

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

*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

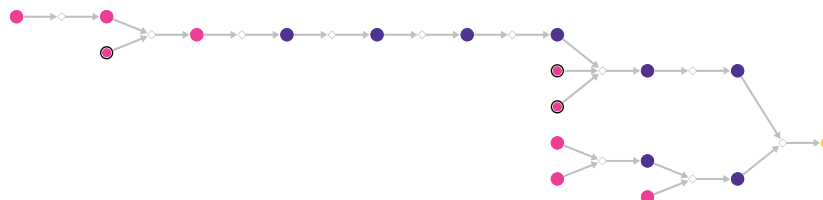
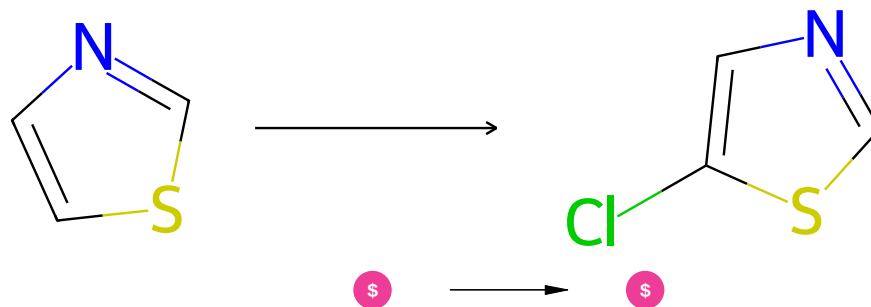


Figure 1: Outline of path 1

2.1.1 Chlorination of aromatic compounds



Substrates:

1. Thiazole - *available at Sigma-Aldrich*

Products:

1. 5-Chlorothiazole - *available at Sigma-Aldrich*

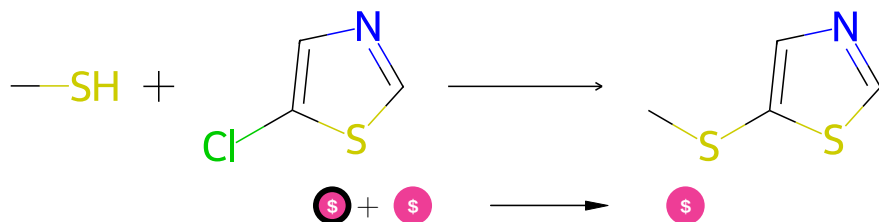
Typical conditions: Cl₂ or other chlorinating agent like NCS

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 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. Methanethiol - *available at Sigma-Aldrich*
2. 5-Chlorothiazole - *available at Sigma-Aldrich*

Products:

1. 5-(Methylthio)thiazole - *available at Sigma-Aldrich*

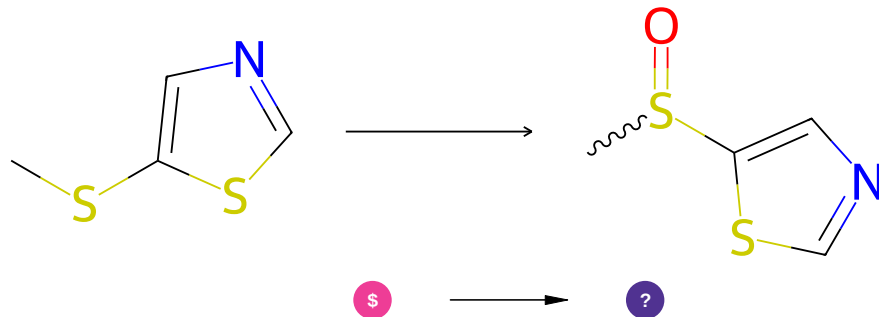
Typical conditions: Pd(OAc)₂.tBuONa.DME.110C

Protections: none

Reference: [10.1021/ja0580340](https://doi.org/10.1021/ja0580340)

Retrosynthesis ID: 1299

2.1.3 Oxidation of sulfides to sulfoxides



Substrates:

1. 5-(Methylthio)thiazole - *available at Sigma-Aldrich*

Products:

1. CS(=O)c1cnsc1

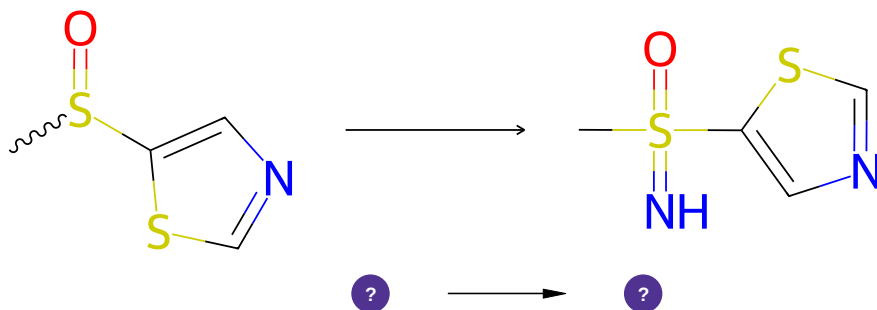
Typical conditions: TaC.H₂O₂.MeOH.45C

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. CS(=O)c1cnsc1

Products:

