

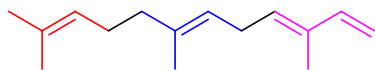


SYNTHESIS OF THE CHAMIGRANE SESQUITERPENE CORE

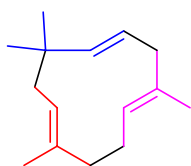
**Philip Williams
Group Meeting
May 30, 2007**

WHAT'S A SESQUITERPENE?

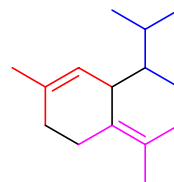
- Sesquiterpenes are terpenes with 3 isoprene units.
- Molecular Formula $C_{15}H_{24}$.
- These terpenes can be a-, mono-, bi-, or tricyclic.



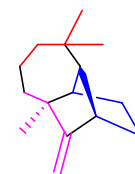
α -Farnesene



Humulene



Cadinene

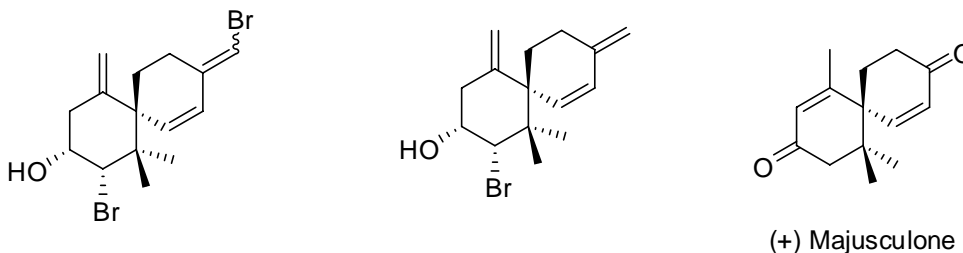


Longifolene



THE INTERESTING ONES...

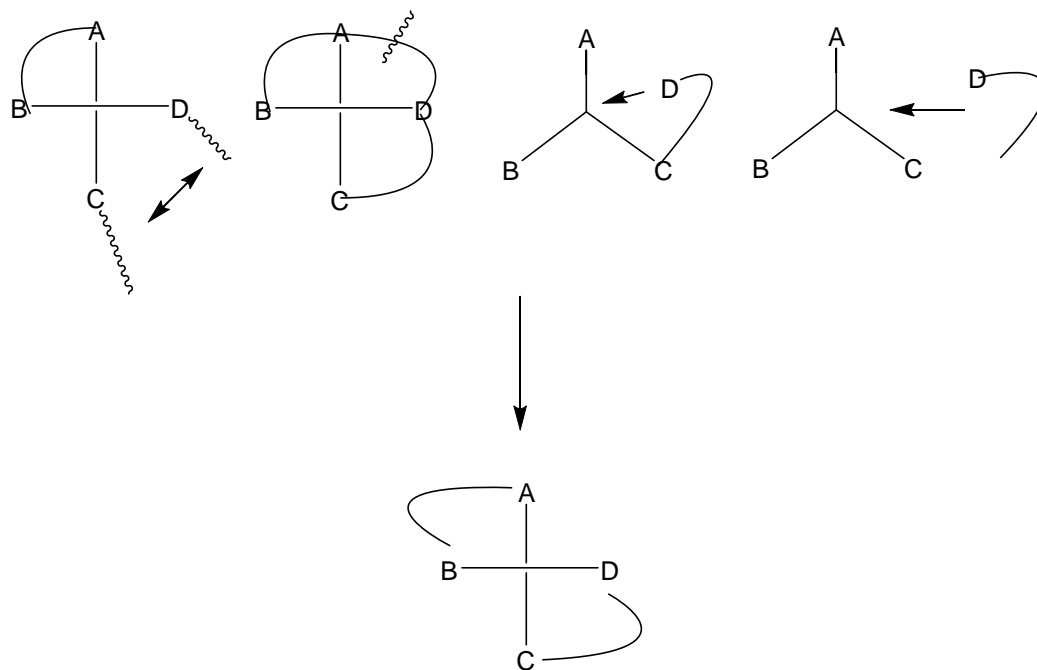
- The chamigrane class of sesquiterpenes is particularly interesting because of the all-carbon spirocenter.
- Some of the halogenated chamigrenes have shown high biological activity, yet they haven't been enantioselectively synthesized until recently (2007).



