

Supporting Information

“Palladium-Catalyzed Regioselective Arylation of Imidazo[1,2-*a*]pyrimidine”

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General: Infrared spectra were recorded on a Nicolet Magna-FT-IR 560 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 MHz spectrometer. Melting points were determined using a Mel-Temp II capillary melting point apparatus and are uncorrected. HPLC analyses were performed on a Hewlett Packard Series 1100 chromatograph. HR-MS was performed on a Finnigan New-Star FT/ICR instrument via ESI.

Materials: All commercial reagents were available from Aldrich Chemical Co. and were used as received. Flash chromatography was performed using silica gel 60 (230-400 mesh) available from EM Science.

HPLC Conditions: Supelco Discovery 4.6x100mm 5 micron column at 30 °C, 1.5 mL/min, gradient elution from 0:100 to 25:75 $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (0.1% HClO_4) over 10 min, followed by gradient elution from 25:75 to 80:20 $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (0.1% HClO_4) over 10 min, then returned to 0:100 $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (0.1% HClO_4) over 0.1 min, with a 3 min post time, detection at 220 nm, injection volume of 10 μL .

General procedure for arylation of imidazo[1,2-*a*]pyrimidine: A mixture of aryl bromide (1.15 mmole), imidazo[1,2-*a*]pyrimidine hydrobromide (1.0 mmole), palladium(II) acetate (0.02 mmole), triphenylphosphine (0.04 mmole), and cesium carbonate (2.0 mmole) in anhydrous 1,4-dioxane (2 mL) was degassed using 5 vacuum/nitrogen back-fill cycles. The slurry was heated to 100 °C and monitored by HPLC. The reaction was aged at 100 °C until imidazo[1,2-*a*]pyrimidine was consumed (12 – 36 hours). The mixture was cooled to room temperature and diluted with water. The mixture was extracted with ethyl acetate (3x). The combined organic layer was dried with MgSO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (5% MeOH in CH_2Cl_2) to give 3-aryl-imidazo[1,2-*a*]pyrimidine.

3-Phenyl-imidazo[1,2-*a*]pyrimidine (7a): off-white solid, mp 125.2-126.5 °C. IR (film) 3053, 1515, 1494, 1282, 1197, 1142, 960, 780, 755, 698 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 6.91 (dd, 1H, $J=4.0, 6.9$ Hz), 7.46-7.49 (m, 1H), 7.53-7.58 (m, 4H), 7.92 (s, 1H), 8.59 (dd, 1H, $J=2.0, 4.0$ Hz), 8.67 (dd, 1H, $J=2.0, 6.9$ Hz). ^{13}C NMR (100 MHz,

CDCl₃) δ 108.8, 124.2, 127.9, 128.3, 128.7, 129.4, 131.1, 133.9, 149.0, 149.4. HR-MS m/z calcd. for C₁₂H₁₀N₃ ([M + H]⁺) 196.0869, found 196.0860.

3-(4-Fluoro-phenyl)-imidazo[1,2-*a*]pyrimidine (7b): white solid, mp 198.6-200.1 °C. IR (film) 3078, 1520, 1480, 1423, 1284, 1143, 833, 809, 767, 588, 555 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.92 (dd, 1H, *J*=4.0, 6.9 Hz), 7.24-7.28 (m, 2H), 7.53 (dd, 2H, *J*=5.2, 8.8 Hz), 7.88 (s, 1H), 8.57 (dd, 1H, *J*=2.0, 6.9 Hz), 8.60 (dd, 1H, *J*=2.0, 4.0 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 109.0, 116.6, 116.8, 123.3, 124.4, 130.0, 130.1, 130.9, 134.0, 149.0, 149.6, 161.6, 164.1. HR-MS m/z calcd. for C₁₂H₉FN₃ ([M + H]⁺) 214.0775, found 214.0771.

4-Imidazo[1,2-*a*]pyrimidin-3-yl-benzonitrile (7c): off-white solid, mp 265-266 °C (decomp.). IR (film) 3085, 3043, 2223, 1607, 1539, 1517, 1474, 1282, 848, 827, 779, 765, 567 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.05 (t, 1H, *J*=5.4 Hz), 7.71 (d, 2H, *J*=8.1 Hz), 7.86 (d, 2H, *J*=8.2 Hz), 8.03 (s, 1H), 8.70 (d, 2H, *J*=5.4 Hz). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 110.1, 110.5, 119.2, 122.7, 128.0, 133.4, 133.6, 133.9, 135.7, 149.8, 151.2. HR-MS m/z calcd. for C₁₃H₉N₄ ([M + H]⁺) 221.0822, found 221.0819.

