Supporting Information

Photoredox-Catalyzed Multicomponent 1,2-Difunctionalization of Activated Alkenes with Silyl Enol Ethers and Oxime Esters

Ming-Xian Zhang,[a] Yu Bao,[a] Tao Wang,[a] Shenghu Yan,[a] Yue Zhang,*[a] and Jia-Yin Wang*[a]

[a]School of Pharmacy, Changzhou University, Changzhou, Jiangsu 213164, China; Email: wjychem@cczu.edu.cn; zyjs@cczu.edu.cn.

General Information

^{1}H NMR (^{13}C NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ with chemical shift (δ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QII HRMS/MS instrument (BRUKER). PE refers to petroleum ether (bp 60-90 °C), and EA refers to ethyl acetate. Other reagents, unless otherwise noted, were purchased from commercial vendors and used without further purification. Silyl enol ether **1** are known compounds and were prepared according to literature procedures (*Adv. Synth. Catal.* 2023, **365**, 3444-3449). All cycloketone oxime esters **3** are known compounds and were prepared according to literature procedures (*Chem. Comm.* **2019**, *55*, 11900-11903). All indanone oxime esters **5** are known compounds and were prepared according to literature procedures (*Green Chem.* **2022**, *24*, 6849-6853).

Images of setup for Photoredox-catalyzed reaction

Figure S1. Photograph of the Reaction Setup (Blue LED, 450-460 nm)

Photoreaction set-up purchased from Lianhua Glass Instrument on the online shopping platform (https://www.cnlhglass.com/index.html). All reactions under light-irradiation conditions were performed as shown in Figure S1.

Luminescence Quenching Experiment

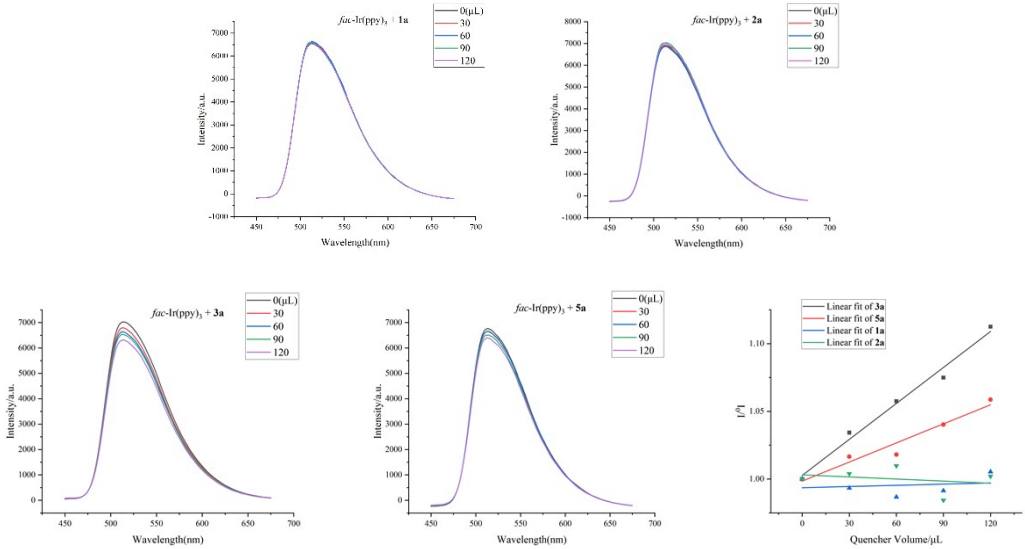


Figure S2. Stern−Volmer analysis for *fac*-Ir(ppy)$_3$ with **1a**, **2a**, **3a** and **5a**

The luminescence quenching experiment was taken using a FS5 Spectrophotometer (Edinburgh FS5). The excitation wavelength was 400 nm, the emission wavelength was 450 nm, and the emission spectra were recorded between 450 and 675 nm. The samples were prepared by mixing *fac*-Ir(ppy)$_3$ (1.0×10^{-3} mol/L) and different amounts of quenchers (**1a**, **2a**, **3a** and **5a**) in CH_3CN (total volume = 2.0 mL) in a light path quartz fluorescence cuvette. The concentration of **3a** stock solution is 1.0×10^{-3} mol/L in CH_3CN. The concentration of **5a** stock solution is 1.0×10^{-3} mol/L in CH_3CN.

Then the emission intensity was collected and the results were presented in **Figure S2**. The observations indicate that the fluorescence intensity of *fac*-Ir(ppy)$_3$ significantly decreases along with the increasing of concentration of **3a** and **5a**. The linear relationships between I_0/I and the concentrations of **1a** and **2a** indicates that the fluorescence intensity of *fac*-Ir(ppy)$_3$ slowly decreases with increasing concentrations of **1a** and **2a** and the *fac*-Ir(ppy)$_3$ is believed to be quenched by **3a** and **5a**.

Light On-Off Experiments

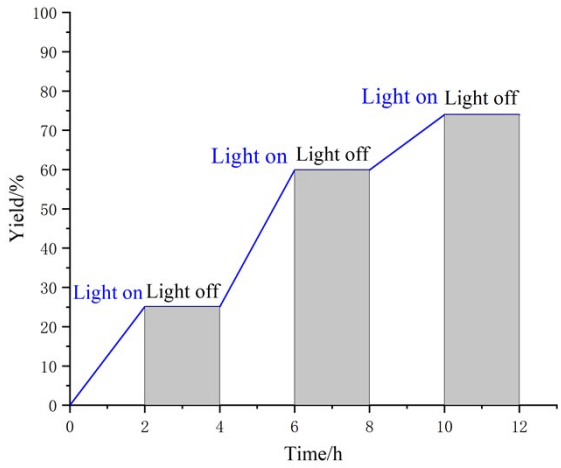
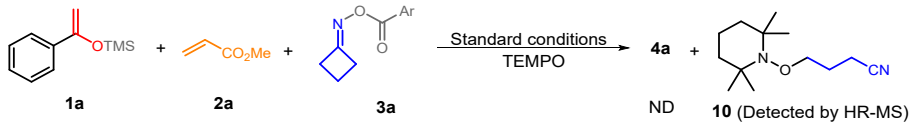


Figure S3. Light On-Off Experiments

Six standard reaction mixtures in 25 mL Schlenk tube were charged with **1a** (0.3 mmol, 1.5 equiv.), **2a** (0.3 mmol, 1.5 equiv.), **3a** (0.2 mmol, 1.0 equiv.), K_3PO_4 (0.3 mmol, 1.5 equiv.), *fac*-Ir(ppy)$_3$ (2 mol %), The tube was then evacuated and back-filled under N_2 flow (this sequence was repeated three times). Subsequently, anhydrous CH_3CN (2.0 mL) were added under N_2. The mixtures were then stirred rapidly and irradiated with a 10 W blue LED (approximately 2 cm away from the light source) at room temperature. After 2 hours, the Blue LED was turned off, and one tube was removed from the irradiation setup for analysis. The remaining five tube were stirred in the absence of light for an additional 2 hours. Then, one tube was removed for analysis, and the Blue LED was turned back on to irradiate the remaining four reaction mixtures. After an additional 2 hours of irradiation, the Blue LED was turned off, and one tube was removed for analysis. The remaining three tube were stirred in the absence of light for an additional 2 hours. Then, a tube was removed for analysis, and the Blue LED was turned back on to irradiate the remaining two reaction mixtures. After 2 hours, the Blue LED was turned off, and one tube was removed for analysis. The last tube was stirred in the absence of light for an additional 2 hours, and then it was analyzed. The yield was obtained by isolated.

Radical-Trapping Experiment



1a 2a 3a

Under N_2 conditions, a dried Schlenk tube was added **1a** (1.5 equiv., 0.3 mmol), **2a** (1.5 equiv., 0.3 mmol), **3a** (1.0 equiv., 0.2 mmol), K_3PO_4 (0.3 mmol, 1.5 equiv.), *fac*-Ir(ppy)$_3$ (2 mol %), TEMPO (3.0 equiv., 0.6mmol), CH_3CN (2.0 mL). The tube was placed exposed to 10 W blue LEDs at room temperature for 12h. The corresponding product **4a** was not detected according to TLC analysis. The TEMPO-trapped product **10** was detected by HR-MS (**Figure S4**). HRMS (ESI) m/z calculated for $C_{13}H_{24}N_2O$ $[M+Na]^+$ 247.1786, found 247.1786.

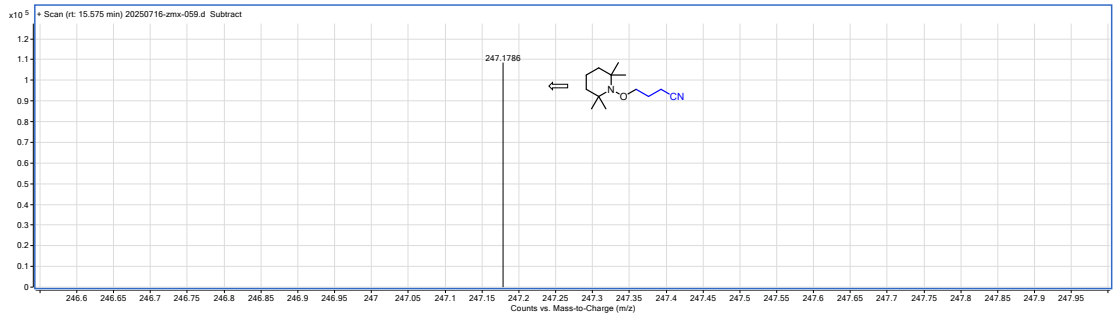
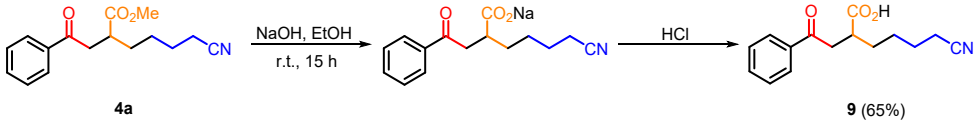


Figure S4. Copy of HR-MS Spectrum of TEMPO adduct **10**

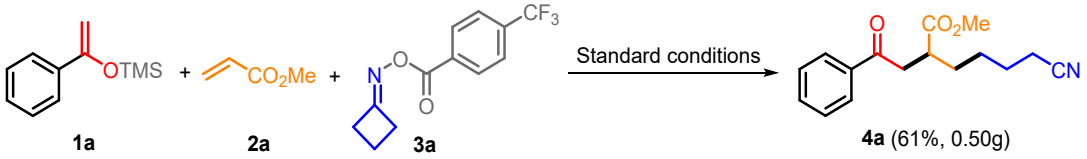
General procedure for the synthesis of compounds 9



4a

A suspension of **4a** (54.7 mg, 0.2 mmol), NaOH (24.0 mg, 1.0 mmol) in mixed solvent EtOH (4 mL) was stirred at ambient temperature for 15 h. After the reaction was complete (by TLC), the mixture was acidified with 0.2M HCl (10 mL), and extracted with DCM. The extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. Purified product **9** was obtained after column chromatography on silica gel (PE/EA= 1/1).

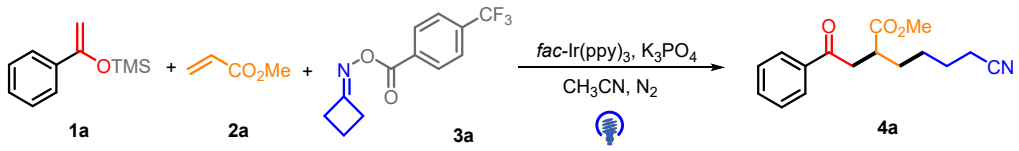
Scale-up Reaction



1a 2a 3a

Under N_2 conditions, A 50 mL oven-dried Schlenk-tube was added **1a** (1.5 equiv., 4.5 mmol., 865.5 mg), **2a** (1.5 equiv., 4.5 mmol., 387.4 mg), **3a** (1.0 equiv., 3 mmol., 771.6 mg), K_3PO_4 (1.5 equiv., 4.5 mmol., 955.2 mg), *fac*-Ir(ppy)$_3$ (2 mol %., 39.3 mg), CH_3CN (30.0 mL). The tube was placed exposed to 10 W blue LEDs at room temperature for 12 h. After the reaction was complete (by TLC), the reaction mixture was washed with water and extracted with DCM. The combined organic layer was washed with brine and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purified product **4a** was obtained after column chromatography on silica gel (PE/EA= 10/1).

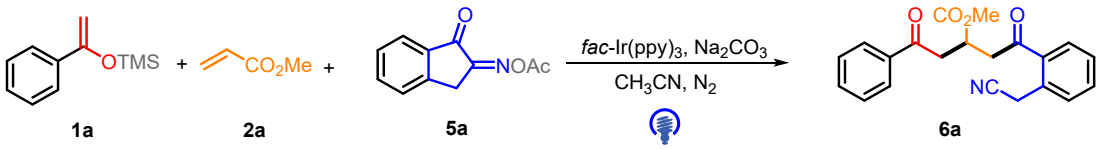
General procedure for the synthesis of compounds 4



Example for the synthesis of **4a**

Under N_2 conditions, a dried Schlenk tube was added **1a** (0.3 mmol, 1.5 equiv.), **2a** (0.3 mmol, 1.5 equiv.), **3a** (0.2 mmol, 1.0 equiv.), K_3PO_4 (0.3 mmol, 1.5 equiv.), *fac*-Ir(ppy)$_3$ (2 mol %), CH_3CN (2.0 mL). The tube was placed exposed to 10 W blue LEDs at room temperature for 12 h. After the reaction was complete (by TLC), the reaction mixture was washed with water and extracted with DCM. The combined organic layer was washed with brine and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purified product **4a** was obtained after column chromatography on silica gel (PE/EA= 10/1).

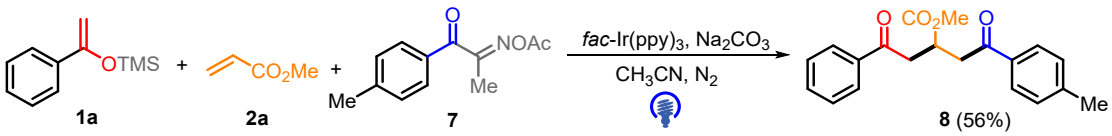
General procedure for the synthesis of compounds 6



Example for the synthesis of **6a**

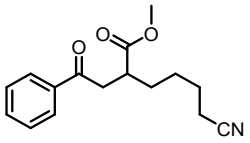
Under N_2 conditions, a dried Schlenk tube was added **1a** (0.3 mmol, 1.5 equiv.), **2a** (0.3 mmol, 1.5 equiv.), **5a** (0.2 mmol, 1.0 equiv.), Na_2CO_3 (0.3 mmol, 1.5 equiv.), *fac*-Ir(ppy)$_3$ (2 mol %), CH_3CN (2.0 mL). The tube was placed exposed to 10 W blue LEDs at room temperature for 12 h. After the reaction was complete (by TLC), the reaction mixture was washed with water and extracted with DCM. The combined organic layer was washed with brine and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purified product **6a** was obtained after column chromatography on silica gel (PE/EA= 10/1).

General procedure for the synthesis of compounds 8



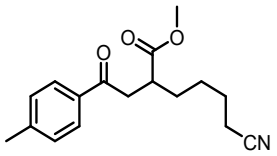
Under N_2 conditions, a dried Schlenk tube was added **1a** (0.3 mmol, 1.5 equiv.), **2a** (0.3 mmol, 1.5 equiv.), **7** (0.2 mmol, 1.0 equiv.), Na_2CO_3 (0.3 mmol, 1.5 equiv.), *fac*-Ir(ppy)$_3$ (2 mol %), CH_3CN (2.0 mL). The tube was placed exposed to 10 W blue LEDs at room temperature for 12 h. After the reaction was complete (by TLC), the reaction mixture was washed with water and extracted with DCM. The combined organic layer was washed with brine and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purified product **8** was obtained after column chromatography on silica gel (PE/EA= 10/1).

Methyl 6-cyano-2-(2-oxo-2-phenylethyl)hexanoate (4a)



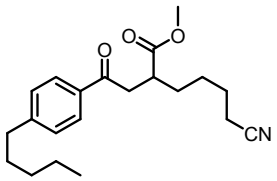
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 40.4 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.96 (d, *J* = 7.6 Hz, 2H), 7.60-7.56 (m, 1H), 7.49-7.45 (m, 2H), 3.72 (s, 3H), 3.51-3.44 (m, 1H), 3.12-3.07 (m, 2H), 2.39-2.35 (m, 2H), 1.78-1.66 (m, 4H), 1.57-1.51 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.9, 175.6, 136.5, 133.4, 128.7, 128.1, 119.5, 51.9, 40.4, 39.9, 31.2, 26.3, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{16}H_{19}NO_3$ $[M+Na]^+$ 296.1263, found 296.1265.

Methyl 6-cyano-2-(2-oxo-2-(p-tolyl)ethyl)hexanoate (4b)



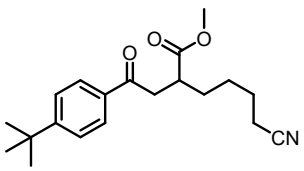
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 35.1 mg, 61% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.86 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 3.71 (s, 3H), 3.48-3.39 (m, 1H), 3.10-3.02 (m, 2H), 2.41-2.34 (m, 5H), 1.77-1.61 (m, 4H), 1.56-1.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.5, 175.7, 144.2, 134.0, 129. 3, 128.2, 119.5, 51.9, 40.3, 39.9, 31.2, 26.3, 25.1, 21.7, 17.0; HRMS-ESI (m/z) calculated for $C_{17}H_{21}NO_3$ $[M+Na]^+$ 310.1419, found 310.1421.

Methyl 6-cyano-2-(2-oxo-2-(4-pentylphenyl)ethyl)hexanoate (4c)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 36.4 mg, 53% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.87 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 3.71 (s, 3H), 3.49-3.39 (m, 1H), 3.11-3.02 (m, 2H), 2.68-2.63 (m, 2H), 2.38-2.34 (m, 2H), 1.80 – 1.60 (m, 6H), 1.56-1.49 (m, 2H), 1.37-1.26 (m, 4H), 0.91-0.87 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.5, 175.7, 149.2, 134.2, 128.7, 128.2, 119.5, 51.9, 40.3, 39.9, 36.0, 31.4, 31.2, 30.8, 26.3, 25.1, 22.5, 17.0, 14.0; HRMS-ESI (m/z) calculated for $C_{21}H_{29}NO_3$ $[M+Na]^+$ 366.2045, found 366.2060

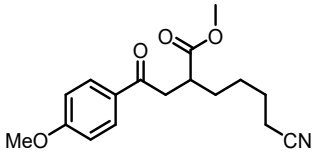
Methyl 2-(2-(4-(tert-butyl)phenyl)-2-oxoethyl)-6-cyanohexanoate (4d)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 32.9 mg, 50% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.90 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 3.71

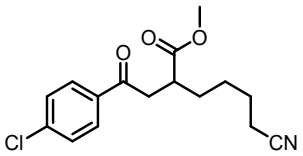
(s, 3H), 3.49-3.39 (m, 1H), 3.10-3.03 (m, 2H), 2.39-2.34 (m, 2H), 1.78-1.62 (m, 4H), 1.57-1.50 (m, 2H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.5, 175.7, 157.1, 134.0, 128.0, 125.6, 119.5, 51.9, 40.3, 39.9, 35.1, 31.1(4), 31.1(7), 26.3, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{21}H_{29}NO_3$ $[M+Na]^+$ 352.1889, found 352.1887.

Methyl 6-cyano-2-(2-(4-methoxyphenyl)-2-oxoethyl)hexanoate (4e)



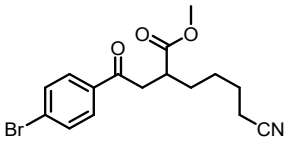
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 30.9 mg, 51% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.95-7.90 (m, 2H), 6.95-6.90 (m, 2H), 3.86 (s, 3H), 3.70 (s, 3H), 3.45-3.35 (m, 1H), 3.10-2.98 (m, 2H), 2.37-2.33 (m, 2H), 1.79-1.60 (m, 4H), 1.55-1.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 196.3, 175.8, 163.7, 130.3, 129.6, 119.5, 113.8, 55.5, 51.9, 40.1, 40.0, 31.2, 26.3, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{17}H_{21}NO_4$ $[M+Na]^+$ 326.1368, found 326.1366.

Methyl 2-(2-(4-chlorophenyl)-2-oxoethyl)-6-cyanohexanoate (4f)



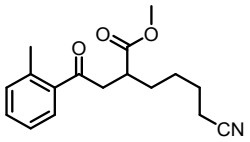
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 34.4 mg, 56% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.89 (d, J = 9.0 Hz, 2H), 7.43 (d, J = 9.0 Hz, 2H), 3.70 (s, 3H), 3.47-3.39 (m, 1H), 3.11-2.98 (m, 2H), 2.38-2.34 (m, 2H), 1.77-1.61 (m, 4H), 1.56-1.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 196.7, 175.5, 139.8, 134.8, 129.5, 129.0, 119.5, 52.0, 40.3, 39.9, 31.2, 26.2, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{16}H_{18}ClNO_3$ $[M+Na]^+$ 330.0873, found 330.0874.

Methyl 2-(2-(4-bromophenyl)-2-oxoethyl)-6-cyanohexanoate (4g)



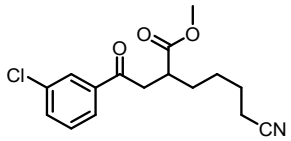
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 43.5 mg, 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.82 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 3.71 (s, 3H), 3.47-3.40 (m, 1H), 3.10-3.00 (m, 2H), 2.39-2.35 (m, 2H), 1.76-1.61 (m, 4H), 1.56-1.50 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm): 196.9, 175.5, 135.2, 132.0, 129.6, 128.6, 119.5, 52.0, 40.3, 39.9, 31.1, 26.2, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{16}H_{18}BrNO_3$ $[M+Na]^+$ 374.0368, found 374.0368.

Methyl 6-cyano-2-(2-oxo-2-(o-tolyl)ethyl)hexanoate (4h)



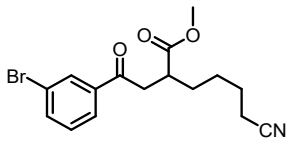
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 25.8 mg, 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.69 (d, *J* = 7.6 Hz, 1H), 7.40-7.39 (m, 1H), 7.29-7.24 (m, 2H), 3.72 (s, 3H), 3.44-3.37 (m, 1H), 3.08-3.03 (m, 1H), 3.01-2.95 (m, 1H), 2.48 (s, 3H), 2.39-2.35 (m, 2H), 1.77-1.68 (m, 4H), 1.56-1.50 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) (δ, ppm): 201.4, 175.5, 138.4, 137.2, 132.0, 131.6, 130.5, 128.6, 128.5, 125.7, 119.5, 52.0, 51.8, 43.9, 43.1, 43.0, 38.9, 38.7, 34.3, 34.0, 32.1, 31.3, 26.2, 25.2, 21.3, 17.0; HRMS-ESI (m/z) calculated for $C_{17}H_{21}NO_3$ $[M+Na]^+$ 310.1419, found 310.1422.

Methyl 2-(2-(3-chlorophenyl)-2-oxoethyl)-6-cyanohexanoate (4i)



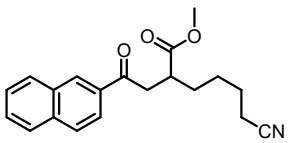
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 25.2 mg, 41% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.93 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.60-7.54 (m, 1H), 7.44-7.39 (m, 1H), 3.72 (s, 3H), 3.47-3.41 (m, 1H), 3.17-2.99 (m, 2H), 2.40-2.35 (m, 2H), 1.76-1.65 (m, 4H), 1.55-1.50 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) (δ, ppm): 196.7, 175.4, 138.0, 135.0, 133.3, 130.0, 128.2, 126.1, 52.0, 40.5, 39.8, 31.1, 26.2, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{16}H_{18}ClNO_3$ $[M+Na]^+$ 330.0873, found 330.0876.

Methyl 2-(2-(3-bromophenyl)-2-oxoethyl)-6-cyanohexanoate (4j)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 27.4 mg, 39% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.08 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.38-7.34 (m, 1H), 3.72 (s, 3H), 3.48-3.42 (m, 1H), 3.10-3.00 (m, 2H), 2.39-2.36 (m, 2H), 1.76-1.66 (m, 4H), 1.57-1.51 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 196.6, 175.4, 138.2, 136.2, 131.2, 130.3, 126.6, 123.0, 119.4, 52.0, 40.4, 39.8, 31.1, 26.2, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{16}H_{18}BrNO_3$ $[M+Na]^+$ 374.0368, found 374.0366.

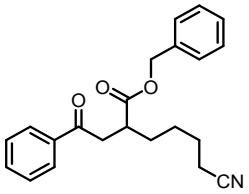
Methyl 6-cyano-2-(2-(naphthalen-2-yl)-2-oxoethyl)hexanoate (4k)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 39.4 mg, 61% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.49 (s, 1H), 8.03-8.00 (m, 2H), 7.91-7.86 (m, 2H), 7.63-7.53 (m, 2H), 3.73 (s, 3H), 3.65-3.57 (m, 1H), 3.25-3.09 (m, 2H), 2.40-2.35 (m, 2H), 1.82-1.64 (m,

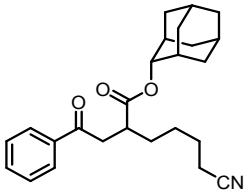
4H), 1.60-1.53 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.8, 175.7, 135.7, 133.8, 132.5, 129.8, 129.6, 128.6(3), 128.6(5), 127.8, 126.9, 123.7, 119.5, 52.0, 40.5, 40.0, 31.2, 26.3, 25.2, 17.0; HRMS-ESI (m/z) calculated for $C_{20}H_{21}NO_3$ $[M+Na]^+$ 346.1419, found 346.1421.

Benzyl 6-cyano-2-(2-oxo-2-phenylethyl)hexanoate (4l)



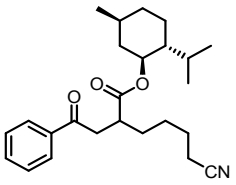
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 55.9 mg, 80% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.95 (d, J = 7.2 Hz, 2H), 7.59-7.55 (m, 1H), 7.48-7.44 (m, 2H), 7.36-7.31 (m, 5H), 5.21-5.10 (m, 2H), 3.51-3.45 (m, 1H), 3.15-3.05 (m, 2H), 2.28-2.25 (m, 2H), 1.75-1.60 (m, 4H), 1.50-1.42 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm): 197.9, 174.9, 136.5, 135.9, 133.4, 128.7, 128.6, 128.4, 128.3, 128.1, 119.5, 66.6, 40.3, 40.0, 31.2, 26.2, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{22}H_{23}NO_3$ $[M+Na]^+$ 372.1576, found 372.1574.

