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Synthesis and photochemical properties of new coumarin-derived ionophores and their alkaline-earth and lanthanide complexes

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Dedicated to the memory of the late professor Jesús-Hilario Rodríguez Ramos

Abstract

Several new ionophores derived from crown ethers and iminodiacetic subunits attached to 3-aroylcoumarins have been synthesized and fully characterized. The alkaline-earth complexes of these new ligands were studied from their UV–visible and fluorescence data. Some systems displayed strong bathochromic shifts upon complexation with Mg^{2+} that may make them useful signaling devices of this cation. The corresponding Eu^{3+} and Tb^{3+} chelates were easily formed and their photophysical properties were measured. In all the cases, lanthanide emission lifetimes were in the range of milliseconds albeit quantum yields were low. Possible energy-transfer mechanisms are discussed.

Keywords: Alkaline-earth; Lanthanide; Chelate; Fluorescence; Stokes' shifts

1. Introduction

In recent years, there have been a number of reports of chromogenic or fluorogenic reagents that respond to alkaline, alkaline-earth and lanthanide metal ions [1]. These compounds are based on a donor–acceptor system whose π-system is perturbed after complexation, the perturbation thus being the transducer of discrete recognition events into spectral shifts. In these host–guests systems, the introduction of a cation into the ionophore cavity can 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 [2].

The coumarin nucleus is a very interesting chromophore due to its photochemical and photophysical properties and has been used to convert crown ethers and cryptands into fluorescent probes for alkaline and alkaline-earth metal ions [3]. In addition, it has been shown that 3-ketocumarins display sensitization properties via triplet–triplet energy transfer [4], which may be applied to excite lanthanide ions, despite the fact that coumarins are, in general, highly fluorescent. Our experience on photoactive macrocycles [5], cryptates [6] and polyaminocarboxylates [7] containing the 3-aroylcoumarin motif suggests that these compounds are in fact useful as triplet sensitizers for Eu^{3+} and Tb^{3+} luminescence.

This paper deals with the synthesis and photophysical study of 3-aroylcoumarin crown ethers and azacrown ethers with pendant iminodiacetate arms to achieve complexation of alkaline-earth and lanthanide ions, respectively. Compounds **1**–**4** (Fig. 1), in which the crown ethers are attached through a conjugated 3-aroyl ring or directly to the coumarin chromophore, are appropriate for studying the alkaline-earth complexes, whereas compounds **5a**–**d** were designed to form luminescent lanthanide(III) chelates. All compounds were studied from their UV–visible and emission data.

2. Synthesis of the ligands

Compounds **1**–**4** were synthesized by condensation of a β-ketoester with a salicylaldehyde in the presence of piperidine (Scheme 1) as it was outlined in a previous communication (see Refs. [5,8]).

Two strategies can give access to branched macrocyclic coumarin **5**. One may start from a cavity-containing β-ketoester to be reacted with a commercial salicylaldehyde or begin with the synthesis of the coumarin nucleus and subsequently build the cavity in the last steps (Scheme 2). The latter method is a more convergent route and, therefore, gave better yields.

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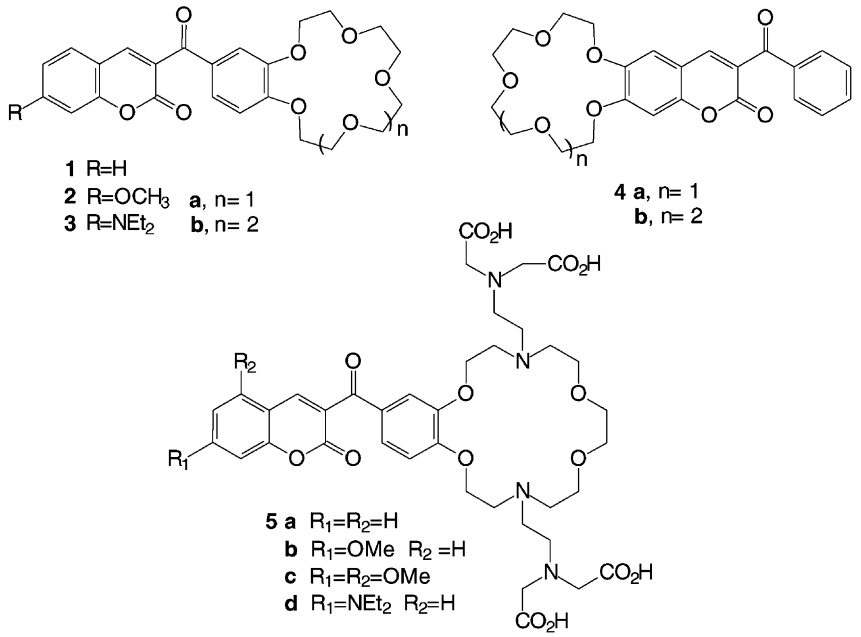


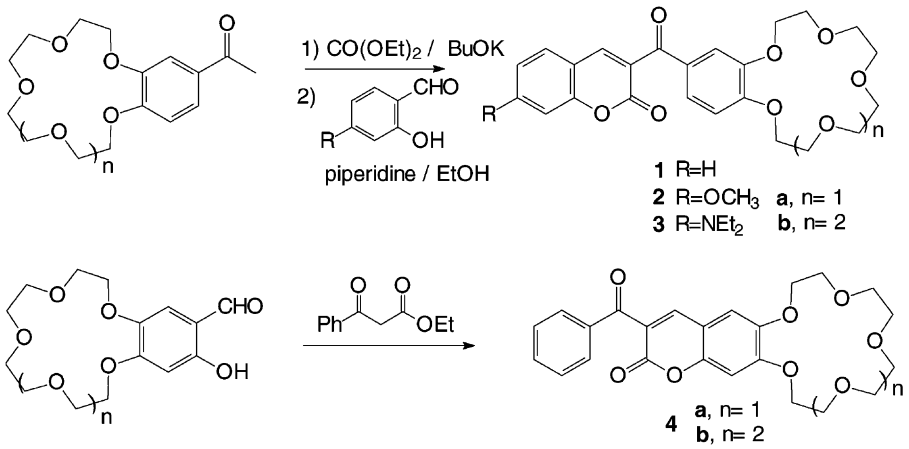
Fig. 1. Compounds studied in this work.

Thus, the reaction of the dimethylated coumarin derivative with 6,9-dioxa-3,12-diazatetradecane-1,14-diol [9] in the presence of sodium carbonate and sodium iodide afforded the macrocycle **6** with yields ranging 55–70% (Scheme 2). The introduction of the amino carboxylate branches was performed after substitution of hydroxyl groups by chlorine atoms and by treatment of the dichloro derivative with di-*tert*-butyliminodiacetate. The resulting *tert*-butyl esters were cleaved to the acids with trifluoroacetic acid in dichloromethane in moderate yields. In all the cases, the analytical data of coumarins **5** and **6** indicated that the isolated compounds enclosed a sodium atom in the azacrown cavity with iodide as counter ion.

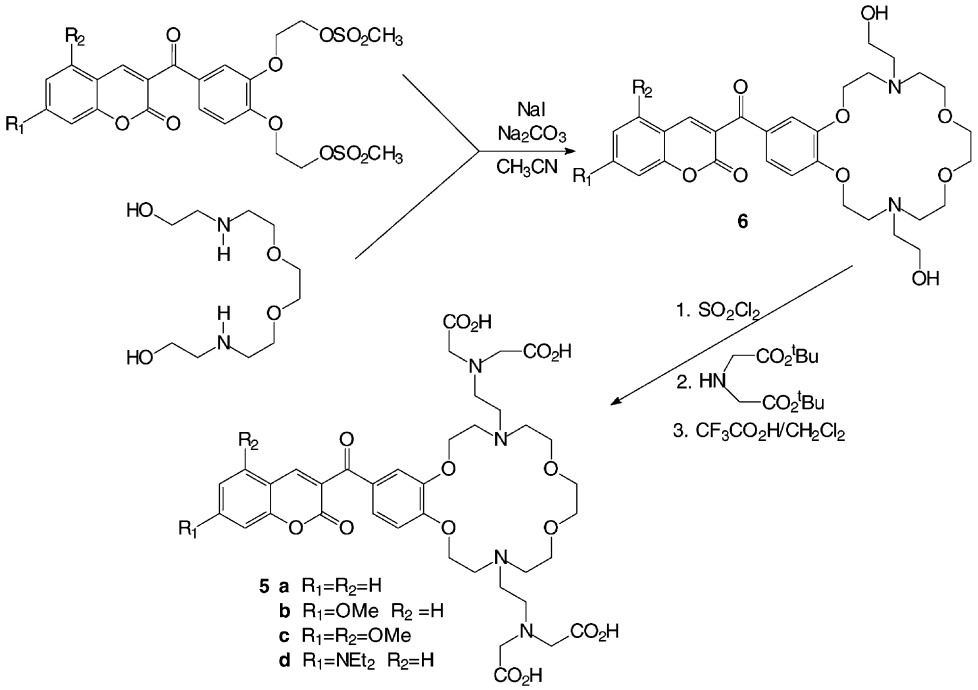
3. Results and discussion

The stoichiometry and stability constants of the complexes of compounds **1**–**4** with alkaline-earth salts was determined by UV–visible in acetonitrile following the method reported by Badaoui and Bourson [10] (Table 1).

The only case in which we observed stoichiometries different from 1:1 were those of the 15-crown-5 derivatives with Ba^{2+}. It appears that the largest metal in the series needs the concurrence of two relatively small 15-membered crowns from two different molecules to form a stable complex. This has been observed in the literature for similar situations [11].



Scheme 1.



Scheme 2.

3.1. UV–visible studies

It has been lately shown that coumarins increase their dipolar moment when excited, but it has been argued [12] that better than the old ICT state it is more likely to propose that the charge-separated resonance forms have simply a superior contribution in the excited state. For compounds with an electron acceptor part conjugated with a donor part, the stabilization of the dipole moment is more important in the excited state than in the ground state. Therefore, excitation of our coumarins should induce the development of higher electron density in the aroyl part and, consequently, a lower density at the other end. In the case of complexes formed by compounds **1**–**3**, whose crowns are located where the electron density increases (hence the bound cation can interact with the negatively charged electron acceptor part of the molecule), the stabilization upon complexation of the excited state is more important than the stabilization of the ground state due to an increase of the dipole moment within the excitation. In agreement with this assumption, Table 2 shows general bathochromic shifts when ligands **1**–**3** form the alkaline-earth metal complexes. The opposite tendency (hypsochromic shifts) showed by compounds **4**, reinforces the interpretation because now the crown is attached where a positive charge should be developed in the excited state, thus making the complexes less stable than the parent ligands **4** when excited.

