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Note

Luminescent europium(III) and terbium(III) ions encapsulated in a 2-aminoethoxy or carbamoyloxy substituted calixarene host ☆

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Abstract

A series of new 2-aminoethoxy and carbamoyloxy substituted calix[4]arenes and calix[6]arenes has been synthesized and used to complex Eu^{3+} and Tb^{3+} ions. Emissive complexes in methanol solvent are obtained. The Tb^{3+} complexes are strongly emissive from a terbium centered excited state. The excited states of the calix[6]arene complexes are less effectively quenched by the addition of water than are those having the calix[4]arene ligands.

Keywords: Luminescence; Europium complexes; Terbium complexes; Calixarene complexes

1. Introduction

Europium(III) and terbium(III) ions are particularly attractive for bioanalytical applications that involve fluorometric techniques. The luminescence properties of Eu^{3+} and Tb^{3+} complexes include large Stokes' shifts, narrow emission line spectra, long wavelength emission and long fluorescence lifetimes [1]. A limitation to the use of these ions for fluoroimmunoassay techniques is the emission quenching by coordinated water molecules. This quenching can be minimized by tightly complexing the metal ion in the cavity of a chelate or macrocyclic ligand [2–4], or by encapsulating it within a calixarene host. The calixarene host that has been used is a *para*-tert-butylcalix[4]arene tetramide where the tertiary amide nitrogens have N-ethyl substituents [5]. A primary amide ligating group is expected to offer stronger ligating properties, but the presence of N–H groups results in vibrational quenching of the excited state [6]. In order to test whether such encapsulated calixarenes can potentially be used with Eu^{3+} and Tb^{3+} ions for fluorometric applications we have now synthesized calixarenes having either carbamoyloxy or 2-aminoethoxy [7] groups appended to the lower rim. These excited state lifetime measurements are the first to be reported for Eu^{3+} or Tb^{3+} encapsulated in a 2-aminoethoxy or carbamoyloxy substituted calixarene.

2. Experimental

All compounds used were of reagent purity and used as supplied. Dry THF was distilled from the ketyl prepared from sodium and benzophenone. IR spectra were recorded on a Mattson Cygnus 100 FTIR spectrometer. ^1H NMR spectra were recorded on GE Omega 400 NMR spectrometer at 400.082 MHz and referenced to tetramethylsilane. Fast atom bombardment (FAB) mass spectra were obtained using a Kratos Concept 1H spectrometer with the sample introduced in an *m*-nitrobenzyl alcohol matrix. Melting points were determined on a MEL-TEMP apparatus in open capillary tubes and are uncorrected.

2.1. 5,11,17,23,29,35-Hexa-tert-butyl-37,38,39,40,41,42-hexacarbamoylmethoxy calix[6]arene (1)

5,11,17,23,29,35-Hexa-tert-butylcalix[6]arene (4.00 g, 4.1 mmol), potassium carbonate (5.11 g, 37.0 mmol) and 2-bromoacetamide (6.84 g, 49.6 mmol) were refluxed under nitrogen for 7 days in 100 ml dry acetone. The reaction mixture was then allowed to cool to ambient temperature and poured into 200 ml of dilute sulfuric

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☆ This paper is dedicated to Professor György Bor on the occasion of his 70th birthday.

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acid. The precipitate which formed was filtered off and washed with water (3×30 ml). This solid residue was then dried in vacuo and recrystallized from hot methanol. Yield 3.25 g (60%); m.p. 275–278 °C dec. ^{1}H NMR ($CDCl_3$): δ 1.18 (brm, 54H, Bu^t); 3.42 and 4.26 (brs, 24H, ArCH_2Ar and OCH_2); 7.15 (brs, 24H, NH_2 and ArH). IR (KBr pellet): ν(CO) 1683, ν(NH) 3340 cm^{-1}. FAB mass spectrum: m/z 1316.7 $(M+\mathrm{H})^+$.

2.2. 5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetracarbamoylmethoxy calix[4]arene (2)

5,11,17,23-Tetra-tert-butylcalix[4]arene (4.00 g, 6.2 mmol), potassium carbonate (5.11 g, 37.0 mmol) and 2-bromoacetamide (6.84 g, 49.6 mmol) were refluxed under nitrogen for 5 days in 100 ml dry acetone. The reaction mixture was then allowed to cool to ambient temperature and poured into 200 ml of dilute sulfuric acid. The precipitate which formed was filtered off and washed with water (3×30 ml). This solid residue was then dried in vacuo and recrystallized from hot methanol. Yield 1.24 g (23%); m.p. 274–276 °C. ^{1}H NMR ($CDCl_3$): δ 0.85 (s, 36H, Bu^t); 3.06 (d, 4H, ^2J(HH) = 12.4 Hz, ArCH_2Ar); 4.18 (s, 8H, OCH_2); 4.22 (d, ^2J(HH) = 12.4 Hz, ArCH_2Ar); 6.66 (s, 8H, ArH); 7.35 (brs, 8H, NH_2); IR (KBr): ν(CO) 1676, ν(NH) 3354 cm^{-1}. FAB mass spectrum: m/z 877.5 $(M+\mathrm{H})^+$.

