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Pb^{2+} Selectivity of Two New Mono Pyrene Acetamide Calix[4]arenes

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ABSTRACT

The synthesis of the mono tert-butyl ester mono pyrene acetamide calix[4]arene 5,11,17,23-tetra(t-butyl)-25-pyrene acetamide-27-tert-butyl ester calix[4]arene, 2 and of its carboxylic acid derivative 5,11,17,23-tetra(t-butyl)-25-pyrene acetamide-27-acid calix[4]arene 3, that both present pyrene fluorescent functionalities, is reported. The binding properties towards a variety of transition and non-transition metal cations have been determined, along with a fluorescence study. Particular selectivity to lead cations was observed.

Indexing terms/Keywords

calixarene; pyrene; fluorescence, complexation.

Academic Discipline And Sub-Disciplines

Organic and supramolecular chemistry

SUBJECT CLASSIFICATION

Host-Guest chemistry

INTRODUCTION

When a spontaneous emission occurs immediately after the excitation of a molecule with a light beam, molecular fluorescence phenomena are observed. **[1]** The fluorescent molecule is characterized by the property of absorbing the excitation energy followed by emission of the fluorescent radiation that results as the molecule returns to its ground electronic state. Fluorescence is used in various fields such as molecular recognition (recognition of cations, anions or neutral molecules). **[2]**

The detection of cations in a sensitive and selective way remains a huge current interest in such diverse fields as biochemistry, the environment and biology, **[3]** and fluorescence offers many advantages in terms of both sensitivity and selectivity. **[4,5]**

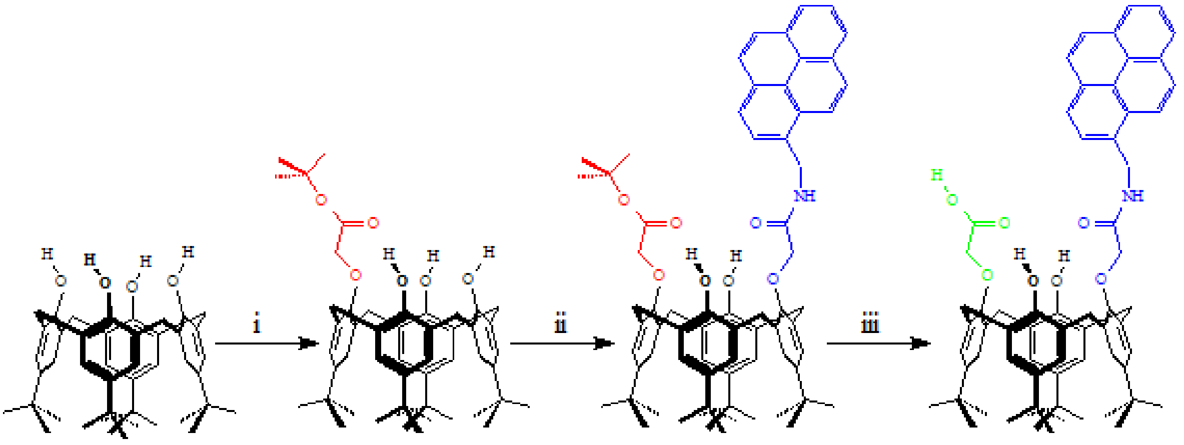
In order to detect cations in solution, it is necessary to design, and synthesize a fluorescent probe, with a complexing entity (e.g. calixarene) covalently bound to a fluorescent entity (e.g. pyrene). **[2, 6-8]** In our study, the system was designed in such way that the complexation of the cation by the calixarene induced the important changes in the fluorescent properties of the attached pyrene. **[8]**

Calixarenes are a class of macrocycles widely used as complexing agents and as substrates for the construction of more elaborate receptors with broader applications; the fluorescent chemosensors for metal ions are usually composed of a cation recognition unit (the ionophore) together with a fluorogenic unit (the fluorophore) and are usually described as fluoroionophores. An effective fluoroionophore must convert the cation recognition by the ionophore into an easily monitored and highly sensitive light signal from the fluorophore. **[8]** As fluorogenic units, pyrenes (Py) are one of the most useful probes due to their relatively efficient excimer formation and emission. **[9]**

