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Green synthesis and self-association of 2,4-diamino-1,3,5-triazine derivatives

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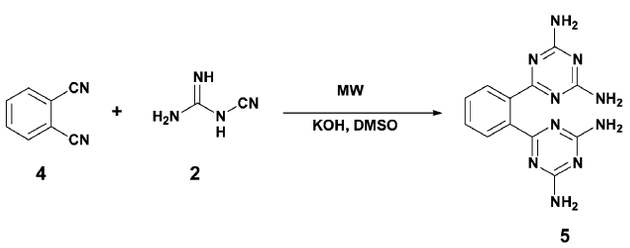
2,4-Diamino-1,3,5-triazines have been prepared by reaction of dicyandiamide with nitriles under microwave irradiation, a method that can be considered as a green procedure due to the reduction in the use of solvents during synthesis and purification, the short reaction time and the simplicity of the procedure. The structures have been confirmed in solution by NMR spectroscopy. Variable temperature experiments have been used to calculate the free energy of activation for rotation about the amino–triazine bond. The crystal structures of three 2,4-diamino-6-R-1,3,5-triazine derivatives (**3a**: R = phenyl, **3i**: R = 1-piperidino and **3g**: R = 1-phenylpyrazol-3-yl) have been determined by X-ray analysis. The N–H···N interactions change from structure to structure, resulting in a variation from pseudo-honeycomb networks to corrugated rosette layers.

Introduction

2,4-Diamino-1,3,5-triazine derivatives have been applied as model systems for flavoenzyme activity[1] and have shown antitumor activity as well as many other types of biological activity.[2] There is also increasing interest in the self-assembly of triazine derivatives through multiple hydrogen bonds. The melamine/cyanuric acid system is one of the best known and most widely studied hydrogen-bonded systems in the literature[3] and its stability has been used to obtain polymers in the solid state[4] and in water.[5] Modification of the system formed by cyanuric acid and/or melamine has allowed non-covalent synthesis to be performed,[6] for example, linear polymers[7] and nanostructures,[8] as well as diastereoselective and enantioselective non-covalent syntheses.[9] The design of quadruple hydrogen-bonded systems by acylation of the amino groups has been described.[10] Furthermore, the introduction of groups that interact strongly with their neighbours in a well-defined way has allowed the preparation of molecular tectonic materials for the creation of new ordered structures by design.[11] Finally, the introduction of nitrogen heterocycles allowed the combination of hydrogen bonding and metal complexes in supramolecular structures.[12]

In this paper we describe the preparation of 6-substituted-2,4-diamino-1,3,5-triazines **3a–j** and **5** by reaction of dicyandiamide with alkyl-, aryl- and heteroarylnitriles under microwave irradiation (Scheme 1). Microwave irradiation has been widely established as a useful energy source in synthetic reactions. The rapid heating induced by the radiation avoids the decomposition of the reagents and/or products, while reactions are cleaner and yields are in many cases higher than those obtained by classical heating.[13] The reaction times associated with microwave-induced reactions are short and

a, phenyl; b, p-methoxyphenyl; c, p-nitrophenyl; d, p-chlorophenyl; e, 2-(pyrazol-1yl)phenyl; f, 3-(pyrazol-1-yl)phenyl; g, 1-phenylpyrazol-3-yl; h, 4-pyridyl; i, 1-piperidino; j; 1-morpholino.



Scheme 1

this results in an energy saving. Furthermore, the microwave technique provides synergy with solvent-free conditions (or reactions at high concentration) and reactions with recyclable solid catalysts.[14] For these reasons the procedure can be designated a green synthetic methodology.[15]

The structures of these compounds were determined by NMR spectroscopy (in solution) and by X-ray crystallography in the cases of compounds **3a**, **3g** and **3i**.

One of the main goals of this study was to identify the patterns created by intermolecular amino···N(triazine) interactions and to assess the ability for self-assembly of the multiple hydrogen bonding units in these compounds. For this purpose, 2,4-diamino-1,3,5-triazine derivatives were selected

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and the nature of the 6-substituent changed: (i) an aromatic substituent in 6-phenyl derivative **3a**, in order to compare the crystal packing with that of the 6-pyridyl derivative **3h**, which has been described previously,[16] as this has almost same size and shape but lacks the coordinating lone pair, (ii) a heteroaromatic unit in the 6-(3-phenylpyrazol-1-yl) compound **3g**, in which the triazine and the phenyl rings are connected by a pyrazole spacer that has a different size and shape and a coordinating lone pair with different directionality and lower coordination ability,[17] and (iii) an aliphatic ring in the 6-(1-piperidino) derivative **3i**, which has a non-planar ring, a chair conformation, and a similar shape but different size to the units in **3a** and **3h**.

