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Design and synthesis of a unique ditopic macrocyclic fluorescent receptor containing furan ring as a spacer for the recognition of dicarboxylic acids

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ABSTRACT

A macrocyclic fluorescent receptor was designed and synthesised and the binding study with three different types of dicarboxylic acids was performed with the receptor being found to have appreciable association constants. Downfield shifts of specific amide protons in 1:1 binding by ^{1}H NMR and the quenching in the fluorescence spectra reveal strong binding and thus unambiguously support the complexation of the receptor **1** with dicarboxylic acids.

1. Introduction

The development of artificial receptors for the detection of biologically and environmentally important substrates like carboxylic acids and carboxylate anion is an important topic in molecular recognition research and such receptors have received considerable attention in supramolecular chemistry.[1] During the last decade, substantial improvement has been made for the recognition of carboxylic acids by a number of synthetic receptors of various architectures. The design of synthetic receptors for neutral molecules involves π–π stacking and hydrogen-bonding interactions between the host and guest.[2] According to their strength and directional nature compared to other intermolecular non-covalent interactions,[3] hydrogen bonds are the most important and are extremely useful to design the structure of molecular crystals. It is worth mentioning that the stability of supramolecular structure can be enhanced by an entropy effect, if additional binding sites are present in the host molecules.[4] Synthetic receptors for monocarboxylic acids and highly selective chiral terpyridine macrocyclic fluorescent sensors have already been reported for the recognition of amino acids and its derivatives.[5,6] Like monocarboxylic acids, di and tricarboxylic acids are also biologically important and their recognition is of contemporary interest among the supramolecular community. The receptors, where 2-aminopyridine derivatives were linked to an isophthalic acid spacer with wide range applications were reported to bind both mono and dicarboxylic acids.[7] A common strategy was applied to design receptors of dicarboxylic acid as well as some biologically active molecules that involved linking two aminopyridine groups through the spacer.[8,9] Photoinduced electron transfer (PET) chemosensors possessing two binding sites were also reported for the recognition of anions like dicarboxylates and pyrophosphate.[10]

Previously, we have successfully applied the Troger's base spacer and also an azo-linked photo responsive spacer using pyridine amides for the chain length selection of dicarboxylic acids.[11] A complete study with discrimination of aromatic dicarboxylic acids over aliphatic dicarboxylic acids in the recognition process of several macrocyclic receptors has also been accomplished previously in our laboratory. We therefore targeted the synthesis of a distinctive macrocyclic receptor to recognise three different types of dicarboxylic acids as well as to selectively choose the chain length. Based on hydrophobic, hydrogen bonding and π-stacking interactions, the designed receptor for neutral molecules is able to complex with the complementary partner.

Such interesting features of carboxylic acid functionality have manifold applications in supramolecular chemistry. For example, being a useful hydrogen-bonding synthon, carboxylic acid has been significantly exploited in generating solid-state supramolecular structures with different architectures.

2. Results and discussion

Macrocyclic molecular receptors, which are formed by cyclic arrays having naphthalene rings, are of interest since they can form

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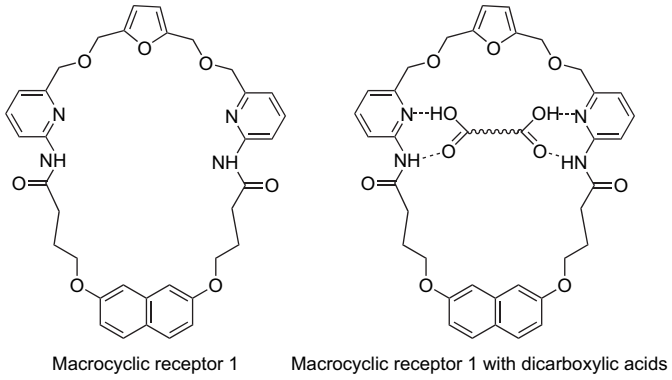
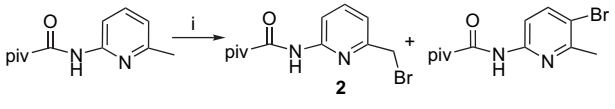


Figure 1. Receptor **1** and its possible complex structure with dicarboxylic acids.

