

Copper (II) bromide/NMO system for α -amination of esters under continuous-flow conditions with reduced catalyst loading

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General Experimental Information. Unless otherwise mentioned, all the solvents, reactants and reagents were purchased from commercial suppliers and used without further purification. DMSO, ethyl acetate, n-hexane and toluene were procured from Sigma/Merck, India. TLC plates were visualized by exposure to ultra violet light (UV) or staining with iodine vapor. ^1H NMR and ^{13}C NMR spectra were obtained by using a JEOL 400 MHz NMR spectrometer. Chemical shifts for protons are reported in parts per million (δ scale) and are referenced to residual protium in the NMR solvents [CDCl_3 : δ 7.26]. Chemical shifts for carbon resonances are reported in parts per million (δ scale) and are referenced to the carbon resonances of the solvent (CDCl_3 : δ 77.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, and coupling constant in Hertz (Hz).

Standard Procedure for α -amination of esters (10) under continuous-flow conditions. Ester compounds **1** (1.0 mmol, 1.0 eq.), amine compounds **9** (1.5 mmol, 1.5 eq.), CuBr_2 (0.05 mmol, 0.05 eq.), DMSO (3.0mL) and NMO (1.0 mmol, 1.0 eq.) were stirred at rt to make homogeneous solution. Then it was pumped from a single pump, and reaction was carried out in a 10mL reactor at 100 °C with residence time of 25min. The reaction mass was allowed to cool to rt, water (3.0mL) was added, filtered. The aqueous layer was extracted with ethyl acetate (3.0mL \times 3), and evaporated under vacuum. The crude mass was purified by silica gel column chromatography, the desired compounds **10** were eluted with 2-5% ethyl acetate in n-hexane.



Figure 1. Flow reactor: VAPOURTEC R series, Instrument serial no. P1720, Software: VI.222, pump: VAPOURTEC R2C.

Reactor volume: 10 mL FEP coil (1.3 mm ID and 1.6 mm OD), Flow rate: 400 μ L/min. residence time: 25min.

Ethyl-2-phenyl-2-(piperidin-1-yl)acetate (10a).¹ The compound **10a** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 83%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.41 (2H, m), 7.32-7.26 (3H, m), 4.18-4.06 (2H, m), 3.93 (1H, s), 2.37 (4H, J = 5.16 Hz, t), 1.60-1.54 (4H, m), 1.42-1.39 (2H, m), 1.17 (3H, J = 7.14 Hz, t). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.9, 136.5, 129.3, 128.6, 128.5, 75.1, 60.9, 52.5, 25.8, 24.4, 14.2.

Ethyl-2-(4-methylpiperidin-1-yl)-2-phenylacetate (10b). The compound **10b** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 73%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.40 (2H, m), 7.32-7.26 (3H, m), 4.20-4.06 (2H, m), 3.93 (1H, s), 2.92 (1H, J = 10.74, 2.10 Hz, dd), 2.70-2.65 (1H, m), 2.09 (1H, J = 11.19, 2.55 Hz, td), 1.85-1.79 (1H, m), 1.60-1.49 (2H, m), 1.36-1.31 (1H, m), 1.26-1.22 (2H, m), 1.19-1.15 (3H, m), 0.88 (3H, J = 5.73 Hz, d). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 172.0, 136.5, 128.9, 128.5, 128.2, 74.9, 60.8, 52.3, 51.6, 34.1, 30.8, 21.9, 14.2, 14.1. HRMS (QTOF) *m/z*: calcd for C₁₆H₂₄NO₂ [M + H]⁺: 262.1807, found: 262.1821. IR: 3051, 2958, 1735, 1262, 1145 cm⁻¹.

Ethyl-1-(2-ethoxy-2-oxo-1-phenylethyl)piperidine-4-carboxylate (10c). The compound **10c** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 63%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.36 (2H, m), 7.30-7.22 (3H, m), 4.15-4.04 (4H, m), 3.97 (1H, s), 2.86-2.70 (2H, m), 2.26-2.14 (2H, m), 2.00-1.94 (1H, m), 1.84-1.71 (4H, m), 1.21-1.13 (6H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 175.1, 171.6, 136.2, 128.8, 128.5, 128.3, 74.2, 60.8, 60.3, 50.7, 41.2, 28.2, 28.2, 14.3, 14.2. HRMS (QTOF) *m/z*: calcd for C₁₆H₂₄NO₂ [M + H]⁺: 262.1807, found: 262.1821. IR: 3050, 2951, 1733, 1260, 1141 cm⁻¹.

Ethyl-2-morpholino-2-phenylacetate (10d).¹ The compound **10d** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 83%. Purified by column chromatography on silica gel (*n*-hexane/EA = 95/5). ¹H NMR (400 MHz, CDCl₃) δ 7.39 (2H, J = 7.26 Hz, d), 7.29-7.23 (3H, m), 4.14-4.02 (2H, m), 3.90 (1H, s), 3.66-3.64 (4H, m), 2.40 (4H, J = 4.28 Hz, d), 1.14-1.11 (3H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.2, 135.5, 128.9, 128.7, 128.5, 74.5, 66.8, 61.0, 51.6, 14.1.

*Ethyl-2-(6,7-dihydrothienof[3,2-*c*]pyridin-5(4H)-yl)-2-phenylacetate (10e)*. The compound **10e** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 81%. Purified by column chromatography on silica gel (*n*-hexane/EA = 97/3). ¹H NMR (400 MHz, CDCl₃) δ 7.50-7.47 (2H, m), 7.37-7.32 (3H, m), 7.04 (1H, J = 5.12 Hz, d), 6.64 (1H, J = 5.12 Hz, d), 4.27 (1H, s), 4.24-4.13 (2H, m), 3.61 (2H, J = 1.87 Hz, t), 2.87-2.80 (4H, m), 1.21 (3H, J = 7.11

Hz, t). ^{13}C { ^1H } NMR (100 MHz, CDCl_3) δ 171.7, 136.2, 133.4, 128.9, 128.7, 128.5, 125.4, 122.8, 73.0, 61.1, 51.0, 48.4, 25.4, 14.2. HRMS (QTOF) m/z : calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_2\text{S}$ [$\text{M} + \text{H}$] $^+$: 302.1215, found: 302.1221. IR: 3056, 2955, 1733, 1540, 1260, 1141, 978, 689 cm^{-1} .

Ethyl-2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-phenylacetate (10f).¹ The compound **10f** was prepared by following general procedure. Physical appearance: orange color oil, Yield: 61%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.54-7.51 (2H, m), 7.39-7.28 (3H, m), 7.13-7.07 (3H, m), 6.95-6.93 (1H, m), 4.25 (1H, $J = 1.99$ Hz, d), 4.23-4.13 (2H, m), 3.72 (2H, $J = 4.28$ Hz, d), 2.91-2.75 (4H, m), 1.26-1.22 (3H, m). ^{13}C { ^1H } NMR (100 MHz, CDCl_3) δ 171.7, 136.2, 134.4, 129.3, 128.9, 128.8, 128.7, 128.5, 126.8, 126.3, 125.7, 73.6, 61.0, 53.9, 48.4, 29.0, 14.3.

Ethyl-2-phenyl-2-(pyrrolidin-1-yl)acetate (10g).² The compound **10g** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 60%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.44 (2H, m), 7.33-7.27 (3H, m), 4.13 (2H, $J = 27.93, 10.81, 7.11$ Hz, ddd), 3.88 (1H, s), 2.57-2.54 (2H, m), 2.43-2.41 (2H, m), 1.80-1.77 (4H, m), 1.17 (3H, $J = 7.11$ Hz, t). ^{13}C { ^1H } NMR (100 MHz, CDCl_3) δ 171.8, 137.5, 128.6, 128.5, 128.3, 74.1, 61.0, 52.6, 23.4, 14.2.

Methyl-2-(4-methoxyphenyl)-2-(piperidin-1-yl)acetate (10h). The compound **10h** was prepared by following general procedure. Physical appearance: orange color oil, Yield: 59%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.33 (2H, $J = 6.65, 2.06$ Hz, dd), 6.84 (2H, $J = 6.65, 2.14$ Hz, dd), 3.89 (1H, s), 3.77 (3H, s), 3.65 (3H, s), 2.35 (4H, $J = 5.35$ Hz, t), 1.58-1.54 (4H, m), 1.41 (2H, $J = 5.35$ Hz, d). ^{13}C { ^1H } NMR (100 MHz, CDCl_3) δ 172.7, 159.6, 130.1, 128.2, 113.9, 74.5, 55.3, 52.5, 52.0, 29.8, 29.5, 25.8, 24.4. HRMS (QTOF) m/z : calcd for $\text{C}_{15}\text{H}_{22}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$: 264.1600, found: 264.1608. IR: 3050, 2948, 1746, 1250, 1164, 1021 cm^{-1} .

*Methyl-2-(6,7-dihydrothieno[3,2-*c*] pyridin-5(4H)-yl)-2-(4-methoxyphenyl) acetate (10i)*. The compound **10i** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 60%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.39 (2H, $J = 6.65, 1.99$ Hz, dd), 7.04 (1H, $J = 5.12$ Hz, d), 6.88 (2H, $J = 6.72, 2.14$ Hz, dd), 6.64 (1H, $J = 5.20$ Hz, d), 4.22 (1H, s), 3.80 (3H, s), 3.70 (3H, s), 3.59 (2H, $J = 6.34$ Hz, d), 2.86-2.76 (4H, m). ^{13}C { ^1H } NMR (100 MHz, CDCl_3) δ 172.4, 159.8, 133.4, 133.3, 130.1, 128.0, 125.4, 122.8, 114.2, 72.3, 55.4, 52.2, 51.0, 48.4, 25.3. HRMS (QTOF) m/z : calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_3\text{S}$ [$\text{M} + \text{H}$] $^+$: 318.1164, found: 318.1174. IR: 3048, 2945, 1746, 1227, 1161, 1052 cm^{-1} .

Methyl-2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-(4-methoxyphenyl)acetate (10j). The compound **10j** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 60%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.42 (2H, $J = 6.72, 2.14$ Hz, dd), 7.11-7.05 (3H, m), 6.94-6.88 (3H, m), 4.16 (1H, s),

3.80 (3H, s), 3.71 (3H, s), 3.66 (2H, J = 5.50 Hz, d), 2.89-2.68 (4H, m). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 172.4, 159.8, 134.3, 130.5, 128.7, 127.8, 126.8, 126.6, 126.3, 125.7, 114.1, 72.9, 55.3, 53.9, 52.2, 48.4, 28.9. HRMS (QTOF) m/z : calcd for $\text{C}_{20}\text{H}_{24}\text{NO}_3$ [M + H] $^+$: 326.1756, found: 326.1776. IR: 3050, 2952, 1743, 1213, 1094, 1032 cm^{-1} .

Methyl 2-(4-methoxyphenyl)-2-morpholinoacetate (10k). The compound **10k** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 62%. Purified by column chromatography on silica gel (*n*-hexane/EA = 95/5). ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.31 (2H, m), 6.87-6.83 (2H, m), 3.88 (1H, s), 3.77 (3H, J = 2.22 Hz, d), 3.72-3.68 (4H, m), 3.65 (3H, s), 2.42-2.39 (4H, m). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 172.0, 159.9, 130.1, 127.3, 114.1, 73.9, 66.8, 55.4, 52.1, 51.7. HRMS (QTOF) m/z : calcd for $\text{C}_{14}\text{H}_{20}\text{NO}_4$ [M + H] $^+$: 266.1392, found: 266.1400. IR: 3051, 2945, 1744, 1227, 1116, 1031 cm^{-1} .

Ethyl-2-(piperidin-1-yl)-2-(4-(trifluoromethyl)phenyl)acetate (10l). The compound **10l** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 52%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.59-7.55 (4H, m), 4.22-4.07 (2H, m), 4.01 (1H, s), 2.37 (4H, J = 5.04 Hz, t), 1.61-1.57 (4H, m), 1.44 (2H, J = 11.42, 5.92 Hz, dd), 1.20 (3H, J = 7.11 Hz, t). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 171.2, 140.7, 130.5, 129.2, 125.5, 125.4, 122.8, 74.6, 61.1, 52.4, 25.9, 24.3, 14.2. HRMS (QTOF) m/z : calcd for $\text{C}_{16}\text{H}_{21}\text{F}_3\text{NO}_2$ [M + H] $^+$: 316.1524, found: 316.1546. IR: 3050, 2952, 1746, 1230, 1051, 1172 cm^{-1} .

Ethyl-2-(4-bromophenyl)-2-(piperidin-1-yl) acetate (10m). The compound **10m** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 68%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.44-7.41 (2H, m), 7.32-7.27 (2H, m), 4.19-4.04 (2H, m), 3.88 (1H, s), 2.34 (4H, J = 4.97 Hz, t), 1.58-1.52 (4H, m), 1.43-1.37 (2H, m), 1.17 (3H, J = 7.13, 1.40 Hz, td). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 172.5, 135.7, 131.9, 130.5, 121.8, 74.4, 61.0, 52.4, 25.8, 24.4, 14.1. HRMS (QTOF) m/z : calcd for $\text{C}_{15}\text{H}_{21}\text{BrNO}_2$ [M + H] $^+$: 326.0756, found: 326.0743. IR: 3062, 1940, 1735, 1475, 1262, 1145, 1072, 1021, 902, 685, 673 cm^{-1} .

Methyl-2-(2-chlorophenyl)-2-(piperidin-1-yl)-acetate (10n). The compound **10n** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 69%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.65 (1H, J = 7.64, 1.91 Hz, dd), 7.35-7.32 (1H, m), 7.26-7.19 (2H, m), 4.59 (1H, s), 3.66 (3H, s), 2.50-2.38 (4H, m), 1.60-1.54 (4H, m), 1.43-1.40 (2H, m). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 171.6, 134.7, 134.2, 130.1, 129.6, 129.1, 127.0, 69.7, 52.3, 52.0, 26.0, 24.4. HRMS (QTOF) m/z : calcd for $\text{C}_{14}\text{H}_{19}\text{ClNO}_2$ [M + H] $^+$: 268.1104, found: 268.1114. IR: 3046, 2951, 1742, 1262, 1116 cm^{-1} .

Methyl 2-(2-chlorophenyl)-2-(4-methylpiperidin-1-yl) acetate (10o). The compound **10o** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 77%. Purified by column chromatography on silica gel (*n*-hexane/EA = 97/3). ^1H NMR (400 MHz, CDCl_3) δ

7.64 (1H, J = 7.68, 1.87 Hz, dd), 7.33 (1H, J = 7.79, 1.45 Hz, dd), 7.26-7.16 (2H, m), 4.59 (1H, s), 3.65 (3H, s), 2.94 (1H, J = 10.85, 2.22 Hz, dd), 2.66 (1H, J = 11.12, 2.10 Hz, dd), 2.16-2.01 (2H, m), 1.61-1.49 (2H, m), 1.36-1.29 (2H, m), 1.26-1.20 (1H, m), 0.88 (3H, J = 6.04 Hz, d). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.6, 134.7, 134.3, 130.0, 129.6, 129.2, 127.1, 69.4, 52.1, 52.0, 51.4, 34.3, 34.2, 30.7, 21.9. HRMS (QTOF) *m/z*: calcd for C₁₅H₂₁ClNO₂ [M + H]⁺: 282.1261, found: 282.1266. IR: 3050, 2955, 1742, 1262, 1164, 751 cm⁻¹.

Methyl-2-(2-chlorophenyl)-2-morpholinoacetate (10p).² The compound **10p** was prepared by following general procedure. Physical appearance: colorless oil, Yield: 70%. Purified by column chromatography on silica gel (*n*-hexane/EA = 95/5). ¹H NMR (400 MHz, CDCl₃) δ 7.60 (1H, J = 7.49, 2.06 Hz, dd), 7.35-7.33 (1H, m), 7.25-7.17 (2H, m), 4.62 (1H, s), 3.67 (4H, J = 4.70 Hz, t), 3.64 (3H, s), 2.56-2.40 (4H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.1, 134.9, 133.2, 130.1, 129.8, 129.5, 127.2, 68.9, 66.9, 52.2, 51.3.

Methyl-2-(2-chlorophenyl)-2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (10q).³ The compound **10q** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 53%. Purified by column chromatography on silica gel (*n*-hexane/EA = 97/3). ¹H NMR (400 MHz, CDCl₃) δ 7.73-7.71 (1H, m), 7.41-7.39 (1H, m), 7.29-7.25 (2H, m), 7.10-7.07 (3H, m), 6.96-6.94 (1H, m), 4.86 (1H, s), 3.72 (3H, s), 3.71-3.67 (2H, m), 2.89-2.81 (4H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.4, 134.8, 134.3, 134.2, 133.9, 130.1, 129.8, 129.5, 128.8, 127.3, 126.7, 126.3, 125.7, 68.5, 53.7, 52.3, 48.4, 29.2.

Methyl-2-(2-chlorophenyl)-2-(pyrrolidin-1-yl)acetate (10r).² The compound **10r** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 57%. Purified by column chromatography on silica gel (*n*-hexane/EA = 95/5). ¹H NMR (400 MHz, CDCl₃) δ 7.69 (1H, J = 7.68, 1.87 Hz, dd), 7.37 (1H, J = 7.79, 1.45 Hz, dd), 7.29-7.20 (2H, m), 4.67 (1H, s), 3.69 (3H, s), 2.67-2.62 (2H, m), 2.51-2.46 (2H, m), 1.84-1.77 (4H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.7, 135.3, 134.0, 130.1, 129.7, 127.3, 125.1, 67.9, 52.3, 52.2, 23.5.

Methyl-2-(2-fluorophenyl)-2-(piperidin-1-yl)acetate (10s). The compound **10s** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 80%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.52 (1H, J = 7.51, 1.76 Hz, td), 7.31-7.25 (1H, m), 7.14 (1H, J = 7.55, 1.17 Hz, td), 7.07-7.02 (1H, m), 4.47 (1H, s), 3.69 (3H, s), 2.47-2.42 (4H, m), 1.63-1.57 (4H, m), 1.44-1.38 (2H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.7, 162.4, 159.9, 130.3, 129.7, 129.6, 124.2, 124.2, 123.0, 122.9, 115.6, 115.4, 66.1, 52.1, 52.0, 29.8, 26.0, 24.3. HRMS (QTOF) *m/z*: calcd for C₁₄H₁₉FNO₂ [M + H]⁺: 252.1400, found: 252.1429. IR: 3052, 2951, 1748, 1221, 1162, 1090 cm⁻¹.

Methyl-2-(2-fluorophenyl)-2-morpholinoacetate (10t). The compound **10t** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 74%. Purified by column chromatography on silica gel (*n*-hexane/EA = 95/5). ¹H NMR (400 MHz, CDCl₃) δ 7.48 (1H, J = 7.45, 1.73 Hz, td), 7.30-7.25 (1H, m), 7.12 (1H, J = 7.55, 1.02 Hz, td), 7.07-7.02 (1H, m), 4.46

(1H, s), 3.69 (4H, J = 4.66 Hz, t), 3.67 (3H, J = 0.92 Hz, d), 2.49 (4H, J = 4.58 Hz, t). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.1, 162.4, 159.9, 130.2, 124.4, 122.0, 115.8, 115.6, 66.9, 65.4, 52.2, 51.1. HRMS (QTOF) *m/z*: calcd for C₁₃H₁₇FNO₃ [M + H]⁺: 254.1192, found: 254.1198. IR: 3050, 2952, 1748, 1227, 1140, 1092 cm⁻¹.

Methyl-2-(piperidin-1-yl)-2-(p-tolyl)acetate (10u).⁴ The compound **10u** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 71%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.29 (2H, m), 7.13 (2H, J = 7.6, d), 4.19 (1H, s), 3.64 (3H, s), 2.40-2.31 (4H, m), 2.20 (3H, s), 1.66-1.54 (4H, m), 1.43-1.39 (2H, m). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 172.6, 138.0, 133.2, 129.3, 128.8, 74.8, 52.5, 52.0, 25.8, 24.4, 21.2. HRMS (QTOF) *m/z*: calcd for C₁₅H₂₂NO₂ [M + H]⁺: 248.1651, found: 248.1662.

Methyl-2-morpholino-2-(p-tolyl)acetate (10v).⁵ The compound **10v** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 87%. Purified by column chromatography on silica gel (*n*-hexane/EA = 95/5). ¹H NMR (400 MHz, CDCl₃) δ 7.28 (2H, J = 8.0, 2H), 7.108 (2H, J = 7.6, d), 3.89 (1H, s), 3.67-3.64 (4H, m), 3.61 (3H, s), 2.39-2.37 (4H, m), 2.27 (3H, s). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 171.9, 138.4, 132.3, 129.4, 128.8, 74.2, 66.8, 52.0, 51.7, 21.2.

*Methyl-2-(6,7-dihydrothieno[3,2-*c*] pyridin-5(4H)-yl)-2-(p-tolyl)acetate (10w)*. The compound **10w** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 72%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.36 (2H, J = 6.42, 1.76 Hz, dd), 7.16 (2H, J = 7.87 Hz, d), 7.04 (1H, J = 5.12 Hz, d), 6.64 (1H, J = 5.12 Hz, d), 4.25 (1H, s), 3.70 (3H, s), 3.61-3.59 (2H, m), 2.89-2.75 (4H, m), 2.34 (3H, s). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 172.3, 138.4, 133.4, 133.3, 133.0, 129.5, 128.8, 125.4, 122.8, 72.7, 52.2, 51.1, 48.4, 25.3, 21.3. HRMS (QTOF) *m/z*: calcd for C₁₇H₂₀NO₂S [M + H]⁺: 302.1215, found: 302.1221. IR: 3055, 2948, 1745, 1223, 1151, 1053 cm⁻¹.

Methyl-2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-(p-tolyl)acetate (10x). The compound **10x** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 58%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ¹H NMR (400 MHz, CDCl₃) δ 7.39 (2H, J = 7.95 Hz, d), 7.18 (2H, J = 8.25 Hz, d), 7.12-7.06 (3H, m), 6.95-6.93 (1H, m), 4.20 (1H, s), 3.72 (3H, s), 3.69 (2H, J = 6.65 Hz, d), 2.90-2.70 (4H, m), 2.36 (3H, s). ¹³C {1H} NMR (100 MHz, CDCl₃) δ 172.3, 138.4, 134.4, 134.3, 133.0, 129.5, 128.8, 128.8, 126.8, 126.3, 125.7, 73.3, 54.0, 52.2, 48.4, 28.9, 21.3. HRMS (QTOF) *m/z*: calcd for C₁₉H₂₂NO₂ [M + H]⁺: 296.1651, found: 296.1666. IR: 3055, 2954, 1744, 1268, 1095 cm⁻¹.

