

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

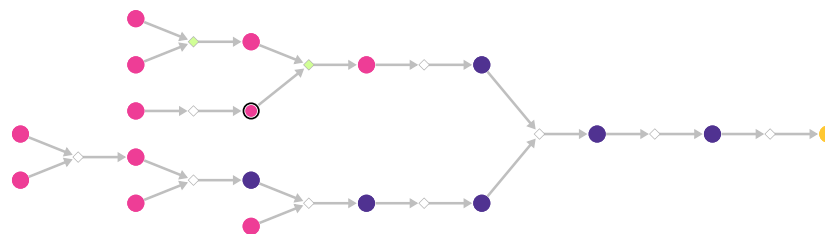
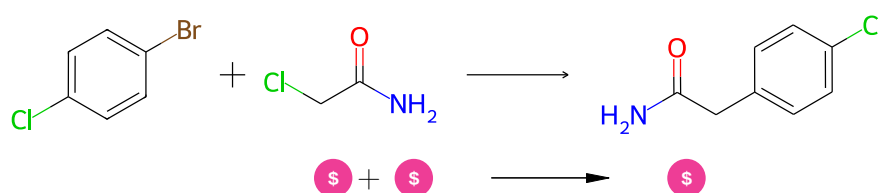


Figure 1: Outline of path 1

2.1.1 Photoredox Cross-Electrophile Coupling of alpha-Chloro Carbonyls with Aryl Halides



Substrates:

1. 1-Bromo-4-chlorobenzene - *available at Sigma-Aldrich*
2. Chloroacetamide - *available at Sigma-Aldrich*

Products:

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

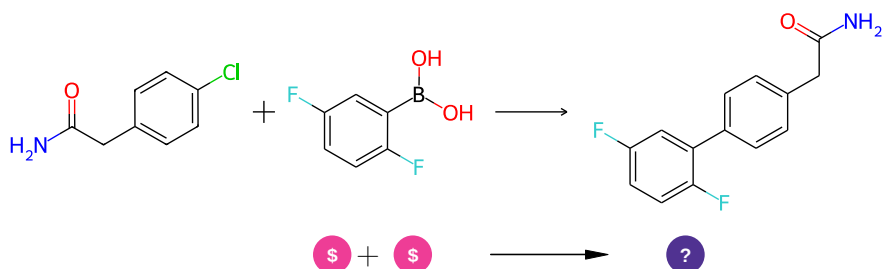
Typical conditions: [Ir]-photocat.[Ni]-cat.silane reagent.base.blue light

Protections: none

Reference: [10.1002/anie.201909072](#)

Retrosynthesis ID: 31016954

2.1.2 Suzuki coupling with aryl chlorides



Substrates:

- 2-(4-Chlorophenyl)acetamide - [available at Sigma-Aldrich](#)
- 2,5-Difluorophenylboronic acid - [Combi-Blocks](#)

Products:

- NC(=O)Cc1ccc(-c2cc(F)ccc2F)cc1

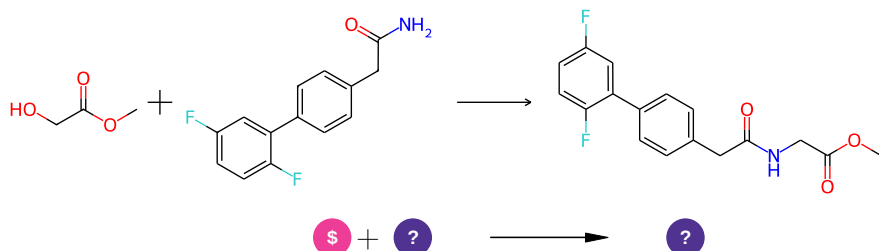
Typical conditions: [Pd].catalyst.base.

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

2.1.3 Alkylation of primary amides



Substrates:

1. Methyl glycolate - *available at Sigma-Aldrich*
2. NC(=O)Cc1ccc(-c2cc(F)ccc2F)cc1

Products:

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

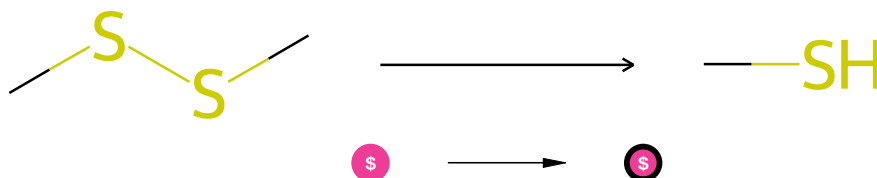
Typical conditions: O(PPh₃)₂. [Ru(p-cymene)Cl₂]₂. MW. heat

