

Carbon-13 Nuclear Magnetic Resonance Spectra and Electronic Densities of Symmetrical Naphthyridines

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The ^{13}C n.m.r. spectra of the four symmetrical naphthyridines have been obtained and assignment of the signals performed by means of heteronuclear decoupling experiments and empirical additivity methods. The shifts were found to depend linearly upon the total charge density on the carbon atoms as calculated by self-consistent molecular orbital INDO and CNDO approximations.

CHARGE and spin density distribution in azanaphthalenes and in the corresponding radical anions have been the subject of a large number of investigations; e.s.r. and ^{13}C n.m.r. spectroscopy are the most suitable experimental techniques for verifying the conclusions of theoretical methods.¹⁻⁶ While for radical anions almost all the isomers of mono-, di-, and tetra-azanaphthalenes have been investigated³⁻⁶ by means of e.s.r. spectroscopy ^{13}C n.m.r. has so far been applied to a more restricted number of derivatives. In this paper we recorded the ^{13}C n.m.r. spectra of the four symmetrical naphthyridines (I)—(IV) in order to determine whether the ^{13}C shifts follow the trend of the carbon charge densities and also to outline the differences in the electronic distribution between the neutral molecules and the corresponding radical anions.

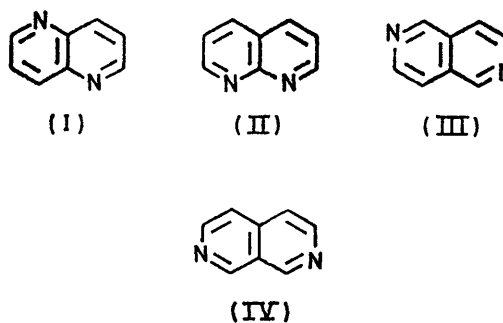
The ^{13}C shifts with respect to benzene (acetonitrile as solvent) are reported in the Table. In order to obtain

¹ R. J. Pugmire, D. M. Grant, M. J. Robins, and R. K. Robins, *J. Amer. Chem. Soc.*, 1969, **91**, 6381.

² W. Adam, A. Grimison, and G. Rodriguez, *Tetrahedron*, 1967, **23**, 2513; J. E. Bloor and D. L. Breen, *J. Amer. Chem. Soc.*, 1967, **89**, 6835; P. S. Pregosin, E. W. Randall, and A. I. White, *J.C.S. Perkin II*, 1972, 1.

³ A. Carrington and J. D. Santos-Vega, *Mol. Phys.*, 1962, **5**, 21; E. W. Stone and A. H. Maki, *J. Chem. Phys.*, 1963, **39**, 1635; F. Gerson and W. L. F. Armarego, *Helv. Chim. Acta*, 1965, **48**, 112; G. D. Zeiss and M. A. Whitehead, *J.C.S. Faraday II*, 1972, 526; F. Gerson, *Mol. Phys.*, 1972, **24**, 444.

an unambiguous assignment of the shifts of carbons bonded to hydrogens selective heteronuclear decoupling



was applied by monitoring the ^{13}C signals while irradiating at the frequency of each group of equivalent protons. In Figure 1 a typical example of these experiments is reported for the 1,8-isomer (II). Figure 1(a) shows the

⁴ L. Lunazzi, A. Mangini, and F. Taddei, *Tetrahedron Letters*, 1968, 1055; J. Chandhuri, S. Kume, J. Jagur-Grodzinski, and M. Szwarc, *J. Amer. Chem. Soc.*, 1968, **90**, 6421; L. Lunazzi, A. Mangini, G. F. Pedulli, and F. Taddei, *J. Chem. Soc. (B)*, 1970, 163.

⁵ J. C. M. Henning, *J. Chem. Phys.*, 1966, **44**, 2139; R. Danieli, L. Lunazzi, and G. Placucci, *J. Amer. Chem. Soc.*, 1971, **93**, 5850.

