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Notes

Calix[2]pyreno[2]pyrrole as a Fluorescence Chemical Probe for Polynitroaromatics

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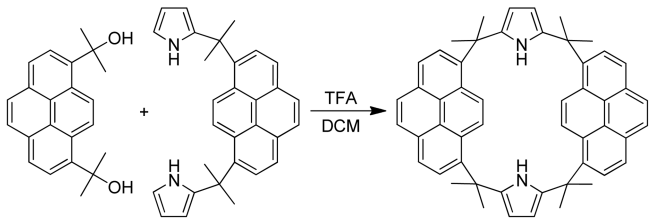
The elevated selectivity and sensitivity for specific analytes are the core requirements for an ideal chemical probes. A signal induced by guest binding must be sensitive enough so that accurate real time monitoring could be satisfactorily achieved.[1] Introduction of signaling units at suitable places in which they can directly interact with the recognition events is critical in designing chemosensors. Among various signaling events, fluorescence changes are often applied for the sensitive detection of various analytes. An easy modulation of the photochemical properties of the signaling units is an additional advantage in compatibility and applications.[2] Chemosensors for the detection of explosives becomes important due to their immediate applications in remedation of explosive manufacturing sites, homeland security or forensic sciences.[3,4] With that in mind, numerous methods for the explosive detection have been reported in recent years.[5] Nevertheless, some detection methods sometimes require sophisticated instrumentation which is not easy for on-site testing.[6-9]

There has been an increasing demand for the development of more convenient and sensitive detection methods. One of them is based on the nanomaterial systems.[10,11] As a part of these efforts, we have recently reported a calix[4]pyrrole-like hybrid macrocycle as potential fluorescence chemosensor for neutral molecule such as fullerenes.[12] The concept of design was based on the replacement of pyrrole rings with fluorophores that bear potential pi-pi interaction site sites. We hypothesized that this substitution would place the fluorophore in a proper location with limited flexibility required for binding and guest selectivity. At the same time, an easy conformational change of the macrocycle can accommodate any neutral guests that bear inherently electron-deficient characteristics. The resulting cavity could be ideal binding site for the guest molecules that bear proper geometry.[13] With these regards, we here report the synthesis of a new fluorescent macrocyclic host, calix[2]pyreno[2]-pyrrole **3** and its guest binding properties.

The designed host **3** exhibits unprecedently high binding affinity for polynitroaromatic compounds including TNT



Scheme 1. Synthesis of receptor **3**.

(*vide infra*).[14-16] The compound **3** was synthesized by typical '3+1' type condensation as shown in Scheme 1. The 1,8-*bis*(2-(hydroxy)propan-2-yl)pyrene **1** was reacted with pyrrole in the presence of catalytic amount of trifluoroacetic acid to afford 1,8-*bis*(2-(1*H*-pyrrol-2-yl)propan-2-yl)pyrene **2** in 28% yield. Condensation of **2** with **1** in the presence of trifluoroacetic acid afforded the target receptor **3** in 12% yield. All the substances prepared in this sequence were characterized by ^{1}H and ^{13}C spectroscopic techniques, and high resolution mass spectrometry. Exceptional down field shift of the pyrrole N-Hs signal seen at 9.48 ppm indicates the existence of the diamagnetic ring current effect of pyrene.

The preliminary anion-binding properties of receptor **3** carried out by using ^{1}H NMR spectroscopic analysis indicates that the pyrrole N-Hs are not participating in the anion binding. This observation is attributed to the conformational rigidity of the macrocycle. This observation led us to test the fluorescence changes upon association with neutral molecules such as polynitroaromatic compounds, since the interaction of electron rich pi-system with electron deficient pi system has been well known.[17] The Figure 1 shows fluorescence titration results of receptor **3** with nitrobenzene and 2,5-dinitro-*p*-xylene. The fluorescence spectra of receptor **3** taken in toluene displayed a typical monomeric emission and the guest-dependent quenching of the fluorescence is obvious. The fluorescence quenching titration was performed with increasing amounts of guest concentration. The spatial arrangement of the two pyrene units must well match

