Paths of analysis*

AS7

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

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

2.1 Path 1

Score: `231.16`

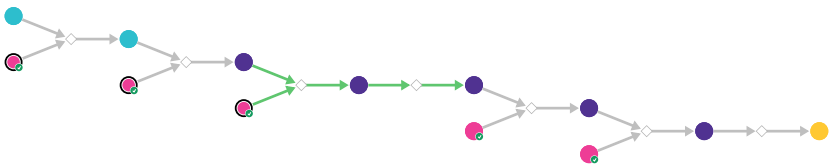
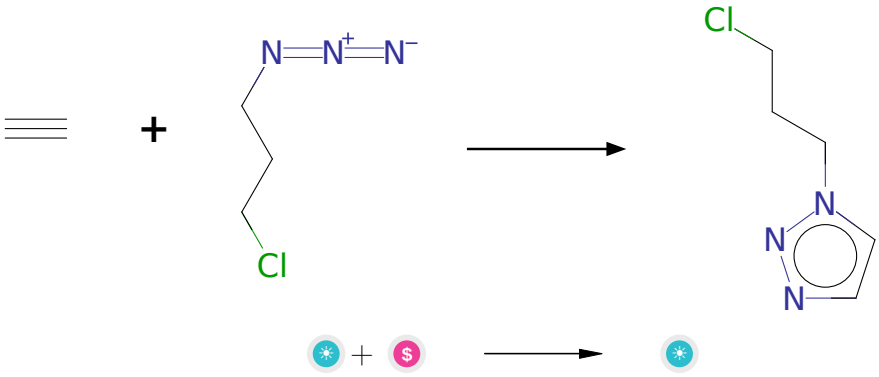


Figure 1: Outline of path 1

2.1.1 Synthesis of triazoles



Substrates:

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

Products:

1. C5H8ClN3

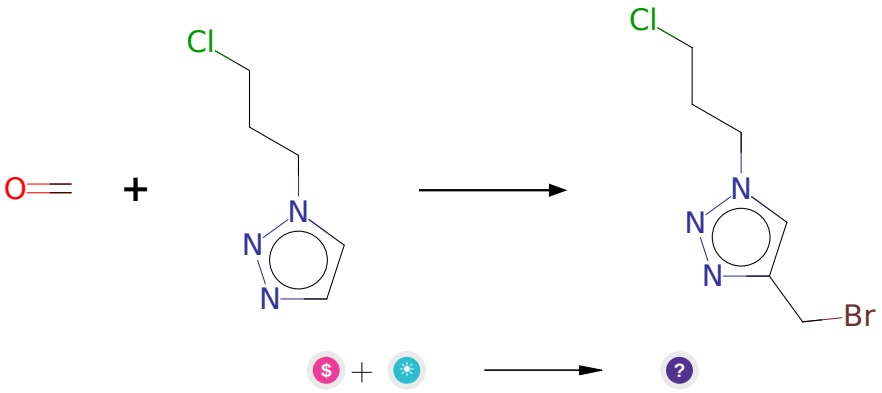
Typical conditions: rt.water.Cu-catalyst

Protections: none

Reference: *10.1039/C4OB01350F*

Retrosynthesis ID: 24030

2.1.2 Blanc bromomethylation



Substrates:

1. Formalin - *available at Sigma-Aldrich*
2. C5H8ClN3

Products:

1. ClCCCn1cc(CBr)nn1

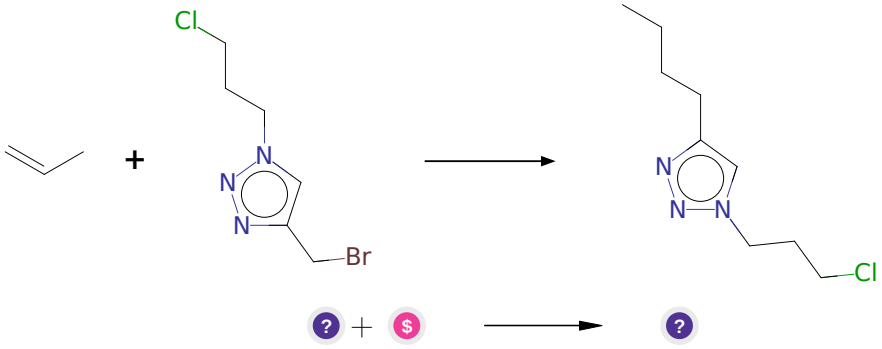
Typical conditions: HBr.heat

Protections: none

Reference: *10.1021/ja011493q* and *10.1021/ma012195g* and *10.1016/S0040-4039(02)01769-0* and *10.1021/ja002069c*

Retrosynthesis ID: 31010730

2.1.3 Suzuki alkyl-alkyl coupling



Substrates:

1. ClCCCn1cc(CBr)nn1
2. Propene - *available at Sigma-Aldrich*

Products:

1. CCCCc1cn(CCCCl)nn1

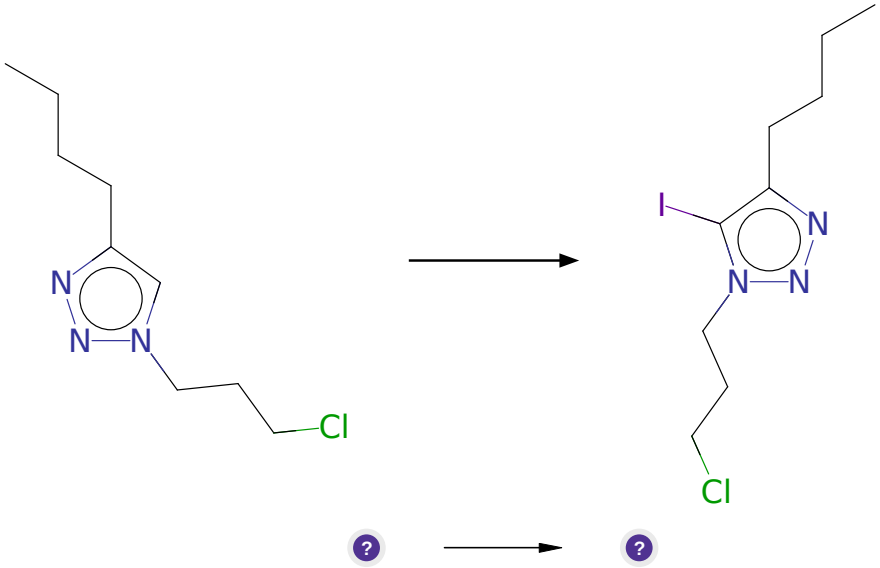
Typical conditions: 1.9BBN-H or pinB-Bpin.Cu 2.[Pd].ligand.base

