Electronic Supplementary Information(ESI)

"An efficient one pot regioselective synthesis of 3,3'-spiro-phosphonyl pyrazole-oxindole framework *via* base mediated [1,3]-dipolar cycloaddition reaction of Bestmann-Ohira reagent with methyleneindolinones"

Anil M. Shelke and Gurunath Suryavanshi*

Chemical Engineering & Process Development Division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, Maharashtra, India- 411008.

*Corresponding author: Tel.: +91 20 25902396; Fax: +91 20 25902676; e-mail: gm.suryavanshi@ncl.res.in

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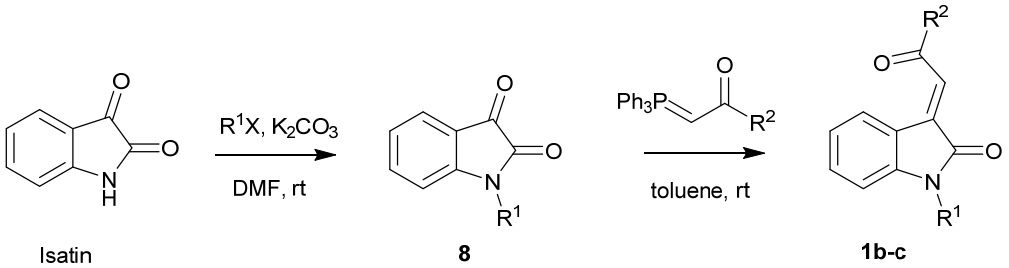
1. General Information

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60–80 °C was used. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded on 200, 400, 500 MHz NMR spectrometers. ^{31}P NMR was recorded on 202.4 MHz NMR spectrometer. HRMS data for new compounds were recorded using Orbitrap mass analyzer associated with Accela 1250 pump. Column chromatography was carried out by using silica gel of the selected particle size of 100-200 mesh or 230-400 mesh. Unless otherwise specified, all reactions were carried out under air atmosphere in oven-dried round-bottom flasks. Dimethyl-2-oxopropylphosphonate and Diethyl-2-oxopropylphosphonate were purchased from commercial sources and used for the synthesis of the Bestmann-Ohira reagent **2**.[26, 27] the reactions were monitored by TLC visualized by UV (254 nm) and/or with iodine. Coupling constants are given in hertz (Hz) and the classical abbreviations are used to describe the signal multiplicities. All commercially available reagents were used as received.

2. Experimental Section:

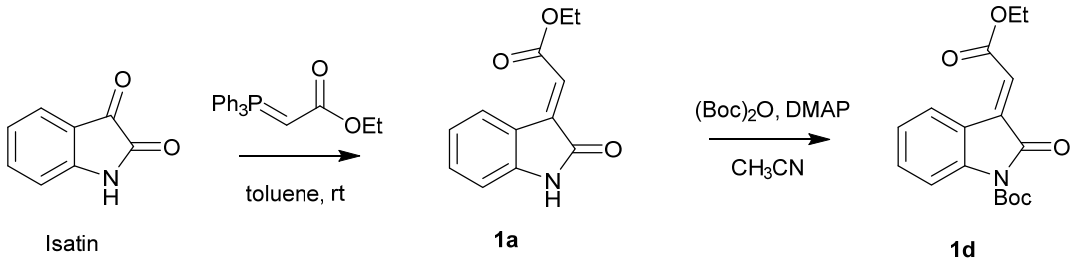
2.1. General procedure for preparation of the methyleneindolinone substrates 1b and 1c[2]



To a stirred solution of isatin (10.0 g, 68 mmol) and K_2CO_3 (18.8 g, 136 mmol) in 50 mL DMF at room temperature were added R^1 X (R^1 X = BnBr, CH_3I) (136 mmol) drop wise and stirred the reaction mixture for 12 hours and monitored by TLC. After the completion of the reaction (12 h), dichloromethane and water was added to the reaction mixture and organic

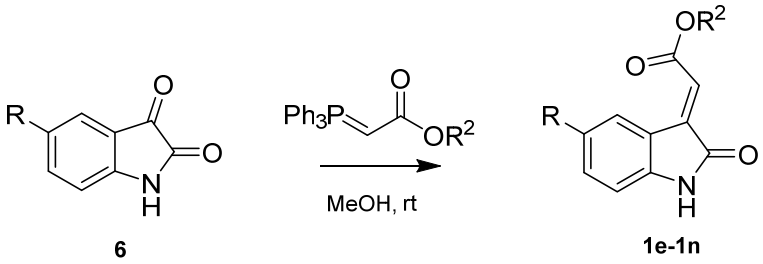
layer was separated. Aqueous layer was further extracted with dichloromethane (2 x 50 mL). The combined organic layers were then washed with saturated brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give viscous oil of crude compound **8**, which was further purified by column chromatography over silica gel using pet ether/EtOAc as eluent (10:1) to give pure compound **8** (85%) as a red solid. Then 1.0 g of compound **8** was mixed with the phosphonium ylide (1.1 equiv.) in toluene (25 mL) and stirred at room temperature for 8-10 hours. The mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (pet ether/EtOAc = 10/1) to give **1b-1c** as orange solid (1.40 g, 75%).

2.2. General procedure for preparation of the methyleneindolinone substrates 1a and 1d[1,3]



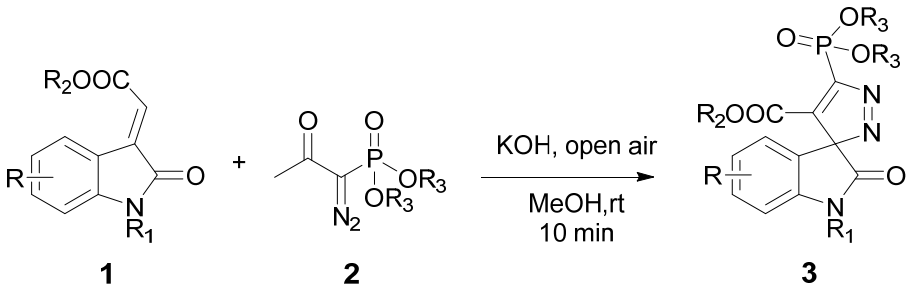
A solution of isatin (1.47 g, 10 mmol) and phosphonium ylide (3.22 g, 11 mmol) in 30 mL toluene was stirred at room temperature for 8 hours. The solvent was evaporated under vaccum and the crude product was purified by using silica gel column chromatography (pet ether/EtOAc = 10/1) to give **1a** (1.24 g, 99%) as a orange solid. To a solution of **1a** (217 mg, 1.0 mmol) and DMAP (11.1 mg, 0.10 mmol) in CH_3CN was added $(Boc)_2O$ (262.2 mg, 1.2 mmol) drop wise for 30 minutes. Then the solution was stirred for 12 hours. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (pet ether/EtOAc = 10/1) to give **1d** (300 mg, 95%) as a red solid.

2.3 General procedure for preparation of the methyleneindolinone substrates 1e-1n[4,5,6]



To a solution of the corresponding substituted isatin **6** (5 mmol, 1equiv.) in methanol (30 mL) was added phosphonium ylide (5 mmol, 1.1 equiv) and the mixture was stirred at room temprature. After the reaction was complete, the solvent was removed under reduced pressure and the residue was purified by flash chromatography directly to afford the purified product **1e-1n** (Petroleum Ether/ EtOAc = 4:1).

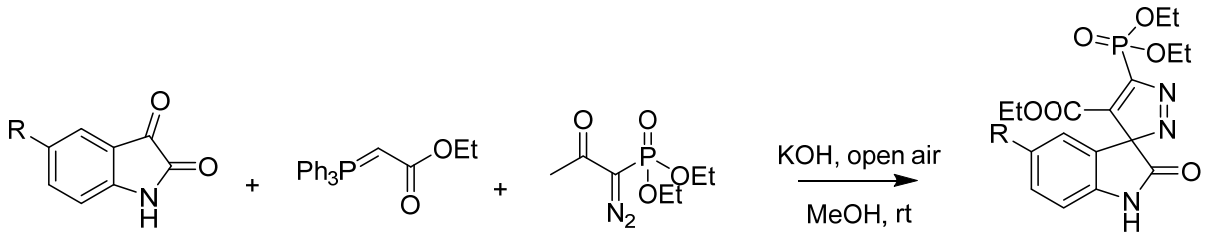
2.4. General experimental procedure for 1,3-dipolar cycloaddition reaction of Bestmann-Ohira reagent 1 with methyleneindolinones 2



To an oven-dried round bottom flask was added methyleneindolinones **1** (0.1 mmol, 1.0 equiv.) dissolved in 3 mL of MeOH. Subsequently, a solution of Bestmann-Ohira reagent **2** (0.2 mmol, 2.0 equiv.) in 2 mL of MeOH was added to the reaction mixture with constant stirring. After the addition of potassium hydroxide (0.2 mmol, 2.0 equiv.), the reaction mixture was stirred at 25 °C for 10 min. The solvent was evaporated and the crude reaction

mixture was extracted using ethyl acetate. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was then purified using column chromatography (100–200 mesh silica gel) using pet ether-ethyl acetate as the eluent.

2.5. General experimental procedure for sequential multicomponent reaction of isatin 6, phosphonium ylide 7, and BOR reagent 2a



6

6a, R=H
6b, R=Cl
6c, R=F
6d, R=Br

7

2a

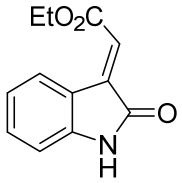
3

3a, 82%
3g, 79 %
3h, 75 %
3f, 77 %

To a solution of the corresponding substituted isatin **6** (5 mmol, 1equiv.) in methanol (30 mL) was added phosphonium ylide **7** (5 mmol, 1.1 equiv) and the mixture was stirred at room temperature for 12 h. Then a solution of Bestmann-Ohira reagent **2a** in 2 ml of MeOH was added to the reaction mixture. After the completion of reaction, as indicated by TLC, the solvent was evaporated and the crude reaction mixture was extracted using ethyl acetate. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified using column chromatography (100–200 mesh silica gel) using pet ether-ethyl acetate as the eluent.

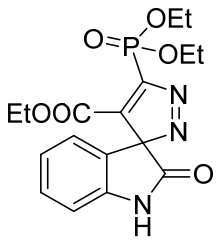
Ethyl (*E*)-2-(2-oxoindolin-3-ylidene) acetate (1a)[1]

Yield: 99%; Orange solid; mp: 183-185 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ:1.37 (t, *J* = 7.2 Hz, 3H), 4.31 (q, *J* = 7.1 Hz, 2H), 6.83 (dd, *J* = 7.1 Hz, 2H), 7.02 (t, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 8.26 (br s, 1H), 8.55 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.3, 61.1, 109.9,



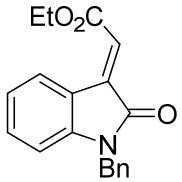
120.6, 122.7, 122.7, 129.3, 132.5, 138.2, 143.3, 165.4, 168.9; HRMS (ESI) calcd for $C_{12}H_{12}NO_3$ $[M+H]^+$ 218.0817; found 218.0812.

Ethyl 5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3a)



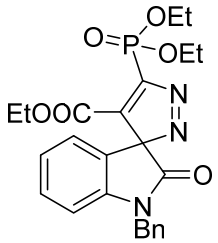
Yield: 84%; White solid; mp: 120-122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.36-1.39 (m, 6H), 1.46 (t, J = 7.6 Hz, 3H), 4.28- 4.34 (m, 4H), 4.45 (q, J = 7.6 Hz, 1H), 7.19-7.21 (m, 1H), 7.46 (m, 2H), 8.76-8.77 (m, 1H), 11.4 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.6, 16.9 (d, J_{C-P} = 6.4 Hz), 17.0 (d, J_{C-P} = 6.4 Hz), 62.6, 64.3 (d, J_{C-P} = 5.9 Hz), 64.4 (d, J_{C-P} = 5.9 Hz), 112.3, 117.1, 124.5, 127.2, 132.5, 135.5, 145.1, 150.4, 163.3; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.59; HRMS (ESI) calcd for $C_{17}H_{20}N_3O_6NaP$ $[M+Na]^+$ 416.0982; found 416.0979.

Ethyl (*E*)-2-(1-benzyl-2-oxoindolin-3-ylidene)acetate (1b)[2]



Yield: 75%; Orange solid; mp: 98-100 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.37 (t, J = 7.6 Hz, 3H), 4.33 (q, J = 7.6 Hz, 2H), 4.93 (s, 2H), 6.67 (d, J = 7.9 Hz, 1H), 7.00 (s, 1H), 7.22-7.32 (m, 7H), 8.56 (ddd, J = 7.8, 0.6 & 0.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.3, 43.9, 61.1, 109.0, 120.1, 122.8, 127.2, 127.7, 128.8, 129.0, 132.3, 135.5, 137.8, 145.2, 165.5, 167.6; HRMS (ESI) calcd for $C_{19}H_{17}NNaO_3$ $[M+Na]^+$ 330.1106; found 330.1102.

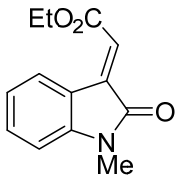
Ethyl 1-benzyl-5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3b)



Yield: 82%; White solid; mp: 168-170 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.41-1.51 (m, 9H), 4.29-4.37 (m, 4H), 4.48 (q, J = 7.5 Hz, 2H), 5.59 (s, 2H), 7.28-7.36 (m, 2H), 7.48-7.53 (m, 1H), 9.01- 9.03 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.3, 15.6 (d, J_{C-P} = 6.6 Hz), 15.8 (d, J_{C-P} = 6.6 Hz),, 47.5, 61.5, 63.0 (d, J_{C-P} = 6.0 Hz), 63.1(d, J_{C-P} = 6.0 Hz), 112.1, 114.9, 123.5, 125.9, 127.1 (d, J_{C-P} = 12.5 Hz), 127.3 (d, J_{C-P} = 12.5 Hz), 128.4,

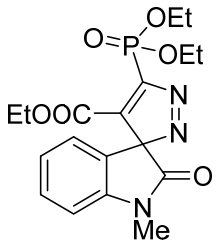
131.5, 134.1, 135.0, 144.5, 162.2; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.12; HRMS (ESI) calcd for $C_{24}H_{26}N_3O_6NaP$ $[M+Na]^+$ 506.1451; found 506.1451.

Ethyl (*E*)-2-(1-methyl-2-oxoindolin-3-ylidene) acetate (1c)[2]



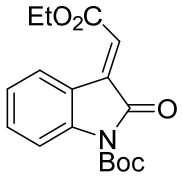
Yield: 75%; Orange solid; mp: 75-78 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.34 (t, *J* = 7.2 Hz, 3H), 3.23 (s, 3H), 4.27 (q, *J* = 7.2 Hz, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.89 (s, 1H), 7.01-7.09 (m, 1H), 7.31-7.40 (m, 1H), 8.54 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2, 26.2, 61.0, 107.9, 119.9, 122.4, 122.8, 128.9, 132.3, 137.9, 145.9, 165.5; HRMS (ESI) calcd for $C_{13}H_{14}NO_3$ $[M+H]^+$ 232.0974; found 232.0976.

Ethyl 5'-(diethoxyphosphoryl)-1-methyl-2-oxospiro [indoline-3,3'-pyrazole]-4'-carboxylate (3c)



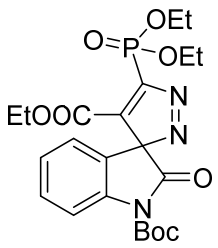
Yield: 78%; White solid; mp: 210-212 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.40-1.53 (m, 9H), 3.84 (s, 3H), 3.92- 4.40 (m, 6H), 7.59-7.67 (m, 1H), 8.94- 8.98 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.8, 16.1(d, J_{C-P} = 6.4 Hz), 16.3 (d, J_{C-P} = 6.4 Hz), 31.4, 61.8, 63.3 (d, J_{C-P} = 6.1 Hz), 63.4 (d, J_{C-P} = 6.1 Hz), 112.3, 113.7, 114.4, 123.8, 127.3, 132.0, 136.1, 140.3, 144.4, 150.1, 162.6; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.17; HRMS (ESI) calcd for $C_{18}H_{22}N_3O_6NaP$ $[M+Na]^+$ 430.1138; found 430.1137.

Tert-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (1d)[3]



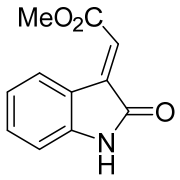
Yield: 95%; Red solid; mp: 71-73°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.35 (t, *J* = 7.3 Hz, 3H), 1.65 (s, 9H), 4.27 (q, *J* = 7.2 Hz, 2H), 6.8 (s, 1H), 7.14-7.26 (m, 1H), 7.31-7.47 (m, 1H), 7.89-7.93 (m, 1H), 8.67-8.71(m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2, 28.1, 61.2, 84.5, 114.9, 120.1, 123.0, 124.5, 128.4, 132.6, 136.5, 141.9, 148.8, 165.2, 165.5; HRMS (ESI) calcd for $C_{17}H_{19}NO_5Na$ $[M+Na]^+$ 340.1161; found 340.1162.

1-(tert-butyl) 4'-ethyl 5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-1,4'-dicarboxylate (3d)



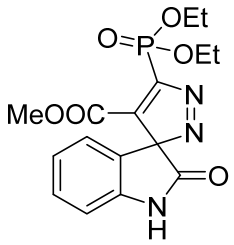
Yield: 80%; White solid; mp: 155-157 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.17 (t, *J* = 7.6 Hz, 3H), 1.32-1.41 (m, 6H), 1.46 (s, 9H), 4.18- 4.35 (m, 6H), 7.05-7.09 (m, 1H), 7.30-7.40 (m, 1H), 7.55-7.67 (m, 1H), 7.99-8.01 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.8, 16.32 (d, J_{C-P} = 6.6 Hz), 16.39 (d, J_{C-P} = 6.6 Hz), 28.3, 61.0, 63.7 (d, J_{C-P} = 6.0 Hz), 63.8 (d, J_{C-P} = 6.0 Hz), 80.4, 122.8, 128.3, 130.0, 130.9, 136.7, 153.2, 162.3; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 5.03; HRMS (ESI) calcd for $C_{22}H_{28}N_3O_8NaP$ $[M+Na]^+$ 516.1512; found 516.1515.

Methyl (*E*)-2-(2-oxoindolin-3-ylidene)acetate (1e)[4]



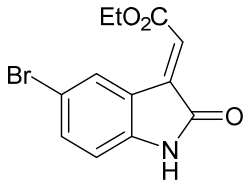
Yield: 95%; Orange crystals; mp: 177-179 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.8 (s, 3H), 6.84-6.88 (m, 2H), 7.00-7.09 (m, 1H), 7.28-7.36 (m, 1H), 8.53 (s, 1H), 8.57 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 52.1, 110.0, 122.0, 122.9, 129.2, 130.5, 132.6, 150.8, 165.9, 169.1; HRMS (ESI) calcd for $C_{11}H_{10}NO_3$ $[M+H]^+$ 204.0661; found 204.0663.

Methyl 5'-(diethoxyphosphoryl)-2-oxospiro [indoline-3,3'-pyrazole]-4'-carboxylate (3e)



Yield: 77%; Yellow orange powder; mp: 178-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.34-1.42 (m, 6H), 4.0 (s, 3H), 4.28-4.35 (m, 4H), 7.36-7.43 (m, 2H), 7.50-7.56 (m, 1H), 8.78-8.85 (m, 1H), 11.0 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.3 (d, J_{C-P} = 6.9 Hz), 16.4 (d, J_{C-P} = 6.9 Hz), 52.5, 63.82 (d, J_{C-P} = 6.4 Hz), 63.87 (d, J_{C-P} = 6.4 Hz), 117.7, 116.3, 124.2, 126.8, 132.1, 134.6, 144.5, 163.0; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.26; HRMS (ESI) calcd for $C_{16}H_{18}N_3O_6NaP$ $[M+Na]^+$ 402.0825; found 402.0846.

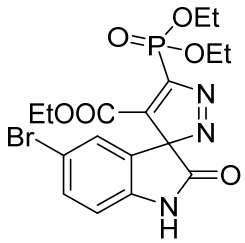
Ethyl (*E*)-2-(5-bromo-2-oxoindolin-3-ylidene) acetate (1f)[1]



Yield: 90%; Yellow orange solid; mp: 207-209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, *J* = 7.7 Hz, 3H), 4.27 (q, *J* = 7.7 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.79 (s, 1H), 7.32 (s, 1H), 7.36 (dd, *J* = 2, 8 Hz, 1H), 8.62 (d, *J* = 2 Hz, 1H),; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 61.7, 111.8, 115.3, 122.2,

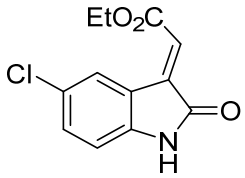
123.8, 131.9, 135.3, 138.0, 143.4, 165.4, 165.6; HRMS (ESI) calcd for $C_{12}H_{11}BrNO_3$ $[M+H]^+$ 295.9922; found 295.9920.

Ethyl 5-bromo-5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3f)



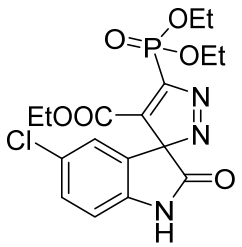
Yield: 81%; White solid; mp: 175-177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.35-1.50 (m, 9H), 4.29-4.33 (m, 4H), 4.46-4.50 (q, J = 7.2 Hz, 2H), 7.39-7.55 (m, 2H), 9.00-9.03 (m, 1H), 11.6 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 16.34 (d, J_{C-P} = 5.4 Hz), 16.39 (d, J_{C-P} = 5.4 Hz), 62.1, 63.80 (d, J_{C-P} = 6.1 Hz), 63.85 (d, J_{C-P} = 6.1 Hz), 113.1, 116.6, 118.2, 129.2, 131.9, 134.1 (d, J_{C-P} = 16.4 Hz), 134.8 (d, J_{C-P} = 16.4 Hz), 140.8, 143.9, 148.7, 162.2; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.52; HRMS (ESI) calcd for $C_{17}H_{20}N_3O_6BrP$ $[M+H]^+$ 472.0268; found 472.0265.

Ethyl (*E*)-2-(5-chloro-2-oxoindolin-3-ylidene)acetate (1g)[1]



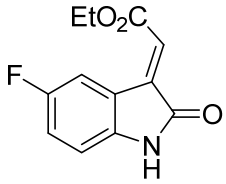
Yield: 80%; Orange solid; mp: 160-162 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.33 (t, J = 7.7 Hz, 3H), 4.27 (q, J = 7.7 Hz, 2H), 6.69 (d, J = 8.4 Hz, 1H), 6.79 (s, 1H), 7.32 (s, 1H), 7.36 (dd, J = 2, 8 Hz, 1H), 8.62 (d, J = 2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d^6) δ: 13.9, 61.2, 111.6, 120.9, 122.1, 125.7, 127.5, 132.3, 137.4, 143.7, 164.8, 167.3; HRMS (ESI) calcd for $C_{12}H_{10}ClNO_3Na$ $[M+Na]^+$ 274.0241; found 274.0238.

Ethyl 5-chloro-5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3g)



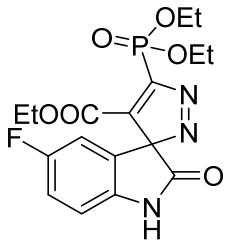
Yield: 80%; White solid; mp: 190-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.35-1.50 (m, 9H), 4.27-4.33 (m, 4H), 4.45-4.50 (q, J = 7.2 Hz, 2H), 7.37-7.47 (m, 2H), 8.86 (d, J = 2.0 Hz ,1H), 11.6 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 16.32 (d, J_{C-P} = 6.4 Hz), 16.38 (d, J_{C-P} = 6.4 Hz), 62.0, 63.83 (d, J_{C-P} = 5.7 Hz), 63.89 (d, J_{C-P} = 5.7 Hz), 112.7, 118.0, 126.2, 129.2, 132.0 (d, J_{C-P} = 22.6 Hz), 133.7 (d, J_{C-P} = 22.6 Hz), 140.9, 143.7, 146.5, 148.8, 162.2; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.45; HRMS (ESI) calcd for $C_{17}H_{20}N_3O_6ClP$ $[M+H]^+$ 428.0775; found 428.0773.

Ethyl (*E*)-2-(5-fluoro-2-oxoindolin-3-ylidene)acetate (1h)[1]



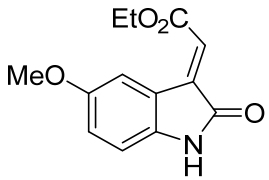
Yield: 78%; orange solid; mp: 182-184 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.35 (t, *J* = 7.0 Hz, 3H), 4.29 (q, *J* = 7.0 Hz, 2H), 6.73 (dd, *J* = 4.0, 8.4 Hz, 1H), 6.9 (s, 1H), 6.99-7.09 (dt, *J* = 2.5, 8.0 Hz, 1H), 7.79 (m, 1H), 8.35-8.41 (dd, *J* = 2.7, 9.0 Hz, 1H),; ^{13}C NMR (50 MHz, DMSO-d_6) δ: 13.9, 61.2, 111.0, 114.6, 115.1, 119.1, 120.2, 122.1, 138.0, 141.4, 164.9, 167.6; HRMS (ESI) calcd for $C_{12}H_{10}FNO_3Na$ $[M+Na]^+$ 258.0542; found 258.0547.

Ethyl 5'-(diethoxyphosphoryl)-5-fluoro-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3h)



Yield: 76%; White solid; mp: 194-196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.35-1.49 (m, 9H), 4.29-4.33 (m, 4H), 4.44- 4.50 (q, *J* = 7.0 Hz, 2H), 7.19-7.23 (m, 1H), 7.49-7.52 (m, 1H), 8.60-8.63 (m, 1H), 11.6 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 16.30 (d, J_{C-P} = 6.1 Hz), 16.37 (d, J_{C-P} = 6.1 Hz), 62.0, 63.7 (d, J_{C-P} = 6.5 Hz), 63.8 (d, J_{C-P} = 6.5 Hz), 112.6, 118.3, 120.0, 131.6, 141.4, 143.9, 146.2, 148.8, 157.2, 159.6, 162.3; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 5.50; HRMS (ESI) calcd for $C_{17}H_{20}N_3O_6FP$ $[M+H]^+$ 412.1068; found 412.1065.

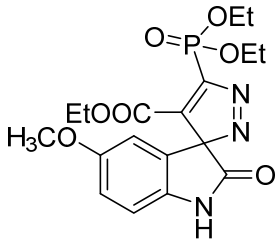
Ethyl (*E*)-2-(5-methoxy-2-oxoindolin-3-ylidene)acetate (1i)[2]



Yield: 82%; Brown solid; mp: 128-130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.37 (t, *J* = 7.0 Hz, 3H), 3.83 (s, 3H), 4.30 (q, *J* = 7.0 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.85-6.88 (m, 2H), 8.21-8.26 (m, 2H),; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.3, 55.8, 61.1, 110.4, 114.4, 119.1, 121.1, 122.8, 137.1, 138.8, 155.8, 165.4, 169.1; HRMS (ESI) calcd for $C_{13}H_{13}NO_4Na$ $[M+Na]^+$ 270.0742; found 270.0746.

