Paths of analysis*

AS6

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

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

2.1 Path 1

Score: `145.10`

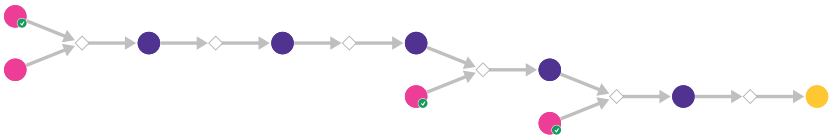
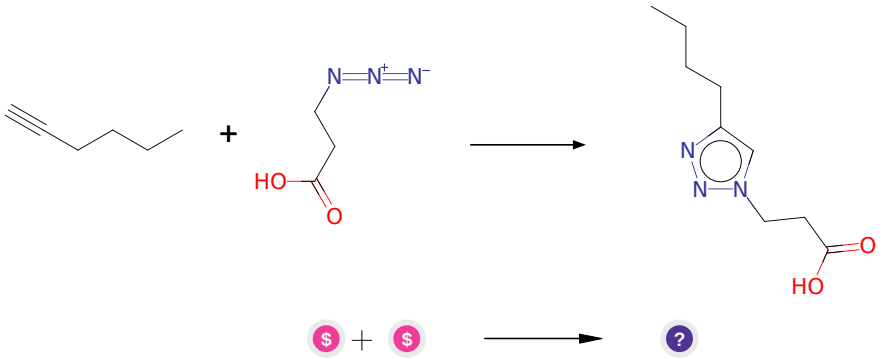


Figure 1: Outline of path 1

2.1.1 Huisgen Cycloaddition



Substrates:

1. 1-Hexyne - *available at Sigma-Aldrich*
2. 3-azidopropanoic acid - *SynthonixCorporation*

Products:

1. CCCCc1cn(CCC(=O)O)nn1

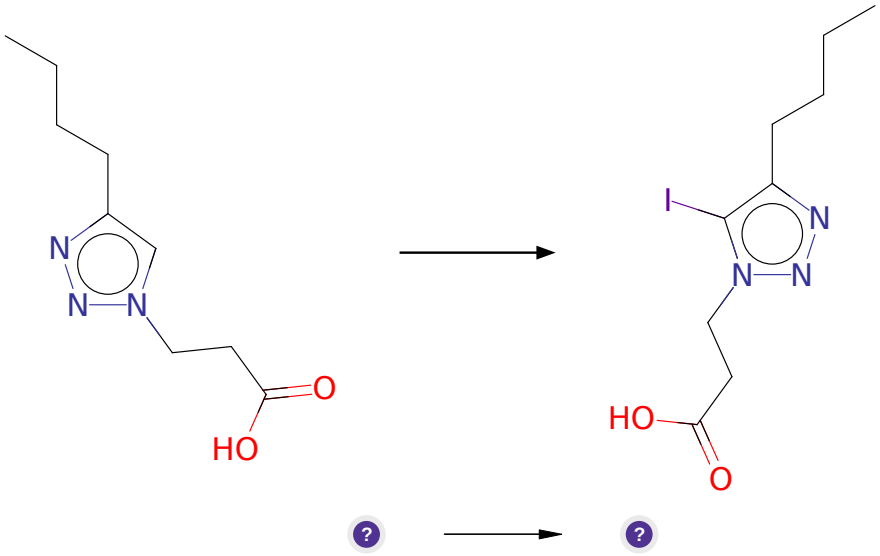
Typical conditions: Cu(I).H2O

Protections: none

Reference: *10.1039/PS9610000357* and *10.1016/S1359-6446(03)02933-7* and *10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5*

Retrosynthesis ID: 10268

2.1.2 Iodination of aromatic compounds



Substrates:

1. CCCCc1cn(CCC(=O)O)nn1

Products:

1. CCCCc1nnn(CCC(=O)O)c1I

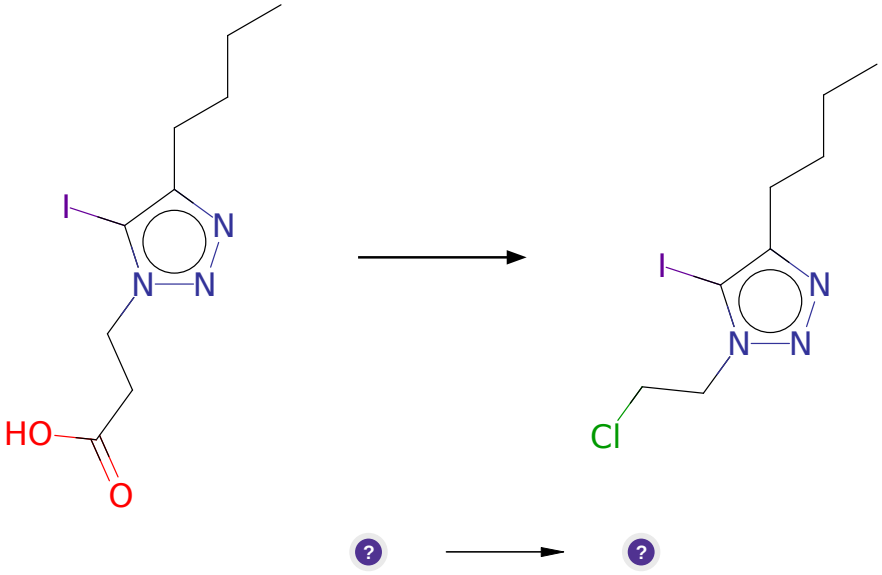
Typical conditions: I2 or other iodinating agent e.g. NIS