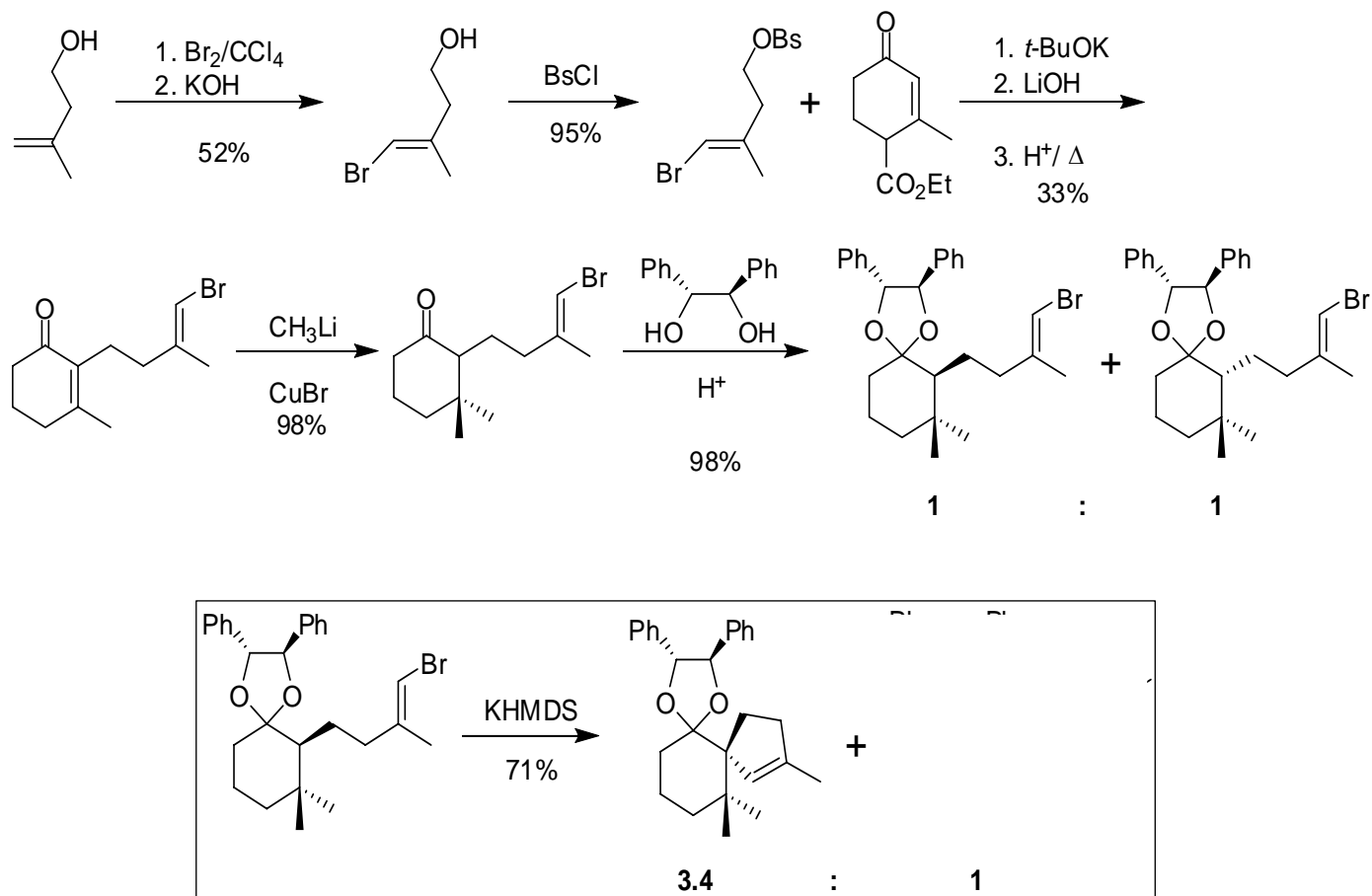
- These examples were purified from the red alga *Laurencia cartilaginea*.
- Taber and coworkers have recently completed the first enantioselective synthesis of (+)-majusculone -- The first chamigrane sesquiterpene to be enantioselectively synthesized.

