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Mechanical Switches of Fluorescence

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Abstract

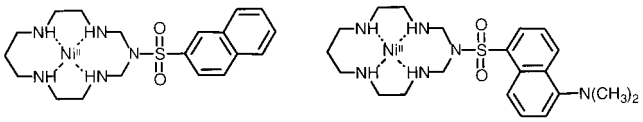
Fluorescence switches are molecular systems containing a light-emitting fragment whose activity can be quenched/revived reversibly, at will, through an external parameter, i.e., a change of pH or the variation of the redox potential. Fluorescence switches can be static (the emission of the fluorophore is switched ON/OFF by a bistable covalently linked control unit) or dynamic (the change in fluorescence is accompanied by an oriented molecular motion). Of the latter class of switches, we will consider the cases (i) of a metal scorpionate and (ii) of systems in which a metal is reversibly translocated between two nonequivalent compartments of a ditopic ligand.

Introduction

The term "switch" is one of the words of the everyday language most used in a chemical context [1]. It refers to a phenomenon in which, following a chemical or physical input, the property of a given substance varies substantially. The world of supramolecular chemistry is populated by a variety of switches and switching properties [2]. We have developed during the last years a defined interest towards molecules which, following a given input, quench/revive the light emission of a built-in fluorescent fragment. Such *switches of fluorescence* can be conceived and designed in a number of ways and may be subject to different classification. For instance, fluorescence switches can be divided into *dynamic* or *static*, depending on whether or not light-emission switching is accompanied by an intramolecular motion. Alternatively, fluorescence switches can be classified according to the input that promotes the phenomenon: thus, there exist pH-switches (quenching-revival of the emission is induced by addition of acid or base) and redox switches (fluorescence switching follows the addition of an oxidising or reducing agent). In the following we will illustrate examples of pH- and redox-switches: the redox switches are static, whereas pH-switches are dynamic.

Redox switches of fluorescence

A redox switch of fluorescence should be constituted of two subunits covalently connected through a spacer [3]. One subunit, Fl, is the fluorescent fragment, the other, C, the control unit, is a redox active moiety, whose oxidised and reduced states, C_{ox} and C_{red}, exhibit a comparable stability and are connected by a fast and reversible one-electron change.



1 **2**

Formula 1.

Figure 1 illustrates a switching situation in which the oxidised control unit, C_{ox}, quenches the emission of the proximate fluorophore through a given mechanism. On the other hand, the reduced form, C_{red}, leaves fluorescence unperturbed: thus, on oxidation, the fluorescence is quenched and, on reduction, the fluorescence is fully restored. Thus, one can switch fluorescence ON/OFF at will, by operating the C_{ox}/C_{red} couple, either chemically (through the consecutive addition of an oxidising agent and of a reducing agent) or electrochemically (by setting at the appropriate value the potential of the working macro-electrode in an experiment of controlled potential electrolysis). That represented in Figure 1 is only one of two switching situations: in the other, it is the reduced control unit, C_{red}, that quenches the fluorophore, whereas the oxidised form, C_{ox}, keeps emission of Fl* intact. Examples of redox switches of fluorescence are illustrated by molecules **1** and **2**.

Each molecule contains a classical fluorophore (either naphthalene, **1**, which emits in the UV region, or dansyl, **2**, which emits in the visible). The fluorophore is connected through a sulphonaza bridge to a cyclam-like macrocycle, which incorporate a Ni^{II} ion. The macrocyclic complex is the redox active unit and controls the emission of the nearby fluorophore. Ni^{II}, when encircled by a cyclam macrocycle,

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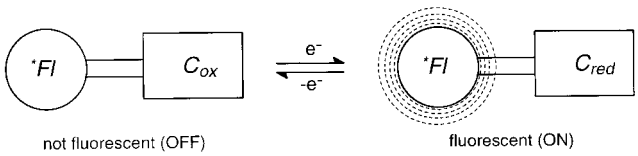


