Effective Na^+ fluorescent sensing by new podand-type receptor connecting two pyrene units and diphenyl ether

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Abstract

A new podand-type receptor for Na^+ detection has been synthesized by connecting two 1-pyrenecarbonylmethyl groups with two hydroxy groups of 2,2'-dihydroxydiphenyl ether. With the addition of Na^+ in the range of 20-200 μM, the increasing monomer emission (423 nm) and the decreasing excimer emission (524 nm) of pyrene were observed. In contrast with the receptor, the fluorescence spectra of the corresponding compound obtained from 2,2'-dihydroxydiphenylmethane are only slightly affected by the addition of Na^+.

Keywords: Chemosensor, podand, pyrene, fluorescence, sodium ion

Introduction

Recently, a number of chemosensors have been developed because of biological, environmental and clinical interests.[1-3] In these chemosensors, guest ions or molecules selectively bind with a monitorable physical change such as an increase and decrease in the absorbance or fluorescence intensities.[4-9] Especially, fluorescence changes by pyrene as a chromophore have received much attention because the pyrene emission can be easily monitored.[10-12]

There are two types of chemosensors for metal ions.[13] One is the chemosensor with chromophores as the monitoring site and a macrocyclic receptor unit such as crown ethers and calixarenes having a fitted cavity for the target guest ions.[14-17] Moon et al. reported the Hg^{2+} sensitive cyclam derivative having two pyrene units as the fluorophore.[18] The other type is the chemosensor with chromophores as the monitoring sites and a non-cyclic binding site such as podands and lariat ethers.[19, 20] For example, Suzuki et al. reported the alkaline earth metal ion sensitive polyoxyethylene derivatives having two pyrene units as the fluorophore.[21] The mercury sensitive imidazole-based non-cyclic derivatives have been reported by Feng et al.[22]

We are interested in a Na^+ detectable fluorescent chemosensor, because the quantification of Na^+ has been very significant especially in the clinical field due to the crucial role plays in the regulation of many physiological phenomena.[23-26] We previously reported the Na^+ sensitive *p-tert*-butylcalix[4]arene derivative having two pyrene units as a fluorophore, which exhibited increasing pyrene monomer and decreasing pyrene excimer emissions with the addition of Na^+.[27] This observation promoted us to investigate the novel podand-type fluoroionophores **1** and **2** in which the two pyrene units are connected to the hydroxy groups of 2,2'-dihydroxydiphenylmethane or 2,2'-dihydroxydiphenyl ether, respectively. The binding abilities of compounds **1** and **2** toward the alkali metal ions (Li^+, Na^+, K^+, Rb^+, and Cs^+) were then investigated.

