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# Synthesis and Single-Crystal X-ray Characterization of 4,4"-Functionalized 4'-(4-Bromophenyl)-2,2':6',2"-terpyridines

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To expand the utility of bis(terpyridine) metal connectivity, the selective symmetrical and unsymmetrical 4,4"-functionalization (-CN, -Me,  $-CO_2Me$ ) of 4'-(4-bromophenyl)-2,2':6',2"-terpyridines was achieved using the Kröhnke synthesis. The final substituted 2,2':6',2"-terpyridines along with their corresponding intermediates, **4a**-**c**, were recrystallized and characterized by <sup>1</sup>H NMR and <sup>13</sup>C NMR as well as X-ray crystallography; COSY correlations were also conducted to permit definitive proton assignment.

#### Introduction

Over the past decade, the coordination and supramolecular chemistry associated with 2,2':6',2''-terpyridines has been studied intensively. However, limited accessibility to unsymmetrically functionalized terpyridines has restricted their potential use in the construction of more complex infrastructures. Because their metal complexes have been shown to possess interesting novel luminescent properties,<sup>1–5</sup> their potential applications as chemosensors<sup>6,7</sup> and fluorescent immunoassay agents,<sup>8–11</sup> as well as their use in catalysis<sup>12–15</sup> and dye-

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synthesized solar cells,<sup>16–21</sup> could be expanded if new poly-functional motifs were available.

Substituted 2,2':6',2"-terpyridines have been synthesized via their *N*-oxide<sup>8,22,23</sup> and 1,2,4-triazine analogues<sup>24</sup> (the Sauer<sup>25</sup> method), the Kröhnke,<sup>26</sup> Potts,<sup>27</sup> and Jameson<sup>28</sup> methods, and

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### SCHEME 1. Preparation of the 4-Substituted 2-Acetylpyridines and Their Pyridinium Iodide Salts<sup>a</sup>



<sup>a</sup> (i) H<sub>2</sub>O/CH<sub>2</sub>Cl<sub>2</sub>, AgNO<sub>3</sub>, MeCOCO<sub>2</sub>H, H<sub>2</sub>SO<sub>4</sub>, (NH<sub>4</sub>)<sub>2</sub>S<sub>2</sub>O<sub>8</sub>, 3 h; (ii) MeCN, paraldehyde, TFA, t-BuOOH, 3 h; (iii) I<sub>2</sub>, pyridine, 3 h, N<sub>2</sub>.

modern Pd<sup>0</sup>-mediated cross-coupling procedures;<sup>29–33</sup> further chemical modifications of substituents have also been reported.<sup>33–35</sup> The two-step Kröhnke<sup>26</sup> synthesis, using modified 2'-azachalcones and pyridinium iodide salts of 2-acetylpyridines, facilitates the potential to create unsymmetrical and symmetrical mono- and disubstituted 4'-phenyl-2,2':6',2"-terpyridines; however, few examples of these procedures are found in the literature.<sup>36–38</sup>

Herein we report the first microwave-assisted solid-state aldol condensation procedure for the preparation of  $-CO_2Me$  and -CN substituted 2'-azachalcones, 4a-b, and the facile synthesis of new mono- and disubstituted 4'-(4-bromophenyl)terpyridines (5a-j; Figure 1) via the two-step Kröhnke<sup>26</sup> method. Different methyl-, methoxycarbonyl-, and cyano-substitution patterns on the 4,4"-positions of 4'-arylterpyridine were initially chosen because these functionalities afforded simple routes to a variety of useful substituted building blocks for higher-ordered supramacromolecular architectures. The X-ray crystal structures for terpyridines 5a, 5c, 5g, and 5j and the crystal packing of diester 5a and the intermediary 2'-azachalcones 4a and 4b are also presented.

## **Results and Discussion**

The initial well-known pyridinium iodide salts of 2-acetylpyridines (**3a**, **3c**, **3d**; Scheme 1) were prepared according to

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FIGURE 1. Substituted 2,2':6',2"-terpyridines (5a-j).

