Tetrahedron Letters No.6, pp. 651-656, 1968. Pergamon Press. Printed in Great Britain.

The Conformation of Cyclic Ketones.

Solvent Shifts in NMR.

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(Received in UK 1 September 1967)

Recently new indications for the existence of preferred, distinct orientations of the carbonyl group in 5-12-membered cycloalkanones was found by the present author[1]. The orientation of the carbonyl group seemed to change in an irregular way within the series, indicating a preferred orientation for each ring size. Some of the results closely paralleled the C^{13} NMR measurements of Dahmi and Stothers[2].

The purpose of the present investigation is to test the above-mentioned findings by an independent method.

Preliminary NMR measurements on the C_5-C_{12} cycloalkanones in carbon tetrachloride gave as expected two main chemical shifts for the ketones: one ranging from 122-152 cps, the other from 120-78. These were ascribed to the alpha- and the other hydrogens respectively. Integration showed for each compound the correct proportion between the two hydrogen types, and the values for the higher cycloalkanones were nearly coincident with those for open-chained aliphatic ketones. A third broad top, centered at about 100 cps below TMS was pronounced only in the highest members. The change in coupling pattern obtained after alpha-deuteration clearly showed that this top was due to the beta-hydrogens, as was found also with open-chained aliphatic ketones.

NMR data of the different cycloalkanones with carbon tetrachloride and benzene as solvents are summarized in Table 1. A coupling constant $J_{\alpha-\beta}$ of ca. 7.0 cps was found for the C_{10}-, C_{11}-, and C_{12}- ring ketones as well as for open-chained ketones, indicating the same conformation, i.e. antiperiplanarity[*] of the carbonyl group and the alpha-methylenes in these cases.

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[*] W. Klyne and V. Prelog, Experentia, 1960, 16, 521.

Table 1

NMR absorptions of cycloalkanones in cps downfield from TMS.

Ring size	Solvent	
	Carbon tetrachloride	Benzene
5	122.5,119.5,116	105,99,88,85,82
6	136,130,121,116,109,106	122,116,80,77.5
7	143.5,101	134.5,78.5
8	147,142,135,116,110,105,94,89	133,129,122,101,97,95,88,85, 77.5,75.5
9	148,144,137,118,110,105,102, 96,87	135,133,130,123,104,98,88,84, 77.5
10	152,148,141,119,110,103,98, 91,82	134.5,131,125,109,105,103,98, 90,85,75
11	151,147,140,117,108,103,98, 91,79	134.5,130,122,105,102,97,92, 85,74
12	149,144,137,115,106,100,94,78	132,128,121,100,94,91,85,72.5
15	147,141,134,110,103,96,90,79	133,126,120,100,93,87,84,76

Comparison of the NMR chemical shifts obtained with carbon tetrachloride and with benzene as solvents shows, as might be anticipated, a typical aromatic solvent shielding effect. Assuming the existence of solute/solvent molecular collision complexes of specific geometry, such an shielding effect can be utilised in conformational analysis[3].

As pointed out recently[4,5], the main rule governing the collision complex geometry is, that a dipole solute molecule will orient itself perpendicular to the plane of an aromatic nucleus with the positive end of its dipole as near as, and the negative end as far from it as possible.

The diamagnetic anisotropy of the aromatic nucleus will then cause an extra chemical shift difference for the various hydrogens depending on their relative locations. For cyclic monoketones with the carbonyl as the only polar group, the situation should be very simple. Different orientations of this group, and of the dipole moment, relative to the alpha- and other ring-hydrogens, should be clearly reflected in different relative variations in chemical shifts when changing from carbon tetrachloride to benzene as solvent.

The experimental results are shown in the figures above. Fig. 1 shows plots of the solvent shift $(\delta_{CCl_4}-\delta_{C_6H_6})$ for the alpha- and the other hydrogens. The shifts are highest for

Fig. 1

NMR solvent shift, ($\delta_{CCl_4} - \delta_{C_6H_6}$) for α - and other hydrogens (H_α and H_o) of cycloalkanones.

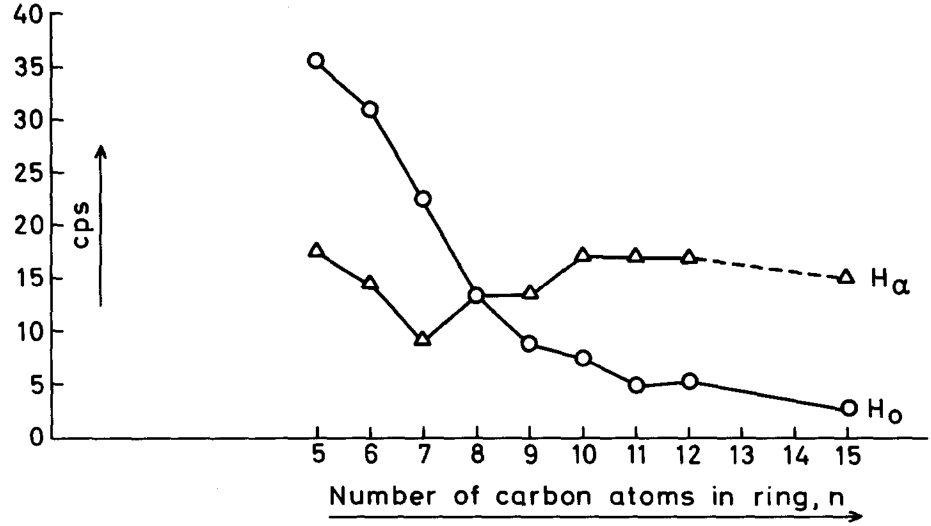


Fig. 2

NMR solvent shift effect on the difference between α - and other hydrogens, Δ ($\delta_{H_\alpha} - \delta_{H_o}$), compared with dipole moment.

