Paths of analysis*

C61

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: 140.27

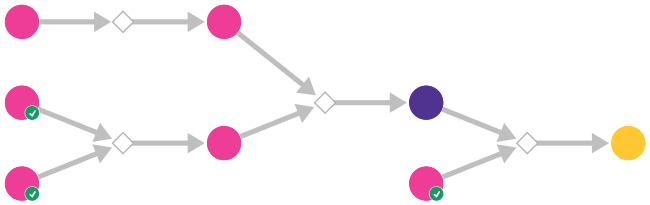
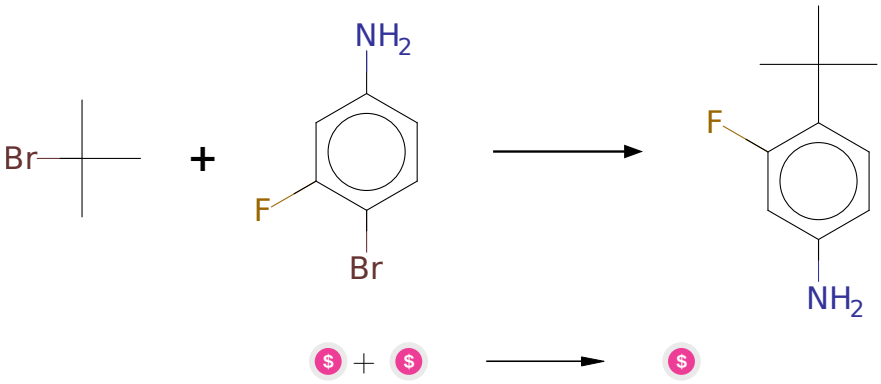


Figure 1: Outline of path 1

2.1.1 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. 4-Bromo-3-fluoroaniline - *available at Sigma-Aldrich*
2. tert-Butyl bromide - *available at Sigma-Aldrich*

Products:

1. 4-tert-butyl-3-fluoroaniline - *Enamine*

Typical conditions: [Ir]-photocat.[Ni]-cat.TTMSS.base.blue light

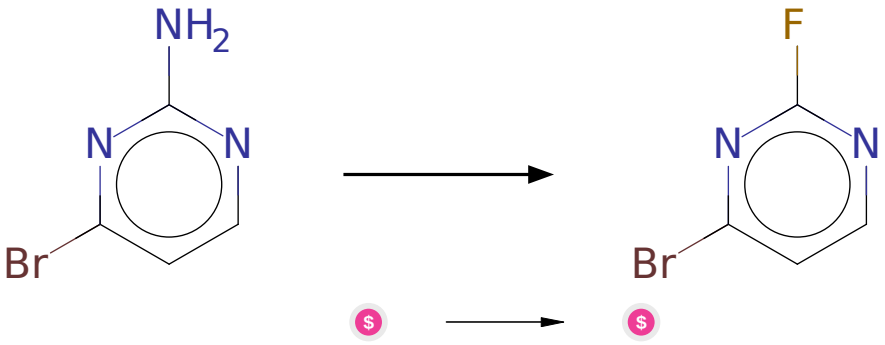
Protections: none

Yield: good

Reference: *10.1021/jacs.6b04818* and *10.1016/j.bbrc.2020.04.028* and *10.1021/acsmedchemlett.8b00183*

Retrosynthesis ID: 31016943

2.1.2 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

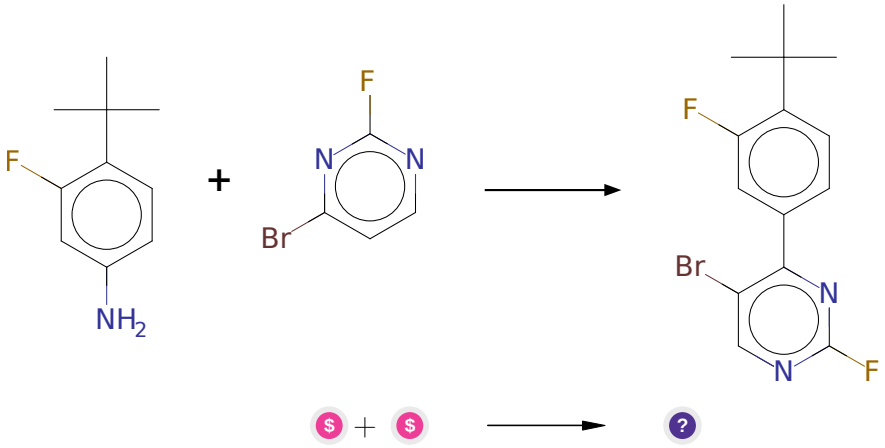
Protections: none

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

2.1.3 Meerwein coupling of diazonium salt with heteroaryl



Substrates:

1. 4-Bromo-2-fluoropyrimidine - *Enamine*
2. 4-tert-butyl-3-fluoroaniline - *Enamine*

Products:

1. CC(C)(C)c1ccc(-c2nc(F)ncc2Br)cc1F

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

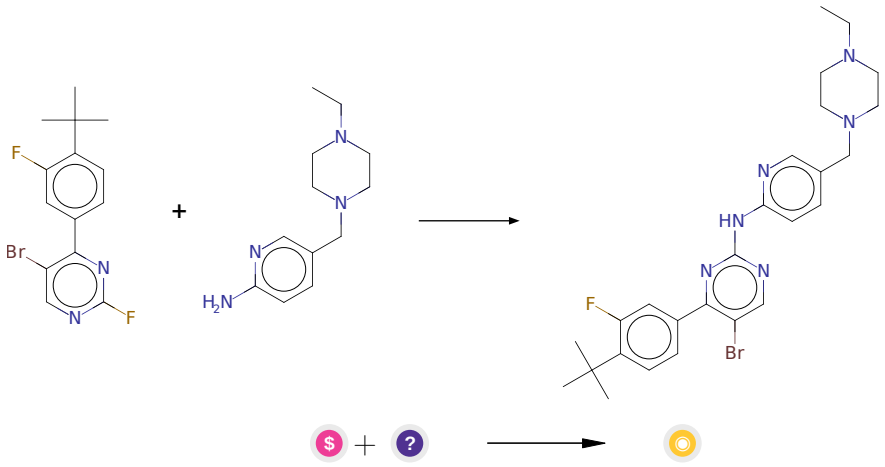
Protections: none

Yield: moderate

Reference: *10.1002/chem.201304120*

Retrosynthesis ID: 10001815

2.1.4 Nucleophilic aromatic substitution



Substrates:

1. 5-((4-Ethylpiperazin-1-yl)methyl)pyridin-2-amine - *available at Sigma-Aldrich*
2. CC(C)(C)c1ccc(-c2nc(F)ncc2Br)cc1F

Products:

1. CCN1CCN(Cc2ccc(Nc3ncc(Br)c(-c4ccc(C(C)(C)C)c(F)c4)n3)nc2)CC1

Typical conditions: Solvent

Protections: none

Yield: good

Reference: *10.1002/9781118093559.ch4*

Retrosynthesis ID: 49476

2.2 Path 2

Score: `176.29`

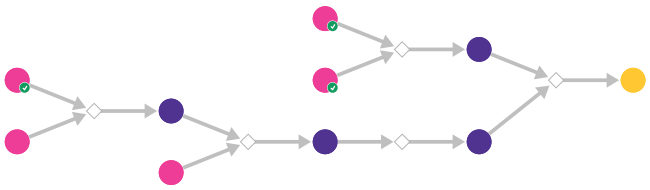
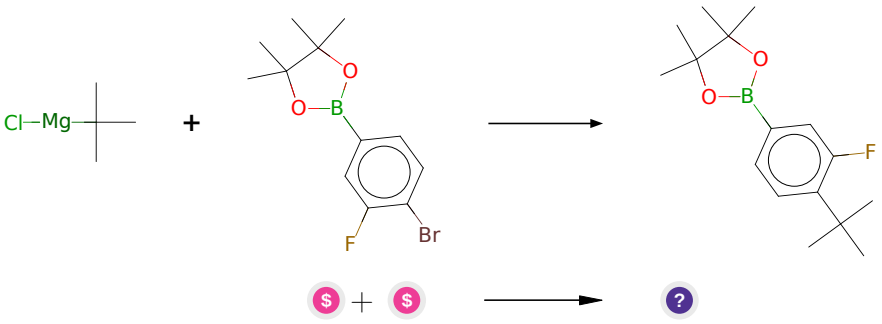


