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A New and Simple 'LEGO' System for the Synthesis of Branched Oligopyridines

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Abstract

The condensation of carboxamidrazones **1** with 1,2-dicarbonyl compounds **2** is the best method for the synthesis of alkyl, aryl or hetaryl substituted 1,2,4-triazines **3** - **7** These 1,2,4-triazines can be easily transformed to pyridines **8** - **12** by [4+2] cycloaddition with bicyclo[2 2 1]hepta-2,5-diene followed by [4+2] cycloreversions of nitrogen and cyclopentadiene This reaction sequence offers a new, simple and general access to branched oligopyridines

Keywords: *Cycloadditions; Oligomers, Pyridines; Triazines*

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

1,2,4-Triazines are easily prepared by heating of carboxamidrazones **1a** - **1e** (Table 1) with 1,2-dicarbonyl compounds **2a** - **2c** (Table 1) in ethanol under reflux for 4-6 hours (Table 2) [7].

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

Compound		Ref	Compound		Ref
1a	pyridine-2-carboxamidrazone	[8]	**1e**	benzene-1,4-dicarboxbisamidrazone	[11]
1b	dicarboxbisamidrazone	[9]	**2a**	1,2-bis-(2-pyridyl)-ethane-1,2-dione	Fluka
1c	pyridine-2,6-dicarboxbisamidrazone	[10]	**2b**	1,2-bis-(2,2'-bipyridin-6-yl)-ethane-1,2-dione	[12]
1d	2,2'-bipyridine-6,6'-dicarboxbisamidrazone	[6]	**2c**	1,2-bis-(2,2',6'-terpyridin-6-yl)-ethane-1,2-dione	[12]

1,2,4-Triazines are known to 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 [6, 13, 14].

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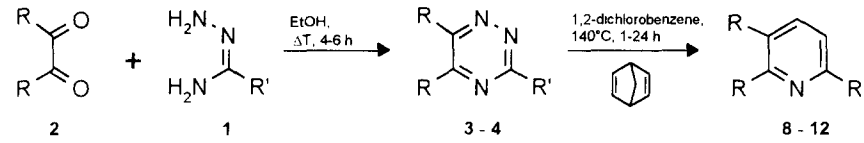
We used bicyclo[2.2.1]hepta-2,5-diene (10 fold excess) in refluxing toluene or p-xylene as a synthetic equivalent for acetylene (Scheme 1).

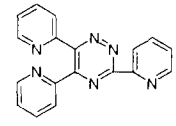
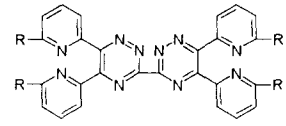
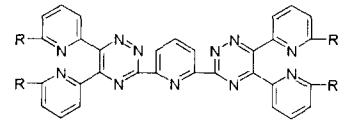
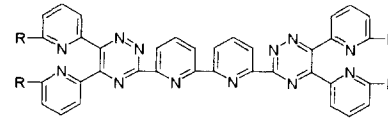
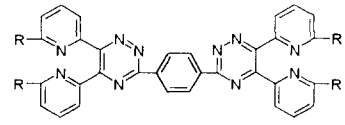


2 1 3 - 4 8 - 12

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

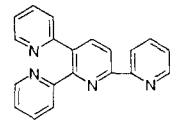
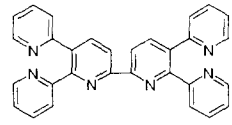
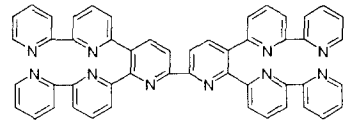
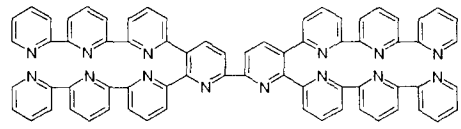
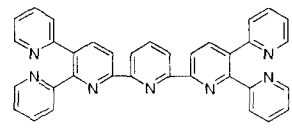
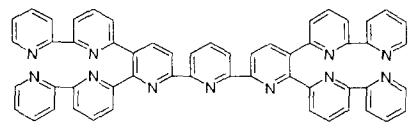
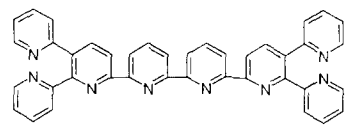
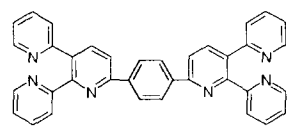
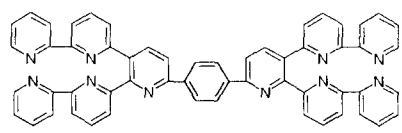
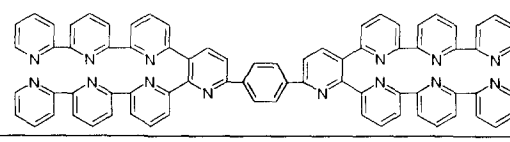
For 1,2,4-triazines with higher molecular weights reaction times were too long and yields too low. In these cases the reactions were performed in 1,2-dichlorobenzene as solvent at 140°C leading to shorter reaction times and higher yields. The results are collected in Table 3.

