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NMR SPECTRA OF CYCLIC NITRONES.
7*. THE INFLUENCE OF SUBSTITUENTS AND A HYDROGEN BOND ON ^{14}N AND ^{17}O CHEMICAL SHIFTS IN DERIVATIVES OF 3-IMIDOAZOLINE 3-OXIDE

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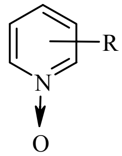
Derivatives of 3-imidazoline 3-oxide have been studied by ^{14}N and ^{17}O NMR methods. Regularities of the influence of substituents and of a hydrogen bond on chemical shifts have been made apparent. The range of changes of the chemical shifts of the nitrogen and oxygen nuclei of the nitrone group has been determined. Both in the ^{17}O and in the ^{14}N NMR spectra the signals of the amino derivatives are the highest field signals for the nitrone group, and the lowest field signals are the signals of the cyano derivatives in the series of derivatives investigated. Depending on the substituent (from amino to cyano group) the ^{17}O chemical shifts varied over a range ~155 ppm, but the interval of change of the ^{14}N chemical shifts for the same substituents was ~110 ppm.

Keywords: 3-imidazoline 3-oxide, nitrones, ^{14}N and ^{17}O NMR spectroscopy.

The high sensitivity of the ^{14}N and ^{17}O nuclear chemical shifts to changes in the electronic structure of molecules makes the NMR method with these nuclei an important instrument for studying the effect of substituents, solvents, and other factors on the electronic state of nitrogen- and oxygen-containing functional groups [2-4]. The ^{14}N (^{15}N) and ^{17}O heterocyclic N-oxides **1** have been studied in fair detail [5-10], while the corresponding data for compounds with a localized azomethine N-oxide (nitrone) group are extremely limited and refer mainly to conjugated C,N-diarylnitrones **2** [3, 11, 12]. In difference to the latter, the derivatives of 3-imidazoline 3-oxide **3** have an isolated nitrone group and there are broad possibilities to vary the substituents both directly at the carbon atom α to the nitrone group and at the more remote positions of the heterocycle. In



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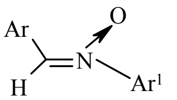

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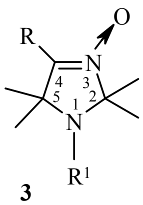

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* For Part 6 see [1].

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the present work, derivatives of 3-imidazoline 3-oxide **3** have been studied by ^{14}N and ^{17}O NMR with the aim of developing general rules for the effect of substituents on chemical shift and also to establish the range of the changes of chemical shift of the nitrogen and oxygen nuclei of the nitrone group.

A correlation was established between the ^{17}O chemical shift and the π-electron density on the oxygen atom, and also the order of the π-bond of the N-oxide group for derivatives of pyridine N-oxide **1** in [6, 7]. The total range of the changes of chemical shift for compounds **1** amounted to 102 ppm [5]. An analogous regularity was also established for C,N-diaryl nitrones **2**, the chemical shifts of which varied in a range of 55 ppm [11, 12]. An approximately three times greater range (155 ppm) of change of ^{17}O chemical shift is observed for 4-R-1,2,2,5,5-pentamethyl-3-imidazoline 3-oxides **3** (Table 1), since variation of substituent R in these compounds occurs directly at the carbon atom α to the nitrone group and not at the remote *para* position of the aryl substituent (Ar) of compounds **2**. In compounds **3**, as in compounds **1** and **2**, the signal of the oxygen atom for amino derivative **3a** (R = NH_2) is at highest field, and the signal for cyano derivative **3i** (R = CN) is at lowest field (Table 1). This is linked with the fact that electron-withdrawing substituents lead to an increase of the order of the π-bond of the N→O group, accompanied by an increase in the frequency of the stretching vibrations of the N→O bond in the IR spectra [13], and consequently by a low field displacement of the signal of the oxygen atom in the ^{17}O NMR spectra (Table 1, cf. [6]). The reverse effect is observed for the action of electron-donating substituents, leading to a reduction in the π-bond order of the N→O group. On forming a hydrogen bond with the N-oxide oxygen atom a reduction is also observed in the double-bonded nature of the N→O group [13], displayed as a high field displacement of the oxygen atom signal when recording the spectra in a protic solvent. The chemical sift of the oxygen atom in compound **3e** in methanol is 256 ppm ($\Delta\delta$ = -54 ppm, see Table 1).

