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STEREOCHEMISTRY AND CONFIGURATIONAL STABILITY OF CYCLIC NH- AND N-DIMETHYLCARBAMOYLDIALKOXYAMINES*

I. I. Chervin, V. S. Nosova, V. F. Rudchenko,
V. I. Shevchenko, and R. G. Kostyanovskii

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On the basis of the data from the ${}^1H$, ${}^{13}C$, and ${}^{15}N$ NMR spectra it was established that perhydro-1,3,2-dioxazine has the chair conformation with the equatorial orientation of the NH proton; the barrier to inversion at the N atom is $\Delta G^{\neq} = 21.9$ kcal/mole. The preferred conformer of its 4-methyl derivative has the 2e,4e configuration. Stereospecific spin–spin coupling constants ${}^4J_{e\text{-HCONH-e}}$, ${}^3J_{{}^{13}\text{CONH-e}}$, and ${}^3J_{{}^{15}\text{NOCH-e}}$ were obtained for these compounds. 1,3,2-Dioxazolidine has a "bent envelope" conformation with the axial orientation of the NH proton; a stereospecific spin–spin coupling constant ${}^4J_{e\text{-HCONH-e}}$ was obtained, and the invariability of the PMR spectrum at 170°C was demonstrated.

Earlier it was shown that the configurational stability of the nitrogen atom in 2-tert-alkyl-1,3,2-dioxazolidines [3] and perhydro-1,3,2-dioxazines [4] is increased in comparison with the acyclic dialkoxyamines [5]. In this connection there was the prospect of finding

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*Communication 58 of the Series "Asymmetric Nitrogen," for Communication 57 see [1]; Communication 35 of the Series "Geminal Systems," for Communication 34, see [2].

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TABLE 1. Chemical Shifts (δ, ppm) of the Protons in Compounds (I-VI)

Structure*	Solvent	4a-H (6a-H)	4e-H (6e-H)	5a-H	5e-H	Others
I**	$CDCl_3$	4,31 (4,31)	4,08 (4,08)	2,07	1,47	8,24 (2e-H)
IIe	$CDCl_3$ C_6D_6	4,25 (4,23) 4,04 (4,10)	1,16 (Me) (4,08) 0,95 (Me) (3,77)	1,68 1,42	1,45 0,79	8,17 (2e-H) 7,85 (2e-H)
IIa	$CDCl_3$ C_6D_6	3,91 (3,93) 3,17 (3,16)	1,24 (Me) (4,31) 0,95 (Me) (4,10)	1,91 —	1,66 —	7,13 (2a-H) 6,67 (2a-H)
III	$C_6D_5CD_3$	3,94		1,28		2,56 (MeN)
IV	$CDCl_3$	4,39 (4,34)	1,23 (Me) (4,22)	1,78	1,52	2,93 (MeN)
Va	$CDCl_3$ C_6D_6	3,91 (AA') 3,01 (AA')		4,21 (BB') 3,52 (BB')		7,22 (2a-H) 6,64 (2a-H)
VI	C_6D_6	3,55 and 4,04 (CH_2O, br. sig.)				2,43 and 2,62 (MeN)

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*Compounds (I, IIe, IIa, IV) were recorded at 400 MHz, and compounds (III, Va,VI) at 80 MHz.

**For the compound not enriched with ^{15}N, $\delta_{^{15}N}$ = 127.9 ppm upfield from $H^{15}NO_3$ as external standard.