Ethyl 2-(1H-indol-3-yl)-2-(piperidin-1-yl) acetate (10y). The compound **10y** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 80%. Purified by column chromatography on silica gel (*n*-hexane/EA = 85/15). ¹H NMR (400 MHz, CDCl₃) δ 9.15 (1H, s), 7.84 (1H, J = 7.87 Hz, d), 7.32-7.30 (1H, m), 7.24-7.13 (3H, m), 4.43 (1H, s), 4.18 (2H, J = 43.88,

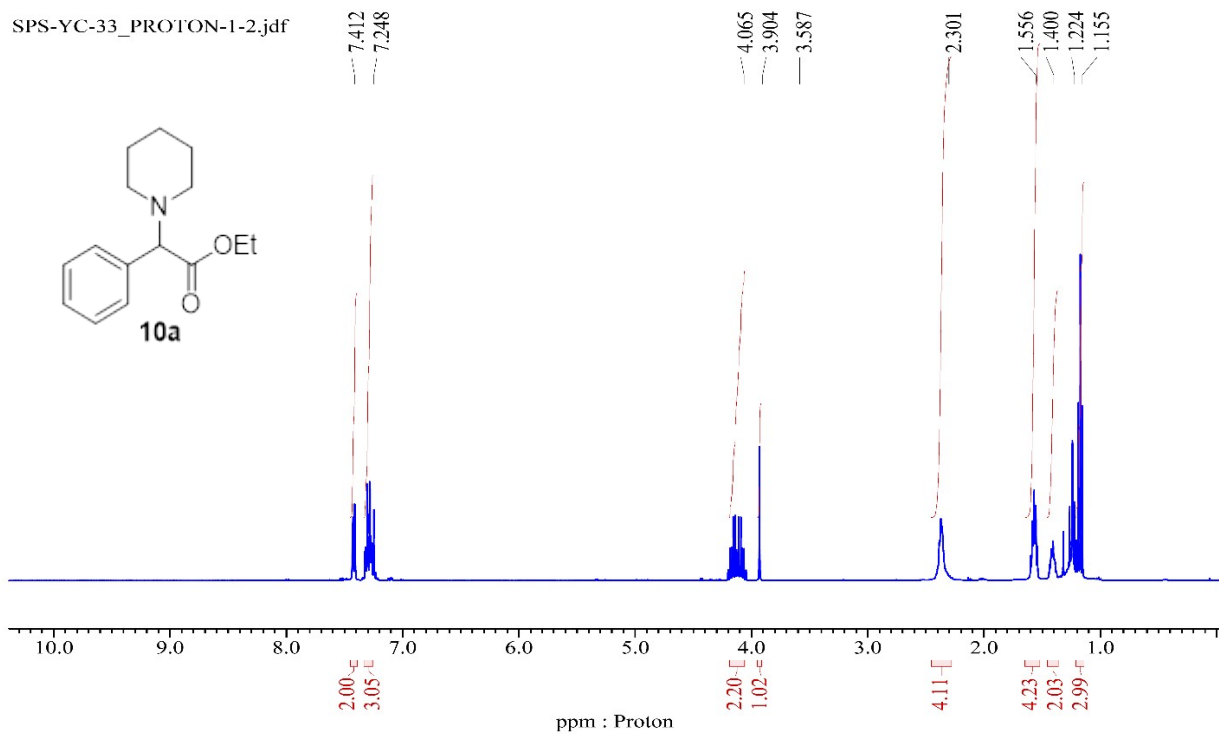
10.83, 7.13 Hz, ddd), 2.62-2.54 (4H, m), 1.61-1.56 (4H, m), 1.45-1.39 (2H, m), 1.20 (3H, J = 7.11 Hz, t). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 172.8, 136.3, 127.6, 124.8, 122.1, 119.7, 119.6, 111.7, 110.2, 66.7, 60.9, 52.5, 25.9, 24.5, 14.3. HRMS (QTOF) m/z : calcd for $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M} + \text{H}]^+$: 287.1760, found: 287.1775. IR: 3051, 2950, 2934, 1734, 1180 cm^{-1} .

Ethyl-2-(thiophen-3-yl)acetate (10z). The compound **10z** was prepared by following general procedure. Physical appearance: yellow oil, Yield: 59%. Purified by column chromatography on silica gel (*n*-hexane/EA = 98/2). ^1H NMR (400 MHz, CDCl_3) δ 7.25 (2H, J = 6.58, 3.14 Hz, dd), 7.16-7.13 (1H, m), 4.22-4.12 (3H, m), 4.11 (1H, s), 2.43-2.37 (4H, m), 1.59-1.54 (4H, m), 1.43-1.38 (2H, m), 1.24-1.20 (3H, m). ^{13}C {1H} NMR (100 MHz, CDCl_3) δ 171.5, 136.9, 128.0, 125.6, 124.1, 70.0, 60.8, 52.1, 25.9, 24.4, 14.3. HRMS (QTOF) m/z : calcd for $\text{C}_{12}\text{H}_{18}\text{NO}_2\text{S}$ $[\text{M} + \text{H}]^+$: 240.1058, found: 240.1061. IR: 3054, 2950, 1732, 1258, 1152 cm^{-1} .

References

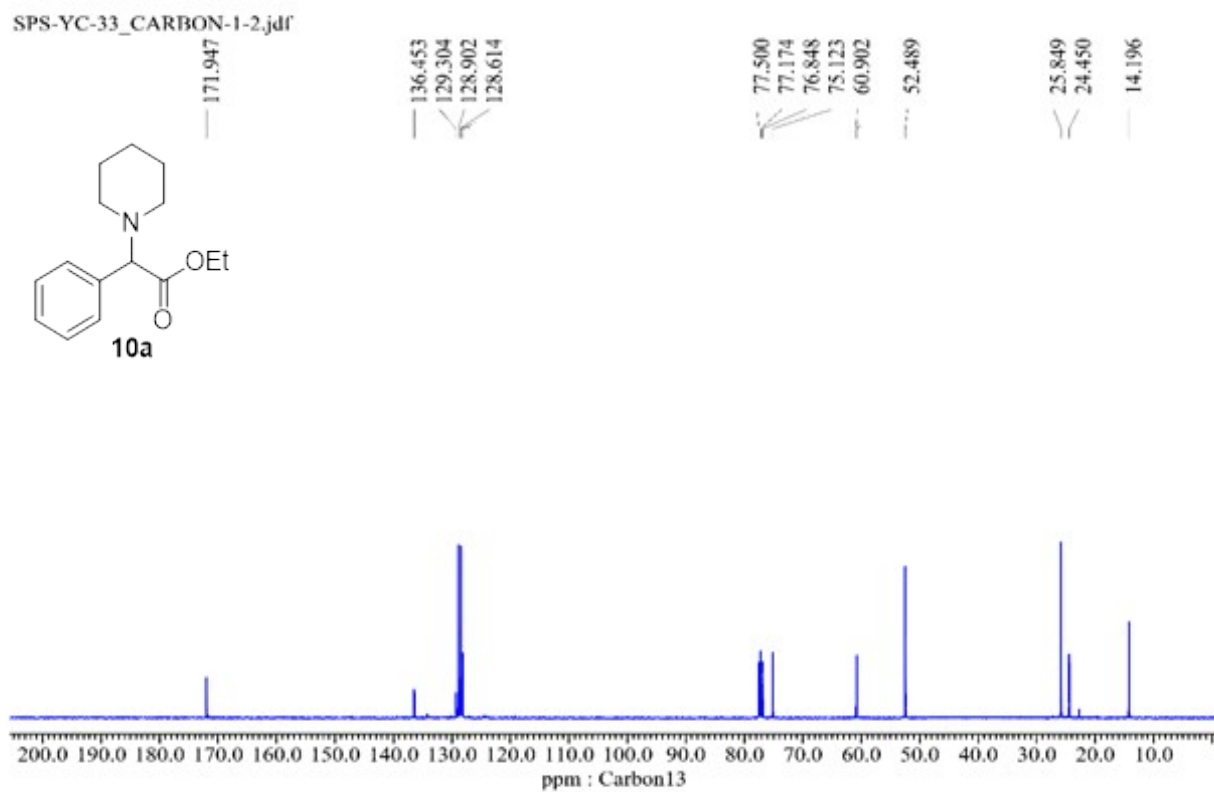
- (1) W.-G. Jia, D.-D. Li, Y.-C. Dai, H. Zhang, L.-Q. Yan, E.-H. Sheng, Y. Wei, X.-L. Mu, K.-W. Huang, Synthesis and Characterization of Bisoxazolines- and Pybox-Copper Complexes and Their Application in the Coupling of α -Carbonyls with Functionalized Amines, *Org. Biomol. Chem.* 12 (2014) 5509–5516, <https://doi.org/10.1039/C4OB01027B>.
- (2) Y. K. Nagare, I. A. Shah, J. Yadav, A. P. Pawar, R. Choudhary, P. Chauhan, I. Kumar, Electrochemical Oxidative Coupling Between Benzylic C(Sp^3)–H and N–H of Secondary Amines: Rapid Synthesis of α -Amino α -Aryl Esters, *J. Org. Chem.* 86 (2021) 9682–9691, <https://doi.org/10.1021/acs.joc.1c00944>.
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SPS-YC-33_PROTON-1-2.jdf

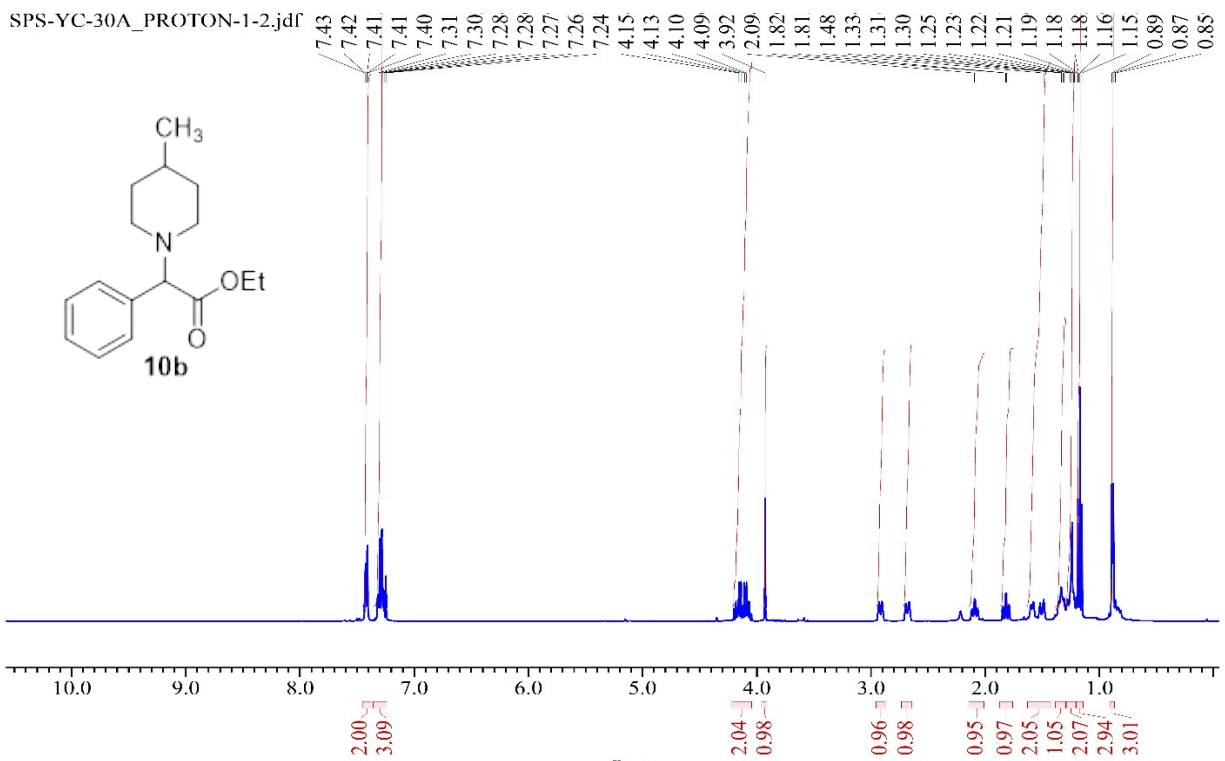


¹H NMR spectrum of **10a**

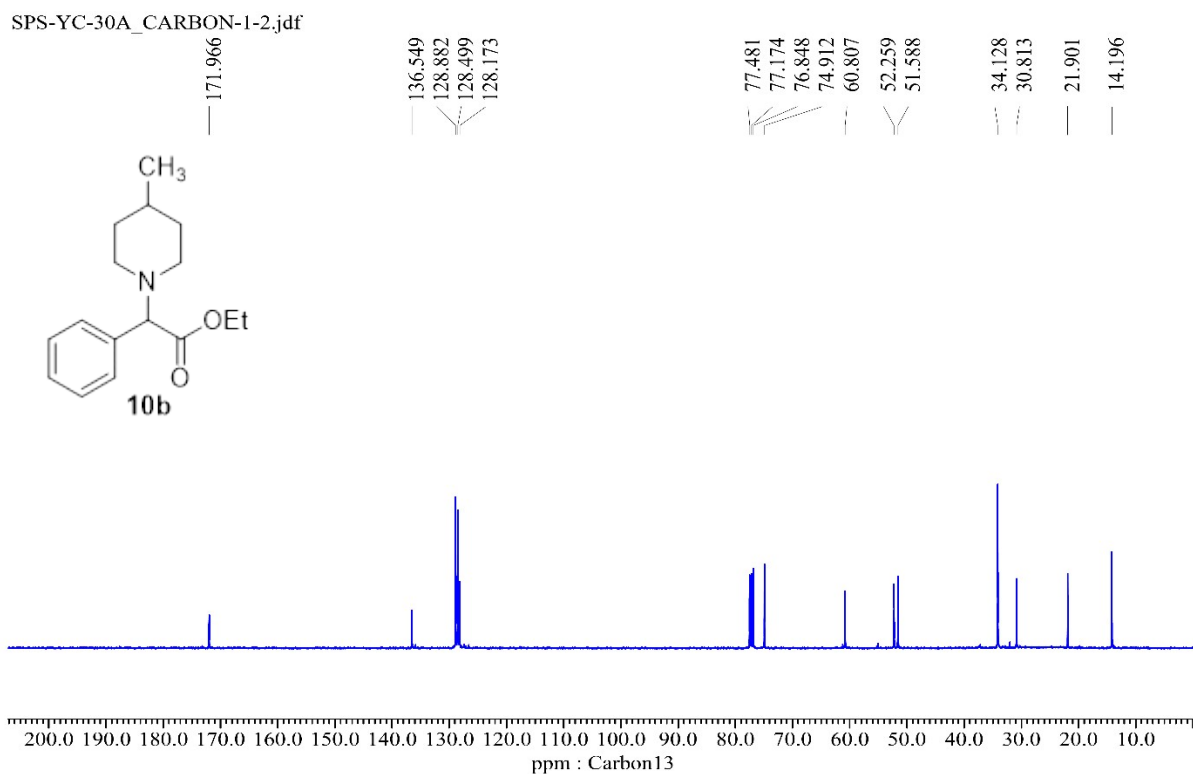
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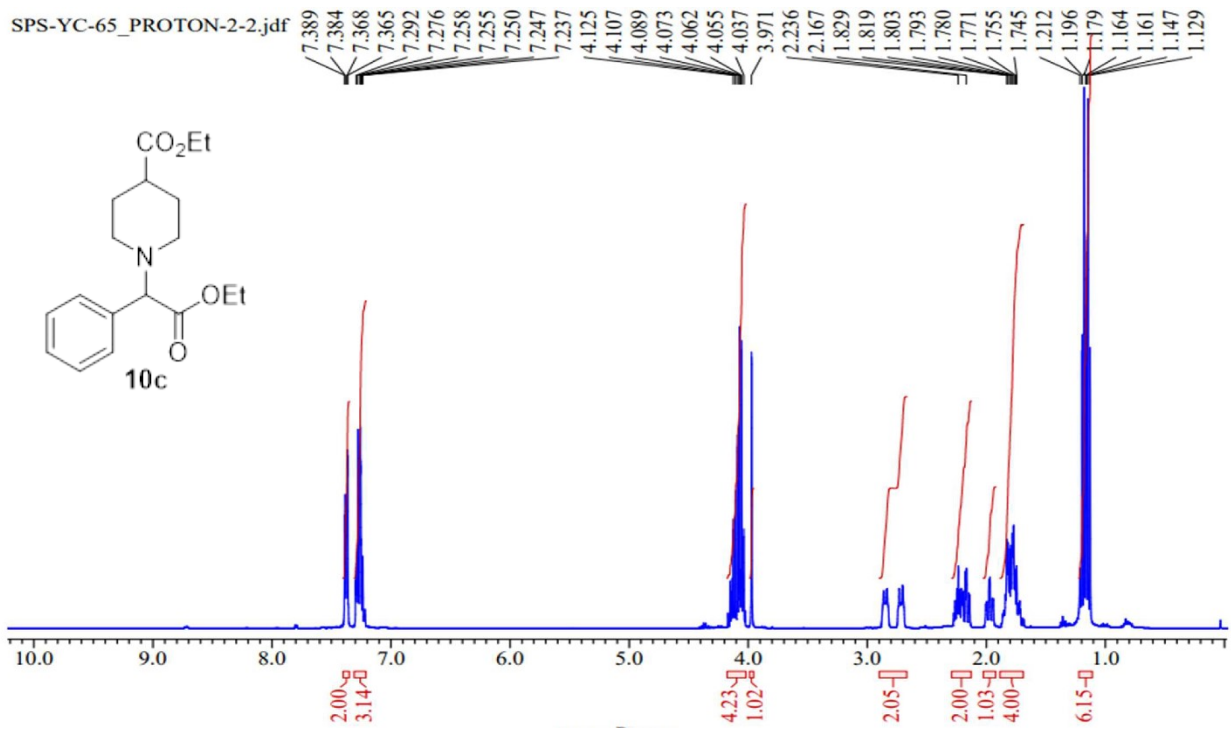
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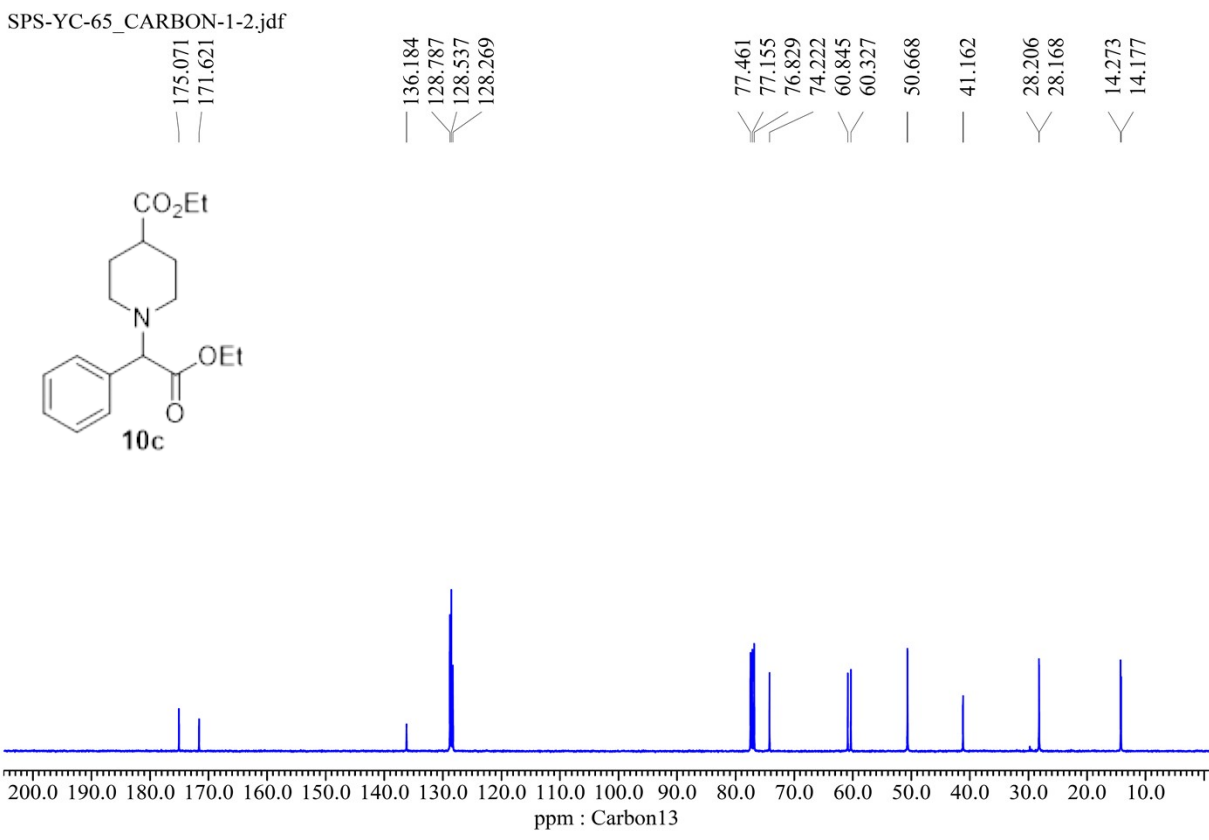
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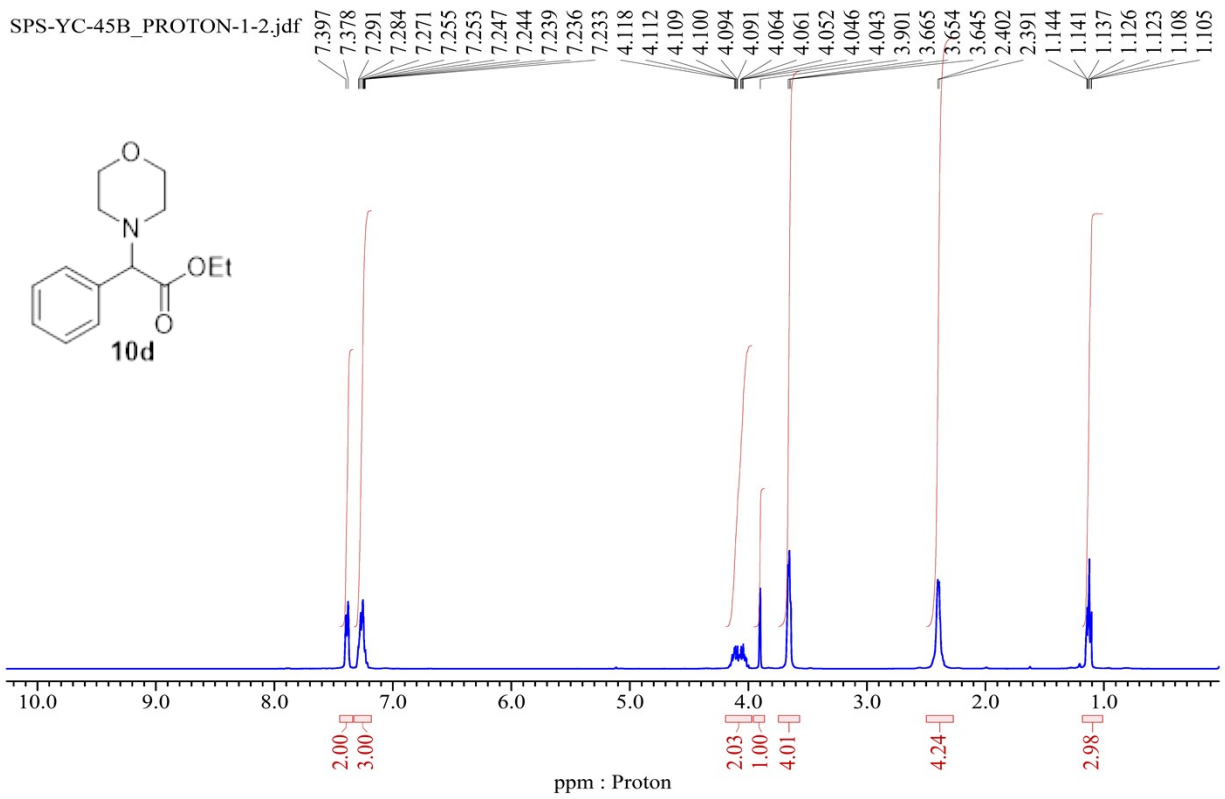
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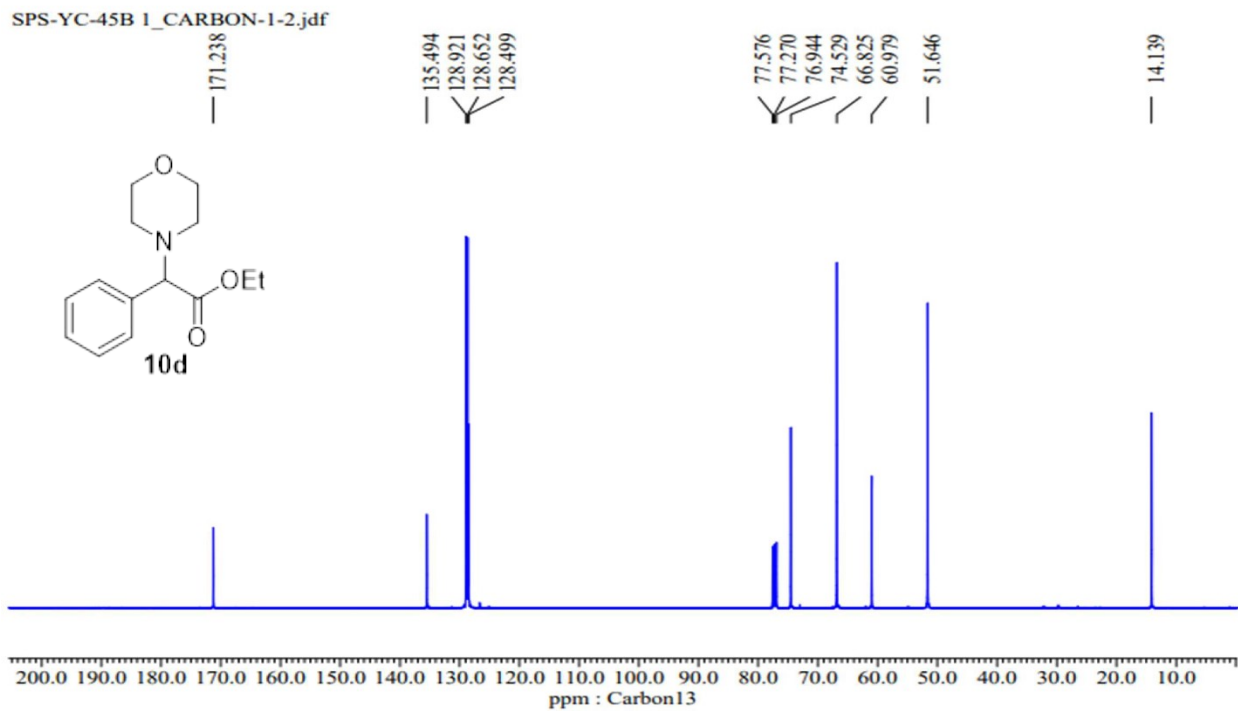
¹H NMR spectrum of **10c**



