SYNTHESIS OF MACROCYCLIC POLYETHER-DIAMIDES AND THEIR MEMBRANE SELECTIVITY

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The preparation of a series of polyether-diamides with different structure of the macrocyclic chain is described. The ion-selective properties of these compounds with respect to ions of the I and II group were investigated electrochemically in poly(vinyl chloride) membranes plasticised with 2-nitro-1-octyloxybenzene. The relationships between the structure of ionophores and their membrane selectivity are discussed.

In recent years, macrocyclic polyethers have become an object of intensive research due to their ability to form complexes with various cations[1,2]. When using them as ionophores in membranes possessing ion-selective properties, we showed that by employing suitable structural changes it was possible to prepare compounds with a high selectivity for potassium ions with respect to sodium ions[3,4]. Changes in structure with a simple polyether macrocyclic ring undisturbed always give rise to compounds which favour alkali metal ions in the formation of complexes and therefore are not suitable for use as potential ligands for alkaline earth ions. We have shown in a recent paper[5] that the introduction of amide groups into the polyether chain modifies the binding properties of these compounds in favour of the alkaline earth cations compared to the alkali metal ions. This paper deals with the preparation of a series of macrocyclic polyether-diamides and investigation of the effect of structure on their selectivity in polymeric membranes with respect to the alkaline earth ions.

EXPERIMENTAL

The melting points were determined on the Kofler hot stage. ^{1}H-NMR spectra were recorded in deuteriochloroform with tetramethylsilane as the internal standard, using a Jeol PS-100 apparatus at 100 MHz. Chemical shifts are given in δ (ppm). Mass spectra were recorded on an AEI-MS 902 mass spectrometer; the most important ions are given in m/e values. Elemental analyses were performed on a CHN Perkin-Elmer 240 analyzer. Column chromatography was carried out on silicagel (60—120 μm), TLC was performed on glass plates precoated with silicagel G (Merck). Spots were detected by spraying with Dragendorff's reagent.

Initial Materials

1,2-Benzenedicarboxylic, butanedioic, hexanedioic and 2,5-furandicarboxylic acids were commercial or laboratory samples. 3,6-Dioxaoctane-1,8-dixarboxylic acid was prepared according to ref.[6]. 4,5-Dimethyl-3,6-dioxaoctanedicarboxylic acid was prepared according to ref.[7], with the only difference that the crude product was distilled *in vacuo* and the fraction having the b.p. 90—99°C/13·3 Pa was saponified by refluxing with 7% KOH in 75% methanol for two hours. The diacid was isolated from acidified aqueous solution with ether in an extractor. After removal of the ether, the remaining viscous oil crystallized upon addition of benzene and the product was recrystallized from the mixture benzene-ethyl acetate. M.p. 85—99°C. For $C_{18}H_{14}O_6$ (206·2) calculated: 46·60% C, 6·84% H; found: 46·59% C, 6·83% H. Acid chlorides were prepared from the respective acids by reaction with thionyl chloride and distilled. Chlorides of oxyalkanedicarboxylic acids were prepared according to ref.[7] each time before cyclization.

1,13-Diaza-4,7,10,16,19-pentaoxacycloheneicosane was prepared according to ref.[6].

N,N'-Dialkylalkylenediamines

These compounds were prepared by the alkylation of the respective N-alkyl-*p*-toluenesulphonamides with 1,5-dibromo-3-oxapentane, 1,8-dibromo-3,6-dioxaoctane, 1,11-dibromo-3,6,9-trioxaundecane or with 1,12-dibromododecane, which was followed by the elimination of the tosyl group with sodium in 2-methylbutane-1-ol. A solution of 0·2 mol of N-alkyl-*p*-toluenesulphonamide in 180 ml of ethanol with 11·8 g of potassium hydroxide and 0·1 mol of dibromide was refluxed for 10 h. 150 ml of 6% NaOH was added after cooling. The oily layer that appeared after this addition was separated, dissolved in benzene and washed with water. Benzene was removed by distillation, and the remaining ditosyl derivative was dissolved in 500 ml of 2-methylbutane-1-ol. To this solution, 40 g of sodium was added in parts at such a rate as to maintain the reaction mixture boiling. After sodium had dissolved and the mixture had been cooled to 90°C, 250 ml of water was added. The organic layer was washed twice with 100 ml of water; 20 ml of concentrated hydrochloric acid was added, and the mixture was concentrated by distillation *in vacuo* to one third of its initial volume. After the addition of ether, dihydrochloride of the respective N,N'-dialkylalkylenediamine crystallized in a yield of 25—30%. Bases were obtained by alkalizing the aqueous solution and extraction into benzene. After the latter had been removed by distillation *in vacuo*, the bases were in most cases used directly in the cyclization reaction.