TABLE 2. Spin–Spin Coupling Constants of the Protons (J, Hz) in the NMR Spectra of Compounds (I-V)

Structure	4a,4e (6a, 6e)	4a, 5a (6a, 5a)	4a, 5e (6a, 5e)	4e, 5a (6e, 5a)	4e, 5e (6e, 5e)	5a, 5e	Others
I*	−11,72 (−11,72)	11,7 (11,7)	2,7 (2,7)	5,1 (5,1)	2,4 (2,4)	−13,4	1,5 [2e, 4e (6e)]
IIe	6,4 (4a, Me) (−11,2)	11,7 (12,2)	2,7 (2,7)	— (5,4)	— (1,5)	−13,4	1,5 (2e, 6e)
IIa	6,4 (4a, Me) (−12,0)	11,7 (11,2)	2,7 (2,7)	— (4,6)	— (2,7)	−13,4	0,7 (2a, 6e)
III	5,3 (CH_2O, CH_2)						
IV	6,4 (4a, Me) (−11,2)	11,7 (12,2)	2,7 (2,7)	— (5,4)	— (1,5)	−13,4	
Va	−7,2 ($^2J_{AB}={}^2J_{A'B'}$); 8,6 (AA') 7,6 (BB'); 6,1 (AB'=A'B)						0,4 (2a, B)

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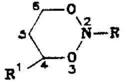
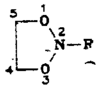
*^{15}N NMR, $^1J_{^{15}N,^1H}$ = 64.7 Hz, $^3J_{^{15}N,4e(6e)}$ = 4.9 Hz.

conformationally and configurationally rigid cyclic systems of a similar type even in the presence of π-electron-accepting N-acyl substituents.

In the present work we studied the stereochemistry and configurational stability of cyclic NH-dialkoxyamines by ^1H, ^{13}C, and ^{15}N NMR spectroscopy. The investigated compounds were perhydro-1,3,2-dioxazines (I, II) and 1,3,2-dioxazolidine (V) and also their 2-dimethylcarbamoyl derivatives (III, IV, VI).


I-IV


V, VI

I, II, V R=H, III, IV, VI R=Me_2NCO; I, III R^1=H, II, IV R^1=Me

The parameters of the PMR spectra of compounds (I-IV) were obtained by homonuclear double resonance and with due regard to the relations between the spin–spin coupling constants *aa* (11-12 Hz) > *ae* (3-5 Hz) > ee (1-2 Hz) for 2-tert-alkylperhydro-1,3,2-dioxazines [3] and 1,3-dioxanes [8] (Tables 1 and 2, Fig. 1) and by computer analysis for the dioxazolidine (V) (Tables 1 and 2, Fig. 2). In the crystal and in the solution the 2-tert-alkyperhydro-1,3,2-dioxazines have the chair conformation with the equatorial orientation of the substituents at

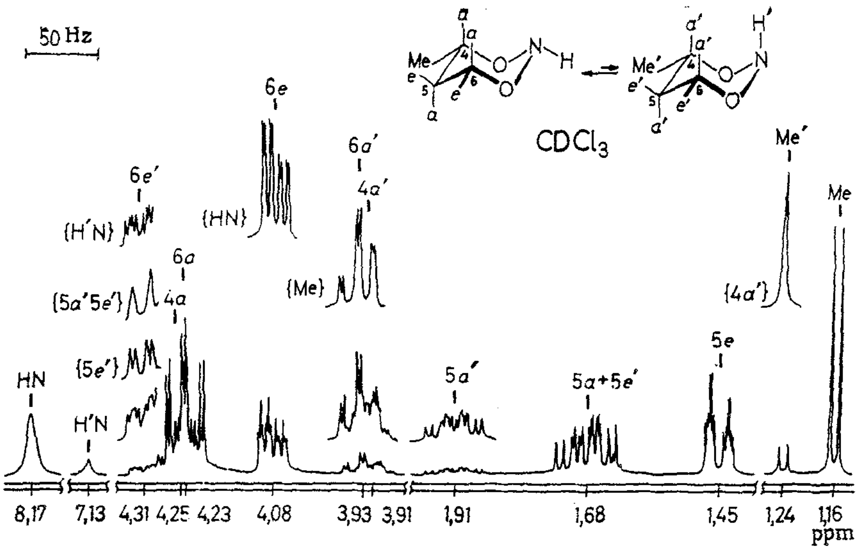


Fig. 1. The PMR spectra of 4-methylperhydro-1,3,2-dioxazine for conformers (IIe) and (II*a*) at 400 MHz.

