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An Anthracene-Based Fluorescent Sensor for Transition Metal Ions Derived From Calix[4]arene

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Abstract: The preparation of anthracene-based fluorescent calix[4]arene **1** combining calix[4]arene element and 9-anthryl unit is reported. The presence of a dioxotetraaza unit allows the chelation of transition metal cations such as zinc and nickel.

As a consequence of the rapid development of supramolecular chemistry, supramolecular technology has developed the synthesis of luminescent probes for metal cations.[1,2] These luminescent probes combine a fluorogenic unit with a cation-selective binding site giving rise to a receptor capable of sensing trace amounts of any particular metal cation in biological materials as well as for medical and environmental applications.[1,2] A number of such fluorescent sensors have been designed for transition metal ions. For instance, Czarnik and co-workers[3] reported the synthesis of several polyazamacrocycles linked to the 9-anthryl unit designed to provide chelation-enhanced fluorescence on complexatio of nonquenching metal ions [e. g., Zn(II) and Cd(II)] in aqueous solutions. For some receptors fluorescence is quenched by addition of Cu(II) and Hg(II). Similar anthracene systems with tetraazadioxa-18-crown-6 have been synthetized by Czarnik and co-workers[4] and their fluorescence titrations with Zn(II), Ca(II), Na(I), Ni(II), Co(II) and Pb(II) ions have been presented. Fabbrizzi and co-workers[5] reported the synthesis of an anthracene-based fluorescent sensor for transition metal ions combining 9-anthryl unit and chelating dioxotetraaza unit. Uncomplexed sensor does not fluoresce and the binding of metal [Mn(II), Cu(II), Co(II) and Ni(II)] resulted in fluoresce by photo-induced-electron transfer. Fabbrizzi and co-workers[6] also constructed fluorescent sensors for 3d divalent metal ions by linking 9-anthryl fragment (signalling subunit) to cyclic or noncyclic dioxotetramine ligand or to a cyclam (receptor centers). Zn(II)-promoted fluorescence enhancement is observed in sensors containing the tetramine subunit.[6]

In the present Note we report the synthesis of anthracene-based fluorescent sensor deriving from calix[4]arene **1** designed for transition metal ions. Preliminary binding properties towards Zn(II) and Ni(II) are also presented.