Figure 2: Outline of path 2

2.2.1 Kumada-Corriu reaction



Substrates:

1. tert-Butylmagnesium chloride solution - *available at Sigma-Aldrich*
2. 4-Bromo-3-fluorophenylboronic acid pinacol ester - *AOBChem*

Products:

1. CC(C)(C)c1ccc(B2OC(C)(C)C(C)(C)O2)cc1F

Typical conditions: NiCl2xH2O.-10C.THF.IL

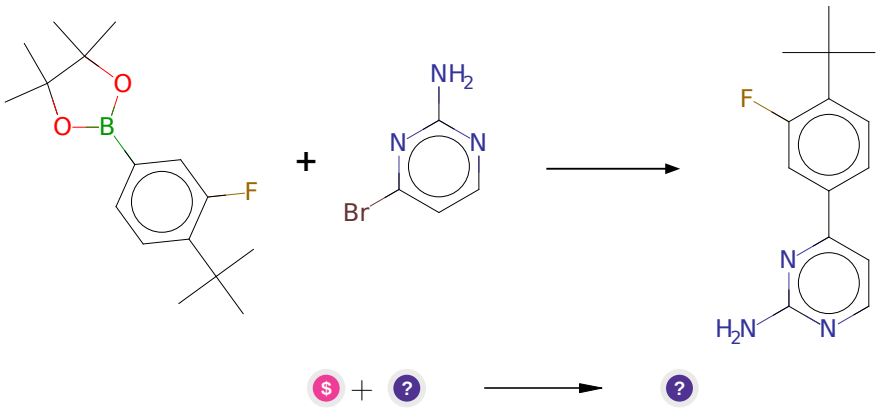
Protections: none

Yield: moderate

Reference: DOI: *10.1021/ja202769t*

Retrosynthesis ID: 1959

2.2.2 Suzuki coupling of arylboronic acids pinacol esters with aryl bromides



Substrates:

1. 4-Bromopyrimidin-2-amine - *Combi-Blocks*
2. CC(C)(C)c1ccc(B2OC(C)(C)C(C)(C)O2)cc1F

Products:

1. CC(C)(C)c1ccc(-c2ccnc(N)n2)cc1F

Typical conditions: Pd catalyst.base.solvent

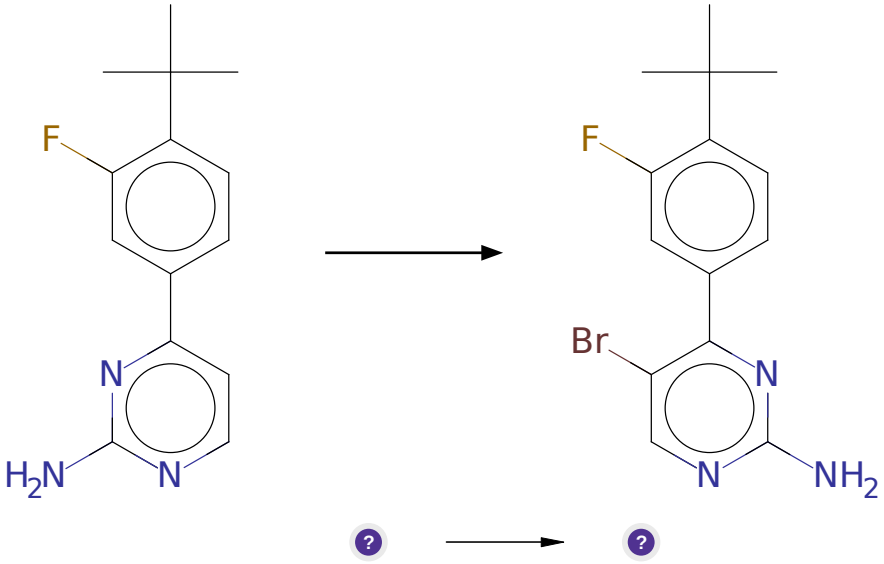
Protections: none

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: 25153

2.2.3 Bromination of aromatic compounds



Substrates:

1. CC(C)(C)c1ccc(-c2ccnc(N)n2)cc1F

Products:

1. CC(C)(C)c1ccc(-c2nc(N)ncc2Br)cc1F

Typical conditions: Br2.Fe

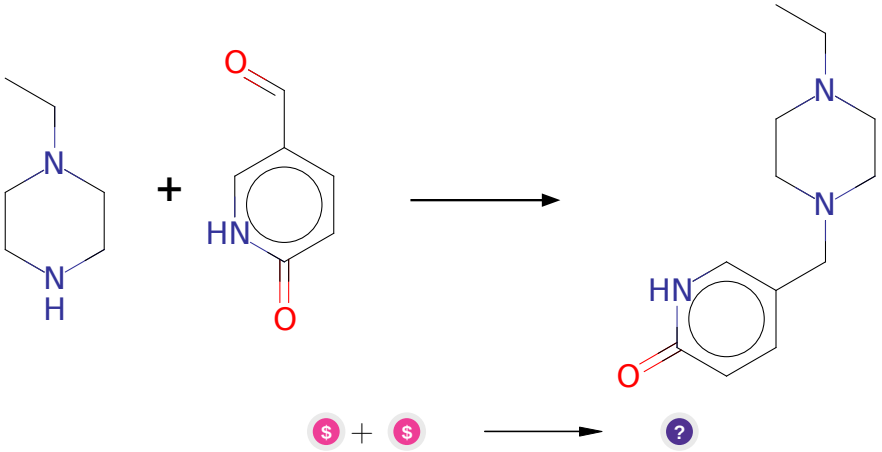
Protections: none

Yield: good

Reference: *10.1021/acs.accounts.6b00120*

Retrosynthesis ID: 7777000

2.2.4 Reductive Amination of Aldehydes with Secondary Amines



Substrates:

1. 6-Oxo-1,6-dihydropyridine-3-carbaldehyde - *available at Sigma-Aldrich*
2. 1-Ethylpiperazine - *available at Sigma-Aldrich*

Products:

1. CCN1CCN(Cc2ccc(=O)[nH]c2)CC1

Typical conditions: NaBH(OAc)3 or NaBH3CN

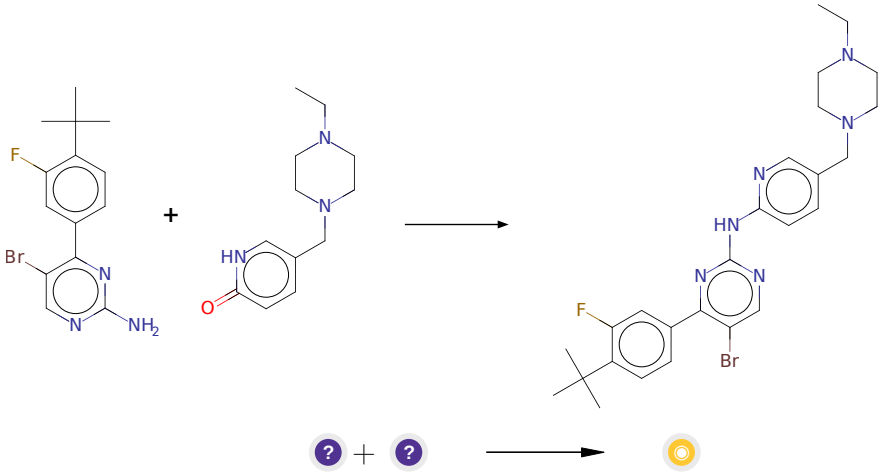
Protections: none

Yield: good

Reference: DOI: *10.1021/jo960057x* and *10.1021/jm7009292* and *10.1073/pnas.1405685111* and *10.1002/ejoc.201101063* and *10.1038/ja.2017.61* and *10.1021/jm4013906*

Retrosynthesis ID: 10019705

2.2.5 Amination of pyridones



Substrates:

1. CCN1CCN(Cc2ccc(=O)[nH]c2)CC1
2. CC(C)(C)c1ccc(-c2nc(N)ncc2Br)cc1F

Products:

1. CCN1CCN(Cc2ccc(Nc3ncc(Br)c(-c4ccc(C(C)(C)C)c(F)c4)n3)nc2)CC1

Typical conditions: 1.PCl5.2.amine

Protections: none

Yield: moderate

Reference: *10.1021/jm300780p* AND *10.3390/molecules170910902* AND *10.1021/jm00392a017*

Retrosynthesis ID: 14886