Figure 1. The multicomponent approach to the design of a *static* redox switch of fluorescence. Switch operativeness requires that the control unit C in its oxidised form, C_{ox}, quenches the nearby photo-excited fluorophore Fl^* and the reduced form C_{red} does not (OFF/ON switch). The other favourable ON/OFF situation can be obtained when C_{red} quenches Fl^* and C_{ox} does not.

can be easily oxidised to the otherwise elusive Ni^{III} state: the potential associated with the Ni^{III}/Ni^{II} couple is moderately positive and the two oxidation states have a comparable stability in solution. It happens that in an MeCN solution, when the metal centre is in the divalent state, both molecules **1** and **2** emit light through their fluorophore: Ni^{II} does not interfere at all with the radiative activity of the fluorescent fragment. But, if the metal centre is oxidised to Ni^{III} through a controlled potential electrolysis experiment, the fluorescent emission is fully quenched for both systems **1** and **2**. However, if the potential is set to an appropriately less positive value, reduction to Ni^{II} takes place and fluorescence is fully restored. Indeed, we are in the presence of a switch, in some way similar to the light switches of everyday life. We can turn ON/OFF light emission operating on the nickel macrocyclic complex (the real switch), in particular oxidising/reducing the metal centre. In the analogy, the fluorophore represents the bulb, and we can choose either an UV emitting bulb (naphthalene, in **1**) or a bulb emitting in the visible (the dansyl subunit, in **2**).

Ni^{III} quenches the excited fluorophore Fl^* through an electron transfer (eT) mechanism. The occurrence of the process can be accounted for on a thermodynamic basis, as the free energy change associated with the eT process: $Ni^{III} + Fl^* \leftrightarrows Ni^{II} + Fl^+$, is distinctly negative: $\Delta G^\circ_{eT} = -2.27$ eV for **1**, and $\Delta G^\circ_{eT} = -1.93$ eV for **2**. On the other hand, the $Ni^{II} + Fl^* \leftrightarrows Ni^{III} + Fl^-$ process is thermodynamically disfavored, the value of ΔG°_{eT} being positive for both **1** and **2**. Figure 2 pictorially illustrates the mechanism of the fluorescence switching process in the case of system **2**.

Other molecular switches of similar type have been developed in this laboratory during the last year: they are based on the two following couples: Ni^{III}/Ni^{II} and Cu^{II}/Cu^{I} [4]. In all cases, it is the oxidised form (Ni^{III} and Cu^{II}) of the control unit that quenches the fluorescence of the proximate light-emitting fragment, whereas the reduced form (Ni^{II} and Cu^{I}) does not interfere with the light emission. Thus, the switches can be defined as of the OFF/ON type. Recently, an ON/OFF switch has been synthesised in our laboratory: it is based on the formal couple Ni^{II}/Ni^{I}, and it is the reduced form that quenches fluorescence, whereas the oxidised one does not [5]. It has to be mentioned that the reduced macrocycic complex, rather than a complex of authentic Ni^{I}, has to be rather considered a complex of Ni^{II} with an anion radical ligand (i.e., on reduction, the electron goes on a π orbital of the unsaturated portion of the macrocycle).

