Application of the Nuclear Overhauser Effect in Establishing the Structure of Heterocyclic Norbornanes

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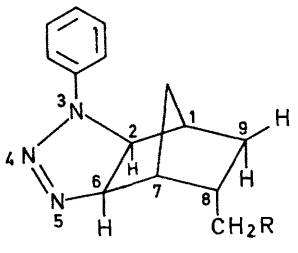
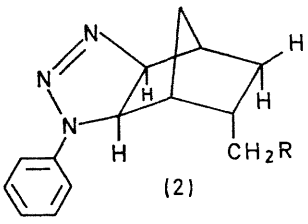
Summary. The nuclear Overhauser effect has becn used in establishing the structure of heterocyclic norbornanes by locating the substituents relative to the *endo*-hydrogen atoms.

WE required heterocyclic norbornanes of the types (1) and (2), and followed the method of Alder and Windemuth[1] in which the strained double bond of bicyclic [2,2,1] systems undergoes ready 1,3-dipolar addition reactions. However, in previous work no supporting evidence was provided for the stereochemistry of the product. A re-examination of this problem now enables us to provide a general method

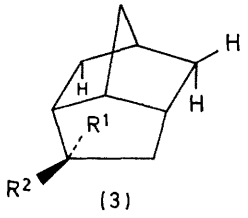


(1)



(2)

a; R = CN
b; R = NH_2



(3)

a; R^1 = Ph, R^2 = H
b; R^1 = H, R^2 = Ph

for elucidating the structure of heterocyclic norbornyl systems and other derivatives of bicyclo[2,2,1]heptane. Thus the structure of the phenyl azide–5-cyanomethylnorborn-2-ene adduct is (1a) from consideration of the n.m.r. spectrum and application of the nuclear Overhauser effect (N.O.E.).

The cyanomethyl group of (1a) is in the *endo*-position as shown by the chemical shift at high field (octet at τ 9·15) of the C-9 *endo*-hydrogen. This abnormal shielding is caused by the anisotropy of the bond from C-8 to the *endo*-methylene group.[2] The heterocyclic ring must assume an *exo*-position, because the protons at C-2 and C-6 form an AB system with doublets centred at τ 5·35 and 6·30 (J 9·0 Hz). This necessitates these protons assuming *endo*-positions where there is virtually no coupling to the hydrogens at C-1 and C-7 (dihedral angle *ca.* 90°).

Although products (1a) and (2a) are possible from the 1,3-dipolar addition reaction, only (1a) was obtained in high yield. However, the n.m.r. spectrum alone does not differentiate between structures (1a) and (2a). The rigid nature of the tricyclic ring system enables the N.O.E. experiments to locate the *endo*-substituent, the hydrogen atoms, and the phenyl group relative to one another. Empirical data[3] suggest that the high-field doublet (τ 6·30) is due to the *endo*-proton at C-2 which is shielded by the phenyl substituent and N.O.E. experiments support this assignment. Thus, double irradiation at the frequency of the most intense peak in the phenyl region (τ 2·85) causes an increase of 8—9% in the integral of the high-field doublet. That the phenyl group is on the opposite side of the molecule to the cyanomethyl, as in structure (1a), was confirmed by double irradiation at the signal of the *endo*-methylene protons. A positive N.O.E. of 15% was observed in the integral of the low-field doublet due to the *endo*-proton at C-6. Final proof in support of structure (1a) was obtained by observing the N.O.E. caused by triple irradiation of the two major peaks due to the C-9 *endo*-proton. This gave rise to approximately 10% enhancement of the integral of the high-field doublet corresponding to the C-2 *endo*-proton.†

By using the N.O.E. in this manner, the stereochemistry of other heterocyclic norbornanes [*e.g.* (1b)] has been established. Furthermore, by using the close proximity of the substituents and neighbouring hydrogens, it may be possible to assign structures (3a) and (3b) unambiguously[4] and to solve other stereochemical problems associated with norbornane adducts.

We thank Allen and Hanbury for a research grant (to J.S.O.) and Professor H. Suschitzky for his interest.

(*Received, September 16th*, 1970; *Com.* 1579.)

† Peak enhancement was deduced using electronic integration by comparing integrals of the C-2 and C-6 *endo*-protons before and after irradiation. Area measurements of the peaks with a planimeter gave slightly higher values.

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[2] R. G. Foster and M. C. McIvor, *Chem. Comm.*, 1967, 280.
[3] P. Scheiner, *Tetrahedron*, 1967, **24**, 349.
[4] P. T. Lansbury and F. J. Caridi, *Chem. Comm.*, 1970, 714.