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STEREOCHEMICAL STUDIES BY PMR SPECTROSCOPY*+ - III**, AXIAL AND EQUATORIAL ACIDS

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THE principal physical methods available at present to find the configuration of a carboxylic acid are (i) by determining the pK value of the acid (1), and (ii) by finding the C-O-stretching frequency of its methyl ester in the IR spectrum (2). The former requires special instruments and experience in the technique and the latter is limited to compounds in which acetates and other interfering esters are absent, and the carboxylic acid was part of a gem-dimethyl group. We are presenting an alternate method for the same, by using the shielding and deshielding effect of the carboxyl group in PMR spectroscopy.

It has been observed in a few cases (3) that a carboxylic acid or its ester shields a methyl group which has a 1,3-diaxial relation with it. We argued that like other electronegative groups as, hydroxyl, halogens etc.(4), the carboxylic acid anion should be able to deshield the same methyl group. Accordingly, when the PMR spectra of the sodium salts of podocarpic acid (V) and abietic acid (VIII) were determined in pyridine solution, it was found that the

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former anion deshields its C_{10}-methyl group by 23 cps when compared to the same C_{10}-methyl signal in podocarpic acid in carbon tetrachloride solution, whereas the latter anion under the same condition showed no such significant effect. But since the sodium salts of many other acids were found insoluble in pyridine, it was thought that the acid itself in pyridine solution should exist largely as the anion and hence should exert the same effect. Spectra of the acids in pyridine solution showed that this assumption was correct although the extent of deshielding was somewhat reduced. To avoid solvent effects, spectra of the acids and their methyl esters were both taken in pyridine solution, and in addition, spectra of the esters were also recorded in chloroform and benzene solutions. The signals of the C_4 and C_{10}-methyl groups found, in ten different axial and equatorial acids in pyridine solution, and in their esters in pyridine, chloroform and benzene solutions are given in Tables 1 to 3.

In the case of the axial acids (I, III, V and VII) it is found that the C_{10}-Me which has a 1,3-diaxial relation with the C_4-carboxyl group suffers a deshielding of 17 cps when the ester is changed to the acid anion (columns e and g). Under the same conditions, the equatorial acids (II, IV, VI and VIII) which has no such relation, shows only a deshielding of ~ 4 cps, thus leaving a net deshielding effect of ~ 13 cps for the axial ester. Comparison of the spectra of otherwise equivalent pairs as I and II or III and IV, or V and VI show that the C_{10}-methyl group is shielded by ~ 12 cps by the axial carboxylic ester in chloroform solution (column a) and about 6 cps in pyridine solution (column e). Hence, that in pyridine solution the carboxylic acid anion apparently moves this methyl signal downfield by ~ 17 cps would mean, that the actual deshielding caused by the anion on the C_{10}-methyl is ~ 7 cps (13-6), from its normal position in pyridine. Thus the advantage of the present method over the simple shielding effect

TABLE I

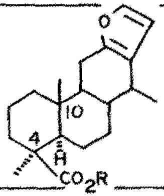
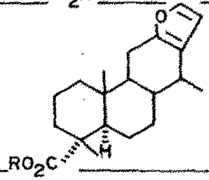
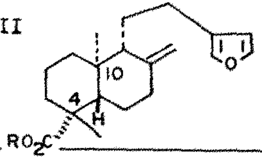
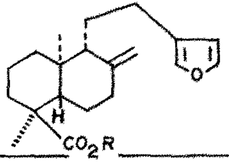
Compound			Chemical shifts observed with the							
			methyl ester in						acid in pyridine	
			Chloroform		benzene		pyridine			
			a C_{10}-Me	b C_4-Me	c C_{10}-Me	d C_4-Me	e C_{10}-Me	f C_4-Me	g C_{10}-Me	h C_4-Me
I		A	43	73	39.5	68	42	71	58.5	83
II		E	57	73.5	48	75.5	48	75.5	53	85.5
III		A	30.5	70	38	64.5	37	70	54	80
IV		E	44	69.5	41	73.5	42.5	73	46	82

TABLE 2

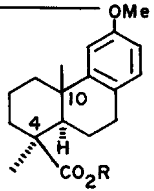
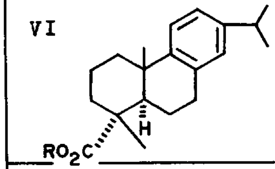
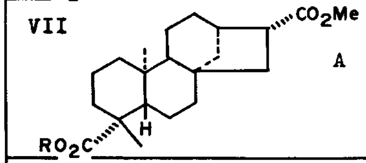
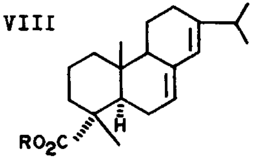
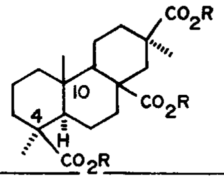
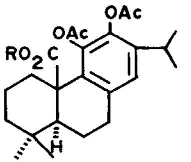
Compound			Chemical shifts observed with the							
			methyl ester in						acid in pyridine	
			chloroform		benzene		pyridine			
			a C_{10}-Me	b C_4-Me	c C_{10}-Me	d C_4-Me	e C_{10}-Me	f C_4-Me	g C_{10}-Me	h C_4-Me
V		A	62.5	77	66	68.5	66	74	83	84.5
VI		E	72.5	76.5	67.5	78.5	71	79.5	74.5	89.5
VII		A	48	70	49	66	49.5	69	66	80
VIII		E	50	75	49.5	80.5	50	80.5	54	89

