

## Synthesis and Complexation Properties of 3-Aroylcoumarin Crown Ethers. A New Class of Photoactive Macrocycles.

Maria Teresa Alonso, Ernesto Brunet, Concepción Hernandez and Juan Carlos Rodríguez-Ubis\*

*Departamento de Química, C-I. Facultad de Ciencias. Universidad Autónoma de Madrid, 28049-Madrid, Spain  
Fax 34 1 397 3966*

**Abstract:** Synthesis of fluoroionophores consisting of 3-benzoylcoumarins fused with crown ethers in two different modes are described. The resulting macrocycles bore emission properties strongly dependent on metal ions and coumarin substitution and may be therefore used as cation dependent fluorescence signaling systems or triplet sensitizers for lanthanide luminescence.

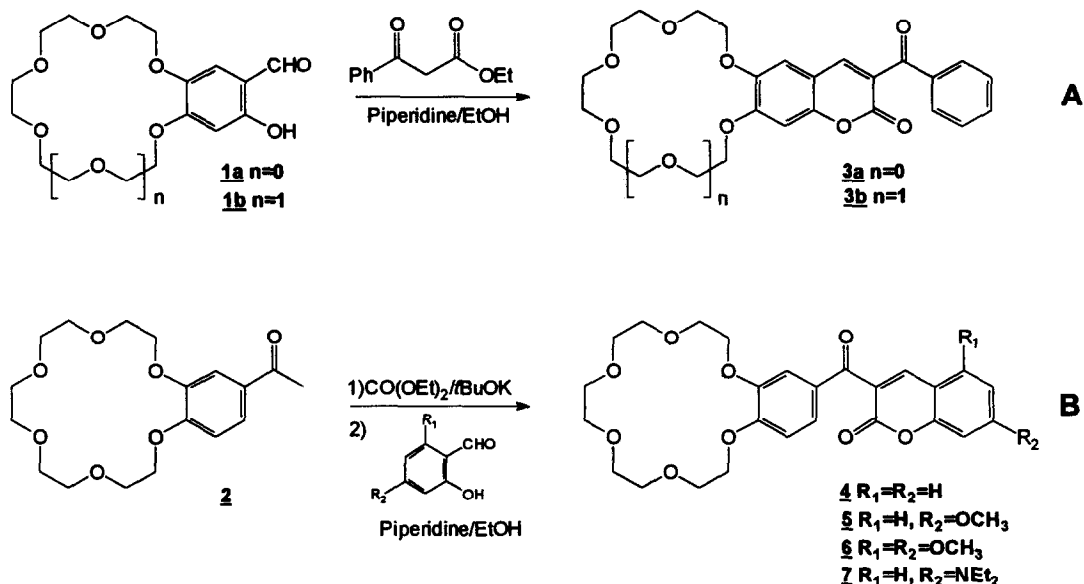
Attachment of a fluorogenic or chromogenic subunit to crown ethers or related species leads to a new class of compounds which is interesting from a theoretical viewpoint as well as for practical purposes.<sup>1</sup> In these host-guest systems, defined as supramolecular species, the structure-specific interactions play a key role in the processes determining the photochemical and photophysical properties. Insertion of a cation into the ionophore cavity can in fact change the absorption spectrum, the luminescence properties, and the photochemical reactivity of the chromophore, opening the way to recognition and determination of metal cations and a variety of other applications.<sup>2</sup>

Coumarins are extremely interesting chromophores by their photochemical and photophysical properties, and have been already used to convert crown ethers and cryptands into fluorescent probes for alkali metal ions.<sup>3</sup> On the other hand, it has been shown that ketocoumarins<sup>4</sup> display sensitization properties, via triplet-triplet energy transfer, which has found numerous industrial applications (crosslinking of many polymers, etc.). This photosensitization might also be applied to excite lanthanide ions in order to enhance their luminescence, a phenomenon with application in fluoroimmunoassay.<sup>5</sup>

The present work deals with the synthesis of 3-aroylcoumarin crown ethers and the preliminary results concerning their luminescence properties. Despite the fact that coumarins are in general highly fluorescent and, therefore, unsuited in principle as lanthanide sensitizers, our results suggest that an adequate selection of substituents in the coumarin nucleus allows the management of the luminescent properties of these molecules.

Two attachment modes of coumarin (**A** and **B** in Scheme) were made in order to compare their complexation and photophysical properties. The key step of the synthesis was the formation of the coumarin nucleus,<sup>6</sup> by condensation of a  $\beta$ -ketoester with a salicylaldehyde derivative in the presence of piperidine (see Scheme). The condensing units **1a-b** and **2**, bearing the crown ether, were obtained in good yields from the reaction in  $\text{Na}_2\text{CO}_3$ /acetone of the corresponding polyethylenoxy diiodides with 2,4,5-trihydroxybenzaldehyde and 3,4-dihydroxyacetophenone, respectively.<sup>7</sup> Lower yields of coumarin crowns were obtained when the macrocyclization reaction was carried out from the respective dihydroxycoumarin.

