Structurally reinforced Macrocyclic Ligands that show greatly enhanced Selectivity for Metal Ions on the Basis of the Match in Size between the Metal Ion and the Macrocyclic Cavity

Robert D. Hancock,* Ann Evers, M. Patrick Ngwenya, and Peter W. Wade

Department of Chemistry, University of the Witwatersrand, Johannesburg, South Africa

Addition of an extra bridging group between nitrogen donors on macrocyclic ligands to give a piperazine-like structure leads to much more rigid ligands which display selectivity for metal ions which is more strongly based on the match between the size of the metal ion and of the macrocyclic cavity than is the case for conventional macrocyclic ligands.

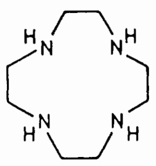
In previous papers[1,2] it has been shown that the formation constants of tetra-azamacrocycles such as L_1 and L_3 do not support the idea of size-match selectivity, *i.e.* that a metal ion would form its most stable complex with the member of the tetra-azamacrocyclic series where there was the closest match between the size of the metal ion and of the macrocyclic cavity. Thus, the largest metal ion examined, Pb^{II}, formed its most stable complex with L_1, which has a cavity much too small for co-ordination with Pb^{II} in the plane of the donor atoms, while the smallest metal ion, low-spin Ni^{II}, formed its most stable complex with L_3, which has a cavity much too big for it.[1,2] Molecular mechanics calculations[3] have shown that the failure to observe size-match selectivity is due to the fact that the metal ions are not constrained to co-ordinate lying in the plane of the ligand, and that this may not even necessarily be the most stable arrangement. Co-ordination of the metal ion in an out-of-plane mode means that the factors controlling selectivity are thus similar to those in open-chain polyamines, namely the size of the chelate rings formed on complex formation.[1,2]

In order to observe genuine size-match selectivity, it is thus necessary to make the macrocyclic ligand more rigid, so that the metal ion is forced to co-ordinate lying in the macrocyclic cavity. The synthesis and some properties of the complex of

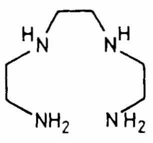
Table 1. Formation constants (log K_1) for some bridged macrocycles and their non-bridged analogues, as well as some open-chain analogues.

	log K_1				
	$Ni^{2+}(S{=}O)$[a]	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
L_5[b,c]	14.3	21.50	10.95	10.07	11.71
L_4[d]	4.68	11.91	5.81	4.51	7.1
log K_{mac} (L_4,L_5)[e]	9.6	9.6	5.1	5.6	4.7
L_1[f]	14.0	23.3	16.2	14.3	15.9
L_2[g]	12.1	20.1	12.0	10.6	10.4
log K_{mac} (L_1,L_2)[h]	1.9	3.2	4.2	3.7	5.5
L_8	—	28.0	—	19.2	—
L_7	—	15.1	—	14.7	—
Ionic radius[i]/Å	0.49	0.57	0.74	0.95	1.18

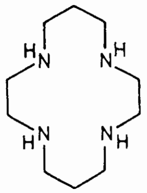
[a] The complex of Ni^{II} with L_4 appears to be entirely low-spin, so that all values listed refer to the stability of the low-spin complex of Ni^{II} so that comparisons can be made. [b] For key to ligands, see structures. [c] This work, 0.1 M $NaNO_3$, 25 °C. [d] In 0.1 M $NaNO_3$ at 25.0 °C, R. D. Hancock, A. Evers, and M. P. Ngwenya, to be published. [e] log K_{mac} = log K_1 (L_5) − log K_1 (L_4). [f] Ref. 1,2, and 10. [g] Ref. 10. [h] log K_{mac} = log K_1 (L_1) − log K_1 (L_2). [i] These are radii for square planar (Cu^{2+}, Ni^{2+}) and octahedral co-ordination (Zn^{2+}, Cd^{2+}, and Pb^{2+}) from ref. 8.



