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Structural Similarity of Hydrogen-Bonded Networks in Crystals of Isomeric Pyridyl-Substituted Diaminotriazines

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ABSTRACT: Crystals of isomeric pyridyl-substituted diaminotriazines 1a-c and elongated analogues 2a-b were grown under various conditions, and their structures were solved by X-ray crystallography. Analysis of the structures revealed three shared features: (1) The compounds favor flattened conformations; (2) they participate in approximately coplanar hydrogen bonding according to motifs characteristic of diaminotriazines; and (3) these interactions play a key role in directing molecular organization. Together, the consistent molecular topologies and the shared presence of a dominant site of association ensure that the compounds crystallize similarly to give structures that feature chains, tapes, and layers. In certain cases, in fact, the molecular organization adopted by different pyridyl-substituted diaminotriazines is virtually identical, even when the length of the molecule or the orientation of the pyridyl group has been changed. Together, these observations show how functional groups such as diaminotriazinyl, which can control association by forming multiple directional intermolecular interactions according to reliable patterns, can be incorporated within more complex molecular structures to determine how crystallization will occur.

Introduction

Isomeric pyridyl-substituted diaminotriazines 1a-c and elongated analogues 2a-b define a coherent series of small molecules with well-defined geometries and a marked ability to associate by forming hydrogen bonds, aromatic interactions, and coordinative bonds to metals. Aryltriazines normally adopt conformations in which the triazinyl ring and aryl substituent are approximately coplanar,¹ and diaminotriazines participate in characteristic patterns of intermolecular hydrogen bonding, as defined by isomeric supramolecular homosynthons I-III.¹⁻⁵ Together, these properties are expected to play a dominant role in determining how isomeric pyridyl-substituted diaminotriazines 1a-c and 2a-b will crystallize, and they should favor a series of related structures in which the compounds adopt flattened conformations and form extensive networks of hydrogen bonds directed primarily within the molecular plane.



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Syntheses of Isomeric Pyridyl-Substituted Diaminotriazines 1a-c and 2a-b. Compounds 1a,⁴ 1b,⁶ 1c,⁷ and 2a⁸ were prepared by methods reported previously. Extended analogue 2b was synthesized in 81% overall yield by Suzuki-Miyaura coupling of 4-bromobenzonitrile with 3-pyridineboronic acid, followed by heating the resulting 3-(4-cyanophenyl)pyridine⁹ with dicyandiamide according to standard procedures.¹⁰

Structure of Crystals of 2,4-Diamino-6-(4-pyridyl)-1,3,5triazine (1a). Previous work reported the structure of crystals of compound 1a, which were grown from EtOH and shown to belong to the monoclinic space group C2/c.^{3,4} We have found that crystals grown from DMSO/MeCN have the same structure. To facilitate comparison of this known structure with new ones, it is presented succinctly in Figure 1, and other crystallographic data are summarized in Table 1. Two crystallographically



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Figure 1. Views of the structure of crystals of 2,4-diamino-6-(4-pyridyl)-1,3,5-triazine (1a) grown from EtOH^{3,4} or DMSO/MeCN. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. (a) View along the *b* axis showing alternating (**AB**)_n chains of independent molecules **A** and **B**, which are held together by hydrogen bonding according to motif **III**. The chains are paired to form tapes, primarily by hydrogen bonding of molecules **A** according to motif **I**. (b) View showing how the association of tapes is directed in part by π -stacking and by edge-to-face N-H···N interactions within a herringbone arrangement of molecules **B**. (c) View showing further association of tapes controlled by head-to-tail π -stacking of molecules **A** along the *b* axis.