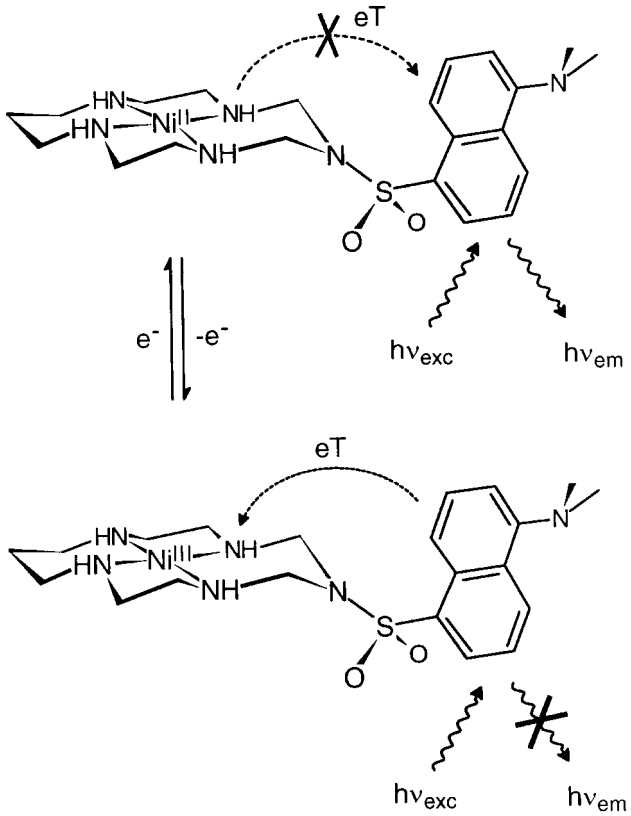
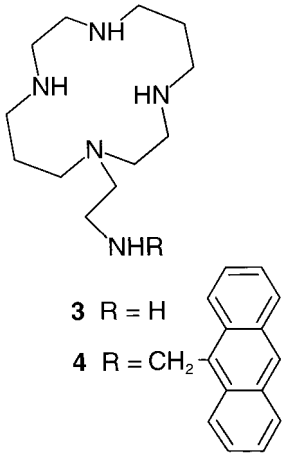


Figure 2. Switching activity of the $[Ni^{III,II}(\mathbf{3})]^{3+,2+}$ system. The Ni^{III} centre promotes a fluorophore-to-metal electron transfer and quenches dansyl fluorescence. On the other hand, the Ni^{II}-to-dansyl electron transfer process is thermodynamically disfavoured. Thus, the Ni^{III}-to-Ni^{II} reduction restores fluorescence.

pH-switches of fluorescence: a nickel(II) scorpionate

Appending a flexible coordinating side-chain to a rigid tetraaza macrocycle generates some interesting properties [6]. For instance, molecule **3**, aminoethylcyclam, can incorporate a metal ion (e.g., Ni^{II}) within the tetramine ring [7]. The ring is that of cyclam and the metal complex which forms profits from the properties of metal cyclam complexes: *in primis*, the extreme inertness and the resistence to the demetallation, even in a strongly acidic solution. On the other hand, the aminoethyl side chain can coordinate the metal centre from the top, giving rise to a five-coordinate species or to a six-coordinate one: in the latter case, a solvent molecule must occupy the sixth coordination position in the octahedral stereochemistry. In contrast to the four Ni^{II}-macrocyle bonds, which are inert, the Ni^{II} interaction with the amine group of the side is labile, to put itself far away from the metal. Thus, on addition of acid the amine group is protonated and, as an ammonium ion, leaves the coordination site. On the other hand, on addition of base, the ammonium deprotonates and goes to coordinate again the metal: the process of attack/detachment of the side chain can be repeated indefinitely on consecutive and appropriate variation of the pH. The similarity of the side chain to a tail biting from the top an already chelated individual accounts for the trivial name of *scorpionand*.



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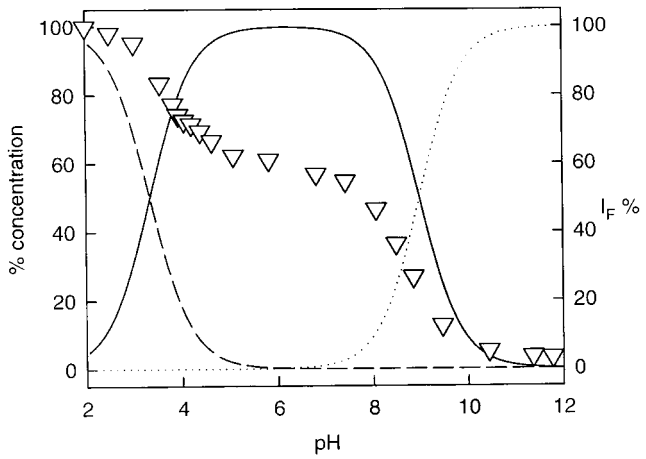


