N-OXIDES OF THE QUINOXALINE SERIES

XVII. IR Spectra of Salts of the Mono- and Di-N-oxides of 2-Aminoquinoxaline*

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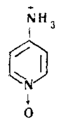
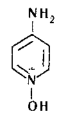
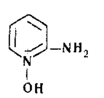
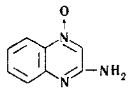
The IR spectra of the hydrochlorides of 2-aminoquinoxaline (II) and its N-oxides are discussed and a comparison of them with the spectra of the analogous sales of 2-aminopyridine and its N-oxide is made. On the basis of the results obtained, it may be concluded that II and its 4-N-oxide are protonated at the cyclic atom of nitrogen $N_{(1)} \rightarrow O$ group.

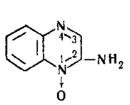
In connection with the study of tautomerism and rearrangement among the N-oxides of 2-aminoquinoxaline [1, 2] it appeared of interest to determine the position of protonation in these compounds. Jaffe [3], using Hammett's equation for calculating the ionization constants of the two possible cations of 4-aminopyridine 1-N-oxide (the base being I and the cations **Ia** and **Ib**), showed that the addition of the proton to the exocyclic nitrogen atom of the amino group of compound I was unlikely and confirmed for its cation the structure **Ib** which had been assumed previously by Japanese workers. Katritzky [5], on the basis of a comparison of the UV spectra of 2-aminopyridine 1-N-oxide and its methyl derivative in neutral and acid media ascribed the analogous structure (**Ic**) to the cation of 2-aminopyridine 1-N-oxide.

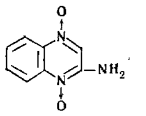

Ia


Ib

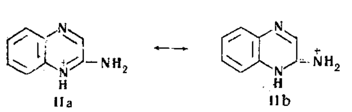

Ic

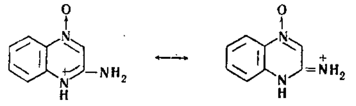

III


IV


V

2-Aminoquinoxaline (II) can form two mono-N-oxides (III and IV) and a di-N-oxide (V). In 2-aminoquinoxaline 4-N-oxide (III), just as in 2-aminoquinoxaline itself (II) there is the amidine grouping $N{=}C{-}NH_2$ that is characteristic for all α-amino derivatives of N-heterocycles. Cheeseman [6], considering the UV spectra of the base II, its cation, and 2-imino-1-methyl-quinoxaline came to the conclusion that in the base II, as in other α-amino derivatives of N-heterocycles [7, 8], the proton adds to the cyclic nitrogen atom, $N_{(1)}$, involved in the amidine grouping, with the formation of the hybrid cation (**IIa** ⟷ **IIb**). The second cyclic nitrogen atom, $N_{(4)}$ of the base II is less basic and cannot compete with $N_{(1)}$ in the addition of a proton (it is known that the basicity of the aromatic N-heterocycles is considerably lower than the basicities of their α- and γ-amino derivatives). In 2-aminoquinoxaline 4-N-oxide (III) one may assume an analogous mechanism of protonation and the formation of the cation (**IIIa** ⟷ **IIIb**).


IIa IIb


IIIa IIIb

In this case, the second competing site of protonation (the oxygen of the N → O group) is still less likely, since the basicity of heterocyclic N-oxides is considerably lower than the basicity of the initial bases.

We have considered the IR spectra of the hydrochlorides of the base II and its N-oxides III–V. The spectra, taken in the form of tablets with KBr or of mulls in paraffin oil, were identical with one another; only in some cases was a splitting of the individual bands observed. The spectra were taken on a UR-10 spectrophotometer. As was to be expected, the hydrochloride of the base II and of 2-aminopyridine have similar spectra in the high-frequency region (see Fig. 1); in these spectra the so-called "immonium" bands of the group $\overset{\setminus + /\!/}{N}{-}H\ldots\bar{X}$ in the 2700–2200 cm^{-1} region are lacking. As a rule, these bands are observed in the IR spectra of salts of aromatic N-heterocycles and are not found in the spectra of the corresponding α- or γ-amino derivatives [9].

