

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

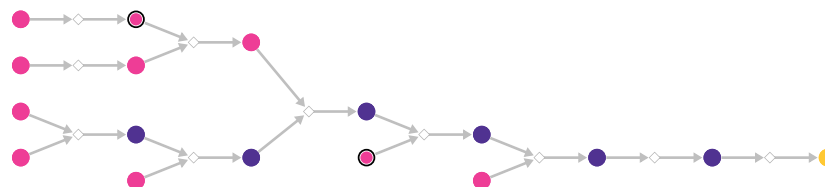
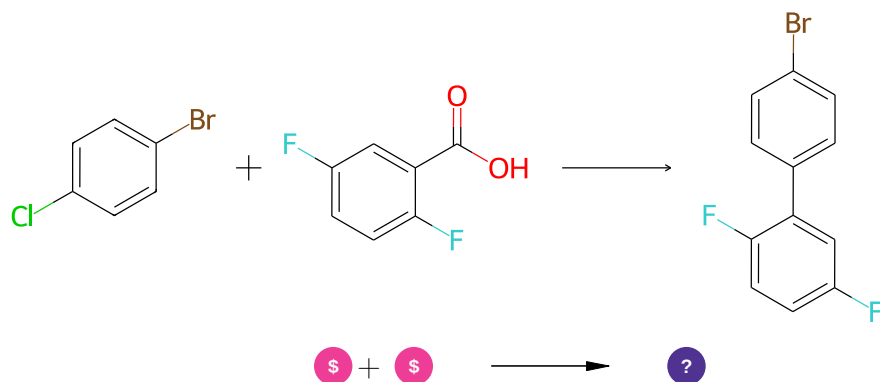


Figure 1: Outline of path 1

2.1.1 Decarboxylative cross-coupling



Substrates:

1. 1-Bromo-4-chlorobenzene - *available at Sigma-Aldrich*
2. 2,5-Difluorobenzoic acid - *available at Sigma-Aldrich*

Products:

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

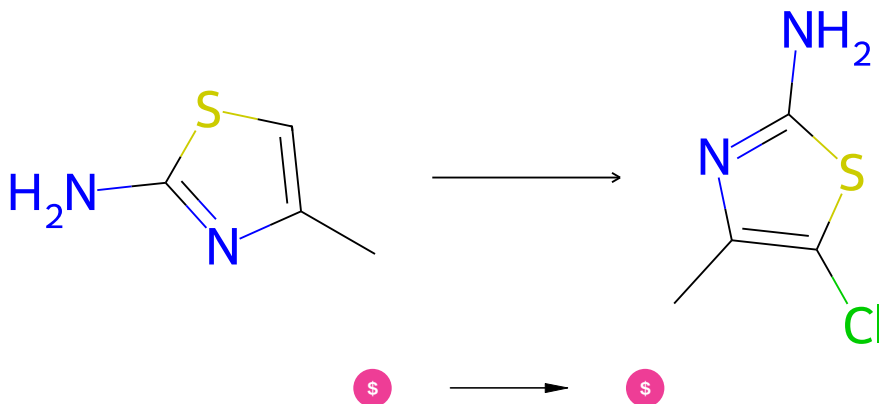
Typical conditions: eg. CuI.PdI2.ligand.K2CO3.NMP.MS.170 deg C

Protections: none

Reference: [10.1039/C1CS15093F](#) and [10.1002/anie.200800728](#) and [10.1021/ja068993+](#)

Retrosynthesis ID: 31019492

2.1.2 Chlorination of aromatic compounds



Substrates:

1. 2-Amino-4-methylthiazole - [available at Sigma-Aldrich](#)

Products:

1. 2-Amino-5-chloro-4-methylthiazole - [available at Sigma-Aldrich](#)

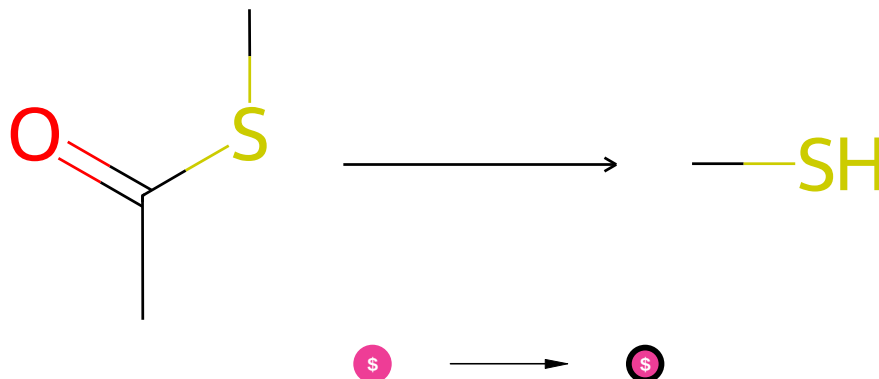
Typical conditions: Cl₂ or other chlorinating agent like NCS

