Molecular Recognition in the Solid State: Controlled Assembly of Hydrogen-Bonded Molecular Sheets

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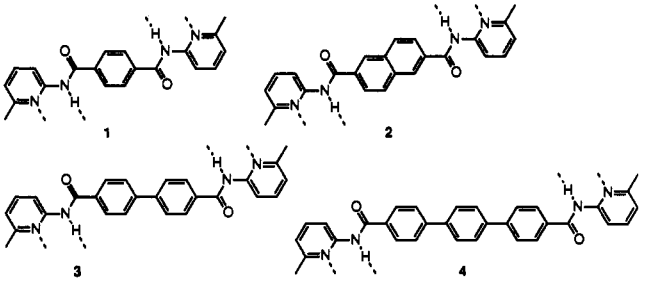
Abstract: A novel hydrogen-bonding motif for the control of solid-state structures has been developed. The motif is based on the hydrogen bonding complementarity of carboxylic acids with 2-aminopyridine derivatives. Linking two aminopyridine groups through a rigid aromatic spacer provides a receptor unit that can complex dicarboxylic acids. When there is a good correspondence between the length of the spacer and that of the carboxylic acid, a discrete 1:1 complex is formed. When the dicarboxylic acid is longer than the receptor, an alternating hydrogen-bonded cocrystal occurs with the carboxylates on each diacid binding to different receptors. This motif dominates the cocrystal, forming even when the relative lengths of the diacid and the receptor change. Within the constraints of the alternating ribbon structure, the spatial position of the two components can be varied in a well-defined and predictable manner.

There is intense current interest in the development of new solid-state structures with unusual conductance, nonlinear optical, or magnetic properties.[1] A key to the design of such materials lies in the precise juxtaposition of redox or photoactive components within the crystal lattice.[2] However, at present it is not possible to reliably predict the crystal structure forms of organic molecules. There is a strong need to develop new molecular motifs that self-assemble into controlled, well-ordered, and predictable solid-state structures. Such motifs should be dominant within the crystal so that even differently shaped or functionalized subunits will form similar lattice structures. A possible solution to this problem lies in using multiple intermolecular interactions between the subunits. Careful choice of complementary binding groups will lead not only to strong but also to discriminating interactions in the solid state.

Directed hydrogen-bonding interactions offer a powerful approach to the control of solid-state structures.[2] Multiple binding sites can be readily incorporated into different subunits to form a range of complementary regions. Recently, patterns of hydrogen bonds between specific functional groups have been identified and rules have been proposed for their formation.[3] For example, primary and secondary diamides, containing either alkyl or aryl spacer groups, frequently show hydrogen-bonding motifs based on an up/down translational arrangement of the amide groups[3b] (Figure 1). The result is an ordered array of single spacer units held in a two-dimensional sheet by predictable intermolecular interactions. Our interest lay in extending this basic structure and in discovering ways to both alter the shape of the sheet and incorporate additional molecular subunits. A key to interposing a second subunit involved imposing a different hydrogen-bonding motif onto Figure 1. The new motif had to be stronger than the single hydrogen bond between each end of a simple diamide. The most direct solution was to attach a second binding site to each amide that could then form a stronger bidentate link to a complementary group on a bis-functionalized spacer. A schematic representation of such a polymeric complex is shown in Figure 2. The result is a linear molecular ribbon made up of alternating subunits and in which the dimensions of the ribbon are imposed by the hydrogen-bonding network. Potential interacting species include the carboxylic acid and 2-aminopyridine groups. These have been widely used in solution for molecular recognition studies.[5,6] Furthermore, Etter[3a] has pointed out that in the solid state the strongest hydrogen bond acceptor will bind to the strongest donor. Thus, the carboxylic acid and aminopyridine groups would be expected to hydrogen bond to each other (e.g. in Figure 2) rather than form symmetrical dimers. A simple family of molecules with the right characteristics would be the bis-(2-amidopyridine) derivatives of different aryl diacids (Figure 3). These could exist either in an anti configuration, with outwardly directed H-bonds able to self-assemble into polymeric complexes (Figure 3a), or in a syn configuration, with inwardly directed binding groups in a position to form 1:1 complexes with complementary substrates (Figure 3b).[5] In this paper we report an investigation of the solid-state characteristics of these molecules and the observation of a recurring hydrogen-bonding motif of the type shown in Figure 2.

Results and Discussion

In order to explore the structural and recognition properties of these bis-(amidopyridines), we have synthesized four derivatives with increasing spacer length: phenyl (**1**), naphthyl (**2**), biphenyl (**3**), and terphenyl (**4**). All were prepared in a single step by the reaction of 2-amino-6-methylpyridine with the corresponding diacid chloride. Crystals were obtained for uncomplexed **1** and



for **1**, **2**, and **3** in association with dicarboxylic acids of different lengths.[7] In the following discussion, each compound or complex

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(1) DiSalvo, F. J. *Science* (*Washington, D.C.*) **1990**, *247*, 608.

