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Synthesis and metal-binding studies of a novel pyrene discotic

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This Letter is dedicated to Professor Douglas C. Neckers on the occasion of his 70th birthday

Abstract—The synthesis of a novel bis-crown quinoxalino[2′,3′:9,10]phenanthro[4,5-*abc*]phenazine discotic and its binding properties to a series of alkali and alkaline-earth metals is reported. A schematic representation of the binding equilibrium of the sensor to the metal is proposed. The binding constant of the sensor to barium(II) was estimated to be $1.4 \times 10^4\ \mathrm{M}^{-1}$ based on ^{1}H NMR studies.

Crown ether derivatives have been exploited for a wide range of applications such as optical[1] and photochromic[2] sensing of metal ions, molecular switches[3] and elevators,[4] two-photon absorption properties,[5] and biomedical applications.[6] Crown-ether-based fluorescent sensors for alkali[7,8] and alkaline-earth[1,8–10] metal cations are an attractive target due to their sensitivity, selectivity, and potential application in real-time monitoring.[11] Rigid rod-like bis-crowns are especially interesting for their ability to form different extended supramolecular arrangements with the metal cations.[12] Recently, we[13] and others[14] have reported novel discotics based on the rigid fluorescent core of quinoxalino[2′,3′:9,10]phenanthro[4,5-*abc*]phenazine. In this Letter, we report the synthesis and binding studies of a novel bis-crown discotic **1** composed of a quinoxalino[2′,3′:9,10]phenanthro[4,5-*abc*]phenazine core furnished with two 18-crown-6 moieties.

The synthesis of **1** (Scheme 1) started with Friedel–Crafts alkylation of pyrene (**2**) to afford 2,7-di-*t*-butylpyrene (**3**) which was oxidized using ruthenium(III) chloride and sodium periodate to yield di-*t*-butyltetraketopyrene (**4**).[15] Nitration[16] of the benzo-18-crown-6 (**5**) produced the 4,5-dinitrobenzo-18-crown-6 (**6**), which was reduced to yield the 4,5-diaminobenzo-18-crown-6 (**7**).[16] The condensation of **4** and **7** in methanol afforded the bis-crown sensor **1**.[17]

The UV–vis spectrum of **1** showed characteristic bands at 286 nm ($\varepsilon = 54{,}400\ \mathrm{M}^{-1}\,\mathrm{cm}^{-1}$), 404 nm ($\varepsilon = 41{,}000\ \mathrm{M}^{-1}\,\mathrm{cm}^{-1}$), and 426 nm ($\varepsilon = 58{,}000\ \mathrm{M}^{-1}\,\mathrm{cm}^{-1}$). The addition[18] of barium(II) to the sensor led to a decrease in the absorption bands at 404 nm and 426 nm, an increase at 340 nm, and a blue shift followed by absorption enhancement at the 286 nm band (Fig. 1). This change in the UV spectrum was observed, with the same trend, even when the concentration of the metal was more than that of the sensor.

On the other hand, the fluorescence spectrum of **1** exhibited a maximum emission at 447 nm upon excitation at 350 nm. The addition[18] of barium(II) to **1** led to a decrease of its emission at 447 nm and to an increase at 525 nm (Fig. 2). When the metal concentration was equal to the concentration of the sensor (but half the effective concentration of the crown), **1** started to regain its fluorescence at 450 nm and to lose the emission at 525 nm. These results suggest that the metal was binding to two crown ethers[7,9,12,19–21] of two molecules to form complexes such as $\mathbf{S_2M}$ and $\mathbf{S_2M_2}$ (Scheme 2). The structure of these complexes forced two chromophores to be in close proximity which led to quenching of the emission at 450 nm and the enhancement at 525 nm. This is similar behavior to pyrene chromophores that formed excimers once the rings were in close proximity.[10,22]

