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STEREOCHEMICAL FACTORS IN THE EPOXIDATION OF SUBSTITUTED CYCLOHEXENES

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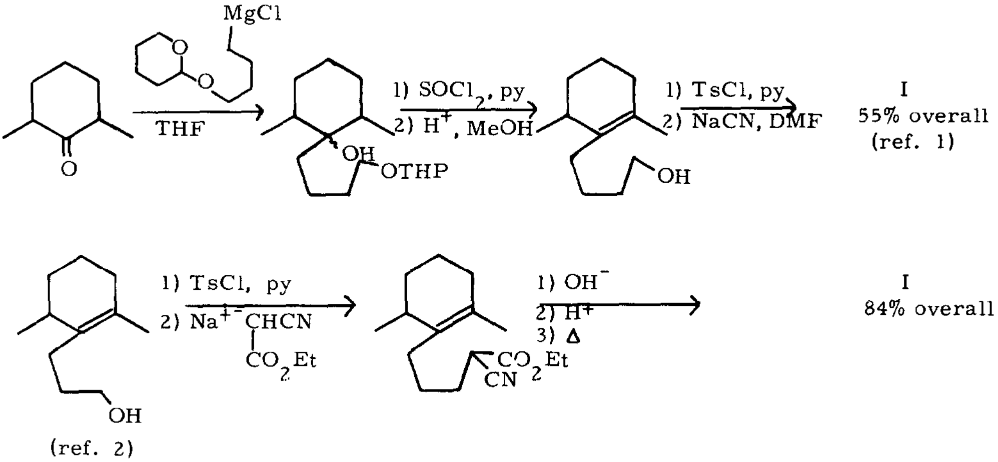
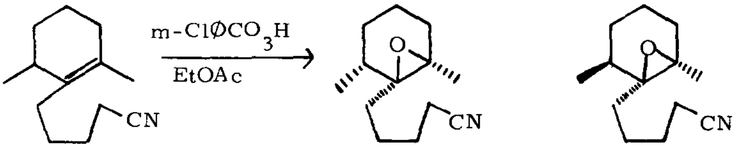
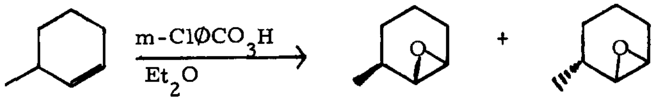
Recently, in connection with the preparation of spiro [4.5] decane compounds, we prepared the epoxide of a cyclohexene derivative I, and obtained an 85:15 mixture of products in 97% yield after distillation. Two routes to I are shown below.



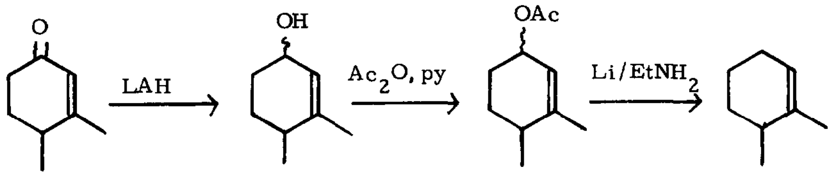


I IIa IIb

At this time we tentatively assigned structure IIa to the major isomer, based on steric considerations. This assignment was purely intuitive, in that Rickborn and Lamke (3) had reported that a 1:1 mixture was obtained from 3-methylcyclohexene.

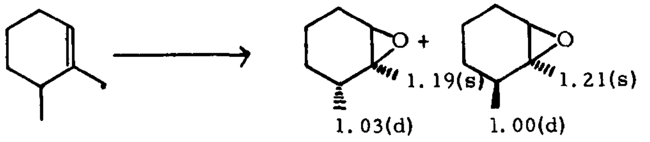


We therefore examined a model more closely related to our system, 1,6-dimethylcyclohexene, IV, prepared in the following manner from the known 3,4-dimethylcyclohexenone III (4).



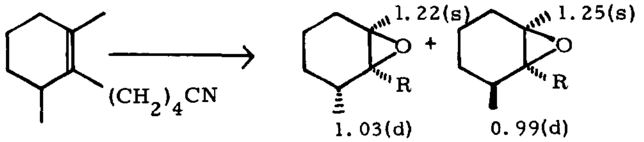
III IV

When IV was epoxidized, a 64:36 product mixture was obtained. That the major epoxide was Vb, i.e. attack of the peracid cis to the secondary methyl group was shown by lithium aluminum hydride reduction and comparison with the known mixture of dimethylcyclohexanols (5) obtained from the reaction of 2-methylcyclohexanone with methyl Grignard. Treatment of both I and IV with aqueous N-bromosuccinimide, followed by potassium t-butoxide dehydrobromination produced mixtures of epoxides in 33 and 64% yields, respectively. The results of the preceding experiments, with pertinent nmr data, are summarized below. The slight upfield shift of the secondary methyl group cis to the epoxide ring (6) in both IIb and Vb also supports the structural assignments.



IV Va Vb

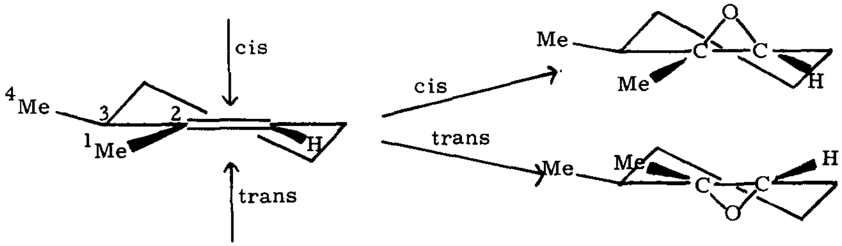
	a/b
peracid	36/64
NBS/base	62/38



I IIa IIb

peracid	15/85
NBS/base	80/20

A possible explanation for the preferential cis attack of the peracid (or positive bromine) is based on the Garbisch model (7) for the addition to substituted cyclohexenes. The sterically favored trans attack decreases the dihedral angle ∠1234, producing a fairly severe eclipsing between the two methyl groups, while cis attack relieves the interaction by increasing the dihedral angle.



The experimental details of all work reported herein can be found in the author's thesis (8).

Acknowledgments:

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References:

1. This route had been previously carried out, using 2-methylcyclohexanone by L. Cama, Ph.D. Thesis, Columbia University (New York, 1964).
2. The preparation of this compound is reported in the accompanying paper.
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