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Pyrrole Azocrown Ethers. Synthesis, Complexation, Selective Lead Transport and Ion-Selective Membrane Electrode Studies

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New 21-membered lipophilic crown ethers, each incorporating a pyrrole unit and two azo groups as macrocyclic ring components, have been synthesized. The complexation behavior of these and two further macrocycles has been investigated in acetonitrile. These ligand systems have been employed as ionophores in transport experiments involving the competitive transport behavior of an equimolar mixture of Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Ag^{+} and Pb^{2+} across a water (pH 4.9)/chloroform/water (pH 3) bulk membrane system. In each case transport selectivity for lead(II) was obtained. The macrocycles have been incorporated in solvent polymeric membrane electrodes and their behavior towards a selection of metal ions, including those mentioned above, is reported.

Keywords: Pyrrole macrocycles; Azocrown compounds; Synthesis; Complexation; Lead transport; Ion-selective electrodes

INTRODUCTION

Polyfunctional molecules that combine dyes and polyether residues to form crown ether analogs represent one category of chromoionophores. Such compounds undergo color changes on complexation with metal ions and are potentially useful as direct metallochromic reagents or as the sensing elements in integrated optochemical sensors. In previous studies such reagents have mainly incorporated hydroxyazobenzene residues along with polyoxyethylene bridges in their structures [1]. Recently, we have described the synthesis and properties of 18- and 21-membered azomacrocyclic chromoionophores (compounds **1** and **2**) that contain a pyrrole residue [2]. In these compounds the pyrrole moiety replaces the phenol residue used previously [3,4]. It was found that in acetonitrile the 18-membered pyrrole derivative **1** (Fig. 1, [2]) binds Ca^{2+}, Sr^{2+} and Ba^{2+} among the alkaline earth cations to induce a spectral change; in contrast, no spectroscopic responses were obtained for the alkali metal cations or for magnesium. The highest stability was found for the strontium complex ($\log K = 3.71$ [2], strontium ionic radius 1.13 Å). Spectroscopically, 21-membered pyrrole derivative **2** (Fig. 1, [2]) was observed to form complexes only with potassium and barium among the alkali and alkaline earth cations.

It is expected that the presence of a pyrrole residue and two azo units (that are an integral part of a macroring) will increase the susceptibility of a crown system towards the binding of transition/heavy metal cations.

An aim of the present study was to investigate the complexation behavior of the pyrrole azocrown ethers **1–4** towards selected transition and heavy metal cations as well as to explore their use as ionophores for metal ion transport across bulk liquid membranes. The lipophilicity of the ionophore is an important factor influencing the efficiency of such a transport system. The 21-membered ionophores **3** and **4** (Fig. 1) were synthesized in an attempt to obtain systems of enhanced lipophilicity relative to **2**. Transport of the following cations Pb^{2+}, Ag^{+}, Cu^{2+}, Cd^{2+}, Co^{2+}, Ni^{2+}, and Zn^{2+} was studied using bulk membranes doped with macrocycles **1–4**. These

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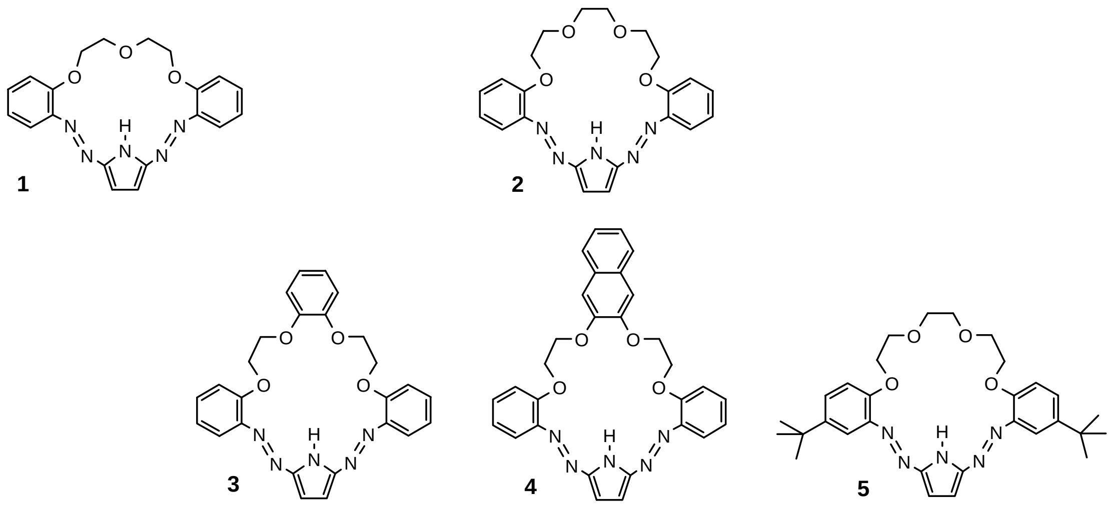


FIGURE 1 Structures of macrocycles studied.

were also employed as ionophores in ion-selective membrane electrodes (ISEs) (compound **5** was also subsequently prepared for use in these latter studies when it was observed that its less lipophilic analogue, **2** showed a tendency to crystallize in the membrane).

