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Synthesis and Selectivity towards Divalent Inorganic Cations of Macrocyclic Dicarboxamides and Disulphonamides Bearing Pendant Electron Donor Groups

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Abstract. Novel carboxamides and sulphonamides derived from 4,13-diaza-18-crown-6 incorporating ligating groups have been obtained and their ion selectivities have been evaluated by membrane techniques indicating their high affinity for Hg(II) cations.

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

1. Introduction

Environmental pollution with heavy metal ions is a most important problem. There is a need for continuous monitoring of such contaminants in soil, water and air. Supramolecular chemistry may contribute substantially to the solution of analytical problems by the synthesis of highly selective ionophores that can serve as heavy metal ion sensors applied in ion-selective electrodes, or ISFET transistors. We have recently demonstrated [1] two ionophores derived from 4,13-diaza-18-crown-6, bearing 2-methylquinolyl-, and 2-methylquinolyl-1-oxide groups on nitrogen atoms, which were selective for Hg(II) ions. It became apparent that altering the substituents on nitrogen of sp^3 hybridization will have little impact, if any, on tuning the selectivity towards Pb(II) or Cd(II) ions, because the parent macrocycle diaza-18-crown-6 forms stronger complexes with Hg(II) as compared to Pb(II) and Cd(II). We therefore changed the character of the nitrogen atoms in the macrocyclic rings by the formation of disubstituted carboxamides and sulphonamides containing electron donor atoms.

2. Experimental

2.1. GENERAL REMARKS

All chemicals were purchased from Fluka or Merck and used without purification, except for the solvents (MeCN, DMF) which were distilled over CaH_2. All new

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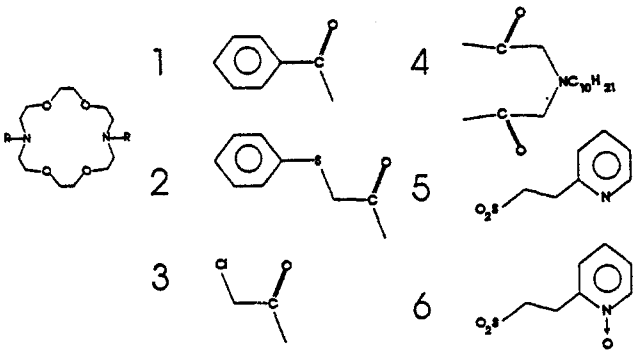

Scheme 1.

side-armed diazacrown ethers were prepared by routine procedures and their general formula is shown in Scheme 1.

The macrocyclic carboxamides were prepared from the respective bis(*N*-chloroacetyl)-4,13-diaza-18-crown-6 and appropriate nucleophiles: thiophenol and decylamine.

The *N*,*N*′-dibenzoyl-4,13-diaza-18-crown-6 was prepared as a reference compound by routine benzoylation. The macrocyclic sulphonamides were synthesized from 2-(2-pyridyl)-ethylsulphochloride prepared *in situ* from sodium 2-(2-pyridyl)ethylsulphonate and thionyl chloride in DMF [2]. The PVC membrane components were the same as described in a previous paper [1].

Melting points are uncorrected. The NMR spectra were obtained on a Bruker AM-500 and Varian Gemini 200 MHz spectrometers in $CDCl_3$ solution with TMS as standard. The IS-561 electrode (Philips, Eindhoven) used for electrochemical studies was coupled with a digital pH meter (Radelkis OP 208) and 16-channel multiplier [3].

2.2. SYNTHESIS

N,N′-Dibenzoyl-4,13-diaza-18-crown-6, **1**

4,13-Diaza-18-crown-6 (524 mg, 2 mmol) and benzoyl chloride (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 70% yield.

