

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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000 * (\text{FILTERS} + \text{CONFLICT} + \text{NON_SELECTIVITY}) + 40 * \text{PROTECT}$

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

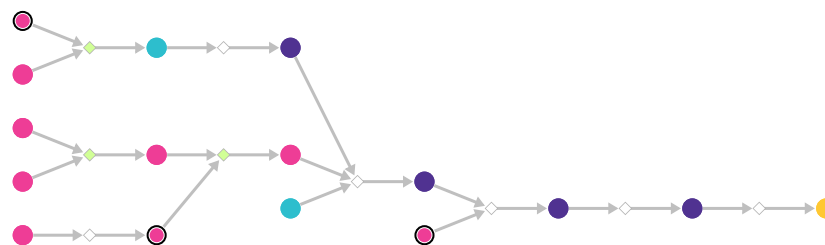
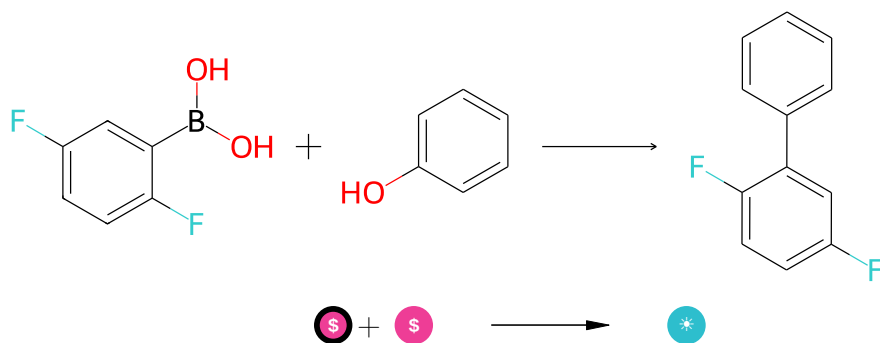


Figure 1: Outline of path 1

2.1.1 Published reaction



Substrates:

1. C₆H₆O - *available at Sigma-Aldrich*
2. 2,5-Difluorophenylboronic acid - *Combi-Blocks*

Products:

1. 2,5-Difluorobiphenyl

Typical conditions: Stage 1: 240 s, 90 degree, Tetrabutylammonium bromide, C45H59Cl1N1P1Pd1, N-Methyl-2-pyrrolidone, Toluene, Water, K3O4P Potassium phosphate, tribasic | Stage 2: null | Stage 3: null

Protections: none

Reference: [10.1002/ANIE.201101480](#)

Retrosynthesis ID: 4345800

2.1.2 Synthesis of thiols from disulfides



Substrates:

1. Methyl disulfide - [available at Sigma-Aldrich](#)

Products:

1. Methanethiol - [available at Sigma-Aldrich](#)

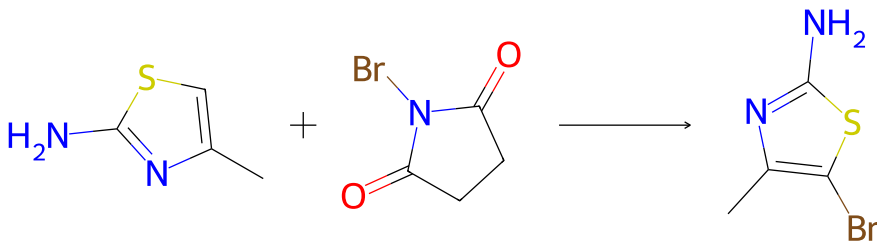
Typical conditions: NaBH₄.THF.0 C or NaBH₄.EtOH.70 C

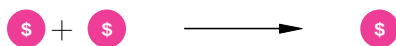
Protections: none

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

Retrosynthesis ID: 10982

2.1.3 Published reaction





Substrates:

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

Products:

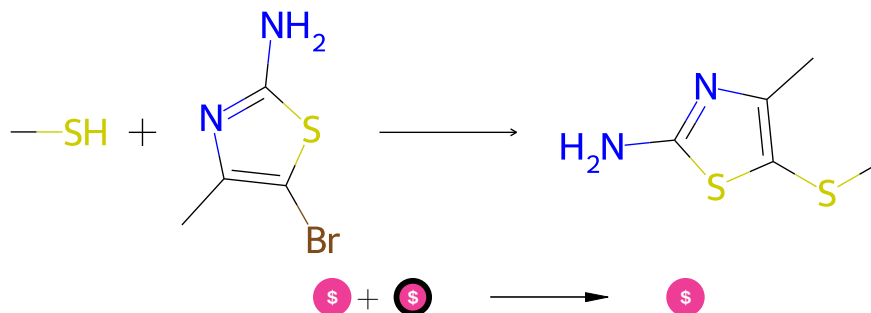
1. 5-Bromo-4-methyl-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US05369107

Retrosynthesis ID: 6299162

2.1.4 Published reaction



Substrates:

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

Products:

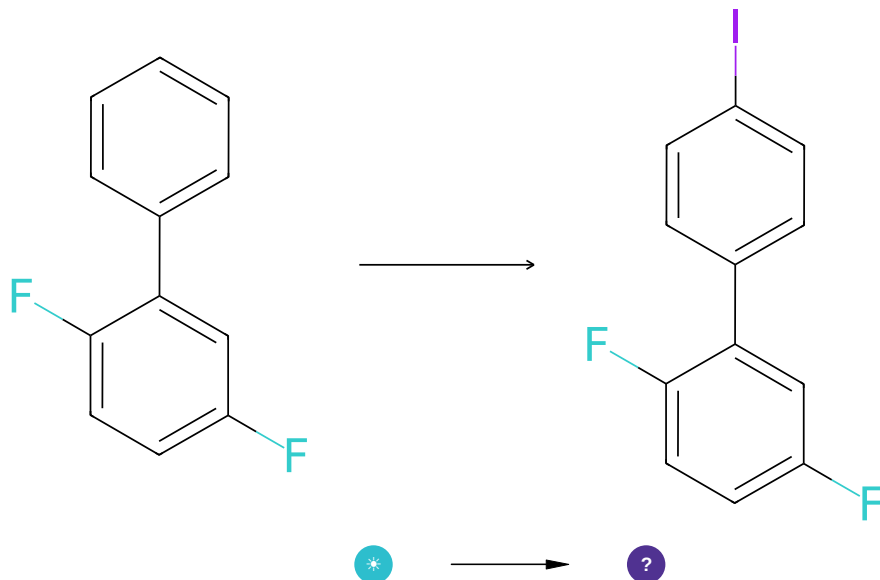
1. 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US20090143448A1

Retrosynthesis ID: 8454157

2.1.5 Iodination of aromatic compounds



Substrates:

1. 2,5-Difluorobiphenyl

Products:

1. Fc1ccc(F)c(-c2ccc(I)cc2)c1

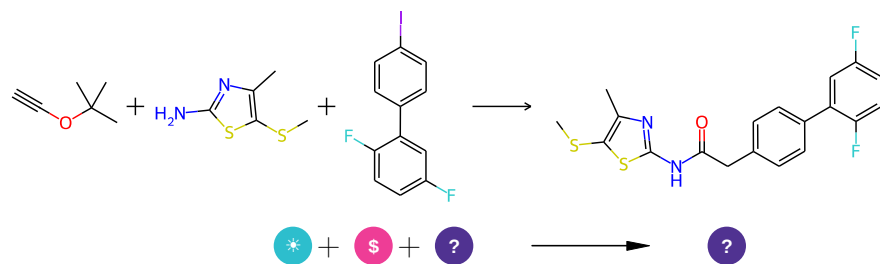
Typical conditions: I₂ or other iodinating agent e.g. NIS

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

2.1.6 Synthesis of amides from aryl iodides through ynol ethers



Substrates:

1. Tert-butoxy-ethyne
2. 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*
3. Fc1ccc(F)c(-c2ccc(I)cc2)c1

Products:

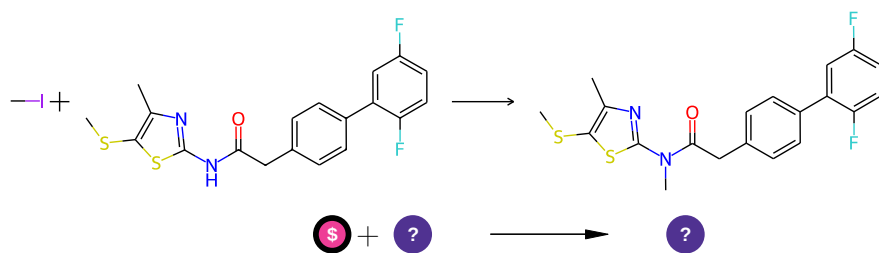
1. CSc1sc(NC(=O)Cc2ccc(-c3cc(F)ccc3F)cc2)nc1C

Typical conditions: [Pd2(dba)3].PPh3.CuI.DIPEA.4A MS 2. amine.75C.toluene

Protections: none

Reference: DOI: [10.1002/anie.201405036](https://doi.org/10.1002/anie.201405036)

Retrosynthesis ID: 1679

2.1.7 N-alkylation of amides**Substrates:**

1. Iodomethane - *available at Sigma-Aldrich*
2. CSc1sc(NC(=O)Cc2ccc(-c3cc(F)ccc3F)cc2)nc1C

Products:

1. CSc1sc(N(C)C(=O)Cc2ccc(-c3cc(F)ccc3F)cc2)nc1C

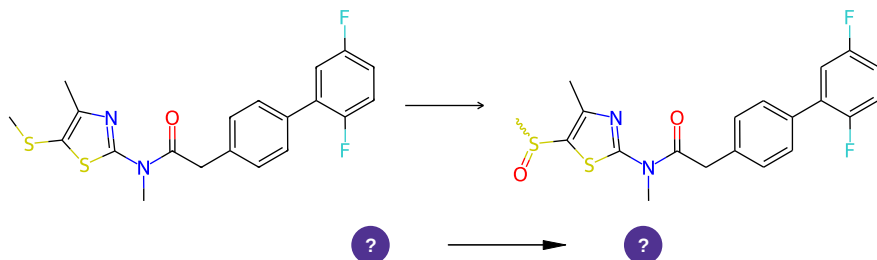
Typical conditions: NaH.DMF

Protections: none

Reference: DOI: [10.1016/j.bmc.2014.03.007](https://doi.org/10.1016/j.bmc.2014.03.007) and [10.1016/j.tetlet.2008.10.057](https://doi.org/10.1016/j.tetlet.2008.10.057)

Retrosynthesis ID: 8841

2.1.8 Oxidation of sulfides to sulfoxides



Substrates:

1. CSc1sc(N(C)C(=O)Cc2ccc(-c3cc(F)ccc3F)cc2)nc1C

Products:

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

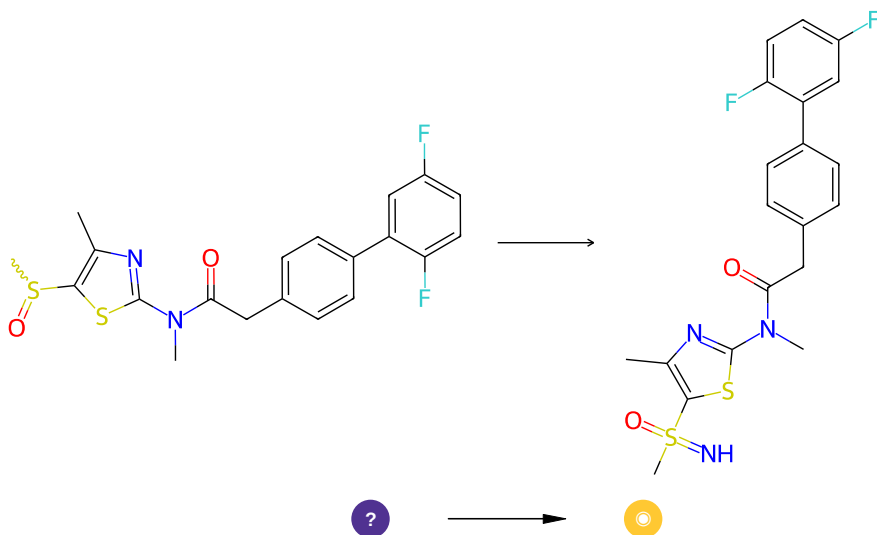
Typical conditions: TaC.H₂O₂.MeOH.45C

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

2.1.9 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