Supporting Information

A base-catalyzed cycloisomerization of 5-cyano-pentyne derivatives: efficient synthesis of 3-cyano-4,5-dihydro-1*H*-pyrroles

Jia Meng,[a,b] Yi-Jin Li,[a] Yu-Long Zhao,*[a] Xiu-Bin Bu[a] and Qun Liu*[a]

[a] Department of Chemistry, Northeast Normal University, Changchun, 130024, China.
[b] Department of Chemistry, Mudanjiang Normal University, Mudanjiang, 157012, China.

e-mail: zhaoyl351@nenu.edu.cn; liuqun@nenu.edu.cn

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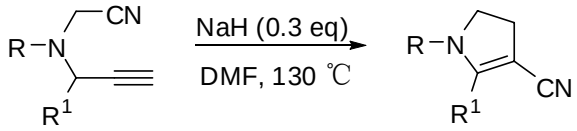
I. General Information

All reagents were commercial and were used without further purification. Chromatography was carried on flash silica gel (300-400 mesh). All reactions were monitored by TLC, which was performed on precoated aluminum sheets of silica gel 60 (F_{254}). Melting points were uncorrected. The ^{1}H NMR spectra were recorded at 500 MHz in $CDCl_3$ and the ^{13}C NMR spectra were recorded at 125 MHz in $CDCl_3$ with TMS as internal standard. All coupling constants (*J* values) were reported in Hertz (Hz). High-resolution mass spectra (HRMS) were obtained using a Bruker microTOF II focus spectrometer (ESI). The compound **2a** was glued on a glass fiber. Data were collected at 293 K using graphite-monochromated Mo Kα radiation (λ = 0.71073Å) and IP technique in the range 2.19° < θ < 27.48°. Empirical absorption correction was applied. The structures were solved by the direct method and refined by the full-matrix least-squares method on F^2 using the SHELXS 97 crystallographic software package. Anisotropic thermal parameters were used to refine all non-hydrogen atoms. Hydrogen atoms were located from difference Fourier maps.

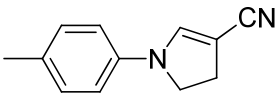
II. General Procedure for the Preparation of 2 from 1 (1a as Example):



1 **2**

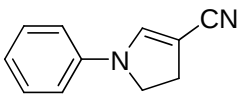
To a stirred solution of 2-(prop-2-ynyl(p-tolyl)amino)acetonitrile **1a** (0.5 mmol, 92 mg) in DMF (2.0 mL) was added NaH (NaH 60%, 0.25 mmol, 6 mg) in one portion. The reaction mixture was stired for 7 h at 130 °C. After **1a** was consumed (monitored by TLC), the reaction mixture was poured into ice-water (20.0 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to yield the corresponding crude product, which was purified by chromatography (silica gel, petroleum ether/ethyl acetate = 10/1, V/V) to give **2a** (85 mg, 92%) as a white solid.

1-p-Tolyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2a):



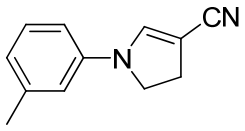
White solid; m.p. 110-112 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.29 (s, 3H), 2.97 (t, J = 10.0 Hz, 2H), 3.92 (t, J = 10.0 Hz, 2H), 6.74 (d, J = 8.5 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.40 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 20.4, 28.7, 48.9, 81.7, 113.9 (2C), 119.0, 130.0 (2C), 131.0, 138.5, 145.1; HRMS (ESI-TOF) Calcd for $C_{12}H_{13}N_2^+$ ($[M + H]^+$): 185.1073. Found 185.1080.

1-Phenyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2b):



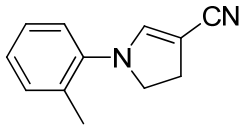
White solid; m.p. 95-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.98 (t, J = 10.0 Hz, 2H), 3.94 (t, J = 10.0 Hz, 2H), 6.83 (d, J = 8.0 Hz, 2H), 6.97 (t, J = 7.0 Hz, 1H), 7.31 (t, J = 7.5 Hz, 2H), 7.43 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.7, 48.7, 82.6, 113.9 (2C), 118.6, 121.4, 129.5 (2C), 140.7, 144.7; HRMS (ESI-TOF) Calcd for $C_{11}H_{11}N_2^+$ ($[M + H]^+$): 171.0917. Found 171.0923.

1-m-Tolyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2c):



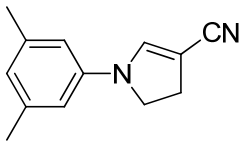
White solid; m.p. 138-140 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.34 (s, 3H), 2.98 (td, J = 10.0, 1.5 Hz, 2H), 3.93 (t, J = 10.0 Hz, 2H), 6.64 (d, J = 7.5 Hz, 2H), 6.79 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.0 Hz, 1H), 7.44 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.6, 28.7, 48.8, 82.4, 111.1, 114.7, 118.8, 122.4, 129.4, 139.6, 140.8, 144.9; HRMS (ESI-TOF) Calcd for $C_{12}H_{13}N_2^+$ ($[M + H]^+$): 185.1073. Found 185.1075.

1-o-Tolyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2d):



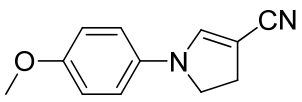
Light yellow liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.31 (s, 3H), 2.95 (td, J = 10.0, 1.5 Hz, 2H), 3.84 (t, J = 10.0 Hz, 2H), 6.97 (dd, J = 7.5, 1.0 Hz, 1H), 7.01 (s, 1H), 7.09-7.13 (m, 1H), 7.13-7.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 18.7, 29.3, 53.0, 80.9, 119.1, 122.5, 125.8, 127.0, 131.7, 131.9, 141.6, 151.3; HRMS (ESI-TOF) Calcd for $C_{12}H_{13}N_2^+$ ($[M + H]^+$): 185.1073. Found 185.1075.

1-(3,5-Dimethylphenyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2e):



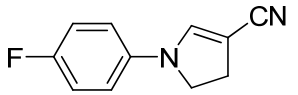
White solid; m.p. 170-172 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.29 (s, 6H), 2.95 (t, J = 10.0 Hz, 2H), 3.90 (t, J = 10.0 Hz, 2H), 6.45 (s, 2H), 6.62 (s, 1H), 7.41 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.4 (2C), 28.7, 48.8, 82.0, 111.9 (2C), 118.9, 123.3, 139.3 (2C), 140.7, 145.0; HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2^+$ ($[M + H]^+$): 199.1230. Found 199.1233.

1-(4-Methoxyphenyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2f):



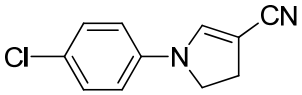
White solid; m.p. 104-106 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.96 (t, J = 10.0 Hz, 2H), 3.77 (s, 3H), 3.90 (t, J = 10.0 Hz, 2H), 6.78 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 9.0 Hz, 2H), 7.33 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.9, 49.5, 55.6, 81.1, 114.9 (2C), 115.5 (2C), 119.1, 134.9, 145.6, 154.8; HRMS (ESI-TOF) Calcd for $C_{12}H_{13}N_2O^+$ ($[M + H]^+$): 201.1022. Found 201.1018.

1-(4-Fluorophenyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2g):



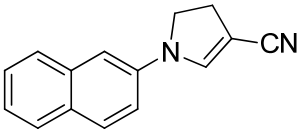
White solid; m.p. 95-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.99 (td, J = 9.5, 1.5 Hz, 2H), 3.92 (t, J = 10.0 Hz, 2H), 6.77-6.79 (m, 2H), 7.02 (t, J = 9.0 Hz, 2H), 7.35 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.9, 49.2, 82.7, 115.2 (d, $^{3}J_{(C\text{-}F)}$ = 7.6 Hz, 2C), 116.2 (d, $^{2}J_{(C\text{-}F)}$ = 22.8 Hz, 2C), 118.6, 137.3, 145.0, 156.8 (d, $^{1}J_{(C\text{-}F)}$ = 239.8 Hz); HRMS (ESI-TOF) Calcd for $C_{11}H_{10}FN_2^+$ ($[M + H]^+$): 189.0823. Found 189.0829.

1-(4-Chlorophenyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2h):



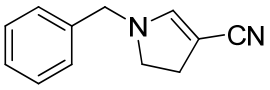
White solid; m.p. 99-101 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.99 (t, J = 10.0 Hz, 2H), 3.92 (t, J = 10.0 Hz, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.37 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.9, 48.9, 83.7, 115.0 (2C), 118.3, 126.4, 129.5 (2C), 139.5, 144.3; HRMS (ESI-TOF) Calcd for $C_{11}H_{10}ClN_2^+$ ($[M + H]^+$): 205.0527. Found 205.0538.

1-(Naphthalen-2-yl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2i):



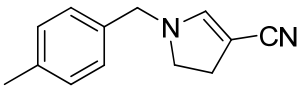
White solid; m.p. 184-186 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.01 (t, J = 10.5 Hz, 2H), 4.02 (t, J = 10.5 Hz, 2H), 7.01 (s, 1H), 7.12 (d, J = 9.5 Hz, 1H), 7.35 (d, J = 7.0 Hz, 1H), 7.43-7.47 (m, 1H), 7.54 (s, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.7, 48.9, 83.0, 109.3, 115.0, 118.7, 124.1, 126.6, 127.0, 127.6, 128.9, 129.6, 134.1, 138.3, 144.7; HRMS (ESI-TOF) Calcd for $C_{15}H_{13}N_2^+$ ([M + H]$^+$): 221.1073. Found 221.1086.

1-Benzyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2j):



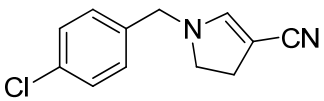
Light yellow liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.77 (t, J = 10.0 Hz, 2H), 3.32 (t, J = 10.0 Hz, 2H), 4.16 (s, 2H), 6.84 (s, 1H), 7.22 (d, J = 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 7.36 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 29.3, 50.9, 54.4, 76.7, 119.7, 127.8 (2C), 127.9, 128.7 (2C), 135.8, 153.3; HRMS (ESI-TOF) Calcd for $C_{12}H_{13}N_2^+$ ([M + H]$^+$): 185.1073. Found 185.1073.

1-(4-Methylbenzyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2k):



White solid; m.p. 86-88 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.34 (s, 3H), 2.75 (t, J = 10.0 Hz, 2H), 3.31 (t, J = 10.0 Hz, 2H), 4.11 (s, 2H), 6.82 (s, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.0, 29.3, 50.8, 54.1, 76.7, 119.8, 127.8 (2C), 129.3 (2C), 132.7, 137.6, 153.2; HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2^+$ ([M + H]$^+$): 199.1230. Found 199.1229.

