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Ethylene spacer-linked *bis*-acetamidopyridine for dicarboxylic acid recognition and polymeric new wave-like *anti-perpendicular* arrangement of a host–guest in the solid state

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In this paper, 1,2-*bis*(2-acetamido-6-pyridyl)ethane, receptor **1**, having an ethylene spacer is reported to recognise dicarboxylic acids. The binding study in the solution phase is carried out using ^{1}H NMR (1:1) and UV–vis experiments and in the solid phase by single-crystal X-ray analysis. In ^{1}H NMR, the downfield shifts of specific amide protons of receptor **1** in 1:1 complexes of receptor and guest diacids, and in the UV–vis experiment, the appearance of an isosbestic point as well as significant binding constants are observed, which thus unambiguously support the complexation of receptor **1** with dicarboxylic acids in solution. Receptor **2**, simple 2-acetamido-6-methylpyridine, has lower binding constants than receptor **1** due to cooperative binding of two pyridine amide groups with two acid groups of diacids. In the solid phase, the ditopic receptor **1** shows a grid-like polymeric hydrogen-bonded network that changes to a polymeric wave-like 1:1 *anti-perpendicular* network instead of the *syn–syn* polymeric 1:1 (Goswami, S.; Dey, S.; Fun, H.-K.; Anjum, S.; Rahman, A.-U. *Tetrahedron Lett.* **2005**, *46*, 7187–7191), *anti–anti* polymeric 1:1 (Goswami, S.; Jana, S.; Dey, S.; Razak, I.A.; Fun, H.-K. *Supramol. Chem.* **2006**, *18*, 571–574; Goswami, S.; Jana, S.; Fun, H.-K. *Cryst. Eng. Comm.* **2008**, *10*, 507–517; Goswami, S.; Jana, S.; Dey, S.; Sen, D.; Fun, H.-K.; Chantrapromma, S. *Tetrahedron* **2008,** *64*, 6426–6433), *syn–syn* 2:2 (Karle, I.L.; Ranganathan, D.; Haridas, V. *J. Am. Chem. Soc.* **1997**, *119*, 2777–2783) or *top–bottom-bound* 1:1 (Garcia-Tellado, F.; Goswami, S.; Chang, S.K.; Geib, S.J.; Hamilton, A.D. *J. Am. Chem. Soc.* **1990**, *112*, 7393–7394) co-crystals.

Keywords: molecular recognition; supramolecular network; pyridine amide; hydrogen bonding; host–guest

1. Introduction

The recognition of biologically important substrates, e.g. dicarboxylic acids, is one of the most important areas of research in supramolecular chemistry (*1*), as well as in the design of new crystal engineering (*2*). Major efforts have been paid due to its application in pharmaceutical science (*3*) and also in molecular biology (*4*). Receptors for neutral molecules are mainly designed based on the hydrogen bonding donor–acceptor array of the guest–host molecules. Among different functional groups, the amide group is mostly used (*5*, *6*) in the recognition of mono- and dicarboxylic acids owing to its presence in proteins. In this regard, pyridine amides have been widely used for carboxylic acid recognition. However, for dicarboxylic acid recognition, it requires two donor and two acceptor binding sites. One common strategy to design the receptor for dicarboxylic acids is the joining of the two pyridine amides through a proper spacer, and this also has received considerable attention in the molecular recognition research field because spacers have a vital role in the design of various supramolecular constructions (*5a–d*, *g*, *6d–g*). Hamilton et al. have reported that if the spacer length of the binding groups of a receptor and that of the dicarboxylic acid have a close match, a 1:1 complex (*5a*) is formed; however, if they do not match well, an alternative mode of binding is observed in the form of infinite ribbon (*5b*, *c*). For this reason, a terephthaloyl dipicolylamide receptor with adipic acid makes a *top–bottom-bound* 1:1 complex with adipic acid (*5a*), whereas the isopthaloyl dipicolamide forms a ribbon or supramolecular helical structure (*5b*). In another study, they have also showed a polymeric 1:1 binding in the co-crystals with long-chain diacids of different lengths with simple phenyl to a more complex naphthyl, biphenyl and terphenyl spacer of different lengths (*5c*). Ranganathan and co-workers have reported a 2:2 tetramer of succinic acid and receptor when a rigid adamantane spacer is used (*5d*).

In this connection, during the course of our ongoing research on dicarboxylic acid recognition, we have successfully used receptors with fluorescent Troger's base (*6a*) spacer, aza-based (*6c*) photo-responsive spacer and also furan spacer (*6h*). We have also reported ether-based (*6d*) spacer and 3,3′-bipyridine amide-based (*6e*, *f*) receptors for dicarboxylic acids. We, however, found that co-crystal of a flexible ether-linked *bis*-amidopyridine with 1,4-phenylenediacetic acid shows a polymeric *syn–syn* network (Figure 1(c)) in the solid state (*6d*), whereas the 3,3′-bipyridine-type rigid *bis*-amide receptor

