

Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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Supporting Information

Oxidative Cross-Coupling of Pyridine *N*-Oxide and Ether between C(sp²)-H/C(sp³)-H Bonds under Transition-Metal-Free Conditions

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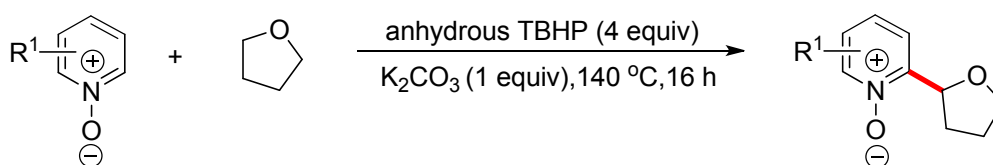
1. General considerations

All ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker FT-NMR spectrometers (400 MHz or 100 MHz, respectively). All chemical shifts are given as δ value (ppm) with reference to tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, J , are reported in Hertz (Hz). High resolution mass spectroscopy data of the product were collected on a Waters Micromass GCT instrument. High resolution mass spectroscopy data of the product were collected on an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS (ESI).

The chemicals and solvents were purchased from commercial suppliers either from Aldrich (USA) or Shanghai Chemical Company (China) without further purification. All the solvents were dried and freshly distilled prior to use. All the reactions were carried out under air atmosphere. Products were purified by flash chromatography on 100–200 mesh silica gels, SiO_2 .

2. General procedure

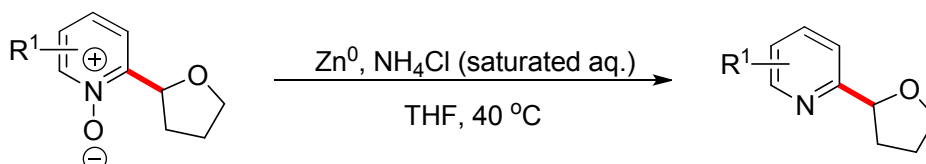
2.1. Typical procedure for the cross-coupling of pyridine *N*-oxide with tetrahydrofuran



All operations are carried out in a glove box under nitrogen atmosphere. To a 25 mL Schlenk tube were added pyridine 1-oxide (0.50 mmol), anhydrous *tert*-butyl hydroperoxide (TBHP, 2.0 mmol, 4.0 equiv) and K_2CO_3 (0.50 mmol, 1.0 equiv). Then tetrahydrofuran (THF, 1.0 mL) was injected into bottom of the tube using a long needle syringe. The mixture was stirred at the preheated oil bath under $140\text{ }^\circ\text{C}$ for 16 h. When the reaction was cooled down to room temperature, the mixture was filtered through a short plug of silica gel and washed with ethyl ether ($3\times 6.0\text{ mL}$) and saturated NaCl solution ($3\times 6.0\text{ mL}$). The

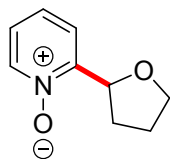
combined organic phase was dried over MgSO_4 and then concentrated under vacuum. The product was purified through flash column chromatography on 200–300 mesh silica gel with petroleum ether/ethyl acetate as eluent with a suitable ratio according to the TLC analysis.

2.2. General procedure for the deoxidative reaction



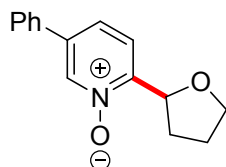
According to the procedure reported in the literature (Y. Aoyagi, T. Abe and A. Ohta, *Synthesis*, 1997, 891), a 20 mL vial was charged with 2-substituted *N*-oxide (0.30 mmol, 1.0 equiv), THF (1.0 mL) and saturated NH_4Cl aqueous solution (1.0 mL). The mixture was stirred under an air atmosphere at 40 °C. Then Zn^0 powder (0.90 mmol, 3.0 equiv) in 4 portions of 0.75 eq. each in 20 minutes interval was added. When the reaction was complete by TLC analysis, the mixture was filtered to remove unreacted Zn^0 and filter cake was washed with THF. The mixture was diluted with EtOAc and organic layer was separated. The organic phase was washed with H_2O (2×5.0 mL), dried with MgSO_4 , filtered and concentrated in vacuo. The residue is then purified via silica gel chromatography using petroleum ether/ethyl acetate mixtures.

