Rapid Oxidative Metal Insertion into a Macrocyclic Ring from a 'Metal-out' Position and Identification of a Stable 'Metal-in' Isomer of a Ni^{II}–Cyclamtetra-acetate Complex

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The previously unknown 'Ni^{II}-in' complex of cyclamtetra-acetate has been prepared from the 'Ni^{II}-out' isomer by oxidative intramolecular (out → in) translocation of Ni and subsequent reduction to Ni^{II}.

Insertion of divalent metal ions into the cavity of an unsubstituted 14-membered tetra-amine macrocycle (cyclam) requires that a high kinetic barrier be overcome,[1—5] although it is thermodynamically feasible.[3,4,6] However, in the presence of acetate groups attached to the secondary tetra-amines (cyclamtetra-acetate),[7] the interacting metal ions do not insert into the macrocyclic ring ('metal-in') but remain outside of the cavity ('metal-out') co-ordinating to the acetate groups.[8—10] Other tetra-*N*-substituted (R) cyclams, adopt a square-pyramidal 'metal-in' structure.[11—13] In light of the low stability constants usually found for these 'metal-in' Ni^{II} complexes, $\log K = 8.6$ for R = Me[14] and 7.3 for R = CH_2CH_2OH,[9] it has been concluded that the stability ($\log K = 15.3$)[7] of the 'metal-out' structure of cyclamtetra-acetate with R = CH_2CO_2H is due to thermodynamic effects.[9]

This communication reports that the previously unknown 'Ni^{II}-in' complex with cyclamtetra-acetate does exist as a stable isomer and that the prohibitively high kinetic barrier for metal insertion is circumvented by oxidation of the metal in the previously identified 'Ni^{II}-out' complex (Figure 1).

The cyclic voltammogram (c.v.) (Figure 2) of a fresh mixture of $NiCl_2$ and a slight excess (1.1 equiv.) of cyclamtetra-acetate solution at pH 5 shows only one peak at +1.0 V *vs.* saturated calomel electrode (s.c.e.) in the first anodic sweep (from +0.4 to +1.2 V). However in the back cathodic sweep, the corresponding reduction wave is much weaker than anticipated for a reversible electrode process, and furthermore a new wave appears at +0.56 V.[†] In the

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[†] The increase in c.v. scan rate (from 50 to 500 mV s^{-1}) decreases the cathodic peak height of the first scan at +0.56 V.

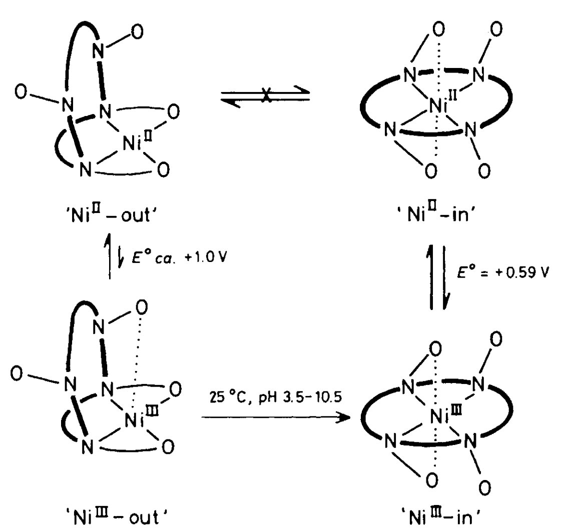

Figure 1. A reaction mechanism for the transformation of the 'Ni^{II}-out' complex to the 'Ni^{II}-in' complex of cyclamtetra-acetate. The 'Ni^{II}-out' complex is postulated[10] as having two amine and two carboxylate groups co-ordinated.

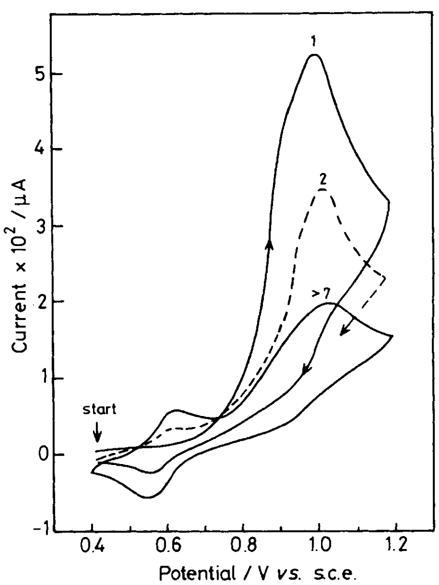

Figure 2. C.v.s of 2.0×10^{-3} M Ni^{II}L-cyclamtetra-acetate solution on a glassy carbon electrode at pH 3.5 and a scan rate of 200 mV s^{-1} with 0.5 M Na_2SO_4 as supporting electrolyte. The numbers 1, 2, and >7 indicate the first, second, and more than seventh sweep, respectively.

second anodic scan, an oxidation peak corresponding to the reduction peak at +0.56 V emerges at +0.63 V. In successive scans, the wave heights at +0.56 V and +0.63 V increase, while the peaks at *ca.* +1.0 V decrease. After seven or eight cycles, no further changes in the peak heights and voltammogram shape were observed.‡ Variation of pH [3.53, 7.25 (phosphate buffer), and 10.52 (borate)] did not affect the peak heights at +0.56 and +0.63 V. We have confirmed that the ligand itself is not oxidized (no CO_2 is evolved) and that anions (*e.g.* Cl^-) have no effect on the c.v. signals.

