Supporting Information for

Solvent- and Halide-free Synthesis of Pyridine-2-yl Substituted Ureas through Facile C–H Functionalization of Pyridine *N*-oxides

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1 General remarks

NMR spectra were recorded at ambient temperature with a Bruker Avance III 400 instrument at 400.13 MHz (^{1}H NMR) and 100.61 MHz (^{13}C NMR, DEPT-135). Chemical shifts (δ) are given in ppm relative to resonances of solvents (^{1}H: δ = 7.26 for the residual $CHCl_3$ peak, δ = 2.50 for the residual DMSO-d_5 peak; ^{13}C: δ = 77.0 for $CDCl_3$, δ = 39.5 for DMSO-d_6). Spin-spin coupling constants (J) are given in Hz. Multiplicities of signals are described as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. The multiplicities of signals in ^{13}C NMR spectra were determined by the DEPT-135 technique. Mass spectra were recorded with a Bruker MicroTOF (ESI) and Bruker maXis HRMS-ESI-QTOF instruments. Mass spectra from TLC plates were recorded employing a Camag TLC-MS interface and a Bruker MicroTOF (ESI) instrument. Infrared spectra were recorded with a Perkin-Elmer spectrum ASCII PEDS 1.60 FT-IR spectrometer. X-ray diffraction data were collected at an Xcalibur Eos diffractometer using Mo-Kα (λ = 0.071073 nm) radiation. The structures were solved by direct methods using the SHELXS and refined with the SHELXL[1] incorporated in the OLEX2 program package.[2] Chromatographic separation was carried out on Macherey-Nagel silica gel 60 (0.063–0.210 mm). Analytical TLC was performed on unmodified Merck ready-to-use plates (TLC silica gel 60 F254). Detection was achieved with a UV lamp. Melting points were determined in capillaries with a Stuart SMP 30 apparatus. The solvents were used as received, without purification. The commercially available compounds dimethylcyanamide, diethylcyanamide, piperidine-1-carbonitrile, pyrrolidine-1-carbonitrile, morpholine-4-carbonitrile, pyridine 1-oxide, 2-picoline 1-oxide were used as received without further purification.

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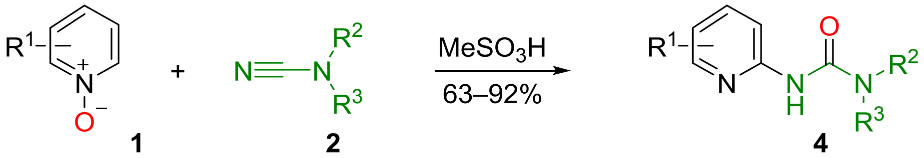
[1] Sheldrick, G. M. *Acta Crystallogr. Sect. A.* **2008**, *64*, 112–122.

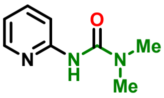
[2] Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard J. A. K.; Puschmann, H. *J. Appl. Cryst.*, **2009**, *42*, 339–341.

2 Experimental procedures

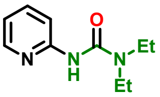
2.1. General procedure for the synthesis of *N*-pyridine-2-yl substituted urea **4** (**GP1**)



A mixture of substituted pyridine *N*-oxide **1** (1.00 mmol) and cyanamide **2** (1.50 mmol) was stirred at r.t. for 2 min and methanesulfonic acid (96.0 mg, 1.00 mmol) was then added dropwise within 3 min. The reaction mixture was then stirred at 60 °C for 2 h, cooled down, diluted with saturated aq. Na_2CO_3 (5.0 mL) and aq. NaCl (20 mL), and extracted with EtOAc (4 × 15 mL). Combined organic fractions were dried over anhydrous Na_2SO_4, filtered, and concentrated on a rotary evaporator. The crude product was subjected to column chromatography on silica gel (EtOAc/hexane, gradient from 50% to pure EtOAc) to give target urea **4** in good to excellent yields.



1,1-Dimethyl-3-(pyridin-2-yl)urea (4a)[3]: From pyridine 1-oxide (**1a**) (95.0 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4a** (147 mg, 89%) was obtained according to GP1 as a yellow oil, which was then crystalized in the freezer to give pale yellow solid, m.p. = 42.6–43.5 °C, lit.[4] m.p. = 44–47 °C (EtOAc/hexane), R_f = 0.25 (EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.00 (s, 6 H, NCH_3), 6.88 (ddd, *J* = 7.3, 5.0, 0.9 Hz, 1 H), 7.30 (br. s, 1 H), 7.60 (ddd, *J* = 8.5, 7.3, 1.9 Hz, 1 H), 8.02 (dt, *J* = 8.5, 0.9 Hz, 1 H), 8.14 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.3 (2 C, CH_3), 113.0 (CH), 118.1 (CH), 138.0 (CH), 147.3 (CH), 152.8 (C), 154.8 (C) ppm. NMR data are consistent with previously reported.[3] **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_8H_{12}N_3O^+$: 166.0975; found: 166.0977.



1,1-Diethyl-3-(pyridin-2-yl)urea (4b)[5]: From pyridine 1-oxide (**1a**) (95.0 mg, 1.00 mmol) and diethylcyanamide (**2b**) (147 mg, 1.50 mmol), compound **4b** (141 mg, 73%) was obtained according to GP1 as a brownish oil, R_f = 0.30 (EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.2 Hz, 6 H, CH_3), 3.35 (q, *J* = 7.2 Hz, 4 H, NCH_2), 6.88 (ddd, *J* = 7.3 5.0, 0.9 Hz, 1 H), 7.16 (br. s, 1 H), 7.59 (ddd, *J* = 8.5, 7.3, 1.9 Hz, 1 H), 8.05 (dt, *J* = 8.5, 0.9 Hz, 1 H), 8.14 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 13.8 (2 × CH_3), 41.5

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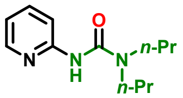
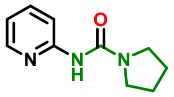
[3] Li, X.; Li, B.; You, J.; Lan, J. *Org. Biomol. Chem.* **2013**, *11*, 1925–1928.
[4] Woods, W. G.; Crawford, R. United States Patents Office. US 3330641, **1967**, [*Chem. Abstr.* **1967**, *67*, 108563].
[5] Han, H.; Chang, S.-B. *Bull. Korean Chem. Soc.* **2010**, *31*, 746–748.

(2 × CH_2), 113.1 (CH), 118.0 (CH), 138.0 (CH), 147.3 (CH), 152.9 (C), 153.7 (C) ppm. NMR data are consistent with previously reported.[5] **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_{10}H_{16}N_3O^+$: 194.1288; found: 194.1280.

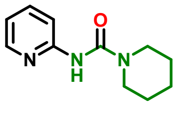


1,1-Dipropyl-3-(pyridin-2-yl)urea (4c): From pyridine 1-oxide (**1a**) (95.0 mg, 1.00 mmol) and dipropylcyanamide (**2c**) (189 mg, 1.50 mmol), compound **4c** (175 mg, 79%) was obtained according to GP1 as a brownish oil, which was then crystalized in the freezer to give pale brown solid, m.p. = 38.5–39.4 °C (EtOAc/hexane), R_f = 0.50 (EtOAc). Compound **4c** is mentioned in lit.[5], but analytical data are absent. **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3225 (w), 2965 (m), 2930 (m), 2875 (m), 1660 (m), 1575 (m), 1535 (m), 1435 (s), 1405 (m), 1305 (s), 1230 (m), 1165 (m), 1105 (w), 995 (w), 895 (w), 782 (m) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.4 Hz, 6 H, CH_3), 1.55–1.71 (m, 4 H, CH_2CH_3), 3.18–3.30 (m, 4 H, NCH_2), 6.89 (ddd, *J* = 7.3, 5.0, 1.0 Hz, 1 H), 7.16 (br. s, 1 H), 7.60 (ddd, *J* = 8.5, 7.3, 1.9 Hz, 1 H), 8.06 (dt, *J* = 8.5, 1.0 Hz, 1 H), 8.15 (ddd, *J* = 5.0, 1.9, 1.0 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 11.3 (2 × CH_3), 21.7 (2 × CH_2), 49.4 (2 × CH_2), 113.2 (CH), 118.1 (CH), 138.0 (CH), 147.2 (CH), 152.9 (C), 154.1 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_{12}H_{20}N_3O^+$: 222.1601; found: 222.1600.



***N*-(Pyridin-2-yl)pyrrolidine-1-carboxamide (4d)**: From pyridine 1-oxide (**1a**) (95.0 mg, 1.00 mmol) and pyrrolidine-1-carbonitrile (**2d**) (144 mg, 1.50 mmol), compound **4d** (176 mg, 92%) was obtained according to GP1 as a pale yellow solid, m.p. = 116.5–116.9 °C (EtOAc/hexane), lit.[6] m.p. = 154–155 °C, R_f = 0.30 (EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.96–1.99 (m, 1 H, NCH_2CH_2), 3.47–3.50 (m, 1 H, NCH_2CH_2), 6.92 (ddd, *J* = 7.3, 5.0, 1.0 Hz, 1 H), 6.99 (br. s, 1 H, NH), 7.63 (ddd, *J* = 8.5, 7.3, 1.9 Hz, 1 H), 8.11 (dt, *J* = 8.5, 1.0 Hz, 1 H), 8.18 (ddd, *J* = 5.0, 1.9, 1.0 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 25.4 (2 × CH_2), 45.7 (2 × CH_2), 112.9 (CH), 118.0 (CH), 137.9 (CH), 147.3 (CH), 152.7 (C), 153.0 (C) ppm.

NMR data are consistent with previously reported.[6] **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_{10}H_{14}N_3O^+$: 192.1131; found: 192.1127.



***N*-(Pyridin-2-yl)piperidine-1-carboxamide (4e)**: From pyridine 1-oxide (**1a**) (95.0 mg, 1.00 mmol) and piperidine-1-carbonitrile (**2e**) (165 mg, 1.50 mmol), compound **4e** (172 mg, 83%) was obtained according to GP1 as a pale yellow solid, m.p. = 84.2–84.8 °C (EtOAc/hexane), lit.[7] m.p. = 85 °C, R_f = 0.50 (EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.17–1.88 (m, 6 H), 3.39–3.47 (m, 4 H, NCH_2), 6.86 (ddd, *J* = 7.3, 5.0, 1.0 Hz, 1 H), 7.51 (br. s, 1 H,

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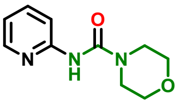
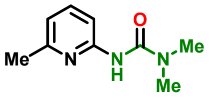
[6] Wei, Y.; Liu, J.; Lin, S.; Ding, H.; Liang, F.; Zhao, B. *Org. Lett.* **2010**, *12*, 4220–4223.

[7] Ohsawa, A.; Arai, H.; Igeta, H. *Heterocycles* **1979**, *12*, 917–920.

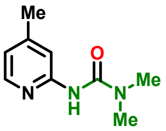
NH), 7.58 (ddd, $J = 8.5, 7.3, 1.9$ Hz, 1 H), 7.98 (dt, $J = 8.5, 0.9$ Hz, 1 H), 8.13 (ddd, $J = 5.0, 1.9, 0.9$ Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): $\delta = 24.2$ (CH_2), 25.6 (2 × CH_2), 45.1 (2 × CH_2), 113.2 (CH), 118.0 (CH), 137.9 (CH), 147.3 (CH), 153.0 (C), 153.9 (C) ppm. **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_{11}H_{15}N_3NaO^+$: 228.1107; found: 228.1099.



***N*-(Pyridin-2-yl)morpholine-4-carboxamide (4f)**: From pyridine 1-oxide (**1a**) (95.0 mg, 1.00 mmol) and morpholine-4-carbonitrile (**2f**) (168 mg, 1.50 mmol), compound **4f** (164 mg, 89%) was obtained according to GP1 as a colorless solid, m.p. = 92.6–93.1 °C (EtOAc/hexane), lit.[8] m.p. = 92 °C, $R_f = 0.35$ (EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$): $\delta =$ 3.45–3.51 (m, 4 H), 3.65–3.71 (m, 4 H), 6.92 (m, 1 H), 7.62 (m, 1 H), 7.66 (br. s, 1 H, NH), 7.98 (d, $J = 8.4$ Hz, 1 H), 8.15 (d, $J = 4.2$ Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): $\delta = 44.1$ (2 × CH_2), 66.4 (2 × CH_2), 113.4 (CH), 118.4 (CH), 138.1 (CH), 147.3 (CH), 152.6 (C), 154.2 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_{10}H_{14}N_3O_2^+$: 208.1081; found: 208.1084.



1,1-Dimethyl-3-(6-methylpyridin-2-yl)urea (4g): From 2-methylpyridine 1-oxide (**1g**) (109 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4g** (147 mg, 82%) was obtained according to GP1 as a pale yellow oil, $R_f = 0.30$ (EtOAc). **IR** (KBr, thin film): $\bar{\nu}_{max}$ 3355 (w), 2925 (w), 1670 (s), 1580 (m), 1530 (s), 1455 (s), 1400 (m), 1305 (m), 1180 (m) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): $\delta = 2.40$ (s, 3 H, CCH_3), 3.03 (s, 6 H, NCH_3), 6.77 (d, $J = 7.4$ Hz, 1 H), 7.28 (br. s, 1 H, NH), 7.52 (dd, $J = 8.3, 7.4$ Hz, 1 H), 7.85 (d, $J = 8.3$ Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): $\delta = 23.7$ (CCH_3), 36.4 (2 × NCH_3), 110.0 (CH), 117.6 (CH), 138.5 (CH), 152.2 (C), 154.9 (C), 156.0 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_9H_{14}N_3O^+$: 180.1131; found: 180.1132.



1,1-Dimethyl-3-(4-methylpyridin-2-yl)urea (4h): From 4-methylpyridine 1-oxide (**1h**) (109 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4h** (140 mg, 78%) was obtained according to GP1 as a gray solid, m.p. = 100.1–100.4 °C (EtOAc/hexane), $R_f = 0.25$ (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3215 (w), 3175 (w), 3020 (w), 2975 (w), 2920 (w), 2800 (w), 1665 (s), 1610 (m), 1575 (s), 1530 (s), 1425 (m), 1365 (s), 1300 (m), 1185 (s), 995 (w), 830 (m), 785 (s), 750 (s), 625 (s) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): $\delta = 2.29$ (s, 3 H, CCH_3), 3.00 (s, 6 H, NCH_3), 6.72 (d, $J = 5.0$ Hz, 1 H), 7.21 (br. s, 1 H, NH), 7.87 (s, 1 H), 8.00 (d, $J = 5.0$ Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): $\delta = 21.3$ (CH_3), 36.3 (2 × NCH_3), 113.5 (CH), 119.5 (CH), 146.9 (CH), 149.4 (C), 152.8 (C), 154.9 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_9H_{14}N_3O^+$: 180.1131; found: 180.1127.

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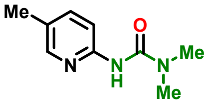
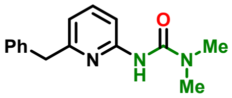
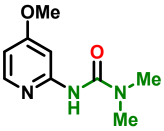
[8] Ohsawa, A.; Arai, H.; Igeta, H. *Chem. Pharm. Bull.* **1980**, *28*, 3570–3575.



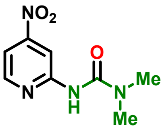
1,1-Dimethyl-3-(3-methylpyridin-2-yl)urea (4i): From 3-methylpyridine 1-oxide (**1i**) (109 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4i** (115 mg, 64%) was obtained according to GP1b as a yellowish solid, m.p. = 61.2–61.7 °C, R_f = 0.20 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3260 (m), 3020 (m), 2950 (m), 2920 (m), 1675 (s), 1590 (s), 1520 (s), 1475 (s), 1370 (s), 1305 (s), 1265 (m), 1180 (m), 1125 (w), 1035 (w), 835 (m), 745 (w), 660 (w), 560 (w), 520 (w) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, CCH_3), 3.02 (s, 6 H, NCH_3), 7.10 (br. s, 1 H, NH), 7.45 (dd, J = 8.5, 1.8 Hz, 1 H, H-4), 7.94 (d, J = 8.5 Hz, 1 H, H-3), 7.99 (br. s, 1 H, H-6) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 17.6 (CCH_3), 36.4 (2 × NCH_3), 112.6 (CH), 127.4 (C), 138.8 (CH), 147.1 (CH), 150.6 (C), 155.0 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_9H_{14}N_3O^+$: 180.1131; found: 180.1124.



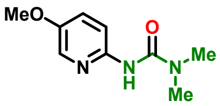
3-(6-Benzylpyridin-2-yl)-1,1-dimethylurea (4j): From 2-benzylpyridine 1-oxide (**1j**) (185 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4j** (181 mg, 71%) was obtained according to GP1 as a colorless solid, m.p. = 90.5–90.9 °C (EtOAc/hexane), R_f = 0.50 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3215 (w), 3060 (w), 3025 (w), 2960 (w), 2930 (w), 2890 (w), 1555 (s), 1640 (s), 1580 (m), 1530 (m), 1450 (s), 1410 (m), 1303 (m), 1190 (m), 740 (m), 700 (m) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.03 (s, 6 H, NCH_3), 4.00 (s, 2 H, $PhCH_2$), 6.73 (d, J = 7.4 Hz, 1 H), 7.14 (s, 1 H, NH), 7.17–7.24 (m, 3 H, H-Ar), 7.26–7.32 (m, 2 H, H-Ar), 7.53 (dd, J = 8.3, 7.4 Hz, 1 H), 7.88 (d, J = 8.3 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.4 (2 × CH_3), 44.1 (CH_2), 110.5 (CH), 117.5 (CH), 126.3 (CH), 128.4 (2 × CH), 129.0 (2 × CH), 138.5 (CH), 139.4 (C), 152.3 (C), 154.9 (C), 158.8 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_{15}H_{18}N_3O^+$: 256.1444; found: 256.1444.



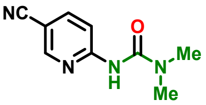
3-(4-Methoxypyridin-2-yl)-1,1-dimethylurea (4k): From 4-methoxypyridine 1-oxide (**1k**) (125 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4k** (168 mg, 86%) was obtained according to GP1 as a colorless solid, m.p. = 47.0–47.2 °C, R_f = 0.15 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3260 (m), 3135 (w), 3035 (w), 2980 (w), 2940 (w), 1665 (s), 1600 (s), 1575 (s), 1515 (s), 1450 (s), 1430 (s), 1415 (s), 1370 (m), 1315 (m), 1305 (m), 1260 (w), 1200 (s), 1180 (s), 1035 (m), 1025 (m), 995 (w), 875 (w), 845 (w), 810 (w), 800 (w), 780 (m), 755 (w) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.01 (s, 6 H, NCH_3), 3.83 (s, 3 H, OCH_3), 6.47 (dd, J = 5.8, 2.1 Hz, 1 H, H-5), 7.24 (br. s, 1 H, NH), 7.70 (d, J = 2.1 Hz, 1 H, H-3), 7.94 (d, J = 5.8 Hz, 1 H, H-6) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.3 (2 × NCH_3), 55.1 (OCH_3), 97.0 (CH), 106.8 (CH), 148.0 (CH), 154.5 (C), 154.9 (C), 167.3 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_9H_{14}N_3O_2^+$: 196.1081; found: 196.1088.



1,1-Dimethyl-3-(4-nitropyridin-2-yl)urea (4l): From 4-nitropyridine 1-oxide (**1l**) (140 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4l** (164 mg, 78%) was obtained according to GP1 as an orange solid, m.p. = 124.7–125.1 °C (EtOAc/hexane), $R_f = 0.40$ (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3330 (m), 3145 (w), 2940 (w), 1665 (s), 1585 (m), 1530 (s), 1415 (m), 1380 (m), 1360 (m), 1270 (m), 1175 (m), 875 (s), 745 (m), 695 (m) cm^{-1}. **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 3.06 (s, 6 H, NCH$_3$), 7.51 (s, 1 H, NH), 7.59 (dd, J = 5.4, 1.5 Hz, 1 H), 8.38 (d, J = 5.4 Hz, 1 H), 8.80 (d, J = 1.5 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, CDCl$_3$): δ = 36.4 (2 × CH$_3$), 106.2 (CH), 110.7 (CH), 149.4 (CH), 154.1 (C), 155.0 (C), 155.3 (C) ppm. **HRMS** (ESI), *m/z*: [M + H]$^+$ calcd. for $C_8H_{11}N_4O_3^+$: 211.0826; found: 211.0822.

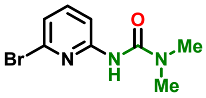


3-(5-Methoxypyridin-2-yl)-1,1-dimethylurea (4m): From 5-methoxypyridine 1-oxide (**1m**) (125 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4m** (140 mg, 72%) was obtained according to GP1 as a yellowish solid, m.p. = 103.0–130.5 °C, $R_f = 0.3$ (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3270 (m), 3020 (w), 2940 (m), 2850 (w), 1660 (s), 1590 (s), 1510 (s), 1485 (s), 1390 (s), 1370 (s), 1280 (s), 1245 (m), 1175 (m), 1120 (m), 1070 (w), 1020 (m), 850 (w), 825 (w), 750 (w), 685 (w) cm^{-1}. **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 3.02 (s, 6 H, NCH$_3$), 3.81(s, 3 H, OCH$_3$), 7.07 (br. s, 1 H, NH), 7.22 (dd, J = 9.1, 2.9 Hz, 1 H), 7.87 (d, J = 2.9 Hz, 1 H), 7.97 (d, J = 9.1 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, CDCl$_3$): δ = 36.3 (2 × NCH$_3$), 55.9 (OCH$_3$), 113.6 (CH), 123.7 (CH), 133.6 (CH), 146.6 (C), 151.9 (C), 155.0 (C) ppm. **HRMS** (ESI), *m/z*: [M + Na]$^+$ calcd. for $C_9H_{13}N_3NaO_2^+$: 218.0900; found: 218.0900.

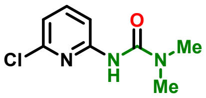


3-(5-Cyanopyridin-2-yl)-1,1-dimethylurea (4n): From 3-cyanopyridine 1-oxide (**1n**) (120 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4n** (152 mg, 80%) was obtained according to GP1 as a yellowish solid, m.p. = 158.5–159.5 °C, $R_f = 0.50$ (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3425 (m), 2225 (m), 1675 (s), 1600 (m), 1580 (m), 1520 (s), 1470 (m), 1385 (m), 1370 (m), 1315 (m), 1270 (w), 1200 (w), 1170 (m), 1355 (w), 1110 (w), 1075 (w), 1020 (w), 950 (w), 850 (w), 750 (w), 580 (w) cm^{-1}. **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 3.08 (s, 6 H, NCH$_3$), 7.50 (br. s, NH), 7.87 (dd, J = 8.9, 1.8 Hz, 1 H), 8.24 (d, J = 8.9 Hz, 1 H), 8.47 (d, J = 1.8 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, CDCl$_3$): δ = 36.4 (2 × CH$_3$), 103.2 (CN), 112.5 (CH), 117.1 (C), 140.9 (CH), 151.4 (CH), 153.8 (C), 155.3 (C) ppm.

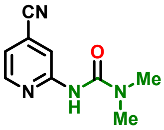
HRMS (ESI), *m/z*: [M + Na]$^+$ calcd. for $C_9H_{10}N_4NaO^+$: 213.0747; found: 213.0738.



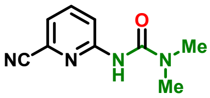
3-(6-Bromopyridin-2-yl)-1,1-dimethylurea (4o): From 2-bromopyridine 1-oxide (**1o**) (174 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4o** (167 mg, 68%) was obtained according to GP1 as a yellowish solid, m.p. = 96.1–96.3 °C (EtOAc/hexane), R_f = 0.55 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3325 (m), 3050 (w), 2930 (w), 1680 (s), 1560 (s), 1595 (m), 1570 (s), 1525 (s), 1440 (s), 1395 (s), 1305 (m), 1265 (w), 1245 (w), 1190 (m), 1160 (m), 1130 (m), 1070 (w), 980 (w), 885 (w), 775 (s), 620 (m) cm^{-1}. **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 3.03 (s, 6 H, NCH$_3$), 7.09 (d, *J* = 7.7 Hz, 1 H), 7.14 (br. s, 1 H, NH), 7.48 (dd, *J* = 8.3, 7.7 Hz, 1 H), 8.03 (d, *J* = 8.3 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, CDCl$_3$): δ = 36.2 (2 × CH$_3$), 111.2 (CH), 121.5 (CH), 138.5 (C), 140.0 (CH), 152.8 (C), 154.1 (C) ppm. **HRMS** (ESI), *m/z*: [M + Na]$^+$ calcd. for C$_8$H$_{10}$BrN$_3$NaO$^+$: 265.9899; found: 265.9891.



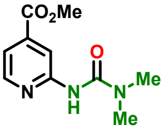
3-(6-Chloropyridin-2-yl)-1,1-dimethylurea (4p): From 2-chloropyridine 1-oxide (**1p**) (130 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4p** (126 mg, 63%) was obtained according to GP1 as a pale yellow solid, m.p. = 73.2–74.1 °C (EtOAc/hexane), R_f = 0.55 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3330 (m), 2930 (w), 1680 (s), 1660 (s), 1590 (s), 1570 (s), 1515 (m), 1440 (s), 1400 (s), 1305 (m), 1250 (m), 1180 (m), 1155 (s), 1135 (m), 985 (m), 780 (s), 750 (w), 625 (m) cm^{-1}. **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 3.00 (s, 6 H, NCH$_3$), 6.90 (d, *J* = 7.6 Hz, 1 H), 7.18 (s, 1 H, NH), 7.54 (t, *J* = 8.1 Hz, 1 H), 7.96 (d, *J* = 8.3 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, CDCl$_3$): δ = 36.3 (2 × CH$_3$), 110.9 (CH), 117.8 (CH), 140.5 (CH), 148.3 (C), 152.7 (C), 154.2 (C) ppm. **HRMS** (ESI), *m/z*: [M + Na]$^+$ calcd. for C$_8$H$_{10}$ClN$_3$NaO$^+$: 222.0405; found: 222.0462.



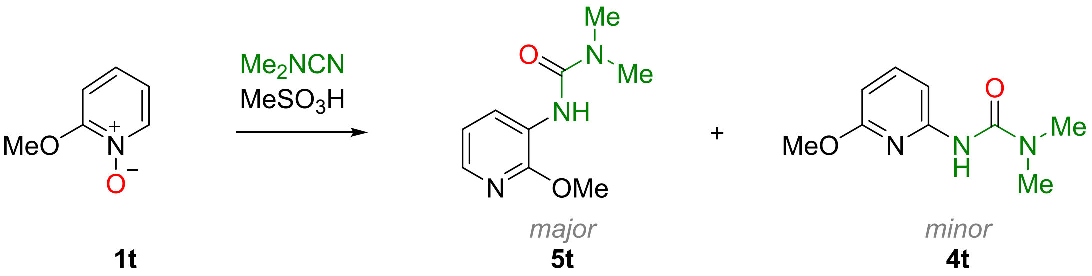
3-(4-Cyanopyridin-2-yl)-1,1-dimethylurea (4q): From 4-cyanopyridine 1-oxide (**1q**) (120 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4q** (137 mg, 72%) was obtained according to GP1 as a pale yellow solid, m.p. = 98.5–99.1 °C, R_f = 0.25 (EtOAc, 5 : 1). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3440 (m), 3155 (w), 3105 (w), 3085 (w), 2935 (w), 2880 (w), 2821 (w), 2235 (w), 1675 (s), 1610 (m), 1555 (s), 1510 (s), 1415 (s), 1365 (s), 1295 (m), 1265 (m), 1215 (m), 1155 (s), 880 (w), 855 (w), 750 (w), 655 (w), 530 (w) cm^{-1}. **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 3.06 (s, 6 H, NCH$_3$), 7.12 (dd, *J* = 5.1, 1.4 Hz, 1 H), 7.32 (br. s, 1 H, NH), 8.31 (dd, *J* = 5.1, 0.8 Hz, 1 H), 8.39 (dd, *J* = 1.4, 0.8 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, CDCl$_3$): δ = 36.4 (2 × CH$_3$), 115.2 (CH), 116.7 (C), 119.4 (CH), 122.0 (C), 148.6 (CH), 153.5 (C), 154.1 (C) ppm. **HRMS** (ESI), *m/z*: [M + Na]$^+$ calcd. for C$_9$H$_{10}$N$_4$NaO$^+$: 213.0747; found: 213.0749. VAR277



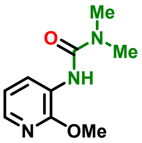
3-(2-Cyanopyridin-2-yl)-1,1-dimethylurea (4r): From 2-cyanopyridine 1-oxide (**1r**) (120 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4r** (158 mg, 83%) was obtained according to GP1 as a colorless solid, m.p. = 122.1.–122.5 °C, R_f = 0.50 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3405 (m), 3120 (w), 3070 (w), 2945 (w), 2245 (w), 1670 (s), 1575 (s), 1530 (s), 1455 (s), 1400 (m), 1310 (m), 1170 (m), 985 (w), 800 (m), 755 (w), 625 (w), 550 (w), 460 (w) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.07 (s, 6 H, NCH_3), 7.27 (br. s, NH), 7.32 (dd, J = 7.5, 0.6 Hz, 1 H), 7.74 (dd, J = 8.5, 7.5 Hz, 1 H), 8.34 (dd, J = 8.5, 0.6 Hz, 1 H)ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.4 (2 × CH_3), 117.0 (CN), 117.1 (CH), 122.8 (CH), 130.9 (C), 138.7 (CH), 153.8 (C), 154.2 (C) ppm. **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_9H_{10}N_4NaO^+$: 213.0747; found: 213.0748.



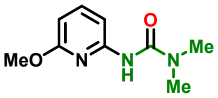
Methyl 2-(3,3-dimethylureido)isonicotinate (4s): From 4-(methoxycarbonyl)pyridine 1-oxide (**1s**) (153 mg, 1.00 mmol) and dimethylcyanamide (**2a**) (105 mg, 1.50 mmol), compound **4s** (176 mg, 79%) was obtained according to GP1 as a colorless solid, m.p. = 93.5–94.1 °C, R_f = 0.30 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3365 (m), 3145 (w), 3085 (w), 3010 (w), 2950 (w), 1720 (s), 1665 (s), 1570 (s), 1535 (s), 1440 (m), 1415 (s), 1370 (m), 1310 (m), 1255(m), 1230 (m), 1170 (m), 1105 (m), 975 (w), 760 (m), 690 (w), 625 (m) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.07 (s, 6 H, NCH_3), 3.92 (s, 3 H, OCH_3), 7.25 (s, 1 H, NH), 7.50 (dd, J = 5.1, 1.5 Hz, 1 H), 8.31 (dd, J = 5.1, 0.7 Hz, 1 H), 8.61 (dd, J = 1.5, 0.7 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.3 (2 × NCH_3), 52.4 (OCH_3), 112.7 (CH), 117.5 (CH), 139.3 (C), 148.0 (CH), 153.6 (C), 154.6 (C), 165.6 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_{10}H_{14}N_3O_3^+$: 224.1030; found: 224.1023.



From 2-methoxypyridine 1-oxide (**1t**) (500 mg, 4.00 mmol) and dimethylcyanamide (**2a**) (420 mg, 6.00 mmol), a mixture of **5t** and **4t** (702 mg, 5 : 1) was obtained according to GP1.



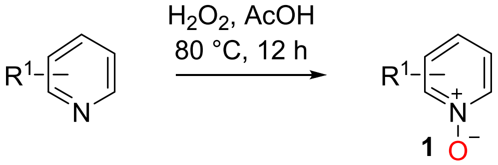
3-(2-Methoxypyridin-3-yl)-1,1-dimethylurea (5t): Recrystallization (2 times) of the mixture of **5t** and **4t** from Et_2O/hexane gave **5t** (328 mg, 42%) as a colorless solid, m.p. = 72.9–73.1 °C, R_f = 0.30 (EtOAc). **IR** (KBr, pellet): $\bar{\nu}_{max}$ 3455 (m), 3115 (w), 3060 (w), 3020 (w), 2990 (w), 2955 (w), 2895 (w), 2850 (w), 1675 (s), 1600 (w), 1585 (w), 1520 (s), 1455 (s), 1400 (m), 1360 (m), 1290 (w), 1270 (w), 1245 (m), 1200 (w), 1170 (m), 1105 (m), 1020 (m), 795 (m), 795 (m), 760 (w), 745 (w), 605 (w), 505 (w), 495 (w) cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.01 (s, 6 H, NCH_3), 3.98 (s, 3 H, OCH_3), 6.84 (dd, *J* = 7.8, 5.0 Hz, 1 H, H-5), 6.92 (br. s, 1 H, NH), 7.73 (dd, *J* = 5.0, 1.6 Hz, 1 H, H-6), 8.38 (dd, *J* = 7.8, 1.6 Hz, 1 H, H-4) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.2 (2 × NCH_3), 53.6 (OCH_3), 117.3 (CH, C-5), 124.2 (C, C-3), 125.0 (CH, C-4), 138.2 (CH, C-6), 152.7 (C, C-2), 155.3 (CO) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_9H_{14}N_3O_2^+$: 196.1081; found: 196.1076.



3-(6-Methoxypyridin-2-yl)-1,1-dimethylurea (4t): Compound **4t** was not isolated in pure form. NMR data extracted from the NMR spectra of the mixture of **5t** and **4t**. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.89 (s, 6 H, NCH_3), 3.69 (s, 3 H, OCH_3), 6.23 (dd, *J* = 7.9, 0.6 Hz, 1 H, H-5), 7.39 (t, *J* = 7.9 Hz, 1 H, H-4), 7.47 (dd, *J* = 7.9, 0.6 Hz, 1 H, H-3) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 35.9 (2 × NCH_3), 53.0 (OCH_3), 103.2 (CH, C-5), 104.1 (CH, C-3), 140.3 (CH, C-4), 150.4 (C, C-2), 154.4 (CO) 162.4 (C, C-6) ppm.

2.2. Synthesis of the starting pyridine *N*-oxides **1**

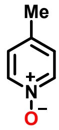
General procedure for the N-*oxidation of pyridine* ***1 (GP2)***



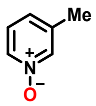
Aq. H_2O_2 (75 mL, 30 %) was added in one portion to the solution of the substituted pyridine (30 g) in glacial CH_3CO_2H (160 mL) and the mixture was stirred at 80 °C for 12 h. Solution was then cooled down and concentrated on a rotary evaporator. The residue was worked up in 2 different ways.

a) The residue was alkalized with saturated aq. Na_2CO_3 (100 mL) and solid K_2CO_3 until pH = 8, and the resulting solution was then extracted with EtOAc (4 × 75 mL). Combined organic fractions were washed with brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by vacuum distillation or recrystallization from a suitable solvent.

b) The residue was diluted with acetone (100 mL) and the precipitate was filtered off.



4-Methylpyridine 1-oxide (1h): From 4-methylpyridine (30.0 g, 322 mmol), compound **1h** was obtained according to **GP2a**. Crude product was purified by recrystallization from acetone/hexane mixture to give **1h** (16.6 g, 47%) as a pale gray solid, m.p. = 182–183 °C, lit.[9] m.p. = 180–181 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 7.02 (m, 2 H), 8.04 (m, 2 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 20.1 (CH_3), 126.6 (2 × CH), 137.4 (C), 138.5 (2 × CH) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_6H_8NO^+$: 110.0600; found: 110.0604.



3-Methylpyridine 1-oxide (1i): From 3-methylpyridine (33.0 g, 354 mol), compound **1i** was obtained according to **GP2a**. Crude product was purified by vacuum distillation to give **1i** (16.6 g, 43%) as a colorless liquid (b.p. = 132–134, 5 mbar), which was then crystallized in the freezer to form colorless solid, m.p. = 36.5–37.5 °C, lit.[10] m.p. = 37–38 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.18 (s, 3 H, CH_3), 6.94–7.09 (m, 2 H), 7.90–7.98 (m, 2 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 18.0 (CH_3), 125.1 (CH), 126.9 (CH), 136.3 (CH), 136.6 (C), 139.0 (CH) ppm. **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_6H_7NaNO^+$: 132.0420; found: 132.0415.

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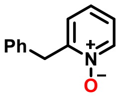
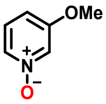
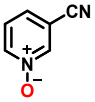
[9] Jain, S.; Joseph, J.; Sain, B. *Synlett* **2006**, *16*, 2661–2663.
[10] Katritzky, A. R.; Beard, J. A. T.; Coats, N. A. *J. Chem. Soc.* **1959**, 3680–3683.



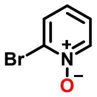
2-Benzylpyridine 1-oxide (1j): From 2-benzylpyridine (15.0 g, 89.0 mmol), compound **1j** was obtained according to **GP2a**. Crude product was purified by recrystallization from hexane to give **1j** (11.8 g, 72%) as a colorless solid, m.p. = 99–100 °C, m.p. = 99–100 °C, lit.[11] m.p. = 98–99 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.20 (s, 2 H, CH_2), 6.88 (m, 1 H), 7.03–7.10 (m, 2 H), 7.18–7.25 (m, 3 H), 7.25–7.32 (m, 2 H), 8.21 (m, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 36.2 (CH_2), 123.3 (CH), 125.1 (CH), 125.6 (CH), 126.8 (CH), 128.6 (2 × CH), 129.4 (2 × CH), 136.1 (C), 139.1 (CH), 151.6 (C) ppm. **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_{12}H_{11}NaNO^+$: 208.0733; found: 208.0730.



3-Methoxypyridine 1-oxide (1m): From 3-methoxypyridine (4.00 g, 36.7 mmol), compound **1m** was obtained according to **GP2a.** The crude product was purified by recrystallization from the mixture of acetone and hexane to give **1m** (3.82 g, 83%) as a colorless solid, m.p. = 102.0–102.6 °C, lit.[10] m.p. = 100–101 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OCH_3), 6.80 (dd, J = 8.7, 1.9 Hz, 1 H), 7.08 (dd, J = 8.7, 6.4 Hz, 1 H), 7.79 (m, 1 H), 7.89 (t, J = 1.9 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 55.9 (OCH_3), 112.6 (CH), 125.2 (CH), 127.6 (CH), 132.2 (CH), 157.8 (C) ppm. **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_6H_7NNaO_2^+$: 148.0369; found: 148.0369.



3-Cyanopyridine 1-oxide (1n): From 3-cyanopyridine (15.0 g, 144 mmol), compound **1n** was obtained according to **GP2b.** The crude product was purified by recrystallization from acetone to give **1n** (12.5 g, 72%) as a coloreless solid, m.p. = 176.5–177.0 °C, lit.[10] m.p. = 174–175 °C. **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 7.60 (ddd, J = 7.8, 6.6, 0.6 Hz, 1 H), 7.81 (ddd, J = 0.9, 1.5, 7.8 Hz, 1 H), 8.48 (ddd, J = 6.6, 1.9, 0.9 Hz, 1 H), 8.86 (ddd, J = 1.9, 1.5, 0.6 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 112.0 (C), 114.9 (C), 127.4 (CH), 128.3 (CH), 141.6 (CH), 143.2 (CH) ppm. **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_6H_4N_2NaO^+$: 143.0216; found: 143.0213.



2-Bromopyridine 1-oxide (1o): From 2-bromopyridine (15.0 g, 95.0 mmol), compound **1o** was obtained according to **GP2a**. The crude product was purified by recrystallization from acetone/hexane mixture to give **1o** (8.30 g, 50%) as a pale brown solid, m.p. = 62–63 °C, lit.[12] m.p. = 132–135 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.02 (ddd, J = 8.1, 7.5, 1.4 Hz, 1 H), 7.17 (ddd, J = 7.5, 6.5, 1.9 Hz, 1 H), 7.56 (ddd, J = 8.1, 1.9, 0.4 Hz, 1 H), 8.25 (ddd, J = 6.5, 1.4, 0.4 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 124.5 (CH), 125.5 (CH), 130.7 (CH), 132.6 (C), 140.1

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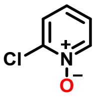
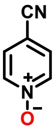
[11] Ohsawa, A.; Kawaguchi, T.; Igeta, H. *J. Org. Chem.* **1982**, *47*, 3497–3503.

[12] Adams, R.; Reifschneider, W. *J. Am. Chem. Soc.* **1957**, *79*, 2236–2239.

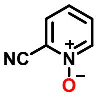
(CH) ppm. NMR data are consistent with previously reported.[13] **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_5H_5BrNO^+$: 173.9549; found: 173.9550.



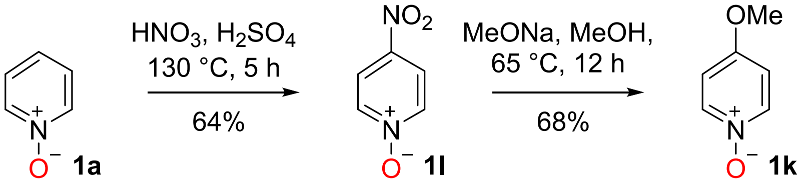
2-Chloropyridine 1-oxide (1p): From 2-chloropyridine (30.0 g, 264 mmol), compound **1p** was obtained according to **GP2a**. The crude product was purified by recrystallization from acetone/hexane mixture to give **1p** (17.4 g, 51%) as a pale gray solid, m.p. = 67–68 °C, lit.[14] m.p. = 66–68 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.13–7.22 (m, 2 H), 7.46 (m, 1 H), 8.30 (m, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 123.9 (CH), 125.7 (CH), 127.1 (CH), 140.5 (CH), 141.9 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_5H_5ClNO^+$: 130.0054; found: 130.0051.

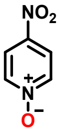


4-Cyanopyridine 1-oxide (1q): From 4-cyanopyridine (15.0 g, 144 mmol), compound **1q** was obtained according to **GP2b.** The crude product was purified by recrystallization from methanol to give **1q** (11.7 g, 68%) as a coloreless solid, m.p. = 227–228 °C, lit.[15] m.p. = 220–222 °C. **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 7.91 (m, 2 H), 8.38 (m, 2 H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 106.3 (C), 116.6 (C), 129.7 (2 × CH), 140.0 (2 × CH) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_6H_5N_2O^+$: 121.0396; found: 121.0398.



2-Cyanopyridine 1-oxide (1r): From 2-cyanopyridine (15.0 g, 144 mmol), compound **1r** was obtained according to **GP2a.** The crude product was purified by recrystallization from methanol to give **1r** (10.8 g, 62%) as a coloreless solid, m.p. = 119–120 °C, lit.[16] m.p. = 116 °C. **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 7.47 (td, *J* = 7.9, 1.0 Hz, 1 H), 7.69 (ddd, *J* = 7.9, 6.7, 2.0 Hz, 1 H), 8.08 (ddd, *J* = 7.9, 2.0, 0.5 Hz, 1 H), 8.45 (ddd, *J* = 6.7, 1.0, 0.5 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 112.6 (C), 124.5 (C), 125.3 (CH), 130.3 (CH), 132.1 (CH), 140.0 (CH) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_6H_5N_2O^+$: 121.0396; found: 121.0401.





4-Nitropyridine 1-oxide (1l): A mixture of pyridine 1-oxide (10.2 g, 107 mmol), concentrated H_2SO_4 (22.7 mL, 417 mmol), and fumaring HNO_3 (11.4 mL) was heated at 130 °C for 5 hours.

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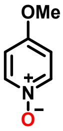
[13] Kokatla, H. P.; Thomson, P. F.; Bae, S.; Doddi, V. R.; Lakshman, M. K. *J. Org. Chem.* **2011**, *76*, 7842–7848.

[14] Connon, S. J.; Hegarty, A. F. *European J. Org. Chem.* **2004**, *2004*, 3477–3483.

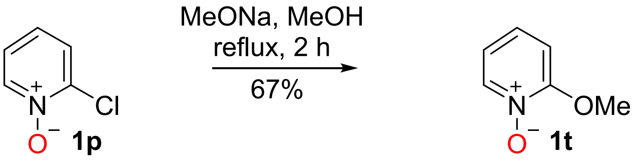
[15] Schnekenburger, J.; Heber, D. *Arch. Pharm.* **1975**, *308*, 33–41.

[16] Duric, S.; Tzschucke, C. C. *Organic Letters* **2011**, *13*, 2310–2313.

The resulting solution was poured into ice, alkalized with saturated aq. Na_2CO_3, and extracted with dichloromethane (3 × 30 mL). Combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by recrystallization from acetone to give **1l** (9.60 g, 64%) as a yellow solid, m.p. = 160.5–161.5 °C, lit.[17] m.p. = 163 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.10 (m, 2 H), 8.25 (m, 2 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 120.8 (2 × CH), 140.1 (2 × CH), 142.1 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_5H_5N_2O_3^+$: 141.0295; found: 141.0290.



4-Methoxypyridine 1-oxide (1k): 4-Nitropyridine 1-oxide (**1l**) (3.00 g, 21.4 mmol) was added by portions to the freshly prepared solution of MeONa, which was obtained from Na (900 mg, 39.1 mmol) and methanol (100 mL). The resulting mixture was heated at 65 °C for 4 h, methanol was distilled off on a rotary evaporator and the residue was diluted with DCM (50 mL). Precipitate was filtered off, washed with DCM (50 mL), mother liquor was concentrated and the crude product was recrystallized from ethyl acetate/hexane mixture to give **1k** (1.83 g, 68%) as a dark green solid, m.p. = 82.5–84.0 °C, lit.[18] m.p. = 81.5–82.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, CH_3), 6.77–6.82 (m, 2 H), 8.09–8.14 (m, 2 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 56.0 (OCH_3), 111.6 (2 × CH), 139.9 (2 × CH), 157.8 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_6H_8NO_2^+$: 126.0550; found: 126.0554.



2-Methoxypyridine 1-oxide (1t): Solution of 2-chloropyridine 1-oxide (**1p)** (13.4 g, 103 mmol) in methanol (30 mL) was slowly added to the freshly prepared solution of MeONa, which was obtained from Na (2.62 g, 114 mmol) and methanol (45 mL). The resulting mixture was stirred under reflux for 2 h. Methanol was distilled off on a rotary evaporator, the residue was diluted with DCM (50 mL) and precipitate was filtered off. Mother liquor was concentrated and the crude product was recrystallized from EtOAc/hexane to give **1t** (8.70 g, 67%) as a colorless solid, m.p. = 59–60 °C, lit.[19] m.p. = 77–78 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.69 (s, 3 H, CH_3), 6.53–6.63 (m, 2 H), 6.94 (m, 1 H), 7.85 (d, J = 6.3 Hz, 1 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 56.4 (CH_3), 107.4 (CH), 116.8 (CH), 127.3 (CH), 139.0 (CH), 157.8 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_6H_8NO_2^+$: 126.0550; found: 126.0552.

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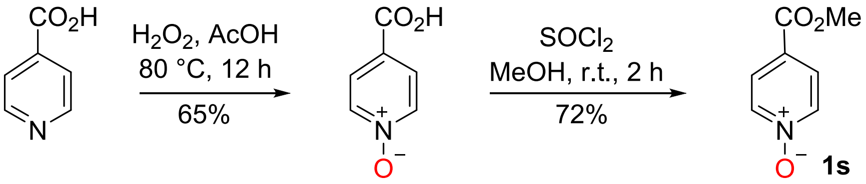
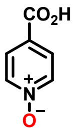
[17] Diemer, V.; Chaumeil, H.; Defoin, A.; Fort, A.; Boeglin, A.; Carré, C. *European J. Org. Chem.* **2008**, *2008* (10), 1767–1776.

