

Friedel-Crafts Reaction of Indoles with Vicinal Tricarbonyl Compounds Generated in Situ from 1,3-Dicarbonyl Compounds and TEMPO: Highly Selective Synthesis of Tertiary Alcohol

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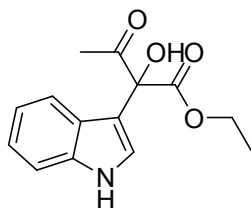
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1. General Considerations.

All ^1H NMR and ^{13}C NMR spectra were measured in CDCl_3 using a Bruker ASCEND 400 spectrometer. Chemical shifts are expressed in ppm and J values are given in Hz. High resolution mass spectra were recorded on Bruker micrOTOF-QIII MS (ESI). Column chromatography was performed with 200-300 mesh silica gel using flash column techniques. Melting points (uncorrected) were determined on a Yalixien X-4 melting point apparatus. All the solvents and reagents were used directly as obtained commercially unless otherwise noted.

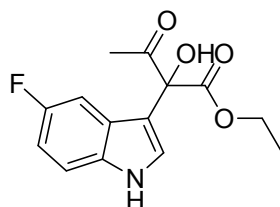
Procedure for the synthesis of **3aa**. A solution of indole (1a) (117 mg, 1.0 mmol), ethyl acetoacetate (2a) (143 mg, 1.1 mmol), and TEMPO (468 mg, 3.0 mmol) in acetic acid (5.0 mL) under an air atmosphere was stirred at 50 °C for 1 h (complete consumption of indicated by TLC). The mixture was then concentrated in vacuo to give a residue that was dissolved in ethyl acetate (50 mL). Washing the ethyl acetate solution with aqueous NaHCO_3 (2×30 mL) followed by drying over sodium sulphate and concentration in vacuo gave a residue that was subjected to flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1 as an eluent) to afford **3aa** as a white solid (85%).

2. Characterization Data of Compounds 3aa-30a:



ethyl 2-hydroxy-2-(1H-indol-3-yl)-3-oxobutanoate (3aa)

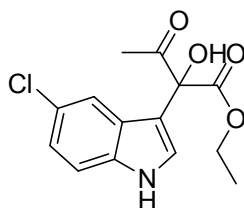
White solid: m.p. 136-137 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.39 (s, 1H), 7.55 (d, $J = 8.0$ Hz, 1H), 7.37 (d, $J = 2.5$ Hz, 1H), 7.31 (d, $J = 8.1$ Hz, 1H), 7.19 (t, $J = 7.4$ Hz, 1H), 7.11 (t, $J = 7.4$ Hz, 1H), 4.81 (s, 1H), 4.42 – 4.24 (m, 2H), 2.25 (s, 3H), 1.31 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.9, 170.4, 136.6, 125.1, 124.3, 122.7, 120.5, 120.3, 111.9, 111.6, 82.3, 62.9, 25.1, 14.2; HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 284.0893, found 284.0907.



ethyl 2-(5-fluoro-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3ba)

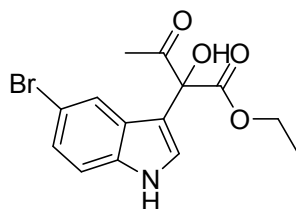
White solid: m.p. 129-130 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.47 (s, 1H), 7.46 (d, $J = 2.7$ Hz, 1H), 7.28 – 7.20 (m, 2H), 6.95 (td, $J = 9.0, 2.5$ Hz, 1H), 4.80 (s, 1H), 4.45 – 4.27 (m, 2H), 2.26 (s, 3H), 1.34 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.4, 170.2, 158.0 (d, $J = 233.9$ Hz), 132.97, 125.83,

125.42 (d, $J = 10.5$ Hz), 112.1 (d, $J = 9.7$ Hz), 111.9 (d, $J = 4.8$ Hz), 110.1 (d, $J = 26.3$ Hz), 105.4 (d, $J = 24.5$ Hz), 82.1, 62.9, 24.8, 14.0; HRMS calcd for $C_{14}H_{14}FNO_4Na$ ($M+Na$)⁺ 302.0799, found 302.0812.



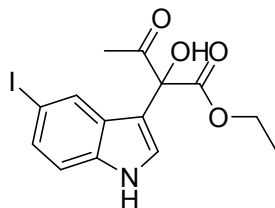
ethyl 2-(5-chloro-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3ca)

White solid: m.p. 144-145 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.54 (s, 1H), 7.55 (s, 1H), 7.34 (s, 1H), 7.18 (d, $J = 8.5$ Hz, 1H), 7.12 (d, $J = 8.6$ Hz, 1H), 4.81 (s, 1H), 4.45 – 4.24 (m, 2H), 2.24 (s, 3H), 1.32 (t, $J = 7.1$ Hz, 3H); ¹³C NMR (101 MHz, Acetone) δ 204.6, 171.1, 136.3, 127.7, 127.0, 125.4, 122.6, 121.1, 113.8, 112.7, 83.5, 62.7, 14.3; HRMS calcd for $C_{14}H_{14}ClNO_4Na$ ($M+Na$)⁺ 318.0504, found 318.0516.



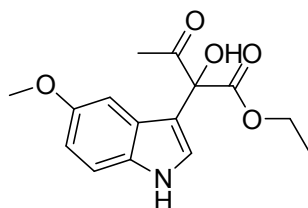
ethyl 2-(5-bromo-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3da)

White solid: m.p. 151-152 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.45 (s, 1H), 7.75 (s, 1H), 7.45 (s, 1H), 7.29 (d, $J = 7.8$ Hz, 1H), 7.21 (d, $J = 8.6$ Hz, 1H), 4.78 (s, 1H), 4.44 – 4.29 (m, 2H), 2.26 (s, 3H), 1.35 (t, $J = 7.1$ Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.3, 170.3, 135.2, 126.9, 125.7, 125.4, 123.1, 113.9, 113.0, 111.7, 82.2, 63.1, 24.9, 14.1; HRMS calcd for $C_{14}H_{14}BrNO_4Na$ ($M+Na$)⁺ 361.9998, found 362.0003.



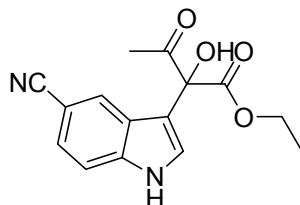
ethyl 2-hydroxy-2-(5-iodo-1H-indol-3-yl)-3-oxobutanoate (3ea)

White solid: m.p. 159-160 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.42 (s, 1H), 7.95 (s, 1H), 7.46 (d, $J = 8.5$ Hz, 1H), 7.42 (s, 1H), 7.13 (d, $J = 8.6$ Hz, 1H), 4.76 (s, 1H), 4.44 – 4.28 (m, 2H), 2.26 (s, 3H), 1.36 (t, $J = 7.1$ Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.3, 170.3, 135.7, 131.2, 129.4, 127.7, 124.9, 113.4, 111.4, 84.2, 82.2, 63.1, 24.9, 14.2; HRMS calcd for $C_{14}H_{14}INO_4Na$ ($M+Na$)⁺ 409.9860, found 409.9862.



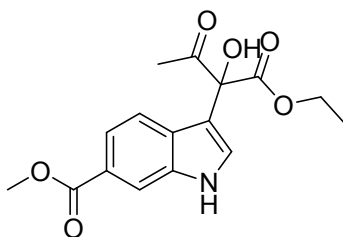
ethyl 2-hydroxy-2-(5-methoxy-1H-indol-3-yl)-3-oxobutanoate (3fa)

White solid: m.p. 108-109 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.40 (s, 1H), 7.35 (d, *J* = 2.7 Hz, 1H), 7.21 (d, *J* = 8.8 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.86 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.81 (s, 1H), 4.45 – 4.26 (m, 2H), 3.82 (s, 3H), 2.27 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.91, 170.32, 154.42, 131.59, 125.48, 124.81, 112.94, 112.24, 111.32, 101.72, 82.27, 77.39, 77.08, 76.76, 62.75, 55.80, 25.00, 14.10; HRMS calcd for C₁₅H₁₇NO₅Na (M+Na)⁺ 314.0999, found 314.1015.



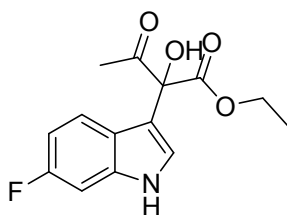
ethyl 2-(5-cyano-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3ga)

Pale solid: m.p. 100-101 °C. ¹H NMR (400 MHz, CDCl₃) δ 9.30 – 8.40 (br, s, 1H), 8.05 (s, 1H), 7.63 (s, 1H), 7.43 (s, 2H), 4.82 (s, 1H), 4.46 – 4.29 (m, 2H), 2.27 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 203.7, 170.0, 138.2, 126.7, 126.4, 125.4, 125.1, 120.5, 112.9, 112.5, 103.6, 82.1, 63.3, 24.7, 14.1; HRMS calcd for C₁₅H₁₄N₂O₄Na (M+Na)⁺ 309.0846, found 309.0860.



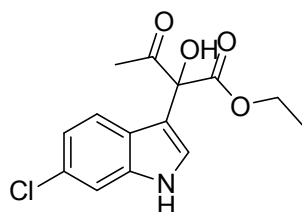
methyl 3-(1-ethoxy-2-hydroxy-1,3-dioxobutan-2-yl)-1H-indole-6-carboxylate (3ha)

White solid: m.p. 135-136 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.91 (s, 1H), 8.12 (s, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 4.85 (s, 1H), 4.46 – 4.26 (m, 2H), 3.95 (s, 3H), 2.25 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.4, 170.3, 168.1, 136.0, 128.8, 127.6, 124.3, 121.4, 120.1, 114.0, 112.3, 82.2, 63.1, 52.2, 24.9, 14.1; HRMS calcd for C₁₆H₁₇NO₆Na (M+Na)⁺ 342.0948, found 342.0951.



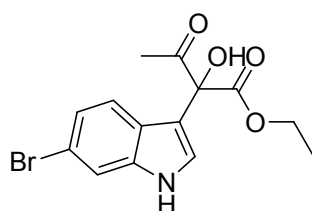
ethyl 2-(6-fluoro-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3ia)

White solid: m.p. 139-140 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.48 (s, 1H), 7.49 (dd, *J* = 8.8, 5.3 Hz, 1H), 7.35 (d, *J* = 2.0 Hz, 1H), 7.00 (dd, *J* = 9.4, 2.2 Hz, 1H), 6.89 (td, *J* = 9.3, 2.3 Hz, 1H), 4.82 (s, 1H), 4.44 – 4.27 (m, 2H), 2.26 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.5, 170.2, 160.0 (d, *J* = 245.6 Hz), 136.5 (d, *J* = 12.3 Hz), 124.5 (d, *J* = 3.3 Hz), 121.6, 121.3 (d, *J* = 10.0 Hz), 112.0, 109.3 (d, *J* = 24.2 Hz), 97.7 (d, *J* = 26.0 Hz), 82.2, 62.9, 24.8, 14.0; HRMS calcd for C₁₄H₁₄FNO₄Na (M+Na)⁺ 302.0799, found 302.0810.



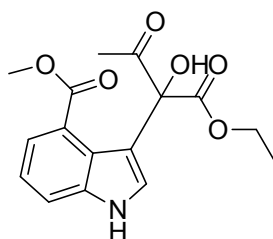
ethyl 2-(6-chloro-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3ja)

White solid: m.p. 132-133 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.42 (s, 1H), 7.50 (d, $J = 8.6$ Hz, 1H), 7.43 (d, $J = 2.5$ Hz, 1H), 7.33 (d, $J = 1.5$ Hz, 1H), 7.09 (dd, $J = 8.6, 1.7$ Hz, 1H), 4.80 (s, 1H), 4.34 – 4.27 (m, 2H), 2.25 (s, 3H), 1.33 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.4, 170.1, 136.9, 128.6, 124.8, 123.7, 121.2, 121.2, 112.1, 111.4, 77.4, 77.0, 76.7, 24.8, 14.1; HRMS calcd for $\text{C}_{14}\text{H}_{14}\text{ClNO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 318.0504, found 318.0514.



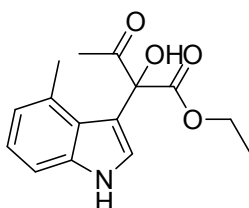
ethyl 2-(6-bromo-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3ka)

White solid: m.p. 153-154 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.36 (s, 1H), 7.52 (s, 1H), 7.46 (d, $J = 8.7$ Hz, 2H), 7.23 (d, $J = 8.6$ Hz, 1H), 4.77 (s, 1H), 4.42 – 4.29 (m, 2H), 2.25 (s, 3H), 1.34 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.5, 170.3, 137.4, 124.8, 124.1, 123.9, 121.8, 116.4, 114.5, 112.3, 82.2, 63.1, 24.9, 14.2; HRMS calcd for $\text{C}_{14}\text{H}_{14}\text{BrNO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 361.9998, found 361.9993.



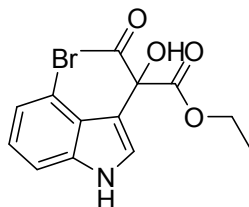
methyl 3-(1-ethoxy-2-hydroxy-1,3-dioxobutan-2-yl)-1H-indole-4-carboxylate (3la)

White solid: m.p. 113-114 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.07 (s, 1H), 7.71 (d, $J = 7.5$ Hz, 1H), 7.27 (d, $J = 7.7$ Hz, 2H), 7.07 (t, $J = 7.8$ Hz, 1H), 6.70 (s, 1H), 6.37 (s, 1H), 4.38 – 4.22 (m, 2H), 3.89 (s, 3H), 2.46 (s, 3H), 1.31 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 206.3, 171.1, 170.6, 137.9, 127.6, 124.1, 122.3, 122.3, 121.2, 117.4, 113.4, 83.62, 77.4, 77.1, 76.8, 62.4, 52.7, 26.2, 14.0; HRMS calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 342.0948, found 342.0954.



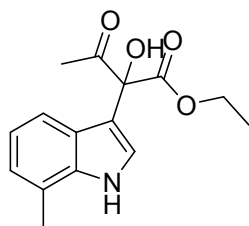
ethyl 2-hydroxy-2-(4-methyl-1H-indol-3-yl)-3-oxobutanoate (3ma)

White solid: m.p. 135-136 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.35 (s, 1H), 7.15 – 7.01 (m, 2H), 6.90 (d, *J* = 5.9 Hz, 1H), 6.82 (d, *J* = 2.2 Hz, 1H), 4.59 (s, 1H), 4.42 – 4.25 (m, 2H), 2.47 (s, 3H), 2.34 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 207.1, 171.1, 137.3, 130.5, 124.9, 124.4, 122.9, 122.7, 113.0, 109.4, 82.8, 62.9, 26.8, 21.5, 14.1; HRMS calcd for C₁₅H₁₇NO₄Na (M+Na)⁺ 298.1050, found 298.1052.



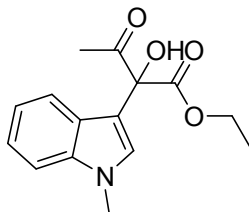
ethyl 2-(4-bromo-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3na)

Pink solid: m.p. 132-133 °C. ¹H NMR (400 MHz, CDCl₃) δ 9.07 (s, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 6.96 (t, *J* = 7.8 Hz, 1H), 6.65 (s, 1H), 4.69 (s, 1H), 4.45 – 4.22 (m, 2H), 2.43 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 206.9, 171.0, 138.2, 126.8, 125.3, 124.1, 123.5, 112.7, 112.2, 111.4, 82.2, 63.1, 27.4, 14.1; HRMS calcd for C₁₄H₁₄BrNO₄Na (M+Na)⁺ 361.9998, found 362.0005.



ethyl 2-hydroxy-2-(7-methyl-1H-indol-3-yl)-3-oxobutanoate (3oa)

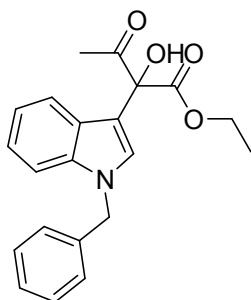
White solid: m.p. 109-110 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.39 (s, 1H), 7.44 – 7.38 (m, 2H), 7.11 – 6.96 (m, 2H), 4.84 (s, 1H), 4.46 – 4.26 (m, 2H), 2.47 (s, 3H), 2.27 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.9, 170.4, 136.1, 124.6, 124.0, 123.1, 120.6, 120.6, 117.9, 112.3, 82.2, 62.7, 25.0, 16.6, 14.1; HRMS calcd for C₁₅H₁₇NO₄Na (M+Na)⁺ 298.1050, found 298.1054.



ethyl 2-hydroxy-2-(1-methyl-1H-indol-3-yl)-3-oxobutanoate (3pa)

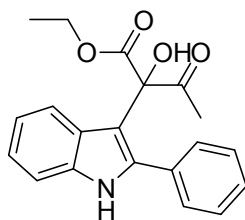
Colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 8.0 Hz, 1H), 7.41 (s, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 4.86 (s, 1H), 4.38 (dddd, *J* = 22.7, 10.7, 7.1, 3.6 Hz, 2H), 3.81 (s, 3H), 2.30 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.4, 170.3,

168.1, 136.0, 128.8, 127.6, 124.3, 121.4, 120.1, 114.0, 112.3, 82.2, 63.1, 52.2, 24.9, 14.1; HRMS calcd for $C_{15}H_{17}NO_4Na$ ($M+Na$)⁺ 298.1050, found 298.1044.



ethyl 2-(1-benzyl-1H-indol-3-yl)-2-hydroxy-3-oxobutanoate (3qa)

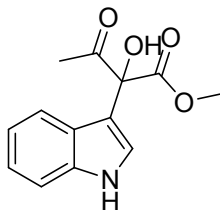
Pale solid: m.p. 64-65 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.49 (s, 1H), 7.38 – 7.29 (m, 4H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 3H), 5.35 (s, 2H), 4.82 (s, 1H), 4.45 – 4.28 (m, 2H), 2.29 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 204.6, 170.4, 136.9, 136.9, 128.8, 128.2, 127.8, 126.8, 125.9, 122.3, 120.6, 120.2, 110.8, 110.0, 82.2, 62.7, 50.3, 24.9, 14.0; HRMS calcd for $C_{21}H_{21}NO_4Na$ ($M+Na$)⁺ 374.1363, found 374.1365.



ethyl 2-hydroxy-3-oxo-2-(2-phenyl-1H-indol-3-yl)butanoate (3ra)

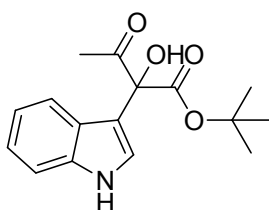
Yellow solid: m.p. 107-108 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.63 – 7.55 (m, 3H), 7.54 – 7.46 (m, 1H), 7.38 – 7.26 (m, 3H), 7.05 – 6.96 (m, 1H), 6.84 (q, *J* = 7.1 Hz, 1H), 6.23 (d, *J* = 7.1 Hz, 1H), 4.99 (s, 0.5H), 4.81 (s, 0.5H), 4.13 – 3.91 (m, 2H), 2.21 (s, 1.5H), 2.19 (s, 1.5H), 1.07 (t, *J* = 7.1 Hz, 1.5H), 0.94 (t, *J* = 7.1 Hz, 1.5H); ¹³C NMR (101 MHz, CDCl₃) δ 203.1, 199.1, 198.6, 198.5, 168.0, 166.0, 160.2, 159.9, 137.4, 137.4, 137.0, 136.9, 136.8, 128.6, 128.5, 127.8, 127.7, 125.1, 125.0, 124.9, 124.9, 119.0, 119.0, 118.7, 111.6, 111.3, 70.2, 70.0, 65.3, 62.6, 61.6, 61.4, 32.7, 30.0, 13.4, 13.1; HRMS calcd for $C_{20}H_{19}NO_4Na$ ($M+Na$)⁺ 360.1206, found 360.1213.

3. Characterization Data of Compounds 4ab-4ah:



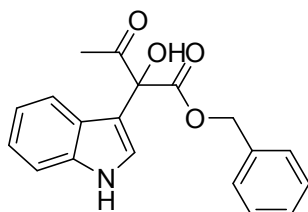
methyl 2-hydroxy-2-(1H-indol-3-yl)-3-oxobutanoate (4ab)

White solid: m.p. 112-113 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.43 (s, 1H), 7.55 (d, $J = 8.0$ Hz, 1H), 7.39 – 7.29 (m, 2H), 7.22 (t, $J = 7.6$ Hz, 1H), 7.14 (t, $J = 7.5$ Hz, 1H), 4.88 (s, 1H), 3.88 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.8, 170.8, 136.5, 124.95, 124.3, 122.6, 120.5, 120.0, 111.6, 111.6, 82.3, 53.4, 25.0; HRMS calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 270.0737, found 270.0745.



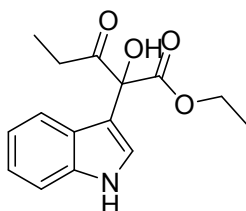
tert-butyl 2-hydroxy-2-(1H-indol-3-yl)-3-oxobutanoate (4ac)

White solid: m.p. 119-120 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.40 (s, 1H), 7.60 (d, $J = 7.9$ Hz, 1H), 7.37 (s, 1H), 7.31 (d, $J = 8.1$ Hz, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 7.12 (t, $J = 7.4$ Hz, 1H), 4.75 (s, 1H), 2.24 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 205.0, 169.5, 136.5, 125.2, 124.1, 122.4, 120.5, 120.2, 112.1, 111.5, 84.2, 82.4, 27.9, 25.1; HRMS calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 312.1206, found 312.1219.



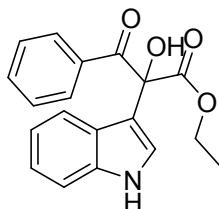
benzyl 2-hydroxy-2-(1H-indol-3-yl)-3-oxobutanoate (4ad)

White solid: m.p. 93-94 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.33 (s, 1H), 7.52 (d, $J = 8.0$ Hz, 1H), 7.36 (s, 5H), 7.33 – 7.29 (m, 2H), 7.20 (t, $J = 7.6$ Hz, 1H), 7.09 (t, $J = 7.5$ Hz, 1H), 5.33 (q, $J = 12.2$ Hz, 2H), 4.87 (s, 1H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.7, 170.1, 136.5, 134.9, 128.7, 128.7, 128.5, 125.1, 124.4, 122.7, 120.5, 120.2, 111.6, 111.6, 82.4, 68.2, 25.1; HRMS calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 346.1050, found 346.1052.



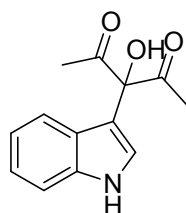
ethyl 2-hydroxy-2-(1H-indol-3-yl)-3-oxopentanoate (4ae)

White solid: m.p. 96-97 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.39 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.41 (s, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 4.87 (s, 1H), 4.45 – 4.24 (m, 2H), 2.80 – 2.67 (m, 1H), 2.58 – 2.46 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 207.8, 170.1, 136.2, 124.8, 124.2, 122.1, 119.9, 119.7, 111.4, 111.4, 81.7, 62.4, 30.3, 13.7, 7.7; HRMS calcd for C₁₅H₁₇NO₄Na (M+Na)⁺ 298.1050, found 298.1064.



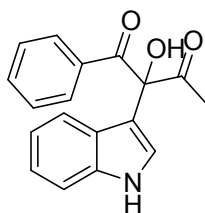
ethyl 2-hydroxy-2-(1H-indol-3-yl)-3-oxo-3-phenylpropanoate (4af)

White solid: m.p. 124-125 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.29 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.50 (s, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.1 Hz, 3H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 5.09 (s, 1H), 4.40 – 4.19 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 195.2, 171.1, 136.1, 133.3, 133.2, 130.0, 127.9, 125.3, 123.9, 122.2, 120.4, 120.0, 113.0, 111.1, 81.0, 62.6, 13.6; HRMS calcd for C₁₉H₁₇NO₄Na (M+Na)⁺ 346.1050, found 346.1056.



3-hydroxy-3-(1H-indol-3-yl)pentane-2,4-dione (4ah)

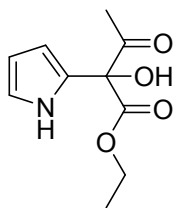
White solid: m.p. 107-108 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.39 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.33 (d, *J* = 2.7 Hz, 1H), 7.27 – 7.21 (m, 1H), 7.18 – 7.11 (m, 1H), 5.36 (s, 1H), 2.36 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 207.3, 136.6, 124.8, 123.7, 122.8, 120.7, 119.8, 112.5, 111.6, 87.3, 26.2; HRMS calcd for C₁₃H₁₃NO₃Na (M+Na)⁺ 254.0788, found 254.0794.



2-hydroxy-2-(1H-indol-3-yl)-1-phenylbutane-1,3-dione (4ai)

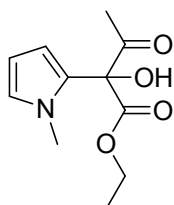
White solid: m.p. 154-155 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.34 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.41 – 7.29 (m, 3H), 7.26 – 7.18 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 5.57 (s, 1H), 2.35 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 207.3, 198.0, 136.4, 134.2, 133.5, 130.9, 128.1, 124.9, 123.7, 122.9, 120.7, 120.1, 113.8, 111.5, 85.2, 26.6; HRMS calcd for C₁₈H₁₅NO₃Na (M+Na)⁺ 316.0944, found 316.0947.

4. Characterization Data of Compounds 6aa and 6ba:



ethyl 2-hydroxy-3-oxo-2-(1H-pyrrol-2-yl)butanoate (6aa)

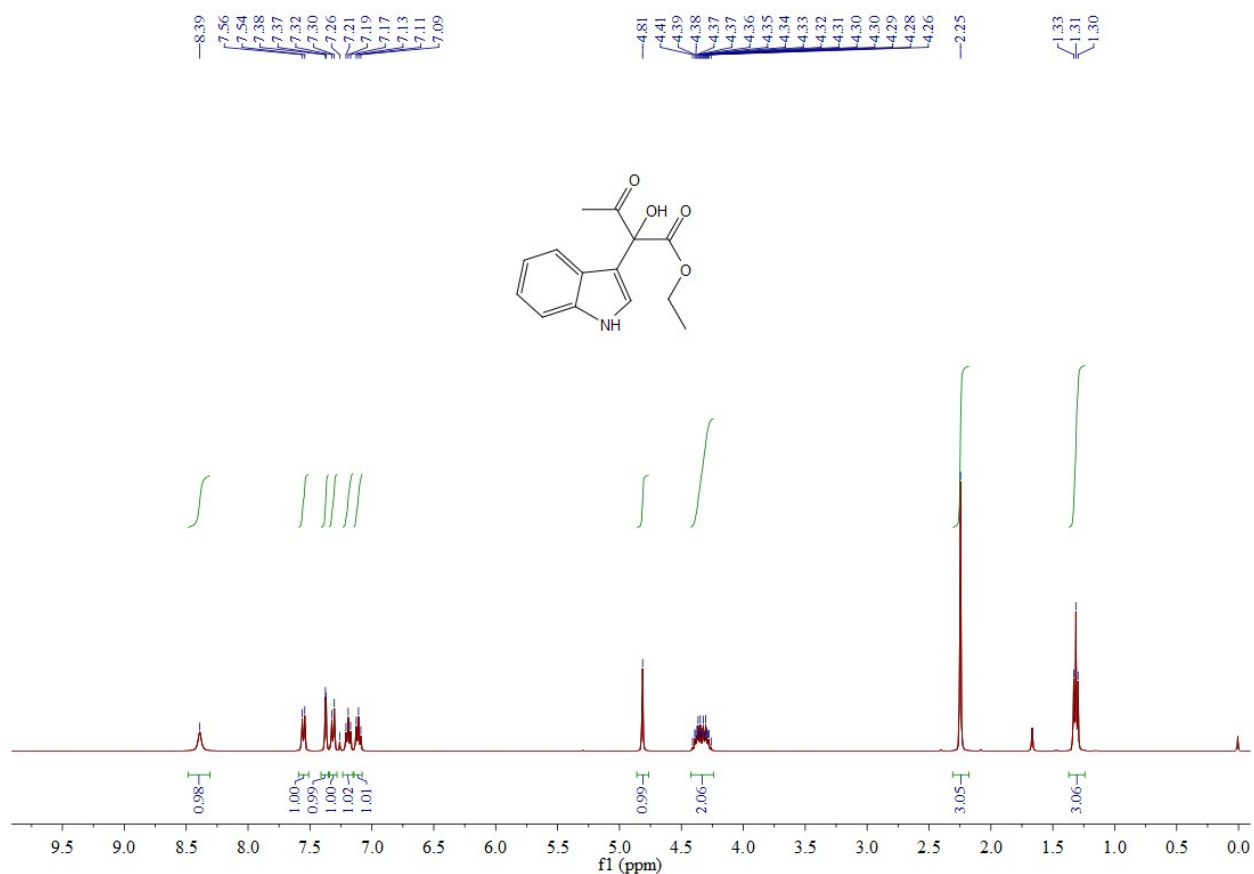
Colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 8.98 (s, 1H), 6.83 (s, 1H), 6.39 (s, 1H), 6.24 (s, 1H), 4.81 (s, 1H), 4.36 (q, $J = 6.8$ Hz, 2H), 2.34 (s, 3H), 1.37 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 202.8, 169.4, 125.6, 118.5, 109.2, 108.1, 81.4, 63.2, 24.4, 14.0; HRMS calcd for $\text{C}_{10}\text{H}_{13}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 234.0737, found 234.0730.



