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LONG RANGE PROTON–PROTON COUPLING IN SUBSTITUTED ANISOLES

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Abstract—The long range coupling, J_{1r}, between the OMe methyl protons and the ortho ring proton has been determined in a series of substituted anisoles. Although this 5-bond coupling is present in all the anisoles, its magnitude is enhanced by the presence of a bulky substituent (Cl, Br, I and NO_2) *ortho* to the methoxy group. The results have been interpreted in terms of restricted rotation, the larger value of J_{1r} being associated with that conformation in which the OMe group is "anti" to the *ortho* substituent.

LONG range proton–proton couplings have been observed in a great variety of compounds, extending over as many as five bonds, in many cases through atoms other than carbon.[1] There is current interest in the occurrence and magnitude of these long range interactions, as well as in the mechanism where by they are transmitted.

The present report is concerned with couplings over five bonds involving the OMe methyl group in some substituted anisoles. This type of long range coupling has been described briefly in the literature, but apparently has not been the subject of any detailed quantitative study. Martin and Dailey suggested that the broadening seen in the ortho-proton region of the spectra of various anisoles is due to a small coupling (0·1–0·2 Hz) between the OMe and ortho-protons.[2] In thioanisole and 2,3,4-trichloroanisole, on the other hand, the corresponding coupling is somewhat larger as indicated by a resolvable splitting of 0·3 Hz.[3] In the non-aromatic, but unsaturated methyl vinyl ether a coupling of 0·3 Hz from the alpha proton to —OMe has been reported.[4] In this instance, however, there is no perceptible coupling to the beta protons analogous to that observed in the anisoles.

We describe here the results of a detailed study of the PMR spectra of sixteen substituted anisoles, with particular emphasis on the long range coupling described above. The data indicate that the conformation of the OMe group is one of the primary factors that determine the magnitude of the long range coupling.

RESULTS

The PMR calculations for the spectral analyses of all the compounds were carried out with the aid of an iterative computer program (PROSPECT 1). Of the sixteen substituted compounds reported, fourteen were completely analyzed, including both the OMe and ring proton regions. 2-hydroxyanisole and 2-methoxyanisole were quite collapsed and consequently not analyzed. We have described fully here only the spectra of the OMe region, since our results for the ring systems agree with most of those reported elsewhere in the literature.[5,6] Table 1 lists the OMe shifts and long range coupling constants, J_{1r}, where the latter could be determined from the observed splittings. In those cases where splitting was not resolved, the width at half height has been listed (Table 1) to serve as an indication of the coupling present.

TABLE 1. CHEMICAL SHIFTS[a] AND LONG RANGE COUPLING IN SUBSTITUTED ANISOLES

Compound	Chemical Shifts	J_{1r} (Hz)	Solvent
2-Chloroanisole	−217·79	0·30	TMS
2-Bromoanisole	−215·65	0·32	TMS
2-Iodoanisole	−223·06	0·30	TMS
2-Nitroanisole	−231·65	0·29	TMS
2,4-Dichloroanisole	−220·75	0·32	TMS
		Width at Half Height (Hz)	
2-Hydroxyanisole	−219·08	0·40	CCl_4
2-Methoxyanisole	−217·23	0·50	CCl_4
2-Fluoroanisole	−219·23	0·75[b]	TMS
3-Methoxyanisole	−214·06	0·60	TMS
3-Bromoanisole	−213·79	0·48	TMS
4-Chloroanisole	−213·79	0·50	TMS
4-Bromoanisole	−215·38	0·47	TMS
4-Iodoanisole	−222·16	0·40	CCl_4
4-Methoxyanisole	−216·61	0·35	TMS
4-Nitroanisole	−233·31	0·45	CCl_4
Anisole	−213·06	0·45	TMS

[a] All chemical shifts are in Hz relative to TMS at 60 MHz.
[b] This value is larger than the others due to interaction with the fluorine.

All the spectra were first analyzed as four spin systems, ignoring the coupling from the OMe group. The resulting spectral fit gave a root mean square deviation of not more than 0·05 Hz between the calculated and observed frequencies for the ring protons and corresponding probable errors in the PMR parameters of 0·05 Hz. In the *ortho*-substituted anisoles (Cl, Br, I and NO_2) where splitting in the OMe methyl region was observed the spectra were treated as $ABCDX_3$ spin systems. A seven spin computer plot appears in Fig. 1 below the observed pattern for *o*-chloroanisole in TMS. This pattern clearly shows the fine structure arising from a long range coupling of 0·30 Hz as observed in those anisoles with bulky substituents. Initially, the ring proton–proton couplings were estimated on the basis of additivity of substituent effects.[6] The satisfactory spectral fits which followed, indicated that the proton assignments were correctly made. Consequently, the appearance of additional fine structure in the ortho-proton and OMe methyl regions unambigously identifies the long range coupling.

