Paths of analysis*

O6

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: `31.25`

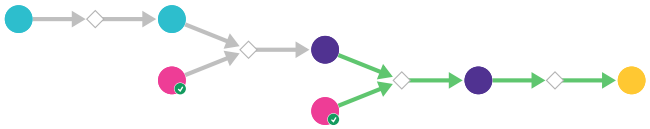
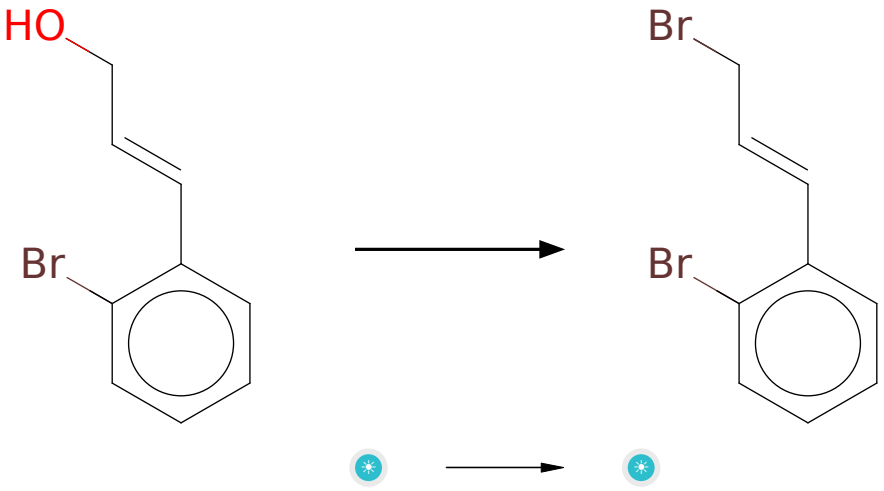


Figure 1: Outline of path 1

2.1.1 Appel Reaction



Substrates:

1. 1-(2-bromophenyl)-1-propen-3-ol

Products:

1. 1-(2-bromophenyl)-1-propen-3-yl bromide

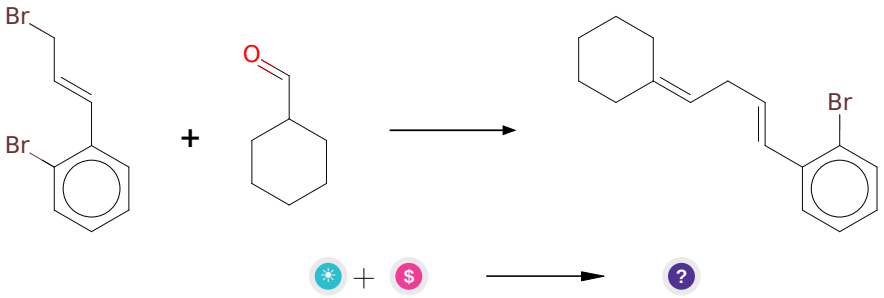
Typical conditions: PPh3.CBr4

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

2.1.2 Shapiro reaction followed by alkyl bromide addition



Substrates:

1. 1-(2-bromophenyl)-1-propen-3-yl bromide
2. Hexahydrobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. Brc1ccccc1/C=C/CC=C1CCCCC1

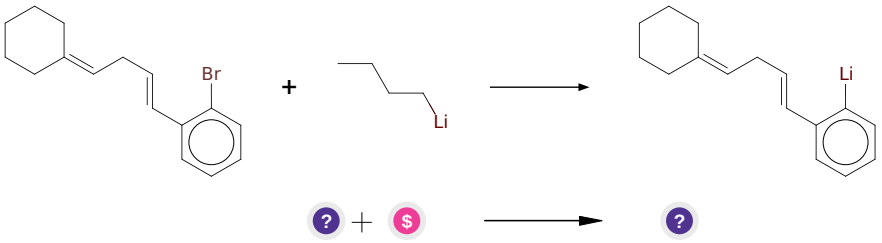
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then alkyl bromide.cooling

Protections: none

Reference: *10.1016/S0040-4039(00)75263-4* and *10.1021/ol300652k* and *10.1021/jo015699l*

Retrosynthesis ID: 9990458

2.1.3 Br/Li exchange



Substrates:

1. Brc1ccccc1/C=C/CC=C1CCCCC1
2. n-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1ccccc1/C=C/CC=C1CCCCC1

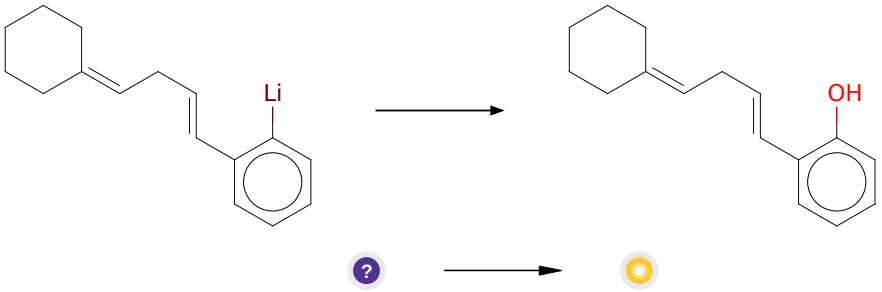
Typical conditions: nBuLi.or.tBuLi.THF.-78C

Protections: none

Reference: *10.1002/ejoc.201101490* and *10.1016/j.tet.2012.03.058* and *10.1016/j.tetlet.2015.01.032* and *10.1021/ja0541175* and *10.1016/j.tetlet.2016.06.123*

Retrosynthesis ID: 30672

2.1.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1ccccc1/C=C/CC=C1CCCCC1

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: B(OMe)3 then H2O2.THF

Protections: none

Reference: *10.1039/C7CC09187G* (SI) and *10.1002/ejoc.201701142* and *10.1021/acscatal.6b03380* (SI,p.10) and *10.1002/chem.201702143* (SI)

Retrosynthesis ID: 10019525

2.2 Path 2

Score: `45.00`

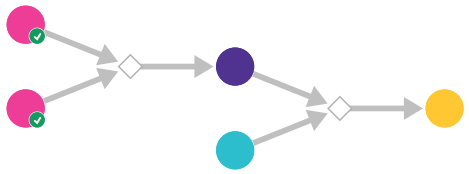
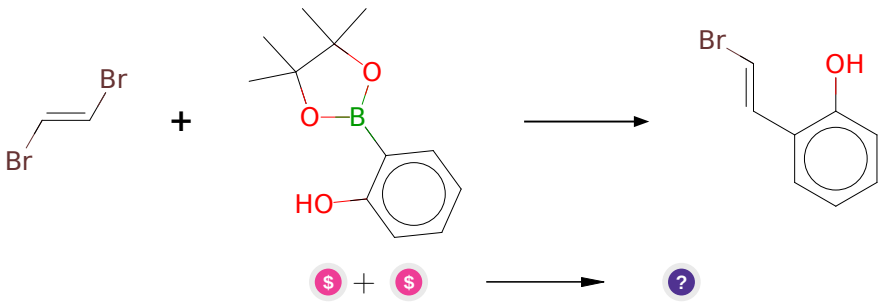


Figure 2: Outline of path 2

2.2.1 Suzuki coupling of arylboronic pinacol esters with vinyl Bromides



Substrates:

1. 2-Hydroxyphenylboronic acid pinacol ester - *available at Sigma-Aldrich*
2. 1,2-Dibromoethylene - *available at Sigma-Aldrich*

Products:

1. Oc1ccccc1/C=C/Br

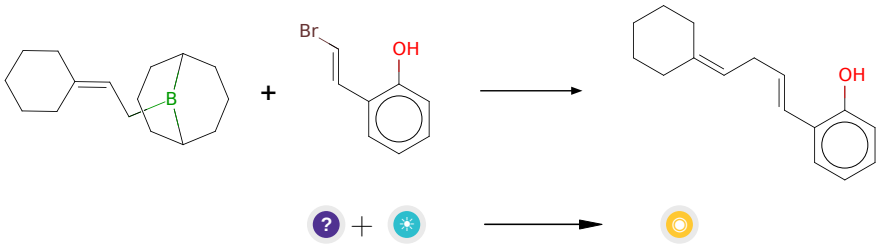
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 10355

2.2.2 Suzuki coupling of alkyl-9-BBNs with vinyl bromides



Substrates:

1. Oc1ccccc1/C=C/Br
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/ja00183a048* and *10.1039/b707338k* and *10.1016/j.tet.2015.05.039* and *10.1021/jo991064z* and *10.1021/ol060290+* and *10.1246/bcsj.65.2863*

