The reaction of sulfamic acid derivatives with epoxides
5.* Reactions of sulfamates with diglycidyl and allylglycidyl ethers and synthesis of the corresponding aminoethers

A. S. Ermakov, P. V. Bulatov, and V. A. Tartakovsky*

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

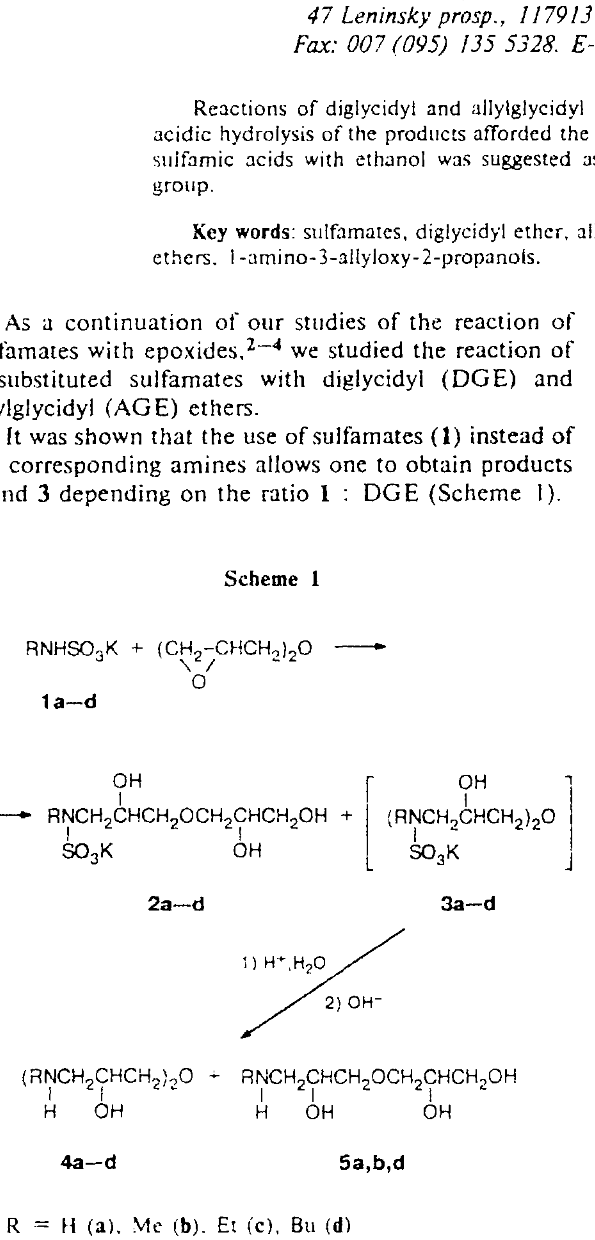
Reactions of diglycidyl and allylglycidyl ethers with salts of sulfamic acid followed by acidic hydrolysis of the products afforded the corresponding aminoethers. The alcoholysis of sulfamic acids with ethanol was suggested as a method for mild elimination of the sulfo group.

Key words: sulfamates, diglycidyl ether, allylglycidyl ether, di(3-amino-2-hydroxypropyl) ethers, 1-amino-3-allyloxy-2-propanols.

As a continuation of our studies of the reaction of sulfamates with epoxides,[2—4] we studied the reaction of *N*-substituted sulfamates with diglycidyl (DGE) and allylglycidyl (AGE) ethers.

It was shown that the use of sulfamates (**1**) instead of the corresponding amines allows one to obtain products **2** and **3** depending on the ratio **1** : DGE (Scheme 1).

Scheme 1



R = H (**a**), Me (**b**), Et (**c**), Bu (**d**)

The reaction in an aqueous medium at a **1** : DGE ratio of (2.5—3) : 1 afforded products **3** that were then hydrolyzed with an aqueous solution of H_2SO_4 without isolation. We failed to isolate disulfamates **3** in pure forms because monosulfamates **2** (10—20%) formed as admixtures that were difficult to separate. A mixture of di- and monoamines obtained after alkaline treatment was extracted with ether to give diaminoethers **4** in high yields (up to 82% with respect to DGE) and monoaminoethers **5** (10—20%) and 3-aminopropane-1,2-diols. Using a **1** : DGE ratio of ~1 : 1, sulfamates **2** were obtained; similar treatment of these afforded the corresponding amines **5**.

