

# Paths of analysis\*

AS3

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.

**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:** 106.04

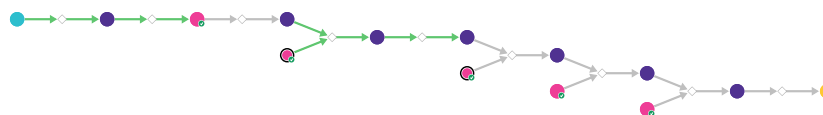
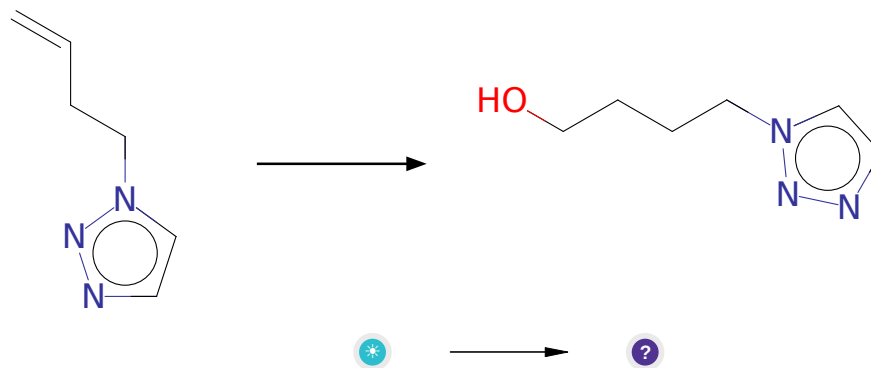


Figure 1: Outline of path 1

#### 2.1.1 Brown Hydroboration of Alkenes



**Substrates:**

- 1-but-3-enyl-1h-(1,2,3)triazole

**Products:**

- OCCCCn1ccnn1

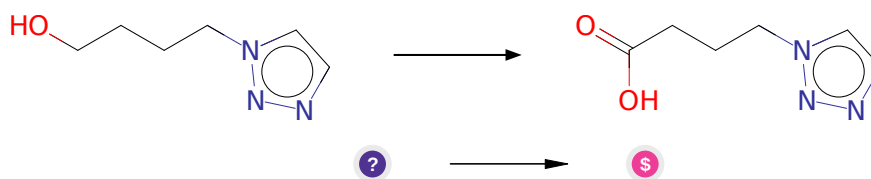
**Typical conditions:** B2H6.H2O2.THF.NaOH

**Protections:** none

**Reference:** [10.1002/9780470638859.conrr118](#)

**Retrosynthesis ID:** 4772

### 2.1.2 Jones Oxidation



**Substrates:**

1. OCCCCn1ccnn1

**Products:**

1. 4-(1H-1,2,3-triazol-1-yl)butanoic acid - *available at Sigma-Aldrich*

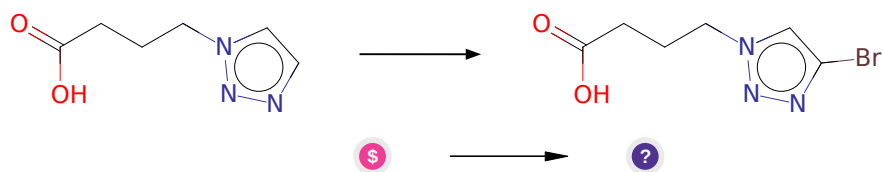
**Typical conditions:** cromate.sulfate.H2O.acetone

**Protections:** none

**Reference:** [10.1002/9780470638859.conrr349](#) and [10.1021/jm00270a004](#)

**Retrosynthesis ID:** 11160

### 2.1.3 Bromination of aromatic compounds



**Substrates:**

1. 4-(1H-1,2,3-triazol-1-yl)butanoic acid - *available at Sigma-Aldrich*

**Products:**

1. O=C(O)CCCN1cc(Br)nn1

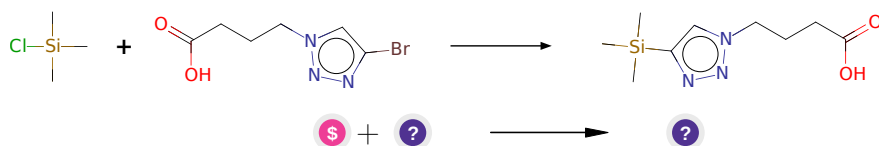
**Typical conditions:** Br2.Fe

**Protections:** none

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

Retrosynthesis ID: 7777000

#### 2.1.4 Synthesis of silanes, stannanes and germanes from Grignard reagents



Substrates:

1. TMS-Cl - *available at Sigma-Aldrich*
2. O=C(O)CCCn1cc(Br)nn1

Products:

1. C[Si](C)(C)c1cn(CCCC(=O)O)nn1

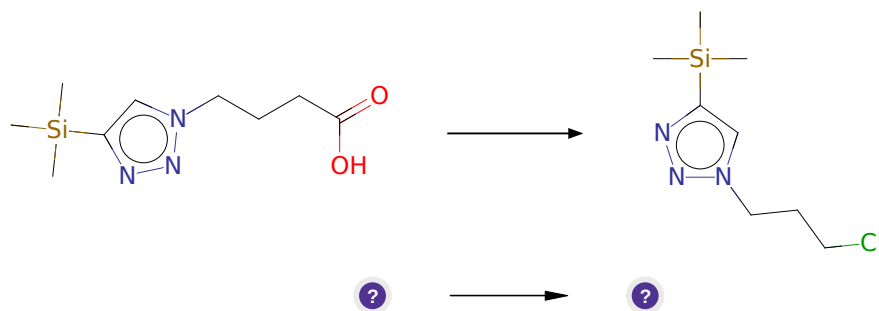
Typical conditions: 1. nBuLi. or. Mg. THF. -78C. 2. Si-Cl. to. rt

Protections: none

Reference: [10.1021/jo802433t](https://doi.org/10.1021/jo802433t) AND [10.1021/ja01108a009](https://doi.org/10.1021/ja01108a009)

Retrosynthesis ID: 5402

#### 2.1.5 Synthesis of alkyl chlorides from carboxylic acids



Substrates:

1. C[Si](C)(C)c1cn(CCCC(=O)O)nn1

Products:

1. C[Si](C)(C)c1cn(CCCCl)nn1

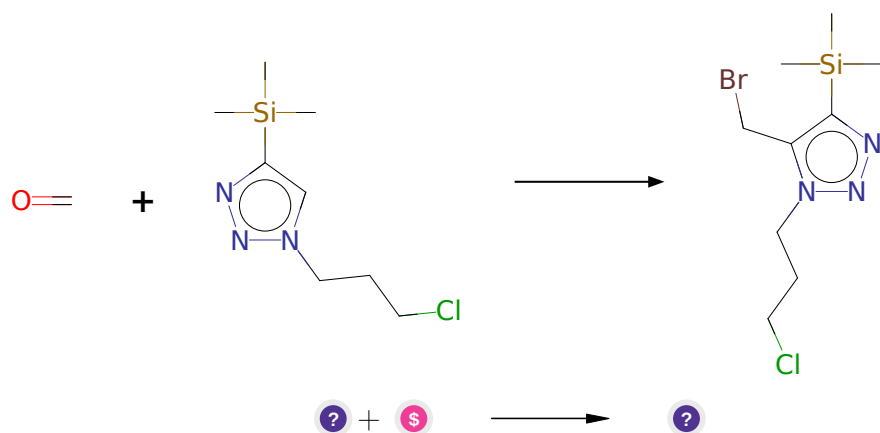
**Typical conditions:** Ag(Phen)2OTf.OtBu.Cl.acetonitrile.RT

**Protections:** none

**Reference:** DOI: [10.1021/ja210361z](https://doi.org/10.1021/ja210361z)

**Retrosynthesis ID:** 11619

### 2.1.6 Blanc bromomethylation



**Substrates:**

1. C[Si](C)(C)c1cn(CCCCl)nn1
2. Formalin - [available at Sigma-Aldrich](#)

**Products:**

1. C[Si](C)(C)c1nnn(CCCCl)c1CBr

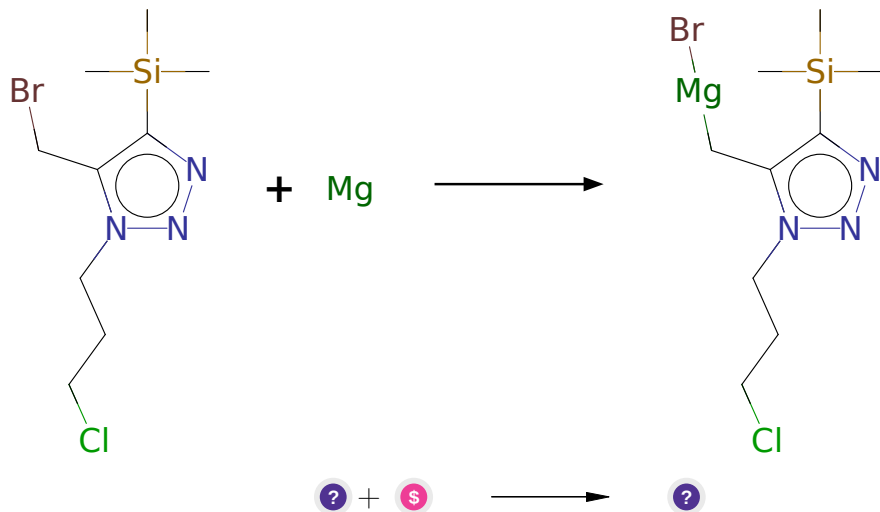
**Typical conditions:** HBr.heat

**Protections:** none

**Reference:** [10.1021/ja011493q](https://doi.org/10.1021/ja011493q) and [10.1021/ma012195g](https://doi.org/10.1021/ma012195g) and [10.1016/S0040-4039\(02\)01769-0](https://doi.org/10.1016/S0040-4039(02)01769-0) and [10.1021/ja002069c](https://doi.org/10.1021/ja002069c)

