Organic Chemistry

The reaction of sulfamic acid derivatives with epoxides
2.* Condensation of sulfamic acids with glycidol, epichlorohydrin and epoxy ethers

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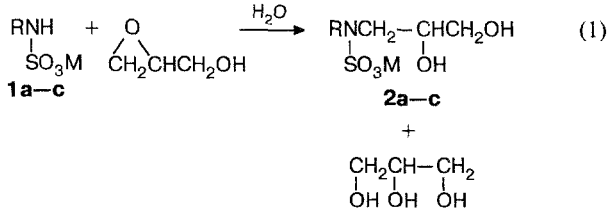
The reaction of the salts of sulfamic acid and *N*-alkylsulfamic acids with glycidol, epichlorohydrin, and epoxy ethers gives the corresponding functionally substituted β-hydroxyalkylsulfamates.

Key words: *N*-alkylsulfamates; glycidol, epichlorohydrin, epoxy ethers; β-hydroxyalkylsulfamates.

Previously[1] we have shown that it is possible to synthesize β-hydroxyalkylsulfamates by the interaction of sulfamic acid derivatives (**1**) with epoxides. In a continuation of these studies, we devoted the present work to the investigation of the condensation of compounds **1** with functionally substituted aliphatic epoxides, such as glycidol, epichlorohydrine, and epoxy ethers.



(1)

The reaction of salts **1a—c** with glycidol was carried out for 10—30 h at 60—80 °C in an aqueous medium.

The yields of the salts of *N*-(1,2-dihydroxypropyl)-*N*-alkylamidosulfoacids (**2a—c**) reached 78—90 % (Table 1). The factors particularly affecting the yield of the reaction products are the pH of the medium and the temperature, whereas varying M in salts **1**, that is, replacing K by Na, Li, or NH_4, changes the rate of the process and its results only insignificantly. The optimum results were obtained at pH ~7. Both in acid and alkaline media the fraction of the side reaction of glycidol with water, which gives rise to glycerol, increases.

Decreasing the reaction temperature (<60 °C) did not diminish the yield of the target product but significantly increased the duration of the synthesis, whereas at temperatures ≥80 °C the target product was significantly contaminated by glycerol.

* For communication 1 see Ref. 1.

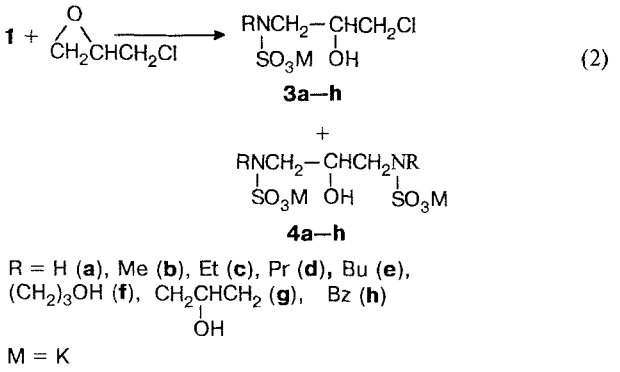
Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 6, pp. 1063—1065, June, 1994.