Table 1
Binding constants and stoichiometries of the complexes of compounds **1**–**4** with alkaline-earth cations in CH_3CN at 20 °C

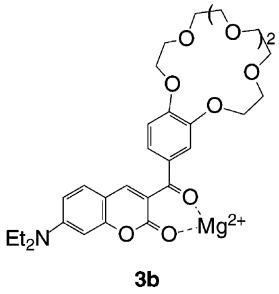
Compound	Log K_s stoichiometry		
	Mg^{2+}	Ca^{2+}	Ba^{2+}
1a	4.90 ± 0.05 ML	5.27 ± 0.03 ML	9.94 ± 0.05 ML_2
1b	–	6.4 ± 0.1 ML	6.9 ± 0.2 ML
2a	5.2 ± 0.1 ML	5.1 ± 0.1 ML	10.2 ± 0.5 ML_2
2b	–	7.0 ± 0.1 ML	7.3 ± 0.1 ML
3a	5.64 ± 0.04 ML	5.35 ± 0.02 ML	11.1 ± 0.1 ML_2
3b	3.99 ± 0.01 ML	6.7 ± 0.1 ML	7.3 ± 0.1 ML
4a	4.6 ± 0.1 ML	4.64 ± 0.03 ML	8.65 ± 0.03 ML_2
4b	–	6.9 ± 0.2 ML	7.6 ± 0.1 ML

Table 2
Wavelength maxima in nanometer of metal ion complexes of coumarins **1**–**4** (acetonitrile)

Compound	Ligand	Complexes		
		Mg^{2+}	Ca^{2+}	Ba^{2+}
1a	287	+6	+6	+6
	324	–	–	–
2a	336	+6	+7	+6
3a	416	+14	+16	+5
			+50 (sh)	
1b	287	0	–	–
	324	0	+6	+6
2b	336	−1	+6	+6
3b	416	+48	+18	+10
			+49 (sh)	
4a	304	−11	−10	−7
	374	−18	−23	−14
4b	304	−1	−9	−8
	374	0	−16	−16

The remarkably large bathochromic shift suffered by **3b** with Mg^{2+} is worthy of a particular comment. It should be noted that we already reported elsewhere [13] that a related 3-aroyl-7-diethylamino coumarin without any crown in its structure displayed the same red-shift. In this case, where no crown is present, the interaction of the metal should be established by the co-operation of chromene and aroyl carbonyl groups. For that reason, it must be assumed that the large 18-crown-6 of **3b** does not play any role in the complex formation with the small Mg^{2+}. The large shift (+48 nm) of **3b** is the highest in the series because the NEt_2 group strongly stabilizes the charge separation as compared with OMe group (**2**) or no substituent (**1**). To sum up, this data indicate a competition between the crown and the two carbonyl groups in complex formation of ligands **1**–**3**, that is controlled by coumarin substitution at 7-position and conditioned by the charge/radius ratio of the metal and the solvent.

Table 3 gathers the absorption maxima for complexes of coumarins **5a**–**d** with sodium, europium and terbium ions. It is noteworthy apparently that the small bathochromic shifts found. One should note that the comparison is established with the sodium complex instead of free ligands as in coumarins **1**–**4** (Table 2). The higher charge/radius ratio of the lanthanides further stabilizes the excited state already stabilized by sodium. Taking into account that sodium is unlikely to interact with the carbonyls, the small stabilization gained with lanthanides suggest that the complexes are formed through the crown and amino polycarboxylate branches and, consequently, the two carbonyl groups do not participate in complexation. However, compound **5d** in methanol showed a shoulder at 466 nm corresponding to a bathochromic shift of +41 (cf. Table 3, Figs. 2 and 3) that does not appear in water. Although, the emergence of a shoulder may be due to various reasons, the regularities found in the bathochromic shifts of a variety of complexes of 7-diethylamino coumarins allow us to point the origin of the shoulder to the participation of species, where the carbonyl groups complex the lanthanide metal. Water is polar enough to hamper this kind of carbonyl coordination and no shoulder was observed in this solvent.



3b

Fig. 2. Idealized structure of magnesium complex of **3b**.

Finally, the lower energy absorption maxima of compounds **5** were red shifted when the solvent was changed from methanol to water, possibly as a consequence of the higher stabilization of S_1 excited state in the more polar solvent.

3.2. Emission spectra

All compounds were fluorescent except **1**, **2** and **5a**–**c** and their corresponding complexes. It can be seen from data collected in Table 4 that complexation induced little changes in fluorescence quantum yields (ϕ values) excluding **4b**, which showed total fluorescence extinction when bound to Ca^{2+} and Ba^{2+}. In general, the presence of the cations should provide new pathways for emission quenching, that might be enhanced if the chromophore and the crown are conjugated

Table 3
Wavelength maxima in nanometer of metal ion complexes of coumarin **5** (solvent methanol or water as indicated in each case)

Compound	Complex		
	Na^+	Eu^{3+}	Tb^{3+}
5a			
MeOH	288	+1	+1
	318	+1	0
H_2O	296	0	0
	323	0	0
5b			
MeOH	338	+1	+1
H_2O	352	+2	+2
5c			
MeOH	357	+1	+1
H_2O	369	+1	+1
5d			
MeOH	425	+6	+6
		+41 (sh)	+41 (sh)
H_2O	439	0	0

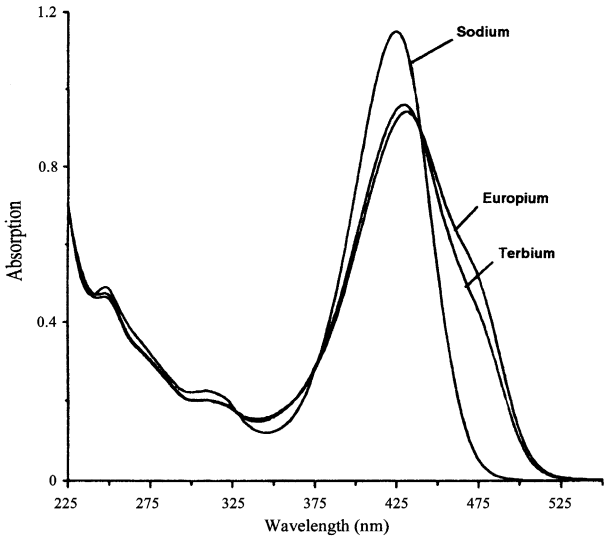


Fig. 3. Absorption spectra of **5d** sodium, europium and terbium complexes in methanol.

Table 4
Emission wavelengths in nanometer, Stokes' shifts ($\Delta\nu \times 10^{-3}\,cm^{-1}$) and quantum yields ($\phi \times 10^2$) of coumarins **3**–**5** (solvent: acetonitrile, unless otherwise indicated)

Compound	Ligand (Na^+ complex)	Complexes				
		Mg^{2+}	Ca^{2+}	Ba^{2+}	Eu^{3+}	Tb^{3+}
3a						
$\lambda_{emission}$	483	491	490	487		
ϕ	6.0	6.0	5.0	6.0		
$\Delta\nu$	3.33	2.89	2.74	3.22		
3b						
$\lambda_{emission}$	483	488	488	488		
ϕ	7.0	11.0	10.0	9.0		
$\Delta\nu$	3.33	1.13	2.55	2.89		
4a						
$\lambda_{emission}$	472	470	470	472		
ϕ	13.0	5.0	14.0	14.0		
$\Delta\nu$	5.55	6.81	7.21	6.59		
4b						
$\lambda_{emission}$	469	471	–	–		
ϕ	11.0	4.0	<1.0	<1.0		
$\Delta\nu$	5.42	5.51	–	–		
5d[a]						
$\lambda_{emission}$	(492)				494	494
ϕ	(5.6)				7.3	7.1
$\Delta\nu$	(3.2)				2.96	2.96
5d[b]						
$\lambda_{emission}$	(489)				488	488
ϕ	(0.7)				0.7	0.7
$\Delta\nu$	(2.33)				2.29	2.29

[a] Methanol.
[b] Water.

and the latter gives the best host–guest fit. To this effect, it is remarkable that **4b** bears the crown that best matches with the larger Ca^{2+} and Ba^{2+} cations directly bonded to the coumarin. It can be also observed that quantum yield of fluorescence decreased 10 times in compounds **5** when the solvent changed from methanol to water.

The variation of Stokes' shifts upon complexation is a phenomenon that has been largely discussed in related compounds [14]. After excitation, the molecule relaxes in a lapse of picoseconds to the lowest vibrational level of the first excited electronic state (S_1). The lowest S_1 state generally has a longer lifetime that allows changes in the local environment. That is why it can be assumed that at room temperature in a polar, non-viscous solvent as acetonitrile, methanol or water solvation interactions are relatively fast and reach equilibrium prior to emission [15]. Therefore, if excitation increases the molecular dipole moment, as it largely occurs in coumarins with strongly donor substituents in 7-position [16], reorganization of the solvent may be involved to stabilize the excited state hence making Stokes' shift larger [17].

But in the cases where the S_1 state gains stability upon complexation (compounds **1**–**3**) the role of solvation should be less important compared to the free ligand and Stokes' shift must be lower. This is the situation of **3a** and **3b** that, upon complexation, exhibited in absorption (Table 2) the highest bathochromic shifts, and a decrease of Stokes' shifts in fluorescence (Table 4). In the contrary, destabilization of S_1 by complexation should increase the need for solvent relaxation, making Stokes' shift larger. This is the case of compounds **4a** and **b** where cation is bound to the crown that is placed where positive charge develops in the excited state. In fact, complexation of **4a** and **b** produced fairly large hypsochromic shifts in absorption (Table 2) and increased Stokes' shifts in emission (Table 4). On the other hand, Mg^{2+} complex of **3b** showed the lowest Stokes' shift (ca. $10^{-3}\,cm^{-1}$, cf. Table 4). This is reasonable considering the structure suggested for this complex (Fig. 2) and assuming that Mg^{2+} confers a high degree of stabilization to the excited state of **3b**. Complexes of coumarins **5** showed lower Stokes' shifts values in water than in methanol, a finding that can be easily explained using the same reasoning that the highest stabilization of the S_1 state is achieved in the more polar solvent.