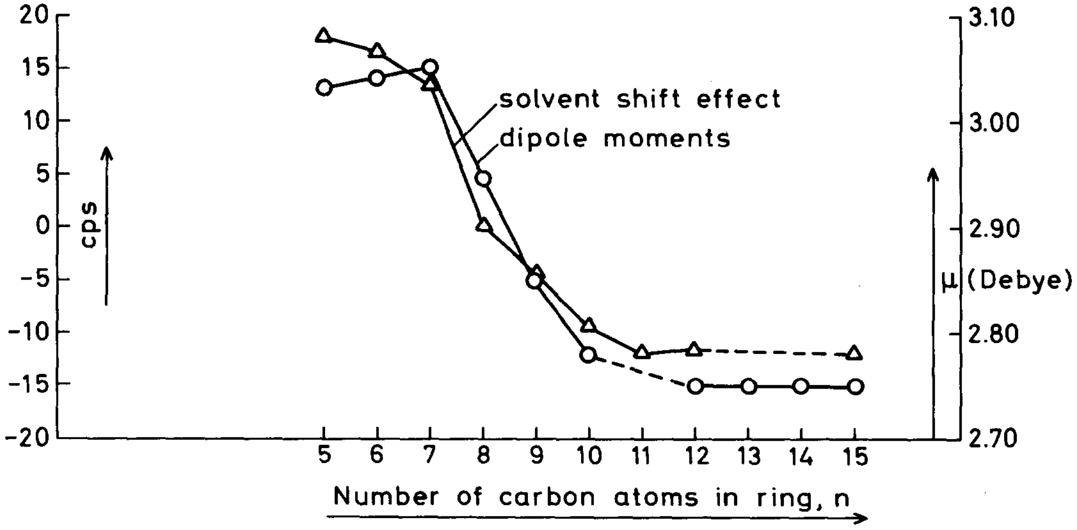


Fig. 3

Increment in solvent shift effect, $\Delta(\delta_{H_\alpha}-\delta_{H_o})$ between n- and n+1- membered cycloalkanone.

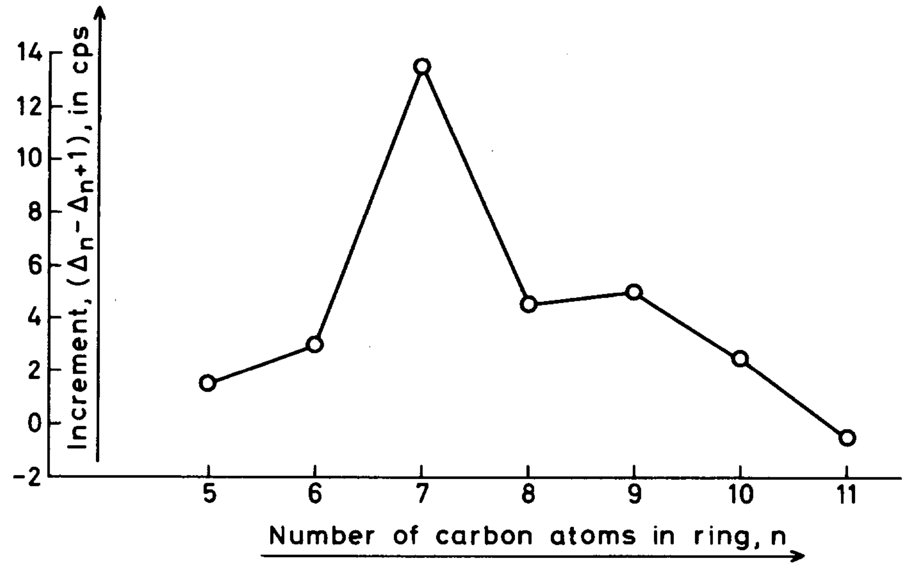
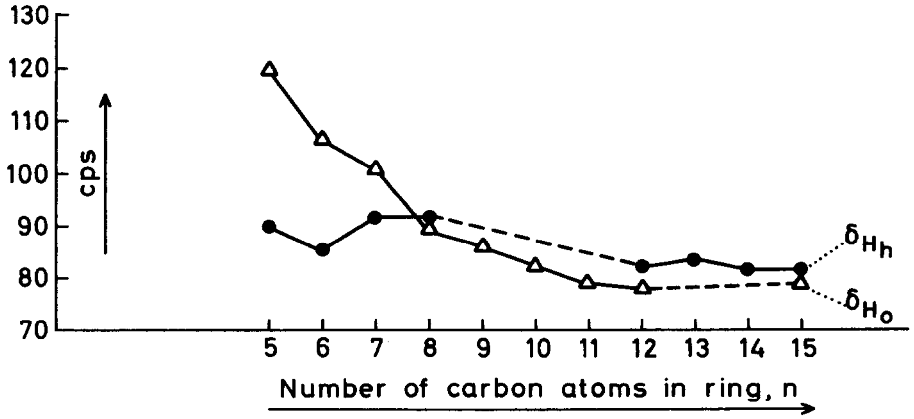


