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A Convenient Synthesis of 2-(Alkylamino)pyridines

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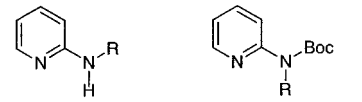
Abstract: The synthesis of a series of 2-(alkylamino)-pyridines (**1**) in three steps from 2-aminopyridine (**4**) is reported. The products were obtained in 67−91% overall yield from **4**.

The asymmetric reduction of prochiral ketones by a complex formed from lithium aluminum hydride, (1*R*,2*S*)-(−)-*N*-methylephedrine, and 2-(ethylamino)pyridine (**1a**, Chart 1) is a useful method for the synthesis of optically pure secondary alcohols.[1,2] In the course of other investigations, we had the need to carry out this reduction on large scale and thus required significant quantities of **1a**.

When choosing among the methods reported for the preparation of **1a**,[1,3,4] it appeared to us that the most straightforward route would be the one illustrated in Scheme 1, which uses inexpensive 2-aminopyridine (**4**) as the starting material.[1] Thus, **4** was treated with acetic anhydride and formic acid[5] to provide the *N*-formyl derivative **5** in 73% yield.[6] This product was then alkylated by reaction with sodium hydride and ethyl iodide affording **6** (85%). Deformylation of **6** by acid hydrolysis gave **1a** in 90% yield. Although the product could be obtained by this route, the modest yield of the formylation step, and its problematic purification by distillation (the distillate often solidified in the condenser), led us to explore an alternate route to **1a**. We report here that substitution of **5** with the readily available *N*-Boc-protected 2-aminopyridine derivative **2** allows for the efficient preparation of **1a** and other 2-(alkylamino)pyridines in high overall yield.

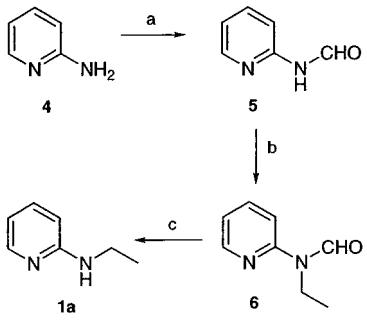
The preparation of carbamate **2** was achieved by reaction of **4** with Boc anhydride in *tert*-butyl alcohol (Scheme 2).[7] Following evaporation of the solvent, the crude solid was recrystallized from isopropyl alcohol, providing **2** in 90% yield. Evaporation of the mother liquors and chromatography of the resulting oil provided additional product, giving **2** in a 98% total yield.

CHART 1



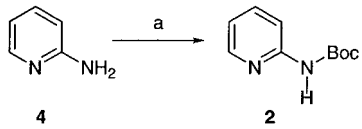
1a, R = CH_2CH_3 — **3a**, R = CH_2CH_3
1b, R = CH_3 — **3b**, R = CH_3
1c, R = $CH_2CH_2CH_3$ — **3c**, R = $CH_2CH_2CH_3$
1d, R = $CH(CH_3)_2$ — **3d**, R = $CH(CH_3)_2$
1e, R = CH_2Ph — **3e**, R = CH_2Ph
2, R = Boc

SCHEME 1[a]



[a] (a) HCO_2H, Ac_2O, 0 °C → rt, 73%; (b) CH_3CH_2I, NaH, DMF, 0 °C → rt 85%; (c) 6 N HCl, 100 °C, 90%.

SCHEME 2[a]



[a] (a) $(Boc)_2O$, *t*-BuOH, rt, 98%.

Alkylation of **2** with various alkyl halides proceeded efficiently upon treatment with sodium hydride in DMF (Table 1). The yields of products (**3**, Chart 1) were, with one exception, uniformly excellent; only isopropyl iodide afforded the corresponding alkylated derivative (**3d**) in less than 90% yield. Following purification of **3a**−**e** by chromatography, cleavage of the Boc group was achieved by treatment with TFA in CH_2Cl_2 containing a small amount of water. In terms of overall efficiency from **4**, compounds **1a**−**1c** and **1e** are obtained in yields of 85% or better. A similar yield of **1a** was also obtained when the crude reaction mixture obtained after the alkylation of **2** with ethyl iodide was directly treated with TFA/water in CH_2Cl_2 (Table 1, entry 6).

