

# Paths of analysis\*

C126

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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\*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: 118.77

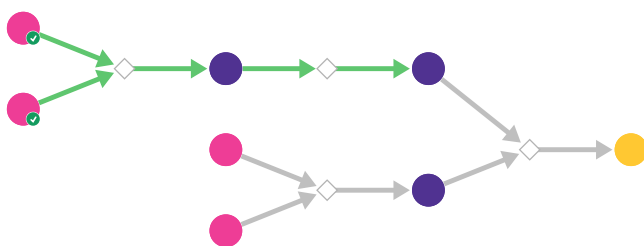
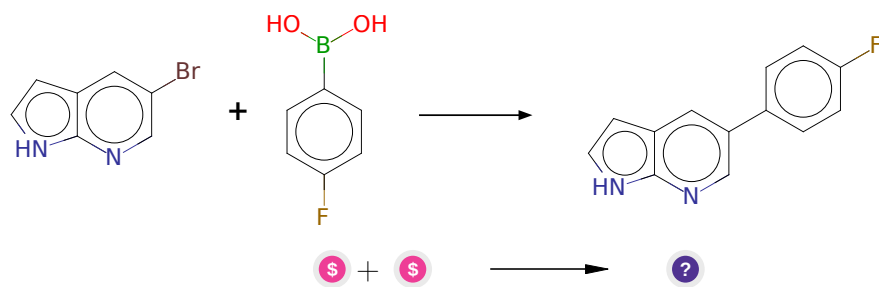


Figure 1: Outline of path 1

#### 2.1.1 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

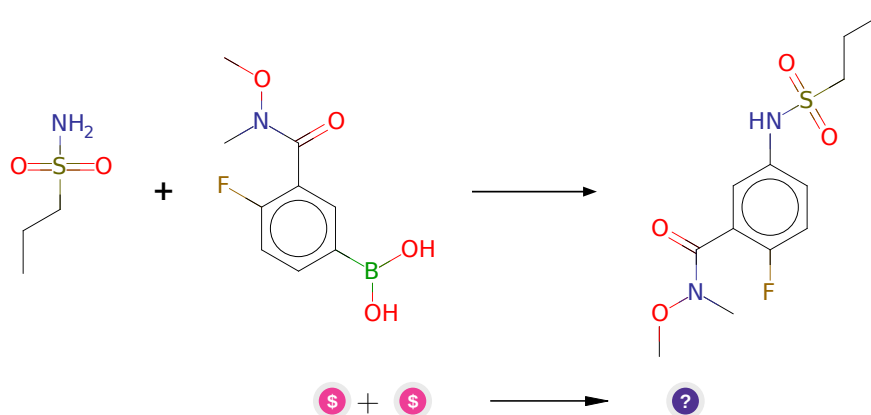
**Protections:** none

**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

### 2.1.2 Chan-Lam Coupling



**Substrates:**

1. Propane-1-sulfonamide - *Combi-Blocks*
2. 4-Fluoro-3-[(N-methoxy-N-methyl)carbamoyl]phenylboronic acid - *AOBChem*

**Products:**

1. CCCCS(=O)(=O)Nc1ccc(F)c(C(=O)N(C)OC)c1

**Typical conditions:** Cu(OAc)<sub>2</sub>.K<sub>2</sub>CO<sub>3</sub>.H<sub>2</sub>O or Cu(OAc)<sub>2</sub>.pyridine.DCM.MS 4A

