

Paths of analysis*

AS1

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

*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.

Strategies: none selected

FGI Coeff: 0

Tunnels 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: 320.54

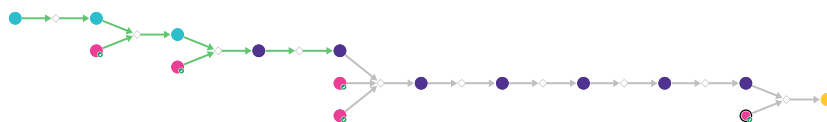
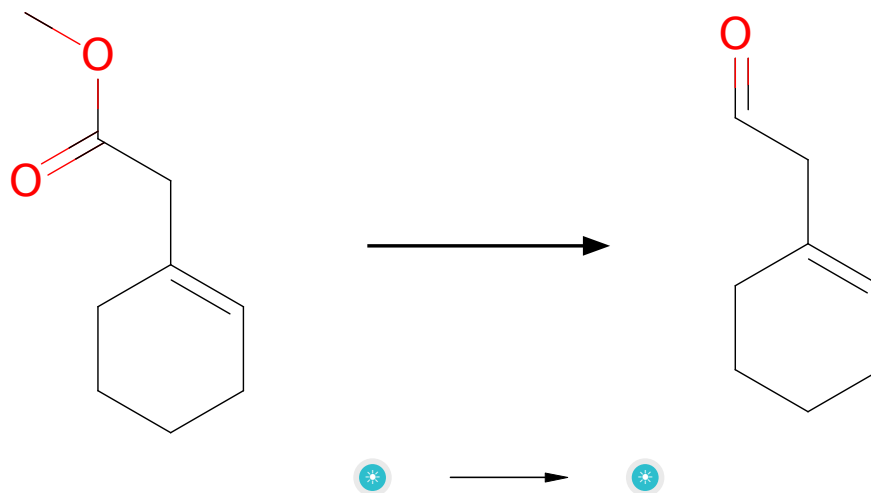


Figure 1: Outline of path 1

2.1.1 Aldehyde Formation



Substrates:

1. cyclohex-1-enyl-acetic acid methyl ester

Products:

1. cyclohex-1-enyl-acetaldehyde

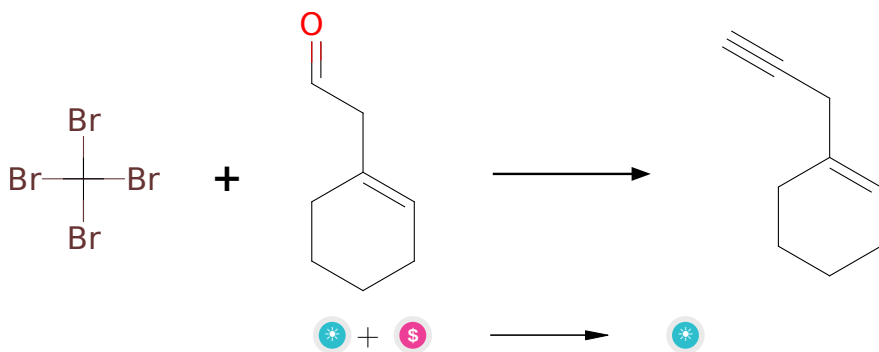
Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Reference: [10.1039/C39940000483](#) and [10.1039/C3CC47867J](#) and [10.1021/jo00222a054](#) and [10.1021/ja9934908](#) and [10.1021/jo902426z](#)

Retrosynthesis ID: 28551

2.1.2 Corey-Fuchs reaction



Substrates:

1. cyclohex-1-enyl-acetaldehyde
2. Tetrabromomethane - *available at Sigma-Aldrich*

Products:

1. 1-prop-2-ynyl-cyclohexene

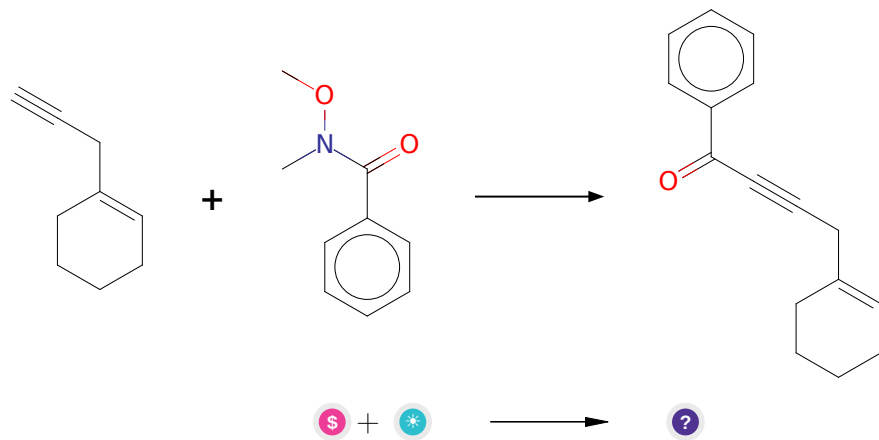
Typical conditions: PPh₃.BuLi.CBr₄

Protections: none

Reference: [10.1002/ejoc.200601137](#) and [10.1016/S0040-4039\(01\)94157-7](#)

Retrosynthesis ID: 10912

2.1.3 Addition of acetylides to Weinreb amides



Substrates:

1. N-Methoxy-N-methylbenzamide - *available at Sigma-Aldrich*
2. 1-prop-2-ynyl-cyclohexene

Products:

1. O=C(C#CCC1=CCCCC1)c1ccccc1

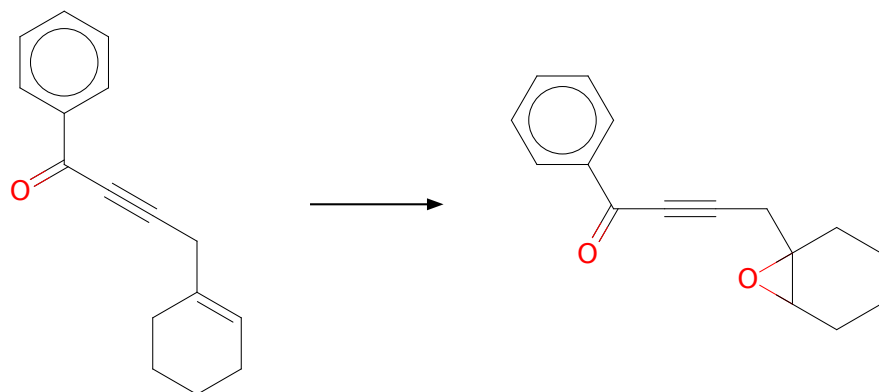
Typical conditions: nBuLi.THF

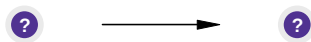
Protections: none

Reference: [10.1055/s-2007-992366](#) and [10.1002/ejoc.201200246](#) and [10.1021/ja9009265](#)

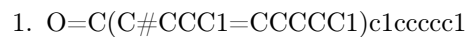
Retrosynthesis ID: 31443

2.1.4 Shi epoxidation

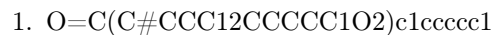




Substrates:



Products:



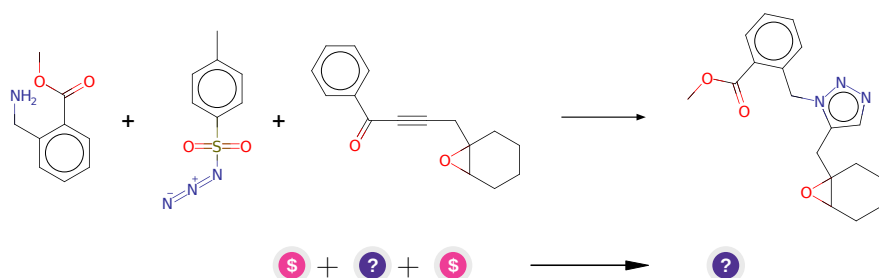
Typical conditions: sugar.based.catalyst.KHSO5.K2CO3.H2O.ACN.0C

Protections: none

Reference: [10.1055/s-0028-1083545](#) and [10.1021/ja972272g](#) and [10.1021/ja003049d](#) and [10.1021/jo972106r](#)

Retrosynthesis ID: 7434

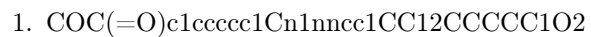
2.1.5 Metal-free multicomponent synthesis of triazoles



Substrates:

1. Tosyl azide solution - *available at Sigma-Aldrich*
2. O=C(C#CCC12CCCCC1O2)c1ccccc1
3. methyl-2-aminomethylbenzoat - *available at Sigma-Aldrich*

Products:



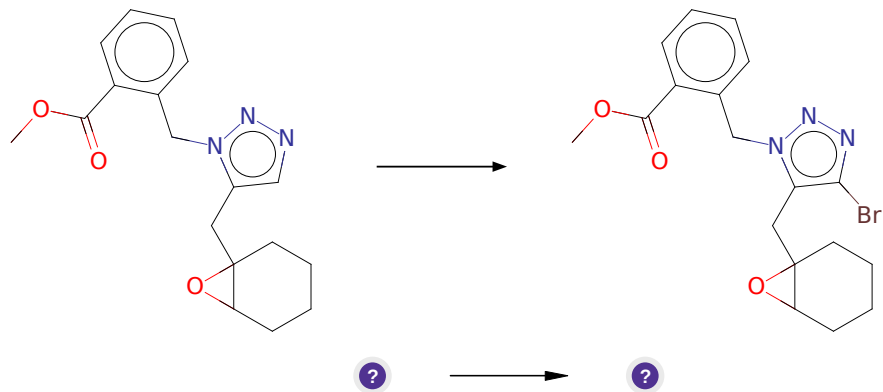
Typical conditions: 1. toluene.80C 2. LiOtBu.RT

Protections: none

Reference: DOI: [10.1002/anie.201307499](#)

Retrosynthesis ID: 6001

2.1.6 Bromination of aromatic compounds



Substrates:

1. COC(=O)c1ccccc1Cn1nncc1CC12CCCCC1O2

Products:

1. COC(=O)c1ccccc1Cn1nnc(Br)c1CC12CCCCC1O2

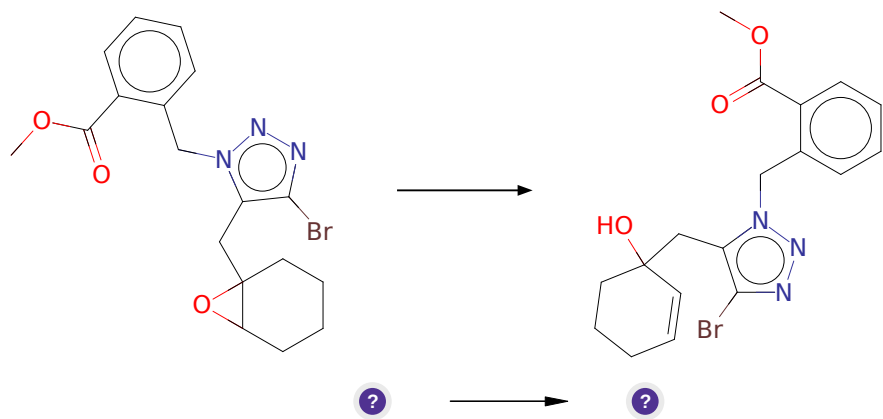
Typical conditions: Br₂.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.1.7 Synthesis of allyl alcohols from epoxides



Substrates:

1. COC(=O)c1ccccc1Cn1nnc(Br)c1CC12CCCCC1O2

Products:

1. COC(=O)c1ccccc1Cn1nnc(Br)c1CC1(O)C=CCCC1

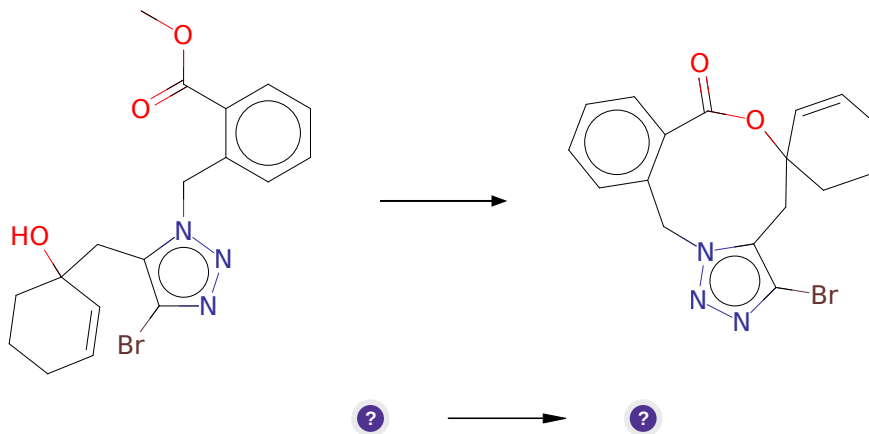
Typical conditions: PhSeNa.then H₂O₂

Protections: none

Reference: [10.1016/j.tetlet.2005.02.058](#) and [10.1016/0040-4020\(82\)85157-0](#) and [10.1016/j.bmc.2008.05.034](#) and [10.1021/ja070022m](#)

Retrosynthesis ID: 27837

2.1.8 Acid catalyzed transesterification



Substrates:

1. COC(=O)c1ccccc1Cn1nnc(Br)c1CC1(O)C=CCCC1

Products:

1. O=C1OC2(C=CCCC2)Cc2c(Br)nnn2Cc2ccccc21

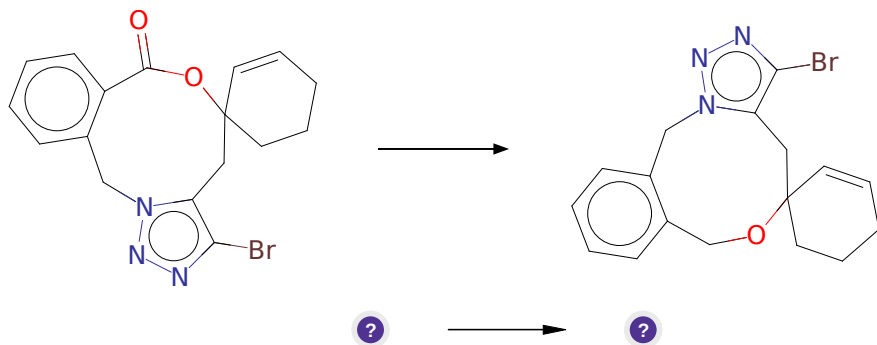
Typical conditions: H⁺

Protections: none

Reference: [10.1021/cr00020a004](#)

Retrosynthesis ID: 50438

2.1.9 Reduction of lactones to ethers



Substrates:

1. O=C1OC2(C=CCCC2)Cc2c(Br)nnn2Cc2ccccc21

Products:

1. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

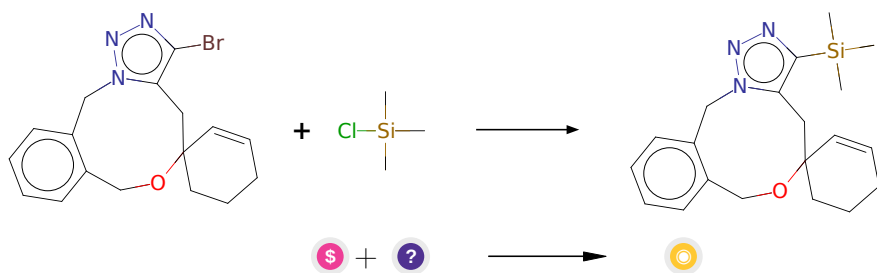
Typical conditions: LAH.THF.reflux

Protections: none

Reference: [10.1002/anie.200352705](https://doi.org/10.1002/anie.200352705) and [10.1016/j.tet.2016.07.036](https://doi.org/10.1016/j.tet.2016.07.036) and [10.5012/bkcs.2013.34.8.2495](https://doi.org/10.5012/bkcs.2013.34.8.2495) and [10.1080/10286020.2016.1232251](https://doi.org/10.1080/10286020.2016.1232251)

