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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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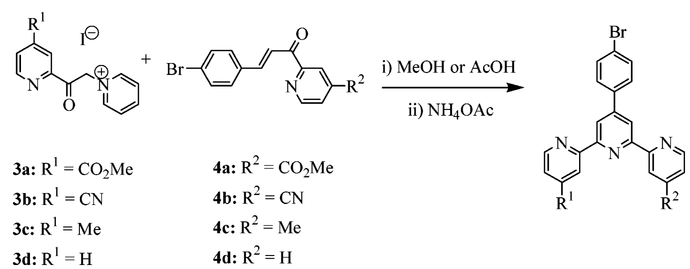

To expand the utility of bis(terpyridine) metal connectivity, the selective symmetrical and unsymmetrical 4,4″-functionalization (−CN, −Me, $-CO_2Me$) of 4′-(4-bromophenyl)-2,2′:6′,2″-terpyridines was achieved using the Kröhnke synthesis. The final substituted 2,2′:6′,2″-terpyridines along with their corresponding intermediates, **4a−c**, were recrystallized and characterized by ^1H NMR and ^{13}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,[1−5] their potential applications as chemosensors[6,7] and fluorescent immunoassay agents,[8−11] as well as their use in catalysis[12−15] and dye-synthesized solar cells,[16−21] could be expanded if new polyfunctional motifs were available.

Substituted 2,2′:6′,2″-terpyridines have been synthesized via their *N*-oxide[8,22,23] and 1,2,4-triazine analogues[24] (the Sauer[25] method), the Kröhnke,[26] Potts,[27] and Jameson[28] methods, and

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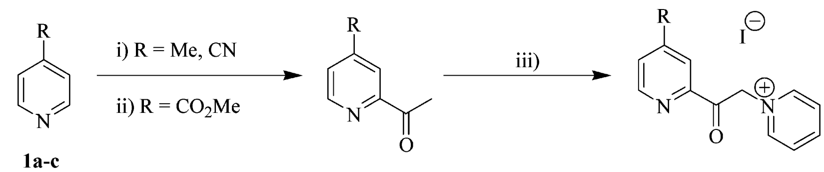
SCHEME 1. Preparation of the 4-Substituted 2-Acetylpyridines and Their Pyridinium Iodide Salts[a]



1a-c

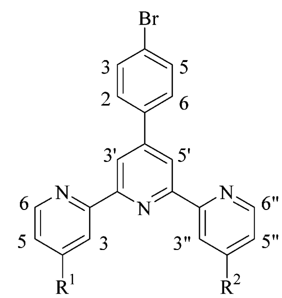
2a: R = CO_2Me (66%)
2b: R = CN (65%)
2c: R = Me (38%)

3a: R = CO_2Me (60%)
3b: R = CN (85%)
3c: R = Me (63%)
3d: R = H (56%)

[a] (i) H_2O/CH_2Cl_2, $AgNO_3$, $MeCOCO_2H$, H_2SO_4, $(NH_4)_2S_2O_8$, 3 h; (ii) MeCN, paraldehyde, TFA, *t*-BuOOH, 3 h; (iii) I_2, pyridine, 3 h, N_2.

modern Pd^0-mediated cross-coupling procedures;[29−33] further chemical modifications of substituents have also been reported.[33−35] The two-step Kröhnke[26] 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.[36−38]

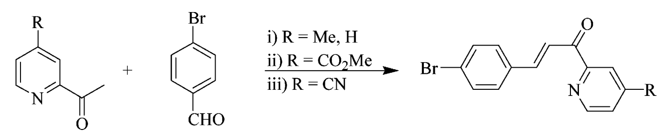
Herein we report the first microwave-assisted solid-state aldol condensation procedure for the preparation of $-CO_2Me$ and $-CN$ substituted 2′-azachalcones, **4a−b**, and the facile synthesis of new mono- and disubstituted 4′-(4-bromophenyl)terpyridines (**5a−j**; Figure 1) via the two-step Kröhnke[26] 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.



