

# Paths of analysis\*

(re)Analysis 1381 - No Filter - Rerun

Synthia

November 28, 2023

## 1 Analysis parameters

**Analysis type:** Automatic Retrosynthesis

**Saved Configuration:** General

**Rules:** Expert-Coded Rules

**Published Reactions:** SPRESI by DeepMatter, USPTO, Enzyme-Catalyzed Reactions

**Filters:** none selected

**Max. paths returned:** 50

**Max. iterations:** 2000

**Commercial:**

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1000 \$/g

**Published:**

1. Max. molecular weight - 1000 g/mol
2. Popularity - 15

**My Stockroom:**

1. Max. molecular weight - 1000 g/mol

**Shorter paths:** no

**Pathway linearity:** COMBO

**Protecting groups:** BALANCED

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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.

**Reaction scoring formula:**  $\text{TUNNEL\_COEF} * \text{FGI\_COEF} * \text{STEP} * 20 + 1000 * (\text{FILTERS} + \text{CONFLICT} + \text{NON\_SELECTIVITY}) + 40 * \text{PROTECT}$

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

**Min. search width:** 400

**Max. reactions per product:** 60

## 2 Paths

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

### 2.1 Path 1

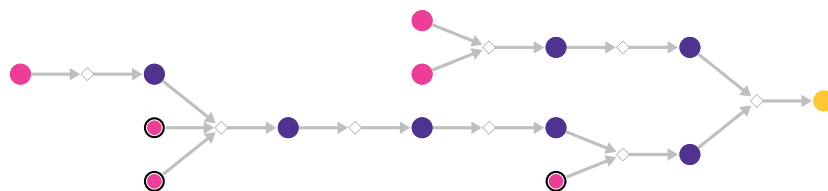
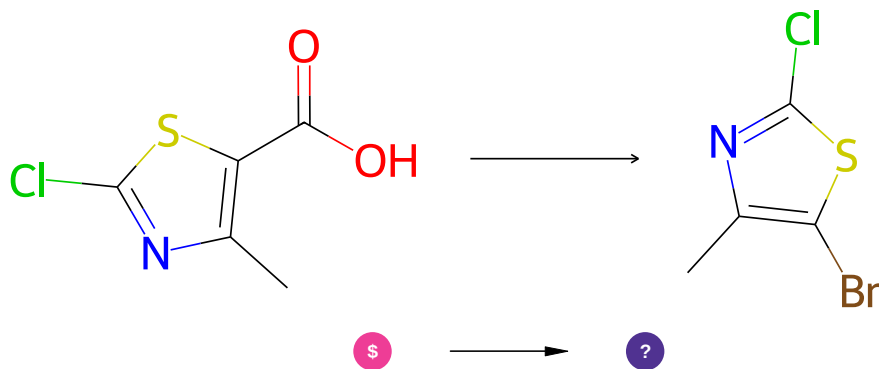


Figure 1: Outline of path 1

#### 2.1.1 Decarboxylative Bromination of Aromatic Carboxylic Acids



**Substrates:**

- 2-Chloro-4-methylthiazole-5-carboxylic acid - *available at Sigma-Aldrich*

**Products:**

- Cc1nc(Cl)sc1Br

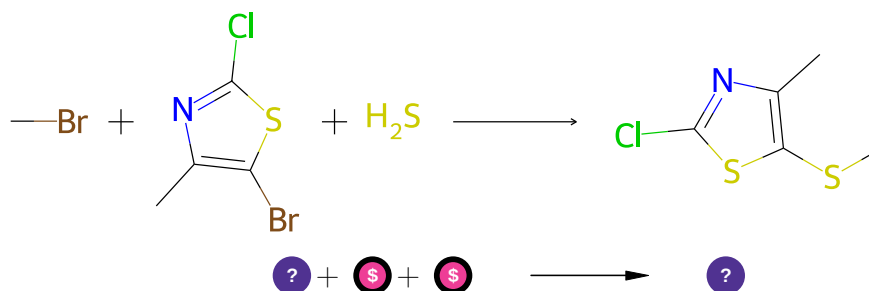
**Typical conditions:** N-hydroxy-2-thiopyridone.AIBN.Trichlorobromomethane.toluene.light.heat

**Protections:** none

**Reference:** [10.1055/s-0037-1610188](#) and [10.1016/S0040-4039\(00\)98266-2](#) and [10.1016/S0040-4020\(01\)90307-2](#)