As the concentration of barium increased, such that more than 1 equiv of the metal was added, the equilibrium shifted toward new complexes in the form of $\mathbf{S_2M_3}$ and $\mathbf{SM_2}$ (Scheme 2). These new conformations

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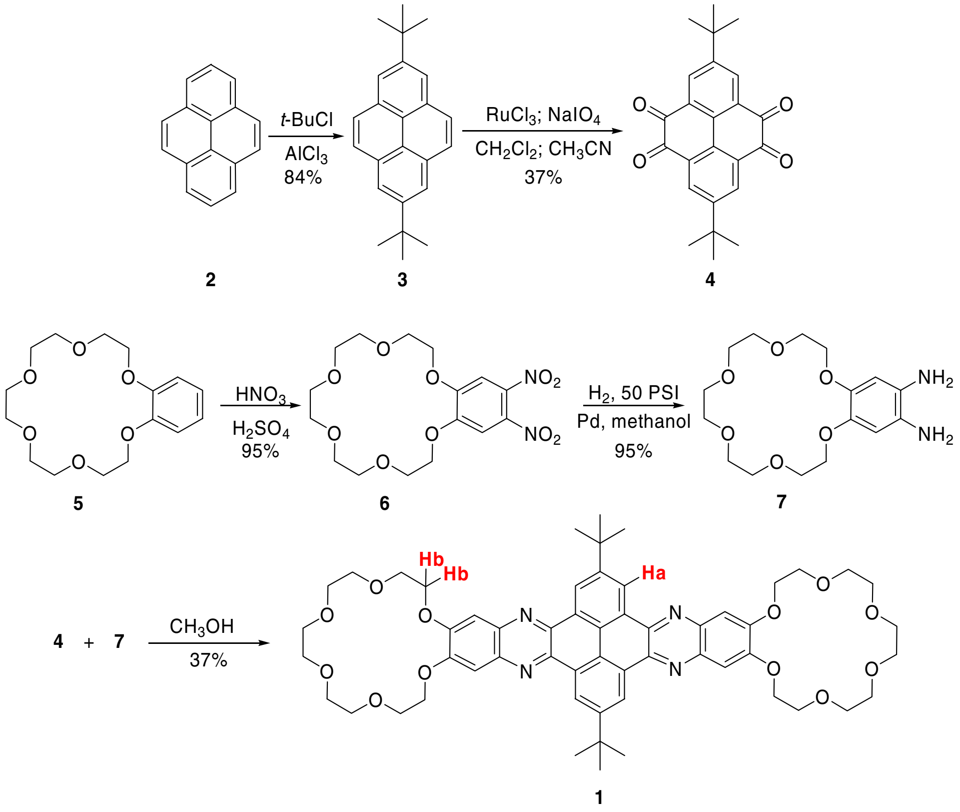


Scheme 1. Synthesis of **1**.

