Paths of analysis*

C37

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: TUNNEL_COEF*FGI_COEF*STEP*20+1000000*(CONFLICT+NON_SELECTIVITY+FILTERS+PROTECT)

Chemical scoring formula: SMALLER^ 3,SMALLER^ 1.5

Min. search width: 400

Max. reactions per product: 60

Strategies: none selected

*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.

FGI Coeff: 0

JSON Parameters: {}

2 Paths

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

2.1 Path 1

Score: 497.50

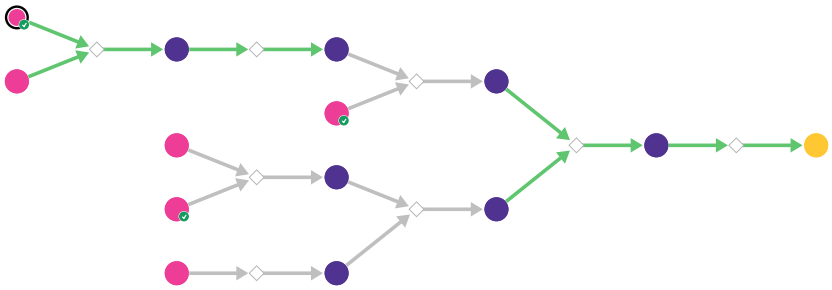
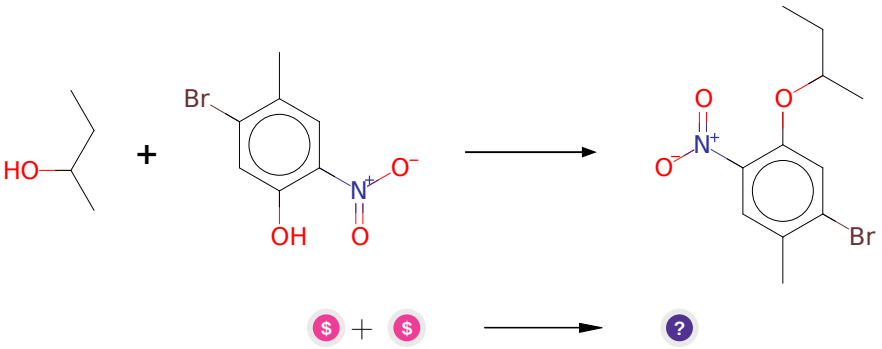


Figure 1: Outline of path 1

2.1.1 Mitsunobu reaction



Substrates:

1. 2-Butanol - *available at Sigma-Aldrich*
2. 5-Bromo-4-methyl-2-nitro-phenol - *Combi-Blocks*

Products:

1. CCC(C)Oc1cc(Br)c(C)cc1[N+](=O)[O-]

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

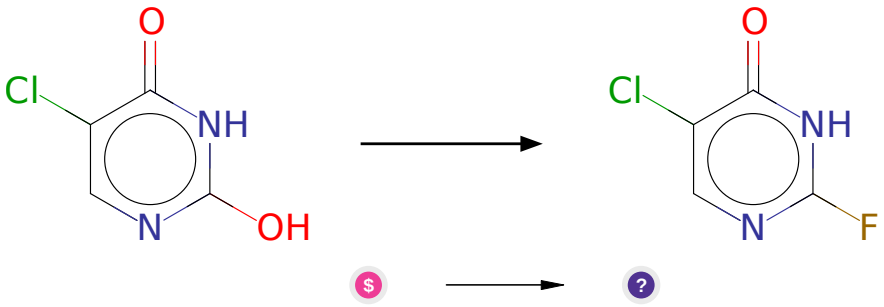
Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo0345751* AND *10.1021/ol0618757*