Only one diaminoether, **4a**, obtained by the reduction of the corresponding dinitrile, is known as yet.[5] It is obvious that this method cannot afford diamines **4** if R = Alk. The direct synthesis from the corresponding primary amine or ammonium and DGE should lead to the formation of a polymeric product since disubstitution is possible both for amine and DGE. The use of sulfamates, where one H atom at the nitrogen is replaced by a sulfo group, allows one to preclude polymerization.

The reactions of sulfamates **1** with AGE proceeded in a similar way (Scheme 2).

Amines **7** obtained according to Scheme 2 have previously been considered as components for polymeric compositions[6,7] and intermediates in syntheses of pharmacological preparations.[8] The known synthetic method[9,10] through the reaction of a corresponding primary amine with AGE is accompanied by side reactions of complete alkylation of the amino group, which decreases the yield of the target amine. The method suggested by us allows one to obtain products **6** in up to 90 % yields. We found that, along with partial deetherification, hydration of the double bond takes place during

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*For Part 4, see Ref. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 3, pp. 508—511, March, 1997.

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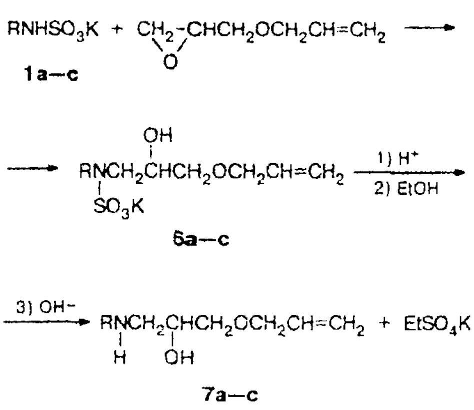
Scheme 2



R = H (**a**), Me (**b**), Et (**c**)

acidic hydrolysis. To get rid of such side reactions, we suggested another method for elimination of the sulfo group, *i.e.*, alcoholysis of the corresponding *N*-substituted sulfamine acid. Earlier[11] a similar reaction was considered as a method for sulfonation of alcohols. The method proposed by us for the removal of the sulfamate protection allows one to obtain amines **7** from products **6** in up to 90 % yields.

The characteristics of the products obtained are given in Tables 1, 2, and 3.

Experimental

^{1}H NMR spectra were recorded on a Bruker WH-250 spectrometer (250.13 MHz) in D_2O.

Di(3-amino-2-hydroxypropyl) ether (4a). A solution of potassium sulfamate (13.5 g, 0.1 mol) and DGE (4.4 g, 34 mmol) in H_2O (15 mL) was heated at 70 °C for 15 h. Then H_2O (35 mL) and 95 % H_2SO_4 (30 g) were added, and the mixture was heated at 100 °C for 5 h. The reaction mixture was then cooled, and an alkaline solution was added to pH 12.2. The mixture was concentrated, the residue was extracted with ethanol (60 mL), and the extract was concentrated. The residue was extracted with an ethanol—ether mixture (50 : 50), and the extract was concentrated to afford 4.5 g (81 %) of diamine **4a**, n_D^{20} = 1.5009.

Compounds **4b—d** were prepared by a similar procedure, except that pure ether was used for the extraction at the last step.

Potassium *N*-ethyl-*N*-[3-(2,3-dihydroxypropoxy)-2-hydroxypropyl]sulfamate (2c). A solution of potassium ethylsulfamate (12.5 g, 76 mmol) and DGE (14.3 g, 0.11 mol) in water (20 mL) was heated for 20 h at 70 °C. Then the mixture was evaporated, and the residue was dissolved in methanol and treated with ether. The residue was washed in acetone to yield 18.5 g (78.4 %) of hygroscopic **2c**.

Compounds **2a**, **2b**, and **2d** were prepared by similar procedures.

1-Butylamino-3-(2,3-dihydroxypropoxy)-2-propanol (5d). H_2SO_4 (95 % solution, 1.35 g) was added to a solution of **2d** (1.11 g, 3.3 mmol) in H_2O (4 mL), and the mixture was heated for 5 h at 100 °C. The mixture was then cooled, and an alkali solution was added to the mixture to pH 12.5. The solution was concentrated, and the residue was extracted with ethanol (10 mL). Ether (15 mL) was added to the extract, inorganic salts were filtered off, and the filtrate was evaporated to yield 0.58 g (80.1 %) of **5d**, n_D = 1.4847.

