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^{14}N-H SPIN COUPLINGS IN PYRAZINE METHIODIDES

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IN the course of the study of total synthesis of Cypridina luciferin (1) extracted from Cypridina hilgendorfii, we have found interesting spin couplings between an aromatic ^{14}N nucleus and ring protons in the PMR spectrum of 2-amino-4-methylpyrazinium iodide (III). Biellmann and Callot have recently reported, however, that ^{14}N-H spin couplings are observed in some N-alkylpyridinium salts having an electron-attracting substituent at C-4 (2). Their paper has driven us to report promptly our results.

In general, it is difficult to observe ^{14}N-H couplings because the signal of a proton interacting with an ^{14}N nucleus is broadened or decoupled by its quadrupolar relaxation. However, ^{14}N-H couplings were clearly observed in some tetra-alkylammonium salts, alkylisonitriles, and trimethylvinylammonium salts in which electric-field gradient at the ^{14}N nucleus is thought to be highly symmetrical, and accordingly, quadrupolar relaxation of the ^{14}N nucleus is relatively slow (3).

We have observed the PMR spectra of 1-methylpyrazinium (I) (4), 2,4-dimethylpyrazinium (II),*[1] 2-amino-4-methylpyrazinium (III) (5), and 1-methylquinoxalinium (IV) iodides in D_2O at 100 MHz.*[2] The assignment of the signals were made by proton magnetic double and triple resonance (PMDR and PMTR) techniques.*[2] On double or triple irradiation at the frequency of methyl-proton signals, ring protons

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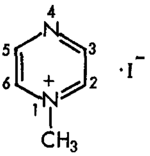
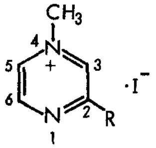
*[1] The compound II were obtained by the procedure similar to that for (I) as a mixture with its 3-methyl isomer in a ratio of about 7 : 1 (from PMR), respectively.

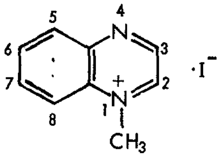
*[2] The PMR spectra were taken with a Varian HA-100 spectrometer operating at 100 MHz by using about 15% (w/v) solutions in D_2O. The PMDR and PMTR experiments were made by using the spectrometer with two Hewlett-Packard 200ABR audio-oscillators in the frequency-swept and DSS-locked mode.



(I)



(II) R=CH_3
(III) R=NH_2



(IV)

ortho to methyl groups become sharper owing to the disappearance of weak benzylic couplings (6). Thus, the $J_{^{14}N,H}$ and $J_{H,H}$ values were determined as listed in the TABLE by the first-order treatments. For example, the spectra of (III) are shown in the FIG. The results indicate that quarternization occurred at position 4 in (II) and (III); this is compatible with that deduced from UV spectroscopy (5). The fact that the $|J_{^{14}N,H(\beta)}|$ values are larger than the corresponding $|J_{^{14}N,H(\alpha)}|$ values (both have probably the positive sign) is in accordance with the result obtained from a study of quinoline-^{15}N ethiodide (7).

TABLE
Coupling Constants, J, in Hz [a]

I	$N_1,H_2 = 1.0_5$	b
	$N_1,H_3 = 2.8$	
II	$N_4,H_3 = 1.0$	$H_3,H_5 = 1.1$
	$N_4,H_5 = 1.1_5$	$H_3,H_6 = 1.1$
	$N_4,H_6 = 2.9$	$H_5,H_6 = 3.6$
III	$N_4,H_3 = 1.0$	$H_3,H_5 = 1.5$
	$N_4,H_5 = 1.2_5$	$H_3,H_6 = 1.0$
	$N_4,H_6 = 3.0$	$H_5,H_6 = 4.0$
IV [c]	N_1,H_2 d	$H_2,H_3 = 3.0$
	$N_1,H_3 = 2.1$	

[a] The coupling constants with respect of methyl groups were not determined because of the complexity of the signals.

[b] The ring protons belong to an A_2B_2 system. The full analysis of the signals will be reported in our full paper.

[c] Determined at 96°.

[d] The H_2 signal appears still as a sharp doublet even at 96° when the methyl protons were doubly irradiated.