To summarize, we describe here an efficient route for the preparation of 2-(alkylamino)pyridines from 2-aminopyridine (**4**) via the readily accessible intermediate **2**. Advantages of this route over the one shown in Scheme 1 are (1) the cumbersome purification of the *N*-formyl derivative **5** is avoided and (2) the protected aminopyridine intermediate (**2**) is a solid that can be readily recrystallized from the crude reaction mixture following its preparation. Furthermore, the overall yields of the final products are, in general, higher than those reported by other methods.[1,3,4,8]

(1) Kawasaki, M.; Suzuki, Y.; Terashima, S. *Chem. Lett.* **1984**, 239.
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(3) Kemal, Ö.; Reese, C. B. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1569.
(4) Watanabe, Y.; Morisaki, Y.; Kondo, T.; Mitsudo, T. *J. Org. Chem.* **1996**, *61*, 4214.
(5) Sheehan, J. C.; Yang, D.-D. H. *J. Am. Chem. Soc.* **1958**, *80*, 1154.
(6) An alternate formylation method, involving heating **4** in formic acid at reflux (Tschitschibabin, A. E.; Knunjanz, I. L. *Chem. Ber.* **1931**, *64*, 2841) provided **5** in only a 43% yield.
(7) Venuti, M. C.; Stephenson, R. A.; Alvarez, R.; Bruno, J. J.; Strosberg, A. M. *J. Med. Chem.* **1988**, *31*, 2136.

10.1021/jo020057z CCC: $22.00
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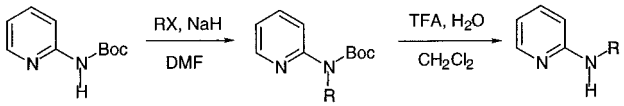
TABLE 1. Alkylation of 2 and Subsequent Deprotection



2 3 1

entry	RX	alkylation yield (%)[a]	alkylation product	deprotection yield (%)[a]	final product	overall yield from **2** (%)
1	CH_3CH_2I	95	**3a**	97	**1a**	92
2	CH_3I	91	**3b**	95	**1b**	87
3	$CH_3CH_2CH_2I$	94	**3c**	96	**1c**	90
4	$(CH_3)_2CHI$	74	**3d**	93	**1d**	69
5	$PhCH_2Br$	96	**3e**	97	**1e**	93
6	CH_3CH_2I	-	-	-	**1a**	88[b]

[a] Isolated yield following chromatography. [b] Overall yield when intermediate alkylated Boc derivative (**3a**) is not purified.

Experimental Section

General. Solvents were distilled from the appropriate drying agents before use. Unless stated otherwise, all reactions were carried out under a positive pressure of argon and were monitored by TLC on silica gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light. Solvents were evaporated under reduced pressure and below 40 °C (bath). Organic solutions of crude products were dried over anhydrous $MgSO_4$. Column chromatography was performed on silica gel 60 (40−60 μM). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Melting points are uncorrected. ^{1}H NMR spectra were recorded at 500.12 MHz and chemical shifts are referenced to TMS (0.00 ppm). ^{13}C NMR spectra were recorded at 125.75 MHz and ^{13}C chemical shifts are referenced to $CDCl_3$ (77.0 ppm). Electrospray mass spectra were recorded on samples suspended in 1:1 THF:MeOH containing NaCl. Elemental analyses were carried out in house.