3.3. Lanthanide emission

Time resolved emission spectra of Eu^{3+} and Tb^{3+} complexes of **5a**–**d** were recorded in methanol and water and data are gathered in Table 5. Unfortunately, the resulting luminescence quantum yields were low in methanol and

Table 5
Excitation wavelengths, lifetimes (τ) and quantum yields ($\phi \times 10^3$) of coumarin **5** (solvent methanol)

Coumarin	Eu^{3+} complex (λ_{ems}: 618 nm)			Tb^{3+} complex (λ_{ems}: 547 nm)		
	λ_{exc} (nm)	τ (ms)	ϕ	λ_{exc} (nm)	τ (ms)	ϕ
5a	289	0.52	1.0	275 (sh)	1.24	3.0
5b	339	0.47	1.0	280 (sh)	1.29	3.0
5c	358	0.46	1.0	284 (sh)	1.18	6.0
5d	431	0.50	$<10^{-1}$	290 (sh)	1.44	2.0

negligible in water. It is well known that the photophysical properties of Eu^{3+} and Tb^{3+} ions markedly depend on their environment, i.e. their luminescence is strongly decreased by the presence of water molecules in the coordination sphere [18]. The low quantum yield values measured thus show that ligands **5a**–**d** do not supply sufficient protection to the lanthanide ions from the O–H water quenchers.

Besides, excitation and absorption spectra only matched for Eu^{3+} complexes suggesting that Tb^{3+} was not sensitized by the expected absorption/energy-transfer/emission (A–ET–E) process from the triplet state of the ligand. In accordance with the long wavelength of their absorption maxima (Table 3), it appears that the excited triplet state of Tb^{3+} complexes results too low for the energy transfer process to the $^5D_4$ emitting levels of this metal to be effectively attained. However, the observed long emission lifetimes, in the range of milliseconds, in particular for Tb^{3+}, suggest that somewhat, there should be a feasible energy-transfer mechanism from the chromophore to terbium. This situation is similar to what we found in related coumarins [6]. An explanation to this behavior can be found if one conceives 3-aroylcoumarins as constituted by two relatively independent chromophores, only formally conjugated through the carbonyl group. Semiempirical calculations of 3-benzoylcoumarin at the AM1 level showed that the preferred conformation of the 3-benzoyl moiety is very far away from planarity with the coumarin nucleus, both in the ground and excited state. Therefore, the 3-aroyl moiety may be considered absorbing light independently by its $S_n(\pi \rightarrow \pi^*)$ transition, much higher in energy, that is able to sensitize Tb^{3+} to little extent, due the low quantum-yield observed. This is supported by our previous results that showed 3,4-dioxaacetophenone chromophore as an excellent sensitizer for terbium [7]. Levels S_1 and T_1, formally coumarin-centered, are too low lying and their energy could be transmitted to europium but not to terbium. To our knowledge, they are a few the examples where a mechanism of energy transfer to lanthanide ions from excited states higher than S_1 or T_1 is proposed [19].

4. Conclusion

Several new ionophores derived from crown ethers and iminodiacetic subunits attached to 3-aroylcoumarins have been synthesized. Some systems displayed significant bathochromic shifts upon complexation with Mg^{2+} and not with the other alkaline-earth cations, a fact that may make them useful in the signaling of this metal. Co-operation between the chromene and the 3-aroyl carbonyl groups is essential for the strong chelation to Mg^{2+}. The comparison of the Stokes' shifts of fluorescence measured in the absorption–emission process of fluorescent compounds and their metal complexes have revealed that the presence of the cation may also change the relative stability of ground and excited state. Sensitized Eu^{3+} and Tb^{3+} emission was observed in methanol with long lifetimes in the range of milliseconds, although with low quantum yield values. Various A–ET–E mechanisms can be at play, in which the coumarin and 3-aroyl chromophores could be formally considered as independently absorbing.

5. Experimental

5.1. General

^{1}*H-NMR and* ^{13}*C-NMR*. Bruker AC-200 (Departamento de Química Orgánica, DCO) and AMX-300 (Servicio Interdepartamental de Invesigación, SIdI). M.S.: VG Autospec spectrometer (SIdI) in FAB mode (L-SIMS$^+$) or EI+. Absorption spectra: Lambda 6 Perkin-Elmer spectrophotometer (DCO). Excitation and emission spectra: LS50 Perkin-Elmer spectrofluorometer (DCO). The excitation spectra were automatically corrected, and the emission spectra were corrected according to the instrument guidebook.

The emission quantum yields were measured by a relative method using the Eu^{3+} and Tb^{3+} complexes of *N*,*N*,*N*′, *N*′-(6,6″-aminomethyl-4′-phenyl-2,2′ 6′,2″-terpyridine) tetrakis (acetic acid) as a standard and referenced to quinine sulfate. The expected errors of this measurement are within 30%. The total luminescence intensities of complexes were determined by integrating the emissions of each lanthanide chelate. Emission lifetimes were measured in methanol and estimated errors are 10%.

Elemental analyses. Perkin-Elmer CHN 2400 automatic analyzers (SIdI). All solvents were purified prior to their use. Alkaline-earth perchlorates, lanthanide chlorides and oxides were purchased from Aldrich and used as received. IUPAC names of compounds were obtained from ChemWeb: http://cwgen.chemweb.com/autonom/autonomsearch.html.

Synthesis of alkakine-earth complexes and absorption and emission measurements. The complexes were formed by addition of 50 equiv. of the corresponding alkaline-earth perchlorate salt in acetonitrile (10^{-2} M) to the coumarin solutions (3.2×10^{-6} M for absorption and 3.2×10^{-7} M for emission). Absorption–emission parameters were analyzed from the same spectroscopic grade solvent. The emission quantum yields were referenced to 1 N H_2SO_4 solution of quinine sulfate ($\phi = 0.546$) [20]. The expected errors of this measurement are within 30%.

Synthesis of lanthanide complexes and absorption and emission measurements. The complexes were formed by addition of equimolecular amounts of the corresponding lanthanide triflate salts in methanol and water (10^{-2} M) to the coumarin solutions (3.2×10^{-5} M for absorption and 3.2×10^{-6} M for emission, except to7-diethylaminoderivatives whose concentration were 1.6×10^{-6} M). The resulting solutions were keep closed at r.t. for 18 h. Absorption–emission parameters were analyzed from the same spectroscopic grade solvent. The emission quantum yields were performed and referenced as above.

5.2. General methods

5.2.1. Synthesis of coumarin ring (Compounds **1**–**3**)

A equimolecular mixture of the corresponding salicylaldehyde and the β-ketoester were dissolved in ethanol. Piperidine (3–5 drops) were added, and the mixture was refluxed for 2–4 h. Filtration of the cooled mixture yields the coumarin crown ether or ethylendioxa as analytically pure crystals.

*Reaction of dimethylated derivatives with 6,9-dioxa-3,12-diazatetradecane-1,14-diol (Compounds **5**)*. A mixture of dimethylated coumarine, 6,9-dioxa-3,12-diazatetradecane-1,14-diol, sodium iodide and sodium carbonate in acetonitrile was heated in an autoclave to 120 °C under argon for 65 h. After solvent evaporation, the crude residue was chromatographed in silica gel (dichloromethane/methanol: 90/10) to give a solid which was triturated with diethyl ether to give the macrocyclic derivatives isolated by filtration as sodium iodide complexes.

Transformation of hydroxyl groups in tert-butyl iminodiacetate groups. A solution of one of compounds **6a**–**d** in dichloromethane was cooled in an ice–salt bath under argon. Thionyl chloride was added with stirring for 10 min. The excess of thionyl chloride and dichloromethane were evaporated and then, *tert*-butyl iminodiacetate, sodium iodide, sodium carbonate and acetonitrile were added in the amounts indicated in each case. The mixture was refluxed under argon for 24 h. After solvent evaporation, the crude residue was chromatographed in silica gel (dichloromethane/methanol: 95/5) to yield the tetraester derivatives in the form of sodium complex with iodide as counterion.

Cleavage of the tert-butyl esters. A mixture of the tetraester derivative and trifluoroacetic acid in dichloromethane was stirred at room temperature for 18 h. Then, the solvent and the excess of trifluoroacetic acid were evaporated. The residue was triturated with THF and the tetra-acid derivatives isolated by filtration as sodium iodide complexes.

5.2.2. Synthesis of the precursors of compounds **1**–**3a** and **b**

1-(3,4-Dihydroxy-phenyl)-ethanone [21]. It was synthesized by means of Fries rearrangement starting from acetic acid 2-acetoxy-phenyl ester [22], m.p.: 119–120 °C (literature, 115–116 °C). ^{1}H-NMR ($CDCl_3$ + 1 drop of MeOD) δ: 7.45–7.40 (m, 2H, H-2, H-6); 6.88 (d, 1H, $J = 8.7$ Hz, H-5); 3.18 (br s, 2H, OH); 2.54 (s, 3H, CH_3).

1-(6,7,9,10,12,13,15,16-Octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecen-2-yl)-ethanone. A mixture of 1-(3,4-dihydroxy-phenyl)-ethanone (0.90 g, 5.92 mmol), 1-(2-iodo-ethoxy)-2-[2-(2-iodo-ethoxy)-ethoxy]-ethane (2.45 g, 5.92 mmol), and Na_2CO_3 (3.14 g, 29.6 mmol) in 60 ml of acetone was heated until 60 °C with stirring for 65 h. The salts were filtered off, and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (75 ml) and washed with water (3 × 50 ml). After solvent evaporation the solid was chromatographed in silica gel column (CH_2Cl_2/methanol: 95/5) yielding the product as a white solid 83%; m.p.: 95–96 °C (literature [23,24], 96–97, 95–96 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.48 (dd, 1H, $J = 2.0$; 8.2 Hz, H-6); 7.42 (d, 1H, $J = 2.0$ Hz, H-2); 6.79 (d, 1H, $J = 8.2$ Hz, H-5); 4.13–4.08 (m, 4H, $ArOCH_2$); 3.86–3.81 (m, 4H, $ArOCH_2CH_2$); 3.70–3.57; 3.68 (m; s, 8H, OCH_2); 2.47 (s, 3H, CH_3). ^{13}C-RMN ($CDCl_3$) δ: 196.1 (CO); 153.0 (C-4); 148.2 (C-3); 130.0 (C-1); 123.1 (C-6); 112.0 (C-2); 111.2 (C-5); 70.6; 69.8; 69.7; 68.8; 68.6; 68.4; 68.1 (CH_2O); 25.7 (CH_3). Anal. calc. for $C_{16}H_{22}O_6$: C, 61.93; H, 7.10. Found: C, 61.55; H, 7.09.