Table 1. Crystallographic Data for Isomeric Pyridyl-Substituted Diaminotriazines 1a-c

compound	1a	2 1a · MeOH	1b	1b	1c	1c·DMSO
crystallization medium	DMSO/CH ₂ Cl ₂ DMSO/MeCN	DMSO/MeOH	DMSO	MeCN	MeCN	DMSO
formula	$C_8H_8N_6$	C ₁₇ H ₂₀ N ₁₂ O	C ₈ H ₈ N ₆	$C_8H_8N_6$	C ₈ H ₈ N ₆	$C_{10}H_{14}N_6OS$
crystal system	monoclinic	triclinic	monoclinic	orthorhombic	monoclinic	monoclinic
space group	C2/c	$P\overline{1}$	$P2_{1}/c$	Pbca	$P2_1/c$	$P2_{1}/c$
a (Å)	27.3388(10)	8.4261(6)	12.063(4)	6.8585(2)	11.9471(9)	11.7704(1)
$b(\dot{A})$	7.1786(3)	10.1297(7)	19.226(5)	13.2958(4)	6.9732(6)	9.0941(1)
$c(\dot{A})$	19.9614(7)	12.2194(10)	7.016(2)	18.5050(5)	21.0822(18)	11.8294(1)
α (°)	90	75.928(4)	90	90	90	90
β (°)	120.433(1)	87.136(4)	95.029(2)	90	101.590(4)	97.160(1)
γ (°)	90	70.451(4)	90	90	90	90
$V(Å^3)$	3377.8(2)	952.8(1)	1620.9(8)	1687.46(8)	1720.5(2)	1256.36(2)
Z	16	2	8	8	8	4
$\rho_{\rm calc} ({\rm g}{\rm cm}^{-3})$	1.480	1.424	1.542	1.482	1.453	1.408
$T(\mathbf{K})$	200	100	100	150	150	100
$\mu (\text{mm}^{-1})$	0.835	0.823	0.870	0.836	0.819	2.299
$R_1, I > 2\sigma(I)$	0.0408	0.0453	0.0516	0.0307	0.0514	0.0360
R_1 , all data	0.0415	0.0523	0.0518	0.0338	0.0538	0.0371
$wR_2, I > 2\sigma(I)$	0.0986	0.1339	0.1202	0.0808	0.1569	0.0963
wR_2 , all data	0.0990	0.1387	0.1203	0.0835	0.1586	0.0992
independent reflections	3056	3252	2842	1474	2989	2215
observed reflections $[I > 2 \sigma(I)]$	2738	2764	2714	1295	2785	2100

independent molecules are present (**A** and **B**), which are linked along the *ac* diagonal into alternating $(AB)_n$ chains by hydrogen bonding according to a distorted form of motif **III** (Figure 1a).

Individual $(AB)_n$ chains are paired to form tapes, primarily by additional hydrogen bonding of molecules A according to motif I (Figure 1a).



Figure 2. Views of the structure of the 2:1 solvate of 2,4-diamino-6-(4-pyridyl)-1,3,5-triazine (**1a**) with MeOH grown from DMSO/MeOH. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, nitrogen atoms in blue, and oxygen atoms in red. (a) View showing how $N-H\cdots N$ hydrogen bonds of type **III** link molecules into chains along the *c* axis, and how sheets are formed by additional $N-H\cdots N$ (pyridine) hydrogen bonds. (b) View along the *b* axis showing the packing of four sheets.

As expected,¹ molecules **A** and **B** both adopt conformations in which the triazinyl ring and pyridyl substituent are nearly coplanar, with torsional angles of approximately 7° and 16°, respectively. In addition, molecules **A** that are paired by hydrogen bonding according to motif **I** lie in essentially the same plane. However, hydrogen bonding of diaminotriazines can accommodate substantial deviations from coplanarity, as illustrated by the distorted geometry of motif **II** in the (**AB**)_n chains (Figure 1a). These deviations do not appear to weaken the hydrogen bonds substantially, and the average N-H···N distances in the nearly coplanar pair **A**₂ are similar to those in the deformed pair **AB** (3.033 and 3.052 Å, respectively).

Cohesion between the tapes is provided in part by an $N-H\cdots N(pyridine)$ hydrogen bond (3.107 Å) involving the pyridyl nitrogen atom of a molecule **B** and the single N-H bond of a nearby molecule **A** not used in motifs **I** and **III**. Association of the tapes is also maintained by unusual $N-H\cdots$ aromatic interactions within a stacked herringbone arrangement of molecules **B** (Figure 1b). In these interactions, the average $N-H\cdots N$ distances (3.177 Å) are significantly longer than those in normal $N-H\cdots N$ hydrogen bonds within tapes (motifs **I** and **III**). The overall network is further stabilized by head-to-tail π -stacking of molecules **A** along the *b* axis (Figure 1c).