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

2.1.3 Synthesis of alkyl chlorides from carboxylic acids



Substrates:

1. CCCCc1nnn(CCC(=O)O)c1I

Products:

1. CCCCc1nnn(CCCl)c1I

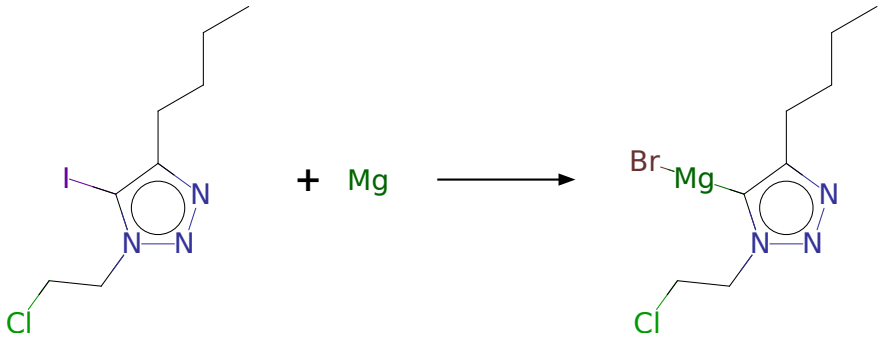
Typical conditions: Ag(Phen)2OTf.OtBu.Cl.acetonitrile.RT

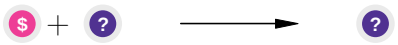
Protections: none

Reference: DOI: *10.1021/ja210361z*

Retrosynthesis ID: 11619

2.1.4 Synthesis of aryl Grignard reagents





Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. CCCCc1nnn(CCCl)c1I

Products:

1. CCCCc1nnn(CCCl)c1[Mg]Br

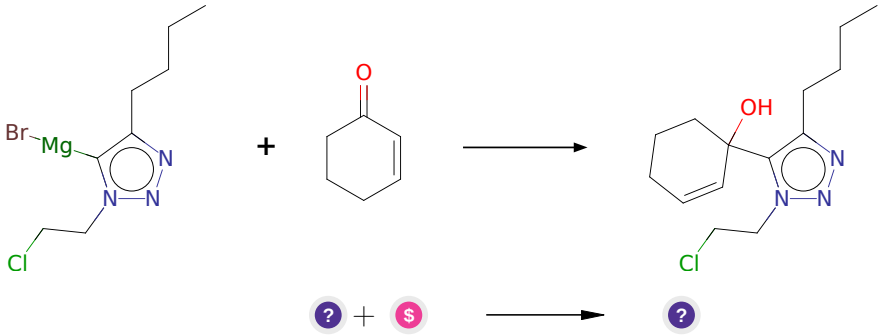
Typical conditions: iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and WO2014123793 p.137 and *10.1021/jm400491x* and *10.3762/bjoc.12.36*

Retrosynthesis ID: 10011460

2.1.5 Grignard-Type Reaction



Substrates:

1. CCCCc1nnn(CCCl)c1[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. CCCCc1nnn(CCCl)c1C1(O)C=CCCC1

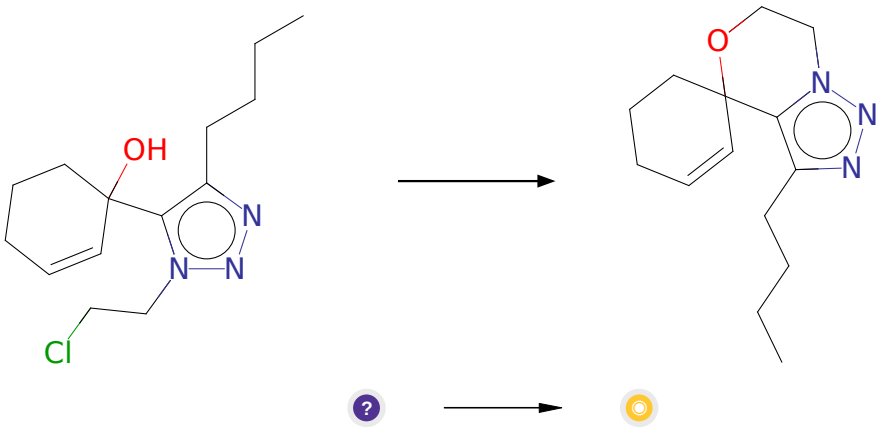
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.1.6 Alkylation of tertiary alcohols



Substrates:

1. CCCCc1nnn(CCCl)c1C1(O)C=CCCC1

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

Typical conditions: K2CO3.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: `193.93`

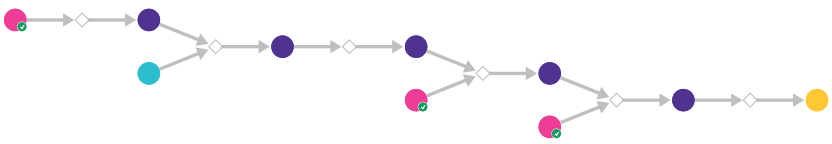
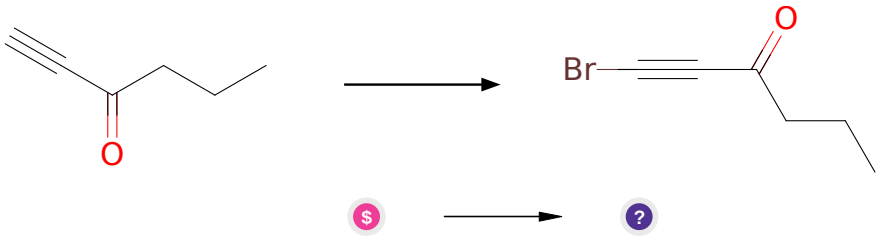


