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# Microwave-assisted synthesis of pyrazolyl bistriazines

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ABSTRACT

Reaction of 6-chloro-*N*,*N*′-bispyrazolyl-[1,3,5]triazine-2,4-diamines with 4-aminobenzylamine under microwave irradiation produces bistriazines in excellent yields. The use of a diamine bearing amino groups with different reactivities allowed the reaction to be carried out in two steps and selectively gave monotriazines, bistriazines with identical substituents and differently substituted bistriazines. The structures of these new compounds have been studied by NMR spectroscopy, mass spectrometry and in one case by X-ray crystallogrphy. These new bistriazines have promising applications in supramolecular chemistry based on hydrogen bonds and/or complexation with metals. The presence of a rigid linker can be used for the efficient preparation of extended supramolecular polymers with interesting fluorescence properties by complexation with cyanuric and barbituric acid derivatives.



## 1. Introduction

Supramolecular chemistry is one of the most important areas in chemistry in the 21st Century.[1] This field was defined by Lehn as the 'Chemistry of molecular assemblies and of the intermolecular bond'. The control of structures using supramolecular interactions is an area of great interest in chemistry, biochemistry and crystal engineering.

*s*-Triazine derivatives have important applications in the most significant fields of Organic Chemistry, including Medicinal,[2,3] Materials[4–6] and Supramolecular Chemistry.[7–11]

The *s*-triazine ring is a remarkable system to produce supramolecular structures[12] and the variety of interactions involving this system has recently been reviewed.[13]

Aminotriazines have also been widely used because they easily form hydrogen bonds[7,9–11] and coordinate to transition metals.[8]

Microwave irradiation has been used with great success in organic synthesis and a wide variety of reactions have been improved under these conditions[14]—including modification of the selectivity.[15]

In recent years we have synthesized a series of pyrazolyl-substituted triazines under microwave irradiation[16] and we subsequently used these compounds to prepare supramolecular structures through the formation of intermolecular hydrogen bonds[17] and coordination with metals.[18]

The use of microwave irradiation permitted the selective preparation of di- and tri-substituted triazines and enabled the design of a green procedure for their preparation.[16]

In this paper we describe the preparation of new bistriazines with pyrazolyl substituents under microwave irradiation conditions. These new polydentate ligands have numerous possibilities in this field. The formation of supramolecular aggregates of bistriazines with barbituric acid derivatives has been reported to give rise to different structures such as 1+1 complexes and folded or extended supramolecular polymers. On using a flexible linker the formation of 1+1 complexes is favoured up to the point where the number of atoms in the linker is 8. After this point an extended supramolecular complex is formed and a folded supramolecular polymer results when the number of atoms in the linker reaches 11.[10] In the present paper we describe the use of a linker with an aromatic ring. The use of a rigid linker is expected to favour the formation of extended supramolecular polymers.

## 2. Results and discussion

4-Aminobenzylamine was selected as the spacer because it possesses two different amino groups, one aliphatic (more nucleophilic) and other aromatic (less nucleophilic); as a consequence, it should be possible to control the reaction and to obtain

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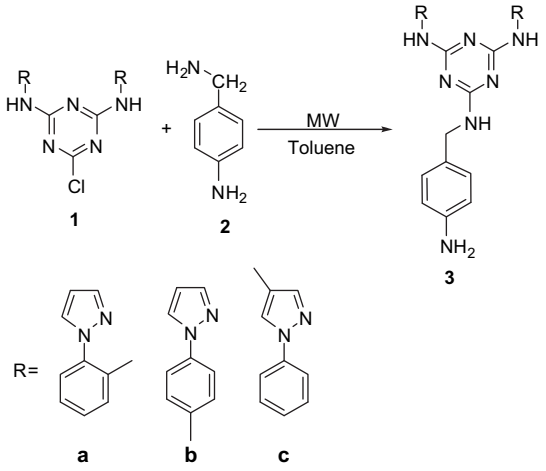
selectively the mono- and di-substitution products. The starting chlorotriazines **1** were previously described by our group and prepared by reaction of cyanuric chloride with the corresponding amine in THF using diisopropylethylamine as the base.[16c]

Monosubstitution reactions were performed under microwave irradiation at 270 W using toluene as the solvent and two equivalents of 4-aminobenzylamine (Scheme 1). A high initial power was used in order to reach the desired temperature in a short time. Reactions were first tried in solvent-free conditions but only moderate yields of triazines **3** were obtained (57–73%) and the starting triazine **1** was not completely consumed (18–33%). We believe that the reaction did not reach completion because the reaction mixture was a highly heterogeneous slurry. As a result, it was decided to use a small amount of toluene (1 mL/mmol) as a solvent, which is transparent to microwaves ($\varepsilon'$=2.408),[19] in order to obtain a homogeneous suspension. Under these conditions excellent yields were obtained using 22 equiv of 4-aminobenzylamine, which acts as both a nucleophile and a base to neutralize the acid liberated in the reaction (Scheme 1). Pure products were obtained simply by precipitation upon the addition of water.




**Scheme 1.**

Substitution through the aromatic amino group required stronger conditions. In this respect, the use of toluene as the solvent produced low yields (6%) in the reaction of **1b** with **3b** even when heated under reflux. In order to attain a higher temperature the polar solvent DMSO was used, again in a small amount (1 mL/mmol) (Scheme 2). The use of an excess of **3b**, again as a nucleophile and a base, made the isolation of the dimeric triazine **4b** difficult as these compounds, **3** and **4**, had the same $R_f$ value in chromatography studies; moreover, the major product was **5b** because elimination of the benzylamino group should be favoured under basic conditions (Table 1, entry 1). Therefore, a hindered amine, diisopropylethylamine (DIPEA), was assessed as a base but **5b** was still the main product (Table 1, entry 2). Finally, the best results were obtained on using DIPEA as the base and an excess of the starting chlorotriazine **1b** (Table 1, entry 3). However, even under these conditions, formation of the aminotriazine **5** was decreased but not completely avoided (Scheme 2).