Results and discussion

Synthesis of 3a–j and 5

2,4-Diamino-1,3,5-triazines have previously been prepared in good yields by reaction of biguanide with esters[2] in methanol or ethanol with long reaction times or by reaction of dicyandiamide with nitriles in 1-pentanol at 413 K for 24 h.[1]

We have prepared triazines **3a**–**j** and **5** in good yields by reacting the appropriate nitrile (**1**) with dicyandiamide **2** under microwave irradiation in 10–15 min (Table 1). Even phthalonitrile (**4**) produced the bistriazine **5** in good yield in only 10 min. Reactions were performed on a 15 mmol scale using 1 mL of DMSO in order to homogenize the reaction mixture and to ensure good absorption of the microwave radiation. Reactions in solvent-free conditions did not give reproducible results because it was impossible to homogenize the reaction mixture, even by sonication of the crude mixture before irradiation. Probably the mixture did not absorb enough microwave radiation to achieve a phase change to an eutectic melt and, as a consequence, a rapid reaction did not take place.[18] Yields can be further improved by using 3 mL of DMSO (Table 1). The pure product was obtained by suspending the crude mixture in boiling water and washing the precipitate with the appropriate solvent. The synthesis here described proceeds with complete atom economy and comparison with previously reported procedures emphasizes its green chemistry characteristics; reaction time was reduced from 24 h to 10–15 min, solvent was reduced from 5 to 0.5 mL/mmol, together with a very simple work-up procedure.

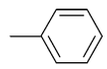
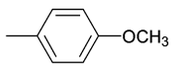
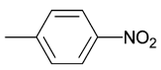
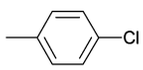
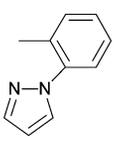
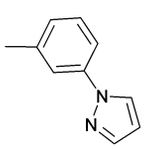
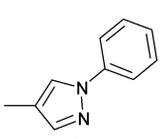
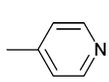
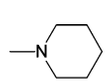
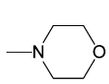
NMR structure determination of triazines 3

The NMR spectra of compounds **3a**–**j** and **5** in $CDCl_3$ and DMSO-d_6 show the presence of the NH_2 group as a broad signal at $\delta = 6.0$–6.9 in each case. The chemical shift can be related with the nature of the substituent (Table 2), with the aliphatic substituents piperidino [**3i** (6.05)] and morpholino [**3j** (6.14)] showing higher shielding due to their donating nature. The shielding of the aromatic substituent can be related with the electron-withdrawing or -donating nature of the substituent in the phenyl ring in the following order: 2-pyrazol-1-yl [**3e** (6.36)], *p*-methoxy [**3b** (6.64)], unsubstituted [**3a** (6.76)], *p*-chloro [**3d** (6.79)], 3-pyrazol-1-yl [**3f** (6.84)] and *p*-nitro [**3c** (6.90)]. Finally, in the heteroaromatic substituents the chemical shift can be related with the π-excessive or π-deficient nature of the heterocyclic ring: 4-pyrazolyl [**3g** (6.65)] and 4-pyridyl [**3h** (6.91)].

The presence of a broad signal can be explained in terms of a restricted rotation of the amine–triazine bond. This restricted rotation has recently been studied in solution[19] and in the solid state[20] in bis- and trisamino-substituted 1,3,5-triazines.

We performed variable temperature experiments on **3a**, **3f**, **3h** and **3j** as models because they are representative of the structural diversity of the compounds studied in this work and also because they are sufficiently soluble in $CDCl_3$.

Table 1 Reaction conditions and yields for the preparation of triazines **3a–j** and **5**

R	Power/W	Time/min	*T*/K	% Yield
 **3a**	60	10	468	85[a]
	60	10	463	91[b]
 **3b**	90	15	493	74[a]
	90	15	493	77[b]
 **3c**	90	15	463	74[a]
	90	15	448	85[b]
 **3d**	90	10	463	82[a]
	90	10	453	88[b]
 **3e**	90	10	463	52[a]
 **3f**	90	10	458	96[a]
	90	10	458	93[b]
 **3g**	90	10	448	83[a]
	90	10	448	99[b]
 **3h**	90	10	478	83[a]
	90	10	463	88[b]
 **3i**	90	10	453	71[a]
	90	10	453	88[b]
 **3j**	90	10	453	71[a]
	90	10	448	73[b]
5	90	10	463	80[b]

[a] DMSO 1 mL/15 mmol. [b] DMSO 3 mL/15 mmol.

Table 2 Chemical shift δ of the NH_2 group

	3a	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**	**5**
δ NH_2	6.76	6.64	6.90	6.79	6.36	6.84	6.65	6.91	6.05	6.14	6.34–6.52

Table 3 Coalescence temperature and calculated $\Delta G^{\ddagger}$ for triazines **3a**, **3f**, **3h** and **3j**

	T_c/K	$\Delta G^{\ddagger}$/kJ mol^{-1}
3a	284	60.71
3f	287	60.26
3h	289	62.58
3j	248	52.97

Coalescence temperatures and calculated activation free energies[21] are collected in Table 3.

Although a wide range of activation free energies was determined (53–61 kJ mol^{-1}), a good linear correlation was observed (Fig. 1) and this is an indication that a single process occurs in all compounds.

X-Ray structure determination of 3a, 3g and 3i

The crystal lattices of **3a**, **3g** and **3i** contain, respectively, 2, 2 and 3 crystallographically independent molecules, hereinafter referred to as molecules **A** and **B** and **A**, **B** and **C** (Fig. 2).

As far as the strong hydrogen bonds (N–H···N) are concerned, only in compound **3g** is every donor and acceptor site available for hydrogen bonding used. In compounds **3a** and **3i**, the number of potential donors is greater than the number of acceptors and one of the two H amino atoms is not involved in strong hydrogen bonding (Table 4).

