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New polydentate and polynucleating *N*-donor ligands from amines and 2,4,6-trichloro-1,3,5-triazine

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Abstract—An efficient synthesis of a novel class of multidentate polynucleating ligands has been developed based on high-yielding chloride substitutions of 2,4,6-trichloro-1,3,5-triazine by primary and secondary amines. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Since the late 1980s, the design and synthesis of supramolecular polynuclear metal complexes has been a topic of growing interest.[1–3] Intramolecular electronic interactions between metal centres can strongly influence magnetic,[4] redox,[5] and spectroscopic[6,7] properties of coordination compounds. The preparation of polymetallic complexes can be achieved by using rationally designed polydentate ligands.[8]

1,3,5-Triazine derivatives are widely used as herbicides,[9] drugs[10] or polymers,[11] like melamine–formaldehyde that has excellent thermal and electrical properties. Furthermore, a very large number of supramolecular noncovalently bond assemblies between melamine and barbituric or cyanuric acid derivatives have been reported[12] but only a few examples of 1,3,5-triazine-containing ligands have been published so far.[13]

The present 1,3,5-triazine-containing compounds are synthesized from 2,4,6-trichloro-1,3,5-triazine **1** and a nucleophile. By controlling the temperature, 2,4,6-trisubstituted triazines can be prepared by sequential selective addition of nucleophiles like amines (Fig. 1). The yield of each substitution often exceeds 95% and the trisubstituted derivatives can be obtained in a one-pot synthesis.

The preparation and characterization of novel polynucleating *N*-donor ligands based on 1,3,5-triazine subunits is reported. Ligands **3a** and **3b** were prepared in high yields in a one-step synthesis as outlined in Scheme 1. Reaction of 3 equiv. of 2,2′-dipyridylamine or di-(2-picolyl)amine with 1 equiv. of 2,4,6-trichloro-1,3,5-triazine **1** in THF under reflux for 2 days, led to the desired pure 2,4,6-(dipyridin-2-ylamino)-[1,3,5]-triazine **3a** and 2,4,6-(di-2-picolylamino)-[1,3,5]triazine **3b** in 72% and 80% yield, respectively. *N*,*N*-Diisopropylethylamine (DIPEA, 'Hünig's base') was used to trap the HCl formed during the substitution reaction (Scheme 1).

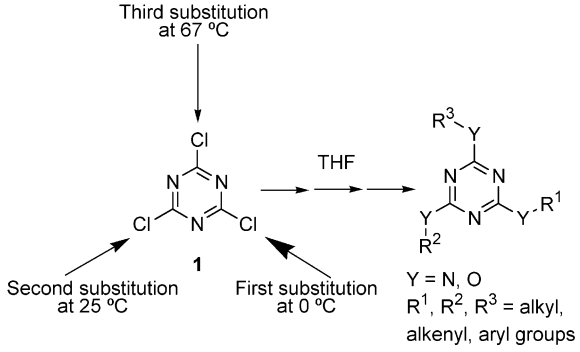
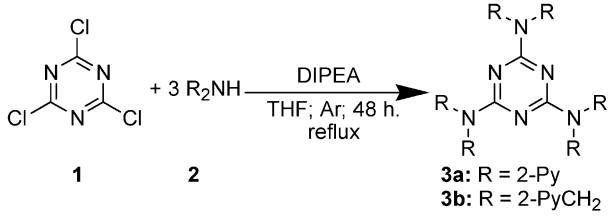


Figure 1. Differential reactivity of 1,3,5-triazines.



Scheme 1. Synthesis of trinucleating hexadentate ligands **2**.

Keywords: 1,3,5-triazine derivatives; *N*-containing ligands; first-generation dendrimer.

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A bis triazine derivative of ligand **3a** was obtained using the synthetic sequence depicted in Scheme 2. The first step consisted in preparing 2-chloro[4,6-(dipyridin-2-ylamino)]-{1,3,5}triazine **4** by substitution of only two chloride atoms of **1**. As for ligands **3a** and **3b**, compound **4** precipitated as a pure product in the reaction mixture (69% yield). Two 2-chloro[4,6-(dipyridin-2-ylamino)]-{1,3,5}triazine units were then bridged employing ethylenediamine **5** as linker where each amino group substituted the third chloride atom. After 48 hours at 80°C in acetonitrile, pure *N*,*N*′-{2,4-di[(dipyridin-2-yl)amine]-1,3,5-triazine}ethylenediamine **6** was isolated by filtration directly from the reaction mixture in an 88% yield.