**Table 1**
Reaction of **1b** with **3b** (DMSO, 1 mL/mmol, time, 10 min, temperature, 140 °C, under microwave irradiation, 270 W)

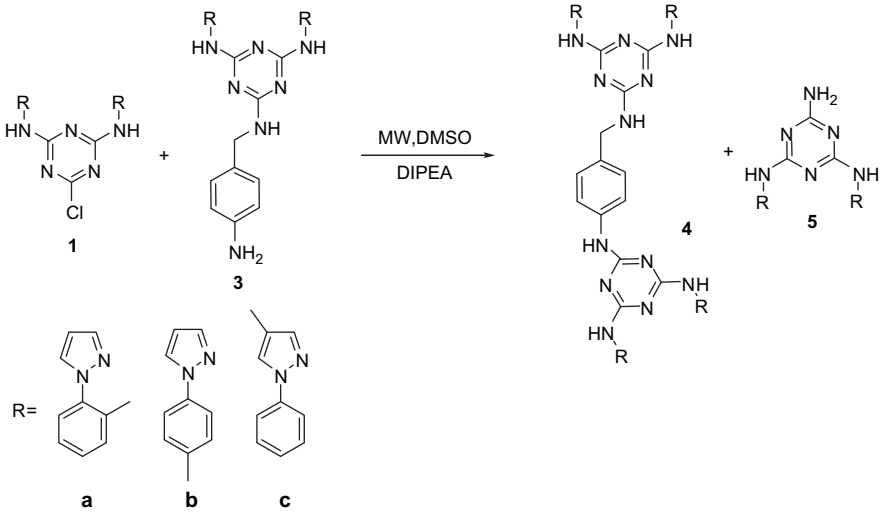
| Entry | **1b**:**3b**:DIPEA | Yield **4b** (%) | Yield **5b** (%) |
|---|---|---|---|
| 1 | 1:2:0 | 36 | 63 |
| 2 | 1:1:1 | 35 | 49 |
| 3 | 2:1:1 | 61 | 38 |

The use of small amounts of a solvent and the simplicity of the isolation procedure (precipitation with water) makes this method a green procedure for the preparation of this kind of compound.

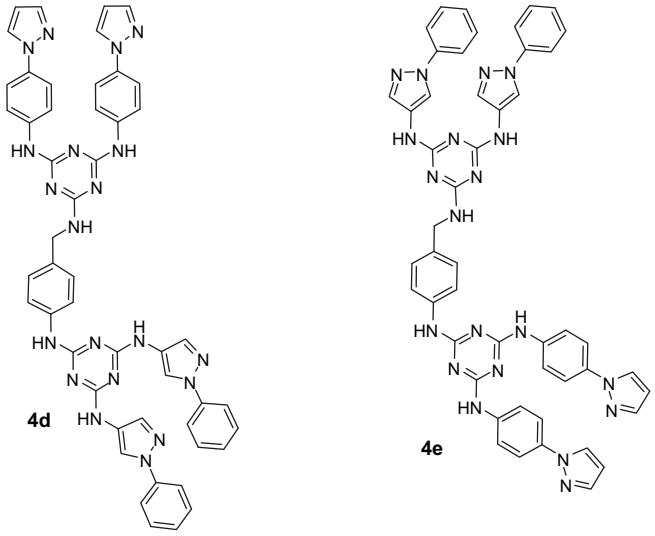
Isolation of monomeric triazines **3** permitted the preparation of asymmetrically substituted dimeric triazines. Under the same conditions, shown in Scheme 2, excellent yields of dimeric triazines **4d** and **4e** were obtained (Table 2 and Scheme 3). It is remarkable that in these reactions the formation of the aminotriazines **5b** and **5c** was not observed.

**Table 2**
Synthesis of mono- and bistriazines **3** and **4**

| Compound | Power (W) | Time (min) | Temp (°C) | Yield (%) |
|---|---|---|---|---|
| **3a** | 270 | 45 | 80 | 84 |
| **3b** | 270 | 15 | 80 | 98 |
| **3c** | 270 | 20 | 80 | 96 |
| **4a**+**5a** | 50 | 10 | 140 | 64 (**4a**)<br>27 (**5a**) |
| **4b**+**5b** | 50 | 10 | 140 | 61 (**4b**)<br>37 (**5b**) |
| **4c**+**5c** | 50 | 10 | 140 | 86 (**4c**)<br>13 (**5c**) |
| **4d** | 50 | 10 | 140 | 98 |
| **4e** | 50 | 10 | 140 | 92 |




**Scheme 2.** Synthesis of symmetrically substituted bistriazines **4a–c**.




**Scheme 3.** Structures of asymmetrically substituted bistriazines **4d–e**.

### 2.1. NMR spectroscopy

The NMR spectra of compounds **3–5** at room temperature show a complex pattern with broad signals as a consequence of the restricted rotation of the triazine–nitrogen bond. The free energy of activation of aminotriazines has been determined by us[16c,e] and others[20] and lies in the range 50–80 KJ mol$^{-1}$. In triazines **3–5**, three rotamers are expected for compounds **5**, four for compounds **3** and up to sixteen rotamers for compounds **4** due to the presence of two triazine rings with four rotamers each (Fig. 1).

The NMR spectra recorded at 135 °C (308 K) show narrow signals for all compounds and chemical shifts and coupling constants can be assigned (Table S-1). Compounds **3–5** show characteristic signals of pyrazole and substituted aryl groups. Compounds **3** and **4** show the simplified AA′XX′ systems of the *p*-phenylene group at 6.60 and 7.07 for compounds **3** and 7.3 and 7.7 for compounds **4**. The aliphatic $NH_2$ group of compounds **3** appears at $\delta$ 4 and is shifted downfield to $\delta$ 8–9 in compounds **4**. Comparison of the NMR spectra of **3** and **5** permits the assignment of all signals in compounds **4** (Figs. 2 and 3).

