

# Paths of analysis\*

PG8

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:** 20.00

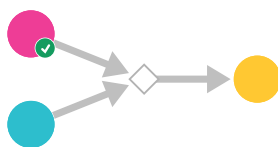
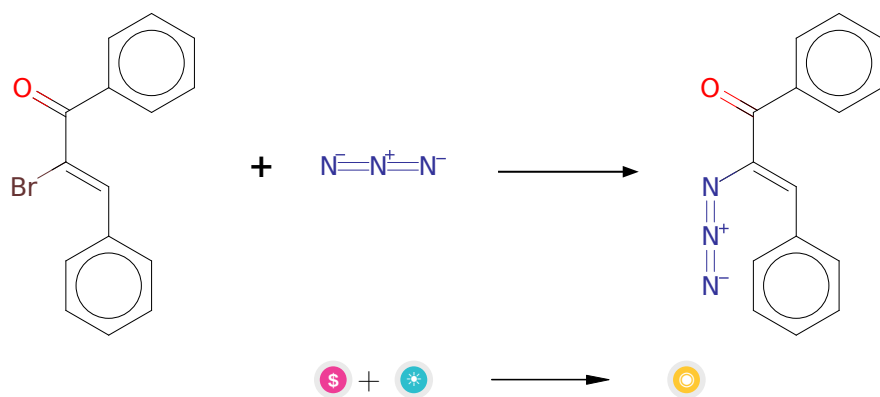


Figure 1: Outline of path 1

#### 2.1.1 Synthesis of azidochalcones from dibromochalcones



**Substrates:**

1. Potassium azide - *available at Sigma-Aldrich*
2. a-bromo-trans-chalcone

**Products:**

1.  $\alpha$ -azidochalcone

**Typical conditions:** NaN<sub>3</sub>.DMF

**Protections:** none

**Reference:** DOI: [10.1016/S0040-4020\(01\)83509-2](https://doi.org/10.1016/S0040-4020(01)83509-2)

**Retrosynthesis ID:** 270

## 2.2 Path 2

Score: 45.00

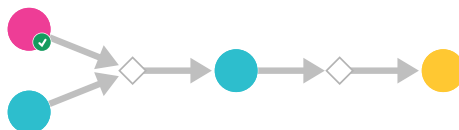
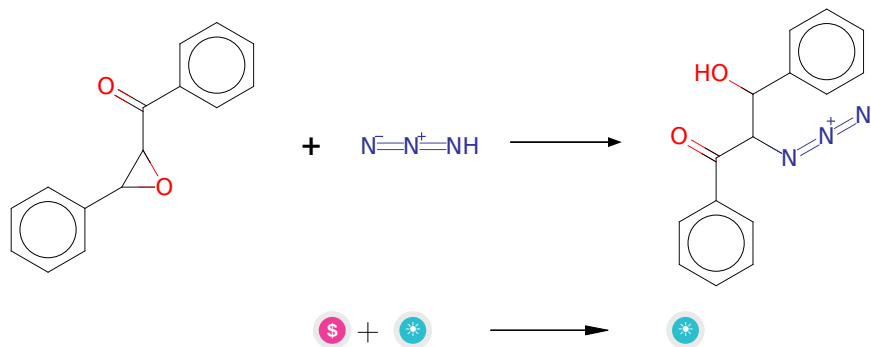


Figure 2: Outline of path 2

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



**Substrates:**

1. 2-Benzoyl-3-phenyloxirane - *available at Sigma-Aldrich*
2. hydrazoic acid

**Products:**

1. C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>

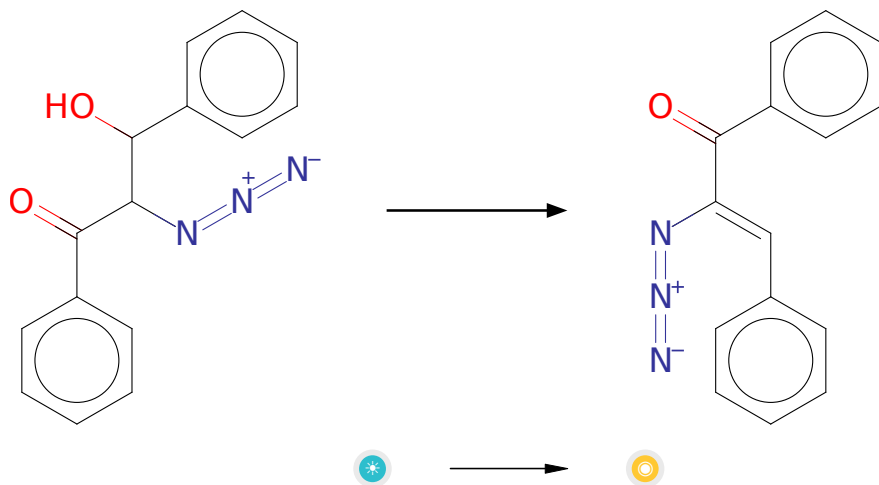
**Typical conditions:** NaN<sub>3</sub>.NH<sub>4</sub>Cl.MeOH.H<sub>2</sub>O.65 C