(2) For general references, see: Wright, J. D. *Molecular Crystals*: Cambridge University Press: Cambridge, 1987. Desiraju, G. D. *Crystal Engineering: The Design of Organic Solids*; Elsevier: New York, 1989.

(3) For discussions of hydrogen bonding in molecular crystals, see: (a) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120. (b) Leiserowitz, L.; Tuval, M. *Acta Crystallogr.* **1978**, *B34*, 1230. (c) Leiserowitz, L.; Hagler, A. T. *Proc. R. Soc. London A* **1983**, *388*, 133.

(4) For a specific example (*N,N'*-diethyladipamide) see: Benedetti, E.; Ciajolo, M. R.; Corradini, P. *Eur. Polym. J.* **1973**, *9*, 101.

(5) Garcia-Tellado, F.; Goswami, S.; Chang, S. K.; Geib, S.; Hamilton, A. D. *J. Am. Chem. Soc.* **1990**, *112*, 7393. Hirst, S. C.; Hamilton, A. D. *J. Am. Chem. Soc.* **1991**, *113*, 382.

(6) For other examples of directed hydrogen bonding in molecular recognition, see: Chang, S. K.; Hamilton, A. D. *J. Am. Chem. Soc.* **1988**, *110*, 1318. Kelly, T. R.; Maguire, M. P. *J. Am. Chem. Soc.* **1987**, *109*, 6549. Rebek, J., Jr. *Acc. Chem. Res.* **1990**, *23*, 399. Adrian, J. C.; Wilcox, C. S. *J. Am. Chem. Soc.* **1989**, *111*, 8055.

(7) At present we have been unable to obtain diffraction-quality crystals of terphenyl **4** or its complexes.

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Table I. X-ray Structure Determination Summary

crystal data	1	1-1,4-diacid	3-1,12-diacid	2-1,12-diacid	2-1,8-diacid
empirical formula	$C_{20}H_{18}N_4O_2$	$C_{26}H_{28}N_4O_6$	$C_{40}H_{48}N_4O_6$	$C_{38}H_{46}N_4O_6$	$C_{34}H_{38}N_4O_6$
fw	346.4	492.5	680.8	654.8	598.7
cryst syst	monoclinic	orthorhombic	triclinic	triclinic	triclinic
cryst size (mm)	0.20 × 0.21 × 0.24	0.22 × 0.25 × 0.38	0.22 × 0.28 × 0.41	0.18 × 0.22 × 0.25	0.40 × 0.40 × 0.40
unit cell dimensions					
a (Å)	7.889 (2)	11.115 (3)	8.109 (2)	8.632 (2)	11.450 (2)
b (Å)	11.264 (3)	13.682 (3)	10.799 (3)	8.932 (2)	11.706 (2)
c (Å)	10.290 (3)	16.144 (4)	10.924 (3)	11.399 (3)	13.881 (3)
α (deg)	90	90	98.31 (2)	92.62 (2)	108.10 (3)
β (deg)	103.86 (2)	90	102.14 (2)	90.26 (2)	100.14 (3)
γ (deg)	90	90	98.06 (2)	99.63 (1)	102.51 (3)
vol (Å^3)	887.7 (5)	2455 (1)	910.9 (5)	865.6 (3)	1666.0 (5)
space group	$P2_1/c$	$P2_12_12_1$	$P\bar{1}$	$P\bar{1}$	$P1$
Z	2	4	1	1	2
density (calcd) (g/cm^3)	1.296	1.33	1.241	1.256	1.193
abs coeff (mm^{-1})	0.664	0.90	0.078	0.652	0.154
F(000)	364	1040	364	350	1272
radiation	Ni-filtered Cu Kα (λ = 1.541 78 Å)	Nb-filtered Mo Kα (λ = 0.710 73 Å)	Nb-filtered Mo Kα (λ = 0.710 73 Å)	Ni-filtered Cu Kα (λ = 1.541 78 Å)	Nb-filtered Mo Kα (λ = 0.710 73 Å)
obsd reflections ($F > 5.0\sigma(F)$)	718	2623	1506	969	3062
no. params refined	155	343	235	217	840
final R indices	R = 6.59%	R = 5.53%	R = 5.45%	R = 7.16%	R = 5.67%
(obsd data)	R_w = 9.13%	R_w = 6.20%	R_w = 7.23%	R_w = 8.86%	R_w = 8.12%
goodness-of-fit	1.39	1.05	1.61	1.47	1.27
largest diff peak	0.23 e Å^{-3}	0.45 e Å^{-3}	0.29 e Å^{-3}	0.30 e Å^{-3}	0.30 e Å^{-3}

