

COUPLING BETWEEN RING FLUORINES AND SIDE-CHAIN PROTONS IN THE PROTON MAGNETIC RESONANCE SPECTRA OF AROMATIC POLYFLUORO-COMPOUNDS

J. BURDON

Chemistry Department, The University, Birmingham

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Abstract—The PMR spectra of aromatic polyfluoro-compounds show that protons in side-chains of the type $-\text{XCH}_2$ ($\text{X} = \text{O}, \text{N}, \text{S}, \text{SO}_2, \text{C}=\text{O}$ and Sn) couple ($J \sim 1\text{--}5$ c/s) with the fluorines *ortho* to the side-chain, and only with these fluorines. In general, the magnitude of the coupling increases with increasing electronegativity of the other ring substituents; rationalizations for this effect are advanced.

ALTHOUGH long-range coupling between ring and side-chain protons is not normally detectable in the NMR spectra of aromatic compounds, it can be observed in aromatic polyfluoro-compounds between ring fluorine atoms and side-chain protons. These interactions have been noted briefly in a few cases before¹ but with the great number of aromatic polyfluoro-compounds available² in this Department it has been possible to rationalize some of the features of these couplings.

In general, protons in side-chains of the type $-\text{XCH}_2$ ($\text{X} = \text{O}, \text{N}, \text{S}, \text{SO}_2, \text{C}=\text{O}, \text{Sn}$) couple only with the fluorines *ortho* to the side-chain. For example, the protons in pentafluoroanisole³ (XXXIX) show a triplet ($J = 1\cdot1$ c/s), and those in 2, 3, 4, 5-tetrafluoro-*NN*-dimethyl-6-nitroaniline³ (X), a doublet ($J = 1\cdot8$ c/s).

In our studies² on replacement reactions of aromatic polyfluoro-compounds, we have found this coupling between *ortho* fluorines and side-chains of the type mentioned above very useful³ as it gives a count of the fluorines *ortho* to the side-chain; when there is no *ortho*-fluorine, the side-chain protons show a singlet, when there is one, a doublet, and two a triplet or a doublet of doublets.

No coupling has been observed between these side-chain protons and *para*-fluorines or adjacent trifluoromethyl-groups. Methyl side-chains, however, couple with both these types of groups, as well as with the *ortho*-fluorines. For example, the protons of pentafluorotoluene show¹ a doublet ($J_{\text{para}} = 1\cdot5$ c/s) of triplets ($J_{\text{ortho}} = 2\cdot5$ c/s) and those of 1,2,4-trifluoro-3,5-bistrifluoro-methyltoluene⁴ a very complex pattern in which the methyl protons are clearly coupling to at least one of the trifluoromethyl-groups as well as the *ortho*-fluorine.

RESULTS

Our detailed results are listed in Tables 1–6.

Most of the spectra have been measured in acetone solution and although this may not seem a good choice of solvent in view of possible interactions between it and

¹ A. G. Massey, E. W. Randall and D. Shaw, *Chem. & Ind.* 1244 (1963).

² J. C. Tatlow, *Endeavour* 22, 89 (1962).

³ J. G. Allen, J. Burdon and J. C. Tatlow, *J. Chem. Soc.* in press.

⁴ J. Burdon, J. G. Campbell and R. Stephens, submitted to *J. Chem. Soc.*

the aromatic polyfluoro-compounds it was the only common solvent in which all the solid compounds were soluble. In fact, in the cases where spectra were measured in carbon tetrachloride or on pure liquids as well, the side-chain protons were shifted at most by 0.07 ppm from their position in acetone. Also, dilution of a number of

