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Water Soluble Molecular Switches of Fluorescence Based on the Ni^{III}/Ni^{II} Redox Change

Luigi Fabbrizzi,*,† Maurizio Licchelli,† Stefano Mascheroni,† Antonio Poggi,† Donatella Sacchi,† and Michele Zema‡,§

Dipartimento di Chimica Generale, Università di Pavia, via Taramelli 12, I-27100 Pavia, Italy, and Centro Grandi Strumenti, Università di Pavia, via A. Bassi 21, I-27100 Pavia, Italy

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The water soluble Ni^{II} complexes of the cyclam derivatives with 1,3-benzodioxole and 1,2,3-trimethoxybenzene display the fluorescent emission typical of the covalently linked fluorophores, which results from a charge transfer excited state. On oxidation to Ni^{III}, the fluorescence is completely quenched due to the occurrence of an electron transfer (eT) process from the excited fluorogenic fragment Fl* to the oxidized metal. Thus, fluorescence can be switched off/on at will, for several cycles, by consecutively oxidizing and reducing the metal center, in controlled potential electrolysis experiments both in acetonitrile and in aqueous 0.1 M $HClO_4$. Occurrence of an eT process from Fl* to Ni^{III} ultimately depends upon the easy oxidation of Fl to Fl^+, whereas failure of the occurrence of an eT process from Ni^{II} to Fl* has to be ascribed to the particular resistance of Fl fragments to the reduction.

Introduction

Fluorescence is an interesting property displayed by a limited number of molecules (fluorophores), which can be conveniently used to generate signals at the molecular level.[1] Signaling requires that an operator be able to modulate fluorescence from the outside by means of a given input: chemical (the variation of the concentration of a species in the solution, e.g., H^+),[2] electrochemical (the variation of the potential of an electrode),[3] or thermal (the change of temperature).[4] The action of the operator needs to be mediated by a molecular subunit, which translates the external input into a language intelligible to the fluorophore. In the case of an electrochemical input, this subunit must be a redox active system, which, according to the value of the potential of the working electrode, exists in either a reduced form (RED) or an oxidized form (OX).

It may happen that the subunit, when in a given state, e.g., OX, quenches the fluorophore, through either an electron transfer (eT) or an electronic energy transfer (ET) mechanism, but, when in the RED state, leaves fluorescence unperturbed. Under these circumstances, appropriate varia-

* Author to whom correspondence should be addressed. E-mail: fabbrizz@unipv.it.

† Dipartimento di Chimica Generale, Università di Pavia.

‡ Centro Grandi Strumenti, Università di Pavia.

§ Present affiliation: Dipartimento di Scienze della Terra, Università di Pavia, via Ferrata 1, I-27100 Pavia, Italy.

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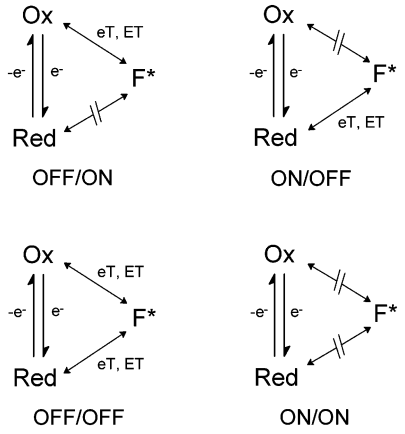
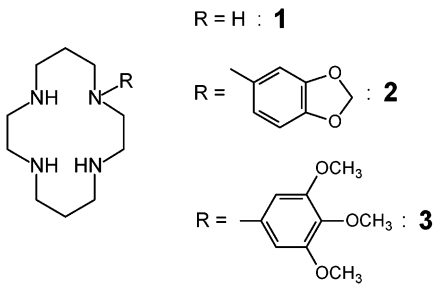


Figure 1. Influence of the oxidation state of the redox active subunit on the emission properties of the covalently linked fluorophore: four different situations are possible.

tions of the potential switch the state of the redox active subunit from RED to OX in a reversible fashion and, accordingly, switch fluorescence ON/OFF, in principle indefinitely. If the fluorophore and the redox active subunit are two distinct particles, fluorescence control results from a bimolecular collision, an event requiring relatively high concentrations of the colliding particles. More conveniently, the fluorophore and the redox active fragment can be covalently linked together by a short spacer: in this case, the control subunit can selectively communicate with the fluorescent moiety by means of an *intramolecular* eT or ET process, either through bond or through space. This can give rise to an efficient molecular switch of fluorescence, which operates through an electrochemical input. Switching situations are achieved when (i) the OX state quenches the fluorophore and the RED state does not (OFF/ON switch); (ii) it is the RED state that quenches the emission of the proximate fluorophore, and the OX form does not (ON/OFF switch). Unfavorable situations, for switching purposes, are those in which both states quench fluorescence (OFF/OFF) or both keep fluorescence unperturbed (ON/ON).[1e,5] The four situations are illustrated by the triangular schemes in Figure 1.



