Supporting Information

A facile one-pot synthesis of *N*-difluoromethyl-2-pyridones

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Experimental section

General: ^1H NMR and ^{13}C NMR spectra were recorded on MERCURY-400 (Varian, ^1H 400 MHz, ^{13}C 100 MHz) or JMN-AL400 (JEOL, ^1H 400 MHz, ^{13}C 100 MHz) in CDCl_3 with chemical shifts referenced to internal standards (^1H : TMS (0 ppm), ^{13}C : CHCl_3 (77.1 ppm)). EI mass spectra were recorded on JMS-700V (JEOL) spectrometer, and ESI mass spectra were recorded on Q-Tof2 (micromass) spectrometer. All materials were obtained from commercial suppliers and used without further purification. Flash-chromatography was performed with a KP-SilTM Silica (Biotage) under the indicated conditions. Analytical HPLC analyses were performed using a Hitachi Model D-7000 under the following conditions: YMC-Pack Pro C18 (Size: 150×4.6 mmI.D., Particle: S-5 μm , 12 nm) with liner gradient system of 10% to 90% CH_3CN in 0.1% aqueous H_3PO_4 over 15 min at a flow rate of 1.0 mL/min. The starting materials **1**, **4a–c**, **4e–i**, and **4k–l** were commercially available compounds. **4d** and **4j** were prepared according to the literature procedure: **4d**,¹ **4j**.²

Difluoromethylation of 5-bromopyridin-2(1H)-one (1) with sodium chlorodifluoroacetate (Scheme 1). To a stirred solution of **1** (500 mg, 2.87 mmol) in anhydrous acetonitrile (15 mL) was added sodium chlorodifluoroacetate (524 mg, 3.44 mmol), and the mixture was heated to reflux for 20 h under a nitrogen atmosphere. The reaction was quenched by addition of saturated aqueous NH_4Cl after cooling down to room temperature, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 20% ethyl acetate in hexanes to give **2a** (53 mg, 8% yield) as colorless prisms and **3** (462 mg, 72% yield) as a colorless oil.

5-Bromo-1-(difluoromethyl)pyridin-2(1H)-one (2a): mp 74–76 °C; ^1H NMR (CDCl_3) δ 6.49 (1H, d, J = 10.0 Hz), 7.40 (1H, dd, J = 2.8, 10.0 Hz), 7.56 (1H, d, J = 2.8 Hz), 7.61 (1H, t, J = 59.6 Hz); ^{13}C NMR (CDCl_3) δ 99.6, 107.1 (t, J = 252 Hz), 122.9, 129.2 (t, J = 4 Hz),

144.1, 159.2; HRMS (ESI): m/z calcd. for $C_6H_5NOF_2Br$ $[M+H]^+$: 223.9523; found: 223.9526.

5-Bromo-2-(difluoromethoxy)pyridine (3): 1H NMR ($CDCl_3$) δ 6.83 (1H, d, $J = 8.8$ Hz), 7.40 (1H, t, $J = 72.7$ Hz), 7.82 (1H, dd, $J = 2.2, 8.8$ Hz), 8.25 (1H, d, $J = 2.2$ Hz); ^{13}C NMR ($CDCl_3$) δ 113.1, 114.0 (t, $J = 255$ Hz), 115.5, 142.7, 147.9, 157.9; HRMS (ESI): m/z calcd. for $C_6H_5NOF_2Br$ $[M+H]^+$: 223.9523; found: 223.9515.

N-[5-bromo-1-(difluoromethyl)pyridin-2(1H)-ylidene]acetamide (5): To a stirred solution of **4a** (1.00 g, 4.65 mmol) in anhydrous acetonitrile (20 mL) was added sodium chlorodifluoroacetate (851 mg, 5.58 mmol), and the mixture was heated to reflux for 18 h under a nitrogen atmosphere. The resulting reaction mixture was concentrated, and the residue was partitioned between saturated aqueous $NaHCO_3$ and ethyl acetate. The layers were separated, and the organic layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 40% ethyl acetate in hexanes to give **5** (1.17 g, 95% yield) as a pale-yellow amorphous. 1H NMR ($CDCl_3$) δ 2.20 (3H, s), 7.38 (1H, dd, $J = 2.4, 10.0$ Hz), 7.68 (1H, d, $J = 2.4$ Hz), 7.79 (1H, d, $J = 10.0$ Hz), 8.00 (1H, t, $J = 60.0$ Hz); ^{13}C NMR ($CDCl_3$) δ 28.2, 107.4 (t, $J = 256$ Hz), 121.3, 129.3 (t, $J = 4$ Hz), 142.9, 144.4, 154.2, 182.0; HRMS (ESI): m/z calcd. for $C_8H_8N_2OF_2Br$ $[M+H]^+$: 264.9788; found: 264.9789.

