CRYSTAL GROWTH & DESIGN

Article

pubs.acs.org/crystal

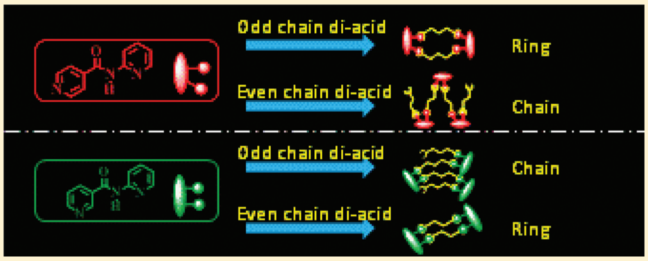
Establishing Supramolecular Control over Solid-State Architectures: A Simple Mix and Match Strategy

Christer B. Aakeröy,* Sheelu V. Panikkattu, Baillie DeHaven, and John Desper

Department of Chemistry, Kansas State University, 213 CBC Building, Manhattan, Kansas 66506, United States

S Supporting Information

ABSTRACT: With the help of robust principles of crystal engineering, it is possible to construct co-crystals where two or more different molecular entities coexist in the same crystalline lattice; the supramolecular assembly is driven by noncovalent interactions, most commonly by hydrogen bonds. We have synthesized two ditopic amide based ligands (*N*-(4-pyridin-2-yl)-isonicotinamide) and (*N*-(3-pyridin-2-yl)nicotinamide) and systematically established their binding preferences when faced with aliphatic dicarboxylic acids with an odd and even number of carbon atoms. Each ligand was co-crystallized with four odd and four even-chain dicarboxylic acids, and 13/16 reactions produced crystals suitable for single-crystal structure determination. On the basis of these results, it is clear that carefully selected systems can be manipulated to produce assemblies in the solid state with very precise control over topology and dimensionality. These ligands can be made to produce either 0-D or 1-D architectures simply by fine-tuning the choice of co-crystallizing agent in the supramolecular synthesis. This mix-and-match strategy allows us to mimic the reliability and versatility of covalent synthesis, in terms of successfully preparing a target with predetermined connectivity and metrics.



Crystal engineering[1,2] involves a combination of synthesis and structural chemistry and requires a detailed understanding of intermolecular interactions. Since any supramolecular synthesis by definition relies on reversible and relatively weak interactions (when compared to most covalent bonds), several problems must be overcome before we can attain a reliability and complexity that begin to approach what can be achieved in conventional covalent synthesis. Despite substantial progress in the last decades, it is still very challenging to utilize specific intermolecular interactions in the construction of solid-state assemblies with desired dimensionality and composition.[3] However, if we were able to develop a larger library of robust and predictable supramolecular synthons,[4] we would undoubtedly get closer to the goal of being able to attach specific molecular-recognition sites onto discrete molecules in such a way that we can preprogram subsequent assembly processes that carry over from solution into the solid state. Hydrogen bonds[5] largely depend on the chemical nature and electronic environment around the binding site, but at the supramolecular level, the relative orientation and geometry of the groups can determine shape, dimension, and metrics of the resulting noncovalent assembly. Therefore, synthesis of a desirable 3-D architecture in the solid state requires a careful choice of target building blocks with complementary geometries and binding patterns. Furthermore, it would be very useful if information about molecular geometry of individual covalent building blocks could be translated into a prediction (or at least an expectation) regarding the structure and properties of the resulting assembly. In short, we need a method for equipping each building block with a code that allows for a specific self-assembly to take place during supramolecular synthesis.[6] An example where molecular geometry has a profound effect on properties is readily observed in the melting points of even-number aliphatic dicarboxylic acids, which decrease monotonically with increasing number of methylene groups in the chain. The melting points of odd-number diacids, however, are significantly lower than their even-number analogues due to considerable differences in crystal structure/packing.[7,8] Similarly, melting points of co-crystals[9] of such diacids with bipyridyl molecules that differ in the total number of carbon atoms connecting the two pyridyl rings[10] display a pattern that can be correlated with the sum of carbon atoms in the repeating unit.

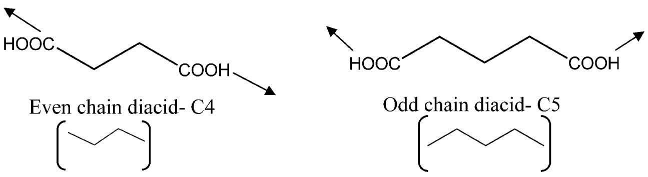
In the present study, we examine how two fundamentally different motifs, rings, and chains can be produced through the appropriate co-crystallizations of odd and even chain aliphatic dicarboxylic acids with two pyridine-based molecules differing in the relative orientation of the two hydrogen-bond acceptor sites. The two synthons employed in the assembly strategy are (a) the carboxylic acid···pyridine synthon[11,12] and (b) the carboxylic acid····2-aminopyridine synthon,[13] and since both have ample precedents in the literature, we can focus primarily on manipulating the relative positions of the binding sites in order to develop direct and rational links between molecular geometry and supramolecular structure. Even-chain diacids

Received: February 7, 2012
Revised: March 8, 2012
Published: March 28, 2012

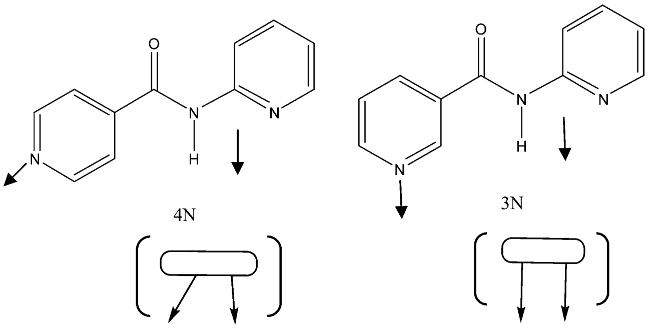
dx.doi.org/10.1021/cg300180b | *Cryst. Growth Des.* 2012, 12, 2579−2587

(referring to the number of carbon atoms in the chain) typically have their molecular recognition sites arranged in a colinear fashion, whereas in odd-chain diacids, they are positioned at an angle of approximately 120°, with respect to each other (Scheme 1). To complement these two types of orientation of hydrogen-bond donor sites, we will examine (*N*-(3-pyridin-2-yl)-nicotinamide), **3N**, where the hydrogen-bond acceptor sites are almost parallel and (*N*-(4-pyridin-2-yl)isonicotinamide), **4N**, where the binding sites are positioned at an angle of approximately 60° with respect to each other (Scheme 2).

Scheme 1



Scheme 2



If these complementary molecules form co-crystals, it is possible to envision different assemblies, depending upon how the donor/acceptor sites are arranged on the two participating tectons. In Scheme 3, we have outlined how the building-blocks could produce either 0-D rings or 1-D chains held together by alternating $-COOH\cdots N(py)$ and $-COOH\cdots N(py)-NH_2$ synthons. The results from the crystal structure determinations of 13 new co-crystals will be analyzed in the context of these postulated architectures.