Finally, a relatively simple route to first-generation dendrimer **9** is described (Scheme 3). The synthetic pathway is once again based on the different chemical reactivities of 1,3,5-triazine derivatives in the nucleophilic aromatic substitution. The temperature-controlled reaction of 2,4,6-trichloro-1,3,5-triazine **1** with 4-aminophenol **7** exclusively led to the formation of compound **8**. This chemoselectivity of the substitutions is due to the huge difference of nucleophilicity between an amine and an alcohol. Thus, after 2 days under reflux in acetone, 2,4,6-tri(4′-aminophenol)-1,3,5-triazine **8** was obtained in 89% yield. Potassium carbonate, a weaker base compared to DIPEA, was used in that case to avoid deprotonation of the phenol group which would have resulted in mixed *N*- and/or *O*-substitution products.

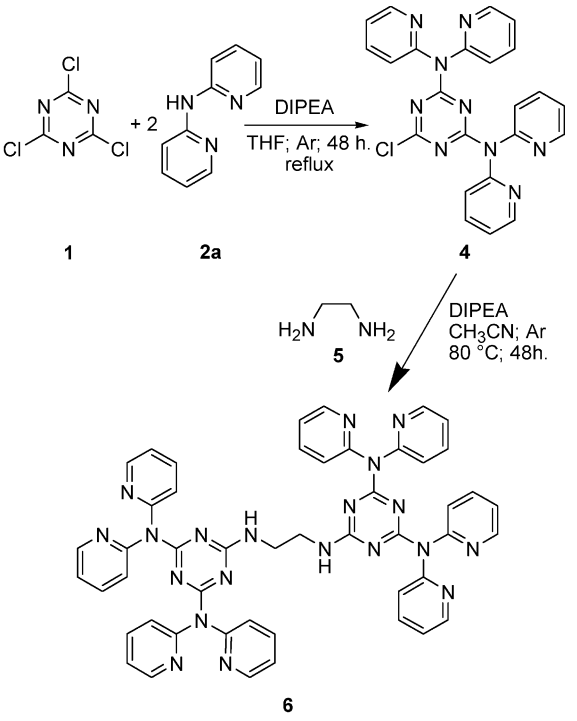
Tris[4-({2′,4′-di[(dipyridin-2″-yl)amine]-1′,3′,5′-triazine-6′-yl}oxy)phen-1-yl]2,4,6-triamino-1,3,5-triazine **9** was prepared in 69% yield by reaction of **8** with 3 equiv. of **4** in pyridine at 85°C for 2 days.

In conclusion, a straightforward and versatile method to synthesize a new class of nitrogen-containing ligands has been developed. These ligands were easily obtained in good yield starting from low-cost commercially available materials. The complexation of the different polynucleating ligands with various metals is under investigation and unprecedented molecular architectures have been recently obtained.[14] The use as catalysts of the polymetallic coordination compounds prepared in oxidation reactions is currently in progress.