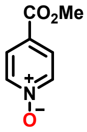
[18] Katritzky, A. R.; Randall, E. W.;.Sutton, L. E. *J. Chem. Soc.* **1957**, *1957*, 1769–1775.

[19] Keith, J. M. *J. Org. Chem.* **2008**, *73,* 327–330.





4-Carboxypyridine 1-oxide: From 4-carboxypyridine (15.0 g, 122 mmol), 4-carboxypyridine 1-oxide (11.0 g, 65%) was obtained according to **GP2b** as a colorless solid, m.p. = 264–265 °C, lit.[20] m.p. = 258–259 °C. **^{1}H NMR** (400 MHz, DMSO-*d$_6$*): δ = 7.81 (m, 2 H), 8.28 (m, 2 H), 13.51 (br. s, 1 H, OH) ppm. **^{13}C NMR** (101 MHz, DMSO-*d$_6$*): δ = 126.7 (C + CH), 139.3 (2 × CH), 164.8 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_6H_6NO_3^+$: 140.0342; found: 140.0345.



4-(Methoxycarbonyl)pyridine 1-oxide (1s): $SOCl_2$ (40 mL) was added dropwise to the suspension of 4-Carboxypyridine 1-oxide (11.1 g, 79.4 mmol) in methanol (150 mL) and the resulting mixture was stirred at r.t. for 2 h. Solvent was distilled off on a rotary evaporator and the crude product was recrystallized from acetone/hexane to give **1s** (8.75 g, 72%) as a colorless solid, m.p. = 106–107 °C, lit.[21] m.p. = 116.5–118.5 °C. **^{1}H NMR** (400 MHz, DMSO-*d$_6$*): δ = 3.83 (s, 3 H, CH_3), 7.89 (m, 2 H), 8.43 (m, 2 H) ppm. **^{13}C NMR** (101 MHz, DMSO-*d$_6$*): δ = 53.0 (CH_3), 126.9 (CH), 127.6 (C), 139.8 (CH), 163.7 (C) ppm. **HRMS** (ESI), *m/z*: $[M + H]^+$ calcd. for $C_7H_8NO_3^+$: 154.0499; found: 154.0496.

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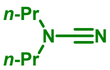
[20] Khrustalev, D. P. *Russ. J. Gen. Chem.* **2009**, *79*, 162–163.
[21] Katritzky, A. R.; Monro, A. M.; Beard, J. A. T.; Dearnaley, D. P.; Earl, N. J. *J. Chem. Soc.* **1958**, 2182–2191.

2.3. Synthesis of the starting cyanamide **2c**



Dipropylcyanamide (2c): Cyanamide (10.51 g, 250 mmol) was added in one portion to the solution of freshly prepared MeONa (13.5 g, 250 mmol) in MeOH (100 mL) and resulted mixture was stirred at r.t. for 15 h. Methanol was removed on a rotary evaporator, the residue was suspended in MeCN (100 mL) and 1-bromopropane (123 g, 1.00 mol) was added. Reaction mixture was stirred under reflux for 2 d, cooled down, and precipitate was filtred off. Vacuum distillation of the filtrate gave cyanamide **2c** (6.02 g, 19%) as a colourless liquid, b.p. = 84–85 °C (10 mbar), lit.[22] b.p. = 60 °C (1 Torr). **^{1}H NMR** (400 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.5$ Hz, 6 H, NCH_3), 1.66 (sextet, $J = 7.5$ Hz, 4 H, CH_2CH_3), 2.94 (t, $J = 7.5$ Hz, 4 H, NCH_2) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): $\delta = 11.0$ ($2 \times CH_3$), 21.0 ($2 \times CH_2CH_3$), 53.2 ($2 \times NCH_2$), 117.9 (CN) ppm. NMR data are consistent with previously reported.[23] **HRMS** (ESI), *m/z*: $[M + Na]^+$ calcd. for $C_7H_{14}N_2Na^+$: 149.1049; found: 149.1051.

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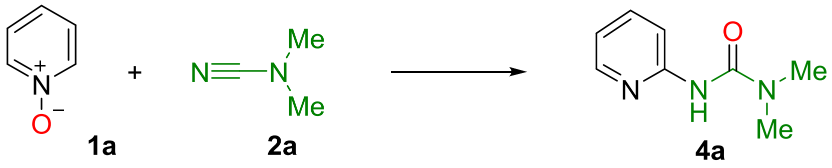
[22] Grigat, E.; Puetter, R. BE 641601, **1964** [*Chem. Abstr.* **1965**, *63*, 10094].

[23] Stolley, R. M.; Maczka, M. T.; Louie, J. *Eur. J. Org. Chem.* **2011**, 3815–3824.

2.4. Optimization of the reaction conditions (full data)

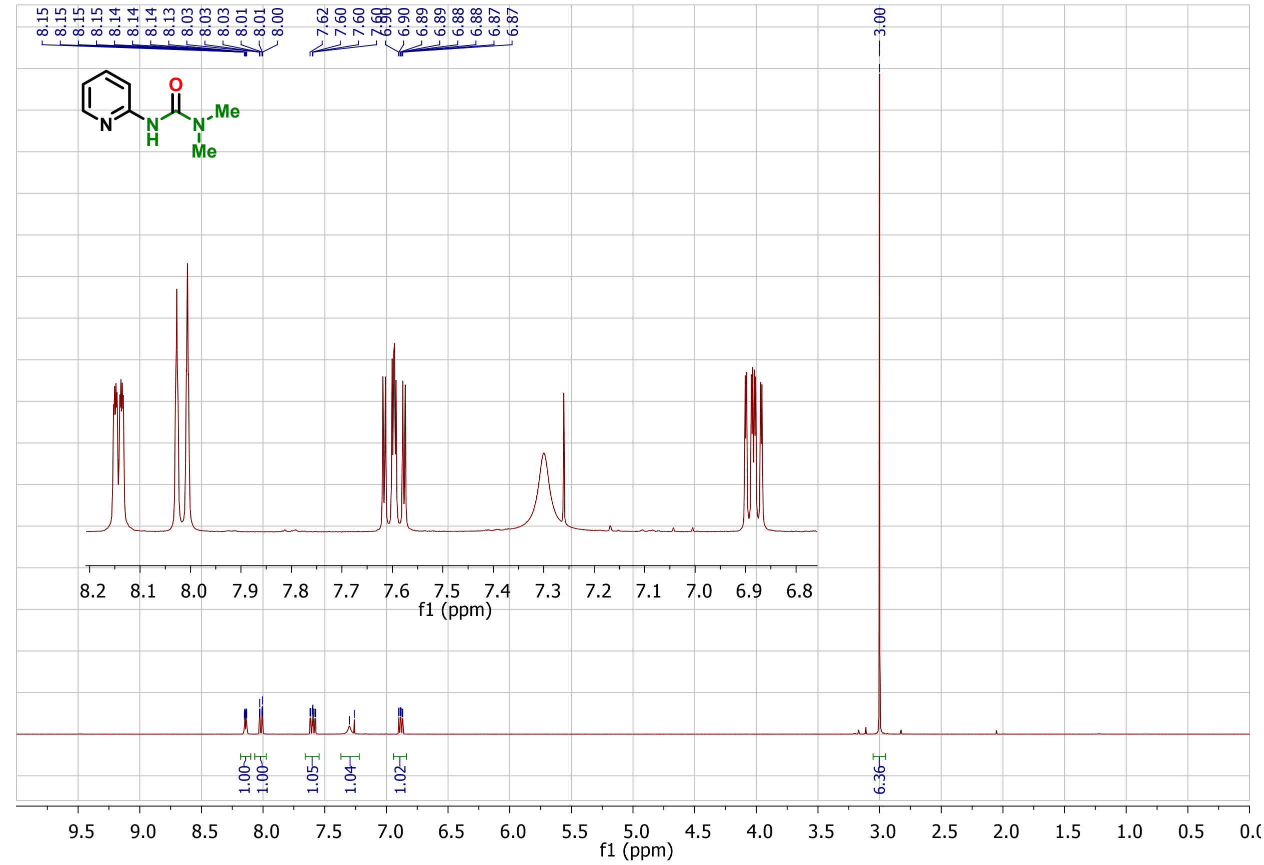


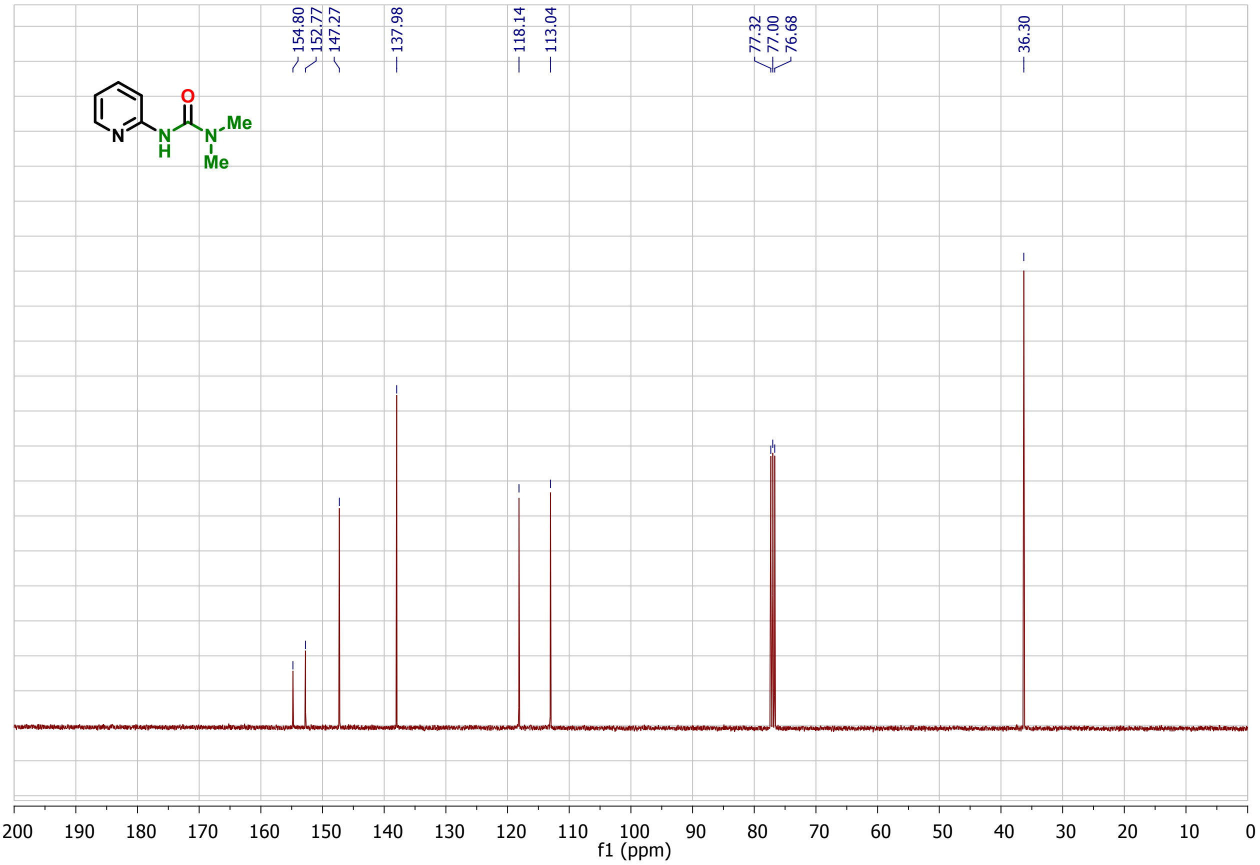
Entry	molar ratio			Conditions
	2a	Acid		(Conversion, %)
1	10	$MeSO_3H$	1.2	60 °C, 3 h (100)
2	1.0	$MeSO_3H$	1.0	60 °C, 3 h (85)
3	1.0	$MeSO_3H$	0.1	60 °C, 3 h (59)
4	1.0	$MeSO_3H$	0.3	60 °C, 3 h (83)
5	1.0	$MeSO_3H$	0.5	60 °C, 3 h (83)
6	1.0	$MeSO_3H$	0.7	60 °C, 3 h (88)
7	1.5	$MeSO_3H$	1.0	60 °C, 3 h (98)
8	2.0	$MeSO_3H$	1.0	60 °C, 3 h (98)
9	1.5	$MeSO_3H$	1.0	r.t., 24 h (0)
10	1.5	$MeSO_3H$	1.0	40 °C, 3 h (56)
11	1.5	$MeSO_3H$	0.1	60 °C, 3 h (46, 9:1[b])
12	1.5	$MeSO_3H$	0.1	60 °C, 8 h (74, 20:1[b])
13	1.5	$MeSO_3H$	0.3	60 °C, 3 h (78, 25:1[b])
14	1.5	$MeSO_3H$	0.7	60 °C, 3 h (88)
15	1.5	CF_3SO_3H	0.1	60 °C, 3 h (92, 16:1[b])
16	1.5	H_3PO_4	0.1	60 °C, 3 h (7)
17	1.5	$MeSO_3H$	1.0	60 °C, 1 h (78)
18	1.5	$MeSO_3H$	1.0	60 °C, 2 h (98)

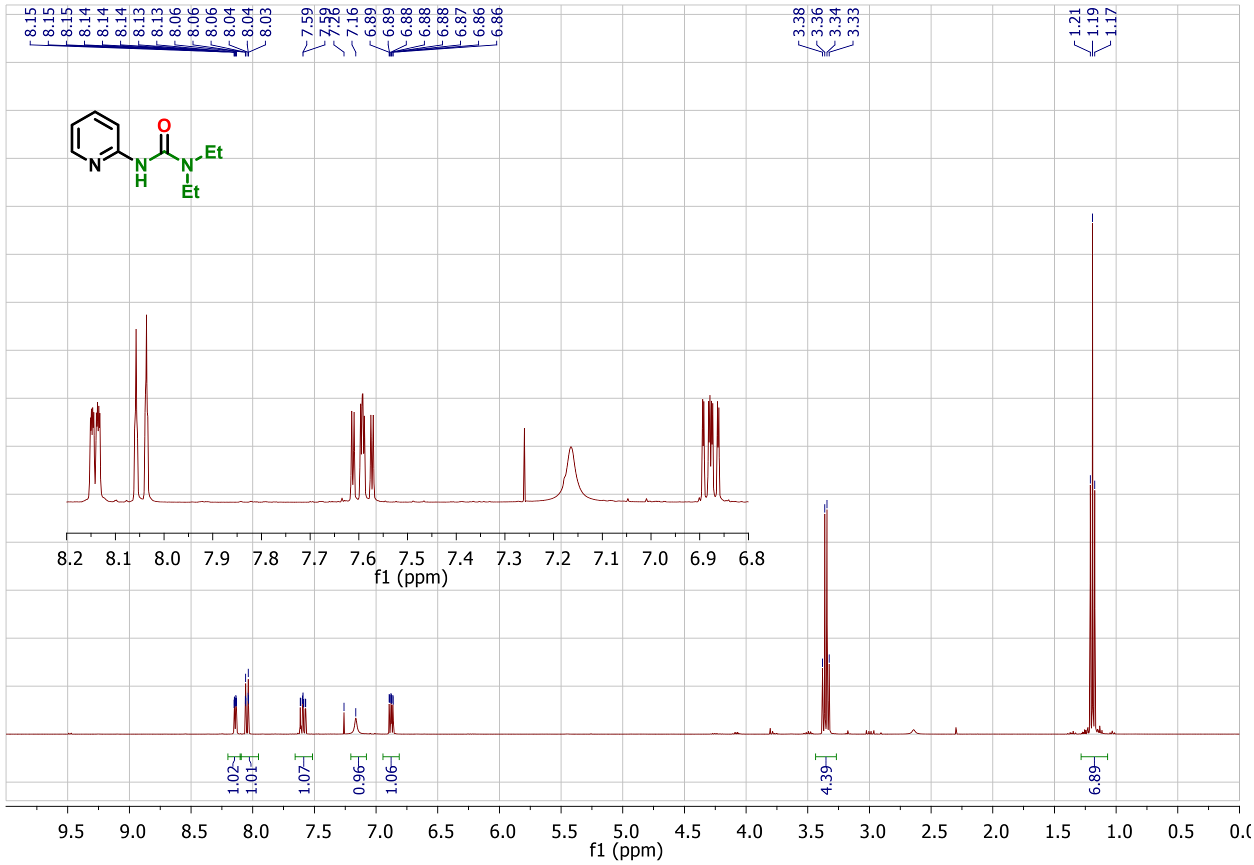
[a] – conversion of the starting material was estimated by ^{1}H NMR; [b] – molar ration of target- and by-product

3 NMR spectra

3.1. Spectra of *N*-pyridine-2-yl substituted ureas **4**







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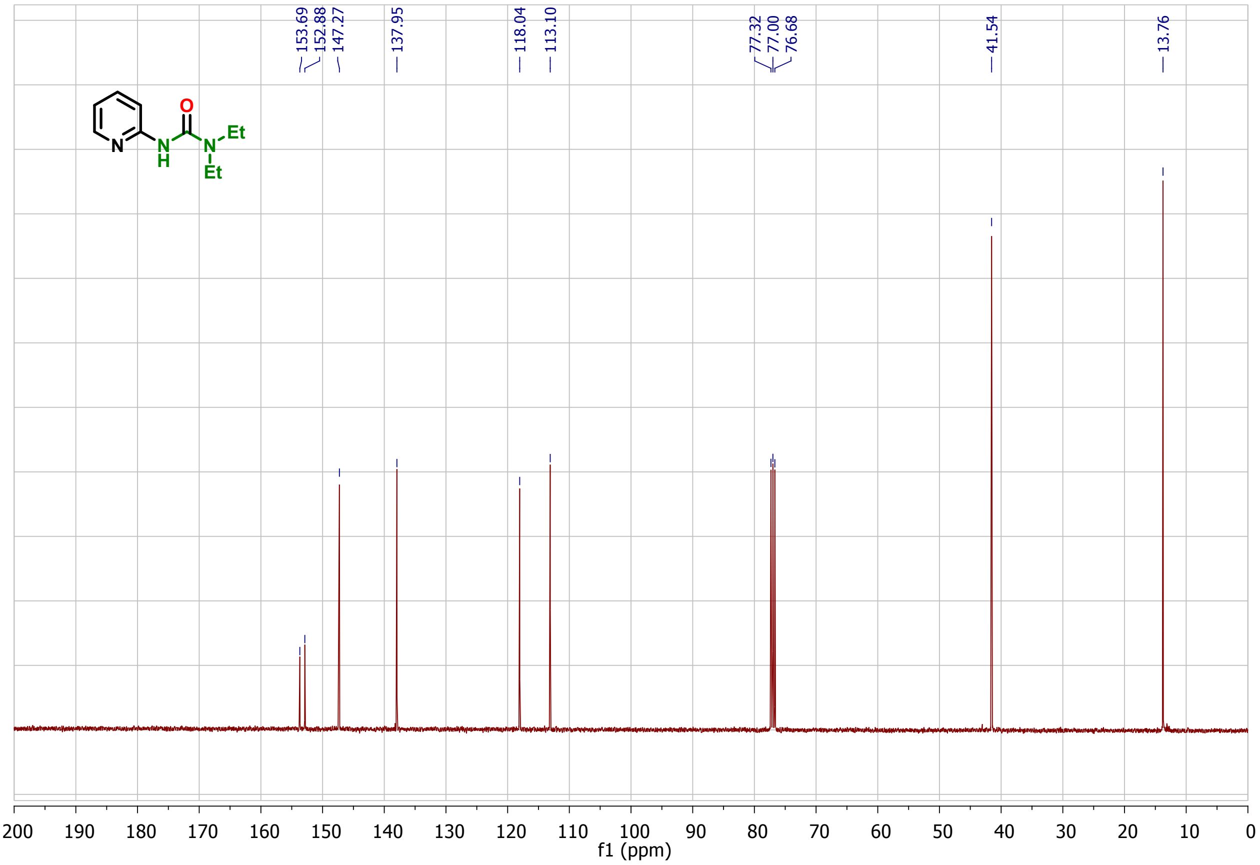

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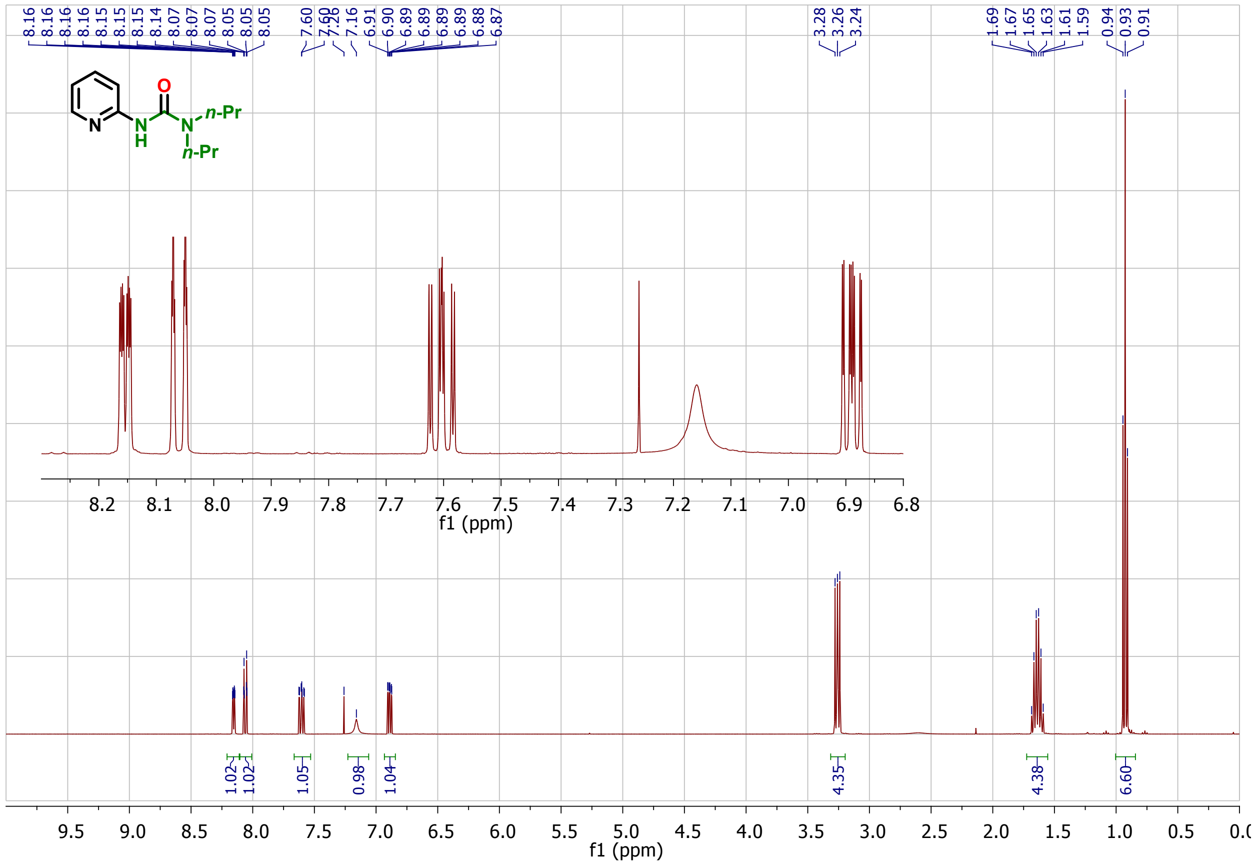
f1 (ppm)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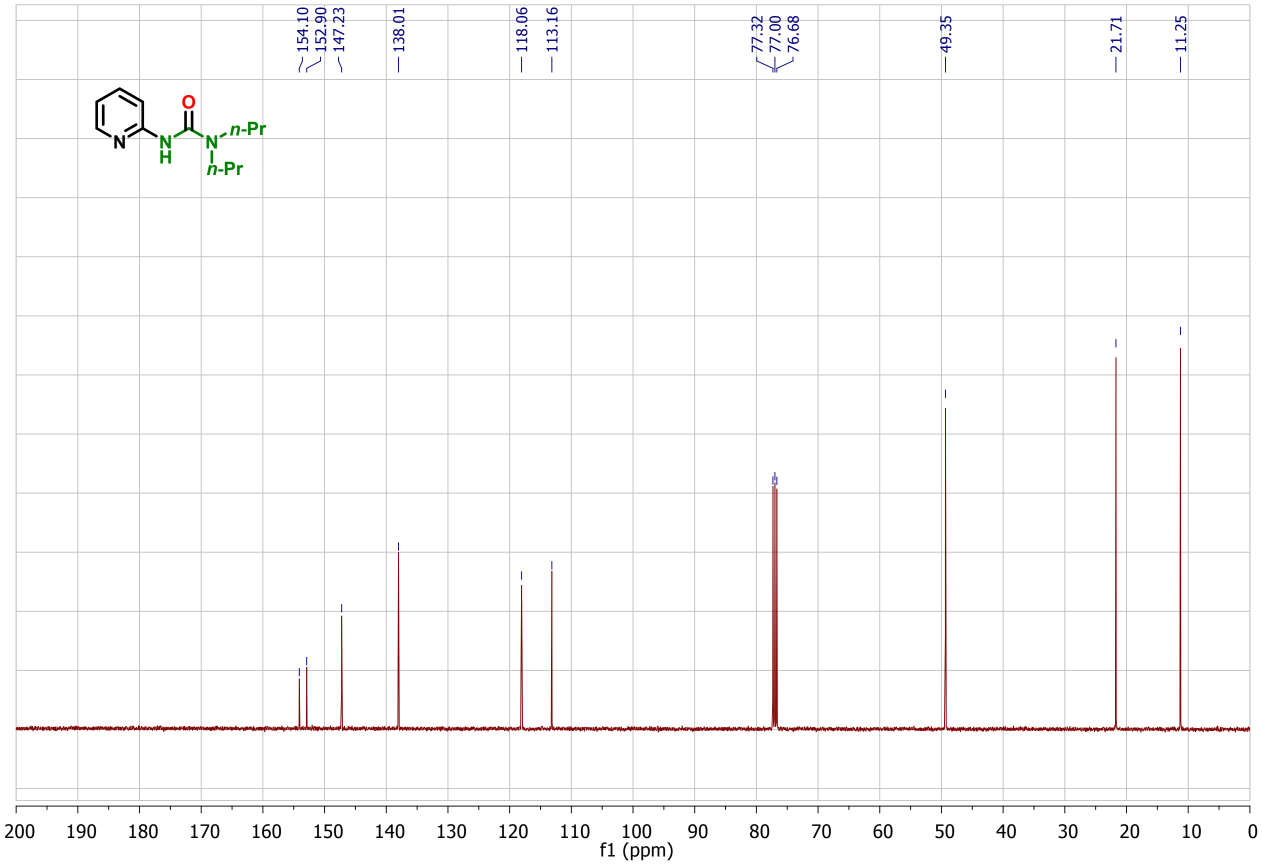
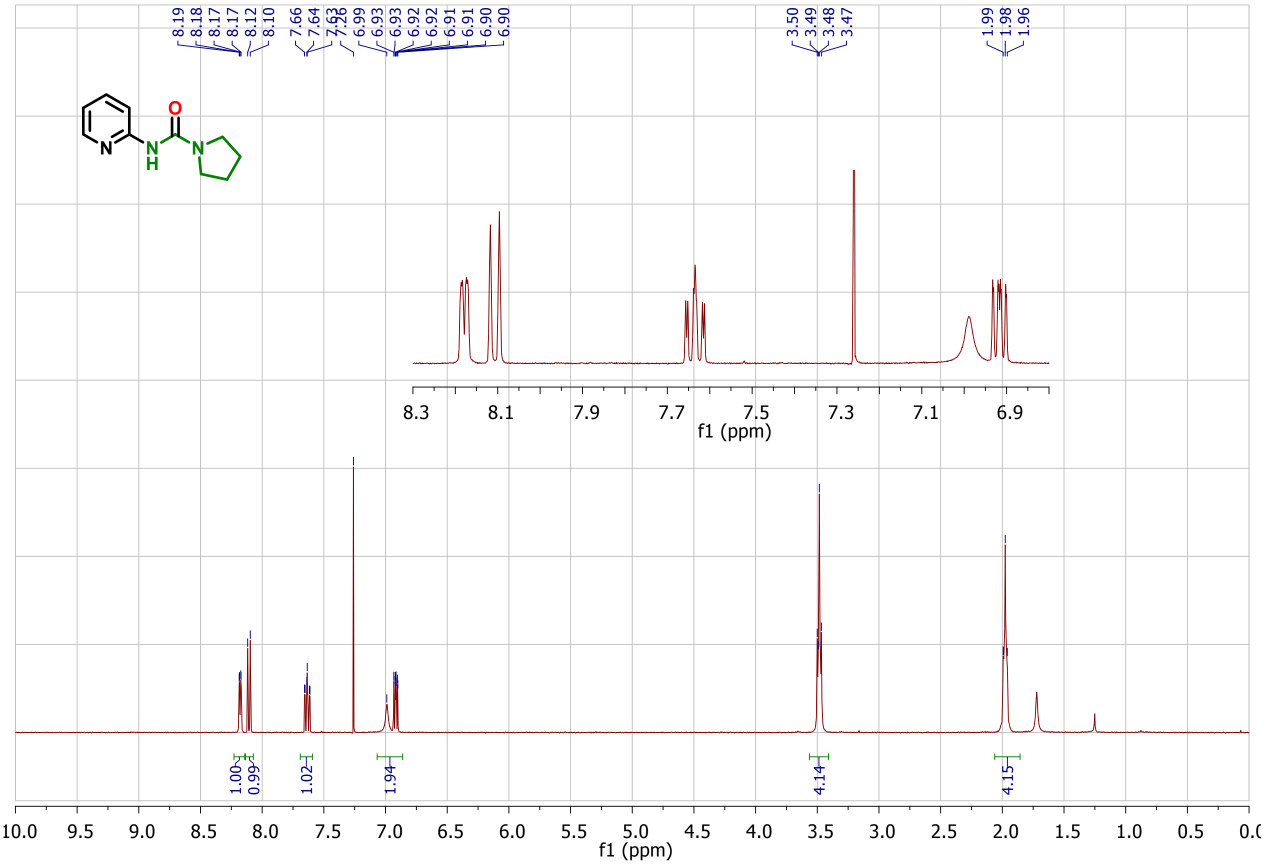
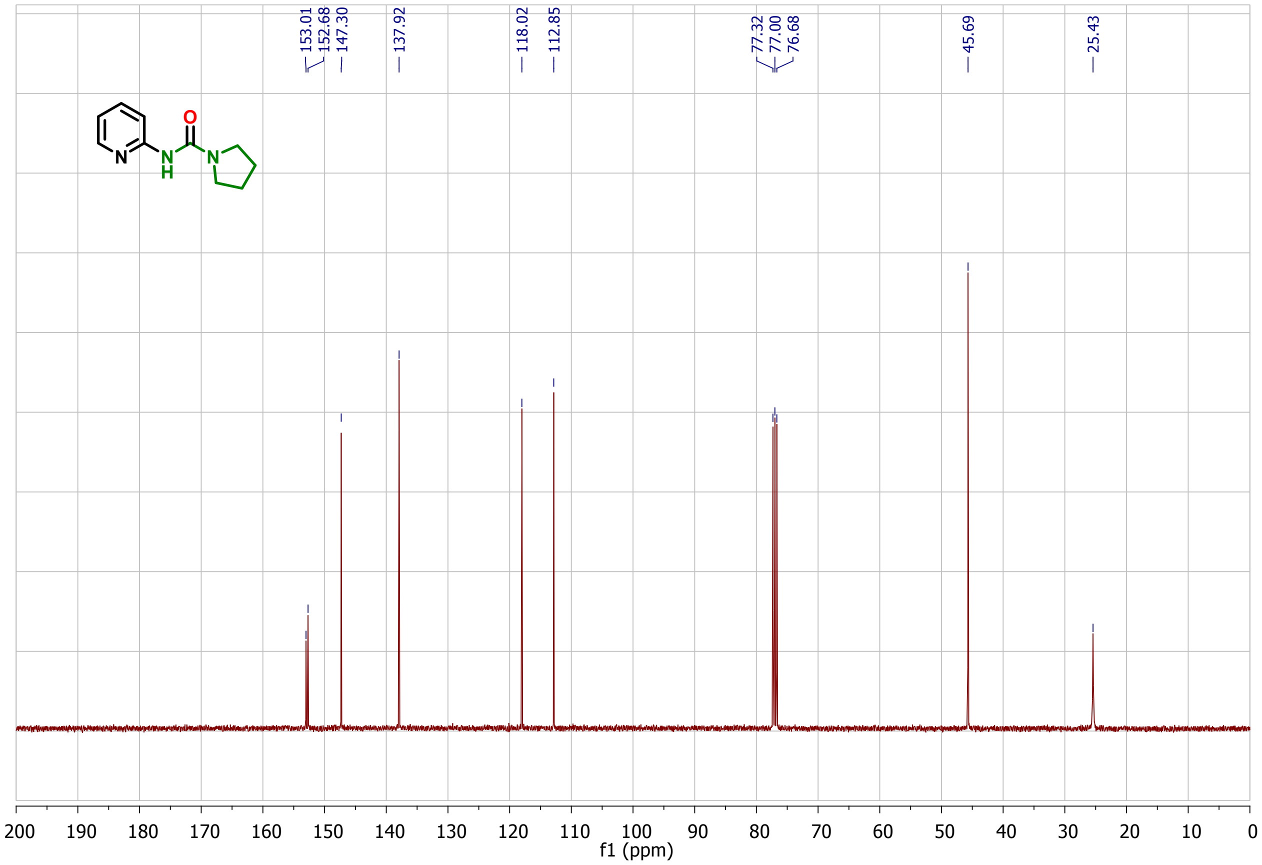
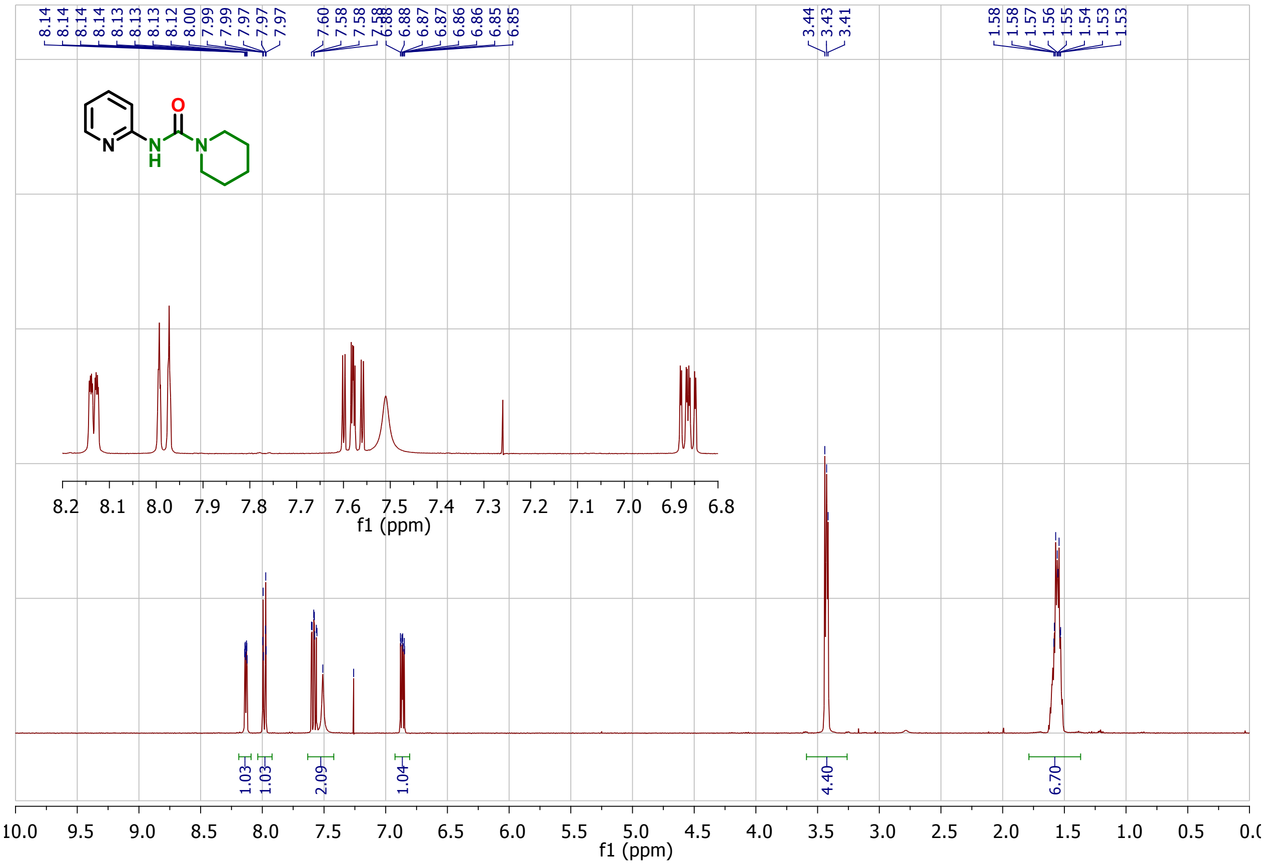
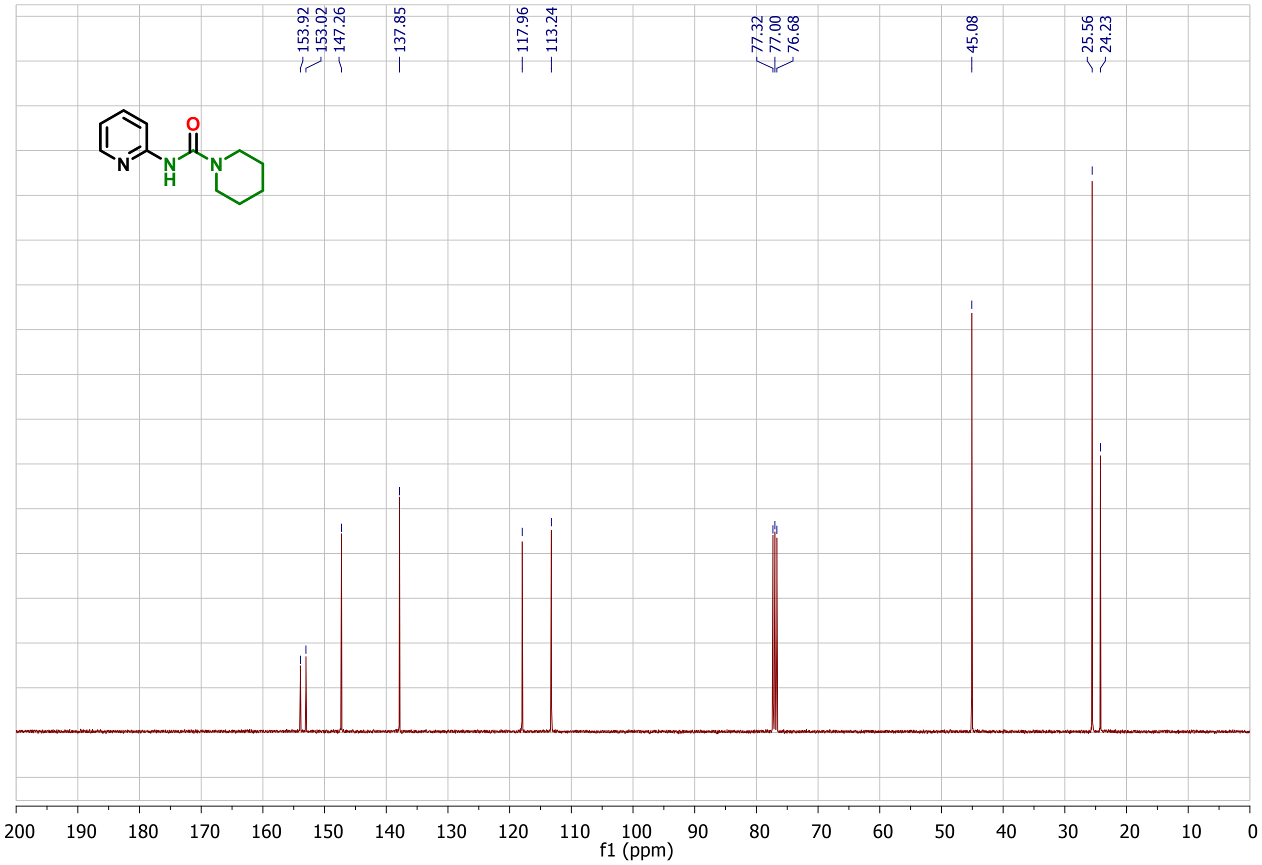
6.89
6.88
6.87
3.28
3.26
3.24
1.69
1.67
1.65
1.63
1.61
1.59
0.94
0.93
0.91
O
N
N
H
N
n-Pr
n-Pr
1.02
1.02
1.05
0.98
1.04
4.35
4.38
6.60
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8

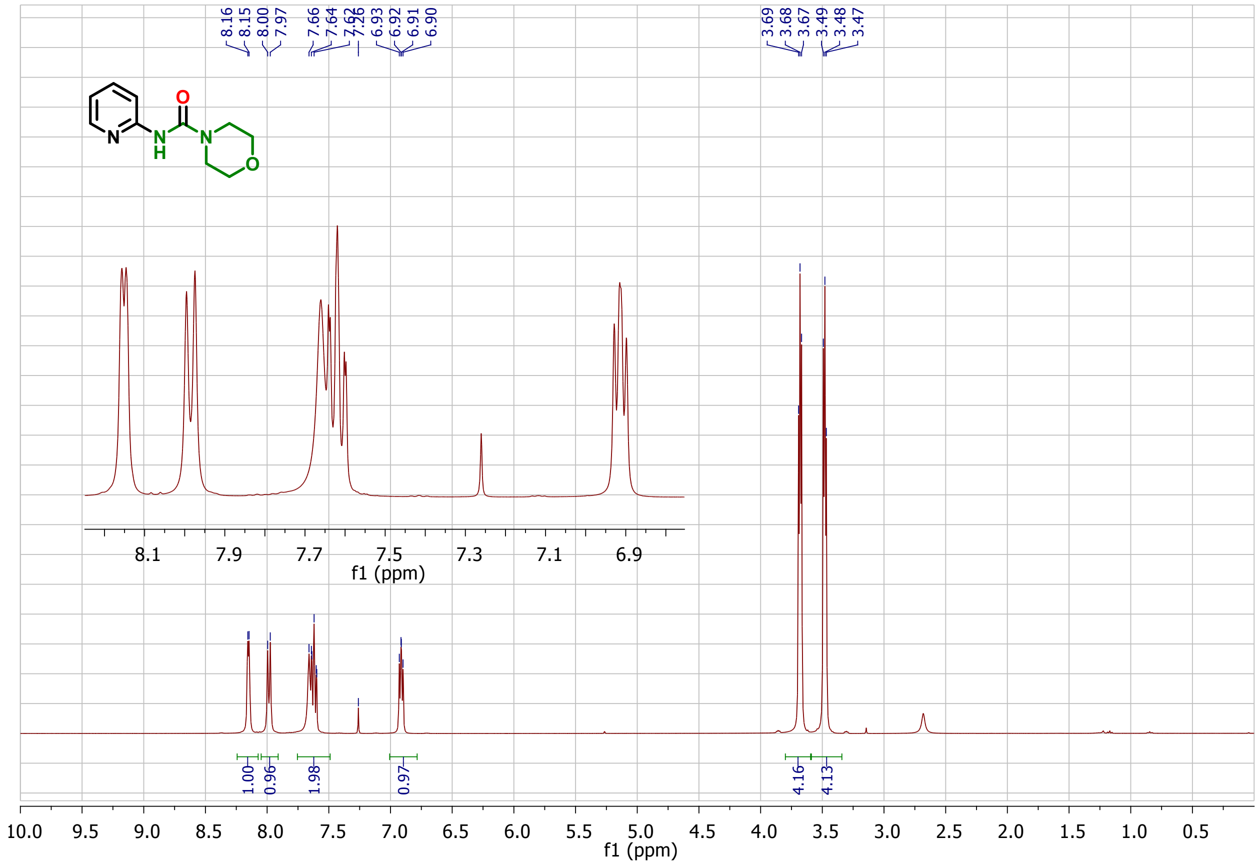

154.10
152.90
147.23
138.01
118.06
113.16
77.32
77.00
76.68
49.35
21.71
11.25
O
N
N
H
N
n-Pr
n-Pr
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

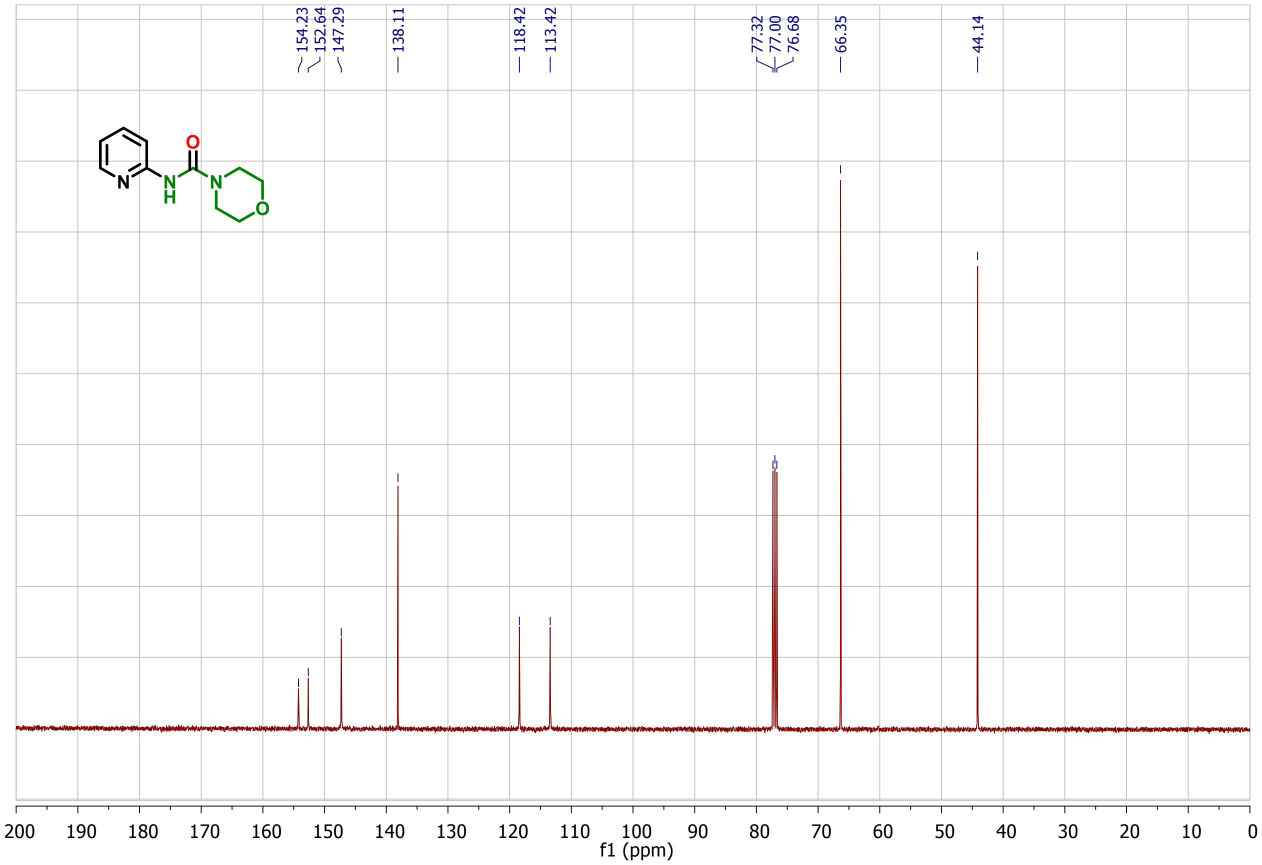

8.19
8.18
8.17
8.17
8.12
8.10
7.66
7.64
7.63
7.26
6.99
6.93
6.93
6.92
6.92
6.91
6.91
6.90
6.90
3.50
3.49
3.48
3.47
1.99
1.98
1.96
N
N
H
O
N
8.3
8.1
7.9
7.7
7.5
7.3
7.1
6.9
f1 (ppm)
1.00
0.99
1.02
1.94
4.14
4.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

