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Synthesis of 2,4,6-Trisubstituted Pyridines by Oxidative Eosin Y Photoredox Catalysis

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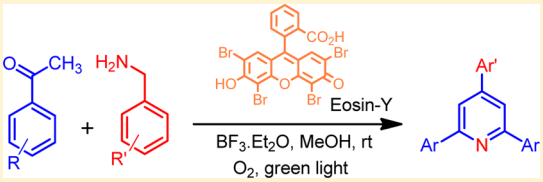
Supporting Information

ABSTRACT: Eosin Y, an organic dye, was activated as a photoredox catalyst in the presence of molecular oxygen using visible light and, when it was used in the reaction of aryl ketones and benzyl amines, afforded good yields (52−87%) of 2,4,6-triarylpyridines (21 examples) at ambient temperature. The aryl groups at the 2- and 6-positions are derived from ketones, while benzyl amine plays the dual role of providing an aryl functionality at the 4-position of pyridine as well as being a nitrogen donor.

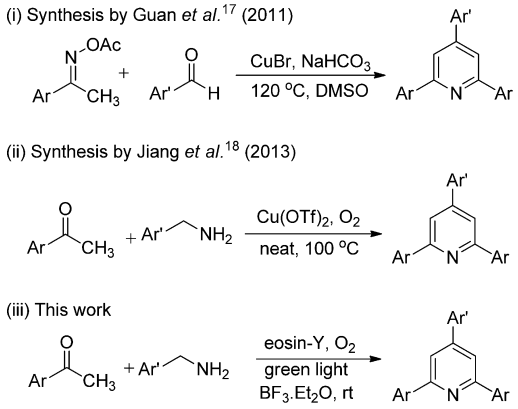


INTRODUCTION

Redox-active organic dyes such as eosin Y, rose bengal, fluorescein, xanthenes, and riboflavin, with strong absorption in the visible part of the spectrum, have been widely used in photochemical organic transformations.[1] These organic photoredox catalysts are less toxic and cheaper in comparison to organometallic and inorganic catalysts.[2] Among these, eosin Y has found wide utility in cell staining, as a pH indicator,[3] and in continuous-flow technology.[4] In addition, synthetic applications of eosin Y involve the formation of reactive intermediates such as aryl radicals, α-carbonyl radicals, iminium ions, trifluoromethyl radicals, and enone radicals in organic transformations as well as in decarboxylation and cycloaddition reactions.[5,6] Our group has demonstrated the use of eosin Y for (a) the formation of C−C and C−P bonds by activation of tetrahydroisoquinoline,[7] (b) enantioselective transformations in combination with organocatalysts,[7c,d] and (c) the synthesis of substituted aromatic heterocycles by intermolecular C−H arylation.[7a,b] As part of our continuing efforts in this area, we herewith report the use of eosin Y−O_2 as a photoredox catalyst, in combination with $BF_3{\cdot}Et_2O$, in the reactions of aryl ketones and benzyl amines to give 2,4,6-triarylpyridines.

Functionalized 2,4,6-triarylpyridines (Krohnke pyridine)[8] have been extensively exploited as chemosensors,[9] as catalysts,[10] as photosensitizers,[11] and as intermediates in the synthesis of therapeutic drugs, insecticides, herbicides, and surfactants.[12] Classic methods[13] for the synthesis of 2,4,6-triarylpyridines include (a) a modified multicomponent Chichibabin pyiridine reaction employing an aldehyde, an enolizable ketone, and an ammonium salt as a nitrogen source using various catalysts at higher temperature,[14] (b) condensation of keto-oximes with aryl aldehydes[15a] or oxiranes[15b] at high temperature, and (c) reaction of amino allenes with aldehydes followed by palladium-catalyzed cyclization.[16] Guan and coworkers reported a copper-mediated coupling of aryl aldehydes with aromatic keto-oxime acetates (Scheme 1, eq 1)[17] for the synthesis of 2,4,6-triarylpyridines. Recently, Jiang and coworkers have reported the copper-catalyzed oxidative cleavage of C−N bonds of benzyl amines that couple with aromatic ketones, giving triarylpyridines at elevated temperature (Scheme 1, eq 2).[18] Our results for the synthesis of 2,4,6-triarylpyridines from aromatic ketones and benzyl amines using eosin Y−O_2 in the presence of visible light are reported herein.