TABLE 3. Parameters of the ^{13}C NMR Spectra (100.61 MHz) for Compounds (I-VI)

Structure*	δ, ppm ($^{n}J_{^{13}C,^{1}H}$, Hz)			
	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	others
I	69,46 (^{1}J=143,3; *a*-H; 145,2, *e*-H) (^{3}J=5,0, 2*e*)	24,59 (^{1}J=124,6; *a*-H; 127,6; *e*-H)	—**	—
II*e*	74,82 (^{1}J=144,7)	31,98 (^{1}J=124,5)	68,72 (^{1}J=144,1; ^{2}J=5,5; *a*-H; ^{3}J=5,5; 2*e*)	19,77 (Me) (^{1}J=126,3)
II*a*	76,43 (^{1}J=144,6)	30,57 (^{1}J=125,7)	70,37 (^{1}J=144,1)	19,72 (Me) (^{1}J=126,3)
III	70,33 (^{1}J=145,3)	24,02 (^{1}J=126,9)	—**	36,45 and 36,82 (MeN) (^{1}J=137,9 and 139,2), 158,7 (C=O) (^{3}J=3,6)
IV	76,42 (^{1}J=146,3; ^{2}J=6,1; 5*a* and 5*e*)	31,83 (^{1}J=125,7)	69,76 (^{1}J=145,3; ^{2}J=4,9; 5*e*)	19,93 (MeC) (^{1}J=126,9), 36,21 and 36,74 (MeN) (^{1}J=139,2), 158,7 (C=O) (^{3}J=3,6)
V*a*	68,95 (^{1}J=150,8; ^{2}J<0,5)			
VI	68,32 (^{1}J=152,6)			36,09 and 36,74 (MeN) (^{1}J=138,9)

*The spectra of compounds (IV, VI) were obtained in hexadeuterobenzene, and those of the others were obtained in deuterochloroform; only the identified long-range constants are given.

**Coincides with $C_{(4)}$.

positions 2 and 4 [4]. The similarity of the parameters in the ^{1}H and ^{13}C NMR spectra of the dioxazines (I-IV) (Tables 1-3) and N-tert-alkyl-substituted compounds [4] indicates the chair conformation for compounds (I-IV). The equatorial orientation of the NH proton in the oxazine (I) is confirmed by the fact that the ^{1}H (Table 2) and ^{13}C (Table 3) NMR spectra contain long-range spin—spin coupling constants for the isochronous protons 4e-H and 6e-H and the carbon atoms $C_{(4)}$ and $C_{(6)}$ with the NH proton.

Conformers with the equatorial (IIe) and axial (II*a*) orientation of NH in a ratio of 5:1 are observed in the ^{1}H and ^{13}C NMR spectra of the 4-methyl derivative of the oxazine (I) at 25°C (Tables 1-3, Fig. 1). The vicinal spin—spin coupling constants of the 4-H proton

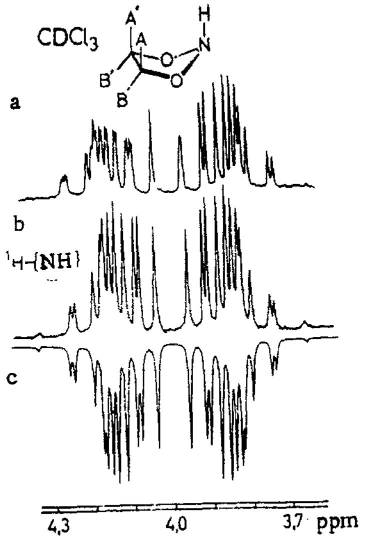


Fig. 2. The PMR spectra of 1,3,2-dioxazolidine (V) at 80 MHz: a) Experimental; b) with suppression of the NH protons; c) theoretical.