M.p.: 94–96°C. ^{1}H-NMR: 7.2 (*m*, 10H 2 × Ph), 3.5 (*m*, 24H 4 × CH_2N, 8 × CH_2O). *Anal. calcd.* for $C_{36}H_{34}N_2O_6$: C66.38 H7.23 N5.96. *Found*: C66.21 H7.36 N5.76. IR $CHCl_3$(3000, 1630, 1120, 1080) cm^{-1}, *m*/*z* (PDMS) 471.3 M$^+$.

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

Compound **3** (1 mmol, 415 mg) and Et_3N (2.2 mmol, 0.31 mL) were dissolved in MeCN (30 mL) and thiophenol (2 mmol, 0.23 mL) was added after cooling to 0°C.

Vigorous stirring was maintained for 24 h at room temperature. Filtration, evaporation and chromatography (SiO_2, 8% EtOH/AcOEt) gave the desired product in 90% yield.

M.p.: 120–121°C. ^{1}NMR 7.2 (*m*10, H 2 × -Ph), 3.8 (*s*, 4H 2 × CH_2CO), 3.6 (*s*, 24H 4 × CH_2N, 8 × CH_2O). *Anal. calcd.* for $C_{28}H_{38}N_2O_6S_2$: C59.79 H6.76 N4.98 S11.39. *Found*: C59.62 H6.71 N5.00 S11.35. IR $CHCl_3$: (3010, 1660, 1220) cm^{-1}, *m*/*z* (PDMS 562.9 M^+.

N,N'Bis(chloroacetyl)-4,13-diaxa-18-crown-6, **3**

4,13-Diaza-18-crown-6 (524 mg, 2 mmol) and Et_3N (0.62 mL, 2 mmol) were dissolved in MeCN (30 mL) and after cooling to 0° chloroacetyl chloride (4 mmol, 0.42 mL) was added. Vigorous stirring was maintained for 2 h at room temperature. Filtration, evaporation and chromatography (Al_2O_3, 2.5% EtOH/AcOEt) gave the desired product in 78% yield.

M.p.: 80–82°C. ^{1}H NMR. 4.2 (*s*, 4H 2 × CH_2CO), 3.6 (*s*, 24H 4 × CH_2N, 8 × CH_2O). *Anal. calcd.* for $C_{16}H_{28}Cl_2N_2O_6$: C46.27 H6.70 N6.75 *Found*: C46.0 H7.01 N6.51. IR $CHCl_3$: (3010, 2870, 1660, 1120, 720) cm^{-1}, *m*/*z* (PDMS) 415.9 M^+.

N,N'-(Diacetylodecylamino)-4,13-diaza-18-crown-6, **4**

Compound **3** (1 mmol, 415 mg) and Et_3N (2.2 mmol, 0.31 mL) were dissolved in MeCN (30 mL) and after cooling to 0°C decylamine (2 mmol, 0.39 mL) was added. Vigorous stirring was maintained for 24 h at room temperature. Filtration, evaporation and chromatography (Al_2O_3, 1% EtOH/AcOEt) gave the desired product in 70% yield.

M.p.: 74–76°C. ^{1}NMR: 3.7 (*m*, 28H 4 × CH_2N, 8 × CH_2O, 2 × CH_2CO), 1.2 (*m*, 18H 9 × CH_2), 0.8 (*s*, 3H 1 × CH_3). *Anal. calcd.* for $C_{26}H_{49}N_3O_6$: C62.52 H10.2 N8.41 *Found*: C61.73 H10.48 N8.7. IR $CHCl_3$: (2930, 1650, 1120) cm^{-1}, *m*/*z* (PDMS) 499.7 M^+.

N,N'-Bis(2-Pyridylethylsulphonyl)-4-13-diaza-18-crown-6, **5**

A solution containing 2-pyridylethylsulphochloride (10 mL), generated from sodium 2-pyridylethanesulphonate (2.09 g) and $SOCl_2$ (0.73 mL) in DMF (50 mL) was added to the solution of 4,13-diaza-18-crown-6 (262 mg) in DMF (10 mL) + Et_3N (0.5 mL). After 1 h the mixture was evaporated and the residue dissolved in $CHCl_3$ (50 mL), shaken with H_2O (5 mL) and evaporated. Chromatography was effected on silica with 5% EtOH in $CHCl_3$. Yield 78%.