## Scheme



The complexation of 3-7 with  $Na^+$  and  $K^+$  was directly observed by  $^1H$ -NMR but, since  $Eu^{3+}$  and  $Tb^{3+}$  complexes were paramagnetic, they had to be indirectly evidenced from the  $^1H$ -NMR spectra of the diamagnetic complexes of  $La^{3+}$  whose coordination chemistry is quite similar.

The absorption spectra of compounds 3-7 in acetonitrile showed in all cases intense bands at wavelengths above 320 nm with significant maxima ranging from 322 to 420 nm (see Table).

**Table.** Absorption and emission spectra of coumarin crown ethers 3-7.

Coumarin	UV/Vis $\lambda_{max}^a$	$\epsilon(10^3)$	Fluor. $\lambda_{max}^a$
<b>3a</b>	372	10.6	471
	306	5.8	
<b>3b</b>	373	15.2	469
	303	8.7	
<b>4</b>	322	17.4	-
	287	21.2	
<b>5</b>	335	23	-
<b>6</b>	351	15.9	-
	269	8.2	
<b>7</b>	420	45.9	485
	314	9.2	

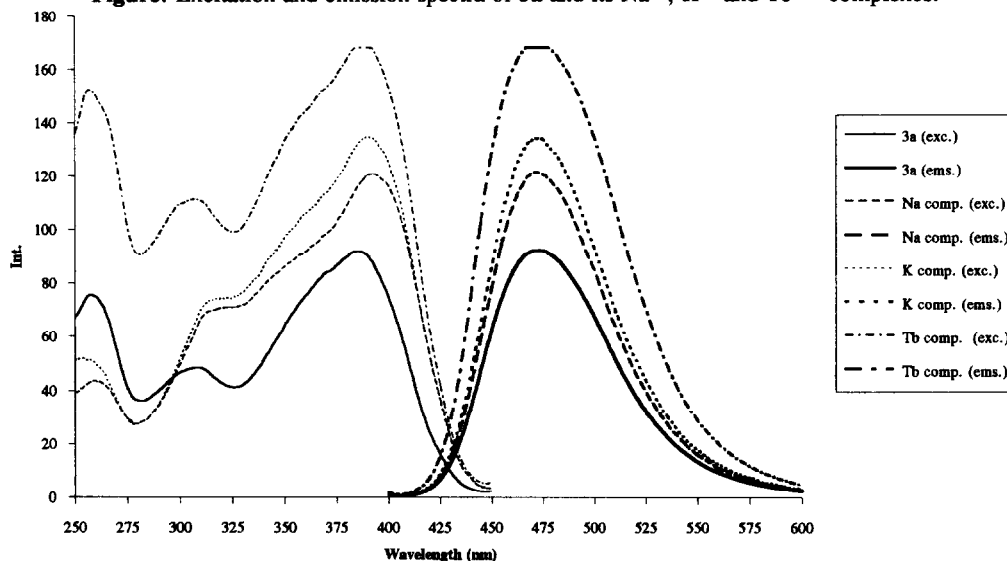
<sup>a</sup> Spectra recorded in acetonitrile solution at  $c = 10^{-5}$ - $10^{-6}$  M.

The  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Eu}^{3+}$  and  $\text{Tb}^{3+}$  complexes did not appreciably change the pattern of the spectra showing very small batho- or hypsochromic effects ( $< 10$  nm) compared to free ligands.

The derivatives **4-6** having alkoxy or no substituents on the coumarin moieties exhibited virtually no fluorescence in acetonitrile at room temperature. The diethylamino derivative **7** showed in turn fluorescence and the 6,7-crown substituted compounds **3a,b** were able to produce room-temperature phosphorescence (483 nm) and/or delayed fluorescence (see below).

Analogously to the absorption spectra, only minor shifts were observed on the emission and excitation wavelengths. However, the intensity was markedly affected by the complexation. In the case of **3a**, as shown in the Figure, the fluorescence intensity increased notably on addition of alkali and lanthanide metal ions ( $10^{-5}$ - $10^{-6}$  M), in the order  $\text{Na}^+ < \text{K}^+ < \text{Tb}^{3+}$ . A plausible explanation for the highest increase observed in the case of  $\text{Tb}^{3+}$  could be the higher rigidity imposed to the complex by this ion because of its higher charge density, making the vibrational deactivation pathways less effective in the complex compared to the free ligand and leading to a more efficient emission process.

**Figure.** Excitation and emission spectra of **3a** and its  $\text{Na}^+$ ,  $\text{K}^+$  and  $\text{Tb}^{3+}$  complexes.



