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Substituent and Solvent Effects in the Proton Magnetic Resonance (PMR) Spectra of Six 2-Substituted Pyridines

DAGFINN W. AKSNES and HÅKON KRYVI

Chemical Institute, University of Bergen, N-5000 Bergen, Norway

The 60 MHz PMR spectra of six 2-substituted pyridines have been recorded and analyzed. The compounds were examined as 10 mol % solutions in a number of solvents of different polarizability and hydrogen bonding character. The spectra were analyzed using the computer program LAOCN3. Substituent effects on the spectral parameters have been observed and discussed. Pronounced solvent effects on the spectral parameters have been observed. However, there seems to be no particular trend in the observed solvent effects on the coupling constants. In the normal pyridines, however, the observed solvent shifts are dominated by reaction field and solvent magnetic anisotropy effects.

The results of this study indicate that 2-hydroxypyridine and 2-mercaptopyridine exist predominantly in the amide form as hydrogen bonded monomers and dimers. The monomer-dimer equilibrium is largely dependent on the hydrogen bonding character of the solvent.

The PMR spectra of pyridine [1–3] and substituted pyridines [4–9] have been the subject of intensive investigations. The various factors that influence the spectral parameters can be grossly divided into substituent and solvent effects. Pyridines have displayed pronounced medium effects in their PMR spectra.[7] The chemical shifts are, in particular, sensitive to solvent effects while the coupling constants of non-tautomeric pyridines are much less affected by solvent. A large part of the reported data on such systems are of little utility when discussing substituent effects because insufficient (if any) allowance for solvent effects has been made.

The observed changes in the chemical shifts upon substitution[1] can generally be interpreted in terms of inductive and mesomeric effects. Anisotropy effects may also be important in some cases.

The chemical shifts of α-protons in pyridine appear at lower field than those of the other protons in the ring. This is due to the magnetic anisotropy at the ring nitrogen. The contribution of this effect to the shielding of the ring protons can be evaluated by studying the PMR spectra in solvents of varying hydrogen-bonding character.

The observed coupling constants in substituted non-tautomeric pyridines are generally similar to those in pyridine.

Nitrogen-14 nuclear quadrupole resonance (NQR) has been observed in several substituted pyridines, including 2-aminopyridine and 2-cyanopyridine.[10,11] The data have been interpreted in terms of changes in σ and π charge densities at the ring nitrogen upon substitution.

In this paper we report the complete analyses of the PMR spectra of six 2-substituted pyridines in a variety of solvents. During the course of this investigation, two papers appeared reporting PMR spectral data on some of these compounds in neutral and acid solutions.[8,9] However, only the chemical shifts were discussed in one of the works.[8] In the other paper,[9] insufficient allowance for solvent effects was made. Furthermore, the effect of solvents on the PMR spectra of 2-substituted pyridines has not been elucidated except for the extreme case of protonation.

EXPERIMENTAL

The six 2-substituted pyridines studied in this paper were all commercially available. The solids were recrystallized from carbon tetrachloride for further purification. The compounds were examined as 10 mol % solutions in carbon tetrachloride, deuterated chloroform, dimethylsulphoxide (DMSO), and acetone, apart from 2-methoxypyridine and 2-mercaptopyridine which were not sufficiently soluble in carbon tetrachloride. The 2-aminopyridine was also studied in 10 mol % solutions in benzene and *N*-methylformamide. The solvents were dried and redistilled under vacuum. A small amount of tetramethylsilane (TMS) was added and used as an internal reference and lock signal source. All samples were thoroughly degassed and sealed under vacuum. No impurities of any significance were detectable in the PMR spectra. The IR spectra of 2-hydroxypyridine and 2-mercaptopyridine in 10 mol % acetone solutions were measured at 0.03 mm path length on a Unicam SP 200 instrument.

