

Proton Chemical Shifts, Long-Range Spin Coupling and π -Electron Distributions in Methoxy Derivates of Salicylaldehyde and *o*-Hydroxyacetophenone

STURE FORSÉN, BJÖRN ÅKERMARK and TORBJÖRN ALM

Research Group for NMR, Division of Physical Chemistry and Division of Organic Chemistry, Royal Institute of Technology, Stockholm 70, Sweden

The proton magnetic resonance (PMR) spectra of the 3, 4, 5, and 6-methoxy derivatives of salicylaldehyde and *o*-hydroxyacetophenone (*cf.* III) have been studied. The chemical shifts of the ring protons — obtained through the use of an iterative ABC computer programme — are comparatively well correlated with π -electron excess charges calculated with the Hückel molecular orbital (HMO) method. Also the ^{13}C shifts in a series of methoxybenzenes are well correlated with π -electron excess charges calculated with the HMO method. The *differences* in the *meta* proton shifts between corresponding salicylaldehyde and *o*-hydroxyacetophenone derivatives do, however, not follow the pattern expected on the basis of commonly used models for the inclusion of methyl groups in the Hückel type MO calculations. Long-range spin couplings between ring protons and the CHO, OH, and OCH₃ protons are observed. It is suggested that the long-range spin coupling of phenolic OH-groups is stereospecific in analogy with the long-range aldehyde couplings. The mechanism of the long-range aldehyde couplings are shortly discussed.

In recent years, the possibility of obtaining information on the π -electron distribution in aromatic and conjugated molecules from nuclear magnetic resonance data, in particular from ^1H and ^{13}C chemical shifts, has received much attention. Chemical shifts of resonances of nuclei in molecules depend in general in a relatively complex manner on the electron distribution around the nucleus and in more distant parts of the molecule.^{1,2} In the early work by Shoolery³ and by Corio and Dailey⁴ on the ring proton shifts in mono-substituted benzenes it was noted, however, that the positions of the ring proton resonances in the spectra could be qualitatively interpreted in terms of the mesomeric and inductive effects of the substituents. It thus appeared likely that the π -electron distribution had an important effect on the ring-proton chemical shifts.

It was later shown that in the isoelectronic series cyclopentadienyl anion ($C_5H_5^-$) benzene (C_6H_6) and tropylium cation ($C_7H_7^+$) there is an approximately linear correlation between the ring proton chemical shifts and the π -electron density on the carbon atoms.⁵

The ^{13}C chemical shifts in the same series of molecules (the ion $C_8H_8^{2-}$ was also studied) similarly show an approximately linear dependence on the π -electron densities.⁶ On the basis of these investigations it was suggested that the shifts $\delta(q)$ of 1H in nuclei (and also of ^{13}C nuclei) in aromatic molecules in general should follow the simple equation

$$\delta(q) = a \cdot q \quad (1)$$

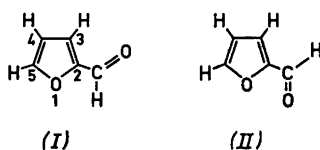
where a is a proportionality constant and q the excess π -electron density on the carbon atom in the C—H bond. When $q = 0$ the shift $\delta(q)$ should equal that in benzene. The value of the proportionality constant a for proton shifts seems to be in the vicinity of 10 ppm/electron — the actual value depends on how corrections are applied for variations in induced “ring currents” and also for solvent effects. (In the rather polar solvents used to dissolve the $C_5H_5^-$ and $C_7H_7^+$ ions in the work by Fraenkel *et al.* the solvent effects may be as large as 0.4 ppm⁷). For ^{13}C chemical shifts a value of $a \approx 160$ ppm/electron has been suggested.⁶ Somewhat higher values have been found by Lauterbur.^{9,10} The value $a \approx 10$ ppm/electron for proton shifts is reasonably consistent with observations by MacLean and Mackor⁸ (*cf.* also Ref.⁷) of chemical shifts in carbonium ions of methyl substituted benzenes.

Eqn. (1) has been applied to estimate π -electron densities at the different carbon atoms in nitrobenzene, aniline, pyridine, azulene, and a number of nitrogen heterocycles⁵⁻⁷ from measured values of 1H and ^{13}C chemical shifts, in the case of azulene corrected for ring current effects. A rough qualitative agreement was obtained between the π -electron densities calculated from the shift data and the densities calculated by the Hückel, Pariser-Parr and other molecular orbital (MO) methods. Later studies of ^{13}C and 1H chemical shifts in monosubstituted benzenes¹¹ and 1H shifts in disubstituted benzenes¹² have indicated that considerable caution must be exercised when conclusions on π -electron distributions are drawn from chemical shift data. There is evidence that some additional effect apart from the π -electron density influences the chemical shift of both 1H and ^{13}C nuclei *ortho* to certain substituents. Thus in the series F, Cl, Br, and I monosubstituted benzenes the *ortho* shifts tend strongly to lower fields as the size of the halogen atom increases.¹¹ A tendency in the opposite direction is expected on the basis of the relative inductive effects of the halogens. Spiesscke and Schneider have suggested that the magnetic anisotropy of the substituents may account for the anomalous *ortho* shifts observed.^{11*}

Additional evidence on the anomalous influence of the substituents on neighbouring ring protons in aromatic systems has recently been found by

* Note added in proof: *Cf.* recent paper by Wu and Dailey, *J. Chem. Phys.* **41** (1964) 2096, in which theoretical and experimental values of 1H , ^{19}F , and ^{13}C shifts in a number of substituted benzenes have been compared. For a number of substituents it is found that other factors than the π -electron densities make important contributions to the shifts in *ortho* and *meta* positions.

