

Paths of analysis*

C56

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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

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: 138.85

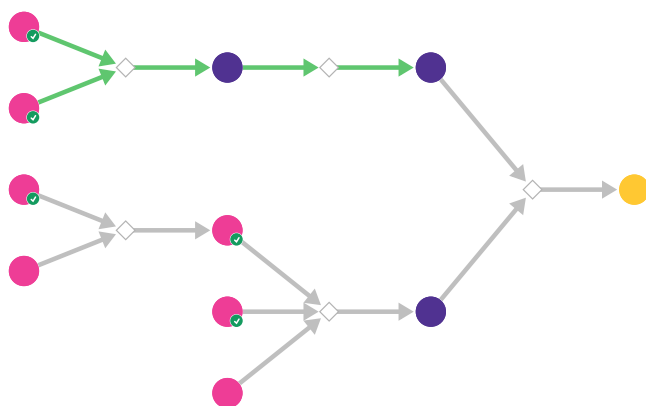
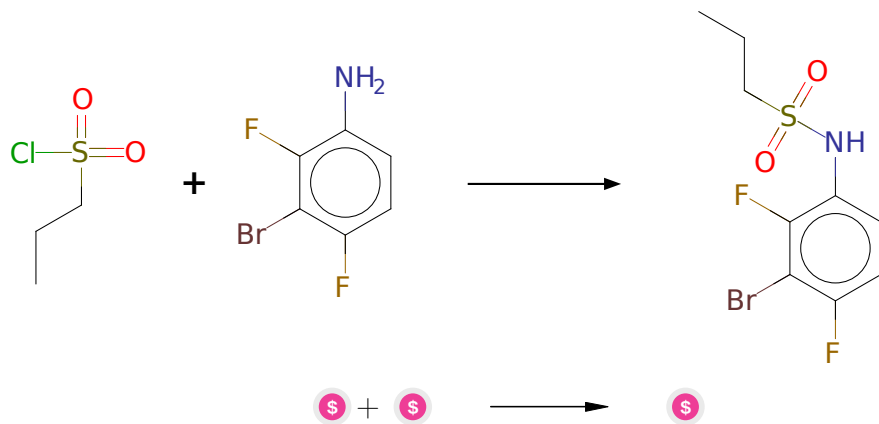


Figure 1: Outline of path 1

2.1.1 N-Sulfonylation



Substrates:

1. 1-Propanesulfonyl chloride - *available at Sigma-Aldrich*
2. 3-Bromo-2,4-difluoroaniline - *AstaTech*

Products:

1. N-(3-Bromo-2,4-difluorophenyl)-1-propanesulfonamide - *available at Sigma-Aldrich*

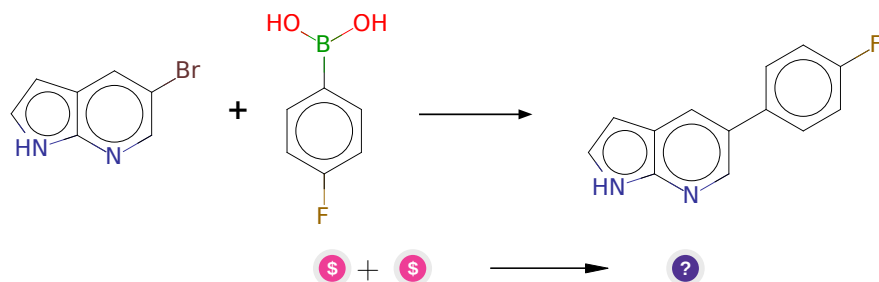
Typical conditions: THF.r.t

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

2.1.2 Suzuki coupling of arylboronic acids with aryl bromides**Substrates:**

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

Products:

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

Typical conditions: Pd catalyst.base.solvent

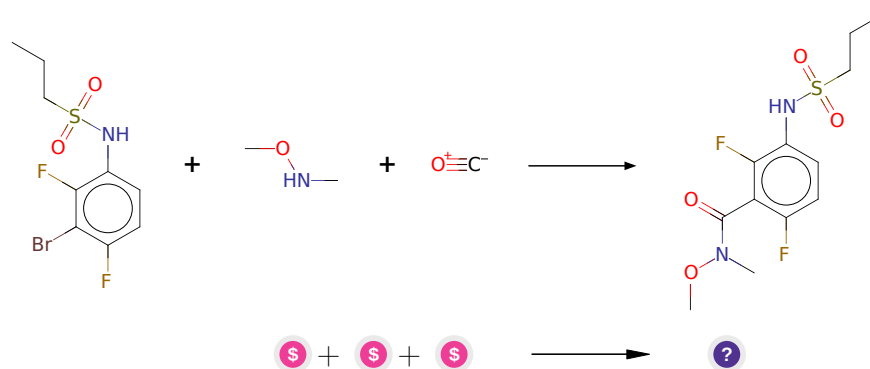
Protections: none

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 Pd-catalyzed conversion of aryl bromides to Weinreb amides



