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Recognition of monocarboxylic acids by imidazole based fluorescent receptors

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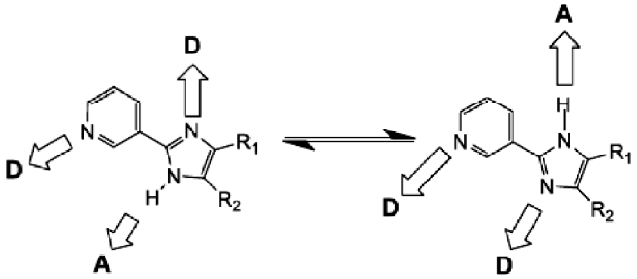
Pyridyl moiety containing substituted imidazole receptors have been synthesized. Their binding properties with monocarboxylic acids have been studied by UV-Vis, fluorescence method as well as ^{1}H NMR study.

Keywords: Imidazole, monocarboxylic acid recognition, fluorescence receptors.

Introduction

The progress of synthetic host molecules for the uncovering of environmentally and biologically significant target molecules like carboxylate anion and carboxylic acid[1–9] is one of the important topics in the ground of molecular recognition research. These types of synthetic host molecules have received substantial interest in supramolecular chemistry. From long period of time, substantial improvement has been made for the detection of carboxylic acids by a huge number of host molecules having diverse architectures[10–13]. Design of artificial sensors for neutral molecules, different non covalent forces such as H-bond, π-π stacking interactions between the host and guest etc. play an important role. Due to their strength and directionality, hydrogen bond is one of the very significant forces in supramolecular design and molecular crystals.

Substituted amidopyridyl moiety in the part of a receptor or isolated is used for the recognition of carboxyl group. In the present paper, imidazole based receptors with different substituent have been synthesized for the detection of mono carboxylic acid. The metal ions coordination of these types of molecules are used for different purposes and their chemistry had been reported[14–17]. The imidazole substituted pyridine moieties contain one acceptor site (pyridine N) and one donor site (the imidazole moiety). These binding sites are arranged as per the position of the substituent (Scheme 1) to the pyridine ring. The acceptor N in it may be used as a donor site and thus can be used for the recognition of monocarboxylic acid. This is possible because of the resonance within imidazole moiety.



Scheme 1. Different tautomeric forms of receptor and its donor (D)-acceptor (A) array.

These receptors may interact in 1:1 or 1:2 mode of hydrogen bonding interaction with carboxyl moiety of carboxylic acid[18]. Probable modes of binding has been shown in Fig. 1. In case of these receptors **1**, **2**, **3** and **4** (Fig. 2) 1:1 as well as 1:2 modes of interactions are possible (Fig. 1). The beak-like structure of the receptor skeletons may help this hydrogen bonding interaction through proper alignments or arrangements.

Synthesis of receptors

Four receptors of similar type with positional variation have been synthesized[18] for the recognition of monocarboxylic acids. Three components one-pot etiquette was applied for

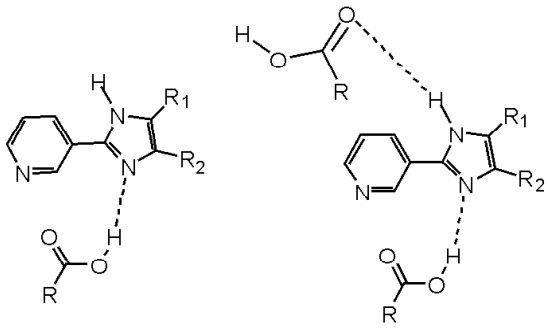


Fig. 1. Probable modes of binding of receptors with carboxyl moiety.

synthesis of these host molecules. The compounds are characterized by spectroscopic data. In case of receptors (Fig. 2), substituted imidazole moiety is attached with the pyridine ring at 3-position. All the pyridine containing receptors have been synthesized (Scheme 2) from pyridine-3-carboxaldehyde, corresponding dicarbonyl compounds and ammonium acetate in glacial acetic acid upon heating at about 95°C.

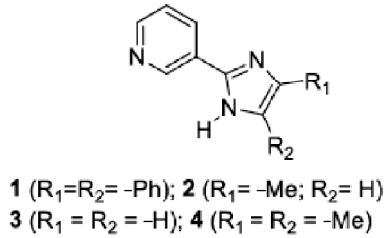


Fig. 2. Receptors with different substituents.

