Pyrene-coumarin Based Calix Fluorophore Emitting Exciplex

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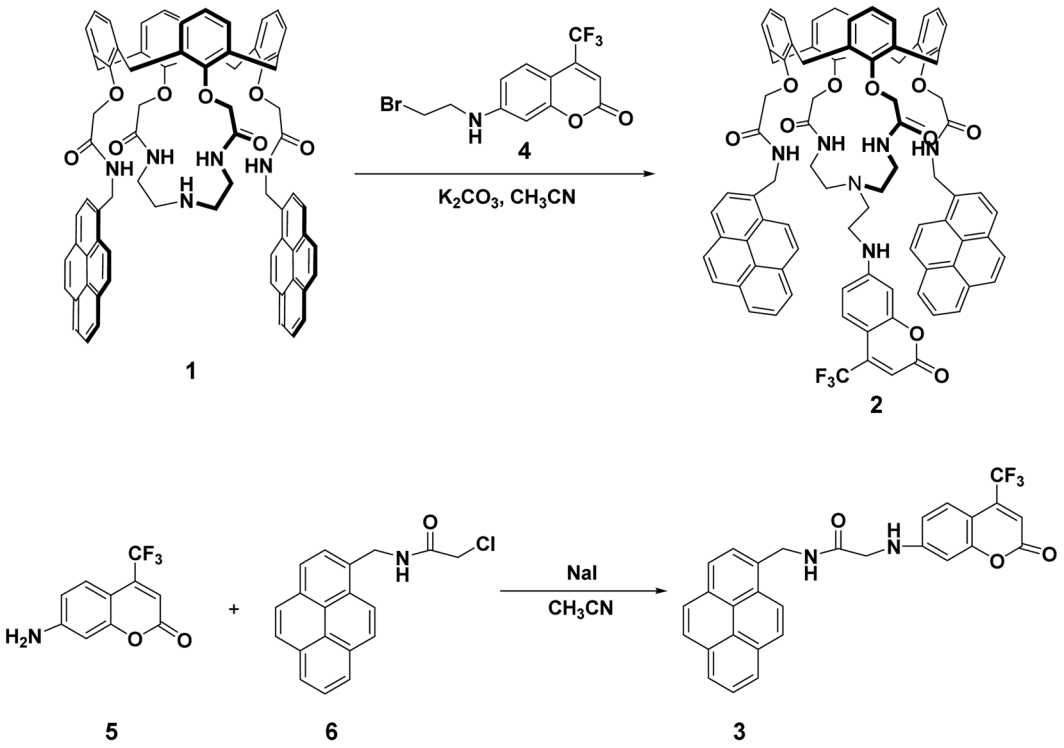
The chemistry of calixarenes, cyclic oligomers composed of phenolic and methylene moieties, has been extensively studied in recent years. The preorganized binding sites, easy derivatization and flexible three-dimensional steric structures make them perfect platforms for sensors to generate fluorescent receptors. Fluorescent chemosensors based on calix[4]arene framework and capability of selectively recognizing heavy metal ions and anions have been studied in fields of chemistry and biology.[1-3]

Calix[4]arenes as host molecules for anions or cations have been of particular interest for the following two different reactive sites: (1) phenolic OHs (lower rim) and (2) *para* positions (upper rim), which can be readily functionalized by various cation-ligating groups such as carboxylic acid, amide, and azacrown ether.[4-12] In this paper, amide groups as a ligating site are known to capture cations through carbonyl oxygen atoms as well as anions through the hydrogen bonding between anion and the acidic hydrogen atoms on nitrogen atom of coumarin.[13]

Most calixarene-based fluorescence sensors have been designed to adopt a photophysical change upon cation or anion binding: PET (photo-induced electron transfer),[6] PCT (photo-induced charge transfer),[7] FRET (fluorescence resonance energy transfer),[8] excimer/exciplex formation and extinction.[11,13] Although an excimer emission from two facing pyrenes has been widely studied, an exciplex emission between pyrene and coumarin has been rarely observed. Here, we report an exciplex formation between pyrene as an electron donor and coumarin as an acceptor followed by disappearance of the exciplex upon the F^- binding which executes "Off" sensing.

As shown in Scheme 1, reaction of **1**[14,15] with 7-[*N*-(2-bromoethyl)amino]-4-trifluoromethylcoumarin (**4**)[9] and K_2CO_3 as a base in MeCN produces **2** in 75% yield. ^{1}H NMR spectrum of **2** exhibits two doublets at 3.79 and 3.29 ppm in AB pattern with coupling constant of 13.14 Hz corresponding to protons of the methylene bridge and there is a peak at 31.3 ppm in the ^{13}C NMR spectrum, suggesting that **2** be in the cone conformation. 2-(4-(Trifluoromethylcoumarin))-*N*-((1-pyrenyl)methyl)acetamide (**3**) as a refer-



Scheme 1. Synthetic routes for fluorescent chemosensor **2**.

ence was also synthesized in 73% yield by the reaction of 7-amino-4-trifluoromethylcoumarin (**5**) with *N*-(1-pyrenylmethyl)chloroacetamide (**6**)[10] in the presence of NaI in MeCN.