Figure 3. Distribution curves of the three Ni^{II} complexes of system **4** (L) in a 4 : 1 MeCN/H_2O solution, v/v (left vertical axis: dashed line: $[Ni^{II}(LH)]^{3+}$, square-planar complex; solid line: $[Ni^{II}(L)(H_2O)]^{2+}$, octahedral complex; dotted line: $[Ni^{II}(L)(OH)]^{+}$ octahedral complex). pH dependence of fluorescence intensity, I_F, of the same solution (right vertical axis, triangles down).

Interesting effects are observed with the complex of **3** with Ni^{II}. In an aqueous solution, when the side chain is coordinated (pH > 3), the complex is octahedral (with a water molecule occupying the second axial position), is high-spin and has a pale blue-violet colour. If the pH is brought below 3, the amine group of the side chain is protonated and goes far away from the metal centre to minimize electrostatic repulsions. The complex has now a square stereochemistry, is low-spin and has a yellow colour. Thus the pH-controlled process of attack-detachment of the side chain can be followed through a neat change of colour, from blue to yellow and *vice versa*.

We were interested to investigate the possible effects of the above described pH- controlled molecular movement on fluorescence and we linked an anthracenyl group to the side chain of **3** to give **4**, a fluorescent scorpionand [8]. Then, we studied the behaviour in solution of the corresponding Ni^{II} complex over the 2–12 pH range. In this pH interval, three species are present in solution and their abundance is shown in the distribution diagram in Figure 3. The dashed line refers to a $[Ni^{II}(LH)]^{3+}$ species, in which the amine group

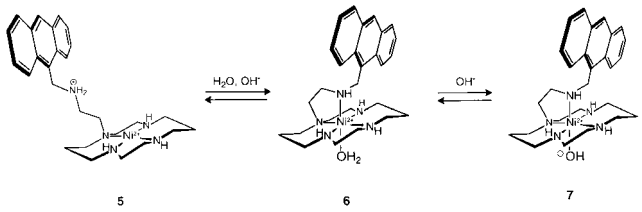
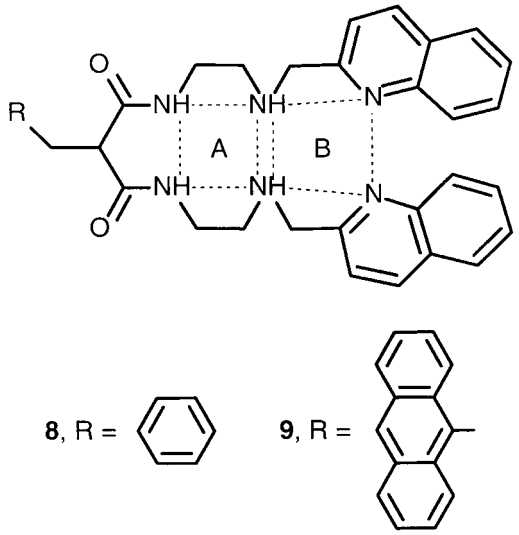


Figure 4. pH controlled movement of the fluorescent side-chain in the Ni^{II} scorpionate complex of ligand **4**. Species **5**, low-spin, square-planar, displays full fluorescence. In complex **6**, high-spin, octahedral, fluorescence intensity is reduced to 60%, due to the occurrence of an electronic energy transfer process involving excited anthracene (An*) and Ni^{II}. In complex **7**, a further contribution operates (Ni^{II}-to-An* electron transfer) and fluorescence is almost completely quenched (less than 2%). Only the first step is characterised by a controlled molecular motion (oscillation of the side-chain).

of the side chain is protonated; the solid line corresponds to the complex in which the amine group is coordinated and a water molecule completes the octahedral coordination, $[Ni^{II}(L)(H_2O)]^{2+}$; the dotted line indicates a species still octahedral, but in which the coordinated water molecule is deprotonated, $[Ni^{II}(L)(OH)]^{+}$.

