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: `20.00`

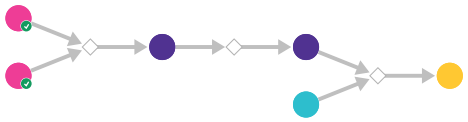
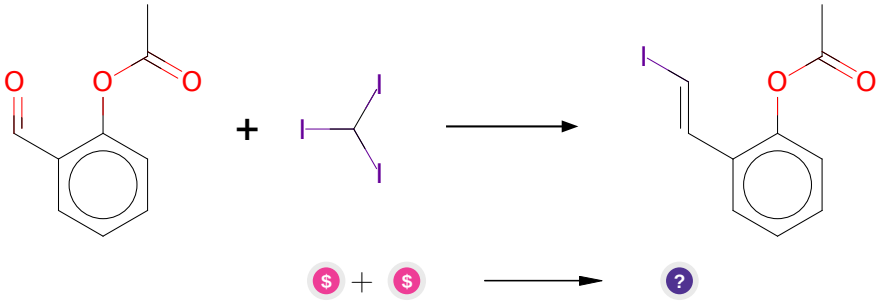


Figure 1: Outline of path 1

2.1.1 Takai olefination



Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. 2-formylphenyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccccc1/C=C/I

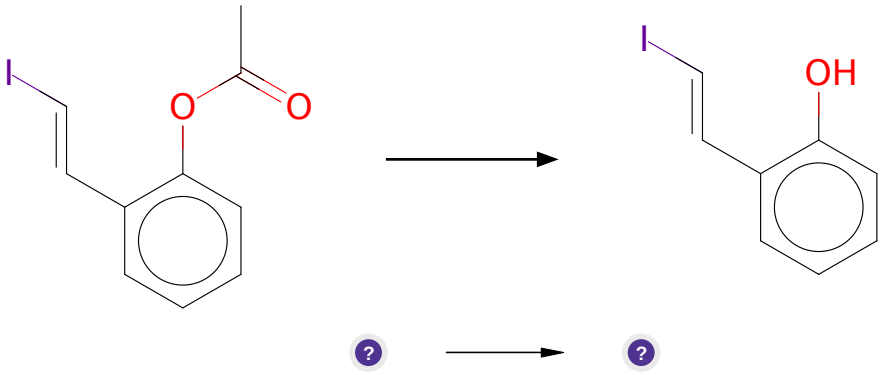
Typical conditions: CrCl2.THF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10497

2.1.2 Hydrolysis of acetates



Substrates:

1. CC(=O)Oc1ccccc1/C=C/I

Products:

1. Oc1ccccc1/C=C/I

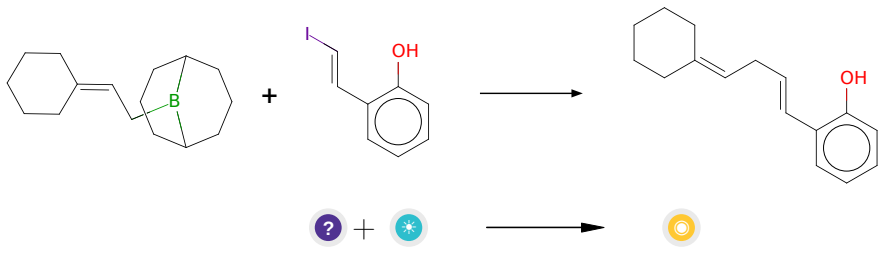
Typical conditions: KOH.MeOH

Protections: none

Reference: *10.3762/bjoc.10.40* and *10.1016/j.bmc.2009.11.035* and *10.1016/S0040-4020(02)01584-3*

Retrosynthesis ID: 32805

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



Substrates:

1. Oc1ccccc1/C=C/I
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/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