TABLE 4. ASIS Effect, $\Delta\delta = \delta_{CDCl_3} - \delta_{C_6D_6}$, ppm

Structure	4*a* (6*a*)	4*e* (6*e*)	5*a*	5*e*	HN
VII* [4]	0,18 (0,18)	0,28 (0,28)	0,32	0,69	
II*e*	0,21 (0,13)	0,21 (Me) (0,31)	0,26	0,66	0,32
II*a*	0,74 (0,77)	0,29 (Me) (0,21)			0,46
V*a*	0,9 (AA')		0,69 (BB')		0,58

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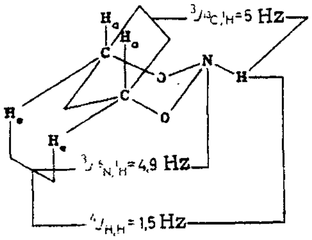
*Methyl 2-(dihydro-1,3,2-dioxazin-2-yl)isobutyrate.

($^3J_{4,5a}$ = 11.7 Hz) for the conformers (IIe) and (II*a*) (Table 2, Fig. 1) demonstrate unambiguously the equatorial orientation for the methyl substituent 4-CH_3 in both conformers.



As for the oxazine (I), long-range spin–spin coupling constants $^4J_{2e6e}$ = 1.5 and $^3J_{^{13}C(6),2e}$ = 5.5 Hz are observed in the ^1H and ^{13}C NMR spectra of the conformer (IIe) (Tables 2 and 3, Fig. 2). In the case of the conformer (II*a*) the $^3J_{^{13}C(6),2e}$ constant is absent (<0.4 Hz), and $^4J_{6e2a}$ = 0.7 Hz is half the value for the conformer (IIe).

The agreement of the long-range spin–spin coupling constants for compounds (I) and (IIe) and their difference in the case of the isomer (II*a*) correspond to the analysis of the geometry on Dreiding molecular models. From this it follows that spin–spin coupling $^4J_{HH}$ of the "W" type is possible between the 4e(6e) and NH protons in the equatorial orientation of the NH proton, and coupling of the "dipper" type is possible in the axial orientation. It is known that for six-membered rings in the chair conformation $^4J_{ee}$ (in the "W" arrangement) > ^4J_e and $^4J_{aa}$ ("dipper") [8, 9]. It can therefore be considered that the observed spin–spin coupling constants $^4J_{4e(6e),NH}$ = 1.5 Hz [for (I)] and $^4J_{6e,NH}$ = 1.5 Hz [for (II)] (Table 2) correspond to the spin–spin coupling constants of the conformers with the equatorial orienta-

TABLE 5. Energy Parameters for Restricted Amide Rotation and Inversion at the Nitrogen Atom in Compounds (I, III-VI)

Compound*	Solvent	Observed group	($J^{\Delta\nu_i}_{AB}$ Hz)	T_c, °C	k, sec^{-1}	$\Delta G^{\neq}_{ro}$ ±0,3**, kcal/mole (25°)	$\Delta G^{\neq}_{in}$ ±0,3**, kcal/mole (25°C)
I	DMSO	CH_2O	43 (11,23)	160	113,3	—	21,9
III	$C_6D_5CD_3$	Me_2N	5,8	14	12,88	15,3	—
		CH_2O	93	−64	208,23	—	9,8
IV	$C_6D_5CD_3$	Me_2N	6,4	12	14,21	15,1	—
V	Ph_2O	The spectrum does not change on heating to 170°C					~28
VI	$C_6D_5CD_3$	Me_2N	14,4	53	31,97	16,9	—
		CH_2O	32,0	44	71,04	—	15,9

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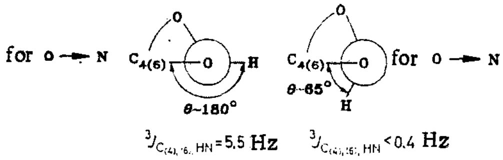
*Compound (I) at 400 MHz, (III, IV, VI) at 80 MHz, (V) at 60 MHz.