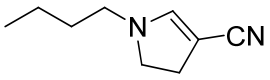
1-(4-Chlorobenzyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2l):



White solid; m.p. 124-126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.77 (t, J = 10.0 Hz, 2H), 3.30 (t, J = 10.0 Hz, 2H), 4.14 (s, 2H), 6.83 (s, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz,

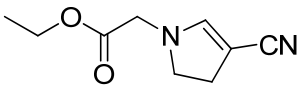
$CDCl_3$) δ: 29.3, 50.8, 53.7, 77.5, 119.4, 128.8 (2C), 129.1 (2C), 133.6, 134.4, 153.1; HRMS (ESI-TOF) Calcd for $C_{12}H_{12}ClN_2^+$ ($[M + H]^+$): 219.0684. Found 219.0680.

1-Butyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2m):



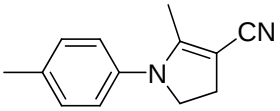
Light yellow liquid; ^1H NMR (500 MHz, $CDCl_3$) δ: 0.92 (t, J = 7.0 Hz, 3H), 1.29-1.34 (m, 2H), 1.46-1.52 (m, 2H), 2.78 (t, J = 10.0 Hz, 2H), 3.01 (t, J = 7.0 Hz, 2H), 3.40 (t, J = 10.0 Hz, 2H), 6.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ : 13.6, 19.7, 29.2, 30.0, 49.9, 51.0, 75.1, 120.3, 153.6; HRMS (ESI-TOF) Calcd for $C_9H_{15}N_2^+$ ($[M + H]^+$): 151.1230. Found 151.1236.

Ethyl 2-(4-cyano-2,3-dihydro-1*H*-pyrrol-1-yl)acetate (2n):



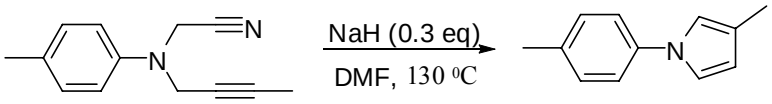
Light yellow liquid; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.29 (t, J = 7.0 Hz, 3H), 2.83 (t, J = 10.0 Hz, 2H), 3.50 (t, J = 10.0 Hz, 2H), 3.78 (s, 2H), 4.21 (q, J = 7.0 Hz, 2H), 6.74 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.1, 29.7, 51.0, 51.7, 61.4, 79.2, 119.1, 153.1, 168.9; HRMS (ESI-TOF) Calcd for $C_9H_{13}N_2O_2^+$ ($[M + H]^+$): 181.0972. Found 181.0971.

2-Methyl-1-p-tolyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (2o):



White solid; m.p. 98-100 °C. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.00 (t, J = 1.5 Hz, 3H), 2.33 (s, 3H), 2.80 (td, J = 9.5, 1.0 Hz, 2H), 3.89 (t, J = 9.5 Hz, 2H), 6.93 (dd, J = 6.5, 1.5 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 13.7, 20.8, 27.3, 54.0, 79.1, 120.6, 129.1 (2C), 129.8 (2C), 134.8, 139.0, 160.6; HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2^+$ ($[M + H]^+$): 199.1230. Found 199.1223.

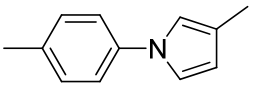
III. General Procedure for the Preparation of 4p and 5p (4p as Example):



1p **4p**

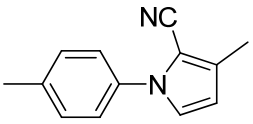
To a stirred solution of 2-(but-2-ynyl(p-tolyl)amino)acetonitrile **1p** (0.5 mmol, 99 mg) in DMF (2.0 mL) was added NaH (NaH 60%, 0.15 mmol, 6 mg) in one portion. The reaction mixture was stired for 7 h at 130 °C. After **1p** was consumed (monitored by TLC), the reaction mixture was poured into ice-water (20.0 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to yield the corresponding crude product, which was purified by chromatography (silica gel, petroleum ether/ethyl acetate = 12/1, V/V) to give **4p** (74 mg, 86%) as a white solid.

3-Methyl-1-p-tolyl-1*H*-pyrrole (4p):



^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.16 (s, 3H), 2.35 (s, 3H), 6.16 (t, J = 2.5 Hz, 1H), 6.83 (d, J = 1.0 Hz, 1H), 6.95 (t, J = 2.5 Hz, 1H), 7.18 (d, J = 8.5 Hz, 2H), 7.22-7.24 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.9, 20.7, 111.5, 117.1, 118.9, 119.9 (2C), 120.7, 129.9 (2C), 134.8, 138.4; HRMS (ESI-TOF) Calcd for $C_{12}H_{14}N^+$ ($[M + H]^+$): 172.1121. Found 172.1131.

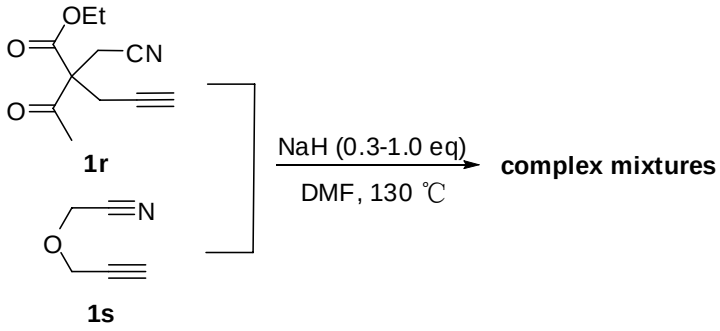
3-Methyl-1-p-tolyl-1*H*-pyrrole-2-carbonitrile (5p):



^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.30 (s, 3H), 2.39 (s, 3H), 6.16 (d, J = 2.5 Hz, 1H), 6.93 (d, J = 2.5 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.9, 20.9, 103.0, 111.4, 113.9, 123.5 (2C), 126.3, 130.1 (2C), 133.9, 136.0, 137.9; HRMS (ESI-TOF) Calcd for $C_{13}H_{13}N_2^+$ ($[M + H]^+$): 197.1073. Found 197.1065.

IV. Results of Cyclization Reactions of 1r or 1s:

In addition, the cyclization reaction of ethyl 2-acetyl-2-(cyanomethyl)pent-4-ynoate **1r** or 2-(prop-2-ynyloxy)acetonitrile **1s** was attempted. However, when the substrate **1r** or **1s** was treated with NaH (0.3-1.0 equiv) in DMF at 130 ^{o}C for 5-10 h, a complex mixture was produced, in which no desired product could be isolated.



V. Crystal data and ORTEP drawing of compound 2a:

Crystal data for **2a**: $C_{12}H_{12}N_2$, white crystal, M = 184.24, Monoclinic, P2(1)/c, a = 7,7787(10) Å, b = 8.3955(11) Å, c = 15.691(2) Å, α = 90.00 º, β = 93.859(2) º, γ = 90.00 º, V = 1022.4(2) Å^3, Z = 4, T = 293(2), F_{000} = 392, R_1 = 0.0523 , wR_2 = 0.1252. CCDC 994058.

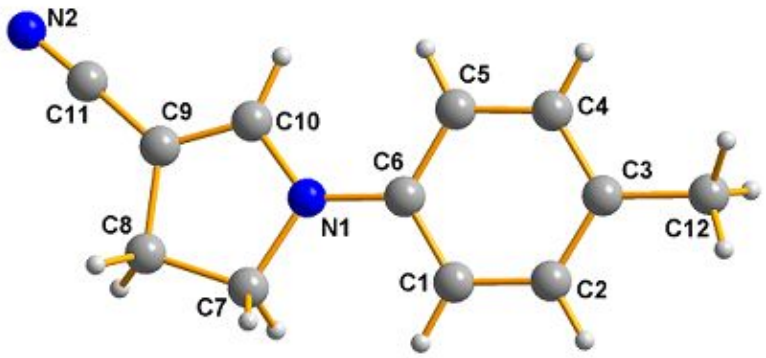


Figure 1 ORTEP drawing of **2a**

VI. ^{1}H and ^{13}C NMR spectra of substrates and products 2, 4 and 5:

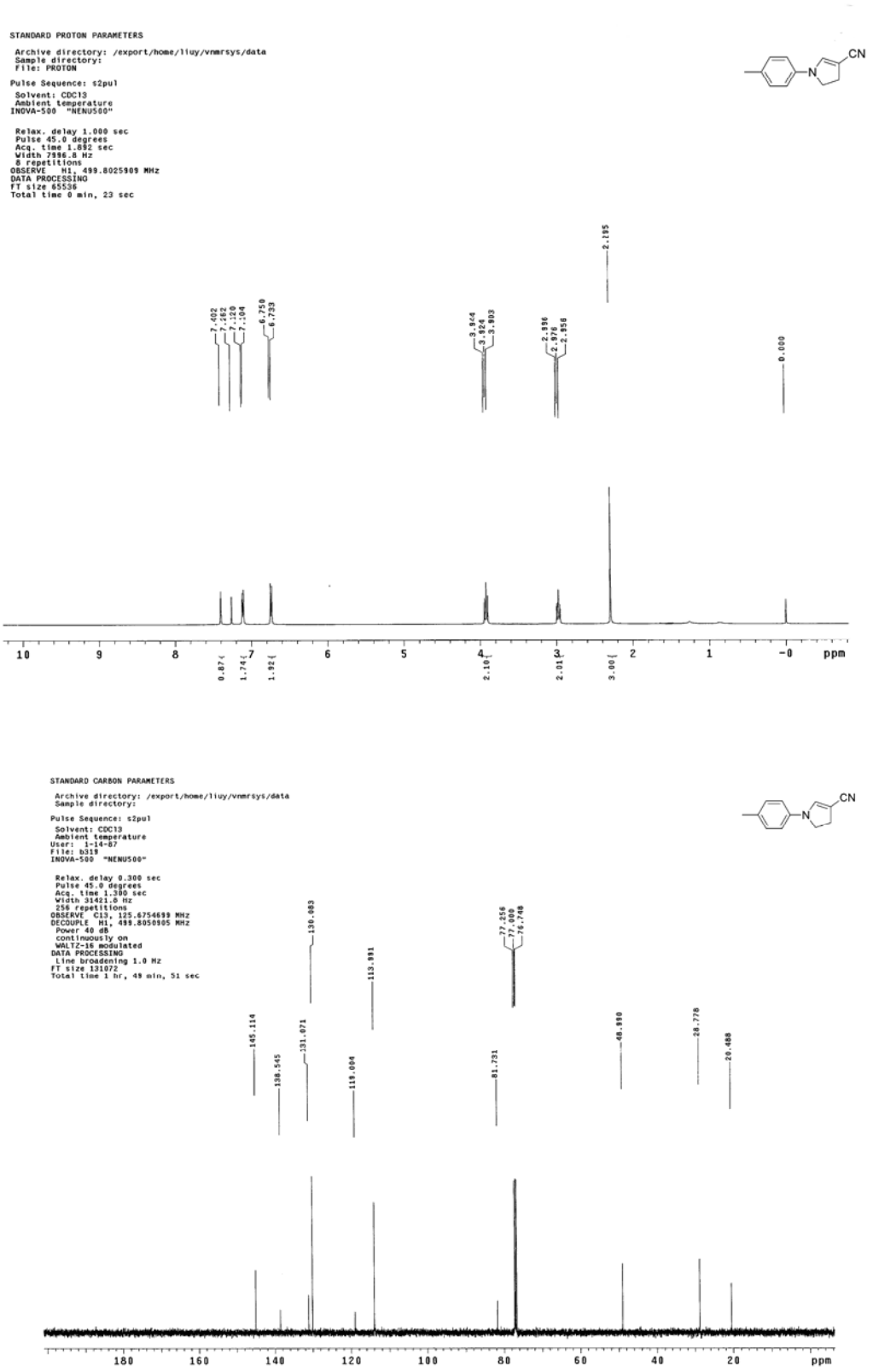


Figure 1. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2a**.

