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Diaza Crown Ethers Bearing Heterocyclic Ligating Groups on Nitrogen Atoms and Their Complexing Properties with Divalent Inorganic Cations

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Abstract. Two nitrogen-substituted 4,13-diaza-18-crown-6 compounds, bearing 2-methylquinolyl and 2-methylquinolyl-1-oxide groups, have been prepared. Ionophore–cation selectivities with a range of inorganic divalent cations have been investigated by means of membrane techniques, demonstrating their high selectivity for the Hg(II) cation.

Key words. Diaza crown ethers, heavy metal-ion selectivity, PVC membranes.

1. Introduction

Lariat crown ethers have attracted considerable attention in recent years [1]. The introduction of a side arm on nitrogen atoms in the monoaza and diaza crown ethers provides a variety of monocyclic molecular receptors with substantially modified complexing properties towards metal ions.

It has been shown that the heteroatoms present in the side arms cooperate in binding the inorganic cations [2], therefore many modifications in the binding strength of lariat ethers can be envisaged. The rational design and synthesis of lariat ethers may lead to host molecules capable of binding a chosen metal ion with a very high selectivity. The transport of inorganic cations through liquid membranes mediated by side-armed macrocyclic ligands has also been studied [3].

We have focussed our efforts on the design and synthesis of 4,13-diaza-18-crown-6 derivatives as potential complexers for heavy metal ions. This work is a part of our project on heavy metal ion-selective molecular receptors.

We selected 2-methylquinolyl and 2-methylquinolyl-1-oxide groups as a ligating and lipophilic side arms.

Simple condensation of 4,13-diaza-18-crown-6 with 2-chloromethylquinoline and 2-chloromethylquinoline-1-oxide led to the desired ligands **1** [3c] and **2** (Figure 1). The *N,N′*-bis(dodecyl)-4,13-diaza-18-crown-6 **3** was taken as a reference compound for the complexation studies.

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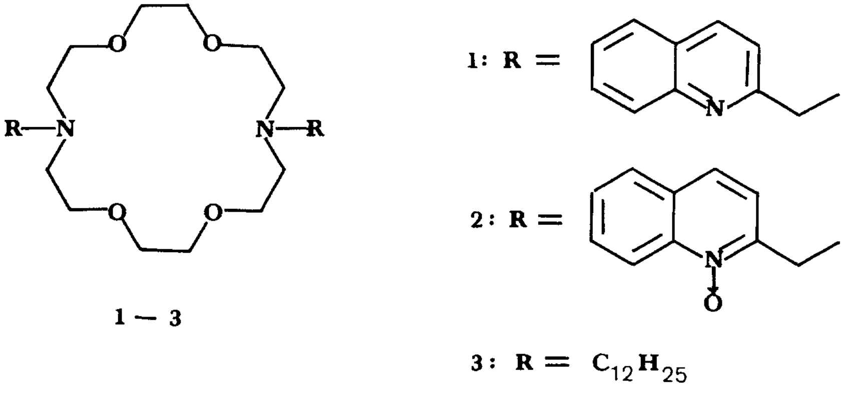

Fig. 1.

2. Experimental

2.1. GENERAL REMARKS

All chemicals were purchased from Fluka or Merck and used without purification except 2-chloromethylquinoline, which was liberated from its hydrochloride by neutralization in EtOH with solid Na_2CO_3. Evaporation, dissolution in $CHCl_3$ and filtration through a shallow layer of silica (Merck) yielded a yellow residue which was crystallized from hexane.

The 2-chloromethylquinoline-1-oxide was prepared by oxidation of 2-chloromethylquinoline with MCPBA in $CHCl_3$ solution. Acetonitrile and THF were distilled over CaH_2 prior to use. The membrane components (PVC of high molecular weight, potassium tetra(*p*-chlorophenyl)borate, and didecyl phthalate) were from Fluka. Inorganic salts of analytical grade were of Polish production.

Melting points are uncorrected. The NMR spectra were obtained on a Bruker 500 MHz spectrometer in $CDCl_3$ solutions, with TMS as internal standard.

The IS-561 electrode (Philips, Eindhoven), used for electrochemical studies, was coupled with a digital pH meter (Radelkis OP 208) and a 16-channel multiplexer described previously [4].