**Determined as in [6, 7].

tion of the NH. This is confirmed by the observation of spin–spin coupling between the $C_{(4)},_{(6)}$ atoms in (I) and the $C_{(6)}$ atom in the conformer (IIe) and the NH proton with $^3J_{^{13}C,^1H}$ = 5.0 and 5.5 Hz, respectively (Table 3). According to the calculated dependence of $^3J_{^{13}C,^1H}$ on the dihedral angle θ_{CCCH} for propane, the maximum value of $^3J_{^{13}C,^1H}$ = 8.8 Hz corresponds to θ = 180° (the trans orientation), while the minimum value of $^3J_{^{13}C,^1H}$ ~ 0 Hz corresponds to θ = 90° (the gauche orientation) [10]. Analysis of the dioxazines (I, IIe, II*a*) shows that with the equatorial orientation of NH Θ_{CONH} ~ 180° (trans) and with the axial orientation Θ_{CONH} ~ 60-70° (gauche).



In addition, according to the ^{15}N NMR spectrum of the unenriched dioxazine (I) the long-range spin–spin coupling constants of the ^{15}N nucleus with the 4e,6e protons is observed ($^3J_{^{15}N,^1H}$ = 4.9 Hz) (Table 2). The absence of spin–spin coupling with the 4*a*,6*a* protons was proved by selective heteronuclear double resonance with successive irradiation of the 4e(6e) and 4*a*(6*a*) protons. According to the data from analysis of models, the dihedral angles amount to θ_{H_eCON} ~ 180° and θ_{H_aCON} ~ 60-70°. According to the calculated dependence of $^3J_{^{14}N,^1H}$ on the dihedral angle θ_{HCCN} for ethylamine [10], the maximum value of $^3J_{^{15}N,^1H}$ must be at θ_{HCON} = 180°. Therefore, the observed $^3J_{^{15}N,^1H}$ value evidently also favors the equatorial orientation of the NH. However, the conformation can only be determined unambiguously from this spin–spin coupling constant if its values are compared for both conformers. On account of the low concentration of the sample of (II) and the small population of the axial conformer it was not possible to measure the ^{15}N NMR spectra of the conformers (IIe) and (II*a*).

An additional test for determining the orientation of the NH proton can be provided by the shift induced by the aromatic solvent (the ASIS effect) (Table 4). The Δδ values for the conformer (IIa) are maximum for the NH, 4*a*, and 6*a* protons, to which the approach of the benzene molecules is not screened by the unshared electron pairs of the N and O atoms. In contrast, in the case of the conformer (IIe) and perhydrooxazine (the equatorial orientation of the N-substituent was demonstrated in [4]) the maximum value of Δδ is observed only for the 5e proton (the only proton to which unhindered approach of the benzene is possible).

The PMR spectra of the dioxazine (I) in octadeuterotoluene and tetradeuteromethanol do not change on cooling to −80°C. This can be explained both by the small population of the conformer with the axial orientation of the NH proton and by the rapid conversion of ring

(I), if it is assumed that the barrier to the conversion is less than for 1,3-dioxazine ($\Delta G^{\neq}$ = 9 kcal/mole at −73°C) [11]. It should be noted that the population of the axial conformer (II*a*) is increased in polar solvents [(II*a*):(IIe) 1:10 (in hexadeuterobenzene), 1:5 (in deuterochloroform), and 1:3 (in hexadeuteromethanol and trideuteroacetonitrile)]. This is evidently explained by the decrease in the energy of the unshared electron pairs of the heteroatoms during solvation and, consequently, by the decrease in their destabilizing interaction. Thus, the preferred equatorial orientation of the substituents at the nitrogen atom in perhydro-1,3,2-dioxazines does not depend on the size of the substituent at this atom. In perhydrodioxazines the bending angle of the ring along the O(1)...O(3) axis is increased by ~20° compared with cyclohexane [4]. This is due to the repulsion of the unshared electron pairs of the N and O atoms and to $n \rightarrow \sigma^*$ interaction. This leads to strong steric syn-axial destabilizing interaction between the ring protons and the N-substituent even with its smallest volume (NH). As in the case of tetrahydro-1,2-oxazine [12], the preferred population of the equatorial conformers is evidently due to the small destabilizing interaction between the unshared electron pairs of the N and O atoms compared with the axial conformers. On the basis of the foregoing it can be supposed that the substituent at the nitrogen atom in the carbamoyl derivatives (III, IV) is also in the equatorial orientation.

