^{19}F Nuclear Magnetic Resonance Studies of Aromatic Compounds. Part V.† Conformational Preferences of Side Chains in *ortho*-Substituted *para*-Fluoro-acetophenones, -α-methylstyrenes, and -αα-dimethylbenzyl Alcohols

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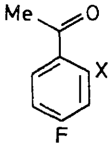
The shielding of *para*-fluorine nuclei in the series of acetophenones and α-methylstyrenes named in the title is used to estimate the interplanar angle between the side chain and the ring in the preferred conformations. In the series of dimethylbenzyl alcohols, an analogous torsion angle (between the C–OH bond and the aromatic ring) is defined and estimated. No information is obtainable from the ^{19}F n.m.r. studies about the cisoid or transoid relationship between the side chain and *ortho*-substituents, since the estimated angles may correspond to either situation. The method of analysis utilises CNDO/2 MO calculations of the way in which charge-density distribution varies with the side chain conformation in a representative member of each series.

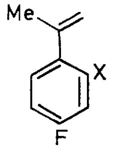
The effect of temperature variation, in the range −40 to 140°, upon the ^{19}F spectra of the series of 2-substituted 4-fluoroacetophenones is studied. The averaging about the zero-point energy of the barrier appears to be temperature-dependent; consequently no information can be obtained about the height of the barrier or the energy differences between conformations.

STERIC effects in conjugated systems have long been the subject of study by many workers using a variety of physical techniques.[1,2] In systems such as acetophenone or α-methylstyrene, the formal single bond betwen the aromatic ring and the side chain has appreciable double-bond character owing to delocalisation of π-electrons over the side chain and ring carbon atoms. There is thus a fairly high barrier to rotation about this bond, which is influenced by the presence of substituents in the *ortho*-positions of the aromatic ring; these substituents also cause the π-conjugation between the side chain and ring to diminish, by making coplanar conformations less available.

In principle, any property of the molecule which is dependent upon the degree of conjugation between the side chain and the aromatic π-system may be used to investigate this phenomenon; studies have been made using dipole moments,[3] u.v. absorption spectroscopy,[4] and ^{13}C and ^{1}H n.m.r. spectroscopy.[5,6] It has been suggested that in a series of *para*-substituted fluorobenzenes the variation in shielding of the fluorine atom which accompanies substituent change is largely caused by variation in the π-electron density on the carbon atom to which the fluorine is bonded, although other effects may also play a part.[7,8] In a series of 2-substituted 4-fluorinated aromatic compounds which have a 1-substituent, X, capable of conformational motion, the 'substituent chemical shift' (SCS) of the group X should therefore be related to the changes resulting from steric interactions, and may provide a method of studying such phenomena. It was decided to prepare a series of *ortho*-substituted *para*-fluoroacetophenones (I) and *ortho*-substituted *para*-fluoro-α-methylstyrenes (II) in order to explore this possibility; a series of *ortho*-substituted *para*-fluoro-αα-dimethylbenzyl alcohols (III) was also prepared, in order to examine the behaviour of a non-π-conjugated side chain in similar circumstances.



(I)



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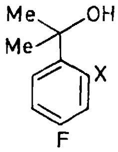

(III)

EXPERIMENTAL

meta-Substituted fluorobenzenes were obtained from Koch–Light Ltd., as was *p*-fluoroacetophenone; these materials were used without further purification.

2′,4′-*Difluoroacetophenone*.—This was prepared by refluxing *m*-difluorobenzene (5·7 g, 0·05 mol), while stirring with anhydrous aluminium chloride (15 g, 0·15 mol) in dry carbon disulphide (20 ml); acetic anhydride (4·1 g, 0·04 mol) was added dropwise during 30 min and stirring was continued for 24 h. The mixture was added to ice and extracted with ether (4 × 15 ml). The extracts were washed with sodium hydroxide solution (2N), dried (Na_2SO_4), and evaporated. The resultant liquid was distilled at reduced pressure to give 2′,4′-difluoroacetophenone (5·14 g, 66%), b.p. 43—44° at 2 mmHg, n^{21} 1·4870.

2′,4′,6′-Trifluoro-, 2′-chloro-4′-fluoro-, 2′-bromo-4′-fluoro-, 4′-fluoro-2′-iodo-, and 4′-fluoro-2′-methyl-acetophenone were prepared by the same method. Products were separated from their 2′-fluoro-isomers (usually the minor product) by chromatography [alumina–petroleum (b.p. 60—80°)] and identified by comparison with literature data, by microanalysis, and by their spectroscopic properties (u.v., i.r., and n.m.r.). 4′-Fluoro-2′-hydroxyacetophenone was prepared by the method of Blatt[9] and identified by comparison with literature data and by its spectroscopic properties.