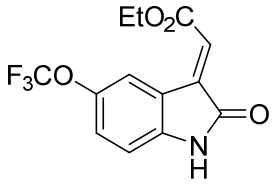
Ethyl 5'-(diethoxyphosphoryl)-5-methoxy-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3i)

Yield: 85%; White solid; mp: 212-214 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.37-1.49 (m, 9H), 3.84 (s, 3H), 4.29- 4.48 (m, 6H), 7.03 (d, *J* = 8.0 Hz,



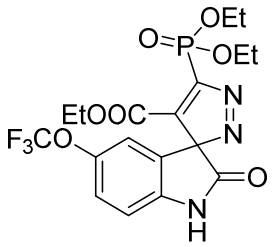
1H), 7.35 (d, J = 8.0 Hz, 1H), 8.48 (s, 1H),11.1 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.0, 14.3, 16.4, 55.6, 61.9, 63.7 (d, J_{C-P} = 6.4 Hz), 63.8 (d, J_{C-P} = 6.4 Hz), 108.7, 112.4, 114.0, 114.2, 117.6, 121.1, 128.7, 142.3, 144.3, 156.0, 162.6; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.52; HRMS (ESI) calcd for $C_{18}H_{22}N_3O_7PNa$ $[M+Na]^+$ 446.1088; found 446.1106.

Ethyl (*E*)-2-(2-oxo-5-(trifluoromethoxy)indolin-3-ylidene)acetate (1j)[5]



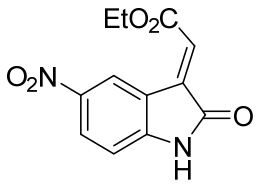
Yield: 78%; Orange solid; mp: 170-172 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.31 (t, J = 7.2 Hz, 3H), 4.26 (q, J = 7.2 Hz, 2H), 6.77-6.80 (m, 2H), 7.10 (d, J = 7.2 Hz, 2H), 8.41(s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 13.9, 61.3, 110.4, 119.4, 121.0, 122.5, 123.8, 125.4, 137.8, 142.7, 144.3, 165.1, 169.1; HRMS (ESI) calcd for $C_{13}H_{10}F_3NO_4Na$ $[M+Na]^+$ 324.0460; found 324.0462.

Ethyl 5'-(diethoxyphosphoryl)-2-oxo-5-(trifluoromethoxy)spiro[indoline-3,3'-pyrazole]-4'-carboxylate (3j)



Yield: 82%; White solid; mp: 164-166 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.37-1.49 (m, 9H), 3.84 (s, 3H), 4.29-4.48 (m, 6H), 7.03 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 8.48 (s, 1H),11.1 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 16.4 (d, J_{C-P} = 6.6 Hz), 16.5 (d, J_{C-P} = 6.6 Hz), 62.1 (d, J_{C-P} = 5.8 Hz), 62.2 (d, J_{C-P} = 5.8 Hz), 64.3, 112.6, 117.8, 118.4, 118.9, 119.3 (d, J_{C-P} = 25.4 Hz), 119.5 (d, J_{C-P} = 25.4 Hz), 121.8, 125.3, 144.9, 153.3, 162.0; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.54; HRMS (ESI) calcd for $C_{18}H_{19}N_3O_7F_3PNa$ $[M+Na]^+$ 500.0805; found 500.0824.

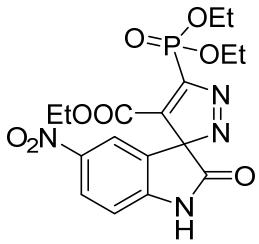
Ethyl (*E*)-2-(5-nitro-2-oxoindolin-3-ylidene)acetate (1k)[5]



Yield: 80%; Yellow solid; mp: 177-179 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.43 (t, J = 7.3 Hz, 3H), 4.43 (q, J = 7.3 Hz, 2H), 6.96 (s, 1H), 7.01 (s, 1H), 8.28- 8.40 (m, 2H), 9.51- 9.52 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.1, 62.5, 110.9, 112.4, 125.0, 125.2, 129.4, 137.8, 146.7, 162.3, 166.2;

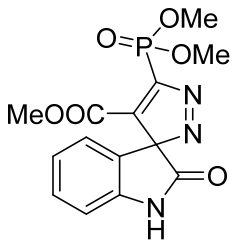
HRMS (ESI) calcd for $C_{12}H_{10}N_2O_5Na$ $[M+Na]^+$ 285.0487; found 285.0490.

Ethyl 5'-(diethoxyphosphoryl)-5-nitro-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3k)



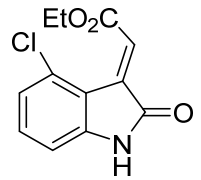
Yield: 79%; Brown solid; mp: 185-187 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.32-1.44 (m, 9H), 3.87 (q, *J* = 7.2 Hz, 2H), 4.13 (m, 4H), 7.68 (s, 1H), 8.02 (d, *J* = 2.0 Hz, 1H), 8.16 (dd, *J* = 2.0, 7.2 Hz, 1H), 9.91 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.7, 16.3 (d, J_{C-P} = 6.5 Hz), 16.4 (d, J_{C-P} = 6.5 Hz), 61.9, 63.4 (d, J_{C-P} = 5.7 Hz), 63.6 (d, J_{C-P} = 5.7 Hz), 111.0, 121.1, 137.1, 139.5, 143.2, 148.1, 165.9, 177.6; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.27; HRMS (ESI) calcd for $C_{17}H_{19}N_4O_8PNa$ $[M+Na]^+$ 461.0838; found 461.0842.

Methyl 5'-(dimethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3l)



Yield: 83%; White solid; mp: 202-204 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.93 (s, 3H), 3.99 (s, 3H), 4.04 (s, 3H), 7.30-7.37 (m, 1H), 7.41-7.60 (m, 2H), 8.85 (d, *J* = 7.2 Hz, 1H), 11.1 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 52.5, 54.13 (d, J_{C-P} = 5.0 Hz), 54.17 (d, J_{C-P} = 5.0 Hz), 111.8, 114.2, 116.3, 124.2, 127.0, 132.1, 134.8, 142.4, 144.5, 146.5, 162.8; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.01; HRMS (ESI) calcd for $C_{14}H_{14}N_3O_6PNa$ $[M+Na]^+$ 374.0512; found 374.0893.

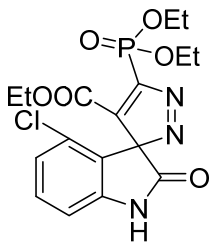
Ethyl (E)-2-(4-chloro-2-oxoindolin-3-ylidene)acetate (1m)



Yield: 78%; Orange solid; mp: 174-176 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.29 (t, *J* = 7.0 Hz, 3H), 4.25 (q, *J* = 7.0 Hz, 2H), 6.59 (s, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 7.36 (dd, *J* = 2.0, 8.0 Hz, 1H), 8.34 (d, *J* = 2.0 Hz, 1H), 10.89 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 13.9, 61.2, 111.6, 120.9, 122.1, 125.7, 127.5, 132.3, 137.4, 143.7, 164.8, 167.3; HRMS (ESI) calcd for $C_{12}H_{10}ClNO_3Na$ $[M+Na]^+$ 274.0241; found 274.0240.

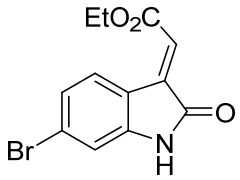
Ethyl 4-chloro-5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3m)

Yield: 79%; White solid; mp: 180-182 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ:



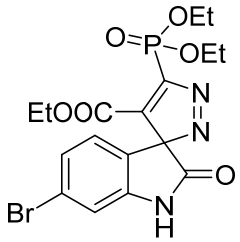
1.34-1.52 (m, 9H), 4.24- 4.55 (m, 6H), 7.39-7.63 (m, 3H), 11.4 (br s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.9, 16.2 (d, J_{C-P} = 6.2 Hz), 16.3 (d, J_{C-P} = 6.2 Hz), 62.0, 63.7 (d, J_{C-P} = 5.2 Hz), 63.8 (d, J_{C-P} = 5.2 Hz), 112.5, 112.6, 112.8, 114.4 (d, J_{C-P} = 28.2 Hz) , 114.6 (d, J_{C-P} = 28.2 Hz), 118.2, 119.7, 120.0, 131.6, 141.3, 143.8, 146.5, 148.7, 157.1, 159.5, 162.2; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 5.50; HRMS (ESI) calcd for $C_{17}H_{20}N_3O_6ClP$ $[M+H]^+$ 428.0775; found 428.0774.

Ethyl (E)-2-(6-bromo-2-oxoindolin-3-ylidene)acetate (1n)[6]



Yield: 90%; Orange solid; mp: 204-206 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.35 (t, J = 7.2 Hz, 3H), 4.29 (q, J = 7.2 Hz, 2H), 6.73- 9.79 (m, 1H), 6.90 (s, 1H), 7.00- 7.09 (m, 1H), 7.79 (br s, 1H), 8.35- 8.41 (m, 1H),; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.7, 61.0, 110.2, 120.8, 122.2, 123.6, 125.1, 142.4, 144.0, 164.8, 168.8; HRMS (ESI) calcd for $C_{12}H_{11}BrNO_3$ $[M+H]^+$ 295.9922; found 295.9918.

Ethyl 6-bromo-5'-(diethoxyphosphoryl)-2-oxospiro[indoline-3,3'-pyrazole]-4'-carboxylate (3n)



Yield: 84%; White solid; mp: 168-170 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.36-1.54 (m, 9H), 4.25-4.57 (m, 6H), 7.41-7.74 (m, 2H), 8.99 (d, J = 8.0 Hz, 1H), 10.5 (br s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.6, 15.9 (d, J_{C-P} = 6.3 Hz), 16.0 (d, J_{C-P} = 6.3 Hz), 61.7, 63.4 (d, J_{C-P} = 5.3 Hz), 63.5 (d, J_{C-P} = 5.3 Hz), 112.2, 112.3, 112.5, 114.1 (d, J_{C-P} = 22.5 Hz), 114.3 (d, J_{C-P} = 22.5 Hz), 117.9, 119.5, 119.7, 131.3, 141.0, 143.6, 146.2, 148.4, 156.8, 159.3, 161.9; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: 6.26; HRMS (ESI) calcd for $C_{17}H_{20}N_3O_6BrP$ $[M+H]^+$ 472.0268; found 472.0266.

3 References for general procedure and experimental data of methyleneindolinone substrates 1a-1n:

1. S. Malhotra, S. Balwani, A. Dhawan, B. K. Singh, S. Kumar, R. Thimmulappa, S. Biswal, C. E. Olsen, E. V. D. Eycken, A. K. Prasad, B. Ghosh and V. S. Parmar, *Med. Chem. Commun*., 2011, **2**, 743.
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3. S. H. Cao, X. C. Zhang, Y. Wei and M. Shi, *Eur. J. Org. Chem*. 2011, **14**, 2668.
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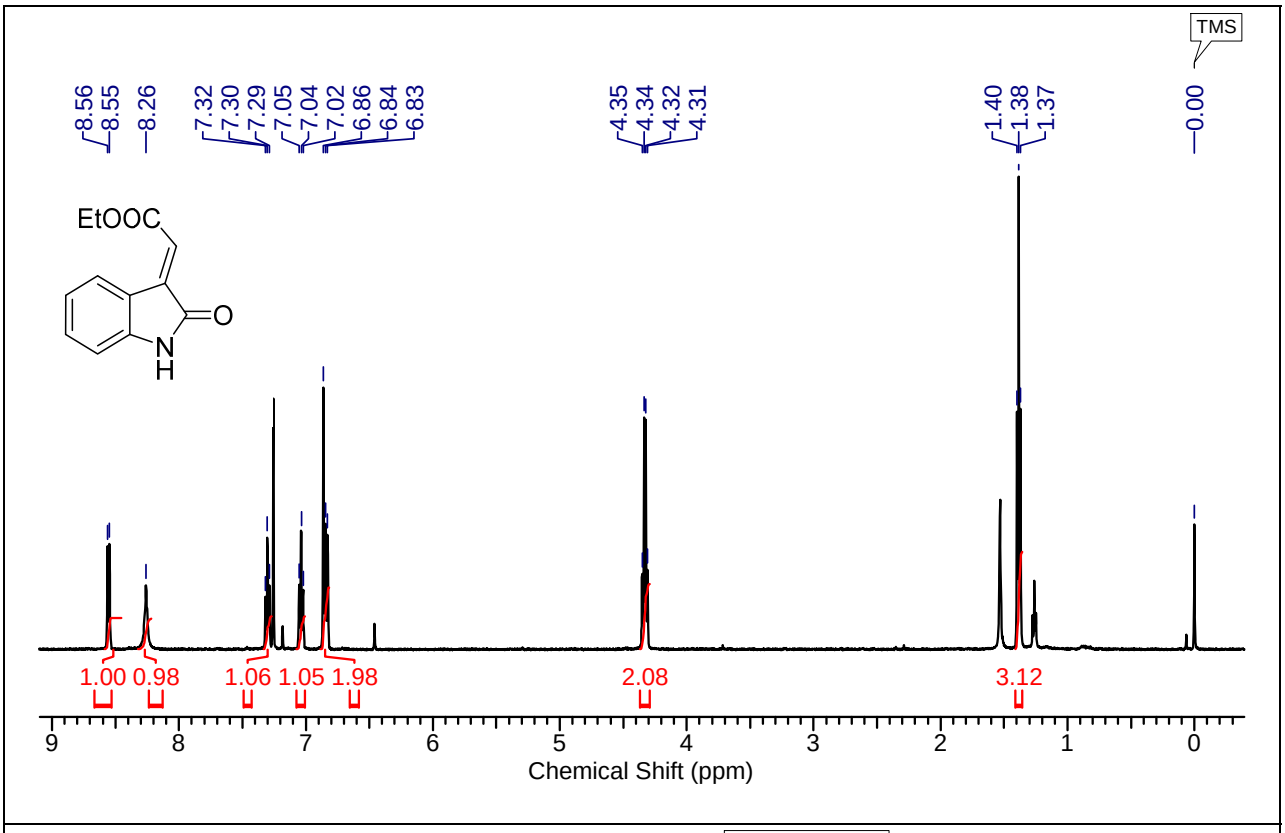
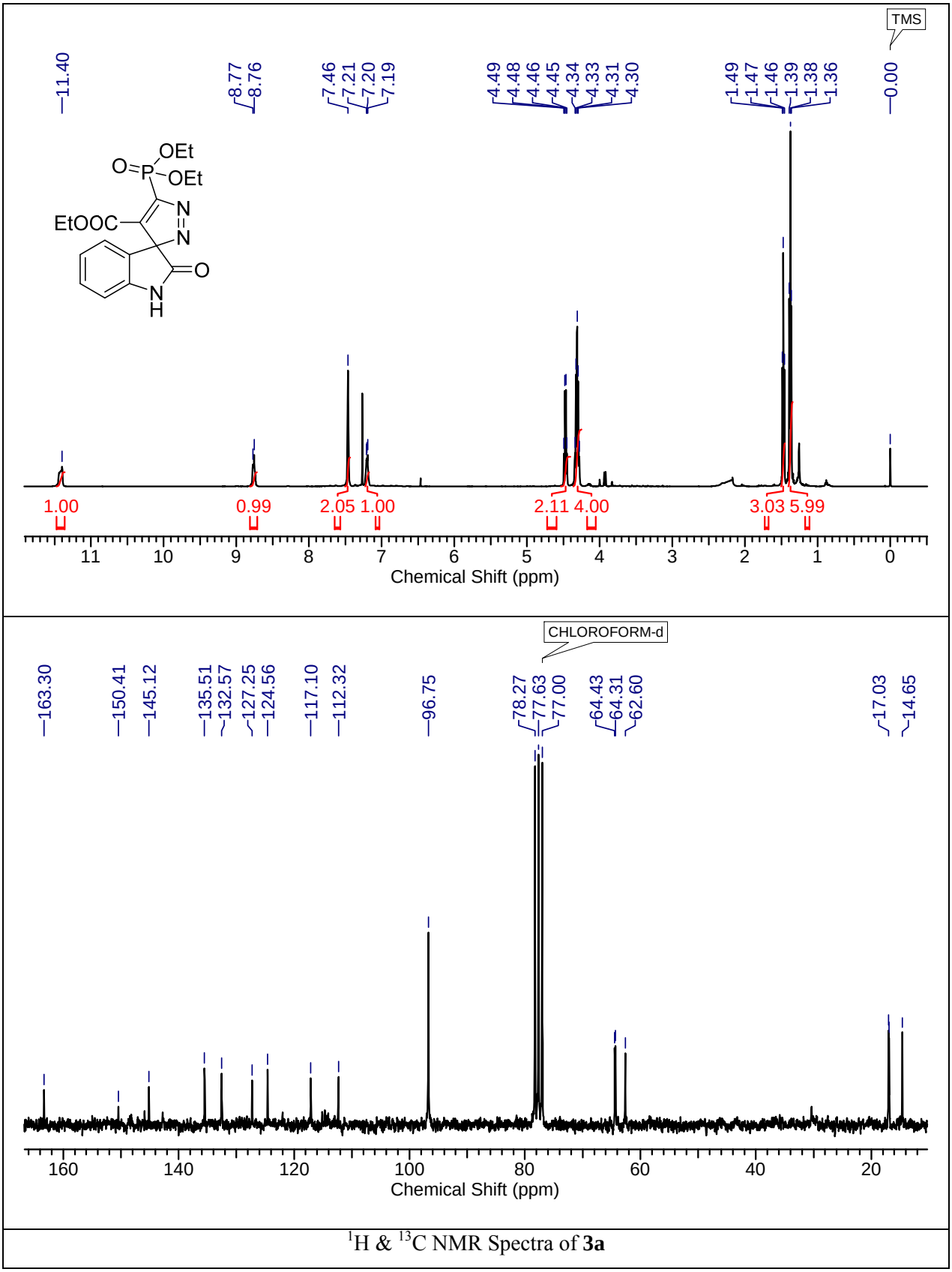
6. A. Singh, A. L. Loomer and G. P. Roth, *Org. Lett*., 2012, **14**, 5266

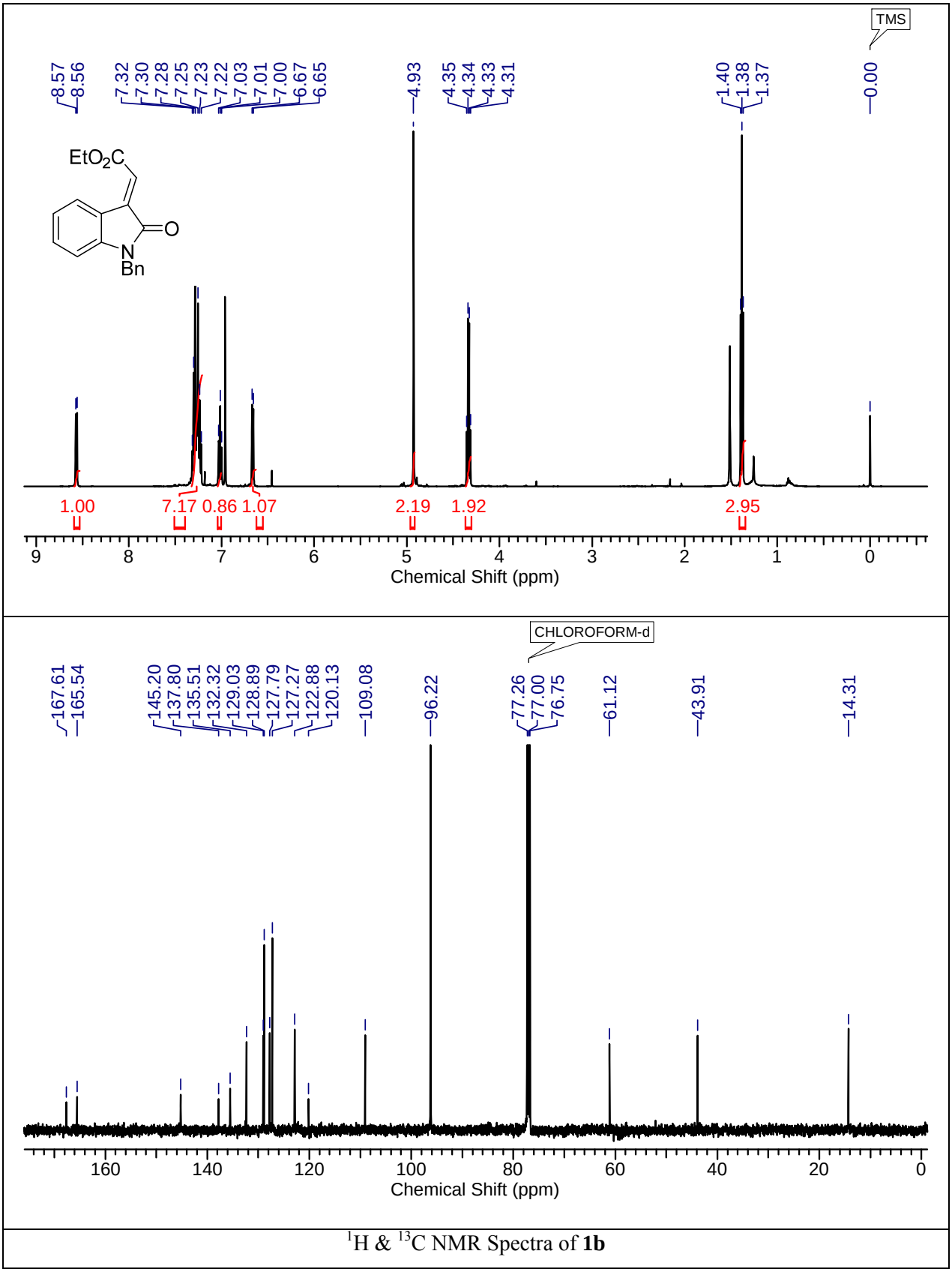
4. NMR Spectra:



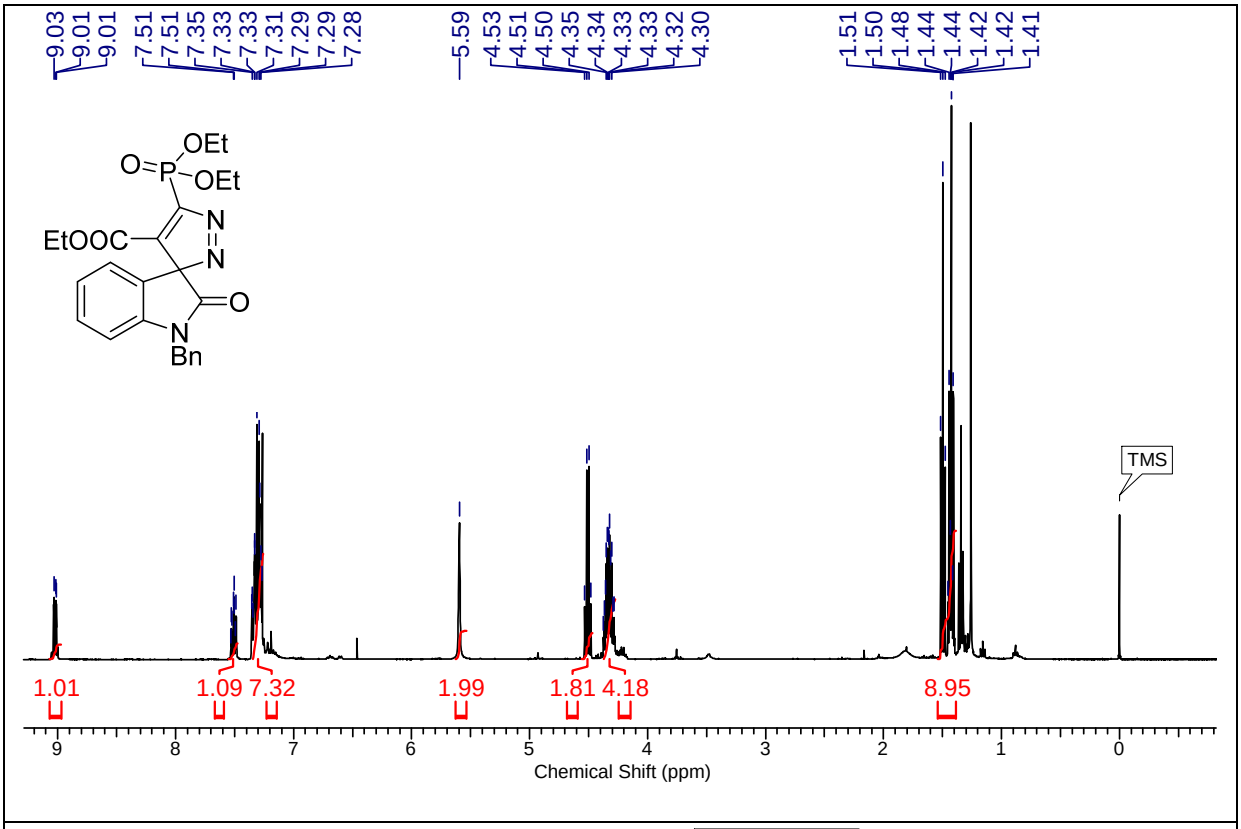
^{1}H & ^{13}C NMR Spectra of **1a**

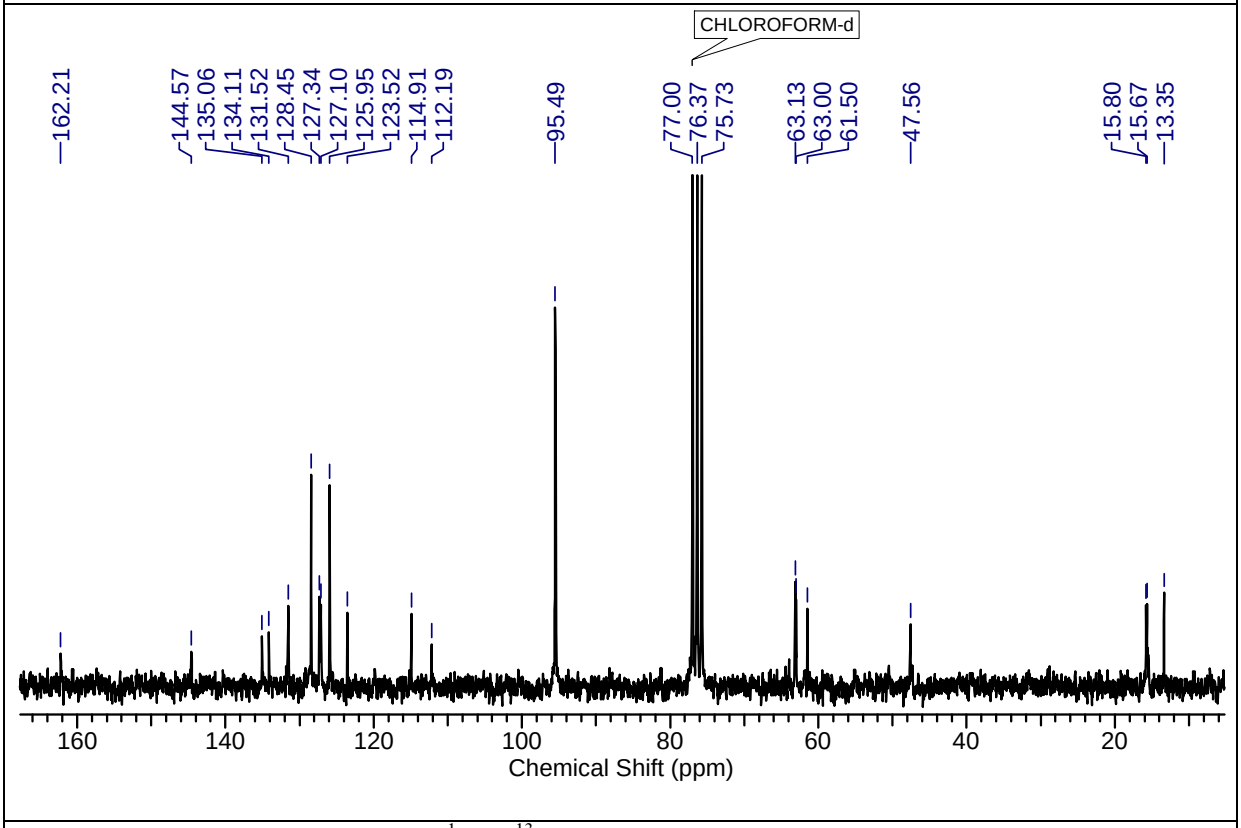


^{1}H & ^{13}C NMR Spectra of **3a**

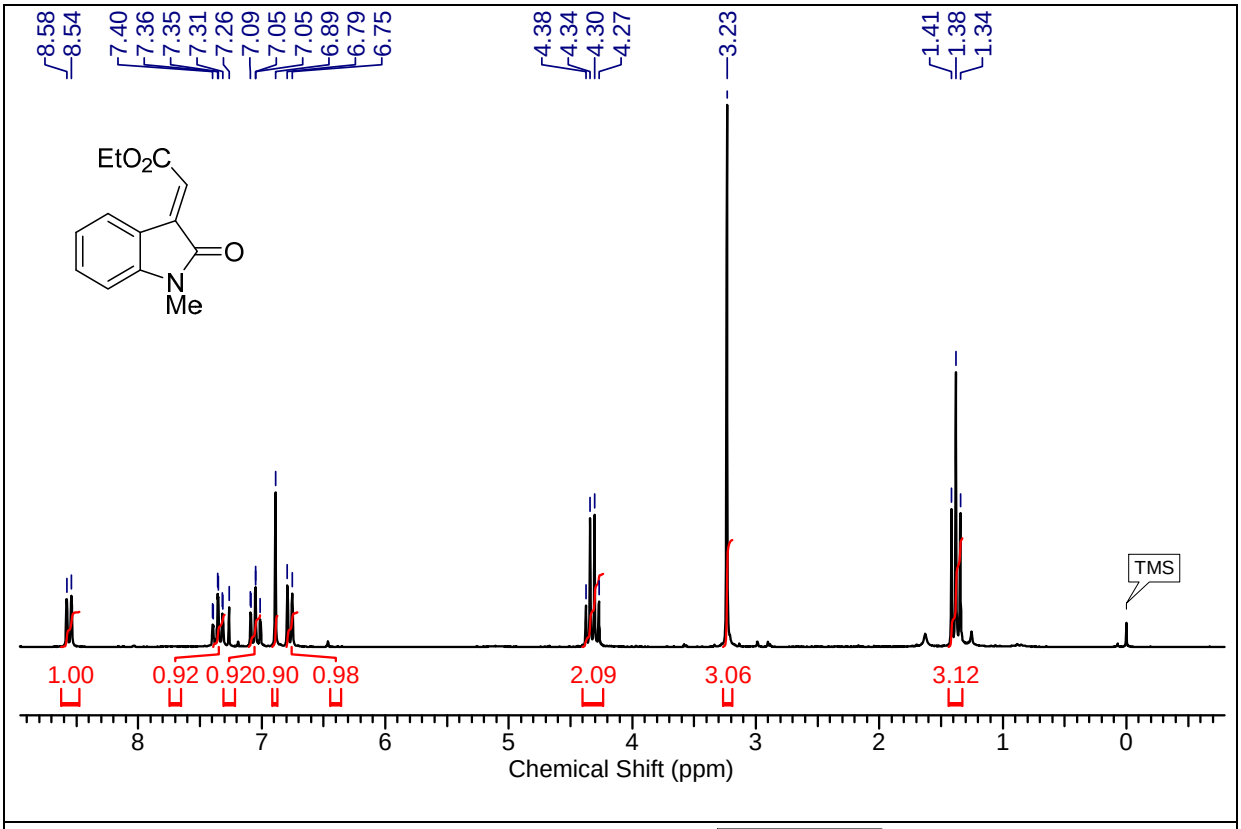


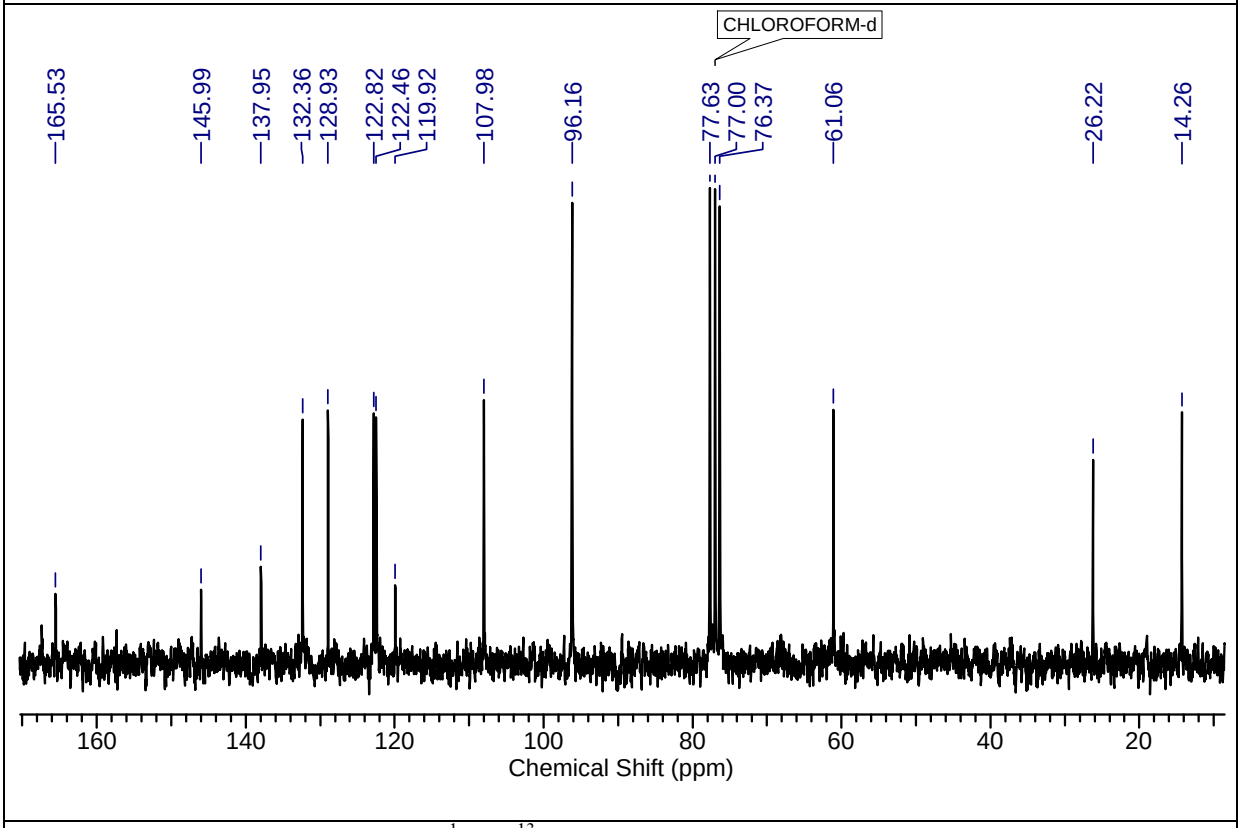
^{1}H & ^{13}C NMR Spectra of **1b**



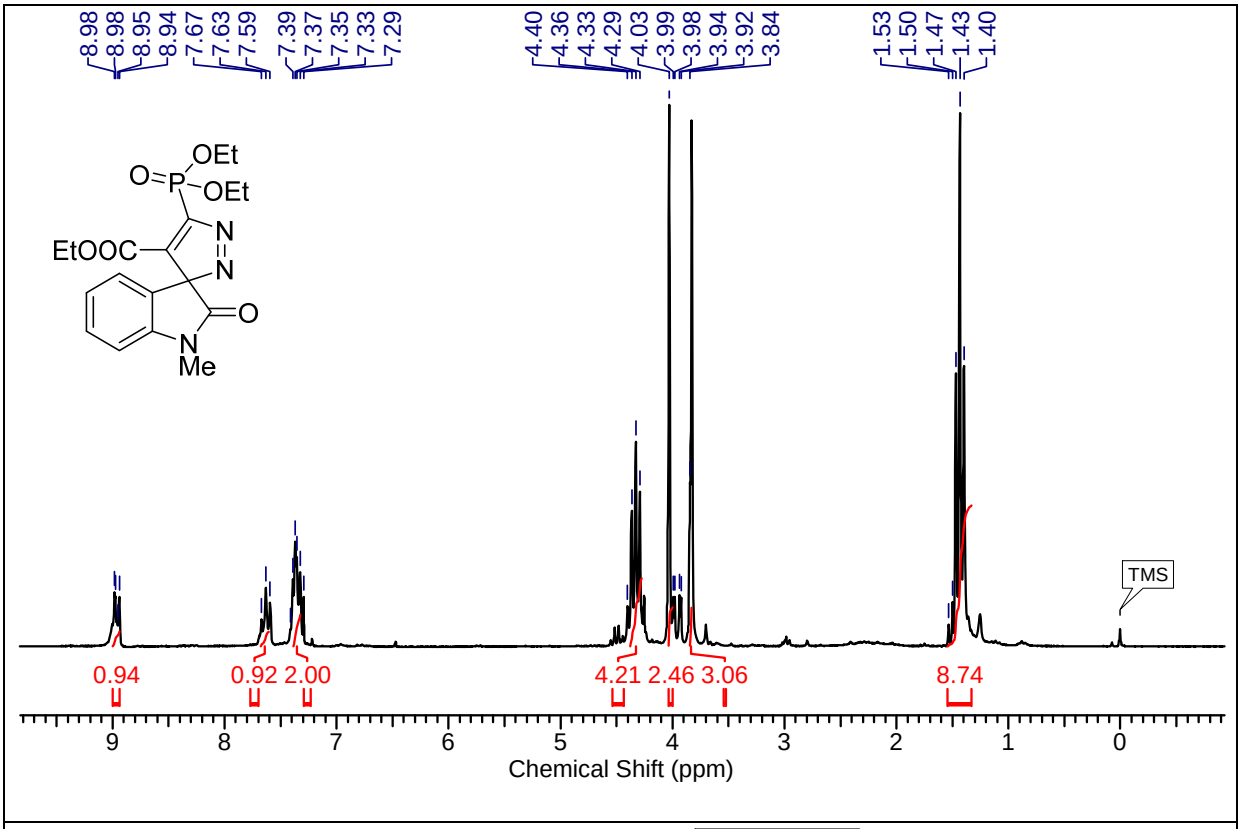


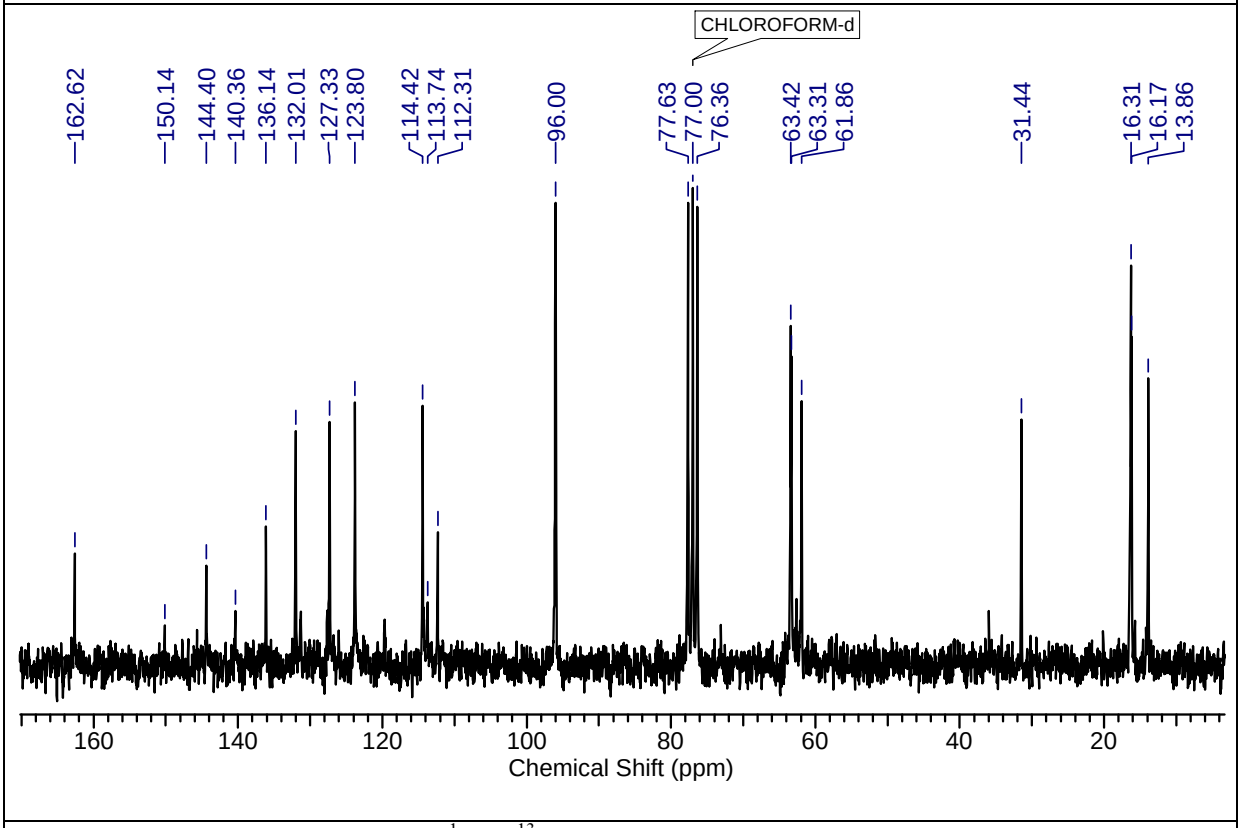
^{1}H & ^{13}C NMR Spectra of **3b**



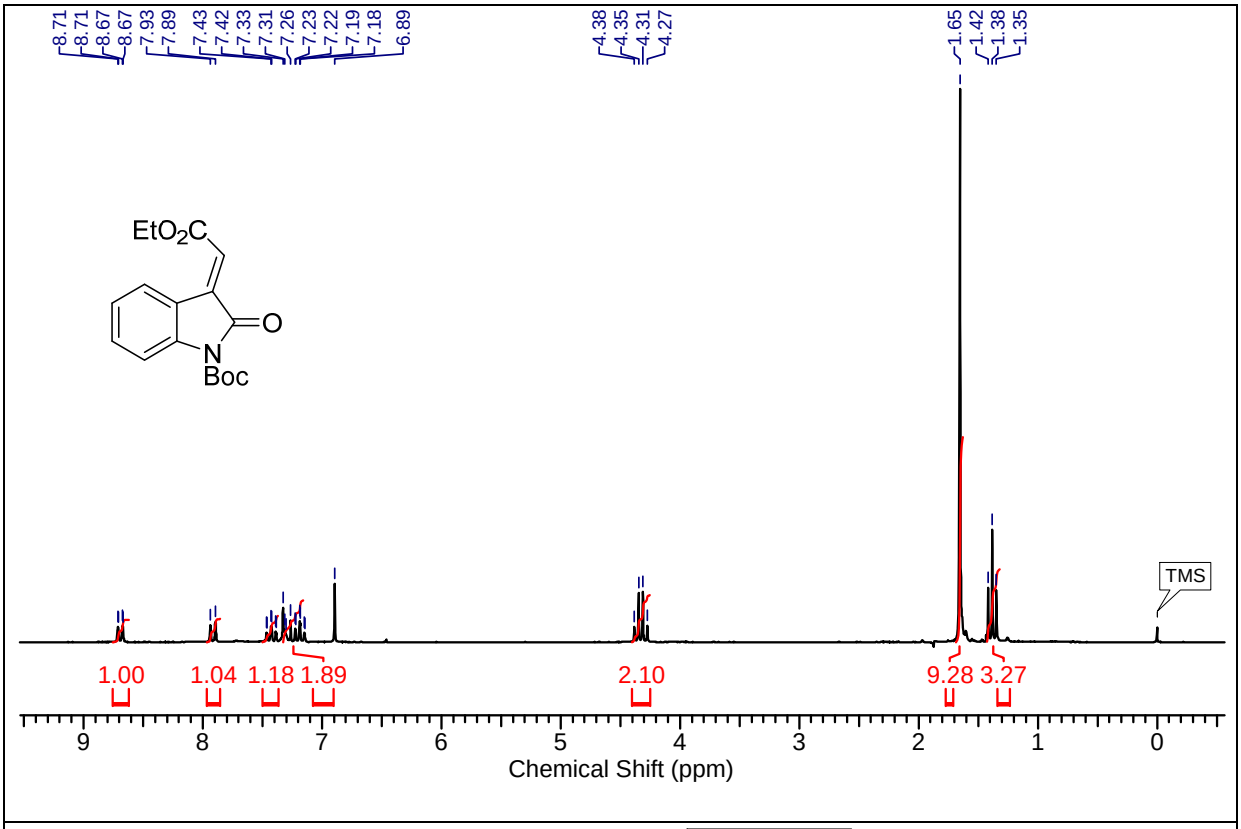


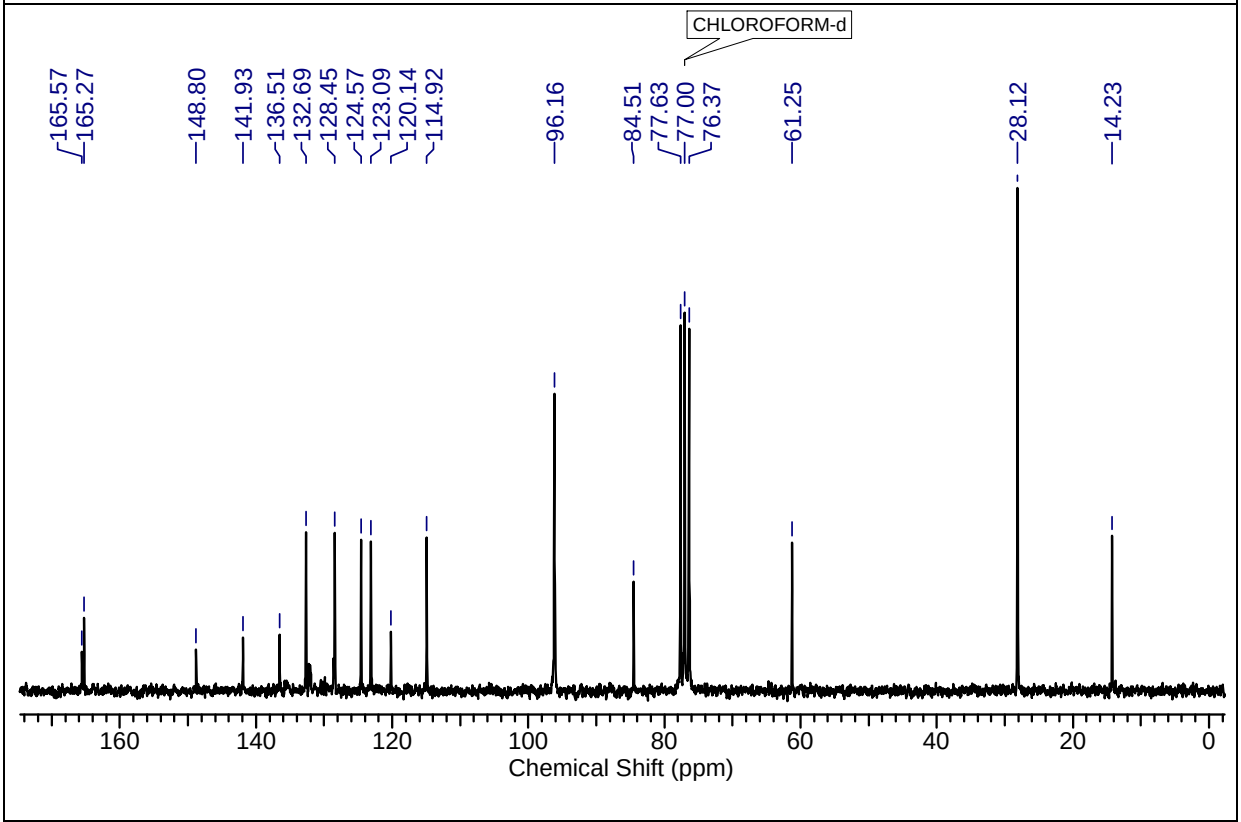
^{1}H & ^{13}C NMR Spectra of **1c**



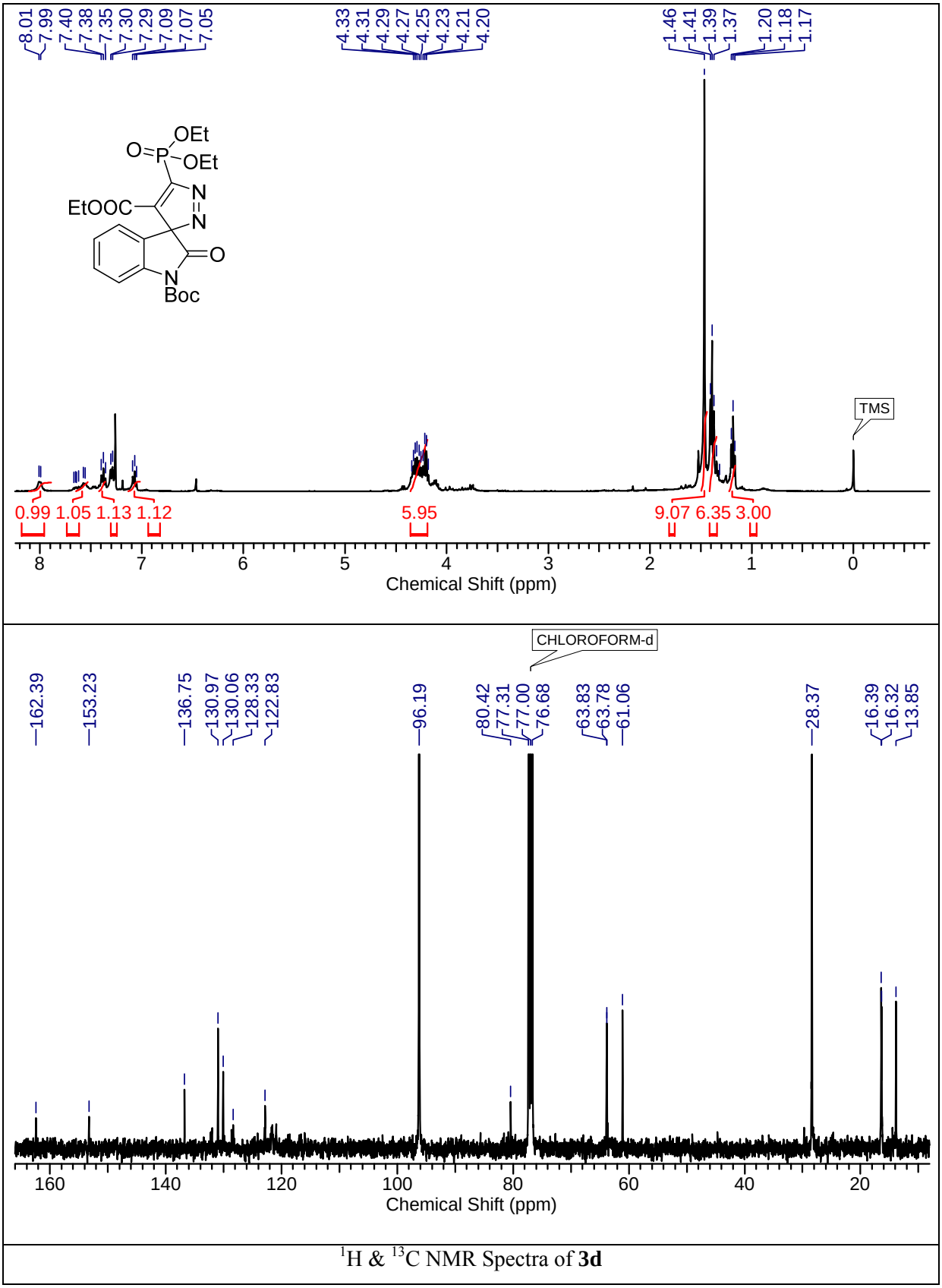