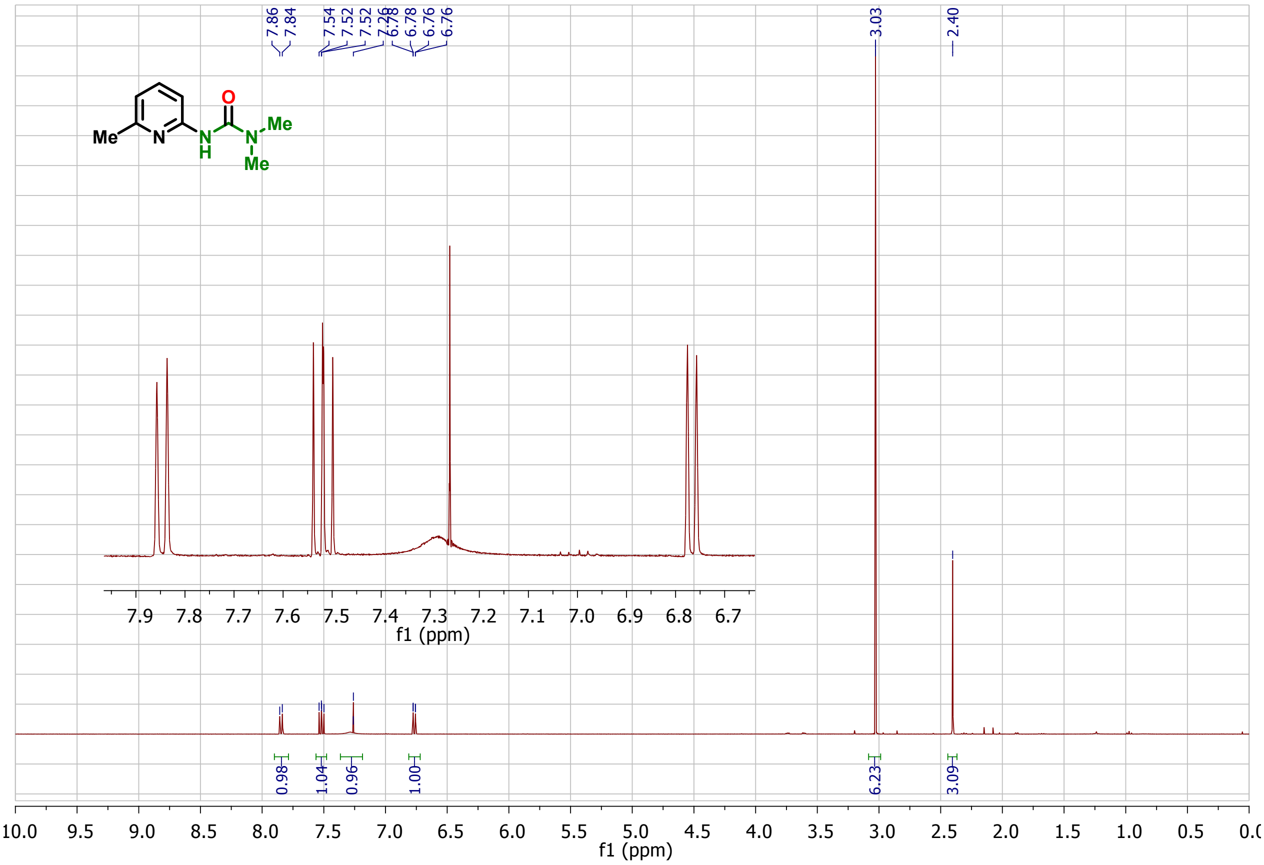

153.01
152.68
147.30
137.92
118.02
112.85
77.32
77.00
76.68
45.69
25.43
N
N
H
O
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

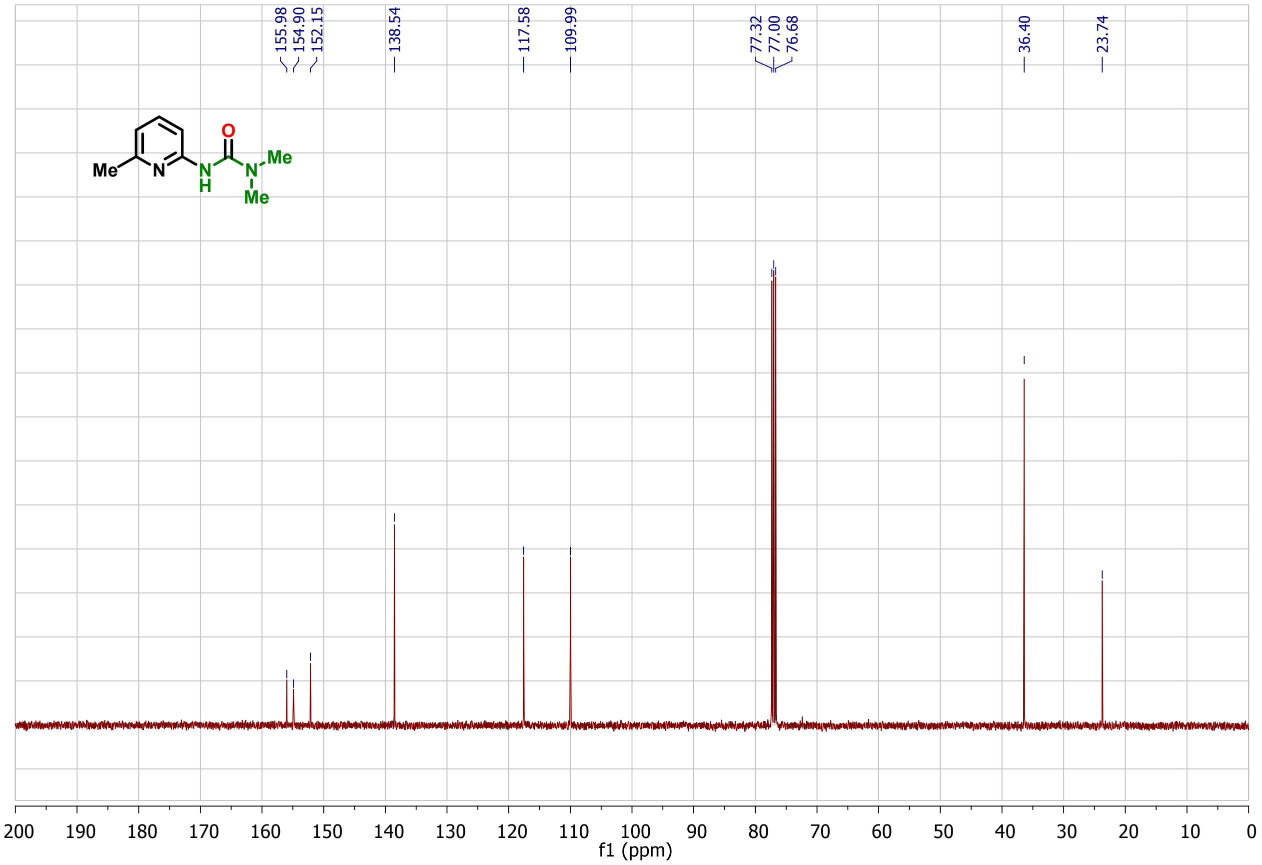

8.14
8.14
8.14
8.14
8.13
8.13
8.13
8.12
8.00
7.99
7.99
7.97
7.97
7.97
7.60
7.58
7.58
7.58
6.88
6.88
6.87
6.87
6.86
6.86
6.85
6.85
3.44
3.43
3.41
1.58
1.58
1.57
1.56
1.55
1.54
1.53
1.53
O
N
N
H
N
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
1.03
1.03
2.09
1.04
4.40
6.70
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

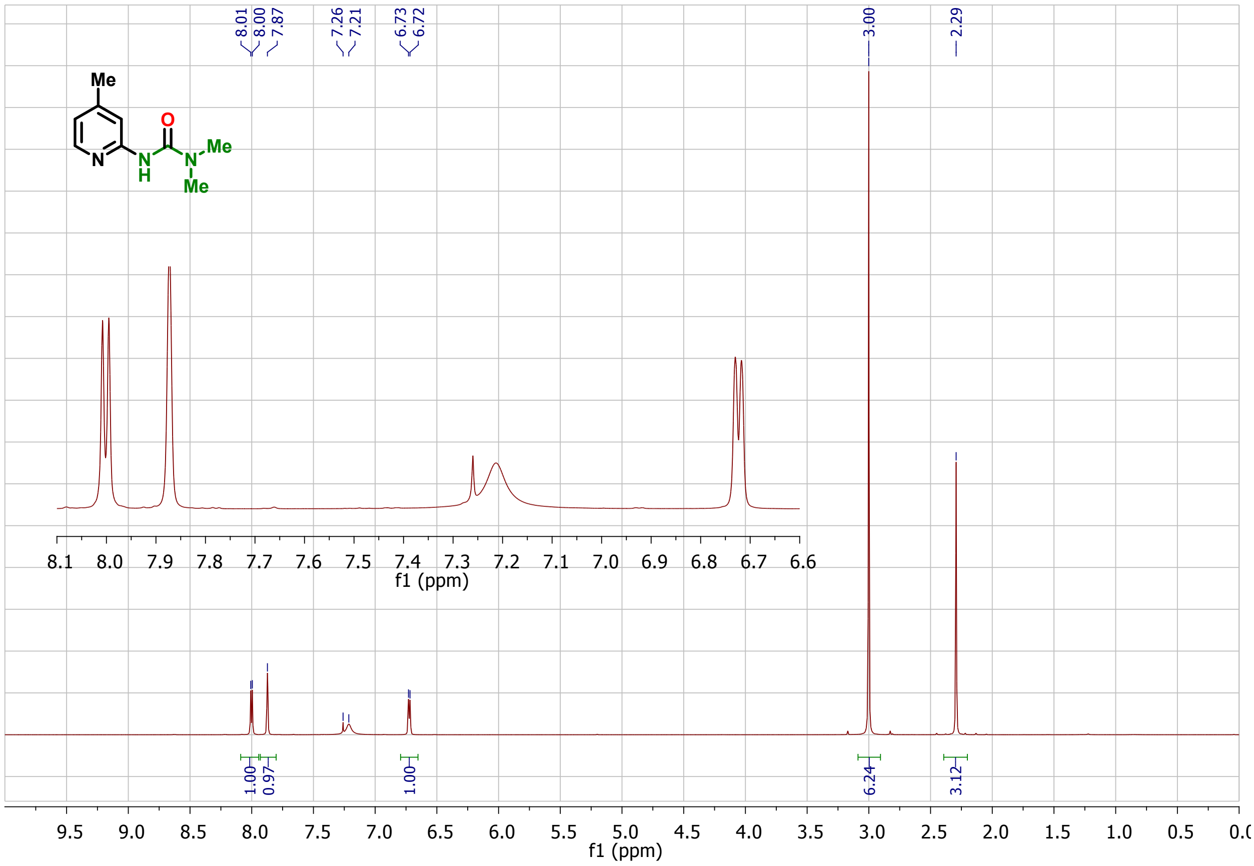

153.92
153.02
147.26
137.85
117.96
113.24
77.32
77.00
76.68
45.08
25.56
24.23
O
N
N
H
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

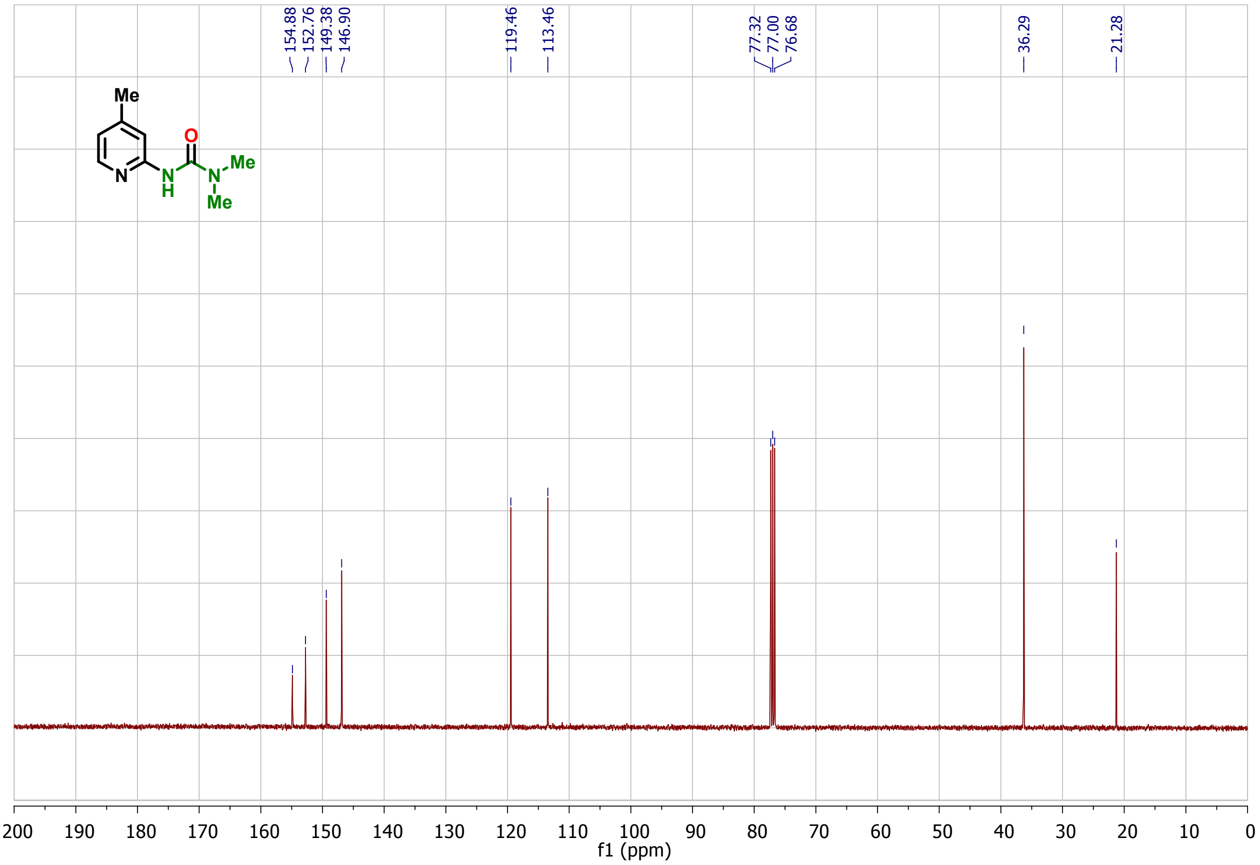

8.16
8.15
8.00
7.97
7.66
7.64
7.62
7.26
6.93
6.92
6.91
6.90
3.69
3.68
3.67
3.49
3.48
3.47
N
N
H
O
N
O
8.1
7.9
7.7
7.5
7.3
7.1
6.9
f1 (ppm)
1.00
0.96
1.98
0.97
4.16
4.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

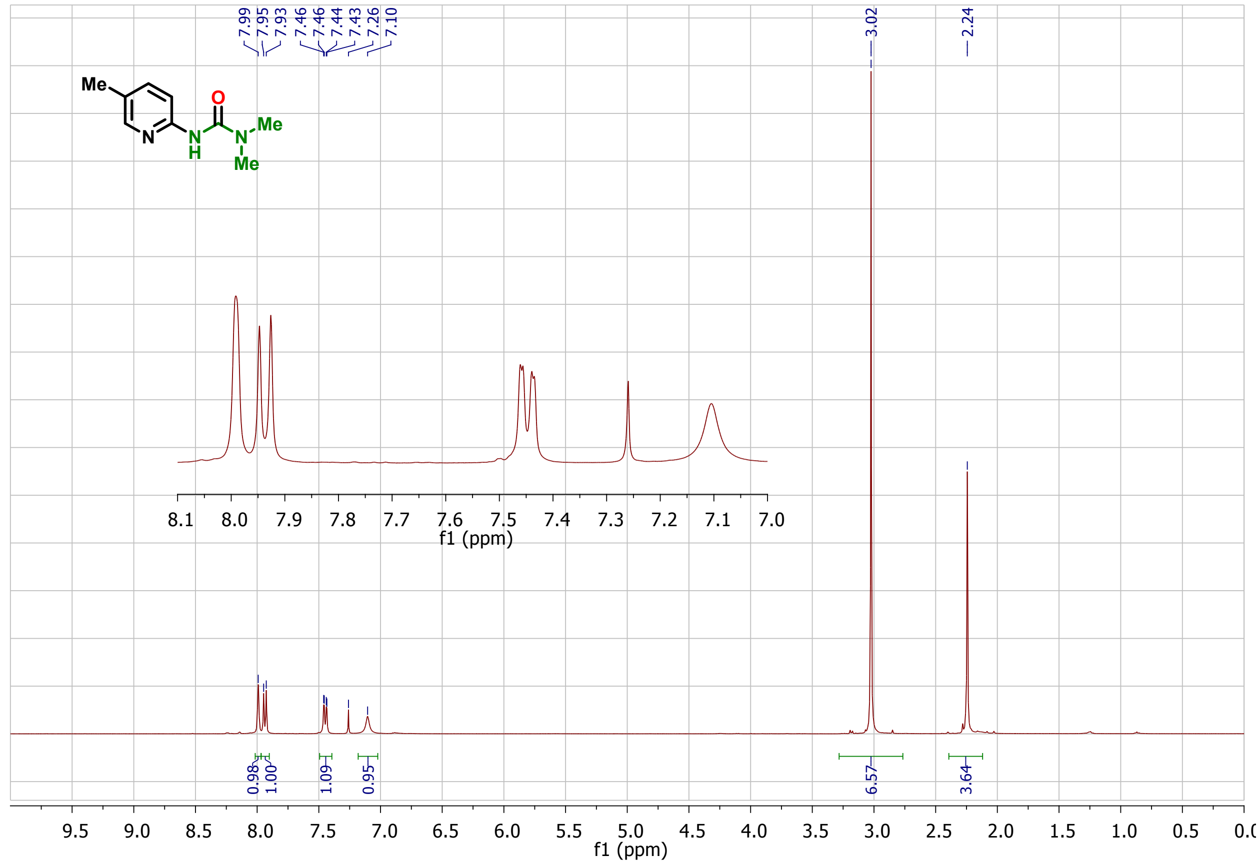

154.23
152.64
147.29
138.11
118.42
113.42
77.32
77.00
76.68
66.35
44.14
N
N
H
O
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

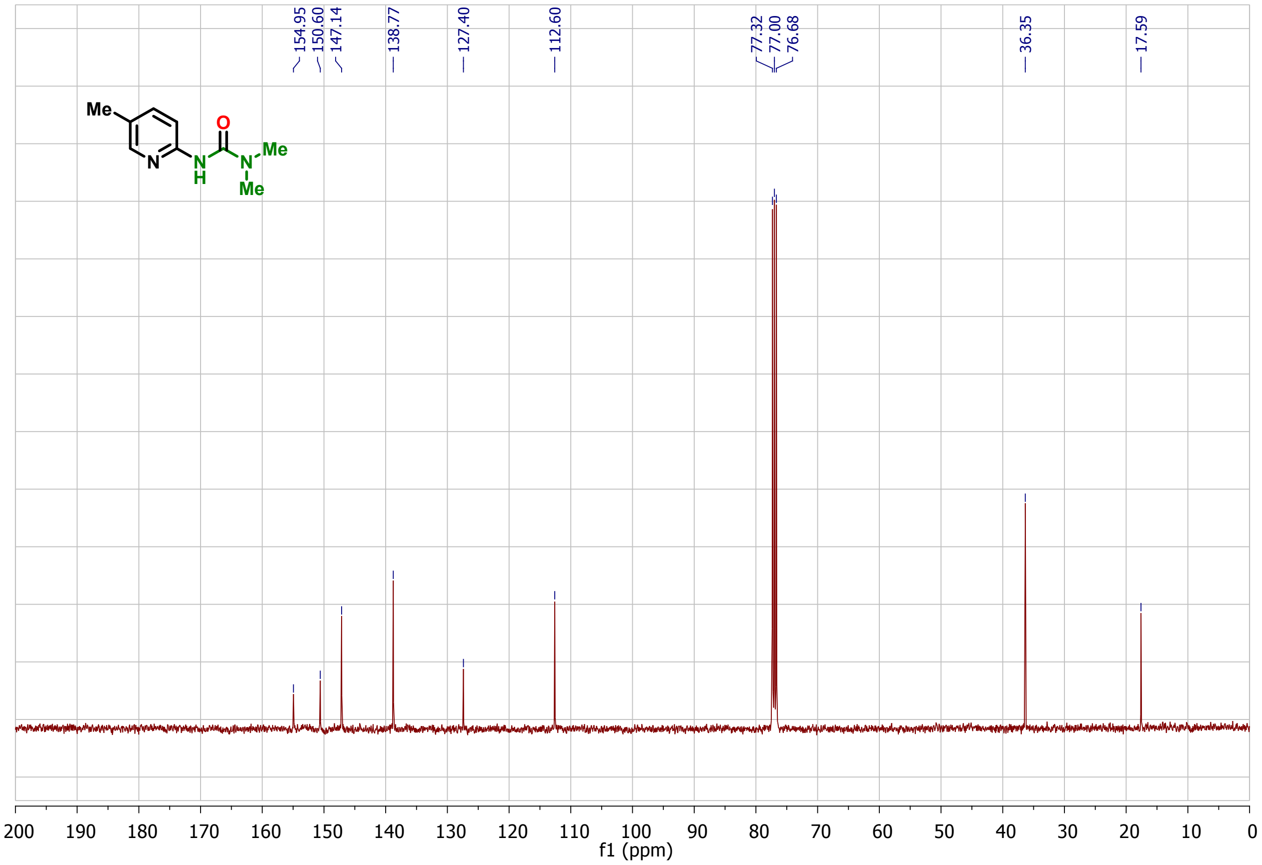

7.86
7.84
7.54
7.52
7.52
7.26
6.78
6.78
6.76
6.76
3.03
2.40
Me
N
N
H
O
N
Me
Me
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
0.98
1.04
0.96
1.00
6.23
3.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

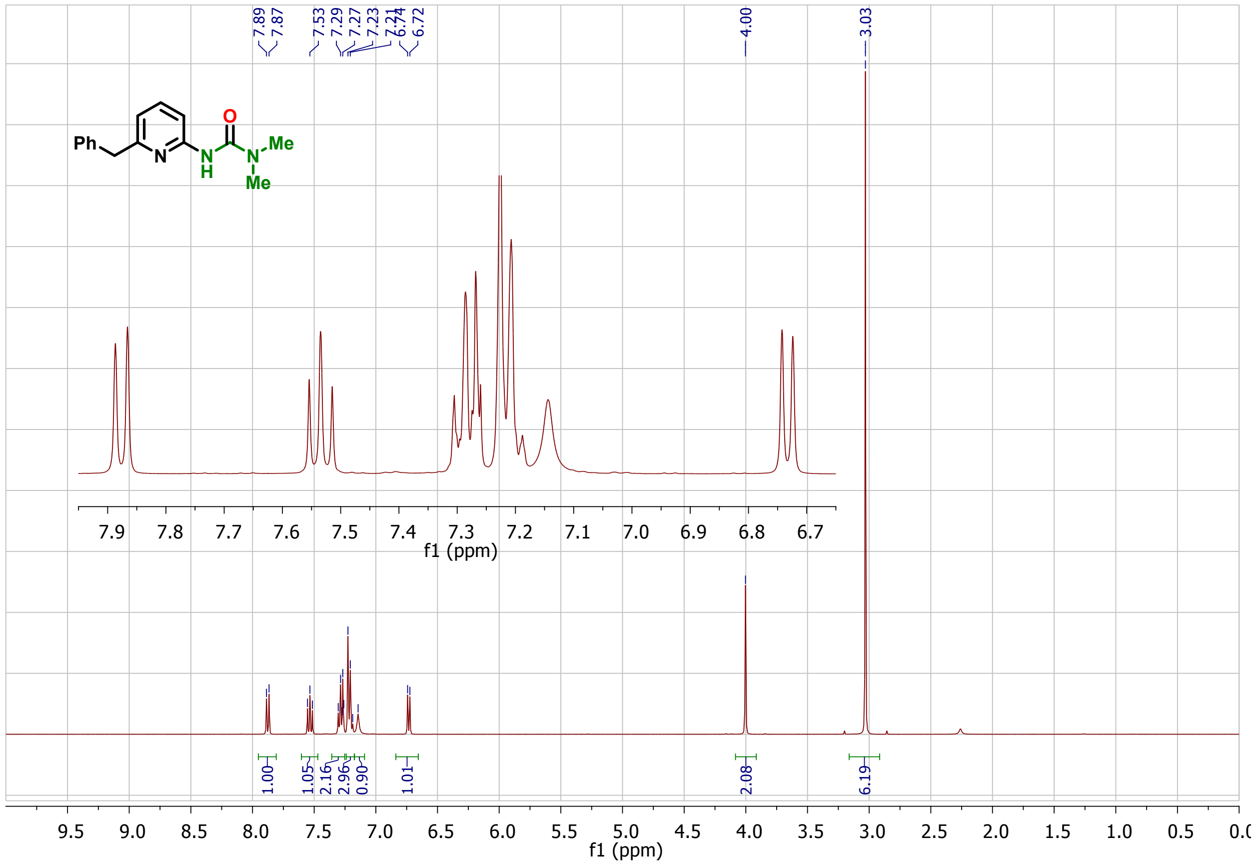

155.98
154.90
152.15
138.54
117.58
109.99
77.32
77.00
76.68
36.40
23.74
Me
N
N
H
O
N
Me
Me
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

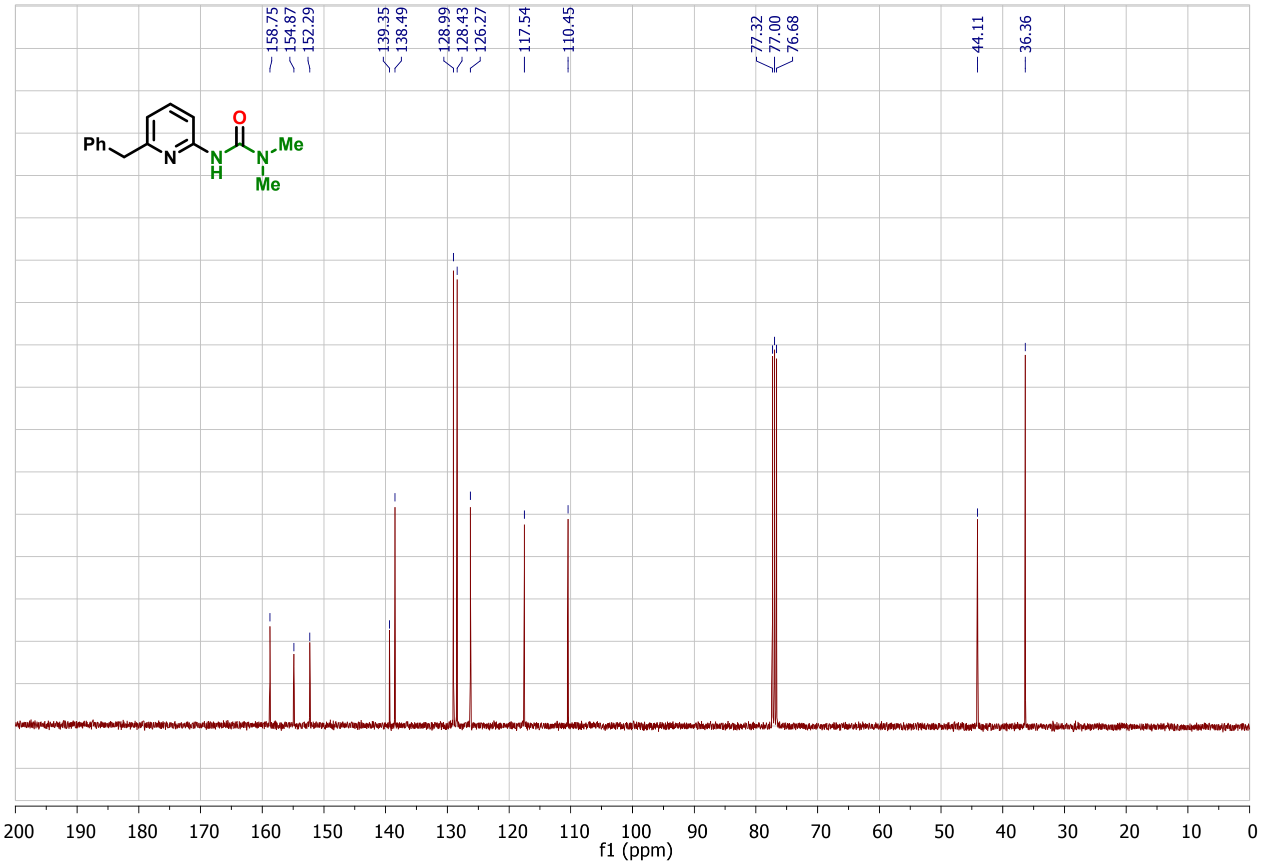

8.01
8.00
7.87
7.26
7.21
6.73
6.72
3.00
2.29
Me
O
N
N
H
N
Me
Me
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
f1 (ppm)
1.00
0.97
1.00
6.24
3.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

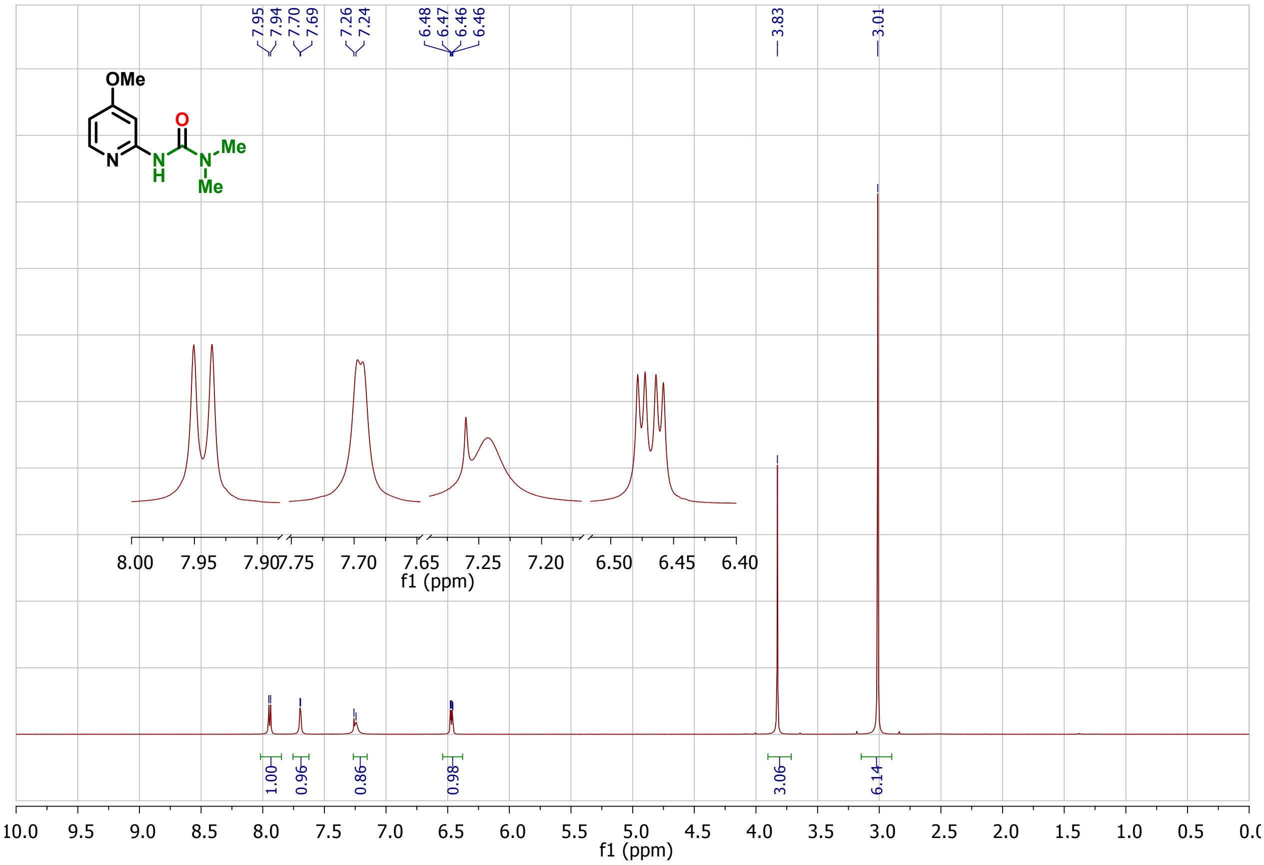

154.88
152.76
149.38
146.90
119.46
113.46
77.32
77.00
76.68
36.29
21.28
Me
O
N
N
H
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

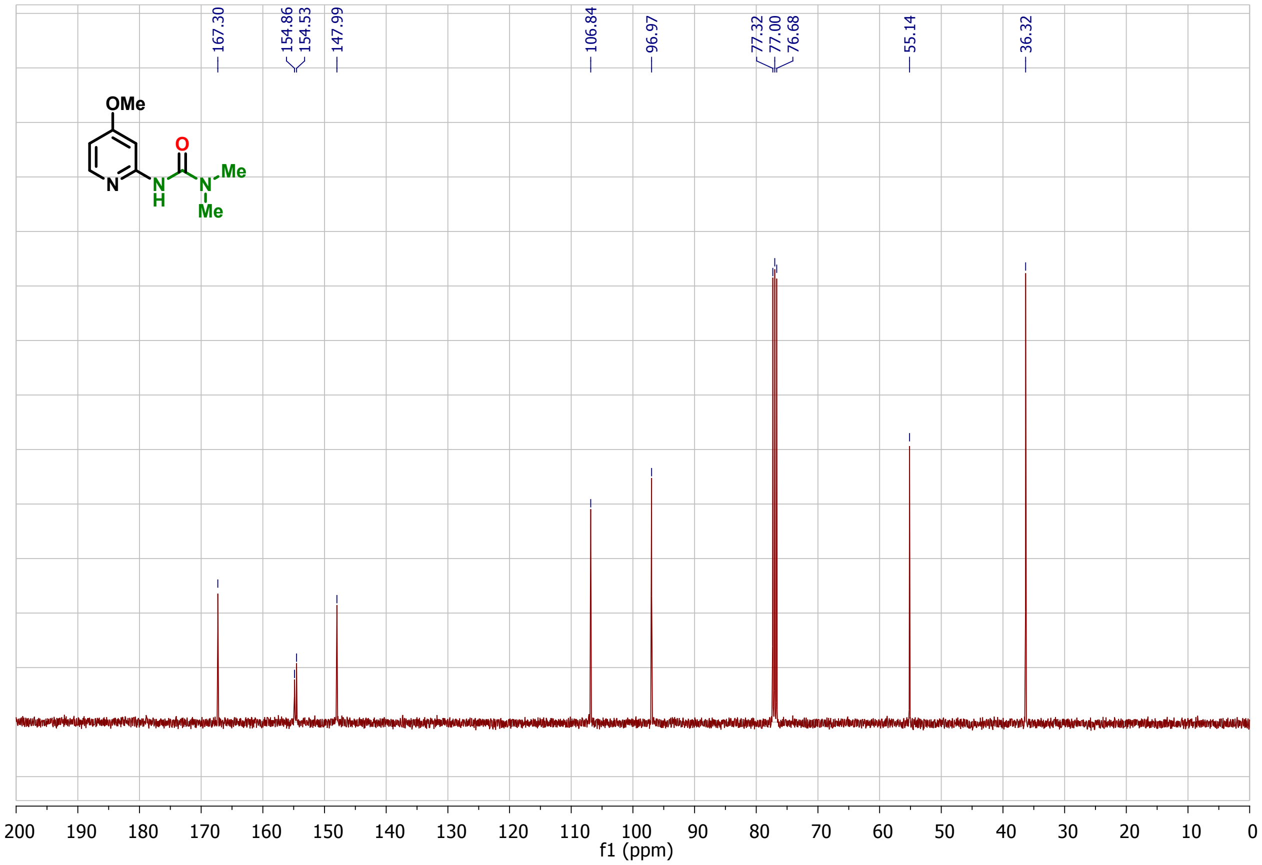

7.99
7.95
7.93
7.46
7.46
7.44
7.43
7.26
7.10
3.02
2.24
Me
O
N
N
H
N
Me
Me
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
0.98
1.00
1.09
0.95
6.57
3.64
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


154.95
150.60
147.14
138.77
127.40
112.60
77.32
77.00
76.68
36.35
17.59
Me
O
N
N
H
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

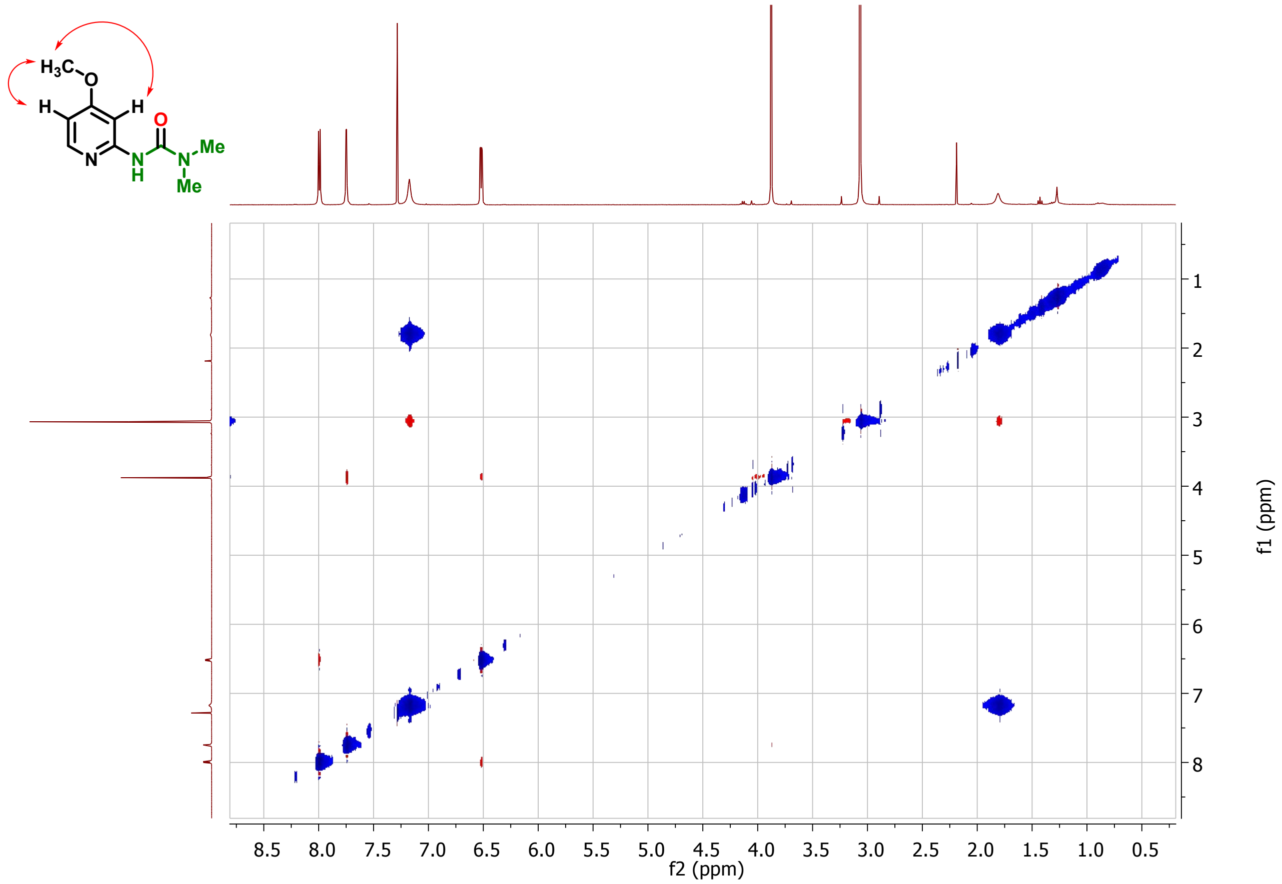

7.89
7.87
7.53
7.29
7.27
7.23
7.21
6.74
6.72
4.00
3.03
Ph
N
N
H
O
N
Me
Me
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
1.00
1.05
2.16
2.96
0.90
1.01
2.08
6.19
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

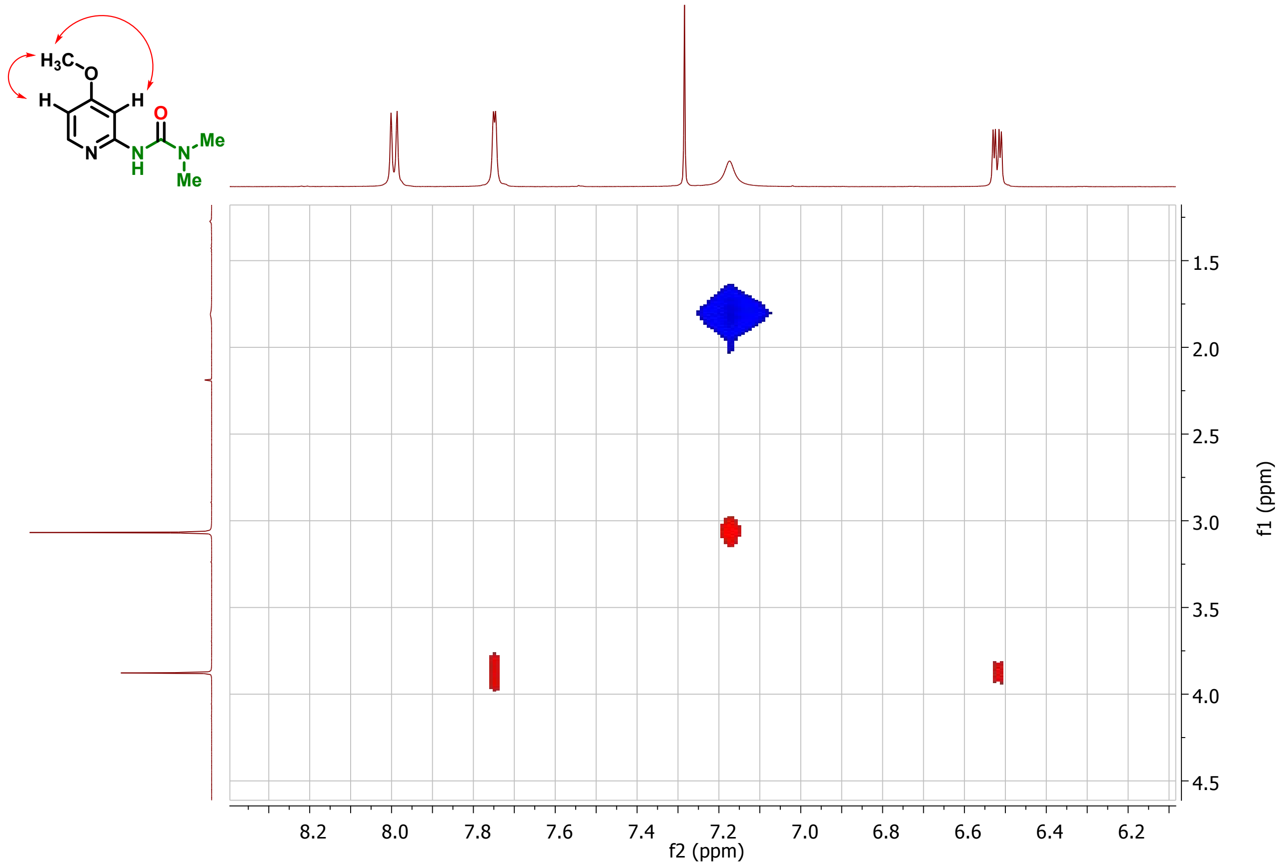

158.75
154.87
152.29
139.35
138.49
128.99
128.43
126.27
117.54
110.45
77.32
77.00
76.68
44.11
36.36
Ph
N
N
H
O
N
Me
Me
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

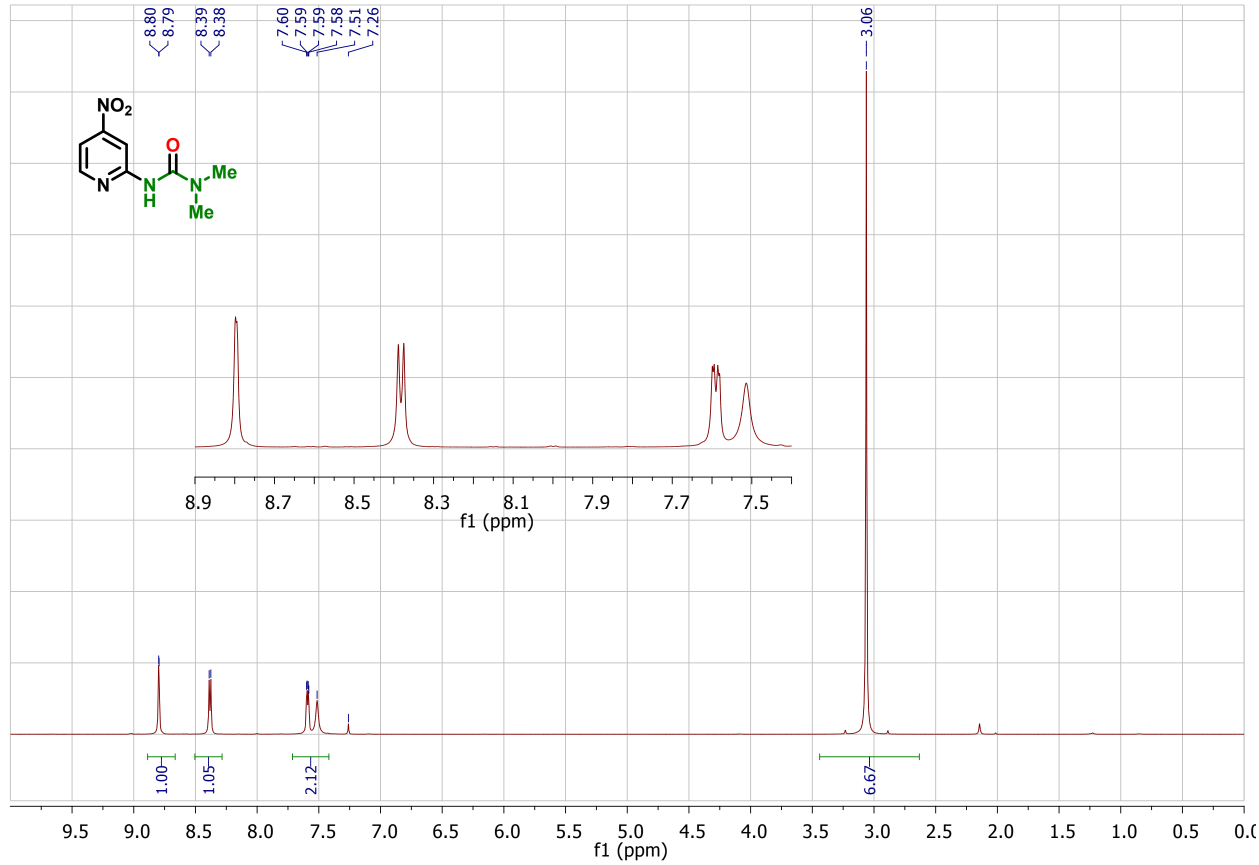

7.95
7.94
7.70
7.69
7.26
7.24
6.48
6.47
6.46
6.46
3.83
3.01
OMe
N
N
H
O
N
Me
Me
8.00
7.95
7.90
7.75
7.70
7.65
7.25
7.20
6.50
6.45
6.40
f1 (ppm)
1.00
0.96
0.86
0.98
3.06
6.14
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