TABLE 1. DIMETHYLAMINO-COMPOUNDS

Compound no.	Compound (group measured in this type)	δ^a	J^b
I	1,2,4-(NMe ₂) ₃ C ₆ F ₃ ⁷	2.75	B
II	2-NMe ₂ -4-NMe ₂ C ₆ F ₃ NO ₂ ⁸	2.75	1.7 (D)
III	<i>m</i> -NMe ₂ C ₆ F ₄ NMe ₂ ⁷	2.80 ^c	1.8 ^c (T)
IV	<i>p</i> -NMe ₂ C ₆ F ₄ NMe ₂ ^{7,8}	2.81	0.9 (Q)
V	<i>m</i> -NMe ₂ C ₆ F ₄ OMe ⁷	2.82	1.7 (T)
VI	<i>o</i> -NMe ₂ C ₆ F ₄ NMe ₂ ⁷	2.83 ^d	0.9 ^d (D)
VII	<i>p</i> -NMe ₂ C ₆ F ₄ OMe ⁷	2.85	1.7 (T)
VIII	C ₆ F ₄ NMe ₂ ^{7,8}	2.90	1.9 (T)
IX	<i>p</i> -NMe ₂ C ₆ F ₄ H ¹⁴	2.91	2.1 (T)
X	<i>o</i> -NMe ₂ C ₆ F ₄ NO ₂ ⁸	2.97	1.8 (D)
II	2-NMe ₂ -4-NMe ₂ C ₆ F ₃ NO ₂ ⁸	2.97	2.5 (T)
XI	4,5-(CF ₃) ₂ C ₆ F ₃ NMe ₂ ¹⁵	3.07	2.8 (T)
XII	<i>p</i> -NMe ₂ C ₆ F ₄ NO ₂ ⁸	3.11	2.8 (T)

TABLE 2. METHYLAMINO-COMPOUNDS

Compound no.	Compound (group measured in this type)	δ^a	J^b
XIII	<i>p</i> -MeNHC ₆ F ₄ NHMe ¹⁶	2.88	B
XIV	C ₆ F ₄ NHMe ¹⁶	3.02	2.6 ^c (T)
XV	<i>o</i> -MeNHC ₆ F ₄ NO ₂ ⁸	3.02	5.4
		2.71 ^f	6.4 ^f } <i>e</i> (D)
		2.28 ^g	6.3 ^g }
XVI	2-MeNH-4-MeNHC ₆ F ₃ NO ₂ ⁸	3.05	7.0 ^c (D)
XVI	2-MeNH-4-MeNHC ₆ F ₃ NO ₂ ⁸	3.18	3.2 ^c (T)
XVII	<i>p</i> -MeNHC ₆ F ₄ NO ₂ ⁸	3.18	3.0
		2.73 ^f	2.9 ^f } <i>e</i> (T)
		2.24 ^g	2.8 ^g }

compounds from about 2 M to 0.05 M in either acetone or carbon tetrachloride lead to shifts of less than 0.03 ppm. There is very little interaction, therefore, between these solvents and the aromatic polyfluoro-compounds. Benzene and bromobenzene, on the other hand caused very marked upfield shifts of almost 1 ppm from the positions in the other solvents in the two cases tried (Table 2); the coupling constants were affected also. These shielding effects are consistent with charge-transfer complex formation between these solvents and the aromatic polyfluoro-compounds; complexes, presumably of this type, are known⁵ to form between hexafluorobenzene and a number of non-fluorinated aromatic hydrocarbons.

The methyl proton lines of the NHMe-compounds (Table 2) were further split into doublets by coupling with the NH-proton. With some compounds it was not obvious which splitting was due to this interaction and which to the methyl/ring-fluorine coupling. In the unambiguous cases, the methyl/NH-coupling lies between

⁵ C. R. Patrick and G. S. Prosser, *Nature, Lond.* **187**, 1021 (1960).

5.2 and 5.6 c/s, and in the ambiguous cases the coupling falling in this range has been attributed to the methyl/NH-interaction and the remaining one to the methyl/ring-fluorine coupling.

The symmetric compounds 2,3,5,6-tetrafluoro-*p*-xylene⁶, 2,3,5,6-tetrafluoro-NNN'-tetramethyl-1,4-phenylenediamine^{7,8} (IV), and 1,2,4,5-tetrafluoro-3,6-dimethoxy-benzene⁹ (XXXV) showed quintets for their proton spectra. This does

TABLE 3. METHYLSULPHONYL-COMPOUNDS

Compound no.	Compound (group measured in this type)	δ^a	J^b
XVIII	<i>p</i> -MeSO ₂ C ₆ F ₄ OMe ¹⁷	3.30	0.7 (T)
XIX	C ₆ F ₅ SO ₂ Me ¹⁸	3.34	0.7 (T)
XX	<i>p</i> -MeSO ₂ C ₆ F ₄ H ¹⁸	3.35	0.8 (T)
XXI	3,6-(CF ₃) ₂ C ₆ F ₂ SO ₂ Me ¹⁸	3.45	1.7 (D)
XXII	4,5-(CF ₃) ₂ C ₆ F ₂ SO ₂ Me ¹⁸	3.47	0.9 (D)