4-Imidazo[1,2-*a*]pyrimidin-3-yl-benzoic acid ethyl ester (7d): white solid, mp 159.2-159.9 °C. IR (film) 2988, 1711, 1610, 1520, 1500, 1364, 1291, 1282, 1314, 1102, 1020, 856, 789, 762, 701 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 1.43 (t, 3H, *J*=7.0 Hz), 4.43 (q, 2H, *J*=7.1 Hz), 6.98 (dd, 1H, *J*=4.3, 6.0 Hz), 7.64 (d, 2H, *J*=7.9 Hz), 7.99 (s, 1H), 8.21 (d, 2H, *J*=7.8 Hz), 8.63 (s, 1H), 8.71 (d, 1H, *J*=6.8 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 14.2, 61.2, 109.2, 123.3, 127.1, 130.3, 130.6, 131.0, 132.4, 134.6, 149.3, 150.0, 165.8. HR-MS m/z calcd. for C₁₅H₁₄N₄O₂ ([M + H]⁺) 268.1081, found 268.1082.

4-Imidazo[1,2-*a*]pyrimidin-3-yl-benzaldehyde (7e): brown solid, mp 248.5-249.6 °C (decomp.). IR (film) 3094, 3043, 2811, 2728, 1695, 1602, 1498, 1420, 1275, 826, 785, 766 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.01 (dd, 1H, *J*=4.0, 6.8 Hz), 7.76 (d, 2H, *J*=8.2 Hz), 8.05 (s, 1H), 8.07 (d, 2H, *J*=8.2 Hz), 8.66 (dd, 1H, *J*=1.9, 3.9 Hz), 8.75 (dd, 1H, *J*=1.7, 6.8 Hz). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 110.2, 123.2, 127.7, 130.8, 133.9, 134.4, 135.5, 135.6, 149.7, 151.2, 193.0. HR-MS m/z calcd. for C₁₃H₁₀N₃O ([M + H]⁺) 224.0818, found 224.0797.

3-(3-Chloro-phenyl)-imidazo[1,2-*a*]pyrimidine (7f): off-white solid, mp 172.1-173.3 °C. IR (film) 3061, 1598, 1517, 1280, 1138, 858, 764, 691 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.96 (dd, 1H, *J*=4.1, 6.9 Hz), 7.43-7.51 (m, 3H), 7.55 (t, 1H, *J*=1.6 Hz), 7.93 (s, 1H), 8.61-8.66 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 109.0, 122.8, 125.8, 127.6, 128.6, 130.0, 130.7, 130.9, 134.3, 135.3, 149.1, 149.7. HR-MS m/z calcd. for C₁₂H₉ClN₃ ([M + H]⁺) 230.0471, found 230.0480.

(4-Imidazo[1,2-*a*]pyrimidin-3-yl-phenyl)-dimethyl-amine (7g): yellow solid, mp 205.4-206.9 °C. IR (film) 2886, 1612, 1521, 1476, 1416, 1232, 1149, 820, 782, 763 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 3.06 (s, 6H), 6.87 (d, 2H, *J*=8.8 Hz), 6.98 (t, 1H, *J*=5.5 Hz), 7.40 (d, 2H, *J*=8.8 Hz), 7.84 (s, 1H), 8.63 (d, 2H, *J*=5.6 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 40.2, 108.5, 112.6, 115.1, 124.8, 129.1, 131.0, 132.3, 148.2, 148.9, 150.5. HR-MS *m/z* calcd. for C₁₄H₁₅N₄ ([M + H]⁺) 239.1291, found 239.1302.

3-(4-Methoxy-phenyl)-imidazo[1,2-*a*]pyrimidine (7h): white solid, mp 149.2-150.1 °C. IR (film) 3098, 1573, 1544, 1516, 1497, 1443, 1307, 1178, 1023, 963, 837, 783, 764 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 3.90 (s, 3H), 6.88 (t, 1H, *J*=5.7 Hz), 7.08 (d, 2H, *J*=8.5 Hz), 7.27 (s, 1H), 7.47 (d, 2H, *J*=8.5 Hz), 7.84 (s, 1H), 8.57 (s, 1H), 8.58 (d, 1H, *J*=4.7 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 55.4, 108.6, 114.8, 120.4, 124.0, 129.4, 130.8, 133.3, 148.6, 149.1, 159.9. HR-MS *m/z* calcd. for C₁₃H₁₂N₃O ([M + H]⁺) 226.0975, found 226.0969.