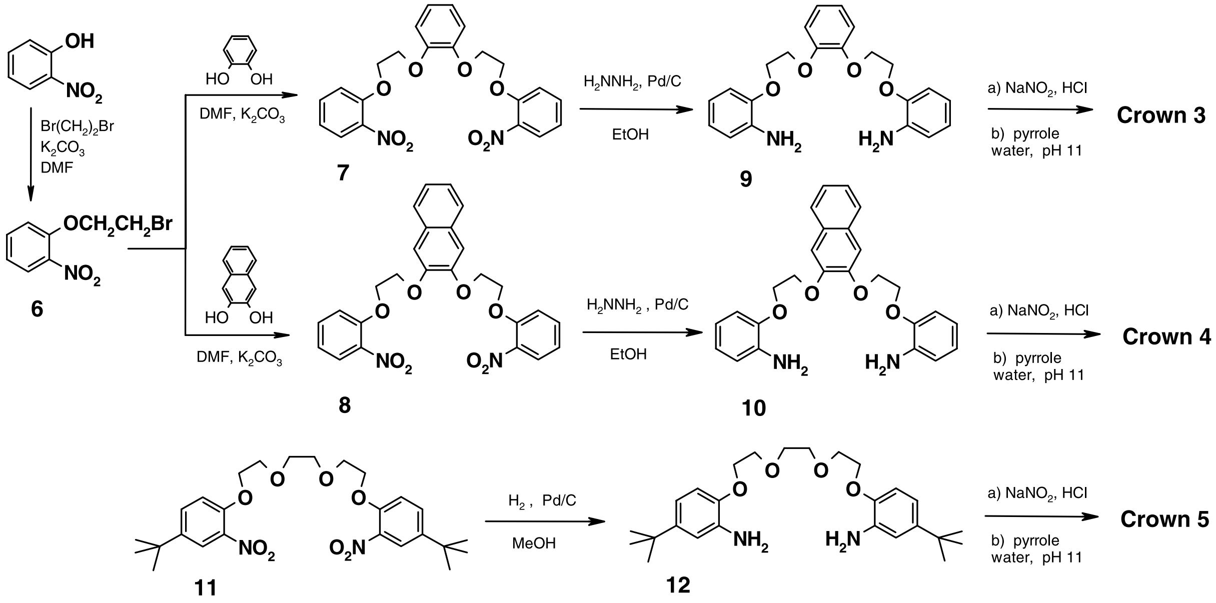
EXPERIMENTAL

General

All materials and solvents used were of analytical reagent grade. Aluminium plates covered with Silica gel 60 F_{254} (Merck) were used for TLC chromatography. NMR spectra were recorded on a Varian instrument at 500 MHz working frequency. Mass spectra were taken on an AMD-604 spectrometer. UV–Vis spectra were recorded on a Unicam UV-300 spectrophotometer in acetonitrile (HPLC grade). IR spectra were registered using a Genesis II (Mattson) instrument. All aqueous solutions for electrode characterization and for transport experiments were prepared with salts of p.a. purity using distilled-deionized water. Atomic absorption spectroscopic measurements were carried out on Varian SpectrAA-800 instrument.

Syntheses

Compounds **1** and **2** were obtained as described previously [2]. The syntheses of compounds **3–5** were performed as shown in Scheme 1.



SCHEME 1 Synthesis of crowns **3–5**. The final step in each case involved formation of a bis-diazonium intermediate.

1-(2-Bromoethoxy)-2-nitrobenzene 6

A mixture of *o*-nitrophenol (10 g, 72 mmol), dibromoethane (40 g, 215 mmol) and anhydrous potassium carbonate (20 g) in dimethylformamide (50 cm^3) was stirred and heated at 60°C for 4 h. The mixture was diluted with water and the insoluble organic components were dissolved in methylene chloride. The organic phase was evaporated and the residue was dissolved in a hot mixture of methylene chloride and hexane. The small amount of bis(2-nitrophenoxy)ethane remaining was filtered off and the filtrate was evaporated. The crude product was purified by column chromatography applying methylene chloride–hexane (1:3) mixture as eluent and was finally crystallized from a small amount of hexane at low temperature. Yield 89%, mp 39–40°C. Lit. mp 40°C [5]; 36–38°C [6]. TLC (methylene chloride) $R_F = 0.87$.^1H NMR ($CDCl_3$), δ [ppm]: 3.68 (2H, t, $J = 6.4$ Hz); 4.42 (2H, t, $J = 6.4$ Hz); 7.07–7.12 (2H, m); 7.54 (1H, t, $J = 7.8$ Hz); 7.84 (1H, dd, $J_1 = 8.3$ Hz, $J_2 = 1.4$ Hz).

1,2-Bis[2-(2-nitrophenoxy)ethoxy]benzene 7

A mixture of catechol (0.72 g, 6 mmol), K_2CO_3 (3 g), 1-(2-bromoethoxy)-2-nitrobenzene **6** (5 g, 20 mmol), and dimethylformamide (10 cm^3) was stirred at 75°C for 24 h. The mixture was diluted with water; the precipitate was collected, washed with water and cold ethanol. The crude product was crystallized from methanol. Yield 94%, mp 126–128°C (lit. mp. 128–130°C [7]; cf. [8]). TLC: $R_F = 0.55$ (methylene chloride). ^1H NMR ($CDCl_3$), δ [ppm]: 4.42–4.56 (8H, m); 6.98–7.05 (6H, m); 7.19 (2H, d, $J = 8.3$ Hz); 7.52 (2H, dt, $J_1 = 8.8$ Hz, $J_2 = 1.5$ Hz); 7.81 (2H, dd, $J_1 = 7.8$ Hz, $J_2 = 1.5$ Hz).

