Effective fluorescent sensing of Na^+ ion by calix[4]arene bearing pyrene and perylene based on energy transfer

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Abstract

A new calix[4]arene having pyrene and perylene moieties has been synthesized as a Na^+ detectable fluorescent ionophore. When excited at the pyrene moiety (342 nm) of the ionophore, a strong fluorescence emission of the perylene moiety (535 nm) was observed due to energy transfer from the pyrene to perylene. By addition of Na^+ at a low concentration in the range of 2.5-10 μM, the fluorescence was remarkably quenched. In contrast to the fluorescent behavior by the ionophore having pyrene and perylene moieties, the excimer emission of a calix[4]arene derivative having two pyrene moieties decreased by the addition of Na^+ with a concentration in the range of 50-200 μM.

Keywords: Ionophore, calix[4]arene, fluorescence, pyrene, perylene, energy transfer

Introduction

The detection and quantification of Na^+ has been a very important subject, especially in the clinical field,[1-5] because Na^+ plays a crucial role in the regulation of many physiological phenomena. Therefore, a number of synthetic receptors for Na^+ having podands, crown ethers, lariat ethers, cryptands, and spherands as binding sites have been developed.[6]

Since calixarenes can be modified by different functionalizations at the lower and/or upper rims of the molecule, the calixarene derivatives provide effective platforms for anchoring a variety of binding units for ions and neutral molecules. For alkali cations, calixarene derivatives incorporating functional groups, such as ester, ether, ketone, amide and carboxylic groups, exhibit excellent binding abilities.[7-17]

Several groups have recently reported the fluorometric detection of Na^+ using the calix[4]arene derivatives bearing pyrenyl groups. On these calix[4]arene-based fluorescence

sensors, Na^+ complexation can be monitored by intramolecular pyrene excimer emission and extinction,[18,19] disruption of the intramolecular photoinduced electron transfer from the pyrene to nitrobenzene,[20] and induction of the intramolecular fluorescence energy transfer from the pyrene to anthracene.[21]

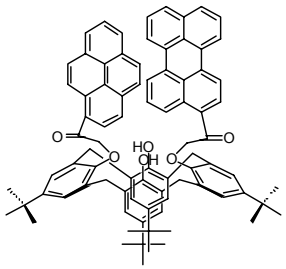


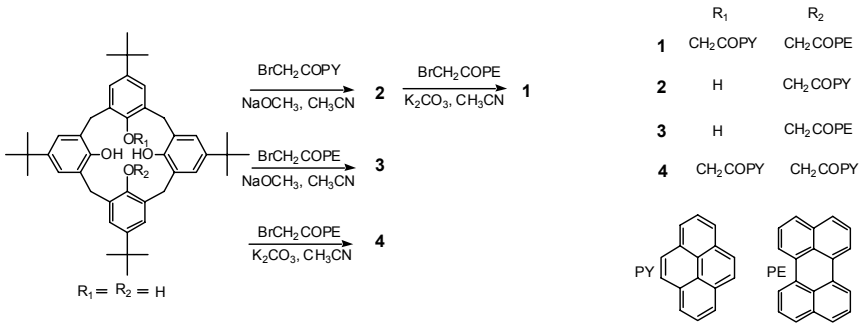
Figure 1. The new calix[4]arene derivative bearing pyrene and perylene.

Perylene exhibits a more intense fluorescence than pyrene, and the fluorescence emission band of perylene significantly overlaps with the absorption band of pyrene. Therefore, when a mixture of pyrene and perylene is excited at the excitation wavelength of pyrene, the strong fluorescence of perylene is observed based on the energy transfer from the pyrene to perylene.[22-24] However, perylene has not used as the fluorogenic unit of calixarene-based ionophores.

In order to construct a new fluorescent ionophore, which detects slight changes in the Na^+ concentration on a micromolar level, we have designed compound **1** (Figure 1) in which the pyrene and perylene are connected to the symmetrical OH groups of the *p-tert*-butylcalix[4]arene.

Results and Discussion

Scheme 1 shows the synthetic routes for the fluorescent ionophore **1** and calixarenes **2**,**3** and **4** as the reference compounds. The reaction of *p-tert*-butylcalix[4]arene with 1-(bromoacetyl)pyrene and 3-(bromoacetyl)perylene in the presence of sodium methoxide in acetonitrile afforded compounds **2** having one pyrene moiety and **3** having one perylene moiety respectively. Compound **2** was subsequently reacted with 3-(bromoacetyl)perylene using potassium carbonate as a base to produce the ionophore **1**. Compound **4** having two pyrenyl groups was prepared by the reaction of *p-tert*-butylcalix[4]arene with two equivalents of 1-(bromoacetyl)pyrene in the presence of potassium carbonate in acetonitrile. The structures of **1**-**4** were determined by their MS and NMR spectra.