3. Characterization data for the products



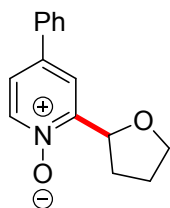
2-(Tetrahydrofuran-2-yl)pyridine 1-oxide

3a: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.22 (d, $J = 6.32$ Hz, 1H), 7.53 (d, $J = 7.68$ Hz, 1H), 7.32–7.28 (m, 1H), 7.21–7.17 (m, 1H), 5.36 (t, $J = 6.42$ Hz, 1H), 4.13–4.08 (m, 1H), 4.00–3.94 (m, 1H), 2.75–2.66 (m, 1H), 2.07–1.99 (m, 1H), 1.92–1.81 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 139.4, 126.2, 123.8, 122.5, 75.3, 69.1, 30.9, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_9\text{H}_{12}\text{NO}_2$: 166.0868, Found: 166.0868.



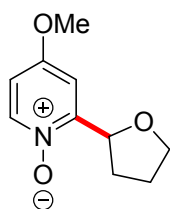
5-Phenyl-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3b: Yellow liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.49 (s, 1H), 7.58–7.56 (m, 1H), 7.54–7.51 (m, 3H), 7.49–7.41 (m, 4H), 5.40 (t, $J = 6.04$ Hz, 1H), 4.14–4.11 (m, 1H), 4.01–3.96 (m, 1H), 2.76–2.70 (m, 1H), 2.04 (br, 1H), 1.90 (br, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 152.2, 138.1, 137.6, 135.3, 129.2, 129.0, 126.8, 125.0, 122.4, 75.3, 69.1, 31.0, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{15}\text{NO}_2$: 242.1181, Found: 242.1179. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{16}\text{NO}_2$: 242.1181, Found: 242.1179.



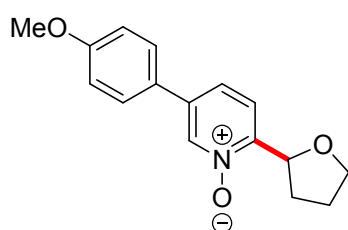
4-Phenyl-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3c: Yellow liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.24 (d, $J = 6.72$ Hz, 1H), 7.75 (s, 1H), 7.62 (d, $J = 7.60$ Hz, 2H), 7.49–7.46 (m, 2H), 7.43–7.40 (m, 2H), 5.39 (t, $J = 6.44$ Hz, 1H), 4.18–4.12 (m, 1H), 4.02–3.97 (m, 1H), 2.80–2.72 (m, 1H), 2.09–2.01 (m, 1H), 1.96–1.85 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 153.7, 139.4, 138.7, 136.8, 129.2, 128.9, 126.5, 121.5, 120.0, 75.4, 69.1, 31.0, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{16}\text{NO}_2$: 242.1181, Found: 242.1176.



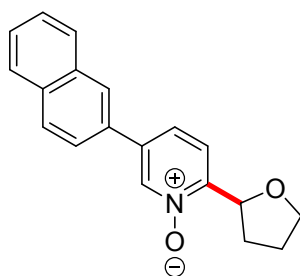
4-Methoxy-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3d: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.08 (d, $J = 6.84$ Hz, 1H), 7.03 (s, 1H), 6.70–6.69 (m, 1H), 5.31 (br, 1H), 4.09–4.08 (m, 1H), 3.95–3.94 (m, 1H), 3.84 (s, 3H), 2.72–2.71 (m, 1H), 2.00 (br, 1H), 1.85 (br, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 158.1, 154.8, 140.2, 110.4, 107.2, 75.4, 69.1, 55.9, 31.0, 25.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{10}\text{H}_{14}\text{NO}_3$: 196.0974, Found: 196.0971.