Figure 2: Outline of path 2

2.2.1 Synthesis of bromoacetylenes



Substrates:

1. hex-1-yn-3-one - *available at Sigma-Aldrich*

Products:

1. CCCC(=O)C#CBr

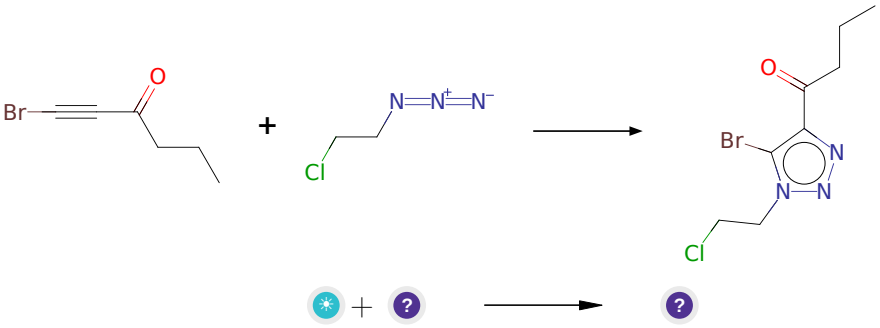
Typical conditions: NBS.acetone

Protections: none

Reference: *10.1021/ja5004747*

Retrosynthesis ID: 5325

2.2.2 Synthesis of triazoles from azides and haloalkynes



Substrates:

1. 1-azido-2-chlor-aethan
2. CCCC(=O)C#CBr

Products:

1. CCCC(=O)c1nnn(CCCl)c1Br

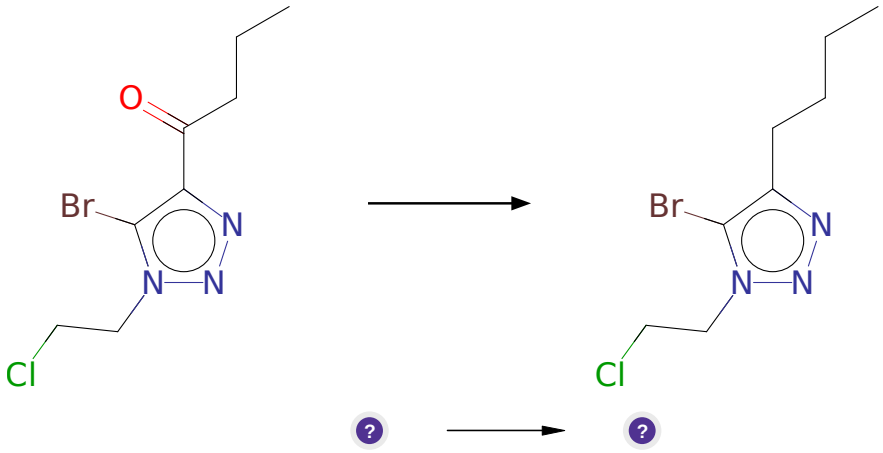
Typical conditions: CpRuCl(cod).ACN

Protections: none

Reference: *10.1002/chem.201402559*

Retrosynthesis ID: 31456

2.2.3 Clemmensen Reduction



Substrates:

1. CCCC(=O)c1nnn(CCCl)c1Br

Products:

1. CCCCc1nnn(CCCl)c1Br

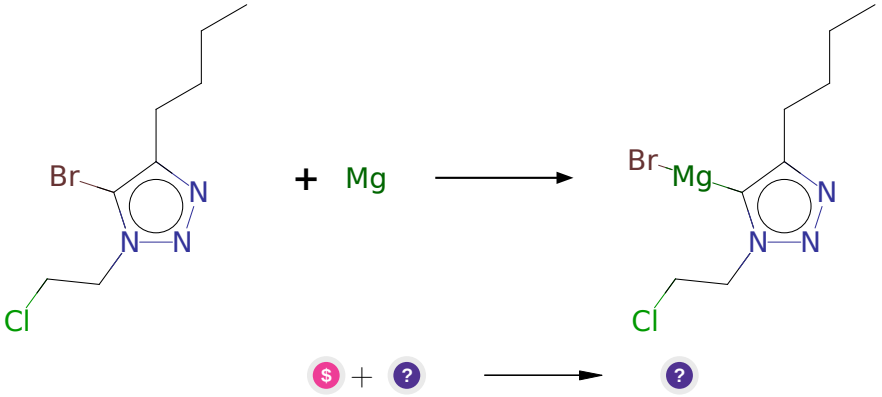
Typical conditions: Zn(Hg).HCl.H2O.EtOH.65 C

Protections: none

Reference: *10.1016/j.bmc.2014.09.022* p. 5873, 5879 and *10.1007/s00044-017-2105-5* p. 828, 819

Retrosynthesis ID: 245

2.2.4 Synthesis of aryl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. CCCCc1nnn(CCCl)c1Br

Products:

1. CCCCc1nnn(CCCl)c1[Mg]Br

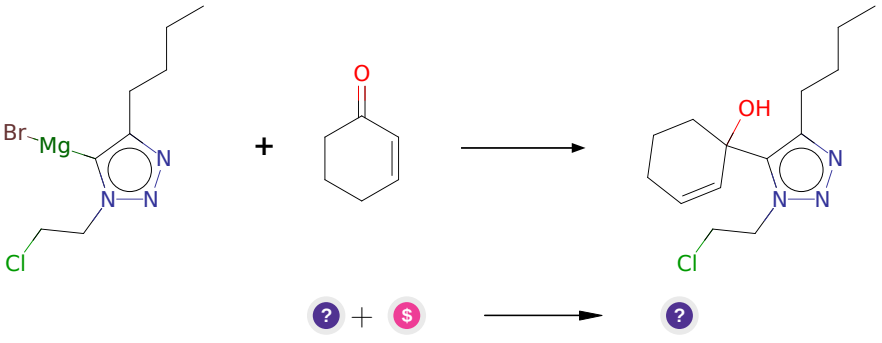
Typical conditions: iPrMgCl.THF or other conditions like BuLi.MgBr2 or Mg.THF

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and *10.1002/anie.200454084* and *10.1021/ol400150z*

Retrosynthesis ID: 10011461

2.2.5 Grignard-Type Reaction



Substrates:

1. CCCCc1nnn(CCCl)c1[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. CCCCc1nnn(CCCl)c1C1(O)C=CCCC1

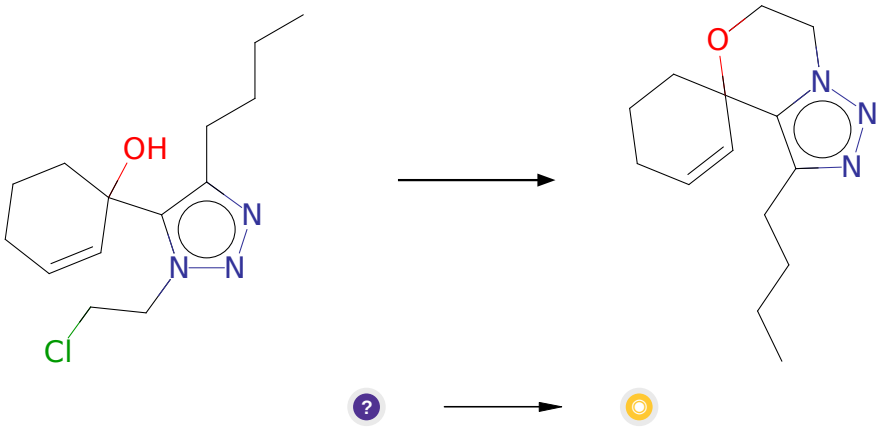
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.2.6 Alkylation of tertiary alcohols



Substrates:

1. CCCCc1nnn(CCCl)c1C1(O)C=CCCC1

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

Typical conditions: K2CO3.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: 193.93

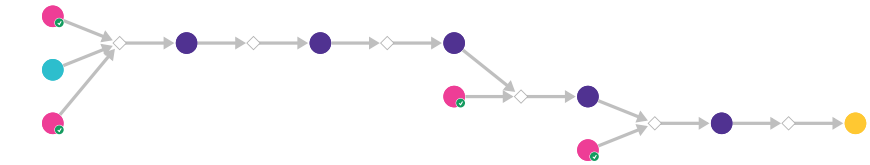
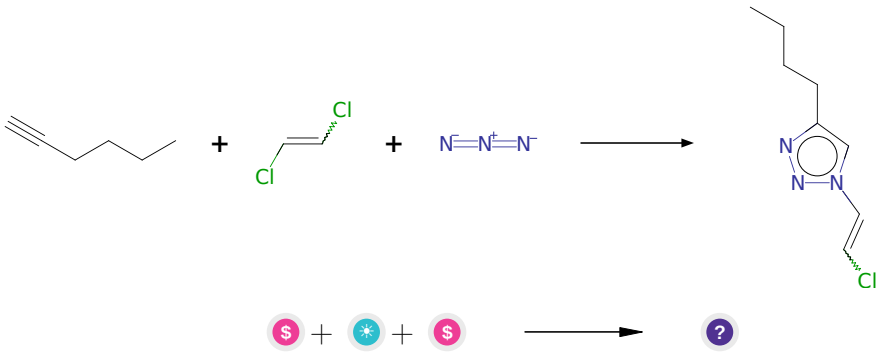


Figure 3: Outline of path 3

2.3.1 One-pot synthesis of triazoles from alkyl halides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. vinylene chloride
3. 1-Hexyne - *available at Sigma-Aldrich*

Products:

1. CCCCc1cn(C=CCl)nn1

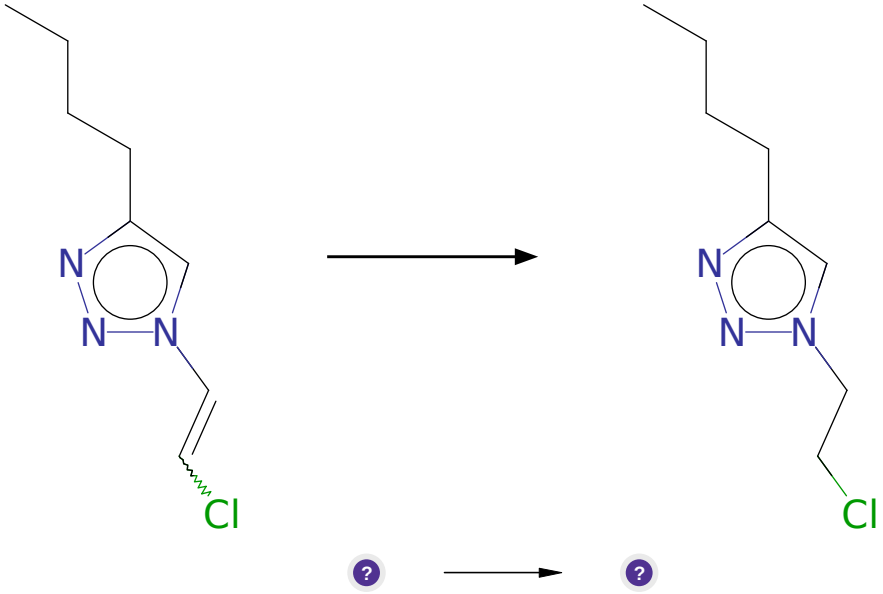
Typical conditions: Cu(II).sodium ascorbate.DMF/H2O

Protections: none

Reference: DOI: *10.1021/ol048859z*

Retrosynthesis ID: 245700

2.3.2 Homogenous Reduction of C=C Double Bond



Substrates:

1. CCCCc1cn(C=CCl)nn1

Products:

1. CCCCc1cn(CCCl)nn1

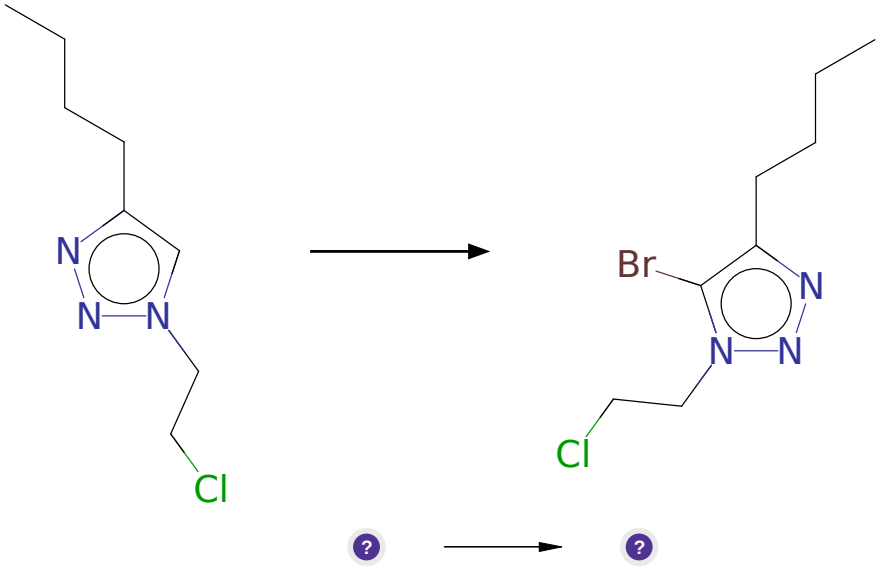
Typical conditions: H2.Pd/C or Pd(OH)2/C

Protections: none

Reference: DOI: *10.1021/ja0629110* and *10.1021/jo0602367* and *10.1021/jo980467g* and *10.1021/ol702231j* (SI, page SI 22) and *10.1002/anie.200503303* and *10.1021/ja011338b* (Pt/C tez)

Retrosynthesis ID: 9995778

2.3.3 Bromination of aromatic compounds



Substrates:

1. CCCCc1cn(CCCl)nn1

Products:

1. CCCCc1nnn(CCCl)c1Br

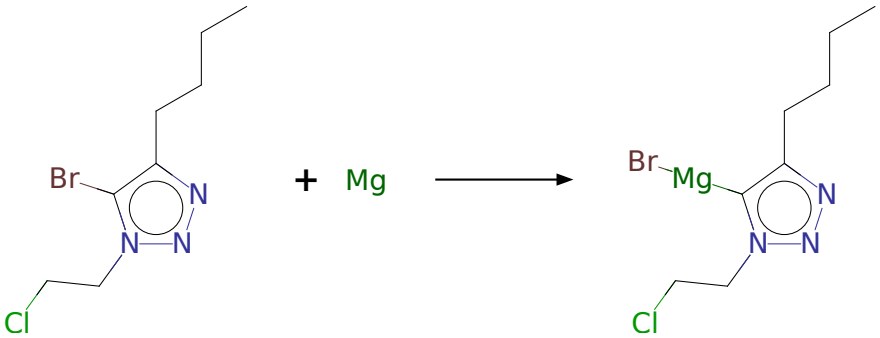
Typical conditions: Br2.Fe

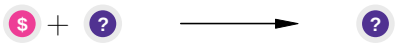
Protections: none

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

Retrosynthesis ID: 7777000

2.3.4 Synthesis of aryl Grignard reagents





Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. CCCCc1nnn(CCCl)c1Br

Products:

1. CCCCc1nnn(CCCl)c1[Mg]Br

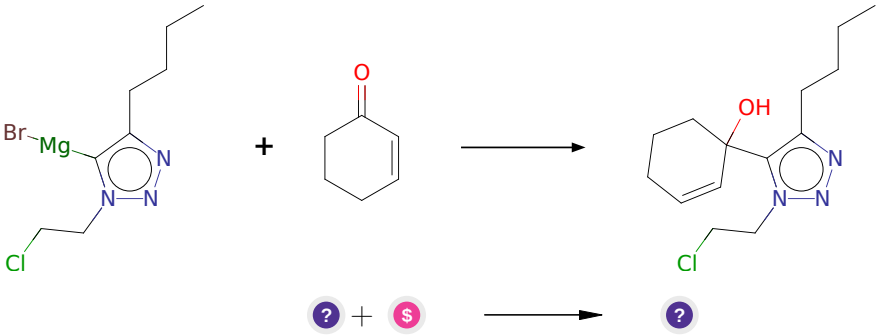
Typical conditions: iPrMgCl.THF or other conditions like BuLi.MgBr2 or Mg.THF

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and *10.1002/anie.200454084* and *10.1021/ol400150z*

Retrosynthesis ID: 10011461

2.3.5 Grignard-Type Reaction



Substrates:

1. CCCCc1nnn(CCCl)c1[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. CCCCc1nnn(CCCl)c1C1(O)C=CCCC1

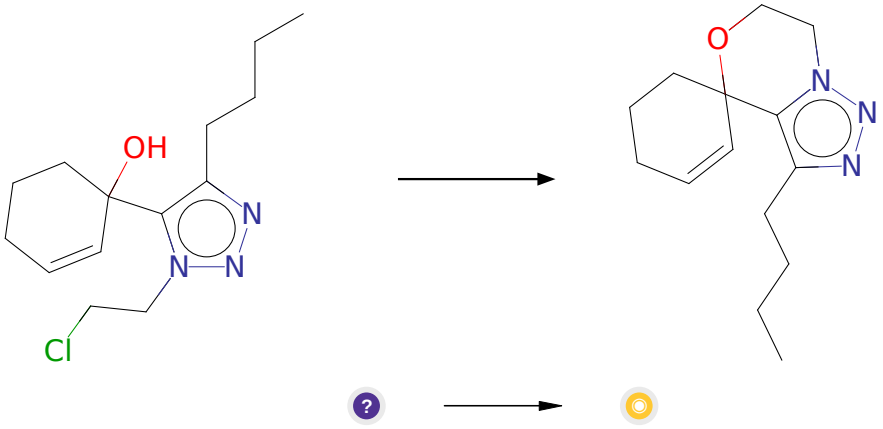
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.3.6 Alkylation of tertiary alcohols



Substrates:

1. CCCCc1nnn(CCCl)c1C1(O)C=CCCC1

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

Typical conditions: K2CO3.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

2.4 Path 4

Score: `210.68`

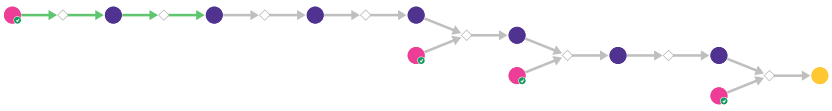
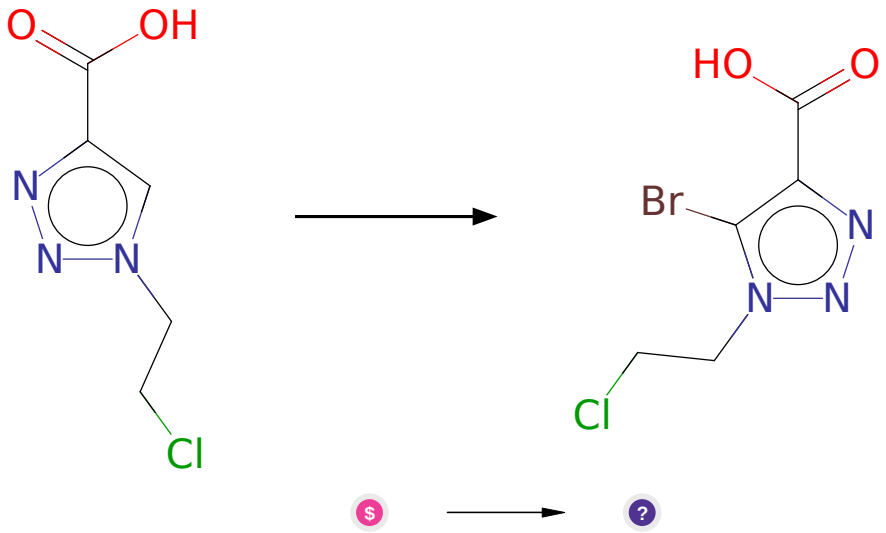


Figure 4: Outline of path 4

2.4.1 Bromination of aromatic compounds



Substrates:

1. 1-(2-chloroethyl)-1H-1,2,3-triazole-4-carboxylic acid - *available at Sigma-Aldrich*

Products:

1. O=C(O)c1nnn(CCCl)c1Br

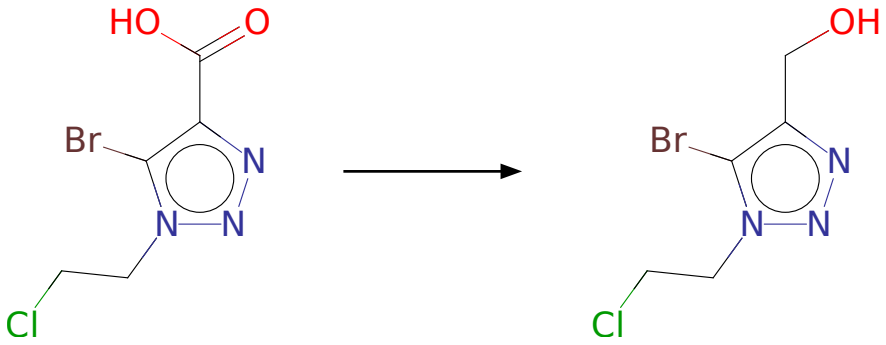
Typical conditions: Br2.Fe

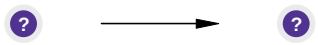
Protections: none

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

Retrosynthesis ID: 7777000

2.4.2 Reduction of carboxylic acids to alcohols





Substrates:

1. O=C(O)c1nnn(CCCl)c1Br

Products:

1. OCc1nnn(CCCl)c1Br

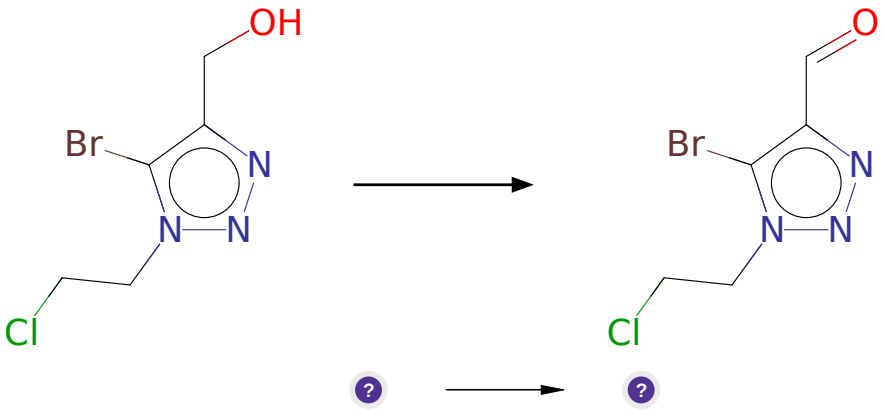
Typical conditions: BH3xTHF.or.ClCOOEt.Et3N.then.NaBH4

Protections: none

Reference: *10.1021/jo00956a011* and *10.1248/cpb.16.492* and *10.1016/S0040-4039(98)01781-X* and *10.1021/ja508846g* and *10.1016/j.bmc.2011.07.054*

Retrosynthesis ID: 9141

2.4.3 Oxidation of primary alcohols with DMP



Substrates:

1. OCc1nnn(CCCl)c1Br

Products:

1. O=Cc1nnn(CCCl)c1Br

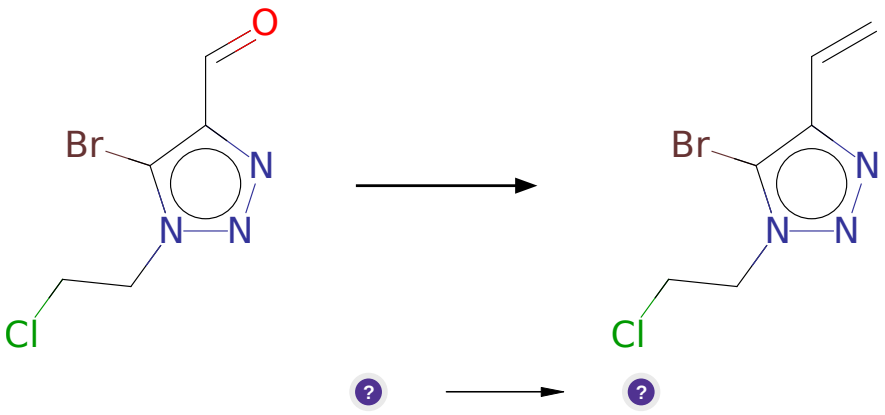
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

Retrosynthesis ID: 50426

2.4.4 Tebbe Olefination



Substrates:

1. O=Cc1nnn(CCCl)c1Br

Products:

1. C=Cc1nnn(CCCl)c1Br

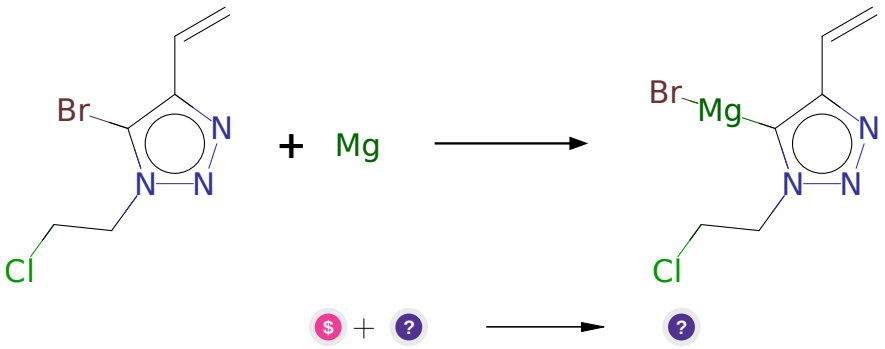
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Reference: *10.1016/j.tet.2007.03.015* and *10.1002/9780470638859.conrr617*

