

# Paths of analysis\*

AS6

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

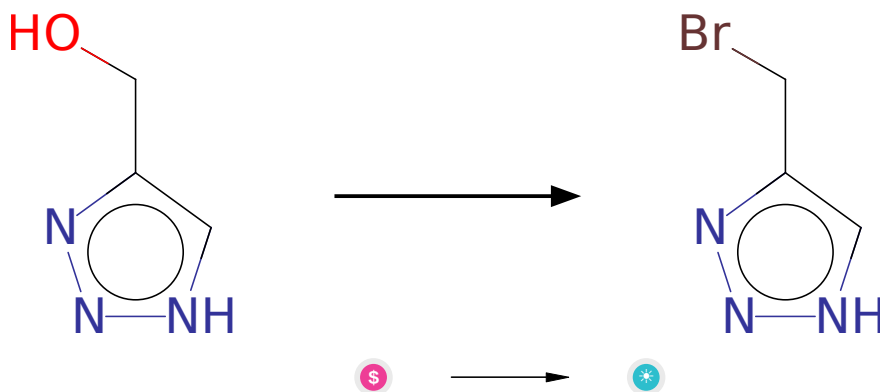
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\*The results stated herein were generated using the proprietary platform owned and maintained by Grzybowski Scientific Inventions, Inc., a subsidiary of Merck KGaA, Darmstadt Germany. The results are provided on an as is basis, and shall be used solely in connection with the rights afforded in the license agreement and for no other purpose.

**JSON Parameters:**  $\{\}$

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

### 2.1.1 Appel Reaction



1. 4-bromomethyl-1h-[1,2,3]triazole

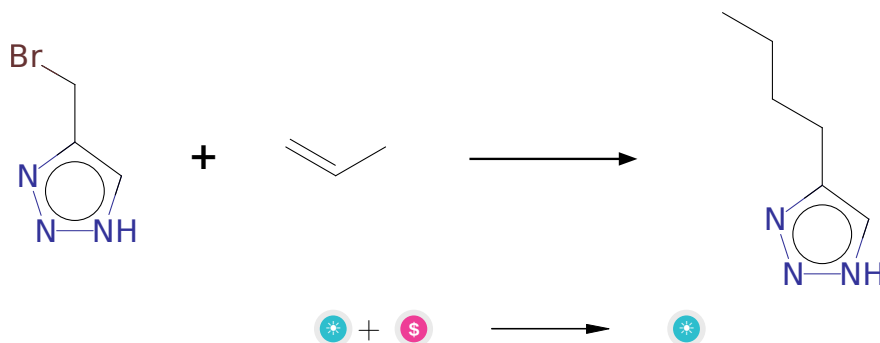
**Typical conditions:** PPh<sub>3</sub>.CBr<sub>4</sub>

**Protections:** none

**Reference:** [10.1021/ja800574m](#) and [10.1016/j.tet.2012.05.010](#) and [10.1016/j.tet.2004.09.021](#) (experimental)

**Retrosynthesis ID:** 9990037

### 2.1.2 Suzuki alkyl-alkyl coupling



#### Substrates:

1. 4-bromomethyl-1h-[1,2,3]triazole
2. Propene - *available at Sigma-Aldrich*

#### Products:

1. 4-butyl-1h-[1,2,3]triazole

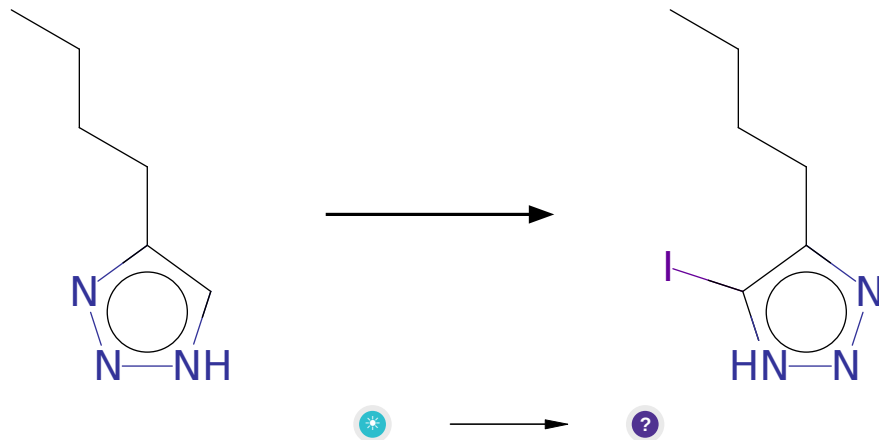
**Typical conditions:** 1.9BBN-H or pinB-Bpin.Cu 2.[Pd].ligand.base

