Supporting Information

$Zn(OAc)_2$-Catalyzed tandem cyclization of isocyanides, α-diazoketones, and anhydrides: a general route to polysubstituted maleimides

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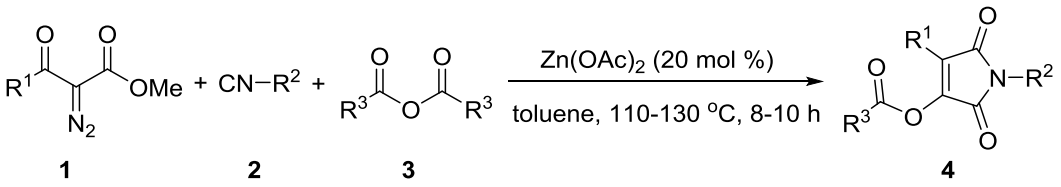
Ⅰ. **General Information**:

All reagents were commercial and were used without further purification. The substrates were prepared according to the previous method reported. Chromatography was carried on flash silica gel (300-400 mesh). All reactions were monitored by TLC, which was performed on percolated aluminum sheets of silica gel 60 (F254). Unless noted, the ^{1}H NMR spectra were recorded at 400 MHz，600 MHz in $CDCl_3$, the ^{13}C NMR spectra were recorded at 151 MHz in $CDCl_3$ with TMS as internal standard. All coupling constants (*J* values) were reported in Hertz (Hz). High-resolution mass spectra (HRMS) were obtained using a Bruker microTOF II focus spectrometer (ESI). The compound **4ka** was glued on a glass fiber. Data were collected at 293 K using graphite-monochromated Mo Kradiation ($\lambda = 0.71073$Å) and IP technique in the range $2.19° < \theta < 27.48°$. Empirical absorption correction was applied. The structures were solved by the direct method and refined by the full-matrix least-squares method on F^2 using the SHELXS 97 crystallographic software package. Anisotropic thermal parameters were used to refine all non-hydrogen atoms. Hydrogen atoms were located from difference Fourier maps.

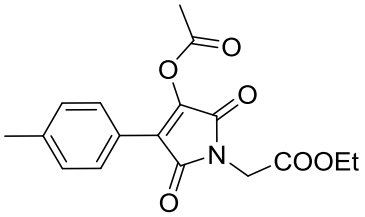
II. Synthetic procedures and analytical data of compounds 4 (4aa as example):



1 2 3 4

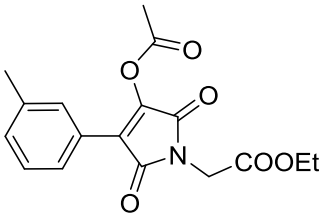
A sealed tube equipped with a magnetic stir bar was charged with **1a** (87.3 mg, 0.4 mmol), **2a** (22.6 mg, 0.2 mmol), **3a** (40.8 mg, 0.4 mmol)，$Zn(OAc)_2$ (7.3 mg, 0.04 mmol), then toluene (2 mL) was added. The reaction was stirred at 110 ℃ for 10 h. After the reaction was complete, the solvent was removed under reduced pressure. The crude residue was purified by silica gel column chromatography (EtOAc/petroleum ether = 1/5, V/V) to afford pure product **4aa** (51.0 mg, 77%) as a white solid.

Ethyl 2-(3-acetoxy-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4aa):



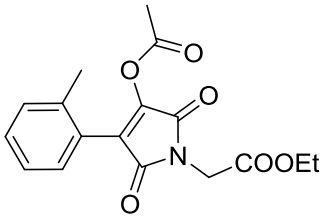
White solid; mp 78-80 °C, 51.0 mg, 77% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 4.33 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 6H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.96, 167.07, 166.65, 164.26, 143.53, 141.17, 129.59, 129.22 (2C), 126.29, 123.83 (2C), 61.97, 38.97, 21.60, 20.44, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{17}H_{17}NNaO_6^+$: 354.0948, found: 354.0957.

Ethyl 2-(3-acetoxy-2,5-dioxo-4-(*m*-tolyl)-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ba):



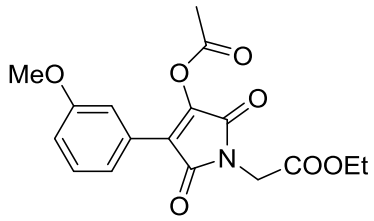
Yellow liquid; 33.7 mg, 51% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.65 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 7.4 Hz, 1H), 4.33 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 2.39 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.87, 167.02, 166.61, 164.17, 144.22, 138.53, 131.43, 129.81, 128.70, 126.48, 126.45, 126.41, 61.98, 39.01, 21.52, 20.43, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{17}H_{17}NNaO_6^+$: 354.0948, found: 354.0957.

Ethyl 2-(3-acetoxy-2,5-dioxo-4-(*o*-tolyl)-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ca):



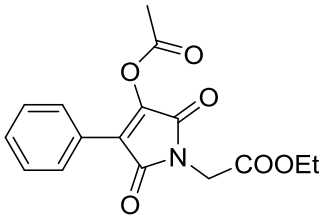
White solid; mp 69-71 ^{o}C, 42.4 mg, 64% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.37 – 7.34 (m, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.23 – 7.20 (m, 1H), 4.34 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 2.27 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.60, 167.00, 166.41, 164.23, 145.98, 137.54, 130.72, 130.18, 129.81, 129.31, 125.83, 125.42, 62.01, 39.18, 20.29, 20.23, 14.08; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{17}H_{17}NNaO_6^+$: 354.0948, found: 354.0952.

Ethyl 2-(3-acetoxy-4-(3-methoxyphenyl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4da):



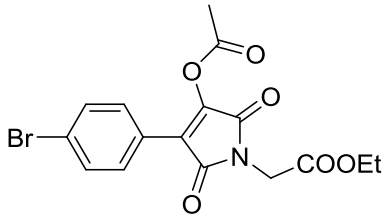
Yellow liquid; 46.5 mg, 67% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.45 – 7.41 (m, 2H), 7.37 (t, *J* = 8.2 Hz, 1H), 7.02 – 6.98 (m, 1H), 4.33 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 2.40 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.74, 166.99, 166.52, 164.04, 159.60, 144.47, 129.83, 127.67, 126.00, 121.73, 116.56, 114.48, 62.00, 55.34, 39.01, 20.44, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{17}H_{17}NNaO_7^+$: 370.0897, found: 370.0905.

Ethyl 2-(3-acetoxy-2,5-dioxo-4-phenyl-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ea):



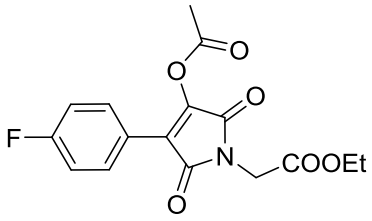
White solid; mp 71-72 ^{o}C, 33.6 mg, 53% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.85 – 7.83 (m, 2H), 7.46 – 7.45 (m, 3H), 4.33 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.79, 166.99, 166.57, 164.10, 144.36, 130.58, 129.28, 128.81 (2C), 126.59, 126.19 (2C), 61.99, 39.02, 20.43, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{16}H_{15}NNaO_6^+$: 340.0792, found: 340.0800.

Ethyl 2-(3-acetoxy-4-(4-bromophenyl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4fa):



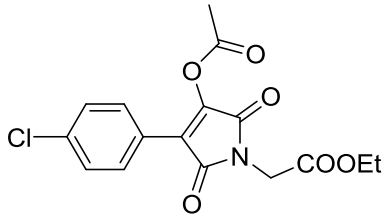
Yellow solid; mp 88-90 ^{o}C, 63.4 mg, 80% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.74 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 4.33 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.50, 166.91, 166.36, 163.82, 144.63, 132.15, 130.67, 125.47 (2C), 125.37, 125.03 (2C), 62.06, 39.04, 20.43, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{16}H_{14}BrNNaO_6^+$: 417.9897, found: 417.9906.

Ethyl 2-(3-acetoxy-4-(4-fluorophenyl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ga):



Yellow liquid; 52.3 mg, 78% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.90 – 7.88 (m, 2H), 7.15 (t, *J* = 8.6 Hz, 2H), 4.33 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.76, 166.97, 166.52, 163.97, 163.82 (d, *J* = 253.2 Hz), 143.98, 131.51 (d, *J* = 8.6 Hz, 2C), 125.07, 122.83 (d, *J* = 3.5 Hz, 2C), 116.15 (d, *J* = 21.9 Hz), 62.04, 39.01, 20.44, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{16}H_{14}FNNaO_6^+$: 358.0697, found: 358.0699.

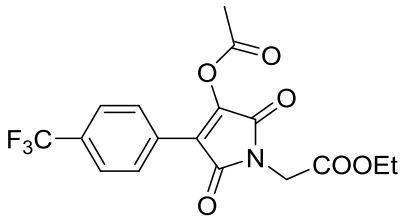
Ethyl 2-(3-acetoxy-4-(4-chlorophenyl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ha):



Yellow solid; mp 78-80 ^{o}C, 52.1 mg, 74% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.82 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 4.33 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H),

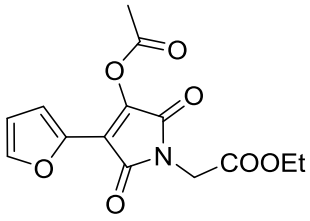
2.41 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.58, 166.92, 166.40, 163.83, 144.55, 136.89, 130.52, 129.19 (2C), 125.05, 124.96 (2C), 62.06, 39.04, 20.43, 14.09; HRMS(ESI-TOF): [M + Na]$^+$ calculated for $C_{16}H_{14}ClNNaO_6^+$: 374.0402, found: 374.0409.

Ethyl 2-(3-acetoxy-2,5-dioxo-4-(4-(trifluoromethyl)phenyl)-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ia):



Yellow liquid; 44.7 mg, 58% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 4.35 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.32, 166.86, 166.31, 163.60, 145.97, 132.03 (q, *J* = 33.22 Hz), 129.92 (d, *J* = 0.6 Hz), 129.56, 125.70 (q, *J* = 3.6 Hz, 2C), 124.60, 123.64 (q, *J* = 272.56 Hz, 2C), 62.12, 39.10, 20.42, 14.08; HRMS(ESI-TOF): [M + Na]$^+$ calculated for $C_{17}H_{14}F_3NNaO_6^+$: 408.0665, found: 408.0669.

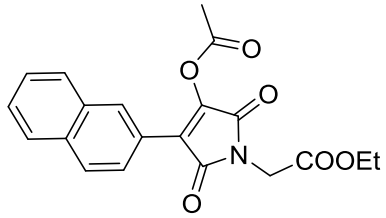
Ethyl 2-(3-acetoxy-4-(furan-2-yl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ja):



Yellow solid; mp 104-106 ^{o}C, 49.8 mg, 81% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.64 – 7.62 (m, 1H), 7.36 (d, *J* = 3.6 Hz, 1H), 6.59 – 6.58 (m, 1H), 4.31 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.95, 166.91, 165.99, 164.63, 146.51, 143.25, 138.43, 118.28, 117.32,

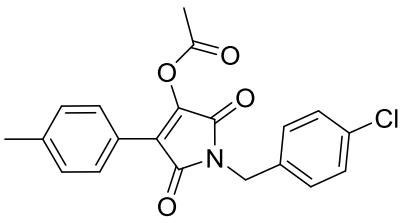
112.62, 62.01, 38.95, 20.43, 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{14}H_{13}NNaO_7^+$: 330.0584, found: 330.0589.

Ethyl 2-(3-acetoxy-4-(naphthalen-2-yl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)acetate (4ka):



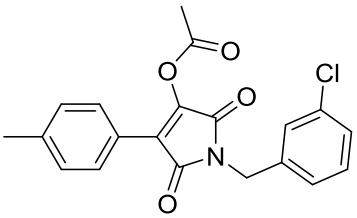
Yellow solid; mp 124-126 ^oC, 44.8 mg, 61% yield; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.48 (s, 1H), 7.92 – 7.88 (m, 2H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.57 – 7.52 (m, 2H), 4.37 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.96, 167.04, 166.63, 164.16, 144.32, 133.84, 132.92, 130.37, 129.14, 128.54, 127.93, 127.71, 126.80, 126.20, 125.16, 124.03, 62.03, 39.07, 20.49, 14.11; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{17}NNaO_6^+$: 390.0948, found: 390.0959.

1-(4-Chlorobenzyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ab):



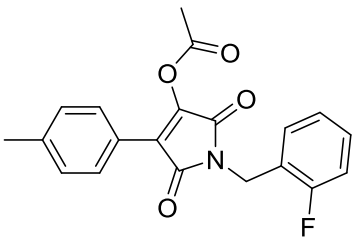
Yellow solid; mp 92-95 ^oC, 60.6 mg, 82% yield; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.25 – 7.22 (m, 2H), 4.68 (s, 2H), 2.38 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.30, 166.75, 164.66, 143.30, 141.11, 134.48, 133.89, 130.00 (2C), 129.57, 129.16, 128.91 (2C), 125.88 (2C), 123.84 (2C), 41.05, 21.57, 20.40; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{16}ClNNaO_4^+$: 392.0660, found: 392.0640.

1-(3-Chlorobenzyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ac):



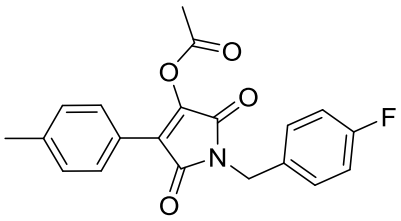
Yellow solid; mp 112-114 ^{o}C, 56.2 mg, 76% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 8.2 Hz, 2H), 7.37 (s, 1H), 7.25 (d, *J* = 8.4 Hz, 5H), 4.70 (s, 2H), 2.39 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.26, 166.74, 164.61, 143.27, 141.13, 137.84, 134.55, 130.04 (2C), 129.57, 129.18, 128.64, 128.20 (2C), 126.68, 125.93, 123.82, 41.15, 21.59, 20.43; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{16}ClNNaO_4^+$: 392.0660, found: 392.0657.

1-(2-Fluorobenzyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ad):



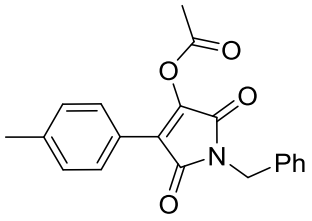
Yellow solid; mp 71-72 ^{o}C, 43.1 mg, 61% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 8.2 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.28 – 7.23 (m, 3H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.08 – 7.03 (m, 1H), 4.83 (s, 2H), 2.39 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.19, 166.76, 164.55, 160.57 (d, *J* = 248.09 Hz), 143.29, 141.06, 130.18 (d, *J* = 3.62 Hz), 129.69 (d, *J* = 8 Hz), 129.55 (2C), 129.19, 125.84, 124.28 (d, *J* = 3.62 Hz), 123.88 (2C), 122.84 (d, *J* = 14.65 Hz), 115.60 (d, *J* = 21.44 Hz), 35.40 (d, *J* = 4.83 Hz), 21.58, 20.43; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{16}FNNaO_4^+$: 376.0956, found: 376.0948.

1-(4-Fluorobenzyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ae):



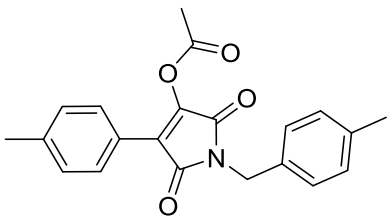
Yellow solid; mp 64-66 ^{o}C, 53.7 mg, 76% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.02 – 6.98 (m, 2H), 4.69 (s, 2H), 2.38 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.34, 166.76, 164.70, 162.43 (d, *J* = 247.64 Hz), 143.28, 141.07, 131.87 (d, *J* = 3.02 Hz), 130.47 (d, *J* = 7.55 Hz, 2C), 129.55 (2C), 129.15, 125.84, 123.85 (2C), 115.61 (d, *J* = 22.65 Hz, 2C), 41.02, 21.57, 20.41; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{16}FNNaO_4^+$: 376.0956, found: 376.0959.

1-Benzyl-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4af):



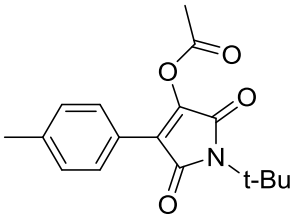
Yellow liquid; 50.3 mg, 75% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.37 (m, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.25 – 7.22 (m, 2H), 4.73 (s, 2H), 2.37 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.39, 166.77, 164.77, 143.33, 140.98, 136.03, 129.54, 129.17 (2C), 128.73, 128.53 (2C), 127.91 (2C), 125.78 (2C), 123.95, 41.75, 21.57, 20.41; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{17}NNaO_4^+$: 358.1050, found: 358.1043.

1-(4-Methylbenzyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ag):



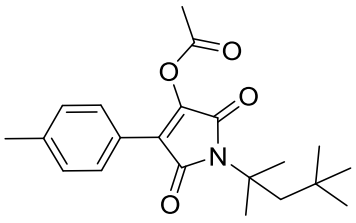
Yellow solid; mp 124-126 ^{o}C, 55.9 mg, 80% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 4.69 (s, 2H), 2.39 (s, 6H), 2.31 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.40, 166.75, 164.78, 143.32, 140.92, 137.65, 133.08, 129.51 (2C), 129.38, 129.15, 128.56 (2C), 125.74 (2C), 123.96 (2C), 41.51, 21.56, 21.13, 20.42; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{21}H_{19}NNaO_4^+$: 372.1206, found: 372.1208.

1-(Tert-butyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ah):



Yellow solid; mp 76-78 ^{o}C, 54.2 mg, 90% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.66 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 2.38 (s, 3H), 2.36 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 169.79, 166.99, 165.91, 142.92, 140.54, 129.41, 129.23 (2C), 124.83, 123.91 (2C), 58.21, 29.03 (3C), 21.54, 20.42; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{17}H_{19}NNaO_4^+$: 324.1206, found: 324.1198.

