Monatshefte für Chemie 115, 1345—1351 (1984)

Monatshefte für Chemie
Chemical Monthly

Hydrogen Bonding and Tautomeric Equilibria of Complexes of Pyridine with Various Proton Donors
A Nitrogen-15 Nuclear Magnetic Resonance Study

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(Received 8 March 1984. Accepted 23 April 1984)

The ^{15}N-NMR-spectra of pyridine in presence of several proton donors are given. The concentration dependence of the chemical shifts can be described formally by a two step mechanism including proton transfer.

(Keywords: Nitrogen-15 nuclear magnetic resonance spectroscopy; Hydrogen bonding; Proton transfer; Pyridine)

Wasserstoffbrückenbindung und Protonenübertragung in Komplexen zwischen Pyridin und verschiedenen Protonendonatoren. Eine Stickstoff-15-NMR-Untersuchung

Die ^{15}N-NMR-Spektren von Pyridin mit einigen Protonendonatoren sind angegeben. Die Konzentrationsabhängigkeit der chemischen Verschiebung kann formal durch ein zweistufiges Gleichgewicht, welches einen Protonenübergang beinhaltet, beschrieben werden.

Introduction

The nitrogen-15 NMR spectra of azine-type nitrogen and especially of pyridine have been investigated widely[1–3]; pyridine was not only one of the first compounds whose N-15 properties were studied in detail, it remains the one that provides excellent tests of the influence of hydrogen bonding, environment and solvent. Pyridine chemical shifts depend very strongly on solvent[4,5], due to interactions with the lone pair of the nitrogen. The most marked changes in chemical shift occur with hydrogen bonded proton donors, partial coordination with the nitrogen unshared

electron pair shields the nitrogen considerably, and this shielding has been used as a probe for hydrogen bonding in different solvents. Semiempirical[6,7] as well as *ab initio* calculations[8,9] have been performed to determine the structure and the energetic behavior of hydrogen bonded complexes. Protonation of the pyridine nitrogen changes the chemical shift also drastically. Whereas at alkylamine nitrogens protonation causes only a small deshielding by diminishing the diamagnetic screening of the lone pair, protonation of pyridine gives rise to a large upfield shift by removing the contribution of the lone pair to the π-electron system.

In the present study we have used the drastic changes of the nitrogen-15 chemical shift of pyridine to study hydrogen bonded complexes of various proton donors with pyridine. The assoziation of proton donors with pyridine can be described by a two step reaction mechanism:

$$Py + A-H \overset{1}{\rightleftharpoons} Py..H-A \overset{2}{\rightleftharpoons} Py-H^+..A^- \qquad (1)$$

$$AN \qquad AZ$$

(*AN* neutral hydrogen bonded complex, *AZ* zwitterionic hydrogen bonded complex).

The primary addition step building up an hydrogen bonded complex is followed by proton transfer within the hydrogen bond forming a highly polar complex *AZ*. In media of low dielectric constant this hydrogen bonded ion pair dissociates only to a very small amount into solvent separated or free ion pairs. Such an assumption of a two step dynamical equilibrium is only an approximation, because additional association phenomena take place depending on the donor-acceptor properties of the compounds used, on their concentrations and finally on the solvent. Therefore we have measured the ^{15}N-nuclear magnetic resonance spectra of the addition complexes of pyridine with various proton donors at different concentration ratios.

Experimental

Commercially available chemicals were purified by destillation. Pyridine was freshly distilled from CaH_2 under argon-atmosphere. Phenol was purified by sublimation. $CDCl_3$ (99.5%, Ueticon) was dried by chromatography (Al_2O_3). The sample solutions were filtered and degassed.

The natural abundance ^{15}N-NMR-spectra were obtained at a frequency of 25.357 MHz on a Bruker-WM-250-NMR-spectrometer equipped with an 80 K ASPECT-2000 computer. All spectra were obtained by 5 ml of 1.0 to 1.25 molar solution of pyridine in $CDCl_3$ containing the proton donor in the range from 0.1 to 6 molar, using 15 mm tubes. The deuterium resonance of the solvent provided the field-frequency lock. A 5 mm concentric tube containing CH_3NO_2 was used as external reference standard. Typical aquisition parameters for refocussed INEPT with broadband decoupling were: pulse width (90°, ^{15}N) = 50 μs; pulse width (90°,

^{1}H) = 42 μs; number of scans: 80–1 000; sweep width: 5 600 Hz. The delays for the refocussed INEPT-experiments were optimized for J = 5–7 Hz (^{15}N−H-system). Typical acquisition parameters for the broadband decoupling with power gating (1.5 W/0.3 W) were: pulse width: 15 μs; number of scans 1 000–10 000.

The sample temperature was 300 K. The reproducibility of chemical shifts is about 0.1 ppm. No correction for diamagnetic susceptibility was performed.

