

Paths of analysis*

(re)Analysis 1381 - No Filter - Rerun

Synthia

November 28, 2023

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Saved Configuration: General

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 - 1000 \$/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

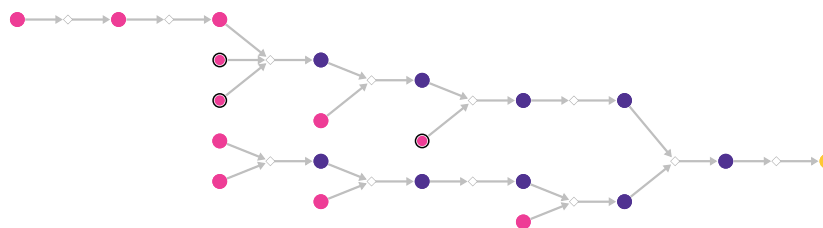
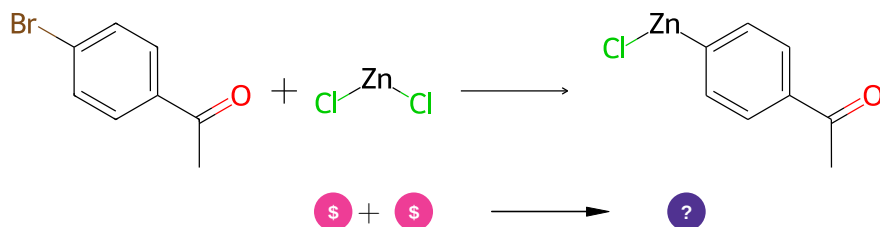


Figure 1: Outline of path 1

2.1.1 Synthesis of Arylzinc compounds



Substrates:

1. Dichlorozinc - *available at Sigma-Aldrich*
2. 4-Bromoacetophenone - *available at Sigma-Aldrich*

Products:

1. CC(=O)c1ccc([Zn]Cl)cc1

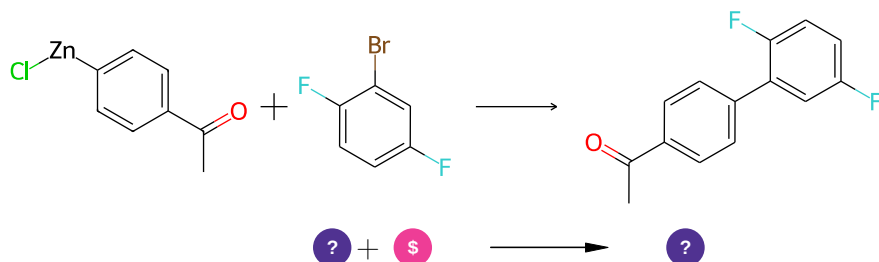
Typical conditions: IPrMgClxLiCl or nBuLi(-78C).ZnCl2.THF

Protections: none

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

Retrosynthesis ID: 10149

2.1.2 Palladium mediated aryl-aryl cross coupling



Substrates:

1. CC(=O)c1ccc([Zn]Cl)cc1
2. 2-Bromo-1,4-difluorobenzene - *available at Sigma-Aldrich*

Products:

1. CC(=O)c1ccc(-c2cc(F)ccc2F)cc1

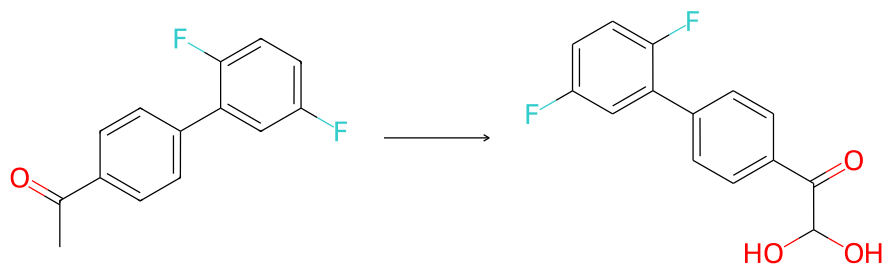
Typical conditions: [Pd].catalyst

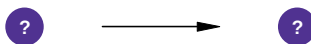
Protections: none

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: 1968

2.1.3 Oxidation of acetophenones to arylglyoxal hydrate





Substrates:

1. CC(=O)c1ccc(-c2cc(F)ccc2F)cc1

Products:

1. O=C(c1ccc(-c2cc(F)ccc2F)cc1)C(O)O

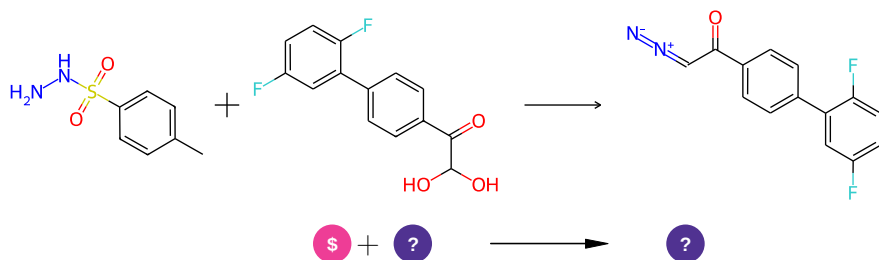
Typical conditions: HBr.DMSO

Protections: none

Reference: [10.1021/jo00225a004](#) and [10.1016/j.tetasy.2010.07.004](#)

Retrosynthesis ID: 9996916

2.1.4 Synthesis of diazoketones from arylglyoxal hydrates



Substrates:

1. Tosylhydrazide - *available at Sigma-Aldrich*
2. O=C(c1ccc(-c2cc(F)ccc2F)cc1)C(O)O

Products:

1. [N-]=[N+]=CC(=O)c1ccc(-c2cc(F)ccc2F)cc1

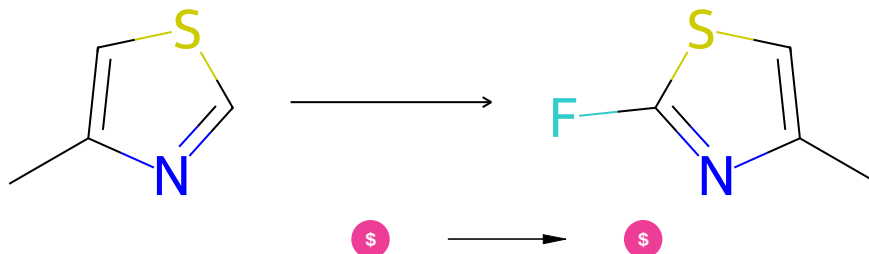
Typical conditions: Cs₂CO₃.chloroform.rt

Protections: none

Reference: [10.1016/j.tet.2014.10.044](#)

Retrosynthesis ID: 9996877

2.1.5 Directed metalation followed by reaction with electrophile



Substrates:

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

Products:

1. 2-Fluoro-4-methyl-1,3-thiazole - *available at Sigma-Aldrich*

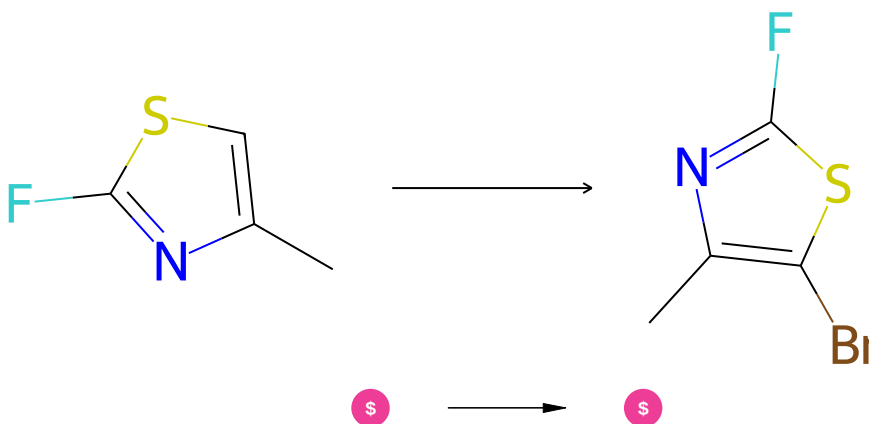
Typical conditions: RLi.or.LiNR₂.-78C.THF.then.NFSI.then.H⁺

Protections: none

Reference: [10.1016/S0040-4039\(01\)02342-5](#) (Fig. 1) and [10.1016/j.tet.2009.06.023](#) (Scheme 2) and [10.1016/j.ejmech.2013.04.054](#) (Scheme 1) and WO2012/138590A1 p. 73 and WO2013/175215A1 p. 77