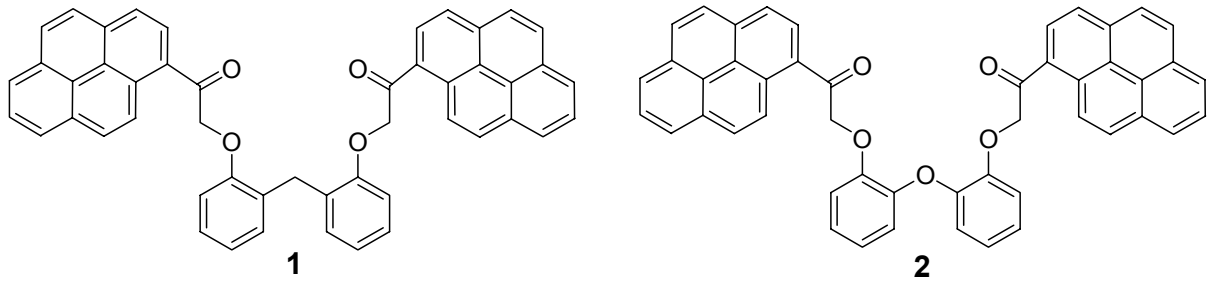
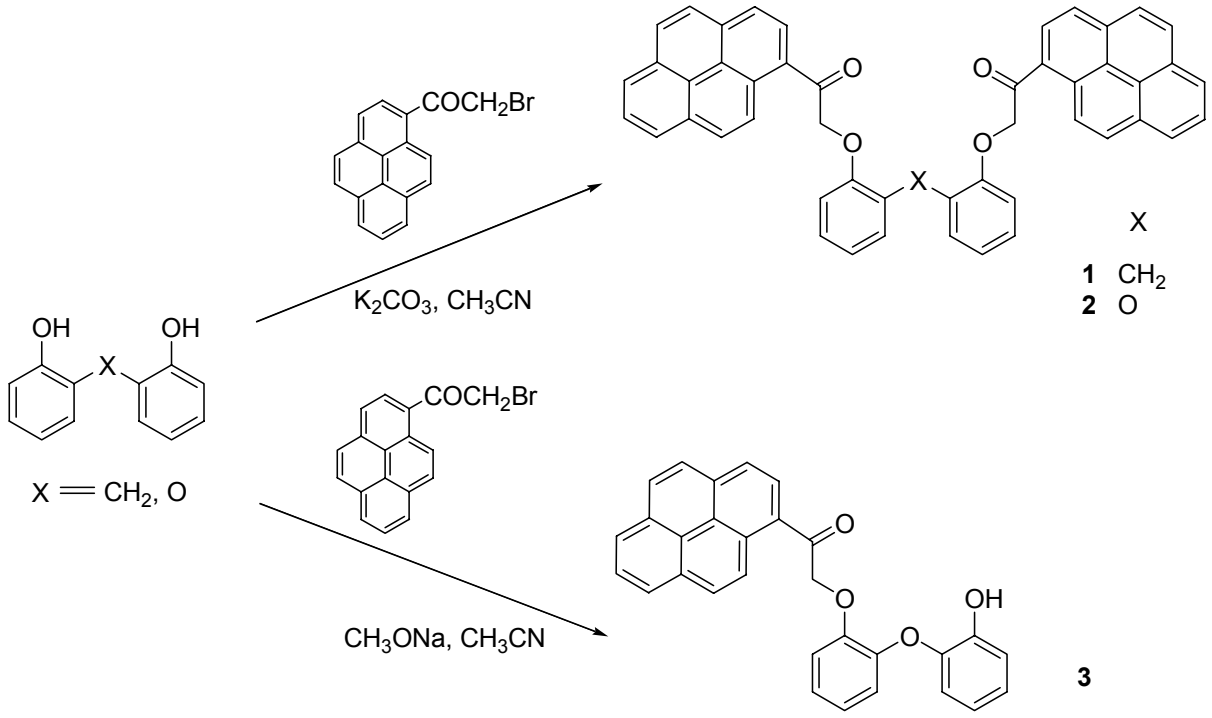


Figure 1. The novel podand-type fluoroionophores **1** and **2** having two pyrene units.

Results and Discussion

Scheme 1 shows the synthetic routes for compounds **1** and **2** having two pyrene units and compound **3** having one pyrene unit as a reference compound. The reaction of 2,2'-dihydroxydiphenylmethane and 2,2'-dihydroxydiphenyl ether with two equivalents of 1-(bromoacetyl)pyrene in the presence of potassium carbonate in acetonitrile afforded compounds **1** and **2** having two pyrene units, respectively. Compound **3** having one pyrene unit was prepared by the reaction of 2,2'-dihydroxydiphenyl ether with one equivalent of 1-(bromoacetyl)pyrene in acetonitrile in the presence of sodium methoxide in order to monodeprotonate the 2,2'-dihydroxydiphenyl ether. The structures of **1**, **2** and **3** were determined by FAB MS and NMR spectroscopies.



Scheme 1. The synthetic routes of **1**, **2** and **3**.

The UV-Vis spectra of 10.0 μM chloroform solutions of compounds **1**, **2**, and **3** are shown in Figure 2. Compounds **1** and **2** having two pyrene units showed an absorption band at 362.5 nm with a shoulder at 392 nm corresponding to the pyrene chromophore.[27] On the other hand, the absorption spectrum of compound **3** having one pyrene unit was slightly red-shifted relative to those of compounds **1** and **2**.

