Paths of analysis*

AS1

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselecitve 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: 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

*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

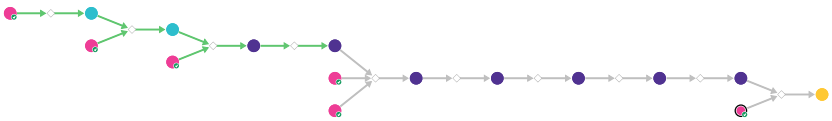
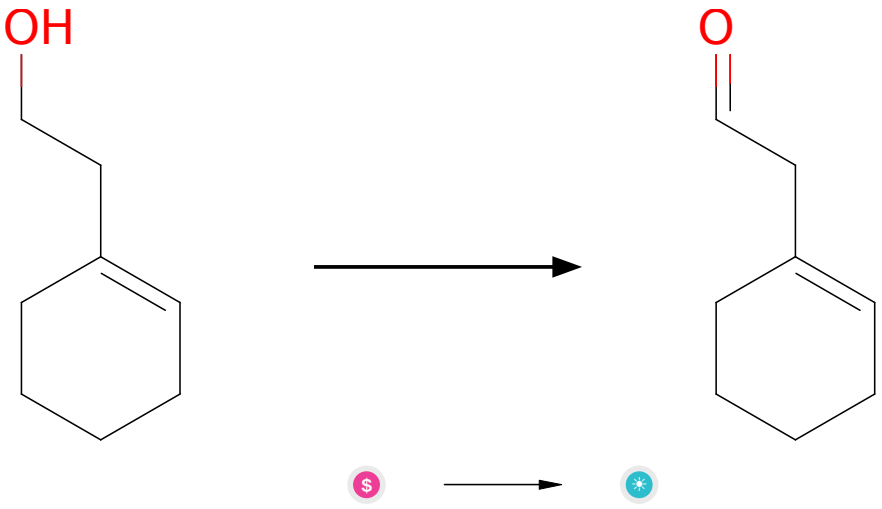


Figure 1: Outline of path 1

2.1.1 Oxidation of primary alcohols with DMP



Substrates:

1. 2-(cyclohex-1-en-1-yl)ethan-1-ol - *available at Sigma-Aldrich*

Products:

1. cyclohex-1-enyl-acetaldehyde

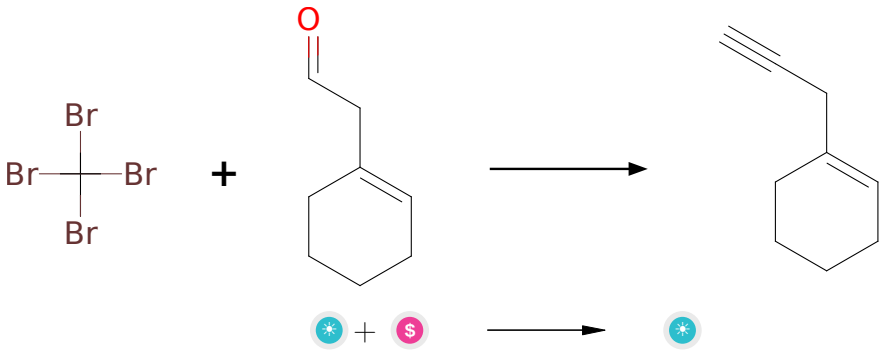
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

Retrosynthesis ID: 50426

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

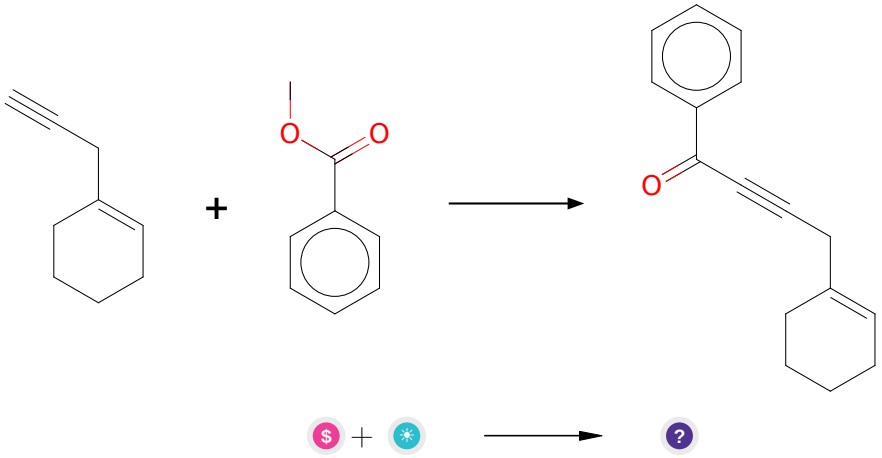
Typical conditions: PPh3.BuLi.CBr4

Protections: none

Reference: *10.1002/ejoc.200601137* and *10.1016/S0040-4039(01)94157-7*

Retrosynthesis ID: 10912

2.1.3 Terminal alkyne addition to ester



Substrates:

1. Methyl benzoate - *available at Sigma-Aldrich*
2. 1-prop-2-ynyl-cyclohexene

Products:

