ACTA CHEMICA SCANDINAVICA 17 (1963) 1907–1916

Hydrogen Bonding Effects Studied by PMR and IR Spectroscopy and the π-Electron Distribution in Methoxy Derivatives of Salicylaldehyde and *o*-Hydroxyacetophenone

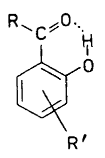
STURE FORSÉN and BJÖRN ÅKERMARK

Research Group for Nuclear Magnetic Resonance, Division of Physical Chemistry and Division of Organic Chemistry, The Royal Institute of Techonology, Stockholm 70, Sweden

The properties of the intramolecular hydrogen bonds in a number of methoxy derivatives of 2-hydroxyacetophenone and 2-hydroxybenzaldehyde have been studied with proton magnetic resonance and infrared spectroscopy. A correlation has been found between the hydroxyl proton chemical shifts, the infrared stretching frequencies of the O–H and C=O bonds and the charge on the carbonylic oxygen as calculated with a semiempirical molecular orbital method of the Hückel type. An attempt is made to interpret the variations of the hydroxyl proton chemical shifts in terms of Poples theory for hydrogen bond shifts.

For a study of the factors that govern the strengths of hydrogen bonds, aromatic molecules containing intramolecular hydrogen bonds offer many advantages. Fairly large variations in hydrogen bond strength can often be accomplished by substitutions in the aromatic nucleus and the changes in electron distribution may to a first approximation be obtained from molecular orbital (MO) calculations on the π-electron system.

In this work an attempt has been made to correlate the relative strengths of the intramolecular hydrogen bond in a number of methoxy derivatives of 2-hydroxyacetophenone and 2-hydroxybenzaldehyde with results from MO calculations of the Hückel type.



R = H and CH_3

R' = H and OCH_3

The relative strength of the hydrogen bonds have been studied with proton magnetic resonance (PMR) and infrared (IR) spectroscopy.

The significance of the IR stretching frequency of O—H and C=O bonds involved in hydrogen bonding as a measure of the strength of the hydrogen bond has been demonstrated in a number of investigations.[1]

Although PMR in comparison with IR spectroscopy has been applied to a very limited number of investigations on hydrogen bonded systems there seems to be general agreement that the change in the chemical shift of a proton upon formation of a hydrogen bond reflects the strength of the hydrogen bond.[2] However, the complex nature of the factors that may contribute to the chemical shift makes it necessary to discuss the PMR results obtained in this work in some detail; in particular the relation between the chemical shift of the hydrogen bonded proton and the electronic distribution in the atoms participating in the hydrogen bond will be discussed.

EXPERIMENTAL

All PMR spectra were recorded at 60 Mc/s using a Varian model "A 60" spectrometer. The temperature of the samples was 33.8 ± 0.3°C.

The spectra were calibrated with the side-band modulation technique [3] employing a Hewlett-Packard model 202 A frequency generator. The modulation frequencies were measured with a Hewlett-Packard electronic counter model 5512 A.

Tetramethylsilane (TMS) was used as internal standard and the shift values are reported as δ-values corresponding to the definition

$$\delta = 10^6 \cdot \frac{H_{\text{TMS}} - H}{H_{\text{TMS}}}$$

The PMR spectra were obtained on 3—6 % solutions in carbon tetrachloride with 0.5 % TMS added. The shift values of the PMR signals were found to be slightly concentration dependent (*cf.* the study of salicylaldehyde by Yamaguchi [4] and the study of anisol derivatives by Heathcock [5]) and the reported shift values have been obtained by extrapolation to infinite dilution. The uncertainty in the reported shift values due to extrapolation errors and to other factors is estimated to be on the order of 0.01—0.02 ppm. The IR measurements were done on a Perkin Elmer No. 21 spectrophotometer equipped with a sodium chloride prism. The instrument was calibrated against air and polystyrene film. Approximately 0.2 M solutions in carbon tetrachloride were measured. A 1 mm cell was used in the 3000 cm^{-1} region and a 0.1 mm cell in the 1600 cm^{-1} region. The uncertainty in the 1600 cm^{-1} region is estimated to be ± 3 cm^{-1}. In four cases the hydroxyl absortion was fairly well defined (Table 1) and the accuracy in absorption frequency is believed to be better than ± 20 cm^{-1}. For the other compounds, the approximate position of the band centre is given with an uncertainty of about 60 cm^{-1}. Although the evaluation of these hydroxyl frequencies is somewhat subjective, it seems probable that the values obtained show the trend of the frequency shift when the substitution is altered.