Then, we measured the fluorescent intensity of the solution along the same pH interval: the values of the relative intensity have been superimposed on the distribution diagram in Figure 3 as triangles down. It is seen that the fluorescence intensity displays a sort of three plateau profile. Each plateau corresponds to one of the three species at equilibrium. The highest emission corresponds to the $[Ni^{II}(LH)]^{3+}$ complex, whose structure is sketched in Figure 4, as **5**. Due to the electrostatic repulsions between the Ni^{II} cation and the ammonium group of the side chain, the anthracene fragment stays far away from the metal centre, whose perturbative effects are minimised. On increasing pH, the $[Ni^{II}(L)(H_2O)]^{2+}$ complex forms, **6**, and the fluorescence intensity decreases to 60% of its original value. The decrease has to be ascribed to the fact that side chain coordination has brought the anthracene fragment much closer to the high-spin Ni^{II} ion, which is now able to quench (partially) fluorescence through an electronic energy transfer mechanism. Complete quenching is observed with the formation of the $[Ni^{II}(L)(OH)]^{+}$ complex, **7**. In this case, a second mechanism contributes to quenching: electron transfer. This is due to the fact that reduction of the electrical charge of the complex (from +2 to +1) makes possible oxidation of Ni^{II} to Ni^{III} and the occurrence of an electron transfer process to the nearby excited fluorophore. Thus, it is the contribution of both mechanisms, electron transfer and energy transfer, that fully quenches fluorescence in complex **7**.

In conclusion, the Ni^{II}-**4** system operates as a three-state switch (HIGH/LOW/OFF): the first operation, which causes 60% quenching, is related to a controlled molecular movement and in this sense the switch is dynamic [9]. In contrast the second operation, which leads to complete quenching, is not related to any movement and is characteristic of a static switch.



Formula 3.

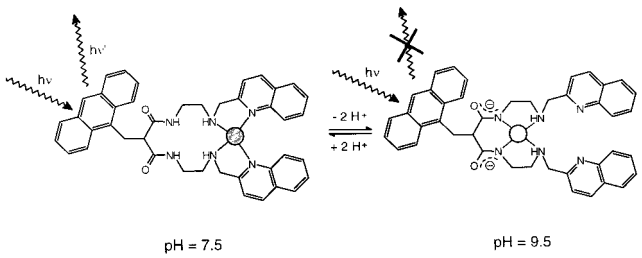


Figure 5. pH driven translocation of the Ni^{II} ion within the ditopic system **9**, which is signalled by quenching/revival of the emission of a fluorescent fragment (the anthracene subunit). When Ni^{II} resides in compartment A^{2-}, the emission is fully quenched, due to the occurrence of a metal-to-fluorophore electron transfer process (eT); when Ni^{II} moves to compartment B, the eT mechanism vanishes and fluorescence is restored.

pH-switches of fluorescence: nickel(II) translocation

In the previous section we have considered an oriented molecular motion (the oscillation of the aminoethyl side-chain of the scorpionand between two fixed positions), which was signalled by a fluorescence change. There exist other systems providing controlled motions, which can generate a fluorescent signal.

A recently reported example is concerned with metal ion translocation [10]. Given a ditopic receptor containing two coordinatively unequivalent compartments, a metal ion can be reversibly translocated from one compartment to the other, following an external input, either a change of pH or the variation of the redox potential. We will consider the translocation promoted by a change of pH. A suitable system should contain two distinct compartments: (i) a compartment B, of moderate coordinating tendencies, and (ii) a compartment AH_n, which displays also the characteristics of a Brønsted acid , according to the equilibrium: $AH_n + nH_2O \leftrightarrows A^{n-} + nH_3O^+$. Then, it should happen that the coordinating tendencies towards the metal M^{n+} decrease along the sequence (1):

$$A^{n-} \gg B \gg AH_n. \qquad (1)$$

Under these circumstances, at lower pH values, when the acid-sensitive compartment is in its protonated form AH_n, the metal prefers staying in compartment B. However, if the pH is raised to a value that allows deprotonation of AH_n, the metal translocates to A^{n-}. On decreasing pH, A^{n-} protonates again, and M^{n+} moves back to B. Thus, it is possible to translocate the metal ion back and forth from one compartment to the other, simply varying the pH in a given interval , often through the addition of a minimum amount of standard acid and base.