**Protections:** none

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

**Retrosynthesis ID:** 858

## 2.2.2 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>

**Products:**

1. a-azidochalcone

**Typical conditions:** TsOH

**Protections:** none

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

**Retrosynthesis ID:** 7732

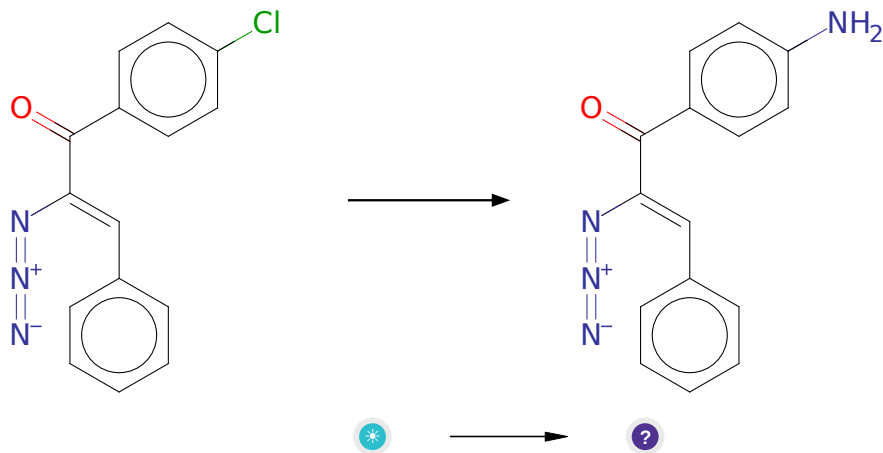
## 2.3 Path 3

**Score:** 45.00



Figure 3: Outline of path 3

### 2.3.1 Amination of aryl chlorides



**Substrates:**

1. C15H10ClN3O

**Products:**

1. [N-]=[N+]=N/C(=C\c1ccccc1)C(=O)c1ccc(N)cc1

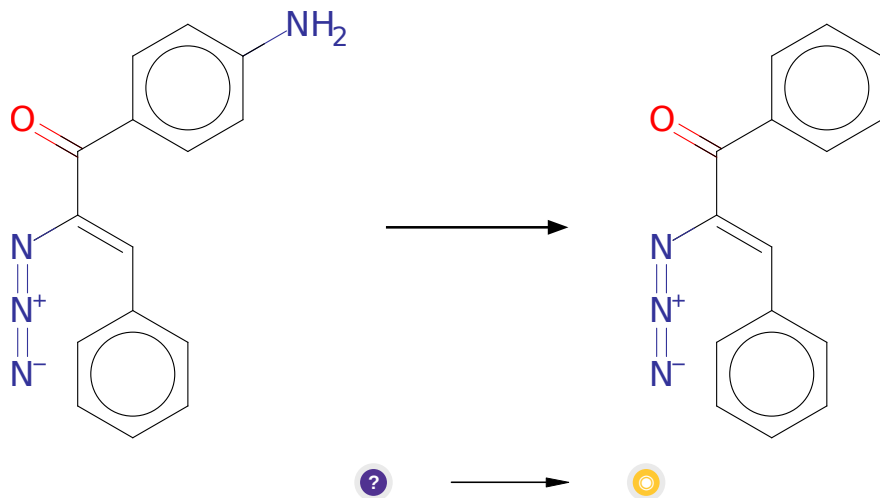
**Typical conditions:** [Pd].Ligand.base

**Protections:** none

**Reference:** [10.1021/ja903049z](#) and [10.1021/jo060945k](#) and [10.1021/jo060190h](#) and [10.1021/ja8055358](#) and [10.1021/ja068926f](#) and [10.1002/anie.200601612](#) and [10.1021/acscatal.0c04280](#)