The NMR spectra were run on a JEOL-C-60H spectrometer at ambient temperature (27°C). The spectra were recorded at 54 Hz sweep width and calibrated using a frequency-counter. Line positions were obtained by averaging the results of four to six scans for each sample.

The spectra, which constitute ABCD and $ABCDX_2$ spin systems, were analyzed in terms of chemical shifts and coupling constants using the computer program LAOCN3.[12] "Stick"-plots based on trial parameters were generated using the computer program KOMBIP.[13] These plots facilitated the analyses. Although the signal from the α-protons was broadened slightly due to residual coupling to the nitrogen atom, the resolution was sufficient to observe the eight expected lines. The analyses were, in general, carried out as previously described.[14]

The root-mean-square deviation for the calculated and experimental lines were about 0.06 Hz or less. The calculated probable errors for the parameters were usually less than 0.06 Hz. Computations were carried out using the IBM-50H computer at the University of Bergen. The graphical output was obtained on a Calcomp Plotter.

RESULTS AND DISCUSSION

The proton chemical shifts and coupling constants for the six compounds studied are compiled in Table 1. The chemical shifts are given in δ values (ppm) down-field from internal tetramethylsilane (TMS). The parameters for unsubstituted pyridine in dilute carbon tetrachloride solution are quoted for comparison.[1] The chemical shifts of the ring protons in the examined series

Table 1. Chemical shifts (ppm) and coupling constants (Hz) of 2-substituted pyridines in 10 mol % solutions.

2-X	Solvent	δ_6	δ_5	δ_4	δ_3	J_{56}	J_{46}	J_{36}	J_{45}	J_{35}	J_{34}	δ_X
H	CCl_4[a]	8.52	7.16	7.54	7.16	4.86	1.85	0.98	7.66	1.36	7.66	
Et	CCl_4[d]	8.42	6.97	7.45	7.02	4.96	1.83	0.93	7.50	1.06	7.82	
	$CDCl_3$	8.51	7.06	7.56	7.12	5.00	1.86	0.89	7.64	1.08	7.89	
	Me_2CO	8.47	7.11	7.61	7.19	4.92	1.76	0.91	7.49	1.10	7.78	
	Me_2SO	8.49	7.17	7.67	7.24	4.86	1.80	0.95	7.46	1.08	7.82	
NH_2	CCl_4[d]	7.93	6.48	7.27	6.33	5.03	1.90	0.76	7.11	0.99	8.31	4.85
	C_6H_6	8.03	6.32	7.02	6.14	5.03	1.98	0.94	7.07	0.91	8.25	5.20
	$CDCl_3$	8.04	6.58	7.36	6.45	5.14	1.89	0.93	7.25	0.97	8.38	4.86
	Me_2CO	7.95	6.50	7.35	6.52	5.07	2.02	0.96	7.12	0.81	8.31	5.28
	Me_2SO	7.91	6.46	7.34	6.46	4.96	1.88	0.79	7.04	1.00	8.44	5.87
	NMF[c]	7.98	6.59	7.44	6.64	5.22	1.87	0.53	7.13	0.87	8.32	5.97
OCH_3	CCl_4	8.06	6.74	7.44	6.63	5.04	2.02	0.81	7.08	0.99	8.35	
	$CDCl_3$	8.18	6.72	7.40	6.72	4.95	2.02	0.83	7.05	1.08	8.43	
	Me_2CO	8.17	6.89	7.62	6.74	5.05	1.99	0.83	7.12	0.93	8.42	
	Me_2SO	8.15	6.93	7.66	6.78	5.03	2.02	0.79	7.10	0.85	8.36	
SH	$CDCl_3$	7.68	6.82	7.42	7.55	6.25	1.83	0.83	7.13	1.20	8.72	13.48
	Me_2CO	7.70	6.76	7.38	7.38	6.40	1.61	1.10	7.51	0.73	8.62	
	Me_2SO	7.67	6.76	7.42	7.32	6.27	1.76	0.84	7.05	1.13	8.79	13.43
OH	$CDCl_3$	7.42	6.27	7.46	6.59	6.46	2.22	0.80	6.70	1.18	9.11	13.23
	Me_2CO	7.56	6.34	7.55	6.53	6.54	2.10	0.76	6.82	1.20	9.49	
	Me_2SO	7.41	6.20	7.45	6.39	6.50	2.24	0.91	6.59	1.17	9.13	
CN	CCl_4	8.69	7.53	7.86	7.69	4.83	1.78	0.92	7.81	1.18	7.85	
	$CDCl_3$	8.75	7.59	7.91	7.75	4.83	1.76	0.92	7.83	1.22	7.77	
	Me_2CO	8.76	7.72	8.06	7.93	4.77	1.73	0.94	7.80	1.17	7.78	
	Me_2SO	8.79	7.76	8.08	8.04	4.86	1.69	1.00	7.99	1.05	7.84	

