# The 13-Membered Macrocyclic Effect. Polarographic Studies of Copper(II)-1,4,7,10-Tetra-azacyclotridecane Complexation

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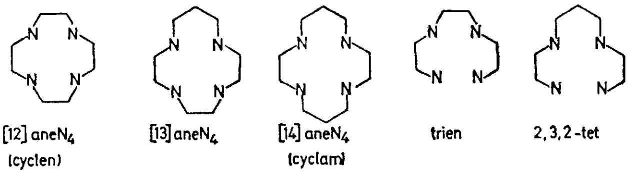
*Summary* Polarographic studies on the $Cu^{II}$-1,4,7,10-tetra-azacyclotridecane ($[13]aneN_4$) complex show that $[13]aneN_4$ has thermodynamic and kinetic properties which are intermediate to those of 1,4,7,10-tetra-azacyclododecane ($[12]aneN_4$) and other less-constrained tetramine ligands.

Recently we reported[1] that the macrocyclic effect used to explain the enhanced complex stabilities of 14-membered cyclic tetramine ligands[2] also occurs for a sterically more constrained 12-membered ligand, $[12]aneN_4$ (cyclen), with a similar order of magnitude. However, the thermodynamic parameters contributing to the macrocyclic effects are different; the enhancement for $[12]aneN_4$ is due to a favourable change in $\Delta S$, whereas for $[14]aneN_4$ (cyclam) it is due to the $\Delta H$ term.[3] On the other hand, the kinetic effects of the 12- and 14-membered cyclic structures are analogous in that dissociations in both systems are greatly retarded. In order to find the origin of the thermodynamic differences and also to investigate the mechanism of complexation we have undertaken polarographic studies on the complexation of $[13]aneN_4$[4] with $Cu^{II}$.

Table 1 Comparison of stability constants, enthalpy and entropy of formation of tetramine complexes at 25 °C

| Complex | log $K_{ML}$ | $\Delta H$/ kcal mol$^{-1}$ | $\Delta S$/cal K$^{-1}$ mol$^{-1}$ |
|---|---|---|---|
| $Cu([13]aneN_4)^{2+a}$ | 29·1 | −29·2 | 33·7 |
| $Cu([12]aneN_4)^{2+b}$ | 24·8 | −18·3 | 51·4 |
| $Cu(2,3,2\text{-tet})^{2+b}$ | 23·9 | −27·7 | 16·5 |
| $Cu(trien)^{2+b}$ | 20·0 | −21·6 | 19·5 |
| $Ni([14]aneN_4)^{2+b}$ | 22·2 | −31·0 | −2·0 |
| $Ni(2,3,2\text{-tet})^{2+b}$ | 15·8 | −19·4 | 7·2 |
| $Ni(trien)^{2+b}$ | 13·8 | −14·0 | 16·0 |

[a] This work, $\mu = 0{\cdot}20$. [b] See ref. 1.



The experimental procedures and conditions are identical to those reported earlier,[1] and the results are consistent with the thermodynamic and kinetic findings for the $[12]aneN_4$ system.[1] From the temperature dependence of the formation constant of the 1 : 1 $Cu^{II}$–$[13]aneN_4$ complex, we have obtained the thermodynamic parameters shown in Table 1. A comparison with other tetramine complexes shows that the 13-membered macrocyclic effect (more than $10^5$-fold stability enhancement) is due largely to the favourable entropy term, but there is significant, though small, contribution from the enthalpy term; a trend which links the 12- and 14-membered macrocyclic effects. The decreased contribution in the entropy term and the increase in the enthalpy term as the ring size expands may indicate the increasing importance of the ligand solvation effect proposed by Hinz and Margerum.[3]

The kinetic behaviour of the $[13]aneN_4$ complex in acetate buffer solution is similar to that of the $[12]aneN_4$ system[1] (equations 1 and 2).

Table 2 Rate constants for the $[13]aneN_4$ and $[12]aneN_4$ systems, $\mu = 0{\cdot}20$, 25 °C.

| Reaction (1) Z | log $k_1$/M$^{-1}$ s$^{-1}$ | log $k_{-1}$/M$^{-1}$ s$^{-1}$ | Relative log $k_{-1}$$^{a}$ | log $K_1$$^{b}$ |
|---|---|---|---|---|
| $[13]aneN_4$$^{c}$ | 6·75 | $-14{\cdot}2_3$ | +2·0 | $20{\cdot}9_8$ |
| $[12]aneN_4$$^{d}$ | 6·30 | −10·9 | 0 | 17·2 |

| Reaction (2) Z | log $k_2$/M$^{-1}$ s$^{-1}$ | log $k_{-2}$/M$^{-2}$ s$^{-1}$ | Relative log $k_{-2}$$^{a}$ | log $K_2$$^{b}$ |
|---|---|---|---|---|
| $[13]aneN_4$$^{c}$ | 1·01 | −9·9 | +3·6 | $10{\cdot}8_8$ |
| $[12]aneN_4$$^{d}$ | −0·74 | −8·2 | 0 | 7·5 |

[a] Relative $k_{-1}$ value $= \dfrac{(k_{-1})[13]aneN_4}{(k_{-1})[12]aneN_4} \times \dfrac{(K_{MZ})[12]aneN_4}{(K_{MZ})[13]aneN_4}$ [b] The first and second protonation constants for $[13]aneN_4$ are 11·1 and 10·1, respectively. [c] This work. [d] Ref. 1.

$$
\begin{array}{l}
\mathrm{Cu(OAc)_2} \\
\quad\uparrow\downarrow \text{ rapid} \\
\mathrm{Cu(OAc)^+} \\
\quad\uparrow\downarrow \text{ rapid} \\
\mathrm{Cu^{2+}}
\end{array}
+
\left\{
\begin{array}{lll}
\mathrm{ZH^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{CuZ^{2+}} + \mathrm{HOAc}, \text{ slow} & K_1 & (1) \\
\mathrm{ZH_2^{2+}} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{CuZ^{2+}} + \mathrm{HOAc} + \mathrm{H^+}, \text{ slow} & K_2 & (2)
\end{array}
\right.
$$

(where Z = [13]ane$N_4$ or [12]ane$N_4$).

The rate of the complex formation is influenced by the protonations, but not as much as for [12]ane$N_4$ (Table 2). This may be due to the less significant proximity effect of the 13-membered ring structure. Also significant for the [13]ane$N_4$ system are the relatively faster dissociation rates. The kinetic behaviour suggests that the 13-membered cyclic tetramine has some properties of non-cyclic tetramine ligands.[5]

The activation parameters for the rate constant, $k_1$, are $\Delta S^\ddagger = +26{\cdot}9$ e.u., $E_a = 17{\cdot}3$ kcal mol$^{-1}$ and for $k_2$ are $\Delta S^\ddagger = -15{\cdot}1$ e.u., $E_a = 12{\cdot}8$ kcal mol$^{-1}$. The strikingly favourable $\Delta S^\ddagger$ overcomes the opposing effect of $E_a$ and is responsible for the dramatic rate acceleration of reaction (1) over reaction (2). The contrast in the activation parameters between reactions (1) and (2) can be explained by assuming that the monoprotonated species ($ZH^+$) has a conformation closer to the transition state than the diprotonated species ($ZH_2^{2+}$) and is more solvated by water molecules to be released at the transition state.

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