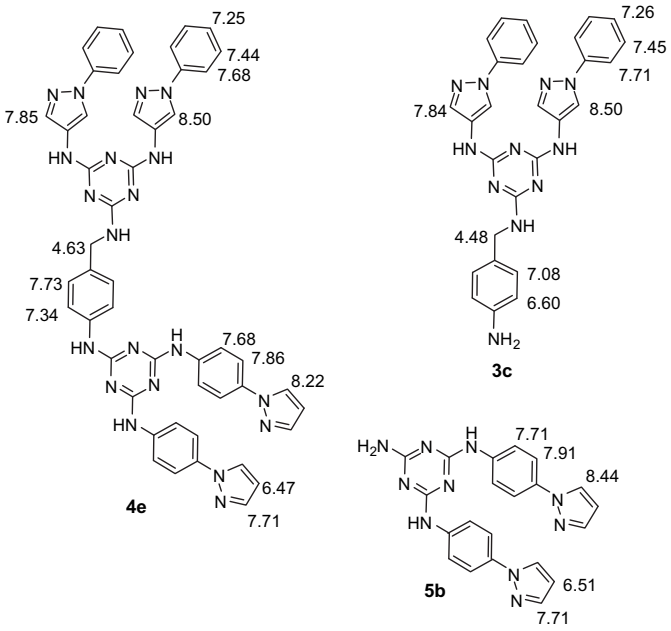



**Figure 2.** NMR assignment of compound **4e** from **3c** and **5b**.

### 2.2. Crystal structure of compound 3a

Compound **3a** crystallizes from a THF/ethanol solution in the monoclinic $P2_1/n$ space group. Crystal data, bond lengths and angles and the packing arrangement are collected in Tables S-2 and S-3 and Figure S2, respectively.

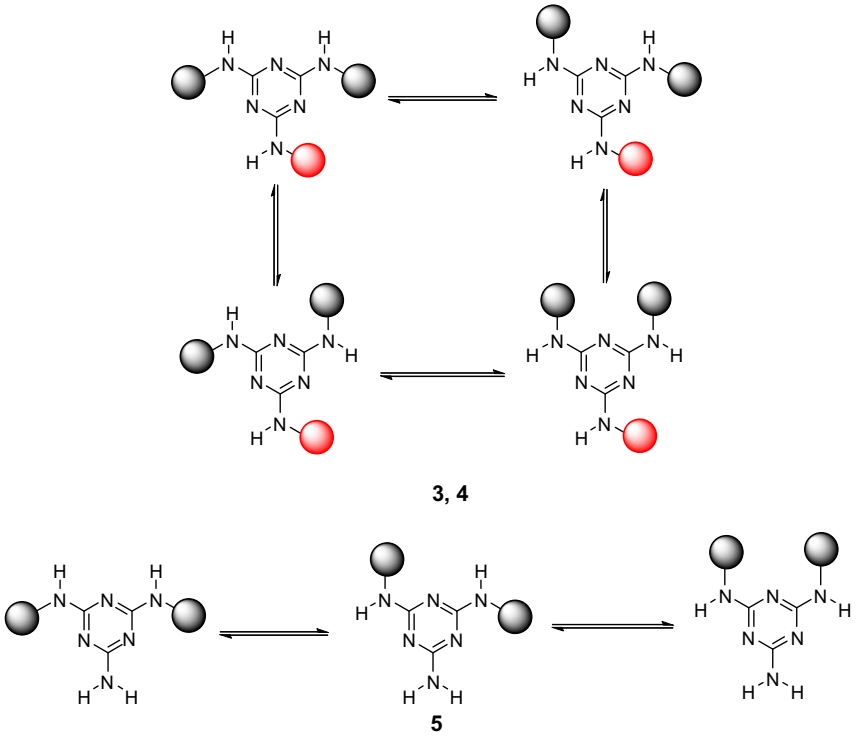



**Figure 1.** Expected rotamers for compounds **3–5**.

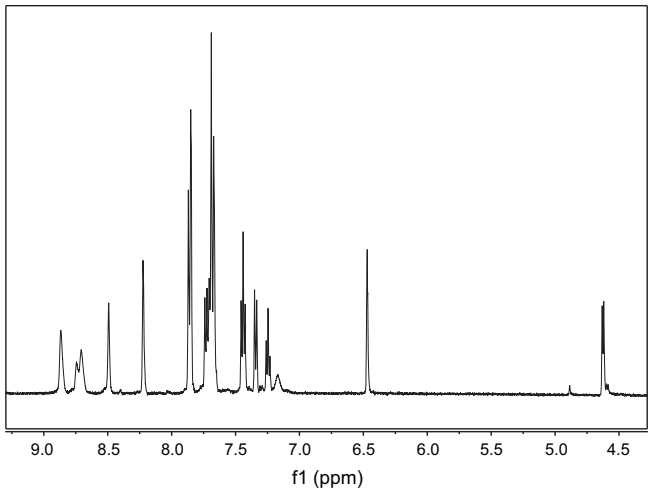



**Figure 3.** NMR spectrum of **4e** recorded at 135 °C in DMSO-$d_6$.

The asymmetric unit shows only one rotamer for compound **3a**, with both aromatic rings in a *trans* conformation with respect to the triazine N1 atom [torsion angles for N1–C1–N4–C11 and N1–C2–N6–C21 are 178.0(2) and 175.4(2)°, respectively] (Fig. 4). All amino groups are coplanar with the triazine ring [0.021(3), 0.009(3) and 0.042(3) Å out of the triazine plane for N4, N5 and N6, respectively]. The dihedral angles between planes C11–C16 and C21–C26 and the triazine ring are 31.9(1) and 33.2(1)°, respectively.