SCHEME 2. Preparation of 4-Bromo-2'-azachalcones by Claisen–Schmidt Aldol Condensation<sup>*a*</sup>



 $^a$  (i) MeOH, 1 M NaOH, 1 h; (ii) acidic Al<sub>2</sub>O<sub>3</sub>, MW 250 W, 60 °C, 15 min; (iii) basic Al<sub>2</sub>O<sub>3</sub>, MW 250 W, THF (2 mL), 15 min.

literature procedures,<sup>36,37,39</sup> whereas the salt of 2-acetyl-4cyanopyridine (**3b**) was prepared starting with a radical carbonylation at the 2 position of 4-cyanopyridine, **1b**, followed by addition to dry pyridine and iodine to give (85%) the new pyridinium iodide salt (**3b**) of 2-acetyl-4-cyanopyridine. Support for the structure of salt **3b** included the appearance of peaks at 6.58 (COCH<sub>2</sub>) and 66.4 (COCH<sub>2</sub>) ppm in the <sup>1</sup>H and <sup>13</sup>C NMR, respectively, and an upfield shift of the COCH<sub>2</sub>-pyridine resonance (198.1  $\rightarrow$  190 ppm, <sup>13</sup>C NMR) that agreed with that of similar conversions in the literature;<sup>36-39</sup> a peak at m/z =224.0836 [M - I]<sup>+</sup> in the HRMS spectrum also confirmed the transformation.

The 4-bromo-2'-azachalcones (**4a**–**d**; Scheme 2) were prepared by Claisen–Schmidt aldol condensation. Synthesis of the ester- and cyano-substituted 2'-azachalcones, **4a** and **4b**, was achieved using microwave irradiation with little or no solvent in the presence of either acidic or basic Al<sub>2</sub>O<sub>3</sub>, respectively, as a catalyst and solid support.<sup>38,40</sup> These protocols were employed

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## SCHEME 3. Preparation of 4,4"-Functionalized 4'-(4-Bromophenyl)-2,2';6',2"-terpyridines by the Kröhnke Method<sup>a</sup>



<sup>a</sup> (i) MeOH, NH<sub>4</sub>OAc, 8 h; (ii) AcOH, NH<sub>4</sub>OAc, 6 h.

instead of using NaOH as a result of potential side reactions, for example, saponification. The reaction mixture of 4-bromobenzaldehyde and ester **2a** was heated to 60 °C, whereas the cyano **2b** was dissolved in a small amount (1–2 mL) of THF to obtain homogeneous mixtures. Then the addition of Al<sub>2</sub>O<sub>3</sub> and irradiation in the microwave at 250 W for 15 min afforded (56%) the desired azachalcones **4a** and **4b**, respectively.<sup>41,42</sup> Methyl-substituted 2'-azachalcone **4c** was prepared by the NaOH-promoted aldol condensation, similar to the literature procedure for 4-bromo-2'-azachalcone (**4d**).<sup>43</sup>

Azachalcones  $4\mathbf{a}-\mathbf{c}$  were characterized (<sup>1</sup>H NMR) by two doublet absorptions (7.78–8.19 ppm) assigned to  $\text{COC}H_A=$  $CH_B$  with large coupling constants ( $J_{A,B} = 15.9-16.2$  Hz) indicative of the trans double bond and a single carbonyl (<sup>13</sup>C NMR) resonance for such constructs in the range of 187.5 to 189.7 ppm.<sup>43</sup> The spectral assignment of **4d** agreed with the literature.<sup>43</sup> HRMS spectra further confirmed the 4-bromo-2'azachalcone structures with peaks at m/z = 367.9899 [M + Na]<sup>+</sup> (**4a**), m/z = 334.9812 [M + Na]<sup>+</sup> (**4b**), and m/z = 323.9992[M + Na]<sup>+</sup> (**4c**); NaI was used in the positive-ion mode.

The pyridinium iodide salts of the modified 2-acetylpyridines,  $3\mathbf{a}-\mathbf{d}$ , were next reacted via a Michael-type addition with the functionalized 4-bromo-2'-azachalcones,  $4\mathbf{a}-\mathbf{d}$ , followed by the ring-closure of the resulting diketone using ammonium acetate in either AcOH or MeOH to afford (33–73%) the desired unsymmetric and symmetric 4'-(4-bromophenyl)-2,2';6',2''-terpyridines ( $5\mathbf{a}-\mathbf{j}$ ; Scheme 3). Most of the reactions proceeded with a higher yield in MeOH than in AcOH as a result of the potential side reactions of the substituents in an acidic and high-temperature environment.