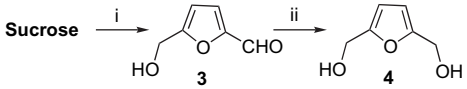
deep, electron-rich cavities. Furthermore, as Glass et al.[12] have recently shown, the fluorescence properties of a naphthalene core can allow the sensitive detection of complexes formed between the guest molecules and such naphthalene ring based receptors.[13] Our particular interest has been in designing new receptors, which could be effective hosts for the recognition of dicarboxylic acids. The designed neutral fluorescent macrocyclic receptor **1** has two pyridyl amide moieties as hydrogen-bonding (HB) points and a naphthalene moiety to encircle the dicarboxylic acids by combined hydrogen bonding to acid carbonyl (HB acceptor) as well as its two NH atoms (HB donor) (Fig. 1). It was also designed on the basis of complementarity between the host and guest involving hydrogen bonding and stacking interactions for specific recognition of aliphatic, aromatic and unsaturated dicarboxylic acids to examine the possible higher association with all types of dicarboxylic acids employing effective multiple points for hydrogen bonding. The incorporation of the fluorescent chromophore naphthalene in receptor **1** was intended to allow possible π-stacking with aromatic dicarboxylic acids.

2.1. Synthesis of the macrocyclic receptor 1

N-(6-Bromomethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (**2**) has been photochemically synthesised in our laboratory using NBS in the presence of a catalytic amount of AIBN refluxing in dry CCl_4. 5-Hydroxymethyl-furan-2-carbaldehyde (**3**) was obtained from sucrose by the reported procedure with the use of I_2 in refluxing dry DMF.[14] Compound **4**, which was prepared by the reduction of compound **3** with $NaBH_4$ in ethanol, was coupled with compound **2** in the presence of NaH using dry THF as solvent under N_2 atmosphere to afford compound **5**. Under refluxing conditions, compound **5** was hydrolysed with 4 M KOH (H_2O–EtOH, 1:1) to give diamino compound **6**. The diamino compound **6** and the diacid chloride of **7** were then coupled using high dilution condition under N_2 atmosphere to obtain the macrocyclic receptor **1** (Schemes 1–4).



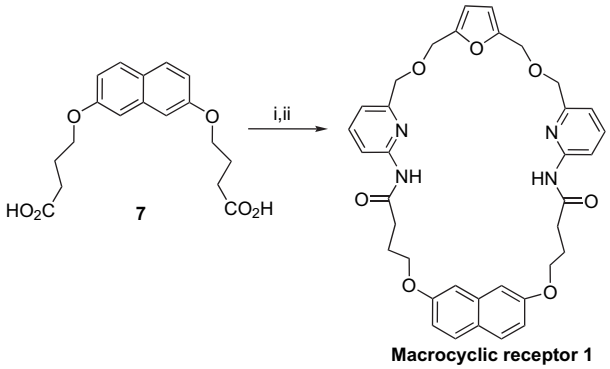
Scheme 1. Reagents and conditions: (i) NBS, AIBN, hν, CCl_4, reflux, 6 h, 60%.



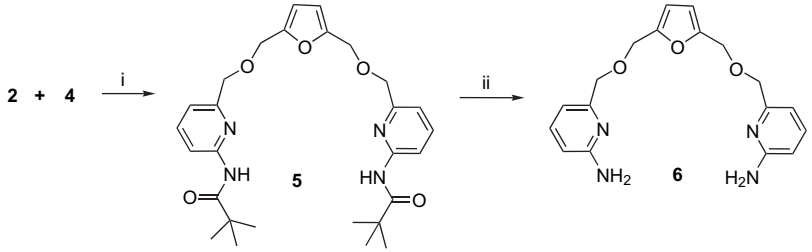
Scheme 2. Reagents and conditions: (i) I_2, DMF, 140 °C, 56%; (ii) $NaBH_4$, EtOH, rt, 12 h, 78%.

2.2. Complexation studies by PCMODEL program

The energy minimisation[15] predicts the stable geometry of the molecule and depending on the electron environment of the receptors and the guests, the geometries of the complexes are found to be different in different complexes. The hydrogen-bonding points are well established in a concave manner (in–in) out of the three possible conformations in–in, in–out, out–out with comparable energy values in MMX energy calculations. The two pyridine rings in the receptor **1** lie in parallel planes to each other, but twisted in the *anti* direction. The distances between the two pyridine ring nitrogens and the two-amide protons are 9.16 Å and 7.91 Å, respectively. The lengths between the two carboxyl moieties in terephthalic acid and isophthalic acid are 5.68 Å and 5.03 Å, respectively. So these two acids can easily be incorporated into the cavity of the receptor **1**. Among these two acids, terephthalic acid might be expected to make a tighter complex with a higher association constant as it has the optimum fitting length. The size and length of 1,4-phenylenediacetic acid is significantly larger, implying it should exhibit a lower association constant. The calculated values of stabilization energy,[15] of the receptor **1** with the acids are reported in the Supplementary data, and the mentioned acids have shown the lowest stabilisation energy. However, on complexation with the carboxylic acids all hydrogen-bonding groups become



Scheme 4. Reagents and conditions: (i) Oxalyl dichloride, DMF (one drop), dry CH_2Cl_2, rt, 4 h; (ii) compound **6**, Et_3N, dry CH_2Cl_2, rt, high dilution, 12%.



