# Paths of analysis*

AS1

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

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**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:** `346.85`

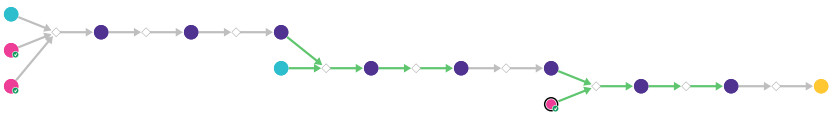
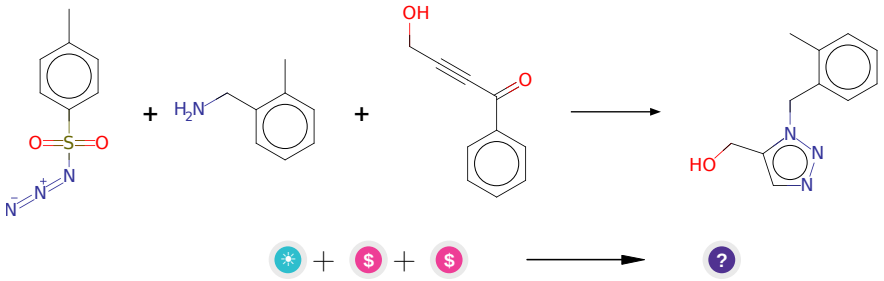


Figure 1: Outline of path 1

### 2.1.1 Metal-free multicomponent synthesis of triazoles




**Substrates:**

1. 4-hydroxybut-2-ynophenone
2. Tosyl azide solution - *available at Sigma-Aldrich*
3. 2-Methylbenzylamine - *available at Sigma-Aldrich*

**Products:**

1. Cc1ccccc1Cn1nncc1CO

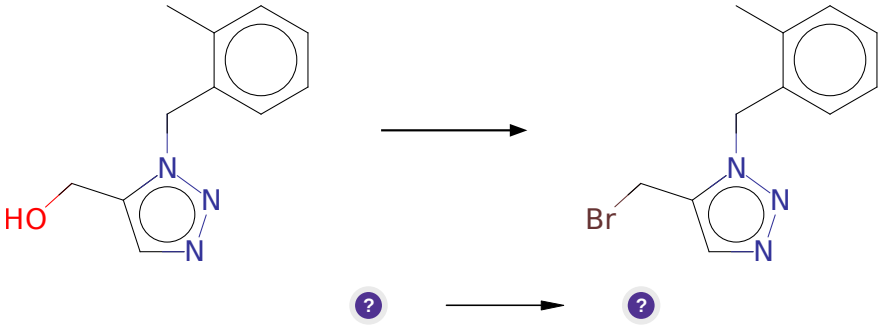
**Typical conditions:** 1. toluene.80C 2. LiOtBu.RT