Scheme 1. The synthesis of **1**, **2**, **3** and **4.**

The ^{1}H NMR spectrum of compound **1** showed four doublets at δ 3.38, 3.39, 4.65 and 4.70 corresponding to the protons of the methylene bridge. This result suggests that **1** exists in the cone conformation.[25,26] Similarly, the methylene hydrogens splitting pattern indicated that compounds **2**, **3** and **4** also adopted the cone conformation.

As shown in Figure 2, the UV-Vis spectrum of compound **1** containing pyrene and perylene shows a broad absorption band corresponding to a superposition of two the spectra of compound **2** having a pyrene moiety and compound **3** having a perylene moiety.

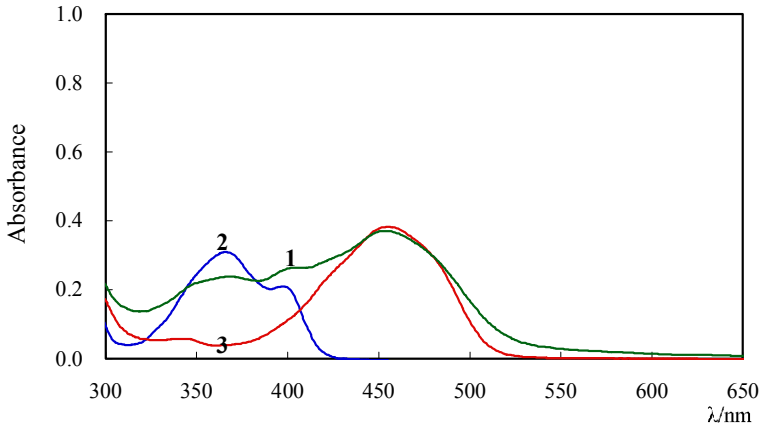


Figure 2. UV-Vis spectra of **1**, **2** and **3** (10 μM in diethyl ether).

Figure 3 shows the excitation and fluorescence spectra of compound **2** having a pyrene moiety and compound **3** having a perylene moiety. The fluorescence emission band (2FL) of **2** at 420 nm significantly overlaps with the excitation band (3EX) of **3** centered at 450 nm.

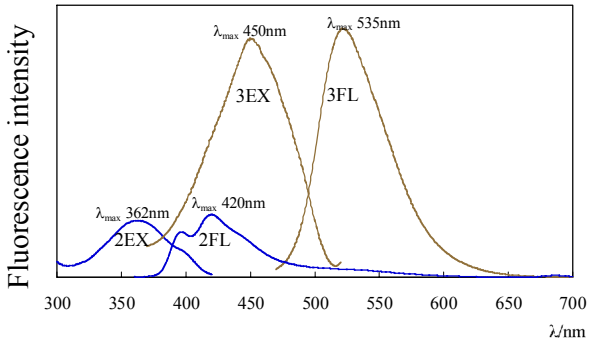


Figure 3. Excitation and fluorescence spectra of **2** (curve 2EX: excitation spectrum detected at 440 nm; curve 2FL: fluorescence spectrum excited at 342 nm) and **3** (curve 3EX: excitation spectrum detected at 530 nm; curve 3FL: fluorescence spectrum excited at 450 nm). The concentrations of **2** and **3** are 1.0 μM in diethyl ether.

These results indicate that a strong perylene emission would be observed due to the intramolecular energy transfer from the pyrene to perylene when the calix[4]arene derivative incorporated pyrene and perylene moieties is excited at the pyrene moiety. The excitation of a 1.0 μM solution of **1** at 342 nm corresponding to the absorption band of the pyrene moiety of **1** induced a strong emission band at 535 nm (Figure 4). This band coincides with the fluorescence of **3** having one perylene moiety observed by excitation at 450 nm. No emission at 535 nm, however, was observed by the excitation of **3** at 342 nm. By excitation of equimoler mixtures of **2** and **3** at 342 nm at the concentration of 2.0 μM, only the monomeric pyrene fluorescence was observed at 380-460 nm. These results indicate that the excitation of compound **1** having pyrene and perylene moeties at 342 nm emits the perylene fluorescence by energy transfer from the pyrene to perylene.