UV-Vis and fluorescence studies for the complexation between the host and the guest and binding constant (K_a) values determination:

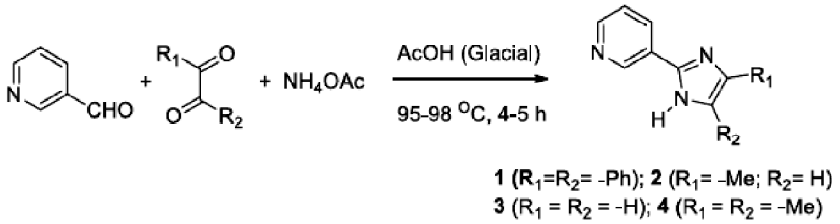
UV-Vis titrations (General procedure):

In order to make stock solution of 10^{-4} *M* in $CHCl_3$, receptors were weighed accurately. Different mono carboxylic acids were dissolved in $CHCl_3$ to prepare the solution of 10^{-3} *M*. The solution of guest molecules is added into the receptor solution. 2 mL of the receptor solution was taken in the UV-Vis cell and the corresponding guest solutions were added through the micropipette with increasing volume to get the corresponding spectrum. From these spectra binding constant (K_a) values were calculated using the particular formula. Each time gradual decrease in absorption was observed in UV spectra. If we plot 1/[G] vs 1/ΔI ([G] = concentration of guest solution and change in intensity {ΔI} of absorbance spectrum obtained through titration) we will be able to calculate the association constants.

Binding behaviors of the synthesized receptors were studied by UV-Vis[19] and fluorescence methods. Receptor **1** showed absorption maxima at ~310 nm, but it gradually decreased upon addition of benzoic acid, phenyl acetic acid, propionic acid and *p*-anisic acid (Fig. 3) solution. Binding constant values could conveniently be calculated from the changes observed in UV-Vis spectrum.

The association constant [K_a (M^{-1})] values for all the receptors with different monocarboxylic acids were determined from the UV-Vis titration values. From the calculated values (Table 1) for receptor **1** it was observed that benzoic acid binds well with all the receptors. The binding constant value is further lowered for *p*-anisic acid due to the presence of methoxy group. Between the phenyl acetic acid and propionic acid, binding constant value for propionic acid is greater than phenyl acetic acid.

The stoichiometry of binding of host with the guest substrates can be determined from the break at the binding graph (Fig. 4). Job's plot also reveals the 1:1 complex formation of receptors with the guest substrates (Fig. 5). From the bind-



Scheme 2. Synthesis of the receptors.