Scheme 3. Reagents and conditions: (i) NaH, dry THF, rt, 12 h, 70%; (ii) 4 M KOH in 1:1 EtOH and H_2O, 6 h, 95%.

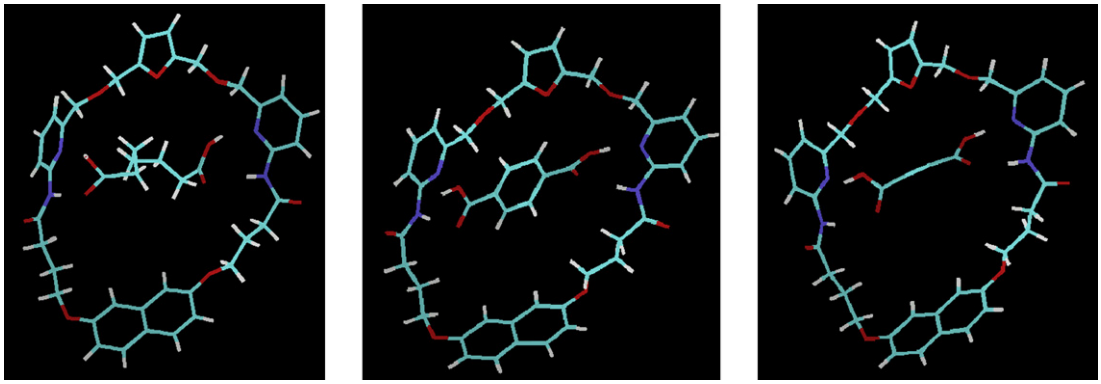


Figure 2. Energy minimised complex structures of receptor **1** with pimelic, terephthalic and acetylenedicarboxylic acids.

properly arranged to make a stable intermolecular complex. The alignments of the π-stacking interaction between the aromatic carboxylic acids with receptor **1** are realised from the docking structures of the receptor–substrate complex (Fig. 2).

2.3. Complexation (1:1) studies in ^{1}H NMR

The ^{1}H NMR spectra of receptor **1** in $CDCl_3$ and 1:1 NMR of the complex with the corresponding acids in 2% DMSO-d_6 in $CDCl_3$ are also reported. The receptor is freely soluble in $CDCl_3$. To solubilise the acids freely and to make the homogeneity in complex's solution we used 2% DMSO-d_6 in all the cases. The amide proton was only displaced towards downfield from its position by 0.06 ppm in 2% DMSO-d_6 in $CDCl_3$ compared to $CDCl_3$ itself. A significant downfield chemical shift of amide proton and *peri* protons of naphthalene ring of receptor **1** was caused by all nine dicarboxylic acids.

Among the three aliphatic dicarboxylic acids, adipic, pimelic and suberic acids, pimelic acid on complexation with receptor **1** shows a larger downfield shift of the amide proton from δ 8.05 ppm to δ 9.41 ppm ($\Delta\delta$ 1.36 ppm) (Fig. 3). The other two acids caused downfield shifts of $\Delta\delta$ 1.10 ppm and $\Delta\delta$ 1.13 ppm, respectively.

The chemical shift of the amide proton in receptor **1** on complexation with terephthalic acid is less than that with 1,4-phenylenediacetic acid ($\Delta\delta$ 1.32 ppm and $\Delta\delta$ 1.45 ppm, respectively). With isophthalic acid the amide proton undergoes a downfield shift ($\Delta\delta$ 0.65 ppm) on complexation. In all the cases, the *peri* protons of the naphthalene ring are also significantly shifted towards downfield on complexation with acids. Significant downfield shifts of the amides and *peri* protons in all cases and the appearance of methylene protons of the guest acids in the spectra are conclusive for the desired complexation. Chemical shifts on complexation of the amide proton of receptor **1** with dicarboxylic acids are summarised in Supplementary data.

