

Paths of analysis*

(re)(re)Analysis 1381 - \$10/g

Synthia

November 28, 2023

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

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 - 10 \$/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

*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

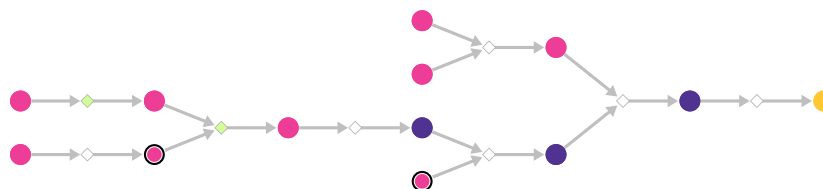
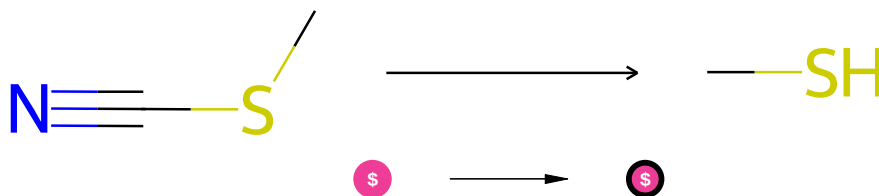


Figure 1: Outline of path 1

2.1.1 Reduction of thiocyanates to thiols



Substrates:

1. Methyl thiocyanate

Products:

1. Methanethiol - *available at Sigma-Aldrich*

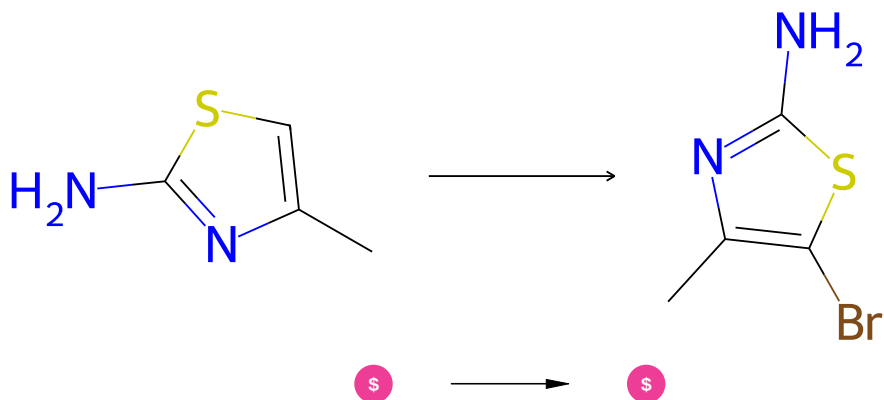
Typical conditions: $\text{NaBH}_4.\text{EtOH}$

Protections: none

Reference: [10.1021/jm100213c](#) p. 4864, 4873 and [10.1016/j.ejmech.2014.09.071](#) p. 308, 310

Retrosynthesis ID: 50811

2.1.2 Published reaction



Substrates:

1. 2-Amino-4-methylthiazole - *available at Sigma-Aldrich*

Products:

1. 5-Bromo-4-methyl-thiazol-2-amine - *available at Sigma-Aldrich*

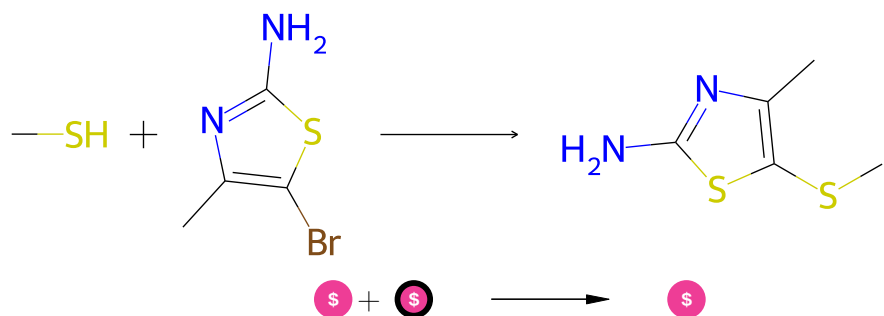
Typical conditions: Br₂

Protections: none

Reference: PATENT: INSTITUT DE RECHERCHES CHIMIQUES ET BIOLOGIQUES APPLIQUEES; FR2658514, 1993

Retrosynthesis ID: 2753330

2.1.3 Published reaction



Substrates:

1. 5-Bromo-4-methyl-thiazol-2-amine - *available at Sigma-Aldrich*
2. Methanethiol - *available at Sigma-Aldrich*

Products:

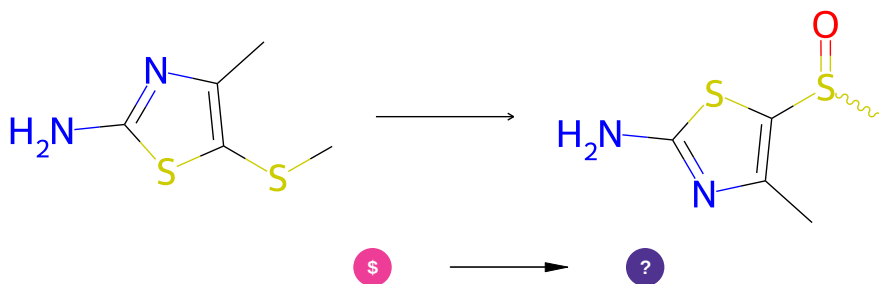
1. 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US20090143448A1

Retrosynthesis ID: 8454157

2.1.4 Oxidation of sulfides to sulfoxides



Substrates:

1. 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*

Products:

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

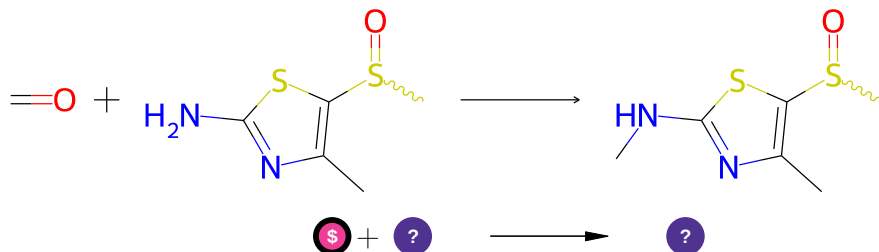
Typical conditions: hexachlorophosphazene.H₂O₂.RT

Protections: none

Reference: DOI: [10.1021/jo1011784](https://doi.org/10.1021/jo1011784)

Retrosynthesis ID: 11037

2.1.5 Reductive alkylation of amines



Substrates:

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

Products:

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

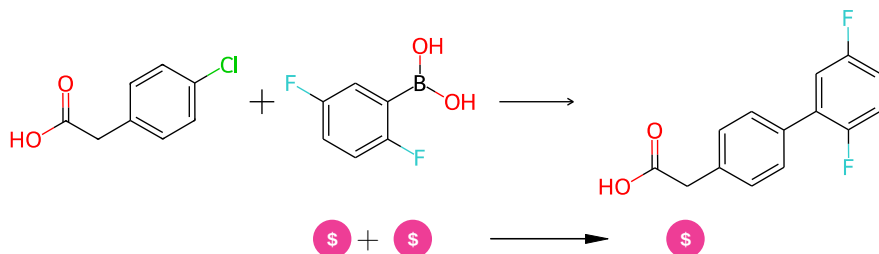
Typical conditions: formaldehyde.NaBH₃CN

Protections: none

Reference: [10.1021/ol048759t](#) and [10.1021/jm050166g](#) and [10.1016/j.ejmech.2011.07.008](#) and [10.1021/ic502998a](#)

Retrosynthesis ID: 26300

2.1.6 Suzuki coupling with aryl chlorides



Substrates:

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

Products:

1. 2',5'-Difluoro-biphenyl-4-acetic acid - *available at Sigma-Aldrich*

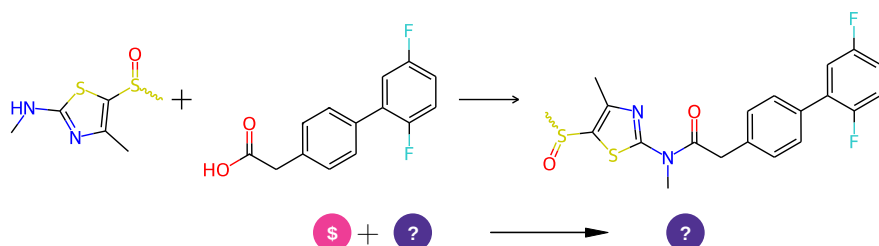
Typical conditions: [Pd].catalyst.base.

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

2.1.7 Amide coupling



Substrates:

1. 2',5'-Difluoro-biphenyl-4-acetic acid - *available at Sigma-Aldrich*
2. CNc1nc(C)c(S(C)=O)s1

Products:

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

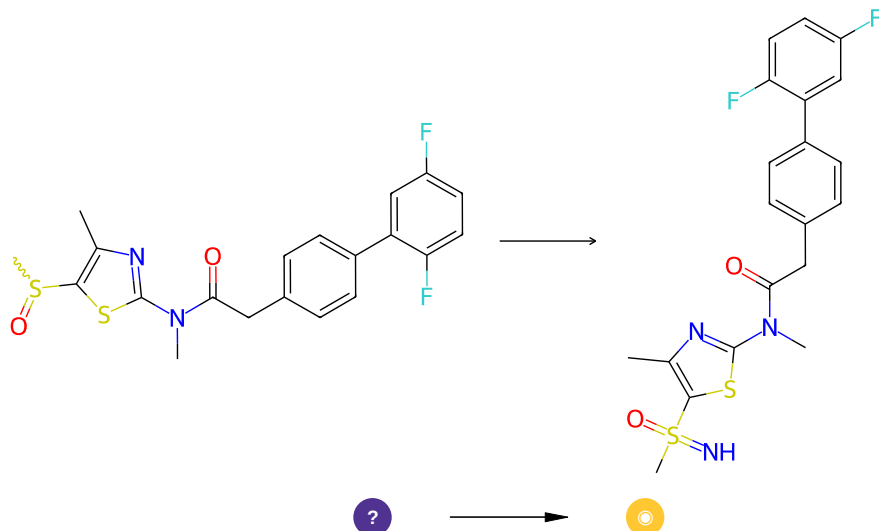
Typical conditions: DCC.DCM or EDC.DCM or SOCl₂.DCM

Protections: none

Reference: [10.1021/ol400686f](#) and [10.1021/jo00200a057](#) and [10.1021/cr100048w](#) and [10.1039/B701677H](#) and [10.1039/C5RA24527C](#) and [10.3727/000000006783981206](#) and [10.1021/np060007f](#) and [10.1021/jo00012a058](#) and [10.1016/j.bmcl.2007.08.037](#) and [10.1039/C0OB00355G](#) and [10.1021/jm500031w](#) (p.3056) and [10.1016/j.tet.2011.03.046](#)

Retrosynthesis ID: 9147

2.1.8 Synthesis of NH-sulfoximines



Substrates:

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

Products:

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

Typical conditions: NaN₃.Eaton's reagent.50C or FeSO₄.1,10-phen.NbzONH₂*TfOH.MeCN or H₂NCO₂NH₄.PhI(OAc)₂.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