(1R,3S,5r,7r)-adamantan-2-yl 6-cyano-2-(2-oxo-2-phenylethyl)hexanoate (4m)



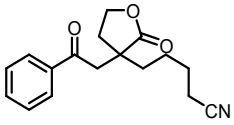
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 45.6 mg, 58% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.95 (d, J = 7.2 Hz, 2H), 7.58-7.54 (m, 1H), 7.48-7.43 (m, 2H), 3.44-3.35 (m, 1H), 3.00-2.90 (m, 2H), 2.38-2.34 (m, 2H), 2.12 (d, J = 13.2 Hz, 9H), 1.76-1.64 (m, 10H), 1.57-1.50 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 198.2, 174.0, 136.8, 133.2, 128.6, 128.1, 119.6, 80.9, 41.3, 41.0, 40.5, 36.2, 31.3, 30.8, 26.2, 25.2, 17.0; HRMS-ESI (m/z) calculated for $C_{25}H_{31}NO_3$ $[M+Na]^+$ 416.2202, found 416.2223.

(1S,2R,5S)-2-isopropyl-5-methylcyclohexyl 6-cyano-2-(2-oxo-2-phenylethyl)hexanoate (4n)



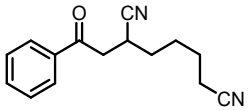
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 38.2 mg, 48% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.96 (d, J = 8.0 Hz, 2H), 7.59-7.55 (m, 1H), 7.48-7.44 (m, 2H), 4.68-4.65 (m, 1H), 3.47-3.43 (m, 1H), 3.04-2.99 (m, 2H), 2.38-2.33 (m, 2H), 2.01-1.94 (m, 1H), 1.78-1.64 (m, 8H), 1.55-1.52 (m, 3H), 1.39-1.34 (m, 1H), 1.06-0.93 (m, 2H), 0.89 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.75-0.71 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm): 197.9, 174.6, 136.6, 133.3, 128.7, 128.1, 119.5, 74.7, 46.9, 40.5, 40.3, 34.2, 31.4, 26.3, 26.0, 25.3, 23.2, 23.0, 22.1, 20.8, 17.1, 16.1, 15.8; HRMS-ESI (m/z) calculated for $C_{25}H_{35}NO_3$ $[M+Na]^+$ 420.2515, found 420.2514.

5-(2-oxo-3-(2-oxo-2-phenylethyl)tetrahydrofuran-3-yl)pentanenitrile (4o)



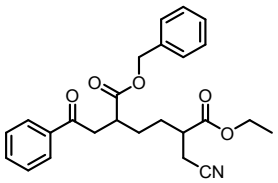
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 20.5 mg, 36% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.96-7.93 (m, 2H), 7.62-7.57 (m, 1H), 7.50-7.45 (m, 2H), 4.58-4.50 (m, 1H), 4.37-4.29 (m, 1H), 3.50-3.34 (m, 2H), 2.45-2.37 (m, 3H), 2.27-2.23 (m, 1H), 1.77-1.67 (m, 5H), 1.53-1.47 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) (δ, ppm): 197.0, 181.0, 136.3, 133.7, 128.8, 128.0, 119.3, 65.6, 44.9, 43.6, 37.0, 31.6, 25.5, 23.4, 17.0; HRMS-ESI (m/z) calculated for $C_{17}H_{19}NO_3$ $[M+Na]^+$ 308.1263, found 308.1261.

2-(2-oxo-2-phenylethyl)heptanedinitrile (4p)



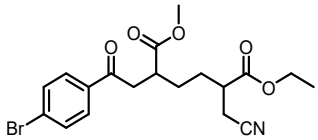
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 29.8 mg, 62% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.95 (d, J = 7.5 Hz, 2H), 7.65-7.60 (m, 1H), 7.53-7.48 (m, 2H), 3.46-3.22 (m, 3H), 2.43-2.39 (m, 2H), 1.79-1.69 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) (δ, ppm): 195.0, 135.7, 134.0, 128.9, 128.1, 121.4, 119.2, 40.6, 31.1, 26.3, 26.1, 24.8, 17.0; HRMS-ESI (m/z) calculated for $C_{15}H_{16}N_2O$ $[M+Na]^+$ 263.1160, found 263.1155.

1-benzyl 6-ethyl 5-(cyanomethyl)-2-(2-oxo-2-phenylethyl)hexanedioate (4q)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 46.4 mg, 55% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.94 (d, J = 8.0 Hz, 2H), 7.59-7.55 (m, 1H), 7.48-7.44 (m, 2H), 7.35 (s, 5H), 5.22-5.10 (m, 2H), 4.20-4.15 (m, 2H), 3.52-3.46 (m, 1H), 3.14-3.04 (m, 2H), 2.70-2.67 (m, 1H), 2.63-2.40 (m, 2H), 1.85-1.72 (m, 2H), 1.69-1.65 (m, 2H), 1.27-1.24 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm): 197.6, 174.5, 172.1, 136.5, 135.9, 133.4, 128.7, 128.6, 128.5, 128.4(9), 128.4(5), 128.3, 128.1, 117.5, 66.7, 61.5, 41.2, 40.2, 39.8, 28.8, 19.4, 19.2, 14.2; HRMS-ESI (m/z) calculated for $C_{25}H_{27}NO_5$ $[M+Na]^+$ 444.1787, found 444.1791.

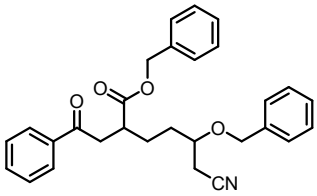
6-ethyl 1-methyl 2-(2-(4-bromophenyl)-2-oxoethyl)-5-(cyanomethyl)hexanedioate (4r)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 39.0 mg, 46% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.82 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 4.24-4.18 (m, 2H), 3.72 (s, 3H), 3.48-3.42 (m, 1H), 3.10-2.99 (m, 2H), 2.79-2.74 (m, 1H), 2.71-2.55 (m, 2H), 1.89-1.64 (m, 4H), 1.31-1.27 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm): 196.7, 175.0, 172.2,

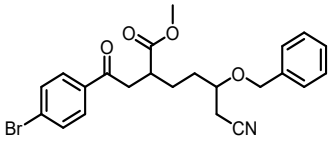
135.1, 132.0, 129.6, 128.6, 117.5(3), 117.5(0), 61.6, 52.1, 41.2, 41.1, 40.2, 40.1, 39.8, 39.7, 28.73, 19.4, 19.3, 14.2; HRMS-ESI (m/z) calculated for $C_{19}H_{22}BrNO_5$ $[M+K]^+$ 462.0318, found 462.0316.

Benzyl 5-(benzyloxy)-6-cyano-2-(2-oxo-2-phenylethyl)hexanoate (4s)



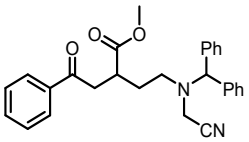
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 50.1 mg, 55% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.94 (d, *J* = 7.5 Hz, 2H), 7.60-7.55 (m, 1H), 7.48-7.43 (m, 2H), 7.35-7.31 (m, 10H), 5.21-5.07 (m, 2H), 4.62-4.46 (m, 2H), 3.66 (s, 1H), 3.48-3.42 (m, 1H), 3.09-2.97 (m, 2H), 2.49-2.42 (m, 2H), 1.80-1.59 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.8, 174.8, 137.4, 136.5, 135.9, 133.4, 128.7, 128.6(0), 128.6(6), 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 117.4, 74.1, 73.7, 72.0, 66.6, 40.3, 40.0, 39.7, 31.8, 31.6, 27.4, 27.3, 22.9; HRMS-ESI (m/z) calculated for $C_{29}H_{29}NO_4$ $[M+Na]^+$ 478.1994, found 478.1990.

Methyl 5-(benzyloxy)-2-(2-(4-bromophenyl)-2-oxoethyl)-6-cyanohexanoate (4t)



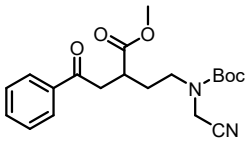
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 33.0 mg, 36% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.80 (d, *J* = 7.8 Hz, 2H), 7.60 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 4.5 Hz, 5H), 4.67-4.51 (m, 2H), 3.70 (s, 4H), 3.47-3.37 (m, 1H), 3.08-2.96 (m, 2H), 2.57 (d, *J* = 5.4 Hz, 2H), 1.77-1.66 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 196.9, 175.4, 137.3, 135.2, 132.0, 129.6, 128.6, 128.1, 128.0, 117.3, 74.1, 73.8, 72.0, 52.0, 40.3, 39.9, 39.6, 31.9, 31.6, 27.4, 27.2, 22.9; HRMS-ESI (m/z) calculated for $C_{23}H_{24}BrNO_4$ $[M+Na]^+$ 480.0786, found 480.0782.

Methyl 2-(2-(benzhydryl(cyanomethyl)amino)ethyl)-4-oxo-4-phenylbutanoate (4u)



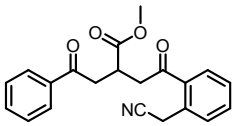
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 46.7 mg, 53% yield; 1H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.89 (d, *J* = 7.2 Hz, 2H), 7.60-7.55 (m, 1H), 7.48-7.42 (m, 6H), 7.31-7.25 (m, 3H), 7.22-7.15 (m, 3H), 4.59 (s, 1H), 3.64 (bs, 5H), 3.39-3.21 (m, 2H), 2.95-2.87 (m, 1H), 2.66-2.61 (m, 2H), 1.97-1.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.8, 175.5, 141.5, 141.3, 136.5, 133.4, 129.0, 128.7, 128.1, 127.8, 127.7, 114.8, 73.3, 52.0, 48.5, 39.8, 39.3, 37.4, 28.9; HRMS-ESI (m/z) calculated for $C_{28}H_{28}N_2O_3$[M+Na]$^+$ 463.1998, found 463.1998.

Methyl 2-(2-((tert-butoxycarbonyl)(cyanomethyl)amino)ethyl)-4-oxo-4-phenylbutanoate (4v)



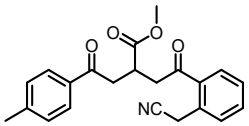
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 41.9 mg, 56% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.96 (d, *J* = 7.2 Hz, 2H), 7.61-7.56 (m, 1H), 7.50-7.45 (m, 2H), 4.19 (s, 2H), 3.71 (s, 3H), 3.54-3.41 (m, 3H), 3.19-3.03 (m, 2H), 2.05-1.95 (m, 1H), 1.91-1.82 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 197.5, 175.0, 136.4, 133.4, 128.7, 128.0, 116.1, 81.9, 52.1, 45.6, 40.3, 37.7, 29.7, 28.2; HRMS-ESI (m/z) calculated for $C_{20}H_{26}N_2O_5$[M+Na]$^+$ 397.1740, found 397.1739.

Methyl 4-(2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6a)



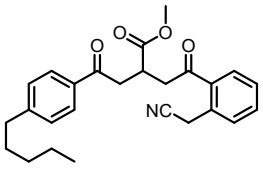
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 44.7 mg, 64% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.99-7.96 (m, 2H), 7.91 (d, J = 7.2 Hz, 1H), 7.61-7.56 (m, 3H), 7.50-7.45 (m, 3H), 4.19-4.04 (m, 2H), 3.71 (s, 3H), 3.68-3.59 (m, 2H), 3.56-3.53 (m, 1H), 3.43-3.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 200.6, 197.7, 174.7, 136.4, 135.3, 133.5, 132.9, 130.7, 130.6, 130.0, 128.7, 128.4, 128.1, 118.0, 52.3, 41.5, 39.5, 36.1, 23.1; HRMS-ESI (m/z) calculated for $C_{21}H_{19}NO_4$ [M+Na]$^+$ 372.1206, found 372.1209.

Methyl 4-(2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-(p-tolyl)ethyl)butanoate (6b)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 50.1 mg, 69% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.82-7.85 (m, 3H), 7.60-7.52 (m, 2H), 7.48-7.42 (m, 1H), 7.28-7.25 (m, 2H), 4.18-4.04 (m, 2H), 3.70 (s, 3H), 3.67-3.56 (m, 2H), 3.54-3.50 (m, 1H), 3.40-3.25 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm) 200.7, 197.3, 174.8, 144.4, 135.3, 133.9, 132.9, 130.7, 130.6, 130.0, 129.4, 128.4, 128.2, 118.0, 52.3, 41.6, 39.4, 36.1, 23.0, 21.7; HRMS-ESI (m/z) calculated for $C_{22}H_{21}NO_4$ [M+Na]$^+$ 363.1471, found 386.1372.

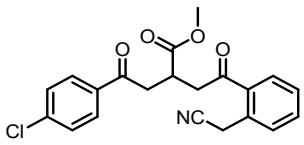
Methyl 4-(2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-(4-pentylphenyl)ethyl)butanoate (6c)



Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 56.2 mg, 67% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.91-7.90 (m, 3H), 7.60-7.53 (m, 2H), 7.48-7.43 (m, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 4.19-4.04 (m, 2H), 3.70 (s, 3H), 3.67-3.57 (m, 2H), 3.54-3.51 (m, 1H), 3.41-3.25 (m, 2H), 2.68-2.63 (m, 2H), 1.68-1.58 (m, 2H), 1.37-1.26 (m, 4H), 0.91-0.86 (m, 3H); ^{13}C NMR (75 MHz, CDCl3) (δ, ppm): 200.7, 197.3, 174.8, 149.3, 135.3, 134.1, 132.9, 130.7, 130.6, 130.0, 128.8, 128.4, 128.3, 118.0, 52.3, 41.6, 39.4, 36.1, 36.0, 31.4, 30.8, 23.1, 22.5, 14.0; HRMS-ESI (m/z) calculated

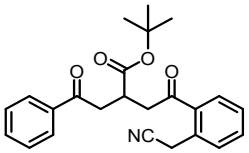
for $C_{26}H_{29}NO_4$ $[M+Na]^+$ 442.1994, found 442.2004.

Methyl 4-(4-chlorophenyl)-2-(2-(2-(cyanomethyl)phenyl)-2-oxoethyl)-4-oxobutanoate (6d)



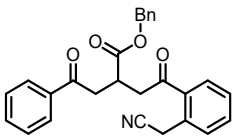
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 47.6 mg, 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.93-7.92 (m, 3H), 7.57 (d, *J* = 4.0 Hz, 2H), 7.50-7.43 (m, 3H), 4.17-4.05 (m, 2H), 3.71 (s, 3H), 3.67-3.62 (m, 1H), 3.59-3.57 (m, 1H), 3.55-3.53 (m, 1H), 3.38-3.30 (m, 2H); ^{13}C NMR (151 MHz, CDCl3) (δ, ppm): 200.5, 196.6, 174.5, 139.9, 135.2, 134.7, 133.0, 130.7, 130.0, 129.5, 129.0, 128.5, 118.0, 52.3, 41.5, 39.4, 36.0, 23.1; HRMS-ESI (m/z) calculated for $C_{21}H_{18}ClNO_4$ $[M+Na]^+$ 406.0822, found 406.0822.

tert-Butyl 4-(2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6e)



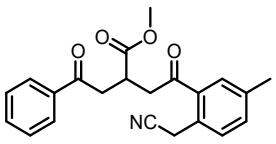
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 51.7 mg, 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.99-7.97 (m, 2H), 7.92-7.90 (m, 1H), 7.60-7.55 (m, 3H), 7.49-7.45 (m, 3H), 4.18-4.06 (m, 2H), 3.58-3.48 (m, 3H), 3.36-3.22 (m, 2H), 1.46-1.42 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 200.9, 198.0, 173.3, 136.6, 135.5, 133.4, 132.8, 130.6, 130.5, 130.0, 128.7, 128.4, 128.1, 118.1, 81.3, 41.6, 39.6, 37.3, 27.9, 23.0; HRMS-ESI (m/z) calculated for $C_{24}H_{25}NO_4$ $[M+Na]^+$ 414.1681, found 414.1682.

Benzyl 4-(2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6f)



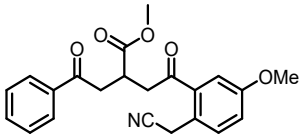
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 46.0 mg, 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.96-7.94 (m, 2H), 7.87 (d, J = 8.0 Hz, 1H), 7.56-7.53 (m, 3H), 7.48-7.41 (m, 3H), 7.33-7.28 (m, 5H), 5.18-5.11 (m, 2H), 4.06-3.93 (m, 2H), 3.75-3.68 (m, 1H), 3.62-3.54 (m, 2H), 3.44-3.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 200.5, 197.7, 174.0, 136.4, 135.7, 135.3, 133.5, 132.9, 130.7, 130.5, 130.0, 128.7, 128.5, 128.4, 128.3(2), 128.3(7), 128.1, 118.0, 66.9, 41.5, 39.5, 36.3, 23.0; HRMS-ESI (m/z) calculated for $C_{27}H_{23}NO_4$ $[M+Na]^+$ 448.1525, found 448.1529.

Methyl 4-(2-(cyanomethyl)-5-methylphenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6g)



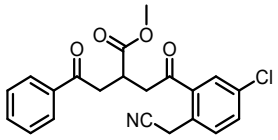
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 50.9 mg, 70% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.99-7.96 (m, 2H), 7.69 (s, 1H), 7.60-7.56 (m, 1H), 7.49-7.42 (m, 3H), 7.35 (d, *J* = 7.8 Hz, 1H), 4.13-3.98 (m, 2H), 3.71 (s, 3H), 3.68-3.64 (m, 1H), 3.61-3.52 (m, 2H), 3.44-3.27 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) (δ, ppm): 200.6, 197.8, 174.7, 138.4, 136.4, 135.1, 133.5(3), 133.5(9), 130.7, 130.5, 128.7, 128.1, 127.7, 118.3, 52.3, 41.5, 39.5, 36.0, 22.7, 21.0; HRMS-ESI (m/z) calculated for $C_{22}H_{21}NO_4$ $[M+Na]^+$ 386.1368, found 386.1374.

Methyl 4-(2-(cyanomethyl)-5-methoxyphenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6h)



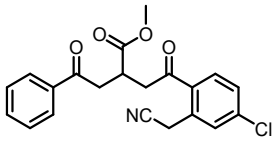
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 51.6 mg, 68% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.99-7.96 (m, 2H), 7.60-7.56 (m, 1H), 7.49-7.44 (m, 3H), 7.40 (d, *J* = 2.8 Hz, 1H), 7.0-7.04 (m, 1H), 4.07-3.95 (m, 2H), 3.86 (s, 3H), 3.71 (s, 3H), 3.67-3.62 (m, 1H), 3.60-3.49 (m, 2H), 3.42-3.26 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm): 200.4, 197.7, 174.7, 159.3, 136.3(4), 136.3(1), 133.5, 131.8, 128.7, 128.1, 122.2, 118.4, 117.3, 116.3, 55.7, 52.3, 41.5, 39.5, 36.0, 22.2. HRMS-ESI (m/z) calculated for $C_{22}H_{21}NO_5$ $[M+Na]^+$ 402.1317, found 402.1328.

Methyl 4-(5-chloro-2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6i)



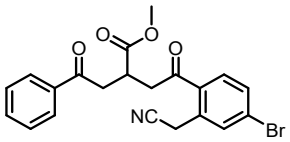
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 36.8 mg, 48% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.98-7.96 (m, 2H), 7.85 (s, 1H), 7.62-7.57 (m, 1H), 7.53 (s, 2H), 7.50-7.46 (m, 2H), 4.13-4.00 (m, 2H), 3.72 (s, 3H), 3.68-3.64 (m, 1H), 3.60-3.51 (m, 2H), 3.44-3.38 (m, 1H), 3.28-3.22 (m, 1H); ^{13}C NMR (151 MHz, CDCl3) (δ, ppm): 199.6, 197.6, 174.5, 136.7, 136.3, 134.5, 133.6, 132.7, 131.8, 129.9, 128.9, 128.7, 128.1, 117.6, 52.4, 41.5, 39.4, 36.0, 22.5; HRMS-ESI (m/z) calculated for $C_{21}H_{18}BrNO_4$ $[M+Na]^+$ 406.0822, found 406.0825.

Methyl 4-(4-chloro-2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6j)



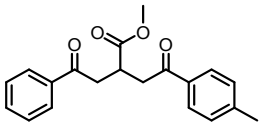
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 49.0 mg, 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.97 (d, *J* = 7.2 Hz, 2H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.61-7.57 (m, 2H), 7.49-7.43 (m, 3H), 4.17-4.04 (m, 2H), 3.71 (s, 3H), 3.66-3.62 (m, 1H), 3.59-3.51 (m, 2H), 3.43-3.37 (m, 1H), 3.28-3.22 (m, 1H); ^{13}C NMR (151 MHz, CDCl3) (δ, ppm): 199.6, 197.6, 174.6, 139.2, 136.3, 133.6, 133.5, 132.8, 131.3, 130.7, 128.8, 128.6, 128.1, 117.4, 52.4, 41.5, 39.5, 36.1, 22.9; HRMS-ESI (m/z) calculated for $C_{21}H_{18}ClNO_4$ $[M+Na]^+$ 406.0822, found 406.0825.

Methyl 4-(4-bromo-2-(cyanomethyl)phenyl)-4-oxo-2-(2-oxo-2-phenylethyl)butanoate (6k)



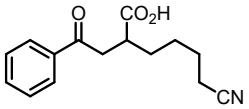
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 49.7 mg, 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.98-7.96 (m, 2H), 7.85 (s, 1H), 7.63-7.57 (m, 1H), 7.53 (d, J = 1.2 Hz, 2H), 7.50-7.46 (m, 2H), 4.13-4.00 (m, 2H), 3.72 (s, 3H), 3.69-3.64 (m, 1H), 3.60-3.51 (m, 2H), 3.44-3.78 (m, 1H), 3.28-3.22 (m, 1H); ^{13}C NMR (151 MHz, CDCl3) (δ, ppm): 199.8, 197.6, 174.6, 136.3, 134.0, 133.6(4), 133.6(0), 132.7, 131.6, 131.3, 128.8, 128.1, 127.7, 117.4, 52.4, 41.5, 39.5, 36.1, 22.8; HRMS-ESI (m/z) calculated for $C_{21}H_{18}BrNO_4$ $[M+Na]^+$ 450.0317, found 450.0312.

Methyl 4-oxo-2-(2-oxo-2-(p-tolyl)ethyl)-4-phenylbutanoate (8)

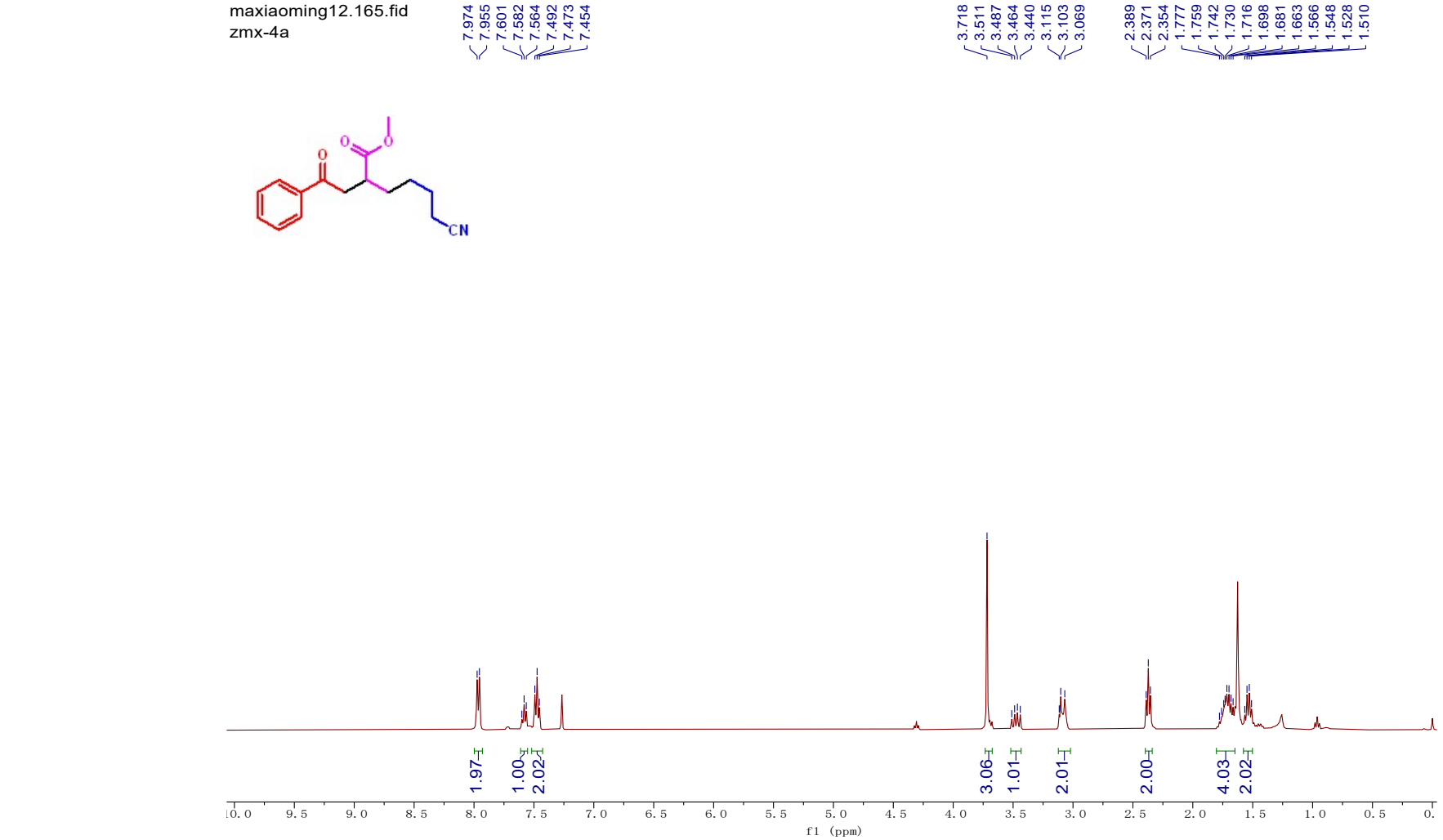


Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 10/1); 36.3 mg, 56% yield; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.96 (d, *J* = 6.9 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 2H), 7.59-7.54 (m, 1H), 7.48-7.43 (m, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 3.70 (s, 3H), 3.67-3.50 (m, 3H), 3.40-3.31 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) (δ, ppm): 197.9, 197.4, 175.0, 144.2, 136.5, 134.0, 133.3, 129.3, 128.6, 128.2, 128.1, 52.2, 39.5, 39.4, 35.9, 21.7; HRMS-ESI (m/z) calculated for $C_{20}H_{20}O_4$ $[M+Na]^+$ 347.1259, found 347.1262.