Results and discussion

a) Compound Syntheses

The synthesis of the compounds **2** and **3** is summarized in Scheme **1**. The starting calix[4]arene was first alkylated in acetonitrile with t-butylbromoacetate to give the monosubstituted ester calixarene derivative **1**, which was isolated in close to 40% yield after work-up and column chromatography. The conversion of **1** into the acatamidopyrene ester calix[4]arene derivative **2** was effected as shown and the product **2** was obtained in a respectable 61% yield. Compound **2** was characterized by ^{1}H-NMR spectroscopy, elemental microanalysis and by MS (see experimental section). The ^{1}H NMR spectrum reveals, via the characteristic coupling constants of the calixarene methylene protons, that a cone configuration is adopted and this is true for all the calixarenes described here. **[10]** The de-esterification of **2**, in a mixture of trifluoroacetic acid in dichloromethane afforded the acatamidopyrene carboxylic acid substituted calix[4]arene derivative, **3** in good yield. Compound **3** was also fully characterized by ^{1}H NMR spectroscopy, by elemental analyses, and by (Maldi-TOF) mass spectroscopy..



1 **2** **3**

Scheme 1 - Preparation of compounds 2 – 3

(i) K_2CO_3, $BrCH_2CO_2C(CH_3)_3$, CH_3CN ; (ii) K_2CO_3, KI, $ClCH_2CONHCH_2C_{16}H_9$, CH_3CN ; (iii) CF_3COOH, CH_2Cl_2

b) Fluorescence studies

The host molecules with the pyrenyl groups exhibit intramolecular excimer emission by two mechanisms. The first mechanism results from π-π stacking of the pyrene rings in the free state, which leads to a characteristic decrease of the excimer emission intensity and a concomitant increase of monomer emission intensity. The second mechanism for excimer emission arises from the interaction of an excited pyrene (Py*) unit with a ground state pyrene (Py) unit. **[8]**

The binding properties of **2** and **3** toward metal ions were investigated by monitoring the fluorescence changes upon addition of the perchlorate salts of a wide range of metallic cations including Fe^{2+}, Co^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+} and

Al^{3+}, all in CH_3CN. In the excitation case, 50 equivalents of metal perchlorate, solubilized in acetonitrile were added to solution of ligands **2** and **3**, both respectively at a concentration of 5.0 x10^{-6} M.

The fluorescence changes are depicted in Figure 1. No specific affinity was observed between mono tert-butyl ester mono pyrene acetamide calix [4] arene **2** and the studied cations. However, the fluorescence complexation study by the ligands **2**, shows a slight affinity for Cd^{2+}, Hg^{2+}, Pb^{2+}. However, no significant changes were observed in the cases of Fe^{2+}, Co^{2+}, Cu^{2+}, Zn^{2+} and Al^{3+} cations.

Addition of Pb^{2+} ion to the CH_3CN solution of **3** bearing acid amido-pyrene induced a remarked ratiometry in which the monomer emission increases while its excimer emission declines. It is postulated that the ratiometric changes observed in **3** are due to conformational changes of the two pyrenyl moieties during Pb^{2+} complexation. In contrast, molecule **2** bearing the ester pyrene amide, shows only a little enhanced emission upon addition of Pb^{2+} ion and with other metal ions, a slight affinity is observed with respect to the ions Cd^{2+}, Hg^{2+}, Pb^{2+}.

