Stereoselective Synthesis of *(Z)*-1,3-bis(α,β-unsaturated carbonyl)-Isoindolines from Aldehydes and Phenacyl azides Under Metal Free Condition

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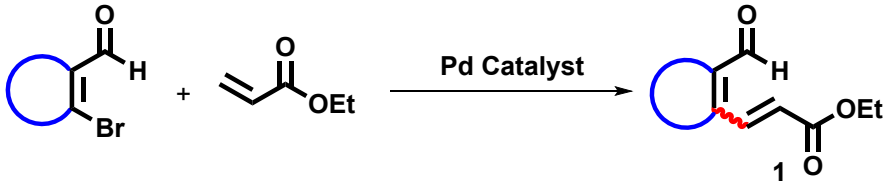
1. General Information:

All the reagents and chemicals were purchased from commercial sources and used without further purification. Common laboratory solvents (LR grade) were purchased from domestic suppliers. Analytical thin layer chromatography was performed with E. Merck silica gel 60 F aluminium plates and visualized under UV 254 nm radiation. NMR spectra were measured with 300, 400, and 500 MHz instruments. Chemical shifts are reported in δ units, parts per million (ppm) downfield from TMS. Coupling constants (*J*) are in hertz (Hz) and are unadjusted; therefore, due to limits in resolution, in some cases there are small differences (<1 Hz) in the measured *J* value of the same coupling constant determined from different signals. Splitting patterns are designed as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; dt, doublet of triplets; tt, triplet of triplets; m, multiplet; br, broad. ESI-MS and ESI-HRMS spectra were obtained on a ion trap mass spectrometer. Melting points were determined on a Kofler block and are uncorrected. All the new compounds were fully characterized by ^{1}H NMR, ^{13}C NMR, Mass-Spectroscopy and HRMS analysis.

3. Genaral experimental procedures:

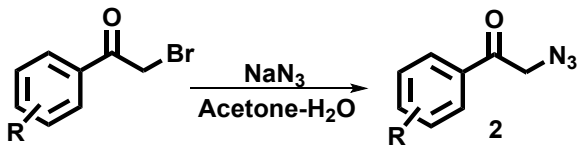
3.1. General experimental procedure for the synthesis of 2-formyl α,β-unsaturated esters

1: All the 2-formyl α,β-unsaturated esters were synthesized from corresponding 2-bromo aldehydes and ethyl acrylate by using reported procedures.[5]

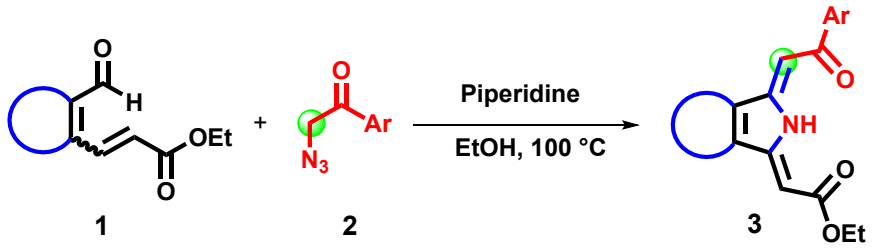


3.2. General experimental procedure for the synthesis of α-azido ketones 2:

All the α-azido ketones were synthesized from corresponding α-bromo ketones and sodium azide by using reported procedure.[6]



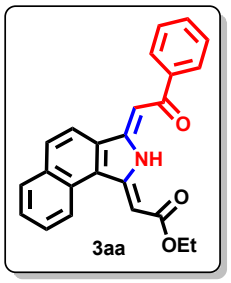
3.3. General experimental procedure for the synthesis of *(Z)*-1,3-bis(α,β-unsaturated carbonyl)-Isoindolines 3:



2-formyl-phenyl acrylate (**1**) (0.5 mmol), α-azido ketone (**2**) (0.6 mmol) and EtOH (2.0-3.0 mL) were taken in a 10 mL round bottom flask then piperidine (0.6 mmol) was added. The reaction mixture was heated upto 100 °C and stirred at this temperature for another 6 hrs. After complete consumption of starting materials, (reaction monitored by TLC) EtOH was removed under reduced pressure and the residue was purified by column chromatography with Hexane/EtOAc to afford the desired *(Z)*-1,3-bis(α,β-unsaturated carbonyl)-Isoindolines **3**.

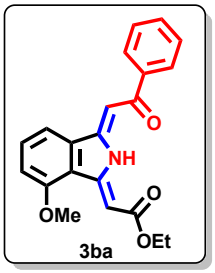
4. ^{1}H and ^{13}C spectral data of compounds:

Ethyl (Z)-2-((Z)-3-(2-oxo-2-phenylethylidene)-2,3-dihydro-1H-benzo[e]isoindol-1-ylidene)acetate (3aa):



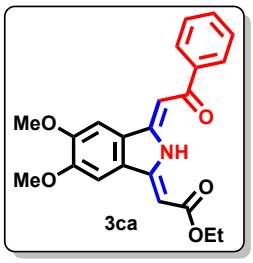
Orange solid, Yield: 92%, M.P: 165−167 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 12.85 (s, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 8.13 – 8.09 (m, 2H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.66 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.57 – 7.52 (m, 1H), 7.52 – 7.47 (m, 2H), 6.84 (s, 1H), 6.31 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 190.05, 168.16, 152.24, 151.48, 139.43, 135.32, 135.25, 132.07, 132.03, 129.74, 129.71, 128.55, 128.51, 127.96, 127.83, 127.20, 123.40, 117.97, 94.29, 91.77, 60.59, 14.58; **HRMS** (ESI) Calcd for $C_{24}H_{20}NO_3$ $[M+H]^+$: 370.14377; Found: 370.14465.

Ethyl 2-((1Z,3Z)-7-methoxy-3-(2-oxo-2-phenylethylidene)isoindolin-1-ylidene)acetate (3ba):



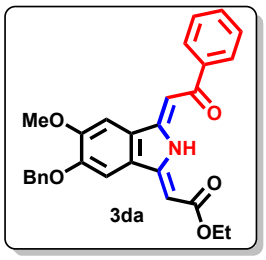
Yellow solid, Yield: 91%, M.P: 133−135 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.50 (s, 1H), 8.08 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.28 (d, *J* = 2.2 Hz, 1H), 7.10 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.74 (s, 1H), 5.66 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 190.10, 167.90, 162.15, 151.97, 150.64, 139.40, 137.02, 132.02, 128.50, 127.77, 122.79, 118.31, 105.52, 91.22, 88.77, 77.62, 60.36, 55.88, 14.57; **HRMS** (ESI) Calcd for $C_{21}H_{20}NO_4$ $[M+H]^+$: 350.1387; Found: 350.1413.

Ethyl 2-((1Z,3Z)-5,6-dimethoxy-3-(2-oxo-2-phenylethylidene)isoindolin-1-ylidene)acetate (3ca):



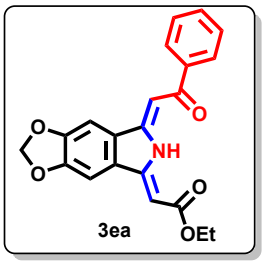
Orange solid, Yield: 87%, M.P: 163−165 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.35 (s, 1H), 8.11 – 8.05 (m, 2H), 7.59 – 7.43 (m, 3H), 7.21 (s, 1H), 7.12 (s, 1H), 6.65 (s, 1H), 5.64 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 3H), 3.98 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.92, 167.74, 152.32, 152.23, 152.00, 150.89, 139.51, 131.91, 128.46, 128.28, 127.96, 127.72, 103.24, 103.14, 90.86, 88.96, 60.37, 56.42, 56.32, 14.56; **HRMS** (ESI) Calcd for $C_{22}H_{22}NO_5$ $[M+H]^+$: 380.14925; Found: 380.14944.

Ethyl 2-((1Z,3Z)-6-(benzyloxy)-5-methoxy-3-(2-oxo-2-phenylethylidene)isoindolin-1-ylidene)acetate (3da):



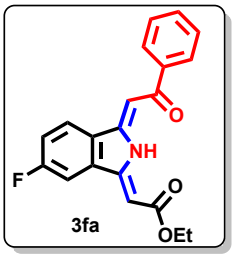
Yellow solid, Yield: 90%, M.P: 134−136 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.35 (s, 1H), 8.07 (d, *J* = 7.3 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.50 – 7.44 (m, 4H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.24 (s, 1H), 7.15 (s, 1H), 6.66 (s, 1H), 5.55 (s, 1H), 5.23 (s, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.96, 167.74, 152.57, 152.30, 151.31, 150.87, 139.46, 136.05, 131.92, 128.80, 128.56, 128.46, 128.31, 127.73, 127.32, 105.40, 103.64, 90.87, 88.90, 77.37, 71.24, 60.38, 56.47, 14.56; **HRMS** (ESI) Calcd for $C_{28}H_{26}NO_5$ $[M+H]^+$: 456.1805; Found: 456.1811.

Ethyl (Z)-2-((Z)-7-(2-oxo-2-phenylethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ea):



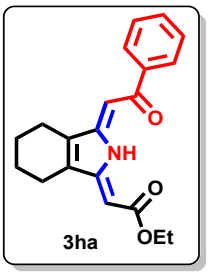
Light yellow solid, Yield: 84%, M.P: 183 − 185 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 12.35 (s, 1H), 8.05 (d, *J* = 6.7 Hz, 2H), 7.58 – 7.40 (m, 3H), 7.17 (s, 1H), 7.05 (s, 1H), 6.60 (s, 1H), 6.10 (s, 2H), 5.57 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 189.93, 167.71, 151.82, 150.87, 150.66, 150.53, 139.43, 131.95, 130.08, 129.68, 128.48, 127.71, 102.47, 101.34, 90.95, 89.16, 77.62, 60.41, 14.56; **HRMS** (ESI) Calcd for $C_{21}H_{18}NO_5$ $[M+H]^+$: 364.1179; Found: 364.1187.

Ethyl 2-((1Z,3Z)-6-fluoro-3-(2-oxo-2-phenylethylidene)isoindolin-1-ylidene)acetate (3fa):



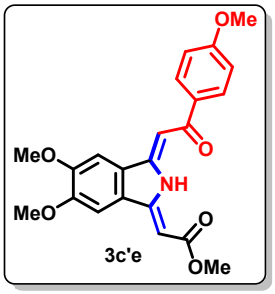
Yellow solid, Yield: 82%, M.P: 119 − 121 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.57 (s, 1H), 8.09 – 8.05 (m, 2H), 7.82 (dd, *J* = 8.5, 4.6 Hz, 1H), 7.54 (dd, *J* = 10.3, 4.3 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.39 (dd, *J* = 7.9, 2.2 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.75 (s, 1H), 5.72 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 190.10, 167.53, 164.52 (d, $J_{C\text{-}F}$ = 251.5 Hz), 151.00, 149.72, 139.24, 132.13, 131.08, 128.54, 127.76, 123.43 (d, $J_{C\text{-}F}$ = 9.5 Hz), 118.43 (d, $J_{C\text{-}F}$ = 24.1 Hz), 108.63 (d, $J_{C\text{-}F}$ = 24.4 Hz), 91.45, 90.33, 77.24, 60.60, 14.51; **HRMS** (ESI) Calcd for $C_{20}H_{17}FNO_3$ $[M+H]^+$: 338.1187; Found: 338.1193.

Ethyl 2-((1Z,3Z)-3-(2-oxo-2-phenylethylidene)-2,3,4,5,6,7-hexahydro-1H-isoindol-1-ylidene)acetate (3ha):



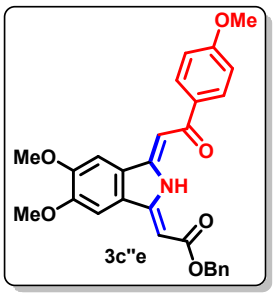
Yellow solid, Yield: 76%, M.P: 168−170 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 11.57 (s, 1H), 8.06 – 7.88 (m, 2H), 7.59 – 7.34 (m, 3H), 6.23 (s, 1H), 5.23 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.48 – 2.24 (m, 5H), 1.89 – 1.76 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 190.20, 167.62, 154.87, 153.83, 139.57, 139.32, 139.15, 131.86, 128.44, 127.66, 92.14, 90.79, 77.25, 60.33, 21.97, 20.87, 20.73, 14.54; **HRMS** (ESI) Calcd for $C_{20}H_{22}NO_3$ $[M+H]^+$: 324.1594; Found: 324.1600.

Methyl 2-((1Z,3Z)-5,6-dimethoxy-3-(2-(4-methoxyphenyl)-2-oxoethylidene)isoindolin-1-ylidene)acetate (3c'e):



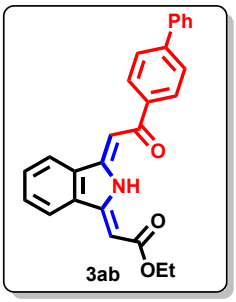
Yellow solid, Yield: 66%, M.P: 155 − 157 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 12.37 (s, 1H), 8.08 (d, *J* = 8.9 Hz, 2H), 7.23 (s, 1H), 7.13 (s, 1H), 6.99 – 6.96 (m, 2H), 6.66 (s, 1H), 5.63 (s, 1H), 4.03 (s, 3H), 3.99 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 188.82, 168.28, 162.80, 151.78, 151.25, 133.40, 132.38, 131.12, 129.90, 128.44, 127.87, 126.58, 114.22, 113.69, 103.22, 90.91, 87.87, 56.35, 55.47, 51.57. **HRMS** (ESI) Calcd for $C_{22}H_{22}NO_6$ $[M+H]^+$: 396.1442; Found: 396.1438.

Benzyl 2-((1Z,3Z)-5,6-dimethoxy-3-(2-(4-methoxyphenyl)-2-oxoethylidene)isoindolin-1-ylidene)acetate (3c''e):



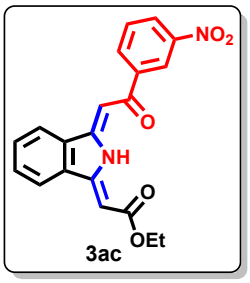
Yellow solid, Yield: 84%, M.P: 155 − 157 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.43 (s, 1H), 8.08 (d, *J* = 8.9 Hz, 2H), 7.49 – 7.45 (m, 2H), 7.41 – 7.30 (m, 3H), 7.22 (s, 1H), 7.11 (s, 1H), 7.00 – 6.94 (m, 2H), 6.66 (s, 1H), 5.68 (s, 1H), 5.32 (s, 2H), 4.03 (s, 3H), 3.97 (s, 3H), 3.88 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 188.73, 167.71, 162.80, 152.11, 152.01, 151.73, 136.57, 132.34, 129.93, 128.55, 128.47, 128.10, 127.82, 113.68, 103.20, 103.15, 91.05, 87.74, 65.93, 56.43, 56.31, 55.48. **HRMS** (ESI) Calcd for $C_{28}H_{26}NO_6$ $[M+H]^+$: 472.1755; Found: 472.1752.

Ethyl 2-((1Z,3Z)-3-(2-([1,1'-biphenyl]-4-yl)-2-oxoethylidene)isoindolin-1-ylidene)acetate (3ab):



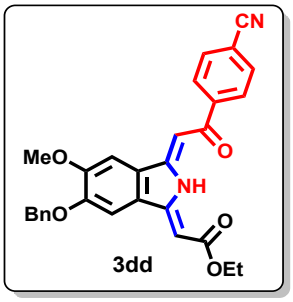
Yellow solid, Yield: 83%, M.P: 155−157 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.61 (s, 1H), 8.16 (d, *J* = 8.3 Hz, 2H), 7.87 (dd, *J* = 5.8, 2.6 Hz, 1H), 7.77 – 7.69 (m, 3H), 7.68 – 7.63 (m, 2H), 7.61 – 7.56 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 3H), 7.40 (t, *J* = 7.3 Hz, 1H), 6.84 (s, 1H), 5.77 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 189.64, 167.80, 151.93, 150.71, 144.75, 140.22, 138.14, 135.16, 134.56, 130.98, 130.67, 128.93, 128.37, 128.03, 127.29, 127.21, 121.63, 121.57, 91.48, 89.70, 60.48, 14.57; **HRMS** (ESI) Calcd for $C_{26}H_{22}NO_3$ $[M+H]^+$: 396.1594; Found: 396.1621.

Ethyl 2-((1Z,3Z)-3-(2-(3-nitrophenyl)-2-oxoethylidene)isoindolin-1-ylidene)acetate (3ac):



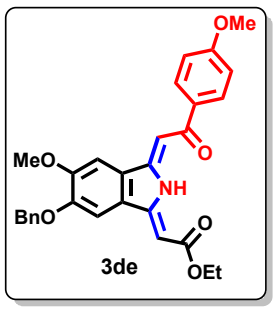
Light yellow solid, Yield: 82%, M.P: 174−176 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.66 (s, 1H), 8.90 (s, 1H), 8.45 – 8.37 (m, 2H), 7.94 – 7.90 (m, 1H), 7.80 – 7.75 (m, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.64 – 7.60 (m, 2H), 6.79 (s, 1H), 5.85 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 187.23, 167.71, 153.52, 150.41, 148.37, 140.69, 134.74, 133.62, 131.48, 130.95, 129.78, 126.33, 122.57, 121.95, 121.69, 91.21, 90.32, 77.26, 60.71, 14.54; **HRMS** (ESI) Calcd for $C_{20}H_{17}N_2O_5$ $[M+H]^+$: 365.1132; Found: 365.1142.

Ethyl 2-((1Z,3Z)-6-(benzyloxy)-3-(2-(4-cyanophenyl)-2-oxoethylidene)-5-methoxyisoindolin-1-ylidene)acetate (3dd):



Yellow solid, Yield: 83%, M.P: 153−155 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.41 (s, 1H), 8.17 – 8.08 (m, 2H), 7.78 – 7.73 (m, 2H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.23 (s, 1H), 7.16 (s, 1H), 6.58 (s, 1H), 5.63 (s, 1H), 5.24 (s, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.03 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 187.83, 167.63, 153.68, 152.70, 151.70, 150.55, 142.92, 135.88, 132.35, 128.84, 128.39, 128.15, 127.83, 127.32, 118.40, 114.96, 105.47, 103.77, 90.39, 90.20, 77.31, 71.31, 60.57, 56.52, 14.52; **HRMS** (ESI) Calcd for $C_{29}H_{25}N_2O_5$ $[M+H]^+$: 481.1758; Found: 481.1770.