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† Part IV, P. J. Mitchell and L. Phillips, preceding paper.

[1] 'Steric Effects in Conjugated Systems,' ed. G. W. Gray, Butterworths, London, 1958.

[2] 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956.

[3] J. W. Smith, ref. 1, p. 141.

[4] E. A. Braude and F. Sondheimer, *J. Chem. Soc.*, 1955, 3754.

[5] K. S. Dhami and J. B. Stothers, *Canad. J. Chem.*, 1965, **43**, 479.

[6] G. Montaudi, P. Finnocchiaro, and P. Maravigna, *J. Amer. Chem. Soc.*, 1971, **93**, 4214.

[7] J. W. Emsley and L. Phillips, *Progr. N.M.R. Spectroscopy*, 1971, **7**, 70.

[8] I. R. Ager, L. Phillips, T. J. Tewson, and V. Wray, *J.C.S. Perkin II*, 1972, 1979.

[9] A. H. Blatt, *Org. Reactions*, 1942, **1**, 342.

2′-Ethoxy-4′-fluoroacetophenone.— 4′-Fluoro-2′-hydroxyacetophenone (0·3 g, 0·0019 mol) was treated with diethyl sulphate (0·6 g, 0·003 mol) in aqueous sodium hydroxide (0·1 g in 2 ml). The mixture was heated for 1 h, cooled, and extracted with ether. Evaporation yielded a crude product which was purified by t.l.c. (silica gel; ether) to give 2′-ethoxy-4′-fluoroacetophenone (0·068 g, 23%), which was recrystallised, m.p. 83—84° (from ethanol). U.v., n.m.r., and i.r. spectral properties were consistent with the proposed structure. The 2′-methoxy-analogue was prepared similarly by use of dimethyl sulphate.

p-*Fluoro-αα-dimethylbenzyl Alcohol.*—*p*-Fluoroacetophenone (5·0 g, 0·036 mol) dissolved in anhydrous diethyl ether (50 ml) was added to a dry ethereal solution (100 ml) of methylmagnesium iodide (6·6 g, 0·040 mol). The mixture was refluxed for 2 days and decomposed with aqueous sulphuric acid (2N). The ethereal layer was separated, and the aqueous layer extracted with ether (5 × 75 ml). The combined ethereal solutions were washed twice with water and dried ($MgSO_4$). Evaporation gave the impure alcohol (4·6 g, 83%). Purification was not possible because of the unstable nature of the compound; spectroscopic properties were consistent with the proposed structure but indicated the presence of *p*-fluoro-α-methylstyrene.

2,4-Difluoro-, 2-chloro-4-fluoro-, 2-bromo-4-fluoro-, 2-iodo-4-fluoro- and 4-fluoro-2-methyl-αα-dimethylbenzyl alcohol were similarly prepared from the corresponding acetophenone derivatives.

p-*Fluoro-α-methylstyrene.*— *p*-Fluoro-αα-dimethylbenzyl alcohol (3·0 g, 0·02 mol) was distilled from a mixture of alumina and phosphorus pentoxide. Dehydration occurred quantitatively; the product (2·6 g, 0·009 mol) was identified by its spectroscopic properties and examined without further purification.

2-Chloro-4-fluoro-, 2-bromo-4-fluoro-, 4-fluoro-2-iodo-, and 4-fluoro-2-methyl-α-methylstyrene were prepared from the corresponding αα-dimethylbenzyl alcohols by analogous procedures.

Attempted Preparations of 2,4-*Difluoro-α-methylstyrene.*— 2,4-Difluoro-αα-dimethylbenzyl alcohol distilled unchanged from a mixture of alumina and phosphorus pentoxide. Dehydration of such tertiary alcohols is usually extremely easy, and the result is surprising. An alternative procedure, in which the alcohol was converted into the corresponding tosylate as an intermediate, yielded oligomers of 2,4-difluoro-α-methylstyrene, but no monomer was isolated.

N.m.r. Measurements.—The ^{19}F n.m.r. spectra were recorded with a modified Varian HA-100 spectrometer operating at 94·1 MHz. The instrument was operated in the extended field-frequency locked mode using full phase correction.[10] Spectra were recorded on dilute solutions in inert solvents; a variety of concentrations was used and the measurements were extrapolated to infinite dilution. Chemical shifts were measured with reference to an internal standard of C_6F_6 by the frequency difference technique using a Beckmann frequency counter. Some variable-temperature experiments were carried out with a Varian XL 100-12 spectrometer.