Table II. Angle between Planes of Pyridine and Aromatic Spacer

1	1-1,4-diacid	3-1,12-diacid	2-1,12-diacid	2-1,8-diacid
57.7°	12.0°/12.2°	9.4°	51.8°	34.1°/30.3° 33.4°/35.4°

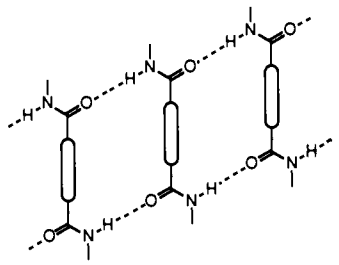


Figure 1. Common hydrogen-bonding pattern for secondary diamides.[3b,4]

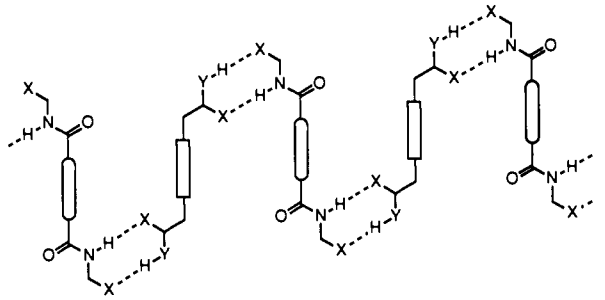


Figure 2.

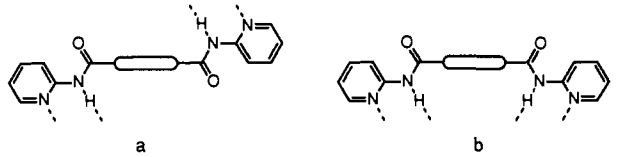


Figure 3.

will be considered in turn, with particular emphasis on both the dependence and the effect of the hydrogen-bonding pattern on the molecular structure. Full crystal and collection details are listed in Table I. None of the molecular structures showed any unusual features.

Phenyl Receptor 1. The closely related diamides diphenylterephthalamide **5** and phenyl receptor **1** have surprisingly different

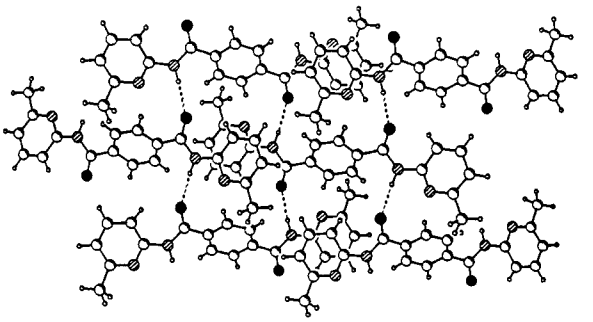
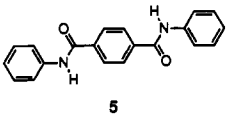


Figure 4. Crystal structure of **1**.

crystal structures. The former takes up a highly regular structure of the type shown in Figure 1, with the amides on each identical subunit in a translational relationship.[8] In contrast, phenyl



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receptor **1** forms a less regular structure (Figure 4). Each molecule resides on an inversion site with one-half molecule per asymmetric unit (two molecules per unit cell). The hydrogen-bonded subunits are related by a C-glide motif[3b] perpendicular to the b axis. The key difference is the methyl group in **1**, which presumably prevents it from achieving the close pyridine–pyridine distance necessary for the more regular structure. The angle between the pyridine and phenyl rings also deviates from planarity to almost 60° (Table II). However, the hydrogen-bond distances in Figure 4 are normal: H···O, 2.13 Å, N···N, 3.06 Å[9] (Table III).

1:1 Complex between 1 and Adipic Acid. When the distance between the amidopyridine groups in the receptor and between the carboxylate groups in the diacid are complementary, a 1:1 complex with a syn arrangement of binding groups (as in Figure 3b) can be formed. This is the case for phenyl receptor **1** and

(8) Harkema, S.; Gaymans, R. J.; van Hummel, G. J.; Zylberlicht, D. *Acta Crystallogr.* **1979**, *B35*, 506.

