Paths of analysis*

C54

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

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

2.1 Path 1

Score: 325.43

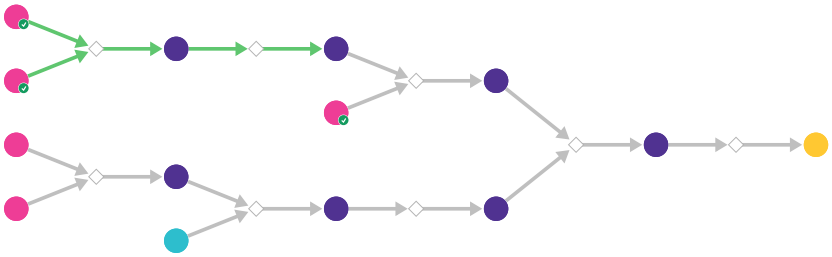
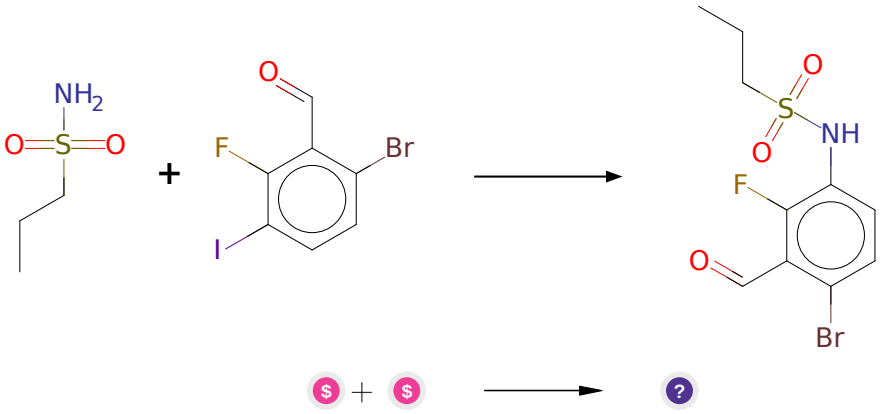


Figure 1: Outline of path 1

2.1.1 Arylation of sulfonamides with aryl iodides



Substrates:

1. 6-Bromo-2-fluoro-3-iodobenzaldehyde - *AOBChem*
2. Propane-1-sulfonamide - *Combi-Blocks*

Products:

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

Typical conditions: Cu.salt.diamine.base.DMF.heat

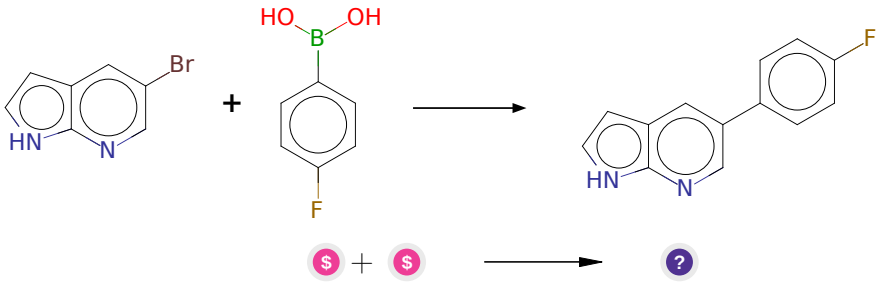
Protections: none

Yield: good

Reference: *10.1016/j.tetlet.2006.04.041* and *10.1016/j.tetlet.2011.10.113* and *10.1016/j.tetlet.2005.08.149* and *10.1021/ol035942y* and *10.1021/acs.jmedchem.6b00685*