¹³C NMR spectrum of **10c**

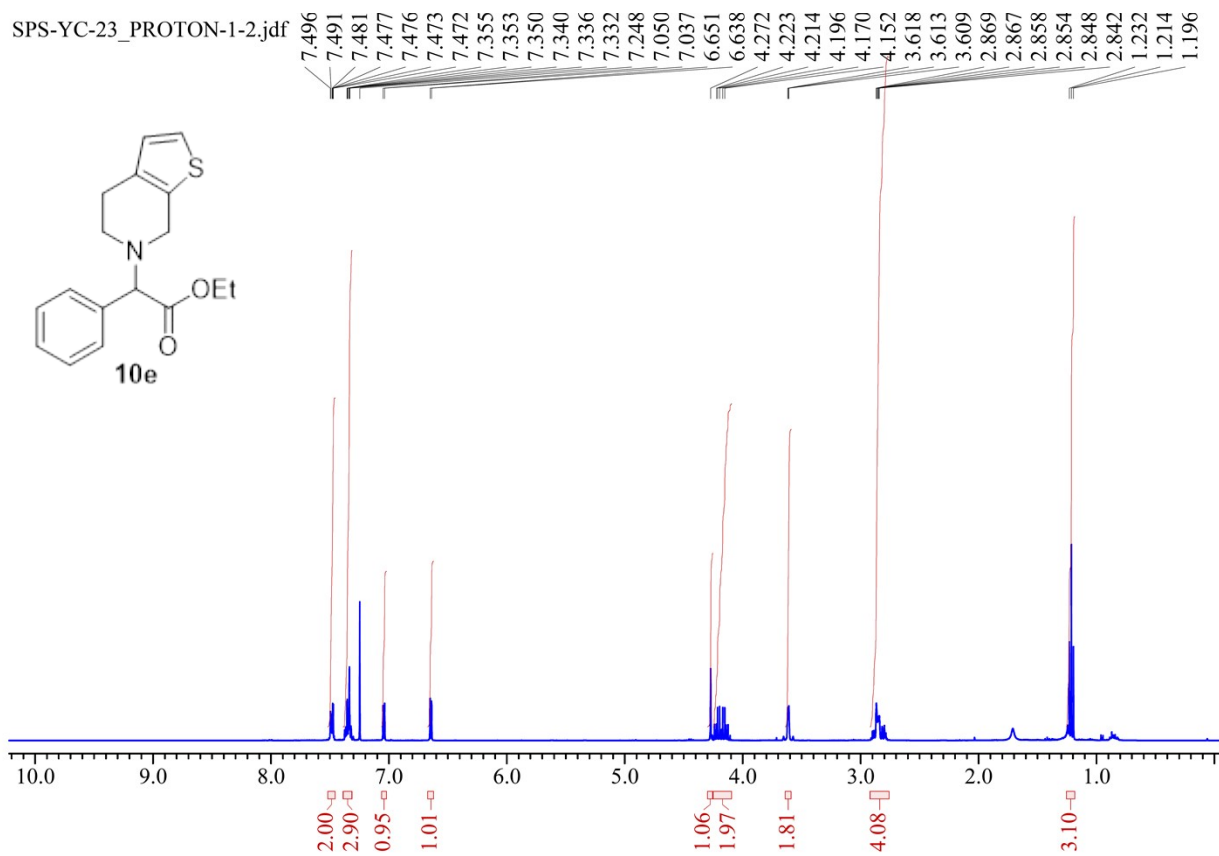


¹H NMR spectrum of **10d**



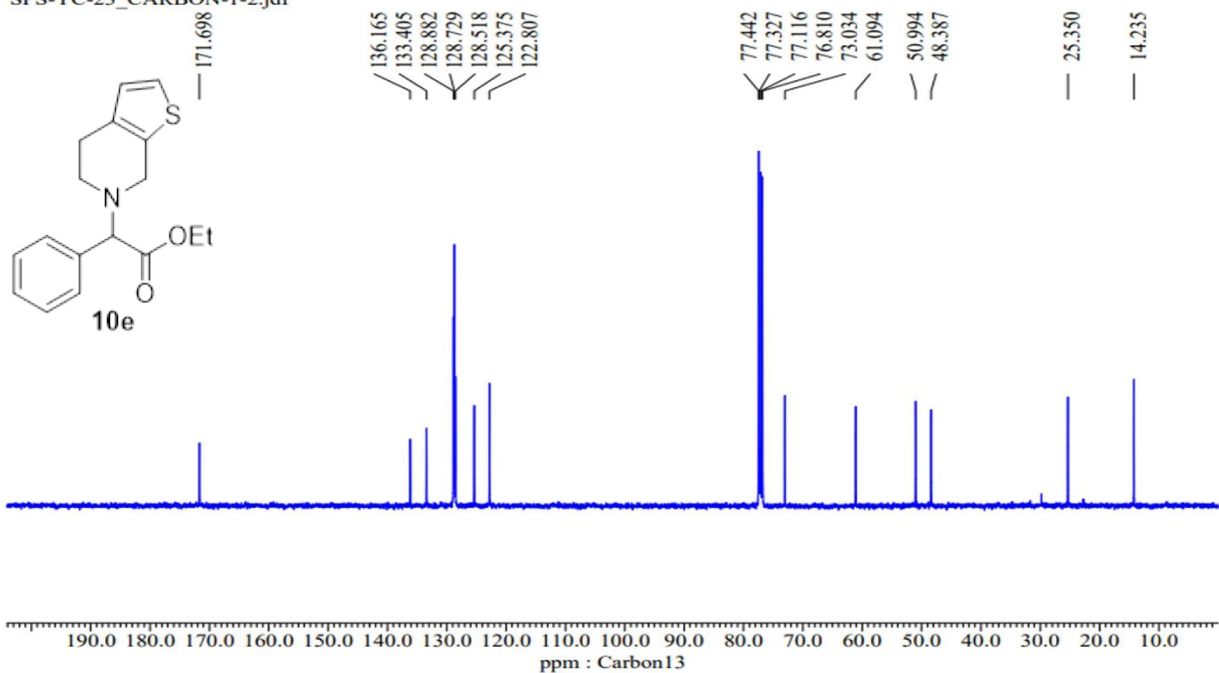
¹³C NMR spectrum of **10d**

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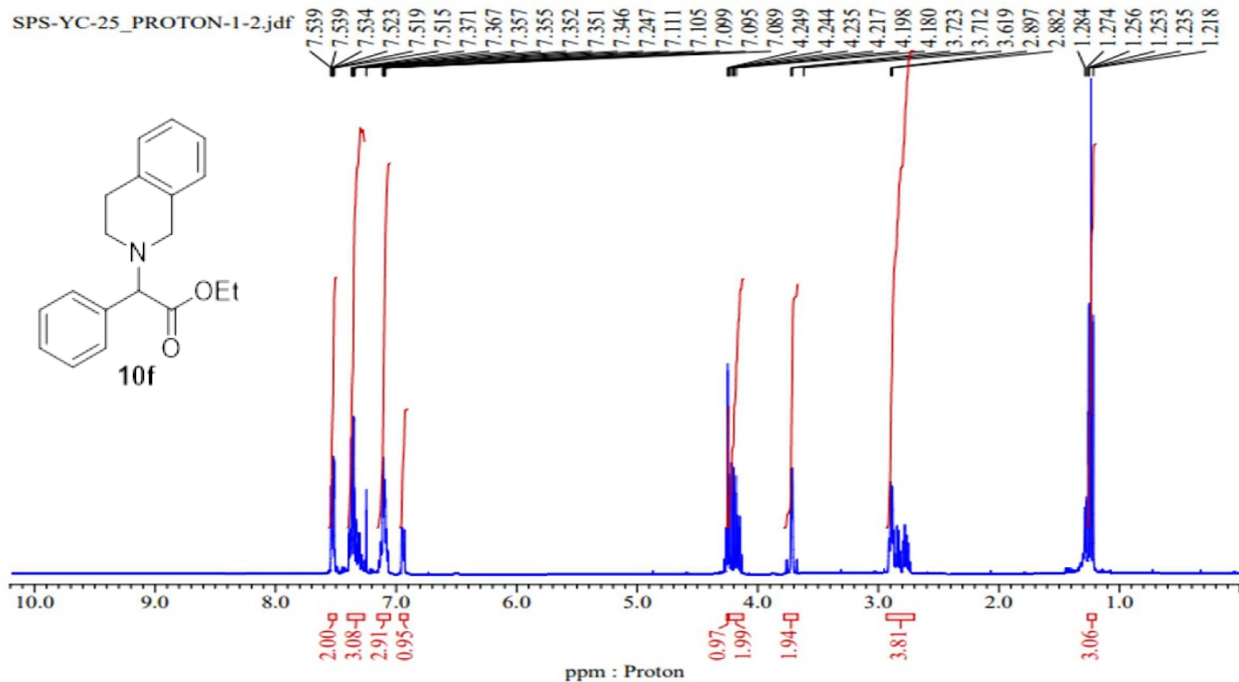


¹H NMR spectrum of **10e**

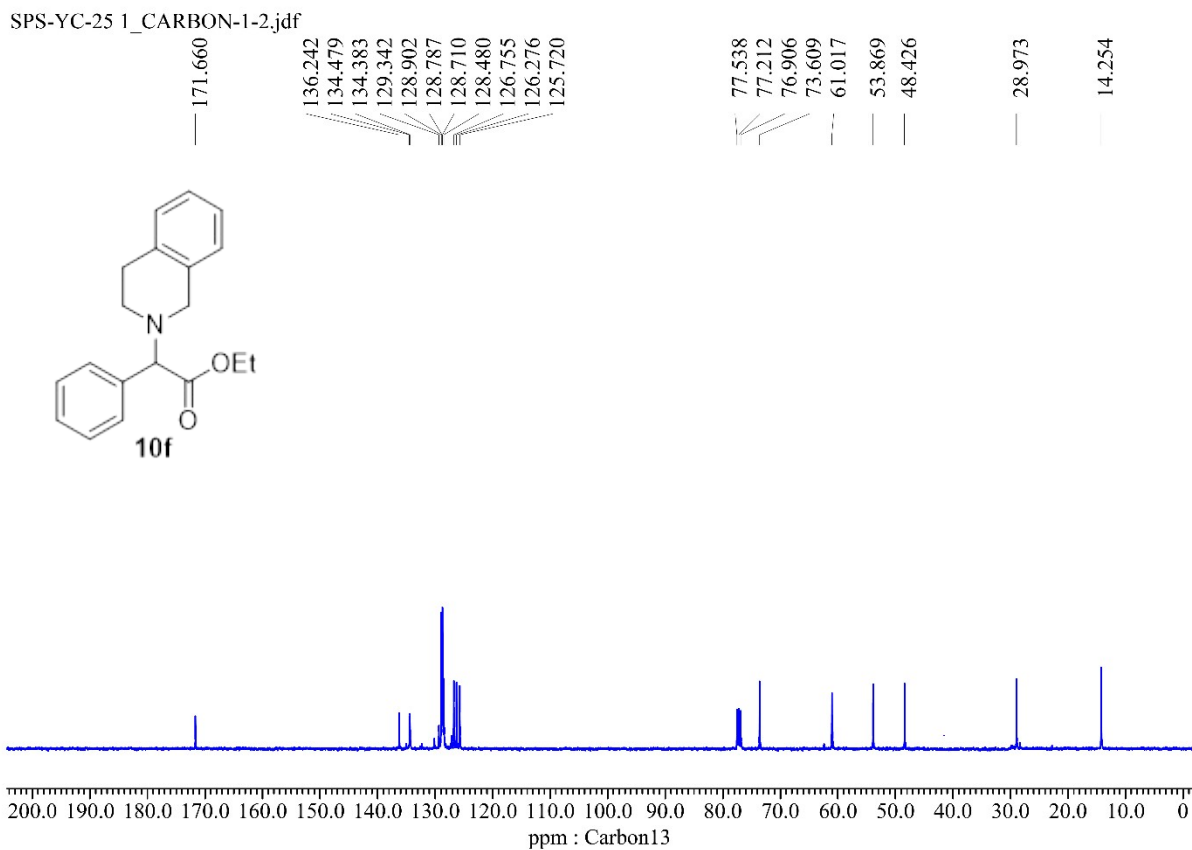
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¹³C NMR spectrum of **10e**

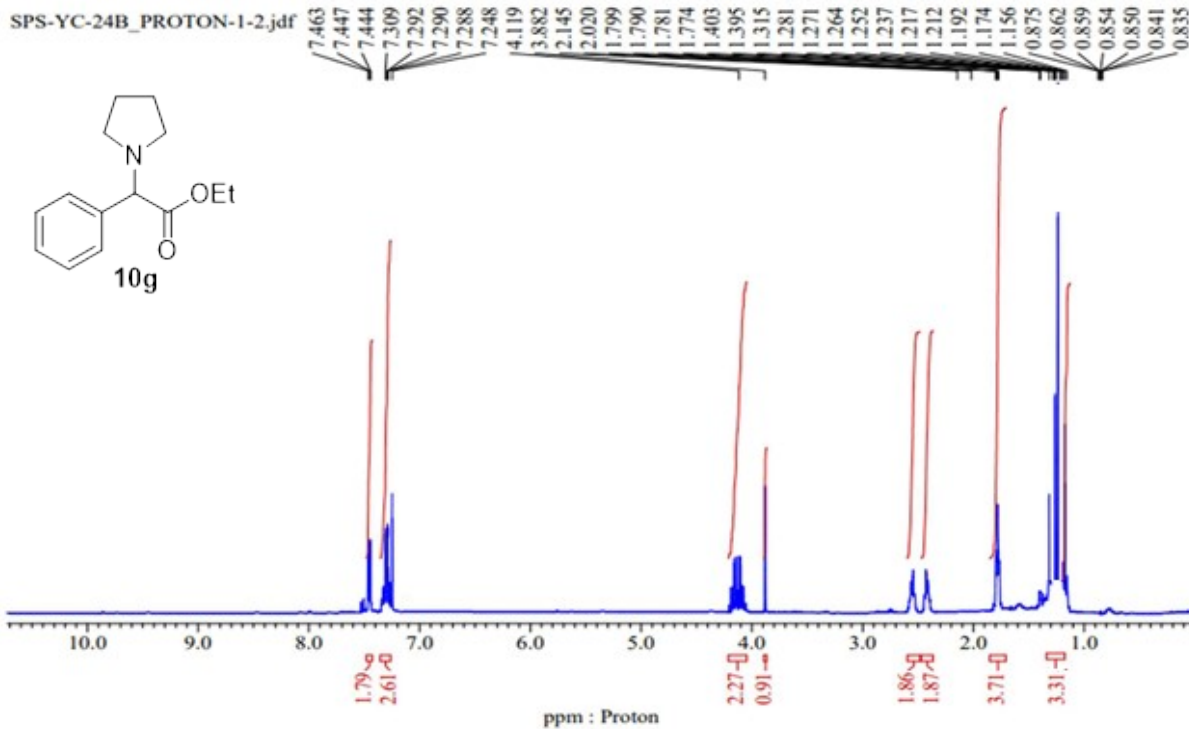


^1H NMR spectrum of **10f**



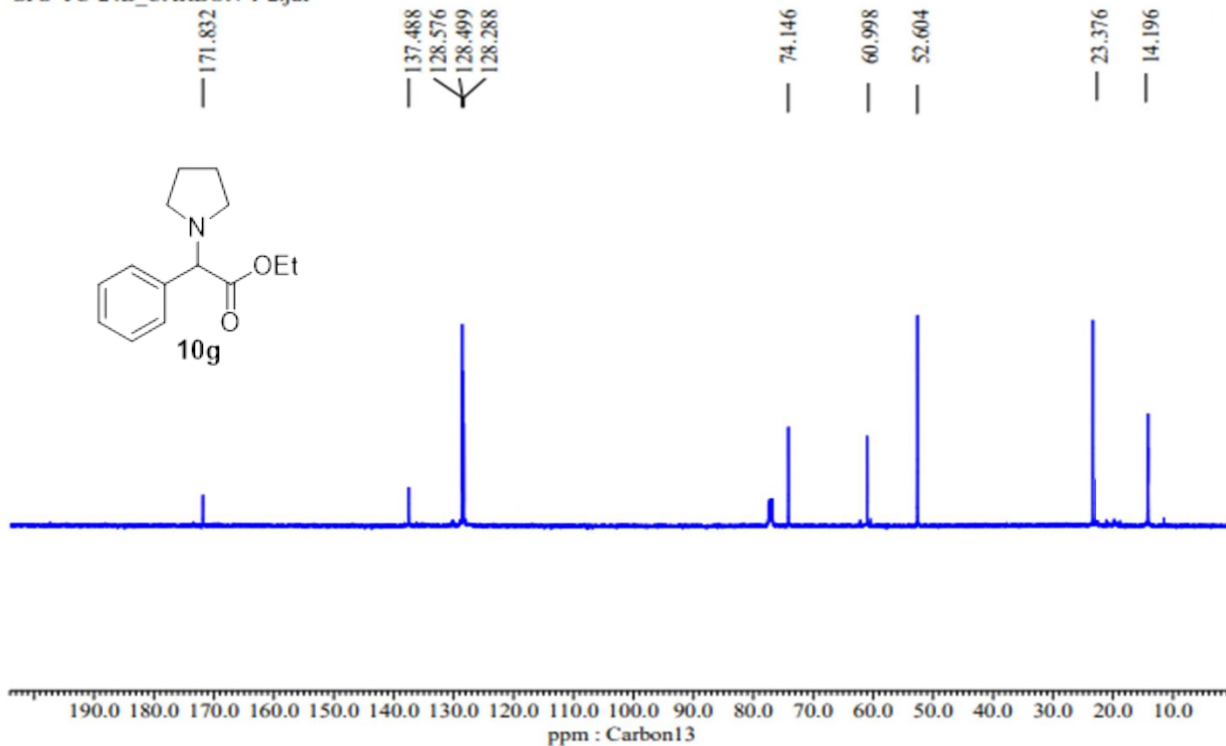
^{13}C NMR spectrum of **10f**

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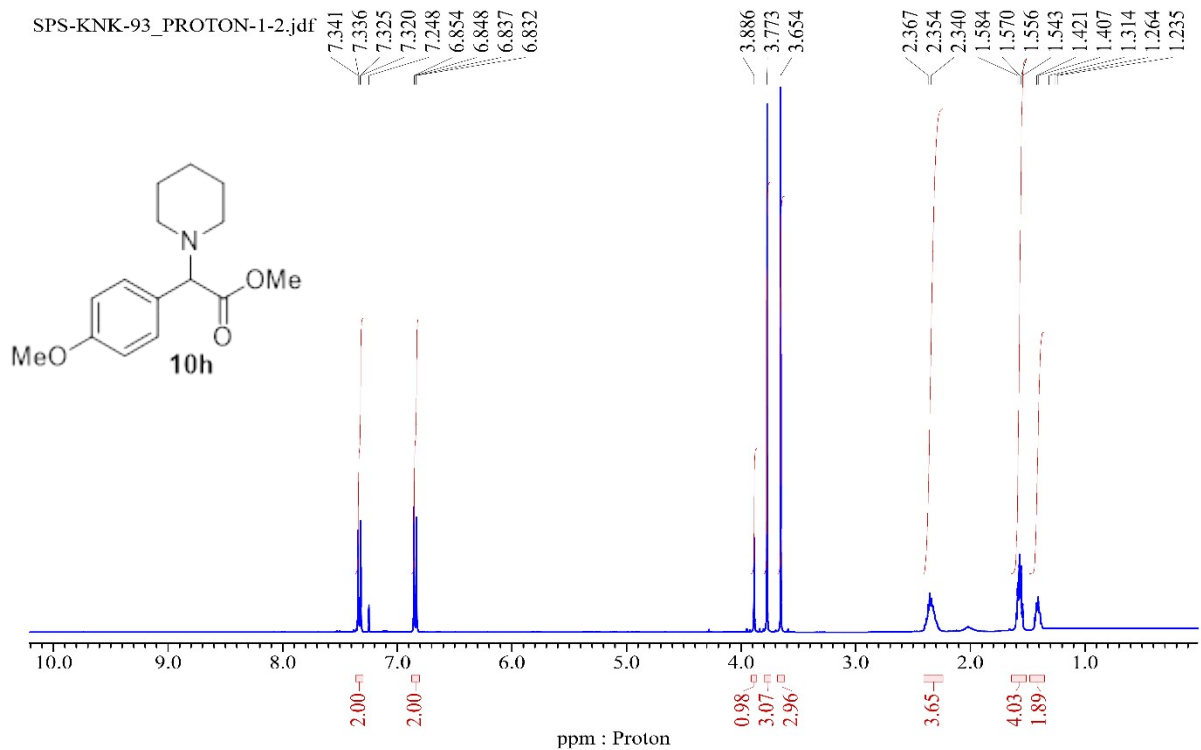


