Synthesis of acyclic quaternary ammonium compounds containing ω-alkoxyethyl and 2-hydroxyethyl substituents at the nitrogen atom*

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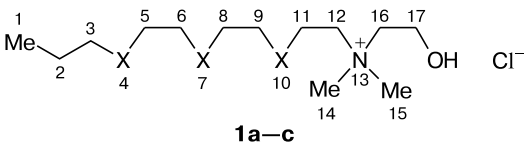
A series of acyclic symmetric quaternary ammonium chlorides $Me_2(HOCH_2CH_2)N^+(CH_2CH_2O)_nR\ Cl^-$ (n = 1, R = n-C_9H_{19}; n = 2, R = n-C_6H_{13}; n = 3, R = n-C_3H_7) was synthesized by alkylation of the corresponding tertiary amines $Me_2N(CH_2CH_2O)_nR$ with ethylene chlorohydrin in a two-phase system, using water as a solvent. The tertiary amines were synthesized in a heterogeneous system organic phase—aqueous phase, using an aqueous solution of Me_2NH and a solid alkali. The intermediate monoethers of ethylene, di- and triethylene glycol were obtained in high yield *via* a phase-transfer alkylation in dioxane, using solid KOH. The proton and carbon atom signals in the NMR spectra of the synthesized amines and ammonium chlorides were assigned based on the data of heteronuclear correlations (^1H, ^{13}C).

Key words: polyethylene glycol monoethers, phase-transfer alkylation, polyethylene glycols, ω-alkoxyethyl chlorides, tertiary amines, quaternary ammonium compounds.

Earlier, it was shown[1] that the introduction of ethylene or diethylene glycol fragments between the nitrogen atom and the dodecyl substituent in the Katinol molecule, $Me_2N^+(n\text{-}C_{12}H_{25})CH_2CH_2OH\ Cl^-$, possessing bactericidal properties leads to a significant increase in the activity of such compounds against *St. aureus*. In the case of *E. coli*, their activity remains virtually on the same level.

In this connection, we carried out the investigations of the relationship between bactericidal properties of such molecules and the number of ethylene glycol units in the 12-membered fragment at the nitrogen atom. For this purpose, we synthesized a series of ammonium chlorides **1a**—**c** analogues to Katinol molecule by a sequential replacement of each third methylene unit counting from the nitrogen atom in the *N*-dodecyl fragment with an oxygen atom.



1a—c

Compound	X(4)	X(7)	X(10)
Katinol	CH_2	CH_2	CH_2
1a	CH_2	CH_2	O
1b	CH_2	O	O
1c	O	O	O

Note that compounds containing such groups in the molecule possess a decreased toxicity to warm-blooded organisms.[2—4]

Results and Discussion

Ammonium chlorides **1a**—**c** were synthesized by a traditional conversion of secondary amines to the tertiary ones **2a**—**c** and their subsequent reaction with ethylene chlorohydrin (Scheme 1). It is known that the most efficient order of the introduction of substituents to the nitrogen atom suggests an initial NH-alkylation of secondary amines with the less active alkylating agents, ω-alkoxyethyl chlorides, while more active reagent is used for the N-alkylation of tertiary amines.[5]

The tertiary amines **2a**—**c** were synthesized in 77—85% yield by the reaction of Me_2NH (used as a 38% aqueous solution) with ω-alkoxyethyl chlorides **3a**—**c** in the heterogeneous system "organic phase—aqueous phase" in the presence of NaOH (110—115 °C, 15 h, a sealed tube) and in the absence of a solvent and a phase-transfer catalyst (Table 1). *N*,*N*-Dimethyl-*N*-(2-nonyloxyethyl)amine (**2a**) obtained by a similar method was described earlier.[5]

* To 90th birthday anniversary of the Corresponding Member of the Russian Academy of Sciences T. A. Mastryukova (1925—2006).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2697—2701, November, 2015.

