

Carbon-13 Chemical Shift Anisotropies of Pyridine and Diazines

Pejman Parhami and B. M. Fung*

Contribution from the Department of Chemistry, University of Oklahoma, Norman, Oklahoma 73019. Received June 17, 1985

Abstract: Diagonal elements of the carbon-13 chemical shift tensor of each carbon atom in pyridine, pyridazine, pyrimidine, and pyrazine have been determined from NMR measurements in liquid crystal solutions. It was found that while the isotropic chemical shift (δ_{iso}) does not correlate well with the inductive effect of the ring nitrogen, the tensorial component perpendicular to the ring (δ_{yy}) does. In pyridine, values of δ_{iso} of the α , β , and γ carbons change irregularly, but those of δ_{yy} decrease regularly in that order. The effects of the two nitrogen atoms on δ_{iso} are not additive for pyridazine and pyrimidine, but their effects on δ_{yy} show better additivities when relative experimental uncertainties are taken into account.

Carbon-13 chemical shift is a quantity very sensitive to molecular structure and is closely related to chemical reactivity.¹⁻³ Isotropic chemical shifts can be easily and accurately determined by NMR study in liquid. The isotropic shift is the trace of the chemical shift tensor

$$\delta_{\text{iso}} = \frac{1}{3}(\delta_{11} + \delta_{22} + \delta_{33}) \quad (1)$$

The availability of the tensorial components would enable one to gain additional knowledge and understanding of the relations between chemical shift and molecular structure and reactivity in a three-dimensional way. A comparison of the tensorial components of a series of analogous compounds often reveals unexpected but very informative trends. For example, the chemical shift component along the C-X axis of the ipso carbon in many monosubstituted and disubstituted benzenes is rather constant,⁴ which is not what one would expect by intuition. In polyatomic linear and pseudolinear molecules, δ_{\parallel} along the C_{∞} axis is also remarkably constant,⁵ even though δ_{iso} varies from -14.6 to +192.8 ppm. The tensorial component perpendicular to the ring for different carbon atoms in benzonitrile⁶ and halobenzenes⁴ is directly related to the inductive effect of the substituents, whereas δ_{iso} is not. In cyclopropanes, a good correlation was found between the tensorial component perpendicular to the CCC plane and the CCC angle at the carbon of interest.⁷

A direct approach to the determination of chemical shift tensors is NMR studies in the solid state. The methods of obtaining carbon-13 chemical shift tensors from single crystals and powders have been reviewed recently.⁸ An ingenious two-dimensional technique based upon rapid flipping of the spinning axis of a powder sample has been proposed independently by two groups.^{9,10} Chemical shift tensors can also be measured by NMR studies in liquid-crystal solutions.¹¹⁻¹³ We have recently shown that car-

bon-13 NMR of solutes in liquid-crystal solutions can be successfully studied in natural abundance¹⁴ and have determined the carbon-13 chemical shift tensor of every carbon atom in benzonitrile⁶ and in halobenzenes.⁴ The present work presents results of a similar study on pyridine and three diazines (pyridazine, pyrimidine, and pyrazine). An advantage of NMR measurements of these compounds in liquid crystal solutions compared to solid-state work is that the carbon-13 signals are rather sharp and are not affected by the dipolar and quadrupolar effects of nitrogen-14.

Experimental Section

p-Ethoxybenzylidene-*p*-*n*-butylaniline (EBBA) was obtained from American Liquid Crystal Co., Kent, OH. NP 1565 TNC and ZL1 1167 were obtained from EM Chemicals, Hawthorne, NY. Pyridine was obtained from Fisher Scientific, Fair Lawn, NJ. Pyridazine, pyrimidine, and pyrazine were obtained from Aldrich Chemical Co., Milwaukee, WI.

All NMR spectra were taken with a Varian XL-300 NMR spectrometer at 298 K. The solvent peaks in the carbon-13 spectra were reduced by using a spin-echo sequence,¹⁴ and the efficiency of proton decoupling was increased by using a phased-alternated broad-band decoupling sequence, ALPHA-26.¹⁵ The variable-angle spinning probe was manufactured by Doty Scientific, Columbia, SC.

