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

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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: `51.25`

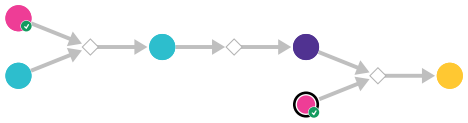
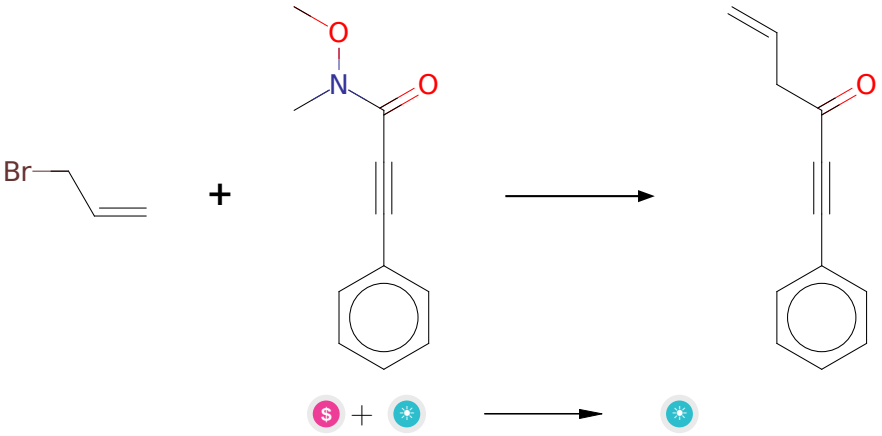


Figure 1: Outline of path 1

2.1.1 Synthesis of ketones from Weinreb amides



Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*
2. n-methoxy-n-methylphenylacetylenecarboxamide

Products:

1. C12H10O

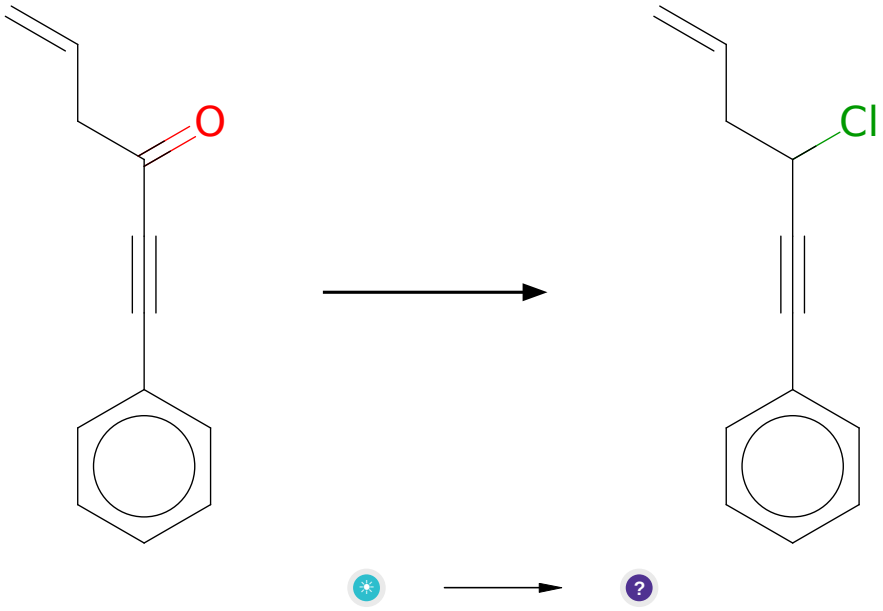
Typical conditions: 1.RmgBr.THF 2.TFA.DCM

Protections: none

Reference: *10.1021/jm051185t* and *10.1021/ol101021v* (supporting info)

Retrosynthesis ID: 6837

2.1.2 Synthesis of alkyl chlorides from ketones



Substrates:

1. C12H10O

Products:

1. C=CCC(Cl)C#Cc1ccccc1

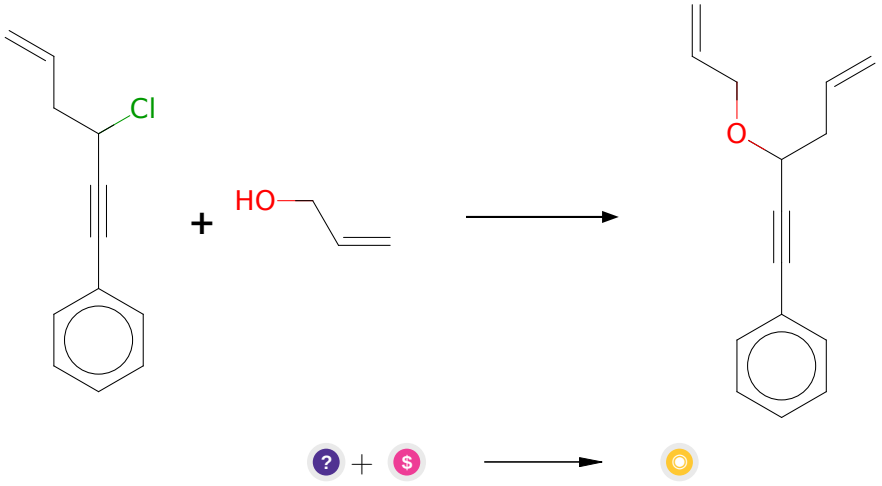
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11620

2.1.3 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

2.2 Path 2

Score: `51.25`

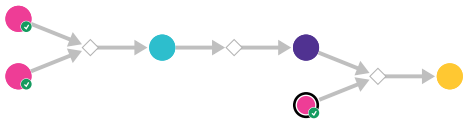
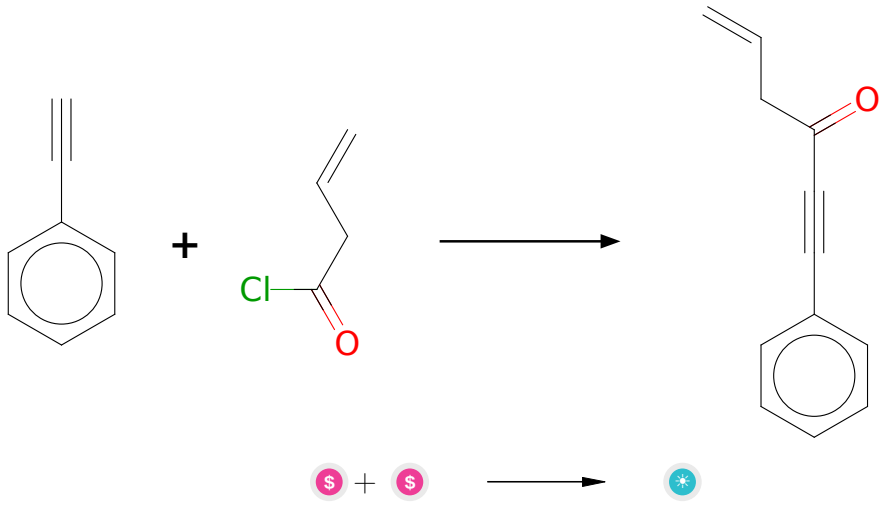


Figure 2: Outline of path 2

2.2.1 Synthesis of acetylenic ketones



Substrates:

1. Ethynylbenzene - *available at Sigma-Aldrich*
2. but-3-enoyl chloride - *available at Sigma-Aldrich*

Products:

1. C12H10O

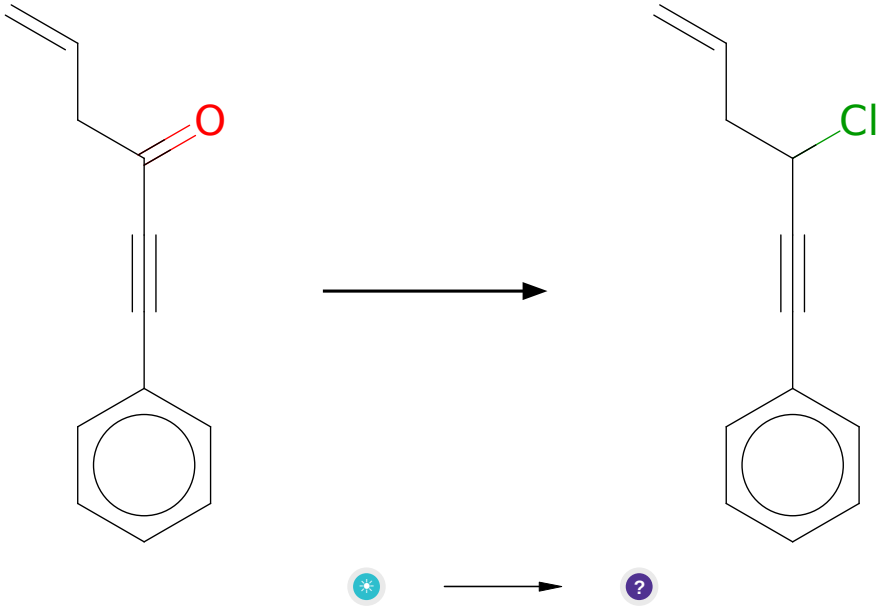
Typical conditions: 1.nBuLi.2.ZnCl2.3.Pd(PPh3)4.RCOCl

Protections: none

Reference: *10.1016/0022-328x(88)80002-0*

Retrosynthesis ID: 5317

2.2.2 Synthesis of alkyl chlorides from ketones



Substrates:

1. C12H10O

Products:

1. C=CCC(Cl)C#Cc1ccccc1

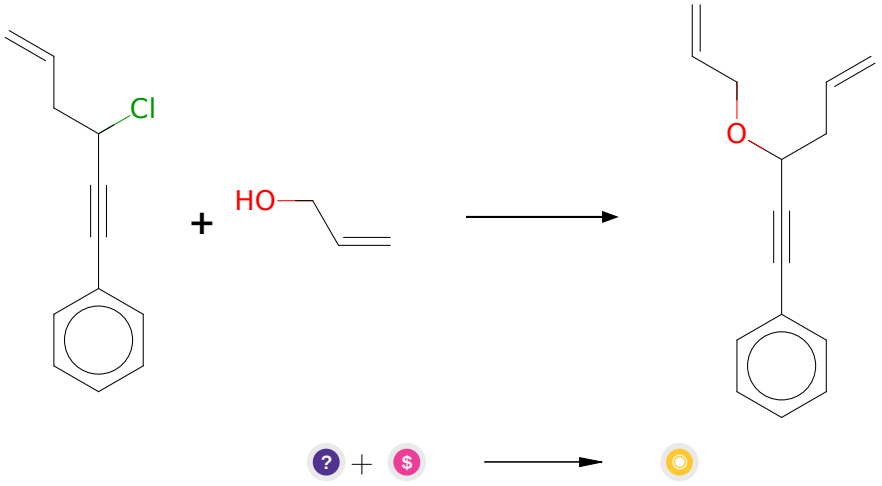
Typical conditions: InO3.chloroform.SiMe2Cl

Protections: none

Reference: DOI: *10.1021/ja0283246*

Retrosynthesis ID: 11620

2.2.3 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

2.3 Path 3

Score: `51.25`

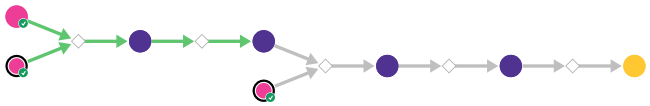
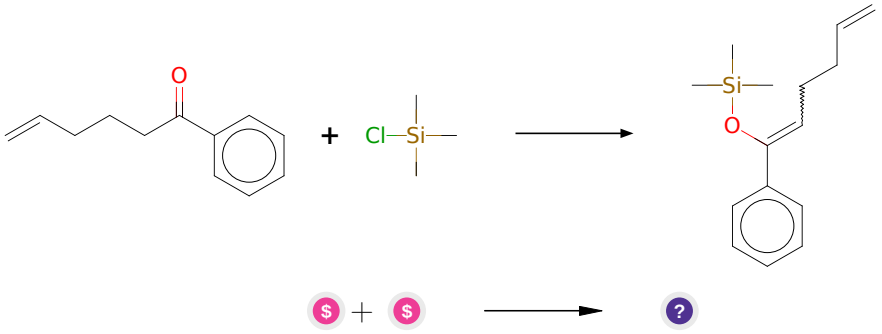


