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Bis(isoquinoline *N*-oxide) Pincers as a New Type of Metal Cation Dual Channel Fluorosensor

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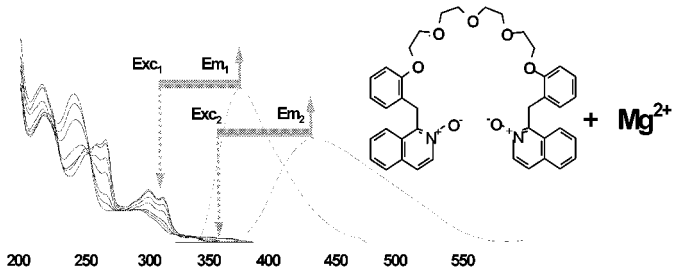
ABSTRACT



A new type of donor-spacer-acceptor podand system has been synthesized and proved as an efficient dual channel fluorosensor for Li^+, Mg^{2+}, and Ca^{2+}. The known ability for the *N*-oxide function to bind Lewis acids is the key step in the appearance of a new emitting charge-transfer (CT) excited state. The occurrence of this CT state for alkaline earth (Mg^{2+} and Ca^{2+}) and not for alkaline metals (Li^+) provided a new type of dual channel fluorosensors.

The application of fluorescence techniques to the detection, identification, and titration of protons and metal ions has fostered a tremendous research activity for the past 12 years.[1] Because of its sensitivity, fluorescence proves very useful for real time sensing of traces for applications in biology and environmental monitoring.[1d,e] Fluoroionophores are known to undergo a change of emission intensity and wavelength on cation binding. Of special interest are systems with two emitting states such as monomer/excimer[2] or locally excited (LE)/internal twisted charge transfer state (TICT).[3] Fluorosensors that allow measurement at two different emission bands permit signal rationing, which can increase the dynamic range and provide built-in correction for environmental effects.[4]

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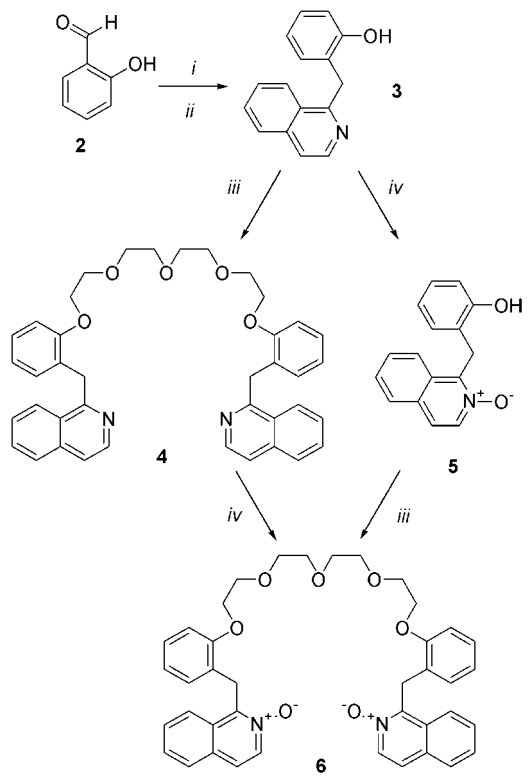
Here we report on the remarkable properties of a new type of dual channel fluorosensor, podand **6** (Scheme 1), which can act as an efficient probe for Li^+, Mg^{2+}, and Ca^{2+}.

Scheme 1[a]



[a] Reagents and conditions: (i) TsCl, CH_2Cl_2, TEBA, 11 N NaOH, then $NaBH_4$, THF, then $SOCl_2$, Δ; (ii) isoquinoline Reissert, PhH, TEBA, 19 N NaOH, then 1 1N NaOH, EtOH, Δ; (iii) NaH, DMF, tetraethylene glycol di-*p*-toluenesulfonate; (iv) *m*CPBA, $CHCl_3$.

Podand **6** was synthesized as shown in Scheme 1. The salicylaldehyde (**2**) was sequentially transformed into the *o*-toluenesulfoniloxy benzyl chloride and coupled to isoquinoline Reissert, to finally obtain the phenolic-benzyl isoquinoline **3** in 65% overall yield. Coupling to tetraethylene glycol di-*p*-toluenesulfonate (TEGDT) to obtain the podand **4** and *N*-oxidation with *m*-chloroperbenzoic acid (*m*CPBA) provided **6** in 55% yield (from **3**). Alternatively, we found that driving first the *N*-oxidation to **5** and subsequent coupling to TEGDT produced a similar overall yield (45%).