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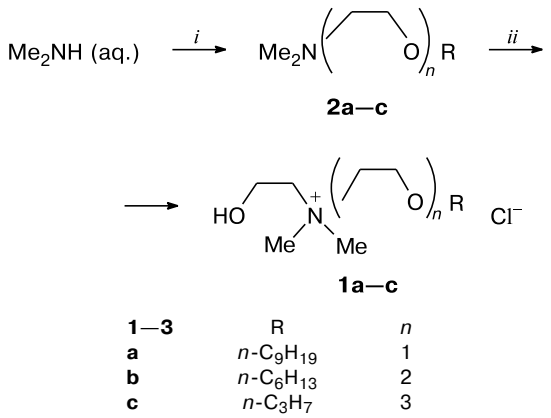
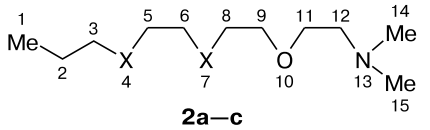
Scheme 1



1—3	R	*n*
a	*n*-C_9H_{19}	1
b	*n*-C_6H_{13}	2
c	*n*-C_3H_7	3

Reagents and conditions: *i*. $Cl(CH_2CH_2O)_nR$ (**3a—c**), NaOH, 110—115 °C, 15 h; *ii*. $ClCH_2CH_2OH$, H_2O, 90—95 °C, 4 h.

The structure and composition of amines **2a—c** were confirmed by ^1H and ^{13}C NMR spectroscopy (see Table 1), as well as by high resolution mass spectrometry (ESI). The ^1H NMR spectra correspond to the structure of these compounds and contain proton characteristic signals for the alkyl and ethylene glycol fragments of the molecules (δ_H 0.79—1.62 and δ_H 3.31—3.69, respectively). The signals in the ^{13}C NMR spectra of tertiary amines **2a—c** were assigned based on the 2D ^1H, ^{13}C correlation spectra (HSQC and HMBC). Thus, the HSQC (^1H, ^{13}C) spectral data allowed us to reliably assign the signals for the carbon atoms of methyl groups 1 and 14, 15, methylene groups 8 and 9 in amine **2a**, 5 and 6 in amine **2b**, and 2 and 3 in amine **2c**, as well as that for the α-carbon atom 12 in all the amines. Chemical shifts of other signals for carbon atoms were assigned based on the cross-peaks in the HMBC spectra (see Table 1).



2a—c

Ammonium chlorides **1a—c** were obtained in 67—88% (Table 2) yield by N-alkylation of tertiary amines **2a—c** with ethylene chlorohydrin in the two-phase system using water as a solvent (see Scheme 1). Their structure was confirmed by ^1H and ^{13}C NMR spectroscopy and high resolution mass spectrometry (ESI) (see Table 2). The ^1H NMR spectra contain the proton characteristic signals of the alkoxy and Me_2N groups, as well as the ethylene glycol fragments, and four proton multiplets of the methylene units 11, 12, 16, 17 in the region δ_H 3.68—4.18, which are attributed to the two structurally similar 2-alkoxy- and 2-hydroxyethyl substituents at the nitrogen atom. These signals were assigned in a separate study[6] based on the 2D

Table 1. Yields and ^1H and $^{13}C\{^1H\}$ NMR spectra ($CDCl_3$) of tertiary amines $R(OCH_2CH_2)_nNMe_2$ **2a—c**