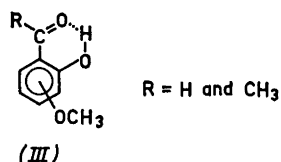
Smith¹³ who has studied the PMR spectra of 5-methyl, 5-bromoethyl, and 5-chloromethyl derivatives of ethyl-2-fuorate. The substitution of one of the methyl hydrogens with halogen is hardly expected to appreciably change the π -electron distribution in the furan ring. However, in the halomethyl derivatives the chemical shift of the hydrogen in the 4-position is about 0.40 ppm and that of the 3-hydrogen about 0.10 ppm to lower fields than in the 5-methyl derivative. A direct observation of the "ortho effect" produced by the aldehyde group in 2-furanaldehyde has recently been made in these laboratories.¹⁴ It was found possible to "freeze" in the two rotational isomers of the aldehyde group in this compound at about -80°C .



The difference in chemical shift of the hydrogen in the 3-position between the two rotamers (I) and (II) was 0.15 ppm.

In the series of monosubstituted benzenes studied by Spiesscke and Schneider¹¹ the chemical shift of ^{13}C nuclei in the *meta* position are completely at variance with the corresponding proton shifts. In the *para* position, on the other hand, the trend of the proton shift closely follows the corresponding ^{13}C shifts. Furthermore the *para* shifts are well correlated with a number of other quantities such as Hammett's σ -constants and *para* ^{19}F shifts.

In an attempt to shed some light on the relation between proton chemical shifts and π -electron densities in substituted benzenes containing OH, OCH_3 , and CHO groups we have in the present work studied the isoelectronic methoxy derivatives of salicylaldehyde and *o*-hydroxyacetophenone:



The chemical shifts and the spin coupling constants of the ring protons have been obtained from an ABC-analysis² of the spectra. In the inert solvent used the $\text{R}-\text{C}=\text{O}$ group is effectively locked in one rotational configuration by the intramolecular hydrogen bond. This should reduce the deshielding effects of the $\text{C}=\text{O}$ bonds¹⁵ on the neighbouring ring protons. The work of Spiesscke and Schneider on anisole indicates that the ring proton shifts are mainly determined by the resonance effects of the OCH_3 group and that the anomalous ortho shifts are comparatively small. This makes a comparison of the experimental shift data calculated π -electron densities seem meaningful.

The π -electron distribution has been calculated by a semiempirical molecular orbital method in the Hückel approximation.^{16,17} Two sets of parameters have been used. One of these sets is essentially that previously used for the same series of compounds in a study of the correlation between the charge distribution and the strength of the intramolecular hydrogen bond.¹⁸

The salicylaldehyde and *o*-hydroxyacetophenone derivatives are interesting in another aspect in that they exhibit long-range spin coupling of the aldehyde group, phenolic OH-group and the OCH₃-group with the ring protons.

In the present work these long-range couplings have been studied in some detail and the characteristics and the possible mechanism of the couplings are discussed.

EXPERIMENTAL

Materials. The preparation of the 3, 4, 5, and 6-methoxy derivatives of salicylaldehyde and *o*-hydroxyacetophenone has been described in a previous paper.¹⁸ The carbon disulphide used as solvent was of highest quality (Merck, *pro analysi*) and was further purified through distillation over calcium oxide. In order to observe the long-range hydroxyl couplings it was found necessary to prepare the solutions less than a day after distillation of the solvent. Tetramethylsilane (Fluka) was used as internal reference. All solutions contained *ca.* 1 % by volume of the reference substance.

NMR procedures. The proton magnetic resonance spectra were recorded at a radio frequency of 60.007 Mc/s on a Varian A 60 spectrometer. The sample temperature $33 \pm 1^\circ\text{C}$. All compounds were measured at a concentration of *ca.* 6 mole-% in carbon disulphide. This concentration was chosen as a compromise between the wish to obtain satisfactory amplitudes of all peaks in the complex spectra of the ring protons and the desire to minimize solvent effects.¹⁹ Studies of the changes in the ring proton shift upon dilution performed in two cases indicated that the shift values obtained on the 6 % solutions do not differ by more than ± 0.01 ppm from the shift values of the "isolated" molecules at infinite dilution.

The samples were deoxygenated by bubbling nitrogen through them for ten minutes before sealing. Line-widths of *ca.* 0.25–0.30 c/s could be obtained in all cases.

In the study of the smallest long-range spin couplings a sweep rate of the magnetic field about half that possible with the commercial A-60 spectrometer was used. The reduction in sweep rate was accomplished by means of a resistor connected in series with the sweep coil in the sweep unit of the spectrometer. This arrangement permitted signals to be recorded at a sweep rate of 0.05 c/s². All spectra were recorded using the lowest possible amplitude of the rf. field to ensure optimum resolution.

Calibration of the spectra was made by the inclusion of side bands from the internal tetramethylsilane reference in the recorded spectra at suitable intervals, and the positions of the individual proton resonance signals were determined by linear interpolation. The side bands were generated through frequency modulation of the rf. oscillator²⁰ with the aid of a Hewlett-Packard model 200 J audio oscillator and the modulation frequency was measured with a Hewlett-Packard model 5512A electronic counter.

The analysis of the ring proton spectra is based upon the assumption that the proton spin coupling constants follow the order $J_{\text{ortho}} > J_{\text{meta}} > J_{\text{para}}$. No contradiction to this empirical rule seems so far to have been encountered.²¹⁻²⁹ It was found possible to fit the observed spectra with positive values of all ring coupling constants within the experimental error. In some cases in the assignment of the observed chemical shifts advantage was also taken of the long-range couplings to the ring protons of the substituents (*cf.* below).