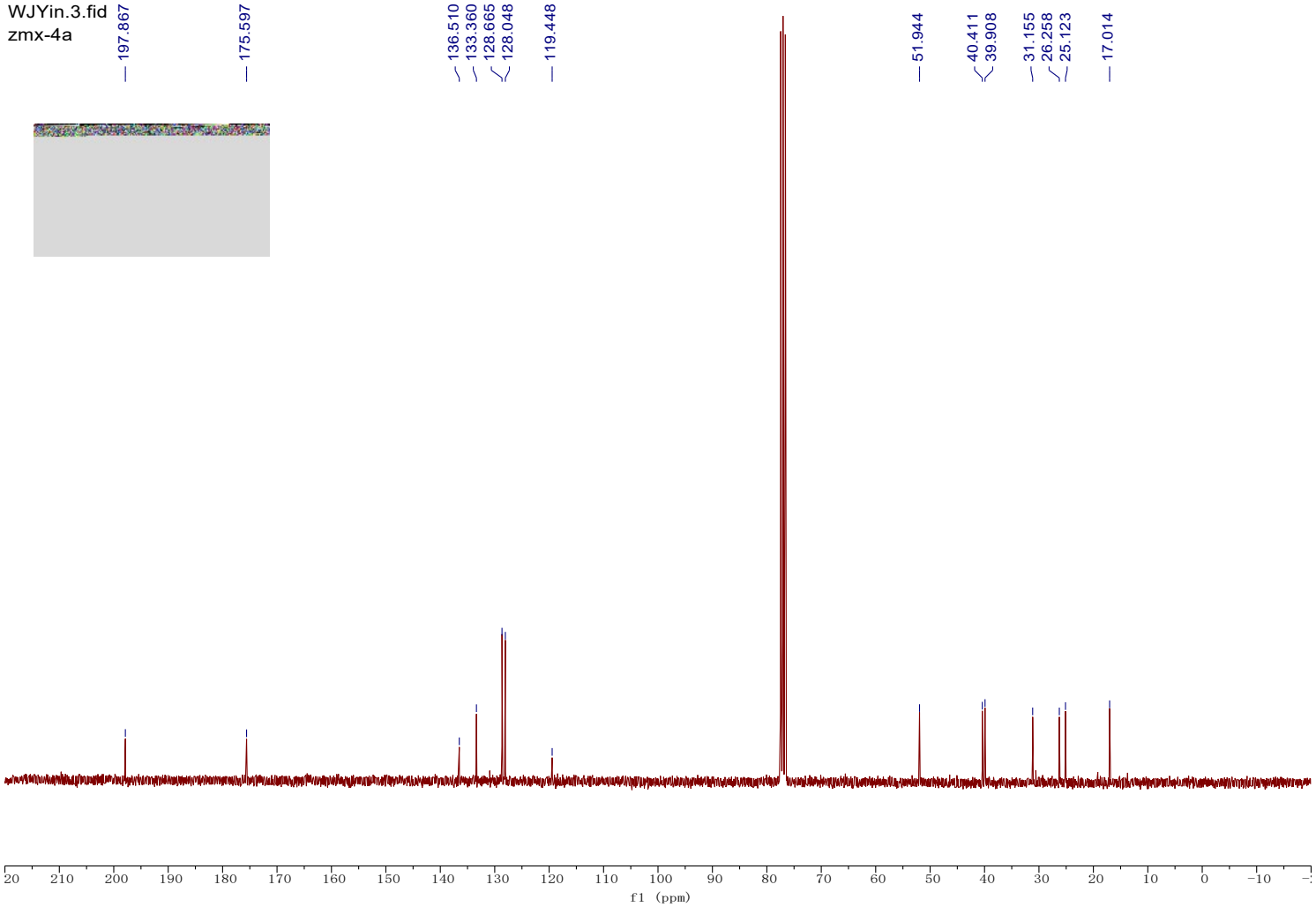
6-Cyano-2-(2-oxo-2-phenylethyl)hexanoic acid (9)



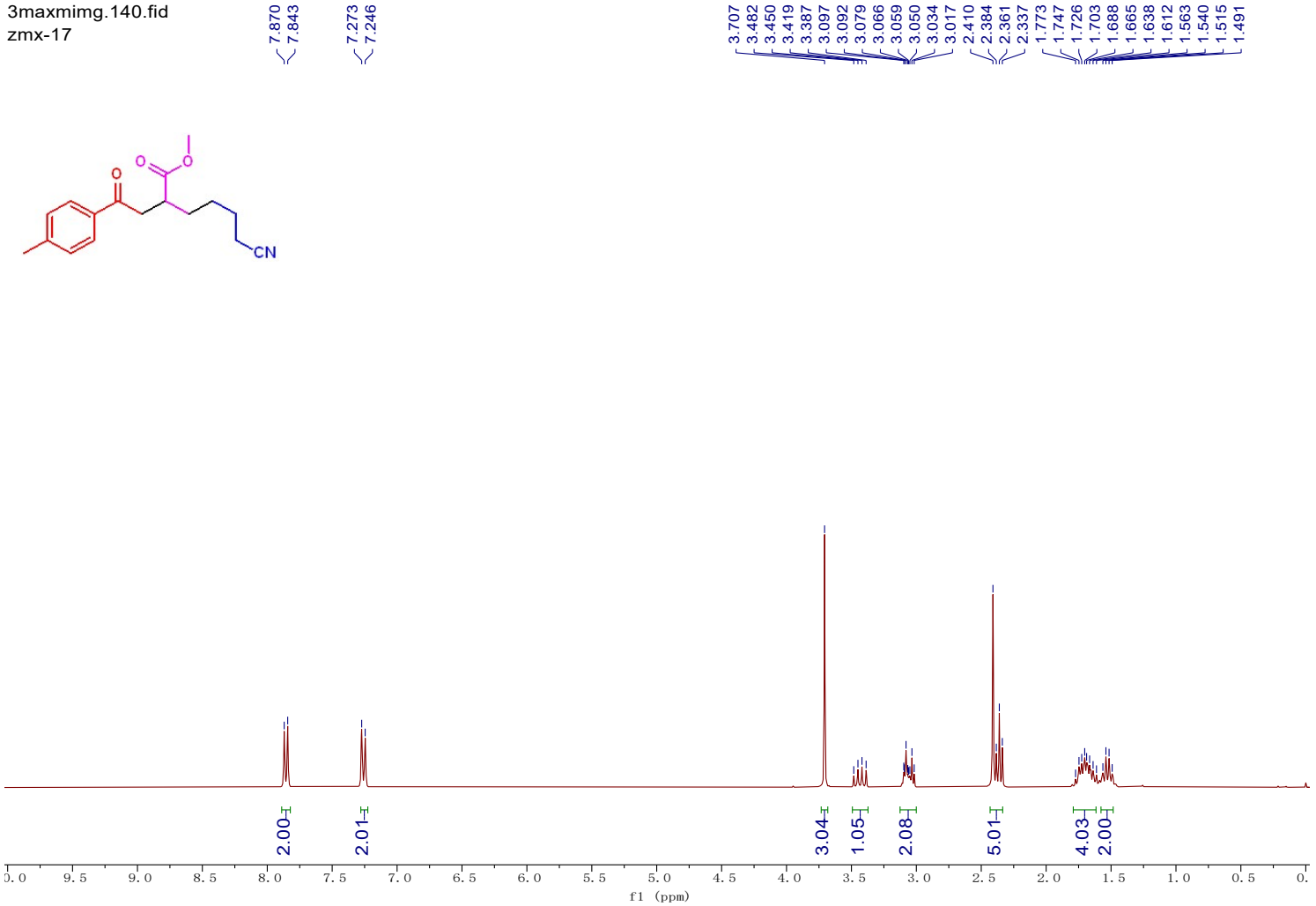
Yellow oil after purification by column chromatography (petroleum ether/ethyl acetate = 1/1); 33.7mg 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.97 (d, *J* = 7.6 Hz, 2H), 7.60-7.56 (m, 1H), 7.49-7.45 (m, 2H), 3.51-3.44 (m, 1H), 3.13-3.08 (m, 2H), 2.39-2.36 (m, 2H), 1.78-1.53 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) (δ, ppm): 197.8, 180.3, 180.2, 136.3, 133.5, 128.7, 128.1, 119.5, 40.1, 39.7, 30.9, 26.2, 25.1, 17.0; HRMS-ESI (m/z) calculated for $C_{15}H_{17}NO_3$ $[M+Na]^+$ 282.1106, found 282.1108.



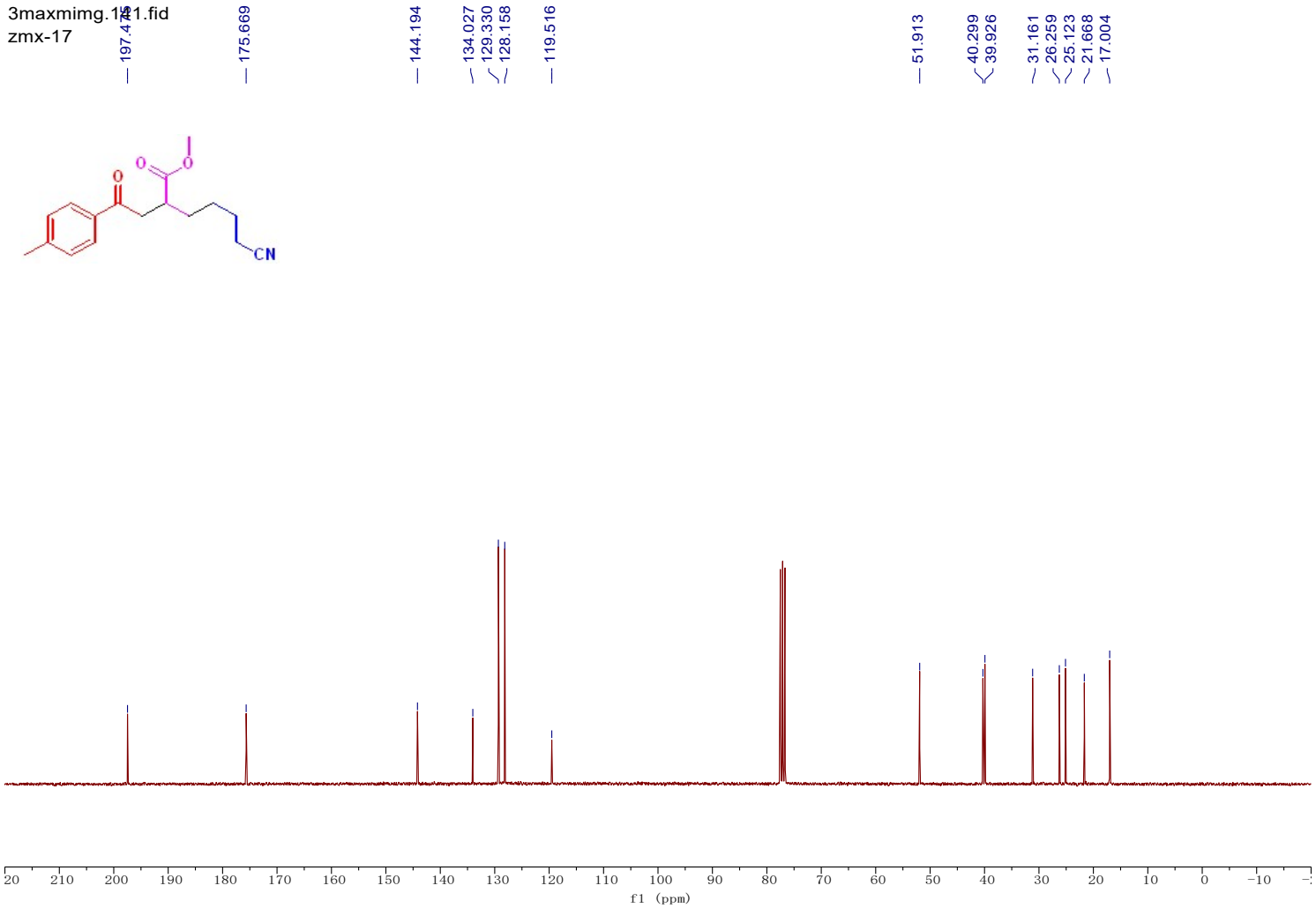
^{1}H NMR Spectrum of Compound 4a (400 MHz, $CDCl_3$)



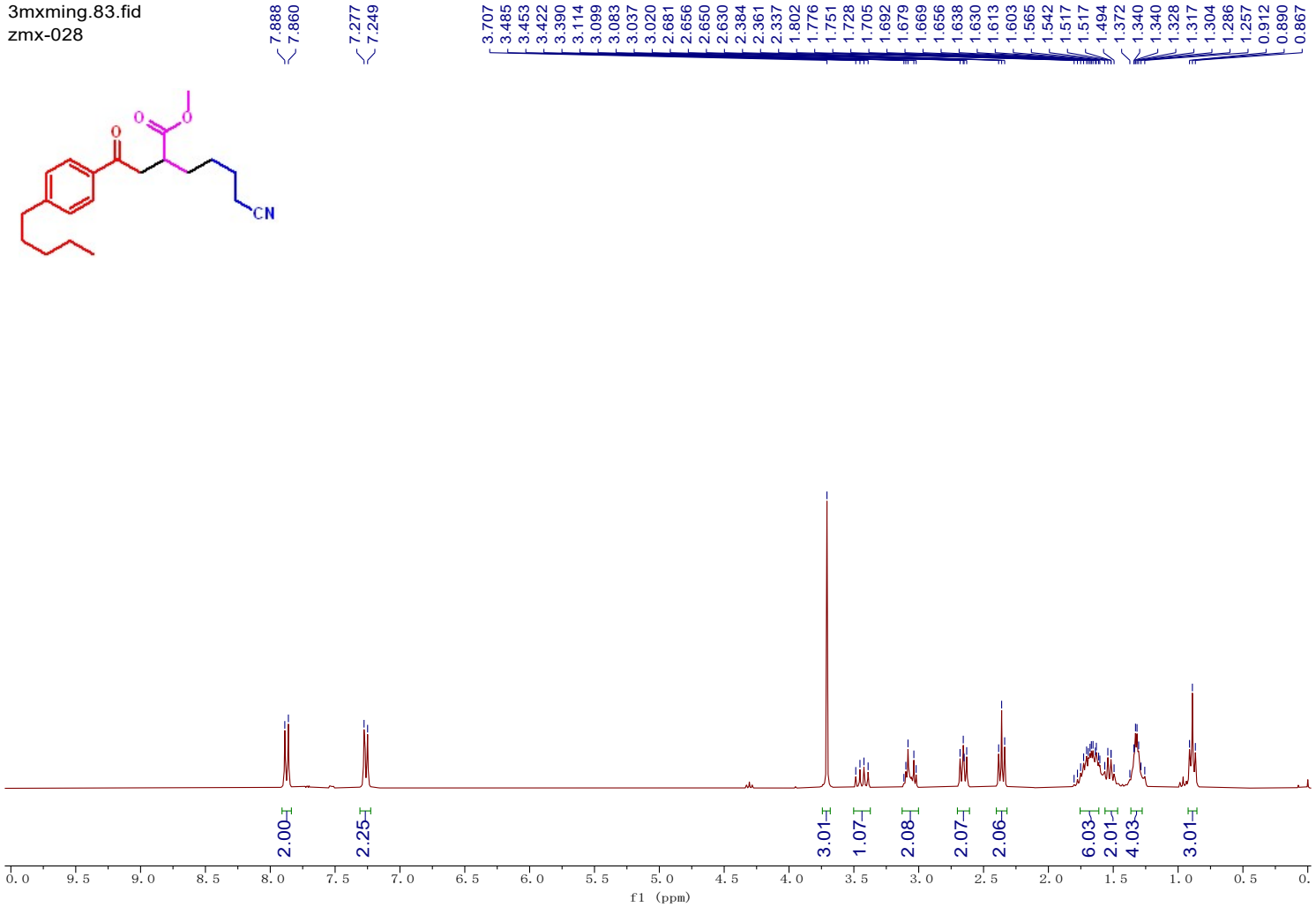
^{13}C NMR Spectrum of Compound 4a (75 MHz, $CDCl_3$)



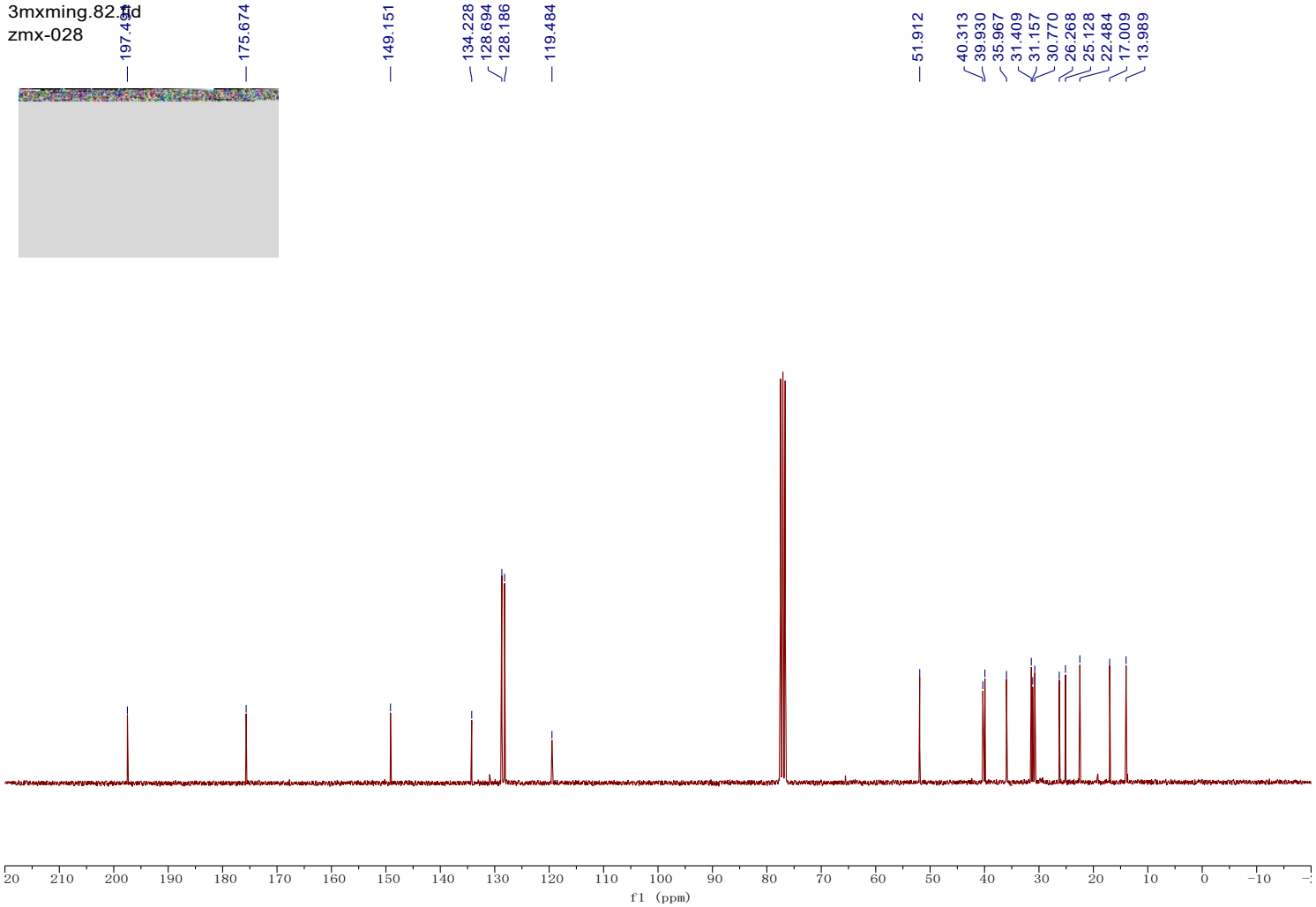
^{1}H NMR Spectrum of Compound 4b (300 MHz, $CDCl_3$)



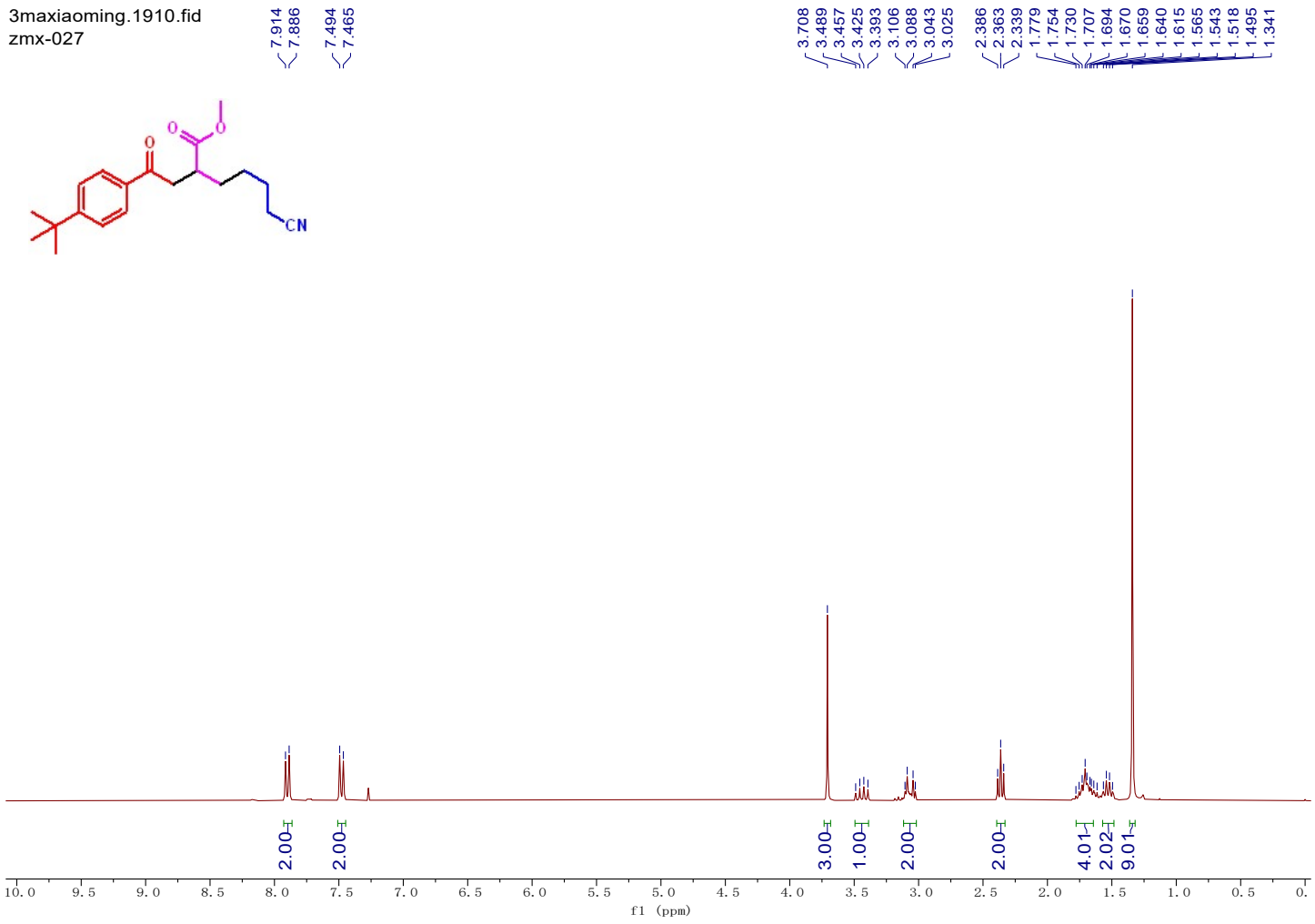
^{13}C NMR Spectrum of Compound 4b (75 MHz, $CDCl_3$)



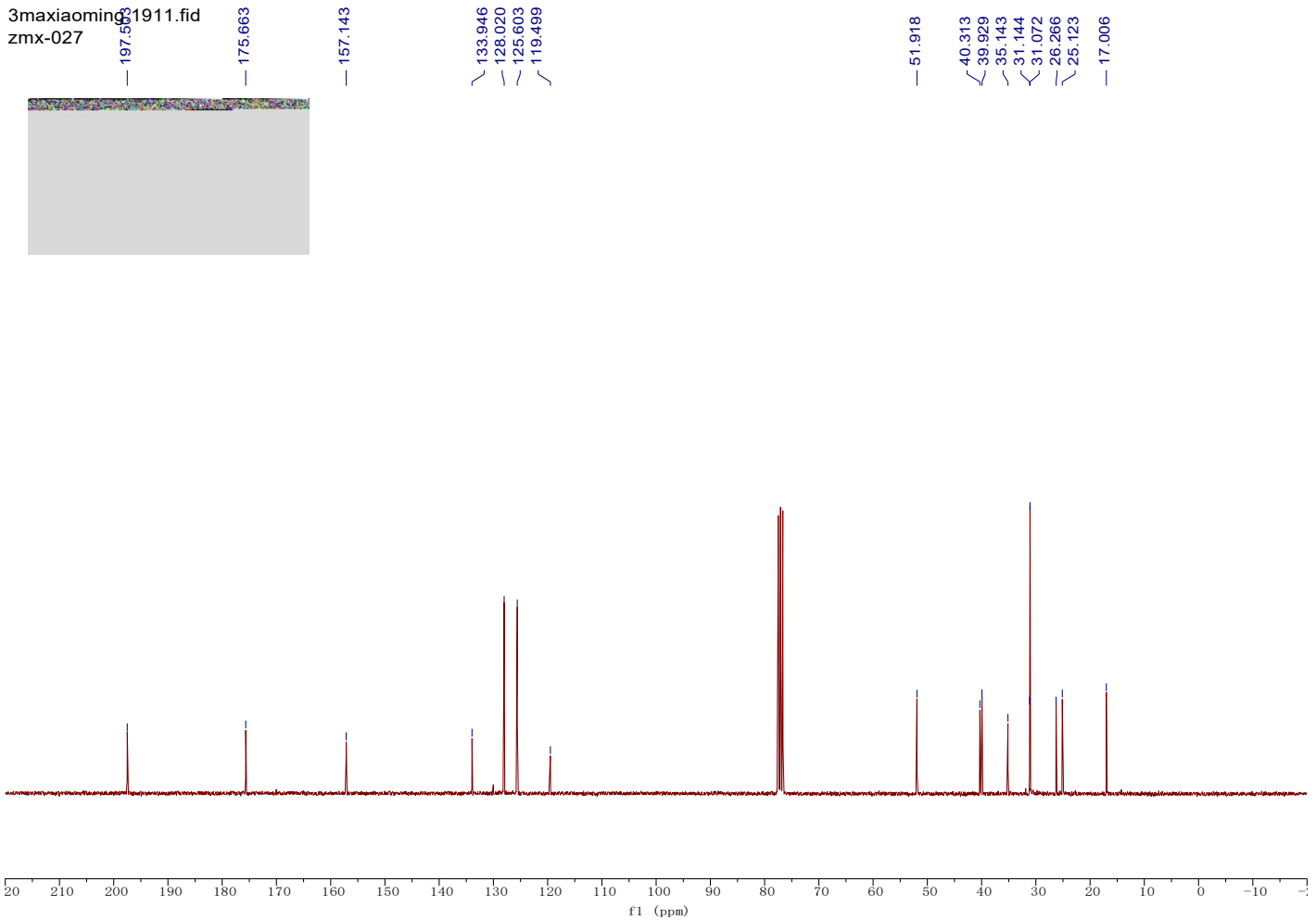
^{1}H NMR Spectrum of Compound 4c (300 MHz, $CDCl_3$)