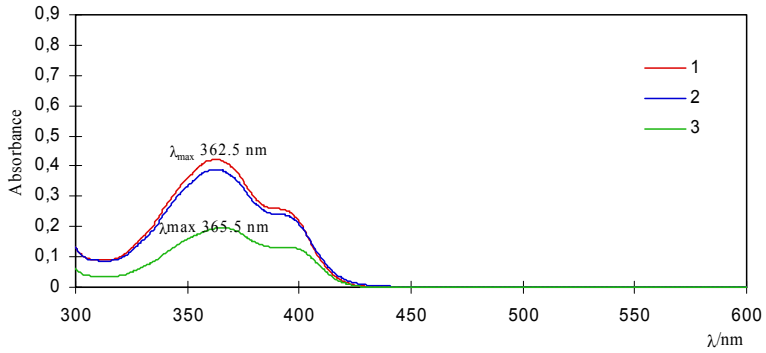


Figure 2. UV-Vis spectra of **1**, **2**, and **3** (10.0 μM in chloroform).

Figure 3 shows the fluorescence spectra of 1.0 μM chloroform solutions of compounds **1**, **2**, and **3** by excitation of 360 nm. Compound **3** having one pyrene unit showed only the monomer

emission at 423 nm. On the other hand, both compounds **1** and **2** having two pyrenyl groups showed two emission bands at 423 and 524 nm. The emission band at 524 nm coincided with the intermolecular pyrene excimer emission band of 1-acetylpyrene observed at the concentration of 10.0 mM in chloroform by excitation of 360 nm. Therefore, the emissions at 524 nm of compounds **1** and **2** are excimer emissions based on the intramolecular interaction between the two pyrene units. It is noteworthy that the fluorescence intensity ratio (I_e/I_m) for compound **2** (2.91) is greater than that of compound **1** (0.44), where I_e and I_m are the fluorescence intensities of the pyrene excimer (at 524 nm) and monomer (at 423 nm), respectively. These results indicate that the two pyrene units in compound **2** must be in close proximity, probably as a result of π-π stacking, while in the compound **1**, they must be separated.

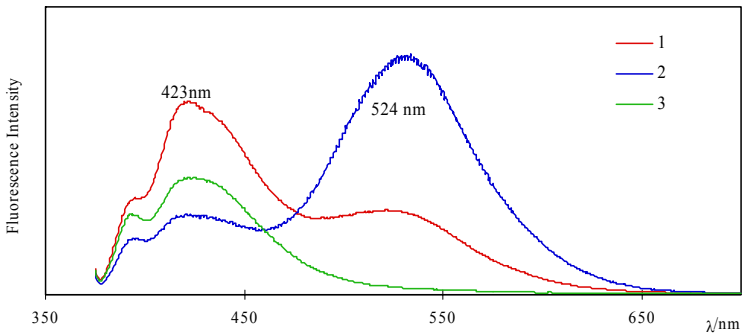


Figure 3. Fluorescence spectra of **1**, **2**, and **3** (1.0 μM in chloroform). Excitation wavelength: 360 nm.

In order to clarify the structures of compounds **1**, **2**, and **3** in detail, the ^{1}H NMR spectra were examined in DMSO-d_6. All proton signals were unambiguously assigned by the ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY and HMBC spectroscopies and the spectra of the pyrene unit are shown in Figure 4. In the spectrum of compound **1** having two pyrene units, the signals for H-10 (δ 8.80), H-2 (δ 8.63), H-4 (δ 8.24), and H-7 (δ 8.14) showed upfield shifts compared to the corresponding protons of compound **3** having one pyrenyl group: Δδ{δ(**3**) - δ(**1**)} = - 0.031 for H-10, - 0.067 for H-2, - 0.027 for H-4, and – 0.023 for H-7. Similar upfield shifts were observed in the spectrum of compound **2**: Δδ{δ(**3**) – δ(**2**)} = - 0.077 for H-10, - 0.12 for H-2, - 0.089 for H-4, and – 0.045 for H-7. These upfield shits indicate that both pyrene units in compounds **1** and **2** would be closely located, because it is well-established that π-stacking interactions between aromatic rings result in shielding of the protons due to the anisotropy of the ring current effect.[28,29] Furthermore, all pyrene protons in compound **2** were remarkably shifted to a higher magnetic field than those in compound **1**. These results and fluorescence spectra described above reasonably indicate that the pyrene units in compound **2** would be located more closely than that in compound **1**.

