Highly Selective Fluorescent Signaling for Al\textsuperscript{3+} in Bispyrenyl Polyether

Hyun Jung Kim, Su Ho Kim, Duong Tuan Quang, Ja Hyung Kim, Il-Hwan Suh,† and Jong Seung Kim*

Department of Chemistry, Institute of Nanosensor & Biotechnology, Dankook University, Seoul 140-714, Korea
*E-mail: jongskim@dankook.ac.kr
†Department of Chemistry, Korea University, Chochiwon 399-700, Korea
Received March 2, 2007

A series of bispyrenyl-polyether have been synthesized and investigated as a fluorescent chemosensor for metal ions. The results showed that bispyrenyl-polyether system is selective towards Al\textsuperscript{3+} ion over other ions tested. In free ligand, excited at 343 nm, it displays a strong excimer emission at around 475 nm with a weak monomer emission at 375 nm. A ratiometry of monomer (375 nm) increase and excimer (475 nm) quenching was shown only when Al\textsuperscript{3+} ion is bound to ligand, because two facing pyrene groups form a less efficient overlap of π--π stacking compared with that of free ligand.

Key Words : Pyrene, Excimer, Fluorescence, Aluminium ion

Introduction

The design of fluorescent chemosensors able to selectively recognize and sense specific cations has attracted considerable interests due to their importance in biological and environmental settings.\textsuperscript{1,2} The main issue in design of effective fluorescent chemosensor is to easily convert molecular recognition into photochemical changes with a high selectivity and sensitivity. On account of their high sensitivity and selectivity,\textsuperscript{3-5} fluorescent chemosensors can be effectively used as a tool to analyze and clarify such roles of charged chemical species in living system as well as to measure the amount of metal ions from the sources contaminated with them.

In the biochemistry centered on the toxicity of the metal ions,\textsuperscript{6} Al\textsuperscript{3+} ion has gained prominence through a possible link to Alzheimer’s disease.\textsuperscript{7} For detection of Al\textsuperscript{3+} ion, we reported a 1,3-alternate calix[4]arene with fluorescent diarylenyl polyether groups showing a complex with Al\textsuperscript{3+} ion. The compounds showed fluorescence change of both the pyrene excimer and its monomer by a conformational change of the ligand to suppress an efficient HOMO-LUMO interaction between two pyrenes (Py-Py\textsuperscript{*}).\textsuperscript{8}

The Pb\textsuperscript{2+} ion has been also considered as one of the important target ions to be selectively removed because of its adverse effects to people, particularly to children.\textsuperscript{9} A wide variety of symptoms which include memory loss, irritability, anemia, muscle paralysis, and mental retardation have been ascribed to lead exposure, suggesting that Pb\textsuperscript{2+} ion affects multiple targets \textit{in vivo}.\textsuperscript{10}

Most of the fluorescent chemosensors for cations are composed of a cation recognition unit (ionophore) together with a fluorogenic unit (fluorophore) and are called fluorionophores.\textsuperscript{11} An effective fluorescence chemosensor must convert the event of cation recognition by the ionophore into an easily monitored and highly sensitive light signal from the fluorophore.

Among fluorophores, pyrenes are known as one of the most useful fluorogenic units because they display not only a well-defined monomer emission at 375 nm but also an efficient excimer emission at around 475 nm.\textsuperscript{12} With an intensity ratio of excimer to monomer emission ($I_E/I_M$) being sensitive to the conformational changes of the pyrene-appended receptor, the $I_E/I_M$ changes upon the metal ion complexation can be an informative parameter in various sensing systems.\textsuperscript{13,14} In addition, polyethers in which the proper-sized polyether oxygen rings are incorporated into the pyrene have attracted intense interest as a selective extractant for specific metal ions.\textsuperscript{15}

From this standpoint, we herein report the synthesis of new series of bispyrene polyether compounds 1-6, which exhibit a unique fluorescence response with Al\textsuperscript{3+} ion. 7 was also synthesized as a reference material to elucidate the binding mechanism of 1-6 to metal cations.