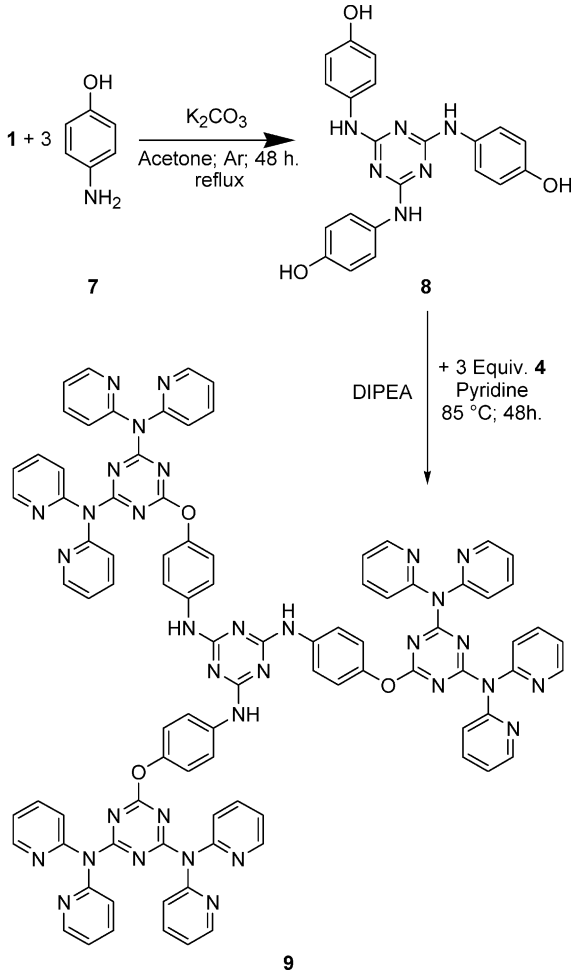
2. Experimental

2.1. Synthesis of ligands 2

2,4,6-Trichloro-[1,3,5]triazine **1** (5.00 g, 27.11 mmol) was dissolved in tetrahydrofurane (50 mL). Three equivalents of *N*-ethyldiisopropylamine (DIPEA) (10.51 g, 81.34 mmol) were added and the two-necked round-bottomed flask was cooled to 0°C. Secondary amine **2** (13.93 g, 81.34 mmol) was added portionwise. After the completion of the addition, the clear reaction mixture was warmed to room temperature and then heated under reflux for 48 h. The slightly yellow precipitate was isolated on a glass filter and washed with ethanol (3×50 mL) to remove *N*-ethyldiisopropylamine hydrochloride.



Scheme 2. Synthesis of bridged ligand **5**.



Scheme 3. Synthesis of first-generation dendrimer **9**.

Data for 2,4,6-(dipyridin-2-ylamino)-[1,3,5]triazine 3a: Yellow powder; yield = 72%; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 7.10 (d, 6H, 3-py-H), 7.43 (dd, 6H, 5-py-H), 7.66 (dd, 6H, 4-py-H), 8.21 (d, 6H, 6-py-H) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 121.1, 122.9, 137.4, 148.2, 154.9 ppm. IR (neat) 3054, 1587, 1538, 1457, 1374, 1291, 1134, 996, 776, 667, 636 cm^{-1}. Elemental analyses, found (calcd): C, 67.05 (67.34); H, 4.15 (4.11); N, 28.44 (28.55).

Data for 2,4,6-(di-2-picolylamino)-[1,3,5]triazine 3b: Light yellow powder; yield = 80%; ^{1}H NMR δ 4.84 (s, 4H, CH_2), 6.97–7.03 (d, 6H, 3-py-H and dd, 6H, 5-py-H), 7.34 (dd, 6H, 4-py-H), 8.40 (d, 6H, 6-py-H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) 52.0, 121.4, 121.5, 136.2, 148.8, 158.5, 165.8 ppm. IR (neat) 3052, 2932, 1591, 1534, 1484, 1408, 1323, 1179, 995, 750 cm^{-1}. Elemental analyses, found (calcd): C, 69.74 (69.62); H, 5.21 (5.39); N, 24.69 (24.98).

2.2. Synthesis of *N*,*N*′-{2,4-di[(dipyridin-2-yl)amine]-1,3,5-triazine}ethylenediamine 5

2.2.1. Synthesis of 2-chloro[4,6-(dipyridin-2-ylamino)]-{1,3,5}triazine 4. 2,4,6-Trichloro-[1,3,5]triazine **1** (5.00 g, 27.11 mmol) was dissolved in tetrahydrofurane (50 mL). Two equivalents of *N*-ethyldiisopropylamine (7.01 g, 54.22 mmol) were added and the two-necked round-bottomed flask was cooled to 0°C. Dipyridin-2-ylamine **2a** (9.28 g, 54.22 mmol) was added portionwise. After the completion of the addition, the clear reaction mixture was warmed to room temperature and then heated under reflux for 48 h. The yellow precipitate was isolated on a glass filter and washed with THF (3×20 mL) and ethanol (3×25 mL) to remove *N*-ethyldiisopropylamine hydrochloride.

Data for compound 4: The product was obtained as a light yellow powder with a yield of 69%. ^{1}H NMR (DMSO-d_6, 200 MHz) δ 7.18 (d, 4H, 3-py-H), 7.22 (dd, 4H, 5-py-H), 7.82 (dd, 4H, 4-py-H), 8.30 (d, 4H, 6-py-H) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 122.1, 123.8, 138.0, 148.6, 154.3, 165.7 ppm. IR (neat) 3084, 1590, 1549, 1501, 1459, 1393, 1258, 1218, 1118, 993, 804, 773, 657 cm^{-1}. Elemental analyses, found (calcd): C, 60.16 (60.86);[15] H, 3.85 (3.55); N, 27.37 (27.77).