Ditopic receptors satisfying the above mentioned requirements are represented by molecules **8** and **9**. In both systems, compartment B consists of two secondary amine nitrogen atoms and two quinoline nitrogen atoms (hybridised sp^2). Compartment AH_2 shares the two secondary amine groups with B and is constituted also by two secondary amide groups. The coordinating tendencies of the amide group are very poor or nil. However, in the presence of divalent metal ions late in the 3d series (e.g., Ni^{II} and Cu^{II}), at a relatively high pH value, the amide group deprotonates and strongly coordinates the metal. Consequently, for both systems **8** and **9** the affinity requirement expressed by Equation (1) is fulfilled ($A^{2-} > B > AH_2$) and a pH-driven translocation can take place reversibly [11].

Of special interest is the case of the Ni^{II} ion. At pH = 7.5 Ni^{II} stays in compartment B: since the ligand field exerted by B is moderate, Ni^{II} is in the *high-spin* state, exhibits an octahedral stereochemistry (two water molecules completing the coordination polyhedron) and displays a pale blue-violet colour. On raising the pH to $\geq$9.5, the solution takes on a yellow colour: the amide groups are now deprotonated and Ni^{II} has now translocated to the A^{2-} compartment. Due to the presence of the two deprotonated amide groups, the compartment A^{2-} exerts especially strong in-plane interactions, which stabilise the *low-spin* state of Ni^{II}, impart square-planar stereochemistry and are responsible for the yellow colour. On changing consecutively the pH from 7.5 to 9.5 and *vice versa* (through the sequential addition of fractions of a drop of standard base and acid), it is possible to translocate the Ni^{II} ion almost indefinitely, without any degradation, between the two compartments.

System **9** is especially interesting in a photophysical context, because it contains a built-in fluorophore, an anthracene fragment linked to the carbon framework of compartment AH_2.

The fluorescence of the anthracene subunit strictly depends upon the position of the Ni^{II} ion, whether in A^{2-} or in B. In particular, when Ni^{II} stays in the distant compartment B, the fluorophore fully displays its characteristic emission, but when it moves to the compartment AH_2, fluorescence is completely quenched. The dynamics of the process is pictorially illustrated in Figure 5. Thus, at a first glance, this behaviour could appear to derive from a mere distance effect: when close, the transition metal interferes easily with the excited fluorophore, but when distant, it cannot. Whereas a contribution from a distance cannot be completely excluded, the origin of the phenomenon is essentially different and refers to the mechanism of quenching: electron transfer.

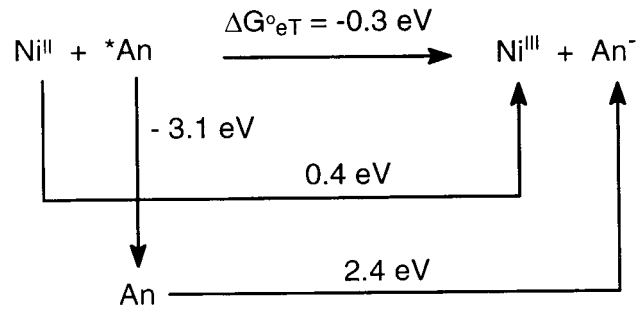


Figure 6. Thermodynamic cycle for the calculation of the free energy change associated with the electron transfer from Ni^{II} in the compartment A^{2-} of the ditopic receptor **9** to the nearby excited anthracene fragment (see Equation (2) in the text). The ΔG°_{eT} value, which results from the appropriate combination of photophysical and electrochemical quantities, is distinctly negative (−0.3 eV) and the process is spontaneous.