Retrosynthesis ID: 7562

2.1.2 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

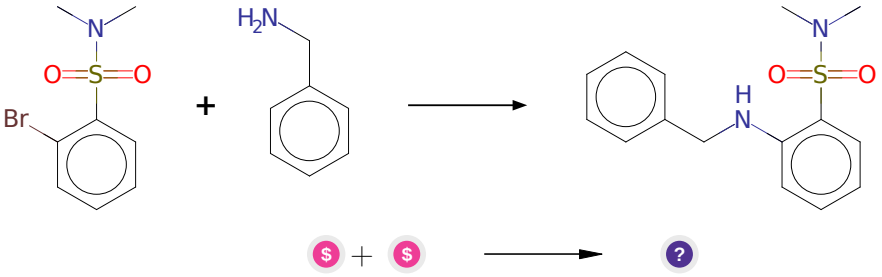
Protections: none

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

2.1.3 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

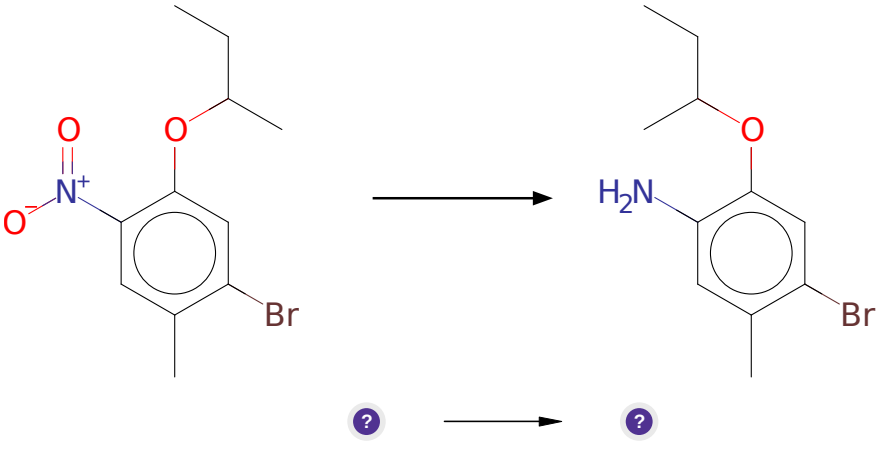
Protections: none

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 Reduction of nitro group



Substrates:

1. CCC(C)Oc1cc(Br)c(C)cc1[N+](=O)[O-]

Products:

1. CCC(C)Oc1cc(Br)c(C)cc1N

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

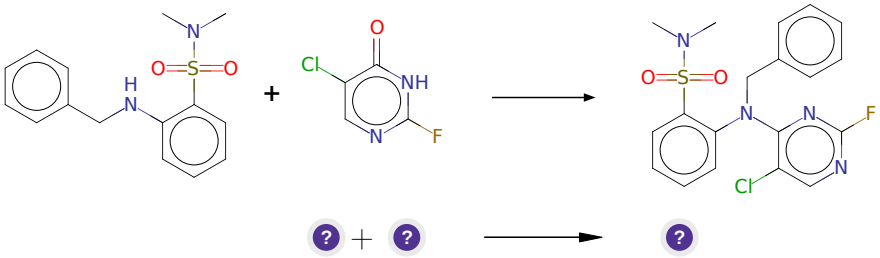
Protections: none

Yield: good

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

Retrosynthesis ID: 6145

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

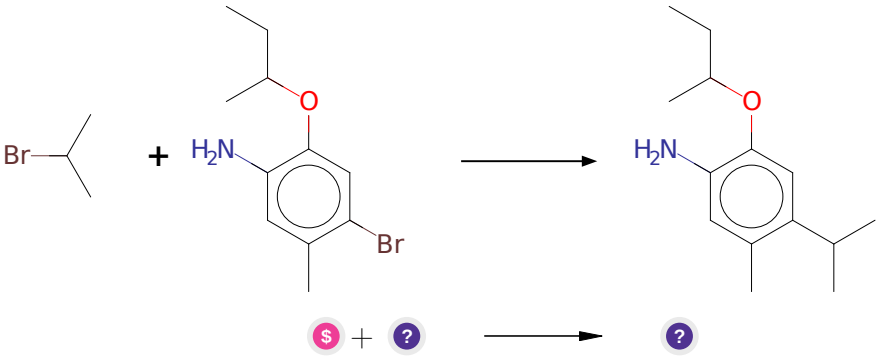
Protections: none

Yield: moderate

Reference: *10.1021/jm300780p* AND *10.3390/molecules170910902* AND *10.1021/jm00392a017*

Retrosynthesis ID: 14895

2.1.6 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. 2-Bromopropane - *available at Sigma-Aldrich*
2. CCC(C)Oc1cc(Br)c(C)cc1N