The redox active subunit must undergo a fast and reversible change, possibly involving one-electron stoichiometry. In this sense, transition metal complexes are ideal candidates to play the role of control subunits, as (i) they present pairs of consecutive oxidation states linked by a fast and reversible change, and (ii) the relative stability of OX and RED can be tuned by modifying the donating tendencies of the ligand(s). We have previously shown that the Cu^{II}/Cu^{I} couple,[6] within a macrocyclic environment containing thioethereal sulfur atoms, and the Ni^{III}/Ni^{II} couple,[7] encircled by a tetramine macrocycle, can selectively control the emission of a polyaromatic fluorophore (naphthalene, anthracene) covalently linked to the ligand framework, giving rise to redox switches of fluorescence of the OFF/ON type. Due to the lipophilic nature of the fluorophore, studies could not be carried out in water, but they could be carried out in nonaqueous solvents like MeCN and alcohols. We report here two new redox switches of fluorescence based on the Ni^{II} complexes of the macrocyclic ligands **2** and **3**, which operate through the Ni^{III}/Ni^{II} couple. The hosting tetramine macrocycle, which possesses the 14-membered framework of cyclam, **1**, is linked through a $-CH_2-$ group to a fluorophore of moderately liphophilic features, which allows the corresponding Ni^{II} and Ni^{III} derivatives to be soluble in water. Water solubility is essential if one intends to utilize fluorescence switches in biologic fluids, in particular for estimating the redox potential of a certain environment. In this connection, it is to be noted that the potential associated with the Ni^{III}/Ni^{II} couple within systems **2** and **3** ranges around 1 V vs SCE.

Experimental Section

General Remarks. Unless otherwise stated, commercially available reagent grade chemicals were used as purchased, without further purification. 1,4,8,11-Tetraazacyclotetradecane (cyclam, **1**) was prepared following the literature method.[8]

Spectrophotometric or fluorimetric grade solvents were used for spectroscopic measurements.

UV−vis spectra were recorded on a Hewlett-Packard 8452A diode array spectrophotometer; emission spectra were taken on a Perkin-Elmer LS-50B luminescence spectrometer.

Corrections for the inner filter effect[9] and in particular for the reabsorption of the emitted light at 315−340 nm by the nickel(III) complexes were evaluated by literature methods.[9,10] In all cases the corrections were lower than 5% of the observed fluorescence intensity (I_F) values.

The relative quantum yields of fluorescence were obtained through the optically diluted method[11] using naphthalene ($\Phi = 0.21$ in EtOH) as reference.[12]

Emission spectra at 77 K were measured in butyronitrile (10^{-5} M), by using quartz sample tubes and the same luminescence spectrometer, equipped with a Perkin-Elmer low-temperature luminescence accessory.

NMR spectra were recorded on a Bruker AMX400 spectrometer.

Mass spectra were obtained using an LCQ DECA ion trap mass spectrometer, equipped with an electrospray ionization (ESI) ion source and controlled by Xcalibur software 1.1 (Thermo-Finnigan).

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Redox potential values were determined by voltammetric techniques, on a Princeton Applied Research model 273 potentiostat−galvanostat. Investigations on MeCN solutions, made 0.1 M in Bu_4NClO_4, were carried out in a conventional three-electrode cell using a platinum microsphere as a working electrode, and a silver wire as a pseudo-reference electrode which was calibrated vs the Fc^+/Fc couple used as an internal standard.[13] Investigations in aqueous solutions (0.1 M $HClO_4$) were performed in the same cell using a glassy carbon working electrode and an SCE as reference.

CPC experiments were carried out on solutions of the nickel(II) complexes ($1-2 \times 10^{-5}$ M) in MeCN (made 0.1 M in Bu_4NClO_4) or in aqueous $HClO_4$ (0.1 M), with a platinum gauze as a working electrode. The counter electrode compartment was separated from the working compartment by a U-shaped bridge filled with the same electrolyte solutions. The reference electrode was a platinum wire dipped in the working cell (its potential was calibrated through CV measurements prior to CPC) for the experiments in MeCN or an SCE for the experiments in aqueous solutions.

SAFETY NOTE! Perchlorate salts of metal complexes are potentially explosive and should be handled with care. In particular, they should never be heated as solids.[14]

1,4,8-Tris(*tert*-butoxycarbonyl)-1,4,8,11-tetraazacyclotetradecane (triBOCcyclam), 4. Cyclam (5 mmol, 1.0 g) was dissolved in dried dichloromethane (200 mL) and triethylamine was added (25 mmol) under a dinitrogen atmosphere. The reaction mixture was stirred, and a solution of *tert*-butoxy-dicarbonate (9 mmol) in dried dichloromethane (60 mL) was added dropwise. After the reaction mixture was cooled to −15 °C, another portion of *tert*-butoxy-dicarbonate (6 mmol) was added, and the mixture was stirred at room temperature overnight. The solution was treated with Na_2CO_3 (0.5 N), and the organic solution was dried over Na_2SO_4. The solvent and the excess of triethylamine were removed in vacuo, and the residue was purified by liquid chromatography (SiO_2, 9:1 ethyl acetate/methanol, R_f 0.5). Yield: 70.5%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.10 (m, 12H, CH_2), 2.70 (t, 2H, CH_2), 2.55 (t, 2H, CH_2), 1.86 (q, 2H, CH_2), 1.63 (q, 2H, CH_2), 1.38 (s, 27H, $C(CH_3)_3$). MS (ESI) *m*/*z*: 501.2 $[M + H]^+$.

5-Bromomethyl-1,3-benzodioxole (Piperonyl Bromide). A solution of CBr_4 (1.66 g, 5 mmol) and Ph_3P (1.31 g, 5 mmol) in diethyl ether (30 mL) was added to a solution of benzo[1,3]dioxole-5-methanol (piperonyl alcohol, 0.76 g, 5 mmol) in diethyl ether (30 mL). The reaction mixture was stirred at room temperature for 3 h and filtered over a sintered glass funnel. The crude product obtained after removing the solvent was purified by liquid chromatography (SiO_2, 1:1 *n*-hexane/diethyl ether, R_f 0.7). Yield: 72.5%. Anal. Calcd for $C_8H_7BrO_2$: C, 44.68; H, 3.28. Found: C, 44.47; H, 3.21.