**Retrosynthesis ID:** 28545

### 2.3.2 Hydrodediazonation



**Substrates:**

1. [N-]=[N+]=N/C(=C\c1ccccc1)C(=O)c1ccc(N)cc1

**Products:**

1. a-azidochalcone

**Typical conditions:** 1) HCl.NaNO<sub>2</sub> 2) H<sub>3</sub>PO<sub>2</sub>

**Protections:** none

**Reference:** [10.1016/j.bmcl.2013.10.058](https://doi.org/10.1016/j.bmcl.2013.10.058) and [10.1021/jm0004906](https://doi.org/10.1021/jm0004906) and [10.1002/ejoc.200600030](https://doi.org/10.1002/ejoc.200600030) and [10.1016/j.tet.2016.02.011](https://doi.org/10.1016/j.tet.2016.02.011)

**Retrosynthesis ID:** 9999757

### 2.4 Path 4

**Score:** 59.06

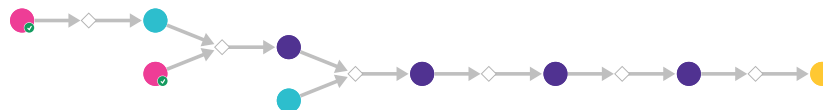
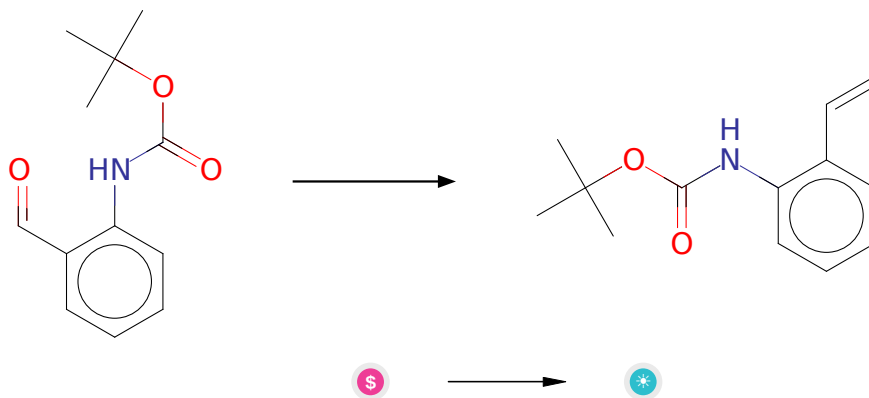


Figure 4: Outline of path 4

### 2.4.1 Tebbe Olefination



**Substrates:**

1. 2-(Boc-amino)benzaldehyde - *available at Sigma-Aldrich*

**Products:**

1. (2-vinylphenyl)carbamate

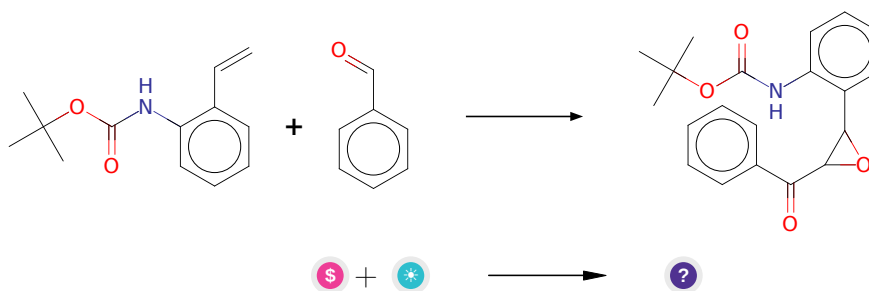
**Typical conditions:**  $\text{Cp}_2\text{TiCl}_2$ .  $\text{AlMe}_3$ . toluene