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1N

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

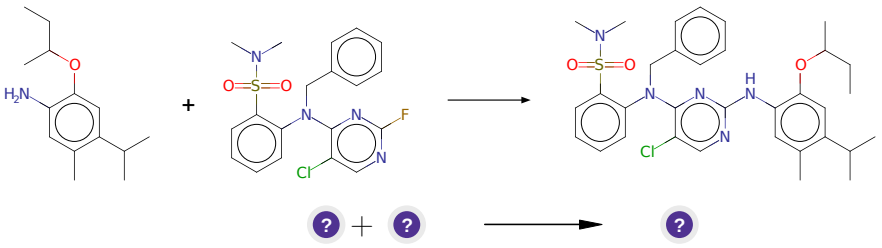
Protections: none

Yield: good

Reference: *10.1021/jacs.6b04818* and *10.1016/j.bbrc.2020.04.028* and *10.1021/acsmedchemlett.8b00183*

Retrosynthesis ID: 31016940

2.1.7 Nucleophilic aromatic substitution



Substrates:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1N

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

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(N(Cc2ccccc2)c2ccccc2S(=O)(=O)N(C)C)n1

Typical conditions: Solvent

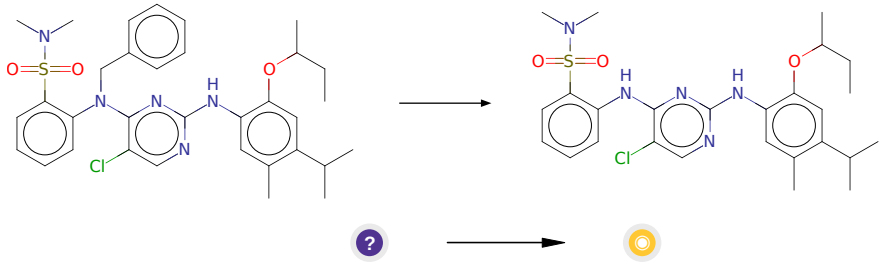
Protections: none

Yield: good

Reference: *10.1002/9781118093559.ch4*

Retrosynthesis ID: 49476

2.1.8 Debenzylation



Substrates:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(N(Cc2ccccc2)c2ccccc2S(=O)(=O)N(C)C)n1

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(Nc2ccccc2S(=O)(=O)N(C)C)n1

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: 502.87

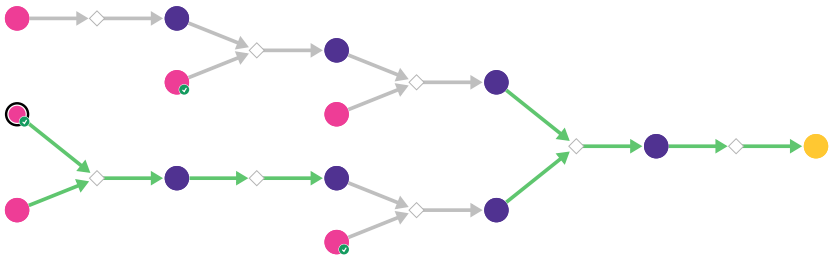
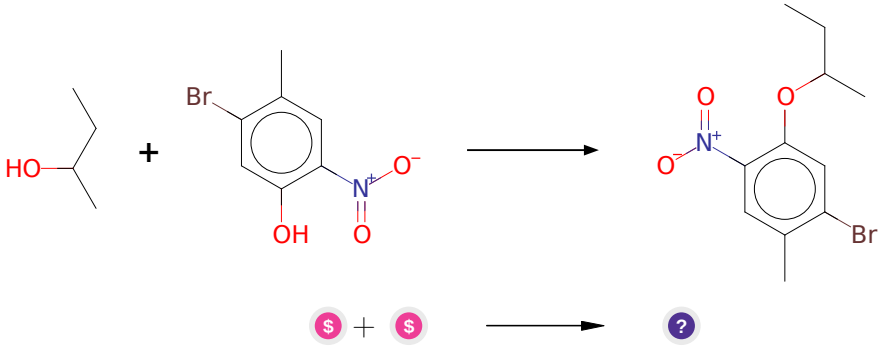