Scheme 1. Synthesis of 2,4,6-Triarylpyridines



RESULTS AND DISCUSSION

Initially, a reaction mixture of acetophenone **1a** (1.0 mmol), benzyl amine **2a** (3.0 mmol), and eosin Y (5 mol %) in the presence of $BF_3{\cdot}Et_2O$ (0.2 mmol) and molecular oxygen in

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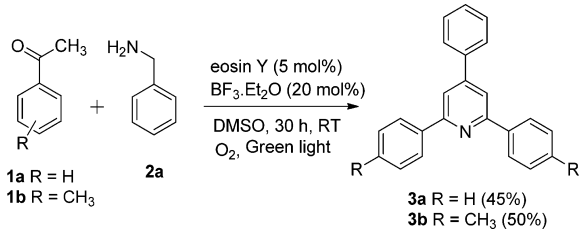
DMSO was irradiated with green LEDs (530 nm) for 30 h at room temperature. Purification of the crude product gave the symmetrically substituted 2,4,6-triphenylpyridine (**3a**) in 45% yield (Scheme 2).

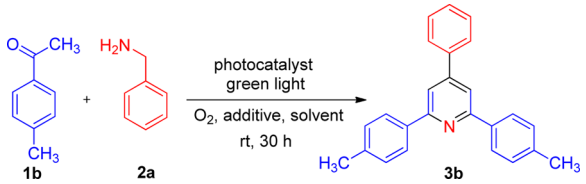
Scheme 2. Synthesis of 2,4,6-Triphenylpyridine



To identify which aryl group is derived from which substrate, we performed the same reaction using 1-(*p*-tolyl)ethanone (1.0 equiv) and benzyl amine (3.0 equiv), yielding 2,4,6-triarylpyridine **3b** in 50% yield, wherein the *p*-methyl phenyl group of the aryl ketone was found to be at the 2- and 6-positions and the phenyl group of benzyl amine was found to be at the 4-position of the pyridine. The benzyl amine played the dual role of phenyl group as well as nitrogen atom donor in the pyridine ring.

Next, the reaction conditions were optimized by variation of the photocatalyst, additives, and solvent to increase the product yield. The results are summarized in Table 1. Reactions of equal amounts of (*p*-methylphenyl)ethanone (1.0 equiv) and benzyl amine (1.0 equiv) as well as reactions of (*p*-methylphenyl)-ethanone (2.0 equiv) and benzylamine (1.0 equiv) afforded low product yields (<20%; Table 1, entries 1 and 2). Therefore, we maintained a 1:3 ratio of aryl ketone and benzyl amine. Other photocatalysts, such as rose bengal (with green light) or the metal complex $Ru(bpy)_3{\cdot}6H_2O$ (with blue light), under identical conditions, afforded **3b** in 30% and 12% yields, respectively (entries 3 and 4). The use of Brønsted acids such as *p*-TSA and acetic acid gave **3b** in 22% and 40% yields, respectively (entries 5 and 6). The use of iodine (2.0 mol %) as an additive afforded a complex product mixture (entry 7). Decreasing the mol % of $BF_3{\cdot}Et_2O$ to 10% in DMSO reduced the yield of the product (entry 9). An increase in the molar ratio of $BF_3{\cdot}Et_2O$ to 50 mol % gave **3b** in 79% yield (entry 10). The use of acetonitrile (entry 11, 60%), DMF (entry 12, 50%), and dichloromethane (entry 13, 48%) as solvents gave lower yields. Better results were obtained using $BF_3{\cdot}Et_2O$ (50 mol %) in MeOH, providing **3b** in 87% yield (entry 14).

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	additive (amt (%))	solvent	yield (%)[b]
1[c]	eosin Y	$BF_3{\cdot}Et_2O$ (20%)	DMSO	<20
2[d]	eosin Y	$BF_3{\cdot}Et_2O$ (20%)	DMSO	<20
3	rose bengal	$BF_3{\cdot}Et_2O$ (20%)	DMSO	30
4	$Ru(bpy)_3{\cdot}6H_2O$	$BF_3{\cdot}Et_2O$ (20%)	DMSO	12
5	eosin Y	*p*-TSA (20%)	DMSO	22
6	eosin Y	AcOH (20%)	DMSO	40
7	eosin Y	iodine (20%)	DMSO	0
8[e]	eosin Y	$BF_3{\cdot}Et_2O$ (20%)	DMSO	50
9	eosin Y	$BF_3{\cdot}Et_2O$ (10%)	DMSO	32
10	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	DMSO	79
11	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	CH_3CN	60
12	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	DMF	50
13	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	DCM	48
14	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	MeOH	87
15	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	neat	40
16	eosin Y	none	MeOH	trace
17	no catalyst	$BF_3{\cdot}Et_2O$ (50%)	MeOH	trace
18	eosin Y	$BF_3{\cdot}Et_2O$ (50%)	MeOH	trace

[a]Conditions unless specified otherwise: aryl ketone **1b** (1.0 mmol), benzyl amine **2a** (3.0 mmol), catalyst (5 mol %), additive, solvent, O_2, green light, 30 °C, 30–40 h. [b]Isolated yields. [c]Aryl ketone **1b** (1.0 mmol), benzyl amine **2a** (1.0 mmol), [d]Aryl ketone **1b** (1.0 mmol), benzyl amine **2a** (2.0 mmol), [e]2 mol % catalyst was used.