^{1}H & ^{13}C NMR Spectra of **3c**

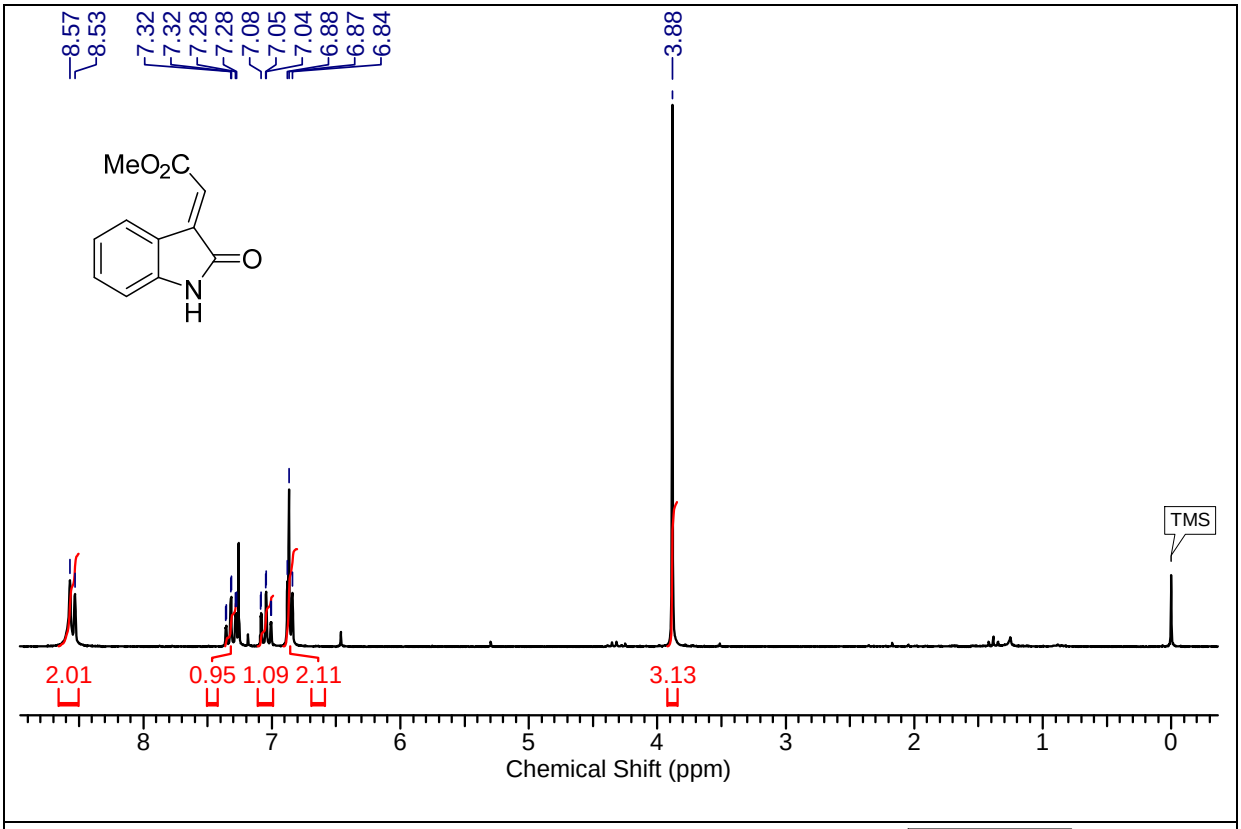


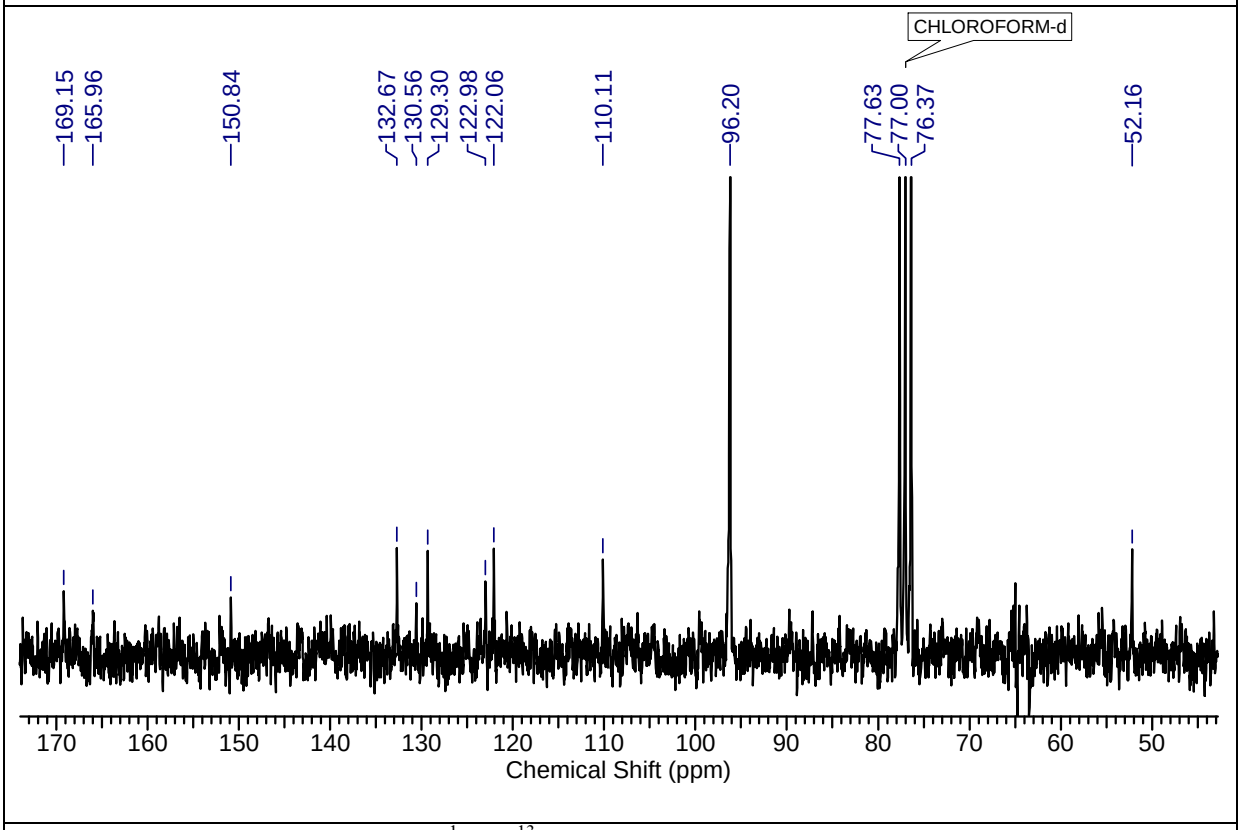


^{1}H & ^{13}C NMR Spectra of **1d**

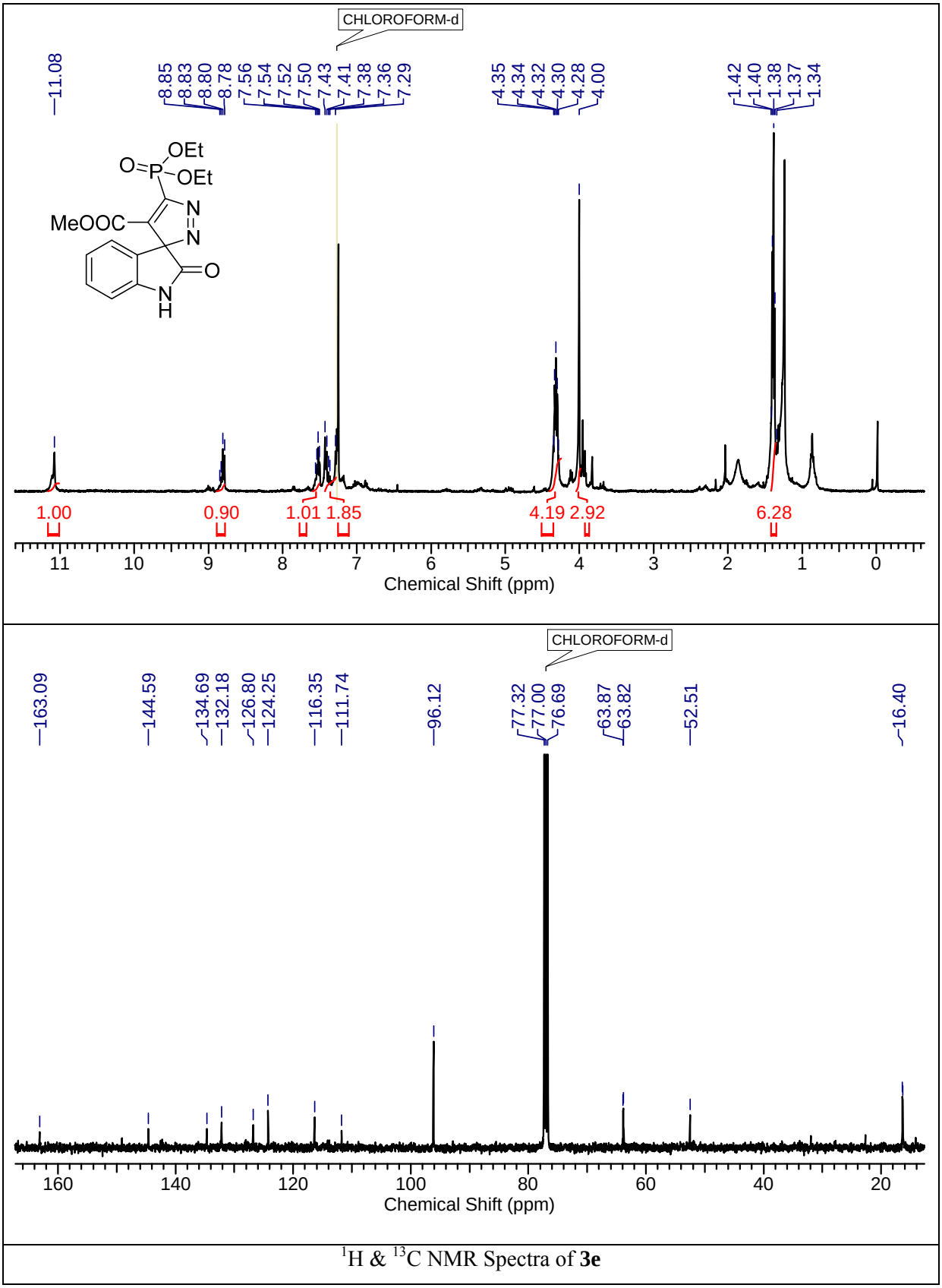


^{1}H & ^{13}C NMR Spectra of **3d**

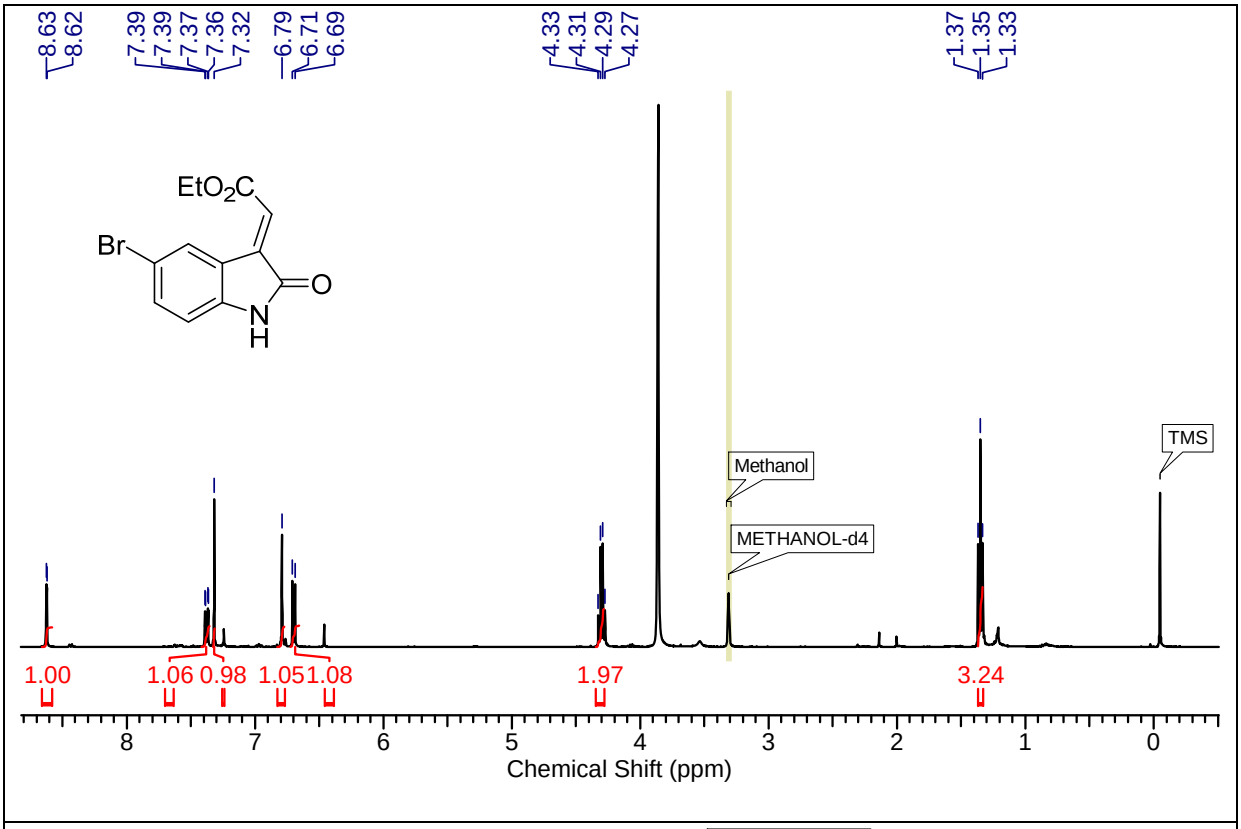


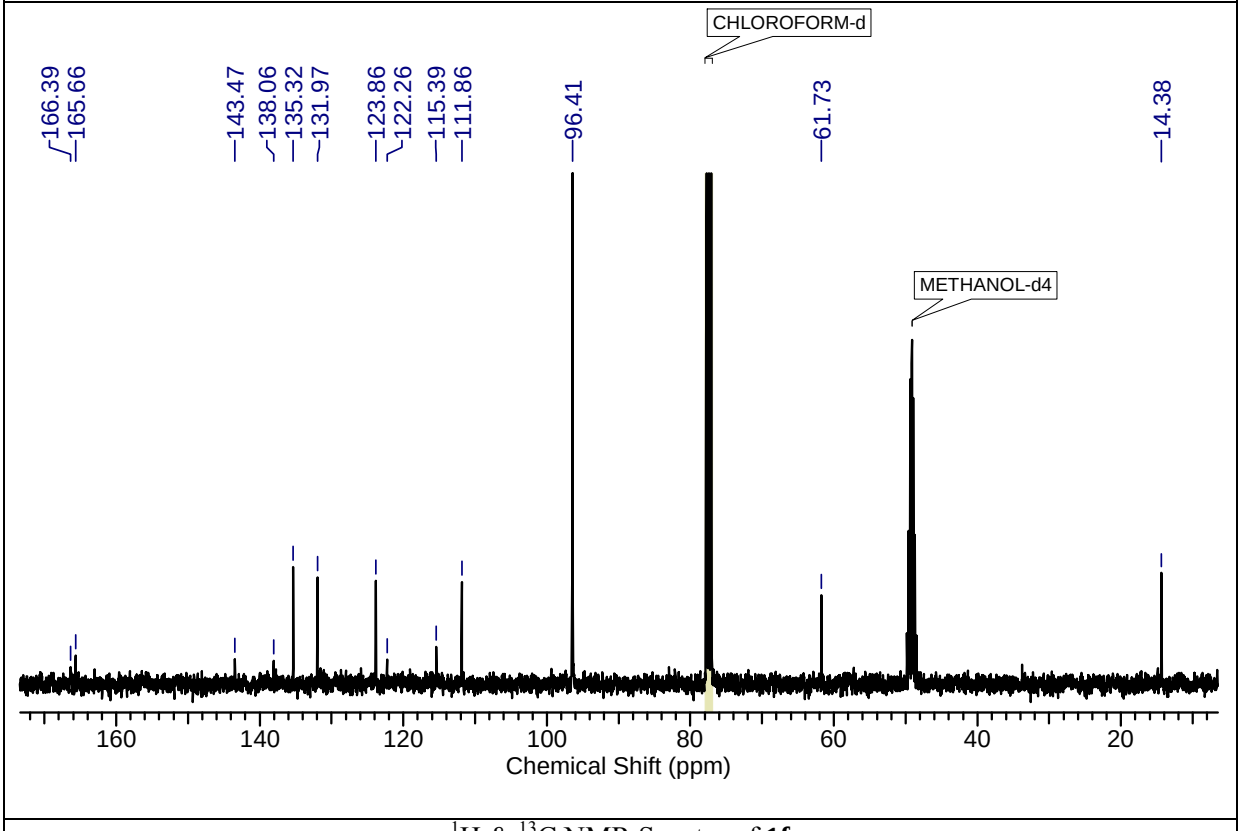


^{1}H & ^{13}C NMR Spectra of **1e**

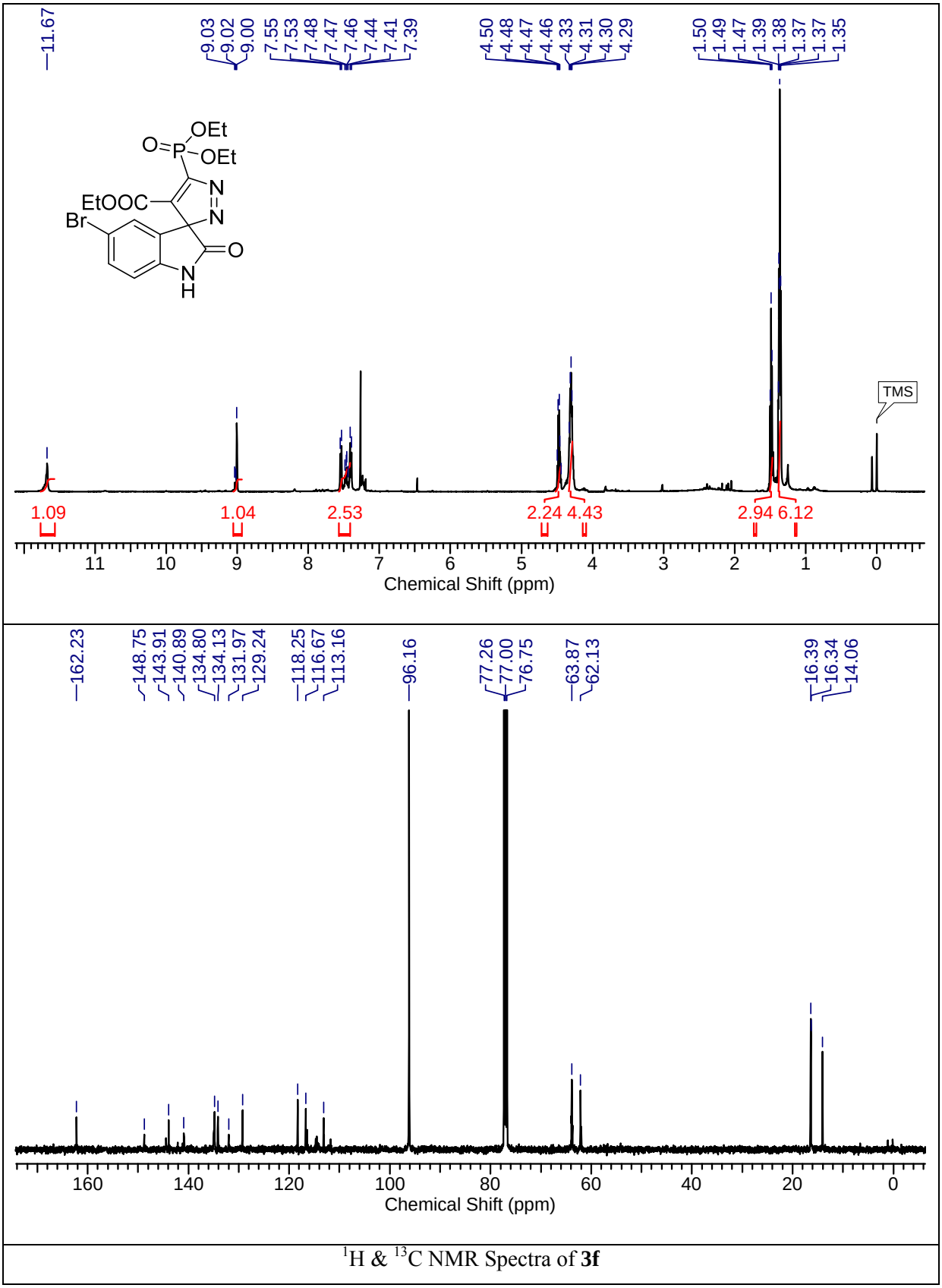


^{1}H & ^{13}C NMR Spectra of **3e**

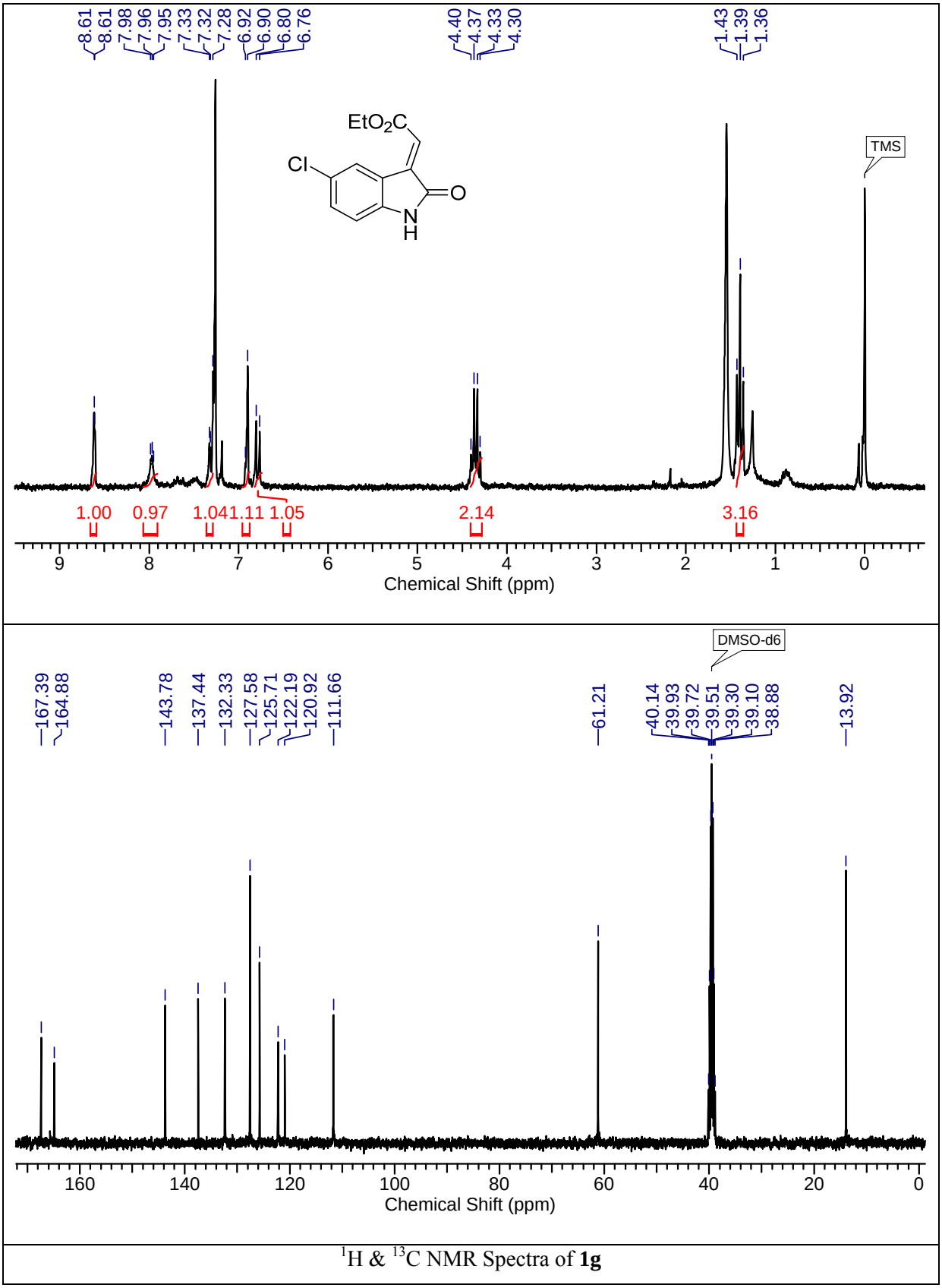




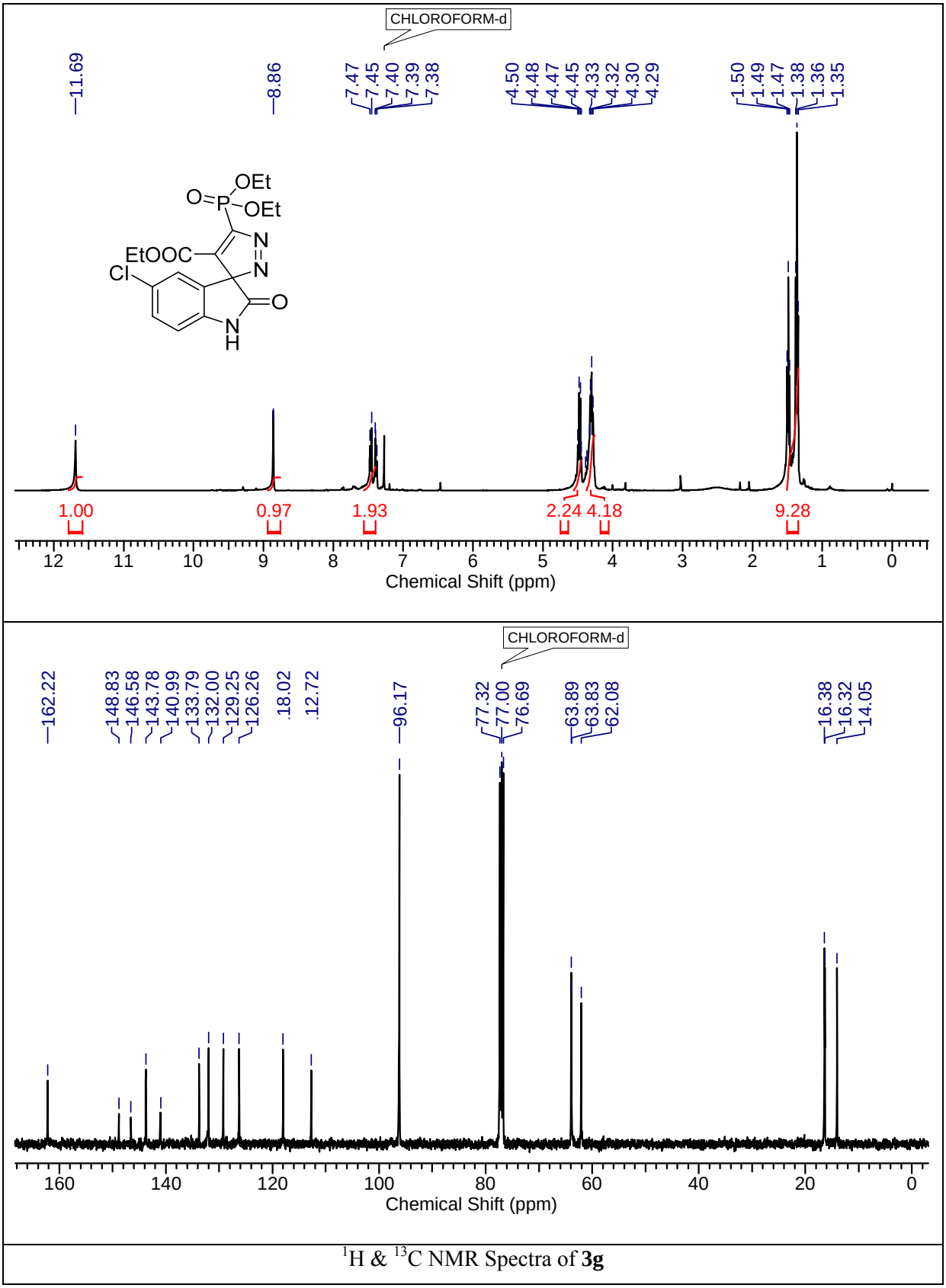
^{1}H & ^{13}C NMR Spectra of **1f**