The <sup>1</sup>H NMR spectra of the symmetric disubstituted 4'-(4bromophenyl)terpyridines (**5a**, **5b**, **5c**; Supporting Information) revealed downfield shifts for the 5,5''-pyrH, 6,6''-pyrH, and 3,3"-pyr*H* (pyr = pyridine) resonance for diester **5a** (7.93, 8.87, and 9.18 ppm) and dicyano **5b** (7.63, 8.92, and 8.89 ppm) as well as upfield shifts for the same signals assigned to the dimethyl terpyridine **5c** (7.19, 8.58, and 8.47 ppm) compared to those of known terpyridines, such as **5d**<sup>43</sup> (7.35, 8.72, and 8.66 ppm) and 4'-phenylterpyridine<sup>44</sup> (7.33, 8.74, and 8.68 ppm). Dimethyl terpyridine, **5c**, showed a similar <sup>1</sup>H NMR pattern as that of 4'-(4-chlorophenyl)-4,4"-dimethylterpyridine, <sup>36</sup> but to confirm the proper assignments, two-dimensional 2D COSY NMR experiments (Supporting Information) were conducted. HRMS spectra also supported the structural assignments of the diester **5a**, m/z = 526.0375 [M + Na]<sup>+</sup>; dicyano **5b**, m/z = 438.0364 [M + H]<sup>+</sup>, 460.0194 [M + Na]<sup>+</sup>; and dimethyl terpyridine **5c**, m/z = 438.0582 [M + Na]<sup>+</sup>.

<sup>1</sup>H NMR spectra of the unsymmetrical monosubstituted 4'-(4-bromophenyl)terpyridines (5g, 5i, 5j; Supporting Information) show unique proton resonances for each pyridine ring as a result of the diminished symmetry. The 5-pyrH resonance ( $^{1}H$  NMR) of ester 5g, cyano 5i, and methyl 5j appears as a doublet, whereas the 5"-pyrH resonance appeared as a doublet of doublets as a result of coupling  $(J_{5'',6''} = 7.5 \text{ Hz}, J_{5'',4''} = 4.8$ Hz) with the adjacent protons. Moreover, the 5-pyrH resonance shifted downfield for ester 5g (7.9  $\rightarrow$  7.35 ppm) and cyano 5i  $(7.56 \rightarrow 7.4 \text{ ppm})$  but upfield for the methyl construct 5j (7.21  $\rightarrow$  7.38 ppm). The 3-pyr*H* resonance follows the same pattern; it shifts downfield for ester 5g (9.14  $\rightarrow$  8.72 ppm) and cyano 5i (8.9  $\rightarrow$  8.63 ppm) and upfield for methyl 5j (8.49  $\rightarrow$  8.66 ppm) when compared to the 3''-pyrH resonance as well as changing from a singlet (3-pyrH) to a doublet (3''-pyrH). Rationale for these shifts is rooted in the deshielding effect of the electron-withdrawing groups for ester 5g and cyano 5i and the shielding effect caused by the electron-donating methyl group in terpyridine 5j. These assignments have been confirmed by 2D COSY NMR experiments (Supporting Information). Furthermore, <sup>1</sup>H and 2D COSY NMR (Supporting Information) spectra of the monosubstituted 4'-(4-bromophenyl)terpyridines

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**FIGURE 2.** Molecular structure of diester **5a** with thermal ellipsoids drawn at 50% probability.

(5g, 5i, and 5j) revealed splitting of the singlet (3',5'-pyr*H*) in the symmetric terpyridines (5a, 5b, and 5c) resulting in two doublets with small meta coupling constants ( $J_{3',5'} = 1.5$  Hz). The ester 5g and methyl 5j showed similar <sup>1</sup>H NMR patterns as that of 4'-(*p*-toluyl)-4-(methoxycarbonyl)terpyridine<sup>37</sup> and 4'-(4-chlorophenyl)-4-methylterpyridine,<sup>36</sup> respectively. HRMS spectra also supported the structural assignments of ester 5g, cyano 5i, and methyl terpyridine 5j with a peak at m/z =468.0331 [M + Na]<sup>+</sup>, m/z = 435.0235 [M + Na]<sup>+</sup>, and m/z =424.0424 [M + Na]<sup>+</sup>, respectively.