With the optimized conditions, the scope of the reaction was studied for the synthesis of substituted 2,4,6-triarylpyridines (Scheme 3). The reaction of (*p*-methoxyphenyl)ethanone (1.0 equiv) with benzyl amine (3.0 equiv), under the optimized conditions, gave the corresponding 2,4,6-triarylpyridine **3c** in 72% yield. Reactions of electron-withdrawing substituted acetophenones such as (*p*-fluorophenyl)-, (*p*-chlorophenyl)-, and (*p*-bromophenyl)ethanones and benzyl amine afforded good yields of products **3d** (68%), **3e** (68%), and **3f** (64%). However, (*p*-nitrophenyl)ethanone was found to be unreactive under the reaction conditions. The effect of an electron-donating ortho group was demonstrated by using sterically hindered (*o*-methoxyphenyl)ethanone as a substrate, which also provided **3m** in 66% yield.

Next, we studied the effect of substituents on the benzyl amine. Thus, the reaction of 4-methoxybenzyl amine with (*p*-chlorophenyl)-, (*p*-fluorophenyl)-, (*p*-methylphenyl)-, and (*p*-methoxyphenyl)ethanone, under the optimized reaction conditions, gave the corresponding 2,4,6-triarylpyridines **3h,i** in good yields (62–80%). The reaction of 4-methoxybenzyl amine with 1-(naphthalen-2-yl)ethanone gave **3o** in 60% yield, and the reaction of 3,4-dichlorobenzyl amine and 4-fluorobenzyl amine with 1-(*p*-tolyl)ethanone provided the corresponding products **3p,q** in 76 and 72% yields, respectively. The scope of the reaction was further studied with aliphatic as well as cyclic ketones. Thus, the reaction of pentan-2-one with benzyl amine afforded product **3t** in 54% yield, while the reaction with cyclohexanone led to a complex mixture of products. Further, the reaction was also studied with a secondary amine, namely dibenzylamine. Thus, the reaction of dibenzylamine (3 equiv) with *p*-methylacetophenone (1 equiv) under the standard conditions gave **3b** in 49% yield. Treatment of 3-picolylamine with (*p*-methylphenyl)ethanone gave the desired product **3r** in 61% yield. Interestingly, when 2-picolyl amine was employed with 1-(*p*-tolyl)ethanone, the desired product **3s** was obtained in 22% yield with deamination cross -coupled product **4** (48%).[18] The formation of product **4** was noticed only in the case of 2-picolyl amine. A possible mechanism is shown in Scheme 4. We believe that, under the reaction conditions, complexation of $BF_3{\cdot}Et_2O$ with acetophenone gives alkenyloxy boron complex **A** with the formation of HF, which reacts with 2-picolyl amine to give ammonium ion species **B**. Further complexation of **A** and **B** leads to the formation of intermediate **C**, which undergoes intramolecular displacement of ammonium ion to give product **4**.

