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SYNTHESIS OF NEW HIGHLY LYPOPHILIC ETHOXYLATED IONIC LIQUIDS AS PROMISING ACTIVE COMPONENTS FOR ION SELECTIVE ELECTRODES

Abtract: The convenient method for preparation of ethoxylated highly lipophilic quaternary ammonium salts has been developed, including alkylation of methyl gallate with dodecyl bromide, hydride reduction of ester group, introduction of the polyethoxylated fragment into the side chain, substitution of the terminal hydroxy group by chlorine and quaternization by a tertiary amine. The salts prepared possess the properties of ionic liquids and can be of interest as active components for ion selective electrode membranes.

Keywords: quaternary ammonium salts, ethoxylated, ionic liquids, ion exchanging membrane components, ion selective electrodes

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СИНТЕЗ НОВЫХ ВЫСОКОЛИПОФИЛЬНЫХ ЭТОКСИЛИРОВАННЫХ ИОННЫХ ЖИДКОСТЕЙ – ПЕРСПЕКТИВНЫХ АКТИВНЫХ КОМПОНЕНТОВ МЕМБРАН ИОНОСЕЛЕКТИВНЫХ ЭЛЕКТРОДОВ

Аннотация: Разработан удобный метод получения этоксилированных высоколипофильных четвертичных аммониевых солей, включающий алкилирование метилгаллата додецилбромидом, гидридное восстановление сложноэфирной группы, введение полиэтоксилированного фрагмента в состав боковой цепи, замещение концевой гидроксильной группы на атом хлора и кватернизацию полученного галогенпроизводного третичным амином. Синтезированные соли обладают свойствами ионных жидкостей и представляют интерес в качестве электроактивных веществ.

Ключевые слова: четвертичные аммониевые соли, этоксилированные, ионные жидкости, электроактивные вещества, ионоселективные электроды

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Introduction. Quaternary ammonium salts have been for a long time used as anion exchanger components of ion selective electrode membranes [1]. According to the previously dominating viewpoint, they are generally considered to have low selectivity, due to nonspecific nature of their interaction with various anions. This viewpoint, however, has been considerably revised during last two decades; in particular, it has been shown [2–5] that some quaternary ammonium salts bearing methyl groups at their cation center and so having improved steric accessibility thereof, can possess increased selectivity to certain kinds of anions (Fig. 1). The methods for relatively simple and easily scalable preparation of such salts have been described [6].

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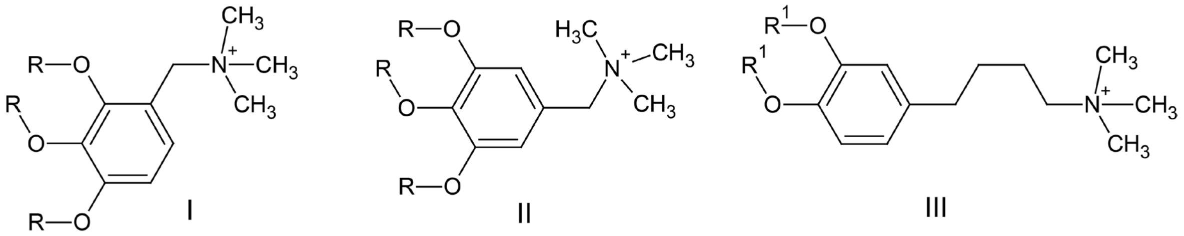

Fig. 1. Highly lipophilic quaternary ammonium salts with improved steric accessibility of the cation center (R = n-$C_{12}H_{25}$, R^1 = *n*-$C_{16}H_{33}$)

However, steric access to the cationic nitrogen atom of these salts may still not be as good as it seems, due to the possibility of long alkyl chains wrapping around the ammonium fragment. This may be particularly true for the structure **I** that has a C_{12} alkoxy chain attached in the position adjacent to the benzyl carbon bearing the ammonium cation, but the same can be a problem for the structure **II** as well. The evidence of this is that for compound **III** where nitrogen atom is attached by a longer carbon chain, some increase of selectivity has been observed [7]. At the same time, trying to improve it further by introducing longer carbon chains between aromatic ring and cationic nitrogen does not seem a feasible approach, due to the lack of conformational stability for non-functionalized chains and, therefore, high probability of their wrapping. Introducing instead, for instance, a relatively rigid polyene fragment is also unpractical due to decreased stability of the compound toward polymerization and oxidation. Additionally, these structural changes make the preparative route to the desired structures much more lengthy and expensive.