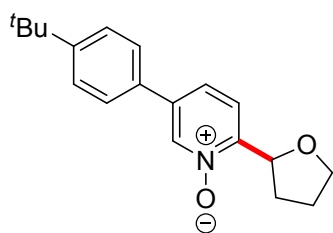
5-(4-Methoxyphenyl)-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3e: White solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.41 (s, 1H), 7.52 (d, $J = 8.24$ Hz, 1H), 7.47–7.41 (m, 3H), 6.98 (d, $J = 8.56$ Hz, 2H), 5.39 (t, $J = 5.82$ Hz, 1H), 4.15–4.10 (m, 1H), 4.00–3.94 (m, 1H), 3.84 (s, 3H), 2.73–2.68 (m, 1H), 2.06–1.99 (m, 1H), 1.92–1.83 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 160.3, 137.6, 137.1, 127.9, 127.6, 124.3, 122.2, 114.6, 75.2, 69.1, 55.3, 31.0, 25.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{16}\text{H}_{18}\text{NO}_3$: 272.1287, Found: 272.1285.



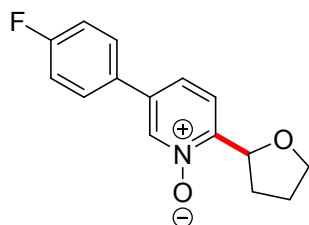
5-(Naphthalen-2-yl)-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3f: Colourless solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.60 (s, 1H), 8.01 (s, 1H), 7.96 (d, $J = 8.52$ Hz, 1H), 7.92–7.88 (m, 2H), 7.64 (dd, $J_1 = 8.56$ Hz, $J_2 = 1.28$ Hz, 1H), 7.61 (br, 2H), 7.57–7.53 (m, 2H), 5.46–5.43 (m, 1H), 4.19–4.14 (m, 1H), 4.04–3.99 (m, 1H), 2.80–2.71 (m, 1H), 2.11–2.03 (m, 1H), 1.98–1.88 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 152.3, 138.0, 137.8, 133.4, 133.2, 132.6, 129.2, 128.3, 127.7, 126.9, 126.8, 126.2, 124.8, 124.2, 122.5, 75.4, 69.2, 31.0, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{19}\text{H}_{18}\text{NO}_2$: 292.1338, Found: 292.1335.



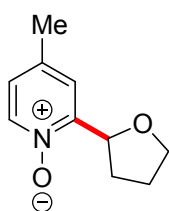
5-(4-(*tert*-Butyl)phenyl)-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3g: White solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.47 (s, 1H), 7.56 (d, $J = 8.24$ Hz, 1H), 7.52–7.47 (m, 5H), 5.43–5.39 (m, 1H), 4.17–4.11 (m, 1H), 4.02–3.97 (m, 1H), 2.76–2.71 (m, 1H), 2.10–2.01 (m, 1H), 1.97–1.90 (m, 2H), 1.36 (s, 9H); ^{13}C NMR (100 Mz, CDCl_3) δ : 152.3, 151.9, 137.9, 137.4, 132.4, 126.5, 126.2, 124.6, 122.3, 75.3, 69.1, 34.7, 31.2, 31.0, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{19}\text{H}_{24}\text{NO}_2$: 298.1807, Found: 298.1803.



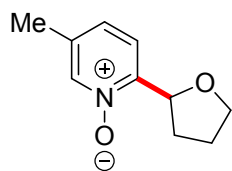
5-(4-Fluorophenyl)-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3h: Yellow solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.41 (s, 1H), 7.56 (d, $J = 8.20$ Hz, 1H), 7.51–7.48 (m, 2H), 7.42 (d, $J = 8.20$ Hz, 1H), 7.18–7.14 (m, 2H), 5.38 (t, $J = 6.38$ Hz, 1H), 4.15–4.10 (m, 1H), 4.01–3.95 (m, 1H), 2.75–2.69 (m, 1H), 2.11–2.00 (m, 1H), 1.95–1.84 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 163.3 (d, $J_{\text{C-F}} = 247.91$), 152.3, 137.4, 137.1, 131.5 (d, $J_{\text{C-F}} = 3.41$), 128.6 (d, $J_{\text{C-F}} = 8.31$), 124.4, 122.5, 116.3 (d, $J_{\text{C-F}} = 21.74$), 75.3, 69.1, 31.0, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{15}\text{FNO}_2$: 260.1087, Found: 260.1087.