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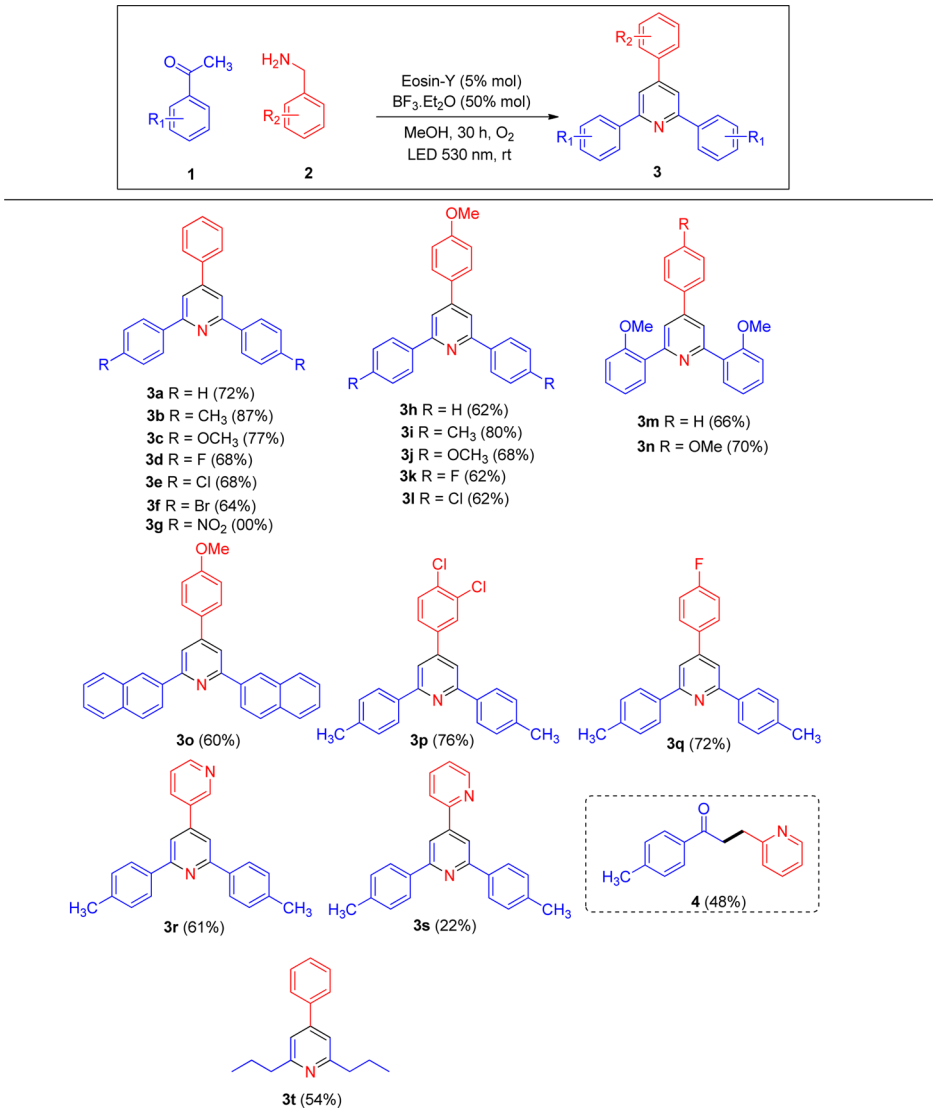
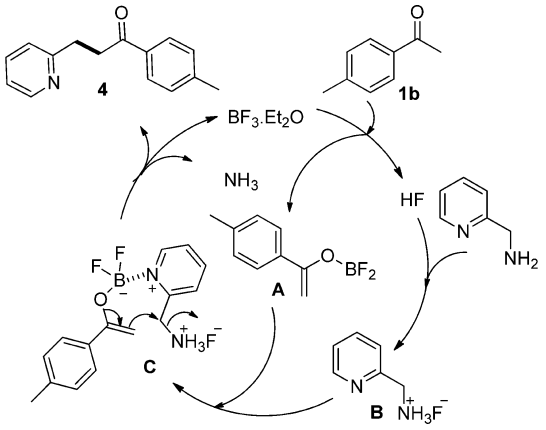
Scheme 3. Substrate Scope for the Synthesis of 2,4,6-Trisubstituted Pyridine



Scheme 4. Plausible Mechanism for Cross-Coupled Product 4



In support of the mechanistic hypothesis, a few control experiments were performed. Thus, the reaction of acetophenone (1.0 equiv) and benzyl amine (3.0 equiv) in the absence of (a) $BF_3{\cdot}Et_2O$ (Table 1, entry 16), (b) eosin Y (entry 17), (c) LED light (entry 18), or (d) molecular oxygen (reaction mixture was purged with and kept under an N_2 atmosphere) failed to give 2,4,6-triarylpyridine. In order to validate the intermediacy of benzaldehyde, as reported by Jiang and co-workers,[18] we performed the reaction of acetophenone (1.0 equiv) and benzyl amine (1.0 equiv) in the presence of *p*-methyl benzaldehyde (1.0 equiv) under the optimized reaction conditions as reported for **3a**. This reaction failed to give either **3a** or **3ab** (Scheme 5, eq a). Increasing the molar ratio of benzylamine (3.0 equiv) gave **3a** in 35% yield, while no trace amount of triarylpyridine **3ab** was detected by LC-MS-MS.[19] This experiment excludes the formation of benzaldehyde in the present protocol by using eosin Y as photoredox catalyst. Next, we explored imine **5** as a possible intermediate.[18] Thus, reaction of acetophenone (1.0 equiv) with imine **5** (2.0 equiv), separately prepared and isolated from benzyl amine and O_2 at 100 °C in DMSO,[20] gave **3a** in 43% yield (Scheme 5, eq b) under the optimized reaction conditions. This indicates imine **5** to be a likely intermediate in the formation of triarylpyridine. The same reaction in the absence of eosin Y failed to give **3a**. To confirm the formation of imine **5** in the reaction, the benzyl amine was irradiated under green light in the presence of eosin