2.2 Path 2

Score: 25.00

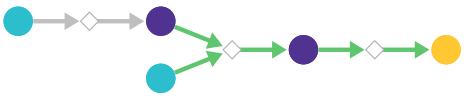
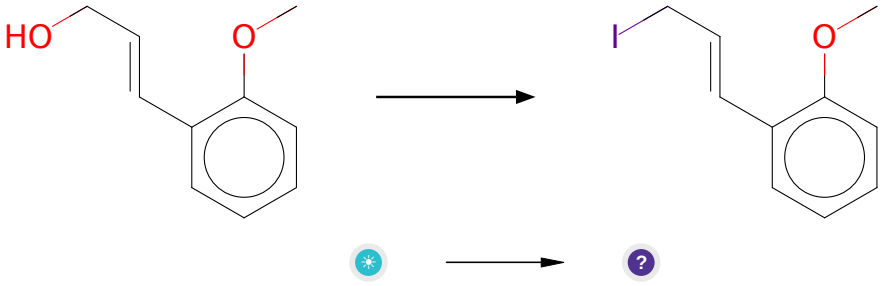


Figure 2: Outline of path 2

2.2.1 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

1. (e)-3-(2-methoxyphenyl)prop-2-en-1-ol

Products:

1. COc1ccccc1/C=C/CI

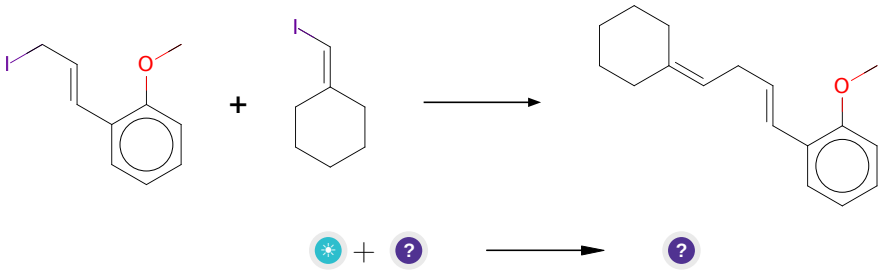
Typical conditions: Imidazole.PPh3.I2

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

2.2.2 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. iodomethylene cyclohexane
2. COc1ccccc1/C=C/CI

Products:

1. COc1ccccc1/C=C/CC=C1CCCCC1

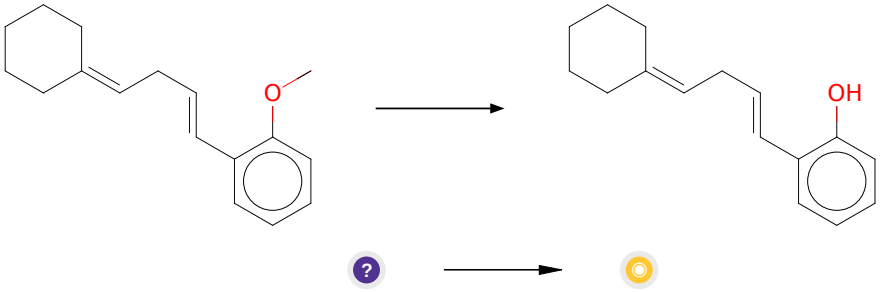
Typical conditions: [Pd].catalyst

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

2.2.3 Demethylation of Phenols



Substrates:

1. COc1ccccc1/C=C/CC=C1CCCCC1

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

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 Path 3

Score: 25.00

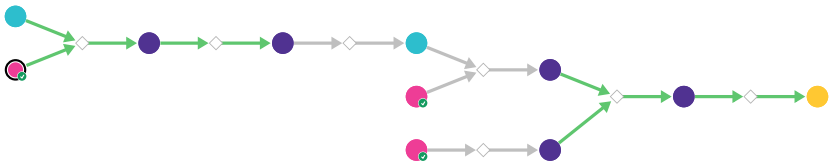
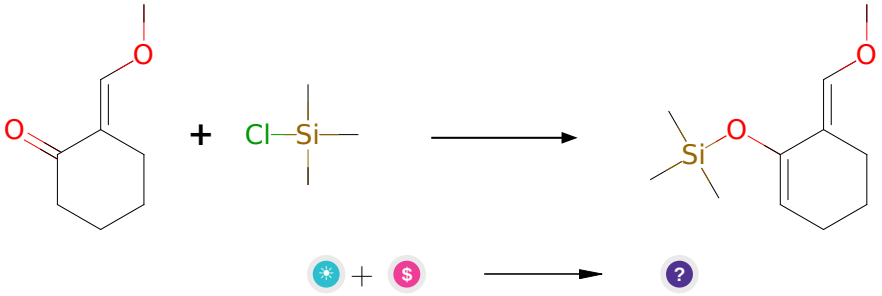


