

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

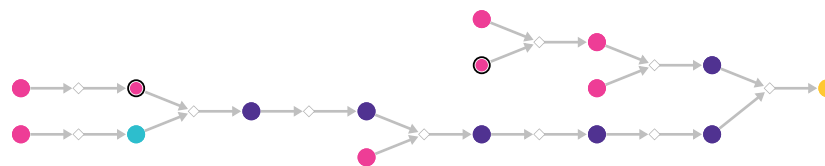
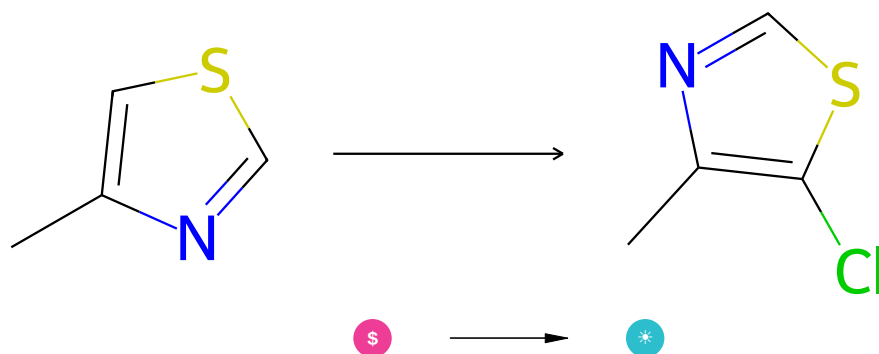


Figure 1: Outline of path 1

2.1.1 Chlorination of aromatic compounds



Substrates:

1. 4-Methylthiazole - *available at Sigma-Aldrich*

Products:

1. 4-Methyl-5-chlorothiazole

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 Synthesis of thiols from disulfides



Substrates:

1. Methyl disulfide - *available at Sigma-Aldrich*

Products:

1. Methanethiol - *available at Sigma-Aldrich*

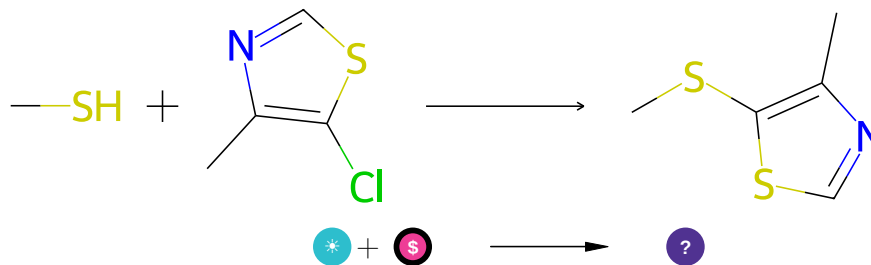
Typical conditions: NaBH₄.THF.0 C or NaBH₄.EtOH.70 C

Protections: none

Reference: [10.1021/jm0510880](https://doi.org/10.1021/jm0510880) p. 4073, 4080 and [10.1016/S0968-0896\(00\)00257-1](https://doi.org/10.1016/S0968-0896(00)00257-1) p. 504, 506

Retrosynthesis ID: 10982

2.1.3 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. 4-Methyl-5-chlorothiazole
2. Methanethiol - *available at Sigma-Aldrich*

Products:

1. CSc1scnc1C

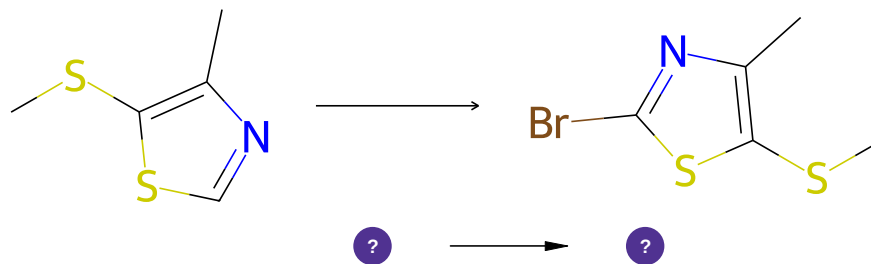
Typical conditions: Pd(OAc)2.tBuONa.DME.110C