In the case of 1,3,2-dioxazolidine (V) the spectrum of the AA'BB' type for the ring protons (Tables 1 and 2, Fig. 2) and also the isochronism of the $C_{(4)}$ and $C_{(5)}$ carbon atoms (Table 3) make it possible to suppose that the five-membered ring has the "bent envelope" conformation. From the analysis of models it can be assumed that the chemical shifts of the 4-H and 6-H protons in the conformers (II*a*) and (IIe) and of the ring protons in (V) are mainly determined by the effect of the unshared electron pairs of the O atoms, and their orientation in relation to the adjacent protons in the five- and six-membered rings is similar. This is confirmed by the inversion of the chemical shifts for the 6*a* and 6e protons in the conformers (IIe) and (II*a*) and by the proximity of the chemical shifts for the 6*a* (3.93) and 6e (4.31 ppm) protons in (II*a*) and protons A (3.91) and B (4.21 ppm) in the spectrum of (V) and also the NH proton [7.13 in (II*a*) and 7.22 ppm in (V)] (Table 1). In the case of the dioxazolidine (V) a larger ASIS effect is observed for the AA' protons than for the BB' protons, and a similar effect to that observed for the conformer (II*a*) is round for the NH proton (Table 4). This indicates that the AA' and NH protons have the axial orientation, and this is confirmed by the similar values of the spin–spin coupling constants $^4J_{4e(5e)2a}$ = 0.4 Hz in (V) and $^4J_{6e2a}$ = 0.7 Hz in (II*a*) (Table 2, Fig. 2) and by the absence of the spin–spin coupling constant $^3J_{^{13}C,\,^1NH}$ in the ^{13}C spectrum of the dioxazolidine (V), as also in the case of the dioxazine (II*a*) (Table 3). The latter agrees with the analysis of the molecule of (V) on the models, according to which Θ_{CONH} ~ 90° with the axial orientation of the NH proton and Θ_{CONH} ~ 150° with the equatorial orientation. Thus, 1,3,2-dioxazolidine (V) has the "bent envelope" conformation with the axial orientation of the NH proton, which is also characteristic of NH-isoazolidines, to judge from the data from photoelectron spectroscopy [12].