Therefore, another approach has been chosen, with a chain of several oxyethane groups inserted as a spacer for removing the aromatic ring from the quaternary ammonium center. In addition to being inexpensive and involving relatively small number of additional synthetic steps, this approach has also the advantage of putting greater distance between the nitrogen atom and the aromatic ring, due to known ability of poly(oxyethane) chains to maintain relatively unfolded, helical or even wholly anti-periplanar conformations [8, 9]. This gave us a hope to expect better steric access to the ammonium center for these products.

Results and discussion. The synthetic route applied has been based on the previously developed method, used formerly for preparation of salt **II** and structurally related compounds [6]. The commercially available reagent, gallic acid methyl ester **IV** (Fig. 2), has been alkylated with dodecyl bromide using slightly modified procedure from [6]. Instead of purification by multiple recrystallization, that could be very laborious and time consuming, particularly when used on large amounts of substance, the product **V** has been purified from phenolic compounds (formed due to incomplete alkylation) by extraction of its heptane solution with potassium hydroxide 5% solution in slightly watered *iso*-propyl alcohol. After this procedure, compound **V** has been found to be pure enough to be used in the next step without further purification.

The ester **V** was then converted into the substituted benzyl chloride **VII** by the two-step procedure taken also from [6]. Enlargement of the side chain has been effected by the reaction with lithium salts of di-, tri- and tetraethylene glycol, respectively, affording compounds **VIII *a-c*** in good yields. The next two steps have been performed as an one-pot procedure, without isolating and characterizing the intermediate alkyl chlorides. Final products **IX *a-c*** were obtained in good to moderate yields as white or off-white crystalline solids with melting points well below 100 ºC (in the case of compound **IX *c***, the m.p. is close to room temperature), that makes them, by definition, ionic liquids. Their structures have been confirmed by ^{1}H NMR and IR spectroscopy.

The preliminary data (to be published elsewhere soon) on ion selectivity of electrodes using compounds **IX** as active components, provide the evidence that their selectivities toward double-charged anions tend to improve with the spacer length increase, as compared to the compound **II** containing no spacer at all.