**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

### 2.1.3 Iodination of aromatic compounds



**Substrates:**

1. 4-butyl-1h-[1,2,3]triazole

**Products:**

1. CCCCc1nn[nH]c1I

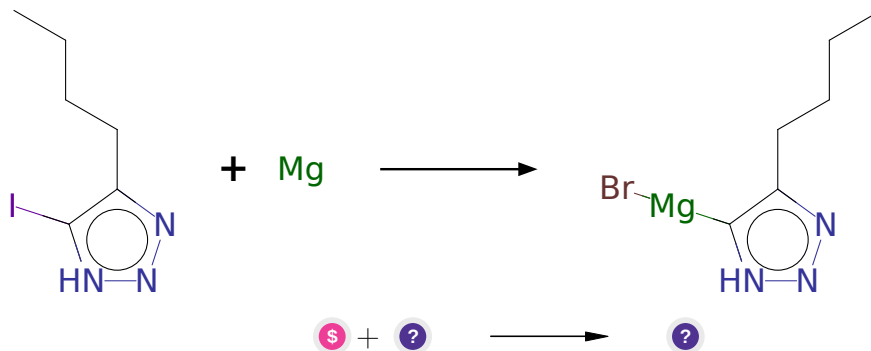
**Typical conditions:** I<sub>2</sub> or other iodinating agent e.g. NIS

**Protections:** none

**Reference:** DOI: [10.1039/C5SC00964B](https://doi.org/10.1039/C5SC00964B) and [10.1016/j.tetlet.2005.05.117](https://doi.org/10.1016/j.tetlet.2005.05.117) and [10.1007/s11178-005-0256-1](https://doi.org/10.1007/s11178-005-0256-1)

**Retrosynthesis ID:** 10697

### 2.1.4 Synthesis of aryl Grignard reagents



**Substrates:**

1. Magnesium - *available at Sigma-Aldrich*

2. CCCCc1nn[nH]c1I

**Products:**

1. CCCCc1nn[nH]c1[Mg]Br

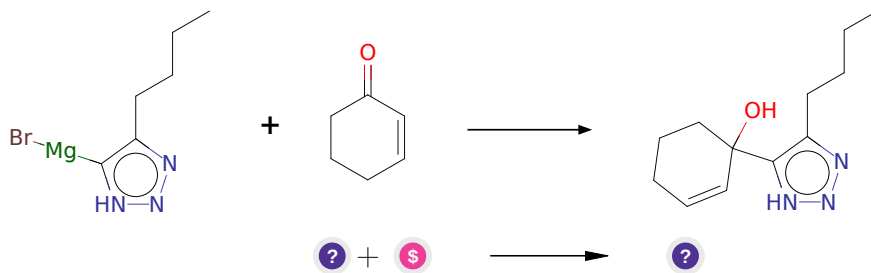
**Typical conditions:** iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

**Protections:** none

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

**Retrosynthesis ID:** 10011460

**2.1.5 Grignard-Type Reaction**



**Substrates:**

1. CCCCc1nn[nH]c1[Mg]Br

2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

**Products:**

1. CCCCc1nn[nH]c1C1(O)C=CCCC1

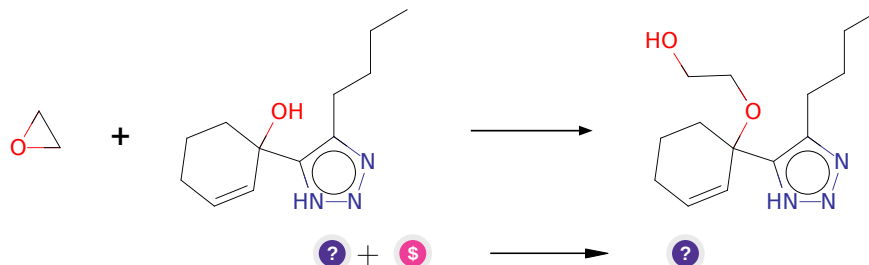
**Typical conditions:** Mg or Li.ether

**Protections:** none

**Reference:** [10.1021/jm061429p](https://doi.org/10.1021/jm061429p) or [10.1016/j.bmc.2012.11.015](https://doi.org/10.1016/j.bmc.2012.11.015) or [10.1016/j.tetasy.2012.05.024](https://doi.org/10.1016/j.tetasy.2012.05.024)

**Retrosynthesis ID:** 25133

### 2.1.6 Ring-opening of epoxides or thiiranes with alkoxides



**Substrates:**

1. CCCCc1nn[nH]c1C1(O)C=CCCC1
2. Oxirane - *available at Sigma-Aldrich*

**Products:**

1. CCCCc1nn[nH]c1C1(OCCO)C=CCCC1

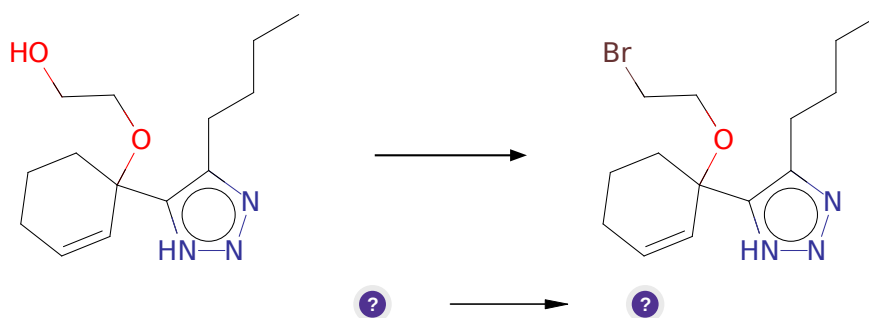
**Typical conditions:** NaH.THF or K<sub>2</sub>CO<sub>3</sub>.DMF.110 C

