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Anthracene-based macrocyclic fluorescent chemosensor for selective sensing of dicarboxylate

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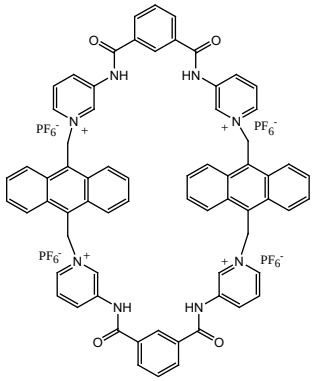
ABSTRACT

An anthracene-based macrocyclic receptor has been designed and synthesized for selective recognition of 1,4-phenylenediacetate ($K_a = 3.34 \times 10^5\ M^{-1}$). The macrocycle binds 1,4-phenylenediacetate selectively at the charged sites of the receptor with a concomitant increase in fluorescence of anthracene. The interaction properties of the macrocycle were evaluated by ^1H NMR, UV–vis and fluorescence spectroscopic methods.

The design and synthesis of fluorescent receptors of particular architectures for the selective sensing and binding of anionic species is an expanding area of research in supramolecular chemistry.[1–4] The precise arrangement of the hydrogen bonding groups near the fluorescent probes is a special art to design a sensor for efficient anion recognition.[5] The recognition and binding of anions are of considerable importance owing to their important roles in biological, industrial and environmental processes.[6,7] In this context, the recognition of dicarboxylate anions is an active area of research in supramolecular chemistry. Dicarboxylates are critical components of numerous metabolic processes including, for instance, the citric acid and glyoxalate cycles. They also play an important role in the generation of high-energy phosphate bonds and in the biosynthesis of important intermediates.[8,9] Considerable effort has been devoted to the development of ditopic fluorescent receptors for dicarboxylates.[10–14] During the last decades, positively charged receptors based on polyammonium,[15] guanidinium,[16] polyprotonated aza crown ether,[17] imidazolium[12] or metal containing species[18] were developed for dicarboxylates. Our ureidopyridyl[19] and pyridyl cinnamide-based receptors[20] for selective recognition of dicarboxylate can be mentioned. Despite the significant progress made in dicarboxylate ion recognition, there is a continuous effort for the synthesis of new designed receptors with interesting properties. In relation to this, pyridinium amide as a binding motif is less explored in anion recognition. To investigate the significance of C–H···O hydrogen bonds in a highly polar solvent for carboxylate ion recognition, Jeong et al. reported the use of pyridinium salt.[21] Later on, Steed et al.[22] pursued the synthesis, anion binding and conformational properties of a series of 3-aminopyridinium based tripodal, tricationic hosts for anions. We have also shown that an anthracene-appended pyridinium salt under an isophthaloyl spacer is able to bind dihydrogenphosphate and aliphatic carboxylates effectively.[23] To explore the pyridinium salt further in the design and synthesis of a new receptor, we report here the synthesis and molecular recognition properties of a new macrocyclic receptor **1**.

The macrocyclic receptor **1** was synthesized according to Scheme 1. Initially, compound **2** was obtained from the reaction of 3-aminopyridine with isophthaloyl diacidchloride in dry CH_2Cl_2.



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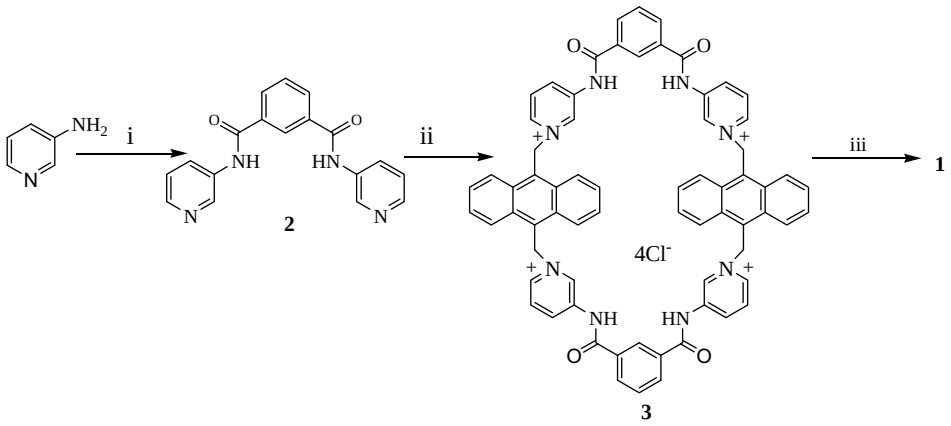

Scheme 1. Reagents and conditions: (i) isophthaloyl diacidchloride, triethylamine, in dry CH_2Cl_2 (isolated yield: 36%), (ii) 9,10-bis (chloromethyl) anthracene in CH_3CN and dry DMF mixture, reflux for 36 h (isolated yield: 39%), (iii) NH_4PF_6, aq CH_3OH (yield 27%).

