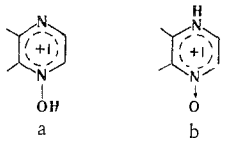
A STUDY OF THE STRUCTURE OF THE CATIONS OF N-OXIDES OF MONOSUBSTITUTED PYRAZINES AND QUINOXALINES BY THE PMR METHOD

T. N. Ul'yanova, G. G. Dvoryantseva,
Yu. N. Sheinker, A. S. Elina, and I. S. Musatova

UDC 547.861'863'822'7'824:543.422.25

The dependence of the chemical shifts of the protons on the concentration of D_2SO_4 in D_2O in a number of N-oxides of monosubstituted pyrazines and quinoxalines has been investigated, and the parameters of the PMR spectra of the neutral and the mono- and diprotonated forms of the compounds investigated have been determined. All the pyrazine and quinoxaline N-oxides considered protonate first at the unoxidized nitrogen atom (N_4). The first protonation of 2-aminopyrazine 1,4-di-N-oxide takes place at the oxygen atom of the N→O group in position 1, and that of 2-methoxypyrazine at the oxygen atom of the N→O group in position 4. The effect of the delocalization of the positive charge in the monocations of the compounds investigated has been considered.

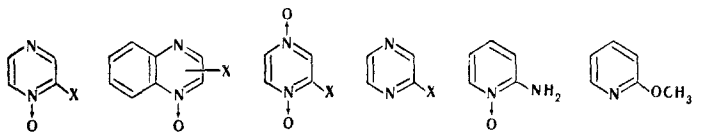
One of the features of the structure of the mono-N-oxides of diazines is the presence in the molecule of two cationic centers: the unoxidized nitrogen atom of the heterocyclic ring and the oxygen atom of the N→O group, corresponding to two possible structures of the monocation:



a b

On the basis of a study of the PMR [1] and electronic [2] spectra it has been established that the protonation of the unsubstituted N-oxides of pyrazine and quinoxaline takes place at the unoxidized nitrogen atom (N_4) with the formation of a monocation of type b.

The introduction of a substituent into position 2 or 3 may lead to a change in the comparative basicities of the centers considered. To study this question, in the present work we have investigated the parameters of the PMR spectrum on the concentration of D_2SO_4 in D_2O (in the range from 0 to 36 N D_2SO_4) for the 1-N-oxides of 2- and 3-methoxyquinolines (IV and V), the 1,4-di-N-oxides of 2-amino- and 2-methoxypyrazines (VI and VII), and the model compounds (VIII-XI).



I-III IV, V VI, VII VIII, IX X XI

I, VI, VIII X = NH_2; II, VII X = OCH_3; III X = Cl; IV X = 2-OCH_3; V X = 3-OCH_3; IX X = $COOCH_3$

The chemical shifts and SSC constants of the protons of the pyrazine ring of the neutral molecules, and the mono- and dications of the compounds investigated, are given in Table 1.

S. Ordzhonikidze All-Union Scientific-Research Institute of Pharmaceutical Chemistry, Moscow.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1115-1123, August, 1973. Original article submitted July 28, 1972.