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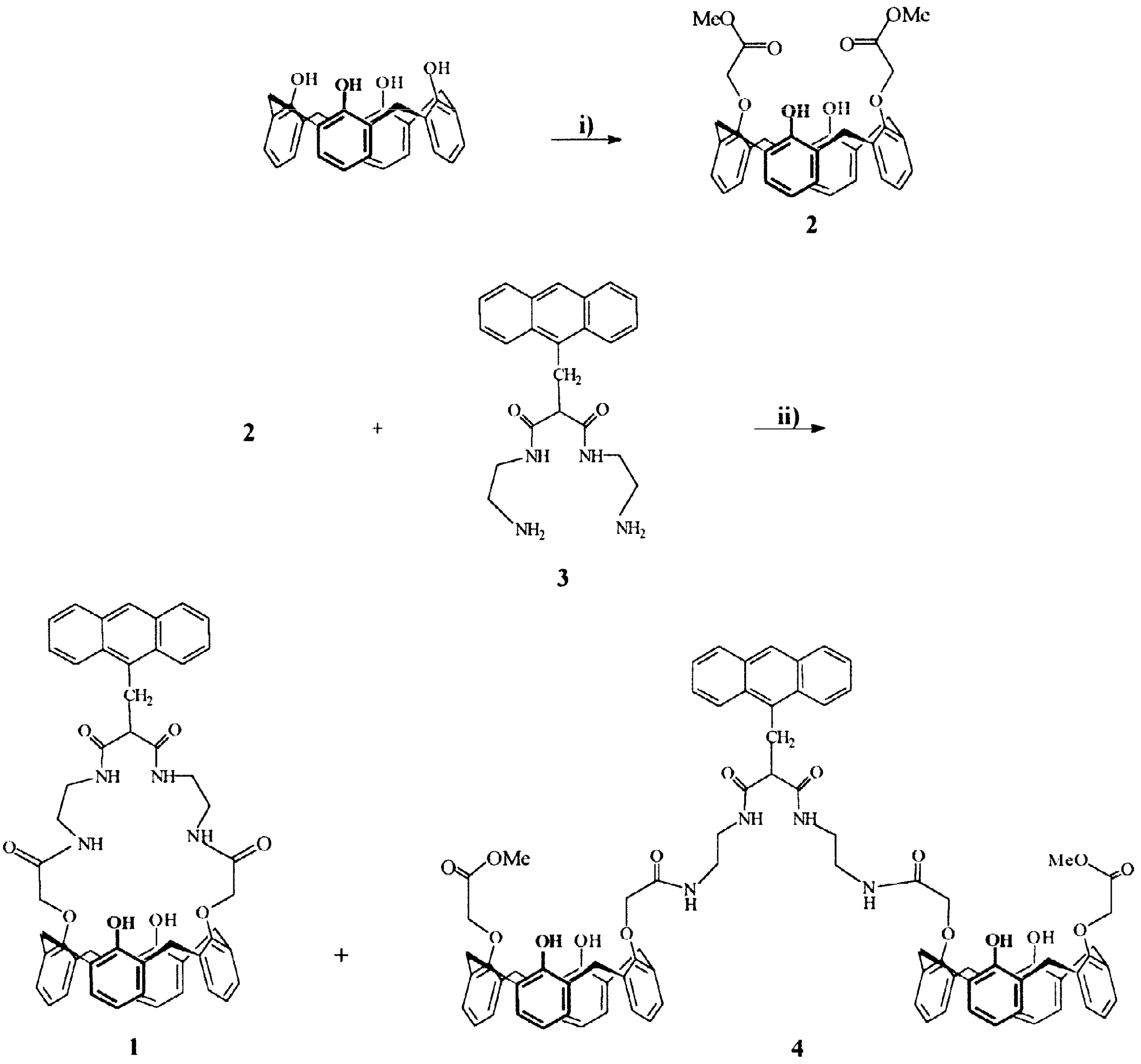
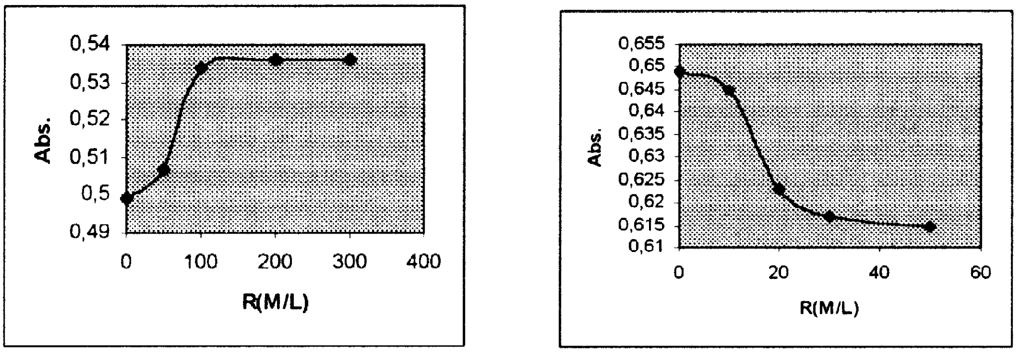


i) $BrCH_2CO_2CH_3$, K_2CO_3, acetone, reflux, 24 hrs
ii) 1:1 toluene-methanol, reflux, 10 days

Scheme 1. Synthetic pathway to **1** and **4**.

The synthesis of **1** is illustrated in Scheme 1 (see experimental[7]). Precursor 1,3-O-dimethyl ester calix[4]arene derivative **2** was prepared by reaction of calix[4]arene with 2 equivs of methyl bromo acetate in the presence of 1 equiv of K_2CO_3 in refluxing acetone for 24 hrs. After filtration, compound **2** was precipitated as a white solid with methanol during evaporation of the solvents of reaction and of washing (acetone and CH_2Cl_2). The yield was 79%. The selective 1,3-di-O-alkylation and the cone conformation of **2** were deduced from the observation in its ^{1}H-NMR spectrum of an AB system at 3.40 ppm and 4.47 ppm (J_{AB} = 13.0 Hz) for $ArCH_2Ar$ protons and two triplets at 6.65 ppm and 6.74 ppm (J = 7.5 Hz) respectively for the *para* protons of the aromatic moieties. Condensation of 9-anthryl diamine **3**[6] on dimethyl ester **2** was achieved by reaction of **2** with 1 equiv of **3** in a 1:1 mixture of toluene and methanol with reflux for 10 days. **1** was eluted on SiO_2 column with 80:20 CH_2Cl_2:acetone as eluent as a white solid in 14% yield. An AB system at 3.40 ppm and 4.37 ppm (J = 13.0 Hz) for the ArCH_2Ar protons indicated compound **1** to be in cone conformation. Double calixarene **4** was also isolated as a by-product in 3.5% yield.