	R^1	R^2
5a:	CO_2Me	CO_2Me
5b:	CN	CN
5c:	Me	Me
5d:	H	H
5e:	CO_2Me	CN
5f:	CO_2Me	Me
5g:	CO_2Me	H
5h:	CN	Me
5i:	CN	H
5j:	Me	H

FIGURE 1. Substituted 2,2′:6′,2″-terpyridines (**5a−j**).

SCHEME 2. Preparation of 4-Bromo-2′-azachalcones by Claisen−Schmidt Aldol Condensation[a]



2a-d

4a: R = CO_2Me (55%)
4b: R = CN (56%)
4c: R = Me (60%)
4d: R = H (80%)

[a] (i) MeOH, 1 M NaOH, 1 h; (ii) acidic Al_2O_3, MW 250 W, 60 °C, 15 min; (iii) basic Al_2O_3, MW 250 W, THF (2 mL), 15 min.

Results and Discussion

The initial well-known pyridinium iodide salts of 2-acetylpyridines (**3a**, **3c**, **3d**; Scheme 1) were prepared according to literature procedures,[36,37,39] whereas the salt of 2-acetyl-4-cyanopyridine (**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_2) and 66.4 (COCH_2) ppm in the ^{1}H and ^{13}C NMR, respectively, and an upfield shift of the COCH$_2$−pyridine resonance (198.1 → 190 ppm, ^{13}C NMR) that agreed with that of similar conversions in the literature;[36−39] a peak at m/z = 224.0836 $[M - I]^+$ 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_2O_3, respectively, as a catalyst and solid support.[38,40] These protocols were employed

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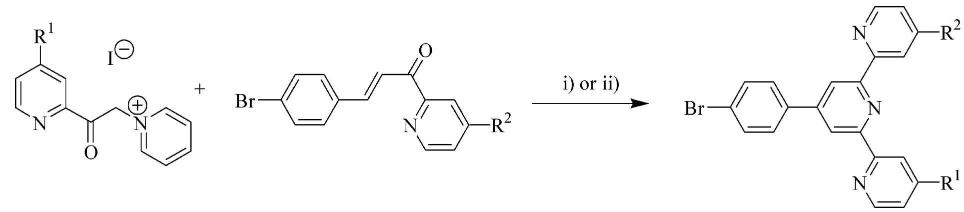
SCHEME 3. Preparation of 4,4″-Functionalized 4′-(4-Bromophenyl)-2,2′;6′,2″-terpyridines by the Kröhnke Method[a]



3a: $R^1 = CO_2Me$
3b: $R^1 = CN$
3c: $R^1 = Me$
3d: $R^1 = H$

4a: $R^2 = CO_2Me$
4b: $R^2 = CN$
4c: $R^2 = Me$
4d: $R^2 = H$

	R1	**R2**	
5a:	CO_2Me	CO_2Me	(51%)
5b:	CN	CN	(48%)
5c:	Me	Me	(33%)
5d:	H	H	(73%)
5e:	CO_2Me	CN	(38%)
5f:	CO_2Me	Me	(39%)
5g:	CO_2Me	H	(37%)
5h:	CN	Me	(41%)
5i:	CN	H	(58%)
5j:	Me	H	(72%)

[a] (i) MeOH, NH_4OAc, 8 h; (ii) AcOH, NH_4OAc, 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_2O_3 and irradiation in the microwave at 250 W for 15 min afforded (56%) the desired azachalcones **4a** and **4b**, respectively.[41,42] Methyl-substituted 2′-azachalcone **4c** was prepared by the NaOH-promoted aldol condensation, similar to the literature procedure for 4-bromo-2′-azachalcone (**4d**).[43]

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

The pyridinium iodide salts of the modified 2-acetylpyridines, **3a−d**, were next reacted via a Michael-type addition with the functionalized 4-bromo-2′-azachalcones, **4a−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 (**5a−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 ^{1}H NMR spectra of the symmetric disubstituted 4′-(4-bromophenyl)terpyridines (**5a**, **5b**, **5c**; Supporting Information) revealed downfield shifts for the 5,5″-pyr*H*, 6,6″-pyr*H*, 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**[43] (7.35, 8.72, and 8.66 ppm) and 4′-phenylterpyridine[44] (7.33, 8.74, and 8.68 ppm). Dimethyl terpyridine, **5c**, showed a similar ^{1}H NMR pattern as that of 4′-(4-chlorophenyl)-4,4″-dimethylterpyridine,[36] 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]$^+$; dicyano **5b**, m/z = 438.0364 [M + H]$^+$, 460.0194 [M + Na]$^+$; and dimethyl terpyridine **5c**, m/z = 438.0582 [M + Na]$^+$.