An analogous effect ($\Delta\delta$ = -60 to -80 ppm) on forming a hydrogen bond is observed in the ^{17}O NMR spectra of pyridine N-oxides **1** [5]. The signal of the oxygen atom of the N→O group linked in an intramolecular hydrogen bond (IMHB) in the 4-carboxy derivative **3g** is also found at higher field compared with the corresponding signal in ester **3h** [14]. The presence of IMHB in compound **3g** leads to the fact that in the ^{17}O NMR spectrum two signals are observed for the oxygen atoms of the carboxyl group at 304 (C=O) and

TABLE 1. Chemical Shifts of Oxygen and Nitrogen Atoms of the Nitrone Group in the ^{17}O and ^{14}N NMR Spectra of 4-R^1-1,2,2,5,5-Pentamethyl-3-imidazoline 3-Oxides **3a-i** (R^1 = Me). The Chemical Shifts of Compounds Enriched in Content of the ^{15}N Isotope are Given in Parentheses

Compound	R	δ ^{17}O, ppm*	δ ^{14}N (^{15}N), ppm*^{2}
3a	NH_2	247	-161
3b	OMe	—	-128
3c	H	283	-74
3d	Me	285	-85 (-90*^{3}; -80*^{4})
3e	Ph	310 (256*^{5})	-81 (-89*^{5})
3f	SMe	337	-78
3g	COOH	353	-66
3h	COOMe	386	-58
3i	CN	401	-50

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* Δf = 1100-3700 Hz.

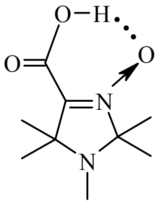
*^{2} Δf = 150-680 Hz (1900 Hz for **3a**).

*^{3} $CHCl_3$.

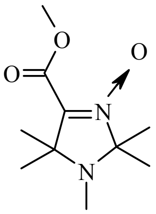
*^{4} CCl_4.

*^{5} MeOH.

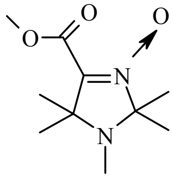
173 ppm (OH), and not one broadened signal at 250 ppm characteristic of carboxylic acids with rapid exchange [2]. The chemical shifts of the oxygen atoms of the ester groups in the spectrum of compound **3h** are observed in the usual ester region [2], at 354 (C=O), 169 and 144 ppm (OCH_3). The presence in the ^{17}O NMR spectrum of two methoxy group signals indicates their nonequivalence, which is probably linked with the existence of compound **3h** in two conformers *s-trans*-**3h** and *s-cis*-**3h**. In the IR spectrum these are displayed as two bands for the C=O groups at 1702 and 1732 cm^{-1} (in CCl_4).



3g



s-trans-**3h**

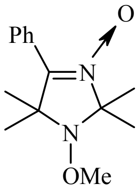


s-cis-**3h**

In the ^{14}N NMR spectra the same tendencies are observed for the nitrogen atom of the nitrone group for changes in chemical shift as for the ^{17}O chemical shift under the action of the same factors. In this case also the extreme positions in a fairly large range of changes of chemical shift (110 ppm) are occupied by aminonitrone **3a** (high field) and cyanonitrone **3i** (low field) (Table 1).

The chemical shift of the nitrogen atom of the amino group in aminonitrone **3a** (-314 ppm) is found at lower field compared with the chemical shifts of alkylamines (from -340 to -350 ppm) [15] and is close to the chemical shift of the nitrogen atoms in aromatic amines (-320 ppm) [3, 4], which indicates significant conjugation of the amino group with the nitrone group. The signal of the cyano group nitrogen atom in the spectrum of compound **3i** is observed at lower field (-82 ppm) compared with the region of values of the chemical shift for nitriles (from -120 to -140 ppm) [3].