The <sup>1</sup>H NMR spectra of the unsymmetric disubstituted 4'-(4-bromophenyl)terpyridines (**5e**, **5f**, **5h**; Supporting Information) showed unique proton resonances for each pyridine ring similar to those of the above monosubstituted counterparts. Moreover, the 5-pyr*H* resonance shifts downfield in the cases of the ester-cyano **5e** (7.95  $\rightarrow$  7.61 ppm), ester-methyl **5f** (7.9  $\rightarrow$  7.2 ppm), and cyano-methyl **5h** (7.58  $\rightarrow$  7.25 ppm) when compared to the 5"-pyr*H* and 3-pyr*H* resonances that show the same pattern; it shifts downfield for the ester-cyano **5e** (9.08  $\rightarrow$  8.9 ppm), ester-methyl **5f** (9.16  $\rightarrow$  8.5 ppm), and cyanomethyl **5h** (8.93  $\rightarrow$  8.47 ppm) when compared to the 3"-pyr*H* resonance. Furthermore, the <sup>1</sup>H and 2D COSY NMR spectra (Supporting Information) of these unsymmetric compounds, **5e**, **5f**, and **5h**, revealed the splitting of the 3',5'-pyr*H* peaks in symmetric terpyridines (**5a**, **5b**, and **5c**) resulting in two doublets with small meta coupling constants ( $J_{3',5'} = 1.5-2.1$  Hz). The HRMS spectra also support the structural assignments of the terpyridines: **5e**, m/z = 493.0274 [M + Na]<sup>+</sup>; **5f**, m/z = 482.0471 [M + Na]<sup>+</sup>; and **5h**, m/z = 449.0384 [M + Na]<sup>+</sup>.

X-ray crystal structures of ester **4a** and cyano azachalcone **4b** (Supporting Information) confirmed the proposed structures. The data showed that ester **4a** and azachalcone **4b** crystallized in a monoclinic cell with a  $P2_1/n$  space group and in a triclinic cell with a P1 space group, respectively. Also, the X-ray data of ester **4a** and azachalcone **4b** revealed a trans double bond configuration with bond lengths (Å) of C(7)–C(8) = 1.312(5) and C(7)–C(8) = 1.342(4), respectively, which is similar to that of the 2'-azachalcone<sup>45</sup> and chalcones<sup>45,46</sup> [1.321(2)–1.329-(4) Å]. Furthermore, the C=O bond lengths (Å) of ester **4a**, O(1)–C(9) = 1.224(4) Å and azachalcone **4b**, O(1)–C(9) = 1.219(3) Å, were in agreement with the literature.<sup>45,46</sup>

X-ray crystal data of the diester **5a** (Figure 2), dimethyl **5c**, ester 5g, and methyl 5j (Supporting Information) confirm the proposed structures. The three pyridine rings showed a transoid arrangement about the interannular C-C bonds, which was also in agreement with the literature.44,47-49 This configuration minimizes electrostatic interactions between the nitrogen lone pairs and the van der Waals interactions between the meta protons.44 The interannular C-C bond lengths of 5a, 5c, 5g, and 5j [1.481-(8)-1.494(4) Å] are comparable with those of the 2,2';6',2"terpyridines [1.480(1)-1.498(3) Å] found in the literature.44,47,48 Moreover, the three pyridine rings are not exactly coplanar and the torsion angles of the two terminal rings with the central pyridine ring are 5.16 and 3.88° for diester 5a, 9.48 and 1.06° for methyl 5c, 2.65 and 3.05° for ester 5g, and 6.59 and 0.97° for methyl 5j, which is comparable to those of 4'-phenylterpyridine<sup>44</sup> (5.7°) and 4'-(4-anilino)terpyridine<sup>48</sup> (2.7 and 7.4°). Furthermore, the 4'-bromophenyl ring connected to the terpyridine is distorted with torsion angles of 22.83° for diester 5a, 39° for dimethyl 5c, 27.48° for ester 5g, and 39.75° for methyl **5j**, which are higher than that of 4'-phenylterpyridine<sup>44</sup> (10.9°), comparable to that of 4'-(4-anilino)terpyridine<sup>48</sup> (27.5°), and lower than those of 4'-(2,4,6-trimethylphenyl)terpyridine<sup>50</sup> (67.5°) and 4'-(2,5-dimethoxyphenyl)terpyridine<sup>51</sup> (50.4°).