1-(6,7,9,10,12,13,15,16,18,19-Decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecen-2-yl)-ethanone. A mixture of 1-(3,4-dihydroxy-phenyl)-ethanone (0.47 g, 3.09 mmol), 1-iodo-2-{2-[2-(2-iodo-ethoxy)-ethoxy]-ethoxy}-ethane (1.42 g, 3.09 mmol) and Na_2CO_3 (2.14 g, 15.5 mmol) in 30 ml of acetone was heated until 60 °C with stirring for 48 h. The salts were filtered off, and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (50 ml) and washed with water (3 × 30 ml). After solvent evaporation, the product was obtained as an analytically pure white solid. Yield 97%; m.p.: 78–79 °C (literature [20], 77–78 °C). ^{1}H-RMN ($CDCl_3$) δ: 7.52 (dd, 1H, $J = 2.0$; 8.3 Hz, H-6); 7.46 (d, 1H, $J = 2.0$ Hz, H-2); 6.84 (d, 1H, $J = 8.3$ Hz, H-5); 4.19–4.15 (m, 4H, $ArOCH_2$); 3.93–3.86 (m, 4H, $ArOCH_2CH_2$); 3.75–3.62; 3.65 (m; s, 12H, OCH_2); 2.51 (s, 3H, CH_3). ^{13}C-RMN ($CDCl_3$) δ: 196.3 (CO); 152.8 (C-4); 148.1 (C-3); 130.0 (C-1); 123.1 (C-6); 112.0 (C-2); 111.3 (C-5); 70.4; 70.2; 68.9; 68.8; 68.6; 68.4 (CH_2O); 25.8 (CH_3). Anal. calc. for $C_{18}H_{26}O_7$: C, 61.02; H, 7.34. Found: C, 60.69; H, 7.56.

3-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-3-oxo-propionic acid ethyl ester. A suspension of sodium hydride (in mineral

oil 60%, 320 mg, 8.0 mmol) in THF (5 ml) was refluxed under argon for 5 min. 1-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-ethanone was added (350 mg, 2.0 mmol) and next, very slowly, diethyl carbonate (0.6 ml, 5.0 mmol). The mixture was heated under reflux for 1.5 h and then 3 h at r.t. Ethanol (3 ml) and HCl (2%, 20 ml) were added and the mixture was stirred for 1 h. At that point the crude mixture was extracted with CH_2Cl_2 (2 × 25 ml), the organic layer dried over sodium sulfate and the solvent evaporated. The residue was column chromatographed in silica gel (ethyl acetate/hexane: 1/2). The product was isolated as a white solid. Yield 74%; m.p.: 55–56 °C. ^{1}H-RMN ($CDCl_3$) (corresponding to mayor tautomer of β-ketoester), δ: 7.43 (d, 1H, J = 2.1 Hz, H-2); 7.42 (dd, 1H, J = 2.1; 9.0 Hz, H-6); 6.86 (d, 1H, J = 9.0 Hz, H-5); 4.29–4.19 (m, 4H, $ArOCH_2$); 4.16 (q, 2H, J = 7.2 Hz, CH_3CH_2O); 3.87 (s, 2H, $OCCH_2CO$); 1.22 (t, 3H, J = 7.2 Hz, CH_3CH_2O). ^{13}C-RMN ($CDCl_3$) (corresponding to mayor tautomer of β-ketoester) δ: 190.8 (ArCO); 167.5 (EtOCO); 148.4 (C-4); 143.3 (C-3); 129.6 (C-1); 122.5 (C-6); 117.7 (C-2 or C-5); 117.2 (C-2 or C-5); 64.5; 63.9 ($ArOCH_2$); 61.2 (CH_3CH_2O); 45.5 ($OCCH_2CO$); 13.9 (CH_3CH_2O). Anal. calc. for $C_{13}H_{14}O_5$: C, 62.40; H, 5.60. Found: C, 62.05; H, 5.49.

3-(6,7,9,10,12,13,15,16-Octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecen-2-yl)-3-oxo-propionic acid ethyl ester. To a solution of 15-crown-5 acetophenone derivative (1.50 g, 4.84 mmol) in diethyl carbonate (30 ml) was added potassium *tert*-butoxide (1.10 g, 9.68 mmol), and it was introduced in a ultrasound bath for 4 h under argon. Then, hexane was added (30 ml) and the orange–red solid was filtered and dissolved in water, HCl 10% was added until pH = 2. This aqueous layer was extracted with CH_2Cl_2 (3 × 50 ml), dried over sodium sulfate and the solvent evaporated. The oily residue was chromatographed in silica gel column (CH_2Cl_2/methanol: 97/3) yielding the product as a yellow oil which solidifies in several hours. Yield 75%; m.p.: 85–86 °C. ^{1}H-RMN ($CDCl_3$) (corresponding to mayor tautomer of β-ketoester) δ: 7.50 (dd, 1H, J = 2.0; 8.4 Hz, H-6); 7.46 (d, 1H, J = 2.0 Hz, H-2); 6.73 (d, 1H, J = 8.4 Hz, H-5); 4.18–4.11 (m, 4H, $ArOCH_2$); 4.16 (q, 2H, J = 7.1 Hz, CH_3CH_2O); 3.92 (s, 2H, $OCCH_2CO$); 3.91–3.85 (m, 4H, $ArOCH_2CH_2$); 3.74–3.63; 3.72 (m; s, 8H, OCH_2); 1.22 (t, 3H, J = 7.1 Hz, CH_3CH_2O). ^{13}C-RMN ($CDCl_3$) (corresponding to mayor tautomer of β-ketoester) δ: 190.7 (ArCO); 167.4 (EtOCO); 153.6 (C-4); 148.5 (C-3); 128.9 (C-1); 123.4 (C-6); 112.3 (C-2); 111.3 (C-5); 70.7; 70.2; 69.8; 68.9; 68.7; 68.5; 68.2 (OCH_2); 61.0 (CH_3CH_2O); 45.3 ($OCCH_2CO$); 13.8 (CH_3CH_2O). Anal. calc. for $C_{19}H_{26}O_8$: C, 59.68; H ,6.81. Found: C, 59.56; H, 6.88.

3-(6,7,9,10,12,13,15,16,18,19-Decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecen-2-yl)-3-oxopropionic acid ethyl ester. It was synthesized following the procedure described above, starting from 18-crown-6 acetophenone derivative (1.06 g, 2.99 mmol) diethyl carbonate (20 ml), and potassium *tert*-butoxide (0.71 g, 5.98 mmol). The product was isolated as a yellow oil. Yield 78%. ^{1}H-RMN ($CDCl_3$) (corresponding to mayor tautomer of β-ketoester) δ: 7.53 (dd, 1H, J = 2.0; 8.2 Hz, H-6); 7.50 (d, 1H, J = 2.0 Hz, H-2); 6.88 (d, 1H, J = 8.2 Hz, H-5); 4.27-4.17 (m, 4H, $ArOCH_2$); 4.20 (q, 2H, J = 7.1 Hz, CH_3CH_2O); 3.97–3.90 (m, 4H, $ArOCH_2CH_2$); 3.94 (s, 2H, $OCCH_2CO$); 3.79–3.66; 3.69 (m; s, 12H, OCH_2); 1.25 (t, 3H, J = 7.1 Hz, CH_3CH_2O). ^{13}C-RMN ($CDCl_3$) (corresponding to mayor tautomer of β-ketoester) δ: 190.9 (ArCO); 167.6 (EtOCO); 153.6 (C-4); 148.6 (C-3); 129.1 (C-1); 123.5 (C-6); 112.4 (C-2); 111.6 (C-5); 70.7; 70.6; 70.4; 69.2; 69.1; 68.8; 68.7 (OCH_2); 61.2 (CH_3CH_2O); 45.6 ($OCCH_2CO$); 13.9 (CH_3CH_2O).

*3-(6,7,9,10,12,13,15,16-Octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecene-2-carbonyl)-chromen-2-one(**1a**)*. It was synthesized following the general method starting from the corresponding β-ketoester (345 mg, 0.9 mmol), salicylaldehyde (100 μl, 0.90 mmol) and ethanol 10 ml. **1a** was obtained as a yellow solid (314 mg, 79%); m.p.: 150–152 °C. ^{1}H-RMN ($CDCl_3$) δ: 7.99 (s, 1H, H-4); 7.68–7.51 (m, 3H, ArH); 7.46–7.28 (m, 3H, ArH); 6.85 (d, 1H, J = 8.4 Hz, H-5′); 4.22–4.18 (m, 4H, $ArOCH_2$); 3.95–3.89 (m, 4H, $ArOCH_2CH_2$); 3.77–3.67; 3.77 (m; s, 8H, OCH_2). ^{13}C-RMN ($CDCl_3$) δ: 189.8 (CO); 158.4 (C-2); 154.3; 154.2 (C-4′; C-9); 148.8 (C-3′); 144.1 (C-4); 133.2 (C-7); 128.9 (C-1′ + C-5); 127.1 (C-10); 125.6 (C-6′); 124.8 (C-6); 118.0 (C-3); 116.6 (C-8); 113.3 (C-2′); 111.4 (C-5′); 71.0; 70.2; 70.0; 69.1; 68.9; 68.8; 68.4 (CH_2O). MS (L-SIMS+): 441.1 ($M + H^+$, 58%); 463.1 ($M + Na^+$, 3%); 573.0 ($M + Cs^+$, 6%); 173.0 (coumarin CO^+, 47%). Anal. calc. for $C_{24}H_{24}O_8$: C, 65.45; H, 5.45. Found: C, 65.24; H, 5.47.