2.3. 5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(2-aminoethoxy) calix[4]arene (3)

To an ice-cooled solution of the tetraamide **2** (1.50 g, 1.7 mmol) in dry THF (50 ml) were added under nitrogen 30 ml of a 1 M borane solution in THF. The mixture was stirred for 3 h at room temperature and then refluxed under nitrogen for a further 18 h. Upon cooling, 30 ml of 6 N hydrochloric acid were carefully added and the mixture was refluxed for another hour. The aqueous layer was saturated with sodium hydroxide, separated and discarded. The THF solvent was removed using a rotary evaporator. The residue was dissolved in chloroform and dried over magnesium sulfate. Evaporation of the chloroform using a rotary evaporator gave **3** as a white solid. Yield 0.91 g (66%); m.p. 179–180 °C (recrystallized from toluene). ^{1}H NMR ($CDCl_3$): δ 1.19 (s, 36H, Bu^t); 3.21 (s, 12H, ArCH_2Ar and NCH_2); 3.61 (s, 8H, D_2O exchangeable, NH_2); 3.95 (brs, 8H, OCH_2); 4.34 (d, ^2J(HH) = 11.6 Hz, 4H, ArCH_2Ar); 6.84 (s, 8H, ArH). IR (KBr): ν(NH) 3362 cm^{-1}. FAB mass spectrum: m/z 822.6 $(M+\mathrm{H})^+$.

2.4. 5,11,17,23,29,35-Hexa-tert-butyl-37,38,39,40,41,42-hexacyanomethoxy calix[6]arene (4)

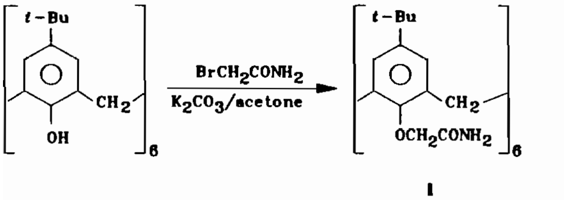
A mixture of 5,11,17,23,29,35-hexa-tert-butylcalix[6]arene (5.00 g, 5.1 mmol), potassium carbonate (4.8 g, 34.7 mmol), potassium iodide (6 g, 36.1 mmol), chloroacetonitrile (3 ml, 56.5 mmol) and dry acetone (120 ml) was refluxed under nitrogen for 5 days. The resulting suspension was filtered through a celite bead, and the filtrate was washed with dichloromethane (2×30 ml). The organic solvents were then evaporated using a rotary evaporator, and the remaining residue was dissolved in chloroform (100 ml), dried over magnesium sulfate, and treated with decolorizing charcoal for several hours. The mixture was filtered again through a celite bead and the filtrate washed with chloroform (3×30 ml). The chloroform solution was then concentrated to approximately 20 ml on a rotary evaporator and 20 ml ethanol were added. The resulting solution upon standing deposited **4** as colorless crystals. Yield 4.26 g (69%); m.p. 282–284 °C. ^{1}H NMR ($CDCl_3$): δ 1.16 (s, 54H, Bu^t); 4.00 (brs, 12H, CH_2); 4.21 (brs, 8H, CH_2); 4.46 (m, 4H, CH_2); 7.02 (s, 12H, ArH). FAB mass spectrum: m/z 1207.8 $(M)^+$.

2.5. 5,11,17,23,29,35-Hexa-tert-butyl-37,38,39,40,41,42-hexa-(2-aminoethoxy) calix[6]arene (5)

To an ice-cooled solution of the hexanitrile **4** (2.00 g, 1.6 mmol) in dry THF (65 ml) were added under nitrogen 45 ml of a 1 M borane solution in THF. The mixture was stirred at room temperature for 3 h, and refluxed under nitrogen for a further 18 h. Upon cooling 30 ml of 6 N hydrochloric acid were carefully added, and the mixture was refluxed for a further hour. The water layer was then saturated with sodium hydroxide, separated and discarded. The THF was removed using a rotary evaporator. The residue was then dissolved in chloroform and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure gave **5** as a white solid. Yield 1.79 g (88%); m.p. 257–259 °C dec. (recrystallized from toluene). ^{1}H NMR ($CDCl_3$): δ 1.04 (brs, 54H, Bu^t); 3.01, 3.40, 3.62 and 4.41 (four brs, 36H, CH_2); 4.24 (brs, 12H, D_2O exchangeable, NH_2); 6.89 (brs, 12H, ArH). FAB mass spectrum: m/z 232.7 $(M+\mathrm{H})^+$.