Only the diester **5a** crystal packing revealed  $\pi - \pi$  interactions (interlayer distances smaller than 3.5 Å).<sup>52</sup> Molecules of diester **5a** (approximately coplanar) are stacked by the overlap of the



**FIGURE 3.** (a) Stacking of diester 5a in the crystal lattice with the distances (Å) between the central pyridine rings and (b) the orientation of diester 5a in adjacent planes in the lattice, viewing along the c axis. Hydrogen atoms are omitted for clarity.

central pyridine rings in consecutive layers with mean interplanar distances of 3.4 Å in the solid state (Figure 3a), which is comparable to those of 4'-(dimethylamino)terpyridine<sup>53</sup> (3.47 Å) and 4'-(4-anilino)terpyridine (3.5 Å). Also, they possess adjacent planes that are parallel to each other in a *head*-to-*tail* fashion (Figure 3b). Moreover, the central pyridine rings are slightly slipped with respect to each other to maximize  $\pi - \pi$  interactions between the stacked pyridine rings.<sup>52</sup>

#### Conclusion

Substituted 2'-azachalcones (4a, 4b) were conveniently synthesized using microwave-assisted solid-state aldol condensation procedures. Symmetrical and unsymmetrical mono- and disubstituted 4'-(4-bromophenyl)terpyridines (5a-j) were constructed by utilizing the two-step Kröhnke<sup>26</sup> methodology with pyridinium iodide salts of substituted 2-acetylpyridines (3a-d) and modified 4-bromo-2'-azachalcones (4a-d). X-ray crystal structures of ester 4a, azachalcone 4b, diester 5a, dimethyl 5c, ester 5g, and methyl 5j, as well as solid-state crystal packing of diester terpyridine 5a, were obtained. Ongoing work utilizes these unsymmetrically disubstituted 4'-(4-bromophenyl)-2,2';6',2''-terpyridines in the assembly of supramacromolecular oligomeric materials.

#### **Experimental Section**

**1-[2-(4-Cyano-2-pyridyl)-2-oxoethyl]pyridinium Iodide (3b).** To a stirred warmed (60 °C) solution of I<sub>2</sub> (4.68 g, 18.5 mmol) in pyridine (27 mL) under N<sub>2</sub> was added 2-acetyl-4-cyanopyridine (**2b**; 2.7 g, 18.5 mmol), which was stirred at 100 °C for 1 h. The crystals that formed upon cooling were filtered and washed with CHCl<sub>3</sub> (2 × 25 mL) and Et<sub>2</sub>O (2 × 25 mL) to give the product **3b** as green crystals: 5.5 g (85%); mp 226–227 °C; <sup>1</sup>H NMR (DMSO $d_6$ )  $\delta$  6.58 (s, 2H, COCH<sub>2</sub>), 8.32 (m, 3H, 5-pyrH, 3,5-ArH), 8.45 (s, 1H, 3-pyrH), 8.78 (t, 1H, 4-ArH, J = 7.8 Hz), 9.07 (d, 2H, 2,6-ArH, J = 6.6 Hz), 9.12 (d, 1H, 6-pyrH, J = 4.8 Hz); <sup>13</sup>C NMR (DMSO- $d_6$ )  $\delta$  66.4, 116.9, 121.1, 123.7, 127.7, 130.4, 146.1, 146.4, 150.6, 151.2, 190. HRMS (EI): [M – I]<sup>+</sup> calcd for C<sub>13</sub>H<sub>10</sub>N<sub>3</sub>O, 224.0824; found, 224.0836.