Figure 3: Outline of path 3

2.3.1 Enol esters and ethers synthesis



Substrates:

1. 2-methoxymethylen-cyclohexanon
2. TMSCl - *available at Sigma-Aldrich*

Products:

1. CO/C=C1\CCCC=C1O[Si](C)(C)C

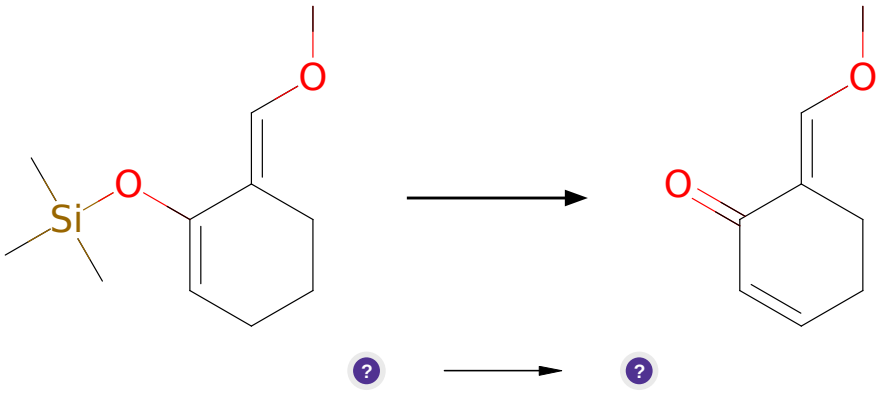
Typical conditions: 1.LDA.2.Electrophile

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. CO/C=C1\CCCC=C1O[Si](C)(C)C

Products:

1. CO/C=C1\CCC=CC1=O

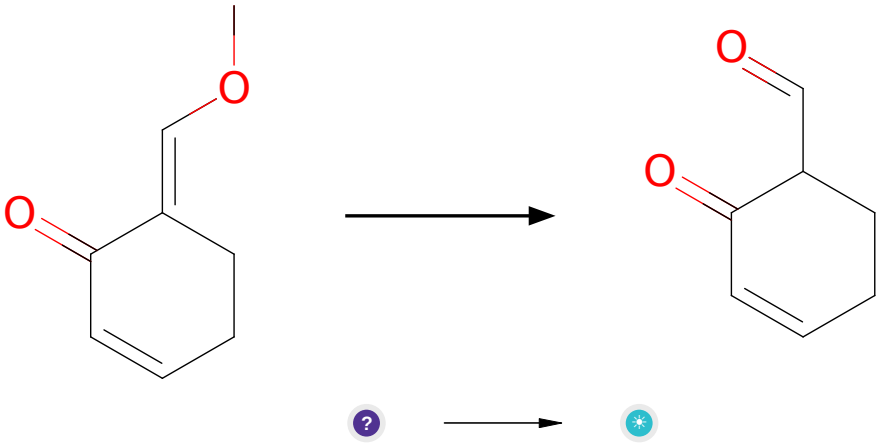
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

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 Synthesis of ketones and aldehydes from enol ethers



Substrates:

1. CO/C=C1\CCC=CC1=O

Products:

1. 6-formyl-cyclohex-2-en-1-on

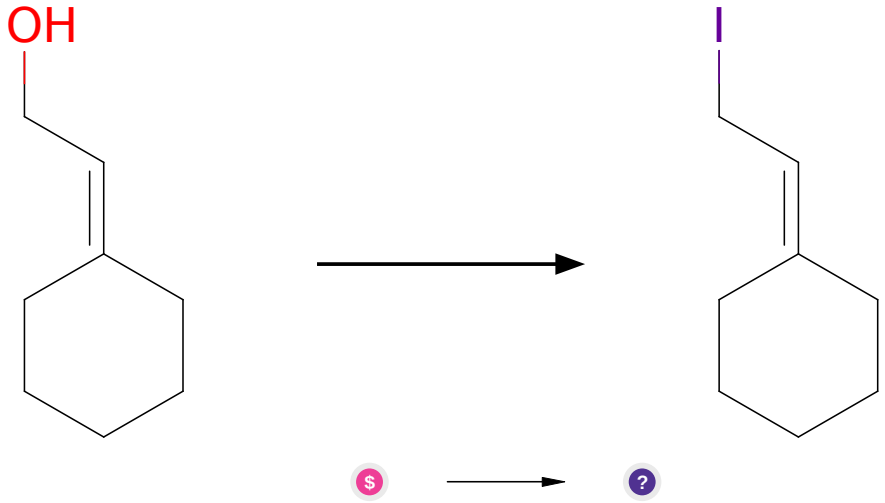
Typical conditions: [H+].THF

Protections: none

Reference: *10.1081/SCC-120023437* AND *10.1016/j.bmcl.2007.11.020* AND *10.1016/j.tet.2011.03.084* AND *10.1021/ja00270a023* AND *10.1055/s-1994-25424* AND

Retrosynthesis ID: 14842

2.3.4 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

1. 2-cyclohexylideneethan-1-ol - *available at Sigma-Aldrich*

Products:

1. ICC=C1CCCCC1

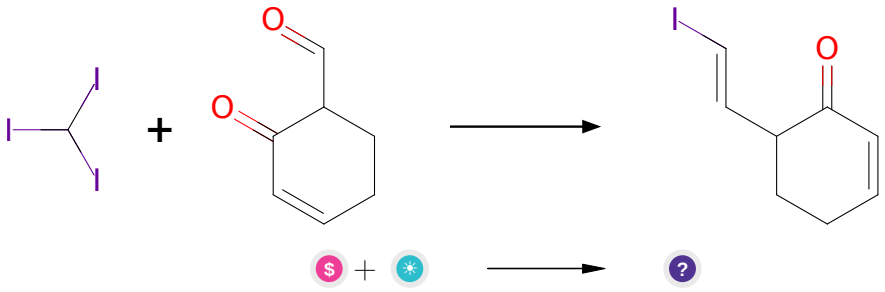
Typical conditions: Imidazole.PPh3.I2

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

2.3.5 Takai olefination



Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. 6-formyl-cyclohex-2-en-1-on

Products:

1. O=C1C=CCCC1/C=C/I

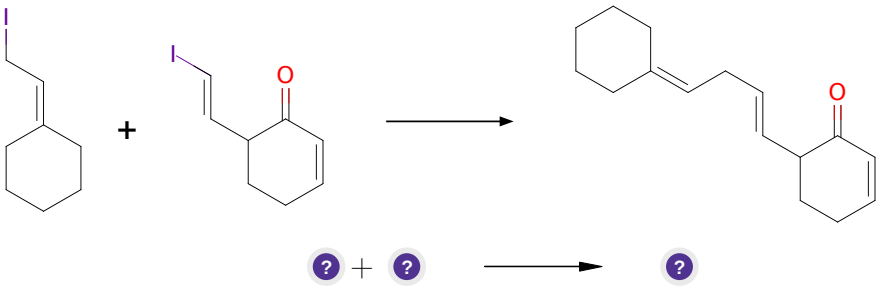
Typical conditions: CrCl2.THF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10497

2.3.6 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. ICC=C1CCCCC1
2. O=C1C=CCCC1/C=C/I