Hydrolysis of 5 with 6 N HCl (Scheme 2). A solution of **5** (400 mg, 1.51 mmol) in 6 N hydrochloric acid (8 mL) was heated to reflux for 0.5 h. The reaction mixture was cooled to 0 °C, neutralized with potassium carbonate, and extracted with ethyl acetate. The organic

layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 50% ethyl acetate in hexanes to give **6** (280 mg, 83% yield) as a brown oil.

5-Bromo-1-(difluoromethyl)pyridin-2(1H)-imine (6): ^1H NMR (CDCl_3) δ 6.17 (1H, d, $J = 10.2$ Hz), 6.45 (1H, brs), 6.73 (1H, dd, $J = 2.4, 10.2$ Hz), 7.25 (1H, d, $J = 2.4$ Hz), 7.69 (1H, t, $J = 60.4$ Hz); ^{13}C NMR (CDCl_3) δ 96.8, 107.5 (t, $J = 252$ Hz), 123.3, 128.0 (t, $J = 4$ Hz), 137.3, 156.4; HRMS (EI): m/z calcd. for $\text{C}_6\text{H}_5\text{N}_2\text{OF}_2\text{Br}$ M^{+} : 221.9604; found: 221.9609.

Hydrolysis of 5 with 1% aqueous KHSO_4 (Scheme 2). To a stirred solution of **5** (400 mg, 1.51 mmol) in acetonitrile (8 mL) was added 1% aqueous KHSO_4 (8 mL), and the mixture was heated to reflux for 3 h. The mixture was concentrated, and the residue was partitioned between 0.5 N hydrochloric acid and ethyl acetate. The layers were separated, and the organic layer was washed with saturated aqueous NaHCO_3 and brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 30% ethyl acetate in hexanes to give **2a** (277 mg, 82% yield) as colorless prisms.

General Procedure for Synthesis of 5-bromo-1-(difluoromethyl)pyridin-2(1H)-one (2a) (entry 2, Table 2). To a stirred solution of **4a** (500 mg, 2.32 mmol) in anhydrous acetonitrile (10 mL) were added sodium chlorodifluoroacetate (424 mg, 2.78 mmol) and 18-crown-6 (122 mg, 0.46 mmol), and the mixture was heated to reflux for 5 h under a nitrogen atmosphere. To the resulting mixture was added 1% aqueous KHSO_4 (10 mL) at room temperature, and the mixture was heated to reflux for 1.5 hours. The reaction mixture was concentrated, and the residue was partitioned between 0.5 N hydrochloric acid and ethyl acetate. The layers were separated, and the organic layer was washed with aqueous NaHCO_3 and brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 30% ethyl acetate in hexanes to give **2a** (440 mg, 85%

yield) as colorless prisms.

Methyl 1-(difluoromethyl)-2-oxo-1,2-dihydropyridine-4-carboxylate (2b): Following the general procedure for **2a** from **4a**, the title compound **2b** was obtained from **4b**. The flash-chromatography was performed with 0% to 40% ethyl acetate in hexanes, and **2b** (78% yield) was obtained as a colorless powder. mp 114–115 °C; ^1H NMR (CDCl_3) δ 3.94 (3H, s), 6.77 (1H, dd, $J = 1.2, 7.2$ Hz), 7.19–7.20 (1H, m), 7.51 (1H, d, $J = 7.2$ Hz), 7.66 (1H, t, $J = 59.9$ Hz); ^{13}C NMR (CDCl_3) δ 53.3, 105.6, 107.4 (t, $J = 252$ Hz), 124.0, 129.9 (t, $J = 4$ Hz), 141.9, 161.0, 164.3; HRMS (ESI): m/z calcd. for $\text{C}_8\text{H}_8\text{NO}_3\text{F}_2$ $[\text{M}+\text{H}]^+$: 204.0472; found: 204.0471.

