AZOLE- AND Δ^2-AZOLINECARBALDEHYDE OXIMES AND THEIR DERIVATIVES

II.* PMR SPECTRA. INFLUENCE OF THE CONFIGURATION AND OF THE IONIZATION OF THE OXIME GROUP ON THE CHEMICAL SHIFTS

N. I. Shapranova, I. N. Somin, and S. G. Kuznetsov

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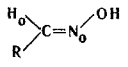
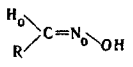
The PMR spectra of the E (syn) and some Z (anti) isomers of 1-methyl-substituted pyrazole-, imidazole-, Δ^2-pyrazoline-, and Δ^2-imidazolinecarbaldehyde oximes and their quaternary and bisquaternary ammonium derivatives in organic solvents and aqueous solutions with various states of the ionogenic groups are described. The influence of the configuration and of the ionization of the oxime group on the chemical shifts of the protons of the quaternary derivatives of the 1-methylazolecarbaldehyde oximes is discussed.

In an investigation of the PMR spectra of oximes of 1-methyl-substituted pyrazolecarbaldehydes (I-III), imidazolecarbaldehydes (IV-VII), Δ^2-pyrazolinecarbaldehydes (VIII), and Δ^2-imidazolinecarbaldehydes (IX) and their quaternary (X-XV) and bisquaternary (XVI, XVII) ammonium derivatives in organic solvents and in aqueous solutions with various states of the ionogenic groups (Table 1), it was found that the oximes of imidazole-2-, pyrazoline-, and imidazolinecarbaldehydes and their derivatives are individual stereoisomers, while the others are mixtures of the E (syn) and Z (anti) isomers.



E (syn)



Z (anti)

The E configuration of the individual isomers (IV, IX, XII, and XV) was established by the most reliable of the existing methods – from the values of the $^{15}N{=}CH_0$ spin–spin coupling constants (SSCCs) (^2J_E < 4 Hz, ^2J_Z > 10 Hz) [2-4]. The same configuration can be ascribed to other individual oximes on the basis of the closeness of the values of their chemical shifts (CSs) to the corresponding values for the oximes (IV, XII, and XV). The assignment of the signals of the ring protons H_4 and H_5 in (IV_0)† is based on literature information [5] and is confirmed by the values of the CSs of the oximes (V_0) and (VI_0).‡

In the analysis of the spectra of the mixtures of isomers, the separation of the signals into two groups corresponding to each isomer was made, as a rule, on the basis of their relative intensities (the use of this criterion is impossible when the E/Z ratio is close to unity). In contrast to the aliphatic aldoximes, in which the H_0 and OH protons resonate in considerably weaker fields than the others [7], in the heteroaromatic aldoximes the H_0 signals and those of the ring protons are grouped in a fairly narrow interval (6.5-8.5 ppm). Their separation proved to be possible because of a difference in intensities (XI) and the

* For Communication I, see [1].

† The lower index denotes the ionic form of the oxime: 0, uncharged form; +, cation; ±, zwitterion.

‡ In contrast to $(IV_0, V_0$, and $VI_0)$, the H_4 signal of (VI_+) is shifted somewhat in the weak-field direction relative to the H_5 signal of (V_+). Thus, the protonation of N_3 shows a greater deshielding influence on the neighboring H_4 proton than on the H_5 proton, which is more remote from it (but adjacent to N_1). This shows the nonequilibrium distribution of the positive charge between N_1 and N_3.

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TABLE 1. Parameters of the PMR Spectra of the Oximes $RCH_0=N_0OH$