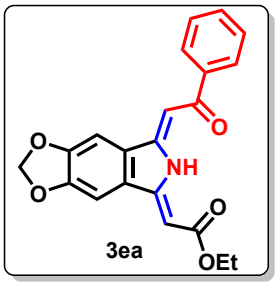
Ethyl 2-((1Z,3Z)-6-(benzyloxy)-5-methoxy-3-(2-(4-methoxyphenyl)-2-oxoethylidene)isoindolin-1-ylidene)acetate (3de):



Yellow solid, Yield: 83%, M.P: 168−170 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.34 (s, 1H), 8.07 (d, *J* = 8.6 Hz, 2H), 7.49 – 7.44 (m, 2H), 7.44 – 7.37 (m, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.23 (s, 1H), 7.14 (s, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.63 (s, 1H), 5.52 (s, 1H), 5.22 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.03 (s, 3H), 3.88 (s, 4H), 1.40 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 188.69, 167.81, 162.74, 152.52, 151.74,

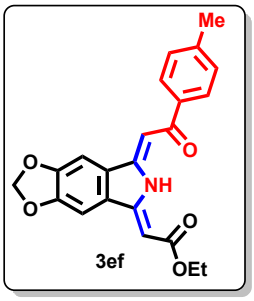
151.19, 150.98, 136.08, 132.39, 129.88, 128.80, 128.30, 127.70, 127.32, 113.66, 105.41, 103.62, 90.80, 88.30, 77.39, 71.24, 60.29, 56.49, 55.47, 14.57; **HRMS** (ESI) Calcd for $C_{29}H_{28}NO_6$ $[M+H]^+$: 486.1911; Found: 486.1920.

Ethyl (Z)-2-((Z)-7-(2-oxo-2-phenylethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ea):



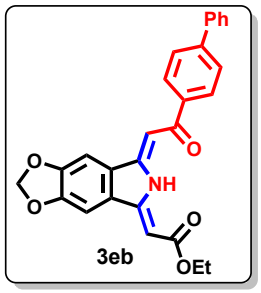
Light yellow solid, Yield: 89%, M.P: 183−185 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 12.35 (s, 1H), 8.05 (d, *J* = 6.7 Hz, 2H), 7.58 – 7.40 (m, 3H), 7.17 (s, 1H), 7.05 (s, 1H), 6.60 (s, 1H), 6.10 (s, 2H), 5.57 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 189.93, 167.71, 151.82, 150.87, 150.66, 150.53, 139.43, 131.95, 130.08, 129.68, 128.48, 127.71, 102.47, 101.34, 90.95, 89.16, 77.62, 60.41, 14.56; **HRMS** (ESI) Calcd for $C_{21}H_{18}NO_5$ $[M+H]^+$: 364.1179; Found: 364.1187.

Ethyl (Z)-2-((Z)-7-(2-oxo-2-(p-tolyl)ethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ef):



Yellow solid, Yield: 90%, M.P: 200−202 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.36 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.18 (s, 1H), 7.06 (s, 1H), 6.60 (s, 1H), 6.10 (s, 2H), 5.57 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.70, 167.77, 151.56, 150.80, 150.62, 150.44, 142.63, 136.84, 130.18, 129.68, 129.21, 127.84, 102.44, 101.38, 91.03, 88.87, 77.26, 60.39, 21.66, 14.58; **HRMS** (ESI) Calcd for $C_{22}H_{20}NO_5$ $[M+H]^+$: 378.1336; Found: 378.1369.

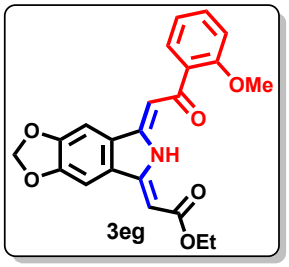
Ethyl (Z)-2-((Z)-7-(2-([1,1'-biphenyl]-4-yl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3eb):



Light yellow solid, Yield: 87%, M.P: 232−234 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.40 (s, 1H), 8.13 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.47 (dd, *J* = 8.1, 6.8 Hz, 2H), 7.39 (dd, *J* = 10.4, 4.3 Hz, 1H), 7.20 (s, 1H), 7.07 (s, 1H), 6.65 (s, 1H), 6.11 (s, 2H), 5.59 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.40, 167.73, 151.82, 150.88, 150.68, 150.55, 144.65, 140.22, 138.19, 130.13, 129.72, 128.92, 128.31, 128.00, 127.28, 127.16, 102.47, 101.40,

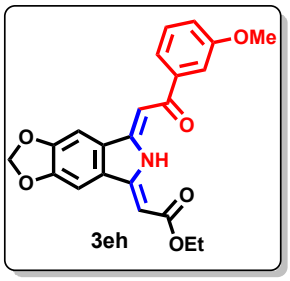
91.01, 89.17, 77.30, 60.42, 14.57; **HRMS** (ESI) Calcd for $C_{27}H_{22}NO_5$ $[M+H]^+$: 440.1492; Found: 440.1503.

Ethyl (Z)-2-((Z)-7-(2-(2-methoxyphenyl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3eg):



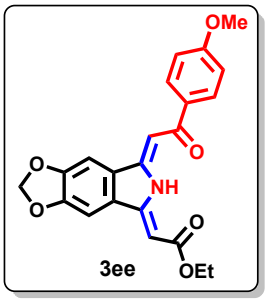
Orange solid, Yield: 87%, M.P: 192−194 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.19 (s, 1H), 7.82 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.12 (s, 1H), 7.06 (s, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.70 (s, 1H), 6.10 (s, 2H), 5.56 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 190.93, 167.74, 157.87, 150.68, 150.55, 150.33, 132.52, 130.77, 130.43, 130.28, 129.69, 120.90, 111.65, 102.37, 101.39, 101.32, 96.65, 88.60, 77.26, 60.36, 55.82, 14.59; **HRMS** (ESI) Calcd for $C_{22}H_{20}NO_6$ $[M+H]^+$: 394.12851; Found: 394.12902.

Ethyl (Z)-2-((Z)-7-(2-(3-methoxyphenyl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3eh):



Light yellow solid, Yield: 89%, M.P: 207−209 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.40 (s, 1H), 7.65 – 7.59 (m, 2H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.18 (s, 1H), 7.11 – 7.06 (m, 2H), 6.60 (s, 1H), 6.11 (s, 2H), 5.60 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.63, 167.76, 159.91, 151.87, 150.89, 150.68, 150.59, 140.90, 130.12, 129.71, 129.37, 120.13, 118.61, 112.17, 102.47, 101.41, 91.06, 89.18, 77.25, 60.40, 55.50, 14.56; **HRMS** (ESI) Calcd for $C_{22}H_{20}NO_6$ $[M+H]^+$: 394.1285; Found: 394.1295.

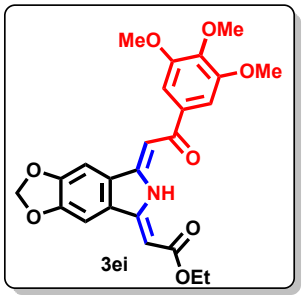
Ethyl (Z)-2-((Z)-7-(2-(4-methoxyphenyl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ee):



Yellow solid, Yield: 91%, M.P: 216−218 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 12.36 (s, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.18 (s, 1H), 7.06 (s, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.59 (s, 1H), 6.11 (s, 2H), 5.56 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 188.74, 167.79, 162.80, 151.30, 150.75, 150.61, 132.37, 130.23, 129.86, 129.69, 113.70, 102.41, 101.37, 101.32, 90.90,

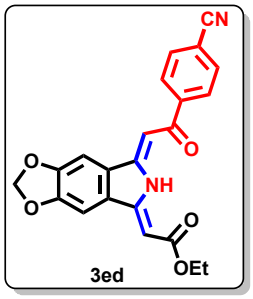
88.60, 77.24, 60.34, 55.47, 14.57; **HRMS** (ESI) Calcd for $C_{22}H_{20}NO_6$ $[M+H]^+$: 394.1285; Found: 394.1299.

Ethyl (Z)-2-((Z)-7-(2-oxo-2-(3,4,5-trimethoxyphenyl)ethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ei):



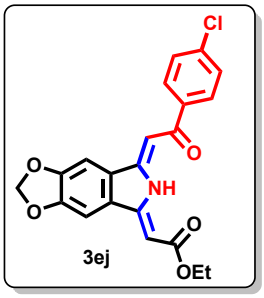
Yellow solid, Yield: 90%, M.P: 238−240 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.47 (s, 1H), 7.33 (s, 2H), 7.22 (s, 1H), 7.09 (s, 1H), 6.55 (s, 1H), 6.13 (s, 2H), 5.61 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 6H), 3.93 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 188.80, 167.83, 153.08, 151.89, 151.20, 150.89, 150.65, 141.69, 134.91, 130.06, 129.70, 105.23, 102.50, 101.44, 90.63, 89.13, 77.27, 61.01, 60.39, 56.42, 14.58; **HRMS** (ESI) Calcd for $C_{24}H_{24}NO_8$ $[M+H]^+$: 454.1496; Found: 454.1509.

Ethyl (Z)-2-((Z)-7-(2-(4-cyanophenyl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ed):



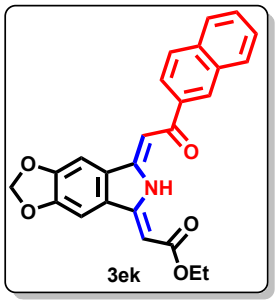
Light yellow solid, Yield: 87%, M.P: 194−196 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.45 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.20 (s, 1H), 7.10 (s, 1H), 6.56 (s, 1H), 6.14 (s, 2H), 5.68 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 187.88, 167.61, 153.21, 151.26, 150.84, 150.22, 142.87, 132.40, 129.84, 128.13, 118.39, 115.05, 114.09, 102.61, 101.51, 90.69, 90.26, 77.36, 60.61, 14.51; **HRMS** (ESI) Calcd for $C_{22}H_{17}N_2O_5$ $[M+H]^+$: 389.1132; Found: 389.1136.

Ethyl (Z)-2-((Z)-7-(2-(4-chlorophenyl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ej):



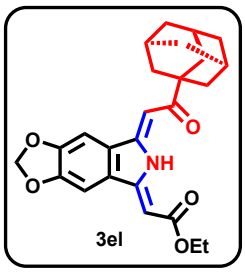
Light yellow solid, Yield: 90%, M.P: 228−230 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.36 (s, 1H), 7.98 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.16 (s, 1H), 7.06 (s, 1H), 6.53 (s, 1H), 6.11 (s, 2H), 5.59 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 188.48, 167.68, 152.25, 150.98, 150.70, 150.41, 138.22, 137.74, 129.93, 129.71, 129.11, 128.73, 102.51, 101.38, 90.45, 89.59, 77.25, 60.46, 14.53; **HRMS** (ESI) Calcd for $C_{21}H_{17}ClNO_5$ $[M+H]^+$: 398.0790; Found: 398.0798.

Ethyl (Z)-2-((Z)-7-(2-(naphthalen-2-yl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3ek):



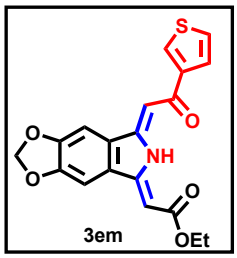
Light orange solid, Yield: 88%, M.P: 177−179 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.44 (s, 1H), 8.55 (s, 1H), 8.15 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.90 (dd, *J* = 14.6, 8.1 Hz, 2H), 7.56 (dq, *J* = 6.8, 5.6 Hz, 2H), 7.25 (s, 1H), 7.07 (s, 1H), 6.77 (s, 1H), 6.12 (s, 2H), 5.60 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.77, 167.74, 151.87, 150.90, 150.69, 150.56, 136.80, 135.17, 132.76, 130.15, 129.74, 129.47, 128.59, 128.31, 127.89, 127.77, 126.55, 124.28, 102.48, 101.39, 91.16, 89.22, 77.36, 60.43, 14.58; **HRMS** (ESI) Calcd for $C_{25}H_{19}NNaO_5$ $[M+Na]^+$: 436.11554; Found: 436.11582.

Ethyl (Z)-2-((Z)-7-(2-((3r,5r,7r)-adamantan-1-yl)-2-oxoethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3el):



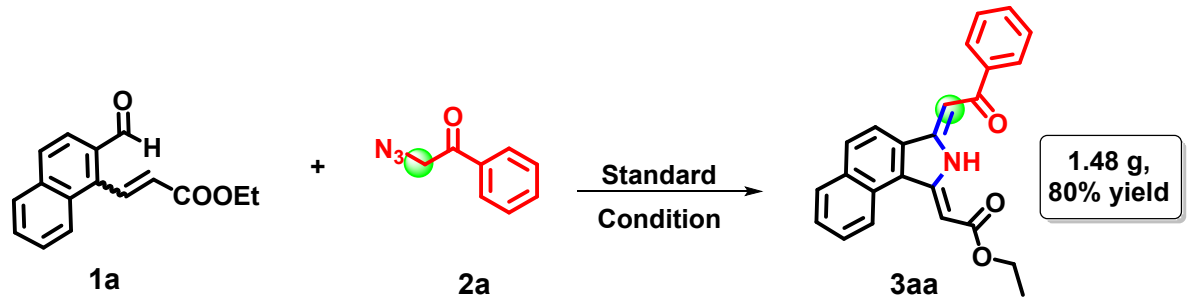
Yellow solid, Yield: 78%, M.P: 172−174 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.15 (s, 1H), 7.12 (s, 1H), 7.03 (s, 1H), 6.11 (s, 1H), 6.10 (s, 2H), 5.51 (s, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.08 (s, 3H), 1.92 (d, *J* = 2.7 Hz, 6H), 1.75 (p, *J* = 12.4 Hz, 6H), 1.62 (s, 2H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 205.43, 167.86, 150.90, 150.86, 150.57, 150.53, 130.34, 129.55, 102.35, 101.28, 89.90, 87.91, 77.25, 60.21, 45.34, 38.95, 36.75, 28.28, 14.54; **HRMS** (ESI) Calcd for $C_{25}H_{28}NO_5$ $[M+H]^+$: 422.19620; Found: 422.19683.

Ethyl (Z)-2-((Z)-7-(2-oxo-2-(thiophen-3-yl)ethylidene)-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-ylidene)acetate (3em):



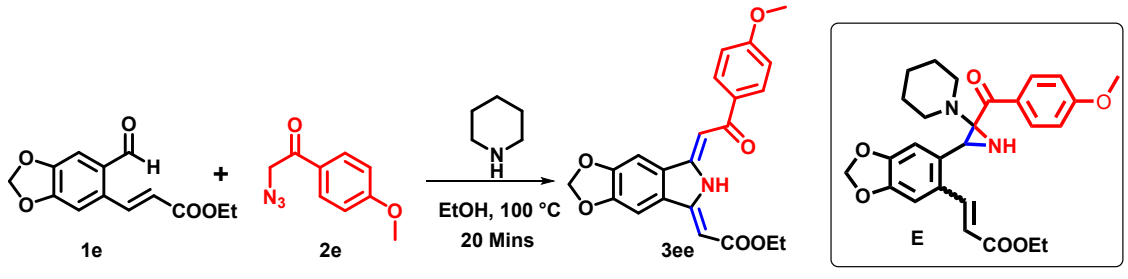
Light yellow solid, Yield: 75%, M.P: 221−223 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.31 (s, 1H), 8.09 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.66 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.34 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.16 (s, 1H), 7.06 (s, 1H), 6.42 (s, 1H), 6.11 (s, 2H), 5.57 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 184.27, 167.74, 151.56, 150.86, 150.64, 150.52, 144.25, 129.96, 129.89, 129.68, 127.11, 126.10, 102.47, 101.35, 92.06, 88.95, 77.26, 60.37, 14.55; **HRMS** (ESI) Calcd for $C_{19}H_{16}NO_5S$ $[M+H]^+$: 370.0744; Found: 370.0757.

Gram Scale Synthesis of ethyl (Z)-2-((Z)-3-(2-oxo-2-phenylethylidene)-2,3-dihydro-1H-benzo[e]isoindol-1-ylidene)acetate (3aa):



ethyl 3-(2-formylnaphthalen-1-yl)acrylate (**1a**, 1.27 g, 5.0 mmol), phenacyl azide (2a, 0.8 g, 5. mmol) and EtOH (30 mL) were taken in a 50 mL round bottom flask then piperidine (6.0 mmol) was added and stirred at this temperature for another 6 hrs. After complete consumption of starting materials, (reaction monitored by TLC) EtOH was removed under reduced pressure and the residue was purified by column chromatography with Hexane/EtOAc to afford the desired *(Z)*-1,3-bis(α,β-unsaturated carbonyl)-Isoindolines **3aa** orange solid (1.48 g) in 80% yield.

In situ HRMS analysis: 2-formylphenyl acrylate (**1e**) (0.124 g, 0.5 mmol), α-azido ketone (**2e**) (0.096 g, 0.5 mmol) and EtOH (2.0-3.0 mL) were taken in a 10 mL round bottom flask then piperidine (0.6 mmol) was added. The reaction mixture was heated upto 100 °C and stirred at this temperature for another 20 mins monitered by TLC (a new spot was observed on TLC other than the desired product spot). Immidetey, the reaction stirring was stopped and EtOH was removed under reduced pressure and a small aliquot from crude product was taken for ESI Mass and HRMS in which a probable intermediate **E** was observed. At this stage we tried to isolate the intermediate E however, all our efforts were unsuccessful.