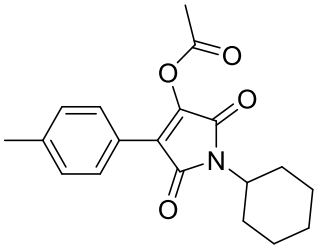
2,5-Dioxo-4-(*p*-tolyl)-1-(2,4,4-trimethylpentan-2-yl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ai):



Yellow liquid; 61.5 mg, 86% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.67 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 3H), 2.36 (s, 3H), 1.92 (s, 2H), 1.71 (s, 6H), 0.97 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 170.26, 166.92, 166.38, 143.19, 140.56, 129.40, 129.25 (2C), 124.81, 123.91 (2C), 61.60, 51.04, 31.54, 31.04 (2C), 29.98 (2C),

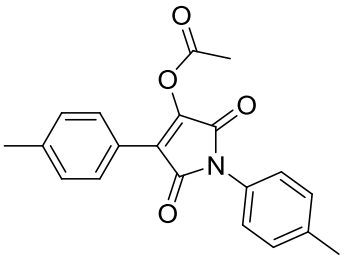
21.54, 20.39; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{21}H_{27}NNaO_4^+$: 380.1832, found: 380.1828.

1-(Cyclohexylmethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4aj):



Yellow solid; mp 86-88 ^oC, 58.3 mg, 89% yield; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 4.00 – 3.95 (m, 1H), 2.39 (s, 3H), 2.38 (s, 3H), 2.11 –2.04 (m, 2H), 1.84 (d, *J* = 13.4 Hz, 2H), 1.75 (d, *J* = 12.7 Hz, 2H), 1.67 (d, *J* = 12.8 Hz, 1H), 1.37 – 1.29 (m, 2H), 1.23 (ddd, *J* = 16.3, 9.7, 3.1 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.65, 166.84, 164.99, 143.14, 140.70, 129.48, 129.14 (2C), 125.14, 124.05 (2C), 51.17, 30.07 (2C), 25.98, 25.11 (2C), 21.55, 20.45; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{19}H_{21}NNaO_4^+$: 350.1363, found: 350.1358.

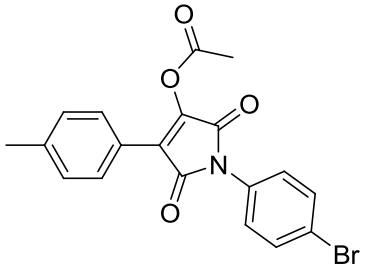
2,5-Dioxo-1,4-di-*p*-tolyl-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4ak):



Yellow solid; mp 102-104 ^oC, 22.8 mg, 34% yield; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.78 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 6H), 2.41 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.69, 166.81, 163.98, 143.31, 141.14, 138.01, 129.74, 129.61 (2C), 129.31, 128.37, 126.09 (2C), 125.74 (2C), 123.84 (2C),

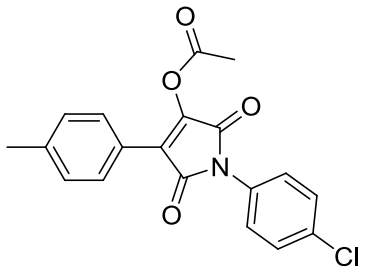
21.60, 21.18, 20.49; HRMS(ESI-TOF): [M + Na]$^+$ calculated for $C_{20}H_{17}NNaO_4^+$: 358.1050, found: 358.1040.

1-(4-Bromophenyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4al):



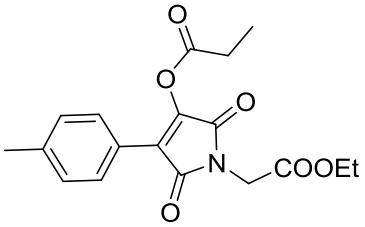
Yellow solid; mp 113-115 ^{o}C, 35.2 mg, 44% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.34 – 7.31 (m, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 2.41 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.19, 166.75, 163.48, 143.31, 141.40, 132.25, 130.15, 129.68 (2C), 129.32, 127.46, 125.96 (2C), 123.60 (2C), 121.59 (2C), 21.63, 20.47; HRMS(ESI-TOF): [M + Na]$^+$ calculated for $C_{19}H_{14}BrNNaO_4^+$: 421.9998, found: 421.9997.

1-(4-Chlorophenyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl acetate (4am):



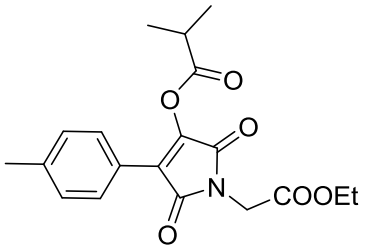
Yellow solid; mp 106-107 ^{o}C, 28.4 mg, 40% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.2 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.39 – 7.36 (m, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.27, 166.77, 163.56, 143.30, 141.40, 133.60, 129.68, 129.61 (2C), 129.32, 129.28, 127.21 (2C), 125.94 (2C), 123.61 (2C), 21.62, 20.47; HRMS(ESI-TOF): [M + Na]$^+$ calculated for $C_{19}H_{14}ClNNaO_4^+$: 378.0504, found: 378.0497.

1-(2-Ethoxy-2-oxoethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl propionate (4ma):



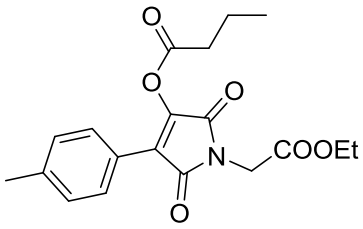
Yellow liquid; 53.1 mg, 77% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 4.32 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.39 (s, 3H), 1.29 – 1.27 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 170.32, 168.00, 167.07, 164.30, 143.74, 141.07, 129.54, 129.20 (2C), 126.14, 123.89 (2C), 61.96, 38.96, 27.29, 21.59, 14.09, 8.84; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{18}H_{19}NNaO_6^+$: 368.1105, found: 368.1114.

1-(2-Ethoxy-2-oxoethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl isobutyrate (4na):



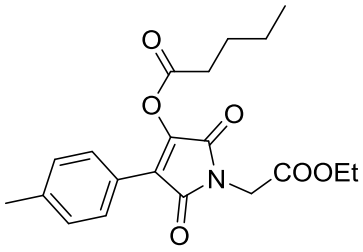
Yellow liquid; 53.9 mg, 75% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 4.32 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.93 – 2.89 (m, 1H), 2.38 (s, 3H), 1.35 (s, 3H), 1.34 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 172.99, 168.01, 167.09, 164.26, 143.94, 141.02, 129.50, 129.19 (2C), 126.08, 123.93 (2C), 61.94, 38.93, 33.97, 21.57, 18.71 (2C), 14.09; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{19}H_{21}NNaO_6^+$: 382.1261, found: 382.1260.

1-(2-Ethoxy-2-oxoethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl butyrate (4oa):



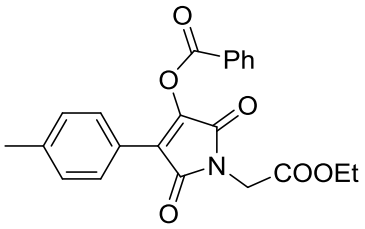
Yellow liquid; 57.5 mg, 80% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 4.32 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.64 (t, *J* = 7.3 Hz, 2H), 2.39 (s, 3H), 1.80 (h, *J* = 7.4 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 169.48, 168.01, 167.07, 164.28, 143.77, 141.05, 129.52, 129.19 (2C), 126.15, 123.91 (2C), 61.93, 38.95, 35.61, 21.56, 18.26, 14.07, 13.45; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{19}H_{21}NNaO_6^+$: 382.1261, found: 382.1263.

1-(2-Ethoxy-2-oxoethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl pentanoate (4pa):



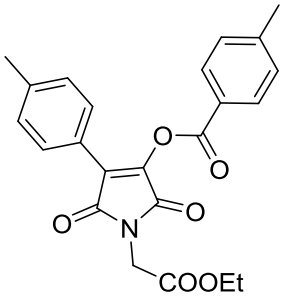
Yellow liquid; 58.3 mg, 78% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 4.32 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.39 (s, 3H), 1.75 (p, *J* = 7.5 Hz, 2H), 1.45 (h, *J* = 7.4 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 169.63, 168.01, 167.07, 164.28, 143.79, 141.05, 129.51, 129.19 (2C), 126.14, 123.92 (2C), 61.93, 38.95, 33.49, 26.70, 22.03, 21.56, 14.08, 13.62; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{20}H_{23}NNaO_6^+$: 396.1418, found: 396.1425.

1-(2-Ethoxy-2-oxoethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl benzoate (4qa):



Yellow liquid; 55.9 mg, 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.19 (d, *J* = 7.3 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 4.37 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.02, 167.10, 164.22, 162.71, 143.81, 141.17, 134.67, 130.76, 129.61 (2C), 129.26, 128.91, 127.30 (2C), 126.61 (2C), 123.92 (2C), 61.98, 39.03, 21.58, 14.11; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{22}H_{19}NNaO_6^+$: 416.1105, found: 416.1109.

1-(2-Ethoxy-2-oxoethyl)-2,5-dioxo-4-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl 4-methyl benzoate (4ra) :



Yellow solid; mp 116-117 ^{o}C, 57.0 mg, 70% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.07 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 4.36 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 3H), 2.36 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.08, 167.12, 164.28, 162.74, 145.81, 143.97, 141.07, 130.82, 129.62 (2C), 129.57, 129.24 (2C), 126.49 (2C), 124.53 (2C), 124.00, 61.95, 39.01, 21.87, 21.55, 14.10; HRMS(ESI-TOF): $[M + Na]^+$ calculated for $C_{23}H_{21}NNaO_6^+$: 430.1261, found: 430.1267.