2,3-Bis[2-(2-nitrophenoxy)ethoxy]naphthalene 8

A mixture of 2,3-dihydroxynaphthalene (0.8 g, 5 mmol), 1-(2-bromoethoxy)-2-nitrobenzene **6** (2.5 g, 10 mmol), K_2CO_3 (2 g) and dimethylformamide (8 cm^3) was stirred and heated at 90°C for 4 h. The mixture was then diluted with water; the precipitate was separated, washed with water and next with methanol. Yield 2.33 g (95%), mp 169–170°C. TLC: $R_F = 0.61$ (CH_2Cl_2). ^1H NMR (DMSO-d_6), δ [ppm]: 4.42–4.55 (8H, m); 7.08 (2H, t, $J = 7.8$ Hz); 7.31–7.35 (2H, m); 7.41 (2H, s); 7.46 (2H, d, $J = 8.3$ Hz); 7.59 (2H, t, $J_1 = 7.8$ Hz, $J_2 = 1.5$ Hz); 7.71–7.75 (2H, m); 7.82 (2H, dd, $J_1 = 8.3$ Hz, $J_2 = 1.5$ Hz). IR (nujol): 1607, 1520, 1350, 1281, 1251, 1164, 1055, 940, 856, 739 cm^{-1}. HRMS [EI]: Found 490.1371; $C_{26}H_{22}O_8N_2$ requires 490.1376.

1,2-Bis[2-(2-aminophenoxy)ethoxy]benzene 9

To a boiling mixture of podand **7** (2.5 g, 5.7 mmol), ethanol (60 cm^3) and Pd/C catalyst, six portions, each of 0.5 cm^3 of 98% hydrazine hydrate was added in 30 min. intervals. Boiling was continued for 4 h and the reaction progress was monitored by TLC. Finally the catalyst was removed and the diamine was crystallized from ethanol. Yield 56%, mp 109–111°C. TLC: $R_F = 0.68$ (methylene chloride – acetone 10:1). ^1H NMR ($CDCl_3$), δ [ppm]: 3.81 (4H, bs); 4.34–4.39 (8H, m); 6.66–6.73 (4H, m); 6.82–6.88 (4H, m); 6.96–7.01 (4H, m). IR (nujol): 3477, 3445, 3379, 3362, 1613, 1505, 1222, 1128, 1056, 931, 735 cm^{-1}.

2,3-Bis[2-(2-aminophenoxy)ethoxy]naphthalene 10

Hydrazine hydrate (98%, 2 cm^3) was added portionwise (0.5 cm^3, each portion at 30 min. intervals) to a suspension of nitropodand **8** (2.4 g, 4 mmol) and Pd/C catalyst in boiling ethanol (40 cm^3). After the reaction was complete (TLC), the hot mixture was filtered and the solid residue was washed with hot ethanol and with chloroform. The combined filtrates were concentrated and allowed to stand whereupon the product crystallized. Yield 1.45 g (85%), mp 165–166°C. TLC: $R_F = 0.38$ (methylene chloride – acetone 30:1). ^1H NMR ($CDCl_3$), δ [ppm]: 3.88 (4H, bs); 4.41–4.51 (8H, m); 6.78–6.80 (4H, m); 6.82–6.87 (2H, m); 6.89–6.93 (2H, m); 7.27 (2H, s); 7.33–7.37 (2H, m); 7.66–7.70 (2H, m). IR (nujol): 3459, 3357, 1617, 1503, 1264, 1211, 1173, 1116, 1053, 945, 864, 740 cm^{-1}.

1,8-Bis(2-amino-4-t-butylphenoxy)-3,6-dioxaoctane 12

The amine was obtained by reduction of 1,8-bis(2-nitro-4-*t*-butylphenoxy)-3,6-dioxaoctane **11** [9] with hydrogen using Pd/C catalyst in methanol. The reaction was carried out for 8 h at room temperature . The product was purified by column chromatography using methylene chloride-acetone (10:1) mixture as eluent. Yield, 88% of an oily product. TLC: $R_F = 0.19$ (methylene chloride–acetone 10:1). ^1H NMR ($CDCl_3$): 1.28 (18H, s); 3.75 (4H, s); 3.86 (4H, t, $J = 4.8$ Hz); 3.92 (4H, bs); 4.15 (4H, t, $J = 4.8$ Hz); 6.70–6.80 (6H, m). IR (film): 3455, 3363, 2958, 2925, 2897, 1614, 1517, 1455, 1428, 1393, 1362, 1293, 1253, 1142, 1079, 942, 865, 798 cm^{-1}.

Pyrrole Azocrown Ether 3

Solution A. Conc. hydrochloric acid (1 cm^3) was added to a suspension of diamine **9** (0.76 g, 2 mmol) in water (40 cm^3). An ice-cooled solution of sodium nitrite (0.28 g, 4 mmol) in water (2 cm^3) was added to the above (cooled) suspension of hydrochloride. The mixture was allowed to stand for 15 min at 5°C.

Solution B. Pyrrole (0.14 cm^3, 2 mmol) and sodium hydroxide (0.2 g) were dissolved in a mixture of 40 cm^3 water and 2 cm^3 ethanol.

