Inorganica Chimica Acta, 43 (1980) 109–112
©Elsevier Sequoia S.A., Lausanne – Printed in Switzerland

The Macrocyclic Effect: Thermodynamic Parameters for the Formation of Zinc(II) Complexes with Macrocyclic Ligands of Varying Ring-size

M. MICHELONI and P. PAOLETTI*

Istituto di Chimica Generale ed Inorganica, University of Florence and Laboratorio C.N.R., Via I. Nardi 39, 50132 Florence, Italy

Received May 5, 1980

The thermodynamic parameters ΔG°, ΔH° and ΔS° for the reactions of the zinc(II) ion with the ligands 1,4,7,10-tetra-azacyclotridecane (L^2) and 1,5,9,13-tetra-azacyclohexadecane (L^5) have been determined at 25 °C by potentiometric techniques and by direct calorimetry. These values combined with those already reported for the other macrocyclic ligands 1,4,7,10-tetra-azacyclododecane (L^1), 1,4,8,11-tetra-azacyclotetradecane (L^3) and 1,4,8,12-tetra-azacyclopentane (L^4) allow, for the first time to discuss the parameters for the complete series of tetra-azamacrocycles L^1–L^5. Finally comparison with the analogous complexes with non-cyclic polyamines is made. The macrocyclic complexes are more stable than the corresponding complexes with non-cyclic polyamines. This extra stability is almost due to a very favourable enthalpy contribution, the entropy being small. In the case of the $[ZnL^5]^{2+}$ complex its extra stability can be assigned to a favourable entropy effect.

Introduction

The term 'Macrocyclic Effect' has been widely used to indicate the greater thermodynamic stability of metal complexes with cyclic polyamine ligands when compared with complexes formed with analogous non-cyclic ligands [1, 2]. There have been many publications on the thermodynamic interpretation of the macrocyclic effect, particularly with reference to copper(II) and nickel(II) complexes [1–8].

In the case of zinc(II) macrocyclic complexes the situation is further complicated by the ease with which the zinc ion is able to change its coordination geometry, and the difficulty in monitoring this, since the spectroscopic techniques (used for Cu(II) and Ni(II) complexes) are not available. In this work we are reporting the thermodynamic parameters ΔG°, ΔH° and ΔS° for the reactions of the zinc ion with the ligands L^2 and L^5 (see Fig. 1) which have been determined by the potentiometric techniques and by direct calorimetry. These values, when taken together with those previously reported for the macrocyclic ligands [5, 7], allow us, for the first time, to look at the parameters for the complete series L^1–L^5 and to make comparison with the analogous non-cyclic polyamines L^6–L^9 [9].

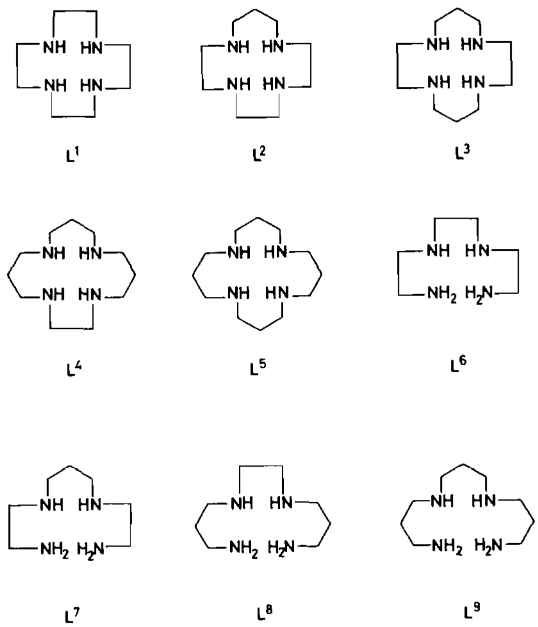

Fig. 1. Tetra-azamacrocycles and open-chain saturated tetramines.

Experimental

Ligands

The ligand L^2 was made by the condensation of the appropriate tosylated segments in alkaline solu-

---

*Author to whom correspondence should be addressed.

tion, following the procedure published by Richman and Atkins [10]. The ligand L^3 (Strem Chemicals) was recrystallised twice from acetonitrile. $L^4 \cdot 4HCl$ was prepared by bubbling gaseous hydrogen chloride through a solution of L^4 (Strem Chemicals) in ether. The crystals of $L^4 \cdot 4HCl$ monohydrate were filtered off and washed with ether. The ligand L^5 was prepared following the procedure already described [11] and was recrystallised from acetonitrile and sublimed twice.

