Journal of Inclusion Phenomena and Macrocyclic Chemistry **41:** 123–127, 2001.

Dependence on pH of the Luminescent Properties of Metal Ion Complexes of 5-Chloro-8-hydroxyquinoline Appended Diaza-18-Crown-6

LUCA PRODI[1]*, MARCO MONTALTI[1], JERALD S. BRADSHAW[2], REED M. IZATT[2]* and PAUL B. SAVAGE[2]*

[1]*Dipartimento di Chimica "G. Ciamician", Università di Bologna, via Selmi, 2, 40126 Bologna, Italy;* [2]*Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT 84602, USA; E-mail: reed_izatt@byu.edu*

(Received: 15 July 2001; in final form: 31 August 2001)

Key words: 5-chloro-8-hydroxyquinoline appended diaza-18-crown-6; metal complexes, luminescence; fluorescence, pH dependence; alkaline earth and post-transition bivalent metal ions

Abstract

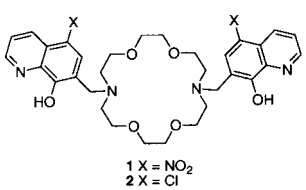
Luminescent properties of 5-chloro-8-hydroxyquinoline (CHQ) free and appended to the amines in diaza-18-crown-6 ($A_2$18C6) were determined. These properties were compared to those of bivalent alkaline earth and post-transition metal ion complexes of the appended macrocycle (CHQ-A218C6). The luminescent properties were found to be pH dependent. In the pH range 3 to 7, CHQ-$A_2$18C6 forms luminescent complexes with only Zn^{2+} and Cd^{2+}. At higher pH values, luminescent complexes were formed with Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}. No luminescent complex was formed by Hg^{2+} over the pH range studied. This lariat macrocycle could find application as a chemosensor for several of the metal ions studied.

Introduction

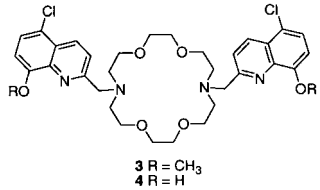
The need for selective, sensitive sensors for a variety of analytes is well recognized. Metal ions constitute an important set of target analytes for sensor development [1] because, while many are essential for biological processes, specific metal ions cause environmental and health concerns when present in uncontrolled amounts. A first step in the preparation of effective sensory devices is the development of effective chemosensors. By taking advantage of fluorescence modulation of 8-hydroxyquinoline derivatives upon metal ion complexation and the ion recognition properties of macrocyclic ligands, we have prepared multiple effective chemosensors for metal ions [2]. Compounds **1** and **2**, with the quinoline groups attached through the C-7 position, selectively bind and respond to Hg^{2+} and Mg^{2+}, respectively [2a, 2b]. Compound **3**, with the quinoline group attached through C-2, is an effective chemosensor for Cd^{2+} [2c].

Compound **4** [3], closely related to Cd^{2+} chemosensor **3**, shows remarkable selectivity for Ba^{2+}. In fact, log K_a for the **4**-Ba^{2+} complex formation is 12.2 in methanol, over five log units greater than that for any of the other ten metal ions tested [3, 4]. Insights into this selectivity may be offered by the solid state structure of the **4**-Ba^{2+} complex in which **4** adopts a 'pseudo-cryptand' conformation, effectively encapsulating the ion [4].

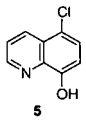
We hoped to take advantage of the selectivity of **4** for Ba^{2+} in the development of a selective chemosensor for this species. Consequently, we investigated the photophysical properties of **4** and its complexes with different metal ions. In our earlier work [2a, 2b], we observed that pH dramatically influenced the fluorescent properties of metal complexes of **1** and **2**. For metal ion complexes of these compounds to fluoresce strongly, deprotonation of both 8-hydroxyquinoline groups, resulting in formation of neutral metal ion complexes, was necessary. The formation of complexes of Hg^{2+} and Mg^{2+} with **1** and **2**, respectively, lowered the pK_a values of the quinoline hydroxyl groups to below 7. Consequently, at pH values of ~7 fluorescent, neutral complexes formed.



