

# Paths of analysis\*

PG6

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

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

### 2.1 Path 1

**Score:** 45.00

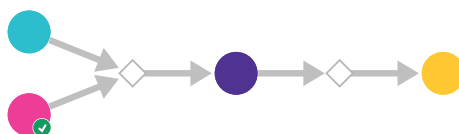
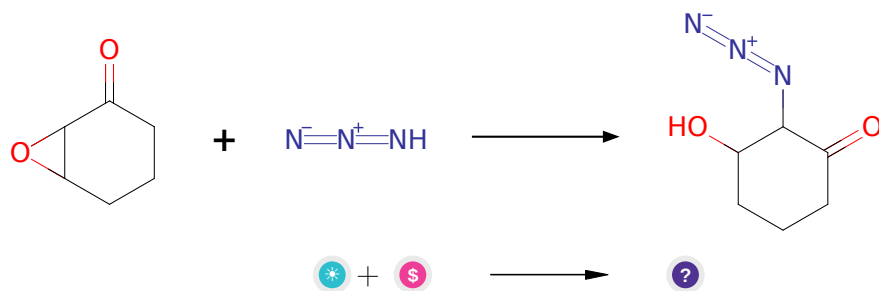


Figure 1: Outline of path 1

#### 2.1.1 Ring-opening of epoxides or thiiranes with azides



**Substrates:**

1. hydrazoic acid
2. 7-Oxabicyclo[4.1.0]heptan-2-one - *available at Sigma-Aldrich*

**Products:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

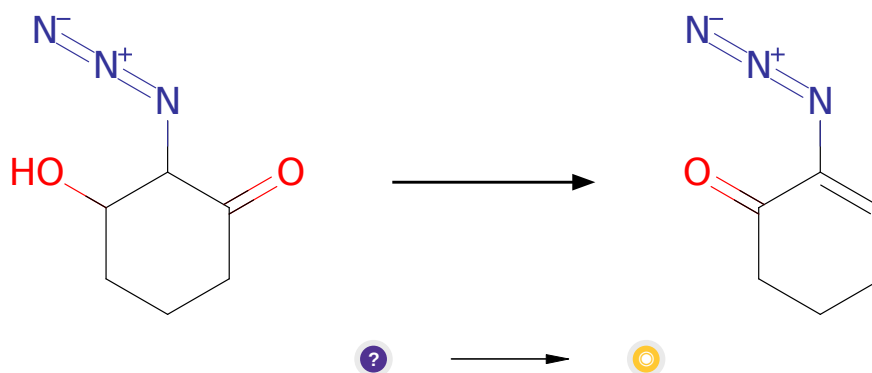
**Typical conditions:** NaN<sub>3</sub>.NH<sub>4</sub>Cl.MeOH.H<sub>2</sub>O.65 C

**Protections:** none

**Reference:** [10.1021/jm400529f](#) p. 4361, 4367 and [10.1021/ja003713q](#) p. 1590, 1594

**Retrosynthesis ID:** 858

### 2.1.2 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

**Products:**

1. 2-azidocyclohex-2-enone

**Typical conditions:** TsOH

**Protections:** none

**Reference:** DOI:[10.1002/anie.201204977](#) AND [10.1021/ol062777o](#)

**Retrosynthesis ID:** 7731

## 2.2 Path 2

**Score:** 76.25

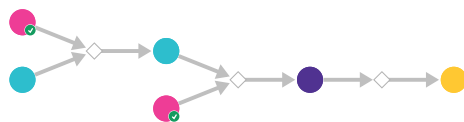
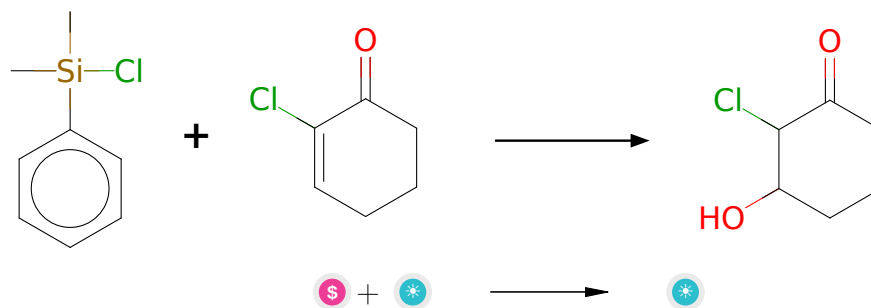