TABLE 1. Chemical Shifts and SSC Constants of the Protons

Comp.	Name	Form of comp.*	Medium	Chemical shifts, δ, ppm				SSC constants		
				3-H	5-H	6-H	OCH_3	$J_{3,5}$	$J_{3,6}$	$J_{5,6}$
I	1-N-oxide of 2-aminopyrazine	N	D_2O	8,33	7,85	8,11	—	<0,5	0,7	4,5
		C	3 *N* D_2SO_4	8,51	8,05	8,62	—	1,4	0,7	5,0
		DC	30 *N* D_2SO_4	9,13	8,23	8,90	—	1,2	0,7	5,2
II	1-N-oxide of 2-methoxypyrazine	N	D_2O	8,61	8,33	8,32	4,25	<0,5	0,6	4,1
		C	7 *N* D_2SO_4	8,74	8,53	8,84	4,33	1,4	0,6	5,0
		DC	35 *N* D_2SO_4	9,25	8,90	9,29	4,74	1,2	0,6	5,0
III	1-N-oxide of 2-chloropyrazine	N	D_2O	8,87	8,57	8,48	—	<0,5	0,6	4,2
		C	12 *N* D_2SO_4	9,13	8,74	8,91	—	1,4	0,6	5,2
IV	1-N-oxide of 2-methoxyquinoxaline	N	D_2O	8,80	—	—	4,37	—	—	—
		C	7 *N* D_2SO_4	9,23	—	—	4,48	—	—	—
		DC	35 *N* D_2SO_4	9,60	—	—	4,88	—	—	—
V	1-N-oxide of 3-methoxyquinoxaline	N	D_2O	8,25†	—	—	4,08	—	—	—
		C	11 *N* D_2SO_4	8,79†	—	—	4,44	—	—	—
VI	1,4-di-N-oxide of 2-aminopyrazine	N	D_2O	8,13	7,72	8,22	—	2,4	0,6	5,6
		C	5 *N* D_2SO_4	8,34	7,77	8,33	—	2,4	0,6	6,0
		DC	30 *N* D_2SO_4	9,03	8,20	8,76	—	2,4	0,6	6,0
VII	1,4-di-N-oxide of 2-methoxypyrazine	N	D_2O	7,81	7,62	8,02	2,90	1,8	0,9	4,9
		C	3 *N* D_2SO_4	8,20	7,69	7,95	2,90	1,8	0,9	5,6
VIII	2-Aminopyrazine	N	D_2O	8,04	7,82	7,95	—	<0,5	1,5	3,0
		C	1 *N* D_2SO_4	8,53	7,97	7,86	—	<0,5	1,1	4,2
		DC	22 *N* D_2SO_4	9,06	8,16	8,54	—	0,7	1,1	5,0
IX	2-Methoxycarbonylpyrazine	N	D_2O	9,27	8,88	8,78	4,02	<0,5	1,5	2,5
		C	12 *N* D_2SO_4	9,51	9,16	9,60	4,14	0,7	1,4	3,0
X	1-N-oxide of 2-aminopyridine‡	N	D_2O	7,00	6,79	7,99	—	1,9	0,6	6,9
		C	3 *N* D_2SO_4	7,18	6,92	8,08	—	1,8	0,6	7,1
XI	2-methoxypyridine	H	CH_2Cl_2	6,72	6,86	8,11	3,91	1,0	0,8	5,0
		K	CH_2Cl_2/30% CF_3COOH	7,42	7,52	8,28	4,22	1,0	<0,5	6,5

*N, neutral molecule; C, monocation; DC, dication.

†Chemical shifts of the 2-H proton.

‡Chemical shifts of the 4-H proton in X: 7.54 (N), 7.83 (C); in (XI): 7.58 (N), 8.51 (C).

The structure of the protonated forms of the compounds under consideration was established on the basis of: 1) the changes in the SSC constants of the protons of the pyrazine ring in the spectra of the neutral molecules; 2) a comparison of the nature of the dependence of the chemical shifts of the corresponding protons on the concentration of the acid at the stage of the first protonation of the molecules under study and of model compounds; and 3) the relative changes in the chemical shifts of the protons present in the α and β positions to the corresponding cationic centers in the molecules under study and model compounds on passing from the neutral compounds to monocations.

Figure 1 shows the experimental curves for the protons of compounds (I-III).

An increase in the concentration of the acid from 0 to 3 N D_2SO_4 is accompanied by a sharp downfield change in the signals of all the protons in 2-aminopyrazine 1-N-oxide. Near the first point of inflection on each curve, which is found at the same concentration of acid (~3 N) for all the protons, there is a change in the SSC constants of the ring protons which is connected with the first protonation of the molecule. Linear sections of the graphs within which the SSC constants remain unchanged and the changes in the chemical shifts are minimal correspond to a range of concentrations of D_2SO_4 from 3 to 10 N. In this range of acidity of the medium, compound (I) is present exclusively in the monoprotonated form. A further rise in the concentration of acid again leads to a downfield displacement of all the signals, and in 30 N D_2SO_4 the molecule passes completely into the form of the dication.