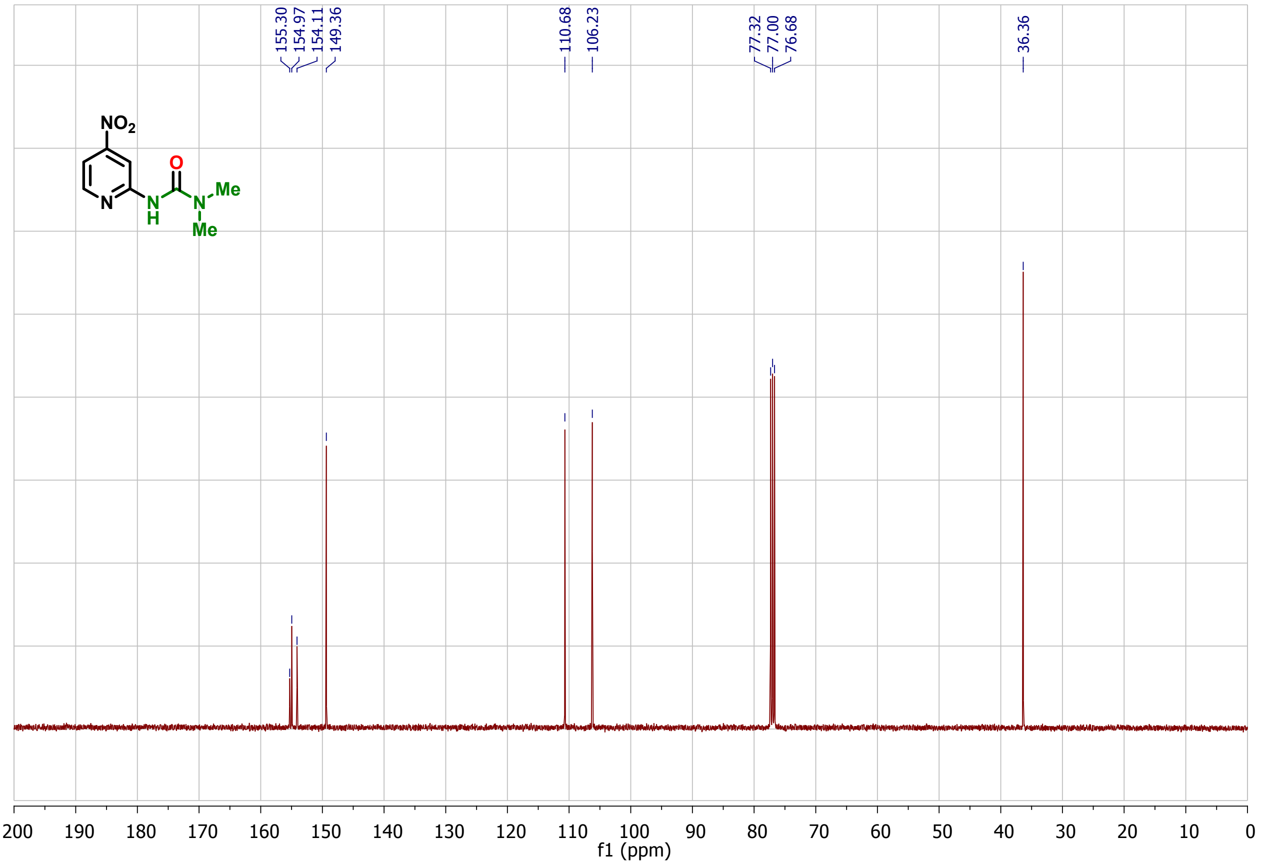

167.30
154.86
154.53
147.99
106.84
96.97
77.32
77.00
76.68
55.14
36.32
OMe
N
N
H
O
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

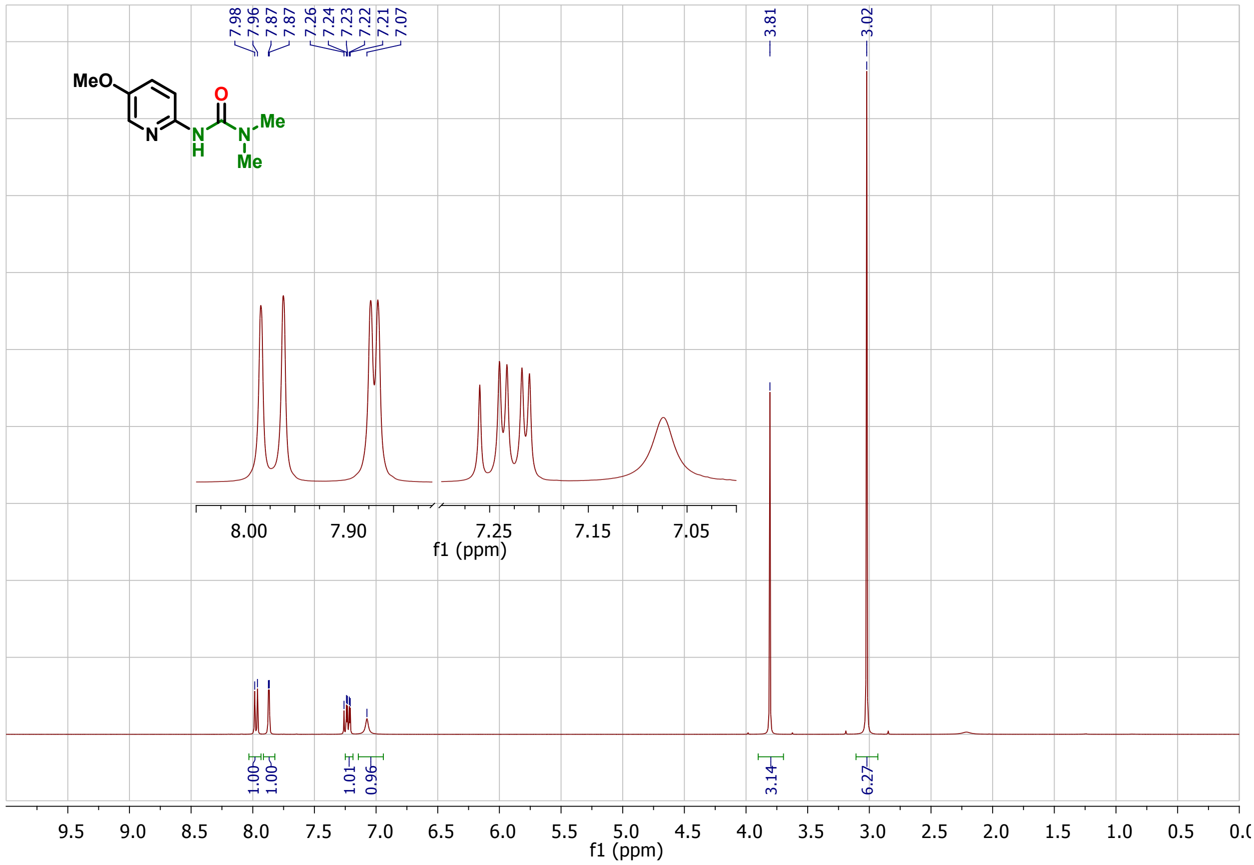
NOESY NMR of 3-(4-Methoxypyridin-2-yl)-1,1-dimethylurea (**4fa**)

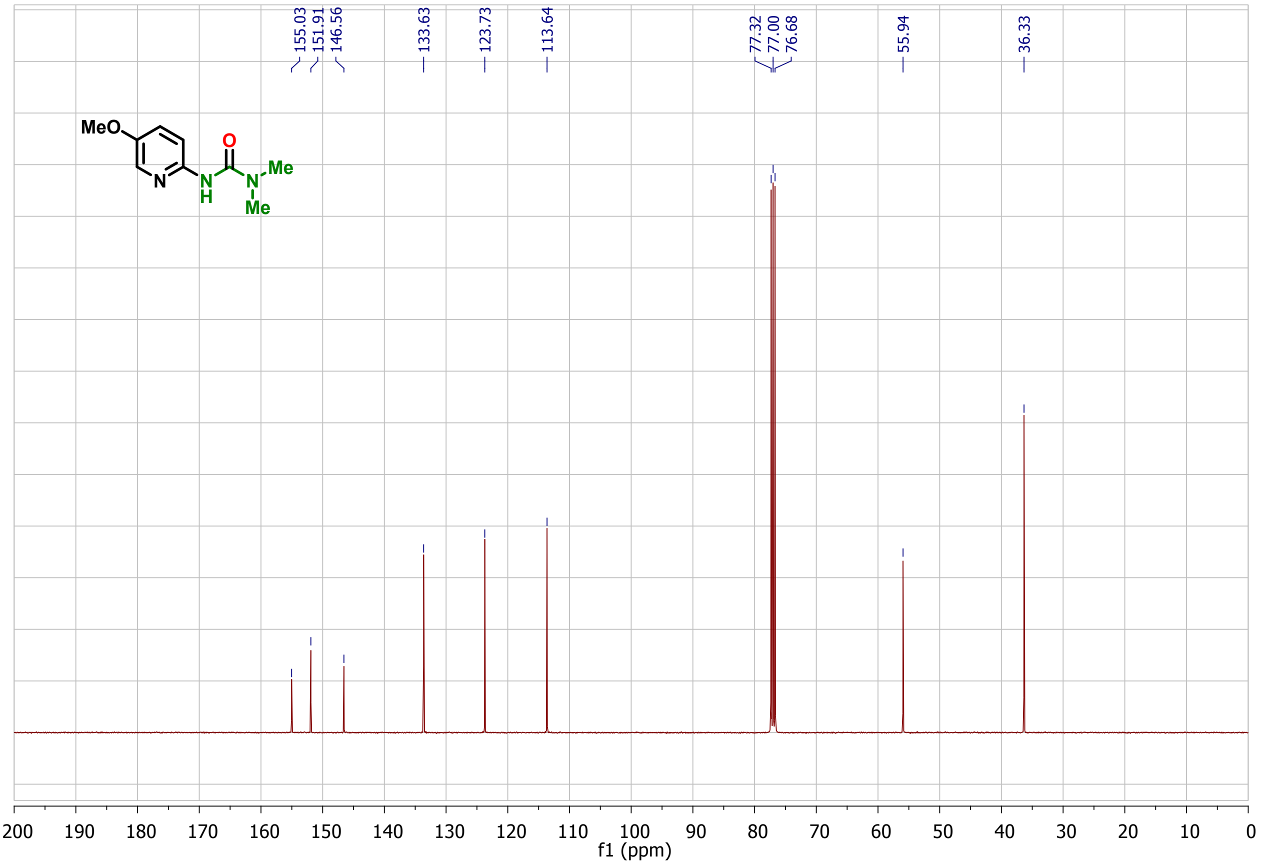


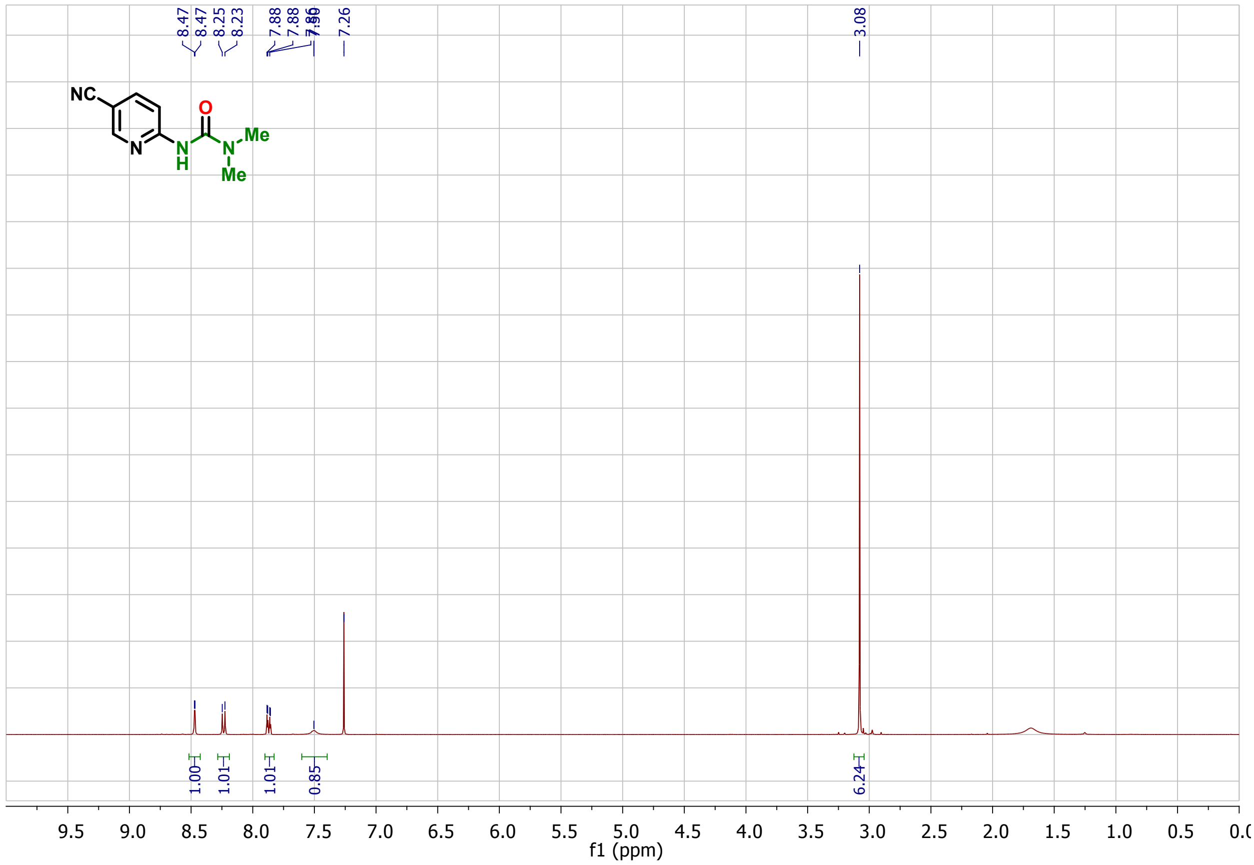


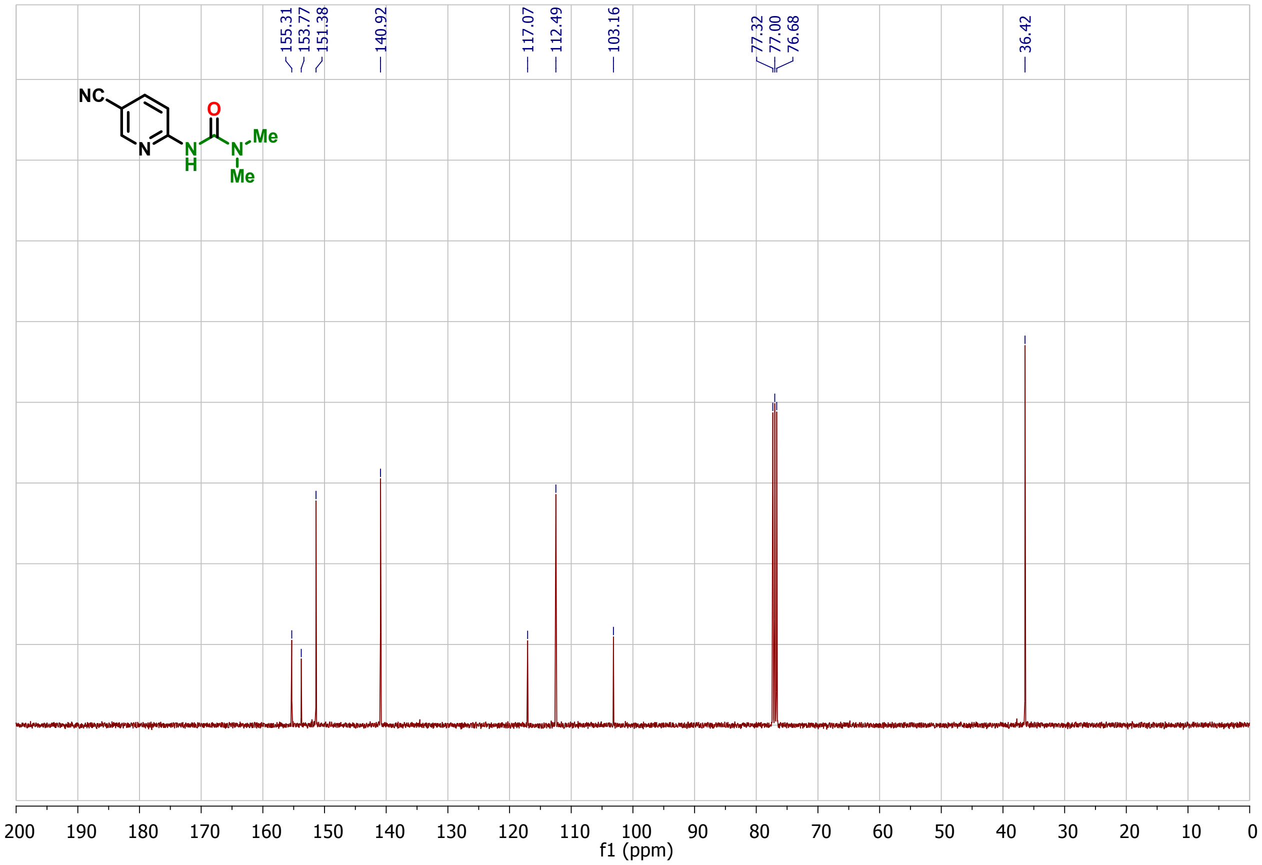

8.80
8.79
8.39
8.38
7.60
7.59
7.59
7.58
7.51
7.26
3.06
NO2
O
N
N
H
N
Me
Me
1.00
1.05
2.12
6.67
8.9 8.7 8.5 8.3 8.1 7.9 7.7 7.5
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

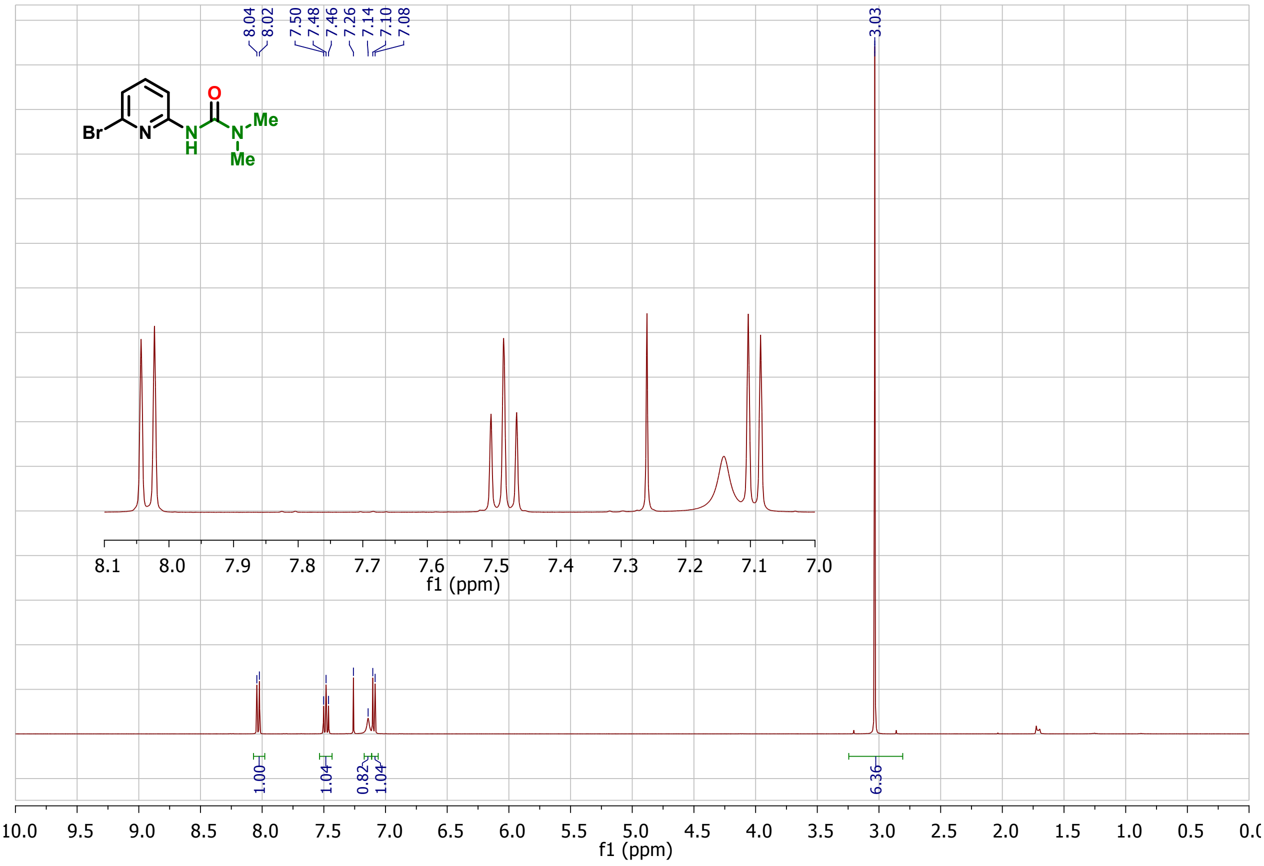

155.30
154.97
154.11
149.36
110.68
106.23
77.32
77.00
76.68
36.36
NO2
O
N
N
H
N
Me
Me
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

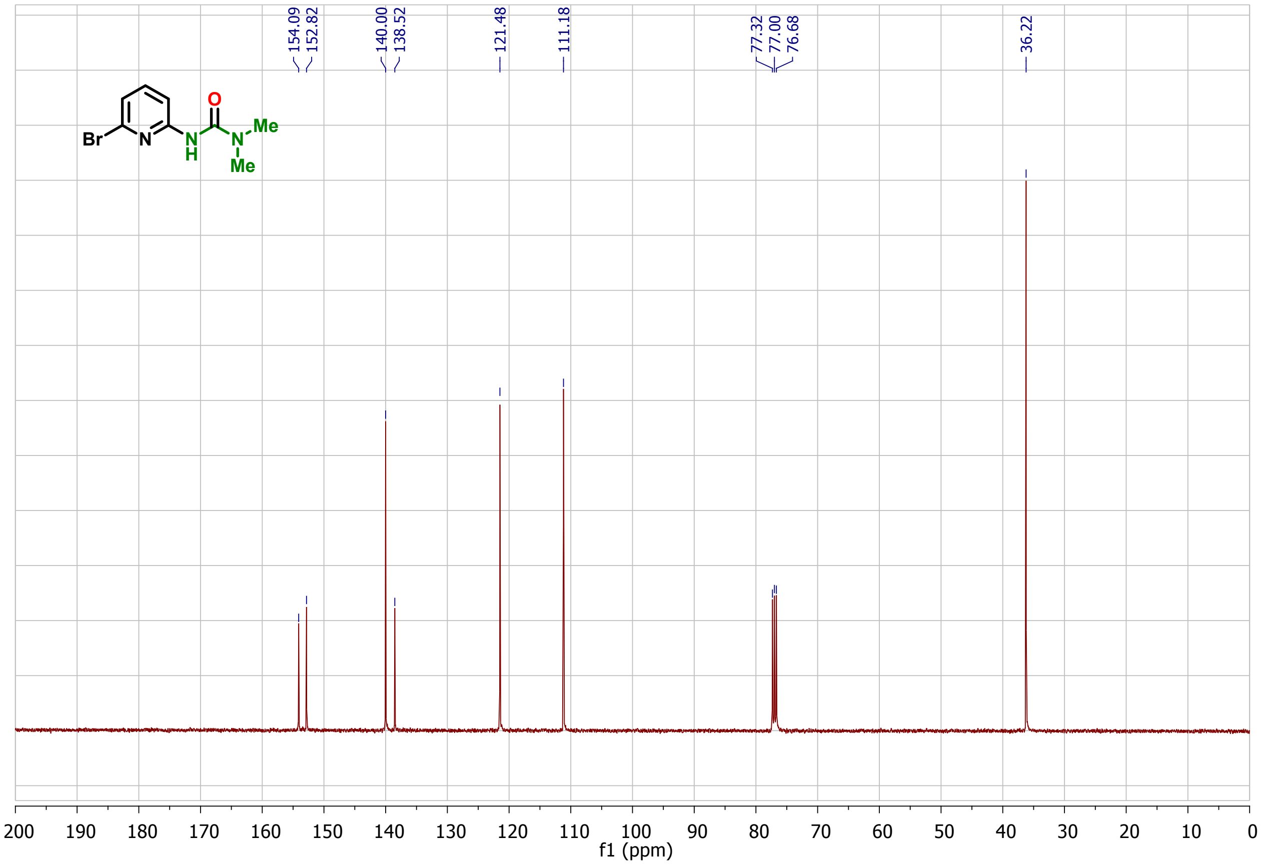

7.98
7.96
7.87
7.87
7.26
7.24
7.23
7.22
7.21
7.07
3.81
3.02
MeO
N
O
N
H
N
Me
Me
8.00
7.90
7.25
7.15
7.05
f1 (ppm)
1.00
1.00
1.01
0.96
3.14
6.27
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


155.03
151.91
146.56
133.63
123.73
113.64
77.32
77.00
76.68
55.94
36.33
MeO
N
O
N
H
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.47
8.47
8.25
8.23
7.88
7.88
7.86
7.50
7.26
3.08
NC
N
O
N
H
N
Me
Me
1.00
1.01
1.01
0.85
6.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


155.31
153.77
151.38
140.92
117.07
112.49
103.16
77.32
77.00
76.68
36.42
NC
N
O
N
H
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.04
8.02
7.50
7.48
7.46
7.26
7.14
7.10
7.08
3.03
Br
N
N
H
O
N
Me
Me
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
1.00
1.04
0.82
1.04
6.36
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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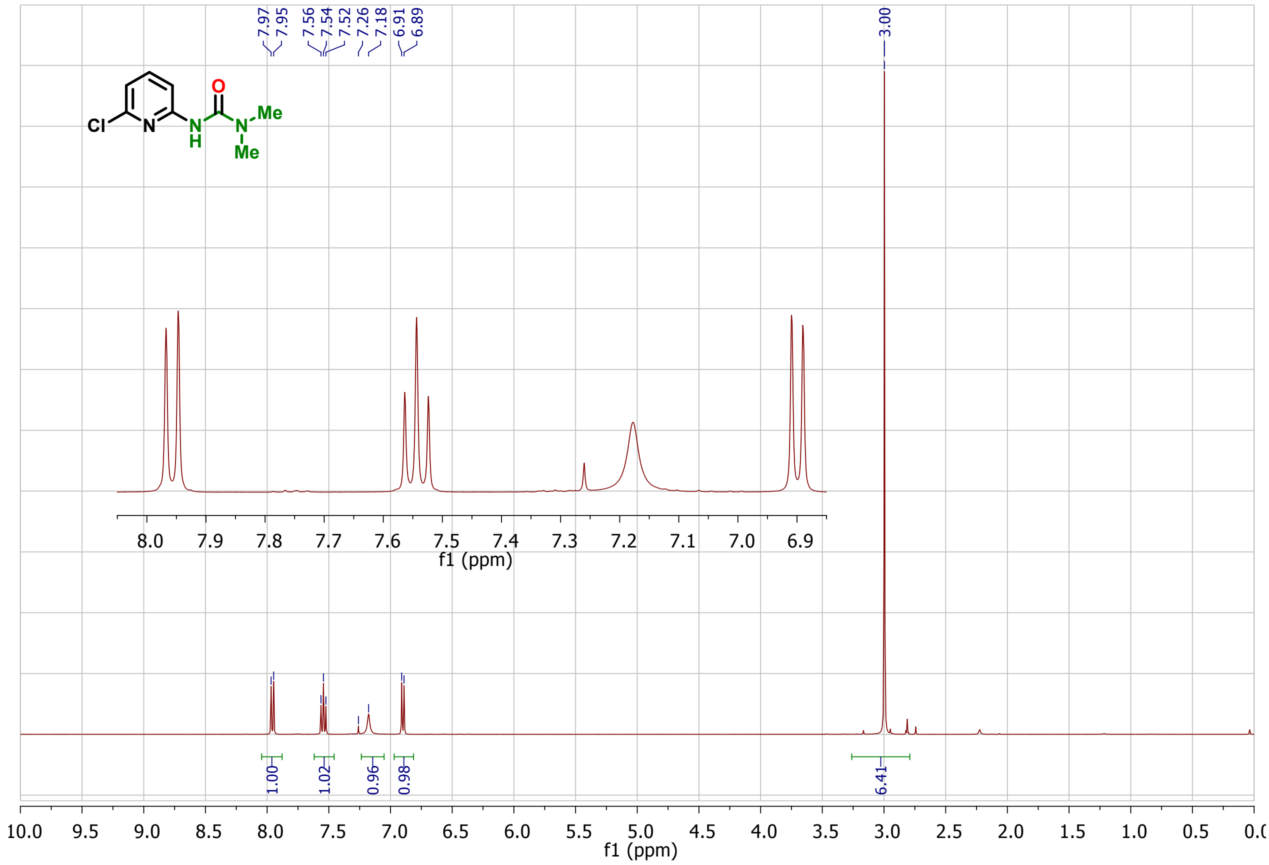
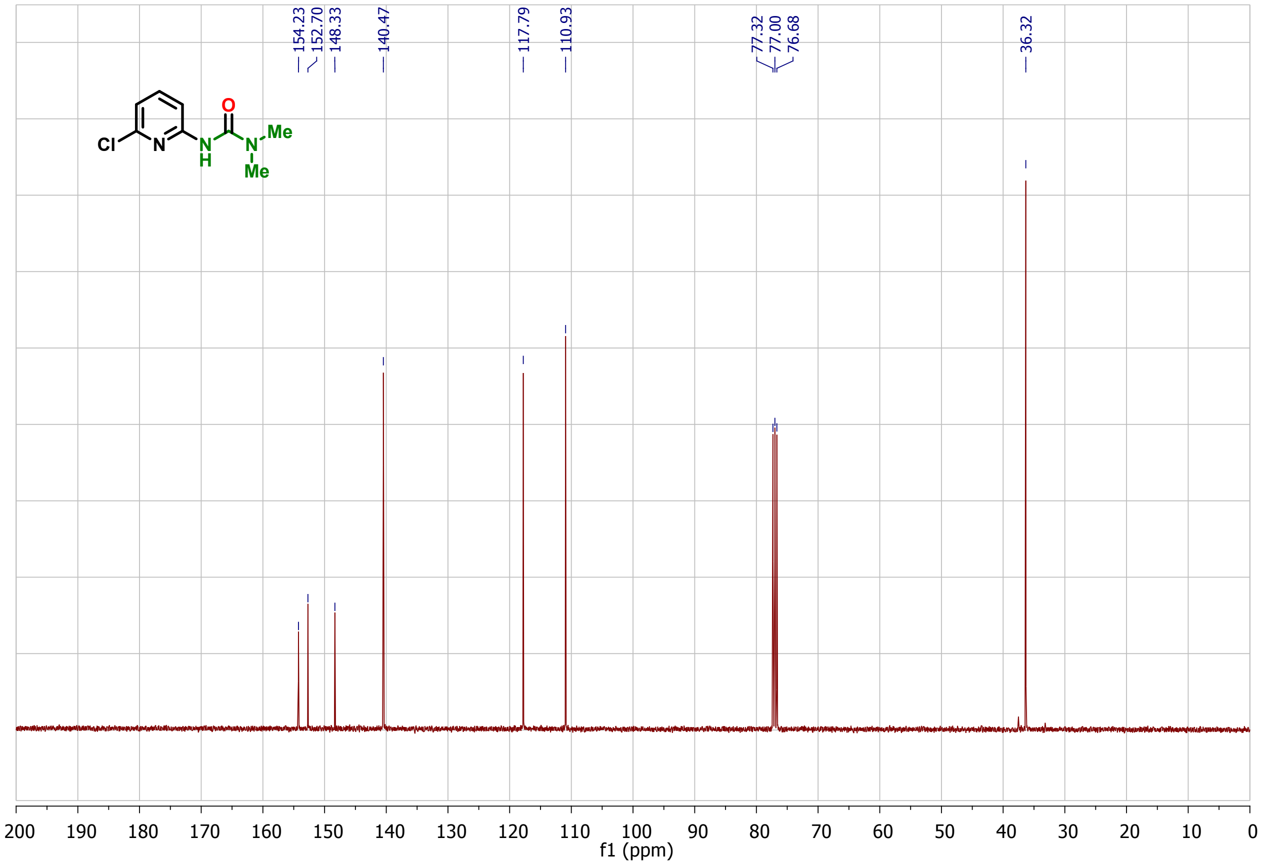
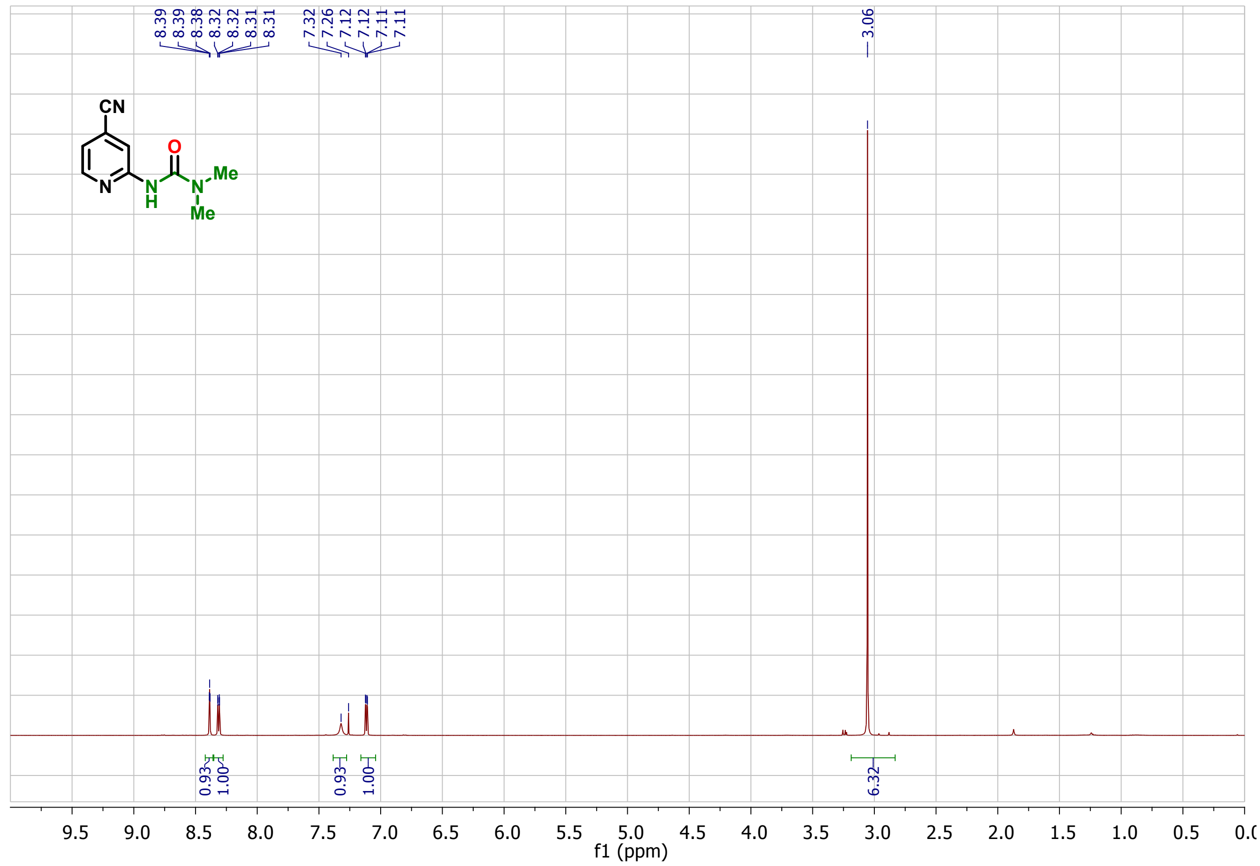
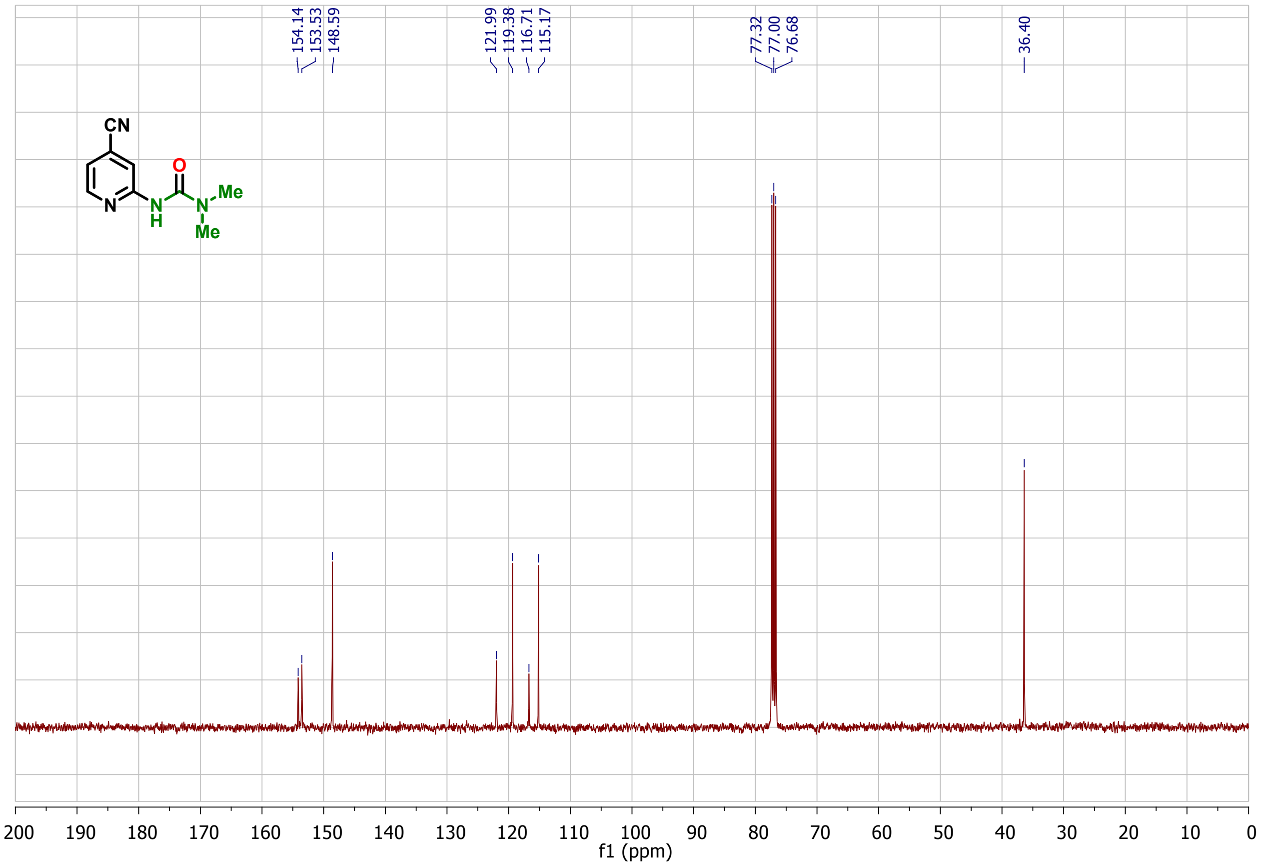
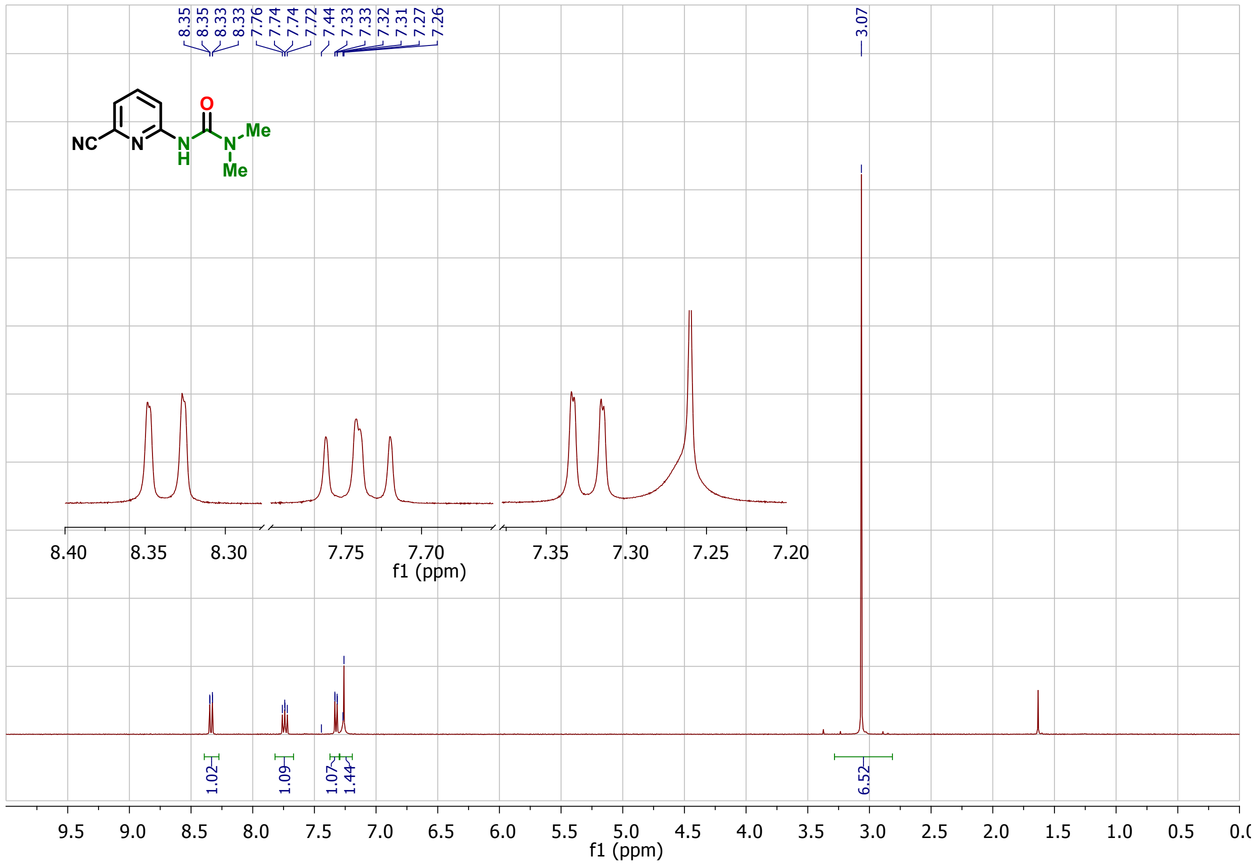
152.82
140.00
138.52
121.48
111.18
77.32
77.00
76.68
36.22
Br
N
N
H
O
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

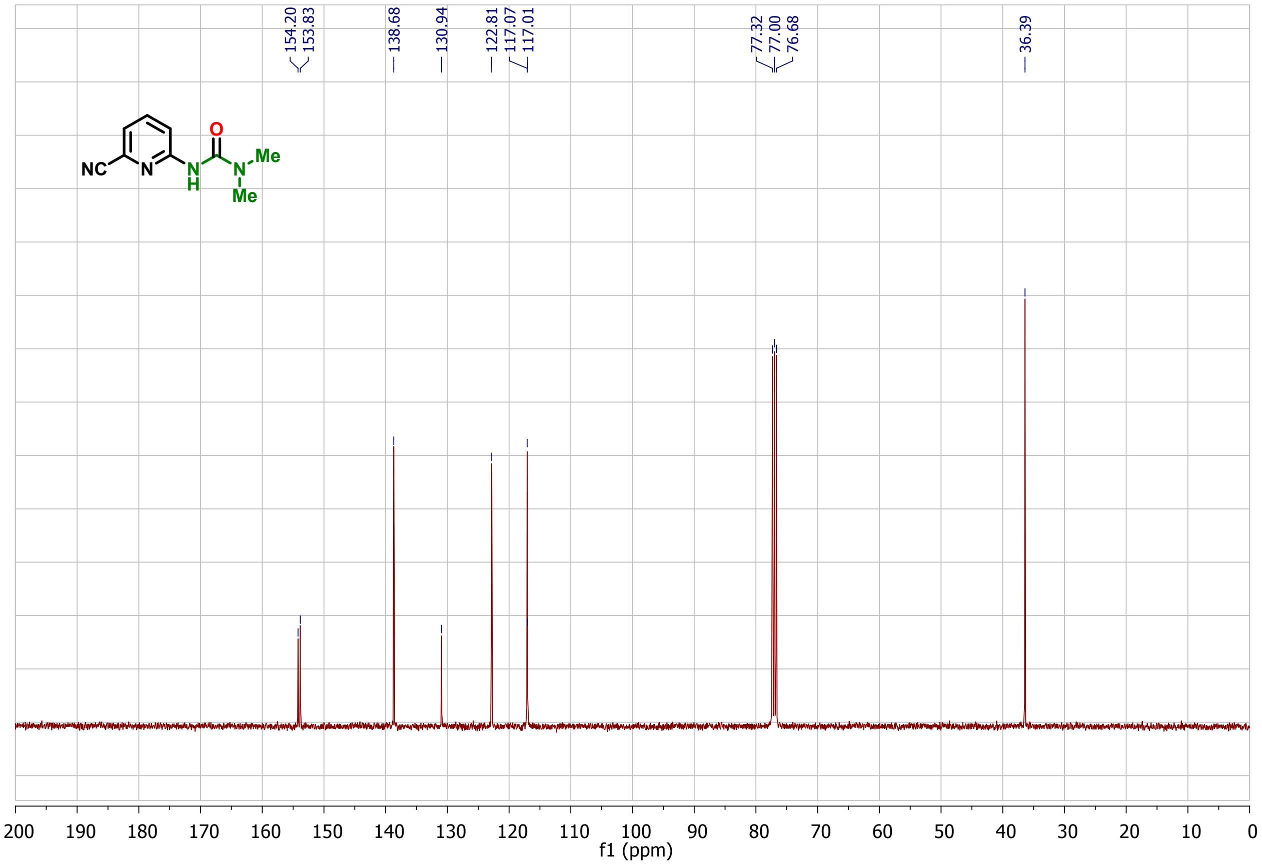

7.97
7.95
7.56
7.54
7.52
7.26
7.18
6.91
6.89
3.00
Cl
N
N
H
O
N
Me
Me
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
f1 (ppm)
1.00
1.02
0.96
0.98
6.41
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

