

Paths of analysis*

O5

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselective 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: $TUNNEL_COEF * FGI_COEF * STEP * 20 + 1000 * (CONFLICT + NON_SELECTIVITY + FILTERS + PROTECT)$

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

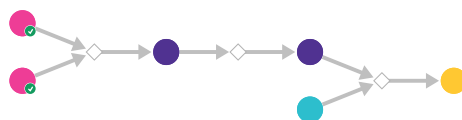
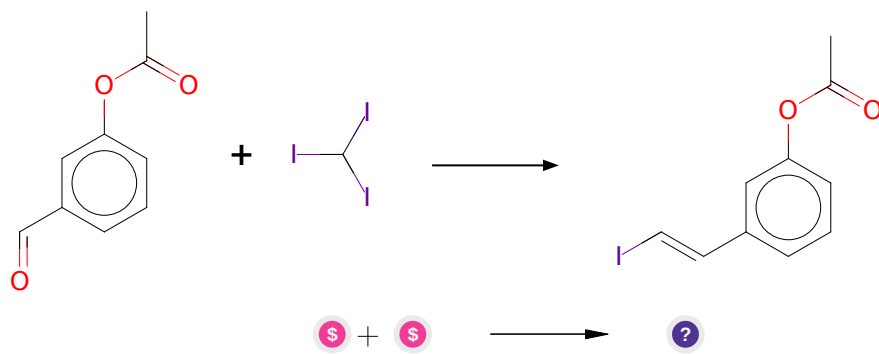


Figure 1: Outline of path 1

2.1.1 Takai olefination



Substrates:

1. 3-Formylphenyl acetate - *available at Sigma-Aldrich*
2. Iodoform - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1cccc(/C=C/I)c1

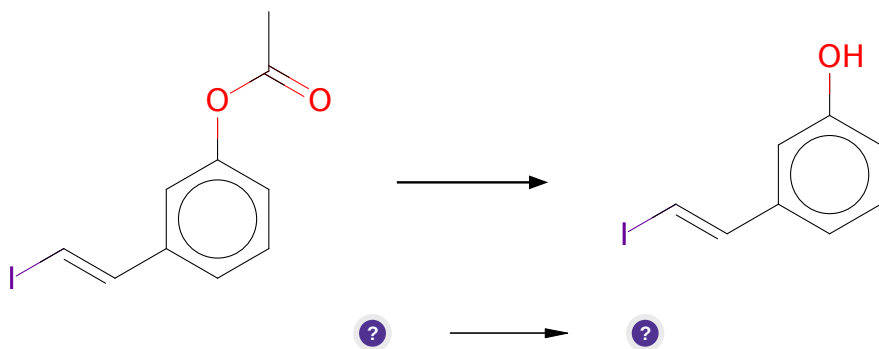
Typical conditions: CrCl₂.THF

Protections: none

Reference: [10.1021/ja00283a046](#) and [10.1021/ja00237a081](#)

Retrosynthesis ID: 10497

2.1.2 Hydrolysis of acetates



Substrates:

1. CC(=O)Oc1cccc(/C=C/I)c1

Products:

1. Oc1cccc(/C=C/I)c1

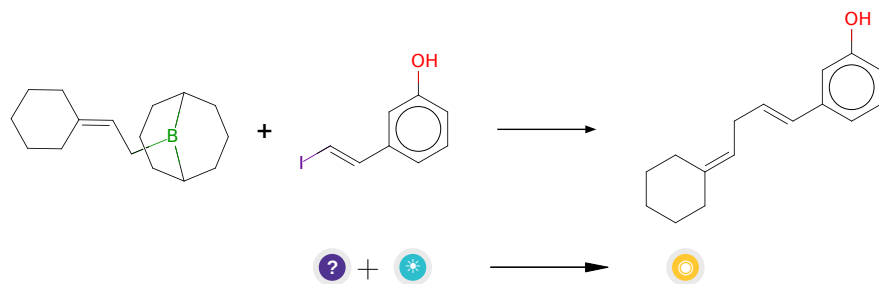
Typical conditions: KOH.MeOH

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. Oc1cccc(/C=C/I)c1
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane

Products:

1. Oc1cccc(/C=C/CC=C2CCCCC2)c1

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

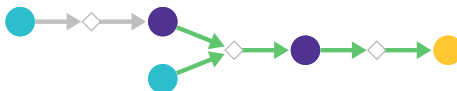
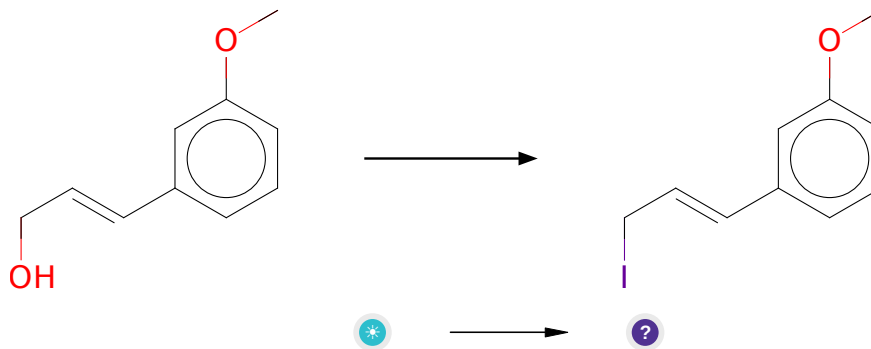


Figure 2: Outline of path 2

2.2.1 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

1. (E)-3-(3-methoxyphenyl)-2-propen-1-ol

Products:

1. COc1cccc(/C=C/CI)c1

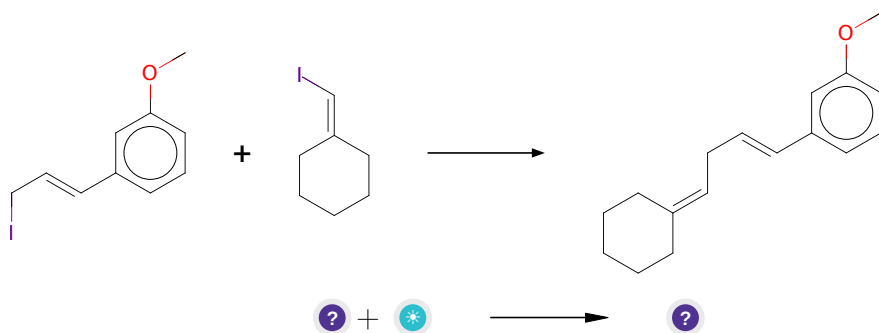
Typical conditions: Imidazole.PPh3.I2

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. COc1cccc(/C=C/CI)c1
2. iodomethylene cyclohexane

Products:

1. COc1cccc(/C=C/CC=C2CCCCC2)c1

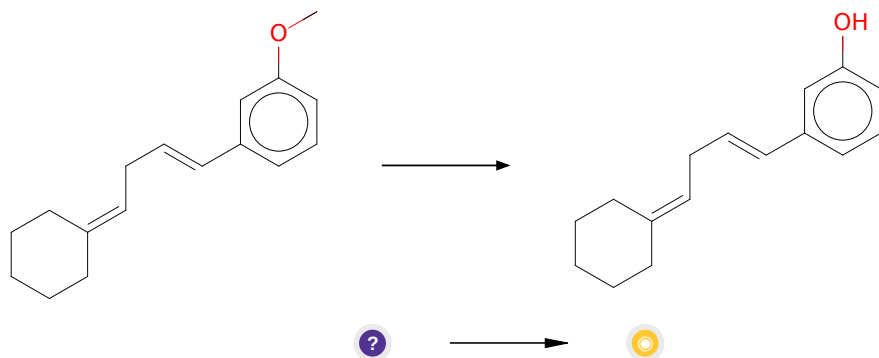
Typical conditions: [Pd].catalyst

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. COC1=CC=C(C=C1)/C=C/CC=C2CCCCC2)c1