Figure 2: Outline of path 2

2.2.1 Mitsunobu reaction



Substrates:

1. 2-Butanol - *available at Sigma-Aldrich*
2. 5-Bromo-4-methyl-2-nitro-phenol - *Combi-Blocks*

Products:

1. CCC(C)Oc1cc(Br)c(C)cc1[N+](=O)[O-]

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

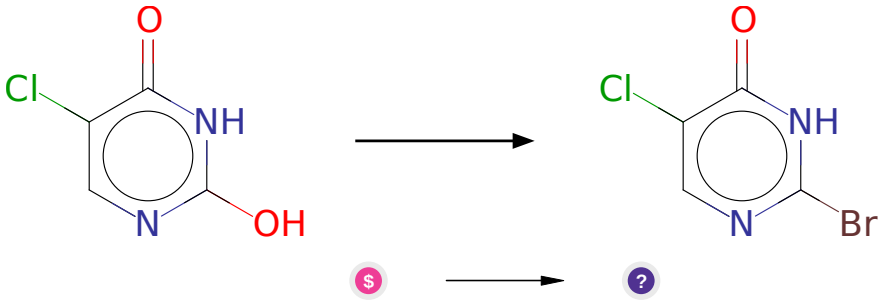
Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo0345751* AND *10.1021/ol0618757*

Retrosynthesis ID: 7562

2.2.2 Synthesis of haloarenes via triflates



Substrates:

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

Products:

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

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

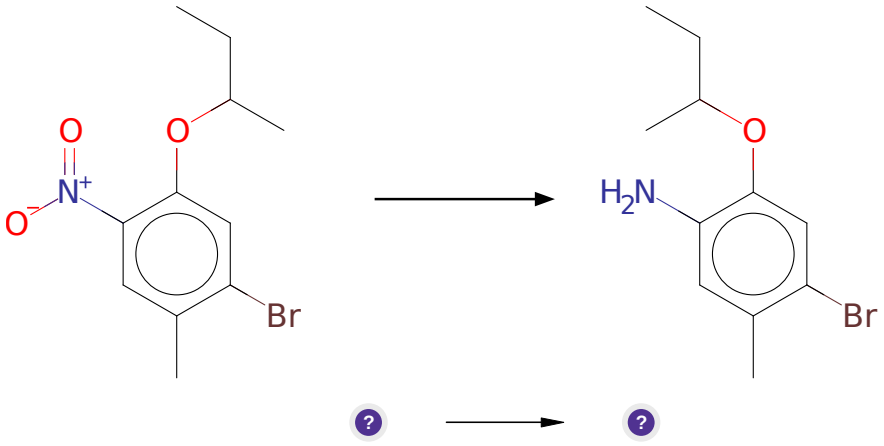
Protections: none

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

2.2.3 Reduction of nitro group



Substrates:

1. CCC(C)Oc1cc(Br)c(C)cc1[N+](=O)[O-]

Products:

1. CCC(C)Oc1cc(Br)c(C)cc1N

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

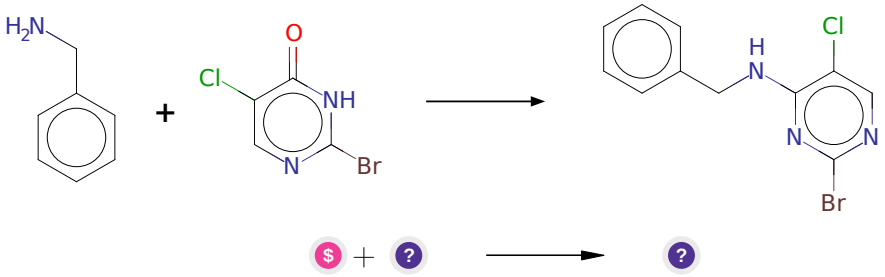
Protections: none

Yield: good

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

Retrosynthesis ID: 6145

2.2.4 Amination of pyridones



Substrates:

1. Benzylamine - *available at Sigma-Aldrich*
2. O=c1[nH]c(Br)ncc1Cl

Products:

1. Clc1cnc(Br)nc1NCc1ccccc1

Typical conditions: 1.PCl5.2.amine

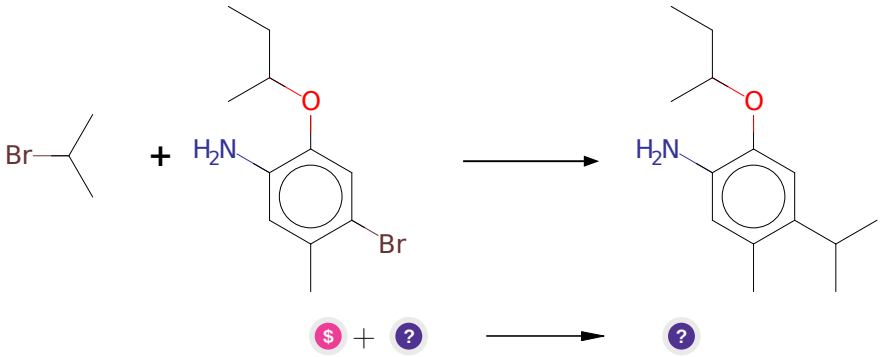
Protections: none

Yield: moderate

Reference: *10.1021/jm300780p* AND *10.3390/molecules170910902* AND *10.1021/jm00392a017*

Retrosynthesis ID: 14887

2.2.5 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. 2-Bromopropane - *available at Sigma-Aldrich*
2. CCC(C)Oc1cc(Br)c(C)cc1N

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1N

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

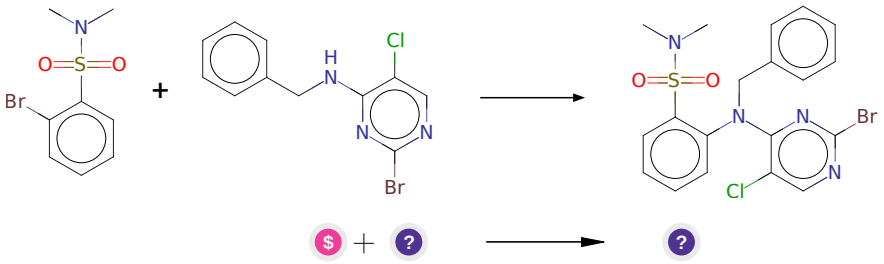
Protections: none

Yield: good

Reference: *10.1021/jacs.6b04818* and *10.1016/j.bbrc.2020.04.028* and *10.1021/acsmedchemlett.8b00183*

Retrosynthesis ID: 31016940

2.2.6 Buchwald-Hartwig amination



Substrates:

1. 2-Bromo-N,N-dimethylbenzenesulphonamide 1g pack - *Combi-Blocks*

2. Clc1cnc(Br)nc1NCc1ccccc1

Products:

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

Typical conditions: Pd(cat).toluene.100C.K2CO3

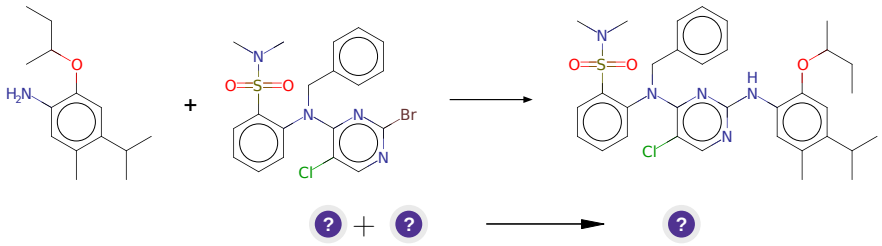
Protections: none

Yield: good

Reference: *10.1021/acs.oprd.9b00161* and *10.1002/anie.201904795* and *10.1021/acs.chemrev.6b00512*

Retrosynthesis ID: 31017516

2.2.7 Amination of aryl bromides



Substrates:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1N
2. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(Br)ncc1Cl

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(N(Cc2ccccc2)c2ccccc2S(=O)(=O)N(C)C)n1