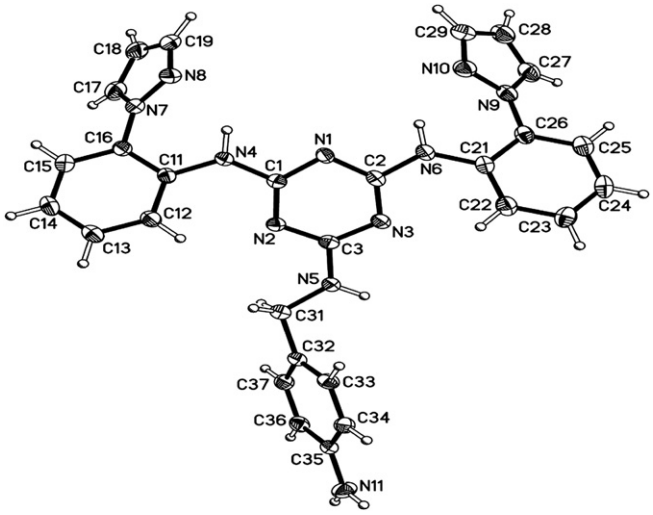



**Figure 4.** ORTEP diagram of **3a** with 30% probability ellipsoids. Dashed lines represent hydrogen bonds.

An interesting supramolecular structure supported by weak interactions is observed. Two intermolecular hydrogen bonds ($N_{11}$–$H_{11a}$···$N_1$ and $N_{11}$–$H_{11b}$···$N_8$) support a supramolecular chain in which the dihedral angle between two adjacent triazine rings is 84.5° (Fig. 5 and Table 3). Therefore $N_8$ is implicated in a bifurcated hydrogen bond with $N_4$–$H_4$ and $N_{11}$–$H_{11b}$ (Table 3).

**Table 3**
Hydrogen bonds for compound **3a**. Distances in Å

| D–H···A | d(D–H) | D(H..A) | <DHA | d(D..A) | Symmetry |
|---|---|---|---|---|---|
| $N_4$–$H_4$···$N_8$ | 0.98 | 2.169 | 131.6 | 2.814(3) | x, y, z |
| $N_6$–$H_6$···$N_{10}$ | 0.98 | 2.074 | 133.1 | 2.735(3) | x, y, z |
| $N_{11}$–$H_{11a}$···$N_1$ | 0.98 | 2.286 | 155.5 | 3.089(3) | x−$^1/_2$ , $^1/_2$ −y, $^1/_2$ +z |
| $N_{11}$–$H_{11b}$···$N_8$ | 0.98 | 2.442 | 149.4 | 3.212(3) | x−$^1/_2$ , $^1/_2$ −y, $^1/_2$ +z |

Each polymeric supramolecular chain interacts with two more polymeric chains through weak π–π and C–H···π interactions. Information for these interactions is collected in Table 4 and Figures 6–8. The π–π interactions are observed between triazine rings that lie in completely parallel planes and have alternate N and C atoms; this corresponds to a $[\sigma-\sigma]^2$ face-to-face geometry, where the stacking interactions involve the heteroatoms and not the two electron-poor ring centroids. This is expected to be the most stable triazine–triazine stack as it has six stabilizing interactions between electron rich N–atoms and electron deficient C–atoms and only one centroid–centroid repulsive interaction (Fig. 6).[13]

**Table 4**
Weak intermolecular interactions

| Interaction | Atoms involved | d(Å) | Dihedral(°) | Symmetry |
|---|---|---|---|---|
| Edge-to-face π···π | D ring···F ring | 4.916 | 75.5 | 1−x, 1−y, 1−z |
| Edge-to-face π···π | E ring···F ring | 4.692 | 72.1 | x+1, y, z |
| π···π | A ring···A ring | 3.594 | 0 | 1−x, −y, 1−z |
| C–H···π | $H_{19}$···F ring | 2.952 | 34.9 | 1−x, −y, 1−z |

