# THE NMR SPECTRA OF CYCLIC NITRONES. 3.* EFFECT OF PROTONATION AND A HYDROGEN BOND ON THE CHEMICAL SHIFTS IN THE $^{13}C$ NMR SPECTRA OF DERIVATIVES OF 3-IMIDAZOLINE 3-OXIDE

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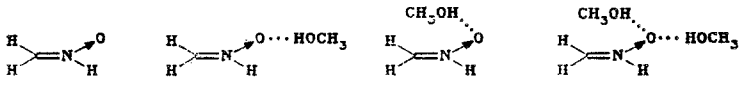
The effect of solvents on the $^{13}C$ NMR spectra of the cyclic nitrones of 3-imidazoline 3-oxide derivatives was studied. It was shown that in solvents capable of forming hydrogen bonds with the N-oxide group the signal for the nitrone carbon atom is shifted downfield by 1.5-2.5 ppm for solutions in chloroform and 5-9 ppm for solutions in methanol. The size of the shift depends on the substituent at position 1 of the imidazoline ring and decreases with increase in its accepting character. Analogous effects are observed during the formation of an intramolecular hydrogen bond with the oxygen atom of the nitrone group. During protonation of the nitrone group the downfield shift of the signal for the nitrone carbon atom amounts to 30-39 ppm.

In [1, 2] the characteristic region of the chemical shifts of the nitrone carbon atoms in the $^{13}C$ NMR spectra of 3-imidazoline 3-oxide derivatives was established. The effect of substituents at positions 1-5 on the electron density distribution in the ground state of the molecules was also studied. The high sensitivity of the chemical shifts in the $^{13}C$ NMR spectra to change in the nature of the solvents is well known for compounds containing groups capable of effective solvation by one or the other solvent [3]. The ability to form hydrogen bonds not only with protic solvents [4] but also with chloroform was established for nitrones on the basis of IR spectroscopy, whereas there are hardly any published data on the effect of solvents and of a hydrogen bond on the $^{13}C$ NMR spectra of nitrones.

In the $^{13}C$ NMR spectra of the majority of compounds containing a C=N group (imines, oximes etc.) the formation of a hydrogen bond and protonation lead to a downfield shift of the signal for the carbon atom of the C=N group, but the opposite effect is observed in certain cases, e.g., for pyridine derivatives [6]. In order to investigate the tendency for the chemical shift to change during the formation of a hydrogen bond with the oxygen atom of the nitrone group we undertook a quantum-chemical calculation of the change in the charges and the associated change in the chemical shifts during the formation of a hydrogen bond with one (B, C) and two (D) molecules of methanol in the model nitrone A (Table 1). In the scheme we give the calculated values of the change in chemical shift during the formation of a hydrogen bond according to the formula $\Delta\delta = f \cdot \Delta Q$, where f = 220 (for $Q_{\sigma+\pi}$) and 160 (for $Q_\pi$) ppm/e (cf. [1, 2]). According to these data a downfield shift of 3-4.5 ppm for the nitrone carbon atom can be expected during the formation of a hydrogen bond with one molecule of methanol and 6-8 ppm with two molecules of methanol.



| | A | B | C | D |
|---|---|---|---|---|
| for $Q_{\sigma+\pi}$ | | $\Delta\delta$=3.4 ppm | $\Delta\delta$=3.2 ppm | $\Delta\delta$=5.8 ppm |
| for $Q_\pi$ | | $\Delta\delta$=4.3 ppm | $\Delta\delta$=4.5 ppm | $\Delta\delta$=7.9 ppm |

*For Communication 2, see [1].

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TABLE 1. Data from Quantum-Chemical Calculation of the Total ($Q_{\sigma+\pi}.10^3$) and π Charges ($Q_\pi.10^3$) (in parentheses)

| Compound | R | $C_{(4)}$ | $N_{(3)}$ | O | $C_{(2)}$ | $C_{(5)}$ | $N_{(1)}$ | $N-CH_3$ | $4-CH_3$ |
|---|---|---|---|---|---|---|---|---|---|
| A | — | −36(−88) | +258(+893) | −406(−805) | | | | | |
| B | — | −21(−61) | +254(+886) | −407(−825) | | | | | |
| C | — | −22(−60) | +254(+885) | −408(−826) | | | | | |
| D | — | −10(−38) | +250(+878) | −407(−840) | | | | | |
| Ib | $CH_3$ | +56(−40) | +167(+781) | −478(−827) | +208 | +99 | −205 | +80 | −34 |
| If | $NO_2$ | +17(−92) | +204(+829) | −447(−796) | +212 | +149 | −188 | | −30 |
| VIIIb | $CH_3$ | +48(+24) | +150(+748) | −469(−870) | +213 | +101 | −205 | +80 | — |
| VIIIb | $CH_3$ | +18(−73) | +190(+814) | −460(−811) | +208 | +102 | −204 | +80 | — |
| IXb | $CH_3$ | +239(+280) | +39(+500) | −153(−972) | +233 | +112 | −196 | +78 | −75 |
| IXf | $NO_2$ | +229(+272) | +80(+546) | −143(−966) | +225 | +139 | −191 | | −77 |
| XIb | $CH_3$ | +73(−38) | +176(+758) | −423(−815) | +205 | +85 | −53 | +71 | −36 |
| XIIIb | $CH_3$ | +259(+282) | +46(+490) | −119(−970) | +235 | +104 | −66 | +58 | −75 |