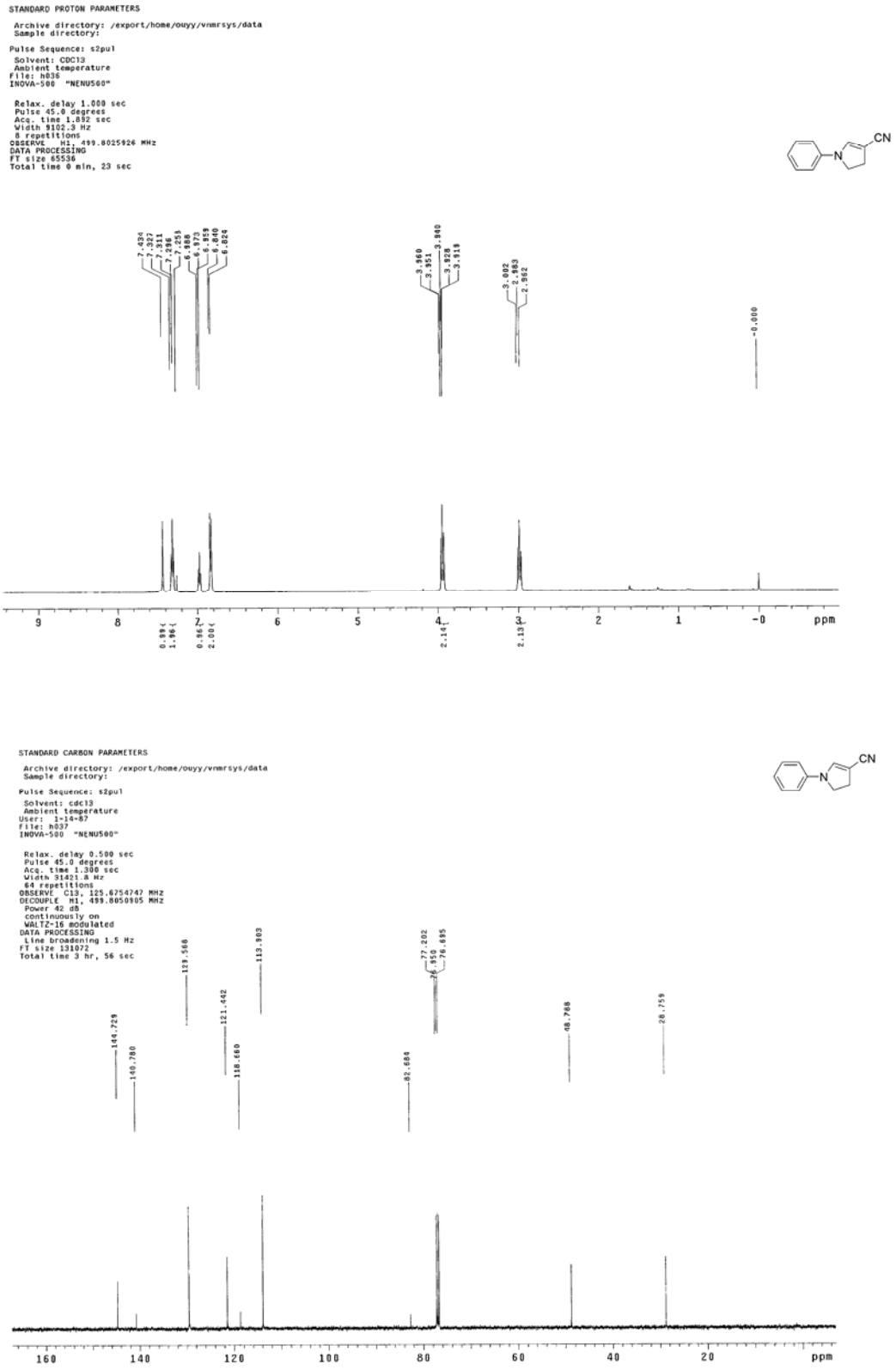


Figure 2. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2b**.

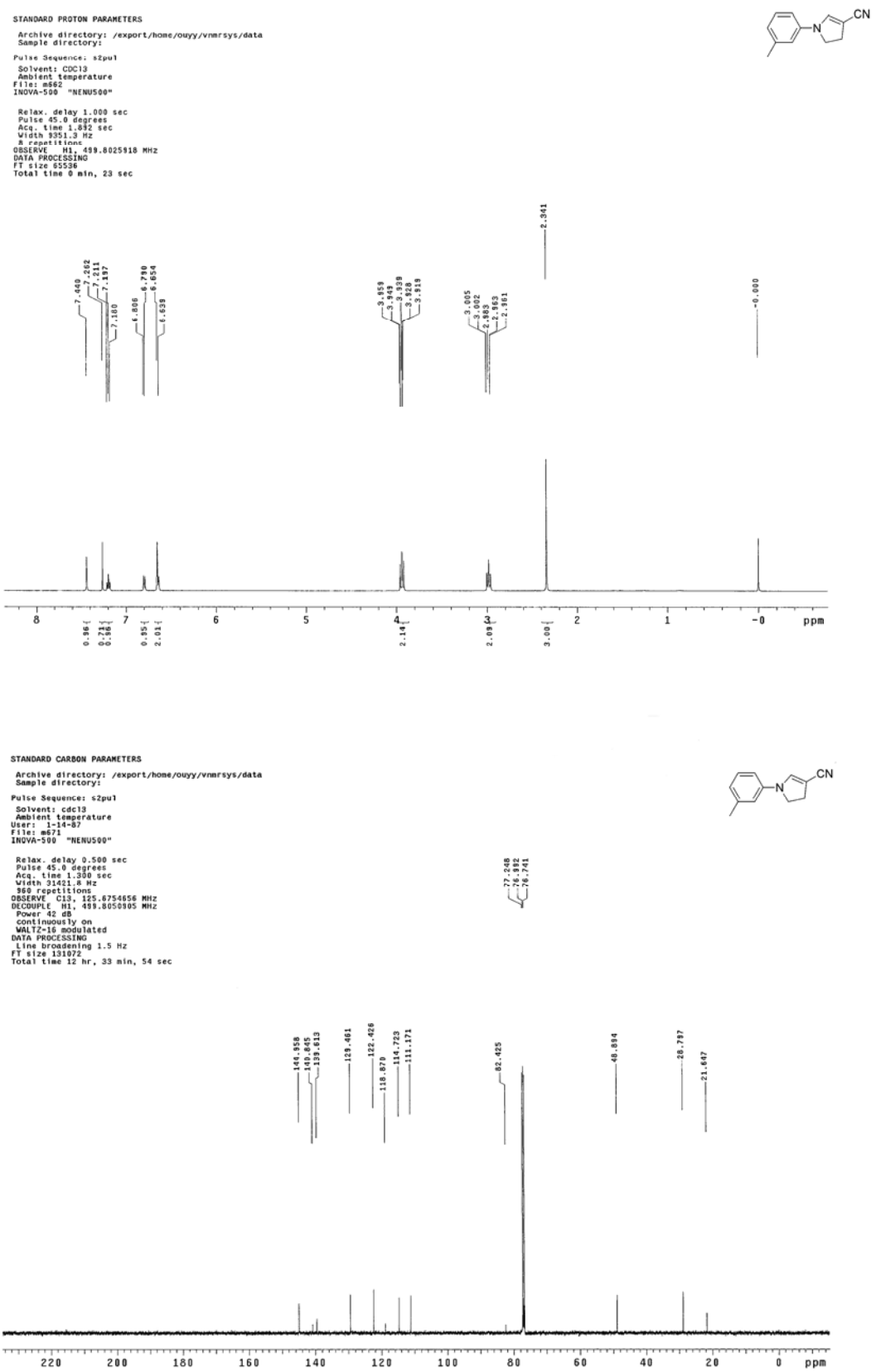


Figure 3. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2c**.