[a] Data from Ref. 1, concentration 10 % wt/wt.
[b] Saturated solution (*ca.* 5 mol %).
[c] NMF = *N*-methylformamide.
[d] $J^o_{H,CH_3} = -0.51$, $J^m_{H,CH_3} = 0.0$, $J^o_{H,CH_3} = -0.52$.

of solvents are displayed in Fig. 1. The use of CCl_4 as solvent for 2-hydroxypyridine and 2-mercaptopyridine was abandoned due to limited solubilities. Throughout this paper, *ortho*, *meta*, and *para* designate the positions relative to the substituent at carbon 2 (C-2), while the α, β, and γ positions refer to the ring nitrogen.

1. Substituent effects

The interpretation of substituent effects is based on the parameters in CCl_4 solutions ($CDCl_3$ for 2-hydroxypyridine and 2-mercaptopyridine) in order to minimize medium effects.

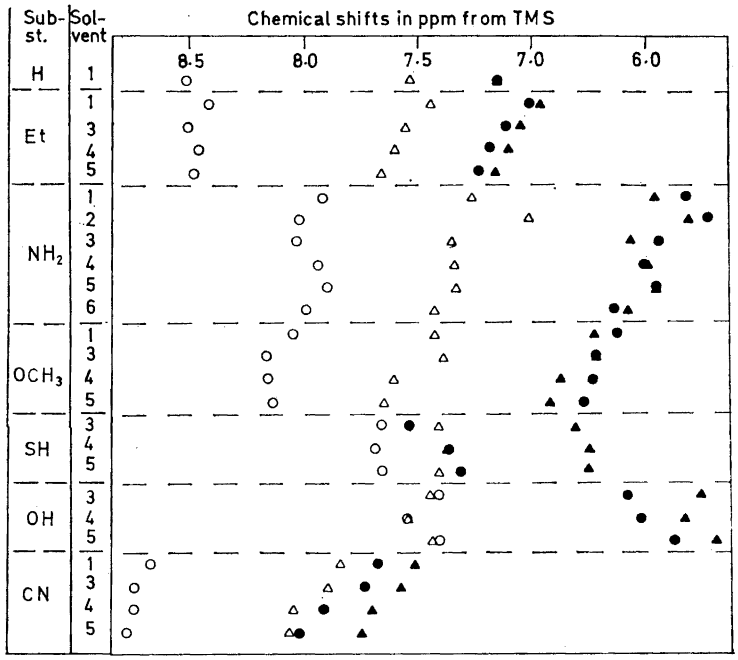


Fig. 1. Chemical shifts of ring protons of 2-substituted pyridines in 10 mol % solutions in carbon tetrachloride (1), benzene (2), deuterated chloroform (3), acetone (4), dimethyl sulphoxide (5) and *N*-methylformamide (6). The dielectric constant of the solvents (ε) increases from top to bottom for each examined compound, ○, α-proton; △, γ-proton; ● and ▲, β-protons at respectively *ortho* and *para* positions to the C-2 substituent.

