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Synthesis of 2-Substituted *N*-Nitrooxazolidines

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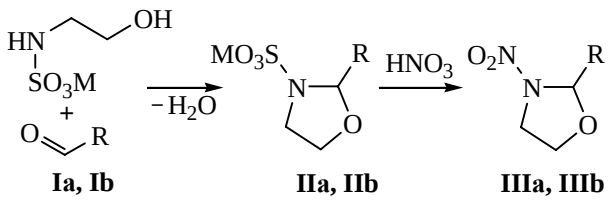
Abstract—A method was developed for preparation of *N*-nitrooxazolidines functionally substituted in position *2* consisting in nitration of reaction products obtained from ***N***-(2-hydroxyethyl)sulfamate and 2-substituted acetaldehydes.

This study is performed in continuation of systematic research on the chemistry and synthetic methods for preparation of *N*-nitrooxazolidines with substituents in various positions [1, 2]. Formerly [1] we demonstrated that the condensation of β-hydroxyalkylsulfamates with formaldehyde afforded N-sulfo derivatives of oxazolidine, and it was established that the governing factor of this reaction was the pH of the medium with an optimum value in the range 7.7–8.2. The subsequent nitration of oxazolidine N-sulfo derivatives furnished respectively *N*-nitrooxazolidine and its 5-substituted homologs. Some compounds of this series are of interest as plasticizers of composite materials [3].

It seemed instructive to extend this approach to the reactions of β-hydroxyalkylsulfamates with other aldehydes. Therefore the target of this study was a development of a rational procedure for preparation of previously unknown 2-substituted *N*-nitrooxazolidines proceeding from the reaction products obtained from sulfamic acid derivatives and 2-substituted aldehydes **I**. By an example of reaction between *N*-(2-hydroxyethyl)sulfamate and chloroacetaldehyde (**Ia)** we found the reaction conditions resulting in the formation of the oxazolidine ring. Similarly to the reaction with formaldehyde here also the governing factor was the pH of the medium with an optimum range 4.0-4.3. The arising compounds **II** prone to hydrolysis were not analyzed but were at once converted by treating with HNO_3 at –35 to –30°C into the corresponding 2-substituted *N*-nitrooxazolidines **III** in overall yields 50-70% (Scheme 1). The formation of the latter products indirectly confirmed the structure of compounds **II**. Compounds **III** obtained were crystalline substances.

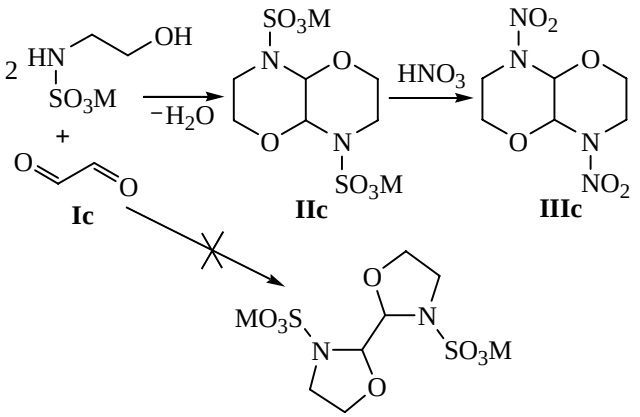
Scheme 1.



R = CH_2Cl (**a**), $CHBg_2$ (**b**), M = K, Na.

It is indicative that the unsubstituted acetaldehyde (R = CH_3) did not enter into the condensation with *N*-(2-hydroxyethyl)sulfamate apparently due to insufficient electrophilicity of the carbonyl group lacking activating electron-acceptor substituents. Unlike that the carbonyl in glyoxal is already sufficiently active for reacting with *N*-(2-hydroxyethyl)sulfamate to furnish finally nitration product **IIIc** in a moderate overall yield (Scheme 2). In keeping with the ^1H NMR spectrum compound **IIIc** was assigned a structure shown on

Scheme 2.



M = K, Na.

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Scheme 2 with a *cis*-junction of two six-membered rings. The signals of two bridging protons appear in the ^{1}H NMR spectrum as a singlet for they are magnetically equivalent and form a degenerate two-spin system A_2. The coupling constants of these protons was measured by the ^{13}C satellites and amounted to 1.5 Hz. For two five-membered rings or six-membered rings with a *trans*-junction the expected value of the coupling constant should have been 7 and 12 Hz respectively according to the angular dependence of the vicinal constants.

