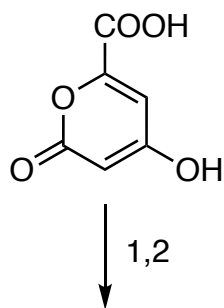


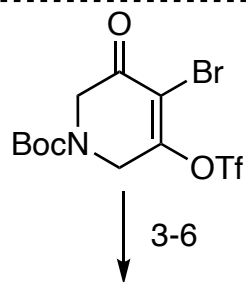
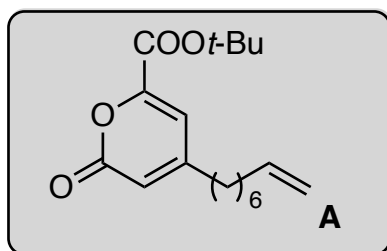
# Total synthesis of lissodendoric acid **A** via stereospecific trapping of a strained cyclic allene

Ippoliti, F. M.; Adamson, N. J.; Wonilowicz, L. G.; Nasrallah, D. J.; Darzi, E. R.; Donaldson, J. S.; Garg, N.K.

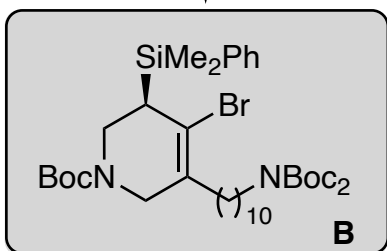
*Science* **2023**, *379*, 261-265



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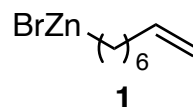


3-6



1) TsCl (excess), TEA, DCM then *t*-BuOH, 40 °C

2) **1**, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (20 mol%), NMI, DMA

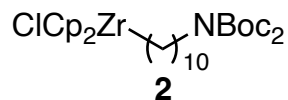


3) **2**, CuBr·SMe<sub>2</sub>, THF, 40 °C

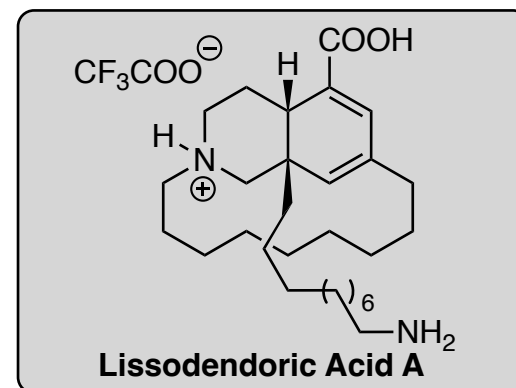
4) (*R*)-CBS cat. (20 mol%), BH<sub>3</sub>·SMe<sub>2</sub>, THF, 30 °C

5) EtOC(O)Cl, pyr., DCM

6) PhMe<sub>2</sub>SiLi, CuCN, PPh<sub>3</sub>, Et<sub>2</sub>O/THF, -78 °C



2) What type of cross-coupling is this reaction? Negishi.

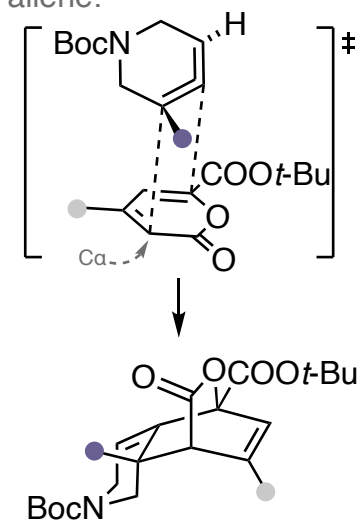


7-14

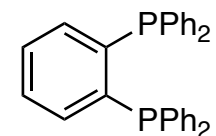


- 7) **A**, CsF, *n*-Bu<sub>4</sub>NBr, MeCN, -20 °C
- 8) PDC, *t*-BuOOH, PhH
- 9) Cu(OAc)<sub>2</sub>·H<sub>2</sub>O, BDP (50 mol%), PMHS, *t*-BuOH, PhMe
- 10) MeCN, 80 °C *then* Cu(OTf)<sub>2</sub> (20 mol%), 40 °C
- 11) acryloyl chloride, TEA, DCM
- 12) Grubb's II (20 mol%), DCM, 40 °C
- 13) Rh(cod)(acac) (50 mol%), PhSiH<sub>3</sub>, DCM, 40 °C
- 14) TFA, DCM, -78 °C to 23 °C

7) Rationalize the regiochemical outcome of this reaction. This reaction proceeds via an inverse electron-demand Diels-Alder (electron-poor diene, electron-rich dienophile), so the more substituted dienophile (the trisubstituted olefin of the allene) reacts. The pyrone carbonyl is thought to provide the dominant electronic effect, guiding bond formation between C $\alpha$  and the more substituted carbon of the cyclic allene:



9) Structure of BDP:



10) *Hint*: 3 eq. CO<sub>2</sub> are liberated throughout this two-part transformation.