Luminescence signalled enantiomeric recognition of chiral organic ammonium ions by an enantiomerically pure dimethylacridino-18-crown-6 ligand

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Acridino-18-crown-6 ligands **1** and **2** are able to bind organic ammonium salts in acetonitrile with high affinity, causing pronounced changes in the luminescence properties of the two partners. Furthermore, enantiomerically pure chiral ligand **2** shows a high enantioselectivity towards chiral organic ammonium ions. The observed changes in the photophysical properties are also an important tool for understanding the interactions present in the adduct. The possibility of monitoring the binding process by means of such a sensitive technique as photoluminescence spectroscopy can gain ground for the design of very efficient enantioselective chemosensors for chiral species.

Introduction

Enantiomeric recognition, as a special case of molecular recognition, is a very important and frequent phenomenon in nature. Examples include the metabolism of single enantiomeric forms of amino acids and sugars in biosynthetic pathways. This phenomenon, which involves the discrimination between the enantiomers of a chiral molecule (guest) by an enantiomerically pure chiral receptor (host), can also be performed using relatively simple synthetic molecules such as crown ethers. Since the pioneering studies of Cram and coworkers on optically pure bis(1,1-dinaphthyl)-22-crown-6 ligands in the early 1970s,[1] a great variety of enantiomerically pure crown ether type host molecules has been prepared with the aim of enhancing their selectivity towards the enantiomers of chiral guest molecules.[2] Among them a number of enantiomerically pure crown ethers have been prepared containing pyridine,[3] pyrimidine,[4] phenanthroline[5] and phenazine[6,7] units. These hosts and their selectivity towards the enantiomers of organic ammonium salts have been extensively studied.[3–8]

Recently the preparation of the new achiral acridino-18-crown-6 ligand **1** and its enantiomerically pure dimethyl-substituted analogue **2** (see below) have been described,[6] but their complexation properties have not been reported.

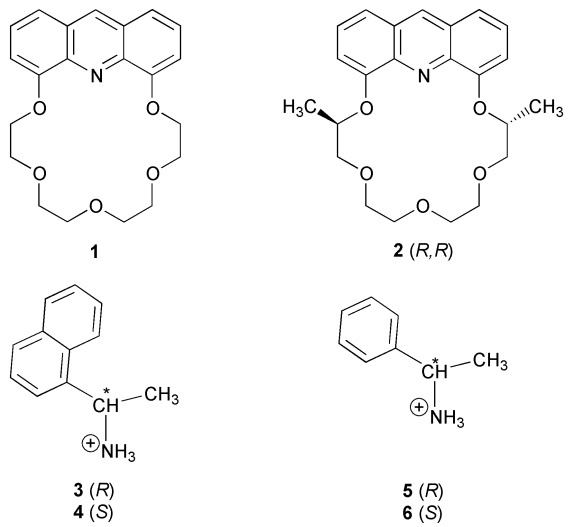
Beside the tripod-like hydrogen bonding which always occurs in the case of analogous crown ethers,[8a,c,e] the extended aromatic ring system of ligands **1** and **2**, securing a strong π–π interaction, also contributes to a great extent to the stability of their complexes with organic ammonium salts containing aromatic moieties. Furthermore, the enhanced rigidity of the enantiomerically pure chiral ligand **2**, especially at the upper part of the macroring containing the stereogenic centers, suggests a high selectivity towards the enantiomers of organic ammonium salts.[8a] In addition, the presence of a luminophoric unit could play a very important role, in fact it could signal the binding event if sufficient interactions are present in the adduct, in order to influence its photophysical properties. This would make the receptor species a very interesting one as a suitable fluorescent chemosensor for enantiomeric recognition, a phenomenon rapidly gaining attention[9–12] in biological, pharmaceutical, analytical and separation sciences, and also in food technology.

We decribe here the application of photoluminescence spectroscopy as a very sensitive tool[13] for monitoring the chiral recognition of the enantiomerically pure crown ether **2** towards the enantiomers of organic ammonium salts.