Figure 2: Outline of path 2

### 2.2.1 Addition of silanes to Michael acceptors followed by oxidation



#### Substrates:

1. DMPSCl - *available at Sigma-Aldrich*
2. 2-chloro-cyclohex-2-enone

#### Products:

1. 2-chloro-3-hydroxy-cyclohexanone

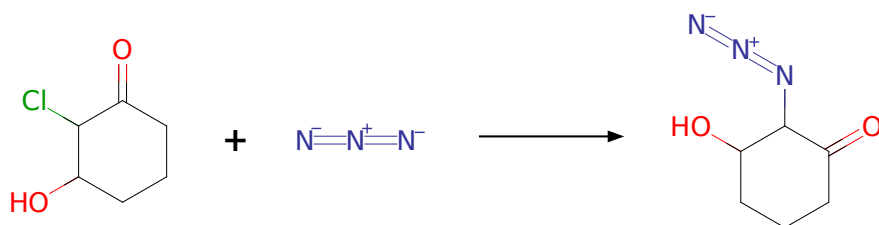
**Typical conditions:** 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

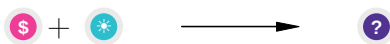
**Protections:** none

**Reference:** [10.1021/ja058370g](#) AND (Oxidation) [10.1021/jo9905672](#) or [10.1021/ol300832f](#)

**Retrosynthesis ID:** 20295

### 2.2.2 Nucleophilic substitution with azides





**Substrates:**

1. Potassium azide - *available at Sigma-Aldrich*
2. 2-chloro-3-hydroxy-cyclohexanone

**Products:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

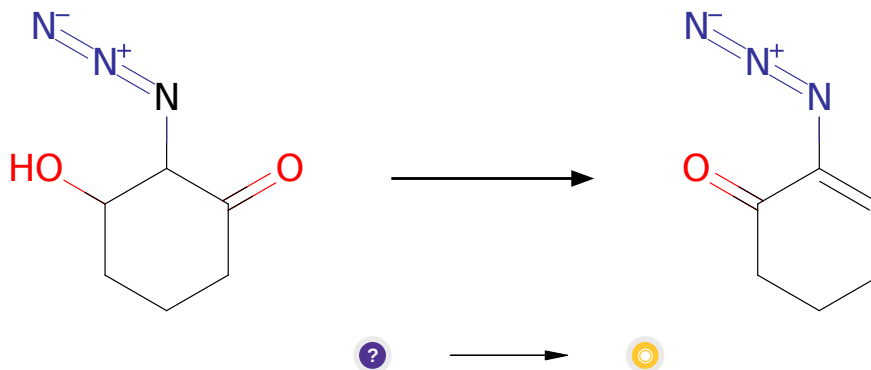
**Typical conditions:** DMF.heat

**Protections:** none

**Reference:** *10.1016/j.tet.2013.11.027* and *10.1021/jo015632y* and *10.3987/COM-06-S(K)18*

**Retrosynthesis ID:** 31011248

### 2.2.3 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

**Products:**

1. 2-azidocyclohex-2-enone

**Typical conditions:** TsOH

**Protections:** none

**Reference:** DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

**Retrosynthesis ID:** 7731

## 2.3 Path 3

Score: 76.25

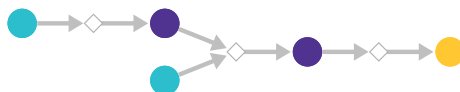
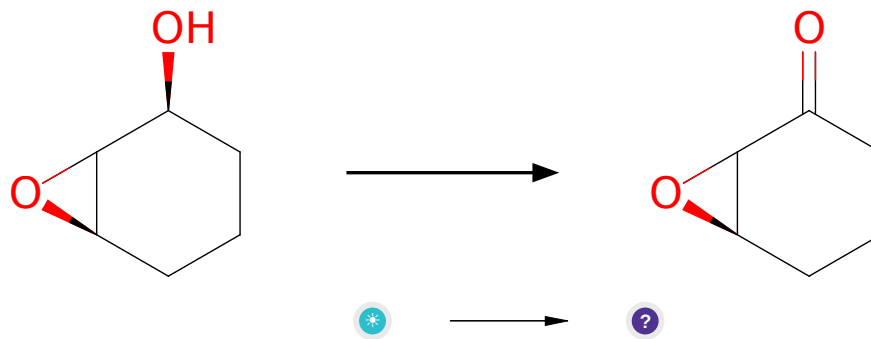