1-(4-Imidazo[1,2-*a*]pyrimidin-3-yl-phenyl)-ethanone (7i): white solid, mp 198.1-198.9 °C. IR (film) 3079, 1675, 1603, 1559, 1540, 1474, 1362, 1270, 1161, 962, 826, 798, 769 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 2.67 (s, 3H), 6.99 (dd, 1H, *J*=4.0, 6.9 Hz), 7.68 (d, 2H, *J*=8.3 Hz), 8.01 (s, 1H), 8.14 (d, 2H, *J*=8.3 Hz), 8.64 (dd, 1H, *J*=1.9, 3.9 Hz), 8.72 (dd, 1H, *J*=1.8, 6.9 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 26.5, 109.3, 123.2, 127.2, 129.3, 131.2, 132.7, 134.7, 136.5, 149.4, 150.0, 197.0. HR-MS *m/z* calcd. for C₁₄H₁₂N₃O ([M + H]⁺) 238.0975, found 238.0967.

3-(2-Nitro-phenyl)-imidazo[1,2-*a*]pyrimidine (7j): yellow solid, mp 187.5-188.5 °C. IR (film) 1653, 1517, 1494, 1340, 1201, 1145, 965, 787, 768, 745 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.91 (d, 1H, *J*=3.9 Hz), 7.59 (d, 1H, *J*=7.1 Hz), 7.72 (t, 1H, *J*=7.5 Hz), 7.80 (t, 1H, *J*=7.0 Hz), 7.86 (s, 1H), 8.02 (d, 1H, *J*=5.9 Hz), 8.24 (d, 1H, *J*=7.9 Hz), 8.64 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 108.8, 119.5, 122.8, 125.3, 130.6, 131.7, 133.8, 134.2, 135.2, 148.7, 149.1, 150.1. HR-MS *m/z* calcd. for C₁₂H₉N₄O₂ ([M + H]⁺) 241.0720, found 241.0723.

3-Phenanthren-9-yl-imidazo[1,2-*a*]pyrimidine (7k): white solid, mp 202.2-203.8 °C. IR (film) 3060, 1616, 1511, 1494, 1425, 1281, 1263, 1144, 781, 766, 752, 727 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.83 (dd, 1H, *J*=4.0, 6.8 Hz), 7.47-7.56 (m, 2H), 7.67-7.78 (m, 3H), 7.91-7.94 (m, 2H), 8.05 (dd, 1H, *J*=3.2, 6.9 Hz), 8.06 (s, 1H), 8.63 (dd, 1H, *J*=2.0, 4.0 Hz), 8.76 (d, 1H, *J*=8.3 Hz), 8.82 (d, 1H, *J*=8.4 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 108.7, 122.4, 122.7, 123.5, 123.9, 125.5, 127.3, 127.5, 128.0, 129.0, 130.2, 130.8, 131.0, 131.1, 131.9, 135.4, 148.9, 149.7. HR-MS *m/z* calcd. for C₂₀H₁₄N₃ ([M + H]⁺) 296.1182, found 296.1186.

3-Pyridin-3-yl-imidazo[1,2-*a*]pyrimidine (7l): off-white solid, mp 159.2-160.3 °C. IR (film) 3068, 1614, 1515, 1493, 1424, 1280, 1194, 1141, 962, 766, 709 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.97 (t, 1H, *J*=5.3 Hz), 7.49 (dd, 1H, *J*=4.9, 7.7 Hz), 7.88 (d, 1H,

$J=7.9$ Hz), 7.96 (s, 1H), 8.62 (d, 1H, $J=5.3$ Hz), 8.63 (s, 1H), 8.70 (d, 1H, $J=3.7$ Hz), 8.85 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 109.3, 120.9, 124.1, 124.7, 130.8, 134.7, 135.2, 148.6, 149.4, 149.8, 150.1. HR-MS m/z calcd. for $\text{C}_{11}\text{H}_9\text{N}_4$ ($[\text{M} + \text{H}]^+$) 197.0822, found 197.0826.