The crystal structure analysis of **3a** shows that the molecules are organized in an analogous way to those in **3h** [2,4-diamino-6-(4-pyridyl)-1,3,5-triazine,[16] TETREP refcode[22]]. The main difference concerns the loss of the hydrogen bond between one hydrogen atom of the N13 amino group in **A** and the nitrogen of the pyridyl ring (Fig. 3), which leaves this hydrogen in **3a** free of N–H···N interactions. The absence of this interaction slightly affects the packing efficiency (packing coefficients of 0.706 and 0.712, respectively). The small differences in the conformations of the phenyl/pyridyl rings with respect to the triazine ring **B** (Table 4), as well as the angle between the triazines **A** and **B**, places the amino group in question further away from the equivalent atom in the phenyl (C10) in **3a** than the nitrogen of the pyridyl ring in TETREP [N13···C10/N = 3.588(8) *vs.* 3.107 Å, respectively].

The supramolecular structure can be described as consisting of ribbons of adjacent rosettes (Fig. 3) formed by four molecules of **A** and two molecules of **B** held together by a double hydrogen-bonding system (Fig. 3). The presence of two ribbons in the cell related by a two-fold screw axis along *b* and those related by unit cell translations [Fig. 4(a)], connected by hydrogen interactions through molecules **B**, results in a distorted honeycomb packing as illustrated in Fig. 4.

The three independent molecules in **3i** pack together in a 3D network that leaves several H amino atoms free of interactions. Molecules **A** and **C** are linked to give chains [Fig. 5(a)] by unit cell translation along *b* and these, in turn, are connected in a helical arrangement through contacts between molecules **B** and **C** (Table 4) sharing chains of molecules.

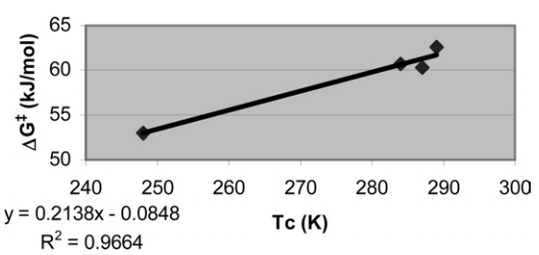


Fig. 1 Coalescence temperature *vs.* $\Delta G^{\ddagger}$ plot for triazines **3a**, **3f**, **3h** and **3j**.

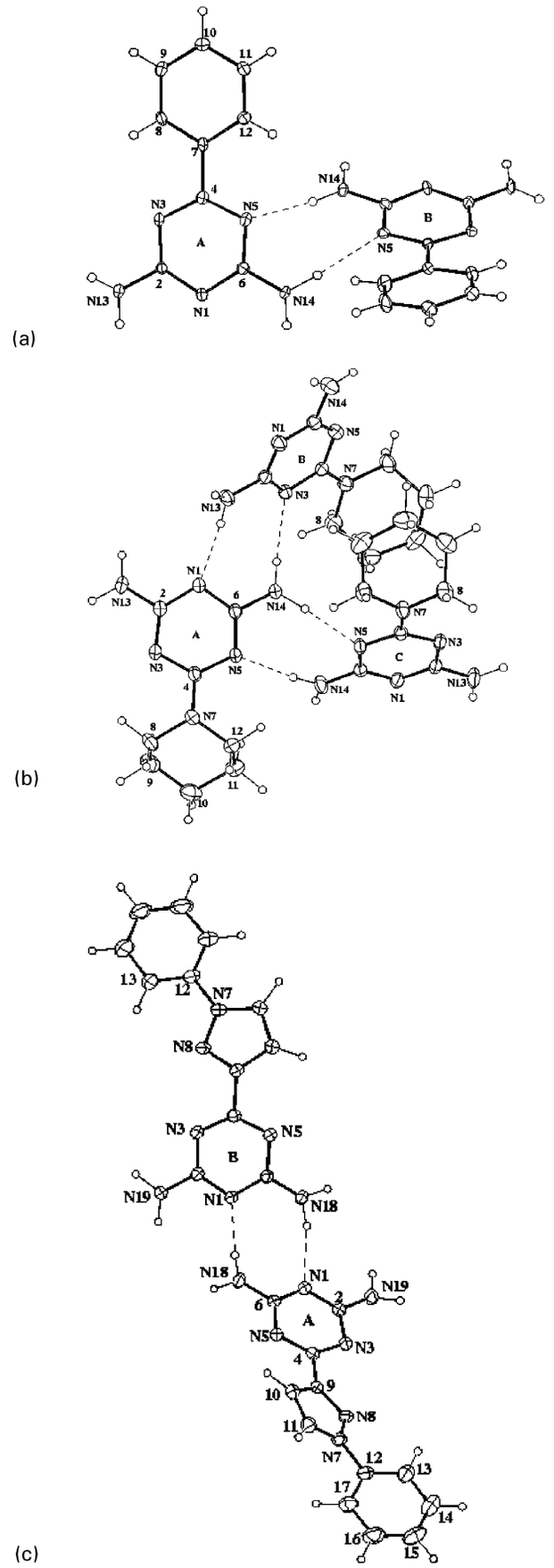


Fig. 2 Asymmetric unit of (a) **3a**, (b) **3i** and (c) **3g**, showing the numbering system. Displacement ellipsoids are drawn at the 30% probability level. Hydrogen bonds are shown with dashed lines.

Table 4 Selected intra- and intermolecular parameters (in Å, °).