The hydroxyl group (in cis form) in maleic acid is intramolecularly hydrogen-bonded with the carboxyl oxygen of another acid group so that the first acidity constant (pK_{a1}=1.9) is more than fumaric acid (pK_{a1}=3.5) that has the two acid groups in the *anti* positions. A different ^{1}H NMR spectrum is identified in the case of fumaric acid on complexation with receptor **1**. The amide protons of receptor **1** appear at two positions, δ 9.47 ppm and δ 9.43 ppm. This indicates that the environments of the two-amide protons are not the same on complexation with fumaric acid. But no extra amide peak is observed in case of the maleic acid complex. Acetylenedicarboxylic acid is a straight chain (sp-hybridised) dicarboxylic acid and shows a downfield δ-shift (from δ 8.05 ppm to δ 9.50 ppm; $\Delta\delta$=1.45 ppm).

2.4. Complexation studies by UV–vis and fluorescence methods and determination of association constants (K_a)

Receptor **1** has absorbance maxima in its UV–vis spectrum at λ_{max}=240 nm and 279 nm in chloroform. In all the cases, a continuous decrease of absorbance is observed on addition of the guest solution (Fig. 4). Here it is to be noted that all dicarboxylic acid guests are dissolved in 1% DMSO in chloroform. This change in UV–vis spectrum could conveniently be used for binding constant calculation, since the lower concentration gives rise to more accurate determination of the value of the association constant of the acids.

Wavelength at 279 nm (λ_{max}) has been selected as the excitation wavelength for all the fluorescence studies. Performing the study, we have achieved an excited state spectrum showing maxima at λ_{max}=345 nm in chloroform. The receptor showed quenching at λ_{max}=345 nm (Fig. 5). Among the six aliphatic dicarboxylic acids [$(CH_2)n$, n=2–6], the maximum association constant was observed for pimelic acid [$(CH_2)n$, n=5]. Adipic and suberic acids have association constant values somewhat less than pimelic acid (Table 1). The association constants are evaluated by a similar method in $CHCl_3$. So according to the chain length and size, among these aliphatic dicarboxylic acids, pimelic acid is found to be best fit for the incorporation into the cavity of the receptor **1**. Though the

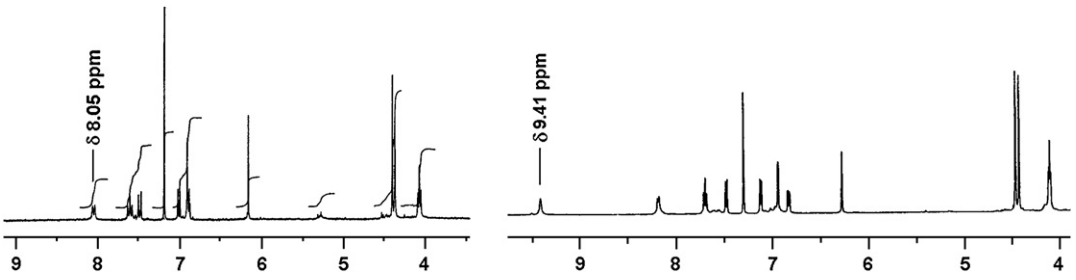


Figure 3. One representative partial ^{1}H NMR spectra of receptor **1** and its complex with pimelic acid in $CDCl_3$ and 2% DMSO-d_6 in $CDCl_3$, respectively.

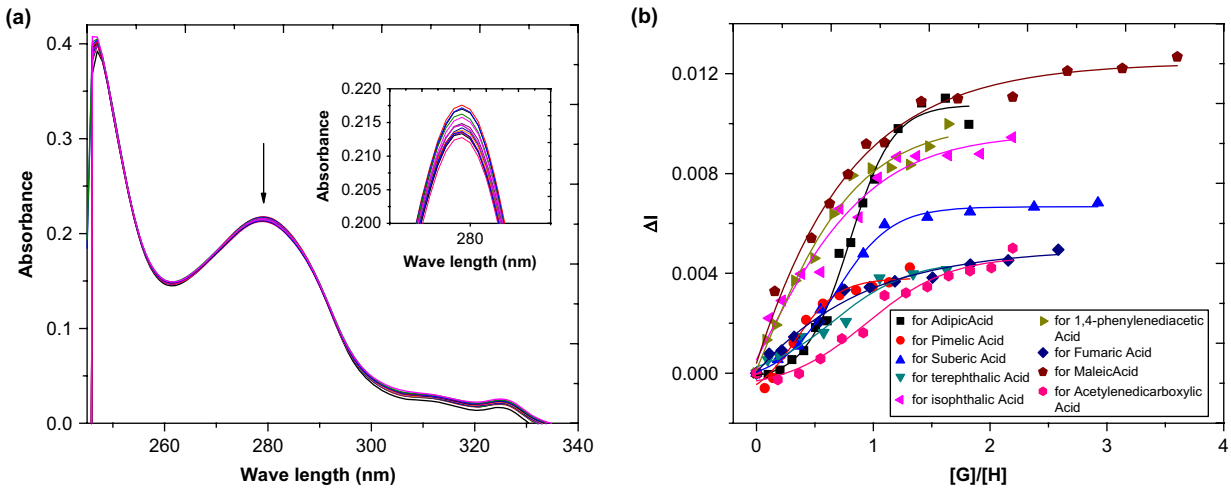


Figure 4. (a) Titration spectra of receptor **1** with pimelic acid and (b) titration curve of receptor **1** with dicarboxylic acids by UV-vis technique. Inset: expanded area (270 nm–290 nm).