**Protections:** none

**Reference:** DOI: *10.1002/anie.201307499*

**Retrosynthesis ID:** 6001

### 2.1.2 Appel Reaction




**Substrates:**

1. Cc1ccccc1Cn1nncc1CO

**Products:**

1. Cc1ccccc1Cn1nncc1CBr

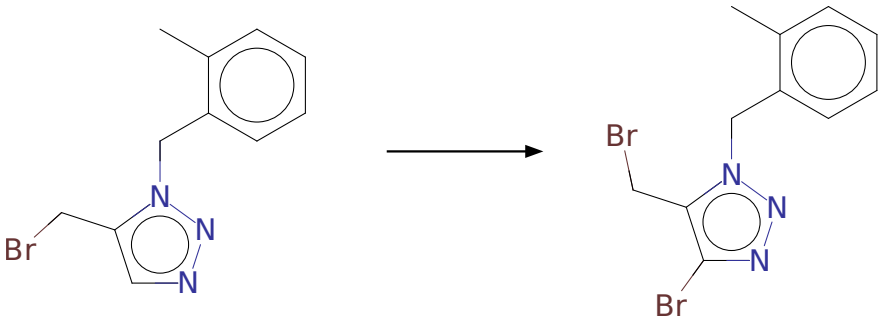
**Typical conditions:** PPh3.CBr4

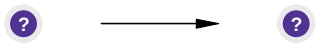
**Protections:** none

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

**Retrosynthesis ID:** 9990037

### 2.1.3 Bromination of aromatic compounds





**Substrates:**

1. Cc1ccccc1Cn1nncc1CBr

**Products:**

1. Cc1ccccc1Cn1nnc(Br)c1CBr

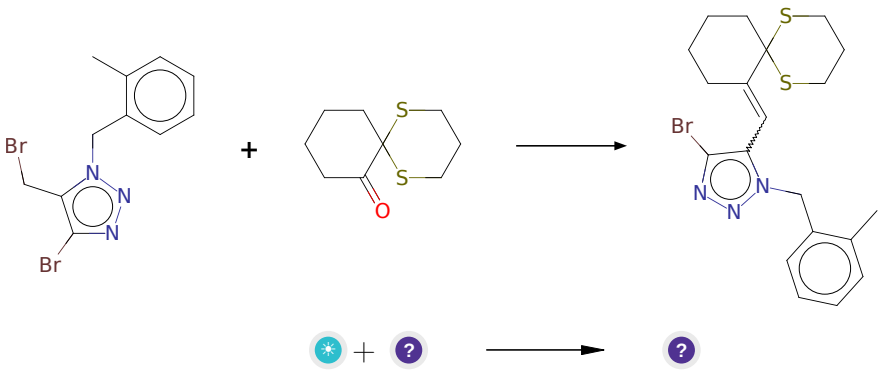
**Typical conditions:** Br2.Fe

**Protections:** none

**Reference:** *10.1021/acs.accounts.6b00120*

**Retrosynthesis ID:** 7777000

### 2.1.4 HWE/Wittig Olefination



**Substrates:**

1. 1,5-dithia-spiro[5.5]undecan-7-one
2. Cc1ccccc1Cn1nnc(Br)c1CBr

**Products:**

1. Cc1ccccc1Cn1nnc(Br)c1C=C1CCCCC12SCCCS2

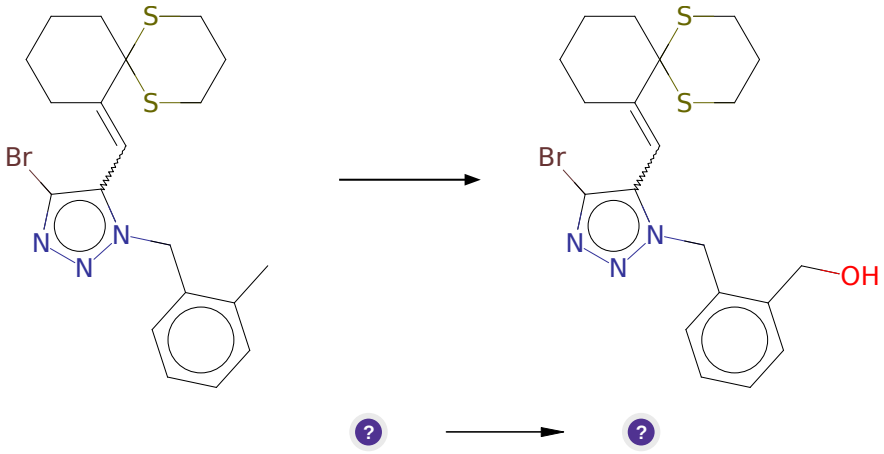
**Typical conditions:** 1.PPh3 or trialkylphosphite.2.base.aldehyde

**Protections:** none

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

**Retrosynthesis ID:** 24425

### 2.1.5 Hydroxylation of benzylic position




**Substrates:**

1. Cc1ccccc1Cn1nnc(Br)c1C=C1CCCCC12SCCCS2

**Products:**

1. OCc1ccccc1Cn1nnc(Br)c1C=C1CCCCC12SCCCS2

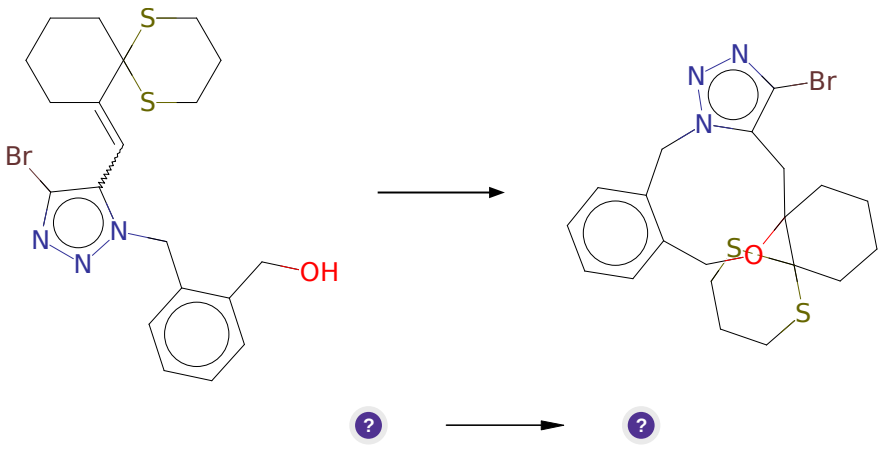
**Typical conditions:** 1.Ce(OTf)4.MeCN.2.NaBH4

**Protections:** none

**Reference:** *10.1039/B008843I* and WO2012137047 p.12

**Retrosynthesis ID:** 27139

### 2.1.6 Synthesis of teriary ethers



**Substrates:**

1. OCc1ccccc1Cn1nnc(Br)c1C=C1CCCCC12SCCCS2

**Products:**

1. Brc1nnn2c1CC1(CCCCC13SCCCS3)OCc1ccccc1C2

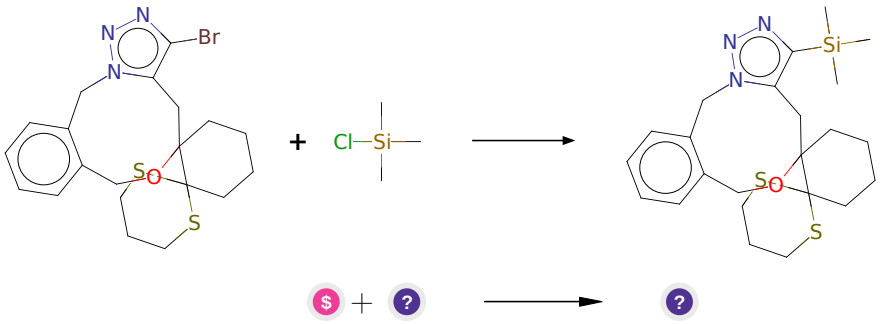
**Typical conditions:** H2SO4

**Protections:** none

**Reference:** *10.1016/j.tet.2009.10.055* and WO2009011551 (p.14 example 5) and *10.1002/chem.201304580* and *10.1021/jm9811209* and US2007/225280A1 p.58 and WO2009/62285A1 p.50 and CN106928032A p.0040