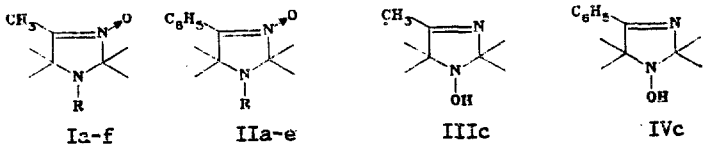
TABLE 2. The $^{13}C$ NMR Spectra of 4-Methyl- and 4-Phenyl-1-R-2,2,5,5-tetramethyl-3-imidazoline 3-Oxides (I, II) in DMSO

| Compound | R | $C_{(4)}$ | $C_{(2)}$ | $C_{(5)}$ | 4-$CH_3$ or $C_{ipso}$ | C ortho | C meta | C para | 2,5-$(CH_3)_4$ | $C_R$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Ia | H | 142.6 | 87.2 | 61.0 | 8.8 | | | | 27.4 | — |
| Ia (in $CCl_4$) | H | 142.0 | 87.5 | 61.2 | 9.0 | | | | 27.9, 27.7 | — |
| Ib | $CH_3$ | 142.1 | 88.3 | 62.9 | 8.6 | | | | 23.6, 23.0 | 26.7 |
| Ib (in $CCl_4$) | $CH_3$ | 141.4 | 88.7 | 63.2 | 9.0 | | | | 24.0, 23.6 | 27.1 |
| Ic | OH | 142.2 | 90.0 | 66.4 | 8.9 | | | | 23.8, 23.4 | — |
| Id | $OCH_3$ | 141.4 | 90.1 | 67.0 | 8.7 | | | | —* | 64.4 |
| Ie | NO | 139.6 | 89.2 | 67.2 | 8.5 | | | | 26.8, 22.0 | — |
| | | 140.0 | 88.6 | 67.8 | 7.8 | | | | 21.4 | — |
| If | $NO_2$ | 140.6 | 89.6 | 68.3 | 8.8 | | | | 22.8, 21.8 | — |
| IIa | H | 140.4 | 87.7 | 61.8 | 128.6 | 127.3 | 128.6 | 129.0 | 29.4, 27.6 | — |
| IIb | $CH_3$ | 140.5 | 89.0 | 63.6 | 128.1 | 127.5 | 128.1 | 129.2 | 24.3, 23.9 | 26.5 |
| IIc | OH | 139.8 | 89.5 | 65.9 | 127.2 | 126.9 | 127.6 | 128.8 | 24.4, 23.7 | — |
| IId | $OCH_3$ | 139.8 | 90.5 | 67.6 | 128.2 | 127.7 | 128.2 | 129.5 | —* | 64.6 |
| IIe | NO | 137.9 | 89.7 | 67.9 | 126.5 | 128.1 | 128.5 | 130.3 | 28.7, 22.2 | — |
| | | 138.8 | 89.2 | 68.7 | 125.8 | — | — | — | 27.6, 22.6 | — |

*They appear in the form of a broad signal [1]).

In the present work we studied the $^{13}C$ NMR spectra of 4-methyl- and 4-phenyl-1-R-2,2,5,5-tetra-methyl-3-imidazoline 3-oxides (I, II) in a series of solvents (carbon tetrachloride, DMSO, chloroform, methanol, trifluoroacetic acid, sulfuric acid, chlorosulfonic acid) in order to establish the scale and the direction of the changes in the chemical shift of the $^{13}C$ carbon during the formation of the hydrogen bond and also during the protonation of the nitrone and other groups. In addition, we considered the possibility of using $^{13}C$ NMR spectroscopy of nitrones to establish the presence of an intramolecular hydrogen bond with the oxygen atom of the nitrone group.

In Table 2 we give data from the $^{13}C$ NMR spectra of 4-methyl- and 4-phenyl-1,R-2,2,5,5-tetramethyl-3-imidazoline 3-oxides (I, II) in DMSO. In Table 3 we give the changes in the chemical shifts with replacement of the solvents in relation to the values of the chemical shifts in DMSO. In order to compare the scale of the relative changes in the chemical shifts in relation to the nature of the solvent in Table 4 we give the changes in the chemical shifts for the 3-imidazoline derivatives (III) and (IV) not containing the N-oxide oxygen. It can be seen that the observed changes for compounds (III) and (IV) during protonation and the formation of the hydrogen bond agree on the whole with existing data on other types of imines [6].