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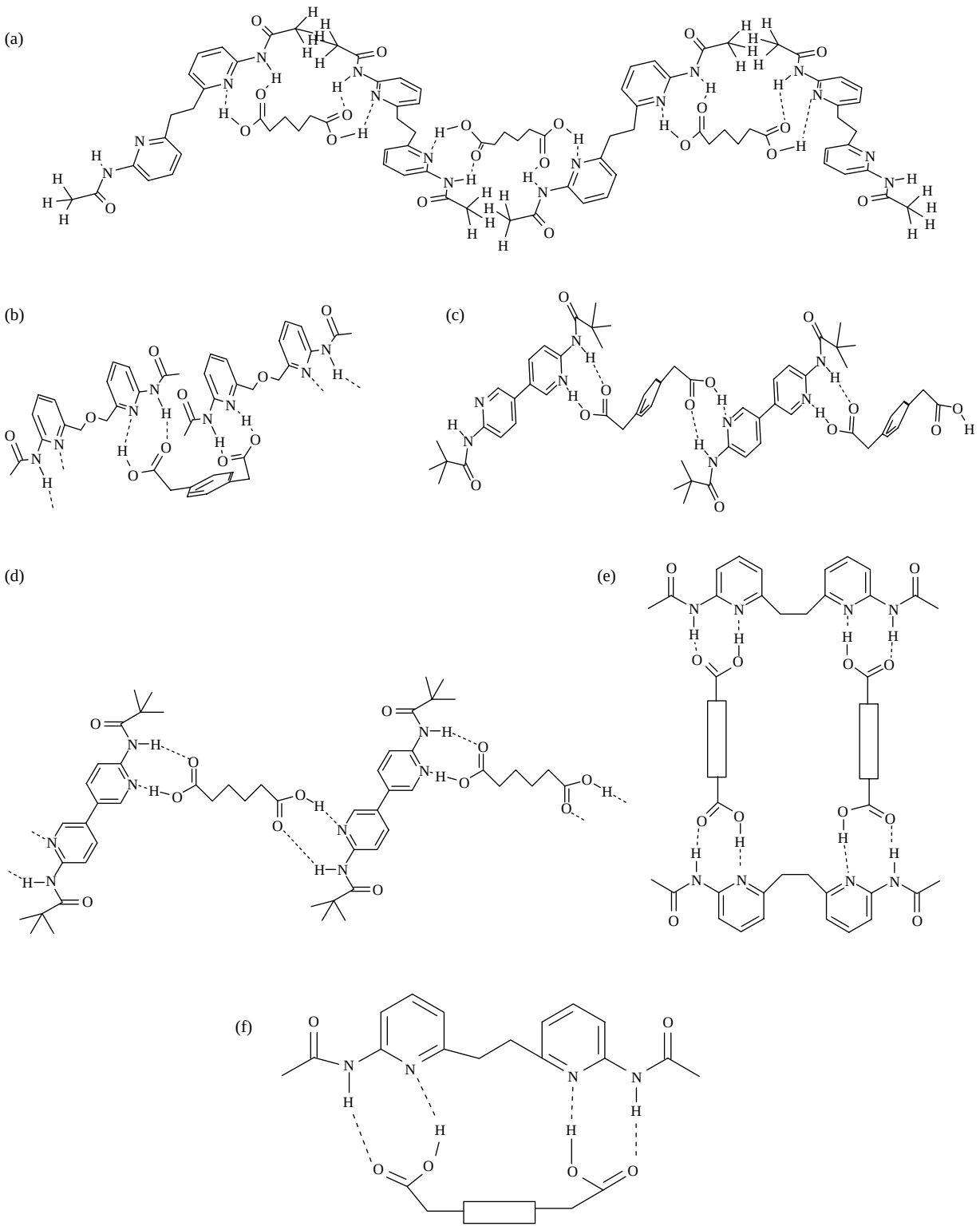


Figure 1. (a) Presentation of a polymeric wave-like *anti-perpendicular* structure of receptor **1** with adipic acid (1:1); (b) *syn–syn* polymeric co-crystal structure of receptor *bis*-2-acetylaminopyridyl-6-methylether with 1,4-phenylenediacetic acid (1:1); (*6d*); (c) *anti–anti* polymeric co-crystal structure of 6,6′-dipivaloylamino-3,3′-bipyridine with 1,4-phenylenediacetic acid (*6e*) (1:1); (d) *anti–anti* polymeric co-crystal structure of receptor **1** with adipic acid (*6f*) (1:1) and (e) hypothetical *syn–syn* tetramer with diacid (2:2) with receptor **1**, (f) hypothetical *syn–syn* dimer with diacid (1:1) with receptor **1**.

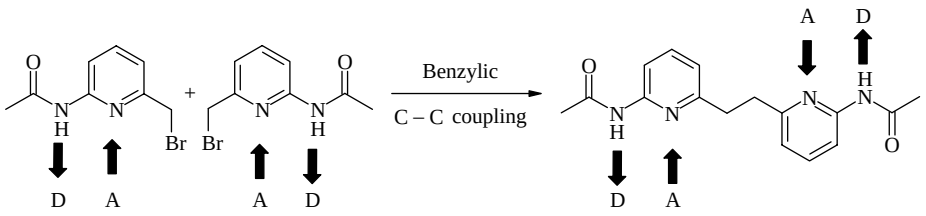
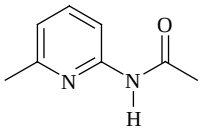


Figure 2. Strategy in the design of receptor **1**.

having no spacer between the pyridine rings binds to the diacids (1,4-phenylenediacetic acid and adipic acid) in a polymeric *anti–anti* (*6e*, *f*) fashion (Figure 1(d) and (e)).

In continuation of this work, we are now interested to examine the binding behaviour of the *bis*-acetamidopyridine having the ethylene spacer (receptor **1**; Figure 2), an intermediate spacer between a flexible ether linkage and a rigid zero [0] spacer (3,3′-bipyridine-type *bis*-amide) between the pyridine rings with dicarboxylic acids in the solution and solid phases. The designed receptor **1** for dicarboxylic acids is able to complex with the complementary partner in solution, confirmed by ^{1}H NMR and UV–vis experiments. The binding property of the receptor to the guest diacid in the solid state is further confirmed by a single-crystal X-ray analysis. Interestingly, in the solid state, the polymeric grid-like network of receptor **1** has been changed into a polymeric wave-like *anti-perpendicular* geometry in the presence of the guest adipic acid. To our knowledge, in this article, we report for the first time an *anti-perpendicular* polymeric arrangement with respect to receptor and the guest adipic acid. The simple ethylene spacer, however, shows a vital role in the binding either in a solution or in a solid state, and receptor **1** exhibits 1:1 binding in solution; in the solid state, receptor **1** is present in the most stable *anti* form either when it is free or complexed (Figure 7(a) and (b)). Thus, here, although the ethylene spacer is intermediate between the flexible ether linkage (*6d*) and the rigid zero (0) spacer (3,3′-bipyridine-type-*bis* amide) (*6e*, *f*), it operates as a sterically constrained type spacer in solid phases due to the stability of the two polar binding pyridine amide groups (two dipoles) in the *anti* form, favouring polymeric hydrogen bonds. To understand the information about the cooperative binding of two pyridine amides in receptor **1** with dicarboxylic acid, simple 2-acetamido-6-methylpyridine (receptor **2**) is synthesised and binding studies with dicarboxylic acids are performed. A general survey on the spacer length in the receptors and the modes of complexation between the receptors and diacids is summarised in Table 1.



The ethylene linked *bis*-acetamidopyridine, receptor **1**, having two acetamido (two hydrogen bond donors) groups and two pyridine rings (two hydrogen bond acceptors) for dicarboxylic acids recognition can be obtained by reductive dimerisation of 2-bromo-6-acetamidopyridine (Figure 2). Receptor **2** is synthesised by acetylation of 2-amino-6-methylpyridine with acetic anhydride at room temperature followed by a usual work-up.

