

ASYMMETRIC INDUCTION FROM PYROLYSES OF
S (+) AND R (-) TRANS-4-METHYLCYCLOHEXYL HYDRATROPATE

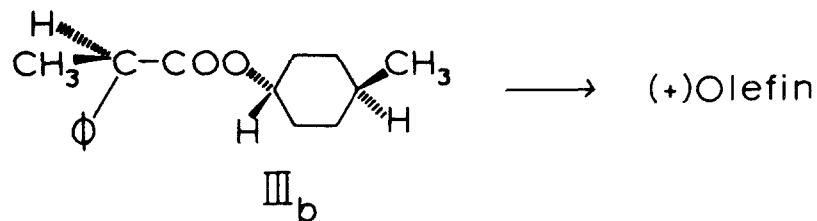
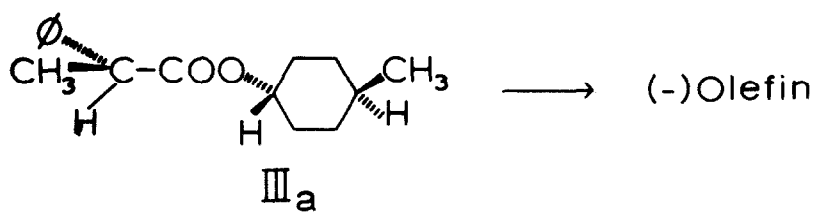
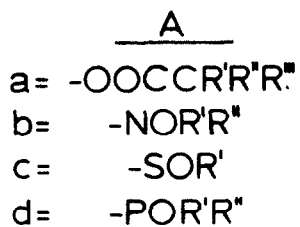
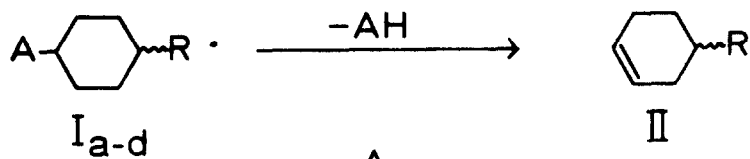
Stanley I. Goldberg and Fuk-Luen Lam
Department of Chemistry, University of South Carolina
Columbia, South Carolina

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Cis-elimination of AH from each of the model systems represented by I would be expected to take place stereoselectively when only one configuration of the asymmetric atom within each A is present. Stereoselective processes are indicated because cis-elimination from such systems would involve, in each case, two diastereomeric transition states possessing a difference in free energy. And a necessary consequence would be formation of optically active 4-substituted cyclohexene (II).

This concept holds the promise of practical utility since assignment of absolute configuration to the asymmetric atom of each A may be possible via selection of the more favored diastereomeric transition state leading to optically active olefin of known absolute configuration.

As a step in the direction of that objective, we wish to report two examples of asymmetric induction via elimination.



\underline{S} (+)Trans-4-methylcyclohexyl hydratropate (III_a) $\{[\alpha]_D^{25.5} +61.8 \pm 0.670^\circ$ ($\underline{c} = 2.02$, benzene) $\}$, prepared from trans-4-methylcyclohexanol (1) and \underline{S} (+)hydratropic acid (2,3) $\{[\alpha]_D^{23} +75.2 \pm 0.7^\circ$ ($\underline{c} = 1.71$, chloroform); lit. (2), $[\alpha]_D^{25} +76.3 \pm 0.6^\circ\}$ via the acid chloride of the latter $\{[\alpha]_D^{20} +104 \pm 0.47^\circ$ ($\underline{c} = 3.44$, benzene); lit. (2), $[\alpha]_D^{22} +101 \pm 0.4^\circ\}$ was carefully pyrolyzed in a column (30 cm. X 1 cm. dia.) packed with Pyrex glass helices by means of the dropping sample method (4) in a stream of nitrogen (12 ml./min.) with contact temperature of $425 \pm 3^\circ$. The pyrolyzate, condensed in a series of cold traps and analyzed gas chromatographically (VPC), was shown to contain 4-methylcyclohexene in about 10% yield. Collection (VPC) of the pure olefin allowed for demonstration of its optical activity, independently determined by each of two disinterested observers* in addition to each of the authors $\{[\alpha]_D^{27} -0.442 \pm 0.152^\circ$ ($\underline{c} = 7.23$, methanol) $\}$.**

Pyrolysis of the enantiomeric ester, \underline{R} (-)trans-4-methylcyclohexyl hydratropate (III_b), prepared in lower optical purity $\{[\alpha]_D^{26} -40 \pm 0.64^\circ$ ($\underline{c} = 1.38$, benzene) $\}$, gave rise to dextrorotatory 4-methylcyclohexene $\{[\alpha]_D^{26} +0.348 \pm 0.269^\circ$ ($\underline{c} = 6.32$, methanol) $\}$.**

The optically active products (presently of unknown absolute configuration) were obtained in states of apparent low optical purity, indicating low degrees of asymmetric induction during the pyrolyses. Considering the rather vigorous conditions required to produce even

* We acknowledge our thanks to Dr. Ruta K. Bly and Mr. Robert F. Moates for these determinations.

** Average of the values obtained by the several independent observers who each made five determinations. The lack of precision is merely a reflection of the difficulty in matching the very small field displayed by the micro-polarimeter cell used for these measurements.

a small yield of olefin and the fact that non-bonded interactions between the α -substituents and the cyclohexyl ring in III are rather long-ranged, it is remarkable that induction is observable at all. We believe, however, that much higher degrees of asymmetric induction will be observed in the systems, I_{b-d}, (work in progress) since these should undergo cis-elimination under milder conditions and since non-bonded interactions between substituents on their asymmetric atoms and the cyclohexyl ring should be more pronounced than in the corresponding ester system (I_a).

This prediction finds support in the recent observation (5) that 3 β -acetoxy-4-cholestene (86% yield) and 3 β -acetoxy-5-cholestene (65% yield) were obtained via pyrolysis of 3 β -acetoxy-(R)5 α -methylsulfinylcholestane and 3 β -acetoxy-(S)5 α -methylsulfinylcholestane, respectively.

With the eventual establishment of absolute configurations of the enantiomeric 4-methylcyclohexenes (experiments in progress) and completion of our pyrolysis work on the enantiomeric cis isomers of III, it should then be possible to begin to evaluate factors which allow one diastereomeric transition state to be favored over the other.

Acknowledgement

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References

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