Ia-f IIa-e IIIc IVc

a R=H, b R=$CH_3$, c R=OH, d R=$OCH_3$, e R=NO, f R=$NO_2$

TABLE 3. The Effectof Hydrogen Bonds and Protonation on the Chemical Shifts of the Carbon Atoms in 1-R-4-Methyl- and 1-R-4-Phenyl-2,2,5,5-tetramethyl-3-imidazoline 3-Oxides (Ia-f) and (IIa-e)

| Compound | Solvent | $\Delta\delta C_i = \delta C_i$(solvent) $- \delta C_i$(DMSO), ppm | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $C_{(4)}$ | $C_{(2)}$ | $C_{(5)}$ | $C_{ipso}$ | $C_{ortho}$ | $C_{meta}$ | $C_{para}$ | $C_R$ |
| Ia | $CHCl_3$ | 1,4 | 0,4 | 0,3 | 0,1 | | | | |
| | $CH_3OH$ | 7,8 | 1,5 | 1,6 | 0,2 | | | | |
| | $CF_3COOH$ | 15,2 | 4,3 | 9,4 | 2,2 | | | | |
| (XIIIa) | $H_2SO_4$ | 36,4 | 6,1 | 12,8 | 5,8 | | | | |
| Ib | $CHCl_3$ | 2,6 | 0,9 | 0,5 | 0,4 | | | | 0,1 |
| | $CH_3OH$ | 8,7 | 1,4 | 1,8 | 0,2 | | | | −0,1 |
| | $CF_3COOH$ | 17,1 | 7,6 | 12,9 | 3,1 | | | | 5,7 |
| (XIIIb) | $H_2SO_4$ | 37,1 | 8,2 | 14,5 | 6,0 | | | | 6,0 |
| Ic | $CH_3OH$ | 8,7 | 1,6 | 1,6 | 0,1 | | | | |
| | $CF_3COOH$ | 20,4 | 6,9 | 10,2 | 2,8 | | | | |
| (XIIIc) | $H_2SO_4$ | 36,2 | 9,4 | 15,0 | 5,1 | | | | |
| Id | $CHCl_3$ | 2,5 | 0,6 | 0,2 | 0,2 | | | | 0 |
| | $CH_3OH$ | 8,7 | 1,9 | 1,7 | 0,1 | | | | 0,3 |
| | $CF_3COOH$ | 33,8 | 5,7 | 7,0 | 3,9 | | | | 2,2 |
| (XIIId) | $H_2SO_4$ | 36,8 | 10,0 | 15,6 | 5,6 | | | | 3,5 |
| Ie | $CHCl_3$ | 1,1 | 0,8 | −0,2 | 0,1 | | | | |
| | | 1,5 | 0,5 | −0,4 | 0 | | | | |
| | $CH_3OH$ | 6,5 | 1,9 | 1,4 | 0,1 | | | | |
| | | 6,9 | 1,5 | 1,2 | 0 | | | | |
| | $CF_3COOH$ | 23,5 | 5,2 | 5,2 | 2,8 | | | | |
| | | 23,5 | 4,5 | 4,7 | 2,7 | | | | |
| If | $CHCl_3$ | 0 | 0 | −0,7 | −0,4 | | | | |
| | $CH_3OH$ | 5,6 | 1,3 | 1,0 | 0 | | | | |
| | $CF_3COOH$ | 26,4 | 4,6 | 4,6 | 3,1 | | | | |
| (IXf) | $H_2SO_4$ | 38,7 | 4,7 | 5,4 | 4,2 | | | | |
| IIa | $CHCl_3$ | 1,8 | 0 | 0,2 | −1,1 | −0,1 | −0,7 | 0,3 | |
| | $CH_3OH$ | 7,1 | 1,2 | 1,5 | −0,7 | 1,5 | −0,2 | 1,5 | |
| | $CF_3COOH$ | 13,6 | 3,7 | 9,9 | −4,1 | 4,0 | 1,3 | 6,0 | |
| (XIVa) | $H_2SO_4$ | 29,6 | 3,5 | 12,0 | −8,6 | 4,1 | 2,5 | 10,3 | |
| IIb | $CHCl_3$ | 2,7 | 0,4 | 0,6 | −0,1 | 0,3 | −0,1 | 0,3 | 0 |
| | $CH_3OH$ | 7,6 | 1,6 | 1,8 | 0,1 | 1,4 | 0,8 | 1,4 | 0 |
| | $CF_3COOH$ | 10,9 | 6,2 | 11,6 | −3,1 | 3,5 | 1,8 | 5,1 | 5,6 |
| (XIVb) | $H_2SO_4$ | 30,4 | 6,3 | 14,3 | −8,1 | 4,1 | 3,1 | 10,1 | 6,0 |
| IIc | $CF_3COOH$ | 15,3 | 7,3 | 11,5 | −2,3 | 4,0 | 2,5 | 5,9 | |
| | $H_2SO_4$ | 30,6 | 8,1 | 15,6 | −7,9 | 4,3 | 3,6 | 10,6 | |
| (XIVc) | $HSO_3Cl$ | 31,2 | 8,3 | 16,5 | −7,0 | 4,4 | 4,4 | 10,9 | |
| IId | $CHCl_3$ | 1,9 | 0,4 | 0,4 | −0,8 | 0,2 | −0,1 | 0 | 0,1 |
| | $CH_3OH$ | 7,8 | −0,3 | 0,7 | 0,6 | 2,1 | 1,8 | 2,3 | 1,3 |
| (Xd) | $CF_3COOH$ | 30,9 | 5,4 | 6,4 | −3,3 | 3,4 | 1,8 | 6,0 | 1,7 |
| (XIVd) | $H_2SO_4$ | 30,3 | 8,1 | 15,5 | −8,4 | 4,1 | 3,3 | 10,5 | 4,0 |
| IIe | $CHCl_3$ | 0 | 0 | 0 | −0,3 | 0 | 0 | 0 | |
| | $CH_3OH$ | 4,5 | 1,3 | 1,2 | 1,9 | 1,2 | 0,8 | −0,7 | |
| | | 5,4 | 1,5 | 1,3 | | | | | |
| | $CF_3COOH$ | 20,7 | 4,7 | 5,9 | −1,6 | 2,8 | 1,6 | 4,6 | |
| | | 21,0 | 5,4 | 5,5 | −1,4 | | | | |