**Retrosynthesis ID:** 10001897

### 2.1.7 Synthesis of arylsilanes




**Substrates:**

1. TMSCl - *available at Sigma-Aldrich*
2. Brc1nnn2c1CC1(CCCCC13SCCCS3)OCc1ccccc1C2

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC13SCCCS3)OCc1ccccc1C2

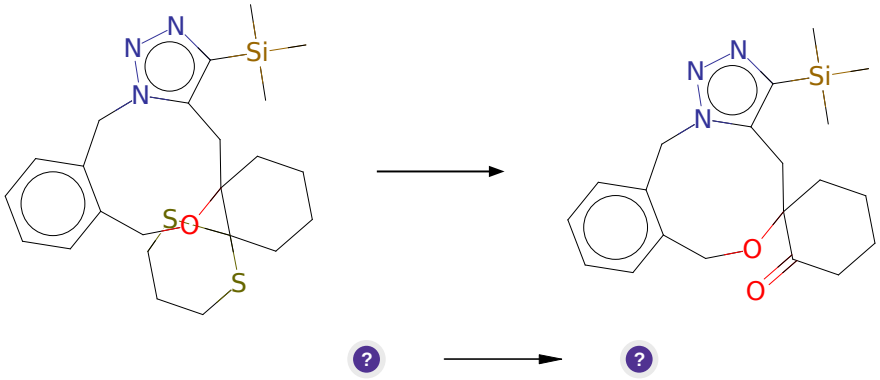
**Typical conditions:** 1.nBuLi.2.ClSnR3

**Protections:** none

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

**Retrosynthesis ID:** 5370

### 2.1.8 Synthesis of ketones from dithianes



**Substrates:**

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC13SCCCS3)OCc1ccccc1C2

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC1=O)OCc1ccccc1C2

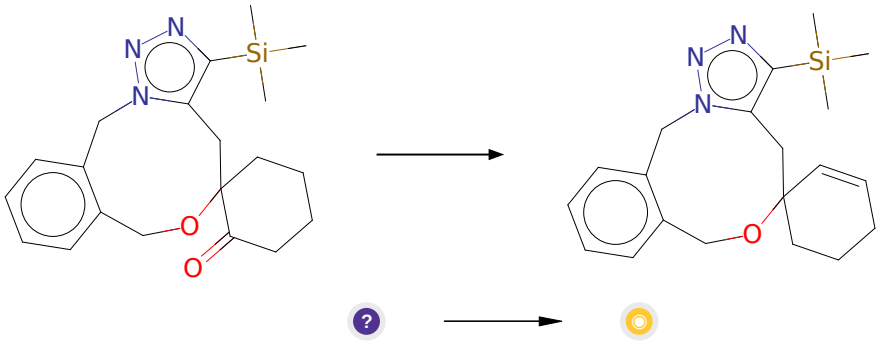
**Typical conditions:** MeI.CaCO3

**Protections:** none

**Reference:** *10.1016/j.tet.2013.09.075* and *10.1021/jo00007a015* and *10.1021/jo0610412* and *10.1021/ol901024t* and *10.1021/ol500553x* and *10.1021/jo0626459*

**Retrosynthesis ID:** 31724

### 2.1.9 Shapiro reaction



**Substrates:**

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC1=O)OCc1ccccc1C2

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

**Typical conditions:** 1.TsNH2NH2.2.N-BuLi

**Protections:** none

**Reference:** *10.1021/jm4008517* and *10.1016/j.bmc.2009.08.038* and *10.1021/jo00350a003*

**Retrosynthesis ID:** 9990398

## 2.2 Path 2

**Score:** `359.64`

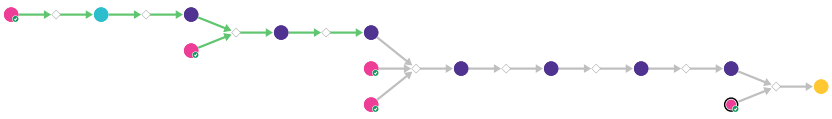
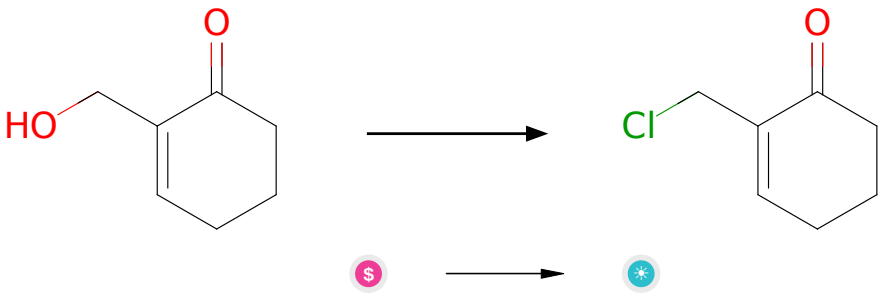