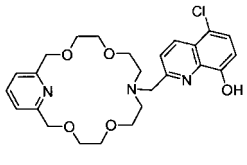
1 X = NO_2
2 X = Cl



3 R = CH_3
4 R = H



5



6

In the crystal structure of the **4**-Ba^{2+} complex, the quinoline hydroxyl groups remained protonated [4]. We hypothesized that if the quinoline hydroxyl groups in the **4**-Ba^{2+} complex were deprotonated then the complex would fluoresce. Consequently, we began an investigation of the UV and fluorescence response to pH of **4** and a variety of its metal ion complexes. Also, as a means of better understanding the photophysical properties of **4**, we studied

* Authors for correspondence.

the influence of pH on the fluorescence of 5-chloro-8-hydroxyquinoline (CHQ, **5**) in protic and aprotic solvents. Due to the limited solubility of **4** in water, the protic solvent methanol was used in the studies. We have observed that metal ion selectivities in methanol correlate well to those in water [5]. As a consequence of using methanol, the reported pH values are apparent pH values.

Results and discussion

We investigated the photophysical properties of **5** at various pH values to identify characteristic signals that could be used to monitor UV and fluorescence responses to pH in more complex macrocyclic systems. The absorption spectrum of **5** changed considerably upon either protonation of the quinoline nitrogen or deprotonation of the phenolic oxygen, yielding in both cases qualitatively similar responses. Under acidic or basic conditions in methanol, **5** gave a new broad absorbance extending into the visible region (centered at 380 nm for the anionic form and at 382 nm for the positively charged form), while the band from the neutral form at 329 nm disappeared. In addition, upon N-protonation or OH-deprotonation, the band at 245 nm shifted to 258 nm.

The pK_a values for nitrogen and hydroxyl deprotonation processes of protonated **5** were determined by following the dependence on pH of the absorbances at 258 and 380 nm in methanol. The same profile was found for both wavelengths giving pK_a values [6] of 2.1 and 12 for deprotonation of the nitrogen and hydroxyl groups, respectively. These values are similar to those determined for **2** in methanol [2b] and they do not differ much from those observed for 8-hydroxyquinoline in methanol [7].

In methanol, **5** showed only a very weak luminescence band at 434 nm ({$\Phi = 2 \times 10^{-3}$) which, after deprotonation (>pH 12), was strongly red shifted (λ_{max} = 540 nm, $\Phi = 2 \times 10^{-3}$) with almost no change in the fluorescence quantum yield. The quenching effect of excited state proton transfer processes on 8-hydroxyquinoline has been reported to be responsible for the weak luminescence signal in protic solvents; some contribution of intramolecular proton transfer processes has also been observed [8]. We carried out additional experiments in acetonitrile designed to prevent excited state proton transfer processes involving the solvent. While only small changes in absorbance were observed for the protonated and neutral species on going from methanol to acetonitrile, the anionic species, obtained by deprotonating the chromophore with tetraethylammonium hydroxide, was strongly luminescent (λ_{max} = 574 nm, $\Phi = 3.4 \times 10^{-2}$). This result suggested that the protic nature of methanol played a central role in quenching the excited state of **5**.

The effects of protonation and deprotonation were also determined with macrocycle **4**. In this compound four basic (two macroring nitrogen atoms and two quinoline nitrogen atoms) and two acidic (two hydroxyl groups on the quinolines) centers are present in the molecule and, as a consequence, more complicated behavior was expected. In methanol basic solutions (pH > 12), we observed that deprotonation of the two hydroxyl groups led to spectral changes very similar to those seen for **5**, i.e., the appearance of bands corresponding to the quinolate (Figure 1). Plots of absorbance of **4** at 264 and 310 nm *vs.* pH revealed variations in absorbance at ca. pH 5.0, 8.5 and 11 (inset, Figure 1). The former two variations were interpreted as arising from changes in the protonation states of the nitrogen atoms in **4**. The identities of the nitrogens involved in these protonation state changes were elucidated by observation of the absorbance of **4** at low pH. At pH 1.0, the band at 264 nm, characteristic of the protonated quinoline, was not observed. Consequently, the minor changes in the absorption spectrum of **4** observed upon changing the pH from 9.0 to 1.0 were likely due to the protonation state changes of the two nitrogen atoms in the macrocyclic portion of the molecule. Protonation of these tertiary amines only slightly influenced, presumably via hydrogen bonding interactions, the absorption properties of the two chromophores. Apparently, protonation of the quinoline nitrogens in **4** was hindered by the presence of the protonated amines on the macrocycle. Protonation of these nitrogen atoms was observed in acetonitrile; after addition of a thousand-fold excess of trifluoromethanesulphonic acid, the bands indicative of the protonated quinoline nitrogens appeared.