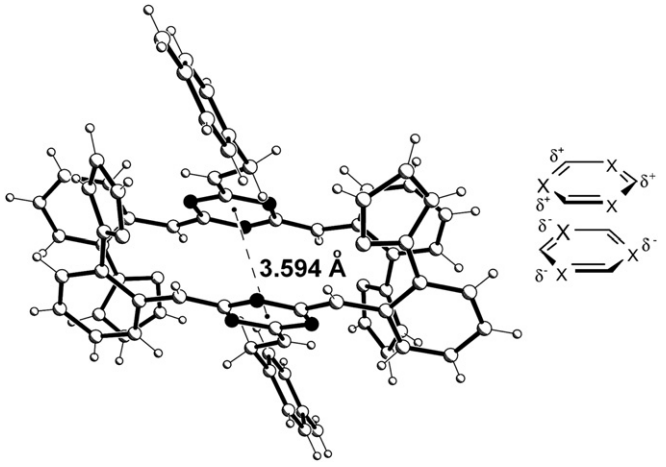



**Figure 6.** π–π Interaction between two triazine rings.

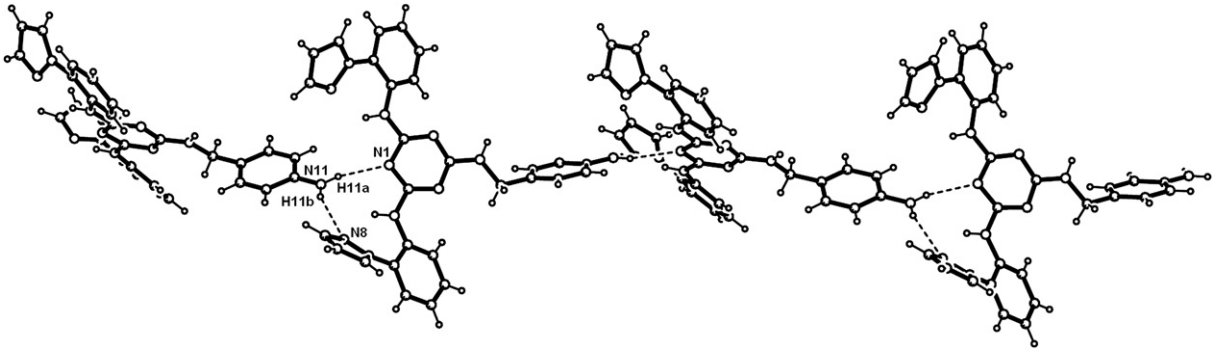



**Figure 5.** Supramolecular chain arrangement of compound **3a** in the crystal structure.

There are two π–π edge-to-face interactions. The phenylene ring and the pyrazolylphenyl group are in an almost ideal orthogonal arrangement, with a distance between centroids of 4.916 Å. The second interaction observed between the phenylene ring and the pyrazolyl group shows a distance between centroids of 4.693 Å (Fig. 7).[21] However, in both cases C–H···π interactions between H27···F ring and H33···D ring ($d$=2.656 Å and 2.708 Å, respectively) could also be present.[22]

Finally, one more C–H···π interaction is observed between a C–H atom of a pyrazolyl group and the *p*-phenylene ring, with a dihedral angle of 34.9° (Fig. 8).[22]

It should be remarked that all weak interactions are observed between two adjacent triazine groups. These weak interactions support the arrangement of the supramolecular chains. The first chain shows C–H···π interactions through F ring and $H_{27}$ with a second chain and C–H···π interactions through D ring and $H_{33}$, with a third chain (Fig. 7).[12]

In conclusion, microwave irradiation provides an efficient and green procedure for the selective preparation of mono- and bistriazines **3** and **4**, respectively. The title compounds were obtained in good to excellent yields in short reaction times and with a simple isolation procedure. Compounds **3** and **4** show restricted rotation of the triazine–amino bond and compound **3a** has an interesting supramolecular structure in the solid state.

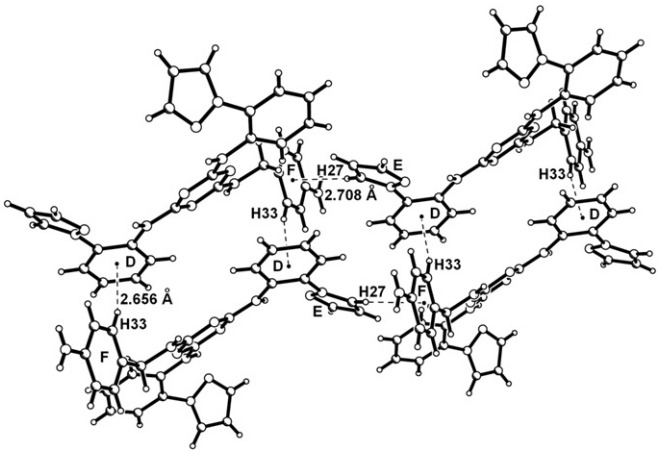



**Figure 7.** π–π edge-to-face interactions of *p*-phenylene with phenyl and pyrazolyl groups.

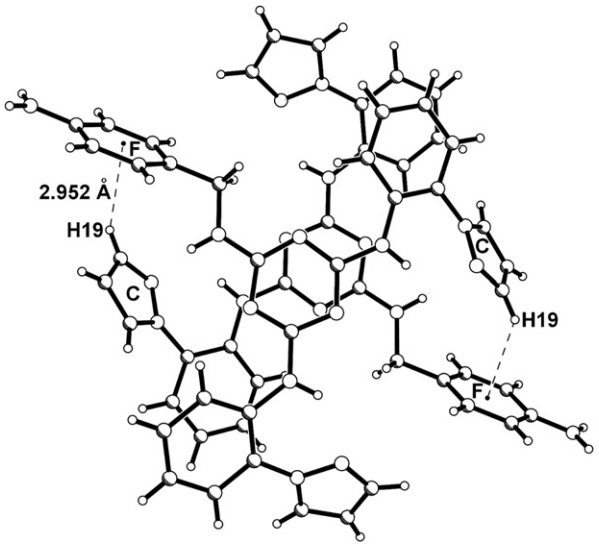



**Figure 8.** C–H···π Interaction between pyrazolyl and a *p*-phenylene group.

These compounds have potential applications in the preparation of supramolecular structures through hydrogen bonding or coordination with metals.

## 3. Experimental section

### 3.1. General

Melting points are uncorrected. NMR spectra were recorded on a spectrometer operating at 499.772 MHz for $^1$H and 125.678 MHz for $^{13}$C with TMS as the internal standard.

Commercially available starting materials were used without purification. 2,4-Bispyrazolyl-substituted-6-chlorotriazines **1** were prepared according to previously described procedures.[16c]

The mass spectra were recorded using electron impact at 70 eV and when the ionization technique was FAB the matrix *m*-nitrobenzyl alcohol was used; determination of exact mass was carried out with polyethylene glycol as the internal standard. Flash column chromatography was performed on silica gel 60 (230–400 mesh).

Reactions under microwave irradiation were performed in a CEM Discover microwave reactor. Temperature was measured with an IR pyrometer.

### 3.2. General procedure for the synthesis of 4-aminobenzylaminotriazines

A mixture of 4-aminobenzylamine (**2**) (2 mmol, 0.244 g), the appropriate 2,4-bispyrazolyl-substituted-6-chlorotriazine **1** (1 mmol) and toluene (1 mL) was introduced into a Pyrex flask and submitted to microwave irradiation at 270 W during the required time (vide infra). The toluene was evaporated under vacuum. The crude mixture was suspended in cold water and the solid was filtered off and washed with water (3×10 mL). The resulting solid was the pure triazine.