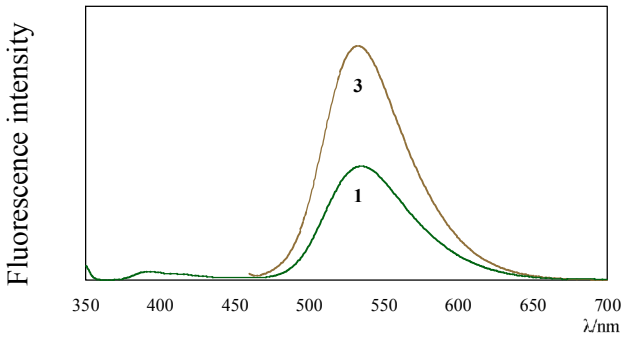


Figure 4. Fluorescence spectra of **1** and **3** (1.0 μM in diethyl ether). Excitation wavelength: 342 nm for **1**, 450 nm for **3**.

On the other hand, a 1.0 μM solution of bispyrenylcalix[4]arene **4** shows a dual emission resulting from a pyrene monomer in the range of 380-460 nm and excimer at 520 nm by excitation of the pyrene moiety of **4** at 342 nm (Figure 5). The excimer emission of **4** must be intramolecular excimer emission, because only the pyrene monomer emission was observed by the excitation of **2** having one pyrene moiety at the concentration of 2.0 μM.

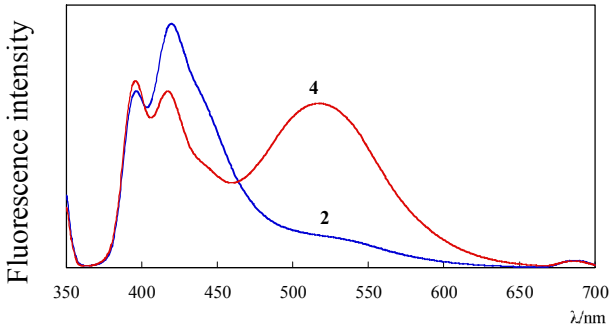


Figure 5. Fluorescence spectra of **2** (2.0 μM) and **4** (1.0 μM). Excitation wavelength: 342 nm for **2** and **4**.

The calixarene derivatives bearing two pyrene groups on the lower rim have been reported to display monomer emissions from 370-425 nm and excimer emissions at around 480 nm, [18,19] while compound **4** showed a monomer emission from 380-460 nm and excimer emission at 520 nm. This result is presumably attributed to the effect of the electron-withdrawing carbonyl group. It is well known that some aromatic hydrocarbons substituted with an electron-withdrawing carbonyl group induce a large bathochromic shift in both the absorption and fluorescence spectra compared to the spectra of the parent aromatic hydrocarbons.[27,28] For the fluorescence sensors using pyrenecarbonyl compounds, the fluorescence spectra shifted to a wavelength longer than the spectra of pyrene itself.[29,30] In our observations, the pyrene monomer and excimer emission of **2** having one pyrenecarbonyl moiety shifted to a wavelength longer than the spectra of pyrene itself (monomer in the 370-425 nm range and excimer at 480 nm). Namely, compound **2** showed the pyrene monomer emission from 380-460 nm and excimer emission at around 520 nm by excitation at 342 nm at the concentration of 1.0 mM.

Figure 6 shows the fluorescence changes in **4** with various Na^+ concentrations by excitation at 342 nm. The fluorescence intensity of the excimer emission at 520 nm of **4** gradually decreased and the intensity of the monomer emission of **4** increased with the increasing Na^+ concentrations ranging from 50 μM to 200 μM. These fluorescence changes were probably caused by the separation of the pyrene moieties from each other by the Na^+ complex formation on the lower rim of **4**.

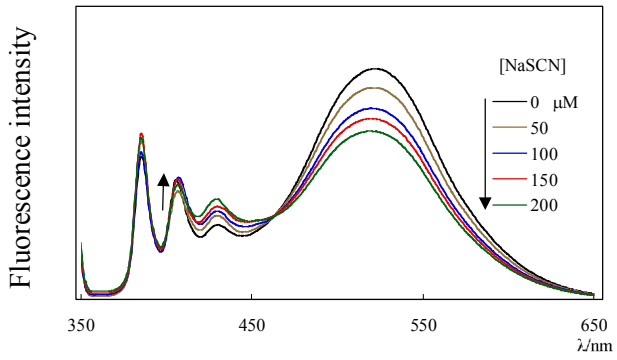


Figure 6. Fluorescence spectral changes of a 1.0 μM solution of **4** in diethyl ether-acetonitrile (97:3 V/V) upon the addition of NaSCN. Excitation wavelength: 342 nm.