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

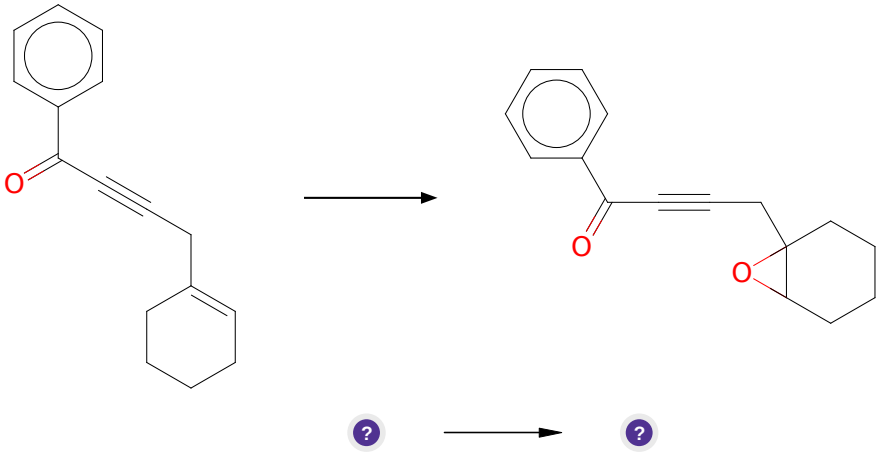
Typical conditions: nBuLi

Protections: none

Reference: *10.1016/j.tet.2013.10.007* and *10.1039/C6CC06591K* (SI p.2) and *10.1021/jo00084a009*

Retrosynthesis ID: 10002012

2.1.4 Shi epoxidation



Substrates:

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

Products:

1. O=C(C#CCC12CCCCC1O2)c1ccccc1

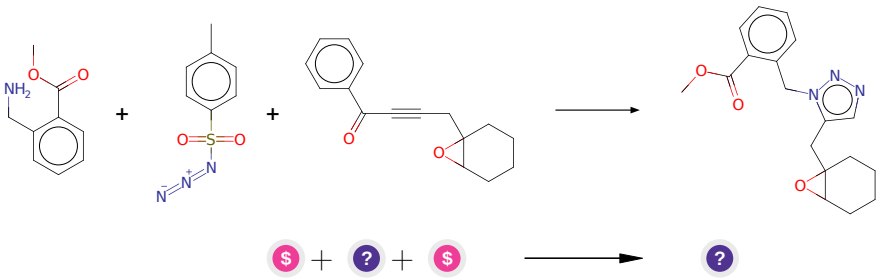
Typical conditions: sugar.based.catalyst.KHSO5.K2CO3.H2O.ACN.0C

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:

1. COC(=O)c1ccccc1Cn1nncc1CC12CCCCC1O2

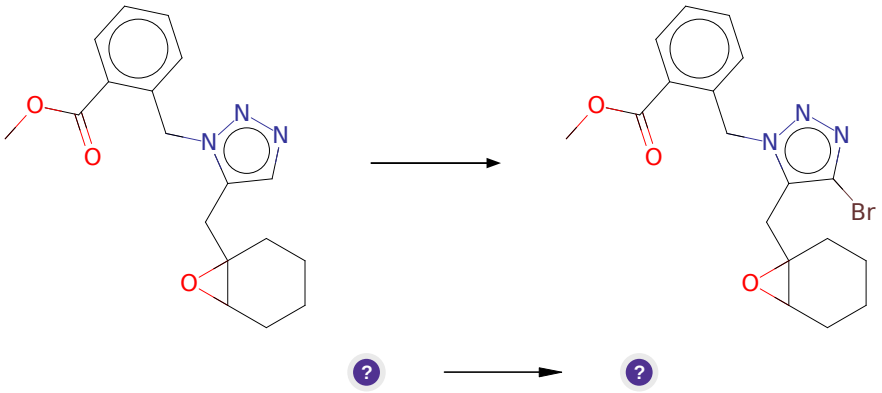
Typical conditions: 1. toluene.80C 2. LiOtBu.RT

