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Molecular events switched by transition metals

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Contents

Abstract

Transition metals can typically give rise to two (or more) distinct states of comparable stability (two consecutive oxidation states; two different stereochemical arrangements). In a multicomponent system, the conversion of one state to the other can modify a given property of a nearby subunit or can induce drastic changes in the system topology. In this sense, the metal behaves as a switch, which can be operated through an external input (the variation of the pH or of the redox potential). Recent examples of molecular switching by transition metals are reviewed: (i) the quenching/enhancement of the emission of a luminescent fragment effected by a nearby metal centred redox couple (e.g. Ni^{II}/Ni^{III}); (ii) the pH driven motion of an aminoalkyl side chain in a Ni^{II} scorpionate complex, which is signalled by the variation of the light emission intensity of an appended anthracenyl fragment; (iii) the pH controlled translocation of a Ni^{II} ion within a multidentate ligand containing two compartments of different coordinating tendencies and (iv) the intramolecular translocation of a Cl^-

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anion between two pre-positioned metal centres Cu^{II} and Ni^{II}, within a ditopic receptor, electrochemically driven through the Ni^{II}/Ni^{III} redox change.

Keywords: Molecular switches; Fluorescence; Molecular motions; Ion translocation; Molecular machines

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1. From template reactions to redox switching of fluorescence

Transition metals, in view of their stereochemical versatility and rich redox reactivity, have an active part in small molecule binding and transport, electron transfer triggering, fine and selective catalysis. Due to these features, transition metals play an essential role in many biological processes and constitute the active sites in most enzymes. In synthetic systems, transition metals, in order to exert their functions, have to be fixed in a preconstructed coordinating framework: this keeps the metal under spatial control, preventing its escaping from the reaction site, and also allows its electronic properties to be modulated, by varying the coordinating tendencies of the frame. One of the most convenient ways to put a transition metal under control is by encircling it with a multidentate macrocycle [1]. In particular, tetramine macrocycles of the type of cyclam, **1**, while firmly incorporating the metal centre and preventing its extrusion even under drastic conditions, leave room above and below the plane of the four nitrogen atoms for the interaction with further ligands. Macrocycles of the desired ring size and of tunable coordinating tendencies can be prepared through multi-step synthetic procedures [2]. As the cyclisation process is intrinsically disfavoured mostly from an entropic point of view, overall yields are relatively low (and the complete process time consuming). In some favourable cases, a transition metal centre can be used as a template, which makes the process much more simple and substantially improves the yield. This is the case of the synthesis of 14-membered tetra-aza macrocycles like **1** [3], which is illustrated in Fig. 1.

The Ni^{II} ion preorganises the open-chain tetramine 3·2·3-tet, by fixing its donor nitrogen atoms at the corners of a square. The two primary amine groups are in the right position to undergo Schiff base condensation with glyoxal, thus allowing cyclisation to occur. Then, the two C=N double bonds are hydrogenated to produce the $[Ni^{II}(cyclam)]^{2+}$ complex. Ni^{II} stays very comfortably inside the cyclam ring, its extrusion being strongly disfavoured from a kinetic point of view. In particular, in spite of the fact that the processes of demetallation and of protonation of the amine groups are on the whole thermodynamically favoured, the $[Ni^{II}(cyclam)]^{2+}$ complex persists almost indefinitely even in strongly acidic solutions: for instance, in a 1 M $HClO_4$ solution, a lifetime of 30 years has been calculated [5]! Moreover, when imprisoned by the cyclam ring, Ni^{II} undergoes an easy one-electron abstraction, thus attaining the otherwise unstable Ni^{III} state [6]. Ni^{II} can be removed from the cyclam ring only under extremely drastic conditions: boiling in presence of excess cyanide. Axial binding of a CN^- ion is the first step of the demetallation process, which eventually leads to the formation of $[Ni^{II}(CN)_4]^{2-}$ [7]. The free macrocycle can be isolated and made to react with other metal ions, if desired. Or it can be functionalised to give a multi-component system, for instance by appending a chosen subunit to one of the amine groups of cyclam. This typically requires the multi-step and tedious procedure of (i) selective protection of the amine groups; (ii) substitution at the unprotected nitrogen atom and (iii) deprotection [8]. Indeed, it could be desirable to have at hand a template reaction that gives in a one-pot process the metal complex of the functionalised macrocycle. Happily, such a reaction exists and its mechanism is illustrated in Fig. 2.

The reaction, which takes place in single passage, under very mild conditions, involves the pre-orientation of the linear tetramine 2·3·2-tet by a metal centre capable of imposing a square coordination (Ni^{II}, Cu^{II}). The two primary groups of the coordinated tetramine undergo Schiff base condensation with formaldehyde. Then, an $\mathbf{AH_2}$ molecule, displaying the properties of a diprotic Brønsted acid, loses its first proton (a base, e.g. triethylamine, is present in the solution) and AH^- gives a nucleophilic attack at one of the C=N double bonds. Subsequently, the covalently bound AH fragment further deprotonates: the A^- fragment that forms attacks the other proximate C=N imine bond, giving rise to the cyclisation. Thus, the AH_2 molecule behaves as a *padlock*, firmly locking the tetramine around the metal centre. The first padlock used was the carbon acid nitroethane, $CH_3\mathbf{CH_2}NO_2$ [9]. Diethylmalonate, $\mathbf{CH_2}(COOEt)_2$, also worked well [10]. Primary amines, $R\mathbf{NH_2}$, which can be formally considered diprotic acids, also gave successful cyclisation processes [11]. However, the most versatile cyclisation was observed when using as padlocks primary amides, both carboxyamides, $RCO\mathbf{NH_2}$ [12], and sulfonamides,

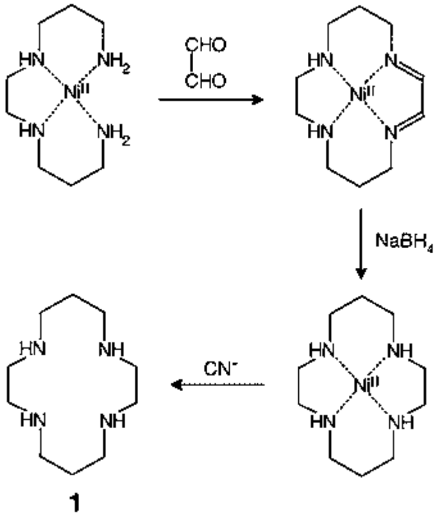

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Fig. 1. The nickel(II) template synthesis of cyclam. The reaction proceeds in two steps: (i) the Ni^{II} directed cyclisation; (ii) the hydrogenation of the two C=N bonds (using $NaBH_4$). The template can be removed in drastic conditions (boiling in presence of excess CN^-) [4].