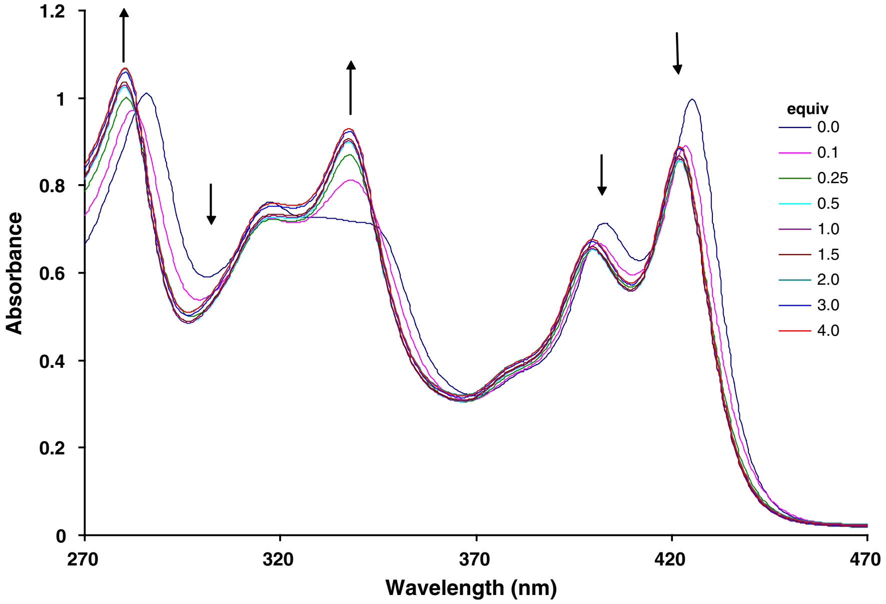


Figure 1. UV–vis spectra of **1** (50 μM) upon the addition of $Ba(ClO_4)_2$ solution (1 mM) in CH_2Cl_2/CH_3CN (1:1).

placed the chromophores far away from each other resulting in enhanced emission at 447 nm and a decrease in the emission at 525 nm. Once the concentration of the metal was double that of the sensor or more, the addition of further metal had little effect on the