**Retrosynthesis ID:** 31010730

### 2.1.7 Synthesis of alkyl Grignard reagents



#### Substrates:

1. C[Si](C)(C)c1nnn(CCCCl)c1CBr
2. Magnesium - *available at Sigma-Aldrich*

#### Products:

1. C[Si](C)(C)c1nnn(CCCCl)c1C[Mg]Br

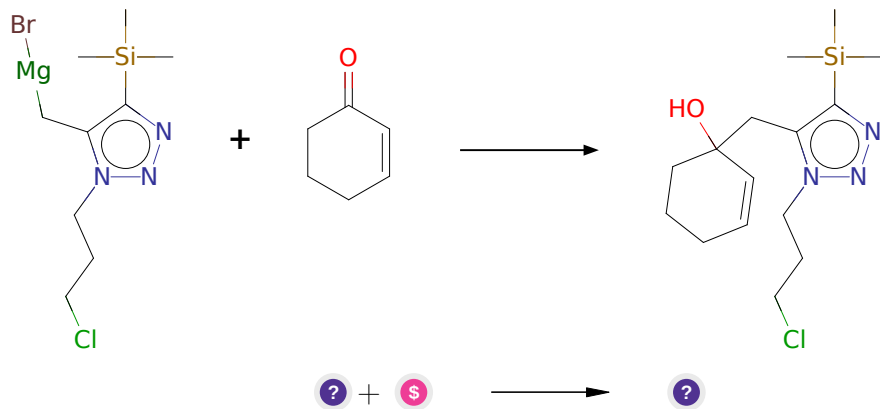
**Typical conditions:** Mg.THF or iPrMgBr

**Protections:** none

**Reference:** DOI: [10.1021/jo00002a039](https://doi.org/10.1021/jo00002a039) and [10.1021/jo047877r](https://doi.org/10.1021/jo047877r) and [10.1021/ol006618v](https://doi.org/10.1021/ol006618v)