Results and Discussion

Carbon-13 and proton NMR spectra of pyridine and three diazines (pyridazine, pyrimidine, and pyrazine) in liquid-crystal solutions were measured. The diagonal elements of each carbon-13 chemical shift tensor were determined according to a method described previously.^{4,6} The procedure is summarized in the following. Anisotropic carbon-13 chemical shifts are determined from the carbon-13 spectrum of each liquid-crystal solution. The proton-proton dipolar coupling constants of the solute are obtained from a computer analysis of the proton spectrum of the same solution measured at the same temperature. From the dipolar coupling constants, the order parameters of the solute can be calculated. In this step, one fixed proton-proton distance for each molecule and isotropic values of J obtained from the literature¹⁶⁻²⁰ were used. For solutes which are described by two or more order parameters, such as pyridine and the diazines, it is important to choose solvents in which the ratio $S_{zz}/(S_{xx} - S_{yy})$ for the solute

(1) Bromilow, J.; Brownlee, R. T. C.; Lopez, V. O.; Taft, R. W. *J. Org. Chem.* **1979**, *44*, 4766.

(2) Ewing, D. F. *Org. Magn. Reson.* **1979**, *12*, 499.

(3) Levy, G. C.; Lichter, R. L.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance Spectroscopy"; 2nd ed.; Wiley-Interscience: New York, 1980.

(4) Fung, B. M.; Kong, C. F. *J. Am. Chem. Soc.* **1984**, *106*, 6193.

(5) Beeler, A. J.; Orendt, A. M.; Grant, D. M.; Cutts, P. W.; Michl, J.; Zilm, K. W.; Downing, J. W.; Facelli, J. C.; Schinder, M. S.; Kutzelnigg, W. *J. Am. Chem. Soc.* **1984**, *106*, 7672.

(6) Fung, B. M. *J. Am. Chem. Soc.* **1983**, *105*, 5713.

(7) Orendt, A. M.; Facelli, J. C.; Beeler, A. J.; Grant, D. M.; Michl, J., in press.

(8) Veeman, W. S. *Prog. Nucl. Magn. Reson. Spectrosc.* **1984**, *16*, 193.

(9) Bax, A.; Szeverenyi, N. M.; Maciel, G. J. *Magn. Reson.* **1983**, *55*, 494.

(10) Terao, T.; Fujii, T.; Onodera, T.; Saika, A. *Chem. Phys. Lett.* **1984**, *107*, 145.

(11) Emsley, J. M.; Linton, J. C. "NMR Spectroscopy Using Liquid Crystal Solvents"; Pergamon Press: Oxford, 1975.

(12) Appleman, B. R.; Dailey, B. P. In "Advances in Magnetic Resonance"; Waugh, J. S., Ed.; Academic Press: New York, 1974; Vol. 7, p 231.

(13) Lounila, J.; Jokisaari, J. *Prog. Nucl. Magn. Reson. Spectrosc.* **1982**, *15*, 249.

(14) Fung, B. M. *J. Magn. Reson.* **1983**, *55*, 475.

(15) Fung, B. M.; Mui, D. S. L.; Bonnell, I. R.; Enwall, W. L. *J. Magn. Reson.* **1984**, *58*, 254.

(16) Diehl, P.; Böisinger, H.; Zimmermann, H. *J. Magn. Reson.* **1979**, *33*, 113.

(17) Burnell, E. E.; de Lenge, C. A. *Mol. Phys.* **1969**, *16*, 95.

(18) Diehl, P.; Björholm, T.; Böisinger, H. *J. Magn. Reson.* **1981**, *42*, 390.

(19) Diehl, P.; Khetrapal, C. L. *Mol. Phys.* **1968**, *14*, 327.

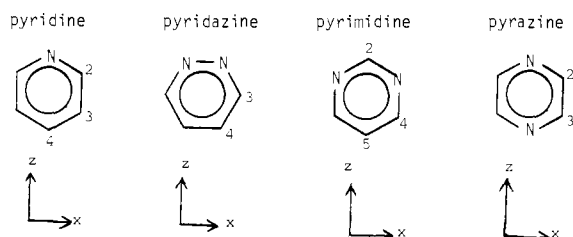
(20) Memory, J. D.; Wilson, N. K. "NMR of Aromatic Compounds"; Wiley-Interscience: New York, 1982.