A pattern similar to this is also found in the spectrum of the hydrochloride of the N-oxide III (see Fig. 1), which confirms for the cation III the structure **IIIa** ⟷ **IIIb**, analogous to the structure of the cations of compounds I and II. Some difference in the high-frequency region of the spectrum of the salt of this N-oxide consisting in the somewhat clearer appearance of the broad band in the 2660–2800 cm^{-1} region possibly indicates a greater localization of the positive charge in the cation **IIIa** ⟷ **IIIb** and a predominance of the **IIIa** form.

In the molecule of 2-aminoquinoxaline 1-N-oxide (IV), by analogy with the N-oxides of 2- and 4-aminopyridine [3, 5], protonation may take place at the oxygen of the $N_{(1)} \rightarrow O$ group with the formation of the cation **IVa.** However, in this N-oxide, in contrast to compound II and the 4-N-oxide III, there is no strongly basic amidine grouping and, in view of this, the pos-

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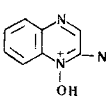
*For part XVI, see [1].

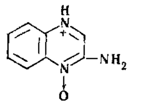
Salts of Quinoxaline Derivatives

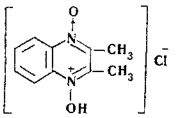
Name	Mp (decomp.), °C	Empirical formula	Found, %		Calculated, %	
			N	halogen	N	halogen
Hydrochloride of 2-aminoquinoxaline 4-N-oxide	242.5 (from anhydrous ethanol).	$C_8H_7N_3O \cdot HCl$	21.01	18.22	21.26	17.94
Hydrochloride of 2-aminoquinoxaline 1,4-di-N-oxide	248 (from anhydrous ethanol).	$C_8H_7N_3O_2 \cdot HCl$	19.55	16.24	19.67	16.60
Hydrochloride of 2-aminoquinoxaline	221 (from anhydrous ethanol).	$C_8H_7N_3 \cdot HCl$	23.02	19.65	23.14	19.53
Hydrochloride of 2,3-dimethylquinoxaline 1,4-di-N-oxide	179—180	$C_{10}H_{10}N_2O_2 \cdot HCl$	12.08	15.39	12.36	15.64
Hydrobromide of 2,3-bis(bromomethyl)quinoxaline 1,4-di-N-oxide	167	$C_{10}H_8Br_2N_2O_2 \cdot HBr$	6.60	56.20	6.53	55.86

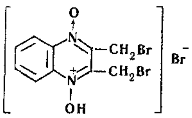
sibility of competition between two centers of protonation—the oxygen of the $N_{(1)} \rightarrow O$ group and the cyclic nitrogen $N_{(4)}$ (the cations **IVa** and **IVb**)—is not excluded. A consideration of the spectrum of the hydrochloride of compound IV shows a marked difference from the spectra of the hydrochlorides of compounds I and II. The stretching vibrations of the NH_2 group in this are shown in the form of well-marked bands in the 3295 and 3095 cm^{-1} regions, being displaced only slightly in comparison with the spectrum of the base IV (3300 and 3130 cm^{-1}), and in the 2560–2680 cm^{-1} region there is a broad intense band (Fig. 2).