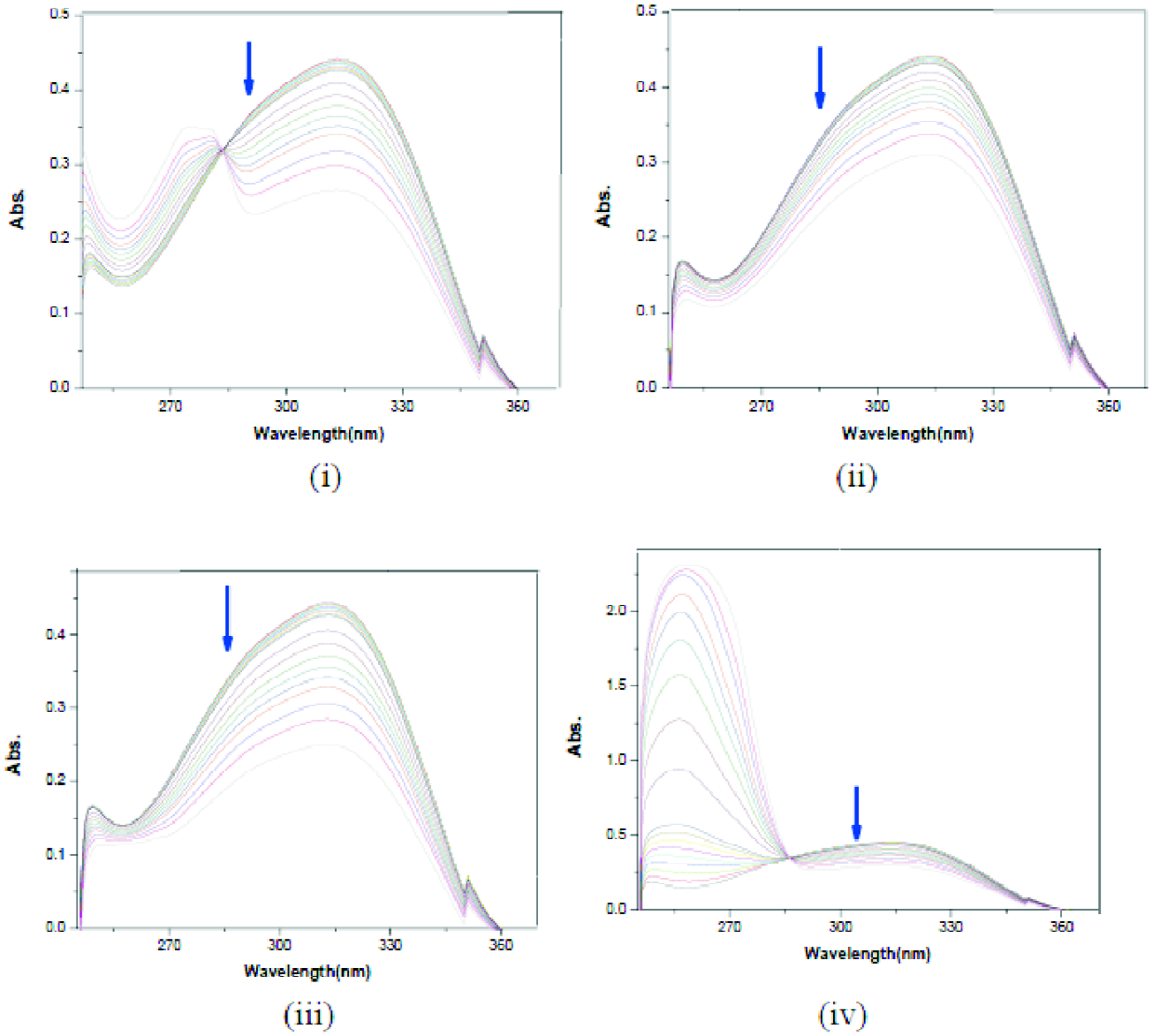


Fig. 3. Titration spectra obtained by UV-Vis of **1** with (i) benzoic acid, (ii) propionic acid, (iii) phenyl acetic acid and (iv) *p*-anisic acid.

Table 1. Binding constants [K_a (M^{-1})][a] at 25°C of host molecules with different monocarboxylic acids by UV-Vis analytical method

Receptors / Guest	**1**	**2**	**3**	**4**
Benzoic acid	$3.4x10^3$	$2.8x10^3$	$5.7x10^3$	$3.2x10^3$
Phenyl acetic acid	$3.9x10^2$	$3.8x10^2$	$4.2x10^2$	$2.9x10^2$
Propionic acid	$2.5x10^3$	$1.9x10^3$	$4.6x10^3$	$2.8x10^3$
p-Anisic acid	$1.7x10^2$	$1.1x10^2$	$2.9x10^2$	$1.5x10^2$

[a]All the errors are ±15%.

ing graph the break at around 1 also reveals the 1:1 binding mode of receptors and the guest monocarboxylic acids (Fig. 4).

Fluorescence studies have also been carried out in the cases of all the receptors with monocarboxylic acids. 2 mL solution of the receptor was taken in the fluorescence cell and the guest solutions were added gradually with the help of a micropipette. Fluorescence spectra were recorded for