Results and Discussion

The general synthetic procedures for 1-7 are summarized in Scheme 1. Starting materials 8-13 were prepared accord-

![Scheme 1](Scheme_1.png)
Compounds iodo propane and NaH in THF provided quantitative yield. Alkylation of 1-pyrenemethanol with 1-
the perchlorate salt of Ag⁺, Cs⁺, K⁺, Li⁺, Na⁺, Mg²⁺, Co²⁺, Ca²⁺, Zn²⁺, Pb²⁺, and Al³⁺ to the CH₃CN solutions of 7 in 74% yield. Comounds 2-6 were prepared by the same method used in 1. All structures were ascertained by ¹H NMR and ¹³C NMR, and Mass spectrometry. Also, the solid-state structure of 1 (Figure 1, Table 1) provided convincing evidence for its conformation.

Excited at 343 nm, 1 displays both monomer and excimer emission at 375 and 475 nm, respectively, whereas 7 emits its only monomer at 375 nm (Figure 2). This means that the excimer emission is formed by the intramolecular not by the its only monomer at 375 nm (Figure 2). This means that the emission at 375 and 475 nm, respectively, whereas changes in both monomer and excimer emissions toward metal ions.

The results are presented in Table 2 and show that they have similar binding properties for the metal ions. On the other hand, 7 hardly responds to the most metal ions tested, indicating that the polyether spacer between two pyrenes plays an important role in the fluorescence ratiometrical changes in both monomer and excimer emissions toward metal ions.

To obtain quantitative insight into the ionic affinity of 1-6, we determined the intensity changes upon complexation of Al³⁺ and Pb⁺. The fluorescence changes of receptors are found to be highly dependent on the polyether spacer length. As shown in Table 3, association constants of Al³⁺ and Pb⁺ increase in order of increasing polyether length. In contrast, addition of Pb²⁺ gives an enhanced association constant with increasing polyether length. Compound 6 responds to metal ion, exhibiting a fluorescence behavior unlikely to that of 1-5. This is presumably because the podand length of 6 is too large to entrap the cations.

On the basis of fluorescence changes upon metal cation complexation, we found that 1-6 exhibit Pb²⁺ and Al³⁺ selectivity over other metal cations tested. Compound 1 with a short spacer is observed to be selective for Pb²⁺ ion in terms of decreasing fluorescence, which is due to the PET effect and the heavy metal ion effect. The fluorescence intensity was gradually decreased by the addition of the Pb²⁺ ion until 1,000 equiv. of ion was added. However, decreasing extent of the excimer emission in 2-6 by Pb²⁺ is much greater than that in 1.