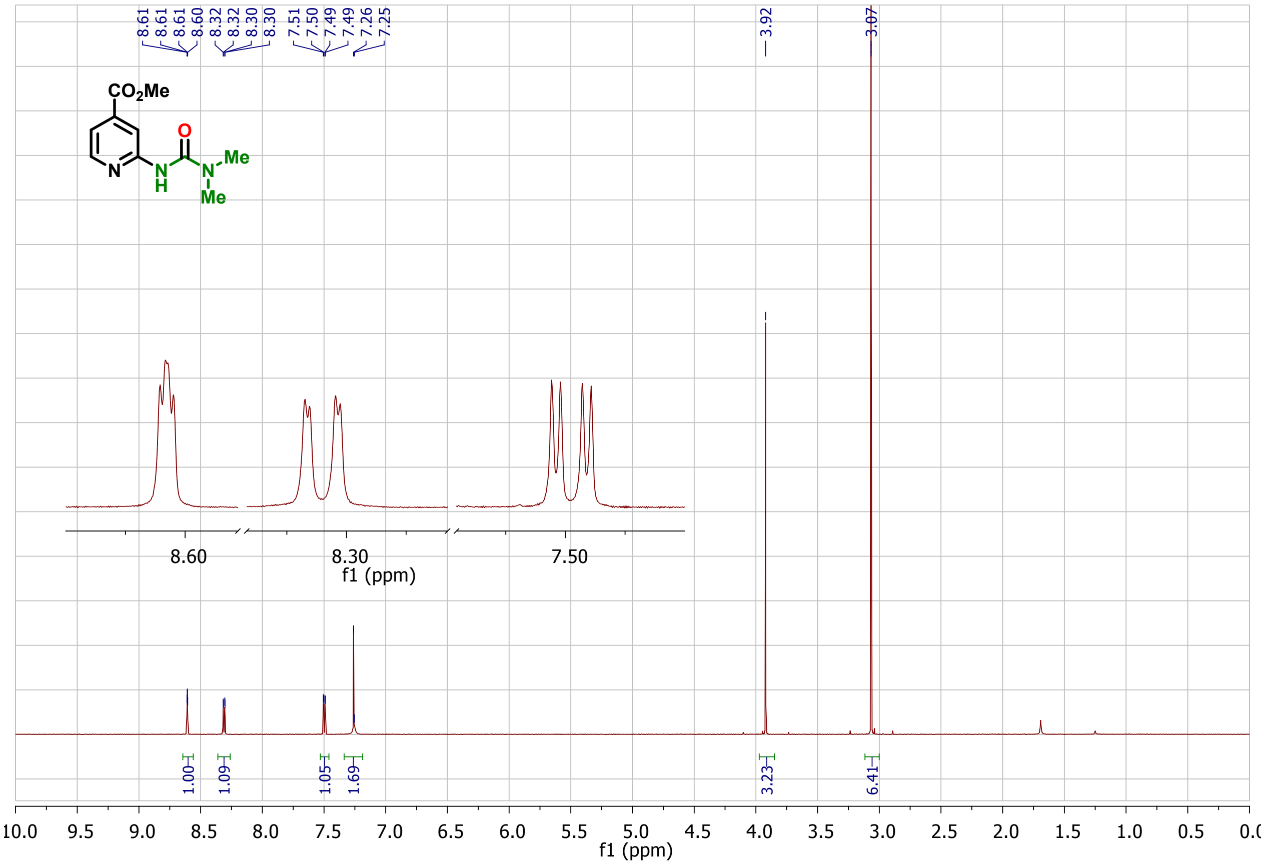

154.23
152.70
148.33
140.47
117.79
110.93
77.32
77.00
76.68
36.32
Cl
N
N
H
O
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

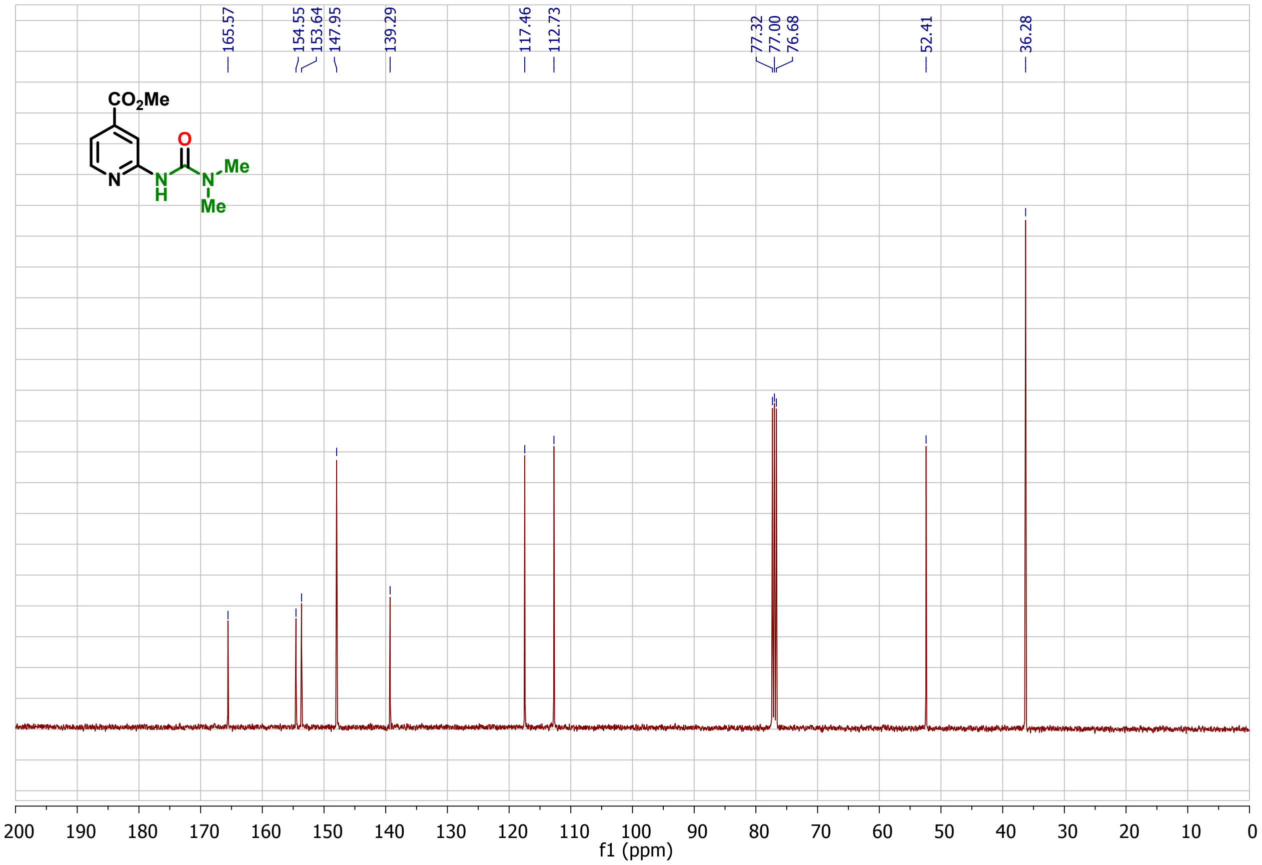

8.39
8.39
8.38
8.32
8.32
8.31
8.31
7.32
7.26
7.12
7.12
7.11
7.11
3.06
CN
O
N
N
H
N
Me
Me
0.93
1.00
0.93
1.00
6.32
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

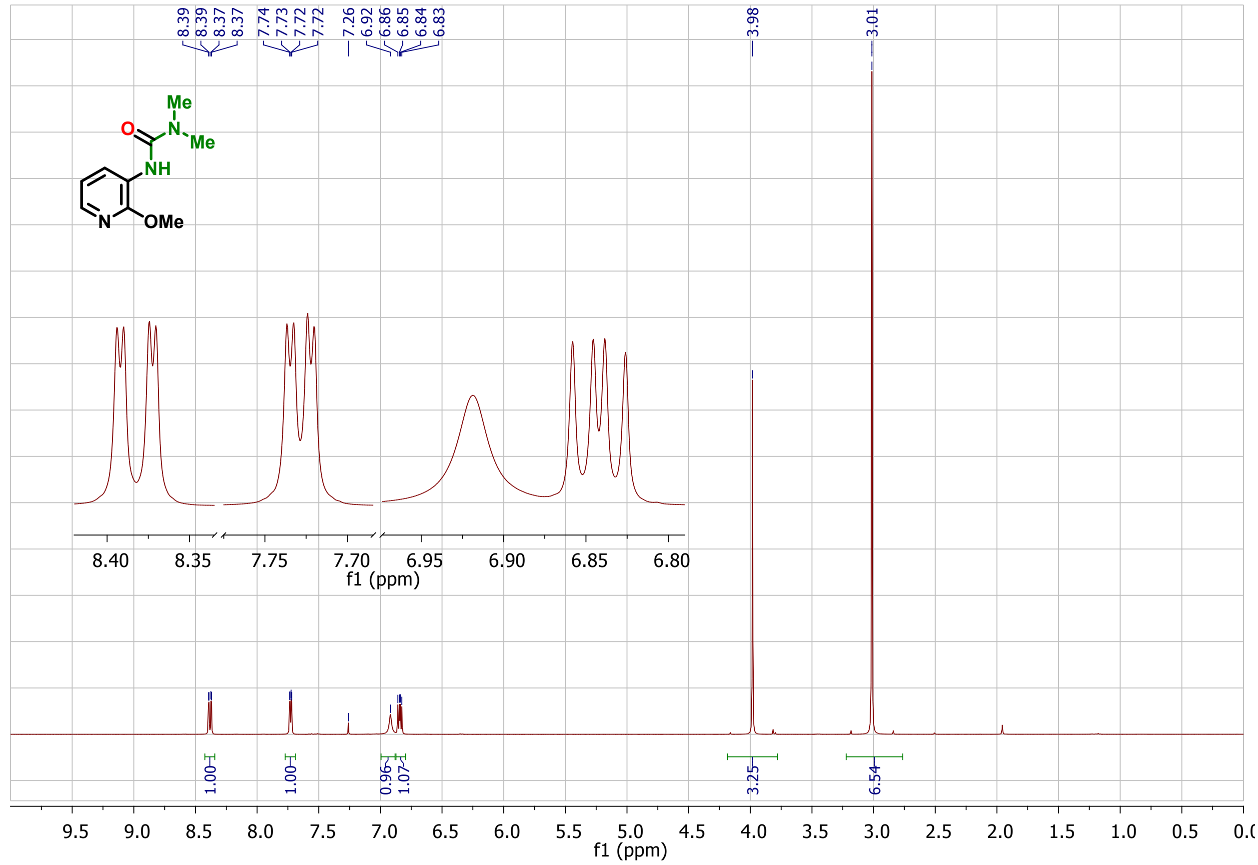

154.14
153.53
148.59
121.99
119.38
116.71
115.17
77.32
77.00
76.68
36.40
CN
O
N
N
H
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

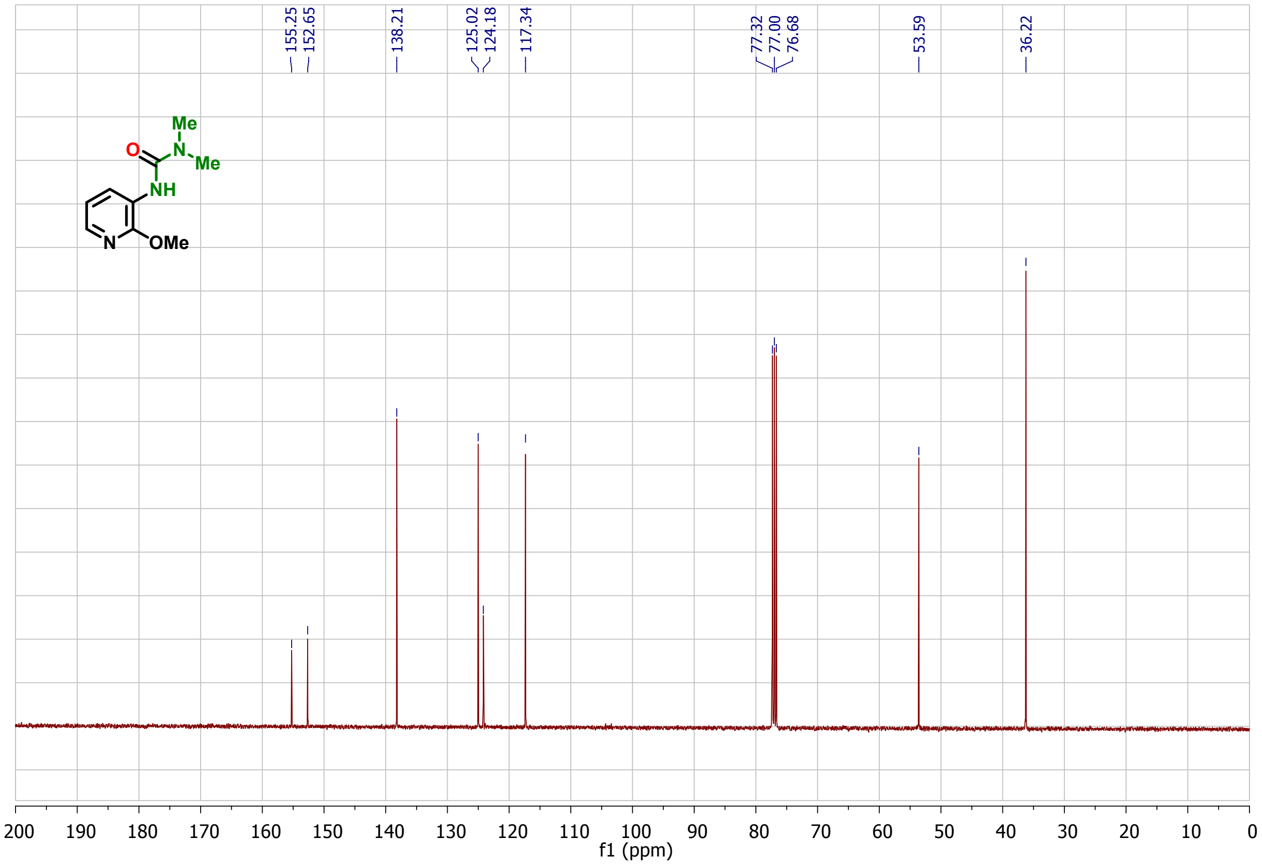

8.35
8.35
8.33
8.33
7.76
7.74
7.74
7.72
7.44
7.33
7.33
7.32
7.31
7.27
7.26
3.07
NC
N
N
H
O
N
Me
Me
8.40
8.35
8.30
7.75
7.70
7.35
7.30
7.25
7.20
f1 (ppm)
1.02
1.09
1.07
1.44
6.52
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


154.20
153.83
138.68
130.94
122.81
117.07
117.01
77.32
77.00
76.68
36.39
NC
N
N
H
O
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

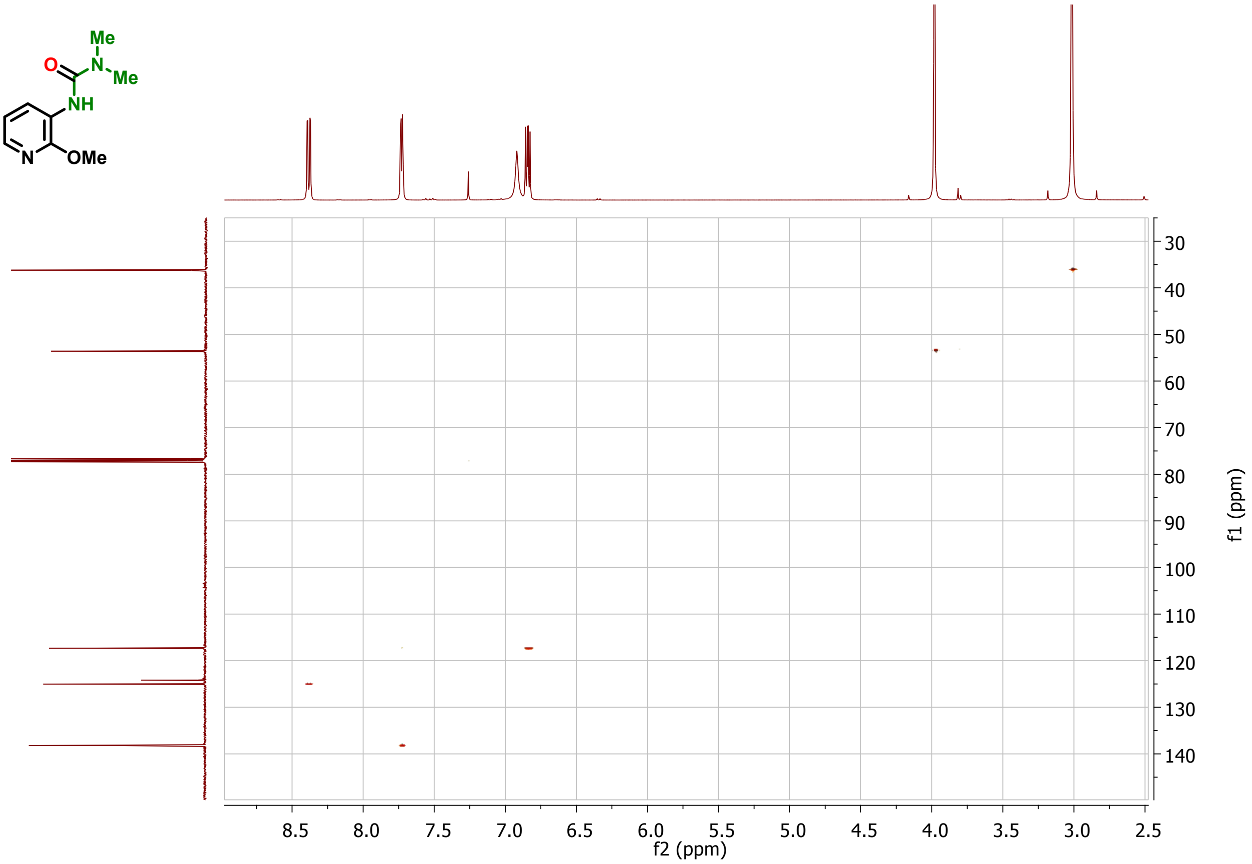

8.61
8.61
8.61
8.60
8.32
8.32
8.30
8.30
7.51
7.50
7.49
7.49
7.26
7.25
3.92
3.07
CO$_2$Me
O
N
N
H
N
Me
Me
8.60
8.30
7.50
f1 (ppm)
1.00
1.09
1.05
1.69
3.23
6.41
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


165.57
154.55
153.64
147.95
139.29
117.46
112.73
77.32
77.00
76.68
52.41
36.28
CO$_2$Me
O
N
N
H
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

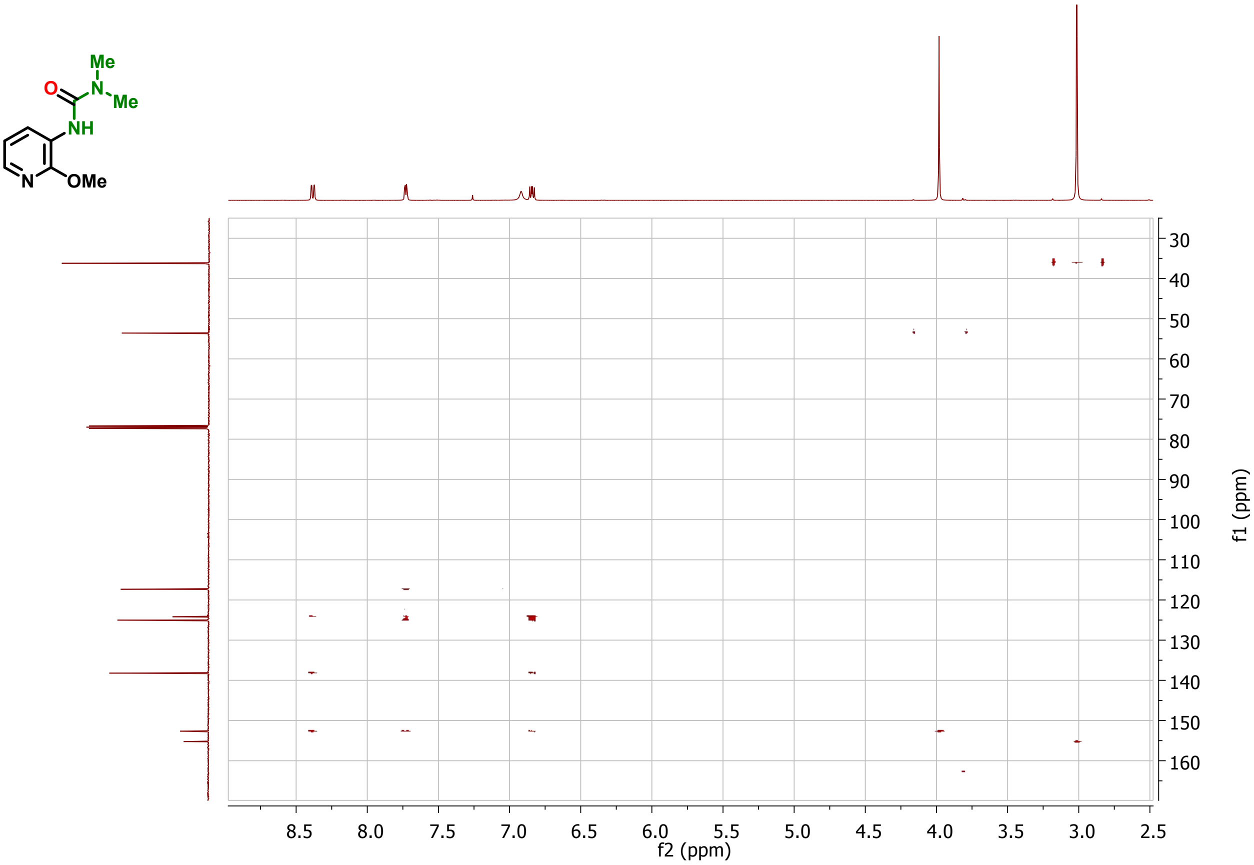

8.39
8.39
8.37
8.37
7.74
7.73
7.72
7.72
7.26
6.92
6.86
6.85
6.84
6.83
3.98
3.01
Me
O
N
Me
NH
N
OMe
8.40
8.35
7.75
7.70
6.95
6.90
6.85
6.80
f1 (ppm)
1.00
1.00
0.96
1.07
3.25
6.54
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


155.25
152.65
138.21
125.02
124.18
117.34
77.32
77.00
76.68
53.59
36.22
Me
O
N
Me
NH
N
OMe
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

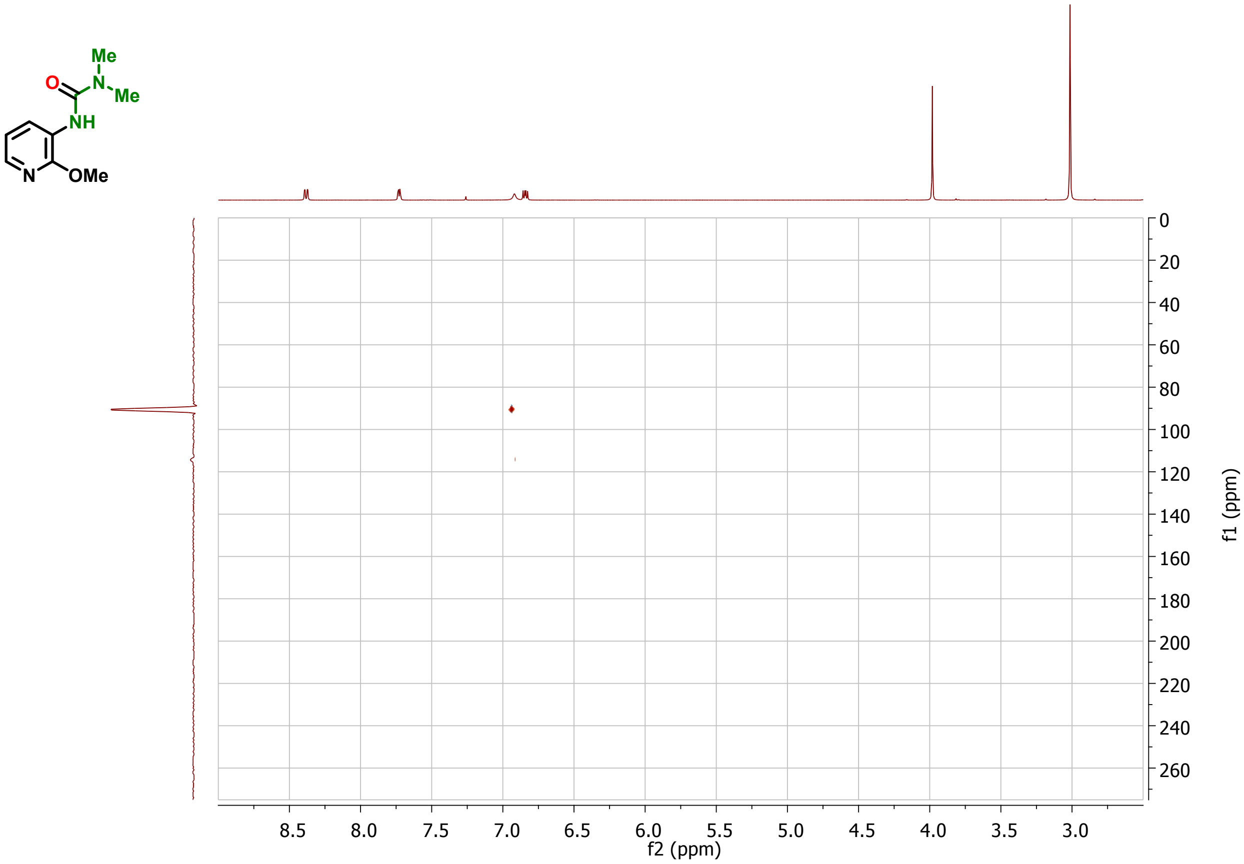
^{1}H–^{13}C HSQC NMR of 3-(2-Methoxypyridin-3-yl)-1,1-dimethylurea (**5t**):



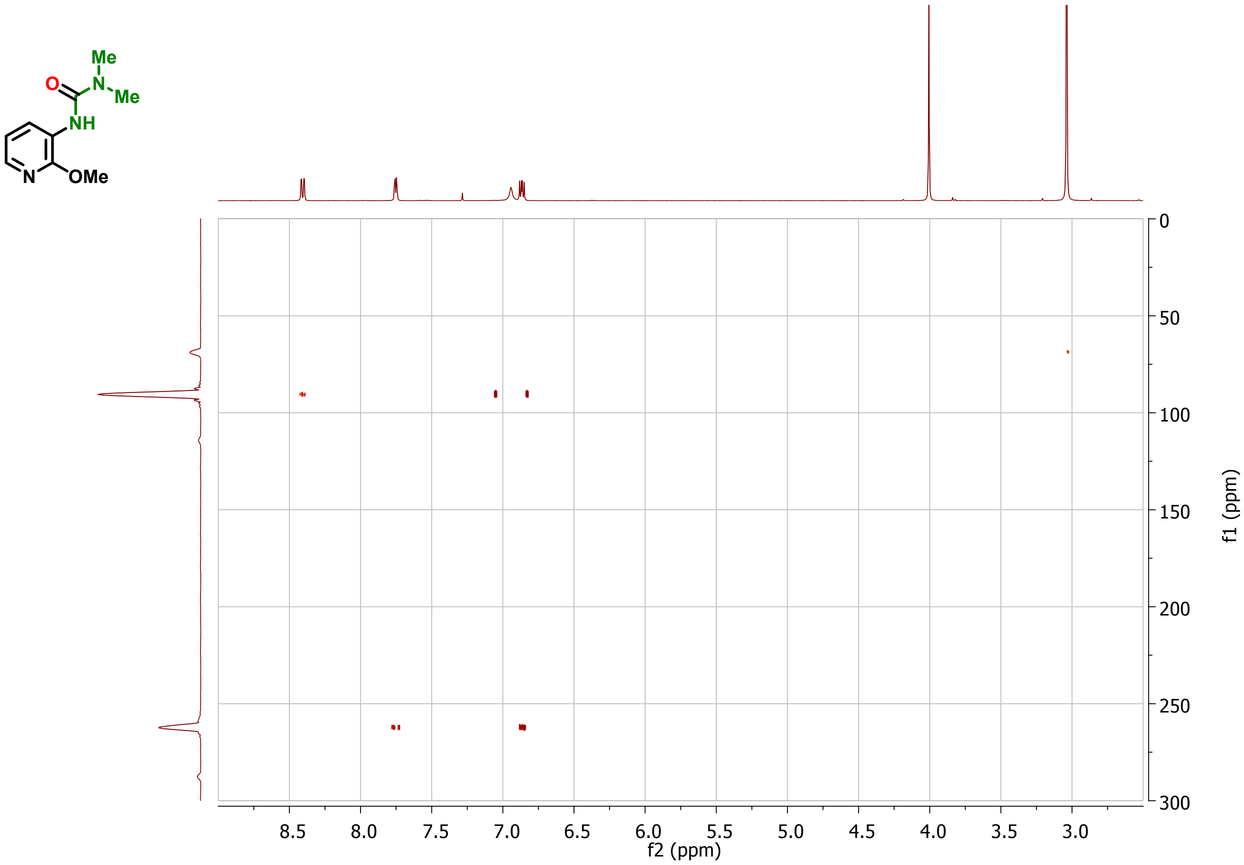
^{1}H–^{13}C HMBC NMR of 3-(2-Methoxypyridin-3-yl)-1,1-dimethylurea (**5t**):



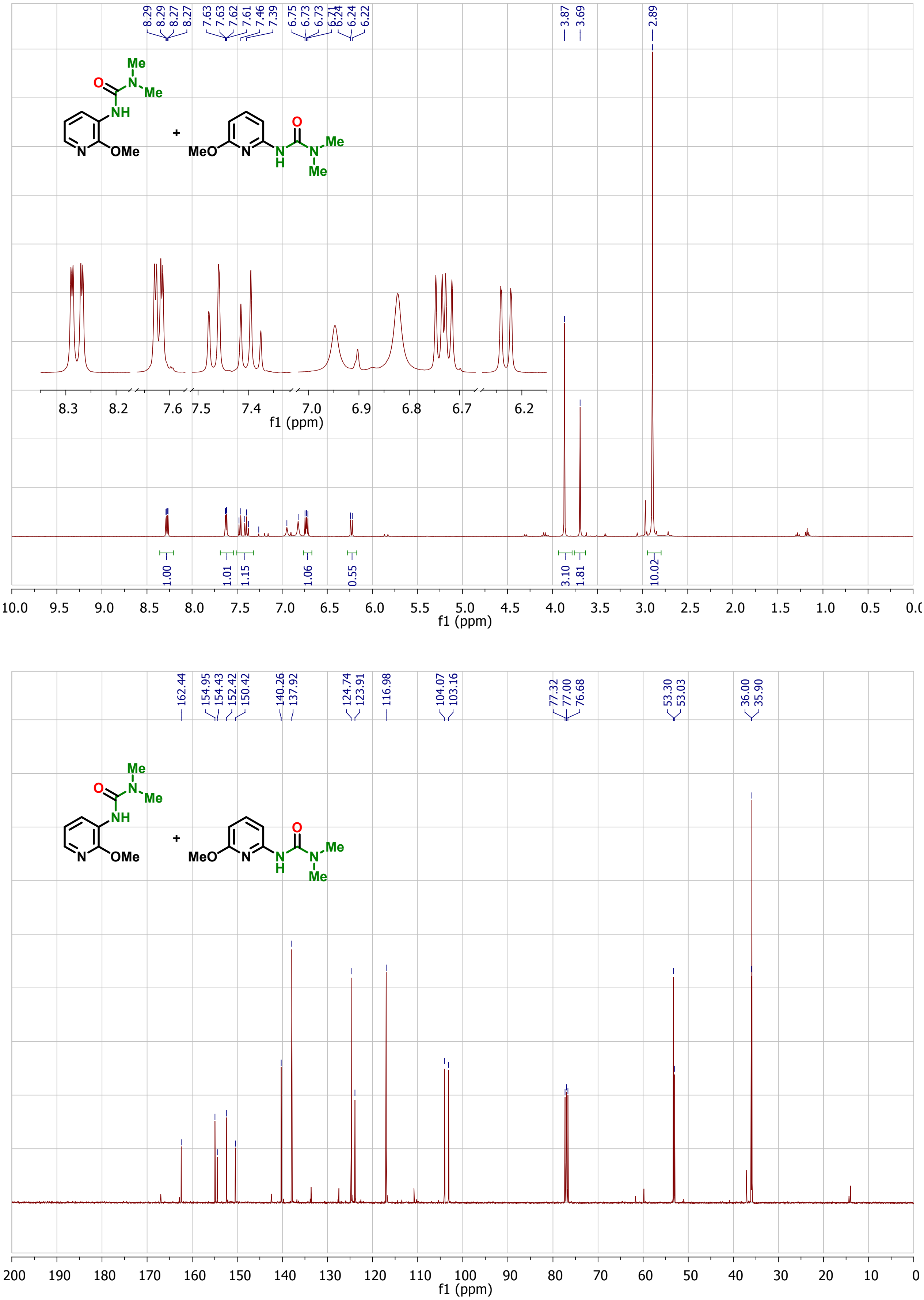
^{1}H–^{15}N HSQC NMR of 3-(2-Methoxypyridin-3-yl)-1,1-dimethylurea (**5t**):



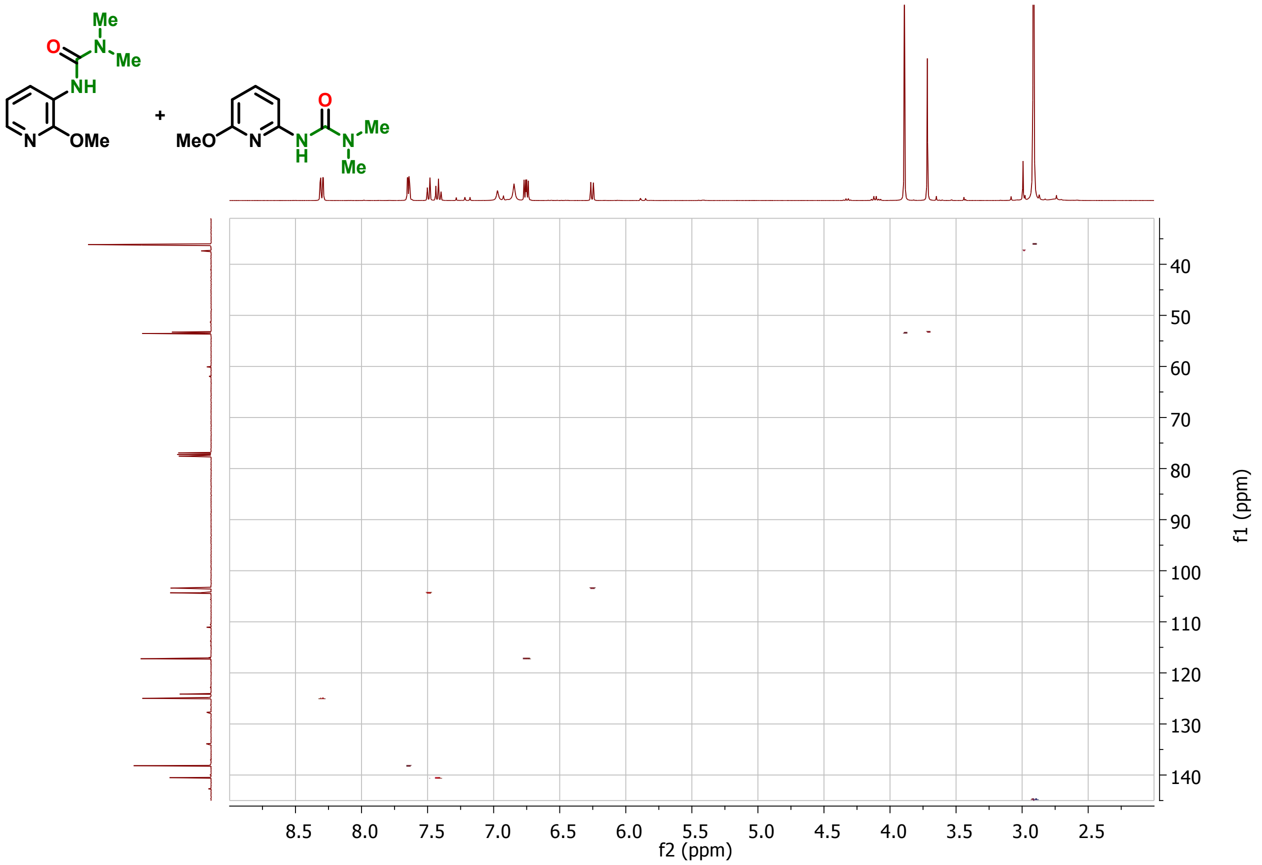
^{1}H–^{15}N HMBC NMR of 3-(2-Methoxypyridin-3-yl)-1,1-dimethylurea (**5t**):



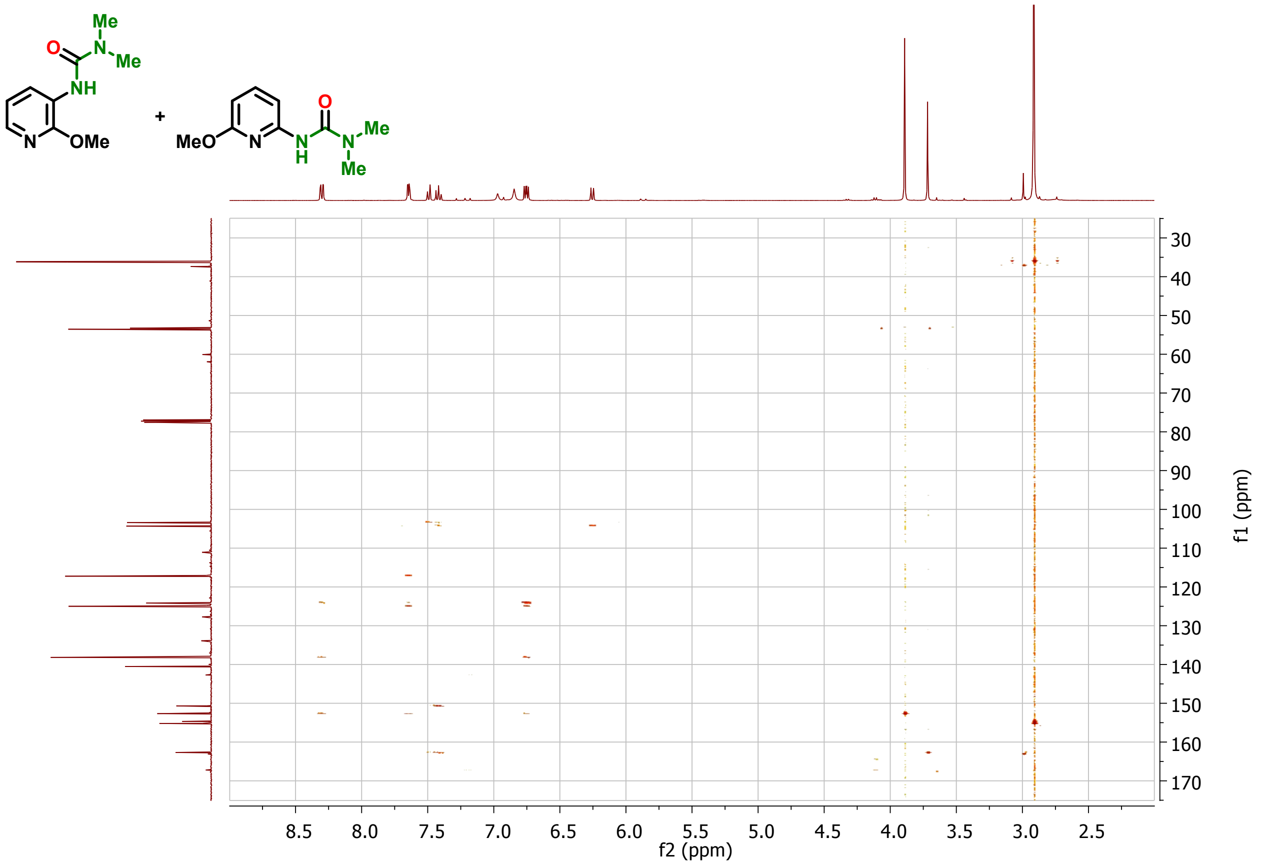
^{1}H and ^{13}C NMR spectra of the mixture of 3-(2-methoxypyridin-3-yl)-1,1-dimethylurea (**5t**, **major**) and 3-(6-methoxypyridin-2-yl)-1,1-dimethylurea (**4t**, **minor**):



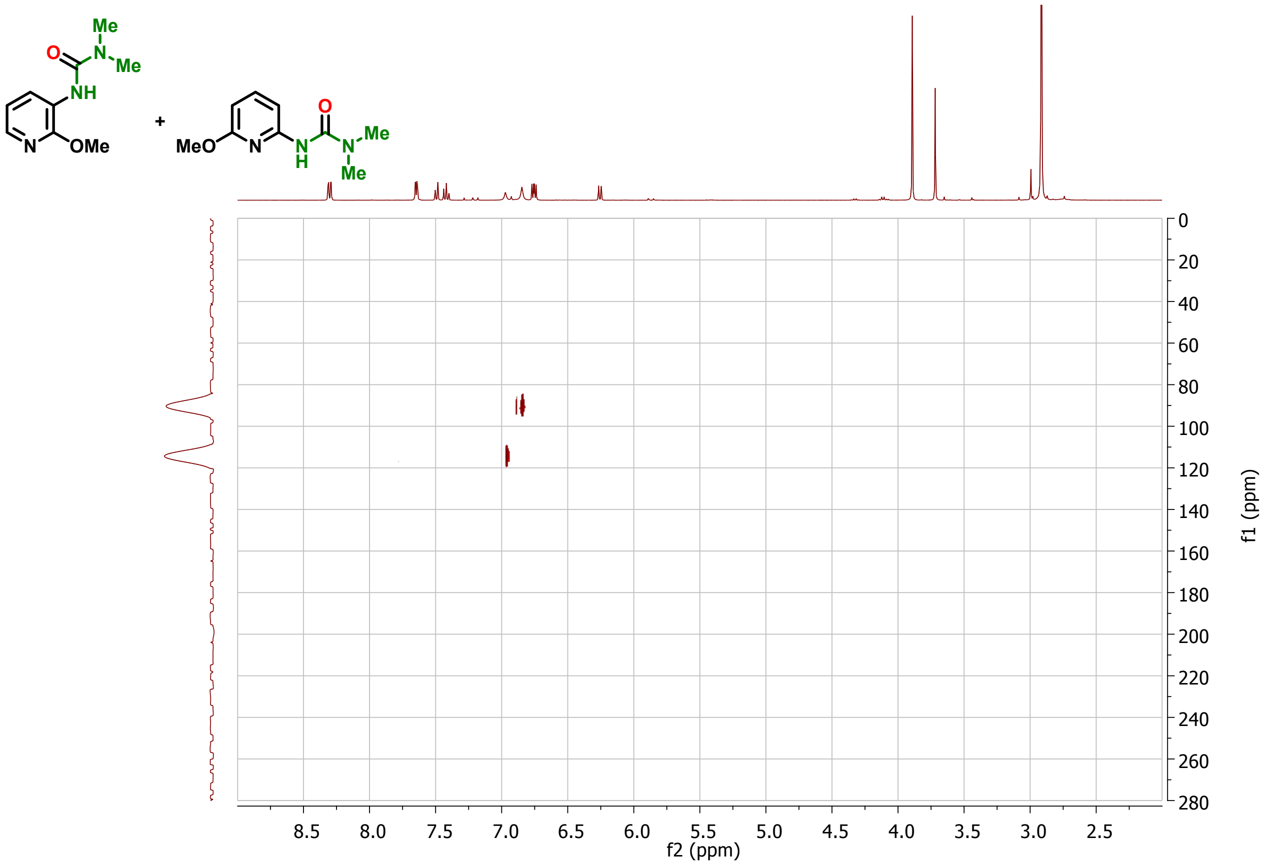
^{1}H–^{13}C HSQC NMR of the mixture of 3-(2-methoxypyridin-3-yl)-1,1-dimethylurea (**5t**, **major**) and 3-(6-methoxypyridin-2-yl)-1,1-dimethylurea (**4t**, **minor**):



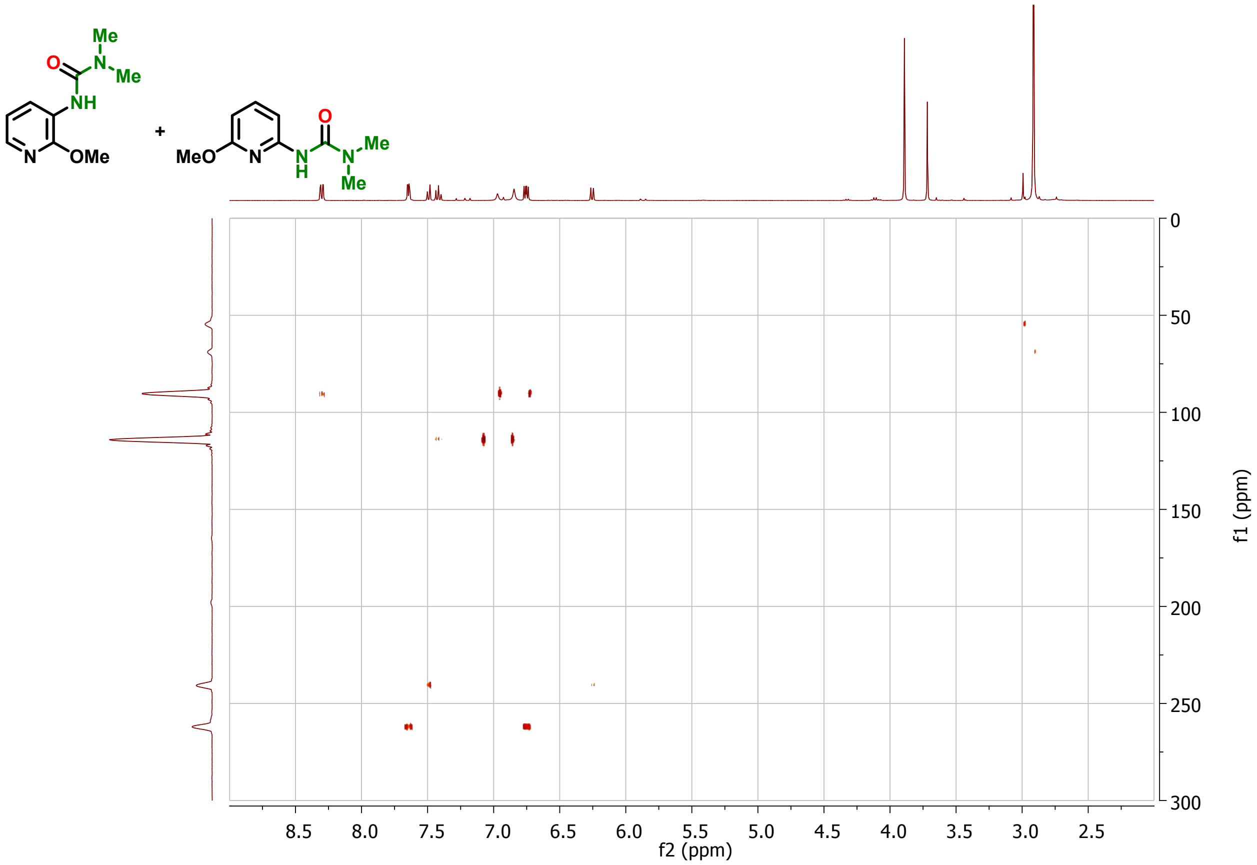
^{1}H–^{13}C HMBC NMR of the mixture of 3-(2-methoxypyridin-3-yl)-1,1-dimethylurea (**5t**, **major**) and 3-(6-methoxypyridin-2-yl)-1,1-dimethylurea (**4t**, **minor**):