Potassium *N*-methyl-*N*-(3-allyloxy-2-hydroxypropyl)sulfamate (6b). A solution of potassium methylsulfamate (1.49 g, 10 mmol) and AGE (1.6 g, 14 mmol) in H_2O (8 mL) and ethanol (3 mL) was heated at 70 °C for 20 h. The reaction mixture was concentrated, the residue was extracted with boiling methanol (2×5 mL), and ether (10 mL) was added to

Table 1. Characteristics of di(3-amino-2-hydroxypropyl) ethers **4**

Compound	Yield (%)*	M.p./°C	Found/Calculated (%) C	H	N	Molecular formula	^{1}H NMR, δ
4a	81	—	—	—	—	$C_6H_{16}N_2O_3$	2.61—2.84 (m, 4 H, CH_2N), 3.50—3.76 (m, 4 H, CH_2O), 3.81—3.91 (m, 2 H, CHO)
4b	61.5	58—59	—	—	10.45 10.56	$C_8H_{20}N_2O_3 \cdot 2HCl$	2.28 (s, 6 H, CH_3N), 2.46—2.60 (m, 4 H, CH_2N), 3.40—3.65(m, 4 H, CH_2O), 3.85—3.95 (m, 2 H,CHO)
4c	54	67—69	—	—	10.78 10.91	$C_{10}H_{24}N_2O_3 \cdot 2HCl$	1.02—1.09 (t, 6 H, Me), 2.52—2.74 (m, 8 H, CH_2N), 3.40—3.65 (m, 4 H, CH_2O), 3.87—4.00 (m, 2 H, CHO)
4d	30.5	37—38	48.03 48.98	9.97 9.98	8.19 8.16	$C_{14}H_{32}N_2O_3 \cdot 2HCl$	0.88—0.98 (t, 6 H, Me), 1.31—1.47 (m, 4 H, CH_2), 1.60—1.75 (t, 4 H, CH_2), 3.03—3.28 (m, 8 H, CH_2N), 3.52—3.77 (m, 4 H, CH_2O), 4.08—4.20 (m, 2 H, CHO)**

* With respect to DGE. ** For dihydrochloride.

Table 2. Characteristics of potassium *N*-[3-(2,3-dihydroxypropoxy)-2-hydroxypropyl]sulfamates and (3-amino-2-hydroxypropyl)-2,3-dihydroxypropyl ethers (**5**)

Compound	Yield (%)	M. p./°C	n_D^{18}	Found Calculated (%)			Molecular formula	^{1}H NMR, δ
				C	H	N		
5a	64	—	1.5055	44.12 43.63	8.99 9.15	—	$C_6H_{15}NO_4$	2.48—2.77 (m, 2 H, CH_2N), 3.36—3.65 (m, 6 H, CH_2O), 3.95 (m, 2 H, CHO)
2b	80	70	—	—	—	4.63 4.71	$C_7H_{16}KNO_7S$	2.73 (s, 3 H, CH_3N), 2.95—3.10 (m, 2 H, CH_2N), 3.50—3.75 (m, 6 H, CH_2O), 3.95—4.10 (m, 2 H, CHO)
5b	80.8	—	1.4814	—	—	—	$C_7H_{17}NO_4$	2.30 (s, 3 H, CH_3N), 2.52—2.63 (m, 2 H, CH_2N), 3.38—3.72 (m, 6 H, CH_2O), 3.70—4.08 (m, 2 H, CHO)
2c	78.4	Hygroscopic	—	—	—	—	$C_8H_{18}KNO_7S$	1.00—1.32 (t, 3 H, Me), 2.95—3.25 (m, 4 H, CH_2N), 3.50—3.86 (m, 6 H, CH_2O), 3.94—4.08 (m, 2 H, CHO)
2d	86.7	Hygroscopic	—	—	—	—	$C_{10}H_{22}KNO_7S$	0.87—0.96 (t, 3 H, Me), 1.22—1.40 (q, 2 H, CH_2), 1.51—1.64 (q, 2 H, CH_2), 2.98—3.19 (m, 4 H, CH_2N), 3.44—3.73 (m, 6 H, CH_2O), 3.86—3.97 (m, H, CHO), 3.98—4.11 (m, H, CHO)
5d	79.5	—	1.4817	—	—	6.20 6.33	$C_{10}H_{23}NO_4$	0.82—0.94 (t, 3 H, Me), 1.19—1.35 (q, 2 H, CH_2), 1.35—1.53 (q, 2 H, CH_2), 2.47—2.73 (m, 4 H, CH_2N), 3.41—3.69 (m, 6 H, CH_2O), 3.77—4.05 (m, 2 H, CHO)