^{1}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-pyr*H* resonance (^{1}H NMR) of ester **5g**, cyano **5i**, and methyl **5j** appears as a doublet, whereas the 5″-pyr*H* resonance appeared as a doublet of doublets as a result of coupling ($J_{5'',6''}$ = 7.5 Hz, $J_{5'',4''}$ = 4.8 Hz) with the adjacent protons. Moreover, the 5-pyr*H* resonance shifted downfield for ester **5g** (7.9 → 7.35 ppm) and cyano **5i** (7.56 → 7.4 ppm) but upfield for the methyl construct **5j** (7.21 → 7.38 ppm). The 3-pyr*H* resonance follows the same pattern; it shifts downfield for ester **5g** (9.14 → 8.72 ppm) and cyano **5i** (8.9 → 8.63 ppm) and upfield for methyl **5j** (8.49 → 8.66 ppm) when compared to the 3″-pyr*H* resonance as well as changing from a singlet (3-pyr*H*) to a doublet (3″-pyr*H*). 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, ^{1}H and 2D COSY NMR (Supporting Information) spectra of the monosubstituted 4′-(4-bromophenyl)terpyridines

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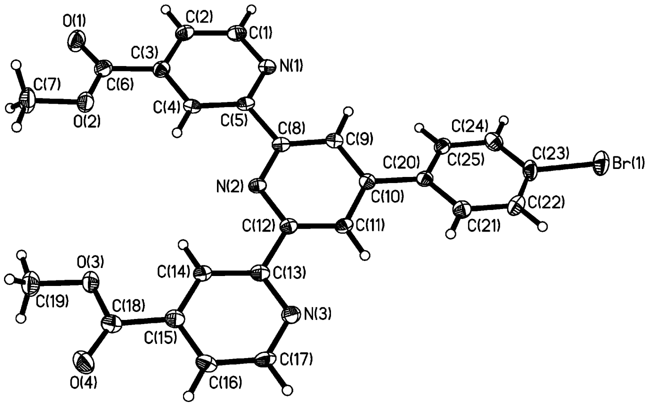

FIGURE 2. Molecular structure of diester **5a** with thermal ellipsoids drawn at 50% probability.

(**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 ^{1}H NMR patterns as that of 4′-(*p*-toluyl)-4-(methoxycarbonyl)terpyridine[37] and 4′-(4-chlorophenyl)-4-methylterpyridine,[36] 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]$^+$, *m*/*z* = 435.0235 [M + Na]$^+$, and *m*/*z* = 424.0424 [M + Na]$^+$, respectively.

The ^{1}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 → 7.61 ppm), ester-methyl **5f** (7.9 → 7.2 ppm), and cyano-methyl **5h** (7.58 → 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 → 8.9 ppm), ester-methyl **5f** (9.16 → 8.5 ppm), and cyano-methyl **5h** (8.93 → 8.47 ppm) when compared to the 3″-pyr*H* resonance. Furthermore, the ^{1}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]$^+$; **5f**, *m*/*z* = 482.0471 [M + Na]$^+$; and **5h**, *m*/*z* = 449.0384 [M + Na]$^+$.

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[45] and chalcones[45,46] [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.[45,46]

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[44] (5.7°) and 4′-(4-anilino)terpyridine[48] (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[44] (10.9°), comparable to that of 4′-(4-anilino)terpyridine[48] (27.5°), and lower than those of 4′-(2,4,6-trimethylphenyl)terpyridine[50] (67.5°) and 4′-(2,5-dimethoxyphenyl)terpyridine[51] (50.4°).

