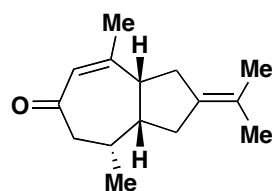


In 1940, Pfau and Plattner proposed structures for β -vetivone, one of the constituents of vetiver oil, an aromatic oil from vetiver grass. The structure was assigned based on extensive degradative studies.

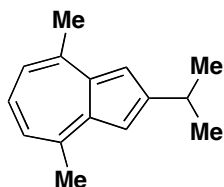


vetiver grass



Proposed structure
of β -vetivone:
a bicyclo[5.3.0]decane

The authors were no doubt misled by the fact that vetivazulene is also a substituent of vetiver oil:



vetivazulene

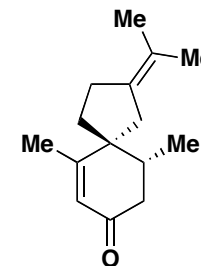


Note: This review is intended to give an historical and chronological account of synthetic work on the spirovetivanes in the class of vetivane sesquiterpenes. The research spans from 1967 to the present, giving us a glimpse at the development of modern synthesis in one small arena. It gives highlights and is not comprehensive.

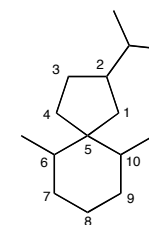


James A. Marshall
Thomas Jefferson Professor
of Chemistry
University of Virginia

In 1967, J. A. Marshall and colleagues synthesized a β -vetivone degradation product as well as its diastereomers, only to discover that it did not match the authentic material. This called into question the structures of the vetivane sesquiterpenes.



β -vetivone: reassigned and
synthetically confirmed structure



vetivane: a spiro[4.5]decane

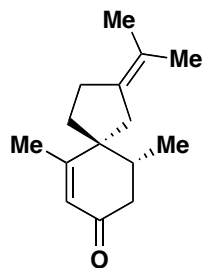
Professor Marshall's personal account of the discovery:

"I remember the day we formulated the spiro structure. At the time it was believed that β -vetivone possessed a 5/7 fused ring system and my graduate student Niels Andersen was completing the final step of a sequence that would provide a synthetic ketone that we had previously obtained from authentic β -vetivone. I wanted to be on hand when Niels made the final comparison of the infrared spectra of the synthetic ketone with that derived from the natural material. We had planned to have a small celebration at my home following the successful comparison to toast the achievement. As is often the case, the workup and isolation of the synthetic ketone took longer than expected, but by 10:30 PM or so all was ready and the sample was placed onto a salt plate and the Infracord Spectrometer was started. As the peaks marched down the paper it became apparent that our sample showed significant differences from the degradation sample and our excitement quickly turned to disappointment. I decided we should go ahead with the gathering as planned, even though it promised to be more of a wake than a celebration, and I instructed Niels and a few other group members involved in the project to meet me at my home in Evanston, some 20 minutes from the lab. As I was driving home to meet my students I mulled over the possible cause of the apparent differences between our degradation and synthetic ketone samples, taking into account the symmetry argument that led to the assignment of a meso structure to dihydrovetivone. It suddenly dawned on me that a spiro[4.5] structure would account for this property as well. This idea was reinforced by the position of the ketone carbonyl absorption in the infrared spectrum of the degradation product, which appeared at a lower wavelength than that of the corresponding absorption band for our synthetic sample of the presumed 5/7 structure. By the time I pulled into my driveway, I had formulated a synthetic route to the alternative [4.5]spiro structure which I excitedly shared with my waiting coworkers.

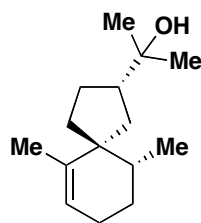
Niels graduated with his PhD a few years later and, after a postdoc position with E. J. Corey, he joined the faculty at the University of Washington where he carried out additional structural studies on vetivane sesquiterpenes."

-James A. Marshall, personal communication

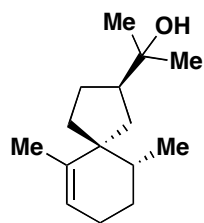
Some of the vetiver oil substituents:



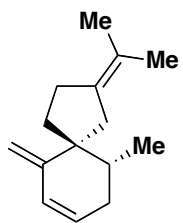
vetivone



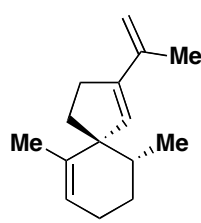
hinesol



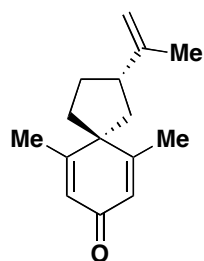
agarospirol



(-)-vetispirene

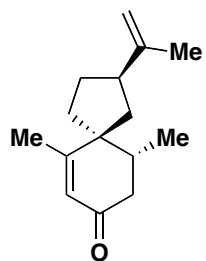


(-)-vetispirene

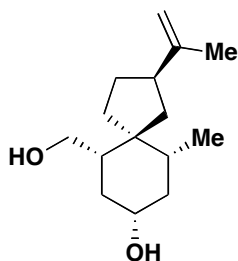


anhydro(-)-rotunol

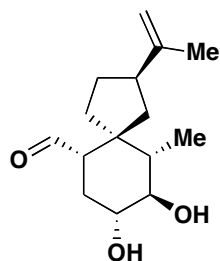
Phytoalexins from diseased potato tubers:



solavetivone

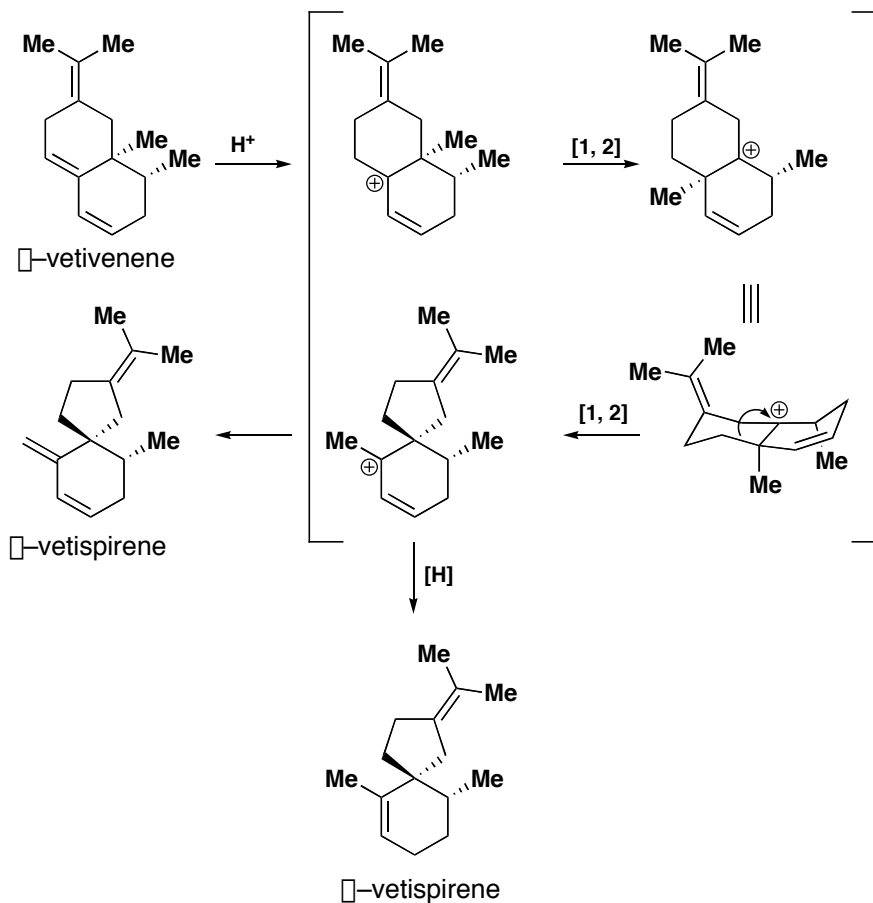


lubiminol

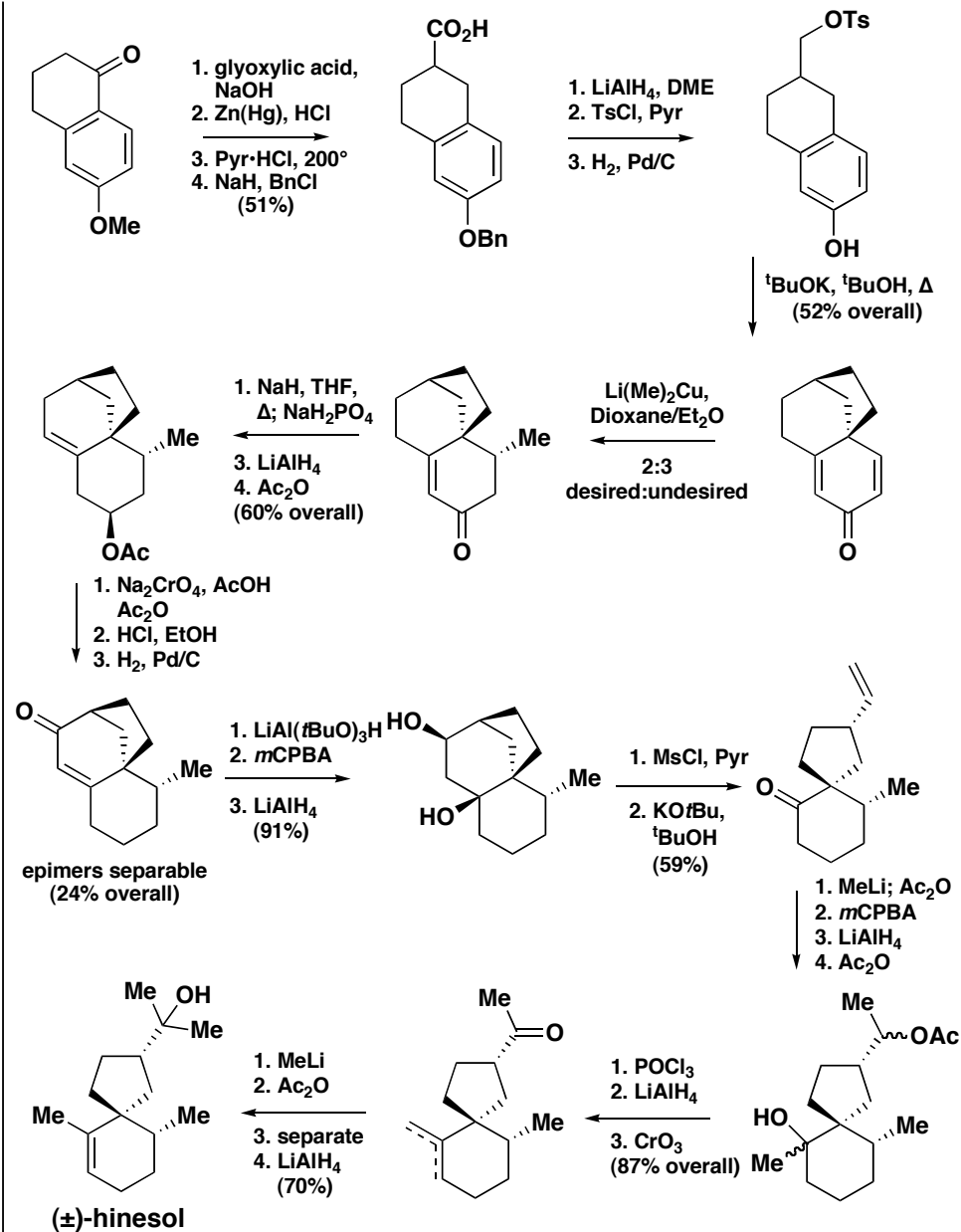
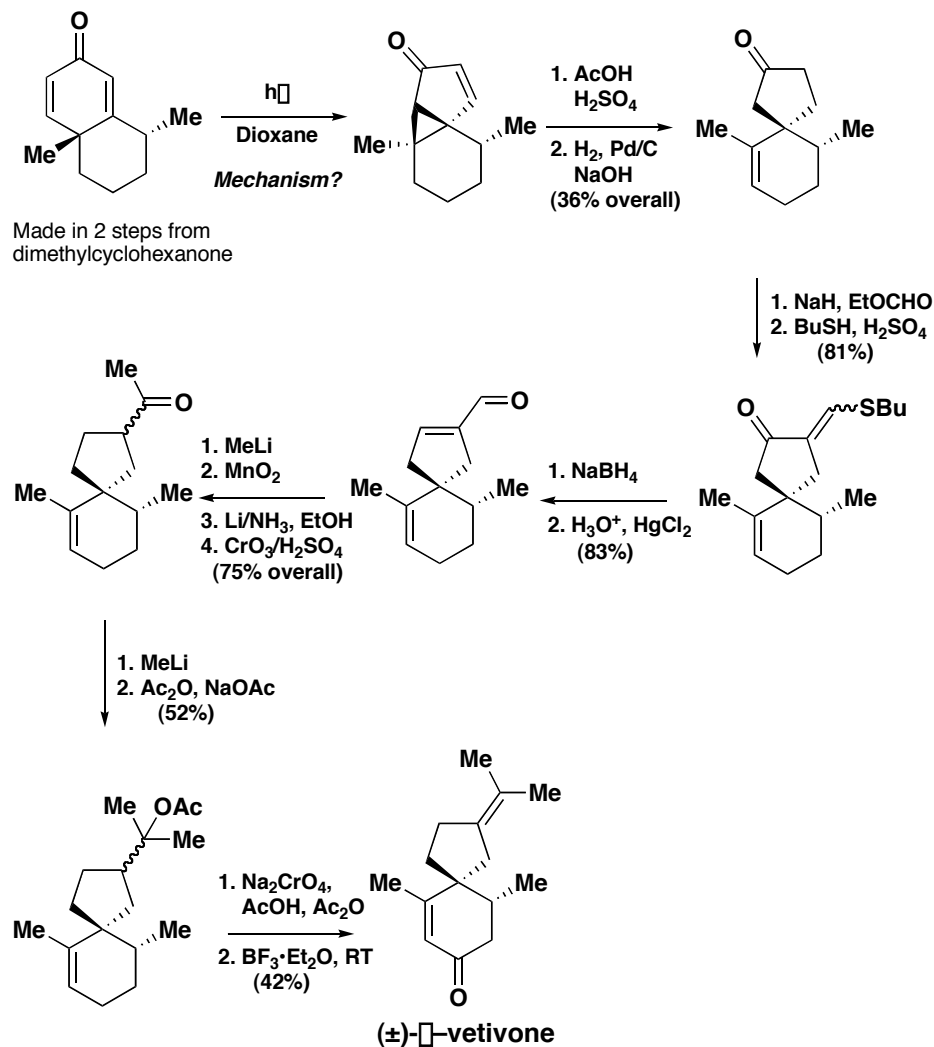