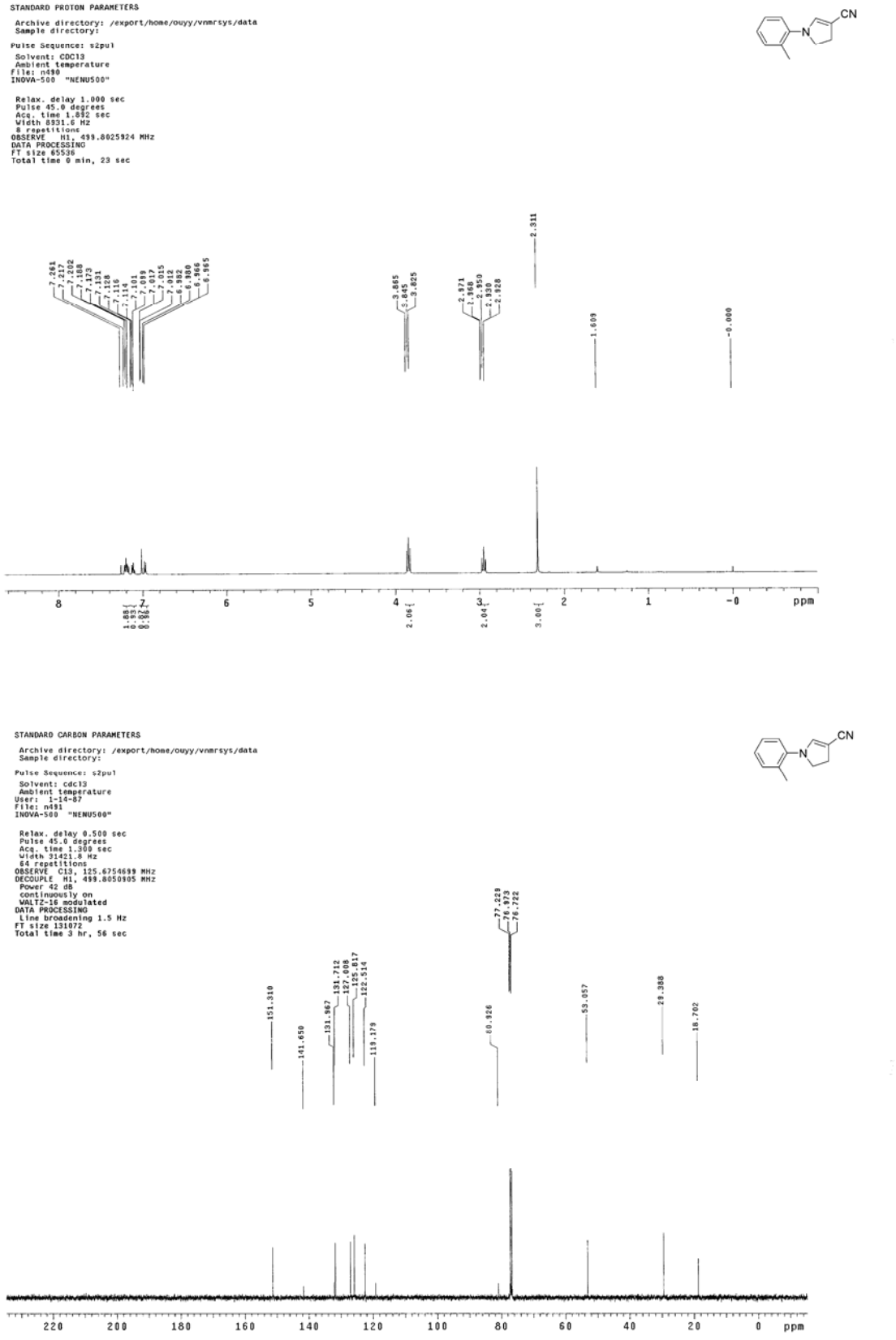


Figure 4. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2d**.

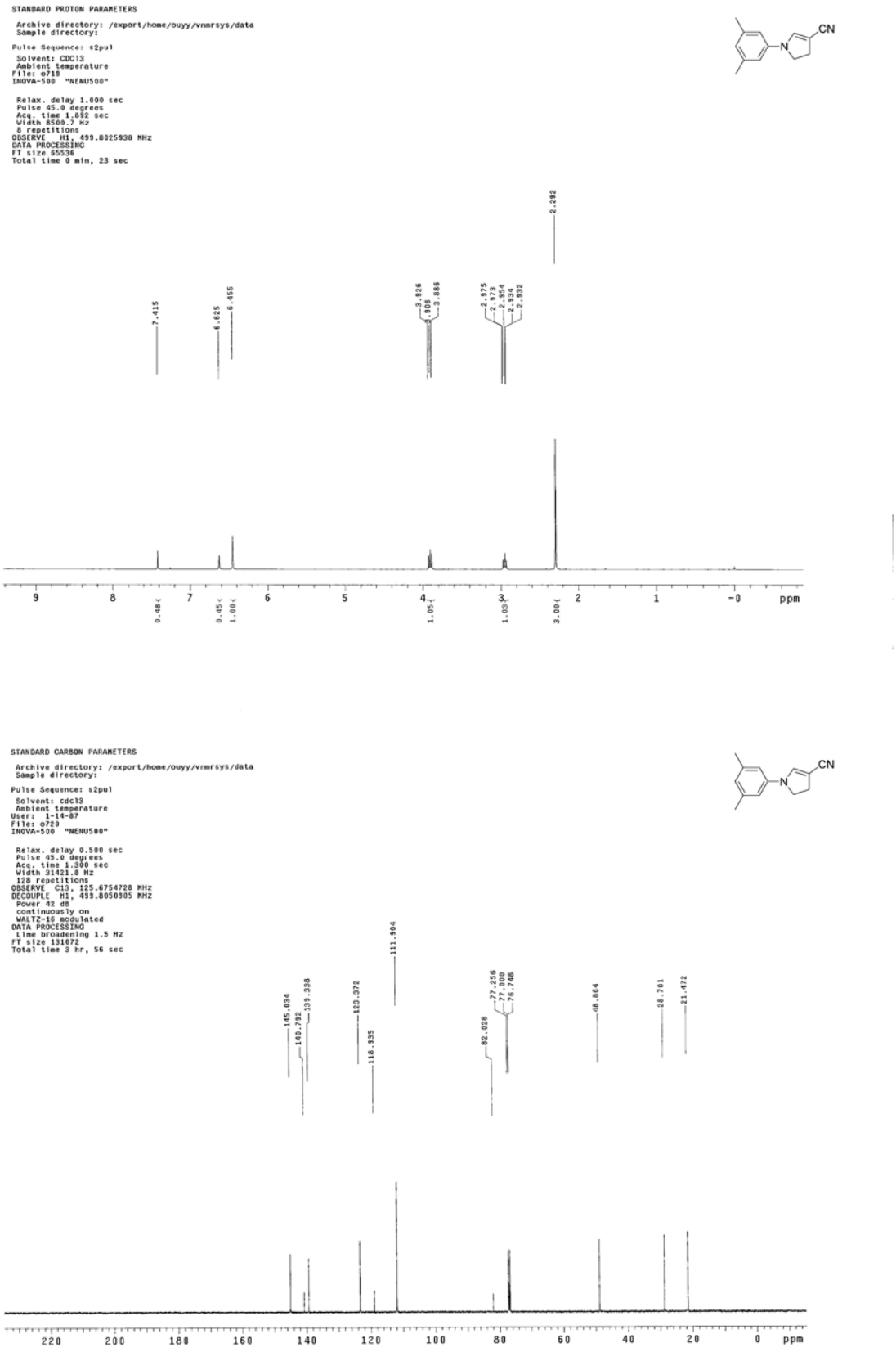


Figure 5. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2e**.

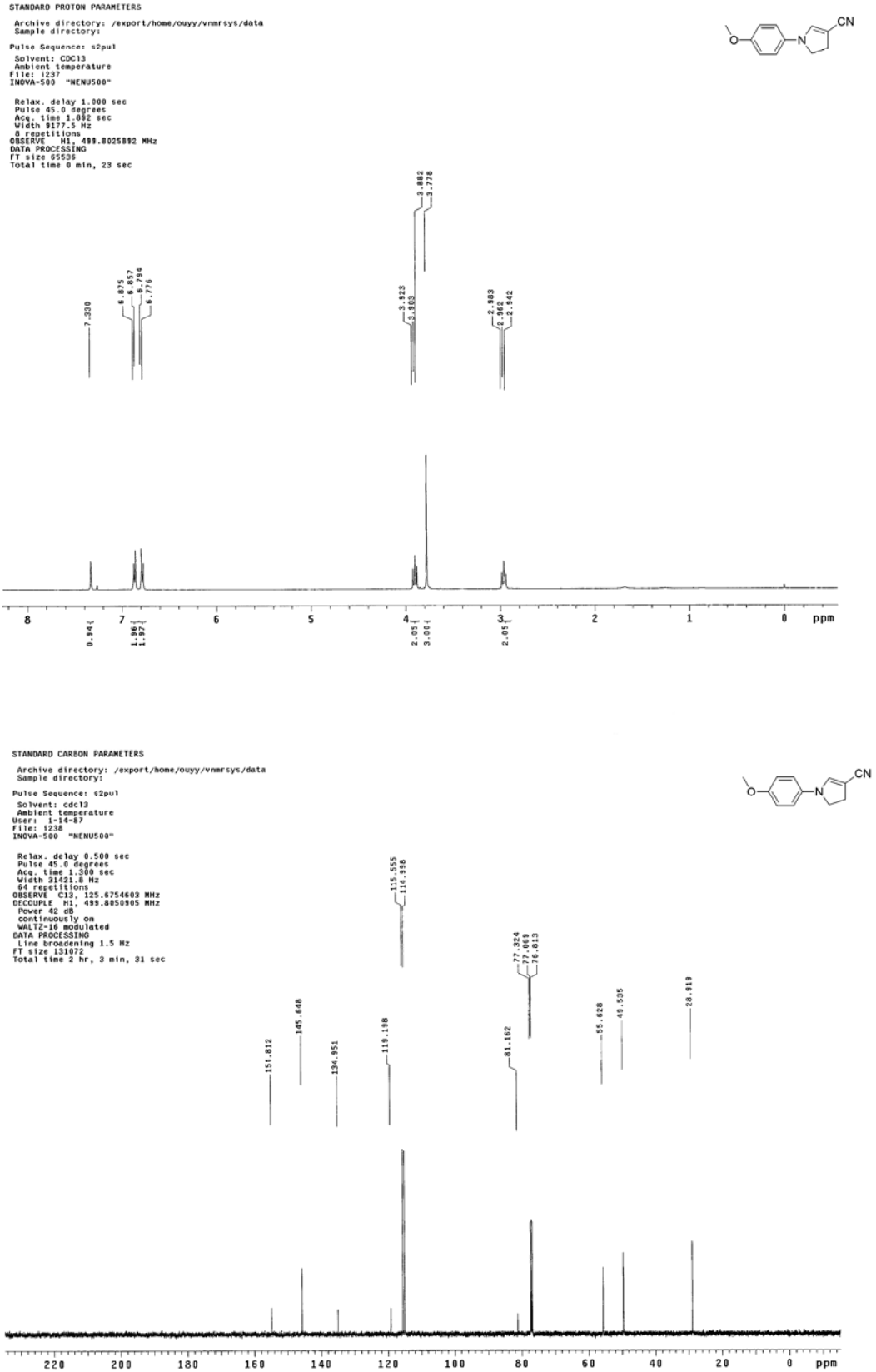


Figure 6. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2f**.