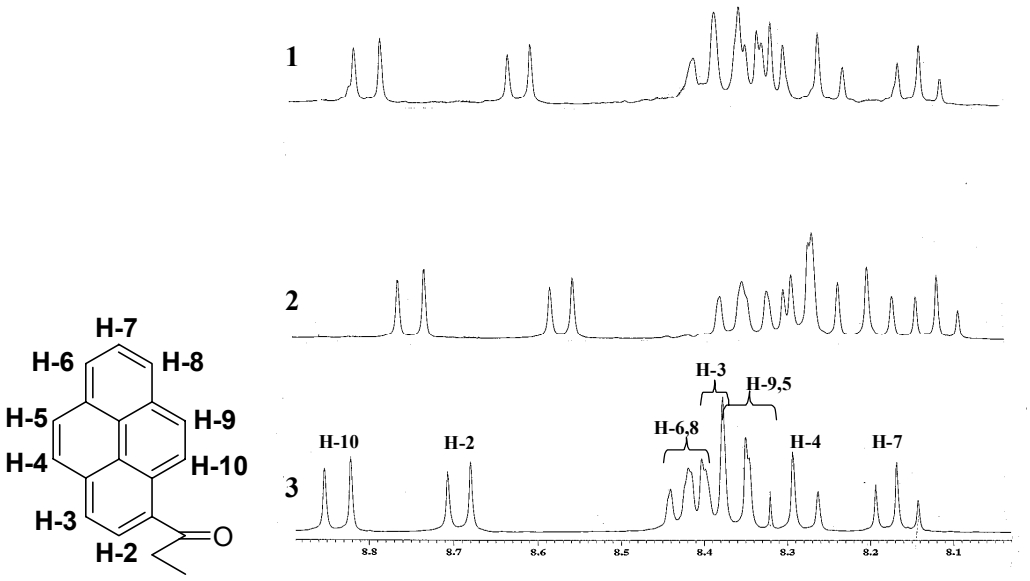


Figure 4. ^{1}H NMR spectra of **1**, **2** (0.02 M in DMSO-d_6), and **3** (0.04 M in DMSO-d_6).

To examine the metal ion binding properties of receptors **1**, **2**, and **3**, we investigated the fluorescence changes. Figure 5 shows the fluorescence emission changes of **1**, **2**, and **3** (1.0 μM, excitation at 360 nm) at 423nm upon the 300 μM addition of alkali metal ions (Li^+, Na^+, K^+, Rb^+, and Cs^+ as thiocyanate salts) in chloroform-acetonitrile (97:3, v/v). The fluorescence changes in compounds **1** and **3** were only slightly observed with addition of the alkali metal ions. On the other hand, the fluorescence intensities of compound **2** having two pyrene units were increased by the addition of Na^+ and K^+. Especially, Na^+ displayed a significant enhancement of the pyrene monomer emission of compound **2**.

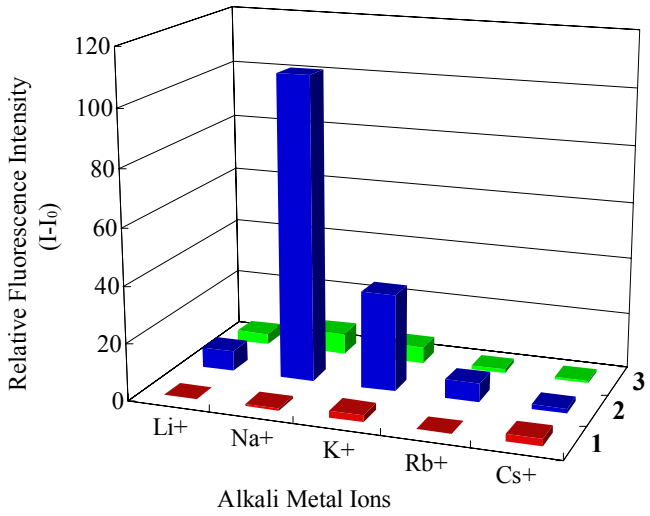


Figure 5. Effect of 300 μM alkali metal ions (Li^+, Na^+, K^+, Rb^+, Cs^+) on the fluorescence spectra of compounds **1**, **2**, and **3** (1.0 μM) in chloroform-acetonitrile (97:3, v/v) at 423 nm. I_0: fluorescence intensity of **1**, **2**, and **3** in the absence of alkali metal ion. I: fluorescence intensity of **1**, **2**, and **3** in the presence of alkali metal ion.