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

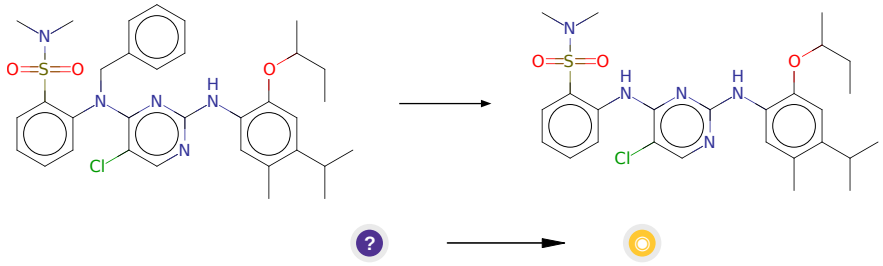
Protections: none

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

2.2.8 Debenzylation



Substrates:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(N(Cc2ccccc2)c2ccccc2S(=O)(=O)N(C)C)n1

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(Nc2ccccc2S(=O)(=O)N(C)C)n1

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

2.3 Path 3

Score: 509.34

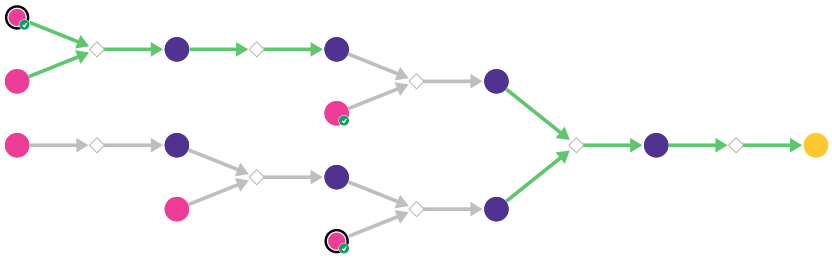
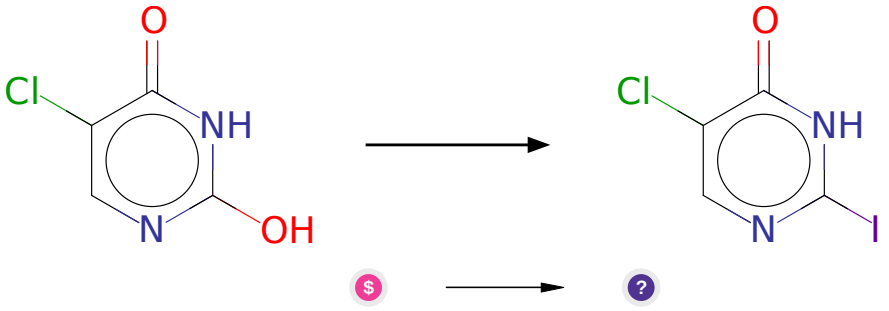


Figure 3: Outline of path 3

2.3.1 Synthesis of haloarenes via triflates



Substrates:

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

Products:

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

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

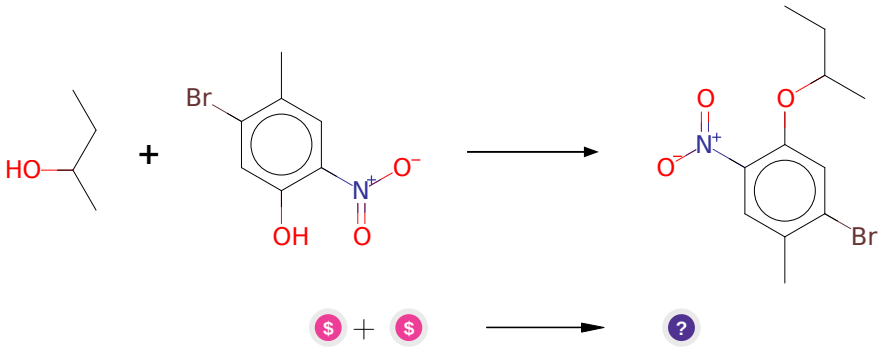
Protections: none

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

2.3.2 Mitsunobu reaction



Substrates:

1. 2-Butanol - *available at Sigma-Aldrich*
2. 5-Bromo-4-methyl-2-nitro-phenol - *Combi-Blocks*

Products:

1. CCC(C)Oc1cc(Br)c(C)cc1[N+](=O)[O-]

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

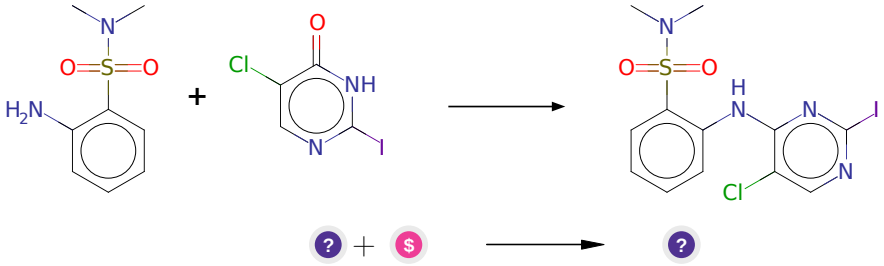
Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo0345751* AND *10.1021/ol0618757*

Retrosynthesis ID: 7562

2.3.3 Amination of pyridones



Substrates:

1. O=c1[nH]c(I)ncc1Cl
2. 2-Amino-N,N-dimethylbenzenesulfonamide - *Combi-Blocks*

Products:

1. CN(C)S(=O)(=O)c1ccccc1Nc1nc(I)ncc1Cl

Typical conditions: 1.PCl5.2.amine

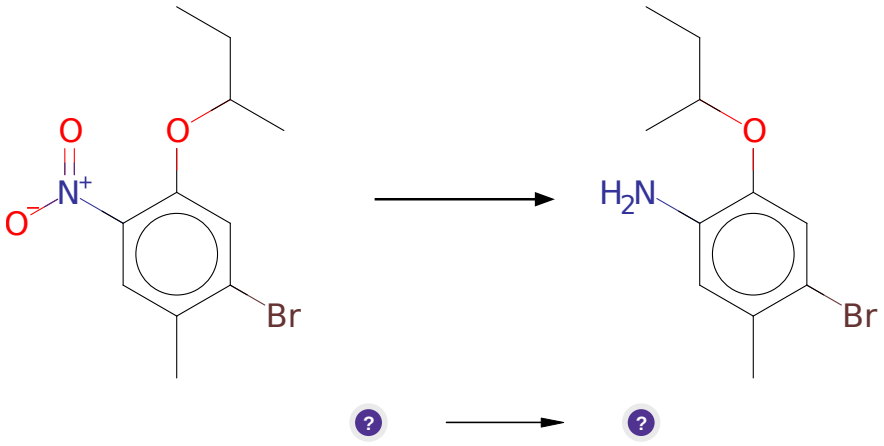
Protections: none

Yield: good

Reference: *10.1021/jm300780p* AND *10.3390/molecules170910902* AND *10.1021/jm00392a017*

Retrosynthesis ID: 14887

2.3.4 Reduction of nitro group



Substrates:

1. CCC(C)Oc1cc(Br)c(C)cc1[N+](=O)[O-]

Products:

1. CCC(C)Oc1cc(Br)c(C)cc1N

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

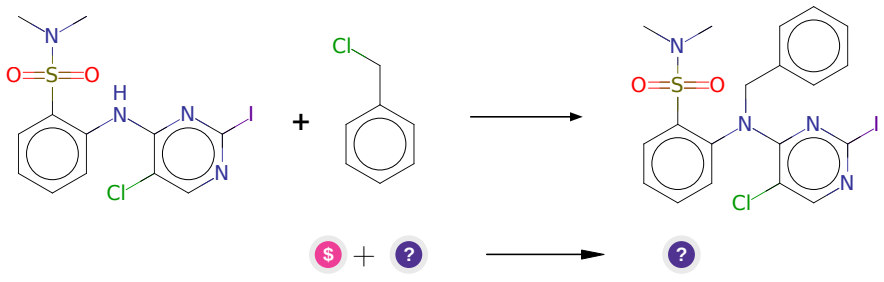
Protections: none

Yield: good

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

Retrosynthesis ID: 6145

2.3.5 Alkylation of amines with alkyl chlorides



Substrates:

1. a-Chlorotoluene - *available at Sigma-Aldrich*
2. CN(C)S(=O)(=O)c1ccccc1Nc1nc(I)ncc1Cl

Products:

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

Typical conditions: KOH. toluene. PTC. catalyst or KI. base e.g. K2CO3

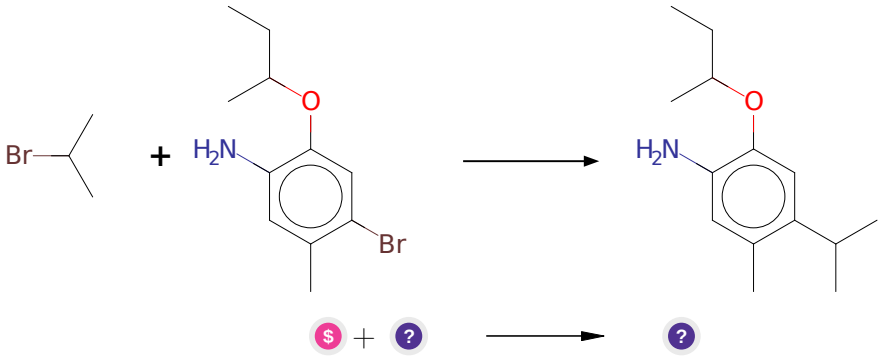
Protections: none

Yield: moderate

Reference: *10.1016/S0040-4020(01)00989-9* and *10.1021/acs.oprd.8b00074* and *10.1016/s0040-4039(00)74286-9* and *10.1080/00397911.2013.828077* and *10.1016/j.bmcl.2012.08.032*

Retrosynthesis ID: 4784

2.3.6 Photoredox Cross-Electrophile Coupling of Unactivated Alkyl Bromides



Substrates:

1. 2-Bromopropane - *available at Sigma-Aldrich*
2. CCC(C)Oc1cc(Br)c(C)cc1N

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1N

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

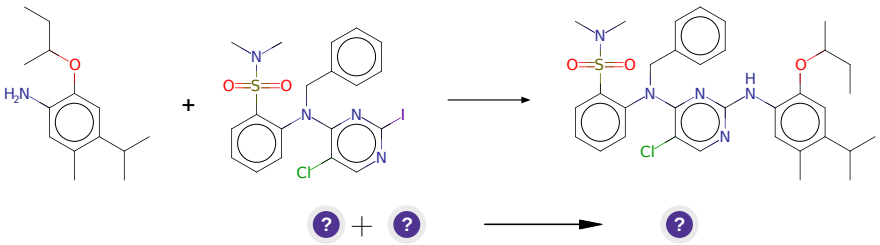
Protections: none

Yield: good

Reference: *10.1021/jacs.6b04818* and *10.1016/j.bbrc.2020.04.028* and *10.1021/acsmedchemlett.8b00183*

Retrosynthesis ID: 31016940

2.3.7 Amination of aryl iodides



Substrates:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1N
2. CN(C)S(=O)(=O)c1ccccc1N(Cc1ccccc1)c1nc(I)ncc1Cl

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(N(Cc2ccccc2)c2ccccc2S(=O)(=O)N(C)C)n1

Typical conditions: [Pd] or CuI.base.solvent

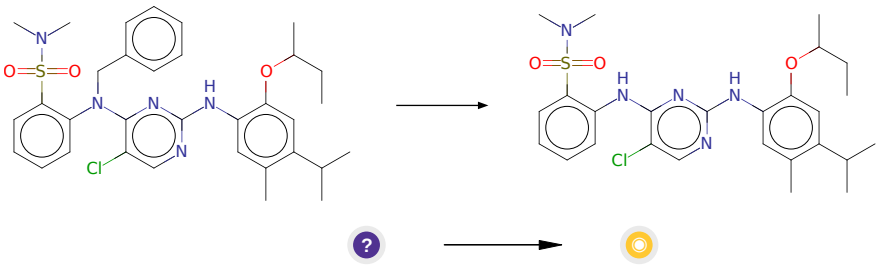
Protections: none

Yield: good

Reference: *10.1016/j.tet.2013.02.040* and *10.1021/ic200966f* (SI) and *10.1021/jo034994y*

Retrosynthesis ID: 1230

2.3.8 Debenzylation



Substrates:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(N(Cc2ccccc2)c2ccccc2S(=O)(=O)N(C)C)n1

Products:

1. CCC(C)Oc1cc(C(C)C)c(C)cc1Nc1ncc(Cl)c(Nc2ccccc2S(=O)(=O)N(C)C)n1

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