1-(1,3-Benzodioxol-5-ylmethyl)-4,8,11-tris(*tert*-butoxycarbonyl)-1,4,8,11-tetraazacyclotetradecane, 5. TriBOCcyclam (0.45 g, 0.9 mmol) was dissolved in toluene (30 mL) in a three-neck round-bottomed flask equipped with a reflux condenser, mechanical stirrer, and dropping funnel, under a dinitrogen atmosphere. Cs_2CO_3 (0.29 g, 0.9 mmol) was added, and the resulting mixture was heated to reflux with vigorous stirring, as a solution of piperonyl bromide (0.2 g, 0.9 mmol) in toluene (10 mL) was dropped through the funnel. Heating and stirring were continued for 12 h, and then the mixture was cooled to room temperature and filtered to remove cesium carbonate. Toluene was distilled off and the crude product purified by liquid chromatography (SiO_2, 95:5 AcOEt/MeOH, R_f 0.75). Yield: 61.3%. MS (ESI) *m*/*z*: 635.3 $[M + H]^+$.

1-(1,3-Benzodioxol-5-ylmethyl)-1,4,8,11-tetraazacyclotetradecane, 2. CF_3COOH (5 mL) was added to a solution of **5** (0.34 g, 0.54 mmol) in CH_2Cl_2 (10 mL), and the resulting mixture was magnetically stirred under a dinitrogen atmosphere for 24 h. The solvent was removed in vacuo, the oily residue was treated with acidic water (0.1 M HCl, 25 mL), and the resulting solution was extracted with diethyl ether (2 × 20 mL). The aqueous layer was made alkaline by addition of NaOH and extracted with CH_2Cl_2 (4 × 20 mL). The organic layer was desiccated over Na_2SO_4, and the product was obtained as a white solid after removal of the solvent. Yield: 95.8%. MS (ESI) *m*/*z*: 335.3 $[M + H]^+$.

1-(3,4,5-Trimethoxybenzyl)-4,8,11-tris(*tert*-butoxycarbonyl)-1,4,8,11-tetraazacyclotetradecane, 6. A solution of triBOCcyclam (0.5 g, 1 mmol) and 3,4,5-trimethoxybenzaldehyde (0.23 g, 1.2 mmol) in MeOH (25 mL) was acidified by addition of CH_3COOH (0.15 mL) and cooled to 0 °C under a dinitrogen atmosphere. $NaBH_3CN$ (0.063 g, 1 mmol) was slowly added with magnetic stirring, and then the solution was allowed to return to room temperature and stirred for 48 h. Solvent was removed at the rotary eveporator and the residue dissolved in aqueous 0.1 M Na_2CO_3 (50 mL). The resulting solution was extracted by CH_2Cl_2 (3 × 25 mL), and the organic layer was dried over Na_2SO_4. The dichloromethane solution was filtered, the filtrate was rotary evaporated to dryness, and the resulting crude product was purified by liquid chromatography (SiO_2, 1:1 *n*-hexane/AcOEt, R_f 0.2, R_f (unreacted aldehyde) 0.8). Yield: 90.5%. MS (ESI) *m*/*z*: 681.4 $[M + H]^+$.

1-(3,4,5-Trimethoxybenzyl)-1,4,8,11-tetraazacyclotetradecane, 3. The macrocyclic ligand **3** was prepared from compound **6**, by the procedure described for **2**. Yield: 96.4%. MS (ESI) *m*/*z*: 381.3 $[M + H]^+$.

[Ni(2)](ClO$_4$)$_2$. A solution of $Ni(ClO_4)_2 \cdot 6H_2O$ (58 mg, 0.17 mmol) in MeOH (3 mL) was slowly added to a solution of **2** (60 mg, 0.16 mmol) in MeOH (5 mL) with magnetic stirring. The resulting solution was refluxed for 2 h and then cooled to room temperature. A yellow-orange precipitate, which was recovered by filtration, was obtained by slow evaporation of the solvent. Yield: 78.6%. MS (ESI) *m*/*z*: 493.1 $[M - ClO_4]^+$, 393.1 $[M - ClO_4 - HClO_4]^+$.

[Ni(3)](ClO$_4$)$_2$. The complex of the trimethoxybenzyl derivative was prepared under the same experimental conditions from ligand **3**. Yield: 83.8%. MS (ESI) *m*/*z*: 539.1 $[M - ClO_4]^+$, 439.2 $[M - ClO_4 - HClO_4]^+$.

Crystallographic Studies. The crystal and molecular structure of the $[Ni^{II}(\mathbf{L3})](ClO_4)_2$ complex has been determined by X-ray diffraction methods. Unit cell parameters and intensity data were obtained on a Philips PW1100 four-circle diffractometer at room temperature using graphite-monochromatized Mo Kα radiation. Calculations were performed with the WinGX-97[15] software. Crystal data and the most relevant parameters used in the crystallographic study are reported in Table 1, whereas important bond lengths and angles are in Table 2. Cell dimensions were determined by least-squares fitting of 48 centered reflections monitored in the range $8.91° < \theta < 15.12°$. Corrections for Lp and empirical absorption were applied.[16] The structure was solved by SIR92.[17] The non-hydrogen atoms were refined anisotropically by full-matrix least-

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Table 1. Crystal and Refinement Data

formula	$NiN_4C_{20}H_{36}Cl_2O_{11}$
fw	638.14
cryst size (mm)	0.16 × 0.21 × 0.56
cryst syst	monoclinic
space group	$P2_1/n$
a (Å)	8.548(4)
b (Å)	21.255(9)
c (Å)	15.257(8)
β (deg)	95.001(8)
V (Å^3)	2762(2)
Z	4
D_{calc} (g cm^{-3})	1.535
T (K)	298(3)
μ (mm^{-1})	0.958
scan type	$\omega-2\theta$
θ range (deg)	2−30
abs correction meth	ψ-scan
index ranges	$-12 \le h \le 12$, $-29 \le k \le 29$, $0 \le l \le 21$
reflns measd/unique	16381/8018 ($R_{int} = 0.0708$)
refinement type	F^2
R1[a]	0.0619
R_{all}	0.1326
wR2	0.1538
GOF[b]	0.990
refined params	454
weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0720P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\text{shift/esd})_{max}$	0.001
max, min $\Delta\rho$ (e Å^{-3})	0.721, −0.556

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$ (calculated on 4380 reflections with $I > 2\sigma_I$). [b] $GOF = S = [\sum[w(F_o^2 - F_c^2)^2]/(n-p)]^{0.5}$, where n is the number of reflections and p is the total number of parameters refined.