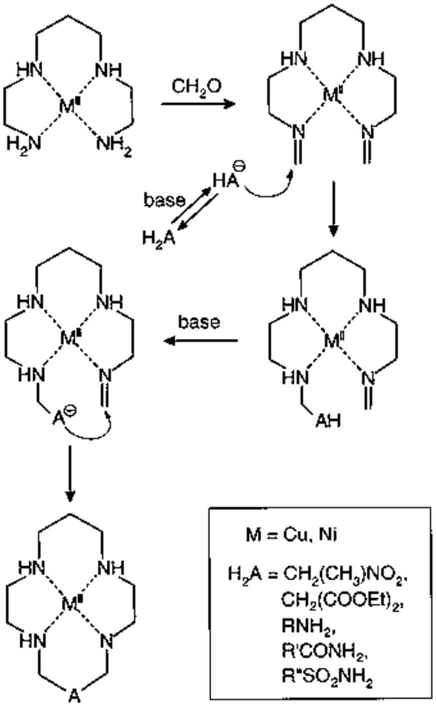
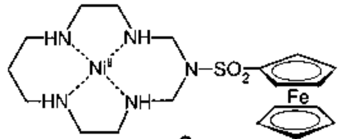


Fig. 2. The metal template synthesis of 14-membered quadridentate macrocycles. The formally diprotic acid H_2A acts as a locking fragment and the A residue (the padlock) remains incorporated in the cyclic framework. Using amides as locking fragments, it is possible to append to the azacyclam ring any wished functionality.

$RSO_2\mathbf{NH_2}$ [13]. The ring that forms (azacyclam) is isostructural with that of cyclam (the amide nitrogen atom merely plays an architectural role and is not involved in coordination) and the metal azacyclam complexes (of Ni^{II} and Cu^{II}) show a behaviour completely analogous to that of the corresponding complexes of cyclam [14]. The good news is that, using this template procedure, almost any kind of functional group can be appended to the 14-membered tetramine framework. In fact, given a desired fragment R, it is always possible to obtain its amide derivative, in particular sulfonamide, RSO_2NH_2, which can be used as a locking fragment in the preparation of the corresponding Ni^{II} or Cu^{II} azacyclam complex. The bad news is that azacyclam complexes do not undergo a clean demetallation to give the free ligand: the azacyclam ring itself is unstable in the absence of a coordinated metal centre and, if demetallated, decomposes. However, azacyclam complexes are per se interesting, in particular those of Ni^{II}. In fact, through the previously outlined template procedure, it is possible to link a redox active site (provided by the Ni^{II}/Ni^{III} couple) to any desired functional group or active subunit R. For instance, on reaction with 1-ferrocenesulfonamide, the conjugate system **2** was obtained, in which two distinct and non-equivalent redox active subunits (through the Ni^{II}/Ni^{III} and ferrocene/ferrocenium couples) are kept at a fixed distance by the sulfonamide spacer [15].



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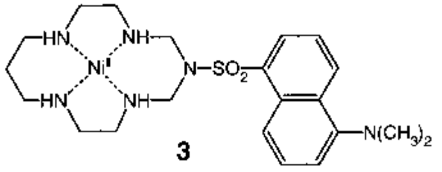

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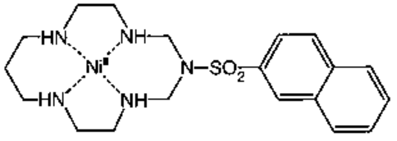

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Luminescent fragments can also be appended to a Ni^{II}-azacyclam system. For instance, reaction of $[Ni^{II}(2{\cdot}3{\cdot}2\text{-tet})]^{2+}$ with dansylamide, in an aqueous ethanolic solution containing excess formaldehyde and stoichiometric triethylamine, at 50°C, gives the complex **3**, as crystalline perchlorate salt [16]. The dansyl fragment, in the conjugate system **3**, displays the typical fluorescent behaviour of the isolated component dansylamide (dns). In particular, when excited at 336 nm (the wavelength of the highest absorption of the naphthalene fragment), an MeCN solution of **3** displays a non-structured emission band centred at 510 nm, which results from a charge transfer excited state. The Ni^{II}-**3** complex can be oxidised to the Ni^{III}-**3** form, through exhaustive electrolysis, by setting the potential of the working electrode (a platinum gauze) at 0.23 V versus Fc^+/Fc (in an MeCN solution made 0.1 M in Bu_3MeNCl). The occurrence of the metal-centred one-electron oxidation process is demonstrated by a colour change of the solution: from yellow (the colour of the square-planar low-spin $[Ni^{II}N_4]^{2+}$ complex) to the intense green-yellow colour of the *trans*-octahedral low-spin $[Ni^{III}N_4Cl_2]^+$ species. More interestingly, following oxidation to Ni^{III}, the emission of the dns subunit is quenched. Quenching has to be ascribed to a fast electron transfer (eT) process from the photoexcited dansyl fragment (dns*) to the nearby Ni^{III} centre. The occurrence of the dns*-to-Ni^{III} eT process is accounted for on the basis of an extremely favourable free energy change ($\Delta G° = -1.9$ eV). On the other hand, the Ni^{II}-to-dns* eT process is thermodynamically prevented in the reduced form of the conjugate system Ni^{II}-**3** ($\Delta G° = 0.7$ eV). Very interestingly, the fluorescence of the dansyl subunit of **3** can be switched on/off at will, through the Ni^{II}/Ni^{III} redox change, i.e. consecutively adjusting the potential of the working electrode at 0.23 and -0.07 V, in a controlled potential electrolysis experiment. The mechanism associated to the redox switching of fluorescence is illustrated in Fig. 3.

The metaphor of the *switch* (very popular in the language of supramolecular chemistry [17]) fits well the behaviour of the multicomponent system **3**. In fact, we can distinguish the light bulb (the luminescent fragment), the electrical wire (the SO_2 spacer), and the real switch (the nickel–azacyclam subunit). The switch can be operated through an external input (the variation of the electrode potential or the addition of a redox reagent) and this results in either light emission (switch on) or quenching (switch off). In everyday life, one wishing to change the type of light simply unscrews the bulb and replaces it with a different one. In the molecular world, the result is obtained through the template reaction illustrated in Fig. 2. For instance, by using as a locking fragment 2-naphthalenesulfonamide, the conjugate system **4** can be obtained in good yield, which behaves as an efficient redox switch of fluorescence: the Ni^{III} derivative quenches the light emission, the Ni^{II} form restores it [16]. Systems **3** and **4** only differ in the wavelength of the emitted light: visible for **3** ($\lambda = 510$ nm), ultraviolet for **4** ($\lambda = 360$ nm).

Further metal centred switches of fluorescence have been recently prepared, in most cases by covalently linking the appropriate components through multistep non-template synthesis. These switches are based on either the Ni^{III}/Ni^{II} or Cu^{II}/Cu^{I} couple and in all cases the oxidised metal quenches the fluorescence of the nearby fluorophore and the reduced form revives it. Quenching takes place through either an eT mechanism (as in the previously discussed systems, **3** and **4**) or an energy transfer (ET) mechanism. The rationale for designing efficient molecular switches of luminescence, responding to chemical inputs, has been recently reviewed in this journal [18].