Figure 2: Outline of path 2

### 2.2.1 Synthesis of alkyl chlorides from alcohols




**Substrates:**

1. 2-(hydroxymethyl)cyclohex-2-en-1-one - *available at Sigma-Aldrich*

**Products:**

1. 2-chloromethyl-2-cyclohexen-1-one

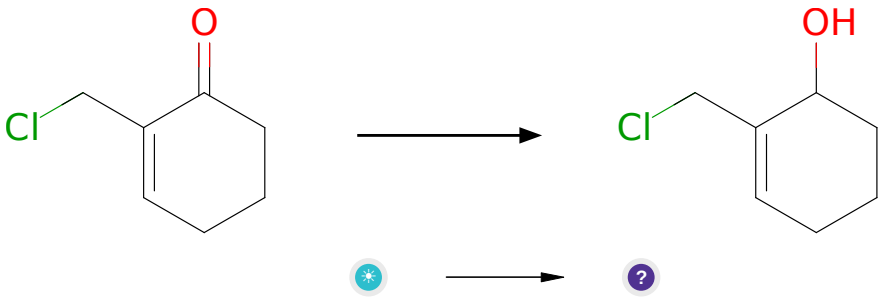
**Typical conditions:** cyanuric chloride.DMF.DCM.RT

**Protections:** none

**Reference:** DOI: *10.1021/ol017168p*

**Retrosynthesis ID:** 11617

### 2.2.2 Luche Reduction




**Substrates:**

1. 2-chloromethyl-2-cyclohexen-1-one

**Products:**

1. OC1CCCC=C1CCl

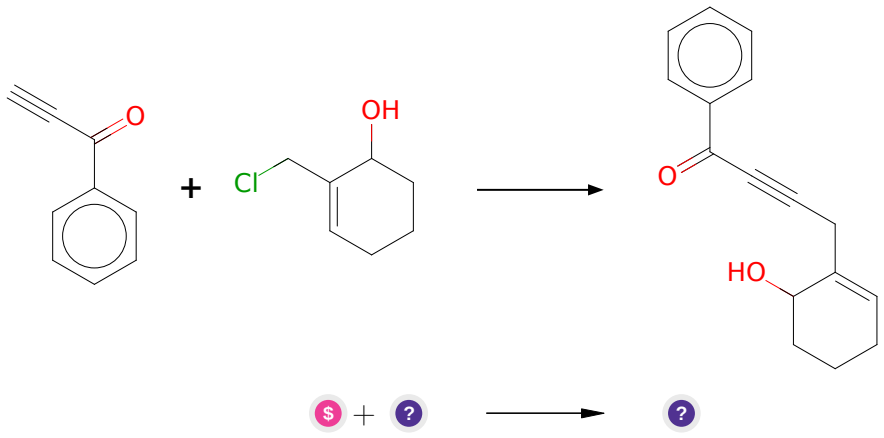
**Typical conditions:** CeCl3.NaBH4.MeOH

**Protections:** none

**Reference:** *10.1002/9780470638859.conrr400*

**Retrosynthesis ID:** 10180

### 2.2.3 Alkylation of terminal Alkynes



**Substrates:**

1. 1-Phenylpropynone - *available at Sigma-Aldrich*
2. OC1CCCC=C1CCl

**Products:**

1. O=C(C#CCC1=CCCCC1O)c1ccccc1

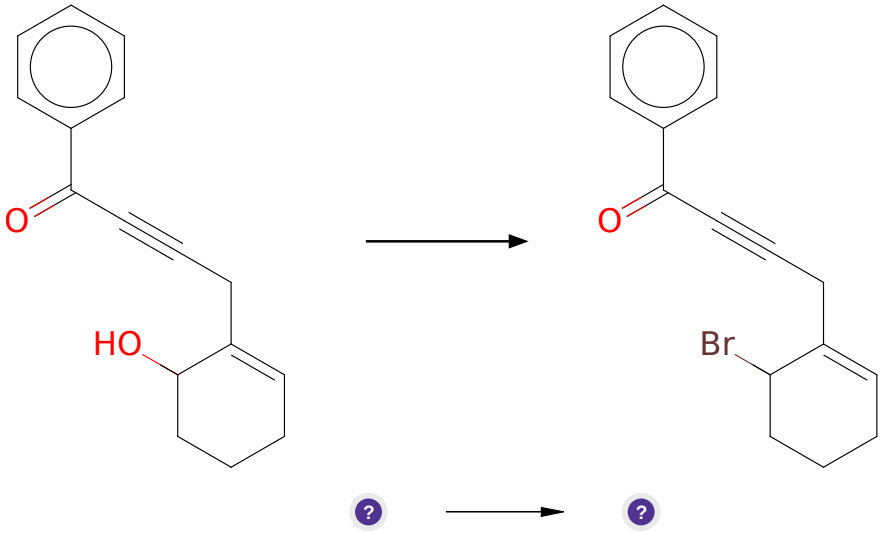
**Typical conditions:** K2CO3.CuI.TBAB.solvent

**Protections:** none

**Reference:** DOI: *10.1021/ja064223m* (SI, page S-3) AND *10.1016/j.tet.2008.01.139* AND *10.1021/ol049474j* AND Patent: US5231232 A1 , page 4

