trans-Pyridyl and Naphthyridyl Cinnamides as Alternatives for Urea in Complexation of Carboxylic Acid and Formation of Water-Templated Assemblies in the Solid State

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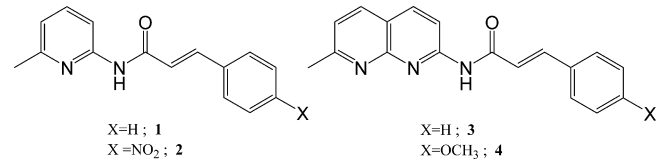
A series of α,β-unsaturated amides of pyridine and naphthyridine (**1**−**4**) derived from *trans*-cinnamic acid and its derivatives has been synthesized. The hydrogen-bonding behavior of these simple amides in the solid state has been established by solving X-ray structures. In solution and in the solid state, the above compounds **1**−**4** were found to bind carboxylic acid utilizing both conventional and unconventional hydrogen bonds. Hence, the possibility has been revealed of using this motif as an alternative of urea for the design of task-specific hosts. The experimental results have been rationalized with an accompanying theoretical study involving density functional calculations on the structure and the relative energies of different rotamers of the host systems as well as the binding energy of the complexes formed with *trans*-cinnamic acid. Generally, small binding energies (0.58−0.70 eV) are calculated for the complexes in the gas phase which become even smaller in chloroform solvent.

1. Introduction

Hydrogen bonding plays an important role in expressing the structure and function of molecules both in the solid state and in solution.[1] The arrangement of small molecules in crystalline solids is controlled by this directional force. In this regard, conventional hydrogen bonding (X−H···Y; X, Y = N or O) is extensively employed to command supramolecular network formation in organic solids.[2] It is of note that the C−H···O hydrogen bond is also well-established in structural chemistry and such hydrogen bonds may contribute significantly along with conventional hydrogen bonds in controlling the structure and function of small molecules of interest.[3] They have been found in many kinds of systems, such as crystals,[3] proteins,[4] and some organic samples.[1] Although the C−H···O hydrogen bond is much weaker in comparison to conventional hydrogen bonds, X−H···Y (X, Y = N, O, F, etc.), this kind of interaction has aroused a great deal of interest recently among researchers working in the area of supramolecular chemistry. However, reports concerning the occurrence of this unconventional C−H···O interaction in solution at ambient temperature are few in number.[5a,b] Recently, Shavitt and co-workers have observed several examples and even quantified the C−H···O interaction in condensed phase. They have also examined them theoretically.[5c]

In the quest for new hydrogen-bonding synthons for complexation of the carboxylic acid motif, we report here the synthesis and supramolecular interaction properties of a series of *trans*-cinnamylamide-based pyridine and naphthyridine molecules **1**−**4**.



Compounds **1**−**4** utilize the amide, the olefin protons of the *trans*-cinnamyl amide moiety, and the pyridine/naphthyridine ring nitrogen for complexation of carboxylic acid. These simple molecules are also found to exhibit water-templated hydrogen-bonded assemblies of different architectures in the solid state involving the same hydrogen-bonding sites. The experimental results are interpreted with the aid of theoretical calculations on different rotamers of systems **1**−**4** and their complexes with *trans*-cinnamic acid, in the gas phase as well as in chloroform.

2. Experimental Section

Synthesis. All the amides were obtained by simple coupling of the amines with the *trans*-cinnamyl chloride and its derivatives in the presence of Et_3N (Scheme 1). The naphthyridine amine was synthesized by the reported method[6] and was used in the coupling reaction as shown in Scheme 1. All the products were characterized by ^1H NMR, ^{13}C NMR, MS, and FTIR spectroscopic data.

***N*-(6-Methylpyridin-2-yl)cinnamamide 1.** To a stirred solution of 2-amino-6-methylpyridine (100 mg, 0.92 mmol) and triethylamine (0.15 mL, 1.02 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise *trans*-cinnamyl chloride (185 mg, 1.11 mmol) in dry CH_2Cl_2 (10 mL) under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 6 h. The solvent was removed under vacuum and the mixture was extracted with $CHCl_3$. The organic layer was washed with 20% $NaHCO_3$ solution, separated, dried over anhydrous Na_2SO_4, and finally removed under vacuum. The crude product was purified

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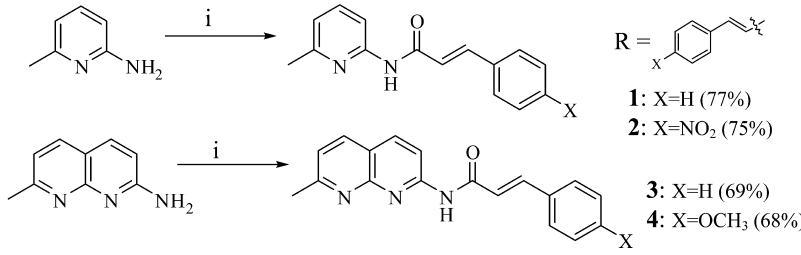
SCHEME 1: Synthesis of 1−4[a]



[a] Reagents and conditions: (i) RCOCl, Et_3N, dry CH_2Cl_2 or $CHCl_3$.

by column chromatography using 15% ethyl acetate in petroleum ether to give compound **1** as an orange gummy product (170 mg, 77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.3 Hz, 1H), 8.08 (s, 1H), 7.76 (d, J = 15.6 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.54 (m, 2H), 7.39 (m, 3H), 6.91 (d, J = 7.5 Hz, 1H), 6.52 (d, J = 15.6 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 157.2, 151.4, 143.2, 139.2, 134.9, 130.5, 129.3, 128.4, 121.1, 119.7, 111.7, 24.3; FTIR ν_{max} in cm^{-1} (neat) 3270, 3061, 3028, 2922, 1681, 1633, 1602, 1577, 1455, 1337, 1157; UV−vis ($CHCl_3$, $c = 1.26 \times 10^{-5}$ M) λ_{max} 281, 304 nm. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.60; H, 5.90; N, 11.74.

(*E*)-*N*-(6-Methylpyridin-2-yl)-3-(4-nitrophenyl)acrylamide 2. *trans*-4-Nitrocinnamic acid (200 mg, 1.04 mmol) was dissolved in dry benzene (10 mL), and $SOCl_2$ (1 mL, 13.76 mmol, excess) was added followed by the addition of one drop of dry DMF. The reaction mixture was refluxed for 12 h under nitrogen atmosphere. The solvent was removed and crude yellow-colored solid (175 mg, 80%) was dried under vacuum and used for the next step.