2. Synthesis of receptor 1

N-(6-Bromomethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (**2**) has been synthesised using NBS in the presence of a catalytic amount of AIBN refluxing in dry CCl_4 photochemically from *N*-(6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide according to the literature procedure (*6h*) (Scheme 1). Compound **3** was prepared by reductive dimerisation of compound **2** by chlorotris(triphenylphosphine)cobalt(I) using dry benzene as the solvent under N_2 atmosphere at 0–12°C according to the literature procedure (*7*) (Scheme 2). Compound **4** (diamine derivative of compound **3**) was obtained after refluxing with 4 (N) KOH:EtOH (1:1) overnight (Scheme 3). Compound **4** was then acetylated with acetic anhydride to afford the desired compound **1** (Scheme 4). Replacement of the pivaloyl group with an acetyl group is done to avoid the bulkiness.

3. Binding studies

3.1 ^{1}H NMR studies

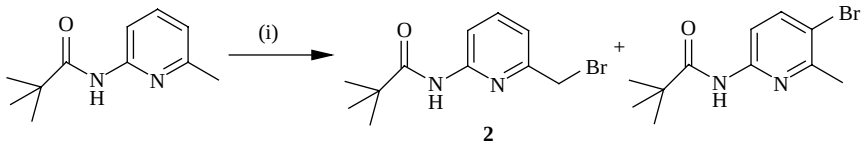
To study the binding behaviour of receptor **1** towards the dicarboxylic acids, the ^{1}H NMR spectra of receptor **1** and a (1:1) complex with various diacids (malonic, succinic, glutaric, adipic, pimelic, suberic and 1,4-phenylenediacetic) are recorded in 1% DMSO-d_6 in $CDCl_3$ to make the solutions homogeneous.[1] The amide proton in ^{1}H NMR of the receptor **1** appearing at $\delta = 8.49$ (Figure 3) ppm shows appreciable downfield chemical shifts ($\Delta\delta = 0.37$–0.67 ppm) of amide protons (Table 2) by all the seven dicarboxylic acids. The downfield chemical shifts in all the cases are conclusive for the desired complexation of receptor **1** with diacids in the solution phase.

3.2 UV–vis studies

To analyse the binding behaviour and to determine the association constants of the receptors with the dicarboxylic acids (malonic, succinic, glutaric, adipic,

Table 1. General survey on the binding of *bis*-amidopyridine bearing different spacers with different diacids in the solid state.

Entry	Spacer used	Guest diacids	Conformation of the receptor in the complex	Binding behaviour of the receptor in the complex
1	Ether linkage (*6d*)	1,4-Phenylenediacetic	*syn*	*syn–syn*, (1:1) polymeric
2	Zero spacer (*6e,f*)	Adipic,1,4-phenylenediacetic	*anti*	*anti–anti*, (1:1) polymeric
3	Ethylene spacer	Adipic	*anti*	*anti-perpendicular*, (1:1) polymeric



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Scheme 1. Reagents and conditions: (i) NBS, AIBN, hγ, dry CCl_4, 58%.

pimelic, suberic and 1,4-phenylenediacetic), UV–vis experiments are performed. One per cent of DMSO–$CHCl_3$ solutions is used to make them homogeneous. Both the receptors have the absorbance maxima at $\lambda_{max} = 280$ nm, which is continuously decreased upon the addition of guest solutions. Changes in the absorbance can be used for the binding constant calculations (*8*), since a low concentration provides more accurate association constant values. From UV–vis titration spectra of malonic, succinic, adipic and pimelic acids with receptor **1**, an isosbestic point is found at $\lambda = 293$ nm (Figure 4(a)) due to the formation of a new species between the host and the guest as a result of complexation; in other cases, a crossover (Figure 4(b)) is observed, which clearly indicates the diacid–receptor interaction. In order to understand the cooperative binding between receptor **1** and dicarboxylic acids, we have performed the UV–vis experiment with receptor **2** with the various diacids (Figure 5). From the association constants (Table 3), it is evident that receptor **1** binds the diacids with larger K_a values compared to receptor **2**. We believe that this is possible if there is a cooperativity between the two pyridine amide binding sites in complexation of diacids. To determine the stoichiometry, we have performed the Job plot (Figure 6(b)) and 1:1 stoichiometry in solution is observed from the Job plot in the case of receptor **1** with various dicarboxylic acids.

3.3 X-ray studies

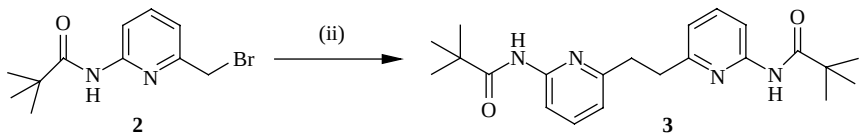
To study the solid-phase interactions between the receptor and the guest, we have developed single crystals of receptor **1** and also the co-crystal of the receptor with adipic acid (complex **A**). The supramolecular behaviour of receptor **1** and its complex is very interesting with respect to their solid-phase architectures. Receptor **1** in the space group $P2_1/c$ (No. 14) presents one molecule in an asymmetric unit (Figure 7(a)). In complex **A**, receptor and adipic acid are present in a 1:1 ratio in the asymmetric unit in the space group of $C2/c$ (No. 15) (Figure 7(b)). The crystallographic data for receptor **1** and complex **A** (receptor **1** with adipic acid) are summarised in Table 4.

*3.3.1 Receptor **1***

Receptor **1** forms a zigzag polymeric chain (Figure 8) where the pyridine moieties interact with others through two amide hydrogen-carbonyl oxygen hydrogen bonds (N2—H1/O1, 2.005 Å) (Table 5) in an angular fashion with two different receptors resulting in polymeric zigzag chains.

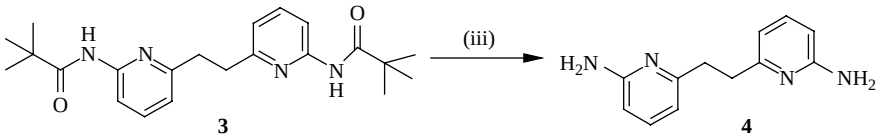
*3.3.2 Complex **A***

The crystal structure of the complex has provided the proof for the recognition interactions. The X-ray analysis of the complex (Figure 9) suggests a supramolecular wave-like structure. The solid-state structure of the



2 **3**

Scheme 2. Reagents and conditions: (ii) $Co(PPh_3)_3Cl$ in dry benzene, nitrogen atmosphere, 0–12°C, 55%.



Scheme 3. Reagents and conditions: (iii) 4 (N) KOH–EtOH (1:1) reflux, overnight, 85%.

