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A STEREOSPECIFIC APPROACH TO CIS-P-MENTH-2-ENE[1]

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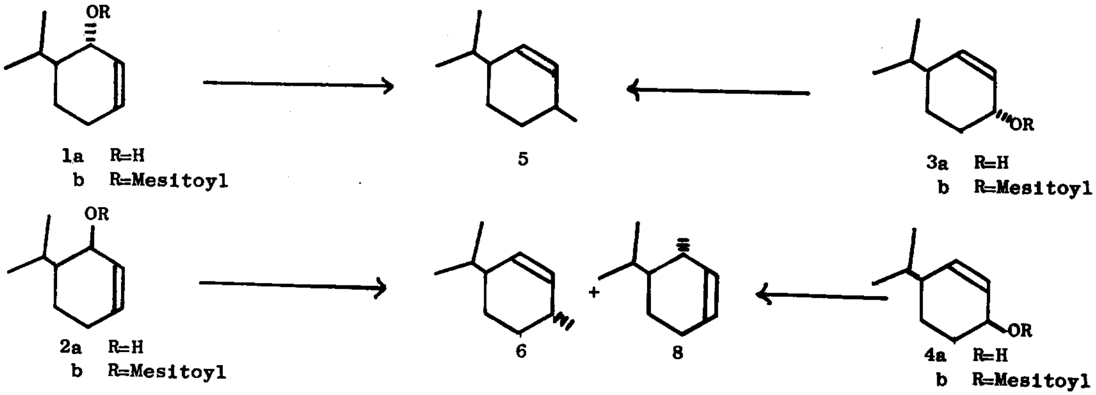
Reaction of lithium organocuprates with allylic esters is a facile method for the formation of new carbon - carbon bonds.[2] The stereochemistry of this reaction has been recently investigated.[3] This data has prompted us to report our relevant findings concerning this reaction in our approach to the synthesis of *p*-menth-2-enes.



1a R=H
b R=Mesitoyl

5

3a R=H
b R=Mesitoyl

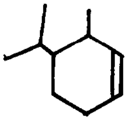
2a R=H
b R=Mesitoyl

6

8

4a R=H
b R=Mesitoyl

The allylic alcohols[4], 1a[5], 2a[6,7], 3a[8] and 4a[8] were first converted (MeLi/Mesitoyl Chloride) to their corresponding mesitoates[7], 1b, 2b, 3b and 4b. Reaction of either 1b or 3b with 1 equivalent of lithium dimethylcuprate in ether at 0°C overnight afforded 67% and 84% yields[9], respectively, of *cis*-*p*-menth-2-ene, 5. None of the allylic isomers, 7, or 8, or the epimer 6, were present.[10] The structural assignment was further corroborated by reduction of 5 to 9a[11,12] by diimide. Reaction of either 2b or 4b with 1 equivalent of lithium dimethylcuprate in ether at 0°C overnight unfortunately afforded[13] in 77% and 57% yields[9], respectively, the same identical 67:33 mixture of 6 and 8. However, none of the *cis*-alkenes 5 and 7 could be detected. The structural assignments were corroborated by reduction of the reaction mixture to the saturated hydrocarbons 9b[11] and 10b[14].



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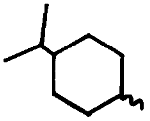
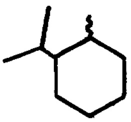
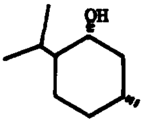


9a -Me
b -Me



10a -Me
b -Me

Previous approaches[17-22] to the *p*-menth-2-enes have all utilized base-induced elimination reactions of esters, halides or quarternary ammonium salts derived from isomeric menthols. While *trans*-*p*-menth-2-ene, 6, can be obtained readily from menthol[17-20,22,13], the *cis*-isomer, 5, is not easily accessible *via* this approach. This is due to either inaccessibility[22] of the precursor, isomenthol, 14, or lack or complete stereospecificity in the elimination reaction of the tosylate of neoisomenthol, 15[22]. Thus, our cuprate approach to *p*-menth-2-enes is the synthetic complement of the traditional elimination approach.



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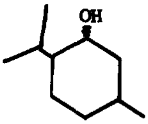

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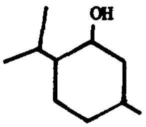

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In addition to the synthetic utility of these results, there are strong mechanistic implications. That the *trans*-allylic mesitoates, 1b and 3b, gave only the same *cis*-alkene, 5, and the *cis* allylic mesitoates, 2b and 4b, gave the same mixture of *trans*-alkenes, 6 and 8, concurs with Goerings proposal[3,23] of a symmetrical intermediate, or its equivalent, which can maintain geometric integrity. However, our results raise new questions about the mechanism of these displacements. Goering's systems, 5-substituted cyclohexenyl substrates, were inherently symmetric with respect to formal SN-2 and SN-2' attack in the proposed intermediate. Our 6-substituted cyclohexenyl substrates clearly show that the relative proportions of formal SN-2 and SN-2' attack can be profoundly influenced by the stereochemistry of an extrinsic asymmetric center.

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References

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4. All compounds are racemic, although only one enantiomer is depicted.
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6. Prepared by triisobutylaluminum reduction of the corresponding en-one, mp 43-45.
7. All new compounds had satisfactory NMR, IR and MS spectra.
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9. Yields were determined by GC using isopropylcyclohexane as an internal standard.
10. The relative GC retention times (10', 1/8", 5% FFAP, 75°C) of 5,6 and 8 were 5.13 min, 4.69 min, and 5.44 min, respectively.
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12. The relative GC retention times (10' 1/8", 5% FFAP, 75°C) of 9a, 9b, 10a and 10b were 4.06 min, 3.50 min, 4.88 min and 4.00 min, respectively.
13. It should be noted the corresponding acetate of 2a gave identical results.
14. Prepared (a 75:25 mixture of 10a and 10b) by catalytic reduction[15] of the corresponding exo-methylene compound[16].
15. For analogous reduction reduction of the α-methyl exomethylene compound: S. Siegal *et al*., J.Org.Chem. 31, 2802 (1966).
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