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The New and Simple 'LEGO' System: Its Application to the Synthesis of Superbranched Oligopyridines

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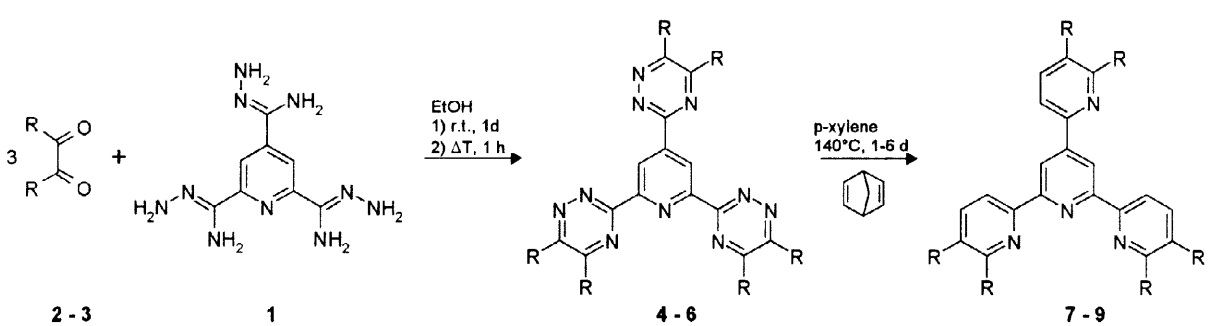
Abstract

The condensation of pyridine-2,4,6-tricarboxtrisamidrazone **1** with 1,2-dicarbonyl compounds **2** - **3** leads to trisubstituted 1,2,4-triazines **4** - **6**. These 1,2,4-triazines can be easily transformed to superbranched pyridines **7** - **9** by [4+2] cycloaddition with norborna-2,5-diene followed by [4+2] cycloreversions of nitrogen and cyclopentadiene. This reaction sequence offers a new, simple and general access to superbranched oligopyridines.

Keywords: *Cycloadditions; Oligomers; Pyridines; Triazines*

A number of reports deal with the synthesis and reactions of polydendate oligopyridines [1,2,3,4]. Here we extend our new and simple 'LEGO' system [5,6] to the synthesis of superbranched oligopyridines and 3,5,6-trisubstituted 1,2,4-triazines as their precursors.

1,2,4-Triazines **4** - **6** are easily prepared by treating of pyridine-2,4,6-tricarboxtrisamidrazone **1** with 1,2-dicarbonyl compounds **2** - **3** (Table 1) in ethanol (Table 2).



2 - 3 **1** **4 - 6** **7 - 9**

Scheme 1. Reaction sequence for the synthesis of pyridines via 1,2,4-triazines.

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Table 1. Starting compounds for synthesis of 1,2,4-triazines: amidrazone and 1,2-dicarbonyl compounds.

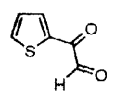
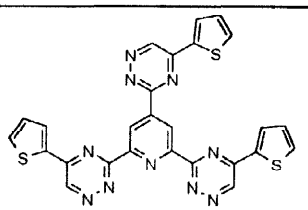
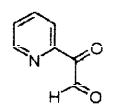
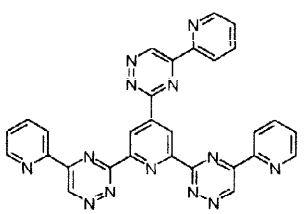
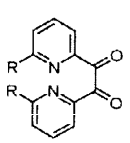
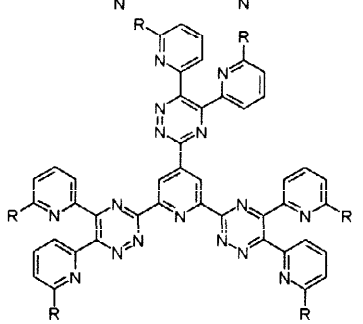
Compound		Ref.	Compound		Ref.
1	pyridine-2,4,6-tricarboxtrisamidrazone	-	**3a**	1,2-bis-(2-pyridyl)-ethane-1,2-dione	Fluka
2a	2-thienyl-glyoxal	[7]	**3b**	1,2-bis-(2,2'-bipyridine-6-yl)-ethane-1,2-dione	[9]
2b	2-pyridyl-glyoxal	[8]			