From the initial concentrations of the proton donor (H−A) and pyridine (Py) and the equilibrium constants K_1 and K_2 the equilibrium concentrations of all reaction partners can be calculated. The chemical shift δ_0 can be expressed from the chemical shift of free pyridine (Py), hydrogen-bonded pyridine (Py−HA), hydrogen-bonded ion pair ($PyH^+ - A^-$) and the equilibrium concentration of each spezies:

$$\delta_0 = \delta_{Py} \cdot \frac{c_{Py}}{c^0_{Py}} + \delta_{Py-HA} \cdot \frac{c_{Py-HA}}{c^0_{Py}} + \delta_{PyH^+-A^-} \cdot \frac{c_{PyH^+-A^-}}{c^0_{Py}} \qquad (2)$$

(c^0_{Py} initial concentration of pyridine).

The chemical shift parameters and the equilibrium constants were fitted simultanously to the experimental values using the SIMPLEX and the MIGRAD routine from the program package MINUIT. The agreement between experimental and calculated chemical shifts was better than 0.1 ppm.

Results and Discussion

Table 1 summarizes the ^{15}N chemical shifts of pyridine and N-methyl pyridinium iodide in different media. Upfield shifts are found for solutions compared with gas phase due to the interaction of the solvent with the lone pair electrons. Evidently the interaction is relatively weak for cyclohexane and stronger for the interaction with solvent molecules with a dipole moment. A large upfield shift can be observed for polar protic solvents as an indication that a hydrogen bond between the pyridine nitrogen and the solvent molecule has been built up. The chemical shift differences in protic solvents are relatively large, also a concentration dependence can be noticed. In strong polar protic solvents a drastic upfield shift occurs caused by proton transfer within the hydrogen bond. The covalent bond together with the positive charge at the nitrogen atom shifts the ^{15}N absorption more than 100 ppm. The same shift can be observed for N-alkylation where a similar covalent bond in the pyridinium cation is established. The chemical shift of the positively charged nitrogen atom is only slightly influenced by media changes. To explain the large differences of the chemical shifts of the hydrogen bonded complexes measurements at different donor-acceptor concentration ratios have been performed.

Fig. 1 shows the dependence of the ^{15}N chemical shifts of pyridine on the concentration ratio of various proton donors and pyridine as proton acceptor. As already mentioned in the introduction and the experimental

part these curves can be described quantitatively by a two-step reaction system according to equ. (1).

In addition step 1 a hydrogen bond between the proton donor and the nitrogen atom of pyridine is formed followed by the proton transfer within the hydrogen bond. Both reaction steps are reversible, a dynamical equilibrium is established in solution. In Table 2 the fitted parameters

Table 1. ^{15}N *chemical shifts of pyridine and N-methylpyridinium iodide in different solvents*[2,4] *(in ppm,* CH_3NO_2 *as reference)*

	Solvent	^{15}N chemical shift
pyridine	gas	−54.6
	cyclohexane	−59.4[a]
	carbon tetrachloride	−62.1[a]
	benzene	−62.3[a]
	pyridine	−63.5[b]
	dimethyl sulfoxide	−64.0[a]
	chloroform	−69.2[a]
	methanol	−79.1[a]
	water	−82.1[a]
	trifluoroethanol	−90.2[c]
	trifluoroethanol	−92.3[a]
	trifluoroacetic acid	−179.0[c]
	trifluoroacetic acid	−182.5[d]
	fluorosulfonic acid	−186.9[d]
N-methylpyridinium iodide		
	dimethyl sulfoxide	−179.9[e]
	trifluoroacetic acid	−182.0[e]

[a] 14.3 mole percent solution; [b] neat; [c] 2 molar solution; [d] 0.5 molar solution; [e] 1 molar solution.

from the titration curve are given. Weak proton donors, trifluoroethanol or phenol show no proton transfer within the hydrogen bond. The concentration dependence of the chemical shift can be described by reaction step 1. The resulting equilibrium constant K_1 includes pre-equilibria like the self-association of the proton donor or the association of pyridine with chloroform. Taking into account per example a dimerization step of phenol, an equilibrium constant $K_1 = 11.3\,M^{-1}$ can be calculated, which is much closer to the value of $K_1 = 17\,M^{-1}$ which has been measured for the single step assoziation in dilute solution[10–12]. Stronger proton donors like carboxylic acids favor proton transfer according to the acid strength of these compounds. In acetic acid the equilibrium constant of reaction step 2 is small, proton transfer is only

