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Anthracene-based ureidopyridyl fluororeceptor for dicarboxylates

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Abstract—Anthracene-labelled ureidopyridyl sensor **1** was designed and synthesized. The emission of the sensor increased in presence of dicarboxylates. The binding properties were studied using ^{1}H NMR, fluorescence and UV–vis spectroscopic methods. The sensor **1** shows modest selectivity for 1,4-phenylenediacetate.

The recognition and sensing of anionic substrates by charged or neutral synthetic molecular receptors has continued to attract significant attention because of the important role of anionic species in chemistry, biology and environmental sciences.[1] Sensors based on anion-induced changes in fluorescence are particularly attractive due to the simplicity and high detection limit of fluorescence. Dicarboxylates are among the most attractive targets for anion recognition and sensing because of their considerable roles in biological systems.[2] In this regard, various reports on sensing of dicarboxylates involving different binding motifs such as polyprotonated azacrown,[3] guanidinium,[4] polyammonium,[5] imidazolium,[6] and urea/thiourea[2b,7] appended to suitable chromophores or fluorophores as signalling probes, are known. However, the use of a ureidopyridyl motif in the construction of a fluorescent receptor for dicarboxylates is unknown to the best of our knowledge. Recently, Steed and co-workers reported ureidopyridyl-based tripodal receptors for selective recognition of chloride ions.[8] In pursuit of developing sensors for dicarboxylates during the course of our work on molecular recognition,[9] we herein report our results on the synthesis and dicarboxylate anion binding behavior of new anthracene-labelled ureidopyridyl receptor **1**.

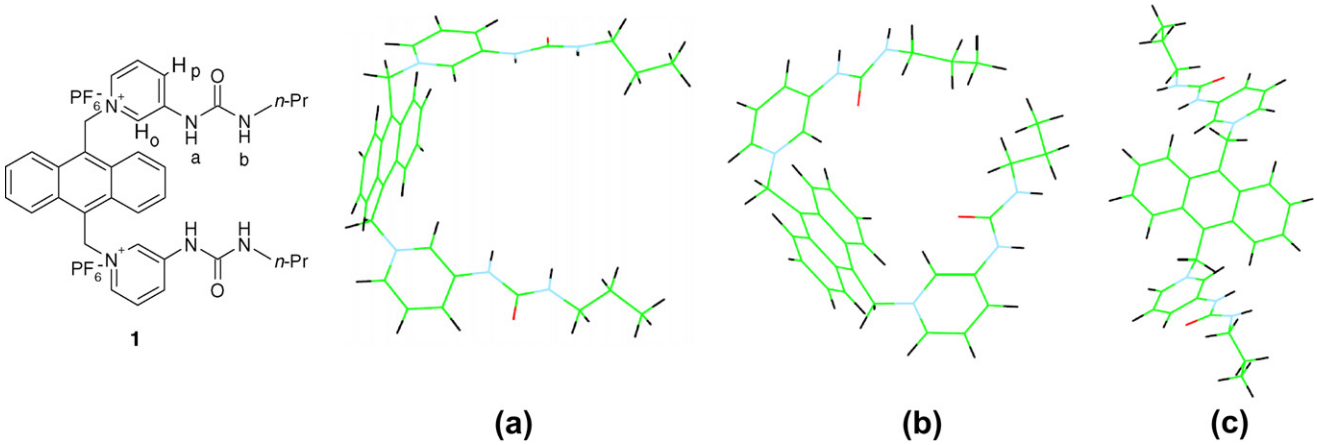

Figure 1. The structure and the AM1 optimized structures of the *syn* rotamers (a) and (b), and the *anti* form (c) of **1**.

Keywords: Ureidopyridyl motif; 1,4-Phenylenediacetate binding; Anion recognition; PET sensor; Anthracene.
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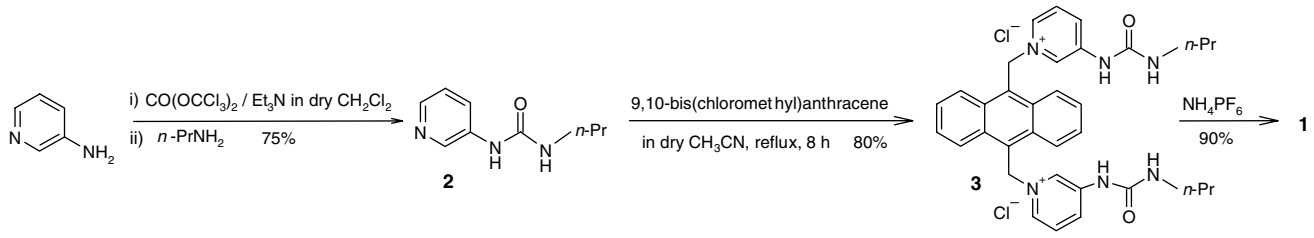

Scheme 1. Synthesis of receptor **1**.