¹H NMR spectrum of **10g**

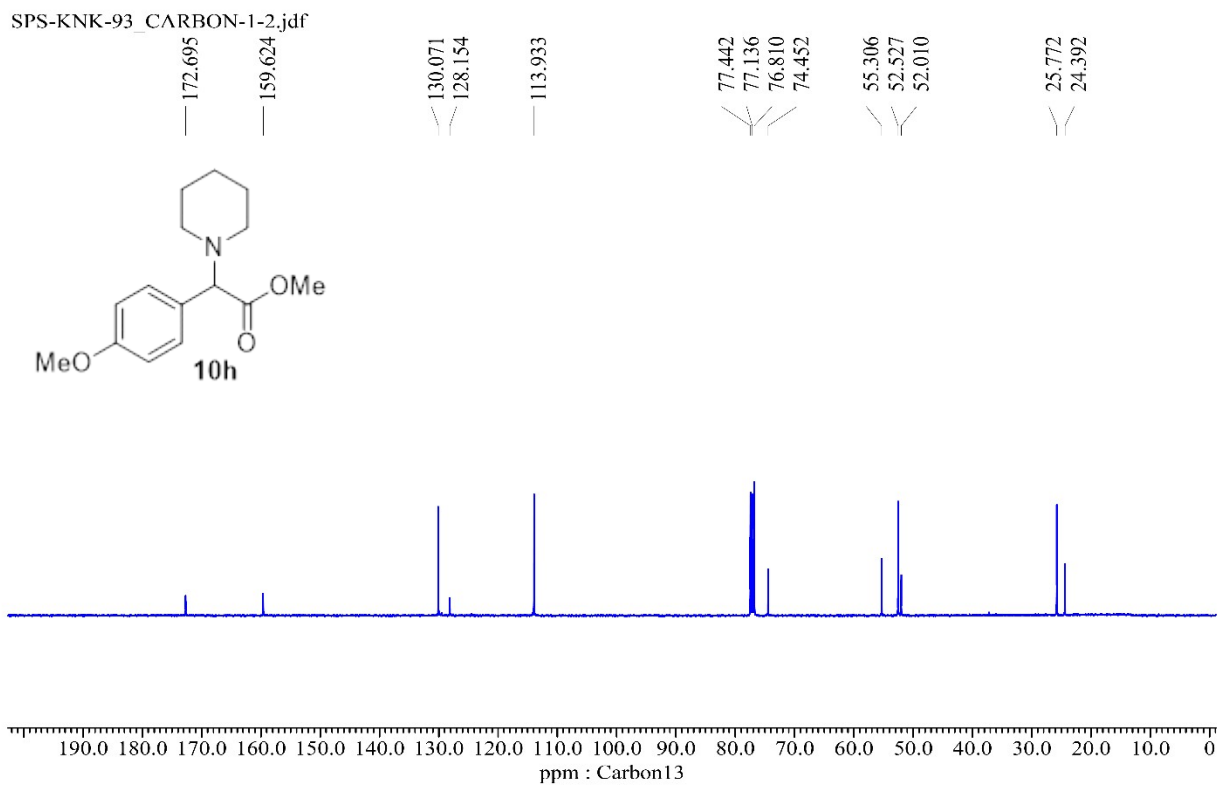
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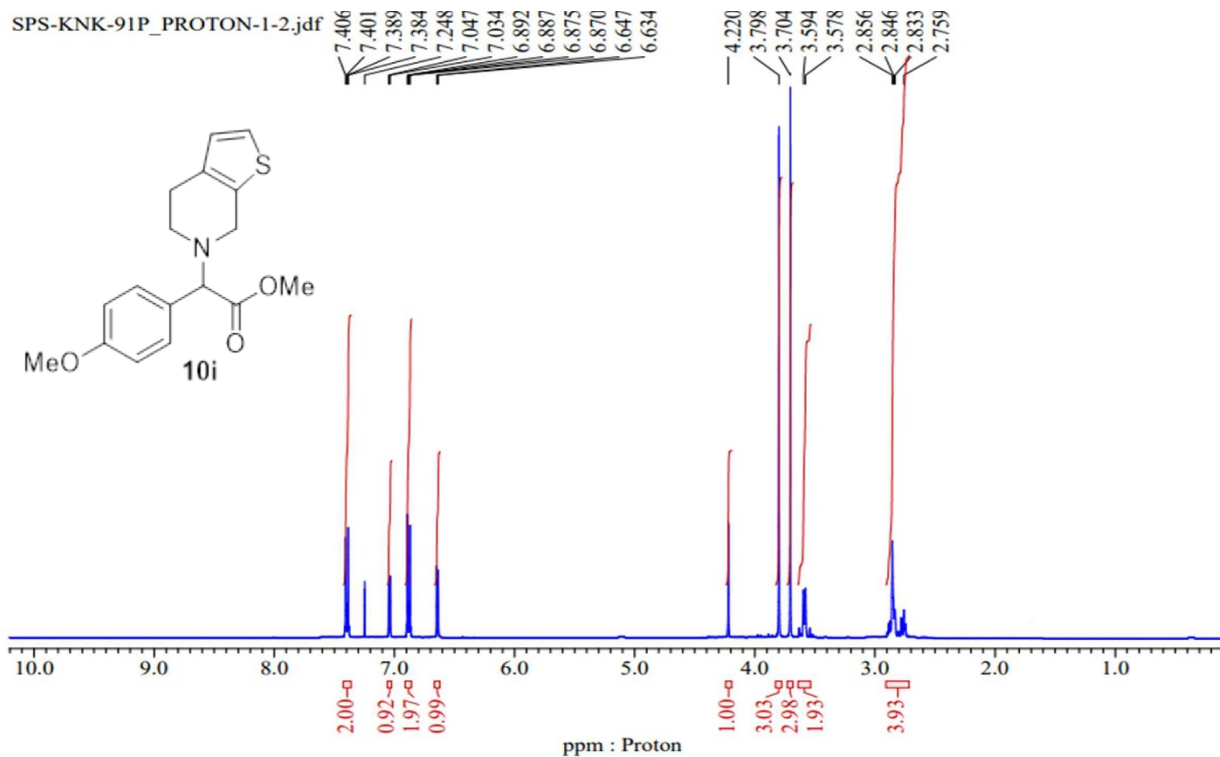
¹³C NMR spectrum of **10g**



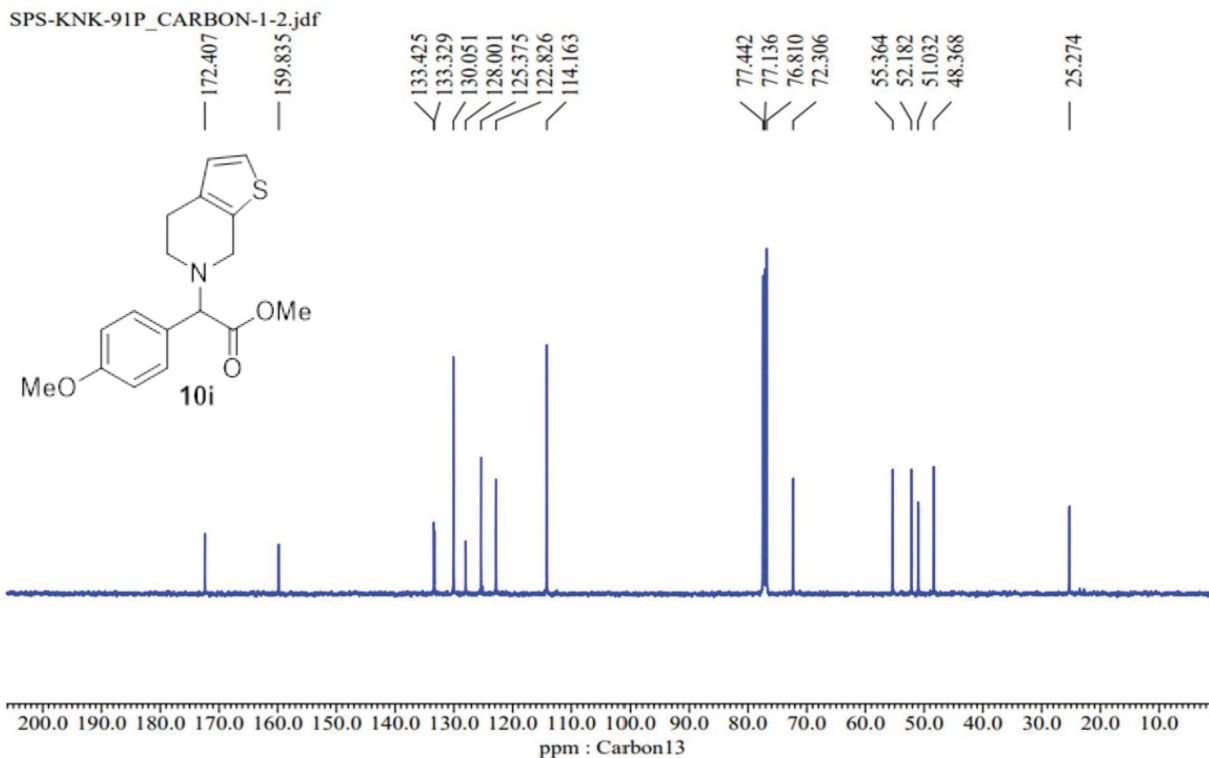
¹H NMR spectrum of **10h**



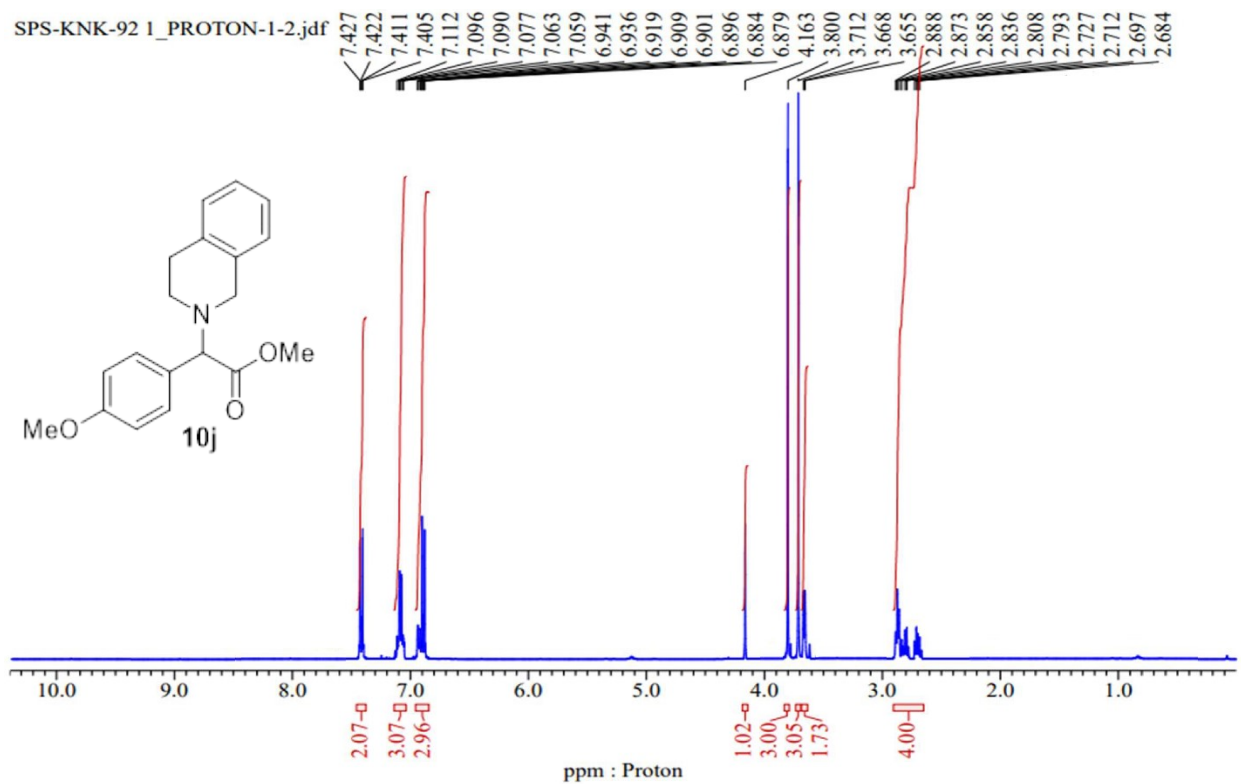
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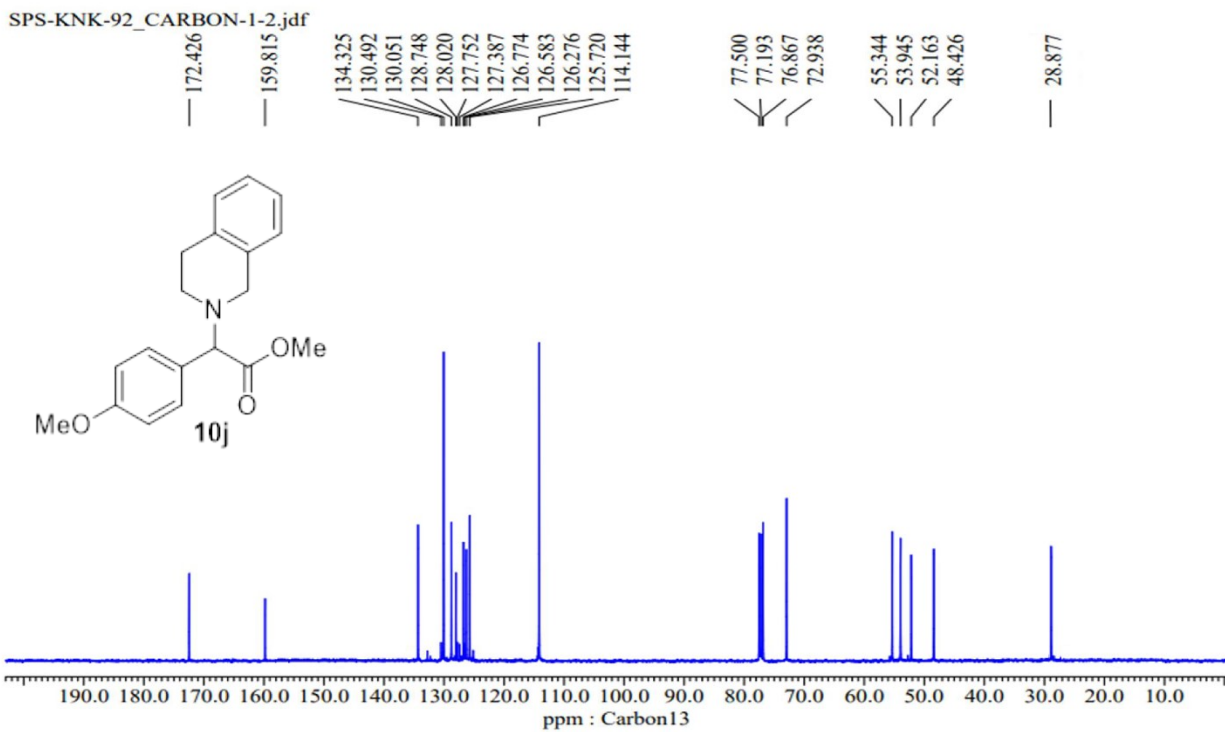
¹H NMR spectrum of **10i**



