

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

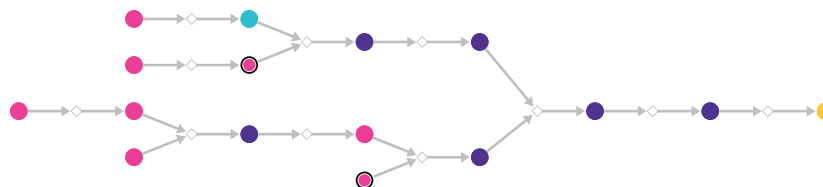
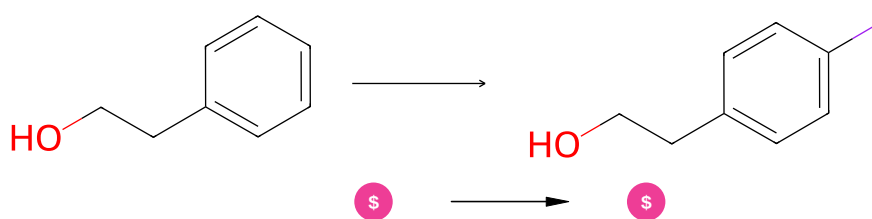


Figure 1: Outline of path 1

2.1.1 Iodination of aromatic compounds



Substrates:

1. Benzylcarbinol - *available at Sigma-Aldrich*

Products:

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

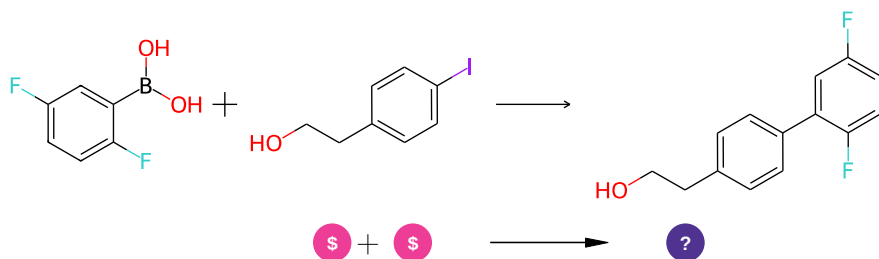
Typical conditions: I2 or other iodinating agent e.g. NIS

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

2.1.2 Suzuki coupling of arylboronic acids with aryl iodides



Substrates:

1. 2,5-Difluorophenylboronic acid - *Combi-Blocks*
2. 2-(4-Iodophenyl)ethanol - *available at Sigma-Aldrich*

Products:

1. OCCc1ccc(-c2cc(F)ccc2F)cc1

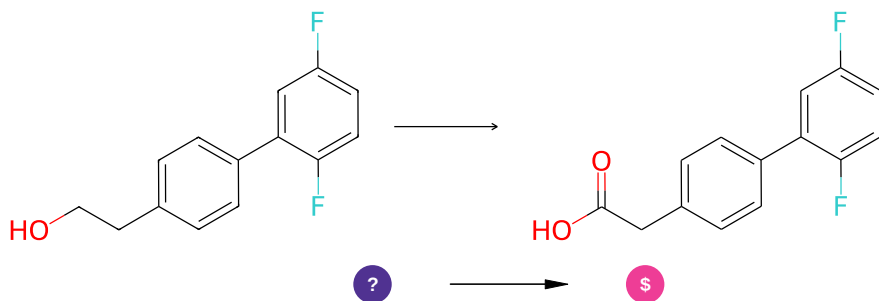
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: [10.1021/cr00039a007](https://doi.org/10.1021/cr00039a007) and [10.1007/3418_2012_32](https://doi.org/10.1007/3418_2012_32) and [10.1021/cr0505268](https://doi.org/10.1021/cr0505268) and [10.1016/j.jfluchem.2016.01.018](https://doi.org/10.1016/j.jfluchem.2016.01.018) and [10.1039/C3CS60197H](https://doi.org/10.1039/C3CS60197H)

Retrosynthesis ID: 25149

2.1.3 Jones Oxidation



Substrates:

1. OCCc1ccc(-c2cc(F)ccc2F)cc1

Products:

1. 2',5'-Difluoro-biphenyl-4-acetic acid - *available at Sigma-Aldrich*

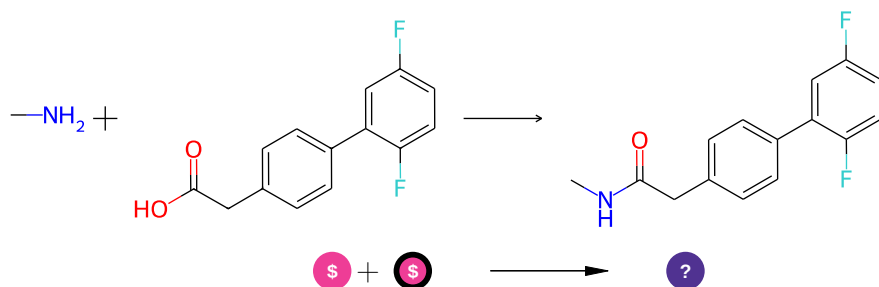
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