Figure 6 shows the fluorescence changes in **2** with various Na^+ concentrations by excitation at 360 nm. The fluorescence intensity of the excimer emission at 524 nm of **2** gradually decreased and the intensity of the monomer emission at 423 nm of **2** dramatically increased with the increasing Na^+ concentrations ranging from 2 μM to 200 μM. The fluorescence emission intensity at 423 nm was saturated at 200 equiv. of Na^+. These fluorescence changes indicate that the pyrene units in compound **2** would be effectively separated from each other by the Na^+ complex formation. In contrast, no spectral changes were observed for compound **1** having two pyrene units and **3** having one pyrene unit by the addition of Na^+. This result suggests that the Na^+ binding ability of **2** would be attributed to the presence of the oxygen atom at the diphenyl ether component in compound **2**.

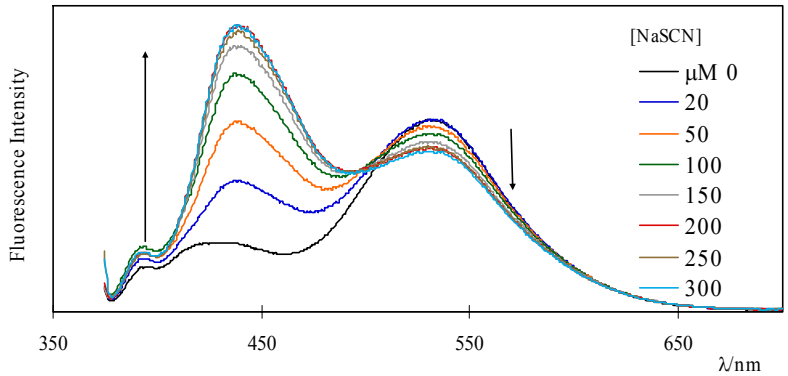


Figure 6. Fluorescence spectral changes of 1.0 μM solution of **2** in chloroform-acetonitrile (97:3, V/V) upon the addition of NaSCN. Excitation wavelength: 360 nm.

The stoichiometry of compound **2** was confirmed by the Job's plots (Figure 7) utilizing the fluorescent titrations of 1.0 μM chloroform-acetonitrile (97:3) solutions of **2** with the 1.0 μM chloroform-aceronitrile solutions of sodium thiocyanate. The Job's plot indicated the formation of a 1:1 complex.

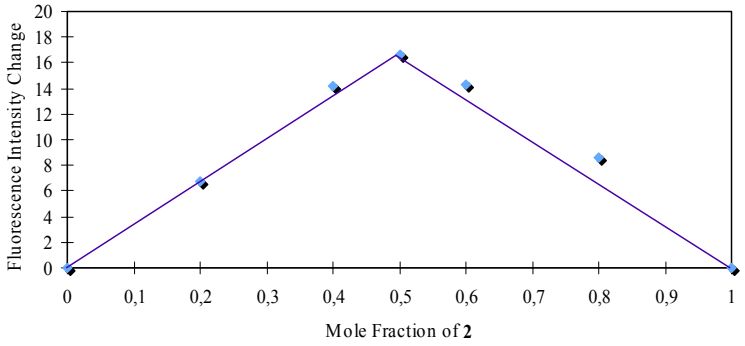


Figure 7. Job's Plot for the binding of Na^+ with **2**.

Figure 8 shows the plots of the fluorescence intensities against the added Na^+ concentration. The association constant of compound **2** for Na^+ was calculated to be 1.14 x 10^4 M^{-1} based on the Benesi-Hildebrand method by plotting the $1/(F-F_0)$ against the $1/[Na^+]$, where F_0 and F are the fluorescence intensities in the absence and presence of Na^+ shown in Figure 8.