*3.2.1. N-(4-Aminobenzyl)-N′,N″-bis-(2-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine* ***3a***. From 6-chloro-*N*,*N*′-bis-(2-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4-diamine **1a**. The mixture was submitted to microwave irradiation for 45 min. Yield 0.441 g (84%): mp 187–188 °C; IR (KBr) 3412, 3348, 1577, 1545 cm$^{-1}$; $^1$H NMR (DMSO, 100 °C) $\delta$ 4.31 (d, $J$=5.7 Hz, 2H), 4.75 (br s, 2H), 6.54 (s, 2H), 6.57 (d, $J$=8.3 Hz, 2H), 7.02 (d, $J$=8.3 Hz, 2H), 7.18 (t, $J$=7.1 Hz, 2H), 7.28 (br s, 2H), 7.35 (t, $J$=7.3 Hz, 2H), 7.49 (d, $J$=8.3 Hz, 2H), 7.85 (d, $J$=1.5 Hz, 2H), 8.12 (d, $J$=2.4 Hz, 2H), 8.36 (d, $J$=7.3 Hz, 2H), 9.16 (br s, 1H); $^{13}$C NMR (DMSO, 25 °C) $\delta$ 43.3, 107.1, 107.1, 113.7, 113.8, 123.0, 123.3, 123.6, 123.7, 123.8, 124.0, 125.3, 126.9, 127.3, 127.4, 127.9, 128.2, 128.3, 128.9, 129.9, 130.1, 131.2, 131.3, 132.0, 132.2, 137.3, 140.9, 141.0, 147.0, 147.4, 163.9, 164.0, 165.6; MS (FAB) $m/z$ 516.0 (M+H$^+$), 1031.0 (2 M+H$^+$); HRMS calcd for $C_{28}H_{25}N_{11}$ $m/z$: 516.2373, found: 516.2367.

*3.2.2. N-(4-Aminobenzyl)-N′,N″-bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine* ***3b***. From 6-chloro-*N*,*N*′-bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4-diamine **1b** (1 mmol, 0.429 g). The mixture was submitted to microwave irradiation for 15 min. Yield 0.505 g (98%): mp 124–127 °C; IR (KBr) 3263, 1620, 1579 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 25 °C) $\delta$ 3.64 (br s, 2H), 4.49 (d, $J$=5.9 Hz, 2H), 5.60 (br s, 1H), 6.43 (s, 2H, $H_4$), 6.61 (d, $J$=8.5 Hz, 2H), 7.10 (d, $J$=8.5 Hz, 2H), 7.28 (br s, 1H), 7.33 (br s, 1H), 7.5 (m, 8H), 7.69 (d, $J$=1.5 Hz, 2H), 7.83 (s, 2H); $^{13}$C NMR ($CDCl_3$, 25 °C) $\delta$ 44.5, 107.3, 115.2, 119.7, 120.9, 121.1, 126.7, 128.4, 128.8, 135.5, 137.3, 140.8, 145.8, 164.1, 164.3, 165.9; MS (EI) $m/z$ 515.2 (M$^+$); HRMS calcd for $C_{28}H_{25}N_{11}$ $m/z$: 516.2373, found: 516.2358.

*3.2.3. N-(4-Aminobenzyl)-N′,N″-bis-(1-phenyl-1H-pyrazol-4-yl)-[1,3,5]triazine-2,4,6-triamine* ***3c***. From 6-chloro-*N*,*N*′-bis-(1-phenyl-

1*H*-pyrazol-4-yl)-[1,3,5]triazine-2,4-diamine **1c**. The mixture was submitted to microwave irradiation for 20 min. Yield 0.490 g (96%): mp 200–201 °C; IR (KBr) 3432, 1597, 1534 $cm^{-1}$; $^1H$ NMR (DMSO, 135 °C) $\delta$ 4.48 (d, $J$=3.9 Hz, 2H), 6.60 (d, $J$=8.3 Hz, 2H), 6.96 (br s, 1H), 7.08 (d, $J$=8.3 Hz, 2H), 7.26 (t, $J$=7.3 Hz, 2H), 7.45 (dd, $J$=7.3, 7.8 Hz, 4H), 7.71 (d, $J$=7.8 Hz, 4H), 7.84 (s, 2H), 8.50 (s, 2H), 8.66 (br s, 2H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 43.1, 113.8, 116.4, 116.8, 117.4, 117.6, 125.5, 125.5, 126.9, 127.2, 128.3, 129.4, 129.5, 133.1, 139.7, 139.9, 147.4, 163.1, 163.3, 163.6, 165.9; MS (FAB) $m/z$ 516.1 (M+$H^+$), 1031.0 (2 M+$H^+$); HRMS calcd for $C_{28}H_{25}N_{11}$ $m/z$: 516.2373; found: 516.2365.

### 3.3. General procedure for the synthesis of bistriazines

A mixture of triazine **3** (0.25 mmol, 0.129 g), the appropriate 2,4-bispyrazolyl-substituted-6-chlorotriazine **1** (0.5 mmol, 0.214 g), diisopropylethylamine (0.25 mmol, 0.031 g) and DMSO (1 mL) was introduced into a Pyrex flask and submitted to microwave irradiation at 50 W for 10 min. The crude mixture was suspended in cold water and the solid was filtered off and washed with water (5×10 mL). The solid was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) gradient ethyl acetate as the eluent.

*3.3.1. N,N-Bis{bis-[4,6-(2-pyrazol-1-ylphenylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4a**.* From *N*-(4-aminobenzyl)-*N*′,*N*″-bis-(2-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine **3a** (0.25 mmol, 0.129 g) and 6-chloro-*N*,*N*′-bis-(2-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4-diamine **1a** (0.5 mmol, 0.214 g).

The solid was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) gradient ethyl acetate as the eluent. *N*,*N*-Bis{bis-[4,6-(2-pyrazol-1-ylphenylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4a**, 0.147 g (64%), was eluted first followed by 2-amino-4,6-bis(2-pyrazol-1-ylphenylamino)-1,3,5-triazine **5a**, 0.028 g (27%).