III. ORTEP Drawing of Compound 4ka:

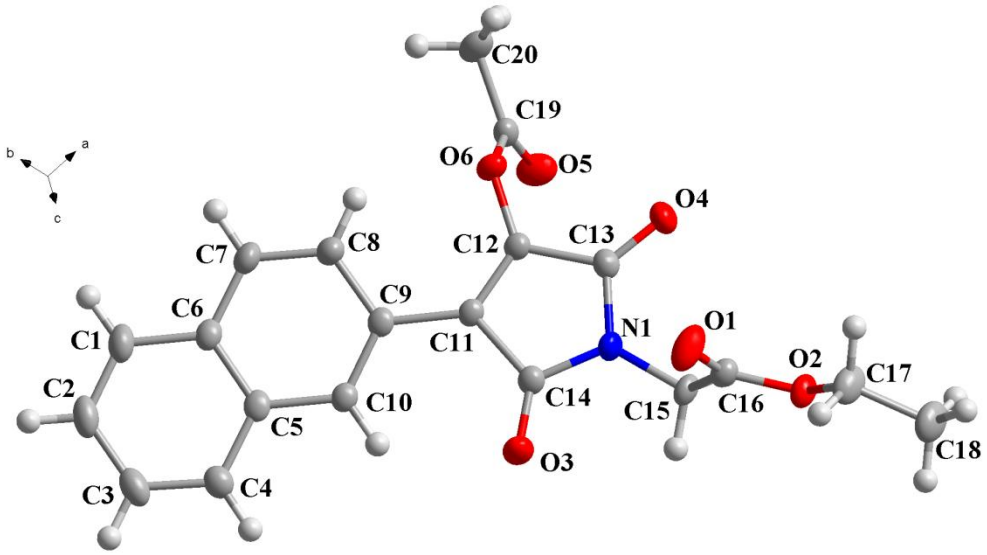


Figure 1. Crystal ORTEP drawing of compound 4ka

IV. Copies of ^{1}H NMR and ^{13}C NMR Spectra of 4:

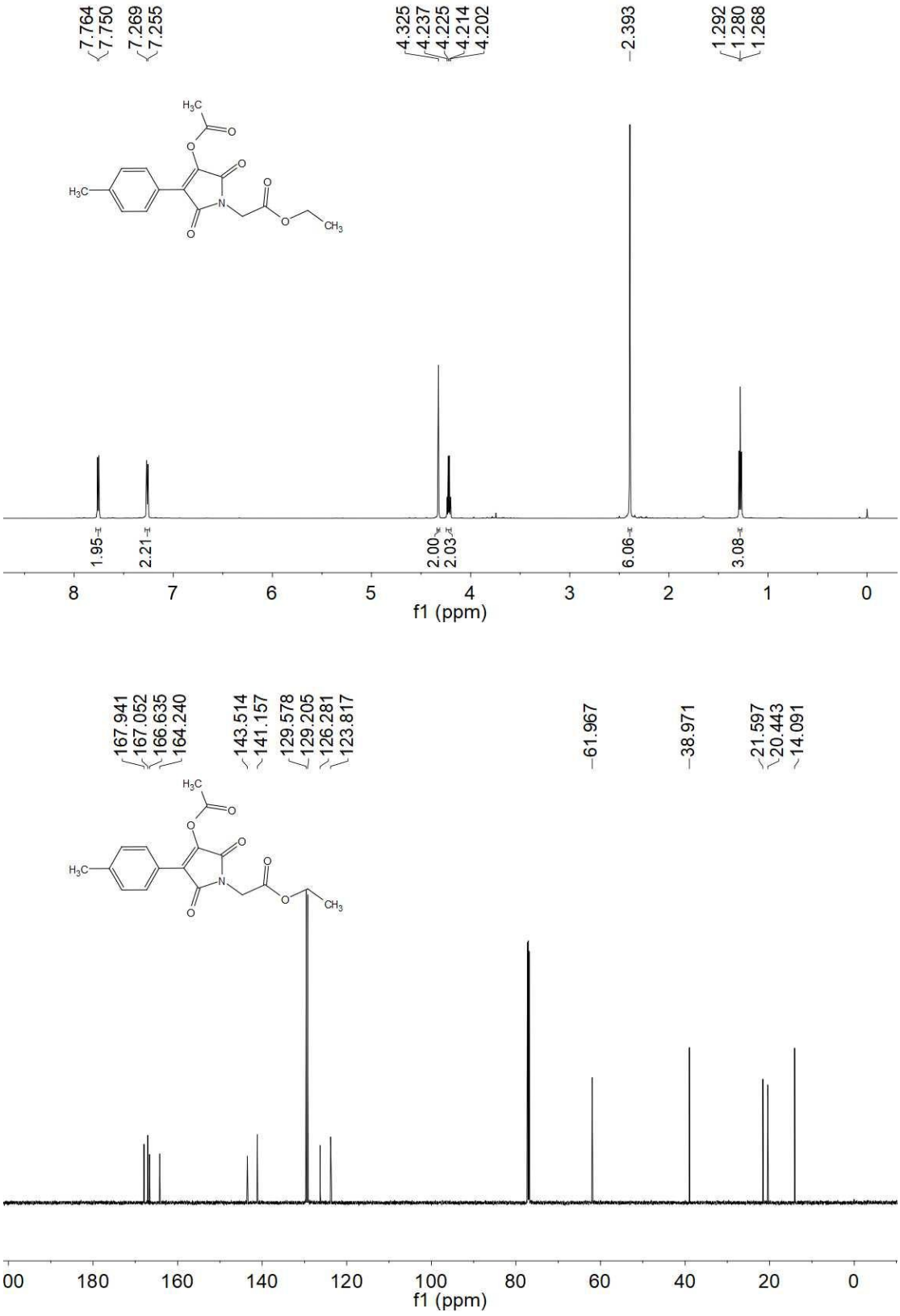


Figure 2. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4aa**

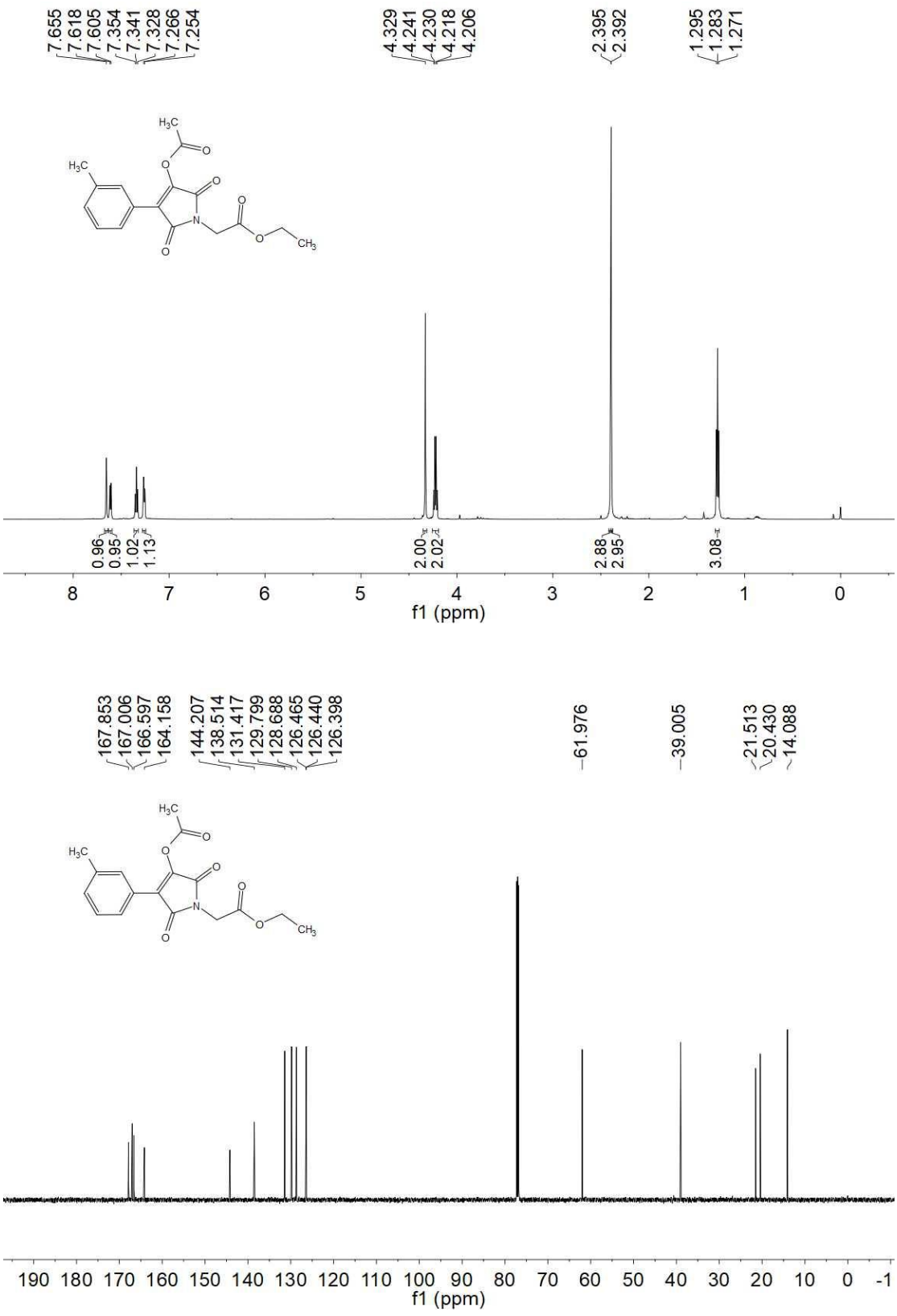


Figure 3. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ba**

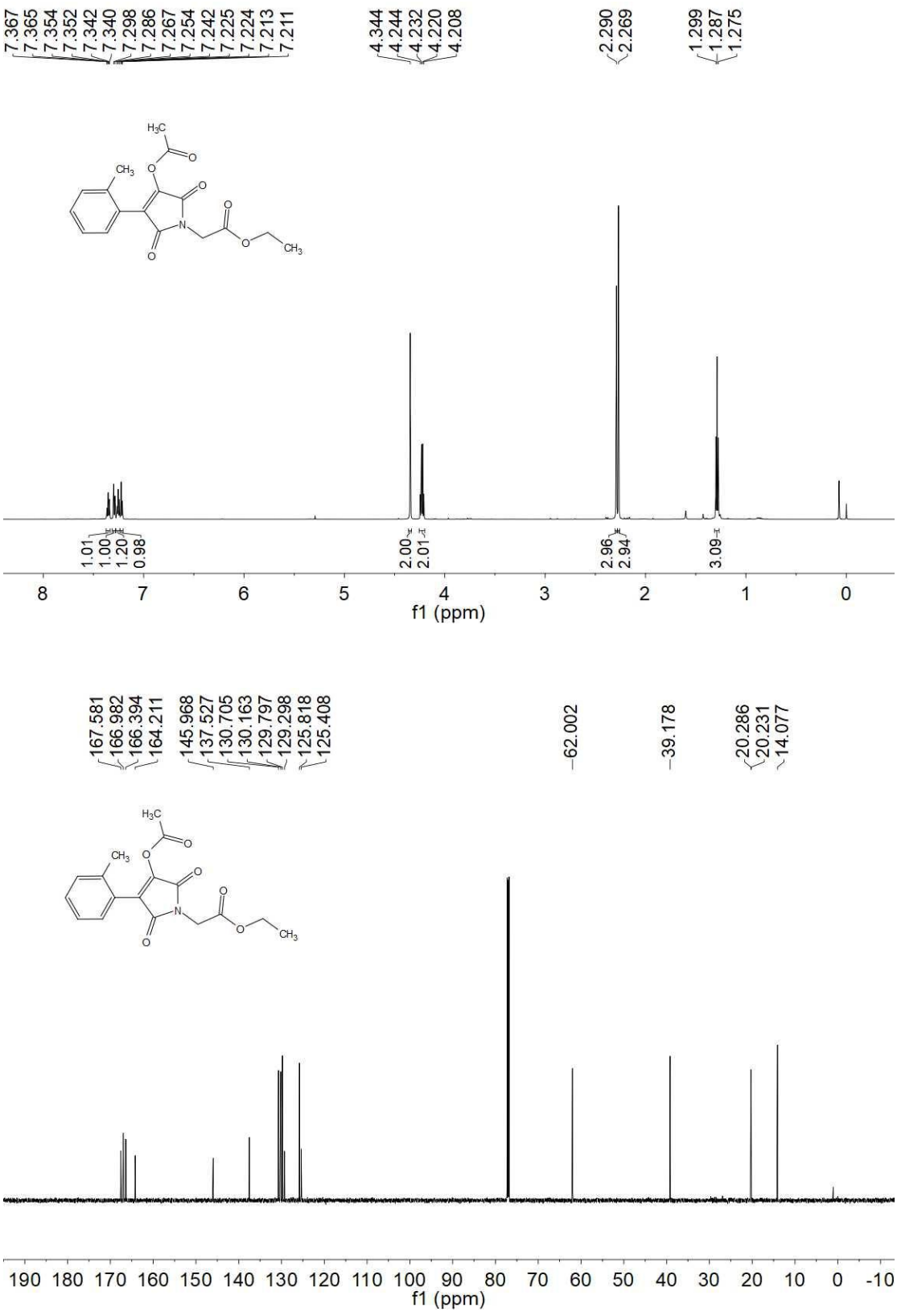


Figure 4. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ca**

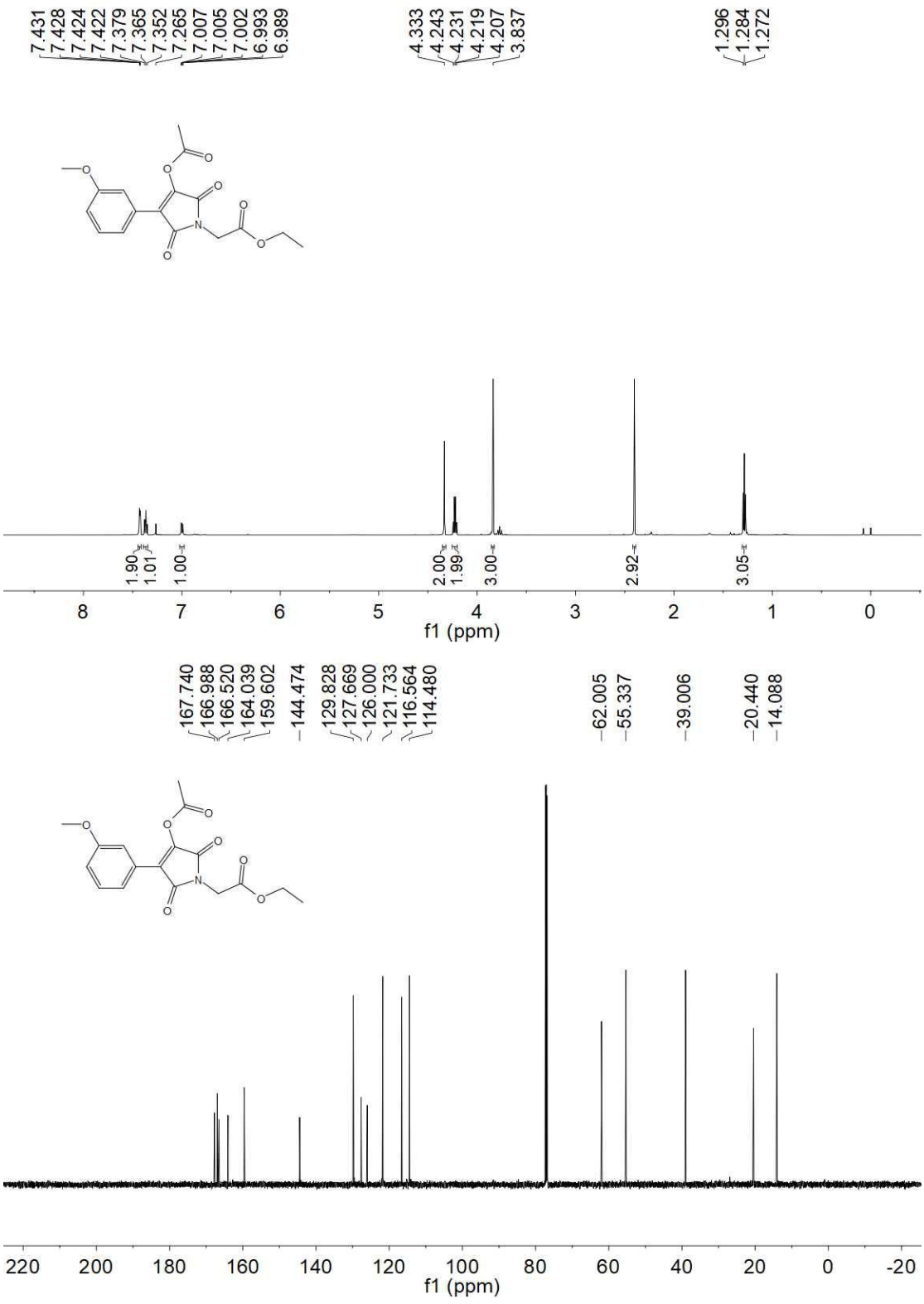


Figure 5. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4da**