Strengthening of the electron-withdrawing character of the substituent at atom C(5) on replacing methyl groups in position 5 of compound **4** by a methoxy group (compound **5**) leads to a displacement by 7 ppm of the N(3) atom signal towards low field, while strengthening the electron-withdrawing character of the substituent at C(2) (compound **6**) displaces the N(3) atom signal towards high field by 8 ppm. Changes in the opposite direction are observed for the chemical shift of atom C(4). Compared with the corresponding signals in compound **4** the C(4) atom signal in compound **5** is displaced by 8.2 ppm towards high field, but the corresponding signal in compound **6** is displaced by 0.5 ppm towards low field. The observed changes in chemical shift are in agreement with the tendencies of changes of charge densities on the C(4) and N(3) atoms [16].



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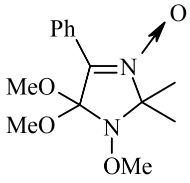

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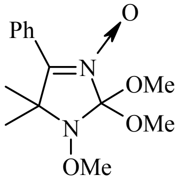
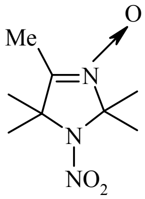


6

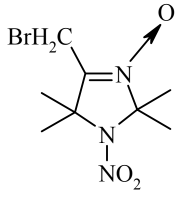
	4	5	6
δ N(3),	–85.9 [14]	–79.3	–94.0
δ C(4),	141.7	133.5	142.2

It must be noted that the reason for the low field displacement of the ^{14}N and ^{17}O atoms of the nitrone group may not only be the growth in electron-withdrawing character of the substituent at the α-carbon atom but also the growth of steric interactions on increasing the bulk of a substituent [17]. Consequently, the displacement towards low field of ~10 ppm for the signal of the N(3) atom on going from the 4-methyl derivative **7** to the 4-bromomethyl derivative **8** is probably the result of the action of both factors.



7

δ N(3), –92.8



8

–83.0

The nature of the substituent R^1 at the N(1) atom has an extremely noticeable influence on the chemical shift of the N(3) atom. Strengthening the electron-withdrawing character of the substituent on going from N(1)H to the N(1)NO_2 derivative leads to a displacement of the N(3) signal by 14 ppm towards high field (Table 2). Consequently the resulting effect of the N(1)R^2 group, with simultaneous substitution at the C(2) and C(5) atoms, coincides in direction with the effect of substitution at C(2) (cf. **4** and **6**). For comparison we note that the effect through C(5) predominates in the resulting effect of the N(1)R^2 groups on the chemical shift of the C(4) atom, but the effect does not exceed 3-4 ppm [16].

The chemical shifts of the nitrogen atoms of secondary and tertiary amino groups (NH and NCH_3) are displaced by 40-60 ppm towards low field relative to the region characteristic for dialkylamines and trialkylamines and appear as broad signals (Δf = 2000-4500 Hz) in the region from -290 to -300 and from -310 to -330 ppm respectively. The chemical shifts of the nitrogen atoms of the N(1)NO group [δN(1) = -105 to -110, δN = 150-165 ppm] are close to the chemical shifts of the nitrogen atoms in diisopropylnitrosamine (-107 and 166 ppm [18], which indicates the similarity of structural and energy parameters of the N(1)NO groups in these compounds. The signal of the N(1) atom in N(1)NO_2 derivatives is found at higher field (from -177 to -181 ppm, Δf = 2000-4000 Hz), in comparison with the N(1) chemical shift in N(1)NO derivatives, which indicates the lower order of the N–N bond [18]. The narrow signal of the NO_2 group (Δf = 40-60 Hz) in derivatives of 1-nitro-3-imidazoline 3-oxide is found at higher field (from -33 to -35 ppm) compared with the signal of dialkylnitroamines (~-26 ppm [18]).

EXPERIMENTAL

Syntheses of the compounds investigated are described in [16, 19]. 1,5,5-Trimethoxy-2,2-dimethyl-4-phenyl-3-imidazoline 3-oxide **5** and 5,5-dimethyl-1,2,2-trimethoxy-4-phenyl-3-imidazoline 3-oxide **6** were obtained by the reduction of the corresponding stable nitroxyl radicals with methylhydrazine [20].