2-(Formylamino)pyridine (5). To an ice-cooled solution of dry formic acid, 99% (115.07 g, 2.50 mol), was added 2-aminopyridine (23.53 g, 0.25 mol) in portions. *Caution*: This process is very exothermic and should be performed with care. This solution was then cooled to 0 °C with vigorous stirring while Ac_2O (38.28 g, 0.38 mol) was slowly added over 1 h at such a rate that the internal temperature never exceeded 10 °C. Upon complete addition, the mixture was brought to room temperature and allowed to stir for 48 h. The mixture was then diluted with water (100 mL) and Et_2O (500 mL). The organic layer was separated and extracted with water, a sat. aqueous $NaHCO_3$ solution, and brine, before being dried and concentrated. The resulting residue was then purified by vacuum distillation to afford **5** (22.28 g, 73%) as a clear, colorless oil that immediately solidified to a white solid upon cooling. Note: During the distillation, the distillate may solidify in the condenser. R_f 0.35 (hexanes/EtOAc, 1:1); mp 70−71 °C [lit.[6] mp 71 °C]; IR ν_{max} (KBr): 3265, 3059, 2968, 1700, 1588, 1462 cm^{-1}. All peaks in the ^{1}H and ^{13}C NMR spectra were doubled. This is presumably due to restricted rotation about the amide bond. ^{1}H NMR (500 MHz, $CDCl_3$, δ) 10.20 (br. s, 1 H), 9.99 (br. s, 1 H), 9.34 (d, 1 H, J = 10.6 Hz), 8.54 (s, 1 H), 8.34 (br. t, 2 H, J = 5.0 Hz), 8.27 (d, 1 H, J = 8.4 Hz), 7.75 (dt, 1 H, J = 9.0, 1.8 Hz), 7.68 (dt, 1 H, J = 7.8, 1.8 Hz), 7.12−7.05 (m, 2 H), 6.94 (d, 1 H, J = 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 163.1, 159.6, 151.1, 151.0, 148.6, 147.4, 138.9, 138.7, 120.2, 119.8, 115.2, 110.6. Anal. Calcd for $C_6H_6N_2O$: C, 59.01; H, 4.95. Found: C, 58.96; H, 5.31. HRMS (ESI) calcd for (M + Na^+) $C_6H_6N_2O$: 145.0372. Found: 145.0373.

2-(Formyl(ethyl)amino)pyridine (6). Compound **5** (1.22 g, 10.0 mmol) was dissolved in anhydrous DMF (30 mL), and the solution was cooled to 0 °C in an ice/water bath. Sodium hydride (0.50 g, 60% suspension in oil, 12.5 mmol) was added in portions such that the internal temperature was maintained <5 °C (vigorous stirring is required to keep the suspension fluid). Upon complete addition, the suspension was stirred vigorously for an additional 20 min while maintaining the temperature below 5 °C and then ethyl iodide (1.79 g, 11.5 mmol) was added dropwise. After stirring for 30 min, the reaction mixture was brought to room temperature over a 1 h period, before water (5 mL) was added. The mixture was then diluted with water (20 mL) and Et_2O (100 mL). The organic layer was separated and extracted with water, 0.1 M HCl, a sat. aqueous $NaHCO_3$ solution, and brine, before being dried and concentrated. The resulting residue was then purified by chromatography (hexanes/EtOAc, 4:1) to afford **6** (1.28 g, 85%) as a clear, colorless oil. R_f 0.29 (hexanes/EtOAc, 2:1); IR ν_{max} (neat): 3059, 2976, 1679, 1589, 1477, 1442 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ) 9.19 (s, 1 H), 8.41 (ddd, 1 H, J = 4.9, 1.9, 0.7 Hz), 7.73 (ddd, 1 H, J = 8.4, 7.2, 1.9 Hz), 7.12 (ddd, 1 H, J = 7.2, 4.9, 0.7 Hz), 7.04 (ddd, 1 H, J = 8.4, 0.7, 0.7 Hz), 4.00 (q, 2 H, J = 7.2 Hz), 1.24 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 161.9, 153.4, 148.8, 138.5, 120.2, 112.4, 37.0, 13.0. Anal. Calcd for $C_8H_{10}N_2O$: C, 63.98; H, 6.71. Found: C, 63.93; H, 6.99. HRMS (ESI) calcd for (M + Na^+) $C_8H_{10}N_2O$: 173.0685. Found: 173.0695.