M.p.: 94–96°C. ^{1}NMR ($CDCl_3$, TMS) δ:3.28 (*m*, 4H 2 × $C\underline{H_2}Py$), 3.49 (*t*, 8H, $J = 5.3$ Hz, 4 × $\underline{CH_2}NSO_2$), 3.50 (*m*, 4H, 2 × $C\underline{H_2}\text{–}SO_2$), 3.59 (*s*, 8H, 2 × $OC\underline{H_2}C\underline{H_2}O$), 3.67 (*t*, 8H, $J = 5.3$ Hz, 4 × CH_2O), 7.13–7.23 (*m*, 4H, 2 × 2H–β-Py), 7.63 (*td*, 2H, $J_{34} = 5.8$ Hz, $J_{42} = 1.82$ Hz, 2 × 1H–γ-Py), 8.53 (bd, 2H, $J_{23} = 4$ Hz). *Anal. calcd.* for $C_{26}H_{40}N_4O_8S_2$: C52.00 H6.72 N9.33 S10.66 *Found*: C52.01 H7.04 N9.17 S10.74. IR $CHCl_3$: (2840, 1600, 1360, 1150) cm^{-1}, *m*/*z* (PDMS) 602.1 M^+.

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

Compound **5** (61.4 mg) was stirred with MCPBA (50,4 mg) in $CHCl_3$ (20 mL). The mixture was worked up after 3 h in the usual manner. The product is highly hydroscopic. Yield 58.0 mg (92%).

M.p.: 138°C (decomp). ^{1}NMR ($CDCl_3$, TMS) δ:3.35 (*m*, 4H 2 × $C\underline{H}Py{-}O$), 3.51 (*m*, 4H, 2 × $C\underline{H}_2{-}SO_2$), 3.52 (*t*, 8H, $J = 4.9$ Hz, 4 × $\underline{CH_2}NSO_2$), 3.60 (*s*, 8H, 2 × $OC\underline{H}_2C\underline{H}_2O$), 3.68 (*t*, 8H, $J = 4.9$ Hz, 4 × CH_2O), 7.21–7.25 (*m*, 4H, 2 × 2H–β-Py–O), 7.35–7.40 (*m*, 2H, 2 × H–γ-Py–O), 8.21–8.25 (*m*, 2H, 2 × H–α-Py–O). *Anal. calcd.* for $C_{26}H_{40}N_4O_{10}S_2$: C49.35 H6.37 N8.85 S10.13 *Found*: C48.79 H6.78 N8.72 S9.89. IR $CHCl_3$:(2880, 1450, 1340, 1150) cm^{-1}, m/z (PDMS) 634.7 M$^+$.

2.3. ELECTROCHEMISTRY

Chemicals

Nitrates of cadmium(II), calcium(II), cobalt(II), copper(II), lead(II), mercury(II), nickel(II), silver(I), sodium(I), zinc(II); chlorides of copper(II), potassium(I), mercury(II) were of analytical grade reagents (supplied by Polskie Odczynniki Chemiczne, Gliwice, Poland). Standard solutions (0.1 M) of metal salts in redistilled water were prepared; working solutions were prepared as required by suitable dilution with redistilled water. The pH of the solution was adjusted with either 0.1 M nitric or hydrochloric acid.

Membrane Materials

High molecular weight poly(vinylchloride) (PVC), potassium tetrakis(*p*-chlorophenyl)borate (KTpClPB) and dodecyl phthalate (DDP), were obtained from Fluka, Buchs, Switzerland. As solvent for membrane components, freshly distilled (THF) – p.a. POCh Gliwice – was used.

