Paths of analysis*

O4

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`

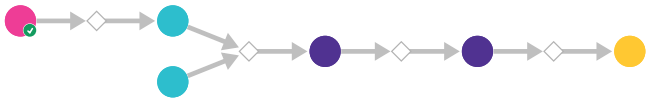
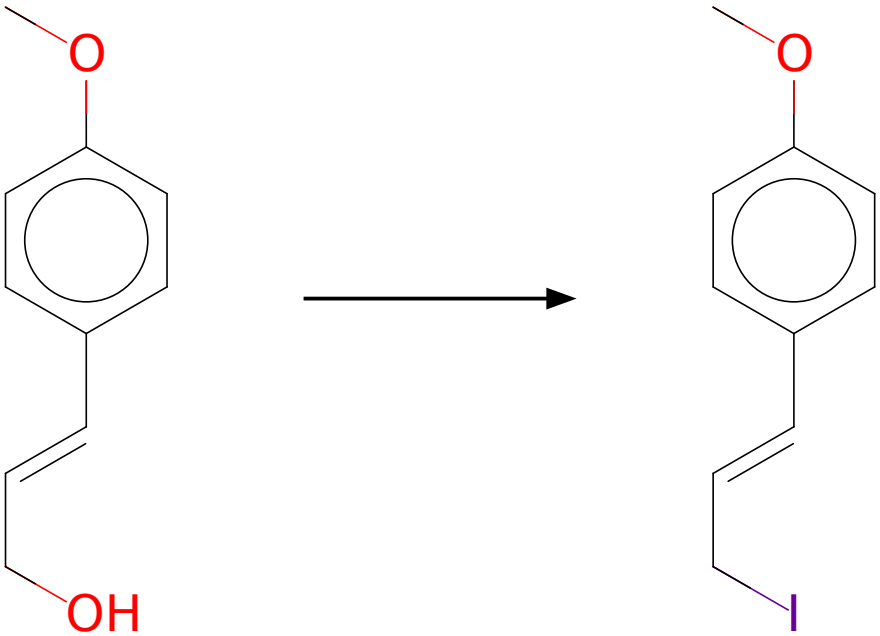
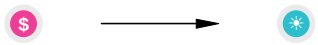


Figure 1: Outline of path 1

2.1.1 Synthesis Of Alkyl Iodides Via Appel Reaction





Substrates:

1. 3-(4-Methoxyphenyl)prop-2-en-1-ol - *available at Sigma-Aldrich*

Products:

1. 1-(3-iodo-propenyl)-4-methoxy-benzene

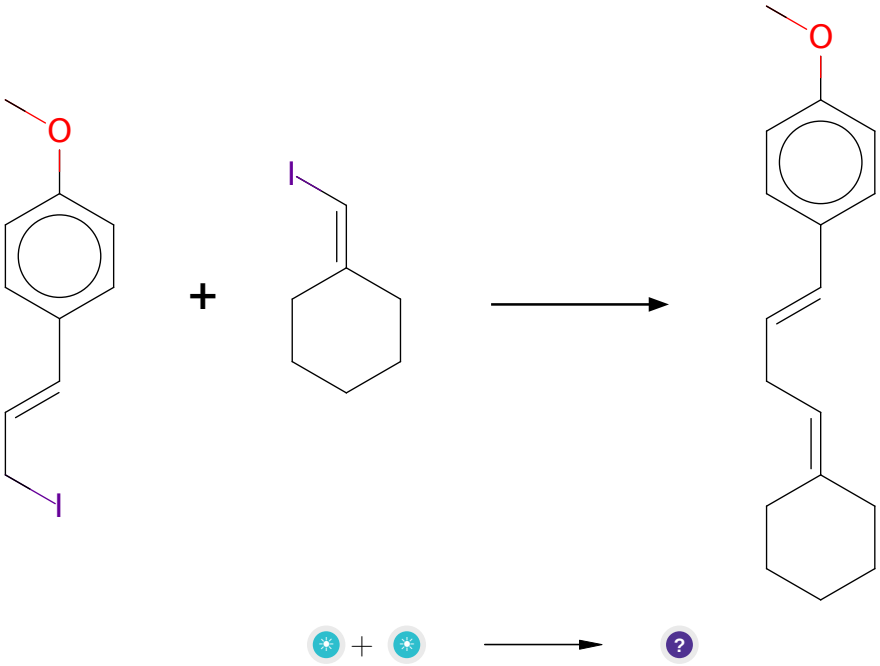
Typical conditions: Imidazole.PPh3.I2

Protections: none

Reference: *10.1002/1099-0690(200102)2001:3<493::AID-EJOC493>3.0.CO2-B* (compound 20) and *10.1016/j.tet.2014.09.030*

