# Paths of analysis*

A1

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

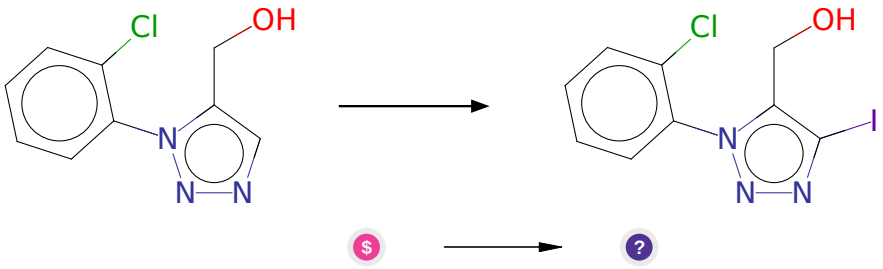
2 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

## 2.1 Path 1

**Score:** `14411533.74`

Figure 1: Outline of path 1

### 2.1.1 Iodination of aromatic compounds




**Substrates:**

1. [1-(2-chlorophenyl)-1H-1,2,3-triazol-5-yl]methanol - *available at Sigma-Aldrich*

**Products:**

1. OCc1c(I)nnn1-c1ccccc1Cl

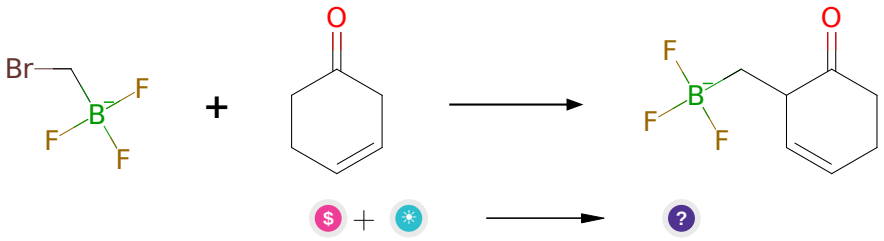
**Typical conditions:** I2 or other iodinating agent e.g. NIS

**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

### 2.1.2 Alkylation of ketones




**Substrates:**

1. Potassium (bromomethyl)trifluoroborate - *available at Sigma-Aldrich*
2. cyclohex-3-enone

**Products:**

1. O=C1CCC=CC1C[B-](F)(F)F

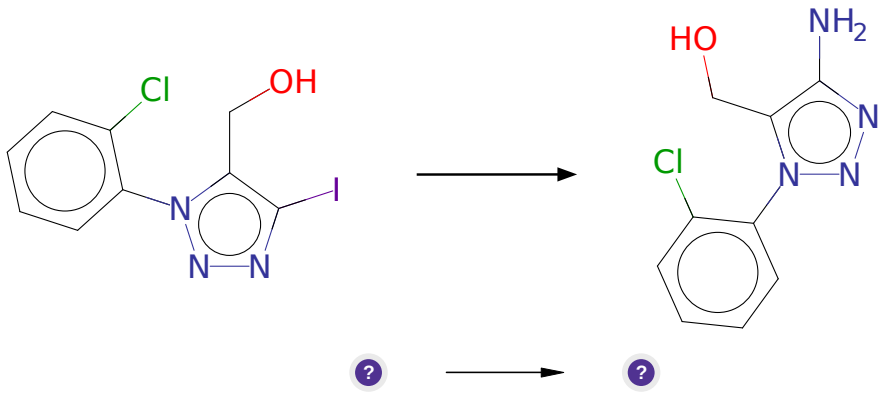
**Typical conditions:** LDA or other base.THF.-78C