The six substituents dealt with in this investigation are of the inductive +I and −I types. If the mesomeric effect is taken into account, a further subdivision results, *viz.*[15]

$+I^+$ type: CH_2CH_3
$-I^+$ type: NH_2, OCH_3, SH, OH
$-I^-$ type: CN

where the superscripts + and − designate the +M and −M effects.

Each of these substituents can conjugate with the π-electron system of the ring through formation of partial double-bonds. In pyridine the ring nitrogen causes charge transfer from the ring π-system to the nitrogen site. A similar ring charge transfer will probably occur in the 2-substituted pyridines also. There may then be a competition between the ring nitrogen and the adjacent substituent for the available σ and π electrons.[10,11] For instance, substituents belonging to the $-I^+$ class are σ-electron attractors, but in the *ortho* and *para* positions are π-electron releasing also. This combination of effects may, in favourable circumstances, give rise to large substituent effects. The present substituents afford the possibility to study the interac-

Table 2. Intramolecular chemical shift differences of 2-substituted pyridines in 10 mol % carbon tetrachloride solutions.[a]

2-X	$\delta_4^m - \delta_3^o$	$\delta_4^m - \delta_5^p$	$\delta_6^m - \delta_5^p$	$\delta_5^p - \delta_3^o$	$\delta_6^m - \delta_4^m$
H	0.38	0.38	1.36	0	0.98
Et	0.43	0.48	1.45	−0.05	0.97
NH_2	0.94	0.79	1.45	0.15	0.66
OCH_3	0.81	0.70	1.32	0.11	0.62
SH[b]	−0.13	0.60	0.86	−0.73	0.26
OH[b]	0.87	1.19	1.15	−0.32	−0.04
CN	0.17	0.33	1.16	−0.16	0.83

[a] Data from Table 1.
[b] Data from $CDCl_3$ solutions.

tion of the electron withdrawing ring nitrogen with electron releasing or electron withdrawing substituents.

(a) Chemical shifts. It is well known that the screening of aromatic protons reflects, to a large extent, changes in π-electron density of the aromatic ring upon substitution. Numerous MO calculations and a large amount of chemical evidence indicate that the α and γ positions in pyridine are the most π-electron deficient, whereas the β position is only slightly affected by the electron withdrawing nitrogen.[10,11,16] The fact that the resonances of the β-protons occur at higher field than the α- and γ-protons in the present compounds, indicates that the substituents do not alter the relative effect of the charge transfer towards the pyridinic nitrogen site.

The studied series of substituents (except CN) are π-electron releasing in the *ortho* and *para* positions. The effect of these substituents should then be to accentuate the differences in screening between the *meta-ortho* and *meta-para* protons relative to unsubstituted pyridine, whereas the differences in screening between the *para-ortho* and *meta-meta* protons should remain fairly constant. The electron withdrawing CN group should have the opposite effect on the chemical shifts. Examination of Table 2 shows results in good agreement with the prediction of classical chemistry. It is, however, seen that 2-hydroxypyridine and 2-mercaptopyridine have a behaviour different from the normal pyridines. This will be commented on later.

The large down-field shift of α-protons in pyridines relative to benzene is caused by the paramagnetic effect of the ring nitrogen.[16] The paramagnetic contribution, σ_p, arises as a result of mixing between the ground state and low-lying excited states of the molecule under the influence of the applied magnetic field. In pyridine the non-bonding (lone-pair) electrons are readily excited into the low-energy antibonding π-molecular orbitals of the ring.

