Paths of analysis*

C130

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: 173.72

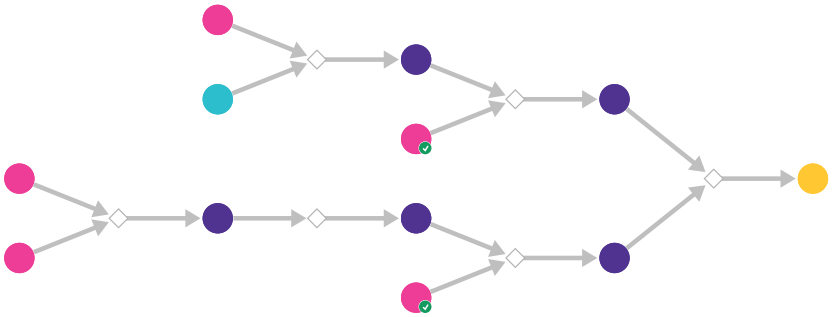
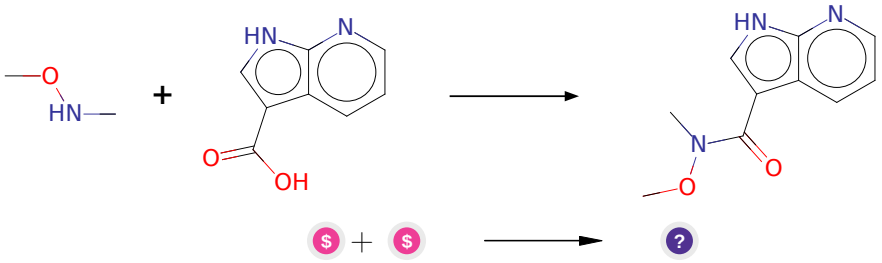


Figure 1: Outline of path 1

2.1.1 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. n-methoxymethylamine - *ChemImpexInternational*
2. 7-Azaindole-3-carboxylic acid - *Combi-Blocks*

Products:

1. CON(C)C(=O)c1c[nH]c2ncccc12

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

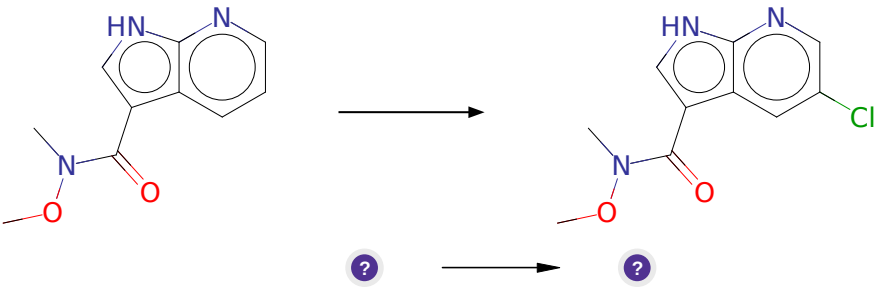
Protections: none

Yield: good

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

Retrosynthesis ID: 1152

2.1.2 Chlorination of aromatic compounds



Substrates:

1. CON(C)C(=O)c1c[nH]c2ncccc12

Products:

1. CON(C)C(=O)c1c[nH]c2ncc(Cl)cc12

Typical conditions: Cl2 or other chlorinating agent like NCS

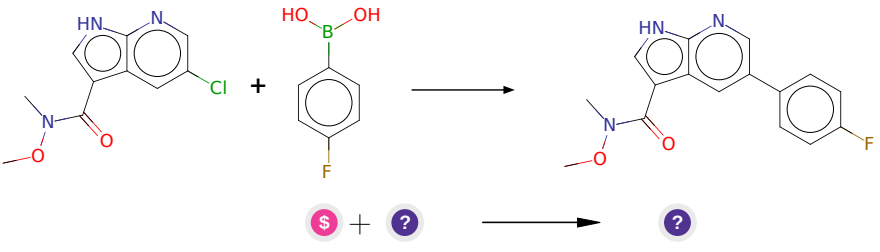
Protections: none

Yield: moderate

Reference: DOI: *10.1007/s11178-005-0256-1*

Retrosynthesis ID: 11125

2.1.3 Suzuki coupling with aryl chlorides



Substrates:

1. (p-Fluorophenyl)boric acid - *available at Sigma-Aldrich*
2. CON(C)C(=O)c1c[nH]c2ncc(Cl)cc12

Products:

1. CON(C)C(=O)c1c[nH]c2ncc(-c3ccc(F)cc3)cc12

Typical conditions: [Pd].catalyst.base.

