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A New Fluoroionophore Derived from 4-Amino-N-Methyl-1,8-Naphthalimide

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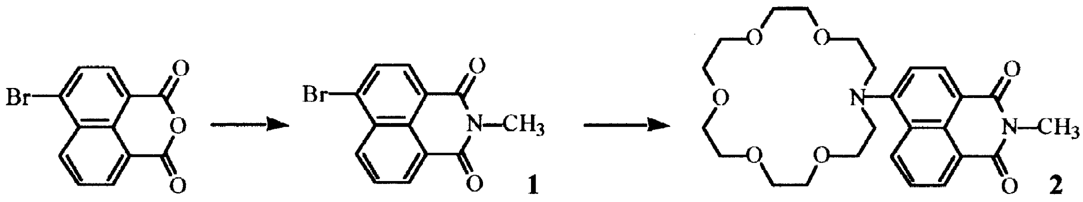
Abstract : A new azacrown ether derived from 1,8-naphthalimide was prepared by a two steps reaction from 4-bromo-1,8-naphthalic anhydride. The spectroscopic properties of this fluoroionophore are described both in the absence and in the presence of cations; the compound shows a strong affinity with Ca^{2+} and Ba^{2+}. © 1998 Elsevier Science Ltd. All rights reserved.

Chromo- and fluoroionophores based on a donor-acceptor system in which the ligand is part of the π system of the chromophore have received considerable attention over the last years[1]. Pertubation of the π system by metal ion complexation leads to spectral shifts and changes of the emissive properties.

1,8-Naphthalimide derivatives are interesting compounds due to their applications in many fields, e.g. as DNA cleaving agents[2], as tumorocidals[3], as brightening agents[4], as laser dyes[5], etc. Substitution by an electron donating group on the 4 position of the naphthalene ring leads to highly fluorescent compounds ($\phi_f \sim 0.8$-1.0)[6].

Here we report on the synthesis and spectroscopic properties of a new azacrown ether derived from 1,8-naphthalimide which particularly shows a strong affinity for Ca^{2+} and Ba^{2+}.

The azacrown **2** was prepared by a two step reaction : at first, 4-bromo-N-methyl-1,8-naphthalimide **1** was obtained by direct condensation of 4-bromo-1,8-naphthalic anhydride with aqueous methylamine at room temperature[7]. In a second step, **1** was treated with aza-18-crown-6 in 2-methoxyethanol under reflux, following a general procedure described for various 4-amino-1,8-naphthalimides[8]. **2** was purified by column chromatography (SiO_2 with CH_2Cl_2-acetone (9:1) as eluant) and characterized by NMR[9].



The spectroscopic properties of **2** are similar to those reported for the 4-dimethylamino-N-substituted-1,8-naphthalimides[8,10]. Both the absorption and emission maxima are red-shifted when increasing the solvent

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polarity (Table 1). Using the Lippert-Mataga equation, one can roughly estimate the difference between the ground state and excited state dipole moments to be 6 Debye. The fluorescence quantum yield and lifetime are strongly sensitive to the solvent ; they both decrease by more than one order of magnitude when passing from an apolar to a polar solvent.

Table 1. Spectroscopic data of **2** in different solvents.

Solvent	Hexane	1,4-Dioxane	CH_2Cl_2	Ethanol	Acetonitrile
λ_{abs} (nm)	403	406	415	419	414
λ_f (nm)	519	529	546	561	558
ϕ_f	0.72	0.53	0.40	0.013	0.069
τ_f (ns)	10.2	8.95	7.2	0.4	1.8

Korol'kova[10c] et al suggested that the interaction between the electron donating group (the substituted amino) and the electron accepting carbonyl groups leads to a mixing of electronic levels, modifying the orbital nature of the radiative states owing to the participation of the nitrogen lone pair. Changing the solvent polarity modifies the energy of the different levels, and therefore the deactivation processes. On the other hand, 4-amino -N-methyl-1,8-naphthalimide and 4-monoalkylamino-N-methyl-1,8-naphthalimide are strongly fluorescent in both polar and apolar solvents. Since the dialkylamino groups are more electron donating than the amino and monoalkylamino groups, one can suggest that in polar solvents the non radiative deactivation process of the dialkylamino derivatives is mainly due to the formation of a non emissive intramolecular charge transfer state(ICT).