TABLE 3

Compound		Chemical shifts observed with the							
		methyl ester in						acid in pyridine	
		chloroform		benzene		pyridine			
		a C_{10}-Me	b C_4-Me	c C_{10}-Me	d C_4-Me	e C_{10}-Me	f C_4-Me	g C_{10}-Me	h C_4-Me
IX 	A	31	65.5,69 (C_4,C_{13})	47	64,67 (C_4,C_{13})	45	68,69 (C_4,C_{13})	78	80,82 (C_4,C_{13})
X 	A	45 (4β)	58 (4α)	47 (4β)	53.5 (4α)	46.5 (4β)	56 (4α)	65.5 (4β)	58.5 (4α)

PMR spectra were taken on a Varian A-60 spectrometer in 10% solution in the solvents given. The signals are recorded in cps from tetramethylsilane as zero.

'A' indicates axial and 'E' equatorial carboxyl group.

I, vouacapenic acid, F.E.King, D.H.Godson and T.J.King, J. Chem.Soc. 1117 (1955); II, vinhaticoic acid, F.E.King, T.J.King and J.M.Uprichard, J. Chem. Soc. 3428 (1958); III, daniellic acid, J. Haeuser, R.Lombard, F. Lederer and G. Ourisson, Tetrahedron 12, 205 (1961); IV, polyalthic acid, K.W. Gopinath, T.R.Govindachari, P.C.Parthasarathy and N.Viswanathan, Helv. Chim. Acta. 44, 1040 (1961); V, podocarpic acid; VI, dehydroabietic acid; VII, an acid related to kaurene, reference (3)b; VIII, abietic acid; IX, a monogynol derivative, reference (3)a; X, salvin, accompanying communication.

The solvent effects observed in columns c and d, compared to a and b in the Tables would be vitiated by the presence of ketone or other unsaturation in the ring.

observed before (3) is that this normal position is not required to be found by reducing the carboxylic acid to a methyl group or by comparing it with an equivalent compound which has no axial carboxyl group, to ascertain whether the carboxyl group actually shields a methyl group (compare e.g. VII and VIII, in column a or e and e to g).

There is no direct physical nor simple chemical method at present, to find whether a carbon bearing a carboxyl group also bears a methyl group on it. In the PMR spectra in $CDCl_3$, this methyl group is deshielded by ~ 20 cps when compared to the compound in which the carboxyl group is reduced to a methyl group (3). But this can be brought about by the paramagnetic anisotropy of a carbonyl group as well [e.g. in 1-keto cholestane, the C_{10}-methyl is deshielded by 21 cps (5) when compared to its signal in cholestane]. Conjugated double bond or other adjacent electronegative groups can also effect such deshielding. We have now found a direct method to find the presence of this methyl group. If the spectra of the acid and its ester are taken in pyridine solution, one finds that this methyl group undergoes a uniform downfield shift of ~ 10 cps in the former due to the polar effect of the anion (compare columns f and h).

The Tables also reveal a simple method to find the conformation of this methyl group. In the axial esters (I, III, V and VII), where the C_4 methyl group is equatorial, we find a consistent shielding of its signal by ~ 5 cps when we change the solvent from chloroform to benzene (columns b and d), whereas in the equatorial esters (II, IV, VI and VIII), where the C_4-Me is axial, it is a similar deshielding that is experienced. Interestingly, this effect is the opposite of what has been observed with respect to a methyl adjacent to a ketone (6).

Thus, by the present methods one can find whether a carbon bearing a carboxyl group also holds a methyl group on it, and if so, what the conformation of this methyl group is. From this, the conformation of the carboxyl can be readily deduced, and if the carboxyl group is axial and at C_4, we can find whether the C_{10} methyl group is in a 1,3-diaxial relation with it. If it is so, then the A/B rings are <u>trans</u>, and if not they are <u>cis</u>.

That these are applicable to carboxyl groups in other positions also, is shown by compounds (IX) and (X). In (X), it is interesting to find that though the methyl groups at C_4 are not attached to the carbon bearing the carboxyl, but are only under its influence, still they follow the same type of shielding and deshielding effects (in chloroform and benzene) according to whether the methyl is equatorial or axial. The high deshielding of 33 cps for the C_{10}-Me, while going from the ester to the acid in pyridine in (IX), which has two carboxylic acid groups in eclipsing positions with the C_{10}-Me, shows that the effect is additive. The Tables also show that while changing the solvent from chloroform to benzene or pyridine, the signal of the C_{10}-Me appears to move downfield with axial esters (except I, which will be dealt with in the full paper) and upfield with the equatorial esters, with the result that the shielding effect is considerably reduced in these solvents (Compare III and IV, or V and VI in column a, and c and e). This should probably be related either to the change of orientation (or increased polarization) of the carboxyl group with change of solvent, or the orientation of the aromatic solvent molecules on the carboxyl group.

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