Compound	X(4)	X(7)	Yield[a] (%)	δ (*J*/Hz)	
				^1H	$^{13}C\{^1H\}$
2a	CH_2	CH_2	81 (oil[b,c])	0.83 (t, 3 H, $H_3C(1)$, $^3J_{H,H}$ = 6.7); 1.15—1.35 (m, 12 H, $H_2C(2)$—$H_2C(7)$); 1.53 (quint, 2 H, $H_2C(5)$, $^3J_{H,H}$ = 6.9); 2.22 (s, 6 H, $H_3C(14)$, $H_3C(15)$); 2.45 (t, 2 H, $H_2C(12)$, $^3J_{H,H}$ = 5.9); 3.38 (t, 2 H, $H_2C(9)$, $^3J_{H,H}$ = 6.8); 3.47 (t, 2 H, $H_2C(11)$, $^3J_{H,H}$ = 5.9)	14.30 (C(1)); 22.86[d] (C(2), C(3)); 26.33 (C(7)); 29.46, 29.68, 29.75 (C(4), C(5), C(6)); 29.80 (C(8)); 32.07[d] (C(2), C(3)); 46.05 (C(14), C(15)); 59.08 (C(12)); 69.97 (C(11)); 71.62 (C(9))
2b	CH_2	O	77 (oil[c])	0.87 (t, 3 H, $H_3C(1)$, $^3J_{H,H}$ = 6.9); 1.20—1.40 (m, 6 H, $H_2C(2)$—$H_2C(4)$); 1.52 (quint, 2 H, $H_2C(5)$, $^3J_{H,H}$ = 7.0); 2.25 (s, 6 H, $H_3C(14)$, $H_3C(15)$); 2.50 (t, 2 H, $H_2C(12)$, $^3J_{H,H}$ = 5.9); 3.44 (t, 2 H, $H_2C(6)$, $^3J_{H,H}$ = 6.8); 3.55—3.60 (m, 6 H, $H_2C(8)$, $H_2C(9)$, $H_2C(11)$)	14.00 (C(1)); 22.58 (C(2)); 25.74 (C(4)); 29.57 (C(5)); 31.66 (C(3)); 45.86 (C(14), C(15)); 58.82 (C(12)); 69.36 (C(11)); 70.05 (C(8)); 70.40 (C(9)); 71.49 (C(6))
2c	O	O	85 (oil[c])	0.87 (t, 3 H, $H_3C(1)$, $^3J_{H,H}$ = 7.4); 1.47 (sext, 2 H, $H_2C(2)$, $^3J_{H,H}$ = 7.1); 2.22 (s, 6 H, $H_3C(14)$, $H_3C(15)$); 2.47 (t, 2 H, $H_2C(12)$, $^3J_{H,H}$ = 5.9); 3.38 (t, 2 H, $H_2C(3)$, $^3J_{H,H}$ = 6.8); 3.52—3.62 (m, 10 H, $H_2C(5)$, $H_2C(6)$, $H_2C(8)$, $H_2C(9)$, $H_2C(11)$)	10.09 (C(1)); 22.14 (C(2)); 46.03 (C(14), C(15)); 58.98 (C(12)); 69.49 (C(11)); 70.17 (C(5)); 70.53 (C(6)); 70.71 (C(8), C(9)); 73.23 (C(3))

[a] Yield of analytically pure products.
[b] Described earlier.[5]
[c] Compounds are very hygroscopic, purified by column chromatography.
[d] According to the HMBC (^1H, ^{13}C) spectrum, the signals belong only to atoms C(2) or C(3).

homo- (^{1}H, ^{1}H) and heterocorrelation procedure (^{1}H, ^{13}C and ^{1}H, ^{15}N), using the gs-COSY, gs-HSQC, and gs-HMBC pulse field gradients. The data obtained allowed us to reliably assign the signals in the low-field part of the ^{1}H NMR spectra to the methylene protons in the following sequence: 16, 12, 11, 17. The most downfield multiplet at δ_H 4.05—4.18 belongs to the protons of the hydroxymethyl group 17 (see Table 2). Note that the conversion of tertiary amines **2a**—**c** to the corresponding ammonium chlorides **1a**—**c** leads to a noticeable downfield shift of the signals for the protons of the α-methylene groups 12 and the methyl groups 14 and 15 by 1.4 and 1.2 ppm, respectively. The signal for the protons of the methyl groups 14 and 15 at the nitrogen atom overlaps with one of the components of the triplet belonging to the protons of the CH_2O methylene groups 9, 6, 3 in compounds **1a**, **1b**, and **1c**, respectively. The signals for the β-methylene protons at position 11 ($NCH_2C\underline{H}_2O$) are only insignificantly (by ~0.4 ppm) shifted toward the low field. Positions of signals for other hydrogen atoms did not change.

The assignment of the ^{13}C signals given in Table 2 is based on the data of heteronuclear (^{1}H, ^{13}C) HSQC and HMBC correlation spectra.[6] The signals for the carbon atoms of the *N*-2-oxy- and *N*-2-hydroxyethyl substituents were found in the following sequences: 17, 11, 12, 16 in the spectrum of salt **1a** with a nonyloxy group and 17, 12, 11, 16 in the spectrum of hexyloxy and propyloxy derivatives **1b** and **1c** (see Fig. 1). The signals for the carbon atoms of the ethylene glycol units in the spectra of salts **1b** and **1c** have the following sequence: 8, 9, 6 and 5, 8, 6, 9. The most downfield signal belongs to the carbon atoms 9, 6 and 3 bonded to the oxygen atom in the OR fragments (see Table 2).

