Supporting Information

Regioselective Synthesis of 3-(2-Hydroxyaryl)pyridines via Arynes and Pyridine *N*-Oxides

*Cristiano Raminelli, Zhijian Liu, and Richard C. Larock**

Department of Chemistry, Iowa State University, Ames, Iowa 50011, USA

larock@iastate.edu

Contents

General methods.....	2S
Procedure for preparation of compounds 3a-q	2S
Characterization data for compounds 3a-q	3S-9S
References.....	10S
Copies of ¹ H and ¹³ C NMR spectra for compounds 3a-q	11S-36S

General methods

The ^1H and ^{13}C NMR spectra were recorded on a spectrometer operating at 300 MHz and 75 MHz respectively. The ^1H NMR spectra were taken in $\text{DMSO-}d_6$ and the chemical shifts are given in ppm with respect to tetramethylsilane (TMS) used as an internal standard. The ^{13}C NMR spectra were taken in $\text{DMSO-}d_6$ and the central peak of the solvent was adjusted to 39.510 ppm and used as a reference. The infrared spectra were obtained using KBr pellets. The high resolution mass spectra were performed on a double focusing magnetic sector mass spectrometer using EI at 70 eV. All melting point values are uncorrected. Column chromatography separations were carried out using 230-450 mesh silica gel. The pyridine *N*-oxides **1a-e**, 2-(trimethylsilyl)phenyl triflate (**2a**) and CsF were used as obtained commercially. 4,5-Dimethyl-2-(trimethylsilyl)phenyl triflate (**2b**),¹ 4,5-dimethoxy-2-(trimethylsilyl)phenyl triflate (**2c**),² 6-(trimethylsilyl)-5-indanyl triflate (**2d**),¹ 4,5-difluoro-2-(trimethylsilyl)phenyl triflate (**2e**),³ 4-methyl-2-(trimethylsilyl)phenyl triflate (**2f**),⁴ 4-methoxy-2-(trimethylsilyl)phenyl triflate (**2g**),⁵ 4-fluoro-2-(trimethylsilyl)phenyl triflate (**2h**)⁶ and 3-methoxy-2-(trimethylsilyl)phenyl triflate (**2i**)³ were prepared according to literature procedures. Acetonitrile was distilled from calcium hydride under a nitrogen atmosphere prior to use.

Procedure for the preparation of compounds 3a-q

To a vial (20 mL) were added the appropriate pyridine *N*-oxide **1a-e** (0.2 mmol), the appropriate silylaryl triflate **2a-i** (0.4 mmol), acetonitrile (3 mL) and CsF (0.1215g, 0.8 mmol). The vial was sealed using a cap and the mixture was stirred for 24 h at room temperature. Afterwards, brine (20 mL) was added to the mixture, which was extracted with ethyl acetate (3 x 20 mL). The organic phase was dried over MgSO_4 . After filtration, the solvent was evaporated under reduced pressure. The residue was impregnated with silica gel and purified by column chromatography on silica gel using 2:1 hexane/acetone as eluent unless otherwise indicated, affording the desired products **3a-q**.

Characterization data for compounds 3a-q

3-(2-Hydroxyphenyl)pyridine (3a):⁷ Yield: 30.0 mg (88%); light yellow solid: mp 173-175 °C (lit.⁷ mp 171-172 °C); ¹H NMR (DMSO-*d*₆) δ 9.77 (s, 1H), 8.75 (d, *J* = 1.5 Hz, 1H), 8.50 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.95 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.43 (ddd, *J* = 7.9, 4.8, 0.7 Hz, 1H), 7.32 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.22 (td, *J* = 7.6, 1.5 Hz, 1H), 6.99 (dd, *J* = 8.2, 0.7 Hz, 1H), 6.92 (td, *J* = 7.5, 1.2 Hz, 1H); ¹³C NMR (DMSO-*d*₆) δ 154.5, 149.5, 147.5, 136.3, 134.1, 130.3, 129.3, 124.3, 123.1, 119.6, 116.1; IR (KBr, cm⁻¹) 3445, 3039-2426, 1450, 1394, 1267, 758; HRMS calcd for C₁₁H₉NO 171.0684, found 171.0687.