N,N'-*Dibenzyl*-1,5-*diamino*-3-*oxapentane dihydrochloride*: m.p. 198—201°C. For $C_{18}H_{26}Cl_2.N_2O$ (357·3) calculated: 60·50% C, 7·33% H, 7·84% N; found: 60·37% C, 7·58% H, 7·52% N.

N,N'-*Dibenzyl*-1,8-*diamino*-3,6-*dioxaoctane dihydrochloride*: m.p. 191—193°C. For $C_{20}H_{30}.Cl_2N_2O_2$ (401·4) calculated: 59·85% C, 7·53% H, 6·98% N; found; 59·79% C, 7·62% H, 6·75% N.

N,N'-*Dibenzyl*-1,11-*diamino*-3,6,9-*trioxaundecane dihydrochloride*: m.p. 174—177°C. For $C_{22}H_{34}Cl_2N_2O_3$ (445·4) calculated: 59·32% C, 7·69% H, 6·29% N; found: 58·89% C, 7·87% H, 6·32% N.

N,N'-*Diphenyl*-1,5-*diamino*-3-*oxapentane*: oil b.p. 172—176°C/13·3 Pa. For $C_{16}H_{20}N_2O$ (256·4) calculated: 74·96% C, 7·86% H, 10·92% N; found: 74·86% C, 7·97% H, 10·90% N.

N,N'-*Dimethyl*-1,11-*diamino*-3,6,9-*trioxaundecane dihydrochloride*: strongly hygroscopic crystals, liquescent in air; the base was prepared directly and used in the preparation of cyclic diamide.

N,N'-*Dibenzyl*-1,12-*diaminododecane*: recrystallized from aqueous ethanol, m.p. 52—52·5°C. Dihydrochloride m.p. 253°C, soluble in hot water. For $C_{26}H_{40}N_2$ (380·6) calculated: 82·05% C, 10·59% H, 7·36% N; found: 81·93% C, 10·87% H, 7·26% N.

Cyclic Diamides

Separate solutions of 6 mmol of dichloride in 180 ml of benzene and 6 mmol of diamine with 18 mmol of triethylamine in 180 ml of benzene were added dropwise at the same rate into 1 000 ml of stirred benzene during 6—7 h. Triethylamine hydrochloride separated during the reaction. On completion of the reaction the mixture was filtered, and benzene was removed by distillation *in vacuo*. The raw product was purified by chromatography on silicagel using benzene–methanol (5 : 1 or 10 : 1) as the eluent; its purity was checked by TLC chromatography. If the products were crystalline, they were moreover recrystallized from a benzene–hexane mixture.

7,13-*Diphenyl*-2,3-*dimethyl*-7,13-*diaza*-1,4,10-*trioxacyclopentadecane*-6,14-*dione* (I): 66%, m.p. 121—125°C. ^{1}H-NMR ($CDCl_3$): 0·9 (q, 6 H, 2 CH_3CH); 3·4 (m, 8 H, 2 NCH_2CH_2O); 3·7 to 3·8 (m, 2 H, 2 $CHCH_3$); 4·17 (m, 4 H, 2 OCH_2CO); 7·38 (s, 10 H, Ar). Mass spectrum: 426 (M^+), 381, 356, 291, 178, 162. For $C_{24}H_{30}N_2O_5$ (426·5) calculated: 67·58% C, 7·09% H, 6·57% N; found: 67·82% C, 7·09% H, 6·30% N.