Protections: none

Reference: *10.1021/ja074008l* and *10.1021/ja011306o* and *10.1002/1521-3773(20011217)40:24<4544::AID-ANIE4544>3.0.CO;2-N* and *10.1021/ol300575d*

Retrosynthesis ID: 8325

2.1.4 Iodination of aromatic compounds



Substrates:

1. CCCCc1cn(CCCCl)nn1

Products:

1. CCCCc1nnn(CCCCl)c1I

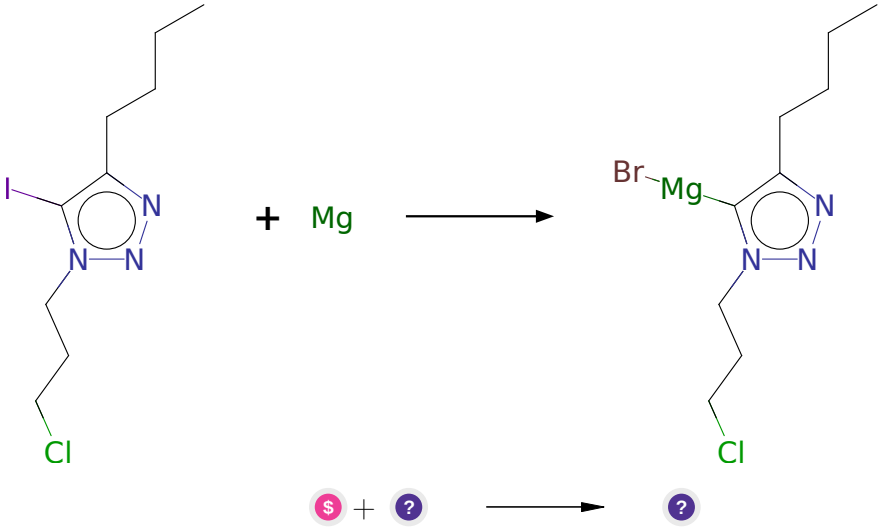
Typical conditions: I2 or other iodinating agent e.g. NIS

Protections: none

Reference: DOI: *10.1039/C5SC00964B* and *10.1016/j.tetlet.2005.05.117* and *10.1007/s11178-005-0256-1*

Retrosynthesis ID: 10697

2.1.5 Synthesis of aryl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. CCCCc1nnn(CCCCl)c1I

Products:

1. CCCCc1nnn(CCCCl)c1[Mg]Br

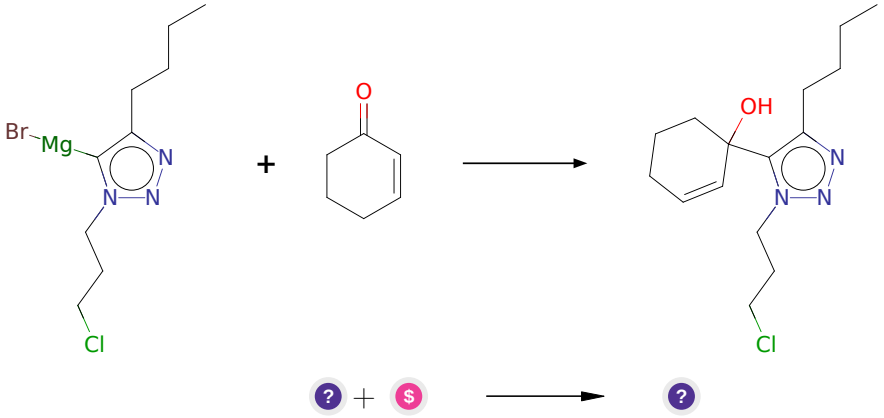
Typical conditions: iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and WO2014123793 p.137 and *10.1021/jm400491x* and *10.3762/bjoc.12.36*

Retrosynthesis ID: 10011460

2.1.6 Grignard-Type Reaction



Substrates:

1. CCCCc1nnn(CCCCl)c1[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. CCCCc1nnn(CCCCl)c1C1(O)C=CCCC1

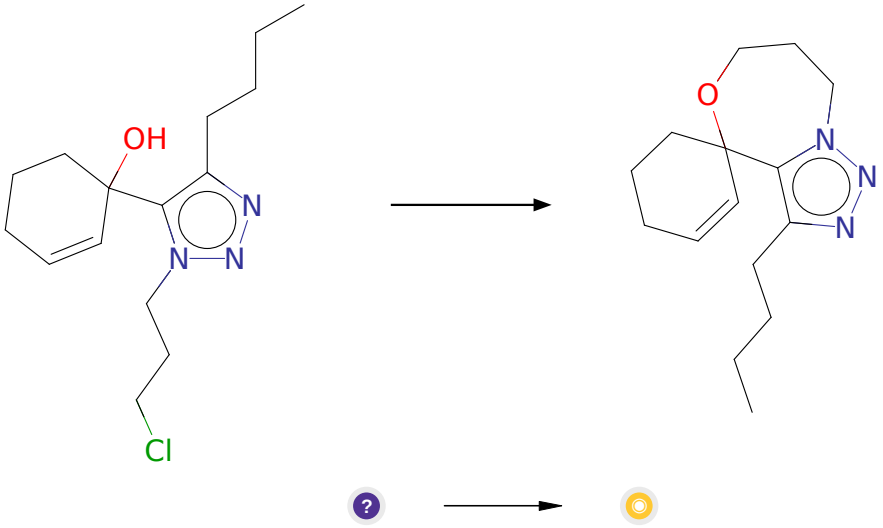
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.1.7 Alkylation of tertiary alcohols