**Protections:** none

**Reference:** [10.1021/acs.orglett.7b00756](https://doi.org/10.1021/acs.orglett.7b00756) SI p. S4, S5 and [10.1021/jm401625b](https://doi.org/10.1021/jm401625b) p. 873, 878

**Retrosynthesis ID:** 833

### 2.1.7 Appel Reaction



**Substrates:**

1. CCCCc1nn[nH]c1C1(OCCO)C=CCCC1

**Products:**

1. CCCCc1nn[nH]c1C1(OCCBr)C=CCCC1

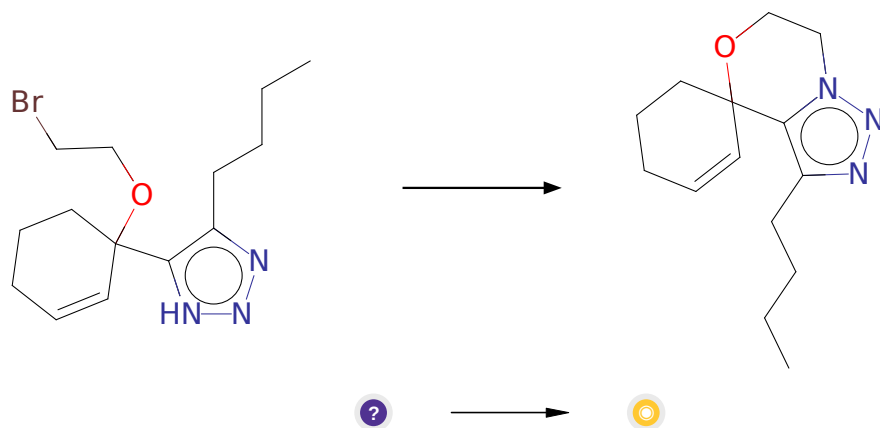
**Typical conditions:** PPh<sub>3</sub>.CBr<sub>4</sub>

**Protections:** none

**Reference:** [10.1021/ja800574m](#) and [10.1016/j.tet.2012.05.010](#) and [10.1016/j.tet.2004.09.021](#) (experimental)

**Retrosynthesis ID:** 9990037

### 2.1.8 N-alkylation of heterocycles



**Substrates:**

1. CCCCc1nn[nH]c1C1(OCCBr)C=CCCC1

**Products:**

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

**Typical conditions:** NaH. DMF

**Protections:** none

**Reference:** [10.1016/j.ejmech.2010.11.014](#) or [10.1039/C6OB01149G](#) (SI) or [10.1246/cl.2005.442](#) or [10.1021/ol403570z](#) (SI) or [10.1016/S0040-4020\(01\)00360-X](#)

**Retrosynthesis ID:** 10000414

## 2.2 Path 2

**Score:** 225.18

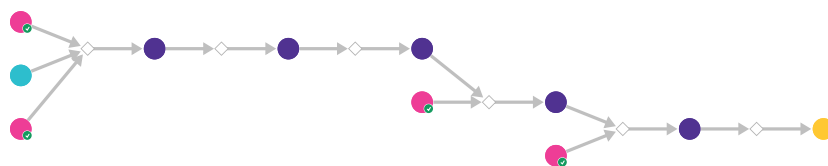
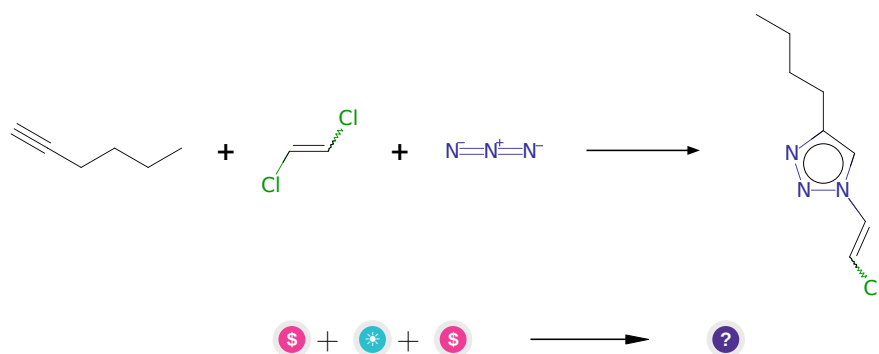


Figure 2: Outline of path 2

### 2.2.1 One-pot synthesis of triazoles from alkyl halides



#### Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. vinylene chloride
3. 1-Hexyne - *available at Sigma-Aldrich*