2-(Ethylamino)pyridine (1a). Compound **6** (1.0 g, 6.7 mmol) was dissolved in 6 M HCl (10 mL) and heated at reflux for 6 h. The mixture was cooled to room temperature, carefully neutralized with 3 M NaOH to pH ∼ 9, and then diluted with Et_2O (100 mL). The organic layer was separated and extracted with water and brine before being dried and concentrated. The resulting residue was purified by chromatography (hexanes/EtOAc, 4:1) to afford **1a** (0.74 g, 90%) as a clear, colorless oil. R_f 0.36 (hexanes/EtOAc, 2:1); IR ν_{max} (neat): 3263, 3088, 2971, 1603, 1515, 1447 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ) 8.07 (ddd, 1 H, J = 5.0, 2.0, 0.8 Hz), 7.40 (ddd, 1 H, J = 8.4, 7.1, 2.0 Hz), 6.54 (ddd, 1 H, J = 7.1, 5.0, 0.8 Hz), 6.38 (ddd, 1 H, J = 8.4, 0.8, 0.8 Hz), 4.57 (br. s, 1 H), 3.28 (dq, 2 H, J = 7.2, 6.3 Hz), 1.25 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 158.9, 148.2, 137.4, 112.6, 106.4, 36.9, 14.9. Anal. Calcd for $C_7H_{10}N_2$: C, 68.83; H, 8.25. Found: C, 68.71; H, 8.06. HRMS (ESI) calcd for (M + H^+) $C_7H_{10}N_2$: 123.0917: Found: 123.0919.

2-[*N*-(*tert*-Butoxycarbonyl)amino]pyridine (2). To a solution prepared from freshly distilled *tert*-butyl alcohol (1.3 L) and di-*tert*-butyl dicarbonate (48.02 g, 0.22 mol) was slowly added 2-aminopyridine (18.82 g, 0.20 mol). This mixture was then allowed to stir for 24 h at 25 °C, and the solvent was then evaporated to an off-white semisolid. Recrystallization from hot 2-propanol (50 mL) afforded **2** (35 g, 90%) as a white needlelike solid. The mother liquor was concentrated to an yellow oil that was purified by chromatography (hexanes/EtOAc, 6:1) giving an additional 3 g (98% total yield) of **2**. R_f 0.44 (hexanes/EtOAc, 4:1); mp 95−97 °C [lit.[7] mp 96−97 °C]; IR ν_{max} (KBr): 3184, 2983, 1721, 1591, 1442, 1234, 1063 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ) 9.28 (br. s, 1 H), 8.34 (ddd, 1 H, J = 5.0, 1.9, 0.8 Hz), 7.99 (ddd, 1 H, J = 8.6, 0.8, 0.8 Hz), 7.66 (ddd, 1 H, J = 8.6, 7.4, 1.9 Hz), 6.94 (ddd, 1 H, J = 7.4, 5.0, 0.8 Hz), 1.55 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 152.7, 147.8, 146.8, 138.3, 118.1, 112.5, 80.8,

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28.4. Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.84; H, 7.26. Found: C, 61.89; H, 7.45. HRMS (ESI) calcd for (M + H^+) $C_{10}H_{14}N_2O_2$: 195.1128. Found: 195.1143.