Materials

Melting points were taken on a Kofler block unless otherwise stated. Liquid compounds were fractionally distilled and solids were fractionally sublimed prior to measurements.

Salicylaldehyde, 2-hydroxy-3-methoxy benzaldehyde, m.p. 41—42°, and 2-hydroxyacetophenone were commercial samples. 2-Hydroxy-4-methoxybenzaldehyde, m.p. 40.5—41.5°, 2-hydroxy-5-methoxybenzaldehyde, m.p. 16—16.5° (in an open capillary), 2-hydroxy-6-methoxybenzaldehyde, m.p. 71.5—72.5°, 2-hydroxy-3-methoxyacetophenone, m.p. 53—54°, and 2-hydroxy-6-methoxyacetophenone, m.p. 57—58.5° were prepared by literature procedures.[6-10]

2-Hydroxy-4-methoxyacetophenone. Resacetophenone (1.05 g, 0.0070 mole) was methylated with methyl iodide and potassium carbonate in dry acetone. The crude product

(1 g) was chromatographed on celite (25 g) impregnated with dimethyl formamide (10 g), yielding pure 2-hydroxy-4-methoxyacetophenone (0.35 g, 32 %) m.p. 46—48°, lit 50°.[11]

2-Hydroxy-5-methoxyacetophenone was prepared by a method similar to that described by Oelschläger.[12] A mixture of 1.4-dimethoxybenzene (15 g, 0.11 mole) and acetic acid (6.6 g, 0.11 mole) was heated to 50° under dry nitrogen, saturated with boron trifluoride (14.5 g, 0.21 mole) and kept at 50° for 5 h. The product was treated with hydrochloric acid (2 N) and ice, extracted with ether, freed from neutral material and steamdistilled, giving 2-hydroxy5-methoxyacetophenone (6.5 g 36%), m.p. 52—52.5°, lit. 52°.

RESULTS AND DISCUSSION

The results of the proton magnetic resonance and infrared measurements are summarized in Table 1.

Table 1. Proton magnetic resonance shifts (δ) and infrared stretching frequencies (ν) of derivatives of *o*-hydroxybenzaldehyde and *o*-hydroxyacetophenone in solutions in carbon tetrachloride. Only the compounds 1, 2, 4 and 6 have fairly well defined O—H absorptions in IR.

Compound	δ_{OH} ppm	δ_{CHO} ppm	δ_{COCH_3} ppm	δ_{OCH_3} ppm	$\nu_{C=O}$ cm^{-1}	ν_{O-H} cm^{-1}
1. 2-Hydroxybenzaldehyde	10.91	9.86	—	—	1670	3140
2. 2-Hydroxy-3-methoxybenzaldehyde	10.82	9.88	—	3.86	1660	3160
3. 2-Hydroxy-4-methoxybenzaldehyde	11.36	9.65	—	3.83	1663	3080
4. 2-Hydroxy-5-methoxybenzaldehyde	10.50	9.74	—	3.73	1669	3180
5. 2-Hydroxy-6-methoxybenzaldehyde	11.84	10.25	—	3.83	1650	3000
6. 2-Hydroxyacetophenone	12.06	—	2.55	—	1645	3040
7. 2-Hydroxy-3-methoxyacetophenone	12.24	—	2.54	3.80	1650	2980
8. 2-Hydroxy-4-methoxyacetophenone	12.54	—	2.48	3.78	1635	2960
9. 2-Hydroxy-5-methoxyacetophenone	11.61	—	2.52	3.72	1655	3060
10. 2-Hydroxy-6-methoxyacetophenone	13.03	—	2.58	3.87	1632	2900

The resonance position of the proton in the intramolecular hydrogen bond (δ_{OH}) is seen to vary over a range of 2.53 ppm among the different salicylaldehyde and *o*-hydroxyacetophenone derivatives, and the variation in δ_{OH} shows nearly the same dependence on the position of the methoxy substituent among the salicylaldehyde derivatives as it does among the *o*-hydroxyacetophenone derivatives. However, the value of δ_{OH} in the *o*-hydroxyacetophenone derivatives is on the average displaced 1.21 ppm towards lower fields.