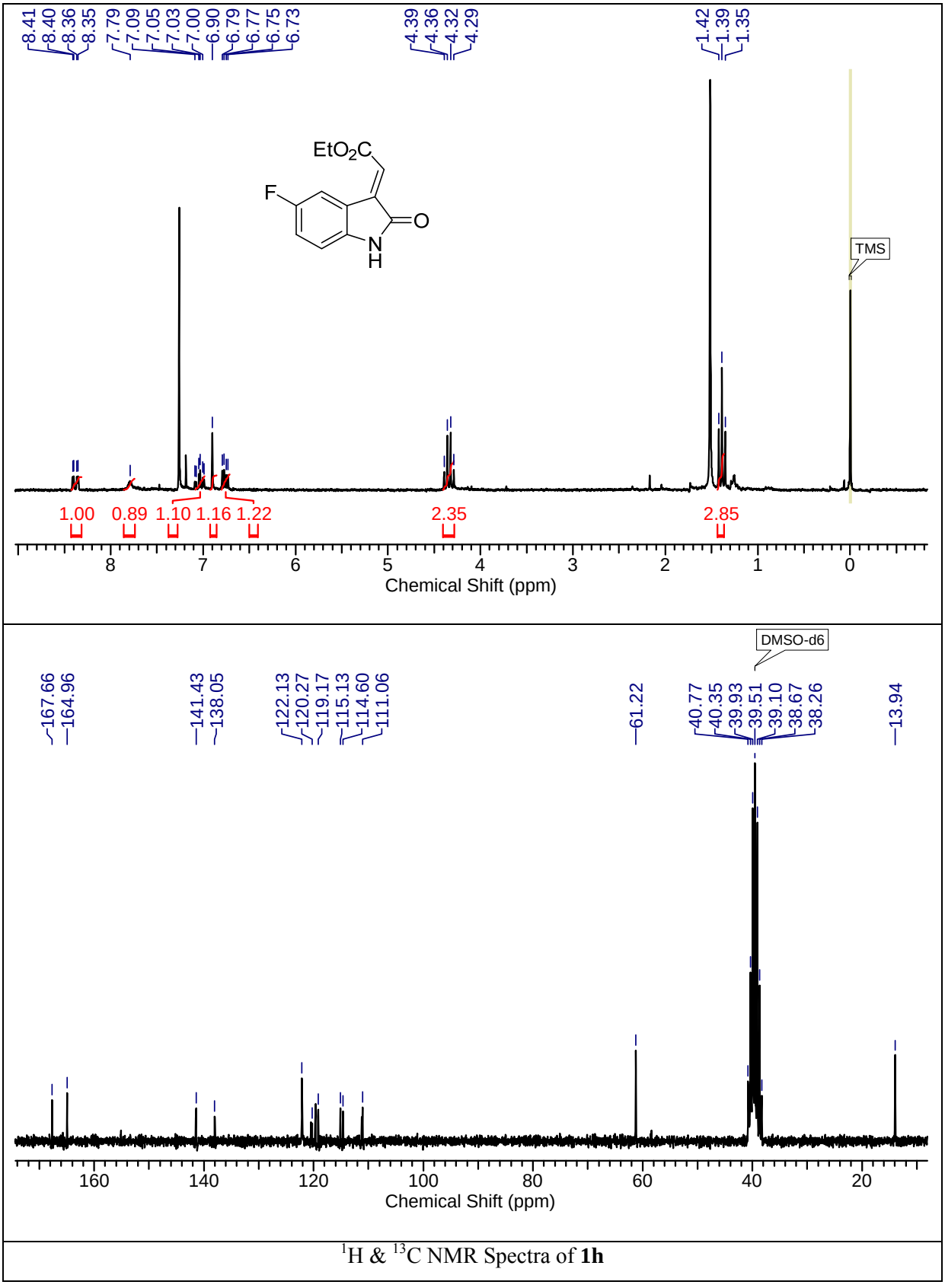
^{1}H & ^{13}C NMR Spectra of **3f**



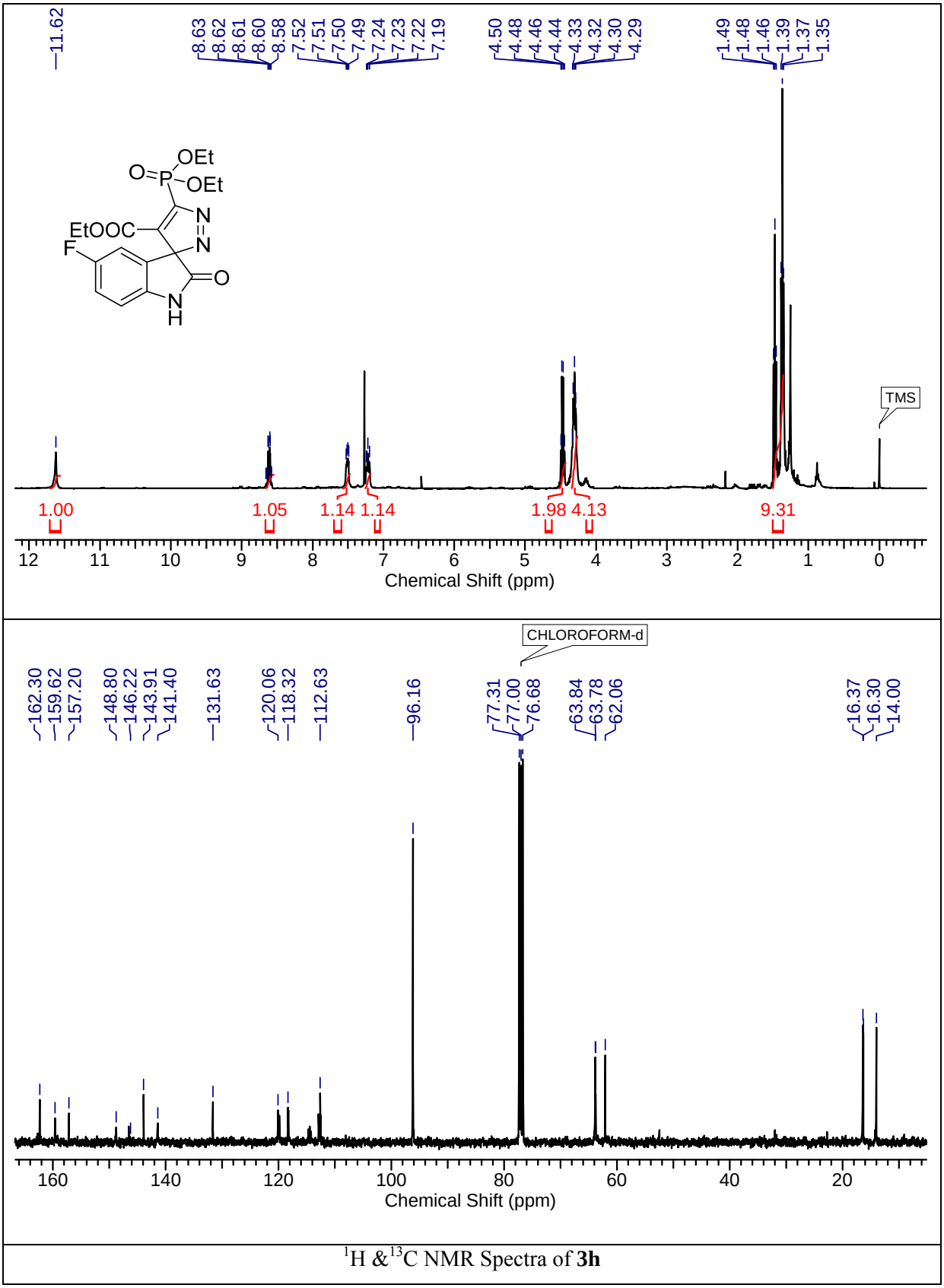
^{1}H & ^{13}C NMR Spectra of **1g**



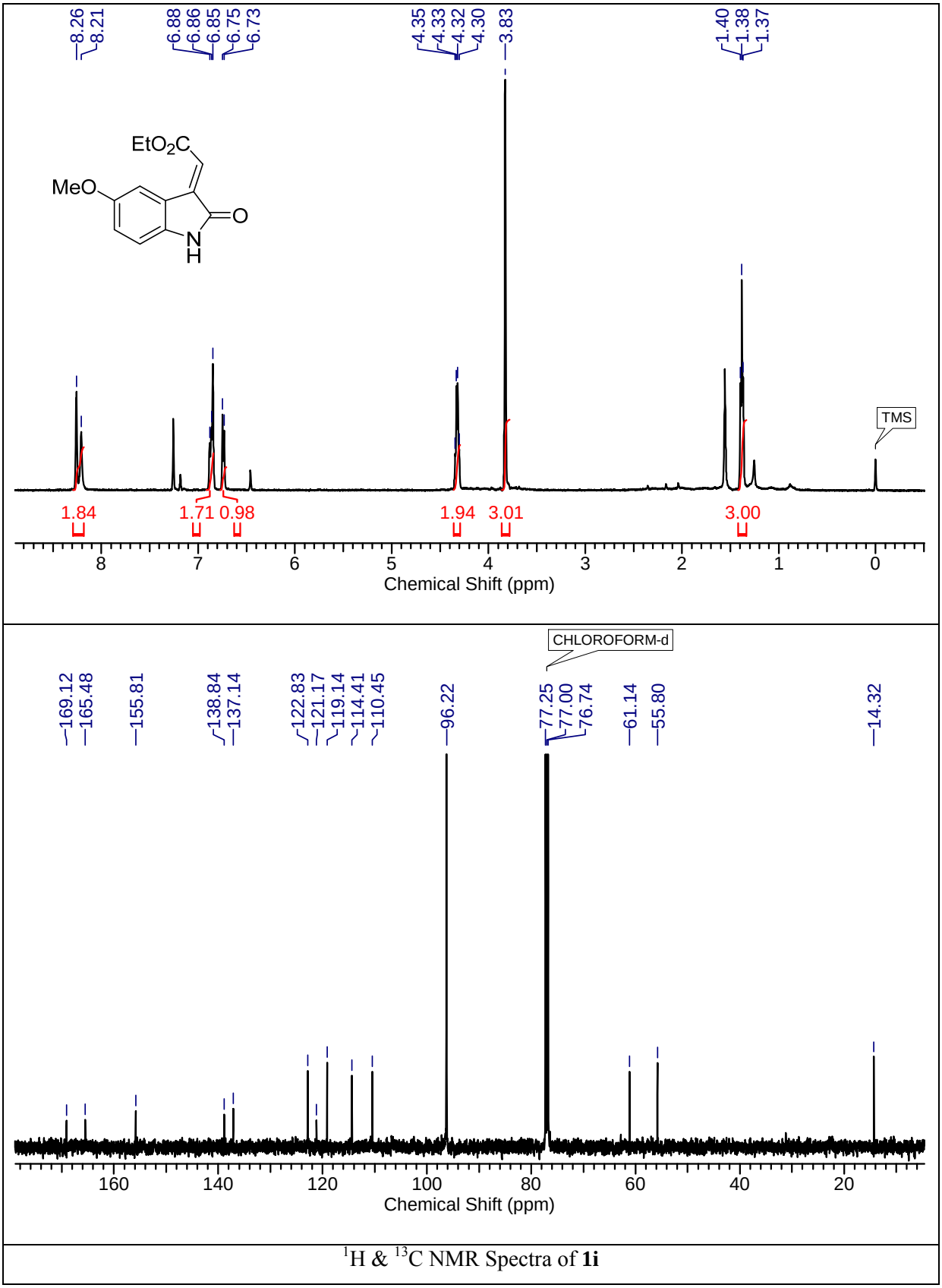
^{1}H & ^{13}C NMR Spectra of **3g**



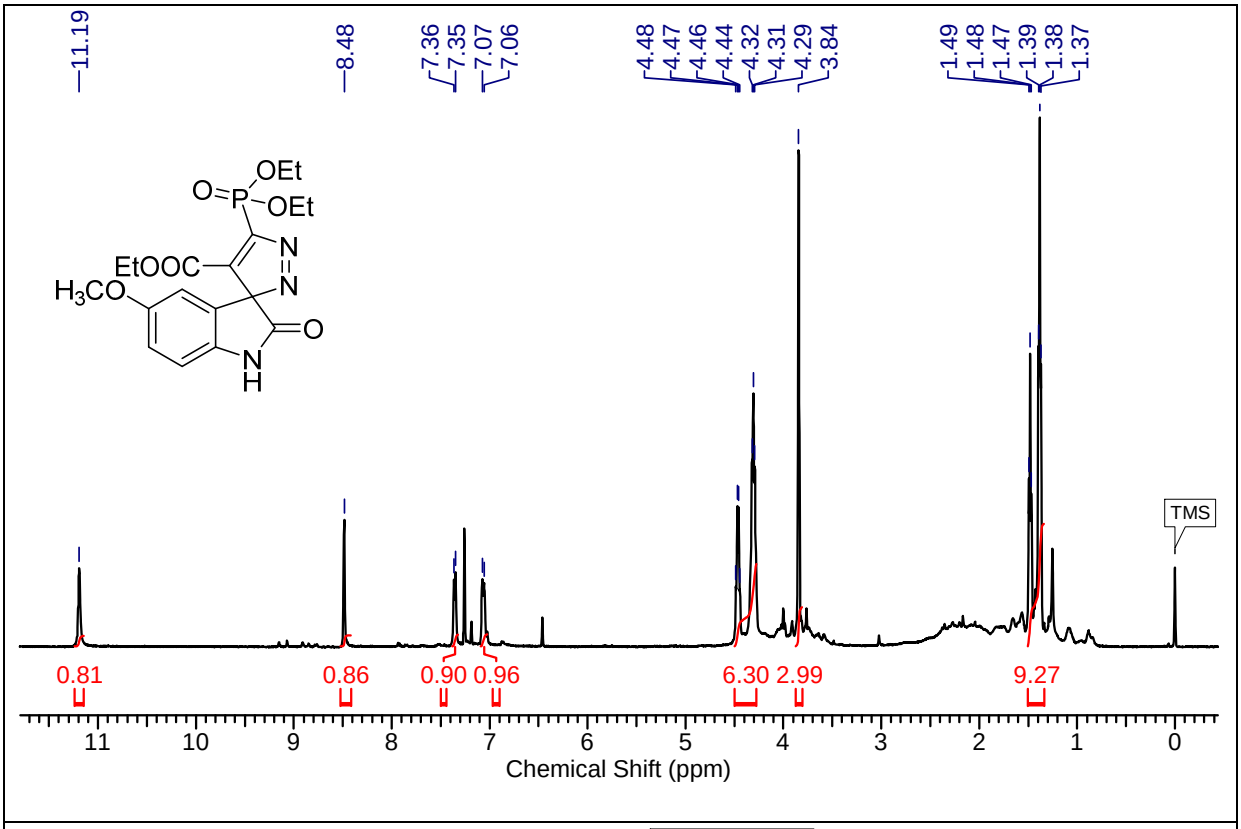
^{1}H & ^{13}C NMR Spectra of **1h**

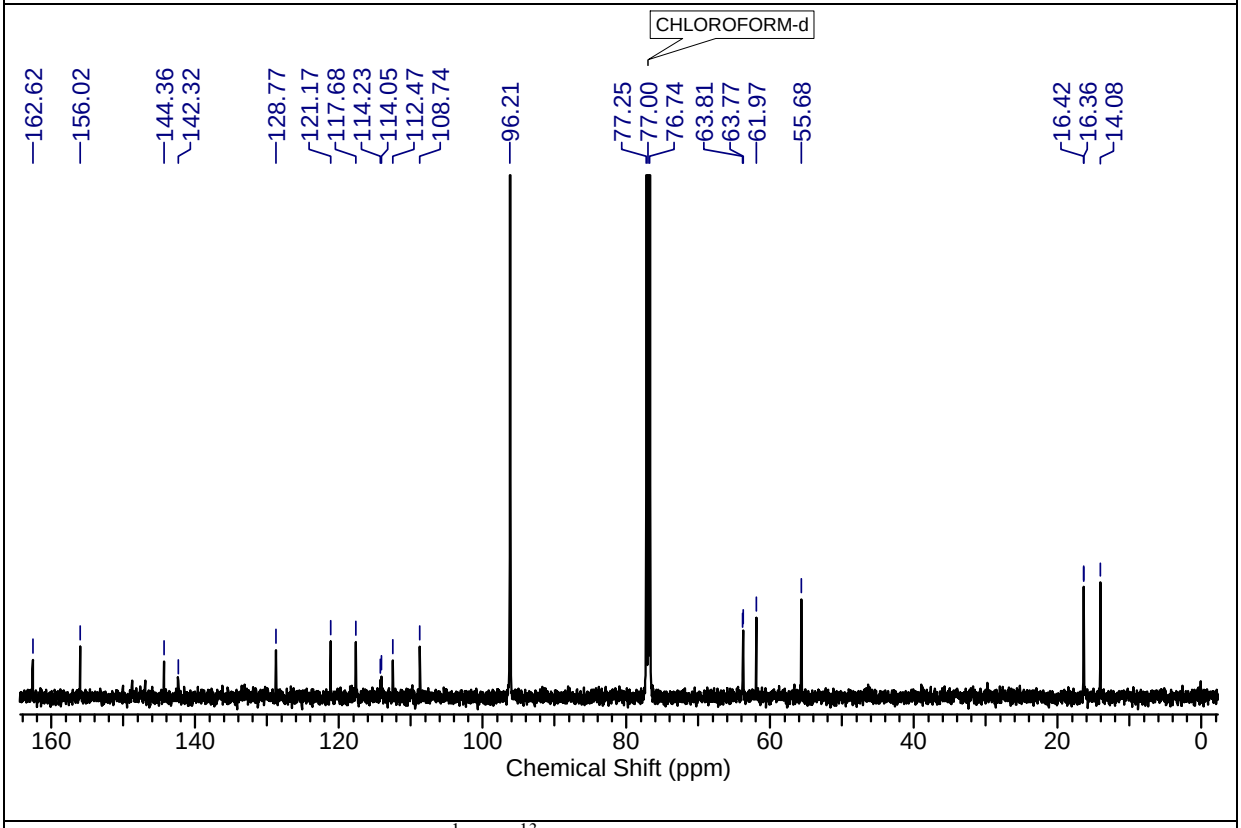


^{1}H &^{13}C NMR Spectra of **3h**

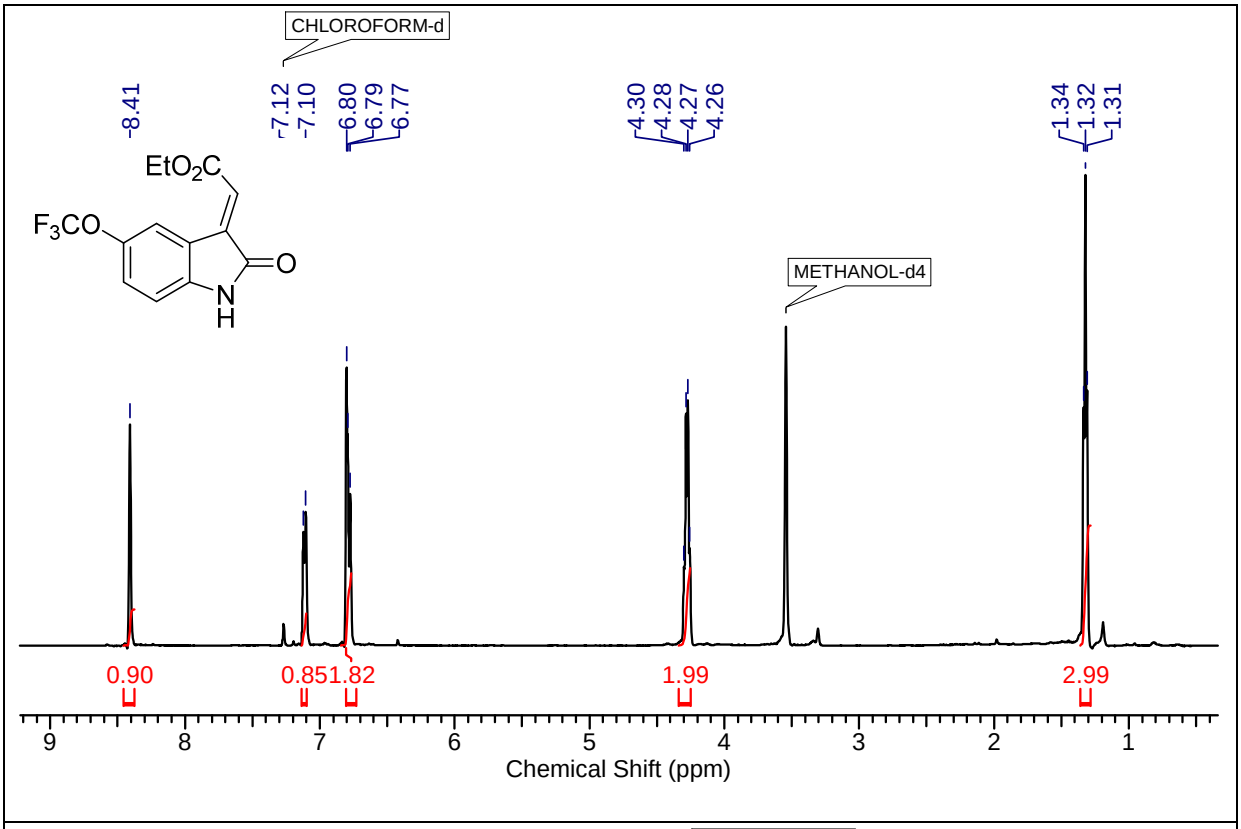


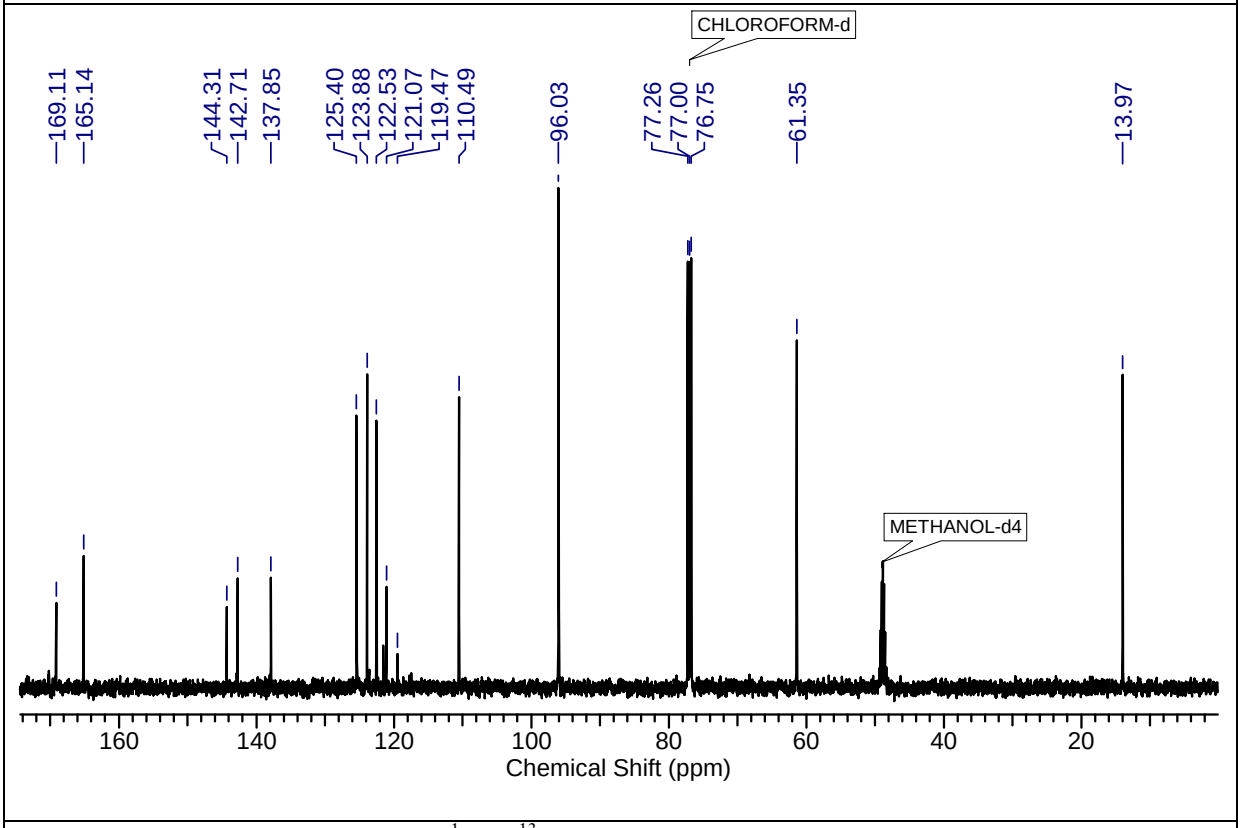
^{1}H & ^{13}C NMR Spectra of **1i**



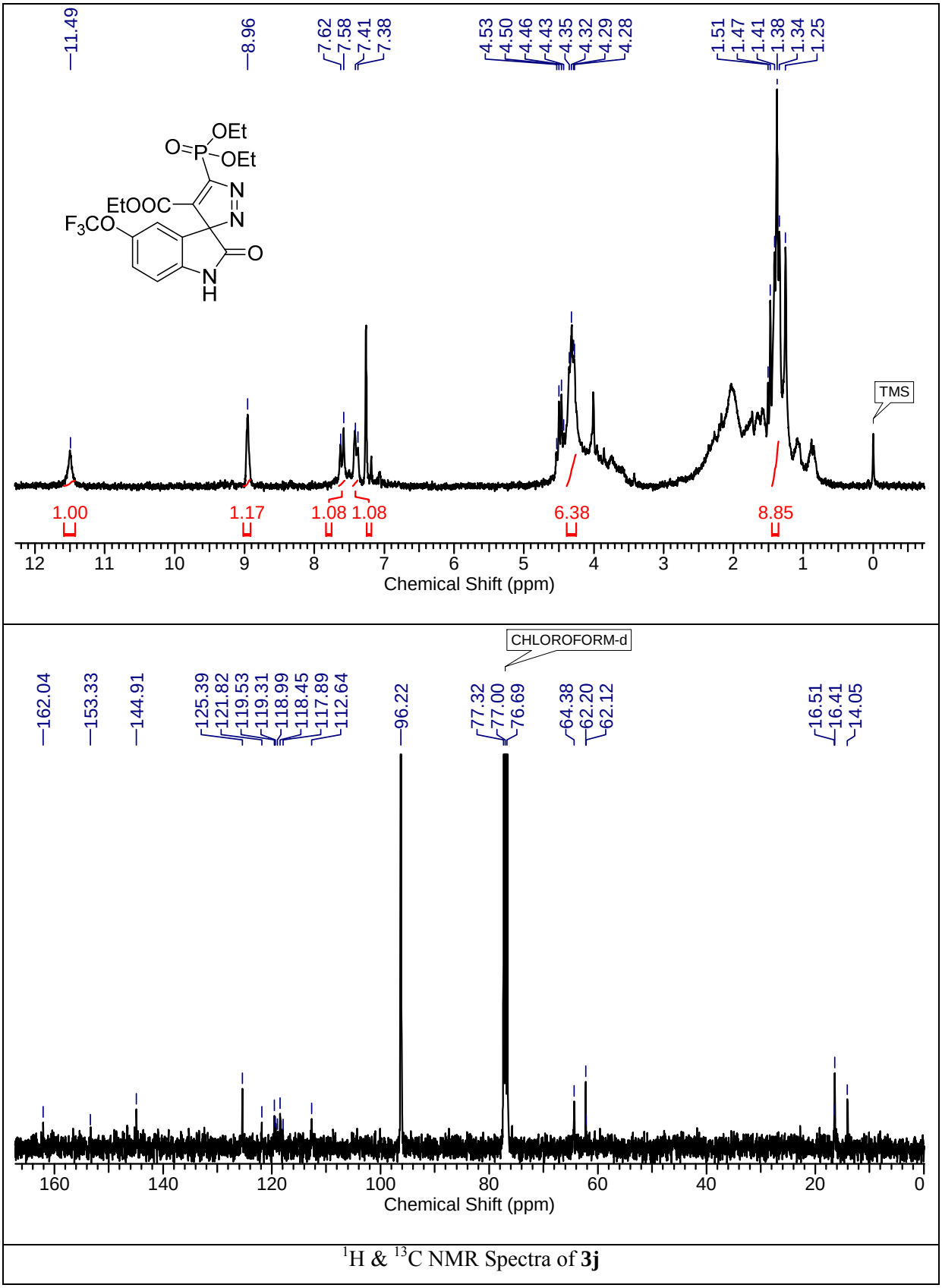


^{1}H & ^{13}C NMR Spectra of **3i**