IDEAS ON CARBON SPIROCYCLES

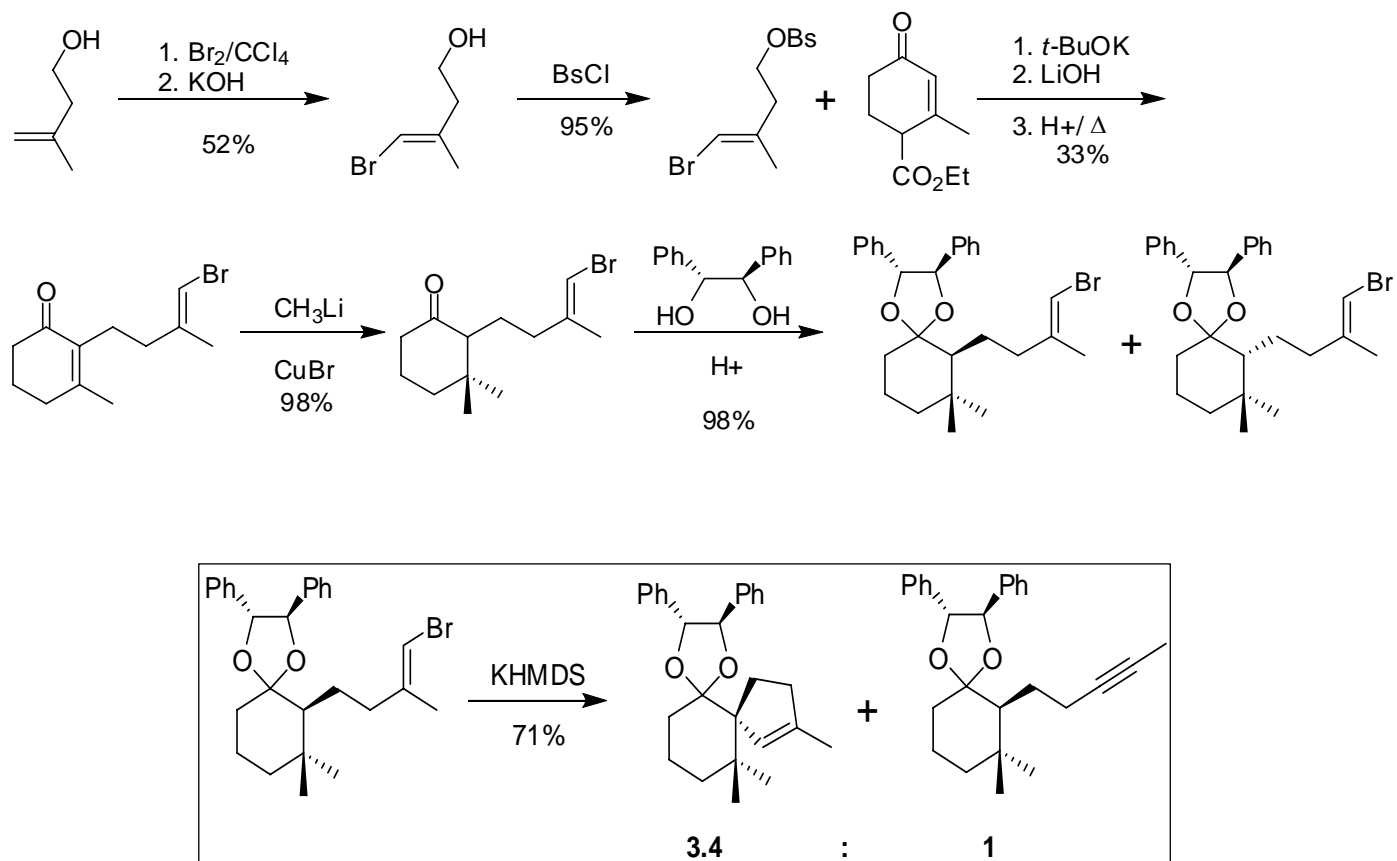
- Basic ideas on how to arrive at a bicyclic carbon spirocenter are as follows:



THE SYNTHESIS OF MAJUSCULONE



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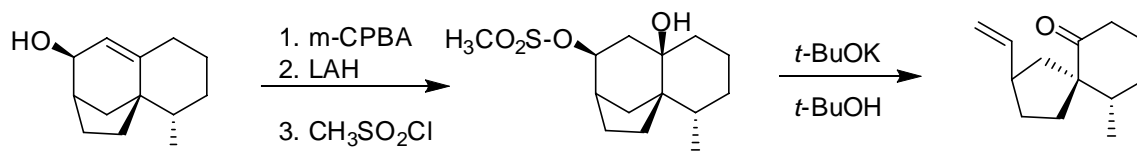
OTHER WORK - 1970

- Marshall and Brady in their total synthesis of Hinesol used the opening of a tricyclic method to install their bicyclic spirocenter.