This average difference in the OH-shift between the salicylaldehyde and *o*-hydroxyacetophenone derivatives does not appear to be explainable as a long range shielding effect due to the replacement of a hydrogen atom with a methyl group. If we neglect the difference in the longitudinal and transverse susceptibilities ($\chi_L - \chi_T$) for C—H bonds a value of -6×10^{-30} cm^3/molecule can be taken for $\chi_L - \chi_T$ in C—C bonds.[13] With a reasonable value of 3 Å for the distance between the OH-proton and the midpoint of the C—CH_3 bond in *o*-hydroxyacetophenone a deshielding effect on the OH-resonance of only *ca.* 0.08 ppm is calculated.

It is thus necessary to seek a different explanation for the fairly large effect on the OH-resonance position caused by the substitution of the aldehydic hydrogen with a methyl group, and it appears likely that the effect is connected with the electron releasing properties of the methyl group. This possibility is further discussed below.

The observed dependence of δ_{OH} on the position of the methoxy substituent in the aromatic nucleus may be expected to be governed by the variation in electron distribution among the derivatives and to some extent also by steric factors, diamagnetic anisotropy and other field effects arising from the atoms and bonds in the methoxy group. These field effects are expected to be most pronounced when the methoxy group is in 3- or 6-position.

There is some reason to believe that the steric "crowding" effects of the methoxy group have relatively little influence on δ_{OH}. One would expect the steric effects to be more pronounced in the 6-methoxy derivative of *o*-hydroxyacetophenone than in the corresponding derivative of salicylaldehyde. The difference in δ_{OH} between the two 6-substituted derivatives (1.19 ppm) has however almost the same value as the average difference in δ_{OH} between the other salicylaldehyde and *o*-hydroxyacetophenone derivatives studied (1.21 ppm).

The methoxy group in the 3-substituted derivatives may modify the resonance position of the OH-proton through direct field effects. Apart from the effect arising from the diamagnetic anisotropy of the C—O bonds there is also a second effect that may be of importance. It appears from suitable molecular models of the 3-methoxysubstituted derivatives that there is a certain restriction of the rotation of the methoxy group around the oxygen-aromatic carbon bond. (This restriction is also apparent in the models of the 6-methoxy derivatives). The preferred orientation of the methoxy group should thus have the oxygen-methyl bond directed away from the neighbouring substituent, which will consequently be exposed to the "lone-pair" electrons of the oxygen atom. Electric distortion effects [14] produced by the lone-pair dipoles may be expected to shift the resonance position of the protons on the substituent towards lower fields. This latter mechanism may account for the exceptionally low field resonance position of the aldehydic proton in 6-methoxysalicylaldehyde (see Table 1) in which the lone-pair electrons of the methoxy group and the aldehydic hydrogen may come fairly close. This interaction between the methoxy group and the aldehydic proton has the characteristics of a weak hydrogen bond.

The electric distortion effect as well as the diamagnetic anisotropy effect of the methoxy groups fall off rapidly with the distance. Their influence on the resonance position of the hydroxyl proton in the 3-methoxy derivatives should be much less than the effect on the aldehydic proton resonance in 6-methoxysalicylaldehyde and the OH-resonance will most probably not be displaced more than about 0.1—0.2 ppm towards lower fields. Although the anisotropy effects and the electric distortion effects of the methoxy groups thus may have some influence on the resonance position of the proton in the intramolecular hydrogen bond — particularly in the 3-methoxy substituted derivatives — it appears however likely that the major factor responsible for the variations in δ_{OH} among the methoxy derivatives is the variation in the electron distribution in the atoms participating in the intramolecular hydrogen bond.

This conclusion is further supported by the fact that there is a good correlation between δ_{OH} and the stretching frequency of the chelated carbonyl group (Fig. 1), and also between δ_{OH} and the stretching frequency of the phenolic OH-group (Fig. 2). The correlations indicate that not only the infrared

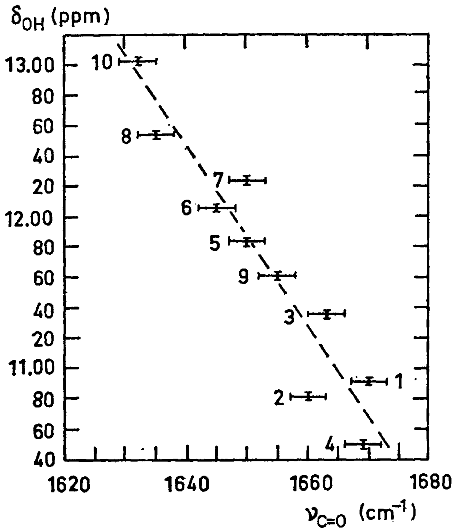


Fig. 1. Correlation of hydroxyl proton chemical shift (δ_{OH}) with infrared stretching frequency of the C=O bond. The numbering of the compounds refers to Table 1.