2.2. SYNTHESIS

N,N′-Bis(2-methylquinolyl)-4,13-diaza-18-crown-6, **1**

4,13-Diaza-18-crown-6 (524 mg, 2 mmol) and 2-chloromethylquinoline (710 mg, 4 mmol) were dissolved in MeCN (30 mL) and anhydrous Na_2CO_3 (0.6 g) was added. Vigorous stirring was maintained for 24 h at 60°C. Filtration, evaporation and crystallization from chloroform–ether yielded the desired product in 60% (655 mg) yield.

M.p.: 83–84.5°C. ^{1}H-NMR: quinolyl protons (12H): 8.096 (*d*, 2H), 8.043 (*d*, 2H), 7.764 (*t*, 4H), 7.682 (*td*, 2H), 7.498 (*td*, 2H), 4.027 (*s*, 4H, 2 × CH_2-quin.), 3.672 (*t*, 8H, 4 × OCH_2CH_2N), 3.610 (s, 8H, 2 × OCH_2CH_2O), 2.937 (*t*, 8H, 4 × NCH_2). Elem. Anal. *calcd* for $C_{32}H_{40}N_4$: C 70.36 H 7.57 N 10.35. *Found*: C 70.31 H 7.53 N 10.29.

N,N'-Bis(2-methylquinolyl-1-oxide)-4,13-diaza-18-crown-6, **2**

The same procedure and molar amounts of reactants were used as previously. The reaction time was 48 h. Yield 65% (750 mg).

M.p.: 128–131°C, decomp. ^{1}H-NMR: quinolyl protons (12H): 8.67 (*d*, 2H), 7.99 (*d*, 2H), 7.72 (*d*, 2H),7.66 (*td*, 2H), 7.607 (*d*, 2H), 7.51 (*t*, 2H); 4.203 (*s*, 4H, CH_2-quin.), 3.698 (*t*, 8H, 4 × OCH_2CH_2N), 3.643 (s, 8H, 2 × OCH_2CH_2O), 2.948 (*t*, 8H, 4 × NCH_2). Elem. anal. *calcd.* for $C_{32}H_{40}N_4O_2{\cdot}2\,H_2O$: C 62.75 H 7.18 N 9.15. *Found*: C 63.04 H 6.64 N 9.16.

X-Ray analysis for the uncomplexed ligands will be described elsewhere.

2.3. ELECTROCHEMISTRY

The following salts were used for the preparation of the stock solutions (10^{-1} and 10^{-2}M) in redistilled water: nitrates; Zn(II), Cd(II), Co(II), Mn(II), Cu(II), Ni(II), Pb(II), Hg(II), Ca(II); chlorides – Cu(II), and Hg(II). Solutions for electrochemical studies were obtained by dilution of stock solutions. The required pH for the solutions was adjusted with diluted solutions of NaOH and HNO_3.

2.4. MEMBRANE AND ELECTRODE PREPARATION

Membrane components (ionophore –1–4%, PVC – 30%, didecyl phthalate (DDP) – 66–69%, and 70 mol% potassium tetra(*p*-chlorophenyl)-borate (KTpClPB) against the ionophore) were dissolved (around 200 mg of overall weight) in THF (2 mL). A clear solution was poured into a glass ring (24 mm in diameter) mounted on a glass plate and left overnight at room temperature for solvent evaporation. Five membranes were cut (7 mm in diameter) and incorporated into the electrode (type IS-561 Philips). The glass tube with an external electrode was filled with internal electrolyte (aqueous solutions: $CuCl_2$, $HgCl_2$ of various concentration and pH) and left overnight in a conditioning solution (redistilled water, or 10^{-3}M solutions of $CuCl_2$, $Cu(NO_3)_2$, $Hg(NO_3)_2$).

For each membrane composition two electrodes were prepared, either with or without KTpClPB.

2.5. POTENTIOMETRIC MEASUREMENTS

Potentials for ionoselective electrodes were measured using the following arrangement:

> Hg; $HgCl_2$; $KCl_{(sat}$/1M KNO_3/solution studied//membrane//internal electrolyte; AgCl; Ag.