Table III. Selected Hydrogen Bond Distances (Å) and Angles (deg)

	1	1–1,4-diacid	3–1,12-diacid	2–1,12-diacid	2–1,8-diacid
O···H	2.13	1.92	2.14	1.90	2.04
		1.88			1.89
					2.02
					2.13
pyrN···H		2.04	1.60	2.33	1.67
		1.99			1.61
					1.65
					1.94
pyrN···H–O		175.1	167.9	96.0	178.2
angle		163.8	167.6		170.7
					175.6
					165.0
O···H–N	175.1	164.4		150.4	165.9
angle		169.5			172.7
					170.4
					176.8

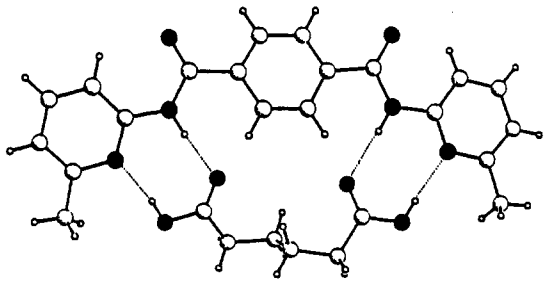

Figure 5. X-ray structure of 1–adipic acid.

adipic acid. In $CDCl_3$ solution, complexation is seen in the ^1H NMR spectra by large downfield shifts of the amide-NH resonances, consistent with the formation of four hydrogen bonds in the complex.[5] The nature of this interaction is confirmed by the solid-state structure, which shows the adipic acid stretched across the face of the receptor to form two bidentate hydrogen bonds to the amidopyridines (Figure 5). The fact that no proton transfer has occurred can be seen by the position of the acidic proton on the carboxylate (located from a difference Fourier synthesis and refined) and the short O–H (0.86 Å) and long PyrN···H (2.02 Å) distances. The hydrogen-bond distances between amideN···O (2.9 Å) and pyrN···O (2.7 Å) also fall in the normal range[9] (Table III). In addition, the entire receptor has become more planar (compared to Figure 4) with just a 12° angle between the phenyl and pyridine planes. A key feature in Figure 5 is the bound conformation of the adipic acid. The normal, low-energy conformation for alkyldicarboxylic acids is all trans.[10] However, adipic acid binds to **1** with two gauche interactions in the chain (across C_2–C_3 and C_4–C_5). The four methylenes retain an all-trans conformation while the two carboxylic acid substituents are well-positioned to rotate through 120° and hydrogen bond to the receptor.

1:1 Cocrystal of Biphenyl 3 and 1,12-Dodecanedicarboxylic Acid. In its fully extended conformation, 1,12-dodecanedicarboxylic acid is too long to form a simple 1:1 complex with **3** as in Figure 5. Instead, the cocrystal takes up an almost flat sheet structure with an alternating arrangement of diacid and diamide linked through a hydrogen-bonding network of the type discussed in Figure 2.[11] Each carboxylic acid forms two hydrogen bonds (NH···O, 2.14 Å; PyrN···H, 1.60 Å) to the aminopyridine group on different receptor molecules. These bidentate acid–pyridine interactions are almost planar as are the planes of the pyridine and phenyl rings (Tables II and III). The overall result (Figure 6a,b) is a highly ordered structure with the polymethylene chains and biphenyl subunits positioned almost parallel to each other. Both the receptor and diacid have crystallographically imposed inversion symmetry with the asymmetric unit consisting of one-half molecule of each. A side view of the structure (Figure 6b) shows a small deviation from planarity with a 13.9° angle between the diacid and receptor.

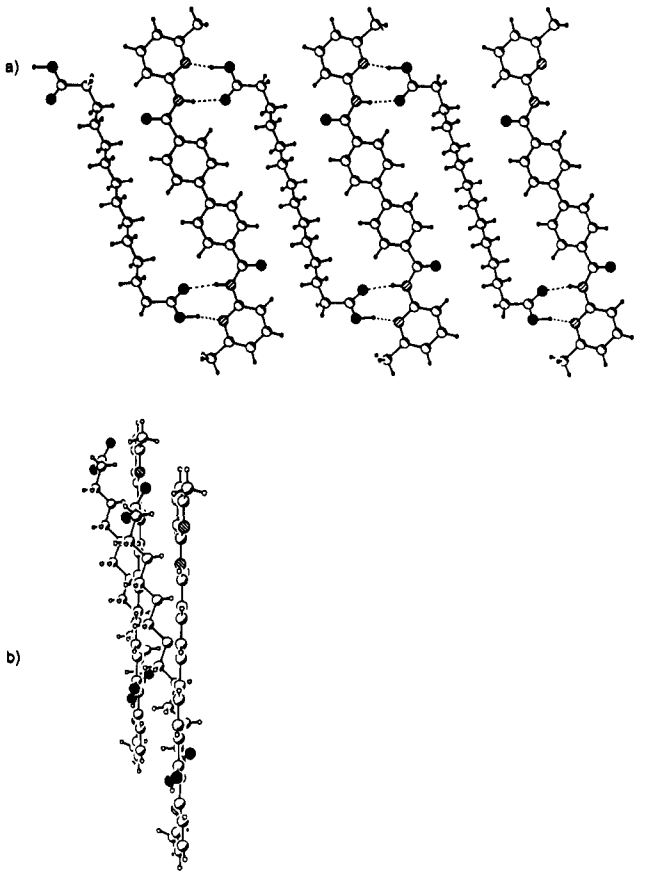

Figure 6. X-ray structure of **3** and 1,12-dodecanedicarboxylic acid: a, top view; b, side view.