Table 2. Selected Bond Distances (Å) and Angles (deg)

Ni1−N1	1.974(3)	Ni1−N3	1.938(3)
Ni1−N2	1.933(3)	Ni1−N4	1.933(3)
N1−Ni1−N2	87.4(1)	N1−Ni1−N3	178.0(1)
N1−Ni1−N4	91.2(1)	N2−Ni1−N3	94.6(1)
N2−Ni1−N4	176.1(1)	N3−Ni1−N4	86.8(1)

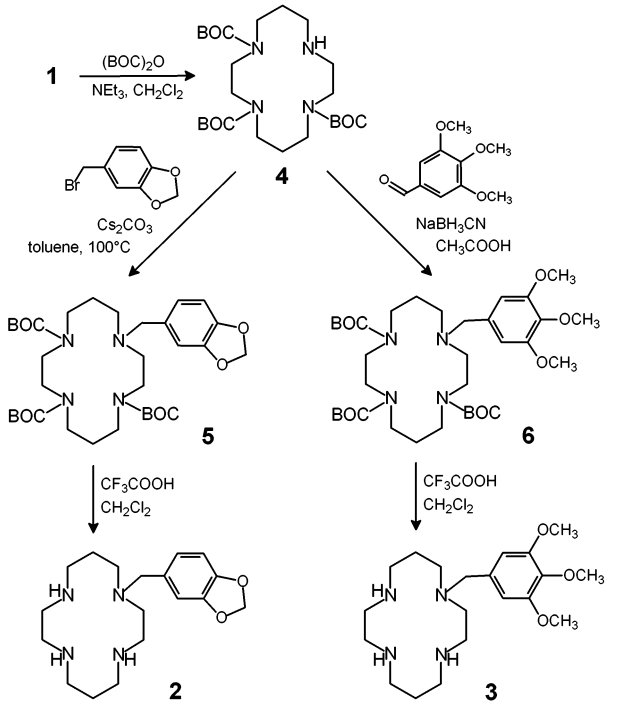
squares using SHELXL-97.[18] Hydrogen atoms were located in the difference Fourier maps and refined isotropically, except those bound to the methyl groups, which were inserted in the calculated positions and refined using a riding model and imposing an isotropic displacement factor proportional (×1.5) to that of their neighboring atom. Atomic scattering factors were taken from *International Tables for X-ray Crystallography*.[19] Diagrams of the molecular structure were produced by the ORTEP-3 program.[20]

Results and Discussion

Syntheses and Crystallographic Studies. Functionalized tetraaza macrocycles **2** and **3** were prepared according to the synthetic pathways reported in Scheme 1. The first step, which was common to both synthetic routes, consists of the protection with *tert*-butyloxycarbonyl (BOC) groups of three secondary amino groups of cyclam and was carried out according to a modified literature procedure.[21]

The fluorogenic subunits were introduced onto the macrocyclic framework by a nucleophic substitution on piperonyl

Scheme 1



bromide (intermediate **5**) or by a reductive amination with trimethoxybenzaldehyde (intermediate **6**)

The use of triBOCcyclam, **4**, allows one to address functionalization reactions toward monosubstituted products. Attempts to prepare tetraazamacrocycle **2** by direct reaction of unprotected cyclam (5-fold excess) with piperonyl bromide always afforded mixtures of polysubstituted products which could not be efficiently separated by common chromatographic methods.

Tris-BOC intermediates, **5** and **6**, were deprotected in trifluoroacetic acid by a standard procedure, affording the macrocyclic ligands **2** and **3** in almost quantitative yield.

Complexes were prepared by simply reacting each ligand with a slight excess of nickel(II) perchlorate in methanol and were isolated as yellow-orange microcrystalline products. Crystals of the $[Ni^{II}(\mathbf{3})](ClO_4)_2$ complex salt, suitable for X-ray investigations, were obtained by slow evaporation of an ethanolic solution. In the case of the $[Ni^{II}(\mathbf{2})](ClO_4)_2$, any attempt to grow X-ray quality crystals afforded yellow-orange needles, which, however, were not of satisfactory quality for crystallographic investigations.

