

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

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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

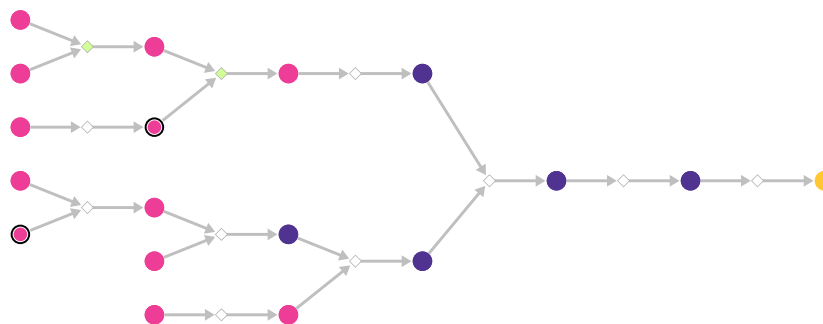
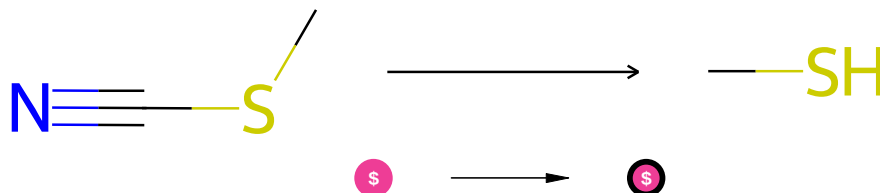


Figure 1: Outline of path 1

2.1.1 Reduction of thiocyanates to thiols



Substrates:

1. Methyl thiocyanate

Products:

1. Methanethiol - *available at Sigma-Aldrich*

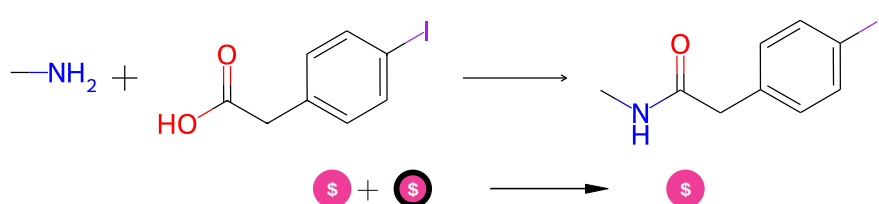
Typical conditions: NaBH₄.EtOH

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 Amide coupling



Substrates:

1. (4-Iodophenyl)acetic acid - *available at Sigma-Aldrich*
2. Methanamine - *available at Sigma-Aldrich*

Products:

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

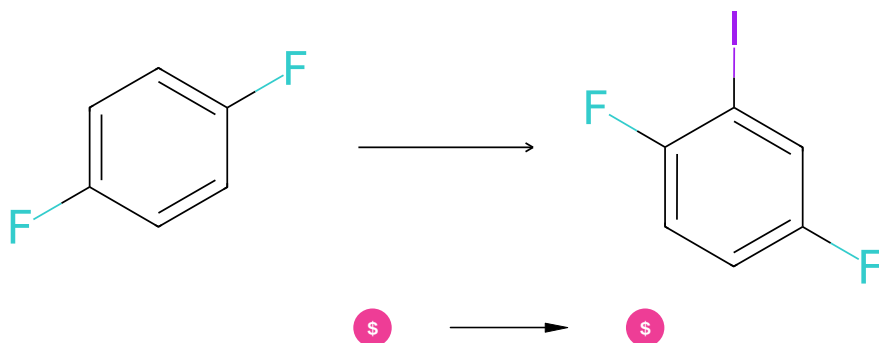
Typical conditions: DCC.DCM or EDC.DCM or SOCl₂.DCM

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

2.1.3 Directed Ortho Metalation followed by Reaction with Electrophile



Substrates:

- 1,4-Difluorobenzene - *available at Sigma-Aldrich*

Products:

- 2,5-Difluoroiodobenzene - *available at Sigma-Aldrich*

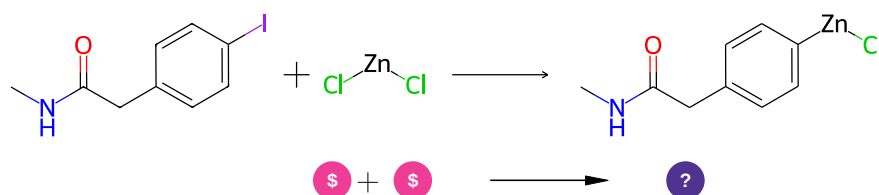
Typical conditions: RLi.or.LiNR₂.-78C.THF.then.I₂

Protections: none

Reference: [10.1016/S0040-4039\(00\)60805-5](#) and [10.1021/om800317v](#)

Retrosynthesis ID: 4366

2.1.4 Synthesis of Arylzinc compounds



Substrates:

- 2-(4-Iodophenyl)-N-methylacetamide - *available at Sigma-Aldrich*
- Dichlorozinc - *available at Sigma-Aldrich*

Products:

- CNC(=O)Cc1ccc([Zn]Cl)cc1

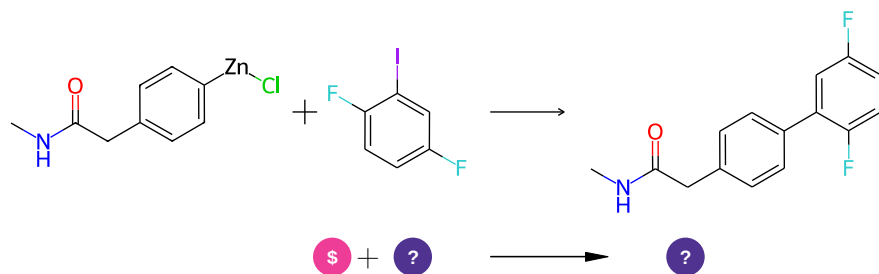
Typical conditions: iPrMgCl.ZnCl₂.THF.-40C

Protections: none

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

Retrosynthesis ID: 10175

2.1.5 Palladium mediated aryl-aryl cross coupling



Substrates:

- 2,5-Difluoroiodobenzene - *available at Sigma-Aldrich*
- CNC(=O)Cc1ccc([Zn]Cl)cc1

Products:

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

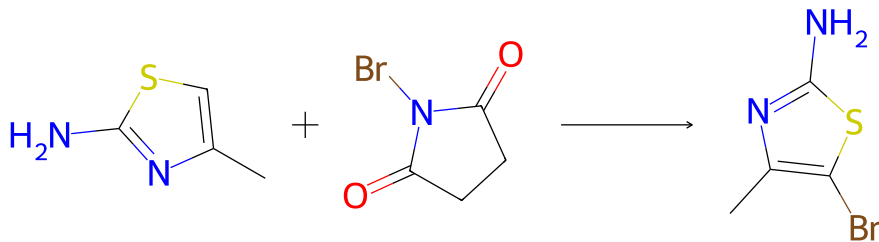
Typical conditions: [Pd].catalyst

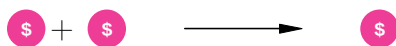
Protections: none

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: 246

2.1.6 Published reaction





Substrates:

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

Products:

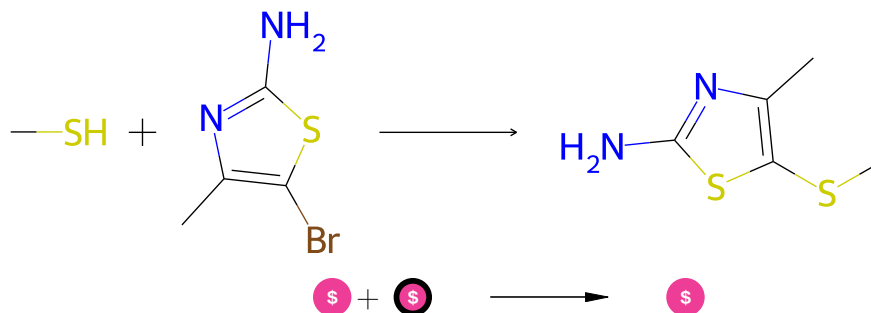
1. 5-Bromo-4-methyl-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US05369107

Retrosynthesis ID: 6299162

2.1.7 Published reaction



Substrates:

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

Products:

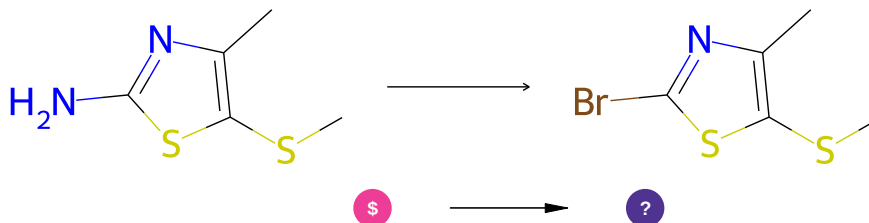
1. 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*

Protections: none

Reference: US20090143448A1

Retrosynthesis ID: 8454157

2.1.8 Sandmeyer Reaction



Substrates:

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

Products:

1. CSc1sc(Br)nc1C

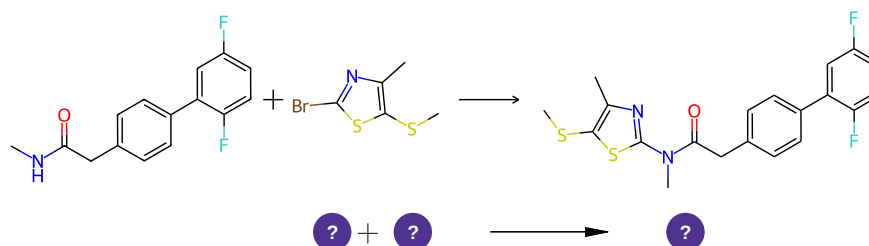
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

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

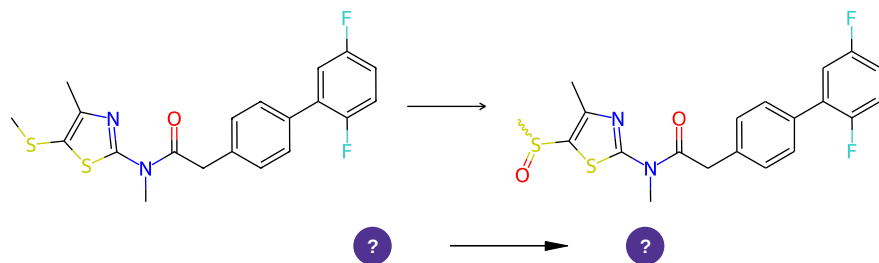
Typical conditions: Cs₂CO₃.CuX₂/CuX.toluene.130C

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

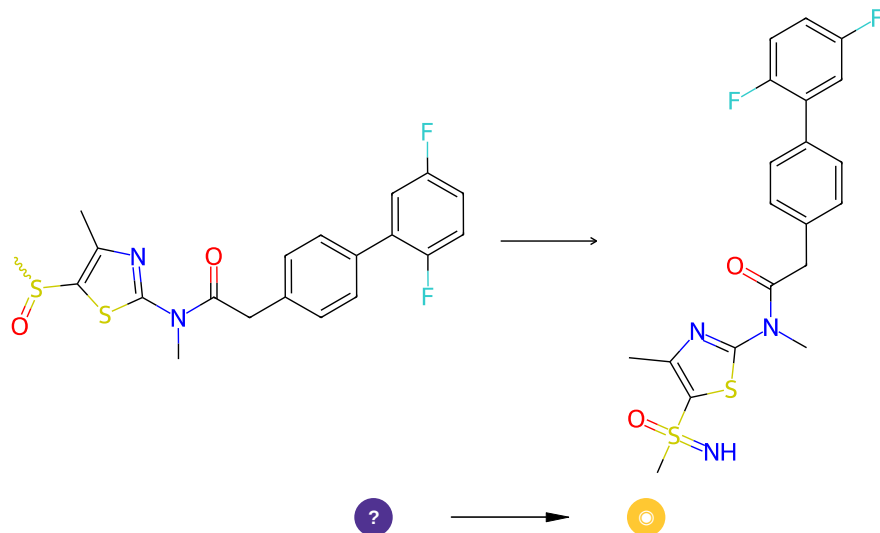
Typical conditions: TaC.H₂O₂.MeOH.45C

Protections: none

Reference: DOI: [10.1055/s-0029-1219947](#) or DOI: [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