7,13-*Dibenzyl*-2,3-*dimethyl*-7,13-*diaza*-1,4,10-*trioxacyclopentadecane*-6,14-*dione* (II): 48%, oil. ^{1}H-NMR: 1·18 (m, 6 H, CH_3CH); 3·4 (m, 10 H, $CHCH_3$, NCH_2CH_2O); 4·18—4·7 (m, 8 H, OCH_2CO, CH_2Ar); 7·2 (s, 10 H, Ar). Mass spectrum: 454 (M^+), 426, 410, 399, 367, 341, 339. For $C_{26}H_{34}N_2O_5$ (454·5) calculated: 68·69% C, 7·53% H, 6·16% N; found: 67·99% C, 7·50% H, 6·04% N.

7,16-*Dibenzyl*-2,3-*dimethyl*-7,16-*diaza*-1,4,10,13-*tetraoxacyclooctadecane*-6,17-*dione* (III): 50%, oil. ^{1}H-NMR ($CDCl_3$): 1·16 (m, 6 H, CH_3CH); 3·46 (m, 14 H, $CHCH_3$, NCH_2, OCH_2CH_2O); 4·0—4·8 (m, 8 H, OCH_2CO, CH_2Ar); 7·2 (s, 10 H, Ar). Mass spectrum: 498 (M^+), 471, 454, 443, 411, 385, 383. For $C_{28}H_{38}N_2O_6$ (498·6) calculated: 67·45% C, 7·68% H, 5·62% N; found: 68·40% C, 7·92% H, 5·34% N.

7,19-*Dibenzyl*-2,3-*dimethyl*-7,19-*diaza*-1,4,10,13,16-*pentaoxacycloheneicosane*-6,20-*dione* (IV): 59%, oil. ^{1}H-NMR ($CDCl_3$): 1·12 (m, 6 H, CH_3CH); 3·5 (m, 18 H, $CHCH_3$, NCH_2, OCH_2.$.CH_2O$); 4·18—4·75 (m, 8 H, OCH_2CO, NCH_2Ar); 7·2 (s, 10 H, Ar). Mass spectrum: 542 (M^+), 515, 498, 487, 455, 429, 427. For $C_{30}H_{42}N_2O_7$ (542·7) calculated: 66·40% C, 7·80% H, 5·16% N; found: 66·11% C, 7·93% H, 5·09% N.

7,20-*Dibenzyl*-2,3-*dimethyl*-7,20-*diaza*-1,4-*dioxacyclododocosane*-6,21-*dione* (V): 55%, m.p. 77 to 80°C. ^{1}H-NMR ($CDCl_3$): 1·24 (m, 26 H, 2 CH_3, 10 CH_2); 3·15 (m, 4 H, 2 NCH_2CH_2); 3·62 (bq, 2 H, 2 $OCHCH_3$); 4·25 (m, 4 H, 2 OCH_2CO); 4·52 (s, 4 H, 2 CH_2Ar); 7·2 (s, 10 H, 2 CH_2Ar). Mass spectrum: 550 (M^+), 495, 464, 437, 435. For $C_{34}H_{50}N_2O_4$ (550·8) calculated: 74·14% C, 9·15% H, 5·08% N; found: 74·23% C, 9·30% H, 4·81% N.

7,19-*Dibenzyl*-7,19-*diaza*-1,4,10,13,16-*pentaoxacycloheneicosane*-6,20-*dione* (VI): 63%, oil. ^{1}H-NMR ($CDCl_3$): 3·45—3·73 (m, 20 H, 2 NCH_2CH_2O, 3 OCH_2CH_2O); 4·38 (m, 4 H, 2 OCH_2CO); 4·54 (s, 4 H, 2 CH_2Ar); 7·2 (s, 10 H, 2 Ar). Mass spectrum: 514 (M^+), 486, 470, 457, 441, 427, 397. For $C_{28}H_{38}N_2O_7$ (514·6) calculated: 65·35% C, 7·44% H, 5·44% N; found: 64·49% C, 7·64% H, 5·21% N.

10,15-*Dibenzyl*-10,15-*diaza*-1,4,7-*trioxacycloheptadecane*-11,14-*dione* (VII): 11%, m.p. 138 to 139°C. ^{1}H-NMR ($CDCl_3$): 2·36—2·94 (m, 4 H, 2 CH_2CO); 3·44 (m, 16 H, NCH_2CH_2O, OCH_2CH_2O); 4·55 (bs, 4 H, CH_2Ar); 7·2 (s, 10 H, Ar). Mass spectrum: 454 (M^+), 426, 370, 363, 322, 264, 263). For $C_{26}H_{34}N_2O_5$ (454·6) calculated: 68·69% C, 7·54% H, 6·16% N; found: 68·87% C, 7·71% H, 6·11% N.