The chemical shifts and spin coupling constants of the aromatic protons were calculated from the obtained spectra using an iterative ABC programme developed for the Swedish electronic computer BESK. The ring proton spectra were initially roughly analysed making use of the property of repeated spacings valid in three-spin systems.³⁰ A number of trial spectra were then calculated, using reasonable values of chemical shifts and spin coupling constants, and compared with the observed spectra. The iterative

procedure was then begun with the best set of preliminary parameters. The small long-range spin couplings due to the substituents, observed in some of the compounds, were neglected in the iterative calculations. The long-range hydroxyl spin-couplings could be suppressed by the addition of a small amount of triethylamine or trifluoroacetic acid (*cf.* Ref.⁴¹) to the solution. The deviations between the line frequencies calculated with the finally obtained set of chemical shift and spin coupling parameters and the frequencies experimentally observed were generally of the order of 0.02–0.04 c/s. Most coupling constants reported here are considered reliable to ± 0.10 c/s and the mean error in the chemical shift values is estimated to be 0.003 ppm.

The computer programmes for the calculation of the trial spectra are written in ALGOL and include a high speed Jacobi routine in the machine code for the calculation of eigenvalues and eigenvectors. In the iterative programme the "pit-mapping" method of Sillén and Ingri³¹ was initially used. In a later version of the programme the LETAGROP-VRID method developed by Sillén³² was included. The final parameter sets were in most cases reached after two to three iterations. No use of the intensities is made in the iterative programme.

RESULTS AND DISCUSSION

The chemical shifts and spin coupling constants derived from the nuclear magnetic resonance measurements as summarized in Table 1. Experimental and theoretical spectra for the four methoxy derivatives of salicylaldehyde are shown in Figs. 1–4. The theoretical spectra have been calculated with the parameters listed in Table 1.

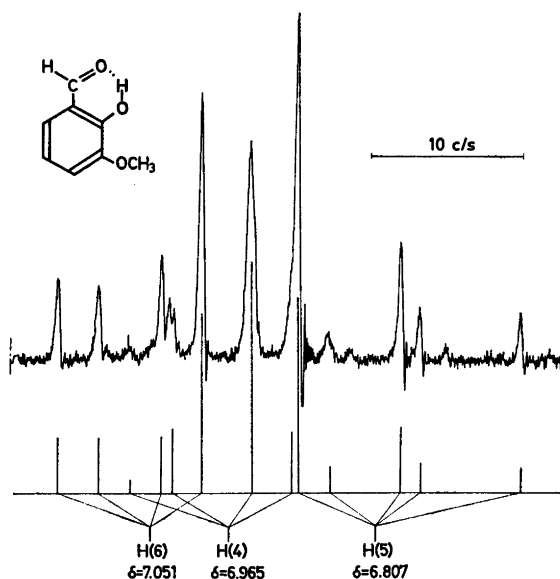
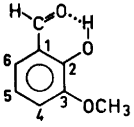
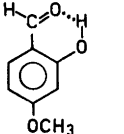
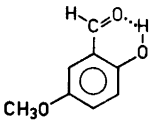
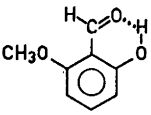
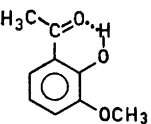
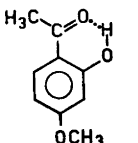
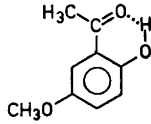
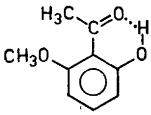


Fig. 1. The PMR spectrum of the ring protons in 3-methoxysalicylaldehyde (triethylamine was added to suppress the long-range spin coupling of the OH hydrogen with the 4-hydrogen; a marked broadening of the 4-hydrogen signals due to long-range coupling with the OCH₃-group is evident.

Table 1. Observed proton chemical shifts (δ) and spin coupling constants (J) in dilute solutions in carbon disulphide. The shift values are given in ppm relative to tetramethylsilane and the spin coupling constants are in c/s.

	$\delta_{\text{H}(4)} = 6.965$	$J_{4,5} = 7.85$	$J_{\text{OH,H}(4)} = 0.50$
	$\delta_{\text{H}(5)} = 6.807$	$J_{5,6} = 7.83$	
	$\delta_{\text{H}(6)} = 7.051$	$J_{4,6} = 1.50$	$J_{\text{OCH}_3,\text{H}(4)} = 0.24$
	$\delta_{\text{H}(3)} = 6.273$	$J_{3,5} = 2.40$	$J_{\text{CHO,H}(3)} = 0.53$
	$\delta_{\text{H}(5)} = 6.427$	$J_{5,6} = 8.84$	
	$\delta_{\text{H}(6)} = 7.303$	$J_{3,6} = 0.18$	
	$\delta_{\text{H}(3)} = 6.751$	$J_{3,4} = 9.16$	$J_{\text{CHO,H}(3)} = 0.57$
	$\delta_{\text{H}(4)} = 6.992$	$J_{4,6} = 3.16$	$J_{\text{OH,H}(4)} = 0.38$
	$\delta_{\text{H}(6)} = 6.855$	$J_{3,6} = 0.38$	
	$\delta_{\text{H}(3)} = 6.352$	$J_{3,4} = 8.55$	$J_{\text{CHO,H}(3)} = 0.62$
	$\delta_{\text{H}(4)} = 7.266$	$J_{4,5} = 8.30$	$J_{\text{OH,H}(4)} = 0.38$
	$\delta_{\text{H}(5)} = 6.249$	$J_{3,5} = 0.82$	$J_{\text{OCH}_3,\text{H}(5)} = 0.26$
	$\delta_{\text{H}(4)} = 6.886$	$J_{4,5} = 7.97$	$J_{\text{OH,H}(4)} = 0.65$
	$\delta_{\text{H}(5)} = 6.652$	$J_{5,6} = 8.23$	$J_{\text{OCH}_3,\text{H}(4)} = 0.25$
	$\delta_{\text{H}(6)} = 7.185$	$J_{4,6} = 1.45$	
	$\delta_{\text{H}(3)} = 6.209$	$J_{3,5} = 2.52$	
	$\delta_{\text{H}(5)} = 6.280$	$J_{5,6} = 8.81$	
	$\delta_{\text{H}(6)} = 7.464$	$J_{3,6} = 0.38$	
	$\delta_{\text{H}(3)} = 6.691$	$J_{3,4} = 9.18$	$J_{\text{OH,H}(4)} = 0.33$
	$\delta_{\text{H}(4)} = 6.920$	$J_{4,6} = 2.83$	
	$\delta_{\text{H}(6)} = 6.966$	$J_{3,6} \leq 1.0$ *	
	$\delta_{\text{H}(3)} = 6.362$	$J_{3,4} = 8.45$	
	$\delta_{\text{H}(4)} = 7.163$	$J_{4,5} = 8.37$	$J_{\text{OH,H}(4)} = 0.37$
	$\delta_{\text{H}(5)} = 6.221$	$J_{3,5} = 1.09$	$J_{\text{OCH}_3,\text{H}(5)} = 0.31$