Table 3.. Characteristics of potassium *N*-(3-allyloxy-2-hydroxypropyl)sulfamates (**6**) and 1-amino-3-allyloxy-2-propanols (**7**)

Compound	Yield (%)	M. p./°C B. p./°C	n_D^{18}	Found Calculated (%)			Molecular formula	^{1}H NMR, δ
		(*p*/Torr)		C	H	N		
6a	90	75—77	—	5.61 5.62	—	—	$C_6H_{12}KNO_5S$	3.01—3.22 (m, 2 H, CH_2N), 3.53—3.78 (m, 2 H, CH_2O), 4.00—4.13 (m, 1 H, CHO), 4.11—4.29 (d, 2 H, CH_2O), 5.32—5.52 (dd, 2 H, CH_2=), 5.97—6.14 (m, 1 H, CH=)
7a	70.9	—	1.4778	—	—	—	$C_6H_{13}NO_2$	2.74—2.97 (m, 2 H, CH_2N), 3.62—3.82 (m, 2 H, CH_2O), 3.93—4.06 (m, 1 H, CHO), 4.21—4.32 (d, 2 H, CH_2O), 5.41—5.61 (dd, 2 H, CH_2=), 6.06—6.28 (m, 1 H, CH=)
6b	73	57—59	—	—	—	5.24 5.31	$C_7H_{14}KNO_5S$	2.69 (s, 3 H, MeN), 2.90—3.09 (m, 2 H, CH_2N), 3.41—3.66 (m, 2 H, CH_2O), 3.96—4.05 (m, 1 H, CHO), 4.00—4.11 (d, 2 H, CH_2O), 5.21—5.39 (dd, 2 H, CH_2=), 5.84—6.04 (m, 1 H, CH=)

(*to be continued*)

Table 3. (*continued*)

Compound	Yield (%)	M. p./°C B. p./°C (*p*/Torr)	n_D^{18}	Found / Calculated (%)			Molecular formula	^{1}H NMR, δ
				C	H	N		
7b	76.8	—	1.4710	—	—	—	$C_7H_{15}NO_2$	2.32 (s, 3 H, MeN), 2.54—2.62 (m, 2 H, CH_2N), 3.42—3.61 (m, 2 H, CH_2O), 3.87—4.02 (m, 1 H, CHO), 4.04—4.13 (d, 2 H, CH_2O), 5.24—5.41 (dd, 2 H, CH_2=), 5.87—6.07 (m, 1 H, CH=)
6c	76.2	67—68	—	—	—	4.91 5.05	$C_8H_{16}KNO_5S$	1.12—1.22 (t, 3 H, Me), 2.96—3.28 (m, 4 H, CH_2N), 3.46—3.72 (m, 2 H, CH_2O), 4.00—4.10 (m, 1 H, CHO), 4.07—4.18 (d, 2 H, CH_2O), 5.26—5.43 (dd, 2 H, CH_2=), 5.90—6.10 (m, 1 H, CH=)
7c	84.1	106—107 (11)	1.4587	60.38 60.35	11.03 10.76	—	$C_8H_{17}NO_2$	1.02—1.11 (t, 3 H, Me), 2.52—2.70 (m, 4 H, CH_2N), 3.42—3.59 (m, 2 H, CH_2O), 3.88—3.97 (m, 1 H, CHO), 4.03—4.10 (d, 2 H, CH_2O), 5.22—5.39 (dd, 2 H, CH_2=), 5.86—6.03 (m, 1 H, CH=)

the extract. The precipitate formed was washed with ether, and the residual ether was removed to give 1.92 g (73 %) of **6b**, m.p. 57 —59 °C.

Compounds **6a,c** were prepared by a similar procedure.

1-Ethylamino-3-allyloxy-2-propanol (7c). Concentrated HCl was added to a solution of **6c** (2.77 g, 10 mmol) in H_2O (3 mL) to pH < 1. The solvent was evaporated, the residue was extracted with ethanol (10 mL), and the extract was evaporated to remove the residual HCl. The resulting *N*-ethyl-*N*-(3-allyloxy-2-hydroxypropyl)sulfamic acid was dissolved in ethanol (10 mL) and refluxed for 12 h. Then KOH (1 g) was added, and the solution was concentrated. The residue was extracted with ether (2×10 mL), and the combined extracts were evaporated to yield 1.34 g (84.3 %) of **7c**, n_D^{20} = 1.4587.

Amines **7a,b** were prepared by a similar procedure.

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Received July 8, 1996
in revised form February 19, 1997