**Protections:** none

**Reference:** DOI: *10.1021/ja0123554*

**Retrosynthesis ID:** 1868

### 2.1.3 Coupling of Ammonia with Aryl Halides




**Substrates:**

1. OCc1c(I)nnn1-c1ccccc1Cl

**Products:**

1. Nc1nnn(-c2ccccc2Cl)c1CO

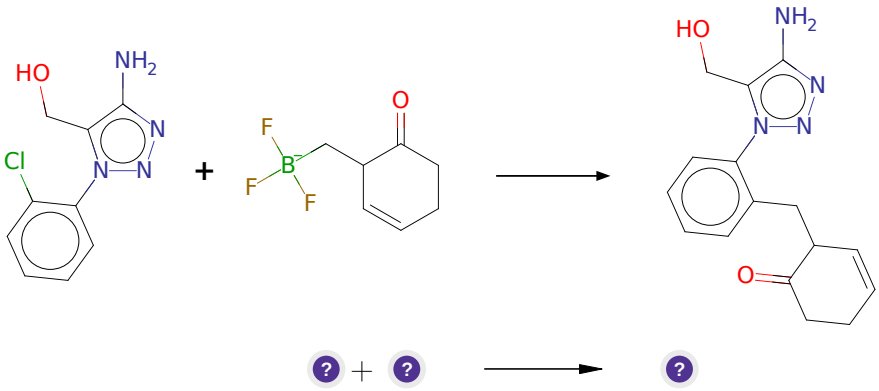
**Typical conditions:** Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

**Protections:** none

**Reference:** *10.1021/ja903049z* and *10.1021/jo9006738*

**Retrosynthesis ID:** 31016464

### 2.1.4 Suzuki Coupling of arylchlorides and alkyltrifluoroborates




**Substrates:**

1. O=C1CCC=CC1C[B-](F)(F)F
2. Nc1nnn(-c2ccccc2Cl)c1CO

**Products:**

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

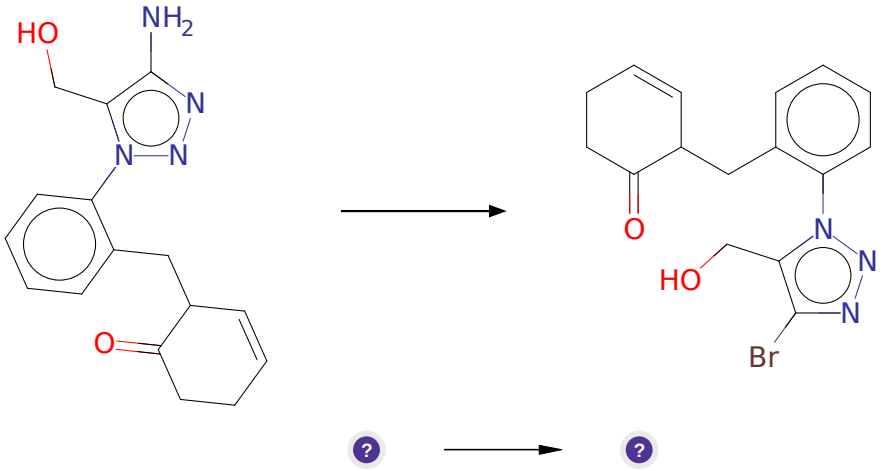
**Typical conditions:** Pd(OAc)2.RuPhos.CsCO3.toluene/H2O.90C

**Protections:** none

**Reference:** *10.1016/j.tet.2015.07.072* and *10.1021/jo900152n*

**Retrosynthesis ID:** 10033514

### 2.1.5 Sandmeyer Reaction




**Substrates:**

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

**Products:**

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

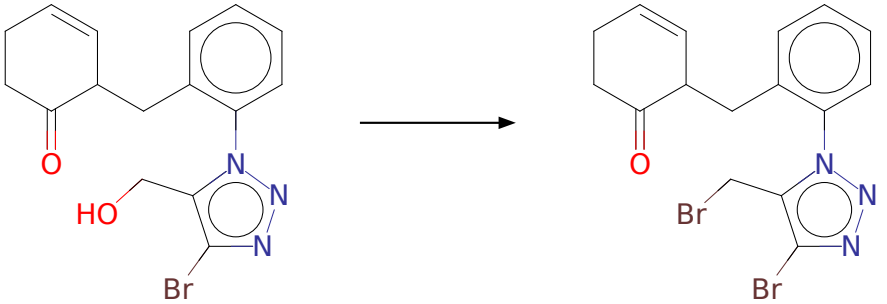
**Typical conditions:** IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