From the data in Table 3 it is seen that replacement of the solvents leads to appreciable changes in the spectra of compounds (I) and (II), and the signals of all the carbon atoms undergo changes. The smallest differences are observed between the chemical shifts of compounds (Ia, b) in carbon tetrachloride and DMSO solutions, i.e., in solvents which differ radically in polarity but are not proton donors. In the transition to solvents capable of forming a hydrogen bond with the nitrone group, however, the changes in the chemical shifts become more significant. Even in the transition from DMSO to chloroform a downfield shift of 1.5-2.5 ppm is observed for the $C_{(4)}$ signal for all the investigated nitrones. This is clearly due to the formation of a weak hydrogen bond between the chloroform and the N-oxide oxygen atom, which was established earlier by IR spectroscopy [5]. In contrast to this, in the spectra of the corresponding derivatives (IIIc) and (IVc) having an imine group the position of the $C_{(4)}$ signal remains practically unchanged in the transition from DMSO to chloroform. In the spectra of methanol solutions of the nitrones (I) and (II) a downfield shift of the $C_{(4)}$signal by 8.7-5.6 ppm

TABLE 4. The Effect of Hydrogen Bonds and Protonation on the Chemical Shifts of the Carbon Atoms in 1-hydroxy-4-methyl- and 1-Hydroxy-4-Phenyl-2,2,5,5-tetramethyl-3-imidazolines (IIIc, IVc)

| Compound* | Solvent | $\Delta\delta_{C_i} = \delta_{C_i}$(solvent) $-\delta_{C_i}$(DMSO), ppm | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | $C_{(4)}$ | $C_{(2)}$ | $C_{(5)}$ | $C_{ipso}$† | $C_{ortho}$ | $C_{meta}$ | $C_{para}$ |
| IIIc | $CHCl_3$ | −0,1 | 0,4 | 0,5 | −0,7 | | | |
| | $CH_3OH$ | 4,1 | 0,8 | 1,5 | −0,1 | | | |
| IVc | $CHCl_3$ | 0,2 | 0,9 | 1,0 | −0,7 | −0,8 | −1,2 | −1,1 |
| | $CH_3OH$ | 4,5 | 1,1 | 1,8 | 0,9 | 0,6 | 0,4 | 0,7 |
| | $HSO_3Cl$ | 8,2 | 6,9 | 14,1 | -11,4 | 5,6 | 5,4 | 13,1 |

*Compounds (IIIc) and (IVc) are unstable in trifluoroacetic acid solutions.
†For compound (IIIc), 4-$CH_3$.

(I) and 7.8-5.0 ppm (II) is observed, whereas the analogous changes for the imines (IIIc) and (IVc) have half the value (Table 4). According to the data from quantum-chemical calculation, the major contribution to the change in the chemical shift of $C_{(4)}$ in the transition from solutions in DMSO to solutions in methanol comes from hydrogen bonds between the N-oxide group and two molecules of methylene (structure D). The signals of the $C_{(2)}$ and $C_{(5)}$ atoms and the signals of the carbon atoms of the phenyl ring in the spectra of compounds (II) also undergo a downfield shift of 1-2 ppm.