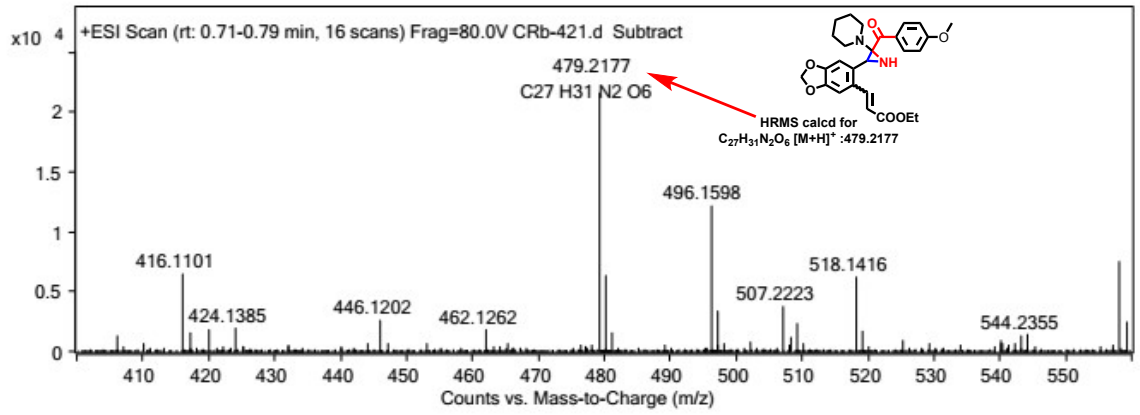


Qualitative Analysis Report

Data File	CRb-421.d	**Sample Name**	
Sample Type	Sample	**Position**	P1-A1
Instrument Name	Instrument 1	**User Name**	CSIR-IICT\Analyst
Acq Method	hrms-pos-method.m	**Acquired Time**	08-07-2021 12:11:32
IRM Calibration Status	Success	**DA Method**	11.m
Comment			
Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)

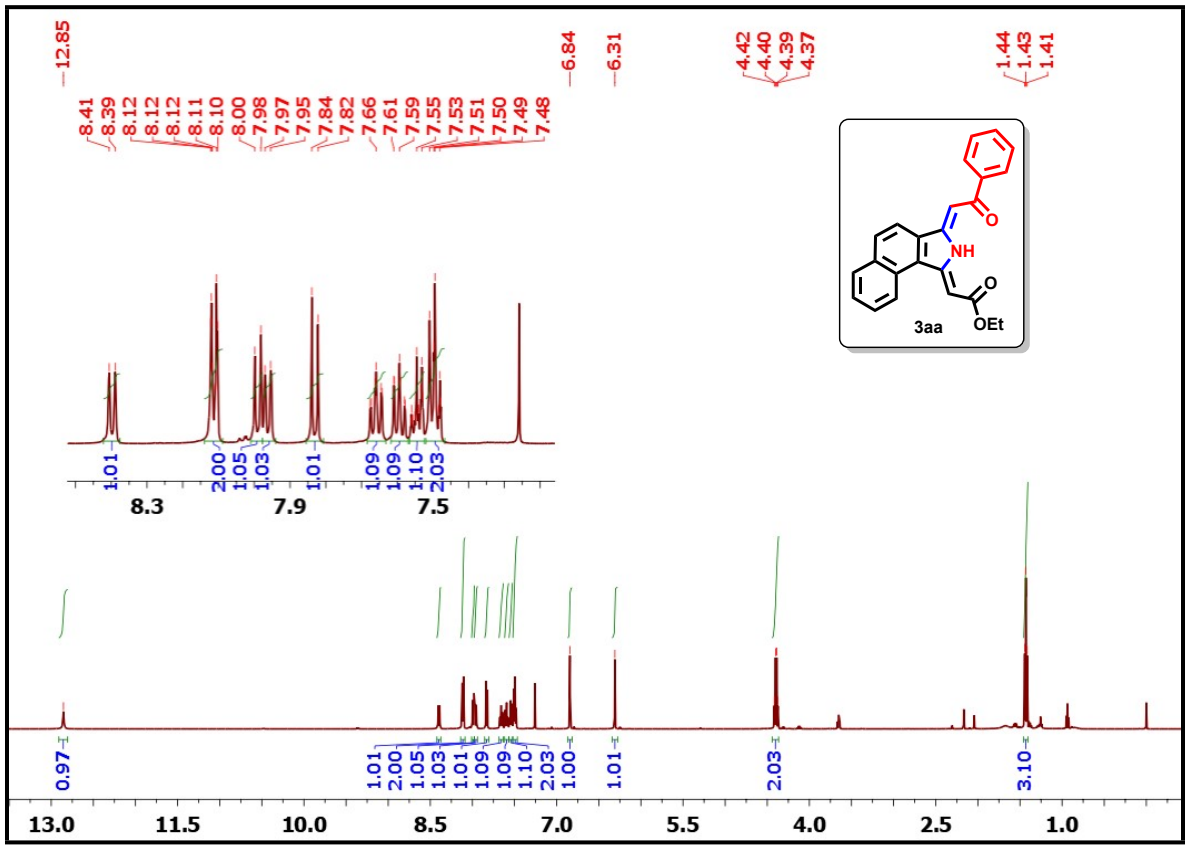
User Spectra

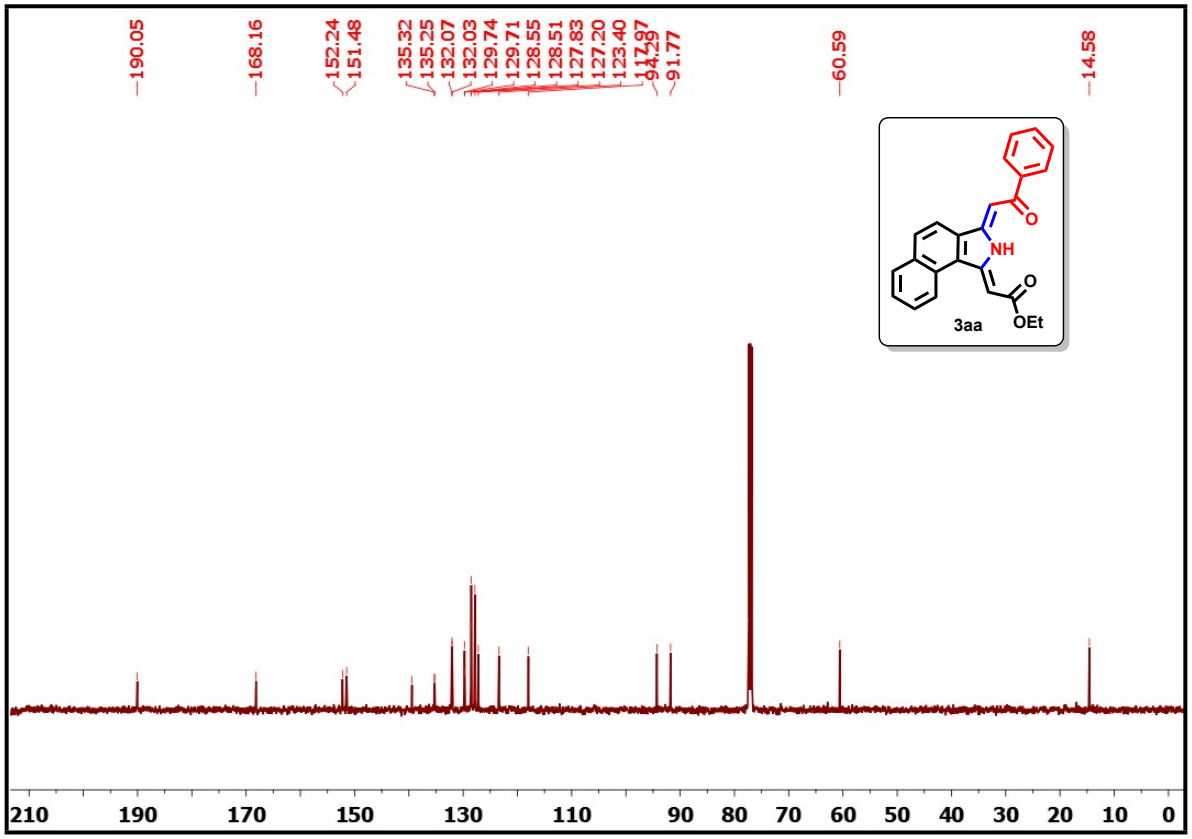
Fragmentor Voltage	Collision Energy	Ionization Mode
80	0	ESI



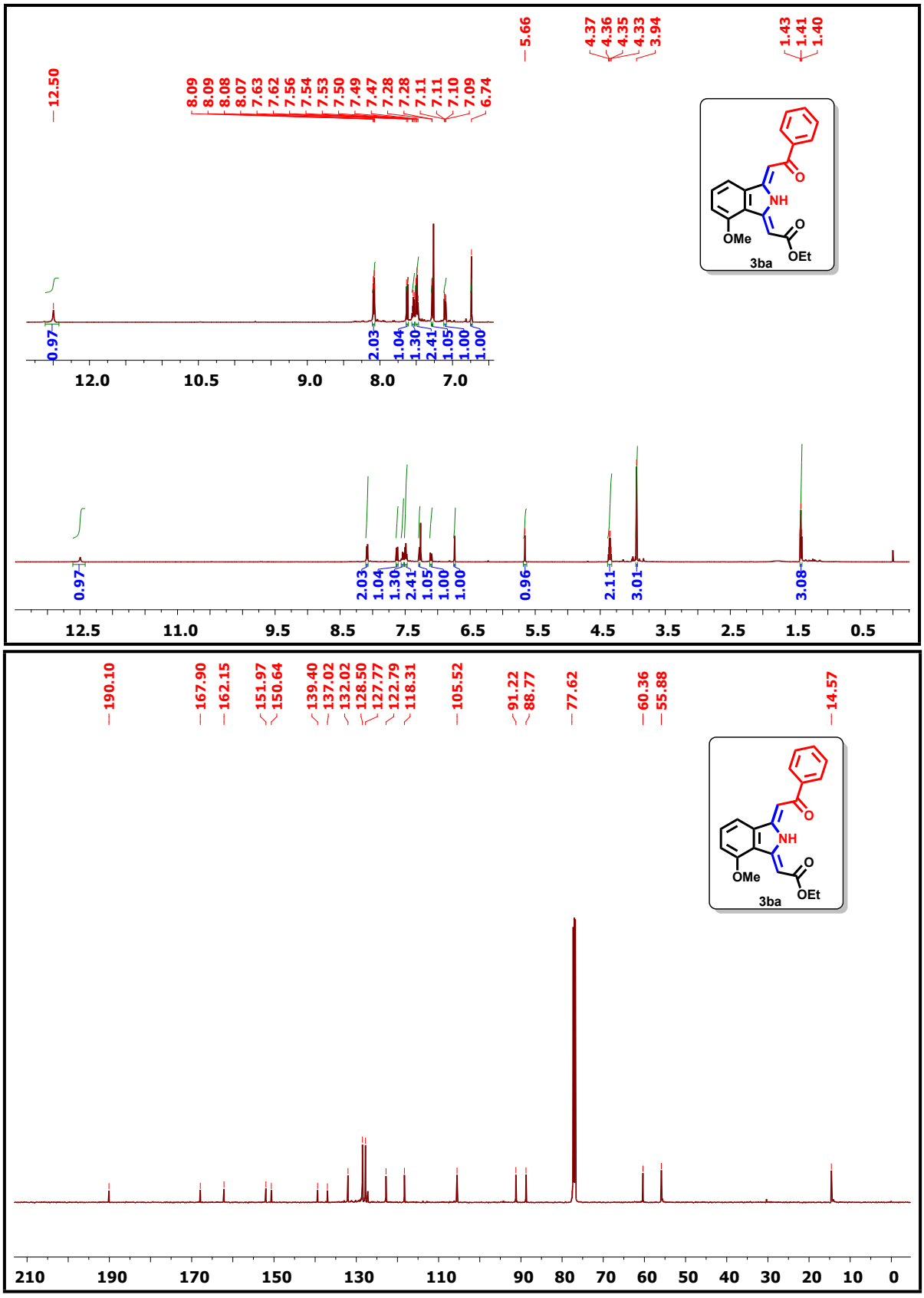
Samples was taken 20 mins after running the reaction under the standard conditions and diluted with MeOH prior to the injection into the mass spectrometer.