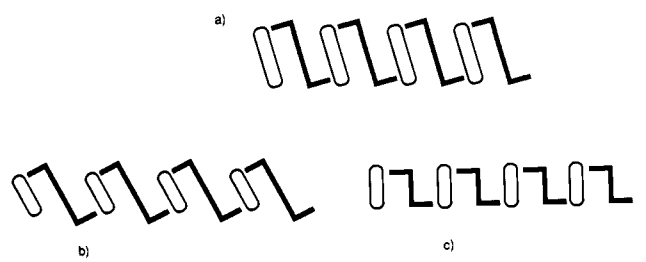

Figure 7. Effect of component length on slip angle.

A key controlling element in the crystal appears to be the relative size of the diacid and diamide subunits. The degree of size matching will determine the slip angle between parallel oligomethylene or biphenyl groups and thus the overall shape of the structure. The magnitude of this effect can be gauged from the angle of the alkane chain (represented as a line drawn between the two terminal methylene carbons) to the horizontal as defined by a line drawn through pyridine N atoms on neighboring receptors. In Figure 6 the diacid is longer than the diamide, and a partially slipped structure with a slip angle of 73.2° is formed (Figure 7a). Reducing the length of the receptor will lead to an increased size differential between diamide and diacid and a decrease in the angle between the cocrystal components and the horizontal (Figure 7b). In contrast, decreasing the length of the diacid will increase the slip angle to the point where the two subunits are well-matched and the angle is 90° (Figure 7c).

1:1 Cocrystal of Naphthyl 2 and 1,12-Dodecanedicarboxylic Acid. Naphthyl receptor **2** represents a shortening of biphenyl

(9) Taylor, R.; Kennard, O. *Acc. Chem. Res.* **1984**, *17*, 320.
(10) Morrison, J. D.; Robertson, J. M. *J. Chem. Soc.* **1949**, 980, 987, 993.
(11) For examples of controlled cocrystallization and self-assembly in the solid state, see: Shimuzu, N.; Nishigaki, N.; Osaki, K. *Acta Crystallogr.* **1982**, *B38*, 2309. Etter, M. C.; Adsmond, D. A. *J. Chem. Soc., Chem. Commun.* **1990**, 589. Lehn, J. M.; Mascal, M.; DeCian, A.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1990**, 479. Zerkowski, J. A.; Seto, C. T.; Wierda, D. A.; Whitesides, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 9025. Gallant, M.; Viet, M. T. P.; Wuest, J. D. *J. Org. Chem.* **1991**, *56*, 2284.

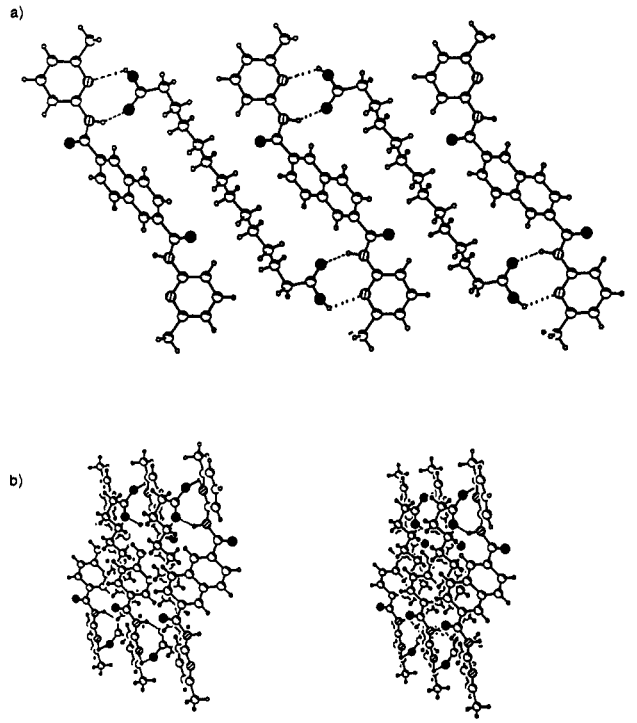

Figure 8. Crystal structure of 2–1,12-dodecanedicarboxylic acid: a, top view; b, stereoscopic representation of side view.