Oxime	R	Solvent[a] (ionic form of the oxime)	Chemical shifts, δ, ppm[b]								J, Hz		
			H_0		H_2 or H_3		H_4		H_5		interacting nuclei (No. of bonds)	E	Z
			E	Z	E	Z	E	Z	E	Z			
I	1-Methylpyrazol-3-yl	acetone (0)	8.10	7,46			6,55 d	7,05 d	7,60d	7,68 d	H_4, H_5 (3)	2,6	2,2
II	1-Methylpyrazol-4-yl	acetone (0)	8,05	7,40	7,75	7,89			7,90	8,27			
		H_2O (+)	8,10	7,87	7,88 br	8,15d			7,98 br	8,40	H_0, $^{15}N_0$ (3)	2,7	10,2
											H_3, H_5 (4)		0,3—0,4
III	1-Methylpyrazol-5-yl	acetone (0)	8.27	7,70	7,45 d	7,47	6,40 d	7,02 d			H_3, H_4 (3)	2,1	2,1
		H_2O (+)	8,36	7,83	8,13 d	8,13	6,55 d	7,15 d				3,0	2,6
IV	1-Methylimidazol-2-yl	DMSO (0)	8,06				7,00 d		7,25 d		H_0, $^{15}N_0$ (3)	2,0	
V	4-Chloro-1-methylimidazol-2-yl	DMSO (0)	7,96						7,31				
		H_2O (+)	8,33						7,59				
VI	5-Chloro-1-methylimidazol-2-yl	DMSO (0)	7,97				7,07						
		H_2O (+)	8,39				7,66						
VII	1-Methylimidazol-5-yl	DMSO (0)	8,12	7,48	7,64		7,15 d	7,74					
		H_2O (+)	8,25	7,75	8,72 m[c]	8,86 m[c]	7,76 d	8,32 d			H_2, H_4 (4)	1,2	1,5
VIII	1-Methyl-Δ^2-pyrazolin-3-yl	H_2O (+)	8,17				4,0—3,5m		4,0—3,5 m				
IX	1-Methyl-Δ^2-imidazolin-2-yl	DMSOd	7,79										
		H_2O (+)	8,09				3,98 m		3,98 m		H_0, $^{15}N_0$ (3)	2,5	
X	1,2-Dimethylpyrazolium-3(5)-yl	DMSO (+)	8.44	7,94			6,99 d	7,39 d	8,47 d	8,52d	H_4, H_5 (3)	3.0	3,1
		H_2O (+)	8,38	7,84			6,98 d	7,47 d	8,20 d	8,28d		3,0	3,2
		H_2O (±)	8,13	7,84			6,84 d	7,44 d	8,06 d	8.12d		3,0	3,0
XI	1,2-Dimethylpyrazolium-4-yl	DMSO (+)	8,03	7,50	8,63	8,85							
		H_2O (+)	8.15	7,59	8,49	8,79					H_0, $^{15}N_0$ (3)	2,4	14,1
		H_2O (±)	7,99	7,60	8,31	8,76						3,2	11,5
XII	1,3-Dimethylimidazolium-2-yl	DMSO (+)	8.43				7,77				H_0, $^{15}N_0$ (3)	2,0	
		H_2O (+)	8,45				7,51					2,0	
		H_2O (±)	8,18				7,37					2,4	
XIII	4(5)-Chloro-1,3-dimethylimidazolium-2-yl	DMSO (+)	8,52				8,14						
		H_2O (+)	8.43				7,68						
		H_2O (±)	8.16				7,52						
XIV	1,3-Dimethylimidazolium-4(5)-yl	DMSO (+)	8,27	7,79	9,23		7,99d	8,42d			H_2, H_4 (4)	1,6	1,6
		H_2O (+)	8.24	7,73	8,80br	8,83br	7,74d	8.36d			H_2, H_4 (4)	1,5—1,6	
		H_2O (±)	8,03 d	7,77d	8,72 e		7,51d	8,46br			H_0, $^{15}N_0$ (3)	1.7	13,0
											H_0, H_4 (4)	0,6	0,5
XV	1,1-Dimethyl-Δ^2-pyrazolium-3-yl	H_2O (+)	8,15				3,68 m		4,16 m				
		H_2O (±)	7,98				4,00 m		4,00 m				
XVI	3,3'-Tetramethylenebis(1-methylimidazolium-2-yl)	DMSO (+)	8,54				7,88 br		7,88 br				
XVII	3,3'-Tetramethylenebis(1-methylimidazolium-5-yl)	DMSO (+)	8,25	7,79	9,30		8,05 d	8,47 d			H_2, H_4 (4)	1,5	1,5

[a]For the preparation of aqueous solutions, H_2O (D_2O) and solutions of HCl (DCl) and NaOH (NaOD) were used. [b]Symbols: d – doublet; m – multiplet; br – broadened singlet; the lower numerical indices of the ring protons correspond to the positions of the protons in the ring. [c]Additional splitting probably because of SSC with $N^+ - H$. [d]Probably a zwitterion; see [6]. [e]Very fast exchange (the signal disappears even in HEO).