Protections: none

Reference: [10.1021/jo102521a](#)

Retrosynthesis ID: 10597

2.1.4 Synthesis of thiols from disulfides



Substrates:

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

Products:

1. Methanethiol - *available at Sigma-Aldrich*

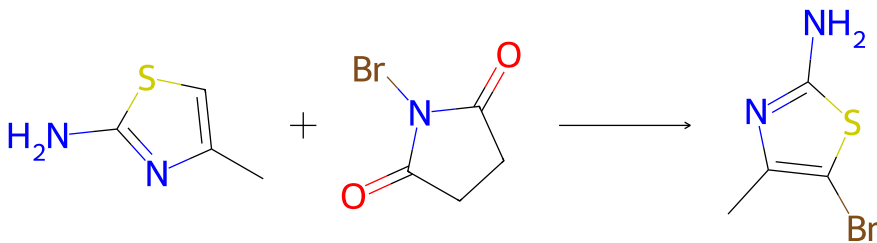
Typical conditions: NaBH₄. THF. 0 °C or NaBH₄. EtOH. 70 °C

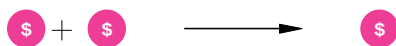
Protections: none

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

Retrosynthesis ID: 10982

2.1.5 Published reaction





Substrates:

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

Products:

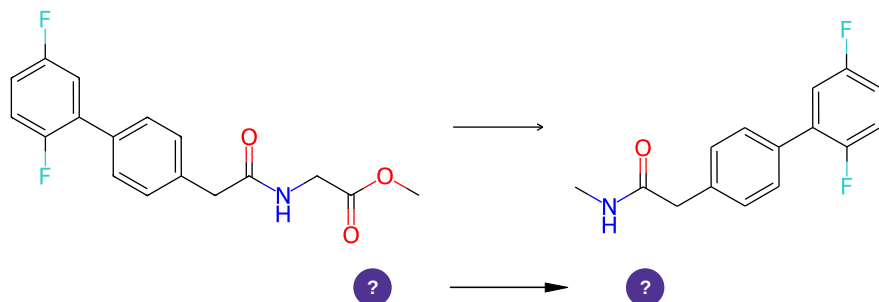
1. 5-Bromo-4-methyl-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US05369107

Retrosynthesis ID: 6299162

2.1.6 Barton decarboxylation



Substrates:

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

Products:

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

Typical conditions:
2.Bu3SnH.AIBN.hv.DMF.rt

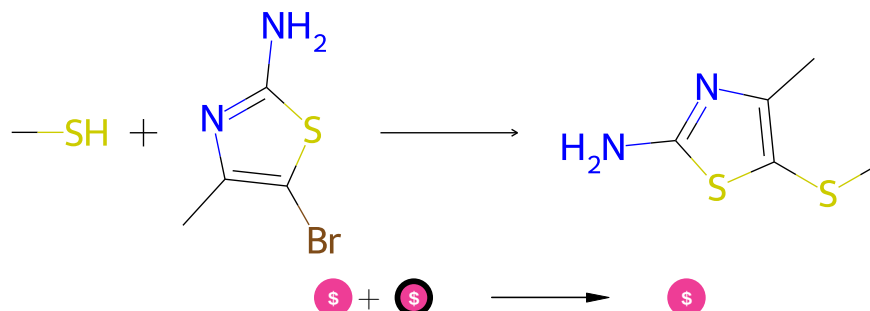
1.2-thiopyridine-N-oxide.NEt3

Protections: none

Reference: *10.1021/ja048084p* AND *10.1021/ol0340235* AND *10.1039/c1ob06370g* AND *10.1039/C39940001687* and *10.1021/ja103428y*

Retrosynthesis ID: 21252

2.1.7 Published reaction



Substrates:

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

Products:

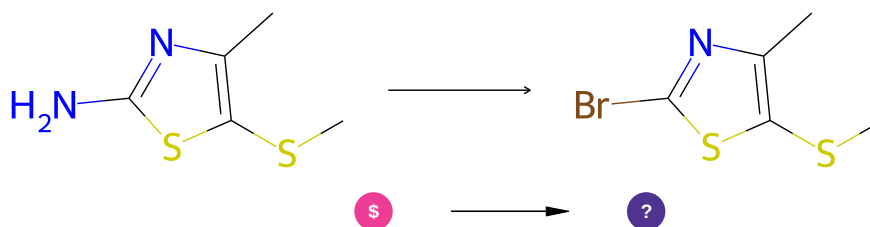
1. 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US20090143448A1

