Organic Chemistry

Synthesis of *N*-3-chloroalkoxy-2-nitroxypropyl-*N*-alkylnitramines and their subsequent azidation

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Nitration of *N*-3-chloroalkoxy-2-hydroxypropyl-*N*-alkylsulfamates gave the corresponding *N*-3-chloroalkoxy-2-nitroxypropyl-*N*-alkylnitramines. Azidation of the latter resulted in *N*-azido-3-azidoalkoxypropyl-*N*-alkylnitramines.

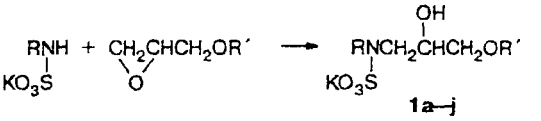
Key words: *N*-alkylsulfamates, glycidic ethers, *N*-3-chloro(or -3-azido)alkoxy-2-hydroxypropyl-*N*-alkylsulfamates, *N*-3-chloro(or -3-azido)alkoxy-2-nitroxypropyl-*N*-alkylnitramines.

N-3-Chloroalkoxy-2-hydroxypropyl-*N*-alkylsulfamates are valuable starting compounds for the synthesis of plasticizers containing nitramino, azido, and nitrate groups, as well as for obtaining various aminoalcohols.

The possibility of addition of sulfamic acid derivatives to epoxides to give *N*-2-hydroxyalkyl-*N*-alkylsulfamates has been shown previously.[1,2] In the present work, a similar procedure was used for the synthesis of *N*-3-chloroalkoxy-2-hydroxypropyl-*N*-alkylsulfamates (**1a—j**) (Scheme 1). 3-Chloroalkylglycidic ethers were synthesized according to the standard procedure[3] and were used in the subsequent reaction without purification. Compounds **1a—j** were characterized by elemental analyses and ^{1}H NMR spectroscopic data (Table 1).

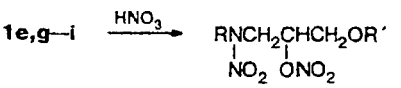
As noted previously,[4] nitration easily transforms *N*-alkylsulfamates to *N*-alkylnitramines. The use of an HNO_3—H_2SO_4 nitrating mixture results in partial nitrolysis of the ether group.[2] For this reason, compounds **1e,g—j** were nitrated with an HNO_3—Ac_2O mixture at 0—7 °C (Scheme 2). The resulting *N*-alkylnitramines were characterized by elemental analyses and ^{1}H NMR spectroscopic data (Table 2).

Scheme 1



1a: R = H, R′ = $(CH_2)_2Cl$; **1b:** R = H, R′ = $(CH_2)_3Cl$; **1c:** R = H, R′ = $CH(CH_2Cl)_2$; **1d:** R = H, R′ = $CH_2CH(Cl)CH_2Cl$; **1e:** R = Me, R′ = $(CH_2)_2Cl$; **1f:** R = Me, R′ = $(CH_2)_3Cl$; **1g:** R = Me, R′ = $CH(CH_2Cl)_2$; **1h:** R = Me, R′ = $CH_2CH(Cl)CH_2Cl$; **1i:** R = Et, R′ = $(CH_2)_2Cl$; **1j:** R = Et, R′ = $(CH_2)_3Cl$

Scheme 2



2a—d

2a: R = Me, R′ = $CH_2CH(Cl)CH_2Cl$; **2b:** R = Me, R′ = $(CH_2)_2Cl$; **2c:** R = Me, R′ = $CH(CH_2Cl)_2$; **2d:** R = Et, R′ = $(CH_2)_2Cl$

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 673—676, April, 1998.