Retrosynthesis ID: 9999753

2.1.10 Synthesis of arylsilanes



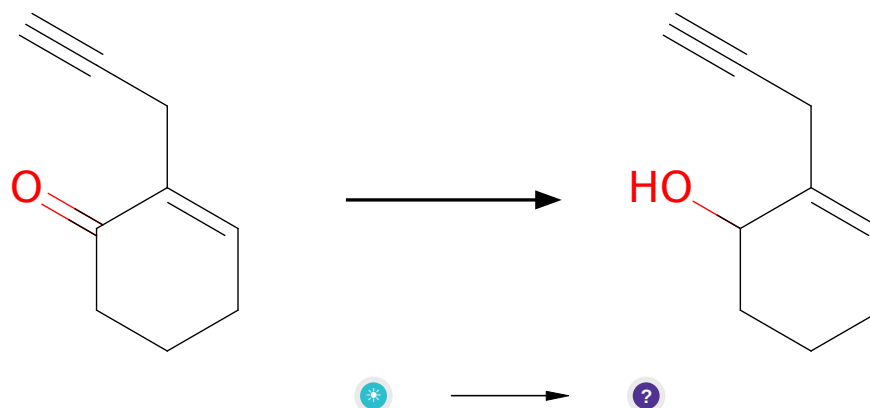
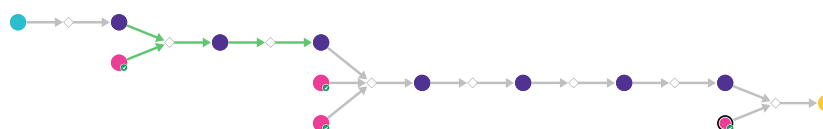
Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

Products:

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

Retrosynthesis ID: 5370

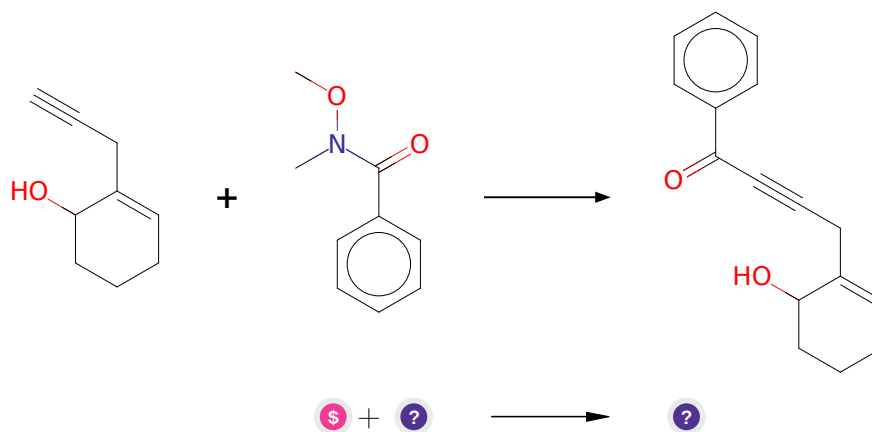


Protections: none

Reference: [10.1002/9780470638859.conrr400](https://doi.org/10.1002/9780470638859.conrr400)

Retrosynthesis ID: 10180

2.2.2 Addition of acetylides to Weinreb amides



Substrates:

1. N-Methoxy-N-methylbenzamide - *available at Sigma-Aldrich*
2. C#CCC1=CCCCC1O

Products:

1. O=C(C#CCC1=CCCCC1O)c1ccccc1

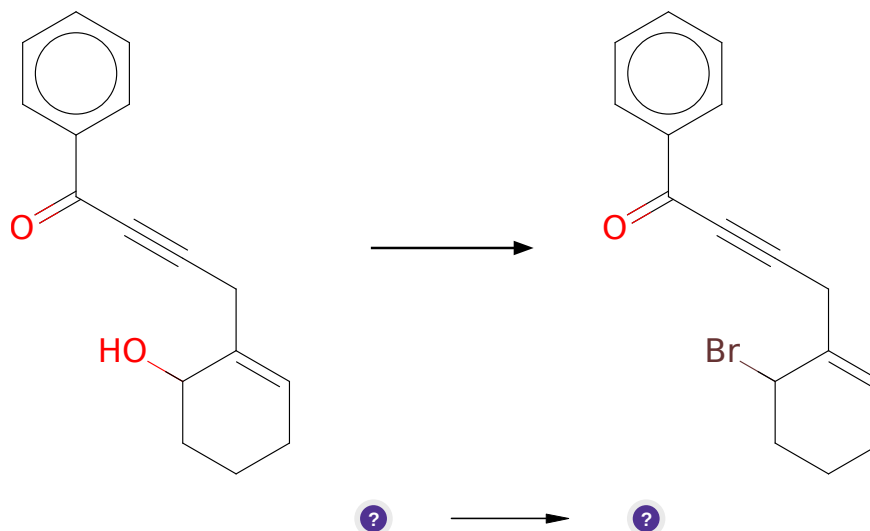
Typical conditions: nBuLi.THF

Protections: none

Reference: [10.1055/s-2007-992366](https://doi.org/10.1055/s-2007-992366) and [10.1002/ejoc.201200246](https://doi.org/10.1002/ejoc.201200246) and [10.1021/ja9009265](https://doi.org/10.1021/ja9009265)