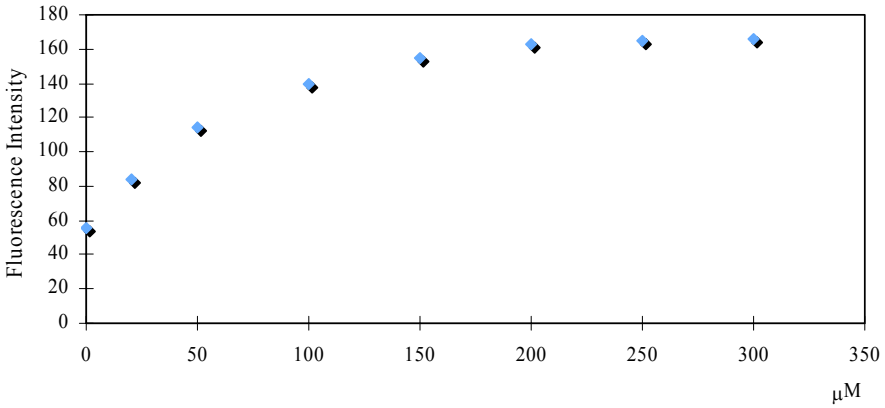


Figure 8. Fluorescence intensity changes of compound **2** (1 μM) in the absence and presence (0-300 μM) of Na^+. The fluorescence intensities were monitored at 423 nm by excitation at 360 nm.

These results demonstrated that a podand-type receptor with a non-cyclic binding site can be applicable as an effective Na^+ fluorescence sensor.

Conclusions

The fluorescence spectra of receptor **1** obtained from 2, 2'-dihydroxydiphenylmethane and two equivalents of 1-(bromoacetyl)pyrene were only slightly affected by the addition of alkali metal ions. However, the receptor **2** obtained from 2, 2'-dihydroxydiphenyl ether and two equivalents of 1-(bromoacetyl)pyrene was highly sensitive to Na^+ over the other alkali metal ions tested and the increasing monomer emission and the decreasing eximer emission of pyrene were observed. These results suggested that the oxygen atom at the diphenyl ether component would play an important role in the Na^+ sensing.

Experimental Section

General Procedures. All melting points were determined using a Hansen & Co., Ltd., MEL-TEMP and were uncorrected. 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 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 used for the synthesis of **1-3**, except for 1-(bromoacetyl)pyrene from Aldrich, were commercially available (Tokyo Chemical Industry Co., Ltd.). All reagents and solvents were used without further purification. The silica gel (70–230 mesh) was from Merck, Ltd., Japan. Elemental analysis was performed by Mitsui Chemical Analysis & Consulting service Inc., Japan.

General procedure for fluorescent study. The stock chloroform solutions of compounds **1-3** (1.03 μM) and acetonitrile solution of the alkali metal salts ($LiSCN{\cdot}2H_2O$, NaSCN, KSCN, RbSCN, and CsSCN) (10 mM) were prepared using a spectroscopic grade solvent (Wako Pure Chemical Industries, Ltd.). Test solutions were prepared by mixing the stock solution (9.7 mL) of **1-3** and the alkali metal salt stock solution in increments of 0.00 mL, 0.02 mL, 0.05 mL, 0.10 mL, 0.15 mL, 0.20 mL, 0.25 mL and 0.30 mL, followed by diluting the solution to 10.0 mL with acetonitrile.

2,2'-Bis(1-pyrenylacetyloxy)diphenylmethane (1). The mixture of 1.52 mmol (0.30 g) of 2,2'-dihydroxydiphenylmethane, 3.10 mmol (1.00 g) of 1-(bromoacetyl)pyrene and 4.56 mmol (0.63 g) of potassium carbonate was refluxed in acetonitrile (300 mL) for 8 h. After evaporation of the solvent, the residue was dissolved in 300 mL of benzene. The benzene solution was washed with water and the solvent was evaporated. The residue was recrystallized from dichloromethane-hexane to afford compound **1**. Yield 10% (0.11 g) of yellow-colored powder; mp 91-92°C dec; UV-vis ($CHCl_3$) λ_{max}/nm 362.5 (ε 4210); ^1H NMR (300 MHz DMSO-d_6) δ 3.90 (s, 2H), 5.70 (s,

4H), 6.73 (td, *J* = 7.4 Hz, 0.8 Hz, 2H), 6.96 (dd, *J* = 7.4Hz, 1.7 Hz, 2H), 7.02 (dd, *J* = 7.7 Hz, 0.8 Hz, 2H), 7.12 (td, *J* = 7.7 Hz, 1.7 Hz, 2H), 8.14 (t, *J* = 7.4 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 2H), 8.30-8.41 (m, 10H), 8.63 (d, *J* = 8.0 Hz, 2H), 8.80 (d, *J* = 9.4 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ; 72.1, 111.7, 120.6, 123.3, 123.9, 124.0, 124.2, 126.2, 126.6, 126.7, 126.8, 126.9, 127.0, 127.1, 128.5, 128.8, 129.1, 129.6, 129.7, 129.8, 130.3, 13.5, 155.6, 199.4; HRMS (FAB) Found ($M^{+\bullet}$): 684.2299; Calcd for $C_{49}H_{32}O_4$: 684.2302. Anal. Calc. for $C_{49}H_{32}O_4$ (684): C, 85.94; H, 4.71 %; Found: C, 85.63; H, 4.79 %.