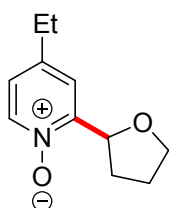
4-Methyl-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3i: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.08 (d, $J = 6.52$ Hz, 1H), 7.31 (s, 1H), 6.97–6.96 (m, 1H), 5.33 (t, $J = 6.60$ Hz, 1H), 4.12–4.07 (m, 1H), 3.98–3.92 (m, 1H), 2.74–2.65 (m, 1H), 2.34 (s, 3H), 2.06–1.96 (m, 1H), 1.92–1.78 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 153.0, 138.7, 137.6, 124.5, 123.0, 75.3, 69.1, 31.0, 25.6, 20.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{10}\text{H}_{14}\text{NO}_2$: 180.1025, Found: 180.1025.



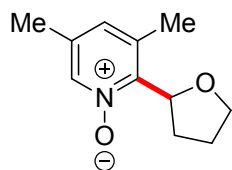
5-Methyl-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3j: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.06 (s, 1H), 7.38 (d, $J = 8.08$ Hz, 1H), 7.10 (d, $J = 8.04$ Hz, 1H), 5.33 (t, $J = 6.48$ Hz, 1H), 4.11–4.06 (m, 1H), 3.97–3.92 (m, 1H), 2.72–2.62 (m, 1H), 2.28 (s, 3H), 2.05–1.95 (m, 1H), 1.91–1.78 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 151.0, 139.2, 134.3, 127.3, 121.9, 75.3, 69.0, 31.0, 25.5, 17.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{10}\text{H}_{14}\text{NO}_2$: 180.1025, Found: 180.1024.



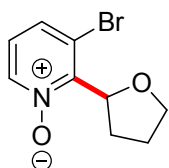
4-Ethyl-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3k: Yellow liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.11 (d, $J = 6.52$ Hz, 1H), 7.33 (s, 1H), 7.00 (d, $J = 5.16$ Hz, 1H), 5.35 (t, $J = 6.46$ Hz, 1H), 4.14–4.09 (m, 1H), 4.00–3.94 (m, 1H), 2.76–2.70 (m, 1H), 2.65 (q, $J = 7.53$ Hz, 2H), 2.07–1.97 (m, 1H), 1.93–1.80 (m, 2H), 1.25 (t, $J = 7.54$ Hz, 3H); ^{13}C NMR (100 Mz, CDCl_3) δ : 153.1, 143.6, 138.9, 123.2, 121.7, 75.3, 69.1, 30.9, 27.7, 25.6, 14.3. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{11}\text{H}_{16}\text{NO}_2$: 194.1181, Found: 194.1183.



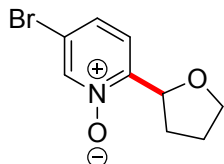
3,5-Dimethyl-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3l: Colourless solid. ^1H NMR (400 MHz, CDCl_3) δ : 7.94 (s, 1H), 6.85 (s, 1H), 5.73 (t, $J = 7.92$ Hz, 1H), 4.10–4.04 (m, 1H), 3.93–3.88 (m, 1H), 2.56–2.48 (m, 1H), 2.39 (s, 3H), 2.21 (s, 3H), 2.10–2.00 (m, 2H), 1.93–1.83 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 148.0, 137.4, 134.6, 133.2, 130.7, 75.5, 68.5, 29.9, 26.6, 18.9, 17.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{11}\text{H}_{16}\text{NO}_2$: 194.1181, Found: 194.1180.



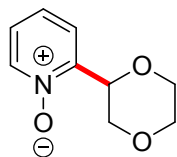
3-Bromo-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3m: Yellow liquid. ^1H NMR (400 MHz, CDCl_3) δ : 7.38 (d, $J = 5.96$ Hz, 1H), 7.20–7.17 (m, 2H), 5.37 (t, $J = 6.72$ Hz, 1H), 4.12–4.07 (m, 1H), 3.98–3.93 (m, 1H), 2.75–2.66 (m, 1H), 2.05–1.95 (m, 1H), 1.91–1.78 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 153.8, 148.9, 125.2, 124.2, 120.0, 75.6, 69.0, 31.0, 25.6. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_9\text{H}_{11}\text{BrNO}_2$: 243.9973, Found: 243.9972.