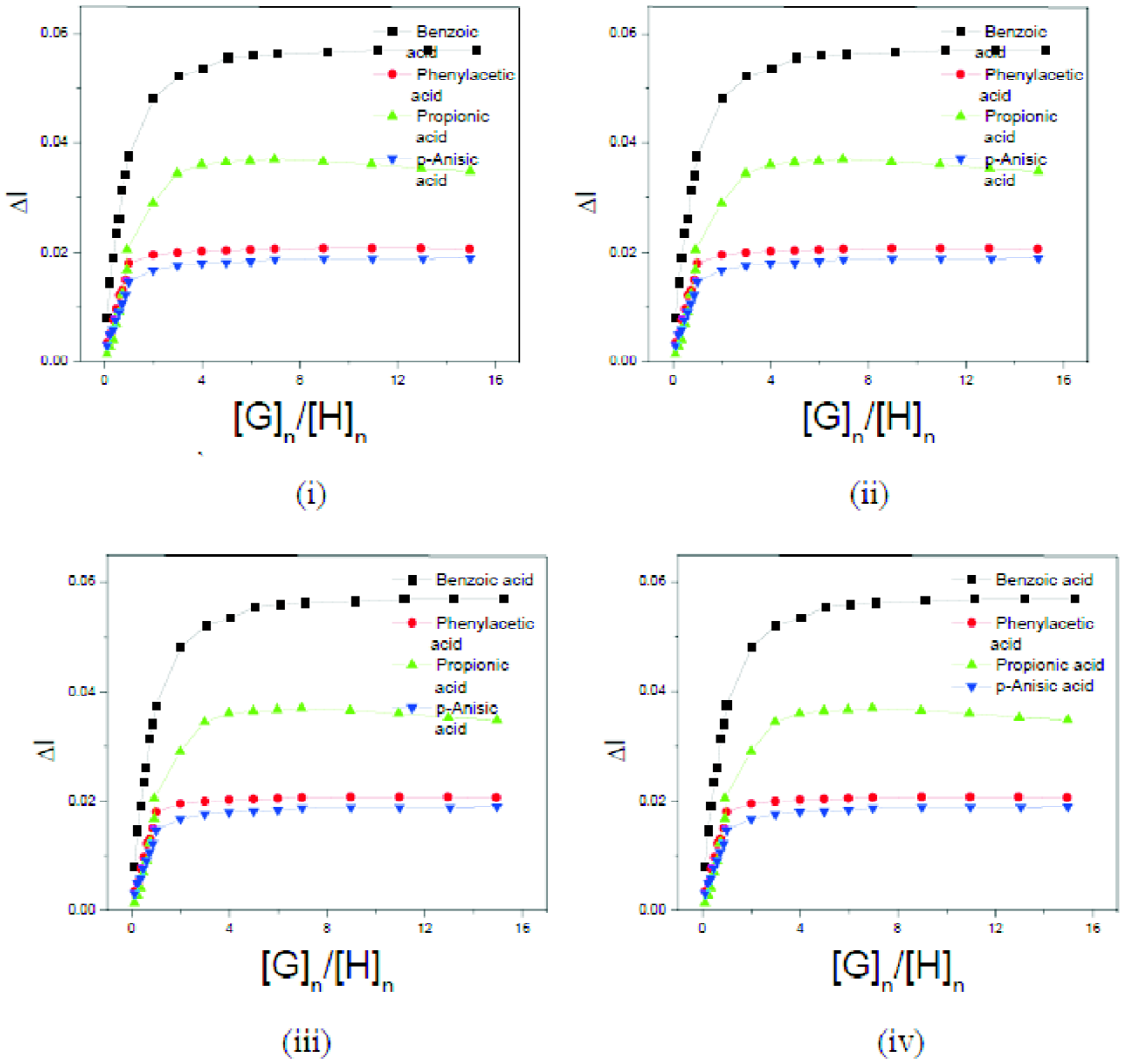


Fig. 4. Binding graph of sensor **1** with (i) benzoic acid, (ii) phenyl acetic acid, (iii) propionic acid and (iv) *p*-anisic acid.

each case. From these series of spectra, for each titration process binding constant values and binding graphs were determined. The titration spectra of receptor **1** have been depicted in Fig. 6.

Fig. 6 depicts the lowering of fluorescence intensity which may be due to some conformational changes (Scheme 1) of the receptor **1** upon gradual addition of guest. The binding phenomena is affected by the occurrence of two tautomeric