**Retrosynthesis ID:** 10011828

### 2.1.8 Grignard-Type Reaction



**Substrates:**

1. C[Si](C)(C)c1nnn(CCCCl)c1C[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

**Products:**

1. C[Si](C)(C)c1nnn(CCCCl)c1CC1(O)C=CCCC1

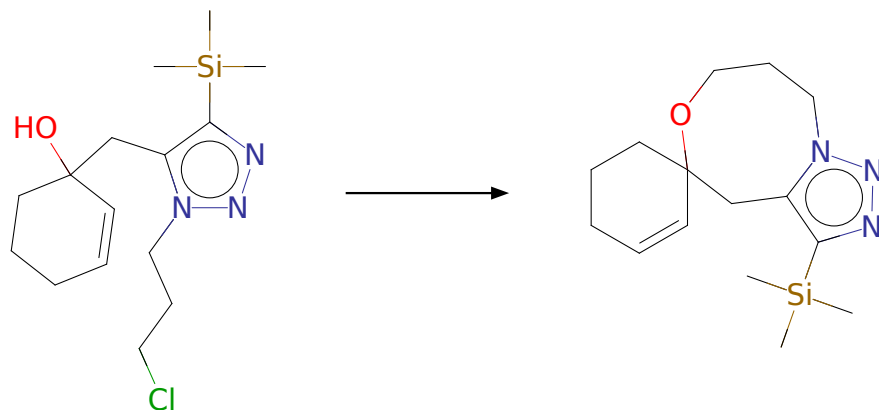
**Typical conditions:** Mg or Li.ether

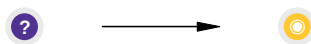
**Protections:** none

**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

### 2.1.9 Alkylation of tertiary alcohols





**Substrates:**

1. C[Si](C)(C)c1nnn(CCCCl)c1CC1(O)C=CCCC1

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCCC2

**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

## 2.2 Path 2

Score: 231.16

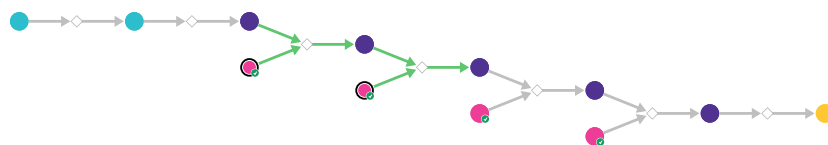
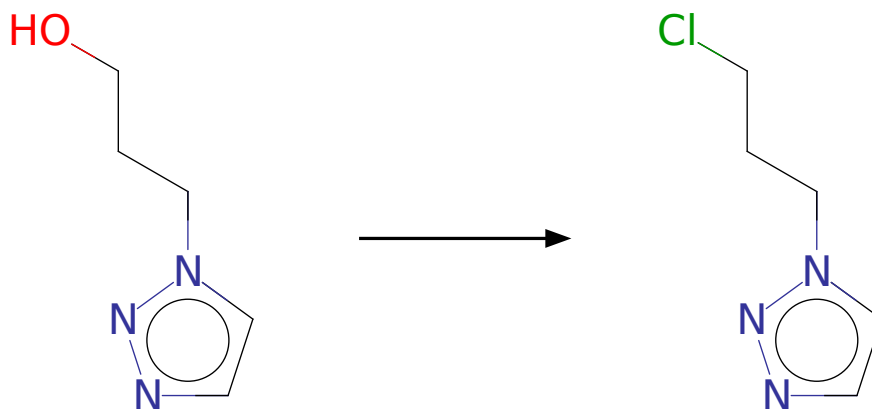
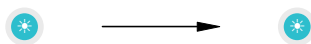


Figure 2: Outline of path 2

### 2.2.1 Synthesis of alkyl chlorides from alcohols







**Substrates:**

1. 3-[1,2,3]triazol-1-yl-propan-1-ol

**Products:**

1. C<sub>5</sub>H<sub>8</sub>ClN<sub>3</sub>

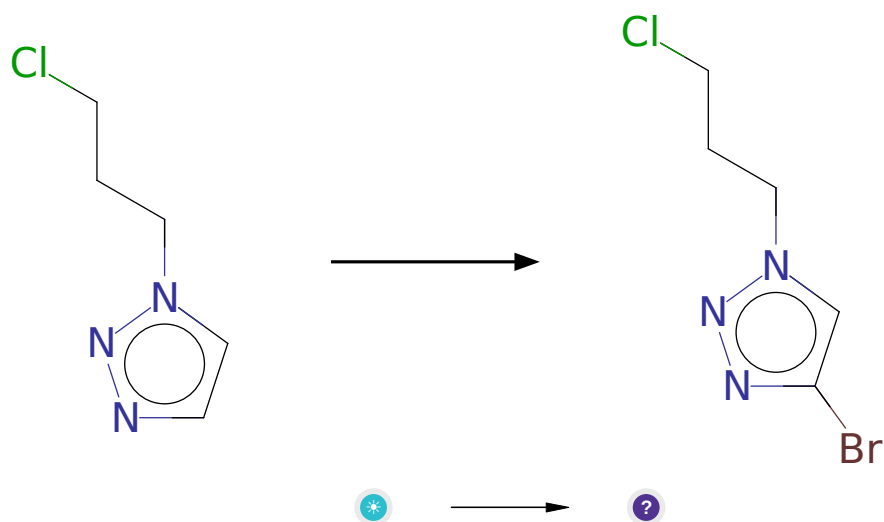
**Typical conditions:** cyanuric chloride.DMF.DCM.RT

**Protections:** none

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

**Retrosynthesis ID:** 11617

## 2.2.2 Bromination of aromatic compounds



**Substrates:**

1. C<sub>5</sub>H<sub>8</sub>ClN<sub>3</sub>

**Products:**

1. ClCCCN1cc(Br)nn1

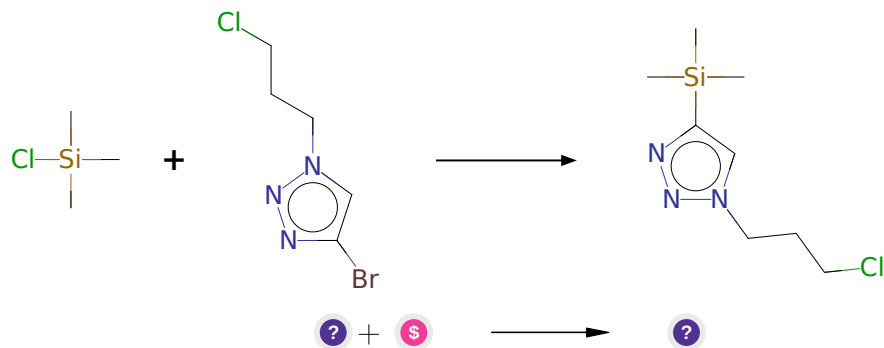
**Typical conditions:** Br<sub>2</sub>.Fe