ω-Alkoxyethyl chlorides **3a**—**c** were obtained in two steps:[5] first, the reaction of phase-transfer monoalkylation of ethylene, di- and triethylene glycol with nonyl, hexyl, and propyl bromide in the presence of KOH with-

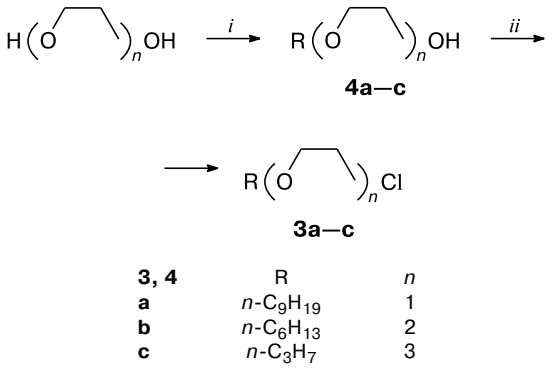
Table 2. Yields and ^{1}H and ^{13}C{^{1}H} NMR spectra ($CDCl_3$) of quaternary ammonium compounds $R(OCH_2CH_2)_nN^+(CH_2CH_2OH)Me_2\ Cl^-$ **1a**—**c**

Compound	X(4)	X(7)	Yield[a] (%)	δ (*J*/Hz)	
				^{1}H	^{13}C{^{1}H}
1a	CH_2	CH_2	67 (oil[b])	0.85 (t, 3 H, $H_3C(1)$, $^3J_{H,H}$ = 6.6); 1.15—1.33 (m, 12 H, $H_2C(2)$—$H_2C(7)$); 1.52 (quint, 2 H, $H_2C(8)$, $^3J_{H,H}$ = 6.6); 3.39[c] (s, 6 H, $H_3C(14)$, $H_3C(15)$); 3.42[c] (t, 2 H, $H_2C(9)$, $^3J_{H,H}$ = 6.6); 3.68—3.80 (m, 3 H, $H_2C(16)$ + OH); 3.85 (br.m, 4 H, $H_2C(12)$ + $H_2C(11)$); 4.05—4.18 (m, 2 H, $H_2C(17)$)	14.14 (C(1)); 22.68[d] (C(2), C(3)); 26.16 (C(7)); 29.28 29.42, 29.46, 29.52 (C(4), C(5), C(6), C(8)); 31.86[d] (C(2), C(3)); 53.02 (C(14), C(15)); 56.04 (C(17)); 64.67 (C(11)); 64.82 (C(12)); 67.26 (C(16)); 71.86 (C(9))
1b	CH_2	O	73 (oil[b])	0.86 (t, 3 H, $H_3C(1)$, $^3J_{H,H}$ = 6.9); 1.20—1.35 (m, 6 H, $H_2C(2)$—H_2C4)); 1.52 (quint, 2 H, $H_2C(5)$, $^3J_{H,H}$ = 7.0); 3.39[c] (s, 6 H, $H_3C(14)$, $H_3C(15)$); 3.40[c] (t, 2 H, $H_2C(6)$, $^3J_{H,H}$ = 6.8); 3.49—3.55 (m, 2 H, $H_2C(8)$); 3.61—3.66 (m, 2 H, $H_2C(9)$); 3.70—3.78 (m, 2 H, $H_2C(16)$); 3.83—3.92 (m, 2 H, $H_2C(12)$);3.93—3.99 (m, 2 H, $H_2C(11)$); 4.08—4.16 (m, 3 H, $H_2C(17)$ + OH)	14.26 (C(1)); 22.82 (C(2)); 25.95 (C(3)); 29.79 (C(5)); 31.84 (C(4)); 53.36 (C(14), C(15)); 56.28 (C(17)); 64.89 (C(12)); 65.25 (C(11)); 67.41 (C(16)); 69.85 C(8); 70.72 C(9); 71.74 (C(6))
1c	O	O	88 (oil[b])	0.90 (t, 3 H, $H_3C(1)$, $^3J_{H,H}$ = 7.4); 1.58 (sext, 2 H, $H_2C(2)$, $^3J_{H,H}$ = 7.1); 3.39[c] (s, 6 H, $H_3C(14)$, $H_3C(15)$); 3.40[c] (t, 2 H, $H_2C(3)$, $^3J_{H,H}$ = 6.6); 3.52—3.70 (m, 8 H, $H_2C(5)$, $H_2C(6)$, $H_2C(8)$, $H_2C(9)$); 3.73—3.81 (m, 2 H, $H_2C(16)$); 3.83—3.92 (m, 2 H, $H_2C(12)$); 3.94—4.04 (m, 2 H, $H_2C(11)$); 4.07—4.18 (m, 2 H, $H_2C(17)$); 4.71 (s, 1 H, OH)	10.65 (C(1)); 22.91 (C(2)); 53.17 (C(14), C(15)); 56.15 (C(17)); 64.72 (C(12)); 65.19 (C(11)); 67.27 (C(16)); 70.09 (C(5)); 70.35 (C(8)); 70.49 (C(6)); 70.65 (C(9)); 73.18 (C(3))