FIGURE 1. ORTEP diagram of compound **3a**.

3-(4,5-Dimethyl-2-hydroxyphenyl)pyridine (3b): Yield: 33.4 mg (84%); light yellow solid: mp 177-180 °C; ¹H NMR (DMSO-*d*₆) δ 9.39 (s, 1H), 8.72 (d, *J* = 1.5 Hz, 1H), 8.45 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.91 (dt, *J* = 6.9, 1.8 Hz, 1H), 7.39 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.08 (s, 1H), 6.76 (s, 1H), 2.17 (s, 3H), 2.16 (s, 3H); ¹³C NMR (DMSO-*d*₆) δ 152.2, 149.4, 147.1, 137.3, 136.1, 134.2, 131.0, 127.0, 123.1, 121.4, 117.3, 19.32, 18.38; IR (KBr, cm⁻¹) 3444, 3006-2569, 1457, 1395, 1308, 710; HRMS calcd for C₁₃H₁₃NO 199.0997, found 199.0999.

3-(4,5-Dimethoxy-2-hydroxyphenyl)pyridine (3c): The eluent used was 1:1 acetone/hexane; yield: 38.8 mg (84%); brown solid: mp 195-197 °C; ^1H NMR (DMSO- d_6) δ 9.36 (s, 1H), 8.77 (s, 1H), 8.44 (d, J = 3.9 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.39 (dd, J = 7.9, 4.9 Hz, 1H), 6.92 (s, 1H), 6.62 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (DMSO- d_6) δ 149.6, 149.5, 148.7, 146.8, 142.3, 136.1, 134.2, 123.1, 115.0, 114.2, 101.3, 56.3, 55.5; IR (KBr, cm^{-1}) 3425, 2976-2605, 1268, 1151, 1046, 637; HRMS calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_3$ 231.0895, found 231.0899.

3-(2-Hydroxyindanyl)pyridine (3d): Yield: 38.0 mg (90%); light yellow solid: mp 167-170 °C; ^1H NMR (DMSO- d_6) δ 9.43 (s, 1H), 8.69 (d, J = 2.1 Hz, 1H), 8.45 (dd, J = 4.9, 1.3 Hz, 1H), 7.90 (dt, J = 8.1, 1.8 Hz, 1H), 7.39 (dd, J = 7.9, 4.9 Hz, 1H), 7.13 (s, 1H), 6.84 (s, 1H), 2.82 (t, J = 7.0 Hz, 2H), 2.79 (t, J = 7.0 Hz, 2H), 2.00 (quint, J = 7.3 Hz, 2H); ^{13}C NMR (DMSO- d_6) δ 153.1, 149.5, 147.0, 145.1, 136.2, 134.8, 134.5, 125.5, 123.0, 122.2, 111.9, 32.4, 31.5, 25.3; IR (KBr, cm^{-1}) 3427, 3014-2567, 1444, 1402, 1323, 713; HRMS calcd for $\text{C}_{14}\text{H}_{13}\text{NO}$ 211.0997, found 211.1001.

3-(4,5-Difluoro-2-hydroxyphenyl)pyridine (3e): Yield: 38.0 mg (92%); brown solid: mp 218-220 °C; ^1H NMR (DMSO- d_6) δ 10.26 (s, 1H), 8.73 (d, J = 1.5 Hz, 1H), 8.52 (dd, J = 4.8, 1.5 Hz, 1H), 7.95 (dt, J = 8.1, 2.0 Hz, 1H), 7.51-7.42 (m, 2H), 6.93 (dd, J = 12.3, 7.2 Hz, 1H); ^{13}C NMR (DMSO- d_6) δ 151.2 (dd, J = 8.5, 1.6 Hz), 149.6, 149.0 (dd, J = 244.7, 13.9 Hz), 148.0, 143.1 (dd, J = 234.8, 12.5 Hz), 136.5, 132.3, 123.2, 120.9 (dd, J = 5.7, 3.4 Hz), 118.3 (d, J = 19.2 Hz), 104.7 (d, J = 19.2 Hz); IR (KBr, cm^{-1}) 3426, 3071-2578, 1453, 1400, 1189, 832; HRMS calcd for $\text{C}_{11}\text{H}_7\text{NOF}_2$ 207.0496, found 207.0499.

