Paths of analysis*

C57

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: 172.08

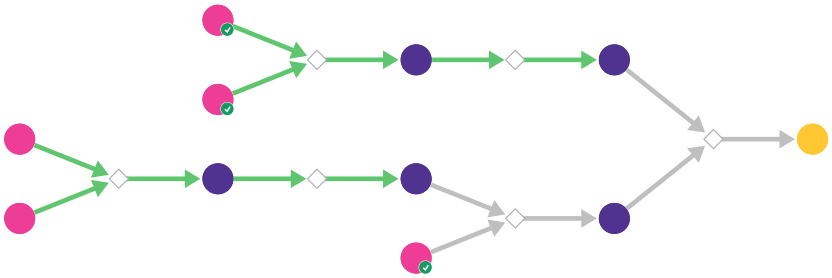
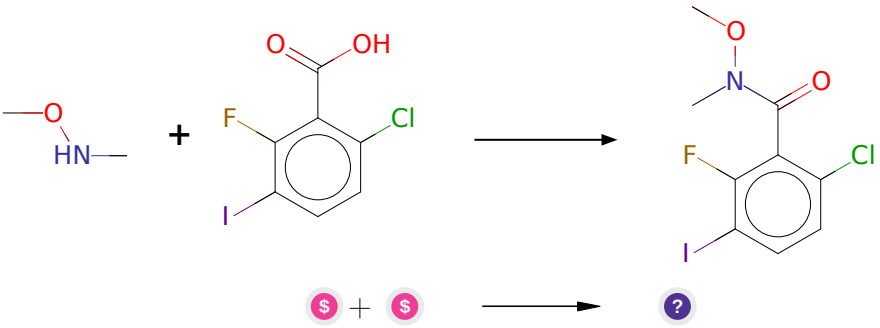


Figure 1: Outline of path 1

2.1.1 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. 6-Chloro-2-fluoro-3-iodobenzoic acid - *AOBChem*
2. n-methoxymethylamine - *ChemImpexInternational*

Products:

1. CON(C)C(=O)c1c(Cl)ccc(I)c1F

Typical conditions: DCC.DMAP or CDI.TEA.DCM

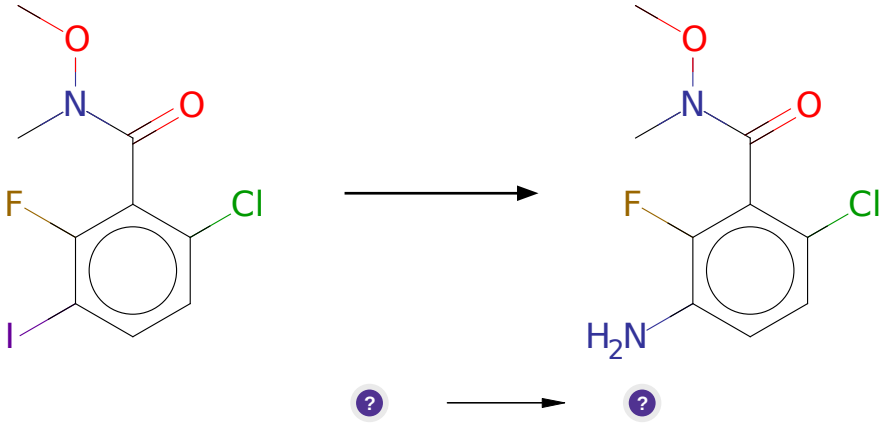
Protections: none

Yield: good

Reference: Patent: WO2007/67333A2, 2007 & *10.1016/j.bmcl.2008.09.100*

Retrosynthesis ID: 1152

2.1.2 Coupling of Ammonia with Aryl Halides



Substrates:

1. CON(C)C(=O)c1c(Cl)ccc(I)c1F

Products:

1. CON(C)C(=O)c1c(Cl)ccc(N)c1F

Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

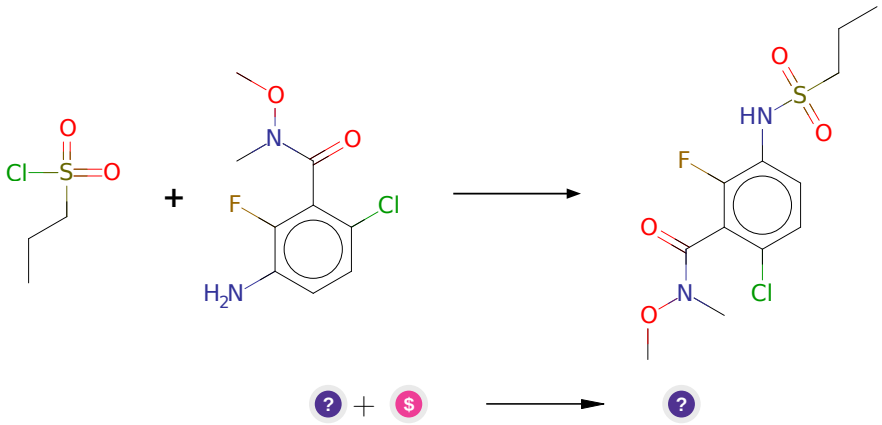
Protections: none

Yield: good

Reference: *10.1021/ja903049z* and *10.1021/jo9006738*

Retrosynthesis ID: 31016464

2.1.3 N-Sulfonylation



Substrates:

1. CON(C)C(=O)c1c(Cl)ccc(N)c1F
2. 1-Propanesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=O)N(C)OC)c1F

Typical conditions: THF.rt

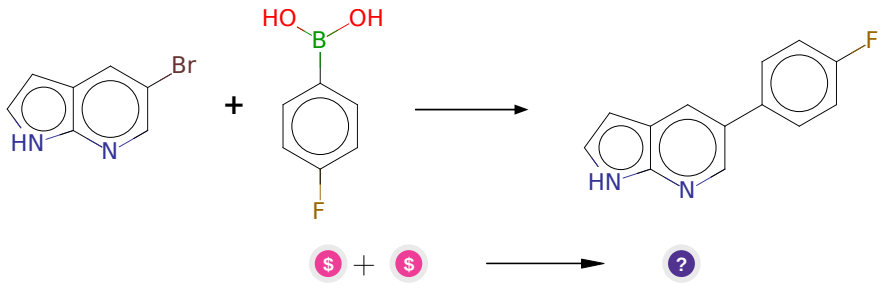
Protections: none

Yield: good

Reference: *10.1055/s-0029-1217565* and *10.1002/(SICI)1099-0690(199806)1998:6<945::AID-EJOC945>3.0.CO;2-3* and *10.1055/s-2001-14567* and *10.1016/j.bmc.2014.07.022*

Retrosynthesis ID: 14717

2.1.4 Suzuki coupling of arylboronic acids with aryl bromides



Substrates:

1. 5-Bromo-7-azaindole - *available at Sigma-Aldrich*
2. (p-Fluorophenyl)boric acid - *available at Sigma-Aldrich*

Products:

1. Fc1ccc(-c2cnc3[nH]ccc3c2)cc1

Typical conditions: Pd catalyst.base.solvent

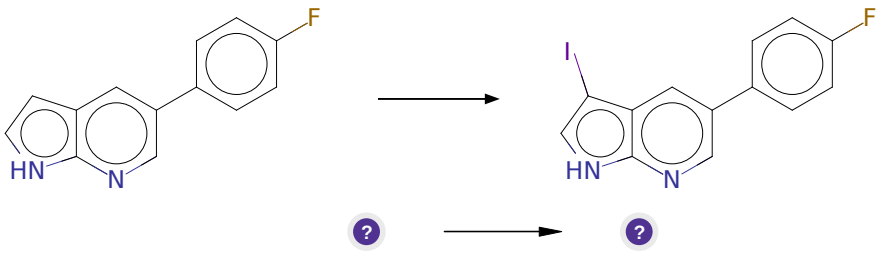
Protections: none

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* and *10.1016/j.ejmech.2018.08.092* and *10.1038/s41929-020-00564-z* (metal-free coupling)

Retrosynthesis ID: 25150

2.1.5 Iodination of aromatic compounds



Substrates:

1. Fc1ccc(-c2cnc3[nH]ccc3c2)cc1

Products:

1. Fc1ccc(-c2cnc3[nH]cc(I)c3c2)cc1

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

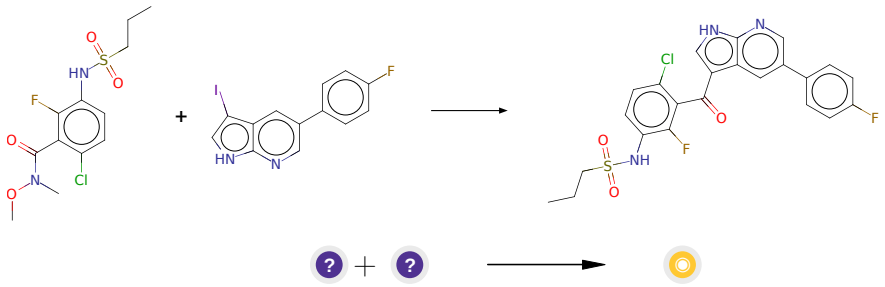
Protections: none

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

2.1.6 Synthesis of ketones from Weinreb amides



Substrates:

1. Fc1ccc(-c2cnc3[nH]cc(I)c3c2)cc1
2. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=O)N(C)OC)c1F

Products:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=O)c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Typical conditions: 1.RmgBr.THF 2.TFA.DCM

Protections: none

Yield: good

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 5060

2.2 Path 2

Score: `371.84`

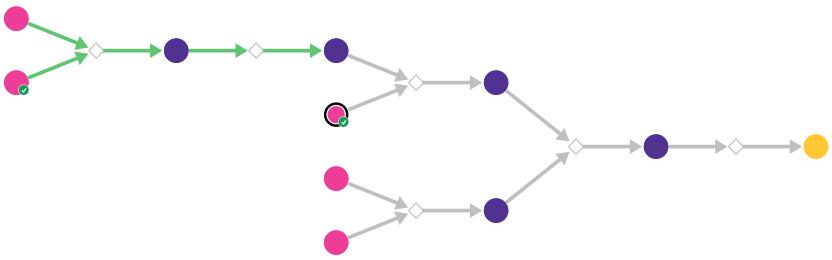
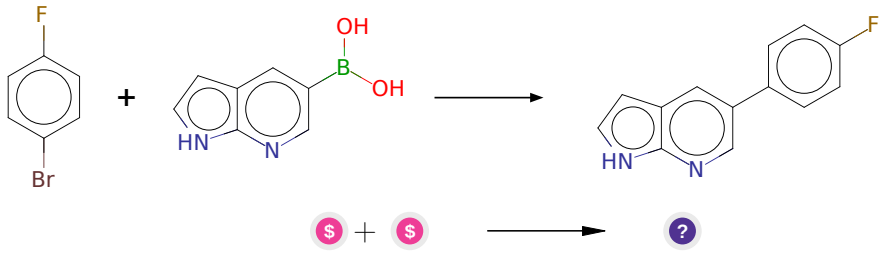


Figure 2: Outline of path 2

2.2.1 Suzuki coupling of arylboronic acids with aryl bromides



Substrates:

1. (1H-Pyrrolo[2,3-b]pyridin-5-yl)boronic acid - *Combi-Blocks*
2. 4-Bromofluorobenzene - *available at Sigma-Aldrich*

Products:

1. Fc1ccc(-c2cnc3[nH]ccc3c2)cc1

Typical conditions: Pd catalyst.base.solvent

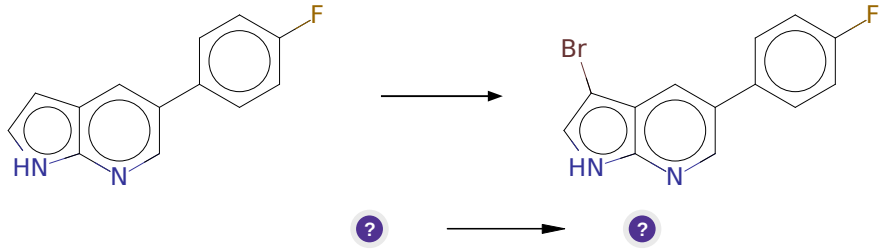
Protections: none

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* and *10.1016/j.ejmech.2018.08.092* and *10.1038/s41929-020-00564-z* (metal-free coupling)

Retrosynthesis ID: 25150

2.2.2 Bromination of aromatic compounds



Substrates:

1. Fc1ccc(-c2cnc3[nH]ccc3c2)cc1

Products:

1. Fc1ccc(-c2cnc3[nH]cc(Br)c3c2)cc1

Typical conditions: Br2.Fe

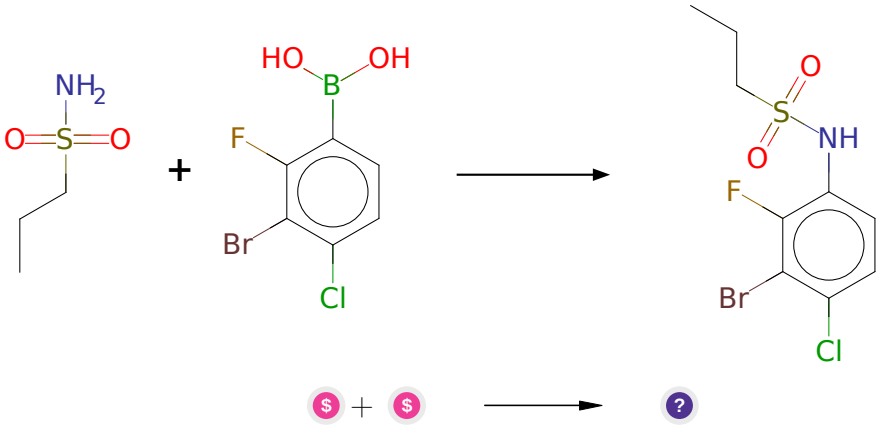
Protections: none

Yield: good

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

Retrosynthesis ID: 7777000

2.2.3 Chan-Lam Coupling



Substrates:

1. Propane-1-sulfonamide - *Combi-Blocks*
2. 3-Bromo-4-chloro-2-fluorophenylboronic acid - *Combi-Blocks*

Products:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(Br)c1F

Typical conditions: Cu(OAc)2.K2CO3.H2O or Cu(OAc)2.pyridine.DCM.MS 4A

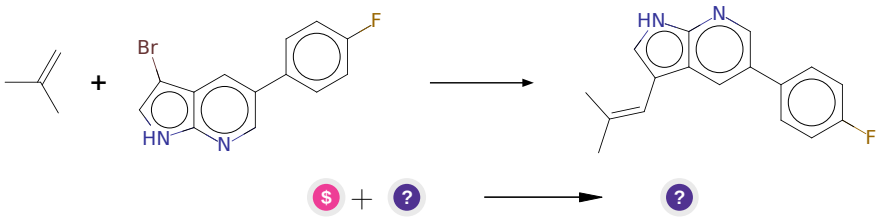
Protections: none

Yield: good

Reference: *10.1016/j.molcata.2014.02.017* and *10.1039/C4RA08137D* and WO2008073956 p.88

Retrosynthesis ID: 31015970

2.2.4 Heck Reaction



Substrates:

1. Isobutylene - *available at Sigma-Aldrich*
2. Fc1ccc(-c2cnc3[nH]cc(Br)c3c2)cc1

Products:

1. CC(C)=Cc1c[nH]c2ncc(-c3ccc(F)cc3)cc12

Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

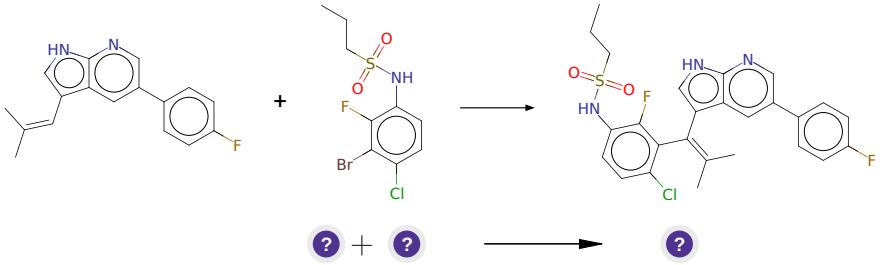
Protections: none

Yield: moderate

Reference: *10.1039/C3GC40493E* *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9177

2.2.5 Heck Reaction



Substrates:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(Br)c1F
2. CC(C)=Cc1c[nH]c2ncc(-c3ccc(F)cc3)cc12

Products:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=C(C)C)c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

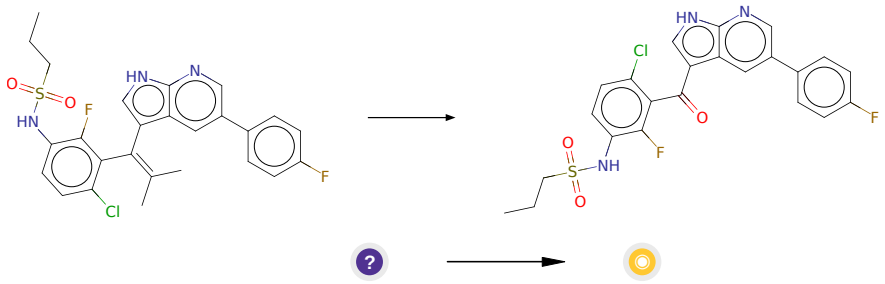
Protections: none

Yield: good

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1021/ja508165a* *10.3390/molecules16108353* or *10.1039/C3GC40493E* *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9174

2.2.6 Ozonolysis



Substrates:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=C(C)C)c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Products:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=O)c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

Protections: none

Yield: good

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5079