STRUCTURE OF 3-PYRAZOLIDONE HYDROCHLORIDES

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UDC 547.775:543.422.4

On the basis of the shift of the bands of the stretching vibrations of the amide group in the IR spectra of the hydrochlorides of 1-phenyl-3-pyrazolidone derivatives in chloroform and in the crystalline state, it was proved that 3-pyrazolidone hydrochlorides are formed through the addition of a proton to the nitrogen atom in the 1 position. The different type of protonation of 3-pyrazolidones as compared with the protonation of 1-phenyl-5-pyrazolones (protonation at the oxygen) is explained by the presence of an aromatic heteroring in the latter compounds and the absence of such a ring in the former.

On the basis of an analysis of the pK_a values of several 3-pyrazolidones, Zaitsev and co-workers [1] have demonstrated that pyrazolidones add a proton at the amine nitrogen in the 1 position. More detailed information regarding the protonation of phenidones, particularly their reaction with HCl, can be obtained by IR spectroscopy. For this, one can use the vibrations of the bonds that include nitrogen atoms (N–H, N^+–H, and C–N) and the vibrations of groups that are sensitive to a change in the state of the indicated nitrogen atoms. Carbonyl groups are particularly groups of this sort. In [1] it was pointed out that the IR spectra of pyrazolidone hydrochlorides in the crystalline state contain bands at 1690-1775 cm^{-1}, while the spectra of chloroform solutions of these hydrochlorides have bands at 1720-1725 cm^{-1}. However, the paper did not contain any data for the hydrochlorides of the individual compounds, the indicated frequency intervals were not adequately discussed, and the completeness of protonation was unknown.

In the present study we have used IR spectroscopy to study the structure of the hydrochlorides of 1-phenyl-3-pyrazolidone derivatives in the crystalline state and in chloroform solutions.

An important factor responsible for the interaction of hydrogen halides with heterocyclic compounds is the basicity of the heteroatoms. The latter depends to a great degree on the environment. Depending on the environment, the heteroatoms in compounds can be found in various states that determine the type of valence orbitals and their inclusion in the molecular electronic system. Of special interest in this respect are compounds with several heteroatoms. In particular, 5-pyrazolones and 3-pyrazolidones are compounds of this sort.

It has previously been pointed out that the state of the nitrogen atom in 5-pyrazolone is determined by the inclusion of an unshared pair of nitrogen electrons in the aromatic system of the pyrazolone ring [1]. The latter circumstance explains the sharp reduction in the basicity of nitrogen atoms, which is confirmed by the ease of protonation of 5-pyrazolone derivatives at the amide oxygen atom rather than at the nitrogen atoms [2].

A distinctive peculiarity of 1-aryl-pyrazolidones is the absence of a closed π-electron system in the pyrazolidone ring. A consequence of this is the fact that phenidone (1-phenyl-3-pyrazolidone) is characterized by the presence of several atoms that have electron-donor properties – the two ring nitrogen atoms and the carbonyl oxygen. These atoms have unshared pairs of electrons that are capable of being supplied to the unfilled or partially vacant orbitals of protons or hydrogen atoms. It should be expected that, of the two nitrogen atoms, the nitrogen atom in the 1 position rather than that in the 2 position has the greatest

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Scientific-Research Institute of Organic Intermediates and Dyes, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 676-680, May, 1972. Original article submitted July 5, 1971.

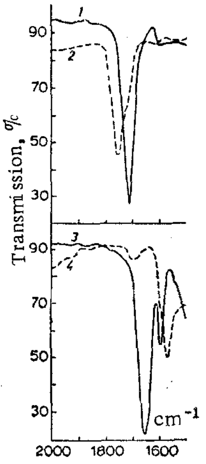


Fig. 1

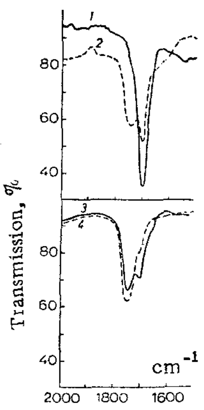
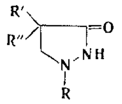


Fig. 2

Fig. 1. $\nu_{C=O}$ bands in chloroform and in chloroform in the presence of HCl: 1) and 2) 1-phenyl-3-pyrazolidone (c 0.00308 M); 3) and 4) antipyrine (c 0.00331 M); 1) and 3) unprotonated forms; 2) and 4) protonated forms.

Fig. 2. $\nu_{C=O}$ band of 1-(o-tolyl)-3-pyrazolidone in chloroform and in chloroform in the presence of HCl (c 0.0028 M): 1) unprotonated form; 2) and 3) partially protonated forms; 4) completely protonated form.