1066-5285/94/4306-0999 $12.50

Table 1. Parameters of the compounds synthesized

Compound	Yield (%)	M.p./°C	^{1}H NMR (D_2O), δ	Molecular formula	Found / Calculated (%)		
					C	H	N
2a	78	114—117	2.87 (m, 2 H, NCH_2); 3.70 ((m, 2 H, CH_2OH); 4.05 (m, 1 H, CHOH)	$C_3H_8KNO_5S$	17.52 17.23	4.07 3.85	6.62 6.69
2b	90	115—118	2.60 (s, 3 H, Me); 2.86 (m, 2 H, NCH_2); 3.72 (m, 2 H, CH_2OH); 4.05 (m, 1 H, CHOH)	$C_4H_{10}KNO_5S$	21.64 21.51	4.36 4.51	—
2c	85	108—111	1.20 (t, 3 H, Et); 3.00 (m, 4 H, CH_2N); 3.68 (m, 2 H, CH_2OH); 4.02 (m, 1 H, CHOH)	$C_5H_{12}KNO_5S$	25.04	5.31	
3a	82	154—156	3.01 (m, 2 H, NCH_2); 3.81 (m, 2 H, CH_2Cl); 4.05 (m, 1 H, CHOH)	$C_3H_7KNO_4SCl$	16.30 15.83	3.32 3.10	5.98 6.15
3b	94	150—152	2.71 (s, 3 H, Me)	$C_4H_9KNO_4SCl$	19.38 19.86	4.16 3.75	5.39 5.79
3c	90	148—150	1.12 (t, 3 H, Me); 2.84 (q, 2 H, CH_2N); 3.02 (m, 2 H, NCH_2); 3.80 (m, 2 H,CH_2OH; 4.02 (m, 1 H, CHOH)	$C_5H_{11}KNO_4SCl$	23.17 23.48	4.57 4.34	
3d	83	146—148	1.0—1.4 (m, 5 H, Pr); 2.84 (m, 2 H, CH_2N); 3.00 (m, 2 H, NCH_2); 3.80 (m, 2 H, CH_2Cl); 4.05 (m, 1 H, CHOH)	$C_6H_{13}KNO_4SCl$	26.64 26.71	5.22 4.86	—
3e	76	144—146	0.8—1.5 (m, 7 H, Bu); 3.01 (m, 4 H, 2 CH_2N); 3.75 (m, 2 H, CH_2Cl); 4.0 (m, 1 H, CHOH)	$C_7H_{15}KNO_4SCl$	29.66 29.52	5.37 5.66	
3f	64	155—157	1.85 (m, 2 H, CH_2CH_2N); 2.88 (t, 2 H, NCH_2); 3.02 (m, 2 H, NCH_2); 3.68 (t, 2 H, CH_2OH); 3.84 (m, 2 H, CH_2Cl); 4.04 (m, 1 H, CHOH)	$C_6H_{13}KNO_5SCl$	25.47 25.22	4.59 5.18	
3g	45	Glassy solid	1.18 (d, 3 H, Me); 3.00 (m, 4 H, 2 CH_2N); 3.84 (m, 2 H, CH_2Cl); 4.00 (m, 2 H, 2 CHOH)	$C_6H_{12}KNO_5SCl$	—	—	—
3h	45	Glassy solid	3.00 (m, 4 H, 2 NCH_2); 3.86 (m, 2 H, CH_2Cl); 4.06 (m, 1 H, CHOH); 6.50—7.05 (m, 5 H, Ph)	$C_{10}H_{13}KNO_4SCl$	37.43 37.80	4.50 4.13	—
5a	71	Glassy solid	3.02 (m, 2 H, NCH_2); 3.38 (s, 3 H, Me); 3.78 (m, 2 H, CH_2O); 4.00 (m, 1 H, CHOH)	$C_4H_{10}KNO_5S$	—	—	—
5b	92	93—95	2.72 (s, 3 H, Me); 3.37 (s, 3 H, MeO); 3.76 (m, 2 H, CH_2O); 4.02 (m, 1 H, CHOH)	$C_5H_{12}KNO_5S$	25.67 25.31	5.46 5.10	
5c	80	102—104	—	$C_6H_{14}KNO_5S$	28.67 28.67	5.56 5.61	—
5d	78	Glassy solid	1.16 (t, 3 H, Me); 3.06 (m, 2 H, NCH_2); 3.70 (m, 4 H, $CH_2OCH_2CH_3$); 4.05 (m, 1 H, CHOH)	$C_5H_{12}KNO_5S$	31.27 31.68	5.98 6.08	—
5e	85	84—86	1.15 (t, 3 H, Me); 2.68 (s, 3 H, MeN); 2.92 (m, 2 H, NCH_2); 3.60 (m, 4 H, 2 OCH_2); 4.02 (m, 2 H, CHOH)	$C_6H_{14}KNO_5S$	—	—	—
5f	81	93—95	1.20 (m, 6 H, 2 Me); 3.00 (m, 4 H, 2 CH_2N); 3.65 (m, 4 H, 2 OCH_2); 4.02 (m, 1 H, CHOH)	$C_7H_{16}KNO_5S$	31.40 31.68	6.42 6.08	
5h	45	Glassy solid	1.15 (t, 3 H, Me); 3.00 (m, 4 H, 2 NCH_2); 3.70 (m, 6 H, CH_2OH, 2 OCH_2); 4.00 (m, 1 H, CH_2OH)	$C_7H_{16}KNO_6S$	30.36 29.89	6.19 5.73	
5i	60	Glassy solid	1.15 (t, 3 H, Me); 1.80 (m, 2 H, CCH_2C); 3.00 (m, 4 H, 2 CH_2N); 3.65 (m, 6 H, CH_2OH, 2 OCH_2); 4.04 (m, 1 H, CHOH)	$C_8H_{18}KNO_6S$	—	—	—
5g	65	Glassy solid	0.8—1.5 (m, 10 H, Bu); 3.0 (m, 4 H, 2 CH_2N); 3.65 (m, 4 H, 2 CH_2O); 4.02 (m, 1 H, CHOH)	$C_9H_{20}KNO_5S$	—	—	—
5j	32	Glassy solid	0.8—1.5 (m, 7 H, Pr); 3.00 (m, 2 H, CH_2N,); 3.65 (m, 4 H, 2 CH_2O); 4.00 (m, 1 H, CHOH)	$C_7H_{16}KNO_5S$	—	—	—
5k	60	Glassy solid	—	$C_9H_{20}KNO_5S$	37.34 36.84	7.13 6.87	—