TABLE 4. METHYLTHIO-COMPOUNDS

Compound no.	Compound (group measured in this type)	δ^a	J^b
XXIII	4,6-(OMe) ₂ C ₆ F ₂ SMe ¹⁹	2.37	0.9 (D)
XXIV	<i>p</i> -MeSC ₆ F ₄ OMe ¹⁷	2.41	0.6 (T)
XXV	2,6-(CF ₃) ₂ C ₆ F ₂ SMe ⁴	2.43 ^c	S ^c
XXVI	C ₆ F ₅ SMe ¹⁸	2.46	0.7 (T)
XXVII	<i>p</i> -MeSC ₆ F ₄ H ¹⁸	2.54	0.9 (T)
XXVIII	4,6-(CF ₃) ₂ C ₆ F ₂ SMe ⁴	2.55 ^c	2.1 ^c (T)
XXIX	4,5-(CF ₃) ₂ C ₆ F ₂ SMe ¹⁸	2.66	1.8 1.2 (DD)

not necessarily mean that there is coupling between the methyl protons and the *meta*-fluorines. Calculations show¹⁰ that in A₃XX'X''X'''A' systems, J_{AX'} can be zero and the A-spectrum still show a quintet with splitting J_{AX/2}. It is suggested that this is the case here; also, doubling of the observed splitting for compounds (IV and XXXV) would fit them more reasonably into the general pattern of coupling constants. The apparent *meta*-coupling does not clearly occur with any of the other compounds, and it would be very laborious to calculate whether it might.

DISCUSSION

For each type of side-chain, XMe, in YC₆F₄XMe compounds, the chemical shift of the XMe protons depends on the electronegativity of Y in the usual way; the more electronegative Y, the further downfield the proton signals. For example, 2,3,5,6-tetrafluoro-4-methoxynitrobenzene³ (XLVII) absorbs at 4.21 ppm (downfield from tetramethylsilane), pentafluoroanisole⁹ (XXXIX) at 4.08, and 2,4,5,6-tetrafluoro-4-methoxyaniline^{3,8} (XXXI) at 3.86. The more highly substituted (that is substituents other than fluorine) compounds fit into the same pattern. There are a few exceptions

⁶ A. K. Barbour, M. W. Buxton, P. L. Coc, R. Stephens and J. C. Tatlow, *J. Chem. Soc.* 808 (1961).

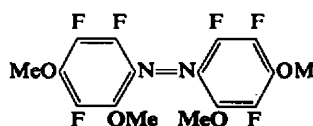
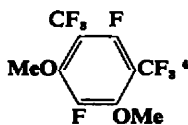
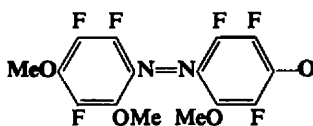
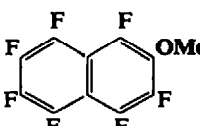
⁷ J. G. Allen, J. Burdon and J. C. Tatlow, submitted to *J. Chem. Soc.*

⁸ L. A. Wall, W. J. Pummer, J. E. Fearn and J. M. Antonucci, *J. Res. Natl. Bur. Standards* 67A, 481 (1963).

⁹ J. A. Godsell, M. Stacey and J. C. Tatlow, *Nature, Lond.* 178, 199 (1956).

¹⁰ F. Ayanadejo and L. F. Thomas, unpublished results.