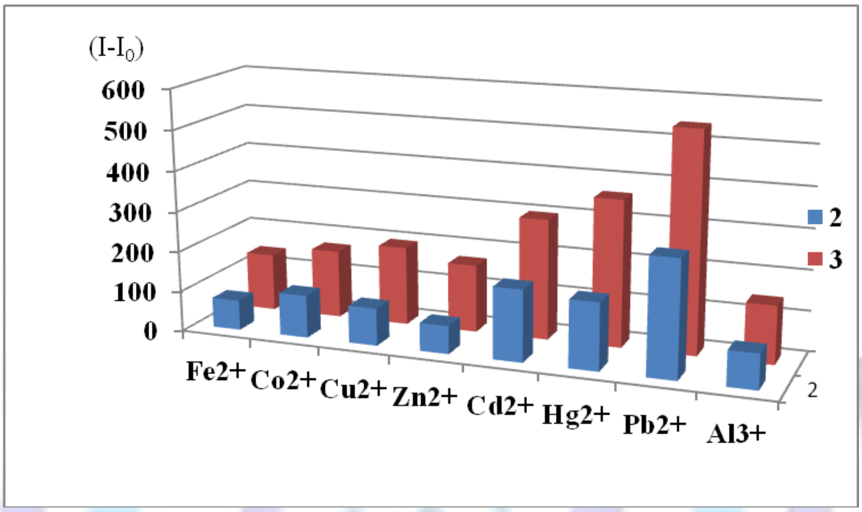


FIGURE 1. Fluorescence changes (*I* – *I*$_0$) of 2 and 3 upon the addition of various metal cations [a]

[a] **2** and **3**: 5.0 µM in CH_3CN; excitation at 340 nm; emission at 375 nm; metal ions, 50 equiv in CH_3CN. I_0: fluorescence emission intensity of free **2** and **3**. *I*: fluorescence emission intensity of metal-ion-complexed **2** and **3**.

The addition of various cation solutions (50 equivalents) to solutions of **3** led to modifications of the free ligand fluorescence spectrum with all studied cations. It was noted that the 420-580 nm wavelengths range was in general slightly affected by complexation. However, the metal complexation highly perturbed wavelengths in the 360 420 nm range, especially with Pb^{2+} (see Fig. 2).

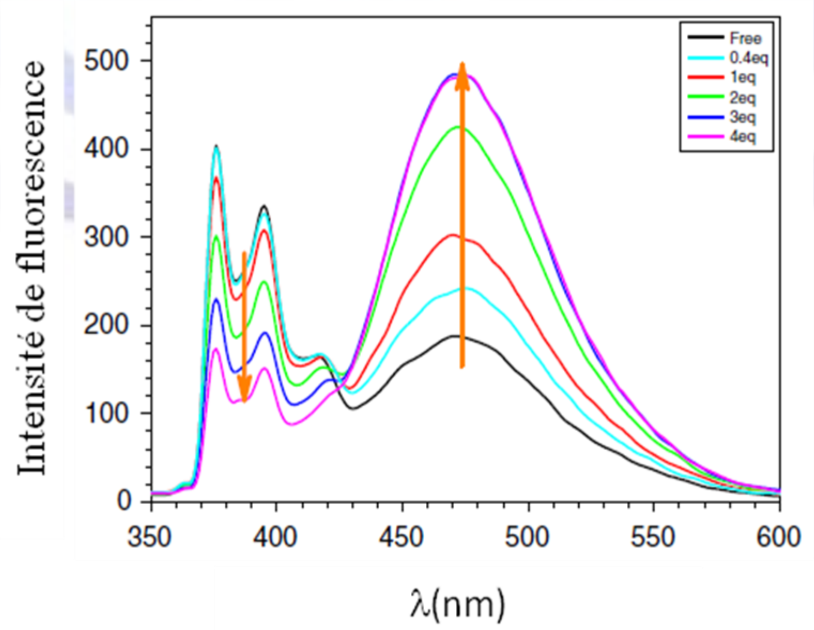


Figure 2. Fluorescence spectra of 3 (5.0 µM) in CH_3CN upon addition of increasing concentrations of $Pb(ClO_4)_2$ (0 ≤ $R_{M/L}$ ≤ 3) with an excitation at 340 nm

Experimental Section

Fluorescence Studies. All reagents and solventes were purchased from Aldrich and used as received. N-(1-pyrenemethyl) chloroacetamide was prepared via the published procedure. **[12]**

Fluorescence spectra were recorded with an RF-5301PC spectrophotometer. Stock solutions (1.00 mM) of the metal perchlorate salts were prepared in CH_3CN. Stock solutions of **2** and **3** (0.05 mM) were prepared in CH_3CN. For all measurements, excitation was at 340 nm with excitation and emission slit widths at 3.0 nm. Fluorescence titration experiments were performed using 5.0 µM solutions of **3** in CH_3CN and various concentrations of metal perchlorate in CH_3CN.**[11]**

^{1}H NMR spectra were obtained on a Bruker SY 300 NMR spectrometer, using $CDCl_3$ as the solvent. Chemical shifts were referenced with respect to TMS as an internal standard.