Protections: none

Reference: DOI: [10.1007/s11178-005-0256-1](#)

Retrosynthesis ID: 11125

2.1.3 Hydrolysis of thioesters



Substrates:

1. S-Methyl thioacetate - *available at Sigma-Aldrich*

Products:

1. Methanethiol - *available at Sigma-Aldrich*

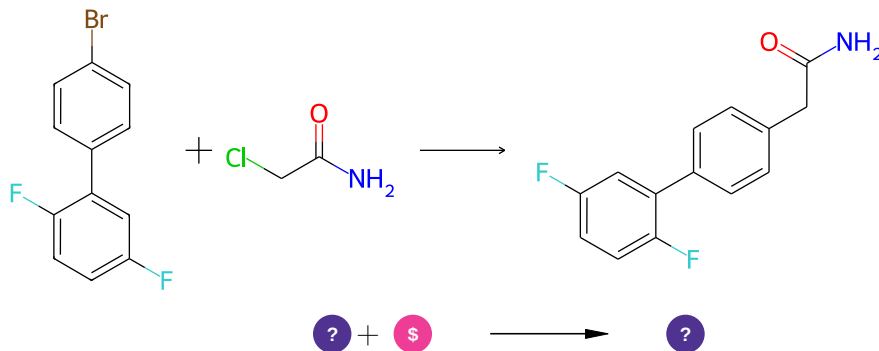
Typical conditions: K₂CO₃.MeOH.rt

Protections: none

Reference: [10.1021/ja2082334](#) (supporting info p14) and [10.1002/anie.200902843](#) (supporting info p5)

Retrosynthesis ID: 22941

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



Substrates:

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

2. Chloracetamide - *available at Sigma-Aldrich*

Products:

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

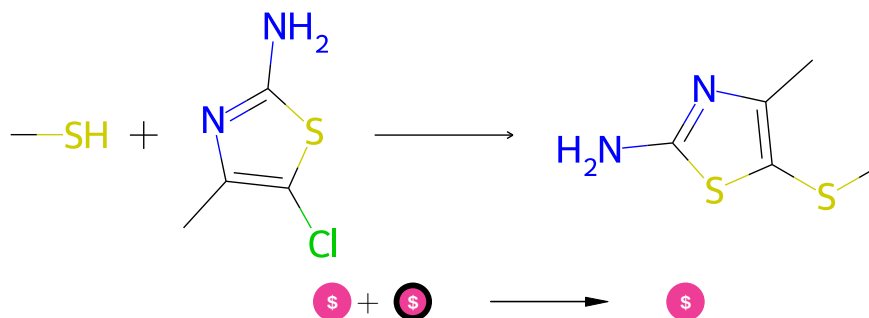
Typical conditions: [Ir]-photocat.[Ni]-cat.silane reagent.base.blue light

Protections: none

Reference: *10.1002/anie.201909072*

Retrosynthesis ID: 31016954

2.1.5 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. 2-Amino-5-chloro-4-methylthiazole - *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*

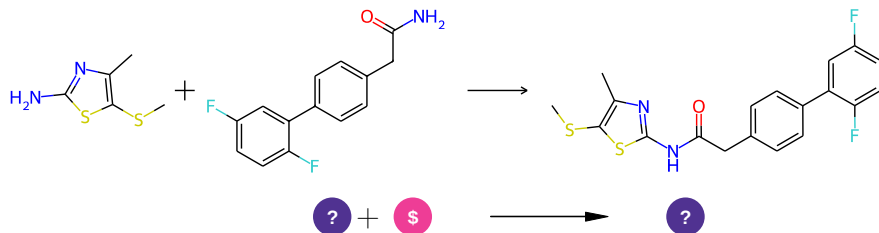
Typical conditions: Pd(OAc)₂.tBuONa.DME.110C

Protections: none

Reference: *10.1021/ja0580340*

Retrosynthesis ID: 1299

2.1.6 Synthesis of N-arylamides from arenediazonium salts



Substrates:

- NC(=O)Cc1ccc(-c2cc(F)ccc2F)cc1
- 4-Methyl-5-(methylsulfanyl)-1,3-thiazol-2-amine - *available at Sigma-Aldrich*

Products:

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

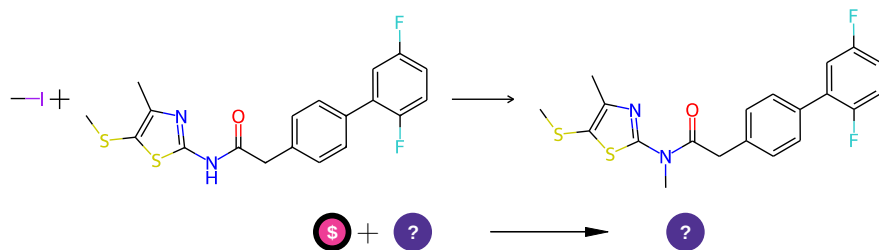
Typical conditions: 1) HCl.NaNO2 2) CuI.TBAI.N,N'-dimethylethane-1,2-diamine.K2CO3.DMSO.110C