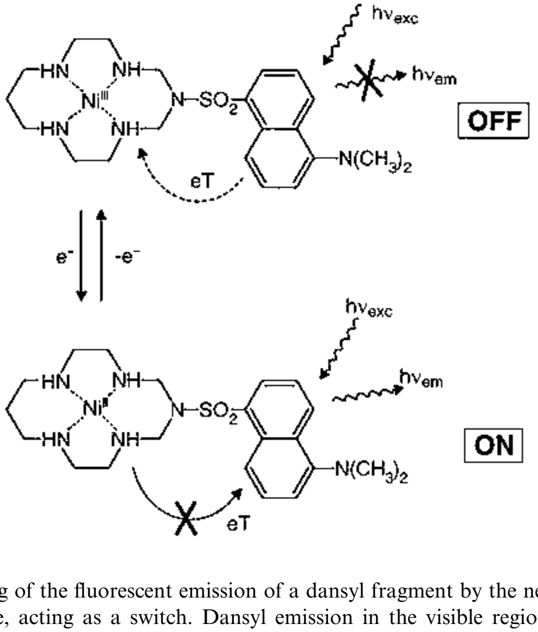
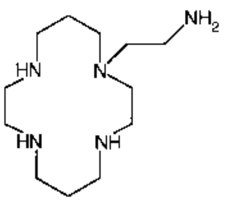


Fig. 3. Redox switching of the fluorescent emission of a dansyl fragment by the nearby covalently linked Ni^{III}/Ni^{II} redox couple, acting as a switch. Dansyl emission in the visible region can be quenched/restored at will through consecutive additions of an oxidising agent and of a reducing agent.

2. pH-controlled molecular movements in metal–scorpionate complexes, signalled through fluorescence quenching-enhancement

There exist molecular systems consisting of mobile and fixed components, in which the movement of the mobile component can be controlled from the outside, through a chemical input (i.e. the variation of the pH or of the redox potential). Recent examples refer to some ingenious objects from supramolecular chemistry: rotaxanes and catenates. Kaifer and Stoddart first reported a rotaxane whose wheel was a π-acceptor cyclophane, containing two methylviologen subunits, and whose axle contained two subunits of different donor tendencies: the more donating 4,4′-benzidine and the 4,4′-dimethoxy-diphenyl fragments [19]. By destroying/regenerating the donor properties of the benzidine portion through either an acid–base reaction or a redox process, the wheel could be made to move, reversibly and without any friction, from one station to the other. In the Sauvage catenate, two rings (one containing a 2,2′-bipyridine subunit and one containing both a 2,2′-bipyridine and a 2,2′:6′,2″-terpyridine subunits) are interlocked around a copper centre, which drives the molecular motion [20]. In fact, when changing the oxidation state of the metal from + 1 to + 2, the two-subunit ring makes a half turn. Further reduction to + 1 makes the turn complete. The redox driven motion presents some hysteresis, essentially due to the stereochemical rearrangement experienced by the Cu^{II} centre. In the two above mentioned examples, the mobile and fixed components (whose definition is relative, since one can only conventionally assess which is the mobile part and which is the fixed one) are held together by supramolecular interactions. Controlled molecular movements can be achieved also in covalently linked multicomponent systems. A relatively old example refers to the metal complexes of the quinquedentate ligand **5**, in which a flexible aminoethyl side-chain has been appended to the rigid cyclam ring [21].



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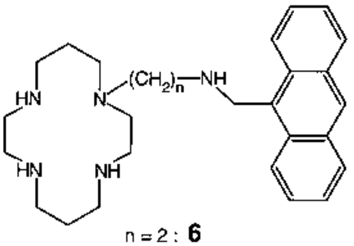


n = 2 : **6**
n = 3 : **7**

When a transition metal is incorporated by the tetramine ring of **5**, the in-plane metal-amine interactions are typically inert, due to the kinetic macrocyclic effect, and the metal cannot be extruded from the ring even in a strongly acidic solution. On the other hand, the pendant arm tends to bind the metal centre from the top, but the M–N bond is labile. Thus, on acidification, the axially bound amine group is protonated and the side-chain bearing the ammonium group moves away from the metal centre. The process is fast and reversible and the pendant arm can be relocated at will into two topologically distinct positions, one on the metal centre,

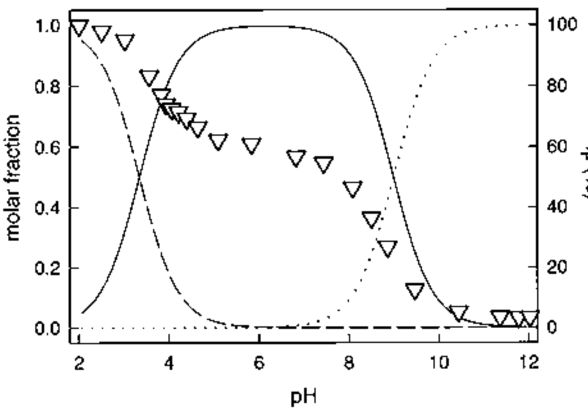


Fig. 4. pH dependance of the relative fluorescence intensity I_F of the anthracene fragment of the Ni^{II} scorpionate complex of ligand **6** (L) (∇, right vertical axis) and distribution curves of the three species present at the equilibrium: $[Ni^{II}(LH^+)]^{3+}$, $[Ni^{II}(L)(H_2O)]^{2+}$, $[Ni^{II}(L)(OH)]^+$ (dashed, full and dotted line, respectively; left vertical axis).

the other far away from it, through a fine variation of the pH: pK_a ± 1. In the case of the Ni^{II}-**5** system (pK_a 2.8), the occurrence of the molecular motion can be visually perceived through a neat colour change. At low pH, Ni^{II} exhibits a square-planar coordination, low-spin state, yellow colour; at $pH > 2.8$, the pendant arm occupies one of the axial positions of the coordination octahedron, the other one being held by a water molecule: the spin state is high, the colour pale blue–violet. The yellow and blue colours can be interconverted at pleasure, through consecutive additions of acid and base [21]. Tetra-aza macrocycles bearing a pendant arm were introduced in the late 1970s by Kaden [22]. Due to the unique feature of an aggressive tail capable of stinging from the top an already chelated individual (the metal ion), ligands of this type were later called *scorpionands* [21]. Metal scorpionate complexes represent a nice example of a controllable molecular motion driven by a pH change and based on the metal–ligand interactions.

We were recently interested in associating the molecular movement of a scorpionate complex with the generation of a luminescent signal. For this reason, we appended an anthracenyl fragment to the aminoethyl side-chain of **5**, to give **6**, and we investigated how the emission of the corresponding Ni^{II} complex was affected by a change of pH [23].

Fig. 4 displays the variation with the pH of the fluorescence intensity, I_F, of the anthracene subunit of the $[Ni^{II}(\mathbf{6})]^{2+}$ complex (open triangles). The highest emission is observed at $pH \leq 2$. Then, I_F decreases to reach a *plateau*, corresponding to 60% of the original emission intensity. A further pH increase induces complete fluorescence quenching ($pH \geq 10$). The presence at the equilibrium of three species was assessed through potentiometric titration experiments: (i) a $[Ni^{II}(LH^+)]^{3+}$ species, having the side arm protonated ($pH \leq 3$); (ii) a $[Ni^{II}(L)(H_2O)]^{2+}$ species, in which the amine pendant arm is axially bound, according to a *trans*-octahedral coordinative arrangement, the other axial position being occupied by a water molecule ($4 \leq \text{pH} \leq 8$); (iii) a species deriving from (ii), through the deprotonation of the axially bound water molecule: $[\text{Ni}^{\text{II}}(\text{L})(\text{OH})]^{+}$. The distribution curves of the three species over the pH 2–12 interval are shown in Fig. 4, while the stereochemical features of the three forms in equilibrium are sketched in Fig. 5. The drawings are inspired from the structures calculated through a semi-empirical procedure.