General Procedure for Alkylation of 2. Compound **2** (1.94 g, 10.0 mmol) was dissolved in anhydrous DMF (30 mL), and the solution was cooled to 0 °C in an ice/water bath. Sodium hydride (0.50 g, 60% suspension in oil, 12.5 mmol) was added in portions such that the internal temperature was maintained <5 °C (vigorous stirring is required to keep the suspension fluid). The suspension was stirred vigorously for an additional 20 min while maintaining the temperature below 5 °C, and then the alkyl halide (11.5 mmol) was added dropwise. After stirring for 30 min, the reaction mixture was brought to room temperature over a 1 h, and then water (5 mL) was added. The reaction mixture was further diluted with water (20 mL) and Et_2O (150 mL). The organic layer was separated and extracted with water, 0.1 M HCl, a sat. aqueous $NaHCO_3$ solution, and brine, before being dried and concentrated. Chromatography (hexanes/EtOAc, 8:1) of the resulting residue afforded the pure product. The product yields for **3a**−**e** are given in Table 1. This procedure is amenable to scale-up by 10-fold; however, a mechanical stirrer should be used to keep the suspension fluid.

2-[*N*-(*tert*-Butoxycarbonyl)-*N*-ethylamino]pyridine (3a). Clear, colorless oil. R_f 0.53 (hexanes/EtOAc, 4:1); IR ν_{max} (neat): 3060, 2977, 1708, 1590, 1472, 1390, 1275, 1148 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.38 (ddd, 1 H, J = 4.9, 1.9, 0.8 Hz), 7.61 (ddd, 1 H, J = 8.3, 7.6, 1.9 Hz), 7.59 (ddd, 1 H, J = 8.3, 0.8, 0.8 Hz), 6.99 (ddd, 1 H, J = 7.6, 4.9, 0.8 Hz), 3.97 (q, 2 H, J = 7.0 Hz), 1.52 (s, 9 H), 1.22 (t, 3 H, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 154.7, 154.1, 147.7, 136.8, 119.9, 119.4, 80.8, 42.0, 28.3, 14.2. Anal. Calcd for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16. Found: C, 64.71; H, 8.48. HRMS (ESI) calcd for (M + H^+) $C_{12}H_{18}N_2O_2$: 223.1441: Found: 223.1439.

2-[*N*-(*tert*-Butoxycarbonyl)-*N*-methylamino]pyridine (3b). Clear, colorless oil. R_f 0.43 (hexanes/EtOAc, 4:1); IR ν_{max} (neat): 3060, 2977, 1710, 1590, 1474, 1352, 1279, 1150 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.37 (ddd, 1 H, J = 4.8, 1.9, 0.8 Hz), 7.66 (ddd, 1 H, J = 8.3, 0.8, 0.8 Hz), 7.61 (ddd, 1 H, J = 8.3, 7.1, 1.9 Hz), 6.99 (ddd, 1 H, J = 7.1, 4.8, 0.8 Hz), 3.40 (s, 3 H), 1.52 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 155.3, 154.4, 147.4, 136.8, 119.3, 119.2, 81.1, 34.2, 28.3. Anal. Calcd for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74. Found: C, 63.63; H, 7.57. HRMS (ESI) calcd for (M + H^+) $C_{11}H_{16}N_2O_2$: 209.1285: Found: 209.1280.

2-[*N*-(*tert*-Butoxycarbonyl)-*N*-propylamino]pyridine (3c). Clear, colorless oil. R_f 0.55 (hexanes/EtOAc, 4:1); IR ν_{max} (neat): 3058, 2969, 1706, 1589, 1471, 1391, 1296, 1147 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.37 (ddd, 1 H, J = 4.9, 1.9, 0.8 Hz), 7.61 (ddd, 1 H, J = 8.3, 7.1, 1.9 Hz), 7.55 (ddd, 1 H, J = 8.3, 0.8, 0.8 Hz), 6.99 (ddd, 1 H, J = 7.1, 4.9, 0.8 Hz), 3.89 (t, 2 H, J = 7.4 Hz), 1.62 (sextet, 2 H, J = 7.4 Hz), 1.52 (s, 9 H), 0.89 (t, 3 H, J = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 154.9, 154.3, 147.7, 136.8, 120.3, 119.5, 80.7, 48.6, 28.3, 22.2, 11.3. Anal. Calcd for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53. Found: C, 65.83; H, 8.40. HRMS (ESI) calcd for (M + H^+) $C_{13}H_{20}N_2O_2$: 237.1598: Found: 237.1609.