1066-5285/98/4704-0652 $20.00

Table 1. Elemental analysis and ^{1}H NMR spectroscopic data for *N*-3-chloroalkoxy-2-hydroxypropyl-*N*-alkylsulfamates

Compound	Yield (%)	Found / Calculated (%) C	H	N	Molecular formula	^{1}H NMR, δ
1a	57	22.09 / 22.10	4.27 / 4.08	5.17 / 5.15	$C_5H_{11}ClKNO_5S$	3.00—3.40 (m, 2 H, NCH_2); 3.50—4.00 (m, 6 H, $CH_2OCH_2CH_2Cl$); 4.20 (m, 1 H, CHOH)
1b	57			4.81 / 4.90	$C_6H_{13}ClKNO_5S$	2.05 (m, 2 H, CCH_2C); 3.00 (m, 2 H, NCH_2); 3.40—3.60 (m, 4 H, CH_2OCH_2); 3.70 (t, 2 H, CH_2Cl); 4.00 (m, 1 H, CHOH)
1c	53			4.37 / 4.37	$C_6H_{12}Cl_2KNO_5S$	3.00—3.30 (m, 2 H, NCH_2); 3.60—4.10 (m, 6 H, CH_2O, 2 CH_2Cl); 4.05 (m, 2 H, CHOH, $OCH(CH_2Cl)_2$)
1d	50	23.07 / 22.50	3.91 / 3.78		$C_6H_{12}Cl_2KNO_5S$	2.90—3.20 (m, 2 H, NCH_2); 3.62 (m, 2 H, $HOCHCH_2O$); 3.80—4.00 (m, 4 H, OCH_2CHCl, CH_2Cl); 4.10 (m, 1 H, CHOH); 4.40 (m, 1 H, CHCl)
1e	85	25.58 / 25.22	4.66 / 4.59		$C_6H_{13}ClKNO_5S$	2.72 (s, 3 H, MeN); 3.05 (d, 2 H, NCH_2); 3.62 (m, 2 H, $HOCHCH_2O$); 3.70—3.90 (m, 4 H, OCH_2CH_2Cl); 4.05 (m, 1 H, CHOH)
1f*	63	27.85 / 28.04	4.98 / 5.04		$C_7H_{15}ClKNO_5S$	2.00 (m, 2 H, CCH_2C); 2.67 (s, 3 H, MeN); 2.95 (d, 2 H, NCH_2); 3.50 (m, 2 H, $HOCHCH_2O$); 3.55—3.70 (m, 2 H, OCH_2, CH_2Cl); 3.95 (m, 1 H, CHOH)
1g**	90	25.51 / 25.15	4.44 / 4.22		$C_7H_{14}Cl_2KNO_5S$	2.73 (s, 3 H, MeN); 3.05 (d, 2 H, NCH_2); 3.60—3.90 (m, 6 H, CH_2O, 2 CH_2Cl); 4.05 (m, 2 H, CHOH, $OCH(CH_2Cl)_2$)
1h***	82	24.47 / 25.15	4.43 / 4.22		$C_7H_{14}Cl_2KNO_5S$	2.66 (s, 3 H, MeN); 3.00 (d, 2 H, NCH_2); 3.58 (m, 2 H, $HOCHCH_2O$); 3.74—3.90 (m, 4 H, OCH_2CHCl, CH_2Cl); 4.00 (m, 1 H, CHOH); 4.36 (m, 1 H, CHCl)
1i	61	27.74 / 28.04	4.85 / 5.04		$C_7H_{15}ClKNO_5S$	1.10 (t, 3 H, MeC); 2.84—3.14 (m, 4 H, CH_2NCH_2); 3.36—3.80 (m, 6 H, $CH_2OCH_2CH_2Cl$); 4.10 (m, 1 H, CHOH)
1j	50			4.48 / 4.46	$C_8H_{17}ClKNO_5S$	1.10 (t, 3 H, MeC); 1.95 (m, 2 H, CCH_2C); 2.86—3.26 (m, 4 H, CH_2NCH_2); 3.30—3.70 (m, 6 H, CH_2OCH_2, CH_2Cl); 3.90 (m, 1 H, CHOH)

* M.p. 102—103 °C. ** M.p. 125—126 °C. *** M.p. 123—124 °C.