In the resulting structure, each molecule **A** participates in a total of seven $N-H\cdots N$ hydrogen bonds with four neighbors, and each molecule **B** engages in nine related interactions (five $N-H\cdots N$ hydrogen bonds and four $N-H\cdots$ aromatic interactions) with five neighbors. Hydrogen bonding of the pyridyl nitrogen atom of compound **1a** plays only a minor role in controlling crystallization, possibly because the diaminotriazinyl groups can compete effectively by forming doubly hydrogen-bonded pairs. This hypothesis is supported by the nearly identical molecular organization found in the structures of compound **1a** and 2,4-diamino-6-phenyl-1,3,5-triazine (**3**), in which the pyridyl group of compound **1a** has been replaced by phenyl.²

Key structural features of pyridyl-substituted diaminotriazine 1a and its phenyl-substituted relative 3, including their rather rigid flattened shape and ability to form multiple coplanar hydrogen bonds of types I-III, help ensure that their options for crystallization are limited to a narrow set of similar possibilities. To test this hypothesis, we grew new crystals of compound 1a from DMSO/MeOH, which proved to belong to the triclinic space group $P\overline{1}$ and to have the composition 2 1a · MeOH. Views of the structure appear in Figure 2, and other crystallographic data are summarized in Table 1. The structure consists of two crystallographically independent molecules A and B, which differ primarily in the torsional angles between the triazinyl and pyridyl rings (approximately 47° and 39°). Both values are atypically high for aryltriazines.¹ Molecules A and B are linked by $N-H\cdots N$ hydrogen bonds of type III with normal average distances (3.098 Å), thereby producing alternating $(AB)_n$ chains that lie along the c axis (Figure 2a). The chains are then connected to form sheets parallel to the bc plane by additional N-H···N(pyridine) hydrogen bonds (2.986 A), and stacking of the sheets is controlled by multiple weak interactions (Figure 2b). As in other structures of pyridylsubstituted diaminotriazine 1a and its phenyl-substituted relative 3, crystals grown from DMSO/MeOH show a preference for molecular organization based on the formation of extensively hydrogen-bonded chains.

Structure of Crystals of 2,4-Diamino-6-(3-pyridyl)-1,3,5triazine (1b). The similar behavior of pyridyl-substituted diaminotriazine 1a and phenyl-substituted analogue 3 established that the pyridyl nitrogen atom does not necessarily play a decisive role in directing crystallization, thereby suggesting that isomeric pyridyl-substituted diaminotriazine 1b should also form a closely related structure. Crystals of compound 1b grown from DMSO were found to belong to the monoclinic space group $P_{2_1/c}$. The molecular organization proved to be essentially identical to that observed in crystals of analogues 1a and 3 (Figure 1). A view of the structure of compound 1b is provided in Figure 3, and other





Figure 4. View along the *b* axis of the structure of crystals of 2,4diamino-6-(3-pyridyl)-1,3,5-triazine (1b) grown from MeCN. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. Chains aligned with the *a* axis are held together by paired hydrogen bonds of type II. $N-H\cdots N(pyridine)$ hydrogen bonds between the chains (not shown) define layers parallel to the *ab* plane, which are connected by additional single $N-H\cdots N(triazine)$ hydrogen bonds to give a three-dimensional network.

Figure 3. View of the structure of crystals of 2,4-diamino-6-(3pyridyl)-1,3,5-triazine (1b) grown from DMSO. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. Alternating (AB)_n chains of independent molecules A and B are held together by hydrogen bonding according to motif III, and the chains are paired to form tapes, primarily by hydrogen bonding of molecules A according to motif I.

crystallographic data are presented in Table 1. The structure incorporates two crystallographically independent molecules A and B with slightly different torsional angles between the triazinyl and pyridyl rings (approximately 2° and 12°, respectively). As in the structures of analogues 1a and 3, molecules A and B are linked into $(AB)_n$ chains by characteristic hydrogen bonding of type III, with an average N- $H \cdots N$ distance of 3.052 Å (Figure 3). The chains are further connected to form tapes aligned with the a axis by additional N-H···N hydrogen bonding (3.096 Å) of molecules A according to motif I (Figure 3). Cohesion of the tapes is ensured by multiple interactions, including (1) $N-H\cdots N$ -(pyridine) hydrogen bonds (3.085 A) involving the pyridyl nitrogen atom of a molecule B and the single N-H bond of a nearby molecule A not used in motifs I and III; (2) π -stacking and edge-to-face $N-H\cdots N$ interactions (3.174 Å) within a herringbone arrangement of molecules B (as in Figure 1b); and (3) head-to-tail π -stacking of molecules A (as in Figure 1c).

