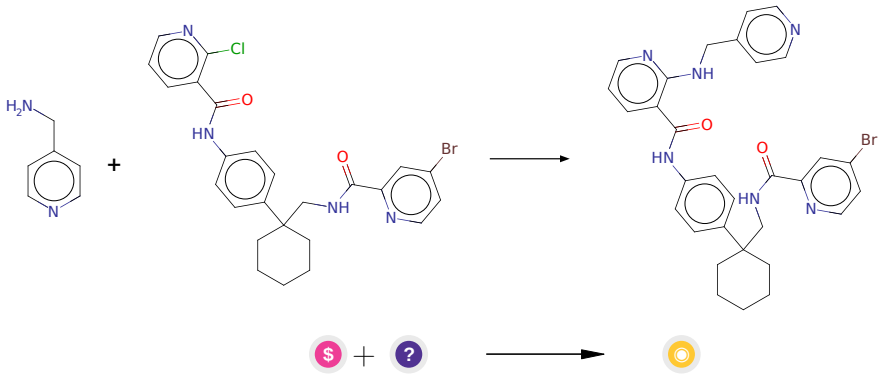
Protections: none

Yield: moderate

Reference: DOI: *10.1055/s-0034-1378556*

Retrosynthesis ID: 1922

2.2.6 Nucleophilic aromatic substitution



Substrates:

1. 4-Picolylamine - *available at Sigma-Aldrich*
2. O=C(NCC1(c2ccc(NC(=O)c3cccnc3Cl)cc2)CCCCC1)c1cc(Br)ccn1

Products:

1. O=C(NCC1(c2ccc(NC(=O)c3cccnc3NCc3ccncc3)cc2)CCCCC1)c1cc(Br)ccn1

Typical conditions: solvent. Heating or pressure

Protections: none

Yield: good

Reference: *10.1021/jm00040a009* or *10.1111/bph.12233* or *10.1246/cl.1987.1187*

Retrosynthesis ID: 5003