Table I. Diagonal Elements of Carbon-13 Chemical Shift Tensors (ppm)^a of Pyridine and Diazines^b

		δ_{iso}	δ_{xx}	δ_{yy}	δ_{zz}
pyridine	C2	149.8 (149.8 ± 0.1)	241 ± 1	35.5 ± 0.6	173 ± 2
	C3	123.6 (123.5 ± 0.1)	205 ± 1	7.5 ± 0.6	158 ± 2
	C4	135.6 (135.6 ± 0.1)	170 ± 3	4.4 ± 1.4	233 ± 4
pyridazine	C3	151.5 (151.5 ± 0.1)	293 ± 6	31 ± 2	130 ± 8
	C4	126.1 (126.1 ± 0.1)	190 ± 10	3 ± 3	186 ± 12
pyrimidine	C2	158.9 (159.0 ± 0.1)	176 ± 5	55 ± 2	246 ± 4
	C4	156.7 (156.7 ± 0.1)	239 ± 6	30 ± 2	201 ± 4
pyrazine	C5	121.4 (121.5 ± 0.1)	138 ± 6	4 ± 2	221 ± 4
	C2	145.0 (145.0 ± 0.2)	223 ± 1	39 ± 1	173 ± 1

^aThe values in parentheses are averages of experimental value; the reference is Me₄Si. ^bSee text for coordinate and numbering systems.

has a considerable variation.⁴ The carbon-13 chemical shifts, order parameters, and values of *J* are listed in the supplementary material. The diagonal elements of the carbon-13 chemical shift tensors in the molecular axes system can be readily calculated from the anisotropic chemical shifts and ordering factors of six liquid-crystal solutions plus the isotropic shifts in six corresponding liquid solutions for each solute.^{4,6} In the calculation, the uncertainties of the tensor components obtained are reduced when the isotropic chemical shift (δ_{iso}) of the solute being studied is directly used.^{4,21} To measure δ_{iso} , one can either study the liquid-crystal solution directly with magic-angle spinning or by adding another organic liquid to change the solution into an isotropic liquid (e.g., adding CDCl₃ to 20%). Data obtained by using these two methods agree with each other within experimental error.²¹ The results for pyridine in ZLI 1167, which is a solvent with no aromatic rings, are shown in Figure 1, parts A and B, respectively. The spectra of pyridine in two liquid-crystal solutions with slow spinning (15 Hz) along the axis of the magnetic field are also shown in the same figure (C and D) for comparison. The exact chemical shifts in a magic-angle spinning experiment depend critically on the exact setting of the angle of the spinning axis. Furthermore, intense solvent peaks often interfere with the solute peaks when liquid crystals containing aromatic rings are used. On the other hand, we have found that solvent interference is not a problem in experiments using isotropic solutions of the same solvents, because the carbon-13 peaks are very sharp and solvent and solute signals can be easily distinguished. Therefore, data obtained from the isotropic solutions were used in the calculation. The numbering and axes systems are given below and the results of the carbon-13 chemical shifts are given in Table I.



The validity of using several different liquid-crystal solutions to determine the elements of the chemical shift tensors of a solute has been carefully tested.²¹ A major source of error in this method may be the effect of local anisotropy of the magnetic susceptibility.²² Since the solute of interest and the reference compound may have different average local environments, there would be an error due to the difference in local susceptibility anisotropy. This effect may not be the same in different liquid-crystal solvents. Fortunately, the anisotropic carbon-13 chemical shifts are quite large and the influence of the anisotropy in local susceptibility is much less than that on proton chemical shift anisotropies.²²

A drawback in the determination of chemical shift tensors by using liquid crystal solutions and polycrystalline solids is that the principal axes system of the tensors cannot be determined. In the