A consideration of the analogous curves for 2-methoxypyrazine 1-N-oxide (II) showed that this compound is present in the form of the monocation in a wide range of concentrations of acid (from 7 to 20 N D_2SO_4) and is transformed completely into the dication in strongly acid media (about 35 N D_2SO_4). These results correspond to the lower basicity of (II) ($pK_a = -0.51$)* than of (I) ($pK_a = 0.79$) [2]. 2-Chloropyrazine 1-N-oxide (III) is the weakest base of the pyrazine mono-N-oxides considered ($pK_a = -1.31$) and over the

*The ionization constants of the compounds under investigation in water were measured by M. M. Kaganskii (Scientific-Research Institute of Pharmaceutical Chemistry, Novokuznetsk) and will be discussed in detail in another paper.

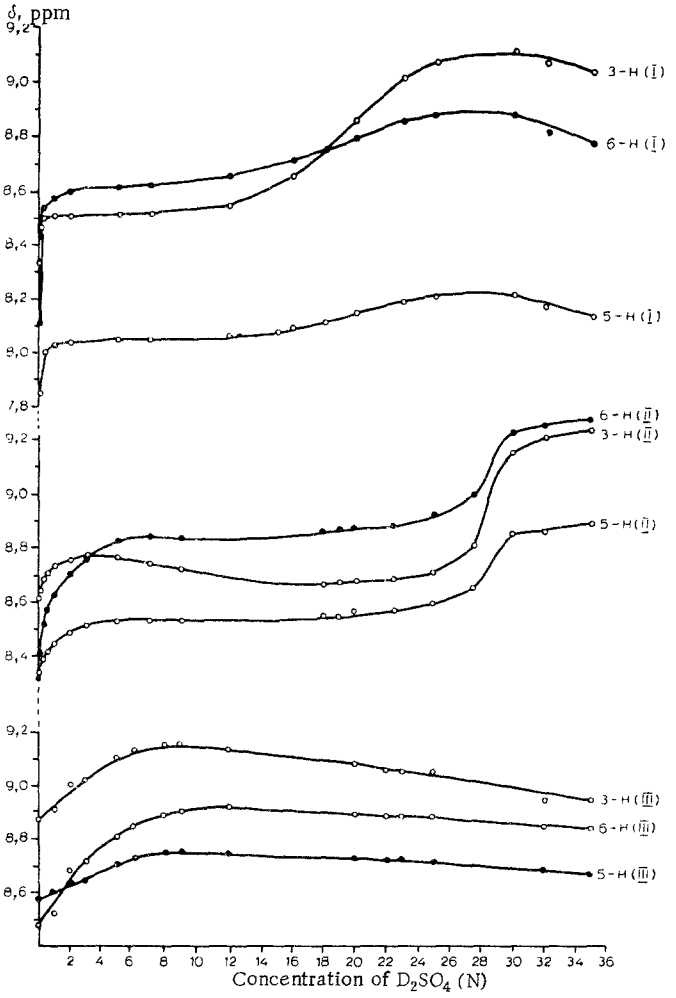


Fig. 1. Dependence of the chemical shifts of the protons of 2-aminopyrazine 1-N-oxide (I), 2-methoxypyrazine 1-N-oxide (II), and 2-chloropyrazine 1-N-oxide (III) on the concentration of deuterosulfuric acid.

whole range of concentrations of acid it gives only the monoprotonated form. Thus, an investigation of the relationships described above enables the measured parameters of the PMR spectra to be assigned reliably to a definite form of the compound. The chemical shifts and SSC constants of the spectra of the mono- and dications given in Table 1 were determined at concentrations of D_2SO_4 corresponding to the linear sections of the graphs close to the points of inflection on the experimental curves, i.e., at the minimum concentrations of acid necessary for the complete conversion of the molecule into the mono- or dicationic form, as the case may be. It must be mentioned that the change in the chemical shifts of the ring protons over the whole of the linear section corresponding to the monocation does not exceed 0.1 ppm and, in the majority of cases, is within the limits of experimental error.