**Protections:** none

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

**Retrosynthesis ID:** 7777000

### 2.2.3 Synthesis of arylsilanes



**Substrates:**

1. ClCCCN1cc(Br)nn1
2. TMSCl - *available at Sigma-Aldrich*

**Products:**

1. C[Si](C)(C)c1cn(CCCCl)nn1

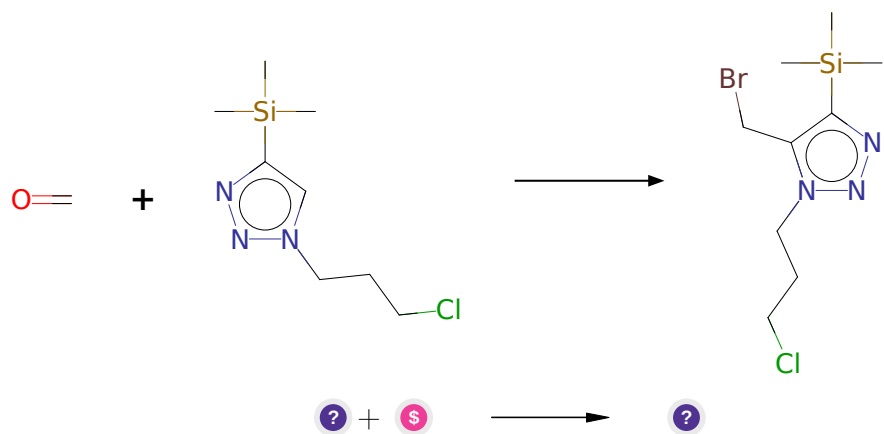
**Typical conditions:** 1. nBuLi. 2. ClSnR3

**Protections:** none

**Reference:** *10.1071/CH9851147*.

**Retrosynthesis ID:** 5370

### 2.2.4 Blanc bromomethylation



**Substrates:**

1. C[Si](C)(C)c1cn(CCCCl)nn1
2. Formalin - *available at Sigma-Aldrich*

**Products:**

1. C[Si](C)(C)c1nn(CCCCl)c1CBr

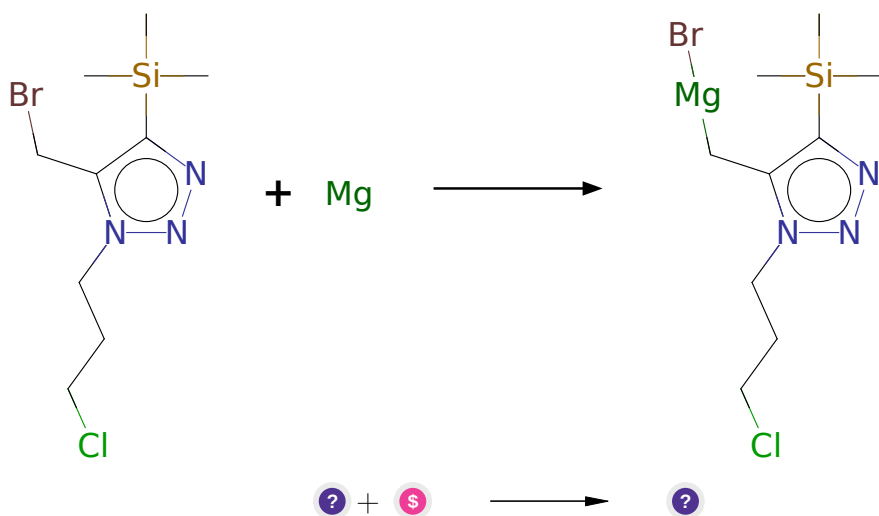
**Typical conditions:** HBr.heat

**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

### 2.2.5 Synthesis of alkyl Grignard reagents



**Substrates:**

1. C[Si](C)(C)c1nn(CCCCl)c1CBr
2. Magnesium - *available at Sigma-Aldrich*

**Products:**

1. C[Si](C)(C)c1nn(CCCCl)c1C[Mg]Br

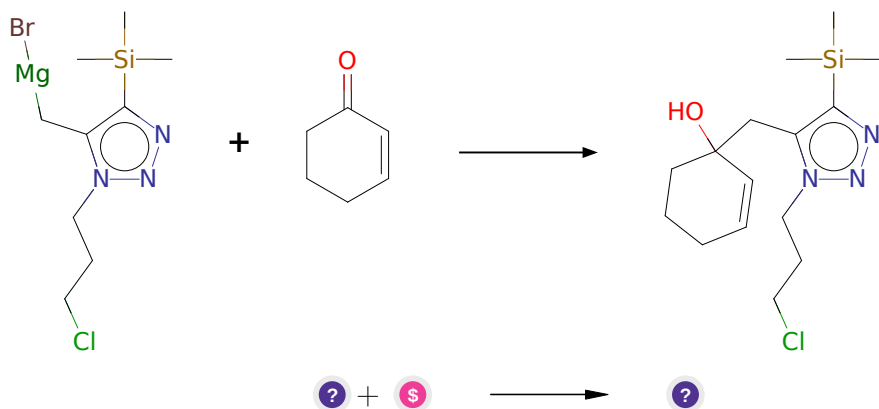
**Typical conditions:** Mg.THF or iPrMgBr

**Protections:** none

**Reference:** DOI: [10.1021/jo00002a039](https://doi.org/10.1021/jo00002a039) and [10.1021/jo047877r](https://doi.org/10.1021/jo047877r) and [10.1021/ol006618v](https://doi.org/10.1021/ol006618v)