Cold solutions *A* and *B* were added drop by drop with the same rate over 45 min. to a vigorously stirred water solution (600 cm^3) adjusted to pH ~ 11 with NaOH. Stirring was continued overnight (the pH was maintained during the initial stages of this coupling procedure). During the first 4 h the temperature was maintained at 5–10°C and was then allowed to rise to 20°C. The reaction mixture was cooled to 5°C, adjusted to pH ~6 with acetic acid and the precipitate that formed collected. The crude product was purified by column chromatography using methylene chloride initially and then a methylene chloride–acetone (30:1) mixture as eluent. Yield 30%, mp 206–208°C (crystallized from propan-2-ol). TLC: $R_F = 0.4$ (toluene – ethyl acetate 5:1). ^1H NMR (acetone-d_6), δ [ppm]: 4.60–4.72 (8H, m); 6.92–6.96 (2H, m); 7.07–7.17 (6H, m); 7.42 (2H, d, $J = 8.3$ Hz); 7.49 (2H, dt, $J_1 = 8.1$ Hz, $J_2 = 1.5$ Hz); 7.78 (2H, dd, $J_1 = 8.3$ Hz, $J_2 = 1.5$ Hz); 12.30 (1H, s). IR (nujol): 3437, 1580, 1379, 1237, 1057, 934, 750 cm^{-1}. UV–Vis (acetonitrile): $\lambda_{max} = 500$ nm, $\varepsilon_{max} = 2.3 \times 10^4$. HRMS [EI]: Found 469.17465; $C_{26}H_{23}N_5O_4$ requires 469.17500.

Pyrrole Azocrown 4

Crown **4** was prepared analogously to **3** starting from bisamine **10**. The crude product was purified by column chromatography using methylene chloride–acetone (30:1) mixture as eluent. The chromatographic separation was repeated and the product was crystallized from propan-2-ol. Yield 15%, mp 227–229°C. TLC: $R_F = 0.82$ (methylene chloride – acetone 50:1). ^1H NMR (acetone-d_6), δ [ppm]: 4.70–4.74 (4H, m); 4.79–4.82 (4H, m); 7.08 (2H, t, $J = 7.6$ Hz); 7.16 (2H, s); 7.30–7.33 (2H, m); 7.37 (2H, d, $J = 8.3$ Hz); 7.47 (2H, s); 7.47–7.52 (2H, m); 7.71–7.74 (2H, m); 7.76 (2H, dd, $J_1 = 7.8$ Hz, $J_2 = 1.6$ Hz); 12.36 (1H, bs). IR (nujol): 3610, 1590, 1260, 1122, 950, 742 cm^{-1}. UV–Vis (acetonitrile): $\lambda_{max} = 498$ nm, $\varepsilon_{max} = 2.0 \times 10^4$. HRMS [EI]: found 519.18830, $C_{30}H_{25}N_5O_4$ requires 519.19065.

Pyrrole Azocrown Ether 5

The synthesis was performed by an analogous method to that used to synthesize **3** or **4** starting from **12**.The coupling reaction was carried out over 2 h at 10°C and 2 h at room temperature. The product was isolated by column chromatography using a methylene chloride-acetone (30:1) mixture as eluent. It was crystallized from acetone/hexane. Yield 13%, mp 159–161°C. TLC: $R_F = 0.46$ (methylene chloride – acetone 50:1). ^1H NMR ($CDCl_3$): 1.35 (18H, s); 3.88 (4H, s); 3.95–4.02 (4H, m); 4.30–4.37 (4H, m); 6.96 (2H, d, $J = 8.8$ Hz); 7.19 (2H, s); 7.41 (2H, dd, $J_1 = 8.3$ Hz, $J_2 = 1.95$ Hz); 7.80 (2H, d, $J = 1.95$ Hz); 12.47 (1H, bs). IR (nujol): 3583, 3493, 1599, 1500, 1259, 1214, 1180, 1139, 1106, 1024, 952, 899, 723 cm^{-1}. UV–Vis (acetonitrile): $\lambda_{max} = 508$ nm, $\varepsilon_{max} = 1.4 \times 10^4$. HRMS [EI]: Found 533.29929; $C_{30}H_{39}N_5O_4$ requires 533.30021.

Competitive Mixed-metal Transport Experiments

Bulk membrane transport experiments were carried out exactly as described elsewhere [10]; the aqueous source phase was buffered at pH 4.9 ± 0.1 (10 cm^3; acetic acid/sodium acetate buffer) and contained a mixture of cobalt(II), nickel(II), copper(II), zinc(II), cadmium(II), silver(I) and lead(II) nitrates, each at concentration of 10^{-2} mol dm^{-3}. The chloroform phase (50 cm^3) contained the pyrrole azocrowns **1**, **2**, **3**, or **4** (1×10^{-3} mol dm^{-3}) and hexadecanoic acid (4×10^{-3} mol dm^{-3}). The receiving phase (30 cm^3) was buffered at pH 3.0 ± 0.1 (formic acid/sodium formate buffer). Transport experiments were terminated after 24 h and atomic absorption spectroscopy was used to determine the amount of metal ion transported over this period. The average results of two independent runs are shown in Table I, with individual values being typically within ±5% of the mean value.

Spectrophotometric Studies of the Complexation of Metal Cations with Macrocycles 1–4 in Solution

A representative set of semi-quantitative complex formation experiments were performed in acetonitrile. UV–Vis titration was carried out by addition of metal perchlorate to the crown ether solution. The composition of species under equilibrium was determined using Job's (continuous variation) method [11]. The UV–Vis titration data analysis was performed with the OPIUM program [12] .

