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Anthracene coupled *trans*-pyridylcinnamide: a new fluororeceptor for selective sensing of dicarboxylates

Kumaresh Ghosh *, Goutam Masanta

Department of Chemistry, University of Kalyani, Kalyani, Nadia 741 235, India

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Abstract

trans-Pyridylcinnamide has been established as an alternative hydrogen bonding synthon, in place of urea for carboxylate binding. This alternative motif has been used in the design and synthesis of new fluorescent 'On–Off' signalling chemical sensor **1**, which is found to bind aliphatic dicarboxylates with moderate binding constants. The recognition ability has been established by fluorescence, UV–vis and ^{1}H NMR spectroscopic methods. The receptor is found to be selective for long chain pimelate.

Keywords: *trans*-Pyridylcinnamide; Anthracene; Dicarboxylate recognition; Fluorescent receptor

The development of new hydrogen bonding synthons and their use in the construction of new chemosensors for the selective recognition of important anions is of great interest in host–guest chemistry.[1–4] In this aspect, dicarboxylates are important target anions because of their considerable roles in numerous metabolic processes such as the generation of high energy phosphate bonds and the biosynthesis of important intermediates.[5–7] Dicarboxylate anion binding by various hydrogen bonding receptors has been demonstrated.[8–11] In general, most of these receptors consist of urea/thiourea,[6,8] imidazolium cations,[12] guanidinium ions[13,14] etc., as the hydrogen bonding synthons attached to different fluorophores. However, the use of the *trans*-pyridylcinnamide motif as a new hydrogen bonding synthon, having both more polar NH and less polar CH groups, in the design of hydrogen bonding fluorescent receptor for anions is unknown to the best of our knowledge. It is well established that the weak C–H···O hydrogen bonds extensively exist just like their strong counterparts[15,16] and are found widely in proteins and many organic crystals.[17–19] Although it is much weaker in comparison to the usual strong hydrogen bond, X–H···Y (X, Y = N, O, F), this kind of interaction has aroused significant interest in recent times. In this aspect, reports concerning the occurrence of this weak C–H···O interaction in solution are still rare.[20,21] Although the idea of such C–H···O interactions is familiar,[22] more recently their existence and importance as a weak, but forceful, secondary interactions has been widely accepted.[23] To explore the scope of such weak interactions in molecular recognition processes we herein report the design and synthesis of new fluororeceptor **1** for the selective sensing of dicarboxylate anions.

Receptor **1** was synthesized according to Scheme 1. The hydrogen bonding site *N*1-(3-pyridyl)-(*E*)-3-phenyl-2-propenamide (also known as *trans*-pyridylcinnamide) **3** was initially prepared by reacting 3-aminopyridine with *trans*-cinnamic acid chloride in the presence of triethylamine in dry CH_2Cl_2. Subsequent coupling of **3** with 9,10-bis-(chloromethyl)anthracene followed by anion exchange using NH_4PF_6 afforded receptor **1** in 85% yield.[24]

Receptor **1** can exhibit different types of conformations in solution. Molecular modelling[25] studies indicate that both the *syn*- and *anti*-forms of receptor **1** are close in

* Corresponding author. Tel.: +91 33 25828750; fax: +91 33 25828282.
E-mail address: ghosh_k2003@yahoo.co.in (K. Ghosh).

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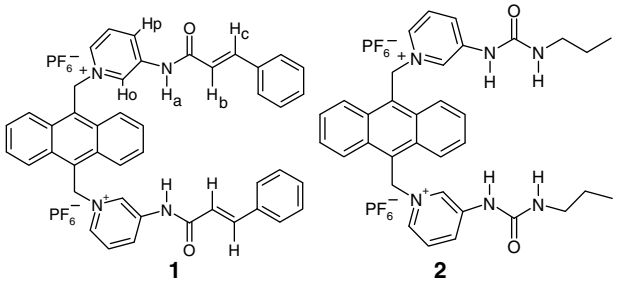


1 2

energy, and the *anti*-form is more stable by 3.87 kcal/mol (Fig. 2). The cavity of the *syn*-form ($E = 127.48$ kcal/mol) can accommodate dicarboxylates of required chain length involving both pyridylcinnamides as binding sites in a cooperative fashion. The non-cooperation of pyridylcinnamide in the *anti*-form of **1** can induce a dynamic supramolecular structure with dicarboxylates that are too short to bridge the binding sites.