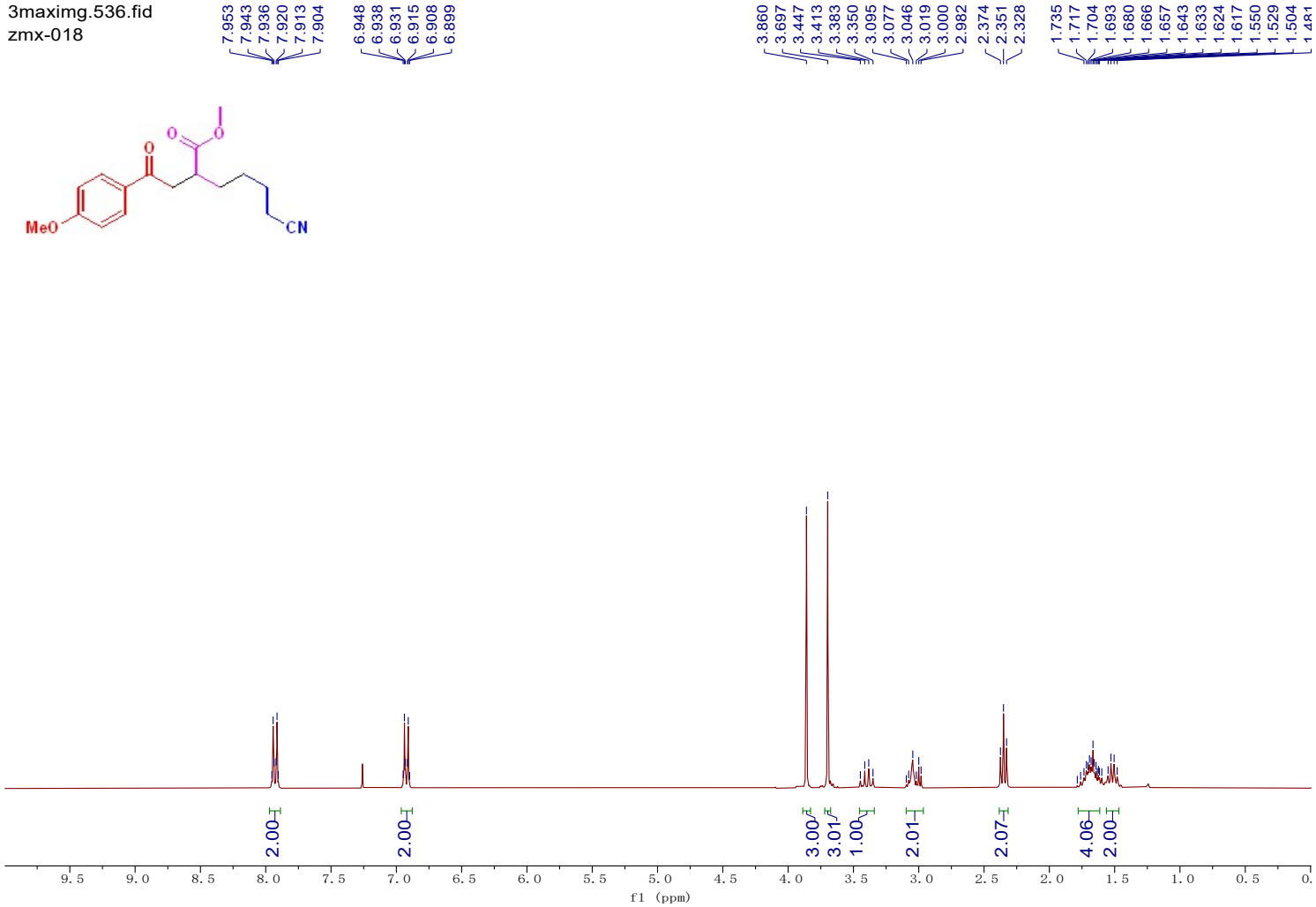
^{13}C NMR Spectrum of Compound 4c (75 MHz, $CDCl_3$)



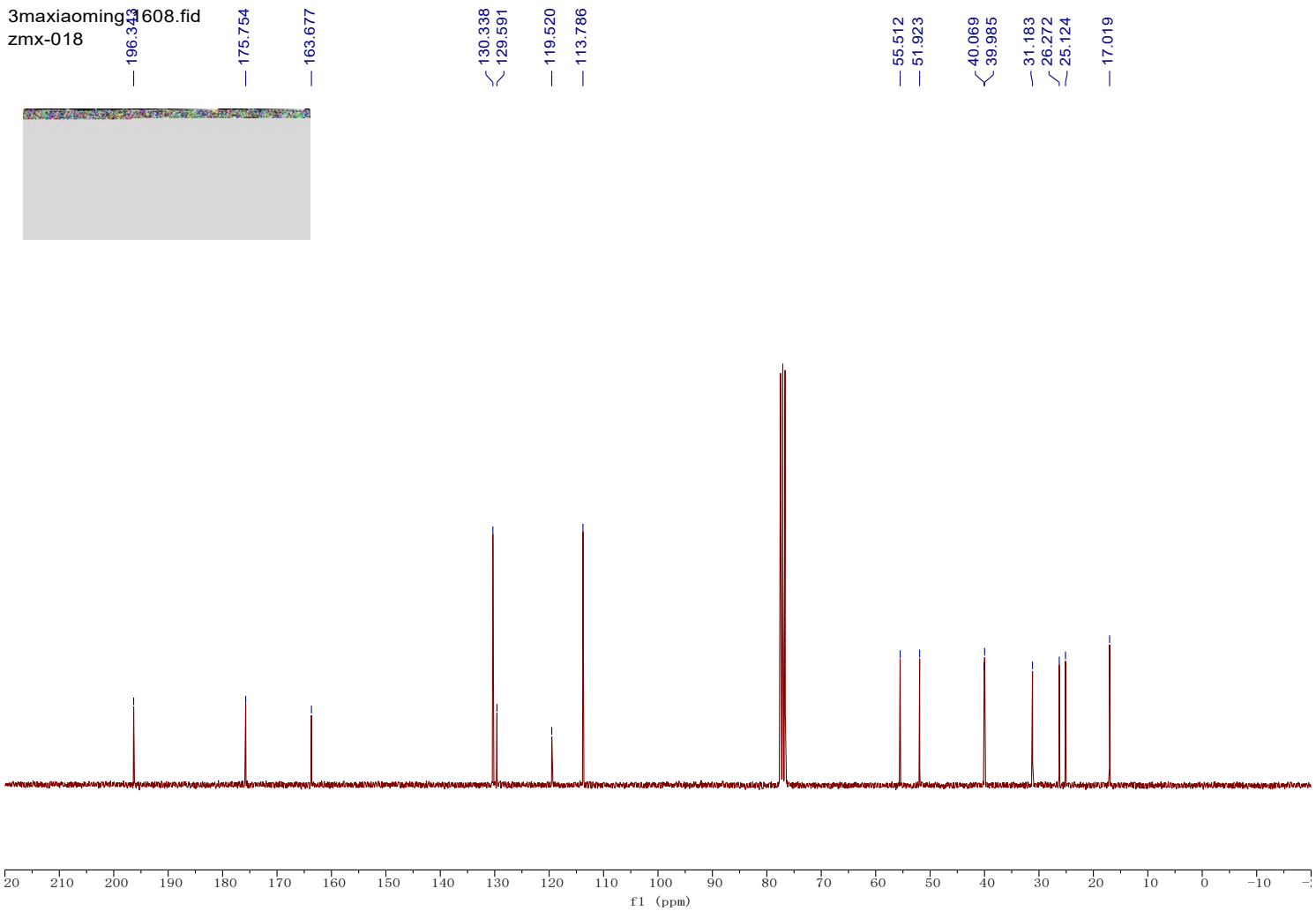
^{1}H NMR Spectrum of Compound 4d (300 MHz, $CDCl_3$)



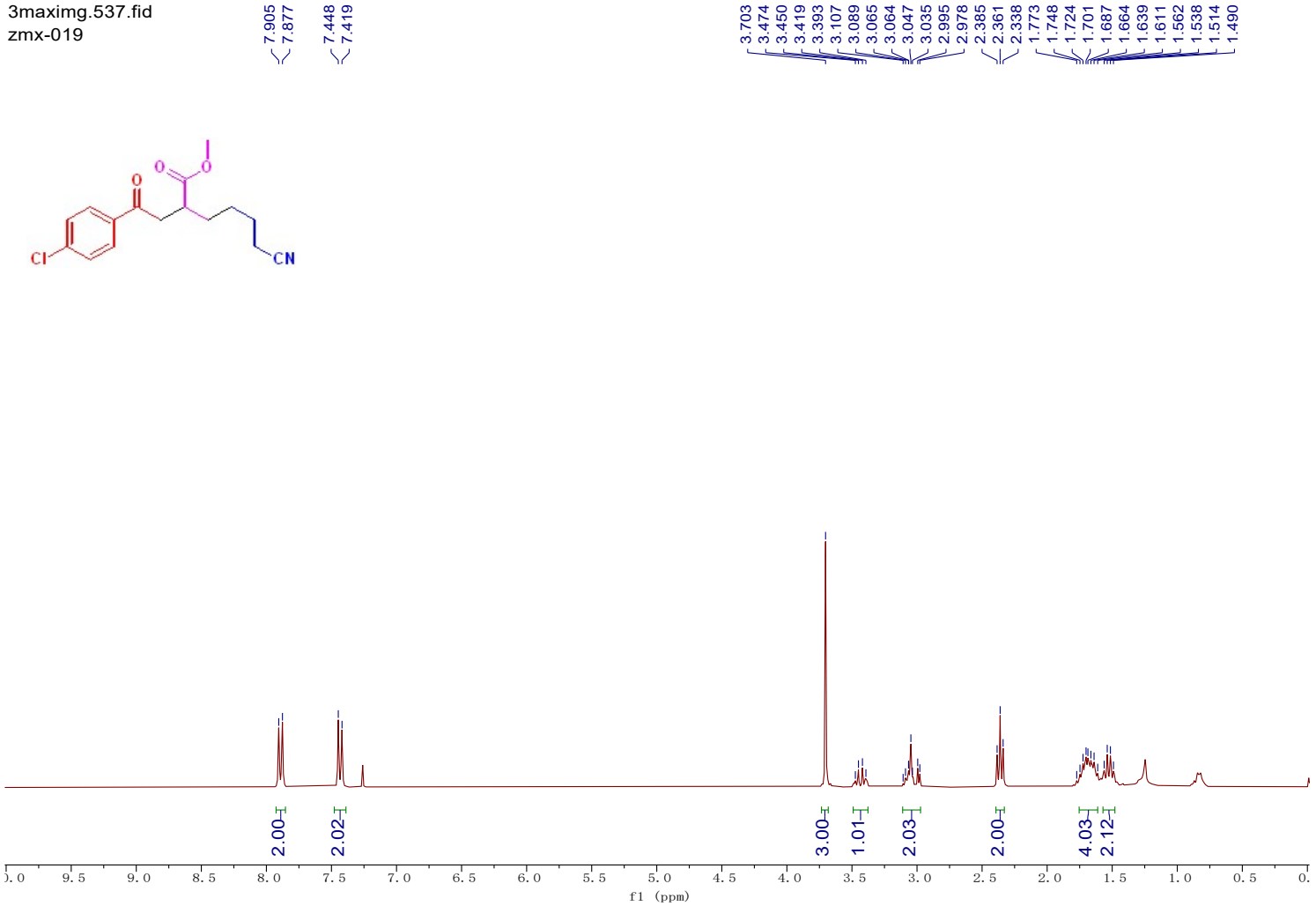
^{13}C NMR Spectrum of Compound 4d (75 MHz, $CDCl_3$)



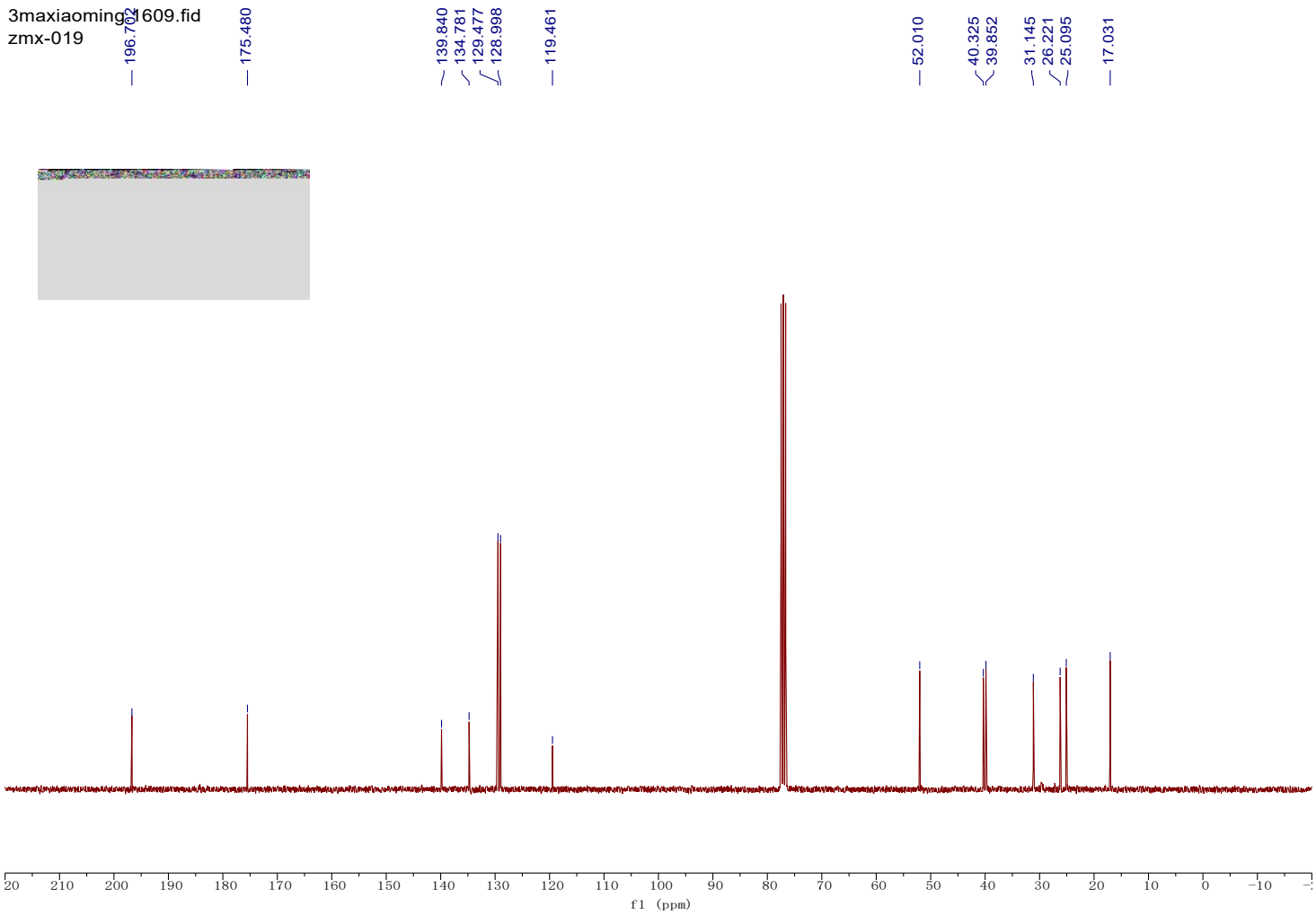
^{1}H NMR Spectrum of Compound 4e (300 MHz, $CDCl_3$)



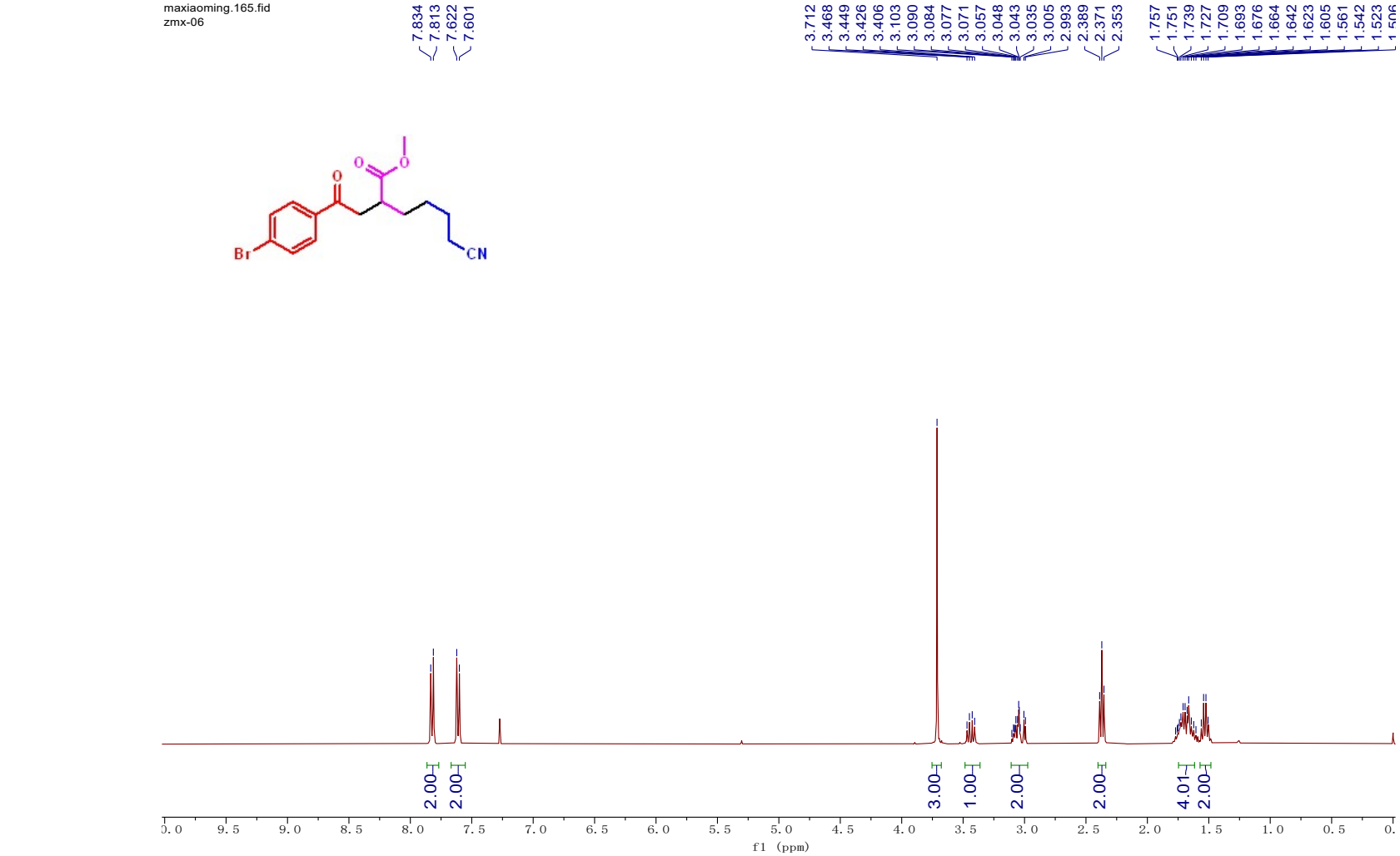
^{13}C NMR Spectrum of Compound 4e (75 MHz, $CDCl_3$)



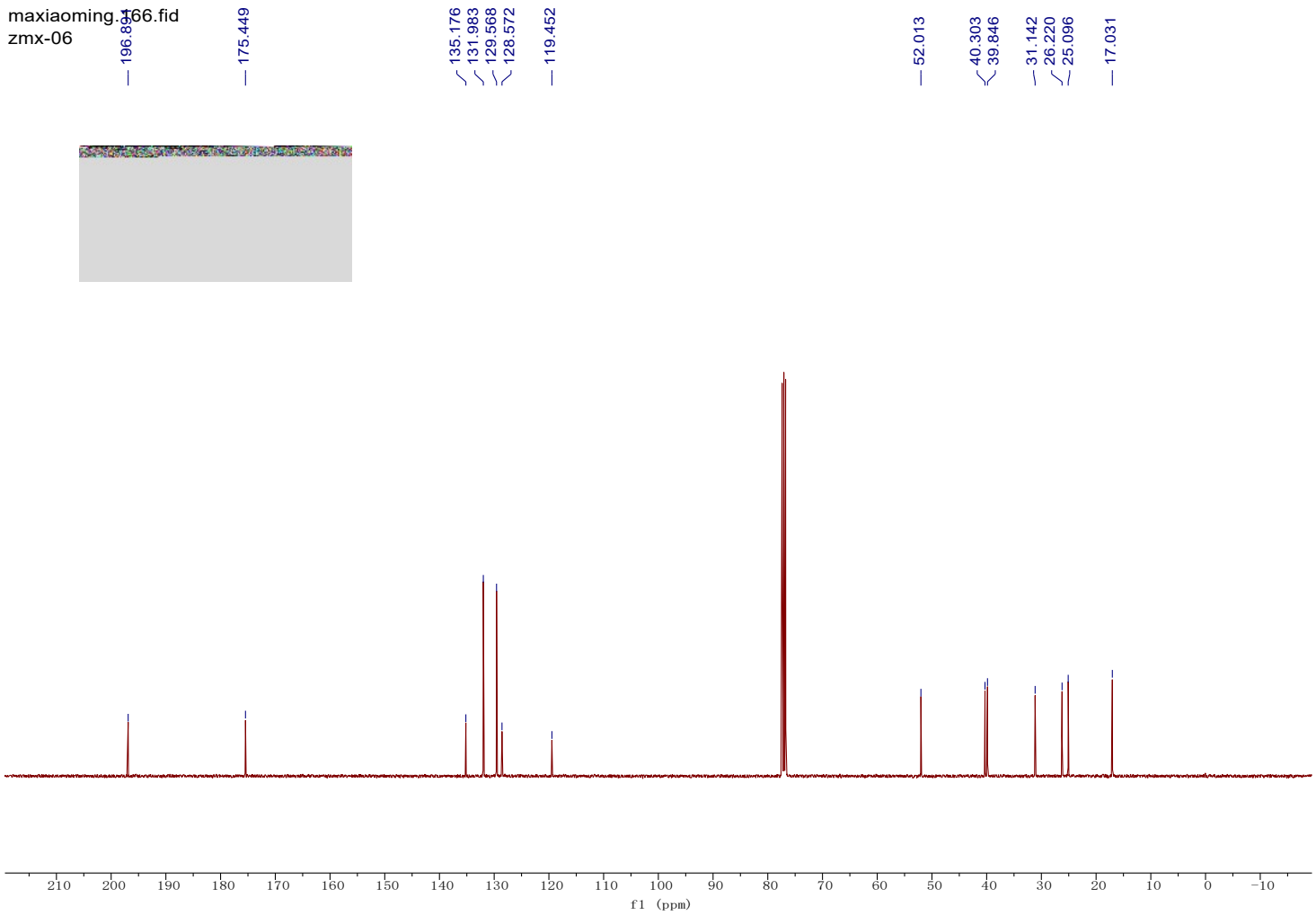
^{1}H NMR Spectrum of Compound 4f (300 MHz, $CDCl_3$)



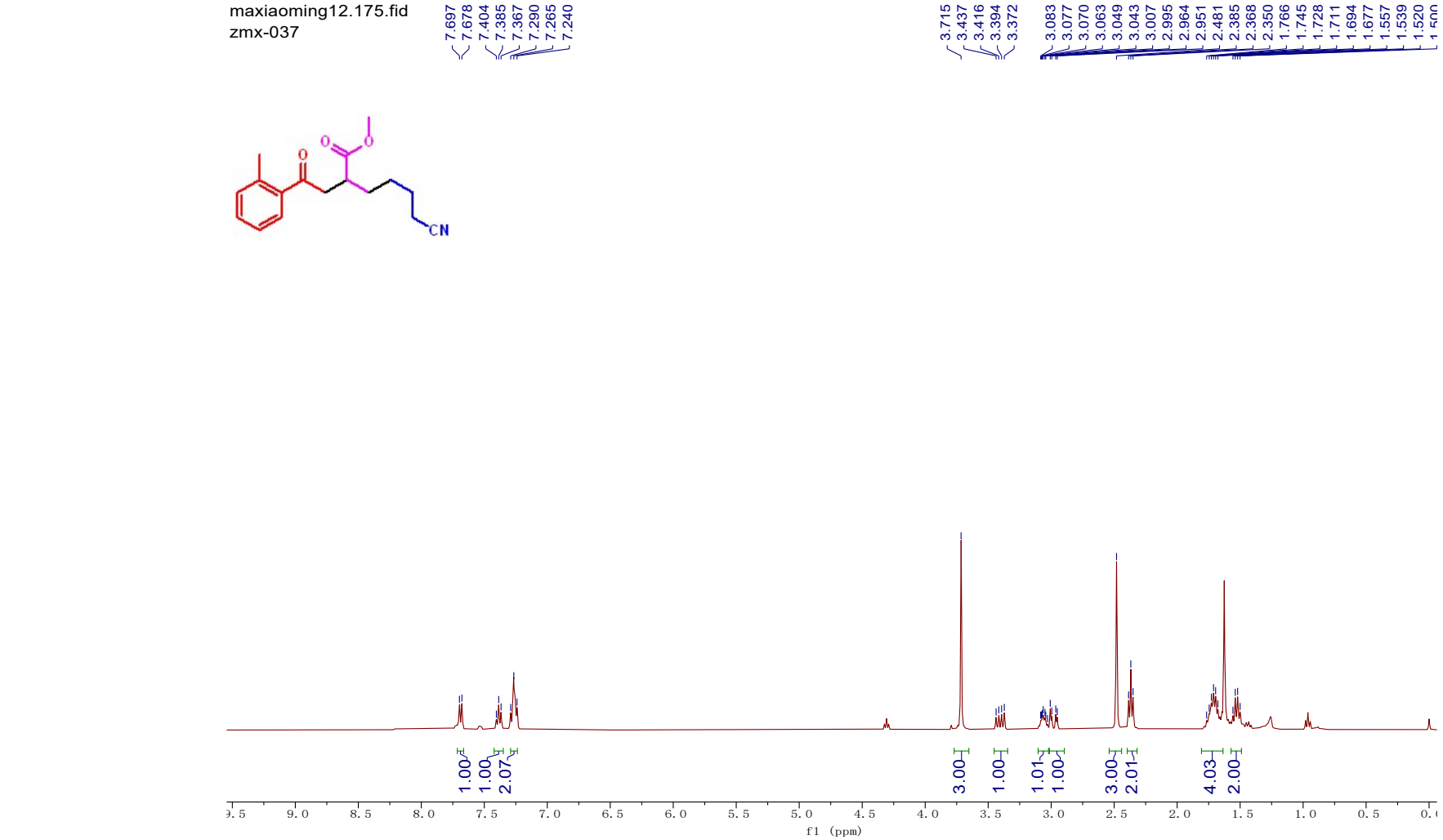
^{13}C NMR Spectrum of Compound 4f (75 MHz, $CDCl_3$)