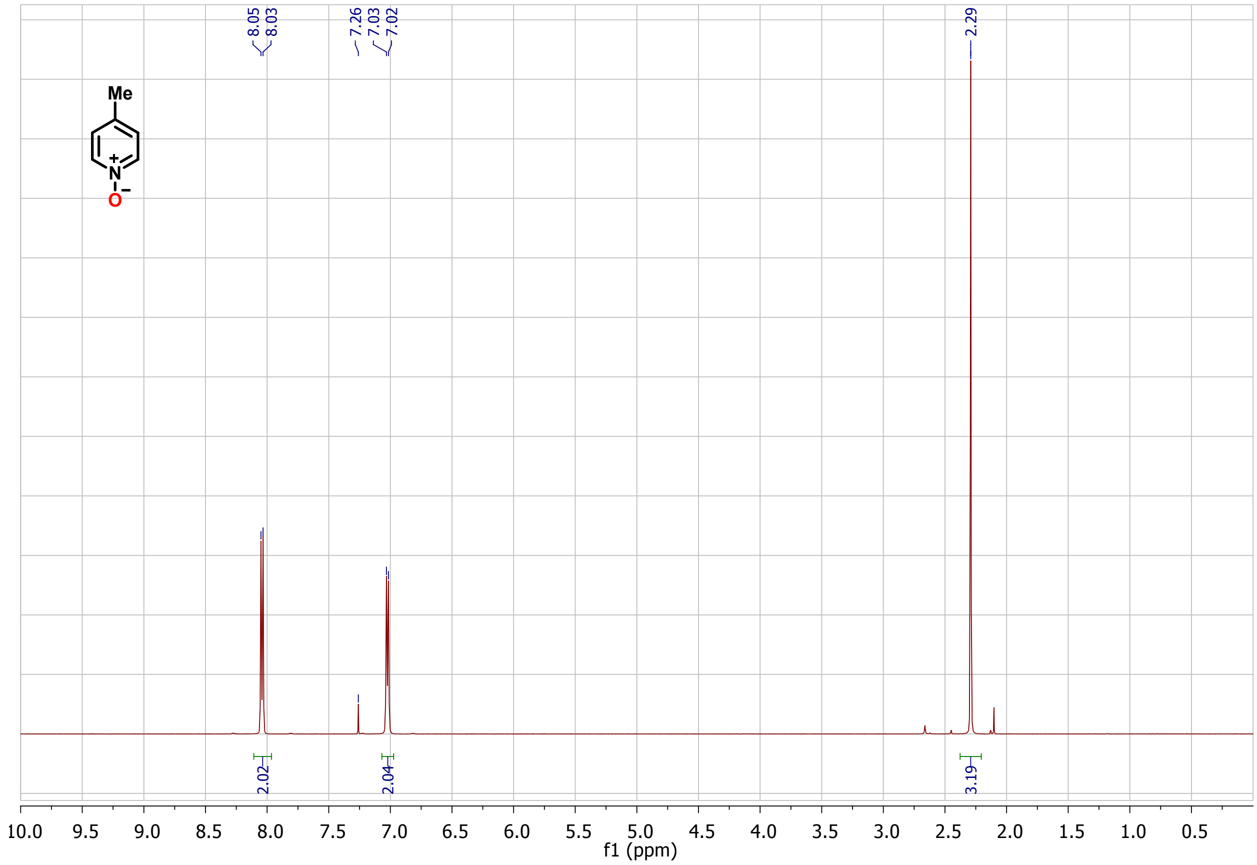
^{1}H–^{15}N HSQC NMR of the mixture of 3-(2-methoxypyridin-3-yl)-1,1-dimethylurea (**5t**, **major**) and 3-(6-methoxypyridin-2-yl)-1,1-dimethylurea (**4t**, **minor**):

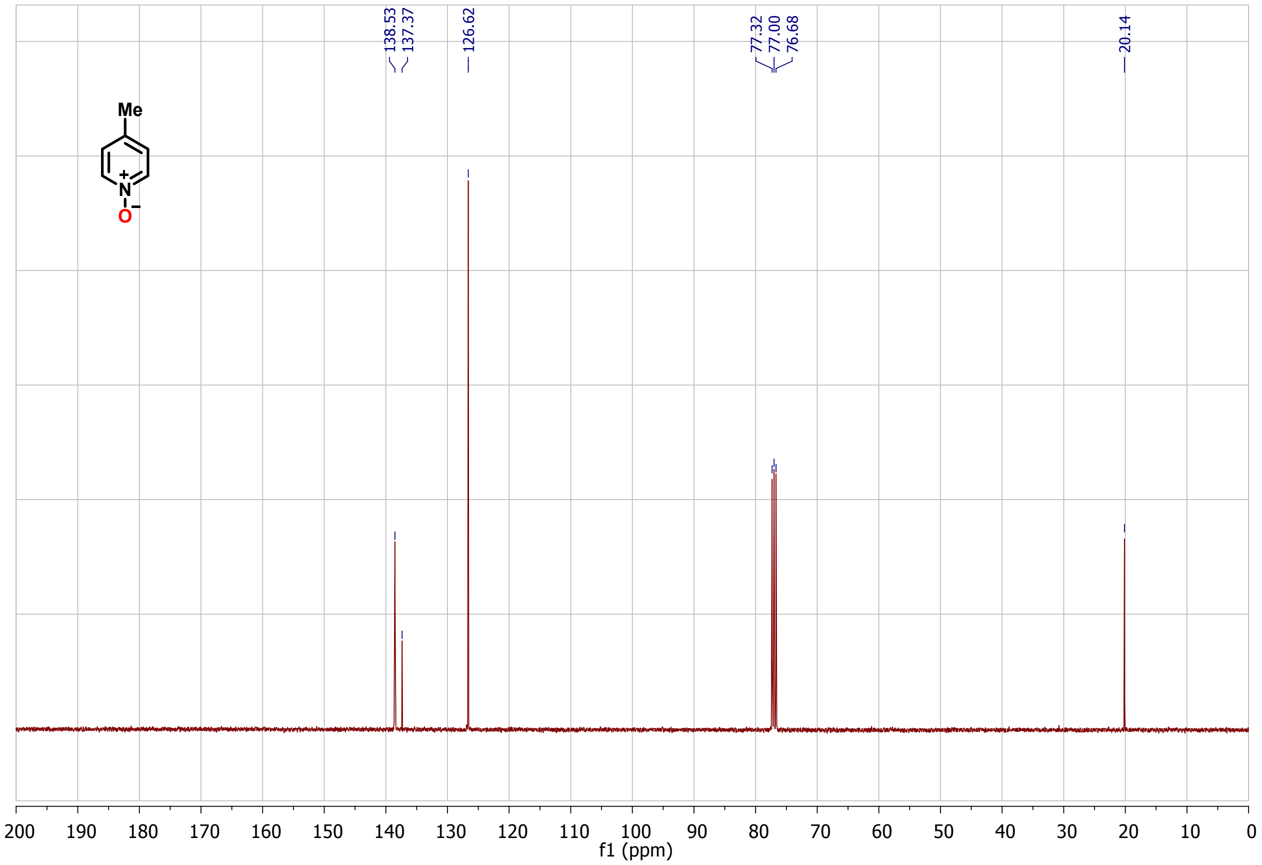


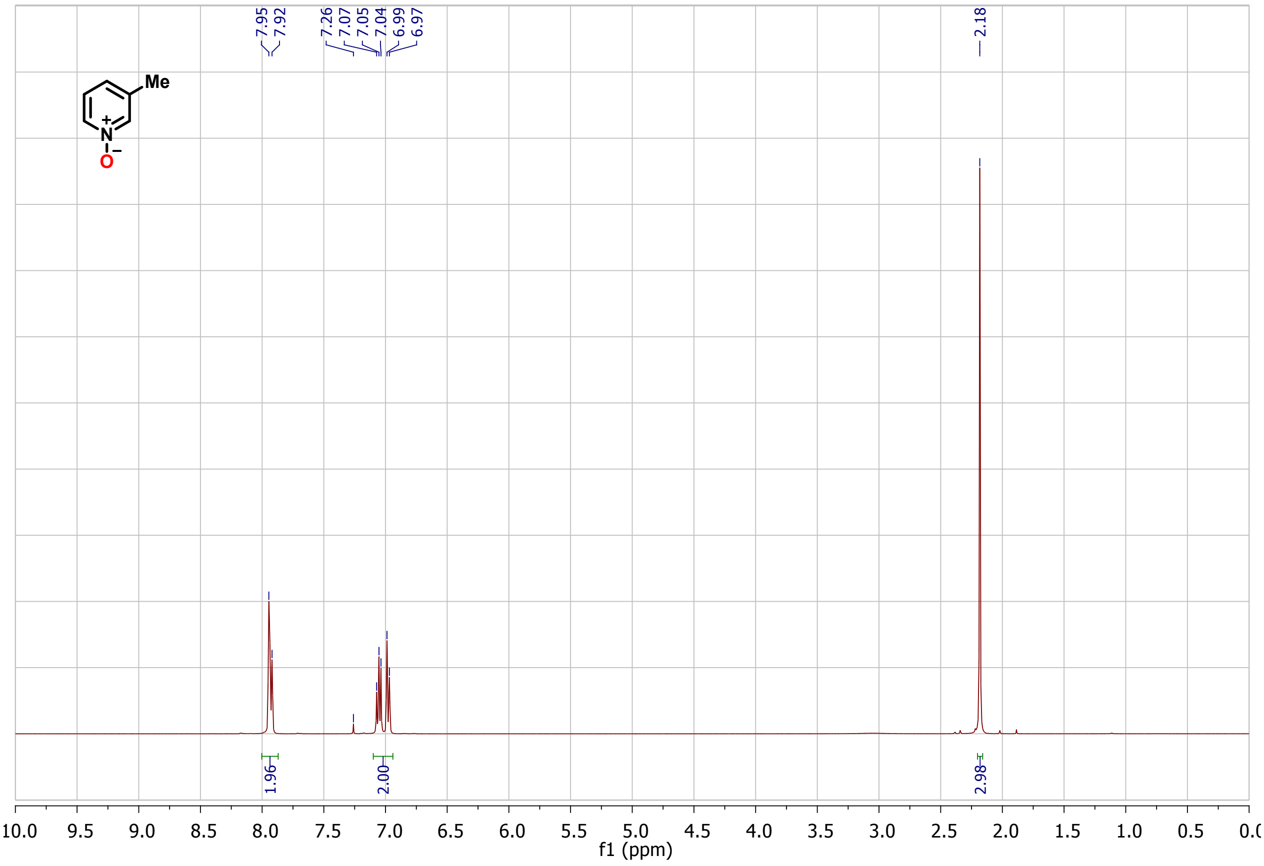
^{1}H–^{15}N HMBC NMR of the mixture of 3-(2-methoxypyridin-3-yl)-1,1-dimethylurea (**5t**, **major**) and 3-(6-methoxypyridin-2-yl)-1,1-dimethylurea (**4t**, **minor**):

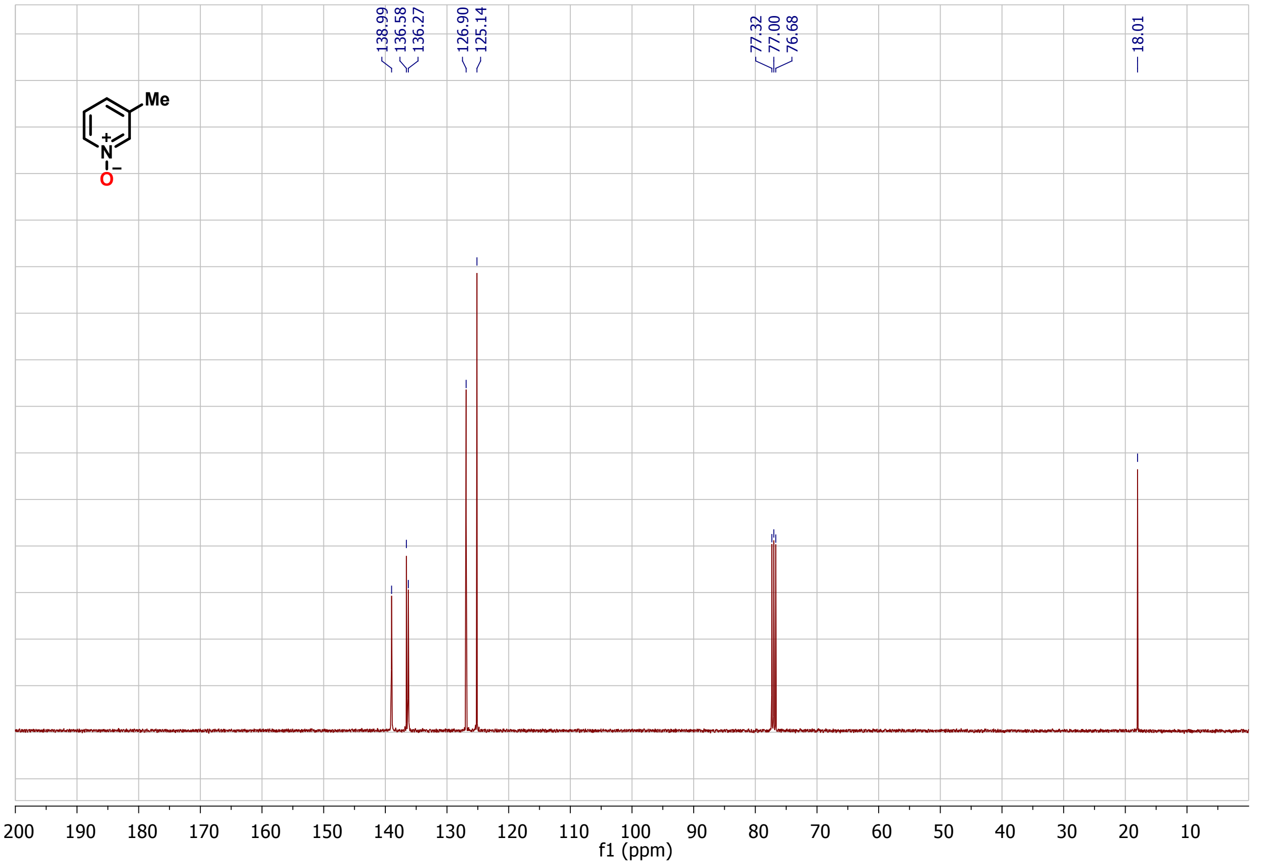


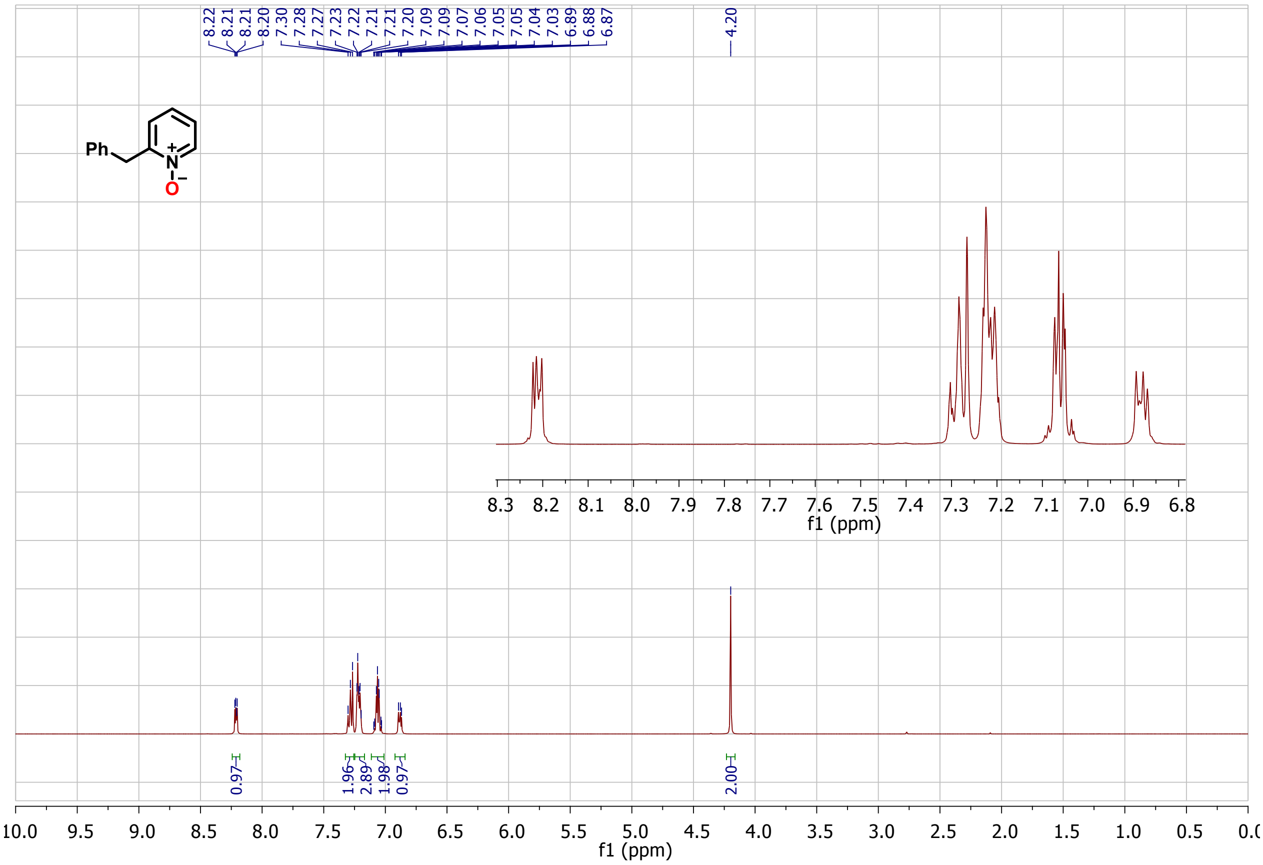
3.2. Spectra of substituted pyridine 1-oxides **1**

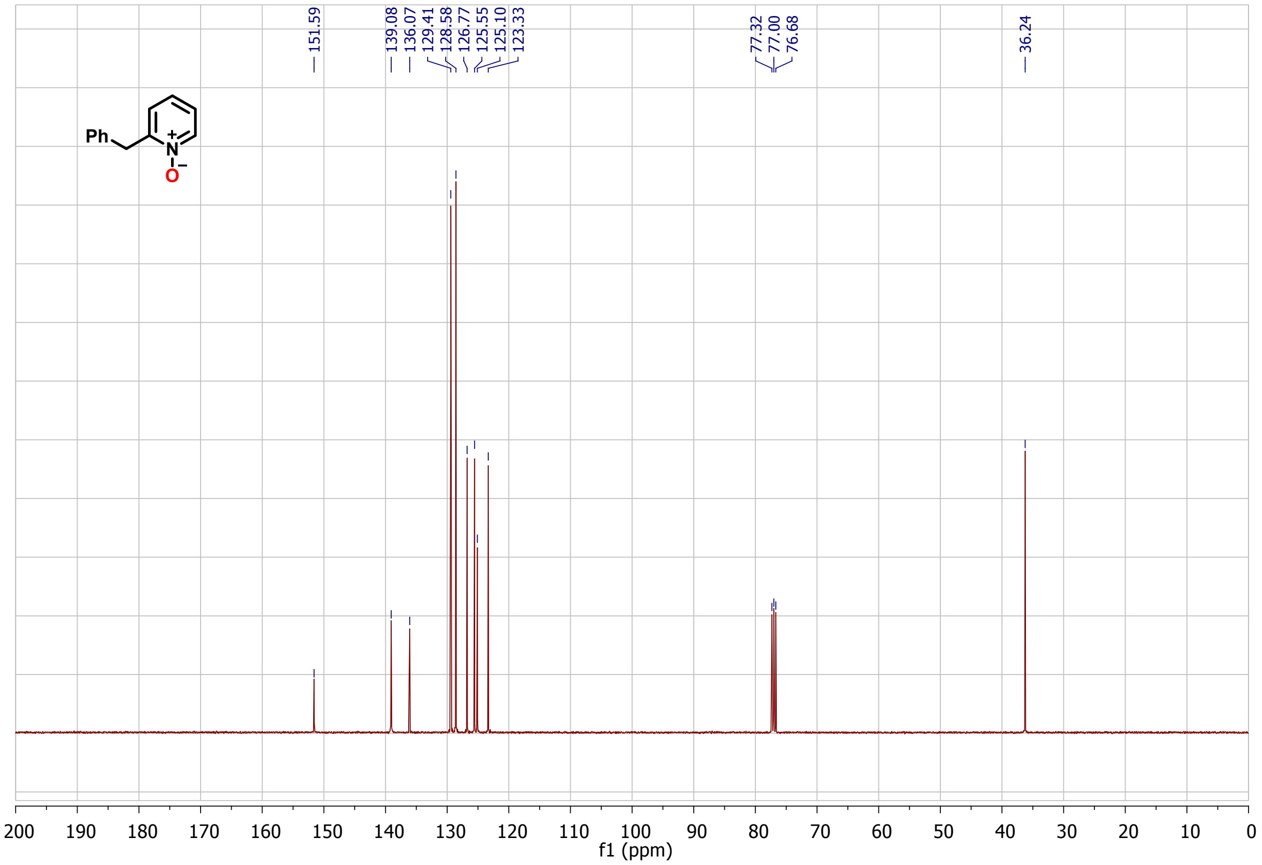


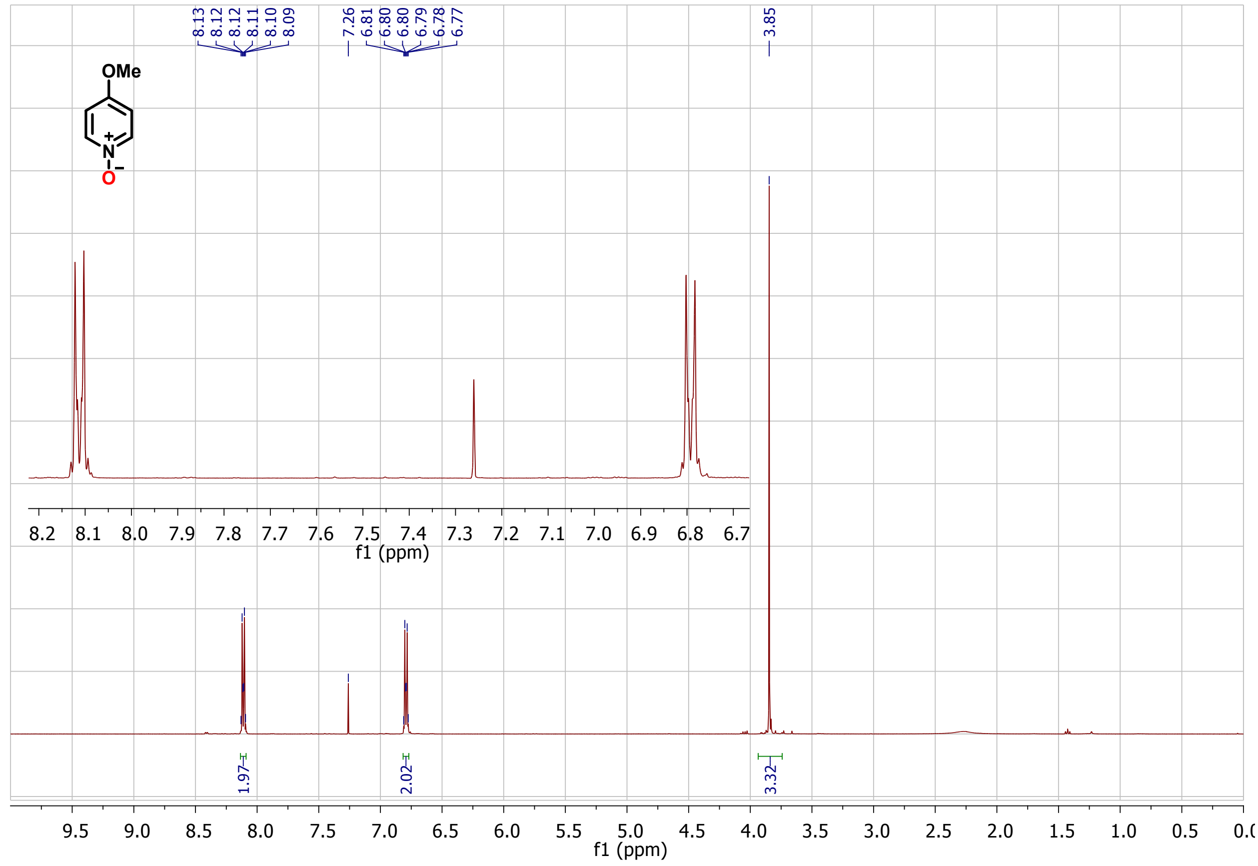


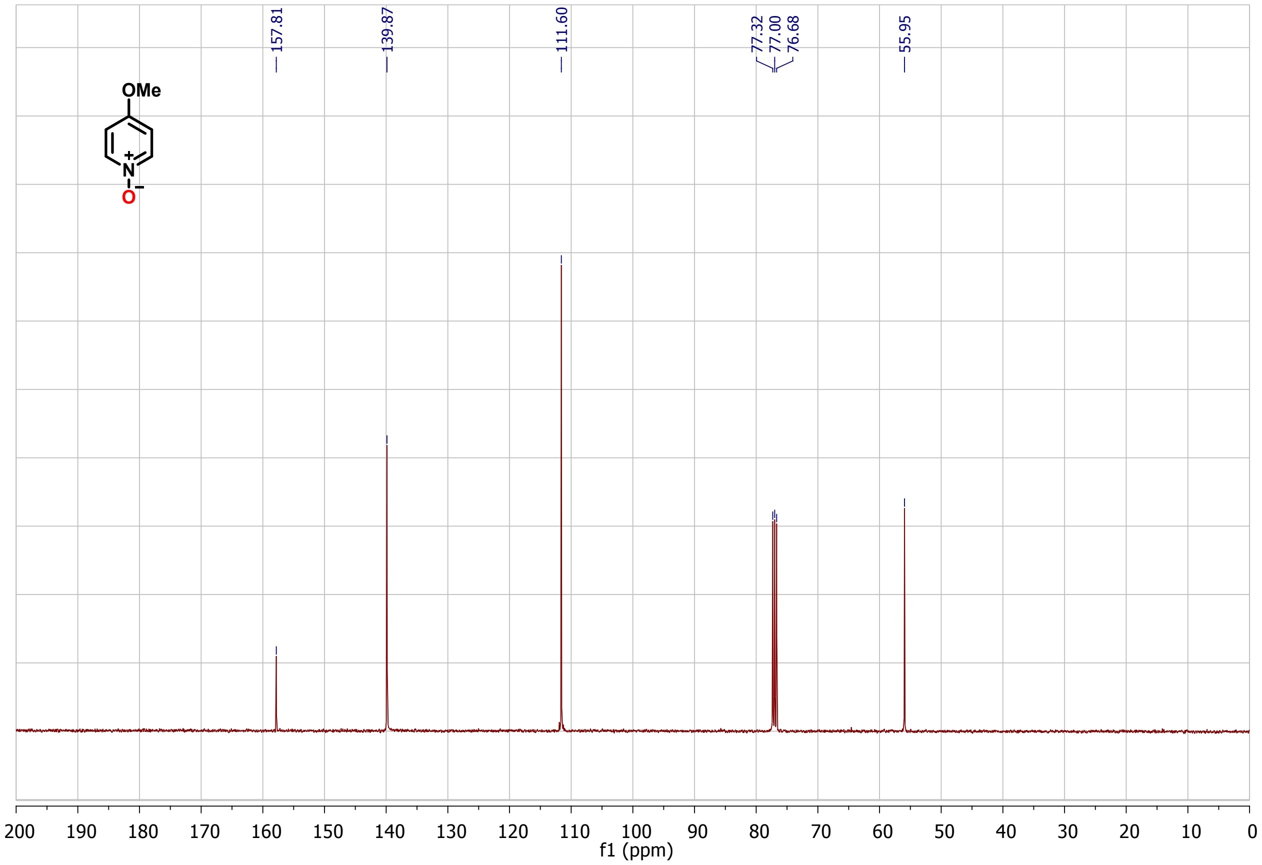

Me
N
+
O
−
7.95
7.92
7.26
7.07
7.05
7.04
6.99
6.97
2.18
1.96
2.00
2.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.(
f1 (ppm)

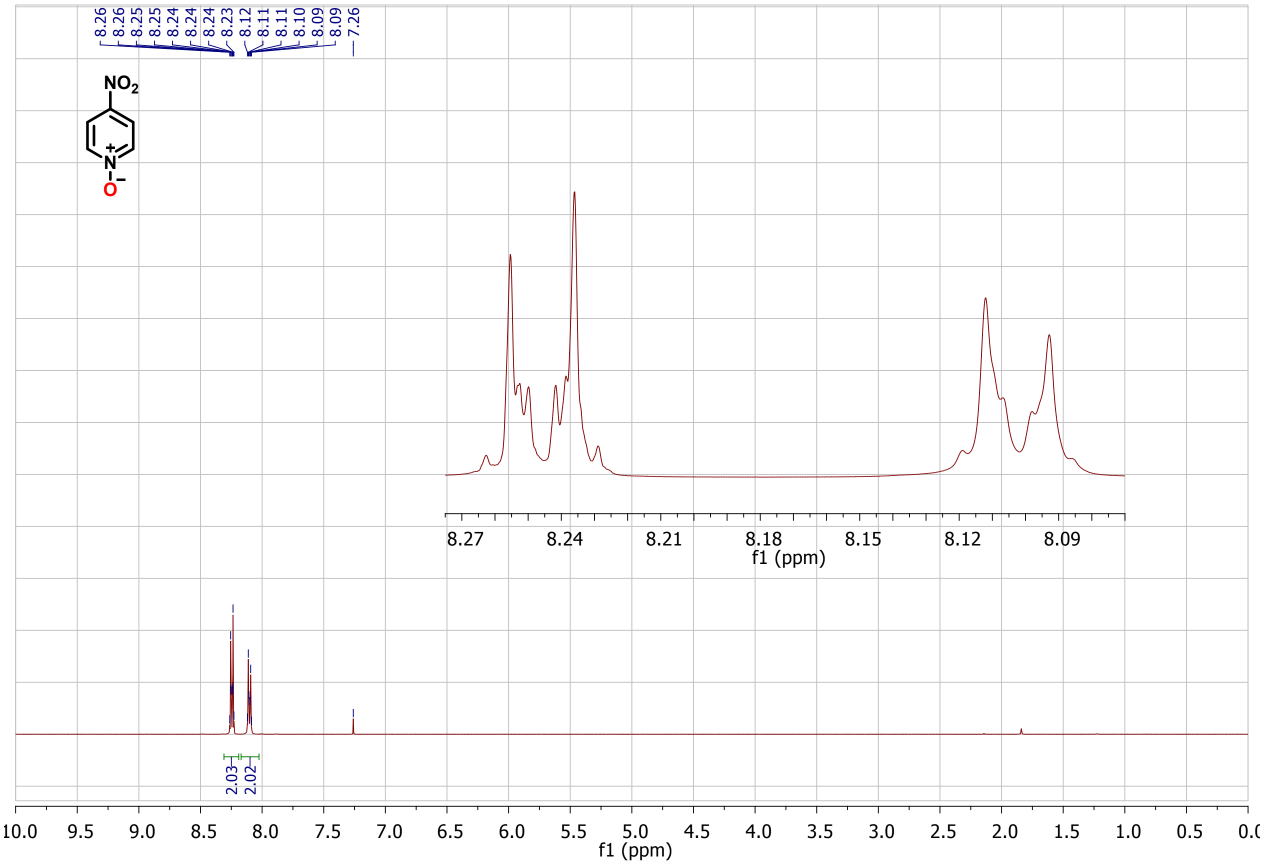

Me
N
+
O
−
138.99
136.58
136.27
126.90
125.14
77.32
77.00
76.68
18.01
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

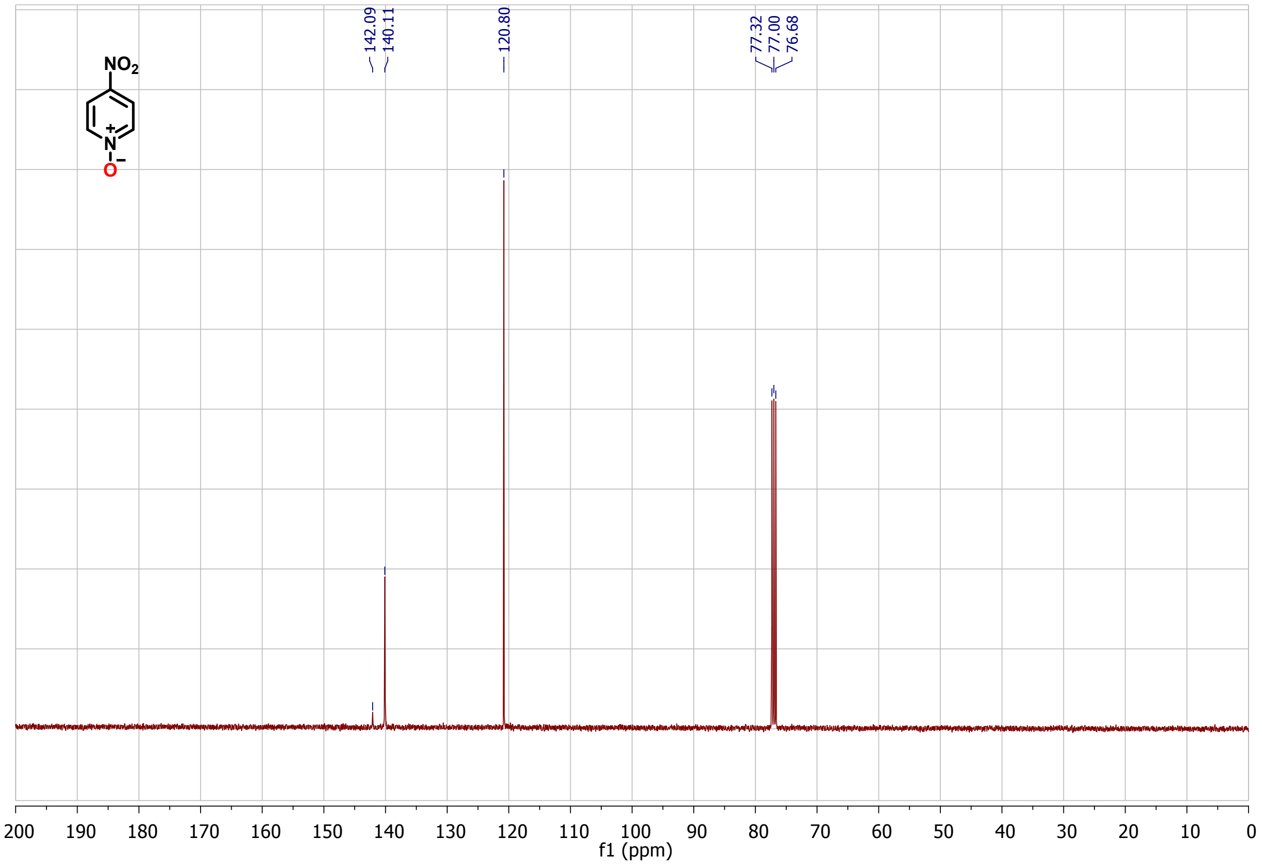

8.22
8.21
8.21
8.20
7.30
7.28
7.27
7.23
7.22
7.21
7.21
7.20
7.09
7.09
7.07
7.06
7.05
7.05
7.04
7.03
6.89
6.88
6.87
4.20
Ph
N
+
O
−
0.97
1.96
2.89
1.98
0.97
2.00
f1 (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8

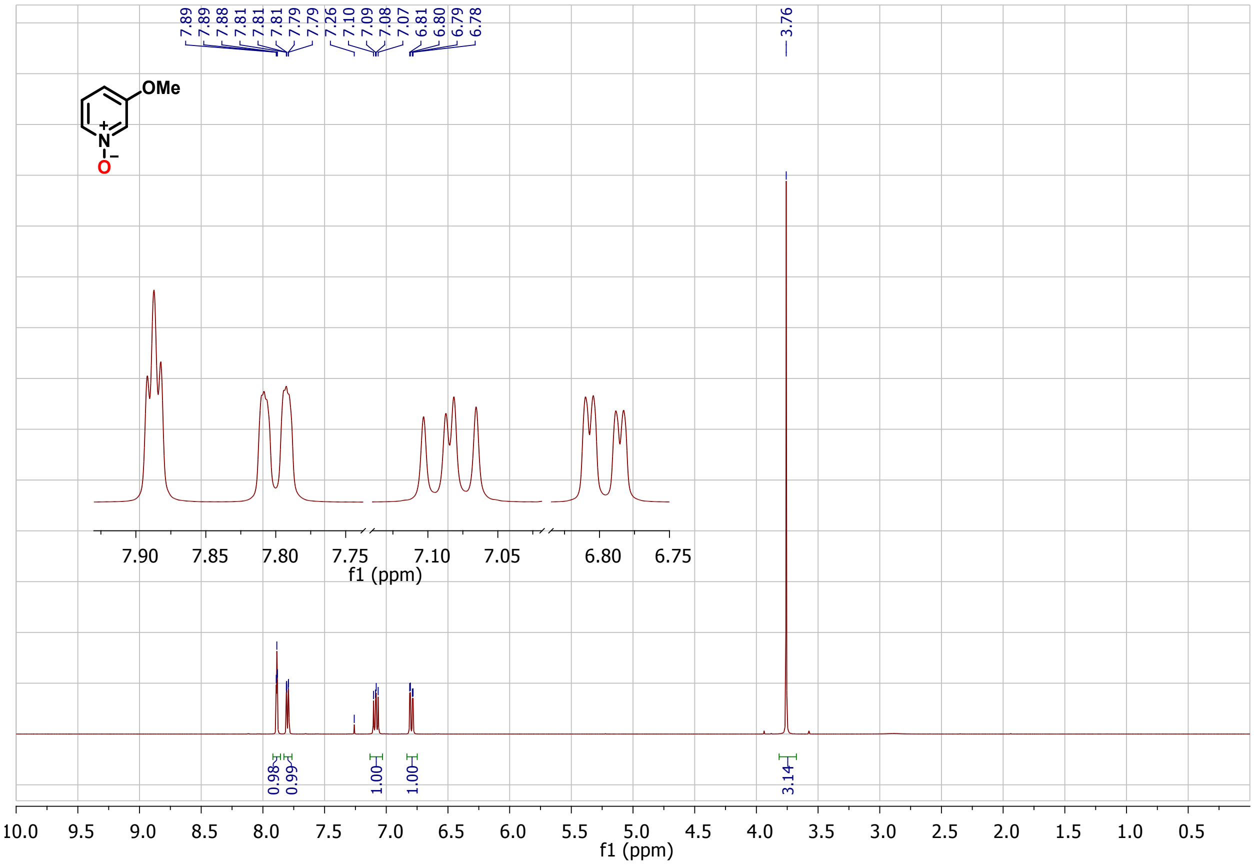

151.59
139.08
136.07
129.41
128.58
126.77
125.55
125.10
123.33
77.32
77.00
76.68
36.24
Ph
N
+
O
−
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

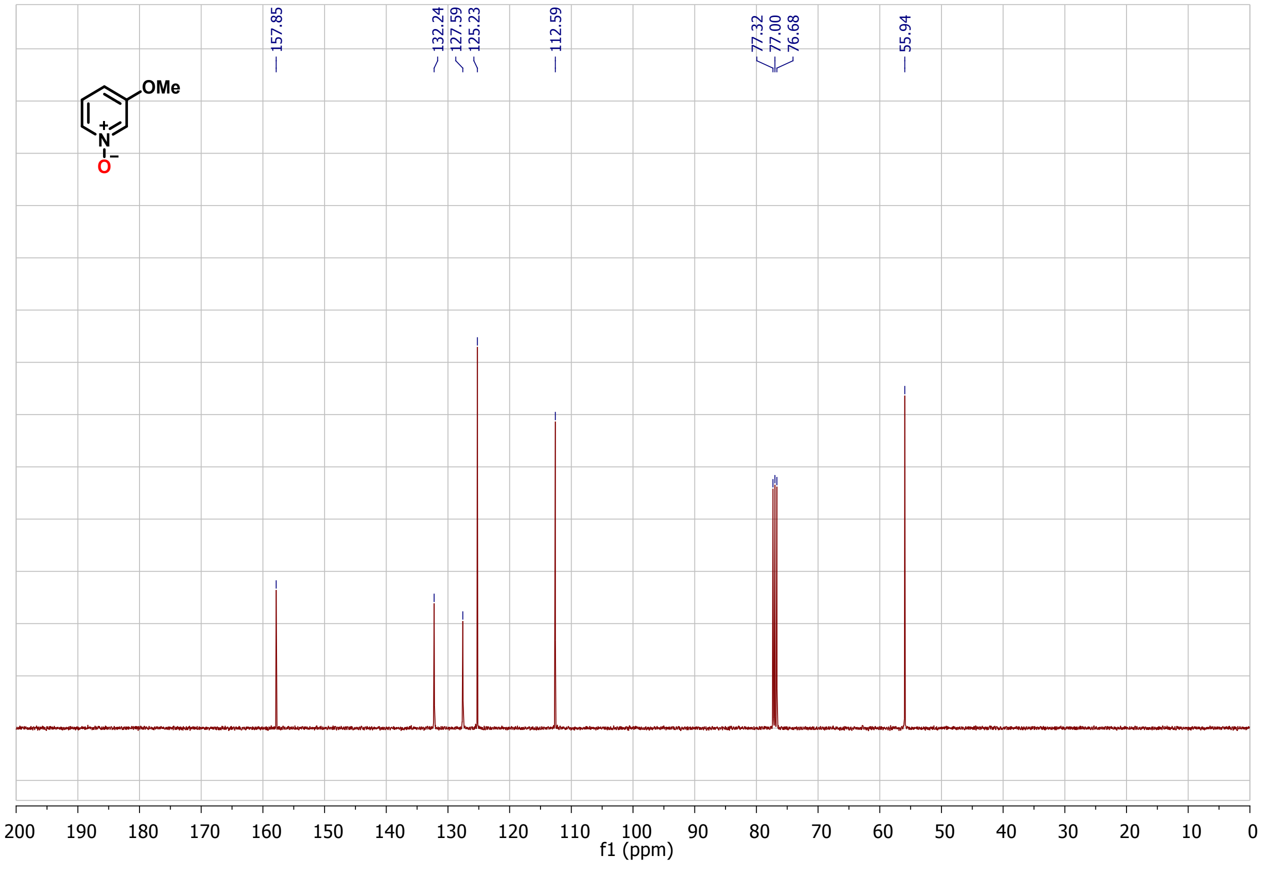

8.13
8.12
8.12
8.11
8.10
8.09
7.26
6.81
6.80
6.80
6.79
6.78
6.77
3.85
OMe
N
O
1.97
2.02
3.32
8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

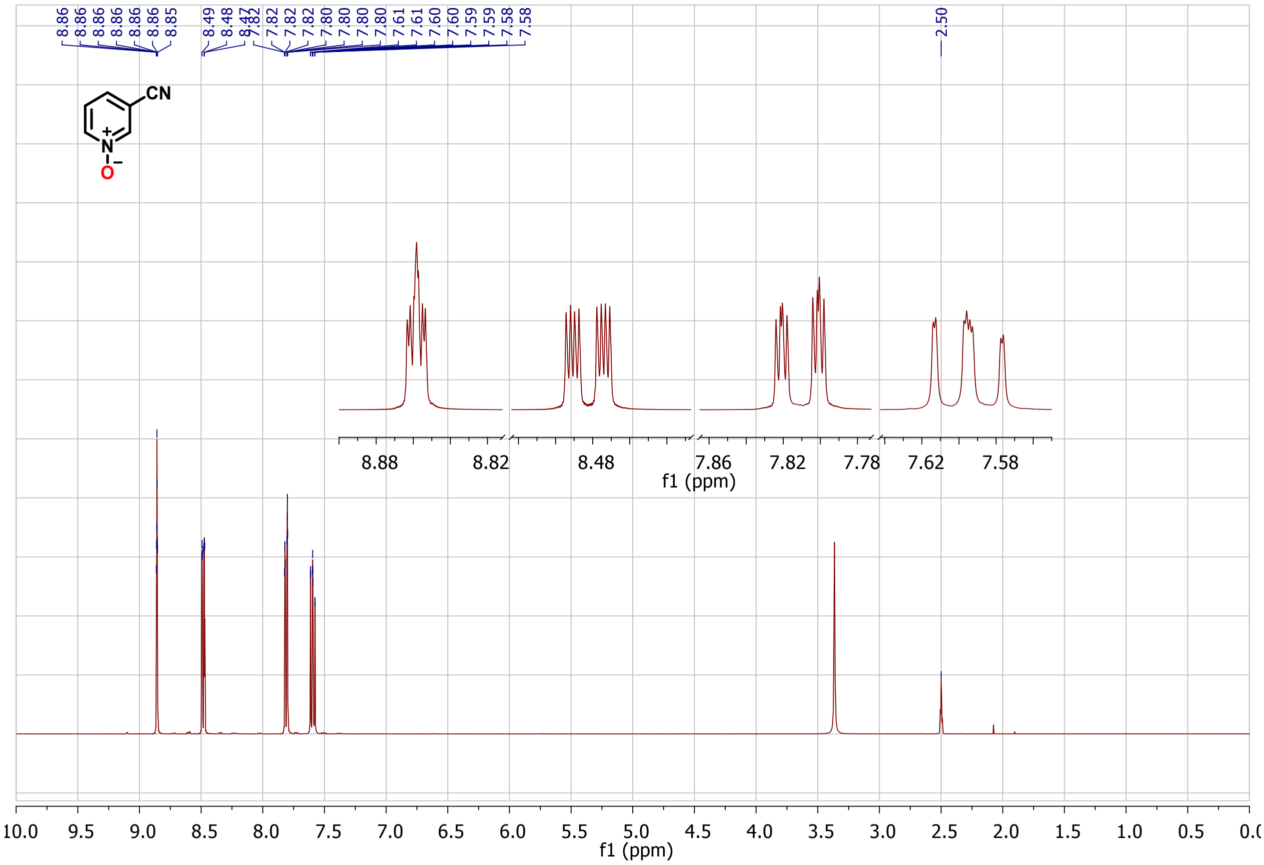

157.81
139.87
111.60
77.32
77.00
76.68
55.95
OMe
N
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

