Brief Communications

Synthesis of *N*-nitrooxazolidines and *N*-nitrotetrahydro-1,3-oxazines from *N*-(2-hydroxyalkyl)- and *N*-(3-hydroxyalkyl)sulfamates

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A method was developed for the preparation of functionally substituted *N*-nitrooxazolidines and *N*-nitrotetrahydro-1,3-oxazines by nitration of the products obtained in the reactions of *N*-(2-hydroxyalkyl)- and *N*-(3-hydroxyalkyl)sulfamates with formaldehyde.

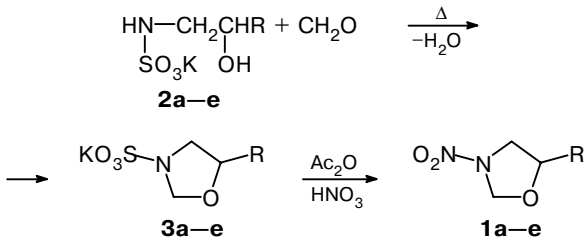
Key words: *N*-nitrooxazolidines, *N*-nitrotetrahydro-1,3-oxazines, *N*-(2-hydroxyalkyl)sulfamates, *N*-(3-hydroxyalkyl)sulfamates, formaldehyde, nitration, ^{1}H and ^{13}C NMR spectroscopy, 2D NMR spectroscopy, IR spectroscopy, mass spectrometry.

The present study was aimed at the search for rational procedures for the preparation of the previously unknown *N*-nitro derivatives of oxazolidine based on derivatives of sulfamic acid. Although procedures for the synthesis of oxazolidine and tetrahydrooxazine derivatives were reported in the literature,[1—3] their *N*-nitro derivatives remain unknown.

Results and Discussion

With the aim of preparing *N*-nitro derivatives of oxazolidines **1**, we studied the reactions of the corresponding *N*-(2-hydroxyalkyl)sulfamates **2** with formaldehyde. These reactions afforded complex mixtures of products. However, we found conditions under which the oxazolidine ring was predominantly formed (the initial components were taken in a ratio **2** : CH_2O = 1 : 1.1, condensation was carried out at pH 7.7—8.2). The resulting compounds **3** were not isolated in individual form because of their instability in solvents. Sulfamates **3** were converted into nitro compounds **1** in a total yield of 50—75% under the action of the HNO_3—Ac_2O mixture as a nitrating agent at the temperature from −10 to −5 °C (Scheme 1), which is indirect evidence in favor of the structure of compounds **3**.

Scheme 1



R = CH_2OMe (**a**); CH_2Cl (**b**); CH_2N_3 (**c**); Me (**d**); H (**e**)

Compounds **1** exist as liquids and were isolated by fractional distillation (Table 1).

Compound **1b** was converted into azidomethyl-substituted compound **1c** in 85% yield upon treatment with NaN_3 in DMF (Scheme 2).

It should be noted that the preparation of azide **1c** through chloride **1b** did not require fractional distilla-

Scheme 2

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Table 1. Physicochemical properties and the yields of *N*-nitrooxazolidines **1** and *N*-nitrotetrahydro-1,3-oxazines **6**

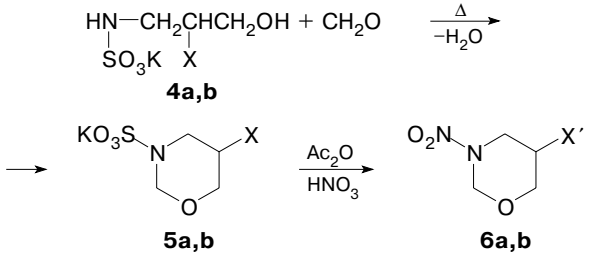
Compound	Yield (%)	B.p./°C (*p*/Torr)	Found / Calculated (%)			Molecular formula
			C	H	N	
1a	47	72—73 (0.7—0.9)	37.09 / 37.04	6.21 / 6.22	—	$C_5H_{10}N_2O_4$
1b	75	93—94 (1.0—1.2)	29.01 / 28.84	4.31 / 4.24	16.80 / 16.82	$C_4H_7N_2O_3Cl$
1c	49 85*	102—103 (0.8—1.0)	28.32 / 27.75	4.28 / 4.08	40.68 / 40.45	$C_4H_7N_5O_3$
1d	48	60—61 (1.0—1.2)	—	—	21.64 / 21.20	$C_4H_8N_2O_3$
1e	61	49—50 (0.7—0.8)	31.11 / 30.51	5.14 / 5.12	23.84 / 23.72	$C_3H_6N_2O_3$
6a	42	**	36.90 / 36.36	6.19 / 6.10	—	$C_4H_8N_2O_3$
6b	42	**	25.01 / 24.88	3.65 / 3.65	21.91 / 21.76	$C_4H_7N_3O_6$

* Prepared from compound **1b** (Scheme 2).
** Crystalline compounds; m.p. were 19.5—20.5 (**6a**) and 89—90 (**6b**) °C.

tion, and compound **1c** was obtained in higher total yield.