#### Products:

1. CCCCc1cn(C=CCl)nn1

**Typical conditions:** Cu(II).sodium ascorbate.DMF/H<sub>2</sub>O

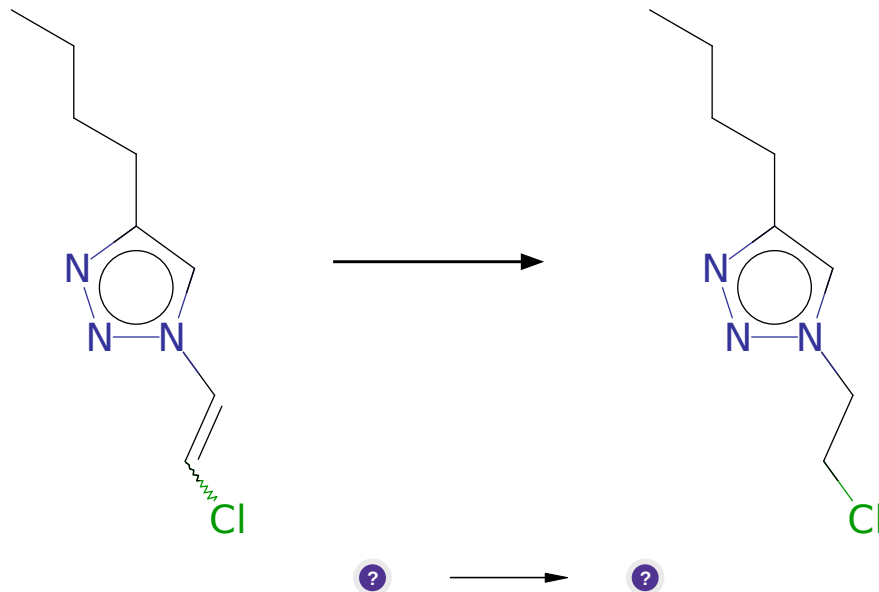
**Protections:** none

**Reference:** DOI: [10.1021/ol048859z](https://doi.org/10.1021/ol048859z)

**Retrosynthesis ID:** 245700



### 2.2.2 Homogenous Reduction of C=C Double Bond



**Substrates:**

1. CCCCc1cn(C=CCl)nn1

**Products:**

1. CCCCc1cn(CCCl)nn1

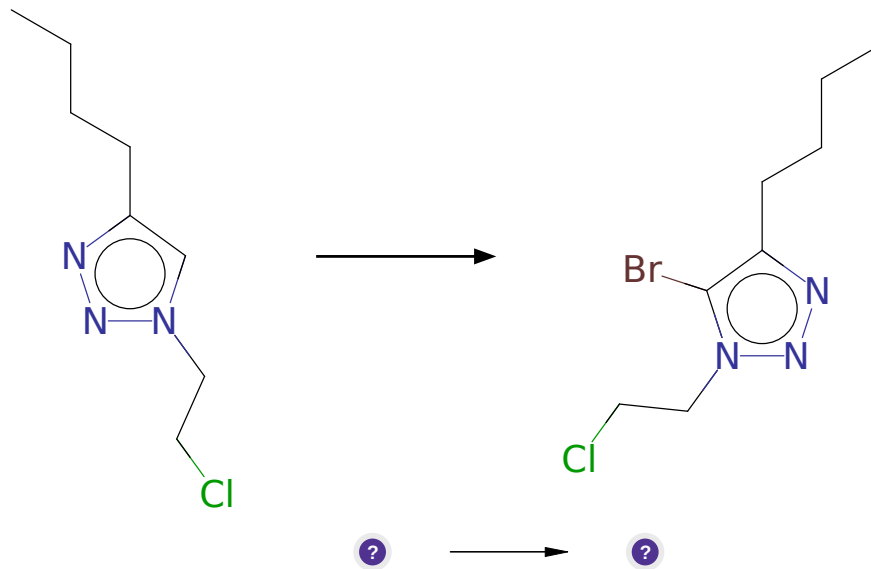
**Typical conditions:** H<sub>2</sub>.Pd/C or Pd(OH)<sub>2</sub>/C

**Protections:** none

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

**Retrosynthesis ID:** 9995778

### 2.2.3 Bromination of aromatic compounds



**Substrates:**

1. CCCCc1cn(CCCl)nn1

**Products:**

1. CCCCc1nnn(CCCl)c1Br

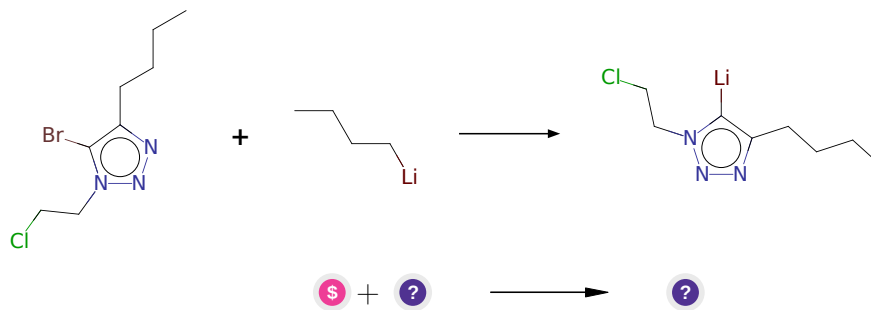
**Typical conditions:** Br<sub>2</sub>.Fe

**Protections:** none

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

**Retrosynthesis ID:** 7777000

### 2.2.4 Br/Li exchange



**Substrates:**

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

**Products:**

1. [Li]c1c(CCCC)nnn1CCCl

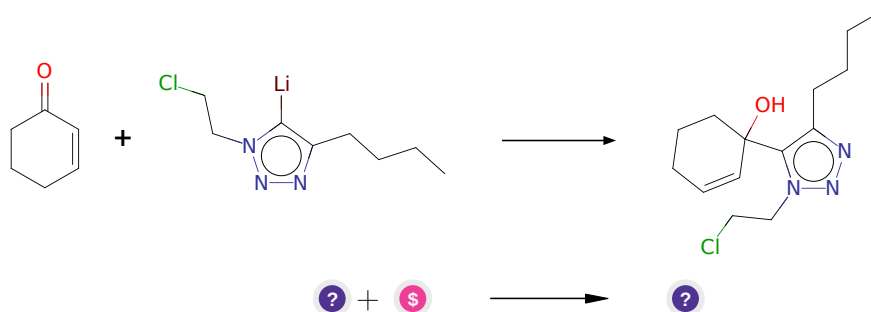
**Typical conditions:** nBuLi.or.tBuLi.THF.-78C