The α-protons in the 2-substituted pyridines suffer considerable shifts relative to unsubstituted pyridine which cannot be attributed to the mesomeric effect of a substituent at *meta* position.[8] Recent calculations based on quadrupole coupling data for 2-substituted pyridines have shown that electron withdrawing substituents, including CN, reduce the σ and π charge densities

Table 3. Differences (in ppm) between the chemical shifts of 2-substituted pyridines and the corresponding shifts of pyridine in CCl_4 solutions.[a]

2-X	$\Delta\delta_6$	$\Delta\delta_5$	$\Delta\delta_4$	$\Delta\delta_3$
Et	−0.10	−0.19	−0.09	−0.14
NH_2	−0.59	−0.68	−0.27	−0.83
OCH_3	−0.46	−0.42	−0.10	−0.53
SH[b]	−0.84	−0.34	−0.12	0.39
OH[b]	−1.10	−0.89	−0.08	−0.57
CN	0.17	0.37	0.32	0.53

[a] Data from Table 1. Positive values indicate down-field shifts relative to the corresponding shifts of pyridine.
[b] Data from $CDCl_3$ solutions.

as well as the total charge excess on the ring nitrogen relative to the unsubstituted pyridine.[11] If a similar reduction in the lone-pair occupation number also occurs, an up-field shift of the α-protons might be anticipated owing to reduced σ_p contribution. Electron releasing groups should give rise to corresponding down-field shifts. These conclusions are completely opposed to the observed α-proton shifts (see Table 3). Evidently there must be some larger compensating effects which have to be taken into account.

Several workers have suggested that the long-range effect of inductive substituents is due to a direct electrostatic interaction across space.[8,17] Smith and Roark argue [8] that the shifts suffered by the α-protons in some 2-substituted pyridines are caused by this field effect which is enhanced by transmission through the lone-pair electrons on the pyridinic nitrogen. It seems that the field effect is the most important mechanism controlling the α-proton shift in the present compounds.

The γ-proton shift is much less affected by electron releasing substituents than the α-proton though both are *meta* to the substituent at C-2. The shift of the γ-proton resonance is, however, of the same magnitude and sign as the *meta* proton shifts in mono-substituted benzenes.

It is seen that the substituent effect on the *ortho* and *para* protons (both at β position) is of similar magnitude. The *ortho* proton shifts have been found to correlate with the empirical parameter Q in substituted benzenes and pyridines.[8] The parameter Q is closely related to the paramagnetic term of the Ramsey shielding equation. A linear relationship has been observed between Q and the *ortho* shift of 2-substituted pyridines.[8] This indicates a considerable paramagnetic contribution to the *ortho* shift.

Below we consider the specific compounds in some detail. The ethyl group has a small but similar effect as the methyl group [8,23] on the chemical shifts. The effect on the chemical shifts is much the same as in the corresponding mono-substituted benzenes.[18,24] The similar methyl proton shifts observed in toluene [19] (2.37 ppm) and α-picoline [23] (2.54 ppm) also indicate the same extent of conjugation with both the aromatic rings.

The amino pyridines have been shown by IR, NMR, and NQR studies to exist in the amino rather than in the imino form.[8–10] This is confirmed by the present results, in that the spectral parameters have values within the expected ranges for normal pyridines. The amino proton resonance in 2-aminopyridine is shifted 1.5 ppm down-field relative to aniline.[20] This observation, and the large shifts suffered by the aromatic protons in 2-aminopyridine, indicate that the strongly electron releasing amino group can conjugate with the electrophilic pyridine ring to a larger extent than with the benzene ring.[10] Similar conclusions were also reached on the basis of dipole moment studies of *para*-substituted pyridines and the corresponding mono-substituted benzenes.[21]

The data of Tables 1, 2, and 3 show that the methoxy group has nearly the same effect as the amino group on the spectral parameters. This is reasonable since both groups are strongly electron releasing and belong to the same $-I^+$ substituent class.

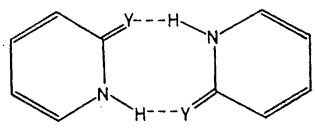
The down-field proton shifts observed for 2-cyanopyridine are in the expected direction. It appears, however, that this group affects the α- and β-proton shifts to a smaller extent than the amino and methoxy groups. This might be partially due to stronger conjugation with the electrophilic pyridine ring of electron releasing substituents than of equally strong electron withdrawing ones.[10]

2-Hydroxypyridine has been shown, by IR, UV, and NMR measurements to exist predominantly in the amide form (pyridone) in neutral solutions.[9,22] This compound has also been reported to exist as hydrogen bonded dimers in the crystalline state as well as in neutral solution [9] (10 mol %).