To obtain insight into the exciplex formation between coumarin and pyrene, we investigated fluorescence changes upon excitation at various wavelengths from 343 nm, the maximum absorption wavelength of the pyrene, to 380 nm. Excited at 343 nm, **1** displays a monomer emission at 375 nm and an excimer emission at 448 nm, whereas **2** develops a new band at 425 nm with a 3-fold higher intensity than the excimer intensity of **1**. There might be two reasons controlling fluorescence changes in this system: a steric effect[15] and an electron transferring interaction between two different fluorophores, pyrenes and coumarin. Since two facing pyrenes are in steric congestion due to the triazacrown unit, the pyene excimer emission of **1** shows a smaller intensity than that of compound without triazacrown group. Besides, the former is blue-shifted in comparison with the latter due to a partial overlap.[15]

When coumarin substituent is introduced on the central nitrogen atom of the triazacrown unit, the resulting product **2** displays a new emission at 425 nm which is conceivable to be originated from an exciplex formation between pyrene to coumarin. This is due to a short distance induced from hydrogen bonding between the amide group linked to pyrenes and the amide groups of the triazacrown ring.[15] The exciplex formation was shown in previous report in which it displayed similar fluorescence spectra induced by a close interval between pyrene as a donor and naphthalene as an acceptor.[16]

Furthermore, when excited from 348 nm to 380 nm, the emissions move from 425 nm to 480 nm with a decrease in intensity. Especially, excited at 380 nm, the maximum absorption of coumarin, **2** displays a coumarin emission at 480 nm with a decreased exciplex emission at 425 nm. This suggests that the large band at 425 nm of **2** be attributed to the exciplex formed from a pyrene as an electron donor to a coumarin as an acceptor.

To elucidate the exciplex of coumarin and pyrene, we have investigated fluorescence experiment with **3** and **6**. Excited at 343 nm, **6** shows a monomer emission of pyrene at 375 nm while **3** develops a distinct coumarin emission at 480 nm with a considerably quenched monomer emission of it. There is no exciplex at 425 nm because **3** does not have a structure able to make short distance between a coumarin and a pyrene as **2** does. Although excitation at 343 nm is not strong enough to excite the coumarin, it displays the coumarin emission at 480 nm due to the FRET (fluorescence resonance energy transfer) from pyrene to coumarin.[17]

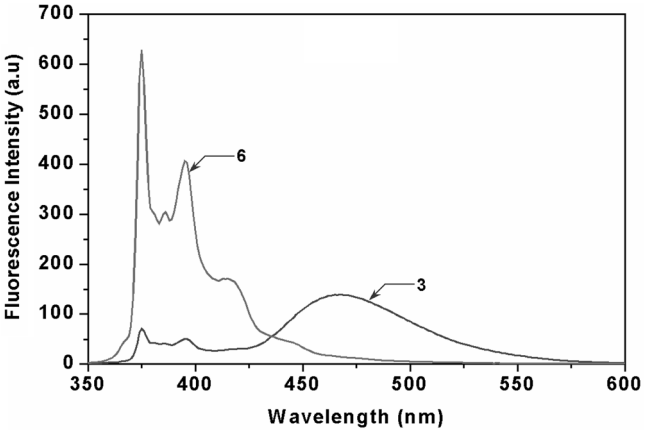


Figure 2. Fluorescence spectra of **3** and **6** (6.0 μM) excited at 343 nm in MeCN.

We investigated binding properties of **2** toward anions with respect to fluorescence changes. Among anions tested, F^-, known as a quenching anion,[13] causes the fluorescence of **2** to be quenched both in the monomer and particularly, in the exciplex. Besides, an unexpected emission appears at 480 nm with weak fluorescence intensity. These results are ascribable to the PET effect from F^- to pyrene units as well as to coumarin as indicated in Figure 3. This change is due to the hydrogen bonding between F^- and the amine hydrogen of the coumarin unit together with amide hydrogen atom of the triazacrown.[13] As a result, **2** does not form the energy transferred-exciplex from pyrene to coumarin. There is an appearance of excimer emission at 480 nm because hydrogen bonding between F^- and the amide groups linked to the pyrene keeps the two fluorophore units overlapping. The accurate binding mechanism of **2** to anion reported in previous experiment indicates that the amine proton