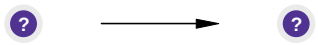
**Protections:** none

**Reference:** *10.1002/chem.201600278* and *10.1016/j.bmcl.2011.12.131* and *10.1016/j.ejmech.2013.01.046* and *10.1021/jm0002782* and *10.1002/ejoc.201300443* and *10.1021/jo052589w*(SI,page S3) and *10.1021/jm800527x* and *10.1016/j.bmcl.2015.04.098* and *10.1021/ja034563x*

**Retrosynthesis ID:** 29904

### 2.1.6 Appel Reaction





**Substrates:**

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

**Products:**

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

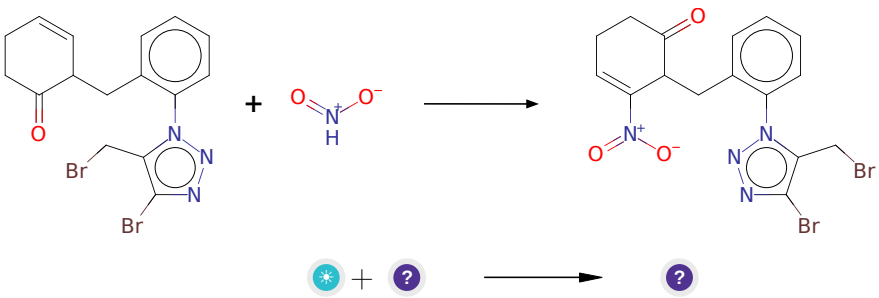
**Typical conditions:** PPh3.CBr4

**Protections:** none

**Reference:** *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

**Retrosynthesis ID:** 9990037

### 2.1.7 Nitration of aliphatic olefins



**Substrates:**

1. HNO2
2. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

**Products:**

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

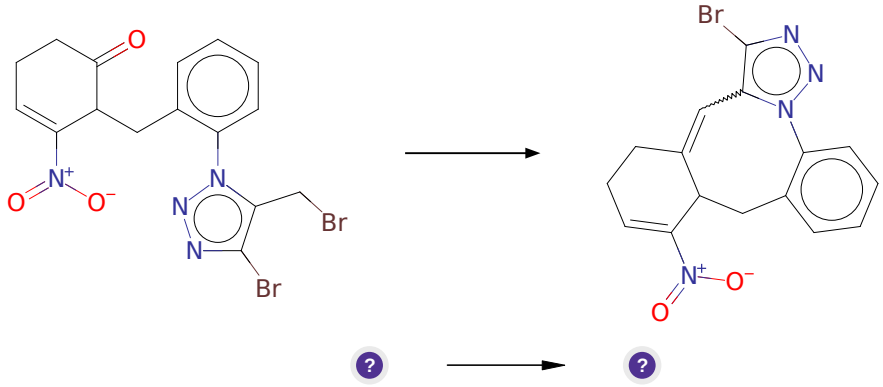
**Typical conditions:** Fe(NO2)3x9H2O.TEMPO.DCE.4A MS.80C

**Protections:** none

**Reference:** DOI: *10.1021/jo400598p*

**Retrosynthesis ID:** 1623

### 2.1.8 HWE/Wittig Olefination



**Substrates:**

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

**Products:**

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

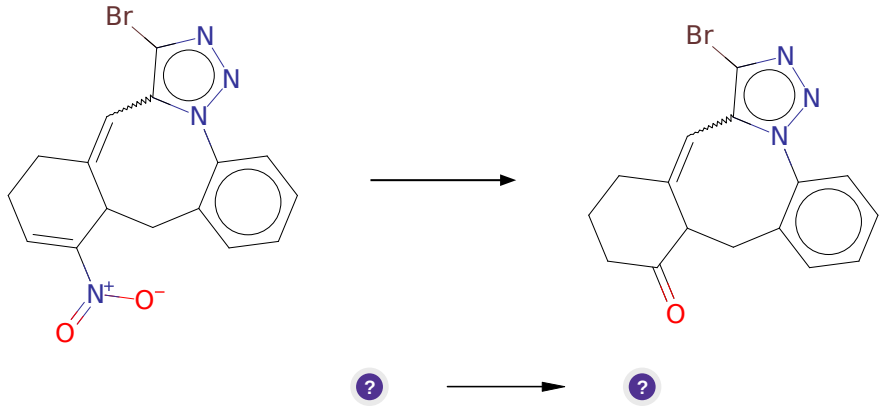
**Typical conditions:** 1.PPh3 or trialkylphosphite.2.base.aldehyde