The closely related behavior of isomeric pyridyl-substituted diaminotriazines 1a-b and phenyl-substituted analogue 3 under various conditions is consistent with the hypothesis that crystallization is controlled primarily by the flattened molecular topology and by the ability of diaminotriazinyl groups to direct the formation of hydrogen-bonded chains. To test this notion further, we grew additional crystals of compound 1b from MeCN, which proved to belong to the orthorhombic space group Pbca. A view of the structure is shown in Figure 4, and other crystallographic data are presented in Table 1. Molecules of compound 1b adopt a flattened conformation with an interaryl angle of approximately 21°, and they associate to form chains along the a axis held together by characteristic paired hydrogen bonds of type II, with an average N-H···N distance of 3.008 Å (Figure 4). Each molecule in a chain participates in a total of four additional $N-H\cdots N(pyridine)$ hydrogen bonds (3.020 Å), which connect the chains to form layers parallel to the *ab* plane.¹¹ The layers are joined by single N-H···N(triazine) hydrogen bonds (3.127 Å) as shown in Figure 4, leading to a threedimensional network in which each molecule of compound 1b engages in a total of eight $N-H\cdots N$ hydrogen bonds with six neighbors. These data provide additional evidence that isomeric pyridyl-substituted diaminotriazines 1a-b and phenylsubstituted analogue 3 are predisposed to adopt similar flattened conformations and to engage reliably in approximately coplanar hydrogen bonds of type I-III, thereby leading to selfassociation that predictably favors the formation of related chains, tapes, and layers.

Structure of Crystals of 2,4-Diamino-6-(2-pyridyl)-1,3, 5-triazine (1c). The closely related behavior of pyridyl-substituted diaminotriazines **1a-b** and phenyl-substituted analogue 3 suggested that isomeric pyridyl-substituted diaminotriazine 1c would also crystallize in a similar way. Crystals grown from MeCN were found to belong to the monoclinic space group $P2_1/c$, and Table 1 provides additional crystallographic data. As confirmed by Figure 5, the molecular organization is virtually identical to that observed in crystals of isomer 1a grown from EtOH or DMSO/MeCN (Figure 1), isomer 1b grown from DMSO (Figure 3), and phenyl-substituted analogue $3.^2$ In the structure of compound 1c, crystallographically independent molecules A and B have flattened conformations with slightly different torsional angles between the triazinyl and pyridyl rings (approximately 15° and 32°, respectively). $(AB)_n$ chains are linked along the *a* axis by characteristic hydrogen bonding of type III, with an average $N-H\cdots N$ distance of 3.068 Å (Figure 5), and the chains are further connected to form tapes by additional N–H···N hydrogen bonding (3.050 Å) of molecules A according to motif I (Figure 5). Association of the tapes involves multiple interactions, including (1) N-H···N(pyridine) hydrogen bonds of normal average distance (3.115 A) involving the pyridyl nitrogen atom of a molecule **B** and the single N-H bond of a nearby molecule **A** not used in motifs I and III; (2) π -stacking and edge-to-face N-H···N interactions (3.326 Å) within a herringbone arrangement of molecules **B** (as in Figure 1b); and (3) head-to-tail π -stacking of molecules A (as in Figure 1c).