N-(3-Hydroxyalkyl)sulfamates **4** behave analogously to *N*-(2-hydroxyalkyl)sulfamates **2**. Compounds **4** can also undergo cyclization in the reactions with formaldehyde to form compounds **5**, which were converted into the corresponding *N*-nitrotetrahydro-1,3-oxazines **6** in 40—45% yields upon treatment with the HNO_3—Ac_2O mixture (Scheme 3). Compounds **6** were obtained in the crystalline form (see Table 1).

Scheme 3



X = X′ = H (**a**); X = OH, X′ = ONO_2 (**b**)

It should be noted that the reaction of sulfamate **4b** with formaldehyde followed by nitration afforded a compound to which the structure of *N*-nitro-5-nitroxytetrahydro-1,3-oxazine (**6b**) was assigned based on the data from ^1H, ^{13}C, and ^{15}N NMR spectroscopy (Table 2), the correlation ^1H—^1H, ^1H—^{13}C, and ^1H—^{15}N NMR spectra (Fig. 1), the IR spectra ((KBr), ν/cm^{-1}: 1284, 1552 (NNO_2); 1636 (ONO_2)), the mass spectra (peaks: 193 $[M]^+$, 131 $[M—ONO_2]^+$, 101 $[M—2NO_2]^+$, 85 $[M—ONO_2—NO_2]^+$), and the data from elemental analysis (see Table 1). Noteworthy is the large difference in the chemical shifts of the magnetically nonequivalent protons of the CH_2 groups at the nitrogen atoms in the

Table 2. ^1H NMR spectra of nitramines **1** and **6**

Compound	δ, *J*/Hz
1a	3.32 (s, 3 H, OMe); 3.58 (m, 2 H, $\underline{CH_2}$OMe, *J* = 2.6, 2.6); 3.82 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −11.7, 7.3); 4.03 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −11.7, 7.3); 4.47 (m, 1 H, CHO); 5.12 (d, 1 H, NCH_2O, *J* = −6.2); 5.40 (d, 1 H, NCH_2O, *J* = −6.2)
1b	3.84 (dd, 1 H, CH_2Cl, *J* = −11.9, 5.2); 3.87 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −11.7, 7.1); 3.90 (dd, 1 H, CH_2Cl, *J* = −11.9, 4.5); 4.21 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −11.7, 6.7); 4.65 (m, 1 H, CHO); 5.20 (d, 1 H, NCH_2O, *J* = −5.8); 5.47 (d, 1 H, NCH_2O, *J* = −5.8)
1s	3.56 (dd, 1 H, CH_2N_3, *J* = −15.0, 7.0); 3.67 (dd, 1 H, CH_2N_3, *J* = −15.0, 5.6); 3.78 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −13.2, 8.0); 4.13 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −13.2, 8.3); 4.58 (m, 1 H, CHO); 5.17 (d, 1 H, NCH_2O, *J* = −7.0); 5.48 (d, 1 H, NCH_2O, *J* = −7.0)
1d[a]	1.38 (d, 3 H, $\underline{Me}$CH, *J* = 7.0); 3.42 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −9.4, 9.4); 4.12 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −9.4, 6.5); 4.40 (m, 1 H, CHO); 5.07 (d, 1 H, NCH_2O, *J* = −6.5); 5.40 (d, 1 H, NCH_2O, *J* = −6.5)
1e	3.95 (t, 2 H, C$\underline{CH_2}$O, *J* = 7.5); 4.18 (t, 2 H, N$\underline{CH_2}$C, *J* = 7.5); 5.20 (s, 2 H, NCH_2O)
6a[a]	1.80 (q, 2 H, $CH_2\underline{CH_2}CH_2$, *J* = 5.7, 5.3, 5.3, 5.7); 3.90 (t, 2 H, O$\underline{CH_2}CH_2$, *J* = 5.3); 4.07 (t, 2 H, N$\underline{CH_2}CH_2$, *J* = 5.7); 5.27 (s, 2 H, NCH_2O)
6b[b]	4.20 (dtd, 1 H, O$\underline{CH_2}$CH, *J* = −13.1, 2.3, 0.7); 4.28 (dd, 1 H, O$\underline{CH_2}$CH, *J* = −13.1, 2.1); 4.28 (br.d, 1 H, N$\underline{CH_2}$CH, *J* = −16.3); 5.01 (br.d, 1 H, NCH_2O, *J* = −12.0); 5.04 (dq, 1 H, N$\underline{CH_2}$CH, *J* = −16.3, 2.5); 5.24 (q, 1 H, $CHONO_2$, *J* = 2.2); 5.89 (dd, 1 H, NCH_2O, *J* = −12.0, 2.1) 48.9 (s, N$\underline{C}H_2$CH); 68.5 (s, O$\underline{C}H_2$CH); 76.9 (s, $\underline{C}HONO_2$); 78.8 (s, N$\underline{C}H_2O$)[c] −26.9 (s, N—$^{14}NO_2$); −45.2 (s, O—$^{14}NO_2$)[d]