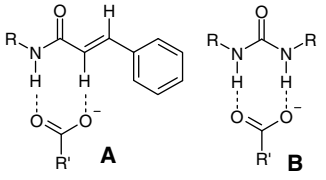
The anion binding ability of **1** was initially established by ^{1}H NMR in DMSO-d_6. To the receptor solution of **1** in DMSO-d_6, aliphatic dicarboxylates of various chain lengths and AcO^- ions were added as their tetrabutylammonium salts in 1:1 stoichiometries. In the presence of acetate ions the amide proton (H_a) underwent a downfield shift ($\Delta\delta = 0.74$ ppm) and became broad. The more acidic vinyl proton (H_b) also showed a downfield shift ($\Delta\delta = 0.08$ ppm). Similar findings were noticed in the presence of dicarboxylate anions. Both the amide (H_a) and the vinyl protons (H_b) of **1** moved downfield in the presence of dicarboxylate anions owing to the formation of receptor–dicarboxylate anion complexes. Surprisingly, the less acidic vinyl proton (H_c) did not show any change in its chemical shift thereby indicating its non-involvement in complexation. The extent of change in the chemical shift of vinyl proton (H_b) was different for aliphatic dicarboxylates of different chain lengths. As can be seen from Table 1, the shift is significant in the case of terephthalate and long chain dicarboxylates such as pimelate and suberate. The amide signal in each case was difficult to detect accurately due to broadening upon complexation. We believe that such measurable downfield chemical shifts of vinyl proton (H_b) are caused by the formation of a weak C–H···O hydrogen bond with the carboxylate anion. The simultaneous involvement of amide proton (H_a) and vinyl proton (H_b) of the *trans*-cinnamide motif in **1** can thus be considered as an alternative hydrogen bonding synthon of urea

Table 1
Change in chemical shift values of receptor **1** in 1:1 complexes with various anions

Guest	$\Delta\delta$ for H_b (ppm)	$\Delta\delta$ for H_o (ppm)	$\Delta\delta$ for H_p (ppm)
Acetate	+0.08	−0.10	+0.10
Malonate	+0.02	−0.09	+0.10
Succinate	+0.0	−0.11	+0.10
Glutarate	+0.14	−0.10	+0.09
Adipate	+0.12	−0.11	+0.18
Pimelate	+0.24	−0.15	+0.31
Suberate	+0.28	−0.14	+0.32
Terephthalate	+0.36	+0.16	+0.35

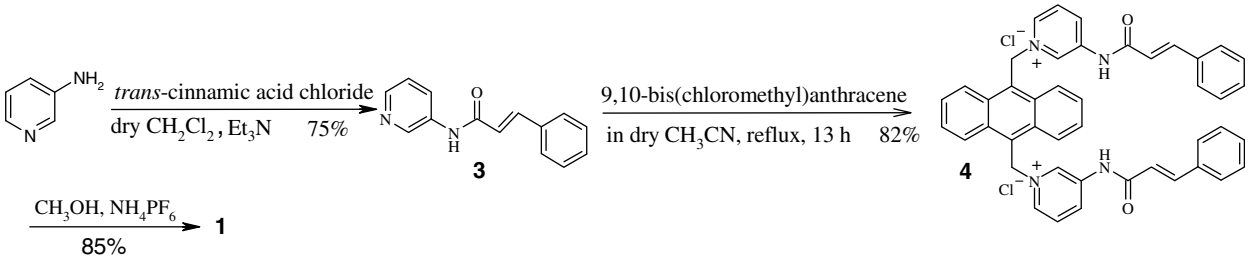
'+' indicates downfield chemical shift.
'−' indicates upfield chemical shift.

for the complexation of carboxylate anions (Fig. 1). Such weak C–H···O hydrogen bonds are not an unusual phenomenon. The result is consistent with the previous reports.[19,26] In this connection, the involvement of the vinyl protons of the α,β-unsaturated amide motif in the complexation of thymine by acrylamido pyridine is worthy of mention.[27] During complexation, the pyridyl *ortho* protons (H_o) showed an upfield shift, presumably, due to either a desolvation effect as DMSO is displaced from the cavity by an anion or a complexation induced conformational change in the receptor. The simultaneous downfield shifts of H_p (Table 1) upon complexation were appreciable. This may be either due to the participation of H_p in the formation of C–H···O hydrogen bonds that stabilize the cinnamylamide–carboxylate complex via the dynamic mode **C** among the other possible equilibrium forms **A** and **B** or closer approach of the amide carbonyl oxygen to H_p upon complexation via mode **A**/**B** (Fig. 3). These observations are consistent with our previously reported urea analogue **2** for dicarboxylates[28] and also with the results reported by Jeong and Cho.[29] The representative spectra of **1** in



A B

Fig. 1. Hydrogen bonding structures of carboxylate with cinnamide (**A**) and urea derivatives (**B**).