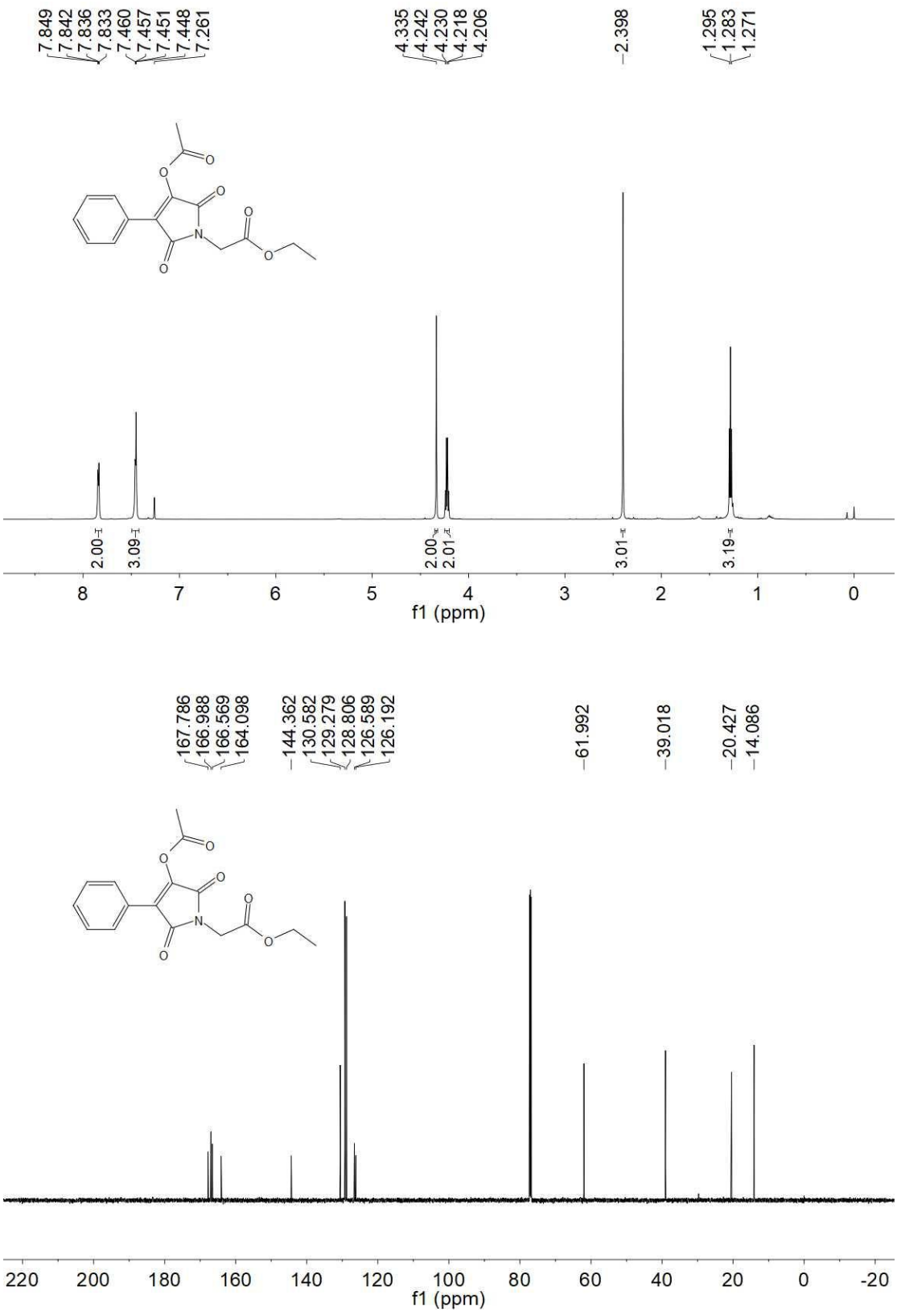


Figure 6. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ea**

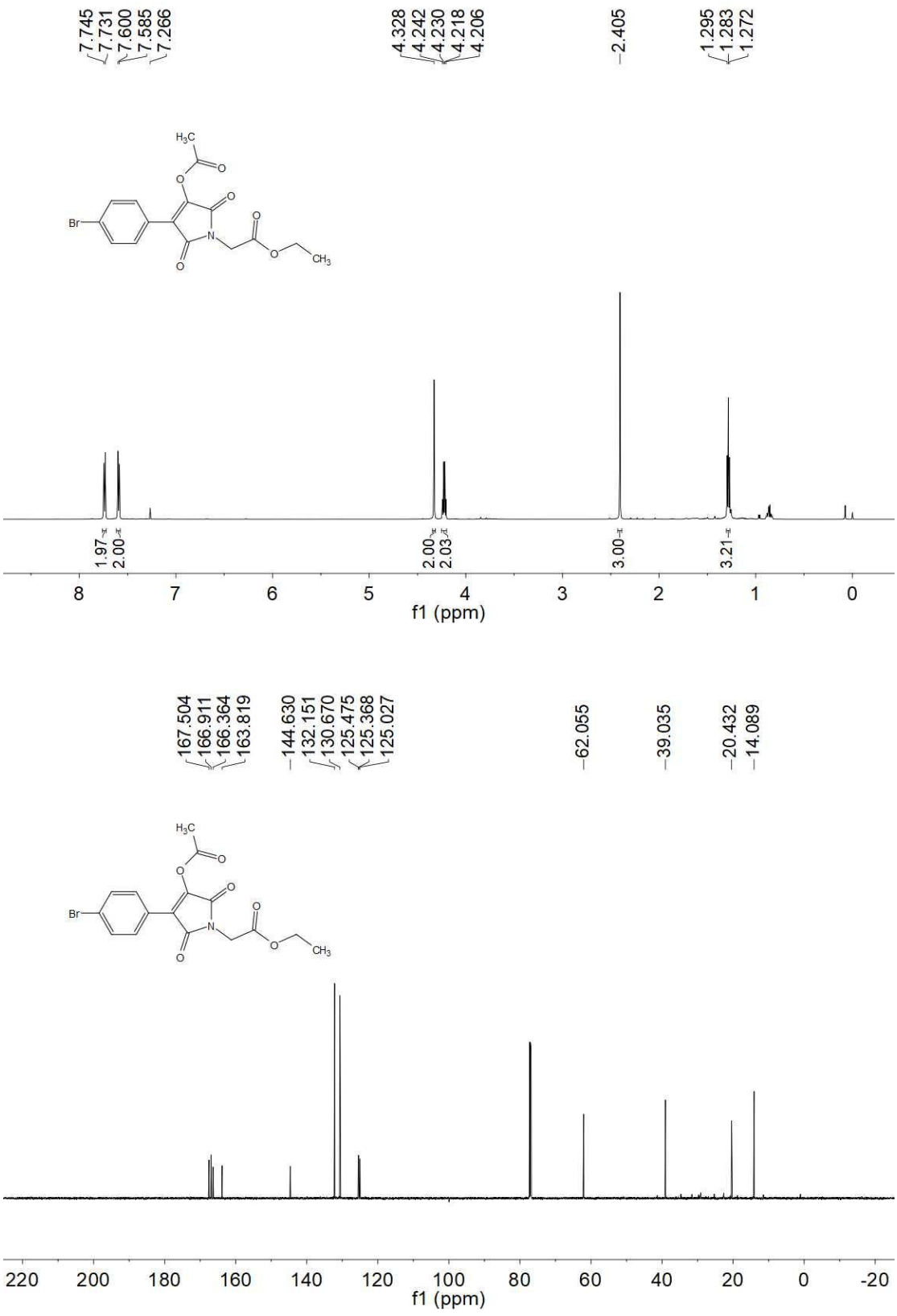


Figure 7. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4fa**

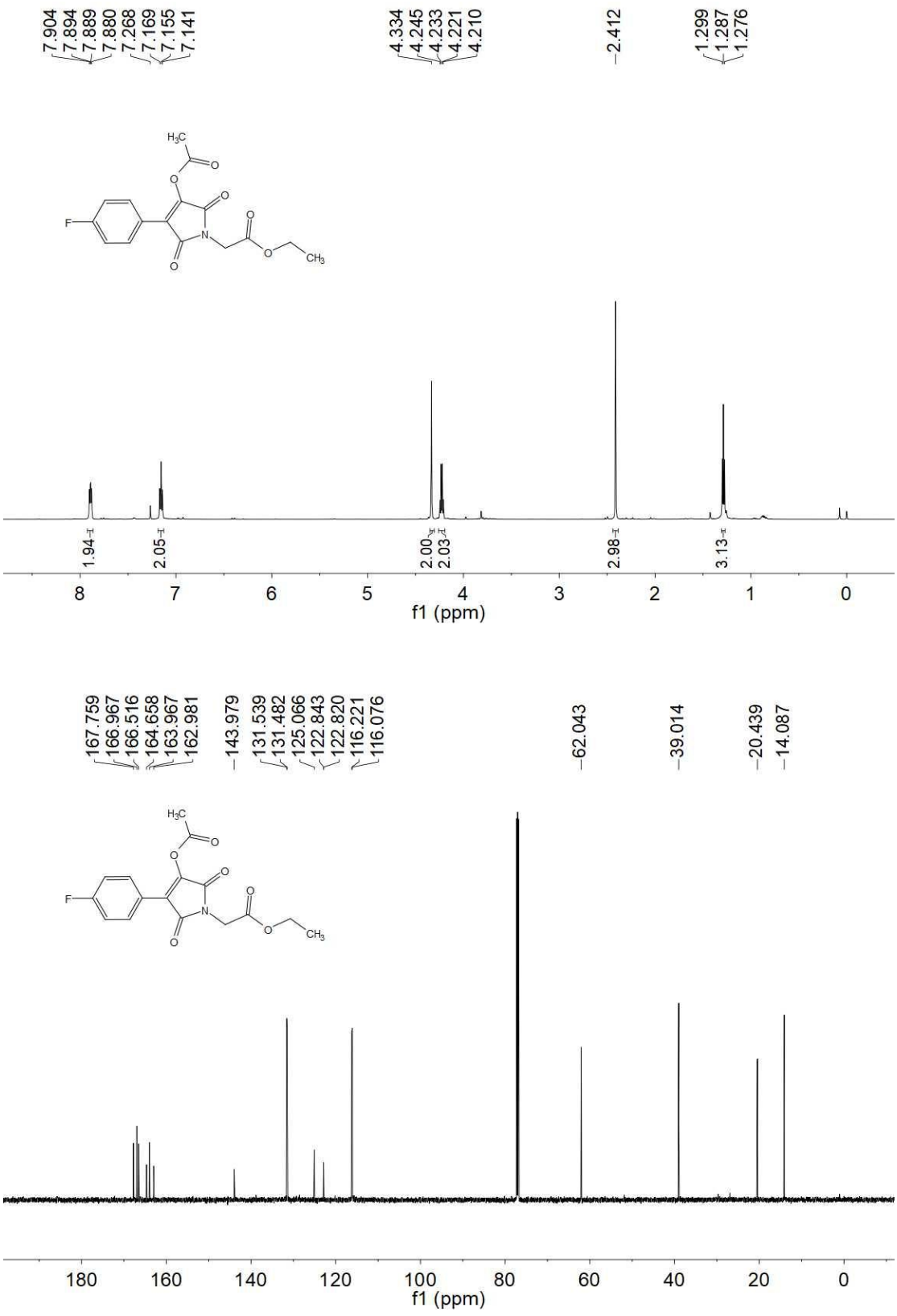


Figure 8. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ga**

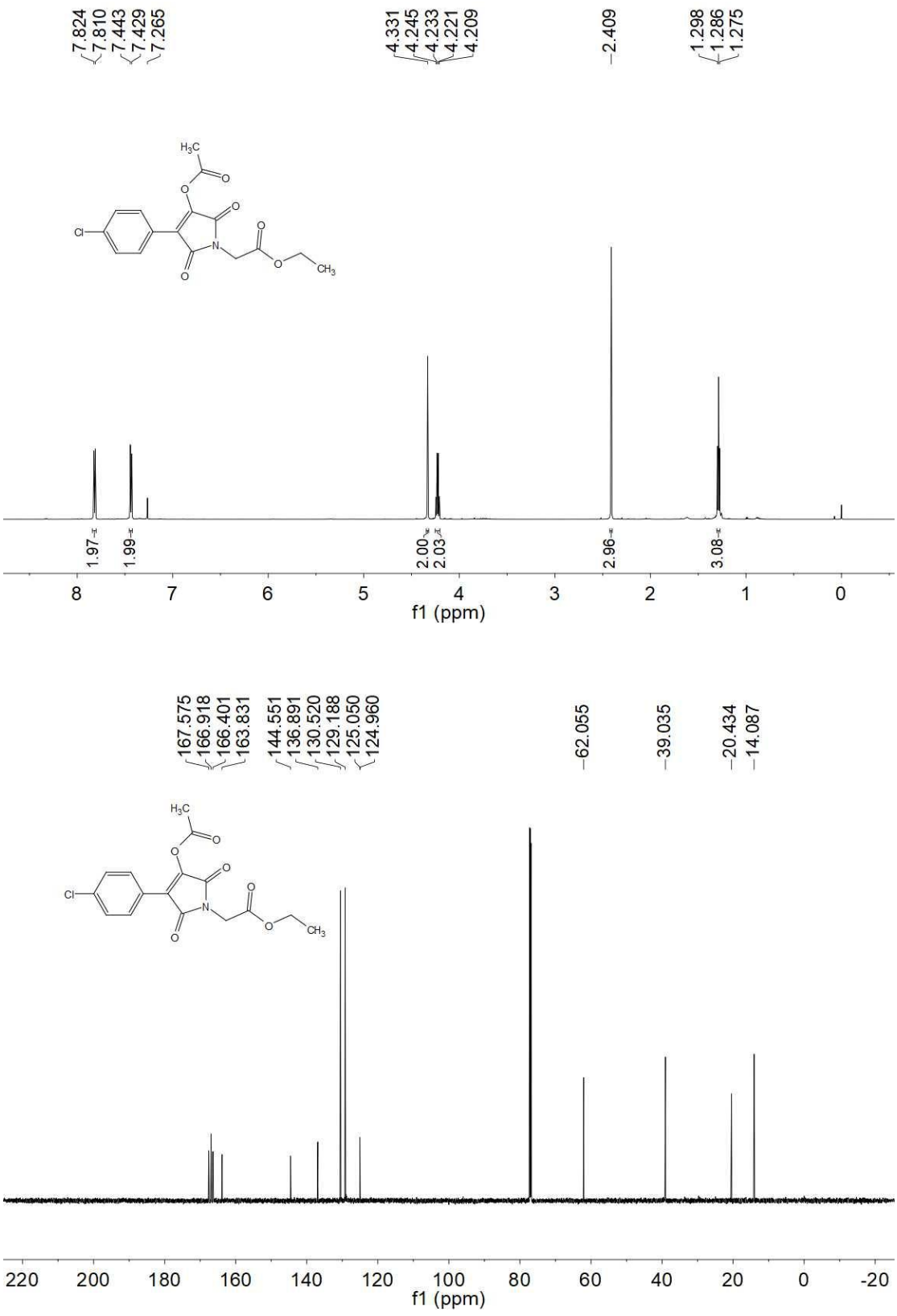


Figure 9. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ha**

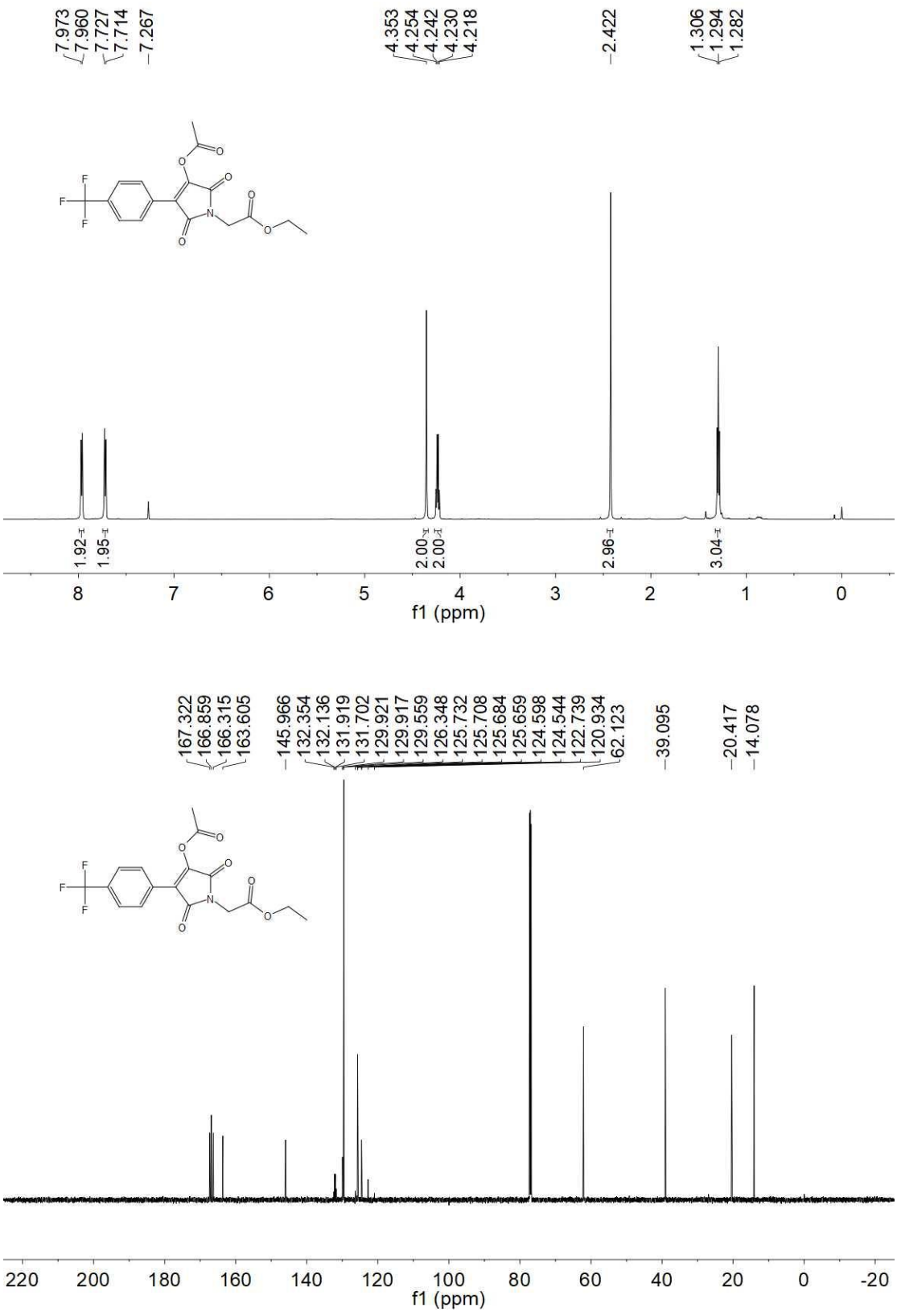


Figure 10. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ia**

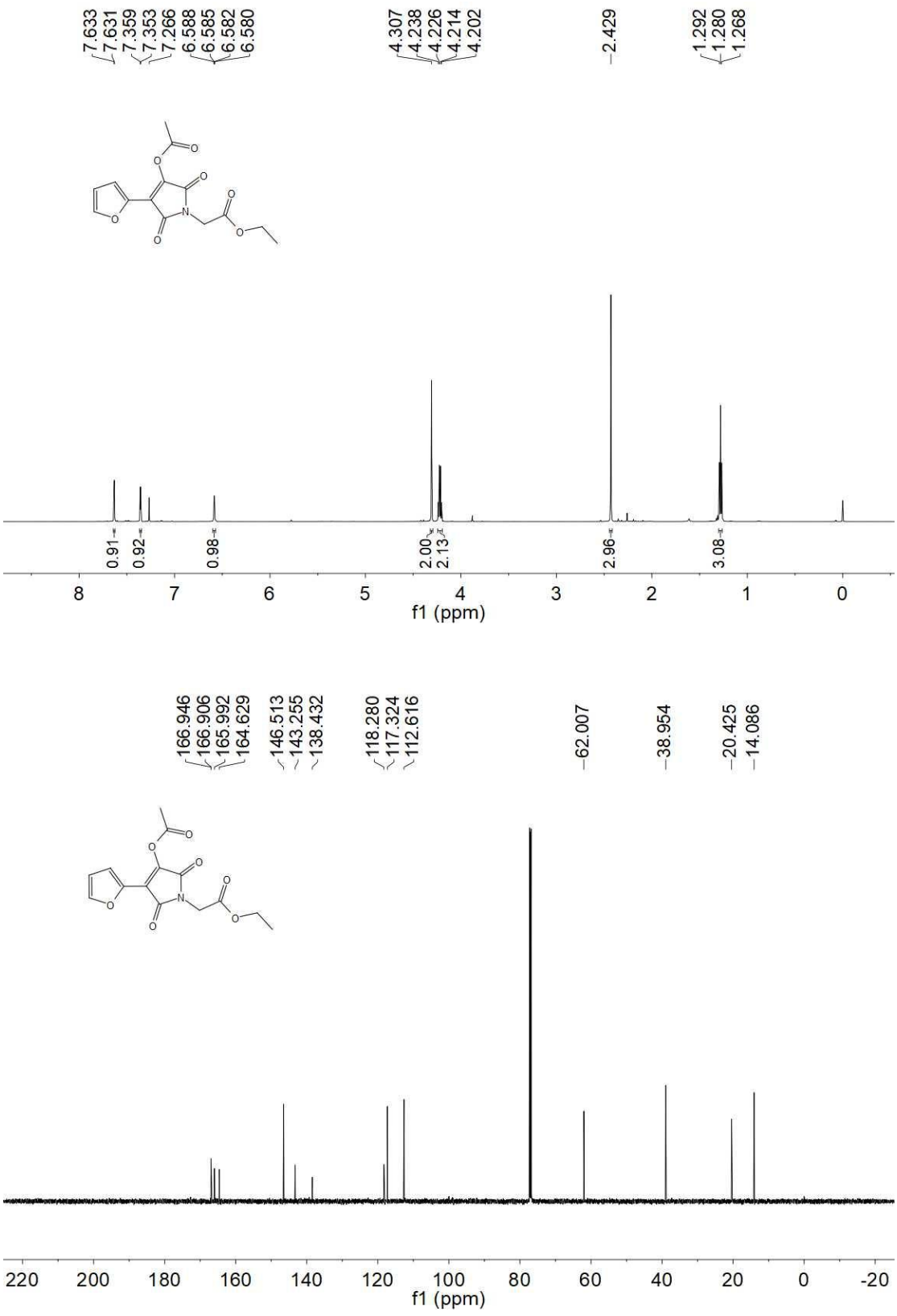


Figure 11. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ja**