Products:

1. O=C1C=CCCC1/C=C/CC=C1CCCCC1

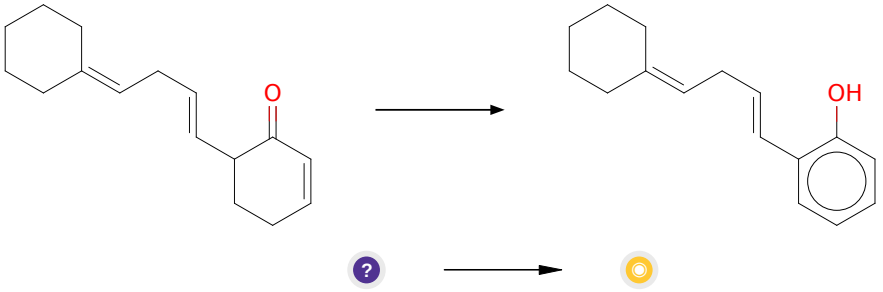
Typical conditions: [Pd].catalyst

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: 25162

2.3.7 DDQ mediated aromatization



Substrates:

1. O=C1C=CCCC1/C=C/CC=C1CCCCC1

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: DDQ

Protections: none

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

Retrosynthesis ID: 9999983

2.4 Path 4

Score: 25.00

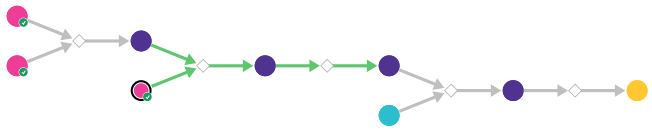
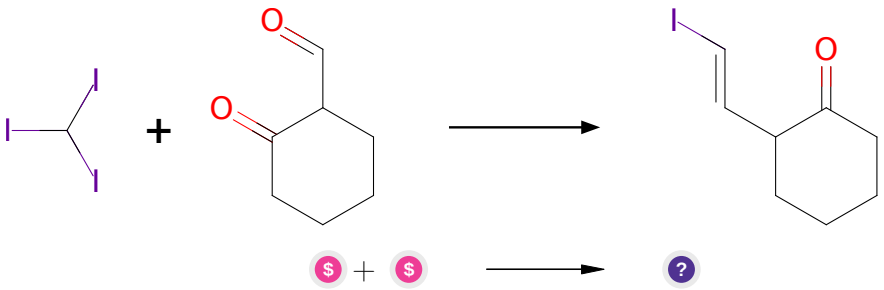


Figure 4: Outline of path 4

2.4.1 Takai olefination



Substrates:

1. 2-Oxocyclohexanecarbaldehyde - *available at Sigma-Aldrich*
2. Iodoform - *available at Sigma-Aldrich*

Products:

1. O=C1CCCCC1/C=C/I

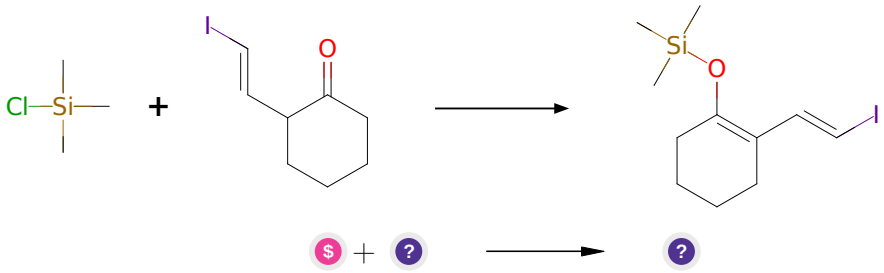
Typical conditions: CrCl2.THF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10497

2.4.2 Enol esters and ethers synthesis



Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. O=C1CCCCC1/C=C/I

Products:

1. C[Si](C)(C)OC1=C(/C=C/I)CCCC1

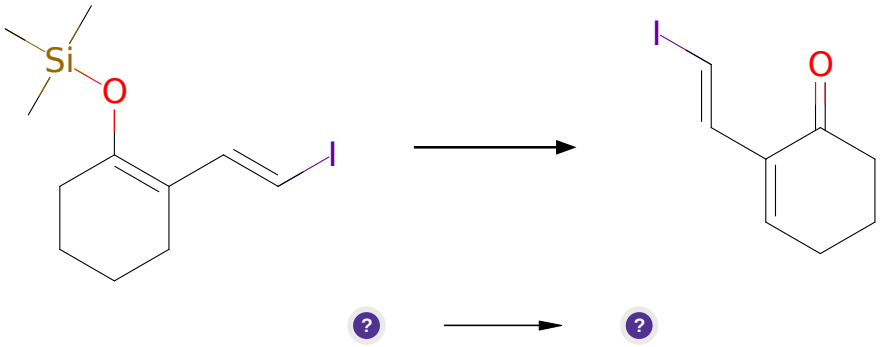
Typical conditions: 1. Et3N.Electrophile

Protections: none

Reference: *10.1016/S0040-4020(03)00977-3* AND *10.1021/ja00056a002*

Retrosynthesis ID: 7799

2.4.3 Dehydrogenation of silyl enol ethers



Substrates:

1. C[Si](C)(C)OC1=C(/C=C/I)CCCC1

Products:

1. O=C1CCCC=C1/C=C/I

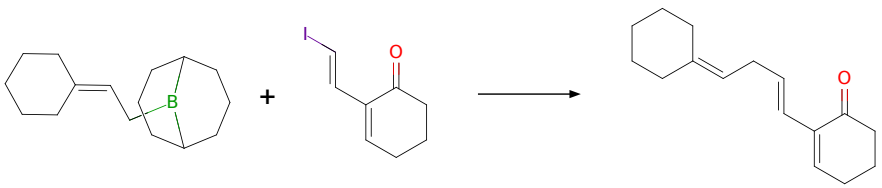
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

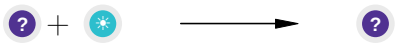
Protections: none

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

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





Substrates:

1. O=C1CCCC=C1/C=C/I
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane

Products:

1. O=C1CCCC=C1/C=C/CC=C1CCCCC1

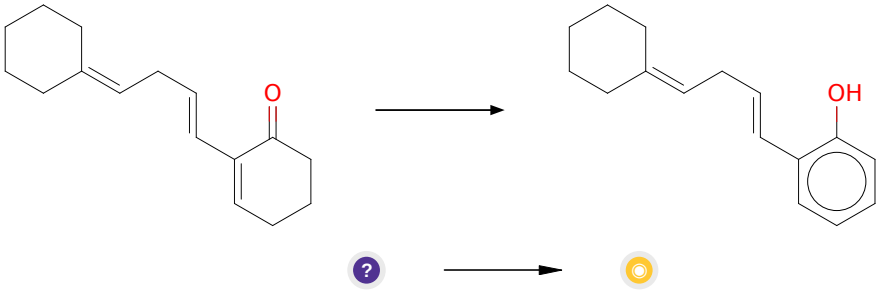
Typical conditions: Pd catalyst.base.solvent

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

2.4.5 DDQ mediated aromatization



Substrates:

1. O=C1CCCC=C1/C=C/CC=C1CCCCC1

Products:

1. Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: DDQ

Protections: none

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

Retrosynthesis ID: 9999983

2.5 Path 5

Score: 31.25

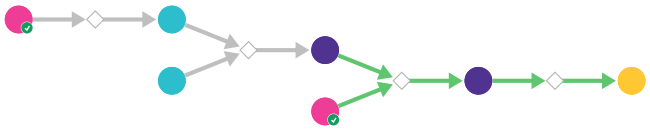
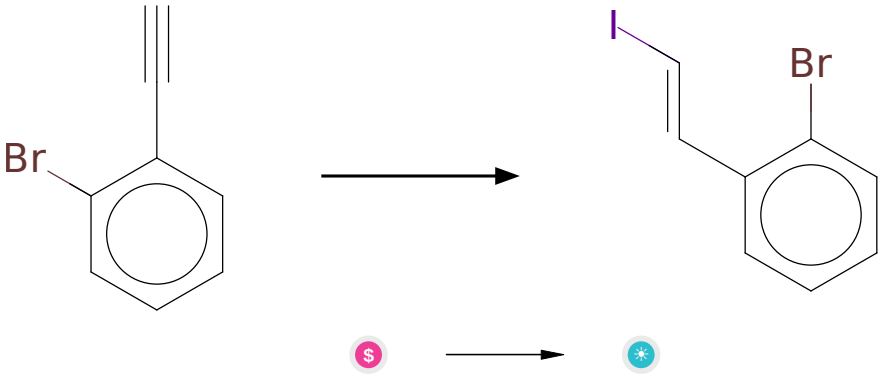


Figure 5: Outline of path 5

2.5.1 Iodination of vinylalanes



Substrates:

1. 1-Bromo-2-ethynylbenzene - *available at Sigma-Aldrich*

Products:

1. C8H6BrI

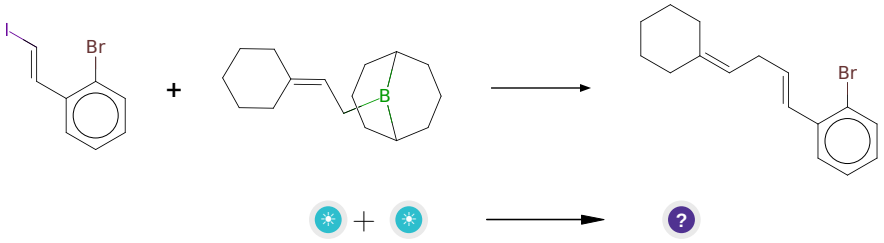
Typical conditions: Schwartz's reagent.then.I2

Protections: none

Reference: DOI: *10.1080/00397910008087318*

Retrosynthesis ID: 7406

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



Substrates:

1. C8H6BrI
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane

Products:

1. Brc1ccccc1/C=C/CC=C1CCCCC1

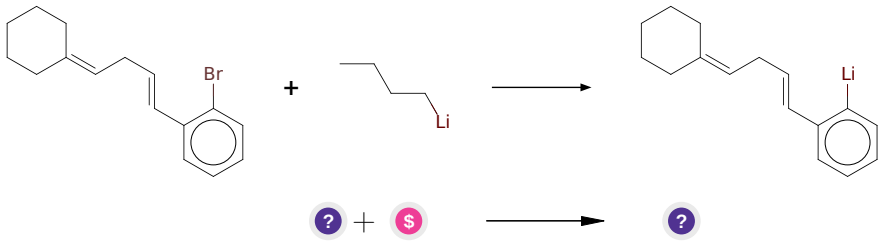
Typical conditions: Pd catalyst.base.solvent

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

2.5.3 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

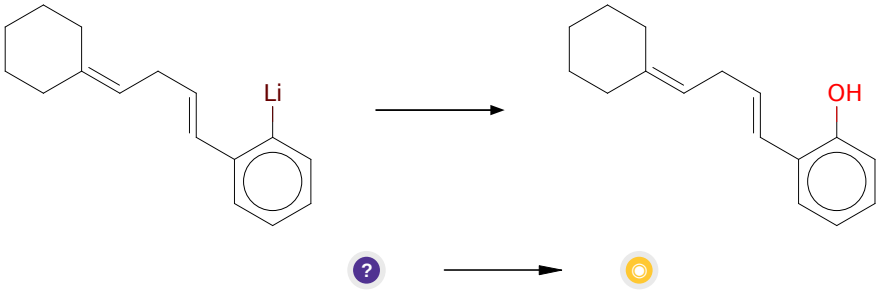
Typical conditions: nBuLi.or.tBuLi.THF.-78C

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

2.5.4 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