[a] Yields of analytically pure products.
[b] Compounds are very hygroscopic, purified by column chromatography.
[c] Overlapped singlet and triplet.
[d] According to the HMBC (^{1}H, ^{13}C) spectrum, the signals belong only to atoms C(2) or C(3).

out a phase-transfer catalyst gave monoethers **4a—c** (70—75%); in the second step, they were treated with thionyl chloride in the presence of pyridine (Scheme 2).

Scheme 2



3, 4	R	*n*
a	*n*-C_9H_{19}	1
b	*n*-C_6H_{13}	2
c	*n*-C_3H_7	3

Reagents and conditions: *i*. RBr, KOH, dioxane, 100—105 °C, 5—10 h; *ii*. $SOCl_2$, PhMe, Py, −5 °C→100 °C, 2 h.

Thus, we synthesized a series of ammonium chlorides with *N*-ω-alkoxyethyl and *N*-2-hydroxyethyl substituents by the alkylation of *N*-(ω-alkoxyethyl)-*N*,*N*-dimethylamines with ethylene chlorohydrin in the two-phase system using water as a solvent. The compounds obtained are of interest as bactericidal agents, as well as for the study of the structure—activity relationship.

Experimental

^1H and ^{13}C NMR spectra of compounds in $CDCl_3$ were recorded on a Bruker Avance III NanoBay spectrometer (300.28 MHz), using signals of residual protons (δ 7.28) and carbon atoms (δ 77.20) of the solvent as a internal reference. 2D Correlation COSY {^1H; ^1H}, HSQC, and HMBC{^1H; ^{13}C} spectra were recorded using a standard Bruker procedure. High resolution mass spectra (ESI) were recorded on a Bruker micrOTOF II instrument. Aldrich silica gel (130—270 mesh, 60 Å) was used for column chromatography. Solvents were purified and dried according to the known procedures.[7] The syntheses of *N*,*N*-dimethyl-*N*-(2-nonyloxyethyl)amine (**2a**), 1-(2-chloroethoxy)-nonane (**3a**), and ethylene glycol monononyl ether (**4a**) were described earlier.[5]

***N*-(2-Hydroxyethyl)-*N*,*N*-dimethyl-*N*-(2-nonyloxyethyl)-ammonium chloride (1a)** was obtained according to the described procedure[5] from amine **2a** (1.2 g, 5.6 mmol), ethylene chlorohydrin (0.5 g, 6.1 mmol), and H_2O (3 mL). The salt **1a** (1.5 g) was purified by column chromatography on silica gel, eluent chloroform—methanol (2 : 1). The yield of product **1a** was 1.1 g (67%) (see Table 2). Found, *m/z*: 260.2573 $[M]^+$. $C_{15}H_{34}NO_2$. Calculated: M = 260.2584.

***N*-[2-(2-Hexyloxyethoxy)ethyl]-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylammonium chloride (1b)** was obtained similarly to compound **1a** from amine **2b** (0.8 g, 3.7 mmol), ethylene chlorohydrin (0.3 g, 4.1 mmol), and H_2O (3 mL). The salt **1b** (1.0 g) was purified by column chromatography on silica gel, eluent chloroform—methanol (2 : 1). The yield of product **1b** was 0.8 g (73%) (see Table 2). Found, *m/z*: 262.2366 $[M]^+$. $C_{14}H_{32}NO_3$. Calculated: M = 262.2377.

***N*-(2-Hydroxyethyl)-*N*,*N*-dimethyl-*N*-{2-[2-(2-propyloxyethoxy)ethoxy]ethyl}ammonium chloride (1c)** was obtained similarly to compound **1a** from amine **2c** (0.6 g, 2.7 mmol), ethylene chlorohydrin (0.2 g, 3.0 mmol), and H_2O (3 mL). The salt **1c** (0.8 g) was purified by column chromatography on silica gel, eluent chloroform—methanol (5 : 1). The yield of product **1c** was 0.7 g (88%) (see Table 2). Found, *m/z*: 264.2170 $[M]^+$. $C_{13}H_{30}NO_4$. Calculated: M = 264.2169.