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

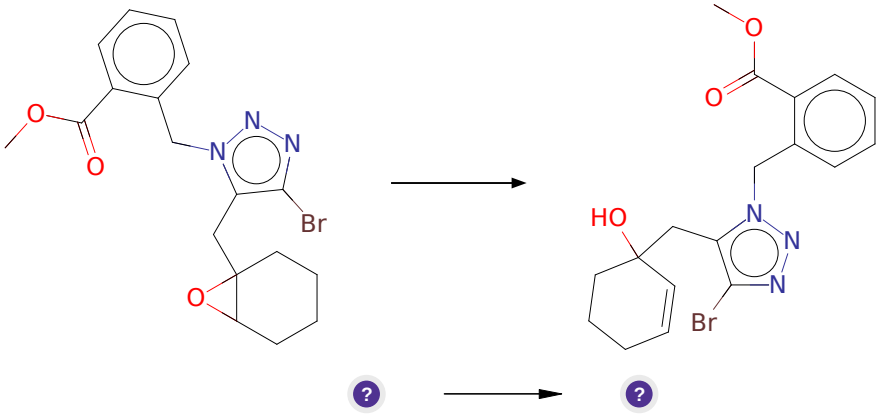
Typical conditions: Br2.Fe

Protections: none

Reference: *10.1021/acs.accounts.6b00120*

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

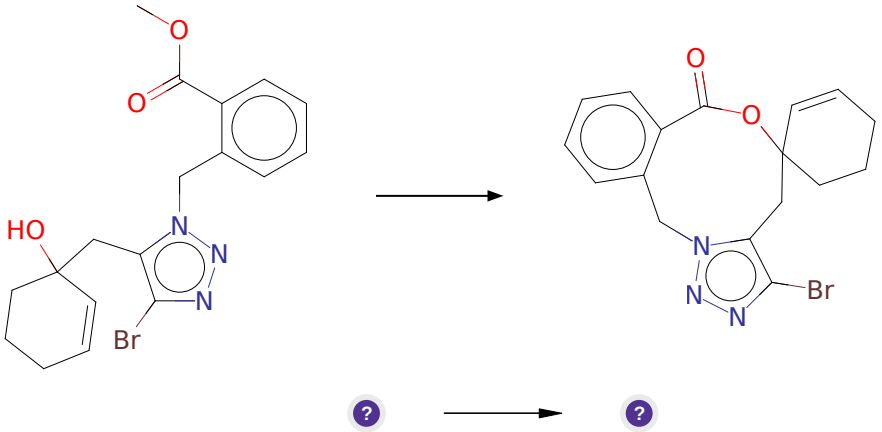
Typical conditions: PhSeNa.then H2O2

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

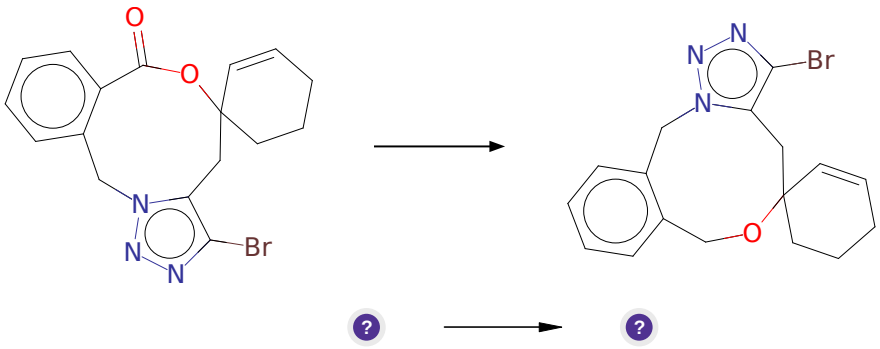
Typical conditions: H+

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

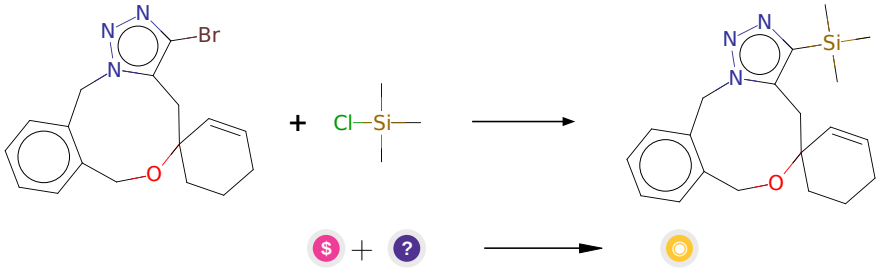
Typical conditions: LAH.THF.reflux

Protections: none

Reference: *10.1002/anie.200352705* and *10.1016/j.tet.2016.07.036* and *10.5012/bkcs.2013.34.8.2495* and *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

Typical conditions: 1.nBuLi.2.ClSnR3

Protections: none

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370

2.2 Path 2

Score: 320.54

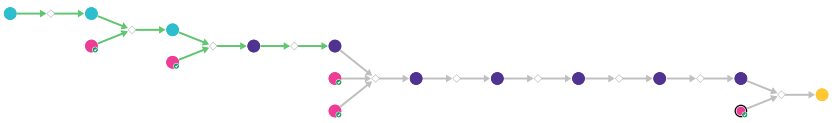
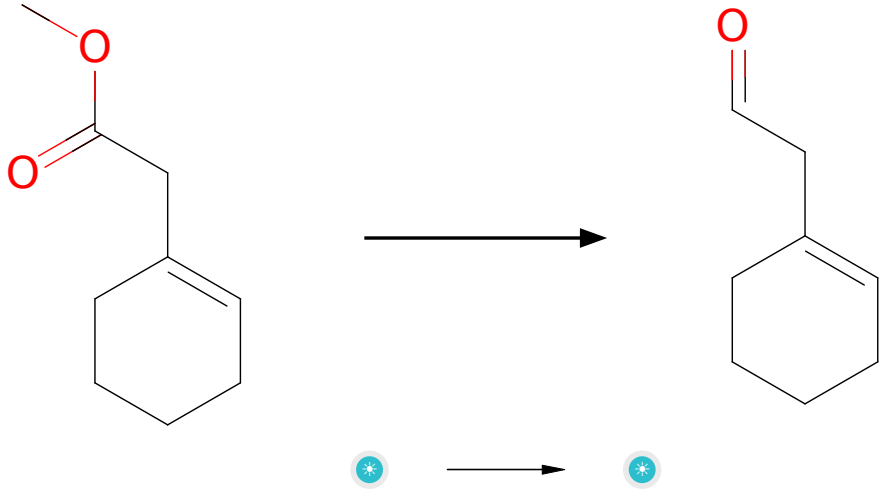


Figure 2: Outline of path 2

2.2.1 Aldehyde Formation



Substrates:

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

Products:

1. cyclohex-1-enyl-acetaldehyde

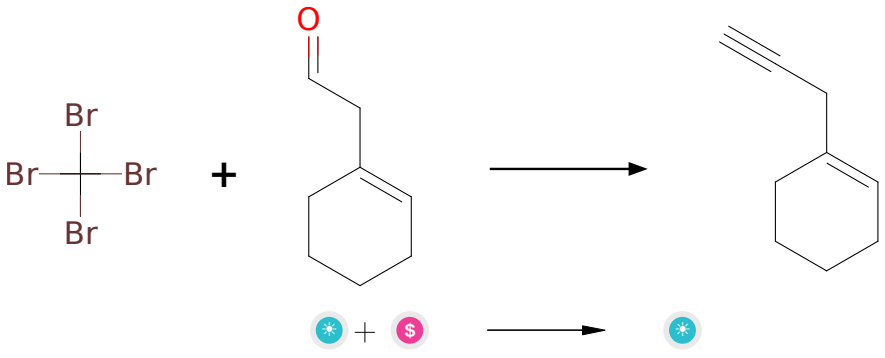
Typical conditions: DIBAL.solvent e.g. DCM

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

2.2.2 Corey-Fuchs reaction



Substrates:

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

Products:

1. 1-prop-2-ynyl-cyclohexene

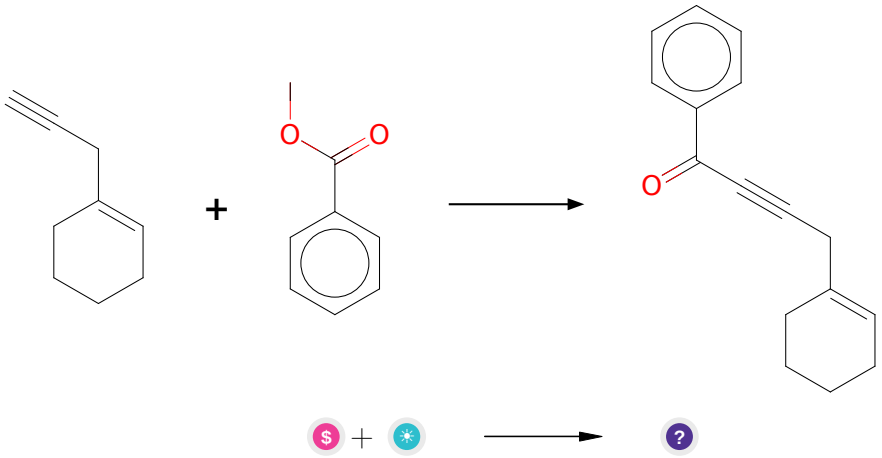
Typical conditions: PPh3.BuLi.CBr4

Protections: none

Reference: *10.1002/ejoc.200601137* and *10.1016/S0040-4039(01)94157-7*

Retrosynthesis ID: 10912

2.2.3 Terminal alkyne addition to ester



Substrates:

1. Methyl benzoate - *available at Sigma-Aldrich*
2. 1-prop-2-ynyl-cyclohexene

Products:

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

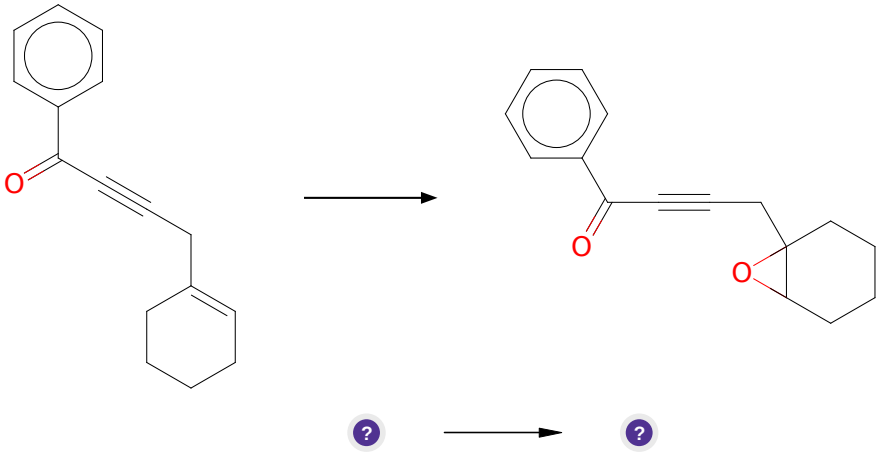
Typical conditions: nBuLi

Protections: none

Reference: *10.1016/j.tet.2013.10.007* and *10.1039/C6CC06591K* (SI p.2) and *10.1021/jo00084a009*

Retrosynthesis ID: 10002012

2.2.4 Shi epoxidation



Substrates:

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

Products:

1. O=C(C#CCC12CCCCC1O2)c1ccccc1

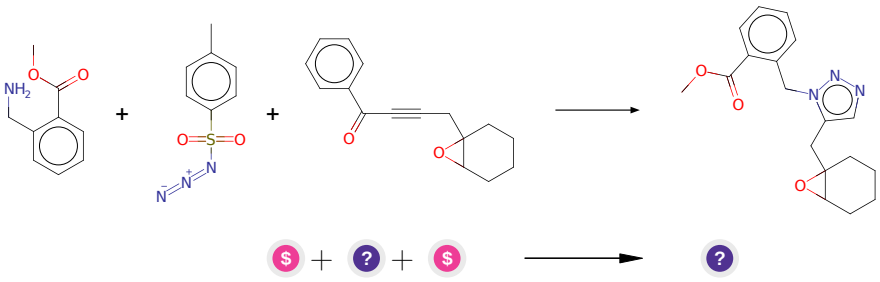
Typical conditions: sugar.based.catalyst.KHSO5.K2CO3.H2O.ACN.0C

Protections: none

Reference: *10.1055/s-0028-1083545* and *10.1021/ja972272g* and *10.1021/ja003049d* and *10.1021/jo972106r*