In contrast to the ionophore **4**, an effective decreasing of the fluorescence of **1** was observed upon the addition of Na^+ at the concentrations ranging from 2.5 μM to 10 μM (Figure 7). The fluorescence change of a 1.0 μM solution of **1** is characterized by a small increasing pyrene monomer emission from 380-460 nm and large decreasing perylene emission at around 535 nm by the excitation of **1** at 342 nm. Interestingly, this Na^+ concentration range on the ionophore **1** is about a hundredth lower than that on the ionophore **4** (Figure 6). Furthermore, these spectral changes indicate that the pyrene and perylene moieties incorporated in **1** are probably separated from each other by the Na^+ complex formation, and the energy transfer from the pyrene moiety to the perylene moiety would be disrupted.

These results clearly indicate that the high sensitive detection toward Na^+ is performed by using the fluorescent ionophore **1** having pyrene and perylene moieties compared to the fluorescent ionophore **4** having two pyrene moieties.

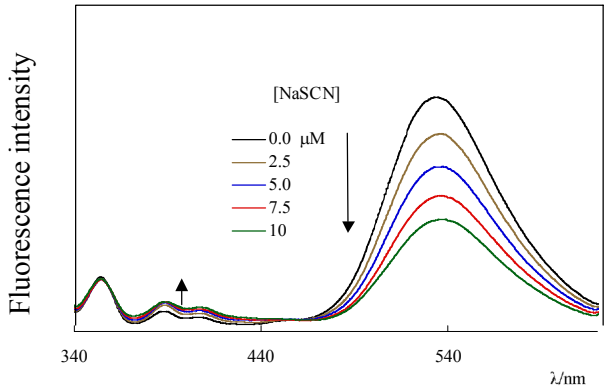


Figure 7. Fluorescence spectral changes of a 1.0 μM solution of **1** in diethyl ether-acetonitrile (97:3 v/v) upon the addition of NaSCN. Excitation wavelength: 342 nm.

Conclusions

We have synthesized a novel calix[4]arere **1** having pyrene and perylene moieties. The fluorescent ionophore **1** can detect Na^+ at low concentrations in the range of 2.5-10 μM (2.5-10 molar equivalent of **1**) with large fluorescence changes based on intramolecular energy transfer from the pyrene moiety to perylene moiety.

Experimental Section

General Procedures. All melting points were determined using a Hansen & Co,. Ltd. MEL-TEMP and were uncorrected. UV-Vis spectra were obtained using the Hitachi U-3010 spectrophotometer. The fluorescence spectra were obtained by a Hitachi F-2500 fluorescence spectrophotometer. The ^1H and ^{13}C NMR spectra were measured by a JEOL-JNM-ECP300 spectrometer (300 MHz and 75 MHz), respectively. The chemical shifts were measured in ppm downfield from the tetramethylsilane as the internal standard. The HRMS (FAB) spectra were measured by a JEOL JMS-SX102A using glycerol or 3-nitrobenzyl alcohol as the matrix. All chemicals for the synthesis of **1**, **2**, **3**, and **4** were from Aldrich and used without further purification. Silica gel (70–230 mesh) was from Merk Ltd. Japan.

General procedure for fluorescent study. The stock solutions of **1** and **3** (1.03 μM) were prepared by using spectroscopic grade diethyl ether (Wako Pure Chemical Industries, Ltd). The NaSCN stock solutions (10 mL) of appropriate concentrations were prepared in spectroscopic grade acetonitrile (Wako Pure Chemical Industries, Ltd). Test solutions were prepared by mixing the stock solution (9.7 mL) of **1** or **3** and the NaSCN stock solution (0.1 mL), followed by diluting the solution to 10.0 mL with acetonitrile.

3-(Bromoacetyl)perylene. To the ground $CuBr_2$ (0.25 g, 1.12 mmol) and ethylacetate (1 mL), a chloroform (180 mL) solution of 3-acetylperylene[31] (0.20 g, 0.670 mmol) was added at room temperature. The reaction mixture was refluxed for 6 h. After removal of the CuBr by filtration, the solvents were removed in vacuo. The residue was purified by silica gel column chromatography with dichloromethane to afford orange colored powder 3-(bromoacetyl)perylene (0.20 g, 95 %); mp 195-196 °C dec; ^1H NMR (300 MHz $CDCl_3$) δ 4.58 (s, 2H), 7.51-8.65 (m, 11H); ^{13}C NMR (75 MHz DMSO-d_6) δ 33.6, 77.2, 118.5, 121.1, 121.4, 122.3, 125.7, 126.7, 127.0, 128.2, 128.4, 128.9, 129.4, 129.7, 129.8, 129.9, 130.7, 130.8, 131.3, 132.5, 134.4, 136.7; HRMS (FAB) Found ($M^{+\cdot}$): 372.0150, 374.0132; Calcd for $C_{22}H_{13}OBr$: 372.0150, ($M^{+\cdot}$+2) 374.0130.