^{1}H NMR & ^{13}C NMR spectrum of compound 3aa

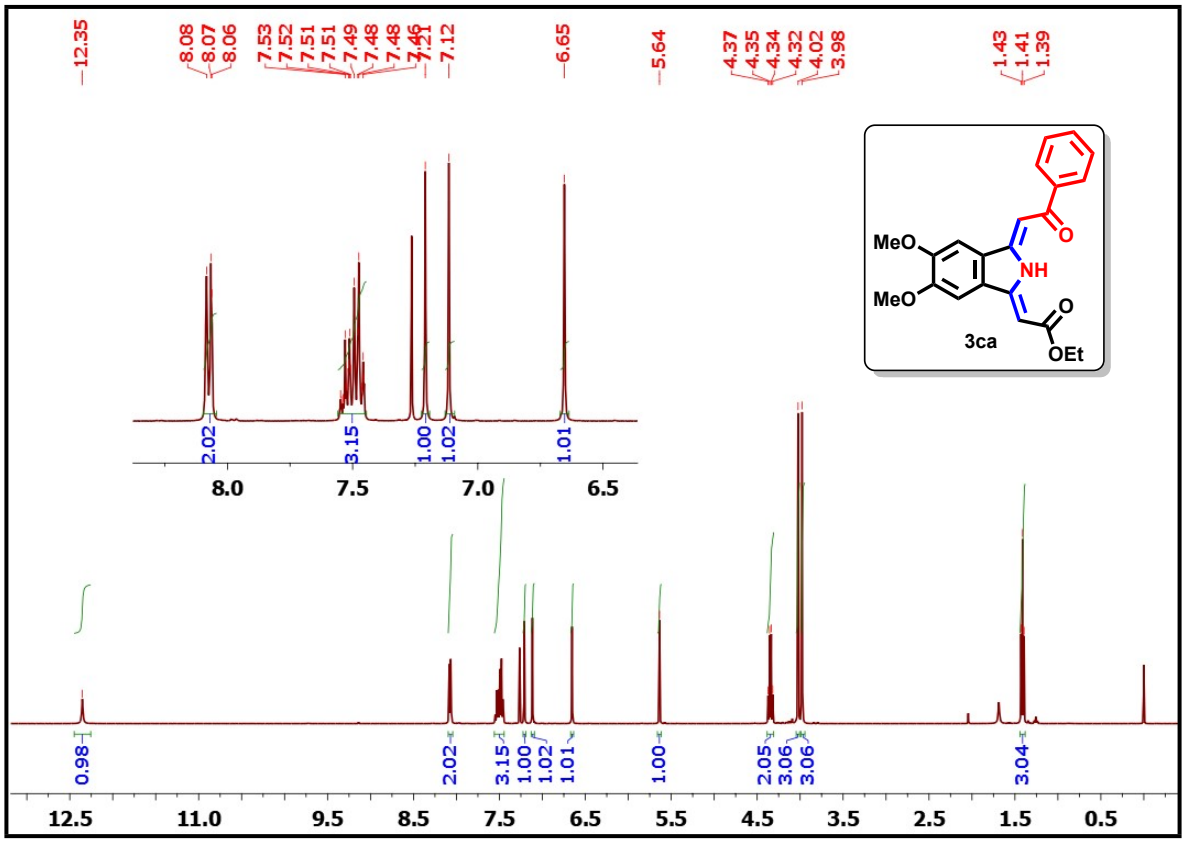


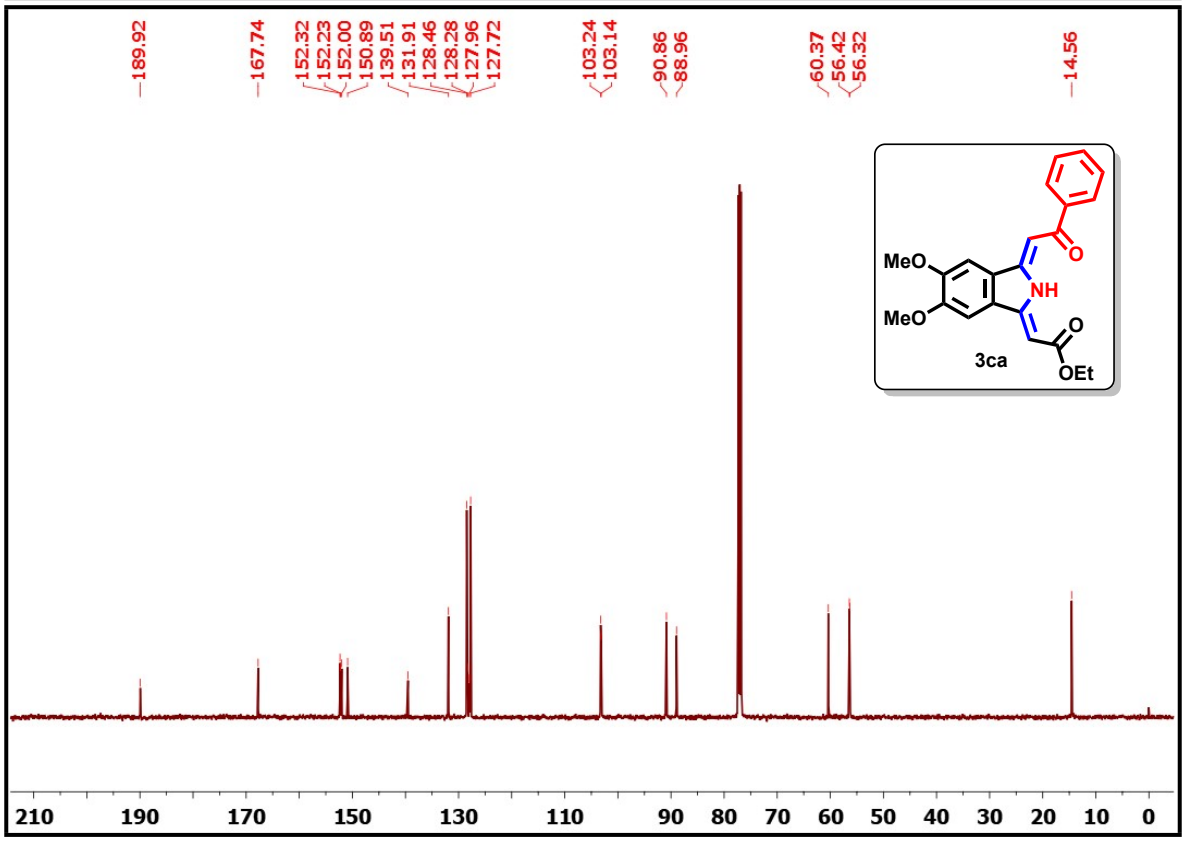


^{1}H NMR & ^{13}C NMR spectrum of compound 3ba

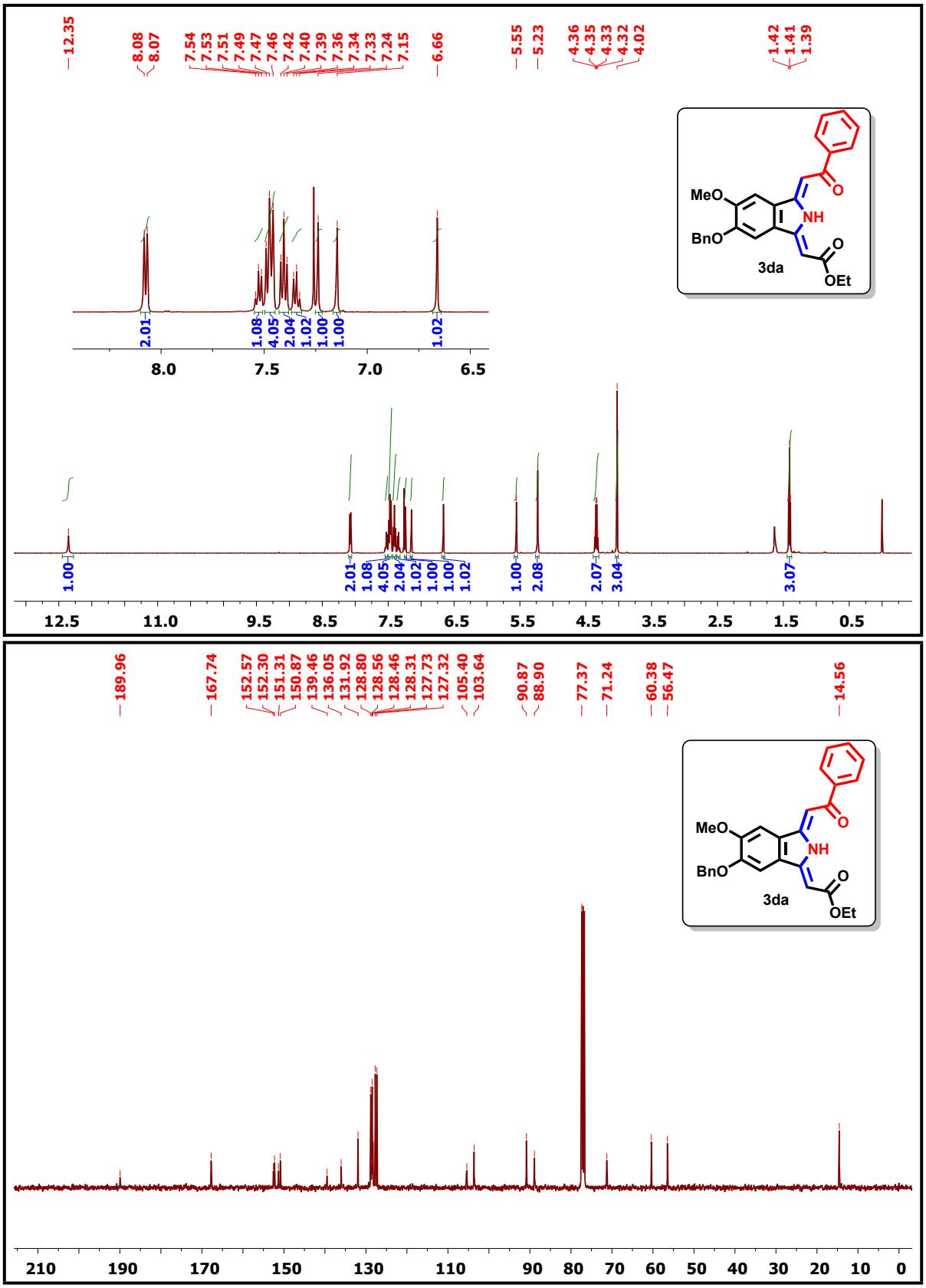


^{1}H NMR & ^{13}C NMR spectrum of compound 3ca

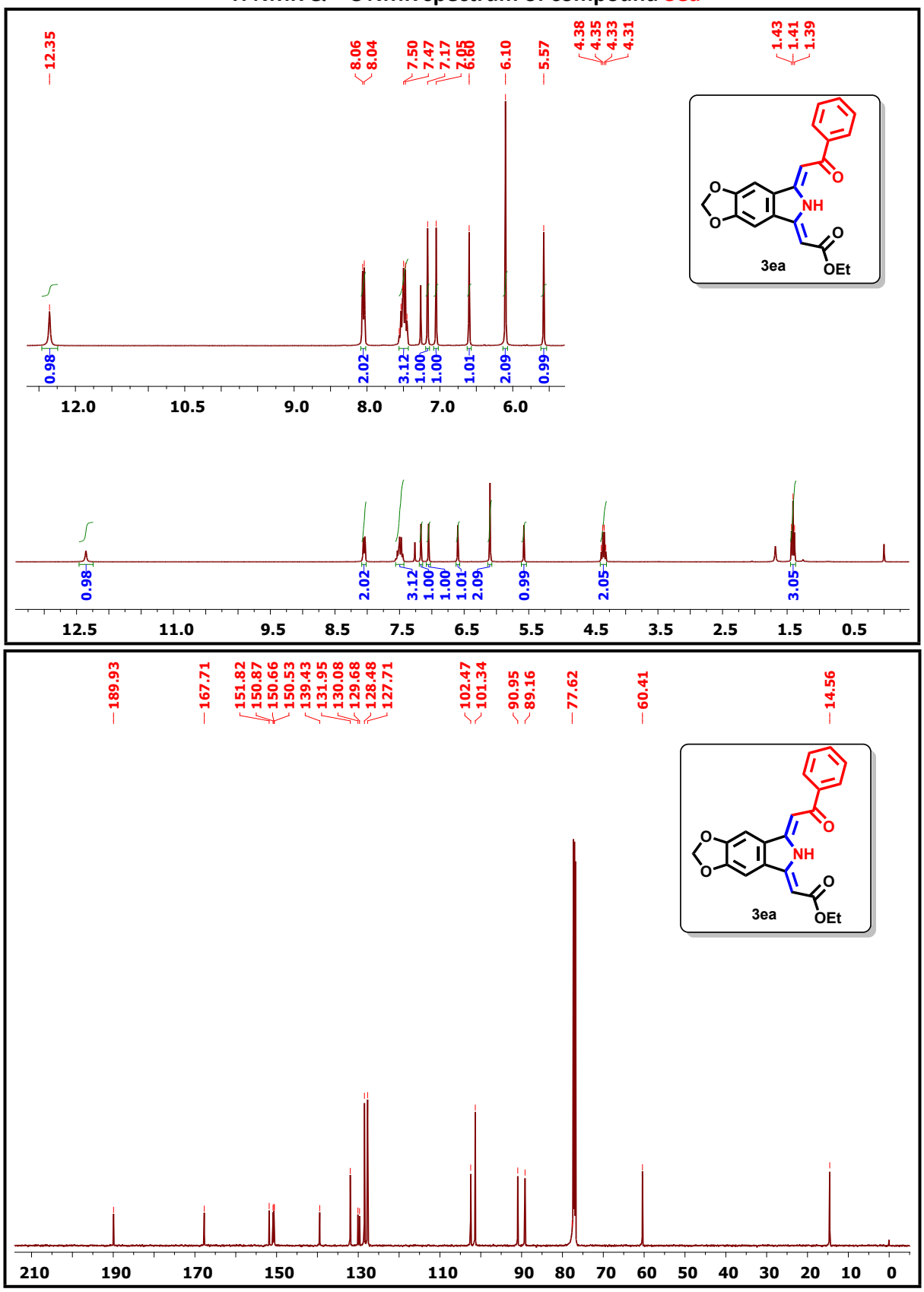




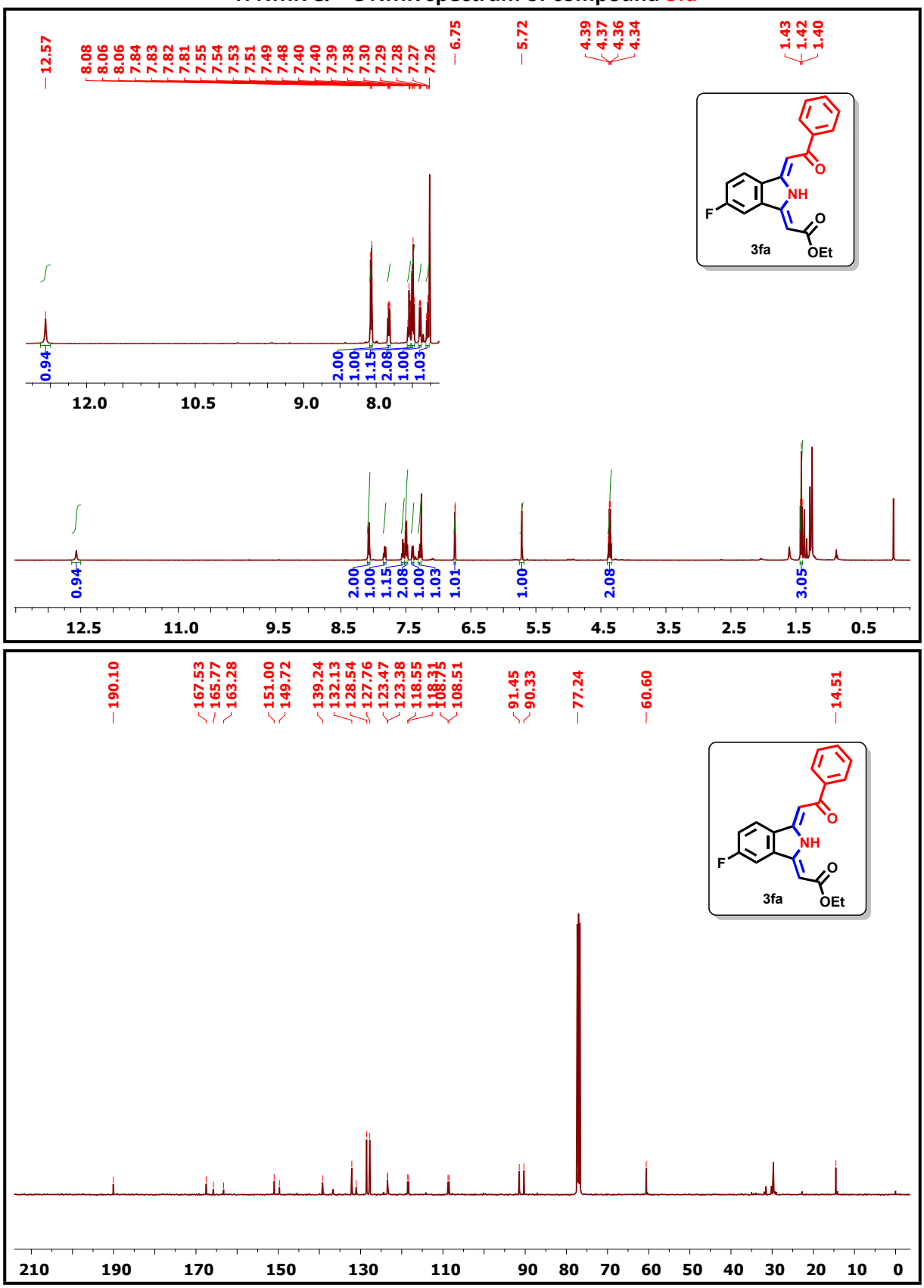
^{1}H NMR & ^{13}C NMR spectrum of compound 3da



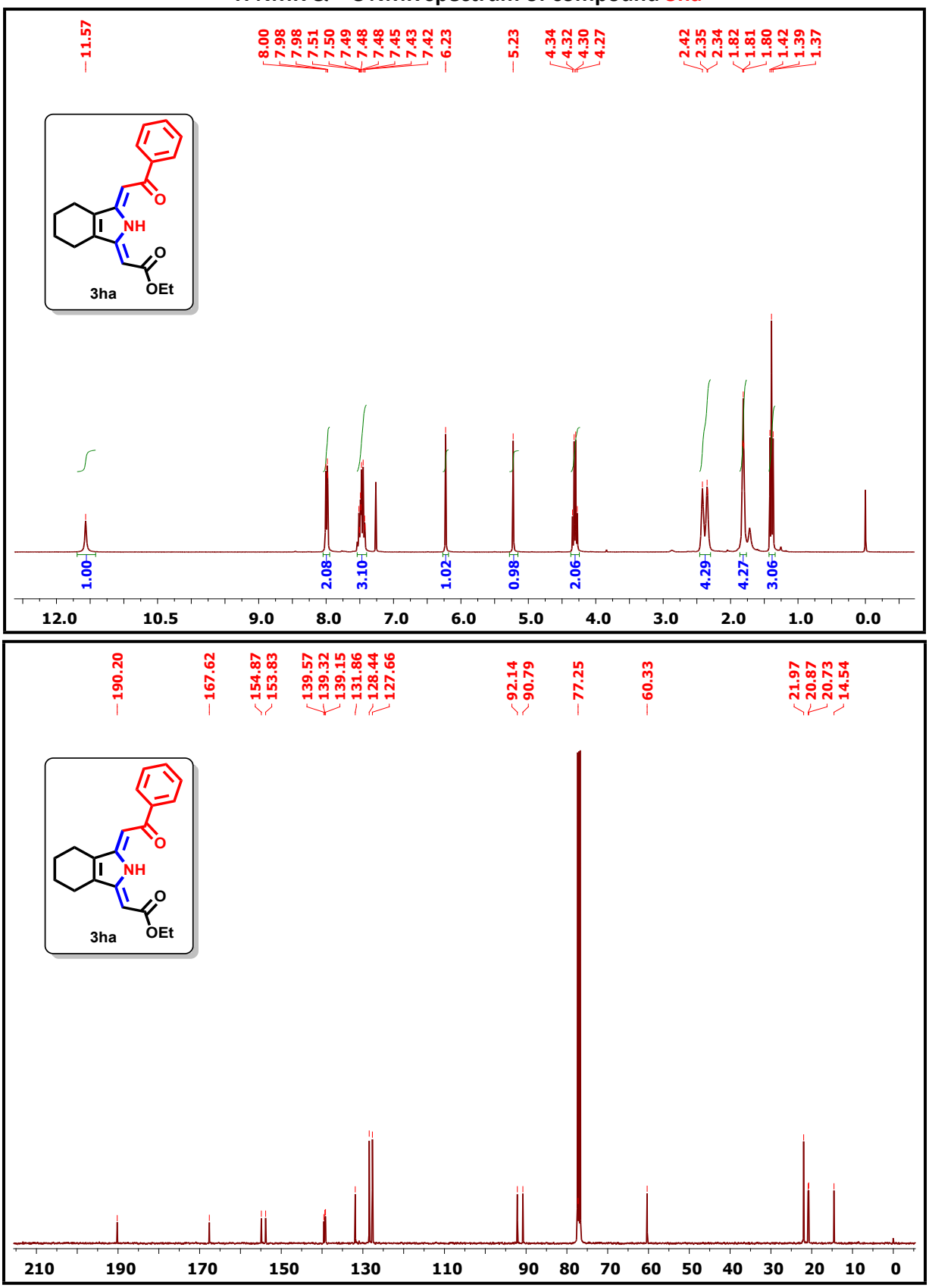
^{1}H NMR & ^{13}C NMR spectrum of compound 3ea



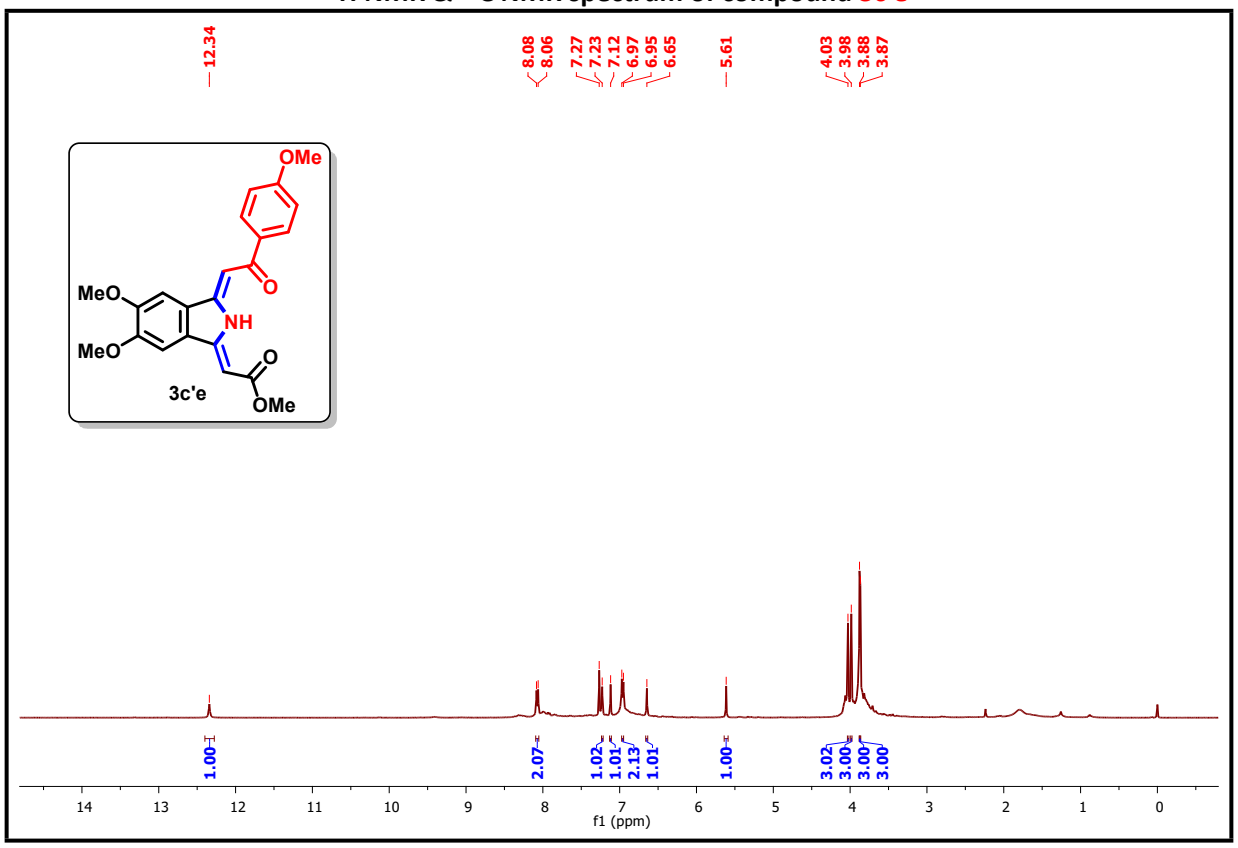
^{1}H NMR & ^{13}C NMR spectrum of compound 3fa

