Macrocyclic Amides as Ionophores for Lead-Selective Membrane Electrodes

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A series of ionophores based on diaza 18-crown-6 units possessing amide and sulfonamide functions were prepared. Their complexing properties were investigated in solvent polymeric membrane electrodes. The influence of the structure of ligands, prepared on the selectivity of complexation, was examined with special respect to lead ions. Substantial changes were observed, when methyl substituent in benzene rings was replaced with hydrogen, bromomethyl or nitro group. All results were rationalized on basis of steric and electronic effects.

Key words: membrane ion-selective electrodes, macrocyclic amides, lead selectivity

The synthesis and complexation studies of supramolecular compounds is of continuous interest [1]. Several types of ionophores were designed for medicine, biochemistry and environmental pollution monitoring [2]. For pollution monitoring some of ionophores, selective towards heavy metal cations, are of general interest. Previously, we have shown that macrocyclic polyether diamides can be readily prepared [3] and successfully applied in ion-selective electrodes [4], showing high selectivity towards Pb²⁺ over other divalent cations. This result prompted us to the conclusion that the introduction of external amide function into the macrocyclic ring can increase the stability of electrodes and improve the complexing properties of ionophores towards divalent cations.

This paper deals with the preparation of a series of external macrocyclic diamides derived from diaza-18-crown-6. Complexing properties of prepared compounds were investigated in ion-selective polymeric membranes system with a special respect to lead cation.

RESULTS AND DISCUSSION

The synthesis of ionophores used in the complexation studies are presented in Scheme 1. Synthetic strategy was based on the functionalization of diaza-18-crown-6 (1) with aromatic acyl chlorides 2 possessing different functional groups. Crude products obtained were purified by chromatography and/or crystallization.
Macrocyclic amides of structure 3 were obtained in 50–88% yield. All compounds possess 18-crown-6 ether rings with two nitrogen and four oxygen atoms and they differ from each other in the phenyl substituents. The presence of various substituents on the phenol groups can be used for ligand structure optimization in order to achieve the highest selectivity towards lead cation. Selectivities of the membranes, containing the investigated ligands 3, were determined by the separate solution method (SSM) using 0.1 M solutions of metal nitrate (see Experimental). The logarithmic values of the selectivity coefficients (expressed as log K_{Pb,M}) are summarized in Figure 1. For comparison, the results for blank membrane (without ionophore) are presented in column 0.

Enhanced selectivity for lead ion over other divalent and some monovalent cations was clearly observed for all ionophores, except ionophore 3e, as compared with the blank membrane. Ligand 3e, with two nitro groups, does not affect the membrane selectivity. This compound can be compared to benzamides: 3a and 3d, whose structures are shown in Scheme 1. The presence of different substituents in para position in benzene rings can influence the complexing properties of ionophores, predominantly due to steric and/or electronic effects. In this case, steric effects can be neglected, since different substituents occur relatively far from the recognition center. Electronic effects of functional groups can decrease or increase the electron density on amide oxygen atoms, decreasing the complexing abilities of ionophores. Nitro groups in compound 3d decrease the difference in selectivity, as compared to blank electrode selectivity. Ionophore 3e with two nitro groups per benzene ring is even worse in this respect. This indicates that such a substitution decreases the electron density on amide oxygen atom and these atoms are no longer involved in the recognition process. Recognition, based predominantly on the ethereal oxygen atoms, is not sufficient for a successful selective complexation, observed as a high selectivity towards specific cations.
From the other hand, methyl groups present in para position of benzene in ionophore 3b should increase the electron density on amide oxygen atom and improve the complexing behaviour of ionophore. This result is clearly observed in Figure 1 for compounds 3a and 3b, where the introduction of the methyl group enhances the membranes selectivity. For electrode with ionophore 3c possessing p-bromo-methyl groups, the highest selectivity towards lead was observed. This electrode is much more selective towards lead than towards sodium or potassium ions. It is possible that bromomethyl substituents modify the electron density on amide oxygen in the best way for the desired selective complexation of the lead ion. Such an interaction previously mentioned in [5] is fully supported by our data.

Figure 1. Selectivity coefficients, log $K_{Pb,M}$, for PVC-membranes with $\alpha$-NPOE (as a plasticizer) and KTpCIPB (70 mol-%). The blank membrane (column 0) is compared to membranes containing the ionophores 3a–e.