**Retrosynthesis ID:** 10617

### 2.2.4 Appel Reaction




**Substrates:**

1. O=C(C#CCC1=CCCCC1O)c1ccccc1

**Products:**

1. O=C(C#CCC1=CCCCC1Br)c1ccccc1

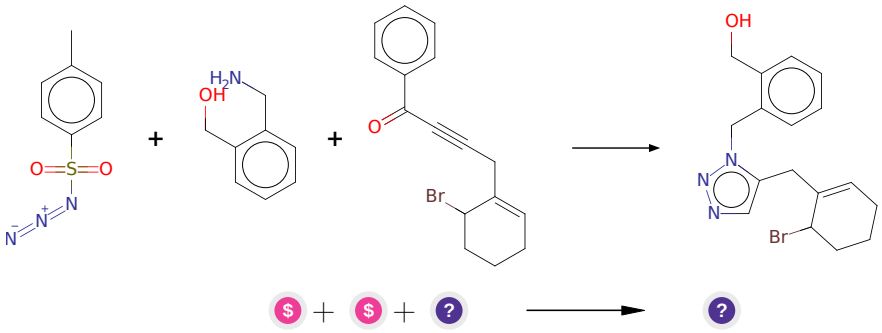
**Typical conditions:** PPh3.CBr4

**Protections:** none

**Reference:** *10.1016/j.jfluchem.2015.03.009* and *10.1016/j.tet.2005.12.006* and *10.1021/jm00161a029* and *10.1055/s-1995-5215*

**Retrosynthesis ID:** 9990042

### 2.2.5 Metal-free multicomponent synthesis of triazoles




**Substrates:**

1. Tosyl azide solution - *available at Sigma-Aldrich*
2. [2-(aminomethyl)phenyl]methanol - *available at Sigma-Aldrich*
3. O=C(C#CCC1=CCCCC1Br)c1ccccc1

**Products:**

1. OCc1ccccc1Cn1nncc1CC1=CCCCC1Br

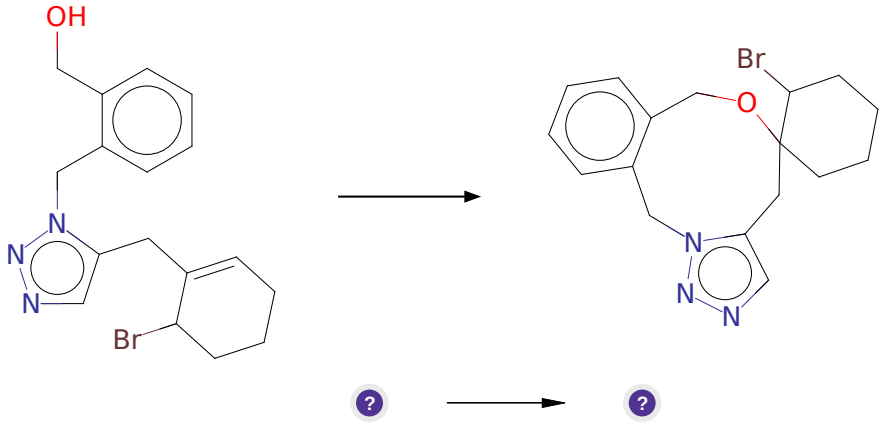
**Typical conditions:** 1. toluene.80C 2. LiOtBu.RT

**Protections:** none

**Reference:** DOI: *10.1002/anie.201307499*

**Retrosynthesis ID:** 6001

### 2.2.6 Synthesis of teriary ethers




**Substrates:**

1. OCc1ccccc1Cn1nncc1CC1=CCCCC1Br

**Products:**

1. BrC1CCCCC12Cc1cnnn1Cc1ccccc1CO2

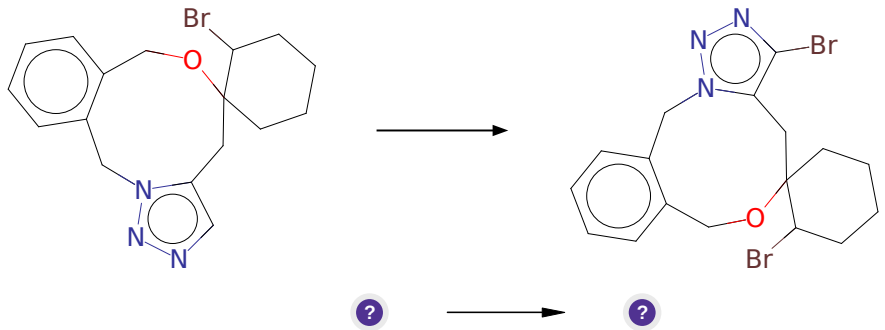
**Typical conditions:** H2SO4

**Protections:** none

**Reference:** *10.1016/j.tet.2009.10.055* and WO2009011551 (p.14 example 5) and *10.1002/chem.201304580* and *10.1021/jm9811209* and US2007/225280A1 p.58 and WO2009/62285A1 p.50 and CN106928032A p.0040

