Organic Chemistry

Synthesis of 3-alkoxy-2-nitroxypropyl-*N*-alkylnitramines

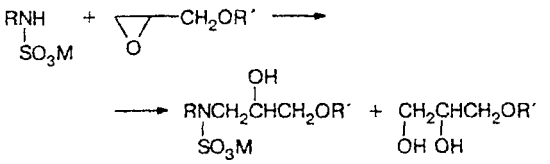
*V. A. Tartakovsky, A. S. Ermakov, and D. B. Vinogradov**

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: 007 (095) 135 5328. E-mail: SECRETARY@ioc.ac.ru

It was shown that 3-alkoxy-2-nitroxypropyl-*N*-alkylnitramines can be prepared by nitration of the corresponding 3-alkoxy-2-hydroxypropyl-*N*-alkylsulfamates.

Key words: *N*-alkylsulfamates; epichlorohydrin; glycidyl ethers; 3-alkoxy-2-hydroxypropyl-*N*-alkylsulfamates; 3-alkoxy-2-nitroxypropyl-*N*-alkylnitramines.

Previously,[1] it has been shown that 3-alkoxy-2-hydroxy-*N*-alkylsulfamates (**1**) can be synthesized by the reaction of *N*-alkylsulfamates with glycidyl ethers in aqueous ethanol.

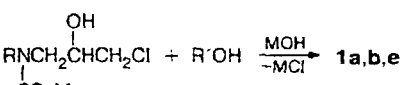


1a—i **2a—i**

M = K, Na
R = Me; R′ = Me (**a**), Et (**b**), Bu (**c**);
R = Et; R′ = Me (**d**), Et (**e**), Bu (**f**);
R = Bu; R′ = Me (**g**), Et (**h**);
R = Hept; R′ = Me (**i**)

To exclude the formation of side products resulting from hydrolysis (**2**), this reaction was studied in anhydrous DMSO (8 h at 110 to 120 °C). However, in this case, it was accompanied by resinification, and the yield of the target product remained the same, *viz.*, ~80%.

To make the preparation of compounds **1** easier, we considered the possibility of the reaction of 3-chloro-2-hydroxy-*N*-alkylsulfamates (**3**) with alcohols in alkaline media; to avoid hydrolysis involving the chlorine atom, anhydrous alcohols were used. In this case, the yields of products **1** reached ~85% (Table 1).



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M = K, Na

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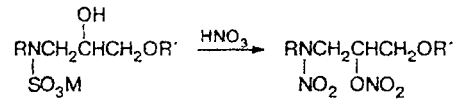
Table 1. Synthesis of 3-alkoxy-2-hydroxy-*N*-alkylsulfamates (**1**)

Compound	Yield (%)	M.p. /°C
1a	85	93—95
1b	80	84—86
1e	77	93—95
1g[a]	60	—[b]
1b[c]	82	84—86

[a] Prepared by the standard procedure.[1] [b] A caramel-like product [c] Prepared in DMSO by a previously described procedure.[1]

Nitration of compounds **1** gave nitramino nitrates (**4**).



1a—i **4a—i**

M = K, Na

As has been reported previously,[2] the sulfamate group can be easily converted into a nitramine group by nitra-

Table 2. Characteristics of 3-alkoxy-2-nitroxypropyl-*N*-alkylnitramines (**4**)