* This value could not be accurately determined from the spectra. The signals from the ring protons in 4- and 6-position were considerably broadened due to unresolved long range spin

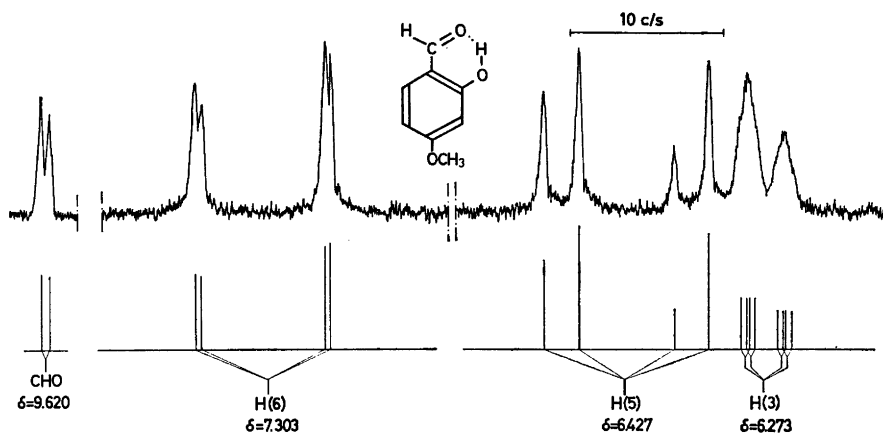


Fig. 2. The PMR spectrum of 4-methoxysalicylaldehyde.

The results of the Hückel MO calculations are summarized in Table 2. The calculations were performed with two basic sets of parameters:

Set 1	Set 2
$\alpha_{=O} = \alpha + \beta$	$\alpha_{=O} = \alpha + \beta$
$\alpha_{OH} = \alpha + 2\beta$	$\alpha_{OH} = \alpha + 1.4\beta$
$\alpha_{OCH_3} = \alpha + 1.9\beta$	$\alpha_{OCH_3} = \alpha + 1.3\beta$
$\beta_{C=O} = \beta$	$\beta_{C=O} = \beta$
$\beta_{C-O} = 0.8\beta$	$\beta_{C-O} = 0.8\beta$

where α is the Coulomb integral for an unperturbed carbon atom and β the carbon-carbon resonance integral.^{16,17} The first of these sets is essentially the "recommended" set of parameters listed by Streitwieser.¹⁷ In the second set of parameters lower values for the Coulomb integrals of hydroxy and methoxy groups have been chosen. Lower values of these parameters than commonly used have recently been suggested by Schug and Deck from a study of proton chemical shifts in hydroxy benzenes.³³ The two parameter sets given above have also been used in a study of the electronic spectra of the same series of compounds as investigated here.⁶⁰

To distinguish between the salicylaldehyde and the *o*-hydroxyacetophenone derivatives in the Hückel calculations, three different models for the acyclic methyl group have been employed (*cf.* Ref.³⁴):

(1) The inductive model where the Coulomb integral for the methyl substituted atom is made numerically smaller. In this work a value of $\alpha_{=C-CH_3} = \alpha - 0.1\beta$ has been used. This value differs from that recommended by Streitwieser¹⁷ ($\alpha - 0.5\beta$) but is in better accordance with the value suggested from a study of the correlation between the hydroxyl proton shift and the π -electron density on the carbonyl oxygen.¹⁸ The above value also leads to changes in

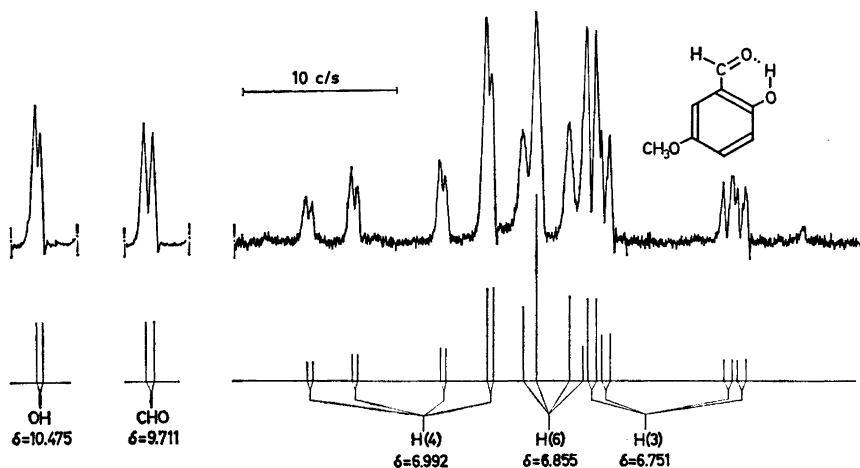


Fig. 3. The PMR spectrum of 5-methoxysalicylaldehyde (also in these latter compounds a broadening of the signals from the ring protons ortho to the OCH₃-group is noted).