Protections: none

Reference: DOI: [10.1055/s-0034-1378556](https://doi.org/10.1055/s-0034-1378556)

Retrosynthesis ID: 1922

2.1.7 N-alkylation of amides



Substrates:

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

Products:

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

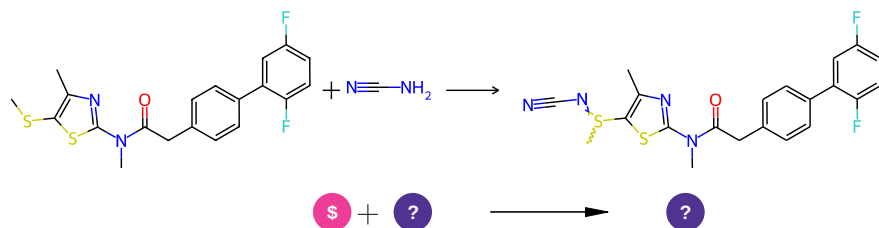
Typical conditions: NaH.DMF

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 Synthesis of N-cyano sulfilimines



Substrates:

1. Cyanamide - *available at Sigma-Aldrich*
2. 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)=NC#N

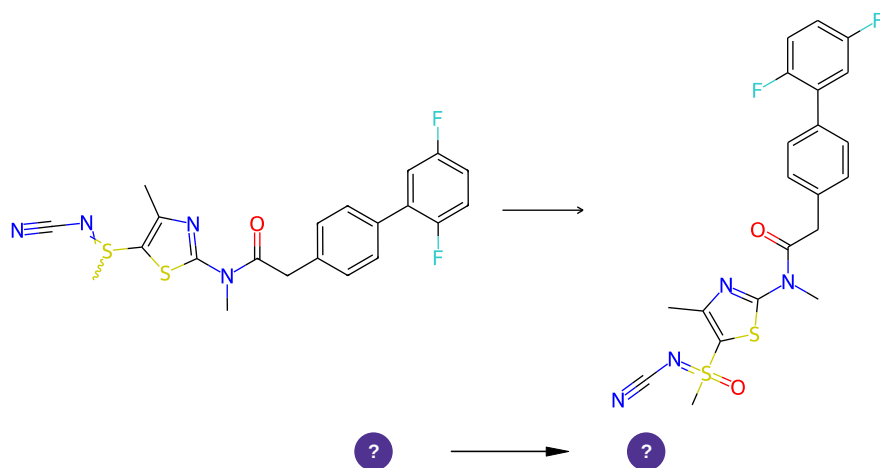
Typical conditions: $\text{PhI}(\text{OAc})_2$.CH₃CN.0C

Protections: none

Reference: US3505401A p.3-6 and [10.1021/ol7016577](https://doi.org/10.1021/ol7016577)

Retrosynthesis ID: 10033463

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



Substrates:

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

Products:

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

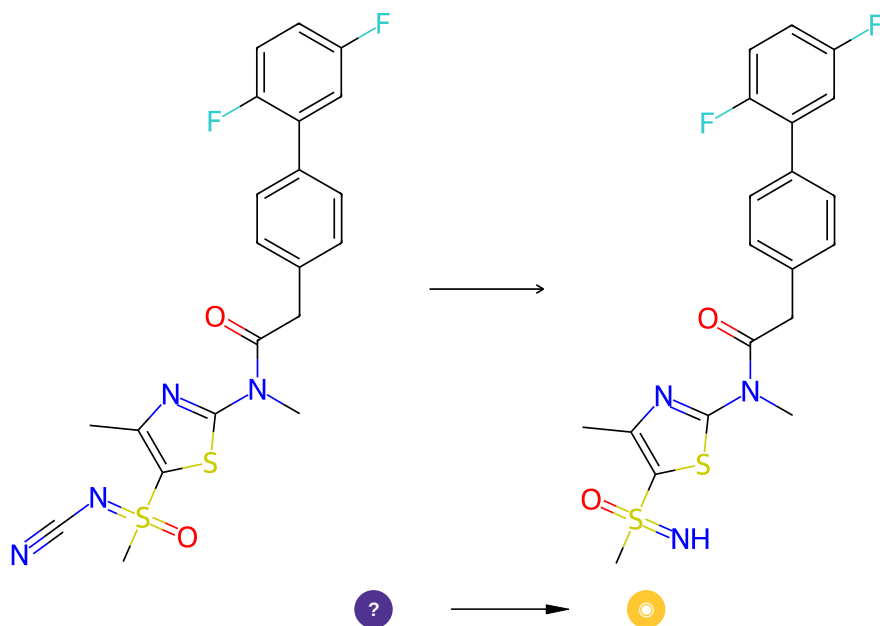
Typical conditions: mCPBA.MeOH.K₂CO₃

Protections: none

Reference: [10.1055/s-0030-1258192](#)

Retrosynthesis ID: 10037382

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



Substrates:

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

Products:

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