Temperature Variation.—It was decided to examine the effects of temperature variation upon the ^{19}F SCS of the acetyl group in the series of *ortho*-substituted *para*-fluoroacetophenones, but it was not possible to find a suitable wide-temperature-range solvent for all the molecules. For low temperatures (35 to −40°) carbon disulphide was used, and for high temperatures (35—140°) *o*-dichlorobenzene.

TABLE 1

Effects of temperature upon the ^{19}F chemical shifts (p.p.m. to low field of internal C_6F_6) and ^{19}F SCS (acetyl) in (a) 2′-bromo-4′-fluoroacetophenone and (b) *m*-bromofluorobenzene

Solvent	Temp. (°C)	^{19}F Chemical shift (a)	^{19}F Chemical shift (b)	SCS	SCS (corr.)
CS_2	−40	55·749	52·656	3·093	3·093
	−25	55·685	52·656	3·029	3·029
	−10	55·600	52·656	2·944	2·944
	5	55·515	52·656	2·859	2·859
	20	55·462	52·656	2·806	2·806
	35	55·356	52·656	2·700	2·700
o-$Cl_2C_6H_4$	35	55·099	51·849	3·250	2·700
	55	55·015	51·870	3·145	2·595
	70	54·973	51·891	3·082	2·532
	85	54·930	51·923	3·007	2·457
	100	54·888	51·934	2·954	2·404
	115	54·814	51·955	2·859	2·309

Solvent effects play an important part in the shielding of ^{19}F nuclei [11] and it is necessary to correct for the effects of changing the medium. In each of the solvents a parallel investigation was made of the effects of temperature variation upon the ^{19}F chemical shifts of the *ortho*-substituted *para*-fluoroacetophenones and the corresponding *meta*-substituted fluorobenzenes. The ^{19}F SCS due to the acetyl group at any one temperature was obtained as the difference between the two chemical shifts at that temperature. A plot of the SCS against temperature is

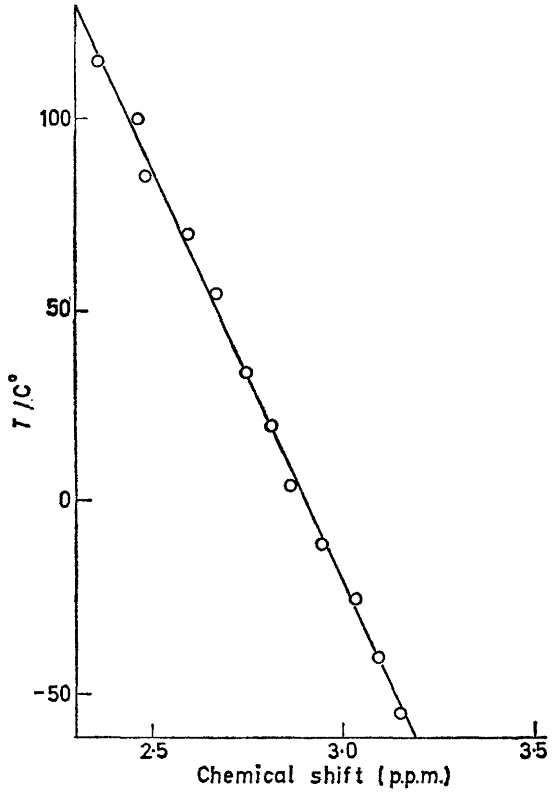

FIGURE 1 Temperature dependence of the corrected ^{19}F chemical shift for 2′-bromo-4′-fluoroacetophenone

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[10] P. N. Jenkins and L. Phillips, *J. Phys.* (*E*), 1971, 530.

[11] R. J. Abraham, D. F. Wileman, and G. R. Bedford, *J.C.S. Perkin II*, 1973, 1027.

sensibly linear *and of the same slope* for solutions in each of the two solvents; a ' solvent correction ' may be made to the data obtained for *o*-dichlorobenzene solutions by adding the difference between the two SCS values at the common temperature of 35 °C. This brings all points onto a common linear plot.

Table 1 shows a typical set of data, obtained for 2′-bromo-4′-fluoroacetophenone and *m*-bromofluorobenzene. Figure 1 shows the plot of ^{19}F SCS due to the acetyl group in this compound, as a function of temperature after correction for the solvent difference.

An independent study of the effect of temperature variation upon the chemical shift of ^{19}F nuclei in fluorobenzene and hexafluorobenzene showed that they have the same temperature coefficient. The experiment was carried out by use of a Varian XL 100-12 instrument with reference to the frequency of an external proton lock whose temperature remained constant; this confirms that in the present study we have indeed eliminated the *intrinsic* effects of temperature upon ^{19}F shielding, and are studying real effects upon the properties of the acetyl side chain.