Membrane Preparation

The membrane components (1% m/m ionophore, 30% m/m PVC, 70 mol-% KTpClPB (with respect to the ionophore), and 68–69% m/m DDP as plasticizer) totalling 200 mg were dissolved in 2 mL of freshly distilled THF. This solution was cast into 24 mm i.d. glass rings resting on a glass plate. After solvent evaporation overnight, the resulting membrane was peeled off from the glass mould and disks of 7 mm diameter were cut out. The membrane disks were mounted in electrode bodies (type IS 561, Philips, Eindhoven, The Netherlands) for EMF measurements. The electrode was left overnight in conditioning solutions of KCl, $CuCl_2$ or $HgCl_2$. Two electrodes were prepared for each composition of membrane.

Emf Measurements

All measurements were carried out at 20°C with cells of the type:

Ag, AgCl; $KCl_{(satd)}$ 0.1 M KNO_3 sample membrane

internal filling solution; AgCl; Ag.

A solution of mercury(II) or copper(II) or potassium chloride at fixed pH was used as an internal filling solution. The potentials were recorded by a custom made 16-channel electrode monitor (resolution 200 μV) equipped with one FET operational amplifier per channel (input impedance $10^{12}\,\Omega/2$ pF). The data acquisition was performed with a 64 kB microcomputer in combination with a Neptun 150 display terminal and a D100 Mera-Błonie matrix printer, and our own software. More details were described in Ref. 2. The selectivity coefficient $k_{\mathrm{Cu,M}}$, was calculated by SSM (separate solution method), measuring potentials in 10^{-2} M solutions of metal nitrates at constant pH = 3 (in case of Hg pH = 2). Values for the coefficients $k_{\mathrm{Cu,M}} > 10^{-3}$ were also determined by means of FIM (fixed interference method), measuring EMF in the Cu(II) solutions within the range of pCu = 1–6 in the presence of a constant (10^{-2} M) concentration of the interfering cation and at pH = 3. Both methods have been described previously [3]. EMF values of electrodes in each of the solutions were measured for 20 minutes at intervals of half a minute. An average of the last five measurement points was used in further calculations.

3. Results and Discussion

The potentiometric selectivity coefficient k_{MN} is defined by the following equation:

$$E = E^0 + \frac{2.303RT}{zF}\log(a_{\mathrm{M}} + k_{\mathrm{MN}}/a_{\mathrm{N}})^{z/n}$$

and determines the scope in which an interfering cation N^{n+} affects the potential of a given electrode sensitive for the ions M^{z+}. A detailed discussion on ion selectivity measurements by means of the membrane technique was published in our previous work [1], therefore we shall briefly discuss only the results obtained.

Membrane techniques are particularly suitable for a rapid screening of the macrocylic ligand selectivities towards inorganic cations, inorganic anions, or organic species. One important feature that should be possessed by the macrocyclic system is a lipophilic function which allows the ligand to remain in the plastic membrane.

The selectivity of the membrane doped with the macrocyclic neutral ionophore is interrelated to the mobility of the cationic complex through the membrane and to complex partitioning between the membrane and the aqueous phase. Furthermore, the membrane ion selectivity will depend on the complex stability constants of the carrier used, and the membrane composition (plasticizer used, lipophilic counter ion and the ionophore concentration).

Figures 1, 2 and 3 show the selectivity coefficients established in three different experimental sets: the internal electrolyte being aqueous KCl, $CuCl_2$, and $HgCl_2$. The membrane conditioning was performed in H_2O, aqueous $CuCl_2$ and aqueous $HgCl_2$, respectively. Compounds **1**, **2**, **3**, and **4** were carboxamides in all cases, and compound **4** was a bicyclic ligand. It is clear that the type of internal electrolyte and conditioning solution have a remarkable impact on selectivity coefficients. When the membrane was conditioned in pure H_2O the highest selectivity was observed for Hg(II) and Ag(I) cations, although compound **2**, containing a sulphur donor atom, exhibited the best selectivity for Ag(I). When the membranes were conditioned in

