

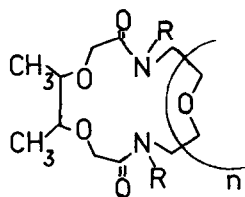
A NEW TYPE OF MACROCYCLIC POLYETHER-DIAMIDE LIGAND -
BINDING PROPERTIES FOR ALKALINE EARTH IONS

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(Received in UK 4 October 1977; accepted for publication 6 October 1977)

Generally, the macrocyclic polyethers (crown ethers) known so far form complexes preferably with alkali metal ions. Structural variation of the macrocyclic ring afford crown ethers possessing a pronounced selectivity for potassium with respect to sodium^{1,2}. However, the simple macrocyclic polyether ring does not seem to be suited for preferential complex-formation with the alkaline earth ions. Recently, crown compounds containing ester groups have been prepared³ as potential ligands for the alkaline earth ions. Latest results show, however⁴, that the selectivity of these compounds towards the above ions is low. We would like to report on a new type of macrocyclic polyether which contains amide groups in the macro-ring, the presence of which modifies the binding properties of the crown compounds in favour of the alkaline earth cations compared to the alkali metal ions.



The following compounds, (I) to (III), have been prepared:

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|------------------------|---|
| I, n=1 | The amide nitrogen atoms of these compounds are |
| II, n=2 | substituted with the benzyl groups in order |
| III, n=3 | to increase their lipophilic character, because |
| R = CH ₂ Ar | we found that the respective compounds with |
| | methyl groups were soluble in water. |

Ligands I-III were prepared by the reaction of 4,5-dimethyl-3,6-dioxaoctane-dicarboxylic acid dichloride with the respective N,N'-dibenzyl-oxa-alkylene diamines using the high dilution technique. The dichloride was prepared according to ref.⁵ from commercial 2,3-butanediol, which was a mixture of meso and racemic forms. The dibenzyl diamines were obtained by alkylation of N-benzyl-p-toluenesulphonamide with di-, tri- and tetraethyleneglycol dibromides, followed by the reductive cleavage of the tosyl group with sodium in isoamyl alcohol. The reaction of dichloride with diamines was carried out as follows: Separate solutions of 9 mmol of dichloride in 180 ml of benzene and of 9 mmol of diamine with 27 mmol of triethyl amine in 180 ml of benzene were added dropwise at the same rate to 1000 ml of rapidly stirred benzene during 6-7 h. The triethylamine hydrochloride was filtered off and benzene was removed under reduced pressure. Macrocyclic products were separated from linear products formed simultaneously in the reaction by chromatography

on silica gel using benzene-methanol (5:1 or 10:1) as eluent; their purity was checked by TLC (detection using Dragendorff's reagent). The isolated products, which were oils or glasses, were characterized by their mass and NMR spectra:

7,13-dibenzyl-2,3-dimethyl-7,13-diaza-1,4,10-trioxacyclopentadecane-6,14-dione (I, 48%).-M.S.: M^+ 454, 426, 410, 399, 367, 341, 339. $^1\text{H-NMR}$ (CDCl_3): 1.18 (m, 6H, CH_3CH), 3.4 (m, 6H, CHCH_3 , NCH_2), 4.18 (s, 4H, OCH_2CO), 4.6 (m, 8H, NCH_2Ar , $\text{NCH}_2\text{CH}_2\text{O}$), 7.2 (s, 10H, Ar).

7,16-dibenzyl-2,3-dimethyl-7,16-diaza-1,4,10,13-tetraoxacyclooctadecane-6,17-dione (II, 50%).-M.S.: M^+ 498, 471, 454, 443, 411, 385, 383. $^1\text{H-NMR}$ (CDCl_3): 1.16 (m, 6H, CH_3CH), 3.46 (m, 10H, CHCH_3 , NCH_2 , $\text{OCH}_2\text{CH}_2\text{O}$), 4.12 (s, 4H, OCH_2CO), 4.6 (m, 8H, NCH_2Ar , $\text{NCH}_2\text{CH}_2\text{O}$), 7.2 (s, 10H, Ar).

7,19-dibenzyl-2,3-dimethyl-7,19-diaza-1,4,10,13,16-pentaoxacycloheneicosane-6,20-dione (III, 59%).-MS.: M^+ 542, 515, 498, 487, 455, 429, 427. $^1\text{H-NMR}$ (CDCl_3): 1.12 (m, 6H, CH_3CH), 3.5 (m, 14H, CHCH_3 , NCH_2 , $\text{OCH}_2\text{CH}_2\text{O}$), 4.18 (s, 4H, OCH_2CO), 4.6 (m, 8H, NCH_2Ar , $\text{NCH}_2\text{CH}_2\text{O}$), 7.2 (s, 10H, Ar).

The selectivity of the compounds prepared in complexing metal ions was determined electrochemically by measuring membrane potentials using a cell of the type: ref.electrode/sample//membrane//inner solution; int.ref.electrode. For these measurements, ligands were incorporated in PVC membranes² using o-nitrophenyl-n-octylether as a membrane solvent. The potentiometric selectivity coefficients $k_{\text{Ca},\text{M}}^{\text{pot}}$ determined by the separate solution technique in 0.1 M aqueous solutions of the chlorides of cations are:

Ligand	Mg	Ca	Ba	Li	Na	K	Rb	Cs
I	0.002	1	2	0.1	0.3	0.7	0.5	0.5
II	0.002	1	0.2	0.2	0.2	0.2	0.2	0.2
III	0.004	1	0.1	0.1	0.05	0.04	0.06	0.06

The values indicate that in complex formation all ligands prefer Ca^{++} and Ba^{++} . An increase in the size of the macrocyclic ring in compound II leads to a preference for Ca^{++} relative to Ba^{++} . Ligand III is ten times more sensitive to Ca^{++} than Ba^{++} . Since, the structures of the complexes are not yet known, the binding sites of the ligands cannot be predicted with certainty. These questions, and the application of the above new group of compounds in ion-selective electrodes, are the object of further study.

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