*7-Methoxy-3-(6,7,9,10,12,13,15,16-octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecene-2-carbonyl)-chromen-2-one (**2a**)*. It was synthesized following the general method starting from the corresponding β-ketoester (345 mg, 0.9 mmol) and 4-methoxy salicylaldehyde (137.4 mg, 0.90 mmol) and ethanol 10 ml. **2a** was obtained as a dark-yellow solid (308 mg, 73%); m.p.: 138–140 °C. ^{1}H-RMN ($CDCl_3$) δ: 7.99 (s, 1H, H-4); 7.50 (d, 1H, J = 2.0 Hz, H-2′); 7.48 (d, 1H, J = 8.3 Hz, H-5); 7.43 (dd, 1H, J = 2.0; 8.4 Hz, H-6′); 6.91 (dd, 1H, J = 2.5; 8.3 Hz, H-6); 6.88 (d, 1H, J = 2.5 Hz, H-8); 6.85 (d, 1H, J = 8.4 Hz, H-5′); 4.22–4.18 (m, 4H, $ArOCH_2$); 3.95–3.89 (m, 4H, $ArOCH_2CH_2$); 3.92 (s, 3H, OCH_3); 3.77–3.67; 3.77 (m; s, 8H, OCH_2). ^{13}C-RMN ($CDCl_3$) δ: 190.2 (CO); 164.2 (C-7); 158.8 (C-2); 156.7 (C-9); 154.0 (C-4′); 148.7 (C-3); 145.2 (C-4); 130.1 (C-5); 129.4 (C-1′); 125.4 (C-6′); 123.2 (C-3); 113.6 (C-6); 113.3 (C-2′); 111.7 (C-10); 111.4 (C-5′); 100.5 (C-8); 71.0; 70.8; 70.2; 69.2; 69.0; 68.8; 68.5 (CH_2O); 55.9 (OCH_3). MS (L-SIMS+): 471.1 ($M + H^+$, 30%); 493.1 ($M + Na^+$, 3%); 509.1 ($M + K^+$, 3%); 603.0 ($M + Cs^+$, 2%); 203.0 (coumarin CO^+, 40%). Anal. calc. for $C_{25}H_{26}O_9$: C, 63.83; H, 5.53. Found: C, 63.41; H, 5.34.

7-Diethylamine-3-(6,7,9,10,12,13,15,16-octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecene-2-carbonyl)-chrom-

*en-2-one (**3a**)*. It was synthesized following the general method starting from the corresponding β-ketoester (345 mg, 0.9 mmol), 4-diethylamine salicylaldehyde (177 mg, 0.90 mmol) and ethanol 10 ml. The reaction mixture was concentrated and cooled. **3a** was obtained as a yellow solid (167 mg, 36%); m.p.: 180–182 °C. ^{1}H-RMN ($CDCl_3$) δ: 7.98 (s, 1H, H-4); 7.46 (d, 1H, J = 2.0 Hz, H-2′); 7.44 (dd, 1H, J = 2.0; 8.4 Hz, H-6′); 7.34 (d, 1H, J = 8.9 Hz, H-5); 6.85 (d, 1H, J = 8.4 Hz, H-5′); 6.62 (dd, 1H, J = 2.2; 8.9 Hz, H-6); 6.50 (d, 1H, J = 2.2 Hz, H-8); 4.21–4.17 (m, 4H, $ArOCH_2$); 3.92–3.88 (m, 4H, $ArOCH_2CH_2$); 3.77–3.67; 3.77 (m; s, 8H, OCH_2); 3.45 (q, 4H, J = 7.0 Hz; CH_3CH_2N); 1.24 (t, 6H, J = 7.0 Hz; CH_3CH_2N).

^{13}C-RMN ($CDCl_3$) δ: 191.0 (CO); 159.6 (C-7); 157.8 (C-2); 153.4 (C-9); 152.1 (C-4′); 148.5 (C-3′); 146.6 (C-4); 130.5 (C-5); 130.4 (C-1′); 124.9 (C-6′); 118.4 (C-3); 114.2 (C-2′); 111.6 (C-5′); 109.4 (C-6); 107.6 (C-10); 96.8 (C-8); 71.1; 70.3; 69.3; 69.2; 68.9; 68.6 (CH_2O); 44.9 (CH_3CH_2N); 12.3 (CH_3CH_2N). MS (L-SIMS+): 512.2 ($M + H^+$, 42%); 534.2 ($M + Na^+$, 3%); 550.1 ($M + K^+$, 1%); 644.1 ($M + Cs^+$, 3%); 244.1 (coumarin CO^+, 100%). Anal. calc. for $C_{28}H_{33}NO_8 \cdot 0.5H_2O$: C, 64.61; H, 6.54; N, 2.69. Found: C, 64.79; H, 6.34; N, 2.67.

*3-(6,7,9,10,12,13,15,16,18,19-Decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecen-2-carbonyl)-chromen-2-one (**1b**)*. It was synthesized following the general method starting from the corresponding β-ketoester (200 mg, 0.47 mmol), salicylaldehyde (50 μl, 0.47 mmol) and ethanol 6 ml. **1b** was obtained as a yellow solid (162 mg, 71%); m.p.: 157–159 °C. ^{1}H-RMN ($CDCl_3$) δ: 7.99 (s, 1H, H-4); 7.69–7.53 (m, 3H, ArH); 7.46–7.27 (m, 3H, ArH); 6.86 (d, 1H, J = 8.4 Hz, H-5′); 4.25–4.21 (m, 4H, $ArOCH_2$); 3.98–3.91 (m, 4H, $ArOCH_2CH_2$); 3.79–3.60; 3.70 (m; s, 12H, OCH_2). ^{13}C-RMN ($CDCl_3$) δ: 189.9 (CO); 158.6 (C-2); 154.5; 154.1 (C-4′;C-9); 148.7 (C-3′); 144.2 (C-4); 133.2 (ArCH); 129.0 (C-1′); 128.9 (ArCH); 127.4 (C-10); 125.6 (C-6′); 124.8 (ArCH); 118.1 (C-3); 116.8 (ArCH); 113.3 (C-2′); 111.5 (C-5′); 70.8; 70.7; 70.5; 69.3; 69.1; 69.0; 68.8 (CH_2O). MS (L-SIMS+): 485.1 ($M + H^+$, 66%); 507.1 ($M + Na^+$, 7%); 523.1 ($M + K^+$, 4%); 617.0 ($M + Cs^+$, 12%); 173.0 (coumarin CO^+, 100%). Anal. calc. for $C_{26}H_{28}O_9$: C, 64.46; H, 5.78. Found: C, 64.51; H, 5.98.

*7-Methoxy-3-(6,7,9,10,12,13,15,16,18,19-decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecen-2-carbonyl)-chromen-2-one (**2b**)*. It was synthesized following the general method starting from the corresponding β-ketoester (105 mg, 0.25), 4-methoxy salicylaldehyde (37.5 mg, 0.25 mmol) and ethanol 3 ml. **2b** was obtained as a dark-yellow solid (97 mg, 76%); m.p.: 167–169 °C. ^{1}H-RMN ($CDCl_3$) δ: 7.99 (s, 1H, H-4); 7.51 (d, 1H, J = 2.0 Hz, H-2′); 7.48 (d, 1H, J = 8.3 Hz, H-5); 7.43 (dd, 1H, J = 2.0; 8.3 Hz, H-6′); 6.91 (dd, 1H, J = 2.3; 8.3 Hz, H-6); 6.87 (d, 1H, J = 2.3 Hz, H-8); 6.86 (d, 1H, J = 8.3 Hz, H-5′); 4.25–4.20 (m, 4H, $ArOCH_2$); 3.98–3.91 (m, 4H, $ArOCH_2CH_2$); 3.92 (s, 3H, OCH_3); 3.82–3.66; 3.70 (m; s, 12H, OCH_2). ^{13}C-RMN ($CDCl_3$) δ: 190.3 (CO); 164.3 (C-7); 158.8 (C-2); 156.8 (C-9); 153.8 (C-4′); 148.6 (C-3′); 145.3 (C-4); 130.1 (C-5); 129.5 (C-1′); 125.3 (C-6′); 123.4 (C-3); 113.6 (C-6); 113.4 (C-2′); 111.8 (C-10); 111.6 (C-5′); 100.6 (C-8); 70.9; 70.8; 70.7; 70.6; 70.5; 69.3; 69.2; 69.1; 68.9 (CH_2O); 55.9 (OCH_3). MS (L-SIMS+): 515.2 ($M + H^+$, 54%); 537.1 ($M+Na^+$, 7%); 553.1 ($M+K^+$, 3%); 647.1 ($M + Cs^+$, 8%); 203.0 (coumarin CO^+, 100%). Anal. calc. for $C_{27}H_{30}O_{10}$: C, 63.03; H, 5.84. Found: C, 63.02; H, 5.83.

*7-Diethylamine-3-(6,7,9,10,12,13,15,16,18,19-decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecen-2-carbonyl)-chromen-2-one (**3b**)*. It was synthesized following the general method starting from the corresponding β-ketoester (200 mg, 0.47 mmol), 4-diethylamine salicylaldehyde (92 mg, 0.47 mmol) and ethanol 6 ml. The reaction mixture was concentrated and cooled. **3b** was obtained as a yellow solid (127 mg, 49%); m.p.: 148–150 °C. ^{1}H-RMN ($CDCl_3$) δ: 7.9 (s, 1H, H-4); 7.47 (d, 1H, J = 2.0 Hz, H-2′); 7.44 (dd, 1H, J = 2.0; 8.2 Hz, H-6′); 7.35 (d, 1H, J = 8.9 Hz, H-5); 6.86 (d, 1H, J = 8.2 Hz, H-5′); 6.62 (dd, 1H, J = 2.5; 8.9 Hz, H-6); 6.52 (d, 1H, J = 2.5 Hz, H-8); 4.24–4.20 (m, 4H, $ArOCH_2$); 3.98–3.90 (m, 4H, $ArOCH_2CH_2$); 3.80–3.69; 3.70 (m; s, 12H, OCH_2); 3.46 (q, 4H, J = 7.1 Hz; CH_3CH_2N); 1.24 (t, 6H, J = 7.1 Hz; CH_3CH_2N). ^{13}C-RMN ($CDCl_3$) δ: 191.0 (CO); 159.8 (C-7); 157.9 (C-2); 152.6 (C-9); 152.2 (C-4′); 148.0 (C-3′); 146.9 (C-4); 130.7 (C-5); 130.5 (C-1′); 124.8 (C-6′); 118.3 (C-3); 113.2 (C-2′); 111.2 (C-5′); 109.4 (C-6); 107.7 (C-10); 96.9 (C-8); 70.4; 69.1; 69.0; 68.3 (CH_2O); 45.0 (CH_3CH_2N); 12.4 (CH_3CH_2N). MS (L-SIMS+): 556.2 ($M + H^+$, 71%); 578.2 ($M + Na^+$, 4%); 594.2 ($M + K^+$, 1%); 688.1 ($M + Cs^+$, 4%); 244.1 (coumarin CO^+, 73%). Anal. calc. for $C_{30}H_{37}NO_9 \cdot 0.5H_2O$: C, 63.83; H, 6.74; N, 2.48. Found: C, 63.48; H, 6.75; N, 2.44.