Retrosynthesis ID: 8454157

2.1.8 Sandmeyer Reaction



Substrates:

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

Products:

1. CSc1sc(Br)nc1C

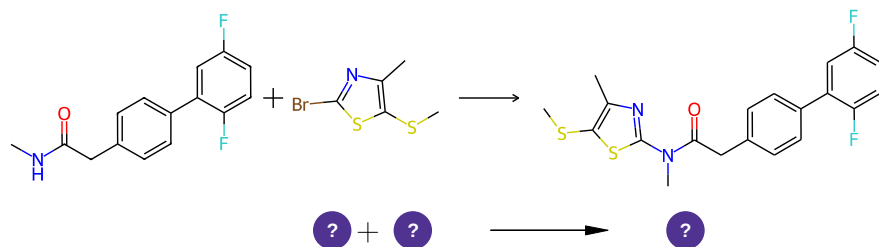
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

Protections: none

Reference: [10.1002/chem.201600278](#) and [10.1016/j.bmcl.2011.12.131](#) and [10.1016/j.ejmech.2013.01.046](#) and [10.1021/jm0002782](#) and [10.1002/ejoc.201300443](#) and [10.1021/jo052589w](#) (SI, page S3) and [10.1021/jm800527x](#) and [10.1016/j.bmcl.2015.04.098](#) and [10.1021/ja034563x](#)

Retrosynthesis ID: 29904

2.1.9 N-arylation of amides



Substrates:

1. CSc1sc(Br)nc1C
2. CNC(=O)Cc1ccc(-c2cc(F)ccc2F)cc1

Products:

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

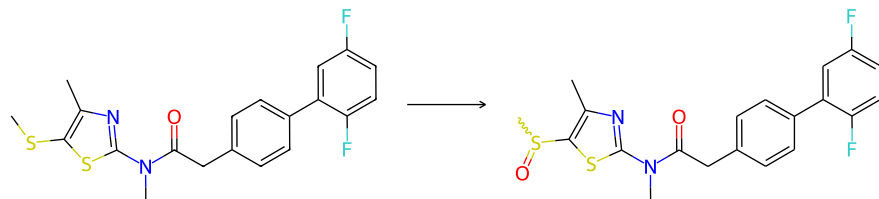
Typical conditions: Cs2CO3.CuX2/CuX.toluene.130C

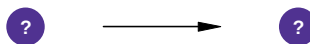
Protections: none

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

Retrosynthesis ID: 10207

2.1.10 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

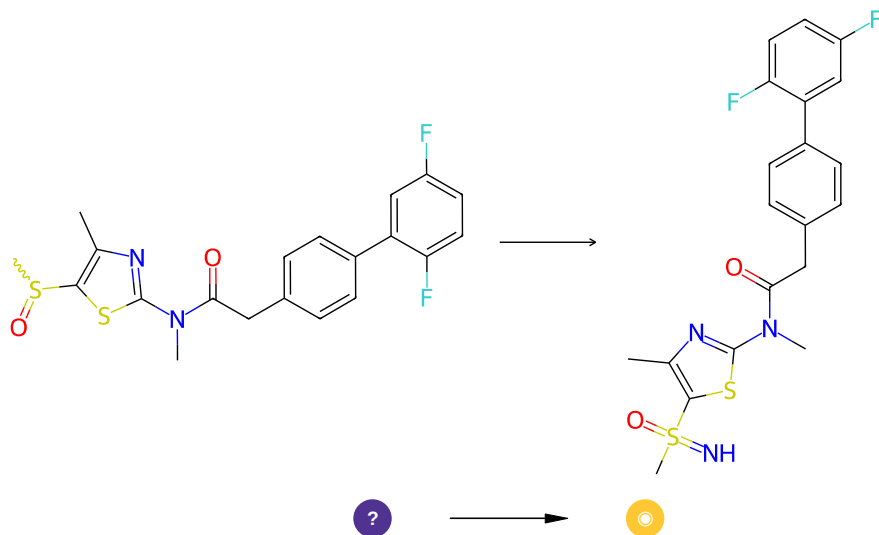
Typical conditions: TaC.H₂O₂.MeOH.45C

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

2.1.11 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