Selectivity coefficients $k^{\mathrm{Pot}}_{\mathrm{Cu/M}}$ were determined by the SSM method (separated solutions method), measuring potentials in 10^{-2}M solutions of the metal nitrates at constant pH = 3. Values for the coefficients $k^{\mathrm{Pot}}_{\mathrm{Cu/M}} > 10^{-3}$ were determined also by means of the FIM method, measuring potentials in the Cu(II) solutions within the range of pCu = 1–6 with the presence of constant (10^{-2}M) concentration of an interfering cation and at pH = 3. Both methods have been described previously [5]. Potentials of the electrode in each solution were measured at 1 min intervals over a period of 10 or 20 minutes and for further analysis a mean value of the last 5 measurements was taken.

The potentials were recorded on a Radelkis OP 208 digital pH-meter and by a custom-made 16-channel electrode monitor (resolution 200 μV) equipped with one FET operational amplifier per channel (input impedance 10^{12} Ω/2pF). The data acquisition was performed with a 65 kB microcomputer in combination with a Neptun 150 display terminal, and a D100 Mera-Blonie matrix printer, and our own software. More details are described in Ref. 3.

3. Results and Discussion

Membrane techniques are of particular importance, since they allow a rapid determination of the selectivity coefficients for lipophilic ionophores with a wide

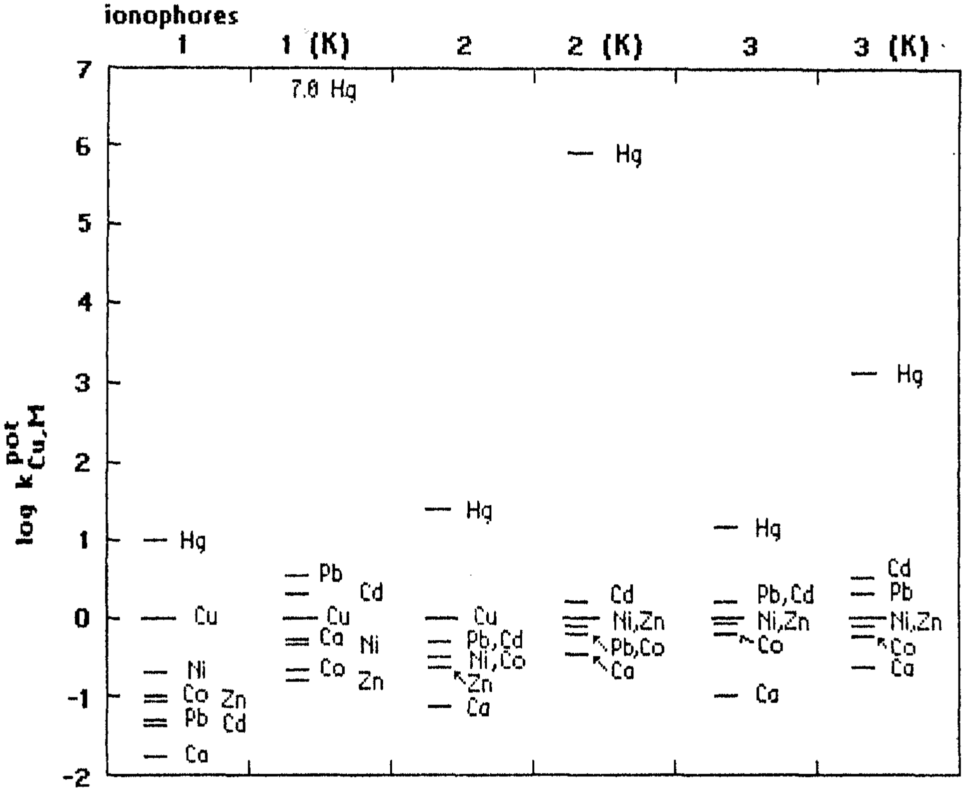

Fig. 2. Values of selectivity coefficients, $\log k_{\mathrm{Cu/M}}$. Conditions: 10^{-2}M $M(NO_3)_2$, pH = 3. Internal electrolyte: 10^{-2}M $CuCl_2$, pH = 3. Membranes were conditioned overnight in 10^{-3}M $CuCl_2$, pH = 3.