***N*-[2-(2-Hexyloxyethoxy)ethyl]-*N*,*N*-dimethylamine (2b).** A mixture of 0.86 g of 38% aqueous solution of Me_2NH (0.32 g, 7.1 mmol), 1-[2-(2-chloroethoxy)ethoxy]hexane (**3b**) (2.00 g, 9.6 mmol), and solid NaOH (0.4 g, 10.5 mmol) was heated in a sealed tube at 110—115 °C for 15 h. Then, the content of the tube was diluted with benzene (15 mL) and water (10 mL). The organic layer was separated, washed with water (3×10 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The residue (1.70 g) was purified by column chromatography on silica gel, eluent chloroform—methanol (4 : 1). The yield of amine **2b** was 1.60 g (77%) (see Table 1). Found, *m/z*: 218.2107 $[M + H]^+$. $C_{12}H_{27}NO_2$. Calculated: M = 218.2115.

***N*,*N*-Dimethyl-*N*-{2-[2-(2-propyloxyethoxy)ethoxy]ethyl}-amine (2c)** was obtained similarly to amine **2b** from 0.86 g of 38% aqueous solution of Me_2NH (0.32 g, 7.1 mmol), 1-{2-[2-(2-chloroethoxy)ethoxy]ethoxy}propane (**3c**) (2.00 g, 9.5 mmol), and solid NaOH (0.42 g, 10.4 mmol). The product (1.90 g) was purified by column chromatography on silica gel, eluent chloroform—methanol (4 : 1). The yield of amine **2c** was 1.80 g (85%) (see Table 1). Found, *m/z*: 220.1917 $[M + H]^+$. $C_{11}H_{25}NO_3$. Calculated: M = 220.1907.

1-[2-(2-Chloroethoxy)ethoxy]hexane (3b) was obtained according to the described procedure[5] from monoether **4b** (6.8 g, 36 mmol), anhydrous pyridine (3.5 mL, 3.4 g, 43 mmol), $SOCl_2$ (3.1 mL, 5.1 g, 43 mmol), and anhydrous toluene (20.0 mL). The product (6.8 g) was distilled *in vacuo* to obtain chloride **3b** (6.4 g, 84%) with b.p. 126—128 °C (13—14 Torr) (*cf.* Ref. 8: b.p. 126 °C (14 Torr)). ^1H NMR, δ: 0.84 (t, 3 H, Me, $^3J_{H,H}$ = 6.9 Hz); 1.20—1.39 (m, 6 H, $C_3\underline{H}_6Me$); 1.55 (quint, 2 H, CH_2Bu, $^3J_{H,H}$ = = 7.1 Hz); 3.42 (t, 2 H, $OC\underline{H}_2C_5H_{11}$, $^3J_{H,H}$ = 6.8 Hz); 3.53—3.65 (m, 6 H, $C\underline{H}_2OC\underline{H}_2C\underline{H}_2OC_6H_{13}$); 3.72 (t, 2 H, $ClCH_2$, $^3J_{H,H}$ = = 5.8 Hz). ^{13}C NMR, δ: 14.18 (Me); 22.77 (CH_2Me); 25.92 (CH_2Et); 29.75 (CH_2Pr); 31.84 (CH_2Bu); 42.82 ($ClCH_2$); 70.23 ($ClCH_2\underline{C}H_2O$); 70.88 ($\underline{C}H_2OC_6H_{13}$); 71.54 ($\underline{C}H_2CH_2OC_6H_{13}$); 71.75 ($O\underline{C}H_2C_5H_{11}$).