diamide **3** by 2.17 Å.[12] This should lead to a decrease in the angle between the subunits and the horizontal as represented in Figure 7b. Figure 8a,b shows the crystal structure formed between **2** and 1,12-dodecanedicarboxylic acid. The main features of the structure are the same as those in Figure 6, reflecting the dominant and organizing influence of the hydrogen-bond network. In this case, however, the hydrogen bonds are longer than those seen above (pyrN···H, 2.33 Å, O···H, 1.90 Å) and the bidentate 8-membered ring arrangement deviates substantially from planarity (Table III). Unlike the almost flat biphenyl receptor, there is a larger angle (51.8°) between the pyridine planes and that of the aromatic spacer. The hydrogen-bonded ribbon shows a small deviation from planarity with a 17.4° angle between the mean planes of the diacid and diamide. However, the slip angle formed between the polymethylene chain and horizontal (defined by a line drawn through the pyridine nitrogens) does indeed decrease to 60.2°, as represented in Figure 7b. The overall effect, compared to the biphenyl cocrystal (Figure 6), is a narrowing and elongation of the hydrogen-bonded ribbon structure.

1:1 Cocrystal of Naphthyl 2 and 1,8-Octanedicarboxylic Acid. The structure of the cocrystal formed between naphthyl receptor **2** and 1,8-octanedicarboxylic acid follows essentially the same features as the two cocrystals discussed immediately above. The structure (shown in Figure 9) is less ordered than those in Figures 6 and 8 and has a noncentrosymmetric *P*1 space group with $Z = 2$. The hydrogen-bonding network links the two components in a similar way to those of Figures 6 and 8 with normal hydrogen-bond lengths: O···H, ~2.0 Å; N···H, ~1.7 Å (see Table III). In this case, however, the closer matching in size of the diacid and diamide leads to an almost perpendicular positioning of the two subunits relative to horizontal (as represented in Figure 7c). The lower symmetry results in two distinct diacid molecules in each unit cell, and thus two slip angles of 89.0° and 77.6° can be measured. The two crystallographically unique naphthyl receptors are coplanar and virtually superimposable, and the pyridine and naphthyl planes in each take up an intermediate angle (~33°) to one other.

In contrast to the previous systems, this cocrystal demonstrates an alternative way for the structure to adapt to variations in the length of the components. In addition to the change in the slip angle, the hydrogen-bonded ribbon takes up a much less planar arrangement. The two distinct diacids deviate from the plane of the receptors by −30.9° and 40.3° (Figure 9b). This allows the interacting groups to avoid overly close contact independently of the slip angle.

(12) Estimated using MacroModel v.2. Still, W. C. Columbia University.

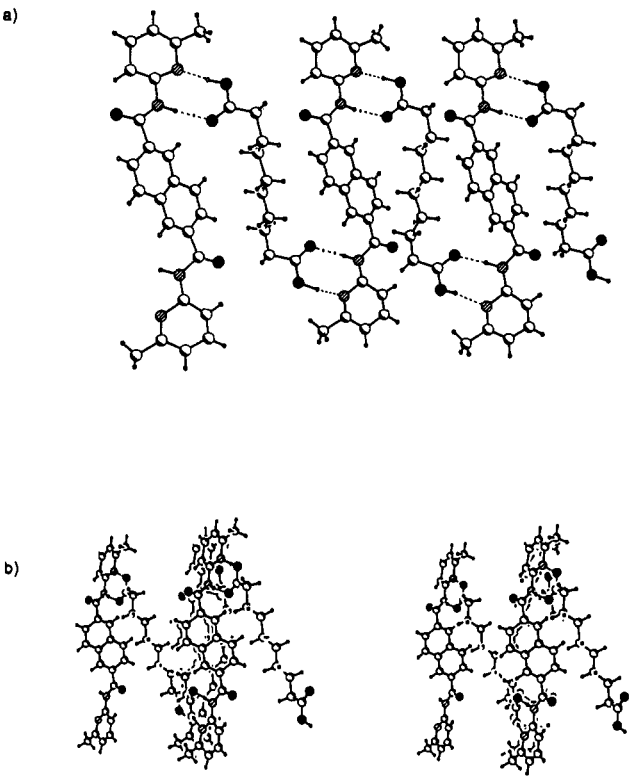

Figure 9. Crystal structure of 2–1,8-octanedicarboxylic acid: a, top view; b, stereoscopic representation of side view.

In summary, we have discovered a recurring hydrogen-bonding network that forms between aliphatic dicarboxylic acids and bis-amidopyridine derivatives. The H-bonding motif is retained despite changes in the sizes of both molecular components. Indeed, careful variation of the length of either the diacid or the diamide leads to almost predictable changes in the angular disposition of the different subunits. The development of molecules that can self-assemble into new solid-state materials is an area of recognized importance.[11] The ability to control both the formation and details of the structure of these materials offers an interesting approach to fine tuning electrical or optical properties in the crystal.