Figure 3: Outline of path 3

### 2.3.1 Oxidation of Chiral Alcohols



**Substrates:**

1. C6H10O2

**Products:**

1. O=C1CCC[C@H]2OC12

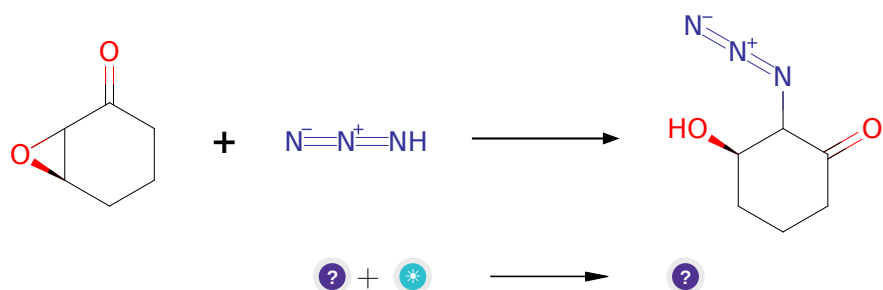
**Typical conditions:** CAN.NaBrO<sub>3</sub>.CH<sub>3</sub>CN or other oxidant e.g. TPAP or NaOCl

**Protections:** none

**Reference:** DOI: [10.1016/S0040-4039\(00\)86883-5](https://doi.org/10.1016/S0040-4039(00)86883-5) or [10.1021/ja00054a005](https://doi.org/10.1021/ja00054a005) or [10.1016/S0040-4039\(00\)85677-4](https://doi.org/10.1016/S0040-4039(00)85677-4)

**Retrosynthesis ID:** 10371

### 2.3.2 Ring-opening of epoxides or thiiranes with azides



**Substrates:**

1. O=C1CCC[C@H]2OC12
2. hydrazoic acid

**Products:**

1. [N-]=[N+]=NC1C(=O)CCC[C@H]1O

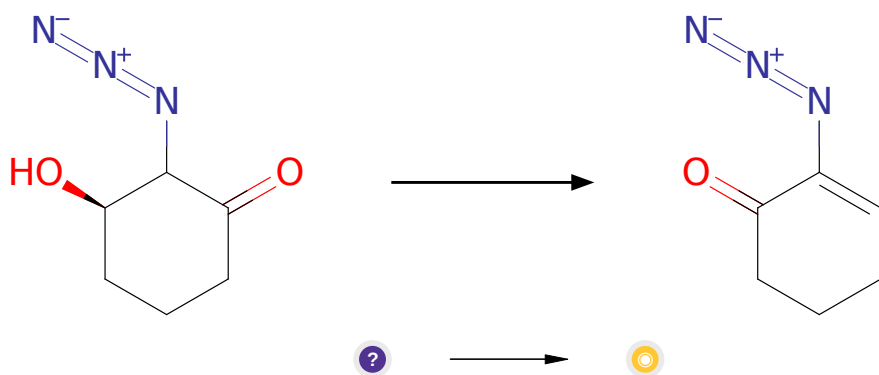
**Typical conditions:** NaN3.NH4Cl.MeOH.H2O.65 C