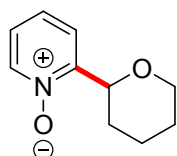
5-Bromo-2-(tetrahydrofuran-2-yl)pyridine 1-oxide

3m': Yellow liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.33 (s, 1H), 7.38 (br, 2H), 5.24 (t, $J = 6.42$ Hz, 1H), 4.10–4.05 (m, 1H), 3.97–3.91 (m, 1H), 2.71–2.61 (m, 1H), 2.06–1.95 (m, 1H), 1.89–1.76 (m, 2H); ^{13}C NMR (100 Mz, CDCl_3) δ : 153.0, 140.6, 128.6, 122.8, 117.9, 75.1, 69.1, 30.7, 25.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_9\text{H}_{11}\text{BrNO}_2$: 243.9973, Found: 243.9966.



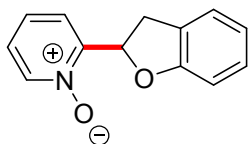
2-(1,4-Dioxan-2-yl)pyridine 1-oxide

3o: Colourless solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.19 (d, $J = 6.36$ Hz, 1H), 7.56 (d, $J = 7.76$ Hz, 1H), 7.32–7.29 (m, 1H), 7.23–7.19 (m, 1H), 5.31–5.28 (m, 1H), 4.52–4.83 (m, 1H), 3.97 (d, $J = 6.24$ Hz, 2H), 3.84–3.81 (m, 1H), 3.75–3.67 (m, 1H), 3.24–3.19 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 148.9, 139.3, 125.9, 124.5, 123.9, 72.2, 68.6, 67.2, 66.4. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_9\text{H}_{12}\text{NO}_3$: 182.0817, Found: 182.0815.



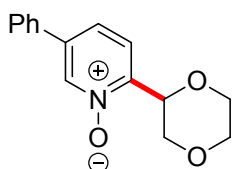
2-(Tetrahydro-2H-pyran-2-yl)pyridine 1-oxide

3p: Colourless solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.19 (d, $J = 6.40$ Hz, 1H), 7.55 (dd, $J = 7.84$ Hz, $J = 1.44$ Hz, 1H), 7.31–7.30 (m, 1H), 7.19–7.15 (m, 1H), 5.00–4.98 (m, 1H), 4.18–4.15 (m, 1H), 3.71–3.65 (m, 1H), 2.45–2.42 (m, 1H), 1.94–1.91 (m, 1H), 1.82–1.79 (m, 2H), 1.64–1.61 (m, 1H), 1.26–1.20 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 139.2, 126.0, 123.7, 123.1, 73.7, 68.9, 29.6, 25.9, 23.1. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{10}\text{H}_{14}\text{NO}_2$: 180.1025, Found: 180.1028.



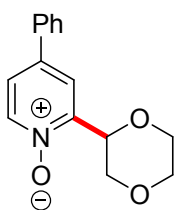
2-(2,3-Dihydrobenzofuran-2-yl)pyridine 1-oxide

3q: Yellow solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.28 (d, $J = 6.12$ Hz, 1H), 7.54 (dd, $J_1 = 7.72$ Hz, $J_2 = 1.28$ Hz, 1H), 7.32–7.28 (m, 1H), 7.26–7.23 (m, 1H), 7.20–7.17 (m, 2H), 6.96 (d, $J = 8.28$ Hz, 1H), 6.93–6.90 (m, 1H), 6.20–6.16 (m, 1H), 4.04–3.97 (m, 1H), 3.19–3.13 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 159.0, 139.5, 128.2, 126.1, 125.9, 125.3, 124.4, 122.7, 121.4, 109.5, 78.0, 35.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{13}\text{H}_{12}\text{NO}_2$: 214.0868, Found: 214.0861.