Both for 4-methyl- and for 4-phenyl-3-imidazoline 3-oxides (I, II) the substituent R has an appreciable effect on the strength of the hydrogen bond between the nitrone group and the methanol, as seen in the relative chemical shift $\Delta\delta_4$. Whereas an approximately identical effect from the hydrogen bond is observed for compounds (Ia-d) and (IIa-d) (7.8-8.7 and 7.1-7.6 ppm respectively), increase in the electron-withdrawing character of the substituent R in the 1-nitroso derivatives (Ie) and (IIe) and the 1-nitro derivative (If) leads to a decrease of 2-3 ppm in the $\Delta\delta_4$ value. Increase in the accepting character of the substituent at position 4, e.g., transition to the 4-methoxycarbonyl derivative (Vb), also leads to a decrease in the relative chemical shift due to the hydrogen bond (Table 5).

The presence of the intramolecular hydrogen bond in the 4-carboxy derivatives (VIb, f) [7] shows up as a downfield shift of 4.3 and 4.4 ppm in the $C_{(4)}$ signal compared with the signals of the corresponding esters (Vb, f). In this case the effect of the substituent R on the $\Delta\delta_C$ value is not observed by virtue of the fact that this substituent affects both the basicity of the nitrone group and the acidity of the COOH group. On the other hand, increase in the accepting effect of the substituent R in the transition from (VIb) to (VIf) leads to a decrease in the basicity of the nitrone group, while the acidity of the COOH group, on the other hand, increases [7], and the two effects (which influence the strength of the hydrogen bond in opposite directions) are mutually compensated. According to the quantum-chemical calculation (Table 1), the formation of the intramolecular hydrogen bond in compound (VIIIb), i.e., the transition from (VIII'b) to (VIIIb), should lead to a downfield shift of 6-7 ppm in the $C_{(4)}$ signal, which agrees satisfactorily with the experimental data (Table 5). In the 4-hydroxymethyl derivatives (VIIIb, f) the effect of the substituent R on the acidity of the hydroxy group is significantly smaller, and the difference in the strength of the hydrogen bond is consequently determined mainly by the basicity of the nitrone group. As a result the value of $\Delta\delta_4 = \delta_4$ (VIII)$-\delta_4$(VII) for the 1-nitro derivative (VIIIf) is 1 ppm smaller than for the 1-methyl derivative (VIIIb).

Compounds (VIIIb, f) proved convenient subjects for comparison of the results from analysis of the $^{13}C$ NMR spectra with the conclusions obtained on the basis of analysis of their IR spectra. In the IR spectrum of (VIIIb) in carbon tetrachloride the intramolecular hydrogen bond between the hydroxy group and the nitrone group appears as a broad band centered at 3300 $cm^{-1}$, whereas the analogous band in the IR spectrum of (VIIIf) is observed at 3375 $cm^{-1}$. The shift of the band for the intramolecular hydrogen bond between the OH group and the nitrone group in the IR spectrum of (VIIIb) toward the longwave region by 75 $cm^{-1}$ compared with the analogous band in the spectrum of (VIIIf) indicates (with identical

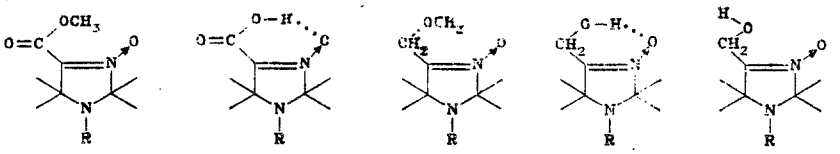
TABLE 5. The Data from the $^{13}C$ NMR Spectra of Compounds (Vb, f-VIIIb, f) in chloroform

| Compound | $C_{(4)}$* | $C_{(2)}$ | $C_{(5)}$ | $CH_2$ | CO | $OCH_3$ | 2,5-$(CH_3)_4$ | $C_R$ |
|---|---|---|---|---|---|---|---|---|
| Vb | 135,6 | 93,0 | 63,4 | | 159,6 | 51,9 | 23,8 | 26,4 |
| Vb† | 137,6 | 93,8 | 64,2 | | 160,0 | 52,1 | 23,9 | 26,3 |
| VI b | 139,7 (4,1) | 92,3 | 63,6 | | 158,0 | | 23,3, 23,8 | 25,8 |
| V f | 132,5 | 93,4 | 68,5 | | 158,0 | 52,6 | 23,5, 22,9 | |
| VI f | 136,9 (4,4) | 93,0 | 69,1 | | 156,3 | | 23,5, 23,0 | |
| VII b | 143,7 | 89,5 | 63,3 | 58,7 | | 63,6 | 23,6, 23,3 | 26,4 |
| VIII b | 147,7 (4,0) | 89,8 | 63,2 | 55,2 | | | 23,7, 23,5 | 26,8 |
| VII f | 141,5 | 90,8 | 68,7 | 59,4 | | 63,8 | 23,3, 22,6 | |
| VIII f | 144,5 (3,0) | 90,8 | 68,0 | 54,3 | | | 23,2, 22,7 | |

*The difference in the chemical shifts is given in parentheses: $\delta_4(VI)-\delta_4(V)$ и $\delta_4(VIII)-\delta_4(VII)$.

