

# 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:**  $\text{TUNNEL\_COEF} * \text{FGI\_COEF} * \text{STEP} * 20 + 100000 * (\text{FILTERS} + \text{CONFLICT} + \text{NON\_SELECTIVITY}) + 40 * \text{PROTECT}$

**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

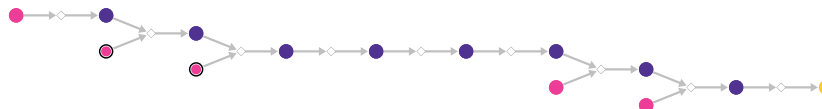
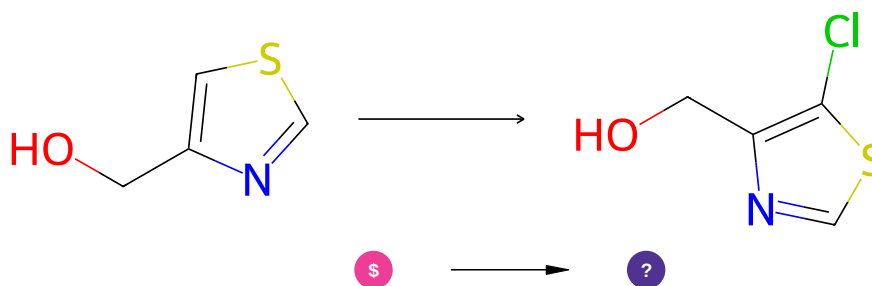


Figure 1: Outline of path 1

#### 2.1.1 Chlorination of aromatic compounds



**Substrates:**

- 1,3-Thiazol-4-ylmethanol - *available at Sigma-Aldrich*

**Products:**

- OCc1ncsc1Cl

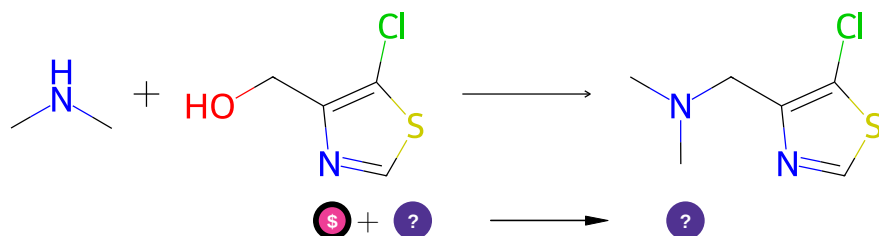
**Typical conditions:** Cl<sub>2</sub> or other chlorinating agent like NCS

**Protections:** none

**Reference:** DOI: [10.1007/s11178-005-0256-1](https://doi.org/10.1007/s11178-005-0256-1)

Retrosynthesis ID: 11125

### 2.1.2 Alkylation of amines with activated alcohols



Substrates:

1. Dimethylamine - *available at Sigma-Aldrich*
2. OCc1ncsc1Cl

Products:

1. CN(C)Cc1ncsc1Cl

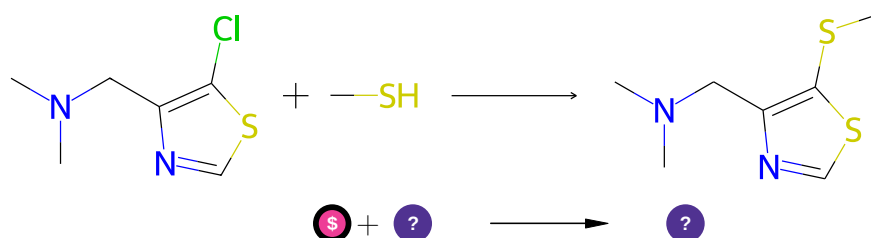
Typical conditions: DCM.2,2,6,6-tetramethyl-1-piperidinol.phenyliodosodiaacetate.RT.Na(acetyloxy)boranyl acetate

Protections: none

Reference: *10.1021/ol201351a*

Retrosynthesis ID: 10059

### 2.1.3 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. Methanethiol - *available at Sigma-Aldrich*
2. CN(C)Cc1ncsc1Cl

Products:

1. CSc1scnc1CN(C)C

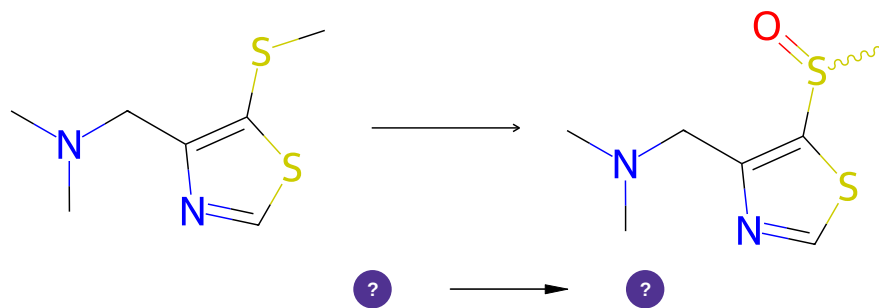
**Typical conditions:** Pd(OAc)<sub>2</sub>.tBuONa.DME.110C

