

Paths of analysis*

AS5

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselective reactions, Tunnels, FGI, FGI with protections

Max. paths returned: 50

Max. iterations: 2000

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1500 \$/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 5

My Stockroom:

1. Max. molecular weight - 1000 g/mol

Reaction scoring formula: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

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

Min. search width: 400

Max. reactions per product: 60

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Strategies: none selected

FGI Coeff: 0

Tunnels Coeff: 0

JSON Parameters: {}

2 Paths

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

2.1 Path 1

Score: 125.08

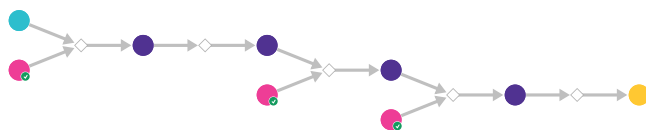
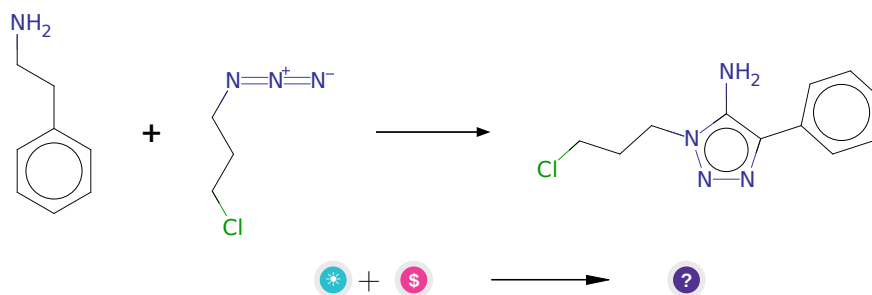


Figure 1: Outline of path 1

2.1.1 Synthesis of 1,2,3-triazoles from azides and nitrile derivatives



Substrates:

1. 1-azido-3-chloropropan
2. Phenethylamine - *available at Sigma-Aldrich*

Products:

1. Nc1c(-c2ccccc2)nn1CCCCl

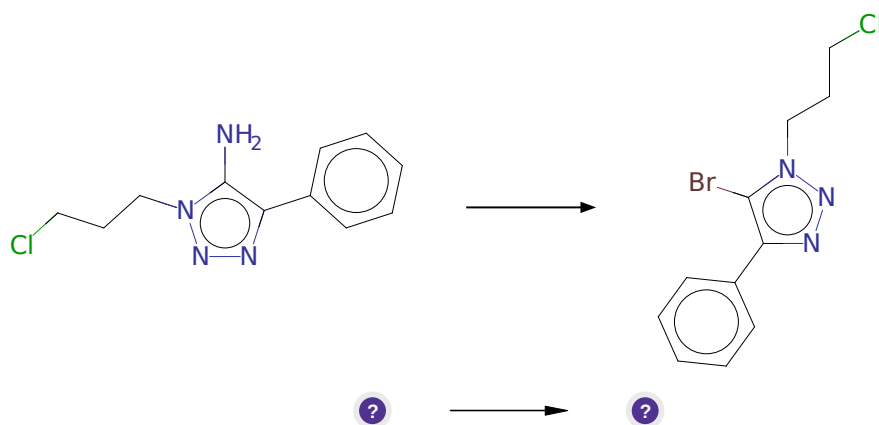
Typical conditions: anhydrous potassium carbonate.DMSO

Protections: none

Reference: DOI: [10.1002/jhet.5570280216](https://doi.org/10.1002/jhet.5570280216)

Retrosynthesis ID: 295117

2.1.2 Sandmeyer Reaction



Substrates:

1. Nc1c(-c2ccccc2)nn1CCCCl

Products:

1. ClCCcn1nc(-c2ccccc2)c1Br

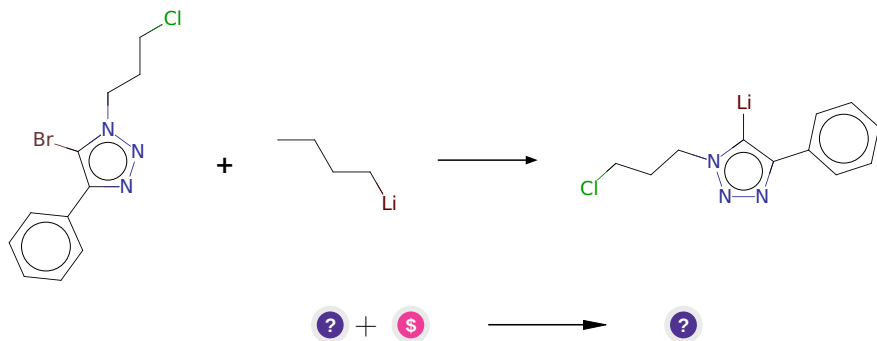
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

Protections: none

Reference: [10.1002/chem.201600278](https://doi.org/10.1002/chem.201600278) and [10.1016/j.bmcl.2011.12.131](https://doi.org/10.1016/j.bmcl.2011.12.131) and [10.1016/j.ejmech.2013.01.046](https://doi.org/10.1016/j.ejmech.2013.01.046) and [10.1021/jm0002782](https://doi.org/10.1021/jm0002782) and [10.1002/ejoc.201300443](https://doi.org/10.1002/ejoc.201300443) and [10.1021/jo052589w](https://doi.org/10.1021/jo052589w)(SI,page S3) and [10.1021/jm800527x](https://doi.org/10.1021/jm800527x) and [10.1016/j.bmcl.2015.04.098](https://doi.org/10.1016/j.bmcl.2015.04.098) and [10.1021/ja034563x](https://doi.org/10.1021/ja034563x)