Substrates:

1. N-(3-Bromo-2,4-difluorophenyl)-1-propanesulfonamide - *available at Sigma-Aldrich*
2. Carbon monoxide - *available at Sigma-Aldrich*
3. n-methoxymethylamine - *ChemImpexInternational*

Products:

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

Typical conditions: Pd(OAc)₂.Xantphos.CO(1 atm).Na₂CO₃.toluene.80C

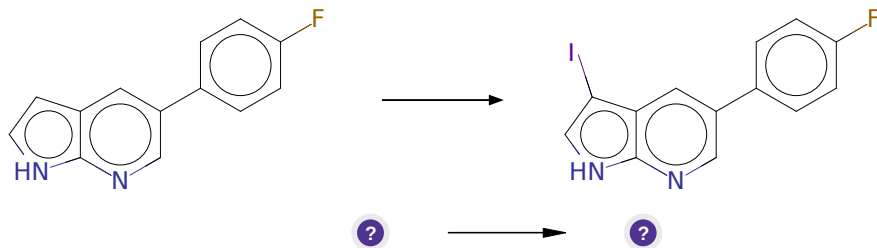
Protections: none

Yield: moderate

Reference: DOI: [10.1021/ol061902t](#)

Retrosynthesis ID: 1688

2.1.4 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

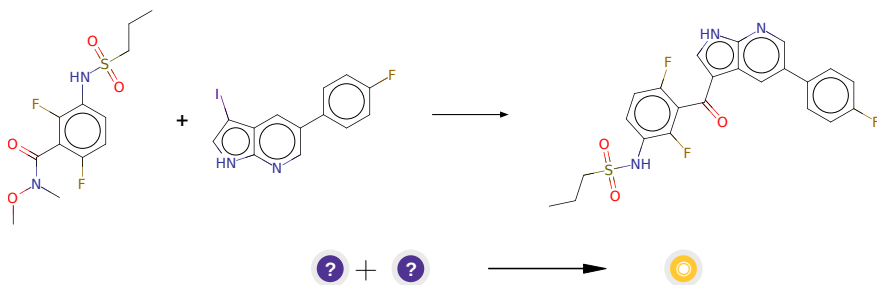
Protections: none

Yield: good

Reference: DOI: [10.1039/C5SC00964B](https://doi.org/10.1039/C5SC00964B) and [10.1016/j.tetlet.2005.05.117](https://doi.org/10.1016/j.tetlet.2005.05.117) and [10.1007/s11178-005-0256-1](https://doi.org/10.1007/s11178-005-0256-1)

Retrosynthesis ID: 10697

2.1.5 Synthesis of ketones from Weinreb amides



Substrates:

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

Products:

1. CCCS(=O)(=O)Nc1ccc(F)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: 162.57

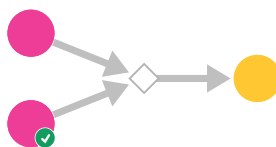
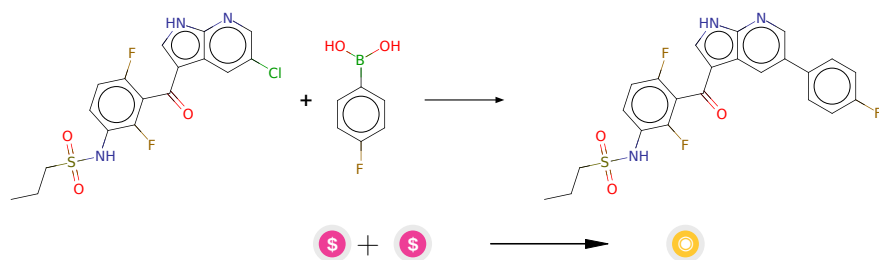


Figure 2: Outline of path 2

2.2.1 Suzuki coupling with aryl chlorides



Substrates:

1. N-[3-[(5-Chloro-1H-pyrrolo[2,3-b]pyridin-3-yl)carbonyl]-2,4-difluorophenyl]-1-propanesulfonamide - [AstaTech](#)
2. (p-Fluorophenyl)boric acid - [available at Sigma-Aldrich](#)

Products:

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

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