SOLVENT EFFECTS ON PROTON CHEMICAL SHIFTS IN THIOPHENES

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ABSTRACT

The effects of various polar and non-polar solvents on the proton chemical shifts in thiophene and its derivatives have been investigated. Results have been interpreted in terms of possible solute-solute, solute-solvent and solvent-solvent interactions in these systems.

INTRODUCTION

When an aromatic solute is dissolved in a non-aromatic solvent, the proton resonance lines due to the former are shifted towards lower field; the effect increases on dilution [Abraham (1961); Bothner-By and Glick (1957); Buckingham et al. (1960); Hutton and Richards (1960); Hutton and Richards (1962); Hutton and Schneider (1962); Khetrapal (1965); Klinck and Stothers (1962); Reeves and Schneider (1957); Schaefer and Schneider (1960); Schneider (1962); Suhr (1963); Zimmerman and Foster (1957)]. On the other hand, the resonance lines due to the solvent protons are shifted towards higher fields. These results have been explained on the basis of magnetic anisotropy of aromatic molecules. In the presence of an external magnetic field, the induced circulation of the pi-electrons generates a secondary magnetic field which reinforces the applied field at a point in the plane of the aromatic ring but opposes it at a point above or below it. When two molecules are close to one another, the intermolecular effect of such ring currents on the chemical shift would depend upon their relative orientation. However, in liquids one observes an average over all possible orientations. Since, the aromatic molecules are disc-shaped, there is a greater probability for a neighbouring molecule to be above or below the molecular plane of the former. This causes the magnetic resonance of the nuclei in the latter to occur at a higher field. This effect would decrease with the increase in the average distances between the two molecules. Thus, the dilution of

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an aromatic compound with a solvent shifts the resonance signals of the former to lower fields. In the limit of infinite dilution, the shift approaches to that of an isolated molecule. An opposite effect is observed when an isotropic solute is diluted with an aromatic solvent. Such studies have been made on benzenes in great detail and to some extent on heterocycles such as picoline, pyrrole and thiophene (Schaefer and Schneider, 1960). The present paper reports a detailed investigation on the effect of various solvents on the proton chemical shifts in thiophene and its derivatives.

**EXPERIMENTAL**

(1) **Chemicals**

(i) Thiophene was obtained from L. Light and Co.

(ii) 2-Iodothiophene and 2-acetylthiophene were prepared by standard methods [Minnis (1932), Hartough (1952)].

(iii) Chloroform, cyclohexane, methyl alcohol and carbon tetrachloride were E. Merck’s G.R. grade reagents.

(iv) Acetone and methyl cyanide were of B.D.H. ‘Analar’ grade. All the chemicals were distilled before use.

(2) **NMR Measurements**

Thiophene, 2-iodothiophene and 2-acetylthiophene were dissolved in different solvents in various proportions and the chemical shifts for both solute and the solvent protons were measured relative to cyclohexane as an external standard on a Varian High Resolution NMR spectrometer, operating at 60 Mc./s. Bulk diamagnetic susceptibility correction was applied to the measured chemical shifts. The shifts were finally expressed relative to the corresponding protons in the pure solute or the pure solvent as the case may be.

The shifts were plotted against the mole fraction of the solute and the curves obtained were extrapolated to infinite dilution to obtain the proton shift in the isolated solute molecule (Khetrapal, 1965). This gives the dilution shift (Δδ) for the solute protons. The dilution shift for the solvent protons (Δδ)_{sol} was obtained in a similar manner.

The experimental error in the estimation of the dilution shift does not exceed ± 0.05 ppm.
RESULTS

The data of dilution shifts for the solvent and the solute protons are given in Tables I, II and III for thiophene, 2-iodothiophene and 2-acetylthiophene systems respectively.

