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## An efficient route to 5,5"-diaryl-2,2':6',2"-terpyridines through 2,6-bis(1,2,4-triazin-3-yl)pyridines

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Abstract—A new route to substituted 2,2':6',2''-terpyridines based on a new method for the synthesis of substituted 2,6-bis(1,2,4-triazin-3-yl)pyridines and their inverse electron demand Diels–Alder reaction is shown to be an efficient strategy for the synthesis of structurally diverse terpyridine ligands.

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2,2':6',2"-Terpyridines (tpy) are undoubtedly among the most widely used ligands in coordination and supramolecular chemistry.<sup>1</sup> In particular, the photophysical properties of terpyridine metal complexes and of terpyridines themselves are especially interesting.<sup>2,3</sup> Among terpyridines, 2,2':6',2"-terpyridines bearing aromatic substituents at the  $\beta$ -positions of the peripheral pyridine rings exhibit the best luminescent properties with emission quantum yields ( $\Phi_f$ ) of up to 0.85, due to the effects of aromatic substituents making the bipyridines attractive as chromophores and 'antennae'.<sup>4,5</sup> Other applications include template synthesis of catenands based on 5.5"-bis(4-hydroxyphenyl)-2,2':6',2"-terpyridine.<sup>6</sup> However, the study of these interesting and useful compounds has been hampered by inefficient chemical synthesis. Cross-coupling approaches or modified Kröhnke syntheses are limited by inaccessible starting compounds, multi-step procedures and low yields.<sup>6,7</sup>

Here we report a new strategy for the synthesis of 5,5"diaryl-2,2':6',2"-terpyridines **1** based on the conversion of 1,2,4-triazines into pyridines via an aza-Diels–Alder reaction.<sup>8</sup> The main step of our strategy is original involving easily synthesized key intermediates—2,6bis(1,2,4-triazin-3-yl)pyridines bearing aryl substituents at position 6 of the peripheral 1,2,4-triazine rings. It should be noted that 2,6-bis(1,2,4-triazin-3-yl)pyridines

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are interesting compounds in their own right due to their application in the separation of lanthanides and actinides in the management of nuclear wastes.<sup>9</sup>



Scheme 1. Reagents and conditions: (i) *i*-PrONO, EtONa, EtOH, 10 °C, then AcOH; (ii)  $N_2H_4$ – $H_2O$ , EtOH, rt; (iii) pyridine-2,6-dicarboxaldehyde, AcOH, reflux (1 min); (iv) 2,5-norbornadiene, xylene, 48 h; (v) 1-(4-morpholino)cyclo-pentene, dioxane, reflux, 6 h.

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Table 1.	Bistriaziny	lpyridines 2a	a-e,	terpyridines	1a,c and	6a,e	produced	via	Scheme	1
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	Procedure	Yield (%)	Mp (°C)	<sup>1</sup> H NMR spectra, $\delta$	Formula	Calculated (%) Found (%)		
						С	Н	Ν
2a	А	66	>290	(CF <sub>3</sub> COOD) 7.80 (m, 6H), 8.33 (m, 4H), 8.86 (t, <i>J</i> = 8.5 Hz,1H), 9.32 (d, <i>J</i> = 8.5 Hz, 2H), 10.04 (s, 2H)	C <sub>23</sub> H <sub>15</sub> N <sub>7</sub>	70.94 70.92	3.88 3.83	25.18 25.20
2b	А	85	260–262	(CF <sub>3</sub> COOD) 2.58 (s, 6H), 7.60 (m, 4H), 8.22 (m, 4H), 8.80 (t, <i>J</i> = 8.4 Hz, 1H), 9.25 (d, <i>J</i> = 8.4 Hz, 2H), 10.03 (s, 2H)	$C_{25}H_{19}N_7$	<i>71.93</i> 71.81	4.59 4.45	<i>23.49</i> 23.61
2c	А	68	>290	(CF <sub>3</sub> COOD) 4.09 (s, 6H), 7.34 (m, 4H), 8.38 (m, 4H), 8.78 (t, <i>J</i> = 8.0 Hz, 1H), 9.22 (d, <i>J</i> = 8.0 Hz, 2H), 10.02 (s, 2H)	$C_{25}H_{19}N_7O_2$	66.81 66.70	4.26 4.20	<i>21.81</i> 21.98
2d	А	65	>290	(CF <sub>3</sub> COOD) 7.92 (m, 4H), 8.19 (m, 4H), 8.89 (t, <i>J</i> = 8.1 Hz, 1H), 9.33 (d, <i>J</i> = 8.1 Hz, 2H), 9.98 (s, 2H)	$C_{23}H_{13}Br_2N_7$	<i>50.48</i> 50.41	2.39 2.42	<i>17.92</i> 17.78
2e	А	73	>290	(DMSO- <i>d</i> <sub>6</sub> ) 8.49 (m, 4H), 8.57 (t, <i>J</i> = 7.8 Hz, 1H), 8.61 (m, 4H), 8.78 (d, <i>J</i> = 7.8 Hz, 2H), 9.75 (s, 2H)	$C_{23}H_{13}N_9O_4$	57.62 57.53	2.73 2.79	26.29 26.17
1a	В	80	218–220	(CDCl <sub>3</sub> ) 7.45 (m, 2H), 7.53 (m, 4H), 7.68 (m, 4H), 7.99 (t, <i>J</i> = 7.6 Hz, 1H), 8.07 (dd, <i>J</i> = 8.2, 2.4 Hz, 2H), 8.46 (d, <i>J</i> = 7.6 Hz, 2H), 8.72 (dd, <i>J</i> = 8.2, 0.9 Hz, 2H), 8.90 (dd, <i>J</i> = 2.4, 0.9 Hz, 2H)	$C_{27}H_{19}N_3$	<i>84.13</i> 84.05	4.97 5.02	<i>10.90</i> 10.72
1c	В	65	281–282 (lit. <sup>6</sup> 280)	(DMSO- $d_6/CCl_4$ ) 3.85 (s, 6H), 7.05 (m, 4H), 7.67 (m, 4H), 8.02 (t, $J = 7.8$ Hz, 1H), 8.12 (dd, $J = 8.2$ , 2.4 Hz, 2H), 8.46 (d, $J = 7.8$ Hz, 2H), 8.65 (d, $J = 8.2$ Hz, 2H), 8.90 (d, $J = 2.4$ Hz, 2H)	$C_{29}H_{23}N_3O_2$	78.18 78.24	5.20 5.25	9.43 9.35
6a	С	75	102–104	(DMSO- <i>d</i> <sub>6</sub> ) 2.06 (m, 4H), 3.04 (t, <i>J</i> = 7.0 Hz, 4H), 3.39 (t, <i>J</i> = 7.0 Hz, 4H), 7.50 (m, 10H), 8.04 (t, <i>J</i> = 7.1 Hz, 1H), 8.20 (d, <i>J</i> = 7.1 Hz, 2H), 8.48 (s, 2H)	$C_{33}H_{27}N_3$	<i>85.13</i> 85.01	5.85 5.70	9.02 9.19
6e	С	55	283–285	(DMSO- $d_6$ /CCl <sub>4</sub> ) 2.08 (m, 4H), 3.08 (t, $J = 7.4$ Hz, 4H), 3.42 (t, $J = 7.4$ Hz, 4H), 7.83 (m, 4H), 8.04 (t, $J = 7.2$ Hz, 1H), 8.23 (d, $J = 7.2$ Hz, 2H), 8.35 (m, 4H), 8.57 (s, 2H)	$C_{33}H_{25}N_5O_4$	<i>71.34</i> 71.25	<i>4.54</i> 4.32	<i>12.61</i> 12.70