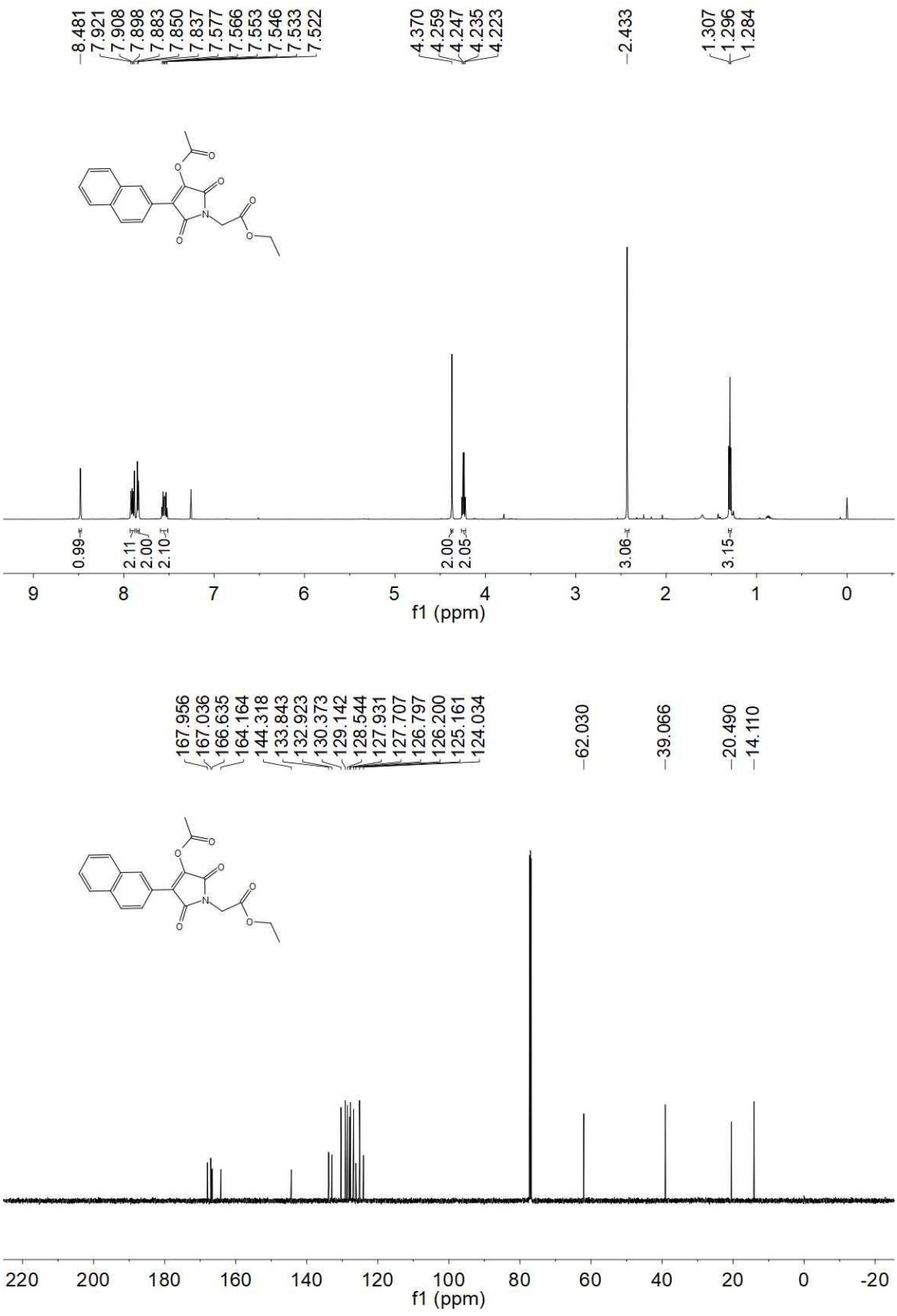


Figure 12. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ka**

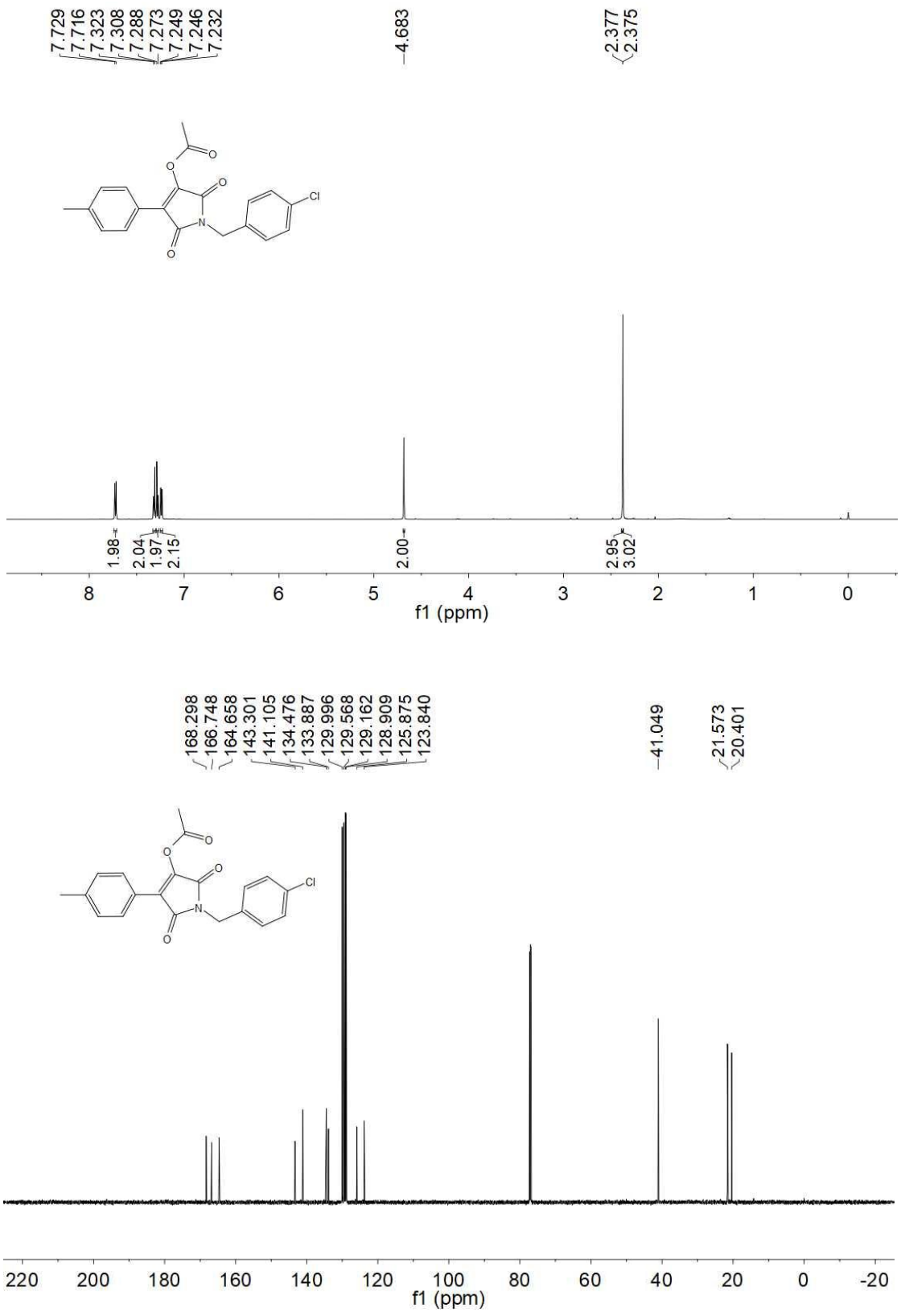


Figure 13. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ab**

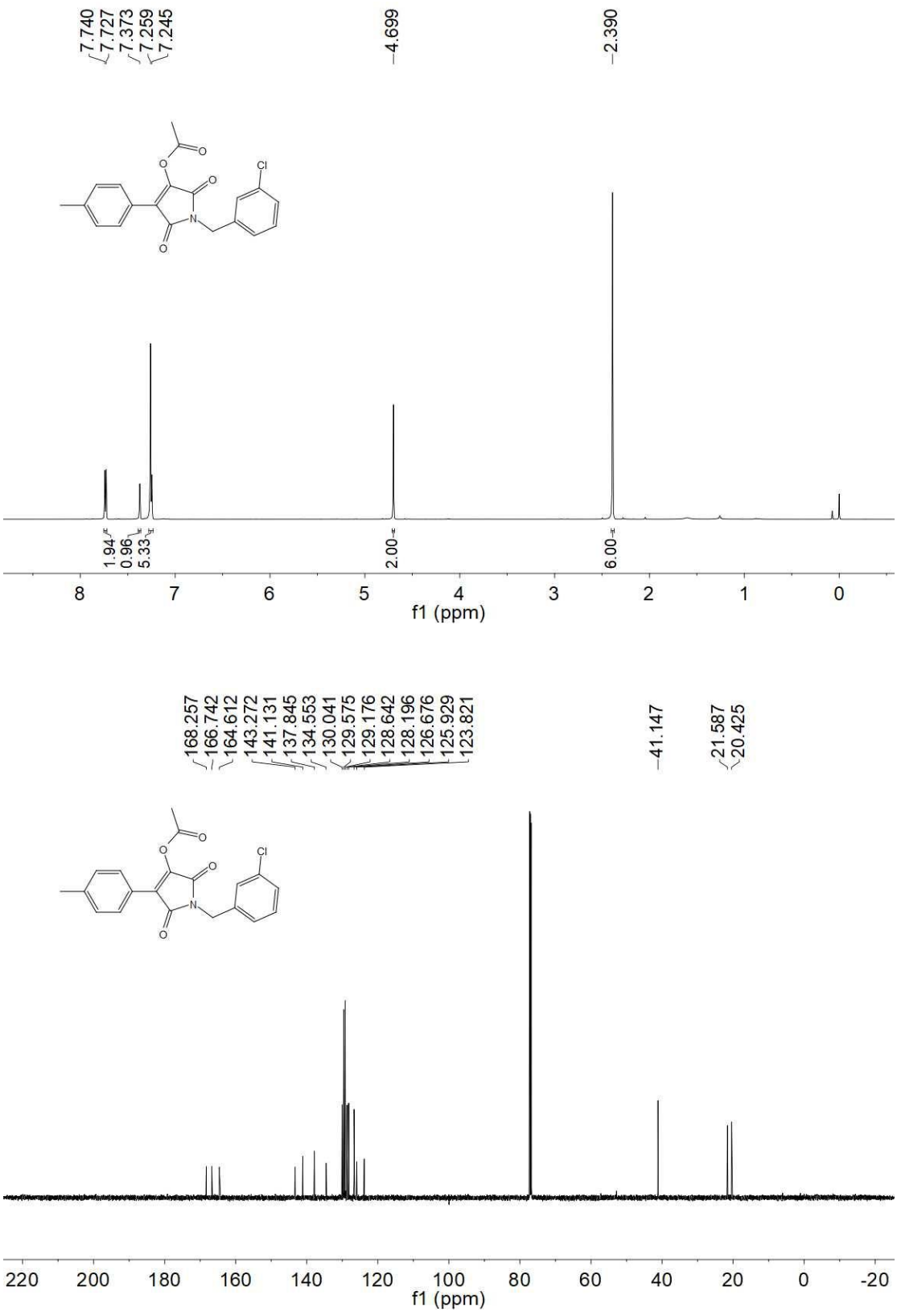


Figure 14. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ac**

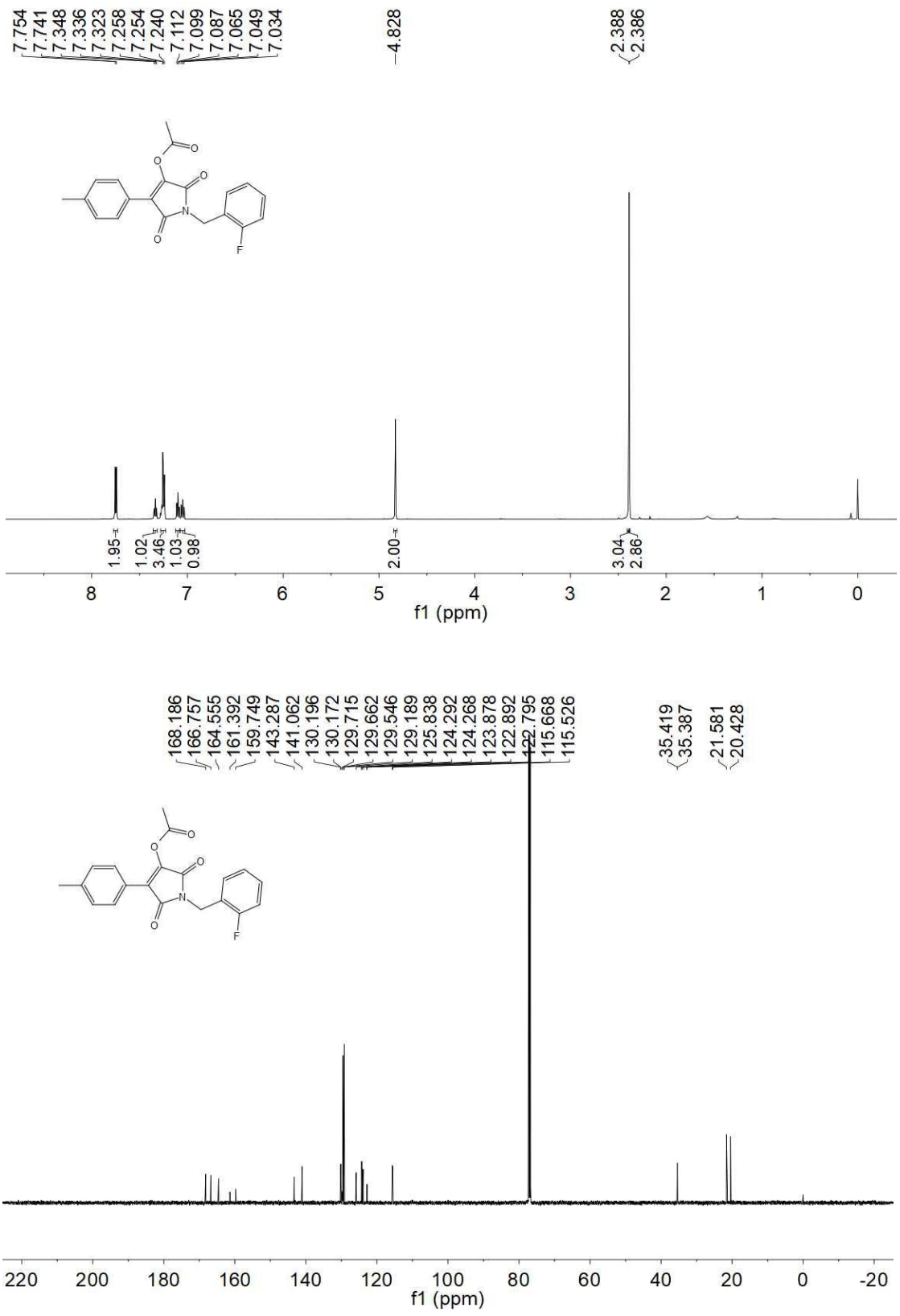


Figure 15. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ad**

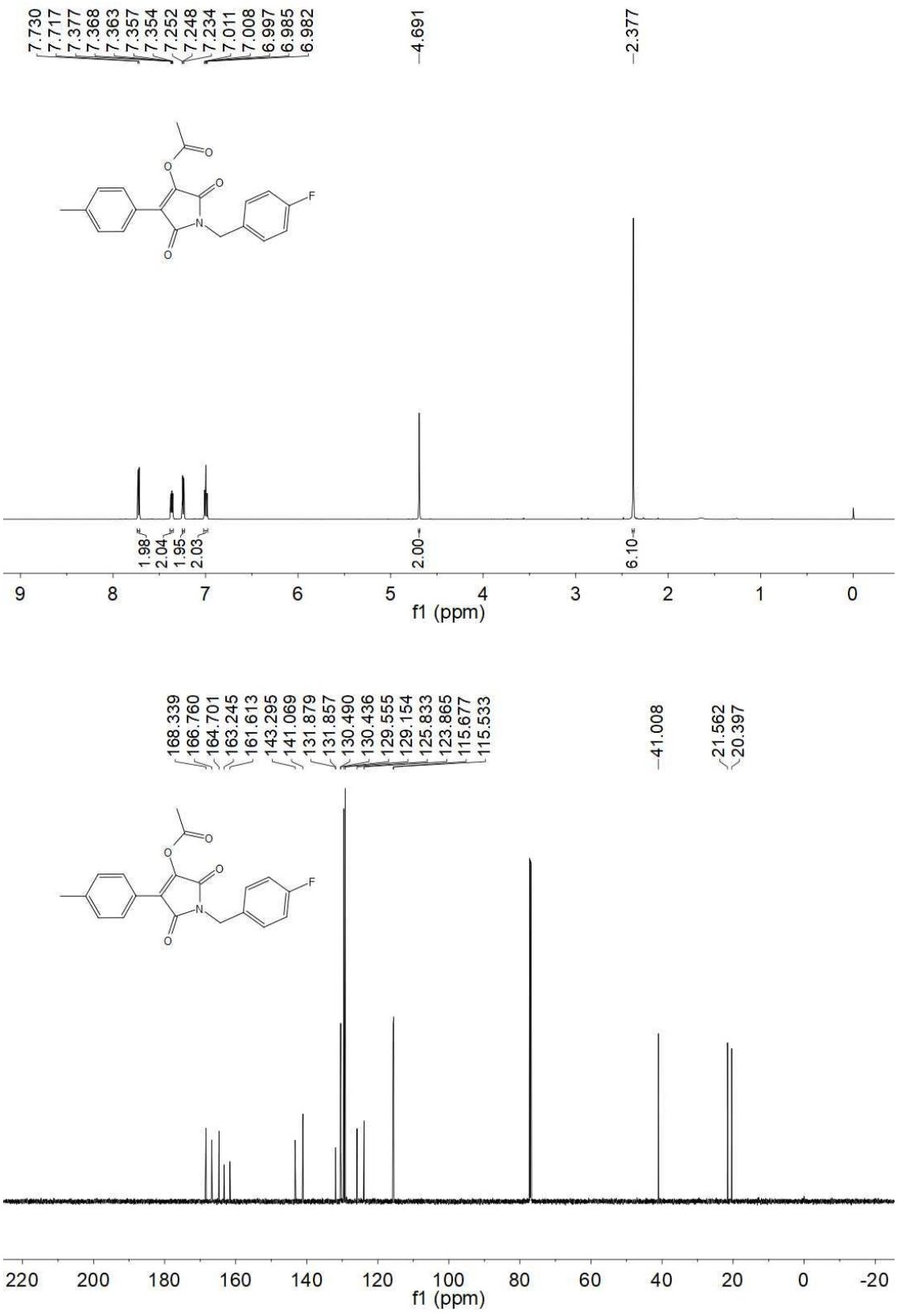


Figure 16. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ae**

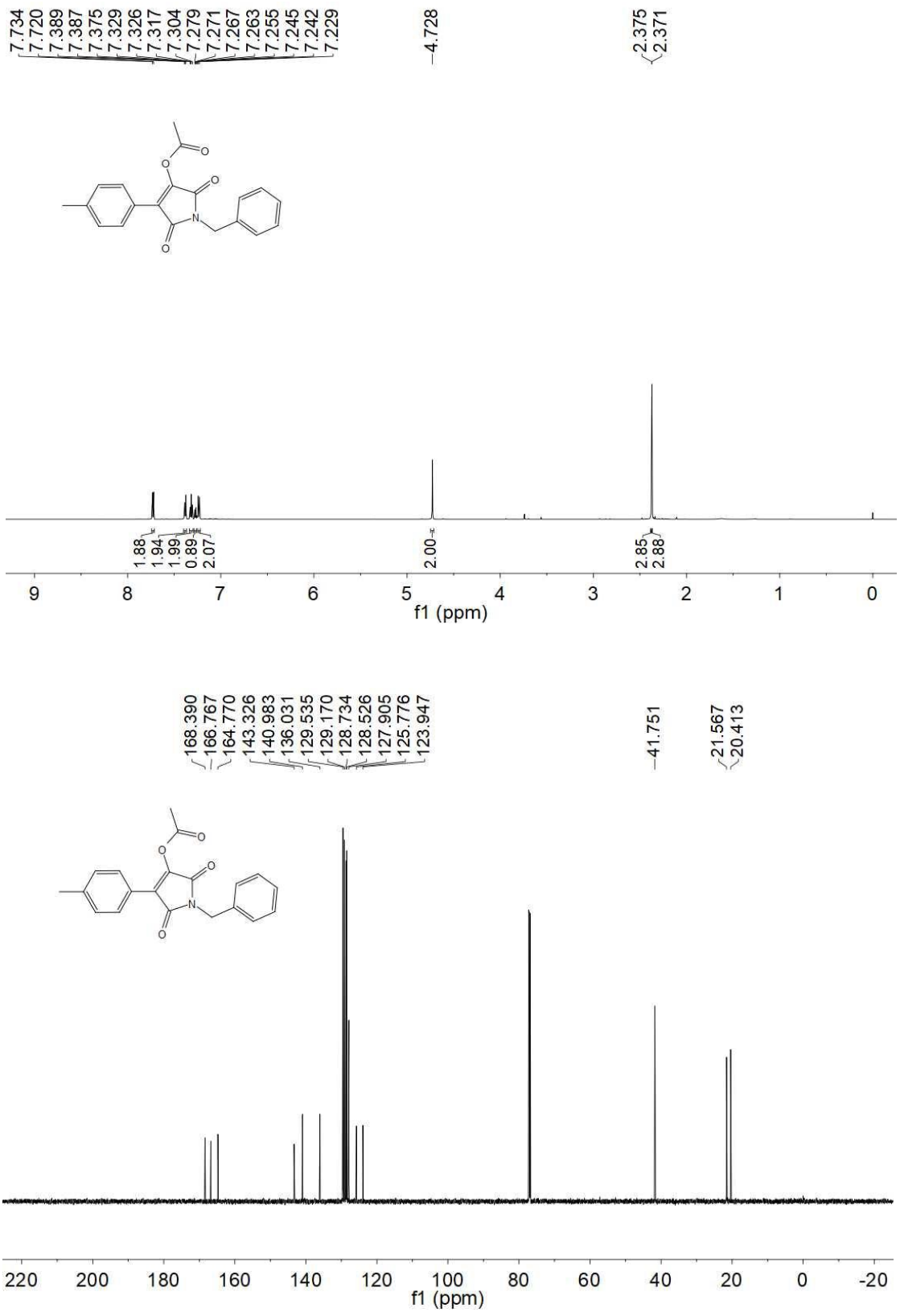


Figure 17. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4af**