Experimental

Chemicals

2,5,8,11,14-Pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}0^{21,25}]-heptacosa-15,17,19,21,22,24(1),26-heptaene (**1**),[6] (3*R*,13*R*)-(−)-dimethyl-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}-0^{21,25}]heptacosa-15,17,19,21,22,24(1),26-heptaene (**2**),[6] (*R*)-1-



1 **2** (*R*,*R*)

3 (*R*)
4 (*S*)

5 (*R*)
6 (*S*)

Scheme 1

(1-naphthyl)ethylammonium perchlorate {(*R*)-NEA, **3**[ClO_4]},[14] (*S*)-1-(1-naphthyl)ethylammonium perchlorate {(*S*)-NEA, **4**[ClO_4]},[14] (*R*)-1-phenylethylammonium perchlorate {(*R*)-PEA, **5**[ClO_4]},[14] and (*S*)-1-phenylethylammonium perchlorate {(*S*)-PEA, **6**[ClO_4]}[14] were available from previous work. Acetonitrile Uvasol (Merck) was used as a solvent. Solutions of hosts **1** and **2** were 1.0×10^{-4} M unless otherwise noted.

Equipment

Absorption spectra were recorded with a Perkin-Elmer lambda 40 spectrophotometer. Uncorrected emission, and corrected excitation spectra were obtained with a Perkin-Elmer LS 50 spectrofluorimeter. The fluorescence lifetimes (uncertainty $\pm$ 5%) were obtained with an Edinburgh single-photon counting apparatus, in which the flash lamp was filled with D_2. Luminescence quantum yields (uncertainty $\pm$ 15%) were determined using quinine sulfate in 1 N H_2SO_4 aqueous solution ($\Phi = 0.546$[15]) as a reference. In order to allow comparison of emission intensities, corrections for instrumental response, inner filter effects, and phototube sensitivity were performed.[13] A correction for differences in the refraction index was introduced when necessary.

Binding studies

UV and luminescence spectra were run on 2.5 ml of a 1×10^{-4} M acetonitrile solution of the crown ether. Aliquots (5–10 μl) of 1×10^{-2} M ammonium salt solution were then added with a micro syringe and the spectra recorded. The luminescence intensity values were read at the maximum of each band, namely 335 nm for the fluorescence bands of **3** and **4** and 440 for the acridino-crowns **1** and **2**. These values were fitted to eqn. (1) and (2)

$$I_{corr}(440) = \psi_{cr}(440)C_{cr} + \psi_{cm}(440)C_{cm} \quad (1)$$

$$I_{corr}(335) = \psi_{naph}(335)C_{naph} + \psi_{cm}(335)C_{cm} \quad (2)$$

where C_{cr} and C_{cm} are the concentrations of uncomplexed and complexed crown, respectively, C_{naph} the concentration of the ammonium ion **3** or **4** when present, and ψ_{cr}, ψ_{cm} and ψ_{naph} are the proportionality constants between the corrected emission intensities (in arbitrary units) and the concentrations of the uncomplexed and complexed crown ether, and of the free ammonium ions **3** or **4**, respectively. C_{cm} satisfies the usual binding expression given in eqn. (3).

$$C_{cm}^2 - (2C_{cm} + C_{cr} + C_{naph} + 1/K_{ass})C_{cm} + (C_{cm} + C_{cr})(C_{cm} + C_{naph}) = 0 \quad (3)$$

Values for the equilibrium constant, K_{ass}, were then obtained by simulation of the data with both K_{ass} and ψ_{cm} as adjustable parameters, using a Newton–Raphson procedure to minimise the sum of squares of residuals.

Results and discussion

Absorption spectra

The absorption spectra of the acridino-18-crown-6 ligands **1** and **2** (for **2** see Fig. 1) are quite similar, although the band in the 340–420 nm region of the latter is less structured. Both are, however, remarkably red-shifted (*ca.* 30 nm) compared to the absorption spectrum of the underivatized acridine in the same solvent.[16,17] As for the acridine parent chromophore,[16] this intense and structured band can be attributed to a $^1\pi$–π^* transition, while the observed red-shift can be explained by the larger delocalisation caused by the oxygen atoms in the 4 and 5 positions. For acridine, a ^{1}n–π^* transition is known[16] to lie in the same spectral region, but it is not separable from

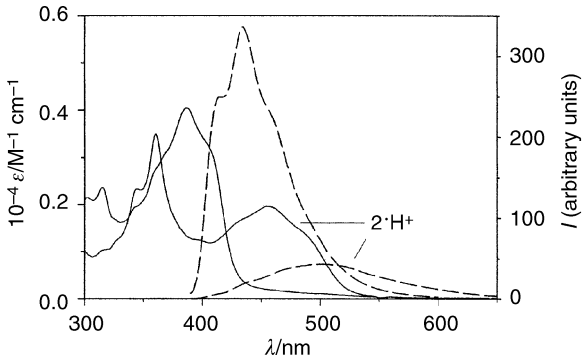


Fig. 1 Absorption (——) and fluorescence spectra (λ_{exc} = 380 nm, – – –) of **2** in acetonitrile before and after addition of trifluoroacetic acid.