General procedure for 25-(Arylacetyloxy)-5,11,17,23-tetra-*tert*-butyl-26,27,28-trihydroxy-calix[4]arenes (2, 3). The mixture of *p-tert*-butylcalix[4]arene and sodium methoxide was refluxed in acetonitrile for 30 min to completely monodeprotonate the *p-tert*-butylcalix[4]arene.

An excess amount of bromoacetylarene was then added to the reaction mixture, followed by stirring at reflux temperature for 8 h. The reaction mixture was neutralized with a few drops of acetic acid, and the solvent was removed. The residue was purified by column chromatography.

25-(1-Pyrenylacetyloxy)-5,11,17,23-tetra-*tert*-butyl-26,27,28-trihydroxycalix[4]arene (2). To an acetonitrile (37.5 mL) solution of the monodeprotonated *p-tert*-butylcalix[4]arene (0.81 g, 1.25 mmol) by sodium methoxide (0.08g, 1.48 mmol), the solution of 1-(bromoacetyl)pyrene (1.00 g, 3.10 mmol) in acetonitrile (600 mL) was added and refluxed. The residue provided by the same procedure described above for the general procedure was purified by silica gel column chromatography with chloroform to afford yellow colored powder **2** (0.33 g, 30 %); mp 144-146°C dec; ^{1}H NMR (300 MHz $CDCl_3$) δ 1.22 (s, 27H), 1.25 (s, 9H), 3.48(d, *J* = 12.6 Hz, 4H), 4.37 (d, *J* = 13.7 Hz, 2H), 4.69 (d, *J* = 12.9, 2H), 5.83 (s, 2H), 7.01 (d, *J* = 2.2 Hz, 2H), 7.08 (s, 2H), 7.09 (d, *J* = 2.5 Hz, 2H), 7.14 (s, 2H), 8.08-9.38 (m, 9H), 9.06 (s, 2H), 10.44 (s, 1H); ^{13}C NMR (75MHz DMSO-d_6) δ 31.0, 31.1, 31.2, 31.4, 31.7, 33.7, 34.1, 78.8, 123.3, 124.1, 124.4, 124.5, 125.2, 125.5, 125.6, 126.2, 126.5, 127.0, 127.2, 127.5, 127.6, 128.0, 128.3, 129.3, 129.9, 130.1, 130.2, 130.6, 133.9, 134.2, 142.8, 143.2, 147.4, 147.7, 147.9, 149.6, 198.2; HRMS (FAB) Found ($M^{+\cdot}$): 890.4906; Calcd for $C_{62}H_{66}O_5$: 890.4912.

25-(3-Perylenylacetyloxy)-5,11,17,23-tetra-*tert*-butyl-26,27,28-trihydroxycalix[4]arene (3). To an acetonitrile (4 mL) solution of the monodeprotonated *p-tert*-butylcalix[4]arene (0.07 g, 0.110 mmol) by sodium methoxide (0.01 g, 0.190 mmol), the solution of 3-(bromoacetyl)perylene (0.10g, 0.270 mmol) in acetonitrile (120 mL) was added and refluxed. The residue provided by the same procedure descrived above for the general procedure was purified by silica gel column chromatography with dichloromethane to afford orange colored powder **3** (0.20 g, 20 %); mp 139-140°C dec; ^{1}H NMR (300 MHz $CDCl_3$) δ 1.21 (d, *J* = 1.4 Hz, 27H), 1.24 (s, 9H), 3.42-3.47 (m, 4H), 4.35 (d, *J* = 13.4 Hz, 2H), 4.64 (d, *J* = 12.9 Hz, 2H), 5.66 (s, 2H), 7.00 (d, *J* = 2.5 Hz, 2H), 7.06 (s, 2H), 7.08 (d, *J* = 2.5 Hz, 2H), 7.13 (s, 2H), 7.53-8.99 (m, 11H), 9.55 (s, 2H), 10.40 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 31.0, 31.1, 31.2, 31.4, 31.7, 33.7, 34.1, 78.4, 119.5, 121.5, 121.9, 123.1, 125.3, 125.4, 125.5, 125.6, 126.1, 127.1, 127.2, 127.4, 127.6, 128.0, 128.3, 128.4, 128.5, 128.7, 129.0, 129.3, 129.6, 129.8, 130.0, 130.5, 130.8, 131.6, 133.9, 134.0, 135.7, 142.8, 143.2, 147.4, 147.7, 147.9, 149.5, 197.3; HRMS (FAB) Found ($M^{+\cdot}$): 940.5063; Calcd for $C_{66}H_{68}O_5$: 940.5069.