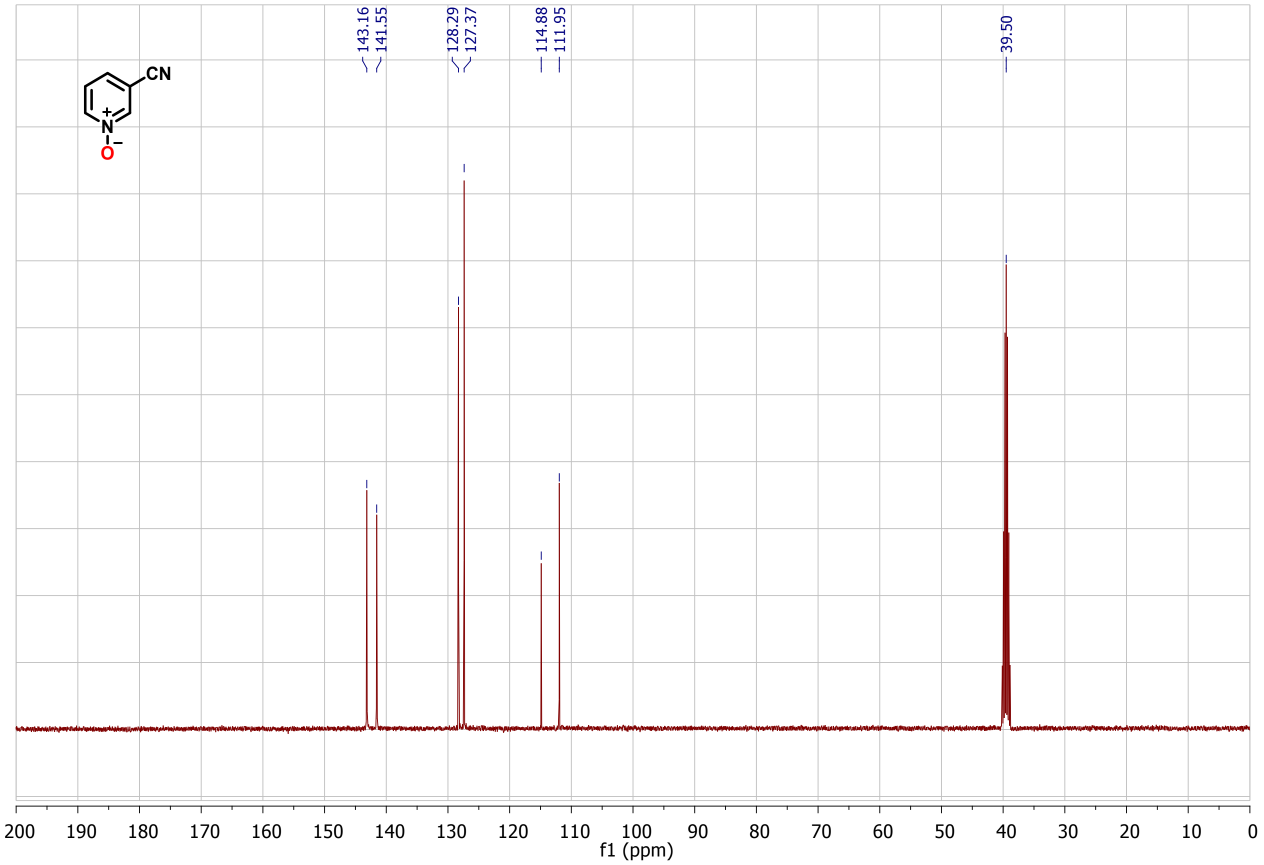

8.26
8.26
8.25
8.25
8.24
8.24
8.24
8.23
8.12
8.11
8.11
8.10
8.09
8.09
7.26
NO2
N+
O−
8.27
8.24
8.21
8.18
8.15
8.12
8.09
f1 (ppm)
2.03
2.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

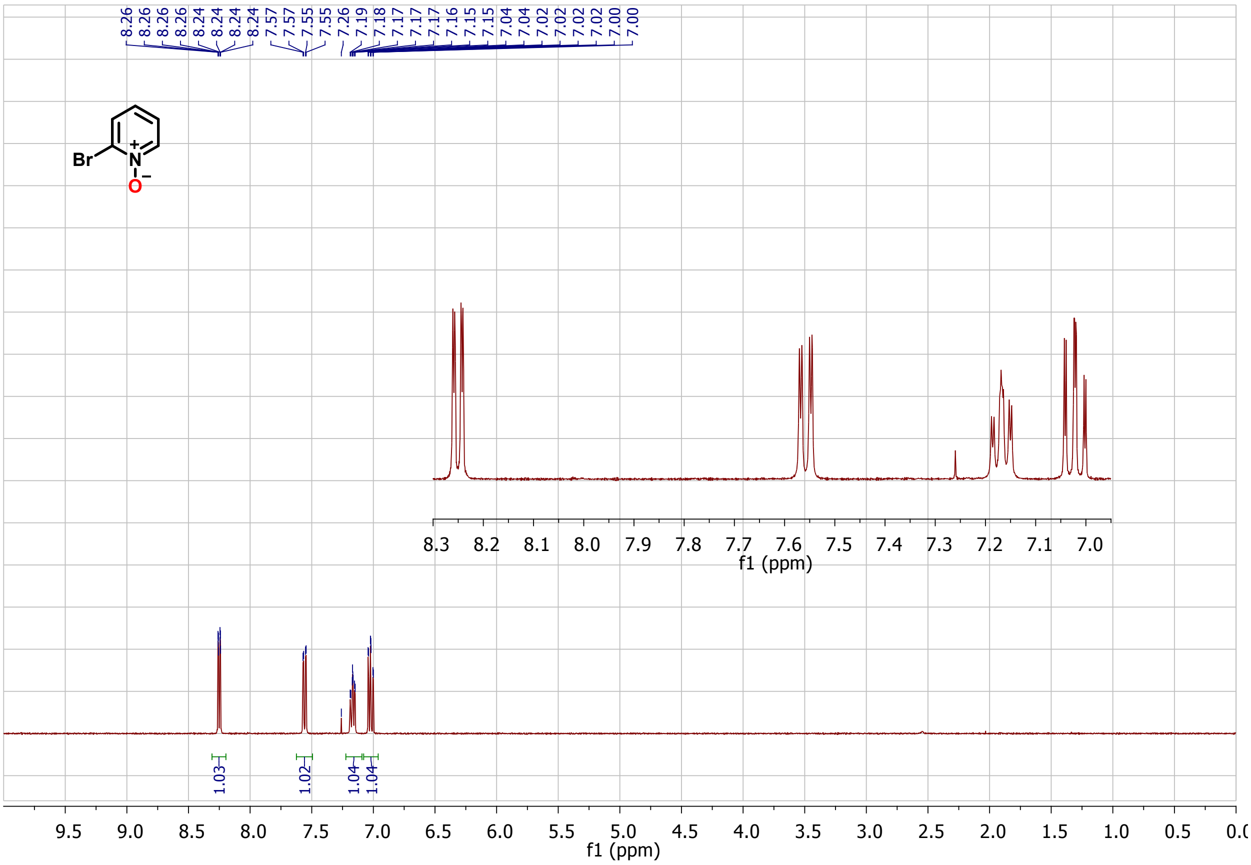

142.09
140.11
120.80
77.32
77.00
76.68
NO2
N+
O−
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

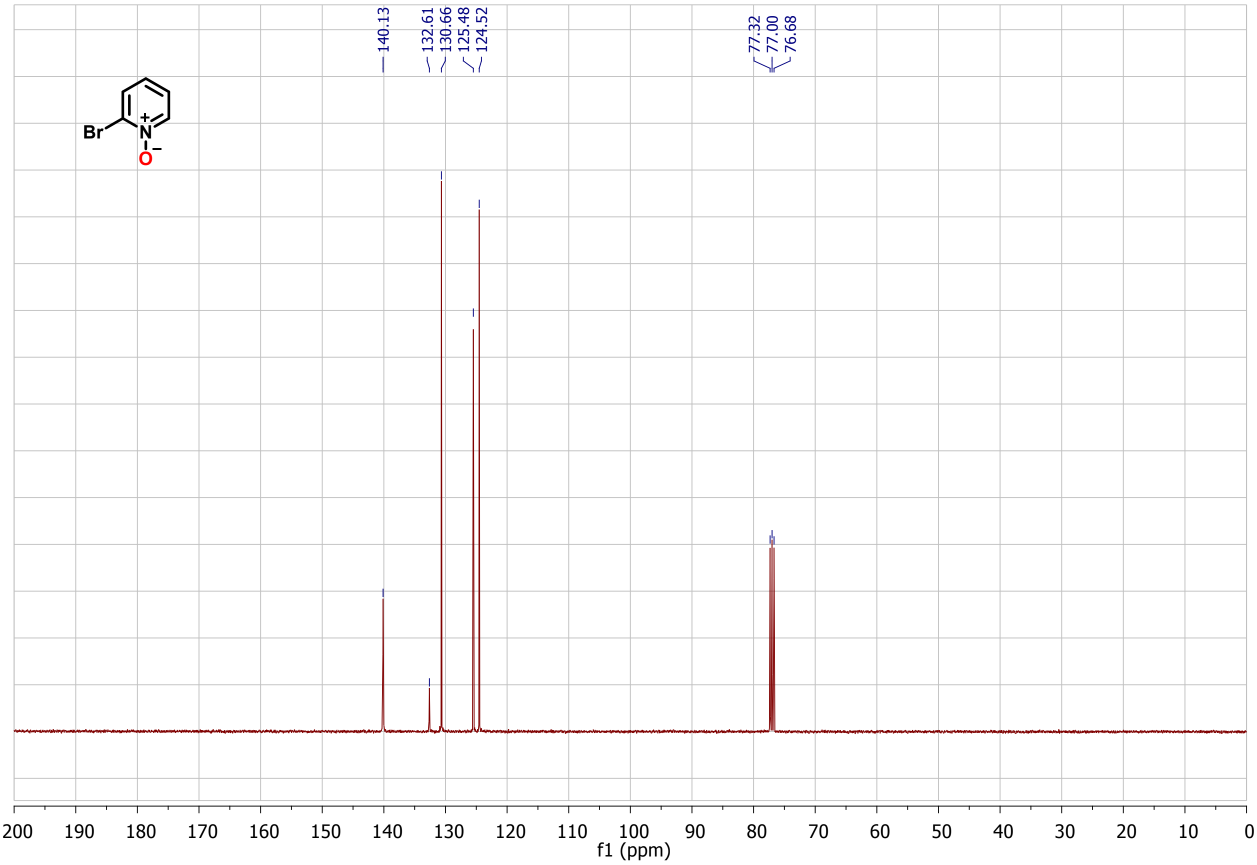

7.89
7.89
7.88
7.81
7.81
7.79
7.79
7.26
7.10
7.09
7.08
7.07
6.81
6.80
6.79
6.78
3.76
OMe
N
O
0.98
0.99
1.00
1.00
3.14
7.90
7.85
7.80
7.75
7.10
7.05
6.80
6.75
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

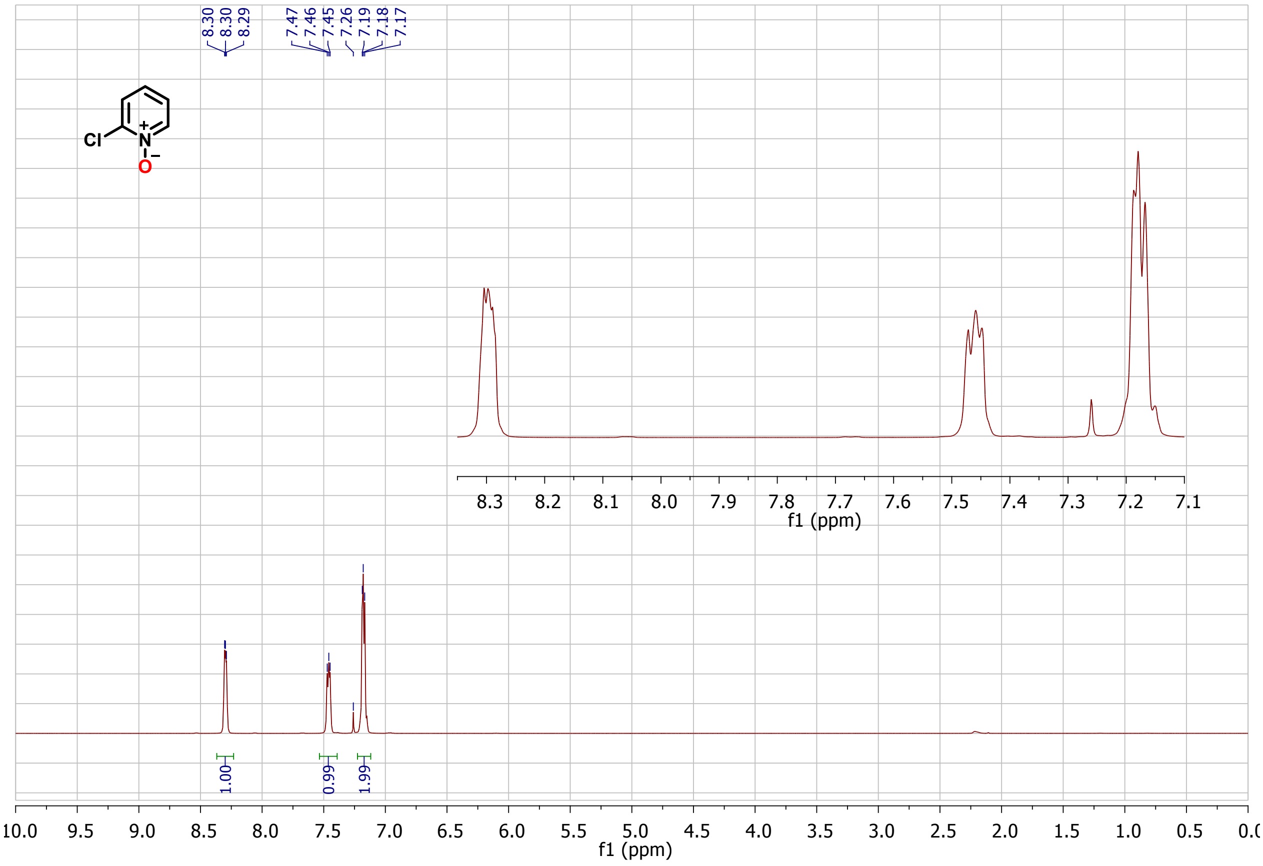

157.85
132.24
127.59
125.23
112.59
77.32
77.00
76.68
55.94
OMe
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

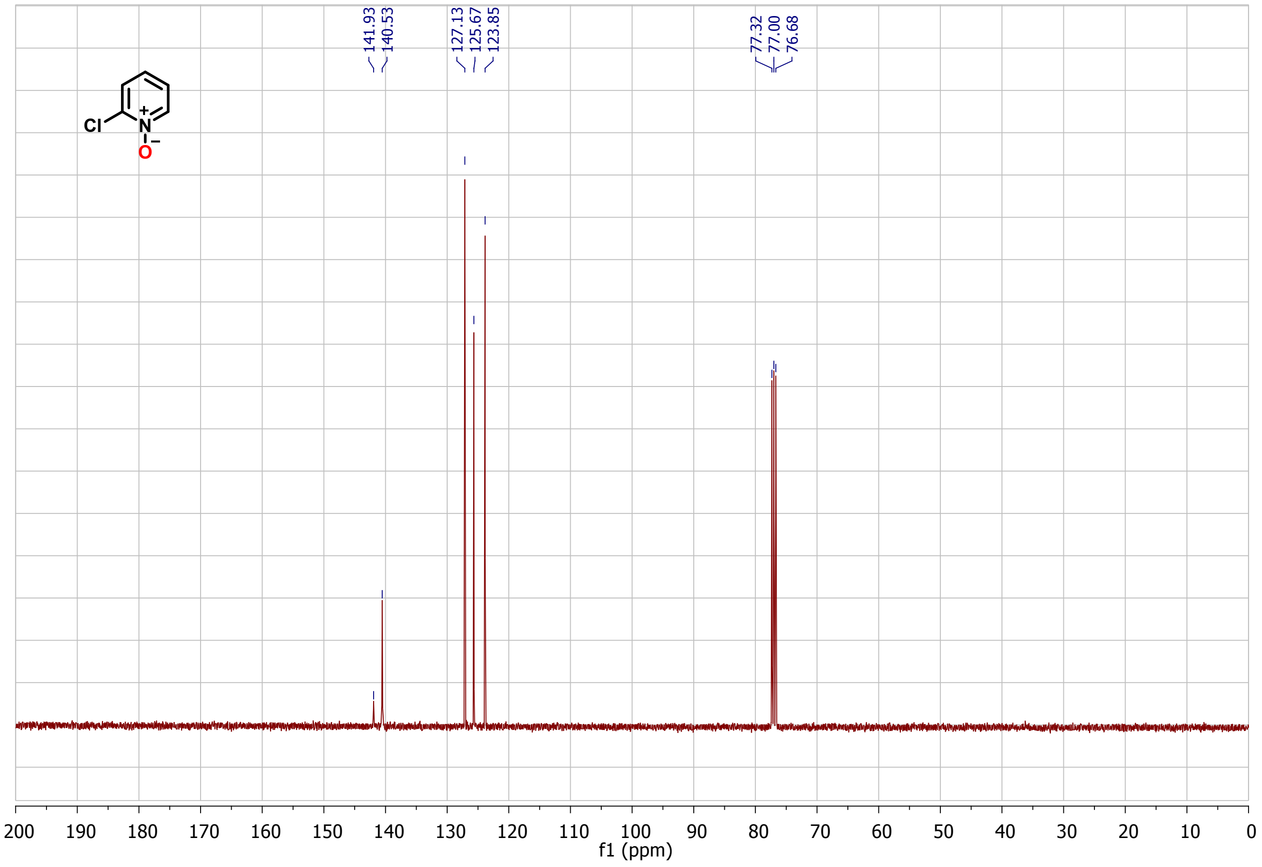

8.86
8.86
8.86
8.86
8.86
8.85
8.49
8.48
8.47
7.82
7.82
7.82
7.80
7.80
7.80
7.61
7.61
7.60
7.59
7.59
7.58
7.58
2.50
CN
N
+
O
−
8.88
8.82
8.48
7.86
7.82
7.78
7.62
7.58
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

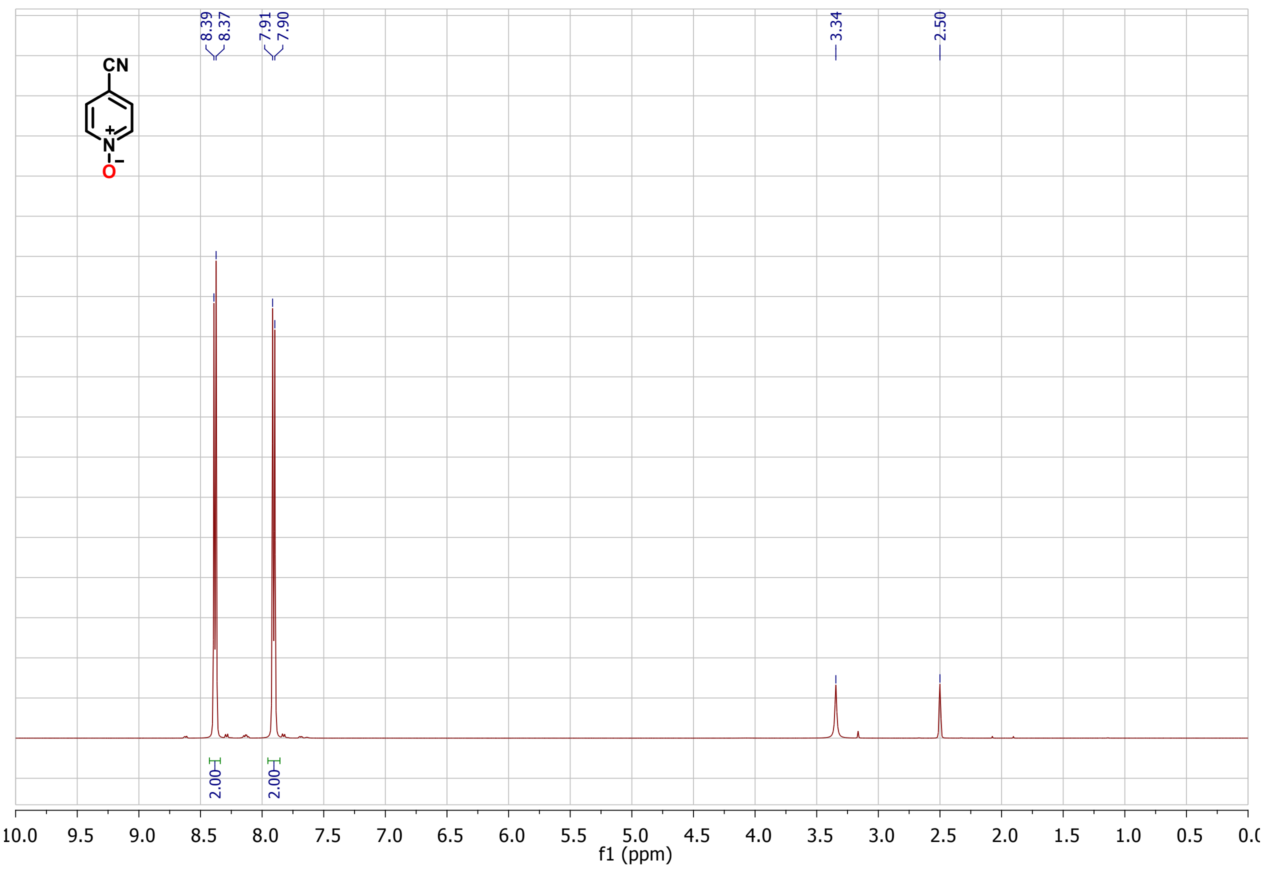

143.16
141.55
128.29
127.37
114.88
111.95
39.50
CN
N
+
O
−
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

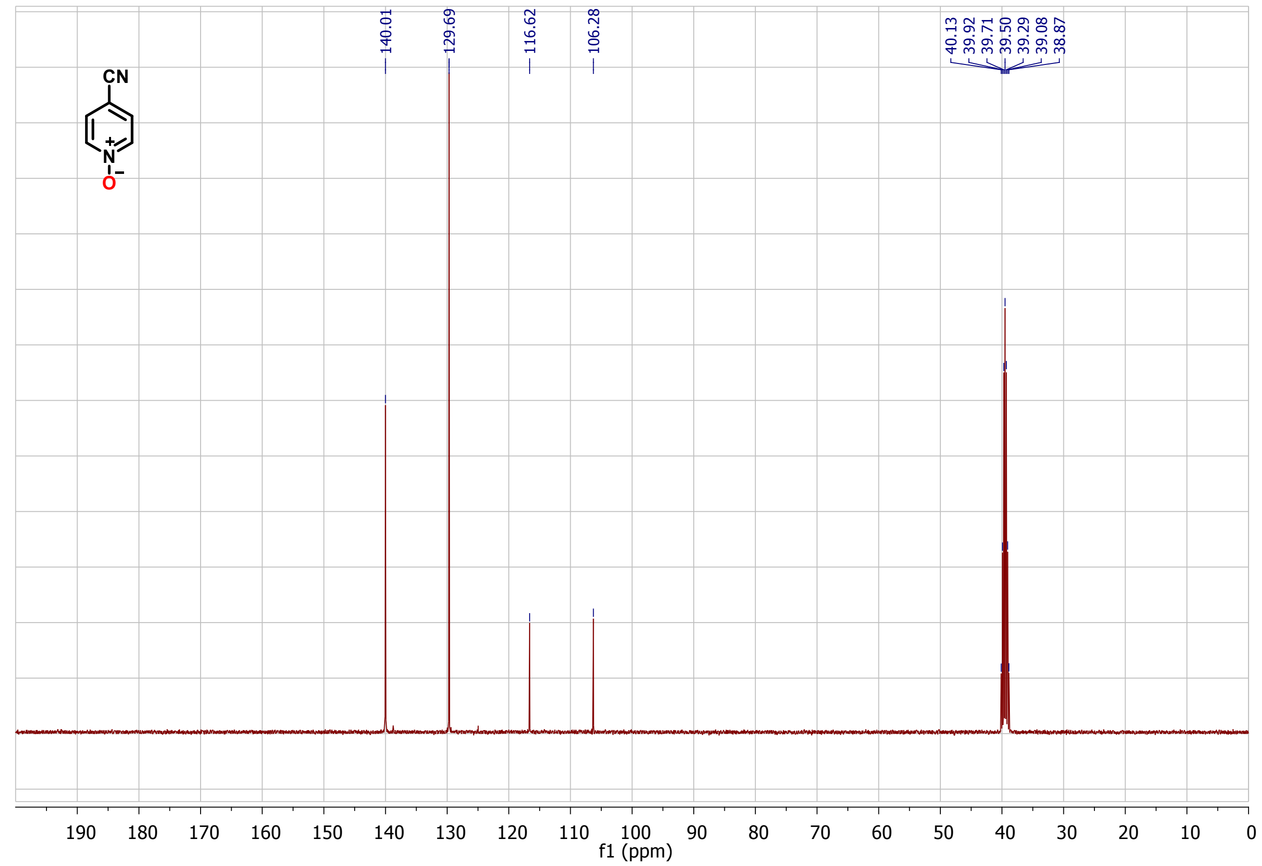

8.26
8.26
8.26
8.26
8.24
8.24
8.24
8.24
7.57
7.57
7.55
7.55
7.26
7.19
7.18
7.17
7.17
7.16
7.15
7.15
7.04
7.04
7.02
7.02
7.02
7.00
7.00
Br
N
+
O
–
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
1.03
1.02
1.04
1.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

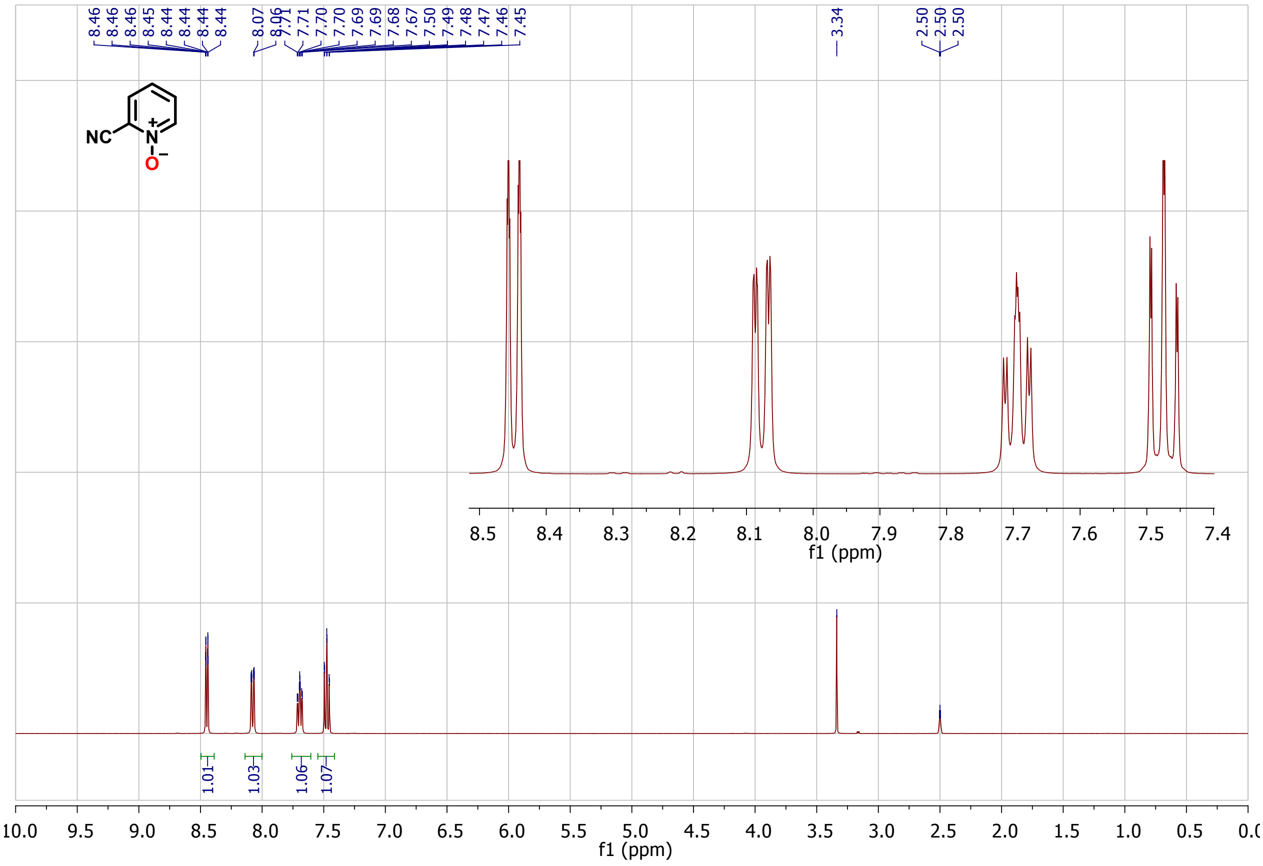

140.13
132.61
130.66
125.48
124.52
77.32
77.00
76.68
Br
N
+
O
–
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

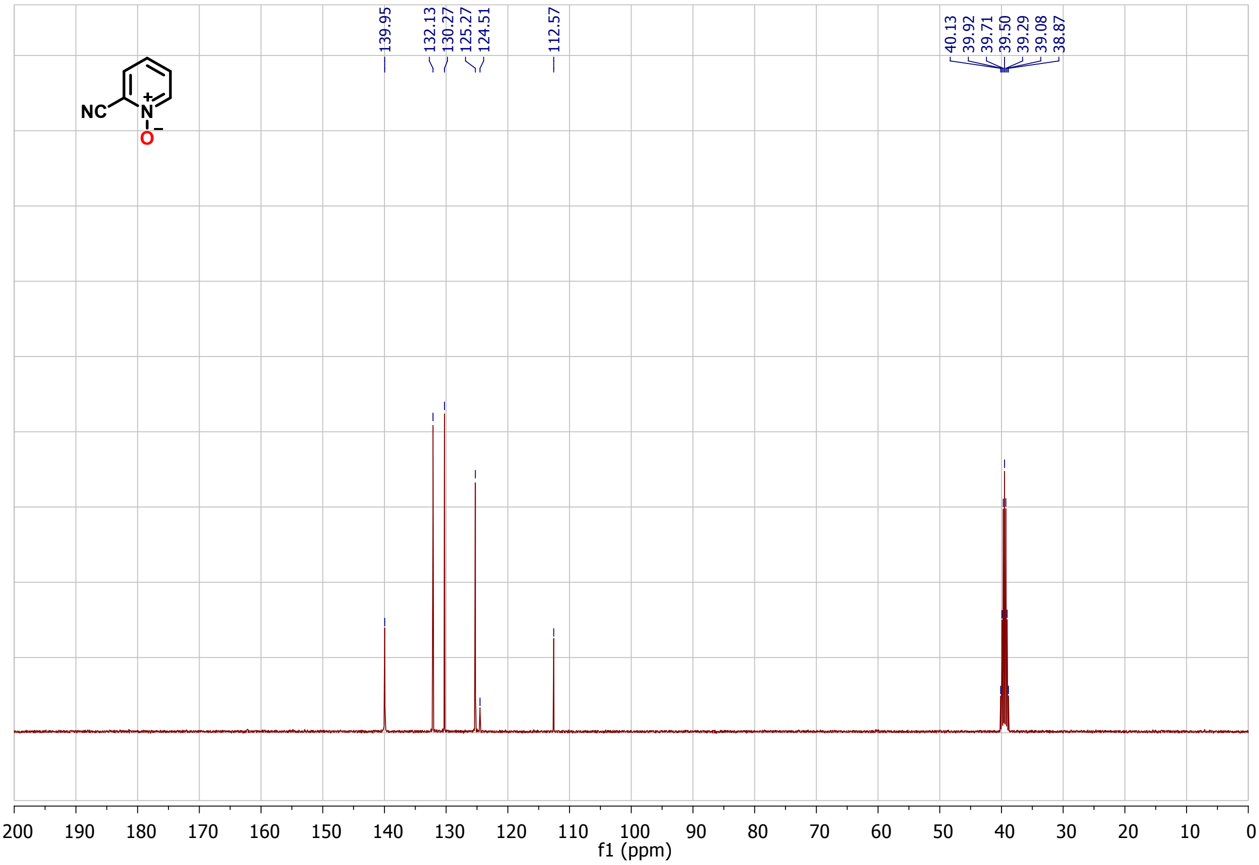

8.30
8.30
8.29
7.47
7.46
7.45
7.26
7.19
7.18
7.17
Cl
N
+
O
−
1.00
0.99
1.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)

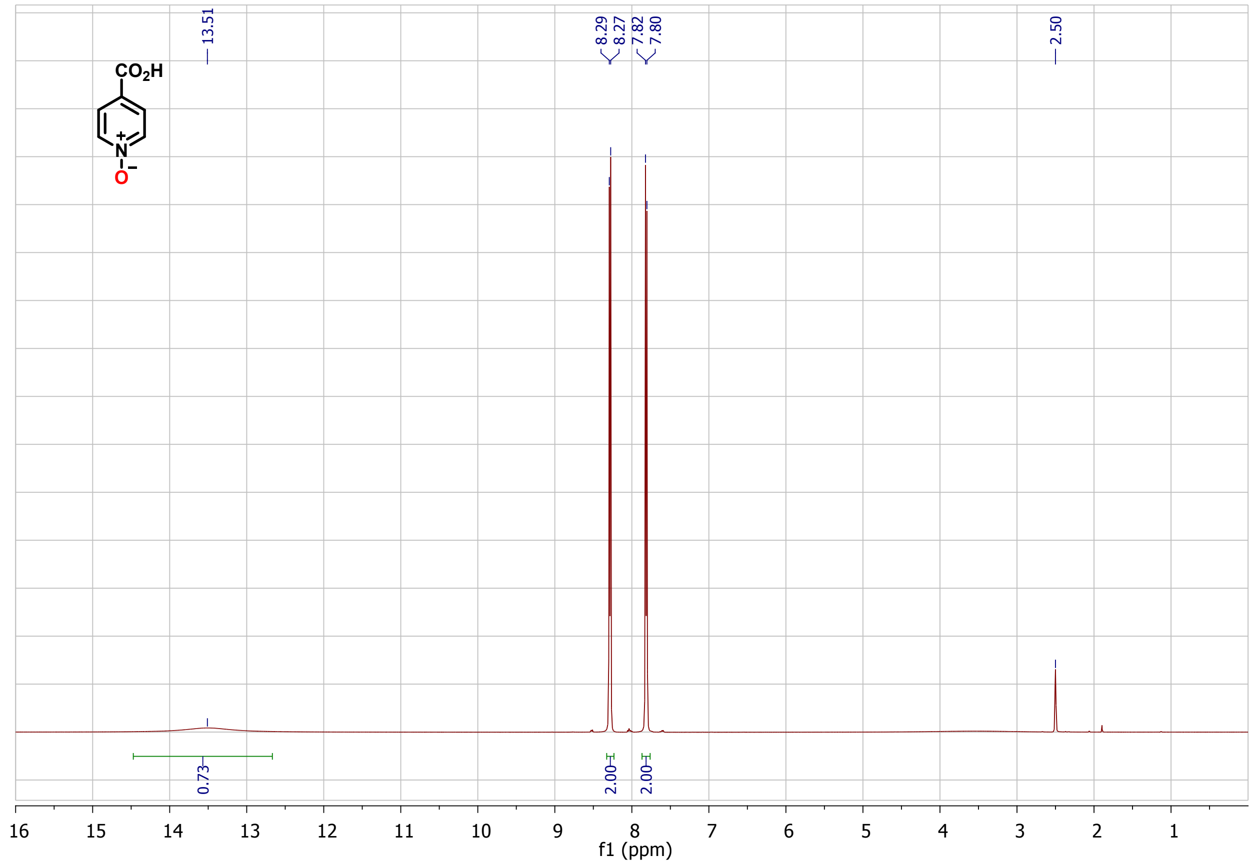

141.93
140.53
127.13
125.67
123.85
77.32
77.00
76.68
Cl
N
+
O
−
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

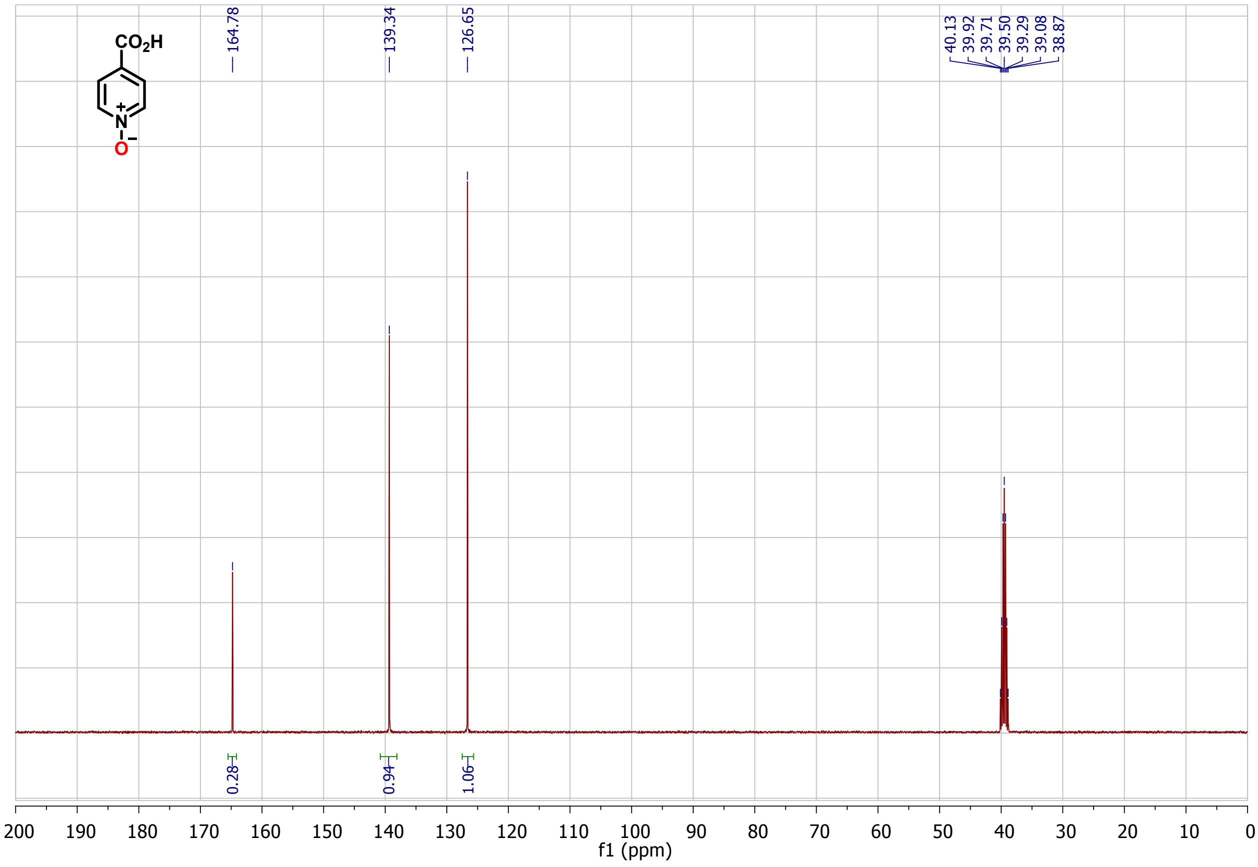

CN
N
+
O
−
8.39
8.37
7.91
7.90
3.34
2.50
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

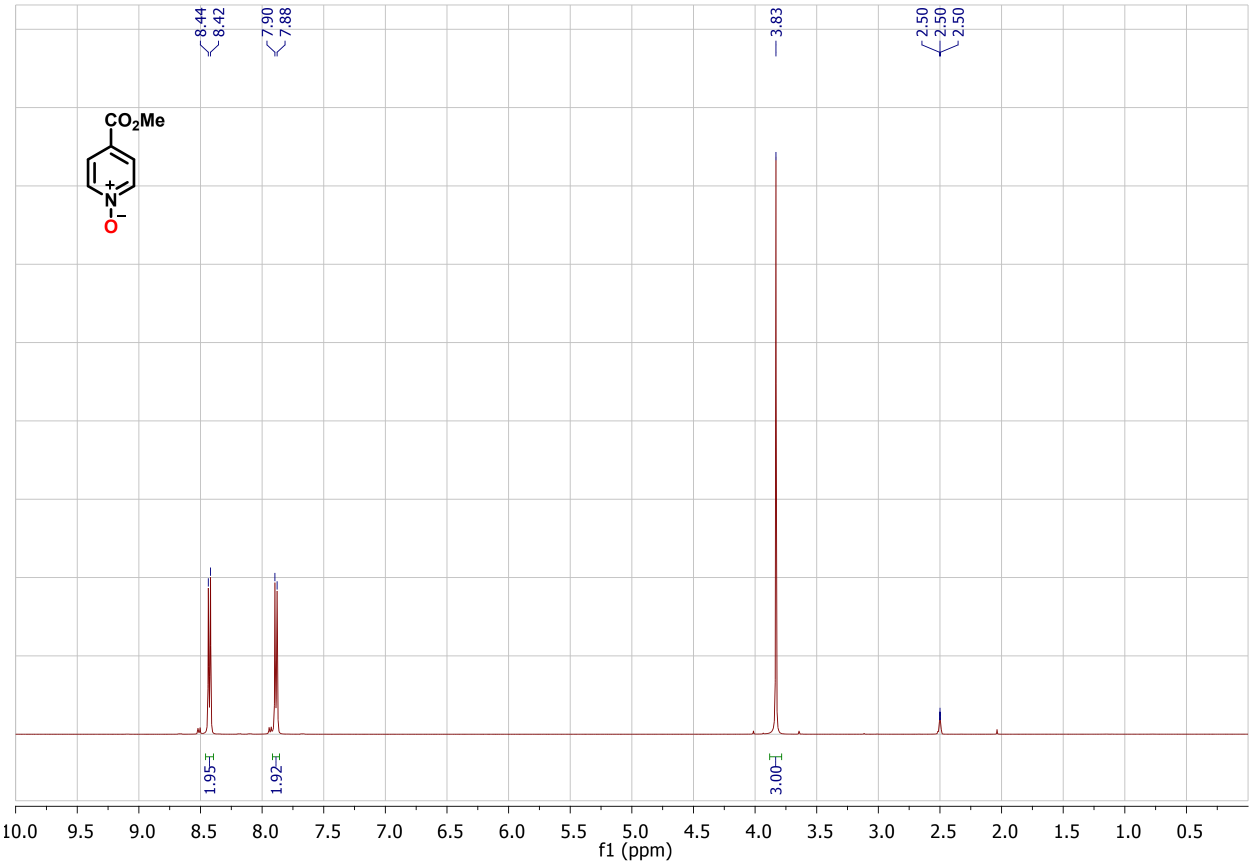

CN
N
+
O
−
140.01
129.69
116.62
106.28
40.13
39.92
39.71
39.50
39.29
39.08
38.87
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

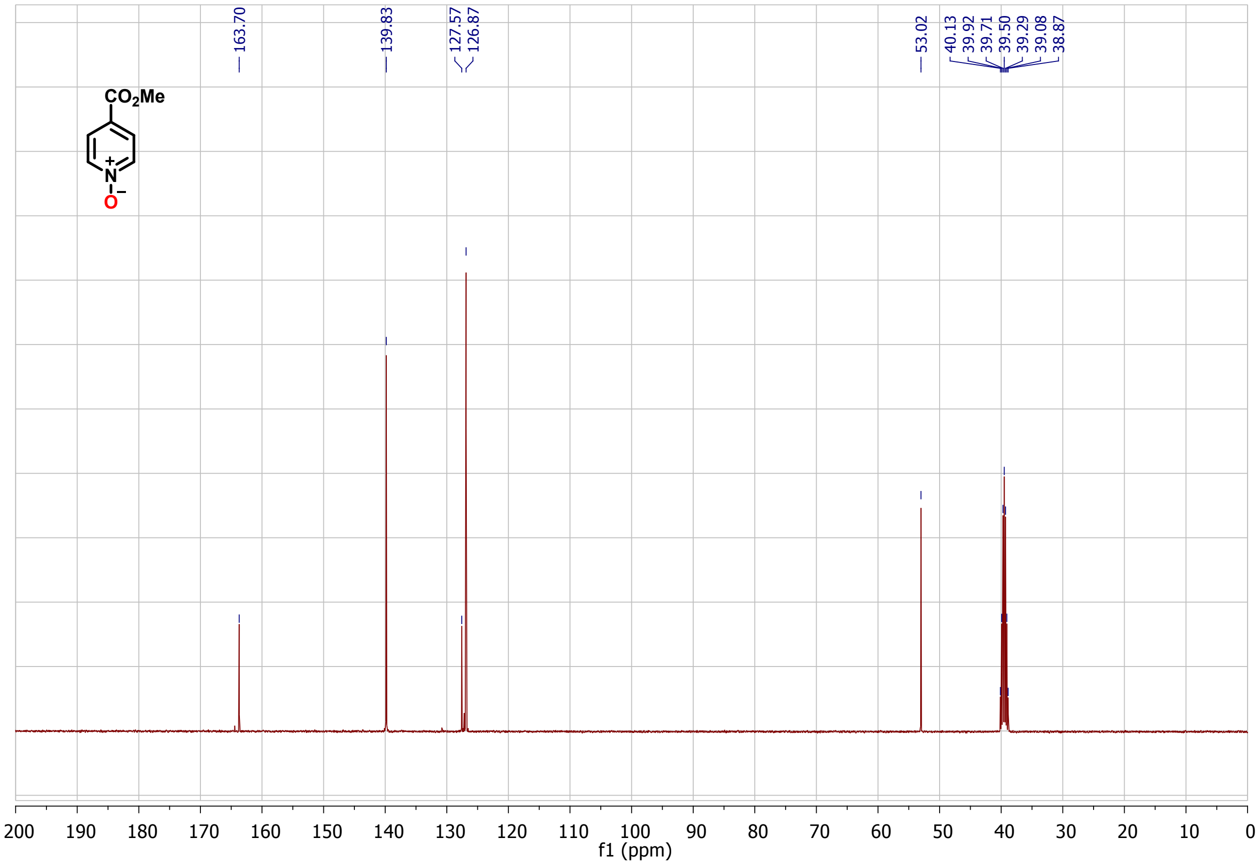

8.46
8.46
8.46
8.45
8.44
8.44
8.44
8.44
8.07
8.06
7.71
7.71
7.70
7.70
7.69
7.69
7.68
7.67
7.50
7.49
7.48
7.47
7.46
7.45
3.34
2.50
2.50
2.50
NC
N
+
O
−
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
f1 (ppm)
1.01
1.03
1.06
1.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