**Protections:** none

**Reference:** [10.1021/jm400529f](#) p. 4361, 4367 and [10.1021/ja003713q](#) p. 1590, 1594

**Retrosynthesis ID:** 858

### 2.3.3 Dehydration of beta-ketoalcohols



**Substrates:**

1. [N-]=[N+]=NC1C(=O)CCC[C@H]1O

**Products:**

1. 2-azidocyclohex-2-enone

**Typical conditions:** 1.MsCl.NEt3

**Protections:** none

**Reference:** [10.1021/ol301090v](#) and [10.1021/ja00521a062](#) and [10.1002/ejoc.201201636](#) (SI)

**Retrosynthesis ID:** 20813

## 2.4 Path 4

Score: 84.06

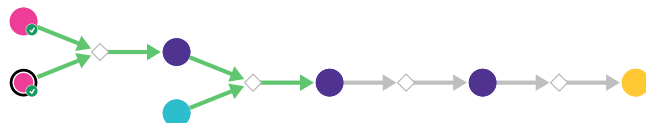
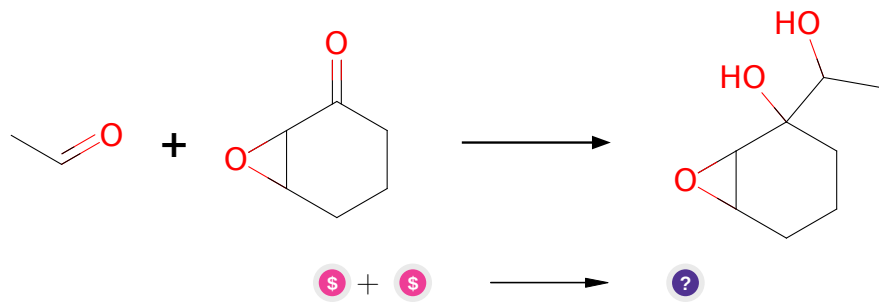


Figure 4: Outline of path 4

### 2.4.1 Pinacol Coupling Reaction



**Substrates:**

1. 7-Oxabicyclo[4.1.0]heptan-2-one - [available at Sigma-Aldrich](#)
2. Ethanal - [available at Sigma-Aldrich](#)

**Products:**

1. CC(O)C1(O)CCCC2OC21



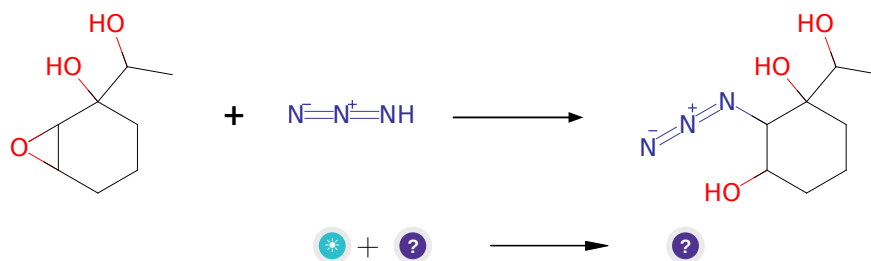
**Typical conditions:** Mg.NH<sub>4</sub>Cl.H<sub>2</sub>O or Mg.SmI<sub>2</sub>.TMSCl.THF.HMPA

**Protections:** none

**Reference:** [10.1021/jo982497p](#) p. 3234, 3236 and [10.1021/ol0506258](#) p. 2366, SI p. S12

**Retrosynthesis ID:** 10205

#### 2.4.2 Ring-opening of epoxides or thiiranes with azides



**Substrates:**

1. hydrazoic acid
2. CC(O)C1(O)CCCC2OC21

**Products:**

1. CC(O)C1(O)CCCC(O)C1N=[N+]=[N-]

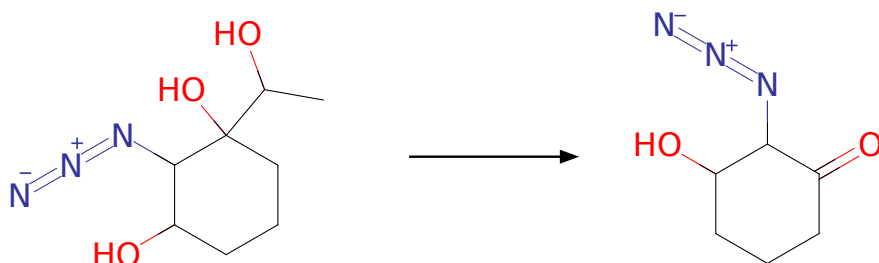
**Typical conditions:** NaN<sub>3</sub>.NH<sub>4</sub>Cl.MeOH.H<sub>2</sub>O.65 °C