10,17-*Dibenzyl*-10,17-*diaza*-1,4,7-*trioxacyclononadecane*-11,16-*dione* (VIII): 25% m.p. 74—77°C. ^{1}H-NMR ($CDCl_3$): 2·36—2·94 (m, 8 H, 2 CH_2CH_2CO); 3·44 (m, 16 H, NCH_2CH_2O, OCH_2.

.CH_2O); 4·55 (bs, 4 H, CH_2Ar); 7·2 (s, 10 H, Ar). Mass spectrum: 482 (M^+), 454, 440,425, 409, 370, 349. For $C_{28}H_{38}N_2O_5$ (482·6) calculated: 69·68% C, 7·93% H, 5·81% N; found: 69·63% C, 7·92% H, 5·88% N.

Benzo-[*l*]-10,15-*dimethyl*-10,15-*diaza*-1,4,7-*trioxacycloheptadecane*-11,14-*dione* (IX): 37%, m.p. 137—138°C. ^{1}H-NMR ($CDCl_3$): 2·85 (s, 6 H, 2 CH_3); 3·65 (m, 16 H, 2 NCH_2CH_2O, 2 OCH_2.CH_2O); 7·25 (m, 4 H, Ar). Mass spectrum: 350 (M^+), 349, 294, 189, 187, 175, 174. For C_{18}.$H_{26}N_2O_5$ (350·4) calculated: 61·69% C, 7·48% H, 7·99% N; found: 61·77% C, 7·65% H, 7·93% N.

3,12-*Dibenzyl*-3,12-*diaza*-6,9,17-*trioxabicyclo*[12,2,1]*heptadeca*-14,16-*diene*-2,13-*dione* (X): 66%, m.p. 108—110°C. ^{1}H-NMR ($CDCl_3$): 3·43 (bs, 12 H, NCH_2CH_2O, OCH_2CH_2); 4·65 (s, 4 H, CH_2Ar); 7·20 (s, 12 H, Ar, furan). Mass spectrum: 448 (M^+), 420, 419, 357, 329, 253. For $C_{26}H_{28}N_2O_5$ (448·5) calculated: 69·63% C, 6·29% H, 6·24% N; found: 70·03% C, 6·39% H, 6·28% N.

3,15-*Dibenzyl*-3,15-*diaza*-6,9,12,20-*tetraoxabicyclo*[15,2,1]-*eicosa*-17,19-*diene*-2,16-*dione* (XI): 68%, glass. ^{1}H-NMR ($CDCl_3$): 3·52 (s, 12 H, OCH_2CH_2O, NCH_2CH_2O ; 3·60 (s, 4 H, NCH_2.CH_2O); 4·70 (s, 4 H, CH_2Ar); 7·2 (s, 12 H, Ar, furan). Mass spectrum: 492 (M^+), 464, 463, 401, 373, 307, 228, 226. For $C_{28}H_{32}N_2O_6$ (492·6) calculated: 68·27% C, 6·54% H, 5·68% N; found: 68·68% C, 6·74% H, 5·38% N.

Benzo[k]-1,13-*diaza*-4,7,10,16,19-*pentaoxabicyclo*[11,8,4]-*pentacosane*-22,25-*dione* (XII): 25%, m.p. 198°C. ^{1}H-NMR ($CDCl_3$): 2·8—4·3 (m, 28 H, NCH_2, OCH_2CH_2O); 7·3 (m, 4 H, Ar). Mass spectrum: 436 (M^+), 348, 335, 306, 291, 218. For $C_{22}H_{32}N_2O_7$ (436·5) calculated: 60·53% C, 7·39% H, 6·41% N; found: 60·91% C, 7·23% H, 6·37% N.