**Protections:** none

**Reference:** *10.1002/anie.200705005* and *10.1021/ol052106a* and *10.1021/jo00075a064* and *10.1021/ol3027297*

**Retrosynthesis ID:** 24425

### 2.1.9 Synthesis of ketones from nitroalkenes



**Substrates:**

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

**Products:**

1. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

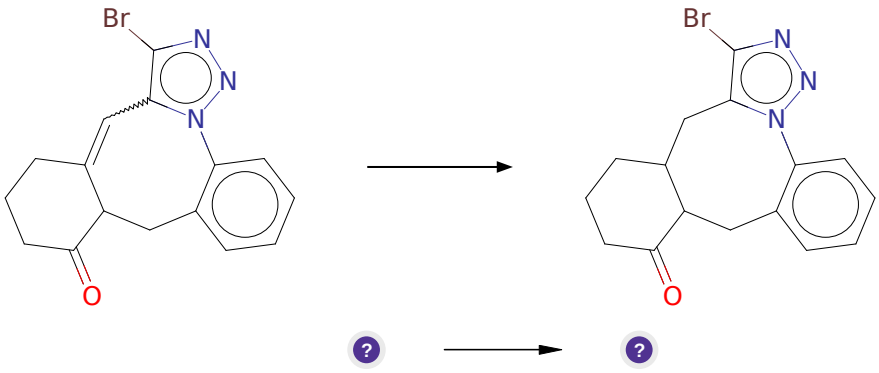
**Typical conditions:** RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

**Protections:** none

**Reference:** *10.1081/SCC-200051681* and *10.1055/s-1993-25981*

**Retrosynthesis ID:** 34041

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




**Substrates:**

1. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

**Products:**

1. O=C1CCCC2Cc3c(Br)nnn3-c3ccccc3CC12

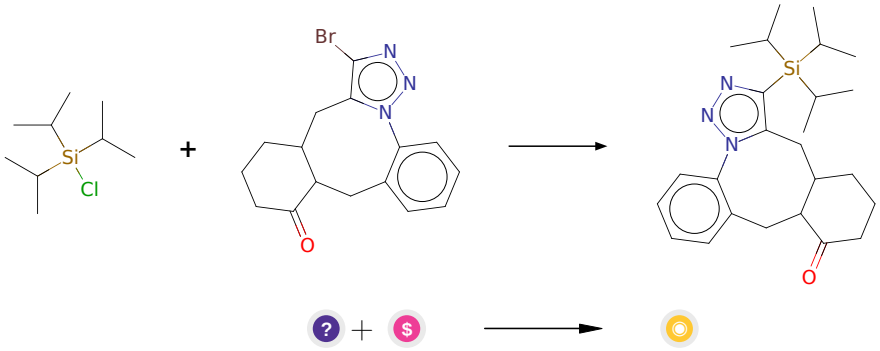
**Typical conditions:** H2.Pd/C or Pd(OH)2/C

**Protections:** none

**Reference:** DOI: *10.1021/jo980467g* and *10.1021/ja00175a039* and *10.1021/ja0296733* and *10.1021/ja049043w* (page S-4) and *10.1021/jo980128n* and *10.1021/ja4029928* and Patent: WO2014/207205 A1, 2014 page 16

**Retrosynthesis ID:** 9995780

### 2.1.11 Synthesis of arylsilanes




**Substrates:**

1. O=C1CCCC2Cc3c(Br)nnn3-c3ccccc3CC12
2. TIPSCl - *available at Sigma-Aldrich*

**Products:**

1. CC(C)[Si](c1nnn2c1CC1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

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

**Protections:**

| Functional group SMARTS | Classification | Protecting groups |
|---|---|---|
| [#6]C([#6])=O | carbonyls | 1.3-Dioxanes |
| | | 1.3-Dioxolanes |
| | | 1.3-Dithianes |
| | | 1.3-Dithiolanes |
| | | Dimethyl Acetals and Ketals |
| | | N,N-Dimethylhydrazones |