Products:

1. Oc1ccccc1/C=C/CC=C2CCCCC2)c1

Typical conditions: BBr₃.CH₂Cl₂

Protections: none

Reference: DOI: [10.1021/ja00105a021](https://doi.org/10.1021/ja00105a021) and [10.1021/jm00176a011](https://doi.org/10.1021/jm00176a011) and [10.1021/jm970277i](https://doi.org/10.1021/jm970277i) and [10.1021/ja0106164](https://doi.org/10.1021/ja0106164) and Patent: US2010/16298, 2010, A1, page 185

Retrosynthesis ID: 10011837

2.3 Path 3

Score: 31.25

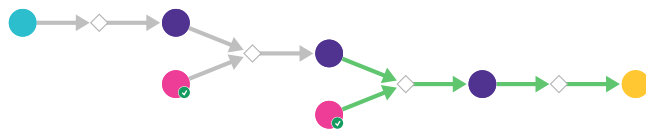
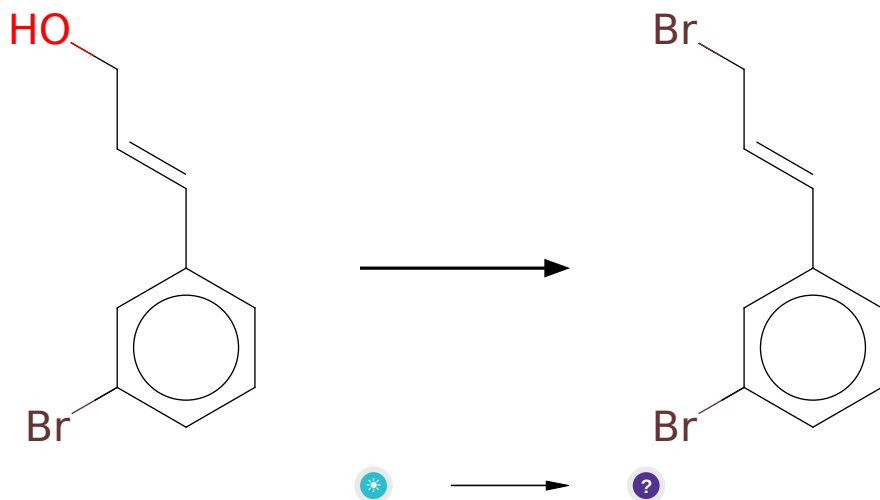


Figure 3: Outline of path 3

2.3.1 Appel Reaction



Substrates:

1. (E)-3-bromocinnamyl alcohol

Products:

1. BrC/C=C/c1cccc(Br)c1

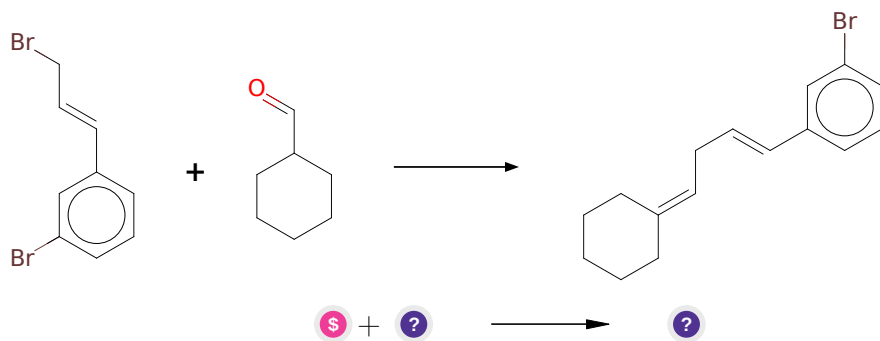
Typical conditions: PPh3.CBr4

Protections: none

Reference: [10.1021/ja800574m](#) and [10.1016/j.tet.2012.05.010](#) and [10.1016/j.tet.2004.09.021](#) (experimental)

Retrosynthesis ID: 9990037

2.3.2 Shapiro reaction followed by alkyl bromide addition



Substrates:

1. Hexahydrobenzaldehyde - *available at Sigma-Aldrich*
2. BrC/C=C/c1cccc(Br)c1

Products:

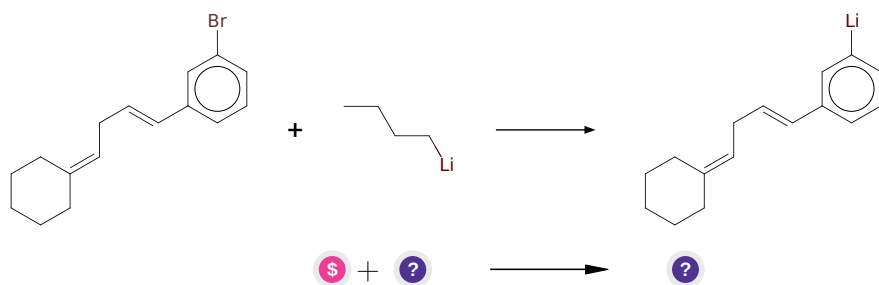
1. BrC1CCCC(/C=C/CC=C2CCCCC2)c1

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

2.3.3 Br/Li exchange**Substrates:**

1. n-BuLi - *available at Sigma-Aldrich*
2. BrC1CCCC(/C=C/CC=C2CCCCC2)c1

Products:

1. [Li]c1cccc(/C=C/CC=C2CCCCC2)c1

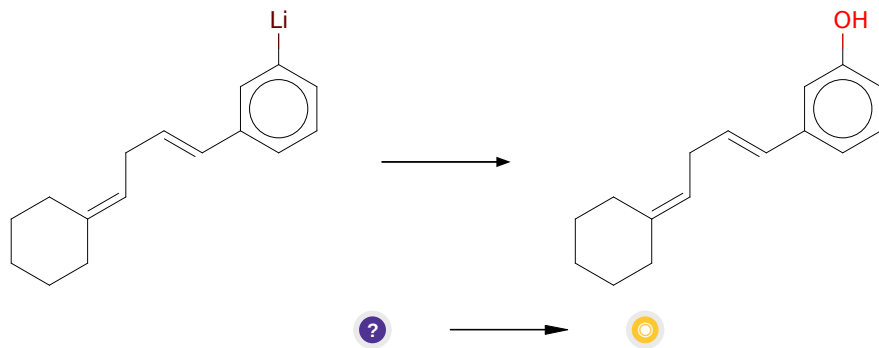
Typical conditions: nBuLi.or.tBuLi.THF.-78C

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

2.3.4 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]c1cccc(/C=C/CC=C2CCCCC2)c1

Products:

1. Oc1cccc(/C=C/CC=C2CCCCC2)c1

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

2.4 Path 4

Score: 31.25

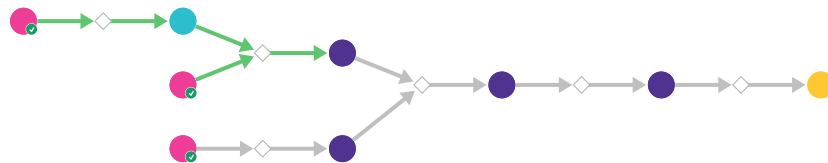
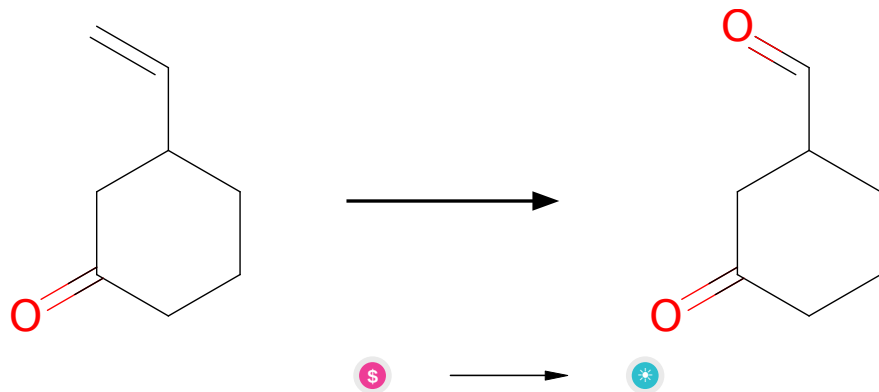