Preparation of 5,11,17,23-tetra(tert-butyl)-25-tert-butyl ester calix[4]arene 1

tert-Butyl calix[4]arene (4.20 g, 6.47 mmol) and K_2CO_3 (0.456g, 3.30 mmol) were stirred at room temperature for 3h in acetonitrile (180 mL). tert-Butyl bromoacetate, $BrCH_2CO_2C(CH_3)_3$, (1.268g, 6.5 mmol) was then added, and the mixture was stirred at reflux for 20 h. The solvent was then evaporated to dryness, and the residue dissolved in dichloromethane and washed with 10% HCl in a separating funnel. The organic layer was separated and dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was subjected to column chromatography on silica gel using dichloromethane as the eluent to afford **1** obtained as a white solid (1.76 g, 38%).

^{1}H-NMR ($CDCl_3$), 10.35 (1H, t, j = 5 Hz, O*H*), 10.25 (2H, t, j = 5 Hz, O*H*), 6.11 (2H, s, Ar*H*), 7.07 (4H, s, Ar*H*), 7.00 (2H, s, Ar*H*), 4.80 (2H, s, ArOCH_2), 4.54 (2H, d, j = 14 Hz, AB system ArCH_2Ar), 3.47 (2H, d, j = 14 Hz, AB system ArCH_2Ar), 3,42 (4H, d, j = 14 Hz, AB system ArCH_2Ar) , 1.63 (9H, s, C(CH_3)$_3$), 1.25 (9H, s, C(CH_3)$_3$), 1.23 (18H, s, C(CH_3)$_3$), 1.21 (9H, s, C(CH_3)$_3$). MS-MALDI-TOF: $C_{50}H_{66}O_6$ m/z = 763.06 (calcd. 763.07). Anal, calcd. for $C_{50}H_{66}O_6$: C, 78.70; H, 8.72; found: C, 78.61; H, 8.66

Preparation of 5,11,17,23-tetra(tert-butyl)-25-pyrene acetamide-27- tert-butyl ester calix[4]arene 2

Mono tert-butyl ester calix[4]arene **1** (457 mg; 0.6 mmol), K_2CO_3 (83 mg, 0.6 mmol) and excess KI were stirred at room temperature 3h in acetonitrile (15 mL). N-(1-pyrenemethyl) chloroacetamide (211 mg, 0.685 mmol) was then added and. the resulting mixture stirred at reflux for 24h. The solvent was then evaporated and the residue extracted with dichloromethane, and then washed with 10% HCl. The organic layer was separated, dried over $MgSO_4$ and the solvent was removed. The residue was passed through a silica gel chromatography column and eluted with dichloromethante to yield the desired compound **2** as a white foamy material (365 mg, 61%)

^{1}H NMR δ (ppm): 9.58 (1H, t, J = 5 Hz, N*H*), 7.70-8.56 (9H, m, $C_{16}H_9$), 7.31 (2H, s, O*H*), 6.92(4H, s, Ar*H*), 6.78 (4H, s, Ar*H*), 5.49 (2H, d, J = 5 Hz, N-CH_2), 4.55 (2H, s, ArOCH_2), 4.43 (2H, d, J = 5 Hz, ArOCH_2N), 4.14 (2H, d, J = 14 Hz, AB system ArCH_2Ar), 4.03 (2H, d, J = 14 Hz, AB system ArCH_2Ar) , 3.25 (2H, d, J = 14 Hz, AB system ArCH_2Ar), 3.13 (2H, d, J = 14 Hz, AB system ArCH_2Ar), 1.43 (9H, s, OC(CH_3)$_3$), 1.26 (18H, s, C(CH_3)$_3$), 0.97(9H, s, C(CH_3)$_3$), 0.95(9H, s, C(CH_3)$_3$). MS-MALDI-TOF: $C_{69}H_{79}NO_7$ m/z = 1034.37 ($M + H^+$), (calcd. 1034.39). Anal, calcd. for $C_{69}H_{78}NO_7$: C, 80.20; H, 7.61; found: C, 80.31; H, 7.46.