The high dilution reaction of compound **2** with 9,10-bis(chloromethyl)anthracene in dry CH_3CN under refluxing conditions afforded a precipitate of chloride salt **3**. The subsequent exchange of the chloride ion by the hexafluorophosphate ion in a hot aqueous methanol solvent yielded the desired macrocycle **1** in 27% yield. The compound **1** was characterized by ^1H NMR, ^{13}C, FTIR and mass spectral analysis (see Supplementary data).

A molecular modelling[24] study shows that macrocycle **1** is flexible enough and exhibits a twisting structure in the gas phase. The phenyl rings of the isophthaloyl spacers maintain the shortest distance of 3.22 Å. In the twisting form (Fig. 1) two binding domains are created for the complexation of carboxylate guests. Figure 1b is a side view of the macrocycle, which shows the narrow channel.

In order to evaluate the noncovalent interaction properties of **1** with diacarboxylates of different dimensions, ^1H NMR spectra of the 1:1 complexes were initially recorded. The amide protons, appearing at 10.85 ppm, underwent a downfield shift to different extents in DMSO-d_6 in the presence of the tetrabutylammonium salts of oxalic, malonic, glutaric, adipic, terephthalic and 1,4-phenylenediacetic acids. In a few cases, the amide protons were too broad to be detected correctly. In the case of oxalate, the downfield chemical shift of the amide protons in **1** was only 0.18 ppm. This was considerable in the case of the long chain dicarboxylates. In the presence of an equivalent amount of terephthalate, 1,4-phenylenediacetate, the changes in the chemical shift of the amide protons of **1** were 0.55 and 0.42 ppm, respectively. Upon the addition of adipate and pimelate, the signal for amide protons was broad and it was difficult to determine the accurate position. During complexation with long chain analogues, the pyridinium *ortho* protons showed an upfield shift (e.g., $\Delta\delta$ = 0.06 ppm in the case of 1,4-phenylenediacetate). In the presence of short chain analogues such as oxalate and malonate, the pyridinium *ortho* protons moved less in the downfield direction ($\Delta\delta$ = 0.01 ppm). This change in the chemical shift of the pyridinium *ortho* protons is ascribed presumably to the conformational change of the receptor during complexation at the diamide cores of **1** involving hydrogen bonding and charge–charge interactions.

After investing the noncovalent interactions of **1** in ^1H NMR both in the presence and absence of dicarboxylate guests, we started our experiments on the exploration of selectivity and sensitivity of **1** towards the dicarboxylate anions in CH_3CN. This was carried out by observing the change in fluorescence emission spectra in CH_3CN. The fluorescence emission spectra of **1** showed a broad peak at 419 nm when excited at 370 nm. Upon the addition of dicarboxylates of different chain lengths to the CH_3CN solution of **1**, the emission of anthracene at 419 nm increased to different extents. Figure 2 shows the change in the fluorescence intensity of anthracene emission at 419 nm in **1** in the presence of increasing amounts of different dicarboxylates. During titration of **1** with adipate, pimelate, terephthalate and 1,4-phenylenediacetate, an additional emission peak at 500 nm was observed. The appearance of this peak was almost negligible in the presence of oxalate, malonate, succinate and glutarate (see Supplementary data). The strong peak at 500 nm in the presence of pimelate, terephthalate and 1,4-phenylenediacetate was attributed to the formation of an excimer between the anthracenes in **1**. The excimer between the anthracenes is reported to appear at 500 nm in the literature.[25] More importantly, the intensity of the excimer was decreased on dilution with CH_3CN. The intensity of this excimer in the presence of 1,4-phenylenediacetate was found significant and compara-