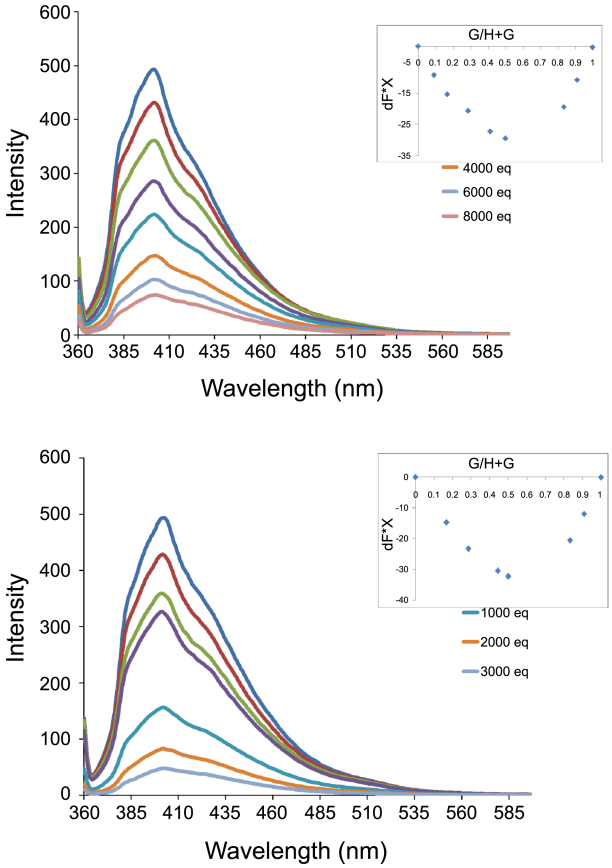


Figure 1. Fluorescence spectral changes of receptor **3** (5.72×10^{-7} M) upon addition of nitrobenzene (top) and TNT (bottom) in toluene ($\lambda_{ex} = 350$ nm).

for the guest binding. The calculated binding constant from the fluorescence titration was found to be $1.2 \times 10^6 \pm 0.14 \times 10^5$ M^{-1} which is large enough to form strong host-anion charge transfer complex.

Next the titration was repeated with 2,4,6-trinitrotoluene (TNT). As shown in Figure 2, the gradual addition of TNT resulted in complete quenching of fluorescence. The calculated binding constant from the fluorescence titration was found to be $1.1 \times 10^6 \pm 0.14 \times 10^5$ M^{-1}, which is almost similar with that of simple nitrobenzene. A Job plot of the data obtained from fluorescence changes of **3** as a function of nitrobenzene concentration was found to exhibit a maximum at *ca.* ~0.5 which is consistent with formation of a 1:1 complex.[18] These results indicate the complex formation between **3** and nitroaromatics is directed by electronic nature of the host and guest. A standard calibration curve for detection of TNT with receptor **3** was constructed by plotting the concentration of TNT against F_0/F in toluene (Figure 2). The detection limit was found to approach up to nanomolar range.

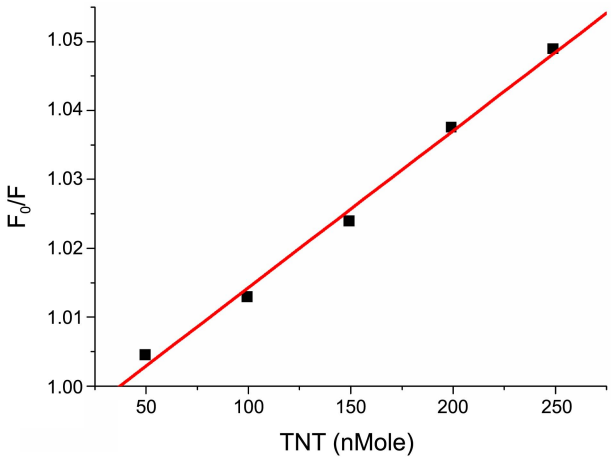


Figure 2. Detection limit of TNT determined from [TNT] against F_0/F in toluene.

In summary, we have demonstrated that the new, readily synthesized and well characterized calix[2]pyreno[2]pyrrole fluorescence molecular probe **3** can detect polynitroaromatic compounds with high affinity. In addition, this highly fluorescent neutral molecular receptor also exhibits enhanced binding affinity towards TNT which is associated with the formation of a pi-complex. The dynamic nature of the current system may enable it to serve as an excellent scaffold for electron-deficient guest molecular binding. Studies for other neutral molecules including metal ions are under in active progress.