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OTHER WORK - 1986

- Julio Martin also has done work on the chamigrane sesquiterpenes. He synthesized the spiro[5.5]undecane system via an intramolecular bromonium initiated cyclization.



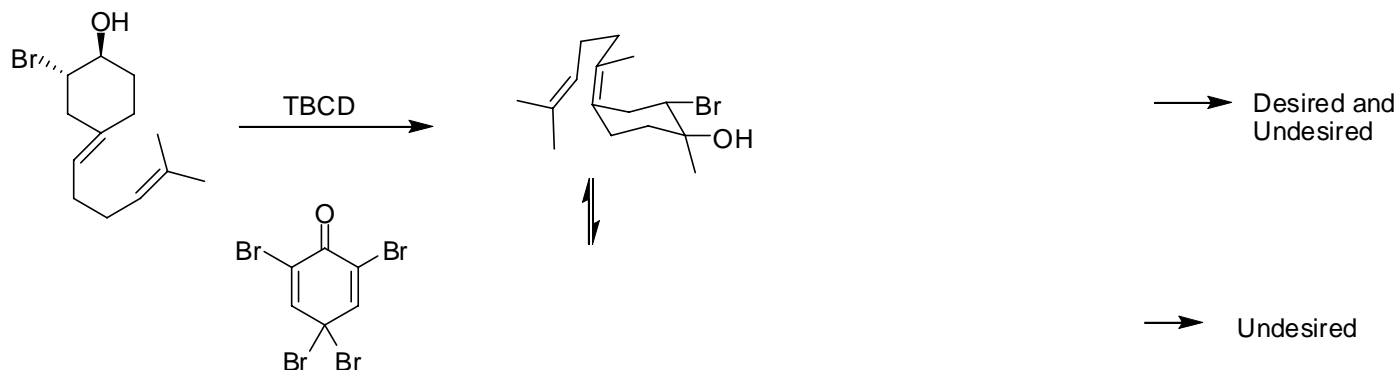
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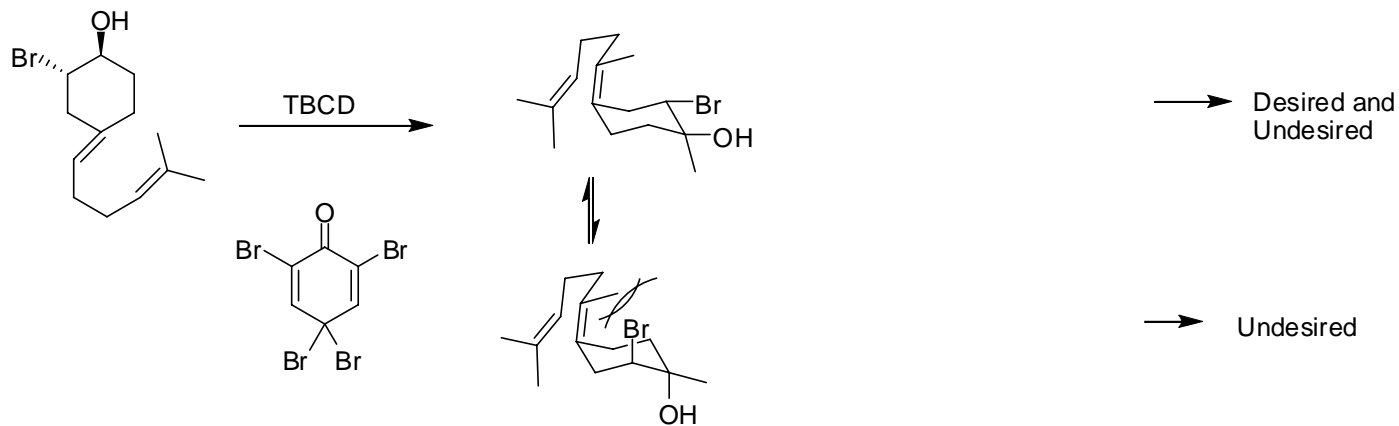