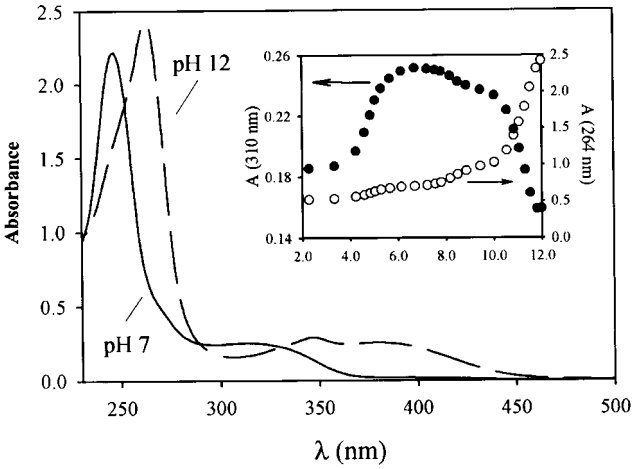


Figure 1. Absorption spectra of methanol solutions of **4** at pH 7 (——) and 12 (- - - - -). Inset: Absorption intensity profiles at 264 nm (○) and 310 nm (●) *vs.* pH.

The pH dependence of the luminescence properties of **4** proved to be very interesting. Similar to **5**, ligand **4** was only weakly luminescent in methanol solution even in the bisquinolate form. In acetonitrile, the addition of a limited amount of base resulted in formation of a monoquinolate form, which gave an absorption band indicative of the deprotonated CHQ group. However, the monoquinolate proved to be only weakly luminescent. At higher pH, the second CHQ group was apparently deprotonated and a significant enhancement of a luminescence band (centered at 567 nm) was observed. The lack of luminescence from **4** containing one quinolate group suggested that deprotonated and neutral CHQ groups within **4** interact causing fluorescence quenching.

Titration experiments of **4** with Ba^{2+} demonstrated how strongly the fluorescence response to complexation could be

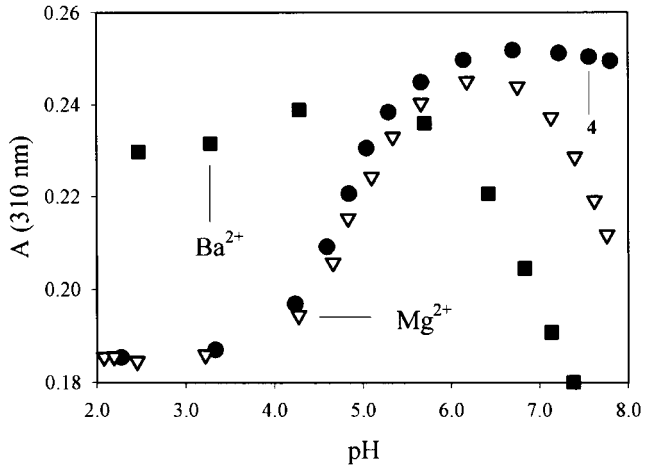


Figure 2. Absorption intensity profiles at 310 nm *vs.* pH of methanol solutions containing **4** (●) and equimolar amounts of Ba^{2+} (■) and Mg^{2+} ions (▽).

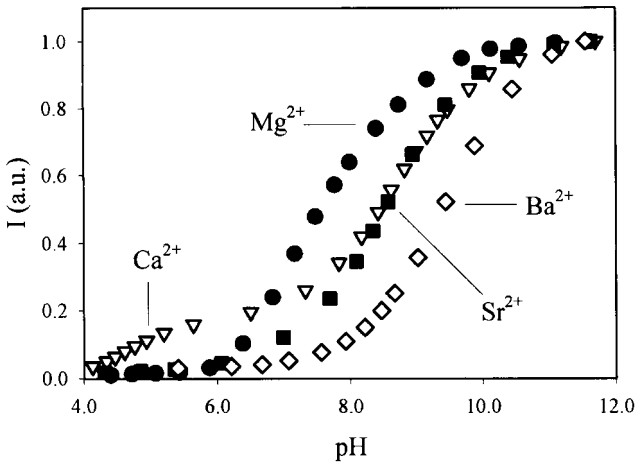


Figure 3. Normalized luminescence intensity profiles (λ_{exc} = 321 nm, λ_{em} = 555 nm) *vs.* pH of methanol solutions containing **4** and equimolar amounts of Ba^{2+} (◇), Sr^{2+} (■), Ca^{2+} (▽), and Mg^{2+} (•) ions.