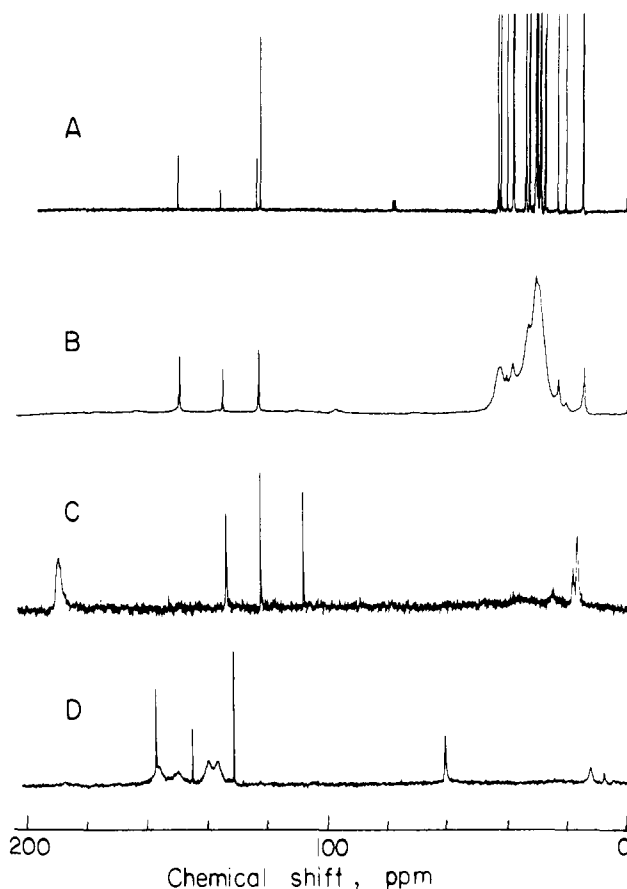


Figure 1. ¹³C NMR spectra of pyridine in several solutions at 75.4 MHz and 298 K. (A) An isotropic solution of ZLI 1167 with 20% CDCl₃; the aliphatic peaks of the solvent are truncated. (B) A nematic solution of ZLI 1167 with magic-angle spinning at the rate of 1 kHz; the CN peak of the solvent is too broad to be observed. (C) A nematic solution of ZLI 1167 with slow spinning (15 Hz) along *B*₀. (D) A nematic solution of EBBA with slow spinning (15 Hz) along *B*₀. A spin-echo sequence was used in taking spectra C and D for the reduction of solvent peaks (ref 14).

study of monosubstituted benzenes, it was assumed that one of the principal axes is the C-X or C-H bond axis and the second one is perpendicular to the ring.^{4,6} It has been shown from single-crystal data that this is a good assumption.²³⁻²⁵ However, in pyridine and diazines, many of the C-H axes further deviate from cylindrical symmetry and the above assumption might not be a good one. The data in Table I are therefore diagonal elements of the tensors in the molecular axis systems only. Nevertheless, the *y* axis, which is the axis perpendicular to the ring, should

(21) Fung, B. M.; Parhami, P. *J. Magn. Reson.* **1985**, *63*, 168.

(22) (a) Buckingham, A. D.; Burnell, E. E. *J. Am. Chem. Soc.* **1967**, *89*, 3341. (b) Buckingham, A. D.; Burnell, E. E.; de Lange, C. A. *J. Am. Chem. Soc.* **1968**, *90*, 2973.

(23) Pausak, S.; Pines, A.; Waugh, J. S. *J. Chem. Phys.* **1973**, *59*, 591.

(24) Pausak, S.; Tegenfeldt, J.; Waugh, J. S. *J. Chem. Phys.* **1974**, *61*, 1338.

(25) van Dongern Torman, J.; Veeman, W. S. *J. Chem. Phys.* **1978**, *68*, 3233.

Table II. A Test for the Additivity of the Effect of the Nitrogen Atoms on the Carbon-13 Chemical Shifts in Diazines^a

		C2	C3	C4	C5
pyridazine	δ_{iso}		145.1 \pm 0.2 (151.5)	157.1 \pm 0.2 (126.1)	
	δ_{yy}		35.9 \pm 2.3 (31.2)	4.8 \pm 2.6 (2.8)	
pyrimidine	δ_{iso}	171.3 \pm 0.2 (159.0)		157.1 \pm 0.2 (156.8)	118.9 \pm 0.2 (121.5)
	δ_{yy}	63.9 \pm 2.3 (54.8)		32.8 \pm 2.6 (29.5)	7.9 \pm 2.3 (4.4)
pyrazine	δ_{iso}	145.1 \pm 0.2 (145.0)			
	δ_{yy}	35.9 \pm 2.3 (39.5)			

^aIn each entry, the first number is calculated according to eq 1 and the number in parentheses is the experimental value, which has an uncertainty of ca. 0.1 ppm for δ_{iso} and 2 ppm for δ_{yy} .

essentially coincide with one of the major axes in the principal coordinate system.