**Retrosynthesis ID:** 10011828

### 2.2.6 Grignard-Type Reaction



**Substrates:**

1. C[Si](C)(C)c1nnn(CCCCl)c1C[Mg]Br
2. 2-Cyclohexen-1-one - [available at Sigma-Aldrich](#)

**Products:**

1. C[Si](C)(C)c1nnn(CCCCl)c1CC1(O)C=CCCC1

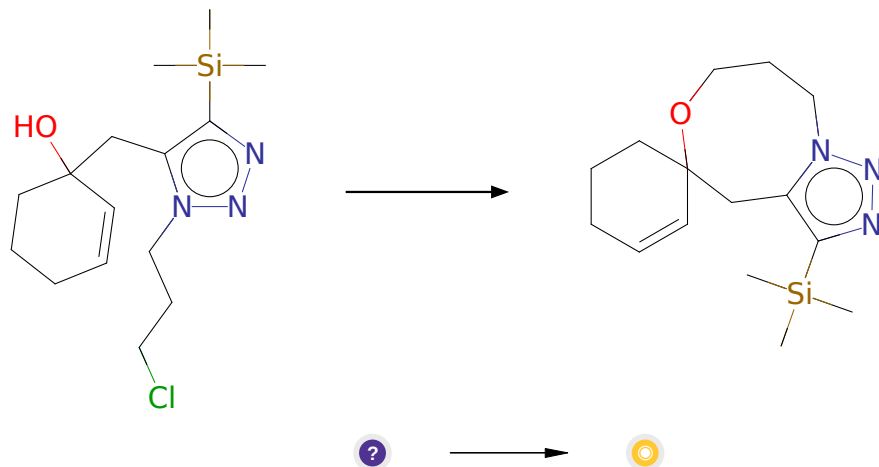
**Typical conditions:** Mg or Li.ether

**Protections:** none

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

**Retrosynthesis ID:** 25134

### 2.2.7 Alkylation of tertiary alcohols



**Substrates:**

1. C[Si](C)(C)c1nn(CCCCl)c1CC1(O)C=CCCC1

**Products:**

1. C[Si](C)(C)c1nn2c1CC1(C=CCCC1)OCCC2

**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:** 231.16

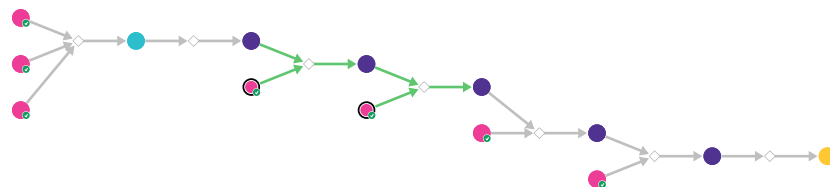
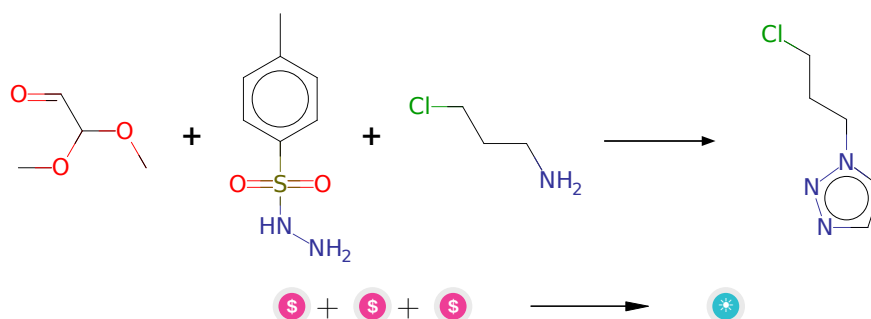


Figure 3: Outline of path 3

### 2.3.1 An azide and acetylene free synthesis of 1-substituted 1,2,3-triazoles



#### Substrates:

1. Glyoxal dimethyl acetal - *available at Sigma-Aldrich*
2. Tosylhydrazide - *available at Sigma-Aldrich*
3. 3-Chloropropylamine hydrochloride - *available at Sigma-Aldrich*