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

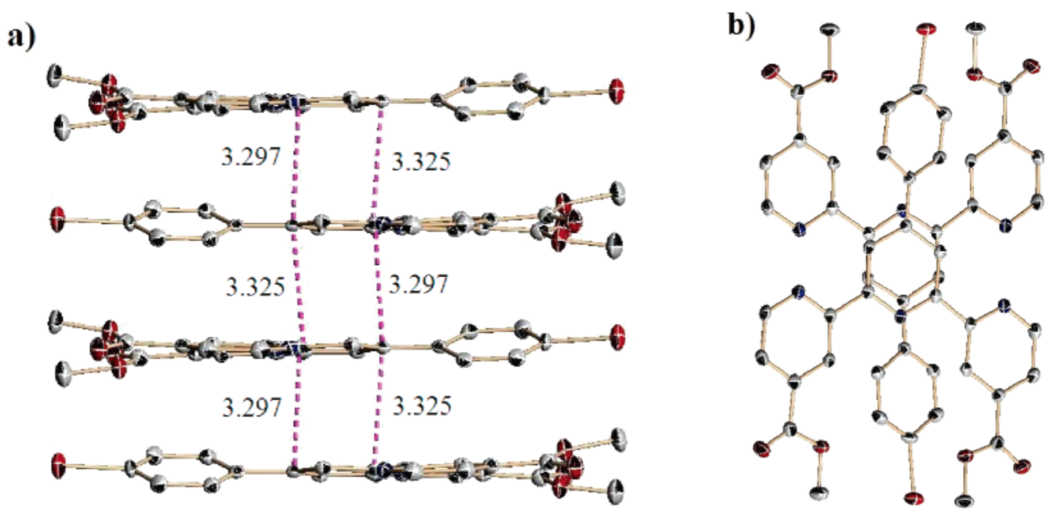

FIGURE 3. **(a)** Stacking of diester **5a** in the crystal lattice with the distances (Å) between the central pyridine rings and **(b)** the orientation of diester **5a** in adjacent planes in the lattice, viewing along the *c* axis. Hydrogen atoms are omitted for clarity.

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[53] (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.[52]

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[26] 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_2 (4.68 g, 18.5 mmol) in pyridine (27 mL) under N_2 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 $CHCl_3$ (2 × 25 mL) and Et_2O (2 × 25 mL) to give the product **3b** as green crystals: 5.5 g (85%); mp 226−227 °C; ^{1}H NMR (DMSO-d_6) δ 6.58 (s, 2H, COC*H*$_2$), 8.32 (m, 3H, 5-pyr*H*, 3,5-Ar*H*), 8.45 (s, 1H, 3-pyr*H*), 8.78 (t, 1H, 4-Ar*H*, J = 7.8 Hz), 9.07 (d, 2H, 2,6-Ar*H*, J = 6.6 Hz), 9.12 (d, 1H, 6-pyr*H*, J = 4.8 Hz); ^{13}C NMR (DMSO-d_6) δ 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]$^+$ calcd for $C_{13}H_{10}N_3O$, 224.0824; found, 224.0836.

1-(3-Oxo-3-[2-(4-methoxycarbonylpyridyl)]propen-1-yl)-4-bromobenzene (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_2O_3 (9.94 g) was added. The mixture was then irradiated in the microwave at 250 W for 15 min. After cooling, $CHCl_3$ (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; ^{1}H NMR δ 4.01 (s, 3H, pyrCO$_2$C*H*$_3$), 7.57 (d, 2H, 3,5-Ar*H*, J = 8.7 Hz), 7.58 (d, 2H, 2,6-Ar*H*, J = 8.4 Hz), 7.92 (d, 1H, COCH═C*H*, J = 16.2 Hz), 8.05 (dd, 1H, 5-pyr*H*, J_1 = 4.8 Hz, J_2 = 1.8 Hz), 8.25 (d, 1H, COC*H*═CH, J = 15.9 Hz), 8.7 (s, 1H, 3-pyr*H*), 8.88 (dd, 1H, 6-pyr*H*, J_1 = 4.8 Hz, J_2 = 0.9 Hz); ^{13}C NMR δ 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]$^+$ calcd for $C_{16}H_{12}BrNO_3Na$, 367.9898; found, 367.9899.