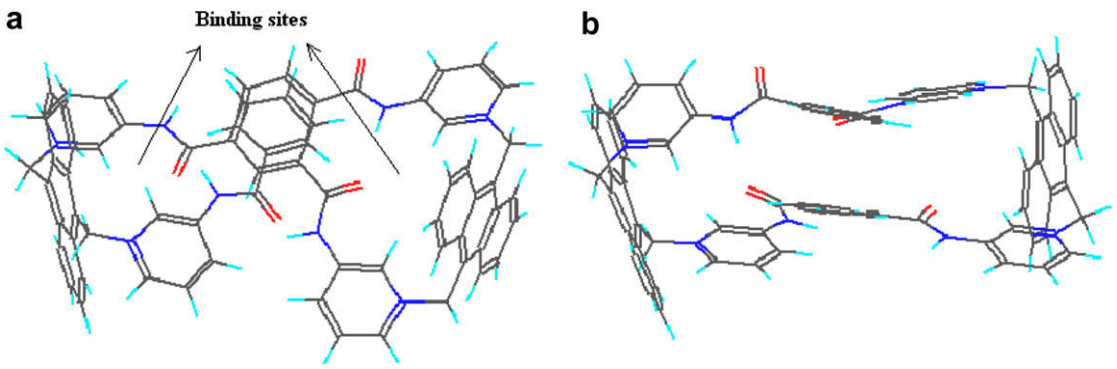

Figure 1. (a) MM2 optimized geometry of 1 (E = 90.33 kcal/mol); (b) side view of the optimized geometry of 1 to focus the internal space for inclusion of guests.

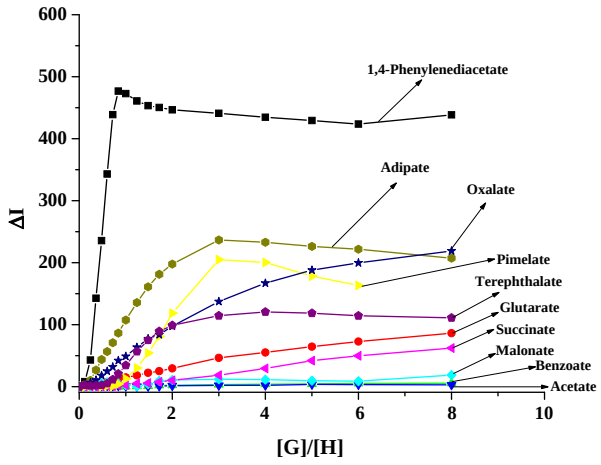

Figure 2. Plot of change in emission of **1** at 419 nm versus the ratio of guest to host concentration.

tively higher than in the cases with adipate, pimelate and terephthalate. Figure 3 exhibits the change in emission of **1** in the presence of increasing amounts of 1,4-phenylenediacetate in CH_3CN. The change in emission of **1** in the presence of monocarboxylates such as acetate and benzoate was negligible as evidenced from Figure 2. The fluorescence enhancement of **1** in the presence of the dicarboxylates is ascribed here to the inhibition of a photo-induced electron transfer (PET) from the binding sites to the excited anthracene. The break of the titration curves at [G]/[H] = 1 in Figure 2 represents the 1:1 stoichiometry of the complexes. Job plots further confirmed the 1:1 stoichiometry of the complexes (see Supplementary data). The inset of Figure 3 demonstrates the job plot from fluorescence. The sharp inflection at 0.5 in the job plot indicates 1:1 stoichiometry of the complex of **1** with 1,4-phenylenediacetate. In order to realize the binding selectivity of **1**, the binding constant values were determined from fluorescence titration.[26] It is evident from Table 1 that the macrocycle, in the present case, has a preference for 1,4-phenylenediacetate over the other dicarboxylates.

A simultaneous absorption study of **1** was followed upon the addition of the same dicarboxylates under identical conditions. During the titration of **1** with oxalate, succinate, glutarate, acetate and benzoate, the absorption peaks for anthracene underwent minor changes (see Supplementary data). On the contrary, the

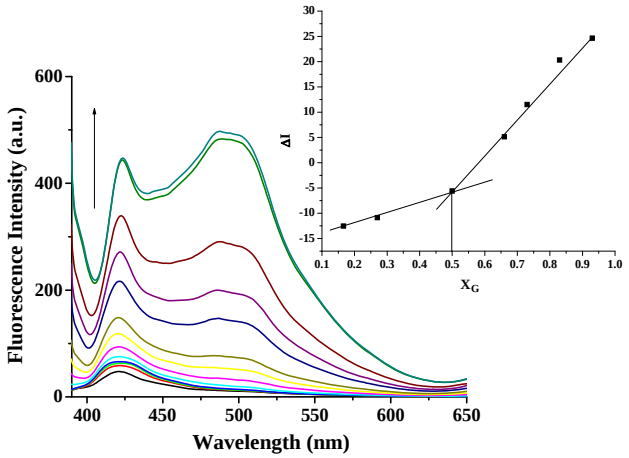

Figure 3. Change in emission of **1** in presence of increasing amounts of 1,4-phenylenediacetate in CH_3CN; inset: fluorescence job of **1** with 1,4-phenylenediacetate.