Receptor **1** was synthesized according to Scheme 1.[10] Initially, the ureidopyridyl motif **2** was prepared by reacting 3-aminopyridine with triphosgene in the presence of triethylamine in dry CH_2Cl_2 followed by slow addition of 1-propylamine. Subsequent coupling of **2** with 9,10-bis(chloromethyl)anthracene followed by anion exchange using NH_4PF_6 afforded the receptor **1** as a light yellow solid.

Molecular modelling shows that the open cavity of receptor **1** possesses an appreciable amount of flexibility due to the presence of the methylene group which acts as a spacer between the anthracene and pyridine moieties.[11] The different conformers obtained from the dispositions of the ureidopyridyl groups around anthracene as well as from rotation of the urea motifs, have close energy values. The *syn* rotamer (Fig. 1a) has the highest energy of all. The *anti* form (Fig. 1c) is only 1.31 kcal/mol lower in energy than the *syn* rotamer (Fig. 1a), and is thus relatively stable. The *syn* rotamer (Fig. 1b) is 8.18 kcal/mol lower in energy than the *syn* rotamer in Figure 1a. The cavity of the *syn* form (Fig. 1a; $d_{NHa–NHa} = 7.59$ Å, $d_{NHb–NHb} = 8.62$ Å) can accommodate dicarboxylates of required chain length involving both the ureidopyridyl groups as binding sites in a cooperative fashion. The alternative *syn* (Fig. 1b) and *anti* forms (Fig. 1c) of **1** may induce the formation of dynamic supramolecular association involving the ureidopyridyl group as the hydrogen-bonding trigger in a non co-operative way.

In order to assess the solution phase binding behavior, ^{1}H NMR spectra of **1** in the presence of aliphatic dicarboxylates of different chain lengths were recorded in DMSO-d_6. Addition of dicarboxylates (malonate, succinate, glutarate, adipate, pimelate, 1,4-phenylenediacetate as their tetrabutylammonium salts) to a solution of receptor **1** (1:1) in DMSO-d_6 resulted in large downfield shifts ($\Delta\delta_{NHa} = 1.47$–$3.50$ ppm and $\Delta\delta_{NHb} = 1.60$–$2.60$ ppm) of the urea protons owing to the formation of a receptor **1**–dicarboxylate complex.

During complexation, H_o of the pyridine ring showed an upfield shift ($\Delta\delta = 0.08$–0.31 ppm), presumably due to either a desolvation effect as DMSO is displaced from the open cavity by an anion or a complexation induced conformational change in the receptor. The downfield chemical shifts of H_p ($\Delta\delta = 0.07$–0.20 ppm) upon complexation were also appreciable. This may be either due to the participation of H_p in the formation of C–H···O hydrogen bonds that stabilize the urea–carboxylate complex via the dynamic mode **C** (Fig. 3) or closer

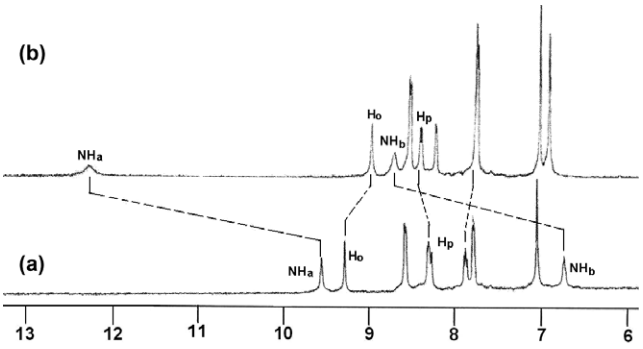

Figure 2. ^{1}H NMR spectra of **1** ($c = 3.52 \times 10^{-3}$ M) with 1,4-phenylenediacetate in DMSO-d_6, (a) **1** only; (b) [G]/[H] = 1.

approach of the urea carbonyl oxygen to H_p upon complexation via mode **A**/**B** (Fig. 3). All the possible forms **A**, **B** and **C** may exist in solution in equilibrium. Representative spectra of **1** in the aromatic region in the presence of 1,4-phenylenediacetate are shown in Figure 2. It is notable that in the presence of 1,4-phenylenediacetate, the anthracene ring protons moved upfield ($\Delta\delta = 0.05$) due to π-stacking interactions.