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

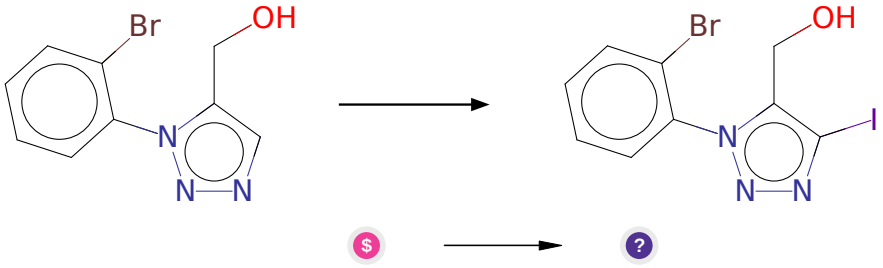
**Retrosynthesis ID:** 5370

## 2.2 Path 2

**Score:** 14411533.74

Figure 2: Outline of path 2

### 2.2.1 Iodination of aromatic compounds




**Substrates:**

1. [1-(2-bromophenyl)-1H-1,2,3-triazol-5-yl]methanol - *available at Sigma-Aldrich*

**Products:**

1. OCc1c(I)nnn1-c1ccccc1Br

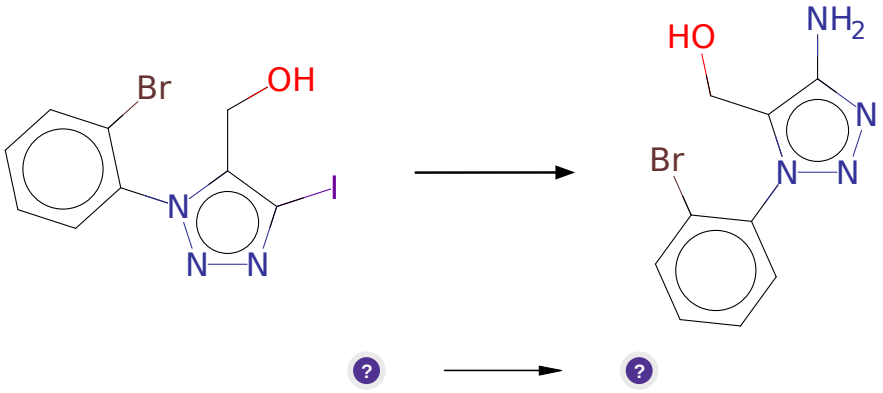
**Typical conditions:** I2 or other iodinating agent e.g. NIS

**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

### 2.2.2 Coupling of Ammonia with Aryl Halides




**Substrates:**

1. OCc1c(I)nnn1-c1ccccc1Br

**Products:**

1. Nc1nnn(-c2ccccc2Br)c1CO

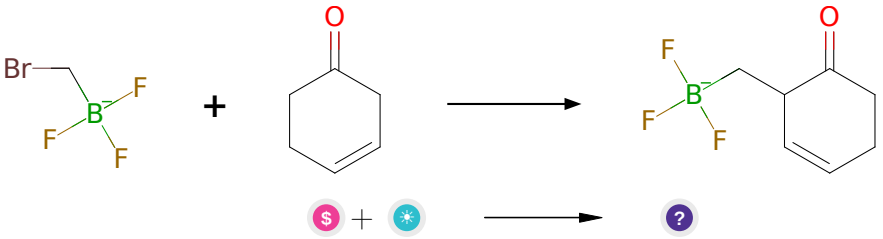
**Typical conditions:** Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