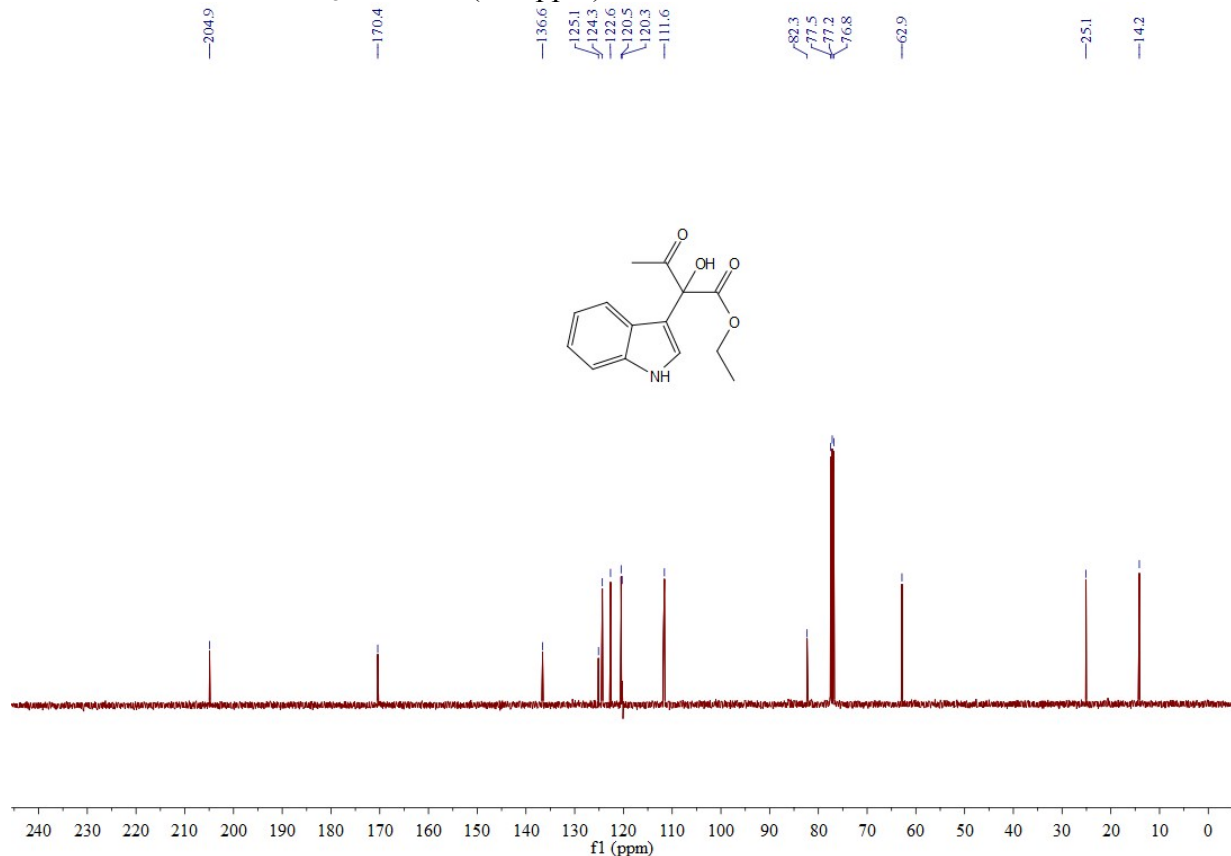
ethyl 2-hydroxy-2-(1-methyl-1H-pyrrol-2-yl)-3-oxobutanoate (6ba)

Colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 6.65 (s, 1H), 6.15 (s, 1H), 6.10 (t, $J = 3.0$ Hz, 1H), 4.50 (s, 1H), 4.39 (qd, $J = 7.0, 2.8$ Hz, 2H), 3.53 (s, 3H), 2.35 (s, 3H), 1.39 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 203.1, 168.4, 125.8, 124.5, 109.8, 106.2, 81.2, 62.2, 34.3, 25.2, 13.2; HRMS calcd for $\text{C}_{11}\text{H}_{15}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 248.0893, found 228.0887.

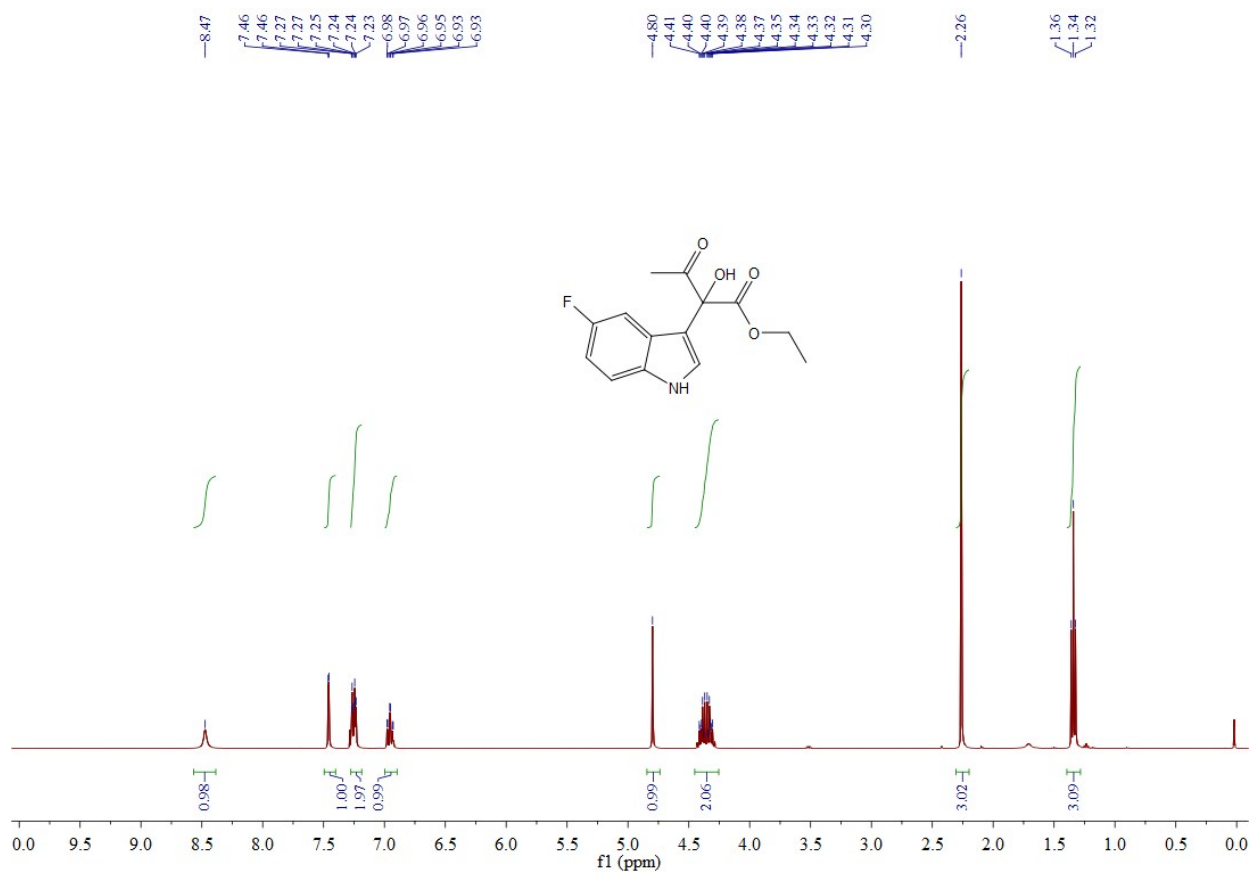
5. ¹H and ¹³C NMR Spectra of Compounds 3aa-3oa



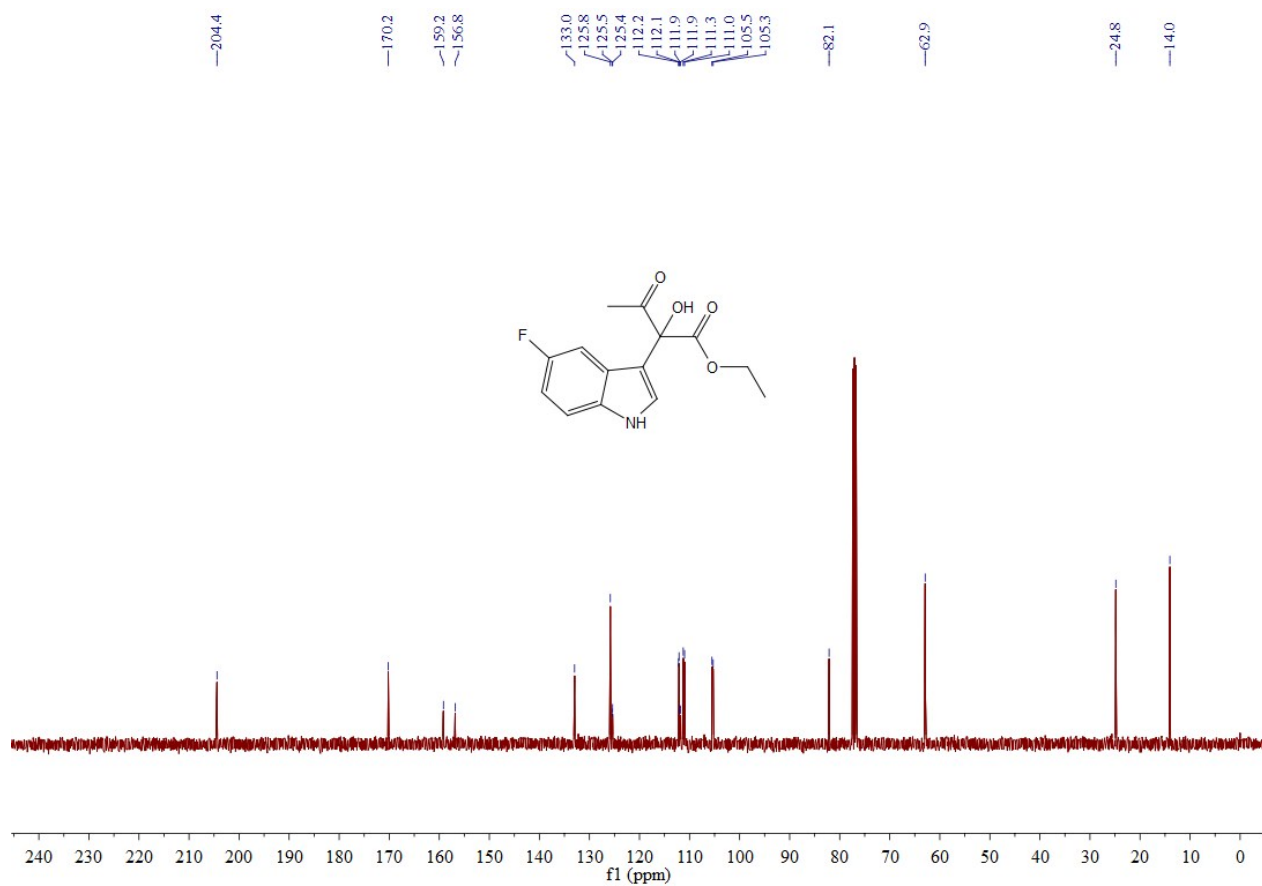
¹H NMR of **3aa** in CDCl₃ at 297 K (δ in ppm).



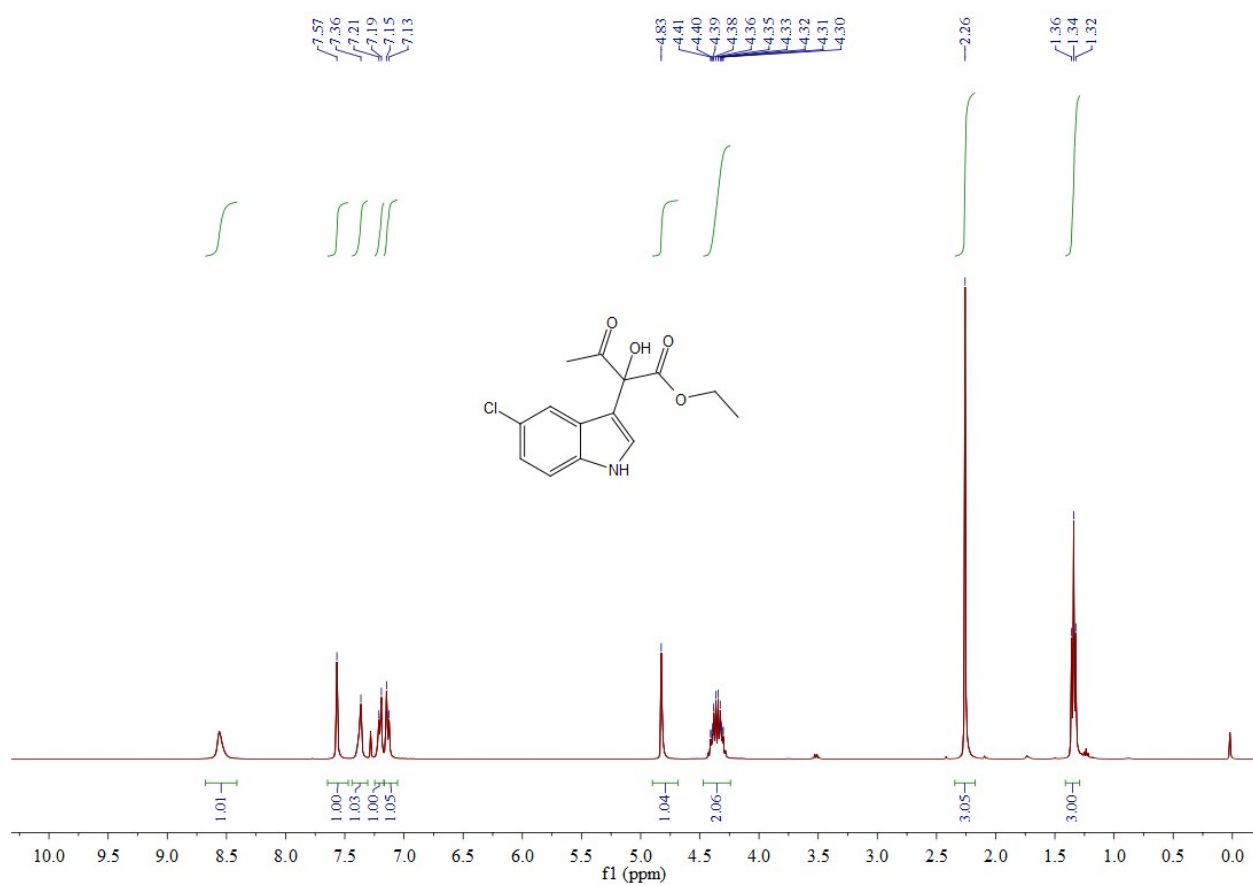
¹³C NMR of **3aa** in CDCl₃ at 299 K (δ in ppm).



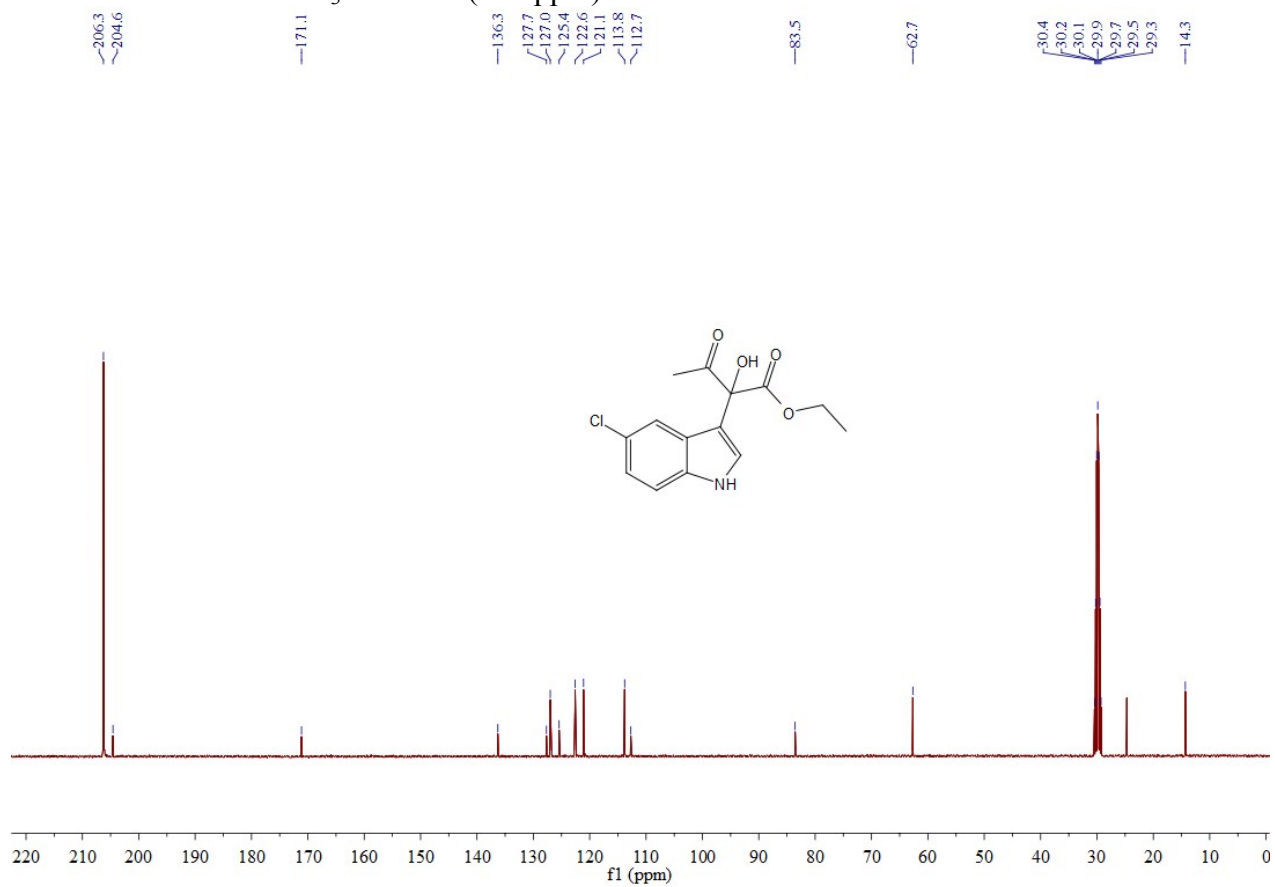
¹H NMR of **3ba** in CDCl₃ at 297 K (δ in ppm).



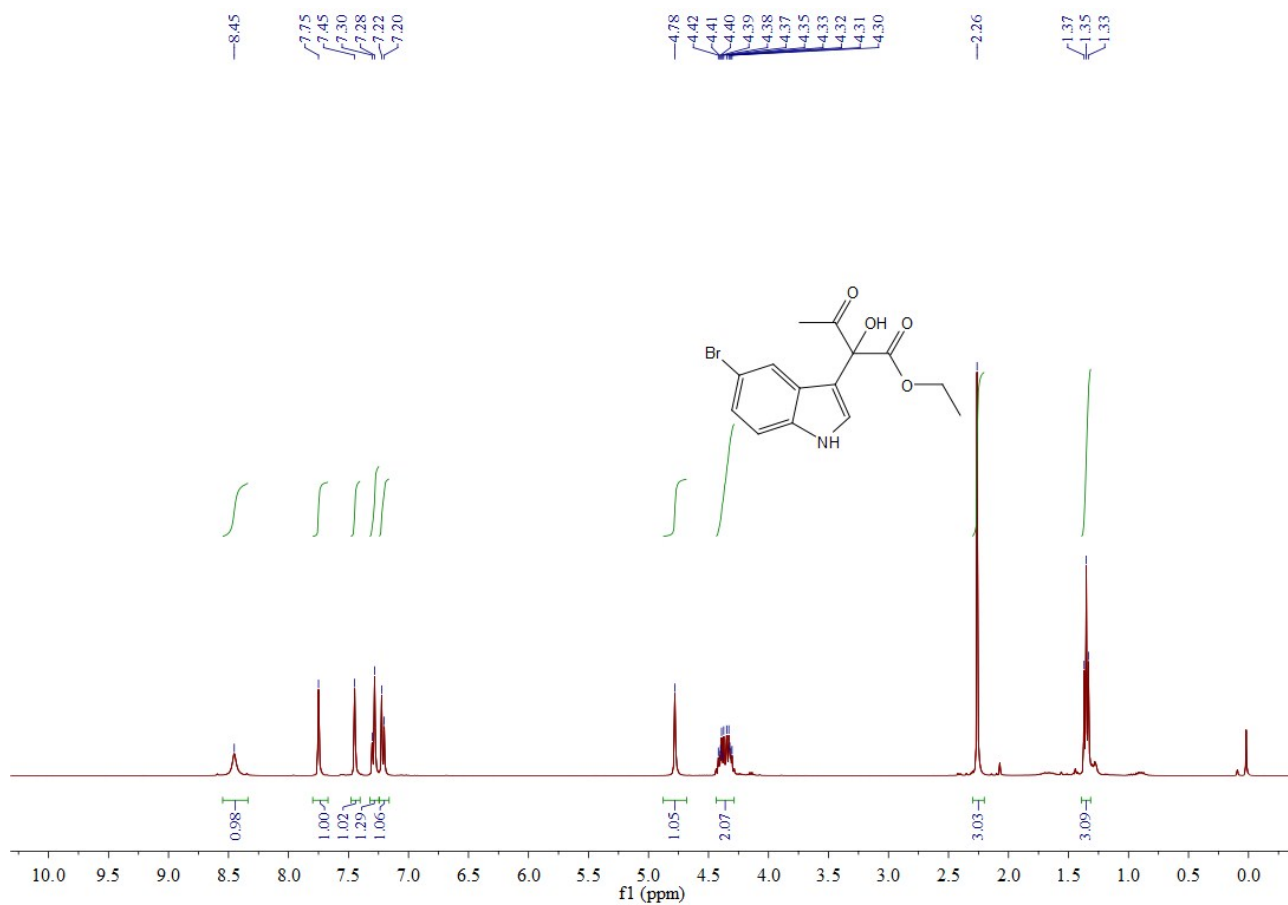
¹³C NMR of **3ba** in CDCl₃ at 299 K (δ in ppm).



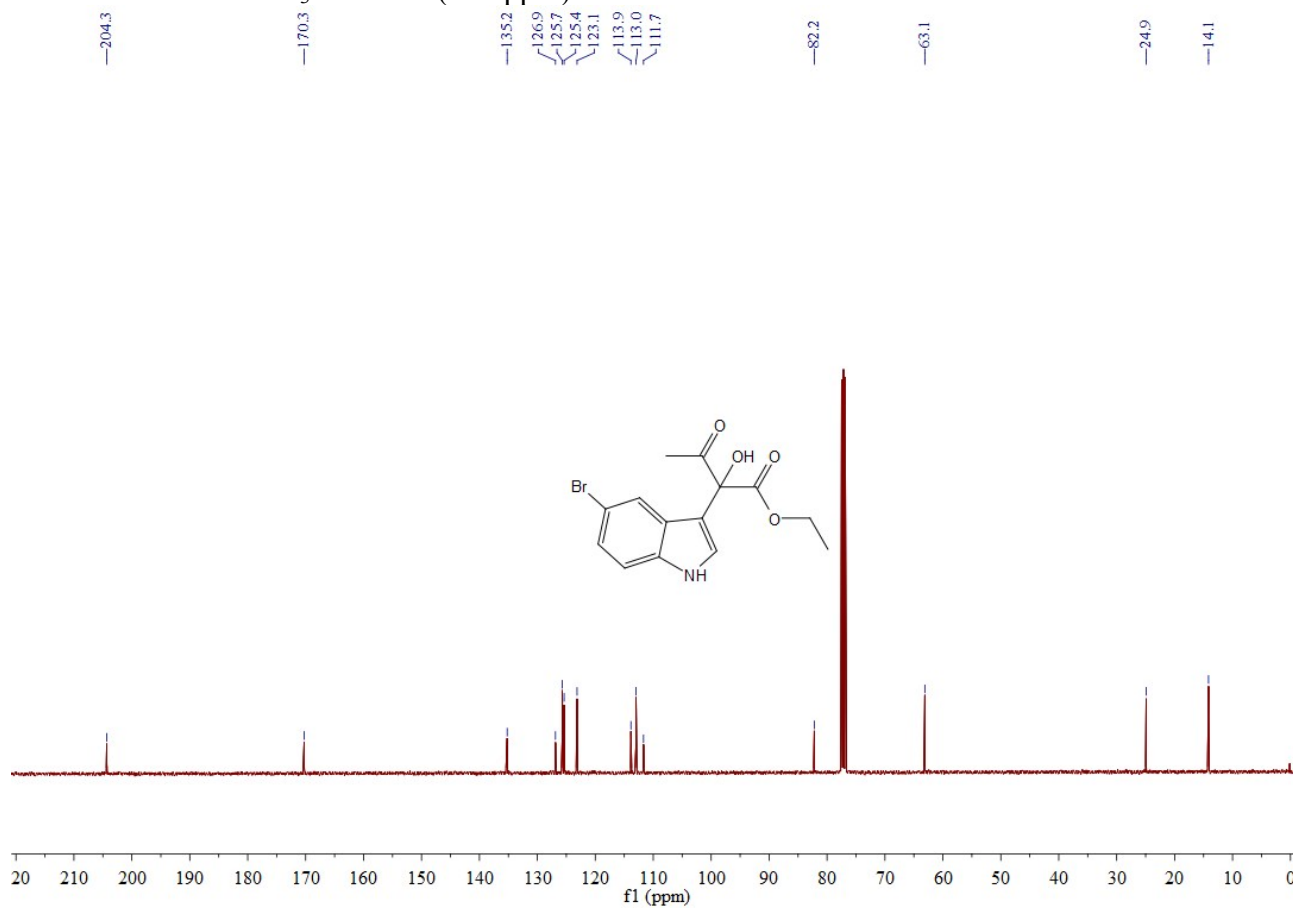
¹H NMR of **3ca** in CDCl₃ at 297 K (δ in ppm).