These observations reinforce the notion that crystallization of isomeric pyridyl-substituted diaminotriazines 1a-cand phenyl-substituted analogue 3 is directed primarily by

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their similar flattened topologies and their shared ability to form approximately coplanar hydrogen bonds directed by diaminotriazinyl groups. As a further test of structural homology, we grew additional crystals of compound **1c** from DMSO, which proved to belong to the monoclinic space group $P2_1/c$ and to have the composition **1c**·1DMSO. Figure 6 shows views of the structure, and Table 1 provides additional crystallographic data. Molecules of compound **1c** have a flattened conformation with an angle of approximately 26° between the average planes of the pyridyl and triazinyl rings. As shown in Figure 6a, chains aligned with the *c* axis result from the formation of typical paired



Figure 5. View of the structure of crystals of 2,4-diamino-6-(2pyridyl)-1,3,5-triazine (1c) grown from MeCN. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. Alternating $(AB)_n$ chains of independent molecules **A** and **B** are held together by hydrogen bonding according to motif **III**, and the chains are paired to form tapes, primarily by hydrogen bonding of molecules **A** according to motif **I**.

hydrogen bonds of type III (average N-H···N distance = 3.086 Å), reinforced by additional N-H···N(pyridine) hydrogen bonds (3.070 Å). Packing of the chains, controlled in part by π -stacking of pyridyl groups, produces a structure with alternating layers consisting of compound 1c and hydrogen-bonded molecules of DMSO (Figure 6b).

Structure of Crystals of 2,4-Diamino-6-[4-(4-pyridy])phenyl]-1,3,5-triazine (2a). Together, our observations confirm that isomeric pyridyl-substituted diaminotriazines 1a-cand phenyl-substituted analogue 3 all inherently favor flattened conformations and participate in approximately coplanar hydrogen bonding according to motifs I–III. As a result, the compounds crystallize similarly under various conditions to give structures that feature chains, tapes, and layers. In certain cases, in fact, the overall molecular organization is virtually identical.

To see if these consistent patterns are maintained when molecular topology is altered, we examined the behavior of elongated pyridyl-substituted diaminotriazine **2a**. Crystallization from wet DMSO under various conditions yielded two polymorphs, as well as a monohydrate and a dihydrate. One of the polymorphs proved to belong to the triclinic space group $P\overline{1}$. A view of its structure is shown in Figure 7, and other crystallographic data are summarized in Table 2. The molecules have flattened conformations and are linked into chains along the *ab* diagonal by hydrogen bonds of type **II** (average N-H···N distance = 3.151 Å). Adjacent chains are further connected by N-H···N(pyridine) hydrogen bonds (average N-H···N distance = 2.950 Å) to give a three-dimensional network.

The second polymorph of elongated pyridyl-substituted diaminotriazine **2a** was found to belong to the monoclinic space group $P2_1/n$. Figure 8 provides a view of its structure, and Table 2 summarizes other crystallographic data. The structure consists of crystallographically independent molecules **A** and **B** that adopt flattened conformations and are paired by hydrogen bonding according to motif **I** (average N-H···N distance = 3.056 Å). Pairs are further connected



Figure 6. Views of the structure of the 1:1 solvate of 2,4-diamino-6-(2-pyridyl)-1,3,5-triazine (1c) with DMSO. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, nitrogen atoms in blue, oxygen atoms in red, and sulfur atoms in yellow. (a) View showing how $N-H\cdots N$ hydrogen bonds of type III and additional $N-H\cdots N$ (pyridine) hydrogen bonds link molecules into chains along the *c* axis. (b) View along the *b* axis showing alternating layers composed of compound 1c and DMSO.

by single N–H···N(pyridine) hydrogen bonds of normal average distance (3.029 Å) to nearly orthogonal adjacent molecules, thereby creating corrugated sheets with extensive edge-to-face aromatic interactions.¹¹ Packing of the sheets introduces additional aromatic interactions.

Crystals of the monohydrate of pyridyl-substituted diaminotriazine **2a** (**2a** · 1H₂O) proved to belong to the triclinic space group $P\overline{1}$. A view of its structure is shown in Figure 9, and other crystallographic data are presented in Table 2. Molecules of compound **2a** are paired by hydrogen bonding of type I (average N-H···N distance = 3.044 Å) to give a layered structure closely similar to that shown in Figure 8, except that hydrogen bonding to pyridyl groups is mediated by intervening molecules of H₂O (Figure 9). This allows the molecular components of each layer to lie approximately in the same plane, giving sheets that pack to create the overall three-dimensional structure.¹¹