**Retrosynthesis ID:** 10001897

### 2.2.7 Bromination of aromatic compounds




**Substrates:**

1. BrC1CCCCC12Cc1cnnn1Cc1ccccc1CO2

**Products:**

1. Brc1nnn2c1CC1(CCCCC1Br)OCc1ccccc1C2

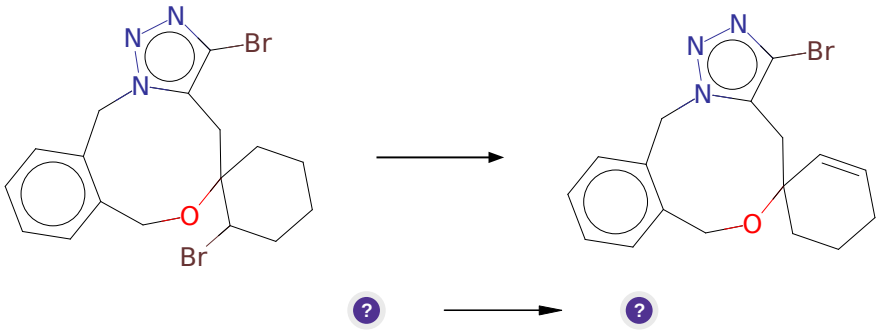
**Typical conditions:** Br2.Fe

**Protections:** none

**Reference:** *10.1021/acs.accounts.6b00120*

**Retrosynthesis ID:** 7777000

### 2.2.8 Elimination of bromide




**Substrates:**

1. Brc1nnn2c1CC1(CCCCC1Br)OCc1ccccc1C2

**Products:**

1. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

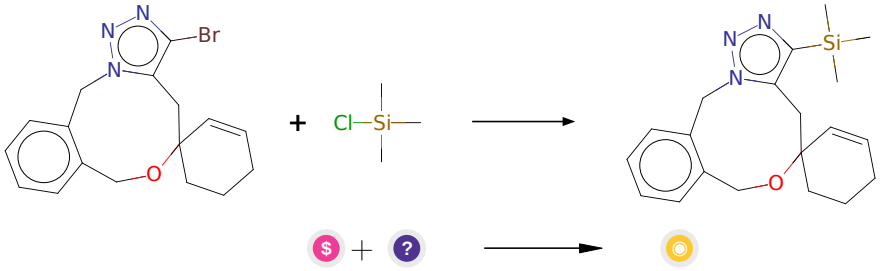
**Typical conditions:** K2CO3.DMF

**Protections:** none

**Reference:** *10.1016/j.jfluchem.2011.08.011* and *10.1039/P19920002971* and *10.1002/cber.19841170909* and *10.1021/ja01570a042*

**Retrosynthesis ID:** 23585

### 2.2.9 Synthesis of arylsilanes




**Substrates:**

1. TMSCl - *available at Sigma-Aldrich*
2. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

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

**Protections:** none

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

**Retrosynthesis ID:** 5370

## 2.3 Path 3

**Score:** 389.45

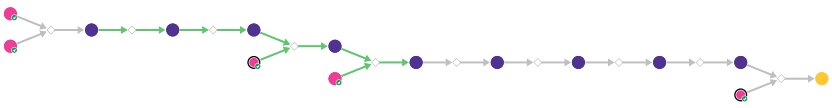
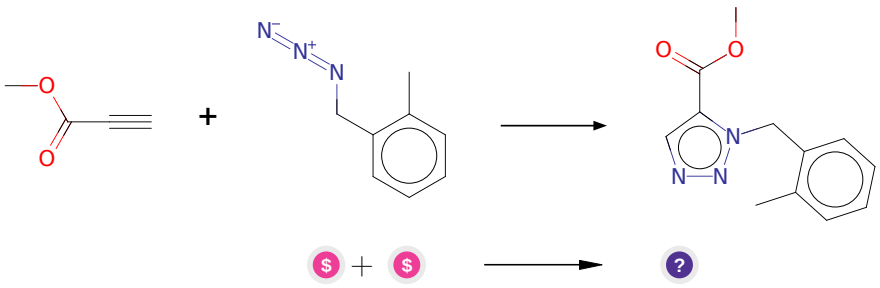


Figure 3: Outline of path 3

### 2.3.1 1,3-Dipolar cycloaddition of azides with electron-deficient alkynes



**Substrates:**

1. Methyl propiolate - *available at Sigma-Aldrich*
2. Azido-o-xylene solution - *available at Sigma-Aldrich*

**Products:**

1. COC(=O)c1cnnn1Cc1ccccc1C

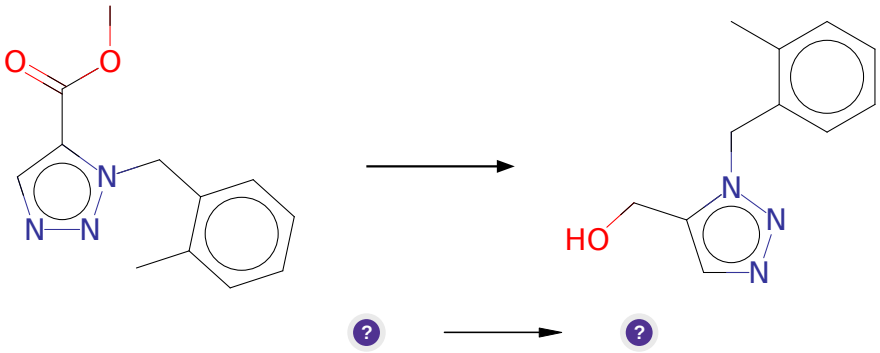
**Typical conditions:** H2O.rt

**Protections:** none

**Reference:** DOI: *10.1016/j.tetlet.2004.02.089*

**Retrosynthesis ID:** 295219

### 2.3.2 Esters reduction with LAH



**Substrates:**

1. COC(=O)c1cnnn1Cc1ccccc1C

**Products:**

1. Cc1ccccc1Cn1nncc1CO

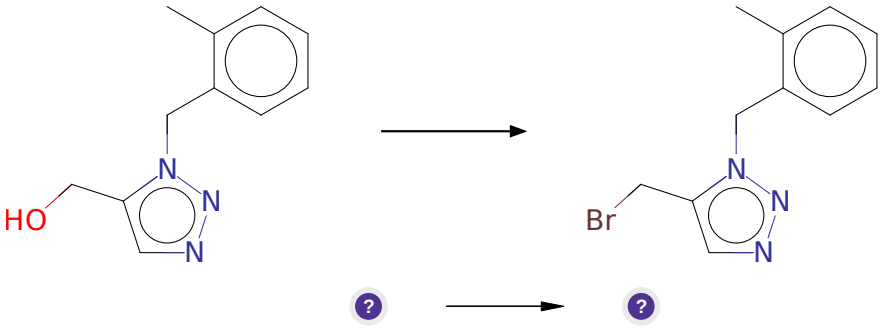
**Typical conditions:** LiAlH4.THF.0-20 C