The appearance of these obvious ^{14}N-H splittings in the compounds is reasonably suggested to result from the presence of an electronegative N atom at the position para to the $^{14}N^+$ atom. The strong electron-attracting ability of the N atom lowers the π-electron density around the $^{14}N^+$ nucleus; this may contribute to make the electric-field gradient at the $^{14}N^+$ nucleus sufficiently symmetrical. This explanation is in harmony with the fact that ^{14}N-H splittings are clearly observed in alkylisonitriles (8), since the π-electron density around the $-\overset{14}{N}{}^+\equiv$ atom would be extremely lowered. Although in the case of N-alkylpyridinium salts, only those having an electron-attracting group at C-4 show the ^{14}N-H splittings (2), the splittings were observed in the PMR spectra of the pyrazinium derivatives having an electron-donating group, such as a methyl or an amino

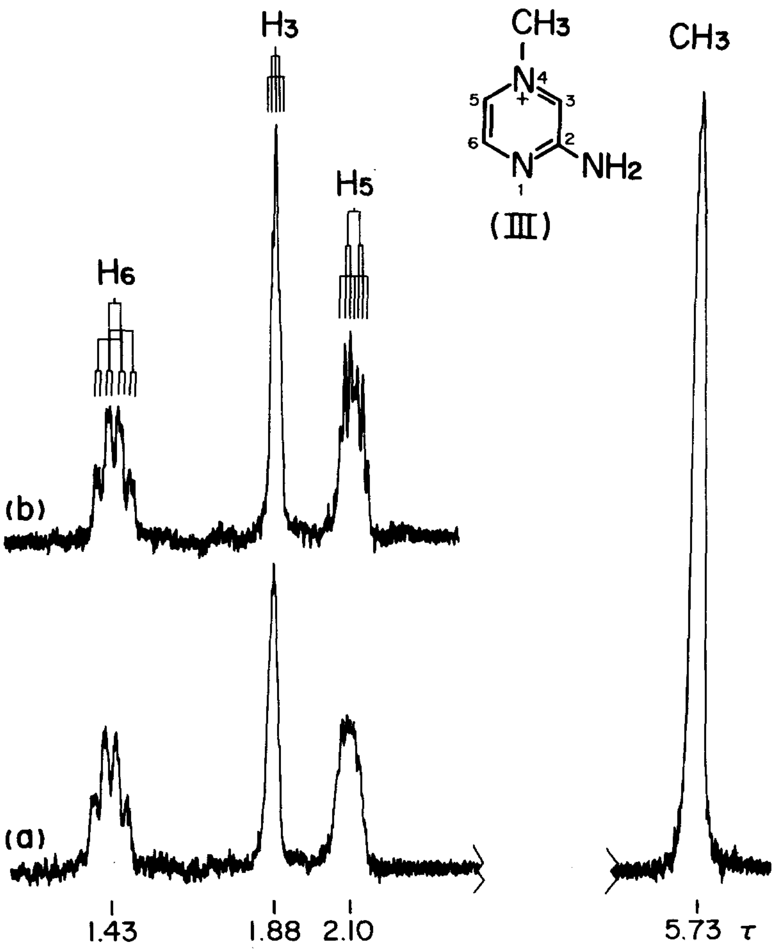


FIG. The PMR spectra of 2-amino-4-methylpyrazinium iodide (III) in D_2O at 100 MHz. (a) Normal spectrum; (b) PMDR spectrum irradiated at the frequency of the methyl resonance.

group, at position 2. This result indicates that electron-attracting power of the N atom would be very strong. In fact, the pK_a values of pyrazine (0.65) and 2-aminopyrazine (3.07) are much lower than those of pyridine (5.21) and 2-aminopyridine (6.82) (9). In our own experience, the spectrum of quinoline ethiodide in D_2O shows a sharp triplet signal for the methyl group even at 100°, while the methyl group in pyridinium ethiodide (2) shows a triplet of triplets, though somewhat broad, at 90°. The benzene ring might distort the electric-field gradient at the $^{14}N^+$ nucleus. On the other hand, in the spectrum of (IV) the ^{14}N-H splittings appeared at elevated temperatures.

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