Reference: [10.1002/9780470638859.conrr349](#) and [10.1021/jm00270a004](#)

Retrosynthesis ID: 11160

2.1.4 Amide coupling



Substrates:

1. 2',5'-Difluoro-biphenyl-4-acetic acid - *available at Sigma-Aldrich*
2. Methanamine - *available at Sigma-Aldrich*

Products:

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

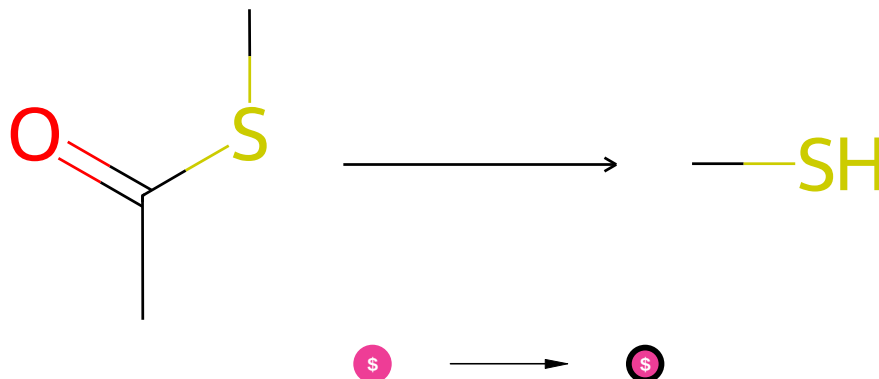
Typical conditions: DCC.DCM or EDC.DCM or SOCl2.DCM

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

2.1.5 Hydrolysis of thioesters



Substrates:

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

Products:

1. Methanethiol - *available at Sigma-Aldrich*

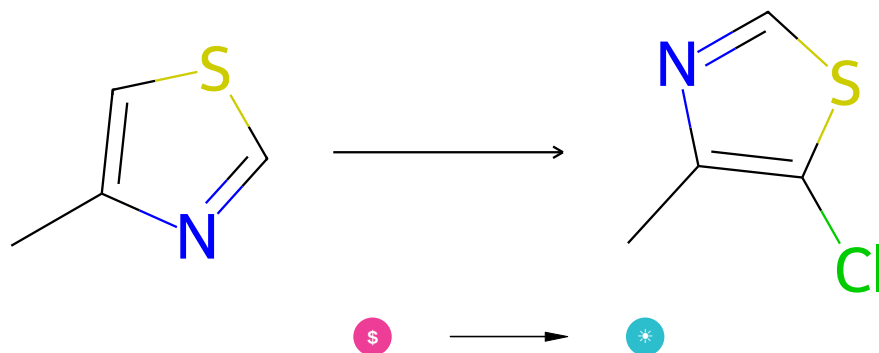
Typical conditions: K₂CO₃.MeOH.rt

Protections: none

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

Retrosynthesis ID: 22941

2.1.6 Chlorination of aromatic compounds



Substrates:

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

Products:

1. 4-Methyl-5-chlorothiazole

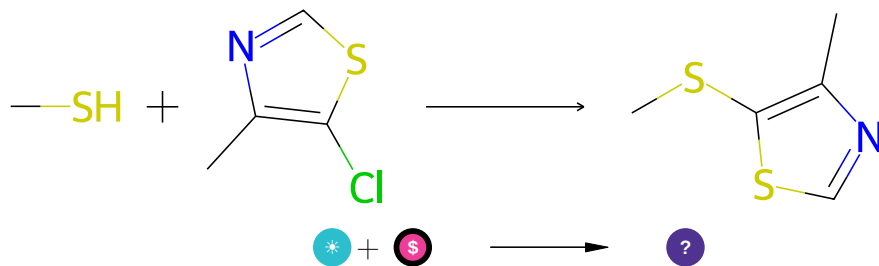
Typical conditions: Cl₂ or other chlorinating agent like NCS

Protections: none

Reference: DOI: [10.1007/s11178-005-0256-1](https://doi.org/10.1007/s11178-005-0256-1)

Retrosynthesis ID: 11125

2.1.7 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. 4-Methyl-5-chlorothiazole
2. Methanethiol - *available at Sigma-Aldrich*

Products:

1. CSc1scnc1C

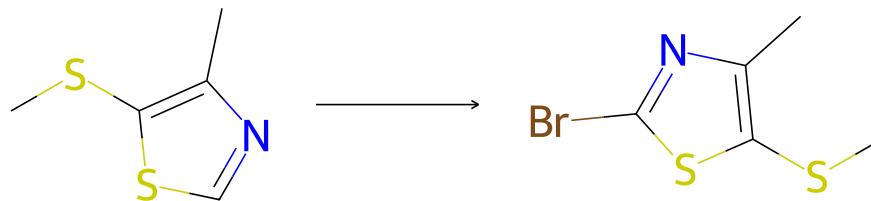
Typical conditions: Pd(OAc)₂.tBuONa.DME.110C

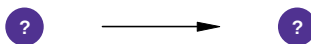
Protections: none

Reference: [10.1021/ja0580340](https://doi.org/10.1021/ja0580340)

Retrosynthesis ID: 1299

2.1.8 Bromination of aromatic compounds





Substrates:

1. CSc1scnc1C

Products:

1. CSc1sc(Br)nc1C

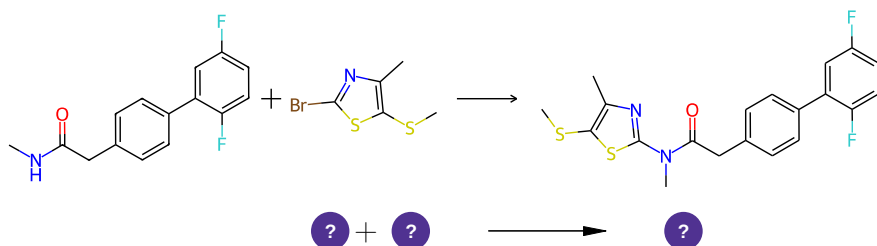
Typical conditions: Br₂.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.1.9 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

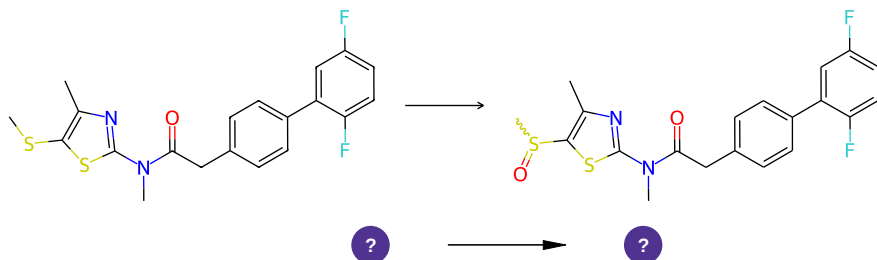
Typical conditions: Cs₂CO₃.CuX₂/CuX.toluene.130C

Protections: none

Reference: [10.1021/ja012610k](https://doi.org/10.1021/ja012610k) and [10.1002/adsc.200700133](https://doi.org/10.1002/adsc.200700133) and [10.1021/jo701573w](https://doi.org/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

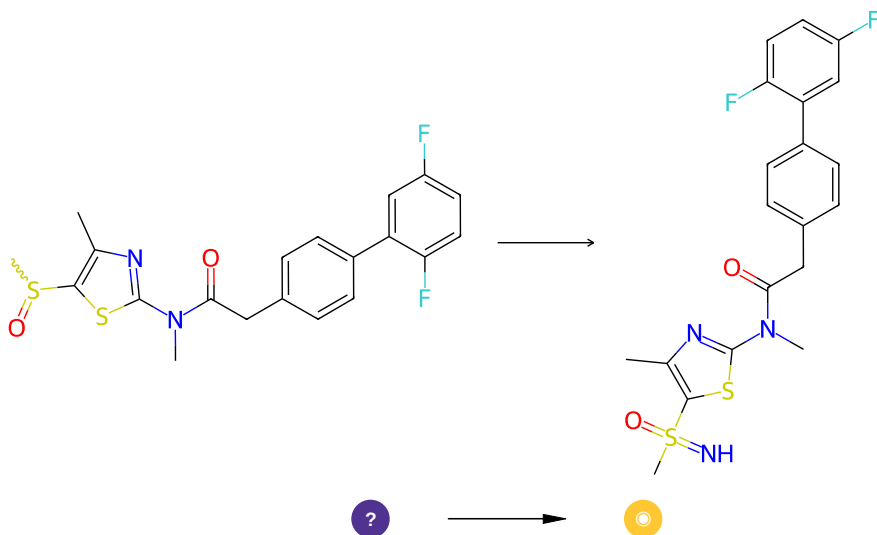
Typical conditions: TaC.H₂O₂.MeOH.45C

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