	A	B	C
Compound **3a**			
N3–C4–C7–C8	−9.3(7)	6.0(7)	
Compound TETREP[a] (**3h**)			
N3–C4–C7–C8	−7.0	12.1	
Compound **3g**			
N3–C4–C9–N8	−20.3(5)	−7.4(5)	
N8–N7–C12–C13	29.7(5)	10.8(6)	
Compound **3i**			
N3–C4–N7–C8	4.6(7)	0.1(7)	3.6(7)
N5–C4–N7–C12	−15.6(7)	6.6(6)	−11.5(7)

Hydrogen interactions	D–H	H···A	D···A	D–H···A
Compound **3a**				
N13A–H32A···N3B (x , $1/2-y$, $-1/2+z$)	0.86(6)	2.31(6)	3.134(6)	161(5)
N14A–H41B···N1A ($1/2-x$, y, $1-z$)	0.91(6)	2.16(6)	3.062(6)	172(5)
N14A–H42B···N5B	1.01(6)	2.15(6)	3.162(6)	175(5)
N13B–H31B···N5B ($1-x$, $-1/2+y$, $3/2-z$)	0.82(6)	2.45(6)	3.255(6)	165(5)
N13B–H32B···N3A (x, $1/2-y$, $1/2+z$)	0.95(6)	2.09(6)	3.023(6)	168(5)
N14B–H41B···N3B ($1-x$, $-1/2+y$, $3/2+z$)	0.92(6)	2.38(6)	3.249(6)	157(5)
N14B–H42B···N5A	1.00(6)	2.02(6)	3.015(6)	170(5)
Compound **3g**				
N18A–H81A···N3B ($-x$, $y-1/2$, $-z+1/2$)	0.95(5)	2.19(5)	3.089(5)	158(4)
N18A–H82A···N1B	0.94(6)	2.16(6)	3.077(5)	165(4)
N19A–H91A···N5B ($-x+1$, $y-1/2$, $-z+1/2$)	0.84(5)	2.34(5)	3.171(5)	168(4)
N19A–H92A···N8A ($-x+1$, $y+1/2$, $-z+1/2$)	0.86(5)	2.36(6)	3.162(5)	155(4)
N18B–H81B···N3A ($-x+1$, $y+1/2$, $-z+1/2$)	0.81(5)	2.27(6)	3.074(5)	172(4)
N18B–H82B···N1A	0.91(5)	2.15(5)	3.024(5)	163(4)
N19B–H91B···N5A ($-x$, $y+1/2$, $-z+1/2$)	0.93(5)	2.09(5)	3.015(5)	177(4)
N19B–H92B···N8B ($-x$, $y-1/2$, $-z+1/2$)	0.82(6)	2.99(6)	3.390(5)	113(5)
Compound **3i**				
N13A–H31A···N3C (x, $y-1$, z)	0.75(7)	2.35(8)	3.098(6)	172(7)
N14A–H41A···N5C	0.84(7)	2.19(7)	3.032(6)	177(6)
N14A–H42A···N3B	0.84(7)	2.19(7)	3.029(6)	175(6)
N13B–H32B···N1C ($x+1/2$, $-y+1/2$, $-z+1$)	1.01(6)	2.16(6)	3.162(7)	169(5)
N13B–H31B···N1A	0.86(6)	2.27(7)	3.124(6)	172(6)
N14B–H41B···N13B ($-x+1$, $y+1/2$, $-z+3/2$)	0.79(7)	2.55(7)	3.343(7)	179(7)
N13C–H32C···N5B ($-x+1/2$, $-y+1$, $z-1/2$)	0.87(7)	2.52(7)	3.389(7)	177(6)
N13C–H31C···N3A (x, $y+1$, z)	0.80(7)	2.48(7)	3.230(6)	158(7)
N14C–H41C···N1B ($x-1/2$, $-y+1/2$, $-z+1$)	0.87(7)	2.44(7)	3.306(7)	178(6)
N14C–H42C···N5A	0.88(7)	2.25(7)	3.109(6)	170(6)

[a] TETREP is the CSD refcode of 2,4-diamino-4-(6-pyridyl)-1,3,5-triazine, **3h**

Twelve molecules are required for one turn [pitch = b axis = 12.042(1) Å] around a channel in which six piperidino units are directed toward the interior [Figs. 5(b) and 5(c)]. However, there are no voids in the structure and the total packing coefficient is 0.671.

In **3g**, hydrogen bonds between one amino group and one nitrogen of the triazine ring of the independent molecules, arranged in a head-to-tail fashion, leads to the formation of dimers [Fig. 2(c)] that expand in sheets of rosettes perpendicular to the c axis [Fig. 6(a)]. The substituents are located on both sides of the sheets [Fig. 6(b)], allowing the formation of hydrogen bonds between amino groups and pyrazole rings of adjacent sheets in an analogous way to compound **3a** (Fig. 3). In a similar way to **3i**, the total packing coefficient is 0.678, illustrating that the molecules in these two compounds are loosely packed with respect to **3a** and the pyridyl analogue **3h**.

Conclusions

The preparation of 2,4-diamino-6-substituted-1,3,5-triazines has been achieved under microwave irradiation in good yield. This procedure can be classified as a green synthesis due to the high yields, short reaction times, reduction of the volume of solvent, and simple work-up procedure.