A comparison of the distribution curves and of the fluorescence intensity profile in Fig. 4 indicates that each level of emission intensity corresponds to a well defined species. In particular, the highest emission is due to the $[\text{Ni}^{\text{II}}(\text{LH}^{+})]^{3+}$ complex, in which the photoexcited anthracene fragment, An*, is at the longest distance from Ni^{II} (see the sketch in Fig. 5) and the metal–fluorophore interaction is minimised. At $\text{pH} > 3$, the pendant arm goes to occupy one of the axial positions of the coordination octahedron, bringing the An fragment much closer to the metal. At this shorter distance, an ET process takes place between Ni^{II} and An*, which reduces the fluorescent emission to 60%. Therefore, the pH driven motion of the side chain of the scorpionate complex is signalled by a distinct decrease of the light emission. On the other hand, the complete quenching of fluorescence which takes places at $\text{pH} \geq 9$ should not be assigned to any molecular movement, but simply to the release of a proton from the axially bound water molecule of the $[\text{Ni}^{\text{II}}(\text{L})(\text{H}_2\text{O})]^{2+}$ complex. As regards the mechanism, it has been suggested that the decrease of the overall electrical charge of the complex makes the Ni^{II}-to-Ni^{III}

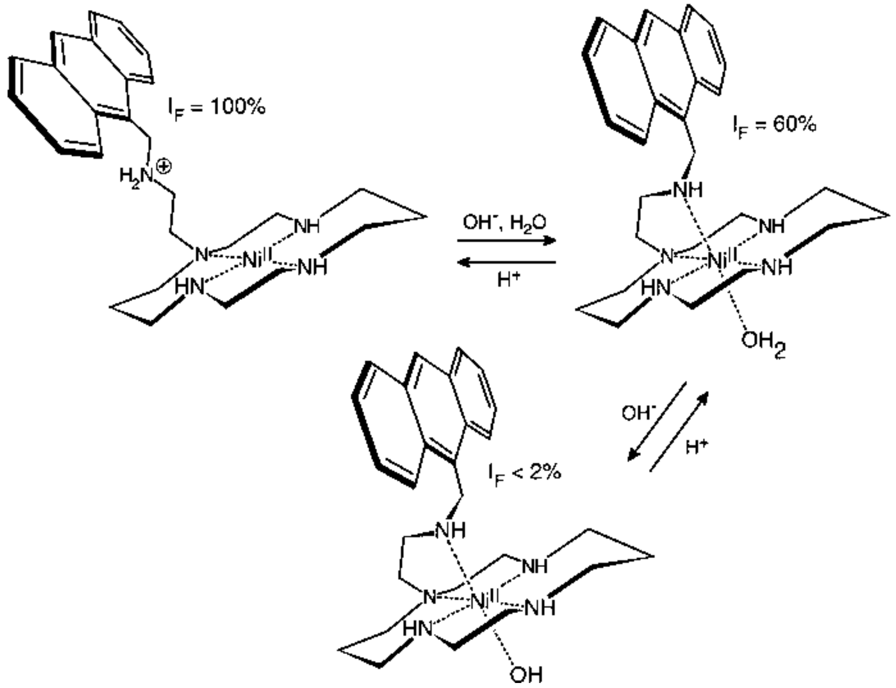


Fig. 5. pH controlled movement of the fluorescent pendant arm in the Ni^{II} scorpionate complex of ligand **6**.

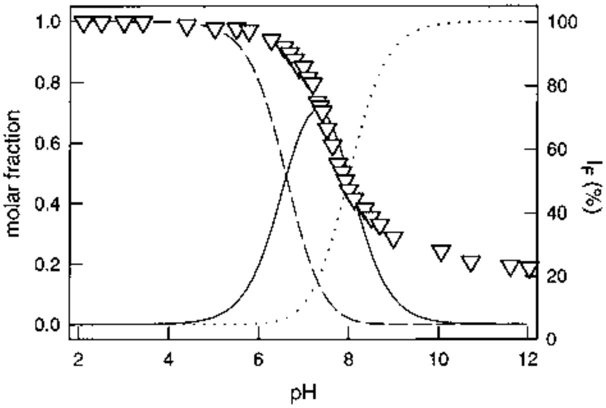


Fig. 6. pH dependance of the relative fluorescence intensity I_F of the anthracene fragment of the Ni^{II} scorpionate complex of ligand **7** (L) (∇, right vertical axis) and distribution curves of the three species present at the equilibrium: $[Ni^{II}(LH^+)]^{3+}$, $[Ni^{II}(L)(H_2O)]^{2+}$, $[Ni^{II}(L)(OH)]^+$ (dashed, full and dotted line respectively; left vertical axis). Compared to system **6**, the intermediate complex $[Ni^{II}(L)(H_2O)]^{2+}$ forms in a narrower pH range, which prevents the formation of the intermediate I_F plateau.

oxidation process distinctly easier, thus making it possible the occurrence of an eT process from Ni^{II} to An*. Notice that this process was thermodynamically disfavoured in the $[Ni^{II}(L)(H_2O)]^{2+}$ complex. Thus, the fluorescence quenching observed for the $[Ni^{II}(L)(OH)]^+$ species results from the concert of two different mechanisms: ET and eT (Ni^{II}-to-An*). The stepwise fluorescence quenching illustrated in Fig. 4 is a quickly, fully reversible process: on addition of standard acid to the non-luminescent solution at pH 12, the fluorescence is first restored at 60%, then, at pH ≤ 2 is fully revived. The Ni^{II}-**6** system is an example of three-position switch of fluorescence, driven by a pH change. The motion of the dangling chain is responsible for the switching effect in the acidic region.

The emission of the fluorescent fragment of a scorpionate complex can be further modulated by varying the coordinating tendencies of the pendant arm. For instance, the ethylenic segment of the side chain of scorpionand **6** can be replaced by a trimethylenic segment in scorpionand **7**. Fig. 6 displays the I_F versus pH profile obtained for the Ni^{II}-**7** system, as well as the distribution curves of the three species which form over the pH 2–12 range: $[Ni^{II}(LH^+)]^{3+}$, $[Ni^{II}(L)(H_2O)]^{2+}$, $[Ni^{II}(L)(OH)]^+$, for which stereochemical arrangements similar to those reported in Fig. 5 can be proposed. The species present at the equilibrium are the same as for scorpionand **6**, their structures are presumably similar, but the I_F versus pH profile is substantially different. In fact, the emission decreases smoothly from pH 6 to 9, where fluorescence is almost completely quenched, and no *plateau* is observed at intermediate pH values. Noticeably such a behaviour is a simple consequence of the reduced coordinating tendencies of the pendant arm. In this connection, it should be noted that an isolated $R_1R_2NH_2^+$ ammonium group behaves as a rather weak acid: as an example, the pK_a for the reference system $AnCH_2NH_2^+C_3H_7$, measured in the same conditions as for scorpionates, is 8.91. Note that for the $[Ni^{II}(LH^+)]^{3+}$