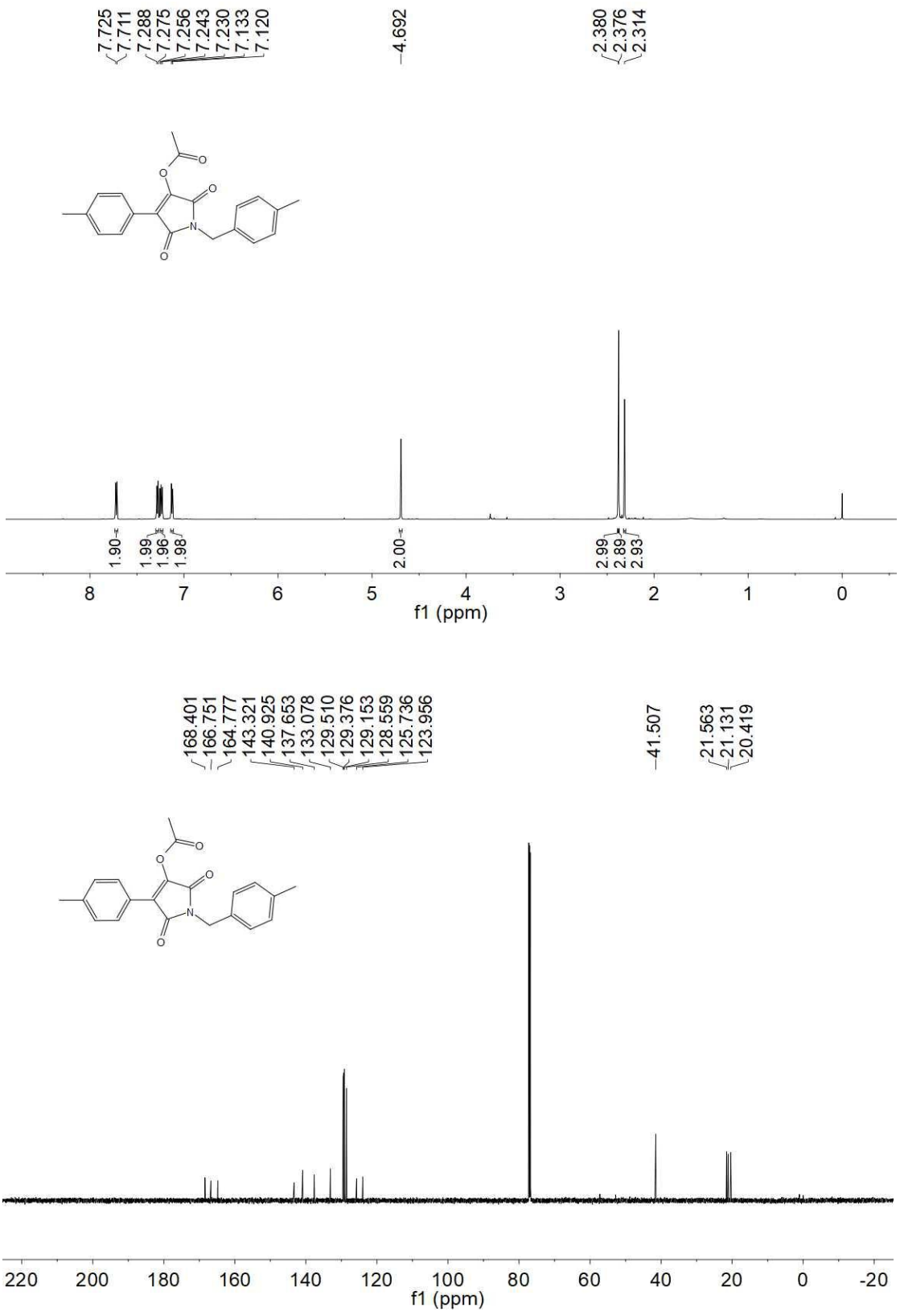


Figure 18. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ag**

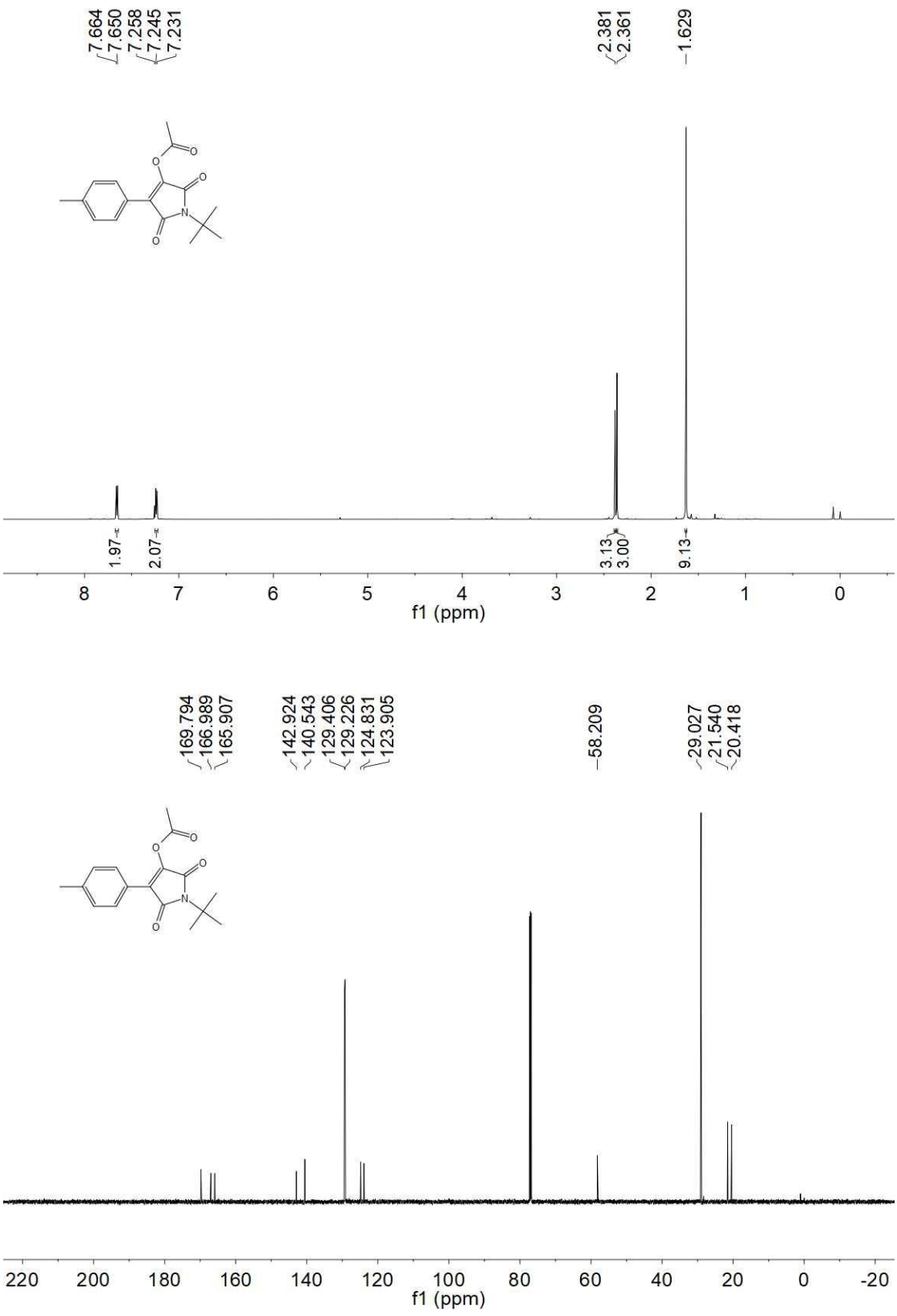


Figure 19. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ah**

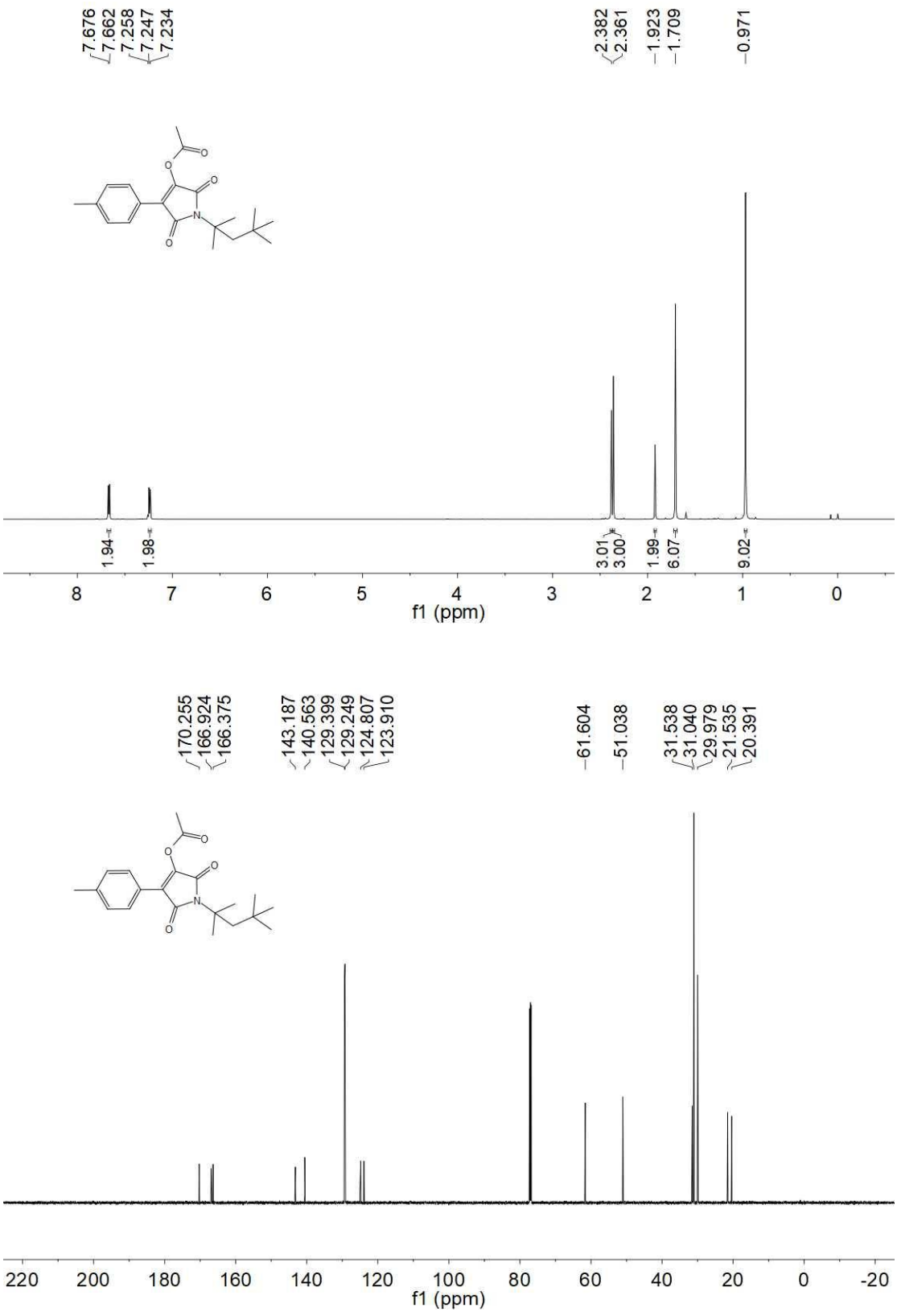


Figure 20. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ai**

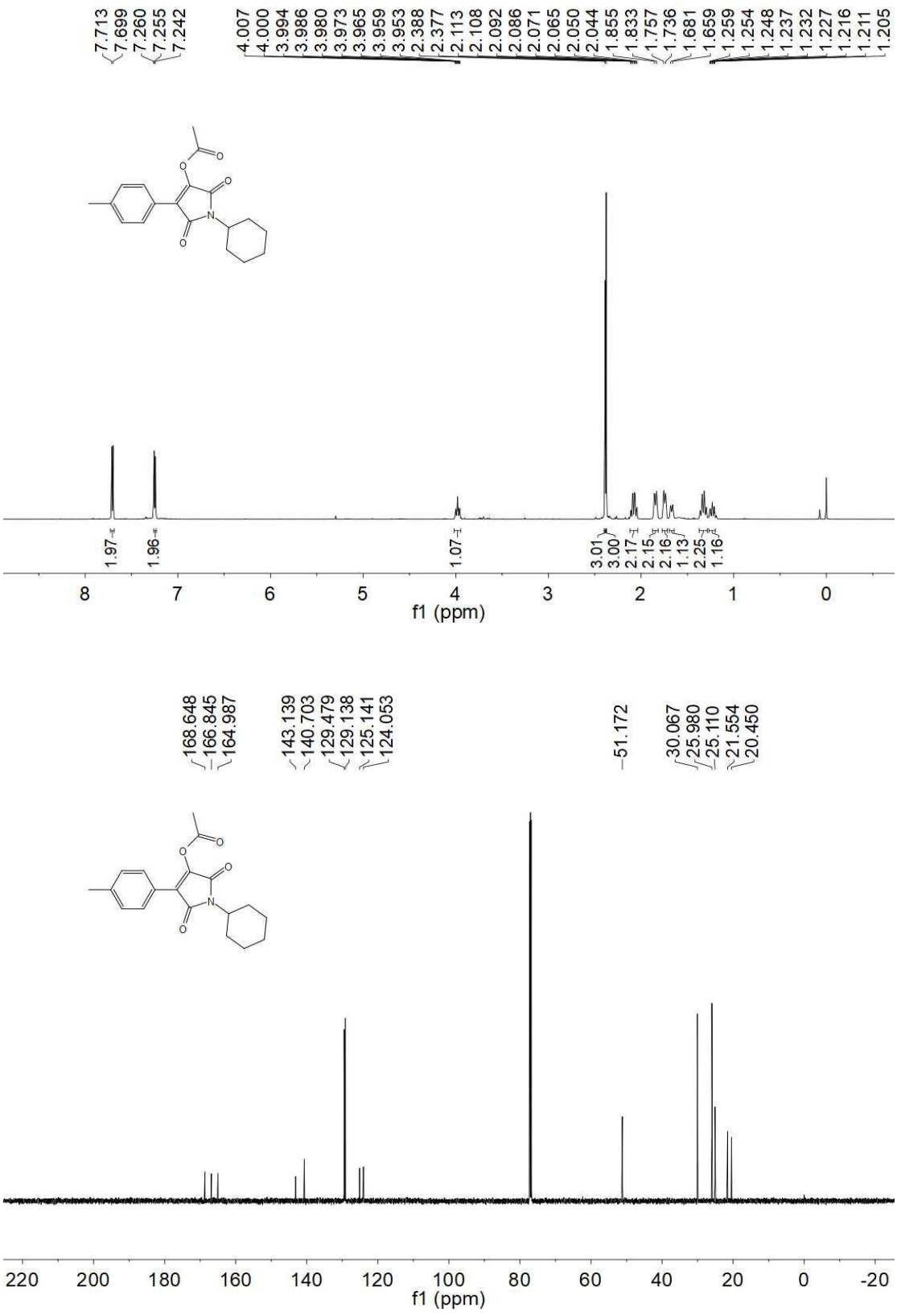


Figure 21. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4aj**

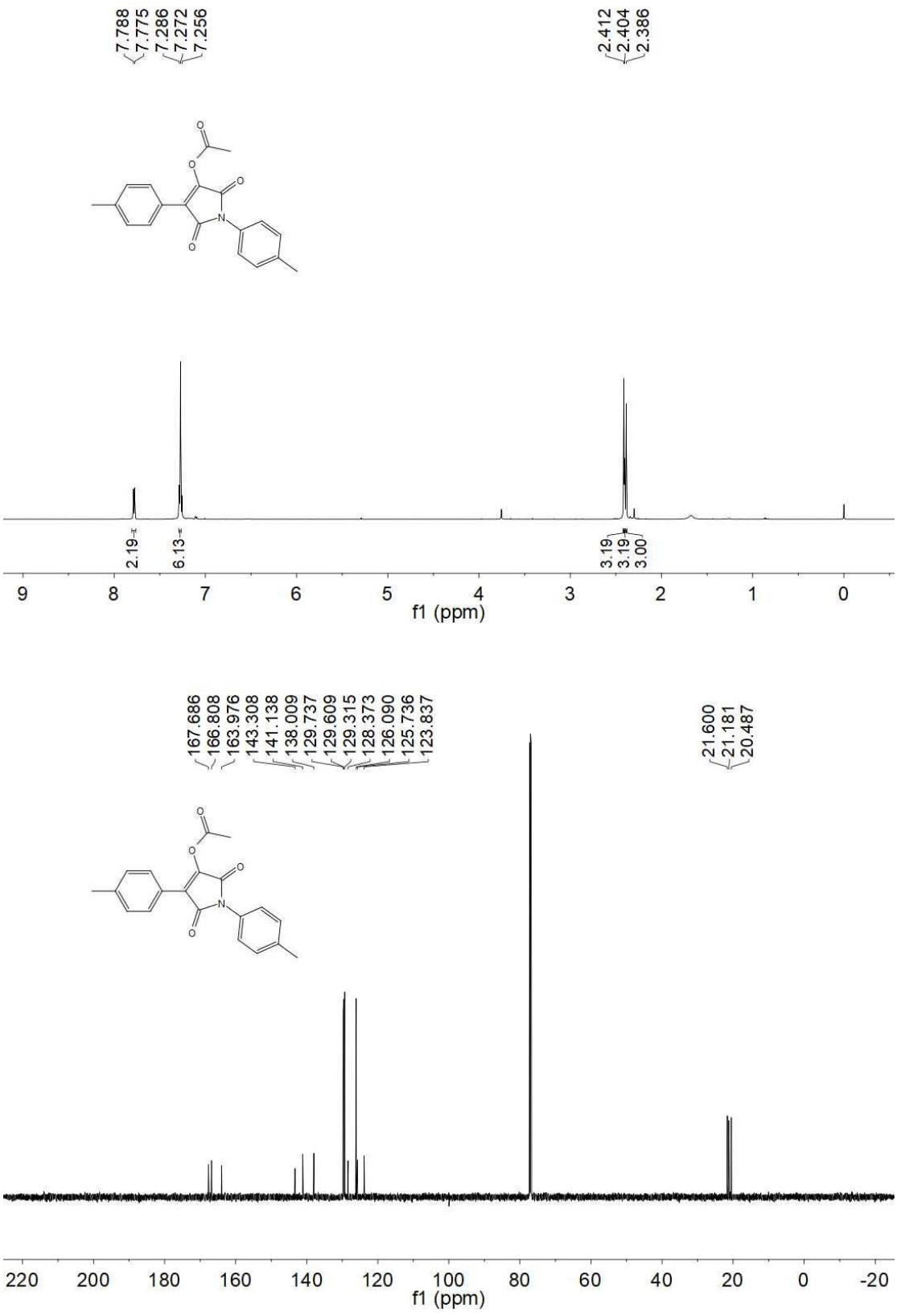


Figure 22. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ak**

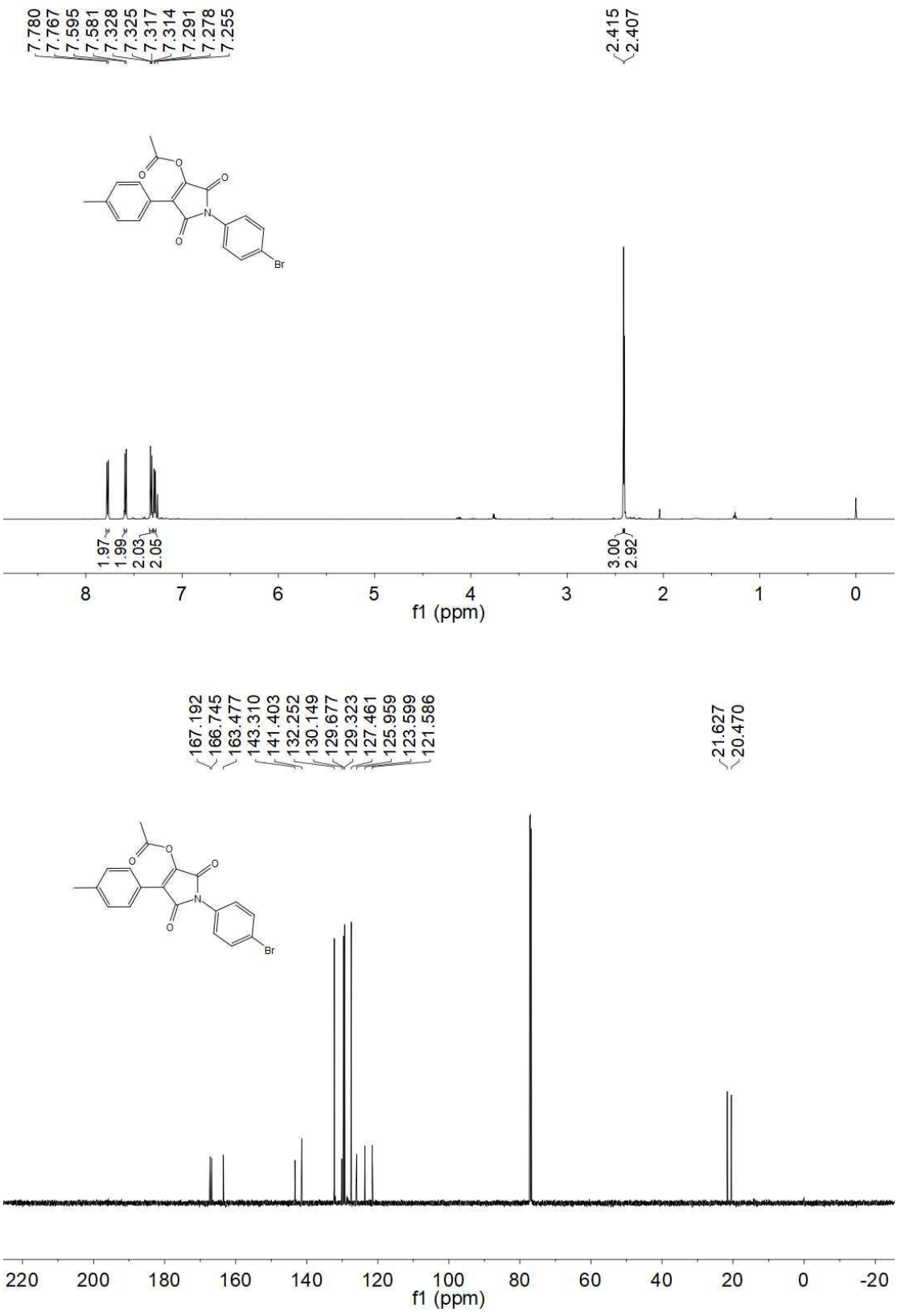