The crystal structures of these 2,4-diamino-6-substituted-1,3,5-triazines show that all crystallize with several independent molecules—a situation that results in a donor:acceptor ratio equal or greater than 1. The secondary structures of **3a**, **3h** and **3i** consist of ribbons in which the molecules are connected through double N–H···N hydrogen bonds that, by means of the remaining amino···N(triazine) bonds, results in a 3D network. However, in **3g** only sheets are observed and these are connected by weaker contacts. The cyclic rosettes observed for **3a**, **3h** and **3i** are one of the possible hydrogen-bonded motifs[10] that could be adopted in the solid by 1,3,5-triazine derivatives, as observed in molecular melamine complexes.[10]

Experimental

General

Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. NMR spectra were recorded on Varian Unity 300 and 500 spectrometers with

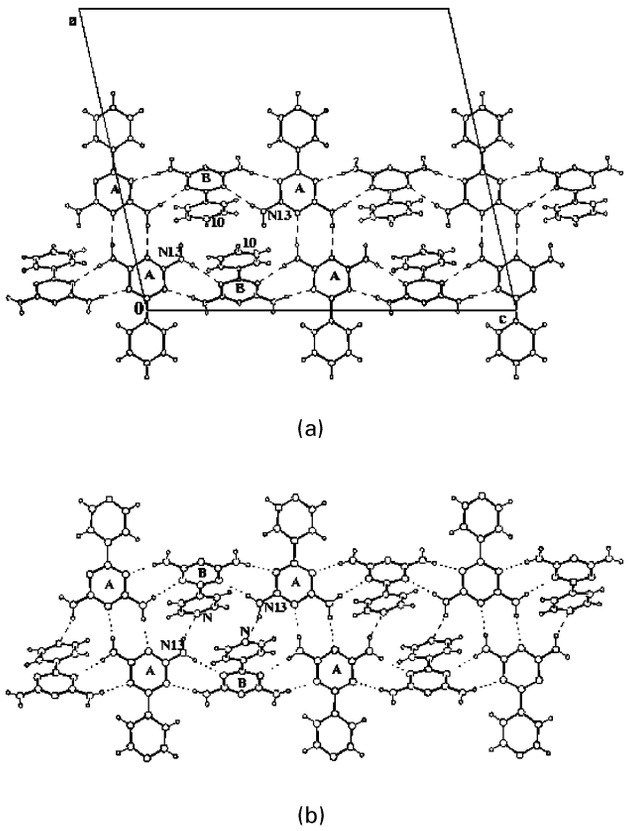


Fig. 3 A fragment of the hydrogen-bonded ribbon of molecules **A** and **B** of (a) **3a** and (b) the TETREP derivative **3h** as projected along *b*. Dashed lines in (b) represent the hydrogen bond between one amino group (N13) in **A** and the nitrogen of the pyridyl ring of **B** with the adjacent ribbons along *b*.

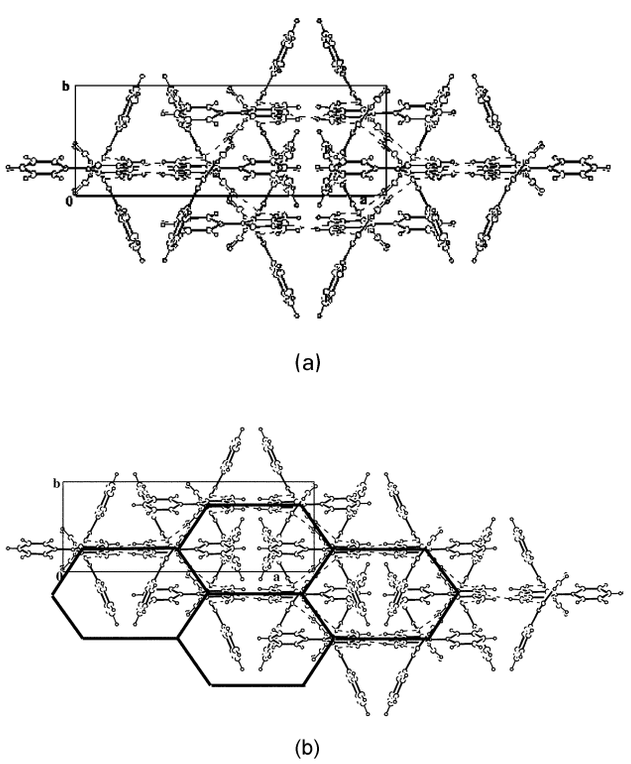


Fig. 4 (a) Assembly of four strands in **3g** leading to the formation of a distorted honeycomb cell. (b) 3D network generated by unit cell translation along *a* and *b* units as represented in (a).