*3.3.1.1. N,N-Bis{bis-[4,6-(2-pyrazol-1-ylphenylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4a**.* Yield 0.147 g (64%): mp 142–143.5 °C; IR (KBr) 3263, 1575, 1505 $cm^{-1}$; $^1H$ NMR (DMSO, 25 °C) $\delta$ 4.35 (d, $J$=5.86 Hz, 2H): 6.55 (m, 4H), 7.1–7.25 (m, 6H), 7.3–7.4 (m, 4H), 7.52 (m, 6H), 7.8–7.95 (m, 5H), 8.1–8.4 (m, 8H), 9.36 (s, 1H), 9.46 (s, 1H), 9.49 (s, 1H), 9.52 (s, 1H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 43.2, 107.1, 120.2, 123.2, 123.6, 123.8, 123.9, 127.3, 127.4, 130.0, 131.3, 131.3, 131.9, 132.1, 133.8, 138.1, 140.9, 163.9, 163.9, 164.0, 164.1, 165.7; MS (FAB) $m/z$ 909 (M+$H^+$), 1817 (2 M+$H^+$); HRMS calcd for $C_{49}H_{41}N_{20}$ $m/z$: 909.3823; found: 909.3843.

*3.3.1.2. N,N′-Bis-(2-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine **5a**.* Yield 0.028 g (27%): mp 163–165 °C; IR (KBr) 3275, 1568, 1487, 1408 $cm^{-1}$; $^1H$ NMR (DMSO, 135 °C) $\delta$ 6.30–6.6 (m, 2H), 7–7.7 (m, 8H), 7.82 (m, 2H), 8.11 (s, 2H), 8.2–8.4 (m, 2H), 8.9–9.3 (m, 2H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 107.1, 123.2, 123.7, 124.0, 127.4, 130.1, 131.3, 131.3, 132.0, 140.9, 141.0, 164.3, 167.0; MS (FAB) $m/z$ 411 (M+$H^+$); HRMS calcd for $C_{21}H_{18}N_{10}$ $m/z$: 411.1794; found: 411.1804.

*3.3.2. N,N′-Bis{bis[4,6-(4-pyrazol-1-ylphenylamino)]-1,3,5-triazin-2-yl}-4-aminobenzyl amine **4b**.* From *N*-(4-aminobenzyl)-*N*′,*N*″-bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine **3b** (0.25 mmol, 0.129 g) and 6-chloro-*N*,*N*′-bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4-diamine **1b** (0.5 mmol, 0.214 g).

The solid was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) gradient ethyl acetate as the eluent. *N*,*N*′-Bis{bis[4,6-(4-pyrazol-1-ylphenylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4b**, 0.135 g (61%), was eluted first followed by *N*,*N*′-bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine **5b**, 0.038 g (37%).

*3.3.2.1. N,N′-bis{bis[4,6-(4-pyrazol-1-ylphenylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4b**.* Yield 0.135 g (61%): mp 175.1–176.4 °C; IR (KBr) 3400, 3269, 1618, 1580 $cm^{-1}$; $^1H$ NMR (DMSO, 25 °C) $\delta$ 4.55 (d, $J$=5.9 Hz, 2H), 6.51 (s, 4H), 7.33 (d, $J$=8.4 Hz, 2H), 7.70 (s, 4H), 7.7–8.0 (m, 22H), 8.41 (d, $J$=2.2 Hz, 4H), 9.2–9.5 (m, 4H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 42.7, 107.4, 118.6, 120.3, 120.7, 127.2, 127.4, 134.0, 134.3, 138.2, 138.4, 140.4, 163.9, 164.0, 165.78; MS (FAB) $m/z$ 909 (M+$H^+$), 1817 (2 M+$H^+$); HRMS calcd for $C_{49}H_{41}N_{20}$ $m/z$: 909.3823; found: 909.3834.

*3.3.2.2. N,N′-Bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4,6-triamine **5b**.* Yield 0.038 g (37%): mp >265 °C; IR (KBr) 3173, 1619, 1583 $cm^{-1}$; $^1H$ NMR (DMSO, 25 °C) $\delta$ 6.51 (t, $J$=2.2 Hz, 2H), 6.66 (br s, 2H), 7.71 (m, 6H), 7.91 (d, 4H, $J$=8.3 Hz), 8.44 (d, 2H, $J$=2.4 Hz), 9.23 (s, 2H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 107.4, 118.7, 120.4, 127.4, 134.1, 138.6, 140.4, 164.4, 166.8; MS (FAB) $m/z$ 411 (M+$H^+$), 821 (2 M+$H^+$); HRMS calcd for $C_{21}H_{18}N_{10}$ $m/z$: 411.1794; found: 411.1806.

*3.3.3. N,N-Bis{bis[4,6-(1-phenylpyrazol-4-ylamino)]-1,3,5-triazin-2-yl}-4-aminobenzyl amine **4c**.* From *N*-(4-aminobenzyl)-*N*′,*N*″-bis-(1-phenylpyrazol-4-yl)-[1,3,5]triazine-2,4,6-triamine **3c** (0.25 mmol, 0.129 g) and 6-chloro-*N*,*N*′-bis-(1-phenylpyrazol-4-yl)-[1,3,5]triazine-2,4-diamine **1c** (0.5 mmol, 0.214 g).

The solid was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) gradient ethyl acetate as the eluent. *N*,*N*-Bis{bis[4,6-(1-phenylpyrazol-4-ylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4c**, 0.196 g (86%), was eluted first followed by *N*′,*N*″-bis-(1-phenylpyrazol-4-yl)-[1,3,5]triazine-2,4,6-triamine **5c**, 0.013 g (13%).