Table 1. Crystal data and structure refinement for 1

<table>
<thead>
<tr>
<th>Identification code</th>
<th>Reflections collected / unique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>Reduction of theta = 28.35°</td>
</tr>
<tr>
<td>Formula weight</td>
<td>Absorption correction</td>
</tr>
<tr>
<td>Temperature</td>
<td>Max. and min. transmission</td>
</tr>
<tr>
<td>Wavelength</td>
<td>Refinement method</td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>Data / restraints / parameters</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>Goodness-of-fit on F²</td>
</tr>
<tr>
<td>Volume</td>
<td>Final R indices [I&gt;2sigma(I)]</td>
</tr>
<tr>
<td>Z, Calculated density</td>
<td>R indices (all data)</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>Absolute structure parameter</td>
</tr>
<tr>
<td>F(000)</td>
<td>Extinction coefficient</td>
</tr>
<tr>
<td>Crystal size</td>
<td>Largest diff. peak and hole</td>
</tr>
<tr>
<td>Formula weight</td>
<td>1</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C₃₀H₁₆O₃</td>
</tr>
<tr>
<td>X-Ray crystal structure of 1</td>
<td>534.62</td>
</tr>
<tr>
<td>Throta range for data collection</td>
<td>233(2) K</td>
</tr>
<tr>
<td>Limiting indices</td>
<td>6083 / 3275 [R(int) = 0.1281]</td>
</tr>
<tr>
<td>Monoclinic, C2</td>
<td>99.7%</td>
</tr>
<tr>
<td>a = 34.72(2) Å</td>
<td>Semi-empirical from equivalents</td>
</tr>
<tr>
<td>b = 4.562(3) Å</td>
<td>0.9983 and 0.1421</td>
</tr>
<tr>
<td>c = 8.472(6) Å</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>z = 90°</td>
<td>1332.6(16) Å</td>
</tr>
<tr>
<td>Monoclinic, C2</td>
<td>3275 / 1 / 187</td>
</tr>
<tr>
<td>a = 1.332 Mg/m³</td>
<td>1.364</td>
</tr>
<tr>
<td>Cell size</td>
<td>0.083 mm⁻¹</td>
</tr>
<tr>
<td>Volume</td>
<td>R₁ = 0.2332, wR₂ = 0.5090</td>
</tr>
<tr>
<td>Absolute structure parameter</td>
<td>1</td>
</tr>
<tr>
<td>Goodness-of-fit on</td>
<td>R₁ = 0.3870, wR₂ = 0.5756</td>
</tr>
<tr>
<td>Reflect ions collected / unique</td>
<td>(10)</td>
</tr>
<tr>
<td>Unique</td>
<td>-10(10)</td>
</tr>
<tr>
<td>Space group</td>
<td>0.13(3)</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>-45 ≤ h ≤ 46, -6 ≤ k ≤ 6, -10 ≤ l ≤ 11 0.967 and -0.683 e.Å⁻³</td>
</tr>
</tbody>
</table>

Figure 1. X-ray crystal structure of 1.

Figure 2. Fluorescence spectra of free 1 and 7 (6.0 μM) in CH₃CN.

The excitation wavelength is 343 nm.
towards Al$^{3+}$ ion. However, in they show same tendency of the fluorescence ratiometry despite a different length of the spacer between two pyrenes, errors in the association constants were less than 10%.

are saturated with more than 1,000 equiv of Al$^{3+}$, whereas in CH$_3$CN; excitation at 343 nm; metal ions, 500 equiv. in CH$_3$CN. The fluorescence spectrum of heavy metal ions and divalent ions. Figure 3(a) shows the fluorescence changes of metal ion-complexed 1-7. (+) and (−) denote fluorescence intensity increase and decrease, respectively.

On the other hand, fluorescence changes of 1-6 for Al$^{3+}$ ion complexation are found to be different from those for heavy metal ions and divalent ions. Figure 3(a) shows the fluorescence spectrum of 1 with increasing amount of Al$^{3+}$. Despite a different length of the spacer between two pyrenes, they show same tendency of the fluorescence ratiometry towards Al$^{3+}$ ion. However, in 3-6, the fluorescence changes are saturated with more than 1,000 equiv of Al$^{3+}$, whereas in the case of 1 and 2 they are with only 200 equiv of Al$^{3+}$, reflecting that 1 and 2 seem to coordinate with Al$^{3+}$ more readily than 3-6 do. When the Al$^{3+}$ ion is entrapped by a pair of polyether units, the two pyrenes seem to cross each other. As a result, the excimer emission of the pyrene is decreased along with the monomer emission increased, causing a suppression of the efficient intramolecular HOMO(π)-LUMO(π*) interaction of two pyrene units.