Experimental Details

1,4-Bis[[(6-methylpyrid-2-yl)amino]carbonyl]benzene (1). A solution of terephthaloyl dichloride (1.45 g, 7.14 mmol) in dry THF (35 mL) was added dropwise under a positive N_2 pressure to a stirred mixture of 2-amino-6-methylpyridine (2.4 g, 22.2 mmol) and potassium carbonate (4.92 g, 35.7 mmol) in dry THF (35 mL). The resulting mixture was stirred for 22 h at room temperature. The solvent was removed by rotary evaporation, and the residue was suspended in water and extracted with CH_2Cl_2. The organic phases were combined and washed with aqueous saturated sodium bicarbonate solution and brine, dried over magnesium sulfate, and filtered. The filtrate was concentrated to give a solid residue from which diamide (**1**) could be isolated by crystallization from a mixture of methanol methylene chloride hexanes as thin needles (2.3 g, 93%): mp 257–259 °C; ^{1}H NMR ($CDCl_3$) δ 8.55 (2 H, s, NH), 8.19 (2, H, d, J = 8 Hz, pyr-3H), 8.06 (4 H, s, tereph-H), 7.68 (2 H, t, J = 8 Hz, pyr-4H), 6.97 (2 H, d, J = 8 Hz, pyr-5H), 2.50 (6 H, s, Me); *m/e* 346 (M^+, 70), 317 (85), 239 (100), 211 (95), 194 (15), 183 (20), 135 (55), 104 (70), 92 (70), 76 (70), 65 (50), 49 (25); HRMS calcd for $C_{20}H_{18}N_4O_2$ (M^+) 346.1430, found 346.1430. Anal. Calcd for $C_{20}H_{18}N_4O_2 \cdot (0.1)CH_2Cl_2$: C, 68.03; N, 15.79; H, 5.17. Found: C, 67.77; N, 15.71; H, 5.26.

2,6-Bis[[(6-methylpyrid-2-yl)amino]carbonyl]naphthalene (2). To 2,6-naphthalenedicarboxylic acid (200 mg; 0.93 mmol) suspended in dry methylene chloride (15 mL) was added oxalyl chloride (0.8 mL) and

dimethylformamide (1 drop), and the mixture was stirred overnight at room temperature under a positive N_2 pressure. Volatile materials were evaporated off and the residue was further dried by standing under high vacuum for 1 h. The solid residue was taken into dry CH_2Cl_2 (10 mL) and dry THF (10 mL), and the solution was added dropwise under a positive N_2 pressure to a stirred mixture of 2-amino-6-methylpyridine (211 mg, 1.95 mmol) and cesium carbonate (1.516 g, 4.7 mmol) in dry THF (10 mL). The resulting mixture was heated with stirring under reflux conditions for 22 h. The solvent was evaporated off, and the residue was suspended in water and extracted with methylene chloride. The organic phases were combined and washed with aqueous saturated sodium bicarbonate solution and brine, dried over magnesium sulfate, and filtered, and the filtrate was concentrated to give the crude naphthyl diamide which was purified by chromatography on neutral alumina. Elution with 2/8 ethyl acetate/methylene chloride (v/v) and crystallization from CH_2Cl_2 hexanes gave 2,6-bis[[(6-methylpyrid-2-yl)amino]carbonyl]naphthalene (**2**) as thin needles (250 mg, 68%): mp 217–218 °C; ^{1}H NMR ($CDCl_3$) δ 8.67 (2 H, s, NH), 8.50 (2 H, s, naphth-2 and 5H), 8.25 (2 H, d, J = 8 Hz, pyr-3H), 8.08 (4 H, s, naphth-3,4,7, and 8H), 7.69 (2 H, t, J = 8 Hz, pyr-4H), 6.98 (2 H, d, J = 8 Hz, pyr-5H), 2.51 (6 H, s, Me); *m/e* 396 (M^+, 100), 367 (60), 289 (80), 261 (45), 233 (15), 217 (2.5), 198 (7), 169 (2.5), 154 (25), 126 (20), 92 (8); HRMS calcd for $C_{24}H_{20}N_4O_2$ (M^+) 396.1586, found 396.1586. Anal. Calcd for $C_{24}H_{20}N_4O_2$: C, 72.71, N, 14.13; H, 5.09. Found: C, 72.61; N, 14.07; H, 5.11.