Crystals of the dihydrate of elongated pyridyl-substituted diaminotriazine **2a** (**2a** \cdot 2H₂O) were found to belong to the monoclinic space group $P2_1/n$. Figure 10 provides a view of its structure, and Table 2 summarizes other crystallographic data. Molecules of compound **2a** are linked into chains along



Figure 7. View of the structure of crystals of the triclinic $P\overline{1}$ polymorph of 2,4-diamino-6-[4-(4-pyridyl)phenyl-1,3,5-triazine (2a) grown from wet DMSO. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. Chains aligned with the *ab* diagonal are formed by hydrogen bonding of type II and are further connected to adjacent chains by N-H···N(pyridine) hydrogen bonds to give a three-dimensional network.

the *ac* diagonal by hydrogen bonding of type **III** (average $N-H\cdots N$ distance = 3.083 Å). The chains are connected to form sheets by further coplanar hydrogen bonding between pyridyl and triazinyl groups, mediated by intervening molecules of H₂O (Figure 10).

The polymorphs and hydrates of elongated pyridylsubstituted diaminotriazine 2a show certain expected features, including a preference for a flattened molecular structure that forms coplanar hydrogen bonds according to standard motifs. However, the behavior of compound 2a is not always completely analogous to that of relatives 1a-c and 3; in particular, the $P2_1/n$ polymorph of compound 2a clearly shows the effects of its increased aromatic surface, which favors a structure with more significant π -stacking and edge-to-face interactions.

Structure of Crystals of 2,4-Diamino-6-[4-(3-pyridyl)phenyl]-1,3,5-triazine (2b). To complete our analysis of the effect of altered molecular topology, we studied the behavior of a second isomer, elongated pyridyl-substituted diaminotriazine 2b. Crystals grown from DMSO/MeCN proved to

Figure 8. View of the structure of crystals of the monoclinic $P2_1/n$ polymorph of 2,4-diamino-6-[4-(4-pyridyl)phenyl-1,3,5-triazine (2a) grown from wet DMSO. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. Pairs of independent molecules A and B are held together by hydrogen bonding according to motif I and are further connected by single $N-H\cdots N(pyridine)$ hydrogen bonds to nearly orthogonal adjacent molecules.

Table 2.	Crystallographi	c Data for Elongated	Isomeric Pyridyl-Sub	stituted Diaminotriazines 2a-b
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2a	2a	$2a \cdot 1H_2O$	$2a \cdot 2H_2O$	2b	
DMSO/H ₂ O	DMSO/H ₂ O	DMSO/H ₂ O	DMSO/H ₂ O	DMSO/MeCN	
$C_{14}H_{12}N_6$	$C_{14}H_{12}N_6$	$C_{14}H_{14}N_{6}O$	$C_{14}H_{16}N_6O_2$	$C_{14}H_{12}N_6$	
triclinic	monoclinic	triclinic	monoclinic	orthorhombic	
$P\overline{1}$	$P2_1/n$	$P\overline{1}$	$P2_1/n$	Pbca	
9.5053(5)	16.9150(7)	9.310(1)	7.2112(2)	7.0142(2)	
14.2146(7)	8.6926(4)	9.719(1)	49.9305(13)	18.5089(4)	
19.4909(9)	17.8433(7)	15.859(2)	11.9101(3)	18.5309(4)	
98.832(2)	90	96.589(2)	90	90	
94.263(2)	109.956(2)	99.854(2)	103.679(1)	90	
104.765(2)	90	111.024(3)	90	90	
2498.5(2)	2466.06(18)	1295.3(3)	4166.70(19)	2405.78(10)	
8	8	4	12	8	
1.405	1.424	1.448	1.436	1.459	
150	150	100	100	100	
0.738	0.748	0.806	0.840	0.766	
0.0721	0.0383	0.0371	0.0547	0.0314	
0.1026	0.0391	0.0372	0.0747	0.0322	
0.1876	0.1104	0.0880	0.1346	0.0845	
0.2050	0.1113	0.0881	0.1466	0.0855	
42622	4269	4604	7516	2190	
30414	4124	4508	5785	2126	
	$\begin{array}{c} \textbf{2a} \\ \hline DMSO/H_2O\\ C_{14}H_{12}N_6\\ triclinic\\ P\overline{1}\\ 9.5053(5)\\ 14.2146(7)\\ 19.4909(9)\\ 98.832(2)\\ 94.263(2)\\ 104.765(2)\\ 2498.5(2)\\ 8\\ 1.405\\ 150\\ 0.738\\ 0.0721\\ 0.1026\\ 0.1876\\ 0.2050\\ 42622\\ 30414 \end{array}$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	