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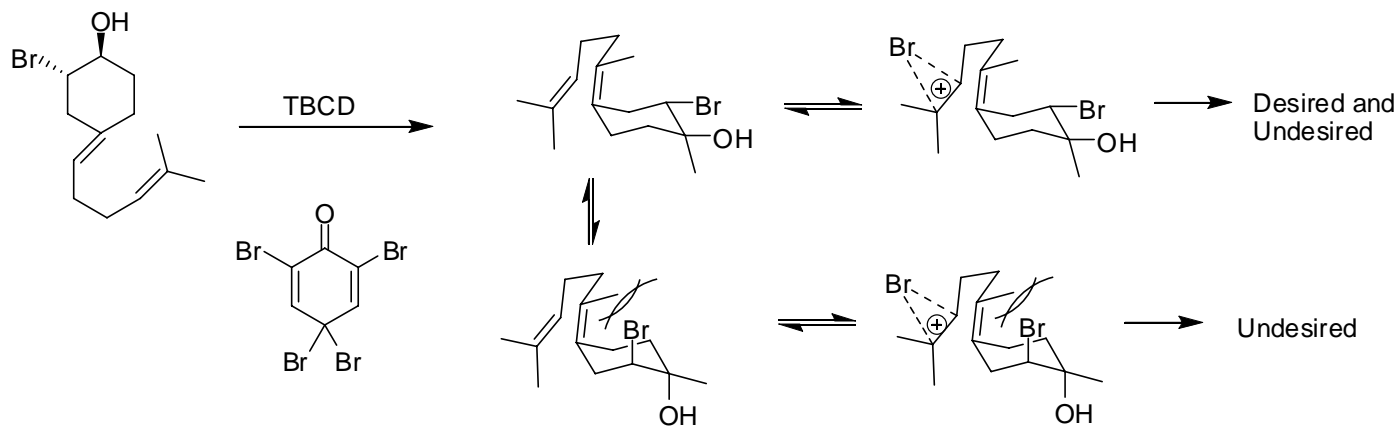
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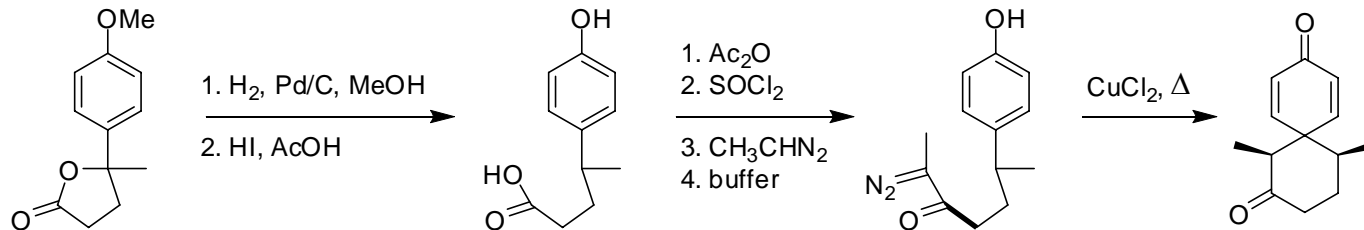
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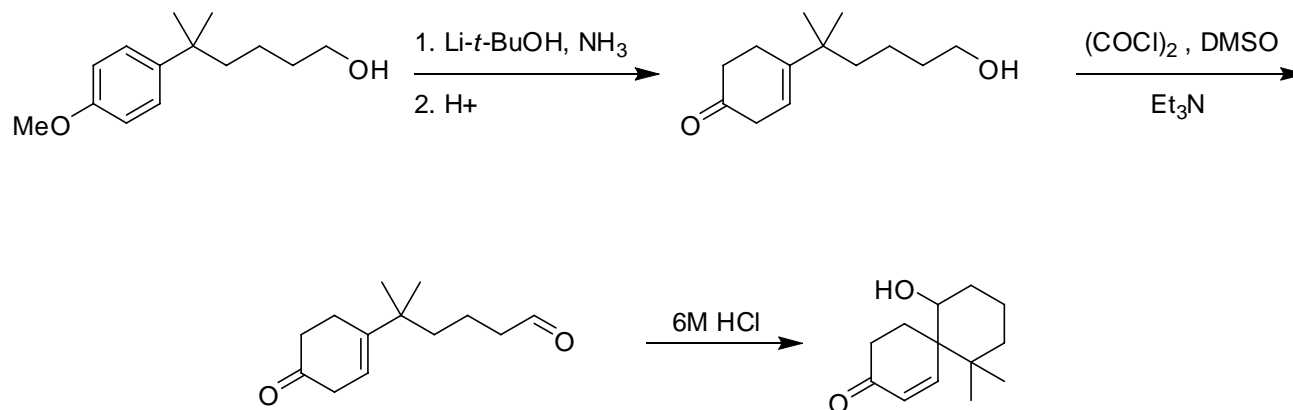
OTHER WORK - 1988