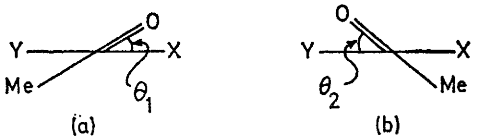


FIGURE 2 Conformations of the acetyl side chain in 2′,6′-disubstituted acetophenones

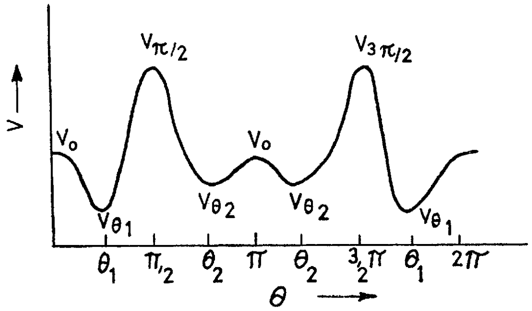


FIGURE 3 Potential energy profile for side-chain rotation in acetophenones

RESULTS AND DISCUSSION

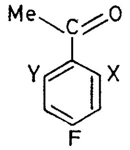
ortho-*Substituted* para-*Fluoroacetophenones*.—It is usually assumed that the potential energy profile for internal rotation of the acetyl side chain in acetophenone and its *ortho*-substituted derivatives possesses two minima which correspond to conformations [5,6,12] shown in Figure 2, in which the side chain is projected onto the plane of the benzene ring and X and Y are the *ortho*-substituents. The barrier is assumed to have the form shown in Figure 3. If the difference between the two energy minima (occurring at θ_1 and θ_2) is greater than 1·5—2·0 kcal mol^{-1}, then almost all the molecules (92—98%) will be in the lower energy conformation at or near θ_1. Obviously there will be a Boltzmann distribution of conformations around θ_1, and any estimate of the ' interplanar angle ' [as first defined by Braude and his co-workers [13] and widely discussed by others (*e.g.* refs. 3—6)] will be a value averaged around this minima. The averaging depends upon the shape of the potential energy profile in this region, and hence to a considerable extent upon the value of ($V_{\pi/2} - V_{\theta_1}$), *i.e.* the energy difference between this minimum and the maximum of the curve; the larger this difference the better defined will be the interplanar angle.

Some idea of the energy differences involved may be obtained from some recent *ab initio* MO calculations of Pople *et al.*; they suggest that for acetophenone itself (X = Y = H), $V_{\pi/2} - V_0 = 4{\cdot}39$ kcal mol^{-1}. Since V_θ is smaller than V_0 this may be taken as a minimum value for $V_{\pi/2} - V_\theta$. Because of the relatively small magnitude of this barrier, the potential energy profile in the region of θ_1 will be rather shallow and extensive averaging will mean that it is rather ill-defined. It is with these limitations in mind that we proceed with the estimation of the ' interplanar angle '; the same reservations should, of course, be applied to all previous studies of this problem and related work where the barrier is small.

In principle, it is possible to obtain information about the difference in energy between the two conformations from a study of the variation with temperature of an averaged n.m.r. parameter; [14] it was decided to perform such an experiment, using the ^{19}F SCS of the acetyl group in the series of *ortho*-substituted *para*-fluoroacetophenones. However, it was not possible to ' freeze out ' the separate conformations before crystallisation from solution occurred (at *ca.* —40 °C) and the necessary parameters for evaluating ΔE are not available. Over the temperature range employed, the plots of SCS against temperature are essentially linear and Table 2 lists the slopes of these as temperature coefficients.

TABLE 2

Temperature coefficients of the ^{19}F SCS (acetyl) in the acetophenones



X	Y	Temperature coefficient (Hz deg^{-1} at 94·1 MHz)
H	H	0·48 ± 0·03
F	H	0·48 ± 0·06
F	F	0·64 ± 0·05
Cl	H	0·46 ± 0·04
Br	H	0·43 ± 0·04
I	H	0·51 ± 0·08
Me	H	0·64 ± 0·07
OH	H	0·17 ± 0·02
OEt	H	0·57 ± 0·12
OMe	H	0·69 ± 0·02

The data in Table 2 show that the behaviour is far from simple. It was anticipated that the effect of temperature variation would be to change the Boltzmann

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[12] E. S. Waight and R. L. Erskine, ref. 1, p. 73.

[13] E. A. Braude, E. R. H. Jones, H. P. Koch, R. W. Richardson, F. Sondheimer, and J. B. Toogood, *J. Chem. Soc.*, 1949, 1890.