**Protections:** none

**Reference:** [10.1021/ja0580340](#)

**Retrosynthesis ID:** 1299

#### 2.1.4 Oxidation of sulfides to sulfoxides



**Substrates:**

1. CSc1scnc1CN(C)C

**Products:**

1. CN(C)Cc1ncsc1S(C)=O

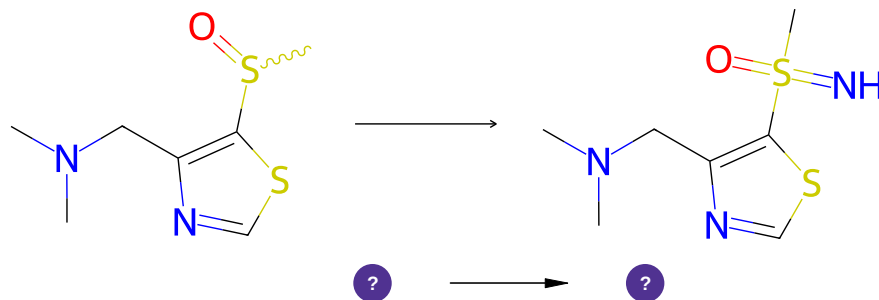
**Typical conditions:** TaC.H<sub>2</sub>O<sub>2</sub>.MeOH.45C

**Protections:** none

**Reference:** DOI: [10.1055/s-0029-1219947](#) or DOI: [10.1055/s-2008-1067019](#)

**Retrosynthesis ID:** 10584

#### 2.1.5 Synthesis of NH-sulfoximines



**Substrates:**

1. CN(C)Cc1ncsc1S(C)=O

**Products:**

1. CN(C)Cc1ncsc1S(C)(=N)=O

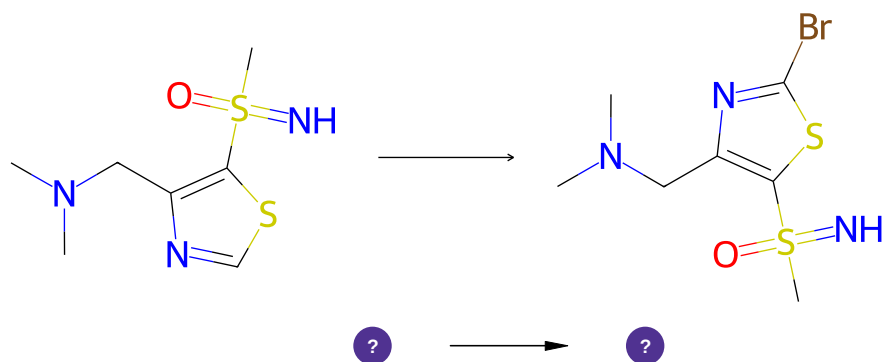
**Typical conditions:** NaN<sub>3</sub>.Eaton's reagent.50C or FeSO<sub>4</sub>.1,10-phen.NbzONH<sub>2</sub>\*TfOH.MeCN or H<sub>2</sub>NCO<sub>2</sub>NH<sub>4</sub>.PhI(OAc)<sub>2</sub>.MeOH

**Protections:** none

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

**Retrosynthesis ID:** 31016630

**2.1.6 Bromination of aromatic compounds**



**Substrates:**

1. CN(C)Cc1ncsc1S(C)(=N)=O

**Products:**

1. CN(C)Cc1nc(Br)sc1S(C)(=N)=O

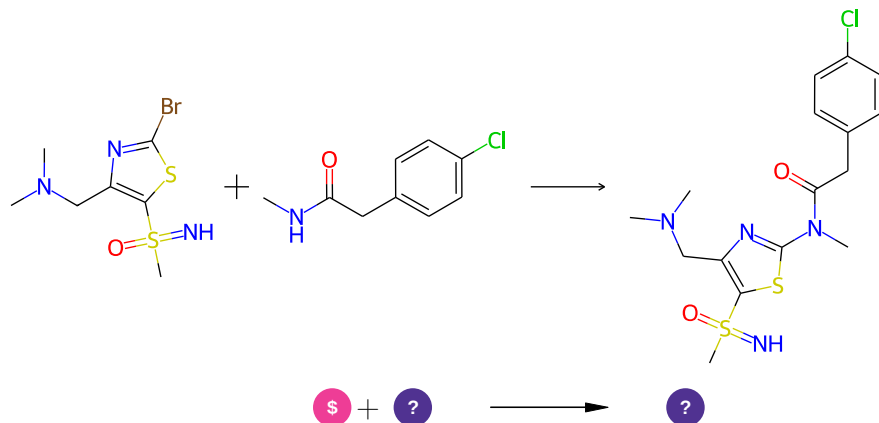
**Typical conditions:** Br<sub>2</sub>.Fe