5.2.3. Synthesis of precursors of compounds **4a** and **b**

3-Hydroxy-6,7,9,10,12,13,15,16-octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecene-2-carbaldehyde. A mixture of 2,4,5-trihydroxybenzaldehyde [25] (0.60 g, 4 mmol), and tetraethylendioxadiiodo (1.67 g, 4 mmol), and K_2CO_3 (2.76 g, 20 mmol) in 250 ml of acetone was heated under argon to 60 °C with stirring for 24 h. The salts were filtered off, and the filtrate was evaporated. The residue was dissolved in dichloromethane and washed with HCl 10%. After drying with magnesium sulfate, the solvent was evaporated and the resulting oil was used in the next step without further purification (94%). ^{1}H-NMR ($CDCl_3$) δ: 3.74 (m, 8H, CH_2); 3.90 (m, 4H, CH_2); 4.14 (m, 4H, CH_2); 6.40 (s, 1H, H-3); 6.97 (s, 1H, H-6); 9.64 (s, 1H, CHO).

3-Hydroxy-6,7,9,10,12,13,15,16,18,19-decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecene-2-carbaldehyde. It was synthesized following the above described method using pentaethylendioxadiiodo as alkylation agent (95%). ^{1}H-NMR ($CDCl_3$) δ: 3.80 (m, 12H, CH_2); 3.99 (m, 4H, CH_2); 4.22 (m, 4H, CH_2); 6.44 (s, 1H, H-3); 7.00 (s, 1H, H-6); 9.70 (s, 1H, CHO).

*3-Benzoyl-7,8,10,11,13,14,16,17-octahydro-1,6,9,12,15,18-hexaoxa-cyclotetradeca[b]naphthalen-2-one (**4a**)*. It was synthesized following the general method starting from ethyl benzoylacetate (0.17 ml, 1 mmol), 3-hydroxy-6,7,9,10,12,13,15,16-octahydro-5,8,11,14,17-pentaoxa-benzocyclopentadecene-2-carbaldehyde (0.30 g, 1 mmol) and ethanol 25 ml. **4a** was obtained as a white-yellow solid (89%). ^{1}H-NMR ($CDCl_3$) δ: 3.78 (s, 8H, CH_2); 3.96 (m, 4H, CH_2); 4.20 (m, 4H, CH_2); 6.84 (s, 1H, H-5); 6.95 (s, 1H, H-8); 7.51 (m, 2H, H-3′, H-5′); 7.61 (m, 1H, H-4′); 7.86 (m, 2H, H-2′, H-6′); 8.06 (s, 1H, H-4). ^{13}C-NMR ($CDCl_3$) δ: 68.52–70.82 (CH_2); 100.43 (C-4); 110.79 (C-5); 111.12 (C-8); 122.54 (C-10); 128.32 (2C, C-3′, C-5′); 129.37 (2C, C-2′, C-6′); 133.34 (C-4′); 136.58 (C-1′); 146.41 (C-9); 146.57 (C-3); 151.65 (C-5); 154.95 (C-7); 159.04 (C-2); 192.22 (COPh). MS(EI+): 440 (M^+, 83%); 308 (M^+-$C_6O_3H_{12}$, 33%); 279 (M^+-$C_6O_3H_{12}$CHO, 41%); 231 (M^+-$C_6O_3H_{12}$Ph, 24%); 203 (M^+-$C_6O_3H_{12}$COPh, 14%); 105 (COPh, 100%).

*3-Benzoyl-7,8,10,11,13,14,16,17,19,20-decahydro-1,6,9,12,15,18,21-heptaoxa-cyclooctadeca[b]naphthalen-2-one (**4b**)*. It was synthesized following the general method starting from ethyl benzoylacetate (0.20 ml, 1.3 mmol), 3-hydroxy-6,7,9,10,12,13,15,16,18,19-decahydro-5,8,11,14,17,20-hexaoxa-benzocyclooctadecene-2-carbaldehyde (0.40 g, 1.1 mmol) and ethanol 25 ml. **4b** was obtained as a white-yellow solid (83%). ^{1}H-NMR ($CDCl_3$) δ: 3.69–3.76 (m, 12H, CH_2); 3.97 (m, 4H, CH_2); 4.20 (m, 4H, CH_2); 6.86 (s, 1H, H-5); 6.95 (s, 1H, H-8); 7.51 (m, 2H, H-3′, H-5′); 7.60 (m, 1H, H-4′); 7.88 (m, 2H, H-2′,H-6’); 8.05 (s, 1H, H-4). ^{13}C-NMR ($CDCl_3$) δ: 68.50–70.80 (CH_2); 100.54 (C-4); 110.82 (C-5, C-8); 122.84 (C-10); 128.38 (C-3′, C-5′); 129.43 (C-2′, C-6′); 133.34 (C-4′); 136.71 (C-1′); 146.30 (C-3, C-9); 151.65 (C-6); 154.74 (C-7); 159.00 (C-2); 192.12 (COPh). MS(EI+): 484 (M^+, 86%); 308 (M^+-$C_8O_4H_{16}$, 36%); 279 (M^+-$C_8O_4H_{16}$CHO, 34%); 231 (M^+-$C_8O_4H_{16}$Ph, 21%); 203 (M^+-$C_8O_4H_{16}$COPh, 11%); 105 (COPh, 100%).

*3-[8,17-Bis-(2-hydroxy-ethyl)-7,8,9,10,12,13,16,17,18,19-decahydro-6H,15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecene-2-carbonyl]-chromen-2-one sodium iodide complex (**6a**)*. It was synthesized following the general method starting from the corresponding dimethylated coumarine (550 mg, 1.04 mmol), 6,9-dioxa-3,12-diazatetradecane-1,14-diol (247 mg, 1.04 mmol), sodium iodide (470 mg, 3.14 mmol), sodium carbonate (554 mg, 5.53 mmol) and 55 ml of acetonitrile. The product was obtained as yellow solid (428 mg, 57%); m.p.: 146–148 °C ^{1}H-RMN ($CDCl_3$) δ: 8.08 (s, 1H, H-4); 7.72–7.63 (m, 2H, H-5, H-7); 757 (d, 1H, J = 2.0 Hz, H-2′); 7.51–7.34 (m, 3H, H-6′, H-8, H-6); 6.3 (d, 1H, J = 8.4 Hz, H-5′); 4.44–4.30 (m, 2H, OH); 4.28–4.16 (m, 4H, $ArOCH_2$); 3.80–3.32 (m, 12H, CH_2O); 2.85–2.62 (m, 12H, NCH_2). ^{13}C-RMN ($CDCl_3$) δ: 189.6 (CO); 158.3 (C-2); 154.1 (C-9); 151.6 (C-4′); 146.7 (C-3′); 144.6 (C-4); 133.3 (C-7); 129.1 (C-1′ + C-5); 126.3 (C-10); 125.6 (C-6′); 124.7 (C-6); 117.8 (C-3); 116.4 (C-8); 111.4 (C-2′); 110.8 (C-5′); 68.4; 67.3 (CH_2O); 65.2; 64.9 ($ArOCH_2$); 58.0 (CH_2OH); 57.5 (NCH_2CH_2OH); 53.1; 52.9 (CH_2N). MS (L-SIMS+): 571.1 (M+H^+, 21%); 593.1 (M + Na^+, 100%); 173.0 (coumarin CO^+, 8%). Anal. calc. for $C_{30}H_{38}N_2O_9$·NaI: C, 50.00; H, 5.28; N 3.89. Found: C, 50.08; H, 5.14; N 3.75.

*3-[8,17-Bis-(2-hydroxy-ethyl)-7,8,9,10,12,13,16,17,18,19-decahydro-6H,15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecene-2-carbonyl]-7-methoxy-chromen-2-one (**6b**)*. It was synthesized following the general method starting from the corresponding dimethylated coumarine (364 mg, 0.65 mmol), 6,9-dioxa-3,12-diazatetradecane-1,14-diol (155 mg, 0.65 mmol), sodium iodide (295 mg, 1.97 mmol), sodium carbonate(347 mg, 3.28 mmol), and 30 ml of acetonitrile. The product was obtained as yellow solid (319 mg, 65%); m.p.: 176–178 °C ^{1}H-RMN ($CDCl_3$) δ: 8.01 (s, 1H, H-4); 7.54 (d, 1H, J = 8.5 Hz, H-5); 7.54 (d, 1H, J = 1.9 Hz, H-2′); 7.48 (dd, 1H, J = 1.9; 8.4 Hz, H-6′); 6.94 (dd, 1H, J = 2.4; 8.5 Hz, H-6); 6.93 (d, 1H, J = 8.4 Hz, H-5′); 6.88 (d, 1H, J = 2.4 Hz, H-8); 4.43–4.30 (m, 2H, OH); 4.25–4.20 (m, 4H, $ArOCH_2$); 3.93 (s, 3H, OCH_3); 3.85–3.30 (m, 12H, CH_2O); 2.88–2.62 (m, 12H, NCH_2). ^{13}C-RMN ($CDCl_3$) δ: 190.2 (CO); 164.4 (C-7); 158.9 (C-2); 156.8 (C-9); 151.5 (C-4′); 146.7 (C-3′); 145.8 (C-4); 130.4 (C-5); 129.8 (C-1′); 125.4 (C-6′); 122.6 (C-3); 113.4 (C-6); 111.7 (C-2′); 110.7 (C-5′ + C-10); 100.6 (C-8); 68.6; 67.6 (CH_2O); 65.2; 65.0 ($ArOCH_2$); 58.5; 58.4 (CH_2OH); 57.7 (NCH_2CH_2OH); 56.0 (OCH_3); 53.4; 53.0 (CH_2N). MS (L-SIMS+): 601.1 (M + H^+, 24%); 623.1 (M + Na^+, 100%); 203.0 (coumarin CO^+, 8%). Anal. calc. for $C_{31}H_{40}N_2O_{10}$·NaI: C, 49.60; H, 5.33; N, 3.73. Found: C, 49.27; H, 5.14; N, 3.40.