⁶ J. A. Pedersen and L. T. Muus, *Mol. Phys.*, 1969, **16**, 589; P. Cavaliere D'Oro, R. Danieli, G. Maccagnani, G. F. Pedulli, and P. Palmieri, *ibid.*, 1971, **20**, 365; D. M. W. Van den Ham, J. J. du Start, and D. van der Mear, *ibid.*, p. 989.

noise decoupled spectrum in which there is one singlet for each of the five types of carbon atoms; in Figure 1(b)—(d) only one type of carbon atom has been decoupled by irradiating at the frequency of the corresponding hydrogen and therefore the signals of the other carbons are almost undetectable owing to the presence of coupling constants and to the lack of appreciable

quinolines [for the isomers (III) and (IV)] placed in suitable positions. By combining the perturbation shifts for the appropriate carbon atoms one obtains the shifts with respect to the α or β positions of naphthalene. Finally, by addition of the naphthalene shifts the calculated values for the various carbon atoms of the naphthyridines are obtained. For instance the shift of

¹³C Shifts and charge densities for naphthyridines (I)—(IV)

Isomer	Carbon atoms	¹³ C Shifts ^a		Charge densities			
		Experimental	Calculated ^b	INDO		CNDO	
				Q_{tot}	Q_{π}	Q_{tot}	Q_{π}
(I)	C-2	-23.2	-23.2	3.8489	0.9531	3.9046	0.9597
	C-3	3.5	3.2	4.0113	1.0097	4.0188	1.0093
	C-4	-11.9	-9.6	3.9672	0.9725	3.9871	0.9742
	C-4a	-15.7	-15.5	3.8967	0.9864	3.9203	0.9870
(II)	C-2	-25.5	-26.2	3.8309	0.9378	3.8903	0.9428
	C-3	5.7	6.1	4.0317	1.0279	4.0354	1.0286
	C-4	-10.4	-7.8	3.9389	0.9532	3.9665	0.9546
	C-8a	-27.9	-35.8	3.7765	0.9550	3.8368	0.9589
	C-4a	5.1	4.8	4.0211	1.0117	4.0077	1.0069
(III)	C-1	-24.1	-23.4	3.8765	0.9596	3.9265	0.9699
	C-3	-16.9	-16.9	3.8606	0.9745	3.9150	0.9811
	C-4	8.6	7.9	4.0464	1.0347	4.0491	1.0329
	C-4a	-2.5	-2.9	3.9529	0.9741	3.9548	0.9718
(IV)	C-1	-24.9	-24.4	3.8537	0.9472	3.9109	0.9575
	C-3	-18.7	-19.9	3.8522	0.9607	3.9070	0.9667
	C-4	8.9	8.9	4.0492	1.0426	4.0497	1.0422
	C-8a	4.2	4.0	4.0390	1.0227	4.0195	1.0174
	C-4a	-10.0	-9.8	3.8878	0.9306	3.9115	0.9321

^a In p.p.m. from benzene. ^b From the empirical additivity method (see text).

nuclear Overhauser enhancement. In this way one can correlate the shifts of the hydrogens, obtained by measuring the frequencies which decouple the ¹³C spectrum, with those obtained from the ¹H spectrum [Figure 1(e)]. Since the assignment of the hydrogens can be made from proton-proton coupling constants and chemical shifts,⁷ unambiguous assignment of the ¹³C signals can be achieved. This technique also allows the identification of bridgehead carbon signals as they are not affected by the irradiation. The results agree with observations on the noise-decoupled spectrum where these signals can be also recognised by the negligible NOE enhancement with respect to that experienced by the hydrogen-bonded carbon atoms.

In the case of molecules (II) and (IV) there is however a further assignment to be made as one must distinguish between two different bridgehead carbon atoms. To remove this uncertainty we used an empirical additivity method successfully employed both for radical anions^{5,6} and neutral molecules¹ closely related to the derivatives here investigated. This method, as we have applied it to naphthyridines, requires the evaluation of the perturbation induced by the nitrogen atom on the ¹³C shifts of naphthalene by comparing the shifts of quinoline and isoquinoline¹ with those of the corresponding positions of naphthalene. One can now build up the naphthyridines (I)—(IV) by using either a pair of quinolines [for isomers (I) and (II)] or a pair of iso-