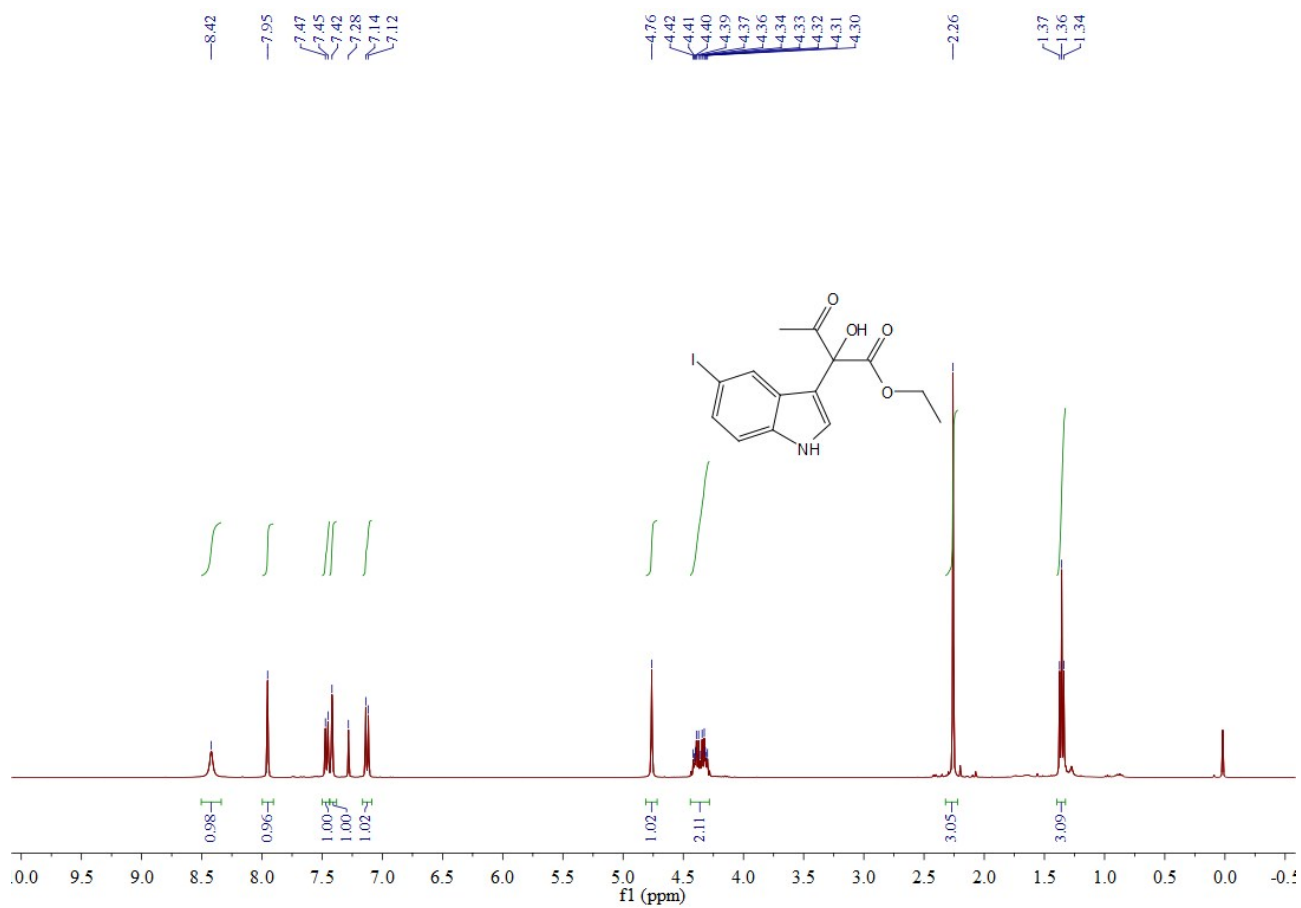
¹³C NMR of **3ca** in CDCl₃ at 299 K (δ in ppm).



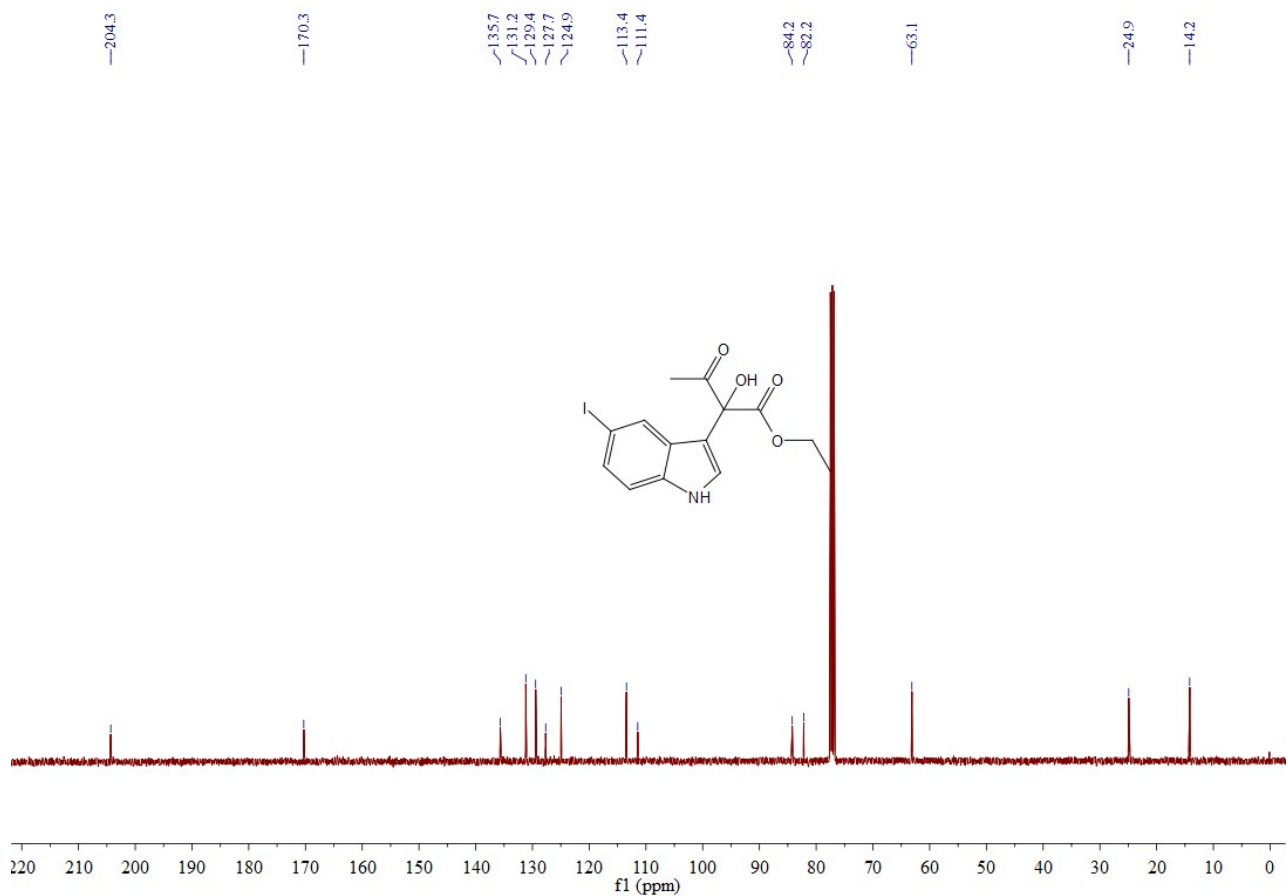
^1H NMR of **3da** in CDCl_3 at 297 K (δ in ppm).



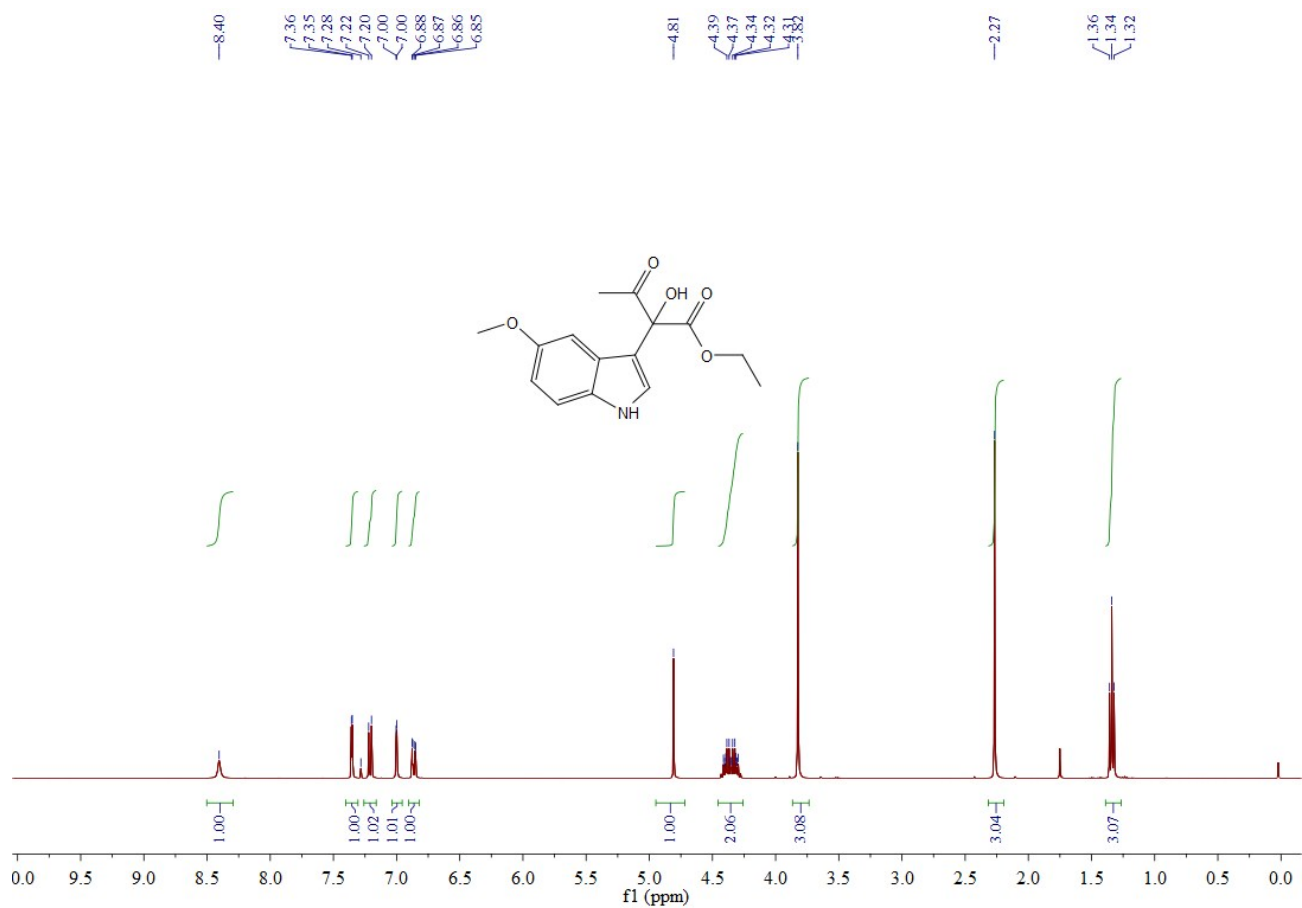
^{13}C NMR of **3da** in CDCl_3 at 299 K (δ in ppm).



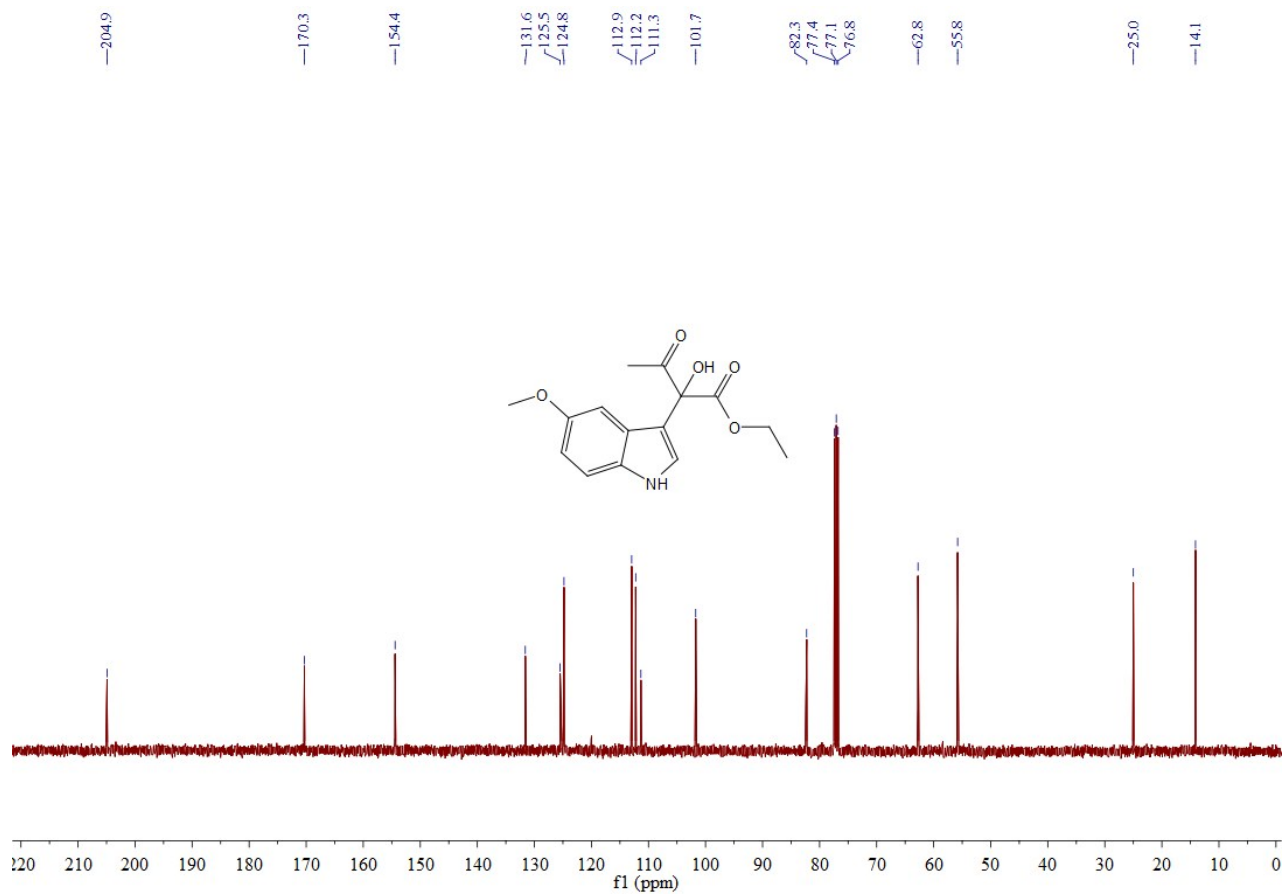
¹H NMR of **3ea** in CDCl₃ at 297 K (δ in ppm).



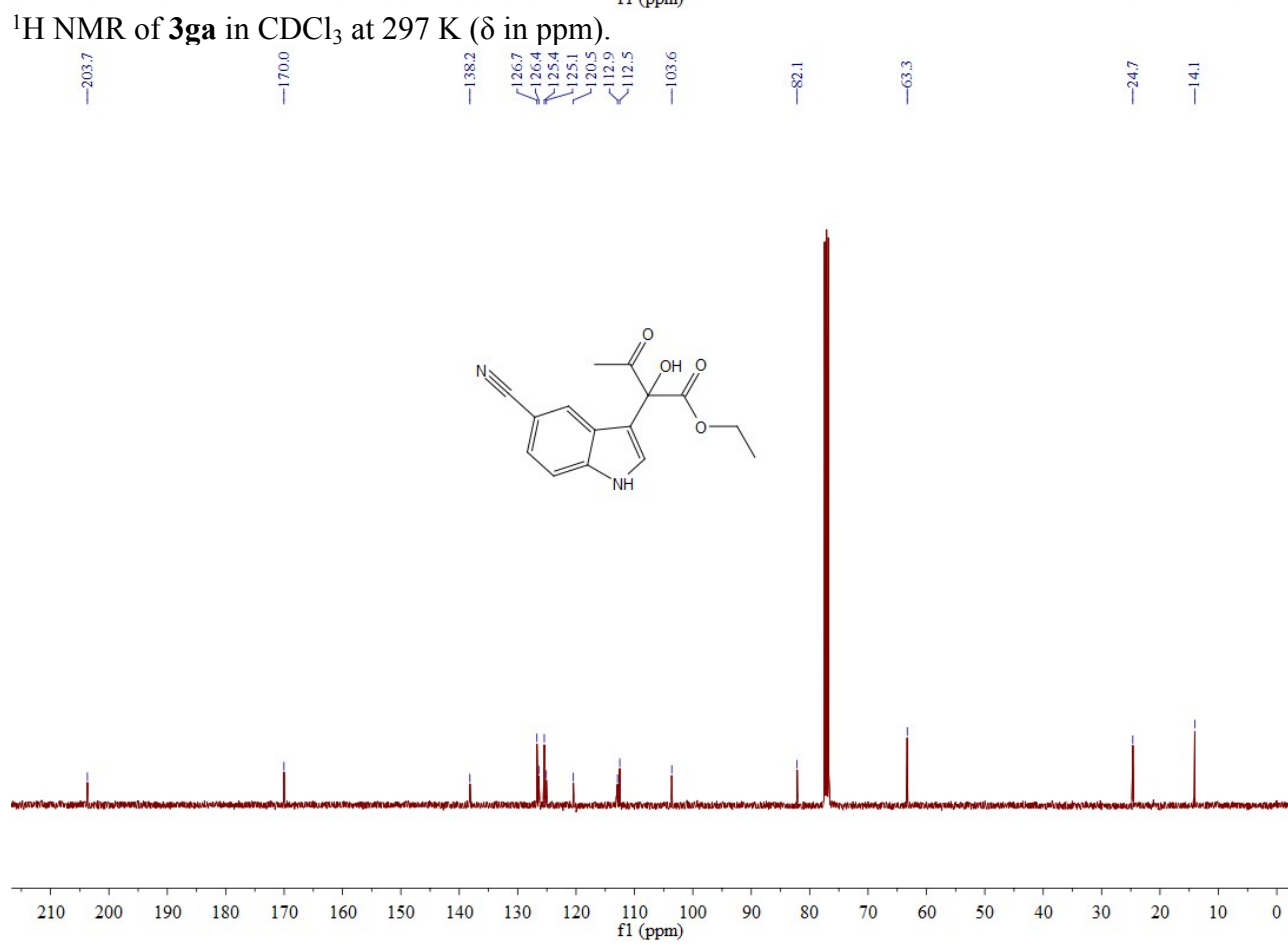
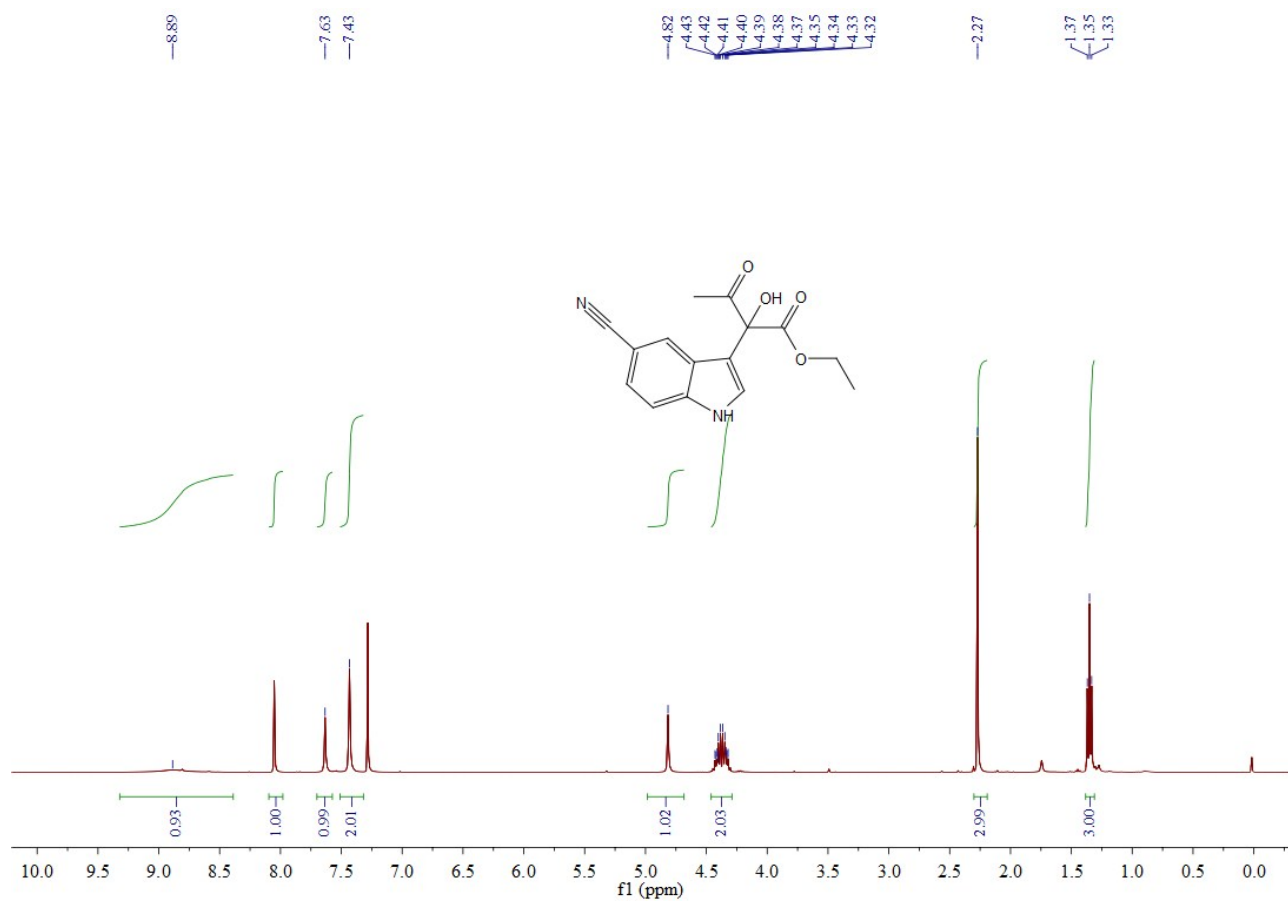
¹³C NMR of **3ea** in CDCl₃ at 299 K (δ in ppm).

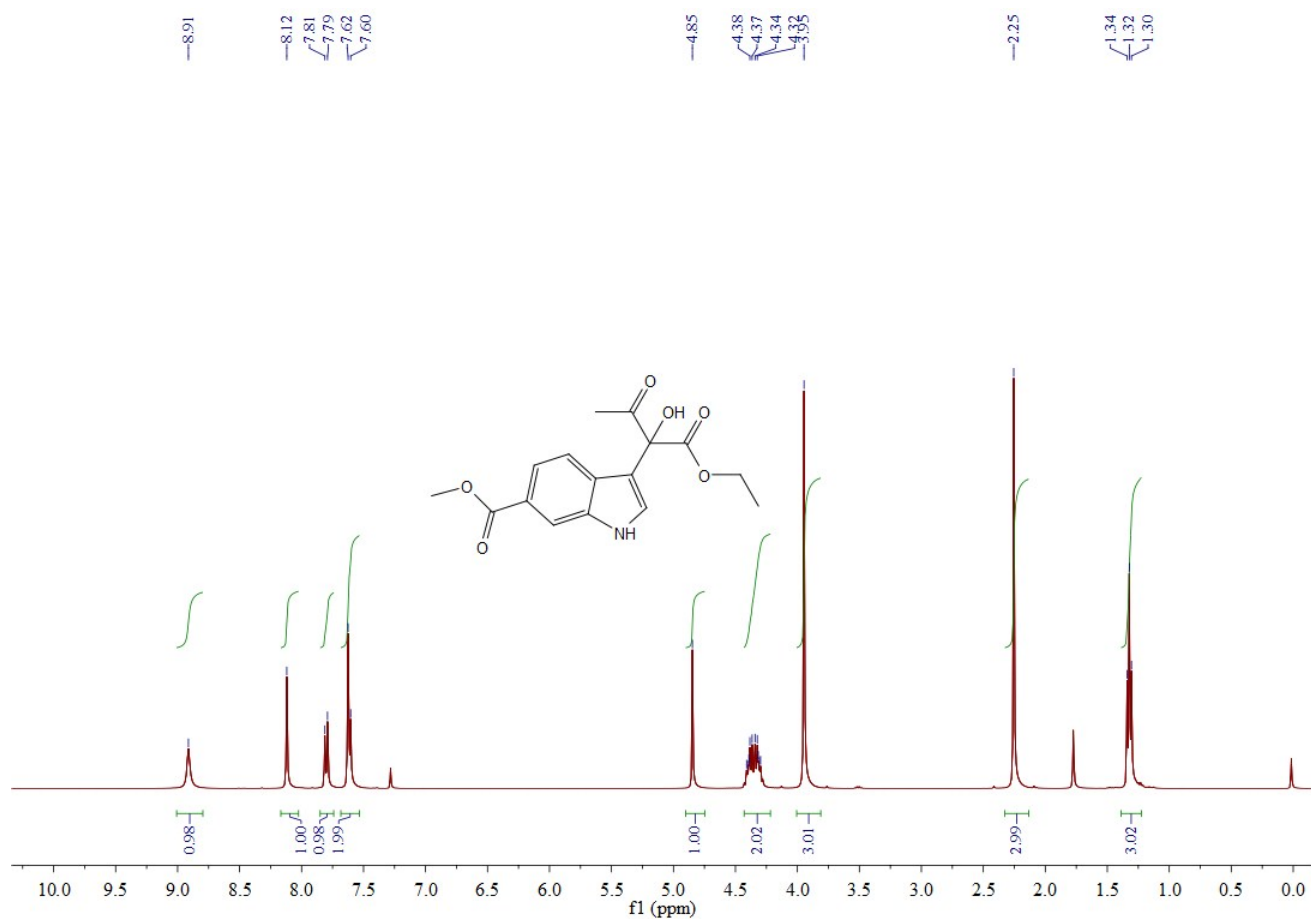


¹H NMR of **3fa** in CDCl₃ at 297 K (δ in ppm).

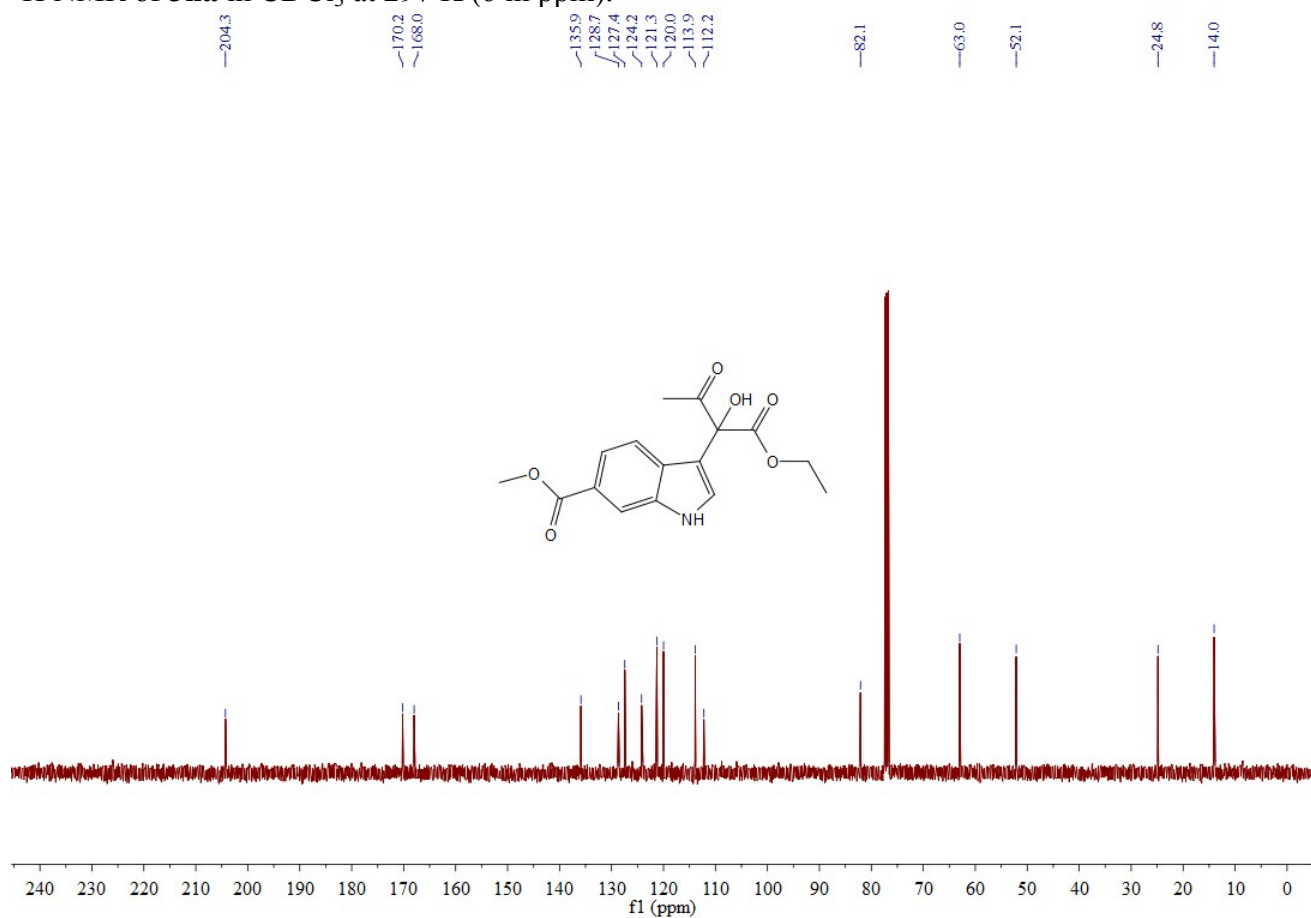


¹³C NMR of **3fa** in CDCl₃ at 299 K (δ in ppm).