Retrosynthesis ID: 29904

2.1.3 Br/Li exchange



Substrates:

1. ClCCCCn1nnc(-c2ccccc2)c1Br
2. n-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl

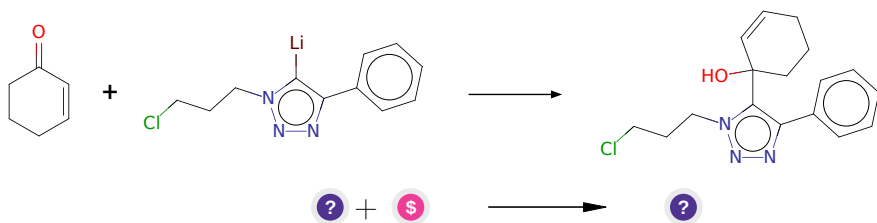
Typical conditions: nBuLi.or.tBuLi.THF.-78C

Protections: none

Reference: [10.1002/ejoc.201101490](https://doi.org/10.1002/ejoc.201101490) and [10.1016/j.tet.2012.03.058](https://doi.org/10.1016/j.tet.2012.03.058)
and [10.1016/j.tetlet.2015.01.032](https://doi.org/10.1016/j.tetlet.2015.01.032) and [10.1021/ja0541175](https://doi.org/10.1021/ja0541175) and [10.1016/j.tetlet.2016.06.123](https://doi.org/10.1016/j.tetlet.2016.06.123)

Retrosynthesis ID: 30672

2.1.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

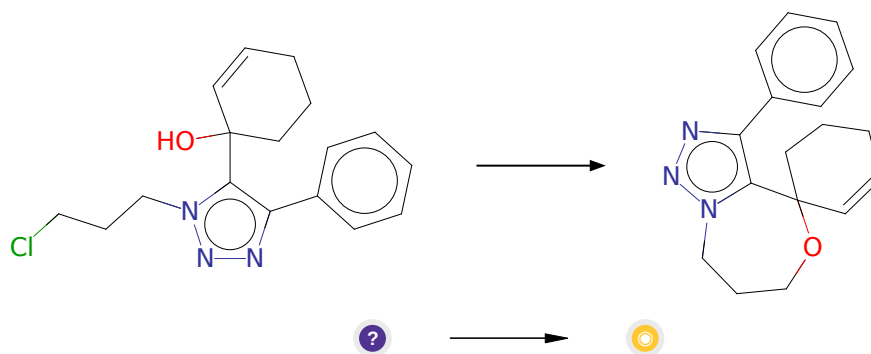
Typical conditions: THF.-78 deg C

Protections: none

Reference: [10.1021/ml300335r](#) and [10.1021/acs.jmedchem.6b00866](#)

Retrosynthesis ID: 31008139

2.1.5 Alkylation of tertiary alcohols



Substrates:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

Products:

1. C1=CC2(CCC1)OCCn1nnc(-c3ccccc3)c12

Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1016/S0040-4020\(01\)90106-1](#) and [10.1021/acs.analchem.5b04461](#)
and [10.3390/molecules24091643](#)

Retrosynthesis ID: 31010930

2.2 Path 2

Score: 125.08

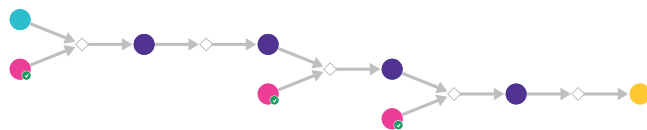
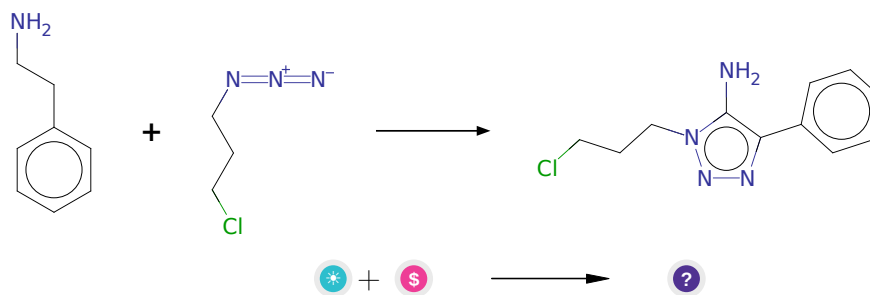


Figure 2: Outline of path 2

2.2.1 Synthesis of 1,2,3-triazoles from azides and nitrile derivatives



Substrates:

1. 1-azido-3-chlor-propan
2. Phenethylamine - *available at Sigma-Aldrich*

Products:

1. Nc1c(-c2ccccc2)nnn1CCCCl

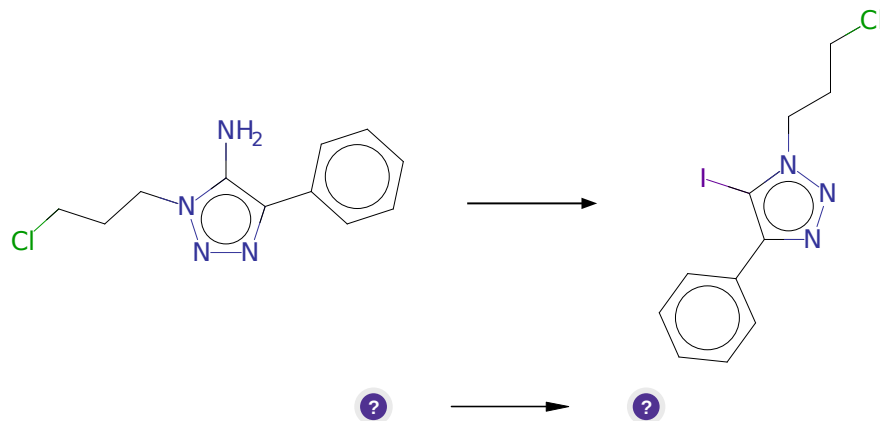
Typical conditions: anhydrous potassium carbonate.DMSO

Protections: none

Reference: DOI: [10.1002/jhet.5570280216](https://doi.org/10.1002/jhet.5570280216)

Retrosynthesis ID: 295117

2.2.2 Synthesis of iodoarenes



Substrates:

1. Nc1nc(CCCCl)c2ccccc12

Products:

1. ClCCCN1N=C(I)C2=CC=CC=C12

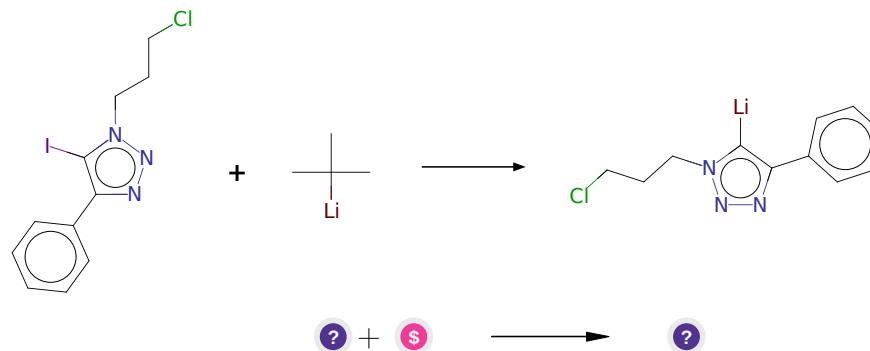
Typical conditions: MeCN.p-TSOH.NaNO₂.KI.0 to 25°C

Protections: none

Reference: [10.1002/anie.201407653](#) (SI, page S2) and [10.1002/anie.201409691](#) and [10.1021/ja312148q](#) and [10.1021/op300198a](#) and [10.1002/ejoc.201001436](#) and [10.1055/s-0028-1087981](#) and [10.1016/j.bmcl.2011.08.006](#) and [10.1021/ja0446404](#) and [10.3762/bjoc.12.36](#) and [10.1021/acs.orglett.5b01248](#) and [10.1055/s-2006-958936](#)

Retrosynthesis ID: 29903

2.2.3 I/Li exchange



Substrates:

1. ClCCCCn1nnc(-c2ccccc2)c1I
2. t-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl

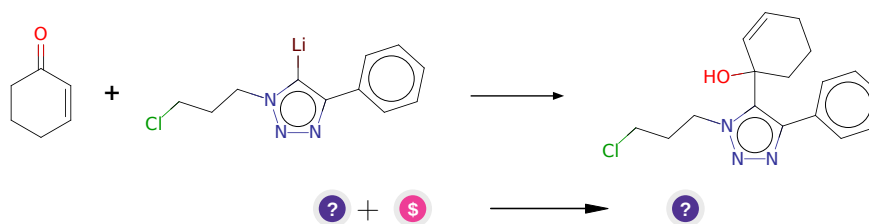
Typical conditions: nBuLi.or.tBuLi.THF.-78C

Protections: none

Reference: [10.1016/j.tet.2004.09.111](#) and [10.1039/c3ob41082j](#) And [10.1016/j.bmc.2012.03.056](#) And [10.1002/chem.201300292](#)

Retrosynthesis ID: 30673

2.2.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

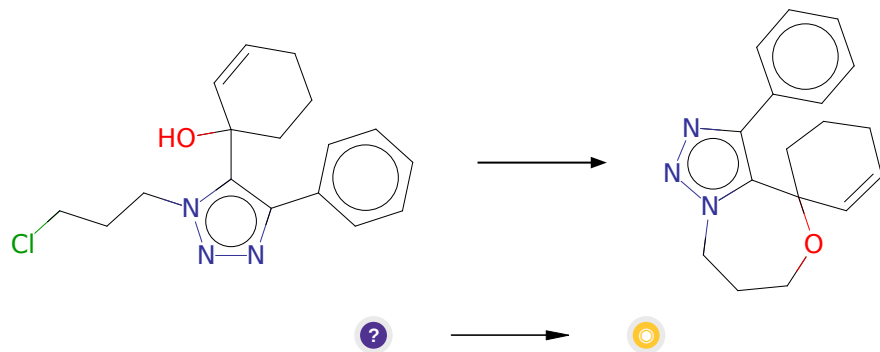
Typical conditions: THF.-78 deg C

Protections: none

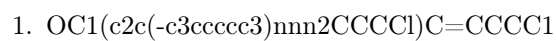
Reference: [10.1021/ml300335r](#) and [10.1021/acs.jmedchem.6b00866](#)

Retrosynthesis ID: 31008139

2.2.5 Alkylation of tertiary alcohols



Substrates:



Products:



Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1016/S0040-4020\(01\)90106-1](#) and [10.1021/acs.analchem.5b04461](#) and [10.3390/molecules24091643](#)

Retrosynthesis ID: 31010930

2.3 Path 3

Score: 151.35

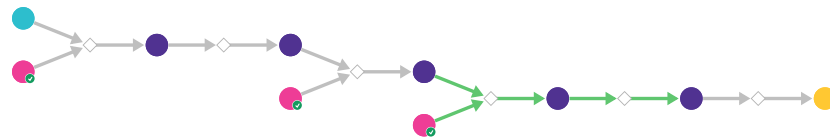
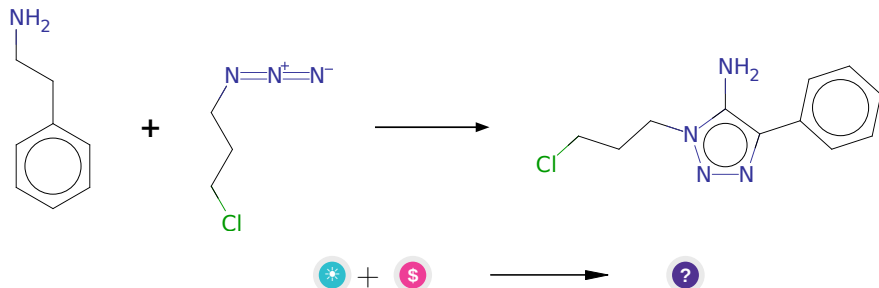


Figure 3: Outline of path 3

2.3.1 Synthesis of 1,2,3-triazoles from azides and nitrile derivatives



Substrates:

1. 1-azido-3-chloropropan
2. Phenethylamine - *available at Sigma-Aldrich*

Products:

1. Nc1c(-c2ccccc2)nn1CCCCl

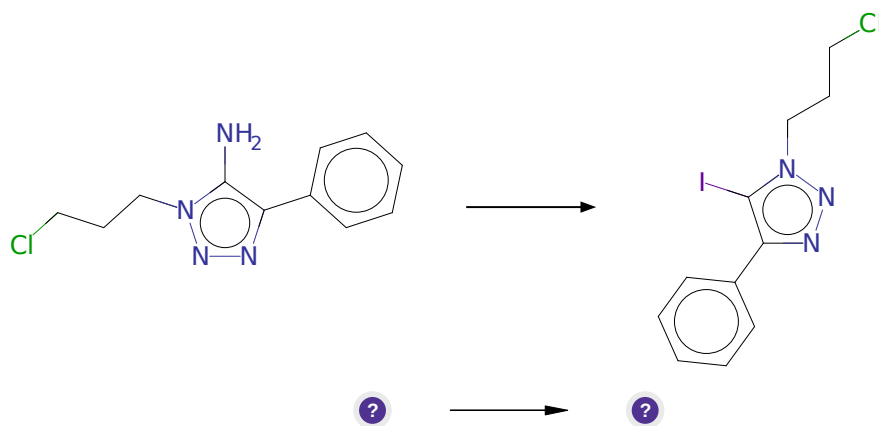
Typical conditions: anhydrous potassium carbonate.DMSO

Protections: none

Reference: DOI: [10.1002/jhet.5570280216](https://doi.org/10.1002/jhet.5570280216)

Retrosynthesis ID: 295117

2.3.2 Synthesis of iodoarenes



Substrates:

1. Nc1c(-c2ccccc2)nn1CCCCl

Products:

1. ClCCCN1nnc(-c2ccccc2)c1I

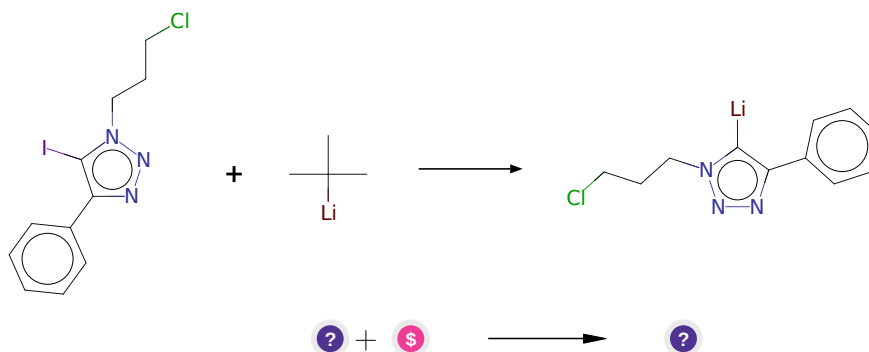
Typical conditions: MeCN.p-TSOH.NaNO₂.KI.0 to 25C

Protections: none

Reference: [10.1002/anie.201407653](#) (SI, page S2) and [10.1002/anie.201409691](#) and [10.1021/ja312148q](#) and [10.1021/op300198a](#) and [10.1002/ejoc.201001436](#) and [10.1055/s-0028-1087981](#) and [10.1016/j.bmcl.2011.08.006](#) and [10.1021/ja0446404](#) and [10.3762/bjoc.12.36](#) and [10.1021/acs.orglett.5b01248](#) and [10.1055/s-2006-958936](#)

Retrosynthesis ID: 29903

2.3.3 I/Li exchange



Substrates:

1. ClCCCN1nnc(-c2ccccc2)c1I
2. t-BuLi - [available at Sigma-Aldrich](#)

Products:

1. [Li]c1c(-c2ccccc2)nn1CCCCl

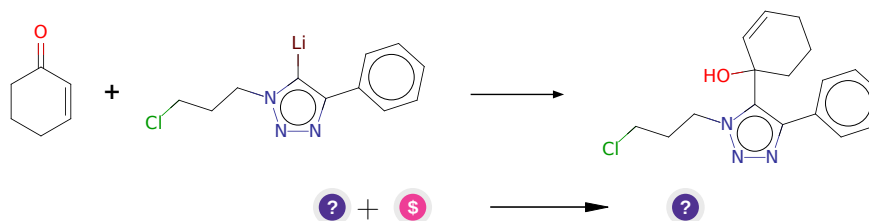
Typical conditions: nBuLi.or.tBuLi.THF.-78C

Protections: none

Reference: [10.1016/j.tet.2004.09.111](#) and [10.1039/c3ob41082j](#) And [10.1016/j.bmc.2012.03.056](#) And [10.1002/chem.201300292](#)

Retrosynthesis ID: 30673

2.3.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

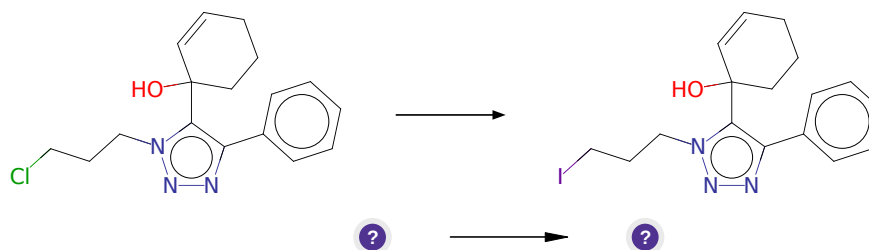
Typical conditions: THF.-78 deg C

Protections: none

Reference: [10.1021/ml300335r](#) and [10.1021/acs.jmedchem.6b00866](#)

Retrosynthesis ID: 31008139

2.3.5 Synthesis of alkyl iodides from alkyl chlorides



Substrates:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCI)C=CCCC1

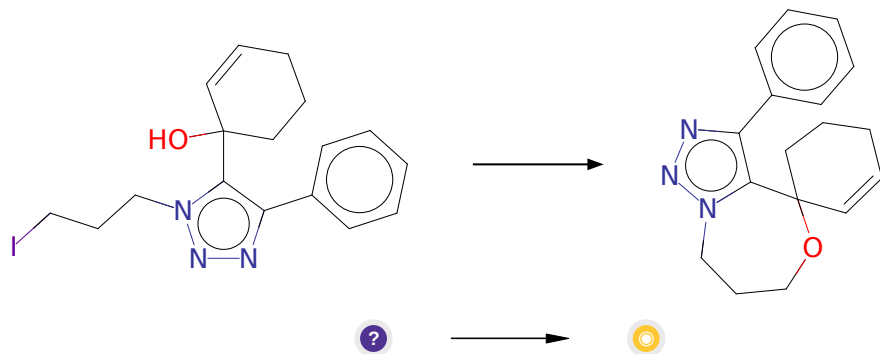
Typical conditions: NaI.acetone.heat

Protections: none

Reference: [10.1039/B812607K](#) and [10.1021/jm030222i](#)

Retrosynthesis ID: 31010848

2.3.6 Alkylation of tertiary alcohols



Substrates:

1. OC1(c2c(-c3ccccc3)nnn2CCCCI)C=CCCC1

Products:

1. C1=CC2(CCC1)OCCn1nnc(-c3ccccc3)c12

Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1039/P29910000147](#) and [10.1038/ncomms7703](#)

Retrosynthesis ID: 31010959

2.4 Path 4

Score: 151.35

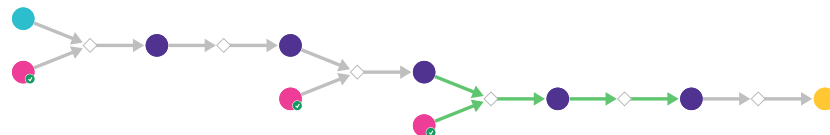
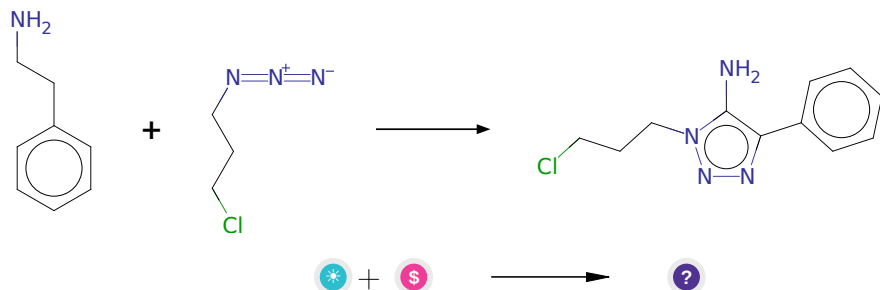


Figure 4: Outline of path 4

2.4.1 Synthesis of 1,2,3-triazoles from azides and nitrile derivatives



Substrates:

1. 1-azido-3-chloropropan
2. Phenethylamine - *available at Sigma-Aldrich*

Products:

1. Nc1c(-c2ccccc2)nn1CCCCl

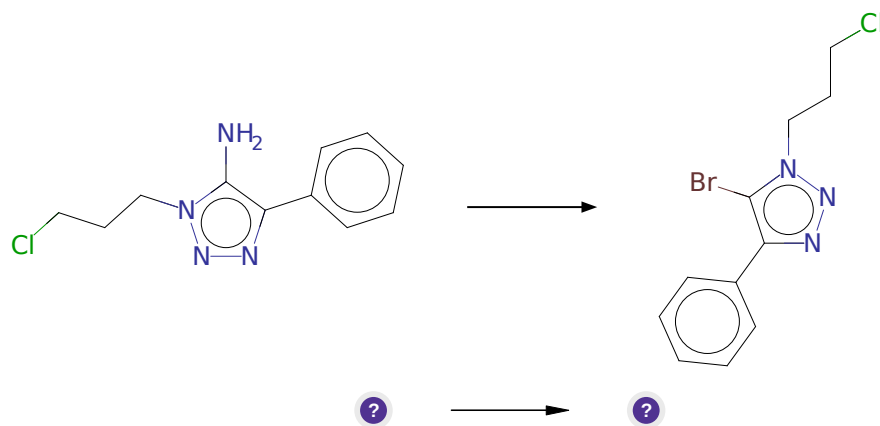
Typical conditions: anhydrous potassium carbonate.DMSO

Protections: none

Reference: DOI: [10.1002/jhet.5570280216](https://doi.org/10.1002/jhet.5570280216)

Retrosynthesis ID: 295117

2.4.2 Sandmeyer Reaction



Substrates:

1. Nc1c(-c2ccccc2)nn1CCCCl

Products:

1. ClCCCN1nnc(-c2ccccc2)c1Br

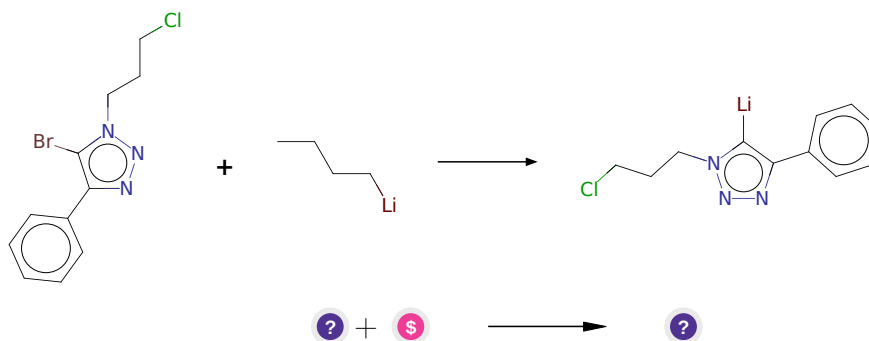
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

Protections: none

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

2.4.3 Br/Li exchange



Substrates:

1. ClCCCN1nnc(-c2ccccc2)c1Br
2. n-BuLi - [available at Sigma-Aldrich](#)

Products:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl

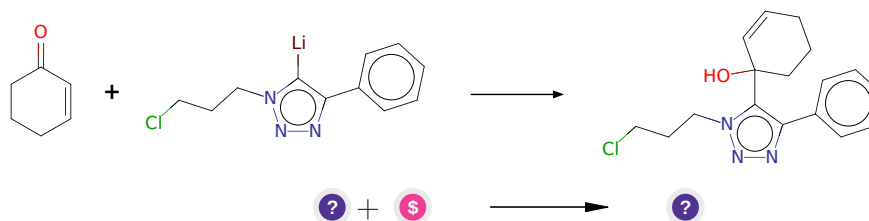
Typical conditions: nBuLi.or.tBuLi.THF.-78C

Protections: none

Reference: [10.1002/ejoc.201101490](#) and [10.1016/j.tet.2012.03.058](#) and [10.1016/j.tetlet.2015.01.032](#) and [10.1021/ja0541175](#) and [10.1016/j.tetlet.2016.06.123](#)

Retrosynthesis ID: 30672

2.4.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

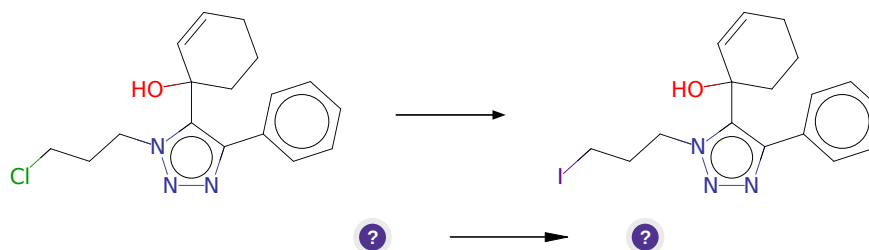
Typical conditions: THF.-78 deg C

Protections: none

Reference: [10.1021/ml300335r](#) and [10.1021/acs.jmedchem.6b00866](#)

Retrosynthesis ID: 31008139

2.4.5 Synthesis of alkyl iodides from alkyl chlorides



Substrates:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCI)C=CCCC1

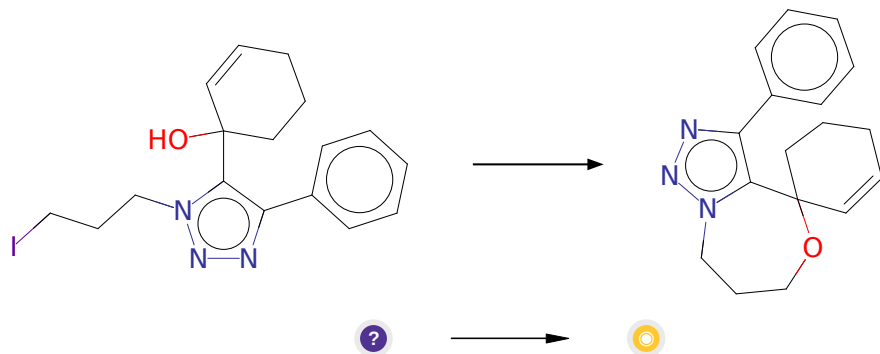
Typical conditions: NaI.acetone.heat

Protections: none

Reference: [10.1039/B812607K](#) and [10.1021/jm030222i](#)