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

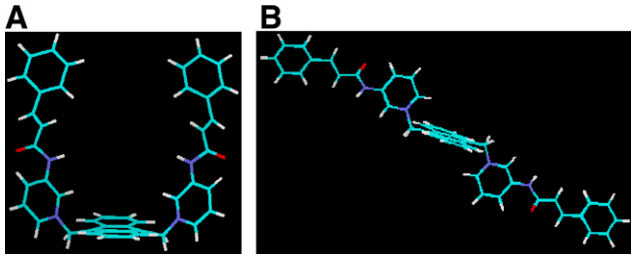


Fig. 2. Energy minimized structures of the *syn*- (A) and *anti*-forms (B) of receptor **1**.

the aromatic region in the presence of both AcO^- and pimelate anions are shown in Figures 4 and 5.

Once it had been established that the vinyl proton (H_b) and the amide proton (H_a) are cooperatively involved in hydrogen bonding with the carboxylate anion like urea (see Fig. 1), the sensitivity and selectivity of receptor **1** was ascertained by fluorescence and UV–vis spectroscopic studies. The UV–vis experiments on receptor **1** with anions were performed in DMSO. As shown in Figure 6, upon complexation of pimelate as its tetrabutylammonium salt with receptor **1** ($c = 3.40 \times 10^{-5}$ M), the absorption peaks at 362 nm, 384 nm and 405 nm for anthracene were increased significantly with a simultaneous decrease of the absorption peak at 306 nm. Similar findings were noted for other anions as mentioned in Table 1. The change in absorbance of the peak at 384 nm as a function of [G]/[H] is shown in Figure 7. From the break of the titration curves (Fig. 7) it is noted that all the anions except pimelate, suberate and terephthalate exhibit 2:1 (host–guest) stoichiometry. The long chain dicarboxylates pimelate, suberate and the aromatic dicarboxylate terephthalate bind in 1:1 stoichiometries. The change in absorption of the peak at 384 nm as a function of added guest concentration was used to determine the binding constant values (Table 2). The results in Table 2 demonstrate that the open cavity of **1** has marked selectivity for the long chain pimelate.

In fluorometric studies, when the solution of **1** ($c = 7.79 \times 10^{-5}$ M) in DMSO was excited at 384 nm, receptor **1** gave a characteristic emission spectrum of anthracene along with a weak emission at 506 nm due to the anthracene–pyridinium complex (exciplex). With a

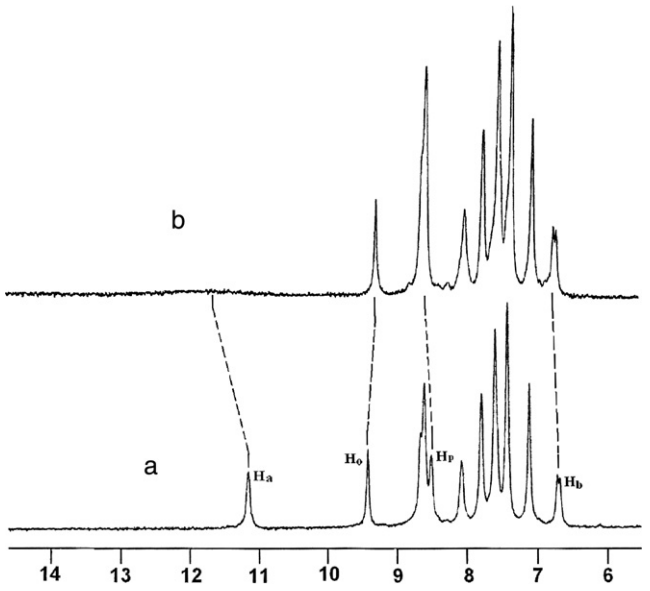


Fig. 4. ^{1}H NMR spectra of **1** ($c = 2.43 \times 10^{-3}$ M) with acetate in DMSO-d_6, (a) **1** only; (b) [G]/[H] = 1.