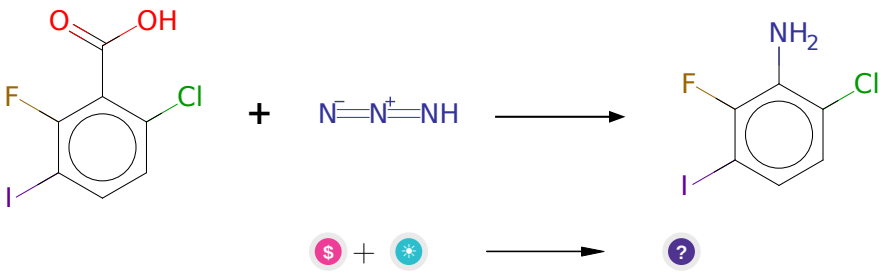
Protections: none

Yield: good

Reference: *10.1002/anie.201108608* and *10.1002/anie.200801465* and *10.1055/s-0033-1338293* and *10.1039/c1cc10708a* and *10.1055/s-0030-1260169* and *10.1016/j.tet.2005.05.071* and *10.1038/s41929-020-00564-z* (metal-free coupling)

Retrosynthesis ID: 26284

2.1.4 Schmidt Reaction



Substrates:

1. 6-Chloro-2-fluoro-3-iodobenzoic acid - *AOBChem*
2. hydrazoic acid

Products:

1. Nc1c(Cl)ccc(I)c1F

Typical conditions: azide.H+.40C

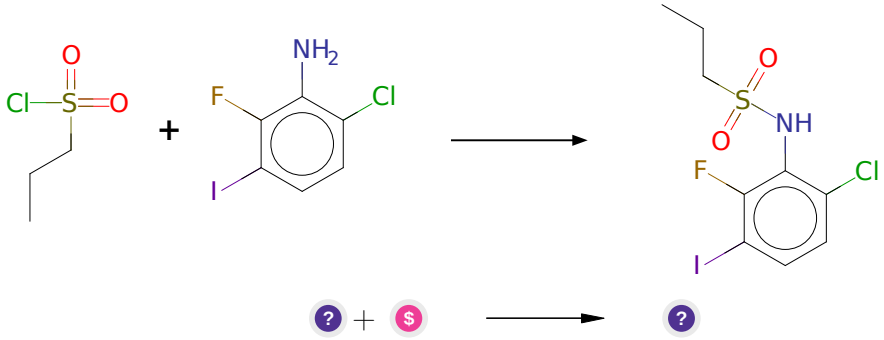
Protections: none

Yield: moderate

Reference: *10.1039/B505080D*

Retrosynthesis ID: 10953

2.1.5 N-Sulfonylation



Substrates:

1. Nc1c(Cl)ccc(I)c1F
2. 1-Propanesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(I)c1F

Typical conditions: THF.rt

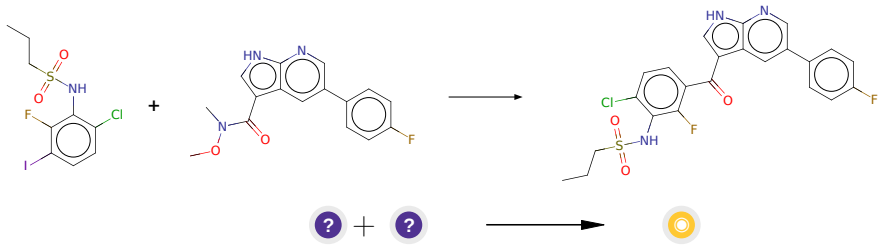
Protections: none

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

2.1.6 Synthesis of ketones from Weinreb amides



Substrates:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(I)c1F

2. CON(C)C(=O)c1c[nH]c2ncc(-c3ccc(F)cc3)cc12

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(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: `236.18`