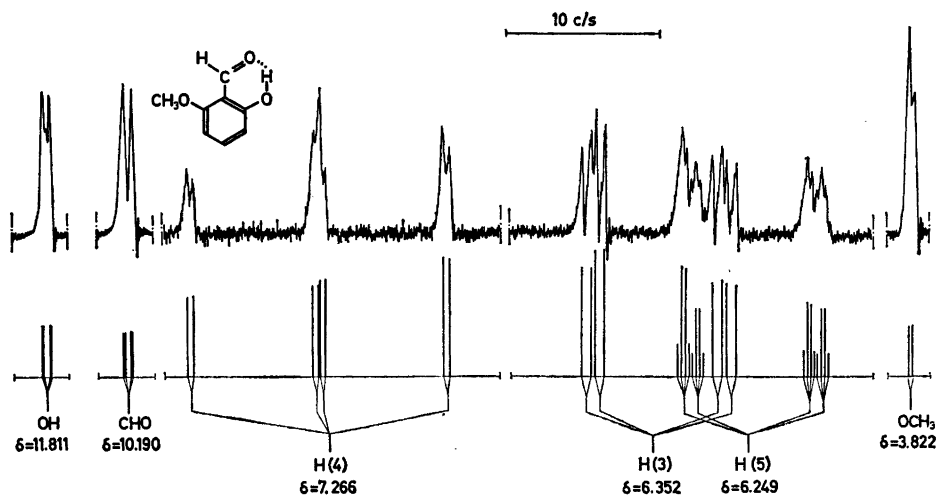
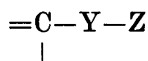


Fig. 4. The PMR spectrum of 6-methoxysalicylaldehyde. In this compound the long-range spin coupling between the OCH₃ hydrogens and the 5-hydrogen is so large as to give rise to a resolvable fine structure.

the calculated π -electron distribution that are in reasonable agreement with changes calculated with other models for methyl groups in the Hückel method.

(2) The hyperconjugation model in which the =C-CH₃ group is treated as a system with two pseudo atoms, Y and Z^{35, 36, 16, 17}



The following parameter values were applied: $\alpha_Y = \alpha$; $\alpha_Z = \alpha - 0.5\beta$

$$\beta_{C-Y} = 0.8\beta; \beta_{Y-Z} = 3\beta$$

(3) The heteroatom model. In this model the methyl group is assumed to behave like a heteroatom (X) with a single electron pair.¹⁷ The following parameters were used: $\alpha_X = \alpha + 2\beta$; $\beta_{C-X} = 0.7\beta$.

A plot of observed ring proton shifts *versus* the calculated π -electron densities for the salicylaldehyde derivatives is shown in Fig. 5. The plots of the corresponding chemical shift and π -electron density data for the *o*-hydroxyacetophenones are very similar to those for the salicylaldehyde derivatives and are not shown. The chemical shift of the ring proton in the 6-position in the two series of methoxy derivatives of salicylaldehyde and *o*-hydroxyacetophenone deviates markedly from the general pattern found for the shifts of the ring protons in the 3-, 4-, and 5-positions. This is shown in Table 3 where the *differences* between the ring proton chemical shifts in the *o*-hydroxyacetophenone and salicylaldehyde derivatives are listed. The chemical shift of the 6-proton in the *o*-hydroxyacetophenone derivatives is throughout found at fields *lower* than that in the corresponding salicylaldehyde derivative. It does not appear likely that this exceptional behaviour is solely due to changes in the π -electron density at the 6-position but more likely is due to the different diamagnetic anisotropy of the C—H bond in the aldehydes and the C—CH₃ group in the *o*-hydroxyacetophenones. An estimate of the magnitude of this anisotropy effect may be made using the point dipole approximation of McConnell.³⁷ From a suitable molecular model of *o*-hydroxyacetophenone (Dreiding) it appears that the distance between the proton in the 6-position and the midpoint of the C—C bond in the CH₃—C=O group is about 2.5 Å. If we assume the diamagnetic anisotropy $\chi_L - \chi_T$ (χ_L and χ_T are the averages of the susceptibility components parallel and perpendicular to the bond axis) to be zero for C—H bonds and take the value $\chi_L - \chi_T = -5 \times 10^{-6}$ cm³ mole⁻¹ for the C—C bond,^{15, 38-40} this leads to a value of 0.18 ppm for the anisotropy effect. The sense of this effect is to displace the chemical shift of the ring proton in the 6-position on the *o*-hydroxyacetophenone derivatives towards lower fields. Even if the above value is somewhat inaccurate it seems credible that the "anomalous" behaviour of the 6-hydrogen shifts in the *o*-hydroxyacetophenones is due to diamagnetic anisotropy effects.

From considerations of molecular geometry there appears to be an appreciable steric interaction between the OCH₃-group and the =C—CH₃ group in the 6-methoxy derivative of *o*-hydroxyacetophenone. Such an interaction seems to account for the large long-range spin coupling constant in this compound between the OCH₃ protons and the ring proton in the 5-position.⁴¹ One would also expect a slight distortion of the CH₃—CO— group out of the plane of the aromatic ring. This would in turn lead to a more uniform π -electron distribution in the aromatic ring (the effect may be demonstrated in the MO calculations by lowering the resonance integral between the carbonyl carbon and the ring carbon in the 1-position) and may account for the "irregular" difference in ring proton chemical shifts between the 6-methoxy derivatives of salicylaldehyde and *o*-hydroxyacetophenone evident in Table 3.