It can be seen from Tables 1, 2, and 3 that the ring proton resonances of 2-hydroxypyridine appear to high field relative to the corresponding resonances of pyridine. The α- and β-protons experience, in particular, large up-field shifts compared to the normal pyridines. The chemical shift of the NH (or OH) proton appears at the low-field value 13.23 ppm. These observations indicate, in agreement with previous conclusions, that 2-hydroxypyridine exist as hydrogen bonded dimers in solution.[9,22]

The NMR spectral parameters of 2-mercaptopyridine are similar to the corresponding values of 2-hydroxypyridine. The α- and β-protons of the former compound also experience the largest effect on the screening relative to the normal pyridines. It is, however, noted that the *ortho* proton in 2-mercaptopyridine suffers a down-field shift in contrast to the corresponding shift of 2-hydroxypyridine. This difference can probably be mainly attributed to magnetic anisotropy effects of the adjacent substituent group.

The chemical shift of the SH (or NH) proton appears at 13.48 ppm, that is, close to the corresponding shift of 2-hydroxypyridine. All these observations suggest that 2-mercaptopyridine, like 2-hydroxypyridine, mainly occurs in the thioamide form as hydrogen bonded dimers as shown below (Y = O, S):



(b) Coupling constants. The values of the coupling constants listed in Table 1 are also of interest. If compared with unsubstituted pyridine,[1–3] all the coupling constants display generally larger variations than observed for the analogous mono-substituted benzenes.[18,24] The larger spread in the coupling constants can be attributed to accentuated substituent interaction with the electrophilic pyridine ring compared to the benzene ring. The same observation has already been noted in the discussion of the chemical shift data.

For the non-tautomeric pyridines the larger changes occur in the values of the vicinal coupling constants J_{34} and J_{45}, which appear to be rather sensitive to the nature of the substituent at C-2. The vicinal coupling constants J_{34} and J_{56} have larger values than in unsubstituted pyridine. The remaining coupling constants generally suffer a decrease on substitution. Again the behaviour of 2-hydroxypyridine and 2-mercaptopyridine is anomalous.

Substituent effects on the coupling constants are usually short-range. It is therefore believed that the variations of these parameters are primarily determined by inductive effects. The propagation of the spin-spin coupling constants therefore presumably involves the σ-electrons. The long-range *para* coupling may, however, get a significant contribution from the π-system.

The data of Table 1 show that the CN, OCH_3, and NH_2 groups have similar effects on the coupling constants in contrast to the observed effect on the chemical shifts. This is reasonable, since these groups belong to the same $-I$ substituent class. The variation in the vicinal coupling constant J_{56} is larger than might be expected on basis of inductive effects alone. It is, however, reasonable to assume that the substituent effect on J_{56} is relayed by the intervening polarizable lone-pair electrons on the pyridinic nitrogen.[17] Castellano and co-workers have, however, reported [1] that the presence of substituents in the α and β positions of the pyridine ring causes only minor variations in the magnitude of the vicinal coupling constant between the remaining α- and β-protons (J_{56}).

2-Hydroxypyridine and 2-mercaptopyridine display much larger variations in the coupling constants. For comparison with the normal pyridines, the coupling constants J_{34}, J_{56}, and J_{45} appear to be most revealing. The large increase in the two former coupling constants, and a corresponding decrease in J_{45} relative to their values in the other 2-substituted pyridines, also constitute strong evidence that the two tautomeric pyridines exist predominantly in the amide form, since this would give the pyridine ring some "diene-like" character, and thus account for the observed changes in the coupling constants.