2-[*N*-(*tert*-Butoxycarbonyl)-*N*-isopropylamino]pyridine (3d). Clear, colorless oil. R_f 0.40 (hexanes/EtOAc, 4:1); IR ν_{max} (neat): 3060, 2975, 1700, 1588, 1471, 1392, 1335, 1176 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.47 (ddd, 1 H, J = 4.9, 2.0, 0.8 Hz), 7.66 (ddd, 1 H, J = 8.0, 7.4, 2.0 Hz), 7.18 (ddd, 1 H, J = 8.0, 0.8, 0.8 Hz), 7.13 (ddd, 1 H, J = 7.4, 4.9, 0.8 Hz), 4.53 (septet, 1 H, J = 6.8 Hz), 1.42 (s, 9 H), 1.26 (d, 6 H, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 154.3, 154.2, 148.3, 137.0, 123.9, 121.3, 80.3, 49.4, 28.4, 22.4. Anal. Calcd for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53. Found: C, 65.81; H, 8.54. HRMS (ESI) calcd for (M + H^+) $C_{13}H_{20}N_2O_2$: 237.1598: Found: 237.1597.

2-[*N*-(*tert*-Butoxycarbonyl)-*N*-benzylamino]pyridine (3e). White solid. R_f 0.57 (hexanes/EtOAc, 4:1); mp 48−50 °C. IR ν_{max} (KBr): 3063, 2977, 1696, 1588, 1472, 1388, 1245, 1164 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.36 (ddd, 1 H, J = 4.9, 2.0, 0.8 Hz), 7.66 (ddd, 1 H, J = 8.3, 0.8, 0.8 Hz), 7.60 (ddd, 1 H, J = 8.3, 7.2, 2.0 Hz), 7.29−7.24 (m, 4 H), 7.21−7.18 (m, 1 H), 6.98 (ddd, 1 H, J = 7.2, 4.9, 0.8 Hz), 5.19 (s, 2 H), 1.51 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 154.5, 154.3, 147.7, 139.5, 136.9, 128.2, 127.2, 126.7, 119.6, 119.5, 81.3, 50.0, 28.2. Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09. Found: C, 71.91; H, 7.03. HRMS (ESI) calcd for (M + H^+) $C_{17}H_{20}N_2O_2$: 285.1598: Found: 285.1615.

General Procedure for the Deprotection of 3a−e. The Boc-protected 2-alkylaminopyridine **3** (5.0 mmol) was dissolved in CH_2Cl_2 (5 mL) and treated with TFA, (95% aqueous solution, 5.0 mL), and the mixture was allowed to stir overnight. *Caution*: the initial mixing is exothermic and should be done with care. The reaction mixture was then cooled to 0 °C and neutralized with 3 M NaOH to pH ∼ 12 before being diluted with Et_2O (100 mL). The organic layer was separated and extracted with water and brine and then dried and concentrated. The products were purified by chromatography using either hexanes/EtOAc, 4:1 (**1a**, **1c**, **1d**, **1e**) or hexanes/EtOAc, 2:1 (**1b**) as the eluant. The product yields for **1a**−**e** are given in Table 1. Note: This procedure is amenable to scale-up by 20-fold; however, complete deprotection may require up to 48 h.

2-(Ethylamino)pyridine (1a). Clear, colorless oil. The spectral and analytical data for this compound were identical to **1a** obtained from **6**.

2-(Methylamino)pyridine (1b). Clear, colorless oil. R_f 0.18 (hexanes/EtOAc, 2:1); IR ν_{max} (neat): 3268, 3042, 2941, 1603, 1520, 1411, 1330, 1289, 1154 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.09 (ddd, 1 H, J = 5.0, 2.0, 0.8 Hz), 7.42 (ddd, 1 H, J = 8.4, 7.1, 2.0 Hz), 6.56 (ddd, 1 H, J = 7.1, 5.0, 0.8 Hz), 6.37 (ddd, 1 H, J = 8.4, 0.8, 0.8 Hz), 4.64 (br. s, 1 H), 2.91 (d, 3 H, J = 5.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 159.7, 148.2, 137.4, 112.7, 106.2, 29.1. Anal. Calcd for $C_6H_8N_2$: C, 66.64; H, 7.46. Found: C, 66.75; H, 7.12. HRMS (ESI) calcd for (M + H^+) $C_6H_8N_2$: 109.0760: Found: 109.0769.