the much more intense symmetry allowed $^1\pi$–π^* transition. For compounds **1** and **2** the same argument applies; in fact even if the ^{1}n–π^* transition is found to be (see below) less sensitive to the presence of substituents, it is still hidden by the much more intense $^1\pi$–π^* transition. This is an expected result, since a conjugative substituent generally causes a small- to moderate blue shift for the n–π^* transitions and a large red-shift for the π–π^* transitions.[17,18]

Addition of trifluoroacetic acid to a solution of **1** or **2** leads to noticeable changes (Fig. 1) in the absorption spectrum, causing the decrease of the absorption band centered at 380 nm and the formation of a new band centered at 460 nm, caused by the protonation of the nitrogen atom of the chromophore. This effect is very similar to that already observed for acridine.[17]

The ammonium ions **3** and **4** present the typical absorption bands of the 1-methylnaphthalene chromophore,[19,20] while ions **5** and **6** show absorption bands very similar to those observed for toluene.[19]

Luminescence spectra and excited state lifetimes

The fluorescence of the parent acridine chromophore is known to be solvent dependent; in particular its quantum yield is very low in low polarity solvents and much higher in protic polar solvents. This behaviour has been suggested, although with some controversy,[21] to derive from an inversion of two close-lying excited states, namely the ^{1}n–π^* state (typically not fluorescent) and the $^1\pi$–π^* state (showing usually stronger fluorescence).[16,17,22–24] The corrected fluorescence spectra of the acridino-18-crown-6 ligands **1** and **2** in acetonitrile (Fig. 1) are similar in shape and intensity ($\Phi = 0.15$ and 0.18, respectively); they differ, however, from the spectrum of acridine in the same solvent, since the fluorescence band of the parent compound is blue-shifted and much less intense ($\Phi = 9.6 \times 10^{-5}$ at 298 K).[16] These differences could be attributed to the conjugative effect caused by the oxygen atoms which, as previously discussed, tends to stabilise the $^1\pi$–π^* excited state with respect to the n–π^* one, leading to the possibility of an inversion between them also in aprotic solvents. Such an inversion in fact can explain both the red-shift and the fluorescence intensity increase observed for **1** and **2**, as already observed for 9-aminoacridine.[17] The excited state decay of **1** and **2** can be satisfactorily fitted only with two exponential terms (7.1 and 1.4 ns). On the contrary, the parent acridine in acetonitrile has only one, very short (61 ps) excited state lifetime.[16] When trifluoroacetic acid is added to the solutions of the acridino-crowns, the fluorescence band at 443 nm disappears, while a new broad and weak band centered at 520 nm shows up (see Fig. 1 for **2**), again in accordance with that observed for the parent acridine.[17]

The fluorescence spectra of the ammonium ions **3** and **4** show the very intense fluorescence band typical of the naph-

thalene chromophore ($\lambda_{max} = 335$ nm), which is due to a $^1\pi$–π^* transition. However, deprotonation of the ammonium salts by means of a suitable base causes the partial quenching of the above mentioned fluorescence band and the formation of a broad, structureless band with λ_{max} at 400 nm. This behaviour is consistent, although less dramatic, with that already found for other (aminomethyl)naphthalene derivatives,[25,26] for which the occurrence of an exciplex was invoked to explain the photophysical changes observed upon protonation.

The ammonium ions **5** and **6** show a fluorescence band in the 290–310 nm region, again very similar to that observed for toluene.[19] Their luminescence properties do not change upon deprotonation of the ammonium group.

Binding studies

Interestingly, addition of the organic ammonium ions **3**–**6** to solutions of the acridino-18-crown-6 ligands **1** and **2** causes a red-shift and a decrease in the intensity of the absorption band of the acridine chromophore (see Table 1 and Fig. 2 for the solution containing **2** and **3**). It is noteworthy that the degree of the observed perturbations depends on the nature and configuration of both the crown ether and the ammonium ion. It is also important to emphasize that the typical absorption bands of the acridinium ion were never observed. This excludes the possible attribution of the observed changes in the absorption spectrum to a simple acid–base process, but points rather to the well known association between primary ammonium ions and crown ethers with the same cavity size as **1** and **2**.[8c] The perturbations shown by acridine absorption bands can instead be attributed to two different effects. The first one is the involvement of the nitrogen atom of the acridine chromophore in the hydrogen bonding process. This kind of interaction is expected to shift the band in the same direction as protonation does, but to a much less extent, as observed in fact in this case. The second effect is a π–π interaction between the chromophoric groups of the ammonium ion and the acridine unit. The importance of the role played by the latter effect is supported by the evidence of a much larger decrease in the absorbance when the naphthyl group, having a more extended π-system, is present as a substituent in the ammonium ion.