Job plot experiments indicate a 1:1 complex formation of 1 or 5 with Al$^{3+}$. Receptors-Al$^{3+}$ complex concentration approached the maximum when the molar fraction of [L]/([L] + [Al$^{3+}$]) was about 0.5, meaning that it formed a 1:1 complex (Figure 4). In addition, one isomissive point at 428 nm in the fluorescence titration spectra supports that the complex stoichiometry for ligand with Al$^{3+}$ ion is 1:1. A 1:1 complex of 1 or 5 with Pb$^{2+}$ is also evidenced by Job plot experiments.

In conclusion, a series of dipyrene spacing with polyethylene glycol units were synthesized and studied for a ratiometric fluorescence changes for metal cations. 1-6 display a high selectivity towards Al$^{3+}$ ion over other metal cations. Table 2. Fluorescence changes (I-$I_0$) of 1-7 upon the addition of various metal cations$^a$

<table>
<thead>
<tr>
<th>Ligand</th>
<th>$\lambda_{ex}$ (nm)</th>
<th>Ag$^+$</th>
<th>Cs$^+$</th>
<th>K$^+$</th>
<th>Li$^+$</th>
<th>Na$^+$</th>
<th>Mg$^{2+}$</th>
<th>Co$^{2+}$</th>
<th>Ca$^{2+}$</th>
<th>Zn$^{2+}$</th>
<th>Pb$^{2+}$</th>
<th>Al$^{3+}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>375</td>
<td>8</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>40</td>
<td>5</td>
<td>-4</td>
<td>865</td>
</tr>
<tr>
<td>2</td>
<td>475</td>
<td>-13</td>
<td>44</td>
<td>62</td>
<td>23</td>
<td>45</td>
<td>47</td>
<td>-176</td>
<td>5</td>
<td>8</td>
<td>-248</td>
<td>-622</td>
</tr>
<tr>
<td>4</td>
<td>475</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>-2</td>
<td>20</td>
<td>-11</td>
<td>93</td>
<td>10</td>
<td>-83</td>
<td>713</td>
</tr>
<tr>
<td>5</td>
<td>475</td>
<td>-52</td>
<td>28</td>
<td>24</td>
<td>-2</td>
<td>-9</td>
<td>70</td>
<td>-168</td>
<td>-75</td>
<td>16</td>
<td>-595</td>
<td>-437</td>
</tr>
<tr>
<td>6</td>
<td>475</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>8</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>-42</td>
<td>304</td>
</tr>
<tr>
<td>7</td>
<td>475</td>
<td>-24</td>
<td>22</td>
<td>23</td>
<td>19</td>
<td>-2</td>
<td>29</td>
<td>-206</td>
<td>-16</td>
<td>21</td>
<td>-609</td>
<td>-332</td>
</tr>
</tbody>
</table>

$^a$Conditions: 1-7: 6.0 $\mu$M in CH$_3$CN; excitation at 343 nm; metal ions, 500 equiv. in CH$_3$CN. $I_0$: fluorescence emission intensity of free 1-7. $I$: fluorescence emission intensity of metal ion-complexed 1-7. (+) and (−) denote fluorescence intensity increase and decrease, respectively.

Table 3. The association constants ($K_a$) of receptors 1-6 with cations in CH$_3$CN$^b$

<table>
<thead>
<tr>
<th>Ligand</th>
<th>$\text{Al}^{3+}(K_a)$</th>
<th>$\text{Pb}^{2+}(K_a)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.94 x 10$^3$ M$^{-1}$</td>
<td>2.56 x 10$^3$ M$^{-1}$</td>
</tr>
<tr>
<td>2</td>
<td>3.21 x 10$^3$ M$^{-1}$</td>
<td>4.22 x 10$^3$ M$^{-1}$</td>
</tr>
<tr>
<td>3</td>
<td>1.01 x 10$^3$ M$^{-1}$</td>
<td>5.12 x 10$^3$ M$^{-1}$</td>
</tr>
<tr>
<td>4</td>
<td>3.52 x 10$^3$ M$^{-1}$</td>
<td>5.54 x 10$^3$ M$^{-1}$</td>
</tr>
<tr>
<td>5</td>
<td>1.23 x 10$^3$ M$^{-1}$</td>
<td>4.52 x 10$^3$ M$^{-1}$</td>
</tr>
<tr>
<td>6</td>
<td>9.29 x 10$^3$ M$^{-1}$</td>
<td>3.17 x 10$^3$ M$^{-1}$</td>
</tr>
</tbody>
</table>