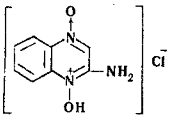
If, by analogy with the cation of 2-aminopyridine N-oxide, the cation of the N-oxide IV is ascribed structure IVa, the broad band at 2560 cm^{-1} must relate to the stretching vibrations for the $\overset{\diagdown + /\!\!/}{N}{-}O{-}H\ldots$ group. Moreover, it is known that in the IR spectra of salts of pyridine N-oxide and its methyl derivatives the bands of the stretching vibrations of this group are generally located in the lower-frequency region, namely 2200–2400 cm^{-1} [10, 11]. The bands of the stretching vibrations of the $\overset{\diagdown + /\!\!/}{N}{-}O{-}H\ldots$ groups in the hydrochloride of 2, 3-dimethylquinoxaline 1, 4-di-N-oxide (VI) (2160 cm^{-1}, Fig. 2) and the hydrobromide of 2, 3-bis(bromomethyl)quinoxaline 1, 4-di-N-oxide (**VII**) (2130–2210 cm^{-1}), which we have prepared, are found in approximately the same region of the spectrum. However, the IR spectra of the hydrochlorides of pyridine and picoline N-oxides and of the di-N-oxide hydrochloride VI and the hydrochloride corresponding to VII can hardly be taken as models for the spectrum of the hydrochloride of the 1-N-oxide IV, since the presence in the latter of an α-amino group may have a substantial effect on the frequency of the vibrations of the $\overset{\diagdown + /\!\!/}{N}{-}O{-}H\ldots$ group. In this case, we may use as model compounds the hydrochlorides of 2-aminopyridine N-oxide and 2-aminoquinoxaline 1, 4-di-N-oxide (**Va**). A comparison of the IR of these compounds with the spectrum of the salt of the N-oxide of IV showed their similarity in the high-frequency region. In the spectrum of **Va**, just as in the spectrum of the hydrochloride of **IV**, there are strong bands of the stretching vibrations of the NH_2 group at 3305 and 3090 cm^{-1} (ν_{NH_2} of the base IV, 3320 and 3120 cm^{-1}) and a broad intense band of the $\overset{\diagdown + /\!\!/}{N}{-}O{-}H\ldots$ group at 2590–2690 cm^{-1} (Fig. 2). These spectra, in their turn, are very similar to the spectrum of the hydrochloride of 2-aminopyridine N-oxide in which the band of the stretching vibrations of $\overset{\diagdown + /\!\!/}{N}{-}O{-}H\ldots$ appears in the form of a broad intense band in the 2530–2650 cm^{-1} region (Fig. 2). Thus, the presence of an α-amino group in the molecules of the salts of heterocyclic N-oxides studied does in fact shift the band of the stretching vibrations of the $\overset{\diagdown + /\!\!/}{N}{-}O{-}H\ldots$ group into the higher-frequency region by approximately 350–400 cm^{-1}. On the basis of the similarity of the bands in the high-frequency region of the spectrum of the hydrochlorides of compounds IV and V and of 2-aminopyridine N-oxide, it may be concluded that the protonation of compound IV takes place at the oxygen atom of the $N_{(1)} \rightarrow O$ group with the formation of the cation **IVa.**


IVa


IV b


VI


VII


Va

In the IR spectra of the bases II, IV, and V three strong absorption bands are found in the region of the deformation vibrations of the NH_2 group and of the stretching vibrations of the C=C and C=N bonds: one at 1645–1660 cm^{-1} and two in the lower-frequency region at 1625–1575 cm^{-1}. In the spectrum of the N-oxide III, there are found bands in the 1625–1560 cm^{-1} region (1625, 1610, 1590, and 1560 cm^{-1}). On the basis of a comparison of the spectra of the deuterated and nondeuterated compounds II, III, IV, and V the bands of highest frequency (1660 in II, 1625 in III, and 1645 cm^{-1} in IV and V must be ascribed to the deformation vibrations of the NH_2 group. The other bands in this region obviously relate to the stretching vibrations of the C=C and C=N bonds of the ring. The bands of the deformation vibrations of the NH_2 groups in the spec-

