

Paths of analysis*

C33

Synthia

March 3, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: FGI, FGI with protections

Max. paths returned: 5

Max. iterations: 300

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1000 \$/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 10

My Stockroom:

1. Max. molecular weight - 1000 g/mol

Reaction scoring formula: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

Min. search width: 400

Max. reactions per product: 60

Strategies: none selected

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FGI Coeff: 0

JSON Parameters: {}

2 Paths

2 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: 341.54

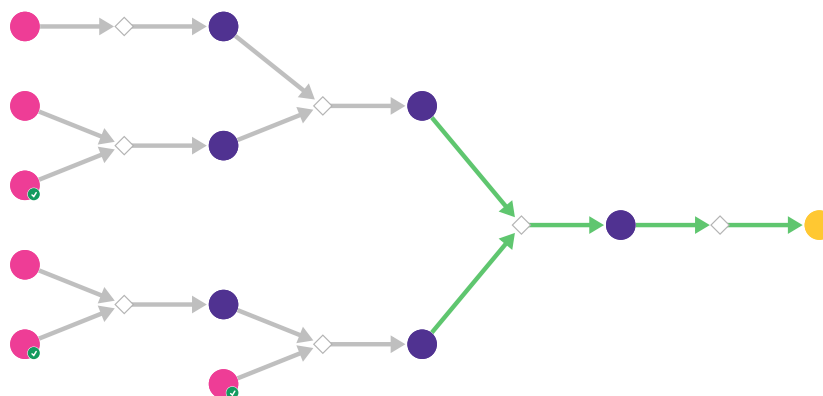
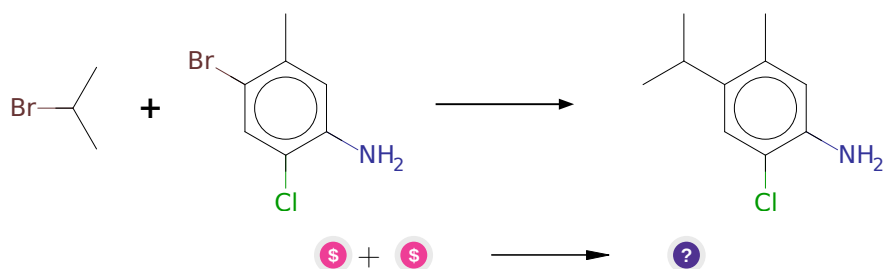


Figure 1: Outline of path 1

2.1.1 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. 4-bromo-2-chloro-5-methylaniline - *Enamine*
2. 2-Bromopropane - *available at Sigma-Aldrich*

Products:

1. Cc1cc(N)c(Cl)cc1C(C)C

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

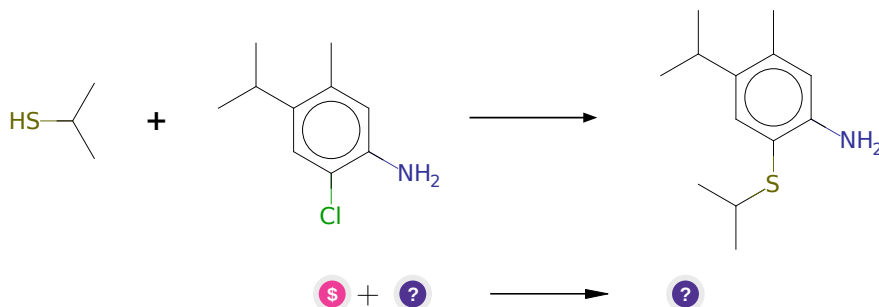
Protections: none

Yield: good

Reference: [10.1021/jacs.6b04818](#) and [10.1016/j.bbrc.2020.04.028](#) and [10.1021/ac-smmedchemlett.8b00183](#)

Retrosynthesis ID: 31016940

2.1.2 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. 2-Propanethiol - *available at Sigma-Aldrich*
2. Cc1cc(N)c(Cl)cc1C(C)C

Products:

1. Cc1cc(N)c(SC(C)C)cc1C(C)C

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

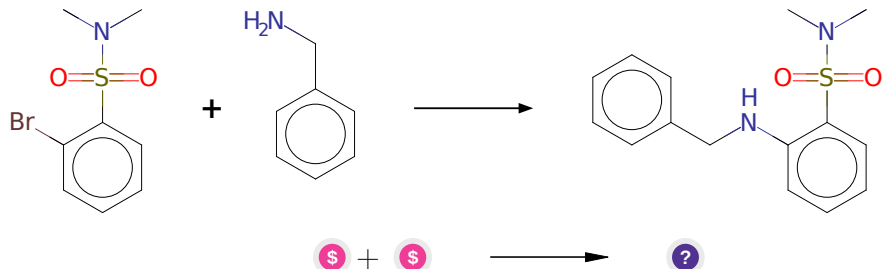
Protections: none

Yield: moderate

Reference: [10.1021/ja0580340](#)

Retrosynthesis ID: 1299

2.1.3 Amination of aryl bromides



Substrates:

1. 2-Bromo-N,N-dimethylbenzenesulphonamide 1g pack - *Combi-Blocks*
2. Benzylamine - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)c1ccccc1NCc1ccccc1

Typical conditions: Pd.ligand.base or CuI.ligand.base

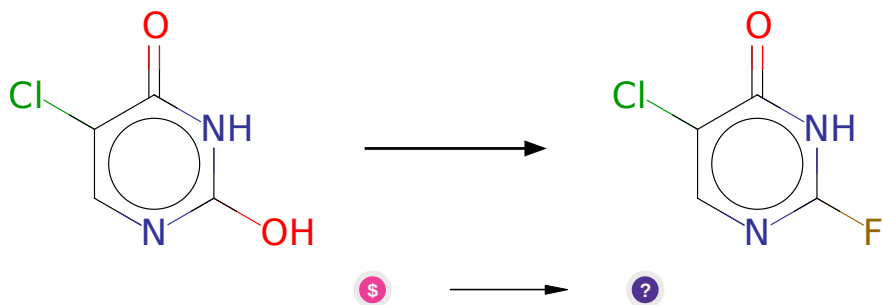
Protections: none

Yield: good

Reference: [10.1021/ja903049z](#) and [10.1021/jo060945k](#) and [10.1021/jo060190h](#) and [10.1039/B923255A](#) and [10.1021/jm8003625](#) and [10.1021/jo9006738](#)

Retrosynthesis ID: 28544

2.1.4 Synthesis of haloarenes via triflates



Substrates:

1. 5-chloro-uracil - *Combi-Blocks*

Products:

1. O=c1[nH]c(F)ncc1Cl

Typical conditions: 1. Tf2O 2. [Pd].MX

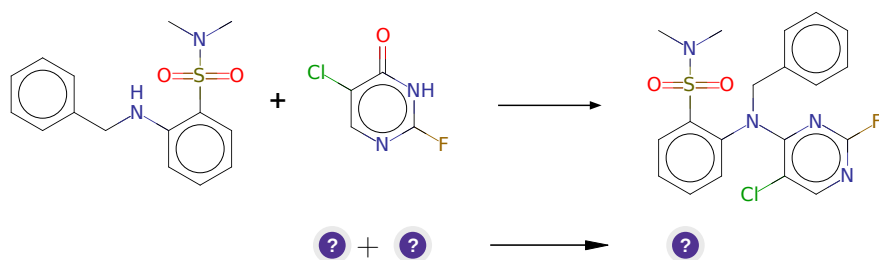
Protections: none

Yield: moderate

Reference: [10.1016/j.tetasy.2012.04.008](#) and [WO2007/136577](#) (p46) and [10.1021/ol202098h](#) and [10.1021/ol402859k](#) and [10.1021/jacs.5b09308](#)

Retrosynthesis ID: 23940

2.1.5 Amination of pyridones



Substrates:

1. CN(C)S(=O)(=O)c1ccccc1NCc1ccccc1
2. O=c1[nH]c(F)ncc1Cl

Products:

1. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(F)ncc1Cl

Typical conditions: 1. PCl5. 2. amine

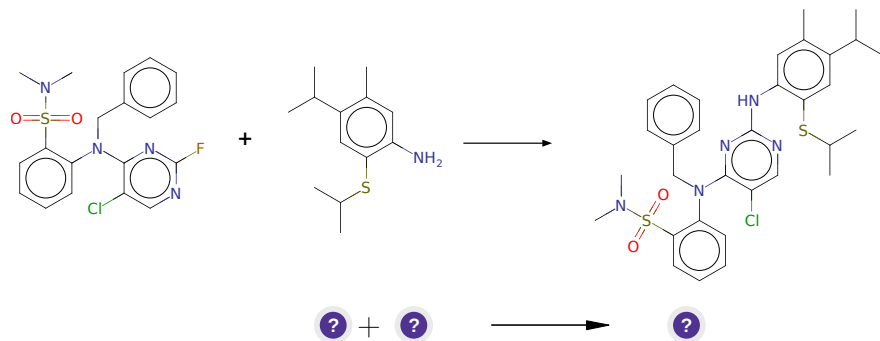
Protections: none

Yield: moderate

Reference: [10.1021/jm300780p](#) AND [10.3390/molecules170910902](#) AND [10.1021/jm00392a017](#)

