

Paths of analysis*

39

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: 396.05

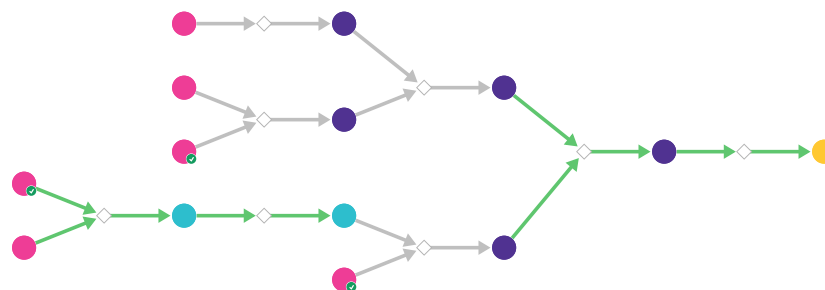
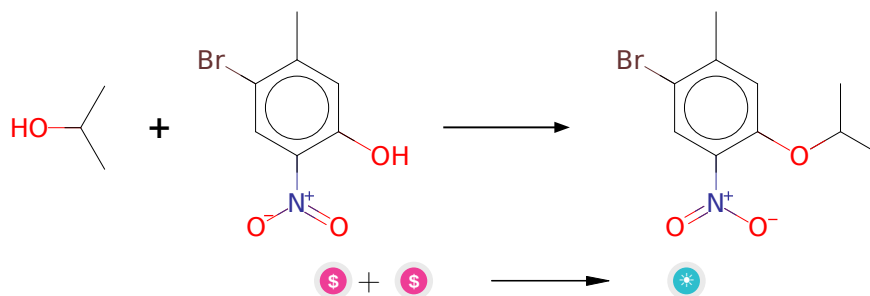


Figure 1: Outline of path 1

2.1.1 Mitsunobu reaction



Substrates:

1. 2-Propanol - *available at Sigma-Aldrich*
2. 4-Bromo-5-methyl-2-nitrophenol - *Combi-Blocks*

Products:

1. C10H12BrNO3

Typical conditions: DEAD.or.DCAD.or.DIAD.PPh3

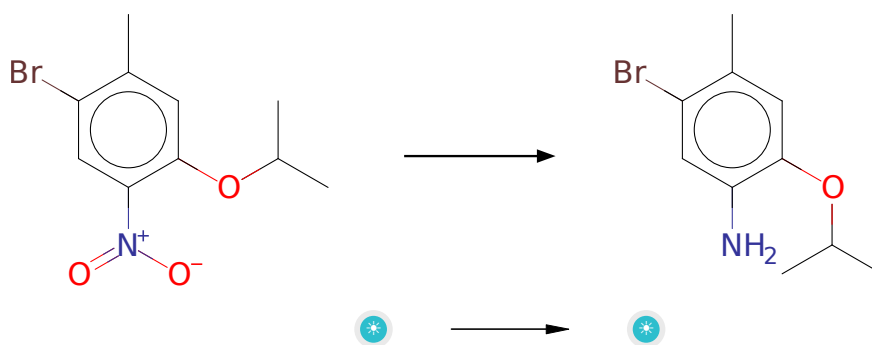
Protections: none

Yield: moderate

Reference: DOI: [10.1021/jo0345751](https://doi.org/10.1021/jo0345751) AND [10.1021/ol0618757](https://doi.org/10.1021/ol0618757)

Retrosynthesis ID: 7562

2.1.2 Reduction of nitro group



Substrates:

1. C₁₀H₁₂BrNO₃

Products:

1. C₁₀H₁₄BrNO

Typical conditions: Zn. aq NH₄. EtOH //Zn.Hcl

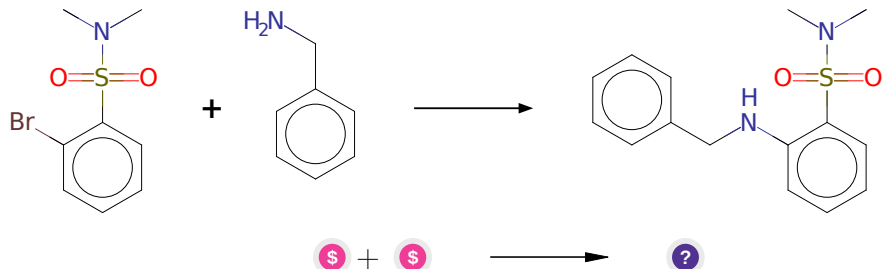
Protections: none

Yield: good

Reference: DOI: [10.1002/anie.201512005](https://doi.org/10.1002/anie.201512005) and [10.1002/anie.201104681](https://doi.org/10.1002/anie.201104681) and [10.3390/molecules17055497](https://doi.org/10.3390/molecules17055497) and [10.3390/molecules19022655](https://doi.org/10.3390/molecules19022655) and [10.1021/ol5033464](https://doi.org/10.1021/ol5033464) (SI,page 3) and [10.5012/bkcs.2013.34.4.1275](https://doi.org/10.5012/bkcs.2013.34.4.1275)

Retrosynthesis ID: 6145

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

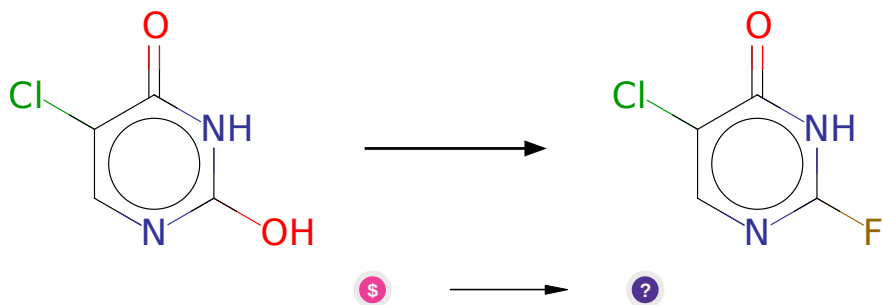
Protections: none

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

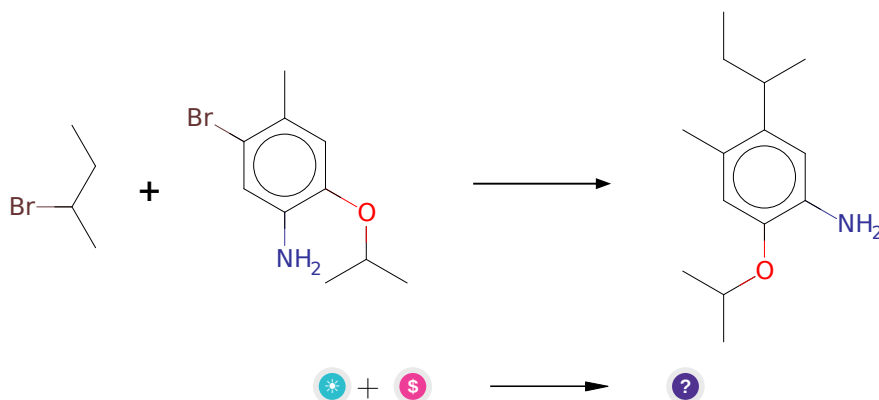
Protections: none

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 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. C₁₀H₁₄BrNO
2. 2-Bromobutane - [available at Sigma-Aldrich](#)

Products:

1. CCC(C)c1cc(N)c(OC(C)C)cc1C

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

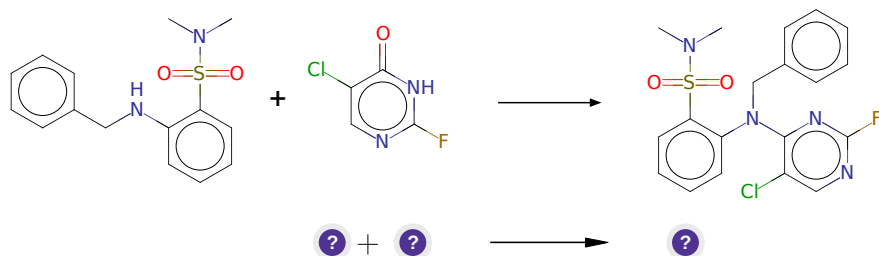
Protections: none

Yield: moderate

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

Retrosynthesis ID: 31016940

2.1.6 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

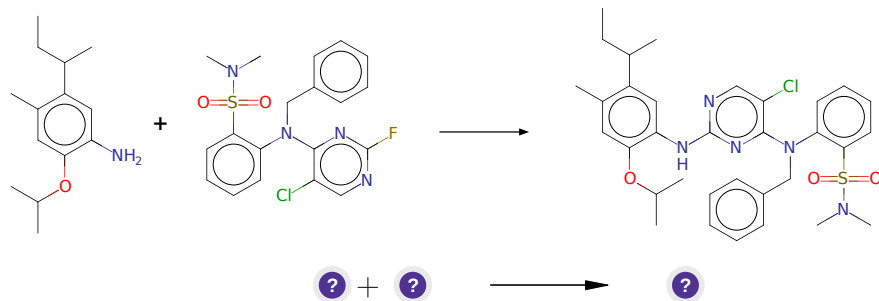
Protections: none

Yield: moderate

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

Retrosynthesis ID: 14895

2.1.7 Nucleophilic aromatic substitution



Substrates:

1. CCC(C)c1cc(N)c(OC(C)C)cc1C
2. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(F)ncc1Cl

Products:

1. CCC(C)c1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: Solvent

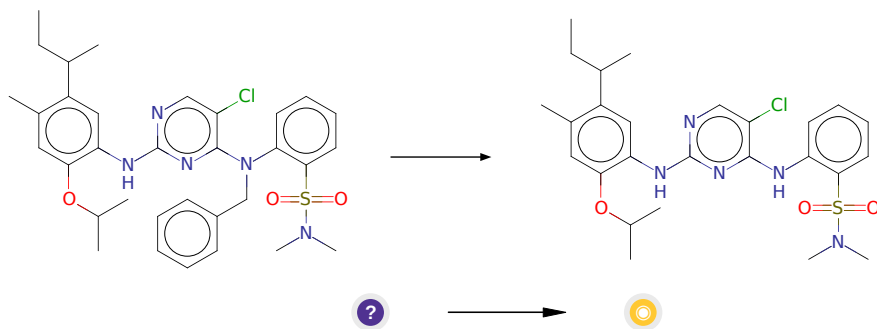
Protections: none

Yield: good

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

Retrosynthesis ID: 49476

2.1.8 Debenzylation



Substrates:

1. CCC(C)c1cc(Nc2ncc(Cl)c(N(Cc3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Products:

1. CCC(C)c1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

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](#) and [10.1021/jo400589j](#) and [10.1021/jm8012932](#) (SI, page S6) and [10.1080/00397911.2016.1261164](#)

Retrosynthesis ID: 9995661

2.2 Path 2

Score: 451.27

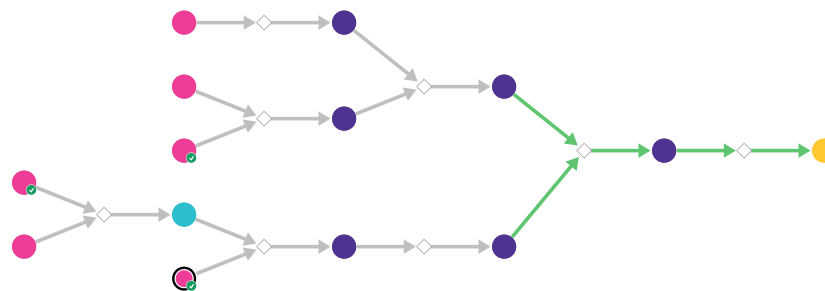
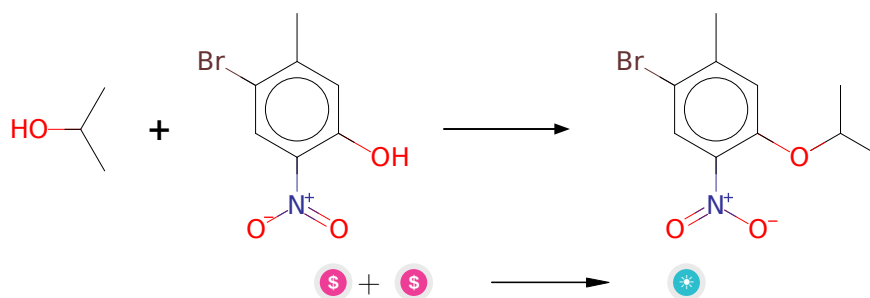


Figure 2: Outline of path 2

2.2.1 Mitsunobu reaction



Substrates:

1. 2-Propanol - *available at Sigma-Aldrich*
2. 4-Bromo-5-methyl-2-nitrophenol - *Combi-Blocks*

Products:

1. C₁₀H₁₂BrNO₃

Typical conditions: DEAD.or.DCAD.or.DIAD.PPh₃

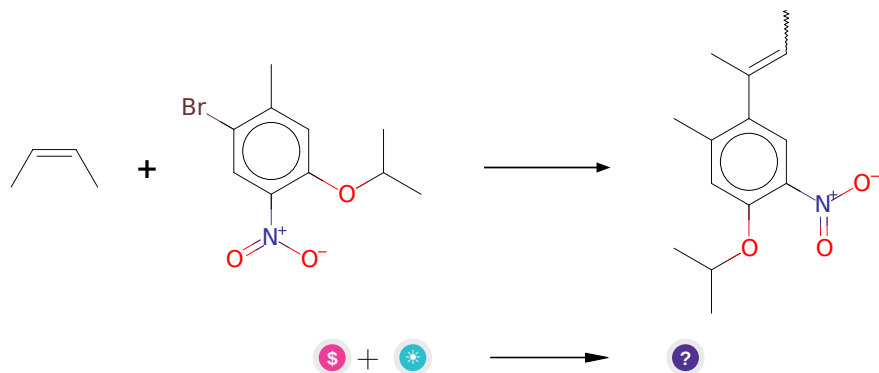
Protections: none

Yield: moderate

Reference: DOI: [10.1021/jo0345751](https://doi.org/10.1021/jo0345751) AND [10.1021/ol0618757](https://doi.org/10.1021/ol0618757)

Retrosynthesis ID: 7562

2.2.2 Heck Reaction



Substrates:

1. *cis*-2-Butene - *available at Sigma-Aldrich*
2. C₁₀H₁₂BrNO₃

Products:

1. CC=C(C)c1cc([N+](=O)[O-])c(OC(C)C)cc1C

Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

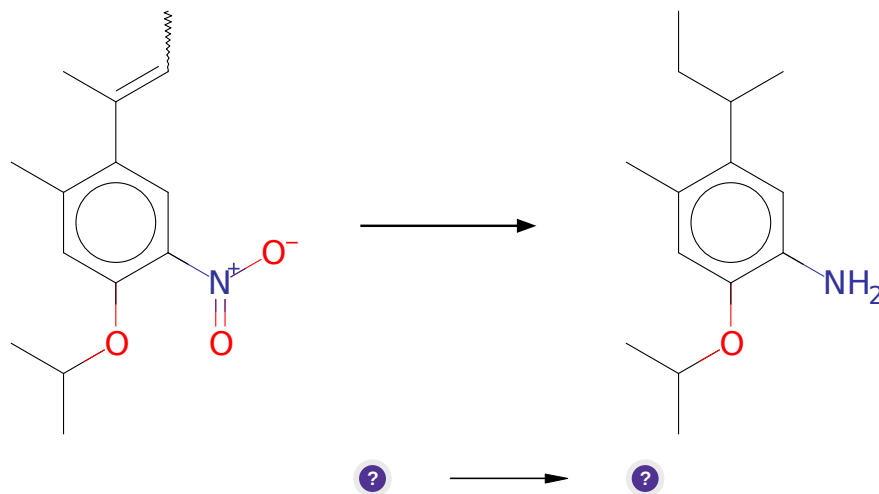
Protections: none

Yield: good

Reference: [10.1016/j.tetlet.2013.01.077](#) or [10.1016/j.tetlet.2013.10.076](#) or [10.1039/C3GC40493E](#) [10.1021/ol0360288](#) or [10.1021/ol702755g](#) or [10.1055/s-0033-1340319](#) or [10.1016/j.tet.2004.10.049](#)

Retrosynthesis ID: 9173

2.2.3 Tandem alkene/nitro reduction



Substrates:

1. CC=C(C)c1cc([N+](=O)[O-])c(OC(C)C)cc1C

Products:

1. CCC(C)c1cc(N)c(OC(C)C)cc1C

Typical conditions: H_2 .Pd/C

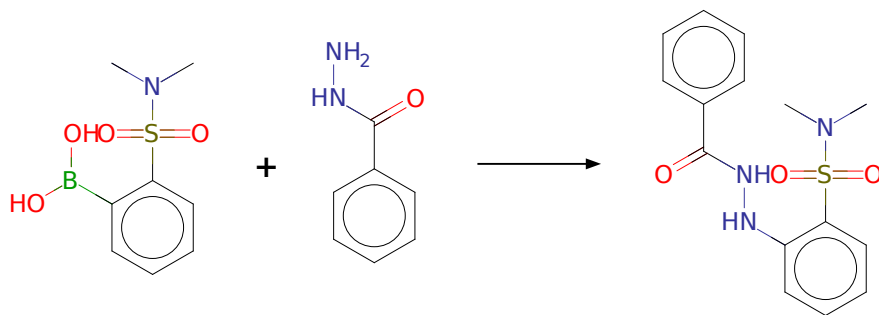
Protections: none

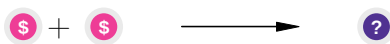
Yield: moderate

Reference: [10.1016/j.bmc.2009.05.066](https://doi.org/10.1016/j.bmc.2009.05.066) and [10.1016/j.cclet.2015.05.003](https://doi.org/10.1016/j.cclet.2015.05.003) and [10.1016/j.bmc.2012.12.025](https://doi.org/10.1016/j.bmc.2012.12.025)

Retrosynthesis ID: 31351

2.2.4 Chan-Lam Coupling





Substrates:

1. 2-(N,N-DIMETHYLSULPHAMOYL)BENZENE BORONIC ACID - *Combi-Blocks*
2. Benzhydrazide - *available at Sigma-Aldrich*

Products:

1. CN(C)S(=O)(=O)c1ccccc1NNC(=O)c1ccccc1

Typical conditions: Cu(Oac)₂.dioxane

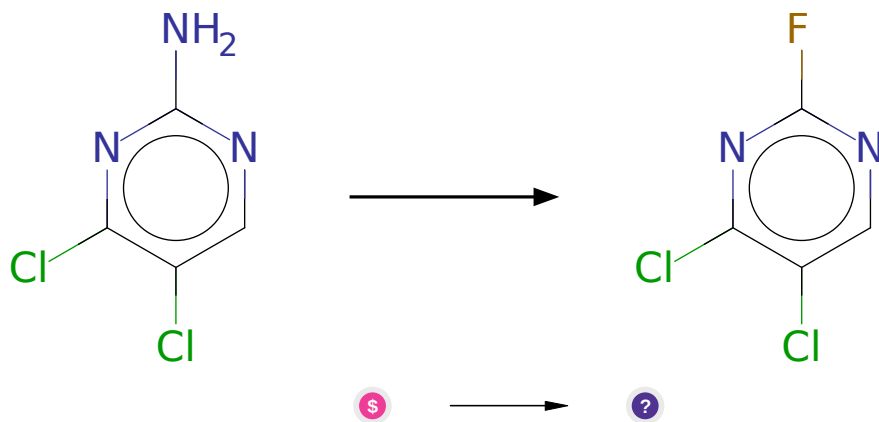
Protections: none

Yield: good

Reference: *10.1039/C4OB02343A*

Retrosynthesis ID: 31015967

2.2.5 Balz-Schiemann Reaction



Substrates:

1. 4,5-Dichloropyrimidin-2-amine - *Combi-Blocks*

Products:

1. Fc1nc(Cl)c(Cl)n1

Typical conditions: NaNO₂.HF-pyridine.-25 to 0C

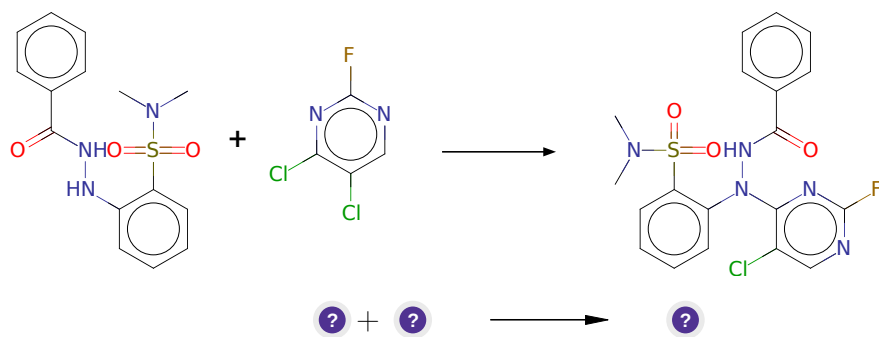
Protections: none

Yield: moderate

Reference: [10.1021/jm100432w](#) and [10.1021/jm5008177](#) and [10.1021/ol401540k](#) and [10.1021/jm401551n](#) (main text and SI, page S8) and [10.1515/chempap-2016-0033](#) and [10.1021/jm0311442](#) and [10.1016/j.jfluchem.2007.03.012](#) and [10.1021/jo00185a023](#)