EXPERIMENTAL SECTION

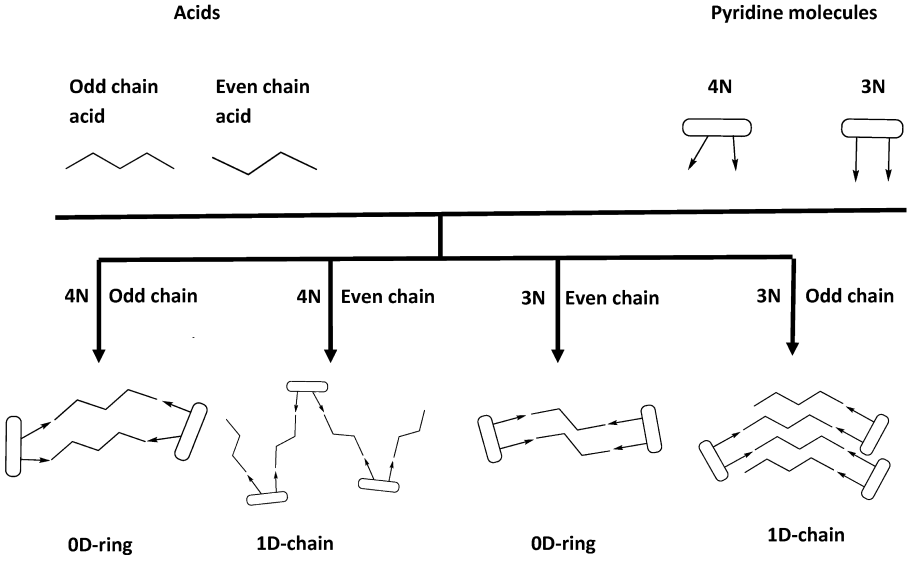
All precursors for the synthesis of **3N** and **4N** were purchased from Aldrich and used without further purification. Melting points were determined using Fischer-Johns Mel-Temp melting point apparatus and uncorrected. ^{1}H NMR spectra were recorded on Varian 400 MHz and 200 MHz spectrometer. IRs of compounds and co-crystals were taken on Nicolet 380 FT-IR.

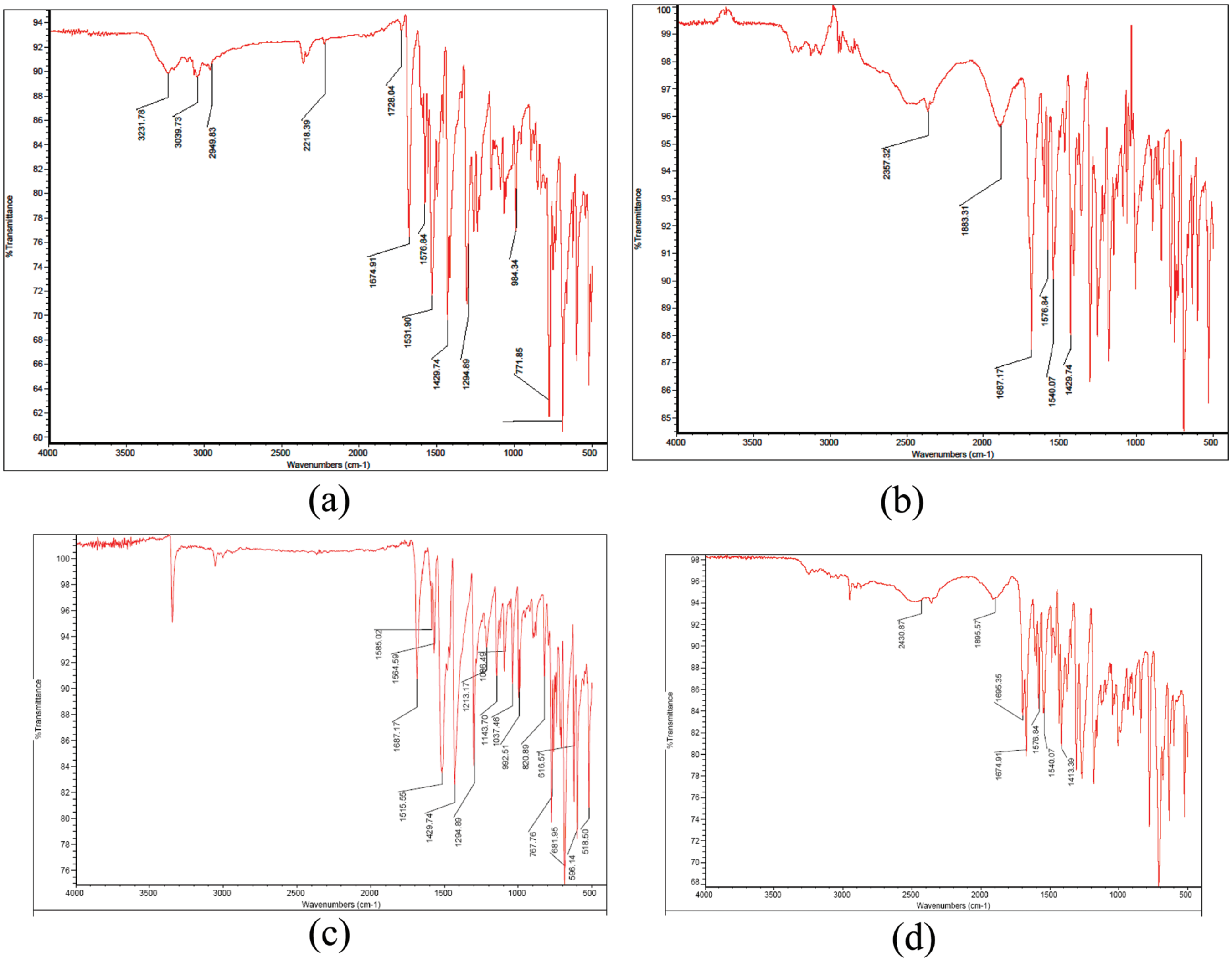
Synthesis of 4N and 3N. *(N-(4-pyridin-2-yl)isonicotinamide), **4N**.* The synthesis of **4N** was carried out using a modified procedure.[14] Isonicotinic acid (1.21 g, 10 mmol) and triethylamine (1.011 g, 10 mmol) were dissolved in 30 mL of chloroform. Thionyl chloride (1.189 g, 10 mmol) was added dropwise under a dinitrogen atmosphere maintaining the temperature between 5 and 10 °C. After the addition was complete, the mixture was heated under reflux for 3 h at the end of which a brown solution was obtained. The mixture was cooled to r.t., then a solution of amino pyridine (1.08 g, 10 mmol), triethylamine (1.01 g, 10 mmol), and acetonitrile (20 mL) was added in situ and stirred at r.t. overnight. The organic layer was washed with water, and the solvent was removed. Column chromatography gave a white powder as the product. Yield 41%, mp 138−140 °C (lit. 136−138 °C).[15] ^{1}H NMR (δH, 400 MHz, MeOD): 8.748 (s, 2H), 8.363 (s, 1H), 8.245 (d, *J* = 8.2 Hz, 1H), 7.902−7.801 (m, 3H), 7.208−7.153 (m, 1H).