Retrosynthesis ID: 31022426

2.1.6 Bromination of aromatic compounds



Substrates:

1. 2-Fluoro-4-methyl-1,3-thiazole - *available at Sigma-Aldrich*

Products:

1. 5-Bromo-2-fluoro-4-methyl-1,3-thiazole - *available at Sigma-Aldrich*

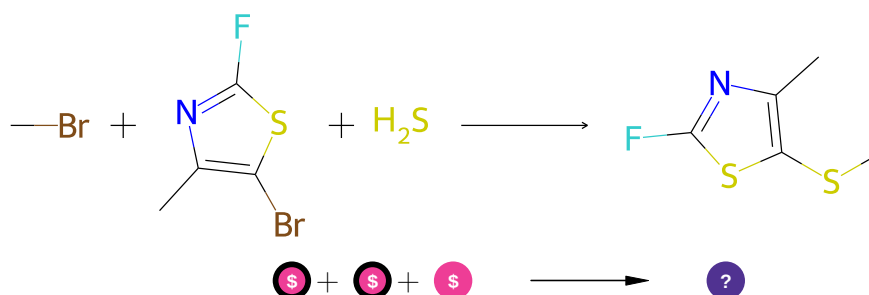
Typical conditions: Br₂.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.1.7 One pot synthesis of aryl-alkyl sulfides



Substrates:

1. Bromomethane - *available at Sigma-Aldrich*
2. Hydrosulfuric acid - *available at Sigma-Aldrich*
3. 5-Bromo-2-fluoro-4-methyl-1,3-thiazole - *available at Sigma-Aldrich*

Products:

1. CSc1sc(F)nc1C

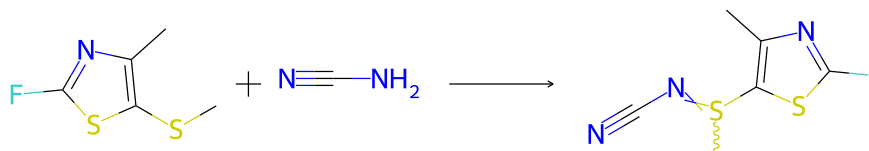
Typical conditions: nBuLi.THF.-78C.then.S.then AlkBr.to.rt

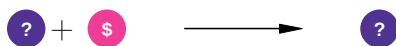
Protections: none

Reference: [10.1021/jo049758h](https://doi.org/10.1021/jo049758h)

Retrosynthesis ID: 5320

2.1.8 Synthesis of N-cyano sulfilimines





Substrates:

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

Products:

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

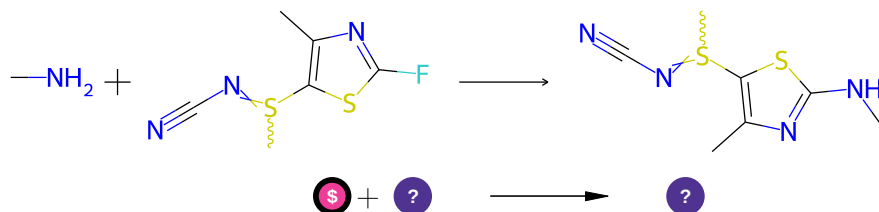
Typical conditions: PhI(OAc)2.CH3CN.0°C

Protections: none

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

Retrosynthesis ID: 10033463

2.1.9 Nucleophilic aromatic substitution



Substrates:

1. Methanamine - *available at Sigma-Aldrich*
2. Cc1nc(F)sc1S(C)=NC#N

Products:

1. CNc1nc(C)c(S(C)=NC#N)s1

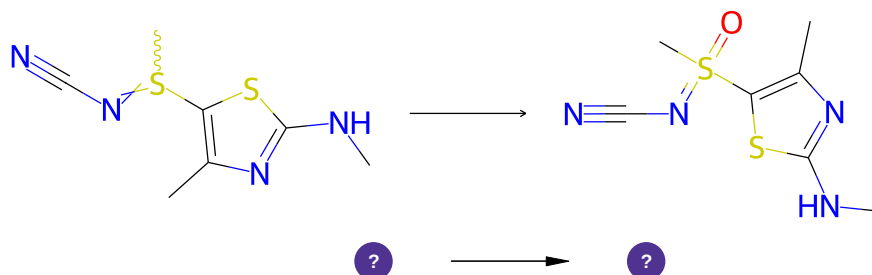
Typical conditions: Solvent

Protections: none

Reference: [10.1002/9781118093559.ch4](#)