#### Products:

1. C<sub>5</sub>H<sub>8</sub>ClN<sub>3</sub>

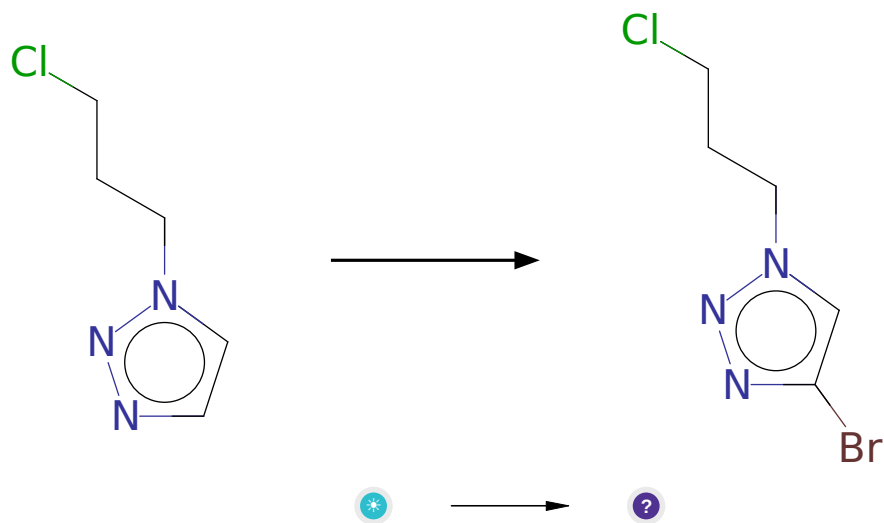
**Typical conditions:** 1. TsNHNH<sub>2</sub>.MeOH.rt 2.Amine.AcOH.heat

**Protections:** none

**Reference:** [10.1016/j.tetlet.2020.152483](https://doi.org/10.1016/j.tetlet.2020.152483)

**Retrosynthesis ID:** 31020968

### 2.3.2 Bromination of aromatic compounds



**Substrates:**

1. C5H8ClN3

**Products:**

1. ClCCCN1CC(Br)NN1

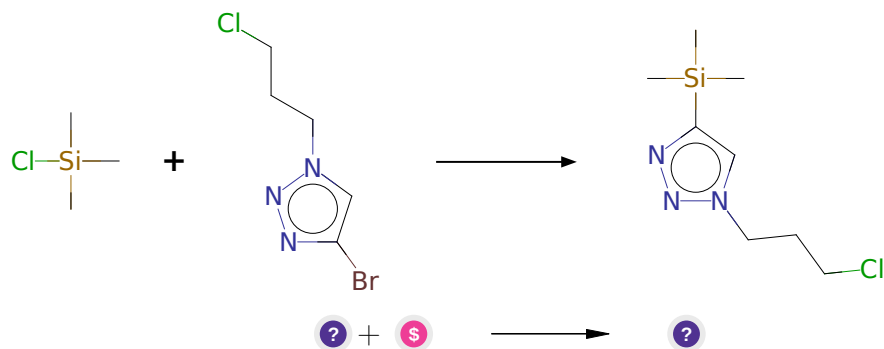
**Typical conditions:** Br2.Fe

**Protections:** none

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

**Retrosynthesis ID:** 7777000

### 2.3.3 Synthesis of arylsilanes



**Substrates:**

1. ClCCCC1cc(Br)nn1
2. TMSCl - *available at Sigma-Aldrich*

**Products:**

1. C[Si](C)(C)c1cn(CCCCl)nn1

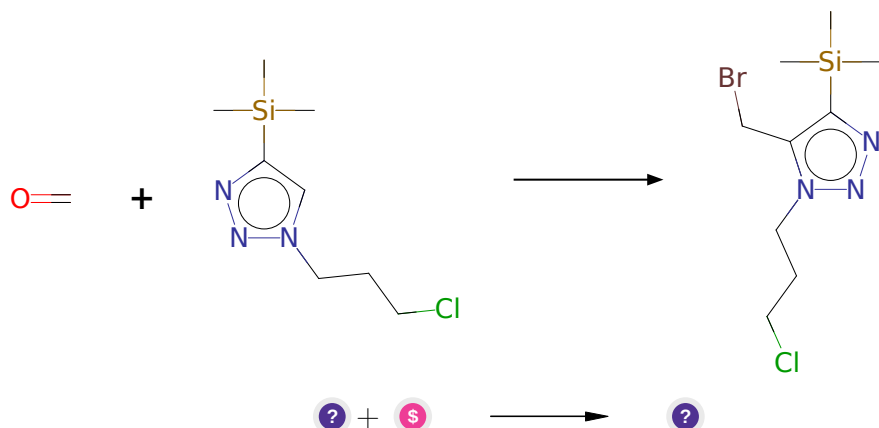
**Typical conditions:** 1.nBuLi.2.ClSnR3

