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BASE CATALYSED DEUTERATION OF NORCAMPHOR AND DEHYDRONORCAMPHOR

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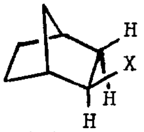
We are prompted by the recent publication of Tidwell[1], to report the results of our work on the base catalysed deuteration of norcamphor and dehydronorcamphor

It is well known[2] that the exo face of a bicyclo[2,2,1]heptane system which has no bulky substituents on the bridge carbon (C_7), is less hindered towards attack by reagents than the endo face. Base catalysed deprotonation in elimination reactions of substituted bicyclo[2,2,1]heptanes of types I and II, where X can be a variety of leaving groups, invariably involves base attack from the exo face[3]. Thomas[4,5] has studied base catalysed deuterium exchange of the bicyclic ketones isofenchone (III) and camphor (IV) and noted that proton exchange was again exo. A study of norcamphor exchange showed some specifity which was tacitly assumed to be exo.



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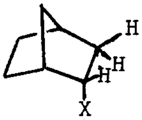

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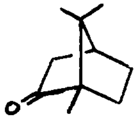

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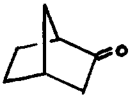

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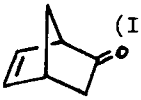

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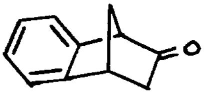

(VII)

When we began our work a major exception to the rule of attack by reagent from the least hindered side appeared to be the base exchange of camphor with its two C_7 methyl groups. This has recently been elegantly explained by

Brown[6,7] so that many of the reactions of the bicyclo[2,2,1]heptane system can now be rationalised in terms of the steric requirements of the reagent and of the bicyclic system itself.

One exception to this rule which was of great interest to us was the implication[8] that while norcamphor (V) did exhibit stereospecific deuterium exchange, dehydronorcamphor (VI) did not. This result was at variance with any explanation based on steric repulsion to base attack since Brown[9] had shown that while attack of borohydride ion on norcamphor is 86% exo; attack on dehydronorcamphor is 95% exo. This is to say that the steric requirements of the π-electrons of the double bond are greater than are those of the saturated bridge.

We were interested to see if this apparently anomalous result, which was in accord with studies on the benzo analogue (VII)[10], might be due to some effect of homoallylic stabilisation of the carbanion or antiaromatic destabilisation of the enolate, and as a first step to this end, treated norcamphor (V) to exchange conditions similar to those used by Thomas[4,5] in his pioneer work. Norcamphor (V) behaved much as reported by Thomas[4], our incorporation figures being 4·0% d_0; 48·0% d_1; 48·0% d_2 by mass spectral analysis after correction for C_{13} natural abundance and the P-1 ion. These results are in line with the values found by Thomas and we have shown that stereospecificity is exo by reducing the ketone to the endo alcohol (II, X = OH) with sodium borohydride[9]. The C$\underline{\underline{H}}$OH absorption which appeared as a sextuplet in the undeuterated material had lost the 9Hz coupling which had been assigned $J_{2\underline{exo},\ 3\underline{exo}}$ by Musher[11]. We also found that pyrolysis of the xanthate of this alcohol gave a product with a very large ion at mass number 95 and a very small ion at mass number 94, in accord with exo deuteration of the ketone (V). The peak at mass number 94 may be due to the d_0 material present and to the small amount of exo-2 alcohol expected from the reduction[9].

Dehydronorcamphor (VI) contrary to expectation[8] gave, under the above conditions, a product containing 84% d_1 and 16% d_2. The predominantly exo nature of attack was obvious from a comparison of the n.m.r. spectra of the endo alcohols derived[9] from the deuterated and undeuterated ketones. The heptet at 7·89τ exhibited by the exo 3H[12] completely disappeared on deuteration and the vicinyl (8Hz) coupling with the $\mathrm{C\underline{\underline{H}}OH}$ proton at 5.51τ[12] and the geminal coupling with the *endo* 3H(12Hz)[12] had also disappeared.

The disagreement between these results and those of Jerkunica,[8] where dehydronorcamphor (VI) underwent dideuteration more readily than did norcamphor, led us to reinvestigate deuteration of these compounds under his conditions, which involved heating with strong alkali in a sealed tube at 100°C.

Dehydronorcamphor under these conditions yielded a product which, from its n.m.r. spectrum, contained bands characteristic of *exo*-3D-*endo*-2-norborneol. This was even more apparent when the reaction was run in $\mathrm{CH_3O\underline{\underline{H}}:\underline{\underline{H}}_2O}$ rather than in deuterated solvents since the characteristic splitting patterns of the 3-*exo*- and 3-*endo* protons were observed.[12] Comparative v.p.c. confirmed this result and integration of the n.m.r. spectrum indicated that there was ca. 25% alcohol. Although Jerkunica reported using n.m.r. spectroscopy to deduce percentage deuteration, we have not been able to do this. Data from integrated gas chromatography-mass spectroscopy on the dehydronorcamphor fraction, however, showed that this was almost entirely dideuterated.

Norcamphor on exchange in the above conditions again gave a product from whose n.m.r. spectrum we hesitated to conclude percentage deuteration figures. Combined gas chromatography-mass spectroscopy led us to the conclusion that norcamphor was also almost entirely dideuterated.

Our results indicate that, although under the forcing conditions used by Jerkunica dideuteration of both ketones was observed together with some reduction and some aldol condensation[13], milder conditions led to attack which was stereospecifically *exo* and was, therefore, in a broad sense, not at variance with expectations based on simple steric considerations.

The finding of reduction of dehydronorcamphor to the *endo* alcohol under the vigorous basic methanolic conditions of Jerkunica is not too surprising. The amount of alcohol obtained increased with increasing base concentration. That very little reduction occurred with norcamphor is in keeping with the relative rates of reduction of the two ketones with sodium borohydride[9].

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