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The Metal Ion Size-dependent Pattern of Stabilization Produced by Adding Alcoholic or Ethereal Oxygen Donors to Ligands

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There has been much interest in ligands with alcoholic 'arms' [1–4] added to macrocyclic structures, such as the 'Lariat Ethers' of Gokel *et al.* [1]. There has, however, to date been no systematic investigation of the effect on complex stability of the addition of neutral oxygen donors in the form of alcoholic 'arms' or how this compares with the stabilization produced by oxygens which are part of a macrocyclic ring. We have recently shown [5] that, whereas small metal ions such as Cu^{II}, Ni^{II}, and Zn^{II}, show little change in complex stability when hydroxyethyl groups are added to ammonia to give triethanolamine as a ligand, a metal ion such as Pb^{II} shows a large increase in complex stability from $\log K_1 = 1.6$ to $\log K_1 = 3.3$. It was conjectured [5] that this increase was size-related, and would be found for large metal ions whether the added neutral oxygen donor was alcoholic or ethereal, or whether it was part of a macrocyclic ring or a pendent donor group.

In order to examine this hypothesis, we have determined the stability of the complexes formed by the ligands THPED and BHP-18-ANE-N_2O_4, shown in Fig. 1, with a wide variety of metal ions. The formation constants of these complexes are reported in this paper.

Experimental

The ligand THPED was obtained from Aldrich. The ligand BHP-18-ANE-N_2O_4 was synthesized by reacting 18-ANE-N_2O_4 (Merck) with a slight excess of propylene oxide in iso-propanol, and was obtained as a clear oil after removal of the solvent and unreacted propylene oxide under vacuum. The C, H, and N analyses were satisfactory. Formation constants were determined by glass-electrode potentiometry as described previously [5]. The protonation constants of BHP-18-ANE-N_2O_4 were found to be $pK_1 = 8.40$ and $pK_2 = 7.15$.

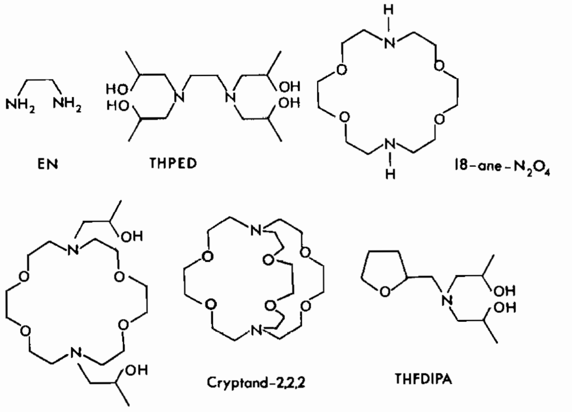

Fig. 1. Ligands discussed in this work. (NOTE abbreviations: EN = ethylenediamine; THPED = *N,N,N',N'*-tetrakis(2-hydroxypropyl)ethylenediamine; 18-ANE-N_2O_4 = 1,4,10,13-tetraoxo-7,16-diazacyclooctadecane; BHP-18-ANE-N_2O_4 = *N,N'*-bis(2-hydroxypropyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane; cryptand-2,2,2 = 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosame).

Results and Discussion

The metal ions in the table of formation constant data have been arranged in order of increasing ionic radius. The ligands in Table I are all diamines, and can, in a sense, be regarded as derivatives of ethylenediamine, the first entry in Table I. The remaining ligands in the table have been arranged in order of increasing structural complexity and rigidity in regard to number of neutral oxygen donors, and of macrocyclic rings. We see that the expected pattern of stabilization [5] is observed, in that small metal ions such as Cu^{II} or Zn^{II} show either a strong decrease or little change in complex stability in passing from a ligand such as EN to THPED. On the other hand, large metal ions such as La^{III}, Ca^{II}, Pb^{II}, or Ba^{II}, show strong increases in complex stability when rings or pendent groups are added bearing neutral oxygen donors. It is particularly interesting to note that the metal ion size-dependent pattern of stabilization is the same whether or not the added oxygens are part of a macrocyclic ring, and whether or not the starting ligand to which the hydroxypropyl groups are added is a macrocycle. We thus see the large increase in stability found for the complexes of large metal ions with THPED as compared to EN. This is shown in the stability of the THPED complex with La^{III}; the metal ion has no aqueous phase chem-