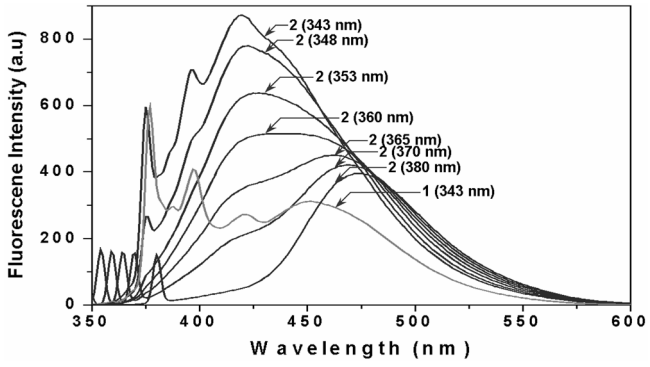
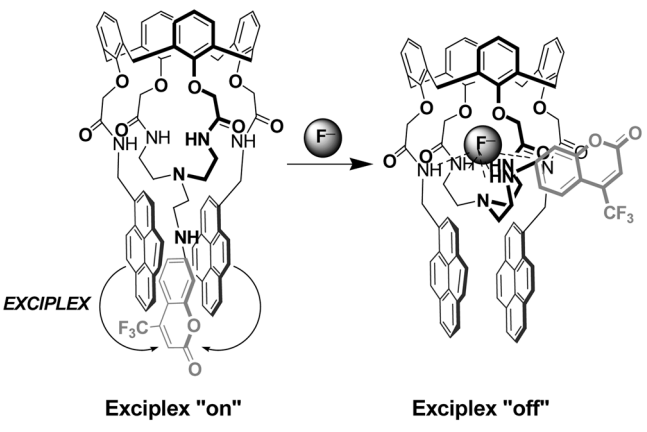


Figure 1. Fluorescence emission spectra of **1** and **2** (6.0 μM) with various excitation wavelengths.



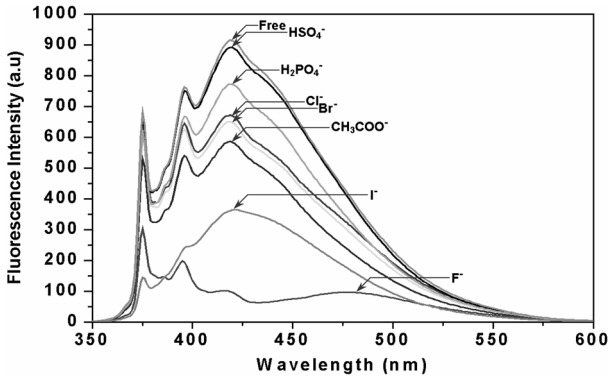


Figure 3. Fluorescence emission spectra of **2** (6 μM) upon addition of various anions of tetrabutylammonium salts of F^-, Cl^-, Br^-, I^-, $CH_3CO_2^-$, HSO_4^-, $H_2PO_4^-$ (6.0 mM) in MeCN.

participates in the binding with F^-.[13]

In conclusion, a new fluorogenic calix[4]triazacrown-5 (**2**) bearing two pyrene amide groups and one coumarin amine group was prepared. Excited at 343 nm, **2** displays the exciplex fluorescence at 425 nm with considerably enhanced intensity because H-bonding between the azacrown unit and the two pyrene amide groups leads the pyrene to locate near coumarin enabling them to overlap. However, complexation of **2** with F^- causes a fluorescence quenching and a decrease in exciplex emission at 425 nm because of a combination of PET and conformational change. The coumarin amine group together with an azacrown unit plays an important role in the selective F^- complexation. Since **2** functions as an anion selective chemo-sensing tool, we believe that this compound can be used in many intriguing systems related to the detection of F^-, which are of general interest in the treatment of industrial waste water.

Experimental Section

Compound **1**[15], **5**[18] and **6**[10] were prepared from the adaptation of the reported procedures.