To a stirred solution of 2-amino-6-methylpyridine (89 mg, 0.82 mmol) and Et_3N (0.13 mL, 0.91 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise *trans*-4-nitrocinnamyl chloride (175 mg, 0.83 mmol) in dry CH_2Cl_2 (10 mL) under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 8 h. The solvent was removed under vacuum and the mixture was extracted with $CHCl_3$. The organic layer was washed with 20% $NaHCO_3$ solution, separated, and dried over anhydrous Na_2SO_4 and finally removed under vacuum. The crude product was purified by column chromatography using 10% ethyl acetate in petroleum ether to give **2** as a light yellow solid (175 mg, 75%): mp 175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.17 (d, J = 8.7 Hz, 2H), 8.07 (d, J = 8.1 Hz, 1H), 7.70 (d, J = 15.6 Hz, 1H), 7.63 (d, J = 8.7 Hz, 2H), 7.56 (t, J = 8.0 Hz, 1H), 6.86 (m, 2H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 157.02, 150.5, 148.4, 140.6, 140.0, 138.9, 128.6, 124.8, 124.2, 119.8, 111.3, 23.9; FTIR ν in cm^{-1} (in KBr) 3456, 3231, 3192, 3056, 1667, 1624, 1604, 1577, 1550, 1515, 1455; UV−vis ($CHCl_3$, $c = 1.20 \times 10^{-5}$ M) λ_{max} 320 nm; MS (LCMS) 284.4 $(M + H)^+$, 266.4. 242.4.

***N*-(7-Methyl-1,8-naphthyridin-2-yl)cinnamamide 3.** *trans*-Cinnamic acid (200 mg, 1.35 mmol) was converted to the acid chloride by following the method as mentioned for the preparation of **1**. Acid chloride (180 mg) was dissolved in $CHCl_3$ and was then added dropwise to a stirred solution of 2-amino-7-methylnaphthyridine (150 mg, 0.94 mmol) and Et_3N (0.15 mL, 1.02 mmol) in dry $CHCl_3$ (15 mL) under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 12 h. Solvent was evaporated and the mixture was extracted with $CHCl_3$. The organic layer was washed with 20% $NaHCO_3$ solution, collected, dried over anhydrous Na_2SO_4, and removed under vacuum. The crude product was purified by column chromatography using 50% ethyl acetate in petroleum ether to give compound **3** as greenish solid (190 mg, 69% yield): mp 197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.60 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 15.6 Hz, 1H), 7.46 (m, 2H), 7.34 (m, 3H), 7.27 (d, J = 7.04 Hz, 2H), 6.7 (d, J = 15.6 Hz, 1H), 2.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 163.4, 154.6, 142.8, 139.1, 136.4, 134.6, 130.0, 128.7, 128.0, 121.5, 118.6, 115.3, 25.4 (two carbons in the aromatic zone are shortage due to overlapping); FTIR ν in cm^{-1} (in KBr) 3444, 1685, 1628, 1610, 1507, 1437; UV−vis ($CHCl_3$, $c = 1.27 \times 10^{-5}$ M) λ_{max} 288, 302, 333, 343 nm; MS (LCMS) 290.4 $(M + H)^+$, 160.4.

(*E*)-3-(4-Methoxyphenyl)-*N*-(7-methyl-1,8-naphthyridin-2-yl)acrylamide 4. *trans*-4-Methoxycinnamic acid (200 mg, 1.12 mmol) was dissolved in dry CH_2Cl_2 (10 mL), and oxalyl chloride (0.15 mL, 1.68 mmol) was added followed by addition of one drop of dry DMF. The reaction mixture was stirred at room temperature (rt) for 12 h under nitrogen atmosphere. The solvent was removed to afford crude yellow solid (177 mg, 80% yield). This was dried under vacuum and used in next step. The acid chloride was redissolved in dry $CHCl_3$ (15 mL) and was slowly added to a solution of 2-amino-7-methylnaphthyridine (135 mg, 0.85 mmol) in dry $CHCl_3$ (10 mL). Reaction mixture was stirred at rt for 12 h in the presence of Et_3N. Solvent was removed and the crude mass was dissolved in $CHCl_3$. The organic phase was washed with 20% $NaHCO_3$ solution, collected, and dried over anhydrous Na_2SO_4. The combined organic layers were concentrated and passed through a silica gel column (eluent 30% ethyl acetate in petroleum ether) to get the pure product **4** as light yellow solid (185 mg, 68% yield): mp 184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.8 Hz, 1H), 8.55 (s, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 16.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 1H), 6.92 (d, J = 8.0 Hz, 2H), 6.46 (d, J = 16.0 Hz, 1H), 3.85 (s, 3H), 2.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 163.3, 161.3, 154.6, 154.4, 142.8, 139.0, 136.4, 129.8, 127.2, 121.4, 118.7, 118.5, 115.1, 114.2, 55.4, 25.5; FTIR ν_{max} in cm^{-1} (KBr) 3422, 3217, 2970, 2933, 2838, 1683, 1603, 1575, 1508, 1436, 1322, 1273, 1159; UV−vis ($CHCl_3$, $c = 1.24 \times 10^{-5}$ M) λ_{max} 270, 317, 344 nm; MS (LCMS): 320.4 $(M + H)^+$, 302.4, 161.4.

X-ray Crystallography. X-ray intensity data sets were collected with a Nonius KappaCCD diffractometer, and the following programs were used: data collection, COLLEC (Nonius B.V., 1998); data reduction, Denzo-SMN;[7] absorption correction, Denzo;[8] structure solution, SHELXS-97;[9] structure refinement, SHELXL-97;[10] graphics, XP (BrukerAXS, 2000).

The details and results of the analysis are presented in Table 1.

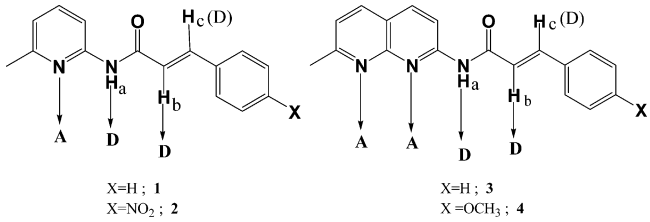


Figure 1. Possible hydrogen-bond donors and acceptors in **1**−**4**.

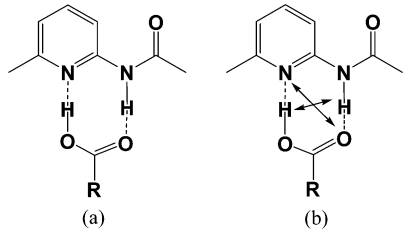


Figure 2. (a) pyridine amide−carboxylic acid complex and (b) secondary repulsive hydrogen-bonding interaction in the complex.