[14] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, ' High Resolution N.M.R. Spectroscopy,' Pergamon, London, 1965, ch. 9.

distribution of molecules between the two conformations [Figure 2(a) and (b)] and hence change the form of the averaged spectrum; obviously if the barrier is symmetrical (X = Y) there can be no conformational preference and there should be no temperature effect. However, when X = Y = H, or X = Y = F, there is a significant temperature variation (0·48 and 0·64 Hz deg^{-1}, respectively); this means that it would not be possible to obtain reliable estimates of the energy difference even if the two conformers were 'frozen out' at a sufficiently low temperature. The effect of temperature variation may be to alter the Boltzmann distribution around the minima in the profile (*i.e.* change the form of the averaging around θ), or perhaps arises from a temperature dependence of the shape of the barrier; it must be concluded that the variation of the relative thermal populations of the two conformations θ_1 and θ_2 plays only a minor part in determining the observed temperature dependence of the SCS. It is conceivable that ^{19}F chemical shifts in aromatic compounds have an intrinsic temperature dependence which is not concerned with the properties of a side chain such as MeC(O); we believe that the referencing procedure used here to determine the SCS at each temperature eliminates this effect (see Table 1 and Figure 1) and the results indicate that the averaging around the potential energy minima varies with temperature, resulting in a temperature variation of the effective interplanar angle of the lower energy conformation. Within these limitations it will be assumed that it is nevertheless valid to discuss the structure of these and the related molecules solely in terms of θ_1.

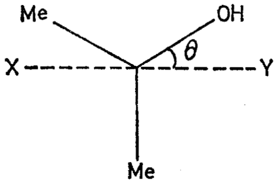

FIGURE 4 Projection of the side chain in αα-dimethylbenzyl alcohols onto the aromatic ring

ortho-Substituted *para*-fluoro-α-methylstyrenes may be discussed in similar terms to the acetophenones, an interplanar angle θ corresponding to the conformation of lowest energy. The series of dimethylbenzyl alcohols is not so simple to describe, but again it is assumed that the molecules exist predominantly in one conformation which is defined in terms of the torsion angle between the C–OH bond and the aromatic ring, shown in Figure 4. In neither of these series was a study made of the effects of temperature variation upon the ^{19}F chemical shift; Table 4 lists the apparent ^{19}F SCS at 35 °C for the side chains in these compounds, together with data for the corresponding acetophenones at −40 and +115 °C.

Calculation of θ.—The three series of compounds were chosen with the object of elucidating a number of different types of substituent effect upon ^{19}F shielding. The MeC(O) side chain is π-conjugated with the aromatic system and, in common with all other side-chains, it can exert a 'π-inductive' or 'orbital penetration' interaction with the aromatic system;[15] the MeC=CH$_2$ group is less polar, but is also π-conjugated and can similarly exert an orbital penetration influence upon the π-system. The Me$_2$C(OH) side chain is not π-conjugated, but it can exert an orbital penetration interaction upon the π-system in the same manner as a t-butyl side chain.[16]

TABLE 3

Values of π-electron density on the *para*-carbon atom of (A) *para*-fluoroacetophenone, (B) *para*-fluoro-α-methylstyrene, and (C) *para*-fluoro-αα-dimethylbenzyl alcohol calculated by using CNDO/2

	π-Electron density		
Angle (θ)	(A)	(B)	(C)
0	0·9510	0·9725	0·9858
10	0·9518	0·9730	
20	0·9541	0·9745	0·9844
30	0·9576	0·9767	0·9828
40	0·9619	0·9793	0·9807
50	0·9664	0·9822	0·9784
60	0·9706	0·9849	0·9762
70	0·9741	0·9872	0·9744
80	0·9763	0·9887	0·9733
90	0·9771	0·9892	0·9729

In order to investigate the consequences of changing conformational properties of the side chain in these systems, CNDO/2 MO calculations were carried out (using the programme of Pople and Segal [17]) for a variety of dihedral angles; in all cases the molecules were *para*-fluoro-derivatives with no *ortho*-substituent (*i.e.* X = Y = H). The torsion angle was varied from 0 to 90°, since, because of the symmetry of the situation, the behaviour will be the same in each quadrant; standard geometries and bond lengths were used for the basic structures.[18] We focus attention upon the π-electron density at the *para*-carbon atom, for reasons outlined earlier; Figure 5 shows the variation of this with torsion angle for all three model compounds (*para*-fluoroacetophenone, *para*-fluoro-α-methylstyrene, and *para*-fluoro-αα-dimethylbenzyl alcohol). Table 3 lists this parameter for the different situations.