**Protections:** none

**Reference:** *10.1021/ja903049z* and *10.1021/jo9006738*

**Retrosynthesis ID:** 31016464

### 2.2.3 Alkylation of ketones




**Substrates:**

1. Potassium (bromomethyl)trifluoroborate - *available at Sigma-Aldrich*
2. cyclohex-3-enone

**Products:**

1. O=C1CCC=CC1C[B-](F)(F)F

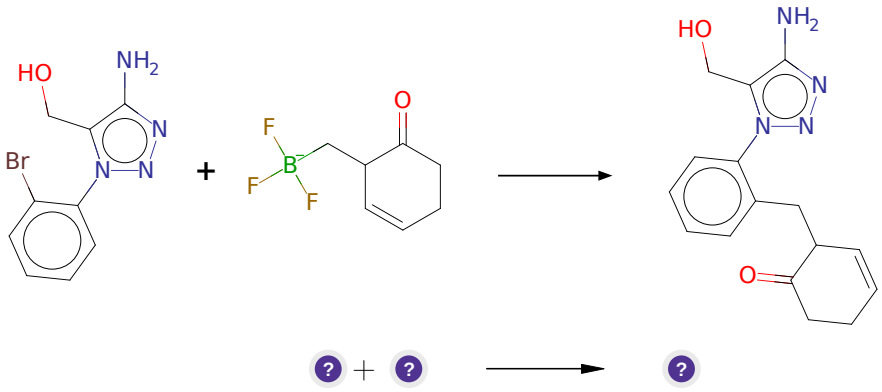
**Typical conditions:** LDA or other base.THF.-78C

**Protections:** none

**Reference:** DOI: *10.1021/ja0123554*

**Retrosynthesis ID:** 1868

### 2.2.4 Suzuki Coupling of arylbromides and alkyltrifluoroborates




**Substrates:**

1. Nc1nnn(-c2ccccc2Br)c1CO
2. O=C1CCC=CC1C[B-](F)(F)F

**Products:**

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

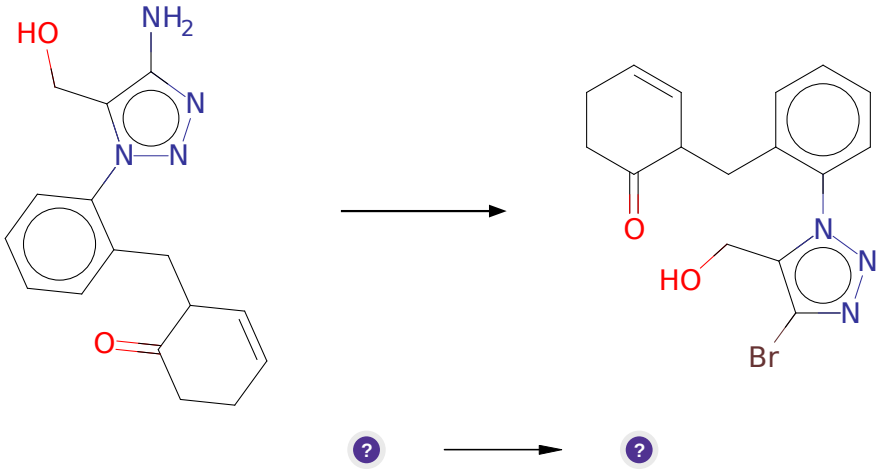
**Typical conditions:** Pd(OAc)2.SPhos.K3PO4.H2O.reflux

**Protections:** none

**Reference:** *10.1021/jo0343331* and EP1867650 p.36

**Retrosynthesis ID:** 10033481

### 2.2.5 Sandmeyer Reaction




**Substrates:**

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

**Products:**

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

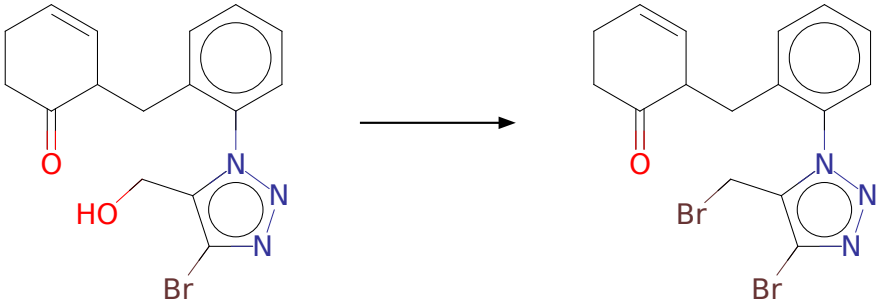
**Typical conditions:** IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