25-(1-Pyrenylacetyloxy)-27-(3-perylenylacetyloxy)-tetra-*tert*-butyl-26,28-dihydroxycalix[4]-arene (1). To an acetonitrile (100 mL) solution of 1-(bromoacetyl)perylene (0.08 g, 0.23 mmol), compound **2** (0.06 g, 0.063 mmol) and potassium carbonate (0.01 g, 0.074 mmol) were added, and the mixture was refluxed for 5 h. After the solvent was removed, the residue was purified by silica gel column chromatography with dichloromethane to afford brown colored powder **1** (0.03 g, 30 %); mp 192-195°C dec; ^{1}H NMR (300 MHz $CDCl_3$) δ 1.14 (s, 27H), 1.19 (s, 9H), δ 3.38 (d, *J* = 12.9 Hz, 2H), 3.39 (d, *J* = 12.9 Hz, 2H), 4.65 (d, *J* = 12.9 Hz, 2H), 4.70 (d, *J* = 12.9 Hz, 2H), 5.58 (s, 2H), 5.73 (s, 2H), 6.91 (s, 4H), 7.07 (d, *J* = 3.0 Hz, 4H), 7.23-8.48 (m, 20H), 8.80 (d, *J* = 9.3 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 30.1, 31.3, 32.0, 33.6, 33.9, 78.2, 78.6, 119.1, 120.4,

121.3, 122.4, 123.0, 123.9, 124.1, 124.9, 125.2, 125.7, 125.9, 126.1, 126.3, 126.6, 126.7, 126.8, 126.8, 126.9, 127.1, 127.6, 127.8, 127.9, 128.0, 128.2, 128.5, 128.9, 129.1, 129.3, 129.4, 129.6, 129.7, 130.0, 130.2, 130.4, 131.2, 132.9, 133.4, 133.5, 133.6, 133.7, 133.8, 133.9, 134.3, 135.0, 141.2, 146.5, 146.6, 146.7, 146.8, 149.9, 150.8, 151.0, 151.9, 197.2, 198.0; HRMS (FAB) Found ($M^{+\cdot}$): 1182.5792; Calcd for $C_{84}H_{78}O_6$: 1182.5801.

25,27-bis(1-Pyrenylacetyloxy)-5,11,17,23-tetra-*tert*-butyl-26,28-dihydroxycalix[4]arene (4). The mixture of *p-tert*-butylcalix[4]arene (0.98 g, 1.52 mmol), potassium carbonate (0.24 g, 1.75 mmol) and 1-(bromoacetyl)pyrene (1.00 g, 3.10 mmol) was refluxed in acetonitrile for 8 h. The solvent was removed in vacuo to yield the crude product, which was purified by silica gel column chromatography with dichloromethane to afford yellow colored powder **4** (1.29 g, 75 %); mp 188-190°C dec; ^{1}H NMR (300 MHz $CDCl_3$) δ 1.17 (d, J = 9.1 Hz, 36H), 3.43 (d, J = 13.2 Hz, 4H), 4.78 (d, J = 13.2Hz, 4H), 5.80 (s, 2H), 6.93 (s, 4H), 7.07 (s, 4H), 7.14-8.06 (m, 20H); ^{13}C NMR (DMSO-d_6) δ 28.7, 29.5, 30.8, 31.5, 31.6, 77.1, 121.7, 121.8, 122.4, 122.7, 123.4, 123.6, 123.7, 124.0, 124.4, 124.6, 126.0, 126.2, 126.3, 127.1, 127.4, 127.9, 128.0, 128.4, 131.3, 131.9, 139.1, 144.9, 149.1, 149.6, 195.5; HRMS (FAB) Found ($M^{+\cdot}$): 1132.5642; Calcd for $C_{80}H_{76}O_6$: 1132.5644.

References and Footnotes

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