Preparation of Membrane Electrodes and EMF Measurements

5 mg of the ligand was dissolved in 0·1 ml of 2-nitro-1-octyloxybenzene and mixed with 5 ml of a 5% (w/v) high-molecular weight poly(vinyl chloride) (PVC) in cyclohexanone. The solution was poured on a horizontal glass plate covering an area of some 30 cm^2. Free evaporation of cyclohexanone at room temperature yields a membrane about 0·15 mm thick, from which suitable discs for the electrodes were cut out. The discs were thermally welded to the end of a PVC tube. The diameter of the effective membrane surface was 5 mm. The electrode units were completed by inserting an internal reference Ag—AgCl were electrode and a 0·01M-$CaCl_2$ filling solution.

EMF was measured on a pHM 4 (Radiometer) pH-meter connected through a 610 C (Keithley Instr.) electrometer. In all the cases cells of the following type were employed: Hg; Hg_2Cl_2, KCl (satd.) /0·1M-NH_4NO_3/ sample solution /membrane/ 0·01M-$CaCl_2$, AgCl; Ag with a saturated calomel electrode OP 815 (Radelkis) in double-junction configuration at 25°C. The separate solution technique[8] on 0·1M solutions of chlorides was employed for determining the potentiometric selectivity coefficients given by

$$\log k_{\mathrm{NM}}^{\mathrm{pot}} = \frac{(E_\mathrm{M} - E_\mathrm{N})\, z_\mathrm{N} F}{2{\cdot}303 RT} - \frac{z_\mathrm{N}}{z_\mathrm{M}} \log a_\mathrm{M} + \log a_\mathrm{N}\,,$$

where RT/F is Nernst factor, a are ionic activities, z_N is the charge of the principal ion, z_M is the charge of the interfering ion, E_M is the EMF of the cell where the sample solution is a solution of chloride of the interfering cation, E_N is the EMF of the cell where the sample solution is a solution of chloride of the main cation.

The activities of all alkaline earth ions were calculated by employing the relation for the dependence of the activity coefficient γ_{Ca} on the ionic strength I,

$$\log \gamma_{Ca} = -2{\cdot}04 \sqrt{I}/(1 + 1{\cdot}55 \sqrt{I}) + 0{\cdot}2I ,$$

the activities of all the cations of alkali metals were determined using the relation for γ_{Na}:

$$\log \gamma_{Na} = -0{\cdot}51 \sqrt{I}/(1 + 1{\cdot}3 \sqrt{I}) + 0{\cdot}06I .$$

RESULTS AND DISCUSSION

Macrocyclic polyether-diamides *I*–*XII* were obtained by reacting dichlorides of dicarboxylic acids with the corresponding N,N'-dialkylalkylenediamines in benzene using high dilution technique, which allowed us to obtain them in a high yield (30 to 65%). A satisfactory elemental analysis could not be obtained for some viscous or glassy compounds owing to the residues of chromatographic solvents, which could not be removed even by employing high vacuum. The structure of all compounds was consistent with ^{1}H-NMR spectra; the mass spectra exhibited a molecular ion corresponding to their mass. Macrocyclic diamides analogous to *X*, *XI* and *XII* but derived from pyridine- and 2,2'-bipyridinedicarboxylic acids were prepared by Vögtle and coworkers[9,10].

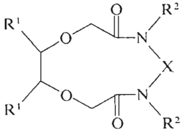
The ion-selective properties of polyether-diamides prepared were investigated electrochemically. Ionophores were incorporated into high-molecular weight poly(vinyl chloride) membranes using 2-nitro-1-octyloxybenzene as solvent and plasticiser.

TABLE I

Selectivity Coefficients k^{pot}_{CaM} of Ligands *I*—*XII* in PVC Membranes with 2-Nitro-octyloxybenzene with Respect to Ions M