*3.3.3.1. N,N-Bis{bis[4,6-(1-phenylpyrazol-4-ylamino)]-1,3,5-triazin-2-yl}-4-aminobenzylamine **4c**.* Yield 0.196 g (86%): mp 161.7–163.4 °C; IR (KBr) 3450, 3269, 1598, 1566 $cm^{-1}$; $^1H$ NMR (DMSO, 25 °C) $\delta$ 4.59 (br s, 2H), 7.1–7.6 (m, 14H), 7.6–7.9 (m, 14H), 8.6–8.9 (m, 4H), 9.2–9.6 (m, 6H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 116.8, 117.4, 117.6, 117.7, 125.1, 125.4, 125.6, 125.7, 129.5, 133.2, 139.9, 163.2; MS (FAB) $m/z$ 909 (M+$H^+$), 1817 (2 M+$H^+$); HRMS calcd for $C_{49}H_{41}N_{20}$ $m/z$: 909.3823; found: 909.3821.

*3.3.3.2. N′,N″-Bis-(1-phenylpyrazol-4-yl)-[1,3,5]triazine-2,4,6-triamine **5c**.* Yield 0.013 g (13%): mp 240 °C (decomposes); IR (KBr) 3414, 3327, 1622, 1496 $cm^{-1}$; $^1H$ NMR (DMSO, 100 °C) $\delta$ 6.42 (br s, 2H), 7.27 (t, $J$=7.1 Hz, 2H), 7.47 (t, $J$=7.3 Hz, 4H), 7.78 (d, $J$=7.3 Hz, 4H), 7.82 (s, 2H), 8.61 (br s, 2H), 8.84 (br s, 2H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 116.9, 117.6, 125.4, 125.5, 129.4, 133.1, 139.9, 163.6, 167.1; MS (FAB) $m/z$ 411 (M+$H^+$); HRMS calcd for $C_{21}H_{18}N_{10}$ $m/z$: 411.1794; found: 411.1783.

### 3.4. Synthesis of mixed bistriazines

*3.4.1. N-[4,6-Bis(1-phenylpyrazol-4-ylamino)-1,3,5-triazin-2-yl]-N′-[4,6-bis(4-pyrazol-1-ylphenylamino)-1,3,5-triazin-2-yl]-4-aminobenzylamine **4d**.* From *N*-(4-aminobenzyl)-*N*′,*N*″-bis-(4-pyrazol-1-ylphenyl)-[1,3,5]triazine-2,4,6-triamine **3b** (0.25 mmol, 0.129 g) and 6-chloro-*N*,*N*′-bis-(1-phenylpyrazol-4-yl)-[1,3,5]triazine-2,4-diamine **1c** (0.5 mmol, 0.214 g).

Yield 0.220 g (98%): mp 157–159 °C; IR (KBr) 3398, 3272, 1574, 1495, 1405 $cm^{-1}$; $^1H$ NMR (DMSO, 135 °C) $\delta$ 4.59 (4d, $J$=6.3 Hz, 2H), 6.47 (t, $J$=2.2 Hz, 2H), 7.26 (t, $J$=7.4 Hz, 2H), 7.34 (d, $J$=8.3 Hz, 2H), 7.46 (t, $J$=7.7 Hz, 4H), 7.66 (m, 4H), 7.67 (m, 2H), 7.71 (d, $J$=8.3 Hz, 4H), 7.74 (d, $J$=8.3 Hz, 2H), 7.85 (m, 2H), 7.86 (m, 4H), 7.87 (m, 2H), 8.53 (s, 2H), 8.68, 8.72, 8.78, 8.85 (br s, 6H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 43.2, 107.3, 113.7, 117.1, 117.7, 118.6, 120.3, 125.1, 125.6, 127.1, 127.3, 128.0, 129.5, 134.0, 138.6, 139.9, 140.3, 140.4, 147.4, 164.0, 165.6,

165.8; MS (FAB) *m*/*z* 908.5 ($M^+$), 909.5 ($M+H^+$); HRMS calcd for $C_{49}H_{40}N_{20}$ *m*/*z*: 908.3745; found: 908.3750.

*3.4.2. N-[4,6-Bis(4-pyrazol-1-ylphenylamino)-1,3,5-triazin-2-yl]-N′-[4,6-bis(1-phenylpyrazol-4-ylamino)-1,3,5-triazin-2-yl]-4-aminobenzylamine* ***4e****.* From *N*-(4-aminobenzyl)-*N*′,*N*″-bis-(1-phenyl-1*H*-pyrazol-4-yl)-[1,3,5]triazine-2,4,6-triamine **3c** (0.25 mmol, 0.129 g) and 6-chloro-*N*,*N*′-bis-(4-pyrazol-1-yl-phenyl)-[1,3,5]triazine-2,4-diamine **1b** (0.5 mmol, 0.214 g).

Yield 0.210 g (92%): mp 181.5–183.3 °C; IR (KBr) 3398, 3277, 1576, 1492 $cm^{-1}$; $^1H$ NMR (DMSO, 135 °C) $\delta$ 4.62 (d, *J*=6.3 Hz, 2H), 6.47 (t, *J*=2.1 Hz, 2H), 7.25 (t, *J*=7.3 Hz, 2H), 7.34 (d, *J*=8.5 Hz, 2H), 7.44 (t, *J*=7.4 Hz, 4H), 7.68 (m, 10H), 7.73 (d, *J*=8.5, 2H), 8.22 (d, *J*=2.0 Hz, 2H), 8.50 (s, 2H), 8.71, 8.75, 8.87 (br s, 6H); $^{13}C$ NMR (DMSO, 25 °C) $\delta$ 43.6, 107.4, 116.8, 117.4, 117.6, 118.6, 120.2, 120.8, 125.6, 127.3, 129.5, 133.2, 134.3, 138.2, 139.9, 140.4, 163.9; MS (FAB) *m*/*z* 908.4 ($M^+$), 909.4 ($M+H^+$); HRMS calcd for $C_{49}H_{40}N_{20}$ *m*/*z*: 908.3745; found: 908.3757.

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## Supplementary Data

$^1H$ and $^{13}C$ NMR spectra and assignments, crystal data and structure of compound **3a**. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2009.11.028.

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