scorpionate complex (L = **6**) the pK_{a_1} is very much lower: 3.34 ± 0.02. The more than five orders of magnitude increase of the acidity constant (corresponding to an energy advantage of 7.6 kcal mol^{-1}) reflects the additional enthalpy contribution due the formation of the Ni^{II}–N axial bond, which immediately follows the deprotonation of the ammonium group. The stronger the metal–amine interaction, the lower the pK_a value. In the $[Ni^{II}(L)(H_2O)]^{2+}$ complex (L = **7**), the coordinated pendant arm forms a six-membered chelate ring, which is less stable than the five-membered ring formed in the corresponding complex of **6**, and this should cause a less exothermic M–N axial interaction. This is reflected in a considerably higher value of pK_{a_1} 6.61 ± 0.02 in the case of system **7**. On the other hand, the less intense axial interaction would make the Ni^{II} centre more ‘acidic’, thus favouring the extrusion of the proton from the axially bound water molecule in the $[Ni^{II}(L)(H_2O)]^{2+}$ complex. It derives that the pK_{a_2} value is distinctly lower for **7** than for **6**: 7.99 ± 0.02 compared to 8.99 ± 0.02. As a consequence of the reduced difference between pK_{a_1} and pK_{a_2} values, the $[Ni^{II}(L)(H_2O)]^{2+}$ form of **7** exists in a narrow pH range and reaches a maximum abundance of only 70% (at pH 7), which prevents the appearance of a *plateau* in the I_F versus pH profile. Thus, it is not possible, from the I_F variation, to detect either the completion of the side chain movement or the inception of the second quenching process. The fluorescence emission monotonically decreases from pH 6 to 9 and, even at higher pH values, it is not completely quenched. In fact, in the $[Ni^{II}(L)(OH)]^{+}$ complex of **7** the Ni^{II}-to-An* eT additional mechanism is not as efficient as in system **6** and some 20% of residual fluorescence persists.

Nickel(II) scorpionate complexes of pentamines **6** and **7** are novel fluorescence switches whose control has a mechanical nature. Both systems allow three states of different emission properties, but only system **6** behaves as a three-position switch (high/low/off): system **7** behaves as a conventional on/off switch.

3. Redox and pH-switched translocation of metal ions

In the everyday language, a *machine* can be defined as ‘a system consisting of fixed and movable parts capable of converting energy into mechanical work’. In this sense, the lever, the millstone, the pulley are among the most ancient and useful machines which have been introduced by the man since the neolithic revolution. Noticeably, the above definition of machine applies well to the systems described in the previous Section (rotaxanes, catenates, scorpionates), which convert chemical energy into mechanical work and can therefore be considered machines operating at the molecular level (even if usefulness and practical application are quite far from being demonstrated, yet).

There exist other ways to produce mechanical work at the molecular level: one involves the controlled displacement of a particle along a predetermined route. In the simplest situation, the particle, e.g. a metal ion, is translocated from a given site to another site of the same molecular system, following a chemical input (an acid–base reaction, a redox process). The redox switched reversible translocation of

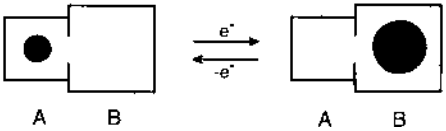


Fig. 7. The redox switched translocation of a metal ion within a two-compartment ligand.

a metal ion in a two-component molecular system is schematically sketched in Fig. 7.

The box in the figure symbolises a system containing two distinct and separate receptor subunits, A and B, which differ in their coordinating properties. For instance, A is a *hard* receptor, and B a *soft* one. Given a metal M possessing two adjacent oxidation states of comparable stability, it will probably happen that, in a solution containing equimolecular amounts of the metal and of the two-compartment system, A–B, the reduced form M^{n+} will go to occupy the soft compartment B. But, if M^{n+} is oxidised, chemically or electrochemically, the harder ion which forms, $M^{(n+1)+}$, will find thermodynamically convenient to move from B to the nearby hard compartment A. Consecutive oxidation and reduction processes would make the metal centre M shuttle back and forth, between A and B, along a determined route. The rate of the translocation process should depend on the nature of the coordinative interactions between M and receptors A and B, whether labile or inert, and on the feasibility of the stereochemical rearrangement which may accompany the metal displacement. Example of redox driven metal ion translocation within a two-component system have been discussed recently.

Lehn has illustrated the possible translocation of a copper centre within the cylindrical macrotricycle **8**, which contains a N_2S_2 ring (the soft receptor, preferred by the Cu^I state) and a N_2O_3 ring (the hard receptor, chosen by the Cu^{II} cation) [24]. The Cu^{II}/Cu^I redox change would make the metal centre translocate reversibly from a site to the other. The hypothesised process is illustrated in Fig. 8.

In the same line, Shanzer has synthesised the tripodal system **9**, which contains a tris-hydroxamate compartment (close to the cap) and a tris-2,2′-bipyridine

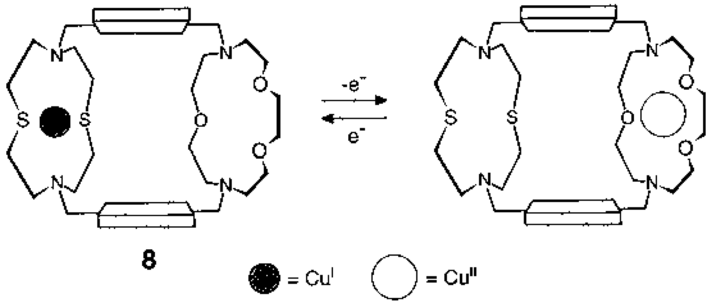


Fig. 8. The redox switched translocation of a copper centre within a cylindrical macrotricycle. Cu^I chooses the soft receptor subunit N_2S_2, Cu^{II} the hard N_2O_3 receptor subunit [24].

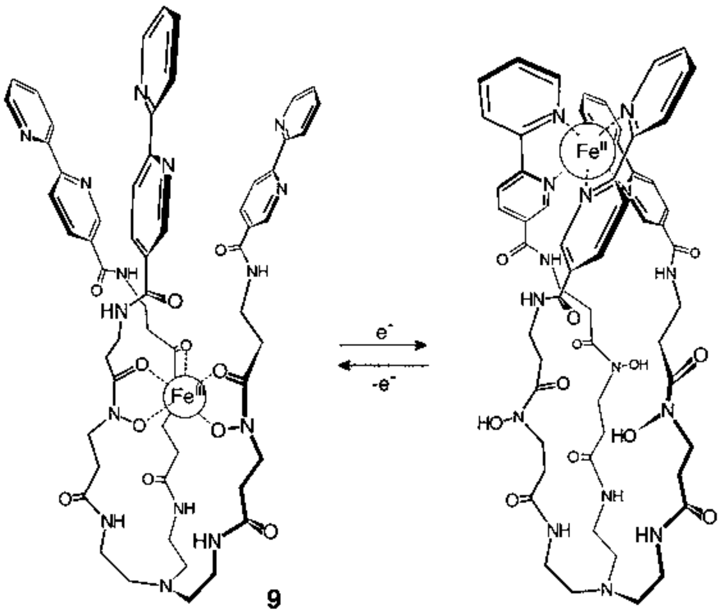


Fig. 9. The redox driven translocation of an iron centre within a ditopic tripodal ligand, based on the Fe^{III}/Fe^{II} redox change. Fe^{III} likes the tris-hydroxamate compartment, Fe^{II} prefers to stay inside the tris-2,2′-bipyridine compartment [25].

compartment [25]. An Fe^{III} centre chooses to occupy the tris-hydroxamate compartment and the solution takes the typical brown colour of iron(III) tris-hydroxamate complexes. On addition of a reducing agent (ascorbic acid), within minutes the solution turns red–violet, the colour of the $[Fe^{II}(bpy)_3]^{3+}$ complex. The mechanism of the process is schematically sketched in Fig. 9. Translocation can be reversed on oxidising Fe^{II} to Fe^{III} with peroxydisulphate, but the process takes several minutes even at 60°C. Sluggishness of the process may be related to the serious conformational changes the tripodal ligand has to experience in the course of the redox driven metal translocation.