TABLE 1: Crystal Data and Structure Refinement for the Complex of 1 with *trans*-Cinnamic Acid and Compounds 2 and 3

	complex **1**−*trans*-cinnamic acid	**2**	**3**
empirical formula	$C_{15}H_{14}N_2O\cdot C_9H_8O_2$	$C_{15}H_{13}N_3O_3\cdot H_2O$	$C_{18}H_{15}N_3O\cdot H_2O$
formula weight	386.44	301.30	307.35
crystal system	monoclinic	triclinic	monoclinic
space group	$P2_1/c$ (No. 14)	P-1 (No. 2)	$P2_1/c$ (No.14)
a (Å)	13.345(1)	7.0295(1)	12.7765(7)
b (Å)	14.802(1)	8.7268(1)	18.7383(9)
c (Å)	10.621(1)	12.5523(2)	6.5565(4)
α	90	73.754(1)	90
β	101.17(1)	81.990(1)	99.574(2)
γ	90	78.751(1)	90
V (Å^3)	2058.3(3)	722.13(2)	1547.8(2)
Z	4	2	4
μ (mm^{-1})	0.667	0.857	0.712
F(000)	816	316	648
temperature (°C)	223(2)	223(2)	223(2)
wavelength (Å)	1.54178	1.54178	1.54178
collected reflections	15697	8806	10903
unique reflections	3621	2536	2738
R_{int}	0.029	0.035	0.036
observed reflections	3384	2414	2612
R_1 [$I > 2\sigma(I)$]	0.039	0.043	0.056
wR_2 (all data)	0.106	0.122	0.140
GooF	1.063	1.054	1.036

3. Results and Discussion

The possible hydrogen-bond donors and acceptors in pyridine- and naphthyridine-based molecules are shown in Figure 1. The hydrogen-bonding characteristics of simple pyridine and naphthyridine amides are well-established.[11] But their *trans*-cinnamyl amides as hydrogen-bonding synthons either in crystal engineering or in complexing carboxylic acids are unknown in the literature. Our ongoing interest in searching for new hydrogen-bonding synthons for complexing carboxylic acids[12] inspired us to deal with compounds **1**−**4** of simple architectures. It is well-established that pyridine amide binds carboxylic acid in the mode as suggested in Figure 2a. The complex is not stable enough due to the occurrence of repulsive secondary hydrogen-bonding interactions (Figure 2b).

To strengthen the complex, the participation of a neighboring hydrogen-bond donor is desirable. In order to do so, urea linkage as exemplified in Figure 3 can be considered. But in practice, the urea functionality at the position-2 of pyridine as well as 1,8-naphthyridine attains a stable six-centered hydrogen-bonded

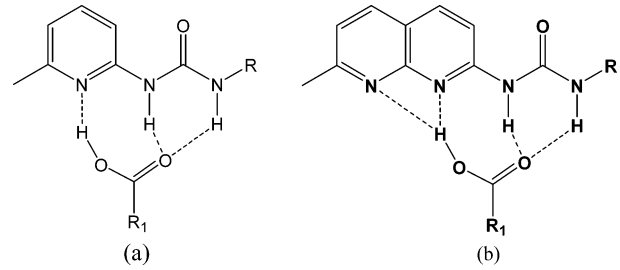


Figure 3. Suggested hydrogen-bonding structures of pyridine- and naphthyridine-based ureas with carboxylic acids.

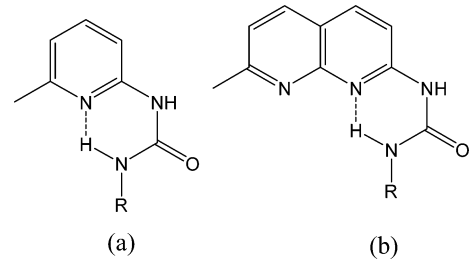


Figure 4. Intramolecular hydrogen-bonding structures of pyridine- and naphthyridine-based ureas.

TABLE 2: Change in Chemical Shift of the Participating Protons of 1−4 in Their 1:1 Complexes with Benzoic Acid

	Δδ (ppm)		
compound	for NH_a	for H_b	for H_c
1	2.47	0.31	0.02
2	1.48	0.12	0.05
3	1.54	0.20	0.02
4	1.69	0.22	0.02

complex (Figure 4).[13] Such intramolecular hydrogen bonding is too strong to allow a heteroassociation in the modes, given in Figure 3.

In contrast to this, *trans*-cinnamylamides of pyridine and naphthyridine behave differently where the olefinic proton of cinnamylamide is involved in hydrogen bonding with the guest carboxylic acid. By virtue of this it can be considered as an alternative of urea with less polar character. The involvement of the olefinic proton of cinnamyl motif in bonding is evident from the systematic study of ^{1}H NMR spectra of compounds **1**−**4** both in the absence and in the presence of the benzoic acid. Upon addition of benzoic acid to the $CDCl_3$ solution of **1**, the amide proton underwent a significant downfield chemical shift. The signal for olefinic proton of cinnamyl motif also moved to downfield direction, although not by a large extent. This was true for the other compounds also. Table 2 shows the change in chemical shift of the interacting atoms. In Table 2 the negligible change in chemical shift of the cinnamyl olefinic proton H_c, in each example, indicates weaker or no interaction during complexation. For example, Figure 5a,b demonstrates the change in ^{1}H NMR spectra of **1** and **3** in the presence of an equivalent amount of benzoic acid. In a similar way, α,β-unsaturated carboxylic acid (e.g., cinnamic acid in the present study) was also found to be involved in hydrogen-bonding complexation with **1**. During complexation the amide proton H_a as well as the olefinic protons H_b and H_c underwent downfield chemical shift. The extent of downfield shift of H_c is smaller than that of H_b (Figure 5).

It is obvious that the *trans*-cinnamyl amides in **1**−**4** may exhibit two different conformations arising due to rotation about a single bond. In the case of **1** and **2**, the rotamers **A** and **B**,

