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PREPARATION OF (+)- AND (-)-4-METHYLCYCLOHEXENE BY ASYMMETRIC PYROLYSIS OF OPTICALLY ACTIVE N-OXIDES

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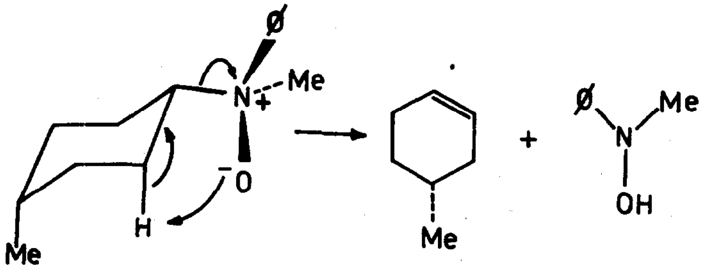
The pyrolysis of N-oxides is a well-known method for the preparation of alkenes, involving a cis-elimination (1) under very mild conditions. As a part of a research program concerning new methods for the asymmetric synthesis of alkenes and halides it appeared promising to investigate the pyrolysis of optically active N-oxides of 4-alkylcyclohexylamines, having two different substituents on nitrogen, as a possible route to active 4-alkylcyclohexenes. Molecular models show that for such compounds the free energies of the ciclic transition states leading to the enantiomeric olefins should differ enough for a fair optical yield.

The diethyl ketal of 4-methylcyclohexanone was transformed with N-methylaniline into the enamine, 4,N-dimethyl-N-phenyl-1-cyclohexenylamine (b.p. 127°/ 4 mm), which was hydrogenated to a mixture of the two diastereoisomeric 4,N-dimethyl-N-phenylcyclohexylamines (b.p. 127-129°/3 mm). Fractional crystallization of the hydrochlorides allowed to separate the major component in a pure state (hydrochloride, m.p. 165-166°). It was tentatively assigned the cis configuration on the basis of the von Auwers-Skita rule (2), as it has higher refractive index and density than mixtures of the two diastereoisomers. This point, however, requires further confirmation.

The pure amine was transformed into its N-oxide (I, monohydrate, m.p. 98-99°) with p-nitroperoxybenzoic acid. Optical resolution was easily achieved with (-)-dibenzoyltartaric acid, which precipitated the crystalline salt of the (+)-N-oxide, m.p. 164-165°, $[\alpha]_D^{18}$ -55.7° ($\underline{c}$ 0.96, dimethylformamide), much less soluble in ethanol than the diastereoisomeric salt. The (+)-N-oxide which was recovered from the salt had m.p. 70-72°, $[\alpha]_{578}^{18}$ +17.4°, $[\alpha]_{365}^{18}$ +64.3° ($\underline{c}$ 0.5, $CHCl_3$). It was pyrolyzed at 110° to give a 60% yield of pure (gas chromatography) (R)(+)-4-methylcyclohexene (II), $[\alpha]_{578}^{18}$ +34.7°, $[\alpha]_{546}^{18}$ +39.5°, $[\alpha]_{436}^{18}$ +68.5°, $[\alpha]_{365}^{18}$ +108.2° ($\underline{c}$ 1.87, $CHCl_3$). Similarly, (S)(-)-4-methylcyclohexene, $[\alpha]_{578}^{18}$ -23.0°, $[\alpha]_{365}^{18}$ -71.5°, was obtained from a (-)-N-oxide of lower optical purity.

If the data of Mousseron (3) ($[\alpha]_{579}$ +106.2°, $[\alpha]_{546}$ +121.1°, $[\alpha]_{436}$ +210.7°) correspond to optically pure (R)(+)-4-methylcyclohexene (a fact which will be checked by correlation with 3-methyladipic acid), the optical purity of our (+)-olefin should be higher than 30%, which would be a rather good result for an asymmetric transformation.



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Our method differs from most of the known kinetic asymmetric transformations as it involves an intramolecular reaction during which the molecule is cleaved in such a way that a symmetric moiety becomes asymmetric and <u>vice-versa</u>.

While the present work was in progress Goldberg and Lam(4) reported an asymmetric degradation based on a similar principle, in which (+)- and (-)-4-methylcyclohexene were obtained from the active *trans*-4-methylcyclohexyl hydratropates. The optical yields were, however, little more than 1/100th of those achieved by our method, probably because much more drastic conditions are required for the pyrolysis of esters and because in these reactions the asymmetrically substituted carbon atom is not part of the cyclic transition state.

Full experimental details will be published at a later date, together with the results of further work which is under way on the scope, limitations, steric requirements, etc. of the preparation of optically active cyclic olefins *via* pyrolysis of N-oxides.

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