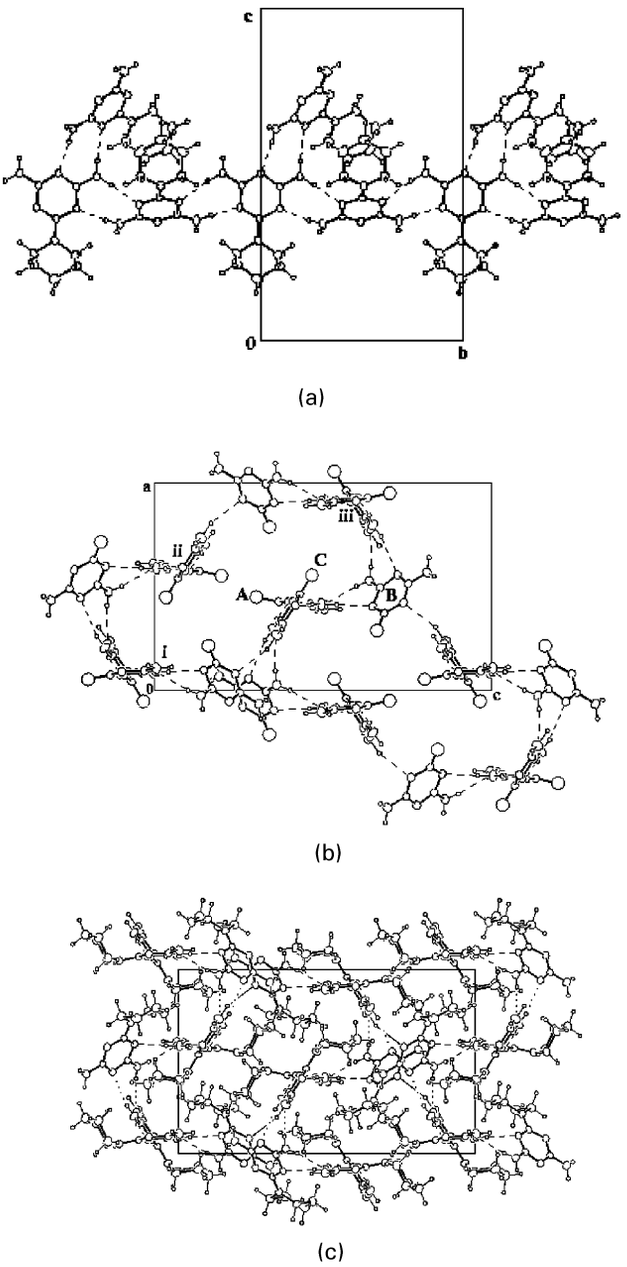


Fig. 5 (a) Chains of molecules of **3i** related by unit cell translation along *b*. (b) The four chains in the unit cell perpendicular to the *ac* plane illustrating the formation of two helices sharing the independent molecules (x, y, z), $i = 1/2-x, 1-y, -1/2+z$, $ii = -x, 3/2+y, -1/2-z$, $iii = 1/2+x, 3/2-y, 1-z$. The piperidino ring has been represented as a sphere for the sake of clarity. (c) Crystal packing down *b*.

TMS as an internal standard. The IR spectra were obtained with a Nicolet-550 FTIR spectrophotometer. Variable temperature experiments were performed at 300 MHz with a probe calibrated with methanol; the coalescence temperatures were determined with a precision of $\pm 0.1^\circ$ and activation free energies were calculated according to Sandström.[21] Flash column chromatography was performed on silica gel 60 (Merck, 230–400 mesh).

X-Ray analysis

Crystals of **3a**, **3g** and **3i** were crystallised from hot ethanol.

X-Ray data for **3a** were collected at 170 K [μ(MoKα) = 0.7107 Å] using a Nonius Kappa CCD diffract-

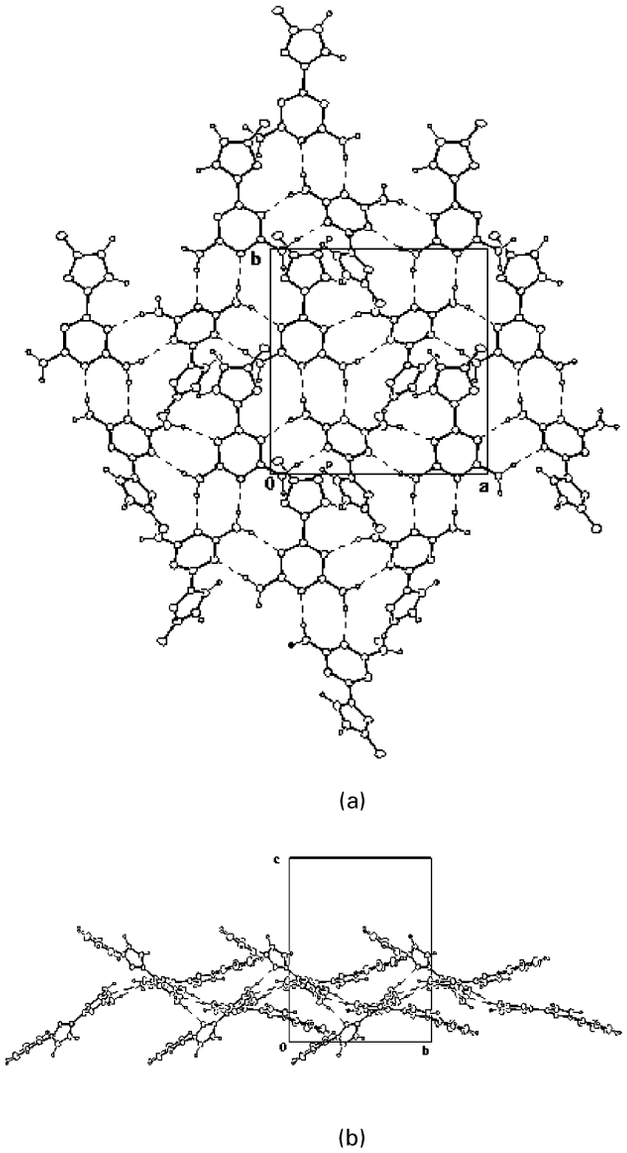


Fig. 6 (a) Crystal packing of compound **3g** illustrating the formation of one corrugated sheet. For clarity, the phenyl ring connected to the pyrazole has been replaced by a sphere. (b) A view down *a* showing the disposition of the pyrazolyl-1-phenyl on both sides of the sheet.