Ligand	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Sr^{2+}	Ba^{2+}
I	$3 . 10^{-2}$	$5 . 10^{-1}$	$5 . 10^{-1}$	$1 . 10^{-1}$	$2 . 10^{-1}$	$2 . 10^{-3}$	$5 . 10^{-1}$	1
II	$4 . 10^{-2}$	$9 . 10^{-2}$	$2 . 10^{-1}$	$1 . 10^{-1}$	$2 . 10^{-1}$	$2 . 10^{-3}$	$5 . 10^{-1}$	1
III	$2 . 10^{-2}$	$1 . 10^{-2}$	$2 . 10^{-2}$	$9 . 10^{-3}$	$1 . 10^{-2}$	$2 . 10^{-3}$	$1 . 10^{-1}$	$3 . 10^{-1}$
IV	$2 . 10^{-2}$	$5 . 10^{-3}$	$3 . 10^{-3}$	$3 . 10^{-3}$	$3 . 10^{-3}$	$1 . 10^{-3}$	$1 . 10^{-1}$	$1 . 10^{-1}$
V	3	$3 . 10^{-1}$	$9 . 10^{-2}$	$4 . 10^{-2}$	$4 . 10^{-2}$	$3 . 10^{-3}$	$3 . 10^{-1}$	$7 . 10^{-1}$
VI	$2 . 10^{-1}$	$2 . 10^{-1}$	$1 . 10^{-1}$	$2 . 10^{-1}$	$2 . 10^{-1}$	$4 . 10^{-3}$	1	$9 . 10^{-1}$
VII	$2 . 10^{1}$	$5 . 10^{1}$	$6 . 10^{1}$	$2 . 10^{1}$	$5 . 10^{1}$	$3 . 10^{-2}$	$6 . 10^{-1}$	3
VIII	5	$4 . 10^{1}$	$8 . 10^{1}$	$7 . 10^{1}$	$2 . 10^{2}$	$7 . 10^{-2}$	1	$1 . 10^{1}$
IX	3	$5 . 10^{1}$	$5 . 10^{2}$	$1 . 10^{3}$	$2 . 10^{3}$	$9 . 10^{-3}$	1	4
X	8	$1 . 10^{2}$	$2 . 10^{3}$	$8 . 10^{2}$	$8 . 10^{2}$	$3 . 10^{-1}$	$8 . 10^{-1}$	9
XI	8	$3 . 10^{1}$	$2 . 10^{2}$	$1 . 10^{2}$	$2 . 10^{2}$	$6 . 10^{-2}$	$8 . 10^{-1}$	6
XII	1	$4 . 10^{1}$	$4 . 10^{2}$	$2 . 10^{2}$	$3 . 10^{2}$	$2 . 10^{-1}$	$3 . 10^{-1}$	2

The selectivity coefficients with respect to Ca obtained by EMF measurements using the separate solution method are summarized in Table I. In order to provide a sufficient lipophilic character needed for ionophores, the amide nitrogen atoms in compounds possessing an aliphatic macrocycle had to be substituted with higher alkyls. N,N'-dimethyl derivatives were still soluble in water. Purely synthetic reasons led to the choice of substitution with the benzyl or phenyl group. As demonstrated by the virtually identical values of the selectivity coefficients of *I* and *II*, there is no perceptible difference between the effect of these two substituents, and substitution with the benzyl group was used with further derivatives. For macrocyclic polyether diamides derived from 3,6-dioxaoctanedicarboxylic acids, the influence of the closing amide chain was examined. An increase in this chain to include eleven members with three oxygen atoms in the case of compound *IV* led to discrimination between the calcium and barium ions and to a rise in the selectivity for calcium with respect to ions of alkali metals (with the exception of lithium ions) compared with *I*–*III*. The omission of ethereal oxygen atoms of the amide chain in V was reflected in an impaired distinction between calcium, barium and alkali metals.



I: $R^1 = CH_3$, $R^2 = Ar$, $X = CH_2CH_2OCH_2CH_2$
II: $R^1 = CH_3$, $R^2 = ArCH_2$, $X = CH_2CH_2OCH_2CH_2$
III: $R^1 = CH_3$, $R^2 = ArCH_2$, $X = CH_2(CH_2OCH_2)_2CH_2$
IV: $R^1 = CH_3$, $R^2 = ArCH_2$, $X = CH_2(CH_2OCH_2)_3CH_2$
V: $R^1 = CH_3$, $R^2 = ArCH_2$, $X = (CH_2)_{12}$
VI: $R^1 = H$, $R^2 = ArCH_2$, $X = CH_2(CH_2OCH_2)_3CH_2$