2,2'-Bis(1-pyrenylacetyloxy)diphenyl ether (2). This compound was prepared by the same procedure used for the synthesis of compound **1** except for using 2,2'-dihydroxydiphenyl ether (0.31 g) instead of 2,2'-dihydroxydiphenylmethane. Yield 54% (0.56 g) of yellow-colored powder; mp 116-118°C dec; UV-vis ($CHCl_3$) λ_{max}/nm 362.5 (ε 3890); ^{1}H NMR (300 MHz DMSO-d_6) δ 5.72 (s, 4H), 6.83 (dd, *J* = 8.0 Hz, 1.7 Hz, 2H), 6.89 (td, *J* = 8.0 Hz, 1.4 Hz, 2H), 7.06 (td, *J* = 8.0 Hz, 1.7 Hz, 2H), 7.17 (dd, *J* = 8.0 Hz, 1.4 Hz, 2H), 8.12 (t, *J* = 7.4 Hz, 2H), 8.18 (d, *J* = 9.1 Hz, 2H), 8.24-8.38 (m, 10H), 8.57 (d, *J* = 8.0 Hz, 2H), 8.75 (d, *J* = 9.3 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 72.5, 115.2, 119.1, 121.7, 123.3, 123.8, 123.9, 124.0, 124.2, 126.2, 126.6, 126.7, 126.8, 127.0, 128.7, 128.8, 129.5, 129.6, 129.8, 130.4, 133.6, 145.7, 148.9, 198.6; HRMS (FAB) Found ($M^{+\bullet}$): 686.2100; Calcd for $C_{48}H_{30}O_5$: 686.2094. Anal. Calc. for $C_{48}H_{30}O_5$ (686): C, 83.95; H, 4.40 %; Found: C, 83.62; H, 4.54 %.

2-(1-Pyrenylacetyloxy)-2'-hidroxydiphenyl ether (3). The mixture of 1.25 mmol (0.25 g) of 2,2'-dihydroxydiphenyl ether and 1.48 mmol (0.08 g) of sodium methoxide was refluxed in acetonitrile (38 mL) for 30 min to completely monodeprotonate the 2,2'-dihydroxydiphenyl ether. The solution of 1-(bromoacetyl)pyrene (1.00 g, 3.10 mmol) in acetonitrile (300 mL) 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 silica gel column chromatography with dichloromethane to afford **3**. Yield 13% (0.07 g) of yellow-colored powder; mp 170-171°C dec; UV-vis ($CHCl_3$) λ_{max}/nm 365.5 (ε 1960); ^{1}H NMR (300 MHz DMSO-d_6) δ 5.80 (s, 2H), 6.66-6.77 (m, 3H), 6.87-6.95 (m, 3H), 7.03 (td, *J* = 7.7 Hz, 1.7 Hz, 1H), 7.17 (dd, *J* = 8.3 Hz, 1.4 Hz, 1H), 8.16 (t, *J* = 7.7 Hz, 1.7 Hz, 1H), 8.27 (d, *J* = 9.0 Hz, 1H), 8.35-8.44 (m, 5H), 8.70 (d, *J* = 8.0 Hz, 1H), 8.83 (d, *J* = 9.3 Hz, 1H), 9.47 (s, 1H); ^{13}C NMR (DMSO-d_6) δ; 72.5, 115.0, 116.9, 118.4, 119.4, 119.5, 121.6, 123.3, 123.4, 124.0, 124.1, 124.2, 124.3, 126.3, 126.7, 126.8, 126.9, 127.2, 128.8, 129.0, 129.5, 129.7, 129.9, 130.6, 133.7, 144.0, 146.2, 148.3, 148.7, 198.9; HRMS (FAB) Found (MH^+): 445.1440; Calcd for $C_{30}H_{21}O_4$; 445.1440. Anal. Calc. for $C_{30}H_{20}O_4$ (444): C, 81.07; H, 4.54 %; Found: C, 80.74; H, 4.57 %.

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