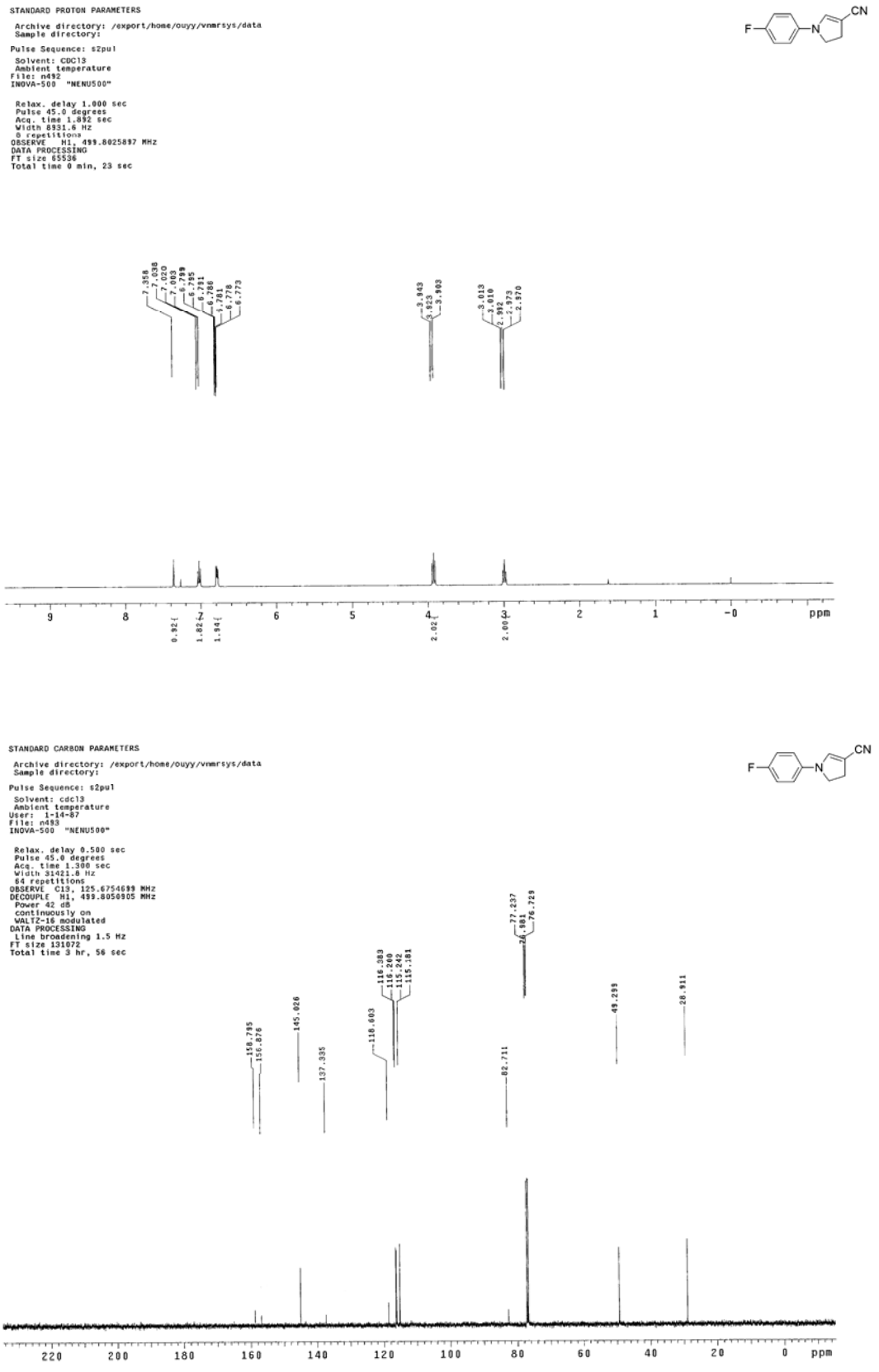


Figure 7. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2g**.

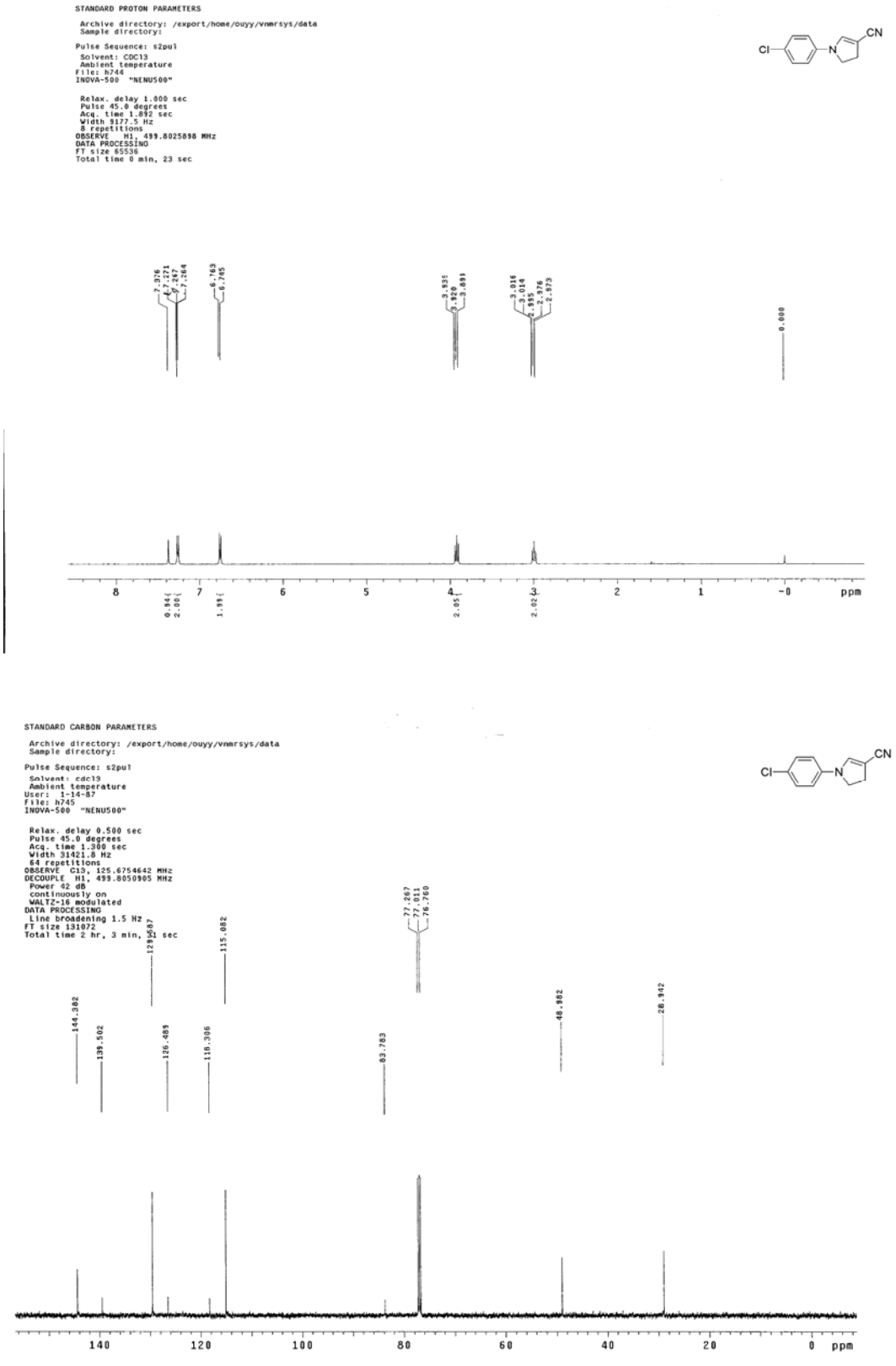


Figure 8. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2h**.