Figure 3: Outline of path 3

2.3.1 Enol esters and ethers synthesis



Substrates:

1. 1-phenylhex-5-en-1-one - *available at Sigma-Aldrich*
2. TMSCl - *available at Sigma-Aldrich*

Products:

1. C=CCCC=C(O[Si](C)(C)C)c1ccccc1

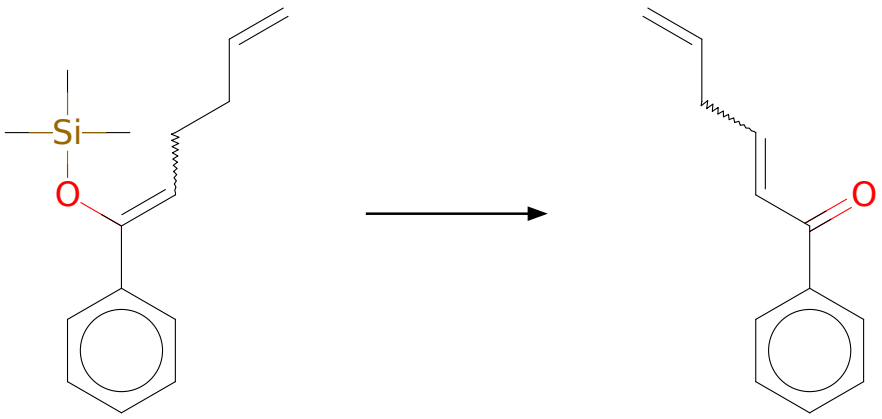
Typical conditions: 1.LDA.2.Electrophile

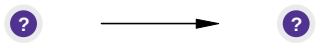
Protections: none

Reference: US2467095A AND WO2014169833a1 AND *10.1016/j.steroids.2011.03.014* AND *10.1021/ol200875m* (SI) AND *10.1021/ja00531a034*

Retrosynthesis ID: 7797

2.3.2 Dehydrogenation of silyl enol ethers





Substrates:

1. C=CCCC=C(O[Si](C)(C)C)c1ccccc1

Products:

1. C=CCC=CC(=O)c1ccccc1

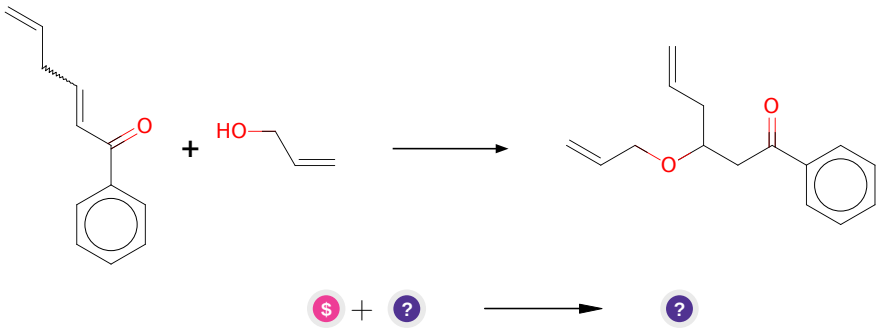
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

Protections: none

Reference: *10.1271/bbb.60.405* and *10.1039/C3CC46778C* and US2015284405 p.40 and *10.1016/S0040-4039(01)81518-5* and US2010204477 p. 15-16 and *10.1016/0040-4039(95)00694-8* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999877

2.3.3 Addition of alcohols or phenols to Michael acceptors



Substrates:

1. 2-Propen-1-ol - *available at Sigma-Aldrich*
2. C=CCC=CC(=O)c1ccccc1

Products:

1. C=CCOC(CC=C)CC(=O)c1ccccc1

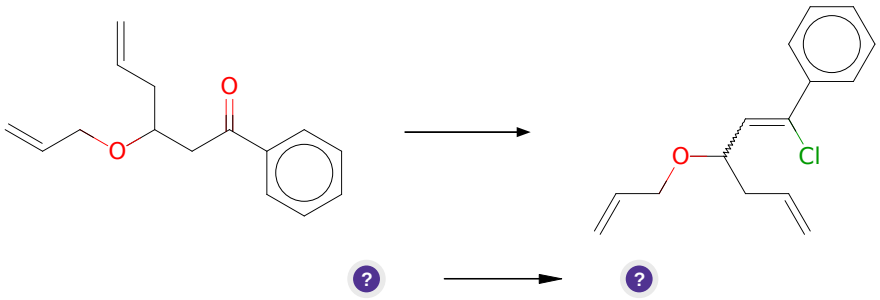
Typical conditions: cat.Na.DMF

Protections: none

Reference: *10.1016/S0957-4166(97)00479-5* AND *10.1016/S0040-4020(98)00817-5* AND *10.1021/np970346w* AND *10.1021/ol049820x*

Retrosynthesis ID: 20266

2.3.4 Shapiro reaction followed by halogen addition



Substrates:

1. C=CCOC(CC=C)CC(=O)c1ccccc1

Products:

1. C=CCOC(C=C(Cl)c1ccccc1)CC=C

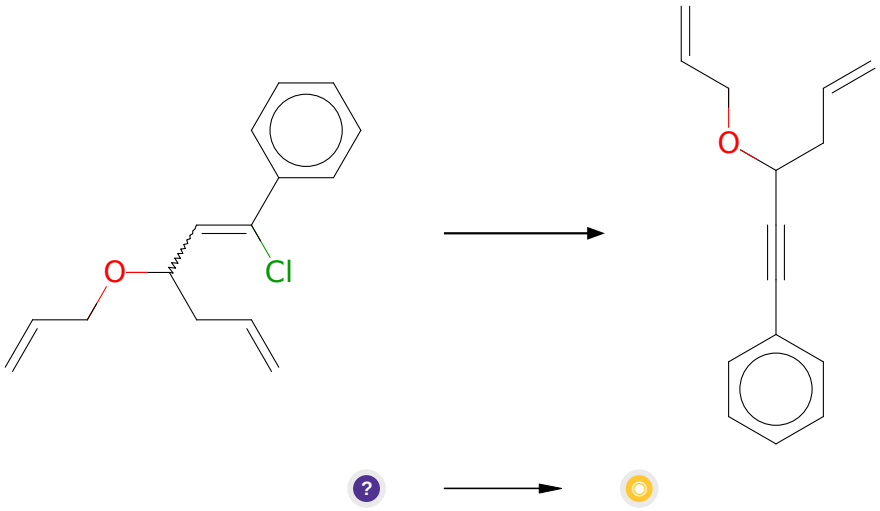
Typical conditions: 1.TsNH2NH2 2.NBS/NCS/NIS.base

Protections: none

Reference: *10.1055/s-1998-1683* and *10.1016/j.tet.2008.02.073* and *10.1021/ol503114n* and *10.1021/ja049694s*

Retrosynthesis ID: 9990471

2.3.5 Synthesis of alkynes via elimination of vinyl chlorides



Substrates:

1. C=CCOC(C=C(Cl)c1ccccc1)CC=C

Products:

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

Typical conditions: Non-aqueous base (NaNH2,LDA,NaOH/ROH)

Protections: none

Reference: WO2005/37758 A1 (p.13) AND WO2007/65661 A1 (p.34) AND *10.1021/ja065015x* AND *10.1055/s-1984-30866* AND *10.1055/s-2002-28518*