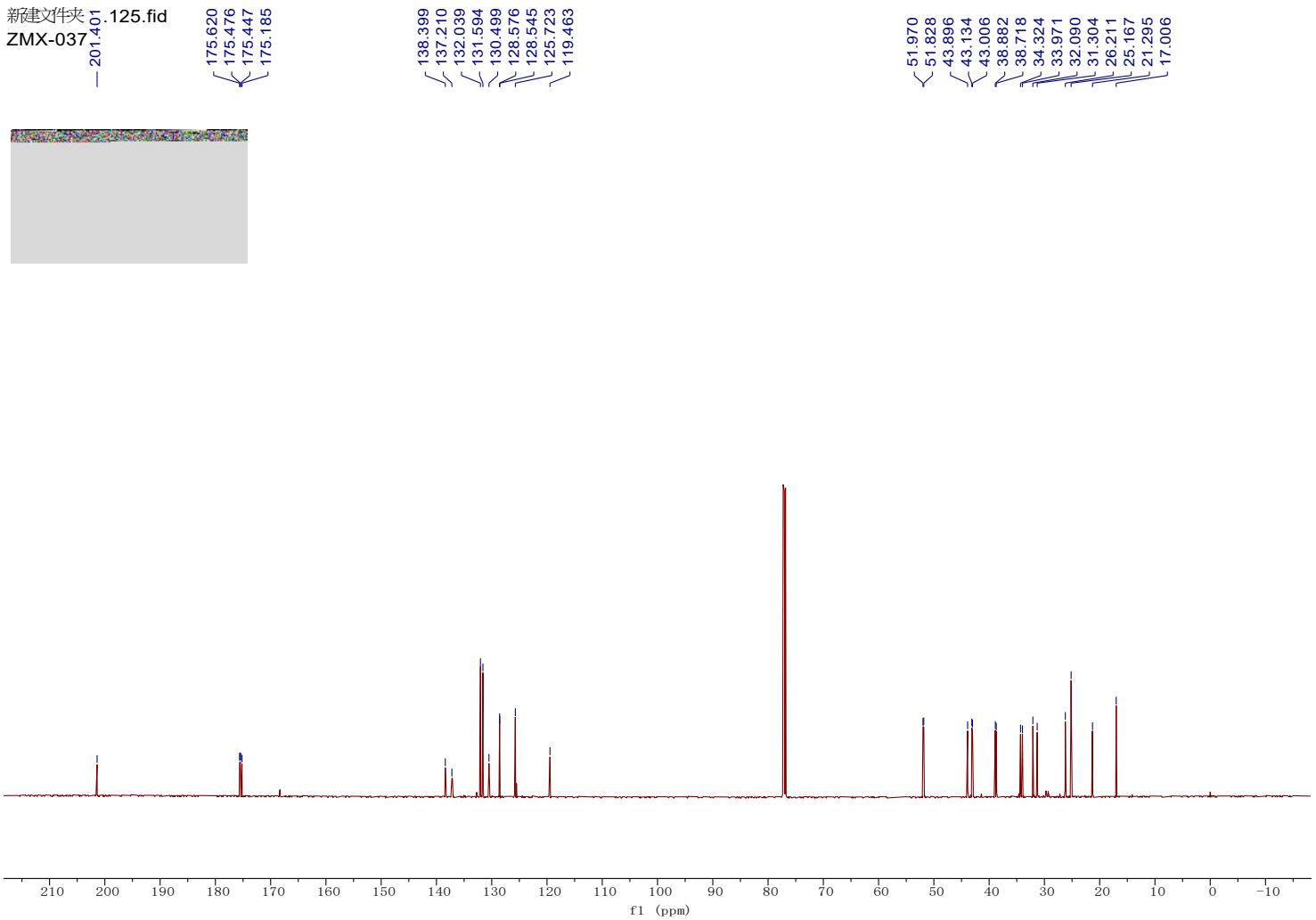
^{1}H NMR Spectrum of Compound 4g (400 MHz, $CDCl_3$)



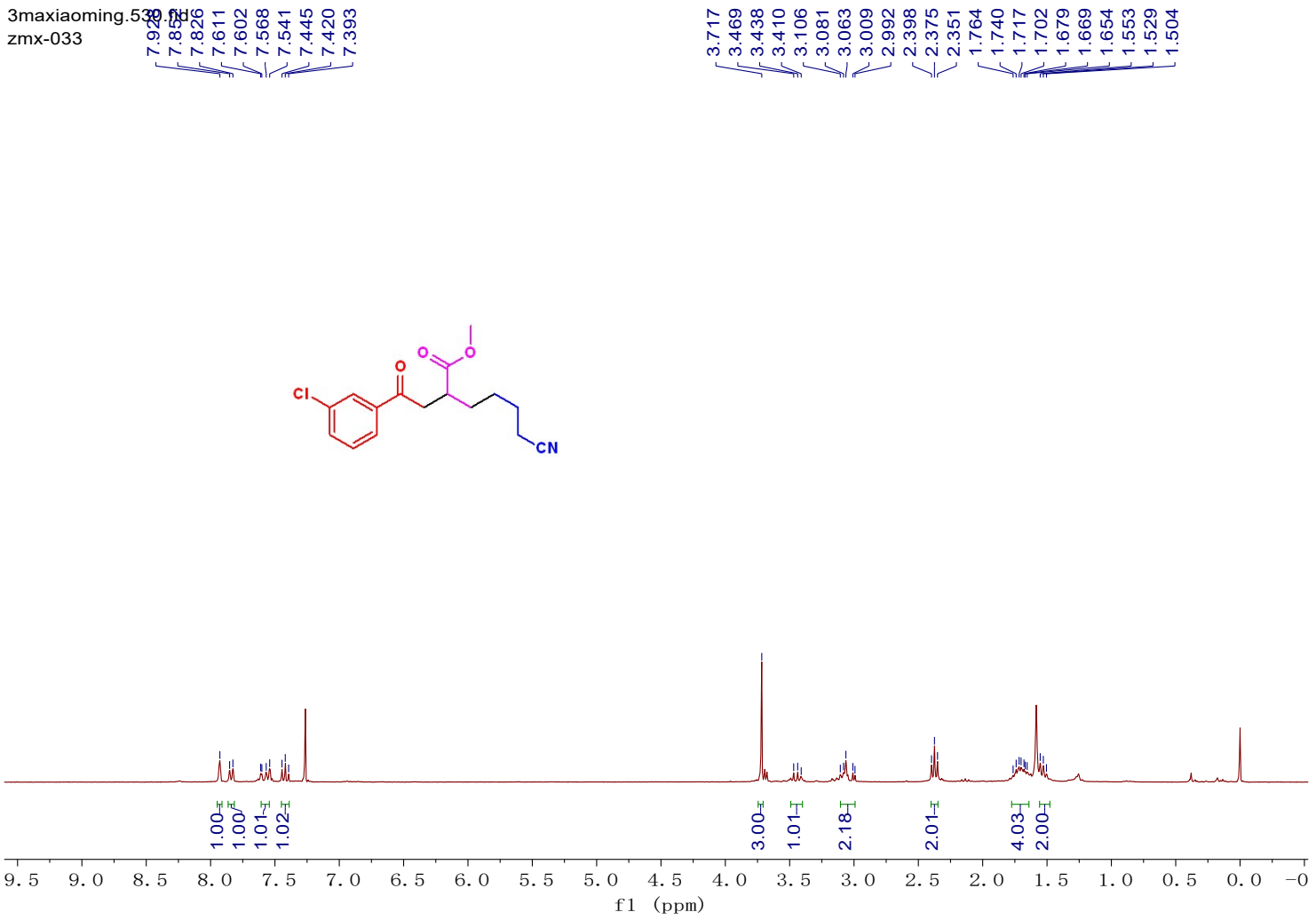
^{13}C NMR Spectrum of Compound 4g (101 MHz, $CDCl_3$)



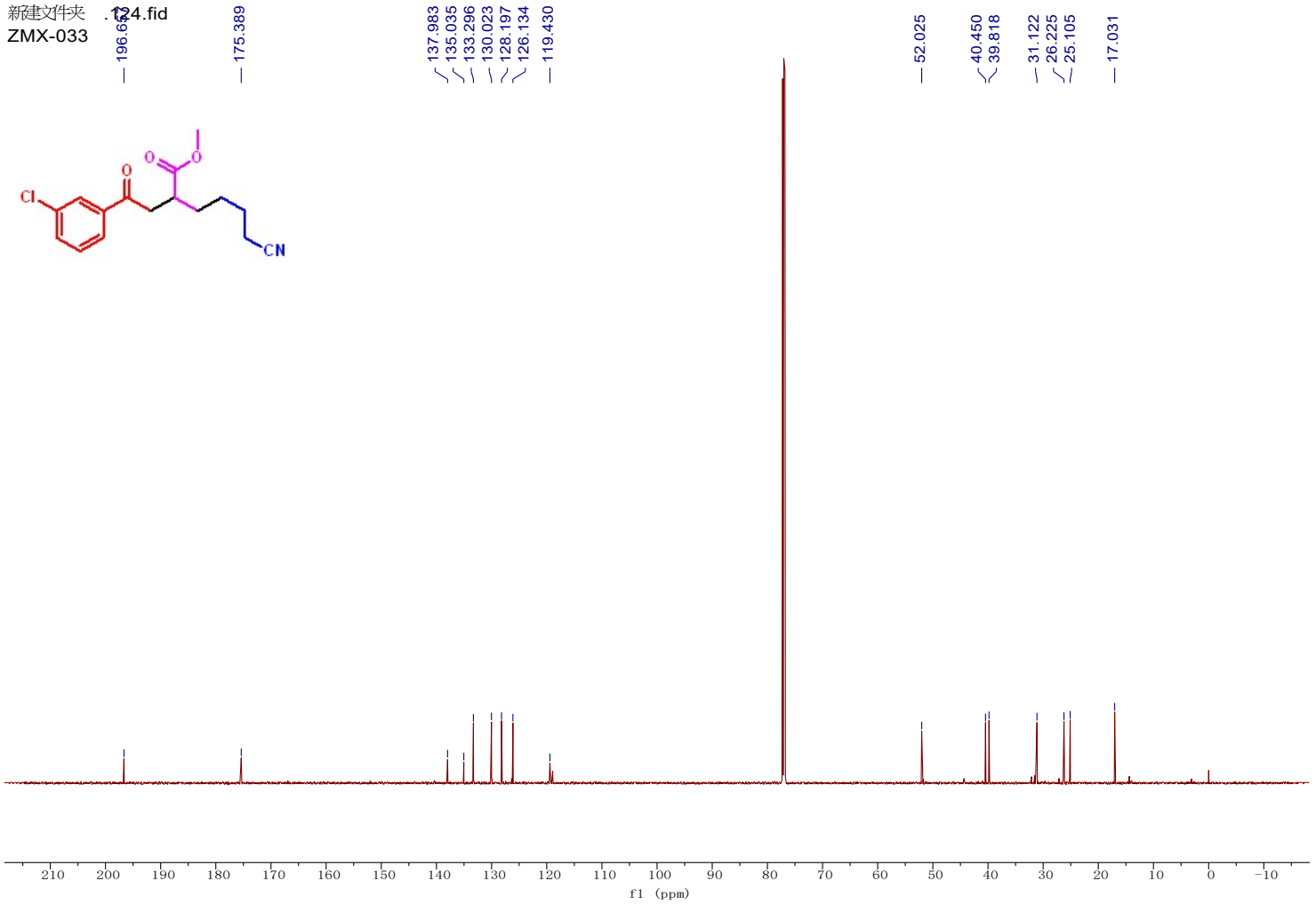
^{1}H NMR Spectrum of Compound 4h (400 MHz, $CDCl_3$)



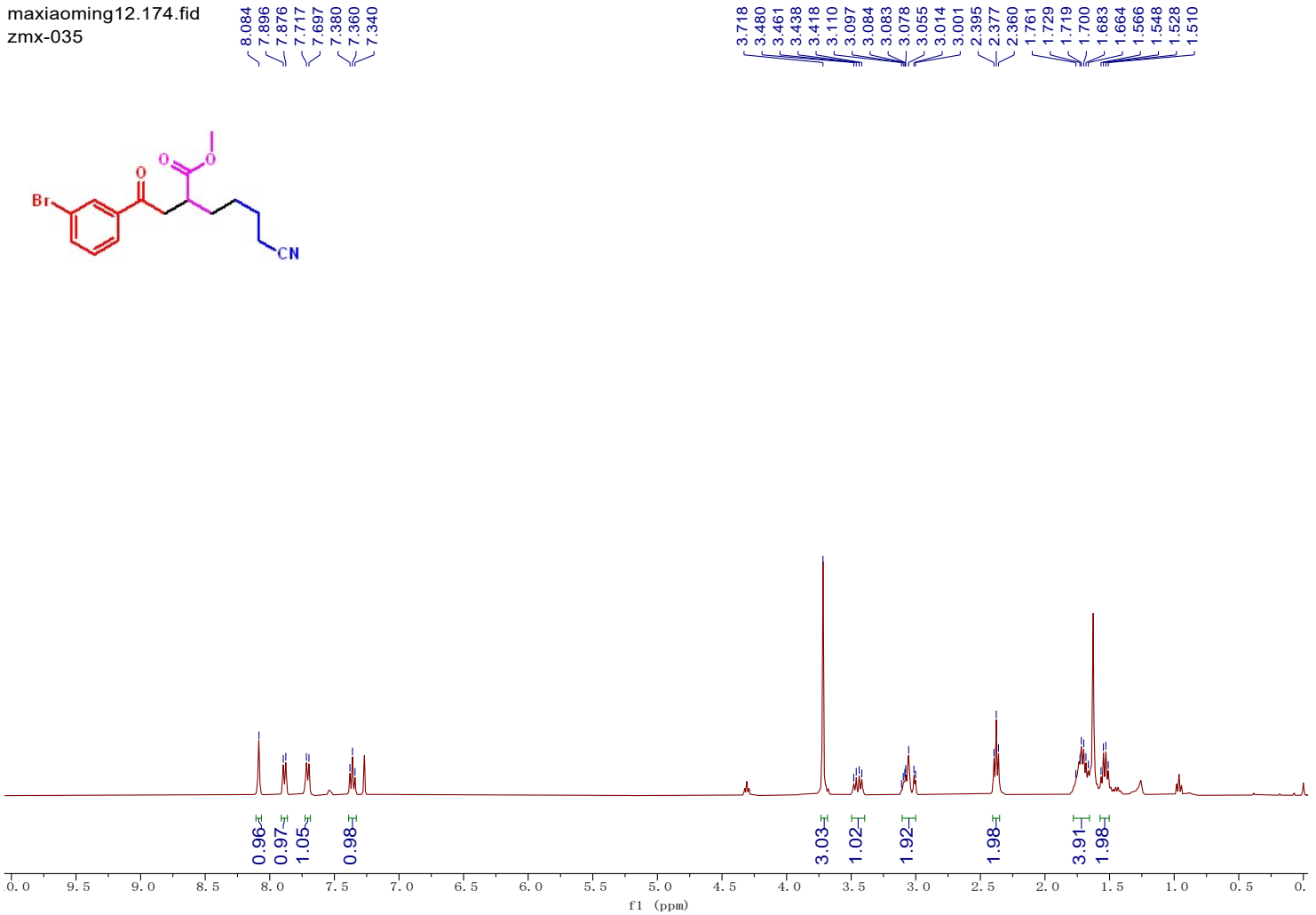
^{13}C NMR Spectrum of Compound 4h (151 MHz, $CDCl_3$)



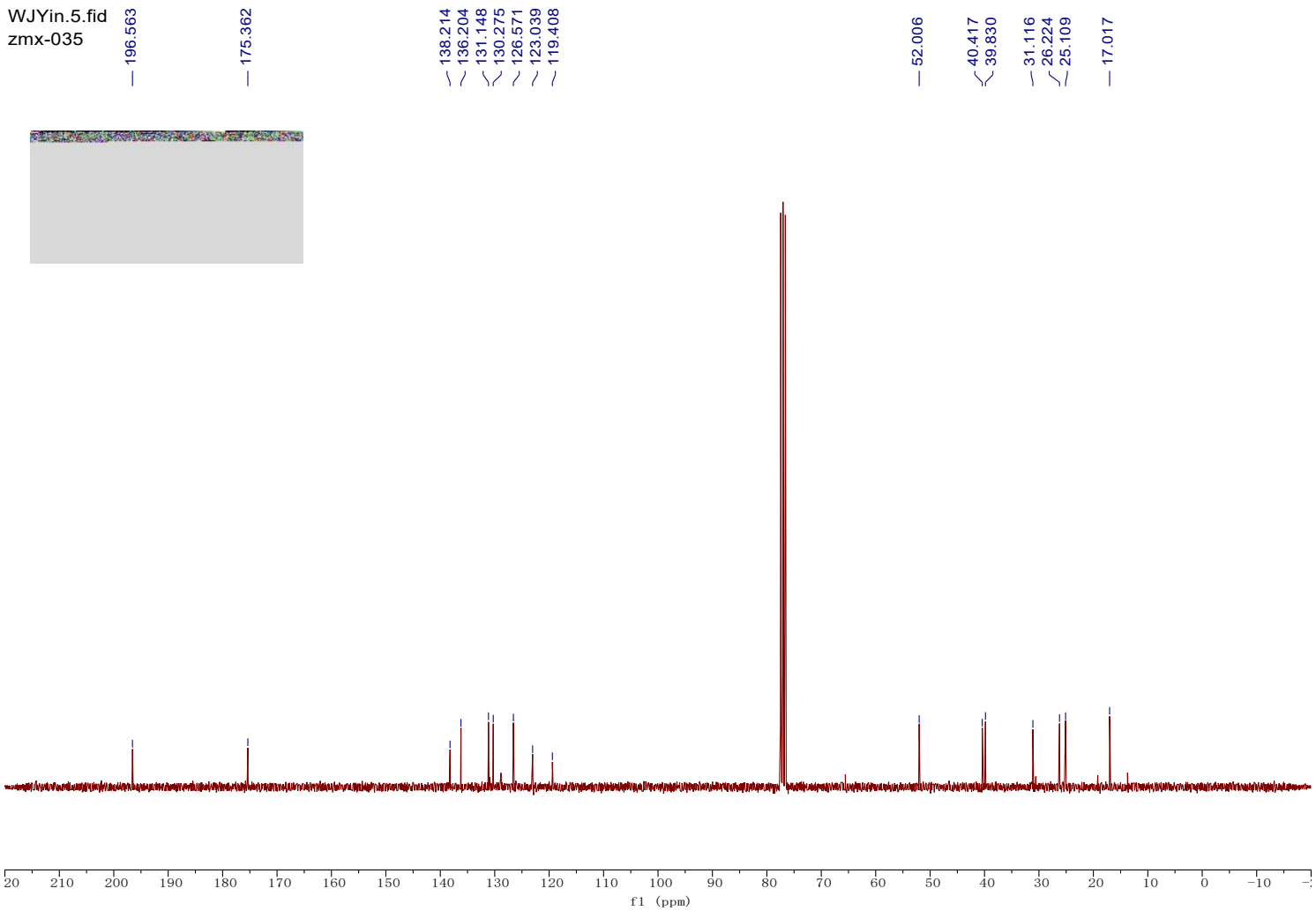
^{1}H NMR Spectrum of Compound 4i (300 MHz, $CDCl_3$)



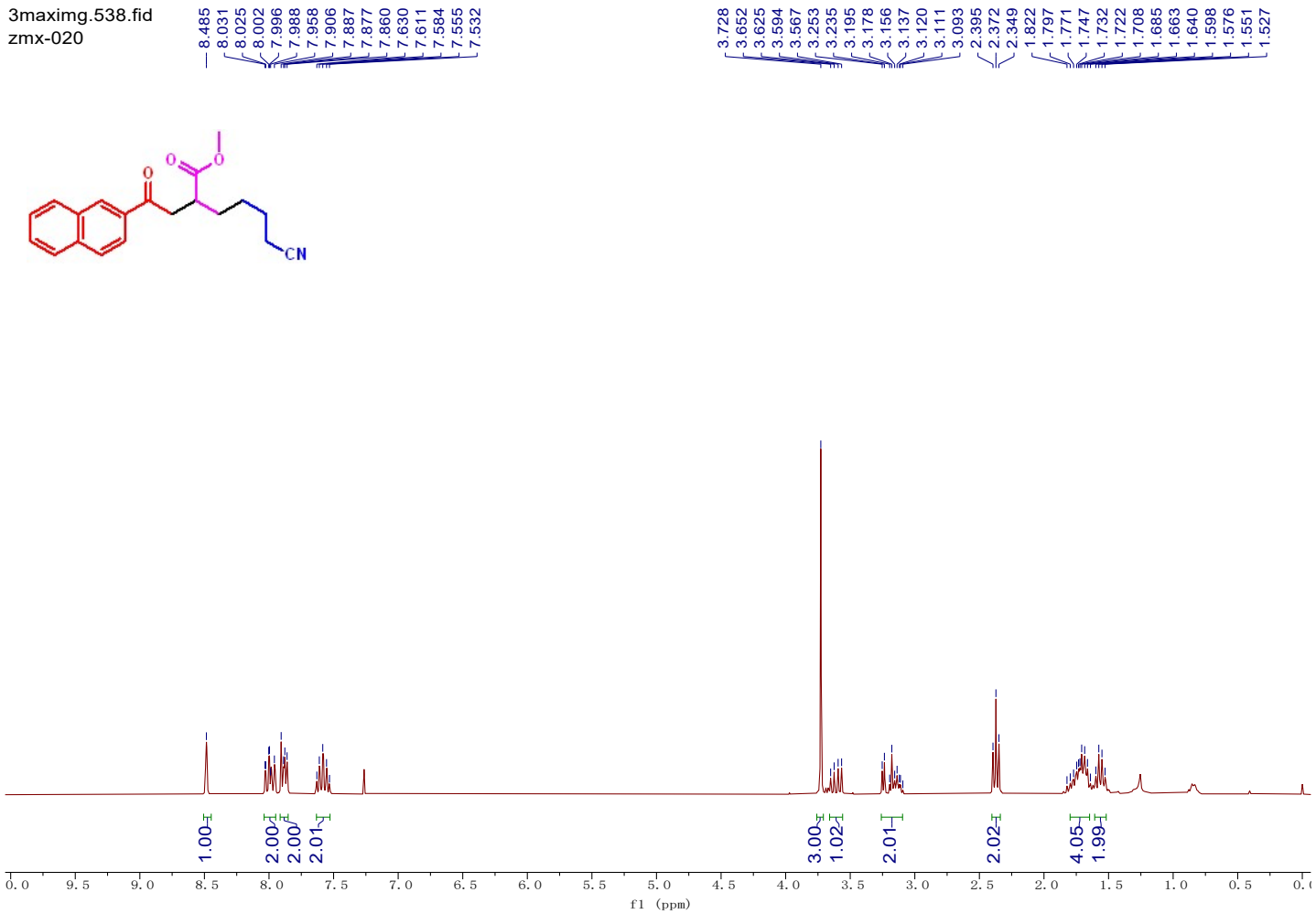
^{13}C NMR Spectrum of Compound 4i (151 MHz, $CDCl_3$)



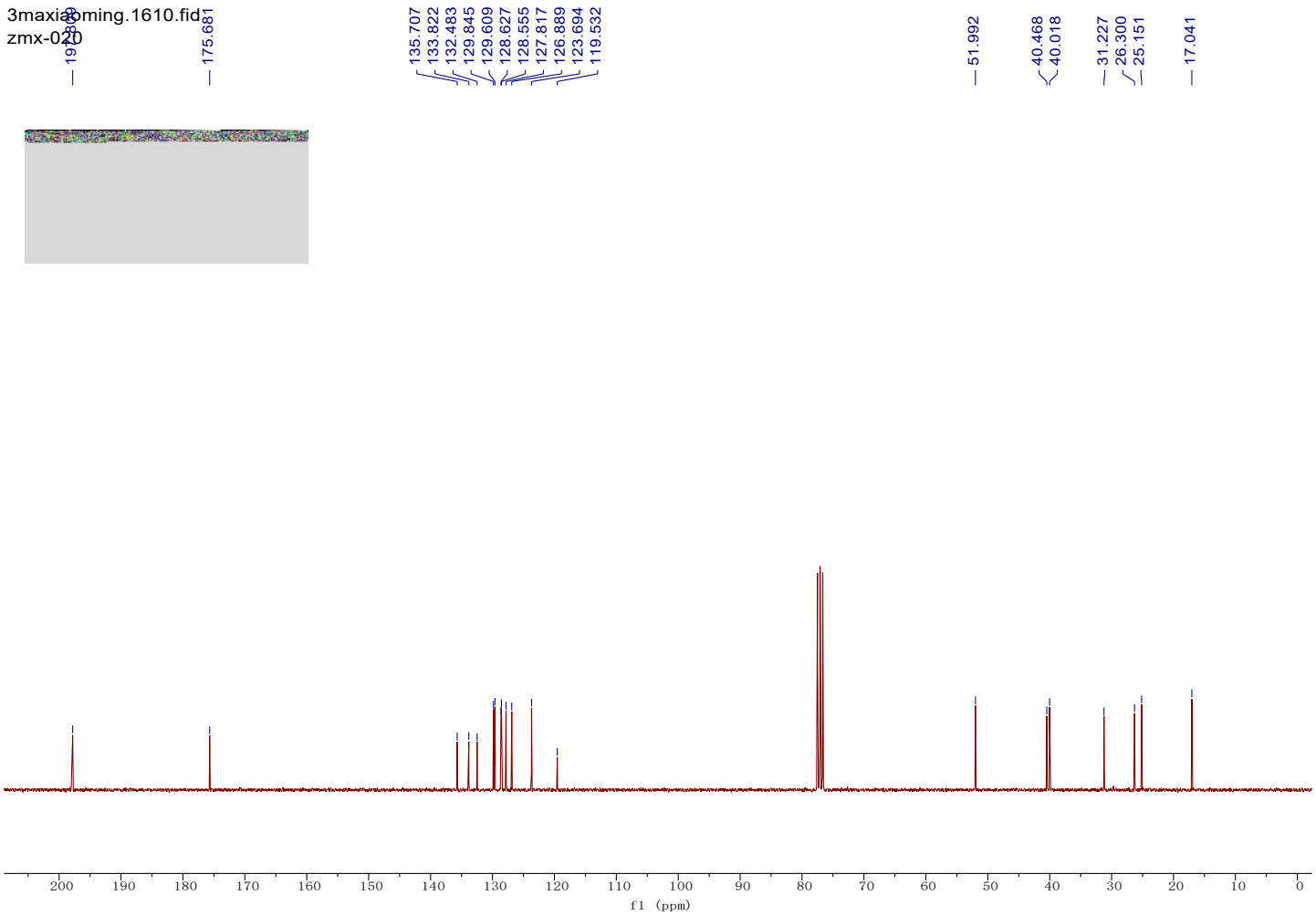
^{1}H NMR Spectrum of Compound 4j (400 MHz, $CDCl_3$)