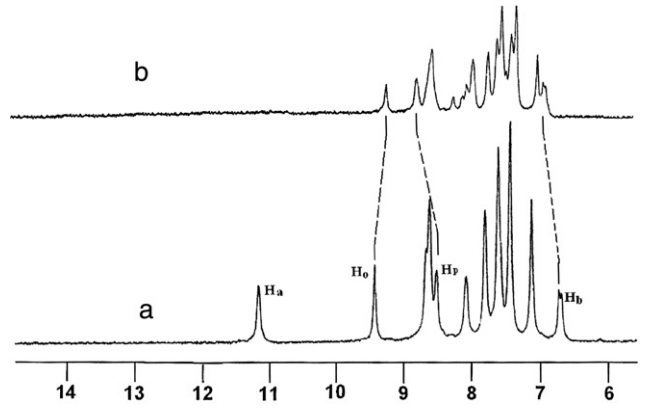


Fig. 5. ^{1}H NMR spectra of **1** ($c = 2.43 \times 10^{-3}$ M) with pimelate in DMSO-d_6, (a) **1** only; (b) [G]/[H] = 1.

gradual increase in the concentration of the guest anions as reported in Table 2, the fluorescent emission of **1** was quenched or *switched off* significantly and behaved oppositely to that of our previously reported receptor **2**.[28] The

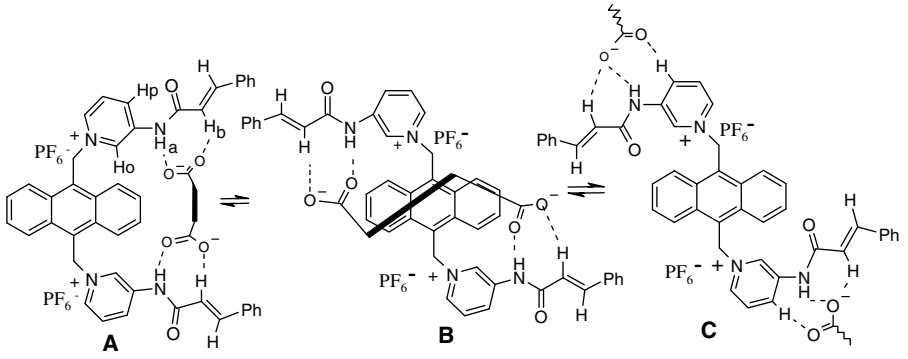


Fig. 3. Possible structures of the hydrogen bonded complexes of **1** with dicarboxylates in solution.

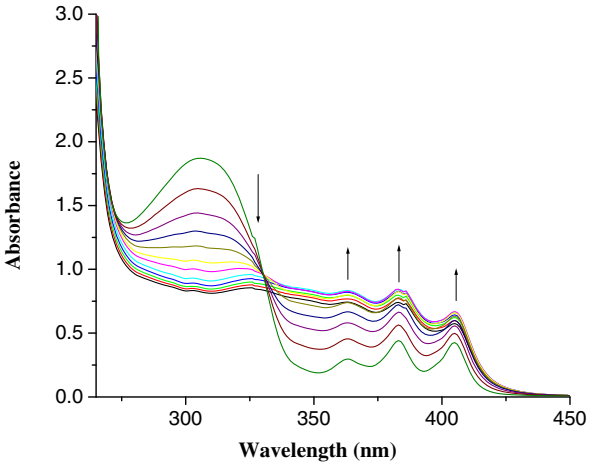


Fig. 6. Changes in the UV–vis spectra of **1** ($c = 3.40 \times 10^{-5}$ M) in DMSO upon the addition of tetrabutylammonium pimelate.

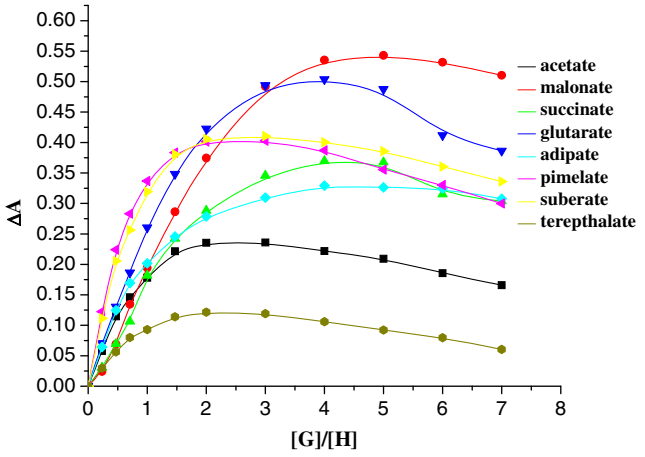


Fig. 7. UV–vis titration curves ([Guest]/[Host] vs change in absorbance) for **1** (measured at 384 nm) with various anions.