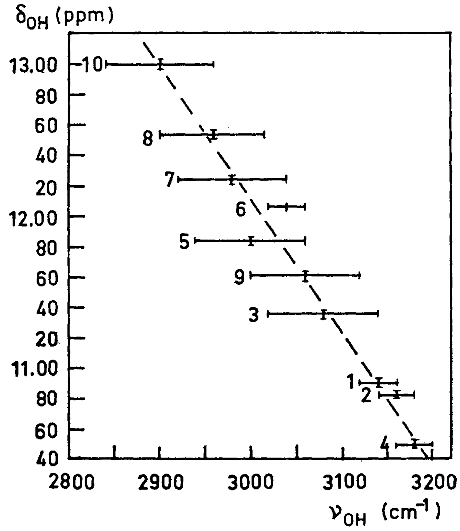


Fig. 2. Correlation of hydroxyl proton chemical shift (δ_{OH}) with the infrared stretching frequency of the O—H bond (ν_{OH}). The numbering of the compounds refers to Table 1.

stretching frequencies of the hydroxyl O—H bond and the carbonyl C=O bond but also the chemical shift of the hydroxyl proton reflect the strength of the hydrogen bond. Similar correlations between IR and PMR data have been obtained in other systems containing inter- and intramolecular hydrogen bonds.[15-19]

MO CALCULATIONS

In order to obtain a qualitative measure of the variations in the electron distribution among the compounds included in Table 1 the electronic densities have been calculated by a semi-empirical MO method in the Hückel approximation. As is common in the semi-empirical MO methods the Coulomb and resonance integrals for the hetero atoms are referred to the Coulomb integral for carbon (α) and the resonance integral for the carbon-carbon double bond (β). Furthermore, it will be assumed that the possible electron delocalisation *via* the intramolecular hydrogen bond may be neglected to a first approximation.

The following basic parameters have been used

$$\alpha_{=O} = \alpha + \beta$$
$$\alpha_{-O-} = \alpha + 2\beta$$
$$\beta_{C=O} = \beta$$
$$\beta_{C-O} = 0.7\beta$$

These or very similar parameters have been widely used in MO calculations of oxygen compounds.[20] It should be noted, however, that the electronic distribution in ketones and aldehydes obtained with more elaborate self-consistent field MO calculations of the Pariser-Parr-Pople type is more uniform than the distribution obtained with Hückel-type MO calculations.[21] The absolute values of the electronic densities calculated in this work should most likely be regarded as less significant than the relative values.

In order to allow for the structural differences between the aldehyde and the keto group in the MO calculations it is necessary to introduce an additional parameter. The problem of allowing for the different effects of hydrogen atoms and methyl groups as substituents on conjugated systems has been solved in a number of ways in MO calculations. A review of the subject is found in the recent book by Streitwieser.[22] In this work the "inductive" model has been used. In this model the effect of a methyl substituent in a conjugated molecule is introduced in the MO calculations by changing the value of the Coulomb integral of the substituted atom so as to make this atom more electro-positive. A range of numerical values for this inductive correction was initially tried in the present calculations but for reasons that will be discussed below a value of -0.075β was finally chosen.

The results of the MO calculations are summarised in Figs. 3—7, in which the numbers within parentheses refer to the acetophenone derivatives.

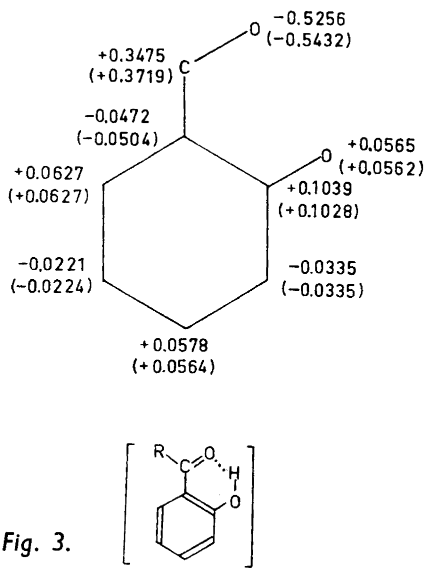


Fig. 3.