Procedure for the preparation of compound **1**: **2,4,6-Tricyanopyridine** [10] (1.66 g, 10.8 mmol) and hydrazine hydrate (100%) (15.7 ml, 16.2 g, 323 mmol) in 200 ml methanol (99%) were stirred magnetically at ambient temperature for 7 d. After suction filtration of the mixture the filtrate was treated with 800 ml 2-propanol and placed in a refrigerator for 7 d. The precipitate formed was isolated by suction filtration, washed thouroghly with cold 2-propanol and dried at 20°C/0.01 Torr. Yield: 1.40 g (5.60 mmol, 52%). Analytical data for **1**: IR (KBr): $\tilde{\nu}$ = 3440, 3290, 3180, 1650, 1610, 1575, 1555, 1450, 1415, 1375, 905, 890, 840, 815 cm^{-1}. ^1H NMR (250 MHz, DMSO-d_6): δ = 5.26 (s, 6 H), 5.65 (s, 1 H), 5.76 (s, 1 H), 6.03 (s, 2 H), 6.10 (s, 1 H), 6.19 (s, 1 H), 8.11 (s, 2 H) ppm. PI-SIMS (Cs^+,glycerine, DMSO); m/z (%): 251.2 (100) [(M + H)$^+$]. $C_8H_{14}N_{10}*H_2O$ (268.31): calcd. C 35.81, H 6.01, N 52.22; found C 35.16, H 6.49, N 51.40.

The NMR spectra of 1,2,4-triazines **4** and **5** show only one singlet for triazine-H^6 and the corresponding pyridines **7** and **8** are confirmed by the expected multiplets for 2,6-disubstituted pyridines [5].

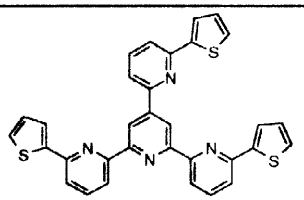
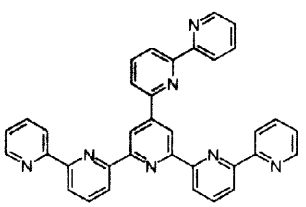
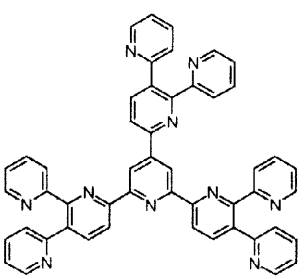
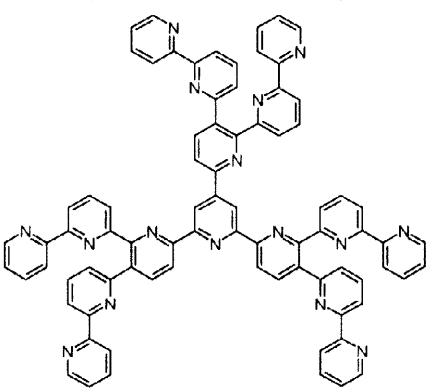
1,2,4-Triazines participate as electron poor dienes in inverse-type Diels-Alder reactions with electron rich and angle strained dienophiles to yield dihydropyridine and pyridine derivatives after extrusion of molecular nitrogen and cyclopentadiene [3,4,11,12]. We used norborna-2,5-diene (10 fold excess) as a synthetic equivalent for acetylene in 1,2-dichlorobenzene or p-xylene as solvent (Scheme 1).

Table 2. Mono-, bi- and bis-[1,2,4]-triazines synthesized according to Scheme 1.

Dicarbonyl compound		Triazine		R	Yield [%]	M.P. [°C]
2a		**4**		-	44	293-295
2b		**5**		-	27	325-328
3a		**6a**		H	20	326-328
3b		**6b**		pyridin-2-yl	40	362-365