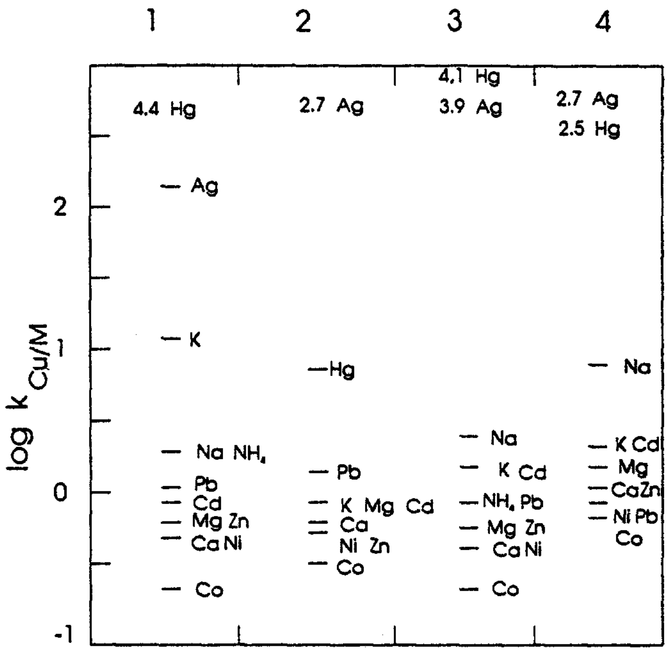

Fig. 1. Values of selectivity coefficients $\log k_{Cu/M}$. Conditions: 10^{-2} M $M(NO_3)_2$; pH = 3. Internal electrolyte: 10^{-1} M KCl, pH = 4. Membrane conditioned for six days in H_2O.

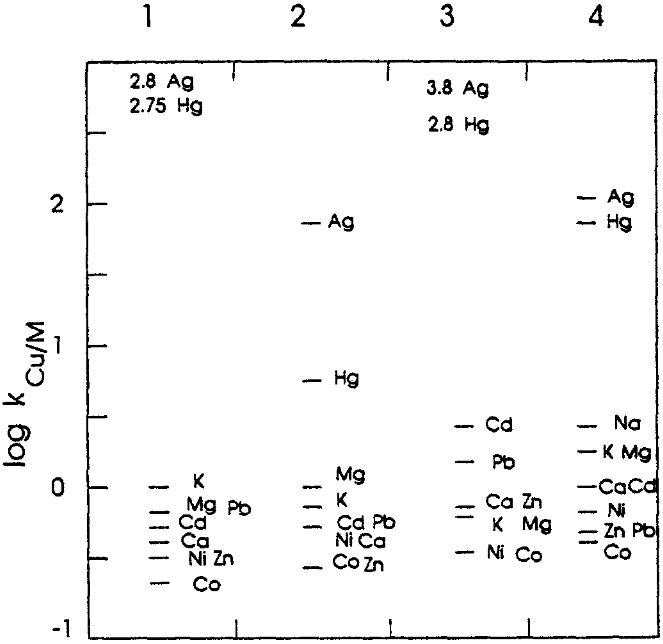

Fig. 2. Values of selectivity coefficients $\log k_{Cu/M}$. Conditions: 10^{-2} M $M(NO_3)_2$; pH = 3. Internal electrolyte: 10^{-2} M $CuCl_2$, pH = 3. Membrane conditioned for two days in 10^{-3} M $CuCl_2$, pH = 4.