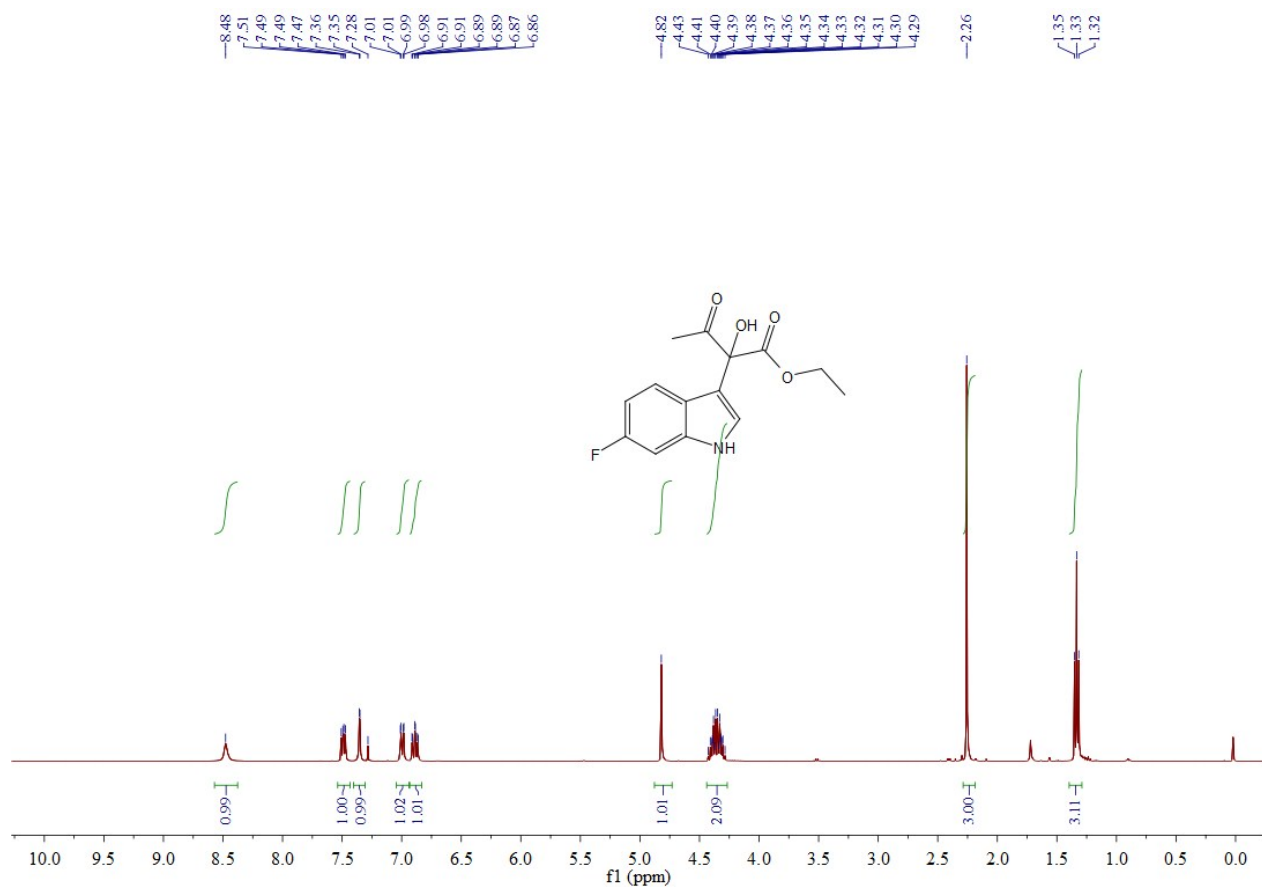




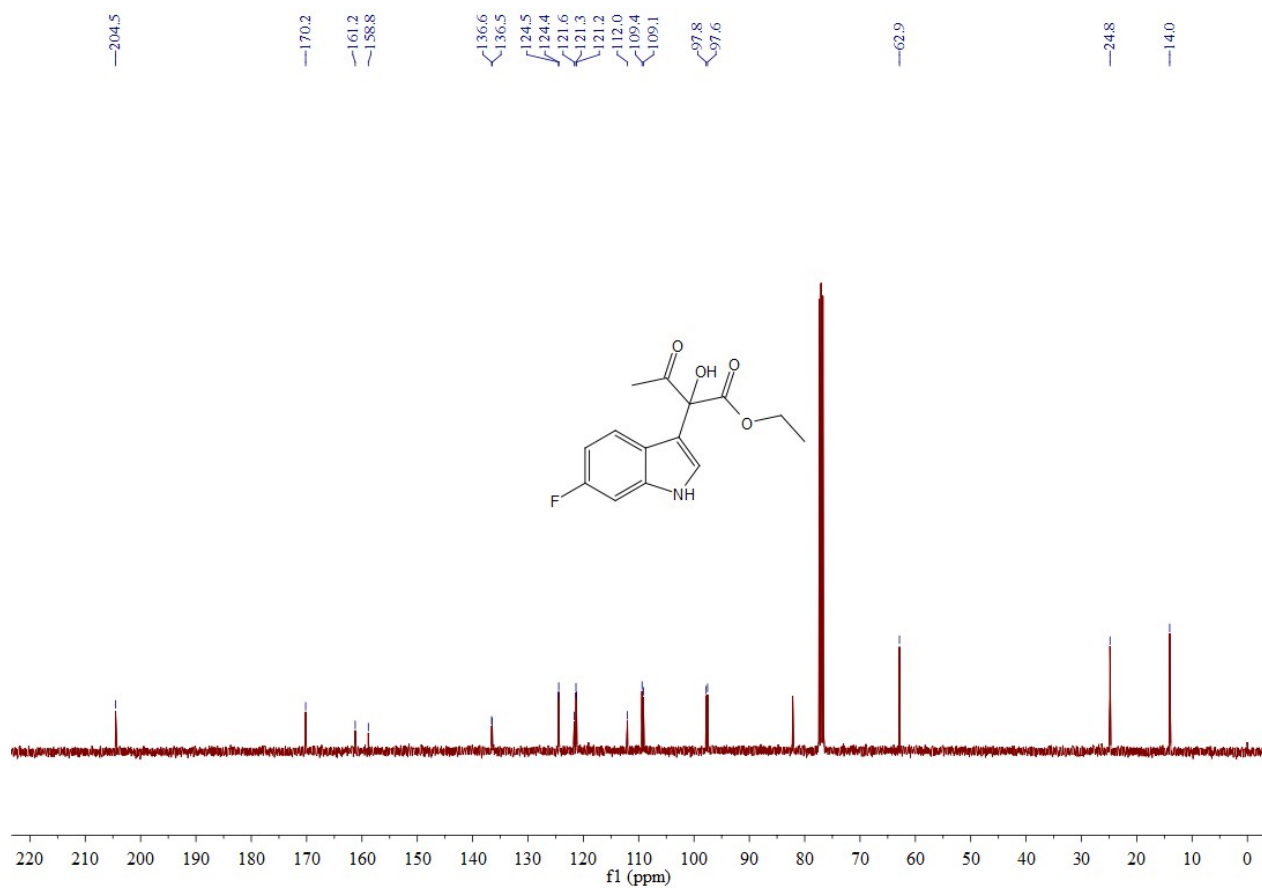
¹H NMR of **3ha** in CDCl₃ at 297 K (δ in ppm).



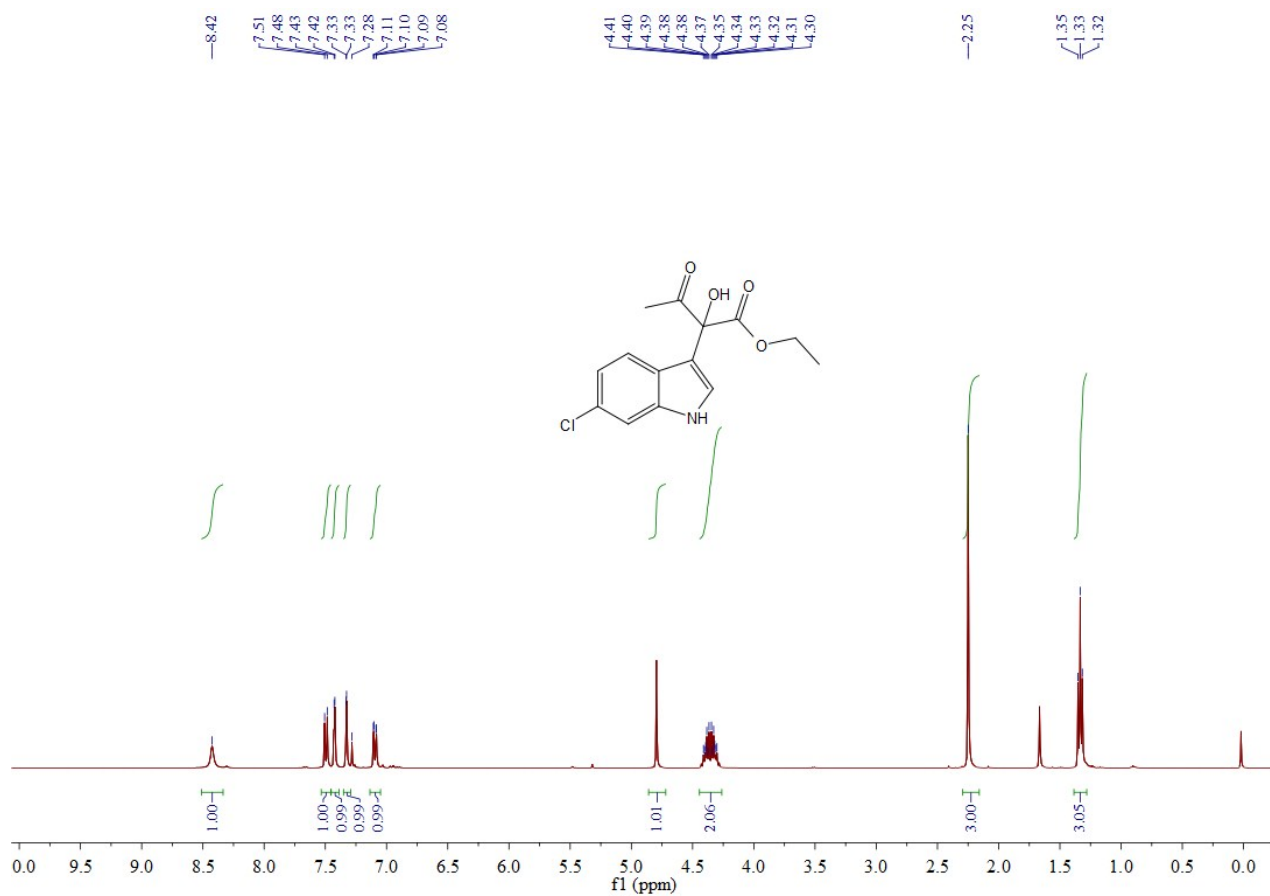
¹³C NMR of **3ha** in CDCl₃ at 299 K (δ in ppm).



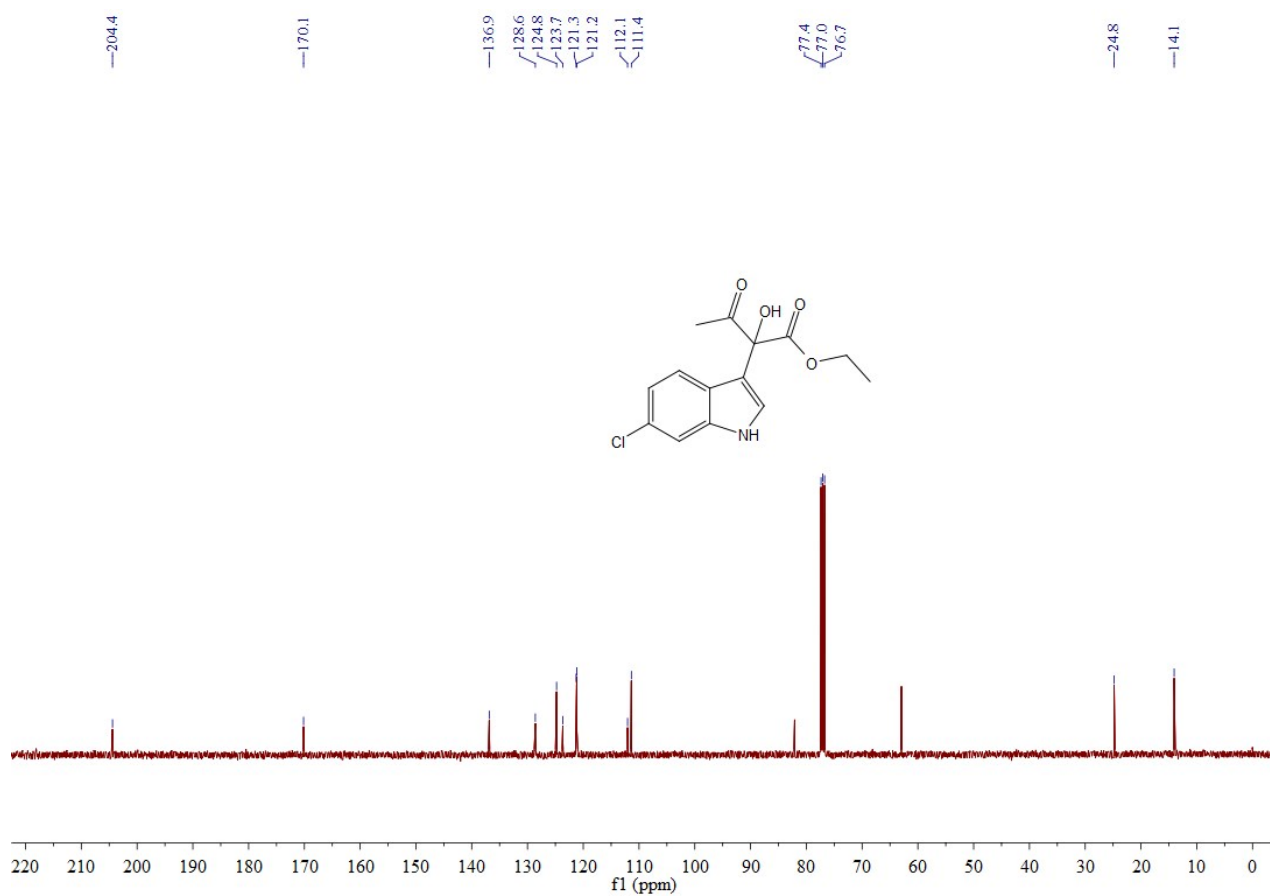
¹H NMR of **3ia** in CDCl₃ at 297 K (δ in ppm).



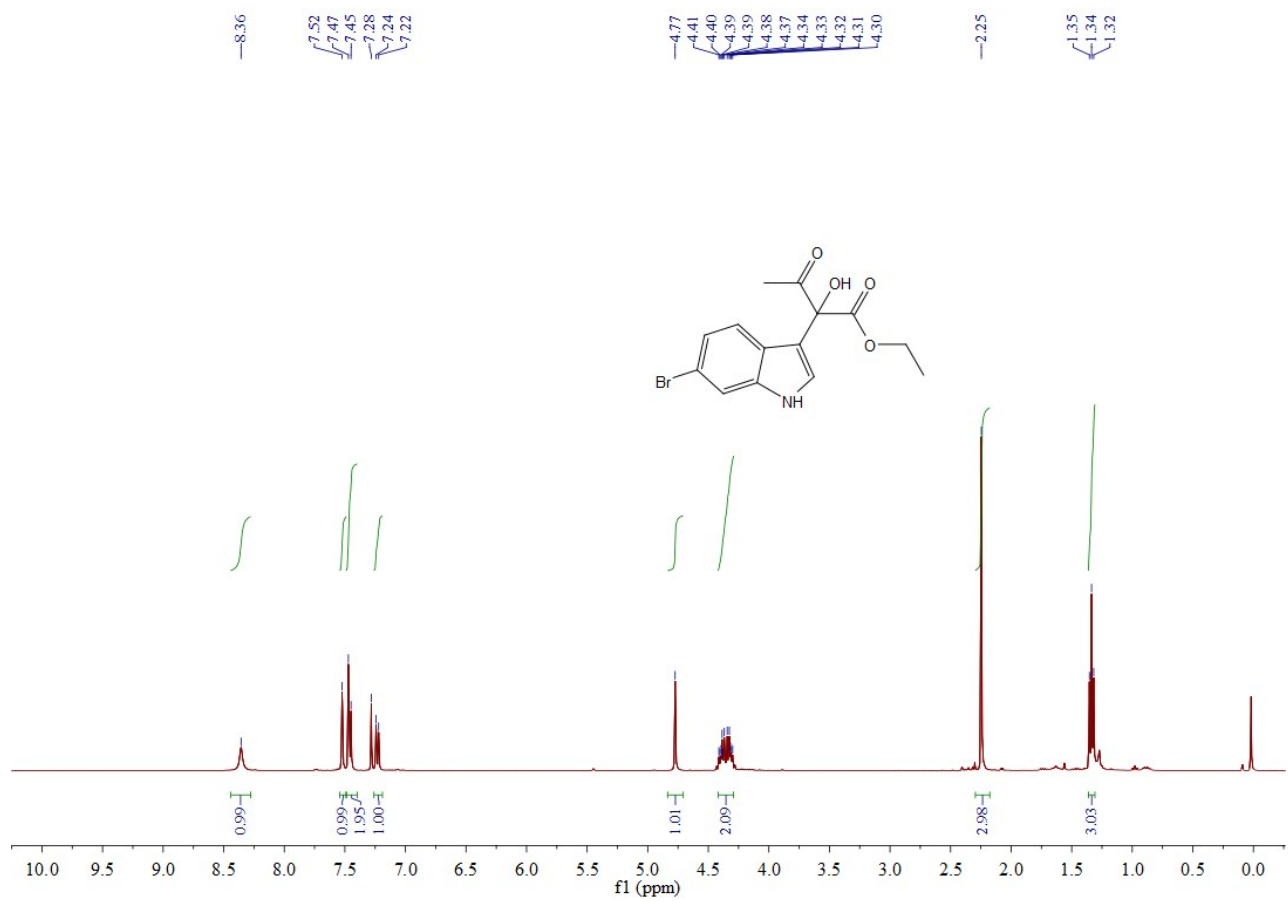
¹³C NMR of **3ia** in CDCl₃ at 299 K (δ in ppm).



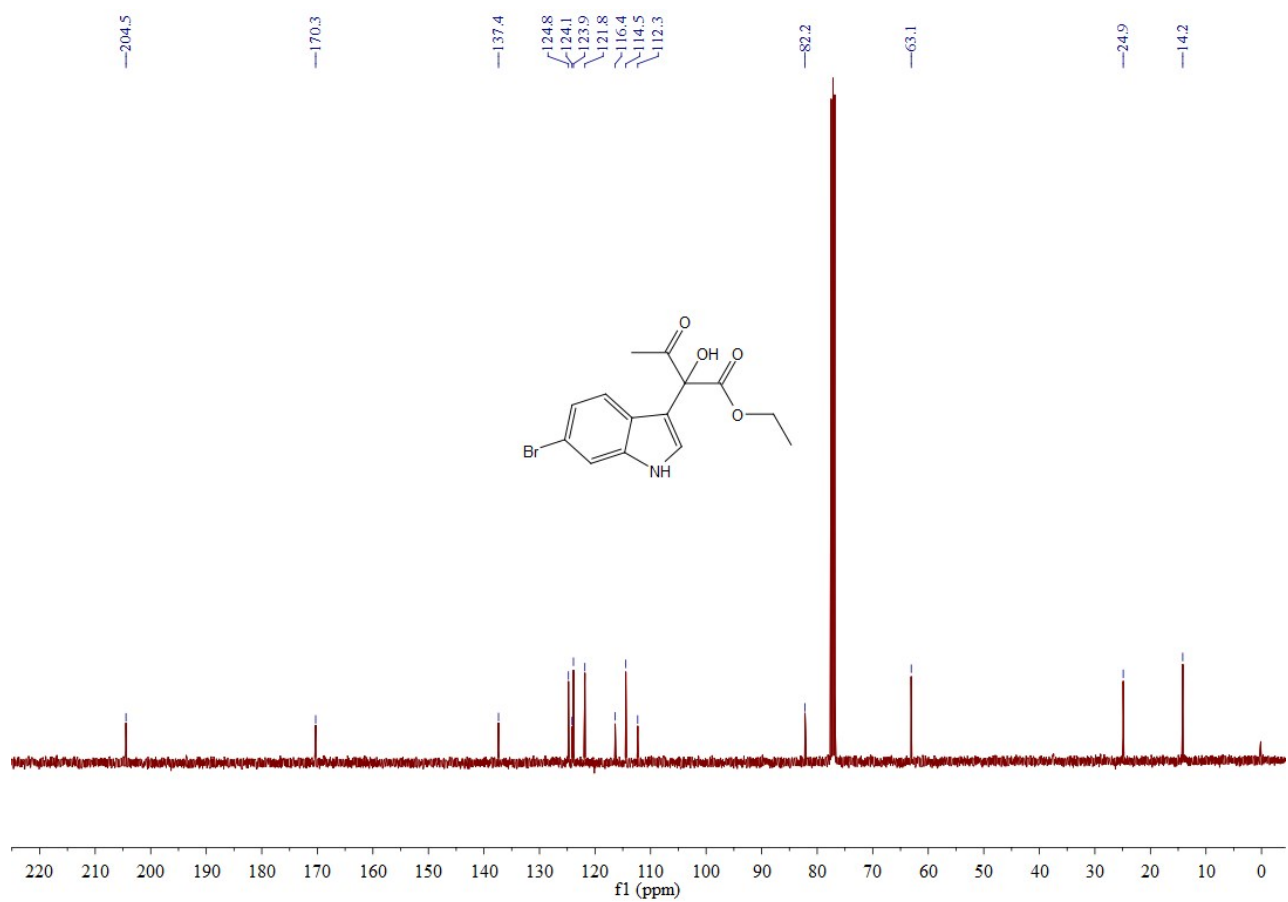
¹H NMR of **3ja** in CDCl₃ at 297 K (δ in ppm).



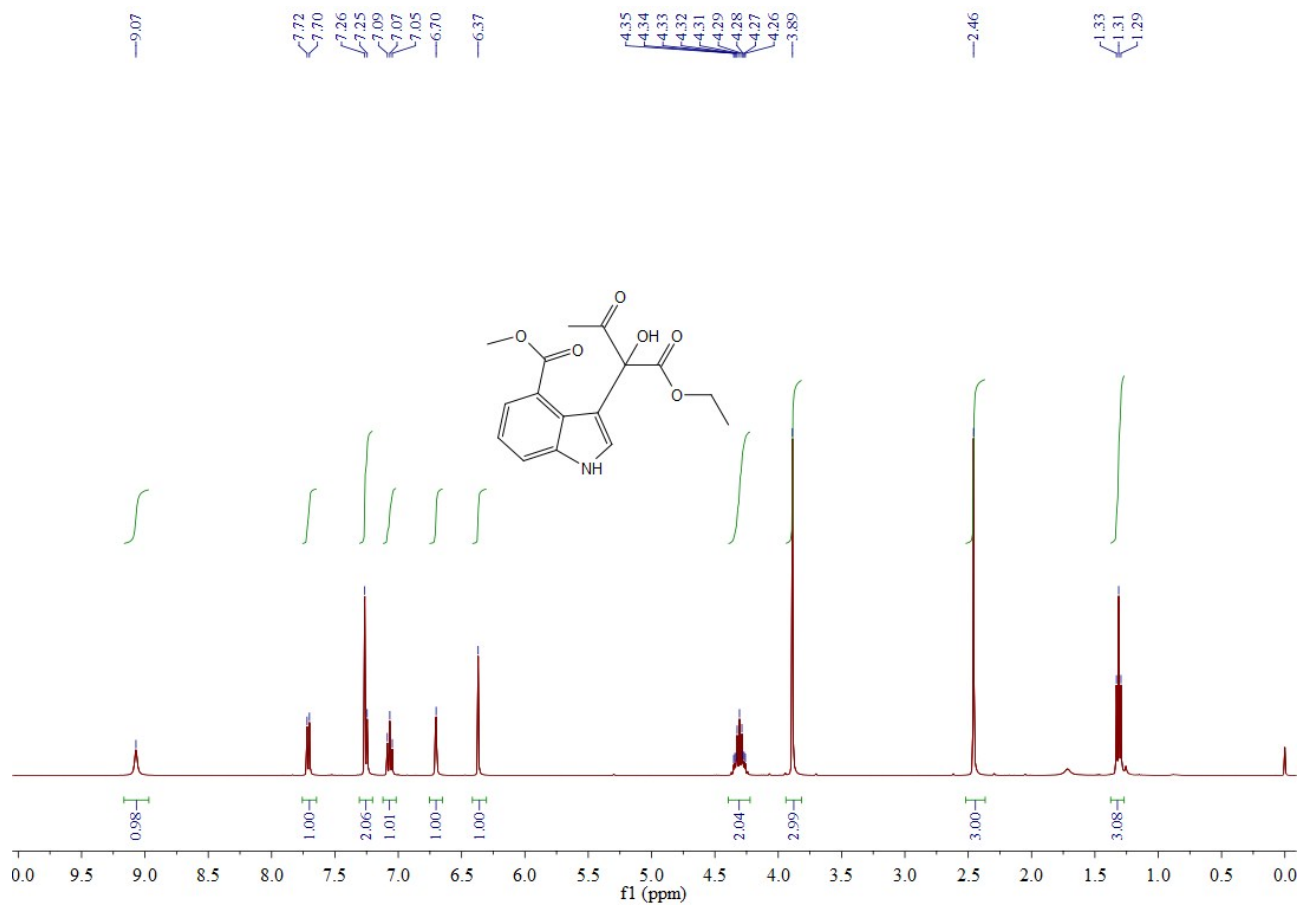
¹³C NMR of **3ja** in CDCl₃ at 299 K (δ in ppm).