**Retrosynthesis ID:** 31021104

### 2.1.2 One pot synthesis of aryl-alkyl sulfides



**Substrates:**

1. Cc1nc(Cl)sc1Br
2. Bromomethane - *available at Sigma-Aldrich*
3. Hydrosulfuric acid - *available at Sigma-Aldrich*

**Products:**

1. CSc1sc(Cl)nc1C

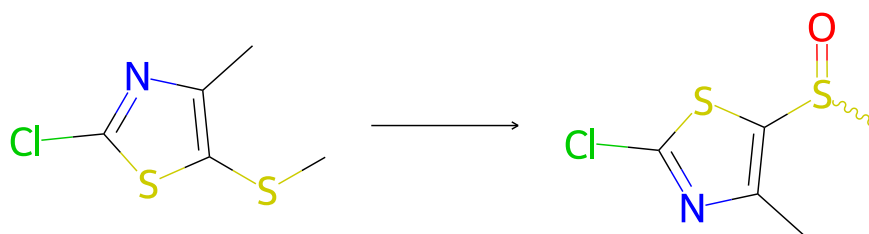
**Typical conditions:** nBuLi.THF.-78C.then.S.then AlkBr.to.rt

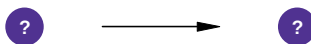
**Protections:** none

**Reference:** [10.1021/jo049758h](#)

**Retrosynthesis ID:** 5320

### 2.1.3 Oxidation of sulfides to sulfoxides





**Substrates:**

1. CSc1sc(Cl)nc1C

**Products:**

1. Cc1nc(Cl)sc1S(C)=O

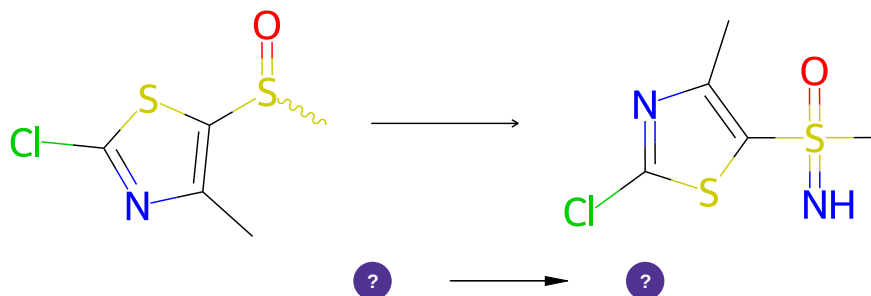
**Typical conditions:** TaC.H<sub>2</sub>O<sub>2</sub>.MeOH.45C

**Protections:** none

**Reference:** DOI: [10.1055/s-0029-1219947](https://doi.org/10.1055/s-0029-1219947) or DOI: [10.1055/s-2008-1067019](https://doi.org/10.1055/s-2008-1067019)

**Retrosynthesis ID:** 10584

#### 2.1.4 Synthesis of NH-sulfoximines



**Substrates:**

1. Cc1nc(Cl)sc1S(C)=O

**Products:**

1. Cc1nc(Cl)sc1S(C)(=N)=O

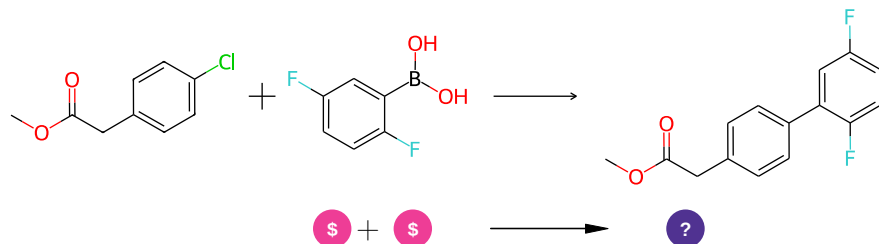
**Typical conditions:** NaN<sub>3</sub>.Eaton's reagent.50C or FeSO<sub>4</sub>.1,10-phen.NbzONH<sub>2</sub>\*TfOH.MeCN or H<sub>2</sub>NCO<sub>2</sub>NH<sub>4</sub>.PhI(OAc)<sub>2</sub>.MeOH

**Protections:** none

**Reference:** [10.1016/j.tetlet.2016.12.031](https://doi.org/10.1016/j.tetlet.2016.12.031) and [10.1002/anie.201710498](https://doi.org/10.1002/anie.201710498) and [10.1002/anie.201602320](https://doi.org/10.1002/anie.201602320) and [10.1055/s-0036-1590874](https://doi.org/10.1055/s-0036-1590874) and [10.1039/C7CC03386A](https://doi.org/10.1039/C7CC03386A)

**Retrosynthesis ID:** 31016630

### 2.1.5 Suzuki coupling with aryl chlorides



#### Substrates:

1. 2,5-Difluorophenylboronic acid - *Combi-Blocks*
2. Methyl 4-chlorophenylacetate - *available at Sigma-Aldrich*

#### Products:

1. COC(=O)Cc1ccc(-c2cc(F)ccc2F)cc1

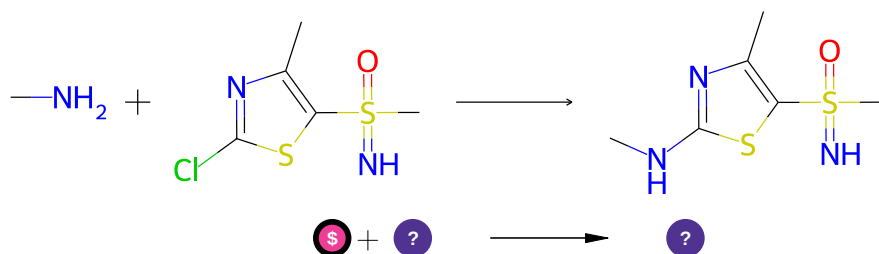
**Typical conditions:** [Pd].catalyst.base.

