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

STURE FORSEN and BJÖRN ÅKERMARK

Research Group for Nuclear Magnetic Resonance, Division of Physical Chemistry and Division of Organic Chemistry, The Royal Institute of Technology, 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 carboxylate 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 $\pi$-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.

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 technique3 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 Yamaguchi4 and the study of anisol derivatives by Heathcock4) 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 absorption 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 Kofer 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.5–10

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
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(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 Oeschläger.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-hydroxy-5-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.

<table>
<thead>
<tr>
<th>Compound</th>
<th>δOH ppm</th>
<th>δCHO ppm</th>
<th>δCOCH₃ ppm</th>
<th>νC=O cm⁻¹</th>
<th>νO—H cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 2-Hydroxybenzaldehyde</td>
<td>10.91</td>
<td>9.86</td>
<td>—</td>
<td>1670</td>
<td>3140</td>
</tr>
<tr>
<td>2. 2-Hydroxy-3-methoxybenzaldehyde</td>
<td>10.82</td>
<td>9.88</td>
<td>—</td>
<td>1660</td>
<td>3160</td>
</tr>
<tr>
<td>3. 2-Hydroxy-4-methoxybenzaldehyde</td>
<td>11.36</td>
<td>9.65</td>
<td>3.86</td>
<td>1663</td>
<td>3080</td>
</tr>
<tr>
<td>4. 2-Hydroxy-5-methoxybenzaldehyde</td>
<td>10.50</td>
<td>9.74</td>
<td>3.73</td>
<td>1669</td>
<td>3180</td>
</tr>
<tr>
<td>5. 2-Hydroxy-6-methoxybenzaldehyde</td>
<td>11.84</td>
<td>10.25</td>
<td>3.83</td>
<td>1650</td>
<td>3000</td>
</tr>
<tr>
<td>6. 2-Hydroxyacetophenone</td>
<td>12.06</td>
<td>—</td>
<td>2.55</td>
<td>1645</td>
<td>3040</td>
</tr>
<tr>
<td>7. 2-Hydroxy-3-methoxyacetophenone</td>
<td>12.24</td>
<td>—</td>
<td>3.80</td>
<td>1650</td>
<td>2980</td>
</tr>
<tr>
<td>8. 2-Hydroxy-4-methoxyacetophenone</td>
<td>12.54</td>
<td>—</td>
<td>3.78</td>
<td>1655</td>
<td>2960</td>
</tr>
<tr>
<td>9. 2-Hydroxy-5-methoxyacetophenone</td>
<td>11.61</td>
<td>—</td>
<td>3.72</td>
<td>1655</td>
<td>3060</td>
</tr>
<tr>
<td>10. 2-Hydroxy-6-methoxyacetophenone</td>
<td>13.03</td>
<td>—</td>
<td>3.87</td>
<td>1632</td>
<td>2900</td>
</tr>
</tbody>
</table>

The resonance position of the proton in the intramolecular hydrogen bond (δOH) is seen to vary over a range of 2.53 ppm among the different salicylddehyde and o-hydroxyacetophenone derivatives, and the variation in δOH shows nearly the same dependence on the position of the methoxy substituent among the salicylddehyde derivatives as it does among the o-hydroxyacetophenone derivatives. However, the value of δOH 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 salicylddehyde 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 (χL—χT) for C—H bonds a value of —6 × 10⁻³⁰ cm²/molecule can be taken for χL—χT 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—CH₃ bond in o-hydroxyacetophenone a de-shielding 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 $\delta_{\text{OH}}$ 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 $\delta_{\text{OH}}$. 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 $\delta_{\text{OH}}$ between the two 6-substituted derivatives (1.19 ppm) has however almost the same value as the average difference in $\delta_{\text{OH}}$ 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 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 $\delta_{\text{OH}}$ 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 $\delta_{\text{OH}}$ and the stretching frequency of the chelated carbonyl group (Fig. 1), and also between $\delta_{\text{OH}}$ and the stretching frequency of the phenolic OH-group (Fig. 2). The correlations indicate that not only the infrared

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1}
\caption{Correlation of hydroxyl proton chemical shift ($\delta_{\text{OH}}$) with infrared stretching frequency of the C=O bond. The numbering of the compounds refers to Table 1.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2}
\caption{Correlation of hydroxyl proton chemical shift ($\delta_{\text{OH}}$) with the infrared stretching frequency of the O–H bond ($\nu_{\text{OH}}$). The numbering of the compounds refers to Table 1.}
\end{figure}

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 ($\alpha$) and the resonance integral for the carbon-carbon double bond ($\beta$). 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

\[ a_{\omega,0} = a + \beta \]
\[ a_{\alpha,0} = a + 2\beta \]
\[ \beta_{\omega,0} = \beta \]
\[ \beta_{\alpha,0} = 0.7\beta \]

These or very similar parameters have been widely used in MO calculations of oxygen compounds.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 $-0.075\beta$ 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.

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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=CH₃). The numbers within parentheses refer to the α-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 δ₂OH, νOH and νC=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 $\delta_{\text{OH}}$, $\nu_{\text{OH}}$ and $\nu_{\text{C}=\text{O}}$. (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 $-0.075\beta$.

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 ($\delta_{\text{OH}}$) and the calculated charge density of the carbonylic oxygen ($q_{\text{C}=\text{O}}$). The numbering of the compounds refers to Table 1.](image)

The approximately linear correlation between $\delta_{\text{OH}}$ and the infrared stretching frequencies $\nu_{\text{C}=\text{O}}$ and $\nu_{\text{OH}}$ demonstrated in Figs. 1 and 2 implies that with the value $-0.075\beta$ 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 $\delta_{\text{OH}}$ 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 $\delta_{\text{OH}}$, $\nu_{\text{OH}}$ and $\nu_{\text{C}=\text{O}}$ indicates that the strength of the intramolecular hydrogen...
H Y D R O G E N   B O N D I N G

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-hydroxycetophenone 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 shield-
ing around the proton.

According to Pople\textsuperscript{24} the chemical shift of a proton in a hydrogen bond
$X - H \ldots Y$ 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\textsuperscript{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 ($\delta_e$)

$$\delta_e = -\frac{881}{216} \frac{a^3 E^2}{m_e c^2}$$

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
$\delta_e$ 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

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

where $r$ is the distance from the point charge to the hydrogen atom. (A con-
venient graph of eqn. (2) is given in Ref.\textsuperscript{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 varia-
tions 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 $\delta_{OH}$ 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.

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