Preparation of 5,11,17,23-tetra(tert-butyl)-25-pyrene acetamide-27-acide calix[4]arene, 3.

Mono tert-butyl ester mono pyrene acetamide calix[4]arene **2** (100 mg, 0.0966 mmol) was stirred at room temperature in a 1:1 mixture of dichloromethane:trifluoroacetic acid (2 mL) for 33h. The solvent was then evaporated to yield pure **3** (77 mg, 82%).

^{1}H NMR δ (ppm): 9.58 9.17 (1H, t, J = 5 Hz, N*H*), 7.64-8.20 (9H, m, $C_{16}H_9$), 6.86 (2H, s, Ar*H*), 6.76 (2H, s, Ar*H*), 6.56 (4H, s, Ar*H*), 6.49 (2H, s, O*H*), , 5.33 (2H, d, J = 5 Hz, N-CH_2), 4.71 (2H, s, ArOCH_2 Acid), 4.07 (2H, s, ArOCH_2N), 3.98 (4H, d, J = 14 Hz, AB system ArCH_2Ar), 3.31 (4H, d, J = 14 Hz, AB system ArCH_2Ar) , 1.17 (18H, s, C(CH_3)$_3$), 0.93 (9H, s, C(CH_3)$_3$), 0.86 (9H, s, C(CH_3)$_3$). MS-MALDI-TOF: $C_{65}H_{70}NO_7$ m/z= 1000.24 $(M + Na)^+$, (calcd. 1000.26). Anal, calcd. for $C_{65}H_{70}NO_7$: C, 79.89; H, 7.22; found: C, 77.83; H, 7.18.

Conclusion

Two new fluorogenic compounds have been prepared, the mono pyrene acetamide calix[4]arene **2** and its related mono pyrene acetamide-mono-acid calix[4]arene derivative **3.** This study demonstrates the affinity of these fluorescent calixarenes heavy metals; a particular selectivity to lead Pb^{2+} cations was observed. The acid derivative **3** exhibited superior selectivity to Pb^{2+} as compared to its related tert-butyl ester compound **2**.

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REFERENCES

[1] Czarnik, A. W., Chem. Biol. 1995, 2, 423-428.

[2] Sahana A., Banerjee A, Lohar S, Guha S, Das Sudipta, Mukhopadhyay S.K. and Das D., Analyst, 2012, 137, 3910-3913.

[3] Chemosensors for Ion and Molecule Recognition. NATO ASI Series, Desvergnes, J. P.; Czarnik, A. W., Eds, Kluwer Academic, Dordrecht, 1997.

[4] Gómez-Machuca H., Quiroga-Campano C., Jullian C., De la Fuente J., Pessoa-Mahana H., Escobar C. A., Dobado J. A., Saitz C., J. Incl. Phenom. 2014, 80, 369-375.

[5] Quiroga-Campano C., Gómez-Machuca H., Jullian C., De la Fuente J., Pessoa-Mahana H., Saitz C., J. Incl. Phenom., 2014, 79, 161-169.

[6] Ozlem S., Mustafa Y., Tetrahedron, 2011, 67, 3501-3508.

[7] Debdeep M., Ashish C., Ravi G., Parimal P., Inorg. Chim. Acta, 2011, 372, 126–135.

[8] Faulkner S., Carrié M.-C., Pope S. J. A., Squire J., Beeby A., Sammes P. G., Dalton Trans., 2004, 9, 1405–1409.

[9] Mareeswaran P.M., Maheshwaran D., Babu E., Rajagopal S., J. Fluoresc. 2012, 5, 1345-1356.

[10] C. D. Gutsche, Ed Stoddart J.F., 1989, The Royal Society of chemistry, London, Vol. 1.

[11] Hamdi A., Kim S. H., Abidi R., Thuéry P., Kim J.S., Vicens J., Tetrahedron, 2009, 65, 2818-2823.

[12] Van der Veen, N. J.; Flink, S.; Deiji, M. A.; Egberink, R. J.; van Veggel, F. C. J.; Reinhoudt, D. N., J. Am. Chem. Soc. 2000, 122, 6112-6113.