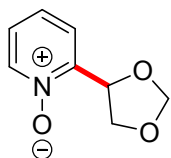
2-(1,4-Dioxan-2-yl)-5-phenylpyridine 1-oxide

3r: Colourless solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.44 (s, 1H), 7.60 (d, $J = 8.24$ Hz, 1H), 7.53–7.44 (m, 6H), 5.36–5.33 (m, 1H), 4.56–4.52 (m, 1H), 3.99 (d, $J = 6.12$ Hz, 2H), 3.86–3.83 (m, 1H), 3.77–3.68 (m, 1H), 3.29–3.24 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 147.1, 138.7, 137.4, 135.1, 129.3, 129.1, 126.8, 124.5, 123.7, 72.2, 68.7, 67.2, 66.4. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{16}\text{NO}_3$: 258.1130, Found: 258.1124.



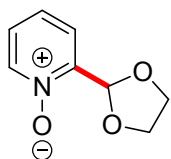
2-(1,4-Dioxan-2-yl)-4-phenylpyridine 1-oxide

3s: White solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.23 (d, $J = 6.76$ Hz, 1H), 7.81–7.80 (m, 1H), 7.63 (d, $J = 7.32$ Hz, 2H), 7.51–7.47 (m, 2H), 7.45–7.41 (m, 2H), 5.36–5.34 (m, 1H), 4.58–4.55 (m, 1H), 4.01 (d, $J = 6.12$ Hz, 2H), 3.87–3.84 (m, 1H), 3.79–3.71 (m, 1H), 3.31–3.26 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 148.7, 139.3, 138.7, 136.5, 129.2, 129.0, 126.5, 122.1, 121.5, 72.4, 68.8, 67.3, 66.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{16}\text{NO}_3$: 258.1130, Found: 258.1127.



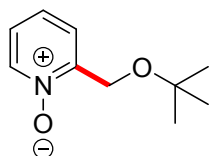
2-(1,3-Dioxolan-4-yl)pyridine 1-oxide

3t: Yellow solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.19 (d, $J = 6.48$ Hz, 1H), 7.52 (d, $J = 7.80$ Hz, 1H), 7.32–7.29 (m, 1H), 7.24–7.20 (m, 1H), 5.40 (d, $J = 6.16$ Hz, 1H), 5.20 (s, 1H), 5.03 (s, 1H), 4.48–4.44 (m, 1H), 3.93–3.90 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 150.9, 139.0, 125.9, 124.4, 122.6, 95.5, 70.8 (d, $J = 232.18$), 65.4 (d, $J = 13.83$). HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_8\text{H}_{10}\text{NO}_3$: 168.0661, Found: 168.0665.



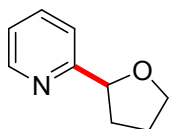
2-(1,3-Dioxolan-2-yl)pyridine 1-oxide

3t' : Yellow solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.24–8.22 (m, 1H), 7.56–7.54 (m, 1H), 7.26 (br, 2H), 6.36 (s, 1H), 4.09 (br, 4H); ^{13}C NMR (100 Mz, CDCl_3) δ : 147.5, 139.8, 125.8, 125.3, 123.6, 97.3, 65.4. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_8\text{H}_{10}\text{NO}_3$: 168.0661, Found: 168.0658.



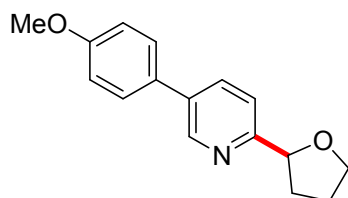
2-(tert-Butoxymethyl)pyridine 1-oxide

3u: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.23 (br, 1H), 7.61 (d, $J = 7.00$ Hz, 1H), 7.30–7.27 (m, 1H), 7.18 (br, 1H), 4.71 (s, 2H), 1.31 (s, 9H); ^{13}C NMR (100 Mz, CDCl_3) δ : 138.8, 125.8, 123.4, 123.3, 74.3, 58.8, 27.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{10}\text{H}_{16}\text{NO}_2$: 182.1181, Found: 182.1179.