Retrosynthesis ID: 14895

2.1.6 Nucleophilic aromatic substitution



Substrates:

- Cc1cc(N)c(SC(C)C)cc1C(C)C
- CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(F)ncc1Cl

Products:

- Cc1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(SC(C)C)cc1C(C)C

Typical conditions: Solvent

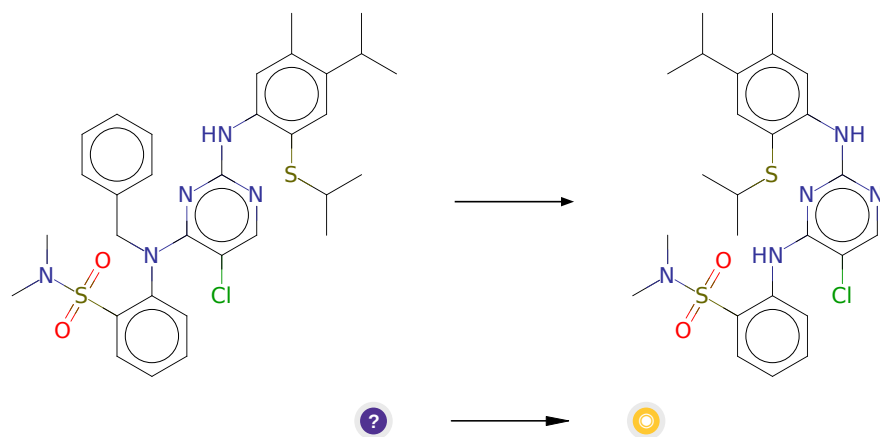
Protections: none

Yield: good

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

Retrosynthesis ID: 49476

2.1.7 Debenzylation



Substrates:

1. Cc1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(SC(C)C)cc1C(C)C

Products:

1. Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)N(C)C)n2)c(SC(C)C)cc1C(C)C

Typical conditions: H₂. Pd/C or Pd(OH)₂

Protections: none

Yield: good

Reference: DOI: [10.1002/1521-3773\(20020603\)41:11<1895::AID-ANIE1895>3.0.CO;2-3](https://doi.org/10.1002/1521-3773(20020603)41:11<1895::AID-ANIE1895>3.0.CO;2-3) and [10.1021/jo400589j](https://doi.org/10.1021/jo400589j) and [10.1021/jm8012932](https://doi.org/10.1021/jm8012932) (SI,page S6) and [10.1080/00397911.2016.1261164](https://doi.org/10.1080/00397911.2016.1261164)

Retrosynthesis ID: 9995661

2.2 Path 2

Score: 513.39

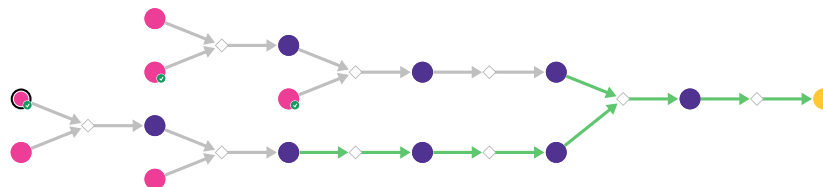
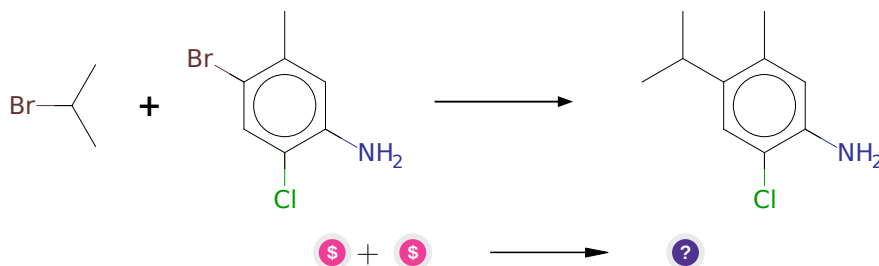