The initially formed violet [$\lambda_{max.}$ 575 nm(ε 17) and 355 nm (ε 25)] Ni^{II}L-cyclamtetra-acetate was presumed to assume a 'Ni^{II}-out' structure.[10,11] Hence, the first anodic peak at *ca.* +1.0 V is assigned to the $Ni^{II} \rightarrow Ni^{III}$ process in the 'metal-out' complex. Application of a constant potential of +1.20 V to the 'Ni^{II}-out' complex solution yields an intense yellow solution [$\lambda_{max.}$ 340 (ε 6.0×10^3, sh) and 277 nm (ε 9.0×10^3)], whose c.v. shows only the reversible wave at +0.59 V, but none at +1.0 V. The cathodic and anodic peaks at +0.59 V are of equal height and increase with the square root of the scan rate. The separation of the two peaks, ΔE, is 65 mV. These facts taken together are indicative of mass-transfer-controlled (one-electron) electrochemical behaviour for the $Ni^{II/III}$ process. Since the $E°$ value of +0.59 V is close to +0.52 V [$I = 0.1$ ($MeCO_2Na$), pH 5.6] and +0.68 V [$I = 0.1$ ($NaClO_4$), pH 4.0] measured (by us) for $Ni^{II/III}$ in the 'metal-in' complex of cyclam, we can assign a similar 'metal-in' structure to the yellow Ni^{III}L-cyclamtetra-acetate complex. The Ni^{III}L-cyclam complex has intense charge transfer absorptions [$\lambda_{max.}$ 370 (ε 6.0×10^3) and 295 nm (ε 1.1×10^4)].[15] The e.s.r. spectrum of the 'Ni^{III}-in' species in frozen solution (−150 °C) with $g_\perp = 2.18$ and $g_\parallel = 2.01$ is similar to that found for Ni^{III}L-cyclam.[15] The half-life of the 'Ni^{III}-in' cyclamtetra-acetate is *ca.* 20 h at pH 3.6, 0.5 M Na_2SO_4, and 25 °C, while that of Ni^{III}L-cyclam is 5 days under the same conditions.[15]

The observed nearly reversible nature of the $Ni^{II/III}$ couple in the 'metal-in' cyclamtetra-acetate complex indicates a stable 'Ni^{II}-in' state. Electrochemical reduction at 0.0 to +0.2 V (*vs.* s.c.e.) or chemical reduction (*e.g.* by ascorbic acid) of the 'Ni^{III}-in' species yields a stable, violet 'Ni^{II}-in' complex solution having a c.v. identical to that of the 'Ni^{III}-in' species. The d–d absorption spectrum of the 'Ni^{II}-in' isomer in pH 7.0 solution ($\lambda_{max.}$ 340, 528 nm) is similar to that of the high-spin Ni^{II}L-cyclam complex measured in the presence of Cl^- anions ($\lambda_{max.}$ 346, 525 nm).[16,17] The solution magnetic moment $\mu_{eff.}$ at 35 °C (using the Evans method)[18] is 2.93, consistent with a high-spin Ni^{II} complex, for which we postulate an octahedral structure with two carboxylate groups in the *trans* position, as depicted in Figure 1. A similar six-co-ordinate structure is reported for a high-spin Ni^{II}L-tetrakis(2-carbamoylethyl)cyclam complex.[14] The kinetic stability of the 'Ni^{II}-in' species is so great that it does not isomerize to the 'Ni^{II}-out' species upon heating on a steam bath for 20 h or acidifying to pH 1. Also the 'Ni^{II}-out' complex cannot be converted into the 'Ni^{II}-in' isomer. The kinetic or/and thermodynamic stability of the 'Ni^{II}-in' complex is distinct from the 'Ni^{II}-out' complex in that at pH 7 the ligand of the 'Ni^{II}-in' complex cannot be displaced with ethylenediaminetetra-acetic acid (edta) (even after 24 h at room temperature), whereas the ligand of the 'Ni^{II}-out' species can,§ as established by c.v. and u.v. spectroscopy. So far we have failed to crystallize the 'metal-in' complexes.

The decrease in size and electronic configurational change of Ni upon oxidation lowers the kinetic barrier for metal insertion into the macrocyclic cavity and at the same time renders the 'metal-in' structure thermodynamically more favourable than the 'metal-out' structure. This explanation accounts for the irreversible c.v. signal at +1.0 V and the immediate occurrence of a reversible c.v. wave at +0.59 V

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‡ The abnormally high peaks at +1.0 V (in comparison with those at +0.56 and +0.63 V) are accounted for by an accompanying H_2O oxidation catalysed by the Ni complex. A control experiment (without the Ni complex or free ligand) confirmed the H_2O oxidation wave at >1 V. Oxidative decarboxylation from the complexed ligand did not occur.

§ The reported complexation constants, log K_{NiL}, are smaller for the 'Ni-out'cyclamtetra-acetate (15.26) than for Ni–edta (18.46) (ref. 7).

(Figure 2). The concentration of the 'metal-out' complexes on the electrode surface decreases while the 'metal-in' isomer concentrations increase, eventually reaching equilibrium with the concentration of the bulk 'Ni^{II}-out' solution after a number of scans.

This oxidative metal entry into the macrocyclic tetra-amines is so far unique to Ni^{II}–cyclam(14-membered-N_4)tetra-acetate. With the Ni^{II}-13- and -15-membered-N_4 tetra-acetate homologues no redox couples of Ni appeared in the region between 0 and +1.2 V. The Cu^{II}, Co^{II}, and Zn^{II} complexes of cyclamtetra-acetate showed no comparable c.v. with no indication of metal entry into the macro ring. This new ligand offers the prospect of devising new highly selective, electrochemically-controllable cation binders.

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