**Protections:** none

**Reference:** [10.1016/j.tet.2007.03.015](#) and [10.1002/9780470638859.conrr617](#)

**Retrosynthesis ID:** 11714

### 2.4.2 Epoxyacylation of alkenes



**Substrates:**

1. Benzaldehyde - *available at Sigma-Aldrich*
2. (2-vinylphenyl)carbamate

**Products:**

1. CC(C)(C)OC(=O)Nc1ccccc1C1OC1C(=O)c1ccccc1

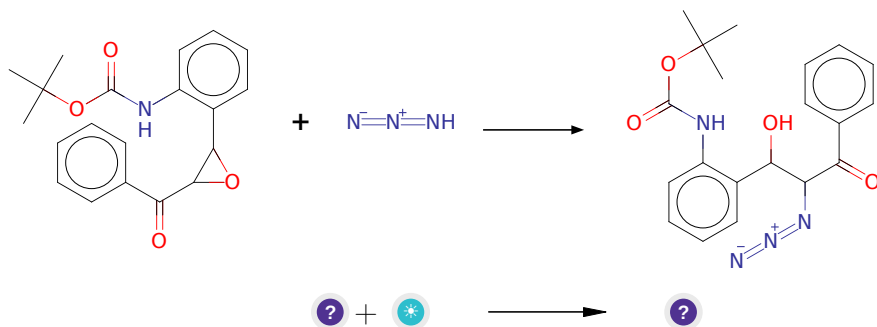
**Typical conditions:** methylene.blue.K2S2O8.K2CO3.H2O.light

**Protections:** none

**Reference:** [10.1021/acs.joc.8b01026](https://doi.org/10.1021/acs.joc.8b01026)

**Retrosynthesis ID:** 10019378

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



**Substrates:**

1. CC(C)(C)OC(=O)Nc1ccccc1C1OC1C(=O)c1ccccc1
2. hydrazoic acid

**Products:**

1. CC(C)(C)OC(=O)Nc1ccccc1C(O)C(N=[N+]=[N-])C(=O)c1ccccc1

**Typical conditions:**  $\text{NaN}_3$ . $\text{NH}_4\text{Cl}$ .MeOH.H<sub>2</sub>O.65 °C

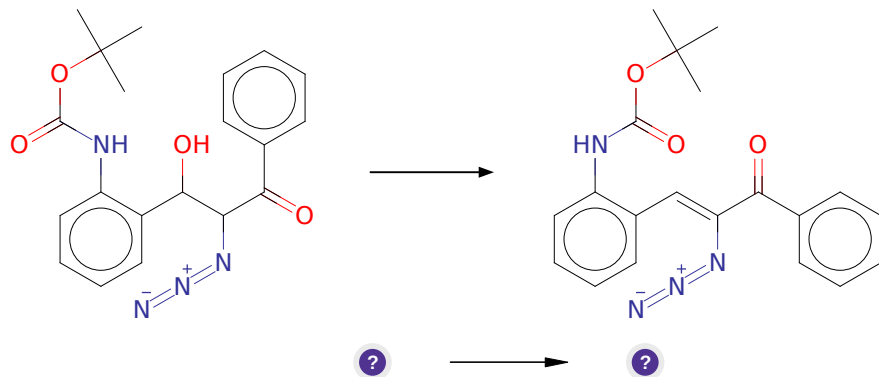
**Protections:** none

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

**Retrosynthesis ID:** 858



#### 2.4.4 Dehydration of Beta Hydroxy Carbonyl Compounds



**Substrates:**

1. CC(C)(C)OC(=O)Nc1ccccc1C(O)C(N=[N+]=[N-])C(=O)c1ccccc1

**Products:**

1. CC(C)(C)OC(=O)Nc1ccccc1/C=C(\N=[N+]=[N-])C(=O)c1ccccc1

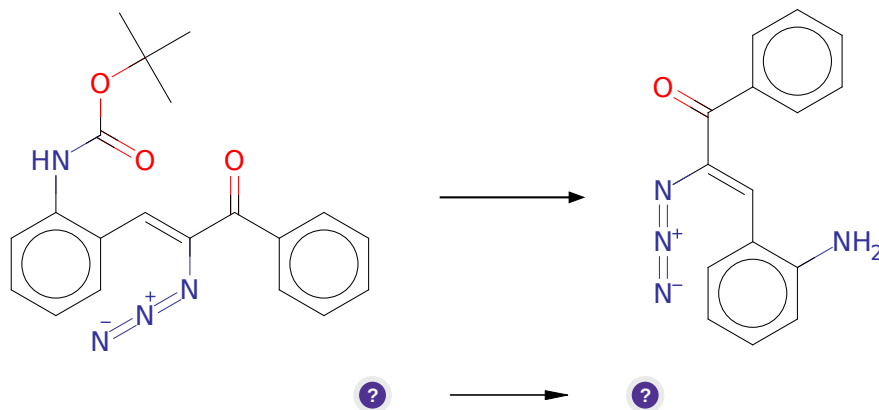
**Typical conditions:** CeCl<sub>3</sub>.NaI.ACN.or.solvent