TABLE 2. Chemical Shifts of the Nitrone Group Nitrogen Atom in ^{14}N NMR Spectra of 4-R^1-1-R^2-2,2,5,5-Tetramethyl-3-imidazoline 3-Oxides **3** and **7**

R/R^1	H	CH_3	OCH_3	NO	NO_2
H		-74		-80	
CH_3	-78	-85		-94	-93
C_2H_5	-78	-90	-91	-91	-92
C_6H_5	-74	-81	-86	-89	

The ^{17}O NMR spectra were recorded on a Bruker CXP 300 (40 MHz) spectrometer in 0.5 M solutions in CCl_4, $CHCl_3$, and CH_3OH at the natural isotope content, external standard was water. The spectrometer operating mode was impulse breadth 20 msec (90° impulse), impulse delay time 30 msec, number of accumulations 20-50 thousand.

The ^{14}N NMR spectra were recorded on a Bruker CXP 300 (30 MHz) spectrometer in solution in $CHCl_3$ and CCl_4, external standard was CH_3NO_2. The spectrometer operating mode was impulse breadth 20 μsec (90° impulse, 30 μsec), impulse delay time 20 msec.

REFERENCES

1. V. A. Reznikov and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, 192 (1991).
2. J.-P. Kintzinger, *Oxygen NMR, Characteristic Parameters and Application,* in: P. Diehl, E. Fluck, and R. Kosfeld (editors), *NMR: Basic Principles and Progress*, Vol. 17, Springer-Verlag, Berlin, Heidelberg, New York (1981), p. 1.
3. M. Witanowski, L. Stefaniak, and H. Januszewski, in: M. Witanowski and G. A. Webb (editors), *Nitrogen NMR*, Plenum Press, London, New York (1973), p. 164.
4. G. J. Martin, M. L. Martin, and J.-P. Gouesnard, in: P. Diehl, E. Fluck, and R. Kosfeld (editors), *NMR: Basic Principles and Progress*, Vol. 18, Springer-Verlag, Berlin, Heidelberg, New York (1981), p. 164.
5. D. W. Boykin, A. L. Baumstark, and P. Balakrishnan, *Magn. Res. Chem.*, **23**, 276 (1985).
6. P. M. Woyciesje, N. Janes, S. Ganapathy, Y. Hiyama, T. L. Brown, and E. Oldfield, *Magn. Res. Chem.*, **23**, 315 (1985).
7. D. W. Boykin, P. Balakrishnan, and A. L. Baumstark, *J. Heterocycl. Chem.*, **22**, 981 (1985).
8. L. Stefaniak, *Spectrochim. Acta,* **A32**, 345 (1976).
9. I. Yavari and J. D. Roberts, *Org. Magn. Res.*, **12**, 87 (1979).
10. W. W. Paudler and M. V. Javanovic, *Heterocycles*, **19**, 93 (1982).
11. M. Thenmozhi, S. Sivasubramanian, P. Balakrishnan, and D. W. Boykin, *J. Chem. Res. (S),* 340 (1986).
12. G. G. Furin, M. A. Fedotov, G. G. Yakobson, and A. A. Zibarev, *J. Fluor. Chem.*, **28**, 273 (1985).
13. M. M. Mitasov, I. A. Grigor'ev, G. I. Shchukin, I. K. Korobeinicheva, and L. B. Volodarskii, *Izv. SO Akad. Nauk SSSR, Ser. Khim. Nauk*, **2**, 112 (1978).
14. I. A. Grigor'ev, V. I. Mamatyuk, G. I. Shchukin, V. V. Martin, and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, 1065 (1986).
15. M. Witanowski and H. Januszewski, *Can. J. Chem.*, **47**, 1321 (1969).
16. I. A. Grigor'ev, G. I. Shchukin, V. V. Martin, and V. I. Mamatyuk, *Khim. Geterotsikl. Soedin.*, 252 (1985).
17. D. W. Boykin, P. Balakrishnan, and A. L. Baumstark, *Magn. Res. Chem*., **23**, 695 (1985).
18. J. P. Gouesnard and G. J. Martin, *Org. Magn. Res.*, **12**, 263 (1979).
19. S. M. Bakunova, I. A. Grigor'ev, I. A. Kirilyuk, and L. B. Volodarskii, *Izv. Akad. Nauk, Ser. Khim.*, 2160 (1999); [*Russ. Chem. Bull.,* **48**, 2136 (1999), (Engl. transl.)].
20. G. I. Shchukin, I. A. Grigor'ev, and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, 478 (1990).