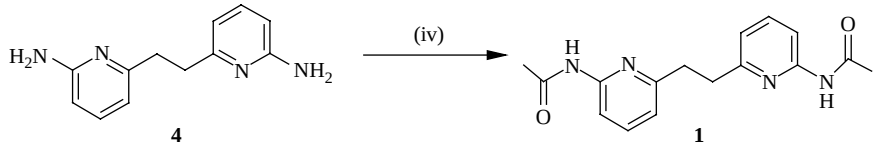
heterosynthon shows that one part of the dicarboxylic acids binds a pyridine amide of one receptor molecule, whereas the other part of the acids binds the pyridine amide of another molecule. The different hydrogen bonding interactions in the complex **A** are given in Table 6. In the complex, the receptor **1** has two planes with respect to the pyridine ring and it is present in the *anti* form with respect to hydrogen-bonding groups (pyridine ring nitrogen and amide groups). In the co-crystal, the pyridine rings joined by the dicarboxylic acids are not planar, rather they are present with a dihedral angle of 49.70° between the mean planes of pyridine (Figure 10). The dicarboxylic acid displays a nearly perpendicular orientation with respect to the acid group with the angle between them being 81.82°. In the complex **A**, the dicarboxylic acid displays one *anti*, one *syn* and another *anti* conformation (about its CH_2—CH_2 bonds). The distance between the nitrogen atoms from each pyridine ring is 5.37 Å and that between hydroxyl groups (—OH···HO—) is 9.71 Å which are very much different. Such an arrangement of the component is ideally suited to the binding of the dicarboxylic acid molecules to two different molecules of receptor **1** from two different planes. Thus, the new motif of a wave-like *anti-perpendicular* (1:1) polymeric co-crystal of the host–guest has been coined instead of the *syn–syn* (1:1) polymeric (*6d*), *anti–anti* (1:1) polymeric (*6e*, *f*), *syn–syn* 2:2 (*5d*) or *top–bottom-bound* 1:1 (*5a*) co-crystals, which were previously reported.

3.4 Model studies

The MMX calculation[2] for receptor **1** with adipic acid (Table 7) in different modes is interesting and supports the experimental results observed in the solid state. The calculation shows that receptor **1** has the E_{min} value of 5.68 kJ mol^{-1} in the *anti* form (Figure 11(a)) and 6.74 kJ mol^{-1} in the *syn* form (Figure 11(b)). Receptor **1** is thus always found to be present in the *anti* form in the solid state, either when it is free or complexed. When it binds with adipic acid (1:1) in the *anti* form, it has the E_{min} value of -8.07 kJ mol^{-1} (Figure 11(c)); however, in the polymeric form, it has the E_{min} value of -10.05 kJ mol^{-1} (Figure 11(d)) due to the formation of an extra number of hydrogen bonds between the receptor and acid groups and thus obtains a better stabilisation. In the *syn* form of the receptor, with adipic acid it has the E_{min} value of -6.54 kJ mol^{-1} (Figure 11(e)) higher than 1:1 (Figure 11(c)) or polymeric (Figure 11(d)) in the *anti* mode which may be due to strain in diacid because diacid now is forced by the receptor to rotate into the higher energy form (*6f*) (Figure 11(e)) compared to the most stable *anti* form (Figure 11(f)). Another important point that supports the polymeric structure in the solid state is that the distance between the hydroxyl groups (—O—H···H—O—) of adipic acid is 10.28 Å (Figure 11(f)) in its most stable *anti* form, whereas the distance between the two pyridine ring nitrogens is 6.03 Å in the most stable *anti* form of the receptor (Figure 11(a)) which are very much different. Thus, a 1:1 dimer of the host and the guest is not found, rather a polymeric nature of binding is present in the solid state observed in the solution state. This calculation thus supports the results obtained with respect to a polymeric 1:1 binding fashion in the crystal structure obtained for receptor **1** in complexation with adipic acid, complex **A** (Figure 11(d)).

4. Discussion

The recognition of dicarboxylic acids by receptor **1** in the solution phase is studied by means of ^{1}H NMR and UV–vis titrations as well as in the solid phase using single-crystal X-ray analysis. From ^{1}H NMR, the downfield shifts ($\Delta\delta = 0.37–0.67$ ppm) of amide protons are observed for all the dicarboxylic acids being studied. In the UV–vis experiment, the appearance of an isosbestic point and calculated binding constants support in favour of binding. Receptor **2** has lower binding constants than receptor **1** calculated by the UV–vis experiment due to the cooperative binding of two pyridine amide groups with two acid groups of diacid. From single-crystal analysis,



Scheme 4. Reagents and conditions: (iii) acetic anhydride, r.t., 4 h, 90%

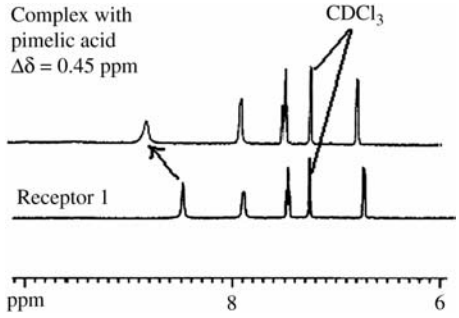


Figure 3. Partial ^{1}H NMR of receptor **1** ($c = 3.12 \times 10^{-3}$ M) and 1:1 complex with pimelic acid at 25°C.

Table 2. Change in chemical shifts in the amide protons of receptor **1** upon the addition of diacids,'+' sign indicates the downfield shifts of the amide protons ($c = 3.12 \times 10^{-3}$ M) at 25°C.

Name of the diacids	Change in chemical shift of amide N—H protons
Malonic	+0.55
Succinic	+0.66
Glutaric	+0.67
Adipic	+0.56
Pimelic	+0.45
Suberic	+0.37
1,4-Phenylenediacetic	+0.44

it is found that receptor **1** is present in the *anti* form, either when it is free or complexed with adipic acid. The ethylene spacer acts as a sterically constrained spacer for such polymeric design in the *anti* form of the receptor to lock the guest adipic acid in a *perpendicular* arrangement about its interacting carboxylic acid group and consequently a new wave-like polymeric (1:1) *anti-perpendicular* geometry is observed, in contrast to other arrangements reported in the literature such as *syn–syn* (1:1) polymeric (*6d*), *anti–anti* (1:1) polymeric (*6e*, *f*), *syn–syn* (*5d*) (2:2) or *top–bottom-bound* (1:1) co-crystals (*5a*).