TABLE 1. Frequencies of the Stretching Vibrations of the C=O Groups in the IR spectra of 3-Pyrazolidone Hydrochlorides*



Compound	R	In $CHCl_3$				In KBr pellets	
		$\nu_{C=O}$, cm^{-1}		$\Delta\nu^a_{1/2}$, cm^{-1}		$\nu_{C=O}$, cm^{-1}	
		unprotonated form	protonated form	unprotonated form	protonated form	unprotonated form	protonated form
I	C_6H_5	1709	1749	29,4	58,8	1695	1756 1710
II	C_6H_5	1710	1748	29,85	55,2	1692	1749 1686
III	C_6H_5	1708	1743	39,2	44,1	1688	1740† 1728 1681
IV	p-$CH_3C_6H_4$	1710	1748	36,4	46,5	1690	1758 1695
V	m-$CH_3C_6H_4$	1710	1753	32,24	53,68	1690	—
VI	o-$CH_3C_6H_4$	1700	1748	31,85	49	1726 1650	1740† 1714
VII	2,4,6-$(CH_3)_3C_6H_2$	1695	1746	30,85	58,4	1723 1712	—
VIII	p-ClC_6H_4	1713	1753	34,3	39,2	1704	1756 1695

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*In II, R' = CH_3, in III, R' = R'' = CH_3, while in I and IV-VIII, R' = R'' = H.

† Shoulder.

capacity for protonation. This is due to the fact that the unshared pair of electrons of the 2-N atom interacts with the carbonyl group, which leads to a sharp decrease in its basic properties and to an increase in the basicity of the carbonyl oxygen. The interaction of 1-N with the phenyl group and with 2-N should be relatively weak, since the phenyl group and 2-N interact much more weakly with the 1-N amine nitrogen than does the carbonyl group with the 2-N atom. As a result, the basicity of 1-N is expected to be quite high (see [1]).

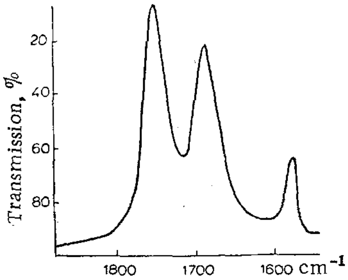
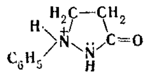


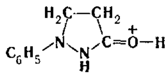
Fig. 3. $\nu_{C=O}$ bands of 1-phenyl-4-methyl-3-pyrazolidone in the crystalline state.

Thus the phenidone molecule has two basic groups that are capable of protonation – the amide and amine groups. Since the pK_a of an aromatic amine is five orders of magnitude greater than the pK_a of the amide, one should expect that the formation of a salt should proceed primarily through the amine 1-N nitrogen and then through the oxygen of the carbonyl group.

The change in the frequencies of the $\nu_{C=O}$ stretching vibrations in the IR spectra was used to prove the type of protonation phenidone undergoes. In doing this, we took into account the dependence of $\nu_{C=O}$ on such factors as 1) the inductive effect due to the $\overset{+}{N}H$ group, 2) the formation of a hydrogen bond, or 3) protonation of the C=O group. The first effect increases $\nu_{C=O}$, while the second and third lower it [3]. Proceeding from these factors, it should be expected that in the case of protonation at the 1-N atom (type A), $\nu_{C=O}$ in the IR spectrum of the protonated phenidone should be shifted to the high-frequency region under the influence of the inductive effect of the $\overset{+}{N}$–H group.



A



B

However, in the case of protonation at the oxygen of the amide group (type B), $\nu_{C=O}$ in the IR spectrum of the protonated molecule should be shifted to the low-frequency region as compared with $\nu_{C=O}$ of the unprotonated molecule. A confirmation of the latter is the disappearance of $\nu_{C=O}$ in the IR spectra of 5-pyrazolone hydrochloride as compared with $\nu_{C=O}$ (1655 cm^{-1}) in the spectrum of 5-pyrazolone in chloroform solution and in the crystalline state, respectively (Fig. 1). In addition, an examination of the IR spectra of 3-pyrazolidone hydrochlorides in the crystalline state and in $CHCl_3$ solutions demonstrates that $\nu_{C=O}$ is shifted to the high-frequency region to 1743-1775 cm^{-1} as compared with $\nu_{C=O}$ (~1690 cm^{-1}) in unprotonated 3-pyrazolidones (Table 1, Figs. 1-3). On the basis of the observed shift of $\nu_{C=O}$, it can be concluded that protonation of 3-pyrazolidones proceeds at the cyclic 1-N atom. As a result of this, salts of the A type rather than of the B type are formed.