The correlations between the observed aromatic proton chemical shifts and the calculated π -electron densities shown in Fig. 5 have some features that are not so easily accounted for. The correlation curves — *i.e.* the straight lines fitted by the method of least squares — do not pass through the shift value of benzene ($\delta = 7.218$ ppm measured on a solution of 6 mole percent in carbondisulphide) when q equals zero. The slope of the fitted straight lines is dependent on the parameter sets used in the MO calculations — with parameter set 1 the slope is 7.1 ppm/electron and with parameter set 2 6.4 ppm/electron, both values slightly lower than those inferred from the series $C_5H_5^-$, C_6H_6 and $C_7H_7^+$.^{5,7}

The least squares treatment of the data in Fig. 5 shows that with parameter set 2 a slightly better fit to a straight line is obtained than with parameter set 1. In order to further illustrate the difference between the two parameter sets we have used the parameter values for the OCH_3 group in sets 1 and 2 to calculate the π -electron distribution in anisole and in *ortho*, *meta*, and *para* di-methoxybenzene for which accurate ^{13}C shifts have been measured by

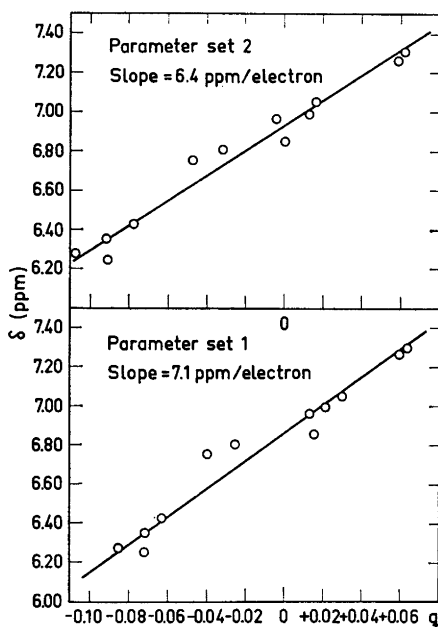


Fig. 5. The correlation between the observed ring proton shifts (δ) and the calculated π -electron excess charges (q) for the 3-, 4-, 5-, and 6-methoxy derivatives of salicylaldehyde.

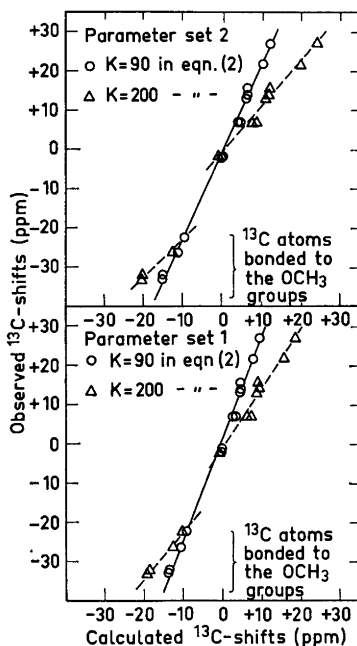


Fig. 6. The correlation between the ^{13}C -shifts observed in anisole, 1,2-, 1,3-, and 1,4-dimethoxybenzene (Lauterbur^{9, 10}) and the ^{13}C -shifts calculated according to the theory of Karplus and Pople (eqn. 2).

Higher values than originally found by Karplus and Pople of the constant multiplying the π -electron excess charge in eqn. 2 leads to better agreement between theory and experiment.

Lauterbur.¹⁰ According to the theory of ¹³C chemical shifts in aromatic hydrocarbons recently developed by Karplus and Pople⁴² the shifts should depend not only in the π -electron density but follow the relation

$$\Delta\sigma_A = K \cdot q_A + 46.0 (F_A - 0.399) \quad (2)$$

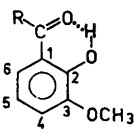
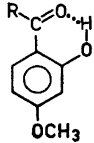
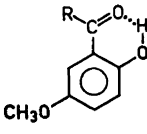
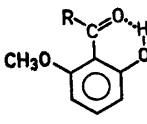
where $\Delta\sigma_A$ is the chemical shift (in ppm) of carbon atom C_A relative to benzene, q_A is the local π -electron excess charge and F_A the free valence index of the atom C_A . K equals $86.7 + 46.0 \lambda_X$ where λ_X is a polarity parameter accounting for the possibility of some ionic character in the C_A-X bond. For $X = H$ the value of λ is probably small — according to Karplus and Pople $0 < \lambda_H < 0.2$. On the basis of electronegativity differences one would expect the polarity parameter to be somewhat larger for C—O bonds than for C—H bonds. We will provisionally leave the question of the values of λ open. The above equation predicts a dependence of ¹³C shifts on the free valence index and this seems to be in agreement with observations of ¹³C shifts in a number of even alternant aromatic hydrocarbons where $q = 0$ for all atoms according to simple MO calculations.⁴² The equation predicts a dependence of $\Delta\sigma_A$ on the π -electron charge q_A in the correct direction but the actual numerical value of K seems to be about half that suggested from ¹³C shift measurements on aromatic molecules.^{6,9,10}

In Fig. 6 is shown a plot of the experimental ¹³C shifts *versus* the shifts calculated by use of eqn. 2. Two values of K have been employed, $K = 90$ and $K = 200$. For ring carbon atoms bonded to hydrogen the main contribution to $\Delta\sigma$ will arise through the first term in eqn. (2) since F_A is here comparatively constant and near 0.4. For the ring carbons bonded to the OCH₃ groups the F_A dependent term will make a larger contribution ($F_A \approx 0.2$).