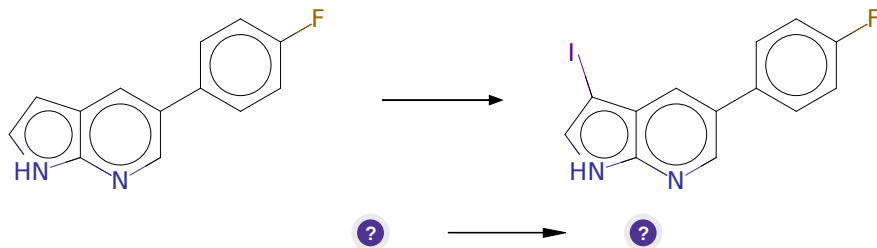
**Protections:** none

**Yield:** good

**Reference:** [10.1016/j.molcata.2014.02.017](#) and [10.1039/C4RA08137D](#) and WO2008073956 p.88

**Retrosynthesis ID:** 31015970

### 2.1.3 Iodination of aromatic compounds



**Substrates:**

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

**Products:**

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

**Typical conditions:** I<sub>2</sub> or other iodinating agent e.g. NIS

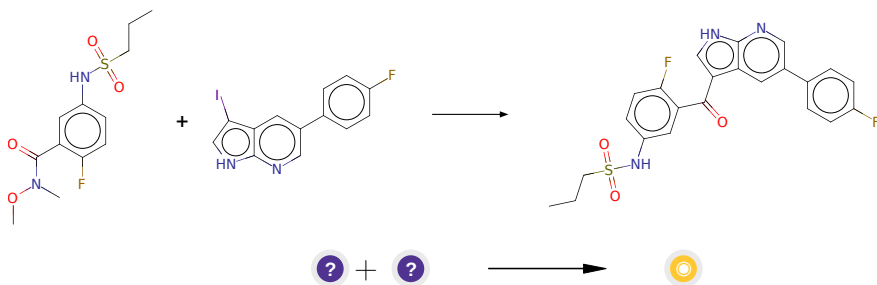
**Protections:** none

**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

### 2.1.4 Synthesis of ketones from Weinreb amides



**Substrates:**

1. CCCS(=O)(=O)Nc1ccc(F)c(C(=O)N(C)OC)c1
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)c1

**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: 169.53

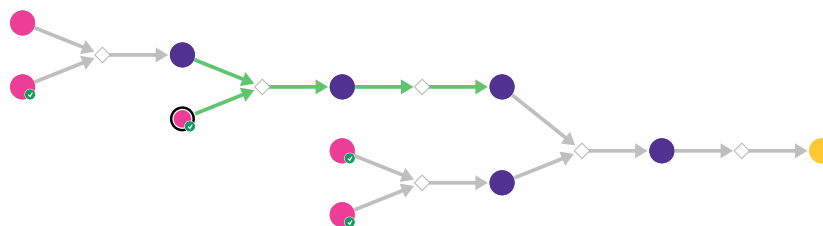
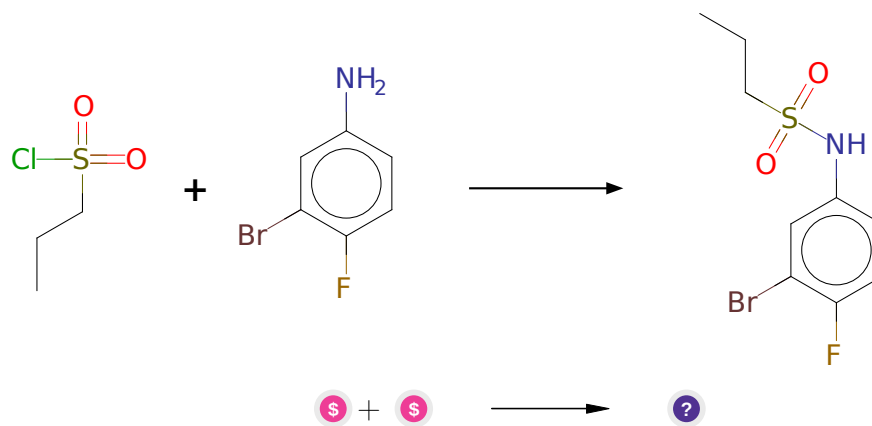


Figure 2: Outline of path 2

### 2.2.1 N-Sulfonylation



**Substrates:**

1. 3-Bromo-4-fluoroaniline - *Combi-Blocks*
2. 1-Propanesulfonyl chloride - *available at Sigma-Aldrich*