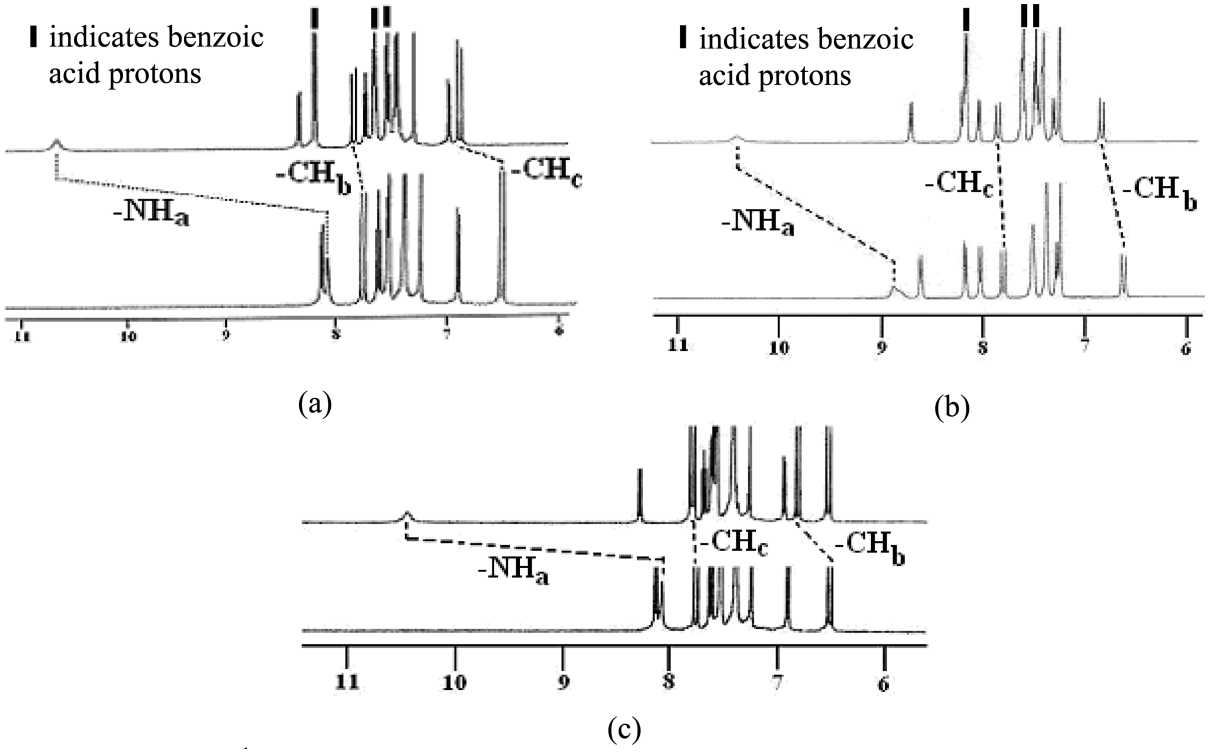


Figure 5. Change in ^{1}H NMR spectra of **1** (a) and **3** (b) in the presence of an equivalent amount of benzoic acid and **1** with an equivalent amount of *trans*-cinnamic acid (c).

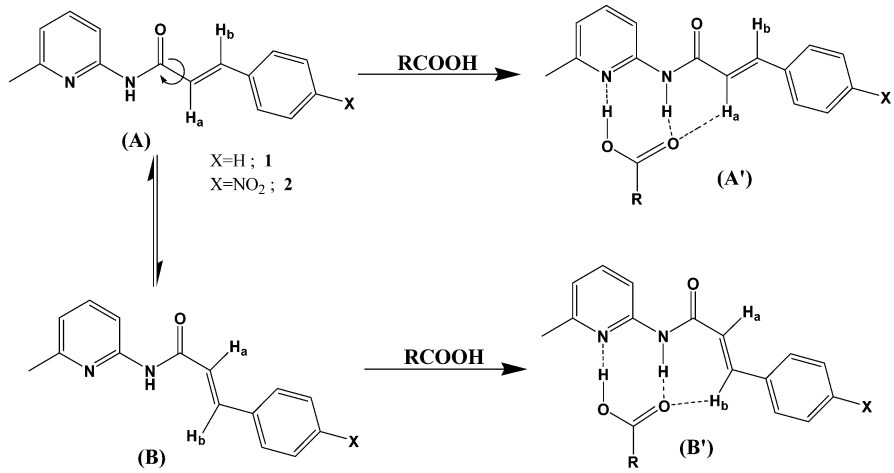


Figure 6. Rotamers of **1** and **2** and their hydrogen-bonding structures with carboxylic acid.

which may remain in equilibrium in solution, can be involved in complexation either in the mode **A′** or **B′** (Figure 6). On the same basis, molecules **3** and **4** will individually exhibit two rotamers, **C** and **D** (Figure 7). The greater downfield shift of H_b than H_c of cinnamyl unit, observed in the ^{1}H NMR study (see Table 2), suggested that the *trans*-cinnamyl amides of pyridine and naphthyridine in solution attain the hydrogen-bonding structures **A′** and **C′**, respectively. To substantiate the involvement of the H_b proton in hydrogen bonding with carboxylic carbonyl in the suggested mode **A′** or **C′** in Figure 6 or 7, compound **1** was crystallized with benzoic and *trans*-cinnamic acids from $CHCl_3$:CH_3OH (5:1 v/v). Only we were able to isolate good-quality crystals of **1** with *trans*-cinnamic acid on slow evaporation of the solvent. Figure 8 shows the single crystal X-ray structure of **1** with *trans*-cinnamic acid. It is evident from Figure 8 that carboxylic acid motif is bound to the pyridine amide site according to the mode **A′** involving N−H···O (1.991 Å), C−H···O (2.55 Å), and O−H···N (1.691 Å) interactions.

Crystallization of the compounds **2** and **3** was also carried out in a chloroform−methanol mixture and $CHCl_3$ solvents, respectively. Suitable crystals grown were analyzed and it was observed that all the *trans*-cinnamylamide derivatives were conformationally different from the urea analogues,[13] cited in the literature.

The formation of six-centered intramolecular hydrogen-bonded structure either **5** or **6** (see Figure 9) like the case of urea in Figure 4 was not found here. This is presumably due to the greater strain imposed upon **5** and **6** upon folding. Close inspection of the packing diagrams for the hydrated crystals of **2** and **3** shows that the inclusion water forms water-templated hydrogen-bonded polymeric assemblies. Interestingly, in the assemblies the heterocyclic ring nitrogen, amide proton H_a and cinnamyl proton H_b are cooperatively involved in hydrogen

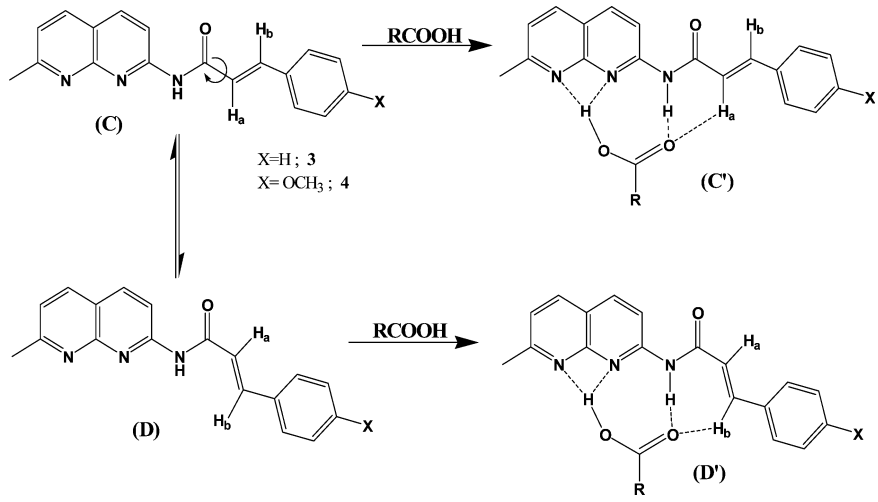


Figure 7. Rotamers of **3** and **4** and their hydrogen-bonding structures with carboxylic acid.