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TABLE I. Formation Constants of some Amines and their Analogues Bearing *N*-(2-hydroxypropyl) Groups with a Variety of Metal Ions[a]

Ligand[b]	Cu^{2+}	Mg^{2+}	Zn^{2+}	Cd^{2+}	Ca^{2+}	La^{3+}	Sr^{2+}	Pb^{2+}	Ba^{2+}
en	10.71[c]	0.37[c]	5.87[c]	5.62[c]	<0[d]	(1.4)[e]	<0[d]	5.04[f]	⩽0[d]
THPED	9.75[g]	⩽0.3[h]	6.09[g]	7.80[g]	1.63[h]	2.90[h]	~0.8[h]	7.66[h]	~0[h]
18-ane N_2O_4	6.1[i]	<0[d]	3.1[i]	5.25[i]	1.74[h]		2.6[i]	6.8[i]	2.97[i]
BHP-18 ane-N_2O_4	5.97[h]	<0[h]	3.0[h]	7.64[h]	3.59[h]	3.24[h]	4.05[h]	8.57[h]	4.65[h]
Cryptand-2,2,2	6.5[c]	<0[d]		6.8[c]	4.45[c]	6.45[c]	8.0[c]	12.0[c]	9.5[c]
Ionic radius[j] of M^{n+} (Å)	0.62	0.72	0.75	0.95	1.00	1.05	1.16	1.18	1.36

[a]Values of log K_1, the formation constant of the 1:1 complex between the metal ion and ligand indicated, at 25 °C and ionic strength 0.1. The metal ions are arranged in order of increasing ionic radius. [b]For key to ligands, see Fig. 1. [c]From ref. 10. [d]Rough estimates by the present authors. [e]Estimated as described in ref. 11. [f]From ref. 12. [g]From ref. 13. [h]This work, 25 °C in 0.1 M $NaNO_3$. [i]From ref. 14. [j]For six-coordination, except for Cu^{2+}, which is for square-planar coordination, from ref. 15.

istry with EN itself. Table I shows that the stability of the complexes of the bicyclic cryptand-2,2,2 is higher than that of its monocyclic analogue, BHP-18-ANE-N_2O_4; this difference, which is the macrobicyclic effect [6], increases as the size of the metal ion increases. Even though the addition of hydroxypropyl groups to 18-ANE-N_2O_4 to give BHP-18-ANE-N_2O_4 does not lead to as large a stabilisation as does the extra ring added to 18-ANE-N_2O_4 to give cryptand 2,2,2, there is still a substantial size-related increase in stability produced by the hydroxyethyl groups. In fact, if we examine Table I, we see for a large metal ion such as Pb^{II} a steady increase in stability as the number of oxygen-donor groups and macrocyclic rings increases, while for small metal ions such as Cu^{II} or Zn^{II} there is usually a strong decrease, or at best only a slight increase. The best interpretation of this at present would seem to be that the alcoholic or ethereal oxygen donor atoms are better Lewis bases than the water molecules which they displace from the metal ion [7]. However, steric crowding is more severe for small metal ions, so that overall they show a decrease in complex stability in the presence of added groups bearing neutral oxygen donor atoms [5].

There is at present also an interest [8] in neutral oxygens other than simple alcohols and ethers. A group of particular interest is the tetrahydrofuran (THF) group, which is present in naturally-occuring, metal-ion-binding antibiotics such as nonactin and monensin [9]. We have examined the complexing properties of ligands such as THFDIPA in Fig. 1, and find that the enhancement in stabilisation produced by THF group is very similar to that of the 2-hydroxypropyl group. It should be noted that the choice of the latter group here, instead of the 2-hydroxyethyl group as a substituent as used in earlier work [1–5], arises from the observation that it produces a uniformly larger effect on complex stability than does the 2-hydroxyethyl group. Thus, log K_1 for *N,N,N′,N′*-tetrakis(2-hydroxyethyl)ethylenediamine with Cd^{II} is 7.04, as compared with 7.80 with THPED. The THF and 2-hydroxypropyl groups contain an optically active carbon, so that substitution of these groups must lead to ligands which are mixtures of different diastereomers. We are at present synthesizing ligands containing the THF group in optically resolved form to see whether the different diastereomers lead to differences in complex stability.

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