A metal ion can be translocated within a two-compartment ligand also by taking profit from a variation of pH. To do that, the ligand should possess the features illustrated in Fig. 10. In particular, one of the two compartments should be an n-protic Brønsted acid AH_n. Whereas AH_n should exhibit negligible coordinating

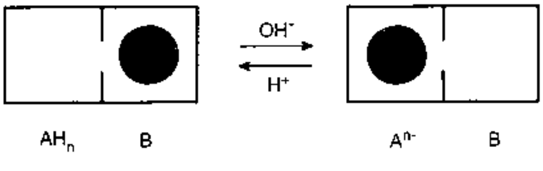
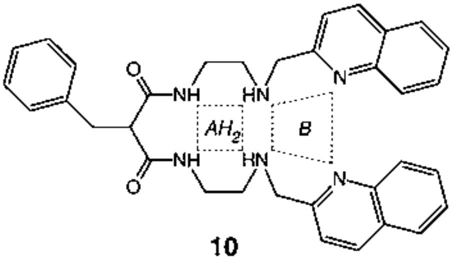


Fig. 10. The pH driven translocation of a metal ion within a two-compartment ligand.

tendencies toward a given metal ion M, its deprotonated form A^{n-} should present strong donor properties, specifically stronger than those exhibited by the adjacent coordinating compartment B. Thus, affinity towards M should decrease along the sequence: $A^{n-} > B > AH_n$.

In such a situation, at low pH the protonated form AH_n is present, and M resides in compartment B. At higher pH, AH_n deprotonates and M moves from B to the more coordinating A^{n-} compartment. Thus, on consecutive addition of standard base (n equiv. of OH^-) and of standard acid (n equiv. of H^+), it should be possible to displace the metal centre back and forth, at will, from a compartment to the other of the ditopic receptor AH_n-B.



10

Preliminary studies have shown that the potentially sexidentate ligand **10** fulfils the requirements of an AH_n–B system and is suitable for the pH-driven intramolecular translocation of a transition metal ion [26]. In **10**, compartment B is represented by the four-coordinating set consisting of two secondary amine nitrogen atoms and two quinoline nitrogen atoms. The set made up by the two amine nitrogen atoms and the two amide groups provides compartment AH_2. In fact, the carboxyamide group –C(O)NH– displays very poor coordinating tendencies towards metal ions, but, in its deprotonated form, $-C(O)N^{-}-$, is a very powerful donor group. Therefore, the recommended order of donor tendencies should be achieved: (deprotonated amide)-(amine) > (amine)-(quinoline) > (amide)-(amine). The Ni^{II} ion, for its electronic properties, seems very appropriate for being translocated within system **10**. The translocation process is depicted in Fig. 11.

In particular, in a water–dioxane solution, at pH 7.2, Ni^{II} resides in the amine–quinoline compartment: the pale violet colour of the solution, as well as the weak d–d bands at 606 and 820 nm, indicate the presence of a high-spin octahedral complex. Probably, two water molecules occupy the axial positions of the elongated octahedron, whose equatorial positions are held by the four nitrogen atoms (two amine and two quinoline). On raising pH up to 9, the solution takes a yellow colour and an intense band at 444 nm develops ($\varepsilon = 116\ M^{-1}\ cm^{-1}$). These features are associated with the formation of a square-planar low-spin Ni^{II} complex and indicate that the metal centre is now coordinated by an especially strong donor set: that consisting of the two amine groups and the two deprotonated amide groups. Thus, the pH change from 7 to 9 has made the Ni^{II} ion move from compartment B to compartment A^{2-}. On adjusting pH at 7 again, through standard acid addition, the metal moves back to B. The Ni^{II} translocation between the two

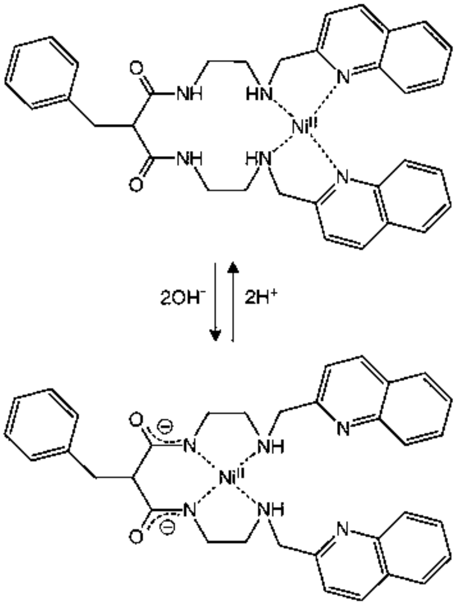


Fig. 11. The pH switched translocation of the Ni^{II} ion within a two-compartment hexa-aza ligand.

compartments of system **10** can be carried out back and forth indefinitely and is visually perceived through the development-disappearance of the yellow colour (increase-decrease of the intensity of the d–d band at 444 nm).

4. Redox switched translocation of anions between metal centres

In principle, nothing hinders the controlled translocation of an anion from a predetermined site to an other in a multicomponent system, in a way similar to that described for metal ions in the preceding Section. One has simply to choose the appropriate receptor subunits for the envisaged anion, and to assemble them according to a convenient geometry. However, the design of an anion receptor is not trivial, and, in any case, is not as simple as in the case of the receptors for transition metal ions. In fact, the recognition of anions is typically based on electrostatic interactions (which include hydrogen bonding) and the design of the receptor involves the elaborate synthesis of concave systems, which contain several positively charged groups (e.g. ammonium, alkylammonium) or hydrogen bonding donors (e.g. amide fragments), placed in geometrically convenient positions [27]. Electrostatic interactions are weak and, in order to avoid the unsuccessful competition with the anion hydration energy, recognition studies have to be carried out in apolar or poorly polar media (e.g. $CHCl_3$, CH_2Cl_2). Moreover, the selective modulation of the receptor binding tendencies, required for translocation, seems rather difficult to achieve in the case of anions. However, there exist other more energetic and versatile interactions suitable for anion binding and recognition: the metal-ligand interactions. Transition metals form stable complexes with most inorganic anions and the intensity of the metal–anion interaction may vary substantially by changing the oxidation state of the metal, a feature which can be profitably employed to carry out translocation experiments. Thus, it may be convenient to equip the receptor platform with a d-block metal centre, which possesses at least one coordination site vacant and available for the incoming anion. Metal containing platforms suitable for anion recognition and sensing have been recently developed [27]. They provide distinct selectivity (which derives in part from the directionality of the binding) and, thanks to the relatively high energy of the metal–ligand interaction, do not suffer from solvational effects, thus working well even in water. Moreover, a gradient of redox potential can be used to promote the anion translocation process in a multimetal system, provided that one of the metal centres chosen as a binding site possesses two consecutive oxidation states displaying a different affinity towards the investigated anion.