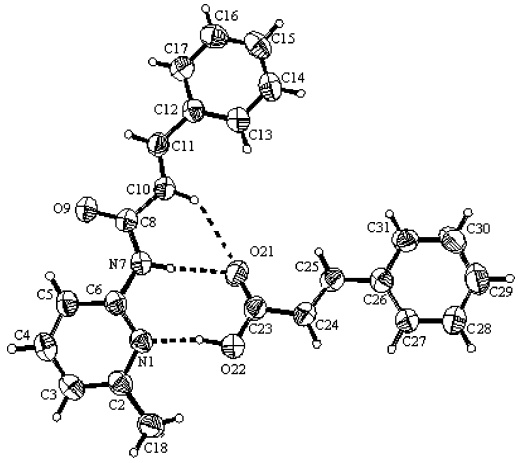


Figure 8. X-ray structure of **1** with *trans*-cinnamic acid.

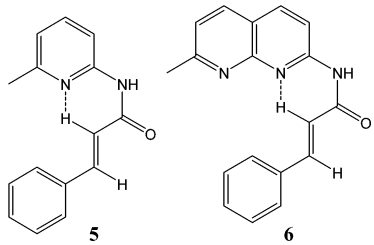


Figure 9. Possible six-centered hydrogen-bonded structures involving olefinic protons of cinnamyl motif.

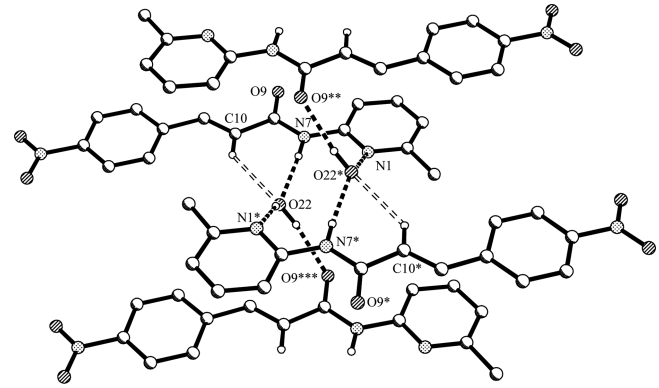


Figure 10. Water-templated hydrogen-bonded assembly of **2** involving olefinic protons of cinnamyl motif (nonbonded hydrogens are omitted).

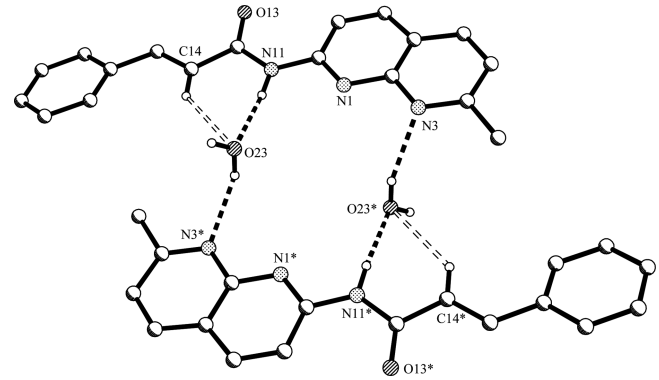


Figure 11. Water-templated hydrogen-bonded assembly of **3** involving olefinic protons of cinnamyl motif (nonbonded hydrogens are omitted).

bonding with water (Figure 10). Such hydrogen-bond-mediated organization of small molecules has some relevance in crystal engineering. In the assembly, the olefinic proton H_b and amide proton H_a are involved in making six-centered hydrogen bonds with water oxygen (C10−H···O22 = 2.57 Å, N7−H···O22 = 2.00 Å) which is already coordinated to the pyridine ring nitrogen of another molecule via a hydrogen bond (O22−H22A···N1* = 2.11 Å). This hydrogen-bonding feature is repeated with another water molecule within the same entities and thus each dimer contains two water molecules. Interestingly, other hydrogen atoms of these two bonded water molecules of the dimer are further connected to another dimer involving hydrogen bonds with amide carbonyl oxygen (O22−H22B···O9** = 2.00 Å). This led to hydrogen-bonded polymeric assemblies. Compound **3**, on the other hand, behaved almost similarly to that of **2** and gave water-templated hydrogen-bonded macrocycle (Figure 11). Each macrocycle is connected involving water as bridging ligand. Thus, the proton H_b of olefinic double bond of *trans*-cinnamyl motif has the tendency of forming hydrogen bonds with guest molecules and the mode of interaction is similar to the hydrogen-bonding feature of urea.

Once it is established that the olefinic protons in the cinnamyl motif are involved in making three-point hydrogen bonding with the carboxylic acid, we carried out UV−vis and fluorescence titration experiments in $CHCl_3$ to determine the binding potencies. The absorbance of receptors **1**−**4** decreased gradually to the different extents upon addition of benzoic acid. In the case of receptors **1** and **2**, the change in absorbance is minor in comparison to receptors **3** and **4**. In all the cases an isosbestic

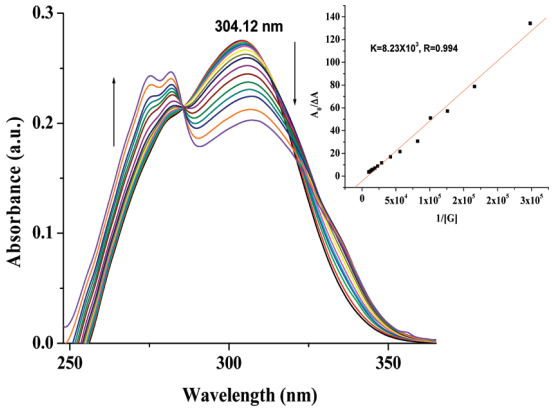


Figure 12. Change in absorbance of **1** ($c = 1.26 \times 10^{-5}$ M) upon gradual addition of benzoic acid. (Inset) The plot of $[A_0/(A - A_0)]$ vs 1/[G].

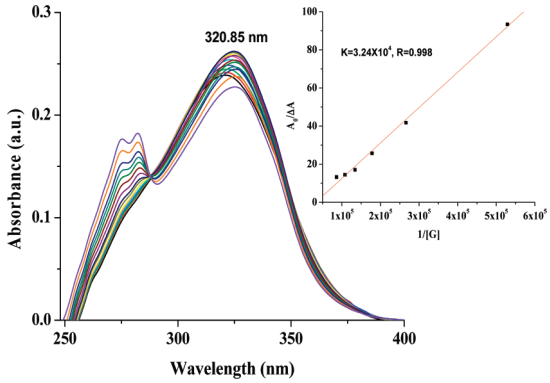


Figure 13. Change in absorbance of **2** ($c = 1.20 \times 10^{-5}$ M) upon gradual addition of benzoic acid. (Inset) The plot of $[A_0/(A - A_0)]$ vs 1/[G].