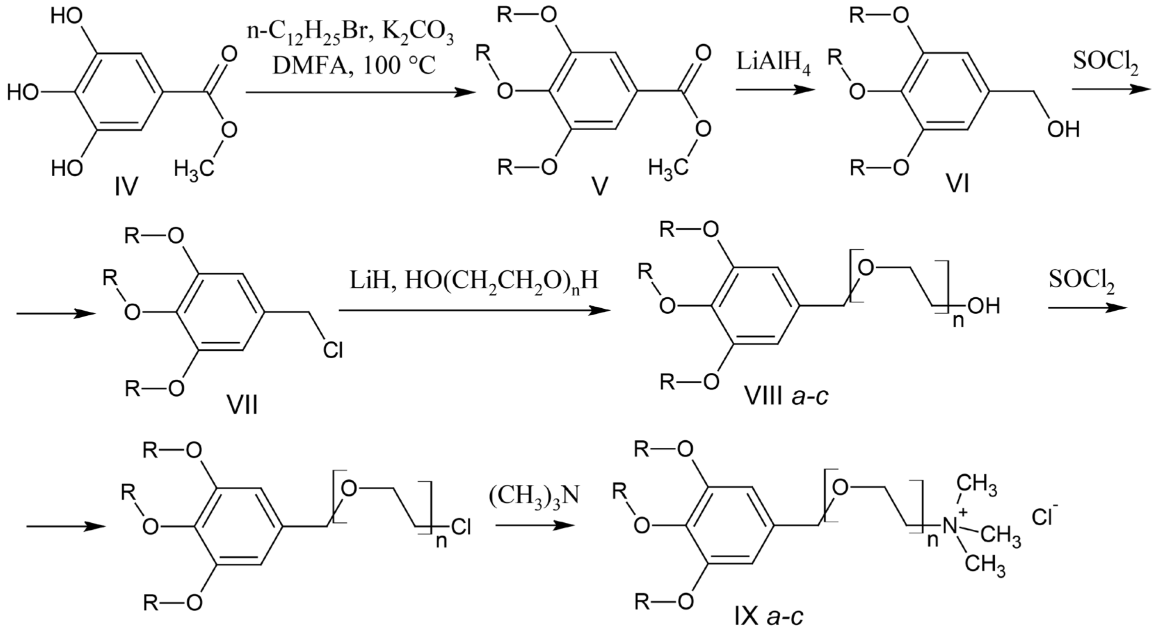

Fig. 2. Synthesis of oligoethoxylated quaternary ammonium salts (R = $C_{12}H_{25}$, n = 2, 3 or 4 for *a*, *b* and *c*, respectively)

Conclusion. We report here the synthetic procedure for preparation of highly lipophilic ethoxylated quaternary ammonium salts as promising ionic liquid components for ion-selective electrode membranes. The procedure developed is convenient, relatively easy to follow and allows wide-range variability of the spacer length, therefore providing a good tool for investigating the effects of the cationic center steric accessibility upon the selectivity of anion exchange extraction.

Experimental. Gallic acid methyl ester (compound **IV**) and dodecyl bromide have been purchased from Acros Organics and had the reagent grade of purity. The reactions were monitored by TLC on Silufol or Kieselgel 60 F_{254} plates. Melting pounts have been determined by the capillary method and are uncorrected. IR spectra were recorded on Bruker ALPHA spectrometer by attenuated total reflection method (ATR Di) in the range from 4000 to 400 cm^{-1}. ^1H NMR (500.03 MHz) spectra were recorded on a Bruker AVANCE-500 NMR spectrometer. $CDCl_3$ was used as a solvent and the residual solvent signals (δ 7.26 ppm) served as an internal reference standard.

3,4-5-tris-Dodecyloxybenzoic acid methyl ester (**V**). To a solution of 18.42 g (0.1 mol) of methyl gallate **IV** in 500 mL of dimethylformamide, 48.30 g (0.35 mol) of potassium carbonate and 74.4 mL (0.31 mol) of dodecyl bromide have been added. The mixture was heated at 100°C with vigorous stirring under reflux for 4 h, then cooled down to room temperature and diluted with 500 mL of heptane. Inorganic salts were filtered off and the filtrate diluted with 500 mL of water. After separation of layers, the lower phase was extracted with heptane (3×100 mL). The combined heptane solution was then extracted with small portions of 5% solution of potassium hydroxide in the *iso*-propyl alcohol-water (9:1) mixture until the alkaline layer was no more turning brown after the extraction. The heptane layer was then washed with water, dried and evaporated, the residue crystallized from *iso*-propyl alcohol affording 61.35 g of compound **V** (yield 89%), with physical constants, IR and NMR ^1H spectra being in accordance with published data [6].

(3,4-5-tris-Dodecyloxyphenyl)methanol (**VI**). To a suspension of 1.10 g (0.029 mol) of lithium aluminium hydride in 200 mL of dry tetrahydrofurane (distilled over lithium hydride), a solution of 10.00 g (0.0145 mol) of the compound **V** in 100 mL of the same solvent has been added dropwise with stirring. The reaction mixture was then refluxed for 2 h, cooled down and treated with 1 mL of NH_4Cl saturated water solution. The inorganic salts were filtered off, the resulting solution dried and evaporated, affording a crude product that has been recrystallized from iso-propyl alcohol giving 8.82 g of compound **VI** (yield 92%) with physical constants, IR and NMR ^1H spectra being in accordance with published data [6].