*(N-(3-pyridin-2-yl)nicotinamide), **3N**.* Nicotinic acid (1.21 g, 10 mmol) and triethylamine (1.011 g, 10 mmol) were dissolved in 30 mL of chloroform. Thionyl chloride (1.189 g, 10 mmol) was added dropwise under a dinitrogen atmosphere maintaining the temperature between 5 and 10 °C. After the addition was complete, the mixture was heated under reflux for 3 h at the end of which a brown solution was obtained. The mixture was cooled to r.t., then a solution of amino pyridine (1.08 g, 10 mmol), triethylamine (1.01 g, 10 mmol), and acetonitrile (20 mL) was added in situ and stirred at r.t. overnight. The organic layer was washed with water, and the solvent was removed, followed by column chromatography to yield an off-white powder as the product. Yield 35%, mp 142−145 °C (lit. 141−143 °C).[16] ^{1}H NMR (δH, 400 MHz, DMSO): 11.094 (s, N−H 1H), 9.135 (s, 1H), 8.761 (d, 1H), 8.409 (d, 1H), 8.340 (d, 1H), 8.120 (d, 1H), 7.845 (t, 1H), 7.541 (t, 1H), 7.189 (t, 1H).

Synthesis of Co-crystals of 4N and 3N. **4N** and **3N** were co-crystallized with four odd-chain diacids (malonic, glutaric, pimelic, and azelaic acid) and four even-chain diacids (succinic, adipic, suberic. and sebacic acid). The reactions included both a melt and a solvent-assisted

Scheme 3. Possible Architectures from Building Blocks 3N and 4N





(a) (b)

(c) (d)

Figure 1. (a) IR spectrum of **4N**; (b) IR of the product resulting from a combination of **4N** and pimelic acid (**4N-PA**) showing two broad stretches near the 1850 and 2500 cm^{-1} regions; (c) IR spectrum of **3N**; (d) IR of the product resulting from the combination of **3N** and adipic acid (**3N-AA**) showing two broad stretches near the 1850 and 2450 cm^{-1} regions.

grinding experiment after which the resulting powder/product was characterized using IR spectroscopy to determine if a co-crystal had formed. A total of sixteen experiments were performed, and all IR spectra displayed broad stretches near 1850 and 2450 cm^{-1} (Figure 1) indicative of intermolecular O−H···N hydrogen bonds confirming co-crystal formation in every case. Stoichiometric amounts of base and acid (1:1) were subsequently dissolved separately in suitable solvents and then mixed together. The resulting solution was warmed and then set aside for slow evaporation at room temperature. Crystals suitable for single-crystal X-ray diffraction were obtained for 13 of the 16 products.

(N-(4-pyridin-2yl)isonicotinamide) Glutaric Acid (1:1), ***4N-GA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with glutaric acid (6.6 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent rod-like crystals were obtained within 20 days. Mp 127−129 °C.

(N-(4-pyridin-2yl)isonicotinamide) Pimelic Acid (1:1), ***4N-PA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with pimelic acid (8.0 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent needle-like crystals were obtained. Mp 123−125 °C.

(N-(4-pyridin-2yl)isonicotinamide) Azelaic Acid (1:1), ***4N-AzA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with azelaic acid (9.41 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent needle-like crystals were formed after 45 days. Mp 92−95 °C.

(N-(4-pyridin-2yl)isonicotinamide) Succinic Acid (1:1), ***4N-SA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with succinic acid (5.9 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent needles were obtained. Mp 122−125 °C.

(N-(4-pyridin-2yl)isonicotinamide) Adipic Acid (1:1), ***4N-AA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with adipic acid (7.31 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent block-shaped crystals were formed. Mp 142−145 °C.

(N-(4-pyridin-2yl)isonicotinamide) Suberic Acid (1:1), ***4N-SuA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with suberic acid (8.71 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent rod-shaped crystals were obtained within few weeks. Mp 133−135 °C.

(N-(4-pyridin-2yl)isonicotinamide) Sebacic Acid (1:1), ***4N-SeA***. A solution of **4N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with sebacic acid (10.11 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent rod-like crystals were formed. Mp 104−107 °C.

(N-(3-pyridin-2yl)nicotinamide) Malonic Acid (1:1), ***3N-MA***. A solution of **3N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with malonic acid (5.23 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent rod-like crystals were obtained within few weeks. Mp 125−127 °C.

(N-(3-pyridin-2yl)nicotinamide) Pimelic Acid (1:1), ***3N-PA***. A solution of **3N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was

Table 1. Hydrogen Bond Geometries of the Co-Crystals of 4N[a]

structure	D−H···A	D-H (Å)	H···A (Å)	D···A (Å)	D−H−N (deg)
4N-GA	O31 H31 N11	0.962(17)	1.712(17)	2.6713(11)	174.6(14)
	N17 H17 O36_#1	0.855(14)	2.164(14)	3.0103(11)	170.7(13)
	O35 H35 N21_#1	0.898(15)	1.786(15)	2.6570(11)	162.9(15)
4N-PA	N17 H17 O32	0.90(3)	2.08(3)	2.970(3)	173(2)
	O31 H31 N21	0.95(3)	1.74(3)	2.679(3)	169(3)
	O37 H37 N11	1.10(3)	1.57(3)	2.665(3)	172(2)
4N-AzA	O31 H31 N21	0.942(15)	1.738(15)	2.6756(11)	173.6(13)
	N17 H17 O32	0.862(14)	2.063(14)	2.9200(12)	172.7(12)
	O39 H39 N11_#1	0.957(15)	1.785(15)	2.7413(12)	176.3(13)
4N-SA	N17_1 H17_1 O52_1	0.89(2)	2.12(2)	3.005(2)	174(2)
	N17_2 H17_2 O52_2	0.92(2)	2.13(2)	3.050(2)	174.8(19)
	N17_3 H17_3 O52_3	0.91(2)	2.09(2)	3.001(2)	176.5(18)
	O51_1 H51_1 N21_1	0.97(2)	1.70(2)	2.661(2)	170(2)
	O51_2 H51_2 N21_2	0.96(2)	1.75(2)	2.691(2	165(2)
	O51_3 H51_3 N21_3	1.00(2)	1.69(2)	2.681(2)	170(2)
	O54_1 H54_1 N41_1	0.98(2)	1.72(2)	2.685(2)	171(2)
	O54_2 H54_2 N41_2	0.97(2)	1.74(2)	2.679(2)	162.4(19)
	O54_3 H54_3 N41_3	0.94(2)	1.79(2)	2.702(2)	165(2)
	O61_1 H61_1 N11_1	0.96(2)	1.72(2)	2.667(2)	173(2)
	O61_2 H61_2 N11_2	0.93(2)	1.75(2)	2.668(2)	170(2)
	O61_3 H61_3 N11_3	0.97(2)	1.72(2)	2.683(2)	173(2)
	O64_1 H64_1 N31_1_#1	0.90(2)	1.80(3)	2.688(2)	168(2)
	O64_2 H64_2 N31_2_#1	0.93(2)	1.74(2)	2.670(2)	175(2)
	O64_3 H64_3 N31_3_#1	0.94(3)	1.72(3)	2.659(2)	170(2)
4N-AA	N17 H17 O42	0.856(18)	2.058(18)	2.9131(14)	177.4(17)
	O31 H31 N11	0.98(2)	1.73(3)	2.6945(15)	169(2)
	O41 H41 N21	0.94(2)	1.74(2)	2.6772(14)	172.3(19)
4N-SuA	O31 H31 N11	1.03(2)	1.69(2)	2.7133(15)	179.3(18)
	N17 H17 O39_#1	0.850(16)	2.077(16)	2.9228(13)	173.6(14)
	O38 H38 N21_#2	1.120(17)	1.541(17)	2.6583(13)	175.3(14)
4N-SeA	O31 H31 N11	0.999(15)	1.674(15)	2.6693(12)	174.2(13)
	N17 H17 O41_#1	0.855(14)	2.002(14)	2.8556(12)	176.2(13)
	O40 H40 N21_#2	1.013(15)	1.626(15)	2.6327(12)	172.0(13)