1-(3-Oxo-3-[2-(4-methoxycarbonylpyridyl)]propen-1-yl)-4bromobenzene (4a). A neat, stirred mixture of 2-acetyl-4-(methoxycarbonyl)pyridine (2a; 550 mg, 3.07 mmol) and 4-bromobenzaldehyde (570 mg, 3.08 mmol) was heated to 60 °C, and then acidic Al<sub>2</sub>O<sub>3</sub> (9.94 g) was added. The mixture was then irradiated in the microwave at 250 W for 15 min. After cooling, CHCl<sub>3</sub> (3 × 50 mL) was added and the mixture was filtered. The filtrate was concentrated in vacuo to give a solid, which was washed with MeOH (3 × 25 mL) to afford the product 4a as a light yellow solid: 580 mg (55%); mp 163–164 °C; <sup>1</sup>H NMR  $\delta$  4.01 (s, 3H, pyrCO<sub>2</sub>CH<sub>3</sub>), 7.57 (d, 2H, 3,5-ArH, J = 8.7 Hz), 7.58 (d, 2H, 2,6-ArH, J = 8.4 Hz), 7.92 (d, 1H, COCH=CH, J = 16.2 Hz), 8.05 (dd, 1H, 5-pyrH,  $J_1$  = 4.8 Hz,  $J_2$  = 1.8 Hz), 8.25 (d, 1H, COCH=CH, J = 15.9 Hz), 8.7 (s, 1H, 3-pyrH), 8.88 (dd, 1H, 6-pyrH,  $J_1$  = 4.8 Hz,  $J_2$  = 0.9 Hz); <sup>13</sup>C NMR  $\delta$  53.1, 121.4, 122.4, 125.3, 126.2, 130.4, 132.4, 134.2, 139, 144, 150, 155.3, 165.3, 188.6. HRMS (EI): [M + Na]<sup>+</sup> calcd for C<sub>16</sub>H<sub>12</sub>BrNO<sub>3</sub>Na, 367.9898; found, 367.9899.

1-(3-Oxo-3-[2-(4-cvanopyridyl)]propen-1-yl)-4-bromobenzene (4b). To a stirred solution of 4-bromobenzaldehyde (2.07 g, 11.2 mmol) and 2-acetyl-4-cyanopyridine (2b; 1.72 g, 11.8 mmol) in THF (2 mL) at 25 °C was added quickly basic Al<sub>2</sub>O<sub>3</sub> (15 g). The mixture was then irradiated in the microwave at 250 W for 15 min. After cooling, CHCl<sub>3</sub> ( $3 \times 50$  mL) was added, and the mixture was filtered. The filtrate was concentrated in vacuo to give a solid, which was washed with MeOH (3  $\times$  25 mL) to afford the product **4b** as a light yellow solid: 1.92 g (56%); mp 184-185 °C; <sup>1</sup>H NMR  $\delta$  7.57 (s, 4H, 2,3,5,6-Ar*H*), 7.71 (dd, 2H, 5-pyr*H*,  $J_1 = 4.8$ Hz,  $J_2 = 1.5$  Hz), 7.93 (d, 1H, COCH=CH, J = 16.2 Hz), 8.19 (d, 1H, COCH=CH, J = 15.9 Hz), 8.39 (s, 1H, 3-pyrH), 8.91 (dd, 1H, 6-pyr*H*,  $J_1 = 5.1$  Hz,  $J_2 = 0.9$  Hz); <sup>13</sup>C NMR  $\delta$  116.1, 120.5, 122.1, 124.9, 125.6, 128.2, 130.5, 132.5, 133.9, 144.9, 150.1, 155.1, 187.5. HRMS (EI):  $[M + Na]^+$  calcd for  $C_{15}H_9BrN_2ONa$ , 334.9796; found, 334.9812.