Table 1
Binding constant values of **1** with the guests in CH_3CN

Guests	K_a (M^{-1})[a]	K_a (M^{-1})[b]
Oxalate	3.89×10^3	7.94×10^3
Malonate	9.20×10^3	[c]
Succinate	[c]	[c]
Glutarate	[c]	[c]
Adipate	3.31×10^3	5.78×10^3
Pimelate	7.95×10^3	2.59×10^4
1,4-Phenylenediacetate	3.63×10^4	3.34×10^5
Terephthalate	5.23×10^3	8.16×10^3
Acetate	[c]	[c]
Benzoate	[c]	[c]

[a] Determined from UV method.
[b] Determined from fluorescence.
[c] Not determined due to irregular and minor changes.

change in the absorption of anthracene was significant in the presence of malonate, adipate, pimelate and 1,4-phenylenediacetate. With regard to this, the change in absorbance of **1** in the presence of increasing amounts of 1,4-phenylenediacetate is shown in Figure 4. During complexation with 1,4-phenylenediacetate, a slight red shift of the anthracene absorption was observed (Fig. 4). The downward running of the curve in the plot showing the change in absorbance with [G]/[H] (Fig. 4: inset) is thought to be due to decomplexation either due to the flexible character of receptor **1** or deprotonation of the amide protons of **1** at high concentrations of guests. Analysis of the UV titration data resulted in the binding constant values,[26] which were of a similar trend to that observed in fluorescence (Table 1). Importantly, the receptor shows a better

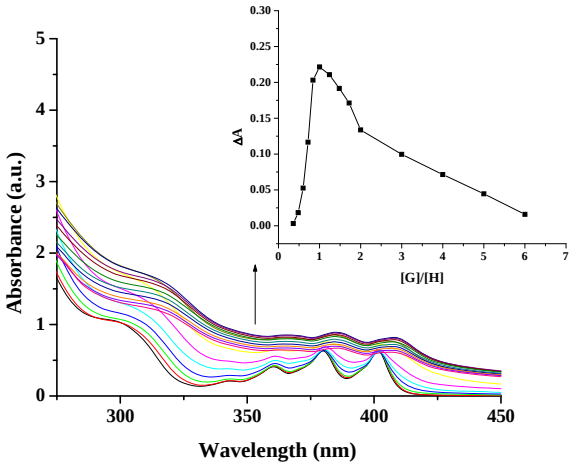

Figure 4. Change in absorbance of **1** in the presence of increasing amounts of 1,4-phenylenediacetate; inset: plot of change in absorbance versus [G]/[H].

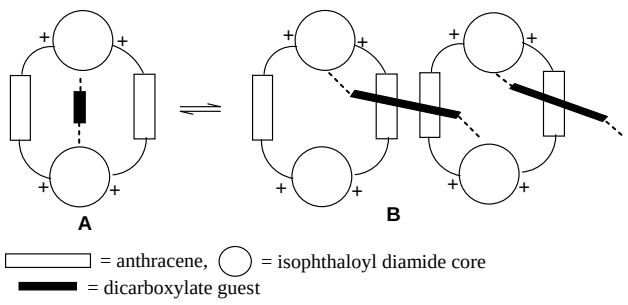

Figure 5. A schematic representation on the binding mode of **1** with tetrabutylammonium 1,4- phenylenediacetate in solution.

selectivity towards the dicarboxylates in the excited state and gives a higher binding constant value with 1,4-phenylenediacetate. This is due to the strong hydrogen bonding interactions of the carboxylate groups at the isophthaloyldiamide cores followed by a weak π-stacking interaction between the anthracene and phenyl ring according to the suggested mode **A** in Figure 5. The possibility of other binding modes of form **B** which may remain in equilibrium with form **A** in solution cannot be ruled out. An experimentally observed peak at around 500 nm for the excimer during complexation supports the existence of dynamic supramolecular structure **B** (Fig. 5).

A small upfield shift of the anthracene ring protons ($\Delta\delta$ = 0.01-0.02 ppm) upon complexation suggested the influence of weak π-stacking interactions in the binding event.

In conclusion, a new anthracene coupled pyridinium-based macrocycle **1** has been designed and synthesized for the selective sensing of dicarboxylate. The macrocycle displays effective selectivity for 1,4-phenylenediacetate showing a large change in fluorescence. The excimer emission with significantly higher intensity clearly discriminates 1,4-phenylenediacetate from the other anions, particularly from adipate, pimelate and terephthalate. Such strong interaction is attributed to the synergistic effect of hydrogen bonding, weak π-stacking and charge–charge interactions in the macrocyclic receptor **1**.

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Supplementary data

Experimental procedure for the synthesis of **1** and the characterization data, Figures showing the change in absorption and fluorescence spectra and the job plots of receptor **1** in the presence of the dicarboxylates are available. Supplementary data associated with this article can be found, in the online version, at doi: 10.1016/j.tetlet.2008.10.135.

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