A comparison of the spectra of the neutral and protonated forms of the pyrazine 1-N-oxides (I-III) and the N-unoxidized compounds (VIII) and (IX) has shown that the position of the cationoid center in a molecule of this type can be established unambiguously from the change in the SSC constant of the meta protons of the ring through the unoxidized hetero nitrogen atom ($J_{3,5}$). It is known that in neutral molecules of azines this constant does not exceed 0.5 Hz in absolute magnitude [3-5]. In the 2-substituted pyrazines, the value of $J_{3,5}$ lies between 0.01 and 0.46 Hz [4]. The N-oxidation of the heteroaromatic ring, both in the pyridine series [6] and in the diazines [5, 7] leads to a considerable increase in the SSC constant of the meta protons through the oxidized nitrogen atom. In the 2-substituted pyrazine 4-N-oxides, the constant $J_{3,5}$ amounts to 1.4-1.8 Hz [5]. At the same time, the N-oxidation of the pyrazine molecule in position 1 has little influence on $J_{3,5}$; in the 2-substituted pyrazine 1-N-oxides, the absolute values of $J_{3,5}$ are in the same range as in the corresponding N-unoxidized azines [5]. Since N-protonation, just like N-oxidation, takes

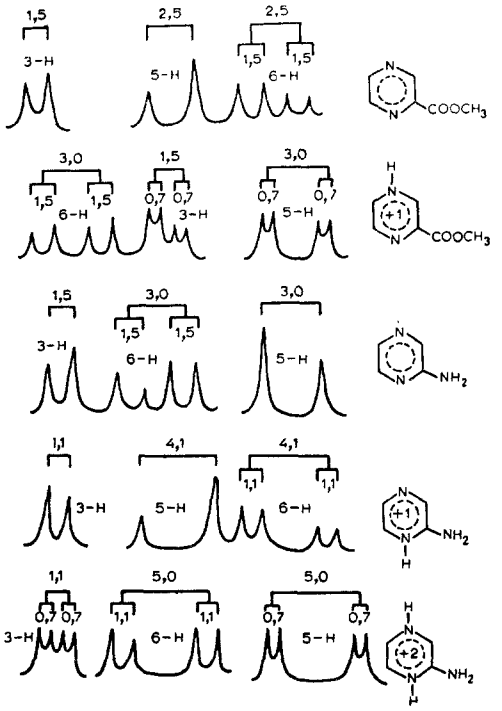


Fig. 2. Signals of the ring protons in the PMR spectra of pyrazine derivatives and of the corresponding cations.

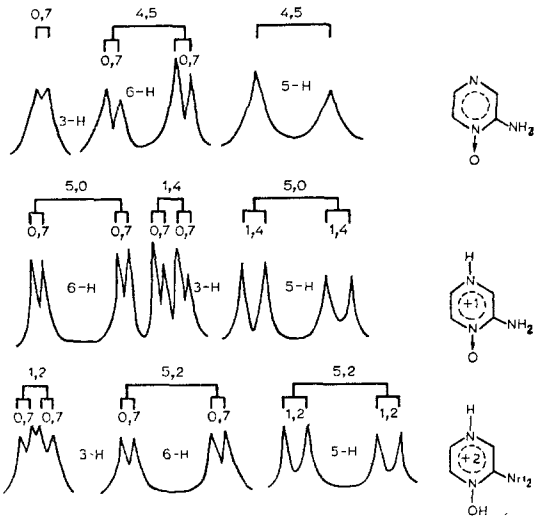


Fig. 3. Signals of the ring protons in the PMR spectra of the base and of the mono- and dications of 2-aminopyrazine 1-N-oxide.

place at the lone pair of the heteroatom, it is natural to expect an analogy in the influence of these processes on the SSC of the meta protons through the nitrogen atom, as is actually found in a consideration of the spectra of the neutral molecules and cations of the 2-substituted pyrazines (VIII) and (IX) (see Table 1 and Fig. 2). In the spectra of the neutral molecules of these compounds the constant $J_{3,5}$ is close to 0 and the signals of the 3-H and 5-H protons form doublets with the SSC constants $J_{3,6} = 1.5$ Hz and $J_{5,6} = 2.5$-3.0 Hz. In the spectrum of the monocation of 2-methoxycarbonylpyrazine (IX), the signals of these protons are observed in the form of quartets with the constant $J_{3,5} = 0.7$ Hz, which shows the addition of the proton to N_4. In the spectrum of the monocation of 2-aminopyrazine, just as in the spectrum of the neutral molecule, the signals of the protons in positions 3 and 5 are observed in the form of doublets. The change in the multiplicity of these signals and the appearance of the signal $J_{3,5} = 0.7$ Hz take place only at the stage of the second protonation of the molecule of (VIII). These facts unambiguously show that the first protonation of 2-aminopyrazine takes place at the N_1 atom and the second at N_4, and they fully correspond to the structure of the monocations of 2-aminopyrazine and 2-aminoquinoxaline established through their UV spectra [8, 9].