2.2.2. Synthesis of *N*,*N*′-{2,4-di[(dipyridin-2-yl)amine]-1,3,5-triazine}ethylenediamine 6. To a stirred solution of **4** (2.67 g, 5.89 mmol) and *N*-ethyldiisopropylamine (0.76 g, 5.89 mmol) in acetonitrile (130 mL), ethylenediamine **5** (0.18 g, 2.94 mmol) was added. This mixture was heated to 80°C for 2 days. The precipitate was filtered under reduced pressure, washed with acetonitrile (3×25 mL) and collected to give compound **6** as a white powder.

Data for compound 6: Yield = 88%; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.96 (s, 4H, CH_2), 7.12 (d, 8H, 3-py-H), 7.16 (s, 2H, NH), 7.43 (dd, 8H, 5-py-H), 7.70 (dd, 8H, 4-py-H), 8.22 (d, 8H, 6-py-H) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 40.4, 121.9, 124.0, 138.5, 149.2, 156.6, 166.7 ppm. IR (neat) 3314, 1579, 1542, 1463, 1431, 1368 cm^{-1}. MS (MALDI-TOF): m/z 895 (M^+). Elemental analyses, found (calcd): C, 64.13 (64.42); H, 4.30 (4.28); N, 31.26 (31.30).

2.3. Synthesis of tris[4-({2′,4′-di[(dipyridin-2′′-yl)amine]-1′,3′,5′-triazine-6′-yl}oxy)phen-1-yl]2,4,6-triamino-1,3,5-triazine 9

2.3.1. Synthesis of 2,4,6-tri(4′-aminophenol)-1,3,5-triazine 8. Two equivalents of 2,4,6-trichloro-[1,3,5]triazine **1** (5.00 g, 27.11 mmol) were dissolved in acetone (150 mL). Three equivalents of potassium carbonate (5.62 g, 40.60 mmol) were added and the two-necked round-bottomed flask was cooled to 0°C. 4-Aminophenol **7** (8.88 g, 81.30 mmol) was added portionwise. After the completion of the addition, the suspension mixture was warmed to room temperature and then heated under reflux for 48 h. The solid obtained was filtered under reduced pressure and washed with water (3×50 mL) to remove the potassium chloride. The product **8** was dried overnight at 50°C under reduced pressure.

Data for compound 8: White powder; yield = 89%; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 6.65 (d, 6H, 4,5 Ph-H), 7.46 (d, 6H, 2,6 Ph-H), 8.71 (s, 3H, NH); 9.03 (s, 3H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 115.0, 122.7, 131.7, 152.9, 164.0 ppm. IR (neat) 3389, 3345, 1622, 1602, 1587, 1512, 1490 cm^{-1}. Elemental analyses, found (calcd): C, 62.76 (62.68); H, 4.78 (4.51); N, 20.95 (20.88).

2.3.2. Synthesis of first-generation dendrimer 9. To a stirred solution of **8** (0.15 g, 0.37 mmol) and *N*-ethyldiisopropylamine (0.14 g, 1.10 mmol) in pyridine (50 mL), **4** (0.50 g,1.10 mmol) was added and the mixture was allowed to react at 85°C for 2 days. The solvent was evaporated under reduced pressure. Ethanol was added to the remaining solid. After stirring for 30 min, the crude was filtered and dissolved in acetonitrile (50 mL). This acetonitrile solution was added dropwise to 200 mL of distilled water leading to the formation of a precipitate. The precipitate was filtered and dried overnight at 50°C under reduced pressure.

Data for compound 9: Slightly brown powder; yield = 69%; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.13 (d, 12H, 3-py-H and d, 6H, 2,6-PhH), 7.52 (dd, 12H, 5-py-H), 7.73 (dd, 12H, 4-py-H and d, 6H, 3,5-PhH), 8.25 (d, 12H, 6-py-H), 9.31 (s, 3H, PhNH) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 122.0, 122.5, 122.6, 124.0, 138.3, 138.7, 147.6, 149.3, 155.8, 165.2, 167.8, 171.6 ppm. IR (neat) 1581, 1558, 1494, 1362, 1281, 1195, 998, 808, 775, 740, 666 cm^{-1}. MS (MALDI-TOF): m/z 1654 (M^+).

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15. Several elemental analyses on compound **4** have led to disparate and too low experimental percentages of carbone (up to 2%). This might be due to the violent decomposition of **4** above 250°C.