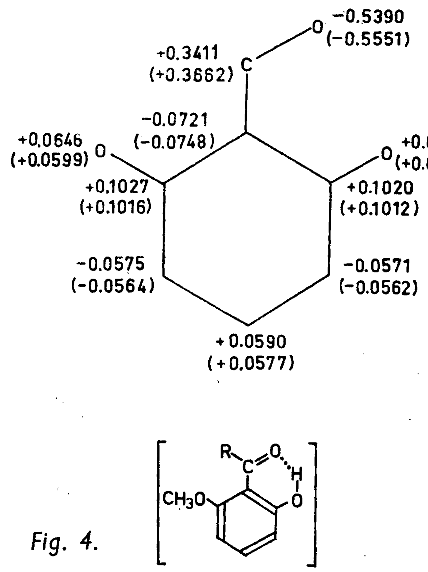
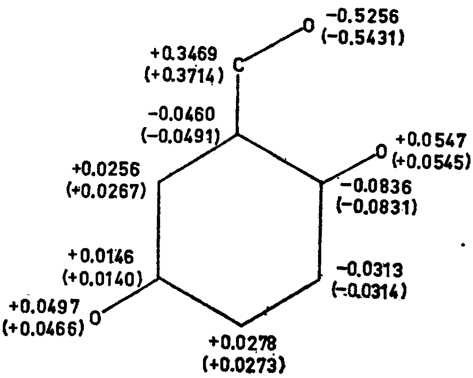


Fig. 4.



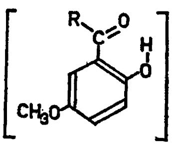
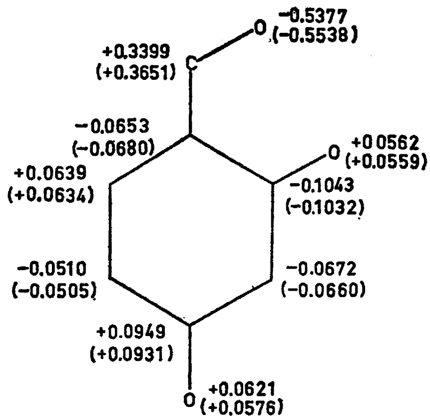


Fig. 5.



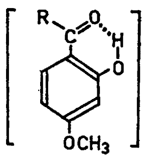
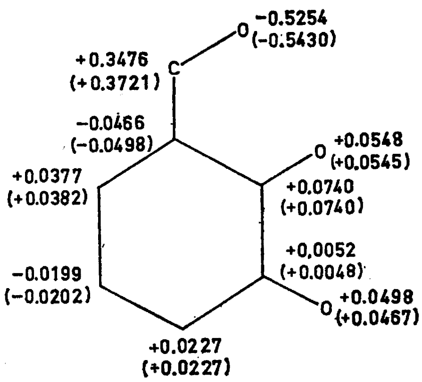


Fig. 6.



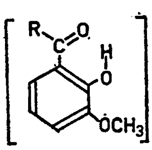


Fig. 7.

Figs. 3–7. Charge distributions of the π-electron system in derivatives of salicylaldehyde (R=H) and *o*-hydroxyacetophenone ($R=CH_3$). The numbers within parentheses refer to the *o*-hydroxyacetophenone derivatives.

The variations in the charge density of the phenolic oxygen are calculated to be very small and there is no apparent correlation between δ_{OH}, ν_{OH} and $\nu_{C=O}$ and the charge on the phenolic oxygen. On the other hand there is a definite correlation between the calculated charge density on the carbonylic oxygen and the value of δ_{OH}, ν_{OH} and $\nu_{C=O}$. (It is hardly to be expected that the correlation should be rigorous). The correlation is in the sense that an increased charge on the carbonylic oxygen accompanies a displacement of the OH-resonance towards lower fields, and the infrared stretching vibrations of the OH and C=O bonds towards lower frequencies.