Addition of alkaline and alkaline-earth perchlorates to acetonitrile solution of azacrown **2** leads to a hypsochromic shift of the long wavelength absorption band. This shift increases with the size of the cation, in both series of mono- and di-cations ; the largest effects are observed in the case of Cs^+ and Ba^{2+}, reflecting a strong interaction of the nitrogen lone pair with the cation. This interaction leads to a decrease of the conjugation of the amino group with the naphthalimide, which induces a blue-shift of the absorption of the complex when compared to the free ligand. In the case of Cs^+, the absorption of the complex is almost similar to the structured absorption of N-methyl-1,8-naphthalimide (λ_{max} = 342 nm in CH_3CN), while in the case of Li^+, almost no change is observed in the absorption spectrum (Table 2). Observation of isobestic points in all the experiments is a clear indication of the formation of a 1:1 complex ; the association constants have been determined using the general method described in the litterature[11] (the optical density (OD) is measured at a wavelength where its variation by addition of the cation is maximum and K_{ass} is determined from the plot of OD versus the cation concentration). The highest values are obtained with the divalent cations, Ca^{2+} and Ba^{2+}. The magnitude of the spectral shifts does not vary in a same way as the association constants, indicating that the participation of the oxygen of the crown ether moiety dominates the complexing abilities, while the participation of the nitrogen lone pair dominates the spectral characteristics.

The fluorescence emission of the azacrown **2** is also hypsochromically shifted (6-43 nm) in the presence of cations. This blue-shift is more important with the divalent cations than with the monovalent cations. In the former case, the fluorescence maximum is located almost at the same position than that of 4-amino-N-methyl-1,8-naphthalimide (λ_{max} = 520 nm in CH_3CN), and its intensity progressively increases with the addition of cation. Due the high values of K_{ass} with Ca^{2+} and Ba^{2+}, the fluorescence quantum yield and lifetime of the fully complexed compounds (5×10^{-4} M of added cation) have been determined ; they are much higher than those of **2**, and come close to the values of 4-amino-N-methyl-1,8-naphthalimide (ϕ_f = 0.64 and τ_f = 10.6ns in CH_3CN).

Table 2: Spectroscopic properties of **2** in presence of the different cations in acetonitrile.

	Li^+	Na^+	K^+	Cs^+	Mg^{2+}	Ca^{2+}	Ba^{2+}
λ_{abs} (nm)	414	400	378	344	387	385	360
λ_f (nm)	540	535	538	552	525	515	520
K_{ass} (M^{-1})	165	5.7×10^3	3.6×10^3	565	230	4.9×10^5	1.8×10^5
ϕ_f		0.29				0.75	0.38
τ_f (ns)		4.8				8.3	4.7

This result indicates that, following the excitation, the nitrogen lone pair breaks its bond with the cation (as already reported for other fluoroionophores[12]), but the cation is obviously not excluded from the crown ether since the fluorescence does not have the characteristics of the free ligand **2**. In the excited state, the cation is still bonded with the oxygenated part of the crown ether, and the proximity of this positive charge does not favor the formation of an intramolecular charge transfer state, even in a polar solvent. Therefore, the complexes exhibit a higher fluorescence quantum yield and lifetime than the crown ether **2**, and their spectroscopic properties are close to those of the 4-amino-N-alkyl-1,8-naphthalimide and 4-monoalkylamino-N-alkyl-1,8-naphthalimide for which intramolecular charge transfer does not deactivate the excited state. In the case of the monovalent cations, only the fully complexed compound with Na^+ (5×10^{-3} M of added cation) has been characterized. Its spectroscopic properties are similar to those of the other complexes. By adding K^+ (up to 5×10^{-4} M) to the acetonitrile solution of **2**, the fluorescence intensity first increases by a factor 1.5, and then decreases. This result suggests a change of the medium properties at high concentration of the salt. With Cs^+, the fluorescence maximum is only slightly blue-shifted and its intensity progressively decreases with the increase of cation concentration. The complex with Cs^+ does not fluoresce, and the decrease of the fluorescence intensity follows the decrease of the concentration of the free ligand. Apparently in this latter case, there is no break, in the excited state, of the interaction between the nitrogen lone pair and the cation, which explains that no enhancement of the fluorescence intensity is observed.

Both the absorption and emission properties of the crown ether **2** are modified in the presence of alkaline and alkaline-earth cations, and the association constants reach their highest values with Ca^{2+} and Ba^{2+}. The selectivity of **2** toward Ca^{2+} versus other cations of biological interest (Na^+, K^+, Mg^{2+}) is high in acetonitrile. However, in order to make this compound suitable as a probe for biologists, its solubility in aqueous medium has first to be improved by changing the nitrogen substitution, and its complexing properties have also to be confirmed in such a medium. The size of the crown ether will also be modified in order to change the selectivity profile of the compound.

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