- At Osaka University, Iwata has put together the chamigrane core using copper catalyzed elimination of α -diazoketones.
- The stereochemistry of the reaction could not be controlled. Though this work enabled the elucidation of the structures of a number of halogenated chamigranes



OTHER WORK - 1991

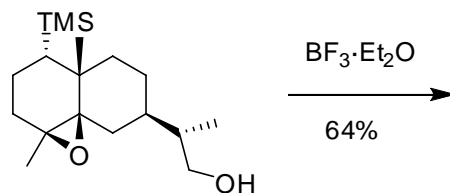
- In 1971, Yamada at Nagoya University, in his attempt to synthesize seychellene he also synthesized a spiro[5.5]undecane system by accident.
- Niwa, also at Nagoya University, used that result, an acidic cyclization, to form the spiro[5.5]undecane core structure of a number of brominated chamigrane sesquiterpenes.



OTHER WORK - 2004

- Pedro and coworkers utilized a silyl-stabilized ring contraction to construct the spiro system.

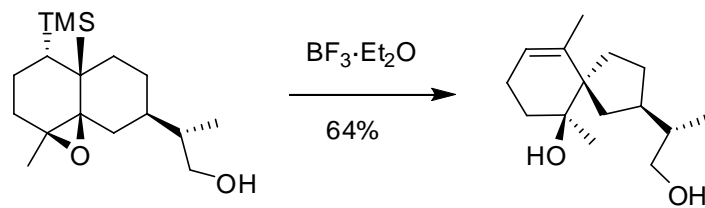
coplanar.



OTHER WORK - 2004

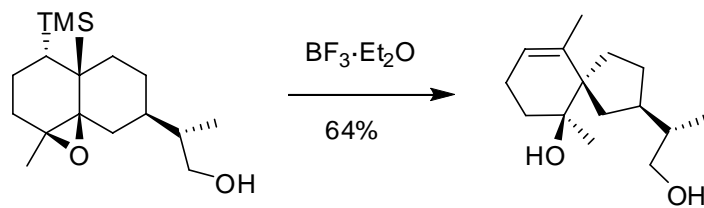
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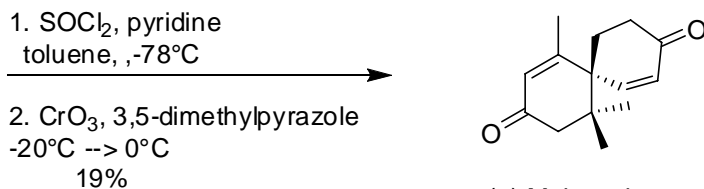
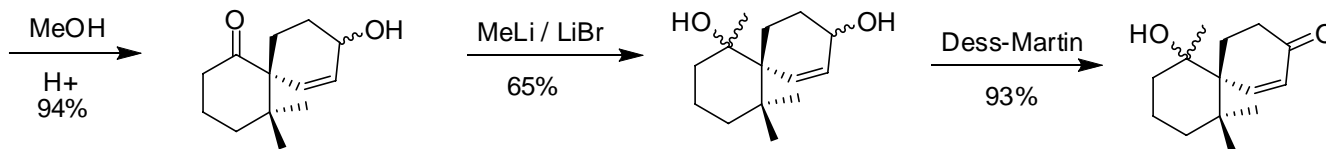
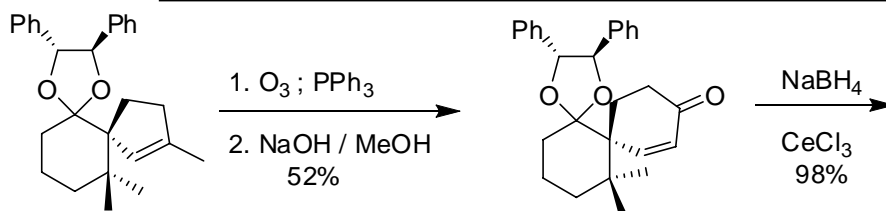
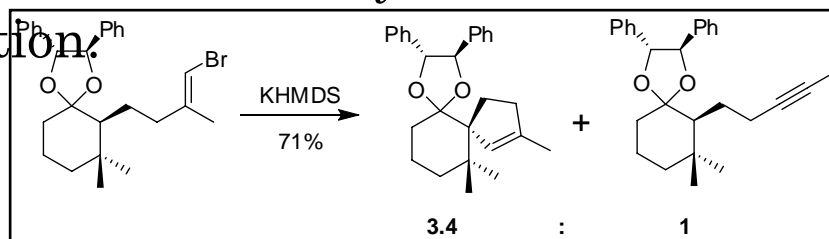
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- He reports that the silyl group doesn't have to be *anti* coplanar with the developing positive charge. In this case it works as *syn* coplanar.