5. Conclusion

Thus, the synthetic receptor **1**, ethylene-linked *bis*-acetamidopyridine, binds with dicarboxylic acids in the solution state. In the solid state, the polymeric host–guest association is found from single-crystal analysis in complex **A**. This happens due to the simple but unique ethylene spacer which directs the receptor **1** to bind to the guest in an *anti* mode. Thus, a conclusion can be drawn about the length of the spacer and the flexibility of it, i.e. when the spacer is ether linkage (*6d*) (three linking atom, —C—O—C—), it is flexible, and when the spacer length is zero the spacer is rigid (*6e*, *f*); however, when the spacer is ethylene also (two linking atom, —C—C—), it behaves now also as a rigid spacer and makes the receptor to stay in the *anti* conformation (i.e. the binding pyridine amide dipoles are in *anti*). Thus, when the linking atoms between the pyridine rings are changed from zero (*6e*, *f*) to 2 in number, the rigidity of the spacer remains, but when it is 3 it is flexible enough to bind the diacid guest in a *syn* fashion about the binding sites of the receptor (*6d*). Another important point is that due to the ethylene spacer, a new motif of polymeric wave-like *anti-perpendicular* supramolecular network is obtained in the solid state in complex **A**. This finding is thus important in designing new supramolecular assemblies involving new wave-like polymeric (1:1) *anti-perpendicular* geometry of the host–guest instead of the *syn–syn* (1:1) polymeric, *anti–anti* (1:1) polymeric, *syn–syn* 2:2 tetramer or *top–bottom-bound* 1:1 dimer co-crystals, which were previously reported by us and other groups.

6. Experimental

6.1 General

Melting points (mp) were recorded on an A. D. and Co. hot-coil stage melting point apparatus and are uncorrected.

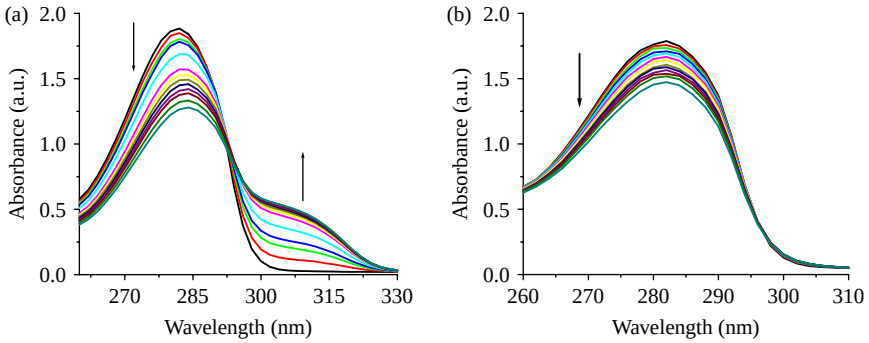


Figure 4. Representative of UV–vis titration spectra showing the change in the absorbance of receptor **1** upon addition of (a) succinic acid and (b) 1,4-phylenediacetic acid.

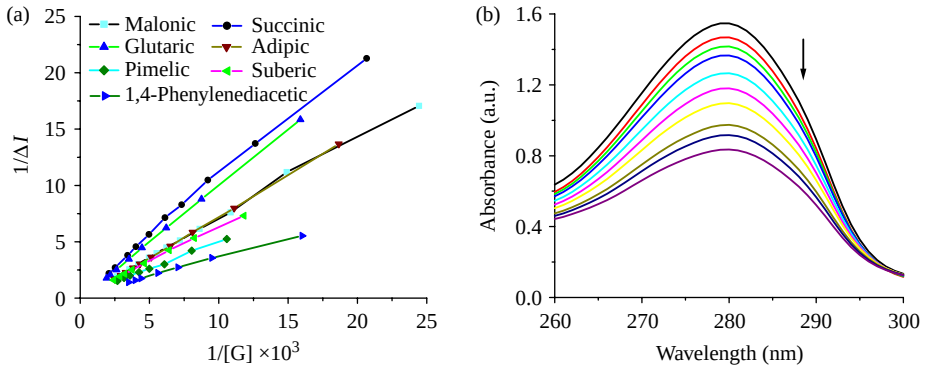


Figure 5. (a) Binding constant calculation curves of receptor **2** with different diacids and (b) UV–vis titration spectra of receptor **2** upon addition of 1,4-phenylenediacetic acid.

Table 3. Association constant (K_a) values of receptors **1** and **2** with different diacids at 25°C in (M^{-1}).

Entry	Dicarboxylic acid	K_a of receptor **1** (M^{-1})	K_a of receptor **2** (M^{-1})
1	Malonic acid	2.19×10^3	1.45×10^2
2	Succinic acid	9.45×10^2	4.61×10^2
3	Glutaric acid	1.03×10^3	4.73×10^2
4	Adipic acid	9.67×10^2	2.40×10^2
5	Pimelic acid	1.23×10^3	5.36×10^2
6	Suberic acid	1.53×10^3	3.65×10^2
7	1,4-Phenylenediacetic acid	1.91×10^3	4.32×10^2

NMR spectra were recorded in $CDCl_3$, unless otherwise mentioned, with TMS as the internal standard with a Bruker AM 500 MHz NMR instrument. Chemical shifts are given in δ (ppm) scale and J values in Hz. IR spectra were measured in a KBr disc with a JASCO FT/IR-460 plus spectrometer. UV–vis spectra were recorded on a JASCO V-530. HR-MS of receptor **1** and compound **3** were recorded on a Qtof Micro YA263 instrument. All solvents were dried prior to use by common methods. Silica gel (100–200 mesh) was used for all chromatographic purifications. Starting materials are commercially available (purchased from Fluka and Aldrich, Secunderabad, Andhra Pradesh, India).

6.1.1 *General procedure for UV–vis titration*

A stock solution of receptor **1** was prepared at a concentration of c. 1×10^{-4} mol/dm^3 in 1% DMSO in $CHCl_3$. Acids were dissolved in 1% DMSO in $CHCl_3$ in c. 1×10^{-3} mol/dm^3 concentration. DMSO (1%) was added to make a homogeneous solution. The guest solutions were then added to the receptor solution (taking 2.0 ml in the

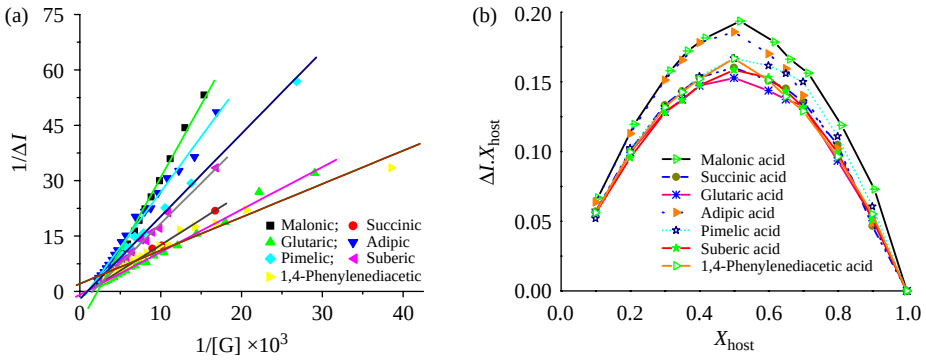


Figure 6. (a) Binding constant calculation curves and (b) the Job plot by the UV–vis method of receptor **1** with various dicarboxylic acids.