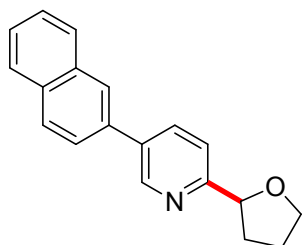
2-(Tetrahydrofuran-2-yl)pyridine

4a: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.52 (d, $J = 3.36$ Hz, 1H), 7.66–7.62 (m, 1H), 7.41 (d, $J = 7.80$ Hz, 1H), 7.14–7.11 (m, 1H), 5.00 (t, $J = 6.06$ Hz, 1H), 4.11–4.06 (m, 1H), 3.98–3.93 (m, 1H), 2.41–2.38 (m, 1H), 1.97–1.96 (m, 3H); ^{13}C NMR (100 Mz, CDCl_3) δ : 162.9, 148.9, 136.5, 121.9, 119.7, 81.2, 68.9, 32.9, 25.7. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_9\text{H}_{12}\text{NO}$: 150.0919, Found: 150.0921.



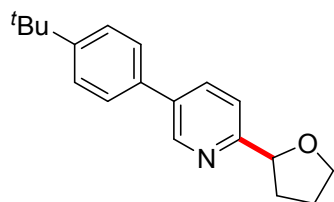
5-(4-Methoxyphenyl)-2-(tetrahydrofuran-2-yl)pyridine

4e: White solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.75 (s, 1H), 7.82 (d, $J = 8.00$ Hz, 1H), 7.52–7.47 (m, 3H), 7.01 (d, $J = 8.20$ Hz, 2H), 5.07 (t, $J = 6.16$ Hz, 1H), 4.16–4.11 (m, 1H), 4.03–3.98 (m, 1H), 3.86 (s, 3H), 2.49–2.39 (m, 1H), 2.09–2.00 (m, 3H); ^{13}C NMR (100 Mz, CDCl_3) δ : 161.0, 159.6, 147.1, 134.6, 134.4, 130.2, 128.1, 119.7, 114.5, 81.2, 69.0, 55.3, 33.0, 25.8. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{16}\text{H}_{18}\text{NO}_2$: 256.1338, Found: 256.1340.



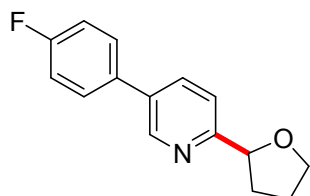
5-(Naphthalen-2-yl)-2-(tetrahydrofuran-2-yl)pyridine

4f: White solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.92 (s, 1H), 8.05 (s, 1H), 8.02–7.89 (m, 4H), 7.72 (d, $J = 8.36$ Hz, 1H), 7.58–7.53 (m, 3H), 5.14–5.10 (m, 1H), 4.20–4.15 (m, 1H), 4.06–4.01 (m, 1H), 2.53–2.47 (m, 1H), 2.13–2.03 (m, 3H); ^{13}C NMR (100 Mz, CDCl_3) δ : 161.9, 147.7, 135.2, 135.1, 135.0, 133.6, 132.8, 128.8, 128.2, 127.7, 126.6, 126.3, 126.0, 125.1, 119.8, 81.2, 69.1, 33.1, 25.8. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{19}\text{H}_{18}\text{NO}$: 276.1388, Found: 276.1393.



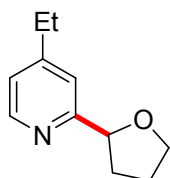
5-(4-(*tert*-Butyl)phenyl)-2-(tetrahydrofuran-2-yl)pyridine

4g: Colourless solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.79 (s, 1H), 7.87 (d, $J = 7.88$ Hz, 1H), 7.55–7.50 (m, 5H), 5.08 (t, $J = 6.46$ Hz, 1H), 4.18–4.12 (m, 1H), 4.04–3.99 (m, 1H), 2.52–2.41 (m, 1H), 2.11–2.01 (m, 3H), 1.38 (s, 9H); ^{13}C NMR (100 Mz, CDCl_3) δ : 161.4, 151.0, 147.4, 134.9, 134.8, 134.8, 126.7, 126.0, 119.8, 81.2, 69.1, 34.6, 33.0, 31.3, 25.8. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{19}\text{H}_{24}\text{NO}$: 282.1858, Found: 282.1856.