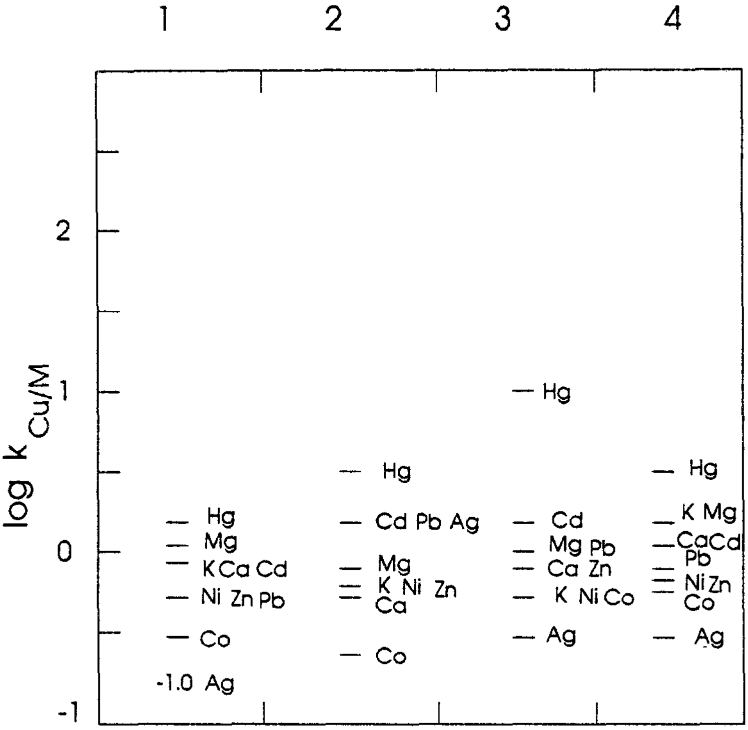

Fig. 3. Values of selectivity coefficients $\log k_{Cu/M}$. Conditions: 10^{-2} M $M(NO_3)_2$; pH = 3. Internal electrolyte: 10^{-2} M $HgCl_2$, pH = 3. Membrane conditioned for five days in 10^{-2} M $HgCl_2$, pH = 4.

aqueous $CuCl_2$, the highest selectivity was observed for Ag(I) ions, although selectivity for Hg(II) ions was also very high. The membrane conditioning in aqueous $HgCl_2$ led to high selectivity for Hg(II) ions.

Compounds **5**, **6**, and 18-crown-6 (for comparison) depicted in Figures 4, 5, and 6 were macrocyclic sulphonamides (except 18C6). The selectivities were assigned in the same manner as shown in Figures 1, 2, 3. In all cases the new compounds **5** and **6** displayed the highest selectivity for Hg(II) ions. It is somewhat surprising that an ‘all oxygen’ macrocycle, 18-crown-6, also exhibited a very high affinity for the Hg(II) cation, although ‘all oxygen’ crown ethers are rather poor binders for the Hg(II) cations.

It appears that the change of the nitrogen character in the diaza-crown ether from sp^3 to sp^2 has practically no effect on suppressing the high affinity for mercury cations and for silver. These two cations were particularly well recognized, in contrast with other divalent cations, such as transition metals and alkaline earth metal cations. The presence of tetra(*p*-chlorophenyl)borate is essential to achieve pronounced selectivity of the ionophores for Hg(II). Further design will involve monoazacrown ethers with linear ether pendant arms as ligating groups. It is well documented that mercury does not form strong complexes with oxygen-donor binding sites.

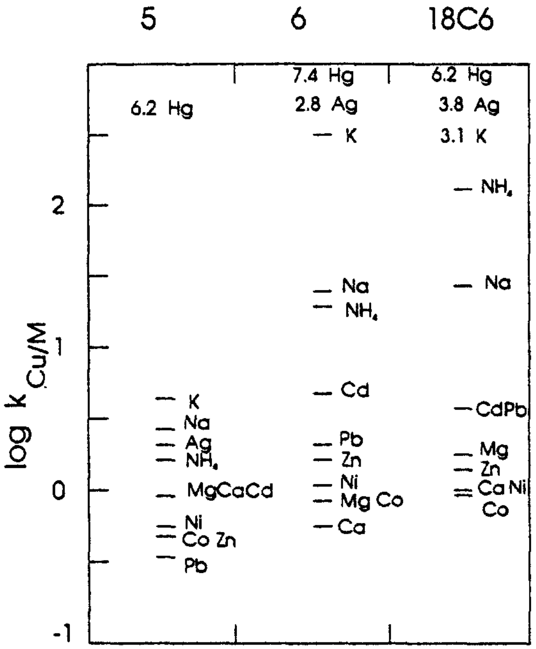

Fig. 4. Values of selectivity coefficients $\log k_{Cu/M}$. Conditions: 10^{-2} M $M(NO_3)_2$; pH = 3. Internal electrolyte: 10^{-1} M KCl, pH = 4. Membrane conditioned for two days in H_2O.