**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

**2.2.5 Addition of electrophiles to lithiated arenes/heteroarenes**



**Substrates:**

1. [Li]c1c(CCCC)nnn1CCCl
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

**Products:**

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

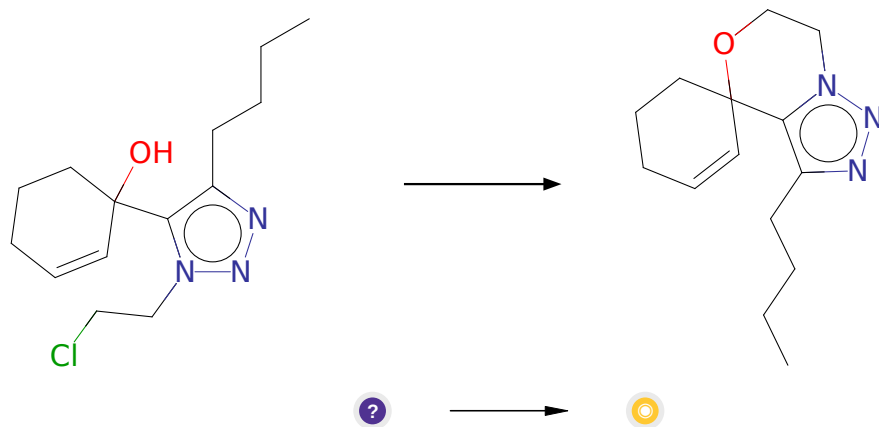
**Typical conditions:** THF.-78 deg C

**Protections:** none

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

**Retrosynthesis ID:** 31008139

### 2.2.6 Alkylation of tertiary alcohols



**Substrates:**

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

**Products:**

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

**Typical conditions:** K<sub>2</sub>CO<sub>3</sub>.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:** 225.18

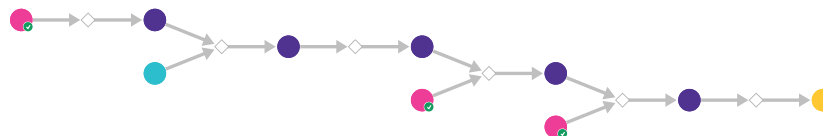
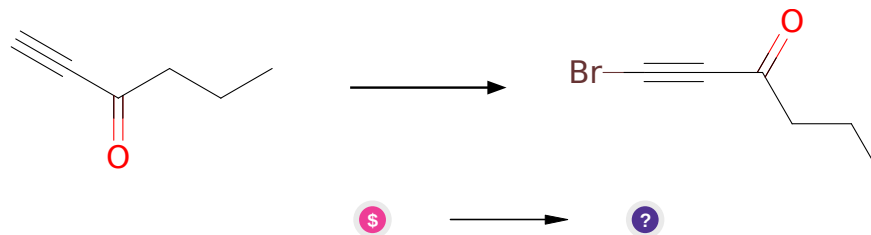