†In $CH_3OH$.

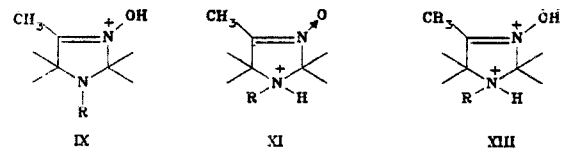
geometry in the chelate ring) a stronger hydrogen bond in (VIIIb), and this agrees with the NMR data.



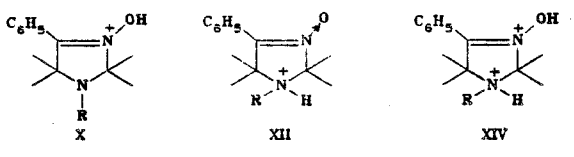
b,f b,f VII b,f VIII b,f VIII b,f

In the derivatives of 3-imidazoline 3-oxide there are two groups capable of protonation; depending on the substituent at $N_{(1)}$ and on the strength of the acid, protonation can either occur only at the nitrone group or at the $N_{(1)}$ atom with the formation of the cations (IX, X) and (XI, XII), or exhaustive protonation can occur with the formation of the dications (XIII) and (XIV).

Table 1 gives calculated data for all three cases of protonation in the 4-methyl derivatives of (I), i.e., (IXb, f), (XIb), and (XIIIb). According to these data, protonation of the nitrone group must be accompanied by a considerable downfield shift of the $C_{(4)}$ signal: $\Delta\delta_4$ = 40-46 ppm.



IX XI XIII



X XII XIV

In concentrated sulfuric acid solutions ($H_0$ = -11) the 3-imidazoline 3-oxide derivatives (Ia-d) and (IIa-d) are protonated both at the nitrone and at the amino and hydroxylamino groups with the formation of the corresponding dications (XIIIa-d) and (XIVa-d). With increase in the acidity of the medium in the transition to solutions in chlorosulfonic acid ($H_0$ = -13) there are hardly any changes in the spectra of compounds (IIc) in comparison with the spectrum in concentrated sulfuric acid. This confirms the exhaustive protonation of compounds (I) and (II) in these acids with the formation of the dications (XIII) and (XIV). If the 1-nitroso derivatives (Ie) and (IIe) are dissolved in concentrated sulfuric acid, the nitroso group is rapidly removed, as shown by the identity of the spectra obtained here with the spectra of (XIIIa) and (XIVa). The removal of the nitro group when (1f) is dissolved in sulfuric acid takes place fairly slowly (several hours), and the signals of both the dication (XIIIa) and the cation (IXf) are observed in the spectrum.

During the protonation of the nitrone group the $C_{(4)}$ signal undergoes a downfield shift of 36-39 and 30-31 ppm both in the spectra of the dications (XIIIa-d) and (XIVa-d) and in the spectrum of the cation (IXf); this is approximately four times larger than the analogous effect in the protonation of the imino group (Table 4 and published data [6]). During the protonation of the 3-imidazoline 3-oxide ring only in the nitro group in the 1-nitro derivative (1f), i.e., during the formation of the cation (IXf), the $C_{(2)}$ and $C_{(5)}$ signals are shifted downfield by 4.7 and 5.4 ppm respectively, whereas protonation of the amino and hydroxylamino groups in parallel with the nitrone group with the formation of the dications (XIIIa-d) and (XIVa-d) leads to an additional downfield shift of these signals to 6-10 and 12-15 ppm.

The protonation of the tertiary amino group and also of the hydroxylamino group leads to the appearance of magnetic nonequivalence in the gem-$CH_3$ groups at positions 2 and 5, which appear in the form of four different signals in the spectra of (XIVb-d): 24.2, 22.6, 21.6 and 20.2 (XIVc); 23.9, 22.6, 21.6 and 20.2 (XIVc); 25.7, 24.6, 22.5 and 21.0 (XIVd). The signals of the H-$CH_3$ and $>\overset{+}{N}H$-$OCH_3$ groups undergo a downfield shift of the 6 and 4 ppm. The signals for the methyl groups at position 4 undergo a shift of the same magnitude and direction during protonation of the nitrone group. The nature of the change in the chemical shifts of the carbon atoms of the aromatic ring during the protonation of the α-phenylnitrone group is similar to that in protonated α-phenylimines (Table 4, cf. [6]); the $C_{ipso}$ signal is shifted upfield by 7-8 ppm, whereas the signals of the ortho-, meta-, and para-carbon atoms are shifted downfield, while the largest shift is found in the signals for the carbon atom at the para position and the smallest is found in the signals of the carbon atoms at the meta position: $\Delta\delta_{para} > \Delta\delta_{ortho} > \Delta\delta_{meta}$.