¹³C NMR spectrum of **10i**

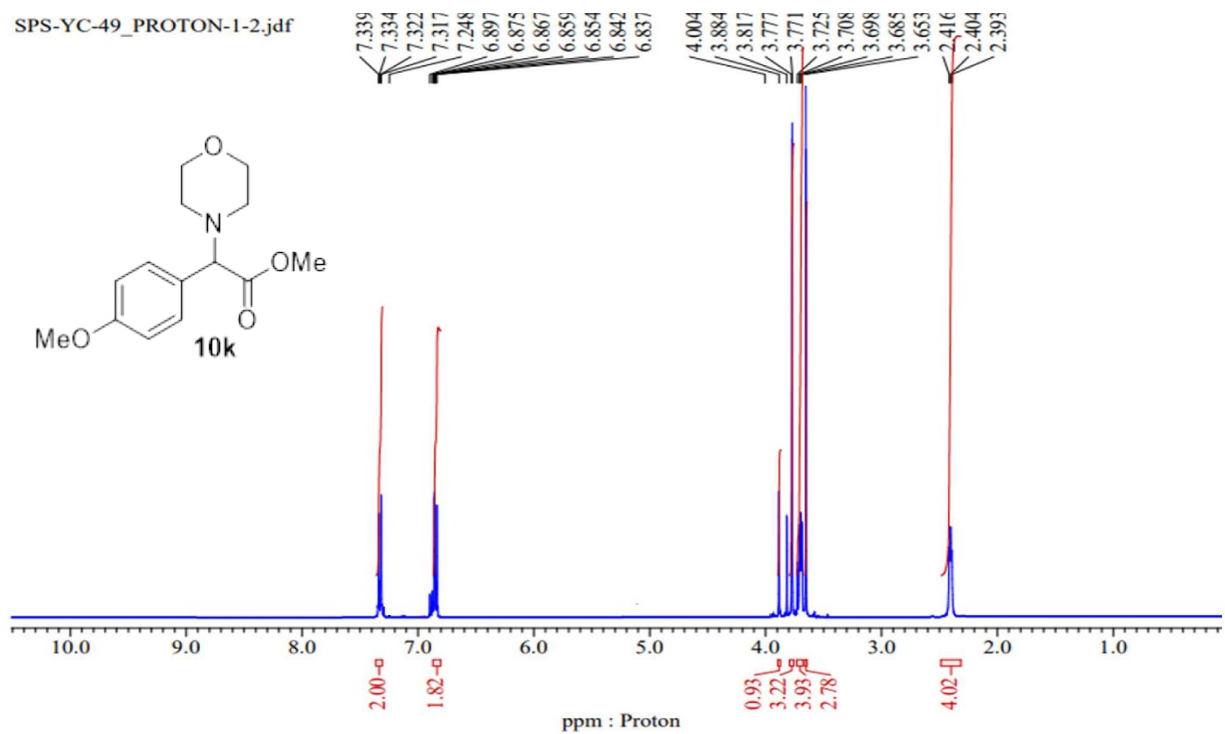


^1H NMR spectrum of **10j**



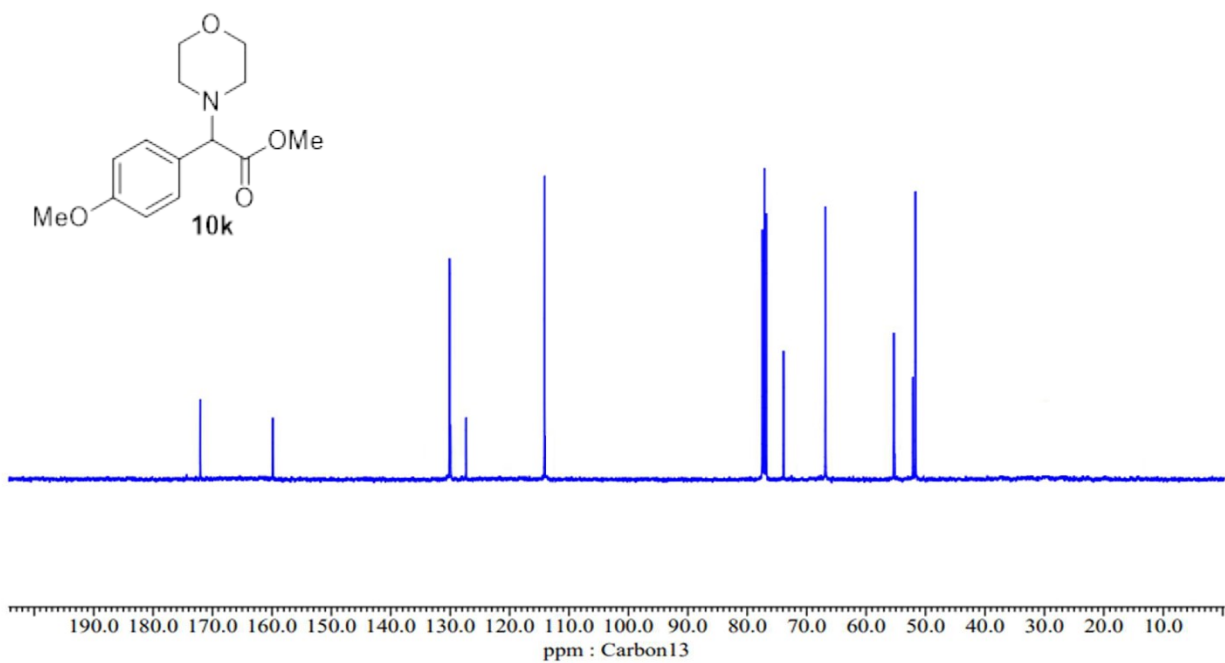
^{13}C NMR spectrum of **10j**

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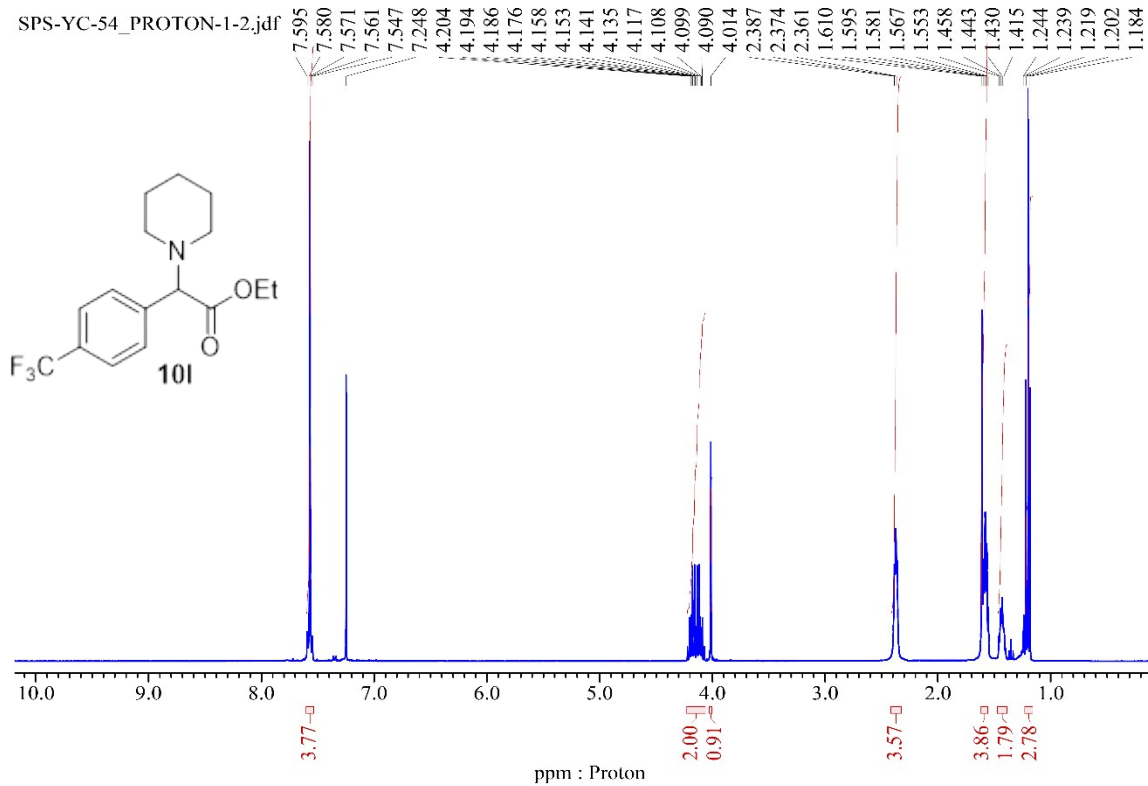


¹H NMR spectrum of **10k**

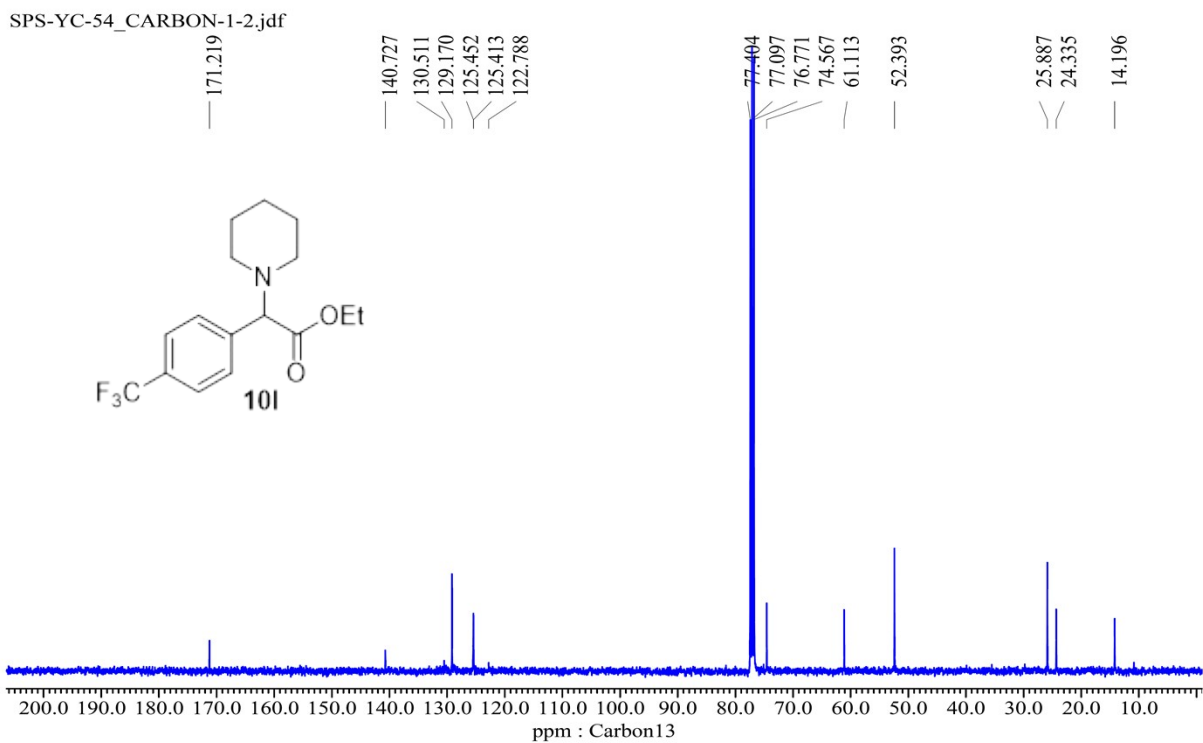
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¹³C NMR spectrum of **10k**

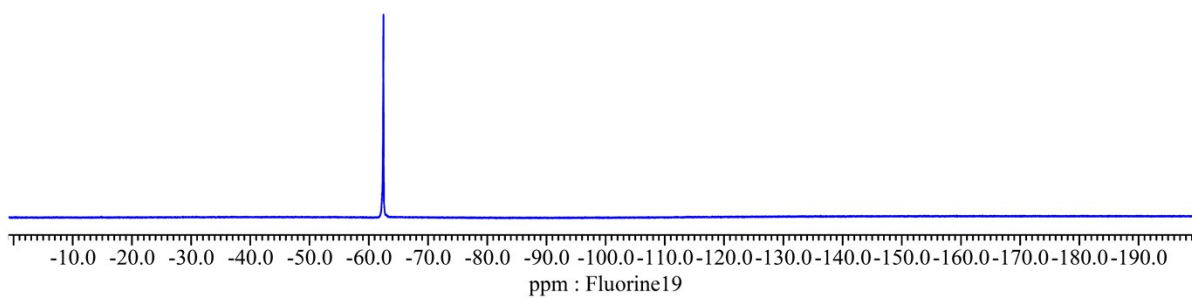
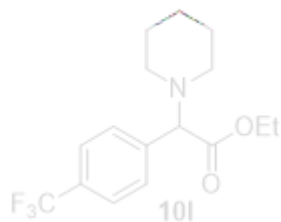


¹H NMR spectrum of **101**

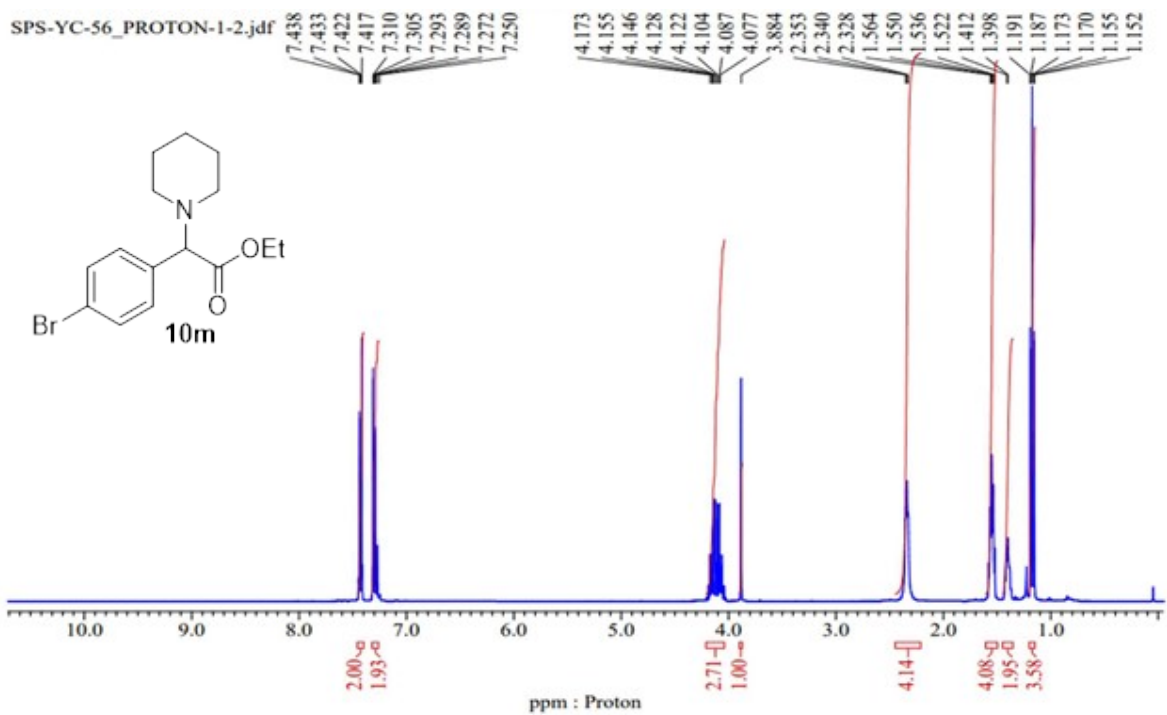


¹³C NMR spectrum of **101**

-62.471

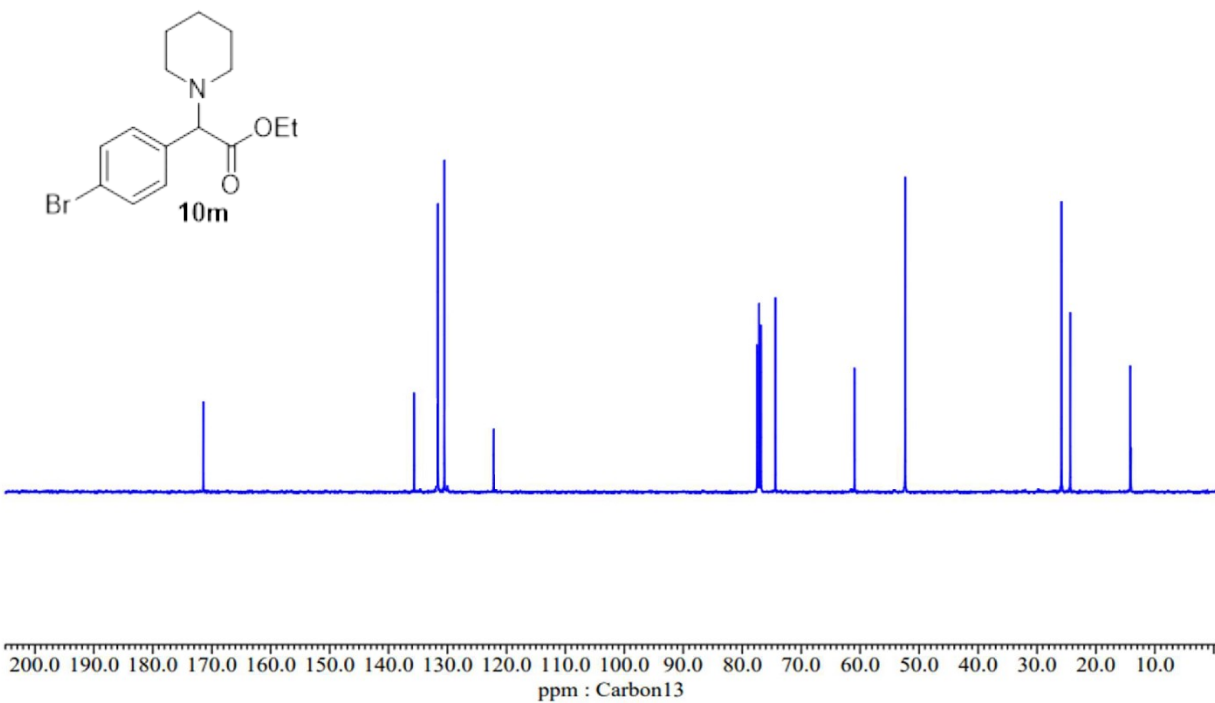


^{19}F NMR spectrum of **101**

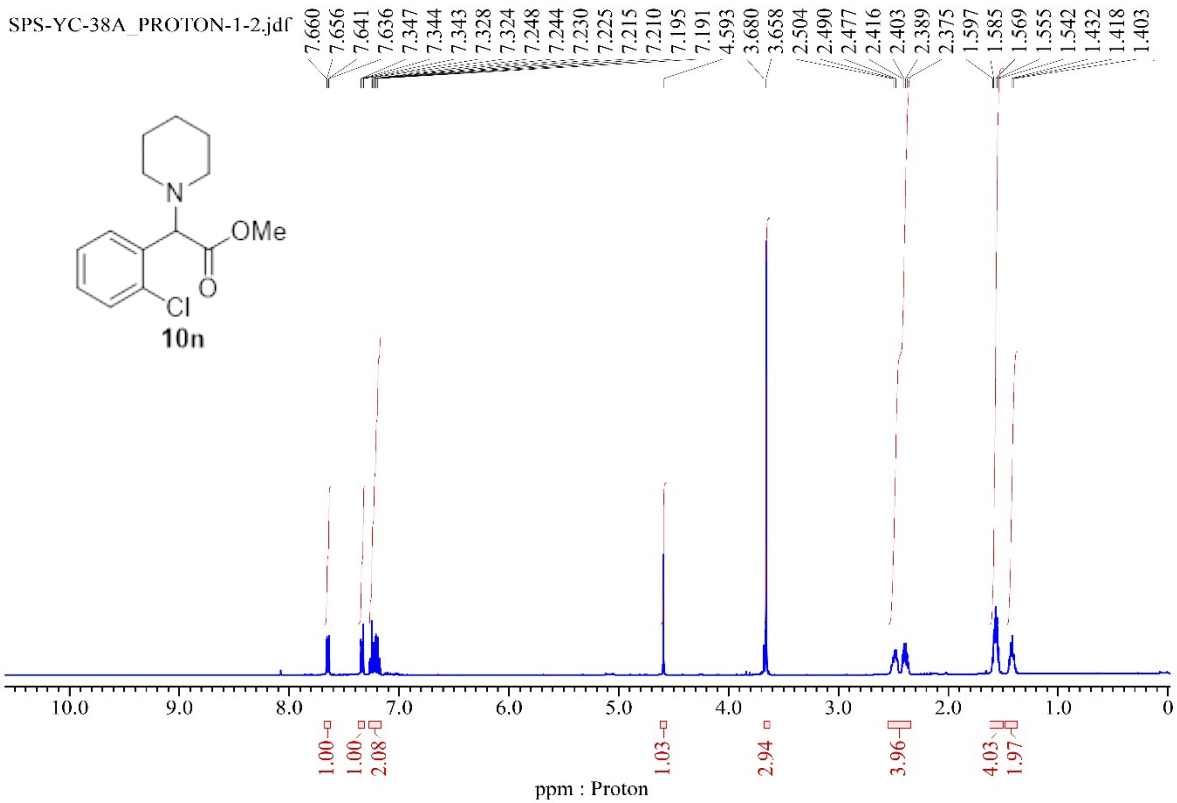


^1H NMR spectrum of **10m**

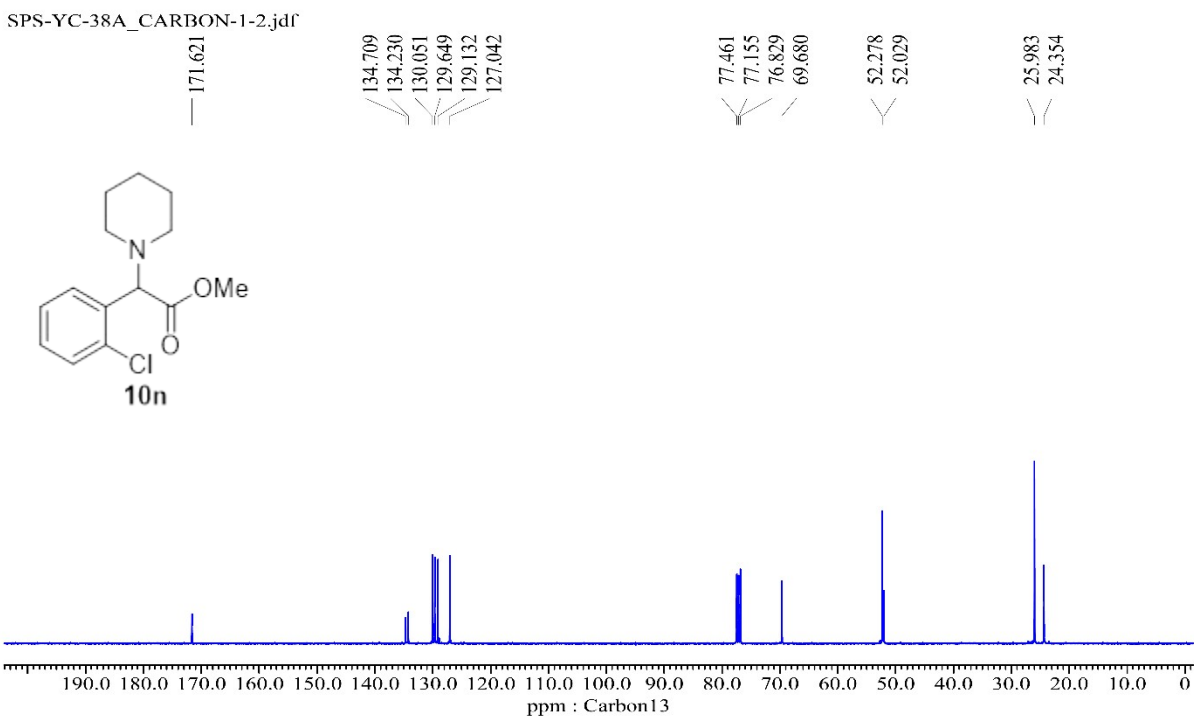
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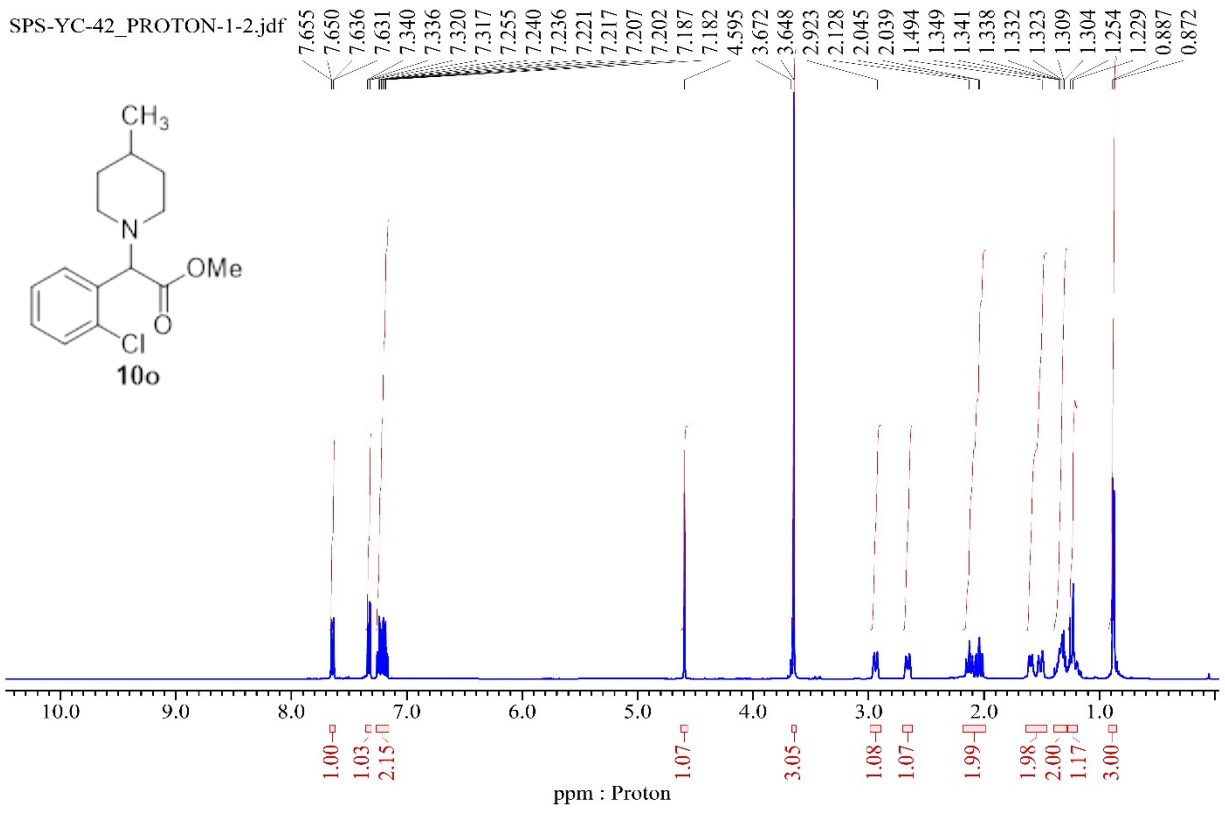
^{13}C NMR spectrum of **10m**