We consider first the series of acetophenones; as the torsion angle increases, the π-electron density upon the *para*-carbon atom also increases from 0·951 at θ = 0° to 0·977 at θ = 90°. A similar calculation on fluorobenzene suggests that the π-electron density upon the analogous carbon atom (*i.e.* that bound to fluorine) is 0·969, and so the acetyl side chain is electron-withdrawing compared with H at a torsion angle of 0° but electron-releasing (or repelling) at θ = 90°. This suggests that as the π-conjugative interaction decreases, the π-inductive interaction (which is repulsive and leads to π-electron build up upon the *para*-carbon atom) increases; this is qualitatively satisfying.

In the case of *para*-fluoro-α-methylstyrene, a similar trend is observed but the group is always electron-

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[15] M. Godfrey and J. N. Murrell, *Proc. Roy. Soc.* (*A*), 1964, 64.

[16] J. N. Murrell, 'The Theory of Electronic Spectra of Organic Molecules,' Methuen, London, 1963, p. 254.

[17] J. A. Pople and G. A. Segal, *J. Chem. Phys.*, 1966, **44**, 3289.

[18] J. A. Pople and D. L. Beveridge, 'Approximate Molecular Orbital Theory,' McGraw-Hill, New York, 1970, p. 111.

repelling compared with H. Thus at θ = 0° the π-electron density is 0·972 (*cf.* 0·969 for H) and at θ = 90° it is 0·989. This build up of electron density as the side chain is taken out of formal conjugation with the ring is surprising, and can best be explained as a consequence of the increasing importance of the π-inductive (or orbital penetration) interaction as the side chain atoms increase their overlap with the aromatic π-system. This phenomenon has been alluded to elsewhere.[19]

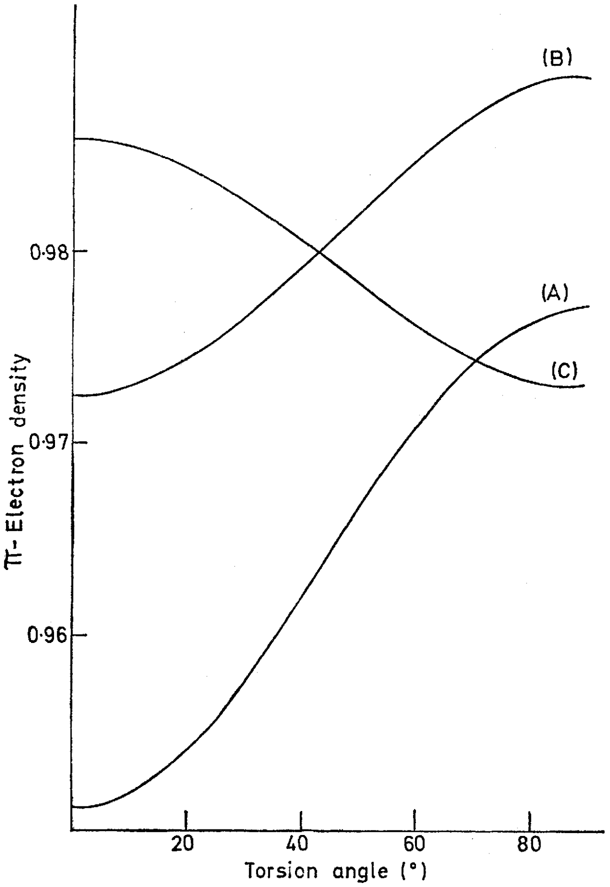

FIGURE 5 Plots of the π-electron density upon the *para*-carbon atom against the torsion angle for (A) *para*-fluoroacetophenone, (B) *para*-fluoro-α-methylstyrene, and (C) *para*-fluoro-αα-dimethylbenzyl alcohol

In the *para*-fluoro-αα-dimethylbenzyl alcohol case, at θ = 0° (*i.e.* the C–OH bond in the plane of the ring) the group is appreciably electron-repelling compared with H (*para*-carbon atom π-density is 0·986, *cf.* 0·969 for C-1 in fluorobenzene); as θ increases it becomes less electron-repelling until at a torsion angle of 90° its effect is comparable to that of the α-methylvinyl side chain at 0° The overall π-electron density change is of the same size as that in the π-conjugative system!

The n.m.r. data reflect these calculations well; thus, as the size of the *ortho*-substituent is increased in the series of acetophenones and α-methylstyrenes the SCS of the acetyl side chain increases in a positive fashion, *i.e.* it becomes more shielding towards the *para*-fluorine nucleus. The case of the alcohol series is more complex, and will be discussed later.