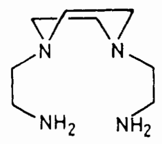
L_1



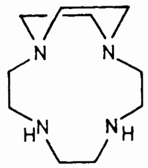
L_2



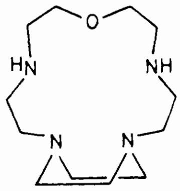
L_3



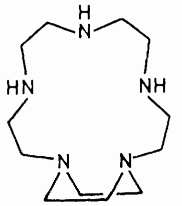
L_4



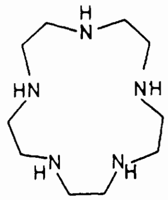
L_5



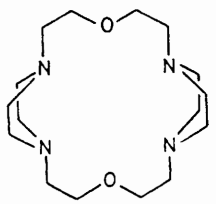
L_6



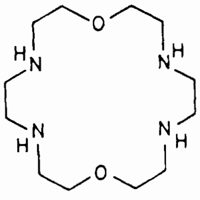
L_7



L_8



L_9



L_{10}

Ni^{II} with L_5 have recently been reported.[4] We have synthesized the ligands L_6 and L_7 by conventional means whereby the ditosylate of *N*,*N*′-bis(2-aminoethyl)-piperazine has been condensed[5] with the tosylates of diethanolamine and diethylenetriamine, and detosylated using glacial acetic-hydrobromic acid mixtures.[6] The ligand L_9 was synthesized by reacting L_{10} with dibromoethane as described for the synthesis of L_5.[4] Formation constants (Table 1) were determined for Cu^{II}, Ni^{II}, Zn^{II}, Cd^{II}, and Pb^{II} with these ligands by the usual glass-electrode potentiometric procedures,[1,2] except that equilibration times with L_5 were very slow, and an out-of-cell procedure was followed.[1]

The thermodynamic manifestation of the macrocyclic effect, $\log K_{mac}$, is taken[7] to be $\log K_1$ for the complex with the macrocycle minus $\log K_1$ for that with the open-chain analogue. Table 1 shows that $\log K_{mac}$ for L_1 shows a tendency to increase with increasing size[8] of the metal ion. This runs contrary to the expectations from size-match selectivity, since the cavity in L_1 is in fact too small[9] even for low-spin Ni^{II}, the smallest metal ion used. On the other hand, $\log K_{mac}$ for L_5 is largest for the very small metal ions Cu^{II} and low-spin Ni^{II}, and much smaller for the larger metal ions, in accord with expectations based on the idea of size-match selectivity. The values of $\log K_{mac}$ for L_5 with Cu^{II} and Ni^{II} are far higher than those in the literature for normal tetra-azamacrocycles, which do not exceed six log units. This may relate to the free ligand L_5 already having the high-energy boat conformation in its piperazine ring, which is required for co-ordination to a metal ion, while L_4 in its free ligand form is likely to have the piperazine-like ring in the lower energy chair conformation.

Models of ligands such as L_6 or L_7 show that the piperazine ring acts much like a spring which tends to hold the cavity in the ligand open. Ligands such as L_8 are able to co-ordinate to small metal ions such as Cu^{II} by folding, which is much more difficult for L_7. We thus see in Table 1 that the small metal ion Cu^{II} suffers a drop of some thirteen orders of magnitude in $\log K_1$ in passing from L_8 to L_7, whereas for the large metal ion Cd^{II} which fits the large cavity in L_7 without the need of folding, the drop in $\log K_1$ is only some four log units. The addition of double bridges almost always leads to a drop in $\log K_1$, possibly resulting from the need for the piperazine part of the ligand to assume the energetically unfavourable boat conformation. The doubly bridged ligand L_9 has a $\log K_1$ of 5.0 with Pb^{II} while the non-bridged analogue L_{10} has $\log K_1$ 9.0. However, no complex formation can be detected for any other metal ion studied with L_9 (Cu^{II}, Ni^{II}, Zn^{II}, Cd^{II}, Ca^{II}, Sr^{II}, or Ba^{II}), whereas L_{10} complexes the smaller of these metal ions such as Cu^{II} ($\log K_1 = 16.3$) or Ni^{II} ($\log K_1 = 12.5$) very strongly. This illustrates the very strong size-selectivity which double bridging can achieve. (It should be noted that the non-complexation of Sr^{II} or Ba^{II} by L_9 must relate to their low affinity for N-donors, as they are also co-ordinated only very weakly by L_{10}.)

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