TABLE 5. METHOXY-COMPOUNDS

Compound no.	Compound (group measured in this type)	δ^a	J ^b
XXX	2-MeO-4-MeOC ₆ F ₃ NH ₂ ^{5,22}	3.78	B
V	<i>m</i> -MeOC ₆ F ₄ NMe ₂ ⁷	3.85	0.9 (T)
XXXI	<i>p</i> -MeOC ₆ F ₄ NH ₂ ^{7,8,22}	3.86	0.6 (T)
XXIII	4-MeO-6-MeOC ₆ F ₂ SMe ¹⁹	3.87	1.2 (T)
VII	<i>p</i> -MeOC ₆ F ₄ NMe ₂ ⁷	3.88	1.0 (T)
XXXII	<i>o</i> -MeOC ₆ F ₄ OMe ¹⁰	3.91	B
XXXIII	<i>m</i> -MeOC ₆ F ₄ NH ₂ ⁷	3.93	0.9 (T)
XXXIV		3.93	0.7 (D)
XXXV	<i>p</i> -MeOC ₆ F ₄ OMe ⁹	3.96	0.5 (Q)
XXXVI	<i>p</i> -MeOC ₆ F ₄ CH ₃ ²⁰	3.98	1.2 (T)
XXIII	4-MeO-6-MeOC ₆ F ₂ SMe ¹⁹	3.99	1.3 (T)
XXXVII	4-MeO-6-MeOC ₆ F ₂ NO ₂ ⁸	3.99	1.7 (D)
XXIV	<i>p</i> -MeOC ₆ F ₄ SMe ¹⁷	4.05	1.5 (T)
XXXVIII	<i>o</i> -MeOC ₆ F ₄ NO ₂ ⁸	4.07	2.1 (D)
XXXIX	C ₆ F ₅ OMe ⁹	4.08 (4.12) ¹	1.1 (T)
XL	<i>o</i> -MeOC ₆ F ₄ Cl ²⁴	—	1.7 (D)
XLI	<i>p</i> -MeOC ₆ F ₄ Cl ²⁴	—	1.4 (T)
XLII	<i>p</i> -MeOC ₆ F ₄ H ²¹	4.10	1.5 (T)
XLIII	<i>p</i> -MeOC ₆ F ₄ CO ₂ H ¹⁴	4.10	1.8 (T)
XXXVII	4-MeO-6-MeOC ₆ F ₂ NO ₂ ⁸	4.11	1.7 (T)
XLIV		4.11	2.9 (D)
XXXIV		4.11	1.6 (T)
XLV		4.12	0.9) 1.9) (DD)
XLVI	4,4'-MeOC ₆ F ₄ N=NC ₆ F ₄ OMe ²²	4.16	1.8 (T)
XVIII	<i>p</i> -MeOC ₆ F ₄ SO ₂ Me ¹⁷	4.16	2.0 (T)
XLVII	<i>p</i> -MeOC ₆ F ₄ NO ₂ ⁸	4.21	2.0 (T)
XLVIII	4,6-(CF ₂) ₂ C ₆ F ₂ OMe ⁴	4.21 ^d	3.4 ^d (D)
XLIX	4,5-(CF ₂) ₂ C ₆ F ₂ OMe ²⁰	4.21	2.4) 1.2) (DD)
L	<i>p</i> -MeOC ₆ F ₄ C ₆ F ₅ ²³	4.22	2.0 (T)

to this rule, all concerned with *ortho*-substituted compounds, and they will be discussed later.

A similar trend is shown by the coupling constants; with a given XMe, the more electronegative Y, the greater the coupling between the XMe protons and the *ortho* fluorines. For the three examples in the previous paragraph, the coupling constants

TABLE 6. MISCELLANEOUS COMPOUNDS

Compound no.	Compound (group measured in this type)	δ^a	J^b
LI	$C_6F_5OCH_2CH_3$ ¹² 	4.21	0.6 (T)
LII		4.39	S
LIII		3.92	S
LIV	$C_6F_5COCH_3$	2.57	1.7 (T)
LV	$(C_6F_5)_2Sn(CH_3)_2$ ¹	—	0.4 (Q) ¹
LVI	$C_6F_5Sn(CH_3)_2Cl$ ¹	—	0.4 (T) ¹

^a Chemical shift of indicated protons in ppm down field from tetramethylsilane as internal reference in acetone solution. ^b Coupling constant in c/s between indicated protons and *ortho*-fluorines; D = doublet; T = triplet; Q = quintet; S = singlet; B = broad line; DD = doublet of doubles. ^c Carbon tetrachloride solution. ^d Measured on pure liquid. ^e All these lines were further split into doublets ($J = 5.2$ – 5.6 c/s) by coupling with the NH-protons. ^f Bromobenzene solution. ^g Benzene solution.

are 2.0, 1.1 and 0.6 c/s (all triplets). The same trend is followed by the more highly substituted compounds and, again, some of the *ortho*-substituted compounds are exceptional.

It is suggested that all these couplings are "through space" and not through the five bonds. The "through space" coupling would be expected to be larger, the closer

¹¹ J. Burdon, V. Damodarin and J. C. Tatlow, *J. Chem. Soc.* 763 (1964).

¹² J. M. Burchall and R. N. Hazeldine, *J. Chem. Soc.* 13 (1959).