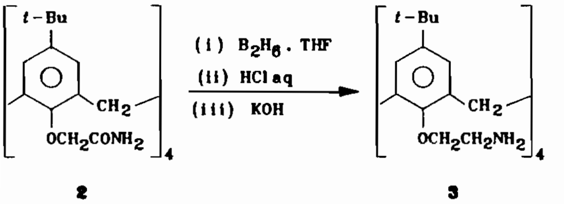
3. Results and discussion

The synthetic route to the carbamoyloxy substituted calix[6]arene involves reacting *para*-tert-butylcalix[6]arene with bromoacetamide in the presence of potassium carbonate as base (Eq. (1)). The amide **1** is obtained in 55% yield and is characterized from its IR and ^{1}H NMR spectra. The IR spectrum shows a band for ν(CO) at 1683 cm^{-1} and one for ν(NH) at 3340 cm^{-1}. The ^{1}H NMR spectrum shows resonances



(1)

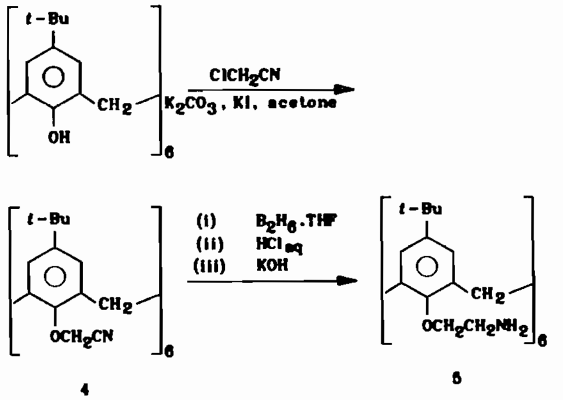
at δ 1.18 (brs, 54H, Bu^t); 3.42 and 4.26 (brs, 24H, $ArCH_2Ar$ and OCH_2); 7.15 (brs, 24H, NH_2 and ArH). The carbamoyloxy substituted calix[4]arene **2** has been obtained in 23% yield, and again characterized from its IR and ^{1}H NMR spectra. The IR spectrum shows



(2)

a band for ν(CO) at 1676 cm^{-1} and one for ν(NH) at 3354 cm^{-1}. The ^{1}H NMR spectrum shows resonances at δ 0.85 (s, 36H, Bu^t); 3.06 (d, 4H, ^2J(HH) = 12.4 Hz, $ArCH_2Ar$), 4.18 (s, 8H, OCH_2); 4.22 (d, ^2J(HH) = 12.4 Hz, $ArCH_2Ar$); 6.66 (s, 8H, ArH); 7.35 (brs, 8H, NH_2). The calix[4]arene amine **3** is obtained by a similar synthetic procedure where the intermediate amide **2** is subsequently reduced to the amine (Eq. (2)). The amine **3** is characterized from its IR and ^{1}H NMR spectra. The IR spectrum shows a band due to ν(NH) at 3362 cm^{-1}. The ^{1}H NMR spectrum shows resonances at δ 1.19 (s, 36H, Bu^t); 3.21 (s, 12H, $ArCH_2Ar$ and NCH_2); 3.61 (s, 8H, (D_2O exchangeable), NH_2); 3.95 (brs, 8H, OCH_2); 4.34 (d, ^2J(HH) = 11.6 Hz, 4H, $ArCH_2Ar$); 6.84 (s, 8H, ArH).

For the calix[6]arene amine **5** an alternate route via the nitrile **4** (Eq. (3)) is preferred. Both the nitrile **4**



(3)

and the amine **5** are characterized by their ^{1}H NMR spectra. The ^{1}H NMR spectrum of **4** shows resonances at δ 1.16 (s, 54H, Bu^t); 4.00 (brs, 12H, CH_2); 4.21 (brs, 8H, CH_2); 4.46 (m, 4H, CH_2); 7.02 (s, 12H, ArH). The IR spectrum of **5** shows a band due to ν(NH) at 3385 cm^{-1}. The ^{1}H NMR spectrum of **5** shows resonances at δ 1.04 (brs, 54H, Bu^t); 3.01, 3.40, 3.62 and 4.41 (four brs, 36H, CH_2); 4.24 (brs, 12H, (D_2O exchangeable, NH_2); 6.89 (brs, 12H ArH).