[a] Symmetry Codes: 4N−GA: #1 $1 - x, -y, 1 - z$. 4N−PA: #1 $2.5 - x, -0.5 + y, 1.5 -$ z. 4N−AzA: #1 $-1 - x, -y, 1 - z$. 4N−SA: #1 $-1 + x, -1 + y, z$. 4N−SuA: #1 $0.5 - x, -0.5 + y, 1.5 - z$. #2 $0.5 - x, 0.5 + y, 1.5 - z$. 4N−SeA: #1 $0.5 - x, 0.5 + y, 1.5 - z$. #2 $0.5 - x, -0.5 + y, 1.5 - z$.

mixed with pimelic acid (8.0 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent rod-like crystals were obtained. Mp 119−120 °C.

(N-(3-pyridin-2yl)nicotinamide) Azelaic Acid (1:1), ***3N-AzA.*** A solution of **3N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with azelaic acid (9.41 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Needle-like crystals were formed. Mp 90−93 °C.

(N-(3-pyridin-2yl)nicotinamide) Succinic Acid (1:1), ***3N-SA.*** A solution of **3N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with succinic acid (5.9 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent needle-shaped crystals were obtained. Mp 145−147 °C.

(N-(3-pyridin-2yl)nicotinamide) Adipic Acid (1:1), ***3N-AA.*** A solution of **3N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with adipic acid (7.31 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Transparent block-shaped crystals were formed. Mp 140−142 °C.

(N-(3-pyridin-2yl)nicotinamide) Sebacic Acid (1:1), ***3N-SeA.*** A solution of **3N** (10 mg, 0.05 mmol) in 2 mL of ethyl acetate was mixed with sebacic acid (10.11 mg, 0.05 mmol) in 2 mL of ethyl acetate and warmed. Needle-shaped crystals were formed. Mp 104−106 °C.

X-ray Crystallography. X-ray data were collected on a Bruker SMART APEX II (for **4A-GA**, **4N-SuA**, **3N-AA**, **4N-AzA**, **3N-SeA**, and **3N-MA** or Bruker Kappa APEX II CCD (for **4N-PA**, **4N-SeA**, **4N-AA**, **3N-SA**, **4N-SA**, **3N-PA**, and **3N-AzA**) diffractometer at 120 K using, in all cases, a fine-focus molybdenum K_α tube. Data were collected using APEX2[17a] software. Initial cell constants were found by small widely separated matrix runs. Scan speed and scan width were chosen based on scattering power and peak rocking curves. Unit cell constants and orientation matrix were improved by least-squares refinement of the reflections threshold from the entire data set. Integration was performed with SAINT,[17b] using this improved unit cell as a starting point. Precise unit cell constants were calculated in SAINT from the final merged data set. Lorenz and polarization corrections were applied. Laué symmetry, space group, and unit cell contents were found with XPREP. Data were reduced with SHELXTL.[17c] The structures were solved in all cases by direct methods without incident. Coordinates for the amide and carboxylic acid protons were allowed to refine; all other hydrogen atoms were assigned to idealized positions and were allowed to ride. Heavy atoms were refined with anisotropic thermal parameters. Selected hydrogen bond geometries are shown in Tables 1 (**4N**) and 2 (**3N**), and crystallographic parameters of **4N** and **3N** co-crystals are listed in Tables 3 and 4, respectively.

■ RESULTS

Three crystal structures (out of four possible) were obtained from combinations of **4N** with an odd-chain diacid; **4N-GA**, **4N-PA**, and **4N-AzA**. No proton transfer was observed, which was consistent with the information obtained from the IR data, Table 5.

In the structure of **4N-GA**, the two primary intermolecular interactions (−COOH···N(py) and −COOH···N(py)-NH_2),

Table 2. Hydrogen Bond Geometries of the Co-Crystals of 3N[a]

structure	D–H···A	D–H (Å)	H···A (Å)	D···A (Å)	D–H–N (deg)
3N-MA	N17 H17 O32	0.921(16)	2.225(16)	3.1144(13)	162.1(13)
	O31 H31 N21	0.969(16)	1.647(16)	2.5945(13)	164.8(14)
	O33 H33 N11_#1	0.971(17)	1.666(17)	2.6344(13)	174.9(15)
3N-PA	N17_1 H17_1 O32_1	0.90(2)	2.08(2)	2.975(2)	172.3(19)
	N17_2 H17_2 O32_2	0.89(2)	2.06(2)	2.943(2)	172(2)
	O31_1 H31_1 N21_1	1.04(2)	1.63(2)	2.6672(19)	172.5(19)
	O31_2 H31_2 N21_2	0.88(2)	1.78(2)	2.6611(19)	176(2)
	O37_1 H37_1 N11_2	0.91(2)	1.77(2)	2.672(2)	172.1(19)
	O37_2 H37_2 N11_1_#1	1.01(2)	1.64(2)	2.647(2)	172.7(18)
3N-AzA	O31 H31 N11	1.00(2)	1.71(2)	2.7055(17)	171.3(18)
	N17 H17 O40_#1	0.906(19)	2.074(19)	2.9785(17)	176.7(16)
	O39 H39 N21_#2	0.95(2)	1.71(2	2.6491(17)	169.6(19
3N-SA	O31 H31 N11	0.96(2)	1.70(2)	2.6581(19)	172(2)
	N17 H17 O35_#1	0.85(2)	2.12(2)	2.9674(19)	170(2)
	O34 H34 N21_#1	0.90(2)	1.79(2)	2.6702(18)	169(2)
3N-AA	O31 H31 N11	0.909(17)	1.780(17)	2.6832(12)	172.0(14)
	N17 H17 O36_#1	0.924(14)	2.009(14)	2.9271(11)	172.2(12)
	O37 H37 N21_#1	0.970(17)	1.721(17)	2.6785(11)	168.6(14)
3N-SeA	O31 H31 N11	0.898(18)	1.795(18)	2.6898(14)	174.4(16)
	O41 H41 N21_#1	0.89(2)	1.79(2)	2.6579(14)	166.3(18)
	N17 H17 O42_#1	0.88	2.05	2.9131(13)	168.0