**Products:**

1. CCCS(=O)(=O)Nc1ccc(F)c(Br)c1

**Typical conditions:** THF.r.t

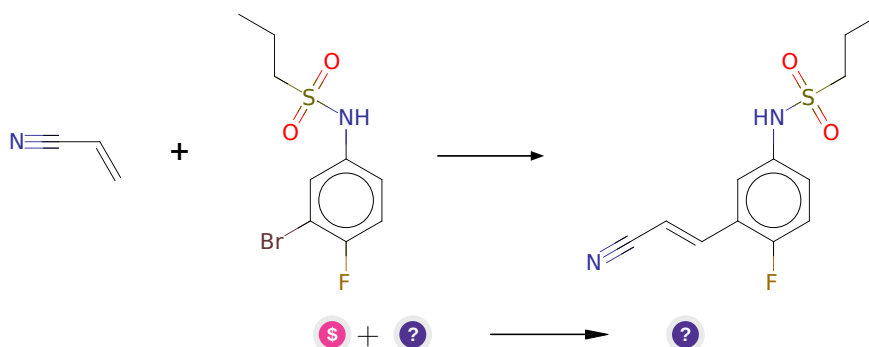
**Protections:** none

**Yield:** good

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

**Retrosynthesis ID:** 14718

**2.2.2 Heck Reaction**



**Substrates:**

1. Acrylonitrile - [available at Sigma-Aldrich](#)
2. CCCS(=O)(=O)Nc1ccc(F)c(Br)c1

**Products:**

1. CCCS(=O)(=O)Nc1ccc(F)c(/C=C/C#N)c1

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

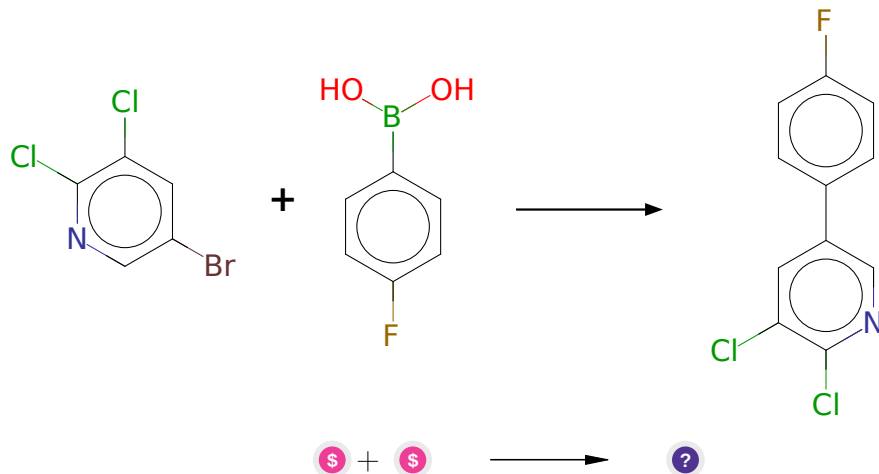
**Protections:** none

**Yield:** moderate

**Reference:** DOI: [10.1039/C3GC40493E](https://doi.org/10.1039/C3GC40493E) DOI: [10.1021/ol0360288](https://doi.org/10.1021/ol0360288) or DOI: [10.1021/ol702755g](https://doi.org/10.1021/ol702755g) or DOI: [10.1055/s-0033-1340319](https://doi.org/10.1055/s-0033-1340319) or DOI: [10.1016/j.tet.2004.10.049](https://doi.org/10.1016/j.tet.2004.10.049)