Ion-selective Membrane Electrodes

The solvent polymeric membranes evaluated for ion response are composed of ionophore (**1**–**5**) 1.5 mg, potassium tetrakis-*p*-chlorophenylborate (KTpClPB) 0.75 mg, plasticizer (*o*-nitrophenyl-octyl ether– *o*-NPOE, bis-butylpentyl adipate–BBPA or bis-ethylhexyl phthalate – DOP) 0.1 cm^3 and 50 mg PVC. The membrane components were dissolved in

TABLE I Average fluxes of metal cations promoted by crown ethers **1**–**4**

Ligand	Average fluxes $J^* 10^7$, mol/24 h						
	Pb	Ag	Cu	Cd	Co	Ni	Zn
1	15.0	1.5	0.5	0.1	0.5	0.4	0.3
2	32.9	1.1	1.65	0.1	0.5	0.5	0.55
3	25.8	1.25	1.35	0.1	0.55	0.35	0.4
4	21.1	12.8	0.25	0.15	2.1	0.55	0.75

TABLE II Stability constants of crown ethers **1–4** complexes with lead(II) in acetonitrile at 25 ± 0.5°C

Crown ether	**1**	**2**	**3**	**4**
Log K	18.1 ± 0.01	21.1 ± 0.09	18.3 ± 0.01	19.5 ± 0.04

freshly distilled THF (2 cm^3). This solution was placed in a glass ring (15 mm i.d.) over a glass plate. After evaporation of the solvent overnight, the resulting membrane was peeled from the glass mold and discs of 7 mm diameter were cut out. These membrane discs were mounted in conventional ISE electrode bodies (IS 561 type; SPR Moeller) for EMF measurements. A Radelkis OP-08201 reference electrode was employed and various bridging electrolytes.

All measurements were performed at ambient temperature (20°C) using a galvanic cell of the following form:

$Ag|AgCl_{(s)}|1\,M\ KCl|$ bridge electrolyte|sample| ion-selective membrane| internal electrolyte| $AgCl_{(s)}|Ag$.

The bridge electrolytes were: 0.1 M KNO_3 for electrodes with *o*-NPOE or DOP plasticizers and 1 M NH_4NO_3 for electrodes with BBPA.

The composition of the internal electrolyte is shown in Table III. Electrodes were conditioned in 10^{-2} M $Pb(NO_3)_2$ solution for 2 days, then soaked for 1 h in HNO_3 solution (pH 5.0) before undertaking measurements. All measurement were performed using a sample pH of 5.3 ± 0.1 (adjusted with HNO_3). The selectivity coefficients were determined using the SSM method [13] at $a = 10^{-3}$ M.

RESULTS AND DISCUSSION

Previously macrocycle mediated transport experiments [14] have had as their focus silver/lead discrimination – metals that occur together in nature [15,16]. From an environmental point of view ideally Zn^{2+} should not compete with the removal of Pb^{2+} (or Cd^{2+}) [17]. Indeed, highly selective separation of lead in the presence of zinc has been achieved using *tetrakis*-(carboxymethyl)- *tetrakis*-(*p-tert*-octyl)calix[4]arene [18]. In another study, preferred transport of lead over cadmium and zinc employing polymer inclusion membranes doped with calix[4]-crown-6 derivatives has also been observed [19]. High Pb^{2+} transport selectivity over Fe^{3+}, Cu^{2+} and Zn^{2+} has been reported for binary metal systems containing equimolar ratios of lead and the competing cations using dicyclohexano-18-crown-6, dithia-18-crown-6 or diketopyridino-18-crown-6 as ionophores [20]. Contrary to the above observations, lead transport has been shown to be less efficient for systems employing neutral thia- and azacrown ethers relative to other transition and post-transition metal cations [21].

Our competitive transport experiments were performed as described [10] using **1–4** (Fig. 1) as the ionophores. Palmitic acid was added to the chloroform membrane in four-fold excess (4×10^{-3} mol dm^3) relative to the concentration of crown ether (10^{-3} mol dm^3) present. The presence of the palmitic acid avoids the need to co-transport nitrate ion from the aqueous source phase (the palmitic acid loses a proton to the aqueous phase). Palmitic acid at the above concentration in the absence of macrocycle has been shown not to transport any of the metals listed in Table I [10]. Normally, we have arbitrarily chosen a flux of 20×10^{-7} mol/24 h as the value below which experimental error means that a given result is uncertain. The experimental values for cations (Cu, Cd, Co, Ni, Zn) other than lead are all much lower then the 20×10^{-7} limit while the value for silver is only marginally lower for system employing **4**.

Under the conditions employed compounds **2**, **3**, and **4** are moderately effective ionophores for Pb^{2+} relative to the other metal ions present. The respective lead(II) fluxes are 33, 26 and 21×10^{-7} mol/24 h while **1** transports this ion to a lesser extent ($\sim 15 \times 10^{-7}$ mol/24 h). It is noted that monovalent silver (ionic radius 1.26 Å) is negligibly transported by **1**, **2**, and **3**. However, in the absence of further studies it appears inappropriate to speculate about the reason for this behavior.