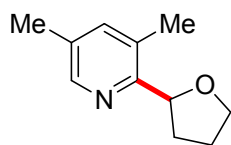
5-(4-Fluorophenyl)-2-(tetrahydrofuran-2-yl)pyridine

4h: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.73 (s, 1H), 7.83 (d, $J = 8.08$ Hz, 1H), 7.56–7.51 (m, 3H), 7.19–7.15 (m, 2H), 5.08 (t, $J = 6.32$ Hz, 1H), 4.17–4.12 (m, 1H), 4.04–3.99 (m, 1H), 2.50–2.41 (m, 1H), 2.09–1.98 (m, 3H); ^{13}C NMR (100 Mz, CDCl_3) δ : 162.8 (d, $J_{\text{C-F}} = 247.82$), 161.8, 147.3, 134.8, 134.0 (d, $J_{\text{C-F}} = 17.60$), 128.7 (dd, $J_{\text{C-F}} = 8.07$, $J_{\text{C-F}} = 1.90$), 119.8 (d, $J_{\text{C-F}} = 1.84$), 116.1, 115.9 (d, $J_{\text{C-F}} = 1.89$), 81.1, 69.1 (d, $J_{\text{C-F}} = 1.80$), 33.0 (d, $J_{\text{C-F}} = 1.78$), 25.8 (d, $J_{\text{C-F}} = 1.89$). HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{15}\text{FNO}$: 244.1138, Found: 244.1132.



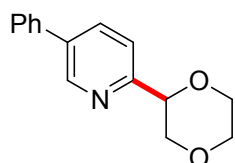
4-Ethyl-2-(tetrahydrofuran-2-yl)pyridine

4k: Colourless liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.38 (d, $J = 4.84$ Hz, 1H), 7.24 (s, 1H), 6.95 (d, $J = 4.60$ Hz, 1H), 4.95 (t, $J = 6.30$ Hz, 1H), 4.10–4.04 (m, 1H), 3.96–3.90 (m, 1H), 2.60 (q, $J = 7.59$ Hz, 2H), 2.43–2.32 (m, 1H), 1.94 (br, 3H), 1.20 (q, $J = 7.58$ Hz, 3H); ^{13}C NMR (100 Mz, CDCl_3) δ : 162.6, 153.5, 148.8, 121.6, 119.2, 81.2, 68.8, 32.9, 28.2, 25.6, 14.2. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{11}\text{H}_{16}\text{NO}$: 178.1232, Found: 178.1234.



3,5-Dimethyl-2-(tetrahydrofuran-2-yl)pyridine

4l: Yellow liquid. ^1H NMR (400 MHz, CDCl_3) δ : 8.26 (s, 1H), 7.25 (s, 1H), 5.10 (t, $J = 7.08$ Hz, 1H), 4.15–4.10 (m, 1H), 3.94–3.89 (m, 1H), 2.34 (s, 3H), 2.27 (s, 3H), 2.24–2.17 (m, 2H), 2.15–2.09 (m, 1H), 2.06–1.96 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 155.5, 147.0, 138.8, 131.6, 130.5, 78.4, 68.6, 30.5, 26.2, 18.2, 17.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{11}\text{H}_{16}\text{NO}$: 178.1232, Found: 178.1231.



2-(1,4-Dioxan-2-yl)-5-phenylpyridine

4r: White solid. ^1H NMR (400 MHz, CDCl_3) δ : 8.79 (s, 1H), 7.91 (d, $J = 7.92$ Hz, 1H), 7.58 (d, $J = 7.48$ Hz, 2H), 7.54 (d, $J = 8.12$ Hz, 1H), 7.51–7.47 (m, 2H), 7.43–7.40 (m, 1H), 4.83–4.80 (m, 1H), 4.21–4.18 (m, 1H), 4.03–3.95 (m, 2H), 3.86–3.75 (m, 2H), 3.62–3.57 (m, 1H); ^{13}C NMR (100 Mz, CDCl_3) δ : 156.6, 147.5, 137.6, 135.8, 135.1, 129.1, 128.1, 127.1, 120.7, 78.0, 71.2, 67.0, 66.4. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. For $\text{C}_{15}\text{H}_{16}\text{NO}_2$: 242.1181, Found: 242.1185.

4. ^1H and ^{13}C NMR spectra of the products