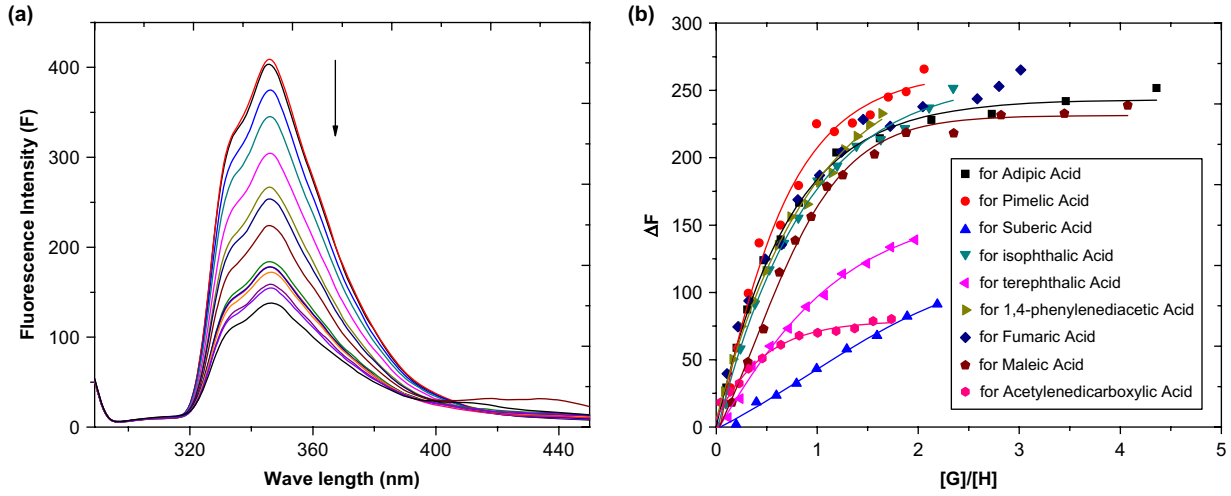


Figure 5. (a) Titration spectra of receptor **1** with pimelic acid and (b) titration curve of receptor **1** with dicarboxylic acids by fluorescence technique.

spacer in aliphatic dicarboxylic acids is flexible, chain length selectivity can thus be observed.

Though the edge-face π-stacking interaction is a common factor for the three common aromatic acids like isophthalic, terephthalic and 1,4-phenylenediacetic acids, the geometry of the acid groups, steric factor and also the length cause differences in association. Both terephthalic and 1,4-phenylenediacetic acids have the two acid groups straight, but there is an angle (120°) between the two acid groups in isophthalic acid, which may cause it to have a lower binding constant. No geometrical problem has been indicated for the first two acids and the cavity size, almost significant to accommodate terephthalic acid, is not big enough for 1,4-phenylenediacetic acid. When the same receptor's solution was excited at 279 nm, we got similar spectra with regular quenching of the fluorescence intensity (λ_{max}=345 nm). But overall association constant values of terephthalic acid are higher compared to the other aromatic dicarboxylic acids.

A similar result with the aromatic acids was obtained with regular quenching (λ_{max}=345 nm). Among the three acids, acetylenedicarboxylic acid possesses the highest association constant (K_a) values, which may be due to the strongest acidity of CO_2H group (sp-hybrid acetylenic carbon is more electronegative than sp^2 carbon in fumaric or maleic acid).