[a] Symmetry Codes: 3N–MA: #1 *x*,1 − *y*,−0.5 + z. 3N–PA: #1 −2 + x, 1 + y, 1 + z. 3N–AzA: #1 −0.5 −*x*, 0.5 + *y*, 0.5 − *z*. #2 −0.5 − *x*, −0.5 + *y*, 0.5 − *z*. 3N–SA: #1 −*x*, 1 − *y*, 1 − *z*. 3N–AA: #1 −*x*, 1 − *y*, −*z*. 3N–SeA: #1 2 − *x*, 1 − *y*, 1 − *z*.

Table 3. Crystallographic Parameters of 4N Co-Crystals

	4N-PA	4N-GA	4N-SeA	4N-AA	4N-SA	4N-AzA	4N-SuA
formula moiety	$(C_{11}H_9N_3O)$ $(C_7H_{12}O_4)$	$(C_{11}H_9N_3O)$ $(C_5H_8O_4)$	$(C_{11}H_9N_3O)$ $(C_{10}H_{18}O_4)$	$(C_{11}H_9N_3O)$ $(C_6H_{10}O_4)$	$(C_{11}H_9N_3O)$ $(C_4H_6O_4)$	$(C_{11}H_9N_3O)$ $(C_9H_{16}O_4)$	$(C_{11}H_9N_3O)$ $(C_8H_{14}O_4)$
empirical formula	$C_{18}H_{21}N_3O_5$	$C_{16}H_{17}N_3O_5$	$C_{21}H_{27}N_3O_5$	$C_{17}H_{19}N_3O_5$	$C_{15}H_{15}N_3O_5$	$C_{20}H_{25}N_3O_5$	$C_{19}H_{23}N_3O_5$
molecular weight	359.38	331.33	401.46	345.35	317.30	387.43	373.40
color, habit	colorless plate	colorless prism	colorless prism	colorless prism	colorless prism	colorless prism	colorless prism
crystal system	monoclinic	triclinic	monoclinic	monoclinic	triclinic	triclinic	monoclinic
space group, *Z*	*P*2(1)/*n*, 4	$P\bar{1}$, 2	*P*2(1)/*n*, 4	*P*2(1)/*c*, 4	$P\bar{1}$, 12	$P\bar{1}$, 2	*P*2(1)/*n*, 4
a (Å)	7.5855(12)	5.1663(6)	11.0319(11)	11.9508(11)	11.2578(7)	5.6707(3)	11.4438(7)
b (Å)	21.675(3)	9.9211(10)	9.9500(9)	19.8752(19)	19.6623(11)	10.8221(6)	10.1874(5)
c (Å)	11.1031(16)	15.8829(17)	18.7354(18)	7.3996(8)	19.8130(12)	17.0848(10)	16.5671(9)
α (deg)	90.00	75.339(3)	90.00	90.00	93.236(3)	104.161(2)	90.00
β (deg)	96.050(9)	82.551(3)	90.323(4)	105.384(4)	91.236(3)	94.599(2)	95.023(3)
γ (deg)	90.00	78.820(3)	90.00	90.00	90.298(3)	104.840(2)	90.00
volume ($Å^3$)	1815.4(5)	769.84(14)	2056.5(3)	1694.6(3)	4377.6(5)	971.22(9)	1924.02(18)
X-ray wavelength	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
μ (mm^{-1})	0.097	0.108	0.093	0.101	0.111	0.096	0.094
absorption corr	none	none	none	none	multiscan	none	none
reflections							
collected	16 010	15 920	23 866	29 113	88 500	22 510	23 456
independent	4889	5171	6752	6437	27578	6431	6179
observed	2078	3934	4902	3940	14 241	4786	4312
threshold expression	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$
R_1 (observed)	0.0558	0.0470	0.0452	0.0511	0.0646	0.0486	0.0488
wR_2 (all)	0.1850	0.1416	0.1240	0.1626	0.1850	0.1509	0.1507
Δ*ρ* max/min	0.238/−0.185	0.341/−0.340	0.292/−0.271	0.325/−0.253	0.433/−0.386	0.400/−0.272	0.236/−0.214

Table 1, combine to give rise to a tetrameric 0-D ring, (Figure 2a). The very same synthons and overall supramolecular motif were also found in the crystal structure of **4N-AzA** (Figure 2b). The one outlier in this series of three is the structure of **4N-PA**, where the building blocks were assembled into an infinite 1-D chain (Figure 3).

All four reactions between **4N** and an even-chain diacid produced crystals suitable for single-crystal structure analysis;

Table 4. Crystallographic Parameters of 3N Co-Crystals

	3N-AA	3N-SeA	3N-MA	3N-SA	3N-PA	3N-AzA
formula moiety	$(C_{11}H_9N_3O)$ $(C_6H_{10}O_4)$	$(C_{11}H_9N_3O)$ $(C_{10}H_{18}O_4)$	$(C_{11}H_9N_3O)$ $(C_3H_4O_4)$	$(C_{11}H_9N_3O)$ $(C_4H_6O_4)$	$(C_{11}H_9N_3O)$ $(C_7H_{12}O_4)$	$(C_{11}H_9N_3O)$ $(C_9H_{16}O_4)$
empirical formula	$C_{17}H_{19}N_3O_5$	$C_{21}H_{27}N_3O_5$	$C_{14}H_{13}N_3O_5$	$C_{15}H_{15}N_3O_5$	$C_{18}H_{21}N_3O_5$	$C_{20}H_{25}N_3O_5$
molecular weight	345.35	401.46	303.27	317.30	359.38	387.43
color, habit	yellow plate	yellow prism	gold plate	gold plate	colorless prism	colorless prism
crystal system	triclinic	triclinic	monoclinic	triclinic	triclinic	monoclinic
space group, Z	$P\bar{1}$, 2	$P\bar{1}$, 2	$C2/c$, 8	$P\bar{1}$, 2	$P\bar{1}$, 4	$P2(1)/n$, 4
a (Å)	8.9361(8)	7.5703(8)	31.2168(18)	4.8289(5)	7.5711(5)	13.5588(13)
b (Å)	9.8031(9)	9.6882(10)	4.7940(3)	11.1223(11)	11.9820(8)	9.4660(10)
c (Å)	9.8270(9)	13.9977(14)	22.7743(13)	14.3787(14)	20.1758(13)	15.8384(15)
α (deg)	83.130(2)	85.455(4)	90.00	67.856(4)	82.560(4)	90.00
β (deg)	74.507(3)	81.210(4)	128.375(2)	89.550(4)	80.081(4)	105.946(4)
γ (deg)	79.462(2)	79.358(4)	90.00	87.878(4)	85.195(4)	90.00
volume (Å^3)	813.31(13)	995.74(18)	2671.9(3)	714.79(12)	1784.2(2)	1954.6(3)
X-ray wavelength	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
μ (mm^{-1})	0.105	0.096	0.117	0.113	0.099	0.096
absorption corr	none	none	none	none	multiscan	multiscan
reflections						
collected	21 410	13 375	16 865	10 209	42 683	15 672
independent	5266	5863	4729	4585	11 575	6247
observed	4361	4414	3553	3013	6192	3981
threshold expression	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$
R_1 (observed)	0.0465	0.0519	0.0433	0.0576	0.0622	0.0604
wR_2 (all)	0.1432	0.1508	0.1241	0.1907	0.1777	0.1813
$\Delta\rho$ max/min	0.551/−0.240	0.436/−0.297	0.463/−0.246	0.360/−0.381	0.322/−0.316	0.316/−0.321