**Protections:** none

**Reference:** *10.1016/j.ejmech.2019.112011* p. 5, 10 and *10.1016/j.ejmech.2020.112910* p. 3, 7

**Retrosynthesis ID:** 9910006

### 2.3.3 Appel Reaction




**Substrates:**

1. Cc1ccccc1Cn1nncc1CO

**Products:**

1. Cc1ccccc1Cn1nncc1CBr

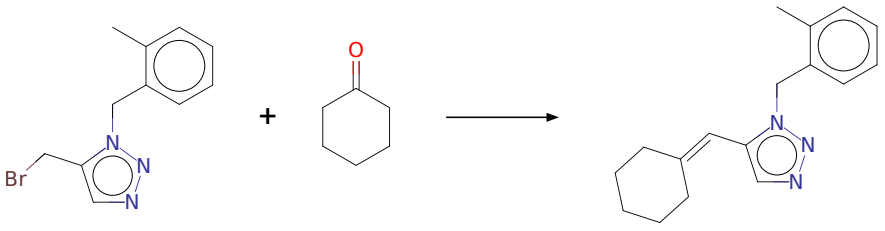
**Typical conditions:** PPh3.CBr4

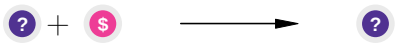
**Protections:** none

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

**Retrosynthesis ID:** 9990037

### 2.3.4 HWE/Wittig Olefination





**Substrates:**

1. Cc1ccccc1Cn1nncc1CBr
2. Cyclohexanone - *available at Sigma-Aldrich*

**Products:**

1. Cc1ccccc1Cn1nncc1C=C1CCCCC1

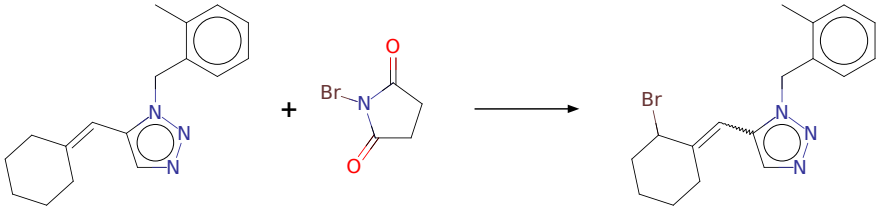
**Typical conditions:** 1.PPh3 or trialkylphosphite.2.base.aldehyde

**Protections:** none

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

**Retrosynthesis ID:** 24425

### 2.3.5 Wohl-Ziegler Bromination




**Substrates:**

1. N-Bromosuccinimide - *available at Sigma-Aldrich*
2. Cc1ccccc1Cn1nncc1C=C1CCCCC1

**Products:**

1. Cc1ccccc1Cn1nncc1C=C1CCCCC1Br

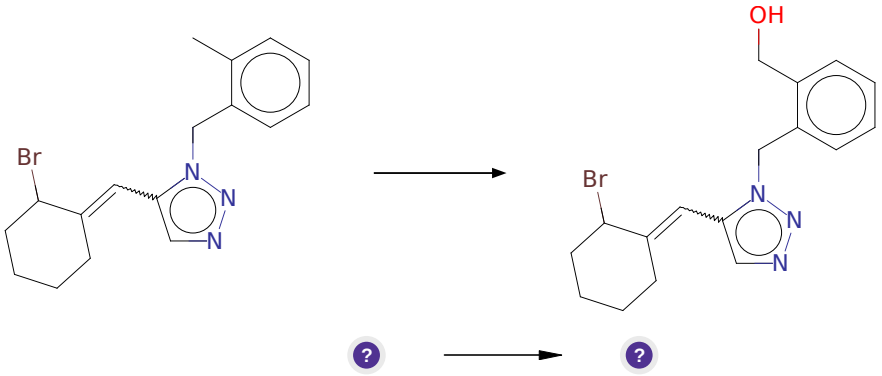
**Typical conditions:** NBS.AIBN or (BzO)2 or heat

**Protections:** none

**Reference:** *10.1002/bscb.19830920407* and *10.1002/prac.19813230417* and *10.1002/cbic.201402000*

**Retrosynthesis ID:** 245553

### 2.3.6 Hydroxylation of benzylic position




**Substrates:**

1. Cc1ccccc1Cn1nncc1C=C1CCCCC1Br

**Products:**

1. OCc1ccccc1Cn1nncc1C=C1CCCCC1Br

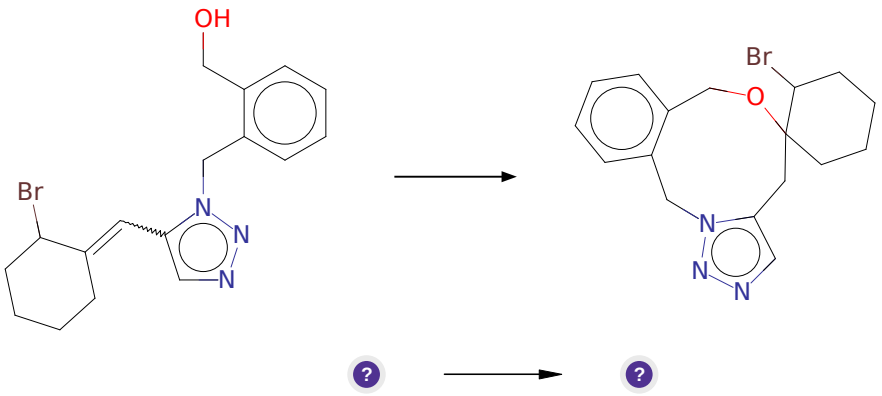
**Typical conditions:** 1.Ce(OTf)4.MeCN.2.NaBH4