The macrocyclic receptor **1** contains one heterocycle furan ring and one naphthalene ring opposite to each other. So there may be some possibility of π-stacking interaction of the guest aromatic acids with naphthalene, which will help increasing the binding constant of aromatic acids. The binding of isophthalic, terephthalic and 1,4-phenylenediacetic acids with receptor **1** has been studied and indicated more selectivity towards terephthalic acid [K_a=1.1×10^5 M^{-1} (UV-vis) and 1.8×10^5 M^{-1} (fluorescence)]. Among the three aliphatic dicarboxylic acids, pimelic acid binds with higher affinity [K_a=4.1×10^4 M^{-1} (UV-vis) and 1.4×10^5 M^{-1}

Table 1
Calculation of the association constant (K_a ±5–8%) values by UV-vis and fluorescence methods

Entry	Guest (dicarboxylic acid)	UV–vis method (K_a, M^{-1})	Fluorescence method (K_a, M^{-1})
1.	Adipic acid	1.4×10^4	1.3×10^5
2.	Pimelic acid	4.1×10^4	1.4×10^5
3.	Suberic acid	1.2×10^4	3.1×10^4
4.	Isophthalic acid	5.4×10^4	1.4×10^5
5.	Terephthalic acid	1.1×10^5	1.8×10^5
6.	1,4-Phenylenediacetic acid	3.9×10^4	1.3×10^4
7.	Fumaric acid	6.2×10^4	2.8×10^5
8.	Maleic acid	9.7×10^3	1.7×10^4
9.	Acetylenedicarboxylic acid	8.7×10^4	5.7×10^5

(fluorescence)], which proves that the chain length of pimelic acid is optimum, corresponding to that of the spacer for the above-mentioned receptor. Acetylenedicarboxylic acid shows strong binding [K_a=8.7×10^4 M^{-1} (UV-vis) and 5.7×10^5 M^{-1} (fluorescence)] than the other two unsaturated acids.

The sigmoidal plots of [*G*]/[*H*] versus Δ*I* in UV-vis and [*G*]/[*H*] versus Δ*F* in fluorescence reveal the 1:1 complexation and linear fit plots of 1/[*G*] versus I_0/Δ*I* in UV-vis and 1/[*G*] versus F_0/Δ*F* in fluorescence help calculating the binding constant values. The binding constant calculations of macrocyclic receptor **1** with the mentioned dicarboxylic acids were performed at λ_{max}=279 nm (in UV) and at λ_{max}=345 nm (in fluorescence).[16]

3. Conclusion

Macrocyclic receptor **1** binds three different types of acids with considerable association constants. Shifting of the NH protons in 1:1 ^{1}H NMR and the quenching of the fluorescence intensity in the excited state unambiguously concluded complexation with the acids. Terephthalic acid shows higher affinity towards receptor **1** among all nine acids. Though the selectivity towards pimelic acid is the unique feature of this type of receptors where furan moiety is used instead of conventional aromatic moiety. The receptor **1** is therefore, an interesting design for complexation with the dicarboxylic acids, which showed interesting physico-chemical behaviour.

4. Experimental

4.1. General

Melting points (mp) were recorded on an A. D. and Co. hot-coil stage melting point apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ unless otherwise mentioned with TMS as the internal standard with either Bruker AM 500 MHz or 400 MHz or 300 MHz NMR instruments. Chemical shifts are given in δ (ppm) scale and *J* values in Hertz. IR spectra were measured in KBr disk with a JASCO FT/IR-460 plus spectrometer. UV–vis and fluorescence spectra were recorded on a JASCO V-530 and Perkin Elmer LS-55, respectively. HRMS of the macrocyclic receptor **1** was recorded on a Qtof Micro YA263 instrument. LC–MS of the compounds was recorded on ABI-Q-Trap (ABI-Applied Bioscience). All solvents were dried prior to use by common methods. Silica gel (60–120 and 100–200 mesh) was used for all chromatographic purifications. For preparative thin layer chromatographic (PTLC) purification, the layer was formed on a glass plate using water gel-GF 254 silica gel. Starting materials were either commercially available (purchased from Fluka and Aldrich) or synthesised according to the cited literature procedures. All the reactions were carried out under nitrogen atmosphere in anhydrous solvents.

4.2. General procedure for UV–vis titration

Stock solution of receptor **1** was prepared at a concentration of ca. 1×10^{-5} mol/mL in $CHCl_3$. Acids were dissolved in 1% DMSO in $CHCl_3$ in ca. 1×10^{-4} mol/dm^3 concentration. DMSO (1%) was added to make a homogeneous solution. Then the guest solution was added to the receptor solution (taking 2.0 mL in the UV-cell) and continuous decreases of absorbance in UV spectra were recorded each time.

4.3. Fluorescence titration and binding study

Receptor **1** (0.7 mg, 4.40252×10^{-5} mmol/mL) was dissolved in dry chloroform (25.0 mL) in a volumetric flask. Then the solution was diluted 10 times to 4.40252×10^{-6} mmol/mL. Taking 2.0 mL portions from this solution, initially the fluorescence spectra were recorded. Then adding the guest solutions (dissolved in different amounts of acids in 1% DMSO–$CHCl_3$ to form solutions of concentrations of ca. 1×10^{-5}) fluorescence titration was carried out for each time for all the guests.

