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# A NOVEL SOLVENT EFFECT IN THE NMR SPECTRA OF SOME N,N-DIMETHYLFORMAMIDINES

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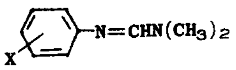
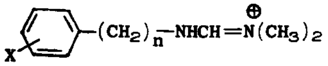
In the course of nmr examination of an N,N-dimethylformamidine derived from a 2-aminophenoxaz-3-one we noticed a striking difference in the appearance of the N-methyl resonances when the solvent was changed from deuteriochloroform to deuterated benzene. We have extended this nmr study to a number of other N,N-dimethylformamidines (I) and, feeling that this solvent effect is unique, wish to present our results in this manuscript.



(I)

The nmr data for the N'-aryl-N,N-dimethylformamidines (I) and for the single N'-aralkyl-N,N-dimethylformamidine II are presented in Table I. The compounds were prepared by the method of Bredereck (1) or of Steiger (2).

The spectra of all the hydrochlorides measured in deuteruim oxide showed the N-methyl substituents as two sharp singlets of approximately equal intensity indicating that the salts in solution exists as (XV) with the two methyl groups non-equivalent because of the expected cis-trans isomerism. In deuteriochloroform the N-methyl resonances of all the formamidines (as the free bases) appeared as a six-proton sharp singlet. The spectrum of compound VII was also measured in deuterated dimethylsulfoxide and in deuterated methanol and, as in deuteriochloroform, the N-methyl groups appeared as a sharp singlet. Distinct differences, however, were noted for the appearance of the N-methyl resonance(s) when the spectra of the



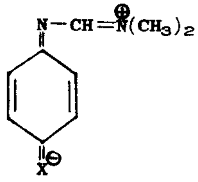
where n = 0 or 2

(XV)

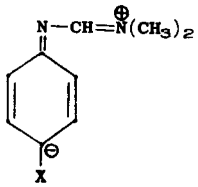
N'-aryl-N,N-dimethylformamidines were run in deuterated benzene. In general, the N-methyl protons were represented by a broad singlet, but the appearance of the peak was markedly dependent on the substituents in the N'-phenyl group. With a sufficiently electronegative group as in compounds XIII and VI, the N-methyl groups showed as two distinct singlets while with groups that are good electron donating groups (e.g. compounds V and XII), the deuterated benzene spectra differed little from the deuteriochloroform spectra and showed the amidine methyl groups as sharp singlets. The spectrum of compound VII in deuterated pyridine also showed the N-methyl broadening strongly suggesting that what is being observed is the general effect of an aromatic solvent. The resolution of the N-methyl peaks in deuterated benzene (but not in deuteriochloroform) was strongly temperature dependent as can be seen in Figure I which shows some of the relevant spectra for compound XI. The appearance of the N-methyl peak for compound II, the only amidine of the series without an N'-aryl group, was precisely the same, a sharp singlet, in both chloroform and benzene.

The combination of solvent and substituent effects noted in the nmr spectra of compounds II-XIV can be rationalized by considering that complex formation between an aromatic solvent and an N'-aryl-N,N-dimethylformamidine enhances the contribution of charge-separated forms such as (XVII), (XVIII), and (XIX) to the structure of the formamidines. We think that the temperature dependence of the spectra in benzene is a reflection of the stability of the complex.

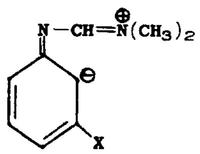
The intensification of the double bond character within the $-CHN(CH_3)_2$ system, then, is responsible for the non-equivalence of the N methyl groups. Strong electron-withdrawing substituents should enhance the double-bond character of the $-CHN(CH_3)_2$ system and lead to a better resolution of the N-methyl peaks as is noted with the p-nitroformamidine XIII . Substituents that tend to donate electrons by resonance effects would tend to decrease that double bond character as is noted with the p-methoxy derivative V ; it is noteworthy that the m-methoxy analog XIV where only an inductive effect via a contributing form like (XIX) would be expected, does give a broadened N methyl peak in deuterated benzene. The β-phenethyl compound II where no direct interaction of the amidine nitrogens and the phenyl ring is possible does



(XVII)



(XVIII)



(XIX)

FIG. I

NMR Spectra of the N,N-Dimethyl Protons of N'-(*p*-Chlorophenyl)-N,N-Dimethylformamidine (Compound XI). A, B, and C in $C_6D_6$, D in $CDCl_3$