The molecular structure of the complex is shown in Figure 2. The tetramine macrocycle is coplanarly coordinated, according to a square geometry. In fact, the metal center lies only 0.033 Å out of the N_4 mean plane, and the four nitrogen atoms are displaced with respect to the plane with distances ranging from 0.025 to 0.034 Å. The Ni^{II}−N distances, ranging over the 1.933−1.974 Å interval, are those expected for a nickel(II) ion in its low-spin state.[22] The two perchlorate ions are located along the axis perpendicular to the four-nitrogen plane, but the long Ni^{II}−O distances (3.037

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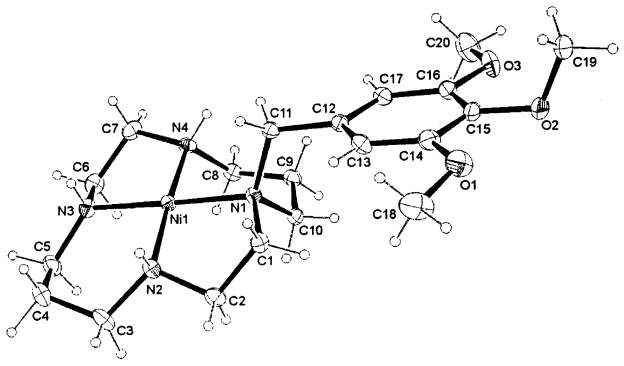

Figure 2. ORTEP view of the $[Ni^{II}(\mathbf{3})]^{2+}$ complex cation.

and 3.272 Å respectively for the two ions) exclude any serious interaction of ClO_4^- with the metal. In other words, the 3,4,5-trimethoxybenzyl substituent does not seem to exert any disturbing effect on coordination. In particular, the fluorogenic fragment points outward with respect to the macrocyclic ring: as a consequence of the presence of the $-CH_2-$ interfacing group, the N_4 macrocyclic ring and the aromatic ring of the fluorophore stay on almost parallel planes (angle between the planes: 15.9°).

Solution Properties of the Nickel(II) Complexes. The two-component systems **2** and **3** possess the framework of the symmetric 14-membered tetramine macrocycle cyclam, **1**. Among polyamine macrocycles of varying denticity and ring size, cyclam and its transition metal complexes exhibit unique properties, which derive from the ligand's ability to place its donor atoms in the positions desired by the metal centers (i.e., the corners of a square) and to establish especially strong coordinative interactions. In particular, (i) cyclam complexes are very resistant to the metal extrusion (as an example, $[Ni^{II}(cyclam)]^{2+}$, in spite of the high basicity of the uncoordinated tetramine, persists in 1 M $HClO_4$ with a half-life of 30 years),[23] and (ii) they can achieve unusually high oxidation states of the encircled metal (e.g., Ni^{III}, Cu^{III}, Ag^{II}, and Ag^{III}); this latter property is strictly related to the capability of cyclam to establish strong in-plane interactions, which raise the energy of the HOMO antibonding orbital, essentially metallic in character, from which the electron is abstracted on oxidation. For istance, the potential of the $[Ni^{III}(cyclam)]^{3+}/[Ni^{II}(cyclam)]^{2+}$ couple in 1 M HCl is 0.71 V vs NHE,[24] something like the familiar $[Fe^{III}(H_2O)_6]^{3+}/[Fe^{II}(H_2O)_6]^{2+}$ couple potential, indicating that the Ni^{II} and the Ni^{III} complex have a comparable stability and are both fairly stable in water.

In systems **2** and **3**, robust fluorophores, 1,3-benzodioxole and 1,2,3-trimethoxybenzene, were linked to one nitrogen atom of the cyclam skeleton, through a methylene group. The two fluorogenic fragments have in common a phenyl ring containing electron donor substituent(s), absorb light in the 200−300 nm interval, and emit light in the 300−350 nm interval, with a relatively high quantum yield (1,2-benzodioxole, $\Phi = 0.31$; 1,2,3-trimethoxybenzene, 0.076). Absorption and emission data in MeCN for $[Ni^{II}(\mathbf{2})]^{2+}$, $[Ni^{II}(\mathbf{3})]^{2+}$, and the plain fluorophores, used as reference compounds, are summarized in Table 3.

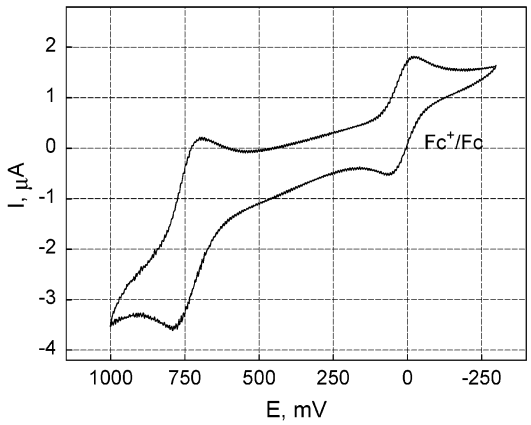

Figure 3. Cyclic voltammetry profile of a 10^{-3} M solution of $[Ni^{II}(\mathbf{3})]^{2+}$ in MeCN made 0.1 M in Bu_4NClO_4. Potential scale is referred to the Fc^+/Fc couple, used as internal reference.

Table 3. Absorption and Emission Data in MeCN for Complexes $[Ni(\mathbf{2})]^{2+}$, $[Ni(\mathbf{3})]^{2+}$, and Reference Compounds 1,3-Benzodioxole and Trimethoxybenzene

	λ_{abs}, nm	ϵ, $M^{-1}\,cm^{-1}$	λ_{em} (λ_{exc}), nm	Φ
1,3-benzodioxole	200	27900	315 (284)	0.31
	232	4380		
	284	4100		
$[Ni(\mathbf{2})]^{2+}$	206	23300	326 (286)	0.21
	236	5140		
	286	4460		
1,2,3-trimethoxybenzene	204	32300	310 (270)	0.076
	268	710		
$[Ni(\mathbf{3})]^{2+}$	208	28600	338 (280)	0.058
	274(sh)			

In diluted solutions ($10^{-5}-10^{-4}$ M), nickel(II) complexes formed by cyclam derivatives **2** and **3** display electronic spectra which are very similar to those of 1,3-benzodioxole and 1,2,3-trimethoxybenzene, respectively (see λ and ϵ values in Table 3). At higher concentrations ($>10^{-3}$ M), a low-intensity band centered at 450−470 nm ($\epsilon = 40-50$ M^{-1} cm^{-1}) is observed. It is typical of the nickel(II) complexes with cyclam derivatives and is ascribed to a d−d transition in a square-planar geometry.