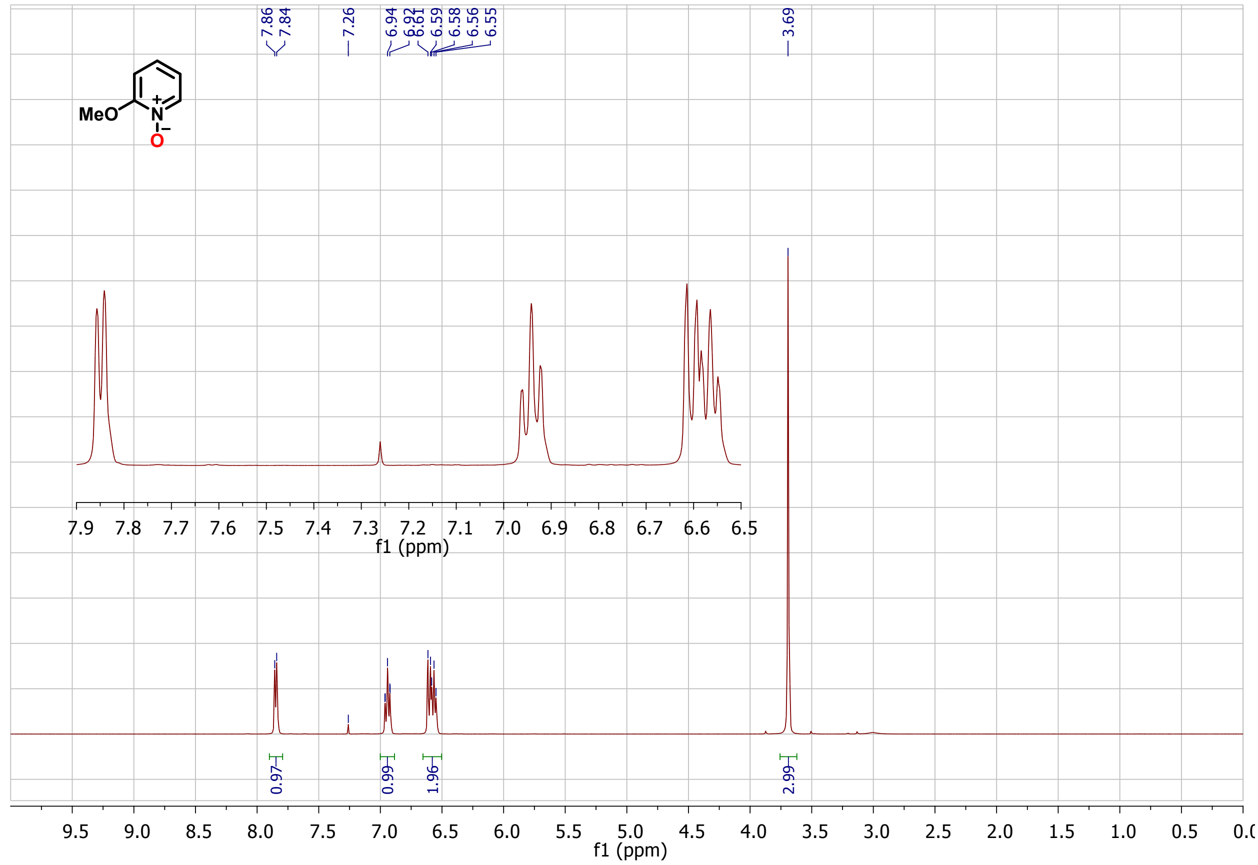

139.95
132.13
130.27
125.27
124.51
112.57
40.13
39.92
39.71
39.50
39.29
39.08
38.87
NC
N
+
O
−
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

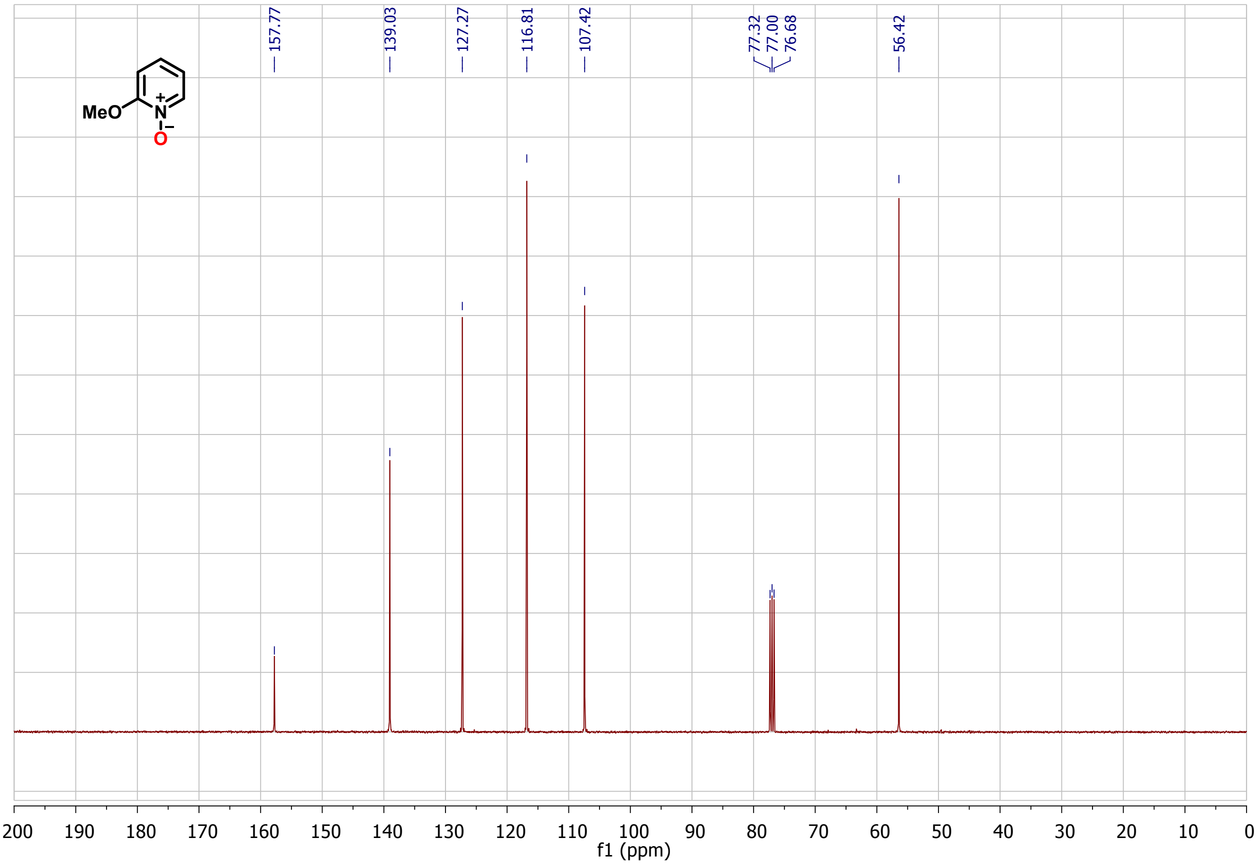

13.51
8.29
8.27
7.82
7.80
2.50
CO$_2$H
N
+
O
−
0.73
2.00
2.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
f1 (ppm)


164.78
139.34
126.65
40.13
39.92
39.71
39.50
39.29
39.08
38.87
CO$_2$H
N
+
O
−
0.28
0.94
1.06
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

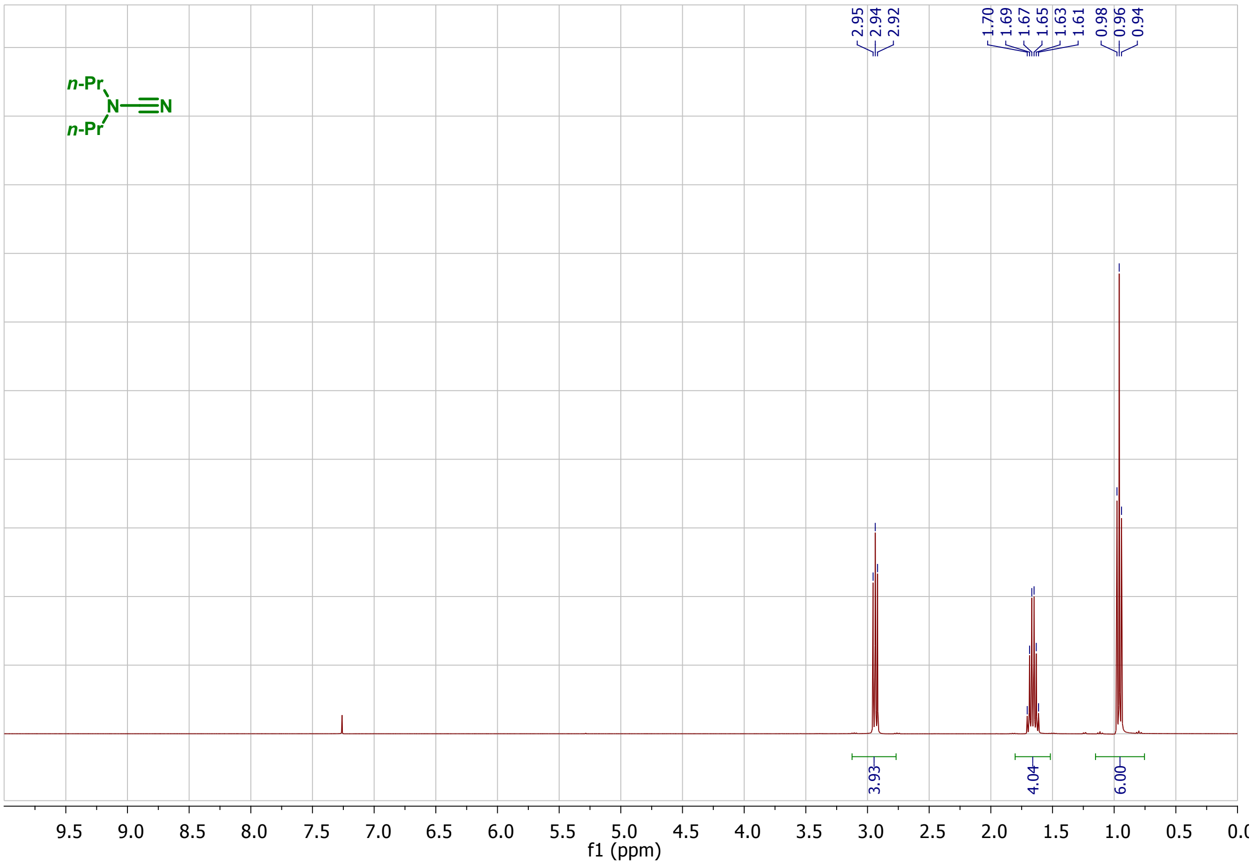

8.44
8.42
7.90
7.88
3.83
2.50
2.50
2.50
CO2Me
N
O
1.95
1.92
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

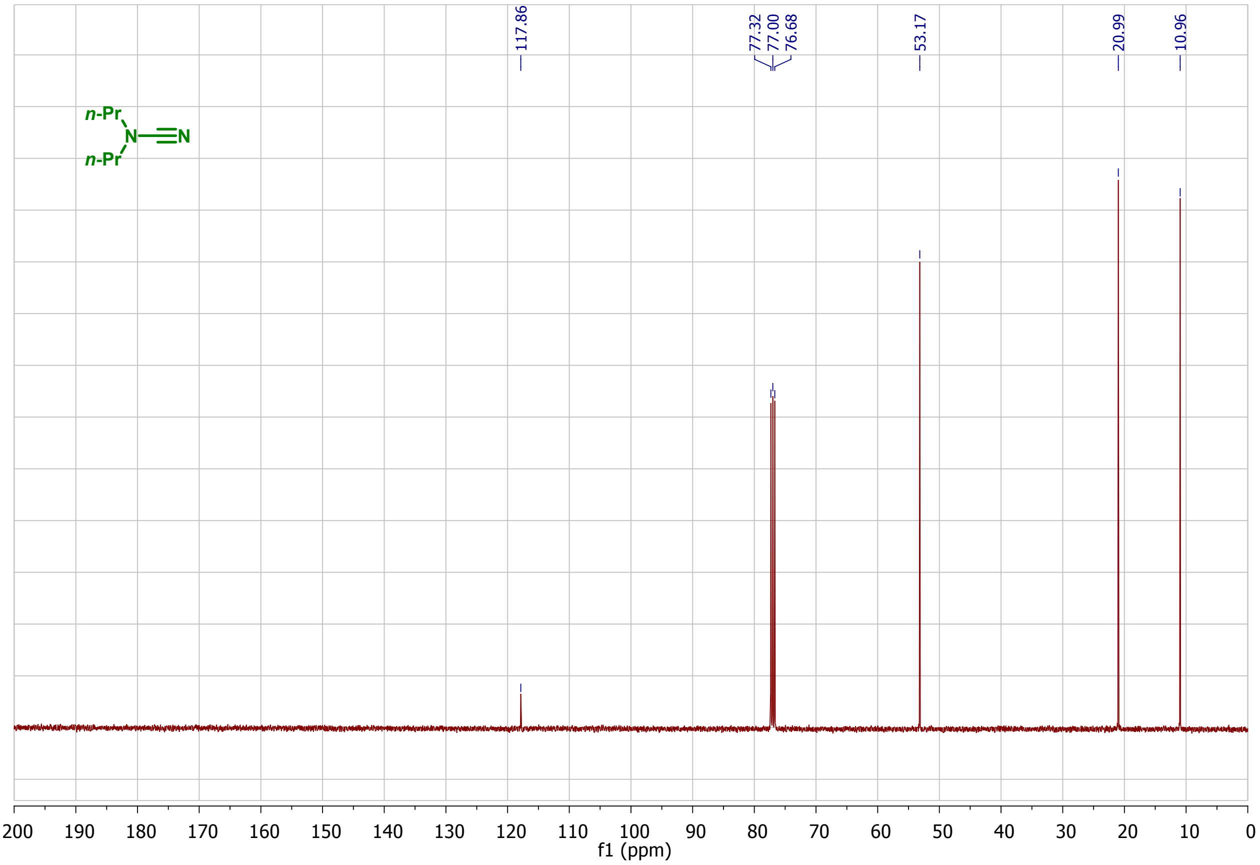

163.70
139.83
127.57
126.87
53.02
40.13
39.92
39.71
39.50
39.29
39.08
38.87
CO2Me
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.86
7.84
7.26
6.94
6.92
6.61
6.59
6.58
6.56
6.55
3.69
MeO
N
+
O
−
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
0.97
0.99
1.96
2.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


157.77
139.03
127.27
116.81
107.42
77.32
77.00
76.68
56.42
MeO
N
+
O
−
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

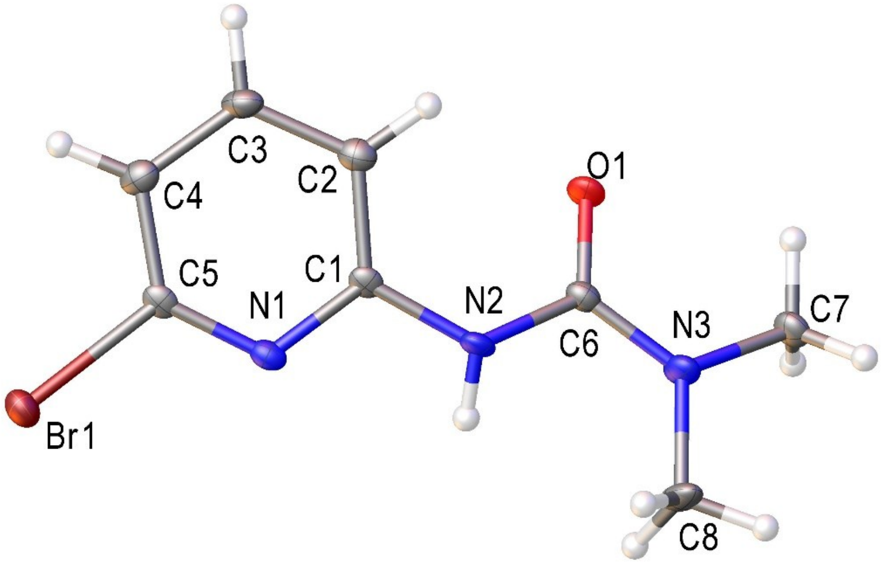
3.3. Spectrum of cyanamide **2c**





4 X-ray data

4.1. X-ray structure of 3-(6-Bromopyridin-2-yl)-1,1-dimethylurea (**4o**)



CCDC: **1473656**

Table S1. Crystal data and structure refinement

Empirical formula	$C_8H_{10}BrN_3O$
Formula weight	244.10
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	4.18964(13)
b/Å	21.1953(8)
c/Å	10.4364(4)
α/°	90
β/°	95.814(3)
γ/°	90
Volume/Å^3	921.99(6)
Z	4
ρ_{calc}g/cm^3	1.759
μ/mm^{-1}	4.421
F(000)	488.0
Crystal size/mm^3	0.36 × 0.28 × 0.14
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.492 to 62.344
Index ranges	$-5 \leq h \leq 5$, $-30 \leq k \leq 30$, $-13 \leq l \leq 14$
Reflections collected	23771
Independent reflections	2504 [R_{int} = 0.0817, R_{sigma} = 0.0532]
Data/restraints/parameters	2504/0/120
Goodness-of-fit on F^2	1.132
Final R indexes [I>=2σ (I)]	R_1 = 0.0503, wR_2 = 0.0946

Final R indexes [all data]	$R_1 = 0.0657$, $wR_2 = 0.1016$
Largest diff. peak/hole / e Å^{-3}	0.90/-0.84

Table S2. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3). U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor

Atom	***x***	***y***	***z***	**U(eq)**
Br$^{(1)}$	4565.8(9)	4934.8(2)	8233.8(4)	19.70(12)
O$^{(1)}$	2791(6)	2410.7(12)	4374(2)	17.6(5)
N$^{(1)}$	4240(7)	3749.1(14)	7140(3)	13.7(6)
N$^{(3)}$	1033(8)	1760.2(15)	5873(3)	17.4(7)
N$^{(2)}$	3485(7)	2717.6(14)	6496(3)	14.1(6)
C$^{(5)}$	5441(8)	4316.5(17)	6977(3)	12.9(7)
C$^{(6)}$	2407(8)	2298.5(17)	5507(3)	13.5(7)
C$^{(4)}$	7208(9)	4496.6(18)	5995(4)	17.6(8)
C$^{(1)}$	4789(8)	3310.1(16)	6265(3)	12.4(7)
C$^{(2)}$	6621(8)	3428.3(18)	5242(4)	15.9(7)
C$^{(7)}$	-393(9)	1329.2(18)	4877(4)	17.2(8)
C$^{(3)}$	7799(9)	4029.6(18)	5112(4)	18.0(8)
C$^{(8)}$	294(10)	1626(2)	7177(4)	23.6(9)

Table S3. Anisotropic Displacement Parameters (Å^2×10^3). The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
Br$^{(1)}$	25.2(2)	17.62(19)	16.5(2)	-4.29(15)	3.31(14)	0.16(15)
O$^{(1)}$	25.3(14)	20.4(13)	7.1(13)	-0.6(10)	1.4(10)	-1.9(11)
N$^{(1)}$	12.4(14)	18.3(15)	10.4(15)	-1.2(12)	0.7(11)	2.4(11)
N$^{(3)}$	23.0(16)	20.9(16)	8.5(16)	-1.9(12)	1.8(12)	-5.1(12)
N$^{(2)}$	18.9(15)	16.9(15)	7.0(15)	-0.4(11)	3.9(12)	1.7(12)
C$^{(5)}$	12.3(15)	17.1(16)	8.2(18)	-0.4(13)	-4.2(13)	2.9(13)
C$^{(6)}$	13.9(16)	16.5(17)	9.8(18)	-1.1(13)	0.2(13)	2.0(13)
C$^{(4)}$	16.5(17)	21.4(18)	14(2)	1.7(14)	-1.2(14)	-4.2(14)
C$^{(1)}$	13.4(16)	15.7(17)	7.3(17)	1.1(13)	-2.8(13)	2.2(13)
C$^{(2)}$	13.1(17)	21.2(18)	13.3(19)	-0.5(14)	0.1(13)	0.6(14)
C$^{(7)}$	21.0(19)	19.7(18)	10.4(19)	-3.0(14)	-1.2(15)	-0.7(14)
C$^{(3)}$	17.5(18)	25(2)	11.5(19)	0.9(15)	2.9(14)	-4.0(15)
C$^{(8)}$	33(2)	29(2)	9.5(19)	-0.2(16)	5.5(16)	-13.8(17)

Table S4. Bond Lengths

Atom	**Atom**	**Length/Å**
Br$^{(1)}$	C$^{(5)}$	1.915(3)
O$^{(1)}$	C$^{(6)}$	1.233(4)
N$^{(1)}$	C$^{(5)}$	1.321(5)
N$^{(1)}$	C$^{(1)}$	1.340(4)
N$^{(3)}$	C$^{(6)}$	1.350(5)
N$^{(3)}$	C$^{(7)}$	1.466(5)
N$^{(3)}$	C$^{(8)}$	1.454(5)

N$^{(2)}$	C$^{(6)}$	1.401(5)
N$^{(2)}$	C$^{(1)}$	1.400(4)
C$^{(5)}$	C$^{(4)}$	1.378(5)
C$^{(4)}$	C$^{(3)}$	1.392(5)
C$^{(1)}$	C$^{(2)}$	1.399(5)
C$^{(2)}$	C$^{(3)}$	1.378(5)

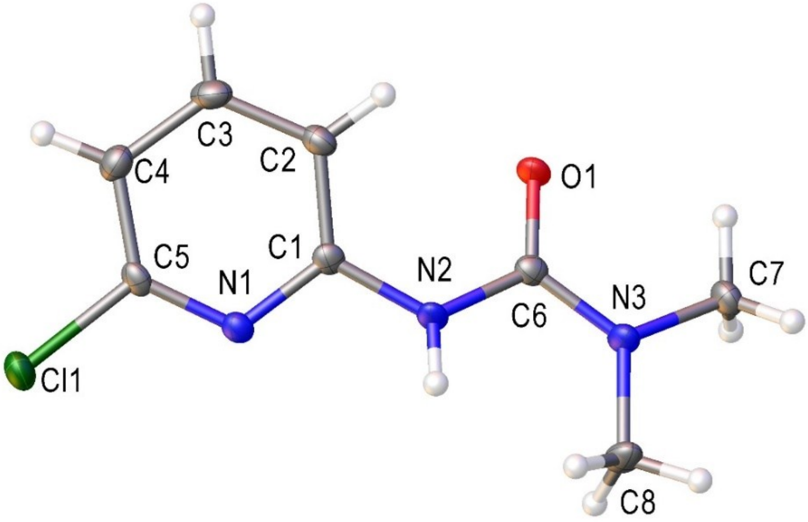
Table S5. Bond Angles

Atom	**Atom**	**Atom**	**Angle/°**
C$^{(5)}$	N$^{(1)}$	C$^{(1)}$	116.8(3)
C$^{(6)}$	N$^{(3)}$	C$^{(7)}$	118.7(3)
C$^{(6)}$	N$^{(3)}$	C$^{(8)}$	124.6(3)
C$^{(8)}$	N$^{(3)}$	C$^{(7)}$	115.6(3)
C$^{(1)}$	N$^{(2)}$	C$^{(6)}$	123.0(3)
N$^{(1)}$	C$^{(5)}$	Br$^{(1)}$	115.6(3)
N$^{(1)}$	C$^{(5)}$	C$^{(4)}$	126.0(3)
C$^{(4)}$	C$^{(5)}$	Br$^{(1)}$	118.3(3)
O$^{(1)}$	C$^{(6)}$	N$^{(3)}$	122.4(3)
O$^{(1)}$	C$^{(6)}$	N$^{(2)}$	121.4(3)
N$^{(3)}$	C$^{(6)}$	N$^{(2)}$	116.2(3)
C$^{(5)}$	C$^{(4)}$	C$^{(3)}$	116.1(3)
N$^{(1)}$	C$^{(1)}$	N$^{(2)}$	114.1(3)
N$^{(1)}$	C$^{(1)}$	C$^{(2)}$	122.8(3)
C$^{(2)}$	C$^{(1)}$	N$^{(2)}$	123.1(3)
C$^{(3)}$	C$^{(2)}$	C$^{(1)}$	118.0(3)
C$^{(2)}$	C$^{(3)}$	C$^{(4)}$	120.2(3)

Table S6. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3)

Atom	***x***	***y***	***z***	**U(eq)**
H$^{(2)}$	2036	2758	7018	17
H$^{(4)}$	7979	4915	5925	21
H$^{(2A)}$	7040	3104	4654	19
H$^{(7A)}$	-2696	1415	4710	26
H$^{(7B)}$	-71	892	5170	26
H$^{(7C)}$	634	1392	4083	26
H$^{(3)}$	9018	4125	4418	22
H$^{(8A)}$	2206	1699	7781	35
H$^{(8B)}$	-378	1185	7234	35
H$^{(8C)}$	-1442	1903	7395	35

4.2. X-ray structure of 3-(6-Chloropyridin-2-yl)-1,1-dimethylurea (**4p**)



CCDC: **1473657**

Table S7. Crystal data and structure refinement for

Empirical formula	$C_8H_{10}ClN_3O$
Formula weight	199.64
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	4.1274(3)
b/Å	20.8167(12)
c/Å	10.4887(6)
α/°	90
β/°	95.909(5)
γ/°	90
Volume/Å^3	896.38(9)
Z	4
ρ_{calc}g/cm^3	1.479
μ/mm^{-1}	0.387
F(000)	416.0
Crystal size/mm^3	0.28 × 0.2 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.528 to 58.2
Index ranges	$-5 \le h \le 5$, $-28 \le k \le 16$, $-13 \le l \le 8$
Reflections collected	4077
Independent reflections	2078 [R_{int} = 0.0240, R_{sigma} = 0.0470]
Data/restraints/parameters	2078/0/120
Goodness-of-fit on F^2	1.075
Final R indexes [I>=2σ (I)]	R_1 = 0.0416, wR_2 = 0.0926
Final R indexes [all data]	R_1 = 0.0552, wR_2 = 0.1028
Largest diff. peak/hole / e Å^{-3}	0.37/-0.43

Table S8. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2\times 10^3$). U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor

Atom	*x*	*y*	*z*	U(eq)
Cl$^{(1)}$	5537.8(12)	4909.1(2)	1674.0(5)	22.90(16)
O$^{(1)}$	7371(3)	2415.9(7)	5469.6(12)	19.1(3)
N$^{(1)}$	5908(4)	3763.9(8)	2691.8(15)	16.0(3)
N$^{(3)}$	9078(4)	1742.1(8)	3978.3(15)	18.0(4)
N$^{(2)}$	6651(4)	2719.8(8)	3356.9(15)	16.6(4)
C$^{(6)}$	7712(4)	2293.2(9)	4338.8(18)	15.5(4)
C$^{(1)}$	5346(4)	3323.5(9)	3576.1(17)	14.7(4)
C$^{(2)}$	3553(4)	3460(1)	4603.4(18)	17.8(4)
C$^{(5)}$	4736(4)	4344.7(10)	2836.6(17)	15.4(4)
C$^{(4)}$	3008(4)	4542.3(10)	3829.0(19)	20.0(4)
C$^{(7)}$	10476(5)	1302.7(10)	4973.0(18)	19.7(4)
C$^{(3)}$	2424(4)	4077.4(10)	4718.1(19)	21.9(5)
C$^{(8)}$	9736(5)	1594.7(11)	2674.8(18)	23.5(5)

Table S9. Anisotropic Displacement Parameters ($Å^2\times 10^3$) . The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl$^{(1)}$	33.5(3)	16.1(3)	19.4(3)	4.7(2)	4.14(19)	-0.2(2)
O$^{(1)}$	30.9(7)	18.3(7)	8.2(7)	0.1(6)	3.1(5)	1.6(6)
N$^{(1)}$	20.9(8)	16.0(8)	11.0(8)	0.4(7)	0.9(6)	-0.6(7)
N$^{(3)}$	26.2(8)	18.1(9)	9.6(8)	1.2(7)	1.8(6)	4.8(7)
N$^{(2)}$	28.3(8)	14.4(8)	7.0(8)	-1.2(6)	1.6(6)	0.8(7)
C$^{(6)}$	17.2(8)	16(1)	13.3(9)	-0.8(8)	1.7(7)	-3.0(8)
C$^{(1)}$	17.5(8)	15.1(9)	10.8(9)	-1.8(7)	-1.4(7)	-1.9(7)
C$^{(2)}$	19.6(9)	20.6(11)	13.5(9)	3.2(8)	2.7(7)	0.0(8)
C$^{(5)}$	18.8(8)	15.7(9)	10.9(9)	3.2(8)	-2.7(7)	-1.7(8)
C$^{(4)}$	23.6(9)	17.2(10)	18.8(10)	-1.4(8)	0.9(7)	4.5(8)
C$^{(7)}$	25.2(10)	18.4(10)	15.4(10)	4.7(8)	1.5(7)	2.3(8)
C$^{(3)}$	22.3(9)	28.2(12)	16.1(10)	-0.8(9)	5.8(7)	5.4(9)
C$^{(8)}$	35.0(11)	24.8(12)	10.8(10)	-1.6(9)	2.5(8)	9.3(9)

Table S10. Bond Lengths

Atom	Atom	Length/Å
Cl$^{(1)}$	C$^{(5)}$	1.7495(19)
O$^{(1)}$	C$^{(6)}$	1.235(2)
N$^{(1)}$	C$^{(1)}$	1.341(2)
N$^{(1)}$	C$^{(5)}$	1.317(2)
N$^{(3)}$	C$^{(6)}$	1.349(2)
N$^{(3)}$	C$^{(7)}$	1.461(2)
N$^{(3)}$	C$^{(8)}$	1.454(2)
N$^{(2)}$	C$^{(6)}$	1.396(2)
N$^{(2)}$	C$^{(1)}$	1.396(2)
C$^{(1)}$	C$^{(2)}$	1.398(3)

$C^{(2)}$	$C^{(3)}$	1.377(3)
$C^{(5)}$	$C^{(4)}$	1.383(3)
$C^{(4)}$	$C^{(3)}$	1.382(3)

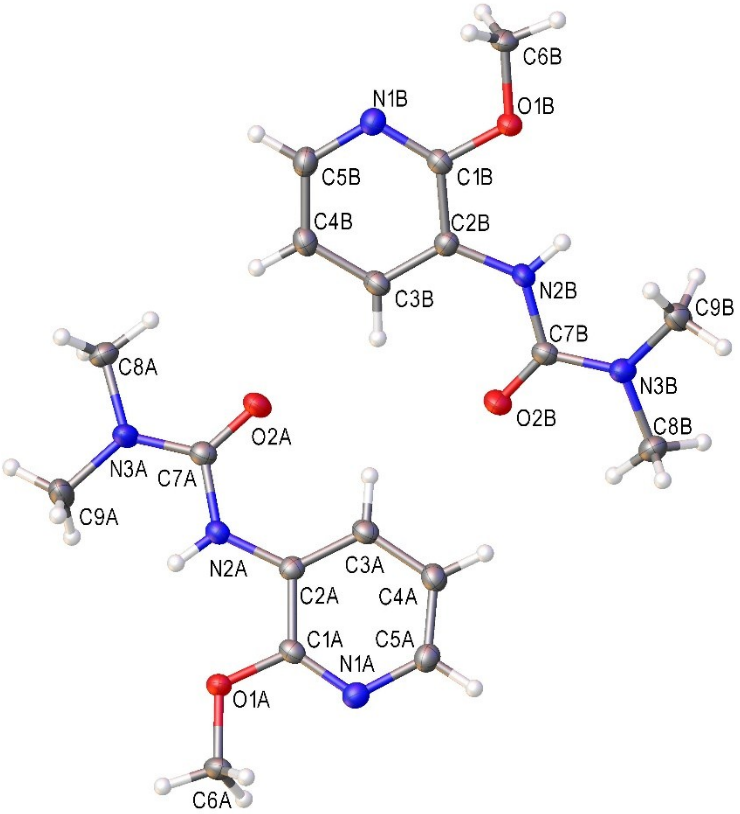
Table S11. Bond Angles

Atom	Atom	Atom	Angle/°
$C^{(5)}$	$N^{(1)}$	$C^{(1)}$	117.13(16)
$C^{(6)}$	$N^{(3)}$	$C^{(7)}$	118.54(16)
$C^{(6)}$	$N^{(3)}$	$C^{(8)}$	124.53(17)
$C^{(8)}$	$N^{(3)}$	$C^{(7)}$	116.18(16)
$C^{(1)}$	$N^{(2)}$	$C^{(6)}$	123.26(16)
$O^{(1)}$	$C^{(6)}$	$N^{(3)}$	122.48(18)
$O^{(1)}$	$C^{(6)}$	$N^{(2)}$	121.25(18)
$N^{(3)}$	$C^{(6)}$	$N^{(2)}$	116.26(16)
$N^{(1)}$	$C^{(1)}$	$N^{(2)}$	113.86(16)
$N^{(1)}$	$C^{(1)}$	$C^{(2)}$	122.48(18)
$N^{(2)}$	$C^{(1)}$	$C^{(2)}$	123.64(17)
$C^{(3)}$	$C^{(2)}$	$C^{(1)}$	117.91(18)
$N^{(1)}$	$C^{(5)}$	$Cl^{(1)}$	115.98(14)
$N^{(1)}$	$C^{(5)}$	$C^{(4)}$	125.73(18)
$C^{(4)}$	$C^{(5)}$	$Cl^{(1)}$	118.28(15)
$C^{(3)}$	$C^{(4)}$	$C^{(5)}$	116.01(19)
$C^{(2)}$	$C^{(3)}$	$C^{(4)}$	120.71(18)

Table S12. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3)

Atom	*x*	*y*	*z*	U(eq)
$H^{(2)}$	6809	2605	2578	20
$H^{(2A)}$	3135	3144	5191	21
$H^{(4)}$	2283	4963	3894	24
$H^{(7A)}$	12791	1364	5105	30
$H^{(7B)}$	10012	868	4710	30
$H^{(7C)}$	9542	1387	5757	30
$H^{(3)}$	1256	4183	5401	26
$H^{(8A)}$	7973	1748	2085	35
$H^{(8B)}$	9948	1138	2581	35
$H^{(8C)}$	11723	1801	2498	35

4.3. X-ray structure of 3-(2-Methoxypyridin-3-yl)-1,1-dimethylurea (**5t**)



CCDC: **1473655**

Table S13. Crystal data and structure refinement

Empirical formula	$C_9H_{13}N_3O_2$
Formula weight	195.22
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.3261(5)
b/Å	20.1659(12)
c/Å	13.1676(8)
α/°	90
β/°	102.555(7)
γ/°	90
Volume/Å^3	1898.8(2)
Z	8
ρ_{calc}g/cm^3	1.366
μ/mm^{-1}	0.099
F(000)	832.0
Crystal size/mm^3	0.18 × 0.15 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.698 to 60.004
Index ranges	$-9 \leq h \leq 10$, $-27 \leq k \leq 27$, $-17 \leq l \leq 18$

Reflections collected	29572
Independent reflections	4907 [R_{int} = 0.0493, R_{sigma} = 0.0394]
Data/restraints/parameters	4907/0/259
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0542, wR_2 = 0.1212
Final R indexes [all data]	R_1 = 0.0737, wR_2 = 0.1325
Largest diff. peak/hole / e $Å^{-3}$	0.32/-0.25

Table S14. Fractional Atomic Coordinates ($\times10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2\times10^3$) . U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor

Atom	***x***	***y***	***z***	**U(eq)**
$O^{(1A)}$	6263.7(17)	9730.3(5)	3567.0(9)	22.6(3)
$O^{(1B)}$	8690.9(17)	4745.5(5)	6439.4(9)	23.2(3)
$O^{(2A)}$	4330.7(18)	7438.6(6)	3777.7(9)	29.1(3)
$O^{(2B)}$	7881.1(19)	7114.5(6)	6768.4(9)	30.4(3)
$N^{(2A)}$	5053(2)	8502.1(7)	3395.8(10)	21.0(3)
$N^{(1A)}$	7404(2)	9678.7(7)	5347.8(11)	22.7(3)
$N^{(2B)}$	8567(2)	6006.9(7)	6871.3(10)	23.8(3)
$N^{(1B)}$	7348(2)	4866.7(7)	4688.7(11)	23.8(3)
$N^{(3A)}$	3338(2)	7823.0(7)	2125.3(11)	26.6(3)
$N^{(3B)}$	9595(2)	6696.2(7)	8283.7(11)	25.3(3)
$C^{(1B)}$	7927(2)	5135.5(8)	5610.9(12)	20.5(3)
$C^{(2A)}$	5945(2)	8716.6(8)	4390.6(12)	18.8(3)
$C^{(7A)}$	4244(2)	7884.7(8)	3134.1(13)	21.3(3)
$C^{(3B)}$	7051(2)	6229.5(8)	5013.6(13)	22.4(3)
$C^{(7B)}$	8640(2)	6642.3(8)	7278.0(13)	21.4(3)
$C^{(3A)}$	6314(2)	8347.2(8)	5298.4(13)	22.2(3)
$C^{(1A)}$	6562(2)	9387.8(8)	4479.6(12)	19.3(3)
$C^{(2B)}$	7840(2)	5821.0(8)	5835.5(12)	20.1(3)
$C^{(4A)}$	7222(2)	8649.6(8)	6229.1(13)	24.3(4)
$C^{(5A)}$	7725(2)	9305.2(9)	6227.2(13)	24.6(4)
$C^{(6B)}$	8775(3)	4044.6(8)	6233.2(13)	24.6(4)
$C^{(4B)}$	6422(2)	5951.6(8)	4027.9(13)	24.0(4)
$C^{(8B)}$	9576(3)	7330.6(9)	8813.5(13)	28.0(4)
$C^{(6A)}$	6966(3)	10400.7(8)	3632.5(13)	24.0(4)
$C^{(5B)}$	6586(2)	5278.6(9)	3896.9(13)	25.4(4)
$C^{(8A)}$	2485(3)	7191.7(8)	1762.0(14)	28.3(4)
$C^{(9B)}$	10700(3)	6167.2(9)	8867.4(14)	27.5(4)
$C^{(9A)}$	3132(3)	8356.2(9)	1362.5(14)	34.3(4)

Table S15. Anisotropic Displacement Parameters ($Å^2\times10^3$) . The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
$O^{(1A)}$	30.2(6)	16.2(5)	20.3(6)	0.7(4)	3.0(5)	-3.5(5)
$O^{(1B)}$	31.5(6)	16.0(5)	20.5(6)	0.9(4)	1.6(5)	2.1(5)
$O^{(2A)}$	38.0(7)	18.7(6)	27.2(6)	5.8(5)	-0.8(5)	-2.8(5)
$O^{(2B)}$	43.5(8)	18.0(6)	26.2(6)	3.0(5)	-0.1(6)	3.3(5)

$N^{(2A)}$	25.7(7)	17.1(6)	19.6(6)	2.4(5)	3.9(6)	-0.9(5)
$N^{(1A)}$	23.6(7)	21.0(7)	22.8(7)	-1.4(5)	3.4(6)	-0.4(6)
$N^{(2B)}$	35.3(8)	16.2(6)	18.3(6)	2.8(5)	2.5(6)	1.2(6)
$N^{(1B)}$	26.7(7)	22.9(7)	21.1(7)	-0.9(6)	3.5(6)	0.4(6)
$N^{(3A)}$	34.6(8)	18.0(7)	23.8(7)	2.6(6)	-1.4(6)	-5.8(6)
$N^{(3B)}$	30.8(8)	18.2(7)	23.9(7)	0.1(6)	-0.9(6)	0.4(6)
$C^{(1B)}$	21.2(8)	19.6(8)	21.2(8)	2.7(6)	5.6(6)	0.5(6)
$C^{(2A)}$	17.7(7)	17.8(7)	20.8(7)	-0.9(6)	3.8(6)	2.5(6)
$C^{(7A)}$	21.5(8)	18.4(8)	23.6(8)	1.3(6)	4.2(6)	0.8(6)
$C^{(3B)}$	26.2(8)	18.5(8)	23.1(8)	3.8(6)	6.8(7)	1.9(6)
$C^{(7B)}$	24.3(8)	16.9(7)	23.4(8)	2.0(6)	5.7(6)	-1.4(6)
$C^{(3A)}$	25.2(8)	17.7(7)	23.8(8)	2.5(6)	5.2(7)	2.8(6)
$C^{(1A)}$	19.4(7)	17.1(7)	22.4(8)	3.1(6)	6.9(6)	2.3(6)
$C^{(2B)}$	21.5(8)	19.8(8)	19.2(7)	0.0(6)	4.9(6)	-1.9(6)
$C^{(4A)}$	26.9(9)	23.6(8)	21.6(8)	2.8(6)	3.6(7)	3.8(7)
$C^{(5A)}$	24.7(8)	25.7(8)	21.6(8)	-1.6(7)	1.4(7)	1.7(7)
$C^{(6B)}$	30.9(9)	14.6(7)	26.7(8)	0.6(6)	2.5(7)	2.7(6)
$C^{(4B)}$	24.6(8)	25.5(8)	20.9(8)	4.6(7)	2.7(7)	1.7(7)
$C^{(8B)}$	34.8(10)	22.5(8)	25.1(8)	-2.8(7)	2.8(7)	-4.0(7)
$C^{(6A)}$	31.5(9)	16.5(7)	24.5(8)	0.9(6)	6.7(7)	-4.5(7)
$C^{(5B)}$	27.0(9)	28.1(9)	19.8(8)	-0.4(7)	2.5(7)	0.6(7)
$C^{(8A)}$	35.1(10)	20.6(8)	26.8(8)	-3.9(7)	1.2(8)	-4.0(7)
$C^{(9B)}$	28.5(9)	23.8(8)	27.0(9)	4.1(7)	-0.9(7)	-0.9(7)
$C^{(9A)}$	45.1(11)	28.4(9)	23.9(9)	7.3(7)	-4.8(8)	-9.2(8)

Table S16. Bond Lengths

Atom	**Atom**	**Length/Å**
$O^{(1A)}$	$C^{(1A)}$	1.3618(18)
$O^{(1A)}$	$C^{(6A)}$	1.4426(19)
$O^{(1B)}$	$C^{(1B)}$	1.3626(19)
$O^{(1B)}$	$C^{(6B)}$	1.4429(19)
$O^{(2A)}$	$C^{(7A)}$	1.2280(19)
$O^{(2B)}$	$C^{(7B)}$	1.226(2)
$N^{(2A)}$	$C^{(2A)}$	1.399(2)
$N^{(2A)}$	$C^{(7A)}$	1.390(2)
$N^{(1A)}$	$C^{(1A)}$	1.313(2)
$N^{(1A)}$	$C^{(5A)}$	1.358(2)
$N^{(2B)}$	$C^{(7B)}$	1.385(2)
$N^{(2B)}$	$C^{(2B)}$	1.403(2)
$N^{(1B)}$	$C^{(1B)}$	1.313(2)
$N^{(1B)}$	$C^{(5B)}$	1.355(2)
$N^{(3A)}$	$C^{(7A)}$	1.355(2)
$N^{(3A)}$	$C^{(8A)}$	1.452(2)
$N^{(3A)}$	$C^{(9A)}$	1.457(2)
$N^{(3B)}$	$C^{(7B)}$	1.361(2)
$N^{(3B)}$	$C^{(8B)}$	1.459(2)

$N^{(3B)}$	$C^{(9B)}$	1.454(2)
$C^{(1B)}$	$C^{(2B)}$	1.418(2)
$C^{(2A)}$	$C^{(3A)}$	1.384(2)
$C^{(2A)}$	$C^{(1A)}$	1.424(2)
$C^{(3B)}$	$C^{(2B)}$	1.383(2)
$C^{(3B)}$	$C^{(4B)}$	1.397(2)
$C^{(3A)}$	$C^{(4A)}$	1.401(2)
$C^{(4A)}$	$C^{(5A)}$	1.373(2)
$C^{(4B)}$	$C^{(5B)}$	1.377(2)

Table S17. Bond Angles

Atom	**Atom**	**Atom**	**Angle/°**
$C^{(1A)}$	$O^{(1A)}$	$C^{(6A)}$	115.84(12)
$C^{(1B)}$	$O^{(1B)}$	$C^{(6B)}$	116.21(13)
$C^{(7A)}$	$N^{(2A)}$	$C^{(2A)}$	126.60(14)
$C^{(1A)}$	$N^{(1A)}$	$C^{(5A)}$	117.12(14)
$C^{(7B)}$	$N^{(2B)}$	$C^{(2B)}$	126.69(14)
$C^{(1B)}$	$N^{(1B)}$	$C^{(5B)}$	117.05(15)
$C^{(7A)}$	$N^{(3A)}$	$C^{(8A)}$	119.16(14)
$C^{(7A)}$	$N^{(3A)}$	$C^{(9A)}$	124.28(14)
$C^{(8A)}$	$N^{(3A)}$	$C^{(9A)}$	116.56(14)
$C^{(7B)}$	$N^{(3B)}$	$C^{(8B)}$	118.63(14)
$C^{(7B)}$	$N^{(3B)}$	$C^{(9B)}$	124.42(14)
$C^{(9B)}$	$N^{(3B)}$	$C^{(8B)}$	116.92(14)
$O^{(1B)}$	$C^{(1B)}$	$C^{(2B)}$	115.15(14)
$N^{(1B)}$	$C^{(1B)}$	$O^{(1B)}$	119.73(14)
$N^{(1B)}$	$C^{(1B)}$	$C^{(2B)}$	125.11(15)
$N^{(2A)}$	$C^{(2A)}$	$C^{(1A)}$	116.49(14)
$C^{(3A)}$	$C^{(2A)}$	$N^{(2A)}$	127.30(15)
$C^{(3A)}$	$C^{(2A)}$	$C^{(1A)}$	116.20(14)
$O^{(2A)}$	$C^{(7A)}$	$N^{(2A)}$	121.99(15)
$O^{(2A)}$	$C^{(7A)}$	$N^{(3A)}$	123.36(15)
$N^{(3A)}$	$C^{(7A)}$	$N^{(2A)}$	114.64(14)
$C^{(2B)}$	$C^{(3B)}$	$C^{(4B)}$	119.05(15)
$O^{(2B)}$	$C^{(7B)}$	$N^{(2B)}$	122.14(15)
$O^{(2B)}$	$C^{(7B)}$	$N^{(3B)}$	123.12(15)
$N^{(3B)}$	$C^{(7B)}$	$N^{(2B)}$	114.74(14)
$C^{(2A)}$	$C^{(3A)}$	$C^{(4A)}$	119.19(15)
$O^{(1A)}$	$C^{(1A)}$	$C^{(2A)}$	114.99(14)
$N^{(1A)}$	$C^{(1A)}$	$O^{(1A)}$	119.76(14)
$N^{(1A)}$	$C^{(1A)}$	$C^{(2A)}$	125.23(15)
$N^{(2B)}$	$C^{(2B)}$	$C^{(1B)}$	116.00(14)
$C^{(3B)}$	$C^{(2B)}$	$N^{(2B)}$	127.40(15)
$C^{(3B)}$	$C^{(2B)}$	$C^{(1B)}$	116.60(15)
$C^{(5A)}$	$C^{(4A)}$	$C^{(3A)}$	119.63(15)
$N^{(1A)}$	$C^{(5A)}$	$C^{(4A)}$	122.60(15)

$C^{(5B)}$	$C^{(4B)}$	$C^{(3B)}$	119.46(15)
$N^{(1B)}$	$C^{(5B)}$	$C^{(4B)}$	122.73(16)

Table S18. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3)

Atom	***x***	***y***	***z***	**U(eq)**
$H^{(2A)}$	5000	8787	2884	25
$H^{(2B)}$	9025	5687	7307	29
$H^{(3B)}$	6939	6693	5118	27
$H^{(3A)}$	5956	7894	5290	27
$H^{(4A)}$	7489	8402	6858	29
$H^{(5A)}$	8321	9506	6866	29
$H^{(6BA)}$	9505	3972	5702	37
$H^{(6BB)}$	7505	3873	5984	37
$H^{(6BC)}$	9371	3813	6874	37
$H^{(4B)}$	5884	6225	3453	29
$H^{(8BA)}$	10809	7539	8908	42
$H^{(8BB)}$	9273	7258	9494	42
$H^{(8BC)}$	8632	7621	8394	42
$H^{(6AA)}$	6738	10595	2934	36
$H^{(6AB)}$	8313	10398	3933	36
$H^{(6AC)}$	6326	10664	4074	36
$H^{(5B)}$	6148	5095	3223	30
$H^{(8AA)}$	2850	6857	2308	42
$H^{(8AB)}$	2909	7054	1138	42
$H^{(8AC)}$	1121	7239	1595	42
$H^{(9BA)}$	9870	5853	9112	41
$H^{(9BB)}$	11580	6356	9466	41
$H^{(9BC)}$	11397	5936	8418	41
$H^{(9AA)}$	2517	8736	1611	51
$H^{(9AB)}$	2372	8201	699	51
$H^{(9AC)}$	4368	8490	1265	51