2-(Propylamino)pyridine (1c). Clear, colorless oil. R_f 0.40 (hexanes/EtOAc, 2:1); IR ν_{max} (neat): 3265, 3087, 2961, 1603, 1515, 1445, 1332, 1292, 1152 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.06 (ddd, 1 H, J = 5.0, 1.9, 0.9 Hz), 7.39 (ddd, 1 H, J = 8.3, 7.1, 1.9 Hz), 6.53 (ddd, 1 H, J = 7.1, 5.0, 0.9 Hz), 6.35 (ddd, 1 H, J = 8.3, 0.9, 0.9 Hz), 4.62 (br. s, 1 H), 3.21 (dt, 2 H, J = 7.4, 5.5 Hz), 1.63 (sextet, 2 H, J = 7.4 Hz), 0.99 (t, 3 H, J = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 159.0, 148.2, 137.4, 112.6, 106.3, 44.1, 22.8, 11.6. Anal. Calcd for $C_8H_{12}N_2$: C, 70.56; H, 8.88. Found: C, 70.75; H, 8.75. HRMS (ESI) calcd for (M + H^+) $C_8H_{12}N_2$: 137.1073: Found: 137.1064.

2-(Isopropylamino)pyridine (1d). White solid. R_f 0.49 (hexanes/EtOAc, 2:1); mp 83−85 °C. IR ν_{max} (KBr): 3273, 3023, 2959, 1611, 1521, 1488, 1355, 1283, 1150 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.06 (ddd, 1 H, J = 4.8, 1.8, 0.8 Hz), 7.38 (ddd, 1 H, J = 8.4, 7.0, 1.8 Hz), 6.52 (ddd, 1 H, J = 7.0, 4.8, 0.8 Hz), 6.34 (ddd, 1 H, J = 8.4, 0.8, 0.8 Hz), 4.36 (br. s, 1 H), 3.87 (dsextet, 1 H, J = 6.4, 5.6 Hz), 1.22 (d, 6 H, J = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 158.2, 148.3, 137.3, 112.4, 106.8, 43.0, 23.0. Anal. Calcd for $C_8H_{12}N_2$: C, 70.56; H, 8.88. Found: C, 70.27; H, 8.79. HRMS (ESI) calcd for (M + H^+) $C_8H_{12}N_2$: 137.1073: Found: 137.1069.

2-(Benzylamino)pyridine (1e). White solid. R_f 0.36 (hexanes/EtOAc, 2:1); mp 94−96 °C. IR ν_{max} (KBr): 3225, 3024, 2868, 1600, 1528, 1442, 1334, 1152, 1079 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ) 8.09 (ddd, 1 H, J = 4.9, 1.9, 0.9 Hz), 7.38 (ddd, 1 H, J = 8.4, 7.0, 1.9 Hz), 7.35−7.31 (m, 4 H), 7.28−7.25 (m, 1 H), 6.57 (ddd, 1 H, J = 7.0, 4.9, 0.9 Hz), 6.35 (ddd, 1 H, J = 8.4, 0.9, 0.9 Hz), 4.95 (br. s, 1 H), 4.49 (d, 2 H, J = 5.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 158.7, 148.2, 139.2, 137.4, 128.6, 127.4, 127.2, 113.1, 106.8, 46.3. Anal. Calcd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.56. Found: C, 78.40; H, 6.68. HRMS (ESI) calcd for (M + H^+) $C_{12}H_{12}N_2$: 185.1073: Found: 185.1062.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of **1**−**3**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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