We devised a new method for the synthesis of 2,6-bis(6aryl-1,2,4-triazin-3-yl)pyridines 2 starting from readily available acylarenes 3 bearing various substituents on the aryl moiety, for example, bromine, methyl, methoxy or nitro groups. Nitrosation of 3 yielded the corresponding 1-aryl-2-oximino-1-ethanones 4 after which treatment with hydrazine hydrate resulted in the formation of 1-aryl-1-hydrazono-2-oximinoethanes 5 in good yields. Condensation of hydrazones 5 with pyridine-2,6-dicarboxaldehyde followed by dehydration of the intermediates (4-hydroxy-3,4-dihydro-1,2,4-triazines)<sup>10</sup> by briefly refluxing in acetic acid gave the bistriazinylpyridines 2.<sup>11</sup> The aryl substituents of the starting ketones 3 appear at position 6 of the 1,2,4-triazines 2 not position 5, as in typical 1,2,4-triazine synthesis from arylglyoxals.<sup>12</sup>

Conversion of bistriazinylpyridines **2** into terpyridines **1** was achieved by aza-Diels–Alder reaction with the strained dienophile—2,5-norbornadiene—following a typical procedure.<sup>8</sup> The reaction proceeded slowly and at high temperature (refluxing in xylene) to give 5,5"-diaryl-2,2':6',2"-terpyridines **1** cleanly and in good yields.<sup>13</sup> The reaction needs a long time to go to completion due to the very low solubility of bistriazinylpyridines **2**.

Inverse electron demand aza-Diels–Alder reactions<sup>14,15</sup> of **2** with eneamines as dienophiles were used to extend the substituent diversity. Bistriazinylpyridines **2a**, **e** reacted with 1-(4-morpholino)cyclopentene more readily than with norbornadiene (refluxing in dioxane instead of xylene) yielding terpyridines **6a**, **e** with fused five-membered rings (Scheme 1).<sup>16</sup> The solubility of the arylterpyridines was increased in this way (Table 1).

In conclusion, the structural diversity is achieved by variation of three independent components: acylarenes and dienophiles (substituents in peripheral pyridines), as well as pyridinedicarboxaldehyde (substituents on the pyridine). Good yields of all intermediates and products, accessible starting compounds and a relatively easy experimental procedure, together combine to make a useful route for creating libraries of terpyridines suitable for any application.

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- 11. Procedure A. To a solution of 1-hydrazono-2-oximino-1arylethane 5 (20 mmol) in AcOH (30 mL) was added a

solution of pyridine-2,6-dicarboxaldehyde (1.35 g, 10 mmol) in acetic acid (10 mL). The mixture was heated to reflux and allowed to cool to room temperature. The precipitate was filtered off, washed with water and recrystallized from DMSO to give **2**.

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- 13. Procedure B. A mixture of 2,6-bis(6-aryl-1,2,4-triazin-3yl)pyridine **2c** (0.67 mmol), 2,5-norbornadiene (1.33 g, 13.4 mmol) and *o*-xylene (30 mL) was refluxed for 48 h and then cooled to room temperature. The precipitate was filtered off, washed with benzene and recrystallized from acetic acid to give the terpyridine **1**.
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- 16. Procedure C. A mixture of 2,6-bis(6-aryl-1,2,4-triazin-3-yl)pyridine 2 (1.0 mmol), 1-(4-morpholino)cyclo- pentene (612 mg, 4 mmol) and 1,4-dioxane (20 mL) was heated at reflux for 6 h. Then acetic acid (2 mL) was added and the reaction mixture was heated at reflux for 30 min, cooled to room temperature and made basic with aqueous 2 M NaOH. The precipitate was filtered off, washed with water and recrystallized from ethanol to give 6.