Preliminary complexation studies were carried out with UV-visible spectrometry. Various amounts of $Zn(ClO_4)_2$ and $Ni(ClO_4)_2$ were added to a 2 x 10^{-4}M solution of **1** in a 4:1 mixture of acetonitrile:water. Figure 1 shows the variation of absorption of ligand **1** at constant concentration at 276 nm during addition of Zn (figure 1a) and Ni (figure 1b) salts. The data were satisfactorily interpreted assuming the formation of 1:1 complexes in both cases with stability constants of log K = 2.2 for the zinc complex and log K = 2.8 for the nickel complex. The 1:1 stoechiometry of the complexes of **1** with Zn and Ni were confirmed by mass spectrometry.[7] By ^{1}H-NMR the zinc atom was tentatively located nearby the nitrogen atoms due to a large shift (0.80-1.00 ppm) of the CH_2NH protons.



(a) (b)

Figure 1. Variation of the absorption of ligand **1** at 276 nm by progressive addition of (a) $Zn(ClO_4)_2$ and (b) $Ni(ClO_4)_2$

The intensity of the fluorescence of the solutions (same solvent as for UV spectrometry) was modified in the presence of the Zn (enhancement) and Ni (quenching) metallic salts.

Further studies of the fluorescent properties of **1** are currently under investigations and will be presented in due course. Work is also directed towards reduction of the amido functions for better complexation.

References and Notes

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6. Fabbrizzi, L.; Licchelli, M.; Pallavicini, P.; Perotti, A.; Sacchi, D. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1975-1977
7. **General:** Mps, capillaries under nitrogen, Büchi 500. Chromatography, SiO_2 columns with Kiesiegel Merck (Art. 11567). Thin layer chromatography (TLC), SiO_2 Merck plates (Art. 6484). ^{1}H-NMR, Bruker SY200 (δ in ppm, J in Hz). FAB (+), VG-Analytical ZAB HF. Elemental analyses were performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg.

Preparation of 2: Calix[4]arene (12.72 g, 30.00 mmol), K_2CO_3 (4.45 g, 32.00 mmol), $BrCH_2CO_2CH_3$ (9.64 g; 63.00 mmol) and acetone (600 mL) were refluxed for 24 hrs. Solvents were evaporated to dryness and the residue was treated with methanol to yield a white solid (12.36 g, 24 mmol).

Analytical data of compound **2***:* Mp 214-215 °C. ^{1}H-NMR (200 MHz, $CDCl_3$) 7.56 (s, 2H, ArO*H*), 7.05 (d, *J*= 7.5, 4H, Ar*H* meta), 6.91 (d, *J*= 7.5, 4H, Ar*H* meta), 6.79-6.79 (m, 4H, Ar*H* para), 4.75 (s, 4H, $CH_2CO_2CH_3$), 4.47 (d, *J*= 13.0, $ArCH_2Ar$, AB system), 3.88 (s, 6H, $CH_2CO_2CH_3$), 3.40 (d, *J*= 13.0, $ArCH_2Ar$, AB system).

Preparation of 1: 1,3-Dimethyl ester calix[4]arene **2** (2.64 g; 4.60 mmol) was dissolved in a 1:1 mixture of toluene: methanol (920 mL). A solution of 9-anthranyl diamine **3** (1.76 g, 4.60 mmol) dissolved in a 1:1 mixture of toluene:methanol (80 mL) was added dropwise during 30 mn. The mixture was refluxed for 10 days. Solvents were evaporated to dryness. Chromatography, SiO_2, 80:20 CH_2Cl_2:acetone afforded **1** (0.568 g, 0.64 mmol) and **4** (0.120 g, 0.08 mmol) as white solids.