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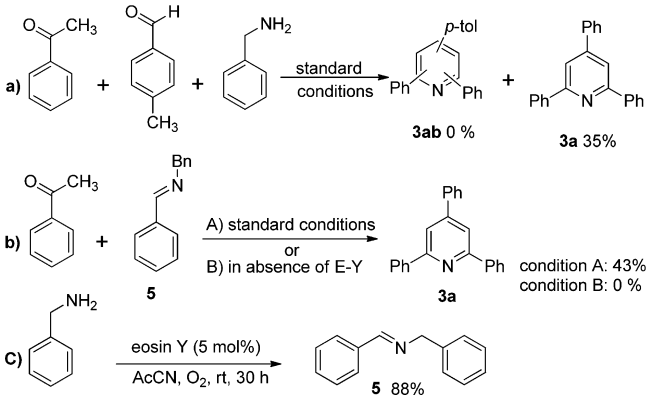
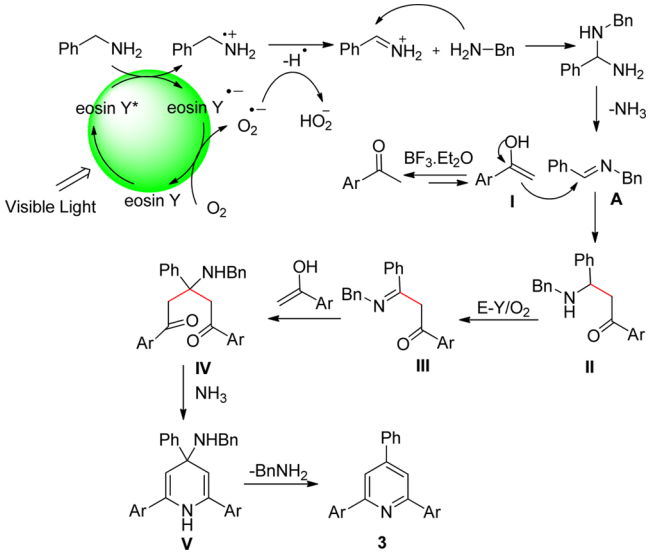
Scheme 5. Control Experiments



Y and O_2 in dry acetonitrile, which afforded imine **5** (^{1}H and ^{13}C NMR and HRMS data are given in the Supporting Information) in quantitative yield (Scheme 5, eq c).

On the basis of these observations, we propose the following plausible mechanism for the formation of triarylpyridines (Scheme 6). Under the reaction conditions, the photocatalytic

Scheme 6. Plausible Reaction Mechanism



oxidative coupling of benzyl amine is induced by eosin Y, generating the iminium ion intermediate **A** and ammonia.[21] Subsequently the addition of enol **I**, facilitated by $BF_3{\cdot}Et_2O$ as an additive, to the iminium ion **A** results in the formation of **II**, which upon photocatalytic oxidation gives **III**. A second addition of enol **I** to **III** leads to the formation of **IV**. The condensation of **IV** with ammonia gives **V**, which on aromatization provides triarylpyridine **3**.

In conclusion, we have demonstrated the use of eosin Y–O_2 as a photoredox catalyst in combination with aryl ketones and benzyl amines, using visible light for the synthesis of triarylpyridines. We presume that the role of $BF_3{\cdot}Et_2O$ is to catalyze the formation of imine and enamine intermediates and the addition–elimination sequence. The reaction proceeds at ambient temperature in high yields and has a wide scope in substituted 2,4,6-triarylpyridines, as the aryl groups at the 2- and 4-positions are derived from the aryl ketones and the aryl functionality at the 4-position is provided by the benzyl amines, in addition to its role as a nitrogen atom donor. The method is a mild, eco-friendly, and reliable alternative to the established procedures for the selective synthesis of triarylpyridines. Further applications of eosin Y as a photoredox catalyst in the synthesis of heteroaromatic compounds are in progress.

EXPERIMENTAL SECTION

General Methods. ^{1}H and ^{13}C NMR spectra were recorded using a 500 MHz NMR spectrometer. The chemical shifts are expressed in δ with reference to TMS as the internal standard. High-resolution mass spectra were obtained with a HRMS TOF mass spectrometer (ESI). Melting points were recorded with a Thomas-Hoover capillary melting point apparatus. TLC was performed using commercially available 100–400 mesh silica gel plates (GF254). Eosin Y (spirit soluble, 99% dye content) was purchased from Sigma-Aldrich. The green light irradiation was performed using high-power LEDs (3 W, λ 530 ± 10 nm).

General Procedure for the Synthesis of 2,4,6-Trisubstituted Pyridines. In a round-bottom flask (10 mL) equipped with a magnetic stirring bar, eosin Y (5 mol %), aromatic ketone **1** (1 equiv), and benzylamine **2** (3 equiv) were dissolved in MeOH (2 mL) and $BF_3{\cdot}Et_2O$ (50 mol %). The round-bottom flask was evacuated and then refilled with oxygen using an oxygen balloon. The reaction mixture was irradiated using 530 nm LEDs at room temperature for 30 h. After completion of the reaction, the methanol was removed under vacuum and the residue was purified by flash column chromatography using ethyl acetate and petroleum ether as eluents to afford pure product **3**.