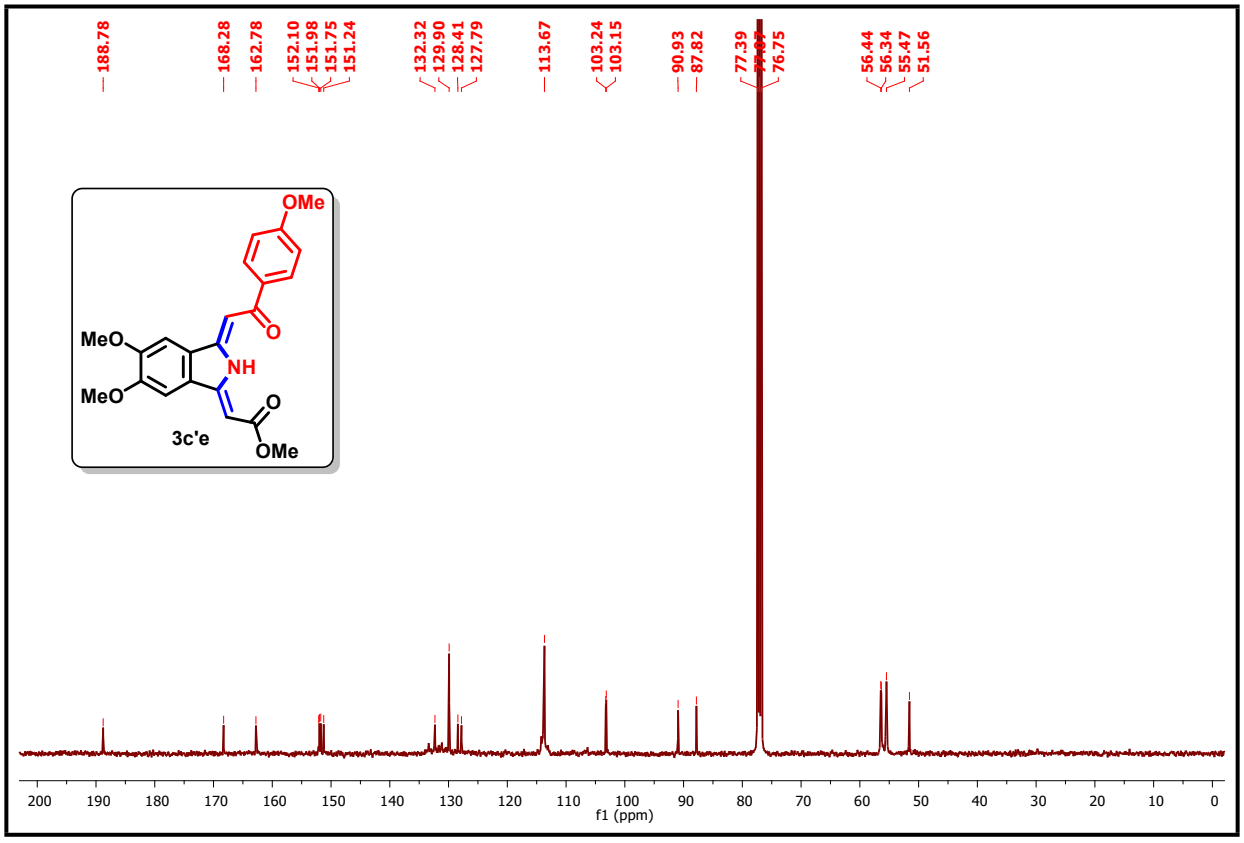


^{1}H NMR & ^{13}C NMR spectrum of compound 3ha

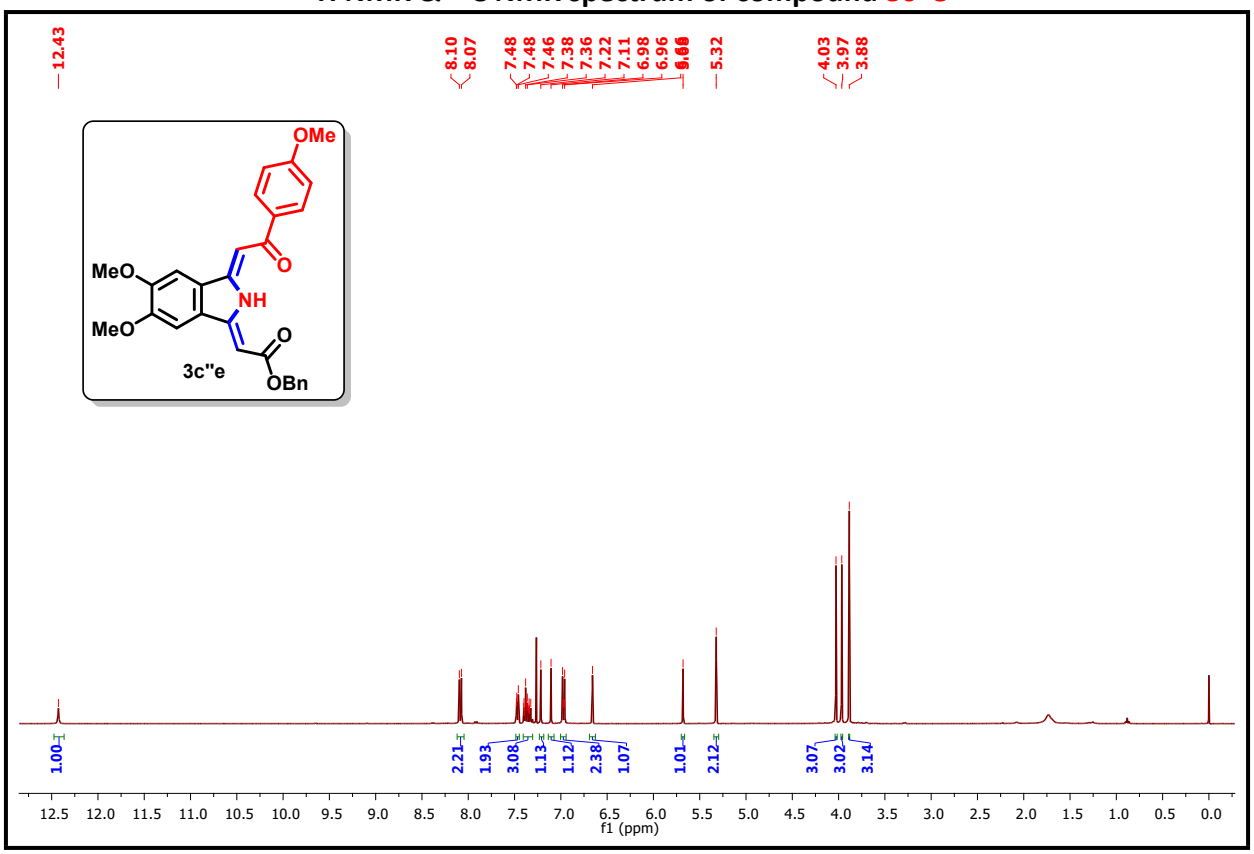


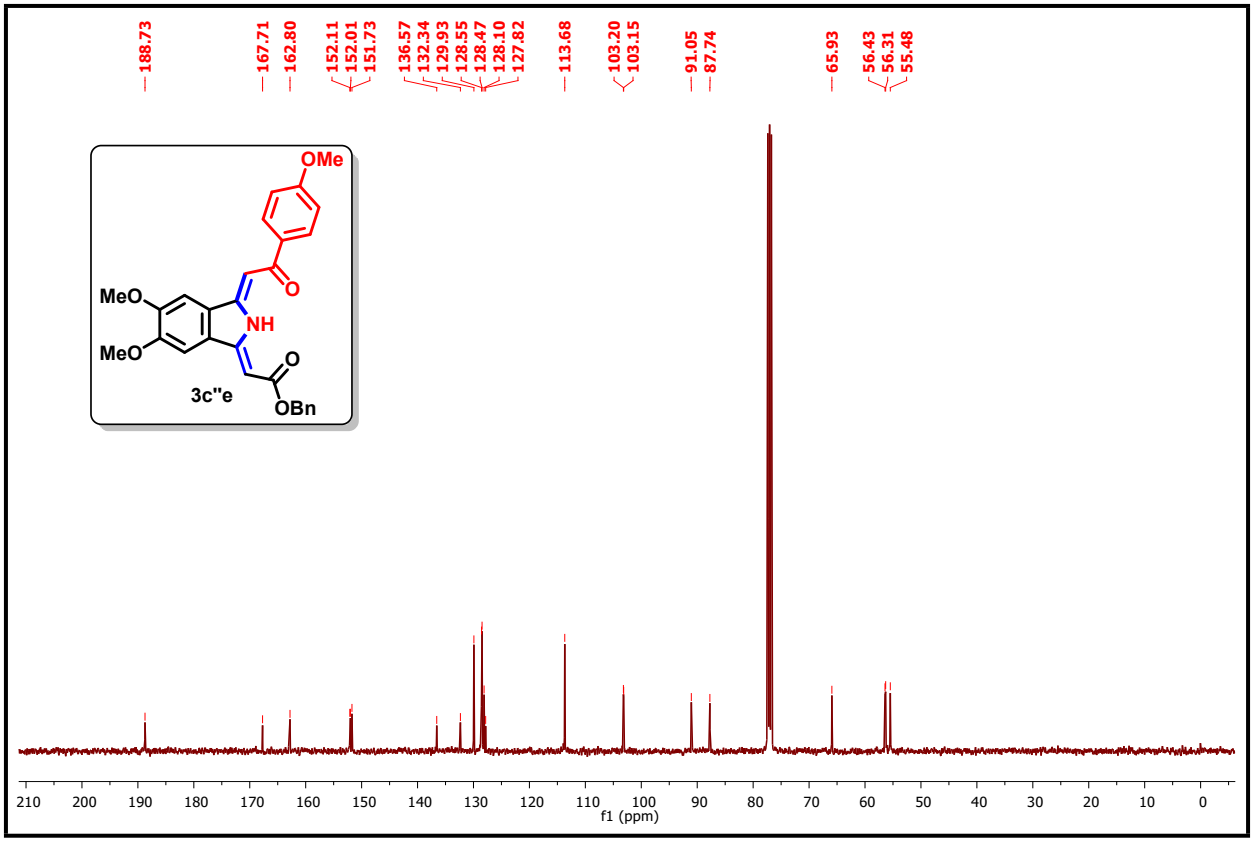
^{1}H NMR & ^{13}C NMR spectrum of compound 3c'e