The emission spectra of $[Ni^{II}(\mathbf{2})]^{2+}$ and $[Ni^{II}(\mathbf{3})]^{2+}$ exhibit broad bands (at 326 and 338 nm in MeCN, respectively), which are only sligthly red-shifted (by 10−20 nm), if compared to the corresponding bands displayed by 1,2-benzodioxole and 1,2,3-trimethoxybenzene, respectively. Moreover, the fluorescence quantum yields corresponding to $[Ni^{II}(\mathbf{2})]^{2+}$ and $[Ni^{II}(\mathbf{3})]^{2+}$ ($\Phi = 0.21$ and 0.058 in MeCN, respectively) are not much lower than those determined for the unsubstituted fluorophores (see Table 3).

Voltammetric studies at solid electrodes were carried out in an MeCN solution (using a platinum microsphere as a working electrode) and in water (using a glassy carbon electrode): in any case, reversible CV profiles were obtained on oxidation (see in Figure 3 the profile obtained for a solution of $[Ni^{II}(\mathbf{3})]^{2+}$ in an MeCN solution, made 0.1 M in Bu_4NClO_4). The measurements in water were performed in

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Table 4. Halfwave Potential Values Related to the Ni^{III}/Ni^{II} Redox Exchange in MeCN and Aqueous 0.1 M $HClO_4$

complex	$E_{1/2}(Ni^{III}/Ni^{II})$, V vs Fc^+/Fc[a]	$E_{1/2}(Ni^{III}/Ni^{II})$, V vs SCE[b]
$[Ni(\mathbf{1})]^{2+}$	0.59[c]	0.75[d]
$[Ni(\mathbf{2})]^{2+}$	0.75	0.94
$[Ni(\mathbf{3})]^{2+}$	0.73	0.93

[a] In MeCN 0.1 M Bu_4NClO_4. [b] In 0.1 M aqueous $HClO_4$. [c] See ref 26. [d] In 1 M aqueous $HClO_4$; see ref 27.

0.1 M $HClO_4$ as the stability of Ni^{III} complexes with respect to the decomposition is distinctly enhanced in acidic solutions.[25]

Half-wave potential values associated with the Ni^{III}/Ni^{II} redox change for complexes of **1**−**3** are reported in Table 4. It is seen that the presence of a benzyl-like substituent on a nitrogen atom (macrocycles **2** and **3**) makes the potential moderately more positive (and the attainment of the Ni^{III} state slightly more difficult) with respect to the corresponding complex of the unsubstituted ligand **1**, cyclam. This is a generally observed behavior and is related to the steric effects exerted by the substituent, which weaken the metal−tertiary nitrogen atom interaction;[28] in fact, in the $[Ni^{II}(\mathbf{3})]^{2+}$ complex, the Ni^{II}−N(tertiary) distance is slightly, but significantly, higher than the Ni^{II}−N(secondary) distance. As a consequence of the less intense in-plane interaction, the HOMO antibonding orbital is destabilized to a lower extent and the abstraction of the electron on oxidation is less favored.

Redox-Driven Fluorescence Switching. Electrochemical investigations showed that Ni^{II} and Ni^{III} states within the cavity of macrocycles **2** and **3** are connected by a fast and reversible redox change, taking place at a not too positive half-wave potential. In order to verify the fluorescence switching behavior, we have now to demonstrate the occurrence of a selective interference of each oxidation state on the emission properties of the proximate fluorophore. This has been carried out by measuring the emission spectra in the course of controlled potential coulometry (CPC) experiments performed on both MeCN and acidic aqueous solutions of $[Ni^{II}(\mathbf{2})]^{2+}$ and $[Ni^{II}(\mathbf{3})]^{2+}$.

As already mentioned, Ni^{II} complexes (RED state) in MeCN solution display almost the same fluorescence spectra as the individual fluorogenic fragments, indicating that the divalent metal center does not seriously interfere with the nearby fluorogenic fragment. Moreover, the emission properties of the complexes in water solution do not substantially differ from those in MeCN (a direct comparison with the plain fluorophores cannot be made due to their poor solubility in water). As an example, the spectrum of the $[Ni^{II}(\mathbf{2})]^{2+}$ complex in 0.1 M aqueous $HClO_4$, prior to the electrolysis, displaying a poorly structured broad emission band centered at $\lambda_{max} = 324$ nm ($\Phi = 0.20$), is shown in Figure 4. In the CPC experiment, the potential of the working electrode (a platinum gauze) was adjusted to the potential of 1.2 V vs SCE (i.e., about 250 mV more positive than the $E_{1/2}$ value determined by CV), in order to perform exhaustive oxidation to Ni^{III}. The emission spectrum of the solution was measured at the end of the electrolysis experiment (after the passage of 1.04 ± 0.05 electrons) showing a distinct decrease of the emission intensity ($\Phi = 0.008$, see Figure 4).

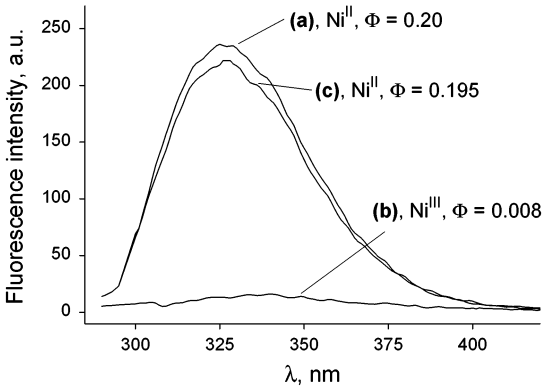

Figure 4. Emission spectra of $[Ni^{II}(\mathbf{2})]^{2+}$, measured during controlled potential coulometry in aqueous 0.1 M $HClO_4$: prior to electrolysis (a); after electrolysis at 1.2 V (b); after electrolysis at 0.7 V (c). λ_{exc}: 286 nm.