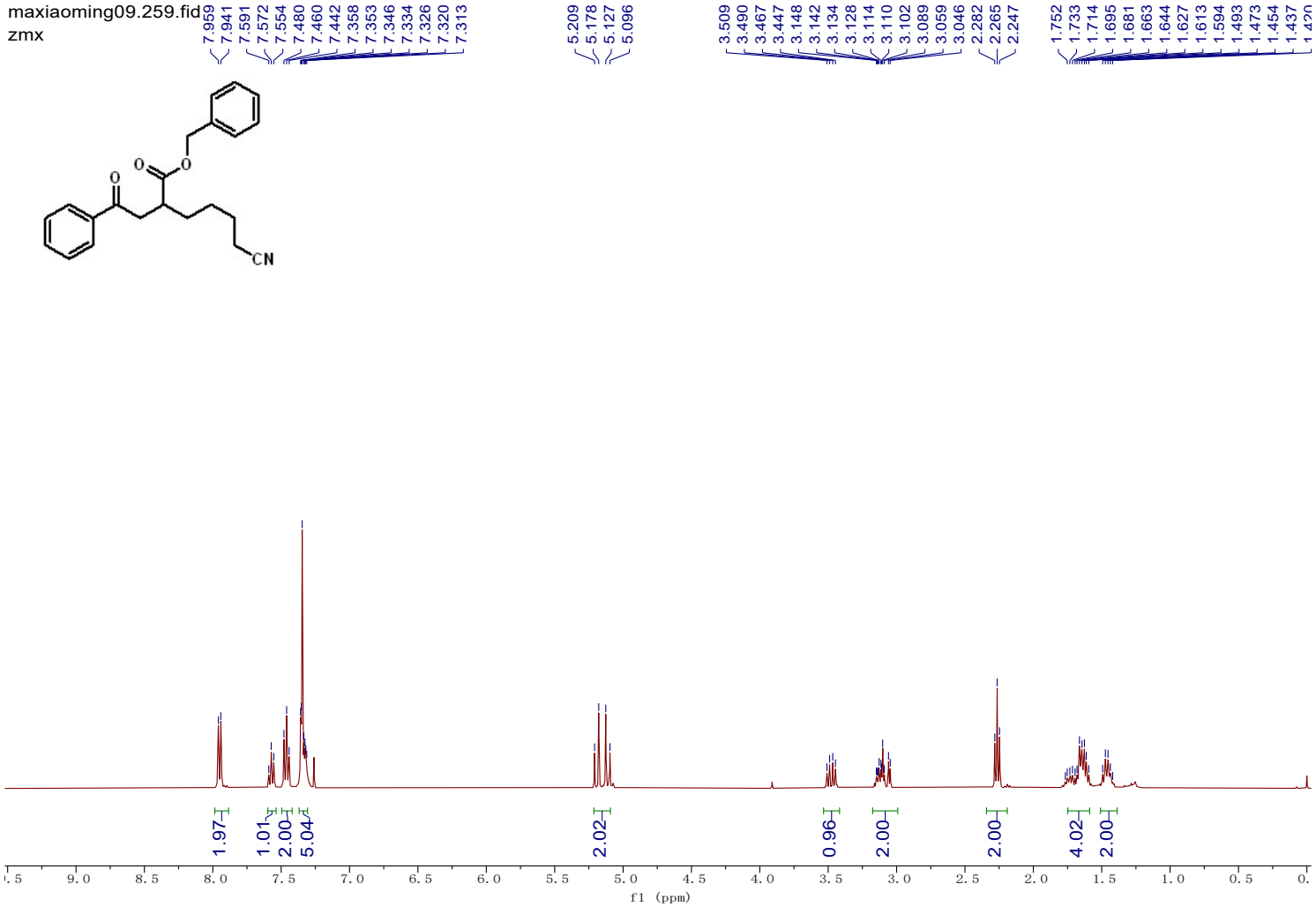
^{13}C NMR Spectrum of Compound 4j (75 MHz, $CDCl_3$)



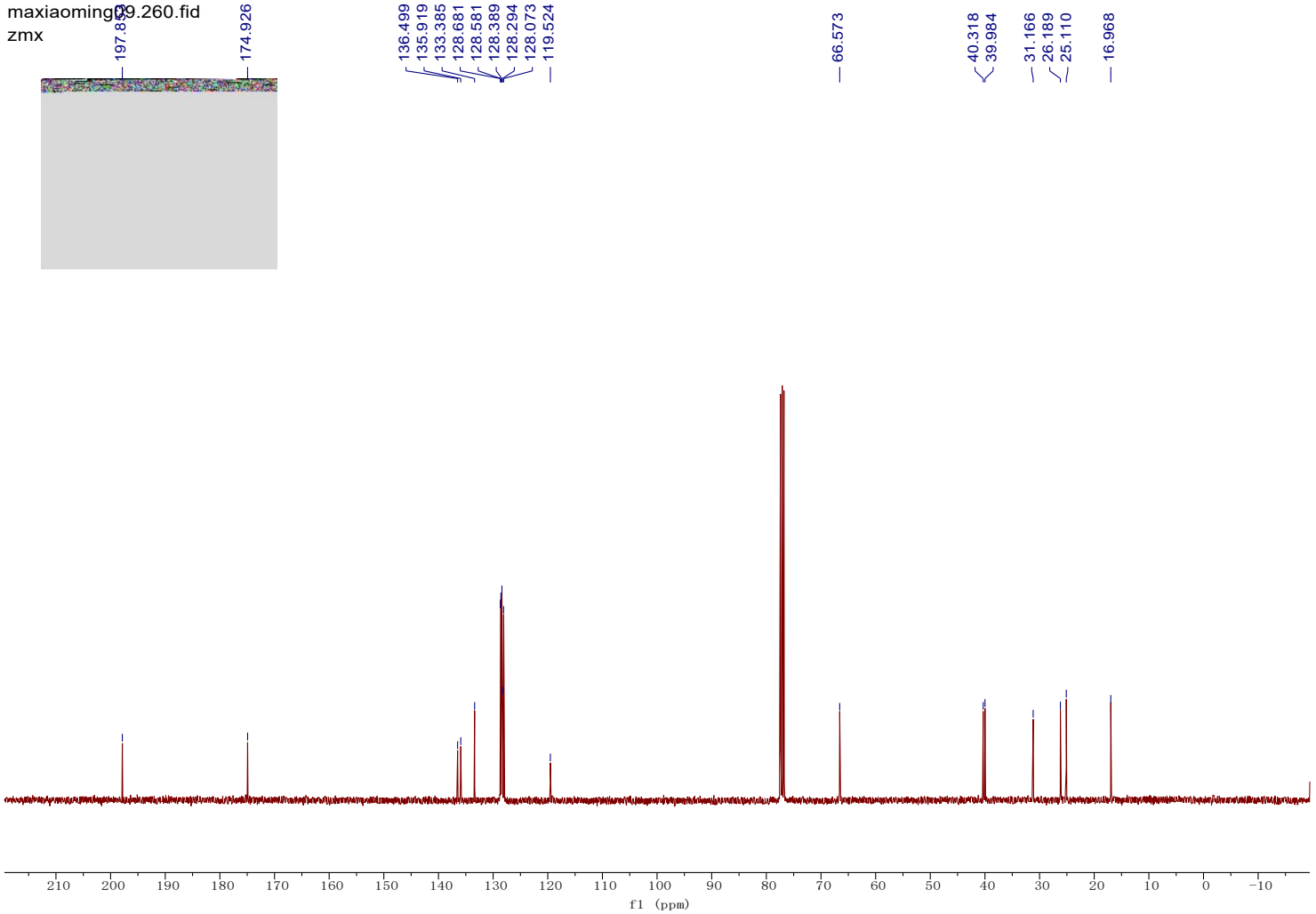
^{1}H NMR Spectrum of Compound 4k (300 MHz, $CDCl_3$)



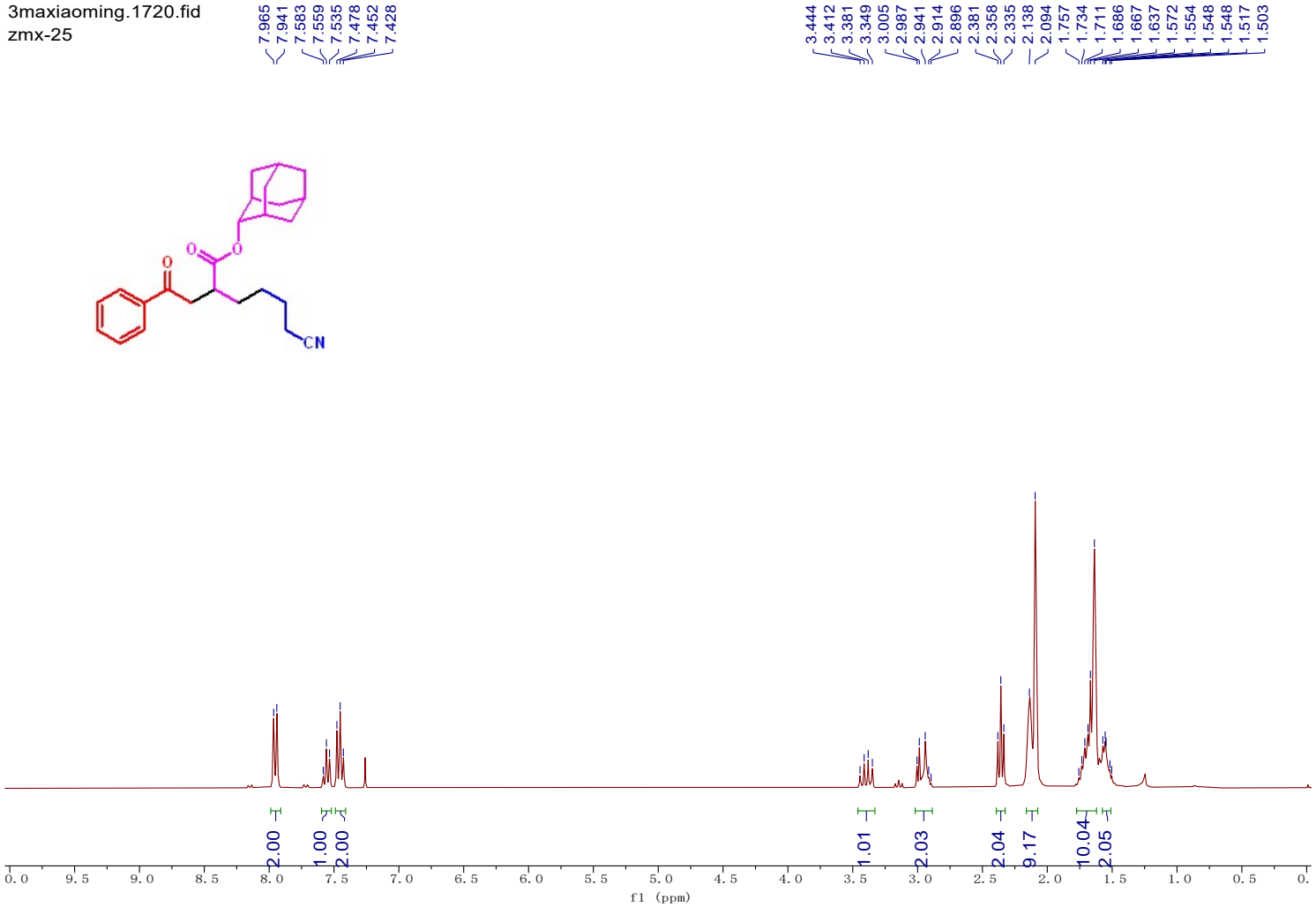
^{13}C NMR Spectrum of Compound 4k (75 MHz, $CDCl_3$)



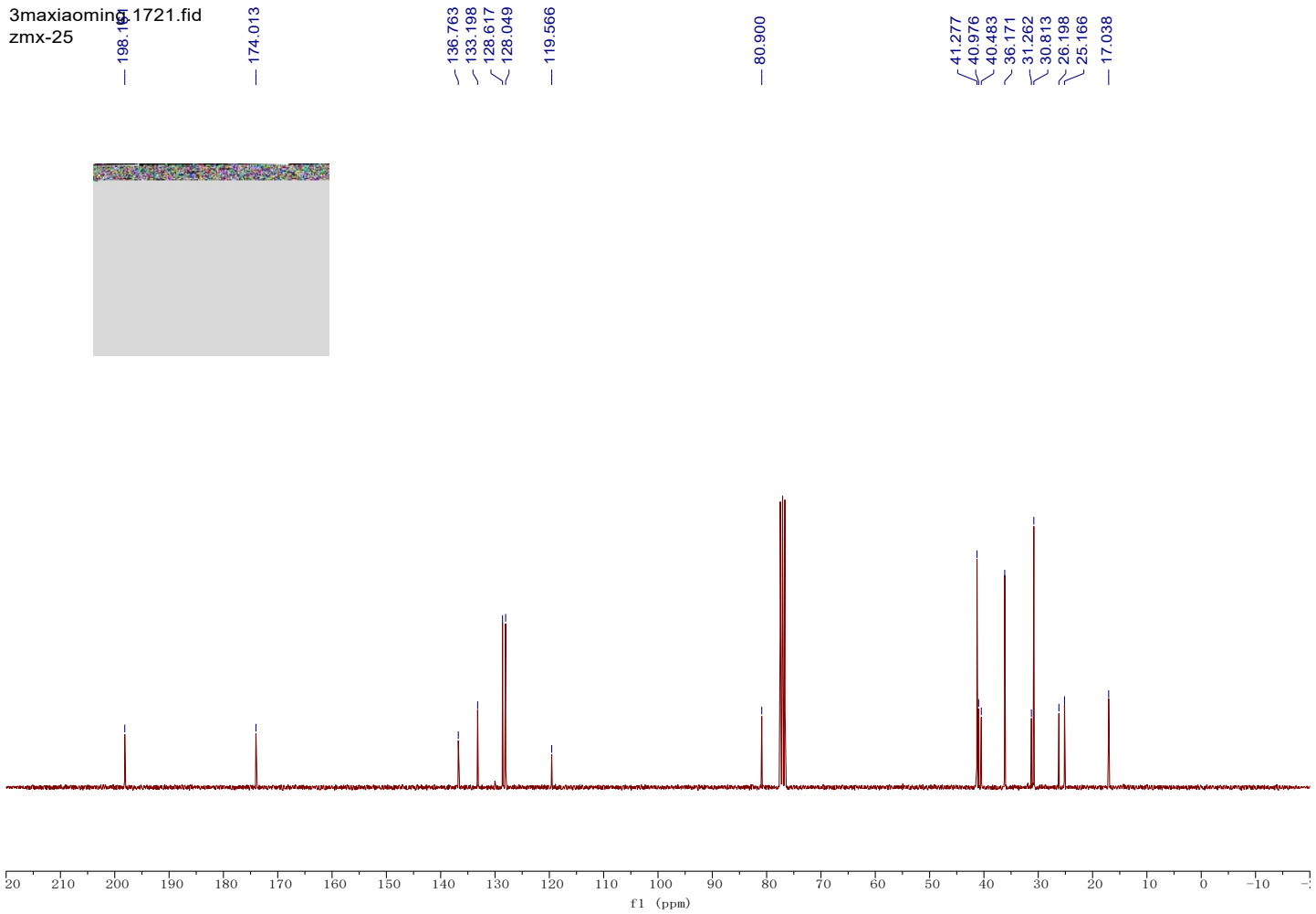
^{1}H NMR Spectrum of Compound 4l (400 MHz, $CDCl_3$)



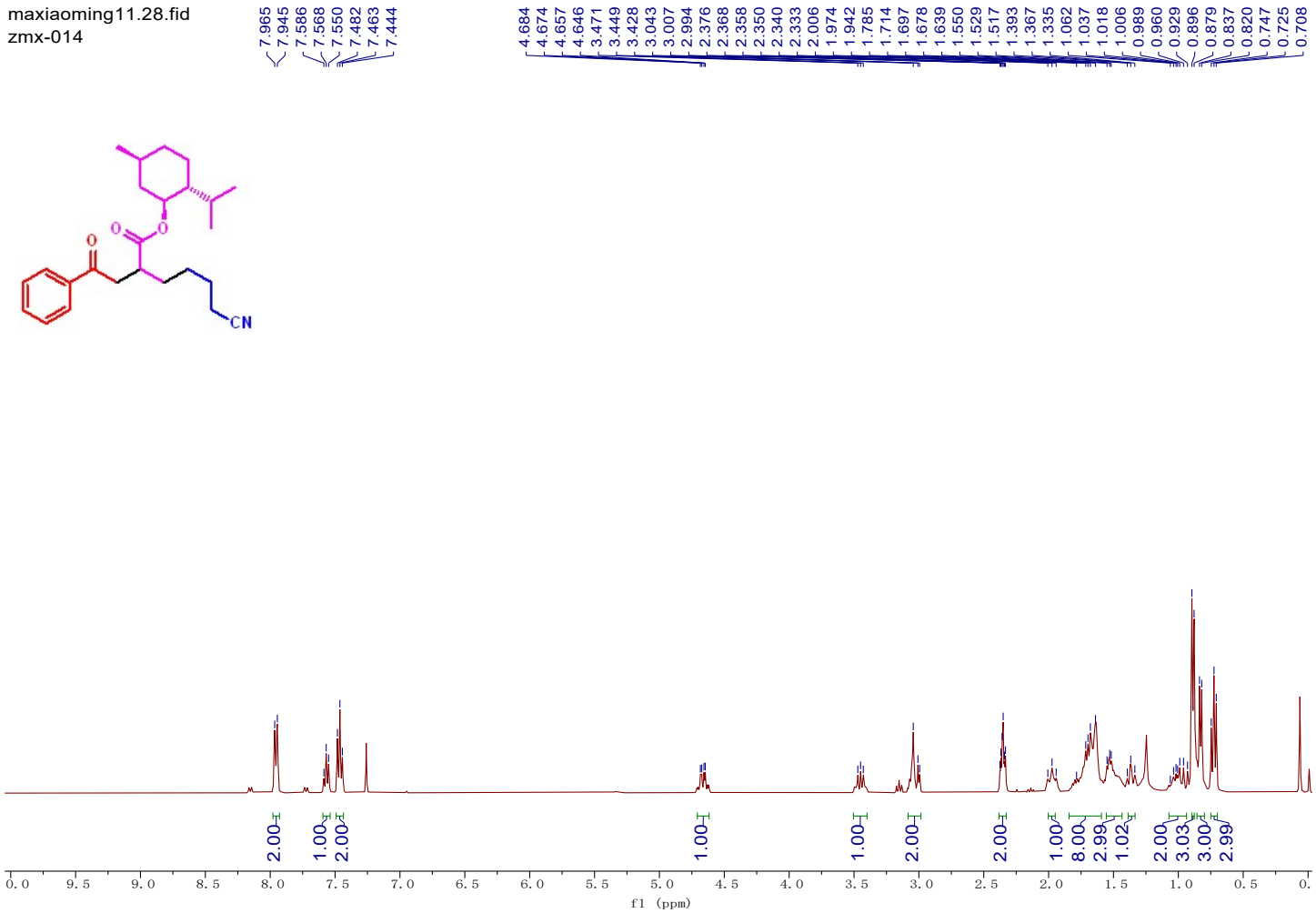
^{13}C NMR Spectrum of Compound 4l (101 MHz, $CDCl_3$)



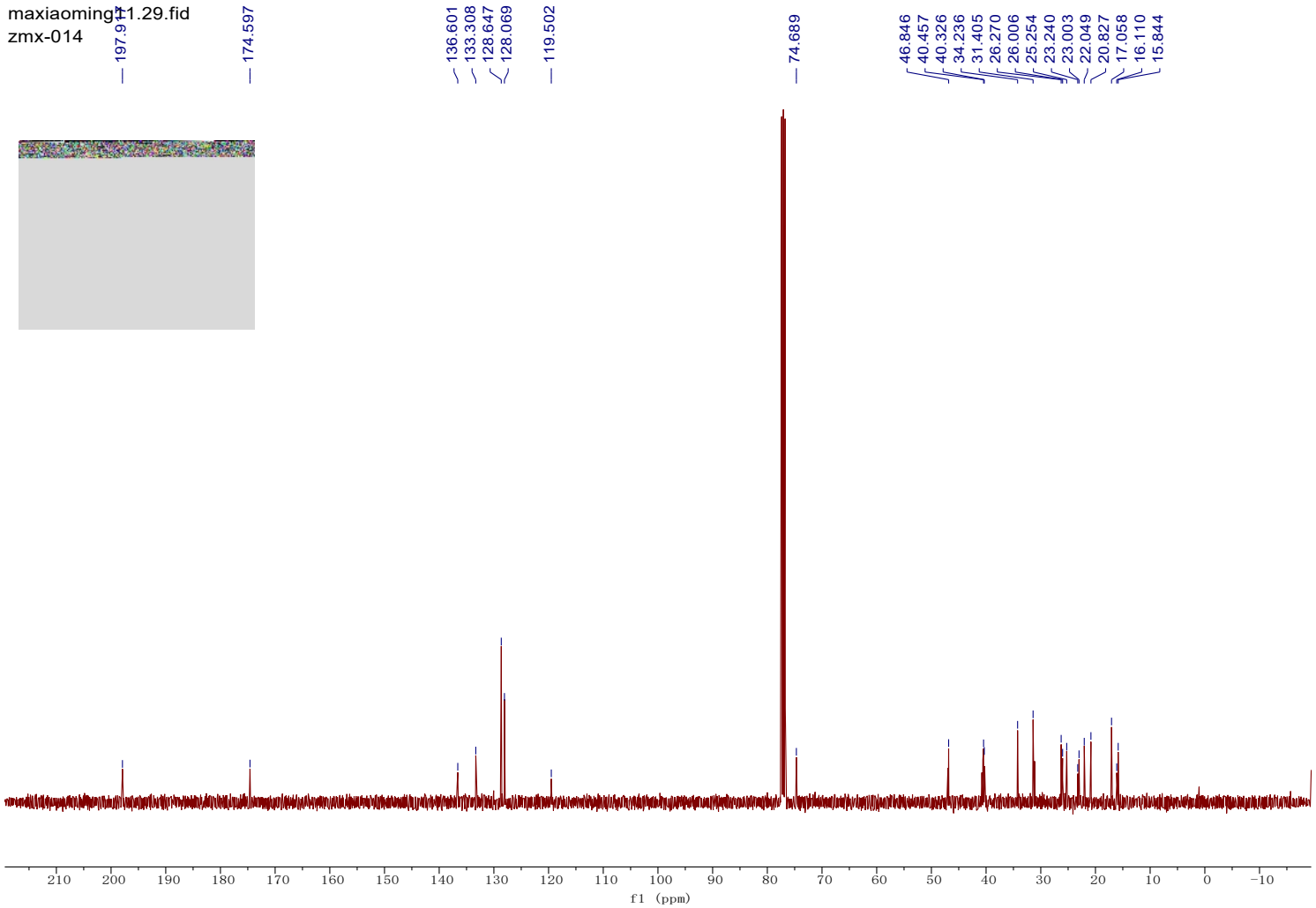
^{1}H NMR Spectrum of Compound 4m (300 MHz, $CDCl_3$)



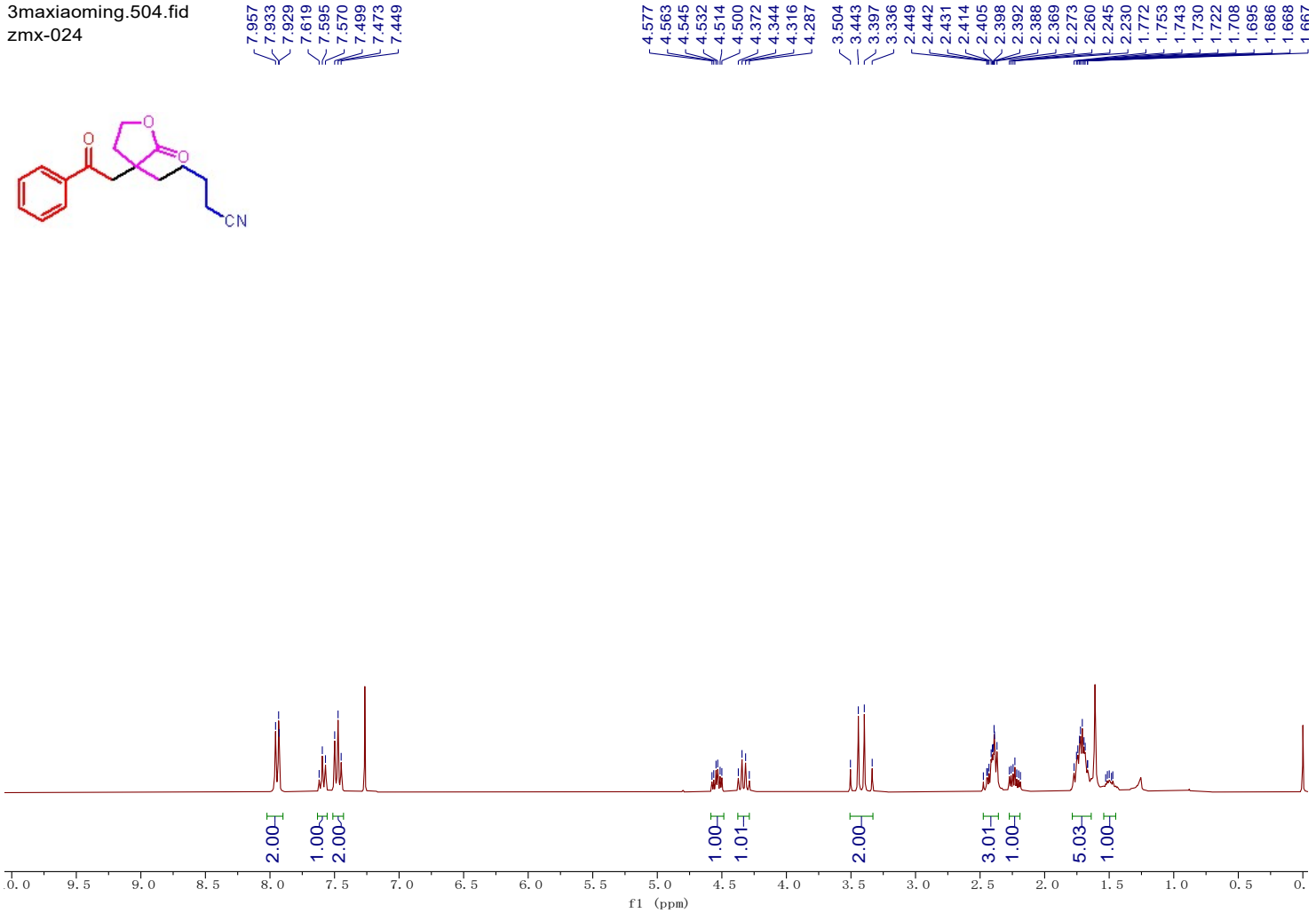
^{13}C NMR Spectrum of Compound 4m (75 MHz, $CDCl_3$)