2. Solvent effects

It is well recognized that solvent effects are much more pronounced in the PMR spectra of heterocyclic unsaturated compounds than in benzenes.[7] The shielding of the ring hydrogen nuclei is, in particular, sensitive to solvent effects. It is, however, often difficult to account for the observed solvent effect on the basis of one particular type of interaction, as there may be several competing factors involved. All we can show is that the proposed effects are in qualitative agreement with experiment. It is seen from Table 1 that the solvent has a significant effect on the measured spectral parameters. However,

Table 4. Intramolecular chemical shift differences of 2-substituted pyridines in various solvents.[a]

2-X	Solvent [b]	$\delta_6^\alpha - \delta_5^\beta$	$\delta_6^\alpha - \delta_3^\beta$	$\delta_6^\alpha - \delta_4^\gamma$
Et	1	1.45	1.40	0.97
	3	1.45	1.39	0.95
	4	1.36	1.28	0.86
	5	1.32	1.25	0.82
NH_2	1	1.45	1.60	0.66
	2	1.71	1.89	1.01
	3	1.46	1.59	0.68
	4	1.45	1.43	0.60
	5	1.45	1.45	0.57
	6	1.37	1.34	0.54
OCH_3	1	1.32	1.43	0.62
	3	1.46	1.46	0.78
	4	1.28	1.43	0.45
	5	1.22	1.37	0.49
CN	1	1.16	1.00	0.83
	3	1.16	1.00	0.84
	4	1.04	0.83	0.70
	5	1.03	0.75	0.71

[a] Data from Table 1.
[b] The solvent number refers to Fig. 1.

there seems to be no particular trend in the observed effects on the coupling constants. Furthermore, the examined solvents appear to affect the coupling constants of tautomeric and non-tautomeric pyridines to about the same extent. The following discussion of solvent effects will therefore be based on the chemical shift data.

Carbon tetrachloride is not completely inert towards all solutes, and may lead to solvent shifts when compared with hydrocarbon solvents [25] (hexane, cyclohexane, *etc.*). However, as far as the present NMR data are concerned, carbon tetrachloride is inactive relative to the other solvents in this investigation.

The results of Table 1 and Fig. 1 for the normal pyridines show that, as the dielectric constant of the solvent increases, there is a marked shift of the β- and γ-proton resonances to lower field whereas the α-proton resonance is barely affected. Benzene is an exception in this respect in that it causes upfield shifts of the β-and γ-protons.

These observations indicate a considerable contribution from reaction field effects.[16,32] Buckingham's theory of the reaction field predicts a deshielding of the β- and γ-protons relative to the α-protons of pyridine as the dielectric constant of the solvent increases.[25–27] The data of Table 4 (except those for the benzene solution) are in agreement with this prediction. It has been sug-

gested that in the absence of any specific solute-solvent interactions, disc-like solvents (*e.g.*, benzene) and rod-like solvents (*e.g.*, acetone, DMSO) will adopt certain preferred solvent-solute orientations.[27]

The solvent magnetic anisotropy may thus give rise to differential shifts. The opposed effect of benzene relative to the other examined solvents, on the β- and γ-proton shifts of 2-aminopyridine cannot be attributed to the reaction field effect. The α- and amino-protons of 2-aminopyridine suffer small down-field shifts in benzene solution relative to the carbon tetrachloride solution. Corresponding differential shifts in benzene solution relative to an inert solvent, have been observed for numerous heterocyclic compounds.[25,27–31] The observed shifts are in accord with benzene solvation of the positive end of the pyridine dipole.[27] The most likely association is one in which the benzene and pyridine molecules are lying in parallel planes. This would cause shielding of the β- and α-protons by the anisotropy of the orientated benzene molecule, while the amino- and ring-protons at the α-position are deshielded or barely influenced,[27,30] in qualitative agreement with experiment.