Retrosynthesis ID: 9990040

2.1.2 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. iodomethylene cyclohexane
2. 1-(3-iodo-propenyl)-4-methoxy-benzene

Products:

1. COc1ccc(/C=C/CC=C2CCCCC2)cc1

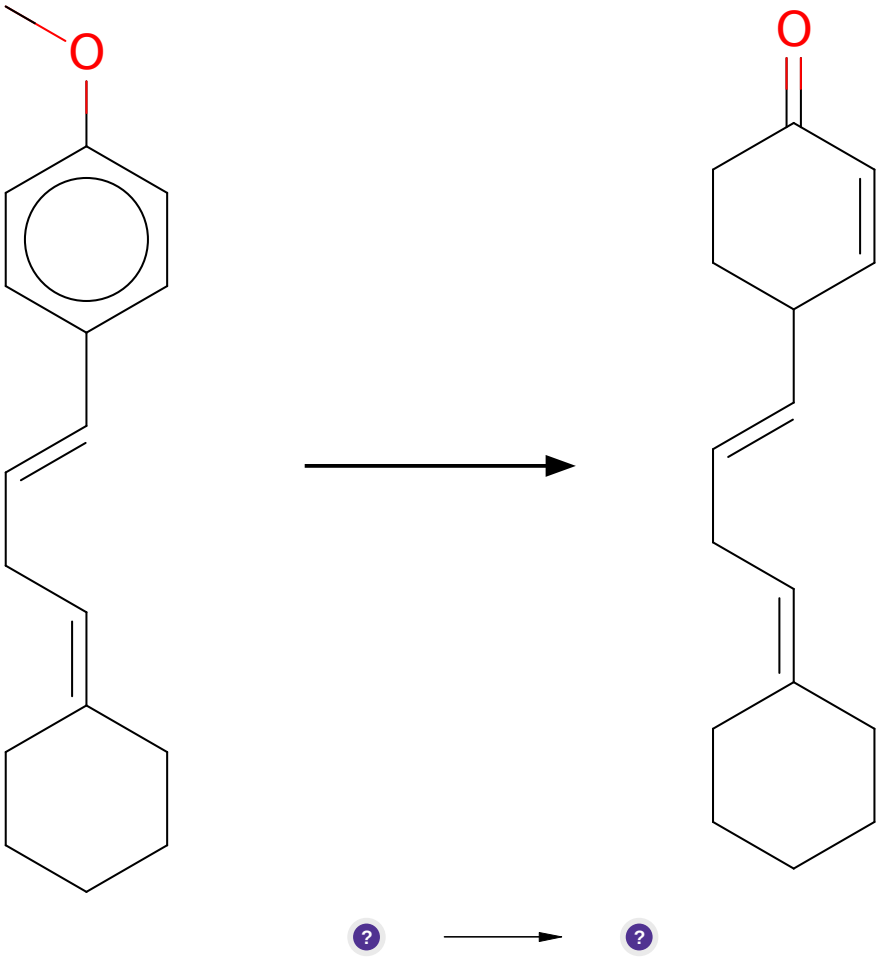
Typical conditions: [Pd].catalyst

Protections: none

Reference: *10.1016/j.bmcl.2005.12.066* and *10.1021/ol052070m* and *10.1021/ol5023195* and *10.1002/anie.200703134* and *10.1016/j.bmcl.2005.09.084* and *10.1021/ol0344873*

Retrosynthesis ID: 25165

2.1.3 Tandem Birch reduction and hydrolysis of enol ethers



Substrates:

1. COc1ccc(/C=C/CC=C2CCCCC2)cc1

Products:

1. O=C1C=CC(/C=C/CC=C2CCCCC2)CC1

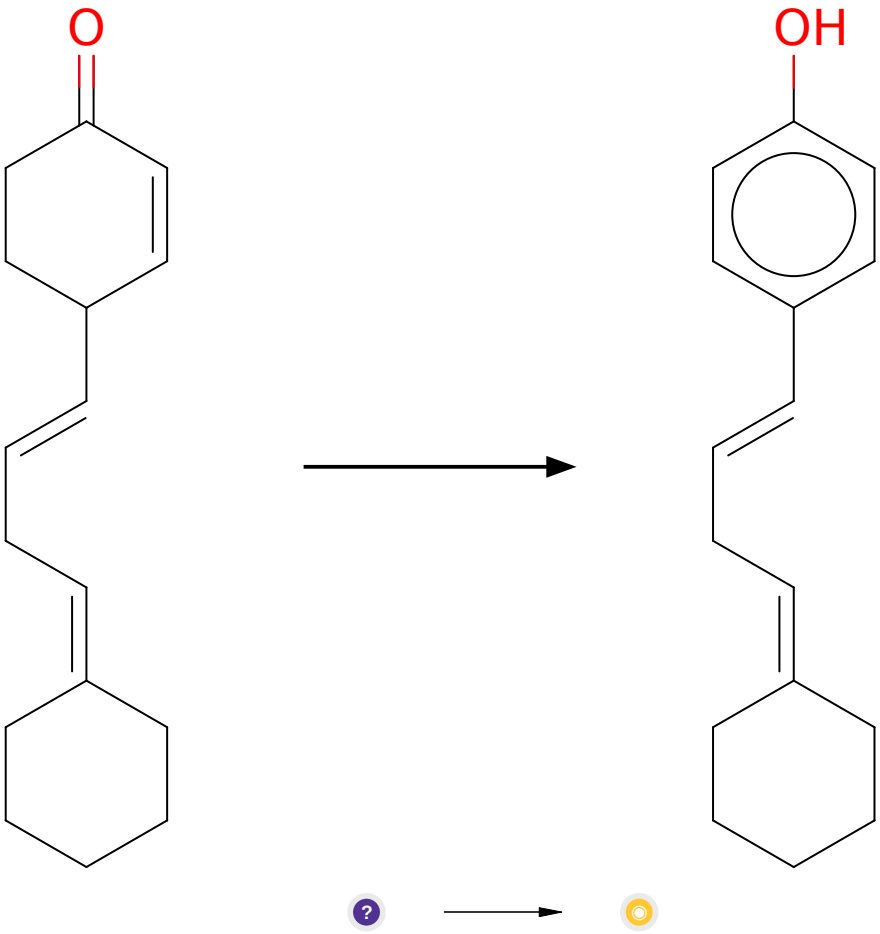
Typical conditions: 1. Li.NH3 2. HCl

Protections: none

Reference: DOI: *10.1002/anie.201304609* and *10.1021/jo00093a027*

Retrosynthesis ID: 6985

2.1.4 DDQ mediated aromatization



Substrates:

1. O=C1C=CC(/C=C/CC=C2CCCCC2)CC1

Products:

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: DDQ

Protections: none

Reference: *10.1021/ja054872i* and *10.1021/ja00311a085* and *10.1021/ja00122a011*

Retrosynthesis ID: 9999983

2.2 Path 2

Score: 31.25

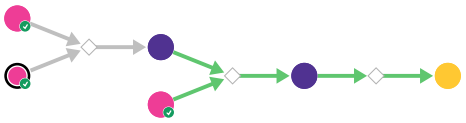
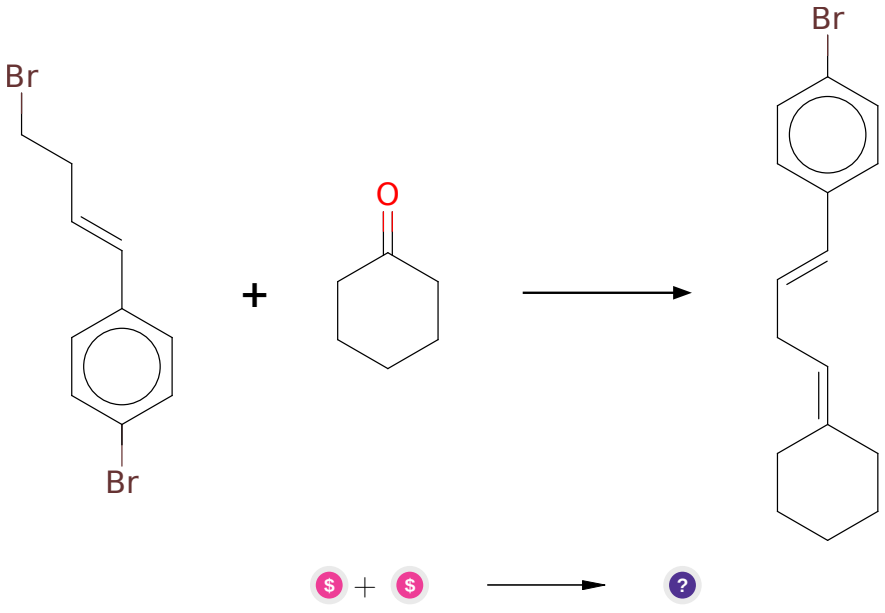