*2,4,6-Triphenylpyridine (**3a**).*[18] In 72% yield (184 mg), white solid (mp 136–137 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 7.1 Hz, 4H), 7.91 (s, 2H), 7.77 (d, J = 7.0 Hz, 2H), 7.57–7.43 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 150.3, 139.5, 139.0, 129.1, 129.1, 129.0, 128.7, 127.2, 127.2, 117.2; HRMS (ESI) calcd $C_{23}H_{18}N$ $[M + H]^+$ 308.1434, found 308.1438.

*4-Phenyl-2,6-di-p-tolylpyridine (**3b**).*[18] In 87% yield (217 mg), white solid (mp 158–159 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 7.9 Hz, 4H), 7.79 (s, 2H), 7.68 (d, J = 7.8 Hz, 2H), 7.49–7.38 (m, 3H), 7.28 (d, J = 7.9 Hz, 4H), 2.39 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 149.9, 139.2, 138.9, 136.8, 129.3, 129.0, 128.8, 127.1, 126.9, 116.4, 21.3; HRMS (ESI) calcd $C_{25}H_{22}N$ $[M + H]^+$ 336.1747, found 336.1753.

*2,6-Bis(4-methoxyphenyl)-4-phenylpyridine (**3c**).*[18] In 77% yield (188 mg), white solid (mp 98–99 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.7 Hz, 4H), 7.79 (s, 2H), 7.75 (d, J = 7.2 Hz, 2H), 7.56–7.45 (m, 3H), 7.06 (d, J = 8.7 Hz, 4H), 3.89 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 156.9, 149.9, 139.3, 132.3, 129.0, 128.8, 128.3, 127.1, 115.6, 114.0, 55.3; HRMS (ESI) calcd $C_{25}H_{21}NNaO_2$ $[M + Na]^+$ 390.1470, found 390.1467.

*2,6-Bis(4-fluorophenyl)-4-phenylpyridine (**3d**).*[18] In 68% yield (168 mg), white solid (mp 100–101 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, J = 8.2, 5.6 Hz, 4H), 7.82 (s, 2H), 7.73 (d, J = 7.6 Hz, 2H), 7.58–7.46 (m, 3H), 7.20 (t, J = 8.5 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6 (d, J $C-F$ = 248.6 Hz), 156.4, 150.4, 138.8, 135.5, 129.1, 129.1, 128.9, 127.1, 116.7, 115.5; HRMS (ESI) calcd $C_{23}H_{16}F_2N$ $[M + H]^+$ 344.1245, found 344.1252.

*2,6-Bis(4-chlorophenyl)-4-phenylpyridine (**3e**).*[18] In 68% yield (165 mg), white solid (mp 183–184 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 7.9 Hz, 4H), 7.85 (s, 2H), 7.72 (d, J = 7.7 Hz, 2H), 7.57–7.46 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 150.6, 138.6, 137.7, 135.3, 129.2, 129.1, 128.9, 128.3, 127.1, 117.1; HRMS (ESI) calcd $C_{23}H_{16}Cl_2N$ $[M + H]^+$ 376.0654, found 376.0658.

*2,6-Bis(4-bromophenyl)-4-phenylpyridine (**3f**).*[13d] In 64% yield (149 mg), white solid (mp 195–197 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.6 Hz, 4H), 7.89 (s, 2H), 7.75 (d, J = 7.0 Hz, 2H), 7.67 (d, J = 8.6 Hz, 4H), 7.58–7.50 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 150.6, 138.6, 138.2, 131.9, 129.2, 129.2, 128.6, 127.1, 123.6, 117.1; HRMS (ESI) calcd $C_{23}H_{16}Br_2N$ $[M + H]^+$ 463.9644, found 463.9645.

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*4-(4-Methoxyphenyl)-2,6-diphenylpyridine (**3h**).*[15a] In 62% yield (173 mg), white solid (mp 100−101 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 7.2 Hz, 4H), 7.88 (s, 2H), 7.72 (d, J = 8.8 Hz, 2H), 7.58−7.46 (m, 6H), 7.07 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 157.3, 149.5, 139.6, 131.1, 128.9, 128.6, 128.2, 127.1, 116.5, 114.4, 55.3; HRMS (ESI) calcd $C_{24}H_{20}NO$ $[M + H]^+$ 338.1539, found 338.1544.