Table 2
Binding constants for **1** with the guest anions

Guest anion	Receptor **1**	
	K_a[a] in M^{-1}	K_a[b] in M^{-1}
Acetate	2.85×10^4	1.94×10^4
Malonate	2.09×10^4	4.80×10^3
Succinate	1.15×10^4	2.10×10^3
Glutarate	4.21×10^4	1.22×10^4
Adipate	4.68×10^4	2.08×10^4
Pimelate	8.60×10^4	3.53×10^4
Suberate	7.29×10^4	2.86×10^4
Terephthalate	4.75×10^4	1.88×10^4

[a] Determined by fluorescence methods in DMSO.[32]
[b] Determined by UV methods in DMSO.[32]

degree of quenching varied with the chain length of the dicarboxylates as evidenced from the Stern–Volmer plot (Fig. 8). The change in emission spectra of **1** upon gradual addition of pimelate is displayed in Figure 9. Receptor **1** falls into the category of the '*receptor–spacer–fluorophore–spacer–receptor*' model as proposed by de Silva and, therefore, the compound could act as a simple PET sensor.[30,31] Thus the quenching of fluorescence of **1** is presumably attributed to the activation of PET (photoinduced electron transfer) either from the electronically rich binding site after complexation to the excited anthracene or the reverse. The changes in fluorescence intensity of **1** as a function of [G]/[H] are plotted in Figure 10 and the sharp break in the curves for pimelate, suberate and terephthalate at [G]/[H] = 1 indicated 1:1 stoichiometry of the complexes. The stoichiometry of the complexes was further confirmed by fluorescence Job plots. In this regard, Figure 11 demonstrates the Job plot for pimelate with receptor **1** which confirms the 1:1 stoichiometry. The lower homologues such as malonate, succinate, glutarate and adipate ions are shown to bind in 2:1 (guest–host) stoichiometries.

The binding constant values were also evaluated by fluorescence titration methods considering the change in emission at 433 nm and showed similar trends to those obtained

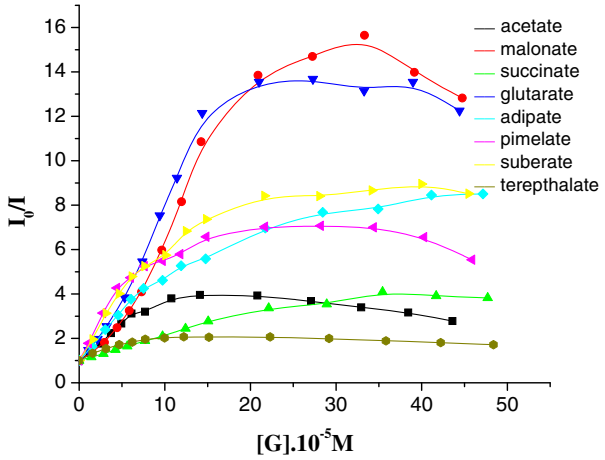


Fig. 8. Stern–Volmer plot for **1** at 433 nm.

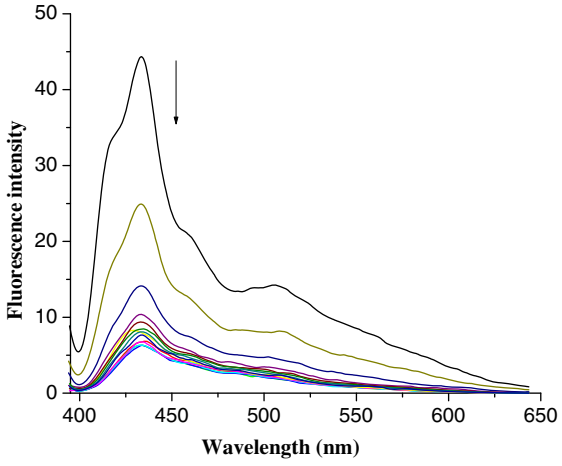


Fig. 9. Changes in the fluorescence spectra of **1** ($c = 7.79 \times 10^{-5}$ M) in DMSO upon the addition of tetrabutylammonium pimelate.