influenced by pH. At pH 10, addition of Ba^{2+} to **4** led to a strong increase in the fluorescence at 561 nm, while at pH 7 no enhancement could be detected. Changes in the absorption spectrum of **4** suggested that effective complexation occurred with Ba^{2+} at both pH values. To gain a better understanding of the properties of **4** as a fluorescent chemosensor, the absorption and luminescence spectra of **4** (1.5×10^{-5} M) in methanol in the presence of one molar equivalent of metal ions were recorded at incrementally varied pH values between 2 and 12. Metal complexes were formed with Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}. Because **4** had shown high selectivity for Ba^{2+}, complexes of **4** with the alkaline earth cations were selected for study. As described, other 8-hydroxyquinoline appended macrocycles formed strong complexes with Zn^{2+}, Cd^{2+} and Hg^{2+}, and consequently complexes of **4** with these metal ions were selected for study.

In the presence of Mg^{2+}, the absorption spectrum of **4** between pH 2 and 7 appeared similar to that of **4** alone (Figure 2). This result suggested that no complexation took place under acidic conditions, which is consistent with our earlier findings in which we found no measurable heat of complex formation for **4** with Mg^{2+} [3]. Upon increasing the pH of the solution above 7, the behavior of **4** with Mg^{2+} differed from that observed with **4** alone. In particular, the pK_a value for deprotonation of both CHQ groups was 8.3, as compared to ca. 12 for the free ligand [6]. In addition, in the presence of Mg^{2+}, deprotonation caused a much stronger increase of the luminescence intensity at 546 nm, indicating that at pH > 8.3 a strongly fluorescent, neutral **4**-Mg^{2+} complex was formed (Figure 3 and Table 1). Ligand **2**, in which the CHQ groups were attached through quinoline position 7 instead of 2, also formed highly fluorescent complexes with Mg^{2+} (λ_{max} = 540 nm, $\Phi = 4.2 \times 10^{-2}$); however, the deprotonation/complexation process was observed at even lower pH (ca 6.0), giving a more stable species (log K_a = 6.8 [3]).

The behavior of **4** in the presence of Ba^{2+} was very different from that in the presence of Mg^{2+}. In the presence of Ba^{2+}, the UV absorbance at 310 nm was relatively constant in the pH region between 2 and 6 (Figure 2), with an extinction coefficient similar to that observed for the neutral macrocycle (i.e., **4** alone between pH 6 and 10). The decrease in absorbance at 310 nm by **4** at pH < 6 was correlated with protonation of the macroring nitrogen atoms; consequently, the lack of change in absorbance of the **4**-Ba^{2+} complex below pH 6 suggested that complexation of Ba^{2+} prevented protonation of the two macroring nitrogen atoms even under acidic conditions. This conclusion is con-

Table 1. Photophysical properties of **4** and its complexes with metal ions in methanol

	λ_{max}[a] (nm)	ϵ[a] (M^{-1} cm^{-1})	λ_{max}[b] (nm)	Φ[b]	τ[b] (ns)
4	264	87,800	530	3×10^{-3}	2.0
	347	9,000			
	378	8,300			
4 Mg^{2+}	264	89,300	546	1.5×10^{-2}	7.4
	346	7,900			
	386	8,000			
4 Ca^{2+}	268	86,800	556	6×10^{-3}	3.4
	348	8,300			
	391	8,100			
4 Sr^{2+}	268	84,300	557	5×10^{-3}	2.9
	348	8,400			
	391	8,100			
4 Ba^{2+}	267	83,200	561	3×10^{-3}	2.0
	348	8,200			
	398	8,500			
4 Zn^{2+}	268	88,200	556	1.1×10^{-2}	6.2
	346	6,500			
	394	7,300			
4 Cd^{2+}	268	87,800	587	3×10^{-3}	2.5
	348	7,800			
	401	8,000			
4 Hg^{2+}	272	77,800	595	$< 1 \times 10^{-3}$	–
	352	7,600			
	418	7,200			

[a] Absorption (pH 10).
[b] Fluorescence (pH 10).