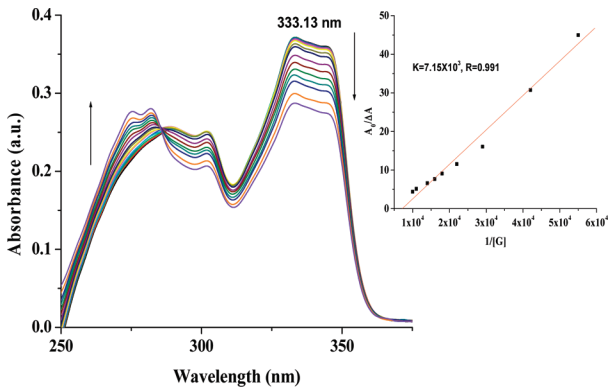


Figure 14. Change in absorbance of **3** ($c = 1.27 \times 10^{-5}$ M) upon gradual addition of benzoic acid. (Inset) The plot of $[A_0/(A - A_0)]$ vs 1/[G].

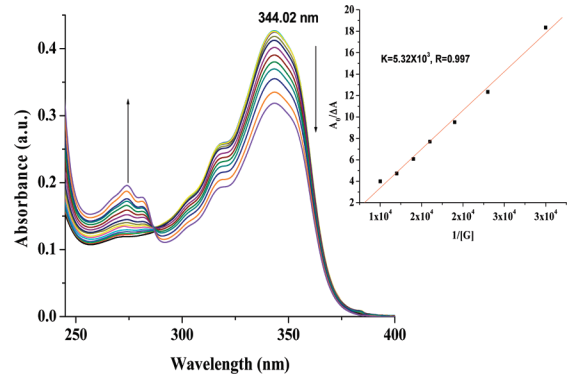


Figure 15. Change in absorbance of **4** ($c = 1.24 \times 10^{-5}$ M) upon gradual addition of benzoic acid. (Inset) The plot of $[A_0/(A - A_0)]$ vs 1/[G].

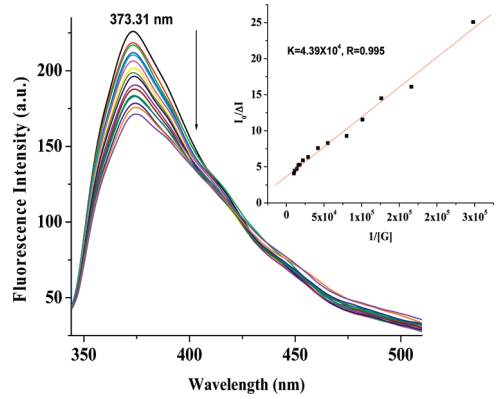


Figure 16. Fluorescence change in $CHCl_3$ of **3** ($c = 1.27 \times 10^{-5}$ M) upon gradual addition of benzoic acid ($\lambda_{ex} = 330$ nm). (Inset) The plot of $[I_0/(I - I_0)]$ vs 1/[G].

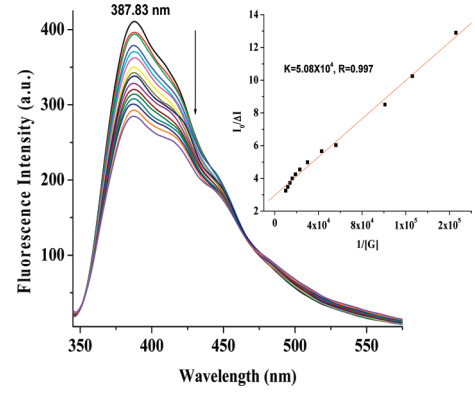


Figure 17. Fluorescence change in $CHCl_3$ of **4** ($c = 1.24 \times 10^{-5}$ M) upon gradual addition of benzoic acid ($\lambda_{ex} = 330$ nm). (Inset) The plot of $[I_0/(I - I_0)]$ vs 1/[G].

point was observed which indicated the formation of a new species of the receptors upon interaction with benzoic acid in solution. The changes in absorbance of receptors **1**−**4** upon addition of benzoic acid are shown in Figures 12−15.

To understand the complexing ability of the receptors toward benzoic acid, UV titration data were used to determine the binding constant values.[14] Insets of Figures 12−15 represent the associated binding constant curves. The linear nature of the plot of $[A_0/(A - A_0)]$ as a function of the inverse of benzoic acid concentrations fits with a linear relationship, indicating the 1:1 stoichiometry of the receptor/benzoic acid complex. Even though the change in absorbance is minor, it gives reasonable binding constant values.

The binding constant values are accumulated in Table 3. Fluorescence titration experiments were also performed with receptors **3** and **4** to understand the change in fluorescence properties of the naphthyridine motif upon interaction with benzoic acid. The titration experiment with benzoic acid shows significant quenching of emission in both the cases. No other spectral changes were observed. The relative changes in fluorescence of receptors **3** and **4** are shown in Figures 16 and 17. The results of the fluorescence titration experiments were also used to determine the binding constant values of the receptors toward benzoic acid. In this context, the insets of Figures 16 and 17 indicate the binding constant curves of the related receptors with benzoic acid.

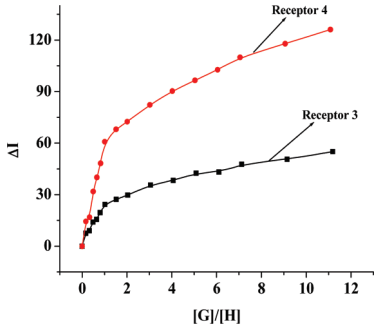


Figure 18. Plot of $(I - I_0)$ vs [G]/[H] for receptors **3** and **4** in $CHCl_3$.

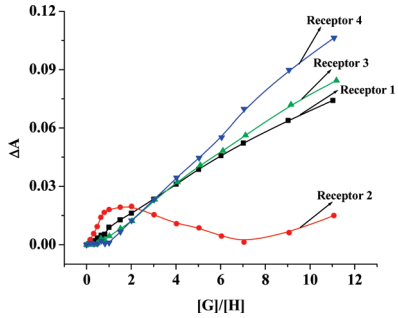


Figure 19. Plot of $(A - A_0)$ vs [G]/[H] for receptors **1**−**4** in $CHCl_3$.

The stoichiometry of the complexes for **3** and **4** was determined from the break of the fluorescence titration curves (Figure 18). Similarly, we plot the change in absorbance vs [G]/[H] from UV titrations in Figure 19 and it is found that the change in absorbance with [G]/[H] is almost linear. This indicated weak interaction in the ground state, and stoichiometries are 1:1.

TABLE 3: Association Constant Values of Receptors 1−4 with Benzoic Acid in $CHCl_3$, Determined by UV−Vis and Fluorescence Methods

	K_a (in M^{-1})	
compound	UV−vis method	fluorescence method
1	8.2×10^3	—[a]
2	3.2×10^4	—[a]
3	7.2×10^3	4.4×10^4
4	5.3×10^3	5.1×10^4

[a] Not determined.