The fluorescence of **6** and the reference compound **1** (Figure 1) is controlled by the unique properties of the donor-spacer-acceptor (D-S-A) system, which displays a charge transfer (CT) fluorescence when the *N*-oxide group is coordinated to a positively charged species.[5]

The fluorescence emission of compound **1** is illustrative of these properties: under neutral conditions a non-structured

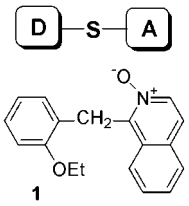


Figure 1. Donor-acceptor covalently linked through methylene spacer reference compound **1**.

emission culminating at 399 nm is recorded whatever the excitation wavelength (inset in Figure 2), but on protonation

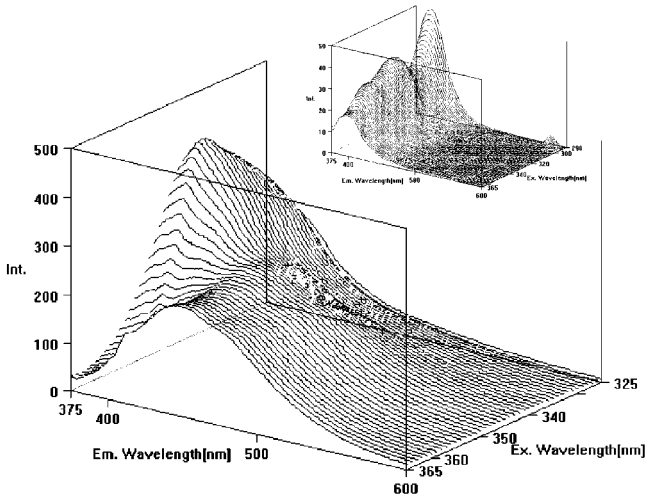


Figure 2. Three-dimensional recording of the emitting wavelength of a 1×10^{-5} M solution of **1** in acetonitrile in the presence of TFA. On going from short to long exciting wavelength the LE emission of the protonated isoquinoline *N*-oxide at about 380 nm is replaced by a CT state emission centered at 450 nm. Only the LE emission of the uncomplexed chromophore (about 400 nm) is observed in absence of coordinating substances (inset). Compound **6** behaves similarly.

of the *N*-oxide function the LE emission ($\pi\pi^*$ transition having a strong internal CT character in isoquinoline *N*-oxide[6]) is blue-shifted to ~380 nm ($\Delta\nu = 1250$ cm^{-1}) for $\lambda_{exc} = 330$ nm and is completely replaced by a new band pointing at $\lambda_{max} \approx 450$ nm ($\Delta\nu = -2850$ cm^{-1}) for $\lambda_{exc} =$ 360 nm. Podand **6** behaves similarly.

A similar result could also be observed with **6** (but not with **1**) in the presence of some alkaline and alkaline earth metal cations. The binding properties of **6** are reflected in a large change of absorption spectra (Figure 3, top), displayed

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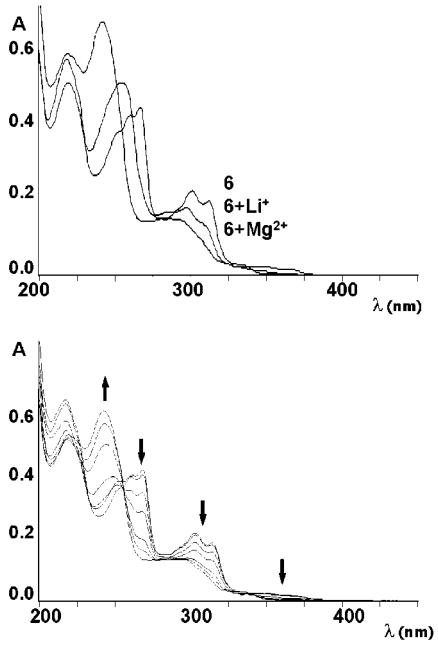

Figure 3. UV absorption spectra of compound **6** in acetonitrile and their modifications in the presence of excess $LiClO_4$ and $Mg(ClO_4)_2$ (top) and spectrophotometric titration with $Mg(ClO_4)_2$ (bottom).

in both a diminution of the optical density and a hypsochromic shifts of the absorption bands. Perceptibly, the highest effect was obtained in the presence of Mg^{2+}, whereas Li^+ induced a moderate modification. These changes (Figure 3, bottom) were used to determine the association constants (Table 1)[7] of the podand−metal complexes, evaluated in

Table 1. Fluorescence Emission Data and Association Constants for **6** and Their Cationic Complexes in Acetonitrile

λ_{exc}		**6**	**6** + Li^+	**6** + Mg^{2+}	**6** + Ca^{2+}
330 nm	λ_{max} (nm)	399	388	371	379
	Φ_f (10^{-3})	3	2	1	1
360 nm	λ_{max} (nm)	399		431	431
	Φ_f (10^{-3})			5.4	6
	K_a (M^{-1})		3.9×10^3	1.4×10^5	1.2×10^5

MeCN at 25 °C. Podand **6** shows a moderate association constant with Li^+ but binds strongly Mg^{2+} and Ca^{2+}; the K_a value (~1.4×10^5 M), comparable to that measured for K^+ and 18-crown-6 in CH_3CN,[8] is very high for an acyclic polyether. This is in agreement with the assumption of the participation of the *N*-oxide function in the coordination process for the Mg^{2+} cation. The involvement of the terminal subunits in playing the role of tweezers significantly contributes to stabilization of the complex.