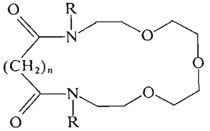
TABLE II

Selectivity Coefficients k^{Pot}_{CaM} of Ligands *II*–*IV* in PVC Membranes with 2-Nitro-1-octyloxybenzene and an Incorporated Anion with Respect to Ions M

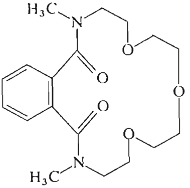
Ligand	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Sr^{2+}	Ba^{2+}
II[a]	$3 . 10^{-3}$	$2 . 10^{-3}$	$1 . 10^{-3}$	$3 . 10^{-3}$	$5 . 10^{-3}$	$1 . 10^{-3}$	$5 . 10^{-1}$	$6 . 10^{-1}$
III[a]	$5 . 10^{-3}$	$1 . 10^{-3}$	$5 . 10^{-4}$	$8 . 10^{-4}$	$1 . 10^{-3}$	$7 . 10^{-4}$	$7 . 10^{-2}$	$5 . 10^{-2}$
IV[a]	$3 . 10^{-3}$	$4 . 10^{-4}$	$1 . 10^{-4}$	$3 . 10^{-4}$	$4 . 10^{-4}$	$2 . 10^{-4}$	$1 . 10^{-1}$	$8 . 10^{-2}$
IV[b]	$3 . 10^{-3}$	$8 . 10^{-4}$	$8 . 10^{-4}$	$2 . 10^{-3}$	$3 . 10^{-3}$	$2 . 10^{-4}$	$1 . 10^{-1}$	$7 . 10^{-2}$

[a] Tetraphenylborate anion incorporated as sodium salt. [b] Tetra(4-chlorophenyl)borate anion incorporated as potassium salt.

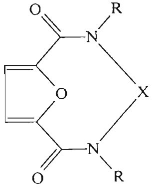
A further object of investigation was the effect of structural changes of dicarboxylic acids used in the preparation of macrocyclic diamides. The impaired selectivity for calcium ions with respect to barium ions and alkali metal ions in the case of *VI*, where two methyl groups in the chain of dioxaoctanedicarbocylic acid have been left out, indicates the importance of substitution in these positions. The steric effect of methyl groups obviously favours the formation of a cavity suited for the complexation of the smaller calcium ions. The substitution of dioxaoctanedicarboxylic acid with butanedioic and hexanedioic acid in the chains of *VII* and *VIII* affects unfavourably the selectivity for calcium ions, while giving preference to barium and alkali metal ions. The ionselective behaviour of *VII* and *VIII* is similar to the simple macrocyclic polyethers-crowns. Macrocyclic polyether-diamides with 1,2-benzenedicarboxylic (*IX* and *XII*) and furanedicarboxylic (*X*, *XI*) acids in the macrocyclic ring behaved in a similar way. The results presented above make it obvious that for Ca-ionophores of this type, at least two oxygen atoms must be present in the chain of dicarboxylic acid used in the preparation of ligands.



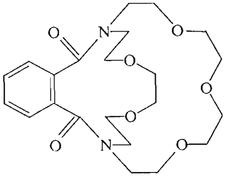
VII, R = $ArCH_2$, $n = 2$
VIII; R = $ArCH_2$, $n = 4$



IX



X; R = $ArCH_2$, X = $CH_2(CH_2OCH_2)_2CH_2$
XI; R = $ArCH_2$, X = $CH_2(CH_2OCH_2)_3CH_2$



XII

As has been demonstrated by Simon and coworkers[11], the selective behaviour of ionophores for bivalent cations with respect to univalent may be favourably affected by the permanent incorporation of a lipophilic anion into the membrane.

Table II documents this effect for selected macrocyclic polyetherdiamides, in which the tetraphenylborate or tetra(4-chlorophenyl)borate anion has been incorporated into the membranes. In all cases the resulting membranes exhibit a pronounced increase in the selectivity for calcium cations with respect to alkali metal ions, as well as a slight increase in the preference of calcium ions with respect to barium ions. No essential difference between the effect of incorporation of both types of anions was observed. An investigation of the influence of the membrane solvent used on the ion-selective properties of ligands of the polyether-diamide type and of the effect of the steric influence of substituents in ionophores derived from dioxaoctanedicarboxylic acid is in progress.

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