*3-[8,17-Bis-(2-hydroxy-ethyl)-7,8,9,10,12,13,16,17,18,19-decahydro-6H,15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecene-2-carbonyl]-5,7-dimethoxy-chromen-2-one (**6c**)*. It was synthesized following the general method starting from the corresponding dimethylated coumarine (500 mg, 0.85 mmol), 6,9-dioxa-3,12-diazatetradecane-1,14-diol (201 mg, 0.85 mmol), sodium iodide (384 mg, 2.56 mmol), sodium carbonate (452 mg, 4.26 mmol) and 50 ml of acetonitrile. The product was obtained as yellow solid (459 mg, 69%); m.p.: 199–201 °C ^{1}H-RMN ($CDCl_3$) δ: 8.42 (s, 1H, H-4); 7.52 (d, 1H, J = 1.9 Hz, H-2′); 7.47 (dd, 1H, J = 1.9; 8.4 Hz, H-6′); 6.92 (d, 1H, J = 8.4 Hz, H-5′); 6.47 (d, 1H, J = 2.1 Hz, H-8); 6.33 (d, 1H, J = 2.1 Hz, H-6); 4.44–4.38 (m, 2H, OH); 4.24–4.19 (m, 4H, $ArOCH_2$); 3.92 (s, 3H, OCH_3); 3.91 (s, 3H, OCH_3); 3.76–3.33 (m, 12H, CH_2O); 2.83–2.69 (m, 12H, NCH_2). ^{13}C-RMN ($CDCl_3$) δ: 190.2 (CO); 165.5 (C-7); 158.8 (C-2); 157.9 (C-5); 157.2 (C-9); 151.1 (C-4′); 146.4 (C-3′); 141.5 (C-4); 129.7 (C-1′); 125.1 (C-6′); 119.7 (C-3); 111.6 (C-2′); 110.6 (C-5′); 103.1 (C-10); 94.7 (C-6); 92.6 (C-8); 68.3; 67.2 (CH_2O); 65.0; 64.8 ($ArOCH_2$); 58.0; 57.8 (CH_2OH); 57.5 (NCH_2CH_2OH); 56.0; 55.9 (OCH_3); 53.1; 52.8 (CH_2N). MS (L-SIMS+): 631.1 (M + H^+, 38%); 653.1 (M + Na^+, 49%); 233.0 (coumarin CO^+, 10%). Anal. calc. for $C_{32}H_{42}N_2O_{11}$·NaI: C, 49.23; H, 5.38; N, 3.59. Found: C, 49.58; H, 5.29; N, 3.28.

3-[8,17-Bis-(2-hydroxy-ethyl)-7,8,9,10,12,13,16,17,18,19-decahydro-6H,15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecene-2-carbonyl]-7-diethylamino-chromen-2-one ***(6d)***. It was synthesized following the general method starting from the corresponding dimethylated coumarine (777 mg, 1.30 mmol), 6,9-dioxa-3,12-diazatetradecane-1,14-diol (307 mg, 1.30 mmol), sodium iodide (585 mg, 3.91 mmol), sodium carbonate (690 mg, 6.51 mmol) and 50 ml of acetonitrile. The product was obtained as yellow solid (609 mg, 59%); m.p.: 204–206 °C ^{1}H-RMN ($CDCl_3$) δ: 8.01 (s, 1H, H-4); 7.48 (d, 1H, $J = 1.9$ Hz, H-2′); 7.48 (dd, 1H, $J = 1.9$; 8.8 Hz, H-6′); 7.39 (d, 1H, $J = 9.0$ Hz, H-5); 6.91 (d, 1H, $J = 8.8$ Hz, H-5′); 6.64 (dd, 1H, $J = 2.4$; 9.0 Hz, H-6); 6.52 (d, 1H, $J = 2.4$ Hz, H-8); 4.45–4.38 (m, 2H, OH); 4.22–4.18 (m, 4H, $ArOCH_2$); 3.76–3.40 (m, 12H, CH_2O); 3.47 (q, 4H, $J = 7.1$ Hz; CH_3CH_2N); 2.86–2.65 (m, 12H, NCH_2); 1.25 (t, 6H, $J = 7.1$ Hz; CH_3CH_2N). ^{13}C-RMN ($CDCl_3$) δ: 190.1 (CO); 159.9 (C-7); 157.9 (C-2); 152.4 (C-9); 150.9 (C-4′); 147.3 (C-3′); 146.5 (C-4); 130.9 (C-1′ + C-5); 124.9 (C-6′); 117.5 (C-3); 112.2 (C-2′); 110.7 (C-5′); 109.6 (C-6); 107.6 (C-10); 96.7 (C-8); 68.6; 67.6 (CH_2O); 65.1; 65.0 ($ArOCH_2$); 58.5; 58.4; (CH_2OH); 57.8 (NCH_2CH_2OH); 53.3; 53.1 (CH_2N); 45.0 (CH_3CH_2N); 12.3 (CH_3CH_2N). MS (L-SIMS+): 642.1 ($M + H^+$, 23%); 664.1 ($M + Na^+$, 8%); 244.0 (coumarin CO^+, 7%). Anal. calc. for $C_{34}H_{47}N_3O_9$·NaI: C, 51.58; H, 5.94; N, 5.31. Found: C, 51.26; H, 6.05; N, 5.11.

({2-[17-[2-(Bis-tert-butoxycarbonylmethyl-amino)-ethyl]-3-(2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-tert-butoxycarbonylmethyl-amino)-acetic acid tert-butyl ester. It was synthesized following the general method starting from macrocyclic coumarine diol **6a** (213 mg, 0.29 mmol), thionyl chloride (0.21 ml, 2.95 mmol) and dichloromethane (10 ml). Further, *tert*-butyliminodiacetate (145 mg, 0.59 mmol), sodium iodide (133 mg, 0.89 mmol), sodium carbonate (157 mg, 1.48 mmol) and acetonitrile (10 ml). The product was obtained as yellow oil (174 mg, 45%). ^{1}H-RMN ($CDCl_3$) δ: 8.10 (s, 1H, H-4); 7.72–7.37 (m, 6H, H-5, H-7, H-2′, H-6′, H-8, H-6); 7.18 (d, 1H, $J = 8.4$ Hz, H-5′); 4.42–4.32 (m, 2H, $ArOCH_2$); 4.32–4.22 (m, 2H, $ArOCH_2$); 3.73–3.15 (m, 16H, OCH_2, NCH_2CO_2); 3.10–2.90 (m, 4H, NCH_2); 2.86–2.59 (m, 12H, NCH_2); 1.46–1.39 (m, 36H, CCH_3). ^{13}C-RMN ($CDCl_3$) δ: 189.2 (CO); 170.5 ($CO_2{}^tBu$); 157.9 (C-2); 153.7 (C-9); 151.8 (C-4′); 147.0 (C-3′); 144.1 (C-4); 132.9 (C-7); 128.9. 128.8 (C-1′, C-5); 126.0 (C-10); 125.5 (C-6′); 124.6 (C-6); 117.4 (C-3); 116.0 (C-8); 111.2 (C-2′ + C-5′); 81.1 (CCH_3); 69.8; 69.1; 67.8; 65.8; 65.2 (CH_2O); 56.9; 55.8 (NCH_2CO_2); 53.2; 52.9; 51.9; 50.5 (CH_2N); 27.5 (CCH_3). MS (L-SIMS+): 1025.8 ($M + H^+$, 50%); 173.0 (coumarin CO^+, 9%) Anal. calc. for $C_{54}H_{80}N_4O_{15}$·2NaI: C, 48.94; H, 6.04; N, 4.23. Found: C, 49.27; H, 5.93; N, 3.87.

({2-[17-[2-(Bis-tert-butoxycarbonylmethyl-amino)-ethyl]-3-(7-methoxy-2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-tert-butoxycarbonylmethyl-amino)-acetic acid tert-butyl ester. It was synthesized following the general method starting from macrocyclic coumarine diol **6b** (214 mg, 0.28 mmol), thionyl chloride (0.21 ml, 2.95 mmol) and dichloromethane (12 ml). Further, *tert*-butyliminodiacetate (140 mg, 0.57 mmol), sodium iodide (129 mg, 0.86 mmol), sodium carbonate (151 mg, 1.43 mmol) and acetonitrile (12 ml). The product was obtained as yellow oil (189 mg, 49%). ^{1}H-RMN ($CDCl_3$) δ: 8.10 (s, 1H, H-4); 7.60 (d, 1H, $J = 8.7$ Hz, H-5); 7.56 (d, 1H, $J = 1.8$ Hz, H-2′); 7.52 (dd, 1H, $J = 1.8$; 8.4 Hz, H-6′); 7.15 (d, 1H, $J = 8.4$ Hz, H-5′); 6.94 (dd, 1H, $J = 2.4$; 8.7 Hz, H-6); 6.88 (d, 1H, $J = 2.4$ Hz, H-8); 4.40–4.30 (m, 2H, $ArOCH_2$); 4.30–4.20 (m, 2H, $ArOCH_2$); 3.92 (s, 3H, OCH_3); 3.70–3.20 (m, 16H, OCH_2, NCH_2CO_2); 3.17–2.92 (m, 4H, NCH_2); 2.87–2.61 (m, 12H, NCH_2); 1.46–1.39 (m, 36H, CCH_3). ^{13}C-RMN ($CDCl_3$) δ: 189.8 (CO); 170.8 ($CO_2{}^tBu$); 164.0 (C-7); 158.5 (C-2); 156.3 (C-9); 151.5 (C-4′); 146.9 (C-3′); 145.4 (C-4); 130.4 (C-5); 129.5 (C-1′); 125.4 (C-6′); 122.2 (C-3); 112.9 (C-6 + C-2′); 111.4 (C-5′ + C-10); 100.4 (C-8); 81.4 (CCH_3); 70.0; 69.3; 68.1; 65.5; 65.3 (CH_2O); 57.2; 55.8 (NCH_2CO_2); 55.7 (OCH_3); 53.7; 53.2; 52.1; 50.8 (CH_2N); 27.7 (CCH3). MS (L-SIMS+): 1055.6 ($M + H^+$, 76%); 1077.5 ($M + Na^+$, 20%); 203.0 (coumarin CO^+, 34%). Anal. calc. for $C_{55}H_{82}N_4O_{16}$·2NaI: C, 48.74; H, 6.06; N, 4.13. Found: C, 48.37; H, 5.73; N, 3.77.