**Protections:** none

**Reference:** *10.1039/B008843I* and WO2012137047 p.12

**Retrosynthesis ID:** 27139

### 2.3.7 Synthesis of teriary ethers




**Substrates:**

1. OCc1ccccc1Cn1nncc1C=C1CCCCC1Br

**Products:**

1. BrC1CCCCC12Cc1cnnn1Cc1ccccc1CO2

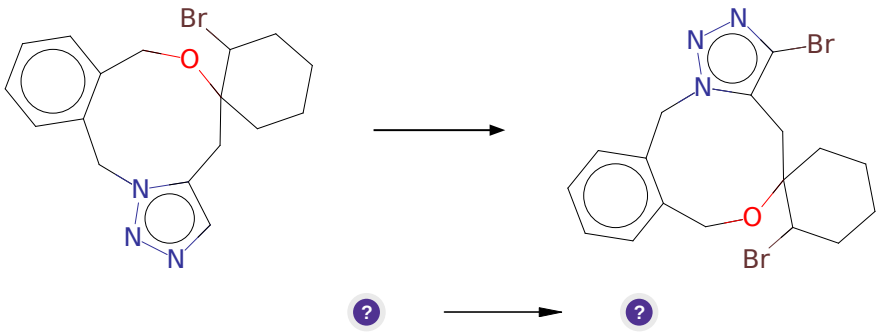
**Typical conditions:** H2SO4

**Protections:** none

**Reference:** *10.1016/j.tet.2009.10.055* and WO2009011551 (p.14 example 5) and *10.1002/chem.201304580* and *10.1021/jm9811209* and US2007/225280A1 p.58 and WO2009/62285A1 p.50 and CN106928032A p.0040

**Retrosynthesis ID:** 10001897

### 2.3.8 Bromination of aromatic compounds




**Substrates:**

1. BrC1CCCCC12Cc1cnnn1Cc1ccccc1CO2

**Products:**

1. Brc1nnn2c1CC1(CCCCC1Br)OCc1ccccc1C2

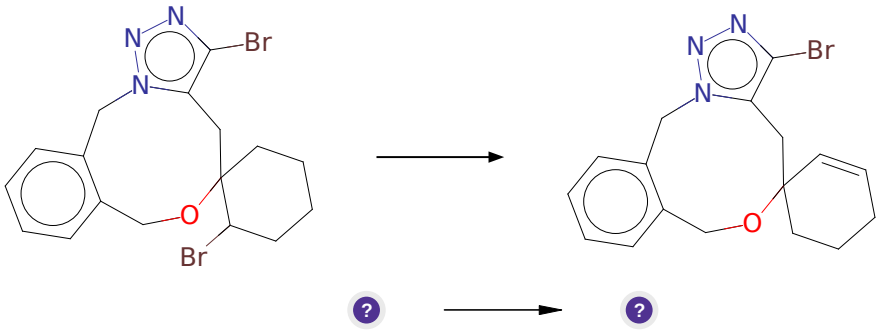
**Typical conditions:** Br2.Fe

**Protections:** none

**Reference:** *10.1021/acs.accounts.6b00120*

**Retrosynthesis ID:** 7777000

### 2.3.9 Elimination of bromide



**Substrates:**

1. Brc1nnn2c1CC1(CCCCC1Br)OCc1ccccc1C2

**Products:**

1. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

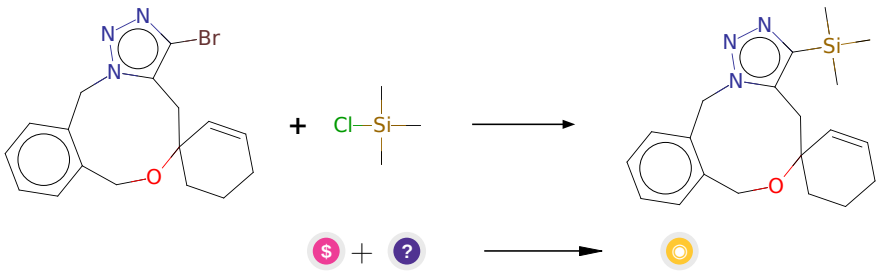
**Typical conditions:** K2CO3.DMF

**Protections:** none

**Reference:** *10.1016/j.jfluchem.2011.08.011* and *10.1039/P19920002971* and *10.1002/cber.19841170909* and *10.1021/ja01570a042*

**Retrosynthesis ID:** 23585

### 2.3.10 Synthesis of arylsilanes



**Substrates:**

1. TMSCl - *available at Sigma-Aldrich*
2. Brc1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

**Products:**

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCc1ccccc1C2

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

**Protections:** none

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

**Retrosynthesis ID:** 5370