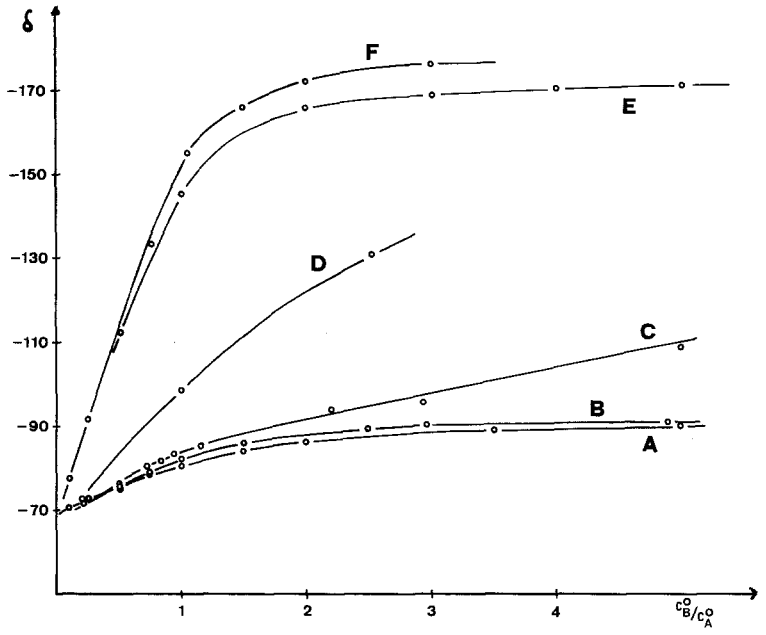

Fig. 1. Nitrogen-15 chemical shifts of pyridine in dependence on different concentrations of various proton donors. *A* phenol as proton donor, solvent $CDCl_3$; *B* trifluorethanol, solvent $CDCl_3$; *C* acetic acid, solvent $CDCl_3$; *D* chloroacetic acid, solvent $CDCl_3$; *E* trifluoroacetic acid, solvent $CDCl_3$; *F* trifluoroacetic acid, solvent *DMSO-d*$_6$

observed at higher concentrations of the proton donor. The overall equilibrium constant K^* can be expressed by equation (3):

$$K^* = K_1 \cdot (1 + K_2) = \frac{c_{Py-HA} + c_{PyH^+-A^-}}{c_{Py} \cdot c_{HA}} \qquad (3)$$

K^* is also given in Table 2. K^* increases with increasing acid strength of the proton donor used. The values of K_1 and K_2 cannot be estimated with the same accuracy as K^* because of the small dependence of the error function on the ratio of these parameters. The association constant K_1 is much lower as in the case of trifluoroethanol, the dimerization constant of the carbon acids as preequilibrium is rather high. In the system trifluoroacetic acid/pyridine the state of hydrogen bonded ion pair is mainly populated, it is therefore evident that the proton transfer constant should be higher than $K_2 > 20\,M^{-1}$. The parameters K_1 and K_2 cannot be fitted simultaneously in this case – they are covariant. Only the equili-

brium constant K^* can be given. The chemical shift values of protonated hydrogen bonded pyridine is more or less equal to the value obtained for *N*-methylpyridinium iodid given in Table 1. In both cases there is also no certain change on chemical shift in chloroform and dimethyl sulfoxide.

Table 2. *Equilibrium constants and* ^{15}N *chemical shifts of the species* (*Py*), (*Py*−H*A*) *and* (*Py*H−*A*) *for the system pyridine−proton donors*

Proton Donor	Solvent	K_1	K_2	K^*	δ_{Py}	δ_{PyHA}	δ_{PyH^+A}
Trifluoroethanol	$CDCl_3$	1.5	<0.01		−68.8	−92.1	–
phenol	$CDCl_3$	0.01	<0.75		−67.0	−91.3	–
acetic acid	$CDCl_3$	(0.04)	(1.6)	0.12	−65.9	(−93.0)	−185.0
chloroacetic acid	$CDCl_3$	(0.09)	(4.1)	0.44	−66.0	(−93.0)	−186.4
trifluoroacetic acid	$CDCl_3$			7.8	−66.2	(−93.0)	−184.9
trifluoroacetic acid	*DMSO*			8.5	−64.1	(−93.0)	−187.1

Significance of the equilibrium constant ± 7%, and of the chemical shift values ± 1.5 ppm (accuracy for equilibrium constants in brackets ± 10%, of chemical shift values in brackets ± 3 ppm).

Conclusion

The reaction of proton donors with pyridine can be modelled formally by a two step reaction mechanism. In the case of weak donors like trifluorethanol or phenol no significant proton transfer occurs, whereas stronger proton donors like carboxylic acids show proton transfer within the hydrogen bond to a large extent. The difference of ^{15}N chemical shifts in various protic solvents is the result of different equilibria of the two step reaction scheme. Neither the ^{15}N chemical shifts of the hydrogen bonded addition complex nor the chemical shifts of the hydrogen bonded ion pair seem to be dependent on the proton donor. The influence of the solvent appears to be small as well.

Acknowledgements

The authors wish to thank Prof. *P. Schuster* for his interest, the *"Interfakultäres Rechenzentrum der Universität Wien"* for computing time, and the *"Fonds zur Förderung der Wissenschaftlichen Forschung in Österreich"* for financial support (Proj. 4009, 3388, and 4940).

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