To ascertain the sensitivity and selectivity we studied the fluorescence and UV–vis behavior of receptor **1** in DMSO both in the presence and absence of dicarboxylates. The receptor **1** falls into the category of the '*receptor-spacer-fluorophore-spacer receptor*' model as proposed by de Silva,[12] and the compound, therefore, could act as a simple PET sensor. The receptor **1** ($c = 7.51 \times 10^{-5}$ M) when excited at 380 nm in DMSO showed structured emission bands at 413, 434 and 460 nm for anthracene along with an additional broad band at 570 nm possibly due to an anthracene–pyridinium complex (exciplex). On gradual increase in the concentration of the dicarboxylate anions, malonate, succinate, glutarate, adipate, pimelate and 1,4-phenylenediacetate (all as tetrabutylammonium salts), the monomer emission of **1** increased to different extents (Fig. 4). This is attributed to the inhibition of PET from the urea binding sites to the anthracene unit owing to the formation of a strong urea–carboxylate hydrogen bonded complex as shown in Figure 3. As displayed in Figure 4, receptor **1** exhibits significant changes in fluorescence emission in the presence of 1,4-phenylenediacetate and long chain pimelate, which form 1:1 complexes, respectively. The stoichiometries of the complexes were confirmed from the break in the titration curve (Fig. 4). One interesting feature of the plot for glutarate

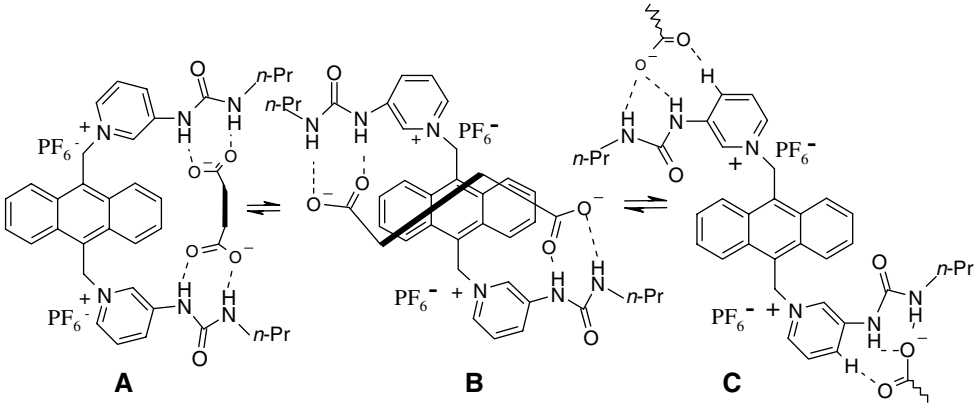

Figure 3. Possible structures of the hydrogen bonded complexes of **1** with dicarboxylates in solution.

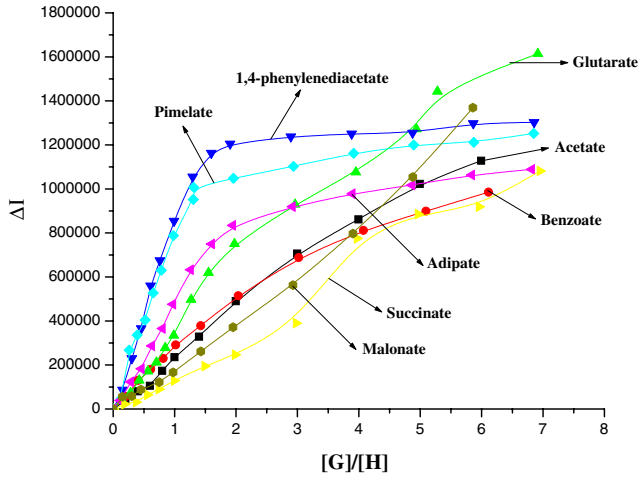

Figure 4. Fluorescence titration curves ([Guest]/[Host] versus change in fluorescence) for **1** (measured at 434 nm) with various anions.

Table 1. Binding constants based on fluorescence analyses

Guest anion	Log *K*
Malonate	4.28
Succinate	4.93
Glutarate	5.73
Adipate	6.87
Pimelate	7.32
1,4-Phenylenediacetate	8.93
Benzoate	5.19
Acetate	5.52

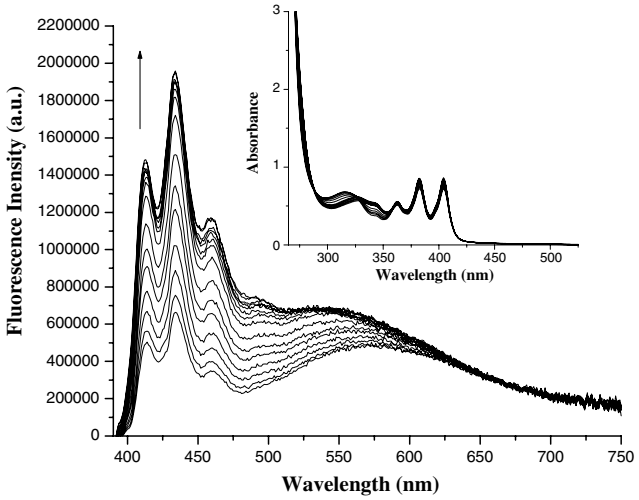

Figure 5. Fluorescence emission spectra of **1** (7.51×10^{-5} M) in DMSO with 1,4-phenylenediacetate and the change in the UV–vis spectra of **1** (7.51×10^{-5} M) (inset) upon addition of 1,4-phenylenediacetate.