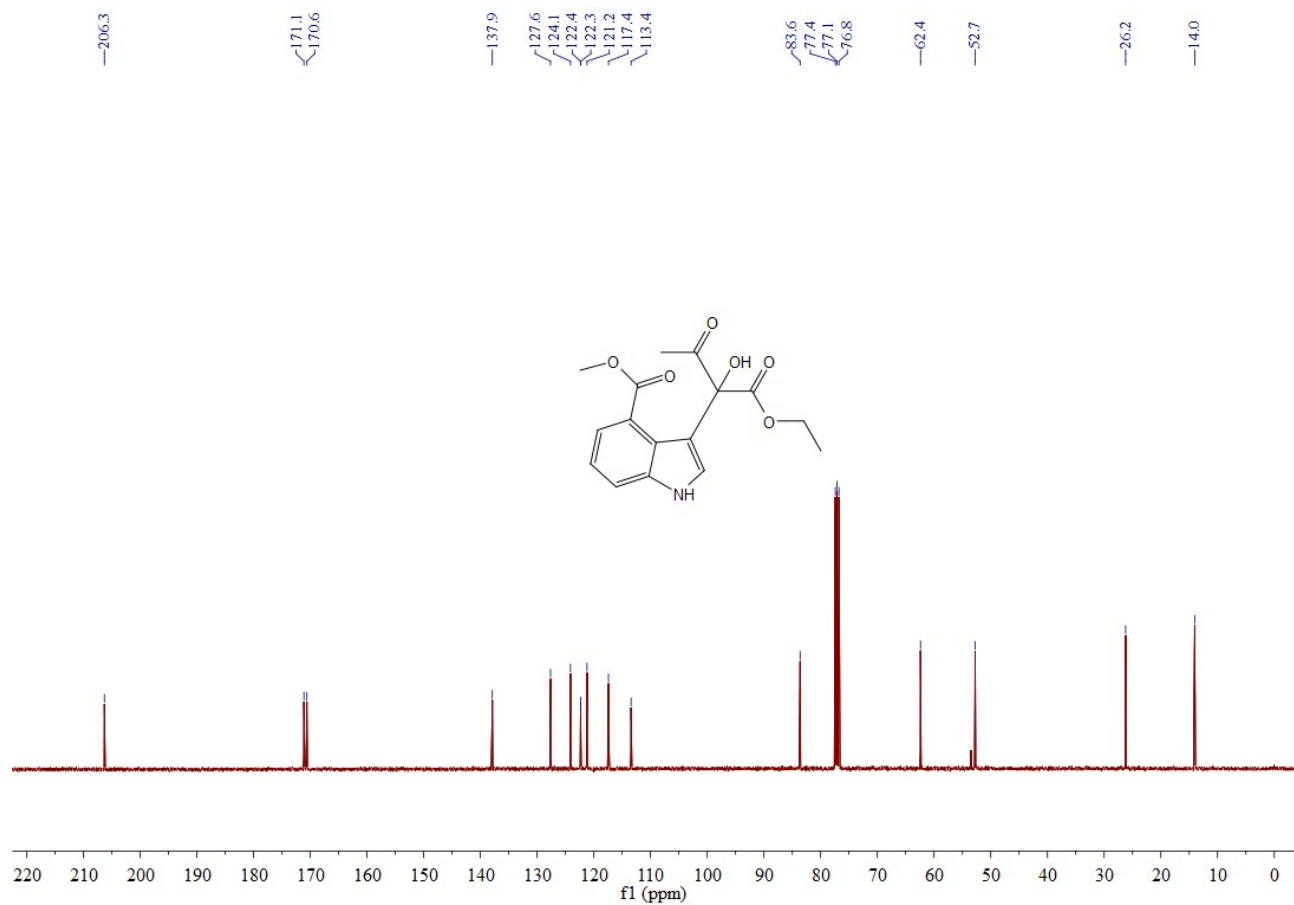
¹H NMR of **3ka** in CDCl₃ at 297 K (δ in ppm).



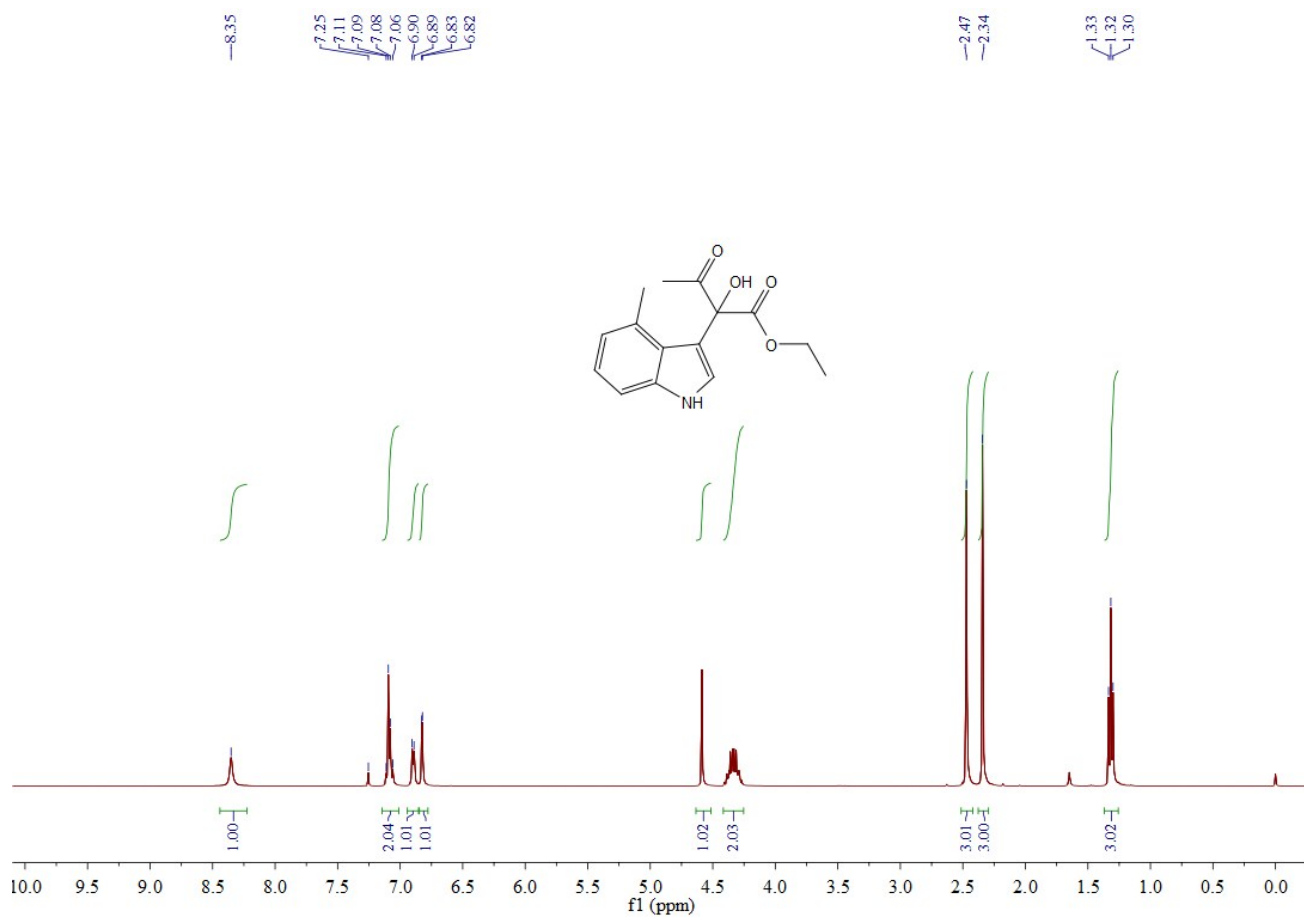
¹³C NMR of **3ka** in CDCl₃ at 299 K (δ in ppm).



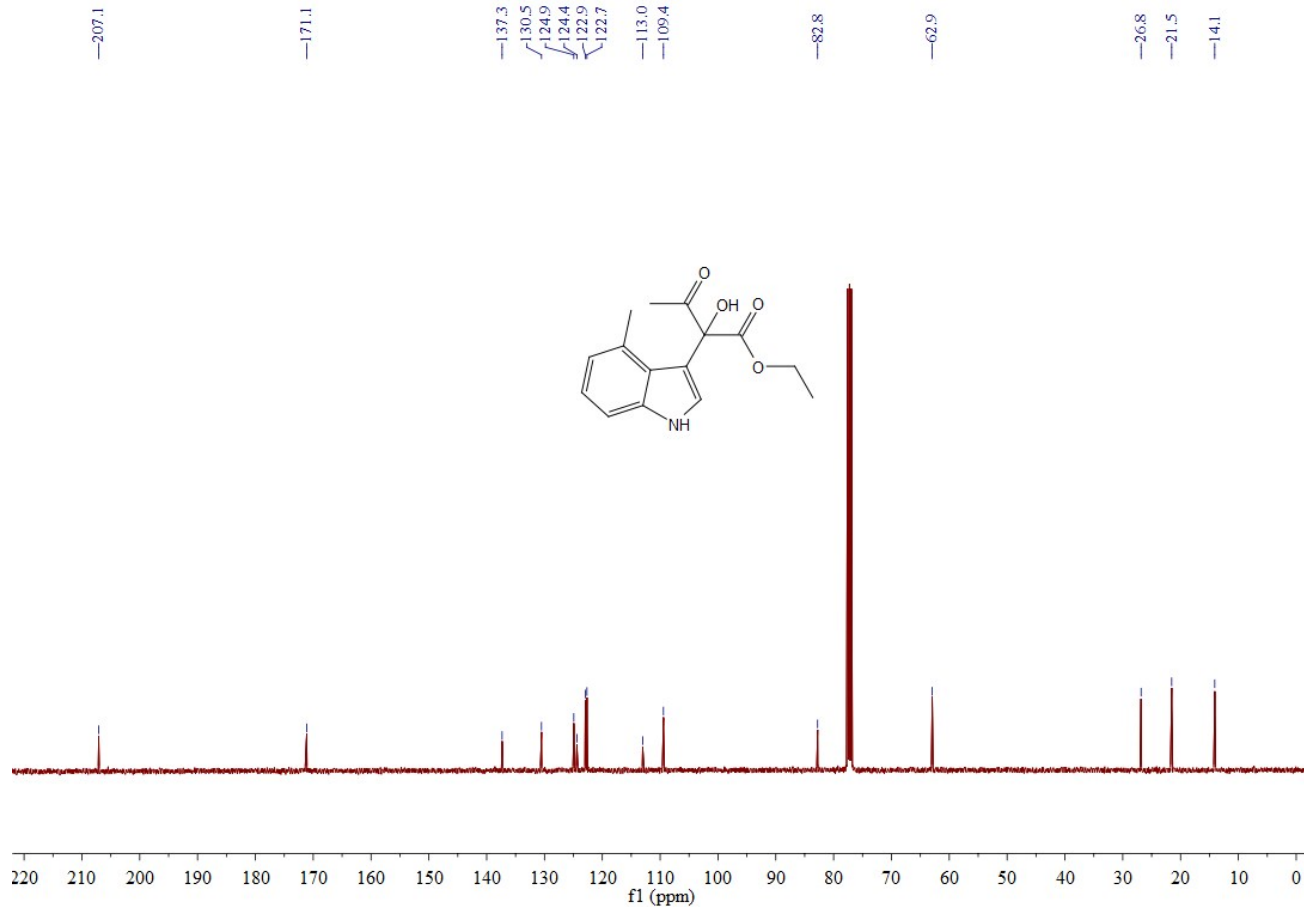
¹H NMR of **3la** in CDCl₃ at 297 K (δ in ppm).



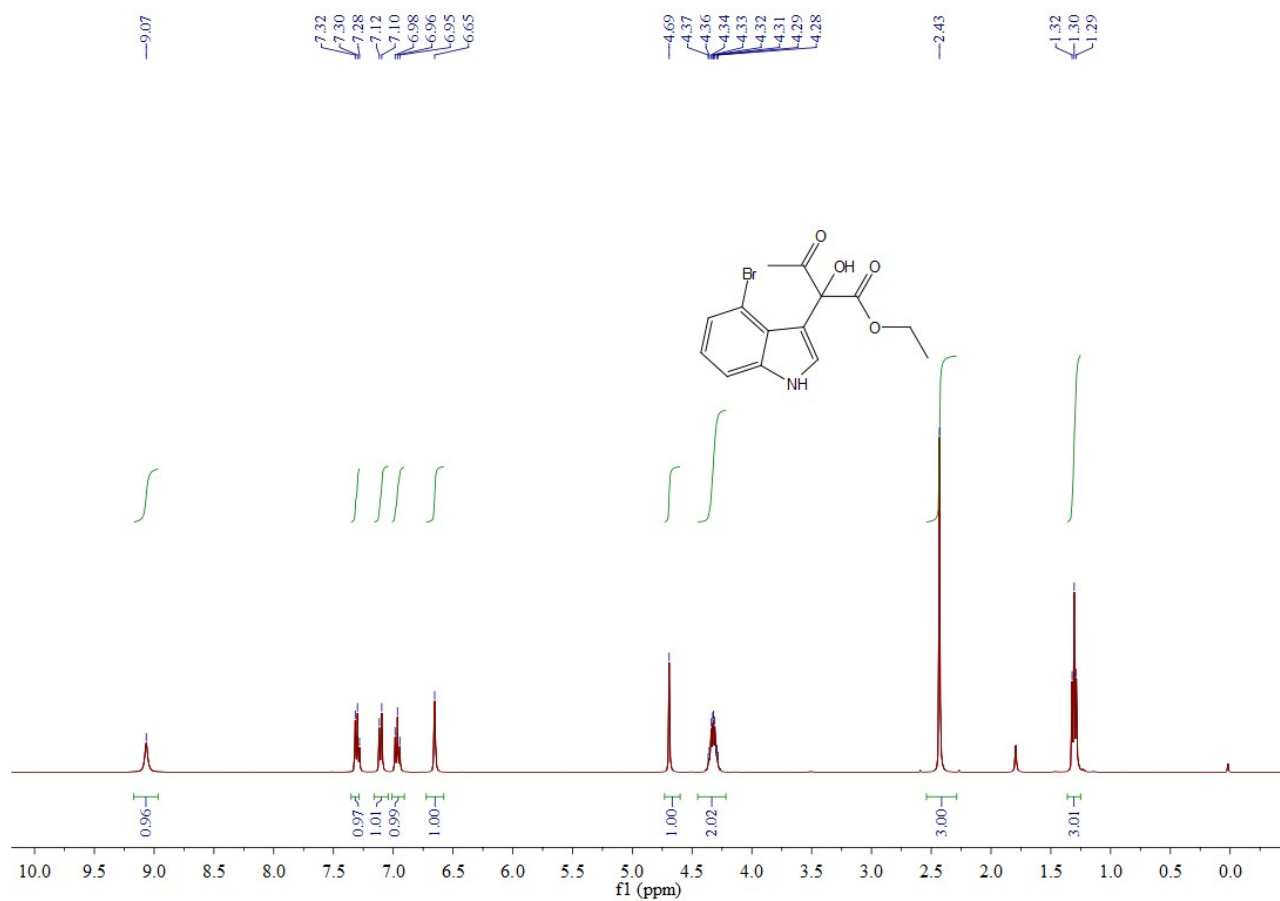
¹³C NMR of **3la** in CDCl₃ at 299 K (δ in ppm).



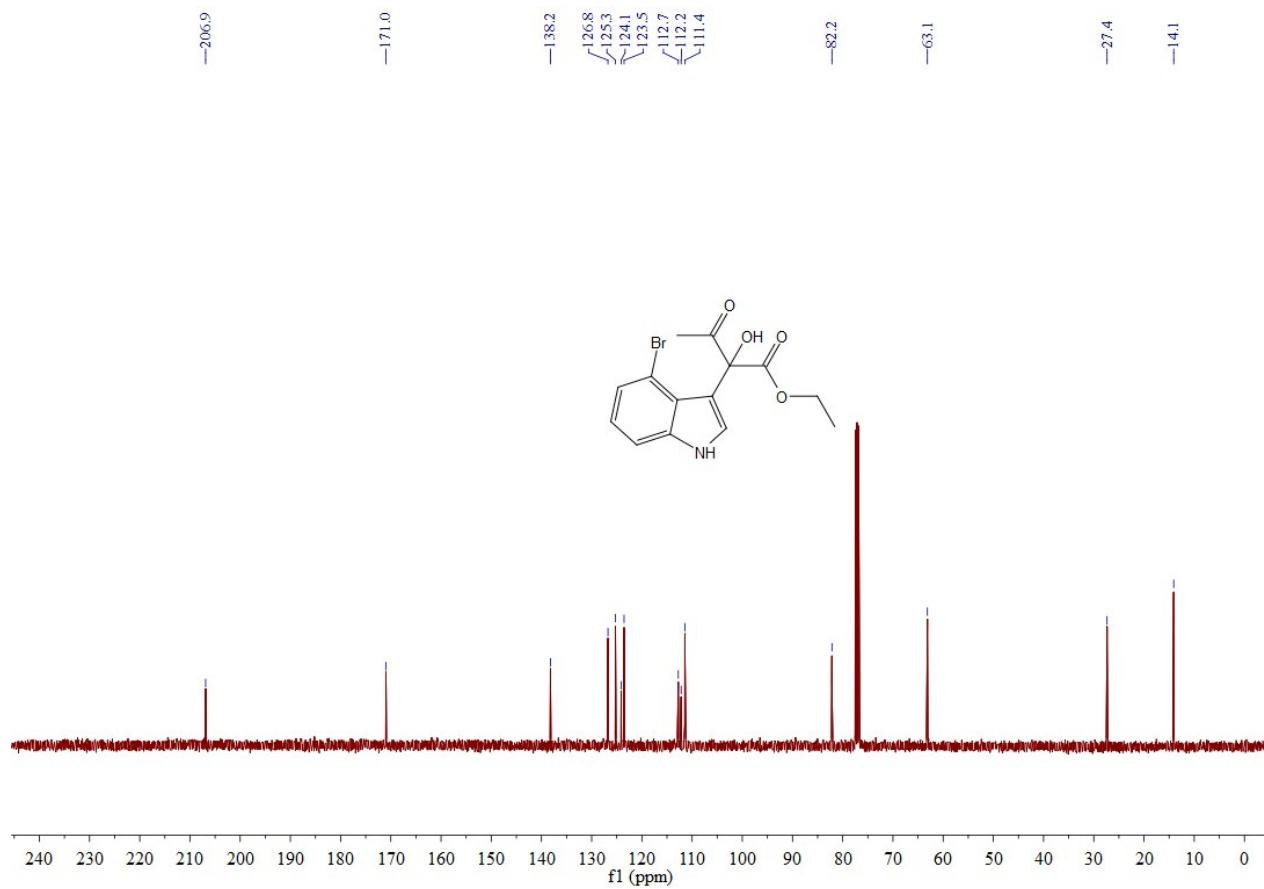
¹H NMR of **3ma in CDCl₃ at 297 K (δ in ppm).**



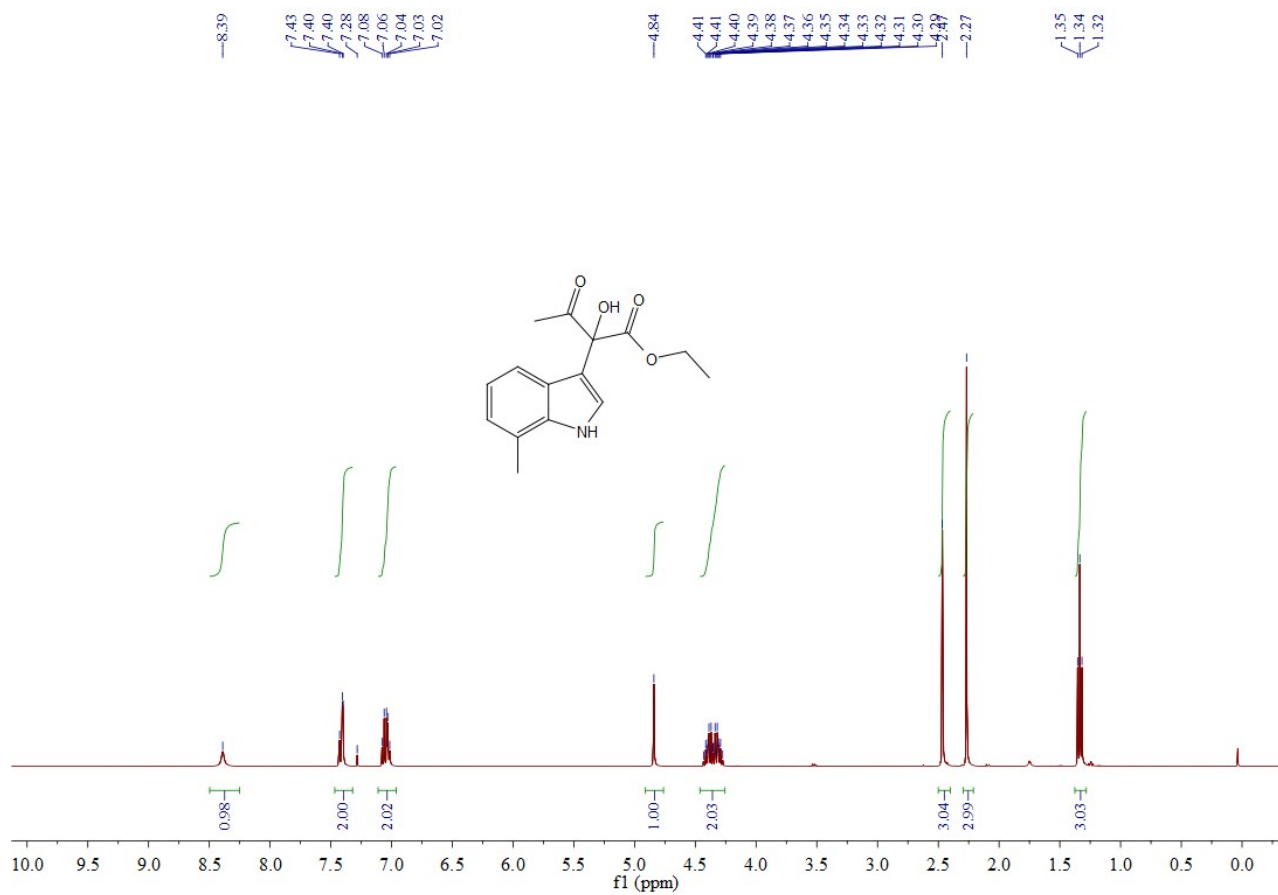
¹³C NMR of **3ma in CDCl₃ at 299 K (δ in ppm).**



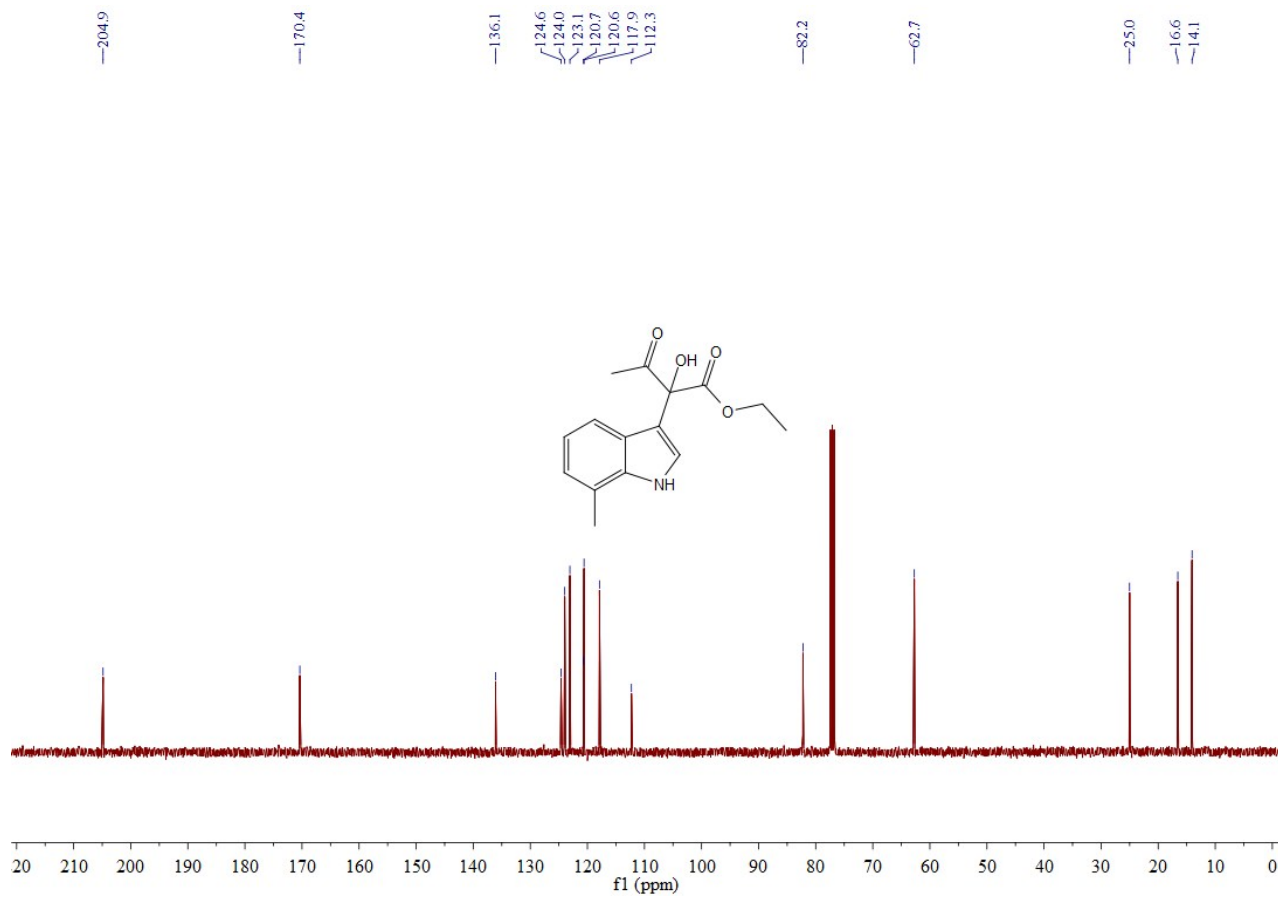
¹H NMR of **3na** in CDCl₃ at 297 K (δ in ppm).



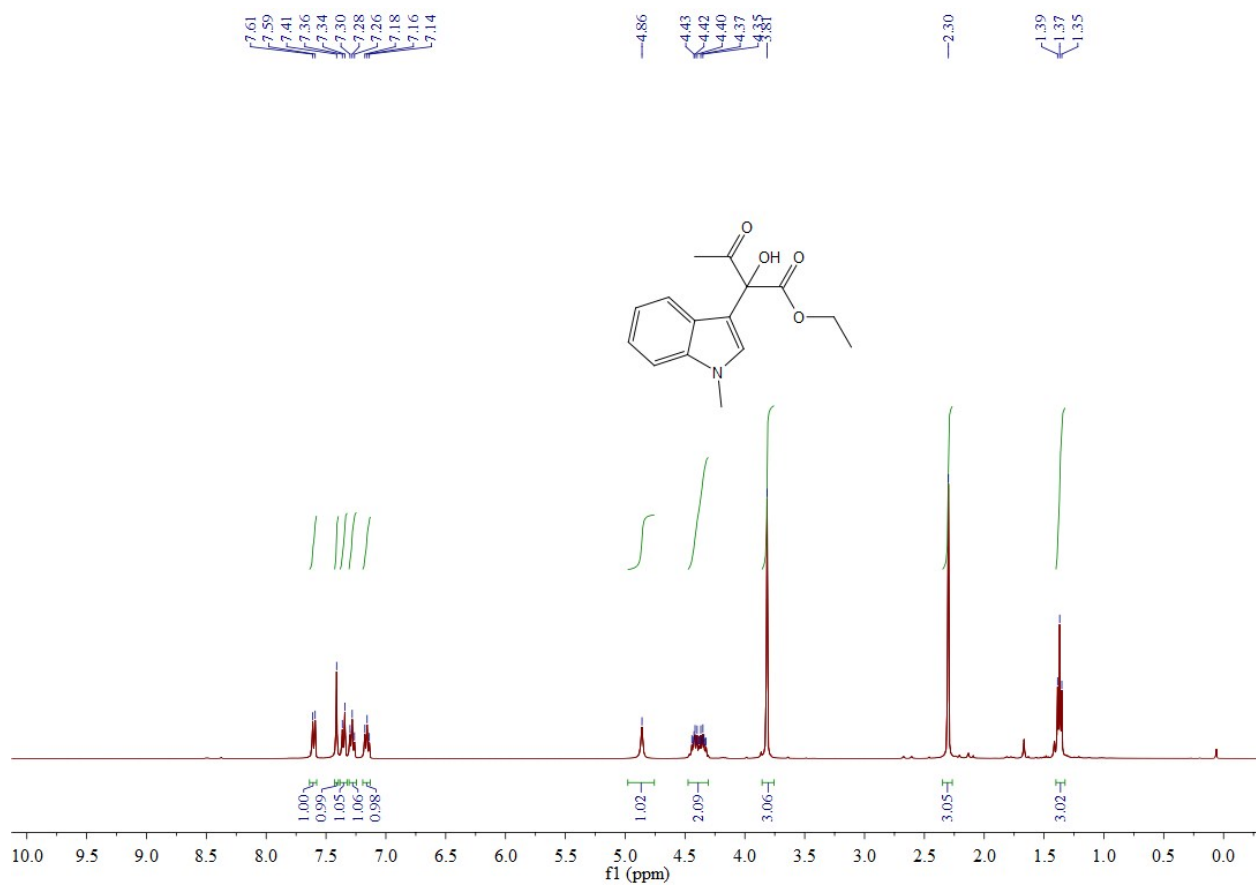
¹³C NMR of **3na** in CDCl₃ at 299 K (δ in ppm).