In our previous works we have shown that δ_{iso} 's of different carbons in benzonitrile⁶ and halobenzenes⁴ do not vary regularly with their positions with respect to the substituent, but the tensorial component perpendicular to the ring (δ_{yy} here) correlates well with the inductive effect of the substituent. The data in Table I show that values of δ_{iso} of the α , β , and γ carbons in pyridine change irregularly, but those of δ_{yy} decrease regularly in that order. It has been shown that each component of the chemical shift tensor depends primarily on electron motion in the plane perpendicular to the direction of that component.^{5,26,27} Therefore, δ_{yy} should be dependent mainly on the σ -electron density, and its correlation with the inductive effect is entirely reasonable.

Each of the diazines contains two nitrogen atoms in a six-membered heterocyclic ring. In view of the difference in the effect of the nitrogen atom in pyridine on δ_{iso} and δ_{yy} , it is of interest to test the additivity (or the lack of it) of the two nitrogen atoms on the carbon-13 chemical shifts. The evaluation can be illustrated by considering the case of pyrazine. In pyrazine, each carbon is α with respect to one nitrogen and β with respect to another. From the data of pyridine in Table I, δ_{iso} of an α -carbon is 21.5 ppm downfield from that of benzene ($\delta_{\text{iso}} = 128.3$ ppm) and δ_{iso} of a β -carbon is 4.7 ppm upfield from that of benzene. Thus, if the effects of the two nitrogens are additive, δ_{iso} of each carbon in pyrazine should be 16.8 ppm downfield from that of benzene, or having the value of 145.1 ppm with respect to Me_4Si . The experimental value is indeed practically the same (145.0 \pm 0.2 ppm). In general, to calculate the additivity of the effects of the two nitrogens in diazines

$$\delta_{\text{cal}} = \delta_i + \delta_j - \delta_0 \quad (2)$$

where δ_i and δ_j are chemical shifts of pyridine; i and j can be α , β , or γ with respect to a nitrogen. δ_0 is the chemical shift of benzene; its isotropic value is 128.3 \pm 0.1 ppm in the solvents we used and its δ_{yy} value is 7.1 \pm 2.1 ppm.²¹ The results of the

additivity test are given in Table II.

The results in Table II show that δ_{iso} for both carbons in pyridazine is nonadditive. The difference between the calculated and experimental values for C4 is very large. On the other hand, δ_{yy} shows better additivities when the relative uncertainties (2–3 ppm for δ_{yy} vs. 0.1–0.2 ppm for δ_{iso}) are taken into account. In pyrimidine, δ_{iso} is additive for C4 only, but δ_{yy} shows reasonable additivities for C4 and C5. While both δ_{iso} and δ_{yy} are nonadditive for C2 in pyrimidine, the difference between the calculated and experimental values with respect to the experimental error is much larger for δ_{iso} than for δ_{yy} . In pyrazine, δ_{iso} is additive. δ_{yy} can also be regarded as additive within experimental error.

In summary, we have determined the carbon-13 chemical shift tensors of pyridine and three diazines in their molecular axes systems. In pyridine, δ_{yy} correlates well with the inductive effect of the ring nitrogen, while δ_{iso} does not. In pyridazine and pyrimidine, the effects of the two nitrogens on δ_{iso} are not additive, but they show much better additivities for δ_{yy} when relative experimental uncertainties are taken into account. From results of this and previous systematic studies,^{4–7,26,28} we conclude that components of the carbon-13 chemical shift tensor may correlate with molecular structure, properties and reactivity better than the isotropic chemical shift.

Acknowledgment. This work was in part supported by the National Science Foundation under Grant No. CHE-8318840. The Varian XL-300 spectrometer was purchased through a grant from the National Science Foundation (CHE-8113507). The variable-angle spinning probe was purchased through a grant from the University of Oklahoma Associates Research/Creative Activity Funds.

Registry No. Pyridine, 110-86-1; pyridazine, 289-80-5; pyrimidine, 289-95-2; pyrazine, 290-37-9.

Supplementary Material Available: Tables of carbon-13 chemical shifts and order parameters of each solute in six liquid crystal solvents and J values for each solute (9 pages). Ordering information is given on any current masthead page.

(26) Strub, H.; Beeler, A. J.; Grant, D. M.; Michl, J.; Cutts, P. W.; Zilm, K. W. *J. Am. Chem. Soc.* **1983**, *105*, 3333.

(27) Honkonen, R. S.; Ellis, P. D. *J. Am. Chem. Soc.* **1984**, *106*, 5988.

(28) Zilm, K. W.; Conlin, R. T.; Grant, D. M.; Michl, J. *J. Am. Chem. Soc.* **1980**, *102*, 6672.