Paths of analysis*

C51

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

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

2.1 Path 1

Score: `159.67`

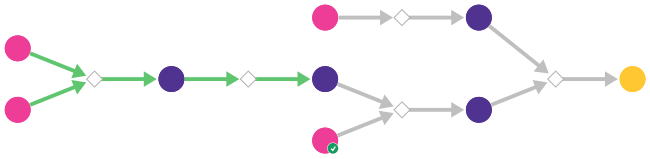
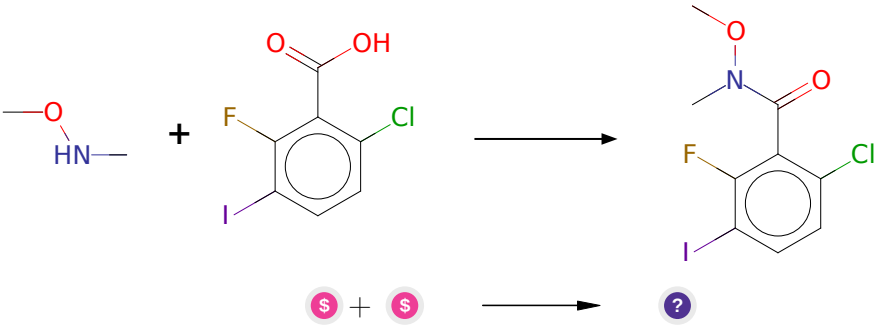


Figure 1: Outline of path 1

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

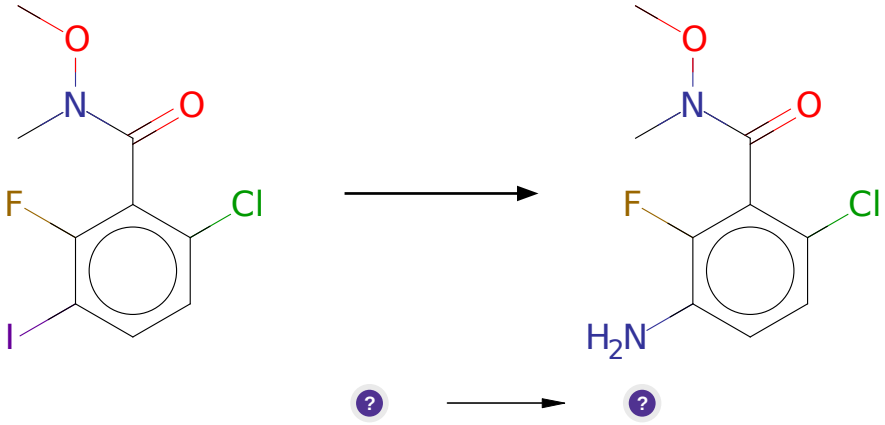
Protections: none

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

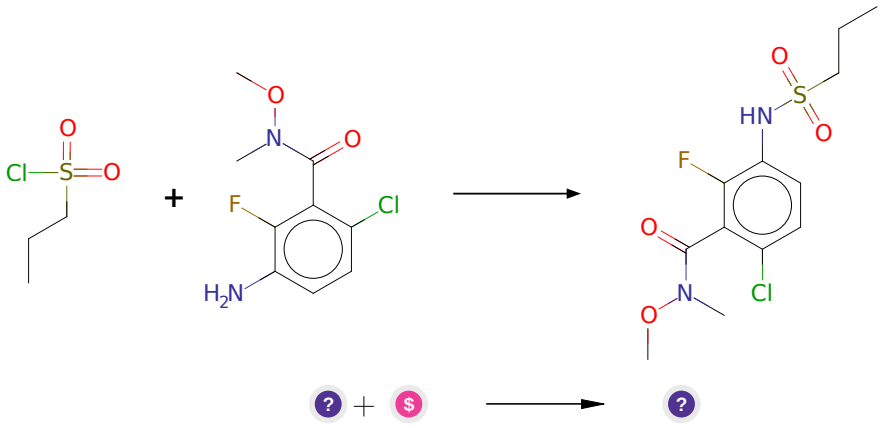
Protections: none

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

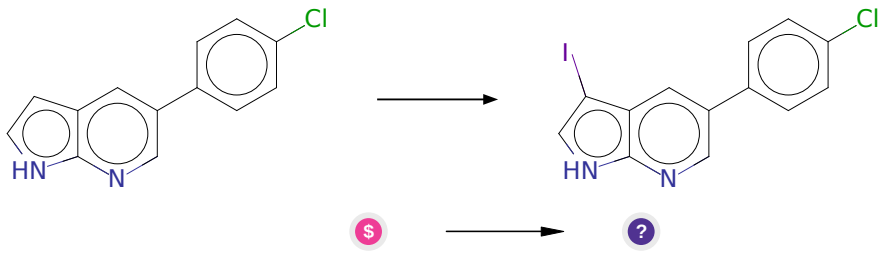
Protections: none

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 Iodination of aromatic compounds