The restricted processes in compounds (I-VI) were investigated by the dynamic NMR method. For the carbamoyl derivatives (III, IV, VI) it was possible to distinguish between the restricted amide rotation and inversion at the nitrogen atom (Table 5), as in the case of the acyclic analogs $Me_2N{-}CON(OR)OR'$ ($\Delta G_{ro}^{\neq}$ ~ 13-14, $\Delta G_{in}^{\neq}$ ~ 10 kcal/mole) [6]. The increase of $\Delta G_{ro}^{\neq}$ in compounds (III, IV, VI) compared with the acyclic N,N-dialkoxyureas agrees with the increase in the s character of the unshared electron pair of the nitrogen atom in the transition from the six- to the five-membered nitrogen heterocycle [13]. On the basis of these data and also of the increase of $\Delta G_{in}^{\neq}$ for the nitrogen atom in the transition from the acyclic alkoxyamines R_2NOR ($\Delta G_{in}^{\neq}$ ~ 10-11 kcal/mole [5]) to the cyclic $(CH_2)_nONR$ (with n = 4, $\Delta G_{in}^{\neq}$ ~ 13 kcal/mole and with n = 3, $\Delta G_{in}^{\neq}$ ~ 15 kcal/mole) [13] and N-alkoxy-1,2-oxazolidines ($\Delta G_{in}^{\neq}$ ~ 28 kcal/mole) [14] an increase could be expected in the configurational stability of the nitrogen atom in compounds (I) and, particularly, (V) compared with the acyclic N,N-dialkoxyamines ($\Delta G_{in}^{\neq}$ ~ 20 kcal/mole) [15]. It was found that $\Delta G_{in}^{\neq}$ for the nitrogen atom in the ring of (I) (Table 5) is only ~1.5 kcal/mole greater than in $RO(R^1O)NH$ [15]. It is not impossible that the insignificance of this difference is due to the contribution from proton exchange of NH at 160°C, although at 100°C the exchange of NH is excluded by the presence of the long-range spin–spin coupling constant $^4J_{4e(6e)NH}$ (Table 2). Unfortunately this spin–spin coupling constant cannot be monitored at higher temperatures on account of the broadening of the signals. In the case of (V) the coalescence of the signals for the ring protons is not reached at 170°C (Table 5). Further increase in the temperature leads to decomposition of the sample. The retention of the anisochronism in the ring protons at 170°C shows that in 1,3,2-dioxazolidine (V) $\Delta G_{in}^{\neq} > 25$ kcal/mole. In the transition from 2-dimethylcarbamoylperhydro-1,3,2-dioxazine (III) to 2-dimethylcarbamoyl-1,3,2-dioxazolidine (VI) $\Delta G_{in}^{\neq}$ is increased by 6.1 kcal/mole, while in the case of 2H-perhydro-1,3,2-dioxazine $\Delta G_{in}^{\neq} = 21.9$ kcal/mole (Table 5). On this basis it is possible to estimate the inversion barrier of the nitrogen in the dioxazolidine (V) as $\Delta G_{in}^{\neq} \sim 28$ kcal/mole. In other words, 1,3,2-dioxazolidine (V) is comparable with N-alkoxy-1,2-oxazolidines in configurational stability [14]. The possibility of the appearance of geminal anisochronism of the ring protons in compounds (I, V) on account of slow conversion of the ring on the NMR time scale is excluded by the fact that the absence of rapid exchange of the NH proton in D_2O and CD_3OD was established in the PMR spectra of compounds (I) and (V). Only the addition of an aqueous solution of potassium hydroxide to solutions of (I) and (V) in CD_3OD leads to exchange of the NH. Here the multiplets for the ring protons of (I) at 20°C are transformed into a triplet (CH_2O) and a quintet (CCH_2C), while the AA'BB' spectrum of the ring protons (V) is transformed into a singlet. From this it follows that the geminal anisochronism of the ring protons observed in the PMR spectra is due to slow inversion at the nitrogen atom (Tables 1, 2, and 5).

Thus, compounds (I) and (V) are the first examples of cyclic N,N-dialkoxyamines containing the O—N—O fragment included in a ring, where it has been possible to detect experimentally and evaluate the barrier to inversion at the nitrogen atom (Table 5).

EXPERIMENTAL

The NMR spectra were measured on Bruker WM-400 (^1H 400.13, ^{13}C 100.61, ^{15}N 40.53 MHz) and WP-80-SY and Jeol C-60-HL spectrometers with TMS as internal standard. The theoretical spectrum of the ring protons in compound (V) was calculated with decoupling from the NH proton using the PANIC program on a ASPECT-2000 computer. The energy parameters of restricted amide rotation and inversion at the nitrogen atom were determined as in [6, 7]. The synthesis of compounds (I, III, VI) was described in [16].