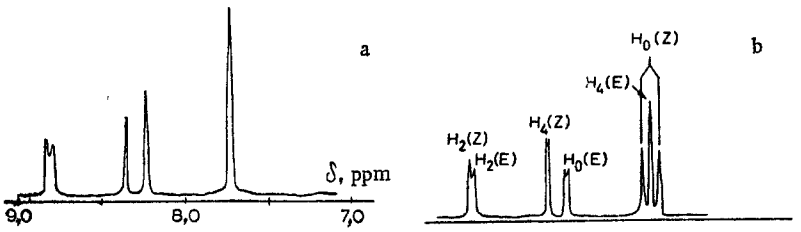

Fig. 1. PMR spectra of (XIV_+) in water (pH ~ 1): a) XIV_+-$^{14}N_0$; b) XIV_+-$^{15}N_0$.

TABLE 2. Differences in the Chemical Shifts $\Delta\delta'$ and $\Delta\delta''$

Oxime	$\Delta\delta'$, ppm						$\Delta\delta''$, ppm					
	H_0		neighboring ring proton		remote ring proton		H_0		neighboring ring proton		remote ring proton	
	$\Delta\delta'_c$[a]	$\Delta\delta'_t$	$\Delta\delta'_c$	$\Delta\delta'_t$	$\Delta\delta'_c$	$\Delta\delta'_t$	$\Delta\delta''_+$	$\Delta\delta''_\pm$	$\Delta\delta''_+$	$\Delta\delta''_\pm$	$\Delta\delta''_+$	$\Delta\delta''_\pm$
X	0,25	0,00	0,03	0,14	0,16	0,14	0,54	0,29	0,49	0,60	0,08	0,06
XI	0,16	−0,01	0,03	0,18	—	—	0,56	0,39	0,30	0,45	—	—
XII	0,27	—	—	—	—	0,14	—	—	—	—	—	—
XIII	0,27	—	—	—	—	0,16	—	—	—	—	—	—
XIV	0,21	−0,04	−0,10	0,23	0,11	0,08	0,51	0,26	0,62	0,95	0,03	0,00

[a]For (XIV) 0.17 ppm; for 2-formyl-1-methylpyridinium oxime 0.26 ppm (our results).

existence of vicinal (I, III, X) or long-range (II_+, XIV_+, XVII) spin–spin coupling between the ring protons. In difficult cases, or for greater reliability, use was made of the replacement of H_0 by deuterium (II, VII) and of the oxime nitrogen by the isotope ^{15}N (II, XIV) (Fig. 1). In a correlation of the signal of the ring proton with the position in the ring, it was considered that the differences in the CSs of the corresponding protons of the E and Z isomers should be considerably higher for the protons adjacent to the anisotropic oxime group than the corresponding differences for the remote protons (I, III, VII, X, and XIV) [8, 10]. The assignment adopted for (I, III, and X) is confirmed by information [11] on the shielding of H_4 relative to H_3 and H_5 in pyrazoles, and the assignment for (VII) and (XIV) by the broadening of the H_2 signal through the electric quadrupole effect of the two neighboring nitrogen atoms. The resonance of H_2 in weaker fields than H_0 and H_4 (VII_+ and XIV_+) and its very fast exchange with deuterium in an alkaline medium ($XIV_\pm$) correspond to the acid nature of H_2 in imidazolium systems [12]. In order to distinguish the H_3 and H_5 signals in (II) it was necessary to have recourse to the replacement of the H_5 by deuterium.

Finally, to assign the signals of the E and Z isomers we used a well-known rule according to which the H_0 protons in the E-aldoximes are deshielded relative to H_0 in the Z isomers [7, 13]. We confirmed the observance of this rule for aldoximes with un-ionized and with ionized hydroxy groups by the independent assignment of $^{15}N{=}CH_0$ on the basis of SSCCs for (II_+, $XI_{+,\pm}$, and $XIV_{+,\pm}$).*