Elemental analyses were as follows:

Anal. Calcd. for L^2: C, 58.0; H, 11.9; N, 30.1%. Found: C, 57.8; H, 12.2; N, 30.4%. *Anal.* Calcd. for L^3: C, 60.0; H, 12.1; N, 28.0%. Found: C, 60.1; H, 12.4; N, 28.1%. *Anal.* Calcd. for $L^4 \cdot 4HCl$: C, 36.7; H, 8.4; N, 15.6%. Found: C, 36.4; H, 8.7; N, 15.5%. *Anal.* Calcd. for L^5: C, 63.1; H, 12.4; N, 24.5%. Found: C, 63.2; H, 12.1; N, 24.4%.

Other Reagents

NaOH–CO_2 free solutions, used for e.m.f. measurements were prepared, stored and standardised as described elsewhere [12].

A 0.5 *M* potassium nitrate stock solution was prepared from potassium nitrate (C. Erba ACS grade) without further purification and used as the ionic medium for potentiometric and calorimetric measurements. A stock solution containing Zn(II) was prepared from solid zinc chloride (C. Erba ACS grade) and standardised by standard gravimetric methods.

E.m.f. Measurements

A full description of the potentiometric apparatus employed has been already reported [12].

For the determination of the equilibrium constants of the Zn–L^2, Zn–L^3, Zn–L^4, Zn–L^5 systems the titration cell was filled with about 100 cm^3 of 0.5 *M* KNO_3 and varying quantities of zinc chloride, ligand and hydrochloric acid; the NaOH solution was dispensed from a Metrohm Multidosimat piston burette graduated to 0.01 cm^3. The equilibrium was reached almost instantaneously in the pH-range investigated. The experimental values of the e.m.f. were not corrected for the liquid junction potential.

The computer program miniquad [13] was used to calculate the equilibrium constants. The criteria adopted in the procedure for selecting the species formed at equilibrium in the system under investigation have already been reported [13, 14].

Calorimetric Procedure

For the calorimetric measurements, LKB BATCH mod. 10700-2 and FLOW mod. 10700-1 microcalorimeters were used. The thermal output of both instruments was amplified by a Keighley 150 B microvolt amplifier and recorded as a trace on a potentiometric recorder. For the batch measurements the heat output was determined by comparison of the area under the heat curve with a similar area produced by electrical calibration. The areas were determined by electronic integration of the voltage output of the amplifier. In aqueous solution reaction between macrocycles and metal ion are very slow, due to the presence of the diprotonated form of the macrocycle H_2L^{2+} in which the presence of two adjacent positive charges causes the insertion of the metal ion into the ligand cavity to be very slow. This problem can be avoided by working in strong alkaline solution, where the macrocycle is uncharged. The most important measurement, that of ΔH°_5, see cycle, was made in the flow calorimeter by passing solutions of Zn(II) and the ligand in 1 mol dm^{-3} NaOH simultaneously through the mixing cell. The flow microcalorimetric apparatus employed has been described previously [15]. In a typical flow experiment, a solution of Zn(II) (1×10^{-2} mol·dm^{-3}) in 1 mol·dm^{-3} NaOH and a solution of the ligand L^2, or its hydrochloride (5×10^{-3} mol·dm^{-3}) were injected in the flow apparatus: the flow rates were changed in such a way to have a metal to ligand ratio ranging from 0.95:1 to 1.4:1.

The batch technique was used to determine the enthalpy of formation of the $[ZnL^5]^{2+}$ complex; a full description of this apparatus and its calibration has been already reported [16]. The reaction between the Zn(II) ion and L^5 is fast; therefore the heat involved in this reaction was measured by mixing an aqueous solution of Zn^{2+} with a solution of the ligand containing NaOH in slight excess only. Under the reaction conditions the species present and their percentages at equilibrium before and after mixing were calculated by means of the Dispol [17] computer program. In a typical batch microcalorimetric experiment 0.4 cm^3 of the Zn(II) solution (1.0×10^{-2} mol·dm^{-3} in 0.5 mol·dm^{-3} KNO_3) was introduced by weight into one side of the calorimetric cell; 2.0 cm^3 of solution of the ligand L^5 (2.2×10^{-3} mol·dm^{-3} in 0.5 mol·dm^{-3} KNO_3) was introduced into the other side. The calorimeter was allowed to equilibrate until a steady base line was obtained on the chosen sensitivity range and the reaction was then started by mixing the reactants. Numerical analysis of the data was handled by means of a computer program written for an IBM 370-168 computer system and the enthalpy of formation of $[ZnL^5]^{+2}$ is reported in Table II. The flow technique was employed to determine the enthalpy of formation of the Zn–L^2 complex by means of the following thermochemical cycle:

TABLE I. Thermodynamic Contribution, ΔH°, ΔS° to the Reaction between Saturated Cyclic and Non-cyclic Tetramines with Zn(II) Ion.