Retrosynthesis ID: 31010848

2.4.6 Alkylation of tertiary alcohols



Substrates:

1. OC1(c2c(-c3ccccc3)nnn2CCCI)C=CCCC1

Products:

1. C1=CC2(CCC1)OCCN1nnc(-c3ccccc3)c12

Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1039/P29910000147](https://arxiv.org/abs/10.1039/P29910000147) and [10.1038/ncomms7703](https://arxiv.org/abs/10.1038/ncomms7703)

Retrosynthesis ID: 31010959

2.5 Path 5

Score: 176.35

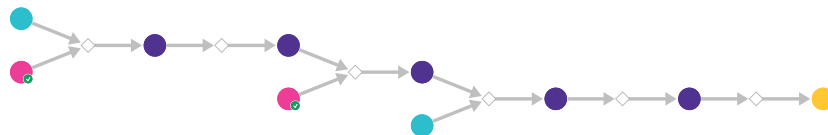
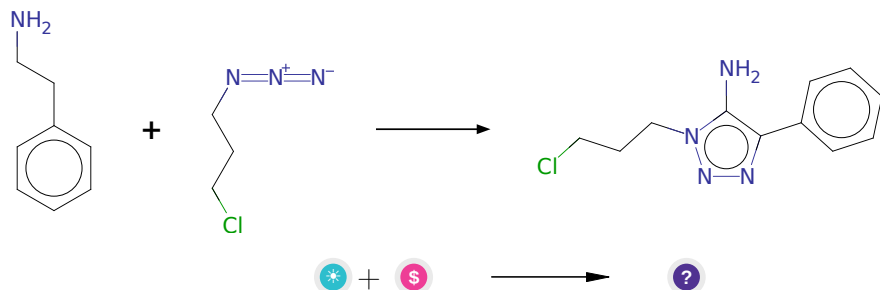


Figure 5: Outline of path 5

2.5.1 Synthesis of 1,2,3-triazoles from azides and nitrile derivatives



Substrates:

1. 1-azido-3-chlor-propan
2. Phenethylamine - *available at Sigma-Aldrich*

Products:

1. Nc1c(-c2ccccc2)nn1CCCCl

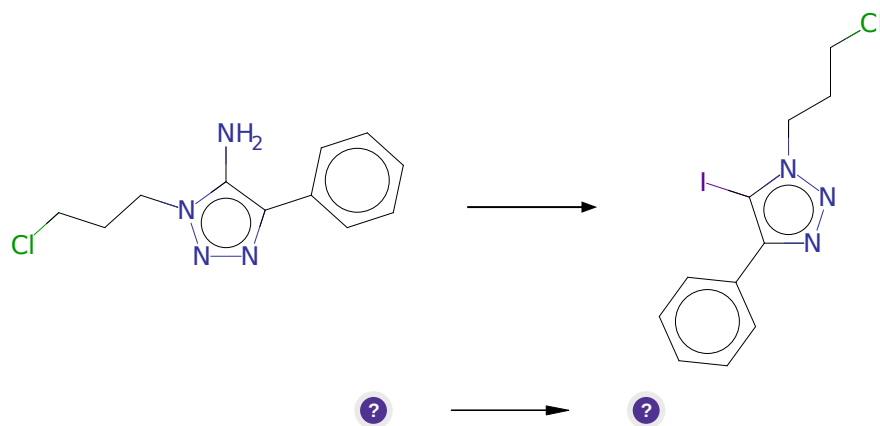
Typical conditions: anhydrous potassium carbonate.DMSO

Protections: none

Reference: DOI: [10.1002/jhet.5570280216](https://doi.org/10.1002/jhet.5570280216)

Retrosynthesis ID: 295117

2.5.2 Synthesis of iodoarenes



Substrates:

1. Nc1c(-c2ccccc2)nn1CCCCl

Products:

1. ClCCCN1nnc(-c2ccccc2)c1I

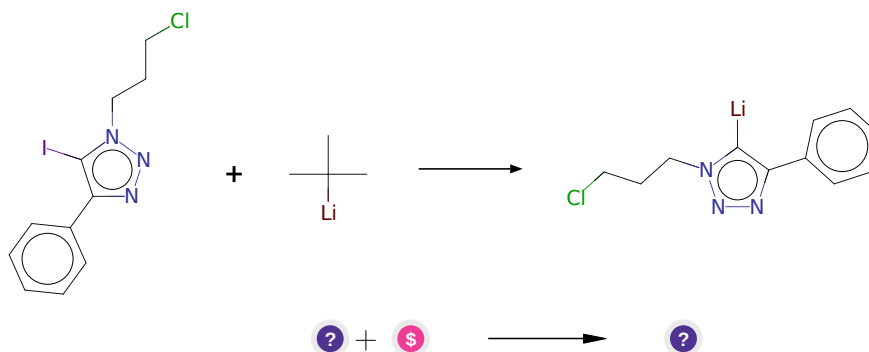
Typical conditions: MeCN.p-TSOH.NaNO₂.KI.0 to 25C