Table 2 gives results characterizing the change in the CSs of the H_0 protons and also the ring protons adjacent to the oxime group and remote from it in aqueous solutions on passing from the cation to the zwitterion ($\Delta\delta' = \delta_+ - \delta_\pm$) and on passing from the isomer with the cis orientation of the proton relative to the oxygen of the oxime group to the isomer with the trans orientation ($\Delta\delta'' = \delta_c - \delta_t$). For the H_0 protons the differences between the values of $\Delta\delta_c'$ and $\Delta\delta_t'$ (i.e., between the E and Z isomers) and between the values of $\Delta\delta_+''$ and $\Delta\delta_\pm''$ (i.e., between the cations and the zwitterions) are, on the whole, analogous to the corresponding differences in aliphatic aldoximes [14]. Thus, the deprotonation of the hydroxyl does not qualitatively change the nature of the magnetic anisotropy of the oxime group: the deshielding of the cis-H_0 relative to the trans-H_0 on passing to the zwitterions is retained ($\Delta\delta_\pm'' > 0$). The magnitude of the effect of anisotropy in this transition decreases ($\Delta\delta_\pm'' < \Delta\delta_+''$). The oximes (X, XI, and XIV) differ from the aliphatic compounds [14] by a more pronounced quantitative difference between $\Delta\delta_c'$ and $\Delta\delta_t'$ and between $\Delta\delta_+''$ and $\Delta\delta_\pm''$. Also characteristic for them is the absence of the expected upfield shift of the signal of the trans-H_0 on the ionization of the oxime group ($-0.04 < \Delta\delta_t' < 0.00$ ppm). The anisotropy of the ionized

*In a paper [15] published while our results were being prepared for the press, the CSs of the oximes (IV) (E), (VII) (E, Z), (XII) (E), and (XIV) (Z) in DMSO are given. The considerable differences from our figures [with the exception of (XII)] are apparently due to the use in this paper [15] as internal standard of 3-(trimethylsilyl)propanesulfonic acid, which reacts with basic groups (downfield shift) and also to the arbitrary and unsubstantiated assignment of the majority of the signals (H_0, H_2, H_4) in the oximes (VII) and (XIV).

oxime group apparently differs from the anisotropy of the un-ionized group the more the higher the degree of delocalization of the negative charge of the oxygen [9, 14]. For onium heteroaromatic aldoximes this delocalization must be more considerable than for aliphatic aldoximes. One must also take into account some noncoplanarity of the C = N bond and the ring in the aromatic Z aldoximes [16]. On the ionization of the oxime group, the increase in conjugation must be accompanied by a decrease in the degree of noncoplanarity. Under these conditions an increase in the deshielding influence of the anisotropy of the aromatic ring on H_0 must be expected.

The figures of Table 2 for the neighboring ring protons, at first sight, show not a decrease but an increase in the effect of anisotropy on ionization: $\Delta\delta_{\pm}'' > \Delta\delta_{+}''$. This ratio is apparently the result of the absence of a diamagnetic shift of the signals of the cis ring protons (in the Z isomers on ionization) ($-0.1 < \Delta\delta_{c}' < 0.03$ ppm). Scale molecular models (Eugon, Hungary) of the Z aldoximes (X, XI, and XIV) show, in the most favorable coplanar conformations, the immediate propinquity of the oxygen atom and a ring proton. This anomaly may therefore be explained by the considerable deshielding contribution of the electrostatic effect [17] of the negatively charged oxygen and (or) the formation (or an increase in the strength) of an intramolecular hydrogen bond between the ring hydrogen and the charged oxygen.

The influence of the anisotropy of the oxime group on the remote ring protons is insignificant: $\Delta\delta'' < 0.1$ ppm (see above). The upfield shifts of the CSs of these protons on ionization ($\Delta\delta'$) are comparable in magnitude with the changes in the CSs of H_0 and the neighboring protons, but they do not much depend on the configuration.

EXPERIMENTAL

The spectra were recorded by I. Yu. Tsereleti,* V. A. Glindin, and Yu. A. Ignat'ev on JNM-3H-60 (Jeol) and HA-100D-15 (Varian) spectrometers. The concentrations of the oximes were 5-10 vol.%. The CSs were reckoned from internal standards – HMDS (0.04 ppm) or (in aqueous solutions) tert-butanol (1.23 ppm), and also from the signal of the solvent (DMSO, 2.50 ppm).

The synthesis of the oximes has been described in the preceding paper [1]. The oximes (II-D_0) and (VII-D_0) were obtained by analogy with the protium derivatives with the aid of DMFA-d_6. The synthesis of (II-D_5) made use of 1-methylpyrazole-d_5, obtained by the decomposition of 1-methylpyrazol-5-yllithium with deuterium oxide. In the preparation of the ^{15}N-isotopomers of (IV, IX, and XII), [^{15}N]hydroxylamine (95% enrichment) was used. In the other cases (II, XI, XIV, XV) the ^{15}N-isotopomers were obtained in situ by isotopic exchange in an acid medium [4] in the presence of [^{15}N]hydroxylamine. The parameters of the spectra of ($XI_{\pm}$-^{15}N) and ($XIV_{\pm}$-^{15}N) were found after the corresponding acid solutions had been made alkaline.

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*Deceased.