The maxima of the $\nu_{C=O}$ absorption bands in the spectra of solutions of protonated 1-aryl-3-pyrazolidones in chloroform lie in a narrow interval (1744-1749 cm^{-1}). At the same time, the interval of $\nu_{C=O}$ values is considerably broader (1695-1713 cm^{-1}) (Table 1) in the spectra of solutions of the unprotonated pyrazolidones in chloroform. As was previously pointed out [4], the broader $\nu_{C=O}$ interval in the latter case is determined by transmission of the interaction of the aryl group through the unshared pair of electrons of the 1-N atom. However, protonation of the 1-N atom leads to blocking of this pair of electrons and, consequently, to disruption of the possibility of interaction of the amide group with the aryl group. As a result, substituents in the phenyl ring will not have an effect on the amide group, and $\nu_{C=O}$ should be determined primarily by the inductive effect of the $\overset{+}{N}H$ group, as a consequence of which the $\nu_{C=O}$ values should be close to one another.

The observed shift ($\Delta\nu_{C=O}$, 39-50 cm^{-1}) is high. In explaining the magnitude of $\Delta\nu_{C=O}$, it is necessary to take into account that it is caused by the electrostatic effect of the positive charge of the proton and removal of the unshared pair of 1-N electrons from conjugation with the amide group.

It should be noted that the interval of $\nu_{C=O}$ values in the IR spectra of solutions of the pyrazolidone hydrochlorides in chloroform presented in [1] does not agree with our data.

In addition to the indicated increase in $\nu_{C=O}$ on protonation of the pyrazolidones in chloroform, we observed an increase in the half widths of the bands of the amide groups ($\Delta\nu_{1/2}$) by a factor of 1.5-2. One of the reasons for the latter is the possibility of the formation of an intermolecular hydrogen bond of the $\overset{+}{N}H \cdots O=CN$ and $NH \cdots O=CN$ types. This is in agreement with the shift in the bands of the stretching vibrations of the NH groups to the low-frequency region (3000-3300 cm^{-1}) on protonation and the appearance of diffuse $\nu_{\overset{+}{N}H}$ bands at 2200-2600 cm^{-1}.

It should be noted that when dry HCl is bubbled into a solution of the 3-pyrazolidones in carbon tetrachloride, a white salt precipitates immediately, during which the $\nu_{C=O}$ bands of the salt or of the starting 3-pyrazolidone are not detected in the spectrum of the solution. When HCl is bubbled into solutions of the 3-pyrazolidones in chloroform, no salt precipitates and, as indicated, $\nu_{C=O}$ bands of only the salt are observed upon sufficient saturation with HCl; i.e., the 3-pyrazolidone is completely protonated.

Two bands at 1690-1700 and 1730-1750 cm^{-1} of about the same intensity are observed in all cases in the region of the stretching vibrations of $C=O$ groups in the spectra of the crystalline salts precipitated from CCl_4 solutions. This can be explained by the formation of stable crystalline associates from the protonated and unprotonated molecules of the $>\overset{+}{N}H \cdots N<$ type. This type of association hinders protonation of the nitrogen atom that is linked by a strong hydrogen bond. The presence of $\overset{+}{N}H$ groups is proved by the very strong bands at 2200-2600 and 2800-3100 cm^{-1}.

EXPERIMENTAL

The investigated 3-pyrazolidones (Table 1) were recrystallized from aqueous alcohol or benzene prior to recording their spectra, and the chloroform was purified by passing it through Al_2O_3. The IR spectra of KBr pellets and chloroform solutions of the 3-pyrazolidone derivatives and their hydrochlorides were obtained with a UR-20 spectrophotometer. The layer thickness of the chloroform solutions was ~ 0.5 cm. The hydrochlorides were prepared by bubbling dry HCl into a solution of the pyrazolidone derivative in $CHCl_3$ and CCl_4 (the phenidone hydrochlorides did not precipitate from $CHCl_3$ solutions). The concentration of the solution of the phenidone in chloroform and in chloroform containing dry HCl was retained unchanged ($\sim 1 \cdot 10^{-3}$ M). The accuracy in the measurement of the frequencies of the carbonyl bands was ± 2 cm^{-1}, while the accuracy in the region of an LiF prism was ± 5 cm^{-1}.

LITERATURE CITED

1. B. E. Zaitsev, S. P. Kozhevnikov, and S. I. Gaft, Zh. Obshch. Khim., **39**, 1835 (1969).
2. B. E. Zaitsev, A. I. Busev, and B. K. Akimov, Zh. Obshch. Khim., **35**, 1548 (1965).
3. L. Bellamy, Infra-Red Spectra of Complex Molecules, Methuen (1958).
4. B. E. Zaitsev, N. A. Andronova, R. B. Zhurin, and L. B. Preobrazhenskaya, Khim. Geterotsikl. Soedin., 1678 (1970).