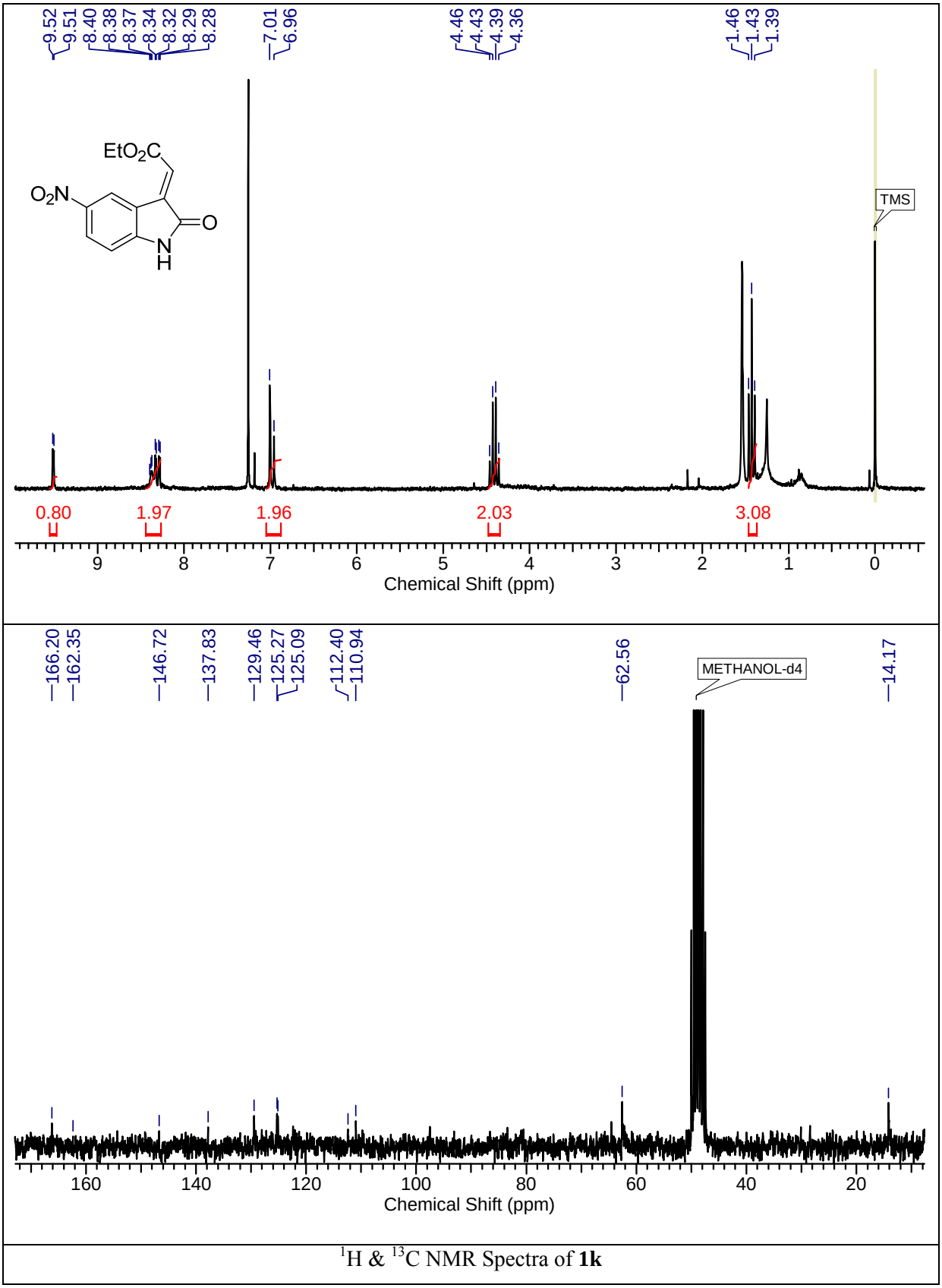




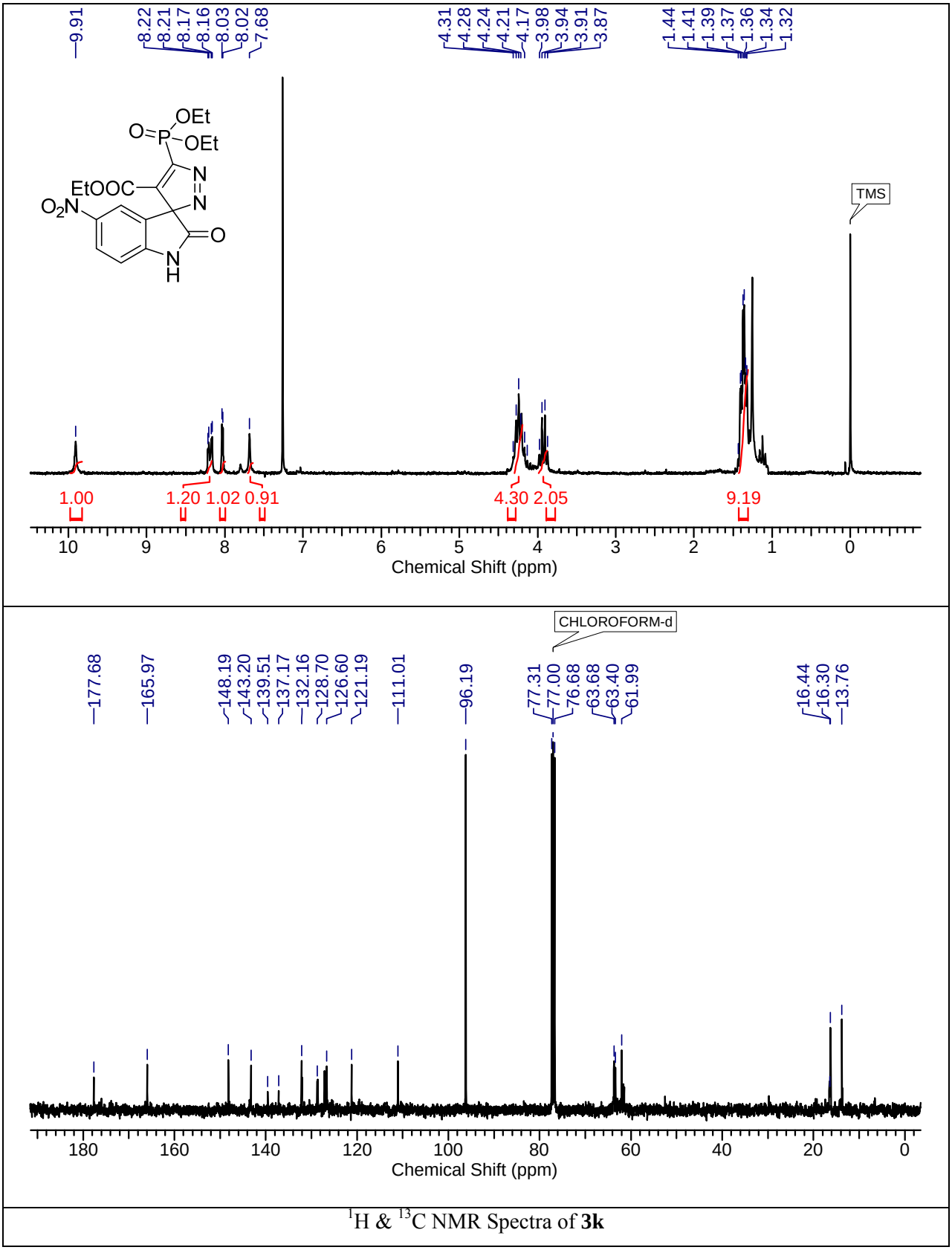
^{1}H & ^{13}C NMR Spectra of **1j**



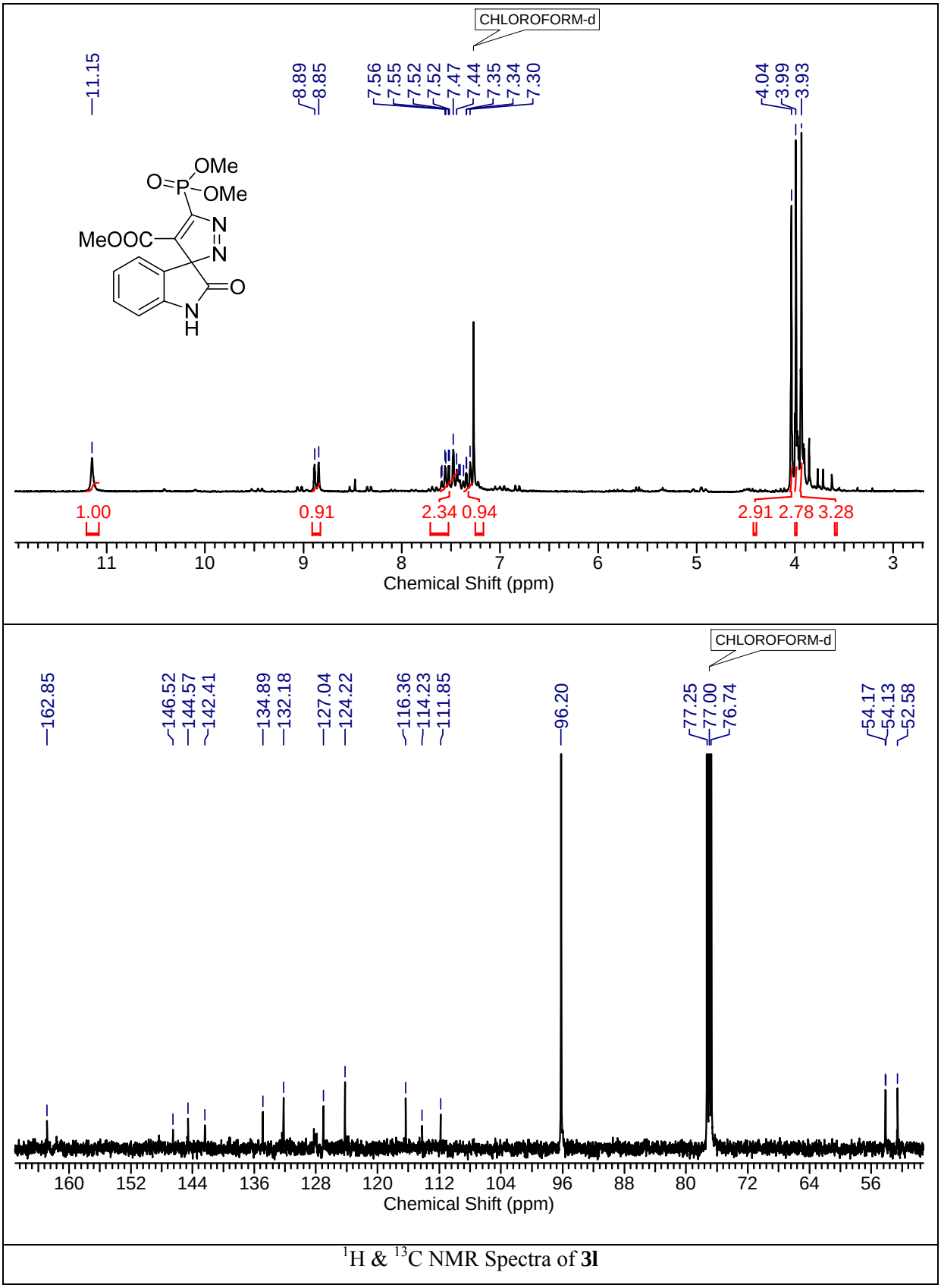
^{1}H & ^{13}C NMR Spectra of **3j**



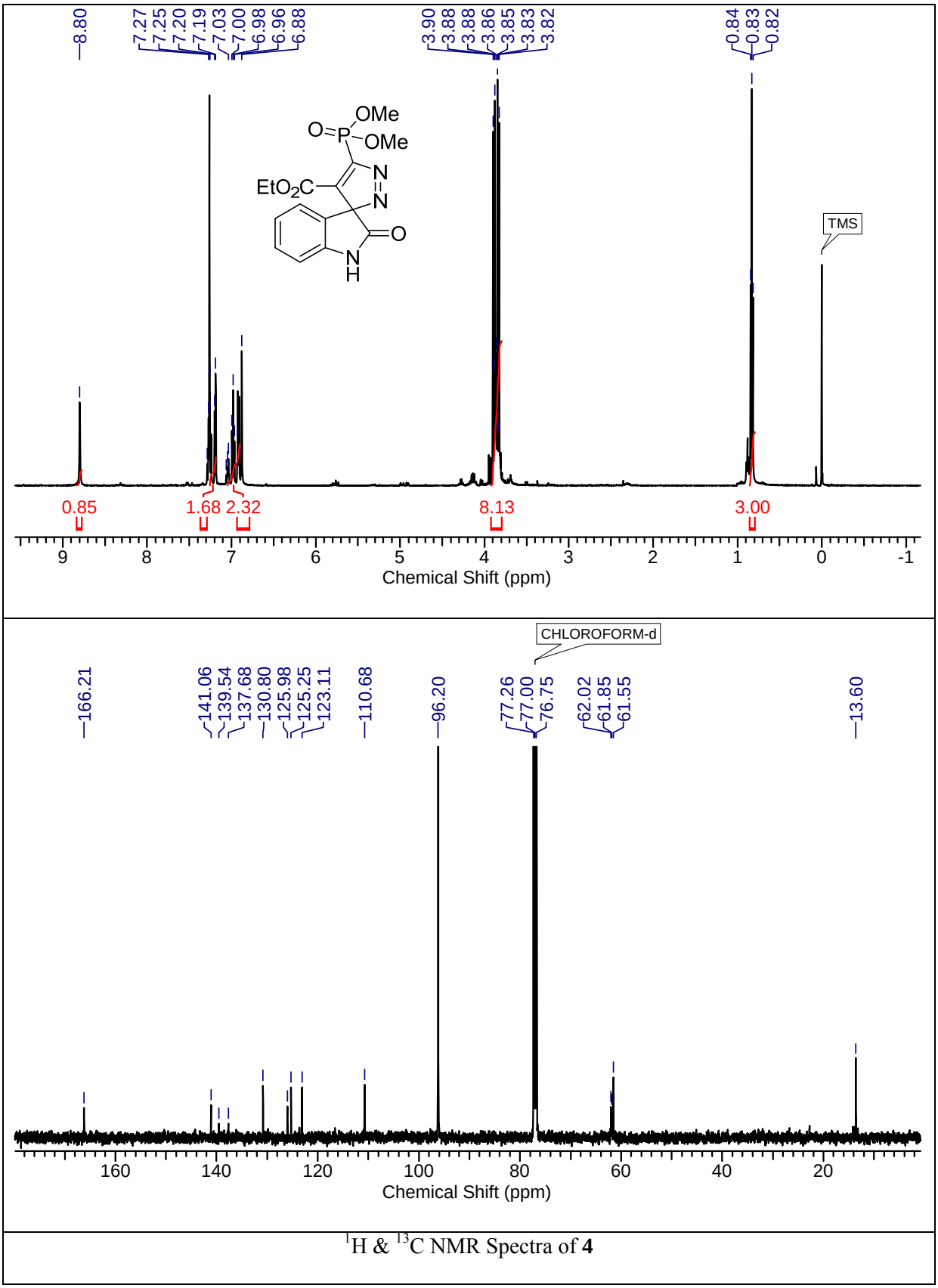
^{1}H & ^{13}C NMR Spectra of **1k**



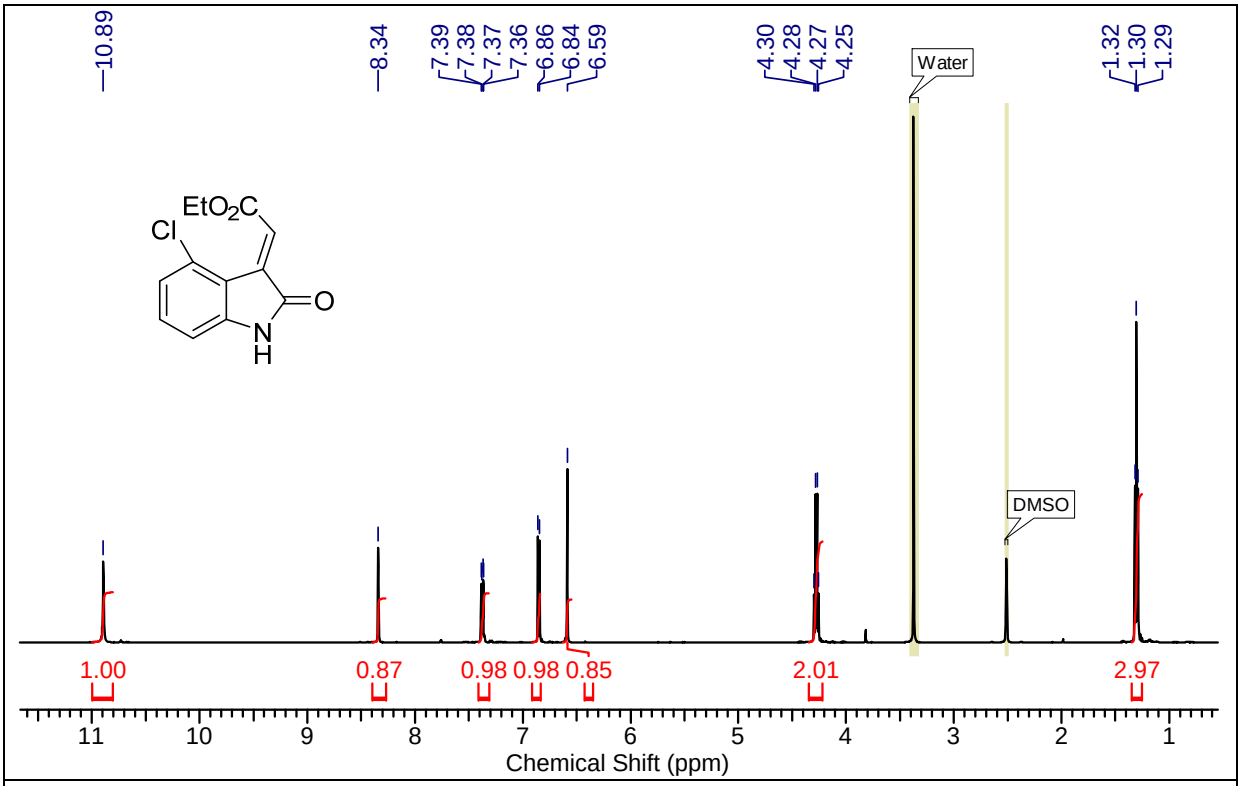
^{1}H & ^{13}C NMR Spectra of **3k**

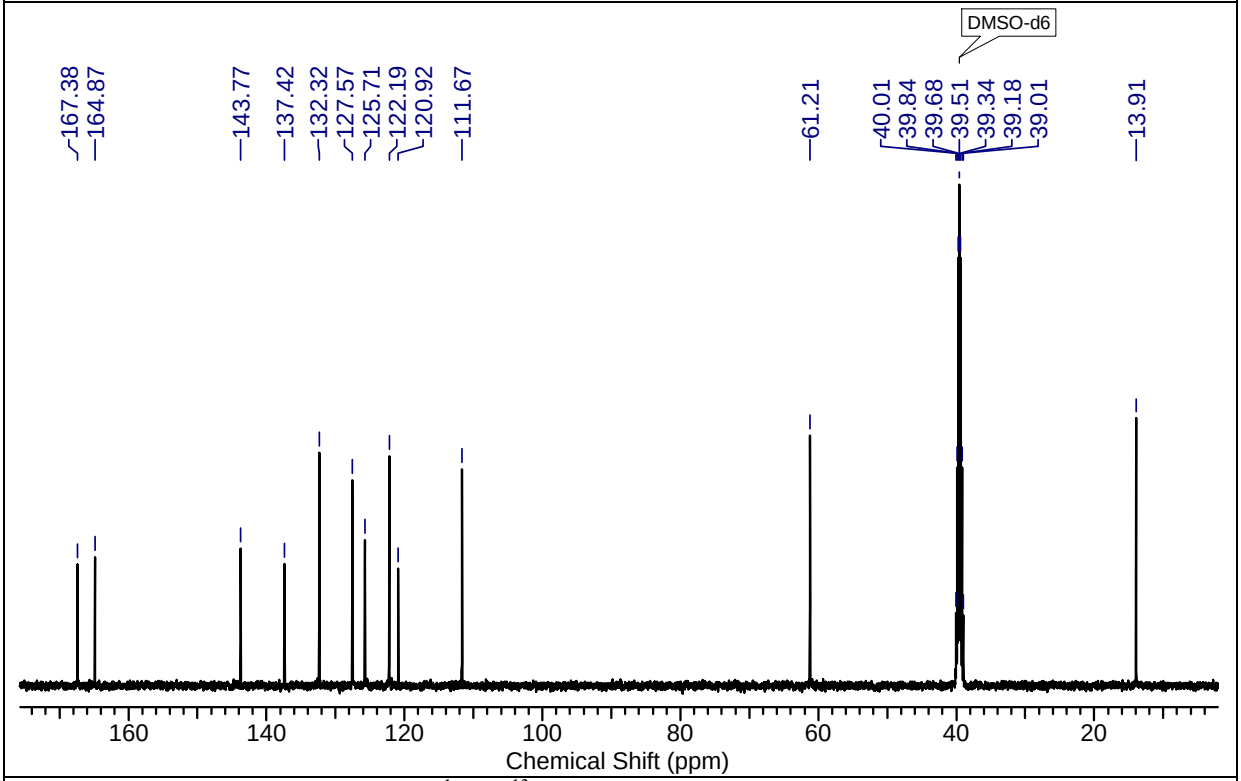


^{1}H & ^{13}C NMR Spectra of **3l**

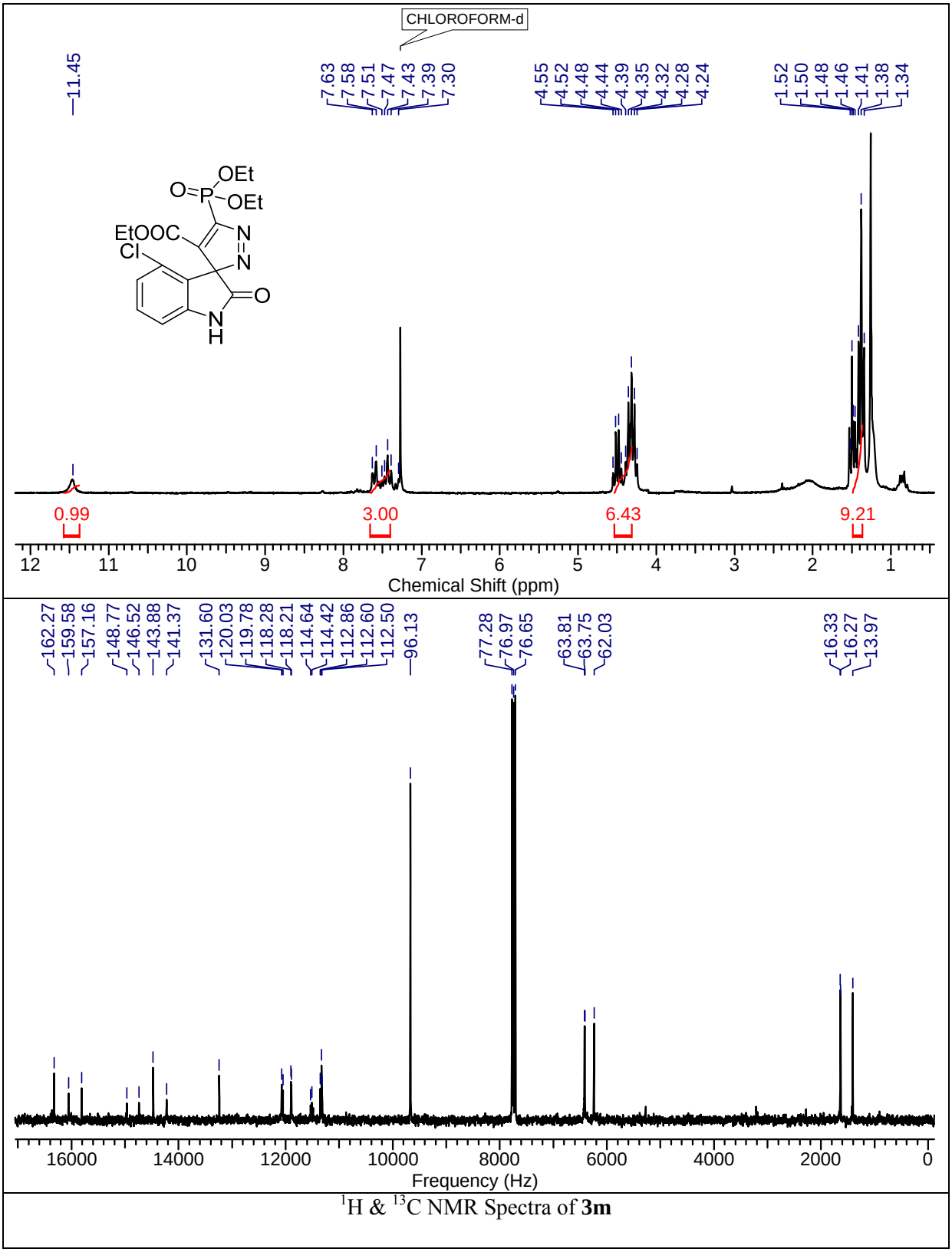


^{1}H & ^{13}C NMR Spectra of **4**

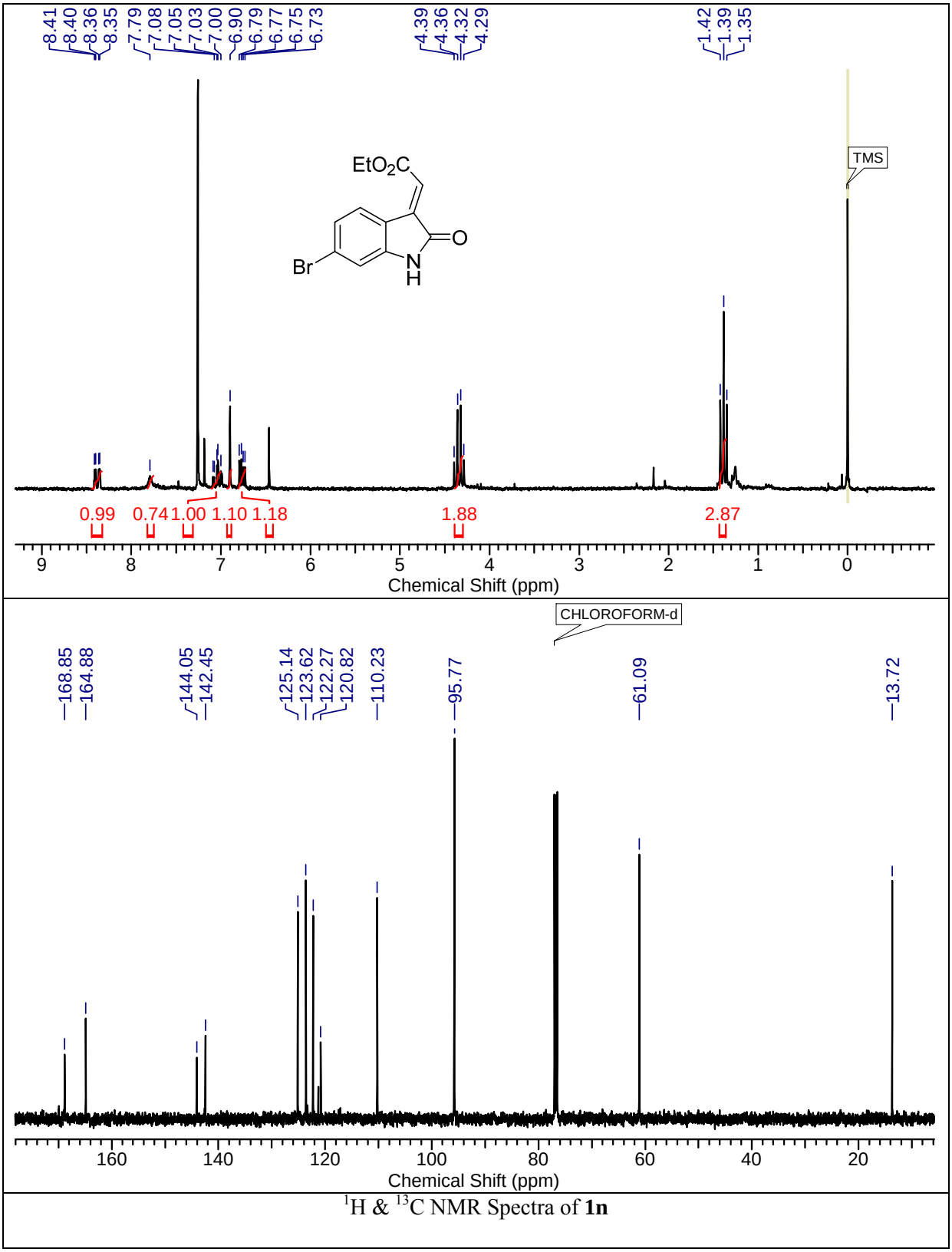