**Protections:** none

**Reference:** [10.1021/acs.accounts.6b00120](#)

**Retrosynthesis ID:** 7777000

### 2.1.7 N-arylation of amides



#### Substrates:

1. 2-(4-Chlorophenyl)-N-methylacetamide - *available at Sigma-Aldrich*
2. CN(C)Cc1nc(Br)sc1S(C)(=N)=O

#### Products:

1. CN(C)Cc1nc(N(C)C(=O)Cc2ccc(Cl)cc2)sc1S(C)(=N)=O

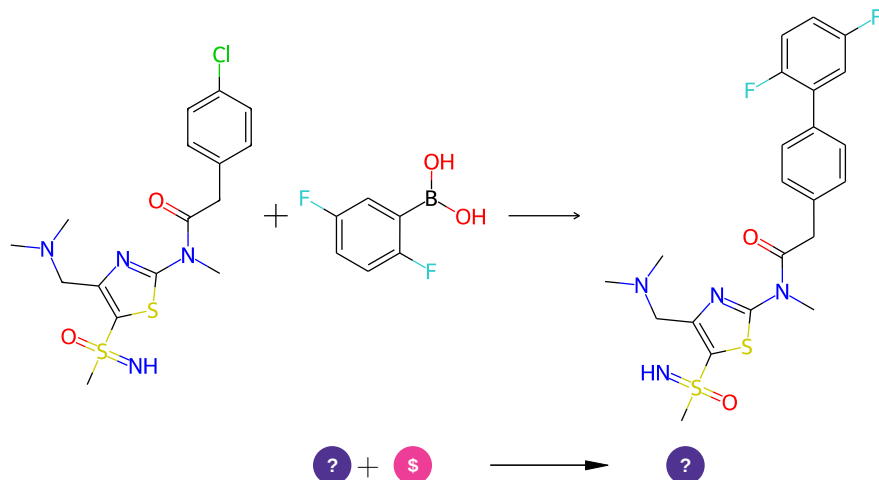
**Typical conditions:** Cs<sub>2</sub>CO<sub>3</sub>.CuX<sub>2</sub>/CuX.toluene.130C

**Protections:** none

**Reference:** [10.1021/ja012610k](#) and [10.1002/adsc.200700133](#) and [10.1021/jo701573w](#)

**Retrosynthesis ID:** 10207

### 2.1.8 Suzuki coupling with aryl chlorides



#### Substrates:

1. CN(C)Cc1nc(N(C)C(=O)Cc2ccc(Cl)cc2)sc1S(C)(=N)=O
2. 2,5-Difluorophenylboronic acid - *Combi-Blocks*

#### Products:

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

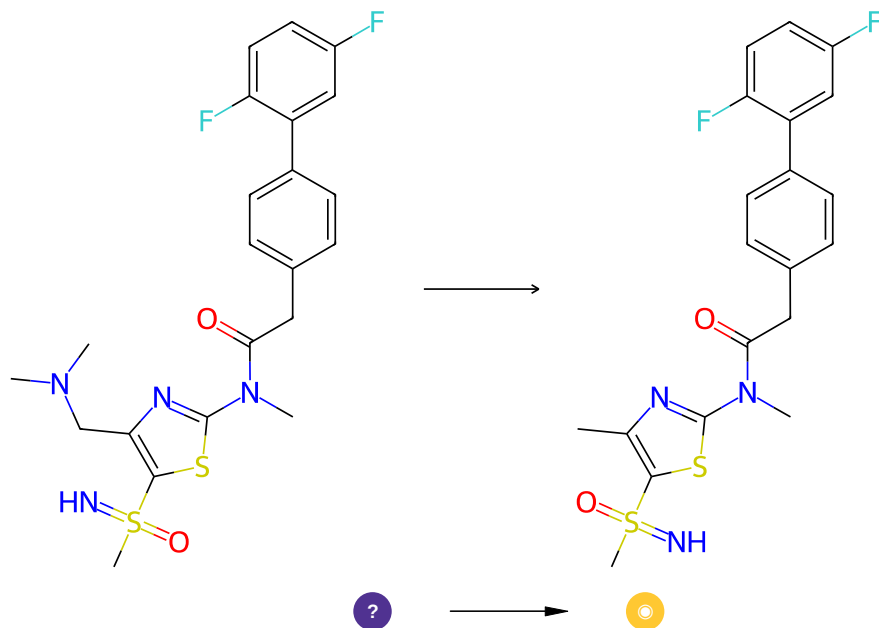
**Typical conditions:** [Pd].catalyst.base.

**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

### 2.1.9 Deamination of benzylic amines



**Substrates:**

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

**Products:**

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

**Typical conditions:** H<sub>2</sub>.Pd/C

**Protections:** none

**Reference:** [10.1021/ja070588a](#)

**Retrosynthesis ID:** 21173