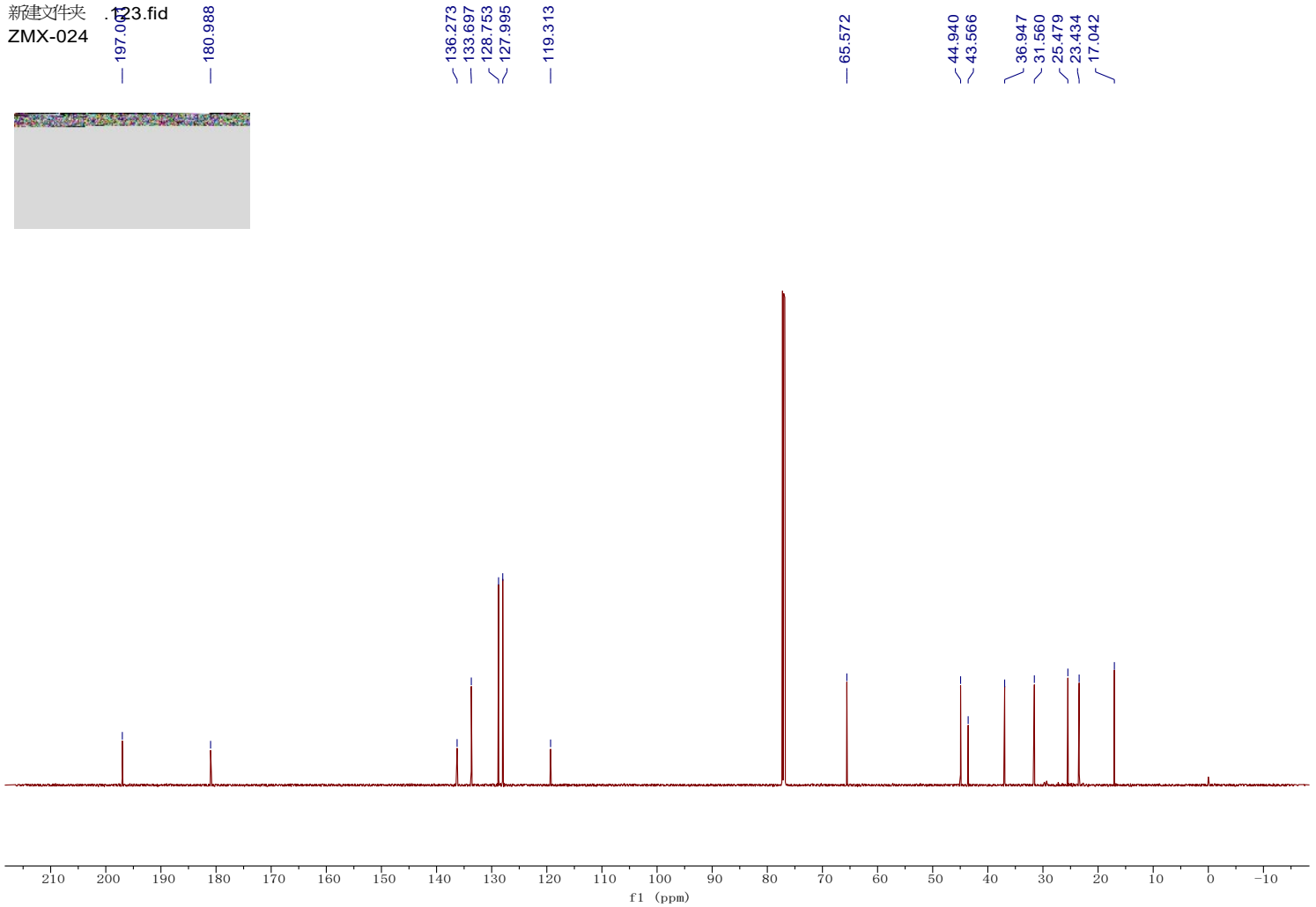
^{1}H NMR Spectrum of Compound 4n (400 MHz, $CDCl_3$)



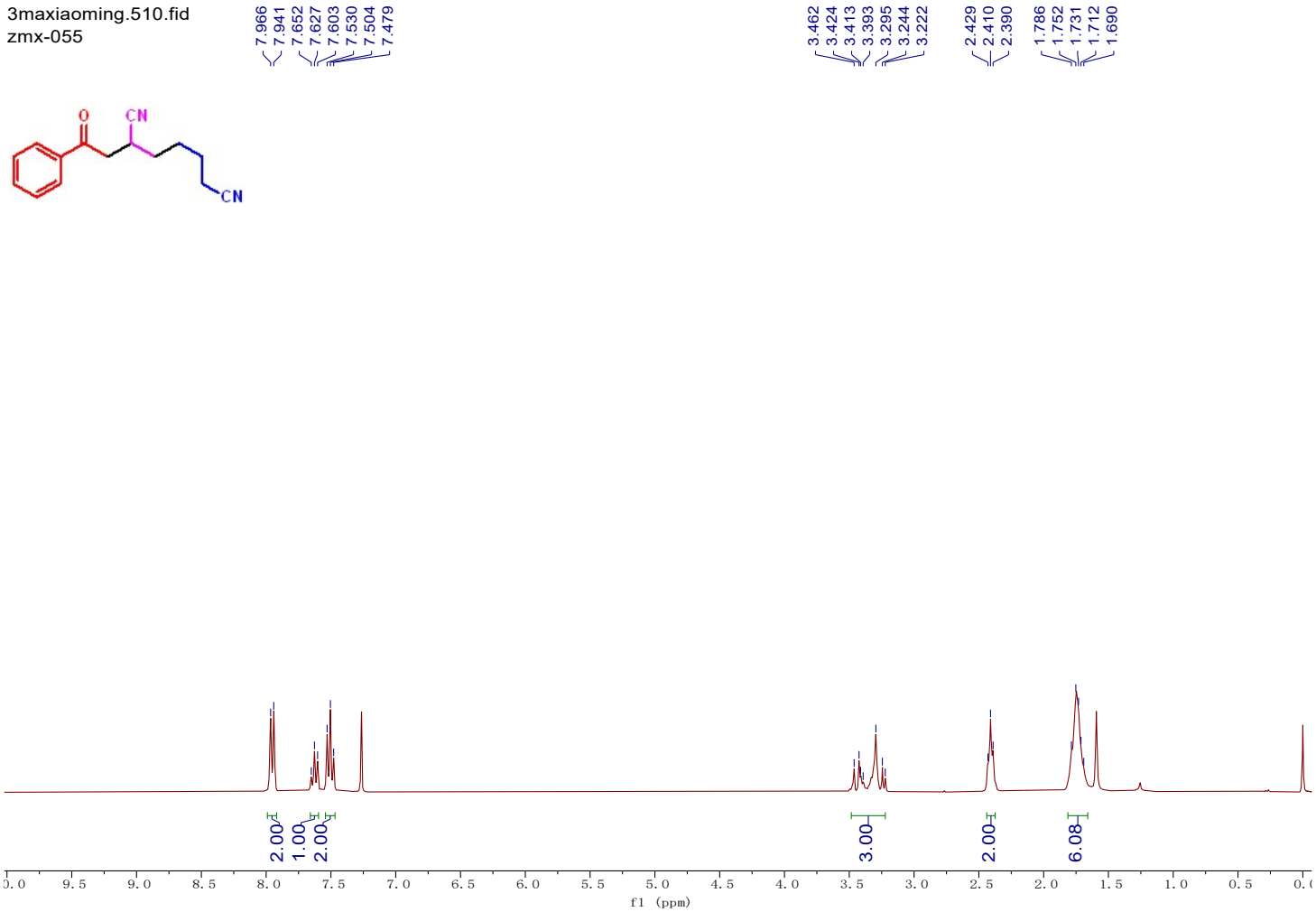
^{13}C NMR Spectrum of Compound 4n (101 MHz, $CDCl_3$)



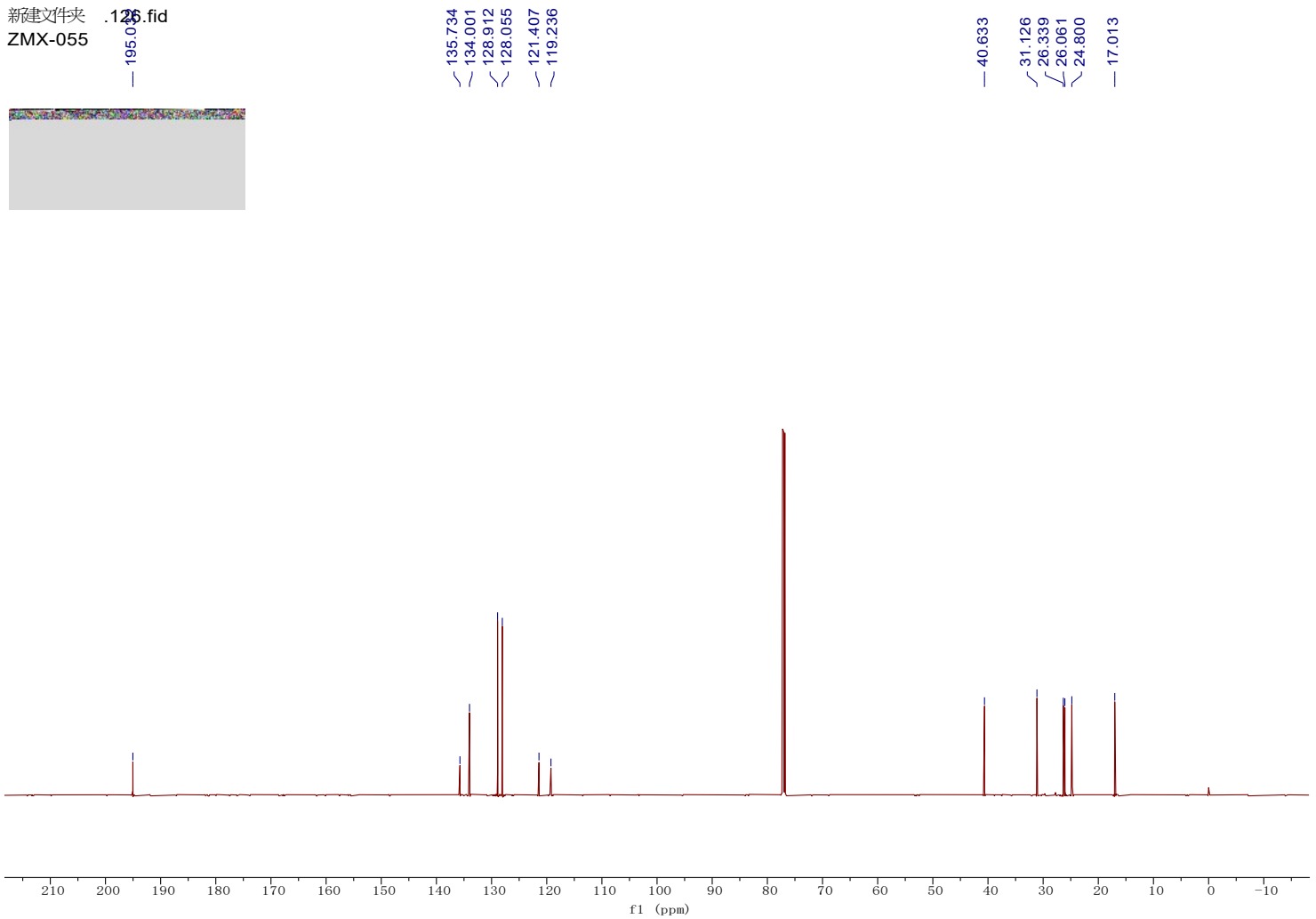
^{1}H NMR Spectrum of Compound 4o (300 MHz, $CDCl_3$)



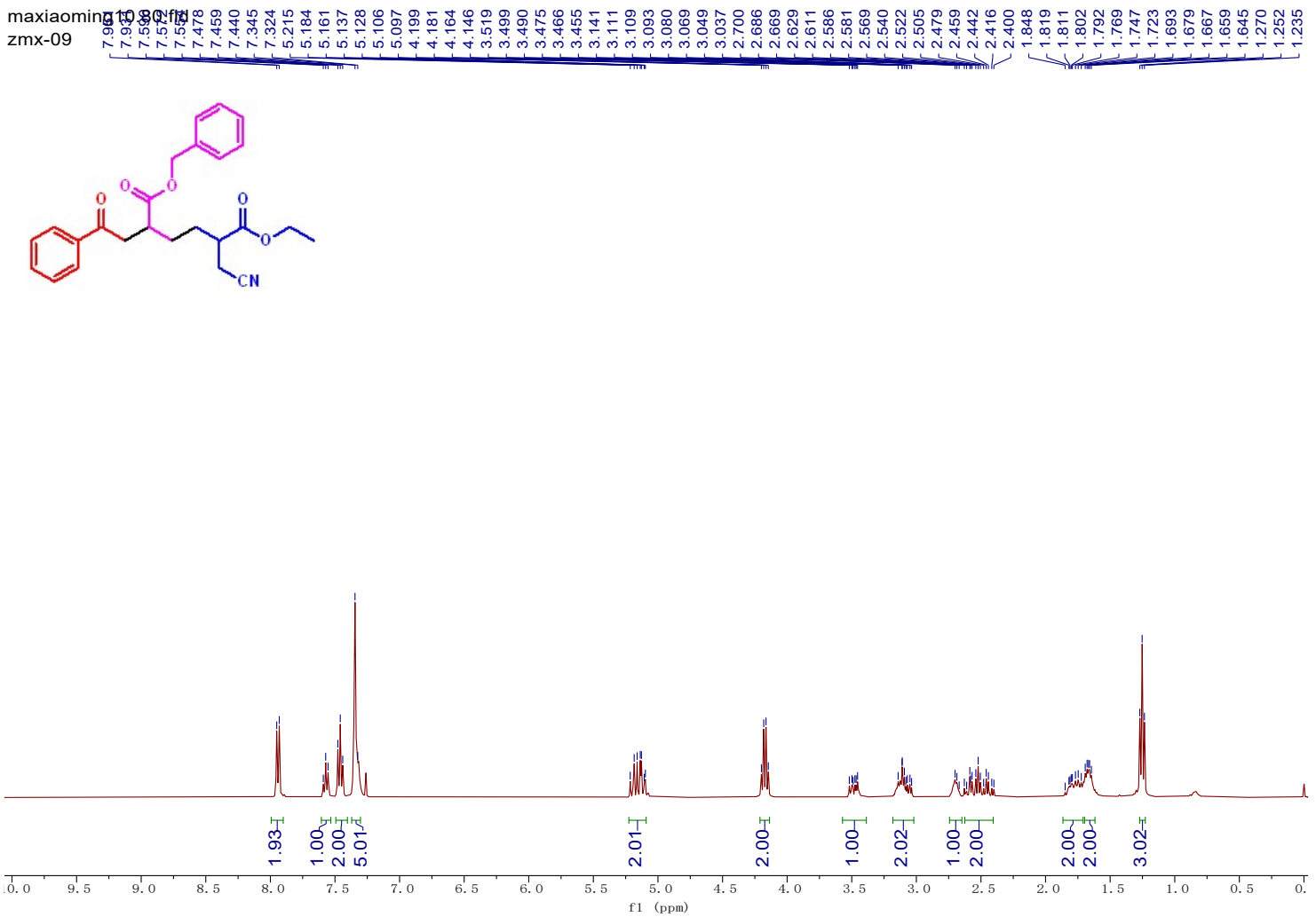
^{13}C NMR Spectrum of Compound 4o (151 MHz, $CDCl_3$)



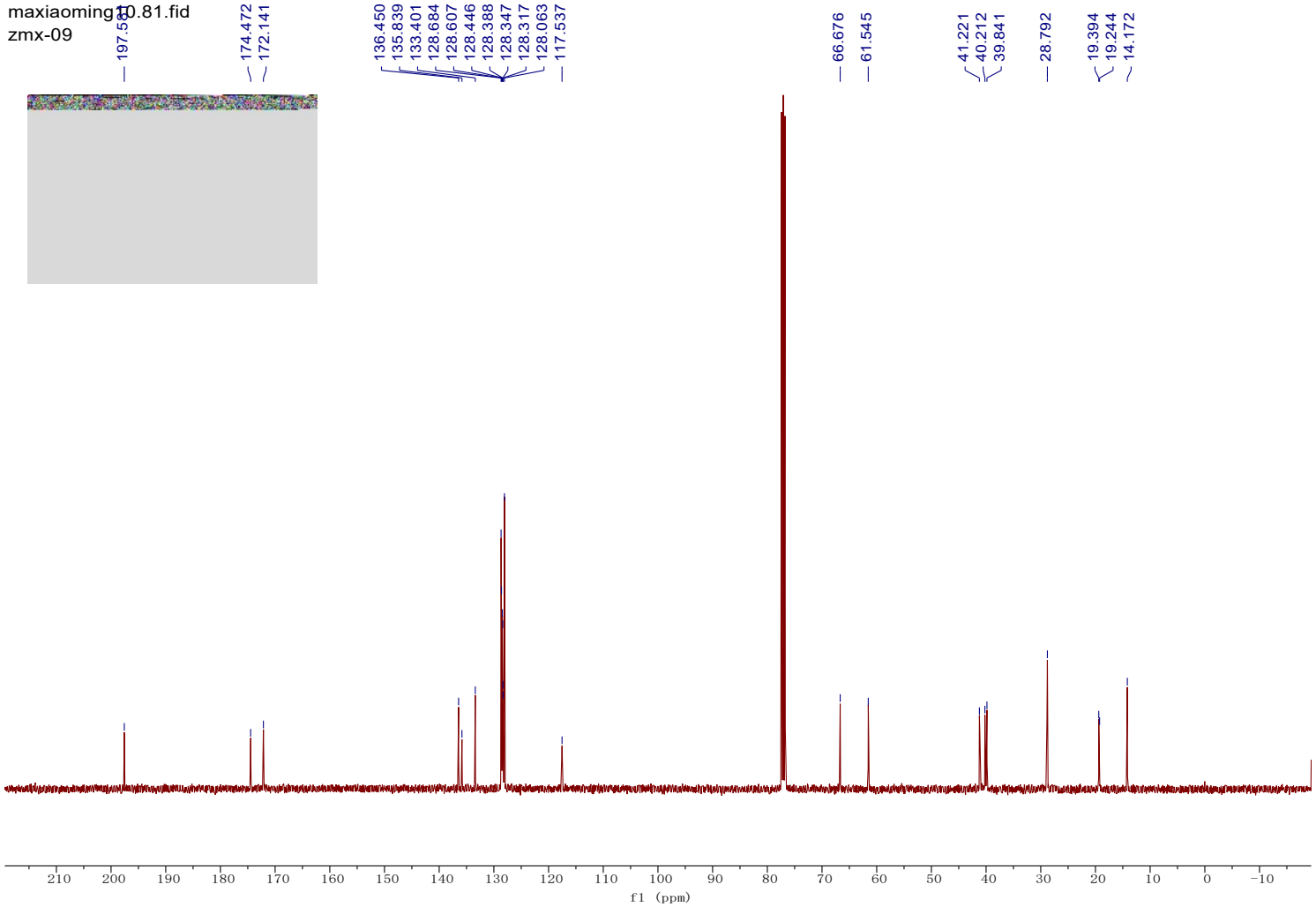
^{1}H NMR Spectrum of Compound 4p (300 MHz, $CDCl_3$)



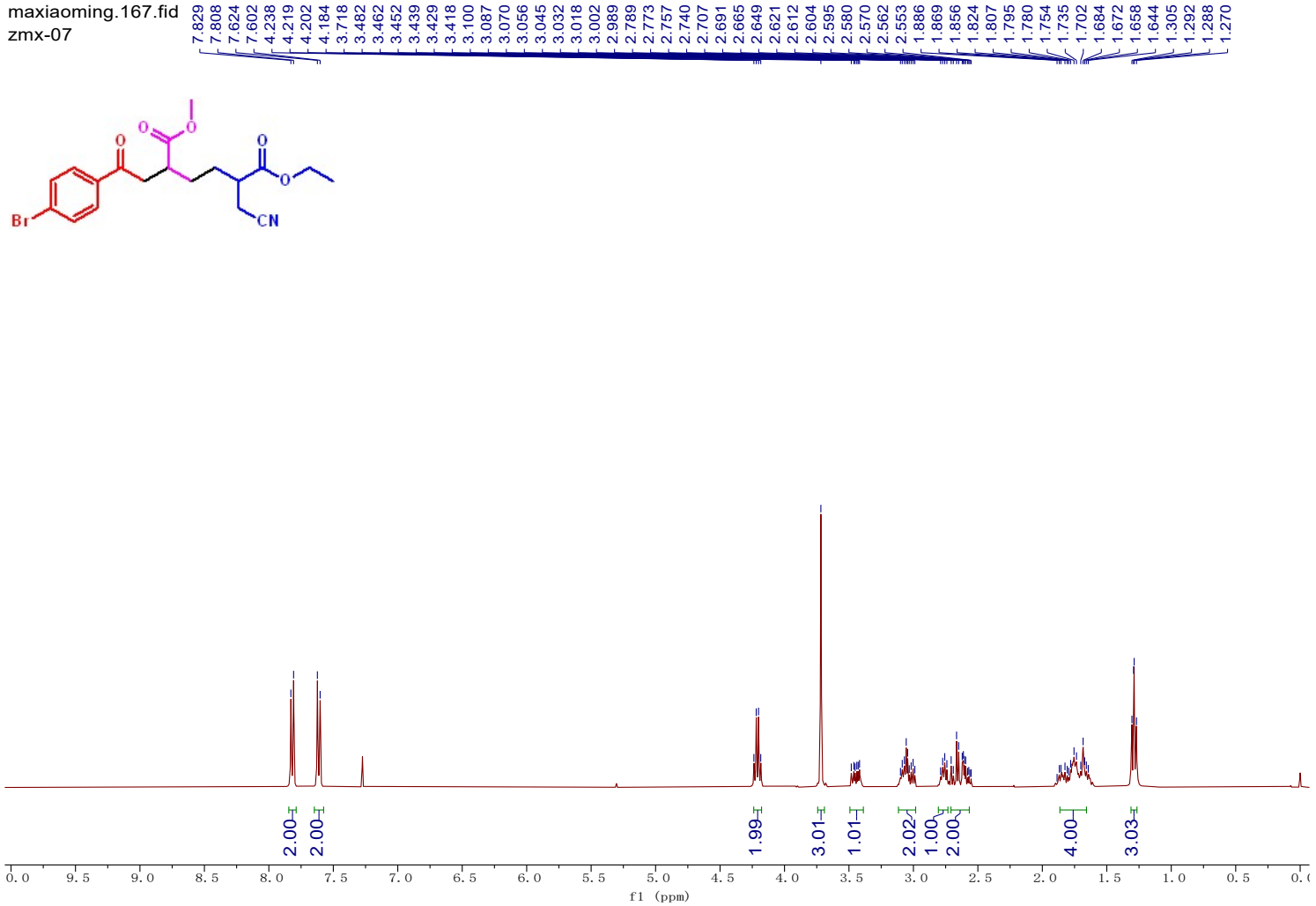
^{13}C NMR Spectrum of Compound 4p (151 MHz, $CDCl_3$)



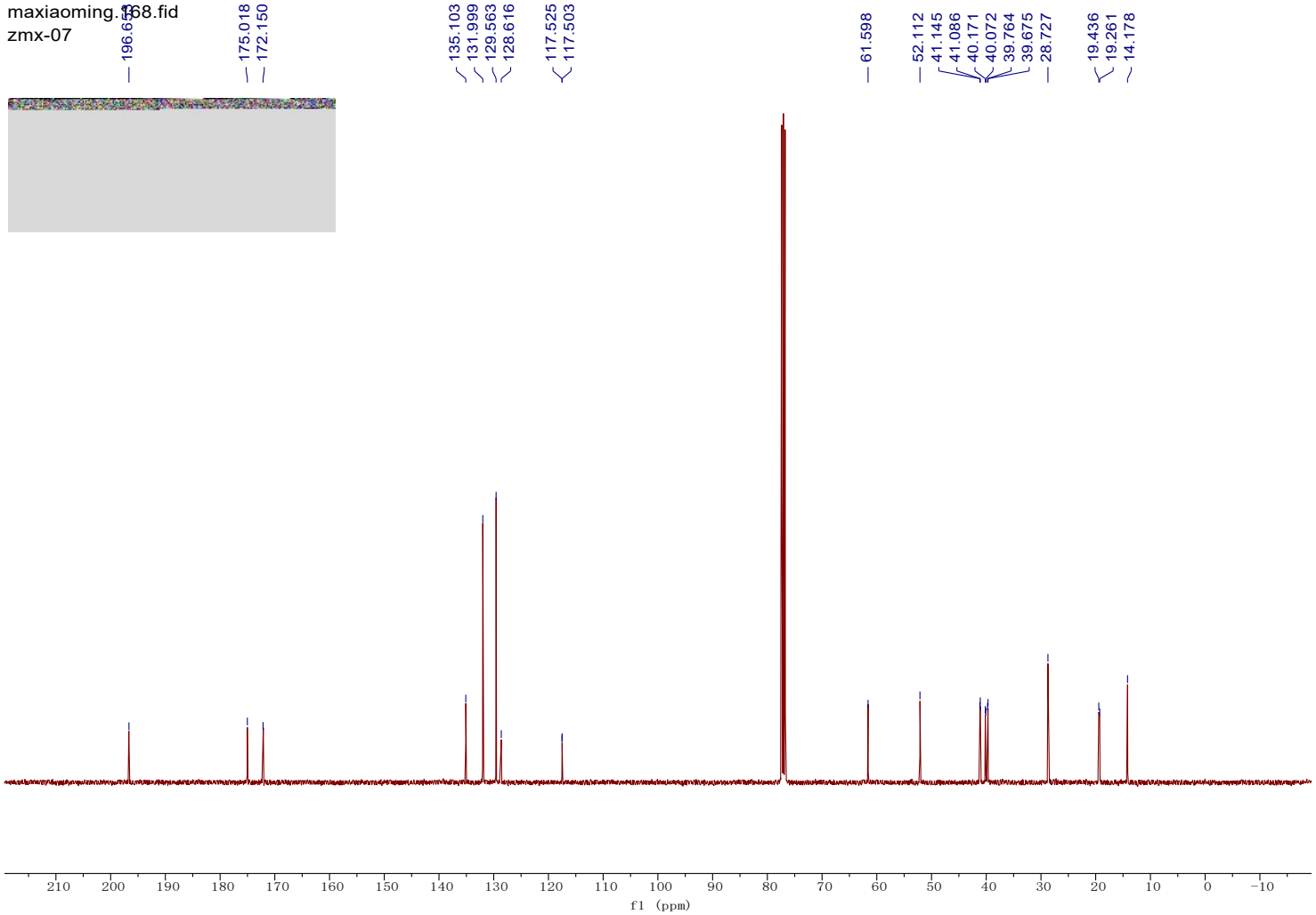
^{1}H NMR Spectrum of Compound 4q (400 MHz, $CDCl_3$)