Fig. 4

NMR chemical shift of cycloalkanes, δ_{H_h} and of the high field hydrogens of cycloalkanones, δ_{H_o}.



hydrogens other than the alphas in the smaller rings and lowest for these same hydrogens in the larger rings. While the solvent shift of other hydrogens is steadily decreasing with increasing ring size, the shift of the alpha hydrogens varies less, but shows minima for the 7-, 8-, and 9-ring. The solvent shift effect on the difference in chemical shift between alpha- and other hydrogens is plotted in Fig. 2. The values, which are positive for the 5-, 6-, and 7-ring ketones, zero for the 8-ring ketone, and negative for the higher ketones, form a curve nearly parallel with that of the dipole moments. The increment in solvent shift effect between neighbouring ketones are plotted versus ring size in Fig. 3. A maximum value is found for the 7-8-ring increment, while the 11-12-ring increment is negative.

The interpretation of the solvent shift results seems clear: In the smaller rings the alpha hydrogens are necessarily located nearer the negative end of the dipole. They are therefore farther away from the benzene nucleus in the ketone/benzene collision complex, and are thus less shielded than the other hydrogens (Fig. 5).

In the 8-ring ketone the alpha- and the other hydrogens have nearly the same mean location relative to the carbonyl group dipole, and are then shielded to the same extent (Fig. 6). In the larger rings the alpha-hydrogens must be nearest the positive end of the dipole as they are shielded much more than the other hydrogens (Fig. 7).

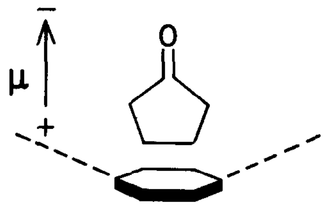


Fig. 5

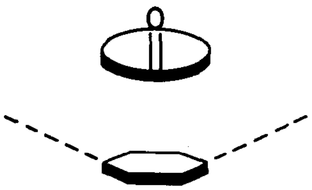


Fig. 6

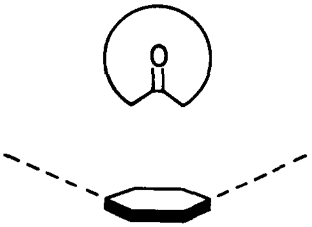


Fig. 7

The conclusion must therefore be: In the 5-ring ketone the carbonyl group is pointing outward with an angle of 0° between its dipole and the ring plane. This angle is steadily increasing for the larger ring ketones, reaching a maximum value for the 11- and the 12-ring ketones, which then may have true "inside-carbonyl"-conformations.

The plots in Fig. 3 reflect the relative variations of carbonyl group orientation in the C_5-C_{12}-cycloalkanones. Provided parallelism between this orientation and solvent shift effect exists, and the angle between carbonyl group and ring plane were exactly determined for both cyclopentanone and cycloundecanone, the corresponding angle of the other cycloalkanones could easily be calculated.

The indicated orientations of the carbonyl groups are assumed to be associated with the conformations of lowest energy, and may thus be one of the factors determining the overall conformations. Substituting a methylene group with carbonyl in cycloalkanes may therefore cause changes in all parts of the molecule. This is in fact seen to be the case from Fig. 4, where the chemical shifts of cycloalkanes are compared with the high field shifts of corresponding cycloalkanones. For cyclooctanone and its higher homologues the introduction of a carbonyl group seems, rather unexpectedly, to cause a lowering of the δ-value. For cycloundecanone and cyclododecanone it is nearly the same as for methylenes in open strain-free chains, *i.e.* *ca.* 78 cps. The first cycloalkane with as low a δ-value as this was found to be the 22-ring alkane.

The chemical shift of the high field methylenes in cyclododecanamine and cyclododecanonoxime was exactly the same as for unsubstituted cyclododecane, *i.e.* 81 cps. Solvent shift for cyclododecanonoxime was 10 cps for two of the alpha hydrogens and -1 cps for the remaining two, while the high field methylenes were shifted 4.5 cps.

New spectroscopic data and a more detailed analysis will be given later.

Experimental.

NMR measurements. *Ca.* 10 % w.w. solutions of the C_5-C_{12} cycloalkanones (p.a. Aldrich) in carbon tetrachloride and benzene respectively (p.a. Merck) were measured with a Varian A 60 A spectrometer at 37 °C with TMS as an internal standard.

Deuteration. The cycloalkanones were stirred with excess D_3PO_4 at 75 °C for 24 h.

References.

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