Methyl 1-(difluoromethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (2c): Following the general procedure for **2a** from **4a**, the title compound **2c** was obtained from **4c**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2c** (79% yield) was obtained as a colorless powder. mp 109–110 °C; ^1H NMR (CDCl_3) δ 3.90 (3H, s), 6.57 (1H, dd, $J = 0.8, 9.6$ Hz), 7.67 (1H, t, $J = 59.9$ Hz), 7.91 (1H, dd, $J = 2.4, 9.6$ Hz), 8.33 (1H, d, $J = 2.4$ Hz); ^{13}C NMR (CDCl_3) δ 52.5, 107.3 (t, $J = 253$ Hz), 111.3, 120.8, 135.0 (t, $J = 3$ Hz), 139.7, 160.3, 163.6; HRMS (ESI): m/z calcd. for $\text{C}_8\text{H}_8\text{NO}_3\text{F}_2$ $[\text{M}+\text{H}]^+$: 204.0472; found: 204.0477.

1-(Difluoromethyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (2d): Following the

general procedure for **2a** from **4a**, the title compound **2d** was obtained from **4d**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2d** (67% yield) was obtained as a colorless powder. mp 146–148 °C; ^1H NMR (CDCl_3) δ 6.63 (1H, d, $J = 9.6$ Hz), 7.40–7.46 (1H, m), 7.59 (1H, t, $J = 59.3$ Hz), 7.95 (1H, d, $J = 2.4$ Hz); ^{13}C NMR (CDCl_3) δ 93.9, 107.0 (t, $J = 256$ Hz), 115.0, 123.2, 137.8 (t, $J = 3$ Hz), 139.8, 158.9; HRMS (EI): m/z calcd. for $\text{C}_7\text{H}_4\text{N}_2\text{OF}_2$ $\text{M}^{+\bullet}$: 170.0292; found: 170.0294.

1-(Difluoromethyl)-5-nitropyridin-2(1H)-one (2e): Following the general procedure for **2a** from **4a**, the title compound **2e** was obtained from **4e**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2e** (53% yield) was obtained as a pale-yellow powder. mp 69–71 °C; ^1H NMR (CDCl_3) δ 6.62 (1H, d, $J = 10.4$ Hz), 7.62 (1H, t, $J = 59.3$ Hz), 8.13 (1H, dd, $J = 3.0, 10.4$), 8.71 (1H, d, $J = 3.0$ Hz); ^{13}C NMR (CDCl_3) δ 107.3 (t, $J = 257$ Hz), 121.5, 132.1 (t, $J = 4$ Hz), 134.5, 159.4; HRMS (EI): m/z calcd. for $\text{C}_6\text{H}_4\text{N}_2\text{O}_3\text{F}_2$ $\text{M}^{+\bullet}$: 190.0190; found: 190.0195.

1-(Difluoromethyl)-4-methylpyridin-2(1H)-one (2f): Following the general procedure for **2a** from **4a**, the title compound **2f** was obtained from **4f**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2f** (62% yield) was obtained as colorless prisms. mp 57–59 °C; ^1H NMR (CDCl_3) δ 2.21 (3H, s), 6.14 (1H, dd, $J = 2.0, 7.6$ Hz), 6.34 (1H, s), 7.34 (1H, d, $J = 7.6$ Hz), 7.67 (1H, t, $J = 59.9$ Hz); ^{13}C NMR (CDCl_3) δ 21.7, 107.4 (t, $J = 250$ Hz), 109.7, 119.4, 128.1 (t, $J = 3$ Hz), 153.0, 160.8; HRMS (ESI): m/z calcd. for $\text{C}_7\text{H}_8\text{NOF}_2$ $[\text{M}+\text{H}]^+$: 160.0574; found: 160.0566.

1-(Difluoromethyl)-5-methylpyridin-2(1H)-one (2g): Following the general procedure for **2a** from **4a**, the title compound **2g** was obtained from **4g**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2g** (71% yield) was obtained as a colorless oil. ^1H NMR (CDCl_3) δ 2.11 (3H, d, $J = 1.2$ Hz), 6.50 (1H, d, $J = 9.4$ Hz), 7.20 (1H, s), 7.25 (1H, dd, $J = 2.4, 9.4$ Hz), 7.68 (1H, t, $J = 60.2$ Hz); ^{13}C NMR (CDCl_3) δ 17.3, 107.5 (t, $J = 250$ Hz), 116.2, 121.3, 126.2 (t, $J = 3$ Hz), 144.2, 160.6; HRMS (ESI): m/z calcd. for $\text{C}_7\text{H}_8\text{NOF}_2$ $[\text{M}+\text{H}]^+$: 160.0574; found: 160.0561.