4.4. *N*-(6-Bromomethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (2)

2,2-Dimethyl-*N*-(6-methyl-pyridin-2-yl)-propionamide (1.0 g, 5.20 mmol) was taken in dry CCl_4 (50.0 mL). Then AIBN (0.20 g, 1.2 mmol) was added as a radical initiator and the solvent was refluxed for 30 min in the presence of 60 W lamp. Recrystallised NBS (0.95 g, 5.20 mmol) was added to the refluxing solution. Then the solution turned brown and the whole system was refluxed for 6 h. After usual work-up the compound was isolated as a brown semi-solid (yield 60%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.16 (d, 1H, *J*=8.2 Hz), 8.02 (br s, 1H), 7.66 (t, 1H, *J*=7.9 Hz), 7.12 (d, 1H, *J*=7.7 Hz), 4.46 (s, 2H), 1.30 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.2, 154.7, 151.3, 139.3, 119.0, 113.3, 39.7, 33.1, 27.3.

LC–MS (*m*/*z*, %): 273.1 (M+2, 100), 271.1 (M$^+$, 90), 255.2 (20), 199.1 (30), 192.2 (15).

4.5. 5-Hydroxymethyl-furan-2-carbaldehyde (3)

Iodine (3.50 g, 0.013 mol) dissolved in dry DMF (10.0 mL) was added to a sucrose solution (150.0 g in 200.0 mL dry DMF) of boiling DMF. This was a strongly exothermic reaction and pouring it into ice water immediately quenched the reaction. After cooling, the mixture was extracted with ethyl acetate continuously several times and dried over sodium sulfate to afford a blackish liquid product (yield 56%).[14]

^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.55 (s, 1H), 7.23 (d, 1H, *J*=3.5 Hz), 6.52 (d, 1H, *J*=3.5 Hz), 4.70 (s, 2H), 3.31 (br s, 1H).

4.6. (5-Hydroxymethyl-furan-2-yl)-methanol (4)

5-Hydroxymethyl-2-furfural **1** (2.50 g, 0.19 mmol) was taken in a round-bottomed flask (50.0 mL). Then ethanol (10.0 mL) and sodium borohydride (0.75 g, 0.2 mmol) were added to it and stirred for 12 h. A more polar compound was produced, which did not respond to UV, but absorbed iodine. Maximum product was solidified when it was dipped into ice. The residue was purified through column chromatography (silica gel 100–200 mesh) using 2% methanol in chloroform. An off-white solid material was isolated (1.98 g, yield 78%, mp 76–78 °C).

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.17 (s, 2H), 4.52 (s, 4H), 3.42 (s, 2H).

^{13}C NMR ($CDCl_3$ + 2 drops DMSO-d_6, 100 MHz): δ 130.0, 115.0, 29.5.

LC–MS (*m*/*z*, %): 130.4 (M+2H$^+$, 71), 120.2 (9), 101.0 (67).

4.7. *N*-(6-{5-[6-(2,2-Dimethyl-propionylamino)-pyridin-2-ylmethoxymethyl]-furan-2-ylmethoxymethyl}-pyridin-2-yl)-2,2-dimethyl-propionamide (5)

To a solution of 2,5-dihydroxymethylfuran **4** (260 mg, 2.0 mmol) in dry tetrahydrofuran (8.0 mL), sodium hydride (240 mg; 10.0 mmol) was added and stirred under nitrogen atmosphere for 1 h. The solution of compound **2** in dry THF was added dropwise to the reaction mixture under nitrogen and stirred for 10 h. After completion of the reaction, THF was removed under vacuum and dichloromethane was added to the crude solid. The organic layer was washed with brine solution several times and dried over anhydrous sodium sulfate. Then the solvent was evaporated and the residue was purified by column chromatography (60–120 silica gel)

by using 8% ethyl acetate in petroleum ether (60 °C–80 °C) to yield a brownish material (semi-solid, 710 mg, yield 70%).

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.15 (t, 2H, J=9.1 Hz), 8.00 (br s, 2H), 7.70 (dd, 2H, J=7.8, 7.9 Hz), 7.16 (dd, 2H, J=7.4, 7.4 Hz), 6.31 (s, 2H), 4.62 (s, 4H), 4.55 (s, 4H), 1.25 (s, 18H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 184.6, 155.9, 151.7, 151.3, 139.2, 117.4, 113.1, 110.4, 71.9, 64.7, 38.4, 27.2.

MS (ESI) (m/z, %): 531.2 (M+Na^+, 80), 421.2 (100).