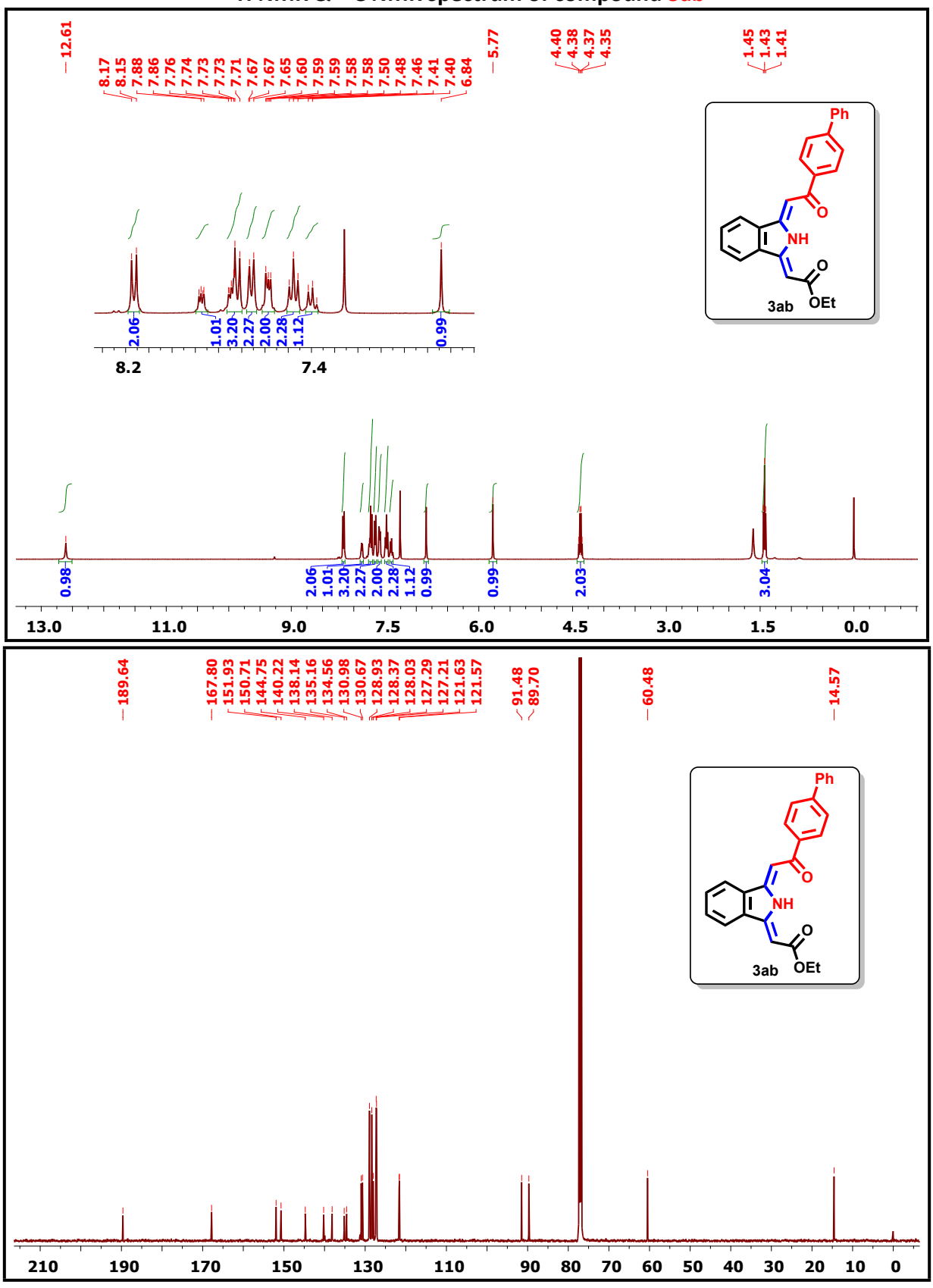


^{1}H NMR & ^{13}C NMR spectrum of compound 3c''e

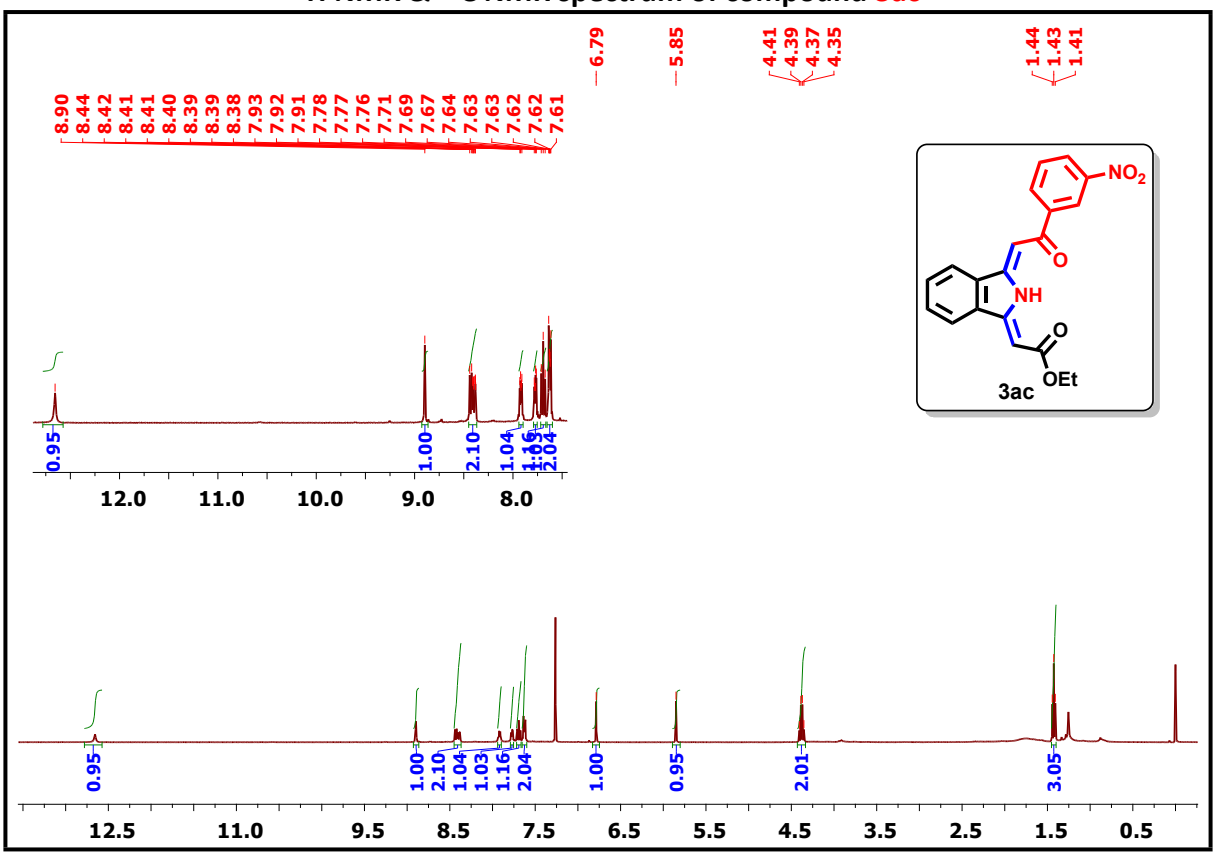


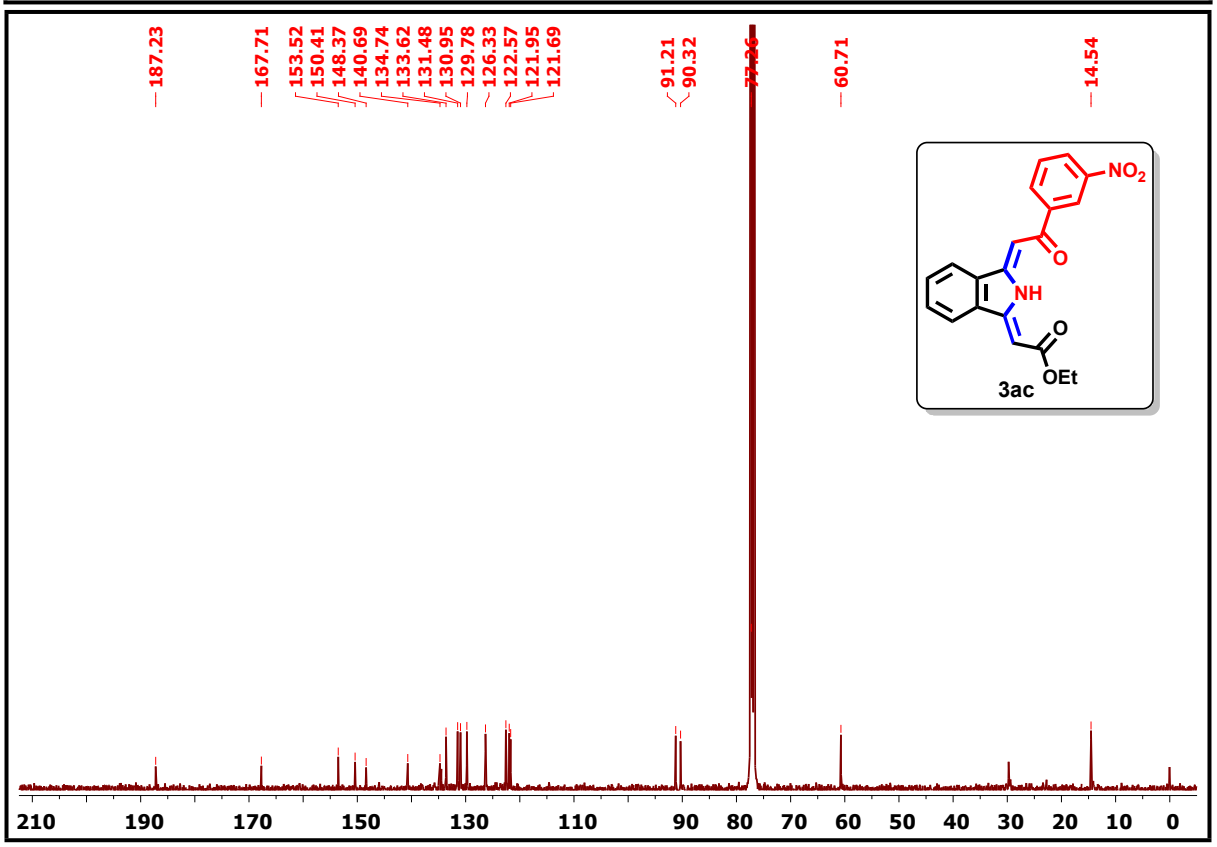


^{1}H NMR & ^{13}C NMR spectrum of compound 3ab

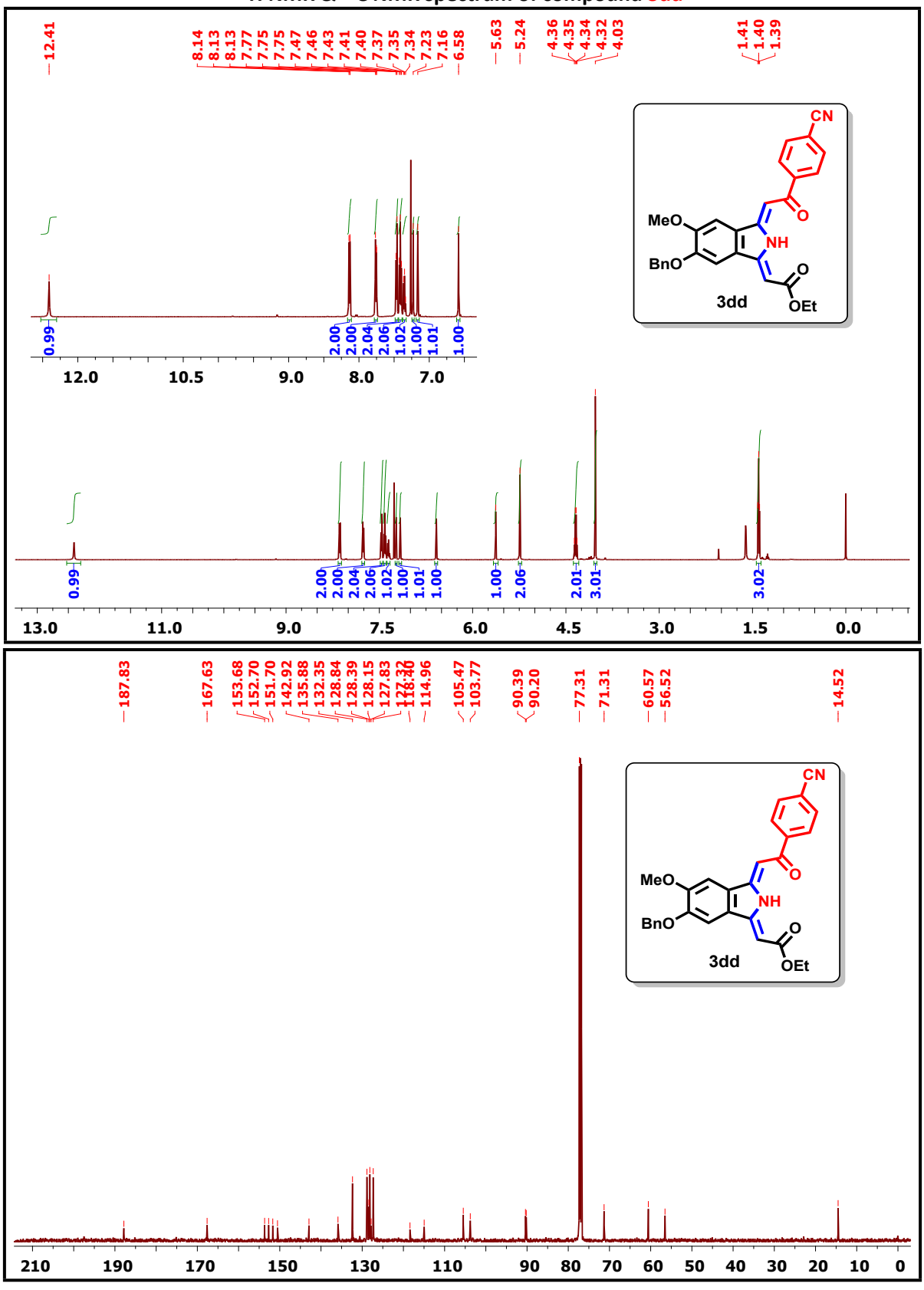


^{1}H NMR & ^{13}C NMR spectrum of compound 3ac

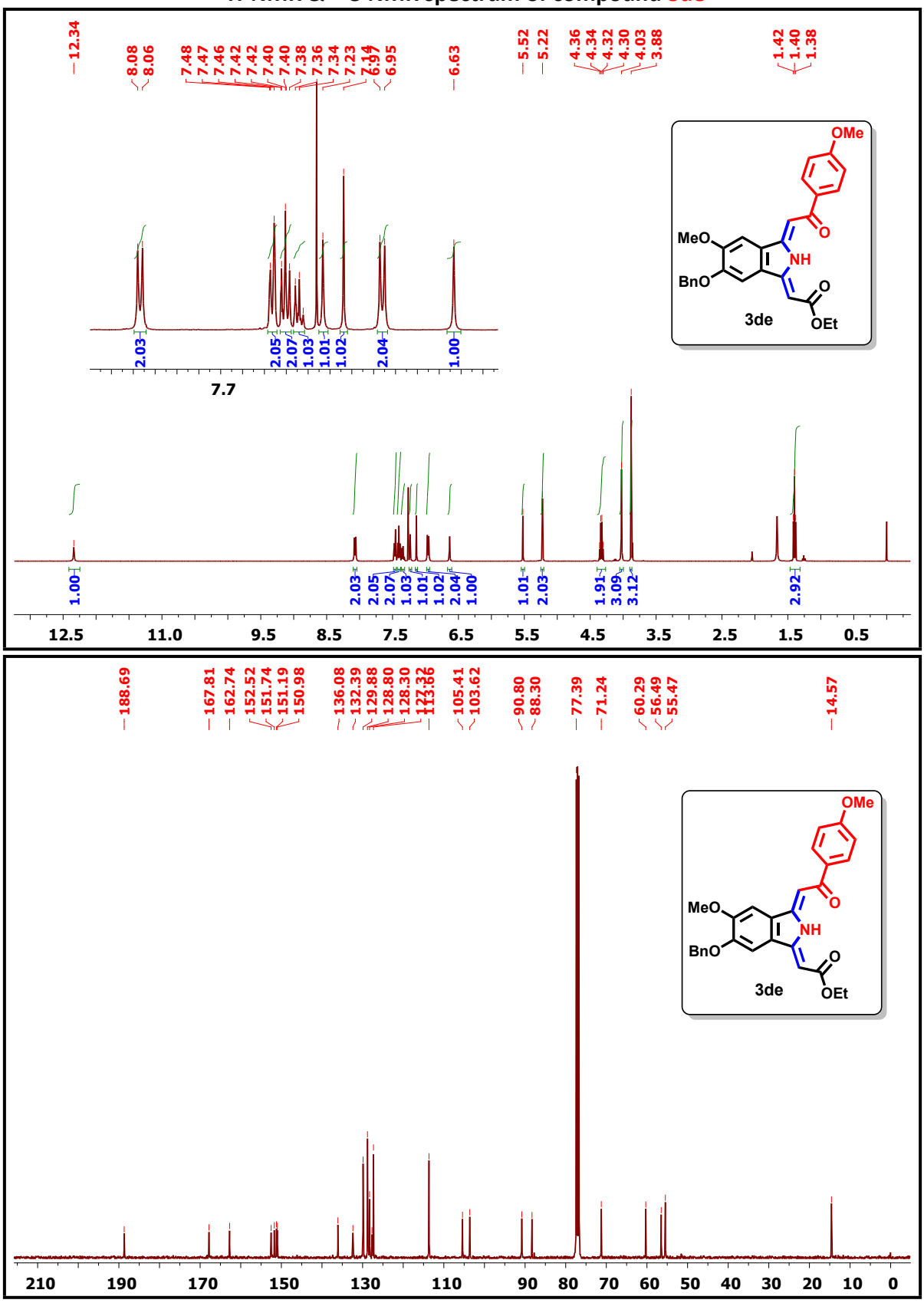




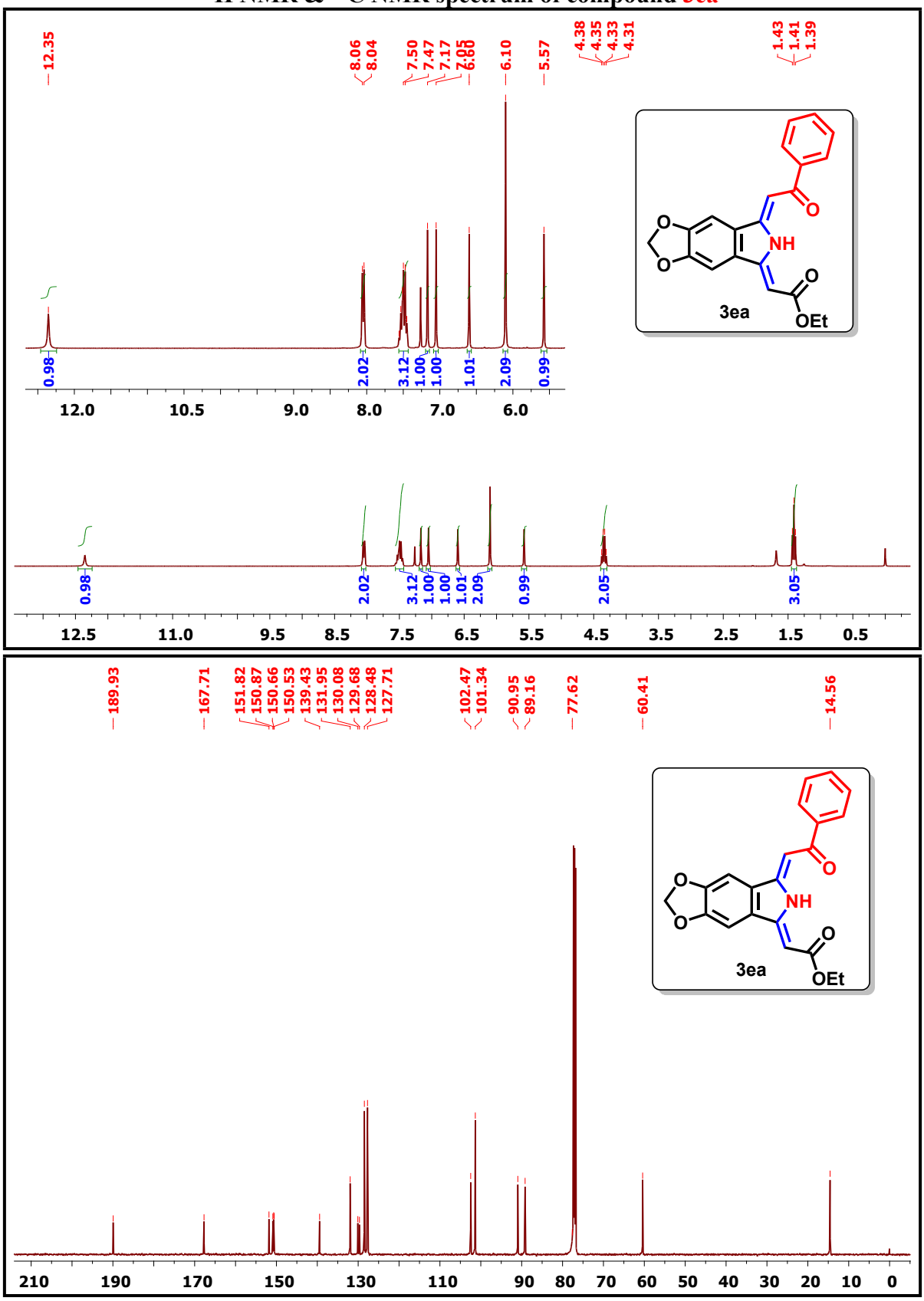
^{1}H NMR & ^{13}C NMR spectrum of compound 3dd



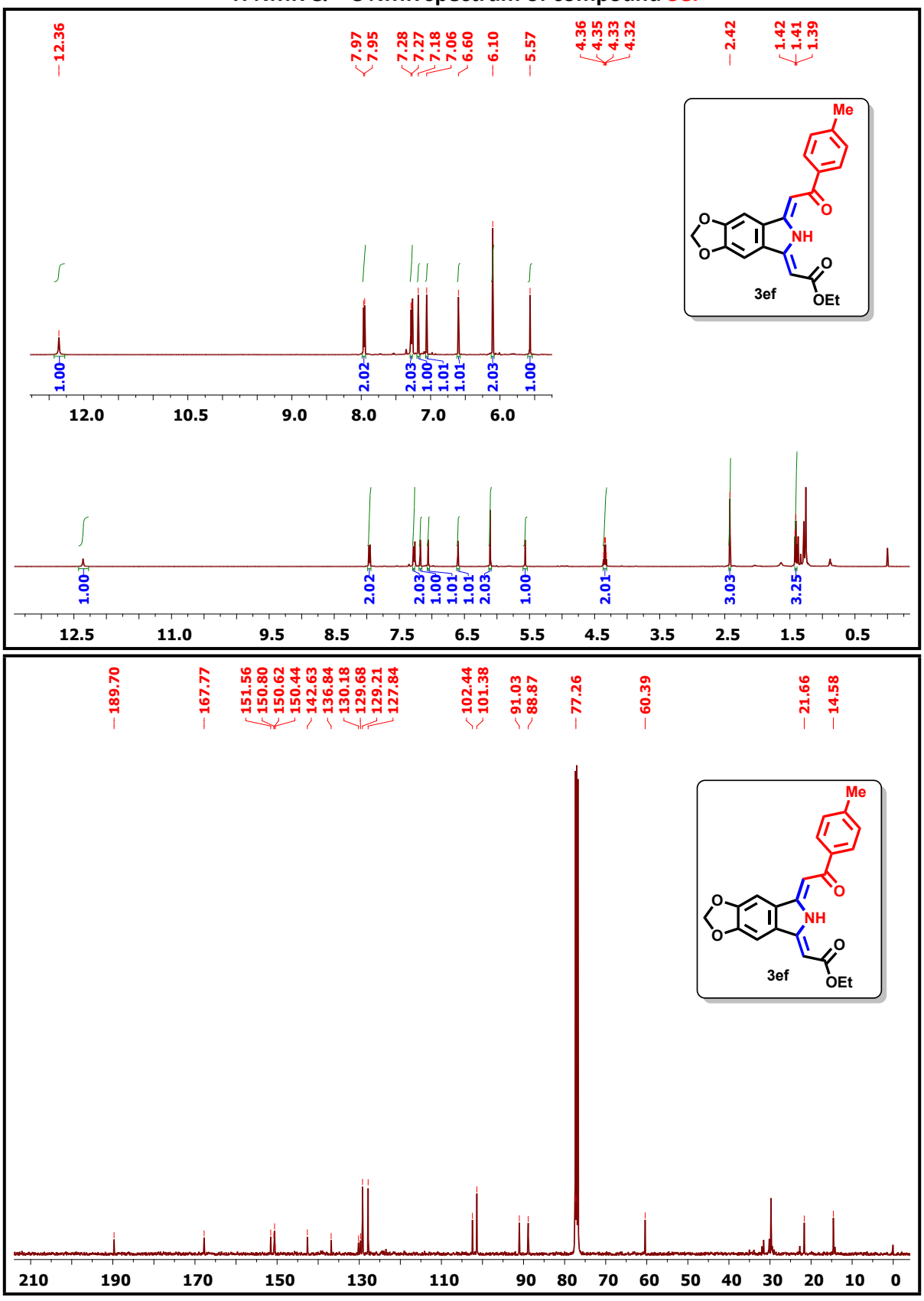
^{1}H-NMR & ^{13}C-NMR spectrum of compound 3de



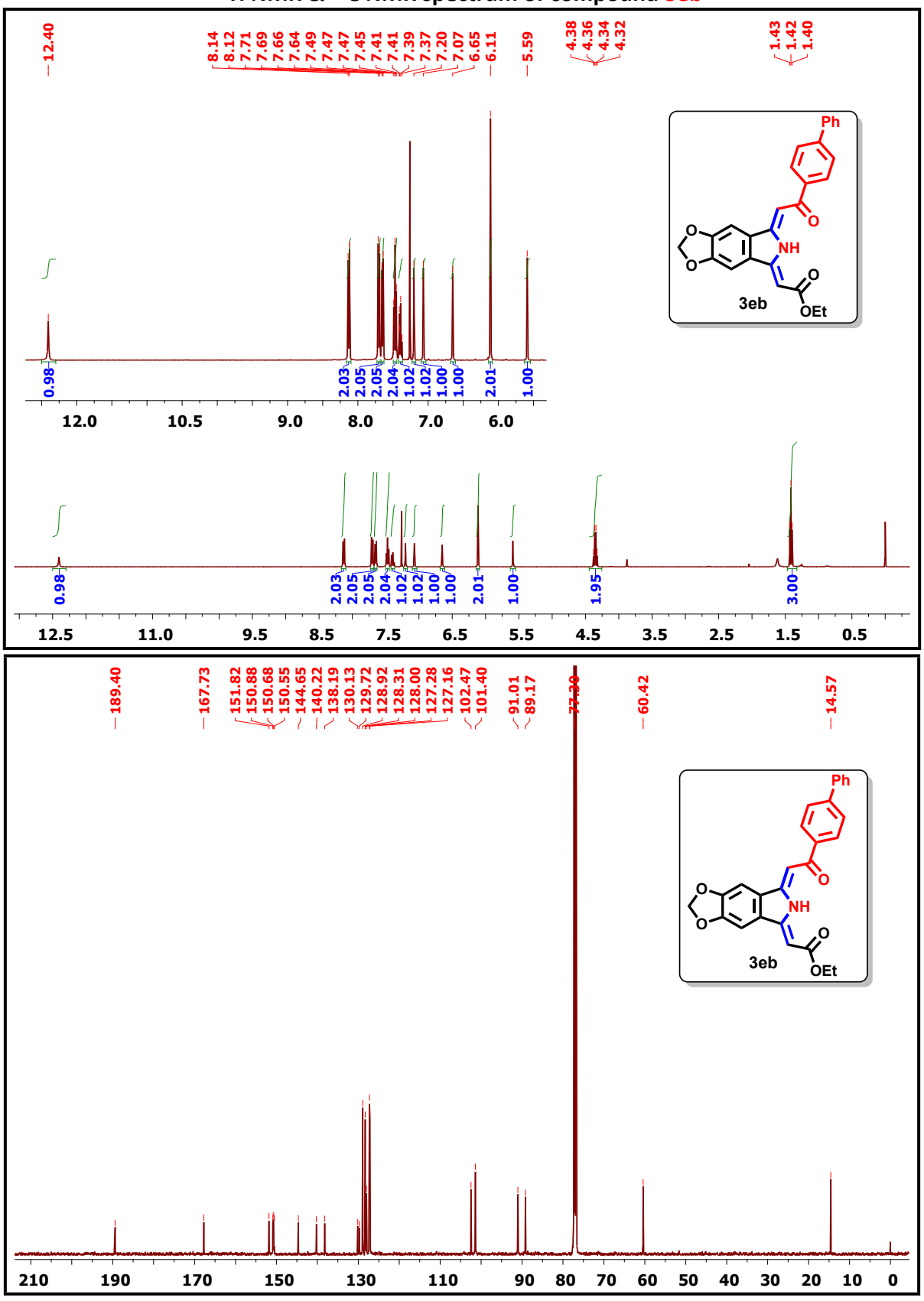
^{1}H NMR & ^{13}C NMR spectrum of compound 3ea