[a] The spectra were recorded on a Bruker AM-300 spectrometer. [b] The spectra were recorded on a Bruker DRX-500 spectrometer. [c] ^1H—^{13}C NMR. [d] ^1H—^{15}N NMR.

N$\underline{CH_2}$O and N$\underline{CH_2}$CH fragments and a rather small difference in these shifts for the CH$\underline{CH_2}$O fragment. The assignment of the signals was made based on the data from the ^1H—^{13}C NMR correlation spectra assuming that the lowest-field and the highest-field ^{13}C signals belong to the N$\underline{CH_2}$O and N$\underline{CH_2}$CH fragments, respectively. This assignment was confirmed by the correlation ^1H—^{15}N NMR spectrum. The cross-peaks between the N—$^{15}NO_2$ group and the protons of the N$\underline{CH_2}$O and N$\underline{CH_2}$CH fragments are observed.

According to the data from ^1H NMR spectroscopy (3.92 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −12.3 and 4.9 Hz); 4.24 (dd, 1 H, N$\underline{CH_2}$CH, *J* = −12.3 and 6.74 Hz); 4.70—4.95 (m, 3 H, $OCHCH_2ONO_2$); 5.22 (d, 1 H, NCH_2O, *J* = 6.0 Hz); 5.45 (d, 1 H, NCH_2O, *J* = 6.0 Hz)), isomeric *N*-nitro-5-nitroxymethyloxazolidine was obtained as an admixture (the yield was ~5%) .

To summarize, a general method was proposed for the preparation of *N*-nitrooxazolidines **3** and *N*-nitro-

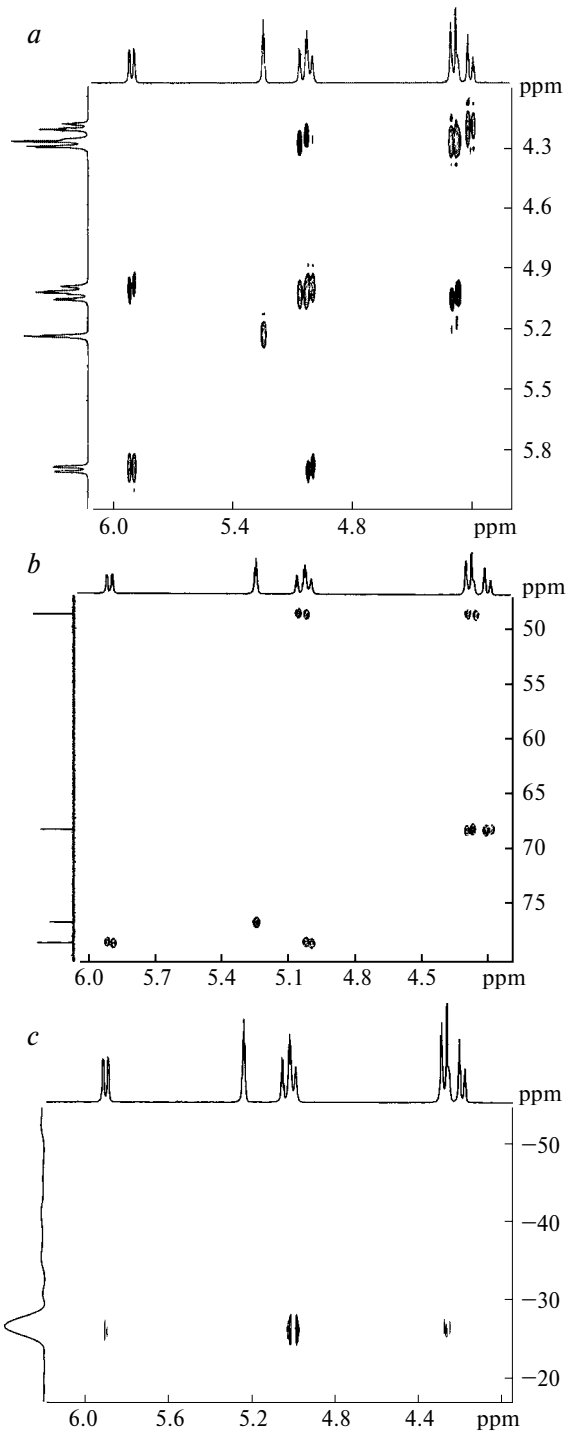


Fig. 1. Correlation NMR spectra of compound **6b**: *a*, $^1H—^1H$ NMR; *b*, $^1H—^{13}C$ NMR; *c*, $^1H—^{15}N$ NMR.

tetrahydro-1,3-oxazines **6** based on hydroxyl-containing *N*-alkylsulfamates.