Figure 4: Outline of path 4

2.4.1 Ozonolysis



Substrates:

1. 3-ethenylcyclohexan-1-one - *available at Sigma-Aldrich*

Products:

1. 3-oxo-cyclohexancarbaldehyd

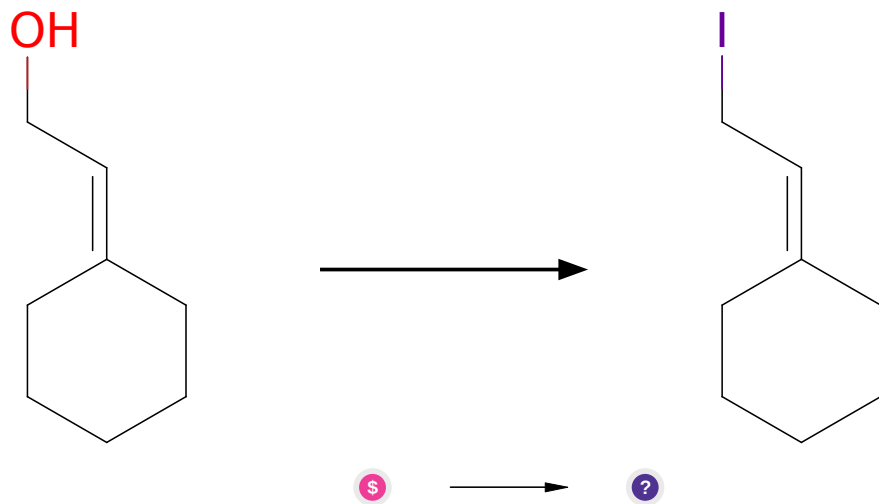
Typical conditions: O₃.MeOH.CH₂Cl₂.PPh₃ or Me₂S.low temperature

Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5074

2.4.2 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

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

Products:

1. ICC=C1CCCCC1

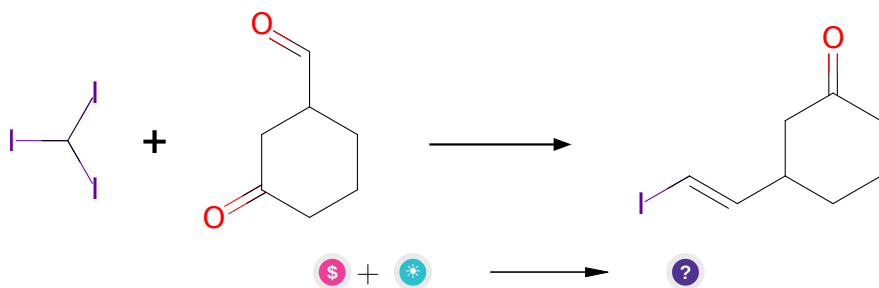
Typical conditions: Imidazole.PPh3.I2

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

2.4.3 Takai olefination



Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. 3-oxo-cyclohexanecarbaldehyde

Products:

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

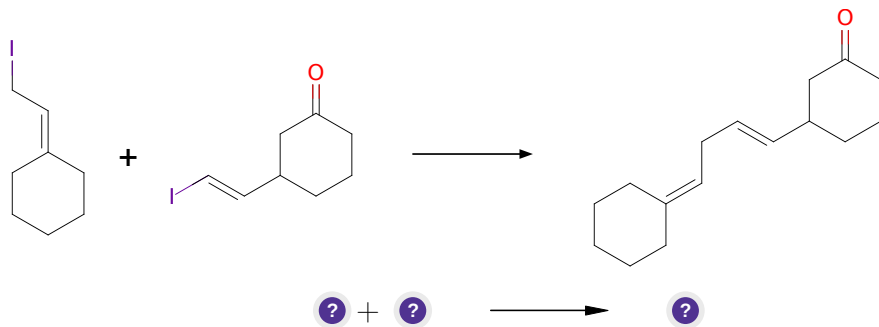
Typical conditions: CrCl2.THF

Protections: none

Reference: [10.1021/ja00283a046](#) and [10.1021/ja00237a081](#)