oxylubimin

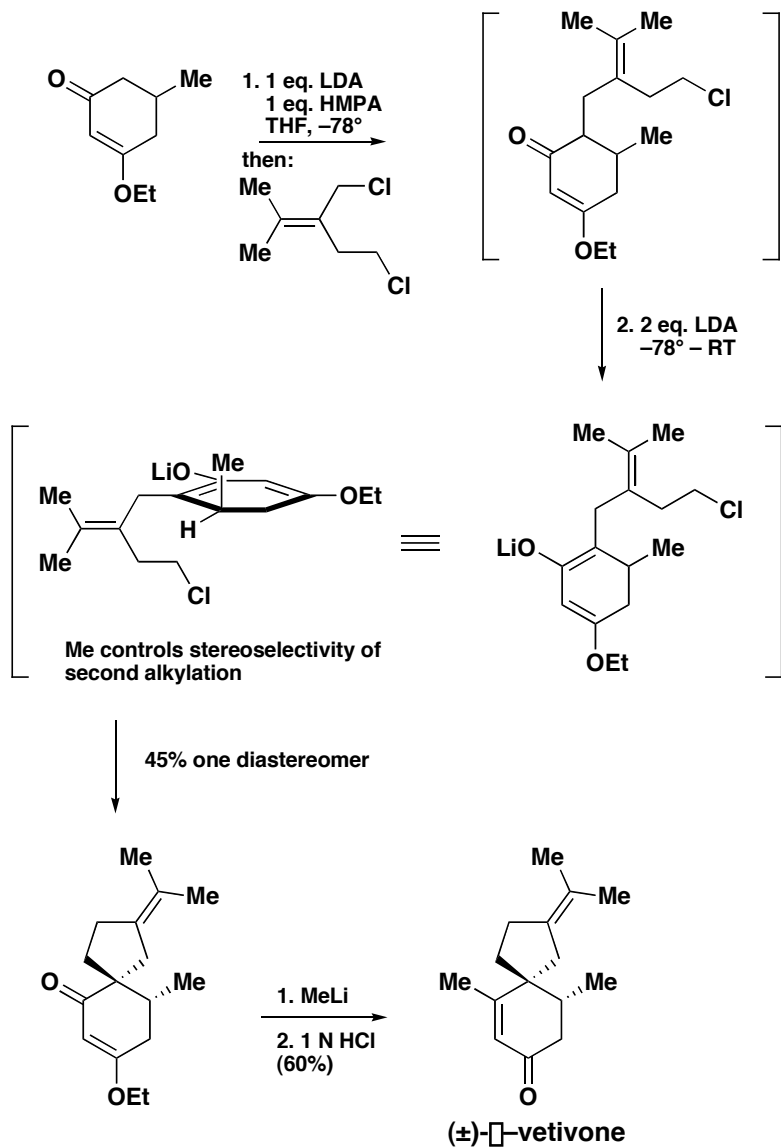
Biogenetic hypothesis of the vetispirenes starting from (-)-vetivenene, the major constituent of vetiver oil:



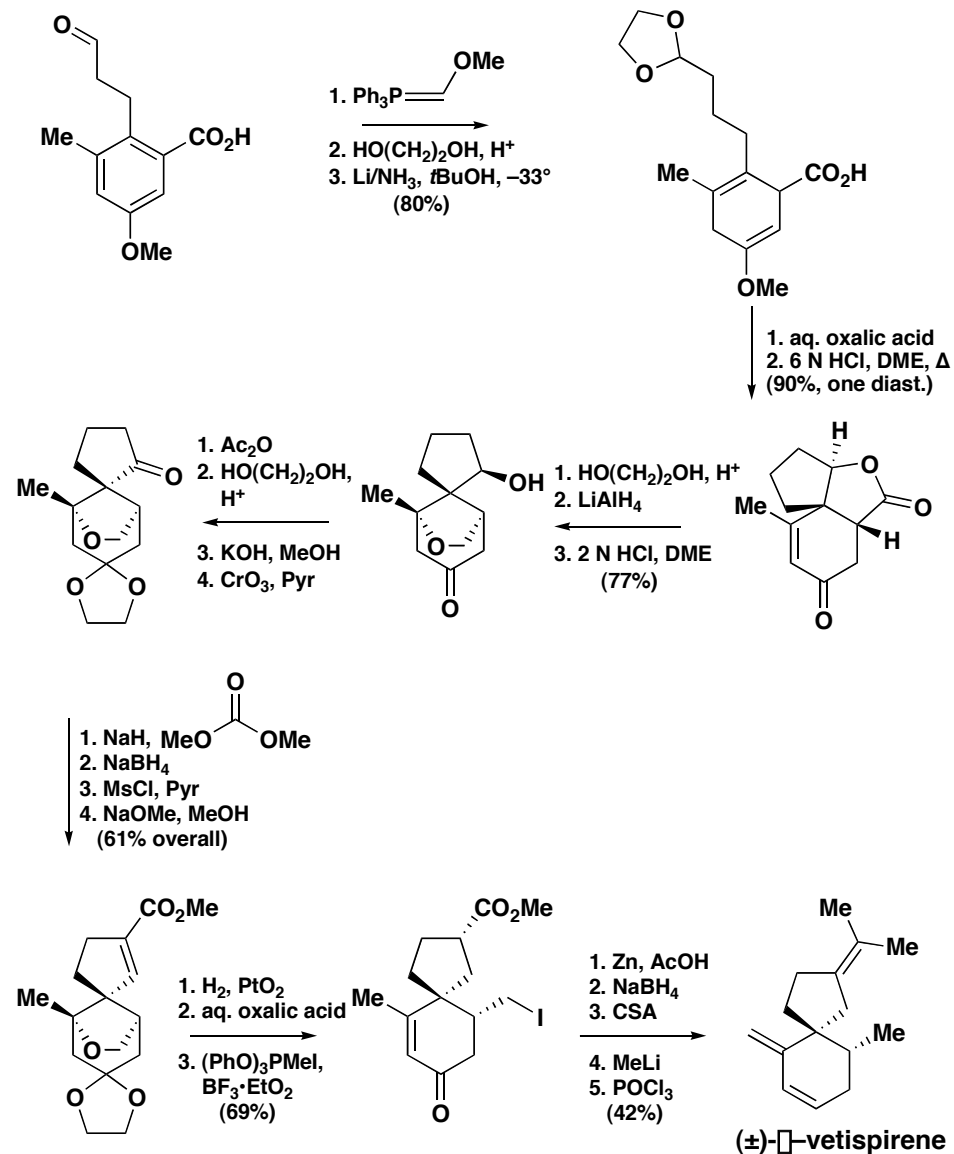
Marshall's pioneering syntheses of (\pm) -vetivone and hinesol, unambiguously confirming the relative stereochemistry of hinesol:



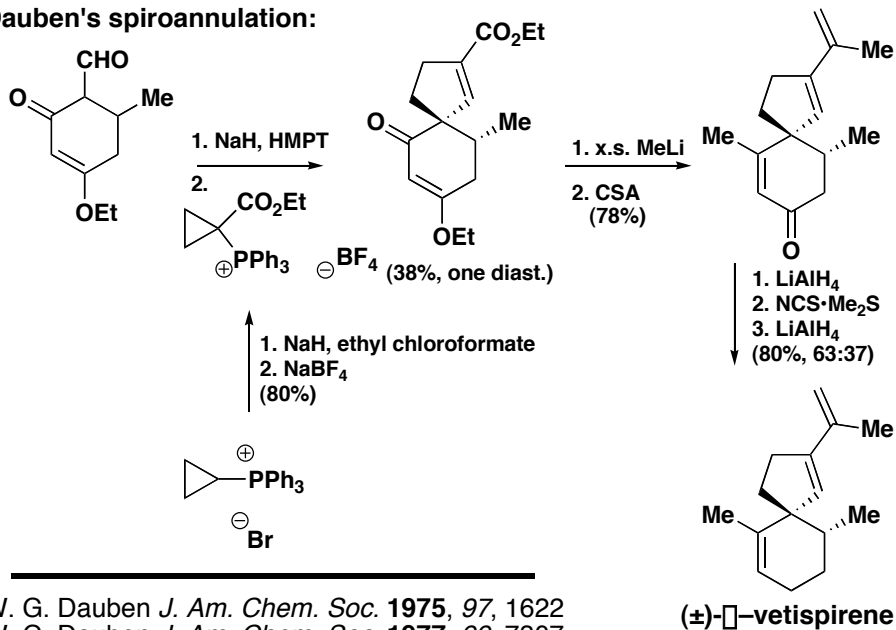
The classic Stork-Danheiser-Ganem synthesis:



Yamada's access to the spirovetivanes:

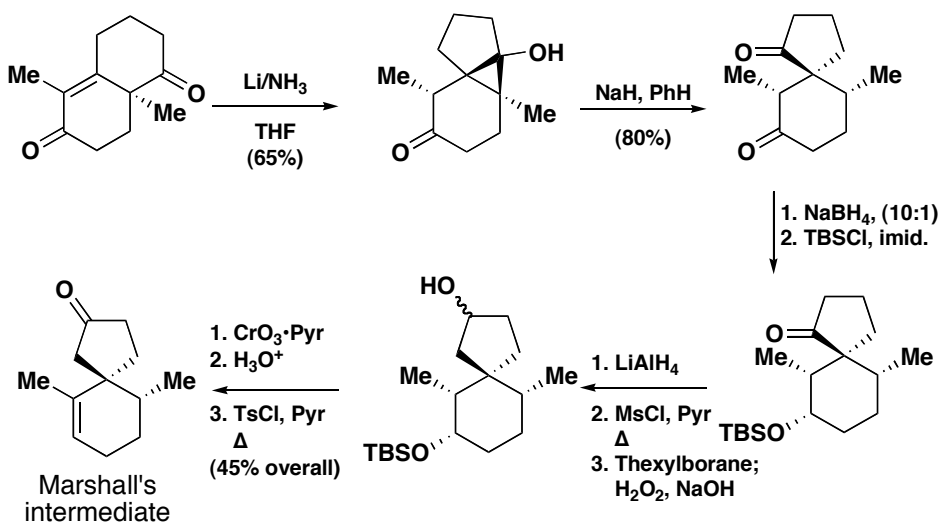


Dauben's spiroannulation:

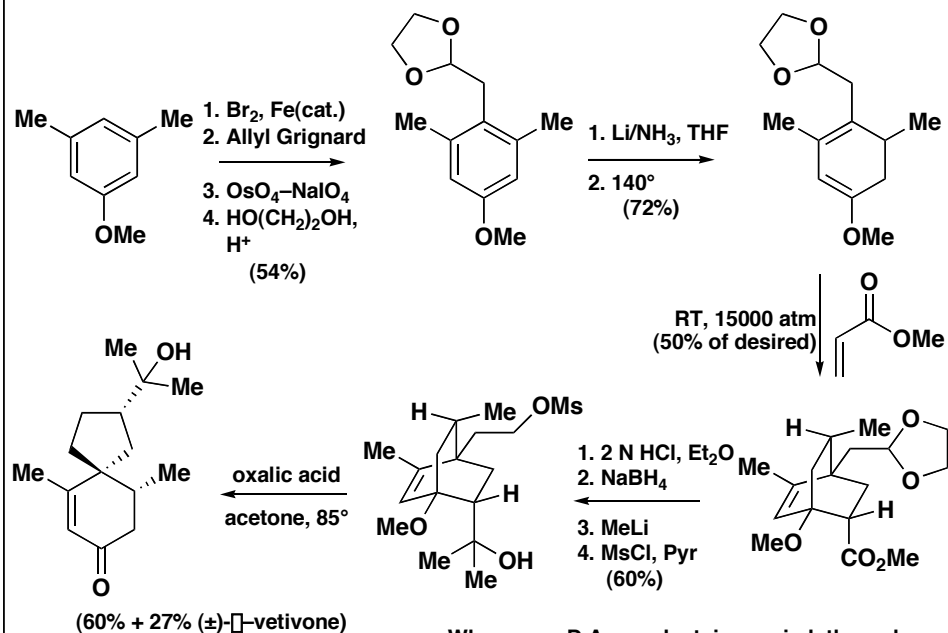


W. G. Dauben *J. Am. Chem. Soc.* **1975**, *97*, 1622
W. G. Dauben *J. Am. Chem. Soc.* **1977**, *99*, 7307

Reusch's formal synthesis:



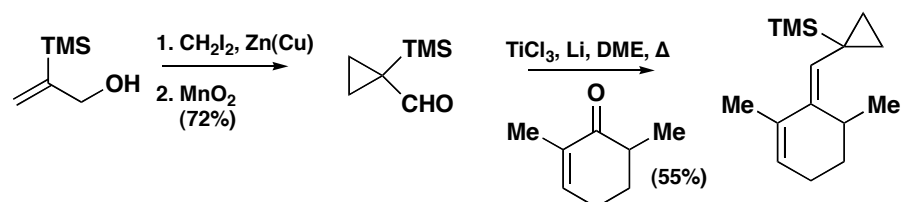
W. Reusch *Tet. Lett.* **1978**, *40*, 3789

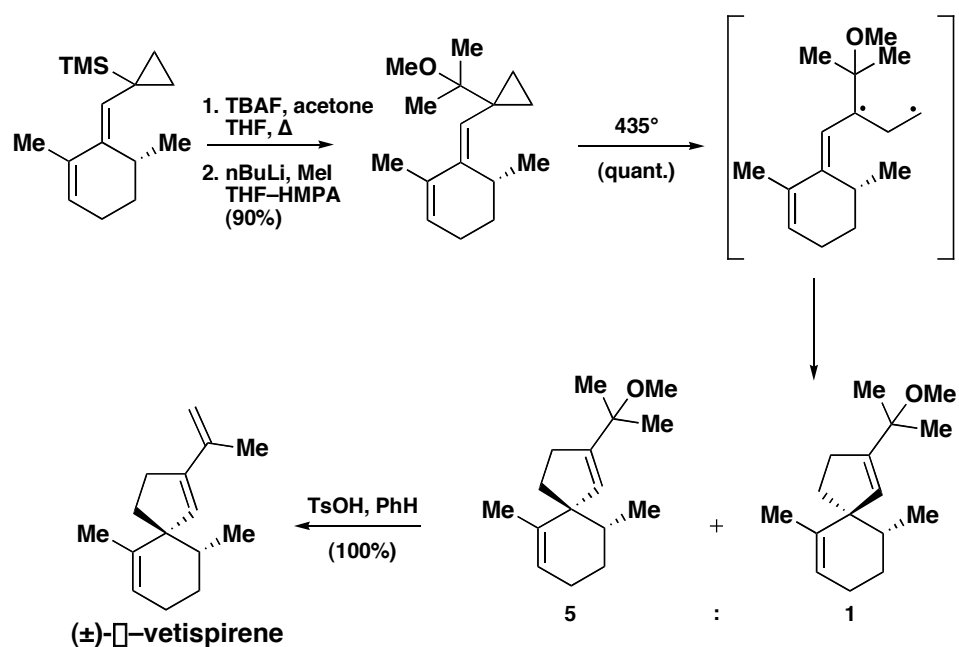
Masamune's Diels-Alder, " π -cyclization" approach:

When *exo* D.A. product is carried through, oxalic acid treatment gives near identical ratio of products. Agarospirol is never seen!

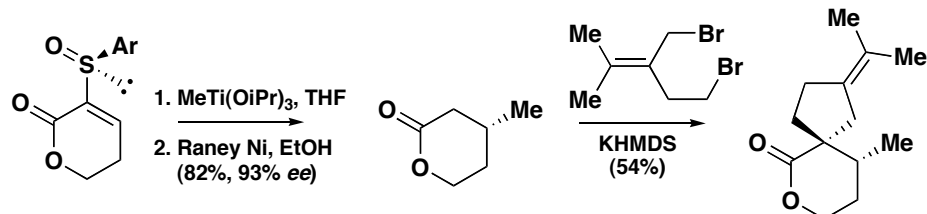
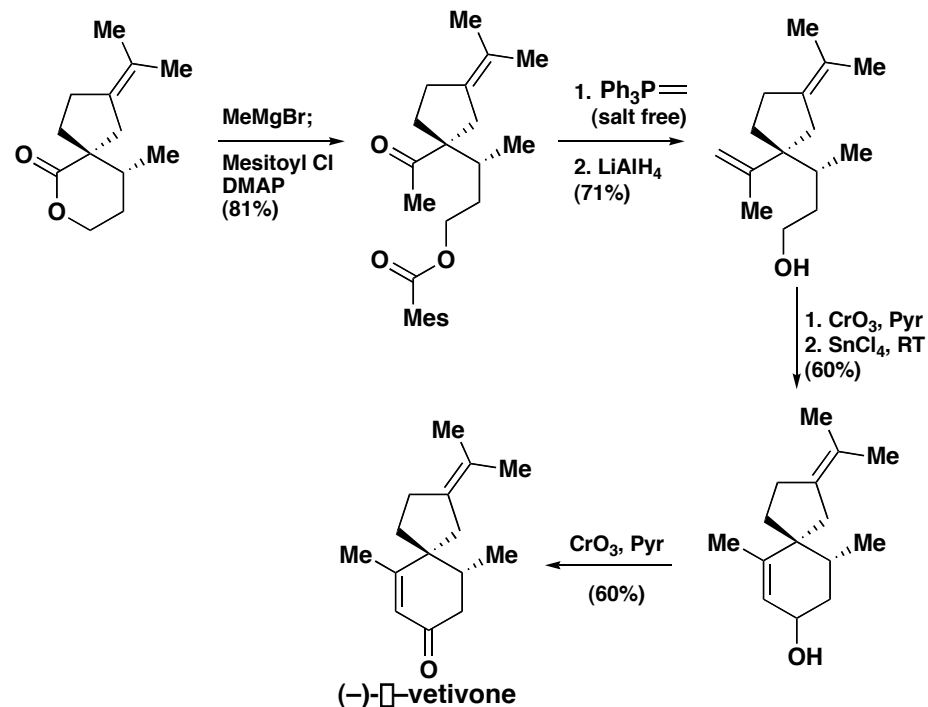
T. Masamune, *Tet. Lett.*, **1981**, *22*, 1033