In the series of acetophenones there is one molecule for which the torsion angle is known with fair certainty, namely 2′-hydroxy-4′-fluoroacetophenone. The ^{19}F n.m.r. spectrum of this molecule shows unusual long-range coupling to the proton of the hydroxy-function, which we have been unable to observe in any other compound in which there is a similar disposition of OH and F. This five-bond coupling (*J* 2 Hz) we believe arises from the coplanarity of the coupling pathway which occurs as a result of the well established hydrogen bonding between an *ortho*-hydroxy-function and a β-carbonyl group when present in an aromatic ring.[20] We may therefore take this molecule as having a torsion angle of 0°, a suggestion which is reinforced by the small temperature coefficient of the SCS of the acetyl group in this case (see Table 2), and the fact that the SCS has its largest negative value (*i.e.* the group is most highly deshielding). At −40 °C the SCS is −1118 Hz, and according to the CNDO/2 calculations this must correspond to a decrease of the π-electron density upon the adjacent carbon atom of 0·018*e* compared with C-1 in fluorobenzene. This implies that the proportionality constant relating π-electron density to observed ^{19}F shift is 62,140 Hz (661·5 p.p.m.) per electron. It is now possible to use the SCS values listed in Table 4 for the acetyl side chain in the various derivatives to estimate the corresponding π-electron density and to interpolate these figures on the appropriate curve in Figure 4 and obtain the torsion angles (θ). These angles are listed in Table 5, and show a reasonable trend; θ for the unsubstituted molecule is 33°; *cf.* the literature value (obtained by u.v. spectroscopy) of 32° for the similar situation in α-methylstyrene.[21] The value of θ for the molecules in which the halogens are *ortho*-substituents increases in the expected order, although the value for the *ortho*-fluorinated

TABLE 4

^{19}F SCS due to the side chains in *ortho*-substituted *para*-fluoro-acetophenones, -αα-dimethylbenzyl alcohols, and -α-methylstyrenes (Hz at 94·1 MHz, positive values to high field)

ortho-Substituent	Acetophenones −40° ‡	Acetophenones 115° §	Alcohols †	Styrenes †
H	−649	−601	+383	+295
F	−699	−624	+316	
Cl	−389	−316	+407	+305
Br	−291	−223	+446	+337
I	−260	−177	+513	+400
Me	−587	−488	+336	+247
OH	−1118	−1093		
OEt	−694	−600		
OMe	−706	−600		

‡ Solutions in CS_2. † Solutions in CCl_4. § Solutions in *o*-$Cl_2C_6H_4$, corrected to CS_2.

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[19] G. K. Hamer, I. R. Peat, and W. F. Reynolds, *Canad. J. Chem.*, 1973, **51**, 915.

[20] A. D. Cross, ' Introduction to Practical Infra red Spectroscopy,' Butterworths, London, 1964, p. 68.

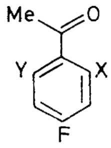
[21] H. Suzuki, *Bull. Chem. Soc. Japan*, 1960, **33**, 613, 619.

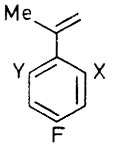
material (31°) is very similar to that obtained for the two *ortho*-oxygenated materials (*ortho*-substituent OMe or OEt) and smaller than that obtained for the unsubstituted molecule.

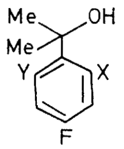
If the conformations are such that the side chain is oriented towards the *ortho*-substituent this phenomenon may well be an example of that reported elsewhere [22,23] which occurs in 1,2-disubstituted ethanes when two small and highly polar substituents (in this case the carbonyl oxygen and the ring fluorine or oxygen) seem to hold a surprising degree of attraction for each other.

TABLE 5

Torsion angles (°) between side chains and aromatic rings calculated by use of Figure 5 and the *para*-fluorine chemical shifts







X	Y	(−40 °C)	(35 °C)	(35 °C) [a]
H	H	33	32	40
F	H	31		48·5
Cl	H	42·5	33	36
Br	H	45	36	30
I	H	47	45	17
Me	H	35	28	45·5
OH	H	0		
OEt	H	31		
OMe	H	31		
F	F	40		

[a] For the definition of these torsion angles see Figure 7.