Retrosynthesis ID: 49476

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



Substrates:

1. CNc1nc(C)c(S(C)=NC#N)s1

Products:

1. CNc1nc(C)c(S(C)(=O)=NC#N)s1

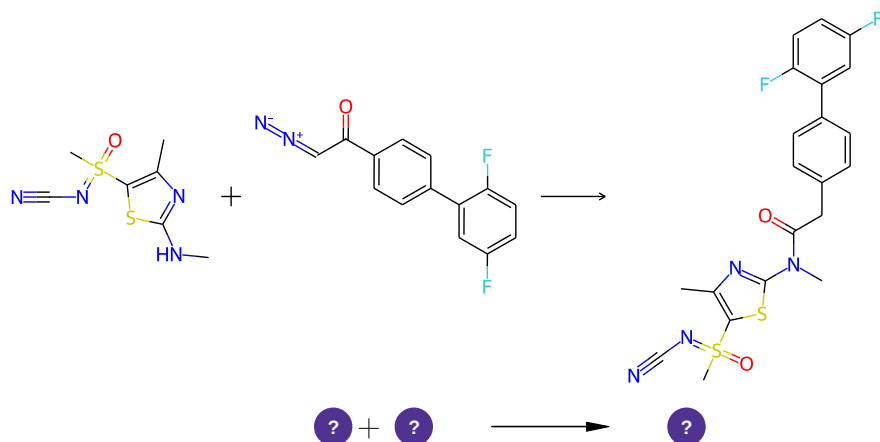
Typical conditions: mCPBA.MeOH.K₂CO₃

Protections: none

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

Retrosynthesis ID: 10037382

2.1.11 Formation of ketenes via Wolff rearrangement followed by amidation



Substrates:

1. [N-]=[N+]=CC(=O)c1ccc(-c2cc(F)ccc2F)cc1

2. CNc1nc(C)c(S(C)(=O)=NC#N)s1

Products:

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

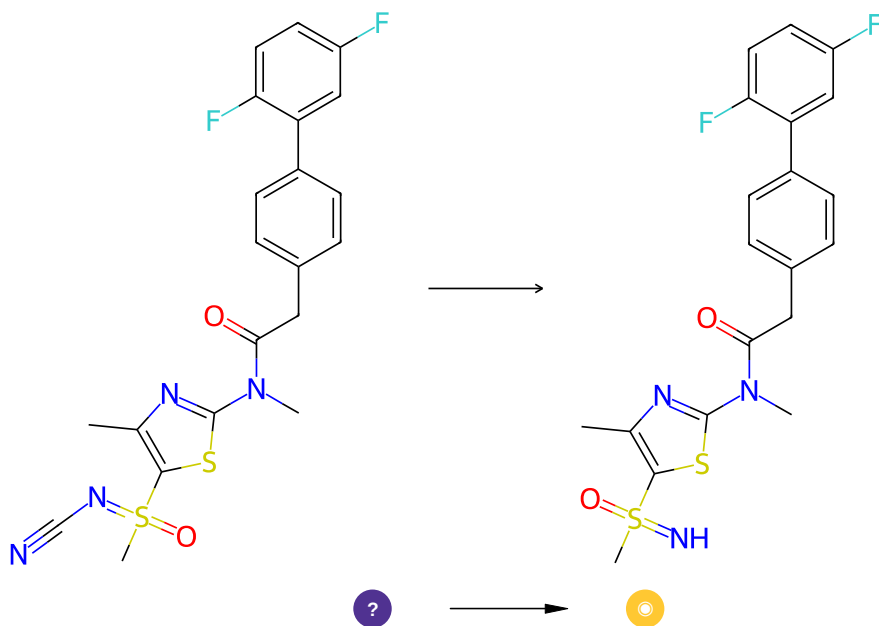
Typical conditions: 1. Ag(I)(cat).hv 2. Amine

Protections: none

Reference: [10.1002/9781118939901.ch3](#) and [10.1002/1099-0690\(200207\)2002:14<2193::AID-EJOC2193>3.0.CO;2-D](#)

Retrosynthesis ID: 31010020

2.1.12 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