$^b$Conditions: 1-6 (6.0 $\mu$M): Determined by fluorescence spectroscopy in CH$_3$CN; excitation at 343 nm; metal ions, 500 equiv. in CH$_3$CN. The errors in the association constants were less than 10%.

Figure 3. Fluorescence spectra of (a) 1 (6.0 $\mu$M) upon the addition of Al$^{3+}$ and (b) 5 (6.0 $\mu$M) upon the addition of Pb$^{2+}$ in acetonitrile. (The excitation wavelength is 343 nm).
ions. In free ligand, they show strong excimer emission at 475 nm with weak monomer emission at 375 nm. The monomer emission increases, concomitantly with an excimer emission decreased when Al^{3+} was bound to dipyrene polyether system. Upon addition of Pb^{2+} ion, both monomer and excimer emissions were decreased, due to a heavy-metal ion effect.

**Experimental Section**

Diethylene glycol bis(1-pyrenylmethyl) ether (1). To a mixture of 1.0 g (2.41 mmol) of 8 and 1.17 g (4.82 mmol) of 1-pyrenemethanol in 100 mL of dry THF, anhydrous NaH (24 mg (24.1 mmol) were added under nitrogen atmosphere. The reaction mixture was refluxed for 24 hours. After removal of the solvent in vacuo, HCl solution (100 mL) and CH2Cl2 (100 mL) were added and organic layer was separated and then washed twice with 50 mL of water. The organic layer was dried over anhydrous MgSO4, and evaporated to give a yellowish oil which was purified by column chromatography on silica gel with ethyl acetate:hexane (1:2) to provide 0.8 g (62.5%) of Compound 1. 

**Propyl 1-pyrenemethyl ether (7).** A mixture of 1-pyrenemethanol (1.00 g, 4.30 mmol), NaH (1.03 g, 42.9 mmol), and THF (60 mL) was stirred magnetically for 20 min, and then 1-iodopropane (2.19 g, 12.8 mmol) was added. The reaction mixture was refluxed for 2 days and evaporated in vacuo to yield 0.87 g (74%) of Compound 7. 

**Octaethylene glycol bis(1-pyrenylmethyl) ether (6).** Compound 6 was prepared by the same method used for 1. 1H NMR (200 MHz, CDCl3): δ 8.35-7.95 (m, 18 H, Ar-H), 5.20 (s, 4H, Ar-CH2-O), 3.73-3.56 (m, 20H, OCH2CH2). 13C NMR (CDCl3): 131.3, 131.1, 130.7, 127.9, 127.5, 127.2, 126.9, 125.9, 125.7, 125.0, 125.0, 124.8, 124.6, 124.3, 123.4, 71.8, 77.0, 76.3, 71.8, 70.8, 69.5 ppm. FAB MS m/z (m+): Calcd, 710.8. Found, 710.5.

**Hexaethylene glycol bis(1-pyrenylmethyl) ether (5).** Compound 5 was prepared by the same method used for 1. 1H NMR (200 MHz, CDCl3): δ 8.39-7.95 (m, 18 H, Ar-H), 5.24 (s, 4H, Ar-CH2-O), 3.72-3.56 (m, 24H, OCH2CH2). 13C NMR (CDCl3): 131.3, 131.2, 130.7, 129.3, 127.5, 127.3, 127.3, 125.9, 125.7, 125.0, 125.0, 124.8, 124.6, 124.3, 123.4, 71.8, 77.0, 76.3, 71.8, 70.8, 69.5 ppm. FAB MS m/z (m+): Calcd, 666.8. Found, 666.5.

