Tetrahedron Letters No.13, pp. 1557-1560, 1968. Pergamon Press. Printed in Great Britain.

SOLVENT SHIFTS IN CYCLIC ETHERS AND OTHER HETEROCYCLIC COMPOUNDS* +

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(Received in UK 12 December 1967)

Although the solvent shift of a methyl group in benzene, relative to that in $CDCl_3$ solution ($\Delta = \delta\ CDCl_3 - \delta\ C_6H_6$) has been found to have a maximum of $\sim +0.3$ PPM when it is axial and slightly negative or nearly zero when it is equatorial, due to a single carbonyl group (1,2), it has recently been observed that in lactones, these shifts are positive in both the cases and have a much higher value for the axial group. In γ-lactones (3), the values are +0.46 ± 0.06 when the methyl group is quasi-axial and +0.23 ± 0.06 when it is quasi-equatorial, and similar results hold good for δ-lactones as well (4). These results in the lactones appeared anamolous, at least as far as the equatorial methyl group is concerned, since it lies close to the reference plane (1,2).

To ascertain whether this difference in behaviour in the lactones can be accounted for by ascribing a positive contribution from the ether oxygen atom of the lactones for both the axial and equatorial groups, a few known and new rigid cyclic ethers without interfering functional groups in the system were prepared and their spectra determined in $CDCl_3$ and benzene solutions. In pyridine solution shifts were found smaller and hence spectra were taken only in one case. The results are given in Table 1.

The data show, as expected, that the ether oxygen atom alone gives a significant positive Δ value to the C_{11}-CH_3. Besides, the solvent shifts of the different groups in the examples, though limited in number, lead to some generalization regarding the Δ of the different groups. If a reference plane is drawn purpendicular to the plane made by the ether oxygen and the two carbon atoms holding it (e.g. C_6 and C_{12} in I to IV) and passing through the mid-points of the C-O bonds, then protons in front of it, i.e. on the same side as the oxygen atom (e.g. $C_{4\alpha}$-CH_3 in I and II) are deshielded and protons lying behind the plane (e.g. C_{11}-CH_3 in I to III) are shielded.

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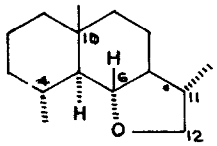
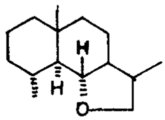
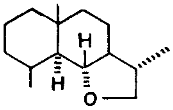
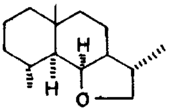
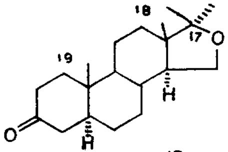
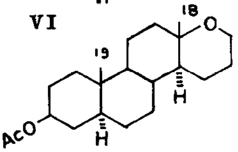
*Communication No.1111 from the National Chemical Laboratory, Poona.

+Stereochemical studies by PMR spectroscopy IX.

TABLE 1

Compound	Solvent	Chemical shift in cps at 60 Mc of the C_4-CH_3	C_6-H	C_{12}-H_2	C_{11}-CH_3	C_{10}-CH_3
I 	$CDCl_3$	59,65	240	197	56,63	51.5
	C_6H_6	76,82	236.5	195	46,53	47
	Shift in C_6H_6	-17	+3.5	+2	+10	+4.5
	Pyridine	70,76	..	..	50,57	48
	Shift in pyridine	-11	..	..	+6	+3.5
II 	$CDCl_3$	59,65	249.5	199.5	51,57	51
	C_6H_6	78,84	245	195	40,46	46.5
	Shift in C_6H_6	-19	+4.5	+4.5	+11	+4.5
III 	$CDCl_3$	58,64	245	199	55,62	57.5
	C_6H_6	62,68	241	197	46.5, 53.5	53.5
	Shift in C_6H_6	-4	+4	+2	+8.5	+4
IV 	$CDCl_3$	59,65	241	197	53,60	59
	C_6H_6	58.5, 64.5	238.5	192	47,54	68
	Shift in C_6H_6	+0.5	+2.5	+5	+6	-9
V 			C_{18}-H		$C_{17}\alpha$-CH_3,$C_{17}\beta$-CH_3	
	$CDCl_3$		54		68,69	
	C_6H_6		44		71,66	
	Shift in C_6H_6		+10		-3, +3	
VI 	$CDCl_3$		69			
	C_6H_6		64			
	Shift in C_6H_6		+5			