Figure 3: Outline of path 3

### 2.3.1 Synthesis of bromoacetylenes



#### Substrates:

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

#### Products:

1. CCCC(=O)C#CBr

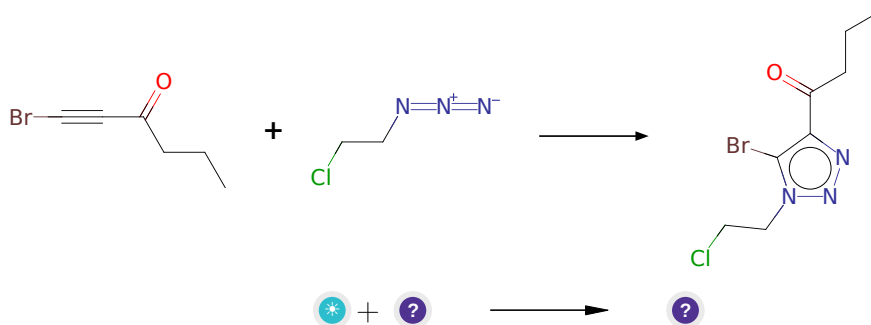
**Typical conditions:** NBS.acetone

**Protections:** none

**Reference:** [10.1021/ja5004747](#)

**Retrosynthesis ID:** 5325

### 2.3.2 Synthesis of triazoles from azides and haloalkynes



#### Substrates:

1. 1-azido-2-chloroethane
2. CCCC(=O)C#CBr

#### Products:

1. CCCC(=O)c1nnn(CCCl)c1Br

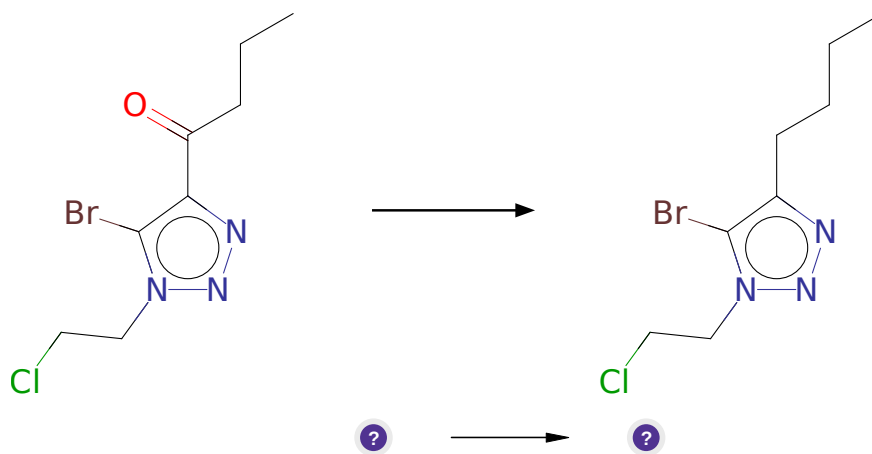
**Typical conditions:** CpRuCl(cod).ACN

**Protections:** none

**Reference:** [10.1002/chem.201402559](#)

**Retrosynthesis ID:** 31456

### 2.3.3 Clemmensen Reduction



**Substrates:**

1. CCCC(=O)c1nnn(CCCl)c1Br

**Products:**

1. CCCCc1nnn(CCCl)c1Br

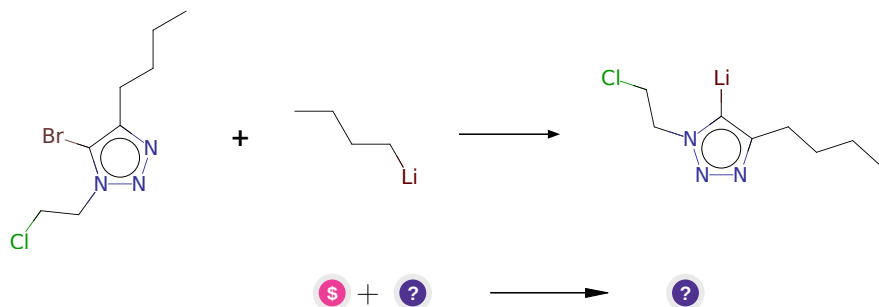
**Typical conditions:** Zn(Hg).HCl.H2O.EtOH.65 C

**Protections:** none

**Reference:** [10.1016/j.bmc.2014.09.022](#) p. 5873, 5879 and [10.1007/s00044-017-2105-5](#) p. 828, 819

**Retrosynthesis ID:** 245

### 2.3.4 Br/Li exchange



#### Substrates:

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

#### Products:

1. [Li]c1c(CCCC)nnn1CCCl

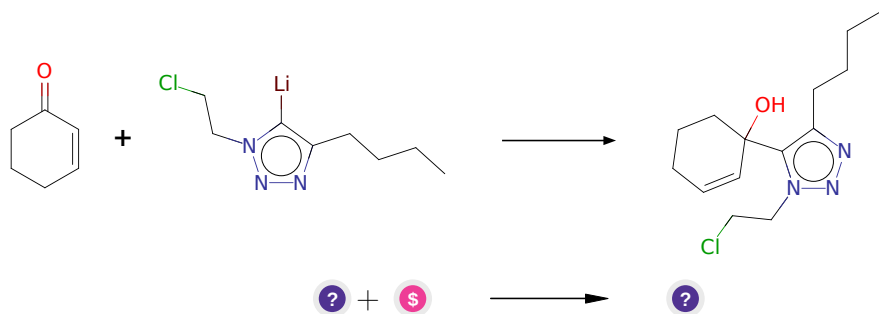
**Typical conditions:** nBuLi.or.tBuLi.THF.-78C