4,4′-Bis[[(6-methylpyrid-2-yl)amino]carbonyl]biphenyl (3). A procedure similar to that for naphthyl **2** was used, employing biphenyl-4,4′-dicarboxylic acid (200 mg, 0.83 mmol), oxalyl chloride (0.8 mL) and dimethylformamide (1 drop). The resulting diacid chloride was dissolved in CH_2Cl_2 (10 mL) and THF (10 mL) and added to 2-amino-6-methylpyridine (188 mg, 1.74 mmol) and cesium carbonate (1.350 g, 4.15 mmol) in THF (10 mL). Purification by chromatography on neutral alumina using ethyl acetate CH_2Cl_2 (5/95 (v/v)) followed by crystallization from CH_2Cl_2 hexanes gave 4,4′-bis[[(6-methylpyrid-2-yl)amino]carbonyl]biphenyl (**3**) as thin needles (210 mg, 60%): mp 225–226 °C; ^{1}H NMR ($CDCl_3$) δ 8.57 (2 H, br s, NH), 8.22 (2 H, d, J = 8 Hz, pyr-3H), 8.06 (4 H, d, J = 8 Hz, biphen-2,2′,6, and 6′H), 7.78 (4 H, d, J = 8 Hz, biphen-3,3′,5, and 5′H), 7.68 (2 H, t, J = 8 Hz, pyr-4H), 6.97 (2 H, d, J = 8 Hz, pyr-5H), 2.51 (6 H, s, Me); *m/e* 422 (M^+, 100), 394 (75), 315 (98), 287 (30), 259 (20), 211 (10), 180 (85), 152 (70), 143 (50), 129 (8), 104 (10), 92 (10), 77 (9), 44 (7); HRMS calcd for $C_{26}H_{22}N_4O_2$ (M^+) 422.1743, found 422.1743. Anal. Calcd for $C_{26}H_{22}N_4O_2 \cdot (0.1)CH_2Cl_2$: C, 72.74; N, 13.01; H, 5.20. Found: C, 72.82; N, 13.10; H, 5.30.

1,4-Bis[4-[[(6-methylpyrid-2-yl)amino]carbonyl]phenyl]benzene (4). 1,1″-Terphenyl diacid chloride[13] (349 mg, 0.98 mmol) in dry THF (15 mL) was added dropwise under a positive N_2 pressure to a stirred mixture of 2-amino-6-methylpyridine (321 mg, 2.98 mmol) and potassium carbonate (540 mg, 3.91 mmol) in dry THF (13 mL). The resulting mixture was stirred under reflux conditions for 9 h. The solvent was evaporated off and the residue was suspended in brine and extracted with methylene chloride. The organic phases were combined and washed with aqueous saturated sodium bicarbonate solution and brine, dried over magnesium sulfate, and filtered. The filtrate was concentrated and purified by flash chromatography. Elution with methylene chloride/methanol (97/3 (v/v)) followed by crystallization from CH_2Cl_2/hexanes gave 1,4-bis-[4-[[(6-methylpyrid-2-yl)amino]carbonyl]phenyl]benzene (**4**) as fine needles (370 mg, 75%): mp 283–284 °C; ^{1}H NMR ($CDCl_3$) δ 8.29 (2 H, d, J = 8 Hz, pyr-3H), 8.09 (4 H, d, J = 8 Hz, *p*-terphen-2,2″,6 and 6″H), 7.79 (4 H, d, J = 8 Hz, *p*-terphen-3,3″,5, and 5″H), 7.78 (4 H, s, *p*-terphen-2′,3′,5′, and 6′H), 7.72 (2 H, t, J = 8 Hz, pyr-4H), 6.98 (2 H, d, J = 8 Hz, pyr-5H), 2.54 (6 H, s, Me); *m/e* 499 (M^+ + 1).

General Crystallization Procedure. Method A. The diacid (0.014 mmol) was added to a solution of the host (0.014 mmol) in dry methylene chloride (1–3 mL), and the resulting mixture was diluted with a small amount of hexanes (the turbidity point was not reached) and allowed to evaporate very slowly to give a good harvest of crystals suitable for X-ray analysis.

Method B. The diacid (0.014 mmol) was added to a solution of the host (0.014 mmol) in dry THF (1–3 mL), and the mixture was carefully deposited in a 10-mL vial, which was placed inside a sealed container (a wide-neck small bottle can be used) charged with hexanes. The pricipitant solvent (hexanes) was allowed to diffuse into the solution from the vapor phase. Crystal formation was slow, requiring, in general, several days to achieve a good harvest of suitable crystals.

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Registry No. 1, 129708-38-9; **1**·1,4-diacid, 129708-39-0; **2**, 134418-78-3; **2**·1,8-diacid, 136631-63-5; **2**·1,12-diacid, 136631-64-6; **3**, 134418-77-2; **3**·1,12-diacid, 136631-65-7; **4**, 136631-66-8.

Supplementary Material Available: Tables of crystal data, isotropic and anisotropic displacement coefficients, and bond lengths and angles (41 pages). Ordering information is given on any current masthead page.

(13) Campbell, T. W. *J. Am. Chem. Soc.* **1960**, *82*, 3126.