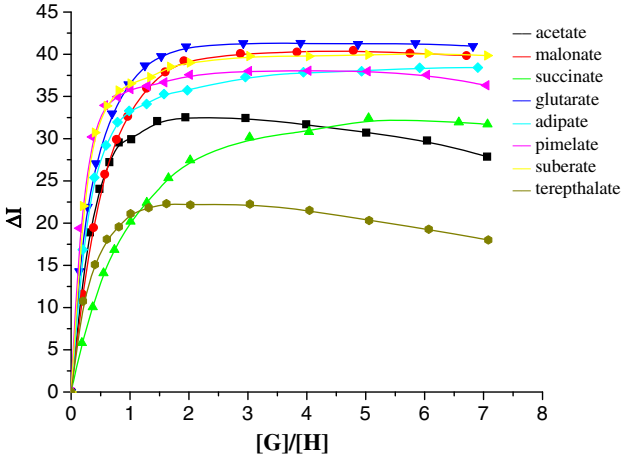


Fig. 10. Fluorescence titration curves ([Guest]/[Host] vs change in emission) for **1** (measured at 433 nm) with various anions.

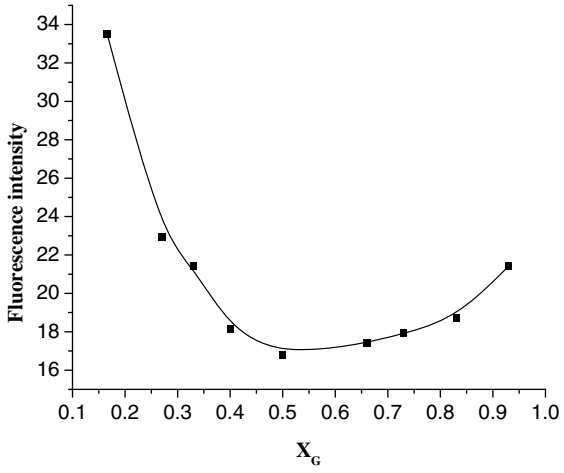


Fig. 11. Fluorescence Job plot of **1** with pimelate.

by the UV method (Table 2). From the values in Table 2, it is clear that the open cleft of receptor **1** has marked selectivity for pimelate over a wide range of dicarboxylates more in the excited state than in the ground state. The conventional N–H···O, unconventional C–H···O hydrogen bonds and the charge–charge interactions are the responsible forces, which cooperatively contribute to the selectivity of **1**.

In conclusion, we have synthesized fluorescent receptor **1** based on a *trans*-pyridylcinnamide motif and investigated its binding properties towards aliphatic dicarboxylates of various chain lengths. It showed moderate selectivity for long chain pimelate over a wide range of dicarboxylates by exhibiting good 'On–Off' switchability, and more importantly, the switching mode was opposite to that of the previously reported urea analogue **2**. This selectivity was attributed to the simultaneous interplay of N–H···O and C–H···O hydrogen bonds and charge–charge interactions during complexation. We are presently exploring the scope of this new hydrogen bonding synthon for the design and synthesis of new task specific receptors.

Acknowledgements

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24. Receptor **1**: Mp 270–274 ° C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.2 (s, 2H, –*NH*CO–), 9.42 (s, 2H), 8.66–8.51 (br m, 8H), 8.08 (br s, 2H), 7.80 (br s, 4H), 7.62 (br s, 6H), 7.45 (br s, 6H), 7.13 (br s, 4H), 6.70 (d, 2H, $J = 16$ Hz); ^{13}C NMR (DMSO-d_6, 125 MHz): 165.5, 143.6, 140.4, 139.4, 135.2, 134.8, 134.5, 132.2, 131.4, 129.9, 129.4, 129.2, 128.9, 127.0, 125.5, 120.9, 57.1; FTIR: ν cm^{-1} (KBr): 3373, 3106, 2926, 1682, 1623, 1589, 1547, 1499, 1454; UV (DMSO): ($c = 3.40 \times 10^{-5}$ M) λ_{max} (nm) 306, 362, 384, 405. Mass (ES^{+}): 797.0 [(M−PF$_6$)+1]$^{+}$, 764.9, 651.2.
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32. For the complexes of receptor **1**, with guests, $[A_0/(A - A_0)]$ as a function of the inverse of carboxylate (guest) the concentration fits a linear relationship, indicating the 1:1 stoichiometry of the receptor/carboxylate complex. The ratio for the intercept versus slope gives the association or binding constant (K_a) for the receptor–guest complex shown in Table 2. In a similar way the emission values obtained during fluorescence titrations of **1** with the same guests were used to evaluate the binding constant values. Chou, P. T.; Wu, G. R.; Wei, C. Y.; Cheng, C. C.; Chang, C. P.; Hung, F. T. *J. Phys. Chem B.* **2002**, *104*, 7818.