Substrates:

1. 5-(4-Chlorophenyl)-1H-pyrrolo[2,3-b]pyridine - *Combi-Blocks*

Products:

1. Clc1ccc(-c2cnc3[nH]cc(I)c3c2)cc1

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

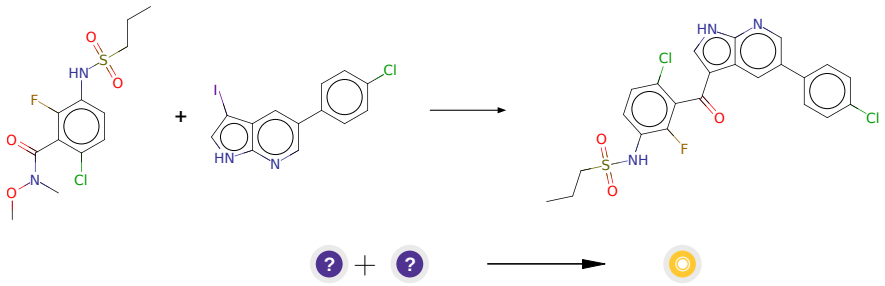
Protections: none

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

2.1.5 Synthesis of ketones from Weinreb amides



Substrates:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=O)N(C)OC)c1F
2. Clc1ccc(-c2cnc3[nH]cc(I)c3c2)cc1

Products:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(C(=O)c2c[nH]c3ncc(-c4ccc(Cl)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: 213.20

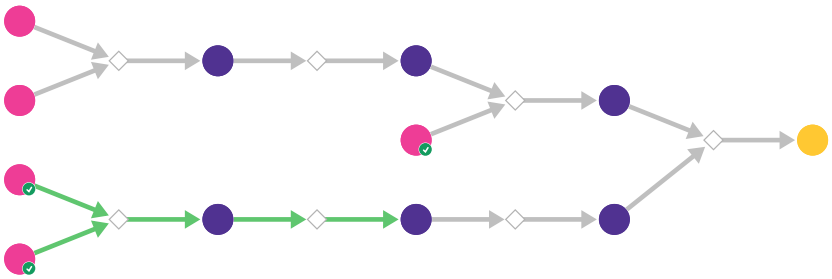
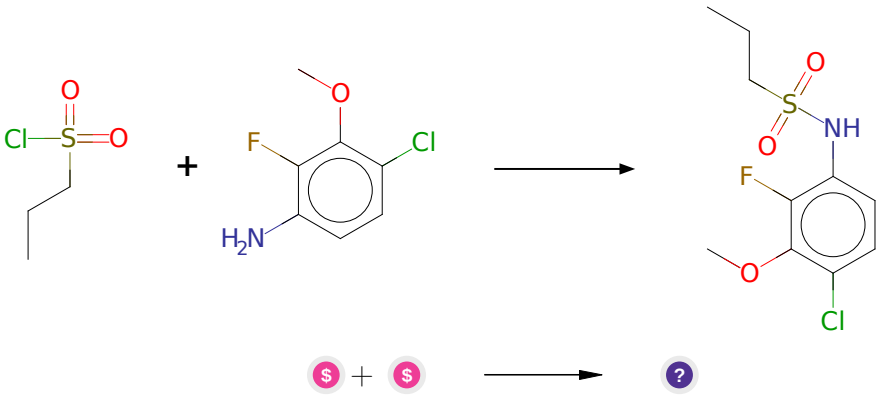


Figure 2: Outline of path 2

2.2.1 N-Sulfonylation



Substrates:

1. 1-Propanesulfonyl chloride - *available at Sigma-Aldrich*
2. 4-Chloro-2-fluoro-3-methoxyaniline 1g pack - *available at Sigma-Aldrich*

Products:

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

Typical conditions: THF.rt

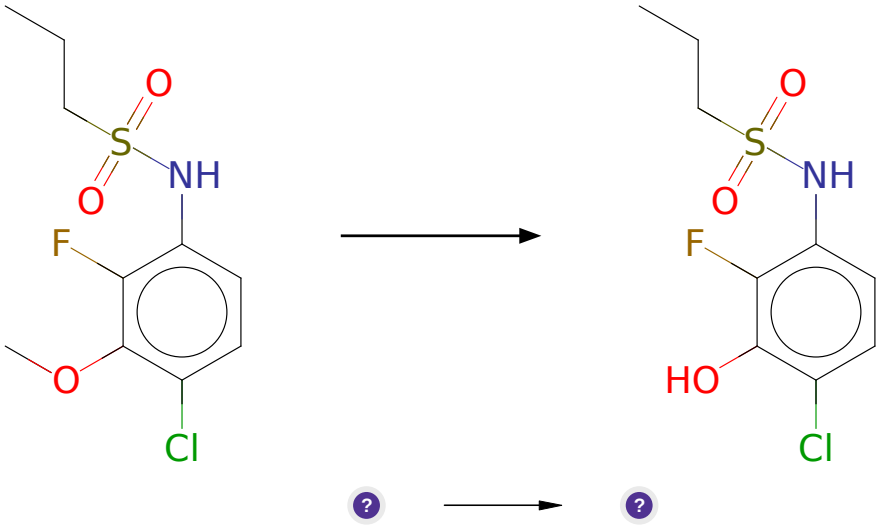
Protections: none

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: 14718

2.2.2 Demethylation of Phenols



Substrates:

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

Products:

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

Typical conditions: BBr3.CH2Cl2

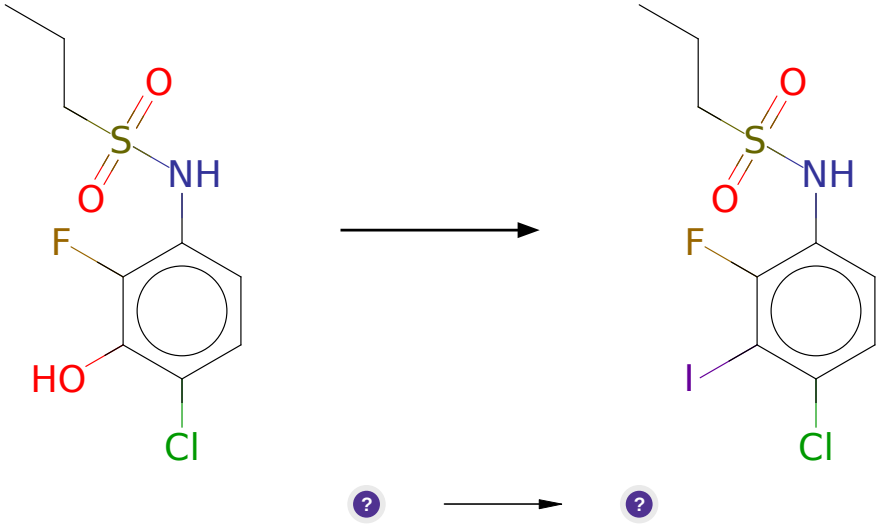
Protections: none

Yield: moderate

Reference: DOI: *10.1021/ja00105a021* and *10.1021/jm00176a011* and *10.1021/jm970277i* and *10.1021/ja0106164* and Patent: US2010/16298, 2010, A1, page 185

Retrosynthesis ID: 10011837

2.2.3 Synthesis of haloarenes via triflates



Substrates:

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

Products:

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

Typical conditions: 1.Tf2O 2. [Pd].MX

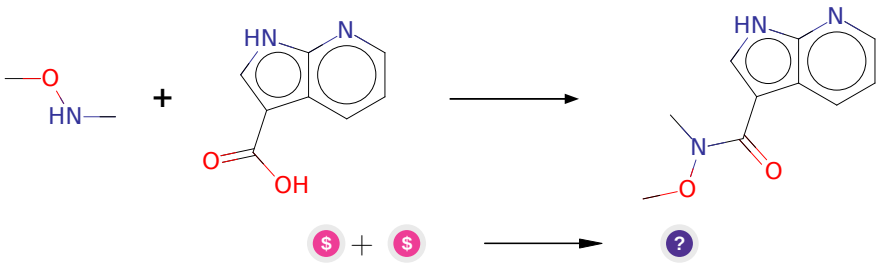
Protections: none

Yield: moderate

Reference: *10.1016/j.tetasy.2012.04.008* and WO2007/136577 (p46) and *10.1021/ol202098h* and *10.1021/ol402859k* and *10.1021/jacs.5b09308*

