Paths of analysis*

C64

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

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

2.1 Path 1

Score: 103.76

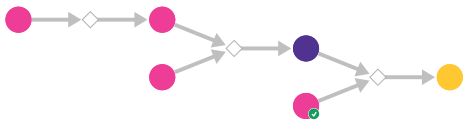
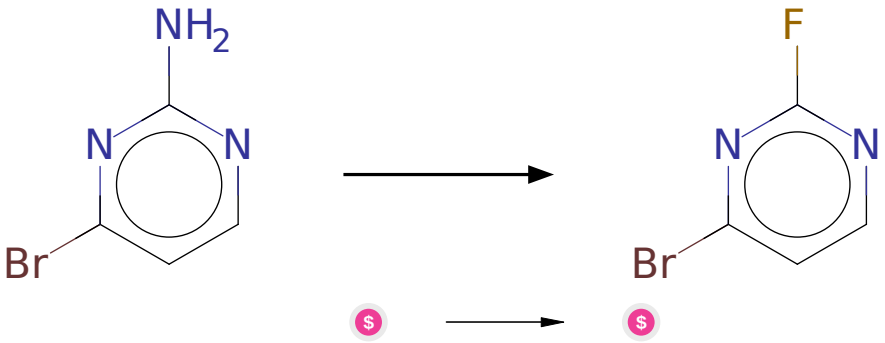


Figure 1: Outline of path 1

2.1.1 Balz-Schiemann Reaction



Substrates:

1. 4-Bromopyrimidin-2-amine - *Combi-Blocks*

Products:

1. 4-Bromo-2-fluoropyrimidine - *Enamine*

Typical conditions: NaNO2.HF-pyridine.-25 to 0C

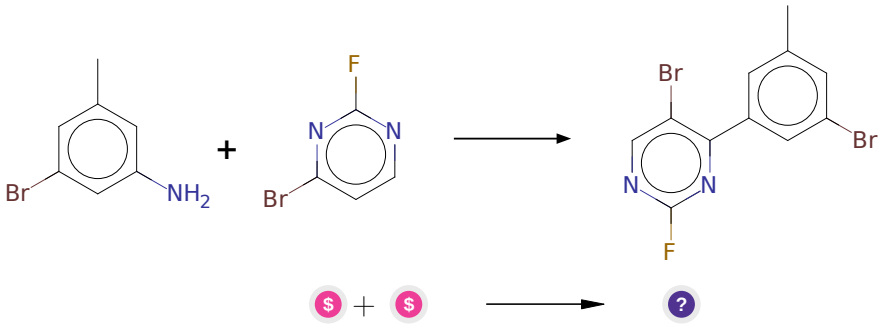
Protections: none

Yield: moderate

Reference: *10.1021/jm100432w* and *10.1021/jm5008177* and *10.1021/ol401540k* and *10.1021/jm401551n* (main text and SI, page S8) and *10.1515/chempap-2016-0033* and *10.1021/jm0311442* and *10.1016/j.jfluchem.2007.03.012* and *10.1021/jo00185a023*

Retrosynthesis ID: 29906

2.1.2 Meerwein coupling of diazonium salt with heteroaryl



Substrates:

1. 4-Bromo-2-fluoropyrimidine - *Enamine*
2. 3-Bromo-5-methylaniline - *Combi-Blocks*

Products:

1. Cc1cc(Br)cc(-c2nc(F)ncc2Br)c1

Typical conditions: 1) HCl.NaNO2 2) [Ru(bpy)3Cl2]*6H2O.45W bulb.H2O.rt

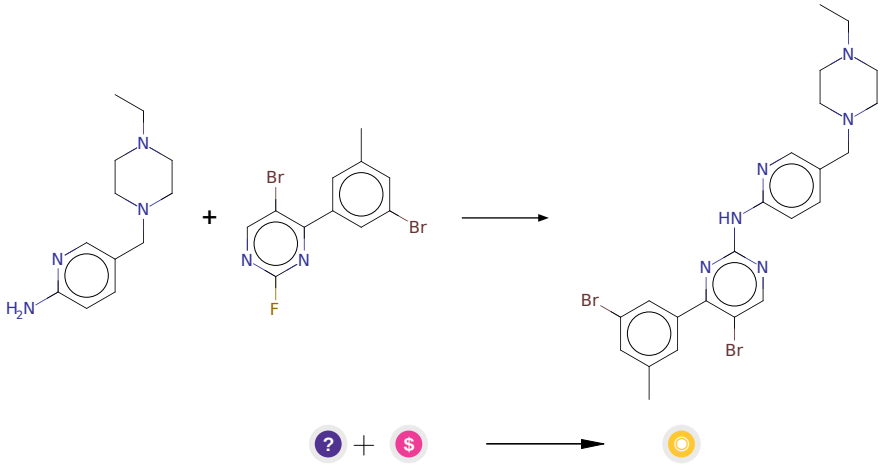
Protections: none

Yield: moderate

Reference: *10.1002/chem.201304120*

Retrosynthesis ID: 10001815

2.1.3 Nucleophilic aromatic substitution



Substrates:

1. Cc1cc(Br)cc(-c2nc(F)ncc2Br)c1
2. 5-((4-Ethylpiperazin-1-yl)methyl)pyridin-2-amine - *available at Sigma-Aldrich*

Products:

1. CCN1CCN(Cc2ccc(Nc3ncc(Br)c(-c4cc(C)cc(Br)c4)n3)nc2)CC1

Typical conditions: Solvent

Protections: none

Yield: good

Reference: *10.1002/9781118093559.ch4*

Retrosynthesis ID: 49476

2.2 Path 2

Score: `149.19`

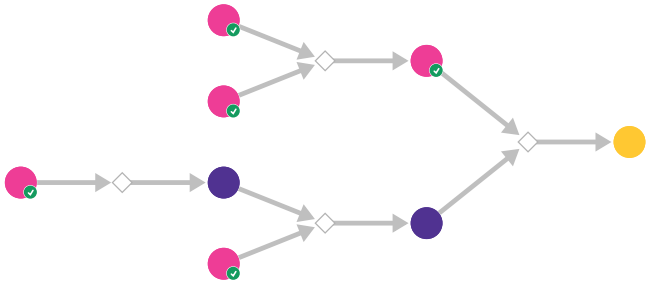
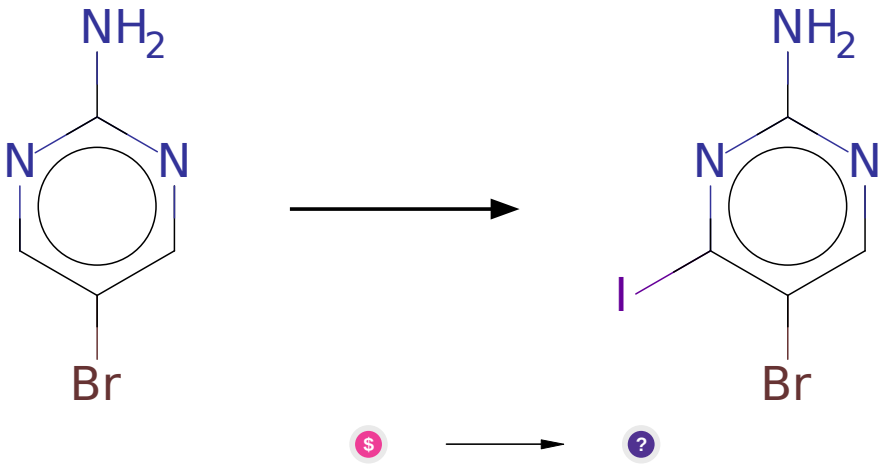


Figure 2: Outline of path 2

2.2.1 Iodination of aromatic compounds



Substrates:

1. 2-Amino-5-bromopyrimidine - *available at Sigma-Aldrich*

Products:

1. Nc1ncc(Br)c(I)n1

Typical conditions: I2 or other iodinating agent e.g. NIS

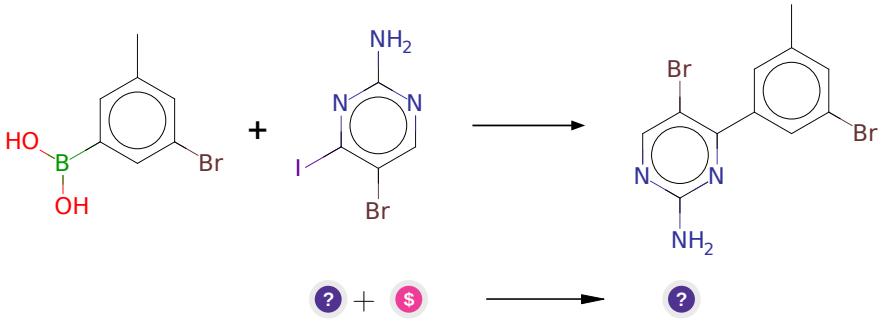
Protections: none

Yield: good

Reference: DOI: *10.1039/C5SC00964B* and *10.1016/j.tetlet.2005.05.117* and *10.1007/s11178-005-0256-1*