Retrosynthesis ID: 31443

2.2.3 Appel Reaction



Substrates:

1. O=C(C#CCC1=CCCCC1O)c1ccccc1

Products:

1. O=C(C#CCC1=CCCCC1Br)c1ccccc1

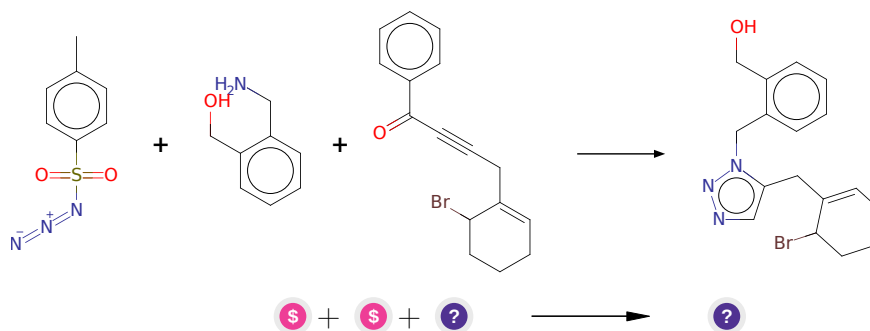
Typical conditions: PPh₃.CBr₄

Protections: none

Reference: [10.1016/j.jfluchem.2015.03.009](https://doi.org/10.1016/j.jfluchem.2015.03.009) and [10.1016/j.tet.2005.12.006](https://doi.org/10.1016/j.tet.2005.12.006) and [10.1021/jm00161a029](https://doi.org/10.1021/jm00161a029) and [10.1055/s-1995-5215](https://doi.org/10.1055/s-1995-5215)

Retrosynthesis ID: 9990042

2.2.4 Metal-free multicomponent synthesis of triazoles



Substrates:

1. Tosyl azide solution - *available at Sigma-Aldrich*
2. [2-(aminomethyl)phenyl]methanol - *available at Sigma-Aldrich*
3. O=C(C#CCC1=CCCCC1Br)c1ccccc1

Products:

1. OCc1ccccc1Cn1nncc1CC1=CCCCC1Br

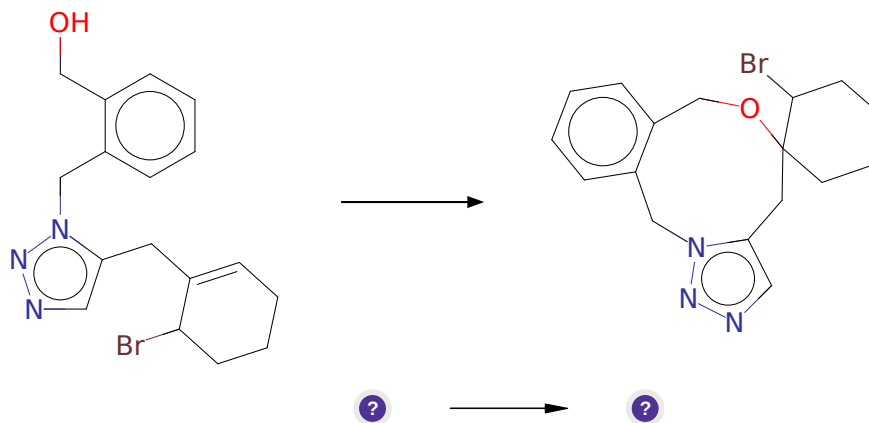
Typical conditions: 1. toluene.80C 2. LiOtBu.RT

Protections: none

Reference: DOI: *10.1002/anie.201307499*

Retrosynthesis ID: 6001

2.2.5 Synthesis of tertiary ethers



Substrates:

1. OCc1ccccc1Cn1nncc1CC1=CCCCC1Br

Products:

1. BrC1CCCCC12Cc1cnmn1Cc1ccccc1CO2

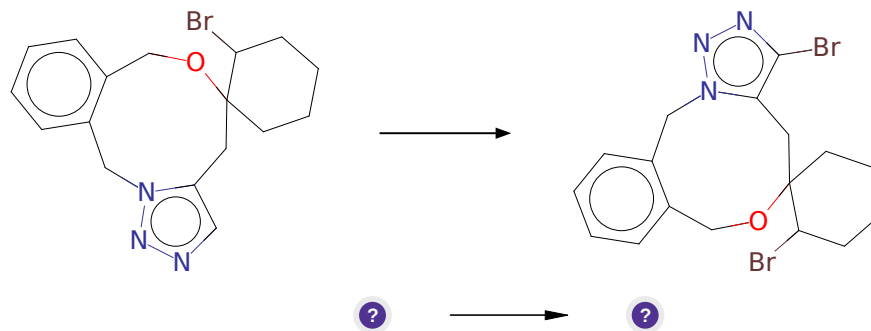
Typical conditions: H₂SO₄

Protections: none

Reference: *10.1016/j.tet.2009.10.055* and WO2009011551 (p.14 example 5) and *10.1002/chem.201304580* and *10.1021/jm.9811209* and US2007/225280A1 p.58 and WO2009/62285A1 p.50 and CN106928032A p.0040

Retrosynthesis ID: 10001897

2.2.6 Bromination of aromatic compounds



Substrates:

1. BrC1CCCCC12Cc1cnnn1Cc1ccccc1CO2

Products:

1. Br1nnn2c1CC1(CCCCC1Br)OCc1ccccc1C2

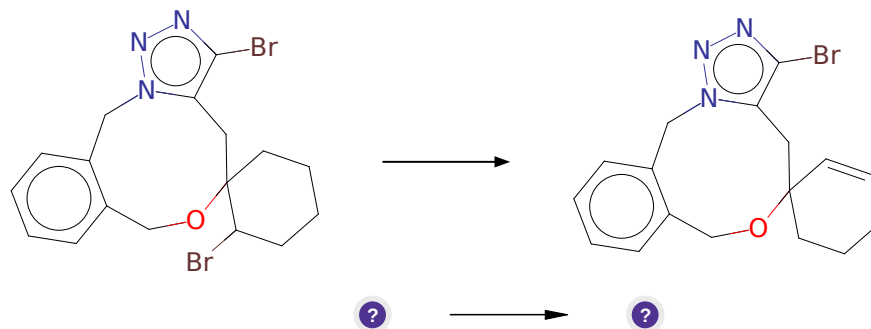
Typical conditions: Br₂.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.2.7 Elimination of bromide



Substrates:

1. Br1nnn2c1CC1(CCCCC1Br)OCc1ccccc1C2

Products:

1. Br1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

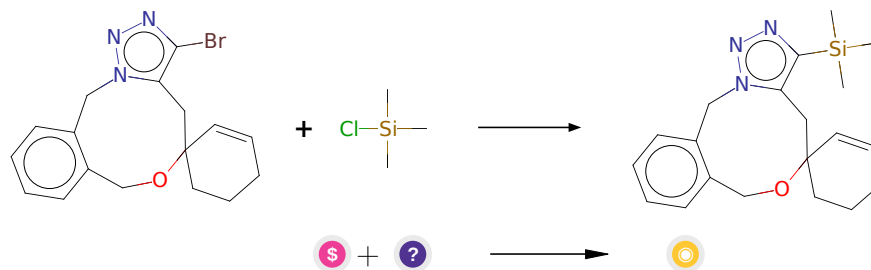
Typical conditions: K₂CO₃.DMF

Protections: none

Reference: [10.1016/j.jfluchem.2011.08.011](#) and [10.1039/P19920002971](#) and [10.1002/cber.19841170909](#) and [10.1021/ja01570a042](#)

Retrosynthesis ID: 23585

2.2.8 Synthesis of arylsilanes



Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

Products:

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

Typical conditions: 1.nBuLi.2.ClSnR₃

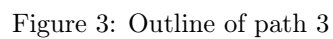
Protections: none

Reference: [10.1071/CH9851147](#).

Retrosynthesis ID: 5370

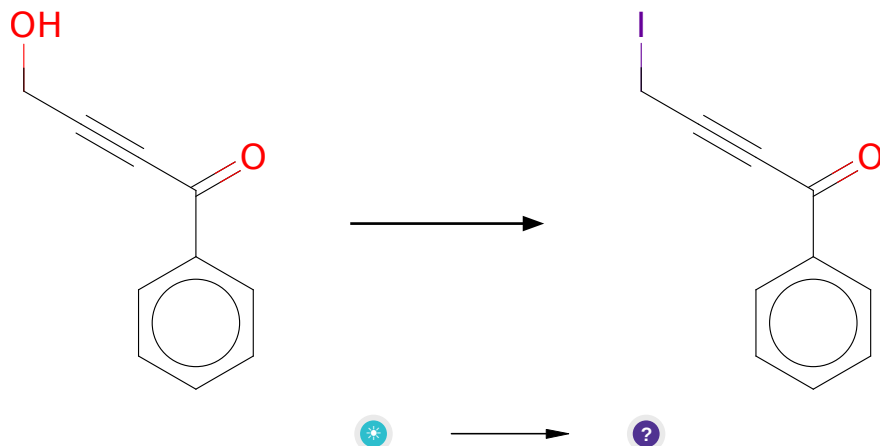
2.3 Path 3

Score: 335.80



Retrosynthesis ID: 10180

2.3.2 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

1. 4-hydroxybut-2-ynophenone

Products:

1. O=C(C#CCI)c1ccccc1

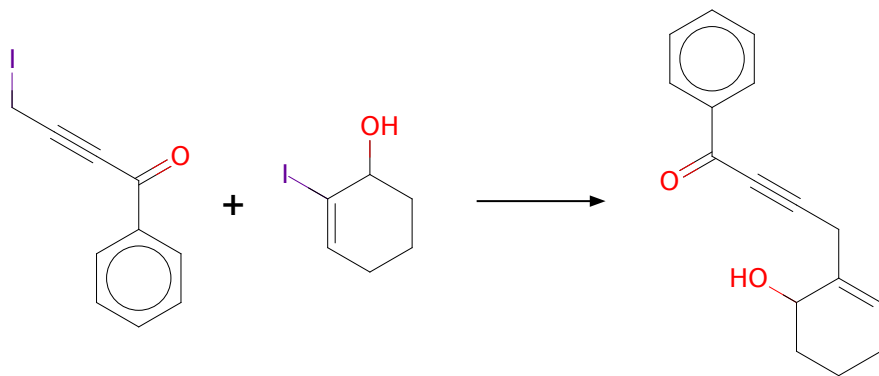
Typical conditions: Imidazole.PPh₃.I₂

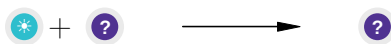
Protections: none

Reference: [10.1002/1099-0690\(200102\)2001:3<493::AID-EJOC493>3.0.CO2-B](#) (compound 20) and [10.1016/j.tet.2014.09.030](#)