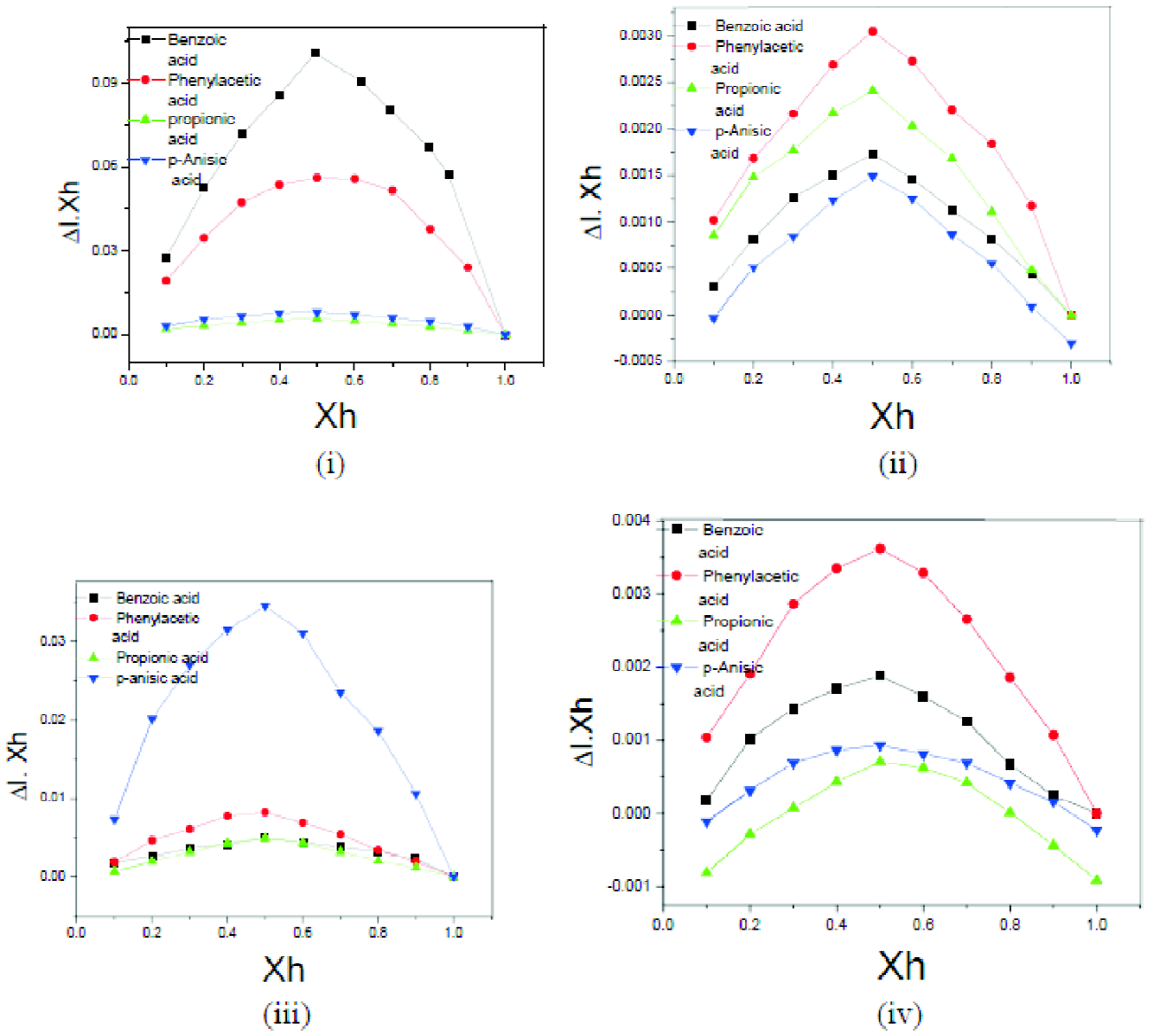


Fig. 5. Job plot of receptor **1, 2, 3** and **4** with benzoic acid, phenyl acetic acid, propionic acid and *p*-anisic acid is depicted in (i), (ii), (iii) and (iv) respectively.

forms of the hosts in presence of the guests which is also supported by the calculated binding constant values (Tables 1 and 2).

From the pK_a values (Table 3) it is clear that benzoic acid is the strongest of all the acids concerned. Normally imidazole or substituted imidazoles behave as mild base. According to the acid-base theory benzoic acid should interact with the receptor more firmly which is also reflected from the binding constant values (Tables 1 and 2).

Table 2. Binding constants [K_a (M^{-1})][a] at 25°C of all the receptors with monocarboxylic acids by fluorescence method

Guests \ Receptors	**1**	**2**	**3**	**4**
Benzoic acid	$3.9x10^3$	$2.1x10^3$	$5.1x10^3$	$3.7x10^3$
Phenyl acetic acid	$3.1x10^2$	$3.3x10^2$	$4.9x10^2$	$2.4x10^2$
Propionic acid	$2.6x10^3$	$1.6x10^3$	$4.9x10^3$	$2.7x10^3$
p-Anisic acid	$1.9x10^2$	$1.4x10^2$	$2.4x10^2$	$1.7x10^2$

[a]All the errors are ±15%.