Table 2. Physicochemical parameters and ^{1}H NMR spectroscopic data for *N*-3-chloro- and *N*-3-azidoalkoxy-2-nitroxypropyl-*N*-alkylnitramines (**2**, **4**)

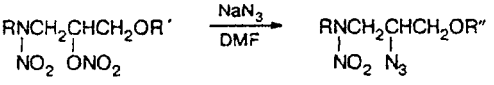
Compound	Yield (%)	n_D^{22} (m.p. /°C)	Found / Calculated (%) C	H	N	Molecular formula	^{1}H NMR, δ
2a	76	1.5035	28.20 / 27.47	4.74 / 4.28	13.83 / 13.73	$C_7H_{13}Cl_2N_3O_6$	3.50 (s, 3 H, MeN); 3.75—4.00 (m, 6 H, CH_2OCH_2, CH_2Cl); 4.10 (m, 2 H, NCH_2); 4.20 (m, 1 H, CHCl); 5.55 (m, 1 H, $CHONO_2$)
2b	77	1.4960			15.84 / 16.31	$C_6H_{12}ClN_3O_6$	3.50 (s, 3 H, MeN); 3.75 (t, 2 H, OCH_2CH_2Cl); 3.85 (m, 2 H, CH_2Cl); 3.95 (m, 2 H, CH_2O); 4.25 (m, 2 H, NCH_2); 5.67 (m, 1 H, $CHONO_2$)
2c	77	1.5040			13.02 / 13.73	$C_7H_{13}Cl_2N_3O_6$	3.50 (s, 3 H, MeN); 3.65—3.95 (m, 7 H, $CH_2OCH(CH_2Cl)_2$); 4.20 (m, 2 H, NCH_2); 5.55 (m, 1 H, $CHONO_2$)
2d	74.5	1.4868	31.53 / 30.95	5.23 / 5.19		$C_7H_{14}ClN_3O_6$	1.25 (t, 3 H, MeC); 3.70—4.00 (m, 8 H, $MeCH_2N$, $CH_2OCH_2CH_2Cl$); 4.20 (m, 2 H, NCH_2); 5.70 (m, 1 H, $CHONO_2$)
4a	71	1.5163	27.02 / 26.34	4.16 / 4.10		$C_7H_{13}N_9O_6$	3.50—3.70 (m, 5 H, MeN, CH_2N_3); 3.65—4.05 (m, 5 H, CH_2OCH_2, CHN_3); 4.25 (m, 2 H, CH_2N); 5.70 (m, 1 H, $CHONO_2$)
4b	75	1.4995			31.86 / 31.81	$C_6H_{12}N_6O_6$	3.40—3.55 (m, 5 H, MeN, CH_2N_3); 3.75 (m, 2 H, $OCH_2CH_2N_3$); 3.95 (m, 2 H, CH_2O); 4.25 (m, 2 H, NCH_2); 5.67 (m, 1 H, $CHONO_2$)
4c	76	(56—57)	26.26 / 26.34	4.18 / 4.10	39.31 / 39.49	$C_7H_{13}N_9O_6$	3.30—3.50 (m, 7 H, 2 CH_2N_3, MeN); 3.65 (m, 1 H, $OCH(CH_2N_3)_2$); 4.20 (m, 4 H, CH_2O, NCH_2); 5.55 (m, 1 H, $CHONO_2$)

Table 3. Physicochemical parameters and ^{1}H NMR spectroscopic data for *N*-3-azidoalkoxy-2-azidopropyl-*N*-alkylnitramines (**3**)

Compound	Yield (%)	n_D^{22}	Found / Calculated (%) C	H	N	Molecular formula	^{1}H NMR, δ
3a	50	1.5223			51.38 51.49	$C_7H_{13}N_{11}O_3$	3.40—3.60 (m, 5 H, MeN, CH_2N_3); 3.65—3.90 (m, 6 H, $N_3CHCH_2OCH_2CHN_3$); 4.00—4.20 (m, 2 H, NCH_2)
3b	55	1.5090	30.28 29.51	5.10 4.95		$C_6H_{12}N_8O_3$	3.30—3.60 (m, 5 H, MeN, CH_2N_3); 3.70—3.90 (m, 4 H, CH_2OCH_2); 4.00—4.20 (m, 3 H, NCH_2CHN_3)
3c	62	1.5245	28.72 28.10	4.47 4.38		$C_7H_{13}N_{11}O_3$	3.40—3.65 (m, 7 H, MeN, 2 CH_2N_3); 3.80—4.20 (m, 6 H, NCH_2CHN_3, CH_2OCH)
3d	63	1.5025	33.13 32.56	5.55 5.46		$C_7H_{14}N_8O_3$	1.30 (t, 3 H, MeC); 3.50 (t, 2 H, CH_2N_3); 3.60—4.40 (m, 9 H, CH_2NCH_2, $N_3CHCH_2OCH_2$)