In the spectra of all the 1-substituted pyrazine 1-N-oxides investigated (I-III) (Table 1, Fig. 3) a change in the multiplicity of the signals of the protons in positions 3 and 5 and the appearance of a constant $J_{3,5} = 1.2$-1.4 Hz are observed at the stage of the first protonation of the molecule. This indicates the addition of the proton to the unoxidized nitrogen atom of the ring (N_4) with the formation of the structure of the monocations (Ib-IIIb). Consequently, an increase in the electron-donating capacity of the substituent in position 2 in the sequence Cl, OCH_3, and NH_2 does not lead to a change in the direction of the protonation of the pyrazine 1-N-oxides.

The position of the center of protonation in the molecules of the methoxy derivatives of quinoxaline 1-N-oxide (IV, V) and pyrazine 1,4-di-N-oxide (VII) was established on the basis of a comparative study of the dependence of the chemical shifts of the protons of the ring and of the OCH_3 group on the concentration of acid. As model compounds we used 2-methoxypyridine (XI) and 2-methoxypyrazine 1-N-oxide (II) with an established structure for the cations. A consideration of the experimental curves, which are given in Fig. 4, showed that the changes in the chemical shifts of the protons of the OCH_3 group at the stage of the first protonation of the molecule depend on the position of this group relative to the cationic center. Thus, on passing from the neutral molecule to the monocation of (XI) (ortho position of the substituent relative to the center of protonation) the signal of this group shifts downfield by 0.3 ppm. In the case of 2-methoxypyrazine 1-N-oxide (meta arrangement of the substituent and the cationic center), the change in the chemical shift of the protons of the OCH_3 group at the first protonation stage is very small (0.07 ppm). The similar downfield shift of the signal of the methoxy group (0.11 ppm) on passing from the neutral molecule to the monocation of 2-methoxyquinoxaline 1-N-oxide shows the similarity of the arrangements of the sub-

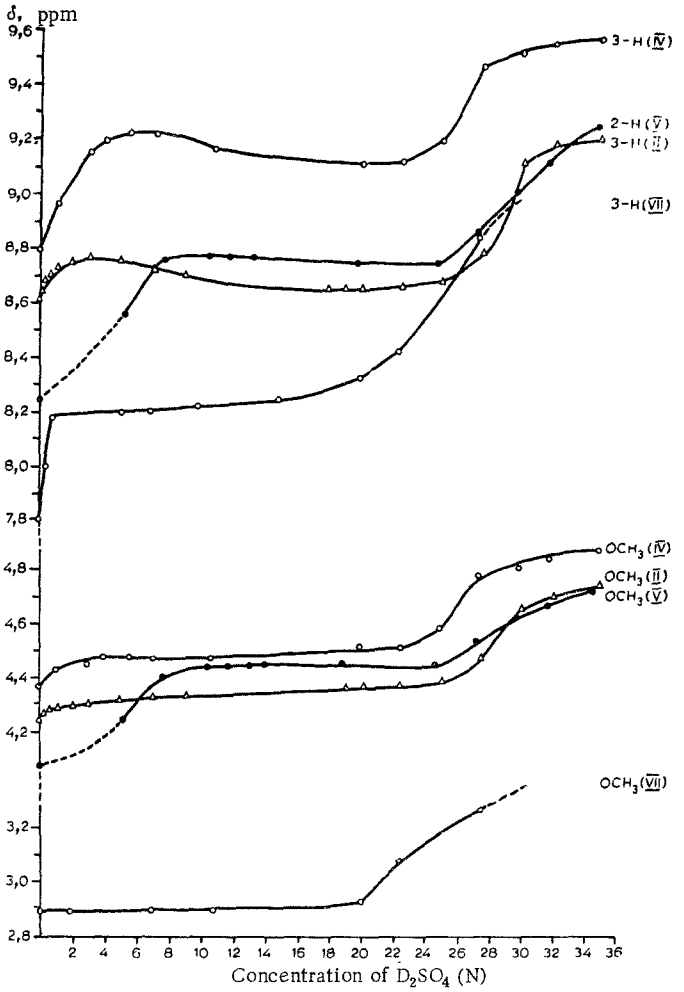
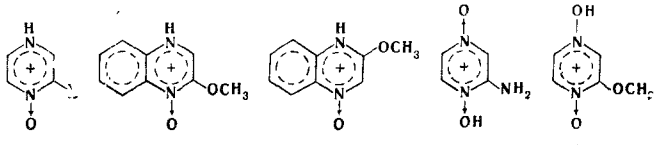