Compound	Yield (%)	n_D^{22}	Molecular formula	Found / Calculated (%)			^{1}H NMR (δ)
				C	H	N	
4a	71	[a]	$C_5H_{11}N_3O_6$	29.17 28.71	5.48 5.78	—	3.35 (s, 3 H, MeO); 3.45(s, 3 H, MeN); 3.70 (m, 2 H, CH_2N) 4.20 (m, 2 H, CH_2O); 5.60 (m, 1 H, $CHONO_2$)
4b	70	1.4780	$C_6H_{13}N_3O_6$	31.95 32.28	5.78 5.87	—	1.15 (t, 3 H, MeC); 3.45 (s, 3 H, MeN); 3.55 (m, 2 H, CH_2O)
4b[b]	75						3.75 (m, 2 H, CH_2N); 4.25 (m, 2 H, CH_2O); 5.60 (m, 1 H, $CHONO_2$)
4c	67	1.4687	$C_8H_{17}N_3O_6$	—	—	16.55 16.80	0.95 (t, 3 H, Me); 1.35 (m, 2 H, CH_2); 1.55 (m, 2 H, CH_2)
4c[b]	55						3.50 (s, 3 H, MeN); 3.70 (t, 2 H, CH_2O); 3.90 (m, 2 H, CH_2N); 4.30 (m, 2 H, CH_2O); 5.55 (m, 1 H, $CHONO_2$)
4d	71	1.4740	$C_6H_{13}N_3O_6$	32.86 32.28	6.14 5.87	—	1.25 (t, 3 H, MeC); 3.45 (s, 3 H, CH_3O); 3.72 (m, 2 H, CH_2N); 3.85 (m, 2 H, CH_2N); 4.15 (m, 2 H, CH_2O); 5.60 (m, 1 H, $CHONO_2$)
4e	68	1.4693	$C_7H_{15}N_3O_6$	35.44 35.44	6.39 6.37	—	1.15 (t, 3 H, Me); 1.25 (t, 3 H, MeC); 3.55 (m, 2 H, CH_2O); 3.70—3.95 (m, 4 H, CH_2NCH_2); 4.15 (m, 2 H, CH_2O); 5.70 (m, 1 H, $CHONO_2$)
4f	67	1.4656	$C_9H_{19}N_3O_6$	—	—	16.29 15.84	1.05 (t, 3 H, MeC); 1.35 (t, 3 H, MeC); 1.50 (m, 2 H, CH_2); 1.70 (m, 2 H, CH_2); 3.60 (m, 2 H, CH_2O); 3.70—3.95 (m, 4 H, CH_2NCH_2); 4.15 (m, 2 H, CH_2O); 5.70 (m, 1 H, $CHONO_2$)
4g[c]	55	1.4707	$C_8H_{17}N_3O_6$	—	—	—	0.95 (t, 3 H, Me); 1.35 (m, 2 H, CH_2); 1.56 (m, 2 H, CH_2); 3.35 (s, 3 H, MeO); 3.70—3.95 (m, 4 H, CH_2NCH_2); 4.15 (m, 2 H, CH_2O); 5.70 (m, H, $CHONO_2$)
4h	69	1.4655	$C_9H_{19}N_3O_6$	41.29 40.75	7.26 7.22		0.95 (t, 3 H, Me); 1.15 (t, 3 H, MeC); 1.35 (m, 2 H, CH_2); 1.65 (m, 2 H, CH_2); 3.50 (m, 2 H, CH_2O); 3.70—3.95 (m, 4 H, CH_2NCH_2); 4.15 (m, 2 H, CH_2O); 5.70 (m, 1 H, $CHONO_2$)
4i	60	1.4665	$C_{11}H_{23}N_3O_6$	45.10 45.04	8.36 7.90	—	0.90 (t, 3 H, MeC); 1.35 (m, 8 H, $(CH_2)_4$); 1.70 (m, 2 H, CH_2); 3.40 (s, 3 H, MeO); 3.70—3.95 (m, 4 H, CH_2NCH_2); 4.15 (m, 2 H, CH_2O); 5.70 (m, 1 H, $CHONO_2$)

[a] M.p. 40—41 °C. [b] Prepared by nitration with an HNO_3—H_2SO_4 mixture. [c] The starting compound was first dissolved in $(MeCO)_2O$, and then HNO_3 was added to the solution.

tion. The nitration of **1b** with a HNO_3—H_2SO_4 mixture gave compound **4b** in a yield of ~75%. However, an increase in the length of the alkoxyl radical (compound **4c**) results in an increase in the rate of nitrolysis, and the yield of the desired compound decreases to 55%. Therefore, a milder nitrating reagent, *viz.*, an HNO_3—$(MeCO)_2O$ mixture, was used. In this case, the proportion of the products of nitrolysis was ≤3%, and the yields of the target products were 60—71%. The resulting compounds **4** were characterized by ^1H NMR spectroscopy and by elemental analysis (Table 2).

Experimental

^1H NMR spectra were recorded on Bruker WM-250 and Bruker AM-300 instruments (250 and 300 MHz) in D_2O, $(CD_3)_2CO$, and $CDCl_3$ using HMDS as the internal standard.