¹³ A. Lewin, *J. Amer. Chem. Soc.* **86**, 2303 (1964).

¹⁴ J. Burdon, W. B. Hollyhead and J. C. Tatlow, to be published.

¹⁵ E. V. Aroskar, M. T. Chaudry, R. Stephens and J. C. Tatlow, *J. Chem. Soc.* 2975 (1964).

¹⁶ G. M. Brooke, J. Burdon, M. Stacey and J. C. Tatlow, *J. Chem. Soc.* 1768 (1960).

¹⁷ P. Robson, T. A. Smith, R. Stephens and J. C. Tatlow, *J. Chem. Soc.* 3692 (1963).

¹⁸ P. Robson, M. Stacey, R. Stephens and J. C. Tatlow, *J. Chem. Soc.* 4754 (1960).

¹⁹ T. A. Smith and R. Stephens, unpublished work.

²⁰ J. Burdon, W. B. Hollyhead, C. R. Patrick and J. C. Tatlow, to be published.

²¹ R. Stephens and J. C. Tatlow, *Chem. & Ind.* 821 (1957).

²² J. Burdon, J. Morton and D. Thomas, submitted to *J. Chem. Soc.*

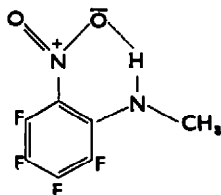
²³ B. R. Letchford, C. R. Patrick and J. C. Tatlow, *J. Chem. Soc.* 1776 (1964).

²⁴ G. M. Brooke, R. D. Chambers, J. Heyes and W. K. R. Musgrave, *Proc. Chem. Soc.* 213 (1963).

²⁵ B. Gething, C. R. Patrick and J. C. Tatlow, *J. Chem. Soc.* 186 (1962).

²⁶ R. Stephens, unpublished work

the proton in the side-chain is to the *ortho*-fluorines. Nearness alone, however, might not be the only factor necessary for large long-range coupling through space; the relative orientation of the C—H and C—F bonds will probably play some part. In the present paper, however, nearness alone will be considered. There are two clear sets of examples which illustrate the importance of this. First, the largest couplings are shown by the *N*-methyl-*o*-nitroanilines³ [(XV) ($J = 5.4$ c/s) and (XVI) ($J = 7.0$ c/s)]. This can be attributed to hydrogen-bond formation:

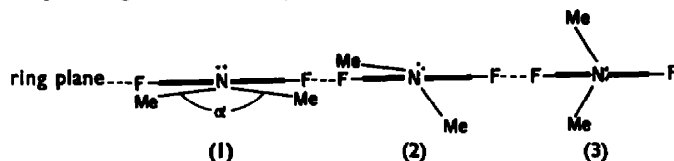


This bonding holds the methyl group close to the *ortho*-fluorine. The corresponding *p*-*N*-methyl-compound (XVII)³ ($J = 3.0$ c/s) and the *NN*-dimethyl-*o*-nitroaniline (X)³ ($J = 1.8$ c/s), neither of which can hydrogen bond in this way, have much smaller coupling constants.

Secondly, neither of the cyclic compounds¹¹ (LII and LIII; Table 6) show any coupling between the protons and the *ortho*-fluorines, whereas the CH₂-group of pentafluorophenetole (LI)¹² does. In the first two cases the protons cannot come close to the *ortho*-fluorines whereas in the third they can.

A number of tentative rationalisations for the correlation between substituent electronegativity and coupling constant may be advanced. They are all based on the same principle; that the more electron-attracting a substituent (that is, a substituent other than fluorine), the more it will force the XMe side-chain to adopt a configuration in which the lone pair on X is in conjugation with the ring. It will be shown that such configurations are also those in which the XMe protons are nearest to the *ortho*-fluorines.