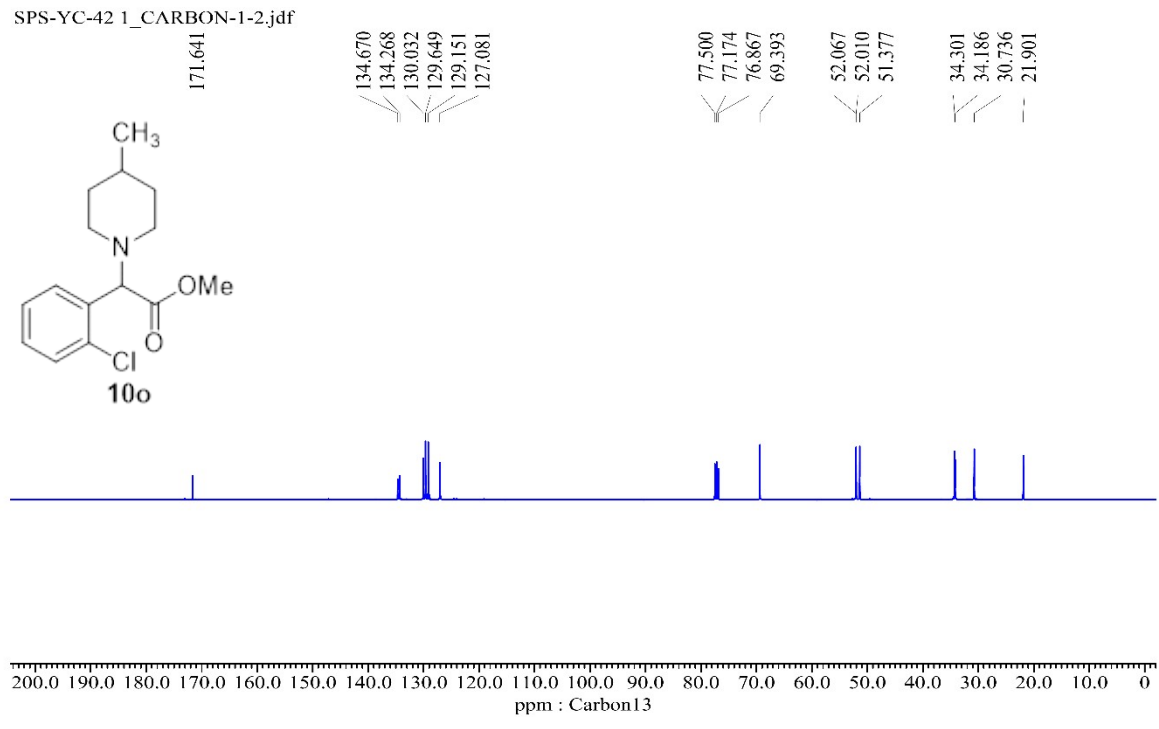
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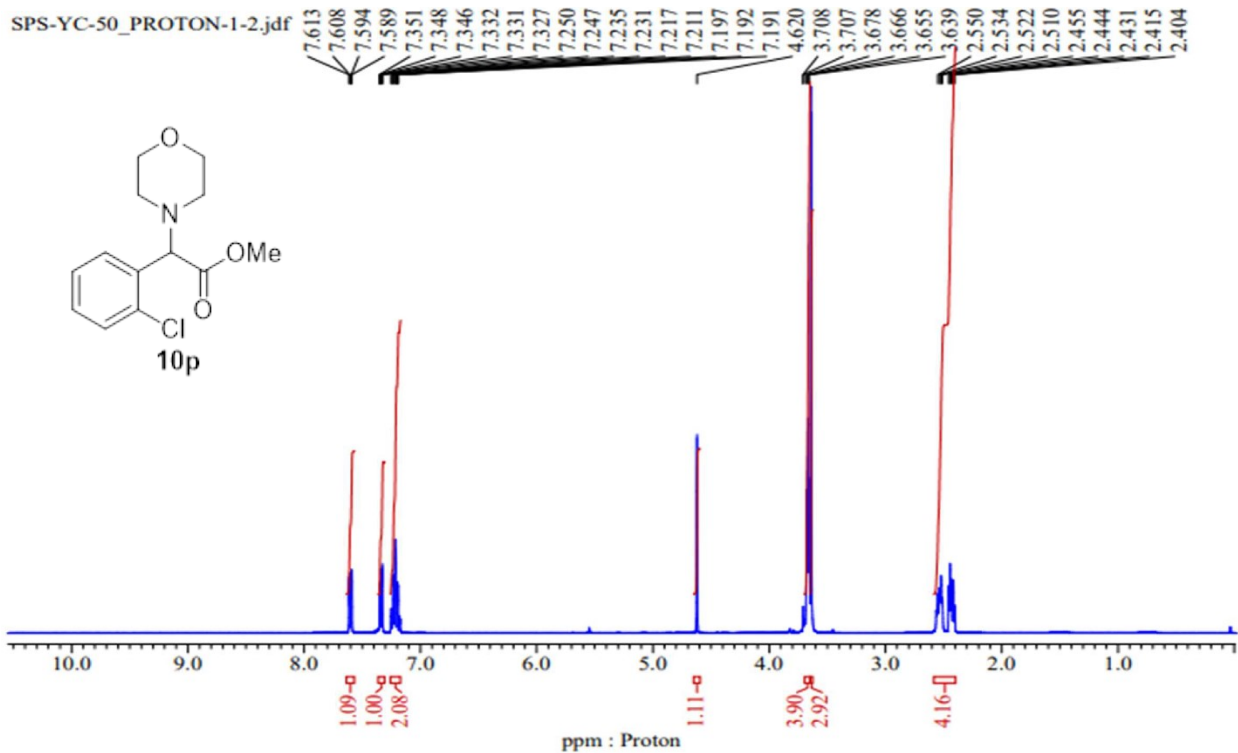
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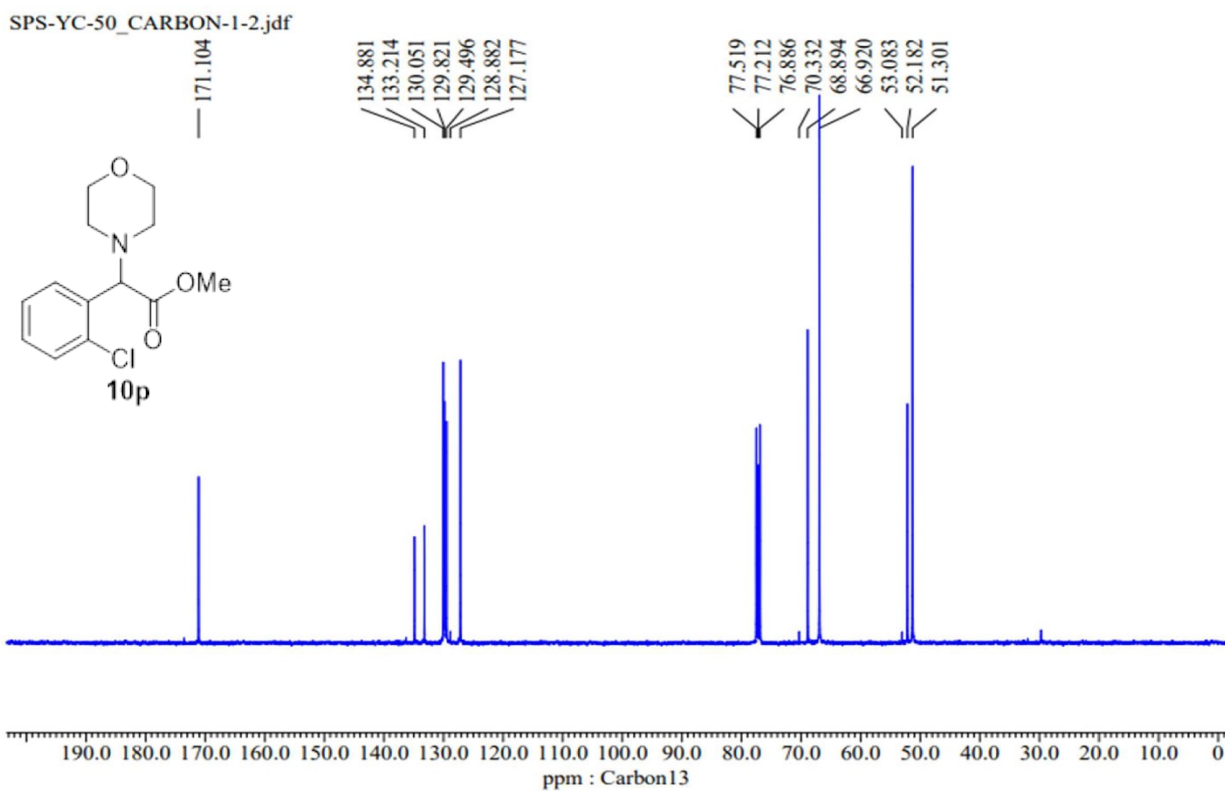
¹H NMR spectrum of **10o**



¹³C NMR spectrum of **10o**

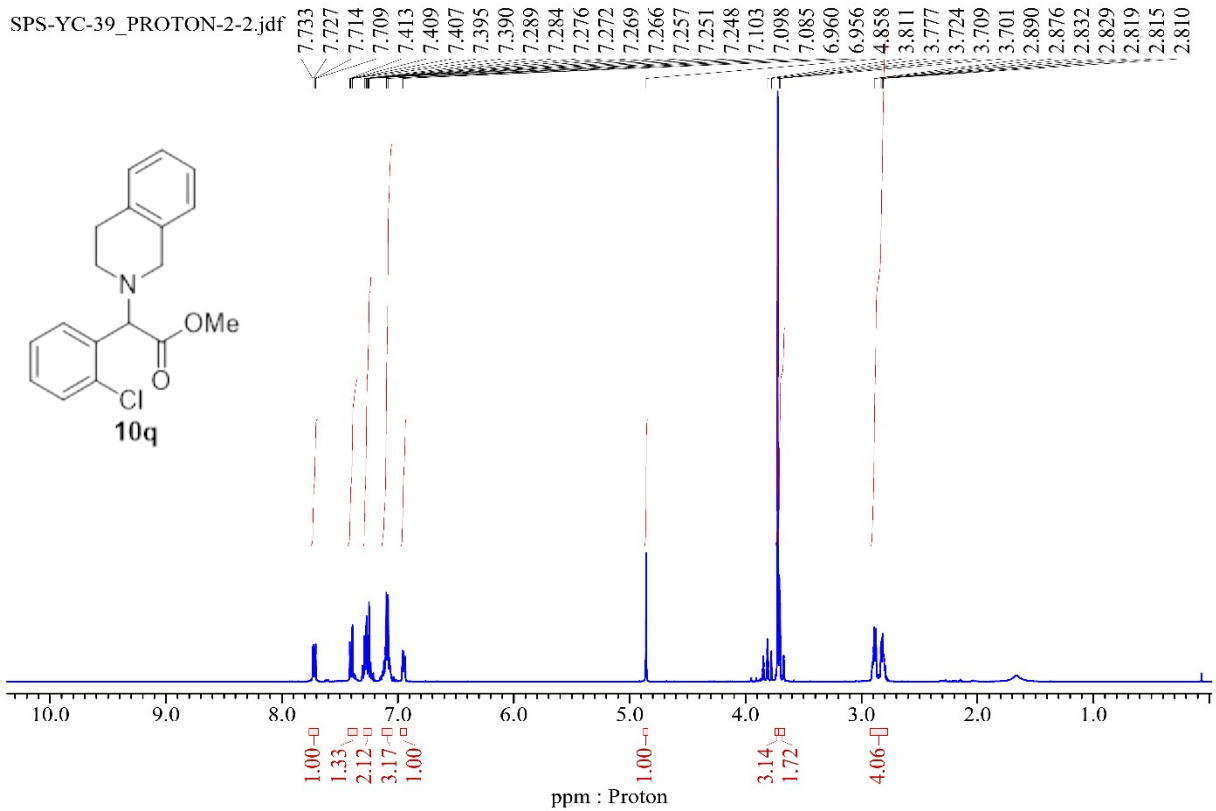


¹H NMR spectrum of **10p**



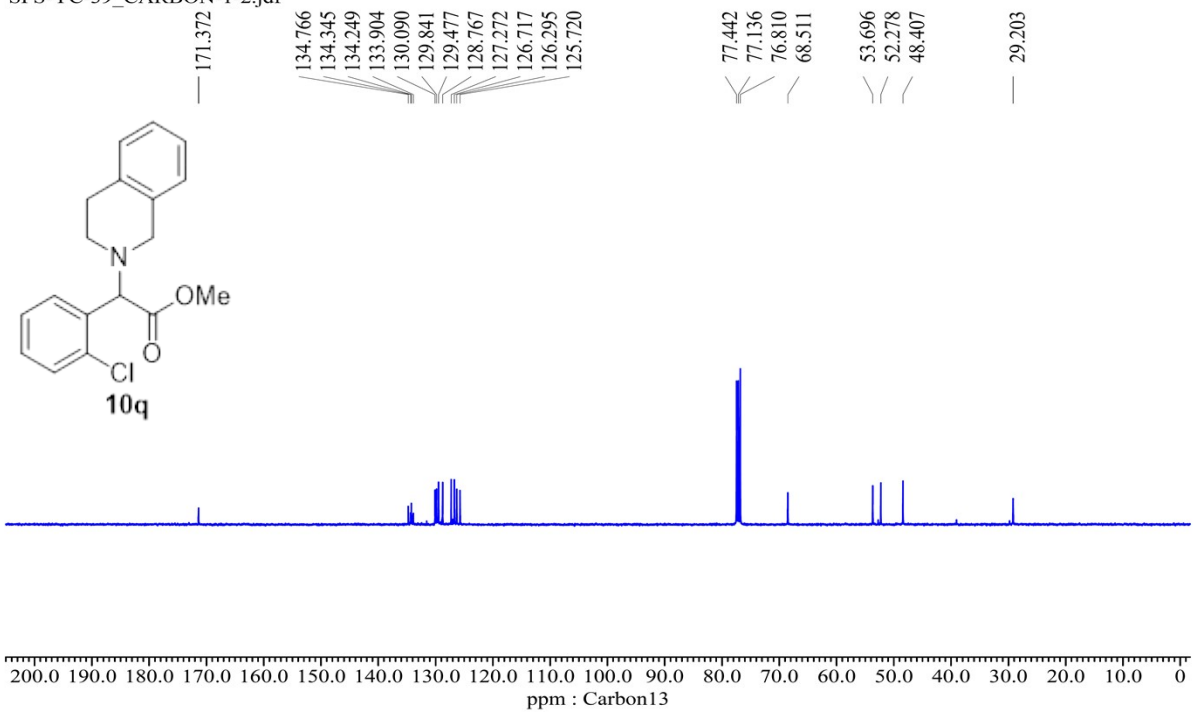
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SPS-YC-39_PROTON-2-2.jdf



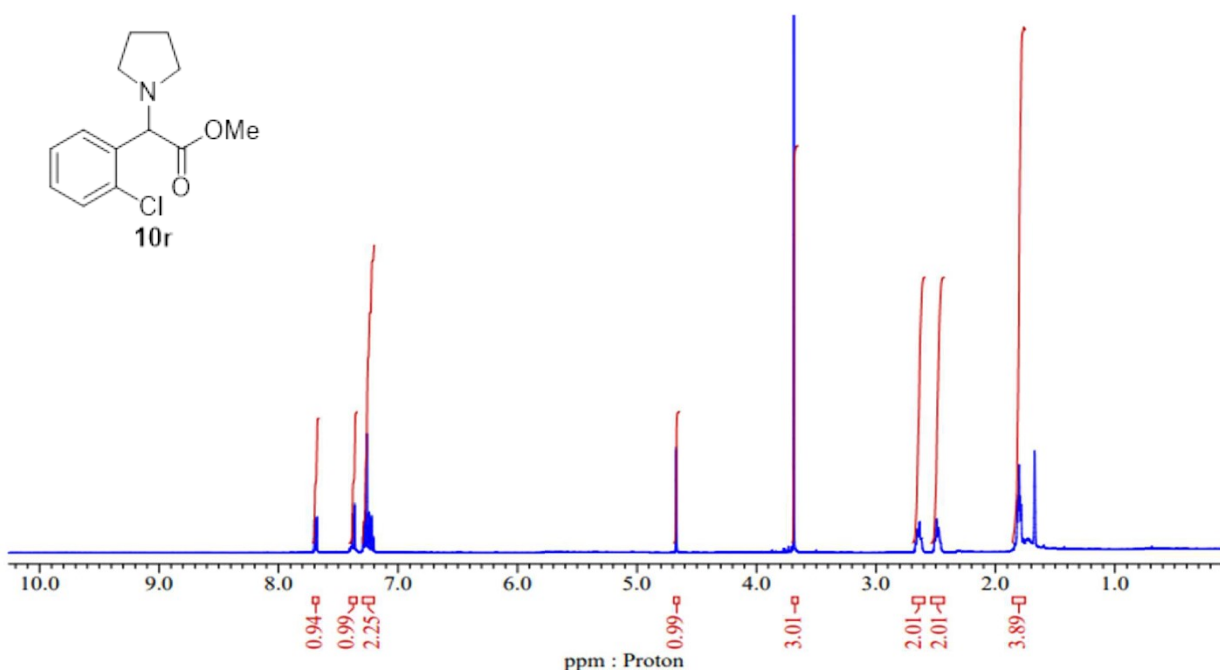
¹H NMR spectrum of **10q**

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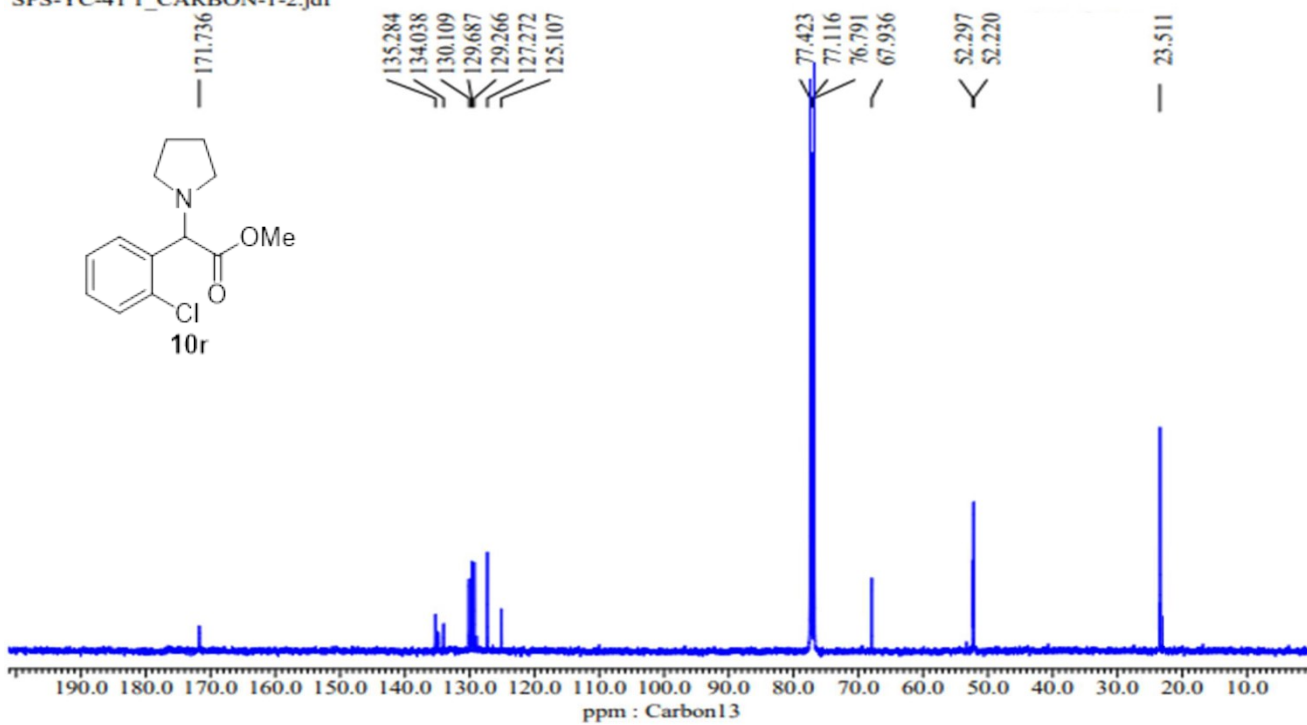
¹³C NMR spectrum of **10q**

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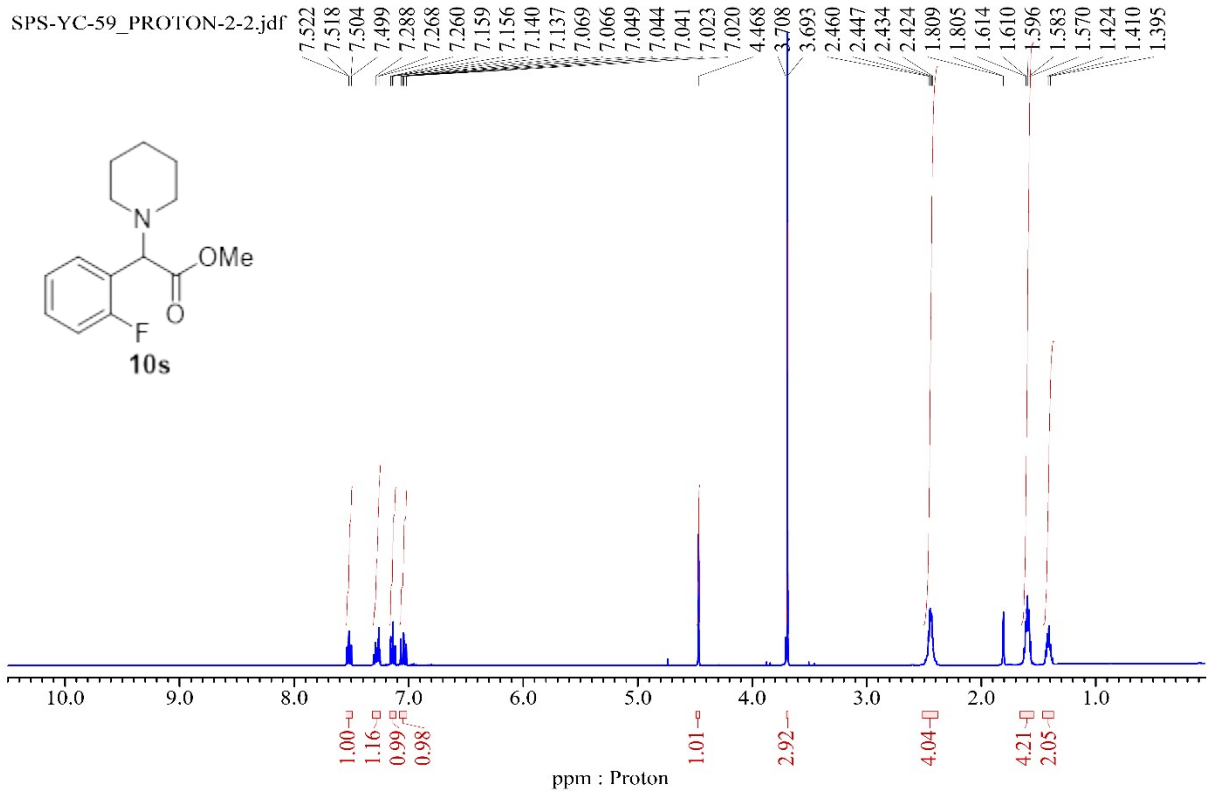