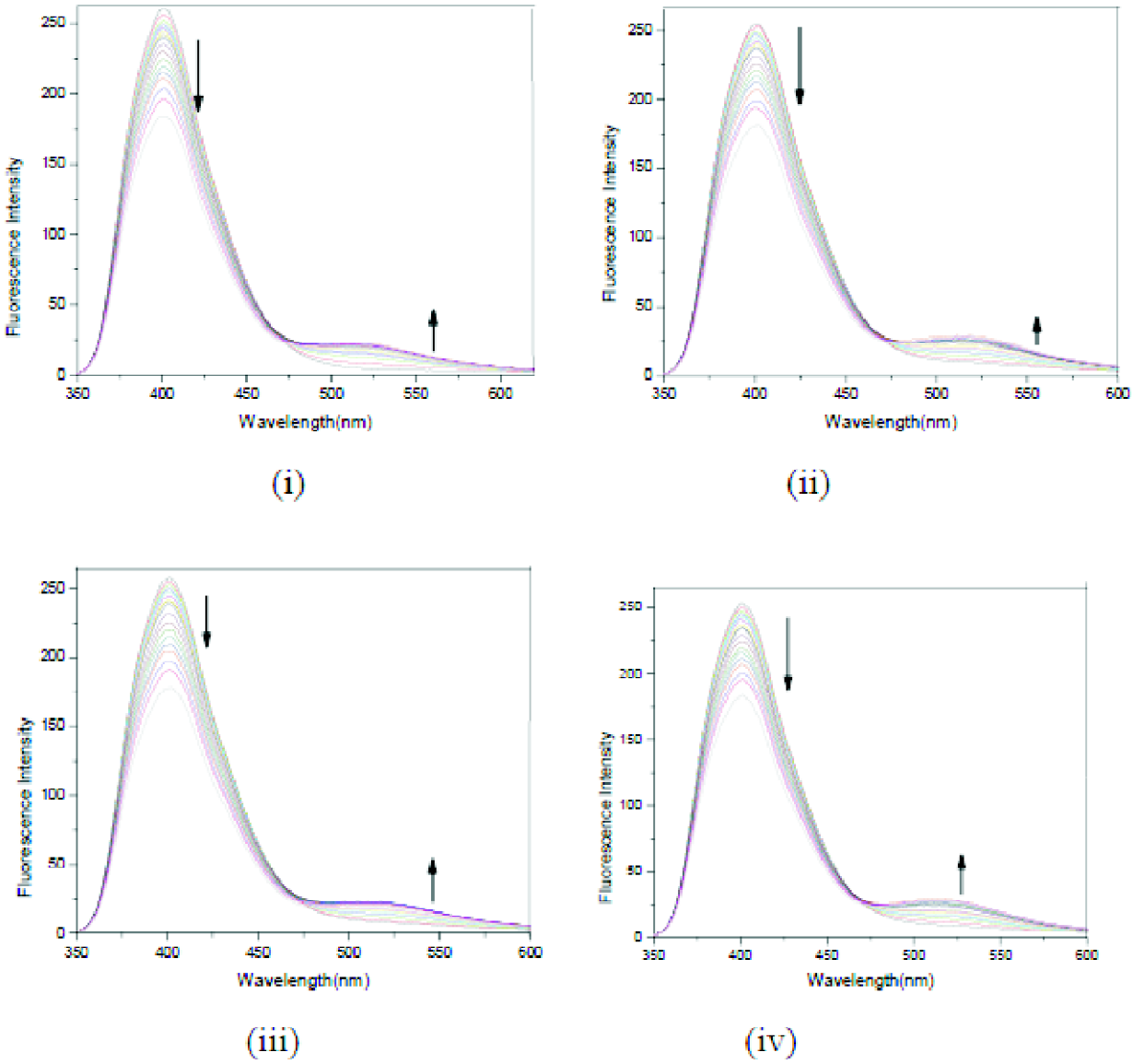


Fig. 6. Fluorescence titration spectra of receptor **1** with (i) benzoic acid, (ii) propionic acid, (iii) phenyl acetic acid and (iv) *p*-anisic acid (excitation wavelength 310 nm).

Table 3. pK_a values of different carboxylic acids under study

Guests	Benzoic acid	Phenyl acetic acid	Propionic acid	*p*-Anisic acid
pK_a	4.20	4.55	4.88	4.50

Fig. 7 represents the study of host-guest complexation between receptor **1** and benzoic acid in DMSO-d_6 solvent in 400 MHz. In the combined spectra "**a**" stands for ^{1}H NMR spectra of pure receptor **1**. On the other hand "**b**", "**c**", and