Fig. 4. Dependence of the chemical shifts of the protons of 2-methoxypyrazine 1-N-oxide (II), 2-methoxyquinoxaline 1-N-oxide (IV), 3-methoxyquinoxaline 1-N-oxide (V), and 2-methoxypyrazine 1,4-di-N-oxide (VII) on the concentration of deuterosulfuric acid.

stituents and the cationic centers in (II) and (IV). On the basis of these facts, the monocation of 2-methoxyquinoxaline 1-N-oxide has been assigned structure (IVb). The effect of the deshielding of the protons of the OCH_3 group on the monoprotonation of 3-methoxyquinoxaline 1-N-oxide (0.36 ppm) proved to be close to that observed in (XI), which corresponds to the ortho position of the substituent relative to the cationic center in (V) (structure Vb).



From a consideration of the curves for the protons of 2-methoxypyrazine 1,4-di-N-oxide it follows that in the range from 4 to 18 N D_2SO_4 the compound exists in the form of the monocation. At the same time, the chemical shift of the protons of the OCH_3 group in this compound scarcely changes as compared with the neutral molecule over the whole range of acidities from 0 to 18 N D_2SO_4. An appreciable downfield shift of this signal is observed only in the range of concentrations of D_2SO_4 above 20 N, which, according to the experimental curve for the ring protons, corresponds to the second protonation of the molecule of (VII). Consequently, the addition of the first proton to 2-methoxypyrazine 1,4-di-N-oxide has practically no influence (within the limits of experimental error) on the shielding of the methoxy group ($\Delta\delta \approx 0$) which indicates an increase in the distance between this group and the center of protonation in (VII) as compared

TABLE 2. Chemical Shifts of the Protons

Compound	Center of protonation	Medium	Chemical shifts, ppm	
			5-H	6-H
Pyridine [10]	N_1	D_2O/18 *N* D_2SO_4	0,72	0,26
Pyridine 1-N-oxide [10]	$N_1 \rightarrow O$	D_2O/18 *N* D_2SO_4	0,40	0,39
2-Methoxycarbonylpyrazine	N_4	D_2O/12 *N* D_2SO_4	0,28	0,82
Pyrazine 1-N-oxide [1]	N_4	D_2O/20 *N* D_2SO_4	0,10	0,39
2-Chloropyrazine 1-N-oxide	N_4	D_2O/12 *N* D_2SO_4	0,17	0,43
2-Methoxypyrazine 1-N-oxide	N_4	D_2O/7 *N* D_2SO_4	0,20	0,52
2-Aminopyrazine 1-N-oxide	N_4	D_2O/3 *N* D_2SO_4	0,20	0,51
2-Aminopyridine [4]	N_1	D_2O/2 *N* DCl	0,35	−0,09
2-Aminopyrazine	N_1	D_2O/1 *N* D_2SO_4	0,15	−0,09
2-Aminopyridine 1-N-oxide	$N_1 \rightarrow O$	D_2O/3 *N* D_2SO_4	0,13	0,09
2-Aminopyrazine 1,4-di-N-oxide	$N_1 \rightarrow O$	D_2O/5 *N* D_2SO_4	0,05	0,11

* $\Delta\delta_i = \delta_i^{(K)} - \delta_i^{(H)}$.

with (II) and (IV) ($\Delta\delta$ = 0.07-0.11 ppm). These facts are in harmony with structure (VIIa) for the monocation of 2-methoxypyrazine 1,4-di-N-oxide.