**TABLE I**

*Dilution shifts in ppm. for various protons in Thiophene-Solvent mixtures*

Solute shifts are relative to \((\delta_1) = 0.00\) ppm. and solvent shifts are relative to \((\delta_1)_{\text{sol.}} = 0.00\) ppm. \([\delta_1] \text{ relative to TMS } = -6.61\) ppm.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>((\Delta \delta)_a)</th>
<th>((\Delta \delta)_b)</th>
<th>((\Delta \delta)_{\text{sol.}})</th>
<th>((\Delta \delta)_{\text{sol.}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane</td>
<td>-0.45</td>
<td>0.13</td>
<td>Negligible</td>
<td>0.35</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>-0.59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>-0.08</td>
<td>0.70</td>
<td>-0.10</td>
<td>0.00</td>
</tr>
<tr>
<td>Chloroform</td>
<td>-0.63</td>
<td>0.05</td>
<td>-0.08</td>
<td>1.19</td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>-0.72</td>
<td>0.06</td>
<td>-0.18</td>
<td>0.60</td>
</tr>
<tr>
<td>Acetone</td>
<td>-0.98</td>
<td>-0.70</td>
<td>-0.28</td>
<td>0.43</td>
</tr>
<tr>
<td>Methyl cyanide</td>
<td>-0.98</td>
<td>-0.70</td>
<td>-0.28</td>
<td>0.43</td>
</tr>
</tbody>
</table>

\((\Delta \delta_1) = 0.60\) ppm.

**TABLE II**

*Dilution shifts in ppm. for various protons in 2-iodothiophene-solvent mixtures*

Solute shifts are relative to \((\delta_1) = 0.00\) ppm. and solvent shifts relative to \((\delta_1)_{\text{sol.}} = 0.00\) ppm. \([\delta_1] \text{ relative to TMS } = -6.45\) ppm. for proton 4 and \(-6.92\) ppm. for protons 3 and 5.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>((\Delta \delta)_4)</th>
<th>((\Delta \delta)_3)</th>
<th>((\Delta \delta)_5)</th>
<th>((\Delta \delta)_{\text{sol.}})</th>
<th>((\Delta \delta)_{\text{sol.}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane</td>
<td>-0.19</td>
<td>-0.20</td>
<td></td>
<td>Negligible</td>
<td>0.21</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>-0.33</td>
<td>-0.31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>0.50</td>
<td>0.50</td>
<td>0.13</td>
<td>0.13</td>
<td>-0.36</td>
</tr>
<tr>
<td>Chloroform</td>
<td>-0.40</td>
<td>-0.36</td>
<td>-0.12</td>
<td>-0.08</td>
<td>0.53</td>
</tr>
<tr>
<td>Acetone</td>
<td>-0.45</td>
<td>-0.43</td>
<td>-0.68</td>
<td>-0.20</td>
<td>-0.18</td>
</tr>
</tbody>
</table>

\((\Delta \delta_1) \sim -0.33\) ppm.)
### Table III

**Dilution shifts in ppm. for various protons in 2-acetyl-thiophene-solvent mixtures**

Solute shifts are relative to \((\delta_1) = 0.00\) ppm. and solvent shifts relative to \((\delta_2)_{sol.} = 0.00\) ppm.

\[ (\delta_4) \text{ relative to TMS} = -6.77 \text{ for proton 4 and } -7.39 \text{ for protons 3 and 5} \]

<table>
<thead>
<tr>
<th>Solvent</th>
<th>((\Delta \delta)_4)</th>
<th>((\Delta \delta)_3) and ((\Delta \delta)_5)</th>
<th>((\Delta \delta)_4)</th>
<th>((\Delta \delta)_3) and ((\Delta \delta)_5)</th>
<th>((\Delta \delta)_{sol.})</th>
<th>((\Delta \delta)_{sol.})</th>
<th>((\Delta \delta)_{sol.}) (Acetyl protons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon tetrachloride</td>
<td>-0.41</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.40</td>
</tr>
<tr>
<td>Chloroform</td>
<td>-0.43</td>
<td>-0.32</td>
<td>(\ldots)</td>
<td>Negligible</td>
<td></td>
<td></td>
<td>-0.25</td>
</tr>
<tr>
<td>Benzene</td>
<td>0.60</td>
<td>0.85</td>
<td>0.27</td>
<td>0.52</td>
<td>-0.25</td>
<td>0.08</td>
<td>-0.13</td>
</tr>
<tr>
<td>Acetone</td>
<td>-0.43</td>
<td>-0.42</td>
<td>-0.53</td>
<td>-0.14</td>
<td>-0.13</td>
<td>-0.24</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.26</td>
<td>0.07</td>
<td>-0.40</td>
</tr>
</tbody>
</table>

\[ (\Delta \delta) \sim -0.37 \text{ ppm.} \]