As far as the fluorescence spectra are concerned, if the excitation is performed in the 340–420 nm region, where only the acridine chromophore absorbs, a change of the luminescence intensity and lifetime is observed (see Table 1 and Fig. 3 for the solution containing **1** and **3**). Again, the observed changes depend on the nature of the compounds involved in the association process (Table 1), and no appearance of the fluorescence band typical of the protonated acridine can be found, in agreement with observations made in the absorption studies. In particular, when the ammonium ions **3** and **4** are added to a solution of an acridino-crown, the fluorescence intensity of the naphthalene chromophore ($\lambda_{em} = 330$ nm) measured upon excitation at 295 nm (where both components absorb) is almost completely quenched in the adduct, while the fluorescence of the acridine moiety ($\lambda_{em} = 440$ nm, $\lambda_{exc} =$ 295 or 380 nm) undergoes only partial quenching (Fig. 4). It is important to note that the excitation spectra recorded at $\lambda_{em} = 445$ nm do not show the absorption of the naphthalene chromophore, indicating that energy transfer from this latter group to the acridine moiety does not occur. Neither can the

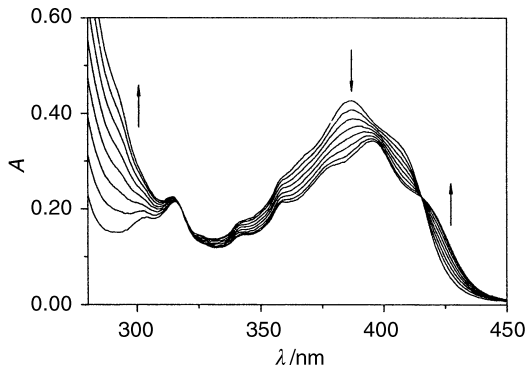


Fig. 2 Absorption spectra of **2** in acetonitrile upon addition of increasing amounts of **3**.

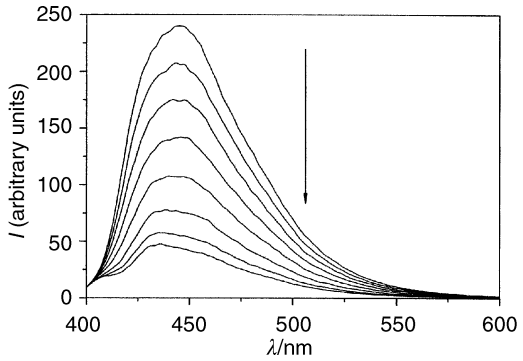


Fig. 3 Fluorescence spectra of **1** in acetonitrile upon addition of increasing amounts of **3**.

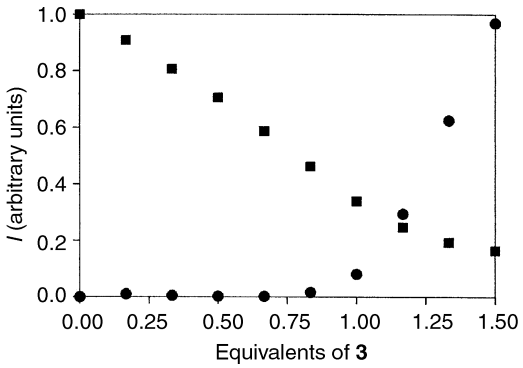


Fig. 4 Fluorescence intensities recorded (■, $\lambda_{exc} = 380$ nm, $\lambda_{em} =$ 440 nm; ●, $\lambda_{exc} = 295$ nm, $\lambda_{em} = 335$ nm) after addition of increasing amounts of **3** to an acetonitrile solution of **1**.