The analogy found in the nature of the curves of the first protonation of 2-aminopyrazine 1,4-di-N-oxide and 2-aminopyridine 1-N-oxide and the similarity of the changes in their UV spectra [2] correspond to the addition of a proton to the oxygen atom of the $N_1 \rightarrow O$ group (structure VIa) in both compounds.

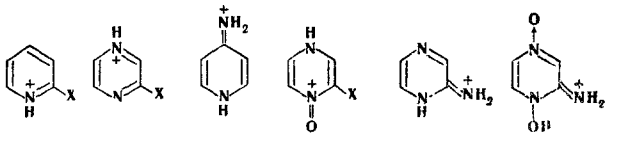
The conclusions concerning the structure of the monocations are confirmed by a comparison of the relative changes of the chemical shifts of the ring protons in the α and β positions to the corresponding cationic center in the compounds investigated and model compounds (see Table 2).

It is known that the protonation of pyridine and of the majority of its monosubstituted derivatives takes place with a considerably greater deshielding of the β proton (5-H) than of the α proton (6-H). The changes in the chemical shifts of the protons in positions 5 and 6 observed on passing from the neutral molecules to the monocations of 2-methoxycarbonylpyrazine and of 2-substituted pyrazine 1-N-oxides correspond to their α and β arrangements relative to the N_4 cationic center.

A consideration of the values of $\Delta\delta_i$ is also of fundamental interest from the point of view of the distribution of the positive charge in the ions. A similarity of the values of $\Delta\delta_\alpha$ and $\Delta\delta_\beta$ in 2-methoxycarbonylpyrazine and those observed in the protonation of pyridine under analogous conditions permits the monocation of (IXb) to be assigned the structure of an ion of the "pyridinium" type corresponding to a considerable localization of the positive charge on the cationoid center. The monoprotonation of the pyrazine 1-N-oxides leads to a smaller deshielding of the ring protons. These results can be explained by some contribution of a structure of the quinoid type (B) with a transfer of positive charge from the cationoid center to the nitrogen atom of the $N \rightarrow O$ group in the ions and, connected with this, a reduction in the effect of the ring currents of the heteroaromatic ring.

Still greater differences from ions of the "pyridinium" type are observed in the monocations of amino derivatives of azines and their N-oxides containing an NH_2 group in the α position to the cationic center. Thus, the protonation of the 2-amino derivatives of pyridine and pyrazine leads to an upfield displacement of the signals of the α protons (6-H) by 0.09 ppm. In these compounds the signal of the β proton is shifted downfield, but this shift (0.15-0.35 ppm) is considerably less than the values of $\Delta\delta_\beta$ characteristic for ions of the "pyridinium" type [10-12].

A similar effect is observed on passing from the neutral molecule to the monocation of 4-aminopyridine, to which, on the basis of IR and PMR spectra, the para-quinoid structure (B) with the localization of the positive charge predominantly (about 90%) on the exocyclic amino group has been ascribed [12]. This analogy is in favor of the predominance of the quinoid structure of the monocation [13] in α-amino derivatives of aromatic azines, as well, which agrees with the results of an investigation of the UV and IR spectra of compounds of this type [8, 13]. Structure C of the monocation (VIIIb) also corresponds to an increased



A B C

value of the ortho constant of SSC $J_{5,6}$ = 4.2 Hz in comparison with the monocation (IXb) (3.0 Hz) and disubstituted pyrazinium ions (3.23-3.56 Hz) [4]. A value of the $J_{5,6}$ constant close to that for (VIIIb) is observed in the spectra of neutral molecules of 2-hydroxypyrazine (3.91 Hz) and 2-hydroxy-3-methylpyrazine (4.20 Hz) [4], which exist in the oxo forms [14].