Retrosynthesis ID: 9990040

2.3.3 Palladium catalysed alkylation of vinyl iodides





Substrates:

1. 2-iodo-2-cyclohexen-1-ol
2. O=C(C#CCI)c1ccccc1

Products:

1. O=C(C#CCC1=CCCCC1O)c1ccccc1

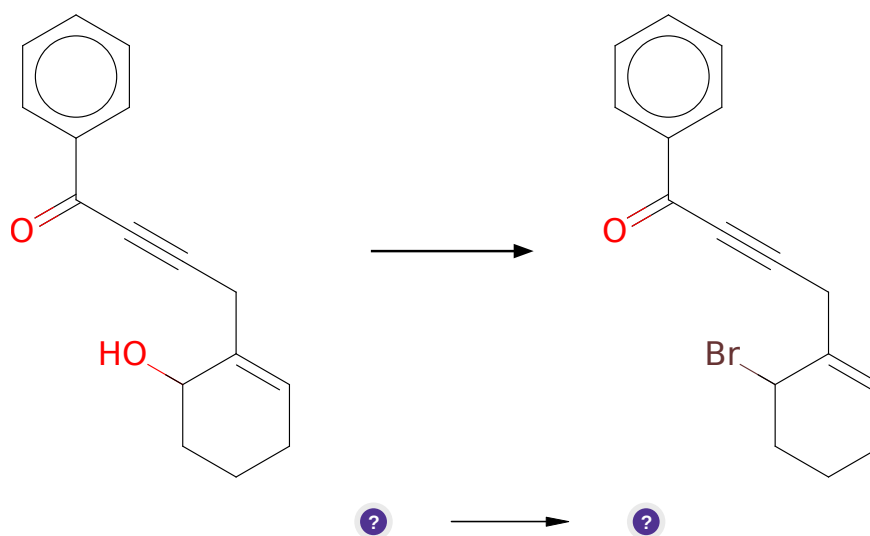
Typical conditions: [Pd].catalyst

Protections: none

Reference: [10.1016/j.bmcl.2005.12.066](#) and [10.1021/ol052070m](#) and [10.1021/ol5023195](#) and [10.1002/anie.200703134](#) and [10.1016/j.bmcl.2005.09.084](#) and [10.1021/ol0344873](#)

Retrosynthesis ID: 25163

2.3.4 Appel Reaction



Substrates:

1. O=C(C#CCC1=CCCCC1O)c1ccccc1

Products:

1. O=C(C#CCC1=CCCCC1Br)c1ccccc1

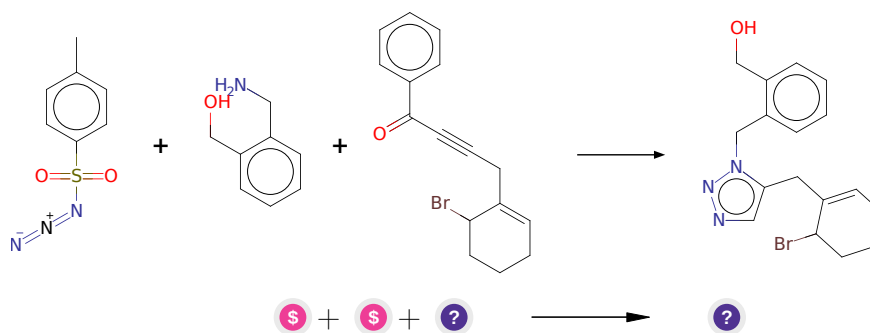
Typical conditions: PPh₃.CBr₄

Protections: none

Reference: [10.1016/j.jftchem.2015.03.009](https://doi.org/10.1016/j.jftchem.2015.03.009) and [10.1016/j.tet.2005.12.006](https://doi.org/10.1016/j.tet.2005.12.006) and [10.1021/jm00161a029](https://doi.org/10.1021/jm00161a029) and [10.1055/s-1995-5215](https://doi.org/10.1055/s-1995-5215)

Retrosynthesis ID: 9990042

2.3.5 Metal-free multicomponent synthesis of triazoles



Substrates:

1. Tosyl azide solution - *available at Sigma-Aldrich*
2. [2-(aminomethyl)phenyl]methanol - *available at Sigma-Aldrich*
3. O=C(C#CCCC1=CCCCC1Br)c1ccccc1

Products:

1. OCc1ccccc1Cn1nncc1CC1=CCCCC1Br

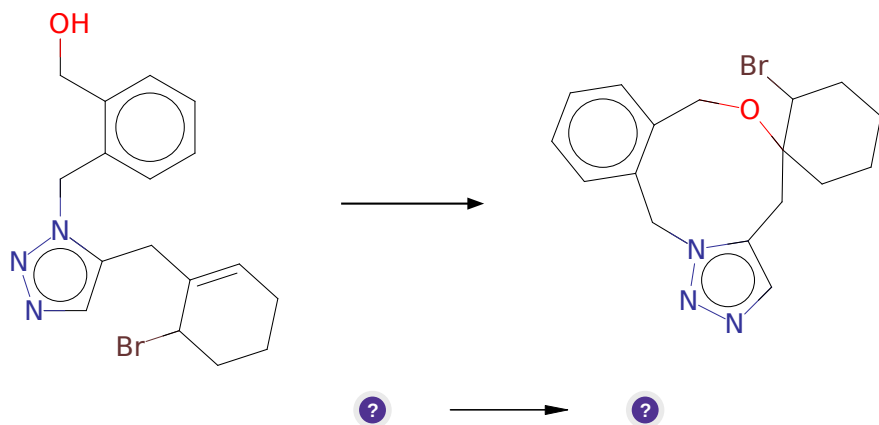
Typical conditions: 1. toluene.80C 2. LiOtBu.RT