Protections: none

Reference: [10.1002/anie.201407653](#) (SI, page S2) and [10.1002/anie.201409691](#) and [10.1021/ja312148q](#) and [10.1021/op300198a](#) and [10.1002/ejoc.201001436](#) and [10.1055/s-0028-1087981](#) and [10.1016/j.bmcl.2011.08.006](#) and [10.1021/ja0446404](#) and [10.3762/bjoc.12.36](#) and [10.1021/acs.orglett.5b01248](#) and [10.1055/s-2006-958936](#)

Retrosynthesis ID: 29903

2.5.3 I/Li exchange



Substrates:

1. ClCCCN1nnc(-c2ccccc2)c1I
2. t-BuLi - [available at Sigma-Aldrich](#)

Products:

1. [Li]c1c(-c2ccccc2)nn1CCCCl

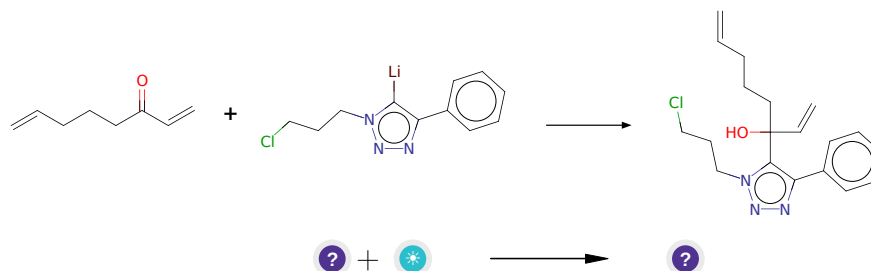
Typical conditions: nBuLi.or.tBuLi.THF.-78C

Protections: none

Reference: [10.1016/j.tet.2004.09.111](#) and [10.1039/c3ob41082j](#) And [10.1016/j.bmc.2012.03.056](#) And [10.1002/chem.201300292](#)

Retrosynthesis ID: 30673

2.5.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1c(-c2ccccc2)nnn1CCCCl
2. octa-1,7-dien-3-one

Products:

1. C=CCCC(O)(C=C)c1c(-c2ccccc2)nnn1CCCCl

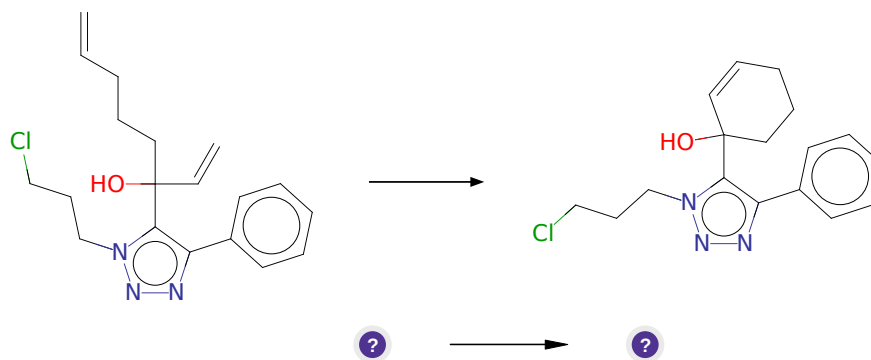
Typical conditions: THF.-78 deg C

Protections: none

Reference: [10.1021/ml300335r](#) and [10.1021/acs.jmedchem.6b00866](#)

Retrosynthesis ID: 31008139

2.5.5 Ring-Closing Metathesis



Substrates:

1. C=CCCC(O)(C=C)c1c(-c2ccccc2)nnn1CCCCl

Products:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

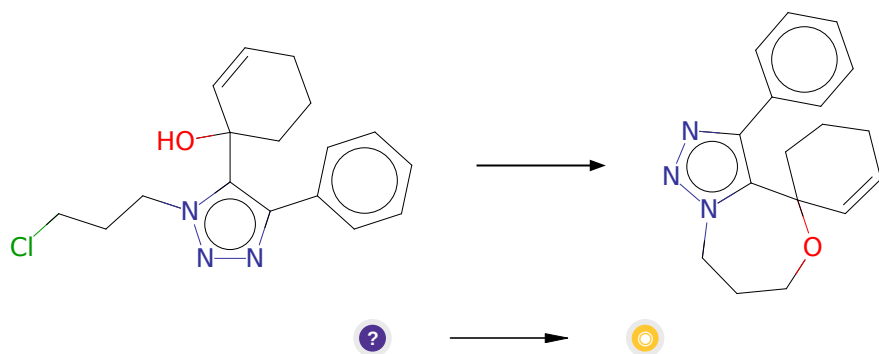
Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH₂Cl₂

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.5.6 Alkylation of tertiary alcohols



Substrates:

1. OC1(c2c(-c3ccccc3)nnn2CCCCl)C=CCCC1

Products:

1. C1=CC2(CCC1)OCCCN1nnc(-c3ccccc3)c12

Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1016/S0040-4020\(01\)90106-1](https://doi.org/10.1016/S0040-4020(01)90106-1) and [10.1021/acs.analchem.5b04461](https://doi.org/10.1021/acs.analchem.5b04461) and [10.3390/molecules24091643](https://doi.org/10.3390/molecules24091643)

Retrosynthesis ID: 31010930