¹H NMR spectrum of **10r**

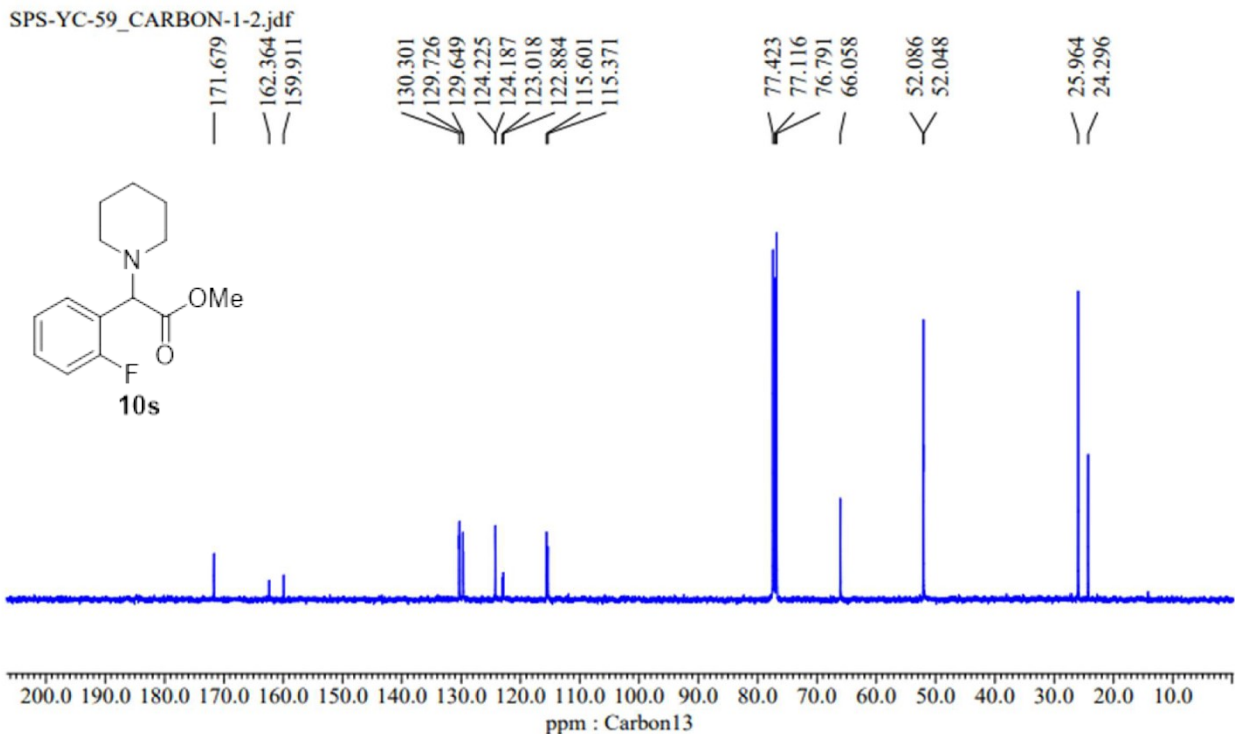
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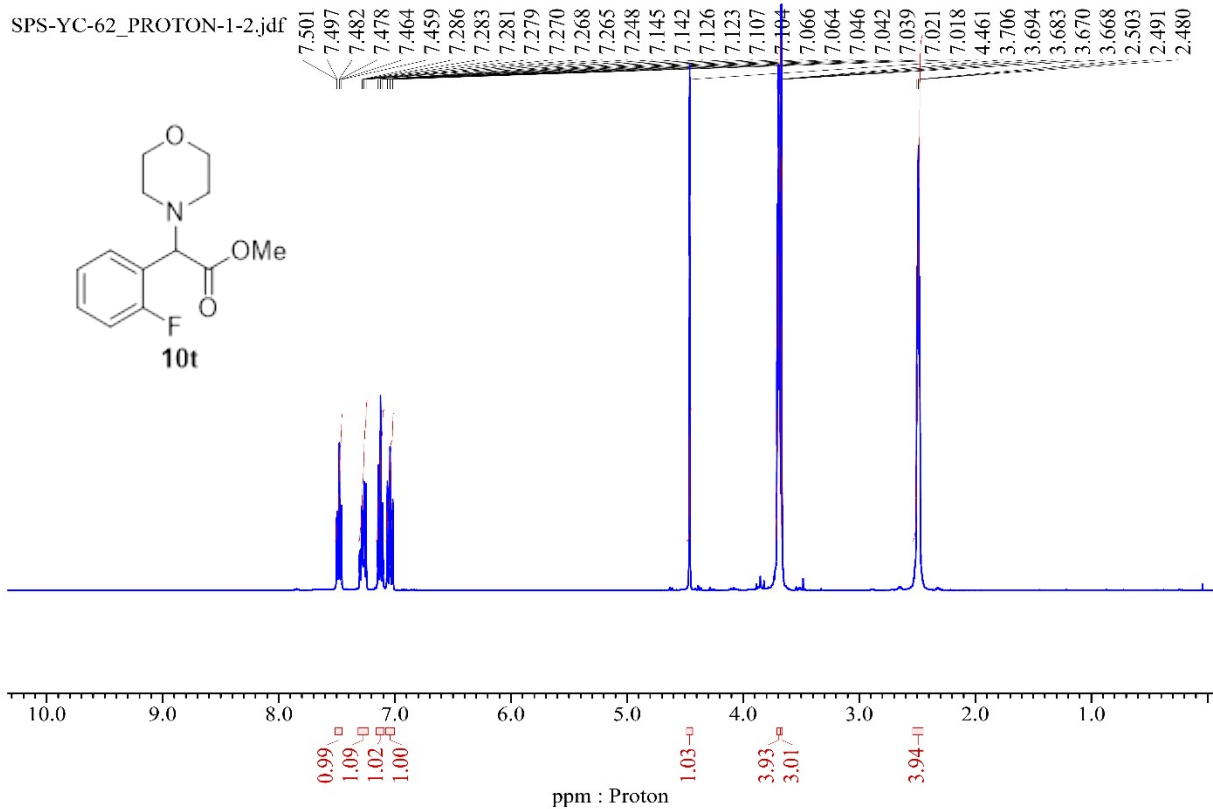
¹³C NMR spectrum of **10r**



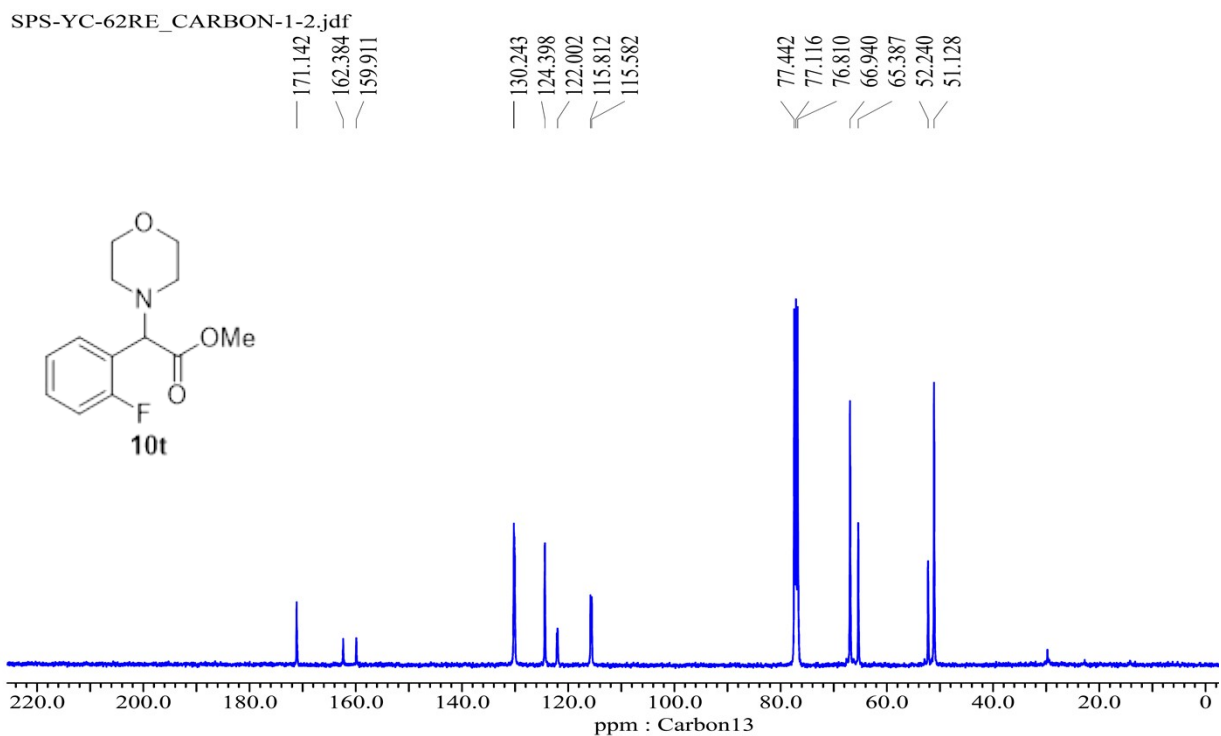
¹H NMR spectrum of **10s**



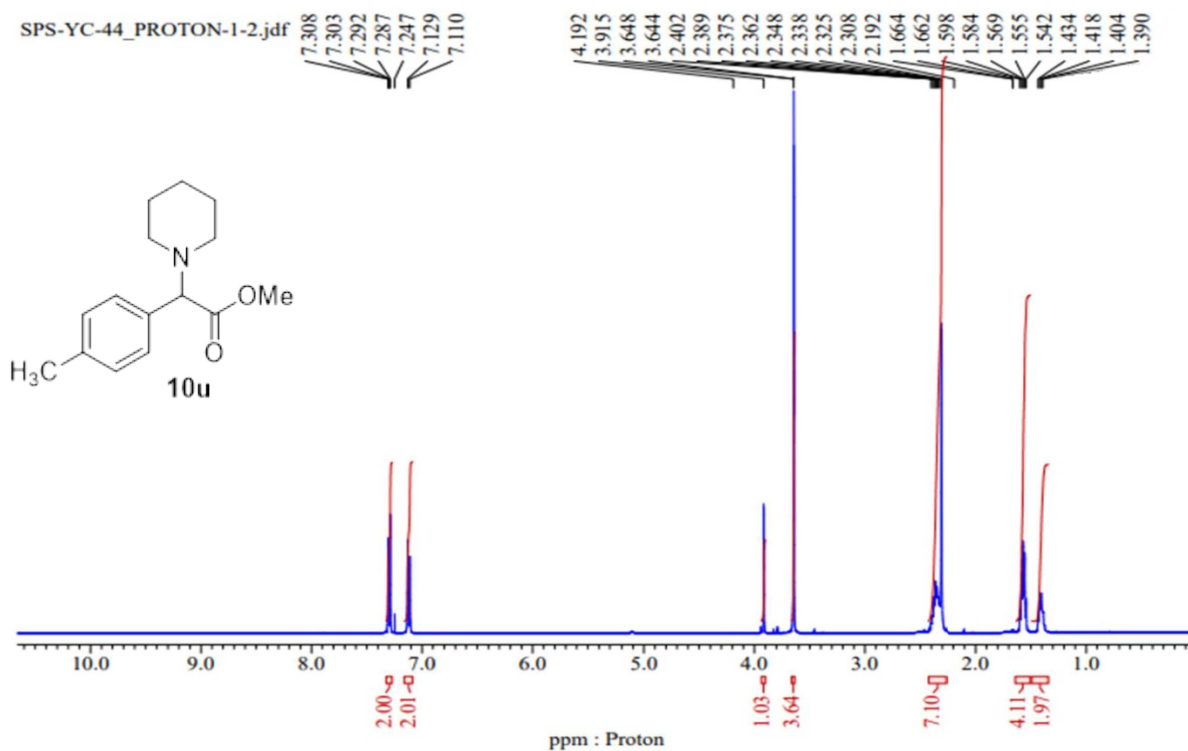
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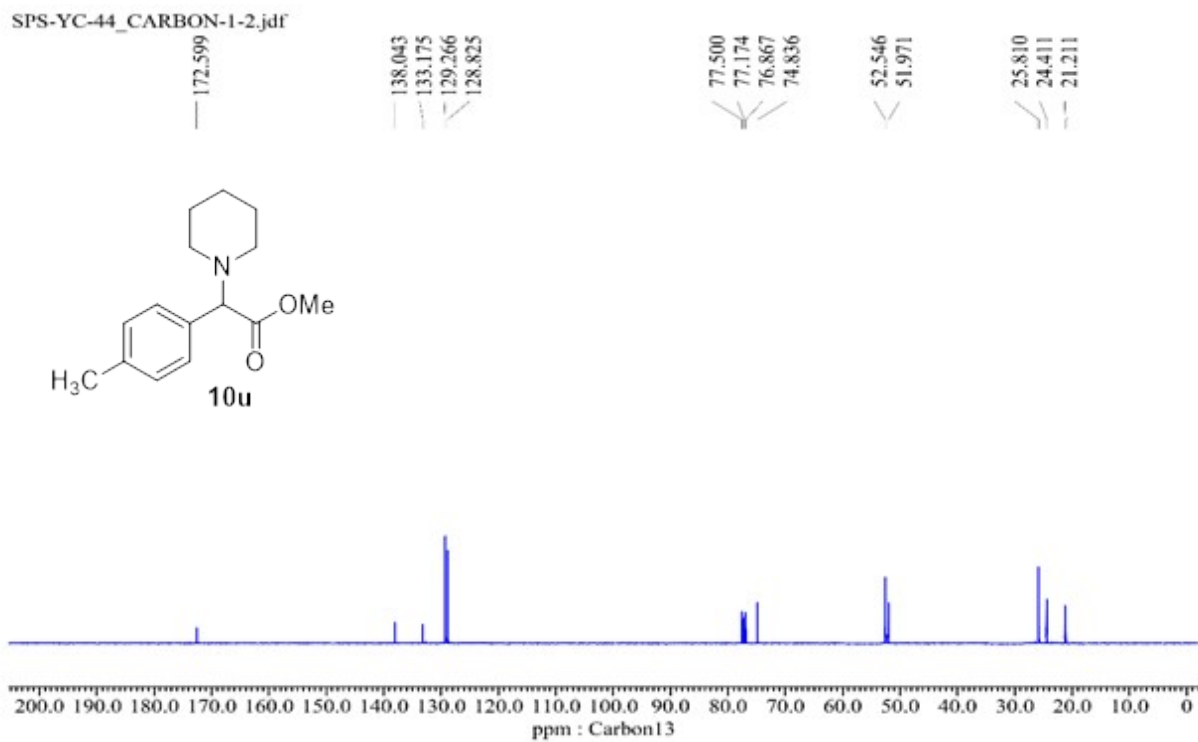
¹H NMR spectrum of **10t**



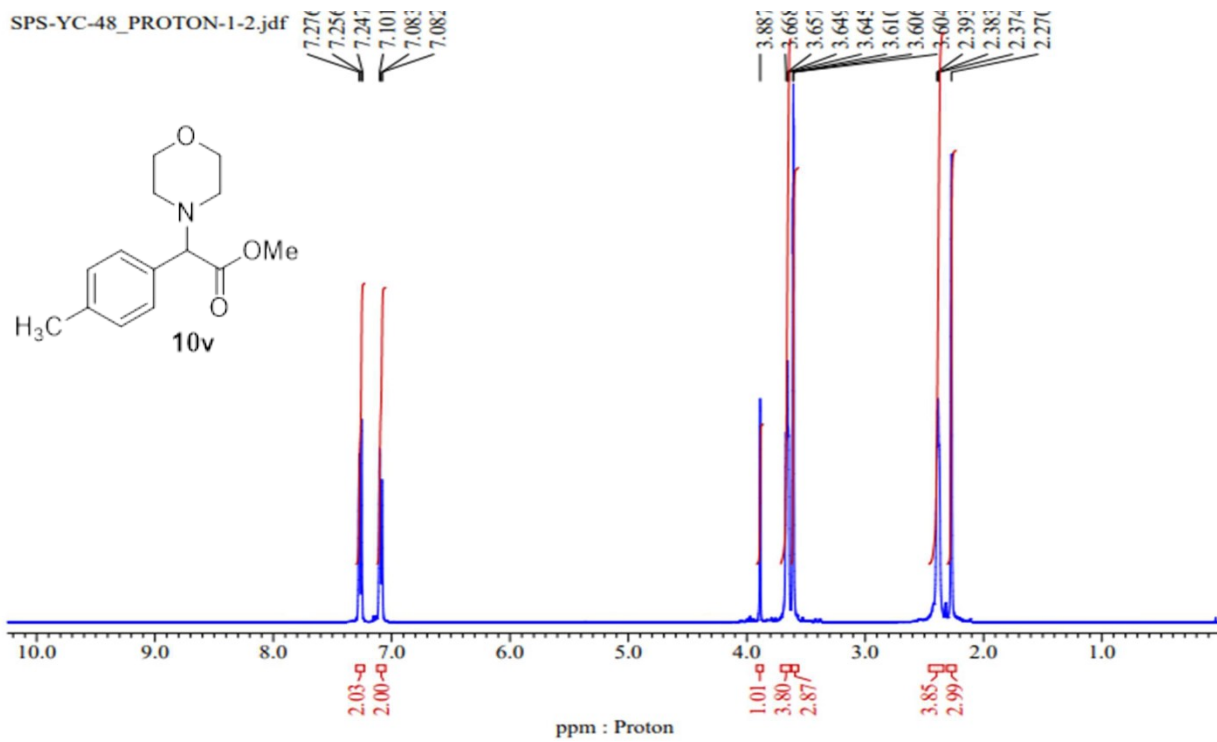
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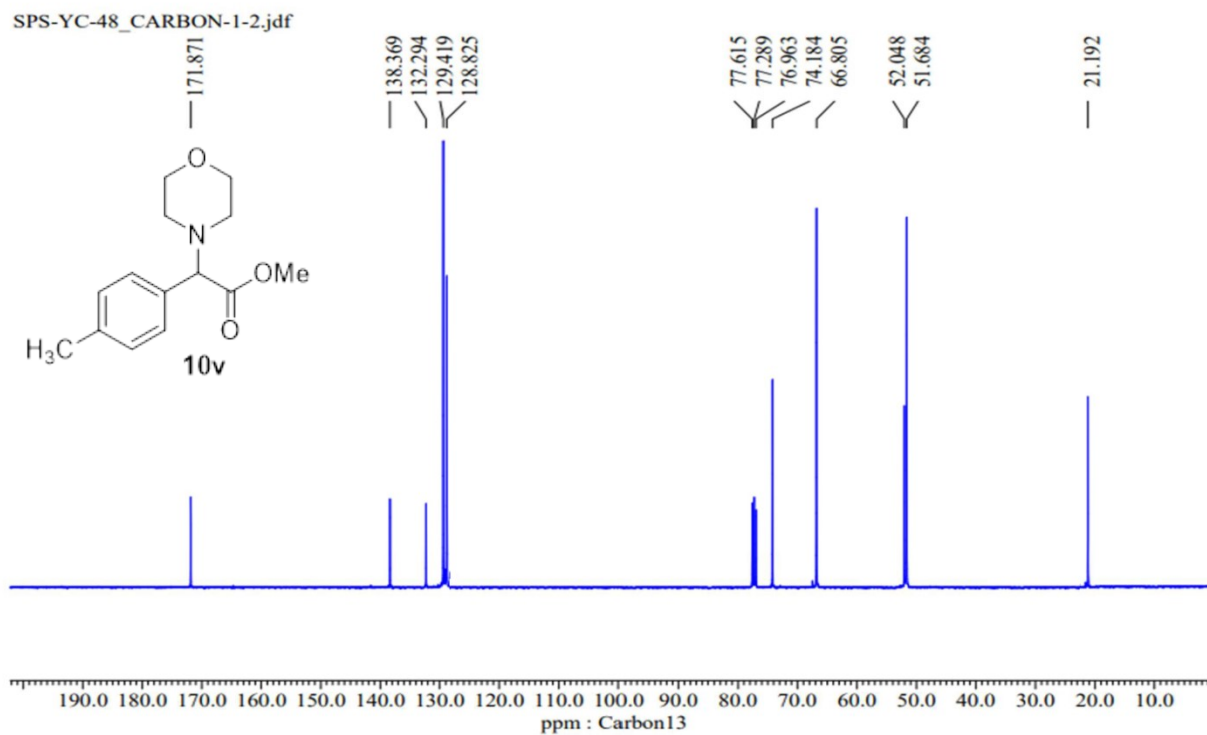
¹H NMR spectrum of **10u**