ometer equipped with an Oxford Cryosystem cryostream because the crystals were very difficult to grow (approximate dimensions $0.05 \times 0.05 \times 0.20$ mm^3). Data reduction and cell refinement was carried out with the programs DENZO[23] and COLLECT.[24] For **3g** and **3i**, data collection was carried out on a Seifert XRD3000-S four circle diffractometer [μ(CuKα) = 1.5418 Å] at room temperature. All structures were solved by direct methods[25] and the refinement process was carried out on F^2 against all data using SHELXL97.[26] The absolute structure of **3i** could not be determined as no significant anomalous scatters were present. All hydrogen atoms were located on difference Fourier maps and were allowed to ride during the last cycles of refinement—the exception being those of the amino groups, which were refined isotropically without restraint.†

† CCDC reference numbers 224695–224697 for **3a**, **3g** and **3i**, respectively. See http://www.rsc.org/suppdata/nj/b3/b315956f/ for crystallographic data in .cif or other electronic format.

General procedure for the synthesis of the 2,4-diamino-1,3,5-triazines

A mixture of potassium hydroxide (3 mmol, 0.168 g), dicyandiamide (18 mmol, 1.51 g), the appropriate nitrile (10 mmol) and DMSO (1 mL) was introduced into a Pyrex flask and irradiated in a modified PROLABO Maxidigest focused microwave reactor.[27] The irradiation conditions are summarised in Table 1. After cooling, the crude mixture was suspended in boiling water and filtered. The corresponding diaminotriazines were purified as described below. Compounds **3a**,[1] **3b**,[1] **3c**,[1] and **3h**[2] have been described previously.

2,4-Diamino-6-(4-chlorophenyl)-1,3,5-triazine, 3d. Prepared from 4-chlorobenzonitrile (1.03 g, 7.5 mmol). The diaminotriazine was washed with diethyl ether (5 mL) and dried. Yield 1.36 g (82%), mp 244–248 °C. IR (KBr) 3488, 3441, 1541 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 6.79 (br s, 4H, NH_2), 7.52 (AA′BB′, J_{AB} 8.9, 2H, $H_{3'}$ and $H_{5'}$), 8.22 (AA′BB′, J_{AB} 8.9, 2H, $H_{2'}$ and $H_{6'}$). ^{13}C-NMR (DMSO) δ 128.26 ($C_{2'}$ and $C_{6'}$), 129.39 ($C_{3'}$ and $C_{5'}$), 135.78 ($C_{4'}$), 135.94 ($C_{1'}$), 167.36 (C_2 and C_4), 169.14 (C_6). Anal. Calcd. for $C_9H_8N_5Cl$: C, 48.77; H, 3.64; N, 31.60. Found: C, 48.69; H, 3.69; N, 32.07. MS (EI) m/z 221.11 (M).

2,4-Diamino-6-[2-(pyrazol-1-yl)phenyl]-1,3,5-triazine, 3e. Synthesized from 2-pyrazolylbenzonitrile (1.27 g, 7.5 mmol). The diaminotriazine was washed with dichloromethane (5 mL) and dried. Yield 1.04 g, (52%), mp 183–185 °C. IR (KBr) 3473, 3316, 1631 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 6.36 (t, J 1.5, 1H, pyrazole-H_4), 6.65 (br s, 4H, NH_2), 6.40 (dt, J 7.3, 1.5, 1H, $H_{5'}$), 7.5–7.6 (m, 4H, pyrazole-H_3, $H_{3'}$, $H_{4'}$ and $H_{6'}$), 7.75 (d, J 2, 1H, pyrazole-H_5). ^{13}C-NMR (DMSO) δ 106.76 (pyrazole-C_4), 124.47 ($C_{3'}$), 126.98 ($C_{5'}$), 129.64 ($C_{1'}$), 130.09 ($C_{6'}$), 130.49 (pyrazole-C_5), 133.23 ($C_{4'}$), 137.89 ($C_{2'}$), 140.15 (pyrazole-C_3), 166.87 (C_2 and C_4), 172.89 (C_6). Anal. Calcd. for $C_{12}H_{11}N_7$: C, 56.91, H, 4.38, N, 38.71. Found: C, 56.40; H, 4.30; N, 38.98. MS (EI) m/z 252.09 (M).

2,4-Diamino-6-[3-(pyrazol-1-yl)phenyl]-1,3,5-triazine, 3f. Prepared from 3-pyrazolylbenzonitrile (1.26 g, 7.5 mmol). The diaminotriazine was washed with dichloromethane (5 mL) and dried. Yield 1.81 g (96%), mp 269–272 °C. IR (KBr) 3391, 3354, 1650 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 6.55 (dd, 1H, J 2.4, 1.5, pyrazole-H_4), 6.84 (br s, 4H, NH_2), 7.56 (t, J 8, 1H, $H_{5'}$), 7.76 (d, J 1.5, 1H, pyrazole-H_3), 7.92 (dd, J 8, 1.7, 1H, $H_{4'}$), 8.15 (d, J 8, 1H, $H_{6'}$), 8.50 (d, J 2.4, 1H, pyrazole-H_5), 8.74 (d, J 1.7, 1H, $H_{2'}$). ^{13}C-NMR (DMSO) δ 107.96 (pyrazole-C_4), 118.00 ($C_{2'}$), 120.57 ($C_{4'}$), 125.29 ($C_{6'}$), 127.76 (pyrazole-C_5), 129.29 ($C_{5'}$), 138.61 ($C_{1'}$), 139.75 ($C_{3'}$), 141.02 (pyrazole-C_3), 167.42 ($C_2$and C_4), 169.49 (C_6). Anal. Calcd. for $C_{12}H_{11}N_7$: C, 56.91; H, 4.38; N, 38.71. Found: C, 56.32; H, 4.12; N, 38.48. MS (EI) m/z 253.13 (M).