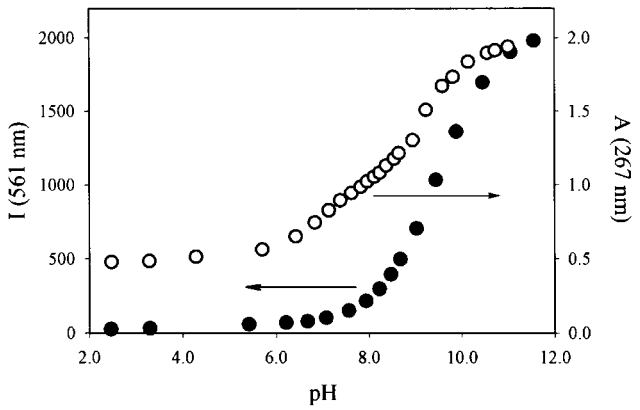


Figure 4. Absorption (λ = 267 nm, ○) and luminescence (λ_{exc} = 321 nm, λ_{em} = 561 nm, ●) intensity profiles vs. pH of a methanol solution containing **4** and equimolar amounts of Ba^{2+}.

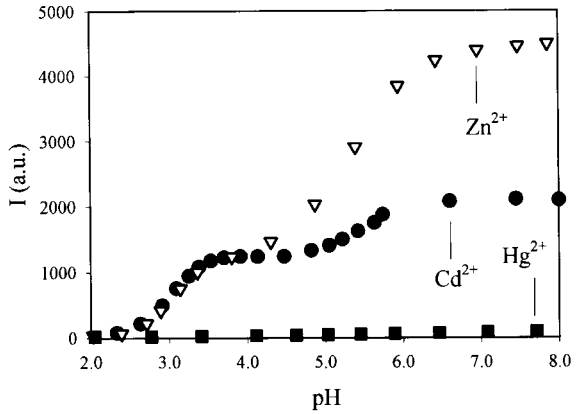


Figure 5. Luminescence (λ_{exc} = 321 nm, λ_{em} = 560 nm) intensity profiles vs. pH of a methanol solution containing **4** and equimolar amounts of Zn^{2+} (▽, Cd^{2+} (●), and Hg^{2+} (■).

sistent with formation of a stable Ba^{2+} complex at low pH. As has been discussed, formation of this Ba^{2+} complex does not induce deprotonation of the two neutral CHQ groups [4], and as expected, the absorption bands indicative of the anionic form of the CHQ group were not observed from the **4**-Ba^{2+} complex in the pH 7 region. Upon increasing the pH, deprotonation of the hydroxyl groups took place in two distinguishable steps. These steps resulted in changes in the absorption intensity at 267 nm (Figure 4). A related pattern was observed in the fluorescence of the complex as pH increased (Figure 4). The system remained non-fluorescent when one of the hydroxyl groups was deprotonated. However, deprotonation of the second hydroxyl group, resulting in formation of a neutral complex, caused a large fluorescence enhancement at 561 nm (Figure 4). This behavior is consistent with that observed with the free ligand in acetonitrile, i.e., deprotonation of both CHQ groups in **4** was required for fluorescence. By analogy with **4**, we hypothesized that when one of the CHQ groups was deprotonated, interaction with the other CHQ group caused fluorescence quenching. Following this argument, the CHQ groups in the **4**-Ba^{2+} complex must have interacted sufficiently to cause quenching of the excited state of the deprotonated CHQ groups (in the solid state [4], the CHQ groups in the **4**-Ba^{2+} complex overlap significantly).

The behavior of **4** in the presence of Ca^{2+} and Sr^{2+} was similar to that with Ba^{2+}; i.e., the complexes only became fluorescent under mildly basic conditions. Changes in fluorescence intensities were attributed to deprotonation of the CHQ hydroxyl groups. Surprisingly, Ba^{2+}, with the highest log K_a value with **4** [3], apparently lowered the pK_as of the hydroxyl groups in **4** less than Mg^{2+}, Ca^{2+} and Sr^{2+} (Figure 3). Consequently, the **4**-Ba^{2+} complex became strongly fluorescent at pH values higher than those at which the complexes of **4** with the other alkaline earth ions became fluorescent.