1-(Difluoromethyl)pyridin-2(1H)-one (2h): Following the general procedure for **2a** from **4a**, the title compound **2h** was obtained from **4h**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2h** (50% yield) was obtained as a colorless oil. ^1H NMR (CDCl_3) δ 6.30 (1H, t, $J = 6.8$ Hz), 6.56 (1H, d, $J = 9.0$ Hz), 7.39 (1H, ddd, $J = 2.4, 6.8, 9.0$ Hz), 7.43–7.46 (1H, m), 7.70 (1H, t, $J = 60.3$ Hz); ^{13}C NMR (CDCl_3) δ 107.1, 107.5 (t, $J = 250$ Hz), 121.9, 129.5 (t, $J = 4$ Hz), 141.1, 161.1; HRMS (ESI): m/z calcd. for $\text{C}_6\text{H}_6\text{NOF}_2$ $[\text{M}+\text{H}]^+$: 146.0417; found: 146.0408.

1-(Difluoromethyl)-3-methylpyridin-2(1H)-one (2i): Following the general procedure for **2a** from **4a**, the title compound **2i** was obtained from **4i**. The flash-chromatography was performed with 0% to 30% ethyl acetate in hexanes, and **2i** (39% yield) was obtained as a pale-yellow oil. ^1H NMR (CDCl_3) δ 2.13–2.15 (3H, m), 6.22 (1H, t, $J = 7.2$ Hz), 7.23–7.26 (1H, m), 7.32–7.36 (1H, m), 7.74 (1H, t, $J = 60.5$ Hz); ^{13}C NMR (CDCl_3) δ 16.9, 106.9, 107.8 (t, $J = 251$ Hz), 126.8 (t, $J = 4$ Hz), 131.0, 137.9, 161.9; HRMS (ESI): m/z calcd. for $\text{C}_7\text{H}_8\text{NOF}_2$ $[\text{M}+\text{H}]^+$: 160.0574; found: 160.0567.

Methyl 1-(difluoromethyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (2j): Following the general procedure for **2a** from **4a**, the title compound **2j** was obtained from **4j**. The flash-chromatography was performed with 0% to 40% ethyl acetate in hexanes, and **2j** (19% yield) was obtained as colorless prisms. mp 54–55 °C; ^1H NMR (CDCl_3) δ 3.92 (3H, s), 6.41 (1H, t, $J = 6.9$ Hz), 7.68 (1H, dd, $J = 2.2, 6.9$ Hz), 7.74 (1H, t, $J = 59.9$ Hz), 8.22 (1H, dd, $J = 2.2, 6.9$ Hz); ^{13}C NMR (CDCl_3) δ 52.7, 106.1, 107.4 (t, $J = 253$ Hz), 122.5, 134.4 (t, $J = 3$ Hz), 146.5, 158.0, 164.5; HRMS (ESI): m/z calcd. for $\text{C}_8\text{H}_8\text{NO}_3\text{F}_2$ $[\text{M}+\text{H}]^+$: 204.0472; found: 204.0461.

1-(Difluoromethyl)quinolin-2(1H)-one (2l): Following the general procedure for **2a** from **4a**, the title compound **2l** was obtained from **4l**. The flash-chromatography was performed with 0% to 20% ethyl acetate in hexanes, and **2l** (73% yield) was obtained as a colorless powder. mp 104–106 °C; ^1H NMR (CDCl_3) δ 6.59 (1H, d, $J = 9.8$ Hz), 7.29–7.33 (1H, m), 7.55 (1H, d, $J = 7.6$ Hz), 7.55–7.58 (1H, m), 7.70 (1H, d, $J = 9.8$ Hz), 7.80–7.90 (1H, m), 8.15 (1H, t, $J = 58.3$ Hz); ^{13}C NMR (CDCl_3) δ 109.9 (t, $J = 250$ Hz), 116.5 (t, $J = 7$ Hz), 120.8, 124.1, 129.2, 131.0, 135.1, 142.0, 161.7; HRMS (ESI): m/z calcd. for $\text{C}_{10}\text{H}_8\text{NOF}_2$ $[\text{M}+\text{H}]^+$: 196.0574; found: 196.0574.