Retrosynthesis ID: 10497

2.4.4 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. O=C1CCCC(/C=C/I)C1
2. ICC=C1CCCCC1

Products:

1. O=C1CCCC(/C=C/CC=C2CCCCC2)C1

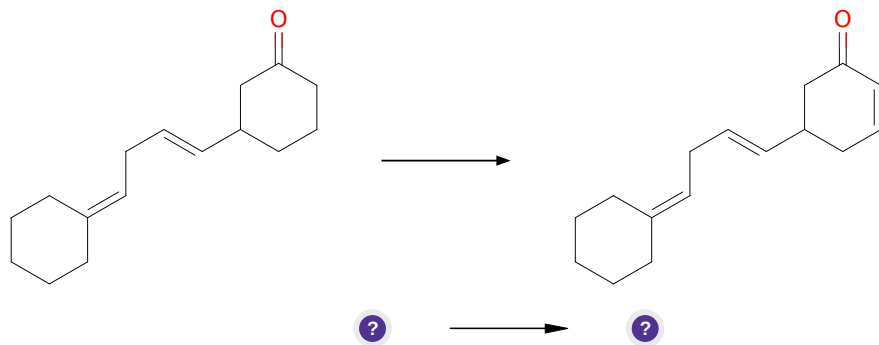
Typical conditions: [Pd].catalyst

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

2.4.5 Synthesis of enones from ketones



Substrates:

1. O=C1CCCC(/C=C/CC=C2CCCCC2)C1

Products:

1. O=C1C=CCC(/C=C/CC=C2CCCCC2)C1

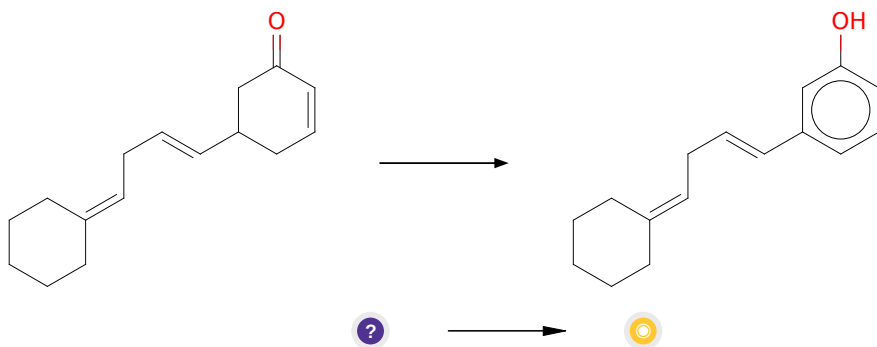
Typical conditions: TMSOTf then oxidant eg PdCl₂.O₂

Protections: none

Reference: [10.1002/anie.201512005](#) and [10.3762/bjoc.10.15](#) and [10.1021/acs.joc.5b02550](#) and [10.1055/s-2002-32603](#)

Retrosynthesis ID: 10004759

2.4.6 DDQ mediated aromatization



Substrates:

1. O=C1C=CCC(/C=C/CC=C2CCCCC2)C1

Products:

1. Oc1cccc(/C=C/CC=C2CCCCC2)c1

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

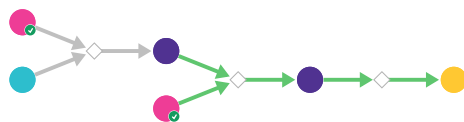
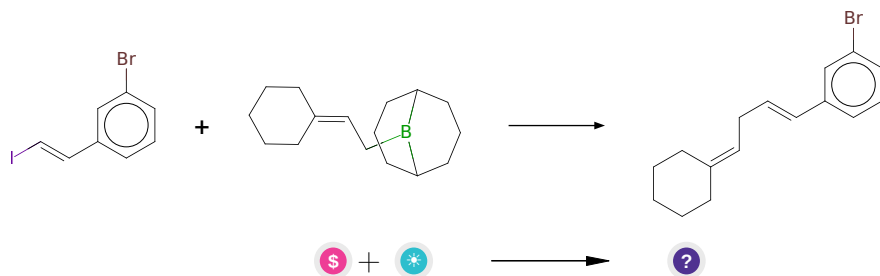


Figure 5: Outline of path 5

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



Substrates:

1. 1-bromo-3-(2-iodoethenyl)benzene - *available at Sigma-Aldrich*
2. 9-(3,3-pentamethyleneallyl)-9-borabicyclo[3.3.1]nonane

Products:

1. BrC1CCCC(/C=C/CC=C2CCCCC2)c1

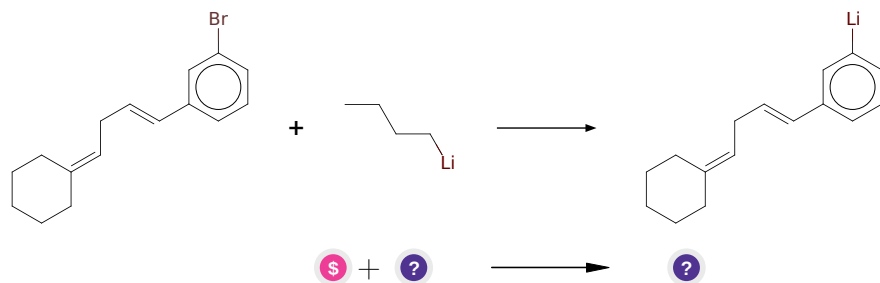
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: [10.1021/jo015995y](https://doi.org/10.1021/jo015995y) and [10.1016/j.tetlet.2010.11.139](https://doi.org/10.1016/j.tetlet.2010.11.139) And [10.1021/ol0600741](https://doi.org/10.1021/ol0600741) and [10.1055/s-2002-32602](https://doi.org/10.1055/s-2002-32602) and [10.1002/anie.200501760](https://doi.org/10.1002/anie.200501760)

Retrosynthesis ID: 25168

2.5.2 Br/Li exchange



Substrates:

1. n-BuLi - *available at Sigma-Aldrich*
2. BrC1CCCC(/C=C/CC=C2CCCCC2)C1

Products:

1. [Li]C1CCCC(/C=C/CC=C2CCCCC2)C1

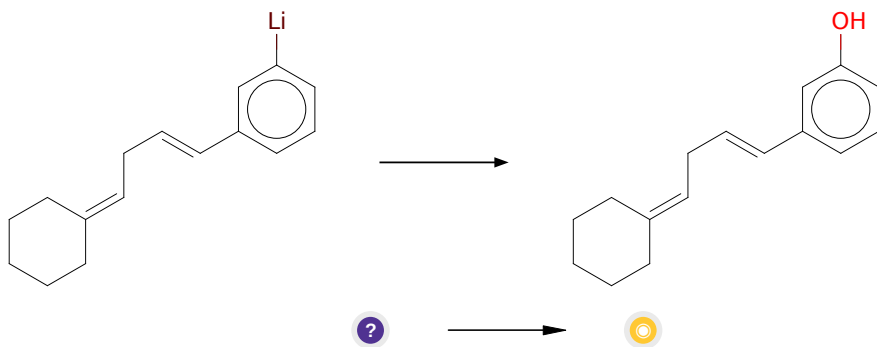
Typical conditions: nBuLi.or.tBuLi.THF.-78C

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

2.5.3 Addition of electrophiles to lithiated arenes/heteroarenes



Substrates:

1. [Li]C1CCCC(/C=C/CC=C2CCCCC2)C1

Products:

1. Oc1cccc(/C=C/CC=C2CCCCC2)c1

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