Through a systematic variation of the value of the inductive parameter for the carbonylic carbon in the *o*-hydroxyacetophenone derivatives it was found that the results for the salicylaldehyde and *o*-hydroxyacetophenone derivatives were best correlated when the inductive parameter was -0.075β.

A graph of the correlation between the phenolic OH-shift and the charge density of the carbonylic oxygen atom is reproduced in Fig. 8.

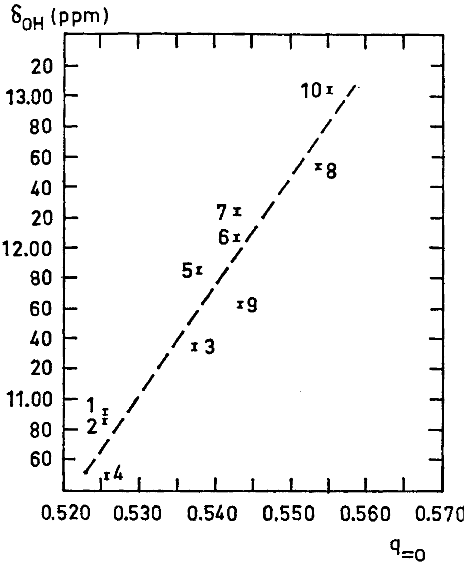


Fig. 8. Correlation of the hydroxyl proton chemical shift (δ_{OH}) and the calculated charge density of the carbonylic oxygen ($q_{=O}$). The numbering of the compounds refers to Table 1

The approximately linear correlation between δ_{OH} and the infrared stretching frequencies $\nu_{C=O}$ and ν_{OH} demonstrated in Figs. 1 and 2 implies that with the value -0.075β for the inductive parameter there is also a approximately linear correlation between the calculated charge on the carbonylic oxygen and the infrared stretching frequencies. This fact seems to justify the procedure of adjustment of the inductive parameter. The fairly small value obtained for the inductive parameter seems furthermore to be in agreement with the results of more advanced MO calculations.[23]

The feasibility of the described procedure of adjustment of the inductive "hyperconjugation" parameter does not necessarily mean that the inductive model is the only "hyperconjugation" model that can account for the changes in δ_{OH} between the salicylaldehyde and *o*-hydroxyacetophenone derivatives. Preliminary calculations indicate that other models may work equally well.

The correlation obtained between the charge on the carbonylic oxygen and δ_{OH}, ν_{OH} and $\nu_{C=O}$ indicates that the strength of the intramolecular hydrogen bond is increased as the negative charge on the oxygen atom increases, and that the differences in hydrogen-bond strengths among the derivatives of salicylaldehyde and *o*-hydroxyacetophenone may be interpreted as due to the different electron-releasing properties of methyl groups and hydrogen atoms. If the strength of the hydrogen bond may be said to a first approximation to be governed by purely electrostatic interactions a correlation of the above type would be expected. In view of the approximations involved in this work it does not appear appropriate to draw too far-reaching conclusions on the nature of the hydrogen bond from the correlations obtained.

THE CHEMICAL SHIFT OF THE HYDROGEN BONDED HYDROXYL PROTON

The factors responsible for the changes in the chemical shift of a proton upon formation of a hydrogen bond are not well understood. Although the change generally is in the direction of reduced diamagnetic shielding it appears far from certain that the change is indicative of a reduced diamagnetic shielding around the proton.

According to Pople [24] the chemical shift of a proton in a hydrogen bond $X-H\cdots Y$ may — apart from a directly reduced diamagnetic shielding — also be effected by the influence of the Y group on the electronic circulation in the X—H bond. In an approximative model for calculating the resulting chemical shift [24,25] the hydrogen bond is assumed to be essentially electrostatic in character and the distorting effect of the donor atom Y on the X—H group is approximated by the distorting effect of a homogeneous electric field on a free hydrogen atom. This model leads to the following equation for the electric distortion shift (δ_e)

$$\delta_e = -\frac{881}{216}\frac{a^3E^2}{m_ec^2} \tag{1}$$

where a is the Bohr radius, E the electric field strength, m_e the electron mass and c the velocity of light. The sign convention is such that a negative value of δ_e means a displacement of the proton resonance towards lower fields.