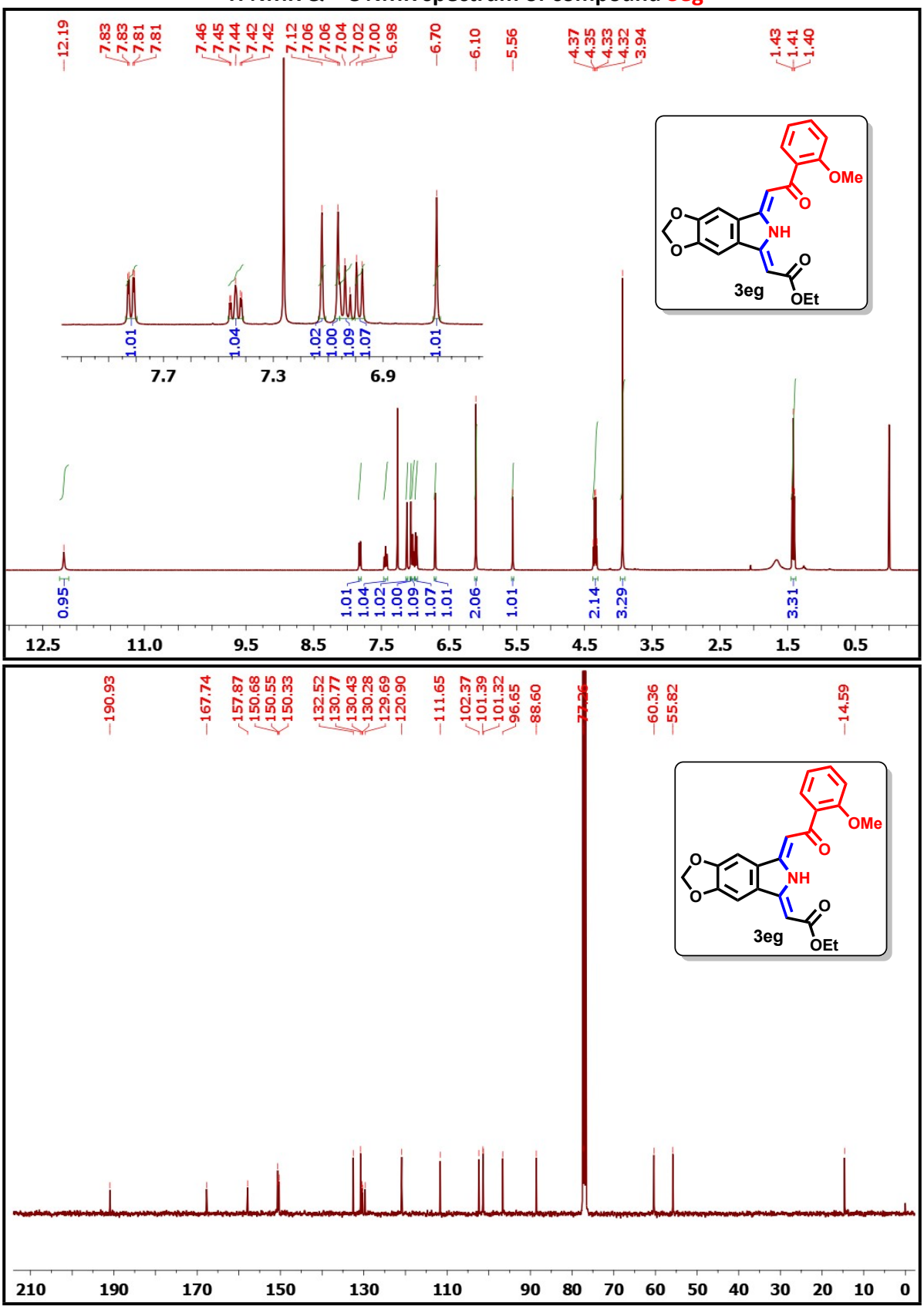
^{1}H NMR & ^{13}C NMR spectrum of compound 3ef



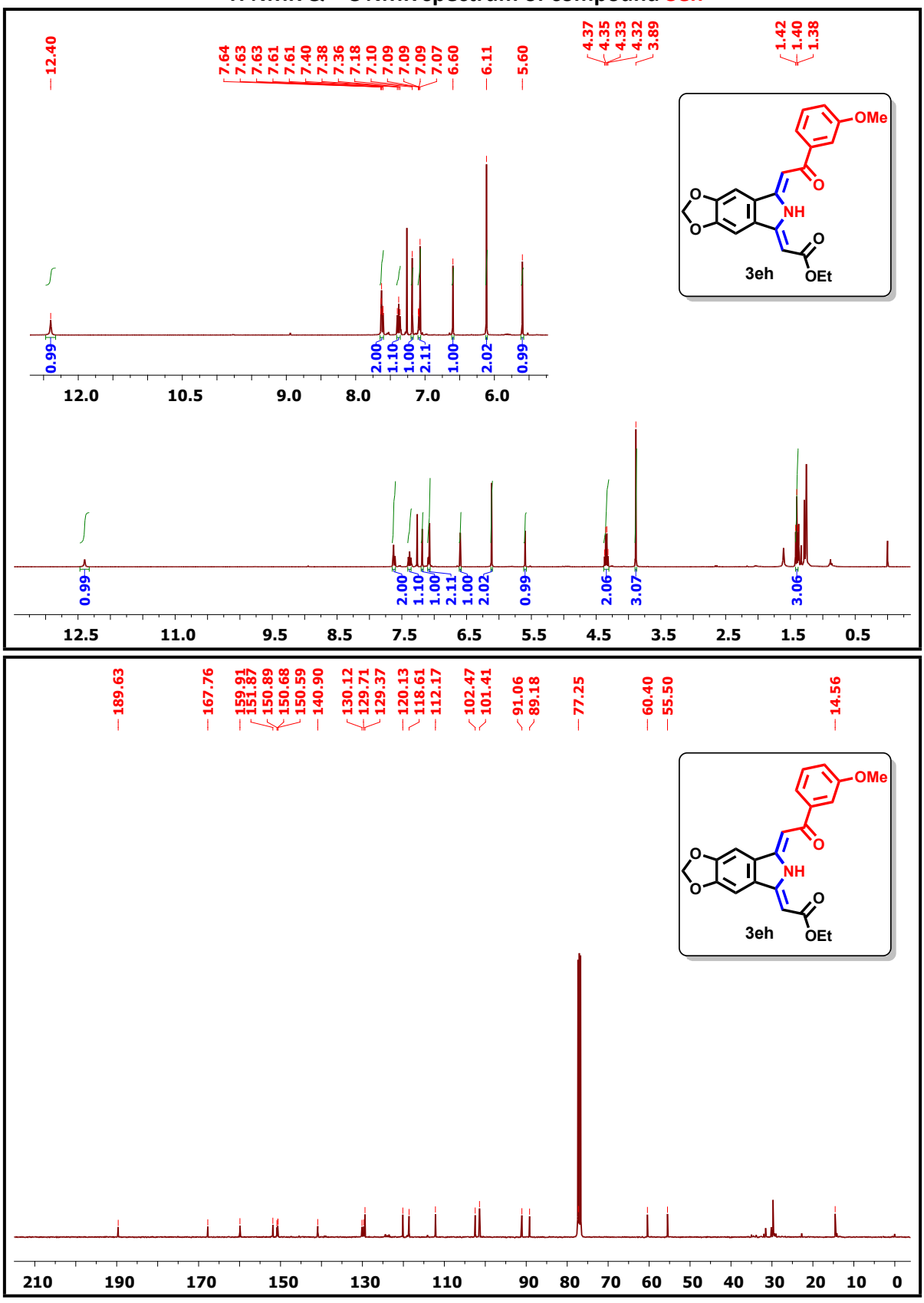
^{1}H NMR & ^{13}C NMR spectrum of compound 3eb



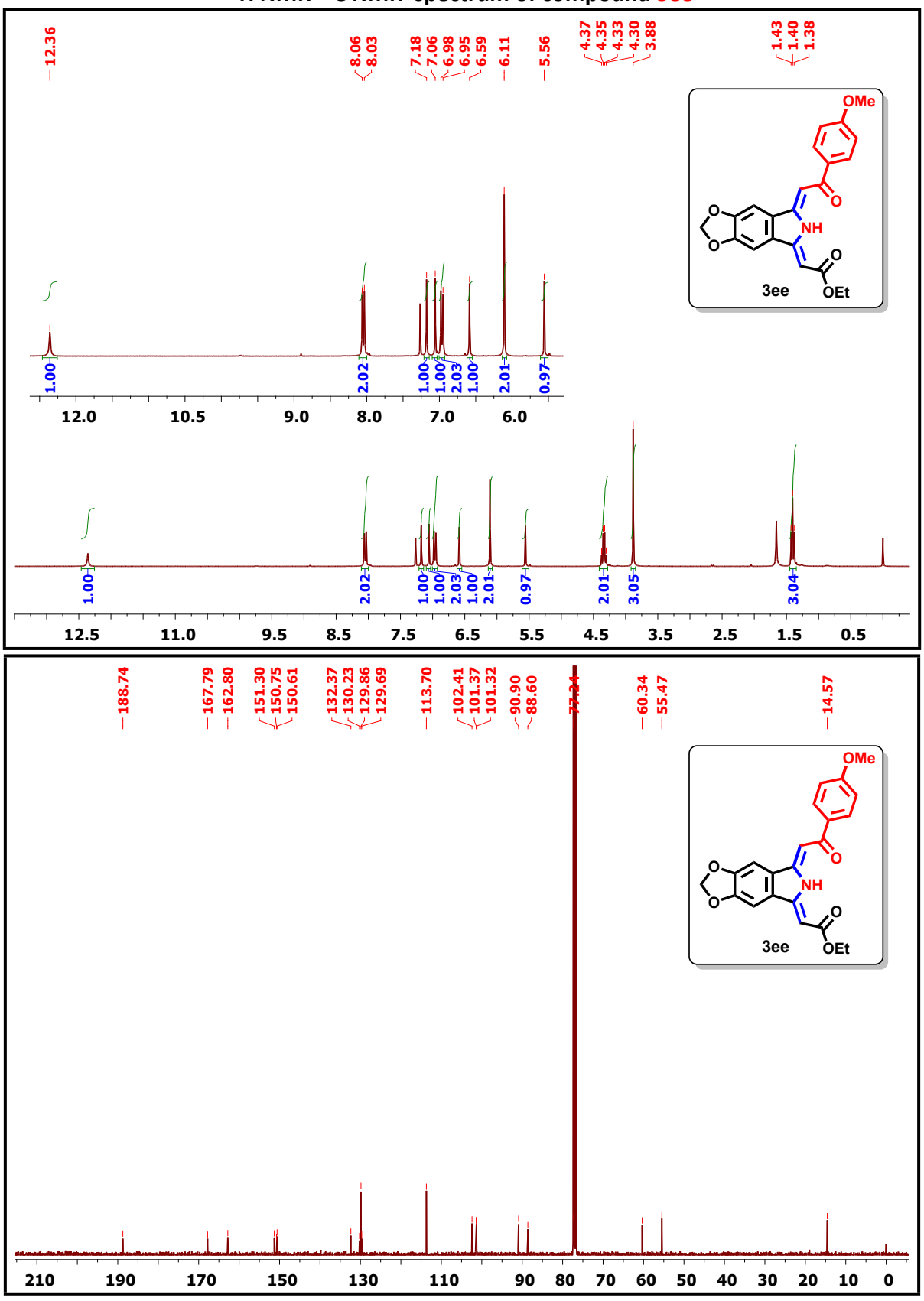
^{1}H NMR & ^{13}C NMR spectrum of compound 3eg



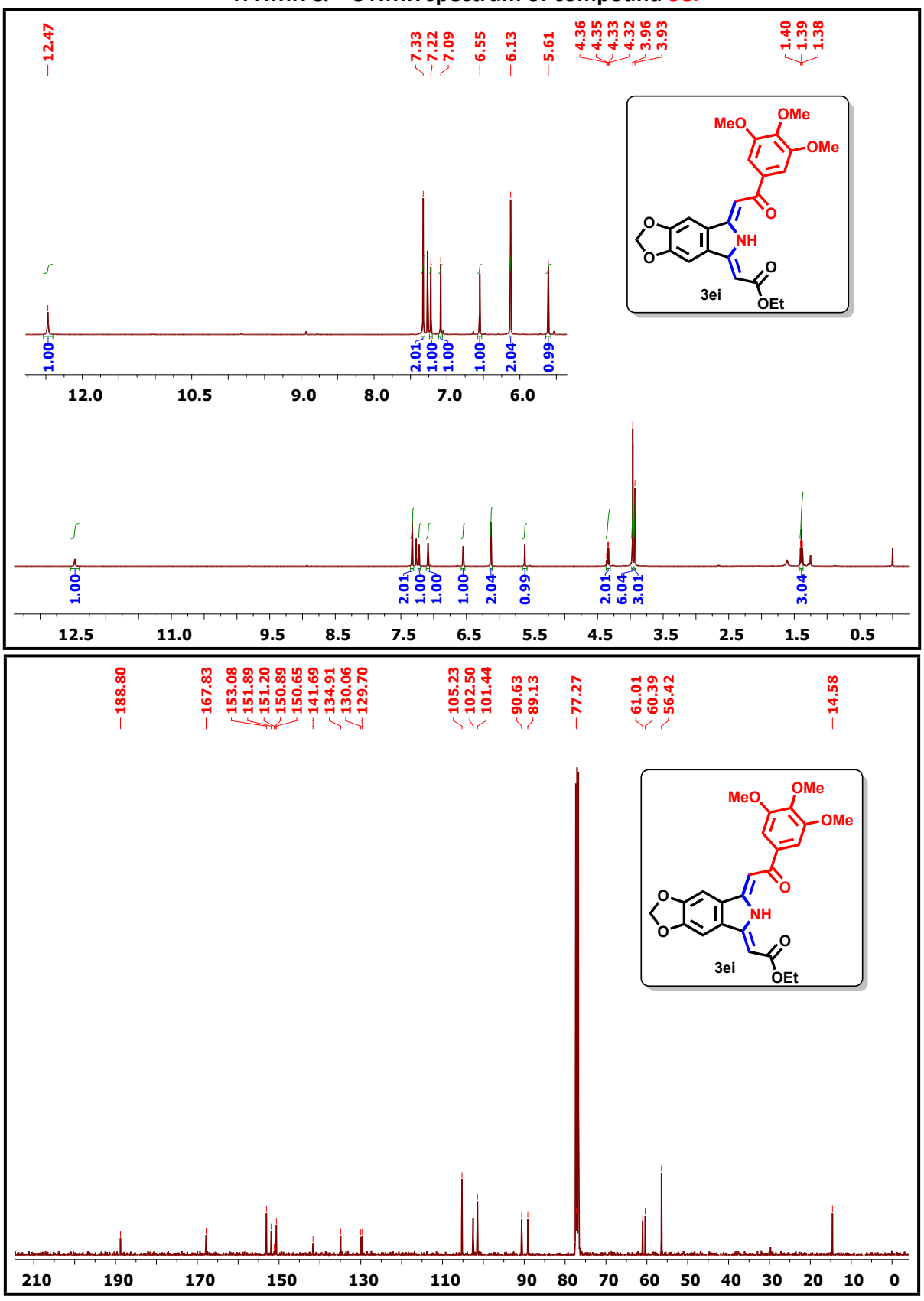
^{1}H NMR & ^{13}C NMR spectrum of compound 3eh



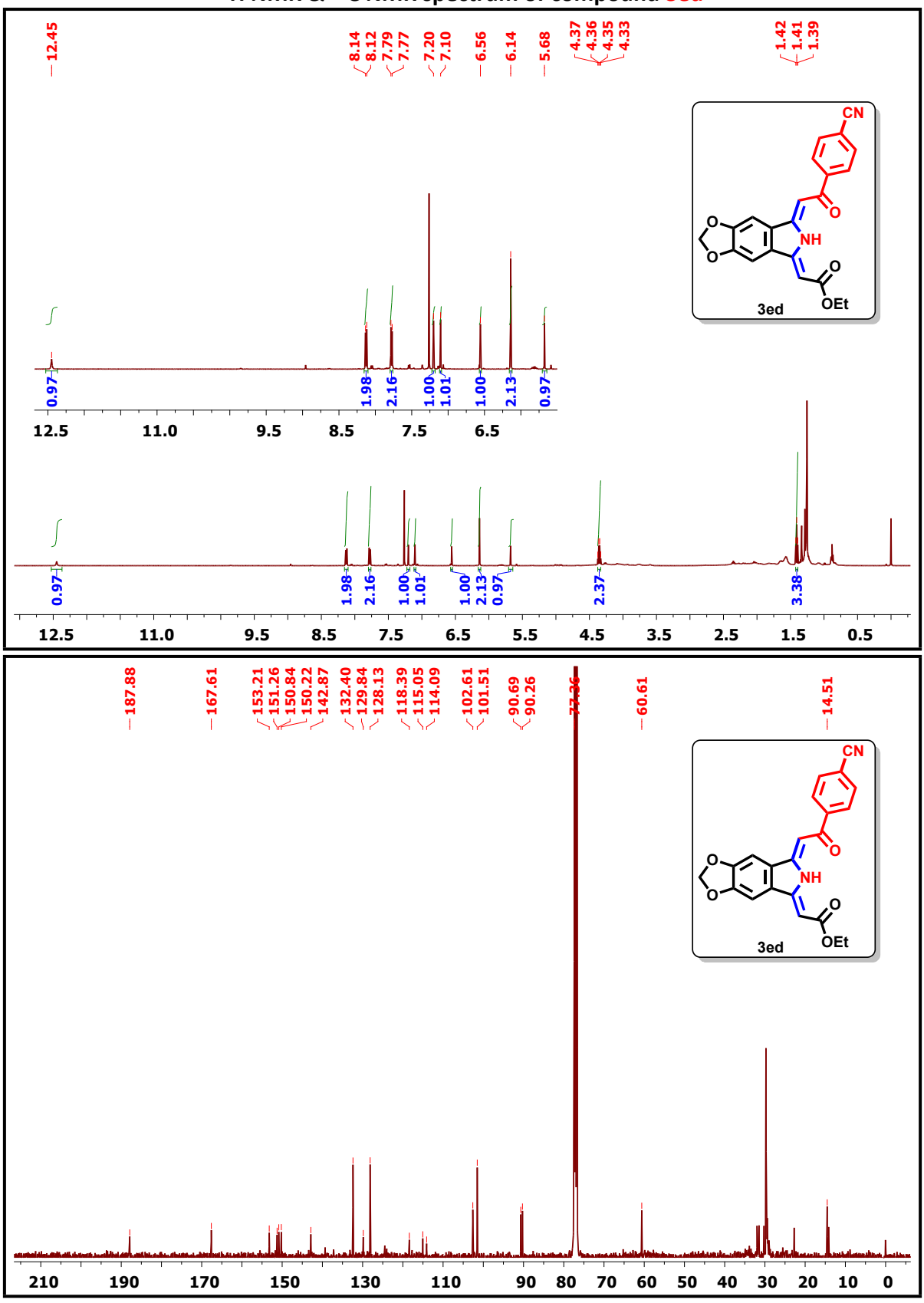
^{1}H NMR ^{13}C NMR spectrum of compound 3ee