*2,6-Bis(4-methylphenyl)-4-(4-methoxyphenyl)pyridine (**3i**).*[18] In 80% yield (217 mg), white solid (mp 156−157 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.1 Hz, 4H), 7.83 (s, 2H), 7.73 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 8.1 Hz, 4H), 7.07 (d, J = 8.8 Hz, 2H), 3.91 (s, 3H), 2.46 (s, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 157.3, 149.4, 138.8, 137.0, 131.5, 129.3, 128.3, 126.9, 116.04, 114.4, 55.4, 21.3; HRMS (ESI) calcd $C_{26}H_{24}NO$ $[M + H]^+$ 366.1852, found 366.1855.

*2,6-Bis(4-methoxyphenyl)-4-(4-methoxyphenyl)pyridine (**3j**).*[15a] In 68% yield (179 mg), white solid (mp 133−134 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 4H), 7.76 (s, 2H), 7.72 (d, J = 8.7 Hz, 2H), 7.12−7.01 (m, 6H), 3.91 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 160.3, 156.9, 149.4, 132.4, 131.6, 128.3, 128.3, 115.2, 114.4, 114.0, 55.4, 55.3; HRMS (ESI) calcd $C_{26}H_{24}NO_3$ $[M + H]^+$ 398.1751, found 398.1759.

*2,6-Bis(4-fluorophenyl)-4-(4-methoxyphenyl)pyridine (**3k**).* In 62% yield (167 mg), white solid (mp 124−125 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, J = 8.8, 5.4 Hz, 4H), 7.82 (s, 2H), 7.72 (d, J = 8.7 Hz, 2H), 7.22 (t, J = 8.7 Hz, 4H), 7.08 (d, J = 8.7 Hz, 2H), 3.92 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6 (d, J_{C-F} = 248.4 Hz), 160.5, 156.4, 149.9, 135.7, 135.7, 131.0, 128.9, 128.8, 128.3, 116.20, 115.6, 115.5, 114.5, 55.4; HRMS (ESI) calcd $C_{24}H_{18}F_2NO$ $[M + H]^+$ 374.1351, found 374.1360.

*2,6-Bis(4-chlorophenyl)-4-(4-methoxyphenyl)pyridine (**3l**).* In 62% yield (162 mg), white solid (mp 180−181 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 8.6 Hz, 4H), 7.84 (s,2H), 7.71 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.6 Hz, 4H), 7.08 (d, J = 8.8 Hz, 2H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 156.3, 150.0, 137.9, 135.2, 130.8, 128.9, 128.3, 128.3, 116.5, 114.6, 55.4; HRMS (ESI) calcd $C_{24}H_{18}Cl_2NO$ $[M + H]^+$ 406.0760, found 406.0766.

*2,6-Bis(2-methoxyphenyl)-4-phenylpyridine (**3m**).*[18] In 66% yield (161 mg), white solid (mp 153−154 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 2H), 8.02 (d, J = 7.6 Hz, 2H), 7.78 (d, J = 7.3 Hz, 2H), 7.58−7.37 (m, 5H), 7.15 (t, J = 7.4 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 3.92 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 155.9, 147.6, 139.4, 131.5, 129.7, 129.6, 128.9, 128.5, 127.3, 121.3, 121.0, 111.4, 55.7; HRMS (ESI) calcd $C_{25}H_{21}NNaO_2$ $[M + Na]^+$ 390.1470, found 390.1464.

*2,6-Bis(2-methoxyphenyl)-4-(4-methoxyphenyl)pyridine (**3n**).* In 62% yield (164 mg), white solid (mp 183−184 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.7, 2.0 Hz, 4H), 7.72 (dd, J = 6.8, 1.9 Hz, 2H), 7.50−7.35 (m, 2H), 7.14 (t, J = 7.0 Hz, 2H), 7.06 (d, J = 8.3 Hz, 4H), 3.93 (s, 6H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 157.1, 155.9, 147.1, 131.7, 131.5, 129.7, 129.6, 128.4, 121.0, 120.9, 114.3, 111.4, 55.7, 55.3; HRMS (ESI) calcd $C_{26}H_{24}NO_3$ $[M + H]^+$ 398.1751, found 398.1755.

*2,6-Bis(naphthalen-2-yl)-4-(4-methoxyphenyl)pyridine (**3o**).* In 60% yield (154 mg), white solid (mp 157−158 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36−8.26 (m, 2H), 7.95 (d, J = 7.5 Hz, 4H), 7.86 (s, 2H), 7.81 (d, J = 7.0 Hz, 2H), 7.77 (d, J = 8.7 Hz, 2H).7.67−7.58 (m, 2H), 7.54 (dd, J = 6.2, 3.3 Hz, 4H), 7.06 (d, J = 8.7 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 159.5, 148.5, 138.9, 133.99, 131.4, 130.5, 128.8, 128.4, 128.4, 127.6, 126.4, 125.8, 125.8, 125.4, 120.9, 114.6, 55.4; HRMS (ESI) calcd $C_{32}H_{24}NO$ $[M + H]^+$ 438.1852, found 438.1856.