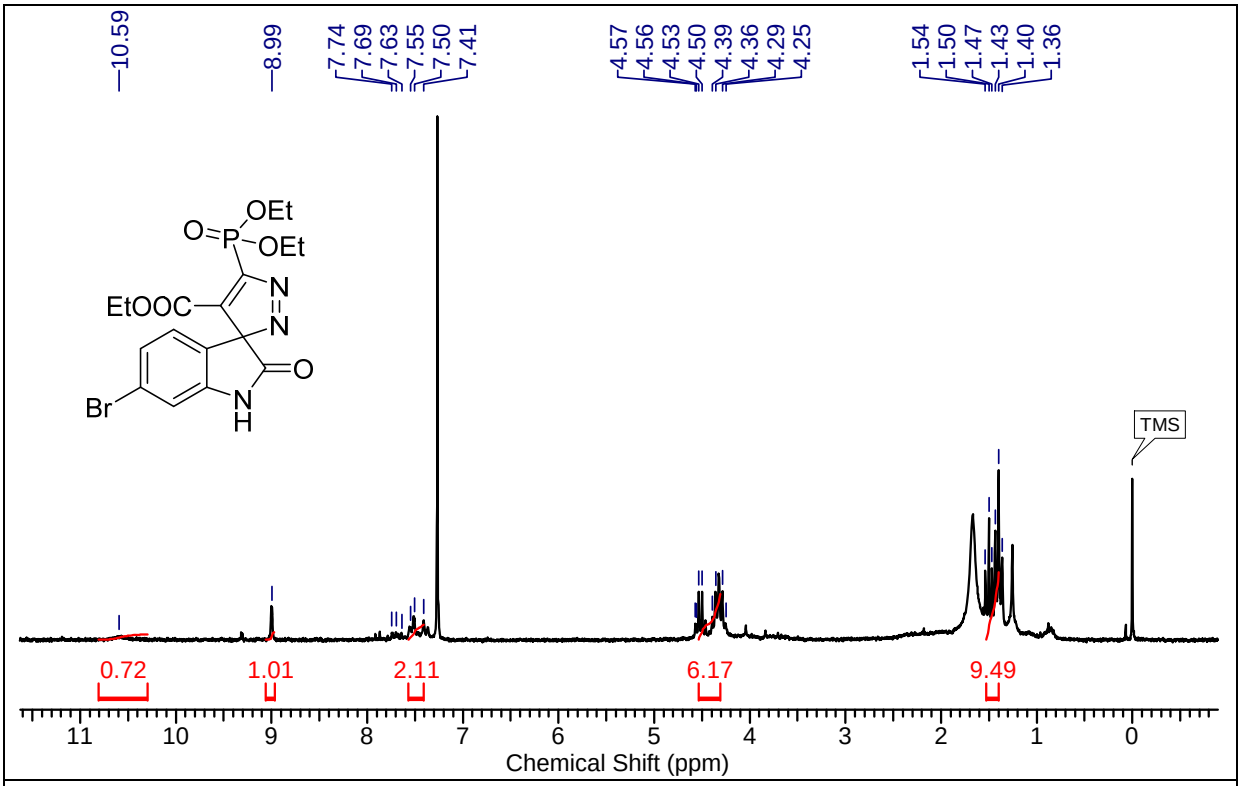
^{1}H & ^{13}C NMR Spectra of **1m**

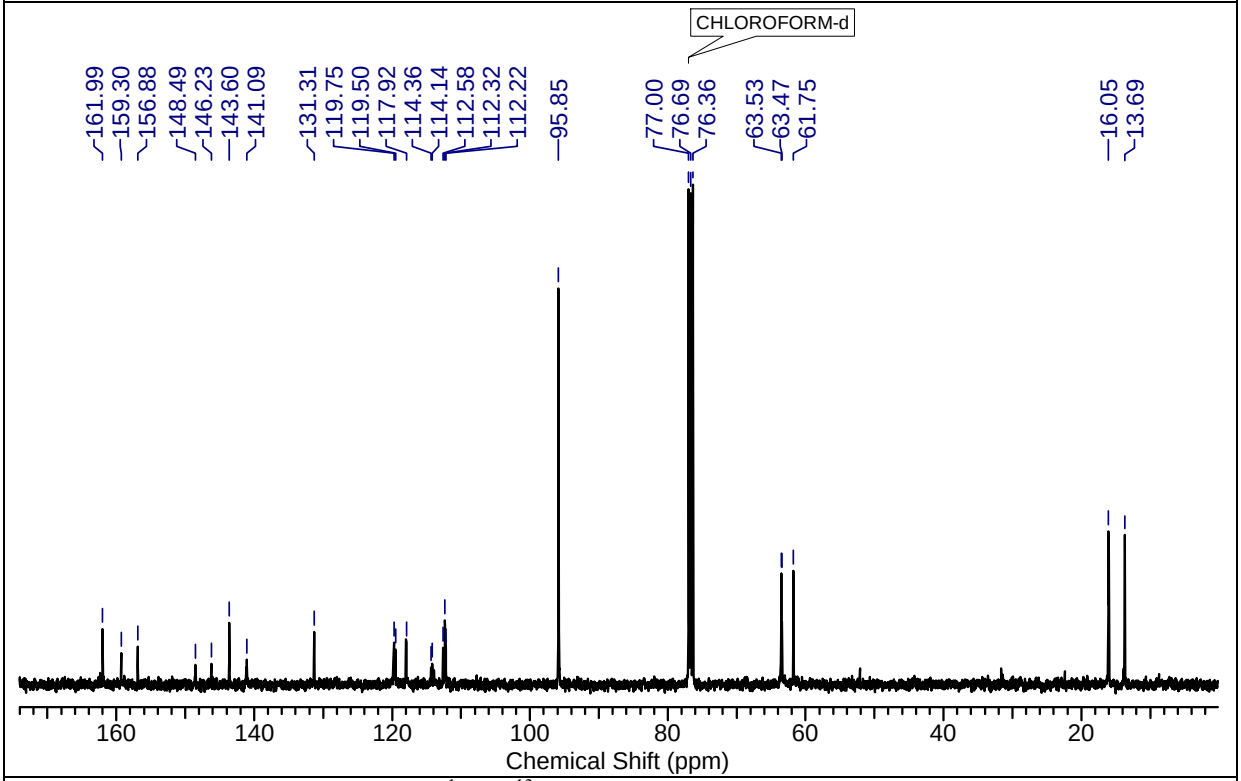


^{1}H & ^{13}C NMR Spectra of **3m**

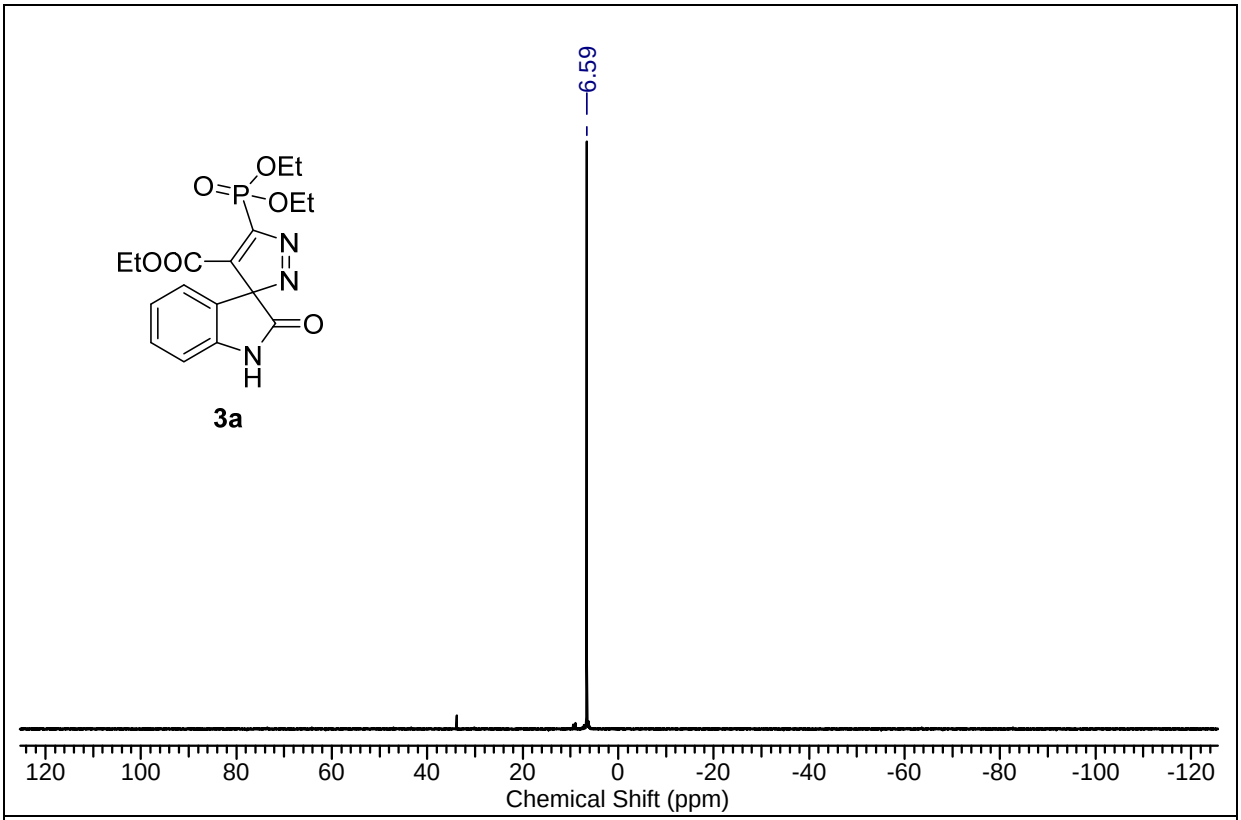


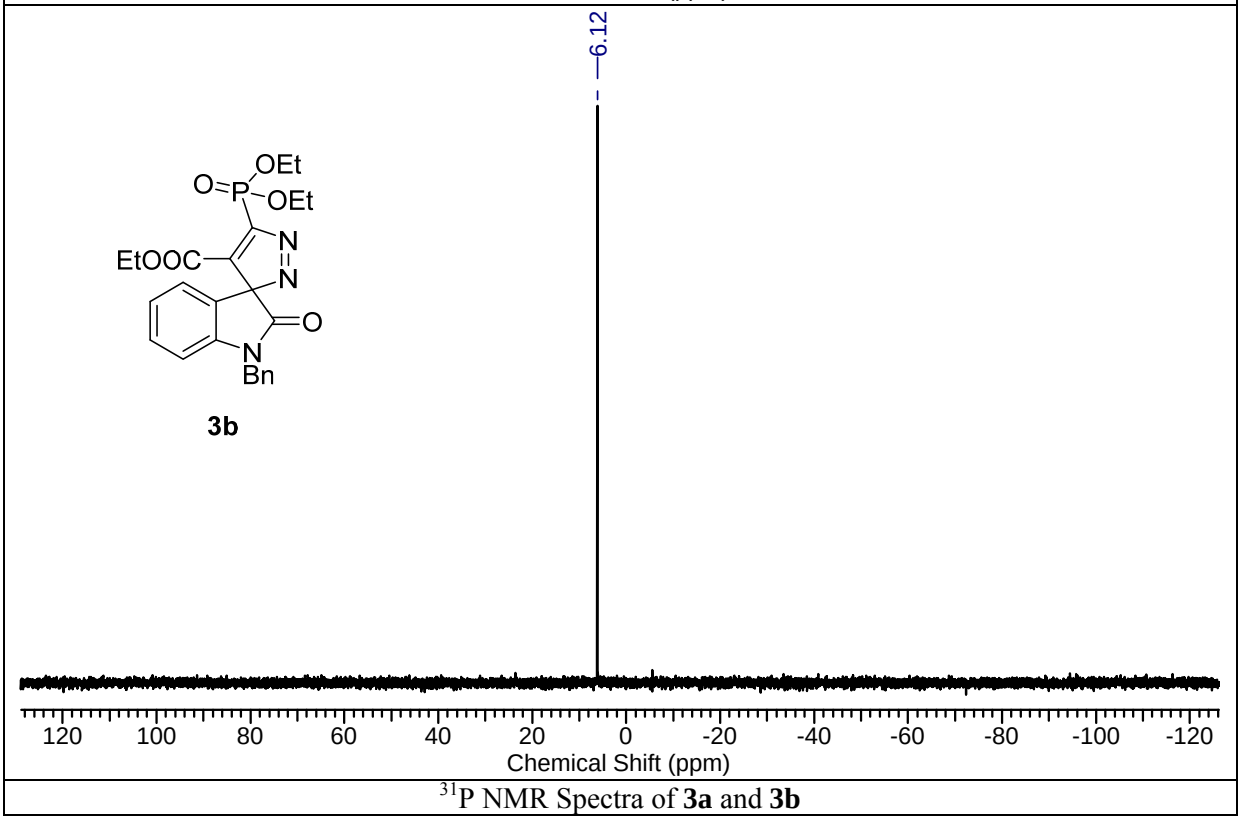
^{1}H & ^{13}C NMR Spectra of **1n**



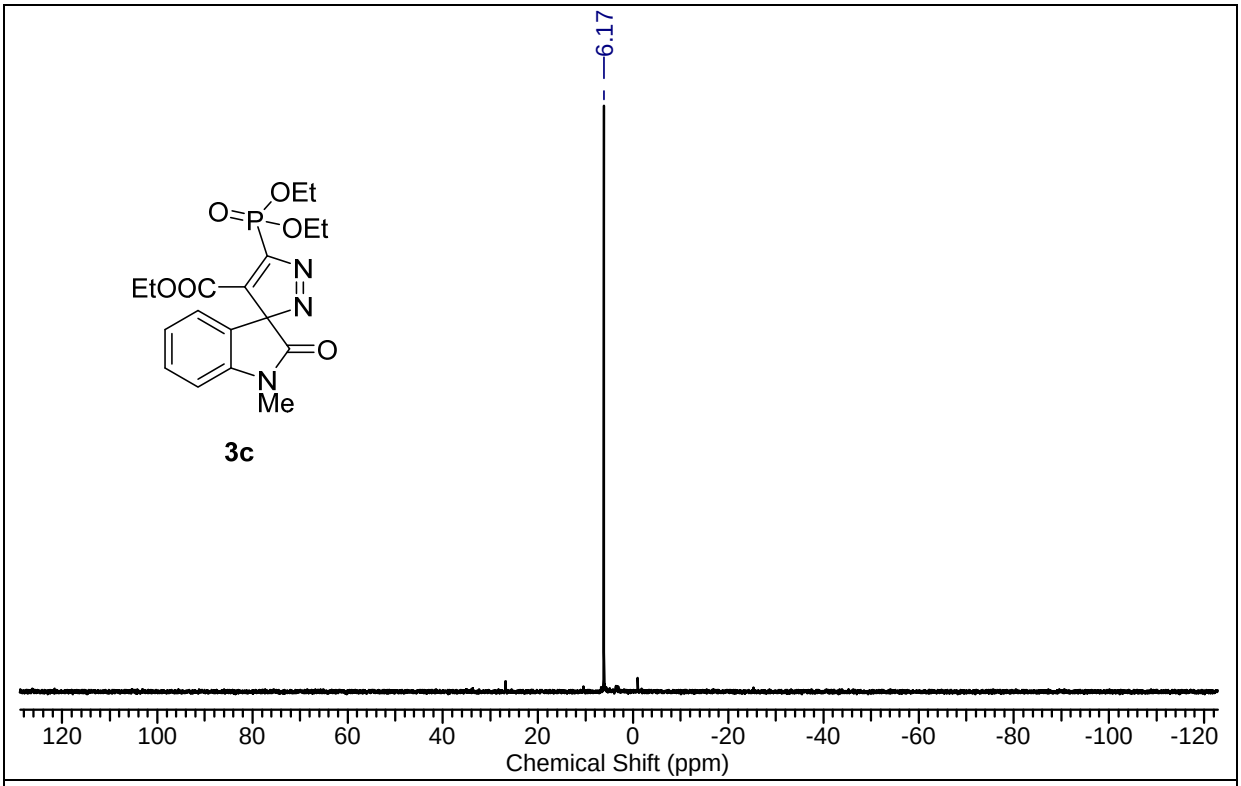


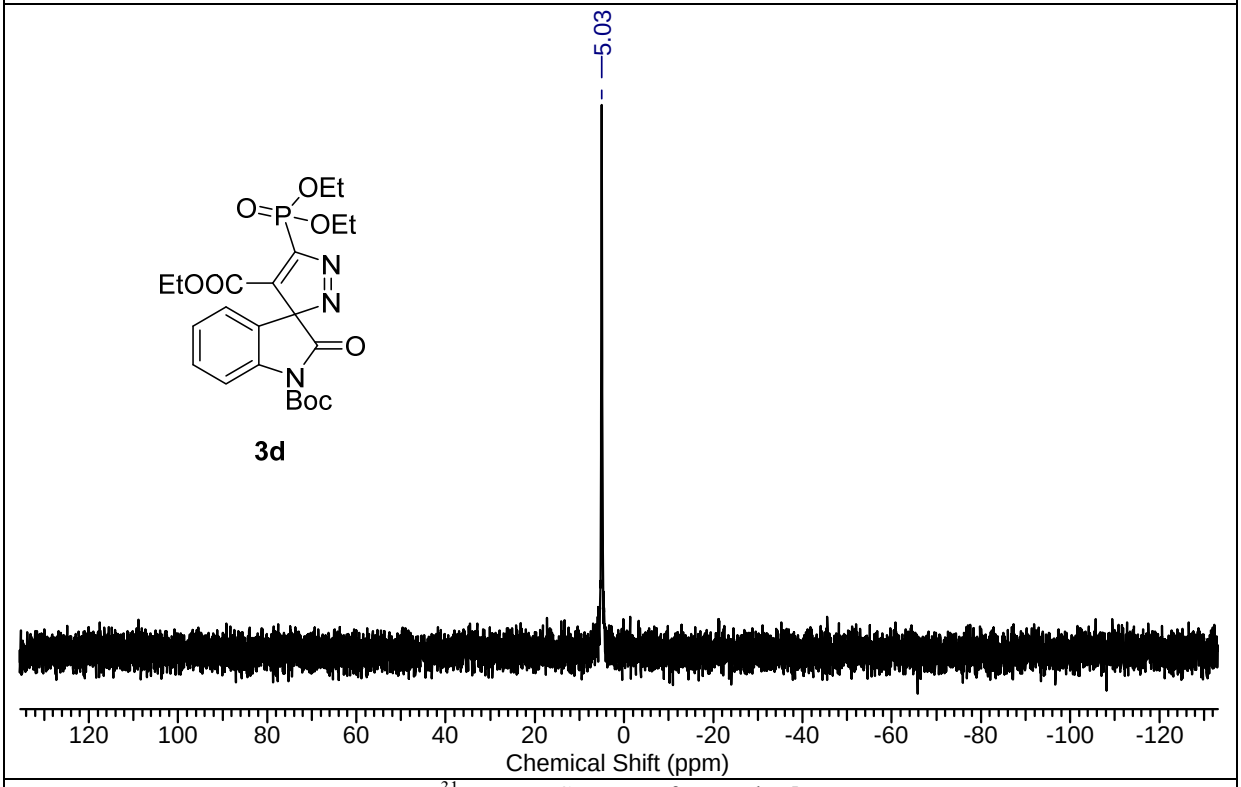
^{1}H & ^{13}C NMR Spectra of **3n**



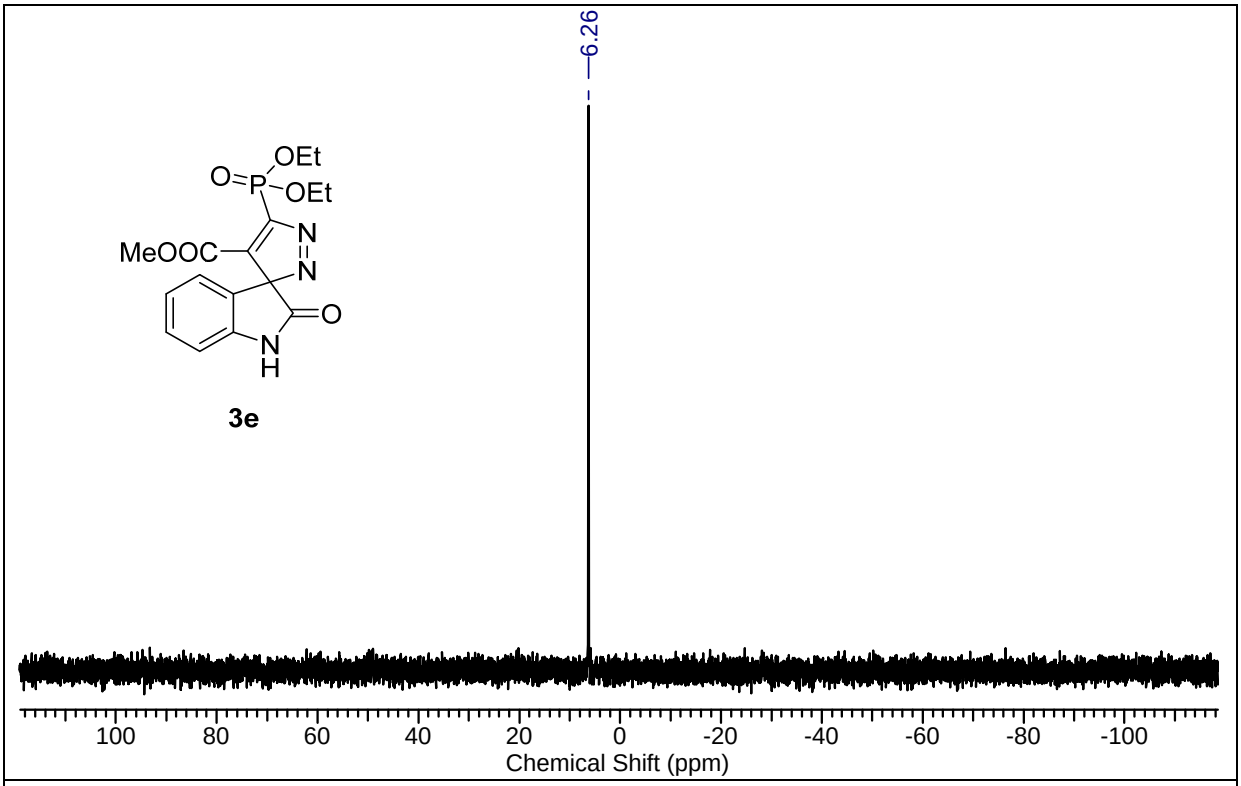


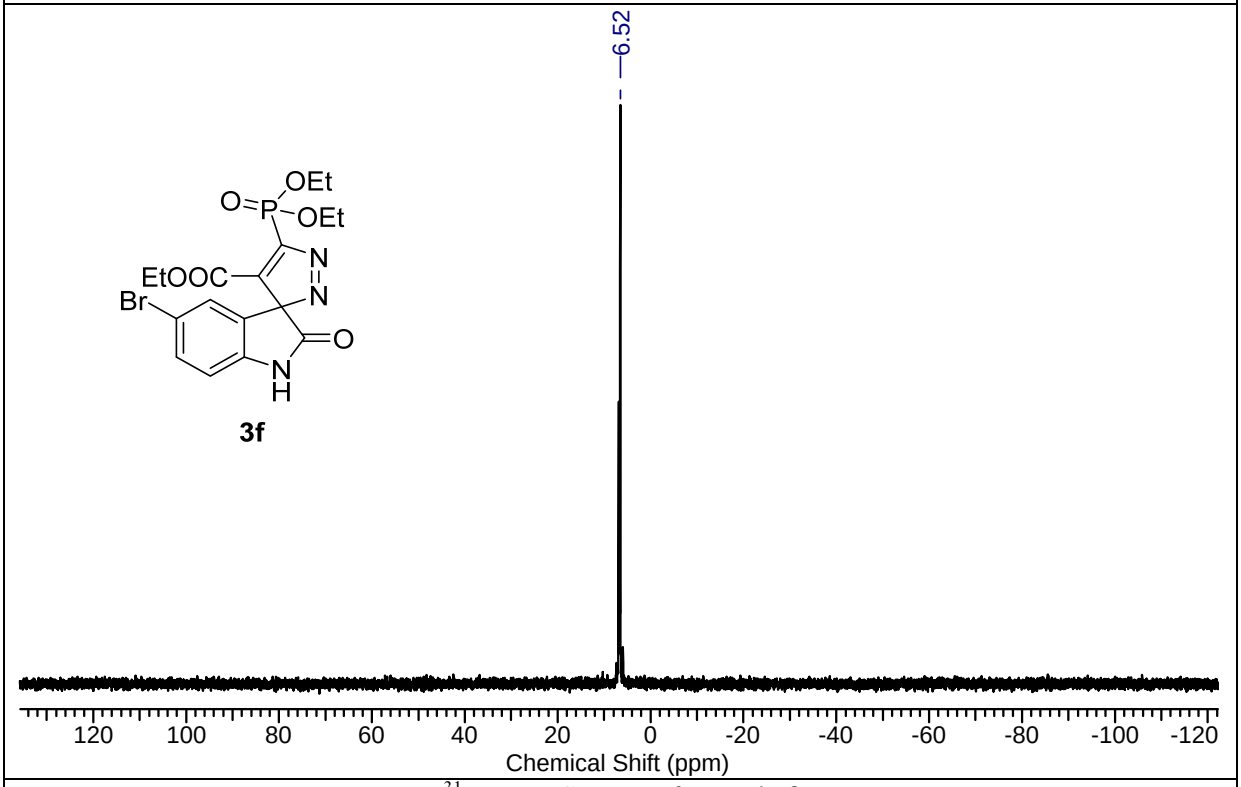
^{31}P NMR Spectra of **3a** and **3b**



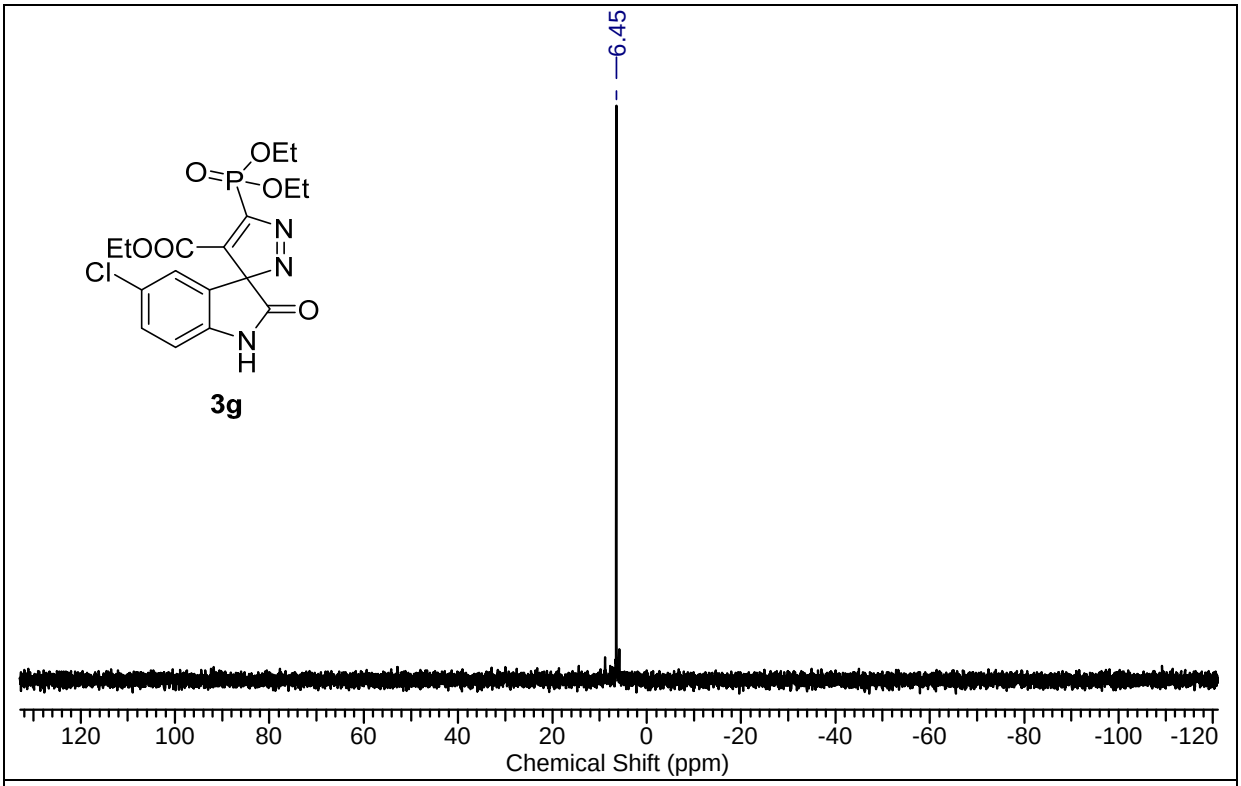