**Protections:** none

**Reference:** *10.1071/CH9851147*.

**Retrosynthesis ID:** 5370

**2.3.4 Blanc bromomethylation**



**Substrates:**

1. C[Si](C)(C)c1cn(CCCCl)nn1
2. Formalin - *available at Sigma-Aldrich*

**Products:**

1. C[Si](C)(C)c1nnn(CCCCl)c1CBr

**Typical conditions:** HBr.heat

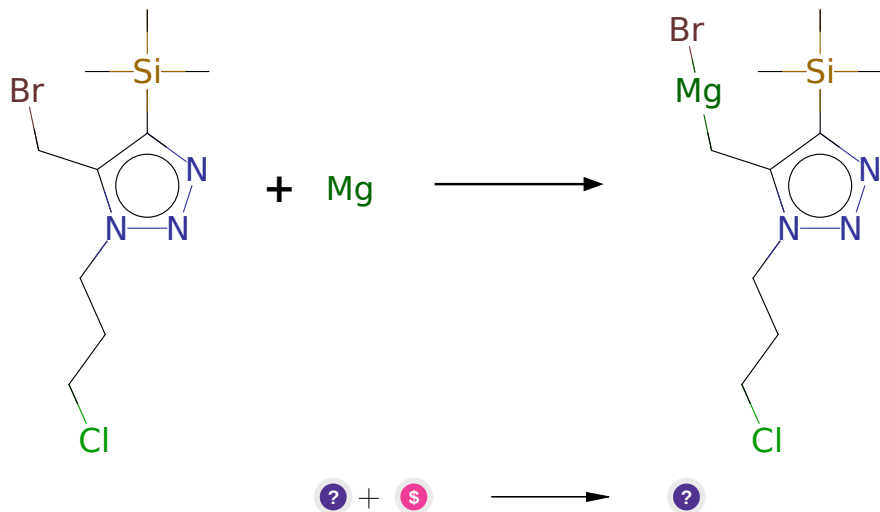
**Protections:** none

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

**Retrosynthesis ID:** 31010730



### 2.3.5 Synthesis of alkyl Grignard reagents



#### Substrates:

1. C[Si](C)(C)c1nnn(CCCCl)c1CBr
2. Magnesium - *available at Sigma-Aldrich*

#### Products:

1. C[Si](C)(C)c1nnn(CCCCl)c1C[Mg]Br

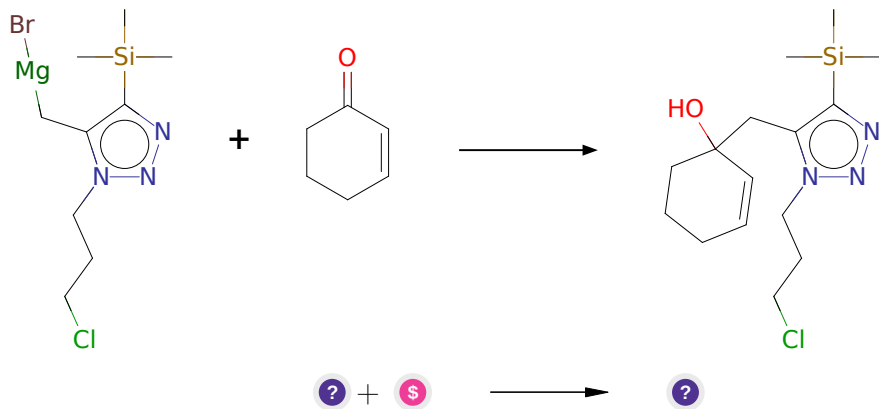
**Typical conditions:** Mg.THF or iPrMgBr

**Protections:** none

**Reference:** DOI: [10.1021/jo00002a039](https://doi.org/10.1021/jo00002a039) and [10.1021/jo047877r](https://doi.org/10.1021/jo047877r) and [10.1021/ol006618v](https://doi.org/10.1021/ol006618v)

**Retrosynthesis ID:** 10011828

### 2.3.6 Grignard-Type Reaction



#### Substrates:

1. C[Si](C)(C)c1nnn(CCCCl)c1C[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

#### Products:

1. C[Si](C)(C)c1nnn(CCCCl)c1CC1(O)C=CCCC1

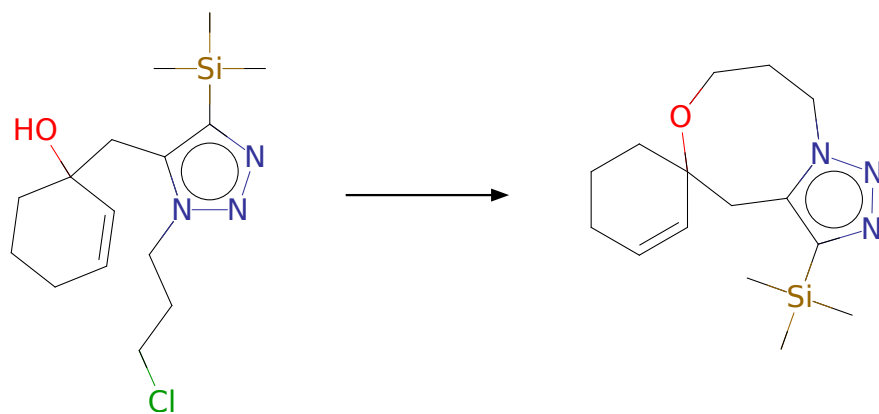
**Typical conditions:** Mg or Li.ether

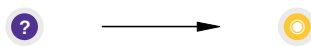
**Protections:** none

**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

### 2.3.7 Alkylation of tertiary alcohols





**Substrates:**

1. C[Si](C)(C)c1nnn(CCCCl)c1CC1(O)C=CCCC1

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCCC2

**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