In fact, when in compartment A^{2-}, the Ni^{II} centre profits from a strong in-plane ligand field that raises the energy of the orbital from which the electron is extracted, thus favouring the oxidation to Ni^{III}. As a consequence, the Ni^{II} centre becomes reducing enough to release one electron to the photoexcited anthracene fragment according to Equation (2):

$$Ni^{II} + An^{*} \rightarrow Ni^{III} + An^{-}. \qquad (2)$$

Essentially due to the low value of the Ni^{III}/Ni^{II} redox potential, the free energy change associated with Equation (2), ΔG°_{eT}, which can be calculated by the thermodynamic cycle illustrated in Figure 6, is distinctly negative and makes the process (2) very favoured from a thermodynamic point of view.

When in B, the Ni^{II} centre profits from rather moderate coordinative interactions and there is no way to accede to the Ni^{III} state, a circumstance which prevents the occurrence of an electron transfer process to the excited anthracene fragment. Thus, rather than by distance, the switching process illustrated in Figure 5 is ultimately regulated by the coordinative tendencies of the two compartments of **9**.

Other interesting aspects are provided by the rate at which the translocation process takes places, depending upon (i) the direction and (ii) the system investigated, whether **8** or **9**. For system **8**, the translocation rate was measured by stopped- flow spectrophotometric experiments, by monitoring the absorption band of the yellow low-spin complex (which increases in the B to AH_2 direction, and decreases when the metal follows the opposite pathway). Rates are significantly different: in particular, the rate of the B-to-AH_2 trip is about one order of magnitude faster that the rate of the A^{2-}-to-B trip: in particular, corresponding lifetimes are $\tau = 0.25 \pm 0.01$ s and $\tau = 2.2 \pm 0.1$ s, respectively. This can be accounted for considering that, whatever the detailed mechanism of the translocation, the first step must be probably *dissociative*. On the other hand, it is well known that a high-spin d^8 cation, like Ni^{II} in compartment B, is much more labile than a low-spin d^8 cation, like Ni^{II} in compartment A^{2-}.

The behaviour of system **9** is roughly the same, in the sense that the B-to-AH_2 trip is much faster than the A^{2-}-to-B trip. However, the time employed by the metal ion for translocating, in both directions, is much higher than observed for system **8**: τ = 12 ± 1 s and τ = 66 ± 12 s, respectively. Again, to explain the paradoxical behaviour, one must refer to the mechanism of the process: in particular, translocation cannot be imagined as the result of the independent long jump of the Ni^{II} cation, high- or low-spin, from one compartment to the other. More plausibly, one should think of ligands **8** and **9** as "books", whose spine is the ideal line joining the two secondary amine groups shared by the two compartments [12]. Each compartment lays on one page and pages oscillate, bringing the metal hosted in a given compartment close enough to the other receiving compartment. The situation in which the 'pages' are at the closest distance and the metal leaves one compartment to reach the other one represents the transition state. The facility to reach the transition state is sterically controlled. In this connection, it is evident that the process is especially difficult (and the energy of the transition state particularly high) in system **9**, which contains the bulky anthracenyl substituent and makes the 'facing pages' mechanism especially demanding. This steric effect may have promising consequences: in particular, one can expect that in the presence of light substituents (for instance less bulky than the benzyl group of **8**) the process of translocation may become particularly fast, a feature of interest in the construction of *molecular machines*. Indeed, systems translocating metal ions, such as those described in this Section, convert (chemical) energy into mechanical work, at will and in a repeatable way: thus, they can be considered molecular machines of a new generation, with respect to rotaxanes and catenanes, as introduced by Stoddart and Balzani [13] and Sauvage [14].

Going back to switches, system **9** represents a novel switch of fluorescence, whose operation is completely mechanical (the displacement of a metal centre between two fixed positions). In this sense, the analogy with the light switches of everyday life seems closer and more convincing.

Acknowledgements

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