belong to the orthorhombic space group *Pbca*. A view of its structure is shown in Figure 11, and other crystallographic data are provided in Table 2. The molecular organization is essentially identical to that of the $P\overline{1}$ polymorph of isomer **2a** (Figure 7). Again, the molecules adopt flattened conformations and form chains linked by hydrogen bonds of type **II** (average N-H···N distance = 3.002 Å). Adjacent chains are further connected by N-H···N(pyridine) hydrogen bonds (3.019 Å) to give a three-dimensional network.

Conclusions

We have found that crystals of isomeric pyridyl-substituted diaminotriazines 1a-c, isomeric elongated analogues 2a-b,

Figure 9. View of the structure of crystals of the monohydrate of 2,4-diamino-6-[4-(4-pyridyl)phenyl-1,3,5-triazine (2a) grown from wet DMSO. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, nitrogen atoms in blue, and oxygen atoms in red. Molecules of compound 2a are paired by hydrogen bonds of type I, and sheets result from additional hydrogen bonds involving molecules of H₂O.

and related phenyl-substituted diaminotriazine **3** have three shared features: (1) The compounds favor flattened conformations; (2) they participate in approximately coplanar hydrogen bonding according to motifs characteristic of diaminotriazines (I–III); and (3) these interactions play a key role in directing molecular organization. Together, the consistent molecular topologies and the shared presence of a dominant site of association ensure that the compounds crystallize similarly under various conditions to give structures that feature chains, tapes, and layers. In certain cases, in fact, the molecular organization adopted by different pyridylsubstituted diaminotriazines is virtually identical, even when the length of the molecule or the orientation of the pyridyl

Figure 11. View of the structure of crystals of 2,4-diamino-6-[4-(3-pyridyl)phenyl-1,3,5-triazine (**2b**) grown from DMSO/MeCN. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, and nitrogen atoms in blue. Chains aligned with the *a* axis are formed by hydrogen bonding according to motif **II**, and adjacent chains are connected by N-H···N(pyridine) hydrogen bonds to give a three-dimensional network.

Figure 10. View of the structure of crystals of the dihydrate of 2,4-diamino-6-[4-(4-pyridyl)phenyl-1,3,5-triazine (2a) grown from wet DMSO. Hydrogen bonds are represented by broken lines, and carbon atoms are shown in gray, hydrogen atoms in white, nitrogen atoms in blue, and oxygen atoms in red. Molecules of compound 2a are linked into chains by hydrogen bonds of type III, and the chains are connected to form sheets by additional hydrogen bonds involving molecules of H₂O.

group has been changed. Together, these observations show how substituents such as the diaminotriazinyl group, which can control association by forming multiple directional intermolecular interactions according to motifs that have a useful degree of reliability, can be incorporated within more complex molecular structures to control how crystallization will occur.

Experimental Section

General Notes. Pyridyl-substituted diaminotriazines 1a, 4 1b, 6 1c, 7 and $2a^{8}$ were prepared by methods reported previously. Elongated compound 2b was made by the procedure summarized below. Other chemicals were purchased from commercial sources and used without further purification.