Paquette's vinylcyclopropane rearrangement:

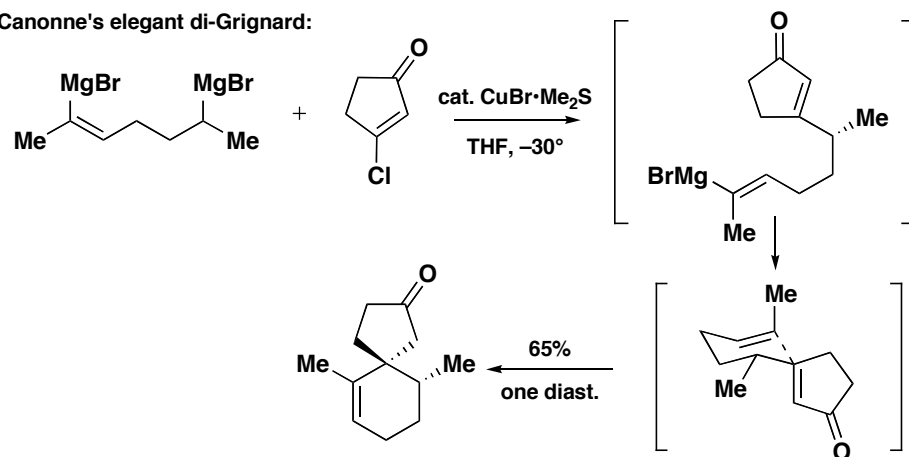


L. Paquette *Tet. Lett.* **1982**, 23, 3227L. Paquette *J. Org. Chem.* **1984**, 49, 3610

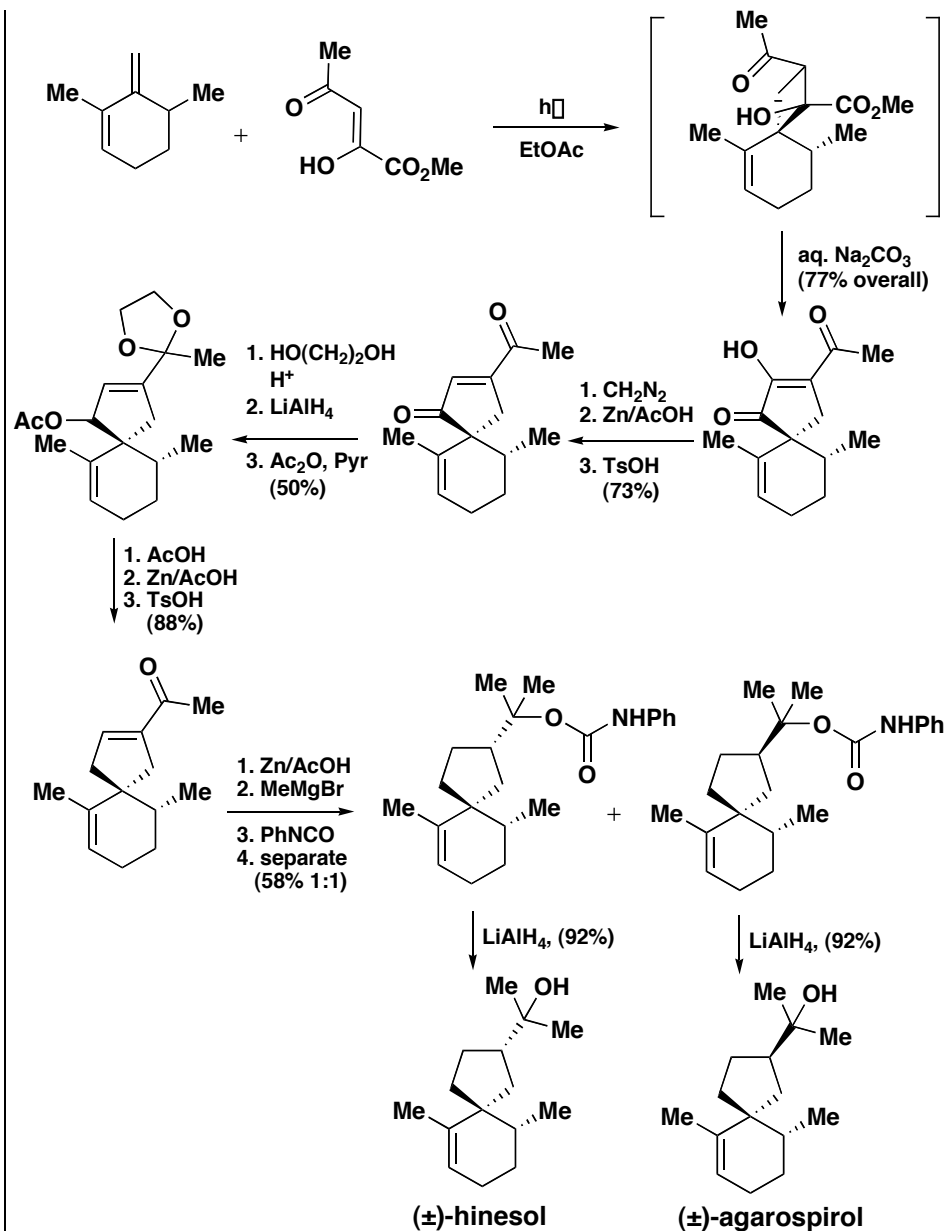
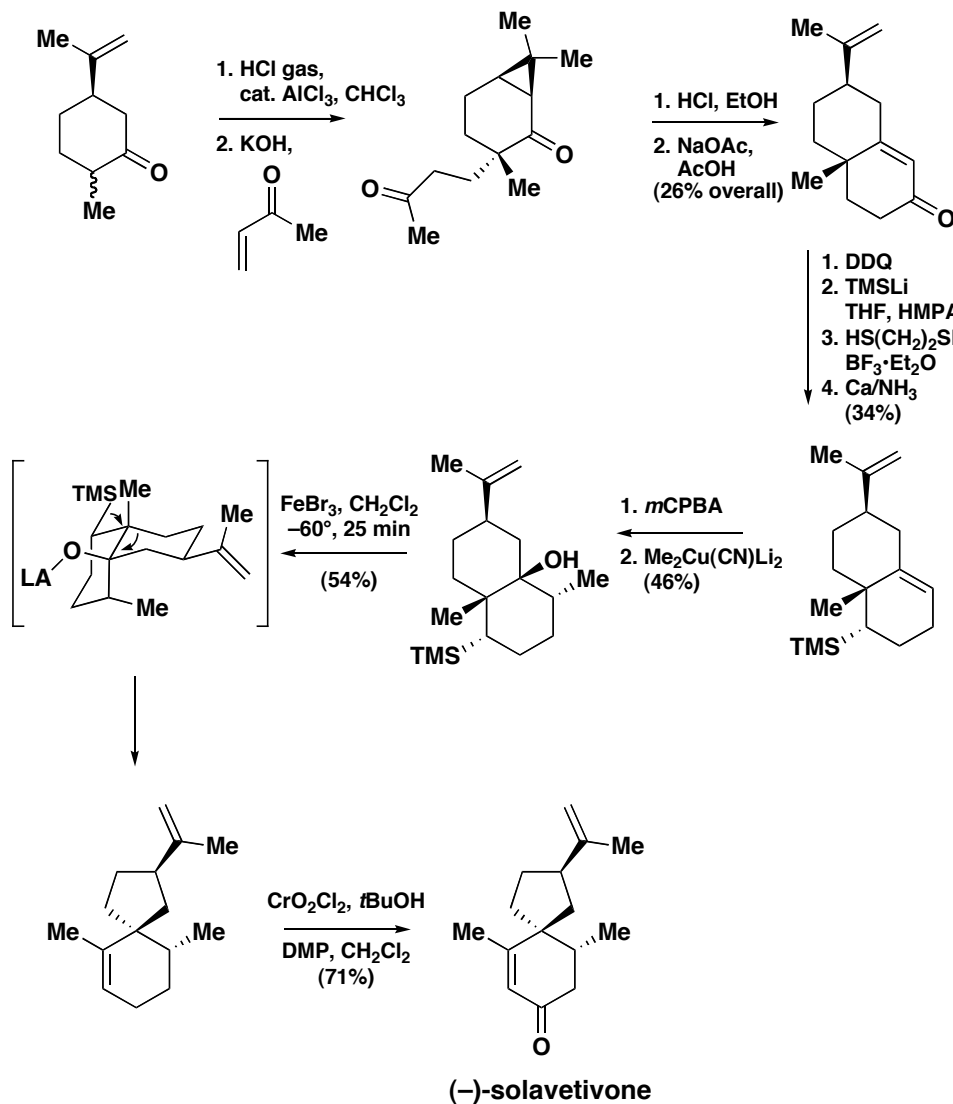
Posner's enantioselective (-)-vetivone:

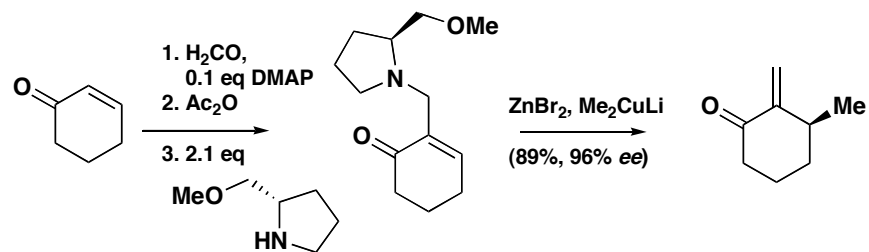
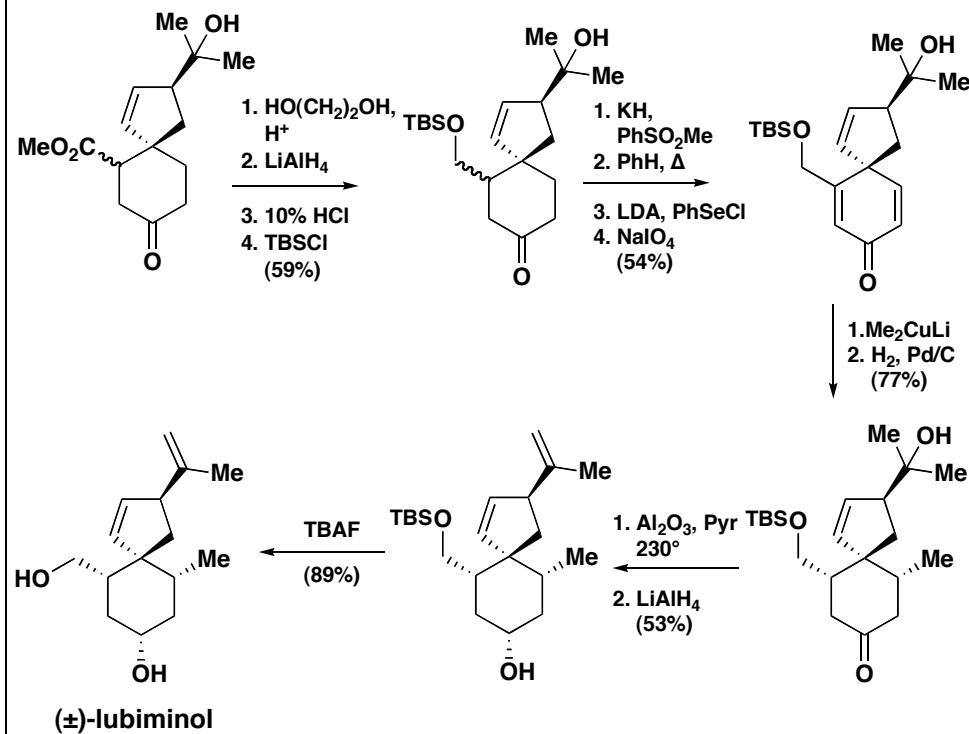
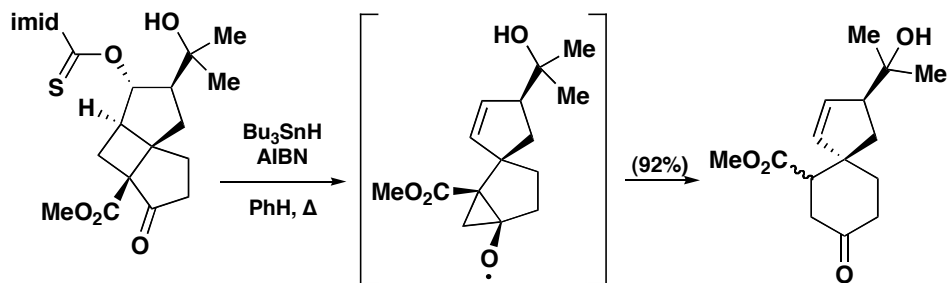
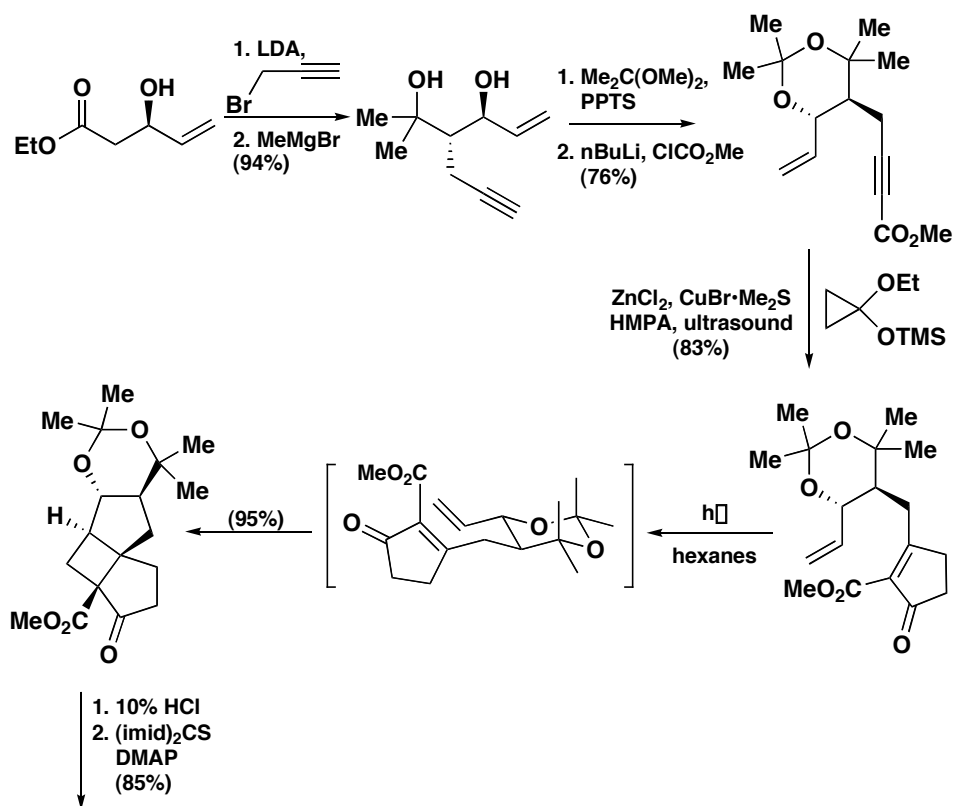
G. H. Posner *J. Org. Chem.* **1988**, 53, 6031