BACK TO (+)-MAJUSCULONE

- The power of this spirocyclization is that the stereochemistry is locked and won't be affected by the acidic conditions required for the deketalization:

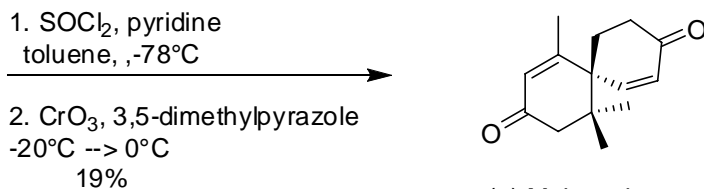
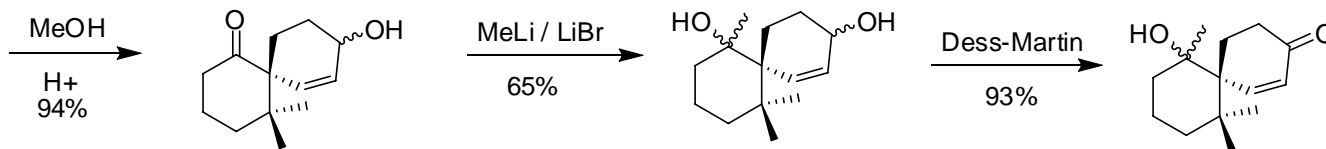
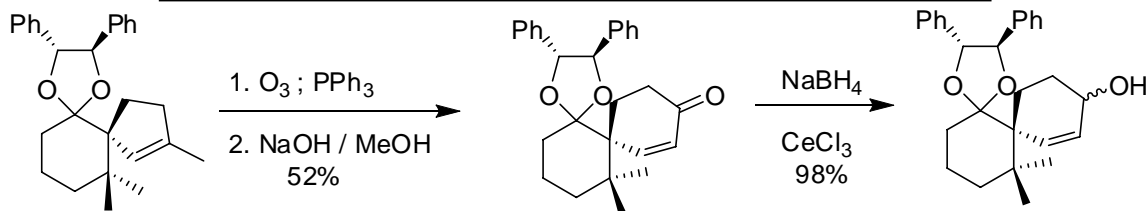
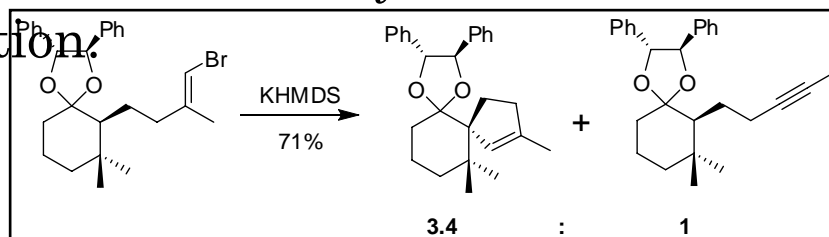


(+) Majusculone



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(+) Majusculone



IN REVIEW

- Bicyclic all-carbon spirocenters are very difficult to construct asymmetrically.
- Few methods exist that are extremely versatile.
- (+)-majusculone is the first chamigrane sesquiterpene to be synthesized enantioselectively.

- Other references:
- Chen, Y., *Tetrahedron* **1996** 52(41), 13181
- Plamondon, J., *Tet. Lett.* **1991** 32(5), 589
- Taber, D., *JACS* **2002** 124, 12416
- Taber, D., *JOC* **1995** 60, 6571
- Pearson, A., *Org. Lett.* **2004** 6(15), 2535 ←





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