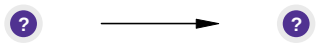
**Protections:** none

**Reference:** *10.1002/chem.201600278* and *10.1016/j.bmcl.2011.12.131* and *10.1016/j.ejmech.2013.01.046* and *10.1021/jm0002782* and *10.1002/ejoc.201300443* and *10.1021/jo052589w*(SI,page S3) and *10.1021/jm800527x* and *10.1016/j.bmcl.2015.04.098* and *10.1021/ja034563x*

**Retrosynthesis ID:** 29904

### 2.2.6 Appel Reaction





**Substrates:**

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

**Products:**

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

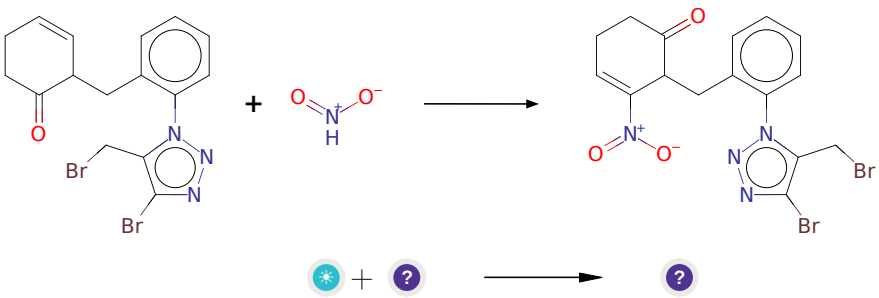
**Typical conditions:** PPh3.CBr4

**Protections:** none

**Reference:** *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

**Retrosynthesis ID:** 9990037

### 2.2.7 Nitration of aliphatic olefins



**Substrates:**

1. HNO2
2. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

**Products:**

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

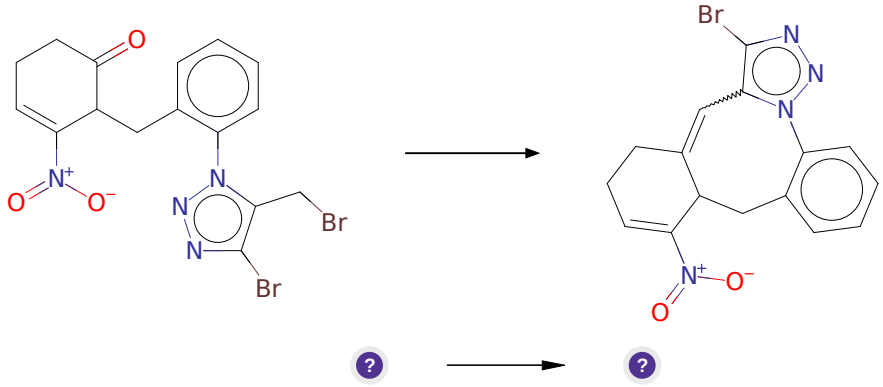
**Typical conditions:** Fe(NO2)3x9H2O.TEMPO.DCE.4A MS.80C

**Protections:** none

**Reference:** DOI: *10.1021/jo400598p*

**Retrosynthesis ID:** 1623

### 2.2.8 HWE/Wittig Olefination



**Substrates:**

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

**Products:**

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

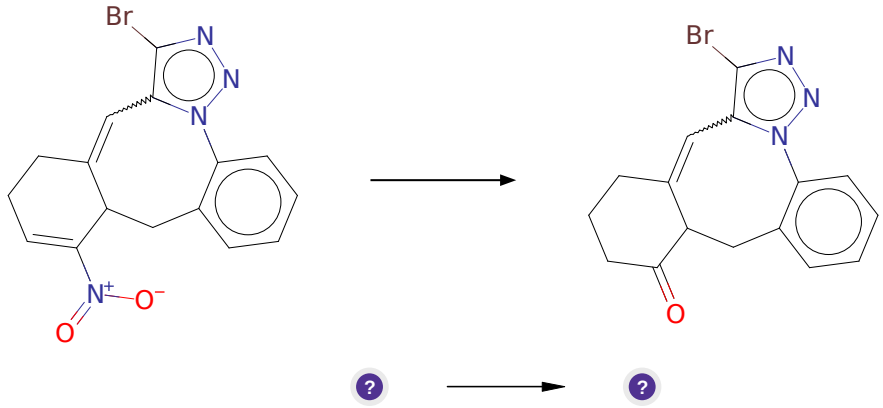
**Typical conditions:** 1.PPh3 or trialkylphosphite.2.base.aldehyde