(3,4-5-tris-Dodecyloxyphenyl)chloromethane (**VII**). To a solution of 6.61 g (0.01 mol) of the compound **VI** in 30 ml of dichloromethane, 1.45 mL (0.02 mol) of freshly distilled thionyl chloride has been added dropwise. The solution was then refluxed for ca. 2 h until no starting material has been detected by TLC, evaporated to dryness, evacuated for a while to remove traces of acidic compounds, and the residue crystalized from acetone, giving 5.71 g (yield 84%) of the product, with physical constants, IR and NMR ^{1}H spectra being in accordance with published data [6].

2-{2-[(3,4,5-tris-dodecyloxybenzyl)oxy]ethoxy}ethanol (**VIII *a***)*, 2-(2-{2-[(3,4,5-tris-dodecyloxybenzyl)oxy]ethoxy}ethoxy)ethanol* (**VIII *b***) *and 2-(2-(2-{2-[(3,4,5-tris-dodecyloxybenzyl) oxy]ethoxy}ethoxy) ethoxy)ethanol* (**VIII *c***).

Into a round-bottom flask, well dried and protected from atmospheric moisture, 0.5 g of lithium hydride, 5,0 mL of dry tetrahydrofurane and 5.0 mL of di-, tri or tetraethylene glycol, respectively, were added (careful, vigorous hydrogen evolution and foaming!). The mixture was refluxed until no more hydrogen evolved, and 15 ml of the compound **VII** (1.00 g, 1.47 mmol) solution in tetrahydrofurane was introduced. The mixture was then refluxed until no more starting material has been detected by TLC, cooled down to room temperature, diluted by water and extracted with dichloromethane. The combined dichloromethane extracts were washed with water, dried and evaporated, giving compounds **VIII *a-c*** as yellowish or yellow oils, sufficiently pure (TLC) to be introduced into the next step without further purification. The yields at this step have not been determined.

Compound **VIII *a***. IR, cm^{-1}: 3397 (broad, OH), 2963, 2917, 2870, 2847 (CH), 1592 (C=C$_{ar}$). NMR ^{1}H: 0.88 (t, 9H, J = 6.0 Hz, CH$_3$), 1.26 (m, broad, 48H, CH$_2$), 1.45 (m, 6H, CH$_2$), 1,75 (m, 6H, CH$_2$), 3,63 (m, 4H, OCH$_2$), 3,72 (m, 4H, OCH$_2$), 3,95 (m, 7H, OCH$_2$+OH), 4.47 (m, 2H, m, C$_{arom}$CH$_2$), 6.53 (s, 2H, C$_{arom}$H).

Compound **VIII *b***. IR, cm^{-1}: 3357 (broad, OH), 2952, 2918, 2870, 2848 (CH), 1592 (C=C$_{ar}$). NMR ^{1}H: 0.88 (t, 9H, J = 6.0 Hz, CH$_3$), 1.27 (m, broad, 48H, CH$_2$), 1.47 (m, 6H, CH$_2$), 1,77 (m, 6H, CH$_2$), 3,62 (m, 6H, OCH$_2$), 3,74 (m, 6H, OCH$_2$), 3,95 (m, 7H, OCH$_2$+OH), 4.47 (m, 2H, m, C$_{arom}$CH$_2$), 6.53 (s, 2H, C$_{arom}$H).

Compound **VIII *c***. IR, cm^{-1}: 3383 (broad, OH), 2957, 2918, 2850 (CH), 1586 (C=C$_{ar}$). NMR ^{1}H: 0.88 (t, 9H, J = 6.0 Hz, CH$_3$), 1.26 (m, broad, 48H, CH$_2$), 1.47 (m, 6H, CH$_2$), 1,76 (m, 6H, CH$_2$), 3,68 (m, 13H, OCH$_2$+OH), 3,95 (m, 6H, OCH$_2$), 4.46 (m, 2H, m, C$_{arom}$CH$_2$), 6.53 (s, 2H, C$_{arom}$H).