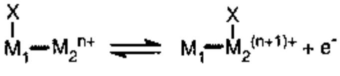
In the following, we will consider the redox driven translocation of a mononegative anion X^- between two pre-positioned metal centres M_1 and M_2. In particular, each metal will be hosted by an appropriate receptor and the two receptor subunits will be covalently linked by a spacer. Thus, the distance between M_1 and M_2 is fixed and determined by the length of the spacer. In order to promote a reversible translocation of X^- within the heterodimetallic system M_1–M_2, the following prerequisites must be fulfilled:

1. M_1 should be coordinatively unsaturated and should display a reasonable affinity towards X^-;
2. M_2 should be redox active through the $M_2^{(n+1)+} + e^- = M_2^{n+}$ change. The oxidised and reduced states should have a comparable stability, i.e. the potential associated to their half-reaction should be neither too high, nor too low. Moreover, the affinity toward X^- should be very high for $M_2^{(n+1)+}$, very low (or nil) for M_2^{n+}.

In particular, the metal–anion affinity should decrease along the sequence:

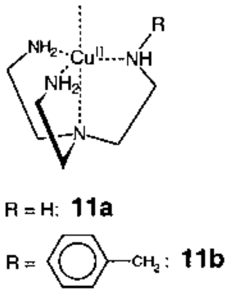
$$M_2^{(n+1)+} > M_1 > M_2^{n+} \qquad (1)$$

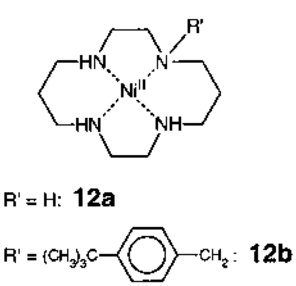
In this situation, it will happen that, when M_2 is in its reduced form, X^- stays on M_1; but, when M_2^{n+} is oxidised, X^- will move to bind the $M_2^{(n+1)+}$ centre. Thus, X^- can be translocated back and forth between M_1 and M_2, at will, through the consecutive oxidation and reduction of the M_2 centre, as outlined in the redox equilibrium (Eq. (2)).



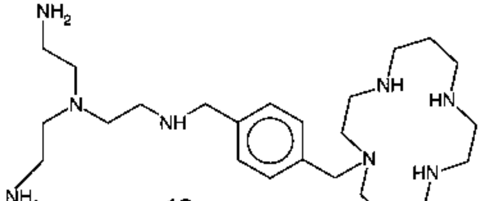
$$\overset{X}{M_1}\text{—}M_2^{n+} \rightleftharpoons M_1\text{—}\overset{X}{M_2}{}^{(n+1)+} + e^- \qquad (2)$$

Notice also that, in order to have a fast and quickly reversible translocation process, the metal-anion coordinative bond must be labile for all the considered





ions: M_1, M_2^{n+} and $M_2^{(n+1)+}$. Such a situation is commonplace with metal ions of the 3d series.



13

We considered that the $[Cu^{II}(tren)]^{2+}$ fragment, **11a**, could be a reasonable M_1 subunit. In fact, when coordinated by the tripodal tetramine tren, Cu^{II} tends to assume a trigonal bipyramidal stereochemistry and one of the axial positions is left available for either a solvent molecule or an anion. In particular, in the case of the Cu^{II} complex with the *N*-substituted tren derivative **11b**, the log *K* value for the $[Cu^{II}L]^{2+} + Cl^- = [Cu^{II}LCl]^+$ equilibrium, in an MeCN solution, is 5.7. On the other hand, a $[Ni^{II,III}(cyclam)]^{2+/3+}$, **12a**, fragment could represent a convenient M_2 centre. The Ni^{II}-to-Ni^{III} oxidation process takes place at a moderately positive potential. Moreover, the low-spin Ni^{II} state prefers a square-planar coordination and has an extremely low affinity to bind anions. On the other hand, the low-spin Ni^{III} state tends to increase its coordination number and to bind one-two ligands in the axial positions. In particular, in the case of the *N*-substituted derivative **12b**, the Ni^{III} complex, when generated in an MeCN solution 0.1 M Bu_4NClO_4 through controlled potential electrolysis, strongly binds a Cl^- anion, according to the equilibrium: $[Ni^{III}(L)]^{3+} + Cl^- = [Ni^{III}(L)Cl]^{2+}$, with a $\log K \gg 7$. The green-yellow five-coordinate $[Ni^{III}(L)Cl]^{2+}$ complex does not bind any further anion even in presence of excess chloride, probably due to the steric repulsive effect exerted by the bulky substituent present on one of the ligand's nitrogen atoms. Therefore, the anion affinity decreases along the series: $Ni^{III} > Cu^{II} > Ni^{II}$, which fulfils the main requirement for the occurrence of the redox driven translocation between metal centres.

Thus, the ditopic receptor **13** was synthesised [28], in which a tren subunit and a cyclam subunit have been covalently linked through the nitrogen atoms by a 1,4-xylyl spacer (in this sense, it was correct to consider the binding characteristics of the *N*-benzyl substituted fragments **11b** ad **12b**). On reaction of **13** with an equivalent of Ni^{II}, the metal centre, among the two covalently linked tetramine receptors, seeks the more strongly donating cyclam subunit (due to the *thermodynamic* macrocyclic effect [29]). The {tren-[Ni^{II}(cyclam)]}$^{2+}$ complex is then reacted with copper(II), at room temperature. Actually, Cu^{II} gives with cyclam a more stable complex than Ni^{II}, but the inertness imparted by the ligand (the *kinetic* macrocyclic effect [30]) prevents metal replacement. Therefore, Cu^{II} has to be satisfied with the coordination by the tripodal tetramine fragment. Thus, the heterodimetallic complex of **13**, {[Cu^{II}(tren)]-[Ni^{II}((cyclam)]}$^{4+}$ (in the following indicated as [Cu^{II}Ni^{II}]) was synthesised and isolated.

In an MeCN solution 10^{-3} M both in [Cu^{II}Ni^{II}] and in Cl, 95% of the anion is bound to the Cu^{II} centre, whose colour is blue–green (absorption band at $\lambda = 465$ nm, $\varepsilon = 180$ M^{-1} cm^{-1} and a broad one centered at about 700 nm). On exhaustive electrolysis, one equivalent of electrons is consumed for the Ni^{II}-to-Ni^{III} oxidation and the solution takes an intense green–yellow colour. The absorption band that develops ($\lambda = 312$ nm, $\varepsilon = 9000$ M^{-1} cm^{-1}) corresponds to the [Ni^{III}(L)Cl]$^{2+}$ chromophore. Thus, the colour change of the solution from blue–green (Cl$^-$ coordinated to Cu^{II}) to intense green–yellow (Cl$^-$ bound to Ni^{III}) signals the occurrence of the Cl$^-$ translocation from Cu^{II} to Ni^{III}. By sequentially adjusting the potential of the platinum gauze working electrode at the appropriate potential (0.40 V vs. Fc$^+$/Fc for oxidation, 0.00 V for reduction), the colour of the solution can be made change indefinitely, thus demonstrating the reversibility of the redox driven translocation, whose stereochemical aspects are sketched in Fig. 12.