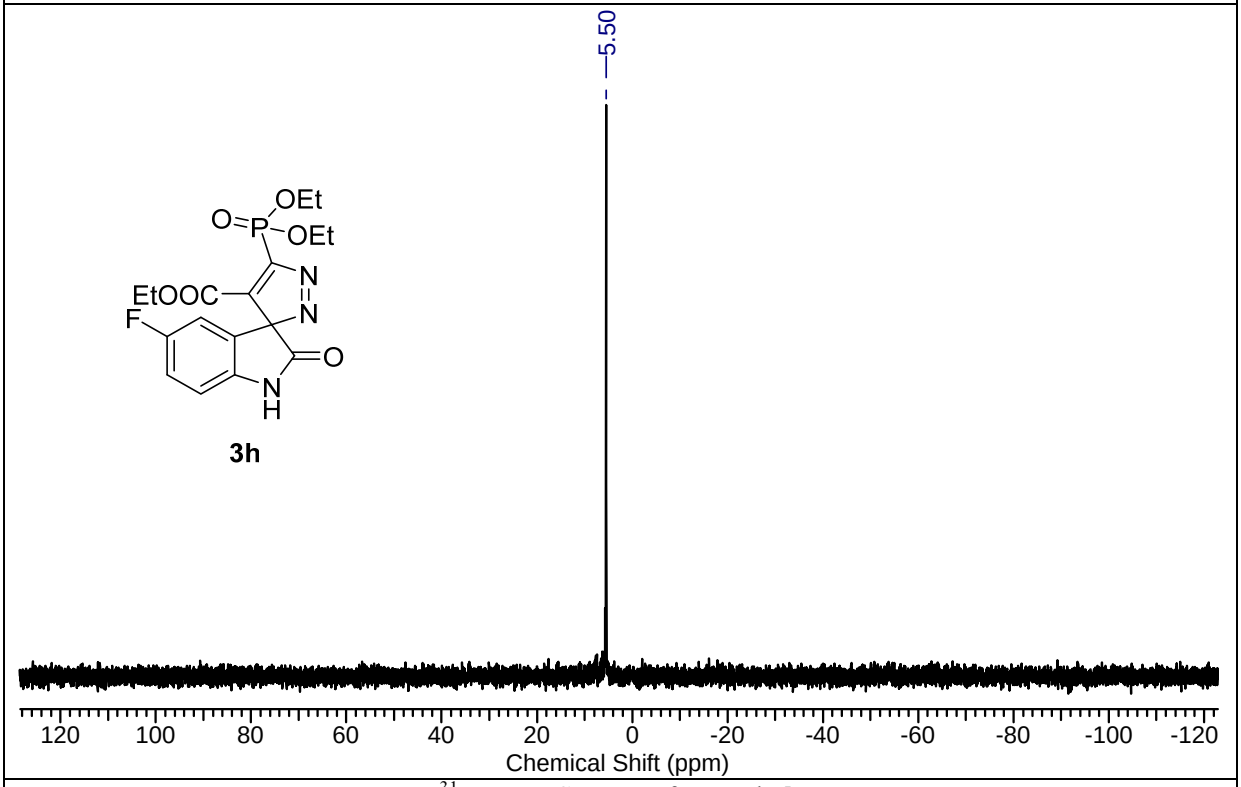
^{31}P NMR Spectra of **3c** and **3d**



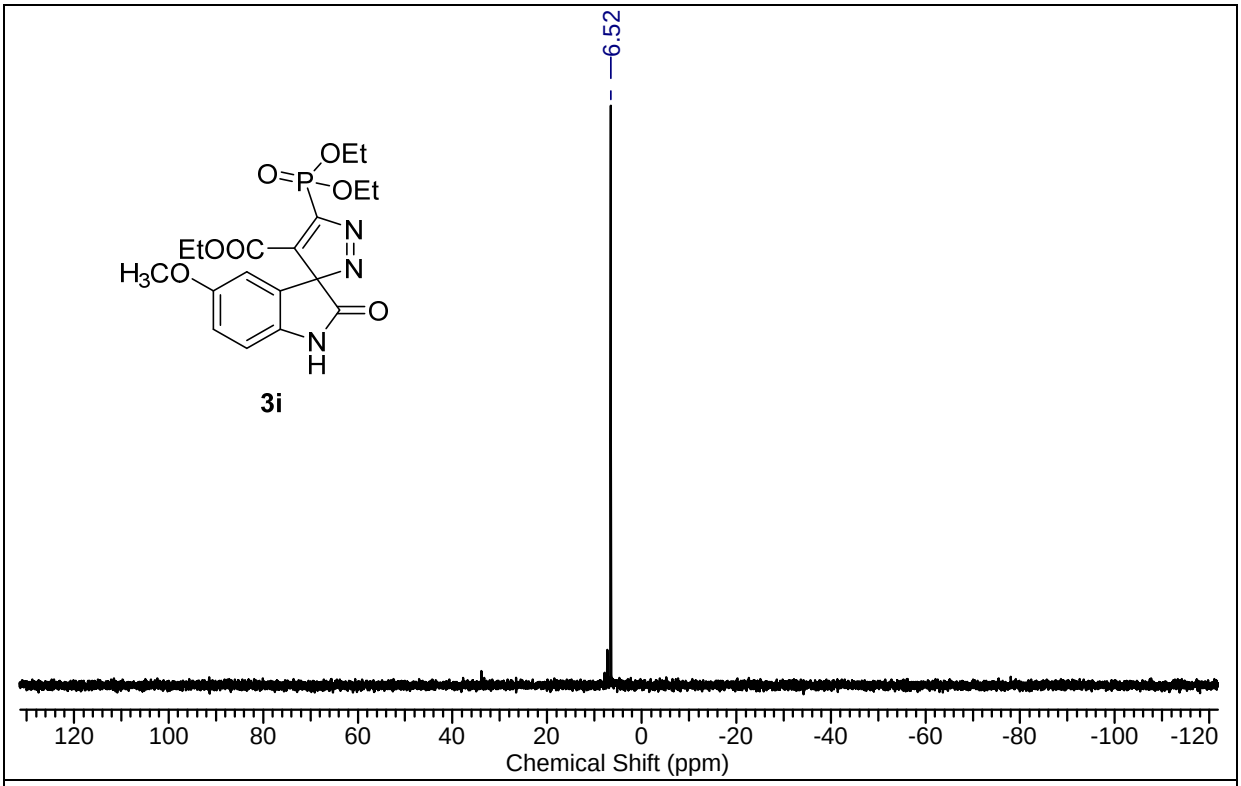


^{31}P NMR Spectra of **3e** and **3f**

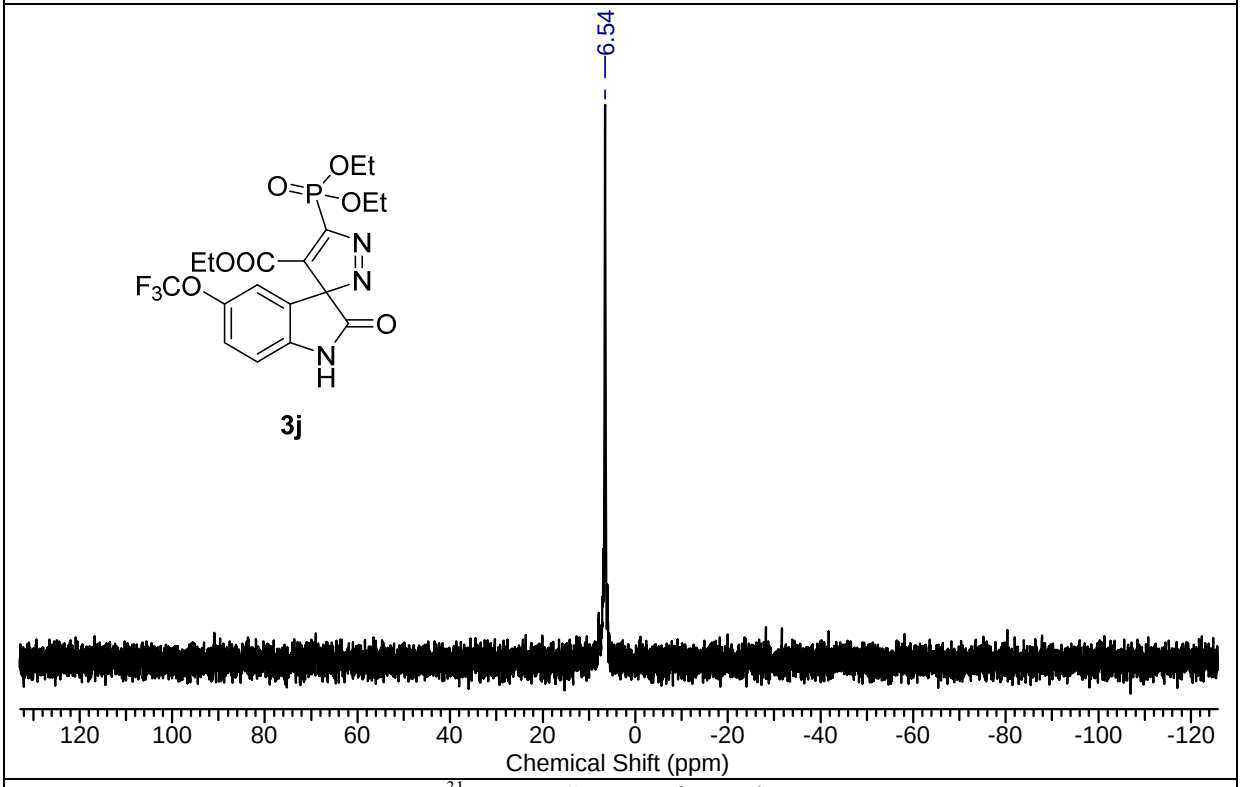




^{31}P NMR Spectra of **3g** and **3h**

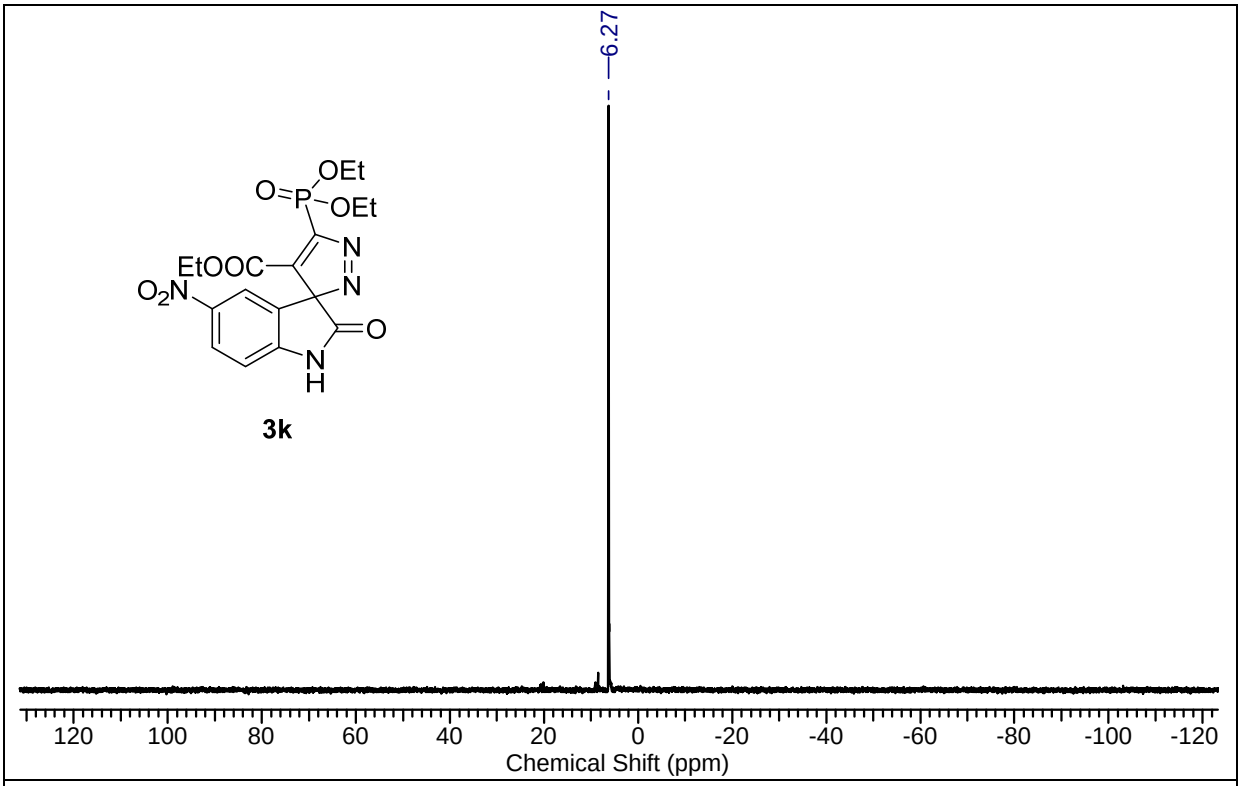


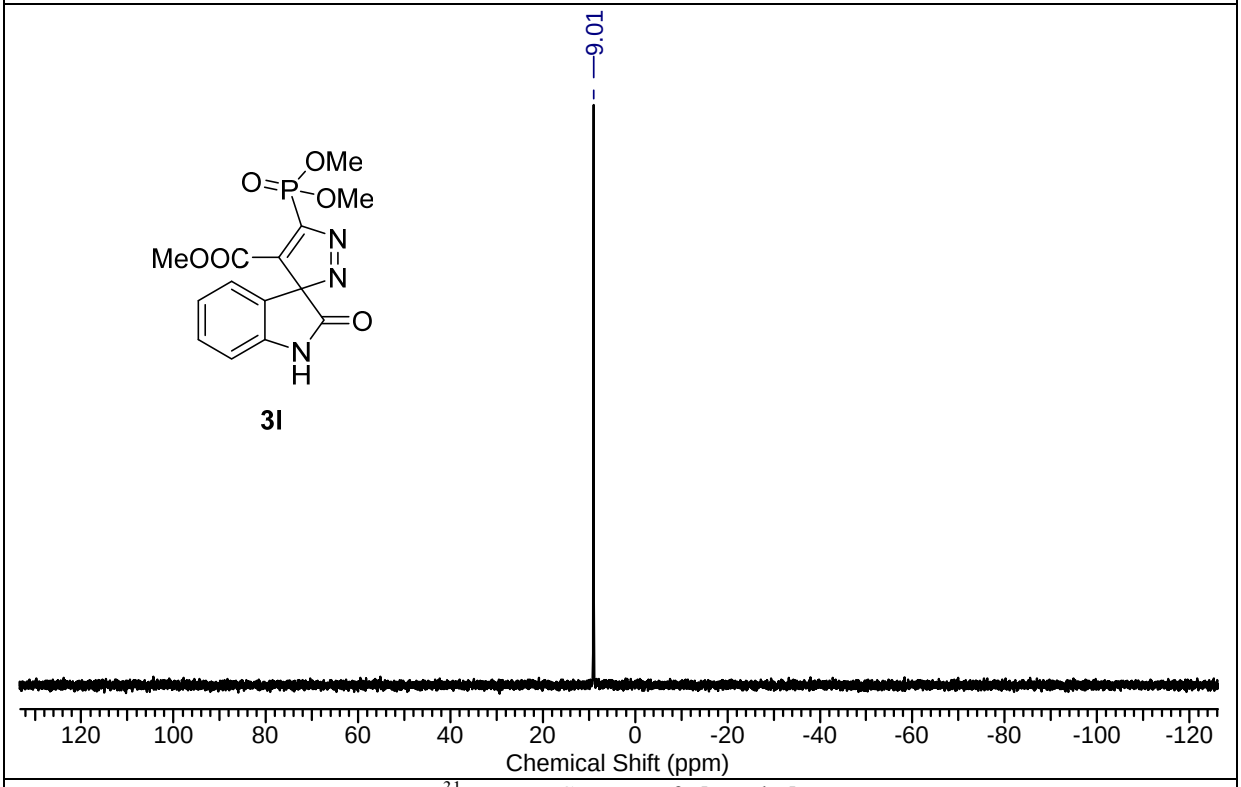
3i



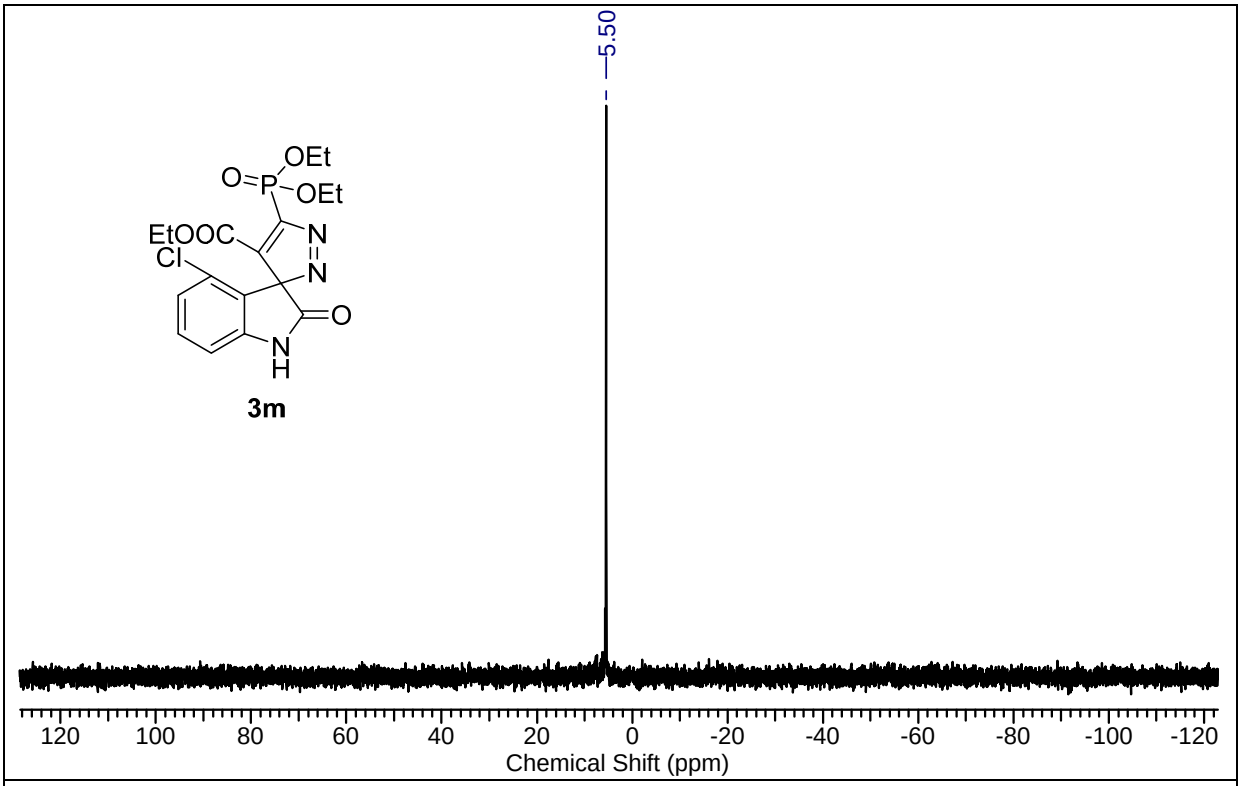
3j

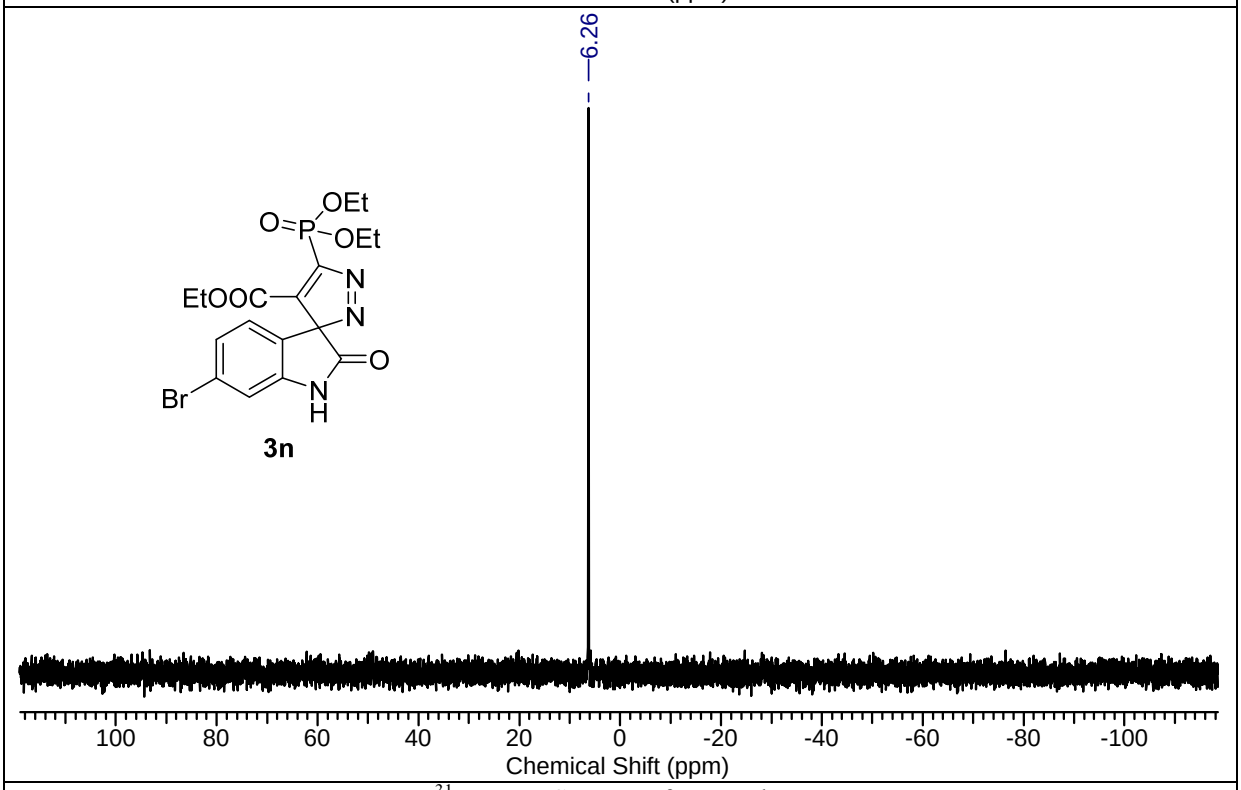
^{31}P NMR Spectra of **3i** and **3j**





^{31}P NMR Spectra of **3k** and **3l**





^{31}P NMR Spectra of **3m** and **3n**

5. X-Ray Crystal Structure of 5