**Retrosynthesis ID:** 9180

### 2.2.3 Suzuki coupling of arylboronic acids with aryl bromides



#### Substrates:

1. (p-Fluorophenyl)boronic 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

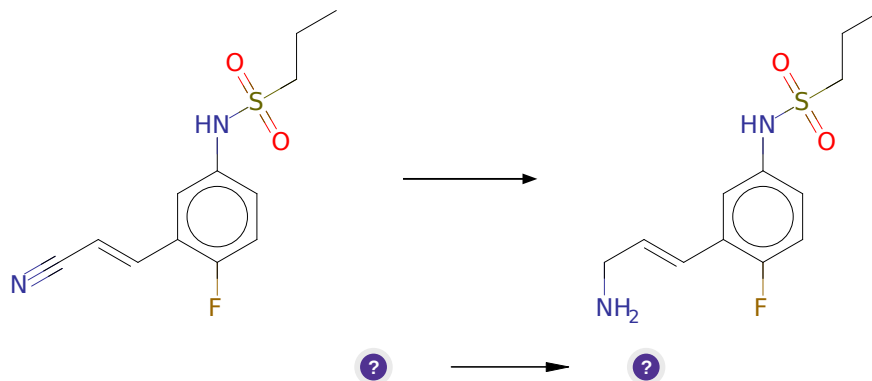
**Protections:** none

**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

## 2.2.4 Reduction of Nitriles to Amines



**Substrates:**

1. CCCS(=O)(=O)Nc1ccc(F)c(/C=C/C#N)c1

**Products:**

1. CCCS(=O)(=O)Nc1ccc(F)c(/C=C/CN)c1

**Typical conditions:** LAH.THF.-78C

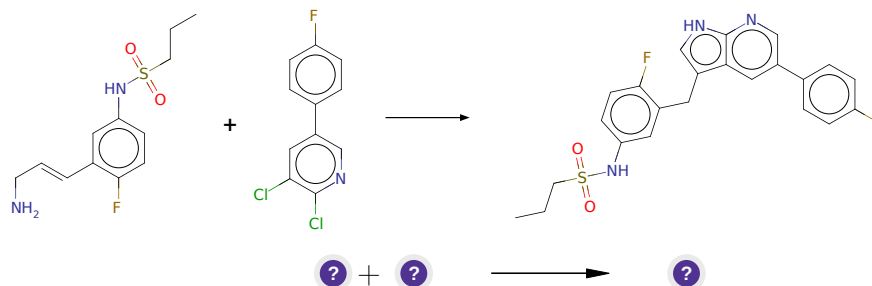
**Protections:** none

**Yield:** moderate

**Reference:** DOI:[10.1021/ja01145a082](https://doi.org/10.1021/ja01145a082)

**Retrosynthesis ID:** 11142

## 2.2.5 Heck-type synthesis of indoles



**Substrates:**

1. CCCS(=O)(=O)Nc1ccc(F)c(/C=C/CN)c1
2. Fc1ccc(-c2cnc(Cl)c(Cl)c2)cc1



**Products:**

1. CCCC(=O)(=O)Nc1ccc(F)c(Cc2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1

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

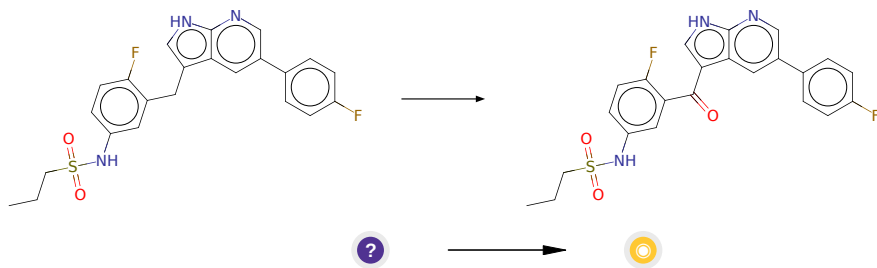
**Protections:** none

**Yield:** good

**Reference:** [10.1002/anie.200703763](#)

**Retrosynthesis ID:** 28942

**2.2.6 Benzylic oxidation to ketone**



**Substrates:**

1. CCCC(=O)(=O)Nc1ccc(F)c(Cc2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1

**Products:**

1. CCCC(=O)(=O)Nc1ccc(F)c(C(=O)c2c[nH]c3ncc(-c4ccc(F)cc4)cc23)c1

**Typical conditions:** oxidant eg. Oxone or O<sub>2</sub> or K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>

**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