The long range coupling as determined from the OMe splitting was 0·30 ± 0·03 Hz for all of the *ortho*-substituted anisoles, except *o*-fluoroanisole, *o*-hydroxyanisole and *o*-methoxyanisole. In the latter two instances, a noticeable broadening indicated the presence of a long range coupling too small to lead to resolved fine structure. Evidence of fine structure was seen in the OMe region of *o*-fluoroanisole, but since there was no accompanying coupling observed in the PMR spectra of the ring, this

was ascribed to interaction with the fluorine. (Examination of the fluorine spectrum provided further support for this interpretation.)

In all of the anisoles examined where only broadening was observed in the OMe methyl pattern (line width of 0·5 Hz at half height) the spectral lines arising from the

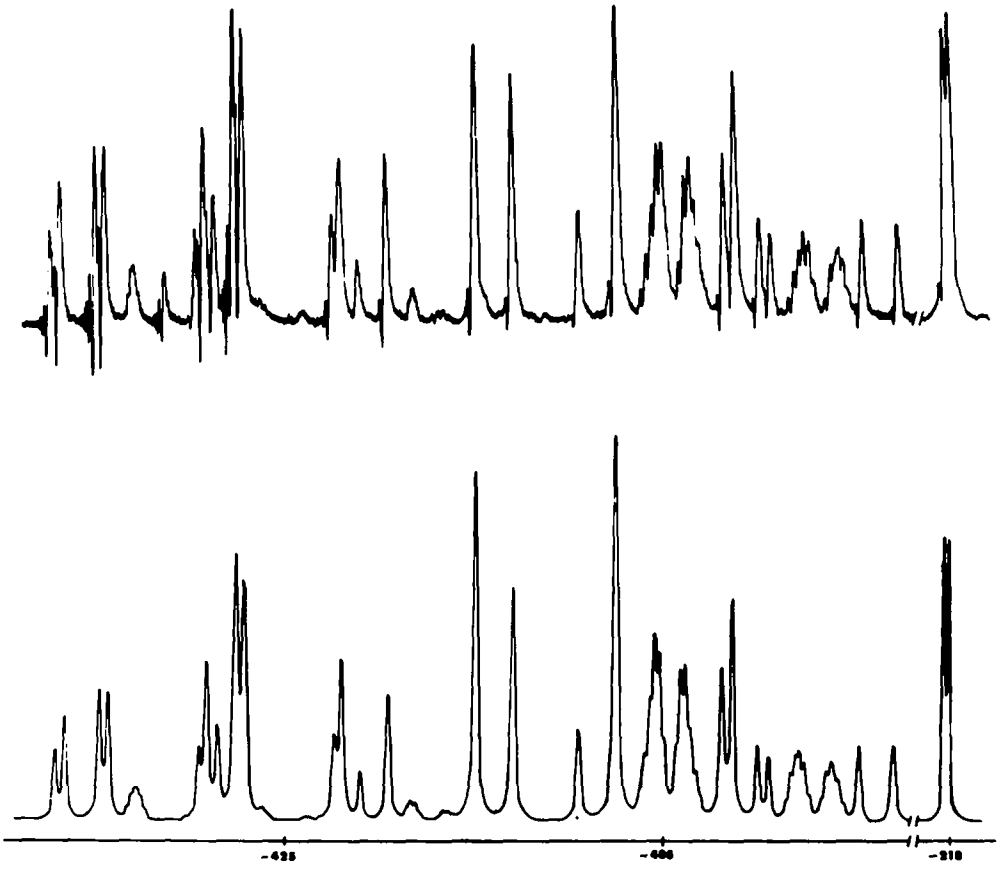

FIG. 1 The observed and computer calculated plot of the 60 Hz PMR spectrum of *o*-chloroanisole (25 mole%) at 38°C showing the methoxy and ring fine structure. Positions labelled A and B denote a small benzene impurity and the methoxy resonance respectively. The intensity scale for the aromatic and methoxy regions are not the same.

ortho ring protons were noticeably broader than those due to the other protons in the aromatic system. This indicates that the long range coupling is present in all of the compounds, but diminished in the absence of a bulky *ortho*-substituent.

DISCUSSION

The experimental evidence presented here indicates that the proposed long range coupling is present in all the anisoles, and is largest for those derivatives with bulky

ortho-substituents. This suggests that J_{1r} may be associated with restricted rotation of the OMe group about the C_{aryl}–O bond. It is unlikely that the OMe group rotates freely even in anisole. Aroney *et al.* inferred a dihedral angle of 18° (between the aromatic ring and C_{aryl}—OMe planes) from both dipole moment and Kerr constant measurements for anisole.[7] Since the PMR results show both *ortho*-protons to be chemically equivalent for anisole and its *para*-substituted derivatives, the OMe group is probably undergoing transitions between two equivalent orientations at a rate which is rapid on the PMR time scale. It is also conceivable that the OMe oxygen atom interacts mesomerically with the aromatic ring, which would tend to stabilize the orientation of the OMe group. However, the extent of such interaction is at present somewhat debatable.[8–10] The introduction of two *ortho* substituents produces observable differences in the UV spectra of the derivatives relative to that of anisole as well as those of the monosubstituted compounds.[11] These effects may possibly be attributed to corresponding changes in the degree of conjugation. However, mesomeric interaction, if it occurs at all does not appear to effect J_{1r}, since PMR fine structure is not even observed in *p*-nitroanisole, a system in which mesomerism is expected to be augmented. It is worth noting that in methyl vinyl ether where mesomeric effects appear to be present on the basis of PMR data, a corresponding five bond coupling does not occur.[4] Instead the OMe protons couple solely with the vinylic alpha protons.