TABLE III Plasticizers, internal electrolytes, linear responses and slopes for electrodes based on compound **2**, **3** and **5**

Electrode number	Ionophore (plasticizer)	Internal electrolyte [mol dm^{-3}]	Range of linear response [log a]	Slope /decade [mV]
2A	**2** (NPOE)	$PbCl_2$ 5×10^{-3}	−6.0 – −1.8	34.2
2B	**2** (BBPA)	$PbCl_2$ 5×10^{-3}	−5.0 – −2.6	25.0
2C	**2** (DOP)	KCl 10^{-2}	−6.0 – −2.0	32.0
3A	**3** (NPOE)	$PbCl_2$ 5×10^{-3}	−5.5 – −1.8	32.2
3B	**3** (BBPA)	$PbCl_2$ 5×10^{-3}	−5.5 – −2.6	30.0
3C	**3** (DOP)	KCl 10^{-2}	−5.0 – −1.8	31.0
5A	**5** (NPOE)	$PbCl_2$ 5×10^{-3}	−5.0 – −1.8	28.5

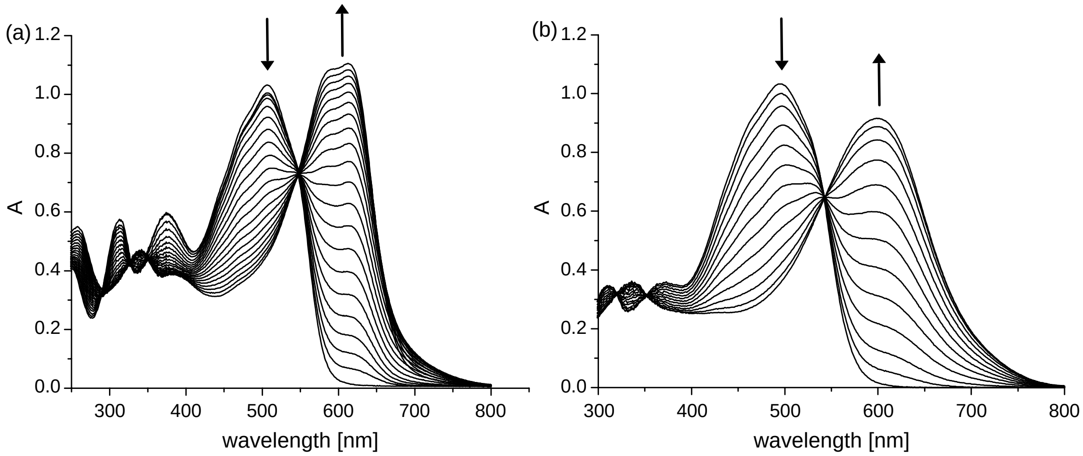


FIGURE 2 UV–Vis titration of crown ethers (starting volume 2.3 mL) with lead(II) perchlorate (titration step 0.01 mL): (a) crown **1** (initial ligand concentration $c_L = 4 \times 10^{-5}\,mol\,dm^{-3}$; $c_{Pb} = 4.2 \times 10^{-3}\,mol\,dm^{-3}$), and (b) crown **2** ($c_L = 3.6 \times 10^{-5}\,mol\,dm^{-3}$; $c_{Pb} = 4.2 \times 10^{-3}\,mol\,dm^{-3}$). The initial spectrum is that of the starting ligand and the final corresponds to the complexed form.

The differences in transport fluxes listed in Table I will very likely be influenced by a number of factors. These include differences in aqueous/organic partition coefficients, variation in the complexation/decomplexation rates between systems, different rates of metal ion diffusion across the aqueous/organic interfaces and the absolute magnitudes of the respective stability constants. For example, in the latter case K values that are too high or too low can both inhibit the transport process. Similarly, slow complexation rates c.f. [22,23] have been implicated previously in selective transport behavior [24].

In view of the above, an attempt was made to investigate spectrophotometrically the relative rates of formation of selected metal complexes involved in the present study with **1**–**4**. Since measurements in chloroform tended to be troublesome, a representative set of semi-quantitative complex formation experiments were performed in acetonitrile.

It was found that lead(II) ion appears completely complexed within the time scale of the initial spectrophotometric measurement. In the presence of lead(II) perchlorate the color changes from red to deep blue. The measured absorption spectra exhibit a well defined isosbestic point which is consistent with the presence of only two UV–Vis active species: ligand and its complex. Spectral changes upon titration with lead(II) perchlorate are exemplified in Fig. 2 for compounds **1** (left) and **2** (right), corresponding to 18- and 21-membered macrocycle ring sizes, respectively.

Figure 3 presents Job's plots for compounds **1** and **2** with apparent x_{max} value of 0.4, corresponding to formation of a 2: 3 (metal: ligand) complex (cf. "club-sandwich" complex [25]).

Data analyses for the UV–Vis titration of ligand solutions with lead(II) perchlorate in acetonitrile were performed assuming the formation of one complex at equilibrium using the OPIUM program [12]. Best fit was obtained for 2:3 (metal:ligand) stoichiometry. The determined stability constants, for the assumed stoichiometry, and their standard deviations are listed in Table II.