Substrates:

1. CCCCc1nnn(CCCCl)c1C1(O)C=CCCC1

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCCC2

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: 252.64

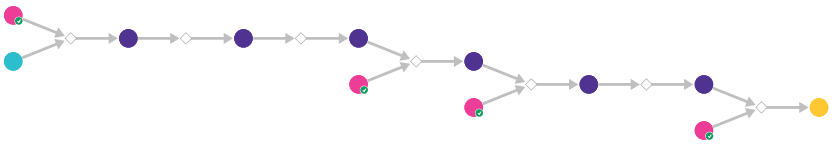
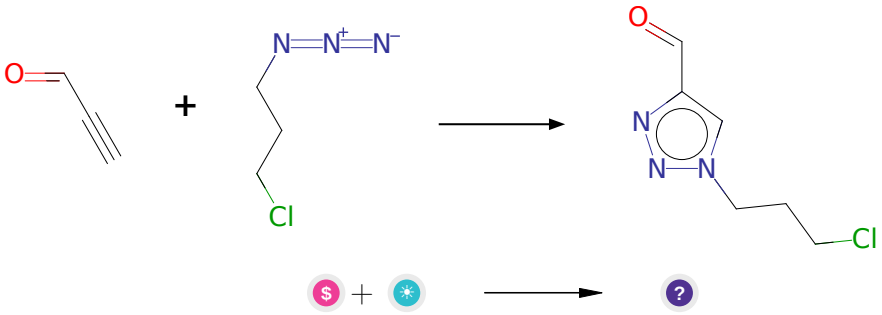


Figure 2: Outline of path 2

2.2.1 Synthesis of triazoles from azides



Substrates:

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

Products:

1. O=Cc1cn(CCCCl)nn1

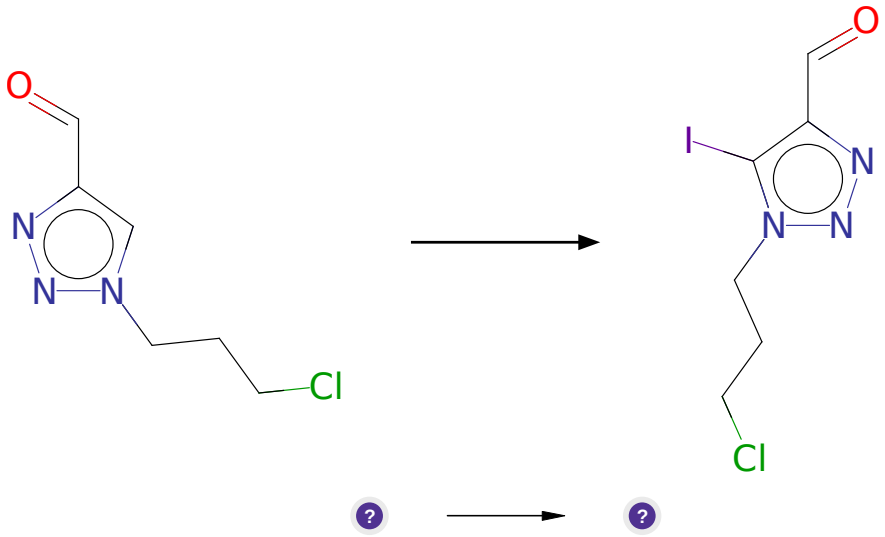
Typical conditions: Cu(I).Et3N.DMF

Protections: none

Reference: DOI:*10.1080/00397911.2013.786090*

Retrosynthesis ID: 295099

2.2.2 Iodination of aromatic compounds



Substrates:

1. O=Cc1cn(CCCCl)nn1

Products:

1. O=Cc1nnn(CCCCl)c1I

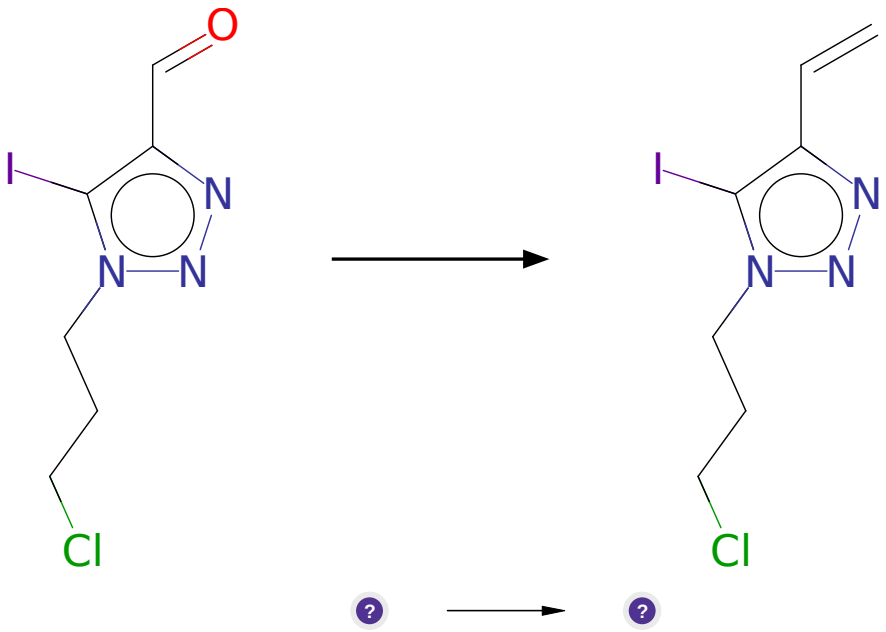
Typical conditions: I2 or other iodinating agent e.g. NIS

Protections: none

Reference: DOI: *10.1039/C5SC00964B* and *10.1016/j.tetlet.2005.05.117* and *10.1007/s11178-005-0256-1*

Retrosynthesis ID: 10697

2.2.3 Tebbe Olefination



Substrates:

1. O=Cc1nnn(CCCCl)c1I

Products:

1. C=Cc1nnn(CCCCl)c1I

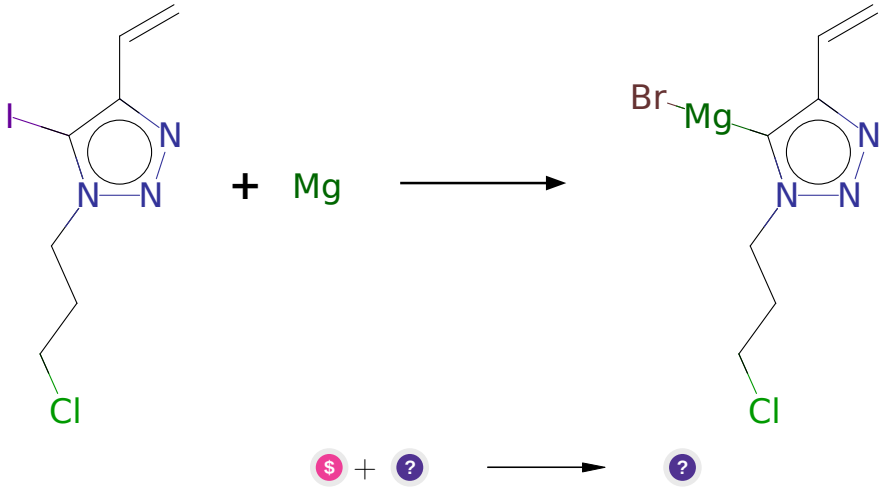
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Reference: *10.1016/j.tet.2007.03.015* and *10.1002/9780470638859.conrr617*

Retrosynthesis ID: 11714

2.2.4 Synthesis of aryl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. C=Cc1nnn(CCCCl)c1I

Products:

1. C=Cc1nnn(CCCCl)c1[Mg]Br

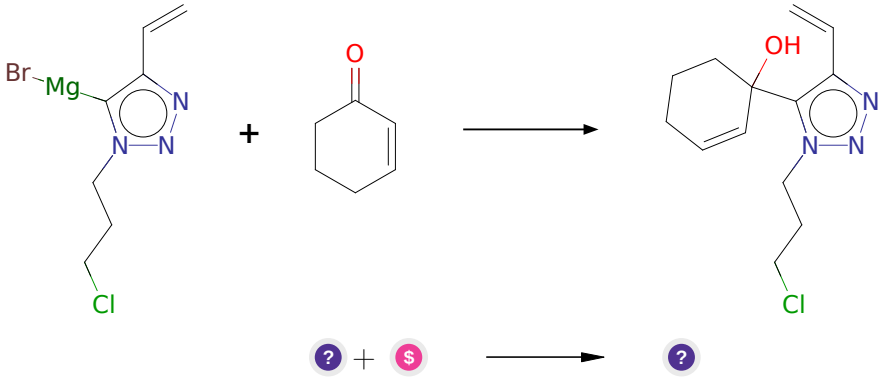
Typical conditions: iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and WO2014123793 p.137 and *10.1021/jm400491x* and *10.3762/bjoc.12.36*

Retrosynthesis ID: 10011460

2.2.5 Grignard-Type Reaction



Substrates:

1. C=Cc1nnn(CCCCl)c1[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. C=Cc1nnn(CCCCl)c1C1(O)C=CCCC1

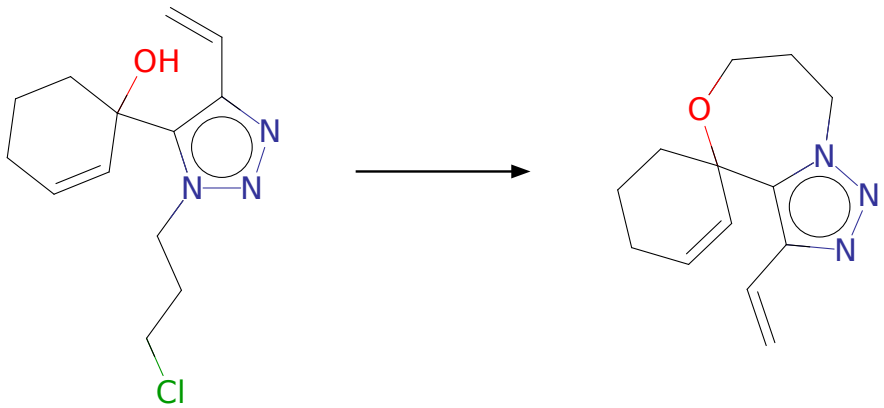
Typical conditions: Mg or Li.ether

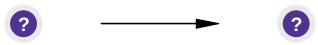
Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.2.6 Alkylation of tertiary alcohols





Substrates:

1. C=Cc1nnn(CCCCl)c1C1(O)C=CCCC1

Products:

1. C=Cc1nnn2c1C1(C=CCCC1)OCCC2

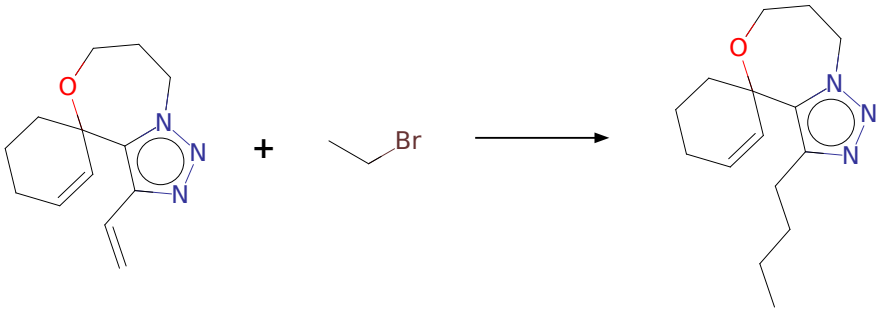
Typical conditions: K2CO3.acetone.heat

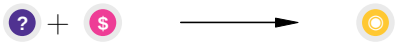
Protections: none

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

Retrosynthesis ID: 31010930

2.2.7 Suzuki alkyl-alkyl coupling





Substrates:

1. C=Cc1nnn2c1C1(C=CCCC1)OCCC2
2. Bromoethane - *available at Sigma-Aldrich*

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCCC2

Typical conditions: 1.9BBN-H or pinB-Bpin.Cu 2.[Pd].ligand.base

Protections: none

Reference: *10.1021/ja074008l* and *10.1021/ja011306o* and *10.1002/1521-3773(20011217)40:24<4544::AID-ANIE4544>3.0.CO;2-N* and *10.1021/ol300575d*

Retrosynthesis ID: 8325

2.3 Path 3

Score: 252.64

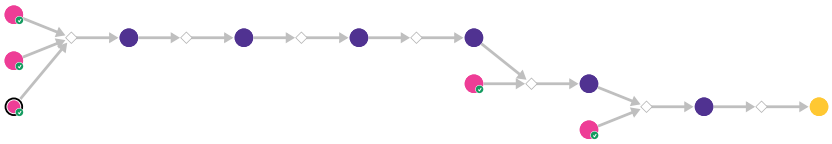
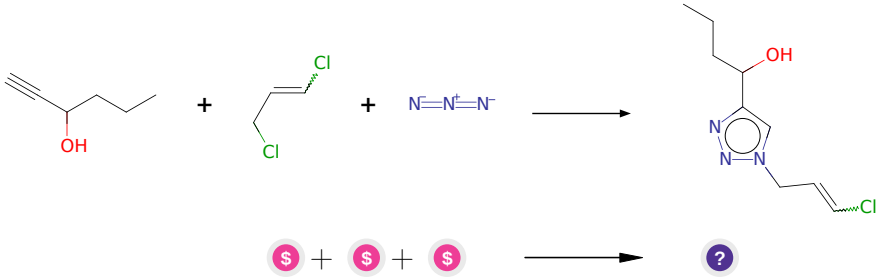


Figure 3: Outline of path 3

2.3.1 One-pot synthesis of triazoles from alkyl halides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. 1-Hexyn-3-ol - *available at Sigma-Aldrich*
3. 1,3-Dichloropropene - *available at Sigma-Aldrich*

Products:

1. CCCC(O)c1cn(CC=CCl)nn1

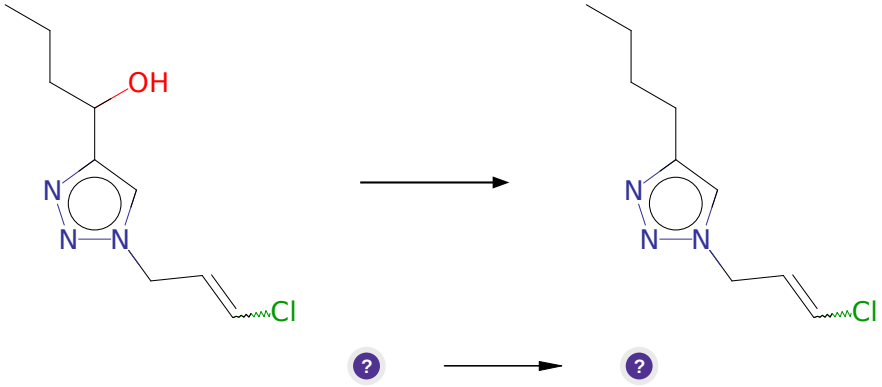
Typical conditions: Cu(II).sodium ascorbate.DMF/H2O

Protections: none

Reference: DOI: *10.1021/ol048859z*

Retrosynthesis ID: 245699

2.3.2 Deoxygenation of alcohols with silanes



Substrates:

1. CCCC(O)c1cn(CC=CCl)nn1

Products:

1. CCCCc1cn(CC=CCl)nn1

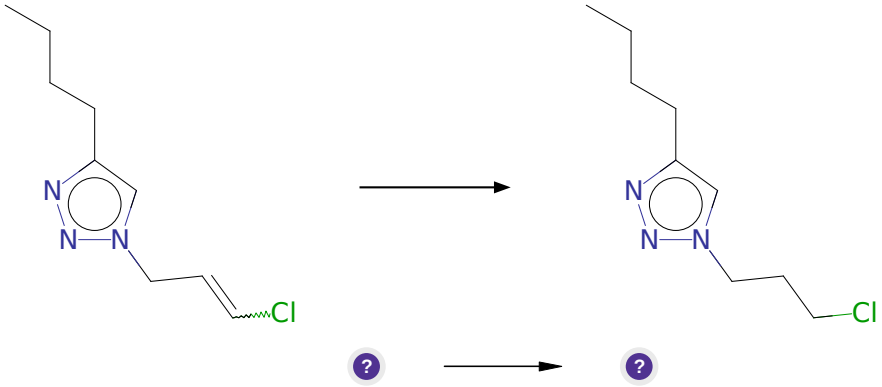
Typical conditions: Et3SiH.Lewis.or.Bronsted.Acid

Protections: none

Reference: *10.1021/jo0158534* AND *10.1021/ol3020144*

Retrosynthesis ID: 8162

2.3.3 Homogenous Reduction of C=C Double Bond



Substrates:

1. CCCCc1cn(CC=CCl)nn1

Products:

1. CCCCc1cn(CCCCl)nn1

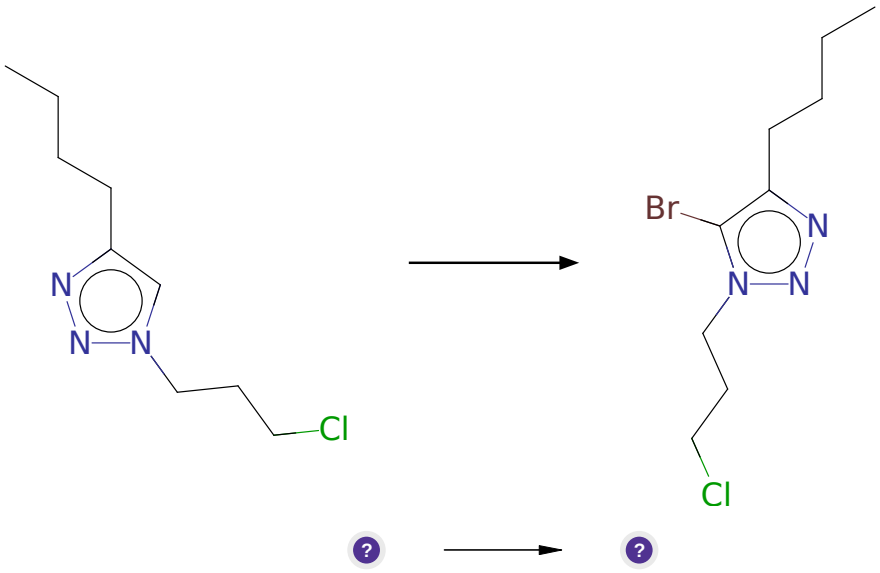
Typical conditions: H2.Pd/C or Pd(OH)2/C

Protections: none

Reference: DOI: *10.1021/ja0629110* and *10.1021/jo0602367* and *10.1021/jo980467g* and *10.1021/ol702231j* (SI, page SI 22) and *10.1002/anie.200503303* and *10.1021/ja011338b* (Pt/C tez)

Retrosynthesis ID: 9995778

2.3.4 Bromination of aromatic compounds



Substrates:

1. CCCCc1cn(CCCCl)nn1

Products:

1. CCCCc1nnn(CCCCl)c1Br

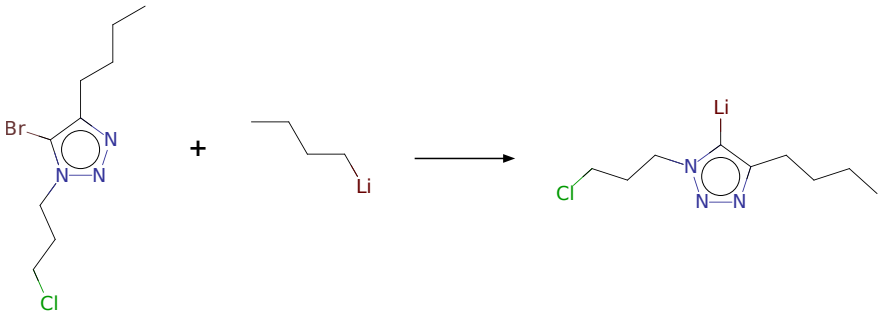
Typical conditions: Br2.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.3.5 Br/Li exchange



Substrates:

1. CCCCc1nnn(CCCCl)c1Br
2. n-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1c(CCCC)nnn1CCCCl

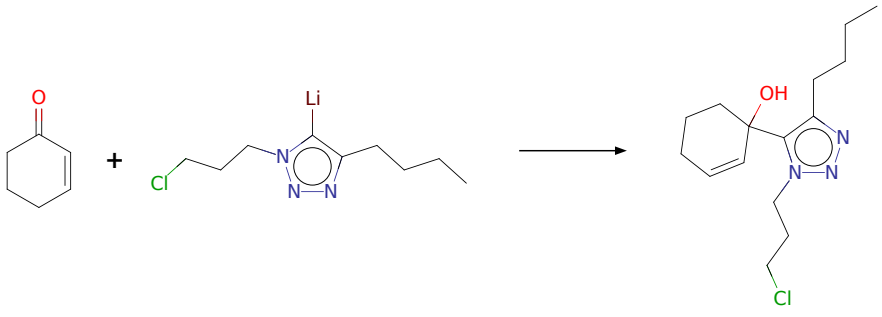
Typical conditions: nBuLi.or.tBuLi.THF.-78C

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

2.3.6 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

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

Products:

1. CCCCc1nnn(CCCCl)c1C1(O)C=CCCC1

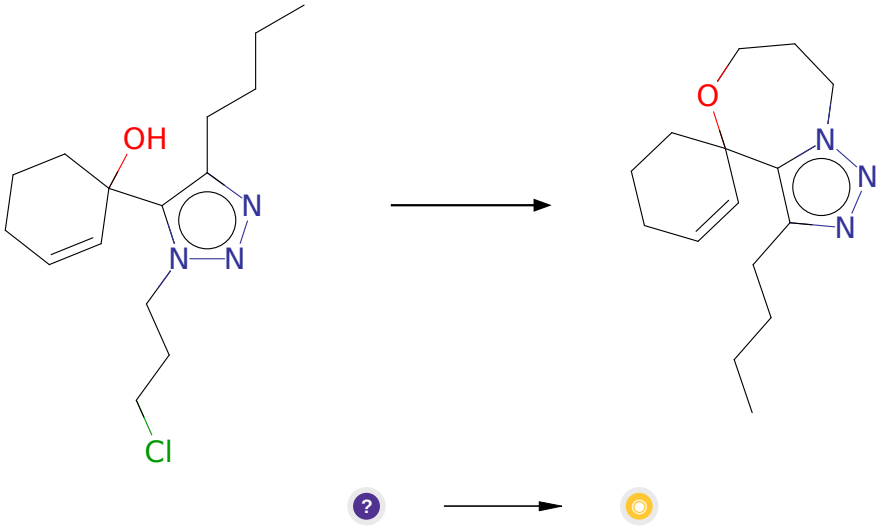
Typical conditions: THF.-78 deg C

Protections: none

Reference: *10.1021/ml300335r* and *10.1021/acs.jmedchem.6b00866*

Retrosynthesis ID: 31008139

2.3.7 Alkylation of tertiary alcohols



Substrates:

1. CCCCc1nnn(CCCCl)c1C1(O)C=CCCC1

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCCC2

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

2.4 Path 4

Score: 252.64

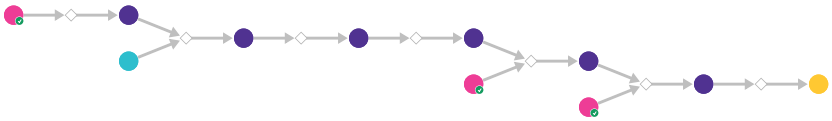
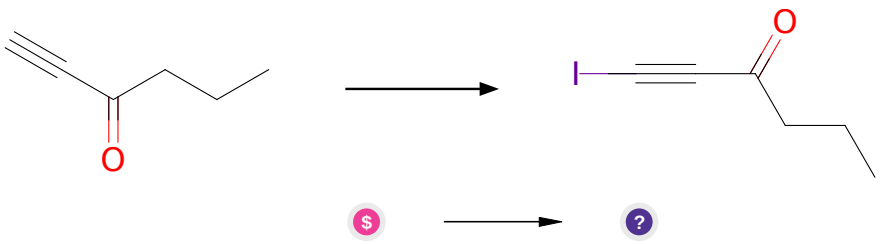


Figure 4: Outline of path 4

2.4.1 Iodination of acetylene



Substrates:

1. hex-1-yn-3-one - *available at Sigma-Aldrich*

Products:

1. CCCC(=O)C#CI

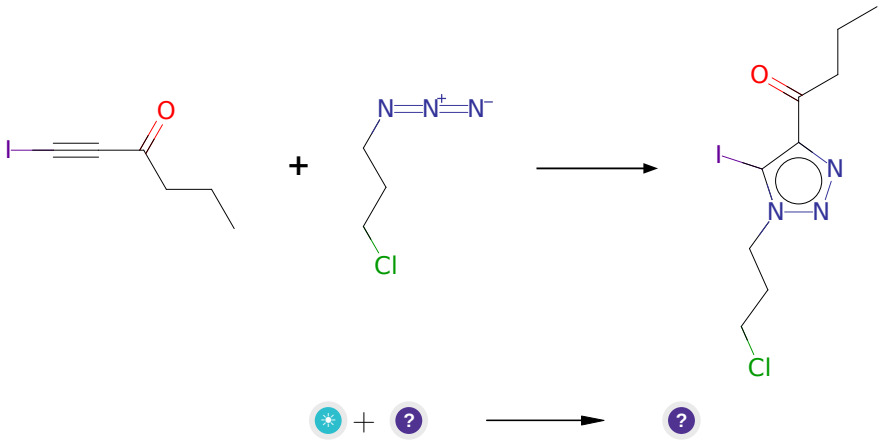
Typical conditions: AgNO3.NIS.THF.rt

Protections: none

Reference: *10.1021/ja960040w*

Retrosynthesis ID: 9900044

2.4.2 Synthesis of triazoles from azides and haloalkynes



Substrates:

1. 1-azido-3-chlor-propan
2. CCCC(=O)C#CI

Products:

1. CCCC(=O)c1nnn(CCCCl)c1I

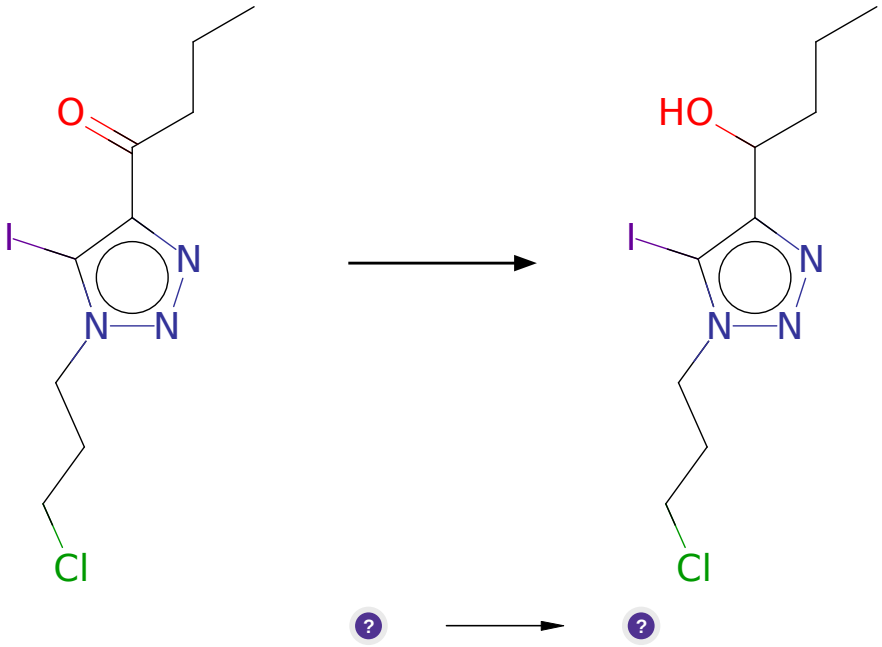
Typical conditions: CpRuCl(cod).ACN

Protections: none

Reference: *10.1002/chem.201402559*

Retrosynthesis ID: 31456

2.4.3 Reduction of ketones with NaBH4



Substrates:

1. CCCC(=O)c1nnn(CCCCl)c1I

Products:

1. CCCC(O)c1nnn(CCCCl)c1I

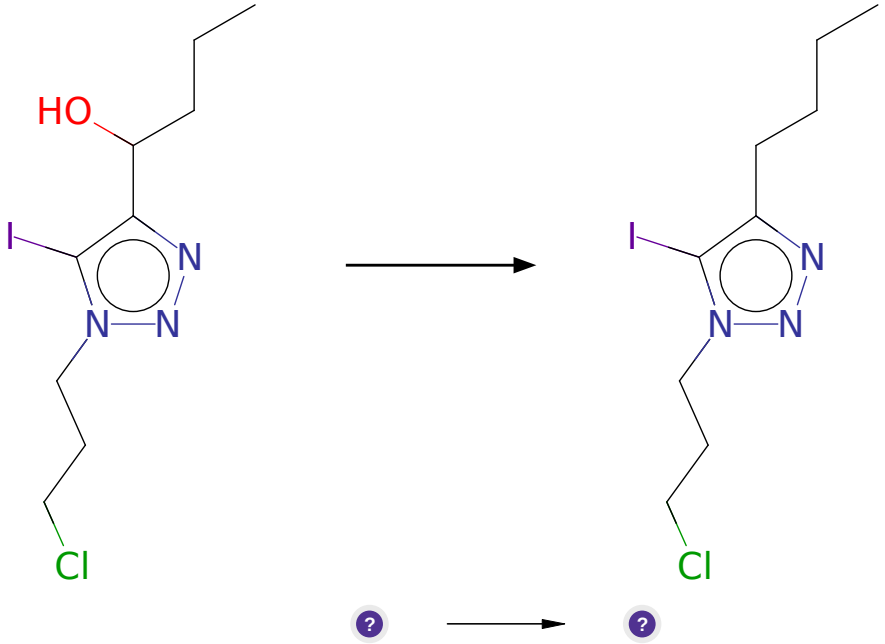
Typical conditions: NaBH4.EtOH.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112360* p. 3, 8 and *10.1016/j.ejmech.2010.10.012* p. 434, 436

Retrosynthesis ID: 50432

2.4.4 Deoxygenation of alcohols with silanes



Substrates:

1. CCCC(O)c1nnn(CCCCl)c1I

Products:

1. CCCCc1nnn(CCCCl)c1I

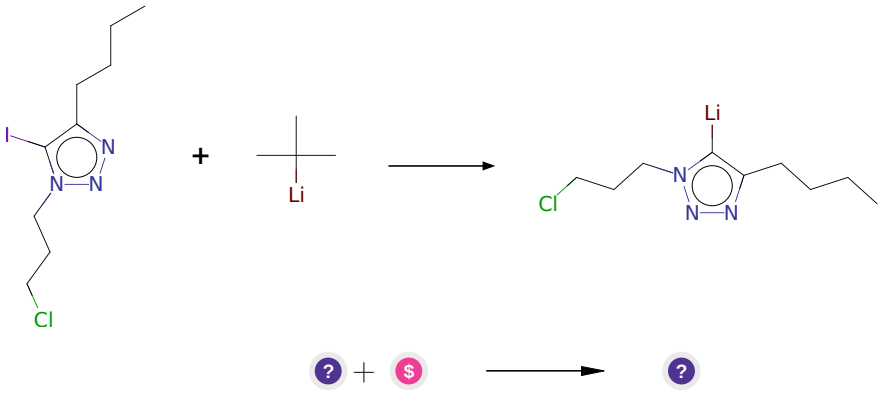
Typical conditions: Et3SiH.Lewis.or.Bronsted.Acid

Protections: none

Reference: *10.1021/jo0158534* AND *10.1021/ol3020144*

Retrosynthesis ID: 8162

2.4.5 I/Li exchange



Substrates:

1. CCCCc1nnn(CCCCl)c1I
2. t-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1c(CCCC)nnn1CCCCl

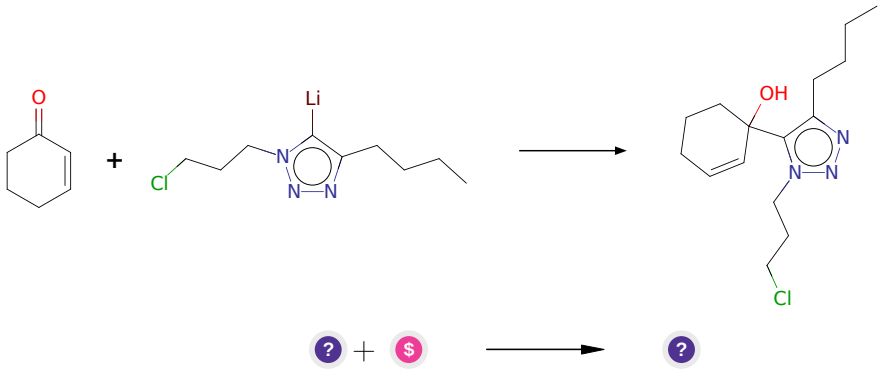
Typical conditions: nBuLi.or.tBuLi.THF.-78C

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

2.4.6 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

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

Products:

1. CCCCc1nnn(CCCCl)c1C1(O)C=CCCC1

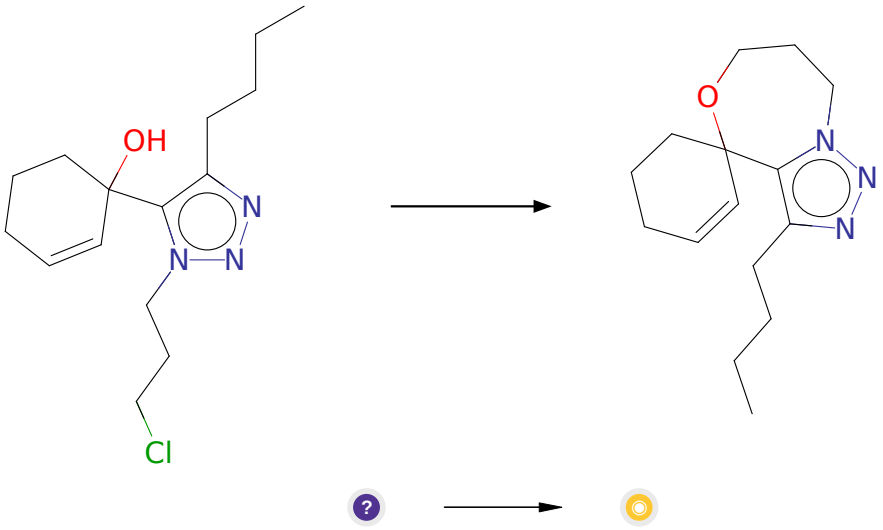
Typical conditions: THF.-78 deg C

Protections: none

Reference: *10.1021/ml300335r* and *10.1021/acs.jmedchem.6b00866*

Retrosynthesis ID: 31008139

2.4.7 Alkylation of tertiary alcohols



Substrates:

1. CCCCc1nnn(CCCCl)c1C1(O)C=CCCC1

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCCC2

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