C-3 (or -7) in (I) will be obtained by combining the perturbation parameters of positions 3 and 7 of quinoline which are, according to ref. 1, +4.4 (*i.e.* +6.95 - 2.56) and -3.8 p.p.m. (*i.e.* -1.24 - 2.56) respectively. The value obtained in this way (+0.6 p.p.m.) gives the shift of C-2 (or -7) in (I) with respect to the β carbon atoms of naphthalene; the latter being +2.56 p.p.m. with respect to benzene,¹ one obtains 3.2 p.p.m. as the calculated shift for C-2 in (I). The agreement with the experimental value (3.5 p.p.m.) is satisfactory. The reliability of this approach can be checked (Table) by comparing the calculated shifts of hydrogen-bonded carbons with the experimental data where unambiguous assignment has been achieved. Since for all the twelve positions involved the assignment is always correct, it is reasonable to rely upon this approximation even when applied to quaternary carbon atoms. Accordingly in compound (II) the downfield shift has been assigned to C-8a and the upfield to C-4a while the opposite has been found in naphthyridine (IV). The value of the ¹³C shift in unsaturated derivatives mainly depends upon the charge density on the carbon atom, the greater the electronic density, the higher the ¹³C shift.^{1,2,8} In order to rationalise theoretically the trend of ¹³C shifts we calculated the charge densities on the different positions by using CNDO and INDO methods.⁹ As knowledge of the geometry is required we first examined derivative

⁸ Z. W. Wolkowski, E. Vauthier, B. Gonbeau, H. Sauvatre, and J. A. Musso, *Tetrahedron Letters*, 1972, 566.

⁹ J. A. Pople and D. L. Beveridge, 'Approximate Molecular Orbital Theory,' McGraw-Hill, New York, 1970.

⁷ (a) W. W. Paudler and T. J. Kress, *Adv. Heterocyclic Chem.*, 1970, 11, 123; (b) W. W. Paudler, D. J. Pokorny, and S. J. Cornrich, *J. Heterocyclic Chem.*, 1970, 7, 291.

(I) whose geometry has been determined by X-ray diffraction.¹⁰ No appreciable difference being observed between the computed charge density of this and the standard geometry,⁹ the latter was employed for all

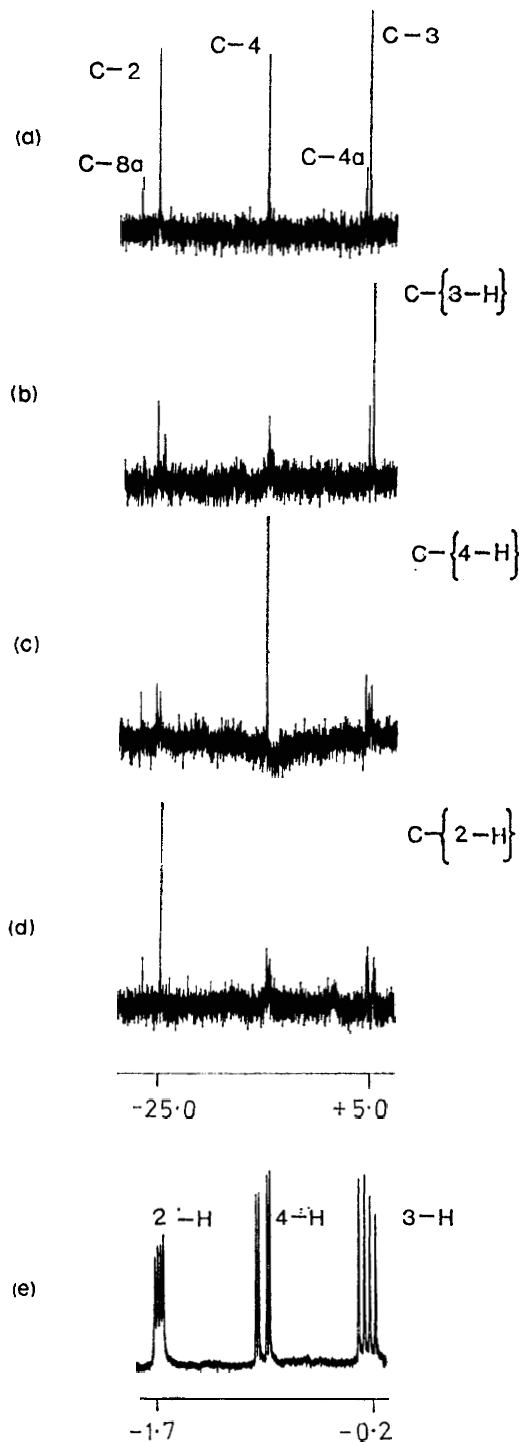


FIGURE 1 (a), 25.2 MHz Noise-decoupled ^{13}C n.m.r. spectrum of 1,8-naphthyridine (II); (b)—(d), the same spectrum obtained by irradiating at the resonance frequencies of 3-, 4-, and 2-H; (e), 100 MHz ^1H n.m.r. spectrum of (II). All the shifts (p.p.m.) are negative when downfield and positive when upfield relative to benzene