Analytical data of compound **1**: Mp 155-156 °C. ^{1}H-NMR (200 MHz, acetone-d_6) 8.45-8.30 (m, 2H, Anth-*H*), 8.09-8.02 (m, 3H, CH_2NH, Anth-*H*), 7.45-7.51 (m, 4H, CH_2NH, Anth-*H*), 7.19 (d, *J*= 7.5, 4H, Ar*H* meta), 7.09 (d, *J*= 7.5, 4H, Ar*H* meta), 7.05-6.98 (m, 4H, Ar*H*, Anth-*H*), 6.75 (d, *J*= 7.5, 2H, Anth-*H*), 6.69-6.54 (m, 2H, Ar*H* para), 5.63 (s, 2H, ArO*H*), 4.51 (s, 4H, $ArOCH_2CONH$), 4.37 (d, *J*= 13.0, 4H, $ArCH_2Ar$, AB system), 4.22 (d, 2H, *J*= 6.5, Anth-CH_2CH), 3.57-3.49 (m, 9H, CH_2CH, $NHCH_2$), 3.40 (d, *J*= 13.0, 4H, $ArCH_2Ar$, AB system). *Anal. Found* C, 69.29; H, 6.46. *Calc.* For $C_{54}H_{50}N_4O_8.2H_2O.2(C_2H_6O)$ C, 70.00; H, 6.68; FAB (+) MS, m/z 883.3 (M^+).

Analytical data of compound **4**: Mp 153-154 °C. ^{1}H-NMR (200 MHz, $CDCl_3$) 8.58 (broad s, 2H, CH_2NH), 8.28 (s, 1H, Anth-*H*), 8.26 (d, *J*= 8.0, 2H, Anth-*H*), 7.95-7.90 (m, 2H, Anth-*H*), 7.70 (s, 4H, ArO*H*), 7.47-7.40 (m, 4H, Anth-*H*), 7.01 (d, *J*= 7.0, 2H, Anth-*H*), 6.96-6.72 (m, 20H, Ar*H* meta and para), 6.65-6.51 (m, 4H, Ar*H* para), 4.55 (s, 4H, $ArOCH_2CONH$), 4.40 (s, 4H, $CH_2CO_2CH_3$), 4.19-4.05 (m, 11H, $ArCH_2Ar$, Anth-CH_2CH, Anth-CH_2CH), 3.77 (s, 6H, $CH_2CO_2CH_3$), 3.56-3.17 (m, 16H, $ArCH_2Ar$, $NHCH_2$). *Anal. Found* C, 70.27; H, 6.30. *Calc.* For $C_{88}H_{82}N_4O_{16}.2H_2O$ C, 70.20; H, 5.89; FAB (+) MS, m/z 1451.5 (M^+).

Preparation of the 1:1 complex of 1 with $Zn(ClO_4)_2$ or $Ni(ClO_4)_2$. 5 mg of compound **1** was dissolved in 1.5 ml of acetone-d_6. Then an excess of zinc perchlorate or nickel perchlorate was added to the solution and a ^{1}H-NMR spectrum was directly recorded. *Analytical data of the 1:1 complex of* **1** *with $Zn(ClO_4)_2$* ^{1}H-NMR (200 MHz, acetone-d_6) 8.81 (broad s, 2H, CH_2NH), 8.59 (s, 1H, Anth-*H*), 8.45-8.40 (m, 4H, CH_2NH, Anth-*H*), 8.14-7.99 (m, 6H, Ar*H* meta, Anth-*H*), 7.47-7.68 (m, 4H, Ar*H* meta), 7.18-7.14 (m, 4H, Ar*H*, Anth-*H*), 6.97 (d, *J*= 7.5, 2H, Anth-*H*), 6.73-6.62 (m, 2H, Ar*H* para), 5.60 (broad s, 2H, ArO*H*), 4.45-4.31 (m, 12H, $ArOCH_2CONH$, $NHCH_2$), 4.16 (d, *J*= 13.0, 4H, $ArCH_2Ar$, AB system), 4.00-3.80 (m, 2H, Anth-CH_2CH), 3.70-3.52 (m, 1H, CH_2CH), 3.43 (d, *J*= 13.0, 4H, $ArCH_2Ar$, AB system). FAB (+) MS, m/z 945.3 ($M-2H^++Zn^{++}+H^+$).

Analytical data of the 1:1 complex of **1** *with $Ni(ClO_4)_2$.* The ^{1}H-NMR spectrum could not be recorded and we only could detected the 1:1 complex through its FAB (+) MS, m/z 939.2 ($M-2H^++Ni^{++}+H^+$)