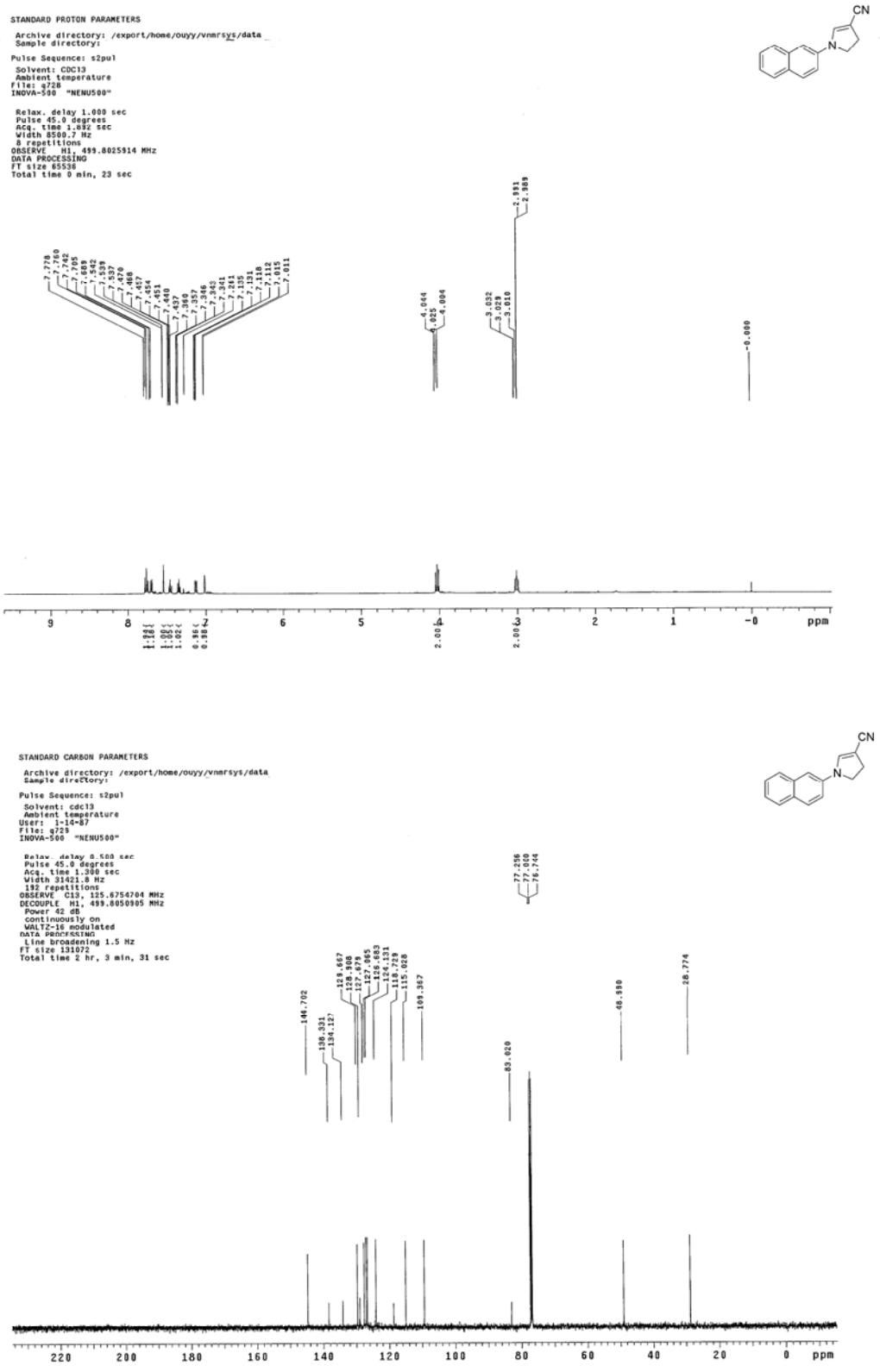


Figure 9. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2i.**

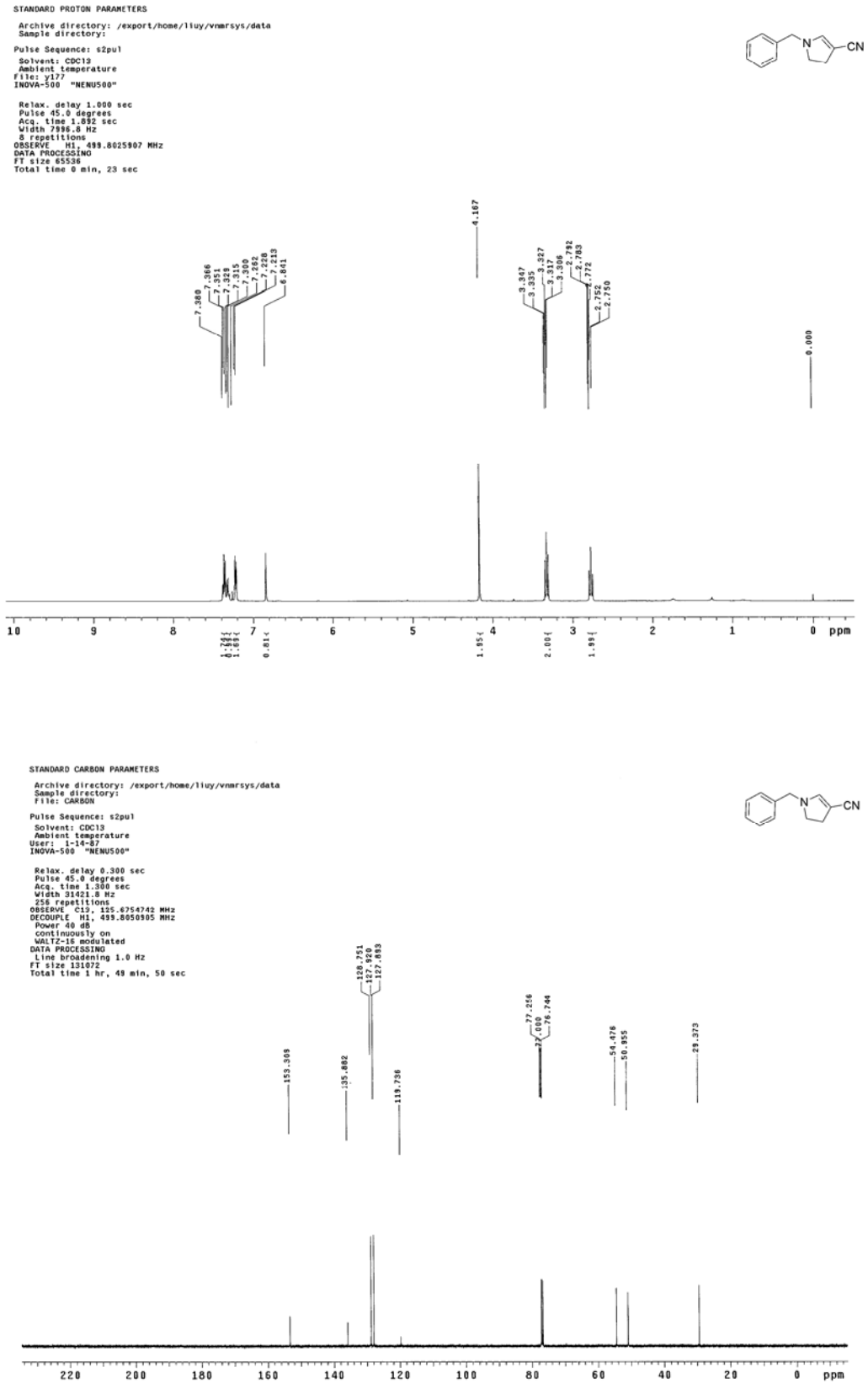


Figure 10. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2j**.

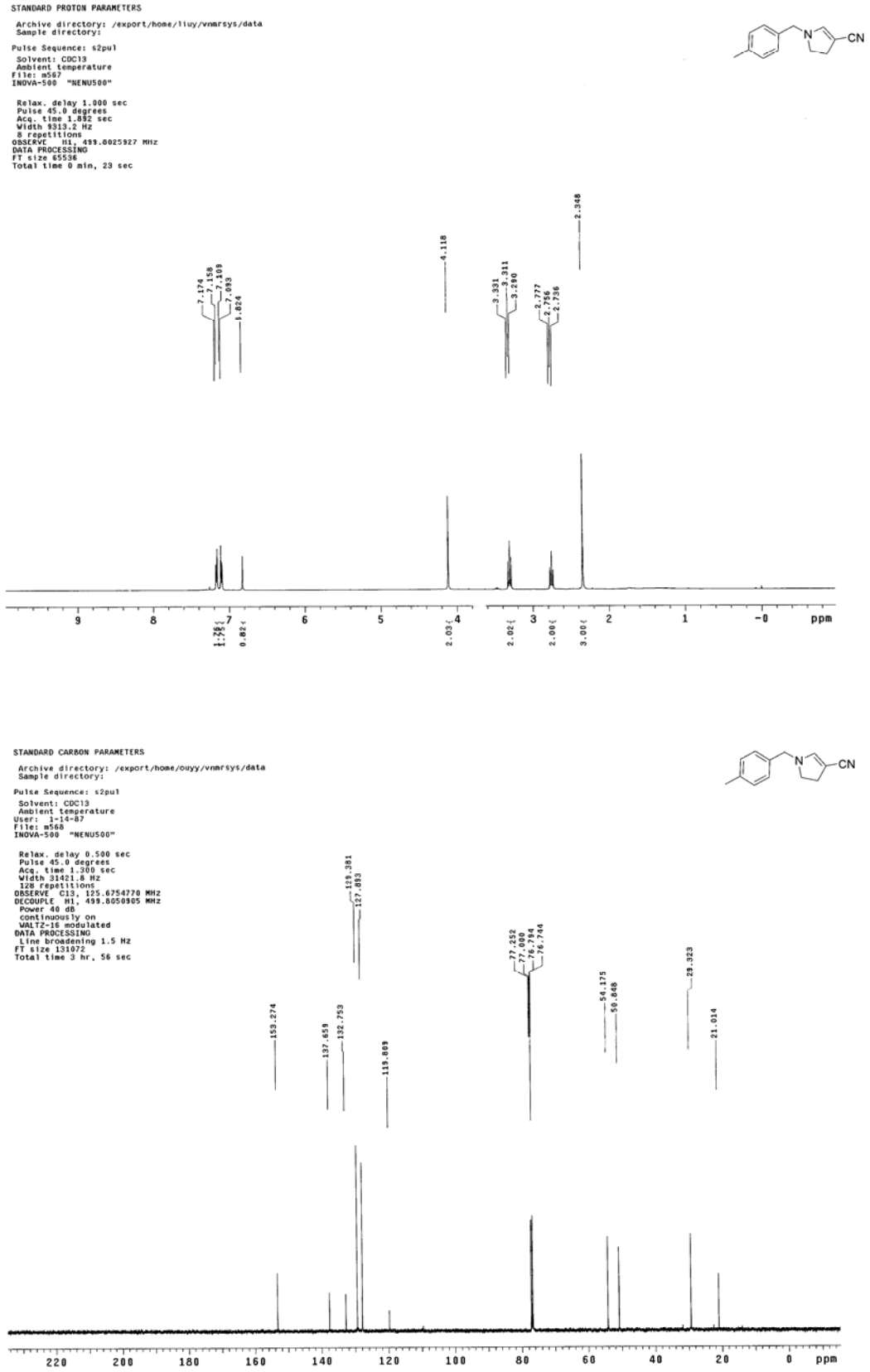


Figure 11. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2k**.