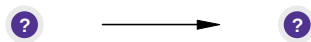
**Protections:** none

**Reference:** [10.1021/jm400529f](#) p. 4361, 4367 and [10.1021/ja003713q](#) p. 1590, 1594

**Retrosynthesis ID:** 858

#### 2.4.3 Cleavage of 1,2-diols with NaIO<sub>4</sub>





**Substrates:**

1. CC(O)C1(O)CCCC(O)C1N=[N+]=[N-]

**Products:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

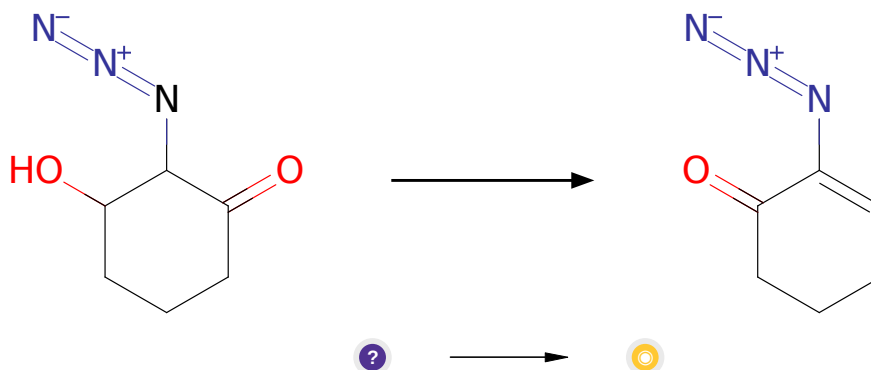
**Typical conditions:** NaIO<sub>4</sub>.solvent

**Protections:** none

**Reference:** [10.1039/C5OB00238A](#) and [10.1002/chem.201301371](#) and [10.1021/ol052106a](#)

**Retrosynthesis ID:** 31017508

#### 2.4.4 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

**Products:**

1. 2-azidocyclohex-2-enone

**Typical conditions:** TsOH

**Protections:** none

**Reference:** DOI: [10.1002/anie.201204977](#) AND [10.1021/ol062777o](#)

**Retrosynthesis ID:** 7731

## 2.5 Path 5

Score: 84.06

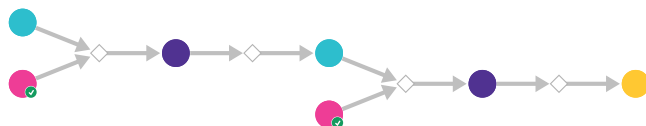
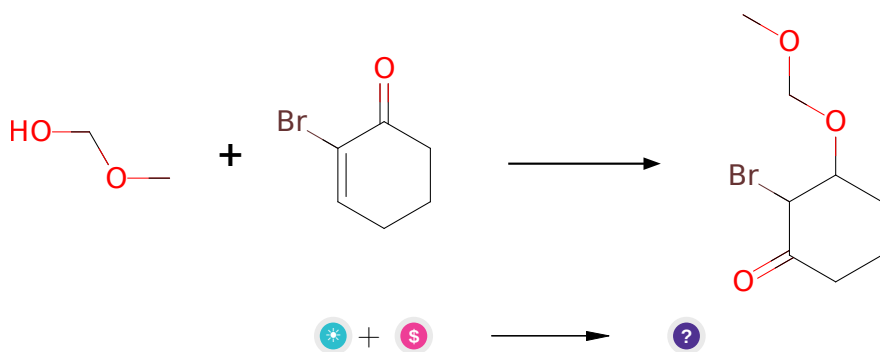