On passing from the neutral molecule to the monocation of 2-aminopyridine 1-N-oxide ($\Delta\delta_6$ = 0.09 ppm, $\Delta\delta_5$ = 0.13 ppm) and of 2-aminopyrazine 1,4-di-N-oxide ($\Delta\delta_6$ = 0.11 ppm, $\Delta\delta_5$ = 0.05 ppm), the α-H and β-H deshielding effects fall by about 0.3 ppm as compared with the corresponding unsubstituted compounds (in pyridine 1-N-oxide, $\Delta\delta_6$ = 0.39 ppm, $\Delta\delta_5$ = 0.4 ppm [10], and in pyrazine 1,4-di-N-oxide, $\Delta\delta_6$ = $\Delta\delta_5$ = 0.35 ppm [2]). By analogy with the α-amino derivatives of N-unoxidized azines, these facts indicate a considerable contribution of structure C with transfer of positive charge to the exocyclic amino group in the monocations (VIa) and (Xa), as well.

The difference that has been discussed in the change in the shielding of the protons of the six-membered aromatic ring on the formation of ions with a quinoid ("pyridonoid") structure as compared with ions of the "pyridinium" type is substantiated by information on the effects of magnetic anisotropy in quinones [15]. The authors concerned showed that the ring currents in the quinones amount to about 75% of the currents in the corresponding hydrocarbons. Making use of the generally accepted value of the chemical shift due to the effect of the ring currents in benzene and its aza derivatives of 1.5 ppm [16-18], it is possible to estimate the increase in the shielding of the protons of a six-membered ring on passing from ions with the "pyridinium" to ions with the "pyridonoid" type of value as about 0.4 ppm. This estimate agrees satisfactorily with the experimental results discussed above.

EXPERIMENTAL

The PMR spectra of the compounds investigated were measured on a C-60 HL spectrometer in 0.1 M solutions of the substances in D_2O/D_2SO_4 mixtures (I-X) and in CH_2Cl_2/CF_3COOH mixtures (XI). As internal standards, sodium 4,4-dimethyl-4-silapentane-1-sulfonate was used for the solutions in D_2O/D_2SO_4, and tetramethylsilane for the solutions in CH_2Cl_2/CF_3COOH.

LITERATURE CITED

1. T. N. Ul'yanova, G. G. Dvoryantseva, L. M. Alekseeva, Yu. N. Sheinker, and A. S. Elina, Khim. Geterotsikl. Soedin., 846 (1971).
2. M. M. Kazanskii, G. G. Dvoryantseva, and A. S. Elina, Dokl. Akad. Nauk SSSR, 197, 832 (1971).
3. W. Brügel, Z. Electrochem., 66, 159 (1962).
4. R. H. Cox and A. A. Bothner-By, J. Phys. Chem., 72, 1642 (1968); 73, 2469 (1969).
5. G. P. Syrova, Yu. N. Sheinker, I. S. Musatova, and A. S. Elina, Khim. Geterotsikl. Soedin., 266 (1972).
6. S. Castellano and R. Kostelnik, J. Amer. Chem. Soc., 90, 141 (1968).
7. A. G. Moritz and B. D. Paul, Austral. J. Chem., 22, 1305 (1969).
8. S. F. Mason, J. Chem. Soc., 219 (1960).
9. G. W. H. Cheesman, Advan. Heterocyclic Chem., 2, 204 (1963).
10. R. A. Abramovitch and J. B. Davis, J. Chem. Soc., B, 1131 (1966).
11. A. R. Katritzky and J. M. Lagowski, J. Chem. Soc., 43 (1961).
12. B. D. Batts and E. Spinner, Austral. J. Chem., 22, 2595 (1969).
13. E. Spinner, J. Chem. Soc., 3119 (1962).
14. Yu. N. Sheinker and Yu. I. Pomerantsev, Zh. Fiz. Khim., 30, 79 (1956).
15. J. J. W. LeFevre and D. S. N. Murthy, Austral. J. Chem., 23, 193 (1970).
16. J. S. Waugh and R. W. Fessenden, J. Amer. Chem. Soc., 79, 846 (1957).
17. C. E. Johnson and F. A. Bovey, J. Chem. Phys., 29, 1012 (1958).
18. G. G. Hall, A. Hardisson, and L. M. Jackmann, Disc. Faraday Soc., 34, 15 (1962).