Retrosynthesis ID: 7434

2.2.5 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:

1. COC(=O)c1ccccc1Cn1nncc1CC12CCCCC1O2

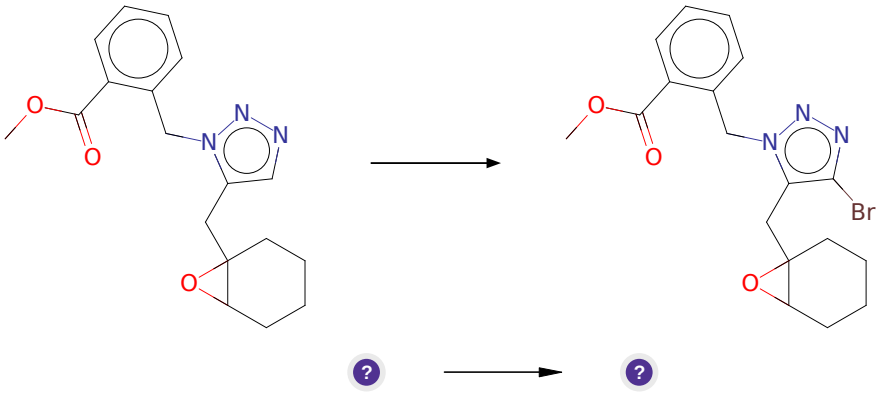
Typical conditions: 1. toluene.80C 2. LiOtBu.RT

Protections: none

Reference: DOI: *10.1002/anie.201307499*

Retrosynthesis ID: 6001

2.2.6 Bromination of aromatic compounds



Substrates:

1. COC(=O)c1ccccc1Cn1nncc1CC12CCCCC1O2

Products:

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

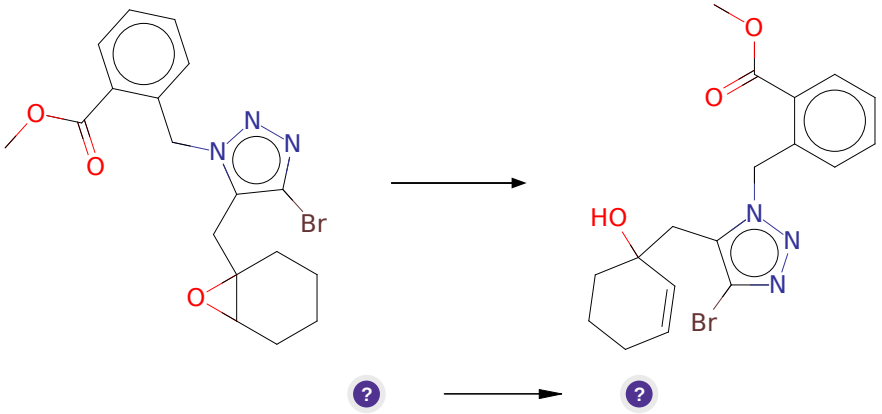
Typical conditions: Br2.Fe

Protections: none

Reference: *10.1021/acs.accounts.6b00120*

Retrosynthesis ID: 7777000

2.2.7 Synthesis of allyl alcohols from epoxides



Substrates:

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

Products:

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

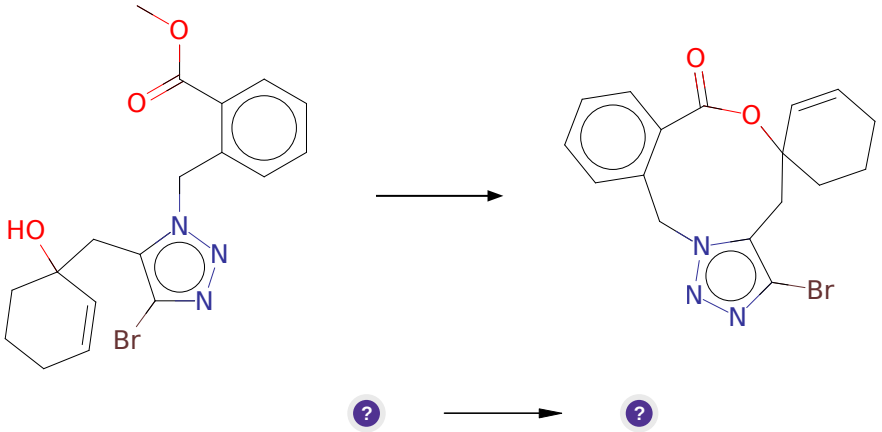
Typical conditions: PhSeNa.then H2O2

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

2.2.8 Acid catalyzed transesterification



Substrates:

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

Products:

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

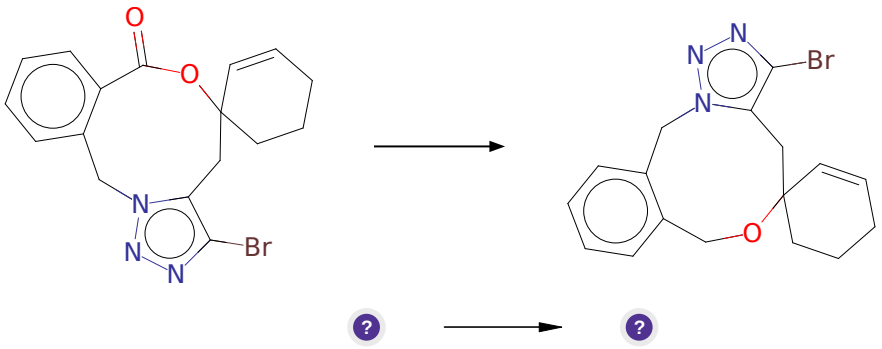
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.2.9 Reduction of lactones to ethers