With decrease in the acidity of the medium, i.e., in the transition to solutions in trifluoroacetic acid ($H_0$ = -3.3), the effect of the solvent and the chemical shift of the carbon atoms in (I) and (II) is more complex in nature. This is due to the fact that in this case, in contrast to the solutions in concentrated sulfuric acid and chlorosulfonic acid, exhaustive protonation of the 3-imidazoline 3-oxide ring does not occur, and one of the functional groups is protonated (fully or partially), depending on the ratio of the basicities of the two groups (the nitrone or the $N_{(1)}$ atom). Thus, in the case of the amines (Ia, b) and (IIa, b)* and the hydroxylamines (Ic) and (IIc) protonation takes place at the amino and hydroxylamino groups more basic than the nitrone groups. This is favored by the high values for the downfield shifts of the $C_{(2)}$ and, particularly, $C_{(5)}$ signals. The magnitude of the downfield shift of the $C_{(4)}$ signal in these cases and also in (Ie, f) and (IIe) indicates partial protonation of the nitrone group.

In compounds (Id) and (IId), in accordance with the known fact the basicity of hydroxylamines decreases during successive substitution with alkyl groups [8], the basicity of the hydroxylamino group becomes lower than in the hydroxylamines (Ic) and (IIc). As a result protonation of the nitrone group becomes predominant. The absence of protonation of the hydroxylamino group in (Id) and (IId) in trifluoroacetic acid is demonstrated by the type of signal for the gem-$CH_3$ groups, which [as in "inert" solvents (DMSO, chloroform, and methanol)] also appear in the form of a broad signal [1], and also by the smaller value for the downfield shift of the $C_{(5)}$ signal compared with the spectra of (Ia-c) and (IIa-c). The downfield shift of the $C_{(4)}$ signal in the spectra of solutions of (Id) and (IId) in trifluoroacetic acid becomes close to the $\Delta\delta_4$ value obtained with full protonation of the nitrone group in solutions in strong acids. The direction of the changes in the chemical shifts of the carbon atoms of the phenyl ring in the spectra of the α-phenyl nitrones in trifluoroacetic acid remains the same as in the solutions in concentrated sulfuric acid, whereas the magnitude of the changes in the $C_{ipso}$ and $C_{para}$ atoms most sensitive to protonation is 1.5-2 times smaller.

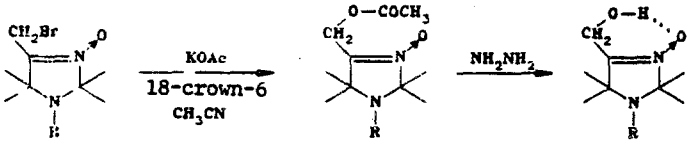
## EXPERIMENTAL

The $^{13}C$ NMR spectra were recorded on a Bruker Physik AG HX-90 spectrometer at 22.63 MHz. For the measurements we used 10-15% solutions of the compounds in the respective

*The $pK_a$ values for the protonation of the amino groups in (IIa) and (IIb) in water at 25°C are 2.06 and 2.25 respectively (measured by K. A. Udachin, Institute of Inorganic Chemistry Suveruab Branch, Academy of Sciences of the USSR).

solvents. To stabilize the resonance conditions at the deuterium nuclei for the spectra in DMSO, chloroform, and methanol we added 10% of the respective deuterated solvent; for the solutions in trifluoroacetic acid, sulfuric acid, and chlorosulfonic acid we used an external standard (in a capillary, 3 mm in external diameter, containing a 1:1 mixture of deuteroacetone and TMS). The chemical shifts for the solutions in DMSO, chloroform, methanol, and trifluoroacetic acid were measured with reference to TMS as internal standard; for the solutions in sulfuric acid and chlorosulfonic acid they were measured with reference to an external standard with correction for the difference in the volume susceptibilities ($\Delta\delta_{\chi_v}$ = 0.7 and 0.3 ppm respectively). The quantum-chemical calculations were performed by the CNDO/2 method without optimization of the geometry by means of the set of VIKING programs (the NMR Laboratory, Moscow State University) on a BESM-6 computer. The geometric parameters of the nitrone group in the model compounds (A-D) and also the geometry of the imidazolines (I, VIII, IX, XI, XIII) were taken from x-ray crystallographic data for 3-imidazoline 3-oxides [9, 10], and the parameters of the substituents were taken from [11]. During the calculation of the complexes of the model nitrone with methanol (B-D) the →O...HO distance was taken as 1.7 Å.