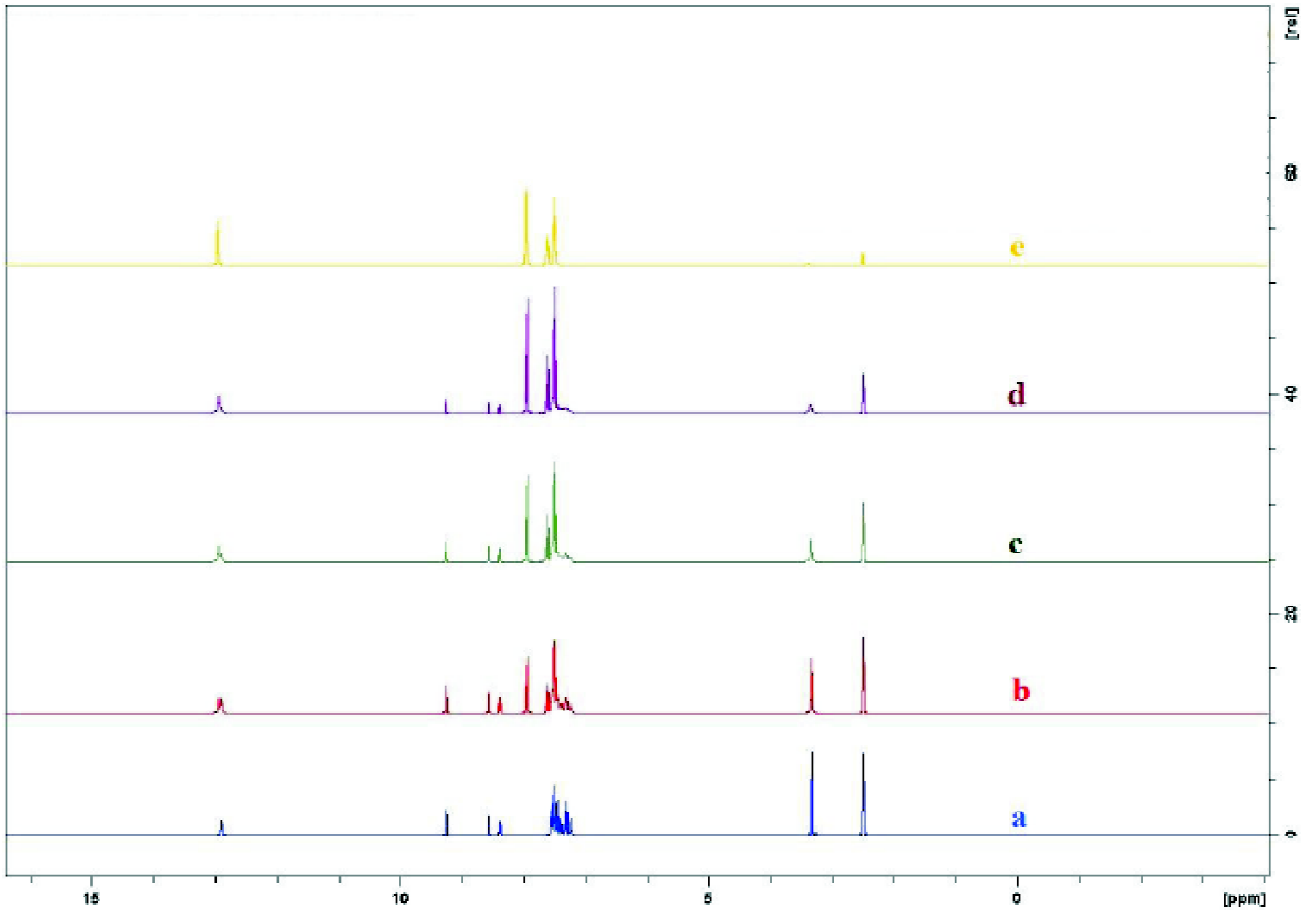


Fig. 7. ^{1}H NMR (400 MHZ) study of receptor **1** with benzoic acid in DMSO-d_6 (**a**: receptor **1**; **b**,**c**,**d**: receptor **1** with benzoic acid; **e**: benzoic acid).

"**d**" represent the ^{1}H NMR spectra on successive addition of benzoic acid into the receptor **1** and "**e**" denotes the spectra of pure benzoic acid.

Fig. 8 represents the partial ^{1}H NMR spectra for the complexation of receptor **1** and benzoic acid. ^{1}H NMR (400 MHz) study of receptor **1** (Fig. 8, a) with benzoic acid (Fig. 8, e) also indicates the binding phenomena. The downfield shift of imidazole -NH proton observed upon gradual addition of benzoic acid in DMSO-d_6 solvent. This indicates the binding of host, receptor **1** with guest benzoic acid.