Compound **IIIa** was further subjected to modification by nucleophilic substitution of chlorine with the other substituents (Scheme 3). Yields of compounds **IIId** and **IIIe** attained ~90%.

Thus we developed a method for preparation of functionally substituted in position *2 N*-nitrooxazolidines **III** based on the corresponding derivatives of acetaldehydes and *N*-(2-hydroxyethyl)sulfamate.

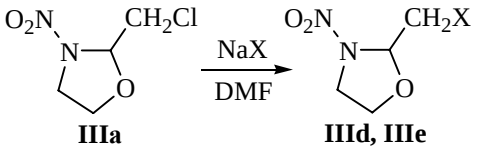
EXPERIMENTAL

^{1}H NMR spectra were registered on spectrometers Bruker AM-300 (300.13 MHz) and Bruker DRX-500 (500.13 MHz) in DMSO-d_6, internal refernce TMS.

2-Chloromethyl-*N*-nitrooxazolidine (IIIa). To a solution of 7 g (39 mmol) of potassium *N*-(2-hydroxyethyl)sulfamate in 23 ml of H_2O was added 8 g of 50% water solution of chloroacetaldehyde. The pH of solution was adjusted to 4.15 (with KOH or HC1), and the mixture was evaporated in a vacuum at 70°C. We obtained 9.20 g of 2-chloromethyl-*N*-sulfooxazolidine potassium salt (**IIa**). To a mixture of 25 ml of 98% HNO_3 and 2.4 ml of $CHC1_3$ in the temperature range from –35 to –30°C was added 9.2 g of compound **IIa**, and the reaction mixture was stirred for 8 min, and then poured into a mixture of 177 ml of ice water and 39 g of KOH. The product was extracted into benzene (4×20 ml). The extract was washed with water and evaporated in a vacuum. The residue was recrystallized from a mixture ether–hexane. Yield 4.28 g (67%), mp 48-49°C, bp 307–108°C (1.3-1.5 mm Hg). ^{1}H NMR spectrum, δ, ppm: 3.75 m (1H, CH_20), 3.92 d (2H, CH_2C1, J 3.7 Hz), 4.20 m (ÇH, NCH_2, CH_2O), 5.67 t (1H, NCH). Found, %: C 28.88; H 4.38; N 17.22. $C_4H_7ClN_2O_3$. Calculated, %: C 28.84; H 4.24; N 16.82.

2-Dibromomethyl-*N*-nitrooxazolidine (IIIb).). To a solution of 1.07 g (6 mmol) of potassium *N*-(2-hydroxyethyl)sulfamate in 10 ml of H_2O was added 7.5 g of 29% water solution of dibromoacetaldehyde. The pH of solution was adjusted to 4.08 (with KOH or HC1), and the mixture

Scheme 3.



IIIa **IIId, IIIe**

X = I (**d**), N_3 (**e**).

was evaporated in a vacuum at 85 °C. We obtained 2.20 g of 2-dibromomethyl-*N*-sulfooxazolidine potassium salt (**IIb**). To 8 ml of 98% HNO_3 in the temperature range from –35 to –30°C was added 2.2 g of compound **IIb**, and the reaction mixture was stirred for 8 min, and then poured into 60 ml of ice water. The precipitated reaction product was filtered off and washed on the filter with water and aqueous sodium carbonate. The precipitate was recrystallized from EtOH. Yield 0.98 g (50%), mp 139-140°C. ^{1}H NMR spectrum, δ, ppm: 3.82 m (1H, CH_2O), 4.22 m (1H, CH_2O), 4.35 m (2H, NCH_2), 5.75 d (1H, NCH), 6.43 m (1H, $CHBr_2$). Found, %: C 16.78; H 2.16; N 9.67. $C_4H\alpha Br_2N_2O_3$. Calculated, %: C 16.57; H 2.09; N 9.66.