Table 5. IR Carbonyl C═O Stretch and O−H···N Bands for Co-Crystals of 3N and 4N

compd	O−H···N stretches (cm^{-1})	C═O stretch (cm^{-1})
4N-GA	2492; 1862	1687
4N-PA	2357; 1883	1687
4N-AzA	2488; 1875	1683
4N-SA	2481; 1890	1685
4N-AA	2492; 1862	1687
4N-SuA	2471; 1907	1683
4N-SeA	2483; 1877	1684
3N-MA	2439; 1871	1701
3N-PA	2487; 1877	1686
3N-AzA	2495; 1887	1684
3N-SA	2406; 1887	1676
3N-AA	2430; 1895	1695
3N-SeA	2509; 1886	1683

(**4N-SA**), (**4N-AA**), (**4N-SuA**) and (**4N-SeA**). As was the case with **4N** and odd-chain acids, the main intermolecular interactions were −COOH···N(py) and −COOH···N(py)-NH_2 synthons, Table 1. The combination of these synthetic vectors resulted, in each case, in infinite 1-D chains, Figure 4a−d.

Three of the four reactions between an odd-chain diacid and **3N** produced crystals suitable for single-crystal structure analysis; **3N-MA**, **3N-PA**, and **3N-AzA**. All three of them contained infinite 1-D chains constructed by a combination of alternating −COOH···N(py) and −COOH···N(py)-NH_2 hydrogen-bond interactions, (Figure 5a−c).

Finally, we obtained structural data for three of the four products obtained when **3N** was allowed to react with even-chain acids; **3N-SA**, **3N-AA**, and **3N-SeA** (Figure 6). Again, the −COOH···N(py) and −COOH···N(py)-NH_2 synthons were the primary intermolecular interactions, Table 2. All three structures contained tetrameric 0-D rings, (Figure 6a−c).

■ DISCUSSION

Combining **3N** and **4N** in stoichiometric amounts with a series of aliphatic diacids can in principle offer three different outcomes, i.e., a co-crystal, a salt, or no reaction at all. Through a systematic IR screen, it is possible to anticipate the outcome before any single crystal data becomes available. For instance, an IR spectrum for a co-crystal shows two very prominent broad O−H···N stretches around the 1850−2500 cm^{-1} region (Figures 1b and 1d; Table 5), and the observed carbonyl C═O stretch for the acid is always above 1675 cm^{-1} (Table 5).

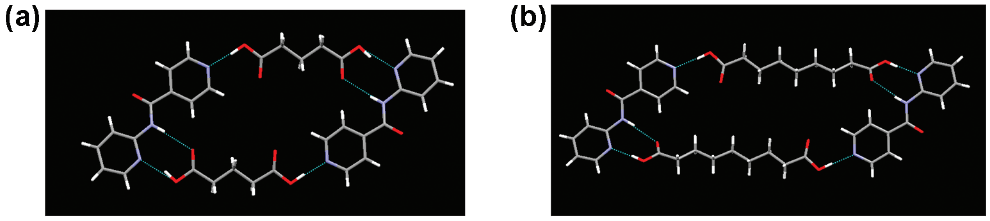


Figure 2. (a) Tetrameric ring in the crystal structure of **4N-GA**. (b) Tetrameric ring in the crystal structure of **4N-AzA**.

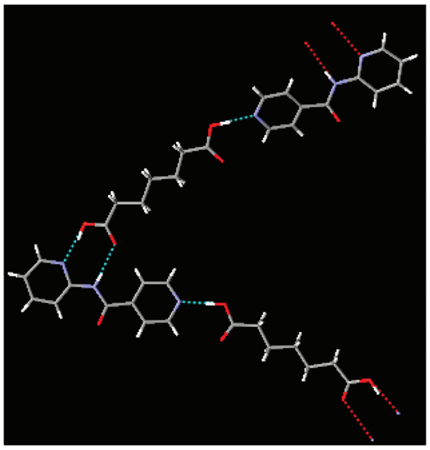


Figure 3. One-dimensional hydrogen-bonded chain in the crystal structure of **4N-PA**.

On the basis of the IR data alone, we could establish that all 16 experiments yielded co-crystals. This assessment was also supported by the result that we obtained from crystallographic data for 13 of these 16 compounds; all were found to be co-crystals. Thus, the IR data is very consistent with the single crystal analysis and can be considered as a reliable tool to detect co-crystal formation.

All 13 crystal structures are assembled through acid−COOH···N(py) and −COOH···N(py)-NH_2 heterosynthons as the primary building block. Two distinctly different types of assemblies i.e., chains (0-D) and rings (1-D) were obtained depending upon the choice of acid−base pair in the co-crystallization experiments.

The following combinations, **4N**-odd acid (pimelic, glutaric, and azelaic acid) and **3N**-even acid (succinic, adipic, and sebacic acid), produce 0-D ring architectures in five out of six structures. The only exception in this series was **4N** with pimelic acid, which gave a chain instead of the expected/intended ring. This preference for a cyclic assembly in five of six structures represents a clear pattern of behavior, especially since we are dealing with molecules with considerable molecular flexibility coupled with the fact that the synthesis is driven by relatively weak and reversible interactions. There is no obvious reason why **4N-PA** contains infinite chains, but it is possible that a ring-containing polymorph could appear if this compound were subjected to a rigorous polymorph screen.