Azido derivatives **3a—d** were synthesized by treatment of compounds **2a—d** and **4a** with NaN_3 in DMF [5] (Scheme 3). Both the nitroxyl group and the Cl atoms were substituted. Products **3a—d** were characterized by elemental analyses and IR and ^{1}H NMR spectroscopic data (Table 3).

Scheme 3

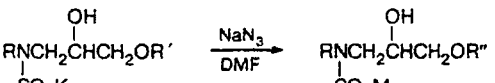


2a—d, 4a **3a—d**

3a: R = Me, R″ = $CH_2CH(N_3)CH_2N_3$; **3b:** R = Me, R″ = $(CH_2)_2N_3$; **3c:** R = Me, R″ = $CH(CH_2N_3)_2$; **3d:** R = Et, R″ = $(CH_2)_2N_3$; **4a:** R = Me, R′ = $CH_2CH(N_3)CH_2N_3$

Of certain interest are nitramines containing both the nitrate and azido groups. Because both functions in (chloroalkoxy)nitrates are replaced by azido groups, we carried out azidation of compounds **1** followed by nitration (Scheme 4).

Scheme 4



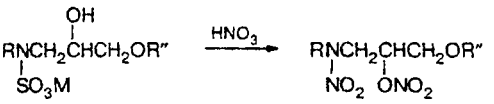
1e,g,h **5a—c**

M = Na, K

5a: R = Me, R″ = $CH_2CH(N_3)CH_2N_3$; **5b:** R = Me, R″ = $(CH_2)_2N_3$; **5c:** R = Me, R″ = $CH(CH_2N_3)_2$

The azidoalkoxy compounds **5a—c** obtained according to Scheme 4 (yields 90—95%) were nitrated with an HNO_3—Ac_2O mixture at −5 to −8 °C without purification (Scheme 5). At higher temperature, the azido groups underwent nitrolysis. Compounds **4a—c** were characterized by elemental analyses and IR and ^{1}H NMR spectroscopic data (see Table 2).

Scheme 5



5a—c **4a—c**

4a: R = Me, R″ = $CH_2CH(N_3)CH_2N_3$; **4b:** R = Me, R″ = $(CH_2)_2N_3$; **4c:** R = Me, R″ = $CH(CH_2N_3)_2$

Experimental

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

Preparation of chloroalkoxyepoxypropanes. Epichlorohydrin (9.25 g) was added dropwise with stirring at ~60 °C to a mixture of 1,3-dichloropropan-2-ol (64.5 g) with a catalytic amount of $BF_3 \cdot OEt_2$, and the mixture was stirred for 1 h. 1,6-Dichloro-5-chloromethyl-4-oxahexan-2-ol was isolated by fractional distillation. The product (17.7 g) was heated to ~60 °C and three portions of KOH (1.5 g each, 40% solution) were added over 20—25 min with vigorous stirring. The organic layer was separated and distilled to give 10 g of 1-(2-chloro-1-chloromethyl)ethoxy-2,3-epoxypropane (b.p. 69—71 °C (0.15 Torr)). 1-(2,3-Dichloropropoxy)-2,3-epoxypropane (b.p. 76—78 °C (0.15 Torr)) and 1-(2-chloroethoxy)-2,3-epoxypropane (b.p. 68—69 °C (18 Torr)) were obtained in a similar way. Their physicochemical parameters agree with literature data.[4]

1-(3-Chloropropoxy)-2,3-epoxypropane was obtained using the same procedure. ^{1}H NMR, δ: 1.95 (m, 2 H, CH_2); 2.55 (m, 2 H, C(3)H_2); 3.05 (m, 1 H, CH); 3.26 (m, 1 H, C(1)H_2); 3.55 (m, 4 H, OCH_2, CH_2Cl); 3.67 (m, 1 H, C(1)H_2).