Calix[4]triaza-crown coumarin (2). Under nitrogen, fluorogenic calix[4]triaza-crown (**1**) (0.1 g, 0.09 mmol), 7-[*N*-(2-bromoethyl)amino]-4-trifluoromethylcoumarin (**4**) (0.03 g, 0.09 mmol) and K_2CO_3 (0.07 mmol) in 50 mL of MeCN were heated to reflux temperature. After refluxing for 24 h, MeCN was removed *in vacuo*. To the resulting yellow solid, water (100 mL) and CH_2Cl_2 (50 mL) were added and the organic layer was separated and washed three times with 50 mL of water. The organic layer was dried over anhydrous $MgSO_4$ and the solvent was evaporated *in vacuo* to give a yellowish solid. Column chromatography on silica gel using EtOAc/hexane (1 : 1) as eluents gave 0.18 g (75% yield) of **1** as a yellowish solid. Mp: 235-239 °C. IR (neat, cm^{-1}): 3440, 1811. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.65 (broad t, 2H, N*H* in triazacrown), 8.31-7.60 (m, 18H, Ar-*H*, pyrene; 2H, *NH*pyrenes; s, 1H, Ar-*H*, coumarin; d, 1H, Ar-*H*, coumarin), 7.02 (d, 4H, Ar-H_m, J = 7.4 Hz), 6.85-6.70 (m, 4H, Ar-H_p; 4H, Ar-H_m; 2H, Ar-*H* in coumarin), 5.19 (d, 4H, NHCH_2-pyrene, J = 5.60 Hz), 4.16 (s, 4H, ArOCH_2), 3.77 (d, 4H, ArCH_2Ar, J = 13.4 Hz), 3.41-3.19 (m, 4H, ArOCH_2; 4H, ArCH_2Ar; 6H, NCH$_2$CH_2NH), 2.87 (broad s, 6H, NCH_2-CH$_2$NH). ^{13}C NMR (50 MHz, $CDCl_3$): 168.7, 154.4, 152.4, 150.7, 132.4, 129.5, 128.2, 127.4, 126.6, 125.2, 124.6, 123.0, 120.8, 67.0, 56.3, 31.3 ppm. FAB MS *m/z* (M^+) Calcd, 1405.5. Found 1405.0. Anal. Calcd. for $C_{86}H_{71}O_{10}N_6F_3$: C, 73.49; H, 5.09. Found: C, 73.51; H, 5.07.

2-(4-(Trifluoromethylcoumarin))-*N*-(1-pyrenylmethyl)-acetamide (3). To a mixture of 1.0 g (4.36 mmol) of coumarin and 1.6 g (4.36 mmol) of *N*-(1-pyrenyl-methyl)-chloroacetamide (**6**) in 50 mL of dry MeCN, a catalytic amount of NaI was added. The reaction was refluxed for 12 h. After removal of the solvent *in vacuo*, the resulting solid was dissolved in CH_2Cl_2 (100 mL) and the organic layer was washed three times with water. The organic layer was dried over anhydrous $MgSO_4$ and evaporated *in vacuo* to give the crude product, which was purified by recrystallization from diethyl ether to give 1.59 g (73%) of **3**. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.23-7.89 (m, 9H, Ar-*H*, pyrene; 1H, N*H*CO), 7.41 (s, 1H, Ar-*H*, coumarin), 6.73 (s, 1H, Ar-*H*, coumarin), 6.50 (d, 1H, Ar-*H*, coumarin, J = 10.9 Hz), 6.30 (s, 1H, Ar-*H*, coumarin), 5.30 (s, 1 H, CH$_2$N*H*coumarin), 5.17 (d, 2H, pyreneCH_2NH, J = 2.0 Hz), 3.67 (d, 2H, COCH_2NHcoumarin, J = 6.0 Hz).

7-[*N*-(2-Bromoethyl)amino]-4-trifluoromethylcoumarin (4). 7-[*N*-(2-bromoethyl)-*N*-tosylamino]-4-trifluoromethyl-coumarin 1.00 g (2.04 mmol) was added to conc. sulfuric acid (10 mL) and the solution was stirred for 12 h at 90 °C. The reaction mixture was cooled and carefully poured into cold water. The mixture was neutralized with a saturated $NaHCO_3$ aqueous solution and extracted with CH_2Cl_2 three times. The organic solution was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*. The residue was recrystallized from H_2O/EtOH to give 0.50 g of yellow powder in 72% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.51 (d, 1H, Ar-*H*, coumarin, J = 8.6 Hz), 6.60 (d, 1H, Ar-*H*, comarin, J = 9.0 Hz), 6.52 (s, 1H, Ar-*H*, coumarin), 6.46 (s, 1H, Ar-*H*, coumarin), 4.80 (broad s, 1H, N*H*), 3.58-3.67 (m, 4H, BrCH_2CH_2NH). FAB MS *m/z* (M^+) Calcd, 336. Found 338. Anal. Calcd. for $C_{12}H_9BrF_3NO_2$: C, 42.88; H, 2.70. Found: C, 42.84; H, 2.73.

General procedures for fluorescence studies. Fluorescence spectra were recored with a RF-5301PC spectrofluoro-photometer. Stock solutions (1.00 mM) of the metal perchlorate salts were prepared in MeCN. Stock solutions of **1** and **2** (0.06 mM) were prepared in MeCN. For all measurements, excitation was at 343 nm with excitation and emission slit widths at 3 nm.

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