Retrosynthesis ID: 23940

2.2.4 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

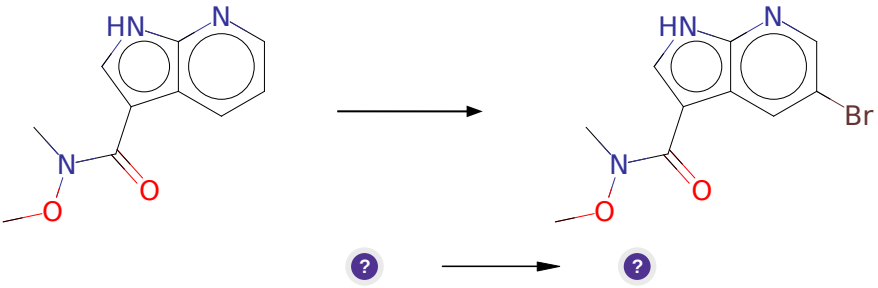
Protections: none

Yield: good

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

Retrosynthesis ID: 1152

2.2.5 Bromination of aromatic compounds



Substrates:

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

Products:

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

Typical conditions: Br2.Fe

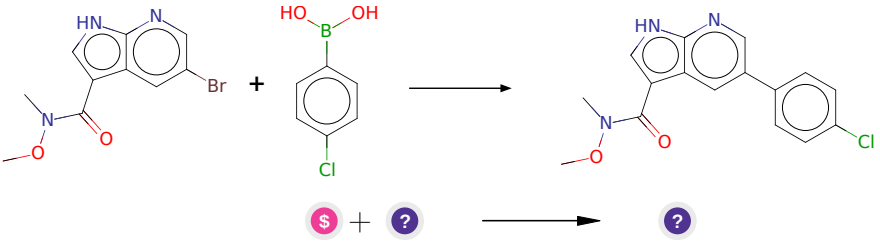
Protections: none

Yield: good

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

Retrosynthesis ID: 7777000

2.2.6 Suzuki coupling of arylboronic acids with aryl bromides



Substrates:

1. 4-Chlorophenylboronic acid - *available at Sigma-Aldrich*
2. CON(C)C(=O)c1c[nH]c2ncc(Br)cc12

Products:

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

Typical conditions: Pd catalyst.base.solvent

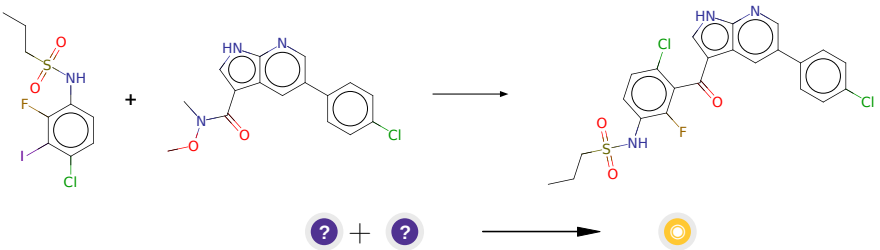
Protections: none

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

2.2.7 Synthesis of ketones from Weinreb amides



Substrates:

1. CCCS(=O)(=O)Nc1ccc(Cl)c(I)c1F
2. CON(C)C(=O)c1c[nH]c2ncc(-c3ccc(Cl)cc3)cc12

Products:

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

2.3 Path 3

Score: `331.10`

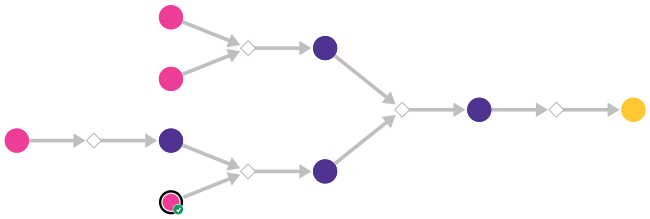
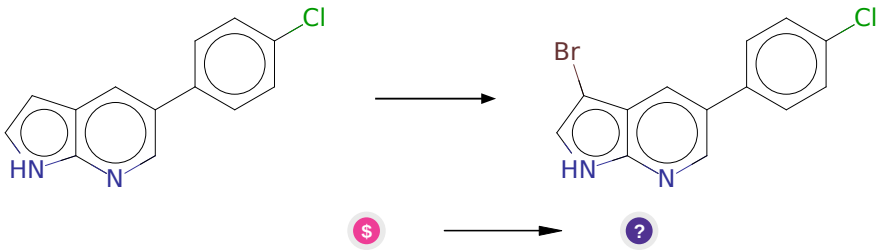


Figure 3: Outline of path 3

2.3.1 Bromination of aromatic compounds



Substrates:

1. 5-(4-Chlorophenyl)-1H-pyrrolo[2,3-b]pyridine - *Combi-Blocks*

Products:

1. Clc1ccc(-c2cnc3[nH]cc(Br)c3c2)cc1

Typical conditions: Br2.Fe

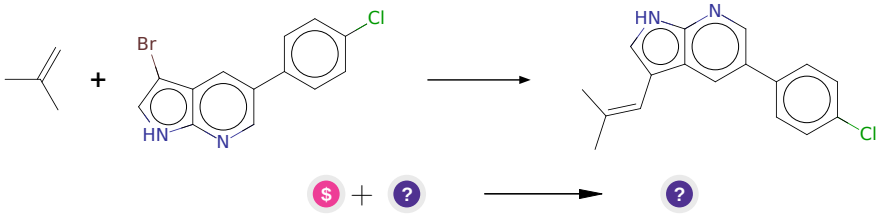
Protections: none

Yield: good

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

Retrosynthesis ID: 7777000

2.3.2 Heck Reaction



Substrates:

1. Isobutylene - *available at Sigma-Aldrich*
2. Clc1ccc(-c2cnc3[nH]cc(Br)c3c2)cc1

Products:

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

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

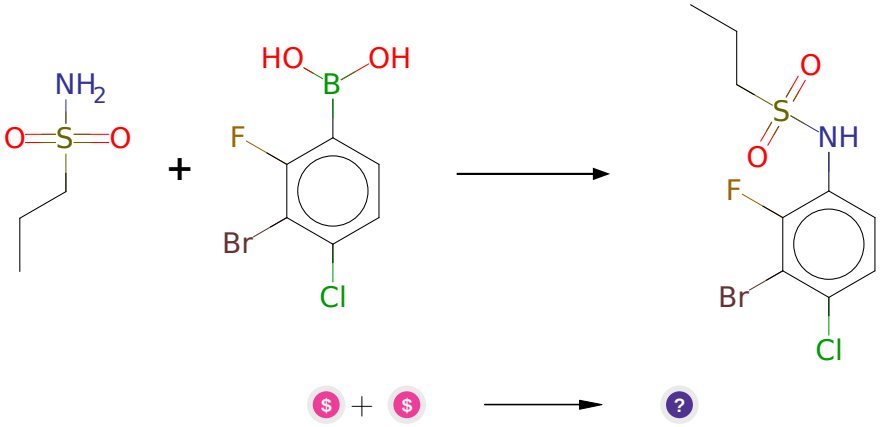
Protections: none

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

2.3.3 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

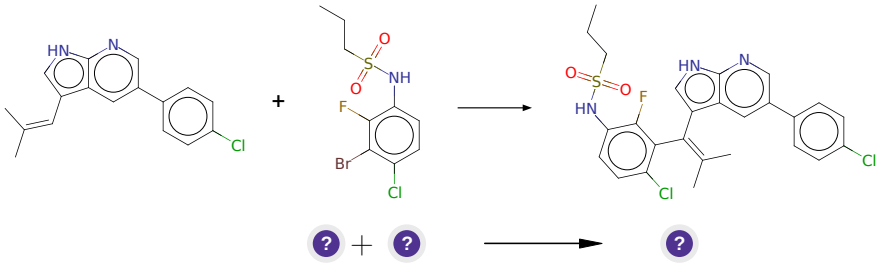
Protections: none

Yield: good

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

Retrosynthesis ID: 31015970

2.3.4 Heck Reaction



Substrates:

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

Products:

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

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

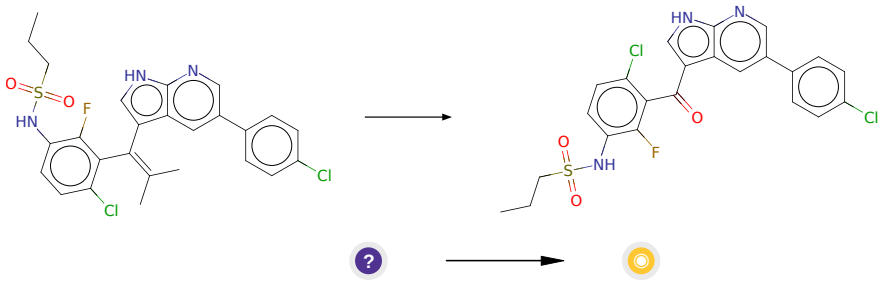
Protections: none

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

2.3.5 Ozonolysis



Substrates:

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

Products:

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