1. CS(=N)(=O)c1cnsc1

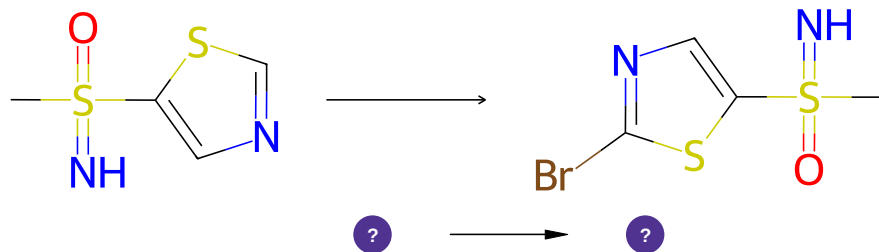
Typical conditions: NaN₃.Eaton's reagent.50C or FeSO₄.1,10-phen.NbzONH₂*TfOH.MeCN or H₂NCO₂NH₄.PhI(OAc)₂.MeOH

Protections: none

Reference: [10.1016/j.tetlet.2016.12.031](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 Bromination of aromatic compounds



Substrates:

1. CS(=N)(=O)c1cncs1

Products:

1. CS(=N)(=O)c1cnc(Br)s1

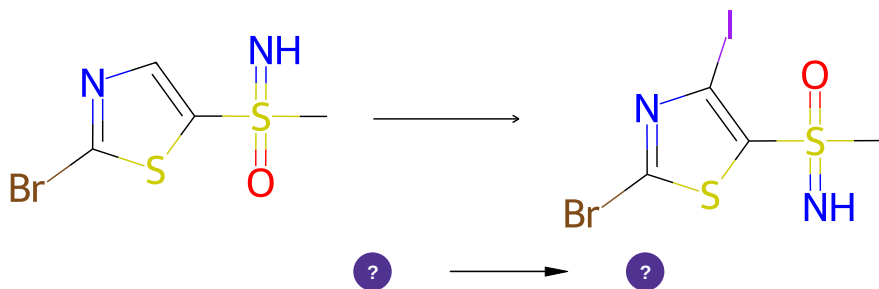
Typical conditions: Br₂.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.1.6 Iodination of aromatic compounds



Substrates:

1. CS(=N)(=O)c1cnc(Br)s1

Products:

1. CS(=N)(=O)c1sc(Br)nc1I

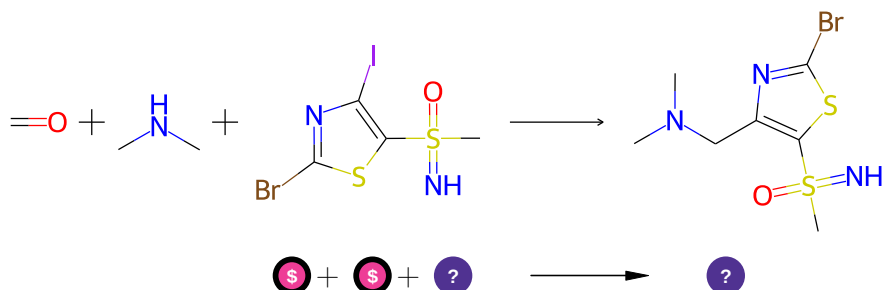
Typical conditions: I₂ or other iodinating agent e.g. NIS

Protections: none

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

2.1.7 Reformatsky-type coupling of aldehydes and amines



Substrates:

1. Dimethylamine - *available at Sigma-Aldrich*
2. Formalin - *available at Sigma-Aldrich*
3. CS(=N)(=O)c1sc(Br)nc1I

Products:

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

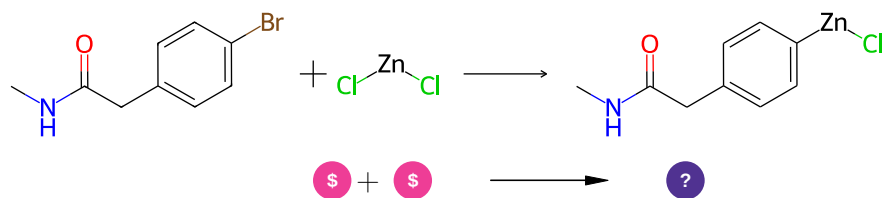
Typical conditions: Zn.ACN.60C

Protections: none

Reference: [10.1055/s-2008-1072582](https://doi.org/10.1055/s-2008-1072582) AND [10.1021/jo901704s](https://doi.org/10.1021/jo901704s)

Retrosynthesis ID: 21135

2.1.8 Synthesis of Arylzinc compounds



Substrates:

1. Dichlorozinc - *available at Sigma-Aldrich*
2. 2-(4-Bromophenyl)-N-methylacetamide - *available at Sigma-Aldrich*

Products:

1. CNC(=O)Cc1ccc([Zn]Cl)cc1

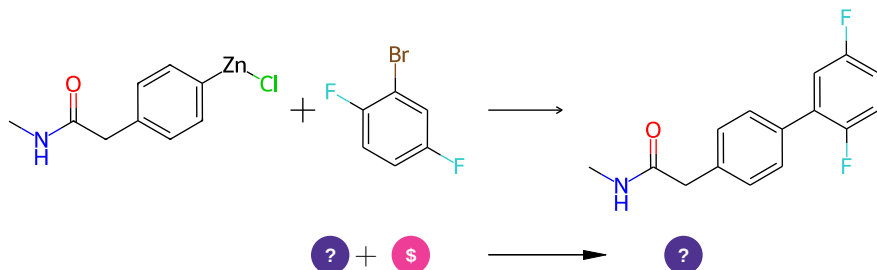
Typical conditions: IPrMgClxLiCl or nBuLi(-78C).ZnCl2.THF

Protections: none

Reference: [10.1016/j.tet.2011.01.030](#) [10.1021/jo801063c](#)

Retrosynthesis ID: 10149

2.1.9 Palladium mediated aryl-aryl cross coupling



Substrates:

1. CNC(=O)Cc1ccc([Zn]Cl)cc1
2. 2-Bromo-1,4-difluorobenzene - *available at Sigma-Aldrich*

Products:

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

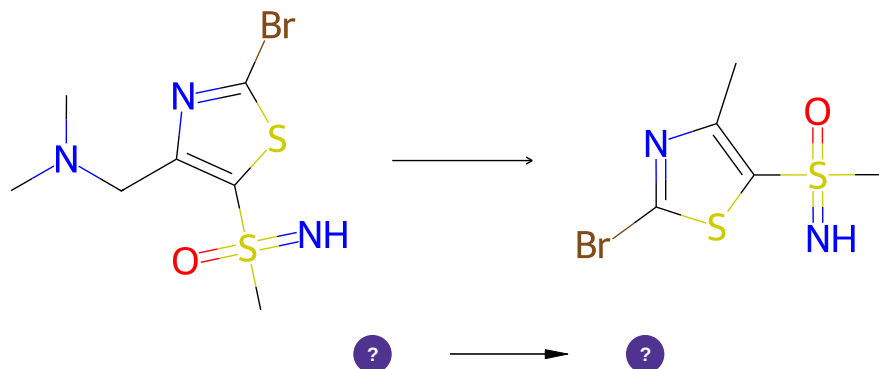
Typical conditions: [Pd].catalyst

Protections: none

Reference: [10.1016/j.tet.2011.01.030](#) and [10.1016/S0040-4020\(01\)00241-1](#) and [10.1021/ol1007026](#) and [10.1021/jo801063c](#) and [10.1002/anie.201207750](#) and [10.1002/9780470638859.conrr456](#)

Retrosynthesis ID: 1968

2.1.10 Deamination of benzylic amines



Substrates:

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

Products:

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

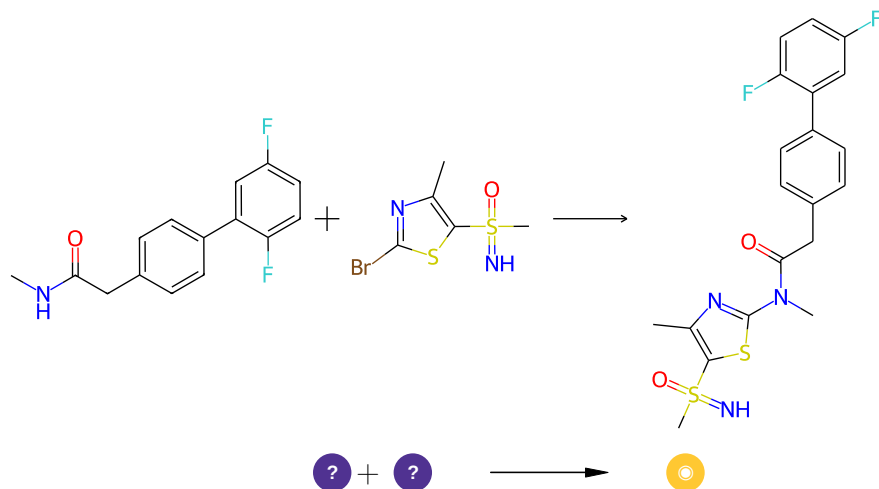
Typical conditions: H₂.Pd/C

Protections: none

Reference: [10.1021/ja070588a](#)

Retrosynthesis ID: 21173

2.1.11 N-arylation of amides



Substrates:

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

2. Cc1nc(Br)sc1S(C)(=N)=O

Products:

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

Typical conditions: Cs₂CO₃.CuX₂/CuX.toluene.130C

Protections: none

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

Retrosynthesis ID: 10207