**Protections:** none

**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

### 2.1.6 Nucleophilic aromatic substitution



#### Substrates:

1. Methanamine - *available at Sigma-Aldrich*
2. Cc1nc(Cl)sc1S(C)(=N)=O

#### Products:

1. CNc1nc(C)c(S(C)(=N)=O)s1

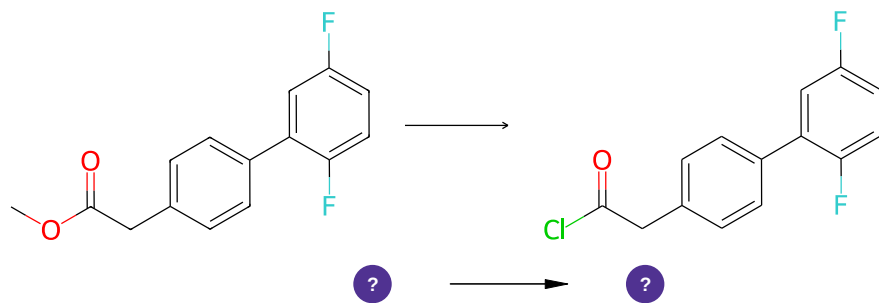
**Typical conditions:** solvent. Heating or pressure

**Protections:** none

**Reference:** [10.1021/jm00040a009](#) or [10.1111/bph.12233](#) or [10.1246/cl.1987.1187](#)

**Retrosynthesis ID:** 5003

### 2.1.7 Synthesis of acid chlorides from esters



**Substrates:**

1. COC(=O)Cc1ccc(-c2cc(F)ccc2F)cc1

**Products:**

1. O=C(Cl)Cc1ccc(-c2cc(F)ccc2F)cc1

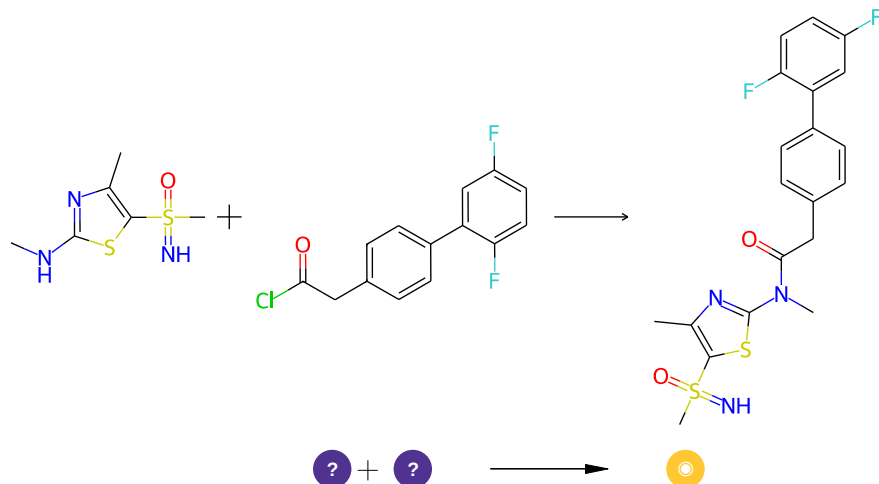
**Typical conditions:** 1. LiOH.H2O.THF. 2. evapo-  
rate. 3. SOCl2. or. oxalyl. chloride

**Protections:** none

**Reference:** [10.1021/ja073476s](#) and [10.1016/j.tet.2007.04.043](#) and  
[10.1002/adsc.200303011](#) and [10.3390/50500714](#)

**Retrosynthesis ID:** 24406

### 2.1.8 Synthesis of tertiary amides from acid chlorides



#### Substrates:

1. O=C(Cl)Cc1ccc(-c2cc(F)ccc2F)cc1
2. CNc1nc(C)c(S(C)(=N)=O)s1

#### Products:

1. Cc1nc(N(C)C(=O)Cc2ccc(-c3cc(F)ccc3F)cc2)sc1S(C)(=N)=O

**Typical conditions:** TEA.DCM.rt

**Protections:** none

**Reference:** DOI: [10.1016/j.bmcl.2008.08.004](https://doi.org/10.1016/j.bmcl.2008.08.004) and [10.1016/j.tetlet.2008.05.010](https://doi.org/10.1016/j.tetlet.2008.05.010)

**Retrosynthesis ID:** 9146