Supplementary data for footnote 12

Table 1. Difluoromethylation of 5-bromopyridin-2(1*H*)-one (**1**)

1		2a	3	7	
entry	reagent	reaction time (h)	2a ^a (%)	3 ^a (%)	7 ^a (%)
1 ^b	BrCF ₂ COOEt	1.5	18	22	3
2 ^{c,d}	FSO ₂ CF ₂ COOH	4.5	trace	77	0

^a Isolated yield. ^b 2.0 equiv of K₂CO₃ was added as a base.

^c The reaction was conducted at rt. ^d 0.2 equiv of Na₂SO₄ was added.

Difluoromethylation of 5-bromopyridin-2(1*H*)-one (1**) with ethyl bromodifluoroacetate (entry 1, Table 1).** To a stirred solution of **1** (1.00 g, 5.75 mmol) in anhydrous acetonitrile (30 mL) were added ethyl bromodifluoroacetate (882 μ L, 6.88 mmol) and K₂CO₃ (0.95 g, 6.88 mmol), and the mixture was heated to reflux for 1.5 h under a nitrogen atmosphere. The resulting mixture was concentrated, and the residue was partitioned between H₂O and ethyl acetate. The layers were separated, and the organic layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 20% ethyl acetate in hexanes to give **2a** (0.23 g, 18% yield) as colorless prisms, **3** (0.28 g, 22% yield) as a colorless oil, and **7** (0.047 g, 3% yield) as a colorless oil.

Ethyl [(5-bromopyridin-2-yl)oxy](difluoro)acetate (7**):** ¹H NMR (CDCl₃) δ 1.30 (3H, t, *J* = 7.2 Hz), 4.35 (2H, q, *J* = 7.2 Hz), 6.90 (1H, d, *J* = 8.8 Hz), 7.84 (1H, dd, *J* = 2.4, 8.8 Hz), 8.19 (1H, d, *J* = 2.4 Hz); ¹³C NMR (CDCl₃) δ 13.8, 63.6, 113.3, 113.7 (t, *J* = 268 Hz), 115.9, 142.8, 147.5, 159.5, 159.9; HRMS (ESI): *m/z* calcd. for C₉H₉NO₃F₂Br [M+H]⁺: 295.9734; found: 295.9725.

Difluoromethylation of 5-bromopyridin-2(1*H*)-one (1**) with 2,2-difluoro-2-(fluorosulfonyl)acetic acid (entry 2, Table 1).** To a stirred solution of **1**

(1.00 g, 5.75 mmol) in anhydrous acetonitrile (30 mL) were added 2,2-difluoro-2-(fluorosulfonyl)acetic acid (713 μ L, 6.90 mmol) and sodium sulfate (82 mg, 0.58 mmol), and the mixture was stirred at room temperature for 4.5 h under a nitrogen atmosphere. The reaction was quenched by addition of saturated aqueous NaHCO_3 , and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 10% ethyl acetate in hexanes to give **3** (0.99 g, 77% yield) as a colorless oil.

Supplementary data for footnote 15

Scheme 1. Difluoromethylation of 5-bromopyridin-2-amine (**8**)

5-Bromo-1-(difluoromethyl)pyridin-2(1H)-imine (6): To a stirred solution of **8** (3.0 g, 17.3 mmol) in anhydrous acetonitrile (120 mL) was added sodium chlorodifluoroacetate (5.3 g, 34.6 mmol), and the mixture was heated to reflux for 15 h under a nitrogen atmosphere. The reaction was quenched by saturated aqueous NaHCO_3 after cooling down to room temperature, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 50% ethyl acetate in hexanes to give **6** (2.14 g, 55% yield) as a brown oil, and the substrate **8** (0.78 g, 26% yield) was recovered.

Table 2. Hydrolysis of 5-bromo-1-(difluoromethyl)pyridin-2(1H)-imine (**6**)

entry	conditions	2a ^a (%)	8 ^a (%)	6 ^a (%)
1	5 N KOH, 100 °C, 2 h	0	63	0
2	6 N HCl, 100 °C, 16 h	0	0	95
3	NaNO ₂ , 40% H ₂ SO ₄ , 0 °C–rt, 12 h, then 100 °C, 0.5 h	32	0	33

^a Isolated yield.