In the presence of Zn^{2+} and under acidic conditions (pH < 3), the absorption spectrum of **4** was nearly identical to that of the free ligand. However, at pH ∼3 complexation apparently took place as observed by changes in the absorption and fluorescent properties of **4** (Figure 5). Alkaline earth ion complexes with **4** were only fluorescent when the CHQ hydroxyl groups were deprotonated, and we attributed the increase in fluorescence of **4** in the presence of Zn^{2+} to formation of the neutral complex. A further increase and a shift in the fluorescence band of the **4**-Zn^{2+} complex was observed beginning near pH 5. Unfortunately, it was not possible to unambiguously identify the process that leads to this increase in fluorescence near pH 5. However, a reasonable explanation is that interaction of Zn^{2+} is stronger with the CHQ groups than with the macroring, leaving the nitrogen atoms in the macroring to be protonated at low pH. The change in fluorescence at pH 5 might be due to the deprotonation of the macroring nitrogen atoms followed by a reorganization of the structure of the complex.

In the presence of Cd^{2+} and at low pH (> 4.5) the dependence of the luminescence intensity of **4** on the pH conditions followed almost the same pattern as that seen for **4** in the presence of Zn^{2+}. This result suggested a very similar behavior for **4** in the presence of these two ions. The primary difference between these complexes was that the luminescence of the **4**-Cd^{2+} complex did not increase significantly at higher pH.

Changes in the absorption spectrum of **4** in the presence of Hg^{2+} suggested that a complex formed (Table 1). However, even at pH > 7 the complex was not fluorescent (Figure 5). A possible rationale for this observation is that complex formation of **4** with Hg^{2+} did not result in a concomitant decrease in the pK_a values of the CHQ hydroxyl groups. Consequently, a fluorescent complex was not formed.

Under basic conditions (e.g., pH 10), Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+} formed neutral complexes with **4** (Table 1). Absorption and fluorescence bands characteristic of the deprotonated chromophores were observed for the complex of **4** with each metal ion, although the exact positions of these bands and their relative intensities varied slightly. Among the alkaline earth ions, an interesting trend was observed: the lowest energy absorption band and the fluorescence λ_{max} were red shifted in the presence of ions with larger radii. It is notable that a similar behavior has been observed for **6** in which only one CHQ group is present,

demonstrating that such an effect cannot be due only to an interaction between two CHQ groups. This trend may be due to interactions of the metal ions with the CHQ groups and the resulting varied stabilization of charge transfer excited states. The strong red shift concomitant with deprotonation of the CHQ hydroxyl groups suggests a partial charge transfer in the lowest energy excited state of the anionic CHQ species. Because larger cations form more stable complexes than the smaller ions, the larger cations presumable interact more strongly with the CHQ oxygen atoms and facilitate stabilization of the fluorescent excited state.

Conclusions

Ligand **4** forms stable complexes with a variety of metal ions including Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}. These complexes display different charge and photophysical properties, depending on the pH conditions. In the pH range from 3 to 7, **4** forms luminescent complexes only with Zn^{2+} and Cd^{2+} ions and could find application as a chemosensor for these two metal ions. At higher pH values, luminescent complexes can also be formed with alkaline earth metal ions. The behavior of **4** in the presence of metal ions is remarkably different than that observed for other structurally similar ligands (e.g., **1–3**), and it can give complementary information concerning the presence of the different metal ions in solution. This complementarity may be applied to the development of arrayed sensory devices, and we are pursuing the application of the useful properties of **4** in the development of metal ion sensors.

Experimental

Ligands **1** [12], **2–4** [3] and **6** [13] were prepared as reported. The experiments reported were performed in MeOH solution and the pH was controlled by addition of methanol solutions of trifluoromethansulfonicacid and/or tetraethylammonium hydroxide.