3-(2-Hydroxy-4-methylphenyl)pyridine (3f) and 3-(2-hydroxy-5-methylphenyl)pyridine (3g): Yield: 28.5 mg (77%); brown solid; ^1H NMR (DMSO- d_6) δ 9.65 (s, 1H), 9.50 (s, 0.7H), 8.73 (td, J = 2.1, 0.7 Hz, 1.7H), 8.48 (dd, J = 4.6, 1.6 Hz, 0.7H), 8.47 (dd, J = 4.9, 1.6 Hz, 1H), 7.95-7.90 (m, 1.7H), 7.41 (ddd, J = 7.8, 4.9, 0.9 Hz, 0.7H), 7.40 (ddd, J = 7.9, 4.8, 0.8 Hz, 1H), 7.20 (d, J = 7.5 Hz, 1H), 7.12 (d, J = 1.8 Hz, 0.7H), 7.02 (ddq, J = 8.6, 2.2, 0.5 Hz, 0.7H), 6.87 (d, J = 7.8 Hz, 0.7H), 6.79 (s, 1H), 6.73 (dq, J = 7.8, 0.7 Hz, 1H), 2.27 (s, 3H), 2.25 (s, 2.1H); ^{13}C NMR (DMSO- d_6) δ 154.4, 152.2, 149.5, 149.4, 147.4, 147.2, 138.9, 136.3, 136.2, 134.3, 134.2, 130.6, 130.0, 129.7, 128.1, 124.0, 123.1, 121.5, 120.5, 116.6, 116.0, 20.9, 20.1; IR (KBr, cm^{-1}) 3418, 3037-2583, 1403, 1293, 799, 709; HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{NO}$ 185.0841, found 185.0843.

3-(2-Hydroxy-4-methoxyphenyl)pyridine (3h) and 3-(2-hydroxy-5-methoxyphenyl)pyridine

(3i): Yield: 30.1 mg (75%); brown solid; ^1H NMR (DMSO- d_6) δ 9.84 (s, 1H), 9.28 (s, 1H), 8.76 (d, J = 1.5 Hz, 1H), 8.70 (d, J = 1.8 Hz, 1H), 8.49 (dd, J = 4.8, 1.5 Hz, 1H), 8.44 (dd, J = 4.5, 1.5 Hz, 1H), 7.96 (dt, J = 7.8, 1.9 Hz, 1H), 7.90 (dt, J = 8.1, 1.8 Hz, 1H), 7.42 (dd, J = 7.4, 4.3 Hz, 1H), 7.39 (dd, J = 7.4, 4.3 Hz, 1H), 7.25 (d, J = 8.1 Hz, 1H), 6.92-6.80 (m, 3H), 6.55-6.50 (m, 2H); ^{13}C NMR (DMSO- d_6) δ 160.2, 155.6, 152.5, 149.6, 149.4, 148.3, 147.5, 146.9, 136.4, 136.0, 134.1, 134.0, 130.9, 124.7, 123.1, 123.0, 117.2, 116.9, 115.1, 114.9, 105.4, 101.8, 55.4, 55.0; IR (KBr, cm^{-1}) 3044-2605, 1437, 1291, 1170, 784, 711; HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{NO}_2$ 201.0790, found 201.0792.