four isomers. Both the π and total charge densities are reported and, as already observed in other cases,^{1,8} the latter give better linear relationships with the ^{13}C shifts. The total charge density calculated from the INDO approximation parallels the trend of the shifts (Figure 2) better than do those from CNDO (correlation coefficients 0.96 and 0.92 respectively).

It is thus reasonable to consider the ^{13}C shift in these isomers a satisfactory measure of the total density on the carbon atoms as the standard deviations of the shifts are only 3.5 and 4.6 p.p.m. for the INDO and CNDO methods respectively over a range of almost 40 p.p.m. Furthermore, the scatter of points about the straight line is statistically distributed so that the few deviations larger than the standard error seem due only to the approximations involved in the theoretical calculations.

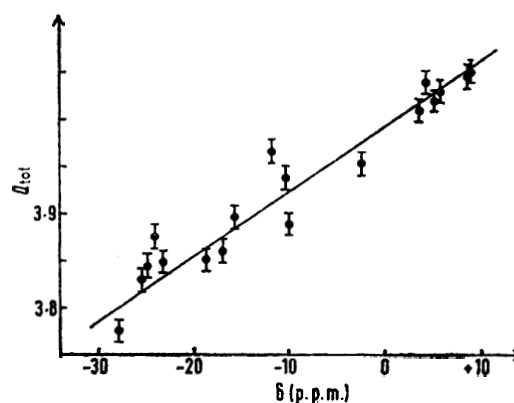


FIGURE 2 ^{13}C Shifts (I)—(IV) vs. the total charge densities computed for the corresponding positions with the INDO approximation

A comparison with the spin densities in the corresponding radical anions shows many differences in the trend of values which by no means depend on the fact that electrons of the neutral molecule are located in bonding orbitals whereas the unpaired electron in the radical anion is in an antibonding orbital. The largest differences are observed for the carbon bonded to nitrogen. The electronegativity of the latter is actually very efficient in modifying the charge density of the vicinal carbon atoms in the neutral naphthyridines and therefore in shifting the ^{13}C signals downfield. On the other hand the hyperfine splittings of the radical anions mainly depend on the spin density distribution of the π orbitals and thus the carbons bonded to nitrogen are less sensitive than in the neutral molecule to the electron-withdrawing power of the nitrogen atom.

EXPERIMENTAL

The ^{13}C spectra have been recorded on a JEOL PS 100 instrument operating at 25.2 MHz in the continuous wave mode. Saturated solutions of acetonitrile in tubes (8 mm) allowed the spectra to be obtained in a single scan. The signal for $\text{CH}_3^{13}\text{CN}$ was used as internal standard and the shifts were then related to benzene whose peak is (for a

¹⁰ M. Brufani, D. Duranti, and G. Giacomello, *Gazzetta*, 1959, **89**, 2328.

solution in acetonitrile) 10.4 p.p.m. downfield from the experimental standard.

The ^1H spectra were recorded for acetonitrile solution and their shifts referred to benzene in order to compare them with the frequencies of the heteronuclear selective decoupling to be performed on the ^{13}C spectra. Relative to the ^1H shifts reported in ref. 7 (CDCl_3 as solvent) those in acetonitrile were slightly displaced downfield (0.1—0.15 p.p.m.). The ^{13}C shifts have been presented with negative

sign when downfield and with positive sign when upfield from that of benzene in order to make them consistent with the analogous data reported in ref. 1, although the opposite practice has been recently recommended.

The four naphthyridines were synthesised according to refs. 6, 7, and 11.

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¹¹ R. Danieli and A. Ricci, *Synthesis*, 1973, **1**, 46.