**Protections:** none

**Reference:** *10.1002/anie.200705005* and *10.1021/ol052106a* and *10.1021/jo00075a064* and *10.1021/ol3027297*

**Retrosynthesis ID:** 24425

### 2.2.9 Synthesis of ketones from nitroalkenes



**Substrates:**

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

**Products:**

1. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

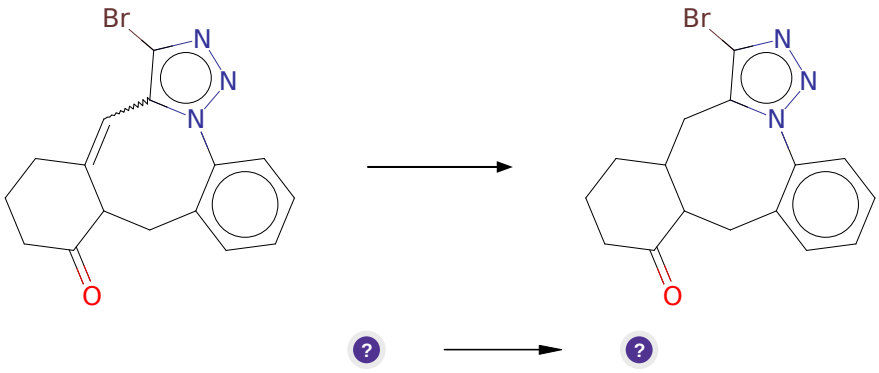
**Typical conditions:** RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

**Protections:** none

**Reference:** *10.1081/SCC-200051681* and *10.1055/s-1993-25981*

**Retrosynthesis ID:** 34041

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




**Substrates:**

1. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

**Products:**

1. O=C1CCCC2Cc3c(Br)nnn3-c3ccccc3CC12

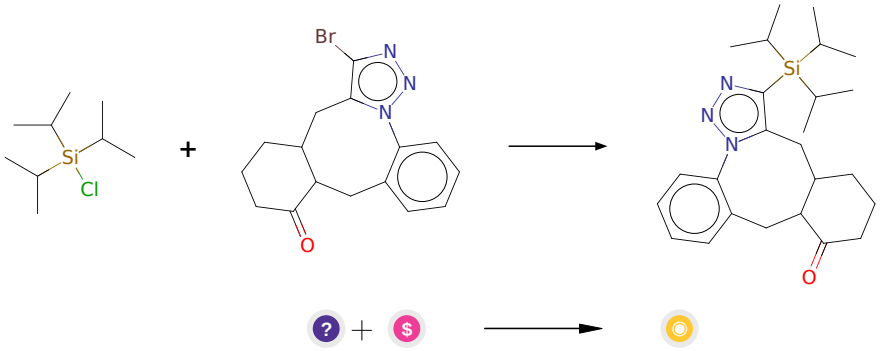
**Typical conditions:** H2.Pd/C or Pd(OH)2/C

**Protections:** none

**Reference:** DOI: *10.1021/jo980467g* and *10.1021/ja00175a039* and *10.1021/ja0296733* and *10.1021/ja049043w* (page S-4) and *10.1021/jo980128n* and *10.1021/ja4029928* and Patent: WO2014/207205 A1, 2014 page 16

**Retrosynthesis ID:** 9995780

### 2.2.11 Synthesis of arylsilanes




**Substrates:**

1. O=C1CCCC2Cc3c(Br)nnn3-c3ccccc3CC12
2. TIPSCl - *available at Sigma-Aldrich*

**Products:**

1. CC(C)[Si](c1nnn2c1CC1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

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

**Protections:**

| Functional group SMARTS | Classification | Protecting groups |
|---|---|---|
| [#6]C([#6])=O | carbonyls | 1.3-Dioxanes |
| | | 1.3-Dioxolanes |
| | | 1.3-Dithianes |
| | | 1.3-Dithiolanes |
| | | Dimethyl Acetals and Ketals |
| | | N,N-Dimethylhydrazones |

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

**Retrosynthesis ID:** 5370