In the combinations of **4N**-even acid (succinic, adipic, suberic, and sebacic acid) and **3N**-odd acid (malonic, pimelic, and azelaic acid), we found 1-D chain architectures in all seven of the crystal structures that we were able to obtain. All the chains are assembled through a combination of −COOH···N-(py) and −COOH···N(py)-NH_2 hydrogen bonds, and the two components alternate throughout each chain. It is interesting to note that in 12 out of 13 crystal structures, the carbonyl group and pyridine N moiety are arranged in an anti-configuration with respect to each other with an exception in the structure of

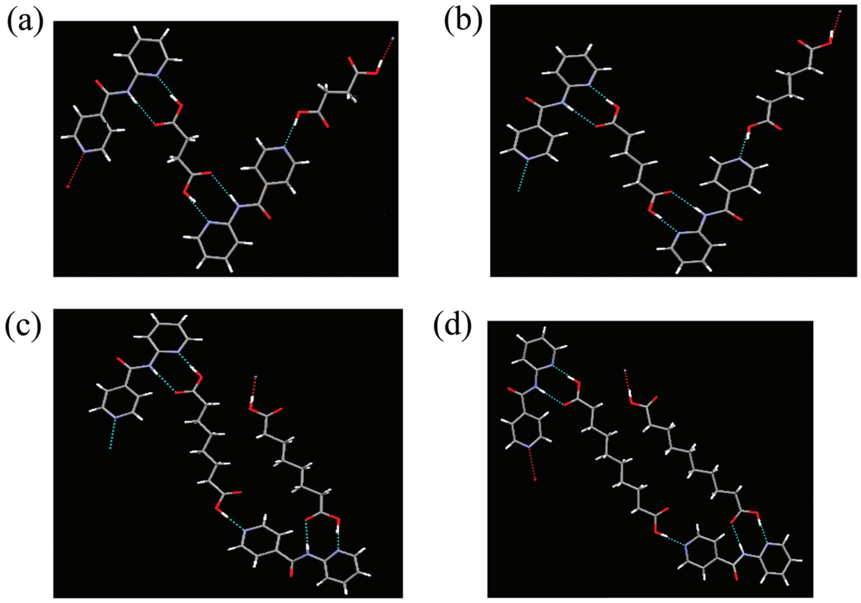


Figure 4. Section of the infinite 1-D chain in the crystal structure of (a) **4N-SA**; (b) **4N-AA**; (c) **4N-SuA**; and (d) **4N-SeA**.

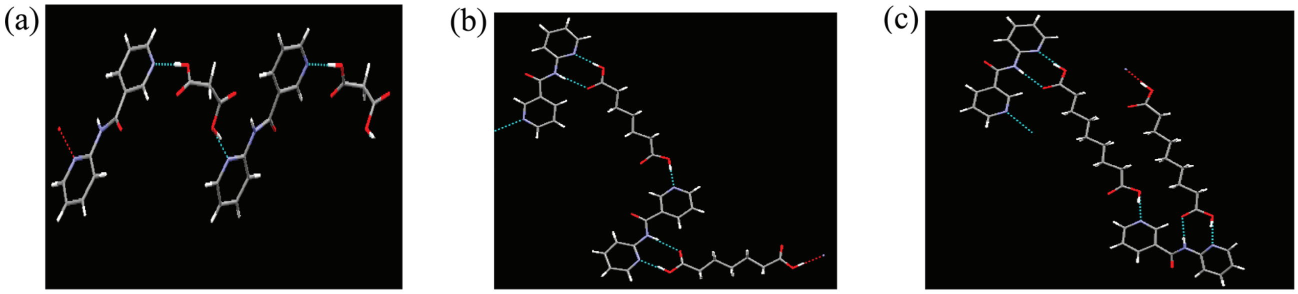


Figure 5. View of the infinite 1-D chain in the crystal structure of (a) **3N-MA**; (b) **3N-PA**; and (c) **3N-AzA**.

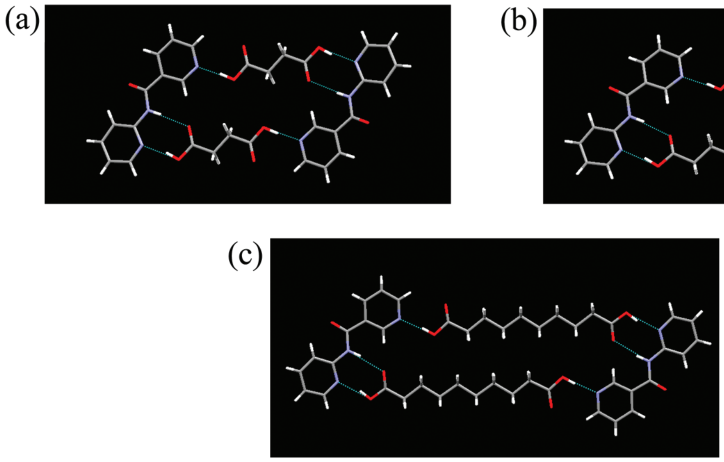


Figure 6. Tetrameric hydrogen bonded rings in the crystal structures of (a) **3N-SA**; (b) **3N-AA**; and (c) **3N-SeA**.

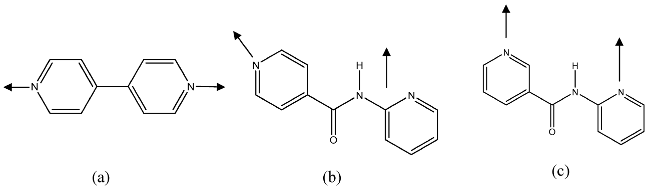
Table 6. Result of Co-Crystallization Experiments of 4N and 3N with Several Even and Odd Chain Diacids

ligand	diacids	chains	rings
4-N	odd-number	1/3	2/3
3-N	even-number	0	3/3
4-N	even-number	4/4	0
3-N	odd-number	3/3	0

3N-malonic acid co-crystal (Figure 5a) where they are syn with respect to each other; however, this discrepancy does not affect the overall assembly, and chains do appear in this structure as expected. A summary of the results is shown in Table 6.

On the basis of the success of our results, we can conclude that the number of carbon atoms within the acid, combined with the precise orientation of the binding sites in the co-crystallizing agent, does indeed control the resulting supramolecular assembly in a very reliable manner. Despite the fact that any number of motifs and assemblies could in principle be formed when **3N** and **4N** are brought together with aliphatic diacids, there is a remarkable consistency to the way in which these flexible molecules recognize, bind, and organize themselves in the solid state. Only two different primary motifs can be identified, rings and chains, and to a very large extent (twelve of thirteen cases), the appearance of one or the other architecture can be rationalized a priori. Such correlations are not always going to be found; for example, attempts to find links between the appearance of tapes or rings and the number of atoms in the participating carbon chains have been made using 4,4′-bipyridyl and carboxylic acids as a test-bed. However, in that case, it was not possible to deduce any obvious connection between the molecular and the supramolecular.[18] It was finally concluded that tape-like structures were preferably formed irrespective of the odd−even nature of the acid. The notable difference between the bipy-system and our **3N**/**4N** compounds is in the relative orientation of the binding sites on the molecule. In the case of 4,4-bipyridine, the two pyridyl binding sites are linear with respect to each other, whereas in the case of **4N** and **3N**, the pyridyl nitrogen and amino pyridine binding sites are at an angle (Scheme 4). This difference in the geometry of the binding sites controls the overall outcome of the assembly process, which is evident from our results. The connections between structural packing and solid-state derived properties are well-known, but it is interesting to note that such fundamental differences extend from homomeric solids[19] to heteromeric co-crystals. Furthermore, the relative orientations of the synthetically important binding sites are clearly dictated by inherent molecular geometries, but these differences can be taken advantage of in a constructive sense when bringing discrete molecular building blocks together into extended solid-state architectures.