is noteworthy. The emission increases until the 1:1 binding stoichiometry is reached. Then again, an increase in emission in the presence of an excess concentration of glutarate was observed. It is believed that when a large excess of glutarate is added, the 1:1 host–guest complex (mode **A**) is disrupted and glutarate begins to bind individually with the ureidopyridyl unit as shown in **C** (Fig. 3). Malonate and succinate are too short to bridge the binding sites and thus bind in a non co-operative fashion. This was evident from the almost linear response of fluorescence change with guest concentration (Fig. 4). This response was not observed for adipate, pimelate and 1,4-phenylenediacetate which indicates that they form 1:1 complexes either in modes **A** or **B** rather than **C**. In contrast, the monocarboxylates (e.g., benzoate and acetate in the present case), bind in 2:1 (guest–receptor) stoichiometries. On the basis of the change in fluorescence intensity, the association constants (K_a) were determined and are shown in Table 1.[13] The values demonstrate that the flexible open cavity of **1** is selective for 1,4-phenylenediacetate among the guests studied. A UV–vis study of **1** in the presence of the same guests cited in Table 1 was carried out in DMSO and the changes in absorbance were minor indicating the insulating role of the methylene groups. The change in the UV–vis spectrum of **1** upon addition of 1,4-phenylenediacetate in Figure 5 (inset) shows the presence of an isosbestic point. This indicated the formation of a 1:1 complex via combination of hydrogen bond formation, π-stacking and electrostatic interactions. The small change in absorbance was not considered when evaluating the binding constant values.

This Letter demonstrates that ureidopyridyl groups can be easily assembled on an anthracene unit to create a fluororeceptor **1** that exhibits fluorescence enhancement in the presence of carboxylates. In the present case the cavity of receptor **1** is selective for 1,4-phenylenediacetate where the complex is stabilized by hydrogen bonding, π-stacking and charge–charge interactions.

Acknowledgments

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10. Mp 196–198 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 9.55 (s, 2H), 9.27 (s, 2H), 8.57–8.54 (m, 4H), 8.29–8.25 (m, 4H), 7.86 (t, 2H, $J = 8$ Hz), 7.78–7.75 (m, 4H), 7.04 (s, 4H), 6.73 (bt, 2H, $J = 8$ Hz), 3.00 (q, 4H, $J = 8$ Hz), 1.41 (m, 4H), 0.84 (t, 6H, $J = 8$ Hz); ^{13}C NMR (DMSO-d_6, 125 MHz): 154.1, 141.9, 134.9, 132.3, 132.1, 131.3, 128.5, 127.9, 125.3, 123.9, 56.4, 41.3, 22.7, 11.1; FTIR: ν cm^{-1} (KBr): 3396, 3138, 3098, 2963, 2934, 2874, 1693, 1591, 1553, 1500, 1453, 1275, 1231; UV (CH_3CN): ($c = 0.634 \times 10^{-5}$M) λ_{max} (nm) 254, 283, 348, 366, 386. Mass (ES^+): 708.2 $[(M-PF_6)+1]^+$, 707.2 $[M-PF_6]^+$, 675.3, 561.3. HRMS (TOF MS ES+) $C_{34}H_{38}N_6O_2PF_6$ $(M-PF_6+H)^+$ requires 708.2698, found 708.1803.
11. Geometry optimization of all conformations of receptor **1** at the AM1 level were carried out using the GAMESS-US (version 2006, R4) software suite. See Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. J.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347–1363.
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13. Binding constants ($\log\beta$) were determined using the equation $\log[(I_{max}-I_F)/(I_F-I_{min})] = \log[\text{guest}]-\log\beta$ (a) Gunnlaugsson, T.; Davis, A. P.; O'Brien, J. E.; Glynn, M. *Org. Biomol. Chem.* **2005**, *3*, 48–56; (b) Cooper, C. R.; James, T. D. *J. Chem. Soc., Perkin Trans. 1* **2000**, 963–969; (c) Wallace, K. J.; Belcher, W. J.; Tumer, D. R.; Syed, K. F.; Steed, J. W. *J. Am. Chem. Soc.* **2003**, *125*, 9699–9715, and references cited therein.