Experimental

The ^1H NMR spectra were recorded on Bruker WM-250 (250.13 MHz) and Bruker AM-300 (300.13 MHz) spectrometers in $(CD_3)_2CO$ with HMDS as the internal standard. The 2D $^1H—^1H$, $^1H—^{13}C$, and $^1H—^{15}N$ NMR spectra were measured on a Bruker DRX-500 spectrometer. The IR spectra were recorded on a Specord-80 instrument in KBr pellets. The mass spectra were obtained on a MS-3 Kratos spectrometer (EI, 70 eV, the temperature of the ionization chamber was 200 °C, the direct inlet system of the samples).

5-Chloromethyl-*N*-nitrooxazolidine (1b). A 28% CH_2O solution (4.36 g, 44 mmol) was added to a solution of *N*-(3-chloro-2-hydroxypropyl)sulfamate (**2b**) (9.68 g, 43 mmol) in H_2O (40 mL) and the pH of the reaction mixture was brought to 7.95 (with KOH or HCl). Then the mixture was concentrated *in vacuo*. Potassium salt of 5-chloromethyl-*N*-sulfooxazolidine **3b** was obtained in a yield of 10.20 g. Thereupon this salt was used without additional purification.

Compounds **3a,c—e** were obtained analogously.

Compound **3b** (10.20 g) was added to a mixture of 97% HNO_3 (13 mL) and Ac_2O (47 mL) at the temperature from −10 to −7 °C. The reaction mixture was stirred for 1 h, poured into ice water (90 mL), and extracted with AcOEt (3×30 mL). The extract was washed successively with H_2O and a solution of Na_2CO_3 and then concentrated *in vacuo*. 5-Chloromethyl-*N*-nitrooxazolidine (**1b**) was obtained in a yield of 5.83 g (75%). The solution was distilled and the fraction with b.p. 93—94 °C (1.0—1.2 Torr) was collected.

Compounds **1a,c—e** were obtained analogously.

5-Azidomethyl-*N*-nitrooxazolidine (1c). 5-Chloromethyl-*N*-nitrooxazolidine (**1b**) (1 g, 6 mmol) was added to a solution of $CaCl_2$ (1.32 g, 12 mmol) and NaN_3 (0.78 g, 12 mmol) in DMF (10 mL) at 95—100 °C. The reaction mixture was stirred for 5.5 h and poured into H_2O (30 mL). The precipitate that formed was filtered off and the filtrate was extracted with benzene (3×15 mL). The extract was washed with H_2O (7×10 mL) and concentrated. 5-Azidomethyl-*N*-nitrooxazolidine (**1c**) was obtained in a yield of 0.88 g (85%).

***N*-Nitro-5-nitroxytetrahydro-1,3-oxazine (6b).** A 28% CH_2O solution (4.45 g, 49.5 mmol) was added to a solution of potassium *N*-(2,3-dihydroxypropyl)sulfamate (**4b**) (9.40 g, 45 mmol) in H_2O (25 mL). The pH of the reaction mixture was brought to 7.50 (with KOH or HCl) and the mixture was concentrated *in vacuo*. Potassium salt of 5-hydroxy-*N*-sulfotetrahydro-1,3-oxazine (**5b**) was obtained in a yield of 9.95 g. The salt was used without purification.

Sulfamate **5a** was prepared analogously.

Sulfamate **5b** was added to a mixture of 97% HNO_3 (15 mL) and Ac_2O (9.95 g, 56 mL) at the temperature from −10 to −7 °C. The reaction mixture was stirred for 1 h, poured into ice water (100 mL), and extracted with AcOEt (3×30 mL). The extract was washed successively with H_2O and a solution of Na_2CO_3 and then concentrated. Nitro-5-nitroxytetrahydro-1,3-oxazine (**6b**) was obtained in a yield of 3.69 g (42%). The residue was recrystallized from EtOH (18 mL). IR (KBr), ν/cm^{-1}: 1284, 1552 (NNO_2); 1636(ONO_2).

N-Nitrotetrahydro-1,3-oxazine (**6a**) was prepared analogously.

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