Paths of analysis*

PG4

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

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

2.1 Path 1

Score: `45.00`

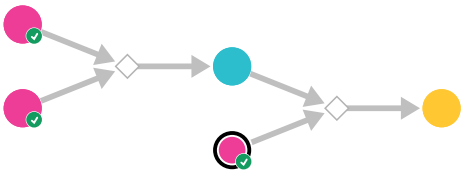
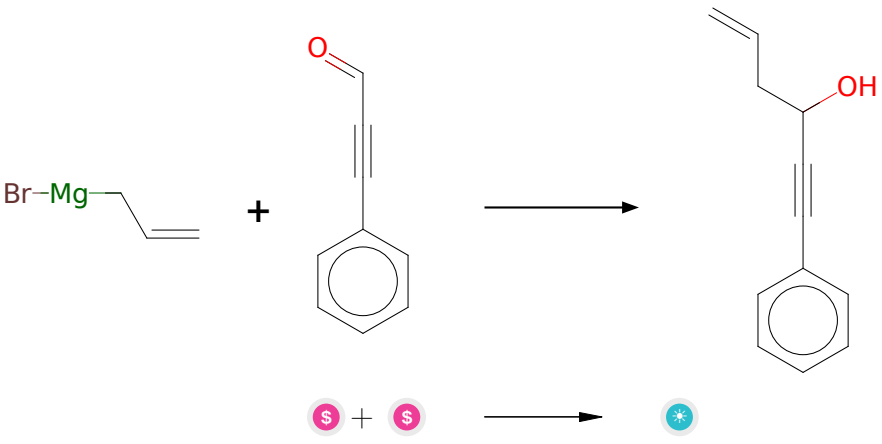


Figure 1: Outline of path 1

2.1.1 Grignard-Type Reaction



Substrates:

1. Allylmagnesium bromide solution - *available at Sigma-Aldrich*

2. 3-Phenyl-2-propynal - *available at Sigma-Aldrich*

Products:

1. 1-phenylethynyl-but-3-en-1-ol

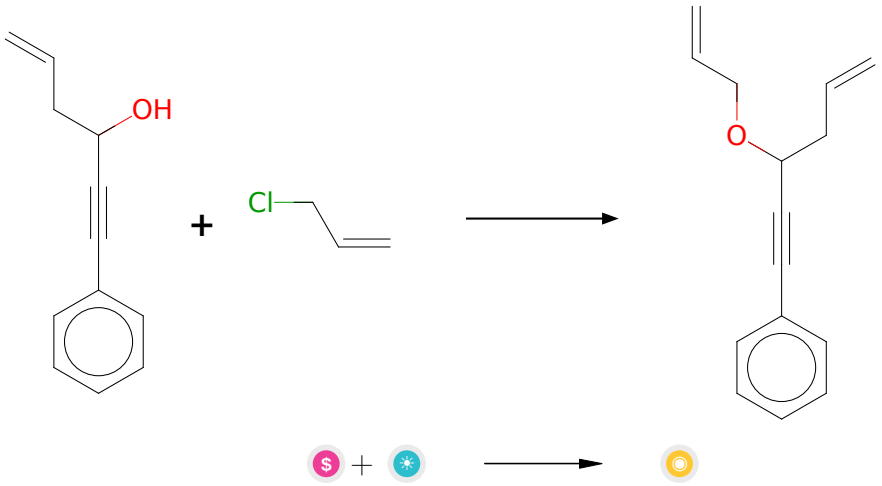
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1016/S0040-4020(99)00197-0* or *10.1055/s-0030-1260809* or *10.1021/ol703056u*

Retrosynthesis ID: 25124

2.1.2 Alkylation of secondary unhindered alcohols



Substrates:

1. Chlorallylene - *available at Sigma-Aldrich*
2. 1-phenylethynyl-but-3-en-1-ol

Products:

1. C=CCOC(C#Cc1ccccc1)CC=C

Typical conditions: K2CO3.acetone.heat

Protections: none

Reference: *10.1016/S0022-1139(00)85021-6* and

Retrosynthesis ID: 31011036

2.2 Path 2

Score: 51.25

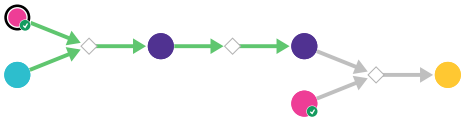
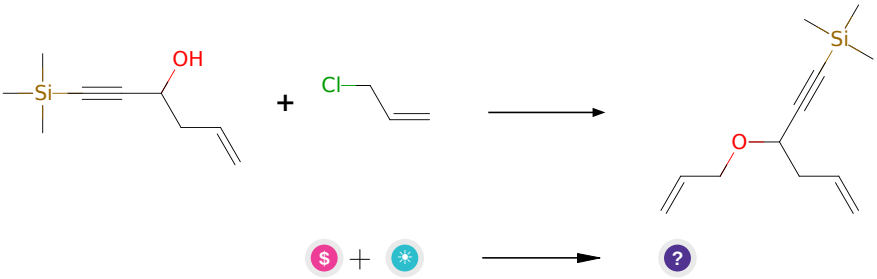


Figure 2: Outline of path 2

2.2.1 Alkylation of secondary unhindered alcohols



Substrates:

1. Chlorallylene - *available at Sigma-Aldrich*
2. 1-trimethylsilyl-5-hexen-1-yn-3-ol

Products:

1. C=CCOC(C#C[Si](C)(C)C)CC=C

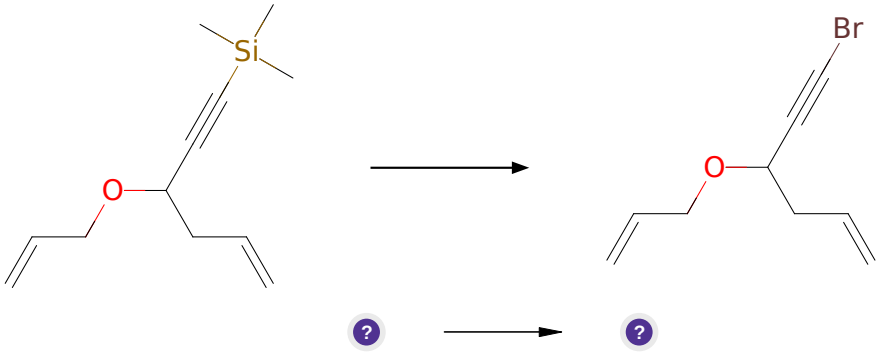
Typical conditions: K2CO3.acetone.heat

Protections: none

Reference: *10.1016/S0022-1139(00)85021-6* and

Retrosynthesis ID: 31011036

2.2.2 Conversion of TMS protected acetylenes to bromoacetylenes



Substrates:

1. C=CCOC(C#C[Si](C)(C)C)CC=C

Products:

1. C=CCOC(C#CBr)CC=C

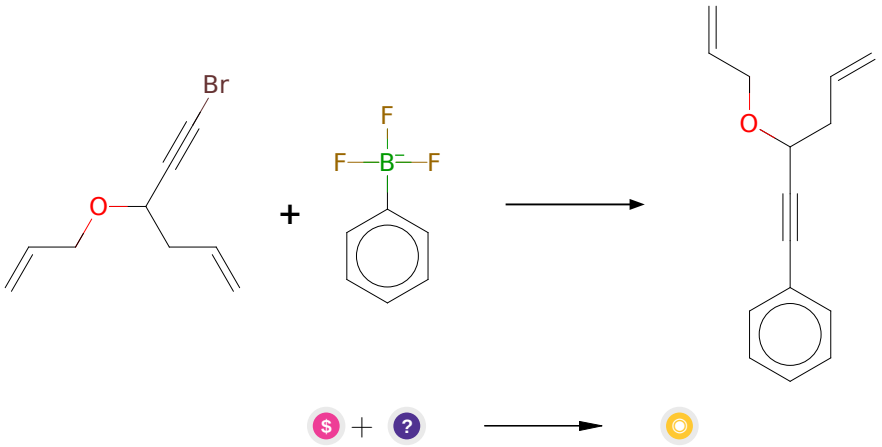
Typical conditions: NBS.Ag2CO3.acetone.rt