**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

### 2.3.5 Addition of electrophiles to lithiated arenes/heteroarenes



#### Substrates:

1. [Li]c1c(CCCC)nnn1CCCl
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

**Products:**

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

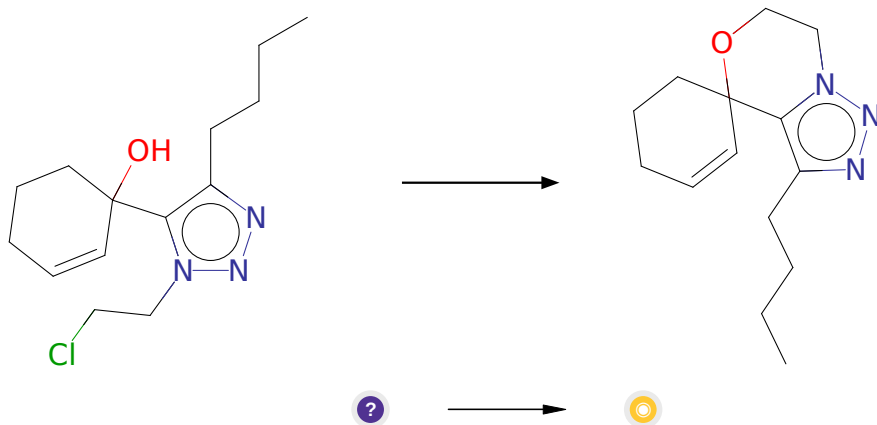
**Typical conditions:** THF.-78 deg C

**Protections:** none

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

**Retrosynthesis ID:** 31008139

**2.3.6 Alkylation of tertiary alcohols**



**Substrates:**

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

**Products:**

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

**Typical conditions:** K<sub>2</sub>CO<sub>3</sub>.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:** 225.18



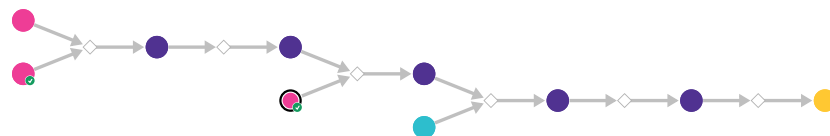
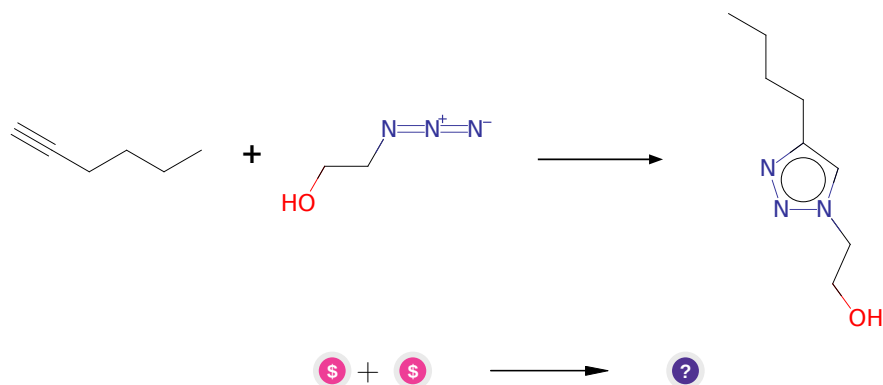


Figure 4: Outline of path 4

### 2.4.1 Huisgen Cycloaddition



#### Substrates:

1. 2-azidoethanol - *Enamine*
2. 1-Hexyne - *available at Sigma-Aldrich*

#### Products:

1. CCCCc1cn(CCO)nn1

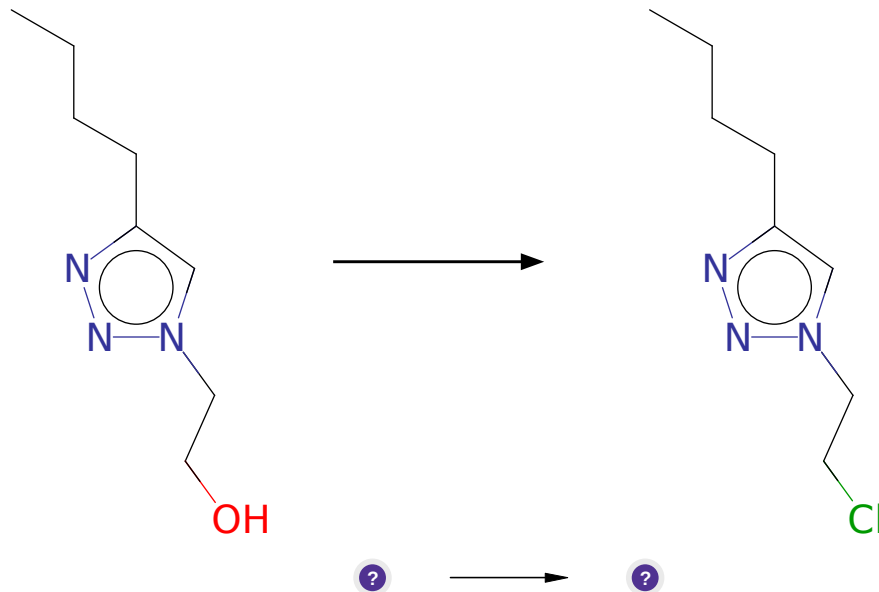
**Typical conditions:** Cu(I).H<sub>2</sub>O

**Protections:** none

**Reference:** [10.1039/PS9610000357](#) and [10.1016/S1359-6446\(03\)02933-7](#) and [10.1002/1521-3773\(20010601\)40:11<2004::AID-ANIE2004>3.0.CO;2-5](#)

**Retrosynthesis ID:** 10268

#### 2.4.2 Synthesis of alkyl chlorides from alcohols



**Substrates:**

1. CCCCc1cn(CCO)nn1

**Products:**

1. CCCCc1cn(CCCl)nn1

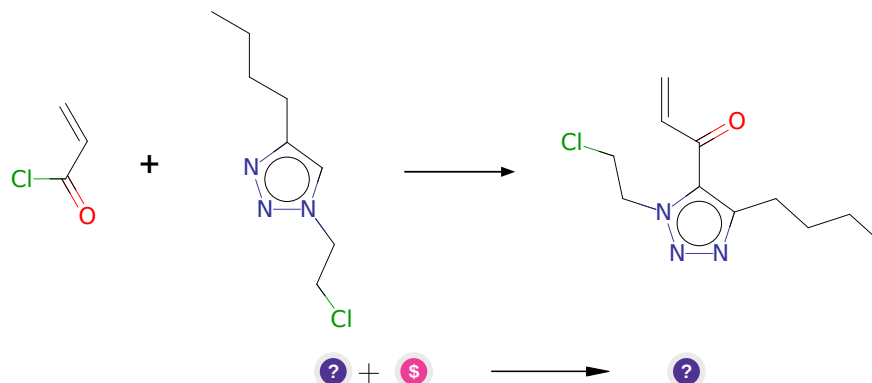
**Typical conditions:** cyanuric chloride.DMF.DCM.RT