TABLE 4: Results of the Calculations Using B3LYP Functional and 6-31+G(d,p) Basis Set[a]

structure	relative energy (eV)	binding energy (eV)	structure	relative energy (eV)	binding energy (eV)
A-1	0.0	–	**A-2**	0.0	
B-1	0.11 (0.12) 0.10[b] (0.12[b])	–	**B-2**	0.10 (0.12)	
A′-1	–	0.64 (0.22) 0.63[b,c] (0.22)	**A′-2**	–	0.69 (0.21)
B′-1	–	0.59 (0.21) 0.58[b] (0.20)	**B′-2**	–	0.63 (0.22)
C-3	0.0		**C-4**	0.0	
D-3	0.10 (0.11)		**D-4**	0.10 (0.11)	
C′-3	–	0.70 (0.21)	**C′-4**	–	0.70 (0.22)
D′-3	–	0.65 (0.18)	**D′-4**	–	0.64 (0.17)

[a] Values in parentheses include chloroform solvent. [b] Values calculated with basis set 6-311+G(d,p). [c] BSSE 0.04 eV.

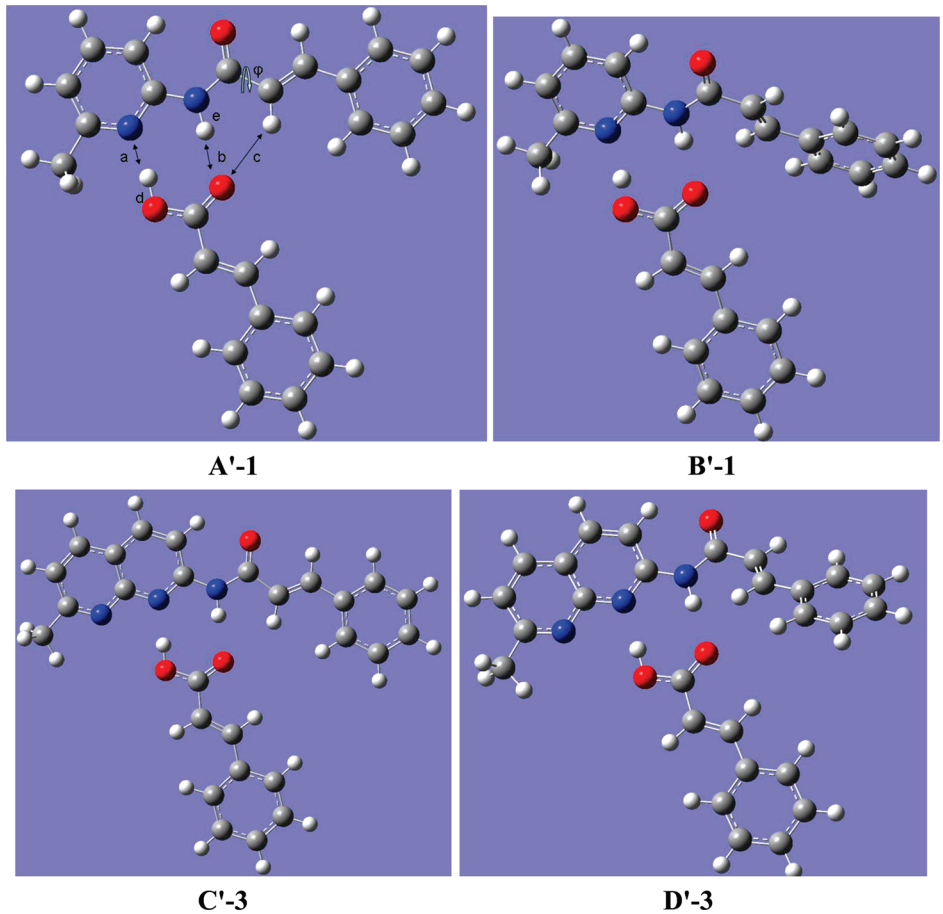


Figure 20. Optimum geometry structures calculated for the complexes of compounds **1** and **3** with *trans*-cinnamic acid. Notation is as in Tables 4 and 5 (unrotated **A′-1** and **C′-3**, rotated **B′-1** and **D′-3**) and Figures 6 and 7.

TABLE 5: Calculated Geometrical Parameters and Dipole Moments[a]

structure	φ, χ	*a*	*b*	*c*	*d*	*e*	*D*
A′-1	0, 0	1.704	1.880	2.560	1.019	1.026	3.94
	(0, 0)	(1.706)	(1.893)	(2.546)	(1.019)	(1.026)	(4.99)
A′-1	0, 0	1.737	1.891	2.538	1.012	1.024	3.97
6311+G(d,p)	(0, 0)	(1.736)	(1.894)	(2.580)	(1.012)	(1.024)	(4.96)
B′-1	157, 35	1.701	1.946	2.353	1.019	1.024	4.77
	(152, 48)	(1.704)	(1.923)	(2.596)	(1.019)	(1.026)	(5.91)
B′-1	158, 35	1.727	1.961	2.348	1.012	1.022	4.42
6311+G(d,p)	(152, 46)	(1.730)	(1.951)	(2.553)	(1.012)	(1.023)	(5.59)
A′-2	0, 0	1.718	1.862	2.500	1.017	1.027	7.16
	(0, 0)	(1.719)	(1.860)	(2.439)	(1.018)	(1.026)	(8.35)
B′-2	154, 40	1.709	1.928	2.368	1.017	1.026	6.83
	(156, 38)	(1.716)	(1.914)	(2.276)	(1.017)	(1.026)	(8.23)
C′-3	0, 0	1.794	1.842	2.524	1.007	1.029	2.37
		(1.781)	(1.853)	(2.527)	(1.010)	(1.028)	(2.79)
D′-3	204, −38	1.775	1.893	2.377	1.003	1.037	3.04
	(204, −47)	(1.770)	(1.882)	(2.477)	(1.010)	(1.027)	(3.83)
C′-4	0, 0	1.793	1.848	2.567	1.008	1.028	1.30
	(0, 0)	(1.773)	(1.866)	(2.538)	(1.010)	(1.028)	(1.37)
D′-4	199, −41	1.800	1.910	2.260	1.007	1.026	3.10
	(199,−41)	(1.800)	(1.908)	(2.266)	(1.007)	(1.027)	(2.73)

[a] Quantities as defined above in **A′-1** of Figure 20 (distances in angstrom, φ angles in deg, χ the dihedral angle between the two rings in deg, *D* dipole moment in debye). Values in parentheses obtained including chloroform solvent.