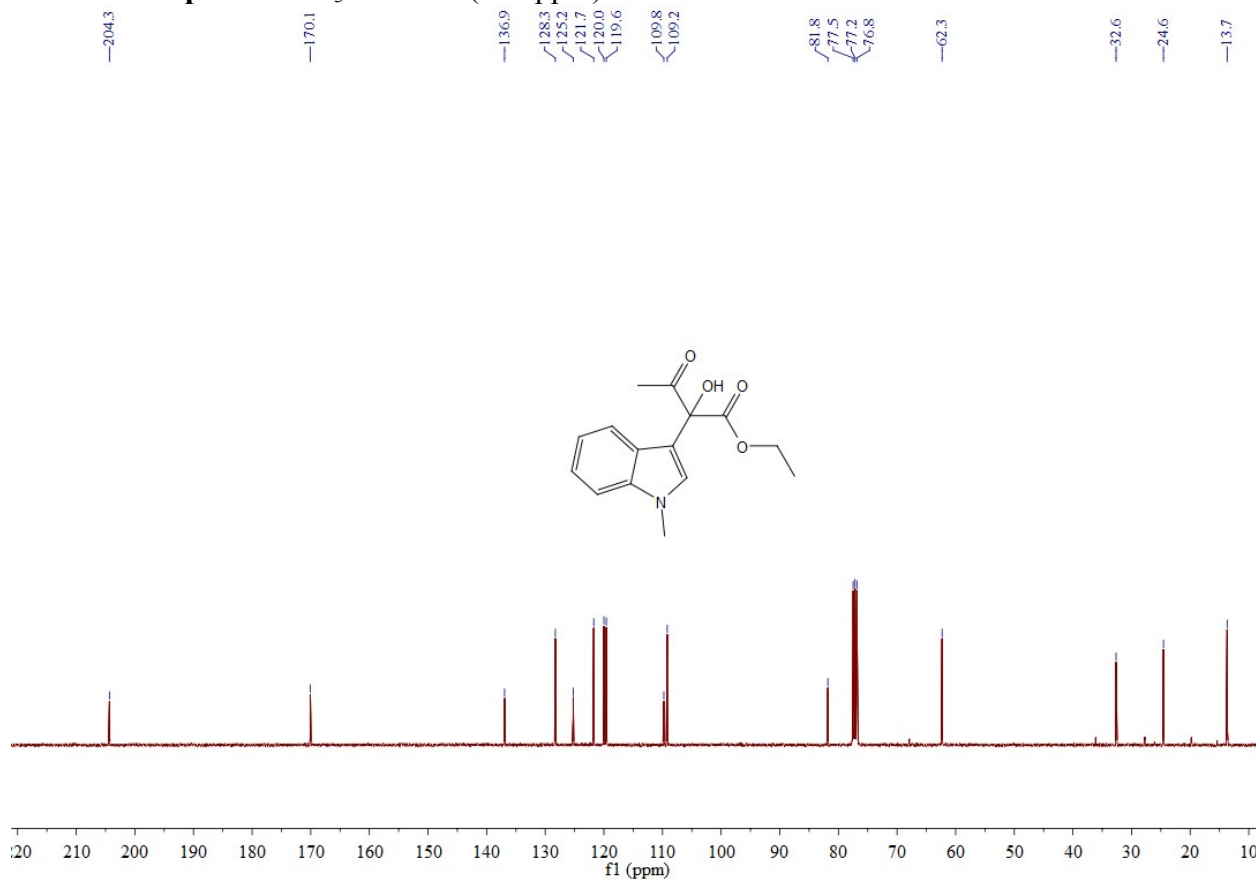
¹H NMR of **30a** in CDCl₃ at 297 K (δ in ppm).



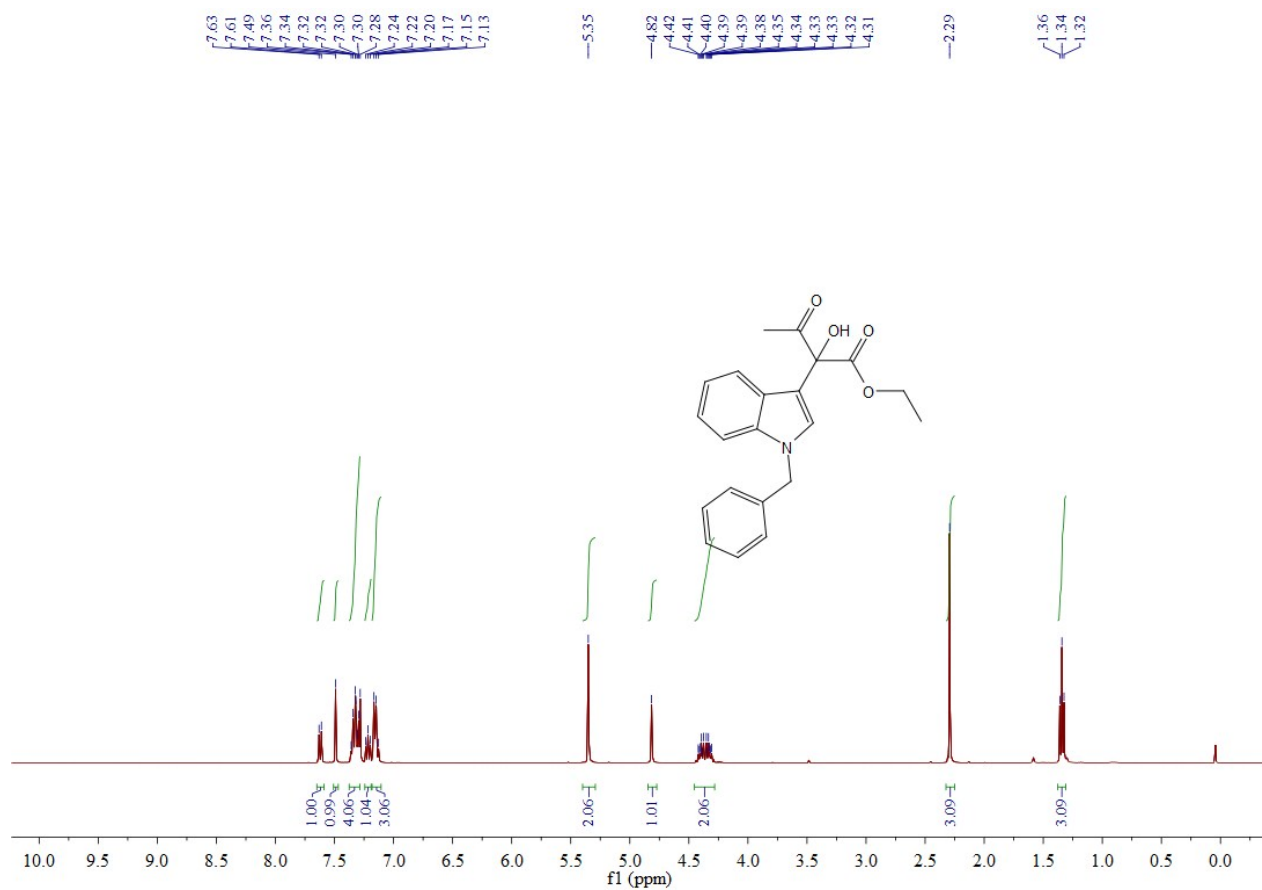
¹³C NMR of **30a** in CDCl₃ at 299 K (δ in ppm).



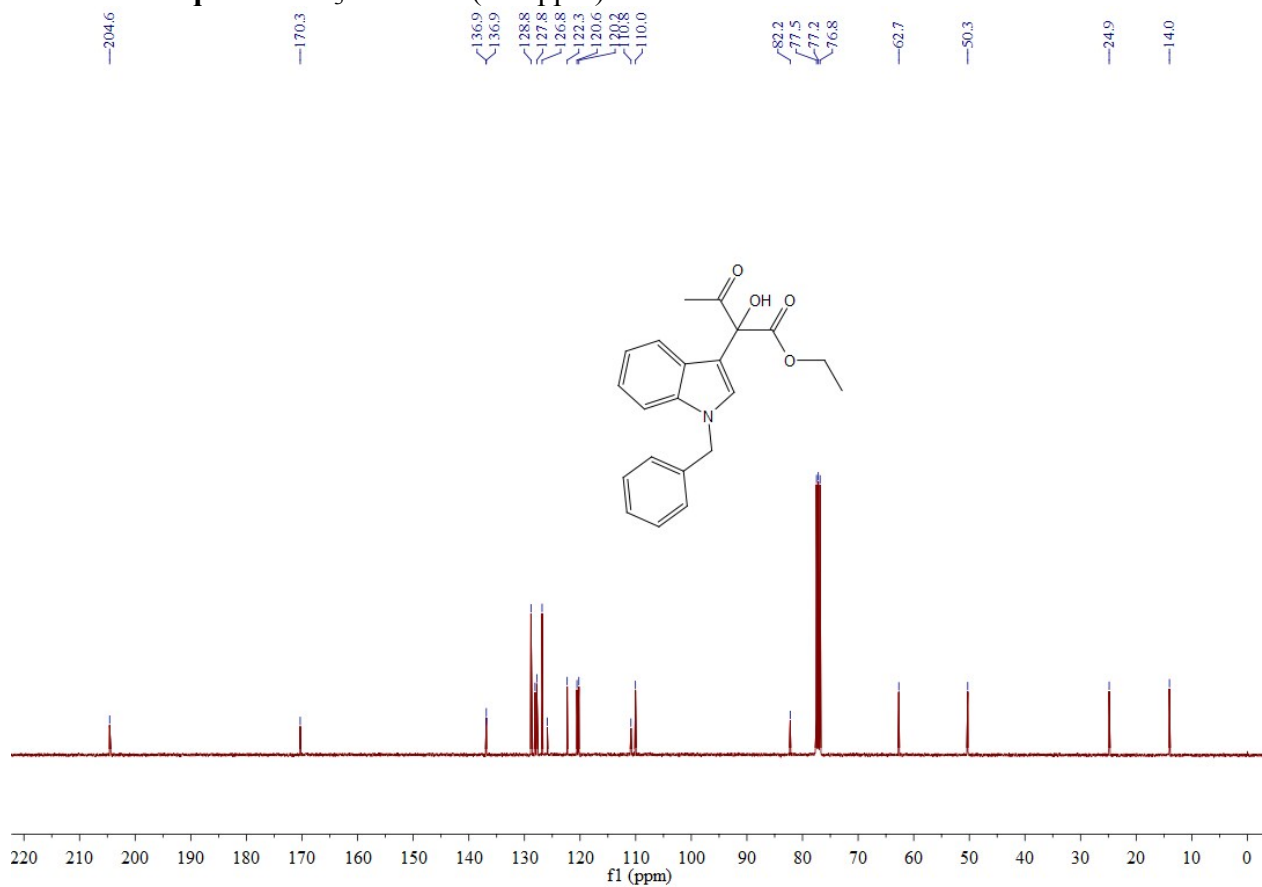
¹H NMR of 3pa in CDCl₃ at 299 K (δ in ppm).



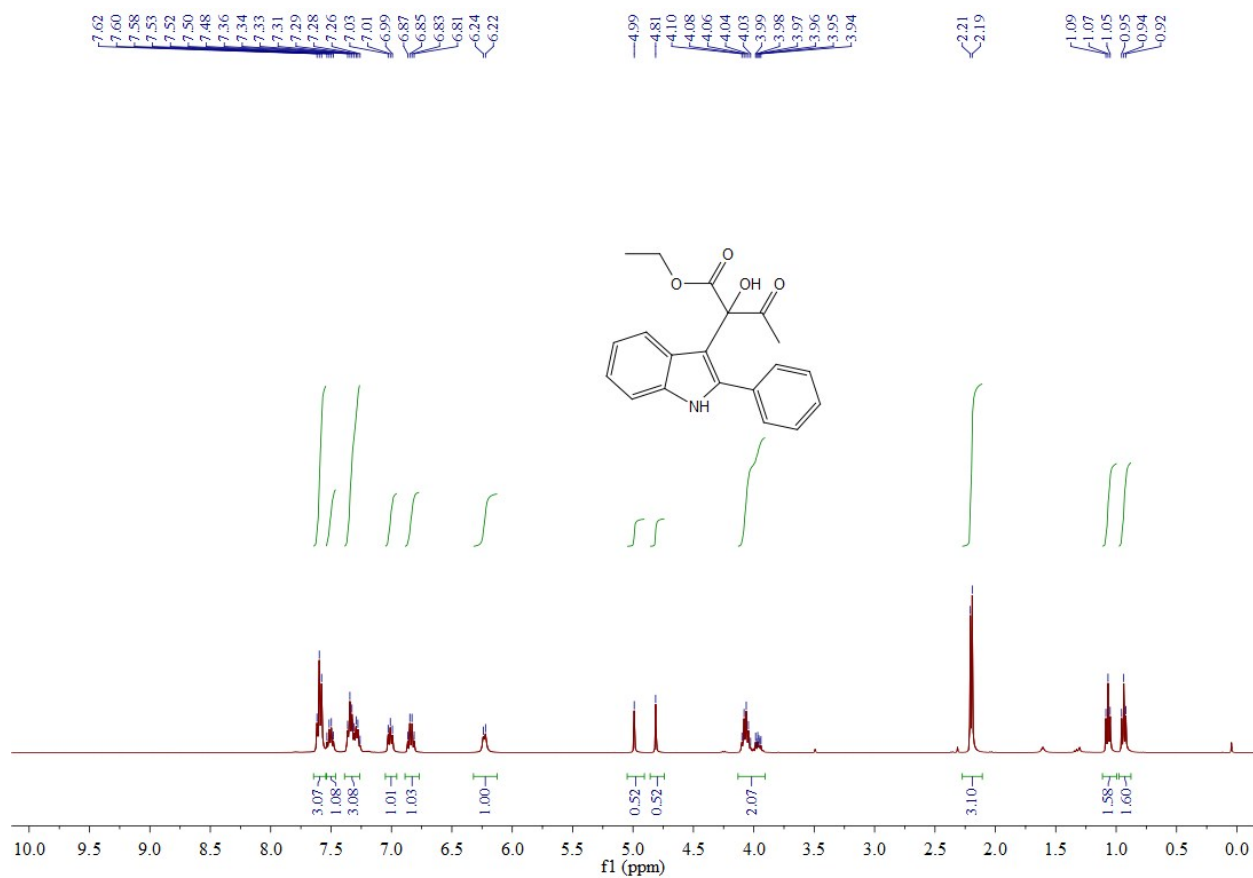
¹³C NMR of 3pa in CDCl₃ at 299 K (δ in ppm).



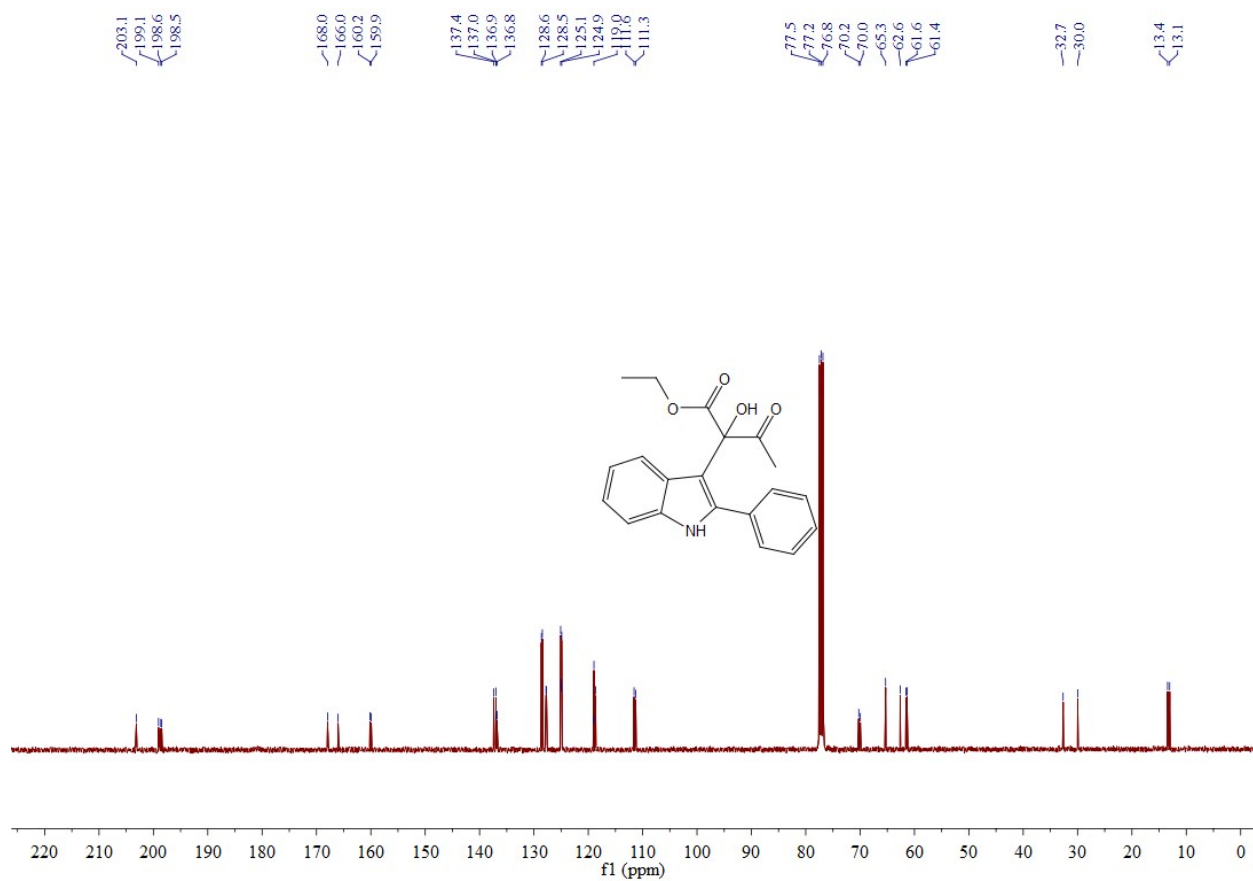
¹H NMR of **3qa** in CDCl₃ at 297 K (δ in ppm).



¹³C NMR of **3qa** in CDCl₃ at 299 K (δ in ppm).

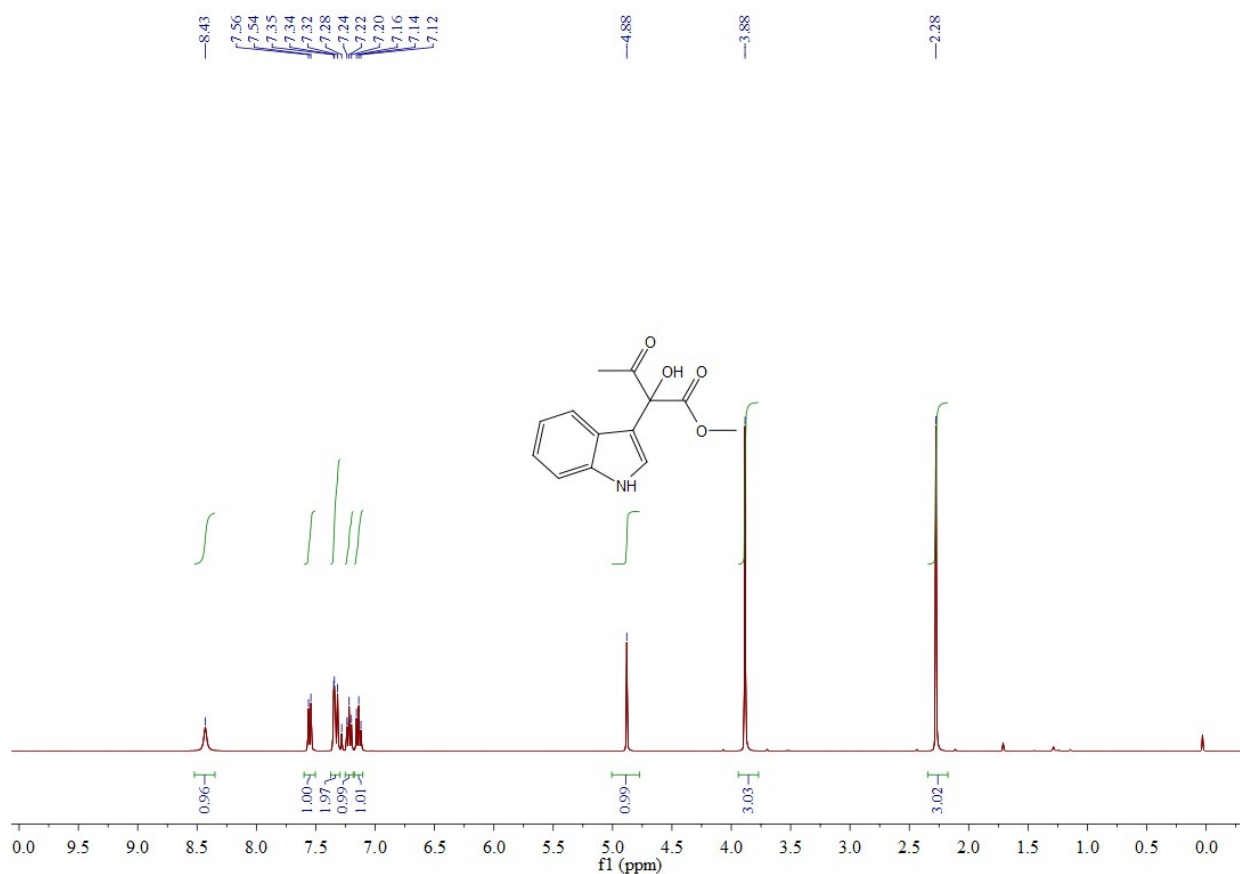


¹H NMR of **3ra** in CDCl₃ at 297 K (δ in ppm).

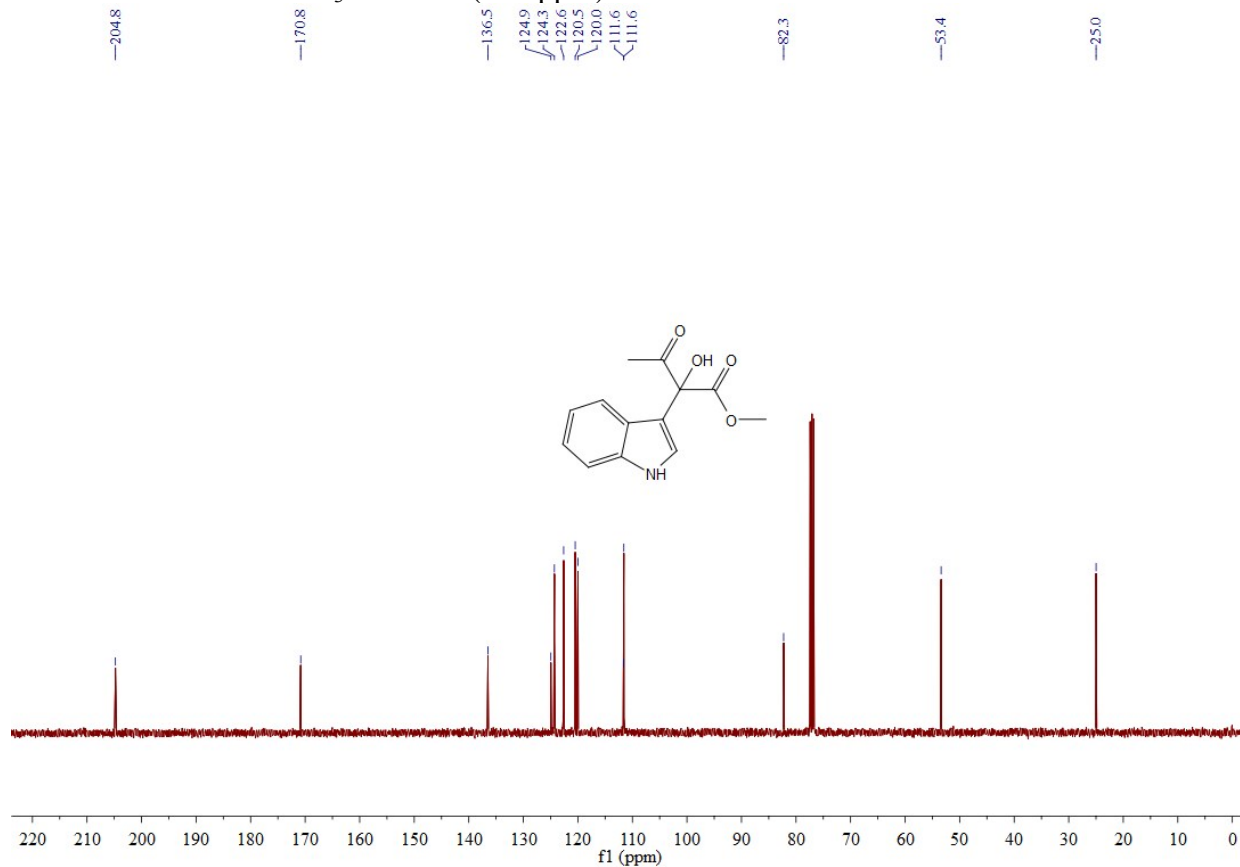


¹³C NMR of **3ra** in CDCl₃ at 299 K (δ in ppm).