Condensation of potassium *N*-butylsulfamate with 1-methoxy-2,3-epoxypropane (1g). 1-Methoxy-2,3-epoxypropane (2.1 g, 24 mmol) was added to a solution of potassium *N*-butylsulfamate (3.51 g, 18 mmol) in a mixture of 3.37 mL of H_2O and 5.4 mL of EtOH at pH 6.96. The reaction mixture was kept for 30 h at 68—70 °C and concentrated on a rotary evaporator. The residue was extracted with a hot Me_2CO—EtOH mixture (2 : 1) to remove the remaining potassium *N*-butylsulfamate. The extract was concentrated on a rotary evaporator, and the residue was recrystallized from a Me_2CO—EtOH mixture to give 2.90 g of compound **1g**. ^1H NMR, δ: 1.20 (t, 3 H, Me); 1.30 (m, 2 H, CH_2); 1.55 (m, 2 H, CH_2); 3.10 (m, 4 H, CH_2NCH_2); 3.40 (s, 3 H, OCH_3); 3.60 (m, 2 H, CH_2O); 4.00 (m, 1 H, CHOH)

Compounds **1a—f,h,i** were prepared in a similar way. Their ^1H NMR spectra corresponded to those reported in the literature.[1]

Condensation of 2,3-epoxy-1-ethoxypropane with potassium *N*-methylsulfamate in anhydrous DMSO (1b). 2,3-Epoxy-1-ethoxypropane (1.33 g, 13 mmol) was added to a solution of potassium *N*-methylsulfamate (1.5 g, 10 mmol) in 10 mL of anhydrous DMSO. The mixture was stirred for 8 h at 115 °C and concentrated using a rotary evaporator with heating on an oil bath. The residue was washed with ether and extracted with a hot EtOH—Me_2CO mixture to remove the remaining *N*-methylsulfamate. The extract was concentrated on a rotary evaporator, and the residue was recrystallized from a EtOH—Et_2O mixture to give 2.06 g of potassium 3-ethoxypropyl-2-hydroxy-*N*-methylsulfamate (**1b**).

Synthesis of potassium 2-hydroxy-3-methoxypropyl-*N*-methylsulfamate (1a) from potassium 3-chloro-2-hydroxypropyl-*N*-methylsulfamate. Potassium 3-chloro-2-hydroxypropyl-*N*-methylsulfamate (2.41 g, 10 mmol) was added to a solution of KOH (0.56 g, 10 mmol) in 5 mL of anhydrous methanol. The mixture was kept for 14 h at 100 °C, neutralized to pH 7.0, and concentrated on a rotary evaporator. The residue was extracted with a hot EtOH—Me_2CO mixture, and the extract was concentrated on a rotary evaporator to give 1.66 g of potassium 2-hydroxy-3-methoxypropyl-*N*-methylsulfamate (**1a**). Compounds **1b,e** were prepared in a similar way.

3-Ethoxypropyl-2-nitroxy-*N*-methylnitramine (4b). Concentrated H_2SO_4 (1.3 mL) was added at −10 °C to fuming HNO_3 (6.5 mL), and then, at −13 to −17 °C, potassium 3-ethoxypropyl-2-hydroxy-*N*-methylsulfamate (1.00 g) was gradually added. The mixture was stirred at −13 to −17 °C for an additional 35 min and poured into a mixture of water and ice, and the product was extracted with MeCOOEt (3×10 mL). The extract was washed with a solution of sodium carbonate to pH ≈ 11 and then with water, and concentrated on a rotary evaporator to give 0.65 g of product **4b**. Compound **4c** was prepared in a similar way.

3-Methoxy-2-nitroxypropyl-*N*-methylnitramine (4a). Fuming HNO_3 (2.78 mL) was gradually added to $(MeCO)_2O$ (9.72 mL) at 0—6 °C. To the resulting solution, potassium 2-hydroxy-3-methoxypropyl-*N*-methylsulfamate (2.00 g) was gradually added at the same temperature; the mixture was stirred for 1 h at 0—8 °C and poured into a mixture of water and ice, and the product was extracted with MeCOOEt (3×13 mL). The extract was washed with a solution of sodium carbonate to pH ≈ 11, and then with water, and concentrated on a rotary evaporator to give 1.25 g of 3-methoxy-2-nitroxypropyl-*N*-methylnitramine (**4a**). Compounds **4b—i** were prepared in a similar way.

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