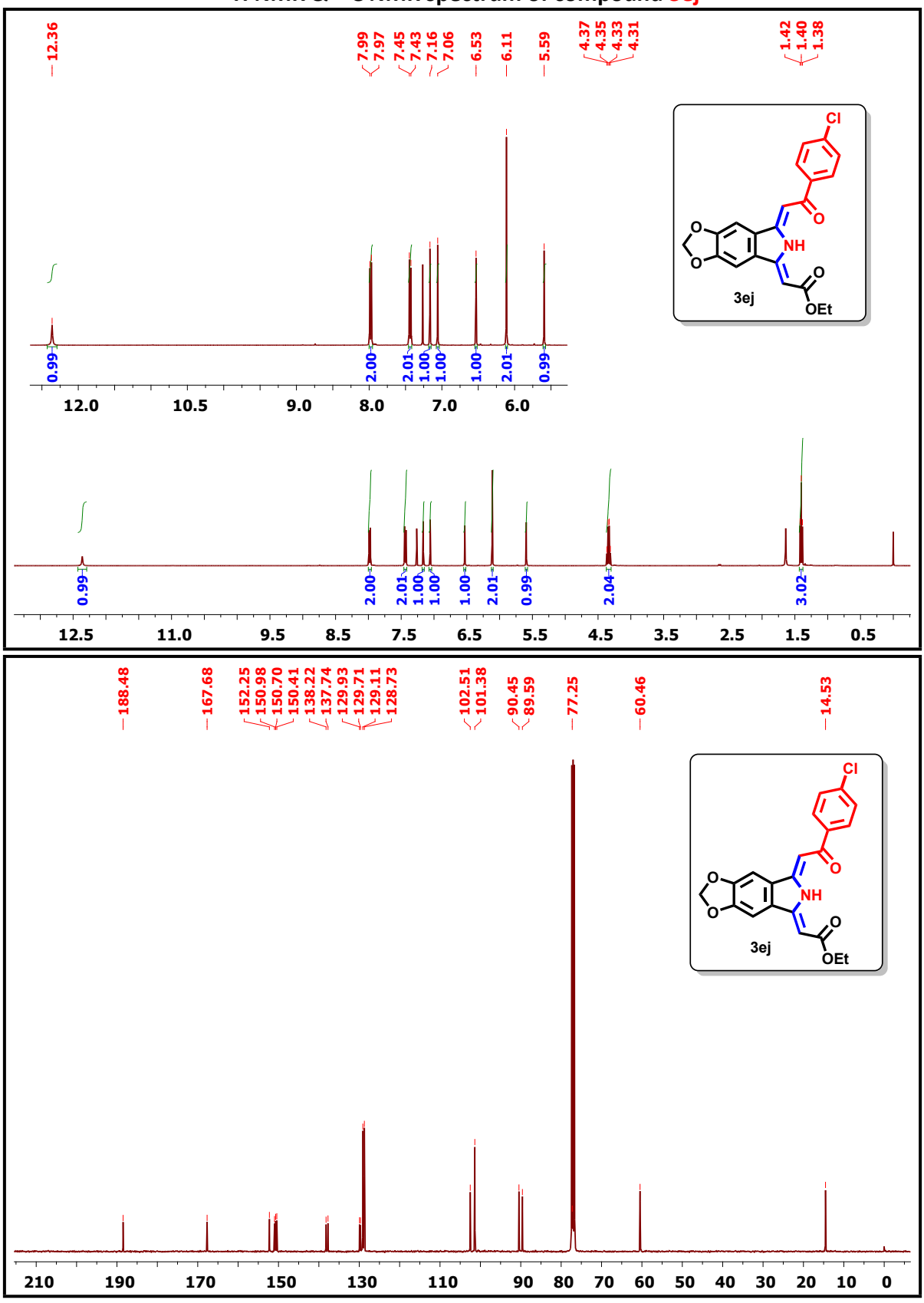
^{1}H NMR & ^{13}C NMR spectrum of compound 3ei



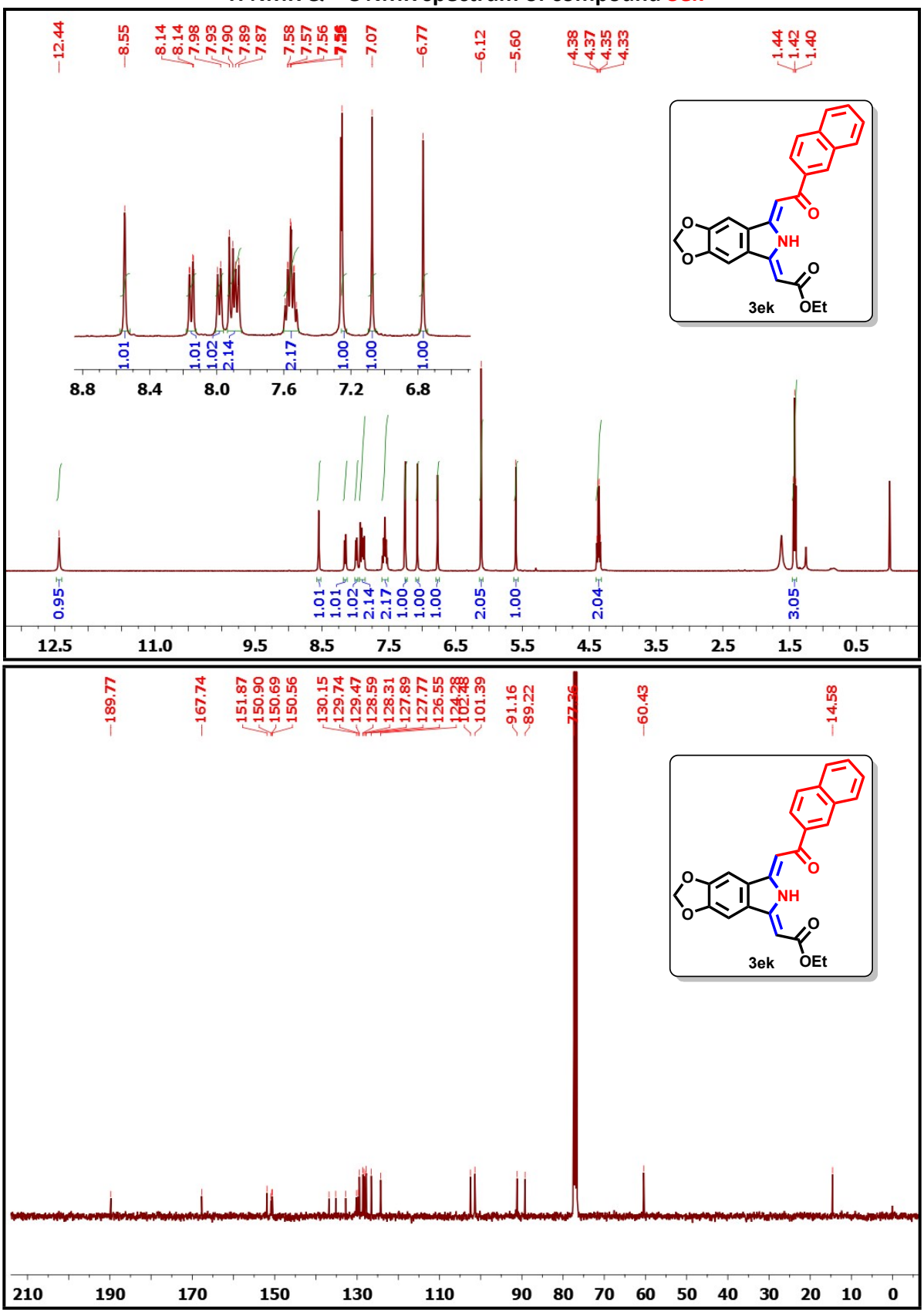
^{1}H NMR & ^{13}C NMR spectrum of compound 3ed



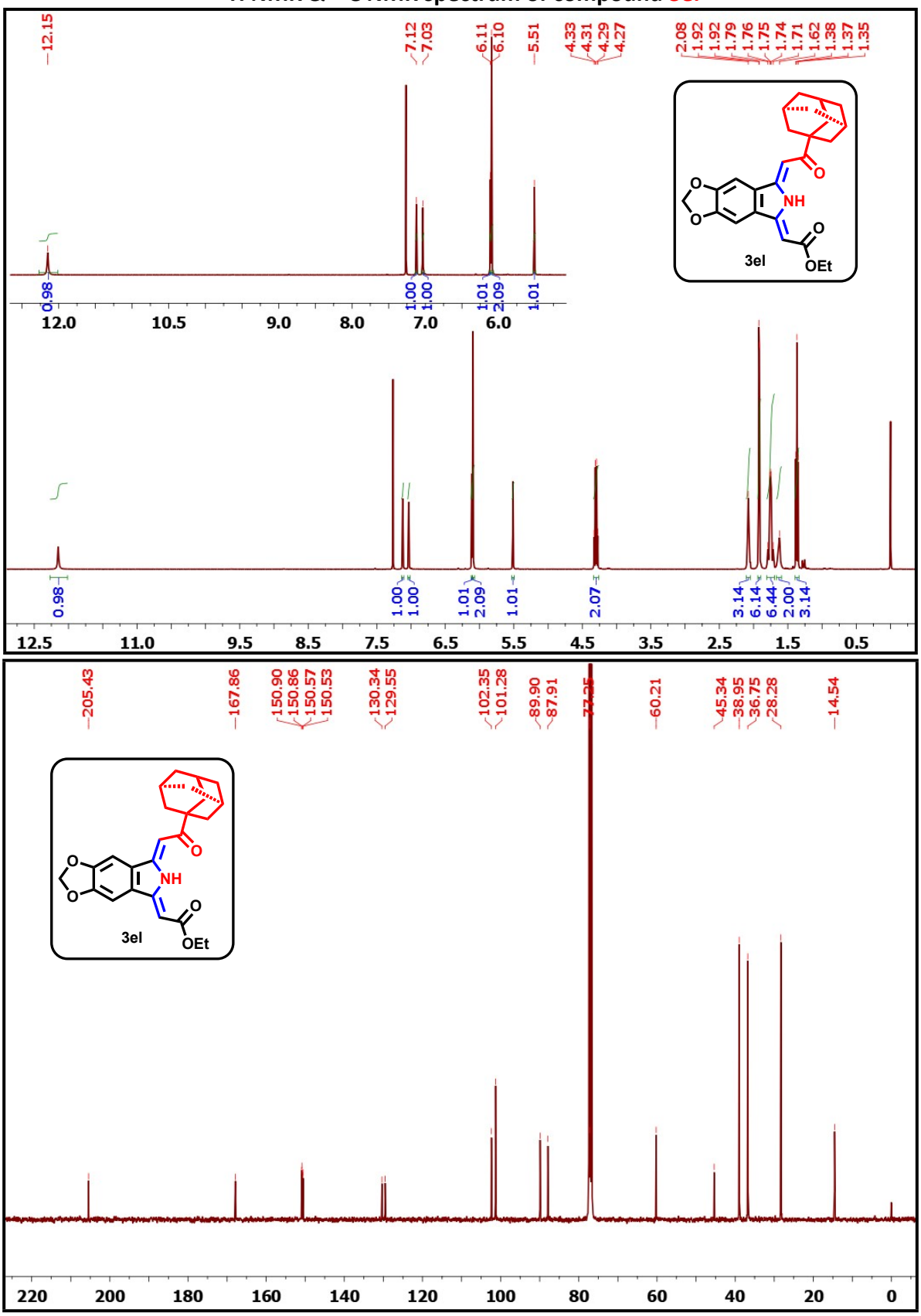
^{1}H NMR & ^{13}C NMR spectrum of compound 3ej



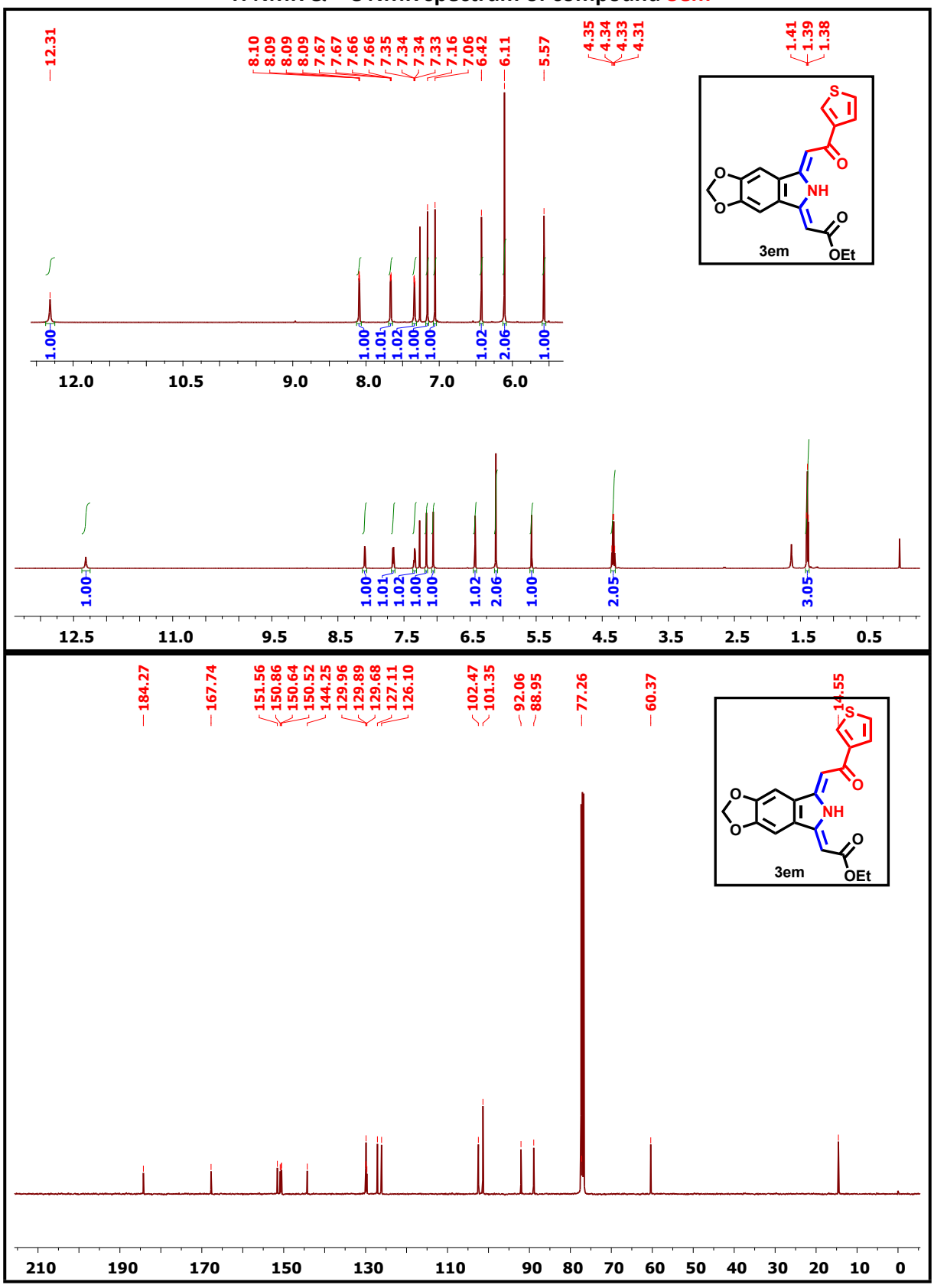
^{1}H NMR & ^{13}C NMR spectrum of compound 3ek



^{1}H NMR & ^{13}C NMR spectrum of compound 3el



^{1}H NMR & ^{13}C NMR spectrum of compound 3em



2. Crystal data of compound 3aa

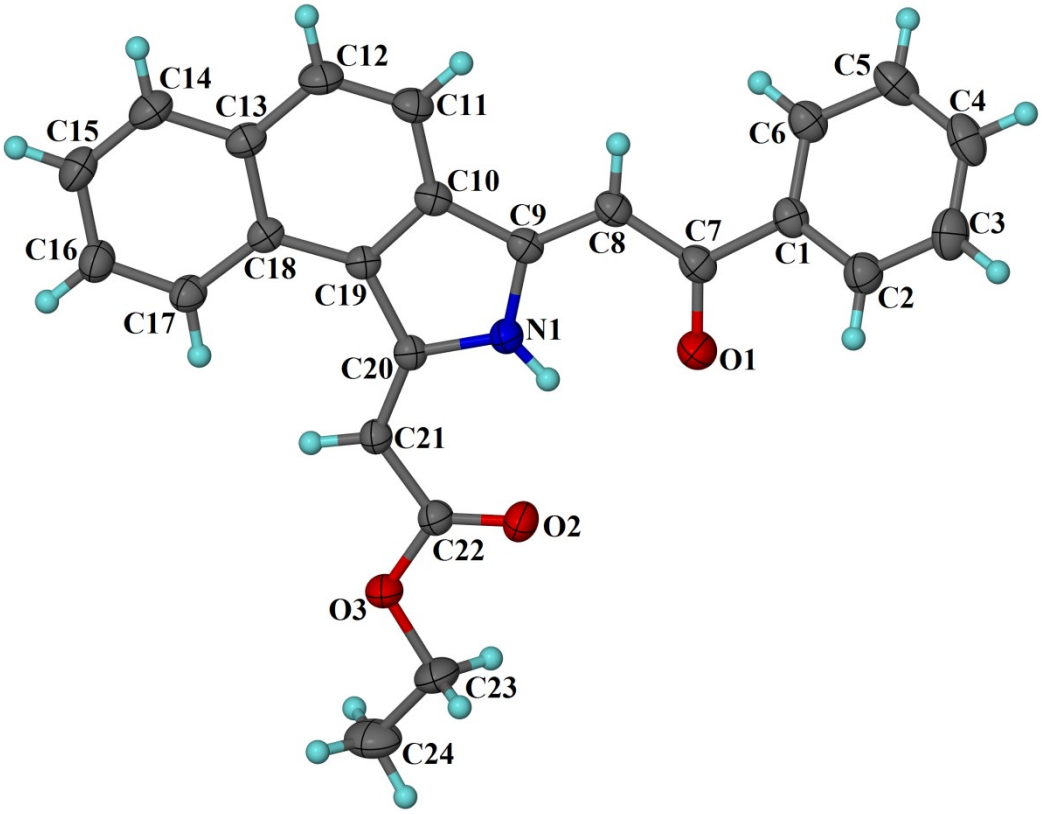


Figure caption: ORTEP diagram of **3aa** compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius.

Crystal data for compound 3aa: $C_{24}H_{19}NO_3$, M = 369.4, size 0. 40 x 0.36 x 0.29 mm^3, Orthorhombic, space group *Pbca* (No.61), a = 19.6210(13)Å, b = 7.3648(5) Å, c = 25.7732(17)Å, $\alpha = \beta = \gamma = 90°$, V = 3724.4(4) Å^3, Z = 8, D_c = 1.318 g/cm^3, F_{000} = 1552, Bruker D8 QUEST PHOTON-100, Mo-Kα radiation, λ = 0.71073 Å, T = 293(2) K, $2\theta_{max}$ = 55.0º, 27104 reflections collected, 4237 unique (R_{int} = 0.0700), Final *GooF* = 1.037, *R1* = 0.0521, *wR2* =0.1169 , *R* indices based on 2777 reflections with I > 2σ(I) (refinement on F^2), 258 parameters, 0 restraints, μ= 0.087 mm^{-1}, largest difference hole and peak = -0.194 and 0.199 e.Å^{-3}. CCDC

2047320 deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Data collection and Structure solution details: Single crystal X-ray data for **3aa** compound were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An Iμs microfocus Mo source (λ=0.71073Å) supplied the multi-mirror monochromated incident beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 8794 reflections. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.[2-4] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. The N bound H atoms were located from the difference Fourier map. CCDC 2047320 deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

6. References:

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3. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.

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