2-Dimethylcarbamoyl-4-methylperhydro-1,3,2-dioxazine (IV). Compound (IV) was obtained by the method described in [16]. A solution of 6.2 g (41.9 mmole) of 1,1-dimethoxy-3,3-dimethylurea (see [16]) and 0.05 g of p-toluenesulfonic acid in 25 ml of 1,3-butylene glycol was kept at 20°C for 3 days with periodic removal of the methanol formed in the reaction under vacuum (20 mm Hg). The mixture was extracted with carbon tetrachloride (4 × 100 ml), the extract was evaporated under vacuum, and the residue was distilled. We obtained 3.24 g (44%) of (IV); bp 117°C (1 mm Hg). The product was characterized by the NMR spectra (Tables 1-3).

4-Dimethylperhydro-1,3,2-dioxazine (II). Compound (II) was obtained by the method in [16]. A solution of 1.53 g (8.8 mmole) of (IV), 1.1 g (19.6 mmole) of potassium hydroxide, and 0.1 g of triethylbenzylammonium chloride in 3 ml of water was kept at 20°C for 24 h and extracted with ether (4 × 40 ml). The extract was dried with magnesium sulfate and evaporated under vacuum (20 mm Hg). The residue was recondensed under vacuum (1 mm Hg) at 20°C. We obtained 0.33 g (36%) of compound (II), which we characterized by means of the NMR spectra (Tables 1-3).

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SYNTHESIS AND TRANSFORMATIONS OF SULFIDES OF THE THIOPHENE SERIES.

42.* SYNTHESIS AND PROPERTIES OF SOME 2-ALKYLTHIO(ALKYLSULFINYL, ALKYLSULFONYL)THIOPHENE-3-CARBONITRILE N-OXIDES

M. M. Krayushkin, M. A. Kalik, V. K. Zav'yalova,
and V. S. Bogdanov

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Thiophene-3-carbonitrile N-oxides containing alkylthio, alkylsulfinyl, and alkysulfonyl groups in the 2-position, which readily undergo 1,3-dipolar cycloaddition to the C=C bond (styrene, N-phenylmaleinimide) to give the corresponding 3,5-disubstituted 2-isoxazolines, were obtained.

The use of organic nitrile oxides in 1,3-dipolar cycloaddition reactions with various dipolarophiles opens up extensive possibilities for the synthesis of the most diverse classes of mono- and polyheterocycles [2]. The number of stable nitrile oxides, particularly in the heterocyclic series, is extremely limited, since the overwhelming majority of them undergo spontaneous dimerization to furoxanes; they are therefore generally prepared in situ. The possibility of the formation of nitrile oxides of the thiophene series only as unstable intermediates was demonstrated in [3]. One of the necessary conditions for the stability of aromatic nitrile oxides is the presence in the ortho position relative to the nitrile oxide group of substituents that sterically hinder their dimerization [4].

In the present paper we describe the synthesis of some thiophene-3-carbonitrile N-oxides with methylthio, methylsulfinyl, or methylsulfonyl groups in the 2 position by two-phase oxidative dehydrogenation of 2-alkylthio(alkylsulfonyl)-5-alkylthiophene-3-aldoximes with sodium hypochlorite by the method in [5]. The starting 2-methylthio-5-methylthiophene-3-aldoxime (I) was obtained by the usual method from the corresponding aldehyde [6] and exists, according to the ^{15}N NMR spectral data ($J_{^{15}NH} = 3.4$ Hz), in the form of the syn isomer [7]. Since both of the oxime and methylthio groups may undergo changes during the reaction, we ascertained the sequence of their oxidation and the effect of the nature of the sulfur fraction on the properties and stabilities of the resulting nitrile oxides.

3-(2-Methylthio-5-methyl-3-thienyl)-5-phenyl-2-isoxazoline (II) was isolated in high yield when oxime I was added to a mixture containing one to two equivalents of NaOCl, styrene, and a small amount of Et_3N in CH_2Cl_2. Its structure was confirmed by data from the mass spectra and the PMR and ^{13}C NMR spectra: in particular, the chemical shifts for the $C_{(4)}$ – trip-

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*See [1] for communication 41.

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