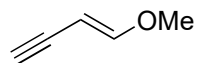


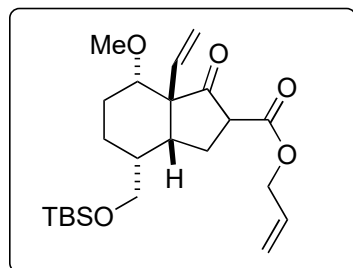
Synthesis of Cossonidine (Davisine)

Kevin G. M. Kou, Jason J. Pflueger, Toshihiro Kiho, Louis C. Morrill, Ethan L. Fisher, Kyle Clagg, Terry P. Lebold, Jessica K. Kisunzu and Richmond Sarpong

J. Am. Chem. Soc. **2018**, 140, 26, 8105–8109.



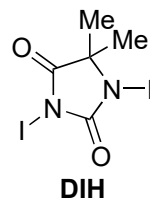
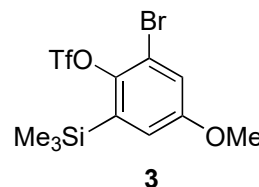
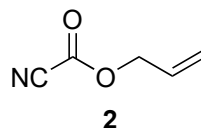
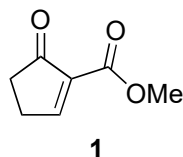
1–8



A

9–16

- 1) *n*-BuLi, then (CH₂O)_n, THF
- 2) LiAlH₄, Et₂O
- 3) TBSCl, ImH, CH₂Cl₂
- 4) **1**, toluene, 100 °C
- 5) LiAlH₄ excess, THF
- 6) TPAP, NMO, CH₂Cl₂
- 7) [Rh(PPh₃)₃]Cl, PPh₃, TMSCHN₂, *i*-PrOH
- 8) LiHMDS, *then* **2**, THF



- 9) **3**, CsF, 70 °C, MeCN
- 10) Pd(PPh₃)₄, PhSiH₃, CH₂Cl₂
- 11) DIH, *hν*, DCE
- 12) TBAF, THF
- 13) TEMPO, PIDA, NH₄OAc, MeCN/H₂O
- 14) LiHMDS, *then* MeI, THF
- 15) CoB, BH₃•*t*-BuNH₂, MeOH
- 16) LiAlH₄, THF, 70 °C

4) What is the name of the reaction? Explain the regioselectivity. [Diels–Alder reaction](#), [see below](#).

7) What is the name of the reaction and the catalyst used? [Lebel olefination](#), [Wilkinson's catalyst](#).

9) What is the reactive species formed? Show the mechanism. [Benzyne](#), [see below](#).

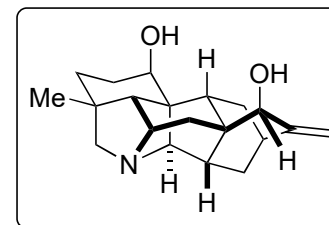
Hint: A seven-membered ring is formed, reminiscent of the Dowd–Beckwith reaction.

10) **Hint:** The ArBr remains intact.

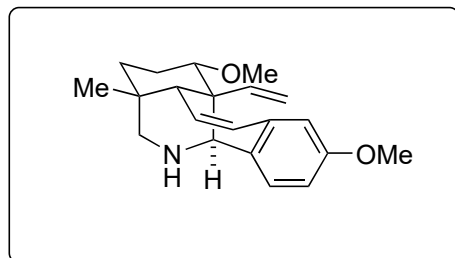
11) **Hint:** The vinyl group remains intact; after the reaction, an elimination occurs resulting in an alkene.

15) **Hint:** Chemoselective reduction of the nitrile group.