Electrodes with ionophores exhibit a linear response within the activity range $10^{-4.5}$–$10^{-1.7}$ M in Pb(NO$_3$)$_2$ solutions (in presence of 0.1 M NaNO$_3$) with the slope of 25–30 mV decade$^{-1}$ (see Figure 2). For electrodes based on ionophores 3d and 3e a poor response for lead cation was observed, what is consistent with the selectivity coefficient studies. The life-time (i.e. reproducible selectivities and performances in time) of the electrodes, based on membranes containing ionophores 3a–3c, does not exceed 2 weeks, due to the relatively low lipophilicity of ionophores. The present results regarding the selectivities of the tested membranes and consequently their abil-
The best result obtained for ionophore 3c, in comparison to similar compounds (3a, 3b), suggests that recognition processes in polymeric membranes are strongly dependent on the nature of substituents in the para position of benzoyl group. Selective functionalization of this position is responsible for stabilities of polymeric membrane electrodes via introduction of long alkyl chain. Also cation selectivity sequence
of electrodes may be easily modified via substitution of benzamide group. The selectivity coefficients of the membranes, based on studied macrocyclic amides, are similar to those reported earlier for membranes containing acyclic [6] and cyclic oxo-amides [4]. In these cases, high lead selectivity over transition metal ions was also observed (log $K_{\text{Pb,M}} < -3$). However, the selectivity of amides derivatives for lead against monovalent cations was lower than that obtained for acyclic oxamides [6] and thioamide functionalized calix[4]arenes [7,8].

**EXPERIMENTAL**

**General.** Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. $^1$H NMR spectra were recorded using a Varian 200 Gemini spectrometer in CDCl$_3$ or CDCl$_3$/C$_6$D$_6$ with TMS as an internal standard. Liquid SIMS spectra were determined on an AMD 604 spectrometer (Cs$^+$, 10 keV).

**Synthesis of diacylaza-18-crown-6. General synthetic procedure:** To the intensively stirred, cooled to 5°C (ice bath) solution of crown 1 (0.624 g, 2 mmol) in methylene chloride (25 ml), containing triethylamine (0.2529 g, 2.5 mmol), a solution of the respective acyl chloride (2.1 mmol) in chloroform (5 ml) was added slowly, while keeping the temperature below 10°C. The solution was stirred at room temperature for 1 h. Water (5 ml) was added followed by 3% sodium hydroxide solution to reach pH 11. Aqueous phase was extracted with chloroform (3×30 ml) and the organic phases were combined and dried (MgSO$_4$). In most cases, pure products were purified by column chromatography on silica gel using chloroform-methanol solvent mixture (95:5, v/v).

**Crown 3a:** $R = -\text{H}$, yield 87%. $^1$H NMR (CDCl$_3$): 3.46–3.65 (16H, m, -OCH$_2$CH$_2$), 3.79 (8H, brs, -OCH$_2$), 7.37 (5H, brs, ArH). $^{13}$C NMR (CDCl$_3$): 46.2, 49.8, 69.8, 70.5, 126.5, 128.2, 128.5, 129.9, 136.6, 172.1. Anal. Caled. for C$_{26}$H$_{34}$N$_2$O$_6$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.35; H, 7.13; N, 5.69.

**Crown 3b:** $R = -\text{4-CH}_3$, yield 88%. $^1$H NMR (CDCl$_3$): 2.36 (6H, s, CH$_3$), 3.45–3.76 (24H, m, -CH$_2$), 7.17, 7.27 (4H, d, J$_{\text{AB}}$ = 8.0, ArH). $^{13}$C NMR (CDCl$_3$): 21.3, 46.2, 46.3, 69.9, 70.6, 126.6, 129.0, 133.8, 139.9, 172.3. EI-Ms m/z 497 ([M-H]$^+$, 2%), 436 (2%), 379 (5%), 250 (12%), 162 (13%), 119 (100%). HR-MS m/z 497.2649 (497.2652 calcd for C$_{28}$H$_{38}$N$_2$O$_6$, [M-H]$^+$).

**Crown 3c:** $R = -\text{4-CH}_2\text{Br}$, yield 83%, m.p. 144–145°C. $^1$H NMR (CDCl$_3$): 3.50–3.66 (16H, m, -NCH$_2$), 3.77–3.80 (8H, m, -OCH$_2$), 4.48 (4H, s, -CH$_2$Br), 7.35, 7.40 (4H, d, J$_{\text{AB}}$ = 8.0, ArH). EI-Ms m/z 655 ([M]$^+$, 1%), 577 (13%), 575 (13%), 118 (100%). Anal. Caled. for C$_{28}$H$_{36}$N$_2$O$_6$Br$_2$: C, 51.23; H, 5.53; N, 4.27. Found: C, 51.11; H, 5.90; N, 4.09.