Protections: none

Reference: DOI: [10.1002/anie.201307499](https://doi.org/10.1002/anie.201307499)

Retrosynthesis ID: 6001

2.3.6 Synthesis of tertiary ethers



Substrates:

1. OCc1ccc(cc1)CN1N=CN=C1

Products:

1. BrC1=CC=CC=C1C1=CC=CC=C1OCC1=CC=CC=C1CN1N=CN=C1

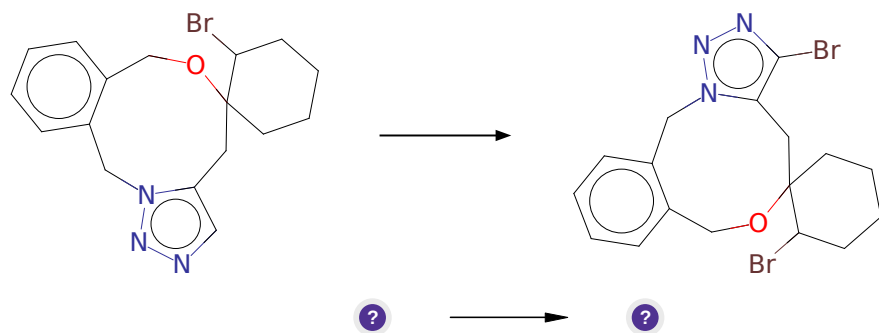
Typical conditions: H₂SO₄

Protections: none

Reference: [10.1016/j.tet.2009.10.055](#) and WO2009011551 (p.14 example 5) and [10.1002/chem.201304580](#) and [10.1021/jm9811209](#) and US2007/225280A1 p.58 and WO2009/62285A1 p.50 and CN106928032A p.0040

Retrosynthesis ID: 10001897

2.3.7 Bromination of aromatic compounds



Substrates:

1. BrC1CCCCC12Cc1cnmn1Cc1cccc1CO2

Products:

1. BrC1nnn2c1CC1(CCCCC1Br)OCc1cccc1C2

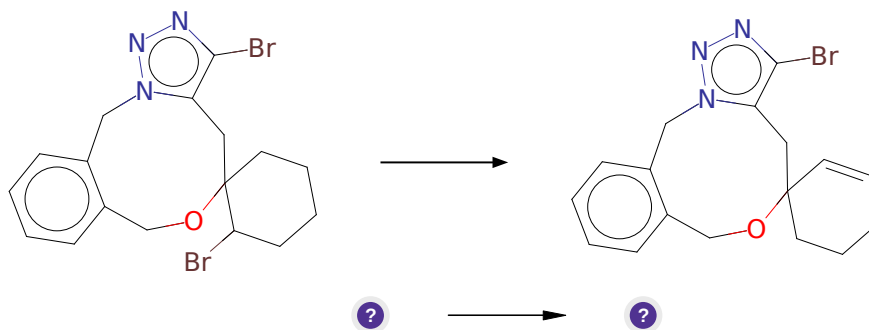
Typical conditions: Br₂.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.3.8 Elimination of bromide



Substrates:

1. BrC1nnn2c1CC1(CCCCC1Br)OCc1cccc1C2

Products:

1. BrC1nnn2c1CC1(C=CCCC1)OCc1cccc1C2

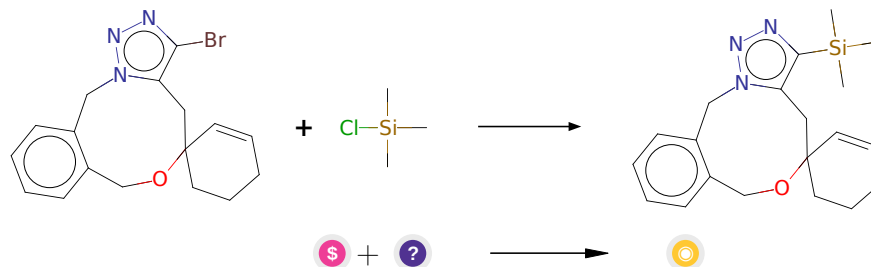
Typical conditions: K₂CO₃.DMF

Protections: none

Reference: [10.1016/j.jfluchem.2011.08.011](https://doi.org/10.1016/j.jfluchem.2011.08.011) and [10.1039/P19920002971](https://doi.org/10.1039/P19920002971) and [10.1002/cber.19841170909](https://doi.org/10.1002/cber.19841170909) and [10.1021/ja01570a042](https://doi.org/10.1021/ja01570a042)

Retrosynthesis ID: 23585

2.3.9 Synthesis of arylsilanes



Substrates:

1. TMS-Cl - *available at Sigma-Aldrich*
2. BrC1=NN=C(C=C1)OCc2ccccc2

Products:

1. C[Si](C)(C)C1=NN=C(C=C1)OCc2ccccc2

Typical conditions: 1. nBuLi. 2. ClSnR₃

Protections: none

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370