Retrosynthesis ID: 11714

2.4.5 Synthesis of aryl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*

2. C=Cc1nnn(CCCl)c1Br

Products:

1. C=Cc1nnn(CCCl)c1[Mg]Br

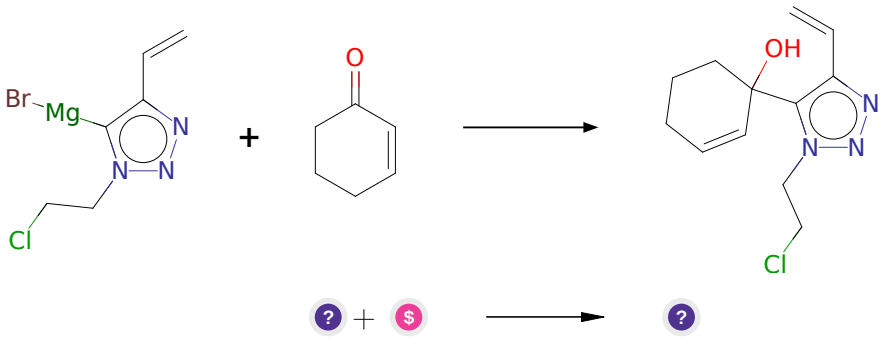
Typical conditions: iPrMgCl.THF or other conditions like BuLi.MgBr2 or Mg.THF

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and *10.1002/anie.200454084* and *10.1021/ol400150z*

Retrosynthesis ID: 10011461

2.4.6 Grignard-Type Reaction



Substrates:

1. C=Cc1nnn(CCCl)c1[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. C=Cc1nnn(CCCl)c1C1(O)C=CCCC1

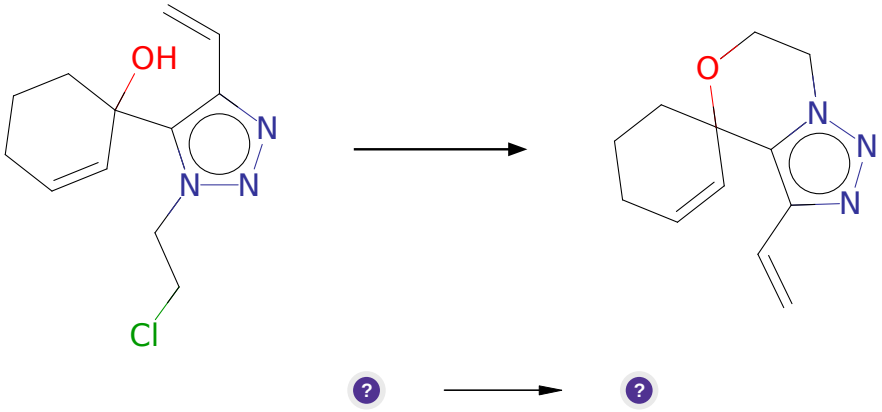
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1021/jm061429p* or *10.1016/j.bmc.2012.11.015* or *10.1016/j.tetasy.2012.05.024*

Retrosynthesis ID: 25133

2.4.7 Alkylation of tertiary alcohols



Substrates:

1. C=Cc1nnn(CCCl)c1C1(O)C=CCCC1

Products:

1. C=Cc1nnn2c1C1(C=CCCC1)OCC2

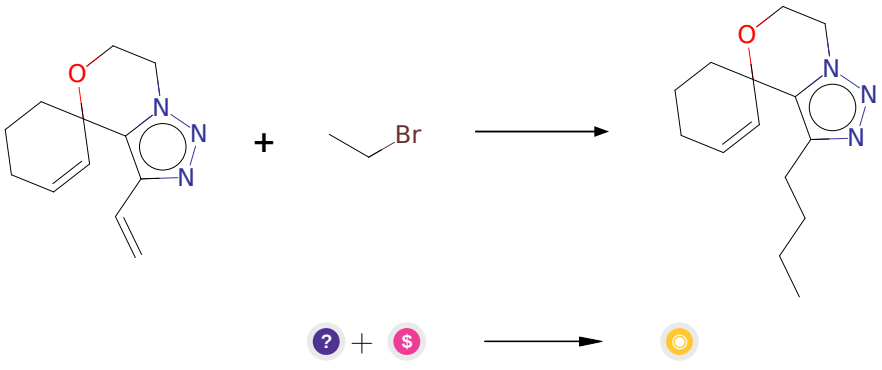
Typical conditions: K2CO3.acetone.heat

Protections: none

Reference: *10.1016/S0040-4020(01)90106-1* and *10.1021/acs.analchem.5b04461* and *10.3390/molecules24091643*

Retrosynthesis ID: 31010930

2.4.8 Suzuki alkyl-alkyl coupling



Substrates:

1. C=Cc1nnn2c1C1(C=CCCC1)OCC2
2. Bromoethane - *available at Sigma-Aldrich*

Products:

1. CCCCc1nnn2c1C1(C=CCCC1)OCC2

Typical conditions: 1.9BBN-H or pinB-Bpin.Cu 2.[Pd].ligand.base

Protections: none

Reference: *10.1021/ja074008l* and *10.1021/ja011306o* and *10.1002/1521-3773(20011217)40:24<4544::AID-ANIE4544>3.0.CO;2-N* and *10.1021/ol300575d*

Retrosynthesis ID: 8325