1-(3-Oxo-3-[2-(4-cyanopyridyl)]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_2O_3 (15 g). The mixture was then irradiated in the microwave at 250 W for 15 min. After cooling, $CHCl_3$ (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 **4b** as a light yellow solid: 1.92 g (56%); mp 184−185 °C; ^{1}H NMR δ 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═C*H*, J = 16.2 Hz), 8.19 (d, 1H, COC*H*═CH, J = 15.9 Hz), 8.39 (s, 1H, 3-pyr*H*), 8.91 (dd, 1H, 6-pyr*H*, J_1 = 5.1 Hz, J_2 = 0.9 Hz); ^{13}C NMR δ 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_2O (15 mL). The precipitate was dissolved in CH_2Cl_2 (150 mL) and extracted with H_2O (2 × 100 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated in vacuo to give the product **4c** as a light yellow solid: 1 g (60%); mp 123−125 °C; ^{1}H NMR δ 2.47 (s, 3H, pyrC*H*$_3$), 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-Ar*H*, J = 8.4 Hz), 7.88 (d, 1H, COCH═C*H*, 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); ^{13}C NMR δ 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_4OAc, 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_2O_3), eluting with $CHCl_3$, 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_4OAc, and the mixture was refluxed overnight. The solution was concentrated in vacuo to give a paste, which was neutralized with Na_2CO_3 (1 M) and extracted with $CHCl_3$. Organic layers were combined and dried ($MgSO_4$), and then the solvent was evaporated in vacuo to give a residue that was column chromatographed (basic Al_2O_3), 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_4OAc (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; ^{1}H NMR δ 4.06 (s, 6H, pyrCO$_2$C*H*$_3$), 7.67 (d, 2H, 3,5-Ar*H*, J = 8.4 Hz), 7.76 (d, 2H, 2,6-Ar*H*, J = 8.7 Hz), 7.93 (dd, 2H, 5,5″-pyr*H*, J_1 = 4.8 Hz, J_2 = 1.5 Hz), 8.73 (s, 2H, 3,3″-pyr*H*), 8.87 (d, 2H, 6,6″-pyr*H*, J = 4.8 Hz), 9.18 (s, 2H, 3′,5′-pyr*H*); ^{13}C NMR δ 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_4OAc (3.47 g). Then, via route A, the product, **5e**, was isolated as a white solid: 240 mg (38%); mp 253−254 °C; ^{1}H NMR δ 4.08 (s, 3H, pyrCO_2CH_3), 7.61 (dd, 1H, 5″-pyr*H*, $J_1 = 3.3$ Hz, $J_2 = 1.5$ Hz), 7.68 (d, 2H, 3,5-Ar*H*, $J = 8.7$ Hz), 7.75 (d, 2H, 2,6-Ar*H*, $J = 8.7$ Hz), 7.95 (dd, 1H, 5-pyr*H*, $J_1 = 3.3$ Hz, $J_2 = 1.8$ Hz), 8.74 (d, 1H, 5′-pyr*H*, $J = 1.8$ Hz), 8.78 (d, 1H, 3′-pyr*H*, $J = 1.8$ Hz), 8.9 (m, 3H, 6,6″,3″-pyr*H*), 9.08 (dd, 1H, 3-pyr*H*, $J_1 = 0.9$ Hz, $J_2 = 0.6$ Hz); ^{13}C NMR δ 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): $[M + Na]^+$ calcd for $C_{24}H_{15}BrN_4O_2Na$, 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_4OAc (4.41 g). Then, via route A, the product, **5g**, was isolated as a white solid: 250 mg (37%); mp 173−174 °C; ^{1}H NMR δ 4.04 (s, 3H, pyrCO_2CH_3), 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*); ^{13}C NMR δ 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): $[M + Na]^+$ calcd for $C_{23}H_{16}BrN_3O_2Na$, 468.0323; found, 468.0331.

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Supporting Information Available: ^{1}H, ^{13}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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