With $K = 90$ the calculated ¹³C shifts are smaller than the experimental values both when parameters sets 1 and 2 are used. The general trend of the ¹³C shift is, however, very well accounted for — the straight line fitted to the points passes very near the zero point. With $K = 200$ the calculated ¹³C shifts for the ring carbons bonded to hydrogen are only slightly smaller than the observed values when q and F_A values are calculated with parameter set 2 — with parameter set 1 the discrepancy is somewhat larger. The ¹³C shifts for the ring atoms bonded to oxygen seem to fall on a separate correlation line which does not pass through the zero point. A larger value of the constant multiplying the F_A -dependent term in eqn. (2) would be required to make the two lines coincide.

Although the MO calculations presented in this work are far from being exhaustive, the choice of Coulomb and resonance integrals that gives the most representative picture of the π -electron distribution appears to be somewhat uncertain. In view of the reasonably good correlation found between the calculated π -electron charges and ring proton shifts — and also between the observed and calculated ¹³C shifts in methoxybenzenes — there seems, however, to be good reason to believe that with both parameter sets the Hückel method gives a good *qualitative* picture of the relative π -electron excess charges in the molecules considered. In view of the many drastic simplifications underlying the Hückel method this is indeed gratifying.

Table 2. Results of the Hückel MO calculations. The parameter sets used are given in the text.

	Basic parameter set	π -electron charge	R = H	R = CH ₃ inductive model	R = CH ₃ hyper- conjugative model	R = CH ₃ heteroatom model
	1	q_4	+ 0.0132	+ 0.0114	+ 0.0116	+ 0.0075
		q_5	- 0.0250	- 0.0254	- 0.0251	- 0.0257
		q_6	+ 0.0305	+ 0.0299	+ 0.0290	+ 0.0262
	2	q_4	- 0.0040	- 0.0056	- 0.0054	- 0.0091
		q_5	- 0.0319	- 0.0325	- 0.0321	- 0.0330
		q_6	+ 0.0165	+ 0.0161	+ 0.0151	+ 0.0130
	1	q_3	- 0.0848	- 0.0849	- 0.0848	- 0.0848
		q_5	- 0.0627	- 0.0635	- 0.0630	- 0.0643
		q_6	+ 0.0638	+ 0.0630	+ 0.0622	+ 0.0594
	2	q_3	- 0.1078	- 0.1079	- 0.1077	- 0.1078
		q_5	- 0.0771	- 0.0783	- 0.0775	- 0.0795
		q_6	+ 0.0620	+ 0.0615	+ 0.0605	+ 0.0582
	1	q_3	- 0.0394	- 0.0394	- 0.0393	- 0.0393
		q_4	+ 0.0215	+ 0.0193	+ 0.0197	+ 0.0149
		q_6	+ 0.0155	+ 0.0152	+ 0.0141	+ 0.0121
	2	q_3	- 0.0474	- 0.0476	- 0.0475	- 0.0476
		q_4	+ 0.0127	+ 0.0103	+ 0.0109	+ 0.0126
		q_6	+ 0.0001	+ 0.0003	- 0.0011	- 0.0022
	1	q_3	- 0.0717	- 0.0718	- 0.0716	- 0.0717
		q_4	+ 0.0596	+ 0.0577	+ 0.0580	+ 0.0539
		q_5	- 0.0719	- 0.0720	- 0.0718	- 0.0719
	2	q_3	- 0.0913	- 0.0914	- 0.0475	- 0.0815
		q_4	+ 0.0581	+ 0.0563	+ 0.0567	+ 0.0534
		q_5	- 0.0913	- 0.0914	- 0.0913	- 0.0807

It appears reasonable that the changes in π -electron distribution in the aromatic ring between the salicylaldehyde and *o*-hydroxyacetophenone derivatives brought about by the substitution of the aldehydic proton with a methyl group should be reflected in the changes in the ring proton shifts. For the ring proton in the 6-position diamagnetic anisotropy effects unfortunately seem to give a large contribution to the shift changes (*cf.* Table 3 and discussions above). Only the order of magnitude of this anisotropy effect can be calculated from the theory in its present state, and the following discussion will be limited to the ring protons in the 3-, 4-, and 5-positions.

From the calculated q values listed in Table 2 it is seen that both from the inductive model and the hyperconjugative model one would predict roughly the same changes in the electron density — the heteroatom model leads to

Table 3. Differences in the ring proton chemical shifts of the methoxy derivatives of salicylaldehyde and *o*-hydroxyacetophenone. Positive sign indicates that the proton shift in the *o*-hydroxyacetophenone derivative is found at higher applied field than the proton shift in the corresponding salicylaldehyde derivative.

Methoxy derivative	Ring proton	Difference in chemical shift (ppm)
3-Methoxy	H(4)	+ 0.079
	H(5)	+ 0.155
	H(6)	-0.134
4-Methoxy	H(3)	+ 0.064
	H(5)	+ 0.147
	H(6)	-0.161
5-Methoxy	H(3)	+ 0.060
	H(4)	+ 0.072
	H(6)	-0.111
6-Methoxy	H(3)	-0.010
	H(4)	+ 0.103
	H(5)	-0.018

slightly more pronounced changes than the two foregoing models. If we assume direct proportionality between the changes in chemical shifts and the changes in π -electron density, taking the proportionality constant to be of the order of 7–10 ppm/electron, we can estimate the changes in π -electron densities from the shift differences listed in Table 3. The changes estimated in this way are much smaller than the changes calculated with the MO method. More noteworthy is, however, the fact that the shift differences indicate changes in π -electron densities for the ring proton *meta* to the aldehyde or acyl groups of the same order of magnitude as the changes in the *para* position. In the 3-methoxy derivative the change in the *meta* proton shift is even nearly twice that in the *para* shift. This is completely at variance with the predictions from the Hückel MO theory.