1-{2-[2-(2-Chloroethoxy)ethoxy]ethoxy}propane (3c) was obtained similarly to chloride **3b** from monoether **4c** (2.3 g, 12 mmol), anhydrous pyridine (1.2 mL, 1.2 g, 14 mmol), $SOCl_2$ (1.0 mL, 1.6 g, 14 mmol), and anhydrous toluene (8.0 mL). The product (1.8 g) was purified by column chromatography on silica gel, eluent chloroform—methanol (49 : 1). The yield of product **3c** was 1.6 g (63%). ^1H NMR, δ: 0.87 (t, 3 H, Me, $^3J_{H,H}$ = 7.4 Hz); 1.56 (sext, 2 H, CH_2Me, $^3J_{H,H}$ = 7.1 Hz); 3.37 (t, 2 H, $OC\underline{H}_2CH_2Me$, $^3J_{H,H}$ = 6.7 Hz); 3.52—3.63 (m, 10 H, $C\underline{H}_2OC\underline{H}_2C\underline{H}_2OC\underline{H}_2C\underline{H}_2OPr$); 3.71 (t, 2 H, $ClCH_2$, $^3J_{H,H}$ = 5.8 Hz). ^{13}C NMR, δ: 10.63 (Me); 22.94 (CH_2Me); 42.83 ($ClCH_2$); 70.17 (CH_2OPr); 70.75 ($O\underline{C}H_2CH_2OPr$); 70.83 ($ClCH_2CH_2O\underline{C}H_2\underline{C}H_2O$); 71.49 ($ClCH_2\underline{C}H_2O$); 73.21 ($OCH_2Et$).

Diethylene glycol monohexyl ether (4b) was obtained according to the described procedure[5] from diethylene glycol (19.1 g, 179 mmol), KOH (3.4 g, 60 mmol), hexyl bromide (9.0 g, 55 mmol), and anhydrous dioxane (19 mL). The product (9.3 g) was distilled *in vacuo* to obtain ether **4b** (7.0 g, 68%) with b.p. 134—135 °C (9 Torr) (*cf.* Ref. 8: b.p. 140—141 °C (16 Torr)). ^{1}H NMR, δ: 0.85 (t, 3 H, Me, $^3J_{H,H}$ = 7.0 Hz); 1.20—1.40 (m, 6 H, $C_3\underline{H}_6Me$); 1.56 (quint, 2 H, CH_2Bu, $^3J_{H,H}$ = 6.8 Hz); 2.66 (s, 1 H, OH); 3.42 (t, 2 H, $OC\underline{H}_2C_5H_{11}$, $^3J_{H,H}$ = 6.8 Hz); 3.53—3.59 (m, 4 H, $OC\underline{H}_2C\underline{H}_2OC_6H_{13}$); 3.61—3.65 (m, 2 H, $HOCH_2C\underline{H}_2O$); 3.67—3.70 (m, 2 H, $HOC\underline{H}_2$). ^{13}C NMR, δ: 14.19 (Me); 22.76 (CH_2Me); 25.90 (CH_2Et); 29.70 (CH_2Pr); 31.82 (CH_2Bu); 61.98 ($HOCH_2$); 70.32 ($HOCH_2\underline{C}H_2O$); 70.64 ($\underline{C}H_2OC_6H_{13}$); 71.77 ($\underline{C}H_2CH_2OC_6H_{13}$); 72.71 ($O\underline{C}H_2C_5H_{11}$).

Triethylene glycol monopropyl ether (4c) was obtained similarly to ether **4b** from triethylene glycol (20.0 g, 133 mmol), KOH (2.7 g, 49 mmol), propyl bromide (5.5 g, 44 mmol), and anhydrous dioxane (22 mL). The product (8.0 g) was purified by column chromatography on silica gel, eluent *n*-hexane—acetone (4 : 1) to obtain ether **4c** (7.0 g, 71%). ^{1}H NMR, δ: 0.82 (t, 3 H, Me, $^3J_{H,H}$ = 7.4 Hz); 1.46 (sext, 2 H, CH_2Me, $^3J_{H,H}$ = 7.2 Hz); 2.91 (br.s, 1 H, O$\underline{H}$); 3.33 (t, 2 H, OCH_2Et, $^3J_{H,H}$ = 6.8 Hz); 3.48—3.53 (m, 4 H, $OC\underline{H}_2C\underline{H}_2OPr$); 3.55—3.57 (m, 2 H, $HOC\underline{H}_2CH_2O$); 3.58 (s, 4 H, $HOCH_2CH_2OC\underline{H}_2C\underline{H}_2O$); 3.65 (t, 2 H, $HOC\underline{H}_2$, $^3J_{H,H}$ = 4.0 Hz). ^{13}C NMR, δ: 10.64 (Me); 22.93 (CH_2Me); 61.91 ($HOCH_2$); 70.16 ($HOCH_2\underline{C}H_2O$); 70.54 ($O\underline{C}H_2CH_2OPr$); 71.79 ($HOCH_2CH_2O\underline{C}H_2\underline{C}H_2O$); 72.68 ($CH_2OPr$); 73.29 ($OCH_2Et$).

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Received June 29, 2015