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

Carbox-amidrazone	Dicarbonyl compound	Triazine [Reference]		R	Yield [%]	M P [°C]
1a	**2a**	**3** [6]		-	80	160-162
1b	**2a**	**4a** [6]		H	85	276-278
1b	**2b**	**4b**		pyridin-2-yl	88	>280
1b	**2c**	**4c**		2,2'-bipyridin-6-yl	80	175-180
1c	**2a**	**5a**		H	94	254-256
1c	**2b**	**5b**		pyridin-2-yl	97	282-283
1d	**2a**	**6**		H	83	331-333
1e	**2a**	**7a**		H	64	>280
1e	**2b**	**7b**		pyridin-2-yl	90	283-285
1e	**2c**	**7c**		2,2'-bipyridin-6-yl	80	269-270

Analytical data for **5b** IR (KBr): ν = 3060, 3020, 1575, 1560, 1510, 1495, 1470, 1450, 1425, 1405, 1370, 1305, 1250, 1145, 1090, 1075, 1055, 1035, 1015, 985, 825, 775, 735, 695 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.12-7.21 (m, 4 H), 7.31 (ddd, 2 H, J = 8.0 Hz, J = 1.2 Hz, J = 1.0 Hz), 7.28-7.34 (m, 6 H), 8.09 (dd, 2 H, J = 7.9 Hz, J = 7.8 Hz), 8.11 (dd, 2 H, J = 7.9 Hz, J = 7.8 Hz), 8.29 (dd, 1 H, J = 8.0 Hz, J = 7.7 Hz), 8.40 (dd, 2 H, J = 7.8 Hz, J = 1.1 Hz), 8.41 (dd, 2 H, J = 7.9 Hz, J = 1.2 Hz), 8.42 (ddd, 2 H, J = 8.0 Hz, J = 1.3 Hz, J = 1.0 Hz), 8.52 (ddd, 2 H, J = 4.8 Hz, J = 1.8 Hz, J = 0.9 Hz), 8.54 (ddd, 2 H, J = 4.8 Hz, J = 1.8 Hz, J = 0.9 Hz), 8.61 (dd, 2 H, J = 7.7 Hz, J = 1.1 Hz), 9.02 (d, 2 H, J = 7.9 Hz) ppm. EI-MS (70eV): m/z (%). 853 (3) [M^+], 825 (7) [M^+ + H - N_2], 491 (23) [M^+ - $C_{22}H_{14}N_4$], 334 (51) [$C_{22}H_{14}N_4$], 333 (51) [$C_{22}H_{13}N_4$ - H], 180 (100) [$C_{12}H_8N_2$], 156 (16) [$C_{10}H$-N_2]; $C_{51}H_{31}N_{15}$ (853.9) calcd C 71.73, H 3.66, N 24.62; found C 71.26, H 3.66, N 24.39. All other 1,2,4-triazines were characterized by the same analytical methods

Table 3. Synthesis of branched oligopyridines according to Scheme 1

Triazine	Pyridine		Reaction conditions and times	Yield [%]	M.P. [°C]
3	**8**		p-xylene, ΔT, 3d	45	122-123
4a	**9a**		toluene, ΔT, 3 d	88	273
4b	**9b**		p-xylene, ΔT, 15 h	88	260-262
4c	**9c**		toluene, ΔT, 24 h	82	169-170
5a	**10a**		1,2-dichlorobenzene, 140°C, 1 h	85	243-244
5b	**10b**		1,2-dichlorobenzene, 140°C, 6 h	94	250-252
6	**11**		1,2-dichlorobenzene, 140°C, 1 d	81	303-305
7a	**12a**		toluene, ΔT, 6 d	49	266-268
7b	**12b**		p-xylene, ΔT, 3 d	63	254
7c	**12c**		toluene, ΔT, 5 d	80	>280