The relatively high values of the stability constants for the lead(II) complexes are comparable to each

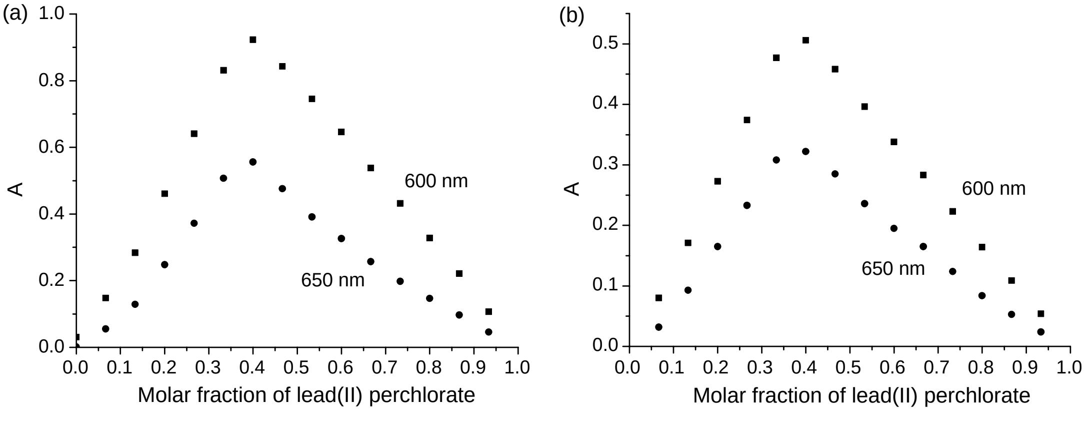


FIGURE 3 Job's plot for lead(II) complexation of compounds **1** (a) and **2** (b) at different wavelengths.

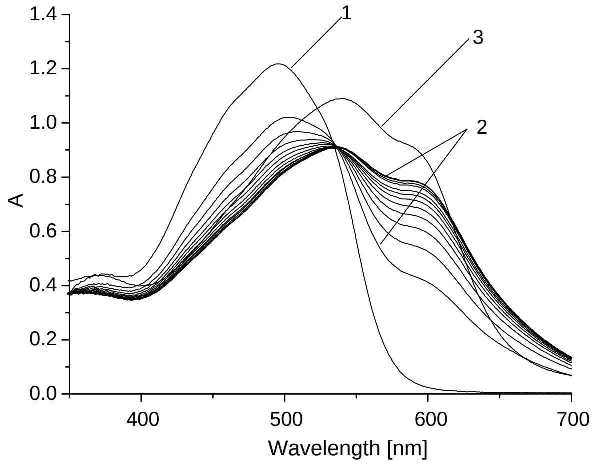


FIGURE 4 Changes in the absorption spectra upon titration of compound **2** ($4.9 \times 10^{-5}\,\mathrm{mol\,dm^{-3}}$, 2.3 mL) with zinc(II) perchlorate ($8.3 \times 10^{-3}\,\mathrm{mol\,dm^{-3}}$, titration step 0.01 mL): 1– free ligand; 2– spectra registered within three minutes after addition of consecutive portions of 0.01 mL of the zinc salt. Spectrum 3 was registered 72 hours after addition of the total volume ($0.1\,\mathrm{cm^3}$) of zinc perchlorate solution.

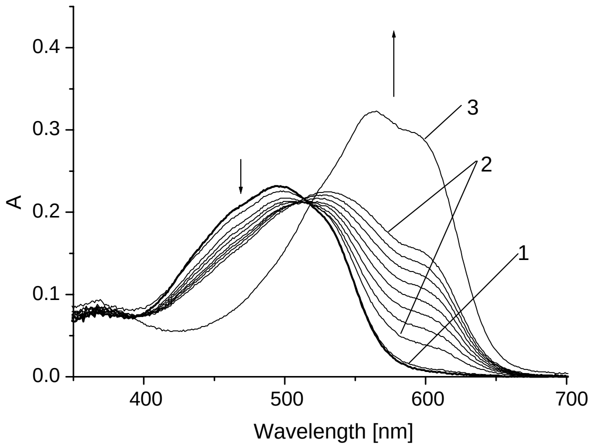


FIGURE 5 Spectral changes indicating slow binding of nickel(II) to crown ether **2** ($c = 7.32 \times 10^{-6}\,\mathrm{mol\,dm^{-3}}$, $v = 2.3\,\mathrm{cm^3}$) in acetonitrile on addition of nickel perchlorate ($c = 1.03 \times 10^{-2}\,\mathrm{mol\,dm^{-3}}$, $v = 0.01\,\mathrm{cm^3}$). The initial spectrum (1) was obtained two minutes after addition of the salt solution. Consecutive spectra (2) were registered at 30 min. intervals after this. Spectrum 3 was taken after 10 h.

other and do not substantially depend on the size of the macrocycle.

Similar experiments were carried out for zinc(II), nickel(II), and cobalt(II). Changes in the absorption spectra upon titration of compound **2** with zinc(II) perchlorate are shown in Fig. 4. Addition of zinc(II) salt resulted in noticeable changes in this ligand's absorption spectrum; however, the observed changes indicated that in this case the system equilibrates much slower than with lead(II). The collection of spectra labeled 2 were obtained after consecutive addition of appropriate amounts of zinc salt solution; the latter resulted in an accompanied color change from red to purple. Spectrum 3 obtained for the final solution after 72 hours does not intersect the isosbestic point (solution color had changed to purple-violet). This thus indicates that a new species forms on allowing the solution to stand for an extended period.

A similar experiment involving nickel(II) leads to only slow changes in the spectrum of compound **2,** as might be expected in view of the well documented more inert nature of this ion. In this case monitoring of the spectrum over time indicated slow kinetics. The spectral changes are shown in Fig. 5. The series of spectra (2) registered at 30 minutes intervals from the initial mixture of ligand and nickel salt show an increasing concentration of complex. Spectrum 3 registered after 10 h does not pass through the isosbestic point and once again indicates formation of a further species.

