Ion-selective electrodes for determination of phenylalanine based on uranyl complexes of phosphoryl-containing podands

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The possibility of phenylalanine determination using membrane ion-selective electrodes based on uranyl complexes with phosphoryl-containing podands was shown. The variation of the procedure of membrane preparation (either entrapping the preliminarily synthesized uranyl—podand complex in the membrane phase or conditioning of the podand-containing membrane in the uranyl solution) was found to have practically no effect on the electrode properties.

Key words: ion-selective electrodes, phenylalanine, metallated carriers, uranyl nitrate, phosphoryl-containing podands.

In the last few years a series of studies on the use of macrocycles and their acyclic analogs, podands, for the determination of various organic substrates has appeared.[1,2] Thus, crown ethers and podands are known to fix compounds with protonated amino groups by hydrogen bonds as host—guest complexes and so can be used as the active components of the membranes of ion-selective electrodes (ISE).[3,4] However, in the case of highly hydrophilic organic guests, e.g., amino acids, it is difficult to achieve effective membrane transport and a reliable analytical signal, as these compounds are too hydrophilic.

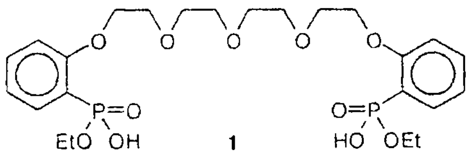
In our opinion, metal complexes with long-chain podands offer promise as reagents for fixing and determination of amino acids and other bifunctional compounds. If some O atoms of the podand polyether chain are not coordinated with the metal, they can fix the ammonium group of the substrate. If the metal ion is coordinationally unsaturated, it can fix the carboxyl group of the substrate. In the ideal case both types of interaction and effective blocking of the hydrophilic groups of the target compounds are feasible and create the prerequisite for effective membrane transfer.

The metal complex itself should be stable, electrically neutral, and highly soluble in organic solvents. The uranyl complexes of long-chain podands meet these demands.[5] The choice of uranyl as the central ion is dictated by its oxophilicity and high coordination potentialities.

We herein report a study on uranyl complexes with podands containing anionogenic or neutral phosphoryl-containing terminal groups as electrode-active components of phenylalanine-sensitive ISE membranes.

Experimental

Reagents and solutions. Phosphoryl-containing podands differing in oxyethylene chain length, 1,11-bis(2-(hydroxyethoxyphosphorylphenoxy)-3,6,9-trioxaundecane) (**1**), 1,14-bis(2-(hydroxyethoxyphosphorylphenoxy)-3,6,9,12-tetraoxatetradecane) (**2**), and 1,14-bis(2-(diphenylphosphorylphenoxy)-3,6,9,12-tetraoxatetradecane) (**3**), were synthesized in the Institute of Physiologically Active Compounds, Russian Academy of Sciences (Chernogolovka). Their purity was controlled by ^{1}H and ^{31}P NMR spectroscopy and elemental analysis.[6] *o*-Nitrophenyl octyl ether (NPOE) (reagent grade, Fluka) and dibutyl sebacate (DBS) (reagent grade, Fluka) were used as plasticizers. Sodium tetraphenylborate (STPB) and dodecylammonium bromide (DAB) were used as lipophilic components. Polyvinyl chloride (PVC) (Selectofor) was used as a polymeric binder for the membrane. The membrane components were dissolved in freshly distilled THF.[7] The solutions of phenylalanine hydrochloride (Phe) (reagent grade) were prepared by the weighing method with subsequent dilution with bidistilled water. The pH value was adjusted by addition of HCl and LiOH. The solution of uranyl



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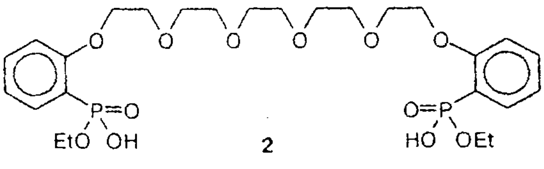

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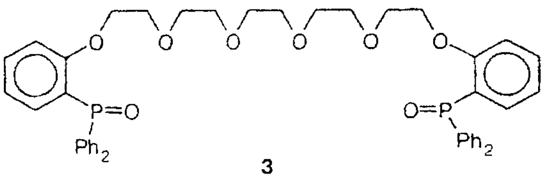

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nitrate was prepared by dilution of an exactly weighed portion of uranous-uranic oxide in HNO_3.

Film PVC-plasticized membranes were prepared by the solution of PVC, the plasticizer, and the carrier (podand) in THF with stirring according to the reported method.[8] The content of the neutral carrier in the membrane was 5% of the total mass; the PVC—plasticizer ratio was 1 : 1. A lipophilic component (2 mol.%) was introduced in some membranes.