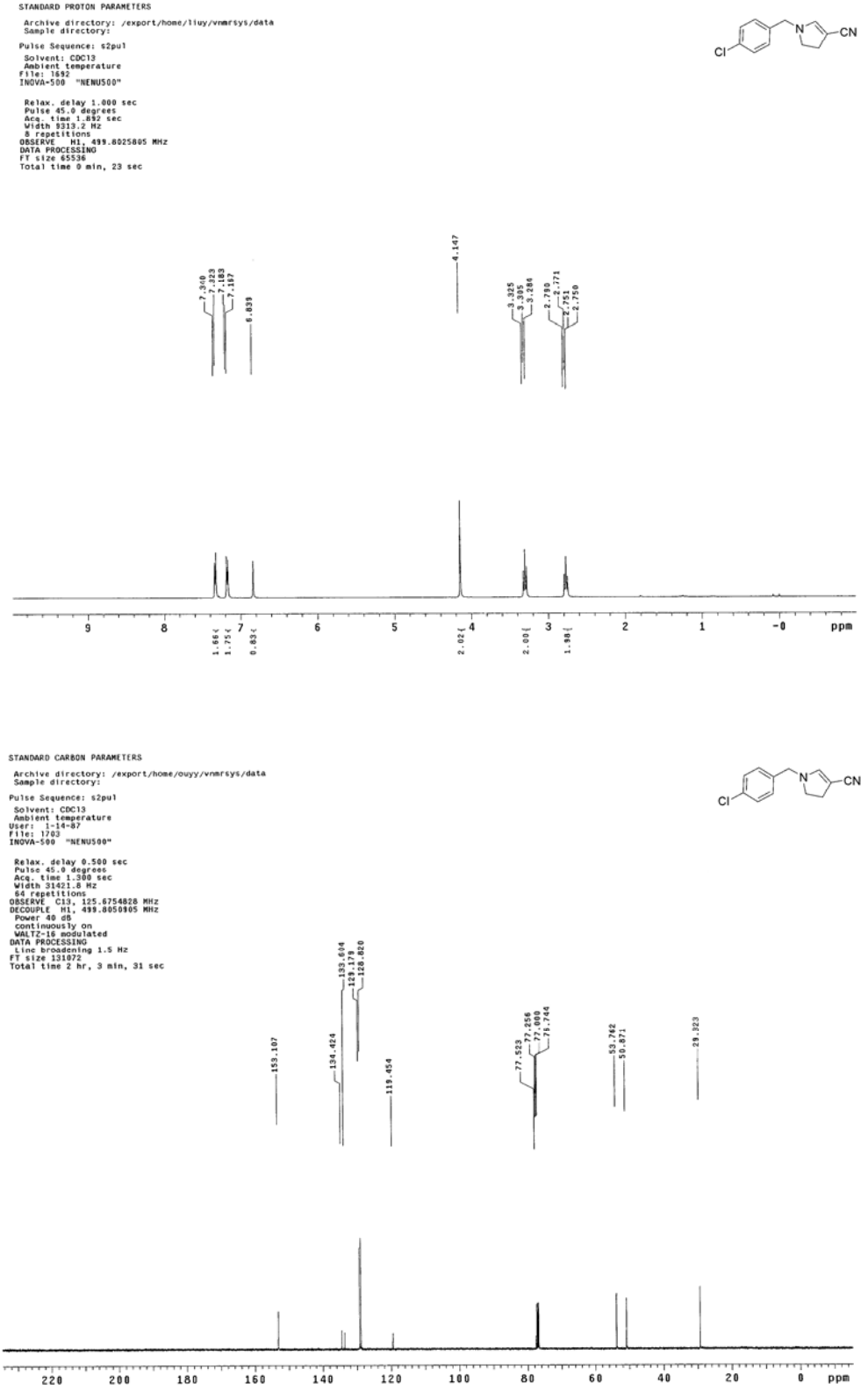


Figure 12. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2l**.

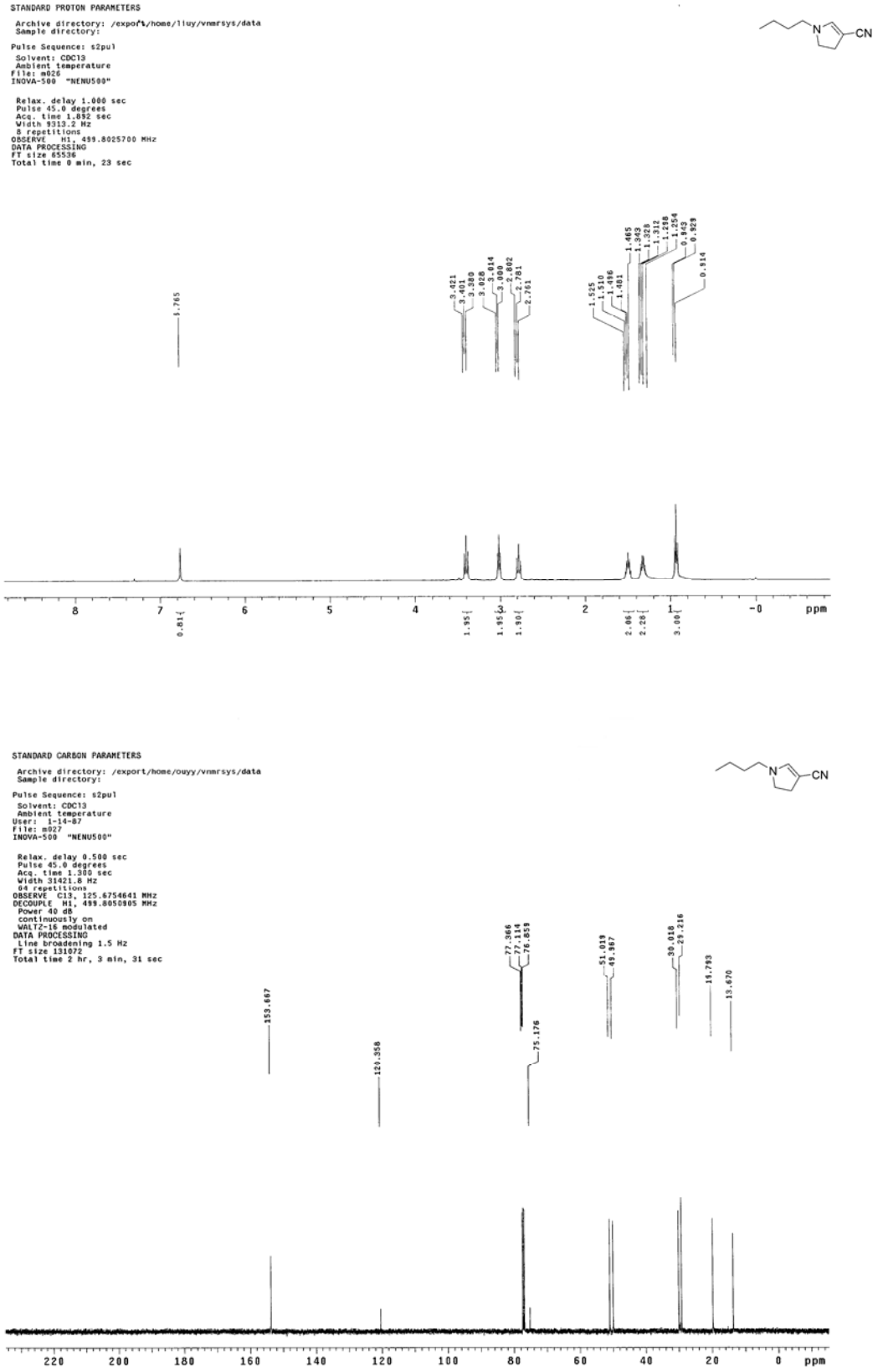


Figure 13. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2m**.