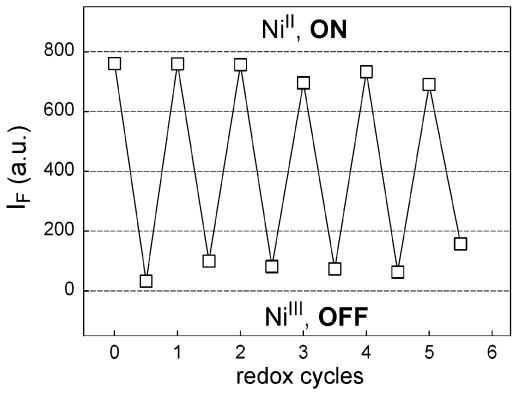

Figure 5. Cyclic variation of I_F (fluorescence intensity) upon consecutive oxidation/reduction processes on the $[Ni^{II}(\mathbf{2})]^{2+}$ complex in aqueous 0.1 M $HClO_4$.

On the other hand, on reduction of Ni^{III} to Ni^{II}, performed by adjusting the potential of the working electrode to 0.7 V (i.e., about 250 mV less positive than the $E_{1/2}$ value), the fluorescence of the solution is progressively restored: in particular, full emission ($\Phi = 0.195$, see Figure 4) is observed after the passage of 1.05 ± 0.05 electrons, on reduction. We carried out up to five complete redox cycles without any apparent degradation of the system: in particular, about 100% of the fluorescence intensity was recovered after each reduction step (see Figure 5).

A completely similar behavior was observed for the $[Ni^{II}(\mathbf{3})]^{2+}$ complex, both in MeCN and in water: the results of the CPC experiment coupled to spectrofluorimetric measurements performed on $[Ni^{II}(\mathbf{3})]^{2+}$ in 0.1 M aqueous $HClO_4$ are illustrated in Figure 6.

Thus, we are in the presence of two new robust and water soluble redox switches of fluorescence.

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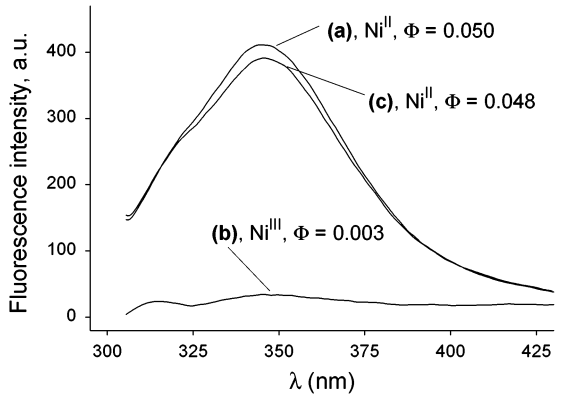

Figure 6. Emission spectra of $[Ni^{II}(\mathbf{3})]^{2+}$ measured during controlled potential coulometry in aqueous 0.1 M $HClO_4$: prior to electrolysis (a); after electrolysis at 1.18 V (b); after electrolysis at 0.68 V (c). λ_{exc}: 280 nm.

We have now to establish through which intramolecular mechanism the Ni^{III} state is able to quench the nearby excited fluorophore. Such an assessment was carried out by measuring the emission spectra of the solutions of both the Ni^{II} and the Ni^{III} complexes (obtained through electrolysis), at room temperature and when frozen at 77 K. Butyronitrile (BuCN) was chosen as a solvent, because, on freezing, it does not crystallize, but forms a transparent glass (thus allowing the measurement of emission spectra). For instance, in the case of the macrocycle **2**, we observed that, at room temperature, the emission intensity at $\lambda_{max} = 324$ nm of the Ni^{II} complex is at least 100 times higher than that of the Ni^{III} species. On the other hand, the BuCN solution frozen at the liquid nitrogen temperature of both Ni^{II} and Ni^{III} complexes shows emission bands, centered at $\lambda_{max} = 315$ nm, which exhibit nearly the same intensity. If the frozen solutions are allowed to warm back to room temperature, a fluorescence quenching is again observed for the Ni^{III} complex since the emission intensity displayed by its BuCN solution is again much lower (by about 100 times) than that corresponding to the Ni^{II} complex.

In other words, freezing of the Ni^{III} complex solution *makes fluorescence revive*. With the exception of few examples of ultrafast eT processes,[29] the reviving of fluorescence in frozen solution is generally expected when an electron transfer (eT) rather than an energy transfer (ET) process is responsible for the fluorescence quenching at room temperature.

In particular, the eT process involves a drastic rearrangement of the system of electrical charges: following the eT process, the positive charge on the metal center is reduced, while a positive charge is formed on the appended donor group. A substantial reorganization of the molecules of the polar solvent (BuCN, in the present case) must accompany the process of electrical charge rearrangement. However, at the liquid nitrogen temperature, the solvent molecules are immobilized, a situation which prevents the occurrence of the electron transfer process from the excited fluorophore to Ni^{III}. Thus, the excited fluorophore releases photonic energy in its normal radiative mode and, in a frozen situation, fluorescence is revived. It has to be noted that the electronic energy transfer mechanism, according to the Dexter mechanism, does not involve any electrical rearrangement and reorganization of the solvation sphere: thus, it takes place both in the liquid and in the glass, quenching fluorescence both at room temperature and at 77 K.