3-(5-Fluoro-2-hydroxyphenyl)pyridine (3j) and 3-(4-fluoro-2-hydroxyphenyl)pyridine

(3k): Yield: 31.4 mg (83%); brown solid; ^1H NMR (DMSO- d_6) δ 10.32 (s, 0.5H), 9.79 (s, 1H), 8.77 (d, J = 1.8 Hz, 1H), 8.70 (d, J = 1.8 Hz, 0.5H), 8.52 (dd, J = 4.6, 1.6 Hz, 1H), 8.50 (dd, J = 4.9, 1.6 Hz, 0.5H), 7.98 (dt, J = 8.1, 1.9 Hz, 1H), 7.92 (dt, J = 8.1, 1.9 Hz, 0.5H), 7.46-7.33 (m, 2H), 7.21 (dd, J = 9.4, 3.1 Hz, 1H), 7.07 (td, J = 8.5, 3.0 Hz, 1H), 6.96 (dd, J = 9.0, 5.1 Hz, 1H), 6.79-6.72 (m, 1H); ^{13}C NMR (DMSO- d_6) δ 162.4 (d, J = 243.1 Hz), 156.0 (d, J = 11.2 Hz), 155.7 (d, J = 232.9 Hz), 150.8 (d, J = 1.6 Hz), 149.5, 149.4, 147.9, 147.6, 136.4, 136.3, 133.3, 133.1, 131.6 (d, J = 10.6 Hz), 125.3 (d, J = 7.5 Hz), 123.1, 121.1 (d, J = 3.1 Hz), 117.0 (d, J = 8.5 Hz), 116.2 (d, J = 23.5 Hz), 115.5 (d, J = 22.4 Hz), 106.3 (d, J = 21.4 Hz), 103.0 (d, J = 23.1 Hz); IR (KBr, cm^{-1}) 3430, 3061-2593, 1446, 1409, 1269, 779; HRMS calcd for $\text{C}_{11}\text{H}_8\text{NOF}$ 189.0590, found 189.0592.

3-(2-Hydroxy-6-methoxyphenyl)pyridine (3l): Yield: 33.0 mg (82%); light yellow solid: mp 229-231 °C; ^1H NMR (DMSO- d_6) δ 9.50 (s, 1H), 8.44 (d, J = 1.2 Hz, 1H), 8.43 (dd, J = 4.9, 1.3 Hz, 1H), 7.66 (dt, J = 7.8, 1.9 Hz, 1H), 7.38 (ddd, J = 7.8, 4.8, 0.9 Hz, 1H), 7.15 (t, J = 8.2 Hz, 1H), 6.59 (t, J = 7.3 Hz, 2H), 3.66 (s, 3H); ^{13}C NMR (DMSO- d_6) δ 157.5, 155.5, 151.2, 147.1, 138.2, 130.4, 129.3, 122.8, 113.6, 108.7, 102.3, 55.6; IR (KBr, cm^{-1}) 3434, 3090-2542, 1463, 1245, 1082, 785, 710; HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{NO}_2$ 201.0790, found 201.0792.

5-(2-Hydroxyphenyl)-2-methylpyridine (3m) and 3-(2-hydroxyphenyl)-2-methylpyridine (3n): Yield: 30.0 mg (81%); light yellow solid; ^1H NMR (DMSO- d_6) δ 9.69 (s, 1H), 9.56 (s, 0.15H), 8.59 (d, J = 2.4 Hz, 1H), 8.41 (dd, J = 4.8, 1.8 Hz, 0.15H), 7.83 (dd, J = 7.9, 2.5 Hz, 1H), 7.49 (dd, J = 7.6, 1.6 Hz, 0.15H), 7.30-7.16 (m, 3.3H), 7.07 (dd, J = 7.6, 1.6 Hz, 0.15H), 6.97-6.85 (m, 2.3H), 2.49 (s, 3H), 2.31 (s, 0.45H); ^{13}C NMR (DMSO- d_6) δ 156.2, 155.7, 154.5, 154.3, 148.7, 147.3, 137.5, 136.6, 133.8, 131.2, 130.6, 130.1, 129.0, 126.6, 124.5, 122.3, 120.9, 119.6, 119.1, 116.0, 115.5, 23.7, 22.8; IR (KBr, cm^{-1}) 3071-2597, 1449, 1376, 1285, 747; HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{NO}$ 185.0841, found 185.0843.