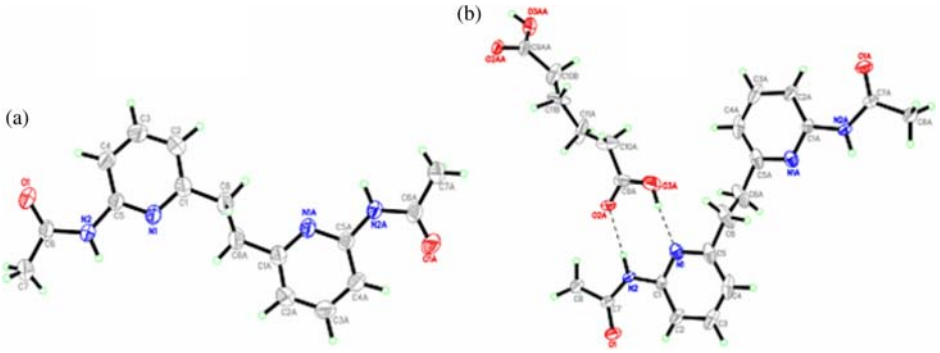


Figure 7. (a) ORTEP diagram (with 50% probability) of receptor **1** and (b) ORTEP diagram (with 50% probability) complex **A**.

UV-cell) and continuous decrease in absorbance in UV spectra was recorded each time.

6.1.2 *General procedure for the Job plot by the UV–vis method*

A stock solution of the same concentration of receptor **1** and the guests were prepared in the order of *ca.* 1×10^{-4} mol/dm^3 in 1% DMSO–$CHCl_3$. The absorbance was recorded in each case with different host–guest ratios but equal in volume (2 ml). In the Job plots, $\Delta I \times X_{host}$ vs. X_{host} were plotted where ΔI is the change in intensity of the absorbance spectrum during titration and X_{host} is the mole fraction of the host in each case, respectively.

6.1.3 *N-(6-Bromomethyl-pyridine-2-yl)-2,2-dimethyl-propionamide (**2**)*

2,2-Dimethyl-*N*-(6-methyl-pyridine-2-yl)propionamide (3 g, 0.016 mmol) and AIBN (1.28 g, 7.79 mmol) were taken in a 250 ml round-bottomed flask. Dry CCl_4 (60 ml)

Table 4. Crystallographic data and structure refinement parameters of receptor **1**, complex **A**.

Compound	Receptor **1**	Complex **A**
CCDC no.	739955	739956
Empirical formula	$C_{16}H_{18}N_4O_2$	$C_{16}H_{18}N_4O_2$, $C_6H_{10}O_4$
Formula weight	298.34	444.48
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$ (No. 14)	$C2/c$ (No. 15)
T [K]	296	100
a [Å]	7.9719 (3)	17.5984 (6)
b [Å]	10.7192 (5)	8.7760 (4)
c [Å]	8.8828 (3)	15.1734 (4)
α [°]	90	90
β [°]	100.620 (3)	108.737 (1)
γ [°]	90	90
Z	2	4
V [Å^3]	746.05 (5)	2219.24 (14)
Wavelength [Å]	0.71073	0.71073
D_{calc} [g/cm^3]	1.328	1.330
F [000]	316	944
Crystal size [mm]	$0.09 \times 0.48 \times 0.50$	$0.17 \times 0.30 \times 0.80$
Theta min–max [°]	2.60, 31.55	2.44, 25.00
μ [mm^{-1}]	0.091	0.098
Index ranges	$-11 \le h \le 11$ $-15 \le k \le 13$ $-12 \le l \le 13$	$-20 \le h \le 20$ $-10 \le k \le 10$ $-18 \le l \le 18$
Reflections collected	9740	17,235
Unique reflections	2495	1959
Observed reflections [$I > 2.0\ \sigma(I)$]	1666	1783
R_1 [$I > 2\sigma(I)$]	0.0496	0.0623
wR_2	0.1454	0.1357
GOF	1.093	1.129

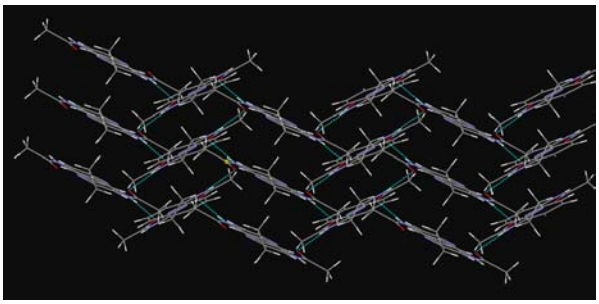


Figure 8. Polymeric zigzag chains of receptor **1** along the crystallographic *a*-axis.

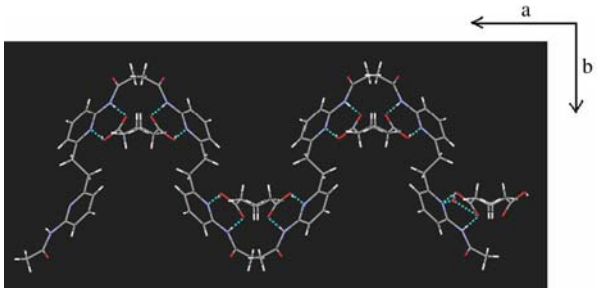


Figure 9. Wave-like structure of the receptor viewed along the crystallographic *c*-axis.

was added to it and the reaction mixture was heated to reflux for half an hour with vigorous stirring in the presence of light. After half an hour, *N*-bromosuccinamide (2.78 g, 0.016 mmol) was added and the reflux was continued for 6 h. Then, the reaction mixture was cooled. After the usual work-up, a brown semi-solid was obtained. This was then purified by column chromatography using silica gel (60–120 mesh) and 1% ethyl acetate in petroleum ether as the eluent to yield a colourless dense liquid (2.4 g), yield 58%.

6.1.4 1,2-bis(2-Pivaloylamino-6-pyridyl)ethane (*3*)

N-(6-Bromomethyl-pyridine-2-yl)-2,2-dimethyl propionamide (500 mg, 1.84 mmol), $Co(PPh_3)_3Cl$ (1.76 g, 2 mmol) was kept in a round-bottomed flask under N_2 atmosphere. Dry, degassed benzene (50 ml) was added dropwise to it, maintaining at 0–15°C temperature around the flask. The reaction was continued for half an hour. The deep green colour turns into blue, an indication of the completion of the reaction. Then, benzene was evaporated and the product was extracted with $CHCl_3$ (20 ml × 4). The solvent was then evaporated and purified by silica gel (100–200 mesh) column chromatography using ethyl acetate and petroleum ether (1:4) as an eluent (mp 216–218°C, 194 mg, 55%).