Retrosynthesis ID: 25174

2.3 Path 3

Score: 51.25

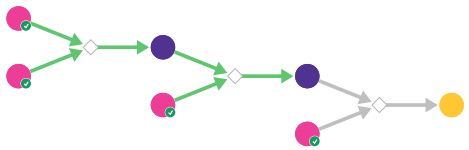
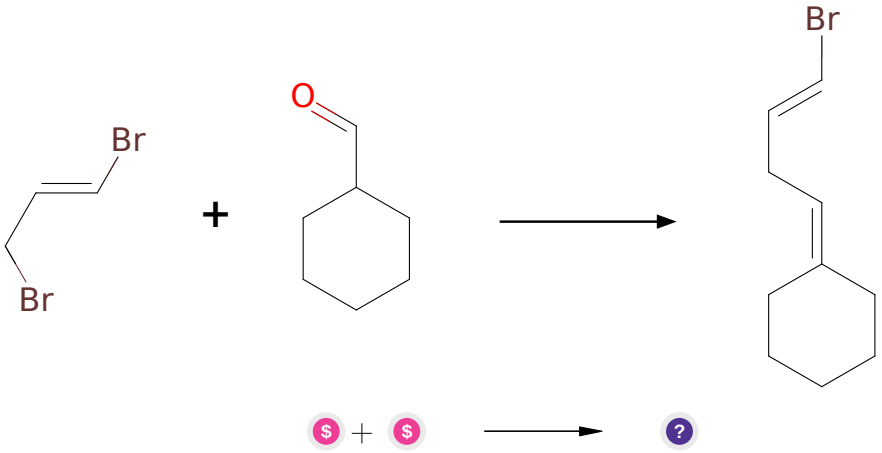


Figure 3: Outline of path 3

2.3.1 Shapiro reaction followed by alkyl bromide addition



Substrates:

1. Hexahydrobenzaldehyde - *available at Sigma-Aldrich*
2. 1,3-Dibromo-1-propene - *available at Sigma-Aldrich*

Products:

1. Br/C=C/CC=C1CCCCC1

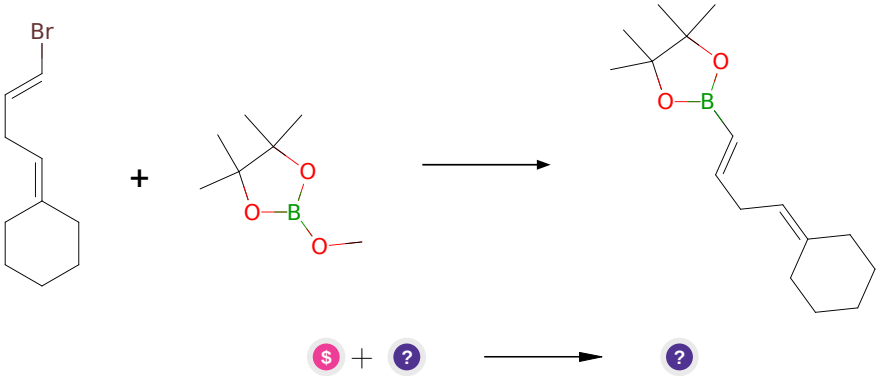
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then alkyl bromide.cooling

Protections: none

Reference: *10.1016/S0040-4039(00)75263-4* and *10.1021/ol300652k* and *10.1021/jo015699l*

Retrosynthesis ID: 9990458

2.3.2 Synthesis of boronic acid esters



Substrates:

1. Methoxyboronic acid pinacol ester - *available at Sigma-Aldrich*
2. Br/C=C/CC=C1CCCCC1

Products:

1. CC1(C)OB(/C=C/CC=C2CCCCC2)OC1(C)C

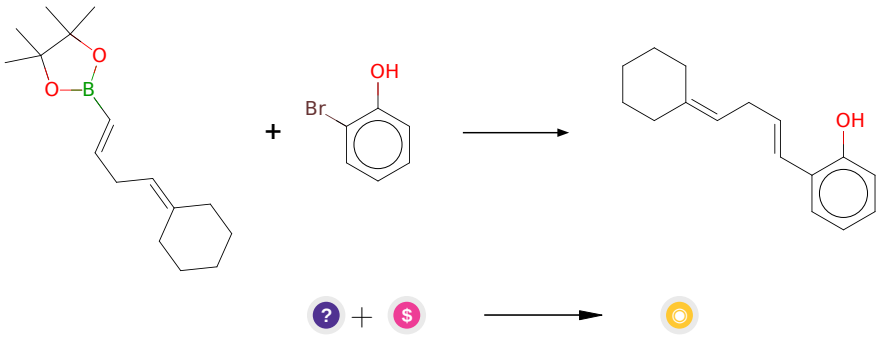
Typical conditions: Mg.THF.-78 C

Protections: none

Reference: *10.1039/B507900D* p. 3167, 3170 and *10.1021/acs.orglett.5b01434* SI p. S6