2,6-Dimethyl-3-(2-hydroxyphenyl)pyridine (3o): Yield: 31.0 mg (78%); light yellow solid: mp 198-200 °C; ^1H NMR (DMSO- d_6) δ 9.49 (s, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.19 (ddd, J = 8.2, 7.2, 1.9 Hz, 1H), 7.08 (d, J = 7.8, 1H), 7.04 (dd, J = 7.6, 1.6 Hz, 1H), 6.93 (dd, J = 7.9, 1.0 Hz, 1H), 6.86 (td, J = 7.2, 1.0 Hz, 1H), 2.45 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (DMSO- d_6) δ 155.4, 155.3, 154.3, 137.9, 130.7, 130.6, 128.8, 126.6, 120.0, 119.0, 115.5, 23.7, 22.7; IR (KBr, cm^{-1}) 3408, 3045-2435, 1446, 1392, 1284, 754; HRMS calcd for $\text{C}_{13}\text{H}_{13}\text{NO}$ 199.0997, found 199.0999.

3-(2-Hydroxyphenyl)-4-methylpyridine (3p): Yield: 19.2 mg (52%); light yellow solid: mp 172-178 °C; ^1H NMR (DMSO- d_6) δ 9.58 (s, 1H), 8.38 (d, J = 5.1 Hz, 1H), 8.26 (s, 1H), 7.27 (d, J = 4.8, 1H), 7.24 (ddd, J = 7.9, 7.5, 1.8 Hz, 1H), 7.08 (dd, J = 7.5, 1.5 Hz, 1H), 6.96 (dd, J = 7.9, 0.9 Hz, 1H), 6.89 (td, J = 7.4, 0.8 Hz, 1H); ^{13}C NMR (DMSO- d_6) δ 154.7, 149.8, 147.9, 145.4, 134.9, 130.8, 129.2, 124.6, 124.5, 119.1, 115.5, 19.14; IR (KBr, cm^{-1}) 3425, 3066-2589, 1446, 1402, 1279, 758; HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{NO}$ 185.0841, found 185.0843.

4-Cyano-2-(2-hydroxyphenyl)pyridine (3q): Yield: 16.5 mg (42%); yellow solid: mp 139-140 °C; ^1H NMR (DMSO- d_6) δ 12.75 (s, 1H), 8.87 (dd, J = 5.1, 0.9 Hz, 1H), 8.67 (s, 1H), 8.07 (dd, J = 7.9, 1.6 Hz, 1H), 7.85 (dd, J = 5.1, 1.5 Hz, 1H), 7.36 (ddd, J = 8.3, 6.9, 1.6 Hz, 1H), 6.99-6.93 (m, 2H); ^{13}C NMR (DMSO- d_6) δ 158.3, 157.6, 148.4, 132.1, 128.2, 123.4, 123.3, 121.1, 119.3, 119.2, 117.8, 116.8; IR (KBr, cm^{-1}) 3439, 3076, 2924, 2854, 2236, 1606, 1545, 1481, 1428, 1382, 1241, 767; HRMS calcd for $\text{C}_{12}\text{H}_8\text{N}_2\text{O}$ 196.0637, found 196.0640.

FIGURE 2. ORTEP diagram of compound **3q**.

References

- (1) Yoshida, H.; Sugiura, S.; Kunai, A. *Org. Lett.* **2002**, *4*, 2767-2769.
- (2) Liu, Z.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 15716-15717.
- (3) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659-2661.
- (4) Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7280-7286.
- (5) Yoshida, H.; Ikadai, J.; Shudo, M.; Ohshita, J.; Kunai, A. *J. Am. Chem. Soc.* **2003**, *125*, 6638-6639.
- (6) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 3935-3938.
- (7) Abramovitch, R. A.; Shinkai, I. *J. Am. Chem. Soc.* **1974**, *96*, 5265.

Copies of ^1H and ^{13}C NMR spectra for compounds 3a-q