Reaction	Log K_{ML}	$-\Delta H°$ (kcal·mol^{-1})	$\Delta S°$ (cal·K^{-1}·mol^{-1})
Zn + L^1	(16.2)^a	14.5^b(7.9)^a	25.5
Zn + L^2	15.74^c(15.6)^a	15.3^c(7.8)^a	20.7
Zn + L^3	15.34^c(15.5)^a	14.8^b(7.6)^a	20.5
Zn + L^4	15.35^c(15.0)^a	16.5^b(8.2)^a	14.9
Zn + L^5	13.05^c	7.1^c	35.9
Zn + L^6	12.02^d	8.9^d	25.1
Zn + L^7	12.83^d	11.9^d	18.8
Zn + L^8	11.25^d	10.6^d	15.9
Zn + L^9	9.32^d	7.4^d	17.8

[a]Values in parentheses are stability constants and enthalpies obtained by polarography, see Ref. 7. [b]Ref. 5. [c]This work. [e]Ref. 9.

TABLE II. Thermodynamic Contributions ΔH°, ΔS° to the Macrocyclic Effect.

Macrocyclic Ligand	Non-cyclic Ref. Ligand	Δ (log K)	Δ (−ΔH°) (kcal·mol^{-1})	Δ(ΔS°) (cal·K^{-1}·mol^{-1})
L^1	L^6	4.19	5.6	0.4
L^2	L^6	3.72	6.4	−4.4
	L^7	2.91	3.4	1.9
L^3	L^7	2.51	2.9	1.7
	L^8	4.09	4.2	4.6
L^4	L^8	4.10	5.9	−1.0
	L^9	6.03	9.1	−2.9
L^5	L^9	3.73	−0.3	18.1

$$\begin{tikzcd}
Zn^{2+}_{(aq)} & + \; L^2_{(aq)} \arrow[r, "\Delta H_1^\circ"] \arrow[dd, "\Delta H_3^\circ"] & {[ZnL^2]^{2+}_{(aq)}} \arrow[dd, "\Delta H_4^\circ"] \\
\Delta H_2^\circ & & \\
Zn^{2+}(1\ \mathrm{mol\cdot dm^{-3}}NaOH) & + \; L^2\ (1\ \mathrm{mol\cdot dm^{-3}}\ NaOH) \arrow[r, "\Delta H_5^\circ"] & {[ZnL^2]^{2+}(1\ \mathrm{mol\cdot dm^{-3}}\ NaOH)}
\end{tikzcd}$$

Discussion

The values of log K, ΔH° and ΔS° for the formation of zinc complexes with the complete series of macrocyclic ligands L^1–L^5 are reported in Table I. The enthalpy values have all been obtained by direct calorimetry and the values are completely different to those which have been reported for some of the complexes, obtained by an indirect, non-calorimetric method [7]. The most stable complex is formed with the smallest ligand and a steady diminution in stability accompanies an increase in ring-size with a larger than usual fall in stability evident between L^4 and L^5.

From the enthalpy data it can be seen that the most exothermic enthalpy of formation occurs for $[ZnL^4]^{2+}$ in which the metal ion is probably located in the cavity of the macrocyclic ligand giving rise to a presumably octahedral arrangement: the low value of the entropy of formation of this complex also helps to advance the hypothesis that this complex is octahedral. For the three complexes with the smallest macrocycles $[ZnL^1]^{2+}$, $[ZnL^2]^{2+}$, $[ZnL^3]^{2+}$, both the enthalpies and entropies of formation are remarkably similar, suggesting that the coordination pattern is the same in all these complexes. On the other hand, the macrocyclic cavity for L^1, L^2 and L^3 is, in all probability, too small to contain a zinc ion and the structure of the zinc complex with a tetramethylated L^3 has been shown to be pyramidal with the zinc ion penta-coordinated and above the plane of the four donor nitrogen atoms [18]. It should also be recorded that for copper(II) complexes the complex with L^3 has the highest enthalpy of formation since the ligand cavity has exactly the correct size to encorporate the copper ion [19]. It would therefore appear that in the zinc complexes, with L^1, L^2 and L^3, the coordination geometry is not octahedral. The higher entropies of formation together with the relative ease with which zinc is known to form pentacoordinate complexes suggests that this is what is happening in this case. In the case of $[ZnL^5]^{2+}$ there is a dramatic reduction in the enthalpy of formation accompanied by a large increase in the entropy of formation compared with that for other complexes. It seems likely in this case that the zinc is tetrahedral and that the high entropy value of 35.9 $\text{cal}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ can be due to the increase in the translational entropy evident in the formation of tetrahedral complexes. It is not so surprising that the tetrahedral arrangement might only be able to be achieved in the case of the largest ligand if one recognises that the larger hydrocarbon bridges between the adjacent nitrogen atoms will make the ligand more flexible and more able to put the four donor nitrogen atoms into the correct position for tetrahedral coordination without expending too much conformational energy.