Experimental Section

All reagents are commercially available and were used as received. All solvents were dried and distilled using common techniques unless otherwise mentioned.

1,8-*Bis*(2-(hydroxy)propan-2-yl)pyrene (1). 1,8-Acetylpyrene (0.50 g, 1.75 mmol) was dissolved in dry THF (50 mL) under N_2 atmosphere, then CH_3MgBr (0.20 mL, 17.5 mmol) was added dropwise over a period of 5 min at 0 °C. The whole mixture was stirred for 12 h at 0 °C. Then, the reaction was quenched by adding aqueous saturated NH_4Cl (10 mL). The mixture was extracted with ethyl acetate and the organic layer was dried (Na_2SO_4) and solvent was removed *in vacuo*. Purification by silica gel column chromatography (CH_2Cl_2/EtOAc = 10/1) yielded **1** (0.13 g, 24%) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 2H), 8.12 (q, 4H, J = 8.56 Hz), 7.99 (s, 2H), 2.16 (s, 2H), 2.02 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.35, 131.08, 127.95, 127.34,126.34, 125.51, 124.49, 123.05, 74.53, 32.24; FAB-MS Calcd for $C_{22}H_{22}O_2$ 318.1620, Found 318.1623 (M).

1,8-*Bis*(2-(1*H*-pyrrol-2-yl)propan-2-yl)pyrene (2). To a solution of compound **1** (0.23 g, 0.72 mmol) and pyrrole (1.0 mL, 14.5 mmol) in CH_2Cl_2 (20 mL) under N_2 atmosphere, $BF_3{\cdot}OEt_2$ (180 μL, 1.45 mmol) was added. The whole mixture was stirred for 15 min at 25 °C. Then, aqueous NaOH (1.0 mL, 0.1 N) was added to the solution. The mixture was extracted with CH_2Cl_2 (10 mL × 3) and the organic layer was dried (Na_2SO_4). The solvent and excess pyrroles were removed *in vacuo*. Purification by silica gel column chromatography (CH_2Cl_2/Hexanes = 1/10) yielded **2** (0.08 g, 28%) in pure form. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, 2H, J = 8.09 Hz), 8.13 (d, 2H, J = 8.08 Hz), 8.00 (s, 2H), 7.79 (s, 2H), 7.31 (s, 2H), 6.40 (m, 2H), 6.22 (m, 2H), 6.19 (m, 2H),

1.93 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.89, 140.84, 130.90, 125.50, 127.25, 126.19, 124.68, 124.41, 124.37, 116.15, 108.00, 102.58, 40.10, 31.99; MALDI-TOF Calcd for $C_{30}H_{28}N_2$ 416.2252, Found 416.5225 (M), 417.5283 (M+1).

Calix[2]pyreno[2]pyrrole (3). Compounds **1** (0.08 g, 0.25 mmol) and **2** (0.10 g, 0.24 mmol) were dissolved in CH_2Cl_2 (20 mL) with stirring, then TFA (0.1 mL, 1.44 mmol) was added. The whole mixture was stirred for 24 h at 25 °C. Then, triethyl amine (0.3 mL) and water (20 mL) were added to the solution. The mixture was then extracted with CH_2Cl_2 (10 mL × 3). The organic layer was dried (Na_2SO_4) and solvent was removed *in vacuo*. Purification by silica gel chromatography (CH_2Cl_2/Hexanes = 1/10) yielded **3** (0.02 g, 12%) in pure form. ^{1}H NMR (300 MHz, Acetone-d_6) δ 9.46 (s, 2H), 8.33 (s, 4H), 7.90 (d, 4H, J = 7.67 Hz), 7.82 (d, 4H, J = 7.85 Hz), 7.73 (s, 4H), 6.34 (s, 4H), 1.87 (s, 12H), 1.77 (s, 12H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 142.32, 141.99, 130.92, 129.46, 127.31, 126.38, 125.25, 124.77, 124.49, 102.59, 40.67, 33.87; MALDI-TOF Calcd for $C_{52}H_{46}N_2$ 698.3661, Found 698.4119 (M), 699.4091 (M + 1).

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