A non trivial question is whether the translocation is *intramolecular* (i.e. the Cl$^-$ ion uptaken by the Ni^{III} centre comes from the proximate Cu^{II} centre) or *intermolecular* (Cl$^-$ comes from the solution, being transferred from a different [Cu^{II}(Cl)Ni^{II}] molecule, following an intermolecular collision). First of all, it should be reminded that the metal-anion interaction is labile for both Cu^{II} and Ni^{III}, which guarantees a continuous exchange of Cl$^-$ and prevents any attempt at anion labelling. However, what can be suggested is that when Ni^{II} is oxidised to Ni^{III} it is the Cl$^-$ ion staying at that particular moment on the proximate Cu^{II} centre that moves *intramolecularly* to Ni^{III}. Such a process is described by the equilibrium in Eq. (3).

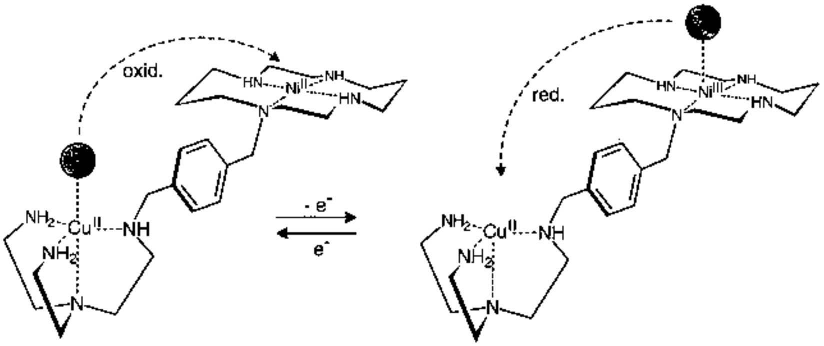


Fig. 12. The redox switched translocation of the chloride ion (sphere) in a copper–nickel dinucleating system. Anion location is controlled by the oxidation state of the nickel centre: when reduced, Cl$^-$ stays on Cu^{II}; when Ni^{II} is oxidised, Cl$^-$ moves to the Ni^{III} centre [28].

$$\overset{\text{Cl}}{\text{Cu}^{\text{II}}}\text{—Ni}^{\text{III}} \rightleftharpoons \text{Cu}^{\text{II}}\text{—}\overset{\text{Cl}}{\text{Ni}^{\text{III}}} \qquad (3)$$

Noticeably, the $\Delta G°$ value associated to the neat anion translocation equilibrium (Eq. (3)) can be calculated from $\Delta E° = E°_{\text{Ni}^{\text{III}}/\text{Ni}^{\text{II}}} - E°_{\text{Ni}^{\text{III}}/\text{Ni}^{\text{II}}}(\text{Cl}^-)$, where $E°_{\text{Ni}^{\text{III}}/\text{Ni}^{\text{II}}}$ is the potential measured in an MeCN solution made 0.1 M in Bu_4NClO_4 and $E°_{\text{Ni}^{\text{III}}/\text{Ni}^{\text{II}}}(\text{Cl}^-)$ the potential measured in a solution containing also Cl^- (potential values being measured by voltammetric techniques). For equilibrium (Eq. (3)), $\Delta G° = F\Delta E° = 11.5$ kcal mol^{-1}, indicating that translocation process (Eq. (3)) is strongly favoured from a thermodynamic point of view. This ΔG° value has to be compared with that associated to the equilibrium (Eq. (4)):

$$[\text{Cu}^{\text{II}}(\mathbf{11})(\text{Cl})]^+ + [\text{Ni}^{\text{III}}(\mathbf{12})]^{3+} = [\text{Cu}^{\text{II}}(\mathbf{11})]^{2+} + [\text{Ni}^{\text{III}}(\mathbf{12})(\text{Cl})]^{2+} \qquad (4)$$

in which the Cl^- anion is transferred from the isolated component $[\text{Cu}^{\text{II}}(\mathbf{11})]^{2+}$ to the other oxidised isolated component $[\text{Ni}^{\text{III}}(\mathbf{12})]^{3+}$. Notice that the anion transfer (Eq. (4)) is much less favoured than translocation process (Eq. (3)), as indicated by the remarkably less negative value of $\Delta G° = 4.0$ kcal mol^{-1}. We ascribe this large energy difference to the fact that process (Eq. (4)) is intermolecular, whereas process (Eq. (3)) is intramolecular. In this connection, it should be noticed that the intermolecular anion transfer of Eq. (4) results from the collision between $[\text{Cu}^{\text{II}}(\mathbf{11})\text{–}(\text{Cl})]^+$ and $[\text{Ni}^{\text{III}}(\mathbf{12})]^{3+}$ ions. The probability that this process occurs increases with the concentration of the reacting species, in the present case 10^{-3} M, which is the concentration typically used in electrochemical investigations. On the other hand, in Eq. (3), translocation may follow the occasional bending of the conjugate system $[\text{Cu}^{\text{II}}(\text{Cl})\text{–Ni}^{\text{III}}]^{4+}$, which makes the Cl^- bound to Cu^{II} intramolecularly collide with the Ni^{III} centre. The occurrence of such a process is very probable, as the local concentration of Cl^- is especially high. In fact, the Cu^{II} bound anion can be considered to move within a sphere, whose centre is Ni^{III} and whose radius is given by the $\text{Cu}^{\text{II}}\text{–Ni}^{\text{III}}$ distance (7.5 Å, as calculated through molecular modelling). The volume of the sphere is 1766 Å^3, to which a 0.94 M local concentration of Cl^- corresponds. In conclusion, we cannot exhibit direct evidence that the process illustrated by Eq. (3) is indisputably intramolecular. However, the very large energy advantage of Eq. (3) with respect to the intermolecular transfer of Eq. (4) strongly suggests that a different mechanism rules the anion translocation: this mechanism can only be intramolecular.

Which other anions can be translocated within the $[\text{Cu}^{\text{II}}\text{Ni}^{\text{II}}]^{4+}$ system? The choice is quite limited. The anion has to be a good ligand for Cu^{II}, but it also has to be resistant to oxidation, the two features being often in conflict. For instance NCO^-, NCS^-, and Br^- are good ligands for the $[\text{Cu}^{\text{II}}(\mathbf{11})]^{2+}$ fragment, but are oxidised at a platinum electrode at a potential too close to that of the $\text{Ni}^{\text{II}}/\text{Ni}^{\text{III}}$ couple, which prevents exhaustive electrolysis. HSO_4^- and NO_3^- are not oxidised, but are rather poor donors for $[\text{Cu}^{\text{II}}(\mathbf{11})]^{2+}$, $\log K < 2$. That means that in a 10^{-3} M solution, less than 40% of the anion is bound to the Cu^{II} centre, a situation which would strongly reduce the intramolecular nature of the anion translocation.

Also, the choice of the M_1–M_2 pair is critical. Given the ditopic polyamine receptor **13**, we cannot see any other working pair than Cu^{II} (M_1) and Ni^{II} (M_2^{n+}). Notice that even the simple inversion of the two metals ($M_1 = Ni^{II}$, $M_2^{n+} = Cu^{II}$) does not provide the right conditions for anion translocation. In fact, it is true that when encircled by the cyclam ring Cu^{II} can be oxidised to Cu^{III} (even if at a distinctly higher potential than Ni^{II}), but the Cu^{III} ion, d^8 low-spin, wants to be square-planar and does not bind anions at all, thus failing the main requirement for anion translocation: $M_2^{(n+1)+}$ must exhibit the highest affinity towards the X anion. Further M_1–M_2 pairs of transition metals can be sought, to promote the redox driven anion translocation process. However, they would require the design of their proper ditopic receptor.

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