1-(3-Oxo-3-[2-(4-methylpyridyl)]propen-1-yl)-4-bromobenzene (4c). To a stirring solution of 4-bromobenzaldehyde (1.02 g, 5.53 mmol) and 2-acetyl-4-methylpyridine (2c; 760 mg, 5.57 mmol) in MeOH (25 mL) at 25 °C was added aqueous NaOH (1 M, 5 mL). The mixture was stirred for 1 h at 25 °C and then filtered and washed with H<sub>2</sub>O (15 mL). The precipitate was dissolved in  $CH_2Cl_2$  (150 mL) and extracted with  $H_2O$  (2  $\times$  100 mL). The combined organic fractions were dried (MgSO<sub>4</sub>) and concentrated in vacuo to give the product 4c as a light yellow solid: 1 g (60%); mp 123-125 °C; <sup>1</sup>H NMR δ 2.47 (s, 3H, pyrCH<sub>3</sub>), 7.32 (d, 1H, 5-pyr*H*, *J* = 4.2 Hz) 7.56 (d, 2H, 3,5-Ar*H*, *J* = 9 Hz), 7.59 (d, 2H, 2,6-ArH, J = 8.4 Hz), 7.88 (d, 1H, COCH=CH, J = 16.2 Hz), 8.03 (s, 1H, 3-pyr*H*), 8.27 (d, 1H, COC*H*=CH, *J* = 16.2 Hz), 8.6 (d, 1H, 6-pyr*H*, J = 4.8 Hz); <sup>13</sup>C NMR  $\delta$  21.3, 121.9, 124, 125, 128.1, 130.3, 132.3, 134.3, 143.3, 148.6, 148.9, 154.1, 189.7. HRMS (EI):  $[M\ +\ Na]^+$  calcd for  $C_{15}H_{12}BrNONa:\ 324.0000;$  found, 323.9992.

General Procedures for the Preparation of 4'-(4-Bromophenyl)-2,2';6',2''-terpyridines. Route A. To a stirred solution of the pyridinium iodide salt of the substituted 2-acetylpyridines 3 and the modified 2'-azachalcones 4 in MeOH or EtOH was added excess NH<sub>4</sub>OAc, and the mixture was refluxed overnight. The precipitate, which was formed upon cooling, was filtered and washed with MeOH. The precipitate collected from the filtration was column chromatographed (basic Al<sub>2</sub>O<sub>3</sub>), eluting with CHCl<sub>3</sub>, to give the product.

**Route B.** To a stirred solution of the pyridinium iodide salt of the substituted 2-acetylpyridines **3** and the modified 2'-azachalcones **4** in AcOH was added excess NH<sub>4</sub>OAc, and the mixture was refluxed overnight. The solution was concentrated in vacuo to give a paste, which was neutralized with Na<sub>2</sub>CO<sub>3</sub> (1 M) and extracted with CHCl<sub>3</sub>. Organic layers were combined and dried (MgSO<sub>4</sub>), and then the solvent was evaporated in vacuo to give a residue that was column chromatographed (basic Al<sub>2</sub>O<sub>3</sub>), eluting with an EtOAc/hexane mixture (1:1), to give the product.

**4'-(4-Bromophenyl)-4,4"-dimethoxycarbonyl-2,2';6',2"-terpyridine (5a).** To a stirred solution of **3a** (1.1 g, 3.2 mmol) and **4a** (1.22 g, 3.2 mmol) in MeOH (30 mL) was added excess NH<sub>4</sub>OAc (8 g, 104 mmol). Then, via route A, the product, **5a**, was isolated as a light yellow solid: 820 mg (51%); mp 280–281 °C; <sup>1</sup>H NMR  $\delta$  4.06 (s, 6H, pyrCO<sub>2</sub>CH<sub>3</sub>), 7.67 (d, 2H, 3,5-ArH, J = 8.4 Hz), 7.76 (d, 2H, 2,6-ArH, J = 8.7 Hz), 7.93 (dd, 2H, 5,5"-pyrH,  $J_1$  = 4.8 Hz,  $J_2$  = 1.5 Hz), 8.73 (s, 2H, 3,3"-pyrH), 8.87 (d, 2H, 6,6"-pyrH, J = 4.8 Hz), 9.18 (s, 2H, 3',5'-pyrH); <sup>13</sup>C NMR  $\delta$  53, 119.5,

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121.1, 123.3, 123.9, 129.1, 132.5, 137.4, 138.8, 149.5, 150.1, 155.9, 157.3, 166; HRMS (EI):  $[M + Na]^+$  calcd for  $C_{25}H_{18}BrN_3O_4Na,$  526.0378; found, 526.0375.