**Protections:** none

**Reference:** DOI: [10.1021/ol005766i](https://doi.org/10.1021/ol005766i)

**Retrosynthesis ID:** 7734

#### 2.4.5 Boc removal



**Substrates:**

1. CC(C)(C)OC(=O)Nc1ccccc1/C=C(\N=[N+]=[N-])C(=O)c1ccccc1

**Products:**

1. [N-]=[N+]=N/C(=C\c1ccccc1N)C(=O)c1ccccc1

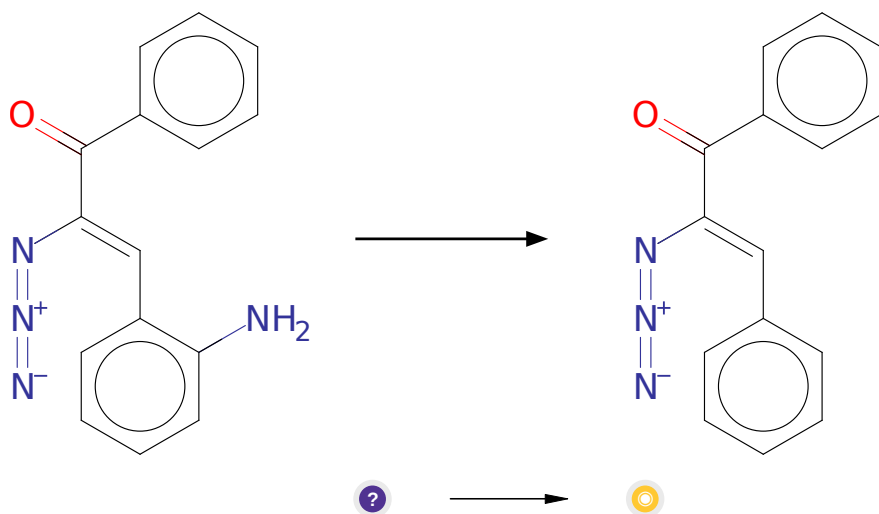
**Typical conditions:** TFA.DCM

**Protections:** none

**Reference:** [10.1016/j.ejmech.2017.06.062](https://doi.org/10.1016/j.ejmech.2017.06.062) and [10.1016/j.bmcl.2008.02.079](https://doi.org/10.1016/j.bmcl.2008.02.079) and [10.1016/j.tetlet.2009.09.087](https://doi.org/10.1016/j.tetlet.2009.09.087) and [10.1016/j.bmcl.2015.06.039](https://doi.org/10.1016/j.bmcl.2015.06.039)

**Retrosynthesis ID:** 10025813

**2.4.6 Hydredediazoniation**



**Substrates:**

1. [N-]=[N+]=N/C(=C\c1ccccc1N)C(=O)c1ccccc1

**Products:**

1. a-azidochalcone

**Typical conditions:** 1) HCl.NaNO<sub>2</sub> 2) H<sub>3</sub>PO<sub>2</sub>

**Protections:** none

**Reference:** [10.1016/j.bmcl.2013.10.058](https://doi.org/10.1016/j.bmcl.2013.10.058) and [10.1021/jm0004906](https://doi.org/10.1021/jm0004906) and [10.1002/ejoc.200600030](https://doi.org/10.1002/ejoc.200600030) and [10.1016/j.tet.2016.02.011](https://doi.org/10.1016/j.tet.2016.02.011)