Retrosynthesis ID: 10012567

2.1.2 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

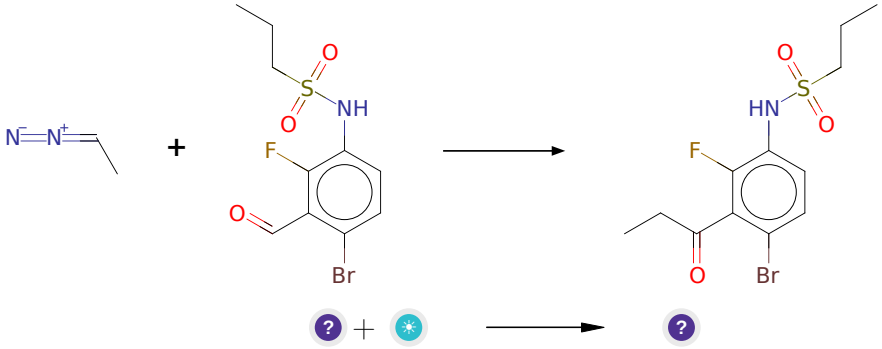
Protections: none

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

2.1.3 Homologation of aldehydes to ketones with diazoalkanes



Substrates:

1. CCCS(=O)(=O)Nc1ccc(Br)c(C=O)c1F
2. diazoethane

Products:

1. CCCS(=O)(=O)Nc1ccc(Br)c(C(=O)CC)c1F

Typical conditions: Lewis.acid

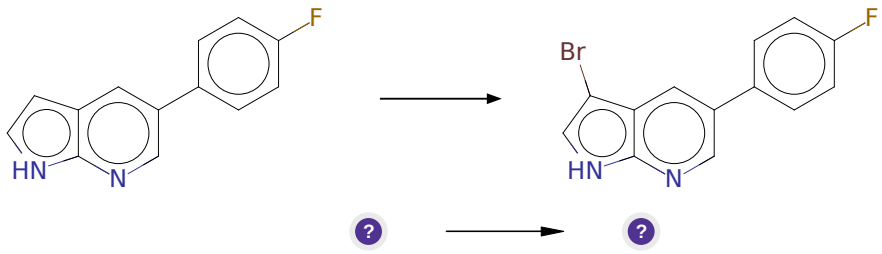
Protections: none

Yield: moderate

Reference: *10.1021/jo00275a006* AND *10.1016/j.tet.2014.05.107* AND *10.1016/j.tet.2014.11.059* AND *10.1021/ol9010932*

Retrosynthesis ID: 15017

2.1.4 Bromination of aromatic compounds



Substrates:

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

Products:

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

Typical conditions: Br2.Fe

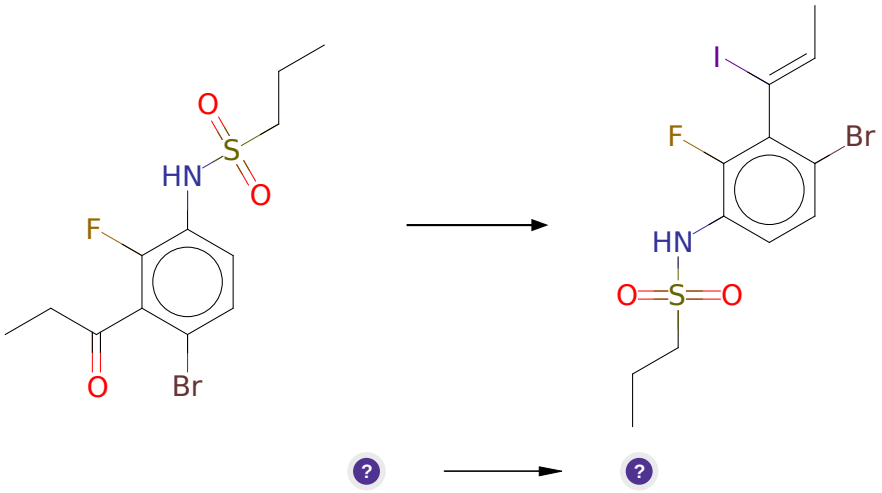
Protections: none

Yield: good

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

Retrosynthesis ID: 7777000

2.1.5 Shapiro reaction followed by halogen addition



Substrates:

1. CCCS(=O)(=O)Nc1ccc(Br)c(C(=O)CC)c1F

Products:

1. C/C=C(\I)c1c(Br)ccc(NS(=O)(=O)CCC)c1F

Typical conditions: 1.TsNH2NH2 2.NBS/NCS/NIS.base

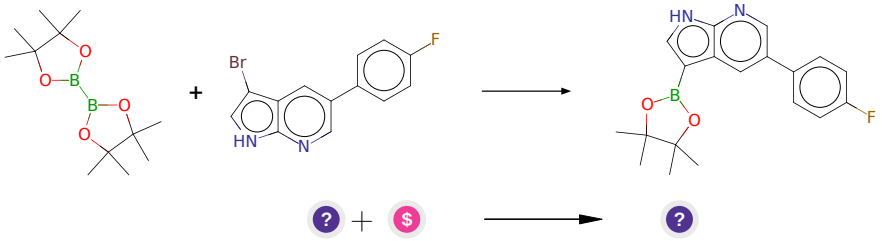
Protections: none

Yield: moderate

Reference: *10.1021/ol503114n* and *10.1016/j.tet.2008.02.073* and *10.1021/ja049694s*

Retrosynthesis ID: 9990472

2.1.6 Miyaura Borylation



Substrates:

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

Products:

1. CC1(C)OB(c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)OC1(C)C

Typical conditions: PdCl2(dppf)2.KOAc.Dioxane or DMSO.80oC

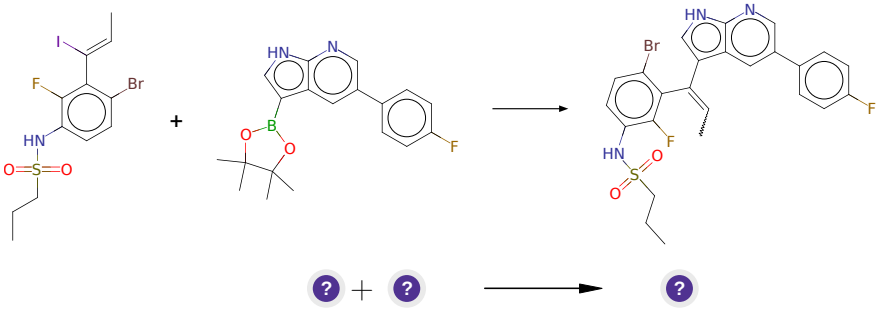
Protections: none

Yield: good

Reference: DOI: *10.1021/ja509198w* and *10.1021/jm800832q* and *10.1021/jm401499g* and *10.1039/C1CC12020D* (SI, page S4) and *10.1055/s-0035-1561355* (SI, page 12) and *10.1021/ol2000556* and *10.1021/jo102070e* and WO2010/75270 A1, 2010 (page 37)

Retrosynthesis ID: 1209

2.1.7 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

1. C/C=C(\I)c1c(Br)ccc(NS(=O)(=O)CCC)c1F

2. CC1(C)OB(c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)OC1(C)C

Products:

1. CC=C(c1c(Br)ccc(NS(=O)(=O)CCC)c1F)c1c[nH]c2ncc(-c3ccc(F)cc3)cc12

Typical conditions: Pd catalyst.base.solvent

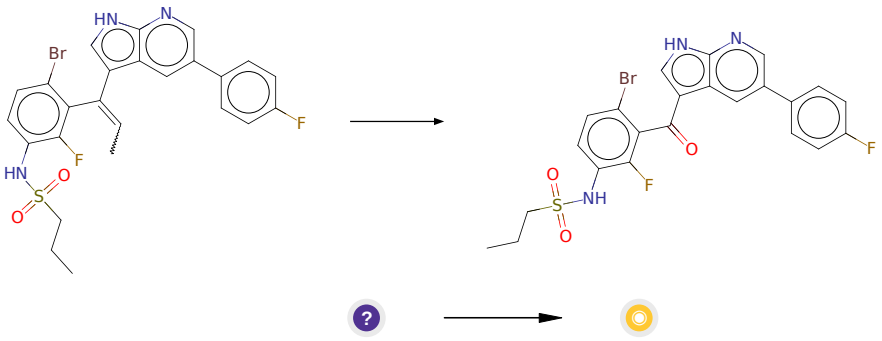
Protections: none

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*

Retrosynthesis ID: 10321

2.1.8 Ozonolysis



Substrates:

1. CC=C(c1c(Br)ccc(NS(=O)(=O)CCC)c1F)c1c[nH]c2ncc(-c3ccc(F)cc3)cc12

Products:

1. CCCS(=O)(=O)Nc1ccc(Br)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: 5078