Figure 2: Outline of path 2

2.2.1 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. 4-bromo-2-chloro-5-methylaniline - *Enamine*

2. 2-Bromopropane - *available at Sigma-Aldrich*

Products:

1. Cc1cc(N)c(Cl)cc1C(C)C

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

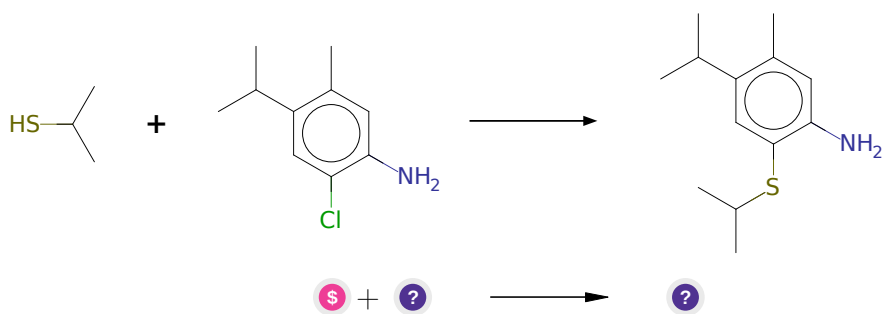
Protections: none

Yield: good

Reference: [10.1021/jacs.6b04818](#) and [10.1016/j.bbrc.2020.04.028](#) and [10.1021/ac-smedchemlett.8b00183](#)

Retrosynthesis ID: 31016940

2.2.2 Pd-catalyzed synthesis of aryl sulfides



Substrates:

1. 2-Propanethiol - *available at Sigma-Aldrich*

2. Cc1cc(N)c(Cl)cc1C(C)C

Products:

1. Cc1cc(N)c(SC(C)C)cc1C(C)C

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

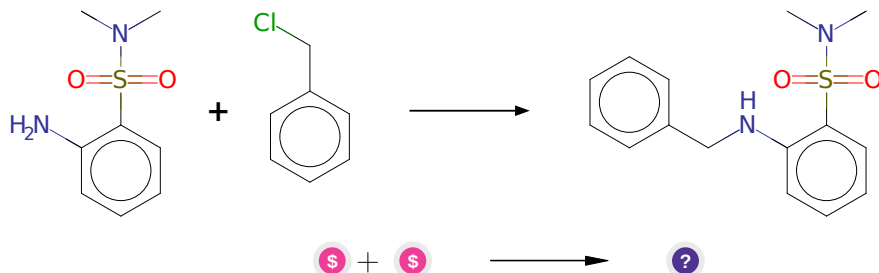
Protections: none

Yield: moderate

Reference: [10.1021/ja0580340](#)

Retrosynthesis ID: 1299

2.2.3 Alkylation of amines with alkyl chlorides (PTC conditions)



Substrates:

1. a-Chlorotoluene - *available at Sigma-Aldrich*
2. 2-Amino-N,N-dimethylbenzenesulfonamide - *Combi-Blocks*

Products:

1. CN(C)S(=O)(=O)c1ccccc1NCc1ccccc1

Typical conditions: NaOH.water.PTC-catalyst

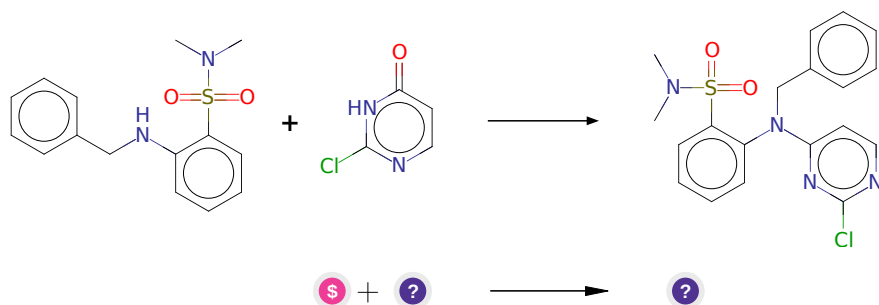
Protections: none

Yield: moderate

Reference: [10.1080/00397911.2013.828077](#) and [10.1002/ejoc.201200202](#) and [10.1080/10799893.2019.1585453](#) and [10.1248/cpb.c14-00754](#)