Absorption spectra were recorded with Perkin Elmer lambda 40 and lambda 16 spectrophotometers. Uncorrected emission, and corrected excitation spectra were obtained with an Spex Fluorolog spectrofluorimeter. The fluorescence lifetimes (uncertainty ±5%) were obtained with an Edinburgh single-photon counting apparatus, in which the flash lamp was filled with D_2. Luminescence quantum yields (uncertainty ±15%) were determined using sulfate in 1 M H_2SO_4 aqueous solution (Φ = 0.546 [9]) as a reference. In order to allow comparison of emission intensities, corrections for instrumental response, inner filter effects, and phototube sensitivity were performed [10]. A correction for differences in the refraction index was introduced when necessary. The determination of binding constants was performed as described [11].

Acknowledgements

The authors acknowledge financial support by the Italian Ministry of University Research and Technology (MURST, *Dispositivi Supremolecolari* project), the University of Bologna (Funds for Selected Topics), CNR (Sensori Fluorescenti Supramolecolari) in Italy and the Office of Naval Research (USA).

References

1. (a) In A.W. Czarnik (ed.), *Fluorescent Chemosensors for Ion and Molecule Recognition*, American Chemical Society, Washington, DC (1992). (b) In J.-P. Desvergne and A.W. Czarnik (eds.), *Chemosensors for Ion and Molecule Recognition*, NATO ASI Series, Kluwer Academic Publishers, Dordrecht (1997). (c) A.P. de Silva, H.Q.N. Gunaratne, T. Gunnlaugsson, A.J.M. Huxley, C.P. McCoy, J.T. Rademacher and T.E. Rice: *Chem Rev.* **97**, 1515 (1997). (d) L. Fabbrizzi and A. Poggi: *Chem. Soc. Rev.* 197 (1995). (e) B. Valeur and I. Leray: *Coord. Chem. Rev.* **205**, 3 (2000). (f) L. Prodi, F. Bolletta, M. Montalti and N. Zaccheroni: *Coord. Chem. Rev.* **205**, 59 (2000). (g) K. Rurack, M. Kollmannsberger, U. Resch-Genger and J. Daub: *J. Am. Chem. Soc.* **122**, 968 (2000).
2. (a) L. Prodi, C. Bargossi, M. Montalti, N. Zaccheroni, N. Su, J.S. Bradshaw, R.M. Izatt and P.B. Savage: *J. Am. Chem. Soc.* **122**, 6769 (2000). (b) L. Prodi, F. Bolletta, M. Montalti, N. Zaccheroni, J.S. Bradshaw, R.M. Izatt and P.B. Savage: *Tetrahedron Lett.* **39**, 5451 (1998). (c) L. Prodi, M. Montalti, N. Zaccheroni, J.S. Bradshaw, R.M. Izatt and P.B. Savage: *Tetrahedron Lett.* **42**, 2941 (2001).
3. A.V. Bordunov, J.S. Bradshaw, X. Xin Zhang, N.K. Dalley, X. Kou and R.M. Izatt: *Inorg. Chem.* **35**, 7229 (1996).
4. X.X. Zhang, A.V. Bordunov, J.S. Bradshaw, N.K. Dalley, X. Kou and R.M. Izatt: *J. Am. Chem. Soc.* **117**, 11507 (1995).
5. X.X. Zhang, R.M. Izatt, K.E. Krakowiak and J.S. Bradshaw: *Inorg. Chim. Acta* **254**, 43 (1997).
6. pK_a values were identified as maxima in the first derivatives of plots of either UV absorbance or fluorescence intensity vs. pH.
7. M. Goldman and E.L. Wehry: *Anal. Chem.* **42**, 1178 (1970).
8. E. Bardez, I. Devol, B. Larrey and B. Valeur: *J. Phys. Chem.* **101**, 7786 (1997).
9. S.R. Meech and D. Phillips: *J. Photochem* **23**, 193 (1983).
10. A. Credi and L. Prodi: *Spectrochimica Acta, Part A* **54**, 159 (1998).
11. L. Prodi, F. Bolletta, N. Zaccheroni, C.I.F. Watt and N.J. Mooney: *Chem. Eur. J.* **4**, 1090 (1998).
12. N. Su, J.S. Bradshaw, X.X. Zhang, H. Song, P.B. Savage, G. Xue, K.E. Krakowiak and R.M. Izatt: *J. Org. Chem.* **64**, 8855 (1999).
13. A.V. Bordunov, P.C. Hellier, J.S. Bradshaw, N.K. Dalley, X. Kou, X.X. Zhang and R.M. Izatt: *J. Org. Chem.* **60**, 6097 (1995).