The fluorescence of podand **6** is strongly affected in the presence of Li^+, Mg^{2+}, and Ca^{2+} (but not with Na^+ and K^+). The addition of Li^+ in excess (Figure 4, top) leads to a blue

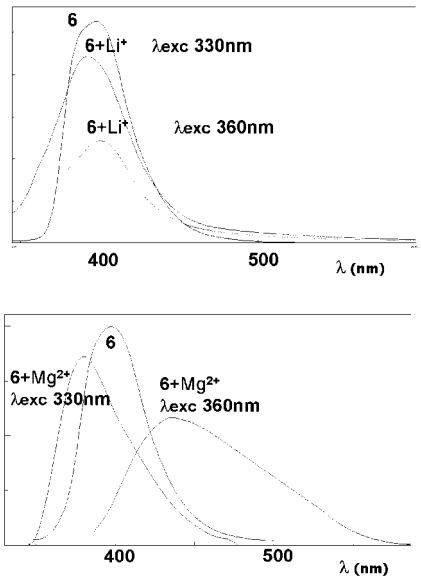

Figure 4. Fluorescence emission spectra of compound **6** in acetonitrile and their modifications in the presence of excess $LiClO_4$ (top) and $Mg(ClO_4)_2$ (bottom). The emission of the free **6** culminates at 399 nm. The Mg^{2+} complex emits at 371 nm (λ_{exc} 330 nm) and 431 nm (λ_{exc} 360 nm).

shift (388 nm, $\Delta\nu \approx 700$ cm^{-1}) of the LE emission band on excitation at 330 nm; no other emission is observed.

In contrast, the addition of an excess of Mg^{2+} (Figure 4, bottom) leads to an enhancement of the hypsochromic shift of the LE emission band ($\Delta\nu \approx 1900$ cm^{-1}) on excitation at 330 nm between the uncomplexed and complexed **6** and a second emission band centered at 431 nm ($\Delta\nu \approx -1860$ cm^{-1}) on exciting at 360 nm. Ca^{2+} shows a similar behavior. The difference of hypsochromic shifts between Li^+ and Mg^{2+} reflects the difference of binding ability.

The second emission is ascribed to an "*interchromophoric*" emitting CT state. Application of the Weller treatment[9] to the energetic of intramolecular electron transfer in this kind of D-S-A systems shows that photoinduced electron transfer is exergonic for the protonated form.[5] The reduction potential of aromatic *N*-oxides is strongly pH-dependent, reduction being easier under acidic conditions, i.e., the protonated *N*-oxide becomes a much better electron acceptor.[10] Therefore, only when the *N*-oxide is effectively coordinated, the isoquinoline *N*-oxide becomes a better acceptor and the CT state is accessible.

(7) The association constants were calculated according with the method previously described: (a) Desvergne, J.-P.; Bouas-Laurent, H.; Perez-Inestrosa, E.; Marsau, P.; Cotrait, M. *Coord. Chem. Rev.* **1999**, *185−186*, 357−379. (b) Perez-Inestrosa, E.; Desvergne, J.-P.; Bouas-Laurent, H.; Rayez, J.-C.; Rayez, M.-T.; Cotrait, M.; Marsau, P. *Eur. J. Org. Chem.* **2002**, 331−344.

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The occurrence of CT state emission when **6** is bound to Mg^{2+} and Ca^{2+} confirms the significant implication of the *N*-oxide function in their coordination. This makes possible the reduction of the isoquinoline *N*-oxide, when transforming it in a better acceptor, and hence the photoinduced electron transfer (PET) from the alkoxybenzene donor moiety, leading to the emitting CT state. However, the *N*-oxide function should not be significantly involved in Li^+ coordination, isoquinoline *N*-oxide remaining as a poor acceptor and inhibiting in this way the PET process. Consequently, a selective response is observed when **6** is coordinated to the cations, being the implication of the *N*-oxide moiety determinant.

(10) For instance, quinoline *N*-oxide $E_{1/2}$ (V) versus SCE (pH) = −1.164 (7), −0.772 (1.8), $\Delta E_{1/2} \approx 0.4$ V; see: *Aromatic Amine Oxides*; Ochiai, E., Ed.; Elsevier: Amsterdam, 1967.

Podand **6** is thus capable of identifying and titrating Li^+ and Mg^{2+} (Ca^{2+}) because of the independent signaling from two emission channels.

Other D-S-A related podands are under study to extend the scope of this new family of fluorosensors and to better understand their photophysical behavior.

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Supporting Information Available: Experimental procedure and full characterization for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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