Figure 23. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4al**

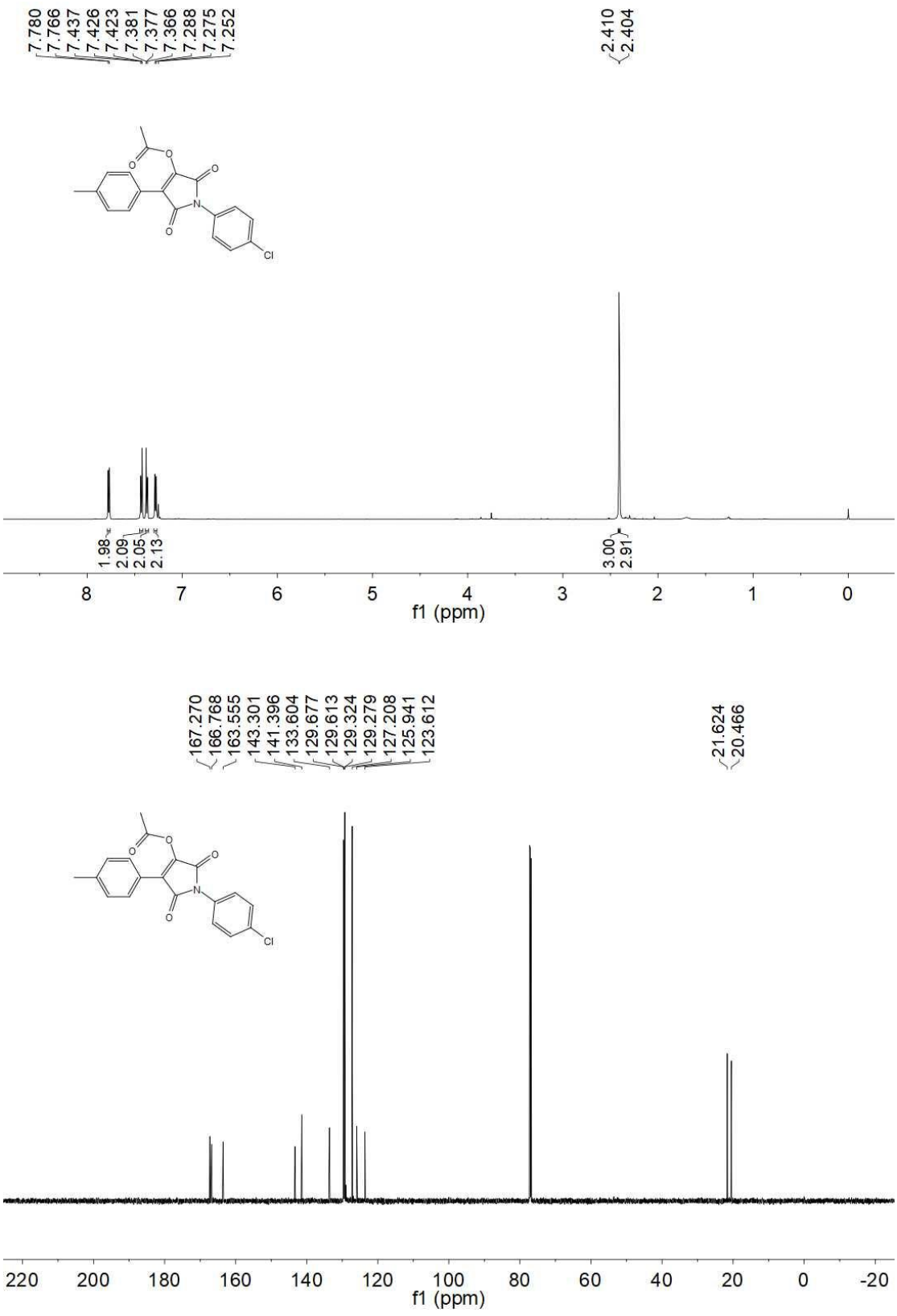


Figure 24. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4am**

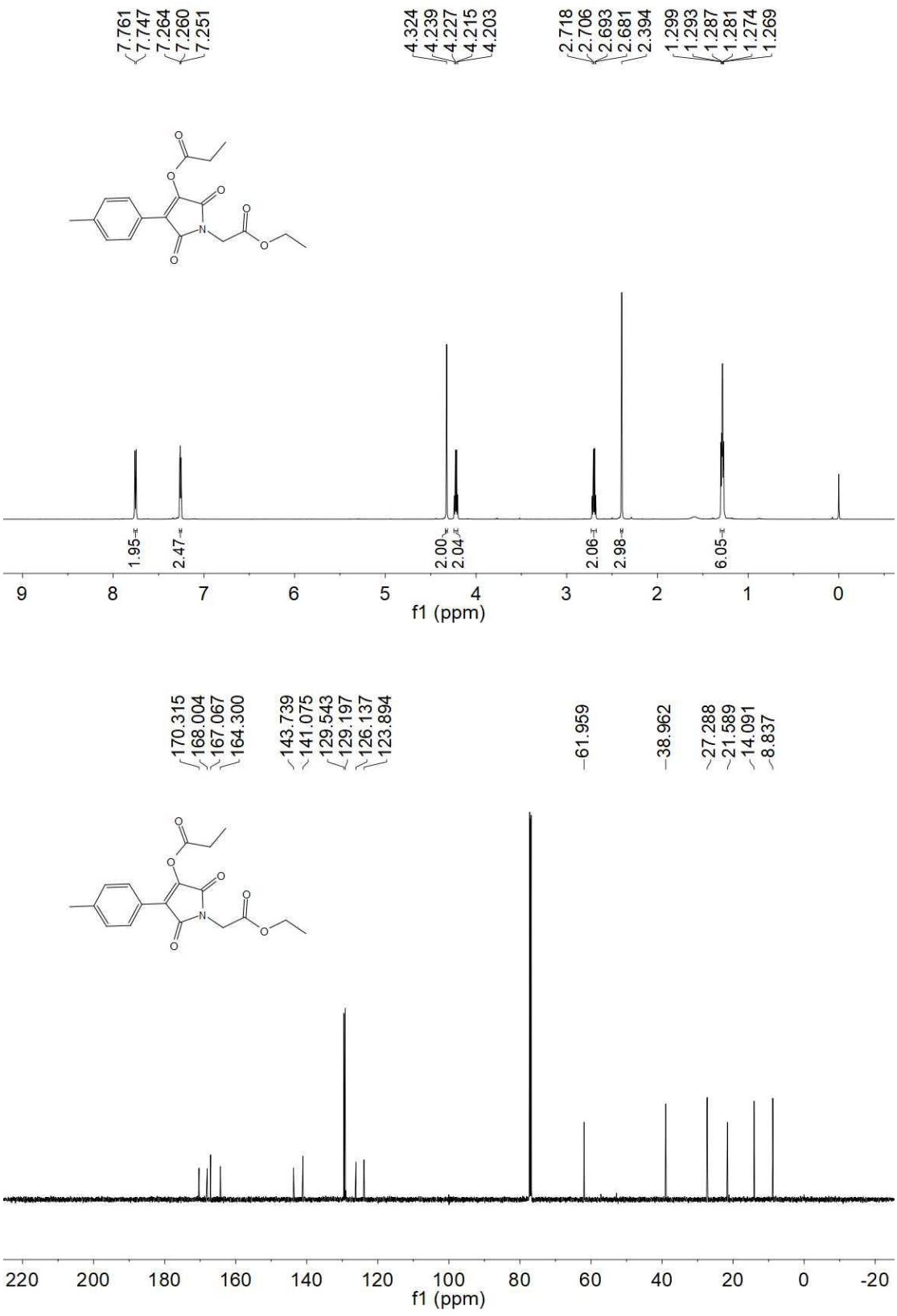


Figure 25. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ma**

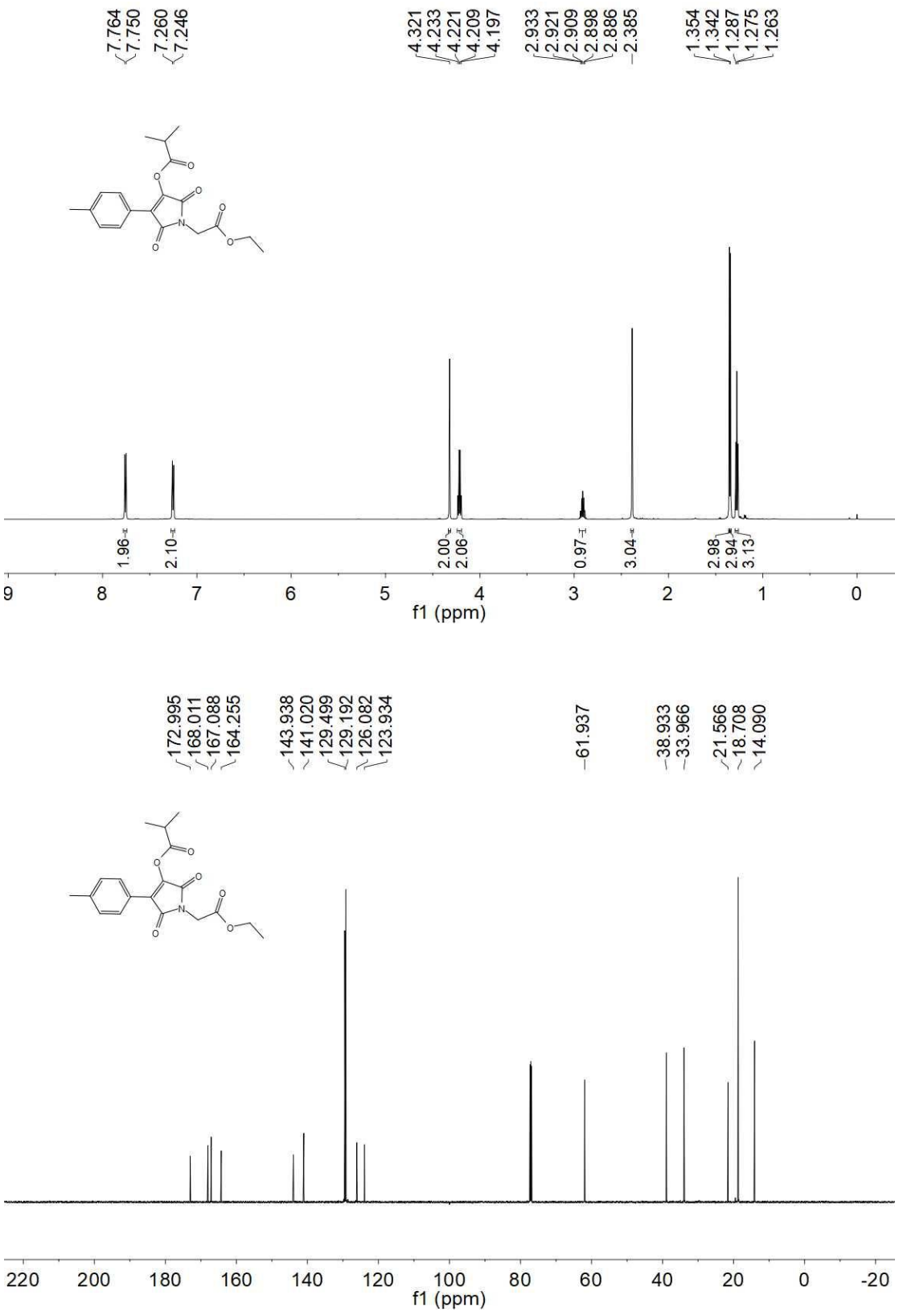


Figure 26. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4na**

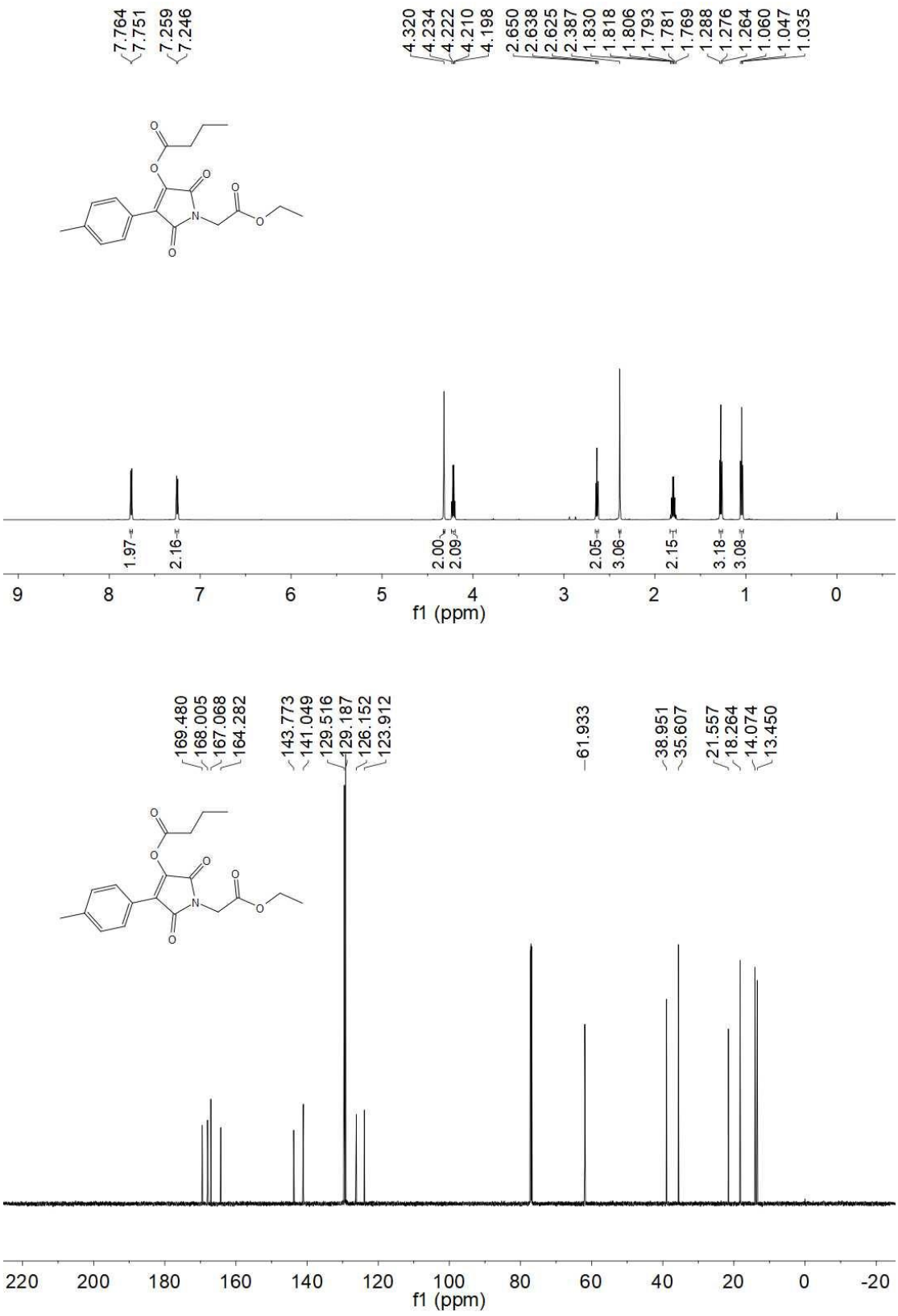


Figure 27. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4oa**

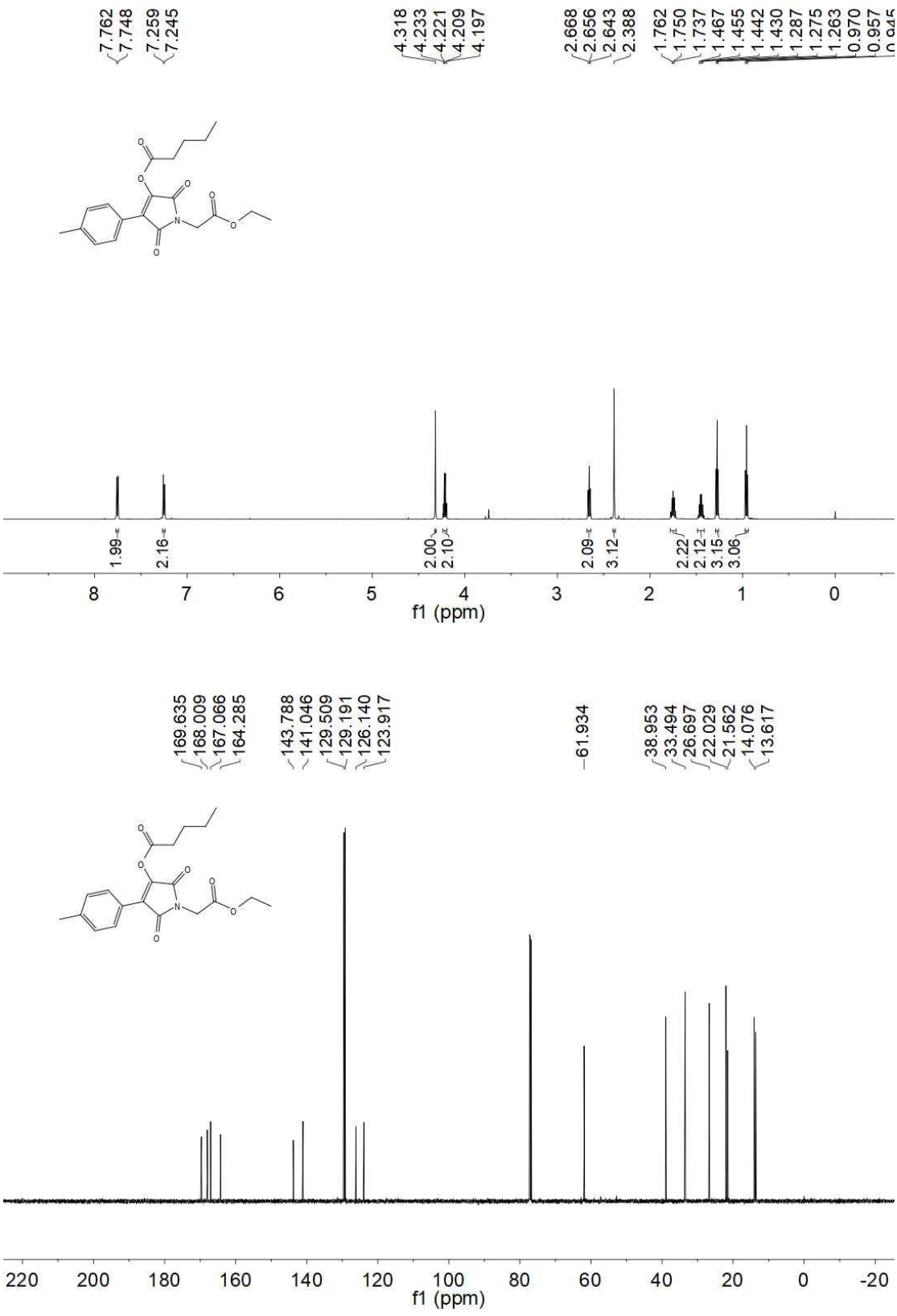


Figure 28. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4pa**

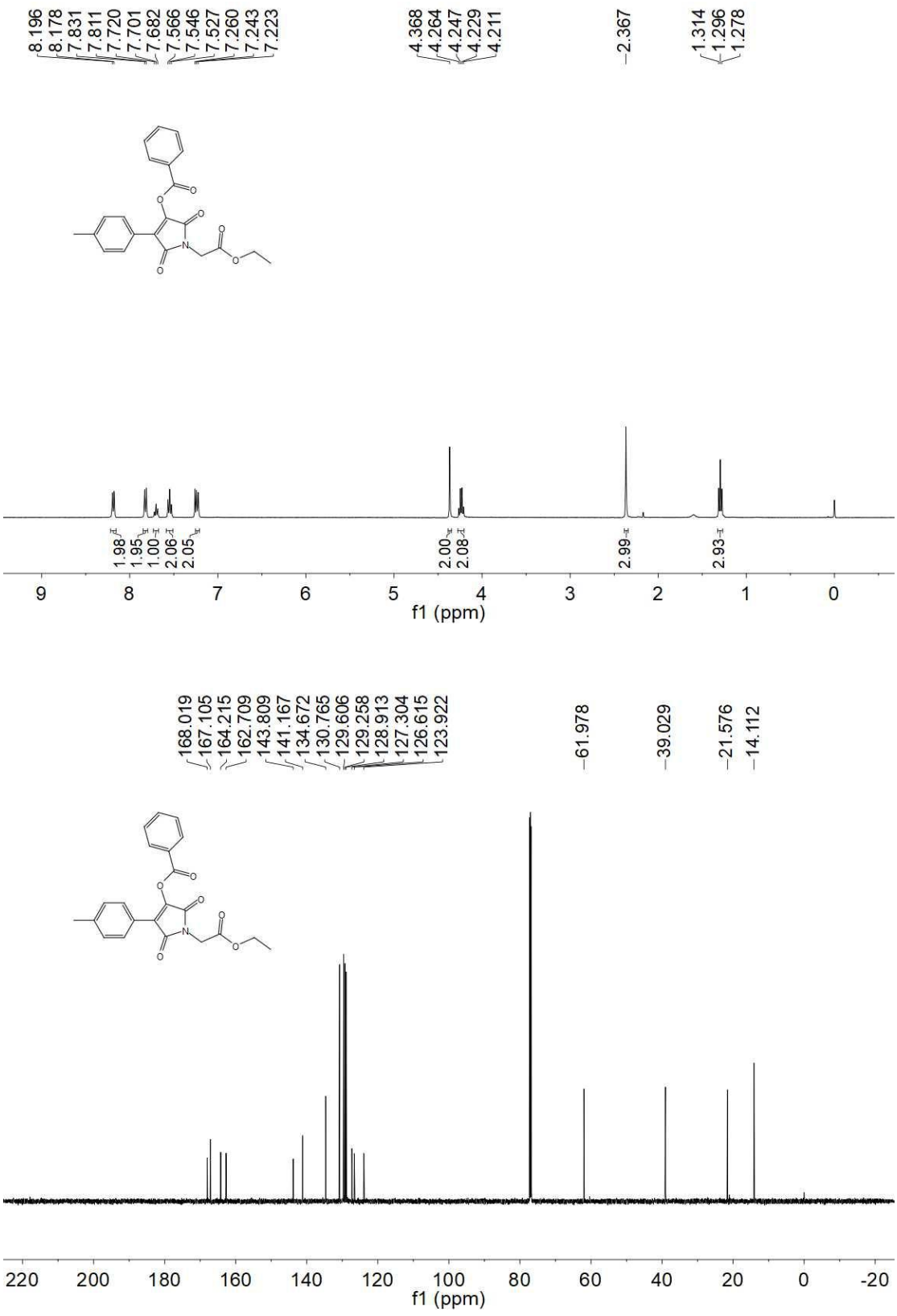