3-(4-Cyanophenyl)pyridine.⁹ A dried pressure tube was charged with Pd(OAc)₂ (0.031 g, 0.14 mmol), 4-bromobenzonitrile (0.50 g, 2.7 mmol), 3-pyridineboronic acid (0.37 g, 3.0 mmol), and SPhos (0.11 g, 0.27 mmol). Toluene (15 mL), water (5 mL), and methanol (5 mL) were added, and the tube was capped with a septum. The mixture was stirred under N2 for 10 min at 25 °C, and then K3PO4 (5.8 g, 27 mmol) was added. The septum was replaced with a screw cap, and the mixture was heated at 110 °C until 4-bromobenzonitrile was consumed, as judged by thin-layer chromatography. The mixture was cooled to 25 °C and extracted with dichloromethane. Solvent was removed from the extracts by evaporation under reduced pressure, and the residue was purified by flash chromatography (silica gel, ethyl acetate/hexane 1:4) to give 3-(4-cyanophenyl)pyridine (0.42 g, 2.3 mmol, 85%) as a colorless solid: mp 96 °C; IR (ATR) 3058, 3039, 2224 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.89 (1H, d, ${}^{4}J = 2.1$ Hz), 8.70 (1H, dd, ${}^{3}J = 4.8$ Hz, ${}^{4}J = 1.6$ Hz), 7.91 (1H, dd, ${}^{3}J = 7.8$ Hz, ${}^{4}J = 2.1$ Hz, ${}^{4}J = 1.6$ Hz), 7.80 (2H, d, ${}^{3}J = 8.6$ Hz), 7.72 (2H, d, ${}^{3}J = 8.6$ Hz), 7.45 (1H, dd, ${}^{3}J = 7.8$ Hz, ${}^{3}J = 4.8$ Hz); ${}^{13}C$ NMR (100 MHz, CDCl₃) δ 150.12, 148.60, 142.69, 135.16, 134.91, 133.27, 128.19, 124.22, 118.96, 112.30; HRMS (ESI) calcd for $C_{12}H_8N_2 + H m/e$ 181.0760, found 181.0763.

2,4-Diamino-6-[3-(pyridinyl)phenyl]-1,3,5-triazine (2b). A mixture of 3-(4-cyanophenyl)pyridine (0.594 g, 3.30 mmol), dicyandiamide (0.555 g, 6.60 mmol), and KOH (0.203 g, 3.62 mmol) in 2-methoxyethanol (30 mL) was heated at reflux for 12 h. The resulting mixture was cooled to 25 °C, the precipitated solid was separated by filtration, and the solid was washed with hot water to give pure 2,4-diamino-6-[3-(pyridinyl)phenyl]-1,3,5-triazine (2b; 0.829 g, 3.14 mmol, 95%) as a colorless solid: mp 320 °C; IR (ATR) 3472, 3289, 3150, 1671, 1623, 1504, 1446, 1382 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.97 (1H, dd, ⁴J = 2.3 Hz, ⁵J = 0.8 Hz), 8.61 (1H, dd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 8.37 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.52 (1H, ddd, ³J = 7.9 Hz, ⁴J = 1.6 Hz), 7.85 (2H, d, ³J = 8.5 Hz), 7.51 (4H, 58), 140.25 (1H, 458), 8.5 (140.25

Crystallization of Pyridyl-Substituted Diaminotriazines 1a-c and 2a-b. All crystallizations were carried out at 25 °C. Crystals of compound **1a** were grown by exposing solutions in DMSO (5 mg/mL) to vapors of MeCN or MeOH in closed vessels. Compounds 1b-c were crystallized by the slow evaporation of solutions in DMSO (5 mg/mL) or in MeCN (saturated). Crystals of compound 2a were obtained in various forms by exposing solutions in DMSO (5 mg/mL) to vapors of H₂O. Crystals of compound 2b were grown by exposing solutions in DMSO (5 mg/mL) to vapors of MeCN.

Analysis of the Structures of Pyridyl-Substituted Diaminotriazines 1a-c and 2a-b by X-ray Crystallography. Crystallographic data were collected at 150 K using a Bruker Microstar diffractometer with Cu K α radiation. The structures were solved by direct methods using SHELXS-97, and non-hydrogen atoms were refined anisotropically with SHELXL-97.¹² Hydrogen atoms were treated by first locating them from difference Fourier maps, recalculating their positions using standard values for distances and angles, and then refining them as riding atoms. In selected structural studies, calculated powder X-ray diffraction patterns were found to closely match those obtained experimentally by analysis of bulk crystalline samples, thereby establishing that the samples consisted primarily of a single phase.¹¹

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Supporting Information Available: Additional crystallographic details (including thermal atomic displacement ellipsoid plots, powder X-ray diffraction patterns, tables of structural data in CIF format, and supplementary figures). This material is available free of charge via the Internet at http://pubs.acs.org.

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