Protections: none

Reference: *10.1021/ja067289q* or *10.1021/ol035752n* or *10.1021/ja0352350*

Retrosynthesis ID: 7577

2.2.3 Suzuki Coupling of aryltrifluoroborates with alkylnyl bromides



Substrates:

1. Potassium phenyltrifluoroborate - *available at Sigma-Aldrich*

2. C=CCOC(C#CBr)CC=C

Products:

1. C=CCOC(C#Cc1ccccc1)CC=C

Typical conditions: CuI.8-quinolinol.Na3PO4.EtOH.80C

Protections: none

Reference: *10.1016/j.tet.2011.05.031* and *10.1055/s-0030-1260138* and *10.1246/cl.2011.941* and *10.1021/jo5011069* and *10.1002/chem.201603627*

Retrosynthesis ID: 10034083

2.3 Path 3

Score: 51.25

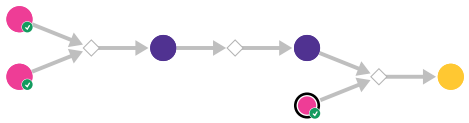
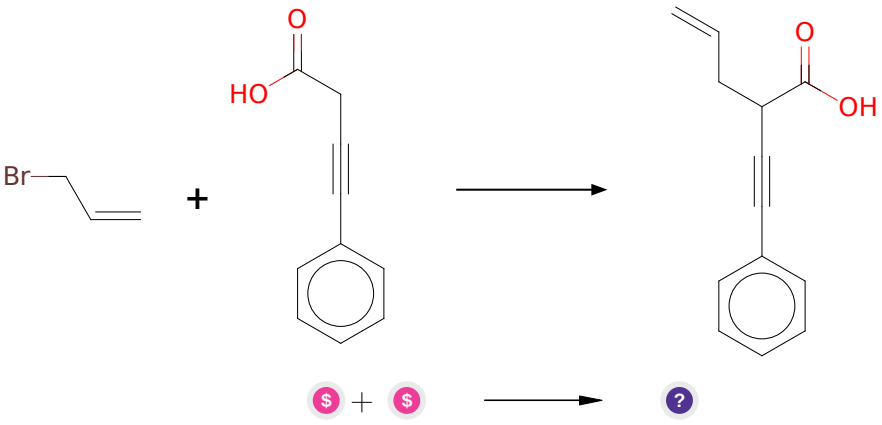


Figure 3: Outline of path 3

2.3.1 Alkylation of carboxylic acids



Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*

2. 4-phenylbut-3-ynoic acid - *available at Sigma-Aldrich*

Products:

1. C=CCC(C#Cc1ccccc1)C(=O)O

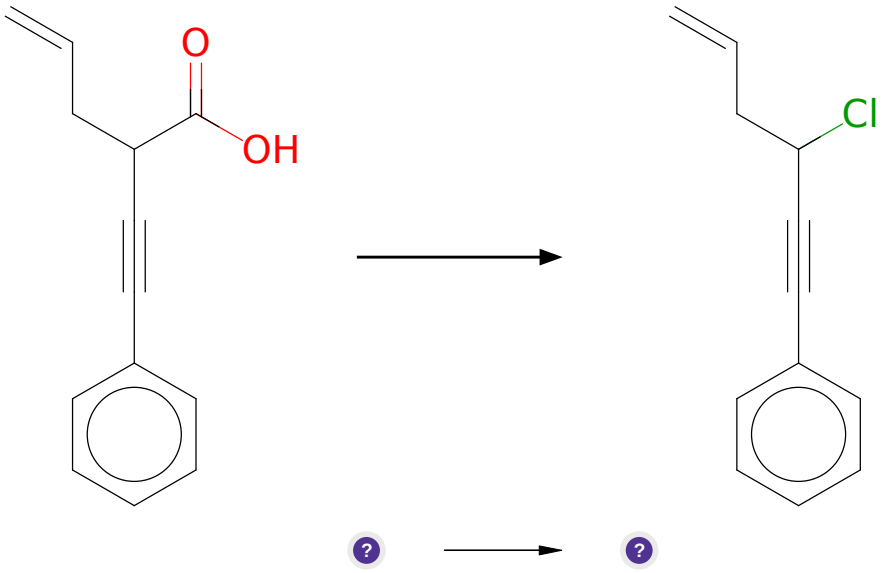
Typical conditions: nBuLi.THF.DIPEA

Protections: none

Reference: *10.1080/15257770.2013.820833* AND *10.1021/jm00078a017* AND *10.1016/j.bmc.2003.12.039* AND *10.1021/ml500411h*(SI,page 11) AND *10.1016/j.tet.2010.12.020* AND *10.1016/j.bmcl.2015.07.101*

Retrosynthesis ID: 28537

2.3.2 Synthesis of alkyl chlorides from carboxylic acids



Substrates:

1. C=CCC(C#Cc1ccccc1)C(=O)O

Products:

1. C=CCC(Cl)C#Cc1ccccc1

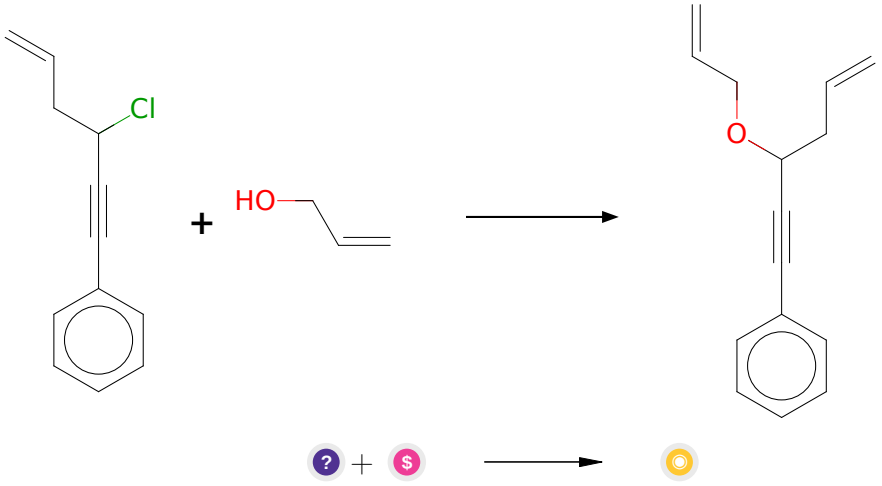
Typical conditions: Ag(Phen)2OTf.OtBu.Cl.acetonitrile.RT

Protections: none

Reference: DOI: *10.1021/ja210361z*

Retrosynthesis ID: 11412

2.3.3 Alkylation of primary alcohols



Substrates:

1. C=CCC(Cl)C#Cc1ccccc1
2. 2-Propen-1-ol - *available at Sigma-Aldrich*

Products:

1. C=CCOC(C#Cc1ccccc1)CC=C

Typical conditions: K2CO3.acetone.heat

Protections: none

Reference: *10.1021/jo00161a028* and *10.1021/acs.orglett.8b03053*

Retrosynthesis ID: 31010998

2.4 Path 4

Score: `51.25`

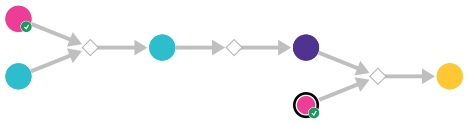
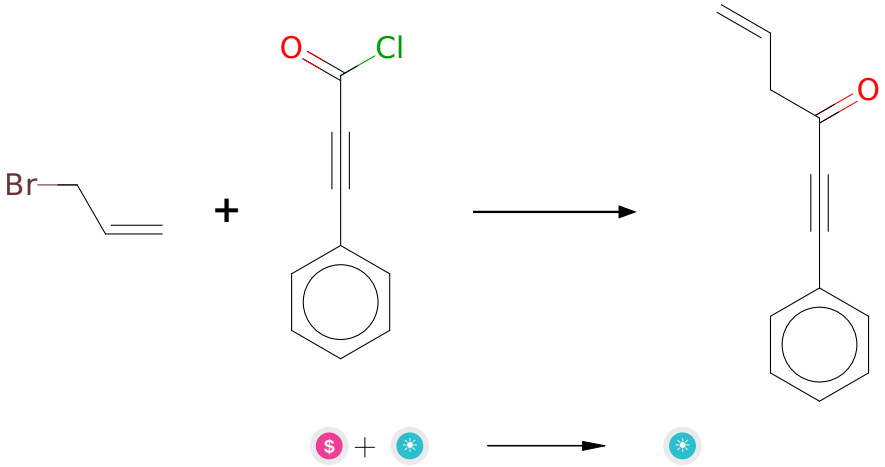


Figure 4: Outline of path 4

2.4.1 Grignard reaction with acyl chlorides



Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*
2. phenylpropynoyl chloride

Products:

1. C12H10O

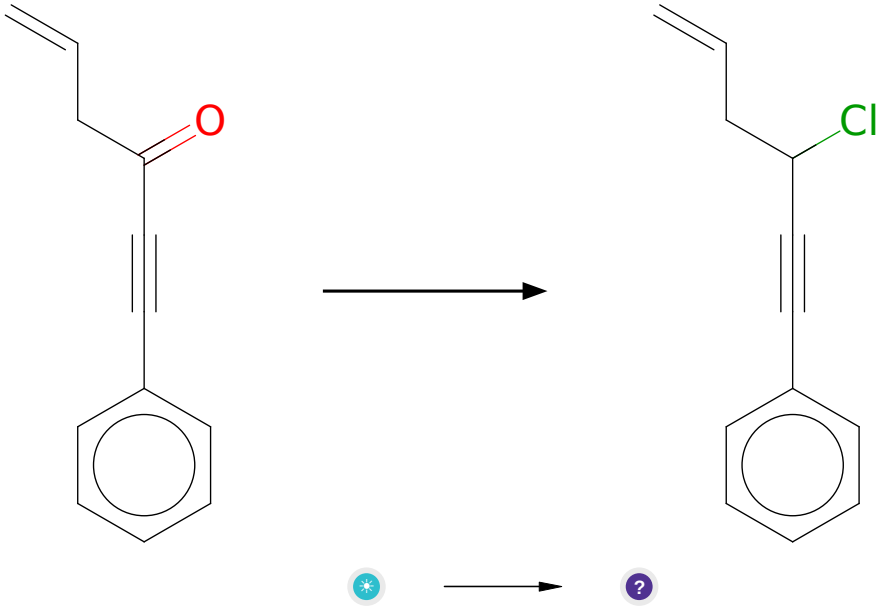
Typical conditions: 1.i-PrMgCl.LiCl 2.ZnCl2 3. CuCl

Protections: none

Reference: *10.1016/0040-4039(94)85361-4* and *10.1016/0040-4039(96)00258-4* and *10.1021/jo3005556* AND *10.1016/0040-4039(96)00689-2*

Retrosynthesis ID: 2530

2.4.2 Synthesis of alkyl chlorides from ketones



Substrates:

1. C12H10O

Products:

1. C=CCC(Cl)C#Cc1ccccc1

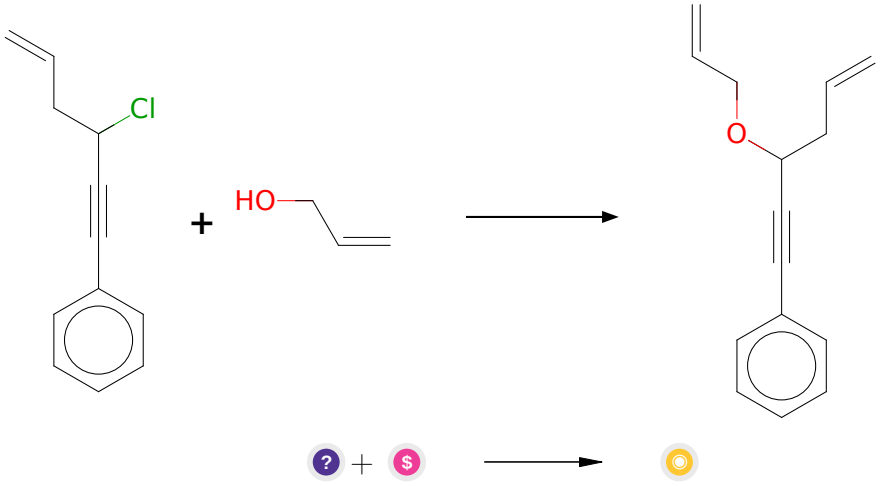
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11620

2.4.3 Alkylation of primary alcohols



Substrates:

1. C=CCC(Cl)C#Cc1ccccc1
2. 2-Propen-1-ol - *available at Sigma-Aldrich*

Products:

1. C=CCOC(C#Cc1ccccc1)CC=C

Typical conditions: K2CO3.acetone.heat

Protections: none

Reference: *10.1021/jo00161a028* and *10.1021/acs.orglett.8b03053*

Retrosynthesis ID: 31010998

2.5 Path 5

Score: `51.25`

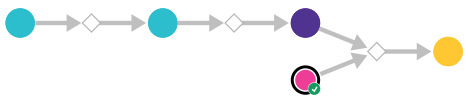
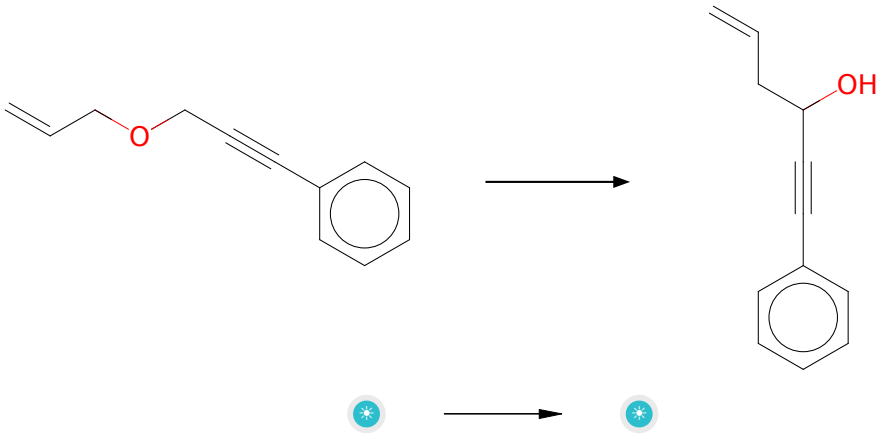


Figure 5: Outline of path 5

2.5.1 [2,3]-Wittig Rearrangement



Substrates:

1. [3-(2-propenyloxy)-1-propynyl]benzene

Products:

1. 1-phenylethynyl-but-3-en-1-ol

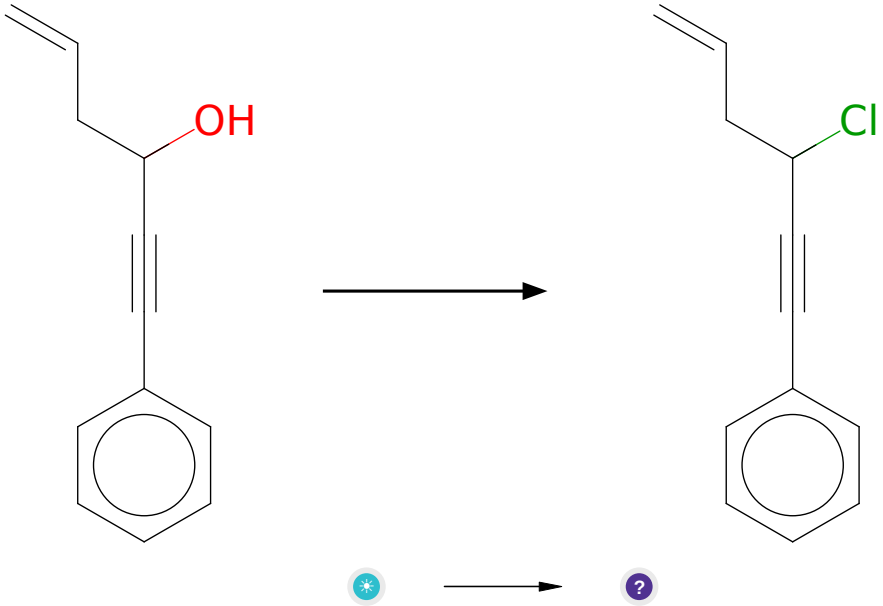
Typical conditions: nBuLi or other base

Protections: none

Reference: DOI: *10.1021/jo00021a002* and *10.1021/ol302432d* and *10.1021/acs.joc.5b00678* and *10.1021/cr00075a011*

Retrosynthesis ID: 10019721

2.5.2 Appel Reaction



Substrates:

1. 1-phenylethynyl-but-3-en-1-ol

Products:

1. C=CCC(Cl)C#Cc1ccccc1

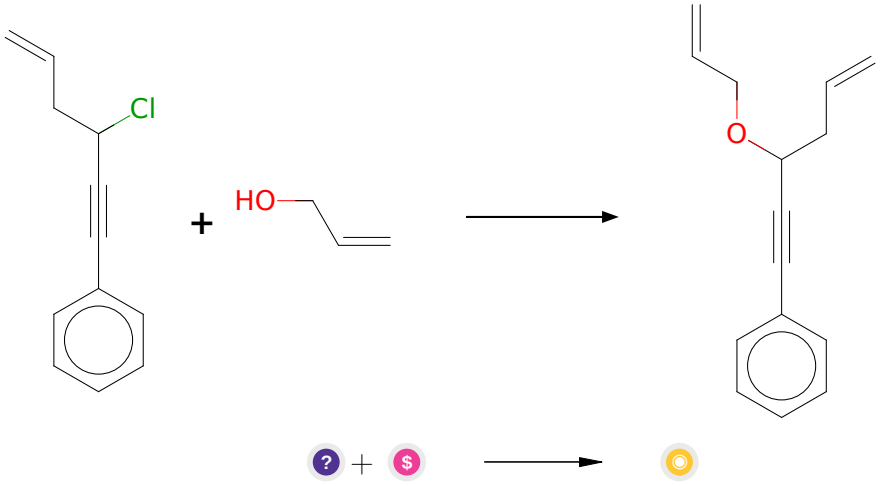
Typical conditions: PPh3.CHCl3

Protections: none

Reference: *10.1021/ja0470158* and *10.1016/j.tet.2015.03.108* and *10.1021/ol9016595* and *10.1081/CAR-120021700*

Retrosynthesis ID: 9990041

2.5.3 Alkylation of primary alcohols



Substrates:

1. C=CCC(Cl)C#Cc1ccccc1
2. 2-Propen-1-ol - *available at Sigma-Aldrich*

Products:

1. C=CCOC(C#Cc1ccccc1)CC=C

Typical conditions: K2CO3.acetone.heat

Protections: none

Reference: *10.1021/jo00161a028* and *10.1021/acs.orglett.8b03053*

Retrosynthesis ID: 31010998