16) **Hint:** Debromination also occurs this is a good point to redraw the molecule

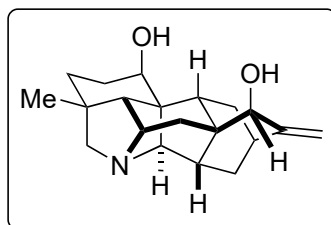


Cossonidine

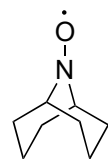


B

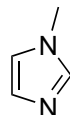
17–24



Cossonidine



ABNO



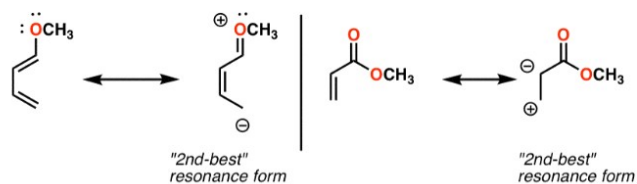
NMI

- 17) *n*-BuLi, $h\nu$, *i*-Pr₂NH, THF
- 18) Na_(s), NH_{3(l)}, *then* HCl
- 19) pyrrolidine, MW, 110 °C, MeOH
- 20) HBr/AcOH, *then* K₂CO₃, MeOH
- 21) Ph₃PCH₃Br, *n*-BuLi, THF
- 22) [Cu(CH₃CN)₄]OTf, ^{MeO}bpy, ABNO, NMI
- 23) LiAlH₄, THF
- 24) SeO₂, 1,4-dioxane

18) Please name the reaction and provide the mechanism. [Birch reduction](#) see below.

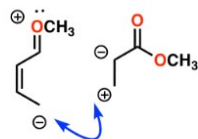
<https://www.masterorganicchemistry.com/2018/11/05/regiochemistry-in-the-diels-alder-reaction/>

How to find these positions? Look at the "2nd-best" resonance forms of each.



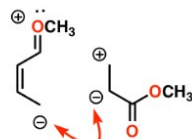
Now, line up the **negative charge from the diene** with the **positive charge on the dienophile**

this way:



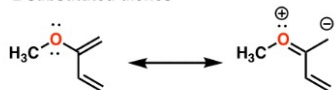
line up opposite charges
results in *ortho*

not this way:



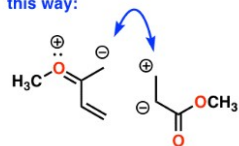
don't line up "like" charges
results in *meta*

2-substituted dienes



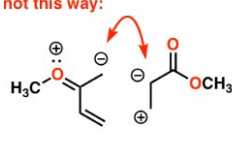
"2nd-best" resonance form

this way:



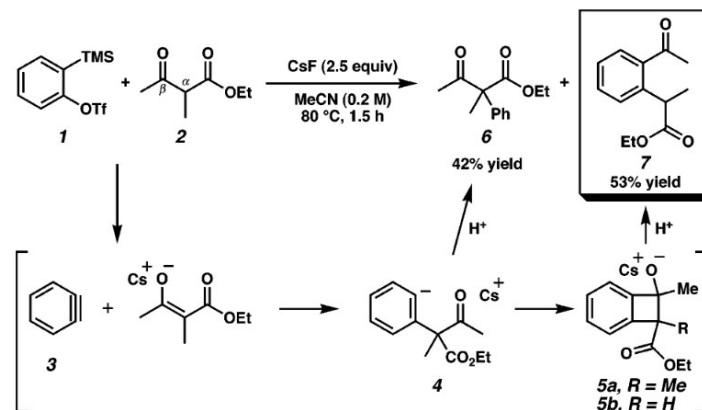
line up opposite charges
results in *para*

not this way:



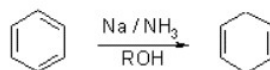
don't line up "like" charges
results in *meta*

https://pubs.acs.org/doi/epdf/10.1021/ja050859m?ref=article_openPDF



<https://www.organic-chemistry.org/namedreactions/birch-reduction.shtm>

Birch Reduction



The Birch Reduction offers access to substituted 1,4-cyclohexadienes.

Mechanism of the Birch Reduction