*2,6-Bis(4-methylphenyl)-4-(3,4-dichlorophenyl)pyridine (**3p**).* In 76% yield (228 mg), white solid (mp 185−186 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.2 Hz, 4H), 7.84 (d, J = 2.0 Hz, 1H), 7.78 (s, 2H), 7.59 (dt, J = 8.3, 5.2 Hz, 2H), 7.35 (d, J = 7.9 Hz, 4H), 2.47 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 147.5, 139.2, 139.2, 136.4, 133.3, 133.1, 131.0, 129.4, 129.0, 126.9, 126.4, 116.0, 21.3; HRMS (ESI) calcd $C_{25}H_{20}Cl_2N$ $[M + H]^+$ 404.0973, found 404.0971.

*2,6-Bis(4-methylphenyl)-4-(4-fluorophenyl)pyridine (**3q**).* In 72% yield (189 mg), white solid (mp 173−174 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.2 Hz, 4H), 7.81 (s, 2H), 7.79−7.69 (m, 2H), 7.35 (d, J = 7.9 Hz, 4H), 7.24 (t, J = 8.7 Hz, 2H), 2.47 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 162.3, 157.4, 148.9, 139.0, 136.7, 135.3, 135.3, 129.4, 128.9, 128.8, 126.99, 116.3, 116.1, 115.9, 21.3; HRMS (ESI) calcd $C_{25}H_{20}FN$ $[M + H]^+$ 354.1658, found 354.1663.

*2,6-Bis(4-methylphenyl)-3,4-bipyridine (**3r**).* In 61% yield (152 mg), yellow solid, (mp 145−146 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.74 (d, J = 4.1 Hz, 1H), 8.13 (d, J = 7.5 Hz, 4H), 8.05 (d, J = 7.7 Hz, 1H), 7.84 (s, 2H), 7.56−7.44 (m, 1H), 7.35 (d, J = 7.6 Hz, 4H), 2.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 149.9, 148.3, 146.8, 139.3, 136.5, 134.9, 134.5, 129.5, 127.0, 123.8, 116.2, 21.3; HRMS (ESI) calcd $C_{24}H_{21}N_2$ $[M + H]^+$ 337.1705, found 337.1703.

*2,6-Bis(4-methylphenyl)-2,4-bipyridine (**3s**).* In 22% yield (55 mg), yellow solid (mp 138−139 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (ddd, J = 4.8, 1.7, 0.9 Hz, 1H), 8.27 (s, 2H), 8.18 (d, J = 8.2 Hz, 4H), 7.99−7.90 (m, 1H), 7.88 (td, J = 7.7, 1.8 Hz, 1H), 7.39 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H), 7.35 (d, J = 7.9 Hz, 4H), 2.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 155.5, 150.0, 147.9, 139.01, 137.0, 136.8, 129.8, 129.5, 129.4, 129.1, 127.0, 126.9, 125.9, 123.6, 121.1, 115.7, 21.3; HRMS (ESI) calcd $C_{24}H_{21}N_2$ $[M + H]^+$ 337.1698, found 337.1699.

*2,6-Bis(propyl)-4-phenylpyridine (**3t**).* In 54% yield (151 mg), yellowish thick liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, J = 5.2, 3.3 Hz, 2H), 7.52−7.41 (m, 4H), 7.20 (s, 2H), 2.85−2.80 (t, J = 7.7 Hz, 4H), 1.87−1.72 (m, 4H), 1.02 (t, J = 7.4 Hz, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 148.8, 139.1, 128.9, 128.6, 127.1, 118.0, 40.6, 23.5, 13.9; HRMS (ESI) calcd $C_{17}H_{21}NNa$ $[M + Na]^+$ 262.1572, found 262.1571.

*1-(4-Methylphenyl)-3-(pyridin-2-yl)propan-1-one (**4**).*[18] In 48% yield (81 mg), yellowish thick liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66−8.42 (m, 1H), 7.91 (d, J = 8.2 Hz, 2H), 7.61 (td, J = 7.7, 1.8 Hz, 1H), 7.27 (dd, J = 12.2, 5.5 Hz, 3H), 7.13 (dd, J = 7.0, 5.4 Hz, 1H), 3.50 (t, J = 7.3 Hz, 2H), 3.25 (t, J = 7.3 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.9, 160.8, 149.2, 143.8, 136.4, 134.4, 129.2, 128.2, 123.4, 121.2, 37.7, 32.1, 21.6; HRMS (ESI) calcd $C_{15}H_{16}NO$ $[M + H]^+$ 226.1232, found 226.1231.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00979.

Characterization of products, ^{1}H and ^{13}C NMR spectra, and HRMS data (PDF)

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Notes

The authors declare no competing financial interest.

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