¹³C NMR spectrum of **10u**

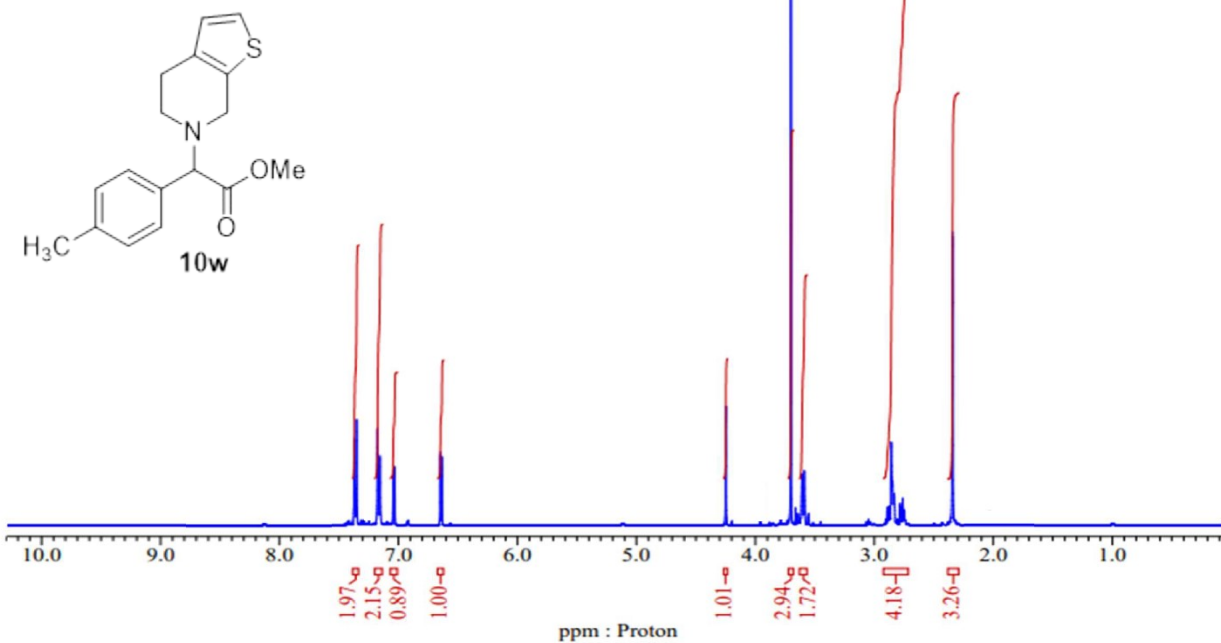


^1H NMR spectrum of **10v**



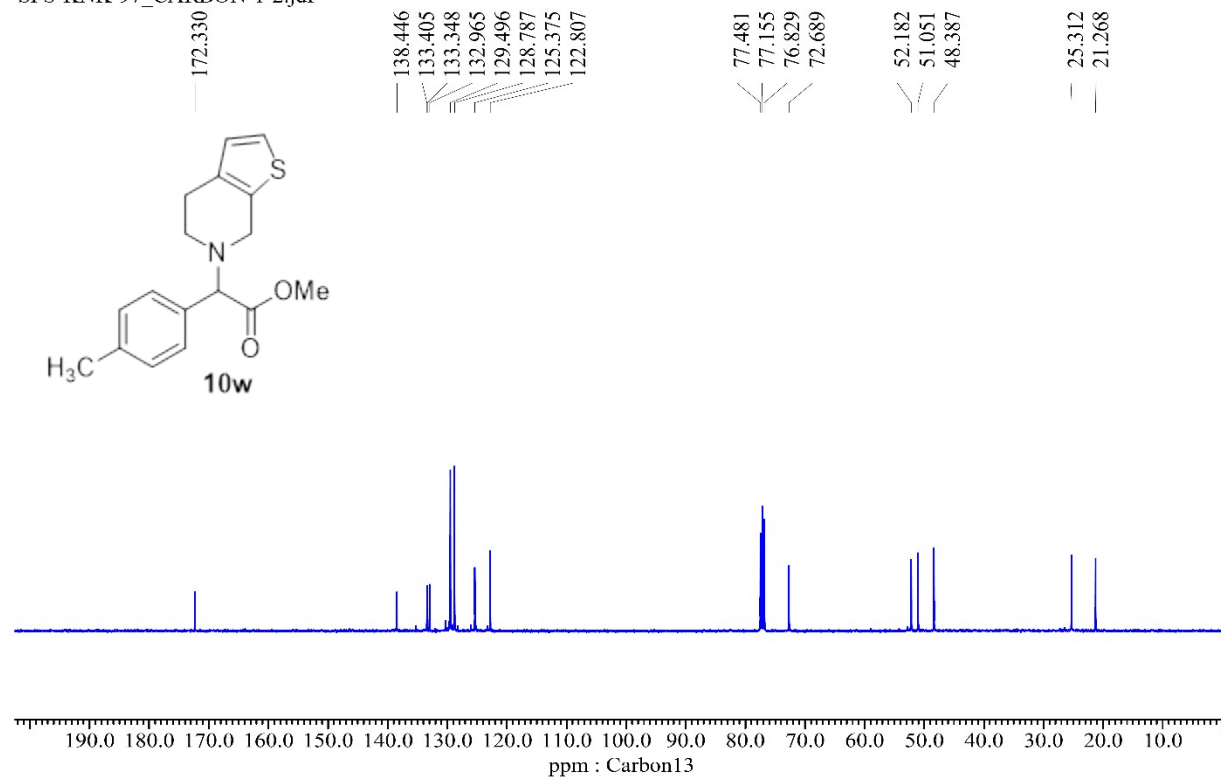
^{13}C NMR spectrum of **10v**

SPS-KNK-97_PROTON-2-2.jdf

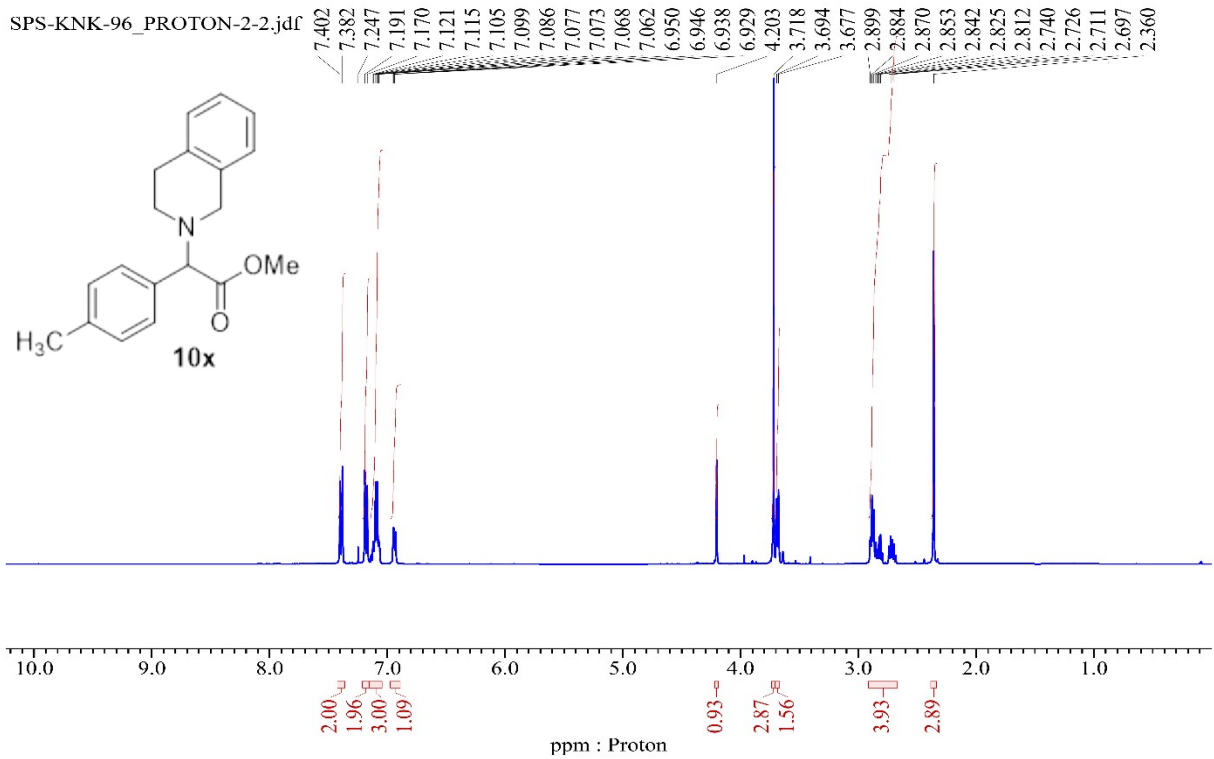


¹H NMR spectrum of **10w**

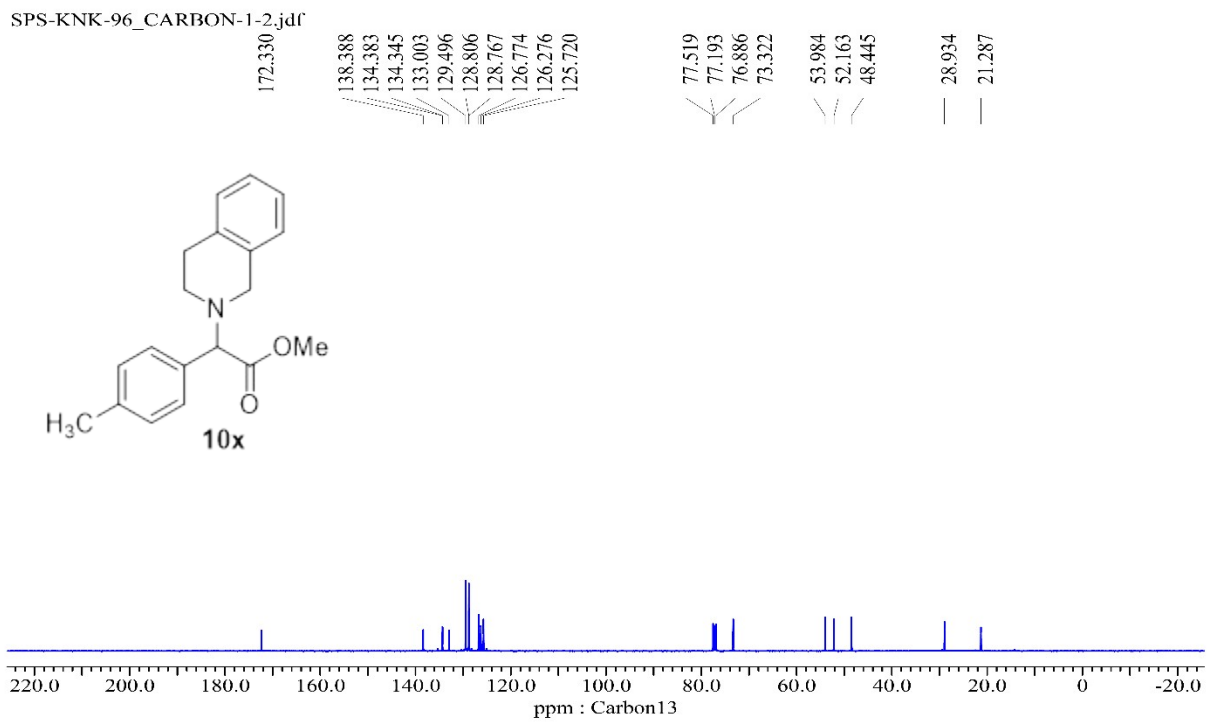
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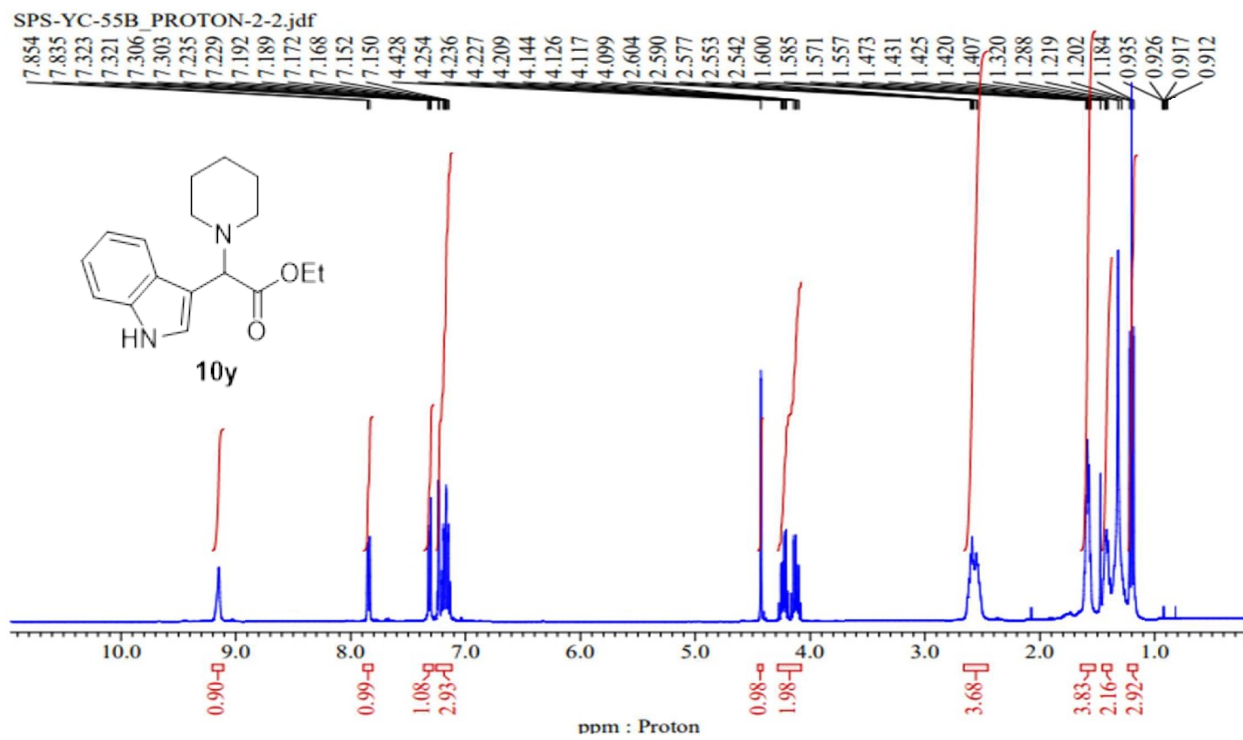
¹³C NMR spectrum of **10w**



¹H NMR spectrum of **10x**

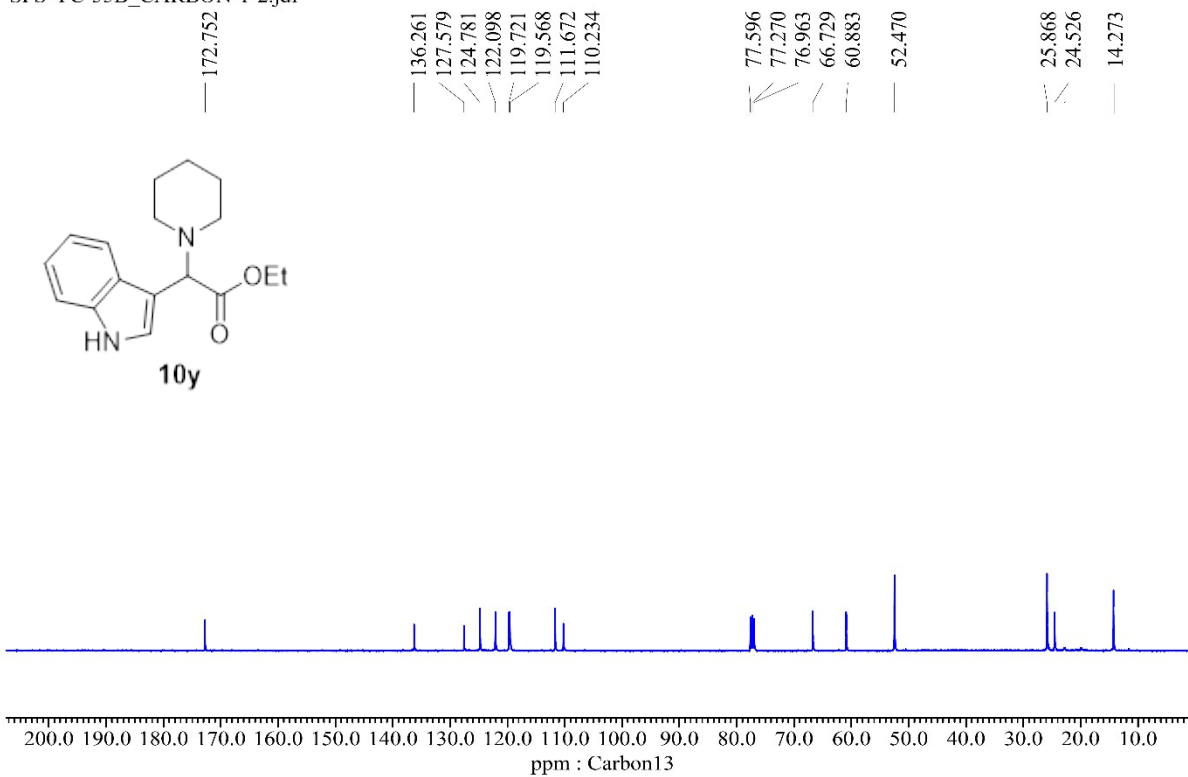


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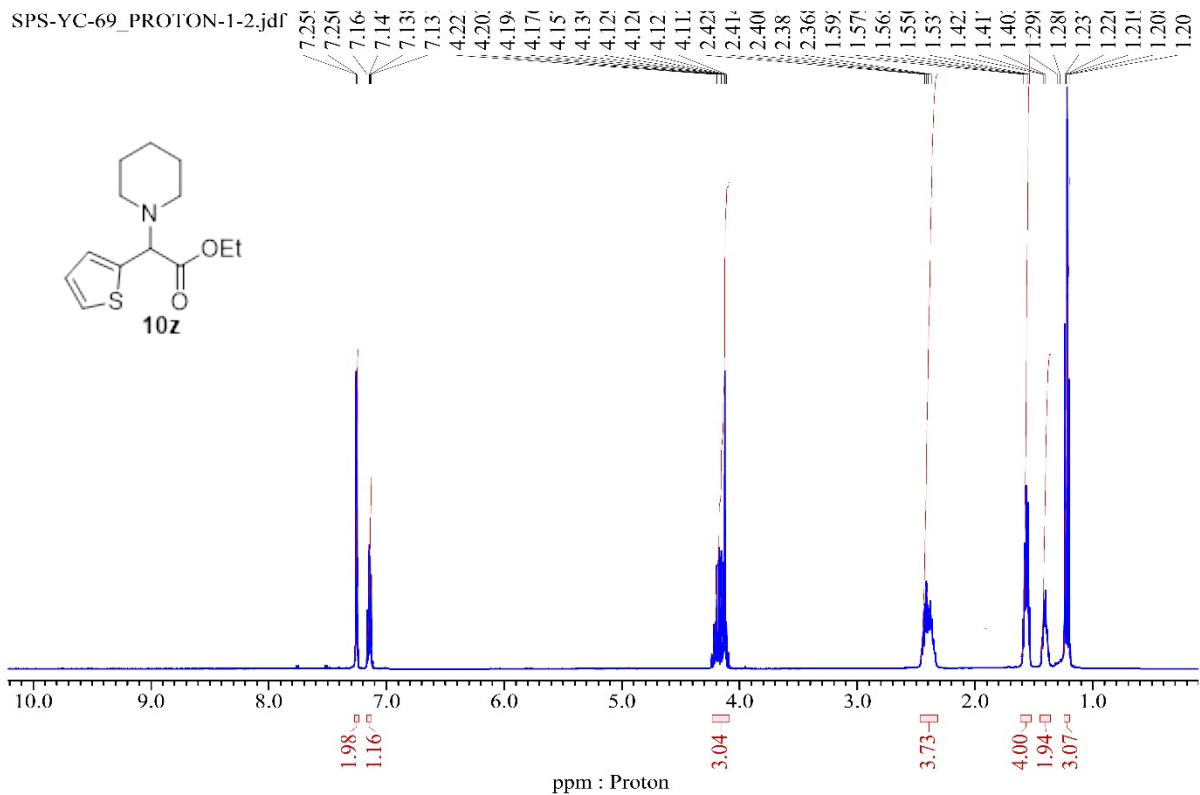


^1H NMR spectrum of **10y**

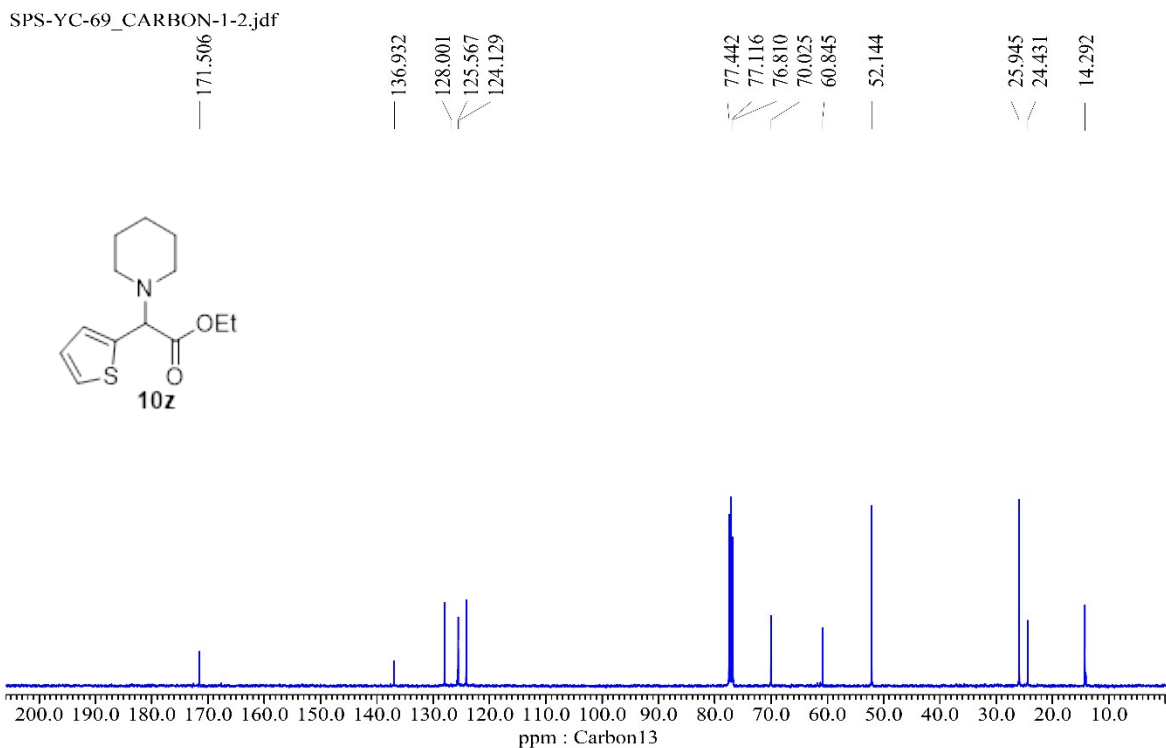
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^{13}C NMR spectrum of **10y**



¹H NMR spectrum of **10z**



¹³C NMR spectrum of **10z**