Scheme 4. From Discrete Building Blocks to Rings and Chains.



■ ASSOCIATED CONTENT

Ⓢ Supporting Information

CIF files of the crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: aakeroy@ksu.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from NSF (CHE-0957607).

■ REFERENCES

(1) Aakeröy, C. B. *Acta Crystallogr., Sect. B: Struct. Sci.* **1997**, *53*, 569−586.

(2) (a) Braga, D. *Chem. Commun.* **2003**, 2751−2754. (b) Aakeröy, C. B.; Champness, N.; Janiak, C. *CrystEngComm* **2010**, *12*, 22−43.

(3) (a) Aakeröy, C. B.; Desper, J.; Fasulo, M.; Hussain, I.; Brock, L.; Schultheiss, N. *CrystEngComm* **2008**, *10*, 1816−1821. (b) Aakeröy, C. B.; Chopade, P.; Ganser, C.; Desper, J. *Chem. Commun.* **2011**, *47*, 4688−4690.

(4) (a) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: Amsterdam, The Netherlands, 1989. (b) Lehn, J. M. *Supramolecular Chemistry*; VCH: Weinheim, Germany, 1995. (c) Desiraju, G. R *Perspectives in Supramolecular Chemistry*; Wiley: Chichester, U.K., 1995; Vol. 2.

(5) (a) Aakeröy, C. B.; Salmon, D. J. *CrystEngComm* **2005**, *7*, 439. (b) MacGillivray, L. R. *CrystEngComm* **2004**, *6*, 77. (c) Lehn, J.-M. *Science* **2002**, *295*, 2400. (d) Desiraju, G. R. *Acc. Chem. Res.* **2002**, *35*, 565. (e) Moulton, B.; Zaworotko, M. J. *Chem. Rev.* **2001**, *101*, 1629. (f) Desiraju, G. R. *Angew. Chem., Int. Ed.* **1995**, *34*, 2311. (g) Wenger, M.; Bernstein, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7966. (h) Childs, S. L.; Hardcastle, K. I. *CrystEngComm* **2007**, *9*, 364. (i) Bosch, E. *CrystEngComm* **2007**, *9*, 191. (j) Aakeröy, C. B.; Desper, J.; Salmon, D. J.; Smith, M. M. *Cryst. Growth Des.* **2006**, *6*, 1033−1042. (k) Aakeröy, C. B.; Desper, J.; Urbina, J. F. *CrystEngComm* **2005**, *7*, 193.

(6) (a) Braga, D.; Desiraju, G. R.; Miller, J. S.; Orpen, G. A. *CrystEngComm.* **2002**, *4*, 500−509.

(7) (a) Thalladi, V. R.; Nüsse, M.; Boese, R. *J. Am. Chem. Soc.* **2000**, *122*, 9227−9236. (b) Vishweshwar, P.; Nangia, A.; Lynch, V. M. *Cryst. Growth Des.* **2003**, *3*, 783−790. (c) Morrison, J. D.; Robertson, J. M. *J. Chem. Soc.* **1949**, *2*, 980. (d) Verweel, H. J.; MacGillavry, C. H. *Nature* **1938**, *142*, 161.

(8) (a) Baeyer, A. *Ber. Chem. Ges.* **1877**, *10*, 1286. (b) Thalladi, V. R.; Nusse, M. *J. Am. Chem. Soc.* **2000**, *122*, 9227−9236.

(9) Desiraju, G. R. *CrystEngComm* **2003**, *5*, 466−467.

(10) (a) Braga, D.; Dichiarante, E.; Palladino, G. *CrystEngComm* **2010**, *12*, 3534−3536. (b) Bond, A. D. *CrystEngComm* **2006**, *8*, 333. (c) Callear, S. K.; Hursthouse, M. B.; Threlfall, T. L. *CrystEngComm* **2010**, *12*, 898−908.

(11) (a) Mei, X.; Wolf, C. *Eur. J. Org. Chem.* **2004**, 4340−4347. (b) Dale, S. H.; Elsegood, M. R. J.; Hemmings, M.; Wilkinson, A. L. *CrystEngComm* **2004**, *6*, 207. (c) Bhogala, B. R.; Nangia, A. *Cryst. Growth Des.* **2003**, *3*, 547. (d) Bensemann, I.; Gdaniec, M.; Lakomecka, K.; Milewska, M. J.; Polonski, T. *Org. Biomol. Chem.* **2003**, *1*, 1425. (e) Hguyen, T. L.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **2001**, *123*, 11057.

(12) (a) Aakeröy, C. B.; Beatty, A. M.; Helfrich, B. A. *J. Am. Chem. Soc.* **2002**, *124*, 14425. (b) Vishweshwar, P.; Nangia, A.; Lynch, V. M. *Cryst. Growth Des.* **2003**, *3*, 783.

(13) (a) Vishweshwar, P.; Nangia, A.; Lynch, V. M. *J. Org. Chem.* **2002**, *67*, 556. (b) Leiserowitz, L.; Nader, F. *Acta Crystallogr., Sect. B: Struct. Sci.* **1977**, *33*, 2719. (c) Huang, C. M.; Leiserowitz, L.; Schmidt, G. M. J. *J. Chem. Soc., Perkin Trans. 2* **1973**, *5*, 503.

(14) Kim, T. H.; Seo., J. *Chem. Mater.* **2007**, *19*, 5815−5817.

(15) Krishna, K.; Jose, D. A.; Dastidar, P.; Das, A. *Langmuir* **2004**, *20*, 10413−10418.

(16) Kushner, S.; Dalalian, H.; Robert, T. C. *J. Org. Chem.* **1948**, *13*, 834−836.

(17) (a) *APEX2*, v2.2.0; Bruker AXS: Madison, WI, 2007. (b) *SAINT*, v7.46a; Bruker AXS: Madison, WI, 2007. (c) *SHELXTL*, v6.10; Bruker AXS: Madison, WI, 2001.

(18) Pedireddi, V. R.; Chatterjee, S.; Ranganathan, A.; Rao, C. N. *Tetrahedron* **1998**, *54*, 9457−9474.

(19) Sarma, J. A. R. P; Nangia, A.; Desiraju, G. R.; Zass, E.; Dunitz, J. *Nature* **1996**, *384*, 320−320.