Equipment and experimental technique. Electromotive force of the galvanic element composed of an ISE with a plasticized membrane fixed in the Teflon case (with 0.1 *M* solution under study as the inner filler and with an Ag/AgCl internal reference electrode) and an EVL-1MZ-1 Ag/AgCl reference electrode was measured by an I-130 pH meter. This instrument with an ESL-63-07 glass electrode was also used for pH control of the solutions.

Results and Discussion

We herein report the results of a study of the electrochemical characteristics of membranes based on uranyl complexes with acidic (containing anionogenic terminal groups) and neutral (containing phosphinoxide terminal groups) podands.

There are two variations of preparation of the membrane compositions based on the metal—podand complexes. The first method includes the preparative synthesis of the complexes (e.g., under extraction conditions) followed by their entrapping into the membrane. An organic phase containing $5 \cdot 10^{-3}$ mol · L^{-1} of a podand in chloroform was saturated with a uranyl nitrate solution with a concentration of $5 \cdot 10^{-4}$ mol · L^{-1}. The saturation was achieved by repeatedly shaking the organic phase with a fresh portion of the aqueous phase up to termination of uranium(VI) extraction (the content of uranium(IV) in the aqueous phase was controlled spectrophotometrically). These experiments showed that 10-fold saturation is necessary for quantitative binding of a podand. The organic phase was filtered off into a dry weighing bottle and kept up to complete evaporation of chloroform.

The second method includes introducing a free podand into the membrane phase and subsequent conditioning of the resulting membrane in the solution of a metal salt.

Preliminary experiments showed a negligible difference in the characteristics of ISE obtained by these two methods (see below). For the most part, we used the simpler second method.

The podand-based electrodes were kept for 48 h in a uranyl nitrate solution at pH 2.5. A lipophilic admixture (STPB), which is known to increase the membrane conductivity, prevent the penetration of anions from the solution under study, and enhance ion-exchange processes at the boundary of the two phases,[1] was introduced into the membrane to improve the ISE characteristics.

Electrodes based on uranyl-modified membranes containing acidic podands. The electrode based on acidic podand **1** with NPOE plasticizer demonstrates a cationic response for Phe in the acidic pH area. The steepness of the electrode function reaches the theoretical value (S = 57) at pH 6.25, the range of Phe concentrations being (10^{-2}—10^{-1}) mol · L^{-1}. Of course, the Phe concentrations, which can be determined, are too high for most practical applications. However, the fact of response is of importance by itself. It is even more interesting that in the pH range of 3—7 Phe exists mainly as an electrically neutral zwitterion, and the electric signal is likely connected with the presence in the solution of a markedly small part of the charged form. In this case, the response should be changed to anionic (in the solution the anionic form of the amino acid begins to prevail), when going to the basic range. As can be seen in Fig. 1, this actually is the case. At high pH values the steepness of the *anionic* electrode function approximates the Nernst value, and the range of determinable amino acid concentrations shifts to lower values. Further studies were performed at pH ~8.5.

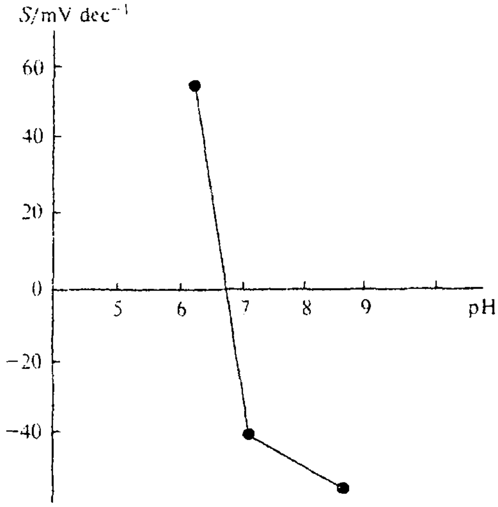

Fig. 1. pH-Dependence of the electrode function steepness.

The electrode based on podand **2** with six O atoms in the polyether chain is also Phe-sensitive, but the electrode characteristics are somewhat changed. Thus, the detection limit decreases, and linearity is observed in the

Table 1. The main characteristics of Phe-reversible ISE, pH = 8.5

EAC	Plasticizer	Steepness /mV dec^{-1}	Linearity interval	C_{min} /mol L^{-1}
1	NPOE	55	10^{-3}—10^{-1}	$5 \cdot 10^{-4}$
2	NPOE	32	10^{-5}—10^{-3}	$3 \cdot 10^{-6}$
2 [a]	NPOE	38	10^{-4}—10^{-2}	$4 \cdot 10^{-5}$
2 [a]	DBS	48	10^{-4}—10^{-2}	$5 \cdot 10^{-5}$
3	DBS	55	10^{-4}—10^{-2}	$5 \cdot 10^{-5}$
3 [b]	DBS	59	10^{-4}—10^{-2}	$5 \cdot 10^{-5}$
3 [b]	DBS	45	10^{-4}—10^{-3}	$4 \cdot 10^{-5}$

[a] With DAB as a lipophilic component.