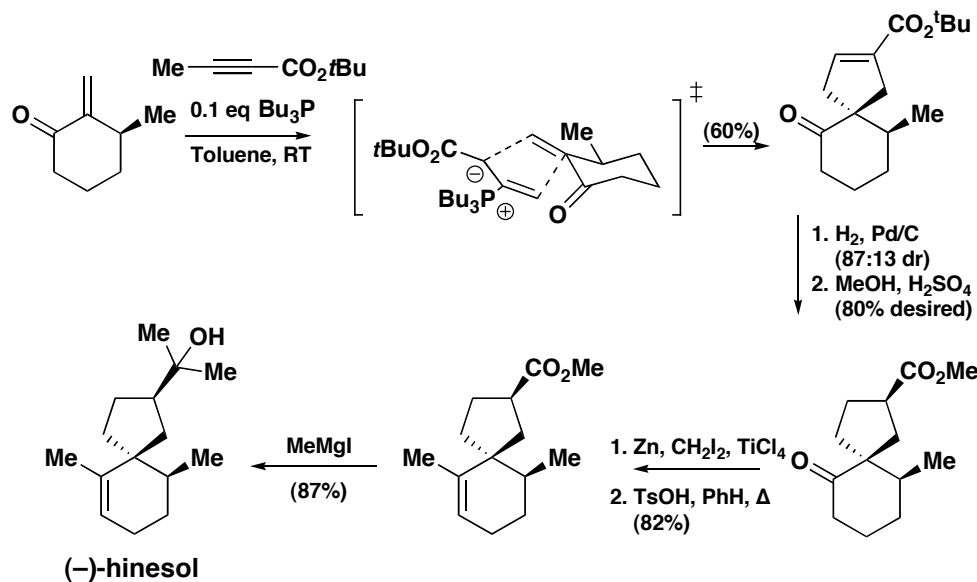
Canonne's elegant di-Grignard:

6 P. Canonne *Tet. Lett.* **1991**, 32, 5861

Wetzel's Si-promoted ring contraction:





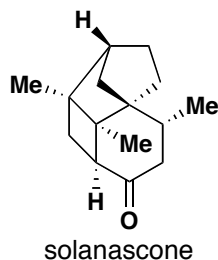


Synthesis references discussed:

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 J. A. Marshall, *ibid.* **1970**, *35*, 4068
 G. Stork *J. Am. Chem. Soc.* **1973**, *95*, 3414
 K. Yamada *Tet. Lett.* **1973**, *49*, 4963, 4967
 W. G. Dauben *J. Am. Chem. Soc.* **1977**, *99*, 7307
 W. Reusch *Tet. Lett.* **1978**, *40*, 3789
 T. Masamune, *Tet. Lett.*, **1981**, *22*, 1033
 L. Paquette *J. Org. Chem.* **1984**, *49*, 3610
 G. H. Posner *J. Org. Chem.* **1988**, *53*, 6031
 P. Canonne *Tet. Lett.* **1991**, *32*, 5861
 J. M. Wetzel *J. Org. Chem.* **1992**, *57*, 922
 H. Takeshita *Bull. Chem. Soc. Jpn.*, **1995**, *68*, 2393
 M. T. Crimmins *J. Am. Chem. Soc.* **1998**, *120*, 1747
 X. Lu *J. Org. Chem.* **2003**, *68*, 6463

Is novel chemistry still possible in work on the spirovetivanes?

An unanswered question:

T. Fujimori *J. C. S. Chem. Comm.* **1978**, 563