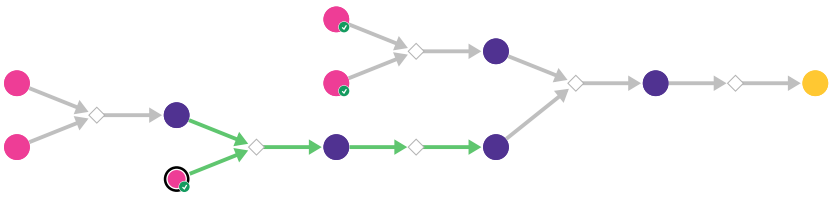
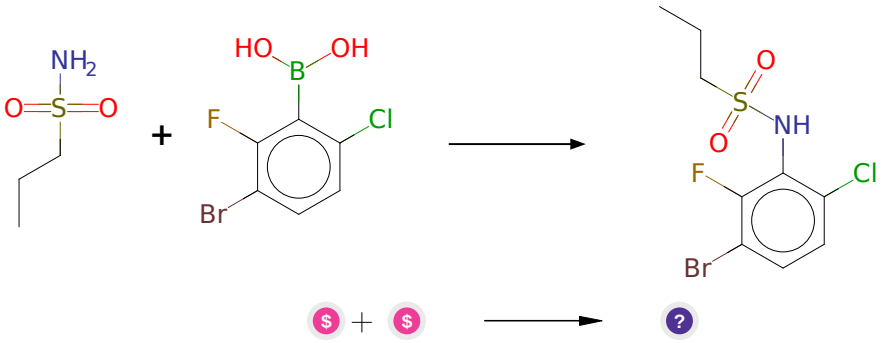


Figure 2: Outline of path 2

2.2.1 Chan-Lam Coupling



Substrates:

1. Propane-1-sulfonamide - *Combi-Blocks*

2. 3-Bromo-6-Chloro-2-fluorophenylboronic acid - *AOBChem*

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(Br)c1F

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

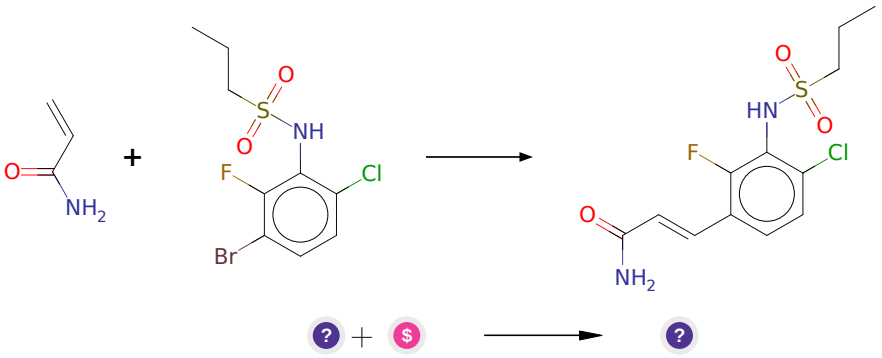
Protections: none

Yield: good

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

Retrosynthesis ID: 31015970

2.2.2 Heck Reaction



Substrates:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(Br)c1F
2. Acrylamide - *available at Sigma-Aldrich*