It is well known that the photophysical properties of  $\text{Eu}^{3+}$  and  $\text{Tb}^{3+}$  ions markedly depend on their environment and, in particular, their luminescence is strongly decreased by the inclusion of water molecules in the coordination shell.<sup>8</sup> However, *typical luminescence of Europium (621 nm) and Terbium (525 nm) was observed for some complexes of 3a-b when irradiated into the lowest energy ligand-centered absorption bands*, even though some of the complexes were fluorescent and the crown ethers were not expected to perfectly isolate the lanthanide ions from the water molecules.<sup>9</sup> Therefore, these crown ethers presented simultaneous fluorescence, room temperature phosphorescence and lanthanide luminescence.

Research is under progress to improve the design of these compounds in order to tune their fluorescence and phosphorescence properties, and the quantum yields of induced lanthanide emission as well, by using novel substituted coumarin nuclei and/or selecting different complexing subunits (chelating groups and cryptands).

### Acknowledgments

This work was supported by a Grant from *Comisión Interministerial de Ciencia y Tecnología* (CICYT). Grant No. PB90-0176.

### REFERENCES AND NOTES

- Löhr, H.G.; Vögtle, F. *Acc. Chem. Res.* **1985**, *18*, 65; Takagi, M.; Ueno, K. *Topics Curr. Chem.* **1984**, *121*, 39; Shinkai, S.; Manabe, O. *ibid.*, **1984**, *121*, 67; Bissell, R.A.; Desilva, A.P.; Gunaratne, H.Q.N.; Linch, P.L.M.; Maguire, G.E.M.; Sandanallake, K.R.A. *Chem. Soc. Rev.*, **1992**, *21*, 187.
- Lehn, J.M. *Angw. Chem. Int. Ed. Engl.*, **1987**, *27*, 89; Balzani, V.; Scandola, S. in *Supramolecular Photochemistry*, Ellis Horwood, Chichester, 1991.
- Masilamani, D.; Lucas, M.E.; Hammond, G.S. U.S. Appl. 80721, PCT Int. Appl. NO 89 00,997, *Chem. Abstr.* **1990**, *112*, P51780t; Göçmen, A.; Bulut, M.; Erk, C. *Pure Appl. Chem.* **1993**, *65*, 447; Bourson, J.; Pouget, J.; Valeur, B. *J. Phys. Chem.* **1993**, *97*, 4552 and previous references in the series.
- Specht, D.P.; Martic, P.A.; Farid, S. *Tetrahedron* **1982**, *38*, 1203.
- Horrocks, Jr., W.DeW.; Sudnick, D.R. *Acc. Chem. Res.* **1981**, *14*, 384; Burroughs, S.E.; Eisenman, G.; Horrocks, Jr. W.DeW. *Biophys. Chem.*, **1992**, *42*, 249; Alpha, B.; Ballardini, R.; Balzani, V.; Lehn, J.-M.; Perathoner, S.; Sabbatini, N. *Photochem. Photobiol.* **1990**, *52*, 299; Davidson, R.S., Hilchenbach, M.M. *ibid.*, **1990**, *52*, 431; Bünzli, J.-C. in *Lanthanide Probes in Life, Medical and Environmental Sciences*, Choppin, G.R.; Bünzli, J.-C.G. eds., Elsevier, Amsterdam, 1989, ch. 7; Sowinska, M.; Lebris, M.T.; Valeur, B. *J. Photochem. Photobiol. A Chem.*, **1991**, *60*, 383.
- General method:** The salicylaldehyde (0.25 mmol) and the  $\beta$ -ketoester (0.25 mmol) were dissolved in 3 ml of ethanol. Piperidine (3 drops) was added, and the mixture was refluxed for 4 h. Filtration of the cooled mixture yields the coumarin crown ether as analytically pure crystals. In selected cases, a second crop of coumarin could be obtained by total evaporation of solvent followed by column chromatography (dichloromethane/methanol 5%). Yields 50-80%. All coumarin crown ethers gave correct  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra and elemental analysis.
- General method:** Tetra- or pentaethyleneglycol diiodide (10 mmol) was added to a mixture of 3,4-dihydroxyacetophenone or 2,4,5-trihydroxybenzaldehyde (10 mmol) and sodium carbonate (50 mmol) in acetone (100 ml). The mixture was heated (50-60°C) for 65 h. Salts were filtered out and the solution was concentrated, re-dissolved in dichloromethane (50 ml) and washed with water (3 X 20 ml). The organic phase was dried, concentrated and purified by column chromatography (dichloromethane/methanol 5%). Yields ca. 90%.
- Haas, Y.; Stein, G. *J. Chem. Phys.*, **1971**, *75*, 3668; Haas, Y.; Stein, G. *ibid.*, **1971**, *75*, 3677; Heller, A. *J. Am. Chem. Soc.*, **1966**, *88*, 2058; Kropp, J.L.; Windsor, M.W. *J. Chem. Phys.*, **1967**, *71*, 477.
- Luminescence measurements were performed in spectra grade acetonitrile (0.5% water content) without further purification;  $\text{Eu}^{3+}$  and  $\text{Tb}^{3+}$  nitrates utilized to form the studied complexes contained seven water crystallization molecules and were used as received.