Retrosynthesis ID: 10697

2.2.2 Suzuki coupling of arylboronic acids with aryl iodides



Substrates:

1. Nc1ncc(Br)c(I)n1
2. 3-Bromo-5-methylphenylboronic acid - *available at Sigma-Aldrich*

Products:

1. Cc1cc(Br)cc(-c2nc(N)ncc2Br)c1

Typical conditions: Pd catalyst.base.solvent

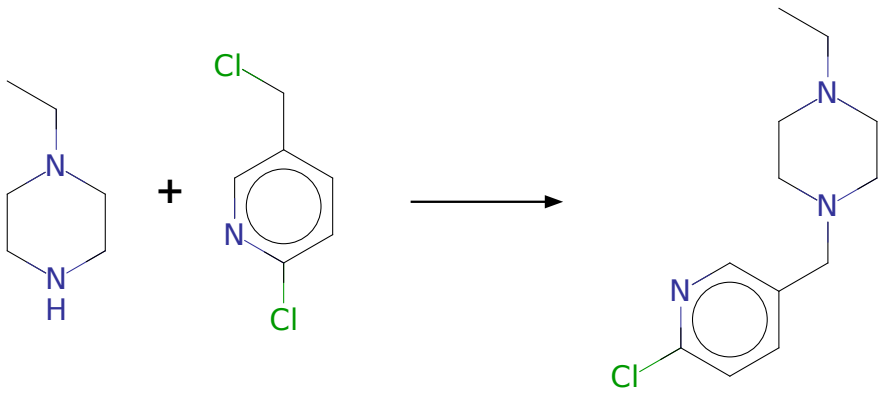
Protections: none

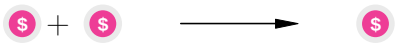
Yield: good

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 25149

2.2.3 Alkylation of amines with alkyl chlorides





Substrates:

1. 2-Chloro-5-(chloromethyl)pyridine - *available at Sigma-Aldrich*
2. 1-Ethylpiperazine - *available at Sigma-Aldrich*

Products:

1. 1-[(6-Chloropyridin-3-yl)methyl]-4-ethylpiperazine - *available at Sigma-Aldrich*

Typical conditions: KOH. toluene. PTC. catalyst or KI. base e.g. K2CO3

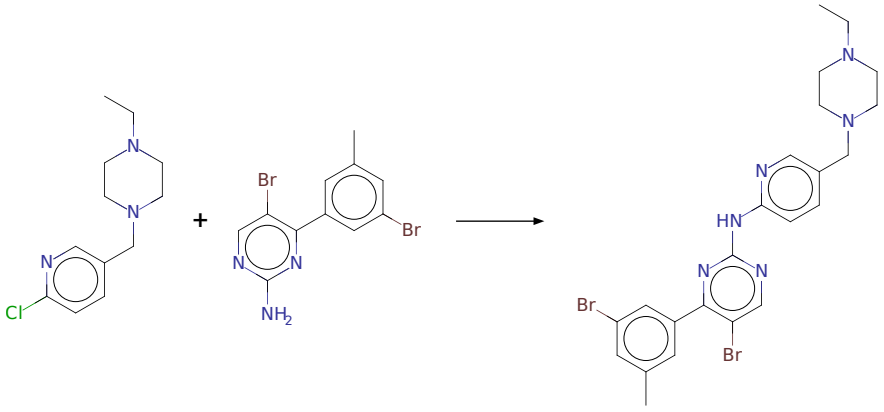
Protections: none

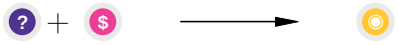
Yield: moderate

Reference: *10.1016/S0040-4020(01)00989-9* and *10.1021/acs.oprd.8b00074* and *10.1016/s0040-4039(00)74286-9* and *10.1080/00397911.2013.828077* and *10.1016/j.bmcl.2012.08.032*

Retrosynthesis ID: 4784

2.2.4 Nucleophilic aromatic substitution





Substrates:

1. Cc1cc(Br)cc(-c2nc(N)ncc2Br)c1
2. 1-[(6-Chloropyridin-3-yl)methyl]-4-ethylpiperazine - *available at Sigma-Aldrich*

Products:

1. CCN1CCN(Cc2ccc(Nc3ncc(Br)c(-c4cc(C)cc(Br)c4)n3)nc2)CC1

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