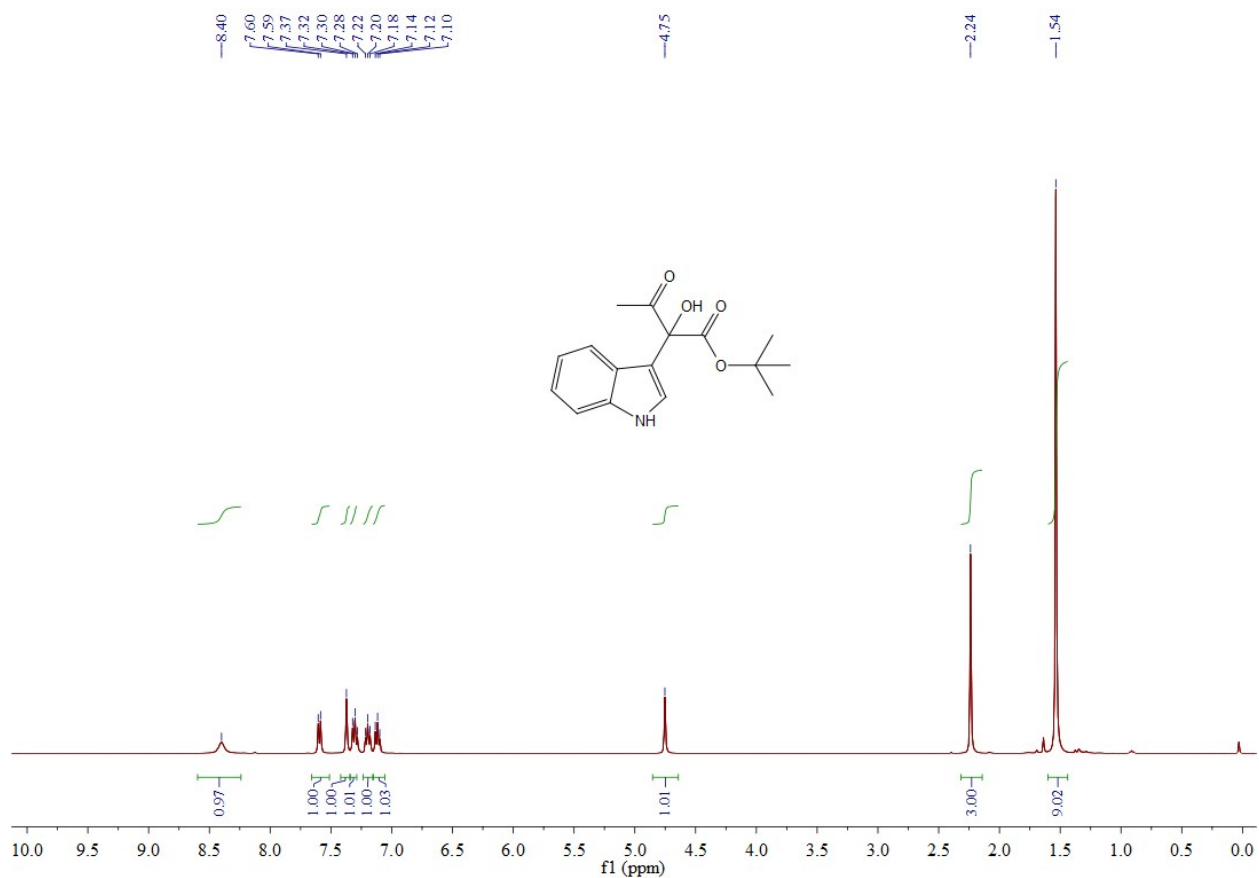
6. ^1H and ^{13}C NMR Spectra of Compounds 4ab-4ai



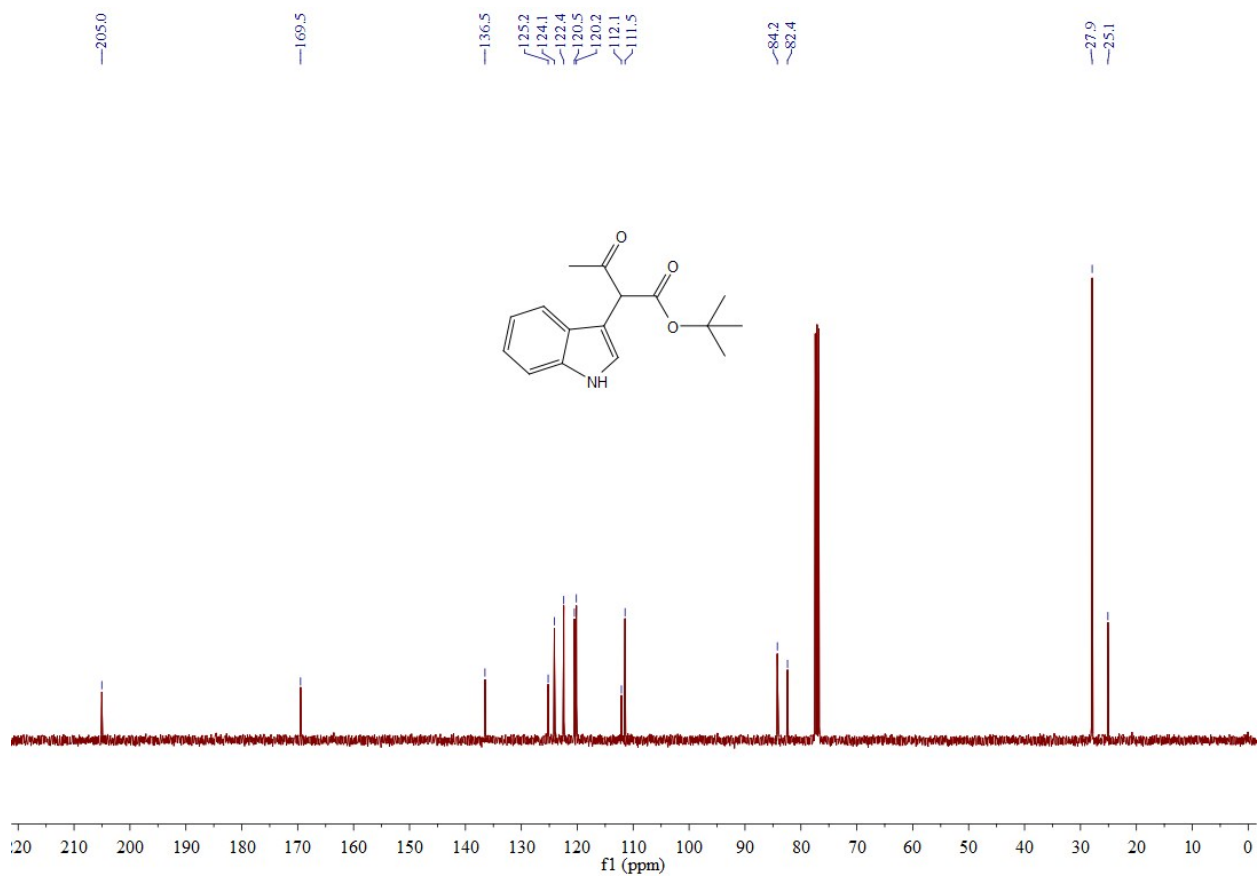
^1H NMR of **4ab** in CDCl_3 at 297 K (δ in ppm).



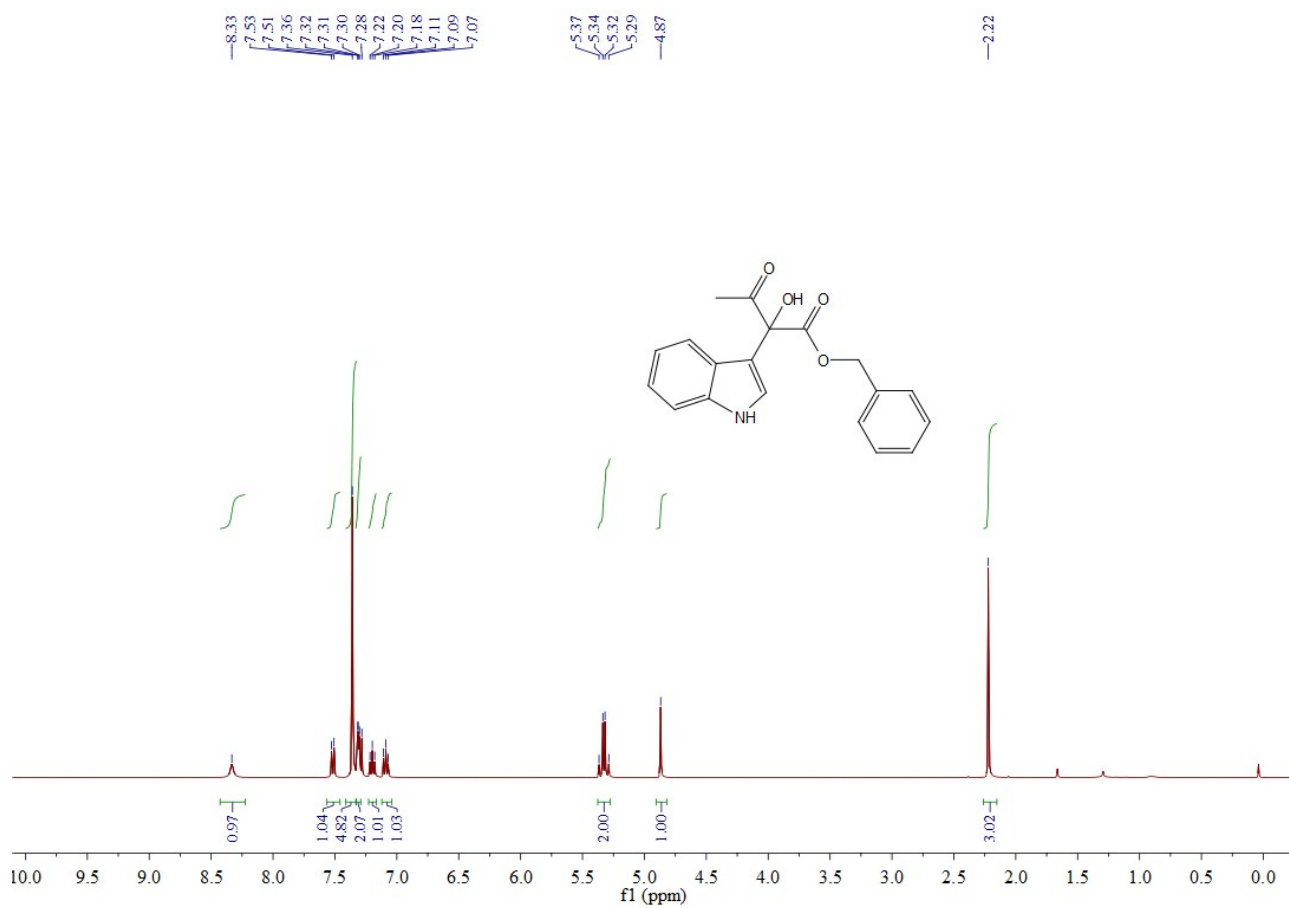
^{13}C NMR of **4ab** in CDCl_3 at 299 K (δ in ppm).



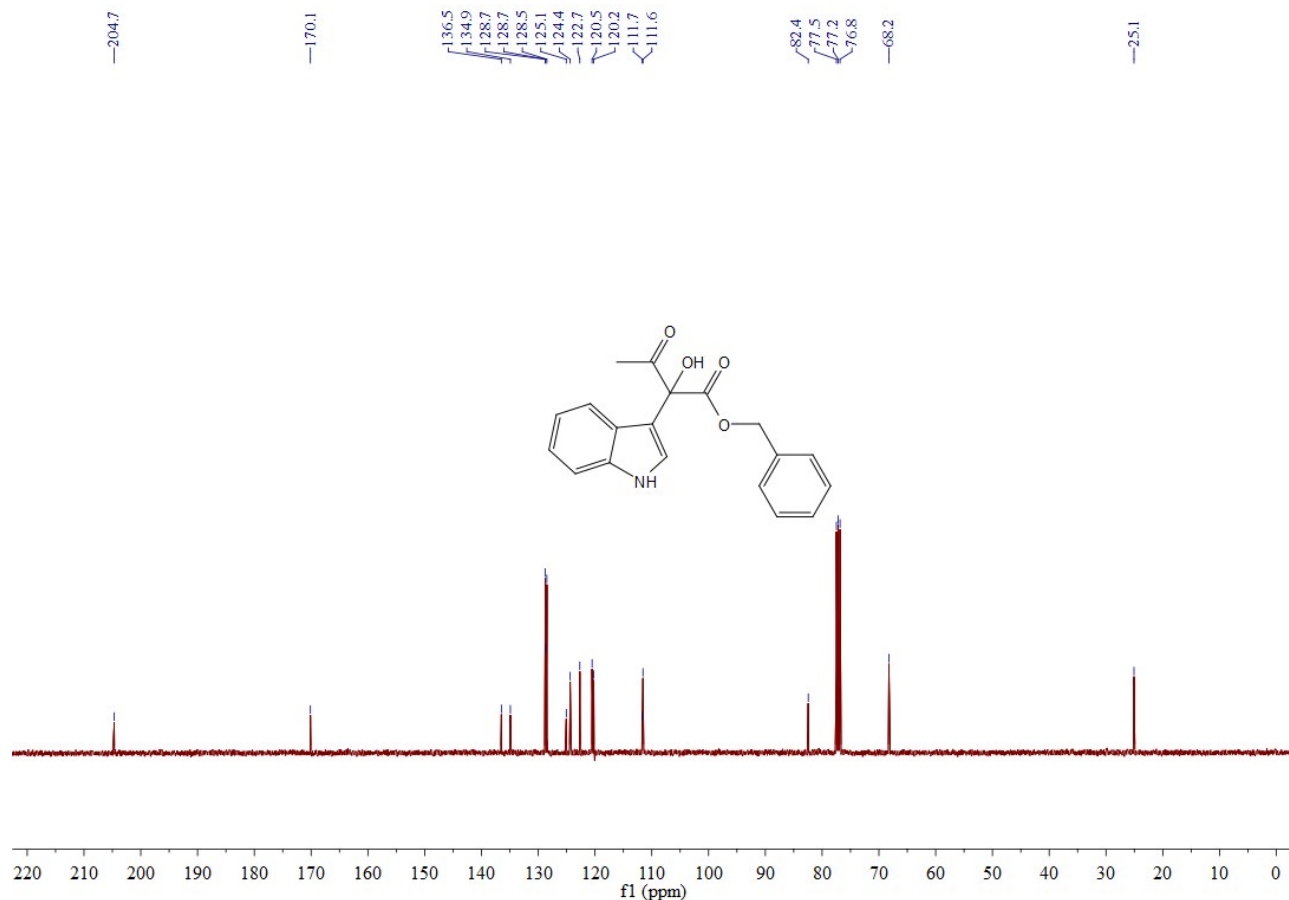
¹H NMR of **4ac** in CDCl₃ at 297 K (δ in ppm).



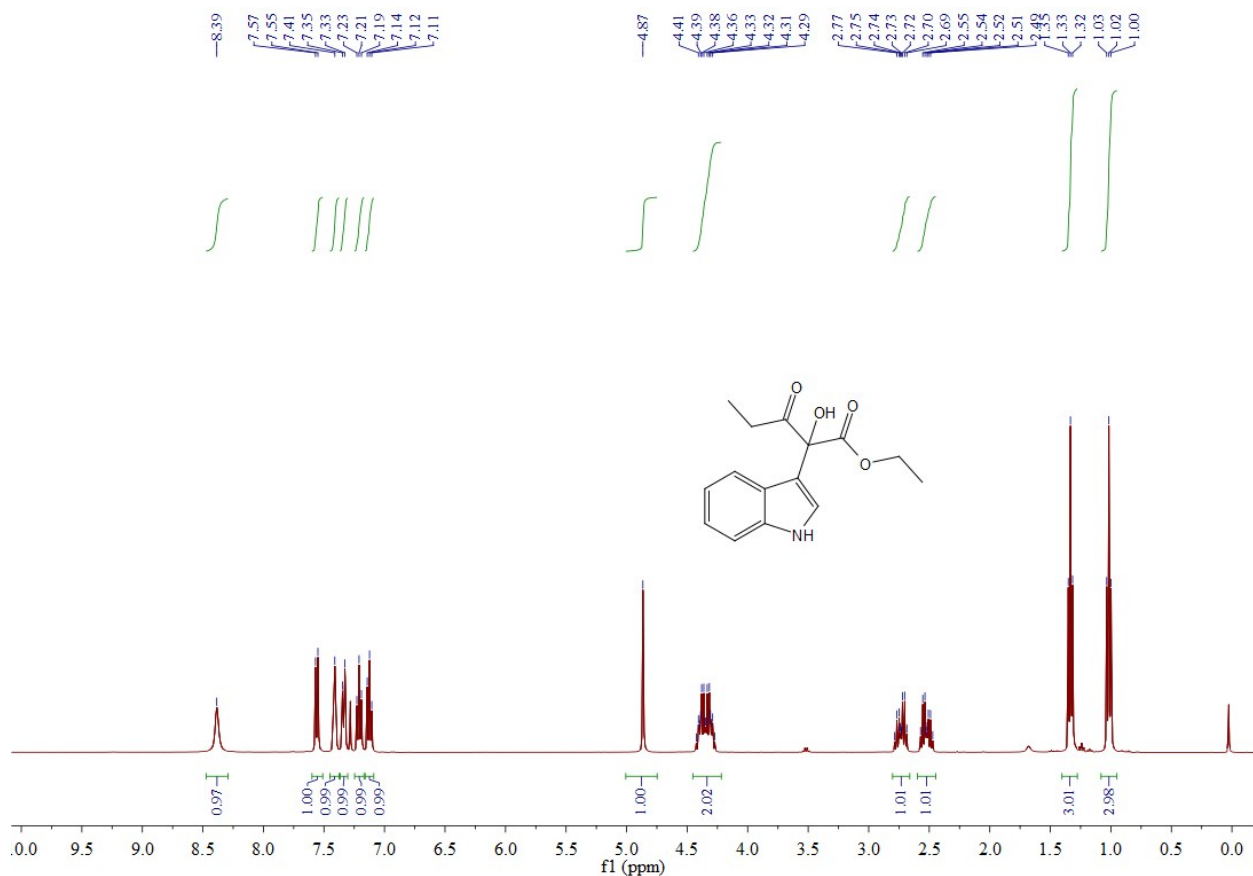
¹³C NMR of **4ac** in CDCl₃ at 299 K (δ in ppm).



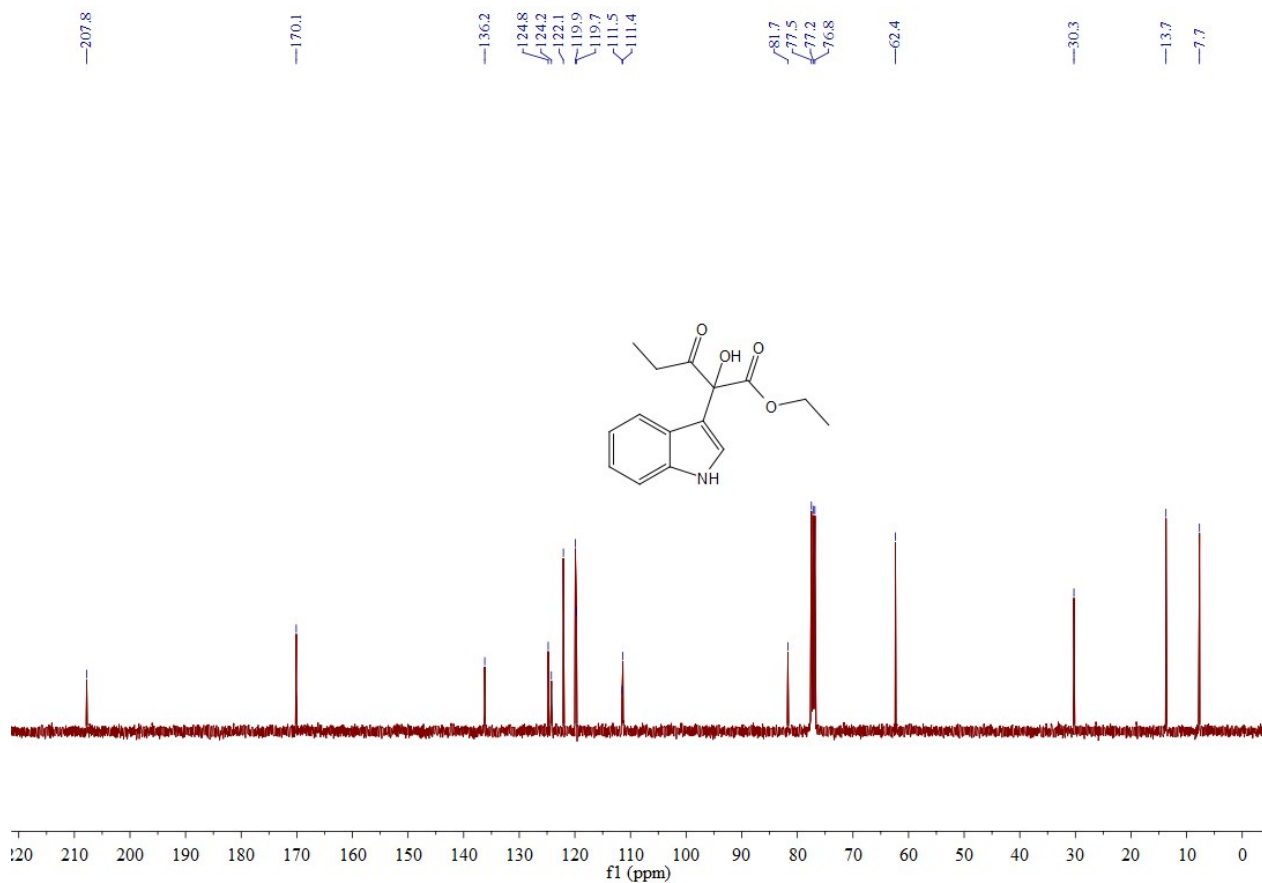
¹H NMR of **4ad** in CDCl₃ at 297 K (δ in ppm).



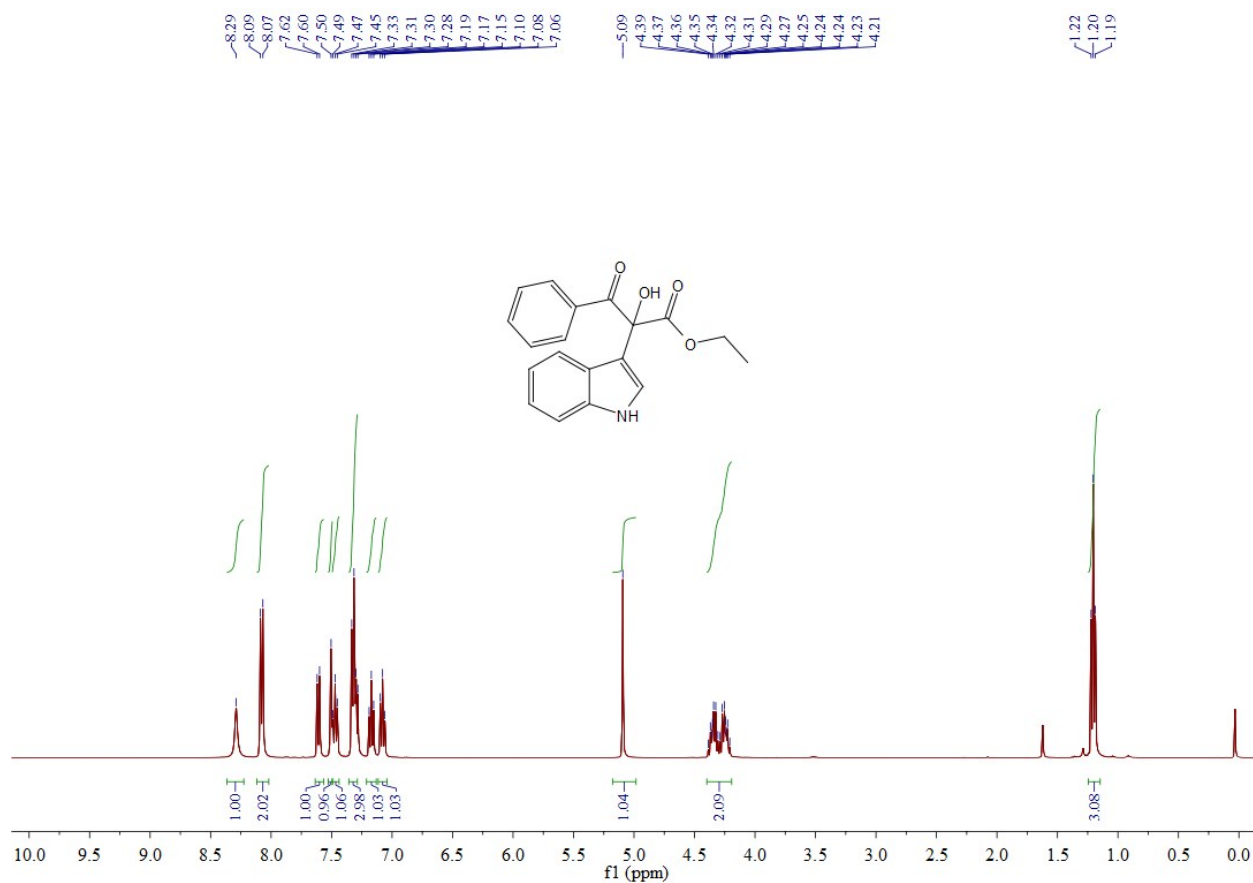
¹³C NMR of **4ad** in CDCl₃ at 299 K (δ in ppm).



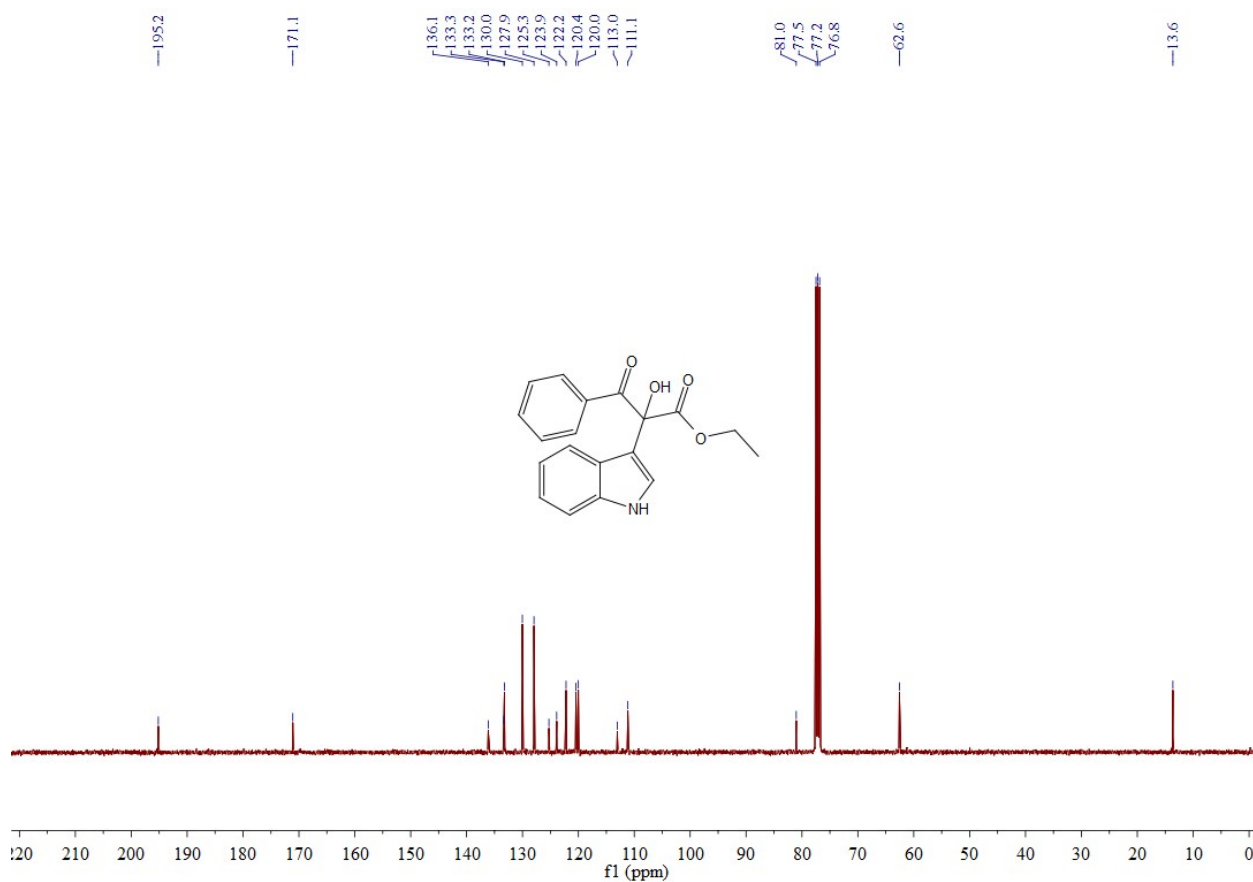
¹H NMR of **4ae** in CDCl₃ at 299 K (δ in ppm).