fluorescence profile of **1** (Fig. 3). All the crowns were then complexed to metals and the main complex present in the solution was in the form of $\mathbf{SM_2}$ (Scheme 2).[9,12]

Titration of **1** with calcium(II) yielded an analogous emission response to that of barium; however, the quenching of fluorescence was to a lower extent

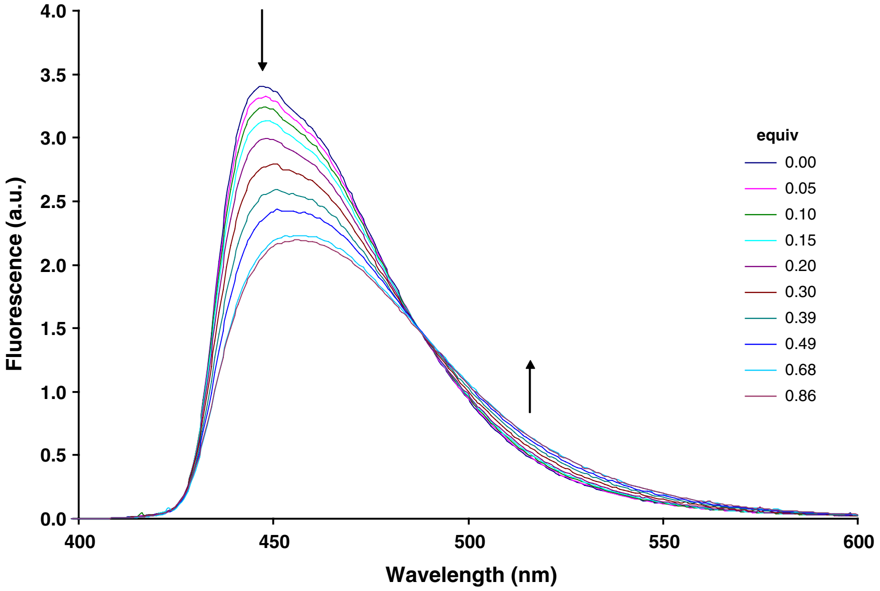
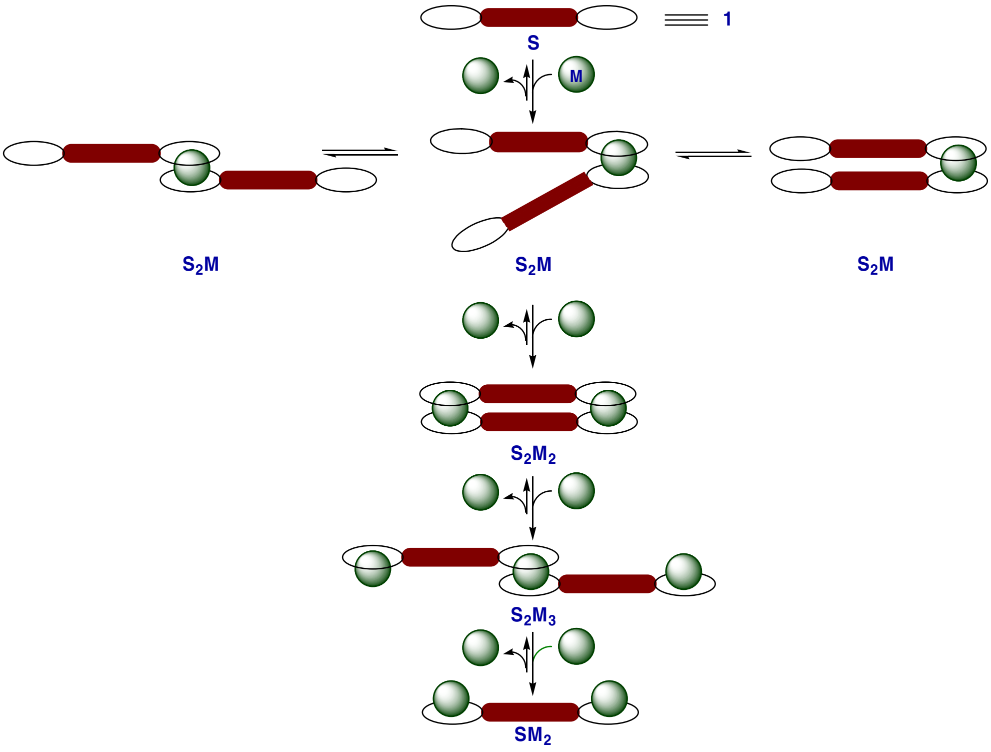