**Pentaethylene glycol bis(1-pyrenylmethyl) ether (4).** Compound 4 was prepared by the same method used for 1. 1H NMR (200 MHz, CDCl3): δ 8.31-7.95 (m, 18 H, Ar-H), 5.20 (s, 4H, Ar-CH2-O), 3.67-3.56 (m, 20H, OCH2CH2). 13C NMR (CDCl3): 131.3, 131.2, 130.7, 129.3, 127.5, 127.3, 127.3, 126.9, 125.8, 125.0, 124.3, 123.4, 71.7, 70.6, 70.5, 70.4, 69.4 ppm. FAB MS m/z (m+): Calcd, 622.7. Found, 622.

Figure 4. Job plot of (a) 1 and (b) 5 with Al^{3+} in CH3CN. The excitation wavelength is 343 nm (Ligand:Al^{3+}=1:1).
were obtained using the computer program ENZFITTER. Fluorescence titration experiments, the association constants
1-6 perchlorate salts were prepared in MeCN. Stock solutions (1.00 mM) of the metal
fluorophotometer. Stock solutions (1.00 mM) of the metal
scence spectra were recorded with a RF-5301PC spectro-
perchlorate in MeCN. After calculating the concentrations of
the free ligands and complexed forms of
1-6 titration experiments were performed using 6 μM solutions of
1-6 in MeCN and various concentrations of metal
perchlorate in MeCN. For all measure-
mnts, excitation was at 343 nm with excitation slit widths at
1.5 nm and emission slit widths at 3 nm. Fluorescence
titration experiments were performed using 6 μM solutions of
1-6 in MeCN and various concentrations of metal
perchlorate in MeCN. After calculating the concentrations of
the free ligands and complexed forms of
1-6 from the
fluorescence titration experiments, the association constants
were obtained using the computer program ENZFITTER.

Acknowledgment. The present research was conducted
by the research fund of Dankook University Alumni Associa-
tion in 2006.

References
1. (a) Chemosensors of Ion and Molecule Recognition, NATO ASI
series; Desvergne, J. P.; Czarnik, A. W., Eds.; Kluwer Academic:
Dordrecht, The Netherlands, 1997; p 492. (b) de Silva, A. P.;
Guararthe, H. Q.; Gunnaugsson, N. T. A.; Huxley, T. M.; McCoy,
2. (a) Prodi, L.; Montalti, M.; Zacheroni, N.; Bradshaw, J. S.; Izatt,
R. M.; Savage, P. B. Tetrahedron Lett. 2001, 42, 2941. (b) Rurack,
65, 2716. (c) Metz, U.; Rigler, R. J. Fluoresc. 1994, 4, 259.

28, 151.
12. (a) Birks, J. B. Photophysics of Aromatic Molecules; Wiley-
Interscience: London, 1970. (b) Lee, Y. O.; Lee, J. Y.; Quang,
27, 1469. (c) Park, H. R.; Oh, C.-H.; Lee, H.-C.; Choi, J. G.;
2002.
(d) Reis e Sousa, A. T.; Castanheira, E. M. S.; Fedorov, A.;
Martinho, J. M. G. J. Phys. Chem. A 1998, 102, 6406. (e) Suzuki,
Yamaguchi, M. Anal. Chem. 2000, 72, 4199. (b) Okamoto, A.;
15. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud-Neu,
F.; Fanni, S.; Schwing, M. J.; Egberink, R. J. M.; de Jong, F.;
16. (a) Kim, J. S.; Lee, W. K.; No, K. H.; Asfari, Z.; Vicens, J.
Trans. 1 1998, 2307.
19. (a) Association constants were obtained using the computer
program ENZFITTER, available from Elsevier-BIOSOFT, 68
Hills Road, Cambridge CB2 1LA, U.K. (b) Connors, K. A.