Retrosynthesis ID: 29906

2.2.6 Nucleophilic aromatic substitution



Substrates:

1. Fc1ncc(Cl)c(Cl)n1
2. CN(C)S(=O)(=O)c1ccccc1NNC(=O)c1ccccc1

Products:

1. CN(C)S(=O)(=O)c1ccccc1N(NC(=O)c1ccccc1)c1nc(F)ncc1Cl

Typical conditions: EtOH.Heat or DMF.K₂CO₃

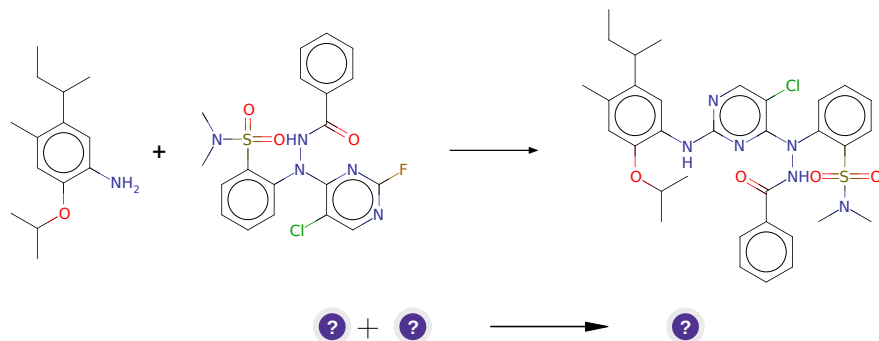
Protections: none

Yield: good

Reference: [10.1016/0040-4020\(95\)00966-3](#) and [10.1002/jhet.5570220420](#) and [10.1021/jo402481t](#)

Retrosynthesis ID: 29647

2.2.7 Nucleophilic aromatic substitution



Substrates:

1. CN(C)S(=O)(=O)c1ccccc1N(NC(=O)c1ccccc1)c1nc(F)nc1Cl
2. CCC(C)c1cc(N)c(OC(C)C)cc1C

Products:

1. CCC(C)c1cc(Nc2nc(Cl)c(N(NC(=O)c3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: Solvent

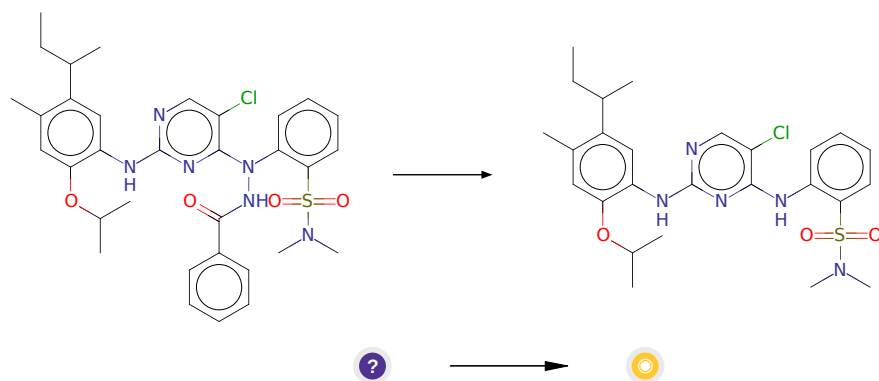
Protections: none

Yield: good

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

Retrosynthesis ID: 49476

2.2.8 Reduction of phenylhydrazines



Substrates:

1. CCC(C)c1cc(Nc2ncc(Cl)c(N(NC(=O)c3ccccc3)c3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Products:

1. CCC(C)c1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)N(C)C)n2)c(OC(C)C)cc1C

Typical conditions: RaNi.H2.MeOH

Protections: none

Yield: moderate

Reference: DOI: [10.1021/ol501424f](https://doi.org/10.1021/ol501424f)

Retrosynthesis ID: 1808