**Protections:** none

**Reference:** DOI: [10.1021/ol017168p](https://doi.org/10.1021/ol017168p)

**Retrosynthesis ID:** 11617

### 2.4.3 Friedel-Crafts Acylation



#### Substrates:

1. CCCCc1cn(CCCl)nn1
2. Acryloyl chloride - *available at Sigma-Aldrich*

#### Products:

1. C=CC(=O)c1c(CCCC)nnm1CCCl

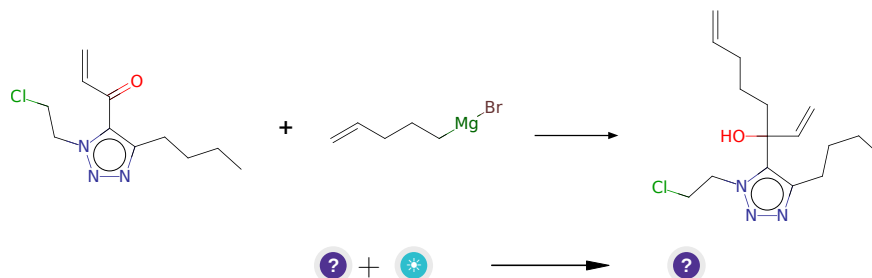
**Typical conditions:** Lewis Acid.solvent

**Protections:** none

**Reference:** [10.1021/jo00085a052](#) and [10.1039/C0OB01107J](#)

**Retrosynthesis ID:** 8722

### 2.4.4 Grignard-Type Reaction



#### Substrates:

1. C=CC(=O)c1c(CCCC)nnm1CCCl
2. pent-4-enylmagnesiumbromide

**Products:**

1. C=CCCCC(O)(C=C)c1c(CCCC)nn1CCCl

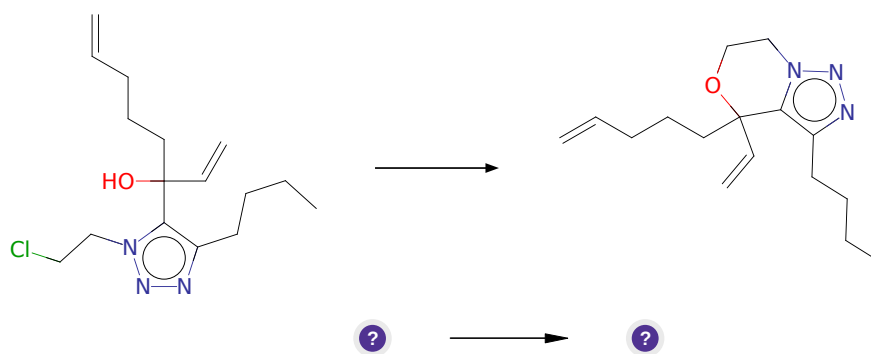
**Typical conditions:** Mg or Li.ether

**Protections:** none

**Reference:** [10.1021/jo010494y](#) or [10.1016/j.steroids.2015.09.009](#) or [10.1021/jo061349t](#) or [10.1021/ja056165v](#) (SI page 19)

**Retrosynthesis ID:** 25134

**2.4.5 Alkylation of tertiary alcohols**



**Substrates:**

1. C=CCCCC(O)(C=C)c1c(CCCC)nn1CCCl

**Products:**

1. C=CCCC1(C=C)OCCn2nnc(CCCC)c21

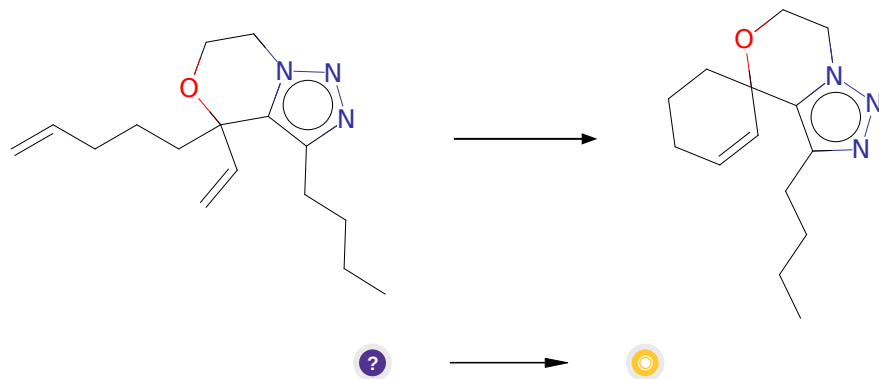
**Typical conditions:** K<sub>2</sub>CO<sub>3</sub>.acetone.heat

**Protections:** none

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

**Retrosynthesis ID:** 31010930

### 2.4.6 Ring-Closing Metathesis



**Substrates:**

1. C=CCCCC1(C=C)OCCn2nnc(CCCC)c21

**Products:**

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

**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