(A) *Thiophene Solutions*

In pure thiophene, the chemical shift between \(\alpha\) and \(\beta\) protons is very small and it is difficult to estimate it. On dilution with non-polar solvents like carbon tetrachloride, cyclohexane and benzene, there is no remarkable change in the relative chemical shift between \(\alpha\) and \(\beta\) protons although the mean chemical shift of the ring protons shows a remarkable change. Dilution shifts the mean chemical shift towards lower field in carbon tetrachloride and cyclohexane solutions but towards the higher field in benzene. In chloroform and methyl alcohol, there is no remarkable change in the relative chemical shift between \(\alpha\) and \(\beta\) protons on dilution. However, when thiophene is diluted with polar solvents like acetone and methyl cyanide, the mean chemical shift as well as the relative chemical shift is found to vary; below 0.8 mole-fraction in acetone and 0.6 mole fraction in methyl cyanide, it is possible to measure the individual shifts of \(\alpha\) and \(\beta\) protons (Khetrapal, 1965).

The chemical shifts of the solvent protons on dilution vary in a direction opposite to that of the solute protons.

(B) *Solutions of Substituted Thiophenes*

In 2-iodo and 2-acetylthiophenes the NMR lines due to proton at C-4 are well separated from those due to other protons. Consequently, the dilution shifts of these protons were estimated separately.

The dilution of 2-iodothiophene with various solvents produces results similar to those discussed for thiophene. The effect of acetone on the spectrum
is well pronounced (cf. that in thiophene) and the individual chemical shifts for protons at C-3 and C-5 could be estimated in quite concentrated solutions.

In 2-acetylthiophene, the effects of the various solvents are in general similar to those observed in the earlier cases. However, dilution with acetone produced comparatively small separation between protons at C-3 and C-5 in this case. The proton peak for chloroform in 2-acetylthiophene shifts towards lower field on dilution whereas in the other cases, it shifts towards higher fields.

**DISCUSSION**

The following three effects may be responsible for causing the dilution shifts in aromatic molecules when they are dissolved in different solvents:—

(a) *Effect due to anisotropy of the solute.*—This is the ring current effect discussed earlier. In non-polar, isotropic solvents like carbon tetrachloride this is the only factor responsible for dilution shifts. Let the contribution to the dilution shift due to this effect be \((\Delta \delta)\).

(b) *Effect due to anisotropy of the solvent.*—If the solvent molecules themselves have a magnetic anisotropy, the field experienced by the isolated solute molecules surrounded by the solvent molecules will be different from that when the solute is placed in an isotropic medium like carbon tetrachloride and this will give rise to a contribution \((\Delta \delta s)\) to the dilution shift. An estimate of \((\Delta \delta s)\) for various solvents can be made by finding out the dilution shifts for the various solvents themselves in carbon tetrachloride. This was estimated for the solvents studied and the results are given in Table I.

(c) *Solute-Solvent interaction.*—Such an interaction is likely to be present in polar solvents. It may either be electrostatic in nature or may involve a complex formation between the solute and the solvent. The contribution to the dilution shift on account of such an interaction \((\Delta \delta s)\) can be estimated by subtracting \((\Delta \delta)\) and \((\Delta \delta s)\) from the total dilution shift \((\Delta \delta)\).

(A) **Solutions of Thiophene**

It is seen from Table I that:

(i) The value of \((\Delta \delta a)\) is about 0.60 ppm. for thiophene.

(ii) In polar solvents like chloroform and methyl alcohol \((\Delta \delta a)\) is not appreciably different from \((\Delta \delta b)\). In these two solvents, therefore, the solvent-solute interaction affects both the \(\alpha\) and the \(\beta\) positions more or less
equally. The magnitude of \((\Delta \delta_\alpha)\) in the two solvents is 0.08 and 0.18 ppm. respectively.

(iii) In solvents like acetone and acetonitrile, the solvent-solute interaction predominantly affects the \(\alpha\)-position. The magnitude of \((\Delta \delta_\alpha)\) for thiophene in acetone and acetonitrile is 0.36 and 0.23 ppm. respectively.

In thiophene solution the following types of solvent-solute interactions are possible:—

(a) Interaction involving the hetero atom.