Figure 5: Outline of path 5

### 2.5.1 Addition of alcohols or phenols to Michael acceptors



**Substrates:**

1. methoxymethanol
2. 2-Bromocyclohex-2-en-1-one - *available at Sigma-Aldrich*

**Products:**

1. COCOC1CCCC(=O)C1Br

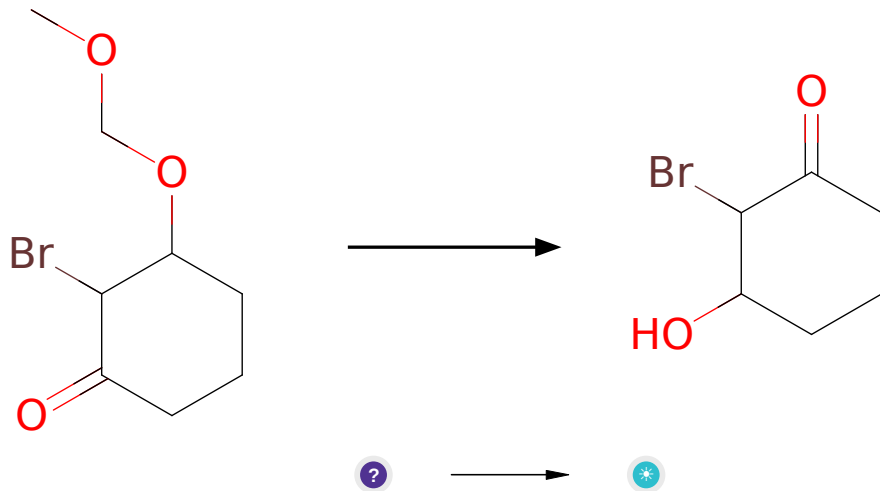
**Typical conditions:** cat.Na.DMF

**Protections:** none

**Reference:** [10.1016/S0957-4166\(97\)00479-5](#) AND [10.1016/S0040-4020\(98\)00817-5](#) AND [10.1021/np970346w](#) AND [10.1021/ol049820x](#)

**Retrosynthesis ID:** 20259

### 2.5.2 Hydrolysis of acetals



**Substrates:**

1. COCOC1CCCC(=O)C1Br

**Products:**

1. 2-bromo-3-hydroxycyclohexanone

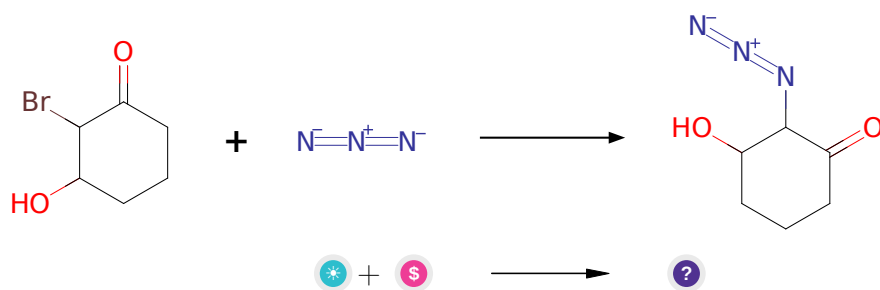
**Typical conditions:** HCl.THF or TFA.DCM

**Protections:** none

**Reference:** [10.1002/ejoc.201301615](#) and [10.3762/bjoc.9.289](#) and [10.1080/00397919808004478](#) and [10.1016/S0040-4039\(99\)02200-5](#) and [10.1055/s-0030-1258583](#) and [10.1016/j.tet.2011.04.072](#)

**Retrosynthesis ID:** 31013131

### 2.5.3 Nucleophilic substitution with azides



**Substrates:**

1. 2-bromo-3-hydroxycyclohexanone
2. Potassium azide - *available at Sigma-Aldrich*

**Products:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

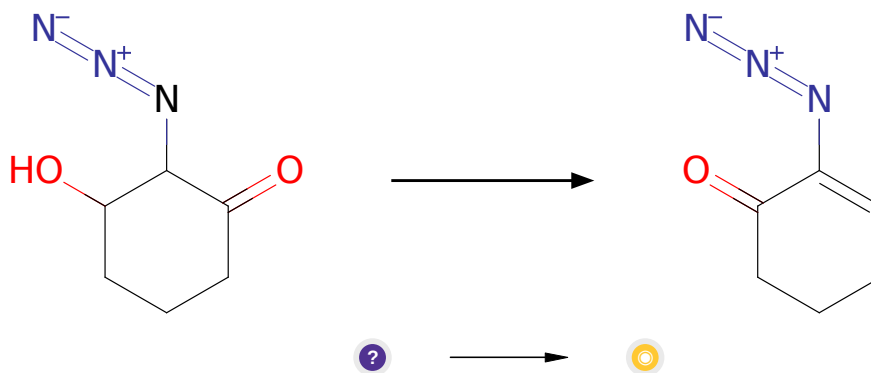
**Typical conditions:** DMF, heat

**Protections:** none

**Reference:** [10.1021/ol049369+](#) and [10.1016/S0040-4039\(00\)61343-6](#) and [10.1016/j.bmcl.2005.03.055](#)

**Retrosynthesis ID:** 31011250

#### 2.5.4 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. [N-]=[N+]=NC1C(=O)CCCC1O

**Products:**

1. 2-azidocyclohex-2-enone

**Typical conditions:** TsOH

**Protections:** none

**Reference:** DOI: [10.1002/anie.201204977](#) AND [10.1021/ol062777o](#)

**Retrosynthesis ID:** 7731