Retrosynthesis ID: 245548

2.3.3 Suzuki coupling of aryl bromides with alkenyl boronic acids pinacol esters



Substrates:

1. CC1(C)OB(/C=C/CC=C2CCCCC2)OC1(C)C
2. 2-Bromophenol - *available at Sigma-Aldrich*

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 11057

2.4 Path 4

Score: 51.25

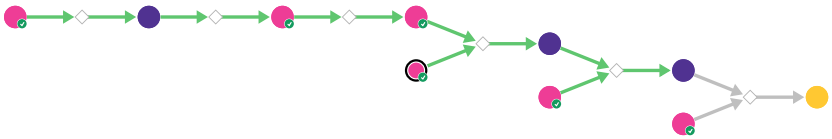
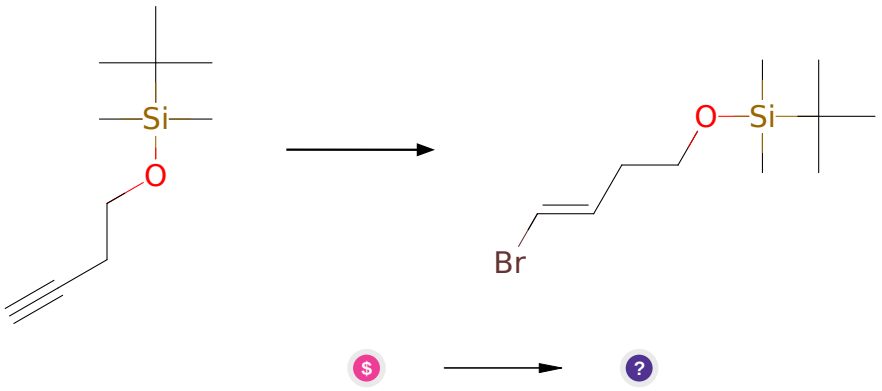


Figure 4: Outline of path 4

2.4.1 Bromination of vinylalanes



Substrates:

1. 4-(tert-Butyldimethylsilyloxy)-1-butyne - *available at Sigma-Aldrich*

Products:

1. CC(C)(C)[Si](C)(C)OCC/C=C/Br

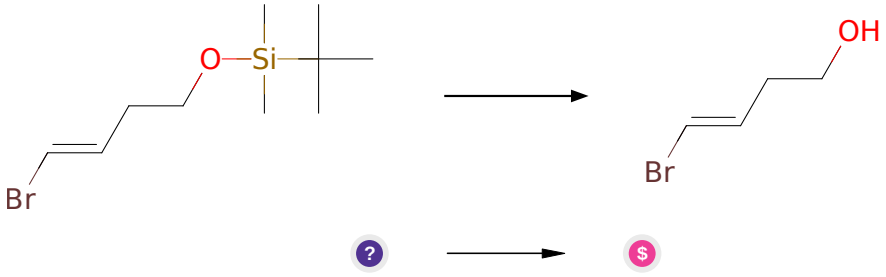
Typical conditions: Schwartz's reagent.then.Br2

Protections: none

Reference: DOI: *10.1039/C2CC36604E* (SI, page S18) AND DOI: *10.1080/00397910008087318*

Retrosynthesis ID: 7405

2.4.2 Deprotection of TBS ethers



Substrates:

1. CC(C)(C)[Si](C)(C)OCC/C=C/Br

Products:

1. 4-bromobut-3-en-1-ol - *available at Sigma-Aldrich*

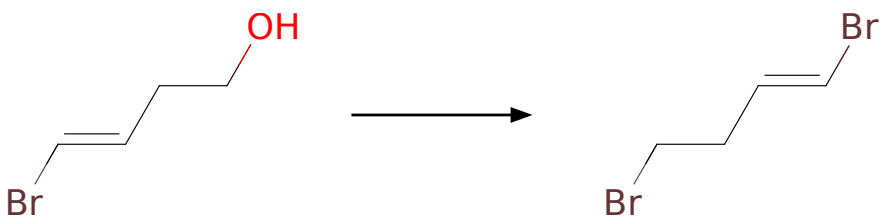
Typical conditions: TBAF.THF

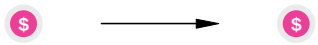
Protections: none

Reference: *10.1016/j.tet.2013.01.017* and *10.1016/j.tet.2004.04.042*

Retrosynthesis ID: 31010160

2.4.3 Appel Reaction





Substrates:

1. 4-bromobut-3-en-1-ol - *available at Sigma-Aldrich*

Products:

1. 1,4-dibromo-but-1-ene - *available at Sigma-Aldrich*

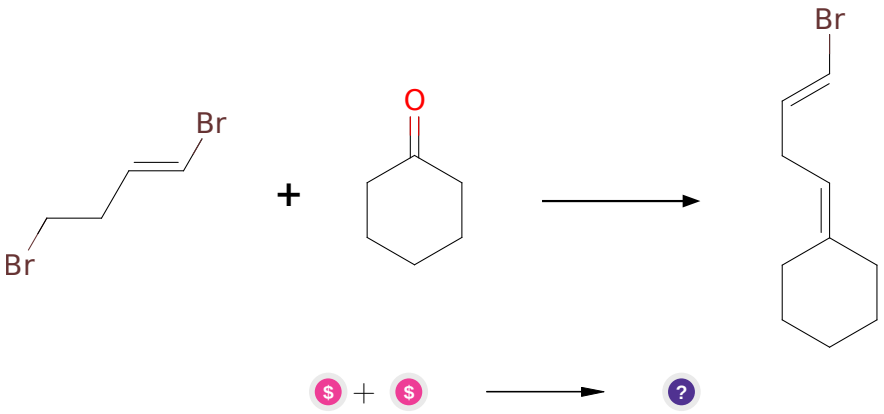
Typical conditions: PPh3.CBr4

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

2.4.4 HWE/Wittig Olefination



Substrates:

1. Cyclohexanone - *available at Sigma-Aldrich*
2. 1,4-dibromo-but-1-ene - *available at Sigma-Aldrich*

Products:

1. Br/C=C/CC=C1CCCCC1

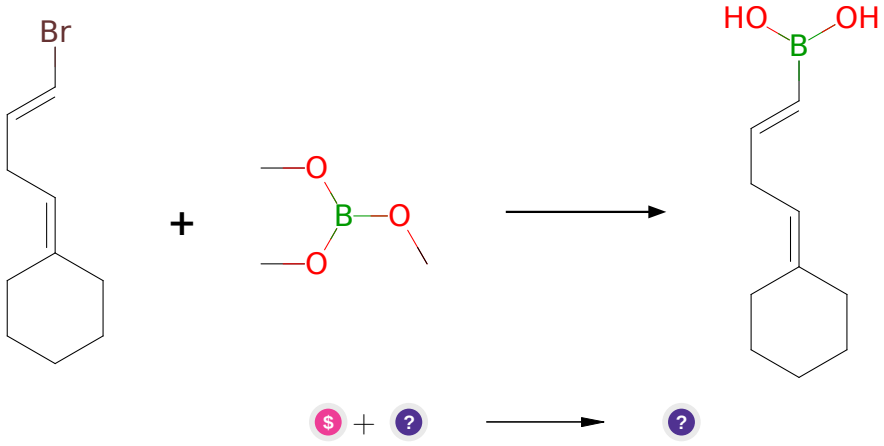
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.4.5 Synthesis of vinylboronic acid from vinyl bromide



Substrates:

1. Methyl borate - *available at Sigma-Aldrich*
2. Br/C=C/CC=C1CCCCC1

Products:

1. OB(O)/C=C/CC=C1CCCCC1

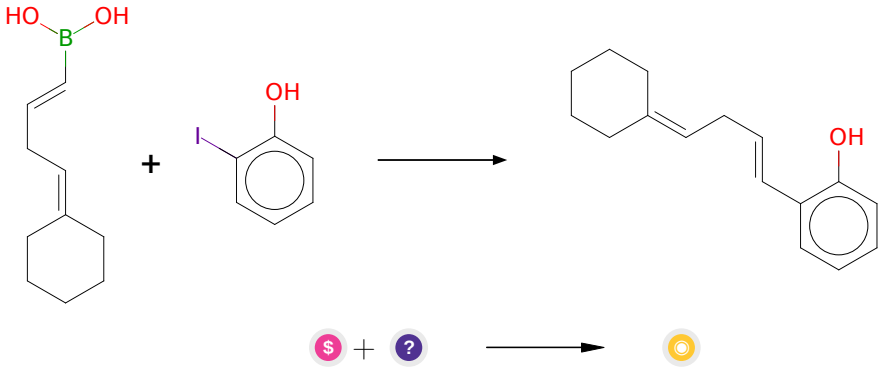
Typical conditions: 1.nBu-Li.THF.cooling.2.(MeO)3B.cooling.3.H+

Protections: none

Reference: *10.1016/j.tet.2010.11.065* and *10.1021/ja806258v* (suppl. Info)

Retrosynthesis ID: 24016

2.4.6 Suzuki coupling of aryl iodides with alkenyl boronic acids



Substrates:

1. 2-Iodophenol - *available at Sigma-Aldrich*
2. OB(O)/C=C/CC=C1CCCCC1

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 24886

2.5 Path 5

Score: 51.25

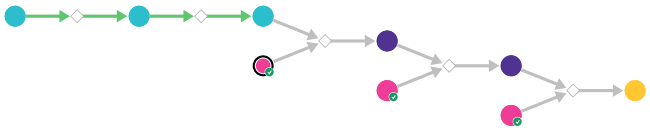
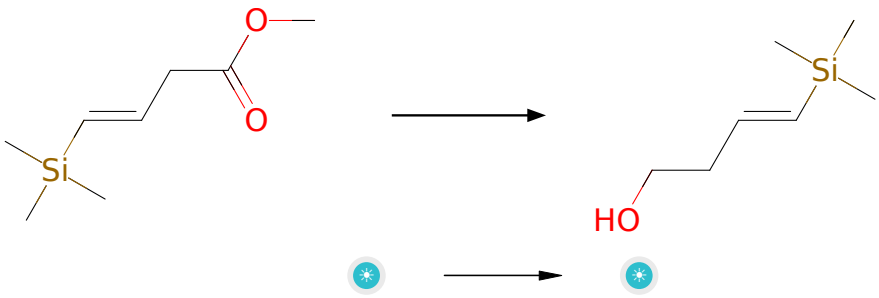


Figure 5: Outline of path 5

2.5.1 Esters reduction with LAH



Substrates:

1. C8H16O2Si

Products:

1. (e)-4-trimethylsilyl-3-buten-1-ol

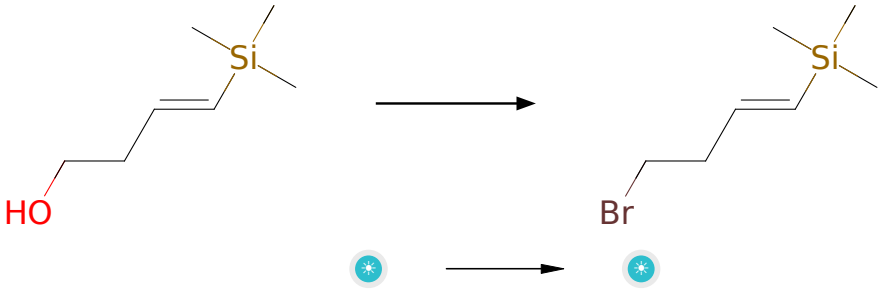
Typical conditions: LiAlH4.THF.0-20 C

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

2.5.2 Appel Reaction



Substrates:

1. (e)-4-trimethylsilyl-3-buten-1-ol

Products:

1. (4-bromo-but-1-enyl)-trimethyl-silane

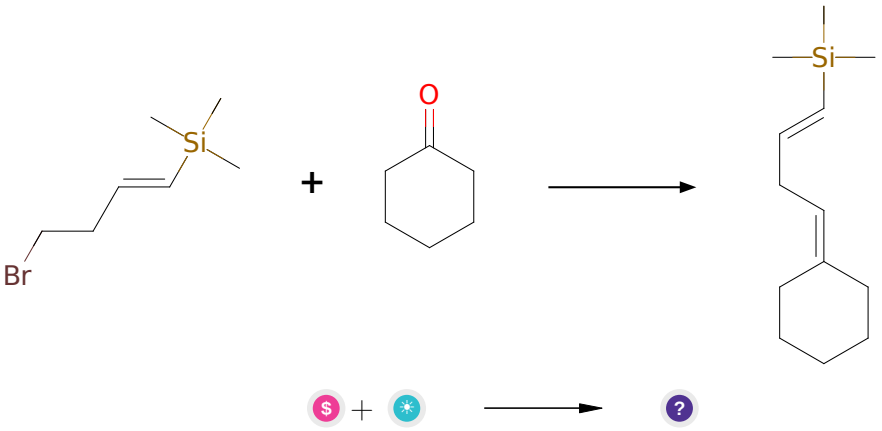
Typical conditions: PPh3.CBr4

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

2.5.3 HWE/Wittig Olefination



Substrates:

1. Cyclohexanone - *available at Sigma-Aldrich*
2. (4-bromo-but-1-enyl)-trimethyl-silane

Products:

1. C[Si](C)(C)/C=C/CC=C1CCCCC1

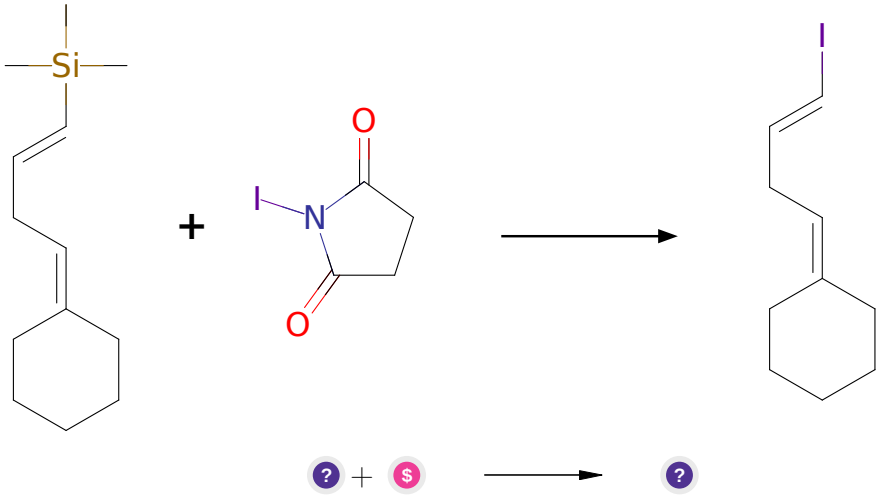
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.5.4 Iodination of Silyl Derivatives



Substrates:

1. C[Si](C)(C)/C=C/CC=C1CCCCC1
2. N-Iodosuccinimide - *available at Sigma-Aldrich*

Products:

1. I/C=C/CC=C1CCCCC1

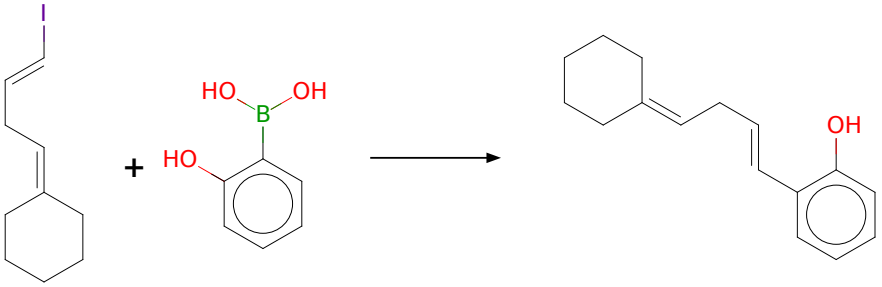
Typical conditions: NIS. 50C. MeCN

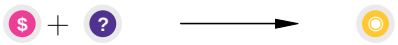
Protections: none

Reference: DOI:*10.1016/j.tetlet.2011.02.057* or DOI: *10.1016/S0040-4039(96)02000-X* or DOI: *10.1016/S0040-4020(02)00334-4*

Retrosynthesis ID: 9211

2.5.5 Suzuki coupling of arylboronic acids with vinyl iodides





Substrates:

1. 2-Hydroxyphenylboronic acid - *available at Sigma-Aldrich*
2. I/C=C/CC=C1CCCCC1

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 11208