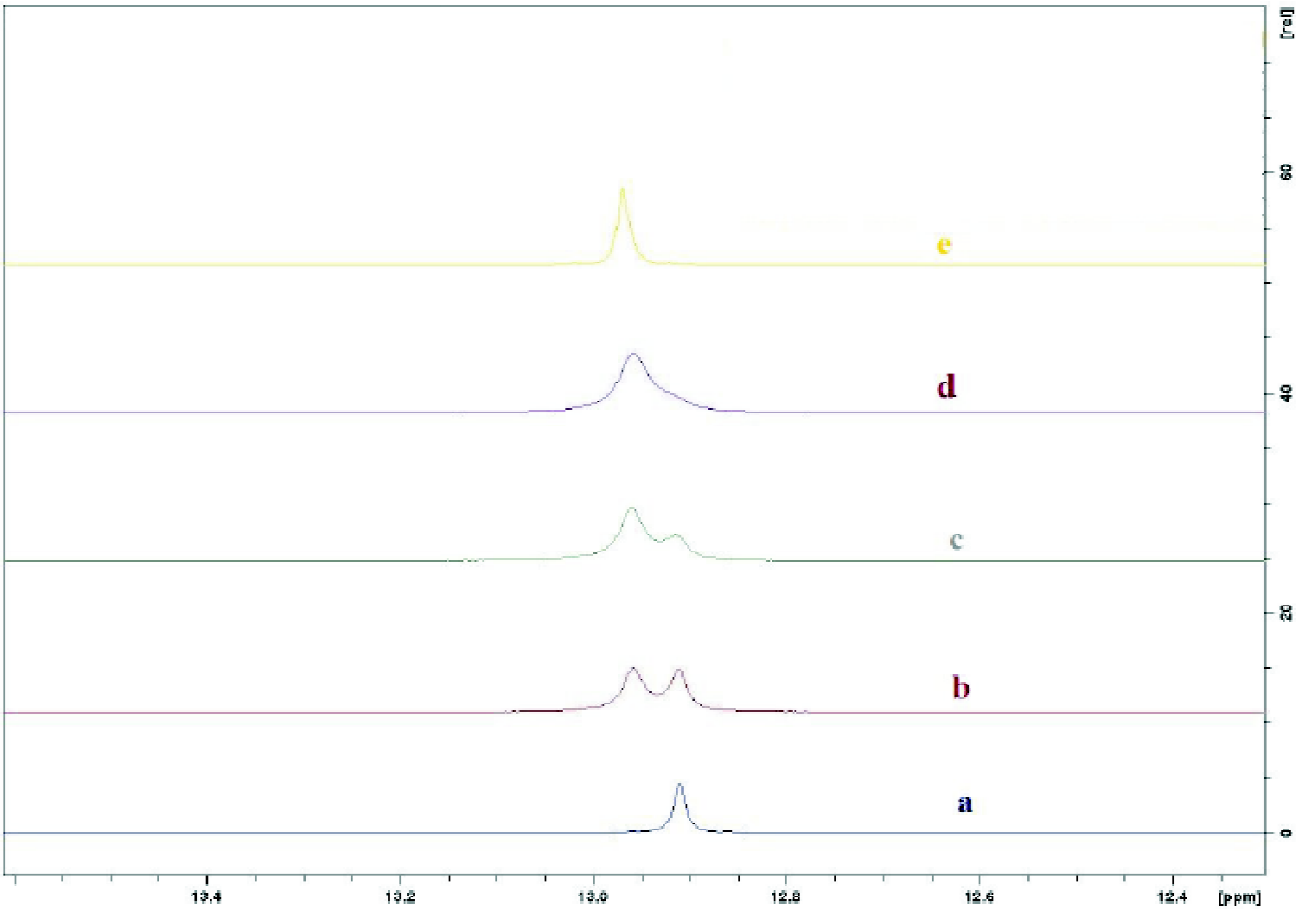


Fig. 8. Partial ^{1}H NMR (400 MHz) study of receptor **1** with benzoic acid in DMSO-d_6 (**a**: receptor **1**; **b**,**c**,**d**: receptor **1** with benzoic acid; **e**: benzoic acid).

Conclusion

From the binding studies, it can be concluded that imidazole moiety containing pyridyl group is another very important motif for the recognition of mono carboxylic acids. Among all the acids, benzoic acid shows higher association constant values. The binding phenomenon is established through UV-Vis, fluorescence and ^{1}H NMR studies.

Acknowledgement

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