Protections: none

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

Retrosynthesis ID: 1299

2.1.4 Bromination of aromatic compounds



Substrates:

1. CSc1scnc1C

Products:

1. CSc1sc(Br)nc1C

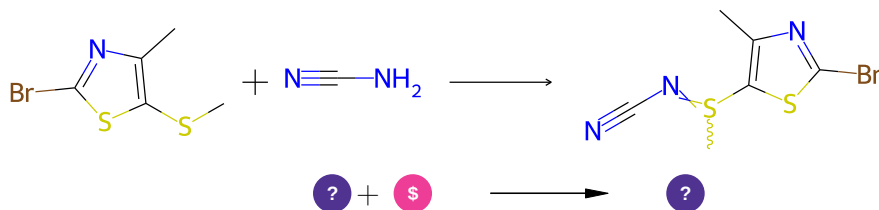
Typical conditions: Br2.Fe

Protections: none

Reference: [10.1021/acs.accounts.6b00120](https://doi.org/10.1021/acs.accounts.6b00120)

Retrosynthesis ID: 7777000

2.1.5 Synthesis of N-cyano sulfilimines



Substrates:

1. CSc1sc(Br)nc1C
2. Cyanamide - *available at Sigma-Aldrich*

Products:

1. Cc1nc(Br)sc1S(C)=NC#N

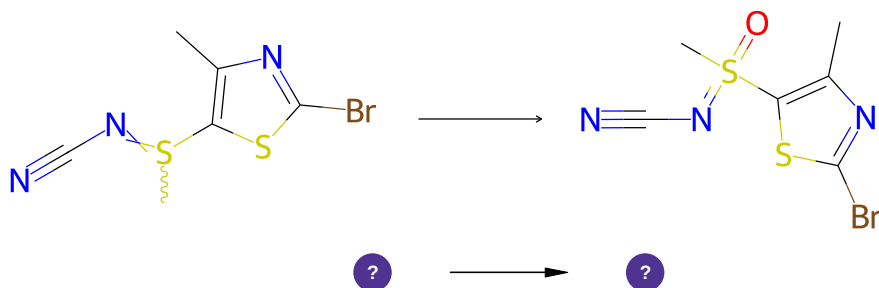
Typical conditions: PhI(OAc)2.CH3CN.0C

Protections: none

Reference: US3505401A p.3-6 and *10.1021/ol7016577*

Retrosynthesis ID: 10033463

2.1.6 Synthesis of N-cyanosulfoximines by oxidation of N-cyano sulfilimines



Substrates:

1. Cc1nc(Br)sc1S(C)=NC#N

Products:

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

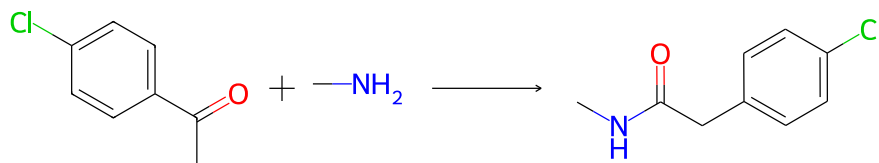
Typical conditions: mCPBA.MeOH.K2CO3

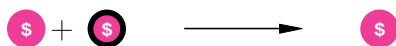
Protections: none

Reference: *10.1055/s-0030-1258192*

Retrosynthesis ID: 10037382

2.1.7 Willgerodt-Kindler Reaction





Substrates:

1. 4-Chloroacetophenone - *available at Sigma-Aldrich*
2. Methanamine - *available at Sigma-Aldrich*

Products:

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

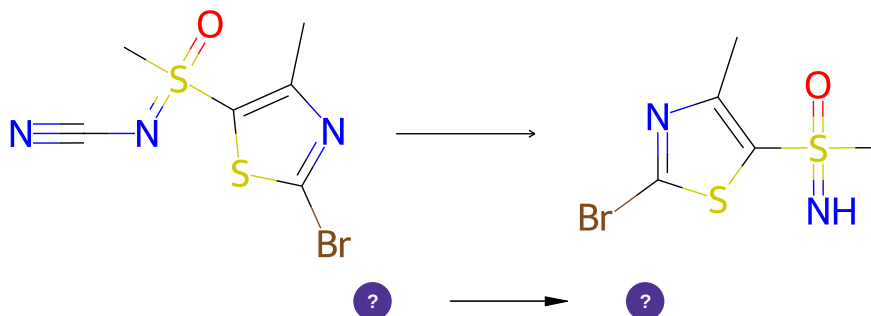
Typical conditions: (NH₄)₂S.H₂O

Protections: none

Reference: *10.1039/C3CS60154D*

Retrosynthesis ID: 11694

2.1.8 Synthesis of NH-sulfoximines by hydrolysis of N-cyano sulfoximines



Substrates:

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

Products:

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

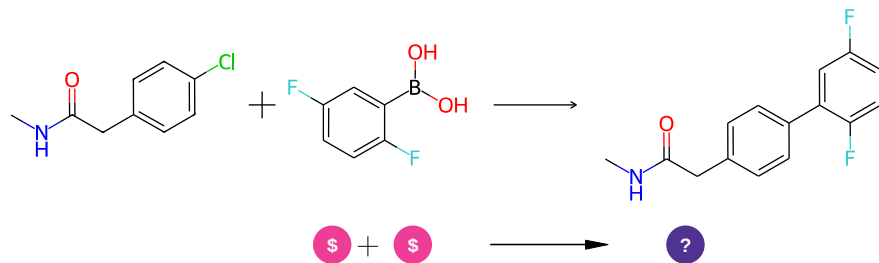
Typical conditions: H₂SO₄.H₂O or HCl.dioxane.H₂O

Protections: none

Reference: *10.1055/s-0034-1378936* and US2009029863 p.11

Retrosynthesis ID: 10037380

2.1.9 Suzuki coupling with aryl chlorides



Substrates:

1. 2-(4-Chlorophenyl)-N-methylacetamide - *available at Sigma-Aldrich*
2. 2,5-Difluorophenylboronic acid - *Combi-Blocks*

Products:

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

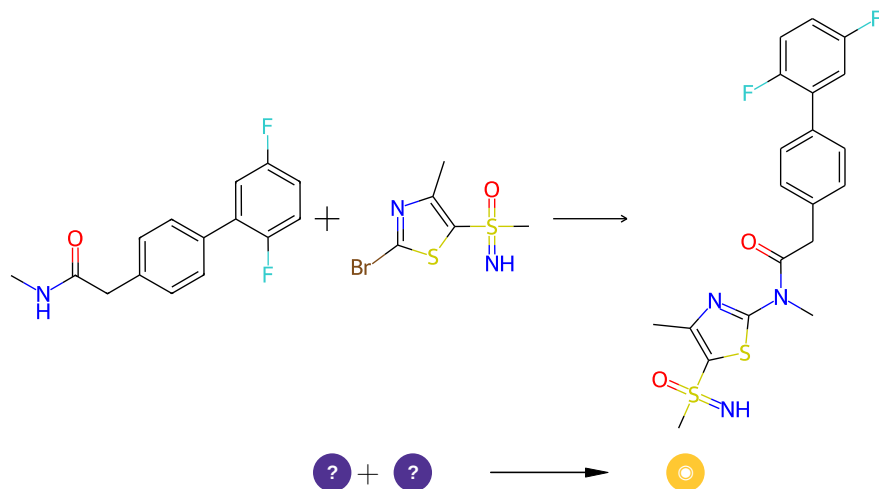
Typical conditions: [Pd].catalyst.base.

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

2.1.10 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