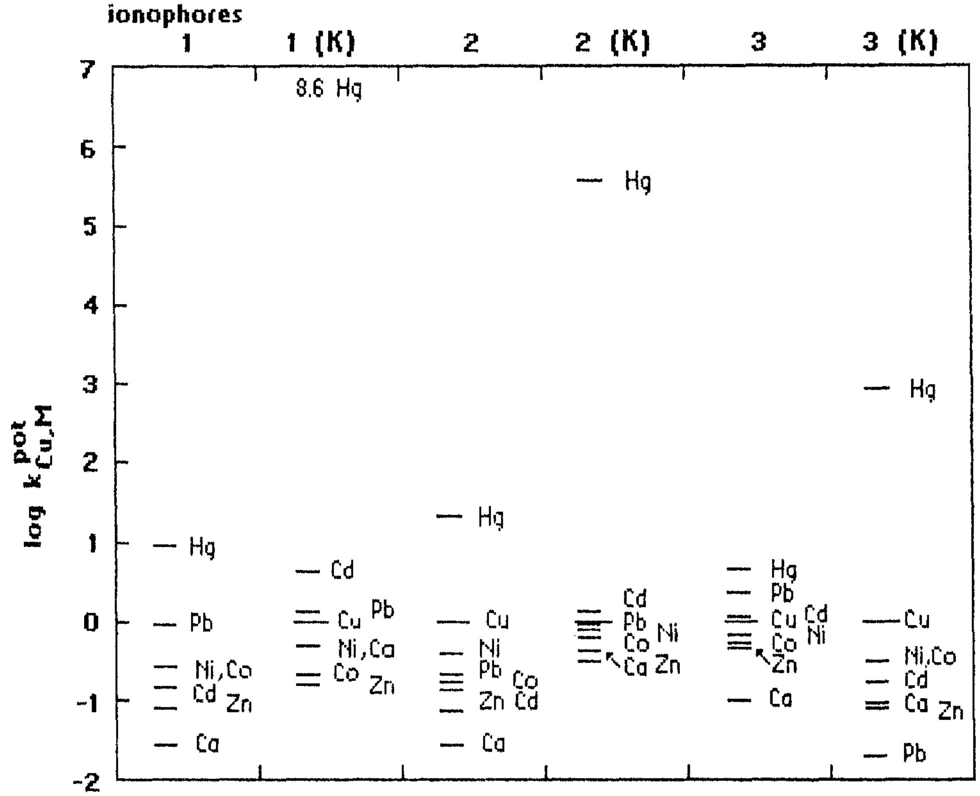

Fig. 3. Values of selectivity coefficients, $\log k_{Cu/M}$. Conditions: 10^{-2}M $M(NO_3)_2$, pH = 3. Internal electrolyte: 10^{-2}M $CuCl_2$, pH = 3. Membranes were conditioned for three days in 10^{-3}M $Cu(NO_3)_2$, pH = 4.

range of species, for instance inorganic cations. Therefore, it is a practical test for the ionophore's usefulness as a sensing component of the ion-selective electrode.

The selectivity of the membrane incorporating a neutral ionophore depends on the mobility of a cationic complex through the membrane and on the complex partitioning between the membrane and the aqueous phase. In most cases, this second parameter determines the membrane selectivity.

Provided that the membrane ion selectivity is related to the free energy of transfer of ions from a water phase to the membrane phase, this selectivity depends on the selectivity behaviour of the carrier ligands used, which can be fully specified by the values of complex stability constants, and on the membrane composition (the concentration of free ligands and lipophilic counter-ion, the extraction properties of the membrane solvent).

The potentiometric selectivity coefficient K_{MN} determines the scope in which an interfering cation N^{n+} affects the potential of a given electrode sensitive for the ions M^{z+}:

$$E = E^0 + \frac{2.303\ \mathrm{RT}}{zF} \log(a_M + K_{MN}/a_N)^{z/n}.$$

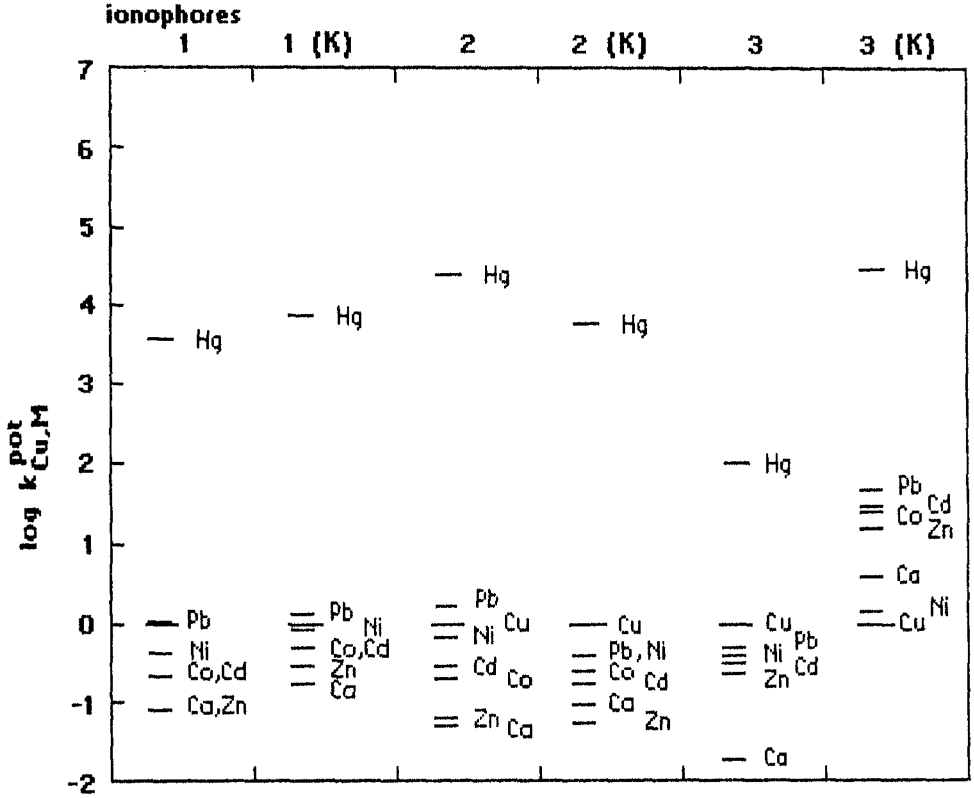

Fig. 4. Values of selectivity coefficients, log $K_{\mathrm{Cu/M}}$. Conditions: 10^{-2}M $M(NO_3)_2$, pH = 3. Internal electrolyte: 10^{-2}M $HgCl_2$, pH = 3. Membranes were conditioned for two weeks in 10^{-3}M $Cu(NO_3)_2$, pH = 4.

We found a pronounced selectivity of the ionophore-doped membranes for Hg(II) ions against transition metal cations and Ca(II) (Figures 2, 3, 4).

It should be noted that the membranes prepared in this work behave as an organic phase in the first extraction step. Symbols 1(K), 2(K), and 3(K) depict the experiments in which membranes contained potassium tetra(*p*-chlorophenyl)borate.

Membranes without ionophores, but with an identical composition of other components, when conditioned in water, did not show any particular selectivity, except Pb(II), for which a plasticizer (DDP) acts as a complexing agent. Further conditioning of such membranes in $Cu(NO_3)_2$ led to a total loss of selectivity.

It is interesting that both ligands **1** and **2** display distinctly higher selectivity towards Hg(II) ions, compared with **3**, but only in the cases where the membranes contained potassium cations. Thus, the presence of potassium tetra(*p*-chlorophenyl)borate is crucial to achieving a high selectivity for Hg(II) ions. This result can be interpreted in terms of very favourable replacement of the potassium cation held in the cavity of **1** or **2**, by a Hg(II) cation.

A further strategy to achieve high selectivities for Pb(II) and Cd(II) needs some comment. It has been demonstrated that *N,N′*-dimethyl-4,13-diaza-18-crown-6 forms a very strong complex with Hg(II) [3a], which means that the array of heteroatoms fits particularly well for this cation. Therefore, the binding properties of nitrogen atoms should be modified by passing from sp^3 character to sp^2, and fine adjustment of the selectivity for Pb(II) and Cd(II) ions might be regulated by careful design and incorporation of appropriate side arms into the basic macrocyclic framework.

Further work in this direction is being pursued.

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