2,4-Diamino-6-(1-phenylpyrazol-4-yl)-1,3,5-triazine, 3g. Formed from 4-cyano-1-phenylpyrazole (1.26 g, 7.5 mmol). The diaminotriazine was washed with dichloromethane (5 mL) and dried. Yield 1.58 g (83%), mp 250–254 °C. IR (KBr) 3469, 3319, 1542 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 6.65 (br s, 4H, NH_2), 7.34 (t, J 7.4, 1H, $H_{4'}$), 7.50 (t, J 7.5, 2H, $H_{3'}$ and $H_{5'}$), 7.88 (d, J 7.6, 2H, $H_{2'}$ and $H_{6'}$), 8.13 (s, 1H, pyrazole-H_3), 8.76 (s, 1H, pyrazole-H_5). ^{13}C-NMR (DMSO) δ 118.73 ($C_{2'}$ and $C_{6'}$), 124.21 (pyrazole-C_4), 126.80 ($C_{4'}$), 128.11 (pyrazole-C_5), 129.60 ($C_{3'}$ and $C_{5'}$), 139.27 ($C_{1'}$), 140.76 (pyrazole-C_3), 166.46 (C_6), 167.10 (C_2 and C_4). Anal. Calcd. for $C_{12}H_{11}N_7$: C, 56.91; H, 4.38; N, 38.71. Found: C, 56.59; H, 4.45; N, 38.73. MS (EI) m/z 253.18 (M).

2,4-Ddiamino-6-piperidino-1,3,5-triazine, 3i. Synthesized from cyanopiperidine (1.44 g, 15 mmol). The diaminotriazine was washed with dichloromethane (5 mL) and dried. Yield 2.57 g (88%), mp 221–223 °C. IR (KBr) 3497, 3427, 1616 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 1.3–1.45 (m, 4H, H_3 and H_5), 1.5–1.6 (m, 2H, H_4), 3.59 (t, J 5.2, 4H, H_2 and H_6), 6.05 (br s, 4H, NH_2). ^{13}C-NMR (DMSO) δ 25.17 ($C_{4'}$), 26.13 ($C_{3'}$ and $C_{5'}$), 43.94 ($C_{2'}$ and $C_{6'}$), 165.73 (C_6), 167.89 (C_2 and C_4). Anal. Calcd. for $C_8H_{14}N_6$: C, 49.47; H, 7.26; N, 43.27. Found: C, 49.18; H, 8.67; N, 43.74. MS (EI) m/z 194.13 (M).

2,4-Diamino-6-morpholino-1,3,5-triazine, 3j. Prepared from cyanomorpholine (1.68 g, 15 mmol). The diaminotriazine was washed with dichloromethane (5 mL) and dried. Yield 2.09 g (71%), mp 221–223 °C. IR (KBr) 3497, 3427, 1660 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 3.5–3.6 (m, 8H, morpholine-H), 6.14 (br s, 4H, NH_2). ^{13}C-NMR ($CDCl_3$) δ 41.04 ($C_{2'}$ and $C_{6'}$), 66.75 ($C_{3'}$ and $C_{5'}$), 166.15 (C_6), 167.83 (C_2 and C_4). Anal. Calcd. for $C_7H_{12}N_6O$: C, 42.85; H, 6.16; N, 42.83. Found: C, 42.94; H, 5.93; N, 42.84. MS (EI) m/z 196.11 (M).

1,2-Bis(2,4-diamino-1,3,5-triazin-6-yl)benzene, 5. Formed from 1,2-dicyanobenzene (1.92 g, 15 mmol). The diaminotriazine was washed with acetone (5 mL) and dried. Yield 3.54 g (80%), mp > 270 °C. IR (KBr) 3465, 3456, 1394 (ν_{NH}) and ($\nu_{C=N}$). ^{1}H-NMR (DMSO) δ 6.34–6.52 (br s, 8H, NH_2), 7.44 (AA′XX′, J 7.8, 6.7, 1.4, 2H, $H_{2'}$ and $H_{5'}$), 7.60 (AA′XX′, J 7.8, 6.7, 1.4, 2H, $H_{3'}$ and $H_{4'}$). ^{13}C-NMR (DMSO) δ 128.36 ($C_{3'}$ and $C_{6'}$), 129.30 ($C_{4'}$ and $C_{5'}$), 138.66 ($C_{1'}$ and $C_{2'}$), 173.90 (C_6), 166.80 (C_2 and C_4). Anal. Calcd. for $C_{12}H_{12}N_{10}$: C, 48.64; H, 4.08; N, 47.27. Found: C, 47.47, H; 4.06, N; 45.95. MS (EI) m/z 296.00 (M).

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