All spectra given in this paper were taken on a Varian A-60 spectrometer in 10% solution in the solvents given. I, from α-santonin, O.Kovacs, V, Herout, M. Horak and F. Sorm, Coll. Czech. Chem. Comm. 21, 216 (1956); III, ether from γ-tetrahydro-α-santonin, G.D. Joshi, M.V. Kadival, S.N. Kulkarni and S.C.Bhattacharya, Tetrahedron 23, 1985 (1967); II, ether prepared in seven steps from β-santonin, like I or III, b.p. 155°/2.5 mm (bath temp.) $(\alpha)_D$ +49.6° IV; ether prepared from 6-epi-α-santonin like the others, b.p. 110-115°/2 mm (bath temp.) $(\alpha)_D$ -32.5°. V, a 16-oxasteroid, R.W.Kierstead and A.Faroane, J. Org. Chem. 32, 704 (1967); VI, G.R.Pettit and T.R. Kasturi, ibid. 26, 4557 (1961).

protons lying not far from the plane suffer relatively small positive (e.g. C_6 and C_{12}-H and C_{10}-CH_3 in I, II and III) or negative shifts ($C_4\beta$-CH_3 in III and C_{10}-CH_3 in IV) according to their location at the back or front of the reference plane. In V, one of the methyl groups at C_{17} lie slightly in front, and the other slightly behind the plane, showing thereby small downfield and upfield shifts respectively, while the C_{18}-protons being definitely behind the plane show larger upfield shift. Since the five membered ether ring can assume slightly different conformations, the plane of the three atoms including the ether oxygen is not very definite and this indefiniteness may extend to the exact angularity of the reference plane with respect to the ring and hence to the relative position of the adjacent groups. However, the above empirical rule qualitatively holds good in general, in all the cases cited. Besides, the Δ values given recently by Williams and Bhacca (5) for the different protons in the D,E,F rings of nine sapogenins can mostly be accounted for, on the above empirical rule when the two reference planes for the five membered and six membered ether rings in the sapogenins are also taken into consideration.

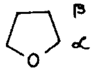
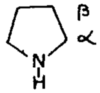
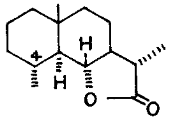
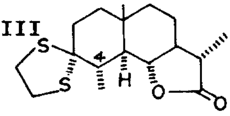
At this stage, it is attractive to consider that the lone pair of electrons on the oxygen atom complexing with the solvent benzene, and holding it in a specific orientation is responsible for the shielding and deshielding effect on protons differently located in the ring. If that is so, other hetero atoms having lone pair of electrons should also be able to induce similar solvent shifts. That this indeed is the case, is shown by the examples in Table 2.

The straight chain compounds being oriented zig-zag, shows significant shifts only for the protons on the α-carbon atom. But in the cyclic ones, protons behind the plane show large upfield shifts and in front, large downfield shifts, whose magnitude, however, appears to vary in O, N and S. Models show that in XIII, the $C_4\alpha$-CH_3 lies in front of the reference plane of the nearer S-atom and it suffers a relative deshielding of 11 c/s compared to XII.

These generalizations could be of considerable use in the structural and stereochemical work on heterocyclic compounds.

Acknowledgement - We are indebted to Drs.R.W. Kierstead for a sample of V, to Prof. G.R. Pettit, for a sample of VI and to Prof.W. Cocker for a generous sample of β-santonin and to Dr.K.N. Iyer for some of the spectra.

TABLE 2

Compound	Chemical shift in cps at 60 Mc of the					
	in $CDCl_3$		in benzene		Solvent shift in benzene of the	
	α-H	β-H	α-H	β-H	α-H	β-H
VII $(\overset{\beta}{CH_3}-\overset{\alpha}{CH_2})_2O$	208	71	200	66	+8	+5
VIII 	224	110	215	89	+9	+21
IX $(\overset{\beta}{CH_3}-\overset{\alpha}{CH_2})_3N$	155	63	147	60	+8	+3
X 	175	103	162	87	+13	+16
XI $\overset{\beta}{CH_3}-\overset{\alpha}{CH_2}-S-H$	154	79	130	59	+24	+20
	C_4-CH_3		C_4-CH_3		C_4-CH_3	
XII 	59,66		65,72		-6	
XIII 	76,83		93,100		-17	

XII & XIII, from α-santonin, vide refce.(3,6).

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