Typical procedure for the preparation of pyridines **8** - **12**: **5b** (250 mg, 293 µmol) and norborna-2,5-diene (0.54 g, 5.86 mmol) were heated at 140°C under an inert atmosphere in 15 ml 1,2-dichlorobenzene for 6 hours. The reaction mixture was cooled and treated with petroleum ether 40/60 until it became cloudy. After standing in a refrigerator for several hours the precipitate was collected by suction filtration, washed with petroleum ether 40/60 and recrystallized from acetonitrile to furnish **10b** as colorless crystals

Analytical data for **10b**. IR (KBr). ν = 3040, 3000, 1565, 1550, 1460, 1445, 1425, 1410, 1365, 1250, 1140, 1105, 1085, 1070, 1035, 1015, 980, 820, 805, 765, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.09-7.14 (m, 2 H), 7.28 (ddd, 2 H, J = 7.5 Hz, J = 4.8 Hz, J = 1.2 Hz), 7.30-7.34 (m, 4 H), 7.36 (dd, 2 H, J = 7.8 Hz, J = 1.7 Hz), 7.71 (dd, 2 H, J = 7.8 Hz, J = 7.8 Hz), 7.72 (ddd, 2 H, J = 7.8 Hz, J = 7.5 Hz, J = 1.8 Hz), 8.01 (dd, 2 H, J = 7.9 Hz, J = 7.7 Hz), 8.05 (t, 1 H, J = 7.8 Hz), 8.19 (ddd, 2 H, J = 8.0 Hz, J = 1.1 Hz, J = 1.1 Hz), 8.27 (dd, 2 H, J = 7.8 Hz, J = 1.0 Hz), 8.32 (d, 2 H, J = 8.1 Hz), 8.30-8.35 (m, 4 H), 8.52 (ddd, 2 H, J = 4.8 Hz, J = 1.7 Hz, J = 1.0 Hz), 8.66 (ddd, 2 H, J = 4.8 Hz, J = 1.8 Hz, J = 0.9 Hz), 8.75 (d, 2 H, J = 7.8 Hz), 8.89 (d, 2 H, J = 8.1 Hz) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, DEPT): δ = 118.86 (2 C, +), 119.84 (2 C, +), 120.41 (2 C, +), 120.98 (2 C, +), 121.27 (2 C, +), 121.65 (2 C, +), 123.52 (2 C, +), 123.67 (2 C, +), 124.06 (2 C, +), 124.15 (2 C, +), 136.20 (2 C, 0), 136.48 (2 C, +), 136.76 (2 C, +), 136.80 (2 C, +), 137.59 (1 C, +), 137.83 (2 C, +), 140.08 (2 C, +), 148.68 (2 C, +), 148.97 (2 C, +), 154.31 (2 C, 0), 155.00 (2 C, 0), 155.09 (2 C, 0), 155.11 (2 C, 0), 155.67 (2 C, 0), 155.74 (2 C, 0), 156.14 (2 C, 0), 157.25 (2 C, 0), 158.54 (2 C, 0) ppm. EI-MS (70eV), m/z (%): 850 (50) $[(M + H)^+]$, 849 (100) $[M^+]$, 848 (87) $[(M- H)^+]$, 821 (2) $[M^+ - N_2]$, 772.4 (41) $[M^+ - C_5H_5N]$, 771 (71) $[M^+ - C_5H_5N]$, 744 (17) $[M^+ - C_5H_5N - N_2]$, 425 (16) $[M^{2+}]$, 385 (12) $[[(M - C_5H_4N)^+]$, 57 (8), 55 (12), 44 (40), 40 (55). $C_{55}H_{35}N_{11}$ (850.0) calcd. C 77.72, H 4.15, N 18.13, found C 76.97, H 4.44, N 17.79. All other oligopyridines were characterized by the same analytical methods.

Further investigations are in progress to examine the variability of this new synthesis with respect to different carboxamidrazones and 1,2-dicarbonyl compounds and the capability of these oligopyridines to act as ligands in metal complexes.

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