Compounds (I-IV) were obtained by the methods in [1]. The 1-R-4-hydroxymethyl-2,2,5,5-tetramethyl-3-imidazoline 3-oxides (VIIIb, f) were synthesized according to the following scheme:




XVI b,f XV b,f XVIIb,f

The 1-R-4-acetoxymethyl-2,2,5,5-tetramethyl-3-imidazoline 3-oxides (XVb, f) were synthesized from 1-R-4-bromomethyl-2,2,5,5-tetramethyl-3-imidazoline 3-oxides (XVIb, f) [1] by reaction with potassium acetate in acetonitrile in the presence of 18-crown-6-ether by the method in [12].

1-R-4-Hydroxymethyl-2,2,5,5-tetramethyl-3-imidazolin-3-Oxides (VIIIb, f). To a solution of 4 mmole of the acetoxy derivative (XVb, f) in 20 ml of alcohol we added 0.5 ml of hydrazine hydrate. The solution was left for 5 h, the solvent was evaporated, 10 ml of water was added to the residue, and the mixture was extracted with chloroform. The extract was dried with calcium chloride and filtered. The residue was chromatographed on a column of silica gel with chloroform as eluant. The yield of (VIIIb) was 40% (an oil). Found %: N 13.7. $C_9H_{18}N_2O_2$. Calculated %: N 14.0. The yield of (VIIIf) was 35%; mp 135-137°C. Found %: C 44.1; H 6.9; N 19.1. $C_8H_{15}N_3O_4$. Calculated %: C 44.2; H 6.9; N 19.4.

1-R-4-Methoxymethyl-2,2,5,5-tetramethyl-3-imidazoline 3-Oxides (VIIb, f). To a solution of sodium methoxide in methanol (from 10 mmole of sodium in 20 ml of methanol) we added 4 mmole of the bromine derivative (XVIb, f). The mixture was left at room temperature until the initial compound had disappeared (monitored by TLC on Silufol UV-254, $R_f$ of initial compound 0.4, $R_f$ of product 0.3 in chloroform). The methanol was evaporated, the residue was dissolved in 10 ml of water, the solution was extracted with chloroform, the extract was dried with calcium chloride and filtered, and the chloroform was evaporated. The residue was chromatographed on a column of silica gel with chloroform as eluant. The yield of (VIIb) was 70% (an oil). Found %: N 9.6. $C_{10}H_{20}N_2O_2$. Calculated %: N 10.0. The yield of (VIIf) was 65% (an oil). Found %: N 18.0. $C_9H_{17}N_3O_4$. Calculated %: N 18.2.

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# ORGANOLITHIUM AND ORGANOSODIUM COMPOUNDS OF N-SUBSTITUTED 2-ALKYLBENZIMIDAZOLES

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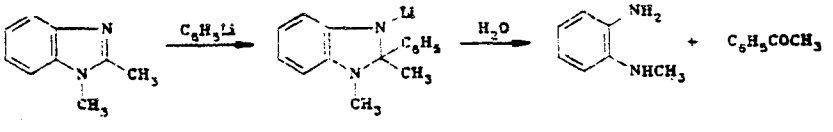
Organolithium and organosodium compounds of 1,2-dimethyl-, 1-methyl-2-ethyl-, 1-methyl-2-propyl-, and 1-phenyl-2-methylbenzimidazole, containing the metal in the alkyl group at position $C_{(2)}$, were obtained by metallation. It was found that metallation can be complicated by the addition of the metalling reagent at the C=N bond of the heterocycle. It was shown that the obtained organometallic compounds can be used for the synthesis of various derivatives of benzimidazole.

It is known that 2-alkylbenzimidazoles are converted into 1-lithio-2-lithioalkylbenzimidazoles by the action of butyllithium [1]. In the present work we describe the metallation of N-substituted 2-alkylbenzimidazoles and some transformations of the obtained organometallic compounds.

Using butyl- and phenyllithium as metallating reagents, we established that the organolithium compounds of N-substituted 2-alkylbenzimidazoles are formed with very low yields at the metallation temperature used for 2-alkylbenzimidazoles (~0°C), except in the case of 2-lithiomethyl-1-phenylbenzimidazole. Calculation of the energies of deprotonation ($\Delta E = E_{HetCH_2} - E_{HetCH_3}$) of 1,2-dimethyl- and 1-phenyl-2-methylbenzimidazole by the CNDO/2 method [2] showed that the latter is a stronger CH acid. The difference in the deprotonation energies of these compounds is 0.12 eV.* With such a difference, calculated by the CNDO/2 method, the rate constants for deuteroexchange of the methyl derivatives of the azoles, which characterize the kinetic CH acidity, may differ by more than an order of magnitude [3].

After hydrolysis of the products from the reaction of phenyllithium with 1,2-dimethylbenzimidazole in the hydrolysis product we found acetophenone and N-methyl-o-phenylenediamine, which are clearly formed according to the following scheme:



*The calculation was performed with the standard bond lengths. A planar model was used for the carbanion.

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