Methanol solutions of Eu^{3+} and Tb^{3+} ions coordinate to **1, 2, 3** and **5** to give luminescent complexes. Methanol solutions of **1, 2, 3** and **5** with the Eu^{3+} ion show only a weak emission. The terbium complexes, however, show a very intense emission in methanol solution. The emission spectrum of a methanol solution of **3** and the Tb^{3+} ion is shown in Fig. 1. The emission spectra of **1, 2** and **5** and the Tb^{3+} ion are very similar. The excited state lifetimes of the terbium complexes are shown in Table 1. They all fall in the microsecond range. The emission of these Tb^{3+} complexes show a biexponential decay which has both a short and long lived component. The short lived component is derived from a ligand centered excited state and the long lived component from a Tb^{3+} centered state. These lifetimes are shorter than those found by Sabbatini et al. for the *N*-ethyl amide substituted calix[4]arene [5], which is likely due to relaxation of the Tb^{3+} centered excited state by coupling with the N–H vibrations of the amine and carbamoyl ligands. In each case the addition of water to the methanol solution results in a partial quenching of the excited state (Table 1). This latter

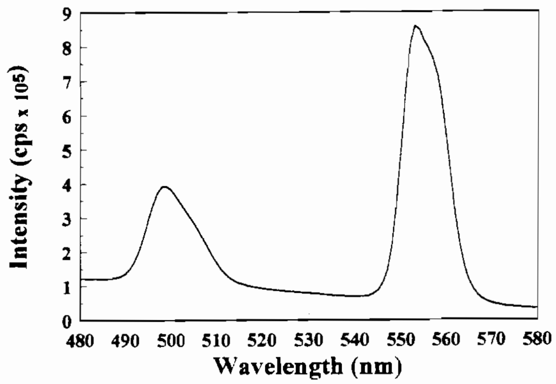


Fig. 1. Emission spectrum of $(3\cdot Tb)^{3+}$ in methanol solvent (λ_{ex} = 266 nm).

Table 1
Excited state lifetime measurements for Tb^{3+} ions encapsulated in calixarene hosts [a]

Complex	Lifetime [b] (μs)
1	639 (365); 76 (66)
2	1785 (242); 124 (62)
3	1021 (409); 62 (30)
5	554 (456); 66 (42)

[a] Lifetimes measured as 5×10^{-3} M solutions in methanol, and in parentheses as methanol/water (95/5) solutions. The excitation is into the ligand band at λ = 266 nm.

[b] Measured at 300 K in the correspondence with the most intense emission band ($^5D_4 \rightarrow {}^7F_5$ at λ = 544 nm).

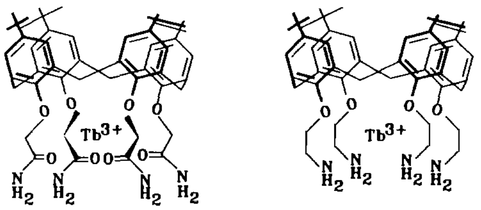


Fig. 2. Proposed structures for the 2-aminoethoxy and carbamoyloxy substituted calix[4]arene complexes of Tb^{3+}.

quenching results from complexation of one or more water molecules to the Tb^{3+} center, with subsequent coupling of the metal centered excited state to ν(OH) in the water molecules. The 2-aminoethyoxy ligand can encapsulate the Tb^{3+} ion by complexation via both the ether and the amine moieties (Fig. 2). By comparison with the work of Sabbatini, the carbamoyl ligand can coordinate via both the ether and amide oxygens. Since, however, we obtain similar excited state lifetimes for both the 2-aminoethoxy and carbamoyloxy substituted calixarenes, we cannot discount the possibility that the carbamoyloxy ligand complexes via the amide nitrogens instead of via the carbamoyl oxygens. Since the excited states of the calix[6]arene complexes are less effectively quenched by the addition of water than are those having the calix[4]arene ligands, it is possible that the larger calix[6]arene more effectively encapsulates the Tb^{3+} ion. From the observed quenching of these excited state emissions by the addition of water, however, it is clear that further chemical modifications must be made to these lower rim modified calixarenes before they can be considered useful for fluoroimmunoassay applications.

Acknowledgement

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