**4'-(4-Bromophenyl)-4-methoxycarbonyl-4''-cyano-2,2';6',2''-terpyridine (5e).** To a stirred solution of **3b** (469 mg, 1.33 mmol) and **4a** (462 mg, 1.33 mmol) in MeOH (20 mL) was added excess NH<sub>4</sub>OAc (3.47 g). Then, via route A, the product, **5e**, was isolated as a white solid: 240 mg (38%); mp 253–254 °C; <sup>1</sup>H NMR  $\delta$  4.08 (s, 3H, pyrCO<sub>2</sub>CH<sub>3</sub>), 7.61 (dd, 1H, 5''-pyrH,  $J_1$  = 3.3 Hz,  $J_2$  = 1.5 Hz), 7.68 (d, 2H, 3,5-ArH, J = 8.7 Hz), 7.75 (d, 2H, 2,6-ArH, J = 8.7 Hz), 7.95 (dd, 1H, 5-pyrH,  $J_1$  = 3.3 Hz,  $J_2$  = 1.8 Hz), 8.74 (d, 1H, 5'-pyrH, J = 1.8 Hz), 8.78 (d, 1H, 3'-pyrH, J = 1.8 Hz), 8.9 (m, 3H, 6,6'',3''-pyrH), 9.08 (dd, 1H, 3-pyrH,  $J_1$  = 0.9 Hz,  $J_2$  = 0.6 Hz); <sup>13</sup>C NMR  $\delta$  53.1, 117, 119.4, 120, 120.7, 121.7, 123.36, 123.45, 124.1, 125.3, 128.9, 132.5, 137, 138.9, 149.6, 150.2, 154.5, 156, 156.8, 157.4, 170. HRMS (EI): [M + Na]<sup>+</sup> calcd for C<sub>24</sub>H<sub>15</sub>BrN<sub>4</sub>O<sub>2</sub>Na, 493.0276; found, 493.0274.

4'-(4-Bromophenyl)-4-methoxycarbonyl-2,2';6',2"-terpyridine (5g). To a stirred solution of 3d (496 mg, 1.52 mmol) and 4a (526 mg, 1.52 mmol) in MeOH (25 mL) was added excess NH<sub>4</sub>-OAc (4.41 g). Then, via route A, the product, 5g, was isolated as a white solid: 250 mg (37%); mp 173–174 °C; <sup>1</sup>H NMR  $\delta$  4.04

(s, 3H, pyrCO<sub>2</sub>CH<sub>3</sub>), 7.35 (dd, 1H, 5"-pyr*H*,  $J_1 = 7.5$  Hz,  $J_2 = 4.8$  Hz), 7.65 (d, 2H, 3,5-Ar*H*, J = 8.4 Hz), 7.76 (d, 2H, 2,6-Ar*H*, J = 8.4 Hz), 7.9 (m, 2H, 5,4"-pyr*H*), 8.72 (m, 4H, 3',5',3",6"-pyr*H*), 8.84 (d, 1H, 6-pyr*H*, J = 5.1 Hz), 9.14 (s, 1H, 3-pyr*H*); <sup>13</sup>C NMR  $\delta$  52.9, 118.8, 119, 120.8, 121.7, 123, 123.8, 124.2, 129, 132.3, 137.1, 137.4, 138.6, 149.16, 149.27, 150, 155.4, 155.9, 156.4, 157.4, 166. HRMS (EI): [M + Na]<sup>+</sup> calcd for C<sub>23</sub>H<sub>16</sub>BrN<sub>3</sub>O<sub>2</sub>Na, 468.0323; found, 468.0331.

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**Supporting Information Available:** <sup>1</sup>H, <sup>13</sup>C, and COSY NMR spectra of all compounds, experimental details of **5b**, **5c**, **5f**, **5h**, **5i**, and **5j**, general remarks, crystallographic data, and CIF files of **4a**, **4b**, **5a**, **5c**, **5g**, and **5j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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