Substrates:

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

Products:

1. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

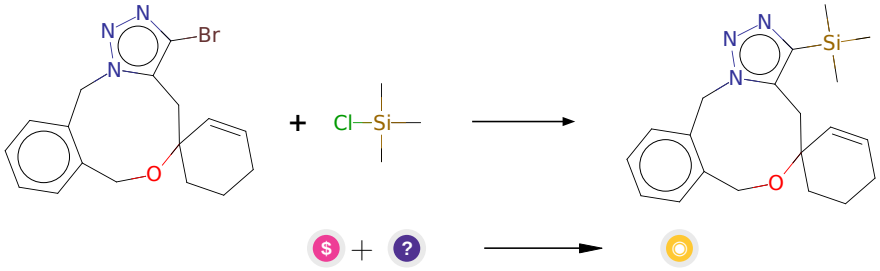
Typical conditions: LAH.THF.reflux

Protections: none

Reference: *10.1002/anie.200352705* and *10.1016/j.tet.2016.07.036* and *10.5012/bkcs.2013.34.8.2495* and *10.1080/10286020.2016.1232251*

Retrosynthesis ID: 9999753

2.2.10 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

Typical conditions: 1.nBuLi.2.ClSnR3

Protections: none

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370

2.3 Path 3

Score: 320.54

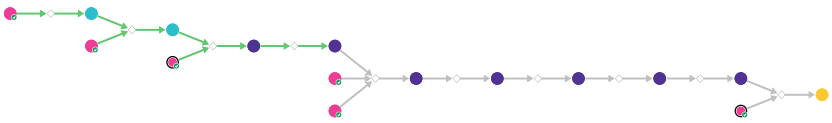
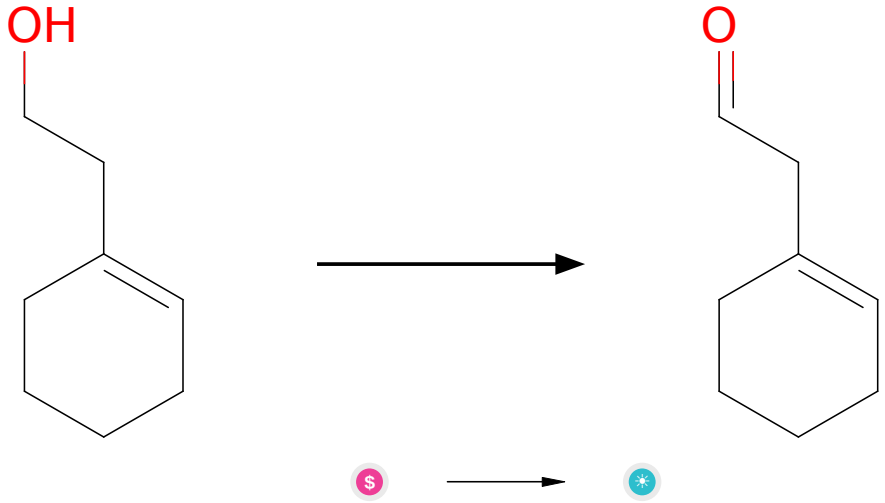


Figure 3: Outline of path 3

2.3.1 Oxidation of primary alcohols with DMP



Substrates:

1. 2-(cyclohex-1-en-1-yl)ethan-1-ol - *available at Sigma-Aldrich*

Products:

1. cyclohex-1-enyl-acetaldehyde

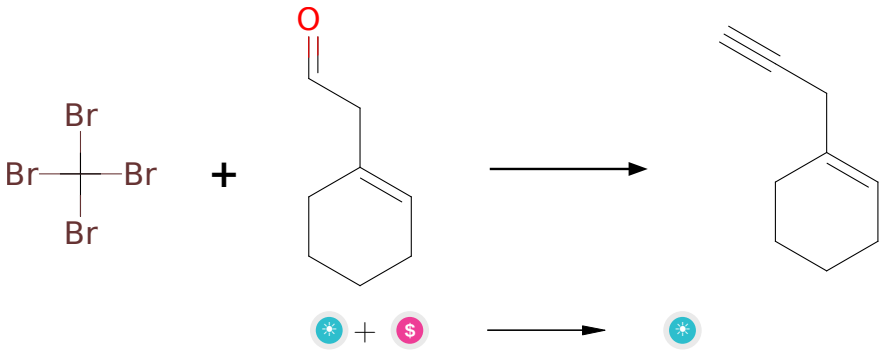
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

Retrosynthesis ID: 50426

2.3.2 Corey-Fuchs reaction



Substrates:

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

Products:

1. 1-prop-2-ynyl-cyclohexene

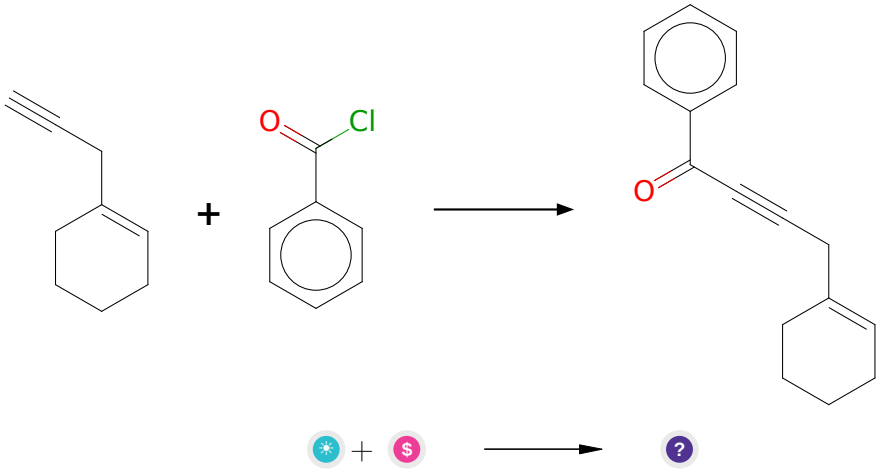
Typical conditions: PPh3.BuLi.CBr4

Protections: none

Reference: *10.1002/ejoc.200601137* and *10.1016/S0040-4039(01)94157-7*

Retrosynthesis ID: 10912

2.3.3 Synthesis of acetylenic ketones



Substrates:

1. 1-prop-2-ynyl-cyclohexene
2. Benzoyl chloride - *available at Sigma-Aldrich*

Products:

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

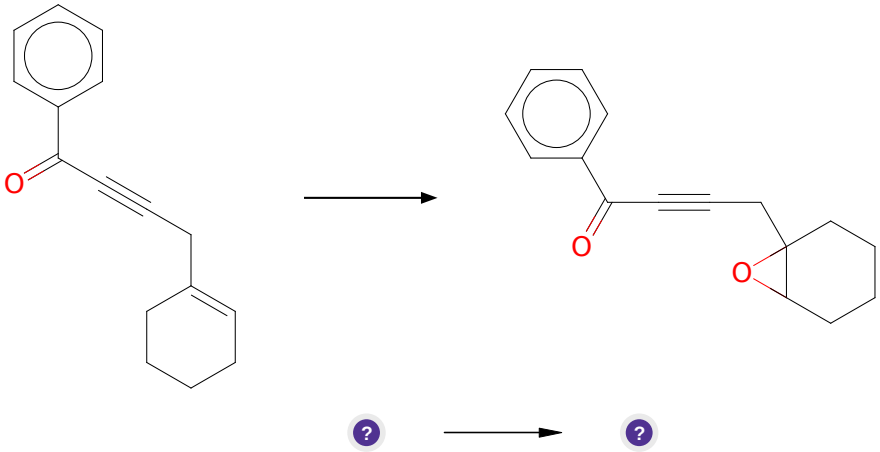
Typical conditions: 1.nBuLi.2.ZnCl2.3.Pd(PPh3)4.RCOCl

Protections: none

Reference: *10.1016/0022-328x(88)80002-0*

Retrosynthesis ID: 5317

2.3.4 Shi epoxidation



Substrates:

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

Products:

1. O=C(C#CCC12CCCCC1O2)c1ccccc1

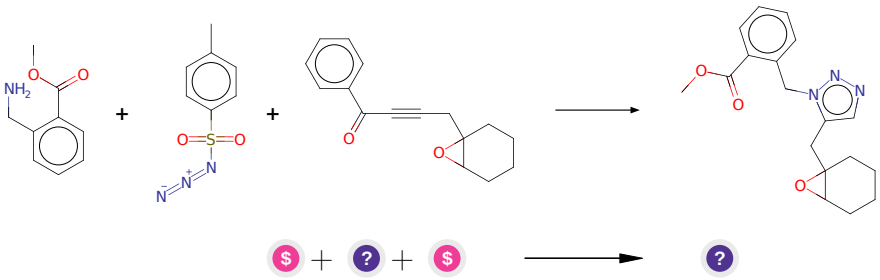
Typical conditions: sugar.based.catalyst.KHSO5.K2CO3.H2O.ACN.0C

Protections: none

Reference: *10.1055/s-0028-1083545* and *10.1021/ja972272g* and *10.1021/ja003049d* and *10.1021/jo972106r*

Retrosynthesis ID: 7434

2.3.5 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:

1. COC(=O)c1ccccc1Cn1nncc1CC12CCCCC1O2

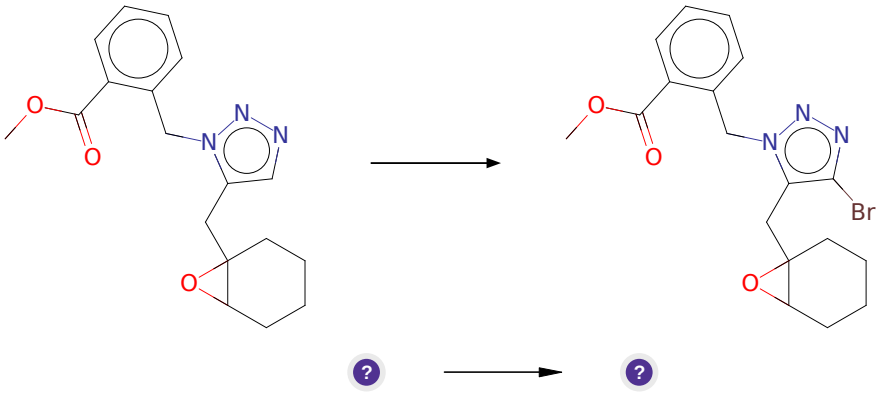
Typical conditions: 1. toluene.80C 2. LiOtBu.RT