**Retrosynthesis ID:** 9999756

## 2.5 Path 5

Score: 76.25

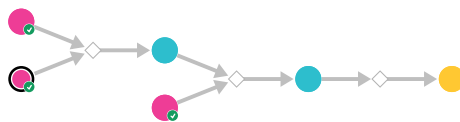
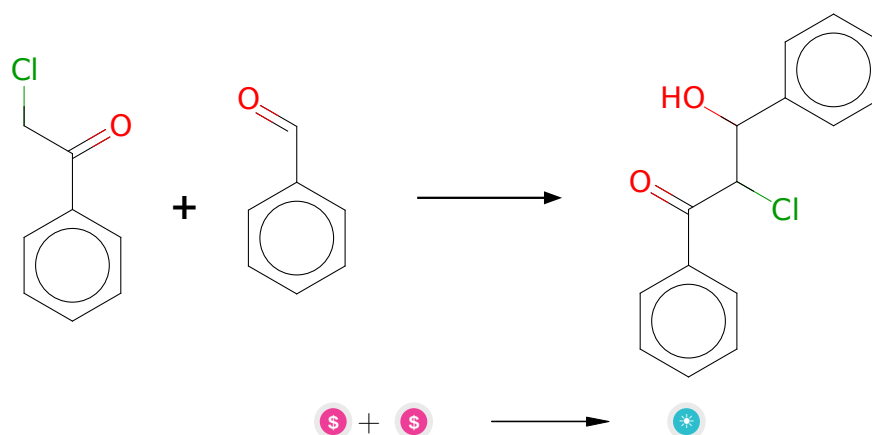


Figure 5: Outline of path 5

### 2.5.1 Aldol Addition



**Substrates:**

1. Benzaldehyde - *available at Sigma-Aldrich*
2. Phenacyl chloride - *available at Sigma-Aldrich*

**Products:**

1. 2-chloro-3-hydroxy-1,3-diphenylpropan-1-one

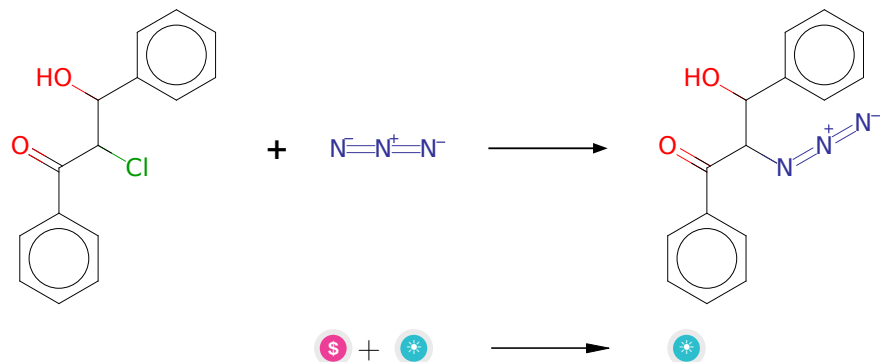
**Typical conditions:** LDA.THF

**Protections:** none

**Reference:** [10.1021/ja991507g](#) and [10.1002/anie.200906662](#) and [10.1007/s10593-011-0669-4](#) and [10.1021/ol0606435](#)

**Retrosynthesis ID:** 14924

### 2.5.2 Nucleophilic substitution with azides



#### Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. 2-chloro-3-hydroxy-1,3-diphenylpropan-1-one

#### Products:

1.  $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_2$

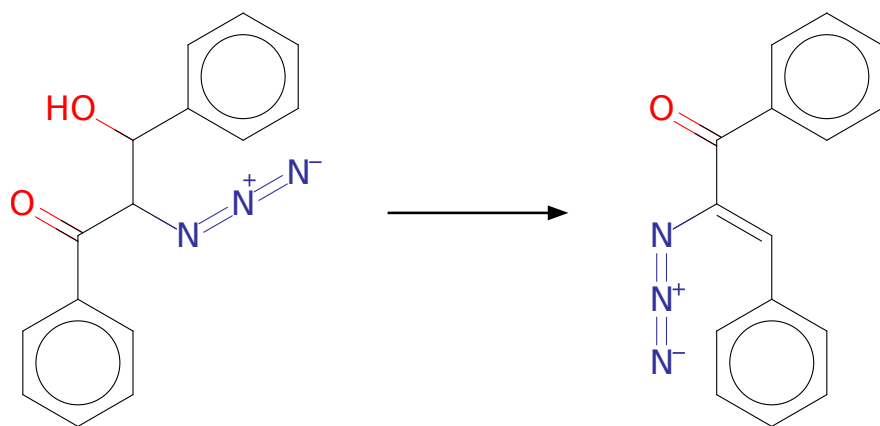
**Typical conditions:** DMF.heat

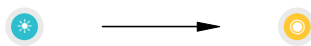
**Protections:** none

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

**Retrosynthesis ID:** 31011248

### 2.5.3 Dehydration of Beta Hydroxy Carbonyl Compounds





**Substrates:**

1. C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>

**Products:**

1. α-azidochalcone

**Typical conditions:** TsOH

**Protections:** none

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

**Retrosynthesis ID:** 7732