Reaction of potassium *N*-methylsulfamate with 1-(2,3-dichloropropoxy)-2,3-epoxypropane. 1-(2,3-Dichloropropoxy)-2,3-epoxypropane (2.42 g, 13 mmol) was added at pH 7.25 to a solution of potassium *N*-methylsulfamate (1.5 g, 10 mmol) in a mixture of water (3.5 mL) and EtOH (4.9 mL). The mixture was kept for 30 h at 68—70 °C and concentrated *in vacuo*. The

residue was extracted with a hot Me_2CO—EtOH mixture (2 : 1) to remove potassium *N*-methylsulfamate. The extract was concentrated on a rotary evaporator, and the residue was reprecipitated with ether from a solution in acetone to give 2.74 g of product **1h**. Compounds **1a—g,i,j** were synthesized in a similar way.

***N*-3-(2-Chloroethoxy)-2-nitroxypropyl-*N*-ethylnitramine (2d).** Potassium 3-(2-chloroethoxy)-2-hydroxypropyl-*N*-ethylsulfamate (**1i**) (1.90 g) was gradually added at 1—7 °C to a mixture of Ac_2O (11 mL) and 98% HNO_3 (3.2 mL). The reaction mixture was stirred for 1 h at 0—7 °C, poured into ice water, and extracted with ethyl acetate (3×15 mL). The extract was washed with aqueous Na_2CO_3 and water, and the solvent was evaporated. The product was purified by reprecipitation with hexane from an ethereal solution to give 1.31 g of *N*-3-(2-chloroethoxy)-2-nitroxypropyl-*N*-ethylnitramine (**2d**). Compounds **2a—c** were synthesized in a similar way.

***N*-3-(2-Azido-1-azidomethyl)ethoxy-2-azidopropyl-*N*-methylnitramine (3c).** NaN_3 (0.95 g) was gradually added at 85—90 °C to a solution of *N*-3-(2-chloro-1-chloromethyl)ethoxy-2-nitroxypropyl-*N*-methylnitramine (**2c**) (0.82 g) in DMF (8 mL). The mixture was stirred for 15 h and poured into water (25 mL). The mixture was filtered and extracted with benzene (4×15 mL). The benzene solution was washed with water and concentrated to give 0.5 g of *N*-3-(2-azido-1-azidomethyl)ethoxy-2-azidopropyl-*N*-methylnitramine (**3c**). Compounds **3a,b,d** were synthesized in a similar way.

Mixed sodium-potassium *N*-3-(2-azidoethoxy)-2-hydroxypropyl-*N*-methylsulfamate (5b). NaN_3 (0.65 g) was added with stirring at 100—105 °C (in the case of compound **5a**, 127—133 °C) to a solution of potassium *N*-3-(2-chloroethoxy)-2-hydroxypropyl-*N*-methylsulfamate (1.20 g) in 8 mL of DMF. The reaction mixture was stirred for 5 h (in the case of **5a**, 15 h) and concentrated. The product was extracted with an Me_2CO—EtOH mixture, 3 : 2 (3×10 mL). The extract was concentrated to give 1.10 g of mixed sodium-potassium *N*-3-(2-azidoethoxy)-2-hydroxypropyl-*N*-methylsulfamate (**5b**). Compounds **5a,c** were synthesized in a similar way.

***N*-3-(2,3-Diazidopropoxy)-2-nitroxypropyl-*N*-methylnitramine (4a).** Potassium 3-(2,3-diazidopropoxy)-2-hydroxypropyl-*N*-methylsulfamate (**5a**) (0.96 g) was gradually added with cooling (−7 to −10 °C) to a mixture of Ac_2O (7 mL) and 98% HNO_3 (2 mL). The mixture was stirred for 1 h at −5 to −8 °C, poured into ice water, and extracted with ethyl acetate (3×10 mL). The extract was washed with aqueous Na_2CO_3 and water, and the solvent was evaporated. The residue was purified by reprecipitation with hexane with an ethereal solution to give 0.65 g of 3-(2,3-diazidopropoxy)-2-nitroxypropyl-*N*-methylnitramine (**4a**). Compounds **4b,c** were synthesized in a similar way.

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Received October 6, 1997