[b] Membrane unmodified with uranyl.

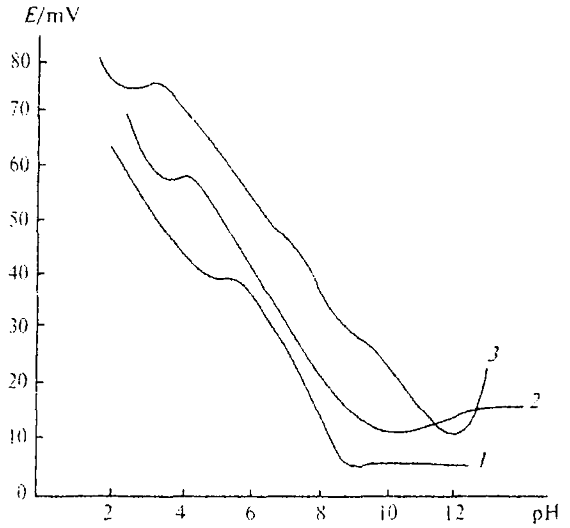

Fig. 2. pH-Dependence of the potential of ISE membranes based on (*1*) podand **2**, (*2*) podand **3**, and (*3*) podand **3** unmodified with uranyl in Phe solutions.

range of lower concentrations. However, the steepness of the electrode function falls (see Table 1).

The potential of the membrane based on compound **2** depends on pH in a sophisticated way (Fig. 2). pH-Dependence has two regions where the acidity does not affect the value of the membrane potential (in the pH range of 4.75—5.5 and at pH > 8.5). Introducing the cationogenic component (DAB) into the membrane phase based on compound **2** results in an increase of the steepness of the electrode function but at the same time causes increase of the detection limit.

Substantially, electrodes unmodified with uranyl display no response under these conditions.

Optimization of the membrane composition. We studied the plasticizer influence on the electrode properties of the membrane based on podand **2** with the lipophilic admixture. The experimental data attest that the use of DBS somewhat enhances the electrochemical characteristics of ISE (see Table 1).

Electrodes based on uranyl-modified membranes containing neutral podands. We also used more traditional guests, phosphoryl-containing podands with neutral diphenylphosphinoxide terminal groups, as electrode-active components of ISE.

The steepness of the electrode function of the uranyl-modified ISE with the membrane based on compound **3** plasticized with DBS was found to approach the Nernst value ($S = 55$) at pH ~8.5. When a lipophilic admixture (DAB) was introduced into the membrane phase, the theoretical value of the steepness was reached. It should be mentioned that the electrode with the membrane unmodified with uranyl also displays response in Phe solutions but has worse electrode characteristics (see Table 1).

The pH-dependence for the electrode based on compound **3** is similar to that of the electrode based on acidic podand. One can observe two plateau in the pH range of 3.3—4.2 and at pH > 9.0 (see Fig. 2). It is interesting to note that in the case of the electrode based on unmodified podand, a plateau is not observed in the region of high pH values, but there is an increase in the electrode potential. This is indirect evidence of the generation of metal complex in the first case and of its role in the formation of the analytical signal.

Electrodes based on preliminarily synthesized metal complexes. Podand metal complexes were prepared under the extraction conditions and were introduced in the membrane composition. Dodecylammonium bromide and sodium dodecyl sulfate (SDS) (10^{-3} mol L^{-1} solution) were used as the internal reference solutions. When DAB was used as the internal reference solution, the reproducibility of results was somewhat better than in the case of the membranes prepared by conditioning in uranyl solutions. The steepness of the electrode function was somewhat higher (it reproducibly reached the theoretical value $S = 56$), but the linearity range was markedly narrower [($2.5 \cdot 10^{-3}$—10^{-2}) mol L^{-1}].

Thus, we showed the possibility of using membranes based on metal complex carriers (uranyl-modified acidic or nonacidic podands) for Phe determination. We have also found that the difference in the methods of membrane preparation (entrapping the preliminarily prepared complex or conditioning the membrane in the uranyl nitrate solution) has practically no effect on the electrochemical characteristics. However, in the first case the reproducibility of results is somewhat higher.

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