N,N,N-trimethyl-2-{2-[(3,4,5-tris-dodecyloxybenzyl)oxy]ethoxy}ethanaminium chloride (**IX *a***)*, N,N,N-trimethyl-2-(2-{2-[(3,4,5-tris-dodecyloxybenzyl)oxy]ethoxy}ethoxy)ethanaminium chloride* (**IX *b***)*, N,N,N-trimethyl-2-(2-(2-{2-[(3,4,5-tris-dodecyloxybenzyl) oxy]ethoxy}ethoxy) ethoxy)ethanaminium chloride* (**IX *c***).

To a solution of compounds **VIII *a, b*** or ***c,*** taken directly from the synthesis described above, in 10 mL of dichloromethane, 0.5 mL of freshly distilled thionyl chloride has been added. The solution was then refluxed for ca. 2 h until no starting material has been detected by TLC, evaporated to dryness, evacuated for a while to remove traces of acidic compounds, and the residue, without isolation or purification, was treated with 10 ml of approx. 2.1 M solution of trimethylamine in *iso*-propyl alcohol. The solution was kept at room temperature for 48 hours, then cooled down to 0 ºC, and the crystals precipitated were collected, washed with the minimum amount of *iso*-propyl alcohol and recrystallized from the same solvent, giving, respectively, 0.51 g (42%) of the compound **IX *a***, 0.60 g (47%) of the compound **IX *b*** and 0.54 g (40%) of the compound **IX *c***, all yields being calculated for three steps, starting from the compound VII.

Compound **IX *a***. White solid, m.p. 41-42ºC. IR, cm^{-1}: 2961, 2927, 2874, 2847 (CH), 1590 (C=C$_{ar}$). NMR ^{1}H: 0.88 (t, 9H, J = 6.0 Hz, CH$_3$), 1.30 (m, broad, 48H, CH$_2$), 1.47 (m, 6H, CH$_2$), 1,70 (m, 6H, CH$_2$), 2,84 (s, broad, 9H, N(CH$_3$)$_3$), 3,63 (m, 2H, OCH$_2$), 3,77 (m, 2H, OCH$_2$), 3.94 (m, 10H, OCH$_2$+NCH$_2$), 4.51 (s, 2H, C$_{arom}$CH$_2$), 6.56 (s, 2H, C$_{arom}$H).

Compound **IX *b***. White solid, m.p. 50–51 ºC. IR, cm^{-1}: 2952, 2918, 2870, 2848 (CH), 1592 (C=C$_{ar}$). NMR ^{1}H: 0.89 (t, 9H, J = 6.0 Hz, CH$_3$), 1.26 (m, broad, 48H, CH$_2$), 1.46 (m, 6H, CH$_2$), 1,73 (m, 6H, CH$_2$), 2,85 (s, broad, 9H, N(CH$_3$)$_3$), 3,63 (m, 4H, OCH$_2$), 3,77 (m, 4H, OCH$_2$), 3.94 (m, 10H, OCH$_2$+NCH$_2$), 4.50 (s, 2H, C$_{arom}$CH$_2$), 6.56 (s, 2H, C$_{arom}$H).

Compound **IX *c***. Yellowish solid, m.p. 29–32 ºC (liquid cryslal formation), 109 ºC (clearing temperature). IR, cm^{-1}: 2957, 2918, 2850 (CH), 1588 ($C{=}C_{ar}$). NMR ^1H: 0.89 (t, 9H, J = 6.0 Hz, CH_3), 1.26 (m, broad, 48H, CH_2), 1.45 (m, 6H, CH_2), 1,77 (m, 6H, CH_2), 2,85 (s, broad, 4H, CH_2) 3.37 (s, broad, 11H, $N(CH_3)_3$+OCH_2), 3,77 (m, 6H, OCH_2), 3,96 (m, 10H, OCH_2+NCH_2), 4.83 (m, 2H, m, $C_{arom}CH_2$), 6.78 (s, 2H, $C_{arom}H$).

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