4,8-Dinitroperhydro[1,4]oxazino[3,2-*b*][1,4]-oxazine (IIIc). To a solution of 1.79 g (10 mmol) of potassium *N*-(2-hydroxyethyl)sulfamate in 15 ml of H_2O was added 0.94 g of 31% water solution of glyoxal. The pH of solution was adjusted to 4.18 (with KOH or HC1), and the mixture was evaporated in a vacuum at 90°C. We obtained 1.92 g of potassium 4,8-perhydro[1,4]-oxazino[3,2-*b*][1,4]oxazine-4,8-disulfonate (**IIc**). To a mixture of 3 ml of 98% HNO_3 and 9 ml of Ac_2O in the temperature range from –10 to –15°C was added 1.92 g of compound **IIc**, the mixture was stirred for 1 h and then poured into 40 ml of ice water and extracted with EtOAc (3×15 ml). The extract was washed with water and aqueous sodium carbonate, and evaporated in a vacuum. The residue was recrystallized from ethanol. Yield 0.53 g (45%), mp 167–168°C. ^{1}H NMR spectrum, δ, ppm: 3.41 d.d.t (2H, $2CH_2O$, *J* –11.2, 3.7 Hz), 3.82 d.d.t (2H, $2CH_2O$, *J* –11.2, 5.6 Hz), 4.15 m (4H, $2NCH_2$), 5.88 s (2H, 2NCH). Found, %: C 31.08; H 4.34; N 24.04. $C_6HioN_4O_6$. Calculated, %: C 30.78; H 4.30; N 23.93.

2-Iodomethyl-*N*-nitrooxazolidine (IIId). To a solution of 8.1 g (48.6 mmol) of 2-chloromethyl-*N*-nitro-oxazolidine (**IIIa)** in 120 ml of DMF was added 49 g (295.2 mmol) of KI. The mixture was stirred at heating to 85–90°C for 14 h and then poured into 410 ml of water. The precipitated reaction product was filtered off and washed on the filter with water (2×100 ml).The precipitate

was dried to obtain 8.5 g of 2-iodomethyl-*N*- nitrooxazolidine (**IIId).** The mother liquor was extracted with benzene, the extract was washed with water (7×70 ml) and evaporated in a vacuum. The residue was combined with the previously obtained precipitate, and the substance was recrystallized from ether. Yield 10.7 g (85%), mp 75.5–76.5°C. ^{1}H NMR spectrum, δ, ppm: 3.61 d (2H, CH_2I, *J* 3.7 Hz), 3.75 m (1H, CH_2O), 4.10–4.30 m (3H, NCH_2, CH_2O), 5.30 t (1H, NCH). Found, %: C 19.03; H 2.73; N 10.86. $C_4H_7IN_2O_3$. Calculated, %: C 18.62; H 2.73; N 10.86.

2-Azidomethyl-*N*-nitrooxazolidine (IIIe). To a mixture of 4.60 g (41.8 mmol) of $CaC1_2$ and 5.15 g (79.23 mmol) of NaN_3 in 27 ml of DMF was added 6.65 g (39.94 mmol) of 2-chloromethyl-*N*-nitrooxazolidine (**IIIa**). The mixture was stirred at heating to 93–97°C for 10 h and then poured into 45 ml of water and filtered from the separated precipitate. The filtrate was extracted with benzene (5×15 ml). The extract was washed with water (7×10 ml) and evaporated in a vacuum. Yield 6.36 g (92%), mp 8-9°C. ^{1}H NMR spectrum, δ, ppm: 3.65 d.d (2H, CH_2N_3, *J* –18.5, 6.2 Hz), 3.77 m (1H, CH_2O), 4.20 m (3H, NCH_2, CH_2O), 5.60 t (1H, NCH). Found, %: N 40.41. $C_4H_7N_5O_3$. Calculated, %: N 40.45.

REFERENCES

1. Tartakovskii, V.A., Ermakov, A.S., Strelenko, Yu.A., Vinogradov, D.B., and Serkov, S.A., *Izv. Akad. Nauk, Ser. Khim.*, 2001, p. 872.
2. Tartakovskii, V.A., Ermakov, A.S., and Vinogradov, D.B., *Zh. Org. Khim.*, 2002, vol. 38, p. 1394. Tartakovskii, V.A, Ermakov, A.S., Vinogradov, D.B., Varfolomeeva, O.N., Denisyuk, A.L., and Rusin, D.L. , RF Patent 2181719, 2002; *Chem. Abstr.*, 2003, vol. 138, 321273.