Molecular models with bulky *ortho*-substituents show considerable steric hinderance to rotation of the OMe group and, as expected on a solely steric basis, indicate that the most favorable conformation for the OMe group would place it "anti" to the substituent. The results of Dhami and Stothers support this type of conformation.[12] These workers found that additivity of ^{13}C chemical shifts, as suggested by Lauterbur, held well for *meta*- and *para*-substituted anisoles, but large deviations were found for the *ortho* compounds. In the *ortho* derivatives the experimental C_6 resonance occurred at higher field, and the corresponding C_2 resonance was at lower field, than predicted by additivity. This failure of additivity was attributed to a preferred conformation in which the OMe group was "anti" to the *ortho*-substituent, leading to greater shielding of C_6 and diminished shielding of C_2. It was also found that the shift of the OMe carbon in the *ortho* compound was very close to that of anisole itself, indicating that the OMe methyl was in a conformation lying farthest from the substituents.

Brouwer *et al.* have reported fixation of the OMe group in 3,5-dimethylanisole cation at −78° as indicated by two chemically nonequivalent ortho proton resonances.[13] Accordingly, we also obtained the PMR spectrum of *o*-chloroanisole at −20° and −55° in an effort to ascertain any temperature dependence of J_{1r}. At these temperatures difficulties were encountered with both resolution and solubility and no fine structure arising from J_{1r} could be observed in the OMe and ortho proton regions. However, from the width of the peaks in these regions it appeared that J_{1r} had not changed appreciably. It is possible that the temperature of −55°, which was the practical limit in our studies, was not sufficiently low to affect J_{1r}. It must also be pointed out that a difference might be expected between the cation and neutral species of anisole.

In view of the now well-established sensitivity of some couplings to the solvent medium it appeared advisable to determine what effect concentration might have on J_{1r}.[14,15] This was done for *o*-chloroanisole in TMS over the range 16–100 mole %.

Although J_{1r} did not change appreciably, significant variations were noticed in the chemical shift of the methoxy protons, which exhibited a minimum value at 66 mole %. Further examination of this effect was not carried out since it was outside the main interest of this study.

For five of the *ortho* anisoles studied, the value of J_{1r} has been determined to be 0·30 Hz with an uncertainty of about 10 %. For the remaining three *ortho* compounds involving hydroxy, methoxy, and fluoro substituents, the value of J_{1r} is definitely smaller, although not precisely determinable. In the latter three compounds the *ortho*-substituent is clearly smaller than in the five derivatives exhibiting the larger value of J_{1r}. Thus, it would appear that the smaller values of J_{1r} are associated with less restricted rotation. In other words the effect of rotational averaging is such as to decrease the value of J_{1r}, which is the general observation for couplings from substituent to ring protons.

EXPERIMENTAL

All the substituted anisoles used in this study were commercially available, and were used without further purification unless the PMR spectra indicated some impurities. The spectra were recorded on a Varian A-60A spectrometer with the probe temp normally at 38°. In general TMS was used as solvent and internal reference. Where solubility in this medium was inadequate, CCl_4 with a few per cent TMS for reference purposes was used instead. All of the solns were made up to a concentration of about 20 mole % and then degassed by bubbling N_2 through the solns. The spectrum of *o*-chloroanisole in TMS was observed at −55° and also −20°. In addition the spectrum of this compound was studied at normal temp over a concentration range of 16–100 mole%.

At least three forward and three reverse sweeps were taken of each soln. The complete spectra (ring and OMe regions) were calibrated using the audio side band method and the six sweeps were averaged to give a standard deviation of not more than 0·05 Hz for the observed line frequencies. The OMe peaks could be measured somewhat more accurately, since a limited sweep range was used (~6 Hz), which consequently allowed less time (120 sec) for instabilities to affect the sweep accuracy.

Note added in proof—After this paper was submitted, Feeney and Sutcliffe reported (*Spectrochimica Acta* **24A**,, 1135 (1968)) long range proton–proton coupling constants from the methoxy Me group to the β protons in methyl vinyl ether. They found coupling values of 0·3 Hz and 0·2 Hz from the Me group to the *cis* and *trans* protons, respectively. Their value of 0·3 Hz is extremely close to the corresponding long range coupling constants we report above for the *ortho*-substituted anisoles. In the latter we have suggested the same conformation for the OMe group as Feeney and Sutcliffe propose for the methyl vinyl ether.

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