If the variation of the electric field over the dimensions of the hydrogen atom is neglected we have for the effect of a point charge q on the chemical shift

$$\delta = -\frac{881}{216}\frac{a^3q^2}{m_ec^2r^4} \tag{2}$$

where r is the distance from the point charge to the hydrogen atom. (A convenient graph of eqn. (2) is given in Ref.[26]).

The result obtained in the present work is in qualitative agreement with eqn. (2) in the sense that an increasing charge on the carbonyl oxygen parallels a displacement of the OH-proton resonance towards lower fields. The variations in the OH-resonance position as calculated from eqn. (2) with reasonable values of r (1.2—1.5 Å) are, however, about one order of ten smaller than the actually observed values, and furthermore the dependence of δ_{OH} on $q_{=O}$ seems to be linear rather than quadratic. It should be remembered, however, that both in the model of the electric distortion effects and in the present MO calculations drastic simplifications have been made.

It would naturally be of interest to calculate the electronic distribution in the compounds included in this work by more elaborate quantum chemical methods. This will be the subject of a forthcoming paper.

Acknowledgements. The authors like to thank Professor H. Erdtman, Dr. E. Forslind and Professor O. Lamm for facilities put at our disposal and Dr. E. Forslind also for valuable discussions. The authors also like to thank Dr. R. Carter for linquistic criticism and Mr. U. Johannesson for technical assistance. The work has been sponsored by a grant from the *Swedish Technical Research Council* and the cost of the NMR spectrometer has been defrayed by a grant from *Knut and Alice Wallenbergs Stiftelse.*

REFERENCES

1. Pimentel, G. C. and McClellan, A. L. *The Hydrogen Bond*, W. H. Freeman and Co, San Francisco 1960.
2. Pople, J. A., Schneider, W. G. and Bernstein, H. J. *High-resolution Nuclear Magnetic Resonance*, McGraw-Hill Book, Co., Inc., New York 1959, Chapter 15.
3. Arnold, J. A. and Packard, M. E. *J Chem Phys.* **19** (1951) 1608.
4. Yamaguchi, I. *Bull. Chem. Soc Japan* **34** (1961) 353.
5. Heathcock, C. *Can. J. Chem.* **40** (1962) 1865.
6. Ott, E. and Nauen, E. *Ber.* **55** (1922) 920.
7. Tiemann, F. and Piest, R. *Ber.* **14** (1881) 1982.
8. Wittig, G. *Angew. Chem.* **53** (1940) 241.
9. Limaye, D. B. *Rasayanam* **1** (1936) 1; *Chem. Abstr.* **31** (1937) 2206; Aurell, A. and Frye, J. B. *Org. Syn.* Coll. Vol. III, p. 281; Nakazawa, K. *J. Pharm. Soc. Japan,* **59** (1939)495; *Chem. Abstr.* **34** (1940) 106.
10. Baker, W., Brown, N. C. and Scott, J. A. *J. Chem. Soc.* **1939** 1922.
11. Tahara, Y. *Ber.* **24** (1891) 2459.
12. Oelschläger, H. *Arch. Pharm.* **288** (1955) 102; *Chem. Abstr.* **50** (1956) 3298 a.
13. Jackman, L. M. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, London 1959, Chapter 7.2.
14. Ref.[2], p. 408.
15. Forsén, S. and Nilsson, M. *Acta Chem. Scand.* **13** (1959) 1383.
16. Reeves, L. W., Allan, E. A. and Strømme, K. O. *Can. J. Chem.* **38** (1960) 1249.
17. Gränacher, I. *Helv. Phys. Acta* **34** (1961) 272.
18. Merrill, J. R. *J. Phys. Chem.* **65** (1961) 2023.
19. Allan, E. A. and Reeves, L. W. *J. Phys. Chem.* **66** (1962) 613.
20. Streitwieser, Jr., A. *Molecular Orbital Theory for Organic Chemists* John Wiley & Sons, New York 1961, Chapter 5.
21. McClelland, B. J. *Trans. Faraday Soc.* **57** (1961) 2073.
22. Ref.[20], Chapter 5.7.
23. Ref.[20], p. 248.
24. Pople, J. A. in Hadzi, D. and Thompson, H. W. (Ed.) *Hydrogen Bonding*, Pergamon Press, London 1959, p. 71.
25. Marshall, T. W. and Pople, J. A. *Mol. Phys.* **1** (1958) 199.
26. Forsén, S. *Arkiv Kemi* **20** (1963) 41.

Received April 5, 1963.