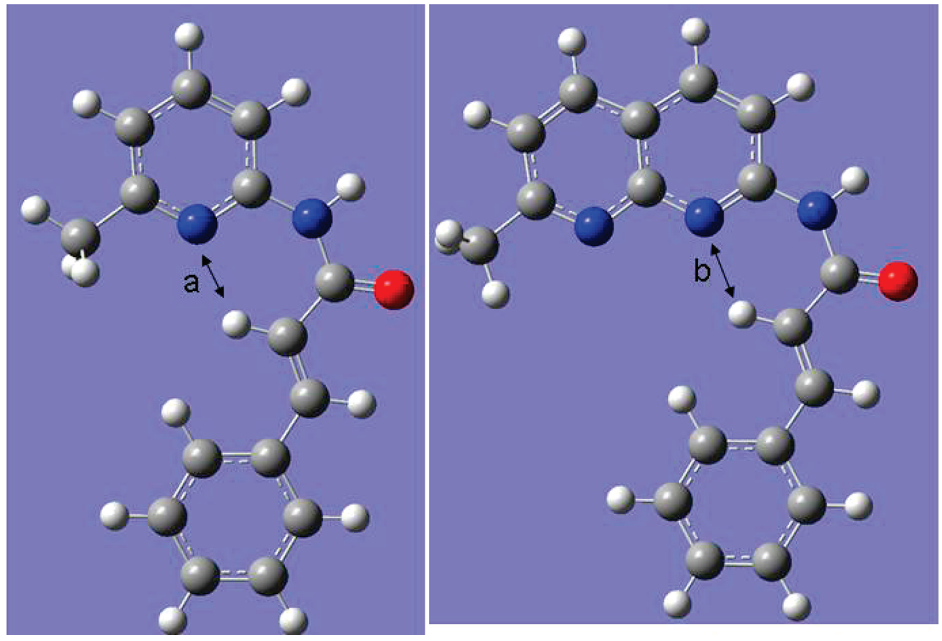


Figure 21. Calculated optimum geometries for the six-centered hydrogen-bonded structures (see Figure 9). The two structures are found to be planar with distance *a* calculated at 2.229 Å and *b* at 2.1967 Å.

Therefore, it is concluded that the olefinic proton of the *trans*-cinnamyl motif is able to form a hydrogen bond with carboxylic acid involving a particular rotamer in a specific manner. These unsaturated amides are considered as an alternative for the urea motif and, therefore, can be introduced in developing receptors without considering the placement of urea as hydrogen-bonding synthon. Even the involvement of these olefinic protons in the solid state is interesting in making water-templated supramolecular assemblies. The contribution of these olefinic protons of cinnamyl motif in the formation of C−H···O hydrogen bonds with acids were also realized by invoking a theoretical investigation.

4. Calculations

Theoretical density functional theory (DFT)[15] calculations have been undertaken in order to establish the relative stability of the different rotamers, e.g., **A** versus **B** and **C** versus **D** (see Figures 6 and 7) as well as the binding energy of the hydrogen-bonded structures with *trans*-cinnamic acid. In the DFT calculations, the B3LYP functional[16] and 6-31+G(d,p) (and for some of the calculations for testing purposes 6-311+G(d,p)) basis set was employed, and all the calculations were carried out with the aid of Gaussian 03.[17] Geometry optimization of the different structures was carried out isolated as well as in the presence of chloroform solvent.[18]

Following the notation of Figures 6 and 7, the results on the relative as well as the binding energies are collected in Table 4. As shown in Table 4, the rotamers **B-1** and **B-2** are calculated to be less stable than **A-1** and **A-2**, respectively, by about 0.10 eV. Similarly, **D-3** and **D-4** are calculated at a higher energy than **C-3** and **C-4** by 0.10 eV. This result persists when the solvent is included and also when a larger basis set is employed. Thus, the relative stabilities of the rotamers are consistent with the experimental result of predominantly forming **A′** and **C′** (rather than **B′** and **D′**). The calculated binding energies also favor complexes **A′** over **B′** and **C′** over **D′**, respectively (see Table 4).

As shown in Table 4, within the accuracy of the calculations, there is no significant difference in the calculated binding energies of the complexes of compounds **1** and **3** with those of compounds **2** and **4**. Thus, the calculated binding energies do not show the trend in the association constants of Table 3, which in any case are for formation of complexes with benzoic acid.

In Figure 20 the optimum geometry structures calculated for the complexes of compounds **1** and **3** with *trans*-cinnamic acid (notation as in Figures 6 and 7) are given, while in Table 5, calculated values for the geometrical parameters relevant to the hydrogen bonds are listed, where the labels *a*−*e* and φ are as exemplified in Figure 20 for structure **A′-1**. As shown in Table 5, the complexes of the unrotated amides (**A** and **C**) are found to be planar. The calculated hydrogen-bond distances for the case of **A′-1**, i.e., the values of *a*, *b*, and *c* (1.704, 1.880, and 2.560 Å, respectively) of Table 5 are in good agreement with the corresponding quantities resulting from the crystallographic analysis, O−H···N (1.691 Å), N−H···O (1.991 Å), and C−H···O (2.563 Å). It might be noted that in the results of the present calculations it is not possible to isolate the contribution of the olefinic C−H···O hydrogen bond to the stability of the complexes. In fact, while the $N-H_a$ bond (under **e** in Table 5) is slightly elongated upon formation of the hydrogen bond in the complex with the *trans*-cinnamic acid (e.g., 1.012 Å in **A** and 1.026 Å in **A′-1**), the $C-H_c$ bond is very slightly shortened upon formation of the complex (e.g., 1.087 Å in **A** and 1.086 in **A′-1**). This was found to be the case in all the systems calculated and also with the larger basis set.

Finally, in Figure 21 the calculated geometries for the six-centered hydrogen-bonded structures of Figure 9 are given. As shown, the two structures are found to be planar with distance *a* calculated at 2.229 Å and *b* at 2.197 Å. These structures are calculated to be local minima both lying higher in energy by 0.20 eV than the corresponding open structures **A** and **C**.

5. Conclusions

We have addressed, for the first time, the hydrogen-bonding behaviors of *trans*-cinnamides of pyridine and naphthyridine both in the solid and solution states. From the experimental observations we have established that *trans*-cinnamides are useful hydrogen-bonding synthons that are alternative of more polar urea motif. In solution and in the solid state the compounds **1**−**4** are found to bind carboxylic acid utilizing both conventional and unconventional hydrogen bonds involving only a particular rotamer. Even this particular rotamer of *trans*-cinnamides of pyridine and naphthyridine is involved in forming water-templated hydrogen-bonded supramolecules of different topologies in the solid state. The results of the calculations show that the unrotated planar structures **A** and **C** are more stable than the corresponding rotated ones, **B** and **D**, and accordingly, predominantly complexes of **A** and **C** are formed with carboxylic acids, in agreement with experiment. Low binding energies are calculated which become even lower in the presence of chloroform solvent. The calculated geometries for the complexes are in good agreement with the crystallographic data, while no evidence is found for the significance of the contribution of the olefinic hydrogen to the stability of the complexes. It is also found that for the systems of interest here the open structures are more favorable than structures involving a six-member ring structure.

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Supporting Information Available: CIF files of complex **1**−*trans*-cinnamic acid and compounds **2** and **3**. This information is available free of charge via the Internet at http://pubs.acs.org.

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