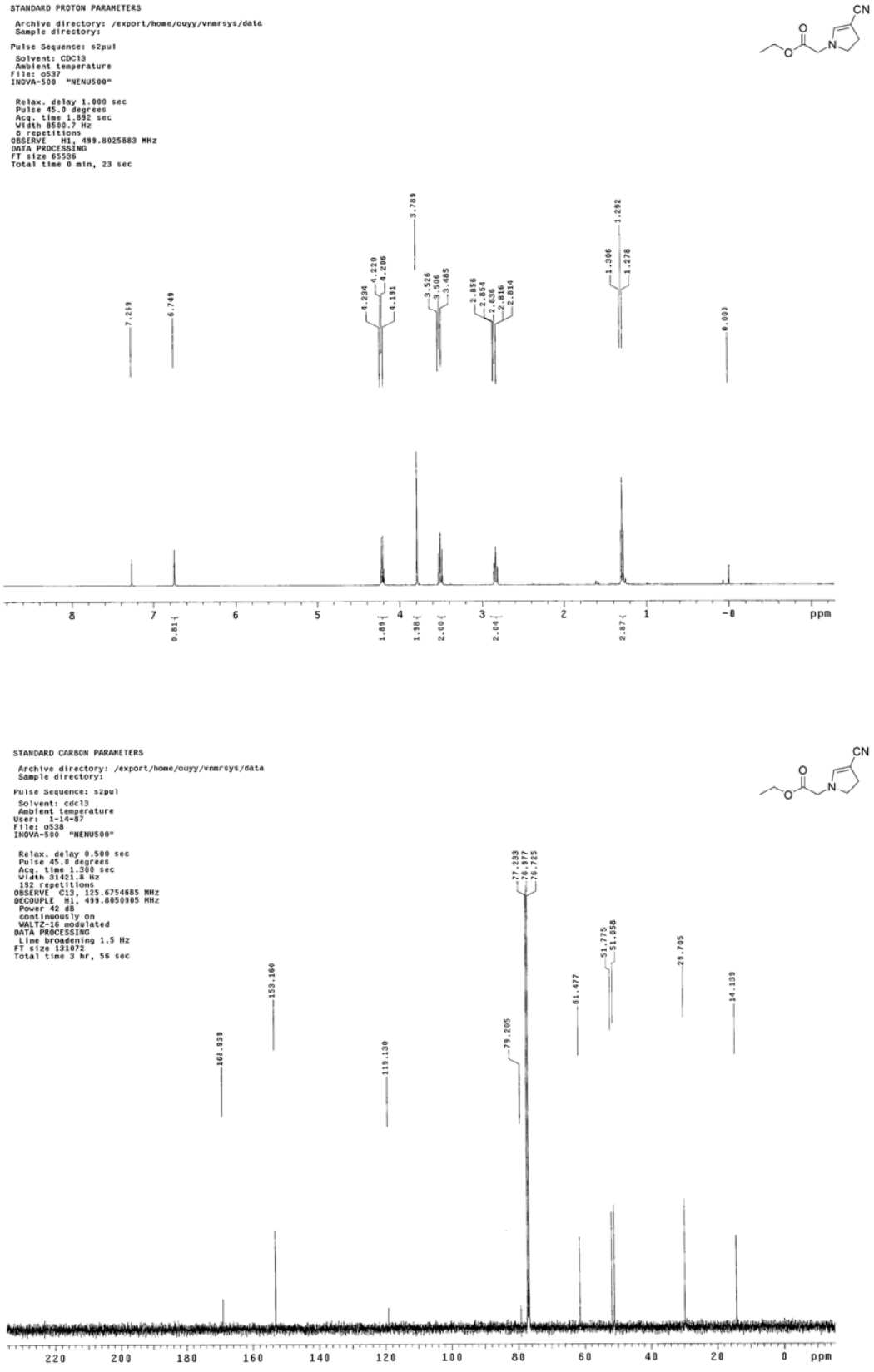


Figure 14. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2n.**

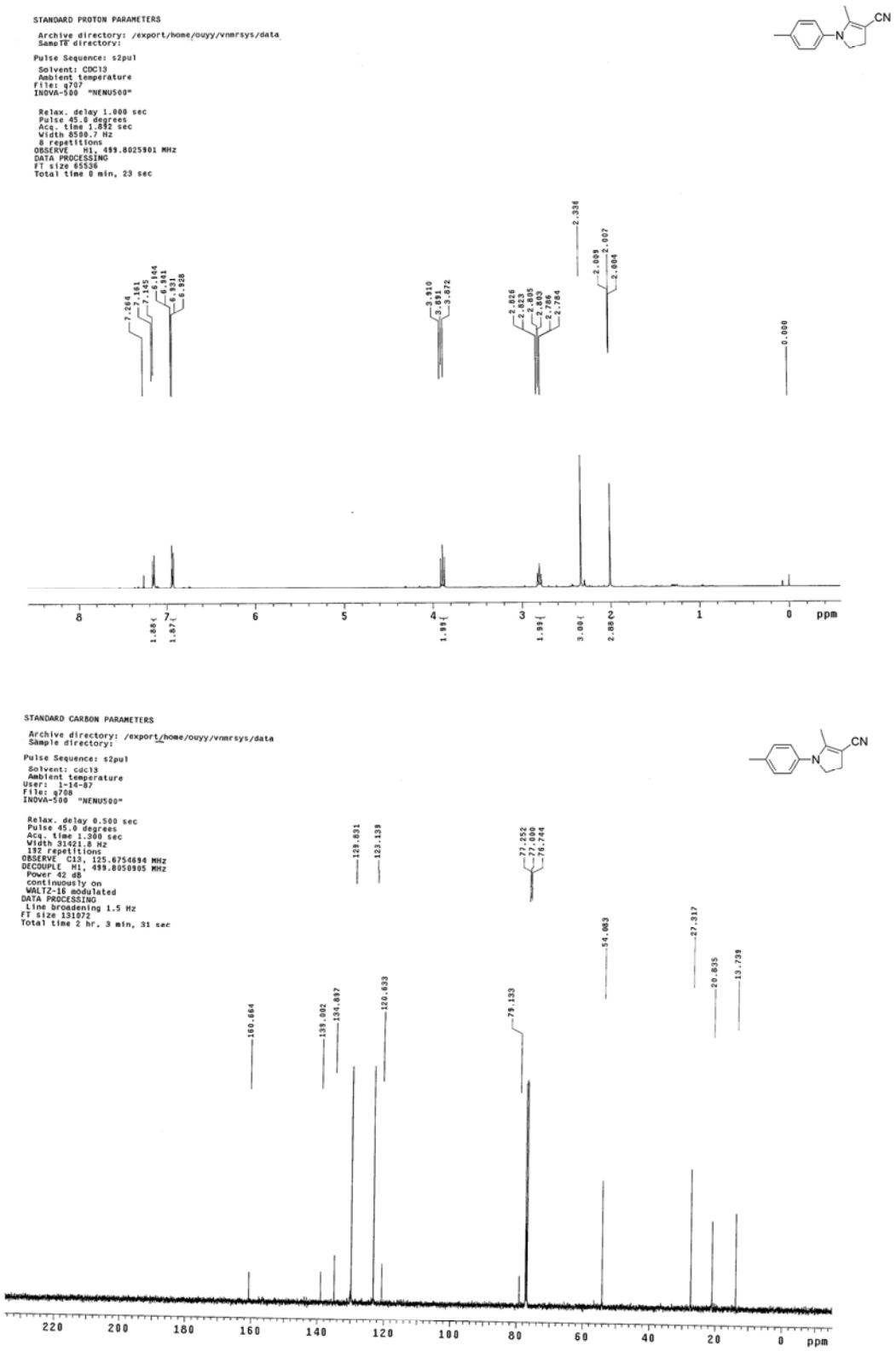


Figure 15. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **2o.**

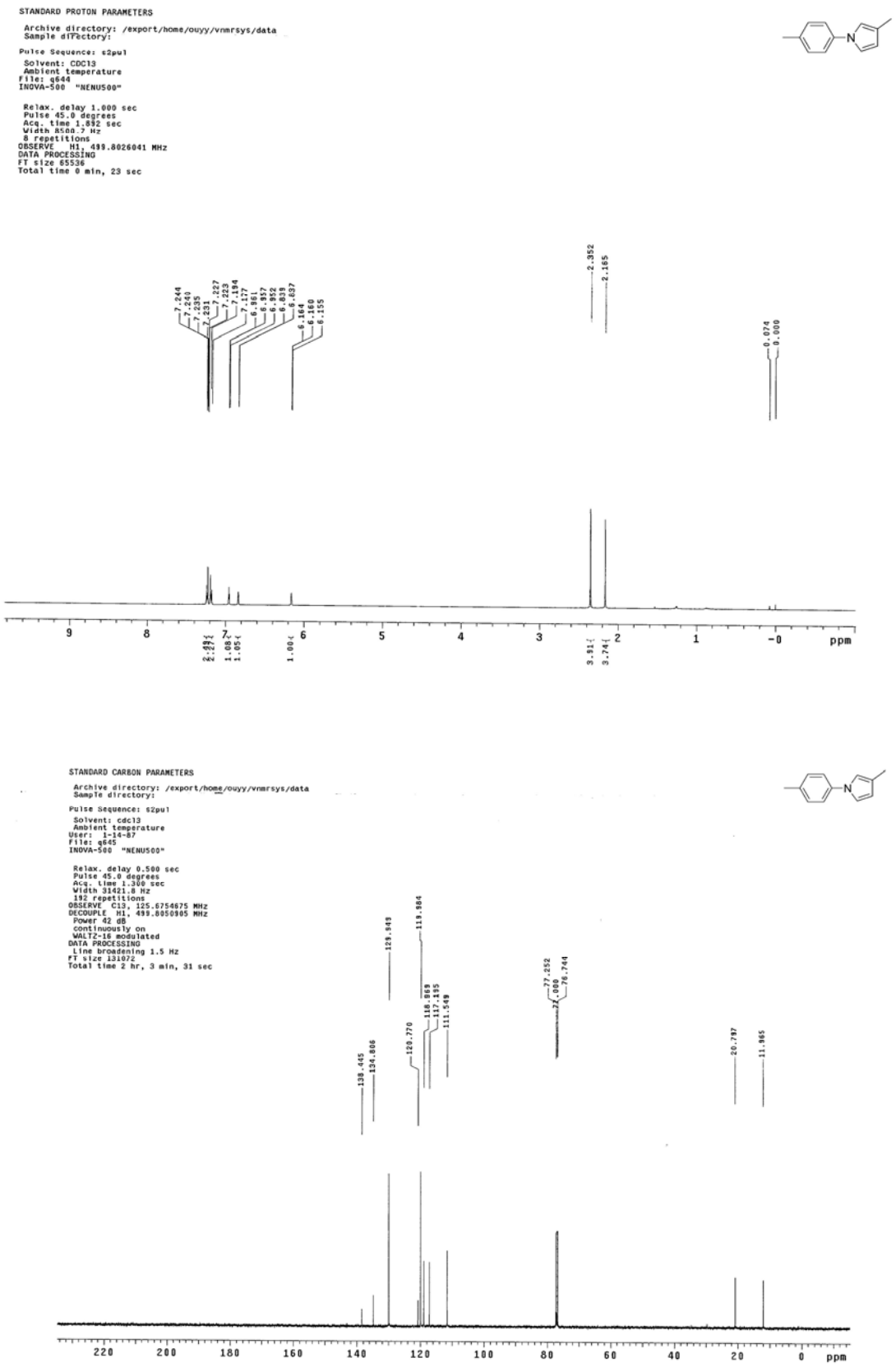


Figure 16. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **4p.**

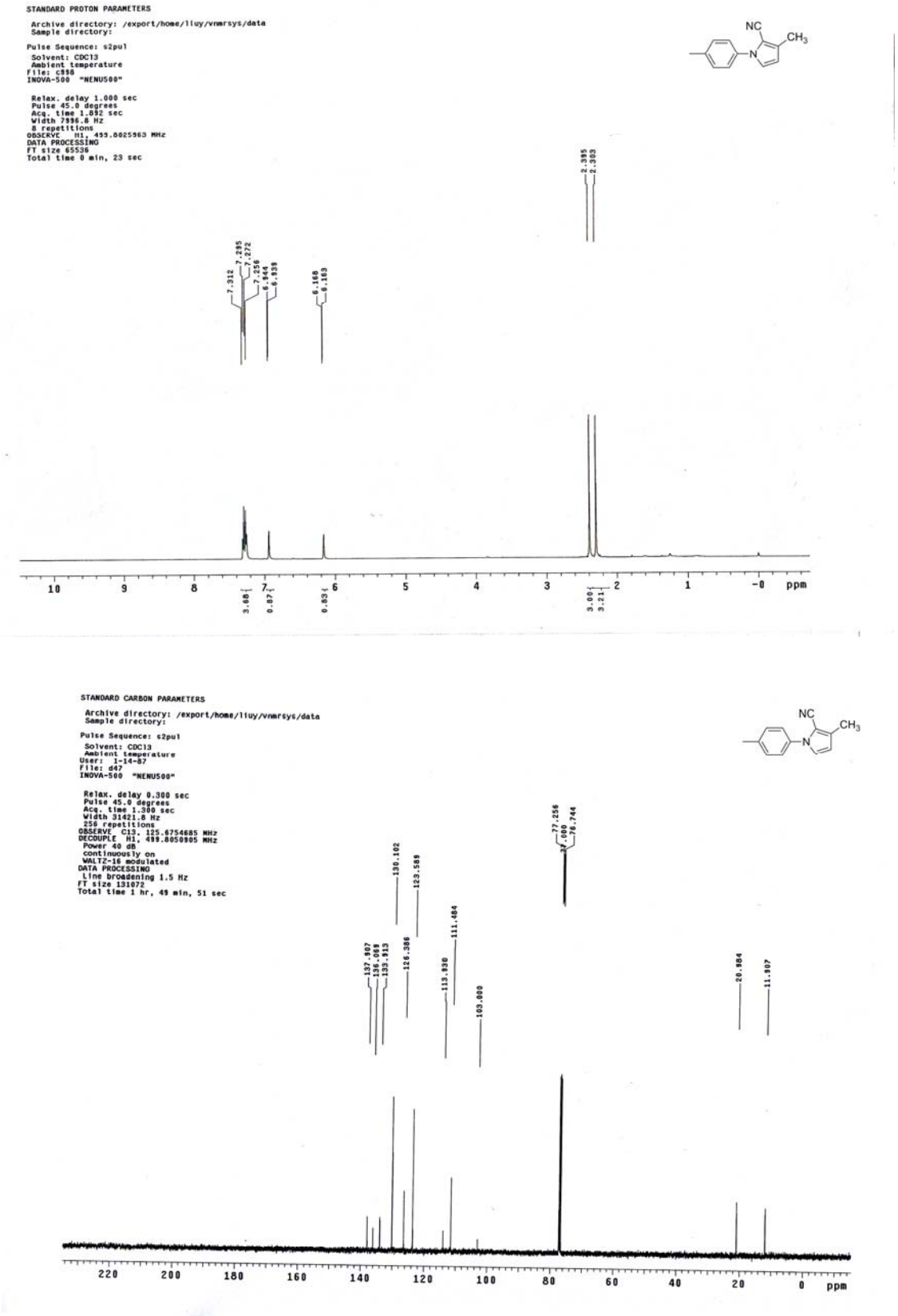


Figure 17. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **5p.**