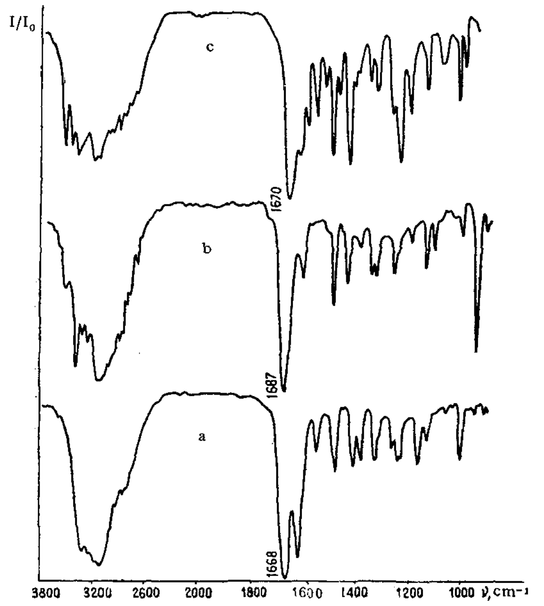


Fig. 1. IR spectra of the hydrochlorides of 2-aminopyridine (a) and 2-aminoquinoxaline (b) and its 4-N-oxide (c) (taken in tablets with KBr).

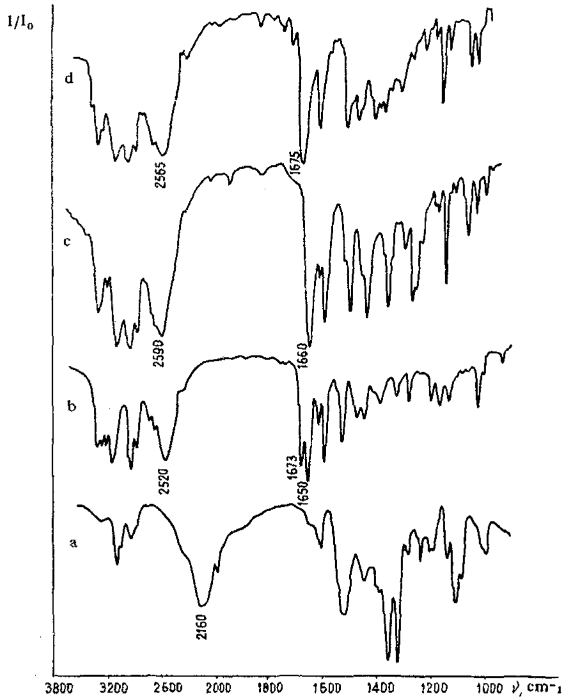


Fig. 2. IR spectra of the hydrochlorides of 2,3-dimethylquinoxaline di-N-oxide (in a tablet with KBr) (a), 2-aminopyridine N-oxide (b), and 2-aminoquinoxaline di-N-oxide (c) and 1N-oxide (d) (taken in a mull in paraffin oil).

tra of the salts of both the initial amine II and its N-oxides III, IV, and V are displaced into the higher-frequency region by 15–45 cm^{-1} as compared with the corresponding bases.

We have shown previously that in the spectra of the N-oxides III, IV, and V there are strong bands in the 1200–1300 cm^{-1} region in which the bands of the stretching vibrations of the N → O group usually appear which are absent from the spectrum of the initial amine II (1220 in III, 1200 cm^{-1} in IV and V) [1]. In the spectrum of 2-aminopyridine N-oxides (1) the very strong band at 1200 cm^{-1} must be ascribed to the vibrations of the N → O group. The formation of a salt has a considerable effect on this region of the spectra. Thus, in the spectra of salts of the N-oxides IV and I in which protonation takes place at the oxygen of the N→O group, these bands have disappeared, and in the spectra of salts of the 4-N-oxide III and the 1, 4-di-N-oxide V, in which protonation takes place at the nitrogen or at one of the N → O group present, the bands of the stretching vibrations of the N → O groups are displaced into the higher-frequency region.

The hydrochlorides were obtained from the corresponding bases by the action on them of an ethanolic solution of hydrogen chloride (the hydrochloride of compound IV has been obtained previously [2]).

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