Figure 2. Fluorescence spectra of **1** (50 μM) upon titration with $Ba(ClO_4)_2$ solution (1 mM) in CH_2Cl_2/CH_3CN (1:1).



Scheme 2. Proposed schematic representation of the binding equilibrium of **1** (**S**) to the metal (**M**).

(Fig. 3). This was attributed to the smaller size of calcium ions, which favored binding to one crown-ether.[7,9,12] Thus, the binding equilibrium (Scheme 2) shifted with calcium toward $\mathbf{S_2M}$ and/or $\mathbf{S_2M_2}$ to a lesser extent than with barium. As expected, potassium had an even lower influence on the emission of **1** than calcium due to the lower charge while sodium and lithium presented insignificant effects (Fig. 3).

The complexation of crown sensors to metal ions was also detected through ^1H NMR spectroscopy.[23,24] The titration[25] with a barium perchlorate solution of **1** led to a significant downfield shift of the methylene protons (H_b, Scheme 1) of the crown ethers from 4.48 ppm to 4.70 ppm. The change in this chemical shift became insignificant after the barium(II) concentration reached double that of the sensor (or the same as the effective

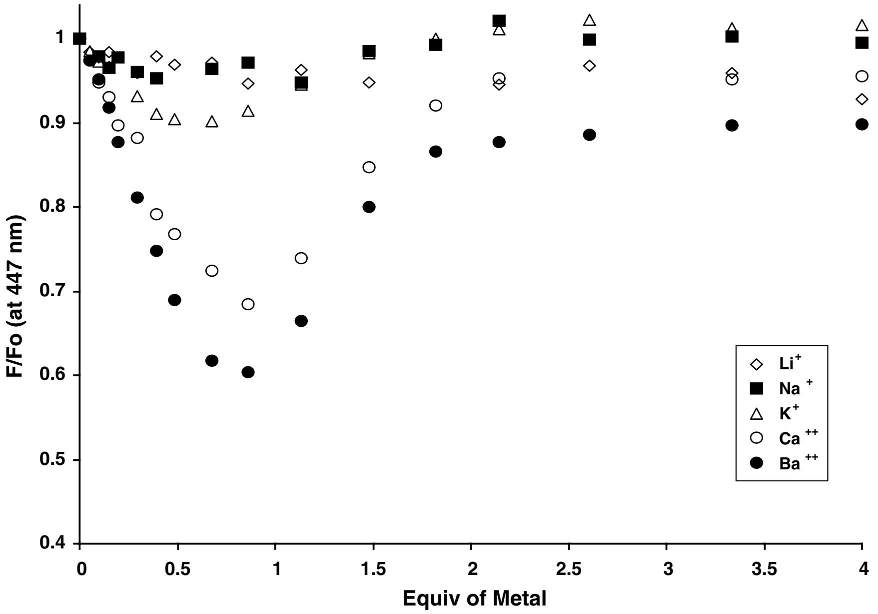


Figure 3. The normalized change in the emission intensity of **1** (50 μM) at 447 nm (F = emission intensity of complex, F_0 = initial emission intensity) upon titration with solutions (1 mM) of $LiPF_6$ (◇), $NaPF_6$ (■), KPF_6 (△), $Ca(ClO_4)_2 \cdot 4H_2O$ (○), and $Ba(ClO_4)_2$ (●) in CH_2Cl_2/CH_3CN (1:1).

concentration of the crown ether) (Fig. 4). This indicated that the metal-crown complexation resulted in a 1:1 complex (**SM_2**) once enough metal had been added. The binding constant for the binding of discotic **1** to barium(II) was estimated to be $1.4 \times 10^4\ M^{-1}$.

On the other hand, the change in the chemical shift of the aromatic protons (H_a, Scheme 1) showed a behavior that supported the suggested dynamic equilibrium observed in the fluorescence studies (Scheme 2). The signals of H_a shifted upfield from 9.69 ppm to 9.65 ppm as the concentration of the metal increased to reach half that of the sensor (Fig. 4). This suggested that when the two crown ethers bound the metal to form complex **S_2M**, the aromatic protons were located in the shielding cone of the ring current[26] of the other molecule producing an upfield shift (an average shift of all the possible conformations of **S_2M**). Then, these signals started to shift downfield as the concentration increased, and reached 7.87 ppm, when 2 equiv of the metal had been added. This implied that when the concentration of the added metal was more than half that of the sensor

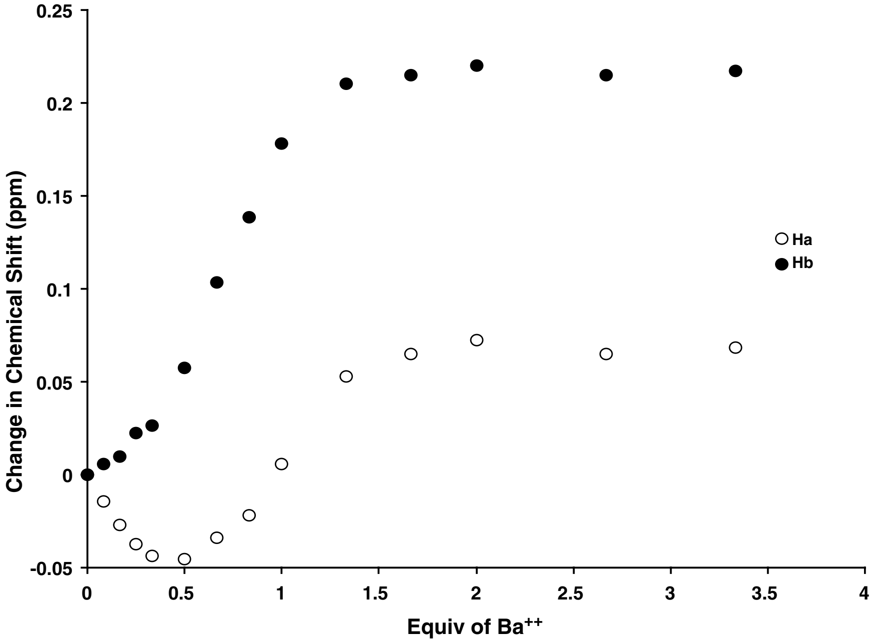


Figure 4. The change in the chemical shifts ($\Delta\delta$) of the aromatic (H_a) and the crown ether protons (H_b) of **1** (1 mM) upon titration with $Ba(ClO_4)_2$ solution (10 mM) in $CDCl_3/CD_3CN$.