Retrosynthesis ID: 4785

2.2.4 Amination of pyridones



Substrates:

1. 2-Chloropyrimidin-4-ol - *Combi-Blocks*
2. CN(C)S(=O)(=O)c1ccccc1NCc1ccccc1

Products:

1. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1ccnc(Cl)n1

Typical conditions: 1.PCl5.2.amine

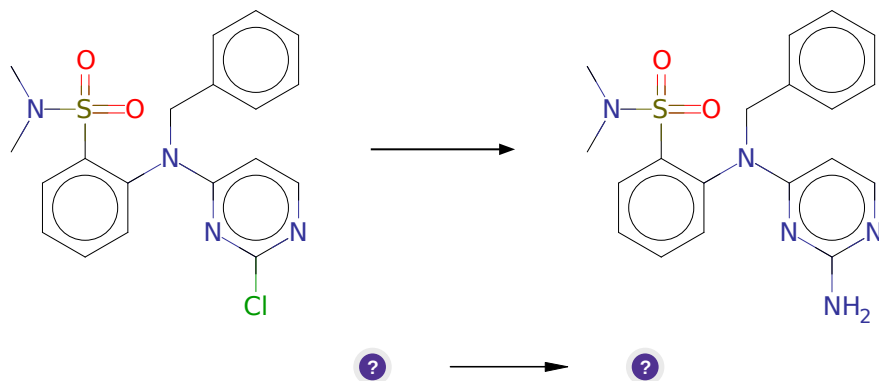
Protections: none

Yield: moderate

Reference: [10.1021/jm300780p](#) AND [10.3390/molecules170910902](#) AND [10.1021/jm00392a017](#)

Retrosynthesis ID: 14895

2.2.5 Nucleophilic aromatic substitution



Substrates:

1. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1ccnc(Cl)n1

Products:

1. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1ccnc(N)n1

Typical conditions: solvent. Heating or pressure

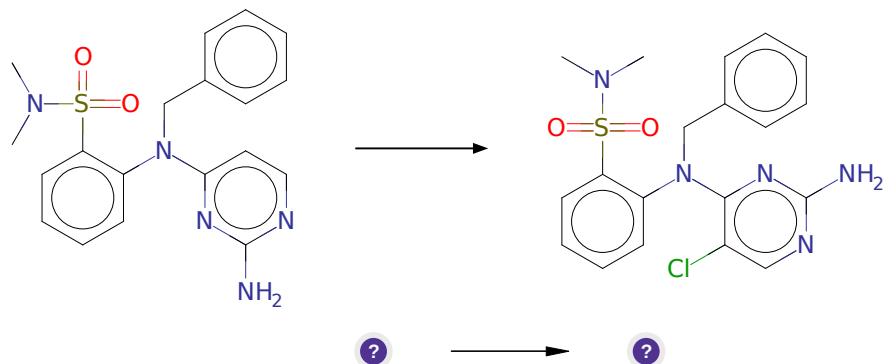
Protections: none

Yield: good

Reference: [10.1021/jm00040a009](#) or [10.1111/bph.12233](#) or [10.1246/cl.1987.1187](#)

Retrosynthesis ID: 5003

2.2.6 Chlorination of aromatic compounds



Substrates:

- CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1ccnc(N)n1

Products:

- CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(N)ncc1Cl

Typical conditions: Cl₂ or other chlorinating agent like NCS

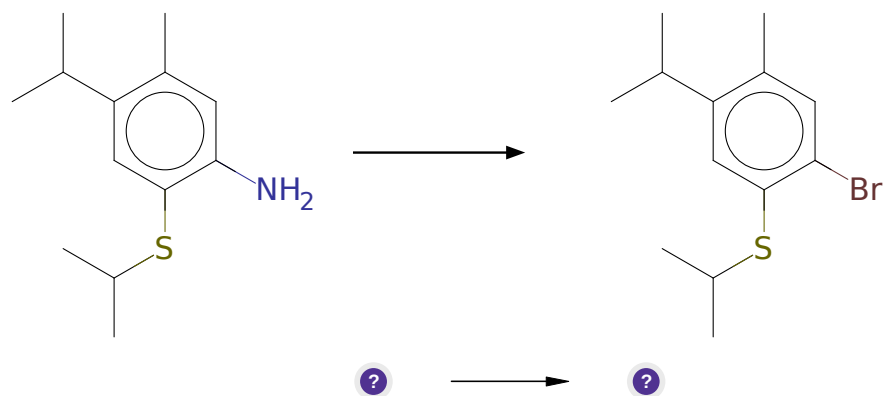
Protections: none

Yield: moderate

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

Retrosynthesis ID: 11125

2.2.7 Sandmeyer Reaction



Substrates:

1. Cc1cc(N)c(SC(C)C)cc1C(C)C

Products:

1. Cc1cc(Br)c(SC(C)C)cc1C(C)C

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

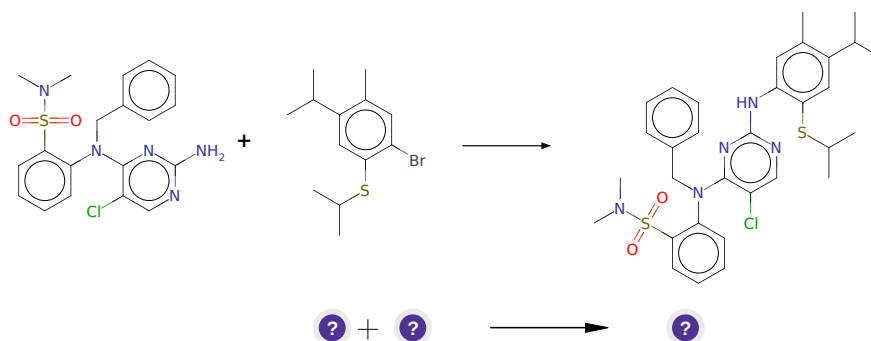
Protections: none

Yield: moderate

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

2.2.8 Amination of aryl bromides



Substrates:

1. Cc1cc(Br)c(SC(C)C)cc1C(C)C

2. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(N)ncc1Cl

Products:

1. Cc1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(SC(C)C)cc1C(C)C

Typical conditions: Pd.ligand.base or CuI.ligand.base

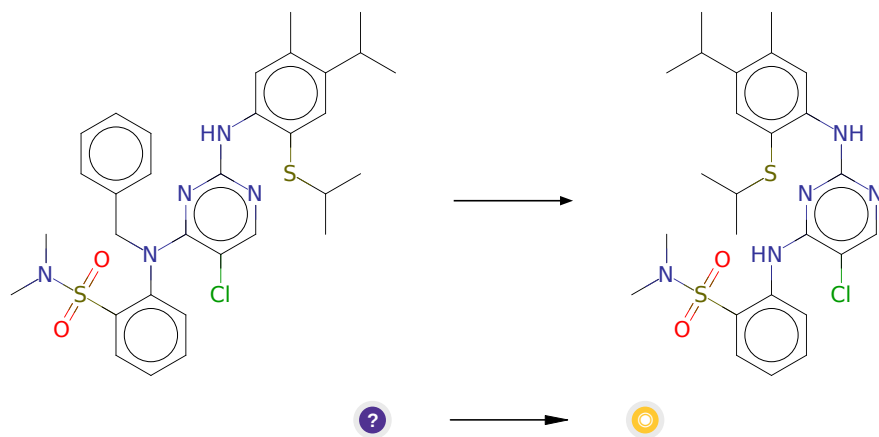
Protections: none

Yield: good

Reference: [10.1021/ja903049z](#) and [10.1021/jo060945k](#) and [10.1021/jo060190h](#) and [10.1039/B923255A](#) and [10.1021/jm8003625](#) and [10.1021/jo9006738](#)

Retrosynthesis ID: 28544

2.2.9 Debenzylation



Substrates:

1. Cc1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(SC(C)C)cc1C(C)C

Products:

1. Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)N(C)C)n2)c(SC(C)C)cc1C(C)C

Typical conditions: H₂. Pd/C or Pd(OH)₂

Protections: none

Yield: good

Reference: DOI: [10.1002/1521-3773\(20020603\)41:11<1895::AID-ANIE1895>3.0.CO;2-3](https://doi.org/10.1002/1521-3773(20020603)41:11<1895::AID-ANIE1895>3.0.CO;2-3) and [10.1021/jo400589j](https://doi.org/10.1021/jo400589j) and [10.1021/jm8012932](https://doi.org/10.1021/jm8012932) (SI,page S6) and [10.1080/00397911.2016.1261164](https://doi.org/10.1080/00397911.2016.1261164)

Retrosynthesis ID: 9995661