(b) Formation of a hydrogen-bonded complex involving an aromatic proton and the donor atom of the solvent similar to the one reported by Schaefer and Schneider (1960) for benzene-acetone mixtures.

(c) The formation of a collision complex similar to that reported by Bhacca and Williams (1965). In these complexes, the pi-electrons of the aromatic rings interact with partial positive charge on the carbon atom in ketones (or other polar solvents) in such a way that the pi-electrons are as far away as possible from the partial negative charge of oxygen (in ketones).

(d) The formation of a pi-complex between the solute as a pi-donor and the solvent as the acceptor, e.g., complexes for benzene in various polar solvents [Schneider (1962); Reeves and Schneider (1957); Klinck and Stothers (1962); Abraham (1961); Hutton and Richards (1960); Hutton and Richards (1962); Hutton and Schneider (1962); Huggins and Pimental (1955)].

In thiophenes, interactions (a) and (b) are expected to be more predominant at \(\alpha\) position as it is more reactive than the \(\beta\). The interactions (c) and (d) would affect both \(\alpha\) and \(\beta\) positions almost equally. In view of the complexity of the systems, it is difficult to say precisely which specific interaction is present in each case. However, it can be concluded broadly that in solutions of chloroform and of methyl alcohol, interactions (c) and/or (d) are more important whereas in solutions in acetone and acetonitrile the interactions (a) and/or (b) may dominate.

(B) Solutions of Thiophene Derivatives

From the dilution shifts in non-polar solvents, the values of \((\Delta \delta_\alpha)\) for 2-iodothiophene and 2-acetylthiophene are \(-0.33\) and \(-0.37\) ppm. respectively. For these compounds also, the results in general indicate a solvent-solute interaction with polar solvents such as chloroform and acetone similar to that observed in thiophene systems. However, the effect of acetone to
separate further the resonances of 3 and 5 position protons is much less pronounced in 2-acetylthiophene. This seems to be due to the presence of intermolecular effect between -COCH₃ group of the molecule of 2-acetylthiophene and the aromatic ring of another solute molecule.

Although \( \Delta \delta_3 \) values for thiophene in benzene and 2-iodothiophene in benzene are quite small, they are quite large in 2-acetylthiophene-benzene mixtures. It appears, therefore, that in the latter system, there is a solvent-solute interaction involving -COCH₃ group and the ring protons of benzene similar to the one suggested for acetone-benzene mixtures (Schaefer and Schneider, 1960). One can come to a similar conclusion from the study of the shift of the line due to the acetyl protons of 2-acetylthiophene in various solvents. \( \Delta \delta_3 \) for these protons is the same in solvents, carbon tetrachloride, acetone and chloroform (\( \sim -0.40 \) ppm). However, it is markedly different in benzene solutions (\( -0.13 \) ppm).

**Effect on chemical shift of solvent protons.**—The dilution shift for the solvent protons \( \Delta \delta_{\text{sol.}} \) can also be represented by the following relation which takes into account the three different contributions as mentioned earlier:

\[
(\Delta \delta)_{\text{sol.}} = - \Delta \delta_1 - \Delta \delta_3 + (\Delta \delta_3)_{\text{sol.}}.
\]

Using this relation, \( \Delta \delta_{\text{sol.}} \) values have been obtained and reported in Tables I, II and III. The results also confirm that solvent-solute interaction is absent in solutions of thiophene and substituted thiophenes in non-polar solvents except for thiophene in cyclohexane, the reason for which is yet not very clear. In polar solvents, however such interactions are present.

The solutions of chloroform with thiophene and 2-iodothiophene show that \( \Delta \delta_{\text{sol.}} \) is positive and large indicating the formation of a molecular complex. The corresponding value in 2-acetylthiophene-chloroform mixtures is, however, negative. It, therefore, appears that in these mixtures in addition to the formation of the molecular complex, there is hydrogen bonding between chloroform and the acetyl group similar to the chloroform-acetone complex studied by Huggins *et al.* (1956) and that the hydrogen bonding effect is predominant.

**References**

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10. ———— Ibid., 1962, 5, 139, 153.
14. Minnis Organic Syntheses, 1932, 12, 44.
(b) ———— Ibid., 1960, 32, 1224.