Salts **1** react with epichlorohydrin in a similar way.



(2)

3a—h

4a—h

R = H (**a**), Me (**b**), Et (**c**), Pr (**d**), Bu (**e**), $(CH_2)_3OH$ (**f**), CH_2CHCH_2 (**g**), Bz (**h**)

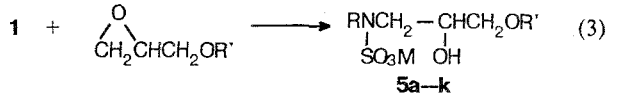
M = K

The yields of the potassium salts of *N*-(1-chloro-2-hydroxypropyl)-*N*-alkylamidosulfoacids (**3a—c**) were 45—90 %.

The basic difference beetween reaction (2) and (1) is the formation of a small amount (~5 %) of disubstituted products (**4**), probably due to the replacement of the chlorine atom in compound **3** by a sulfamate group. For example, the reaction of compound **3b** with potassium *N*-methylsulfamate in an aqueous medium at 100 °C results in dipotassium 4-hydroxy-2,6-diaza-2,6-heptanedisulfonate (**4b**) in 15—20 % yield.

The hydrogen chloride formed in the reaction enables the formation of free sulfamic acids. This inhibits the main reaction and results in the formation of sulfoesters.

The reaction of salts **1** with epoxy ethers was carried out in an aqueous—alcoholic medium.



(3)

5a—k

R' = Me, R = H (**a**), Me (**b**), Et (**c**);
R' = Et, R = H (**d**), Me (**e**), Et (**f**), Bu (**g**), $HO(CH_2)_2$ (**h**), $HO(CH_2)_3$ (**i**)
R' = Bu, R = (**j**), Et (**k**) M = K

It was found that increasing the size of the radical R' in the molecules of epoxy ethers decreases the yields of the salts of *N*-(1-alkoxy-2-hydroxypropyl)-*N*-alkylamidosulfoacids (**5a—k**). This result is explained both by the effect of the steric factor and by the increase in the volume of the solvent required for the complete dissolution of the starting reagents, which, in turn, facilitates side reactions of the solvent with the epoxides.

Experimental

^1H NMR spectra were recorded in D_2O on a Tesla BS-467 spectrometer, working frequency 60 MHz, using $SiMe_4$ as the internal standard.

Condensation of potassium *N*-methylsulfamate with glycidol. Potassium *N*-methylsulfamate (2.98 g, 0.02 mol) was added to a solution of glycidol (1.52 g, 0.0205 mol) in water (6 mL), and the mixture was stirred for 12 h at 70 °C. The reaction mixture was concentrated in a rotary evaporator. The residue was recrystallized from methanol to give 4.01 g of potassium *N*-(1,2-dihydroxypropyl)-*N*-methylamidosulfonate.

Compounds 2a,c, 3a—h, and 5a—k were obtained in the same way as compound **2b**. The yields and properties of the compounds synthesized are presented in Table 1.

^1H NMR spectrum of compound **4a**: 2.71 (s, 6 H, Me); 2.94 (m, 4 H, NCH_2, CH_2N); 4.02 (m, 1 H, C<u>H</u>OH).

References

1. V. A. Tartakovskii, A. S. Ermakov, and N. V. Sigai, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 114 [*Russ. Chem. Bull.*, 1993, **42**, 1104 (Engl. Transl.)].

Received October 21, 1993;
in revised form January 17, 1994