Protections: none

Reference: DOI: *10.1002/anie.201307499*

Retrosynthesis ID: 6001

2.3.6 Bromination of aromatic compounds



Substrates:

1. COC(=O)c1ccccc1Cn1nncc1CC12CCCCC1O2

Products:

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

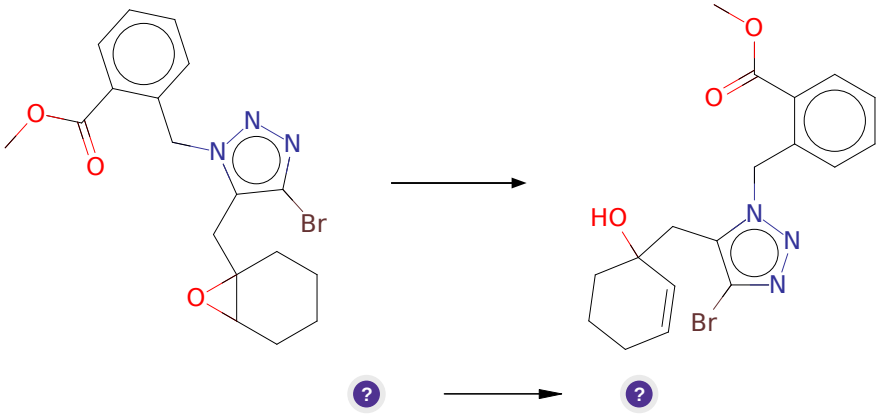
Typical conditions: Br2.Fe

Protections: none

Reference: *10.1021/acs.accounts.6b00120*

Retrosynthesis ID: 7777000

2.3.7 Synthesis of allyl alcohols from epoxides



Substrates:

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

Products:

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

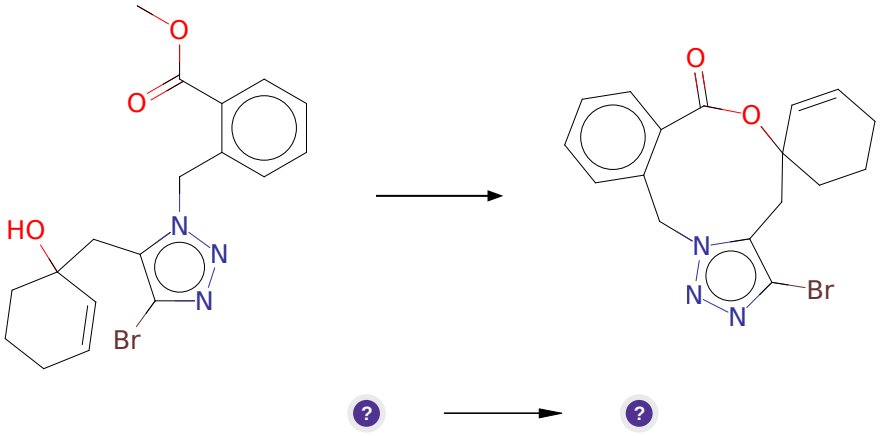
Typical conditions: PhSeNa.then H2O2

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

2.3.8 Acid catalyzed transesterification



Substrates:

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

Products:

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

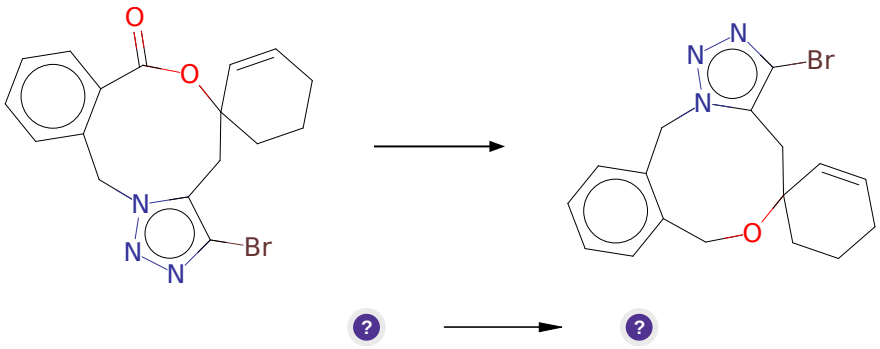
Typical conditions: H+

Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.3.9 Reduction of lactones to ethers



Substrates:

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

Products:

1. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

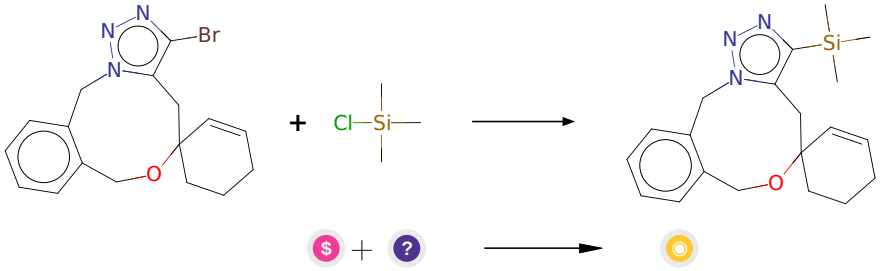
Typical conditions: LAH.THF.reflux

Protections: none

Reference: *10.1002/anie.200352705* and *10.1016/j.tet.2016.07.036* and *10.5012/bkcs.2013.34.8.2495* and *10.1080/10286020.2016.1232251*

Retrosynthesis ID: 9999753

2.3.10 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

Typical conditions: 1.nBuLi.2.ClSnR3

Protections: none

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370