Hydrolysis of 6 with 5 N KOH (entry 1, Table 2): A solution of **6** (500 mg, 2.24 mmol) in 5 N potassium hydroxide (5 mL) was stirred at 100 °C for 2 h. The reaction mixture was cooled to 0 °C, neutralized with 3 N hydrochloric acid, and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 40% ethyl acetate in hexanes to give **8** (244 mg, 63% yield) as a pale orange solid.

Hydrolysis of 6 with 6 N HCl (entry 2, Table 2): A solution of **6** (500 mg, 2.24 mmol) in 6 N hydrochloric acid (5 mL) was stirred at 100 °C for 16 h. The reaction mixture was cooled to 0 °C, neutralized with saturated aqueous NaHCO₃, and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The substrate **6** (473 mg, 95% yield) was recovered.

Hydrolysis of 6 with 40% H₂SO₄ and NaNO₂ (entry 3, Table 2): To a stirred solution of **6** (500 mg, 2.24 mmol) in 40% sulfuric acid (5 mL) was added dropwise sodium nitrite (773 mg, 11.21 mmol) in H₂O (2 mL) at 0 °C. The mixture was warmed slowly to room temperature and stirred for 12 h. The reaction mixture was then stirred at 100 °C for 30 min. The resulting solution was cooled to 0 °C, neutralized with potassium carbonate, and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium

sulfate, and concentrated. The residue was purified by flash-chromatography with 0% to 50% ethyl acetate in hexanes to give **2a** (161 mg, 32% yield) as a pale yellow solid, and **6** (163 mg, 33% yield) was recovered.

References

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¹H NMR spectrum for 5-bromo-1-(difluoromethyl)pyridin-2(1H)-one (**2a**)

¹³C NMR spectrum for 5-bromo-1-(difluoromethyl)pyridin-2(1*H*)-one (**2a**)

¹H NMR spectrum for methyl 1-(difluoromethyl)-2-oxo-1,2-dihydropyridine-4-carboxylate (**2b**)

¹H NMR spectrum for methyl 1-(difluoromethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**2c**)

¹³C NMR spectrum for 1-(difluoromethyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (2d)

¹³C NMR spectrum for 1-(difluoromethyl)-5-nitropyridin-2(1*H*)-one (**2e**)

¹H NMR spectrum for 1-(difluoromethyl)-4-methylpyridin-2(1H)-one (**2f**)

¹H NMR spectrum for 1-(difluoromethyl)-5-methylpyridin-2(1H)-one (**2g**)

¹³C NMR spectrum for 1-(difluoromethyl)-5-methylpyridin-2(1*H*)-one (**2g**)

¹H NMR spectrum for 1-(difluoromethyl)pyridin-2(1H)-one (**2h**)

¹H NMR spectrum for 1-(difluoromethyl)-3-methylpyridin-2(1*H*)-one (**2i**)

¹³C NMR spectrum for 1-(difluoromethyl)-3-methylpyridin-2(1*H*)-one (**2i**)

¹³C NMR spectrum for methyl 1-(difluoromethyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (**2j**)

¹H NMR spectrum for 1-(difluoromethyl)quinolin-2(1*H*)-one (**21**)

¹³C NMR spectrum for 1-(difluoromethyl)quinolin-2(1*H*)-one (**21**)

¹H NMR spectrum for 5-bromo-2-(difluoromethoxy)pyridine (**3**)

¹³C NMR spectrum for 5-bromo-2-(difluoromethoxy)pyridine (3)

¹H NMR spectrum for *N*-[5-bromo-1-(difluoromethyl)pyridin-2(1*H*)-ylidene]acetamide (**5**)

¹³C NMR spectrum for *N*-[5-bromo-1-(difluoromethyl)pyridin-2(1*H*)-ylidene]acetamide (5**)**

¹H NMR spectrum for 5-bromo-1-(difluoromethyl)pyridin-2(1H)-imine (6)

¹H NMR spectrum for ethyl [(5-bromopyridin-2-yl)oxy](difluoro)acetate (7)

¹³C NMR spectrum for ethyl [(5-bromopyridin-2-yl)oxy](difluoro)acetate (**7**)