It is also to be expected that the rod-like solvents, acetone and DMSO, will cause a net down-field shift of the solute protons.[27] The solute molecules will probably orient themselves in planes roughly parallel to the heavy-atom skeleton of acetone and DMSO, so that the negative end of the solute dipole avoids the negative end of the solvent dipole. These solvents should thus tend to augment the effect from the reaction field.

Chloroform, which is widely used as solvent due to its good solubility properties, forms hydrogen bonds with most polar solutes, thus creating extraneous solvent shifts.[25] The results of this study show that chloroform introduces appreciable solvent shifts which may possibly be attributed to hydrogen bonding. When the nitrogen lone-pair electrons become involved in hydrogen bonding, an appreciable high-field shift of the α-proton would be expected due to reduced paramagnetic contribution σ_p.[16] The resonances of the other protons should change little. These predictions are completely opposite to the observed shifts, in that the protons at the α-position of the present compounds experience down-field shifts in chloroform solution. Furthermore, up-field shifts of α-protons would, together with the reaction field effect, result in a reduction of the intramolecular shifts listed in Table 4. This is also contrary to experiment.

It is to be expected that the flow of charge from the α and γ positions will be accentuated when the nitrogen atom is hydrogen bonded to the solvent.[16] The result should be a down-field shift of these protons. This effect cannot, however, account for the observed down-field shifts of the β-protons in chloroform solution. In conclusion, it appears that the solvent shifts observed in the normal pyridines are dominated by reaction field and solvent anisotropy effects.

In 2-hydroxypyridine and 2-mercaptopyridine, the *ortho* proton exhibits the largest solvent effect, whereas the remaining ring protons are less affected. The NH proton signals were broad (when detectable) in acetone and DMSO solutions. The α-proton and NH-proton resonances are displaced to high field in both compounds as the polarity of the solvent increases. These observations indicate that the reaction field effect is not dominant in the polar solvents.

The observed solvent shifts may possibly be attributed to hydrogen bonding effects. The used solvents have, however, different hydrogen bonding characters in that chloroform is a proton donor whereas acetone and DMSO are proton acceptor solvents. Chloroform and the two latter solvents should therefore attach themselves to the solute molecule at different sites. Considerable self-association of solute and solvent may also occur.[25] On a quantitative basis the system would probably have to be described as a monomer-dimer equilibrium. Phenol and thiophenol show fairly large association shifts of the OH and SH proton respectively, in proton acceptor solvents including acetone, thereby indicating appreciable hydrogen bonding with the solvent.[33] It was argued in the last section that 2-hydroxypyridine and 2-mercaptopyridine exist predominantly as hydrogen bonded dimers in chloroform solution. It appears on basis of the observed solvent shifts that the strong proton acceptor solvents acetone and DMSO break the solute dimerization by forming new solute-solvent hydrogen bonds at the NH site. The observed solvent shift of the *ortho* proton is then mainly the result of breaking the hydrogen bond at the C-2 site.

The IR spectra of 2-hydroxypyridine and 2-mercaptopyridine in 10 mol % acetone solutions were recorded using acetone as reference. Both compounds displayed a broad absorption band near 3200 cm^{-1}, which is presumably due to hydrogen bonded N–H stretching. The S–H stretching band was not observed for 2-mercaptopyridine, while a weak and broad band at *ca.* 3250 cm^{-1} in the 2-hydroxypyridine spectrum may indicate hydrogen bonded OH. In the former compound a strong band measured at 1155 cm^{-1} can be attributed to C=S stretching. A strong band (doublet) observed near 1670 cm^{-1} in 2-hydroxypyridine may, similarly, indicate amide C=O stretching.

The obtained NMR and IR data are compatible with the occurrence of 2-hydroxypyridine and 2-mercaptopyridine in the amide form.[9] The amide NH proton is no doubt involved in hydrogen bonding. Furthermore, it appears that these compounds exist predominantly as hydrogen bonded monomers and dimers in the examined proton acceptor and proton donor solvents, respectively.

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