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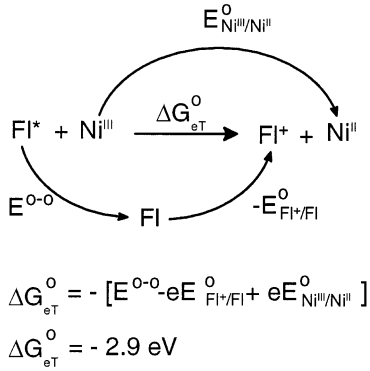

Figure 7. Thermodynamic cycle for evaluating the free energy change $\Delta G°_{eT}$ associated with the intramolecular photoinduced electron transfer in the nickel(III) complex of **3**. $E^{0-0} = 3.6$ eV; $E°(Fl^+/Fl) = 1.43$ V (irreversible peak); $E°(Ni^{III}/Ni^{II}) = 0.73$ V. The Coulombic term has been considered negligible under the present circumstances. A similar cycle can be drawn for the complex $[Ni^{II}(\mathbf{2})]^{2+}$.

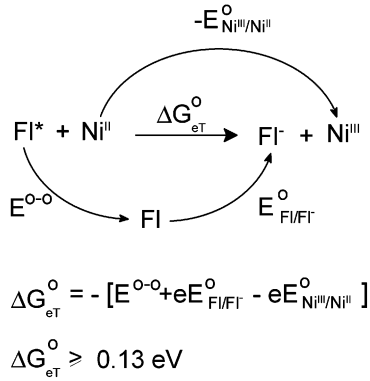

Figure 8. Thermodynamic cycle for evaluating the free energy change $\Delta G°_{eT}$ associated with the intramolecular photoinduced electron transfer in the $[Ni^{II}(\mathbf{3})]^{2+}$ complex. $E^{0-0} = 3.6$ eV; $E°(Fl/Fl^-) \leq 3.0$ V, since no peaks were observed in the cathodic scan in voltammetry experiments until solvent discharge; $E°(Ni^{III}/Ni^{II}) = 0.73$ V. The Coulombic term has been considered negligible under the present circumstances. A similar cycle can be drawn for the complex $[Ni^{II}(\mathbf{2})]^{2+}$.

In particular, the free energy change, $\Delta G°_{eT}$, associated with the eT process can be calculated through the thermodynamic cycle (illustrated in Figure 7 for $[Ni^{III}(\mathbf{3})]^{3+}$), by combining the appropriate photophysical and electrochemical quantities: E^{0-0}, the photonic energy, which is obtained from the emission spectrum; $E°(Ni^{III}/Ni^{II})$ and $E°(Fl^+/Fl)$, which refer to the standard electrode potentials for the redox change involving the macrocyclic complex and the fluorogenic substituent Fl respectively, and are obtained from the corresponding $E_{1/2}$ values. Calculated $\Delta G°_{eT}$ values are all distinctly negative (system **2**, −3.0 eV; **3**, −2.9 eV), and account for the quenching of fluorescence occurring in the Ni^{III} derivatives, through an eT mechanism.

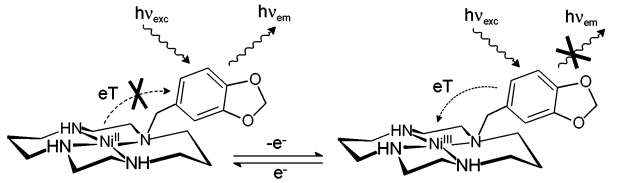

Figure 9. The mechanism of the redox switching of fluorescence in the two-component system $[Ni^{II}(\mathbf{2})]^{2+}$: the oxidized form induces a fluorophore-to-Ni^{III} eT process and causes fluorescence quenching; in the reduced form, the Ni^{II}-to-fluorophore eT process is thermodynamically disfavored. A similar mechanism operates in the $[Ni^{II}(\mathbf{3})]^{2+}$ system.

The thermodynamic approach can also explain why no fluorescence quenching is observed when the system is in the Ni^{II} state. In fact, the possible eT process (from Ni^{II} to the excited fluorophore) is characterized by a positive value of ΔG°_{eT} (system **2**, ≥ 0.05 eV; **3**, ≥ 0.13 eV), as calculated from the appropriate thermodynamic cycle like the one depicted in Figure 8 for the complex $[Ni^{II}(\mathbf{3})]^{2+}$).

The mechanism of the fluorescence switching process for the $[Ni^{II}(\mathbf{2})]^{2+}$ system is pictorially illustrated in Figure 9.

Conclusions

Molecular switches of fluorescence can be constructed by covalently linking a fluorogenic fragment to a redox active subunit. Subunits containing a metal center can provide two consecutive oxidation states of comparable stability and connected by a one-electron fast and reversible redox change. Hopefully, the two states should interact differently with the nearby excited fluorophore. This is the case of the Ni^{III}/Ni^{II} couple in the systems investigated in this work: the oxidized form, Ni^{III}, is capable of establishing an electron transfer process with the charge transfer excited state, Fl* (i.e., from Fl* to Ni^{III}, fluorescence OFF). On the other hand, the occurrence of an eT process involving the reduced state (i.e., from Ni^{II} to Fl*) is prevented by the very endoergonic contribution associated with the reduction of the fluorogenic fragment (fluorescence ON).

Previously reported Ni^{III}/Ni^{II} based switches of fluorescence contained polyaromatic fluorophores with a $\pi-\pi^*$ excited state (e.g., anthracene). The use of aromatic fluorophores containing donor substituents, as described in this work, provides a charge transfer excited state (with a relatively high value of the photonic energy) and produces water soluble systems, an important new feature.

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Supporting Information Available: Crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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