Typical procedure for the preparation of triazines 4 - 6: **3b** (400 mg, 919 µmol) and pyridine-2,4,6-tricarboxtrisamidrazone (82.2 mg, 306 µmol) in 25 ml ethanol (99%) were stirred magnetically at ambient temperature for 1 d. After that the reaction mixture was heated under reflux for 1h. After cooling the yellow precipitate was collected by suction filtration, washed with cold ethanol and recrystallized from *N,N*-dimethylformamide to furnish **6b** (180 mg, 145 µmmol, 40%) as yellow crystals. Analytical data for **6b**: IR (KBr): $\tilde{\nu}$ = 3070, 3020, 1580, 1565, **1515, 1505, 1475,** 1455, 1425, 1375, 1355, 1310, 1255, 1150, 1090, 1080, 1060, **1045, 1035,** 990, 830, 775, 740 cm^{-1}. ^1H NMR (400 MHz, CD_2Cl_2): δ = 7.13-7.22 (m, 6 H), 7.29-7.34 (m, 1 H), 7.35-7.40 (m, 2 H), 7.41-7.45 (m, 1 H), 7.45-7.56 (m, 8 H), 8.08-8.20 (m, 6 H), 8.39-8.61 (m, 18 H), 10.17 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 120.74 (1 C, +), 120.81 (3 C, +), 120.88 (2 C, +), 121.23 (2 C, +), 121.35 (1 C, +), 122.16 (2 C, +), 122.35 (1 C, +), 124.08 (1 C, +), 124.12 (2 C, +), 124.16 (2 C, +), 124.19 (1 C, +), 124.27 (2 C, +), 124.31 (1 C, +), 124.74 (3 C, +), 124.89 (2 C, +), 136.92 (6 C, +), 138.30 (2 C, +), 138.35 (1 C, +), 138.46 (2 C, +), 138.55 (1 C, +), 145.50 (2 C, 0), 149.31 (5 C, +), 149.33 (1 C, +), 154.05 (1 C, 0), 154.39 (2 C, 0), 154.42 (1 C, 0), 154.57 (1 C, 0), 155.29 (1 C, 0), 155.32 (2 C, 0), 155.42 (2 C, 0), 155.59 (1 C, 0), 155.65 (2 C, 0), 155.67 (2 C, 0), 155.75 (2 C, 0), 155.79 (1 C, 0), 156.30 (1 C, 0), 156.41 (2 C, 0), 156.91 (2 C, 0), 157.28 (1 C, 0), 160.35 (2 C, 0), 161.60 (2 C, 0), ppm. FD-MS; m/z (%): 1240 (<50) [M^+], 1212 (<5) [$M^+ - N_2$], 1016 (<10) [$M^+ - N_2 - C_{22}H_{14}N_4$], 620 (100) [$M^{2+}$], 414 (<10) [$M^{3+}$]; $C_{74}H_{44}N_{22}$ (1241.32): calcd. C 71.60, H 3.57, N 24.82; found C 70.66, H 3.93, N 24.63. All other 1,2,4-triazines were characterized by the same analytical methods.

Table 3. Synthesis of superbranched oligopyridines according to Scheme 1.

Triazine	Pyridine	Reaction conditions and times	Yield [%]	M.P. [°C]
4	**7** 	1,2-dichlorobenzene, 145-150°C, 1 d	30	228-229
5	**8** 	p-xylene, reflux, 6 d	46	248-250
6a	**9a** 	p-xylene, reflux, 6 d	49	282-285
6b	**9b** 	p-xylene, reflux, 5 d	61	206-208

Typical procedure for the preparation of pyridines **7 - 9**: **6b** (100 mg, 80.6 µmol) and norborna-2,5-diene (246 µl, 223 mg, 2.42 mmol) in 10 ml absolute p-xylene were heated under reflux in an inert atmosphere for 6 d. The reaction mixture was cooled and treated with petroleum ether 40/60 until it became cloudy. After standing several hours in a refrigerator the precipate was collected by suction filtration, washed with petroleum ether 40/60 and recrystallized from p-xylene to furnish **9b** (61.0 mg, 49.5 µmol, 61%) as colorless crystals. Analytical data for **9b**: IR (KBr): ν = 3070, 3020, 1575, 1560, 1465, 1445, 1425, 1255, 1150, 1090, 1070, 1025, 990, 825, 780, 750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.10-7.16 (m, 3 H), 7.28-7.39 (m, 12 H), 7.73 (dd, 1 H, J = 7.9 Hz, J = 7.9 Hz), 7.74 (dd, 2 H, J = 7.8 Hz, J = 7.8 Hz), 7.72-7.78 (m, 3 H), 7.99 (dd, 1 H, J = 7.8 Hz, J = 7.8 Hz), 8.03 (dd, 2 H, J = 7.8 Hz, J = 7.8 Hz), 8.22-8.27 (m, 3 H), 8.30 (dd, 2 H, J = 7.9 Hz, J = 0.9 Hz), 8.31 (dd, 1 H, J = 7.9 Hz, J = 0.9 Hz), 8.34-8.38 (m, 5 H), 8.38 (d, 2 H, J = 8.0 Hz), 8.46 (dd, 2 H, J = 7.7 Hz, J = 1.0 Hz), 8.50 (dd, 1 H, J = 7.8 Hz, J = 1.0 Hz), 8.53-5.56 (m, 3H), 8.66-8.70 (m, 3H), 8.97 (d, 2 H, J = 8.0 Hz), 9.58 (s, 2 H) ppm. FD-MS: m/z (%): 1235 (100) $[M^+]$. $C_{80}H_{50}N_{16}$ (1235.40): calcd. C 77.78, H 4.08, N 18.14; found C 77.10 , H 4.47 , N 17.63 . All other oligopyridines were characterized by the same analytical methods.

Compound **7** shows an intensive yellow colour on silica gel. The solubility of compounds **9** depends on the solvent in which the reaction is carried out (1,2-dichlorobenzene: high solubility in dichloromethane, p-xylene: low solubility in dichloromethane), which gives rise to different crystal modifications.

Further investigations on these phenomena are in progress to examine the variability of these new compounds as pH-sensors and the capability of these oligopyridines to undergo molecular recognition.

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