The α-methylstyrene series poses a greater problem, for there is no member of the series whose torsion angle can be estimated with the same degree of certainty as that of the *ortho*-hydroxyacetophenone. As already mentioned, for the unsubstituted molecule a value of θ of 32° has been obtained by a u.v. spectroscopic technique, and it is necessary to use this as the starting point. According to Figure 4, a value of $\theta = 32°$ corresponds to a *para*-carbon atom π-electron density of 0·977*e*, *i.e.* 0·008 more than on C-1 in fluorobenzene. The observed side-chain SCS for *para*-fluoro-α-methylstyrene is +295 Hz, which corresponds to a proportionality constant of 36,875 Hz per electron (= 392·2 p.p.m. per electron), *i.e.* about half that obtained for the acetophenone series. Use of this figure leads to the values for θ quoted in Table 5, which show a reasonable trend, with the angle increasing in the expected order for *ortho*-halogen substituents. For an *ortho*-CH_3 group, θ is smaller than in the unsubstituted molecule but this sort of behaviour is not unprecedented.[24] If the proportionality constant derived for the series of acetophenones is used, the values of θ for the α-methylstyrenes appear to be unreasonably small although the correct trend is again observed.

For the series of dimethylbenzyl alcohols, there is no previous study available and no possibility of obtaining an independent assessment of θ for one member of the family. If the proportionality constant derived for the α-methylstyrene series is used, however, some apparently meaningful results are obtained. Use of the appropriate curve in Figure 5 to deduce the torsion angles leads to the values listed in Table 5. At first sight they look peculiar—the angle decreases in the order F > Me > H > Cl > Br > I; however, the calculational procedure does not differentiate between the first and fourth quadrants, *i.e.* the angle θ may correspond to either of two situations shown in Figure 6.

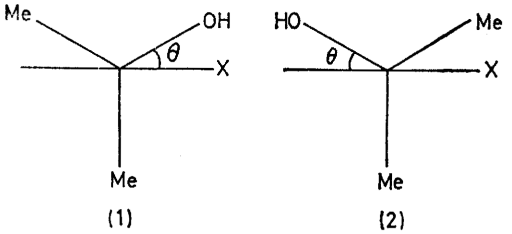


FIGURE 6 Projection of the side chain onto the aromtic ring, showing the two possible orientations

The results are much more sensible if it is taken that conformation (1) of Figure 6 is adopted by those molecules in which the *ortho*-substituent is H, Me, or F and conformation (2) is adopted for Cl, Br, or I. This then predicts that the effects of the group X upon the conformation of the side chain involve a major interaction with the OH function rather than the Me groups, and that this *increases* in the order H < Me < F < Cl < Br < I, which is reasonable. The situation is illustrated in Figure 7. Again we observe that there appears to be an ' attraction ' between an oxygen function and a fluorine atom, although this time a hydrogen bond may be involved. There is no ^1H n.m.r. or i.r. spectroscopic evidence to support this suggestion, but the remarkable thermal stability of the 2,4-difluoro-derivative compared with all other members of the series (see Experimental section) may be indicative of such an interaction.

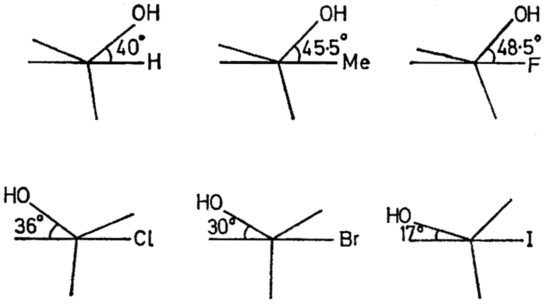


FIGURE 7 Side chain conformations for the *ortho*-substituted *para*-fluoro-αα-dimethylbenzyl alcohols

We have carried out CNDO/2 MO calculations upon this molecule in an attempt to estimate the torsion angle in the minimum energy conformation. Again, standard

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[22] R. J. Abraham and R. H. Kemp, *J. Chem. Soc.* (*B*), 1971, 1240.

[23] L. Phillips and V. Wray, *J.C.S. Chem. Comm.*, 1973, 90.

[24] E. L. Eliel, *J. Chem. Educ.*, 1960, **37**, 126.

geometries were used and the total energy was evaluated as a function of θ for two situations: (i) the OH bond pointing towards the *ortho*-F substituent and (ii) the OH bond pointing away from it. The results show a rather flat potential energy minimum at $\theta = 30$—$50°$ (our empirical calculation suggests $\theta = 48{\cdot}5°$, which is in satisfactory agreement), with the ' OH pointing to F ' conformation (*i.e.* the hydrogen-bonding situation) being more stable than the alternative by about 2·5 kcal mol^{-1}.

In summary, it appears that ^{19}F n.m.r. spectroscopy together with MO calculations of charge density distribution may be a useful tool for conformational analysis of these systems. They are difficult to analyse in other, more conventional, ways. It is not possible, however, to say whether the side chain, in the case of acetophenones or α-methylstyrenes, is oriented towards or away from a single *ortho*-substituent.

[2/505 *Received, 6th March,* 1972]