**Crown 3d:** $R = -\text{4-NO}_2$, yield 67%, m.p. 155–158°C. $^1$H NMR (CDCl$_3$): 3.48–3.82 (24H, m, -OCH$_2$), 7.57, 8.25 (4H, d, J$_{\text{AB}}$ = 8.6, ArH). $^{13}$C NMR (CDCl$_3$): 46.3, 49.9, 69.5, 70.6, 123.7, 127.8, 142.7, 148.1, 169.9. Anal. Caled. for C$_{26}$H$_{32}$N$_4$O$_{10}$: C, 55.71; H, 5.85; N, 9.99. Found: C, 55.59; H, 5.91; N, 9.81.

**Crown 3e:** $R = -\text{3,5-(NO}_2)_2$, yield 57%. $^1$H NMR (CDCl$_3$): 3.41–3.80 (24H, m, -OCH$_2$), 7.87, (2H, s, ArH), 8.99 (1H, s, ArH). $^{13}$C NMR (CDCl$_3$): 46.4, 49.4, 69.9, 71.6, 124.7, 128.8, 146.9, 149.9, 168.8. EI-Ms m/z 650 ([M]$^+$, 8%), 633 (32%), 608 (14%), 454 (12%), 381 (16%), 326 (38%), 238 (56%), 195 (100%). HRMS m/z 650.1818 (650.1820 calcd for C$_{26}$H$_{30}$N$_6$O$_{16}$, [M]$^+$). Anal. Caled. for C$_{26}$H$_{30}$N$_6$O$_{16}$: C, 48.00; H, 4.65; N, 12.92. Found: C, 47.45; H, 4.96; N, 12.96.

**Chemicals:** All inorganic salts used were of analytical grade and were purchased from POCH Gliwice, Poland. The standard stock solutions (0.1 M) of metal nitrates were prepared in redistilled water; working solutions were obtained by dilution of the stock solution with redistilled water. pH was adjusted by the addition of nitric acid, sodium hydroxide or ammonia solutions.
Membrane materials: High molecular weight poly(vinylchloride) (PVC), potassium tetrakis(p-chlorophenyl) borate (KTpClPB) and o-nitrophenyl octyl ether (o-NPOE) were obtained from Fluka, Buchs, Switzerland. As a solvent for membrane component, freshly distilled tetrahydrofuran (THF) p.a. (P.O.Ch. Gliwice) was used.

Membrane and electrode preparation: The membrane contained 1% ionophore, 30% m/m PVC, 70 mol-% KTpClPB (relative to the ionophore), and 67–69% m/m plasticizer. The membrane components, total 200 mg were dissolved in 2 ml of freshly distilled tetrahydrofuran. This solution was placed in a glass ring of 24 mm i.d. placed on a glass plate. After solvent evaporation overnight, the resulting membrane was peeled off from the glass mould and discs of 7 mm i.d. were cut out. Membrane discs were mounted in electrode bodies (Type IS 561; Philips, Eindhoven, The Netherlands) for electromotive force (EMF) measurements. As internal filling solution $5 \times 10^{-3}$ M PbCl$_2$ was used. The electrodes were conditioned overnight in a solution of $10^{-1}$ M Pb(NO$_3$)$_2$. For each membrane composition two electrodes were prepared.

Potentiometric measurements: All measurements were carried out at 20°C with cells of the following type: Ag; AgCl; KCl (0.1 M)/KCl (0.1 M)/sample solution//sensor membrane//internal filling solution; AgCl; Ag. The EMF were measured using a custom made 16-channel electrode monitor. Details of this equipment were published [9]. The EMF of the electrodes in each solution were measured every 20 s during 10 min. The mean value of the final five measurements was taken for further calculations. Potentiometric selectivity coefficients, $K_{\text{Pb,Me}}$, were determined by the separate solution method [10], using $10^{-1}$ M solutions of metal nitrates at a constant pH = 4. The activities of metal ions in aqueous solutions were taken by Debye-Huckel approximation [11]. The performances of the electrodes were examined by measuring EMF of the primary ion solutions within the concentration range $10^{-8}$–$10^{-1}$ M in 0.1 M NaNO$_3$.

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