Figure 2: Outline of path 2

2.2.1 HWE/Wittig Olefination



Substrates:

1. 1-bromo-4-(4-bromobut-1-en-1-yl)benzene - *available at Sigma-Aldrich*
2. Cyclohexanone - *available at Sigma-Aldrich*

Products:

1. Brc1ccc(/C=C/CC=C2CCCCC2)cc1

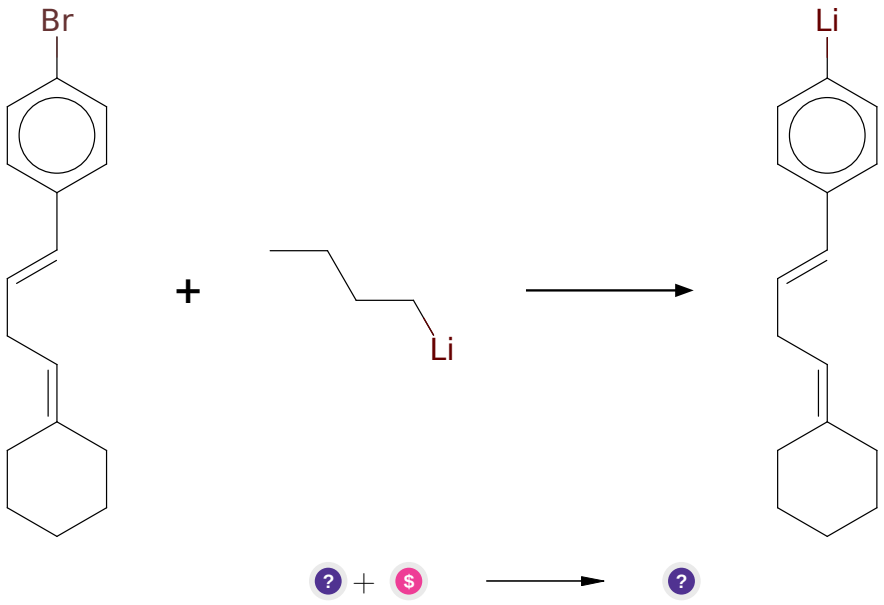
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.2.2 Br/Li exchange



Substrates:

1. Brc1ccc(/C=C/CC=C2CCCCC2)cc1
2. n-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1ccc(/C=C/CC=C2CCCCC2)cc1

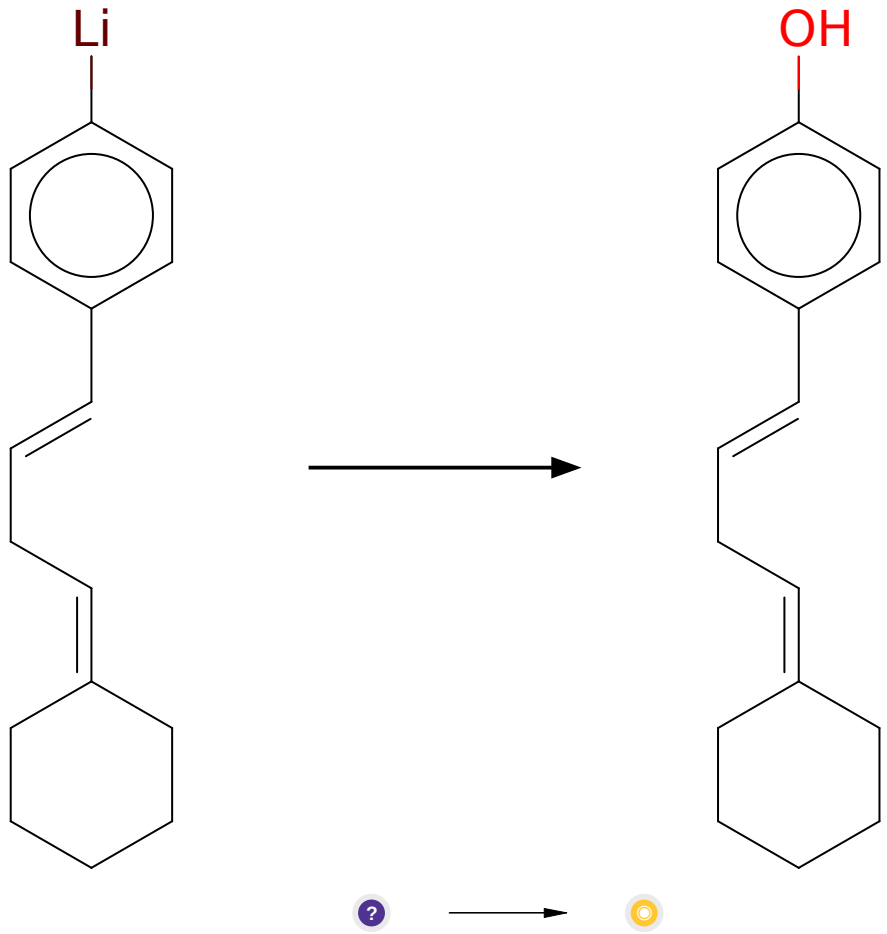
Typical conditions: nBuLi.or.tBuLi.THF.-78C

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

2.2.3 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1ccc(/C=C/CC=C2CCCCC2)cc1

Products:

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

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

2.3 Path 3

Score: `45.00`

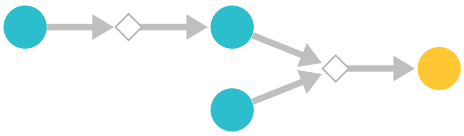
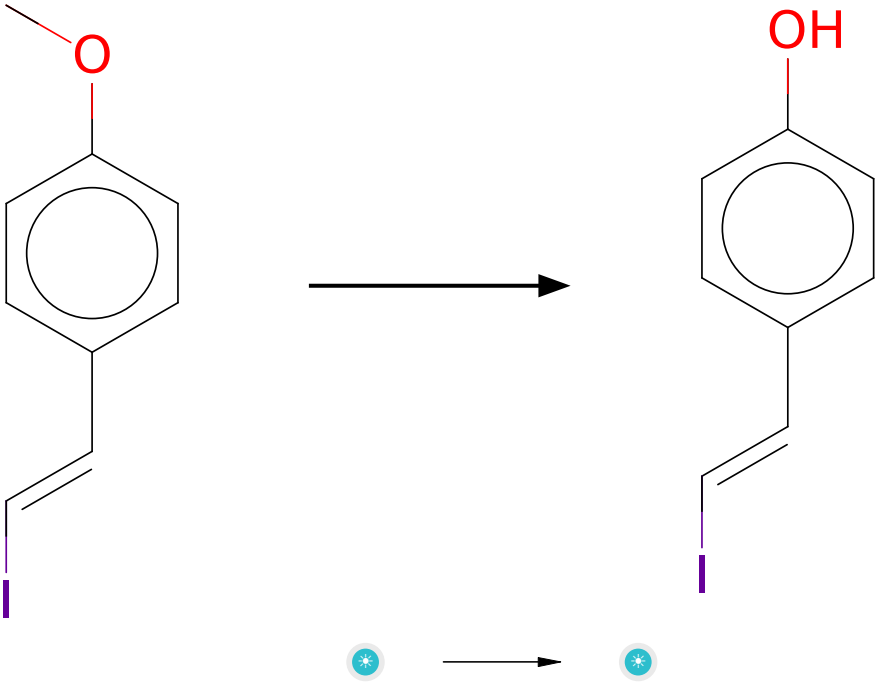


Figure 3: Outline of path 3

2.3.1 Demethylation of Phenols



Substrates:

1. (e)-2-(4-methoxyphenyl)-1-iodo-1-ethene

Products:

1. C8H7IO

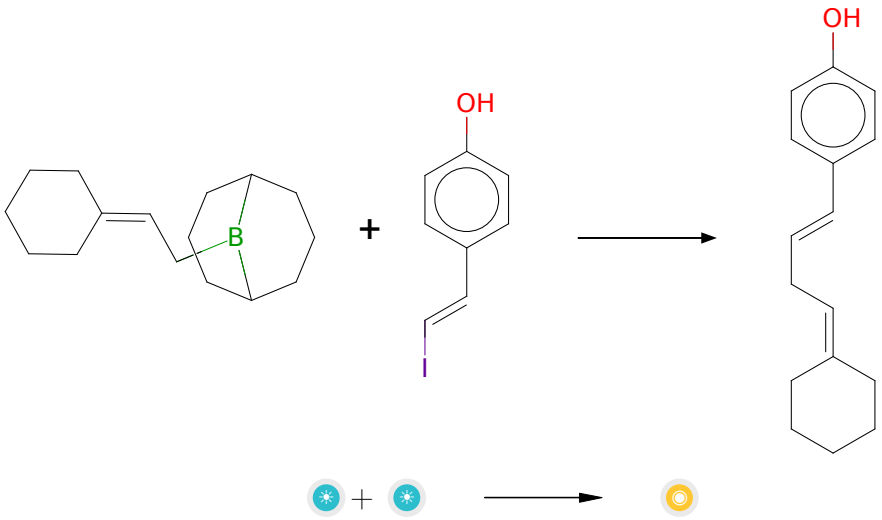
Typical conditions: BBr3.CH2Cl2

Protections: none

Reference: DOI: *10.1021/ja00105a021* and *10.1021/jm00176a011* and *10.1021/jm970277i* and *10.1021/ja0106164* and Patent: US2010/16298, 2010, A1, page 185

Retrosynthesis ID: 10011837

2.3.2 Suzuki coupling of alkyl-9-BBNs with vinyl iodides



Substrates:

1. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane
2. C8H7IO

Products:

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/jo015995y* and *10.1016/j.tetlet.2010.11.139* And *10.1021/ol0600741* and *10.1055/s-2002-32602* and *10.1002/anie.200501760*

Retrosynthesis ID: 25168

2.4 Path 4

Score: 45.00

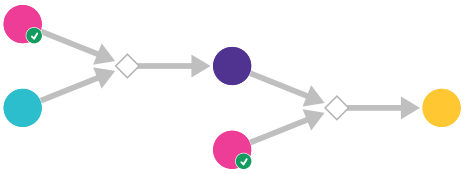
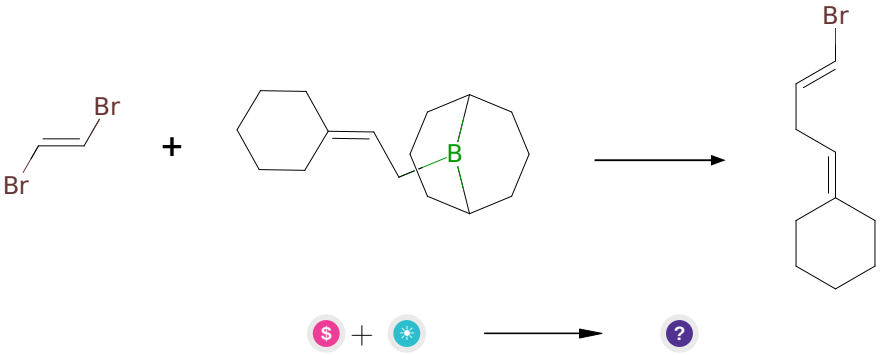


Figure 4: Outline of path 4

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



Substrates:

1. 1,2-Dibromoethylene - *available at Sigma-Aldrich*
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane

Products:

1. Br/C=C/CC=C1CCCCC1

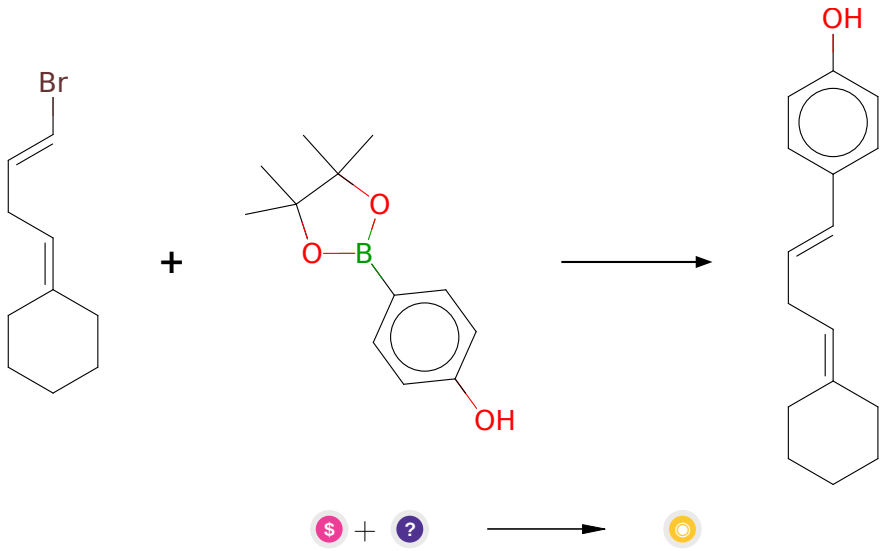
Typical conditions: Pd catalyst.base.solvent

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

2.4.2 Suzuki coupling of arylboronic pinacol esters with vinyl Bromides



Substrates:

1. 4-Hydroxyphenylboronic acid pinacol ester - *available at Sigma-Aldrich*
2. Br/C=C/CC=C1CCCCC1

Products:

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

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

2.5 Path 5

Score: 51.25

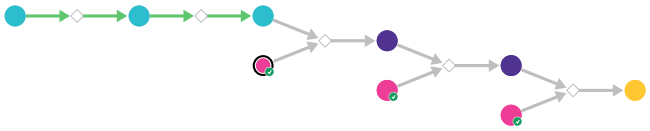
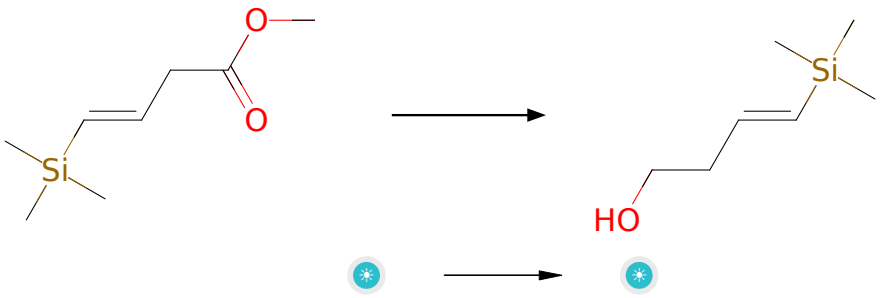


Figure 5: Outline of path 5

2.5.1 Esters reduction with LAH



Substrates:

1. C8H16O2Si

Products:

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

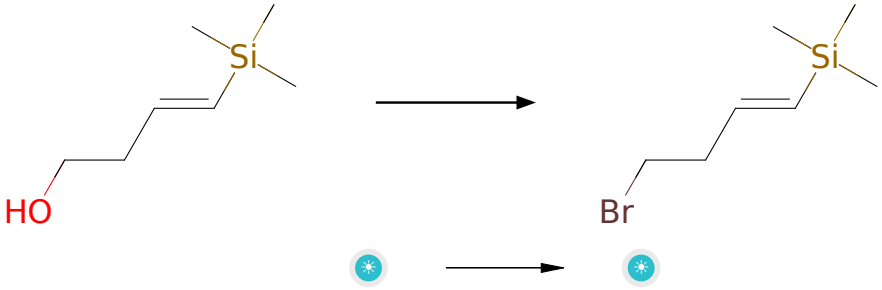
Typical conditions: LiAlH4.THF.0-20 C

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

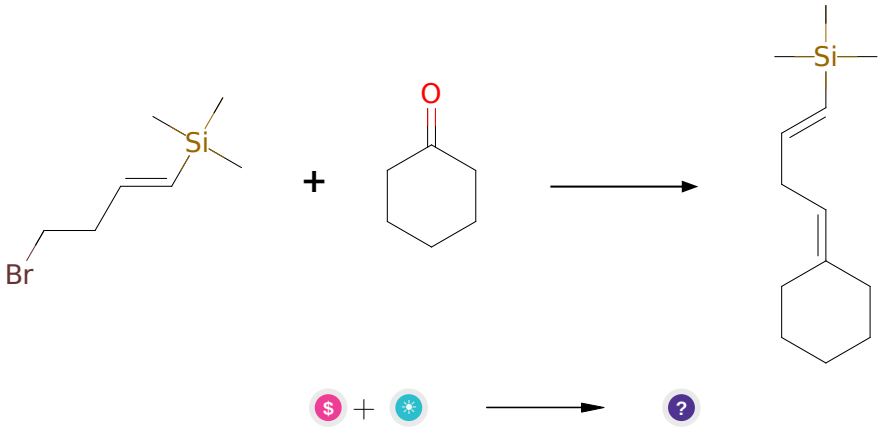
Typical conditions: PPh3.CBr4

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

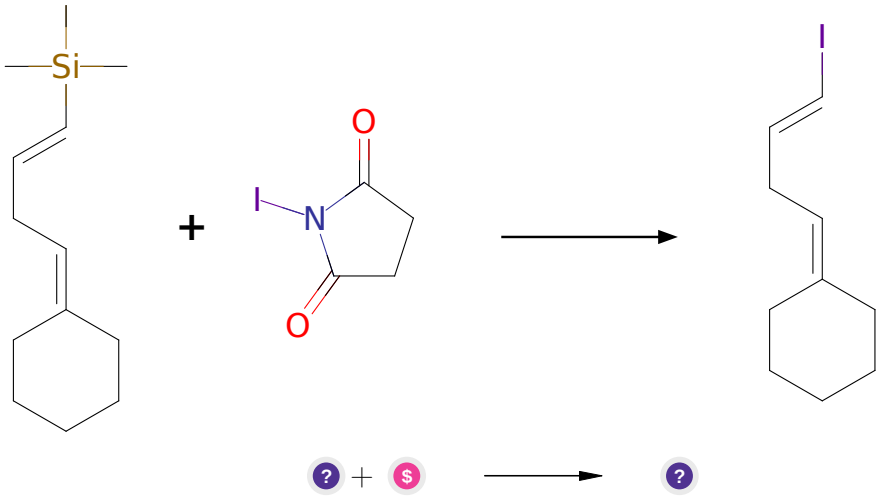
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

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

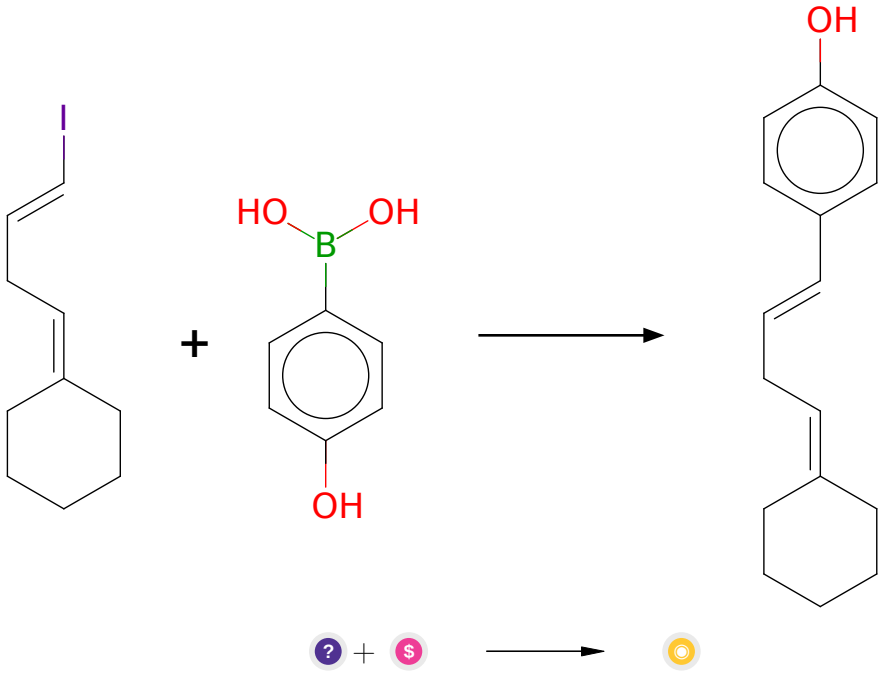
Typical conditions: NIS. 50C. MeCN

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. I/C=C/CC=C1CCCCC1
2. 4-Hydroxyphenylboronic acid - *available at Sigma-Aldrich*

Products:

1. Oc1ccc(/C=C/CC=C2CCCCC2)cc1

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