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 8.2$ Hz, 2H, py-C^{3}H), 7.95 (s, 2H, amide NH), 7.57 (t, $J = 7.6$ Hz, 2H, py-C^{4}H), 6.84 (d, $J = 7.3$ Hz, 2H, py-C^{5}H), 3.07 (s, 4H, methylene H), 1.33 (s, 18H, $C(CH_3)_3$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): $\delta_c = 177.1$ (NH—CO), 159.5 (py-C^2), 151.1 (py-C^6), 138.6 (py-C^3), 118.7 (py-C^5), 111.2 (py-C^4), 39.8 (methylene C), 37.5 (centre carbon of tert. butyl group), 27.6 (CH_3) ppm.

HR-MS (ES^+): Calcd for $C_{22}H_{30}N_4O_2Na$ [M + Na]: 405.2261, Found 405.2263.

FT-IR (KBr): $\nu_{max} = 3103, 2961, 1676, 1596, 1574, 1523, 1452, 1396, 1299, 1157, 808, 697\ cm^{-1}$. Anal. Calcd for $C_{22}H_{30}N_4O_2$: C, 69.08; H, 7.91; N, 14.65. Found: C, 69.12; H, 7.95; N, 14.60.

6.1.5 1,2-bis(2-Amino-6-pyridyl)ethane (*4*)

In a round-bottomed flask, compound **4** (220 mg, 0.57 mmol) was taken. 4 (N) KOH solution (2 ml)

Table 5. Hydrogen-bond parameters (Å, °) of receptor **1**.

D—H···A	D—H	H···A	D···A	D—H···A
N2—H1N2···O1^{i}	0.920 (15)	2.005 (15)	2.9148 (13)	169.7 (13)
C2—H2···N1^{ii}	0.998 (17)	2.624 (17)	3.5836 (18)	161.4 (13)
Intra C4—H4···O1	0.983 (15)	2.257 (15)	2.8714 (16)	119.5 (11)
C7—H7C···O1^{i}	0.927 (18)	2.561 (17)	3.3499 (16)	143.3 (14)

Notes: Symmetry codes: (i) x, $1/2 - y$,$1/2 + z$ and (ii) $1 - x$, $-1/2 + y$,$1/2 - z$.

Table 6. Hydrogen-bond parameters (Å, °) of complex **A**.

D—H···A	D—H	H···A	D···A	D—H···A
O3A—H3A1···N1^{i}	0.84	1.83	2.666 (6)	171
N2—H1N2···O2A^{i}	0.86 (3)	1.98 (4)	2.83 (2)	178 (3)
Intra C2—H2A···O1	0.95	2.27	2.868 (3)	120
C3—H3A···O1^{ii}	0.95	2.50	3.254 (3)	136
C8—H8B···O2A^{i}	0.98	2.57	3.431 (19)	147
C8—H8C···O1^{iii}	0.98	2.40	3.366 (3)	169

Notes: Symmetry codes: (i) $1/2 - x$,$1/2 - y$, $-z$; (ii) $1/2 - x$, $-1/2 + y$,$1/2 - z$ and (iii) $1 - x$,y,$1/2 - z$.

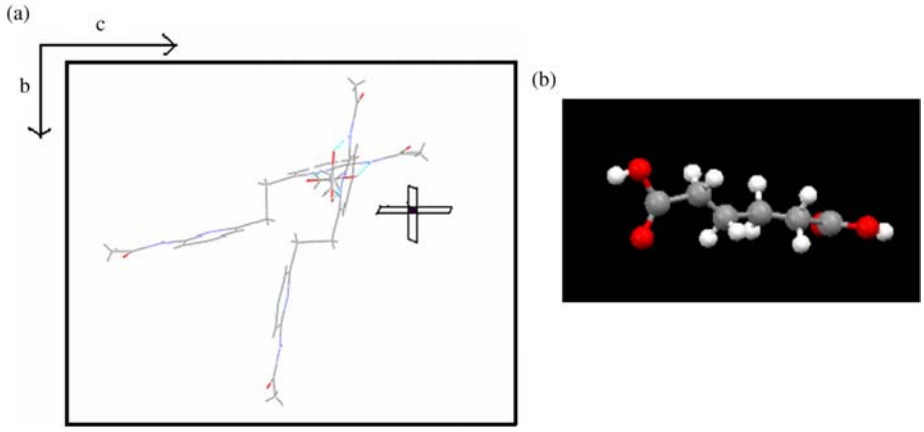


Figure 10. Adipic acid in the complex (a) along the crystallographic *a*-axis and (b) adipic acid itself in the complex (other adjacent receptor molecules are omitted for clarity).

in water and ethanol (2 ml) was added to it and refluxed for 12 h. After the completion of the reaction (monitored by TLC), ethanol was removed and the product was extracted with ethyl acetate, dried over anhydrous sodium sulphate and evaporated to afford the titled compound as a white crystalline solid[1] (105 mg, 85%). This was pure enough for the next step.

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.32$ (t, $J = 7.7$ Hz, 2H, py-C^4H), 6.51 (d, $J = 7.3$ Hz, 2H, py-C^3H), 6.33 (d, $J = 8.0$ Hz, 2H, py-C^5H), 4.45 (s, 4H, methylene H), 2.99 (s, 4H, NH_2) ppm.

6.1.6 1,2-bis(2-Acetylamino-6-pyridyl)ethane (*1*)

Compound **6** (0.50 g) was taken in a round-bottomed flask and acetic anhydride (1.0 ml) was added to it. By examining the TLC, the full conversion of the di-acetylated product was confirmed. Then, it was neutralised and the solid precipitate was filtered. This was then purified through preparative TLC using 6% methanol in chloroform. Ultimately, receptor **1** was isolated as an off-white solid (0.62 mg, mp, 166–168°C, 90%).

^{1}H NMR [500 MHz, 1% (D_6) DMSO in $CDCl_3$]: δ (ppm): 7.80 (d, $J = 8$ Hz, 2H, py-C^3H), 7.90 (s, 2H, amide NHCO), 7.57 (t, $J = 7.75$ Hz, 2H, py-C^4H), 6.83 (d, $J = 7.5$ Hz, 2H, py-C^5H), 3.06 (s, 4H, methylene H), 2.20 (s, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): $\delta_c = 168.6$ (amide CO), 159.4 (py-C^2), 150.8 (py-C^6), 138.8 (py-C^3), 118.8 (py-C^5), 111.2 (py-C^4), 37.4 (methylene C), 24.8 (CH_3) ppm.