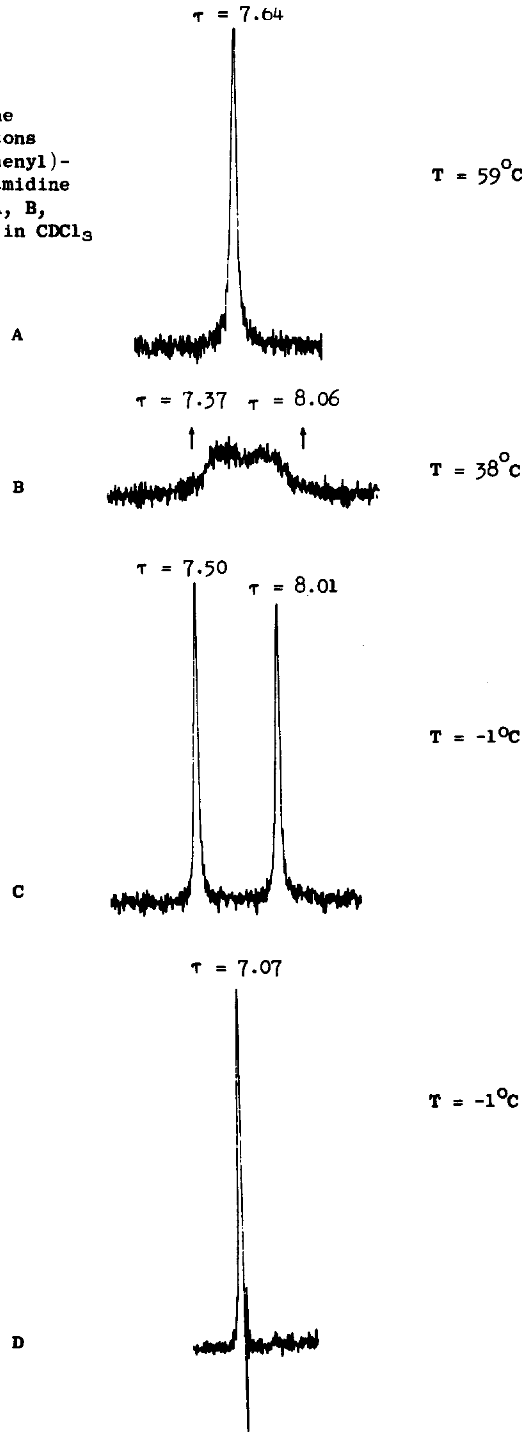


TABLE I

Chemical Shifts for the N,N-Dimethylformamidines

| Compound[a] | $-N{=}\underline{CH}-N(CH_3)_2$ (τ) | | | $-N{=}CH-N(\underline{CH_3})_2$ (τ) | | |
|---|---|---|---|---|---|---|
| | Hydrochloride in $D_2O$[b] | Free Base[c] | | Hydrochloride in $D_2O$[b] | Free Base[c] | |
| | | $C_6D_6$ | $CDCl_3$ | | $C_6D_6$ | $CDCl_3$ |
| II | 6.99, 7.11 | 7.52 | 7.25 | 2.57 | 3.16 | 2.87 |
| III | -- | 7.50[d] | 7.17 | -- | 2.88-2.92[f,g] | 2.62 |
| IV | 6.82, 6.64 | 7.60[e] | 7.19 | 1.88 | 3.18 | 2.80 |
| V | 6.84, 6.66 | 7.50 | 7.19 | 1.88 | 2.95 | 2.78 |
| VI | 6.69, 6.52 | 7.68, 7.40[d] | 7.05 | 1.57 | 3.10 | 2.63 |
| VII | 6.68, 6.57 | 7.81, 7.42[e] | 7.12 | 1.86 | g | g |
| VIII | 6.50, 6.55 | 7.58, 7.34[e] | 7.01 | 1.75 | 2.88 | 2.80 |
| IX | -- | 7.52[d] | 7.07 | -- | 2.96 | 2.69 |
| X | 6.61, 6.55 | 7.47[d] | 6.99 | 2.02 | 3.36 | 2.87 |
| XI | 6.62, 6.52 | 7.53[e] | 7.04 | 1.78 | 2.93 | 2.58 |
| XII | 6.88, 6.69 | 7.46 | 7.10 | 1.88 | 2.80 | 2.50 |
| XIII | -- | 7.70, 7.37 | 6.09 | -- | 3.00 | 2.39 |
| XIV | -- | 7.45[d] | 7.09 | -- | 2.68 | 2.48 |

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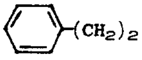
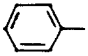
[a] The compounds have the formula $B-N{=}CHN(CH_3)_2$ where B =

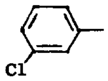
II



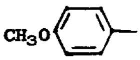
III



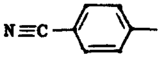
IV



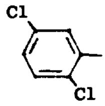
V



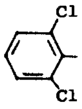
VI



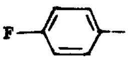
VII



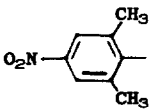
VIII



IX



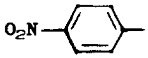
X



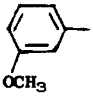
XI

XII

XIII



XIV



[b] Relative to external TMS
[c] Relative to internal TMS
[d] Broadened
[e] Very broad
[f] Within this range
[g] Obscured by the aromatic protons

not show the solvent effect as would be predicted from our postulations. Finally the 4-nitro-2,6-dimethylphenyl formamidine X shows a much reduced ability in resolving the N-methyl peaks as compared to compound XIII . The steric inhibition of contributing forms like (XVII) and (XVIII) can explain this difference in the two compounds. Sandoval and Hanna (3) have postulated complex formation between aromatic solvents and the methyl groups of N,N-dimethylformamide to explain some nmr observations in that system.

When the Hammett $\sigma$ values (4) for the p-monosubstituted formamidines were plotted against the change in chemical shift of the vinyl proton (see Table I) in going from deuteriochloroform to deuterated benzene, there was a good linear relationship with only the p-$NO_2$ substituent being badly displaced from the line. An attempt to correlate this change in chemical shift with Taft's $\sigma^{\rho}$ values (5), inductive effect constants, was less successful emphasizing that both inductive and resonance effects of the substituents must be operating. This is also emphasized by the difference in solvent response of the p-methoxy (compound V) and the m-methoxy (compound XIV) formamidines.

There is a wealth of information available on changes in chemical shifts of substituents with a change in solvent (6). There are also many examples of nuclear magnetic nonequivalence of two methyl groups attached to nitrogen (7). The solvent effect described in this manuscript, however, seems to be unique in that the solvent change affects the chemical shift of a given set of protons as well as bringing about a magnetic nonequivalence.

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6. N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, pp 159-176.

7. J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp 69-71 describes one of the best-studied cases.