({2-[17-[2-(Bis-tert-butoxycarbonylmethyl-amino)-ethyl]-3-(5,7-dimethoxy-2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-tert-butoxycarbonylmethyl-amino)-acetic acid tert-butyl ester. It was synthesized following the general method starting from macrocyclic coumarine diol **6c** (382 mg, 0.49 mmol), thionyl chloride (0.35 ml, 4.90 mmol) and dichloromethane (20 ml). Further, *tert*-butyliminodiacetate (240 mg, 0.98 mmol), sodium iodide (220 mg, 1.47 mmol), sodium carbonate (260 mg, 2.45 mmol) and acetonitrile (20 ml). The product was obtained as yellow oil (271 mg, 40%). ^{1}H-RMN ($CDCl_3$) δ: 8.36 (s, 1H, H-4); 7.51–7.44 (m, 2H, H-2′, H-6′); 7.05 (d, 1H, $J = 8.3$ Hz, H-5′); 6.47 (d, 1H, $J = 2.1$ Hz, H-8); 6.33 (d, 1H, $J = 2.1$ Hz, H-6); 4.53–4.10 (m, 4H, $ArOCH_2$); 3.93 (s, 3H, OCH_3); 3.91 (s, 3H, OCH_3); 3.80–3.20 (m, 16H, OCH_2, NCH_2CO_2); 3.18–2.58 (m, 16H, NCH_2); 1.47–1.41 (m, 36H, CCH_3). ^{13}C-RMN ($CDCl_3$) δ: 190.4 (CO); 171.0 ($CO_2{}^tBu$); 165.7 (C-7); 159.0 (C-2); 158.2 (C-5); 157.7 (C-9); 152.5 (C-4′); 147.3 (C-3′); 141.5 (C-4); 130.4 (C-1′); 125.7 (C-6′); 120.4 (C-3); 111.4 (C-2′); 110.9 (C-5′); 103.6 (C-10); 95.1 (C-6); 92.8 (C-8); 81.7 (CCH_3); 70.3; 68.0; 65.7 (CH_2O); 56.6; 56.4 (NCH_2CO_2); 56.2; 56.0 (OCH_3); 53.7; 52.6; 50.8; 50.6 (CH_2N); 28.0 (CCH3). MS (L-SIMS+): 1085.3 ($M + H^+$, 100%); 1107.3 ($M + Na^+$, 19%); 233.0 (coumarin CO^+, 20%).

({2-[17-[2-(Bis-tert-butoxycarbonylmethyl-amino)-ethyl]-3-(7-diethylamino-2-oxo-2H-chromene-3-carbonyl)-6,7,9,

10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-tert-butoxycarbonylmethyl-amino)-acetic acid tert-butyl ester. It was synthesized following the general method starting from macrocyclic coumarine diol **6d** (135 mg, 0.17 mmol), thionyl chloride (0.12 ml, 1.71 mmol) and dichloromethane (10 ml). Further, *tert*-butyliminodiacetate (84 mg, 0.34 mmol), sodium iodide (77 mg, 0.51 mmol), sodium carbonate (90 mg, 0.85 mmol) and acetonitrile (10 ml). The product was obtained as yellow oil (73 mg, 31%). ^{1}H-RMN ($CDCl_3$) δ: 8.10 (s, 1H, H-4); 7.55–7.38 (m, 3H, H-2′, H-6′, H-5); 7.06 (d, 1H, $J = 8.8$ Hz, H-5′); 6.64 (dd, 1H, $J = 2.2$; 8.6 Hz, H-6); 6.52 (d, 1H, $J = 2.2$ Hz, H-8); 4.40–4.28 (m, 2H, $ArOCH_2$); 4.28–4.20 (m, 2H, $ArOCH_2$); 3.67–3.16 (m, 20H, OCH_2, NCH_2CO_2, CH_3CH_2N); 3.08–2.88 (m, 4H, NCH_2); 2.87–2.54 (m, 12H, NCH_2); 1.46–1.40 (m, 36H, CCH_3); 1.25 (t, 6H, $J = 7.0$ Hz; CH_3CH_2N). ^{13}C-RMN ($CDCl_3$) δ: 190.8 (CO); 171.0 ($CO_2{}^tBu$); 159.7 (C-7); 157.9 (C-2); 152.3 (C-9); 151.2 (C-4′); 147.1 (C-3′+ C-4); 130.8 (C-1′ + C-5); 125.0 (C-6′); 117.4 (C-3); 112.0 (C-2′); 110.6 (C-5′); 109.6 (C-6); 107.5 (C-10); 96.6 (C-8); 81.6 (CCH_3); 69.5; 68.3; 67.8; 65.9; 65.4; 64.7 (CH_2O); 57.3; 56.3 (NCH_2CO_2); 53.8; 53.3; 52.4; 51.2. 50.2 (CH_2N); 44.9 (CH_3CH_2N); 28.0 (CCH3); 12.3 (CH_3CH_2N). MS (L-SIMS+): 1096.5 ($M + H^+$, 12%); 1118.5 ($M + Na^+$, 27%); 1134.8 ($M+K^+$, 28%); 244.1 (coumarin CO^+, 38%).

*({2-[17-[2-(Bis-carboxymethyl-amino)-ethyl]-3-(2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-carboxymethyl-amino)-acetic acid (**5a**)*. It was synthesized following the general method starting from the corresponding coumarine tetraester (172 mg, 0.13 mmol), trifluoroacetic acid (3.0 ml) and dichloromethane (10 ml). The product was obtained as yellow solid (81 mg, 66%); m.p.: 126–128 °C. ^{1}H-RMN (CD_3OD) δ: 8.23 (s, 1H, H-4); 7.82–7.70 (m, 2H, H-5, H-7); 7.66–7.62 (m, 2H, H-2′, H-6′); 7.50–7.42 (m, 2H, H-8, H-6); 7.19 (d, 1H, $J = 8.1$ Hz, H-5′); 4.59 (br s, 4H, $ArOCH_2$); 4.10 (br s, 4H, CH_2O); 3.93; 3.81; 3.67, 3.54; 3.46 (br s′, 24H, CH_2O, NCH_2, CH_2CO_2); 3.13 (br s, 4H, NCH_2). MS (L-SIMS+): 801.7 ($M + H^+$, 2%). Anal. calc. for $C_{38}H_{48}N_4O_{15}$·NaI: C, 48.00; H, 5.05 N, 5.89. Found: C, 48.48; H, 5.06; N, 5.43.

*({2-[17-[2-(Bis-carboxymethyl-amino)-ethyl]-3-(7-methoxy-2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-carboxymethyl-amino)-acetic acid (**5b**)*. It was synthesized following the general method starting from the corresponding coumarine tetraester (158 mg, 0.13 mmol) trifluoroacetic acid (3.0 ml) and dichloromethane (10 ml). The product was obtained as yellow solid (60 mg, 48%); m.p.: 130–132 °C. ^{1}H-RMN (CD_3OD) δ: 8.27 (s, 1H, H-4); 7.71 (d, 1H, $J = 9.4$ Hz, H-5); 7.63–7.59 (m, 2H, H-2′, H-6′); 7.18 (d, 1H, $J = 8.6$ Hz, H-5′); 7.07–7.01 (m, 2H, H-8, H-6); 4.59 (br s, 4H, $ArOCH_2$); 4.09 (br s, 4H, CH_2O); 3.98 (s, 3H, OCH_3); 3.92; 3.81; 3.66, 3.54; 3.46 (br s′, 24H, CH_2O, NCH_2, CH_2CO_2); 3.13 (br s, 4H, NCH_2). MS (L-SIMS+): 831.8 ($M + H^+$, 2%). Anal. calc. for $C_{39}H_{50}N_4O_{16}$·NaI: C, 47.75; H, 5.10; N, 5.71. Found: C, 47.68; H, 5.10; N, 5.30.

*({2-[17-[2-(Bis-carboxymethyl-amino)-ethyl]-3-(5,7-dimethoxy-2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-carboxymethyl-amino)-acetic acid (**5c**)*. It was synthesized following the general method starting from the corresponding coumarine tetraester (250 mg, 0.18 mmol), trifluoroacetic acid (3.0 ml) and dichloromethane (12 ml). The product was obtained as yellow solid (66 mg, 36%); m.p.: 148–150 °C. ^{1}H-RMN (CD_3OD) δ: 8.42 (s, 1H, H-4); 7.60–7.55 (m, 2H, H-2′, H-6′); 7.17 (d, 1H, $J = 8.6$ Hz, H-5′); 6.63 (d, 1H, $J = 2.1$ Hz, H-8); 6.56 (d, 1H, $J = 2.1$ Hz, H-6); 4.59 (br s, 4H, $ArOCH_2$); 4.10 (br s, 4H, CH_2O); 3.98 (s, 3H, OCH_3); 3.97 (s, 3H, OCH_3); 3.92; 3.94–3.48 (s, m, 24H, CH_2O, NCH_2, CH_2CO_2); 3.14 (br s, 4H, NCH_2). MS (L-SIMS+): 861.6 ($M + H^+$, 3%); 883.6 ($M + Na^+$, 2%). Anal. calc. for $C_{40}H_{52}N_4O_{17}$·NaI: C, 47.52; H, 5.15; N, 5.54. Found: C, 47.37; H, 5.26; N, 5.10.

*({2-[17-[2-(Bis-carboxymethyl-amino)-ethyl]-3-(7-diethylamino-2-oxo-2H-chromene-3-carbonyl)-6,7,9,10,12,13,16,17,18,19-decahydro-15H-5,11,14,20-tetraoxa-8,17-diaza-benzocyclooctadecen-8-yl]-ethyl}-carboxymethyl-amino)-acetic acid (**5d**)*. It was synthesized following the general method starting from the corresponding coumarin tetraester (70 mg, 0.05 mmol), trifluoroacetic acid (2.0 ml) and dichloromethane (5 ml). The product was obtained as yellow solid (10 mg, 20%); m.p.: 164–166 °C. ^{1}H-RMN (CD_3OD) δ: 8.23 (s, 1H, H-4); 7.59–7.55 (m, 3H, H-2′, H-6′, H-5); 7.17 (d, 1H, $J = 8.6$ Hz, H-5′); 6.87 (dd, 1H, $J = 2.5$; 8.9 Hz, H-6); 6.67 (d, 1H, $J = 2.5$ Hz, H-8); 4.60 (br s, 4H, $ArOCH_2$); 4.11 (br s, 4H, CH_2O); 3.97; 3.83; 3.69–3.49 (br s, s, m, 28H, CH_2O, NCH_2, CH_2CO_2, CH_3CH_2N); 3.16 (br s, 4H, NCH_2); 1.28 (t, 6H, $J = 7.0$ Hz; CH_3CH_2N). MS (L-SIMS+): 872.5 ($M + H^+$, 4%); 244.1 (coumarin CO^+, 10%). Anal. calc. for $C_{42}H_{57}N_5O_{15}$·NaI·CF_3CO_2H: C, 46.52; H, 5.11; N, 6.17. Found: C, 46.07; H, 4.68; N, 5.70.

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