(but not less than the concentration of **1**) complex $\mathbf{S_2M_2}$ formed. This conformation locked the chromophore rings in a fixed position placing the aromatic protons (H_a) away from the shielding cone of the other ring and caused a downfield shift. Once the concentration of the metal was double or more than that of the sensor, the equilibrium shifted toward the formation of complex $\mathbf{SM_2}$ where the downfield shift of H_a was mainly due to the electrostatic effect of the metal.

In summary, we have reported the synthesis of a novel bis-crown quinoxalino[2′,3′:9,10]phenanthro[4,5-*abc*]-phenazine discotic. We have presented preliminary results on its binding activity and proposed a schematic representation of the binding equilibrium of the sensor to the metal. Further studies on this and other related crowns are currently in progress.

Acknowledgments

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17. Synthesis of 2,25-bis(1,1-dimethylethyl)-7,8,10,11,13,14,16,17,19,20,30,31,33,34,36,37,39,40,42,43-eicosahydro-[1,4,7,10,13,16]hexaoxacyclooctadecino[2″,3″:6′,7′]quinoxalino[2′,3′:9,10]phenanthro[4,5-*abc*][1,4,7,10,13,16]hexaoxacyclooctadecino[2,3-*i*]phenazine (**1**): A mass of 492 mg (1.31 mmol) of **4** was refluxed with 900 mg (2.63 mmol) of **7** in 100 mL of methanol for 48 h under an argon atmosphere. The solution was cooled, filtered, and the solid obtained was washed with cold methanol to afford 480 mg (37%) of a brownish solid **1**, mp >300 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.75 (18H, s), 3.74 (8H, s), 3.79 (8H, m), 3.87 (8H, m), 4.10 (8H, br s), 4.48 (8H, br s), 7.64 (4H, s), 9.72 (4H, s). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.49, 35.91, 69.11, 70.49, 70.76, 71.00, 107.02, 123.06, 124.73, 129.39, 139.01, 140.75, 160.42, 162.97. HRMS-MALDI (*m/z*): $[M+H]^+$: calcd for $C_{56}H_{67}N_4O_{12}$, 987.4750; found, 987.4799.
18. *Spectroscopic titration*. A solution of **1** (50 μM, 2 mL) in CH_2Cl_2/CH_3CN (1:1) placed into a 1 × 1 cm cuvette was titrated with a solution of the metal (1 mM, CH_2Cl_2/CH_3CN (1:1)) that contained **1** (50 μM). Aliquot amounts of the metal solution were added to the cuvette via a syringe until a total of 4 equiv of the metal had been added (the number of additions was around 20 with an increase in the amount of metal solution added). The UV–vis spectrum and emission spectrum ($\lambda_{ex} = 350$ nm) were scanned after each addition.
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25. *^{1}H NMR titration*. A solution of **1** (1 mM, 600 μL) in $CDCl_3/CD_3CN$ (1:1) placed in an NMR tube was titrated with a solution of the metal (10 mM, $CDCl_3/CD_3CN$ (1:1)). Aliquot amounts of the metal solution were added to the NMR tube via a syringe until a total of 4 equiv of the metal were added (the number of additions was around 17 with an increase in the amount of metal solution added). A ^{1}H NMR spectrum was recorded after each addition and the chemical shifts of the aromatic (H_a) and crown-ether (H_b) protons were recorded. The collected data was analyzed using a non-linear least square regression program to fit the data to a theoretical model of a 2:1 crown-to-metal binding process.
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