Table 1 Photophysical properties of the crown ethers **1** and **2** and of their adducts with the ammonium ions **3**–**6**

	Absorption		R.T. Fluorescence		
	λ/nm	ε/M^{-1} cm^{-1}	λ/nm	Φ	K_{ass}/M^{-1}
1	383	4500	446	0.083	
2	386	4300	434	0.10	
1·3 and **1·4**	391	3400	446	0.011	2.3×10^6
1·5 and **1·6**	390	3900	446	0.061	2.0×10^6
2·3	395	3850	434	0.066	4.4×10^5
2·4	395	3600	434	0.066	2.3×10^6
2·5	395	4100	434	0.11	3.4×10^5
2·6	395	4000	434	0.11	1.7×10^6

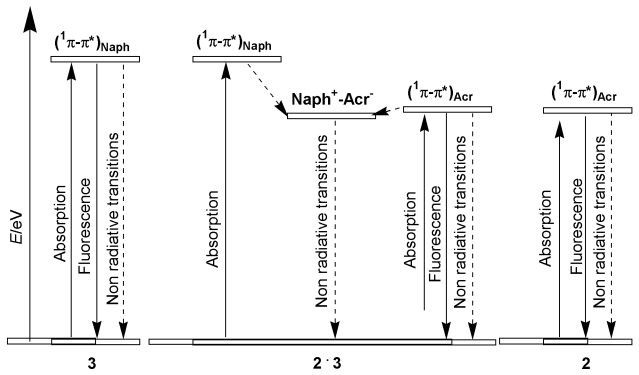


Fig. 5 Schematic representation of the energy levels of **2** and **3**, and of their adduct.

observed quenching of the naphthalene chromophore be due to the partial or complete deprotonation of the ammonium group, since, otherwise, a fluorescence at 400 nm should have been observed. On the other hand, the redox potentials in acetonitrile of the parent chromophores ($E_{ox} = 1.43$ V *vs.* SCE for 1-methylnaphthalene and $E_{red} = -1.62$ *vs.* SCE for acridine[27]) indicate that electron transfer is thermodynamically allowed when the $^1\pi$–π^* excited state of the naphthalene chromophore (3.91 eV) is populated (see Fig. 5). These data suggest that the electron transfer process is the most likely mechanism to explain the complete quenching of naphthalene fluorescence. On the other hand, the acridine fluorescence decrease at 440 nm could be due again to the involvement of the nitrogen atom of the chromophore in hydrogen bonding, or to an electronic interaction between the aromatic systems of the two partners. In particular, the fluorescent $^1\pi$–π^* excited state of the acridine derivative (2.95 eV) is very close in energy to the charge separated state obtained when an electron is transferred from the naphthalene to the acridine. We believe that the latter effect plays a very important role when the naphthyl group is present, and this explains the fact that, when the photoinduced electron transfer process is thermodynamically forbidden, as in the case of **5** and **6** ($E_{ox} = 1.98$ V *vs.* SCE[27] for toluene), modest changes of the fluorescence intensity of the hosts **1** (an intensity decrease) and **2** (an intensity increase) are instead observed. We think that the slightly different behaviour shown by the two crowns **1** and **2** when complexing the phenylethylammonium ions could be due to the bigger steric repulsion introduced by the methyl groups in **2**, resulting in an alteration of the distance and orientation of the two chromophores.

Unfortunately, the fluorescence signal originating from the ions **5** and **6** cannot be used in order to monitor the association process, since their absorption and fluorescence intensities are much weaker and they lie in more unfavourable spectral regions with respect to the bands of the ions containing the naphthalene group.

From the fitting of the fluorescence intensities recorded at 445 nm after addition of increasing amounts of ammonium salts and, where possible, at 330 nm, we were able to obtain the association constant values shown in Table 1. A comparison with the data obtained with chiral crown ethers containing other aromatic units[3,4,5,8] shows that both **1** and **2** have a strong affinity towards organic ammonium ions, and, even more interestingly, the enantiomerically pure chiral crown ether **2** shows high enantioselectivities ($\Delta \log K_a = 0.72$ in the case of the naphthylethylammonium ion, and $\Delta \log K_a = 0.70$ in the case of the phenylethylammonium ion) for chiral organic ammonium ions.

Conclusions

The association process between the acridino-18-crown-6 ligands **1** and **2** and organic ammonium ions causes noticeable changes in the photophysical properties of the single components, and this allows the process to be monitored *via* luminescence spectroscopy with a very high sensitivity. Furthermore, chiral ligand **2** shows high enantioselectivities for chiral organic ammonium ions **3**–**6**, with an important contribution from the π–π interaction between the chromophoric groups of the ammonium ion and the acridine unit. All these features make chiral ligand **2** a suitable fluorescent chemosensor for enantiomeric recognition, a field gaining more and more interest for practical applications.

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