This state of things is not well understood at present. It is perhaps not unlikely that the replacement of a hydrogen atom by a methyl group in a conjugated system leads to more uniform changes in the π -electron distribution which are not adequately described by any of the currently used methods: the inductive model, the hyperconjugative model, or the heteroatom model. Further investigations on this point seem well-motivated.

Spin coupling constants

The values found for the spin-spin coupling constants of ring protons on adjacent carbon atoms (Table 1) range from 7.8 to 9.2 c/s. It has been shown by Jonathan, Gordon and Dailey that in a series of aromatic hydrocarbons there is a good correlation between the π -bond order and the values of the spin

coupling constants for adjacent carbons.^{2,8} We have looked for a corresponding correlation in the present series of compounds but without success.

The values of the *meta* spin couplings show a comparatively larger variation and range from 0.8 to 3.2 c/s.

In the 4-, 5-, and 6-methoxy derivatives of salicylaldehyde the PMR signal of the aldehyde proton is observed as a doublet due to long-range spin coupling with the ring proton in the 3-position. In the case of the 6-methoxy derivative advantage was in fact taken of the observed long-range aldehyde coupling to assign the high field shift to the proton in the 3-position. This interpretation is further supported by the long-range OH and OCH₃ couplings to the ring also observed in this compound (see below). Long-range aldehyde couplings over four to five bonds have previously been observed in a number of substituted benzenes, thiophenes, furans and other aromatic compounds.⁴³⁻⁵¹ The stereo-specific nature of the long-range couplings in benzaldehydes is well established and this fact has been used for the determination of the rotational configuration of the aldehyde group in 3-nitrosalicylaldehyde⁵¹ and in a number of other aromatic aldehydes.⁵³

There has as yet been no satisfactory theoretical interpretation of the mechanism of the long-range aldehyde couplings. The relative sign of the aldehyde coupling in benzaldehydes has not yet been determined.* The signs of the long-range aldehyde couplings in 2- and 3-furanaldehyde⁵⁴ and in 3-bromo-2-thiophene-aldehyde⁵⁵ have recently been determined using proton magnetic triple resonance and transitory selective irradiation techniques. Positive** signs were observed for all long-range coupling constants except for the coupling $J_{\text{CHO}-\text{H}(4)}$ in 3-furanaldehyde. The signs alone do not permit unambiguous conclusions about the coupling mechanism since both long-range coupling transmitted *via* a $\sigma-\pi$ interaction as well as coupling transferred *via* the π -electrons is expected to lead to positive sign for coupling *via* five bonds. The π -electron transmitted coupling of proton spins should, according to theory,⁵⁷ be constant in magnitude but alter its sign of a methyl group is substituted for a directly bonded proton.

By the use of this $=\text{C}-\text{H} \rightarrow =\text{C}-\text{CH}_3$ replacement criterion^{57,58} Hoffman and Gronowitz have concluded that the mechanism of the aldehyde couplings in thiophene and furan aldehydes is not π -electron transmitted.^{49,50} Similarly, in the present case of substituted benzaldehydes, one can argue that the virtual absence of long-range couplings between the $\text{CH}_3-\text{C}=\text{O}$ group and the ring proton in the 3-position in the acetophenone derivatives speaks against a π -electron mechanism for the aldehyde couplings.

Long-range coupling of the phenolic OH proton with the ring proton in the 4-position is observed both in the salicylaldehyde and the *o*-hydroxyacetophenone derivatives. The coupling was in many cases observed only when very pure samples and freshly distilled solvents were used (*cf.* the experimental

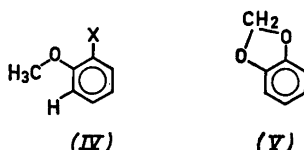
* Note added in proof: The sign of the long-range aldehyde coupling in 5-methoxysalicylaldehyde has recently been shown to be the same as that of the ring couplings. Forsén, S., Gestblom, B., Hoffman, R. A., Rodmar, S. and Alm, T. *To be published.*

** The signs of the aldehyde couplings were determined relatively to the ring coupling constant $J^{4,5}$. The absolute sign of this latter coupling is almost certainly positive in analogy with the *ortho* couplings in benzene.^{54,56}

section). Couplings of OH protons in aromatic molecules have previously been observed in methylsalicylate⁵⁹ and in 3-nitro and 5-nitrosalicylaldehyde.⁵¹

The experimental evidence strongly suggests a stereospecificity for the long-range OH couplings similar to that observed for aldehyde couplings. No theoretical interpretation of the mechanism of the OH couplings has been put forward.

When the phenolic hydrogen is replaced by a methyl group the methyl protons are found to be coupled to the ring proton four bonds away (Table 1). There is some evidence that this long-range methoxy coupling is also stereospecific. In aromatic methoxy derivatives where the OCH_3 group is *ortho* to



a relatively bulky substituent (IV, *e.g.* $\text{X} = \text{COCH}_3$ in 2-hydroxy-6-methoxy acetophenone⁴¹) and where the $\text{O}-\text{CH}_3$ axis should be preferably oriented away from the substituent, comparatively large coupling constants to the neighbouring ring proton are observed. Unfortunately there seems to be no direct way of orienting an OCH_3 group with the $\text{O}-\text{CH}_3$ axis pointing preferably *towards* a neighbouring substituent. However, it is interesting to note that in compounds containing a dioxymethylene ring (V) there seems to be no coupling between the $-\text{CH}_2-$ protons and the ring protons.

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