Macrocyclic Effect

Enthalpy and entropy data pertinent to the metathetical reaction

$$\text{ZnL}_{\text{non-cyclic}} + \text{L}_{\text{cyclic}} \rightarrow \text{ZnL}_{\text{cyclic}} + \text{L}_{\text{non-cyclic}}$$

are reported in Table II. For L^2, L^3, and L^4 the choice of reference ligand rests on the number of 5 or 6 membered chelate rings in each complex and two alternative are available. Both values are given. In general, it can be seen that whatever reference is taken, the macrocyclic complexes are more stable than their non-cyclic counterparts and that this increase in stability arises from a favourable enthalpy term. These results are in direct contrast to those which have been obtaind by determining ΔH° from the temperature dependence of the stability constants [7]. Only in the case of the complex $[ZnL^5]^{2+}$ is the greater stability due entirely to a favourable entropy term. Unfortunately, while the considerations which have been made on the changes in free energy for the formation reaction of the macrocyclic complexes,

$$\text{Zn}^{2+}_{(aq)} + \text{L}_{(aq)} \rightarrow [\text{ZnL}]^{2+}_{(aq)}$$

based on the data in Table I are valid, the comparison between the enthalpy and entropy contributins to the macrocyclic effect can only be properly made if the coordination number and geometry of both the macrocyclic complex and its non-cyclic counterpart are known to be the same. This criterion is properly not met in the case of the zinc(II) ion, given the ease with which this ion can alter its coordination number and geometry to suit the particular ligand with which it is forming a complex.

References

1 D. K. Cabbiness and D. W. Margerum, *J. Am. Chem. Soc., 91,* 6540 (1969).
2 F. P. Hinz and D. W. Margerum, *Inorg. Chem., 13,* 2941 (1974).
3 M. Kodama and E. Kimura, *J. Chem. Soc. Dalton,* 116 (1976).
4 M. Kodama and E. Kimura, *J. Chem. Soc. Dalton,* 2341 (1976).
5 A. Anichini, L. Fabbrizzi, P. Paoletti and R. M. Clay, *J. Chem. Soc. Dalton,* 577 (1978).
6 L. Fabbrizzi, P. Paoletti and R. M. Clay, *Inorg. Chem., 17,* 4 (1978).
7 M. Kodama and E.Kimura, *J. Chem. Soc. Dalton,* 2269 (1977).
8 R. M. Clay, M. Micheloni, P. Paoletti and W. V. Steele, *J. Am. Chem. Soc., 101* (1979).
9 R. Barbucci, L. Fabbrizzi and P. Paoletti, *Inorg. Chim. Acta Rev., 7,* 43 (1973), and references therein.
10 J. E. Richman and T. J. Atkins, *J. Am. Chem. Soc., 96,* 2268 (1974).
11 W. L. Smith, J. D. Ekstrand and K. N. Raymond, *J. Am. Chem. Soc., 100,* 3539 (1978).
12 M. Micheloni, A. Sabatini and A. Vacca, *Inorg. Chim. Acta, 25,* 41 (1977).
13 A. Sabatini, A. Vacca and P. Gans, *Talanta, 21,* 53 (1974).
14 A. Sabatini and A. Vacca, *Coord. Chem. Rev., 16,* 161 (1975).
15 L. Fabbrizzi, M. Micheloni and P. Paoletti, *J. Chem. Soc. Dalton,* 1581 (1979).
16 E. Gallori, E. Martini, M. Micheloni and P. Paoletti, *J. Chem. Soc. Dalton,* in the press.
17 A. Vacca, unpublished results.
18 N. W. Alcock, N. Herron and P. Moore, *J. Chem. Soc. Dalton,* 1282 (1978).
19 L. Fabbrizzi, M. Micheloni and P. Paoletti, *J. Chem. Soc. Dalton,* 1581 (1979).