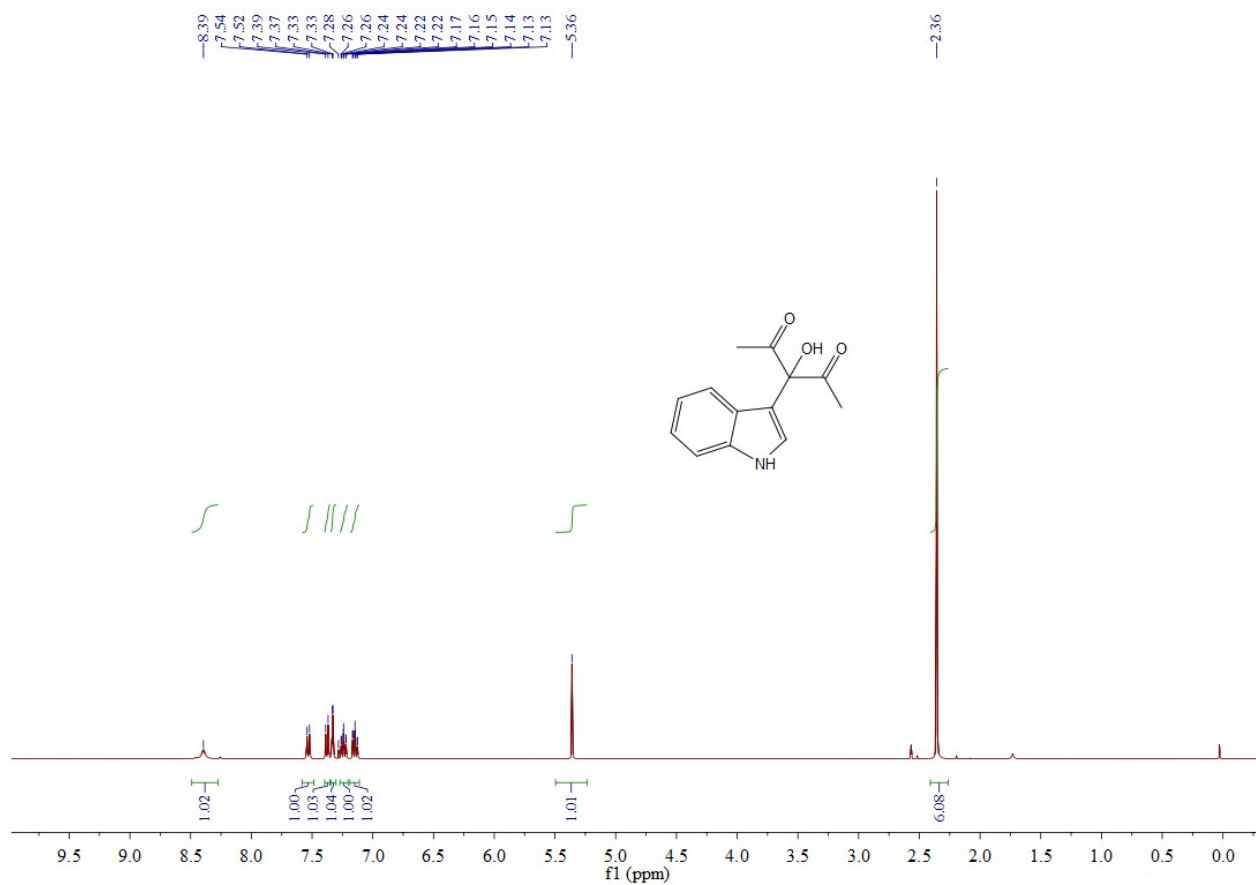
¹³C NMR of **4ae** in CDCl₃ at 299 K (δ in ppm).



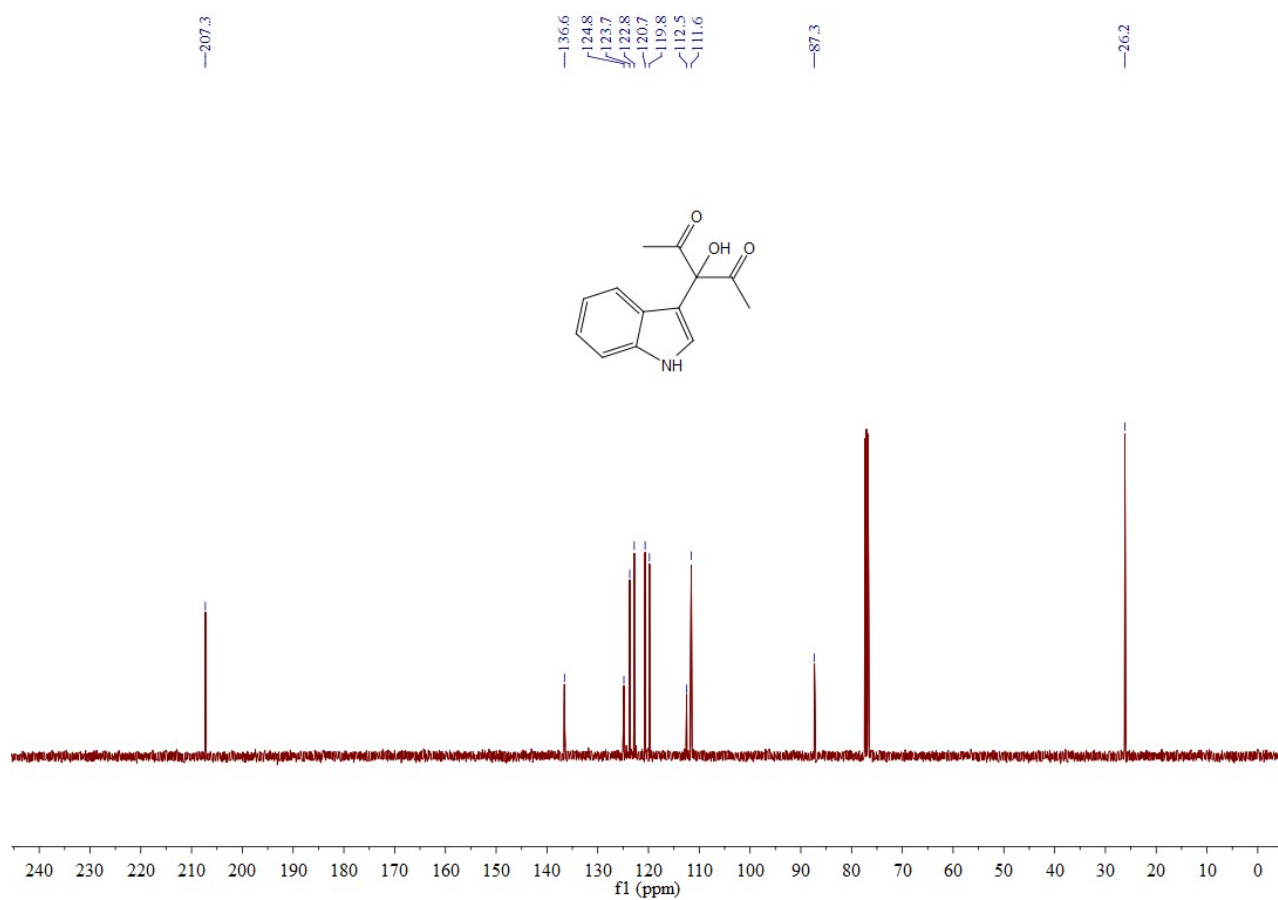
¹H NMR of **4af** in CDCl₃ at 299 K (δ in ppm).



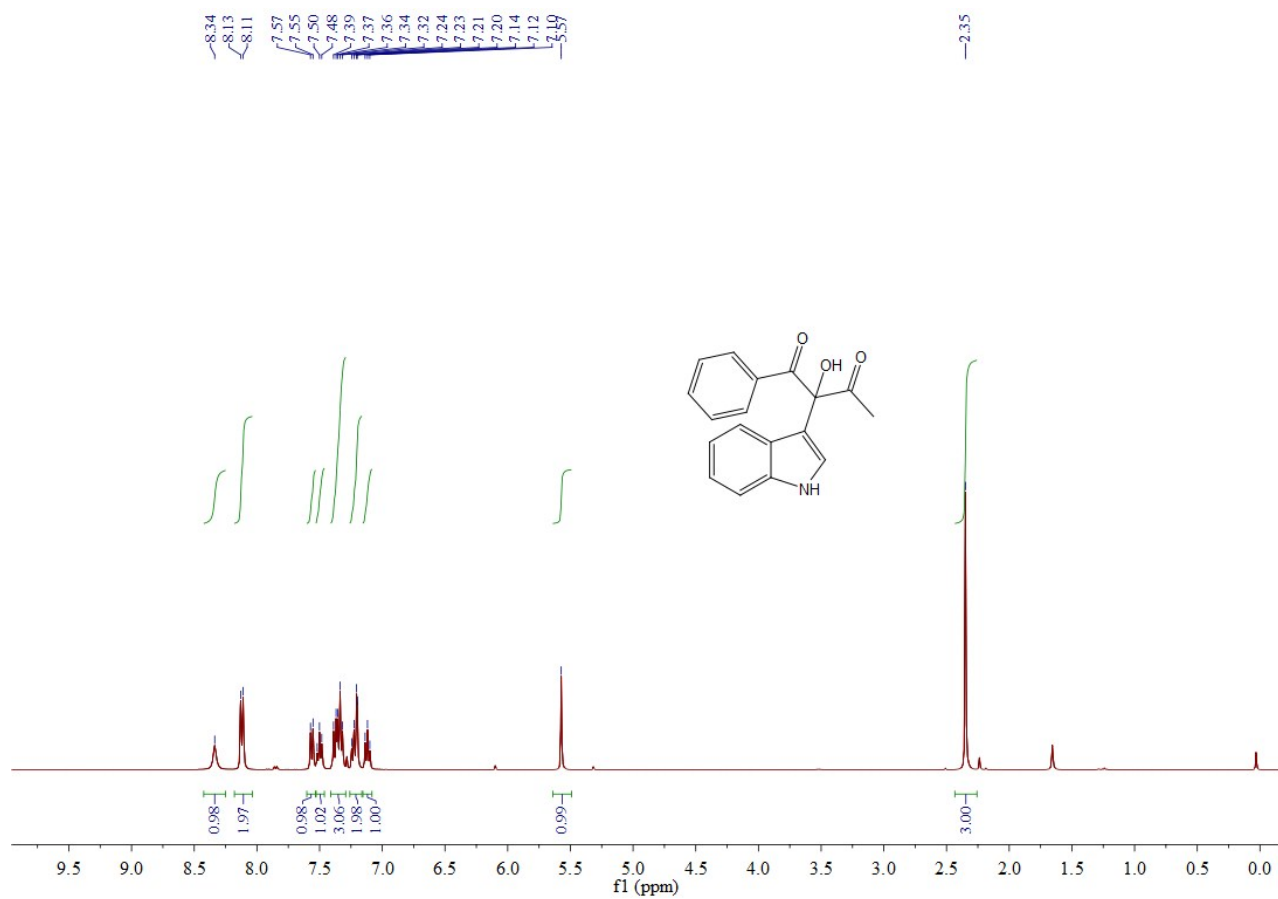
¹³C NMR of **4af** in CDCl₃ at 299 K (δ in ppm).



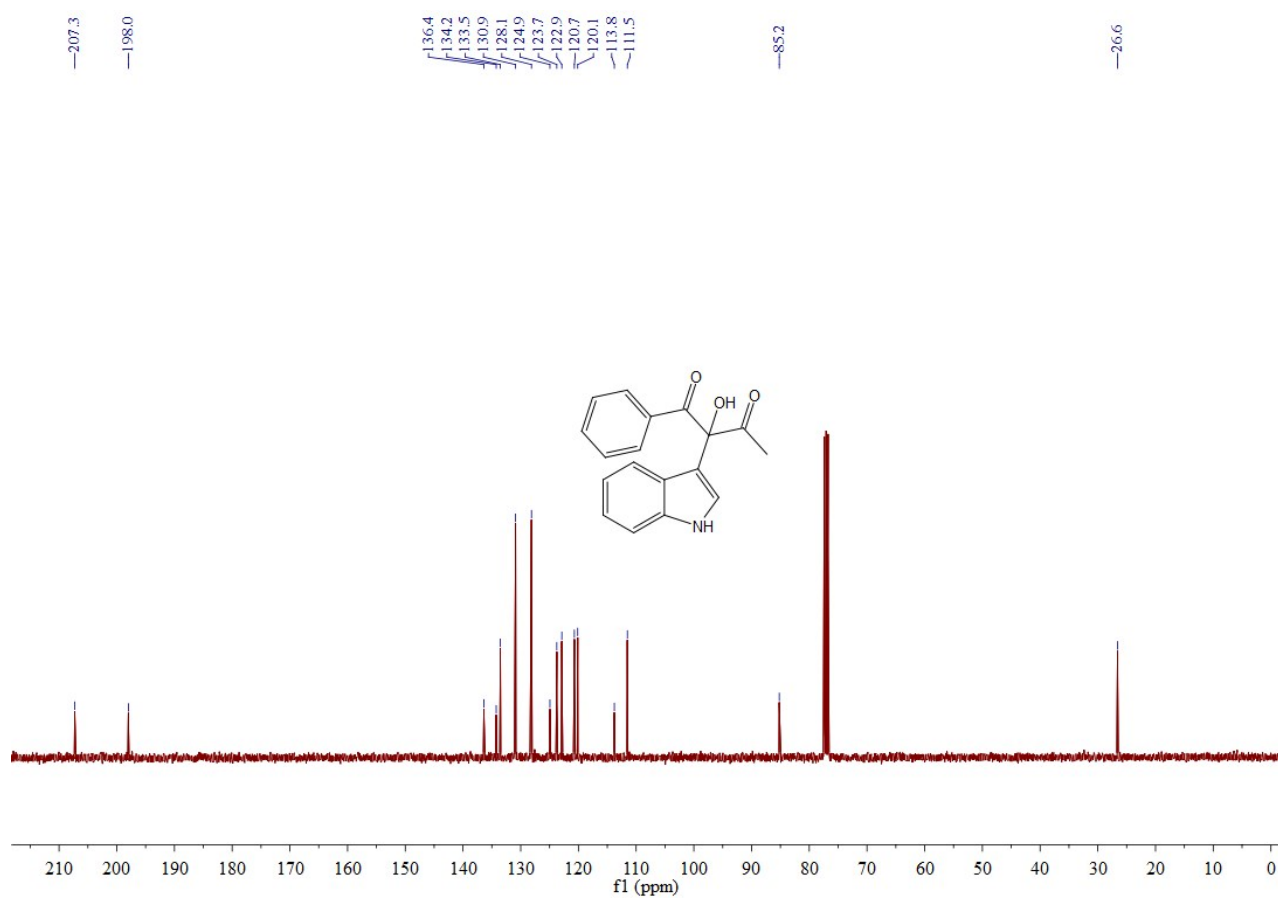
¹H NMR of **4ag** in CDCl₃ at 297 K (δ in ppm).



¹³C NMR of **4ag** in CDCl₃ at 299 K (δ in ppm).

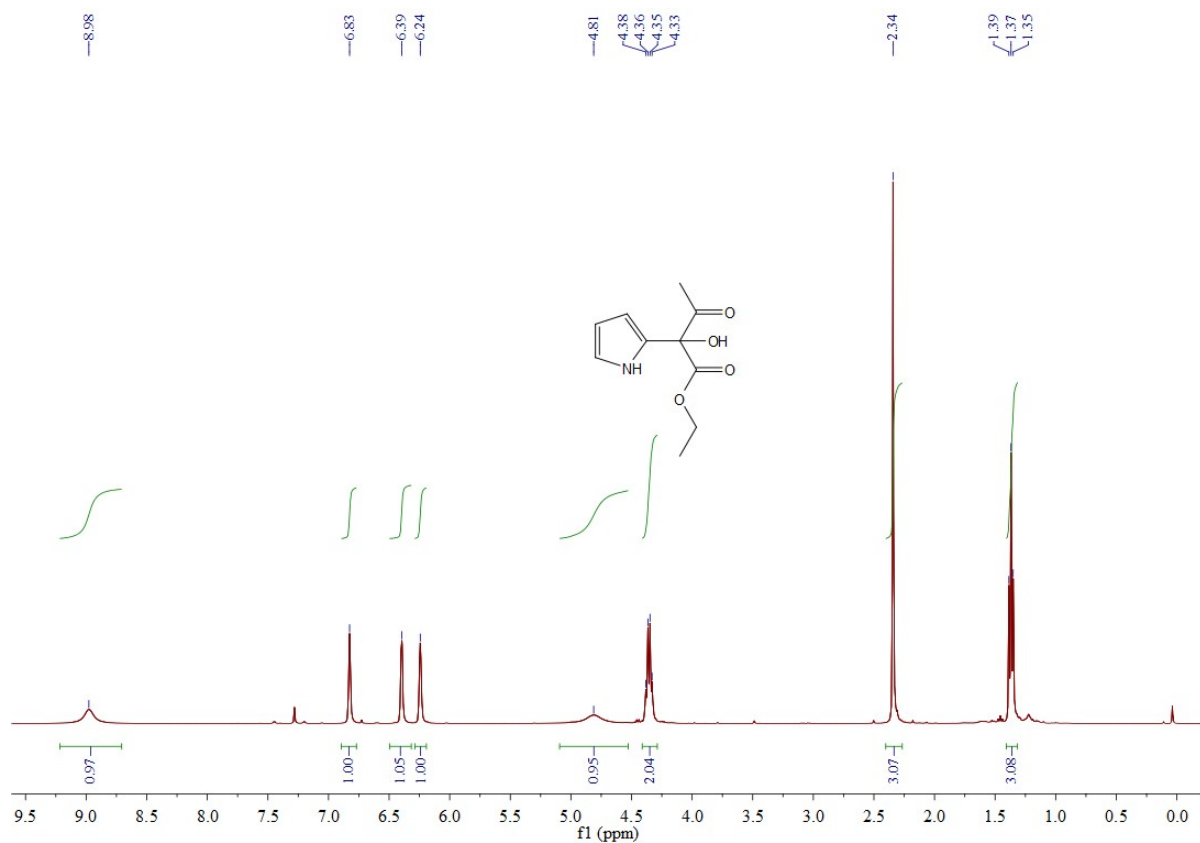


$^1\text{H NMR}$ of **4ah** in CDCl_3 at 297 K (δ in ppm).

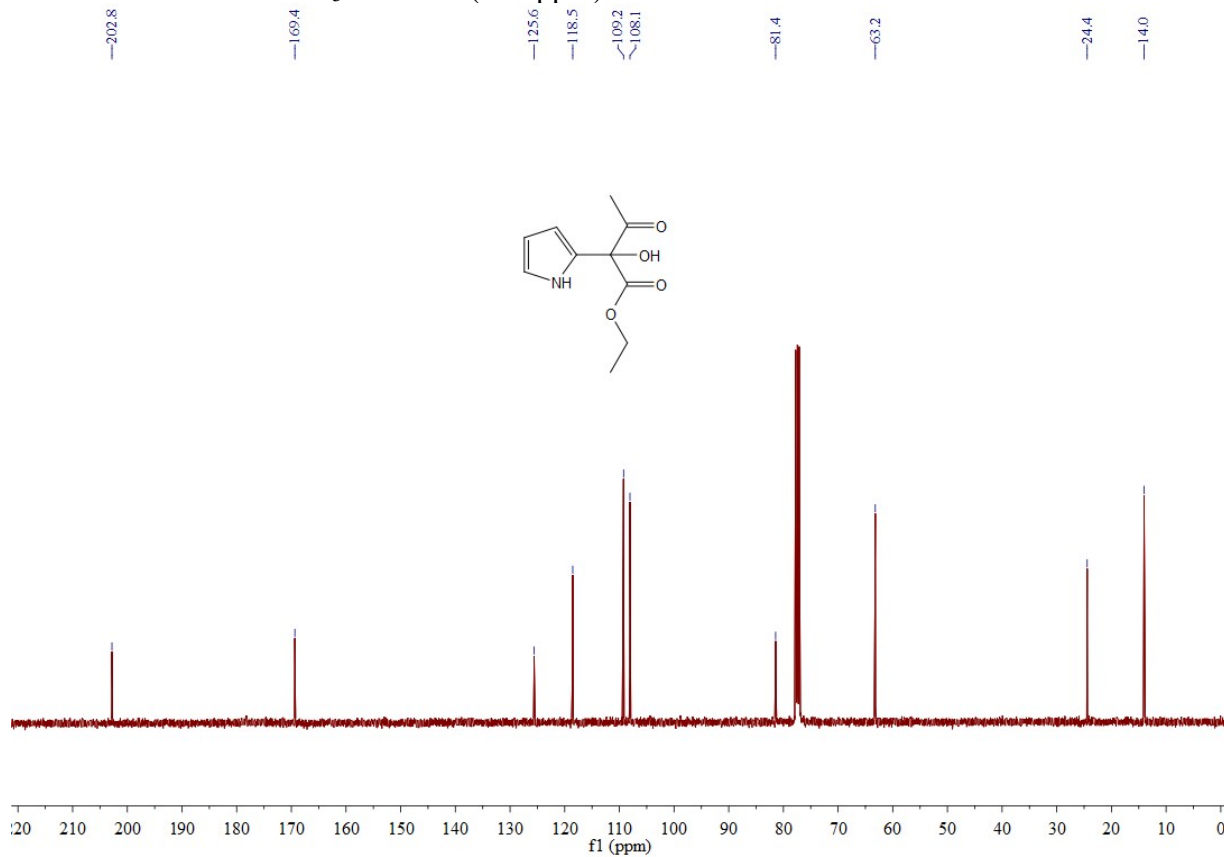


$^{13}\text{C NMR}$ of **4ah** in CDCl_3 at 297 K (δ in ppm).

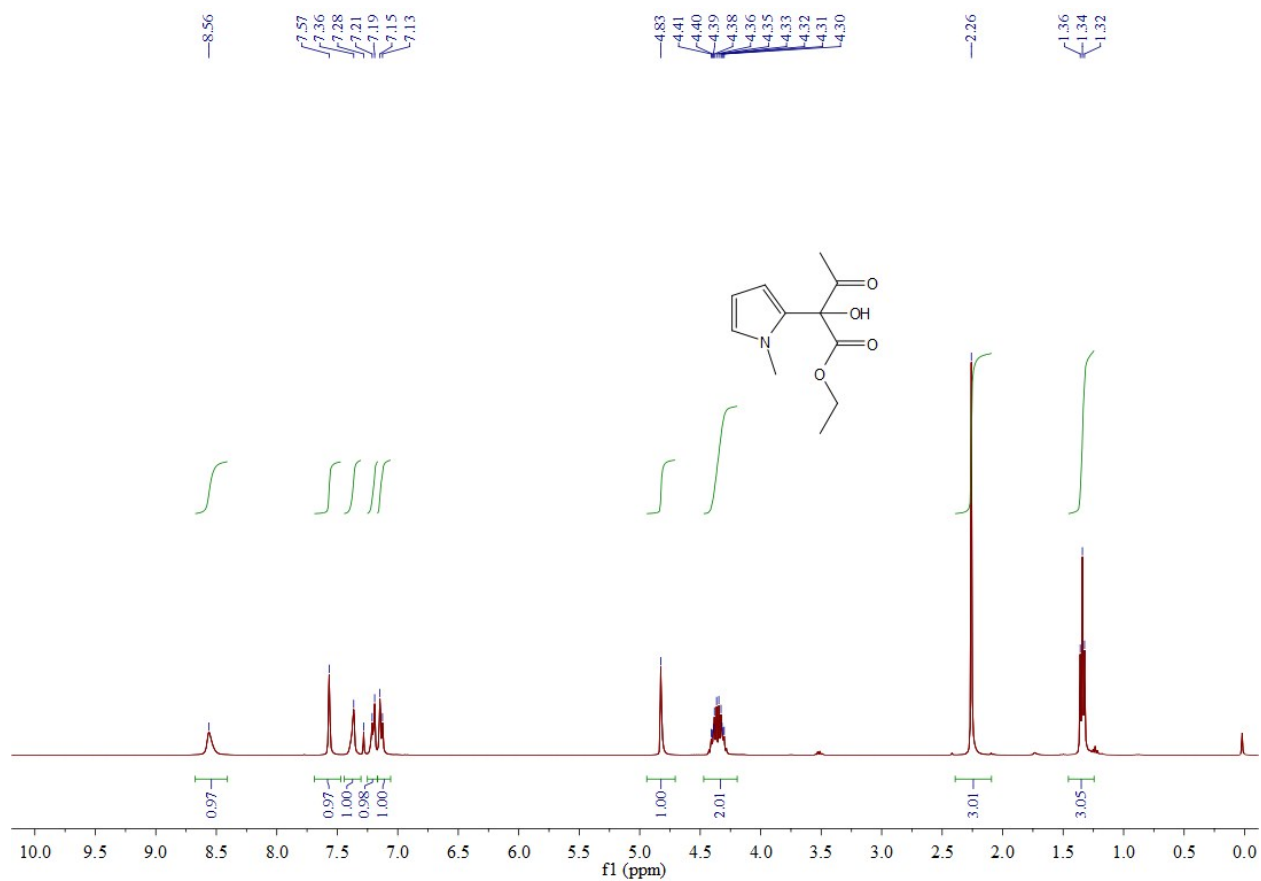
7. ^1H and ^{13}C NMR Spectra of Compound 6aa-6ba



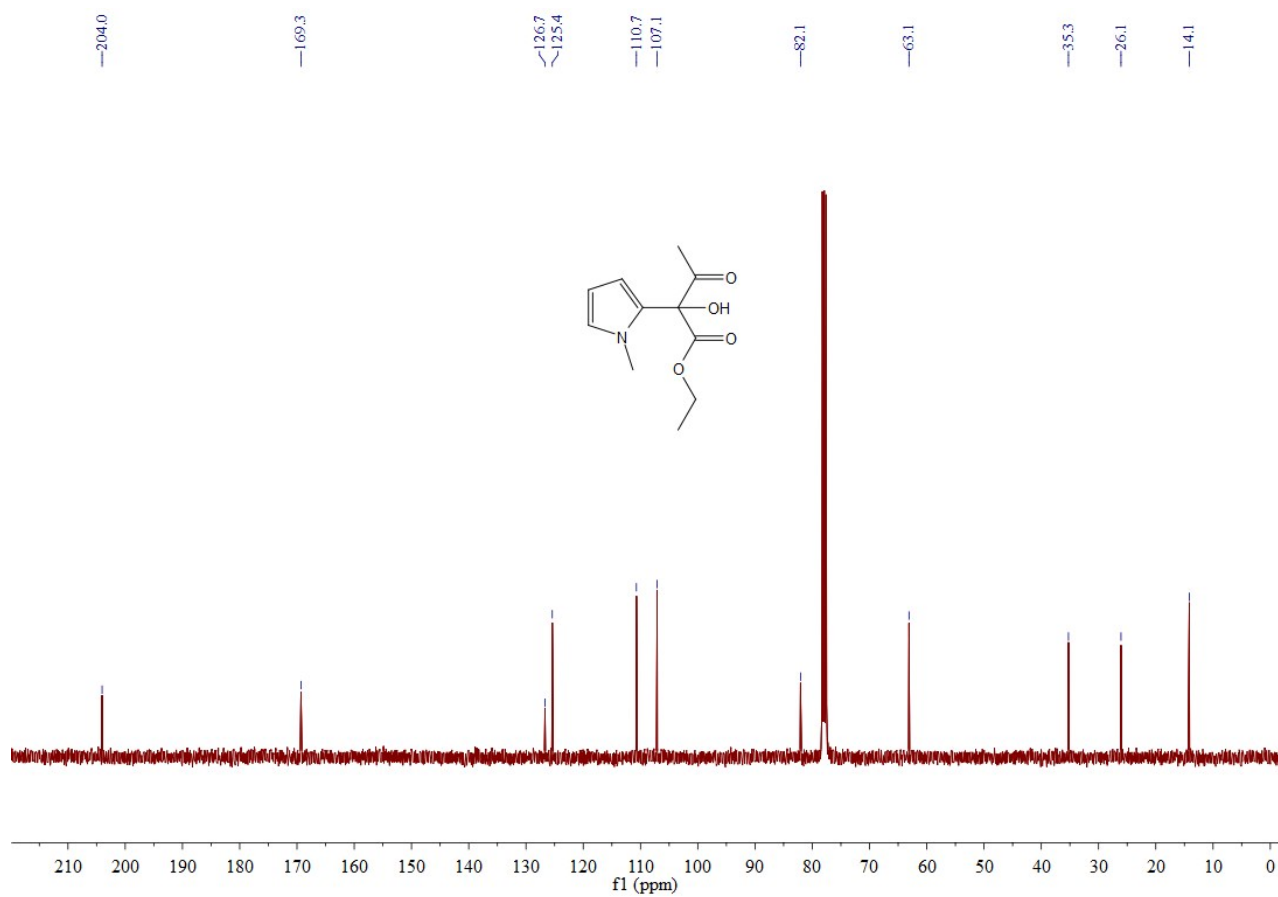
^1H NMR of **6aa** in CDCl_3 at 297 K (δ in ppm).



^{13}C NMR of **6aa** in CDCl_3 at 297 K (δ in ppm).



¹H NMR of **6ba** in CDCl₃ at 299 K (δ in ppm).



¹³C NMR of **6ba** in CDCl₃ at 299 K (δ in ppm).

8. X-ray crystal structure of **3aa**

ORTEP plot of **3aa** shown with ellipsoids at the 30% level.