HRMS (ES^+) Calcd for $C_{28}H_{36}N_4O_5Na$ (M+Na^+): 531.2584. Found: 531.2587.

FTIR (KBr, ν_{max}): 2923, 2852, 2360, 1732, 1716, 1698, 1456 cm^{-1}.

4.8. 6-{[(5-{[(6-Amino-2-pyridyl)methoxy]methyl}-2-furyl)methoxy]methyl}-2-pyridinamine (6)

Compound **5** (1.0 g, 1.96 mol) was dissolved in ethanol (5.0 mL) containing aqueous 4 M KOH (5.0 mL). The mixture was refluxed for 6 h. The solvent was removed and water was added to the residue and extracted with ethyl acetate. The organic layer was separated and dried over anhydrous sodium sulfate and evaporated to yield a brownish solid material (640 mg, yield 95%, mp 118 °C).

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41 (t, 2H, J=7.7 Hz), 6.77 (d, 2H, J=7.3 Hz), 6.38 (d, 2H, J=8.1 Hz), 6.30 (s, 2H), 4.54 (s, 4H), 4.48 (s, 4H) (amine proton not observable).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.0, 156.1, 151.8, 138.4, 111.5, 110.3, 107.5, 72.5, 64.6.

LC–MS (m/z, %): 341.2 (M+H^+, 17), 299.4 (11), 217.3 (100), 189.1 (39).

HRMS (ES^+) Calcd for $C_{18}H_{20}N_4O_3Na$ (M+Na^+): 363.1433. Found: 363.1436.

FTIR (KBr, ν_{max}): 2963, 1619, 1466, 1261, 1094, 1020, 799 cm^{-1}.

4.9. Macrocyclic receptor 1

The acid **7** (58 mg, 0.176 mmol) was taken in a round-bottomed flask (25.0 mL) and to this dry dichloromethane (10.0 mL) was added. The system was kept under nitrogen atmosphere. Oxalyl dichloride (0.10 mL) and one drop of dry DMF were added to the above solution. It was stirred for 3 h. The solvent was removed to get the acid dichloride of compound **7** to be used for the next step.

In a two-necked round-bottomed flask fitted with two dropping funnels, dichloromethane (20.0 mL) was taken and the system was kept under nitrogen. Diamine **6** (60 mg, 0.176 mmol) was dissolved in CH_2Cl_2 (10.0 mL). Then the volume was made up with dry dichloromethane (30.0 mL) and to this, triethylamine (0.10 mL) was added and the mixture was taken in a dropping funnel. Acid dichloride of compound **7** was also dissolved in dry dichloromethane (30.0 mL) and taken in another dropping funnel. Both solutions were added dropwise to the two-necked round-bottomed flask for a period of 2 h and stirred continuously for 10 h at room temperature under nitrogen atmosphere. Then the solvent was removed and fresh CH_2Cl_2 was added to the reaction mixture. Washing with saturated sodium bicarbonate solution, the organic layer was dried over anhydrous sodium sulfate. The solvent was then evaporated to dryness and the crude mixture was purified by preparative TLC using 4% methanol in chloroform (off-white solid; yield 12%, 13.4 mg, mp 142–45 °C).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.05 (d, 2H, 2N*H*, J=8.2 Hz), 7.60 (t, 2H, J=7.9 Hz), 7.48 (4H, d, J=9.7 Hz), 7.18 (s, 2H), 7.01 (d, 2H, J=7.1 Hz), 6.89 (d, 2H, J=7.3 Hz), 6.16 (s, 2H), 4.39 (s, 4H), 4.36 (s, 4H), 4.06 (t, 4H, J=5.9 Hz), 2.59–2.55 (m, 4H), 2.21 (t, 4H, J=6.0 Hz).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.5, 157.5, 156.6, 152.1, 150.9, 139.4, 136.1, 129.5, 124.9, 118.0, 116.5, 112.9, 110.9, 106.8, 72.6, 66.8, 64.9, 34.7, 25.3.

MS (FAB) (m/z, %): 659.1 (M+Na^+, 65), 637.2 (M+H^+, 100), 528.2 (35).

HRMS (ES^+) calcd for $C_{36}H_{36}N_4O_7Na$ (M+Na^+): 659.2482. Found: 659.2482.

FTIR (KBr, ν_{max}): 2923, 2360, 1732, 1698, 1634, 1540, 1456, 1210 cm^{-1}.

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Supplementary data

NMR (^{1}H and ^{13}C) spectra, MS-spectra, UV-vis and fluorescence titration spectra of receptor with dicarboxylic acids, titration curves and the association constants calculation curves (both UV-vis and fluorescence method), and energy minimised structures are also available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.04.086.

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