Retrosynthesis ID: 15106

2.4 Path 4

Score: 59.06

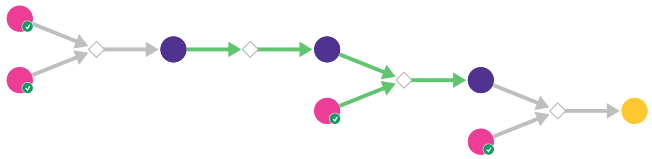
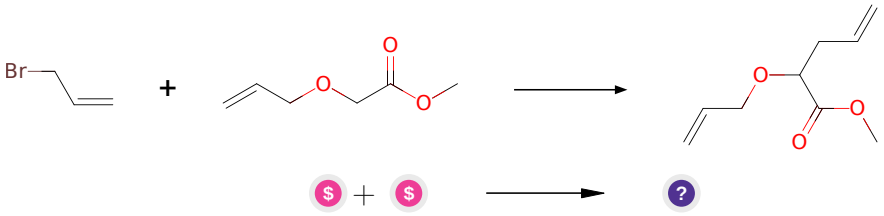


Figure 4: Outline of path 4

2.4.1 Alkylation of Esters



Substrates:

1. Allyl bromide - *available at Sigma-Aldrich*
2. methyl 2-(prop-2-en-1-yloxy)acetate - *available at Sigma-Aldrich*

Products:

1. C=CCOC(CC=C)C(=O)OC

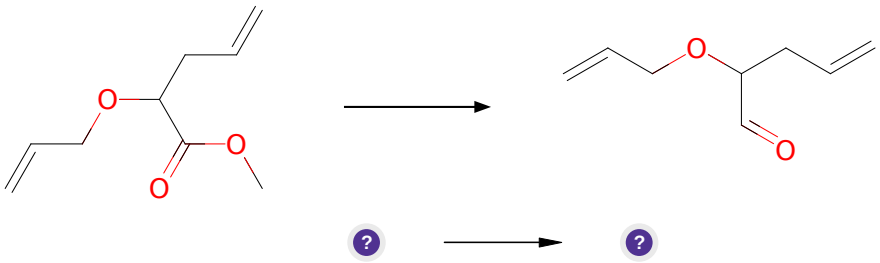
Typical conditions: base e.g. BuLi.THF

Protections: none

Reference: *10.1016/j.tet.2012.05.041* and US2005/288329A1 p. 34 and WO2010/128401A1 p. 50 and WO2019/46330A1 p. 00371 and *10.1021/ja058303m* and *10.1021/acs.orglett.9b03078* and *10.1016/S0040-4020(01)80336-7*

Retrosynthesis ID: 31017110

2.4.2 Aldehyde Formation



Substrates:

1. C=CCOC(CC=C)C(=O)OC

Products:

1. C=CCOC(C=O)CC=C

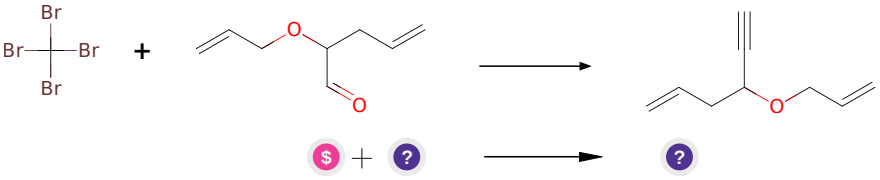
Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Reference: *10.1039/C39940000483* and *10.1039/C3CC47867J* and *10.1021/jo00222a054* and *10.1021/ja9934908* and *10.1021/jo902426z*

Retrosynthesis ID: 28551

2.4.3 Corey-Fuchs reaction



Substrates:

1. Tetrabromomethane - *available at Sigma-Aldrich*

2. C=CCOC(C=O)CC=C

Products:

1. C#CC(CC=C)OCC=C

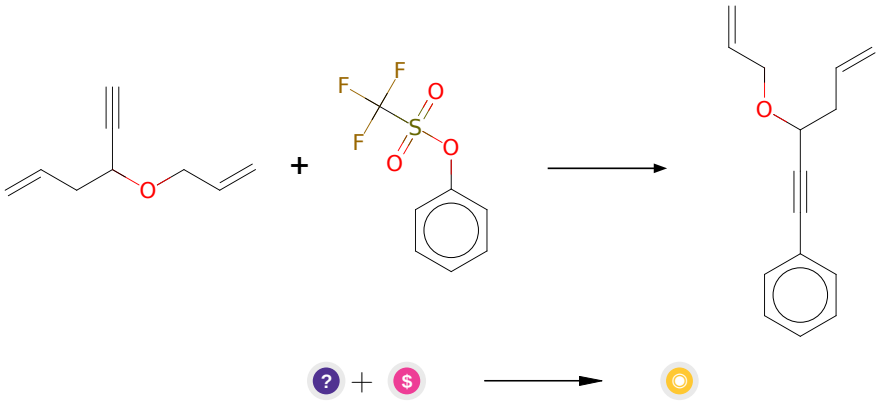
Typical conditions: PPh3.BuLi.CBr4

Protections: none

Reference: *10.1002/ejoc.200601137* and *10.1016/S0040-4039(01)94157-7*

Retrosynthesis ID: 10912

2.4.4 Sonogashira Coupling



Substrates:

1. C#CC(CC=C)OCC=C
2. Phenyl triflate - *available at Sigma-Aldrich*

Products:

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

Typical conditions: [Pd] catalyst.CuI.R3N

Protections: none

Reference: *10.1021/jo902545a* AND *10.1055/s-0033-1340839* AND *10.1021/ol061379i* AND *10.1002/(SICI)1099-0690(199911)1999:11<3117::AID-EJOC3117>3.0.CO;2-O*

Retrosynthesis ID: 5252

2.5 Path 5

Score: 70.31

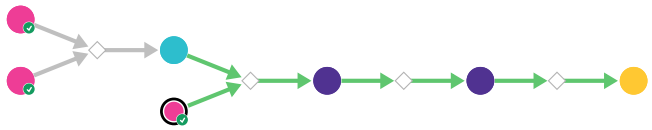
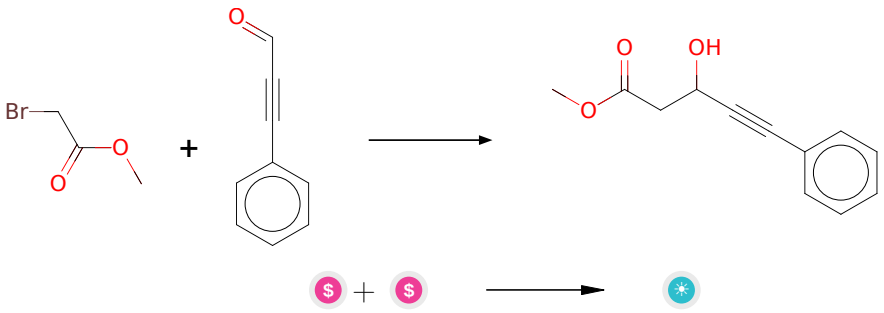


Figure 5: Outline of path 5

2.5.1 Reformatsky Reaction



Substrates:

1. Methyl bromoacetate - *available at Sigma-Aldrich*
2. 3-Phenyl-2-propynal - *available at Sigma-Aldrich*

Products:

1. 3-hydroxy-5-phenyl-pent-4-in-saeuremethylester

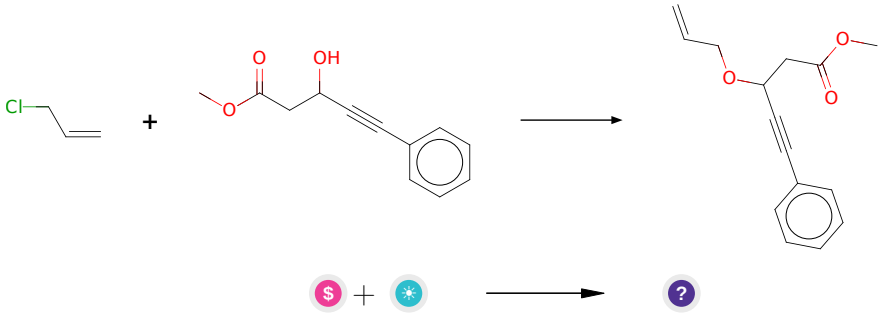
Typical conditions: Me2Zn.B(OMe)3.toluene.Et2O

Protections: none

Reference: *10.1021/jo200774e* p. 6373 and *10.1021/jo00163a019* p. 2522, 2525

Retrosynthesis ID: 11164

2.5.2 Alkylation of secondary alcohols



Substrates:

1. Chlorallylene - *available at Sigma-Aldrich*
2. 3-hydroxy-5-phenyl-pent-4-in-saeuremethylester

Products:

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

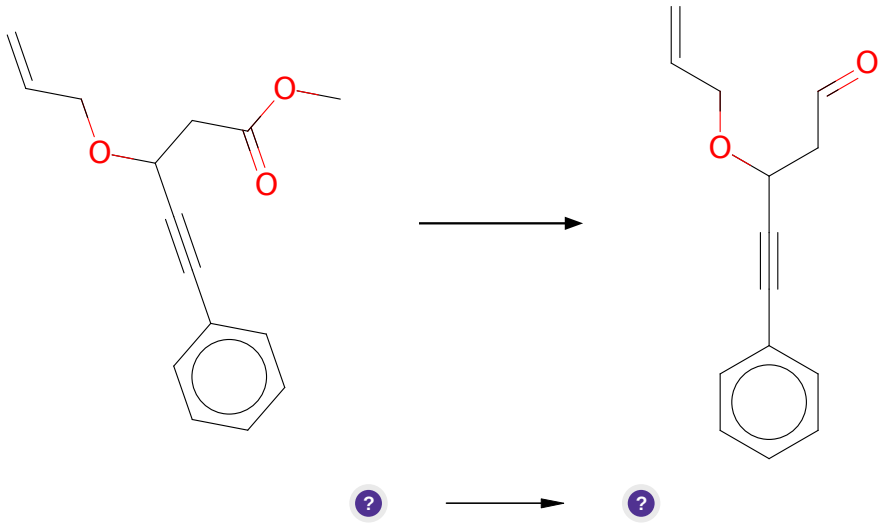
Typical conditions: K2CO3.acetone.heat

Protections: none

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

Retrosynthesis ID: 31011106

2.5.3 Aldehyde Formation



Substrates:

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

Products:

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

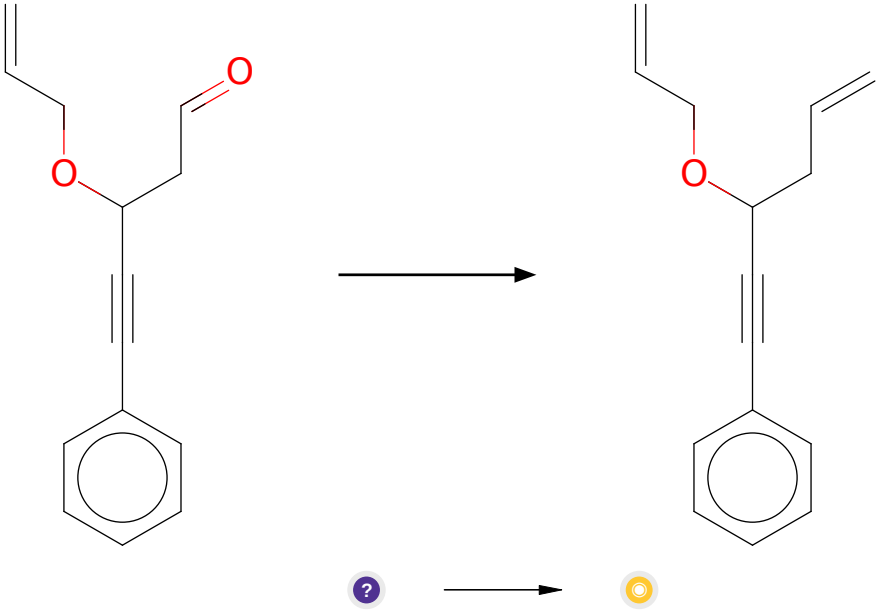
Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Reference: *10.1039/C39940000483* and *10.1039/C3CC47867J* and *10.1021/jo00222a054* and *10.1021/ja9934908* and *10.1021/jo902426z*

Retrosynthesis ID: 28551

2.5.4 Tebbe Olefination



Substrates:

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

Products:

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

Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

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

Retrosynthesis ID: 11714