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NUCLEAR MAGNETIC RESONANCE SPECTRA OF CAGE KETONES AND KETALS

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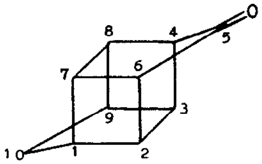
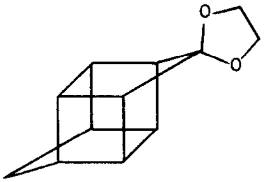
It has previously been reported from these laboratories (1) that carbonyl and cyclic ethylene ketal groups in certain rigid cage compounds cause unexpected magnetic shielding of some of the cage methine protons. The tentative view was put forward that the shielded protons are those situated in the α-position relative to the functional groups. Unfortunately, none of the compounds studied lent themselves to a full assignment of the nmr signals which would confirm this surprising conclusion. We now wish to report a study of the bis-homocubane derivatives 1, 2, and 3, the nmr spectra of which are readily elucidated by spin-decoupling. This work provides strong evidence that in these compounds it is indeed the α-protons (H-4 and H-6) which are shielded by the introduction of the functional groups and consequently resonate at higher field in the ketone 1 and the ketal 2 than in the hydrocarbon 3.

The nmr spectra of 1, 2, and 3 (2) (Table I) show a close triplet or broad singlet at high field, assigned to the methylene protons, and humps or partially resolved multiplets at lower field corresponding to the different types of methine protons. In all the spectra, strong irradiation of one of the methine resonances (which are well separated from one another) causes the collapse of the methylene signal, but irradiation of the other methine resonances leaves the methylene signal unchanged. We believe it is a safe assumption that the major coupling of the methylene protons is to the methine protons vicinal to them. The geometry of the compounds does not favor long range coupling involving the methylene protons (3,4), and the splitting or broadening (5) of the methylene signals is in good agreement with the vicinal coupling (ca. 2 Hz for a 60° dihedral angle) predicted by the modified Karplus equation (6). The remaining methine resonances can be assigned on the basis of their integrated intensities (7).



1



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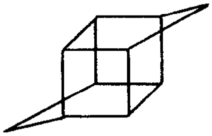

3

TABLE I

Nmr Spectra of Bis-homocubane Derivatives

4% in CCl_4; 100 MHz; δ in ppm from TMS internal standard

	1	2	3
H-10,(5)	1.41[a]	1.37[a]	1.37[b]
H-1,9	3.33[c]	2.88[c]	2.84[c]
H-4,6	2.57	2.44	
H-2,3,7,8	2.77	2.60	2.50

[a] Triplet, 3Hz separation between outer peaks

[b] Singlet, 3 Hz broad at half-height

[c] Irradiation of this resonance caused collapse of the methylene signal to a singlet with width at half-height ≤ 1.5 Hz

The results given in Table I show that the formal conversion of the hydrocarbon 3 to the ketone 1 causes the α-protons (H-4 and H-6) to experience an upfield shift of 0.27 ppm. The remaining protons are shifted downfield, H-2, H-3, H-7 and H-8 by 0.27 ppm, and H-1 and H-9 by 0.49 ppm. Comparison of the ketal 2 with the hydrocarbon shows that the only large shift is experienced by the α-protons (H-4 and H-6), which are moved 0.40 ppm upfield.

In seeking an explanation for the shielding of the α-protons, it should be borne in mind that, apart from inductive effects which should deshield nearby protons, the formal introduction of the functional groups into the hydrocarbon molecule may affect the remaining protons in two ways, (a) by changing the geometry of the system and hence the hybridization of the bonds, (b) by replacing the anisotropy of the methylene group (8) by that of the carbonyl or ketal function. The customary model (9) of the anisotropy of the carbonyl group predicts that it will cause strong deshielding of coplanar α-protons and one might expect this to be the dominant effect in 1. However, newer calculations of carbonyl anisotropy (10), which have recently been expressed in pictorial form (11), show some areas of shielding in the plane of the carbonyl group. To our knowledge, the only simple ketones thus far reported to show the shielding effect are strained structures of the type discussed here. It may be that only in these cases are the coplanar α-protons appropriately placed with regard to the shielding and deshielding zones of the carbonyl. Previous examples of shielding in the plane of the carbonyl group have involved α-bromoketones, where the mutual interaction of the two polar functions may influence the anisotropy of each (12). The strong deshielding of H-1 and H-9 in **1** is surprising in that one would expect all effects of the carbonyl group to be much attenuated at this distance.

The very substantial shielding effect of the ethylene ketal function on the α-protons is without apparent precedent outside the cage area. No great geometric or anisotropic effects would be anticipated for this functional group. However, there may be some long range anisotropic effects associated with the oxygen atoms as discussed in ref. 1b. If this explanation is correct, the shielding would be expected to be observed only when the ketal oxygens form part of a rigid ring. In keeping with this view, preliminary experiments with the dimethyl ketal of **1** show that none of the cage methine protons are greatly shielded with respect to the hydrocarbon.

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2. Compound **2** (mp 32.5-34°) was prepared by lithium dehalogenation of its decachloro derivative [R. J. Stedman, L. D. Davis, and L. S. Miller, *Tetrahedron Letters*, 4915 (1967)], and converted to **1** and **3** by standard procedures (R. J. Stedman, L. D. Davis, and L. S. Miller, *J. Org. Chem.*, in press). Compound **1** was previously reported by G. W. Griffin and A. K. Price, *ibid.*, **29**, 3192 (1964), and compound **3** by W. L. Dilling, H. P. Braendlin, and E. T. McBee, *Tetrahedron*, **23**, 1211 (1967).
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4. In the case of **1** and **2** the methylene signals collapse on irradiation of a *two-proton* methine peak. Thus, if the coupling is not to H-1 and H-9, it must be to H-4 and H-6. Such coupling through five σ-bonds is not commonly observed (3).

5. Virtual coupling [J. I. Musher and E. J. Corey, Tetrahedron, 18, 791 (1962)] may be the cause of the lack of clear resolution of the methylene signal in 3. In this compound the H-1/H-9 and H-4/H-6 pairs are equivalent and may be coupled together through two four-bond pathways.

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7. The assignments in the case of the ketone 1 are supported by the solvent-shifts seen when the spectrum is run in benzene [J. Ronayne and D. H. Williams, Chem. Commun., 712 (1966) and literature cited therein].

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11. G. S. Karabatsos, G. C. Sonnichsen, N. Hsi, and D. J. Fenoglio, J. Am. Chem. Soc., 89, 5067 (1967).

12. N. S. Bhacca, J. E. Gurst, and D. H. Williams, ibid., 87, 302 (1965). These authors draw a careful distinction between the numerous cases of anomalous relative shielding (usually axial compared with equatorial, e.g. cases cited in ref. 1b, and the elegant work of ref. 11), and the rather few examples of net shielding (ketone compared to hydrocarbon) which are much harder to explain.