FT-IR (KBr): $\nu_{max} = 3051$, 1970, 1793, 1667, 1602, 1578, 1551, 1457, 1362, 1305, 1161, 900, 807, 765 cm^{-1}.

HR-MS (ES^+): Calcd for $C_{16}H_{18}N_4O_2Na$ [M + Na] 321.1322, Found 321.1324.

Anal. Calcd for $C_{16}H_{18}N_4O_2$: C, 64.41; H, 6.08; N, 18.78. Found: C, 64.46; H, 6.05; N, 18.81.

6.2 X-ray crystallography

Intensity data of all the compounds were collected with the Bruker SMART APEX II CCD area-detector diffractometer (Mo K_α radiation, $\lambda = 0.71073$ Å) using the APEX2 software (*9*). The low-temperature data for complex **A** were collected using the Oxford Cryosystem Cobra low-temperature attachment. Data reductions were performed using SAINT (*9*). Absorption corrections are performed using SADABS (*9*). The structures were solved by direct methods. The non-hydrogen atoms were refined anisotropically. In receptor **1**, all hydrogen atoms were located from the difference map and were isotropically refined by full-matrix least squares on F_2 using the SHELXTL package (*10*). In complex **A**, the hydrogen atom bound to atom N2 was located from the difference map and was refined freely. The hydrogen atoms bound to atoms O3A and O3B were located from the difference map

Table 7. E_{min} (kJ mol^{-1}) calculated for receptor **1** and its different modes of binding with adipic acid.

Serial no.	Mode of binding	E_{min} for receptor **1** (kJ mol^{-1})
1	Receptor **1** (itself) *anti* form	5.68 (*6a*)
2	Receptor **1** (itself) *syn* form	6.74 (*6b*)
3	(1:1) With adipic acid, *anti* form	−8.07 (*6c*)
4	Polymeric with adipic acid, *anti* form	−10.05 (*6d*)
5	(1:1) With adipic acid, *syn* form	−6.54 (*6e*)

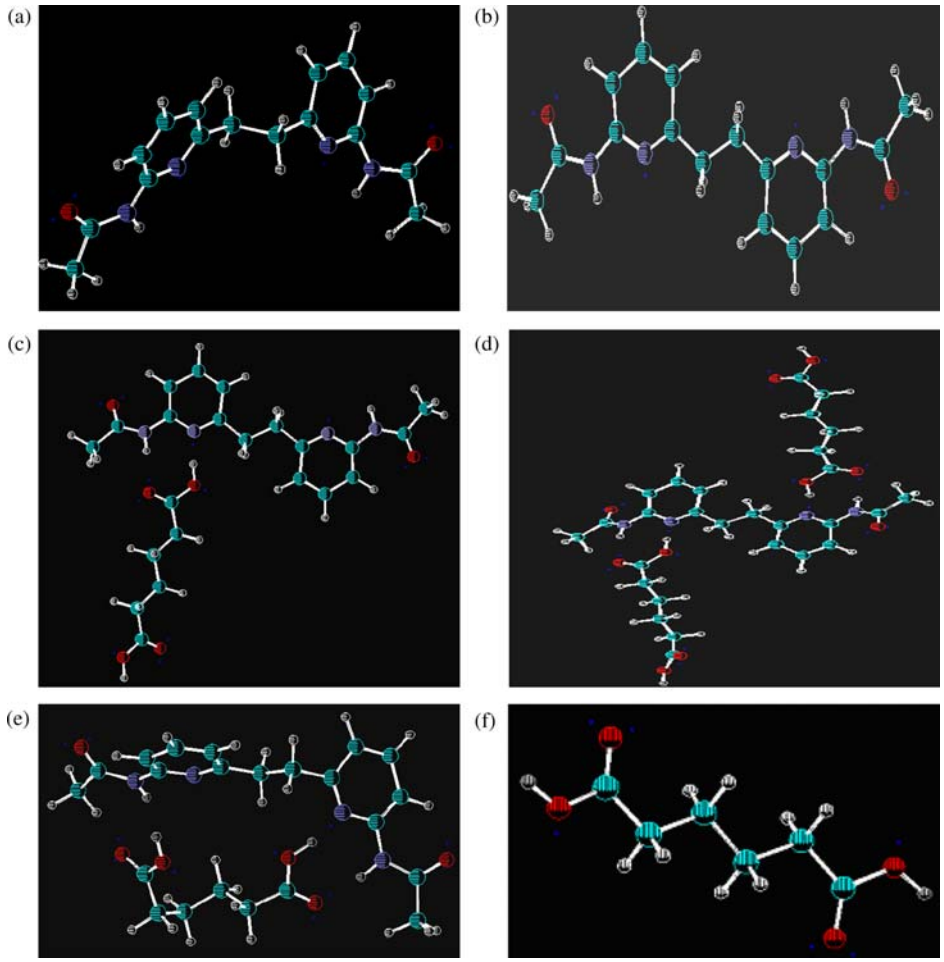


Figure 11. The optimised structures of (a) receptor **1** in the *anti* form; (b) receptor **1** in the *syn* form; (c) 1:1 complex in the *anti* form of receptor **1**; (d) polymeric complex with adipic acid in the *anti* form of receptor **1**; (e) 1:1 complex, *syn* form of receptor **1** and (f) adipic acid.

and then constrained to ride with the parent atoms with $U_{iso} = 1.5\ U_{eq}(O)$, whereas all the other hydrogen atoms were placed in their calculated positions with C—H = 0.95–0.99 Å, and refined using a riding model with $U_{iso} = 1.2$ or $1.5\ U_{eq}(C)$.

In complex **A**, the adipic acid molecule was generated by the crystallographic two-fold rotation (symmetry operation: $-x,y,1/2-z$), and it was further disordered over two positions with a site-occupancy ratio of 0.645 (7):0.55 (7). Initially, all disordered atoms were subjected to similarity and rigid bond restraints. Those restraints were removed after the steady state of refinement has been reached. The Ortep23 figures were plotted using SHELXTL (*10*).

Supporting Information

NMR (^{1}H and ^{13}C) and HR-MS of receptor **1**, compound **3** and ^{1}H NMR of compound **4**, partial ^{1}H NMR of receptor **1** with all dicarboxylic acids studied (1:1) and the UV–vis titration spectra are available online.

Acknowledgements

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Notes

1. The ^{1}H NMR spectra of compounds **2** (*6d*) and **4** (*7b*) is found to be identical to those reported earlier.
2. Energy minimisation (E_{min}) is carried out using MMX (PCMODEL Serena Software 1993). Molecular modelling was performed using standard constants and the dielectric constant was maintained at 1.5.

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