Analogous experiments employing cobalt(II) also showed slow kinetics of complexation with **2**. However, silver(I) cation binds instantly to this ligand in acetonitrile. Experiments with cadmium(II) were not performed due to solubility restrictions.

Several neutral compounds with oxygen, nitrogen and sulfur donor atoms have been examined as ionophores for lead selective electrodes [cf. 26]. The selectivity observed for lead transport and substantial stability constants obtained for the lead complexes prompted us to study the behavior of ion-selective membrane electrodes doped with **1–4**. Initially, preliminary screening aimed at optimizing the composition of the membrane was carried out. This involved varying the plasticizer, the amounts of ionophore and lipophilic salt present and the composition of the internal electrolyte. On the basis of these preliminary studies, membranes of composition: 1.5 mg ionophore, 0.75 mg lipophilic salt KTpClPB per $0.1\,\mathrm{cm^3}$ plasticizer and 50 mg PVC were employed; selectivities were then compared for membranes of this composition but incorporating different plasticizers (*o*-NPOE, BBPA and DOP). The selectivity coefficients were determined using the Separate Solution Method [13] employing metal nitrate solutions of 10^{-3} activity at pH 5.3 ± 0.1. The selectivity coefficients are summarized in Fig. 6. Other properties of the electrodes employed are summarized in Table III.

Compound **1** was observed to be an inefficient ionophore as it was found to readily crystallize in the membrane and in addition leaked to the aqueous solution in the presence of $\mathrm{Pb^{2+}}$ ions. Compound **2** also shows a tendency to crystallize in the membrane; 1.5 mg of this ionophore added to form the membrane was found to be the limit if crystallization was to be avoided. Once again, ionophore **2** was also found to leak from the membrane into the aqueous phase when the membrane was not doped with the lipophilic salt. Nevertheless, both **3** and **4** do not crystallize and are retained in the membrane

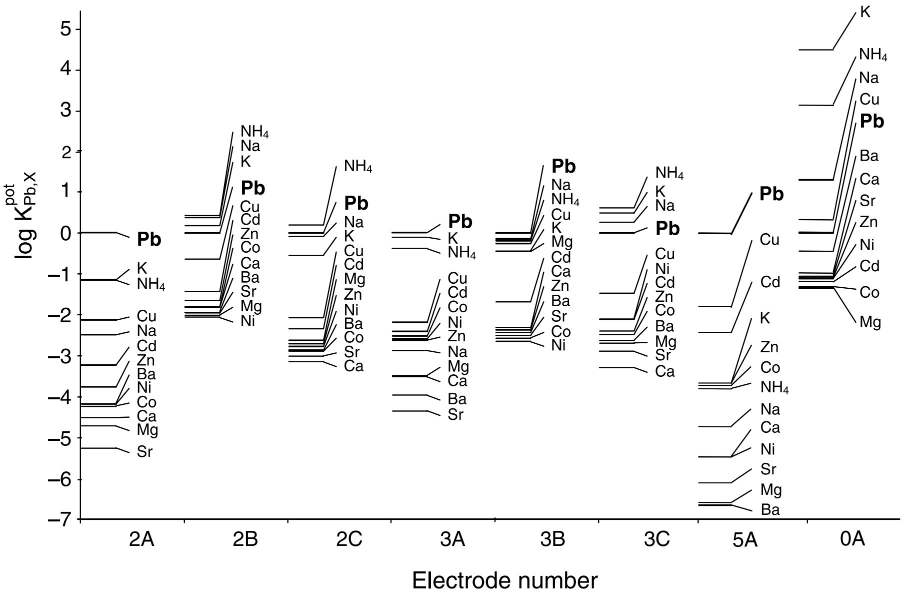


FIGURE 6 Selectivity coefficients log $K^{pot}_{Pb,X}$ for membrane electrodes doped with compound **2**, **3** or **5** (plasticizer: A – *o*-NPOE, B – BBPA, C – DOP). **0** – "blank electrode".

under the above conditions. Electrodes incorporating **1–4** and BBPA or DOP plasticizers show cationic ISE characteristics but the selectivities are not very high. Membranes with compounds **1** and **4** (containing 1.5 mg ionophore and 0.75 mg lipophilic salt) and *o*-NPOE were found to bind Pb^{2+} non-reversibly.

Amongst macrocycles **1–4**, electrodes based on **2** and **3** (KTpClPB as lipophilic salt and *o*-NPOE as plasticizer) were found to possess the best ISE properties (Fig. 6), while a characteristic of electrodes employing **3** is that they appeared the most stable.

Unfortunately, as mentioned above, **2** showed a tendency to crystallize and substantial leakage from the membrane also occurred. In view of this ionophore **5** was synthesized (Scheme 1) as it was predicted to show higher lipophilicity, better solubility in the membrane components as well as a tendency not to crystallize. In fact, membranes based on this compound (containing *o*-NPOE as plasticizer) were subsequently demonstrated to have the best properties as exemplified by the results shown in Fig. 6. These preliminary studies showed that in the absence of Ag^+ ions this electrode is selective towards Pb^{2+} relative to the other cations employed for the transport experiments as well as the alkali and alkaline earth metal cations investigated.

CONCLUSIONS

The stability constants, observed transport fluxes and properties of the ion-selective membrane electrodes collectively indicate that macrocyclic compounds of the present type bearing a pyrrole residue together with oxygen and azo donor atoms show an inherent tendency towards Pb^{2+} cation selectivity, although possible interference from silver may occur.

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