Figure 29. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4qa**

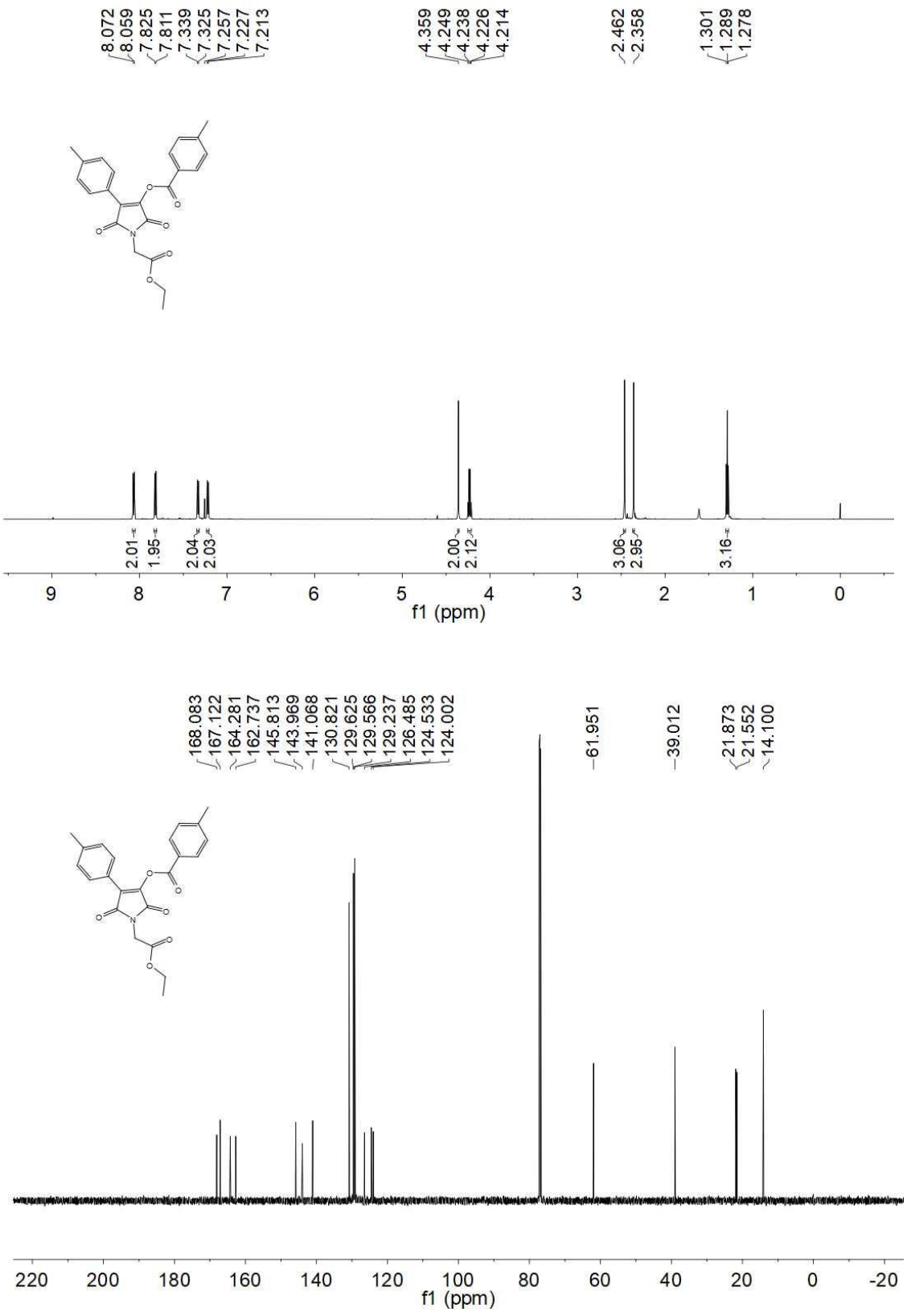
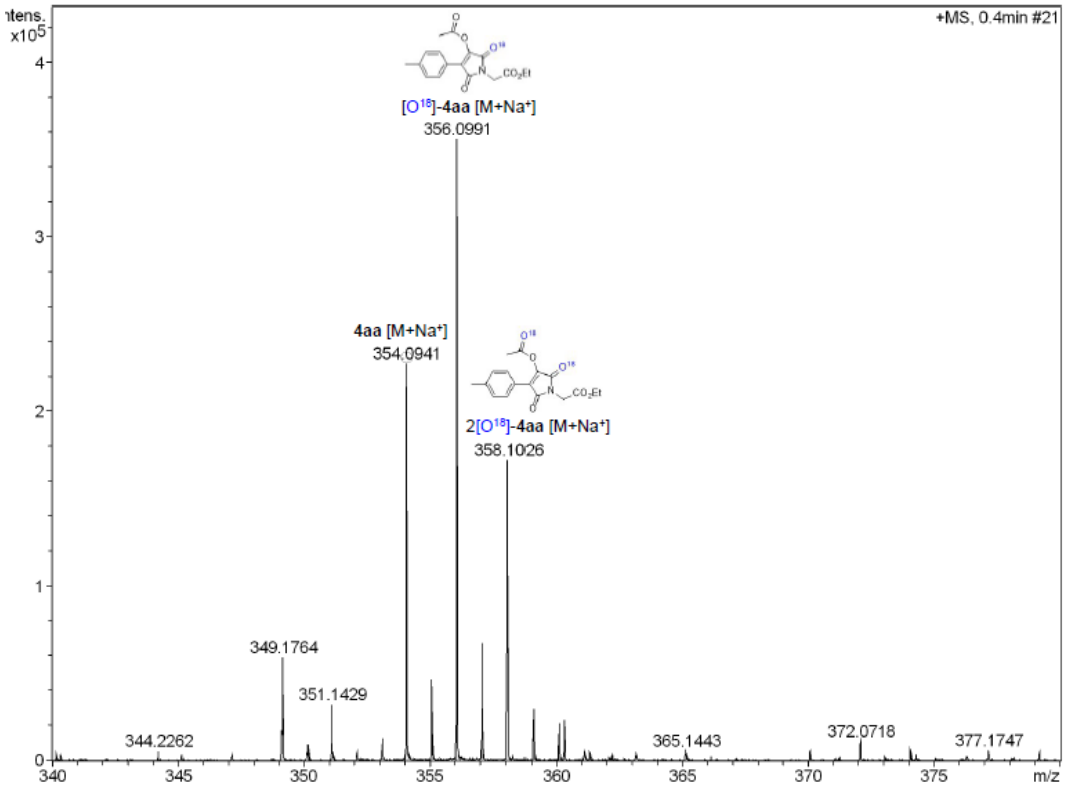


Figure 30. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4ra**

V. Copy of HRMS Spectra of [O^{18}]-4aa and 2[O^{18}]-4aa obtained by reaction with the mixture of $CH_3COO^{18}H$ and $CH_3CO^{18}O^{18}H$:

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Active			Set Dry Heater	180 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	8.0 l/min
Scan End	1500 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule
354.0941	1	C17H17NNaO6	354.0948	-2.0	598.9	1	100.00	9.5	even	ok