The first possibility is based on the existence of discrete rotational isomers of the compounds in question. Unfortunately, these rotamers are not clearly defined. With dimethylamino-compounds, for example, three possible rotamers are (looking down the nitrogen-ring carbon bond):



Rotamers about the methyl-carbon-nitrogen bond will not be considered. In rotamer (1), there is a favourable conjugation of the lone pair with the electronegative ring, and an unfavourable interaction of the methyl groups with the *ortho*-fluorines; these two factors will determine the bond angles in (1). In rotamers (2 and 3) the steric strain has been relieved but the conjugation partly or completely lost. These two configurations may not, however, both represent energy minima; nevertheless there will probably be a rotamer of type (1) in which the conjugation is at a maximum and the distance between the methyl groups and the *ortho*-fluorines is minimal, and also other rotamers, perhaps (2 and 3), in which the conjugation is less and the distance is

greater. If coupling is through space, then the greater the population of rotamer (1) the greater will be the observed coupling constant. Powerful electron-attracting substituents will clearly favour (1) because they attract the lone pair most successfully in this form. Such substituents will therefore give rise to the largest coupling constants, as is observed. Electron-rich substituents, by themselves providing electrons for the remaining ring fluorines, will have the reverse effect.

Alternatively, the variation in coupling could be explained solely on the basis of rotamer (1). The more electronegative a substituent, the more it would tend to increase angle α in order to increase conjugation. This would decrease the proton-fluorine distance and hence increase the coupling constant.

Lewin¹³ has recently pointed out that the UV spectrum of *o*-fluoroacetophenone suggests that the acetyl group is deflected about 25° out of the ring plane. The UV spectra⁷ of pentafluoro-aniline, -*N*-methylaniline and -*NN*-dimethyl-aniline show progressively decreasing extinction coefficients and λ_{max} , while in the analogous non-fluorinated aromatics the trends are in the opposite direction. It seems likely, therefore, that the XMe side-chains in the compounds discussed in this paper are also deflected out of the ring-plane. This effect will modify the rotamer situation discussed above. Electron-attracting substituents might be expected to decrease this deflection by the conjugation effect already discussed and this provides another approach to the coupling constant variation problem.

If discrete rotamers can exist, both *J* and δ should vary with temperature. Preliminary experiments with compounds VIII, XI, XXVII, XXIX and XXXVI over the range -27° to +118° showed no significant change (<0.2 c/s and <0.05 ppm) in either parameter. With the methoxy-compound (XLIX), which shows a doublet of doublets, δ was unchanged over the same temperature range, but the larger coupling constant fell from 2.8 ± 0.2 c/s at -27° to 2.2 ± 0.2 c/s at 118° and the smaller rose slightly (~ 0.2 c/s). No suitable solvent could be found for the *N*-methyl-nitroanilines (XV and XVII). Bromobenzene was finally employed, but this rendered chemical shift measurements valueless and coupling constants suspect because of complex formation⁵ (Table 2). In this solvent, the coupling constant for the *ortho*-isomer (XV) fell from 6.7 c/s at +3° to 4.5 c/s at 118° (assuming that the CH₃/NH-coupling remains at 5.2-5.6 c/s over the temperature range), while for the *para*-compound (XVII), *J* fell slightly (~ 0.2 c/s) over the same temperature range.

As the energy differences between the rotamers would be expected to be small, variations in *J* and δ would also be expected to be small, particularly at higher temperatures. For more significant results, therefore, lower temperatures than those mentioned here are necessary; with the compounds under consideration, this leads to considerable solubility problems.

Examination of the Tables shows that anomalies in both *J* and δ occur with *ortho*-substituted compounds. For all the side-chains, δ for the methyl protons is shifted upfield in the *ortho*-substituted compounds as compared to the *para*-isomers. Coupling constants for the *ortho*-substituted compounds are usually larger than those for the *para*-isomers for the OMe-, SMe-, SO₂Me- and NHMe-side-chains, and smaller for the NMe₂. Owing to the small number of examples these trends should not be regarded as established.

That compounds XXIX, XLV and XLVIII should show doublets of doublets and not triplets seems reasonable, since in each case the two fluorines which are coupled

to the protons are different. However, it is difficult to see why the two couplings should be so different in these cases and so similar with compounds II, XI, XVI and XXIII which show triplets and where the same environment occurs.

EXPERIMENTAL

A Varian A60 instrument with a frequency of 60 Mc/sec was used for all the measurements. The chemical shifts are quoted in ppm downfield from tetramethylsilane as internal reference, and were reproducible within 0.04 ppm. The coupling constants were measured from peak maximum to maximum. This results in low values for incompletely resolved peaks and the constants below about 1 c/s may be ~ 0.1 c/s low; the actual measurements are accurate to ± 0.1 c/s. The sample temp for the results quoted in Tables 1-6 were 36-38°. Some allowance was made for overlapping in the 2-7° and +118° measurements; the coupling constants at these temperatures are accurate to ± 0.2 c/s.