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(/C=C/C(N)=O)c1F

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

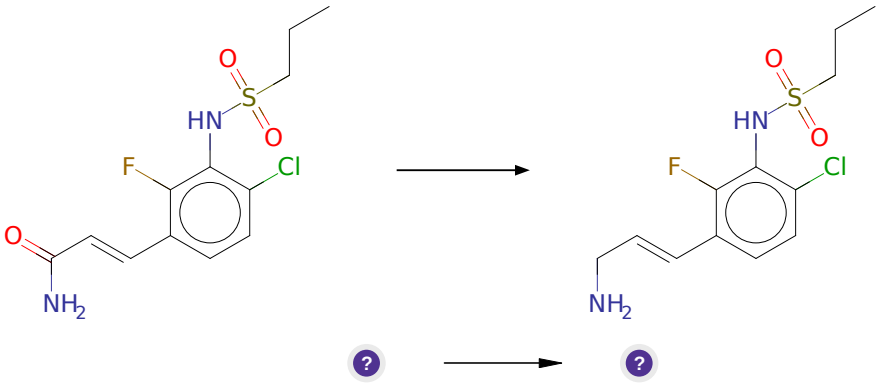
Protections: none

Yield: good

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

Retrosynthesis ID: 9180

2.2.3 Reduction of Amides to Amines



Substrates:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(/C=C/C(N)=O)c1F

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(/C=C/CN)c1F

Typical conditions: LAH.ether.H+.H20

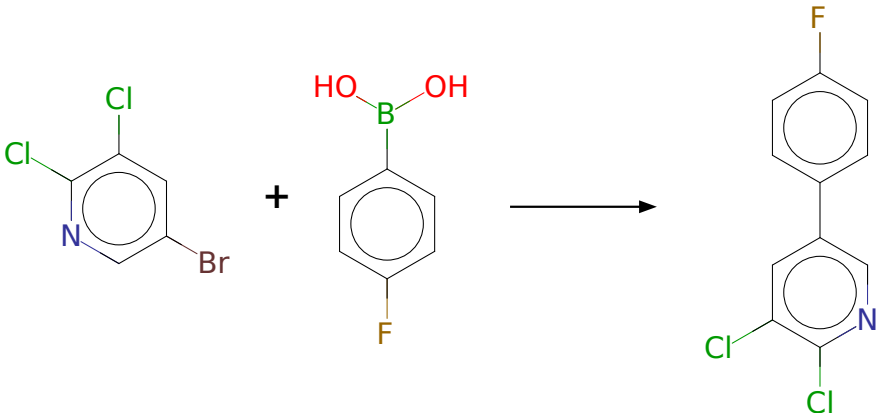
Protections: none

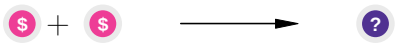
Yield: good

Reference: *10.1021/jo0349633* and *10.1021/op990019q* and *10.1021/op200181f* and *10.1021/op2003826*

Retrosynthesis ID: 10259

2.2.4 Suzuki coupling of arylboronic acids with aryl bromides





Substrates:

1. (p-Fluorophenyl)boric acid - *available at Sigma-Aldrich*
2. 5-Bromo-2,3-dichloropyridine - *available at Sigma-Aldrich*

Products:

1. Fc1ccc(-c2cnc(Cl)c(Cl)c2)cc1

Typical conditions: Pd catalyst.base.solvent

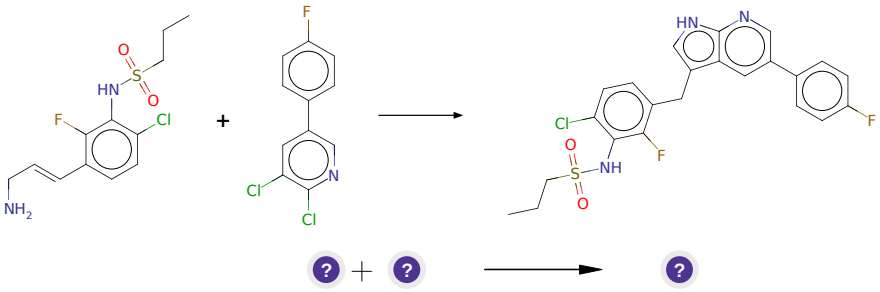
Protections: none

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

2.2.5 Heck-type synthesis of indoles



Substrates:

1. Fc1ccc(-c2cnc(Cl)c(Cl)c2)cc1
2. CCCS(=O)(=O)Nc1c(Cl)ccc(/C=C/CN)c1F

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(Cc2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Typical conditions: Pd2dba3.dppf.NaOtBu.PhMe.140C

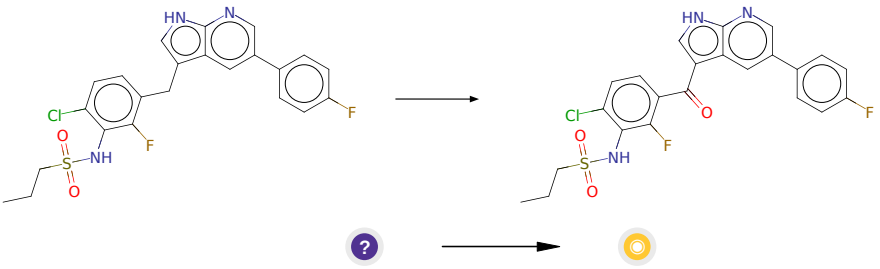
Protections: none

Yield: good

Reference: *10.1002/anie.200703763*

Retrosynthesis ID: 28942

2.2.6 Benzylic oxidation to ketone



Substrates:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(Cc2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Products:

1. CCCS(=O)(=O)Nc1c(Cl)ccc(C(=O)c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1F

Typical conditions: oxidant eg. Oxone or O2 or K2S2O8

Protections: none

Yield: moderate

Reference: *10.1021/ol300853z* and *10.1021/ol0520020* and *10.1055/s-0037-1610678* and *10.1021/acs.orglett.6b02914*

Retrosynthesis ID: 7201