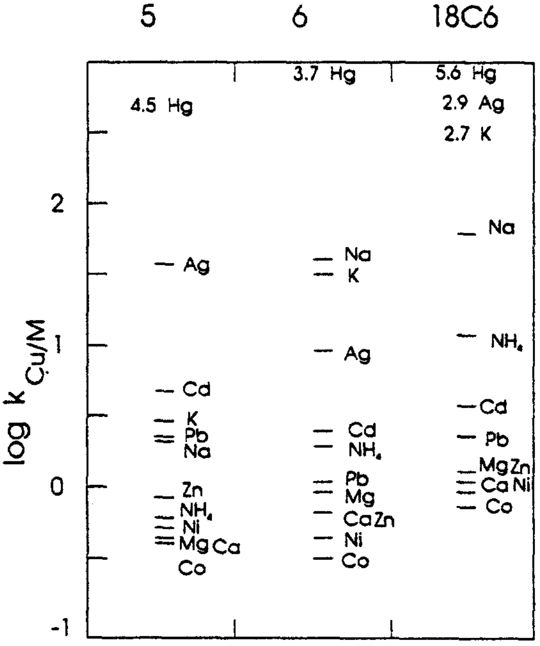

Fig. 5. Values of selectivity coefficients $\log k_{Cu/M}$. Conditions: 10^{-2} M $M(NO_3)_2$; pH = 3. Internal electrolyte: 10^{-2} M $CuCl_2$, pH = 3. Membrane conditioned for three days in 10^{-3} $CuCl_2$, pH = 4.

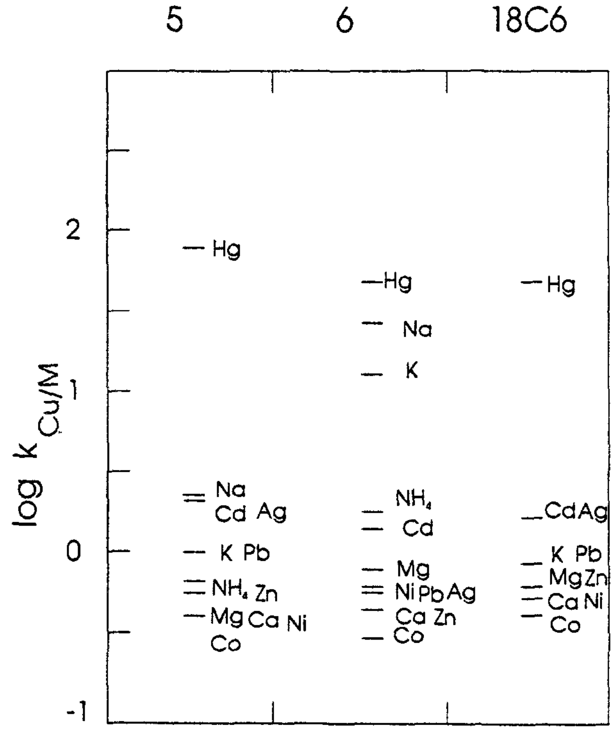

Fig. 6. Values of selectivity coefficients log $k_{Cu/M}$. Conditions: 10^{-2} M $M(NO_3)_2$; pH = 3. Internal electrolyte: 10^{-2} M $HgCl_2$, pH = 3. Membrane conditioned for three days in 10^{-3} $HgCl_2$, pH = 4.

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