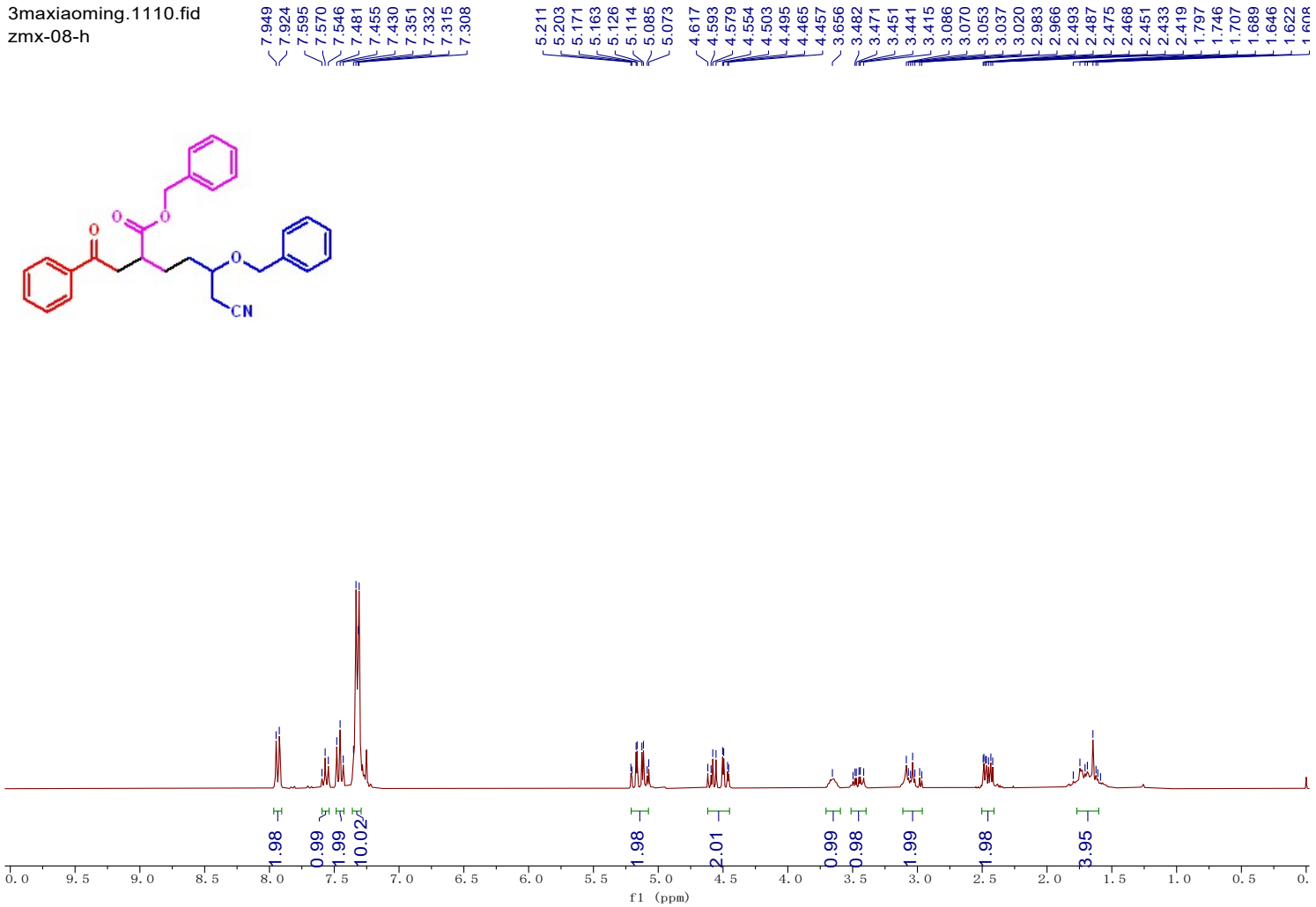
^{13}C NMR Spectrum of Compound 4q (101 MHz, $CDCl_3$)



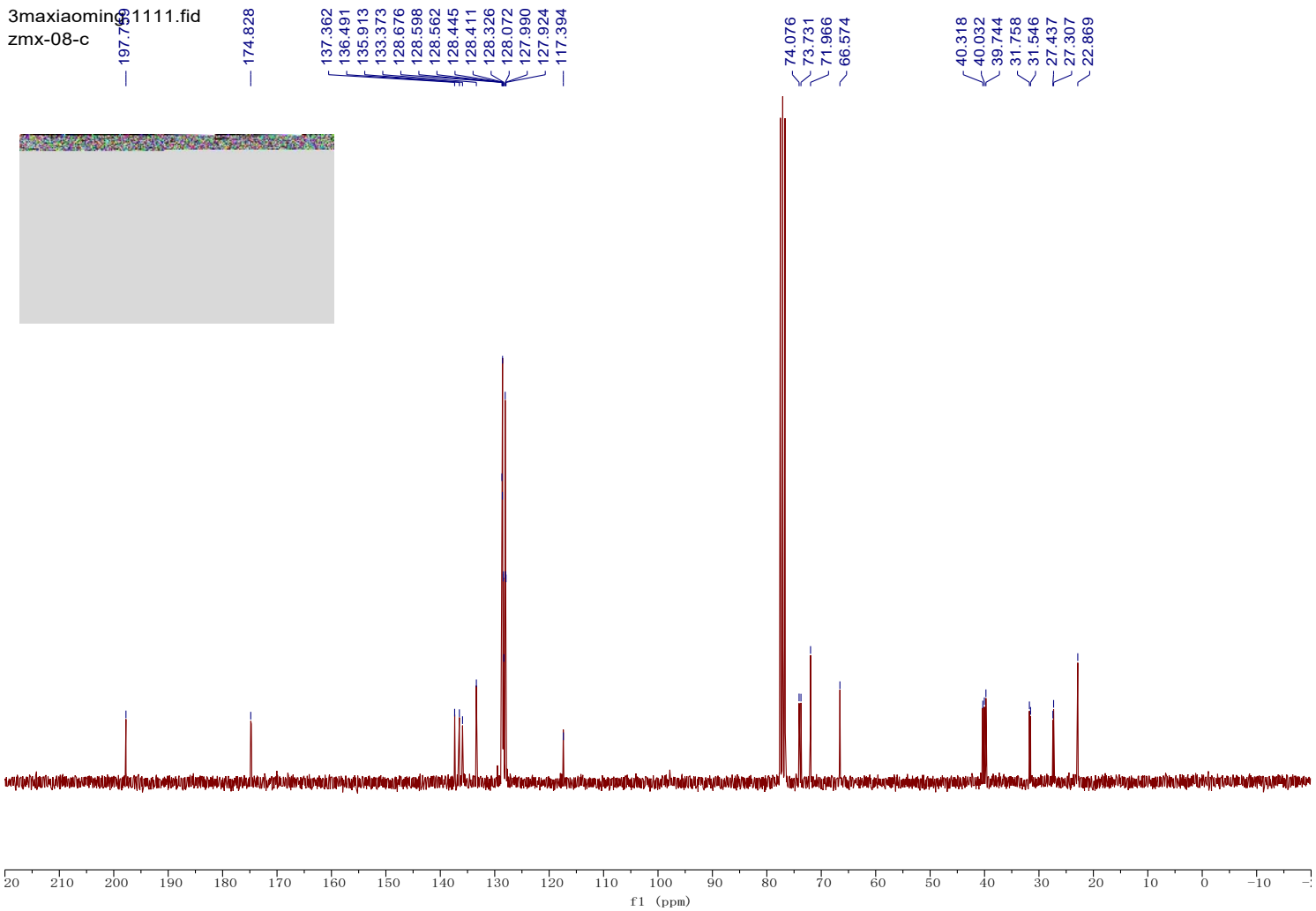
^{1}H NMR Spectrum of Compound 4r (400 MHz, $CDCl_3$)



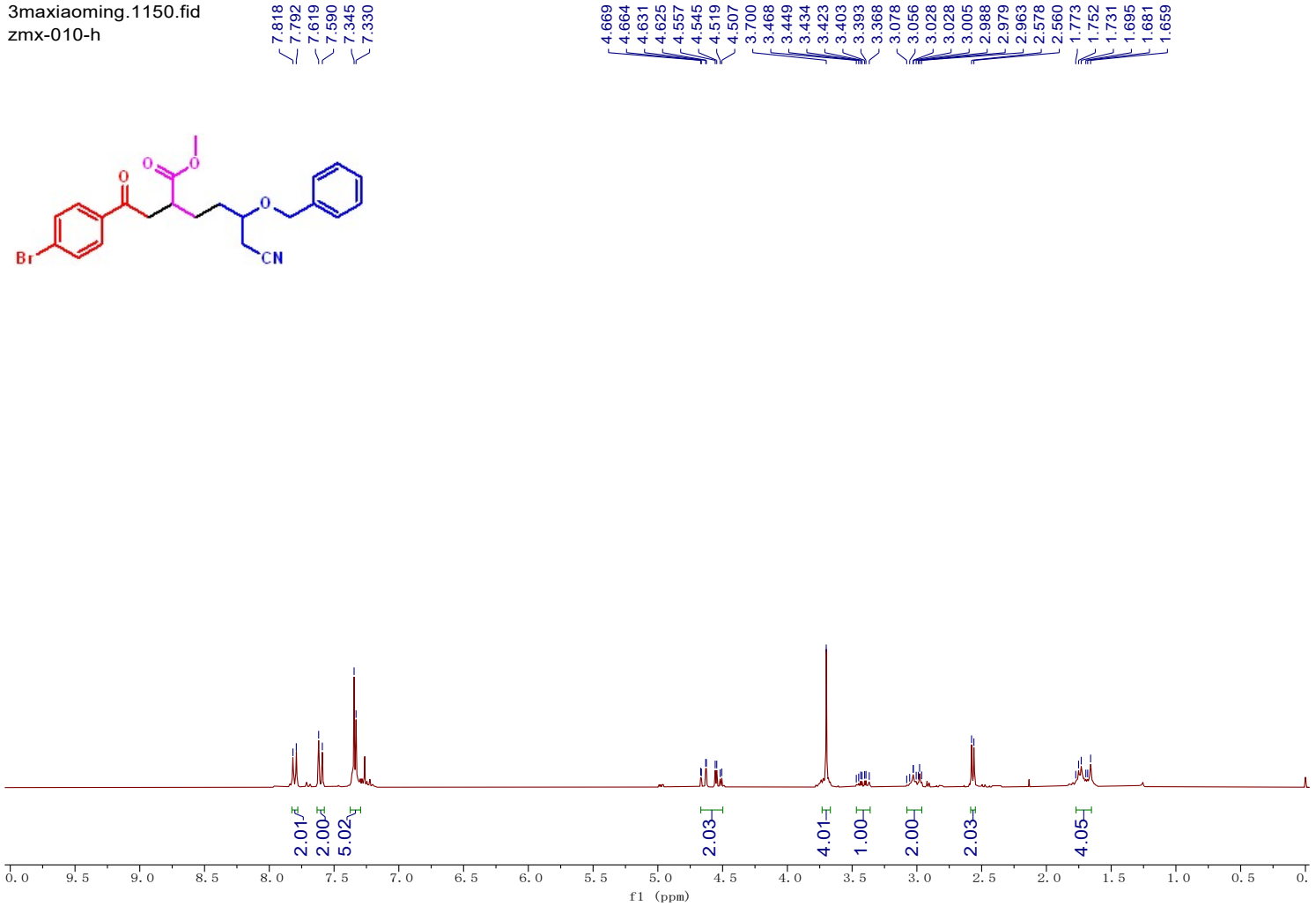
^{13}C NMR Spectrum of Compound 4r (101 MHz, $CDCl_3$)



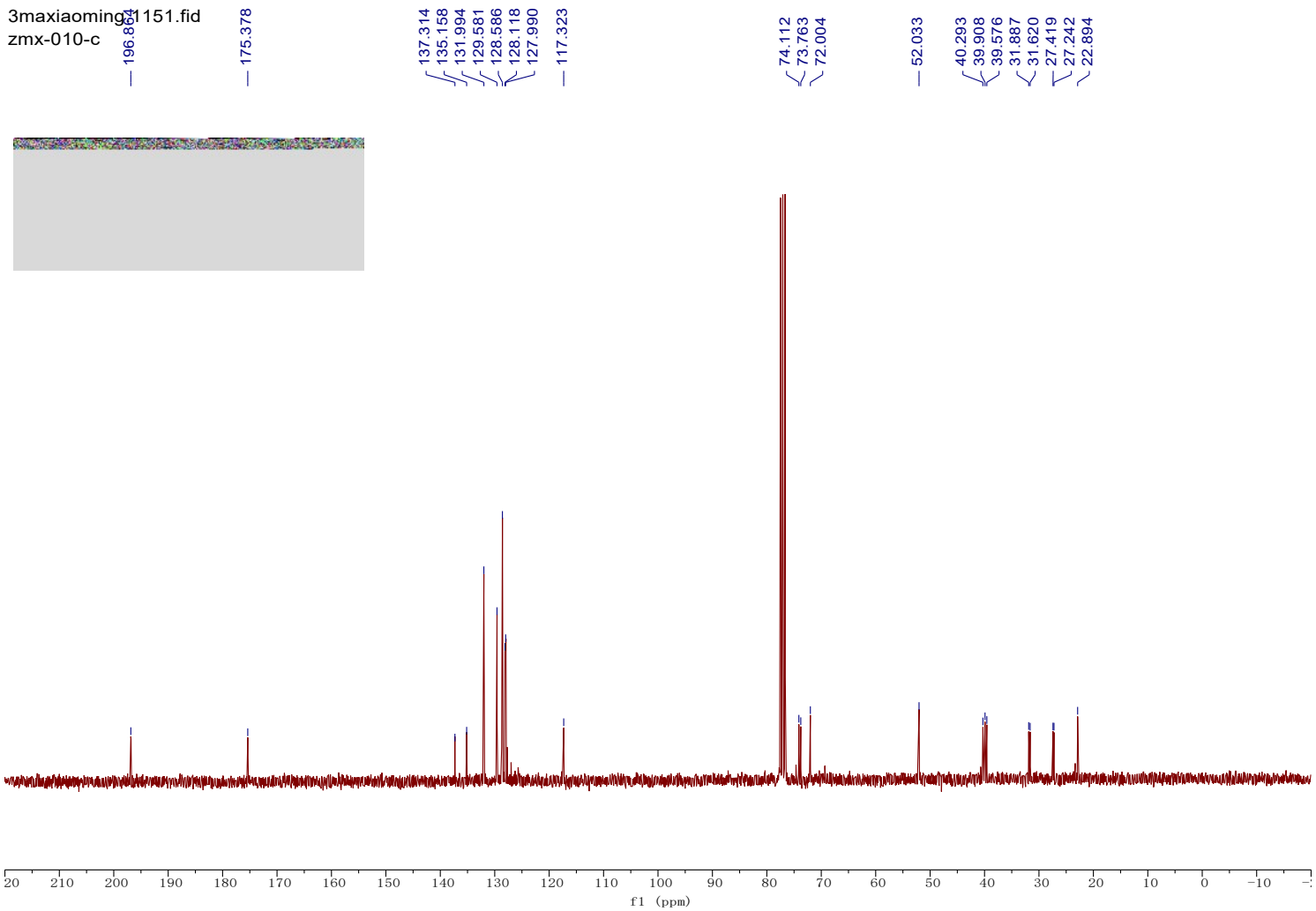
^{1}H NMR Spectrum of Compound 4s (300 MHz, $CDCl_3$)



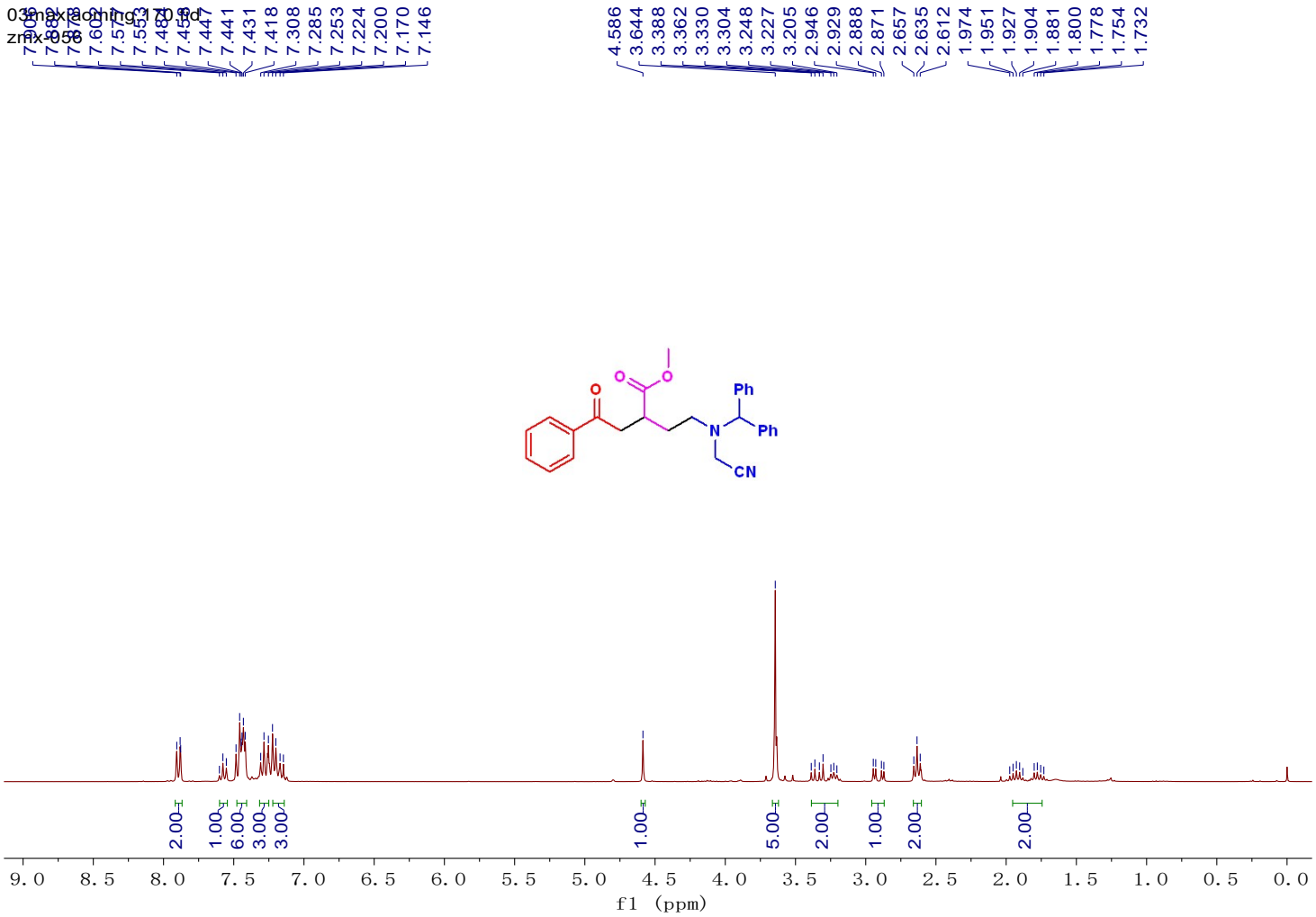
^{13}C NMR Spectrum of Compound 4s (75 MHz, $CDCl_3$)



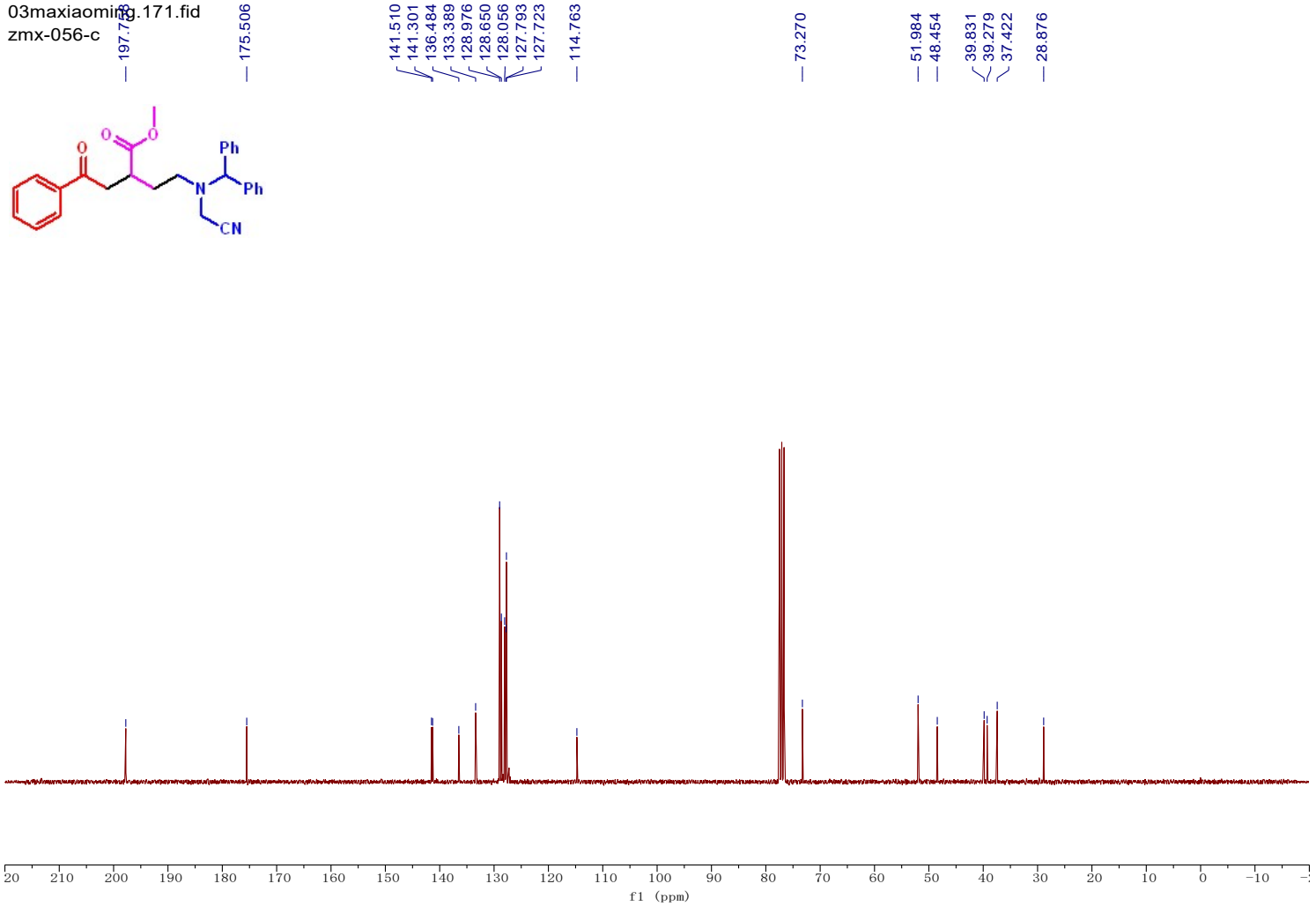
^{1}H NMR Spectrum of Compound 4t (300 MHz, $CDCl_3$)



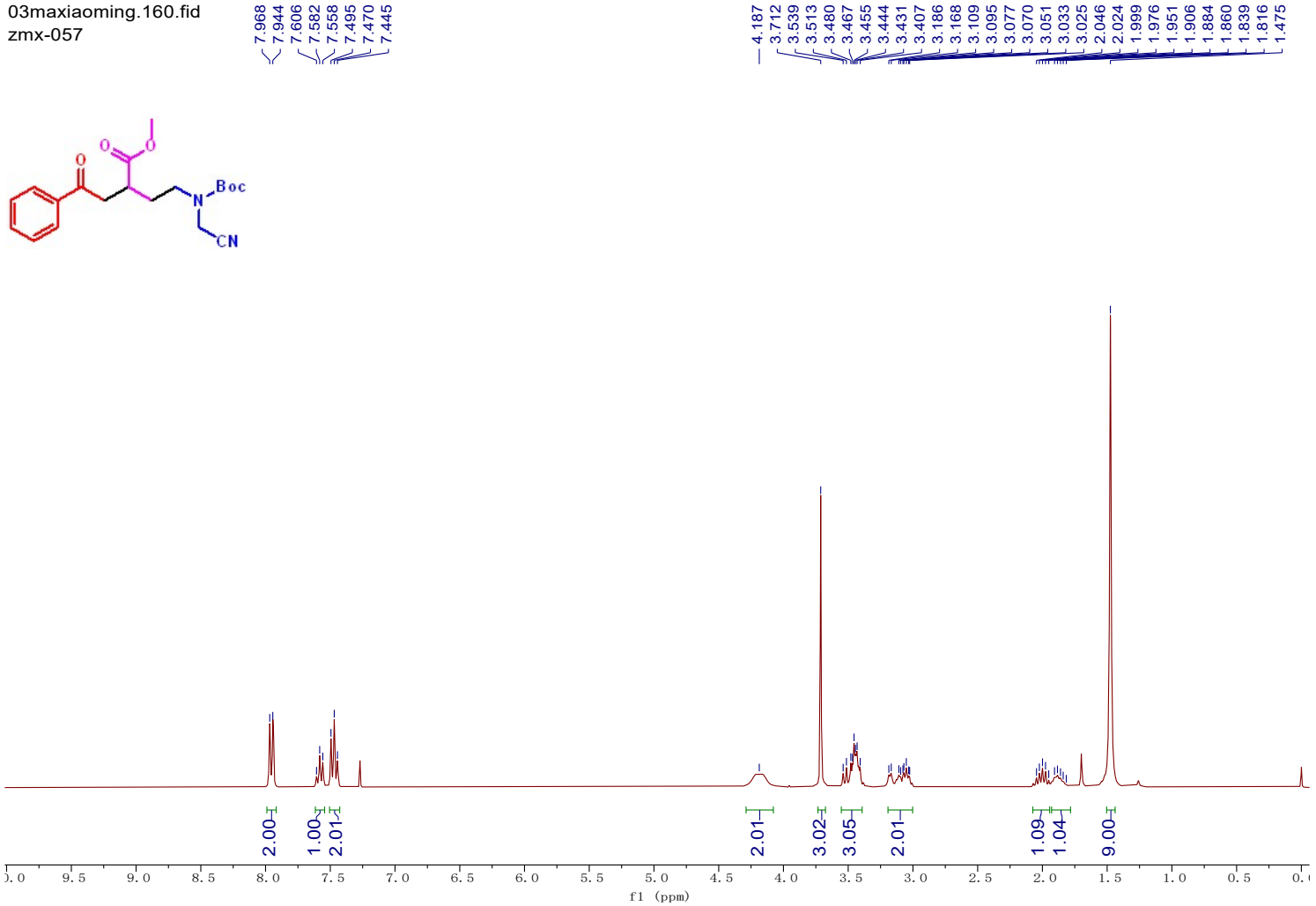
^{13}C NMR Spectrum of Compound 4t (75 MHz, $CDCl_3$)



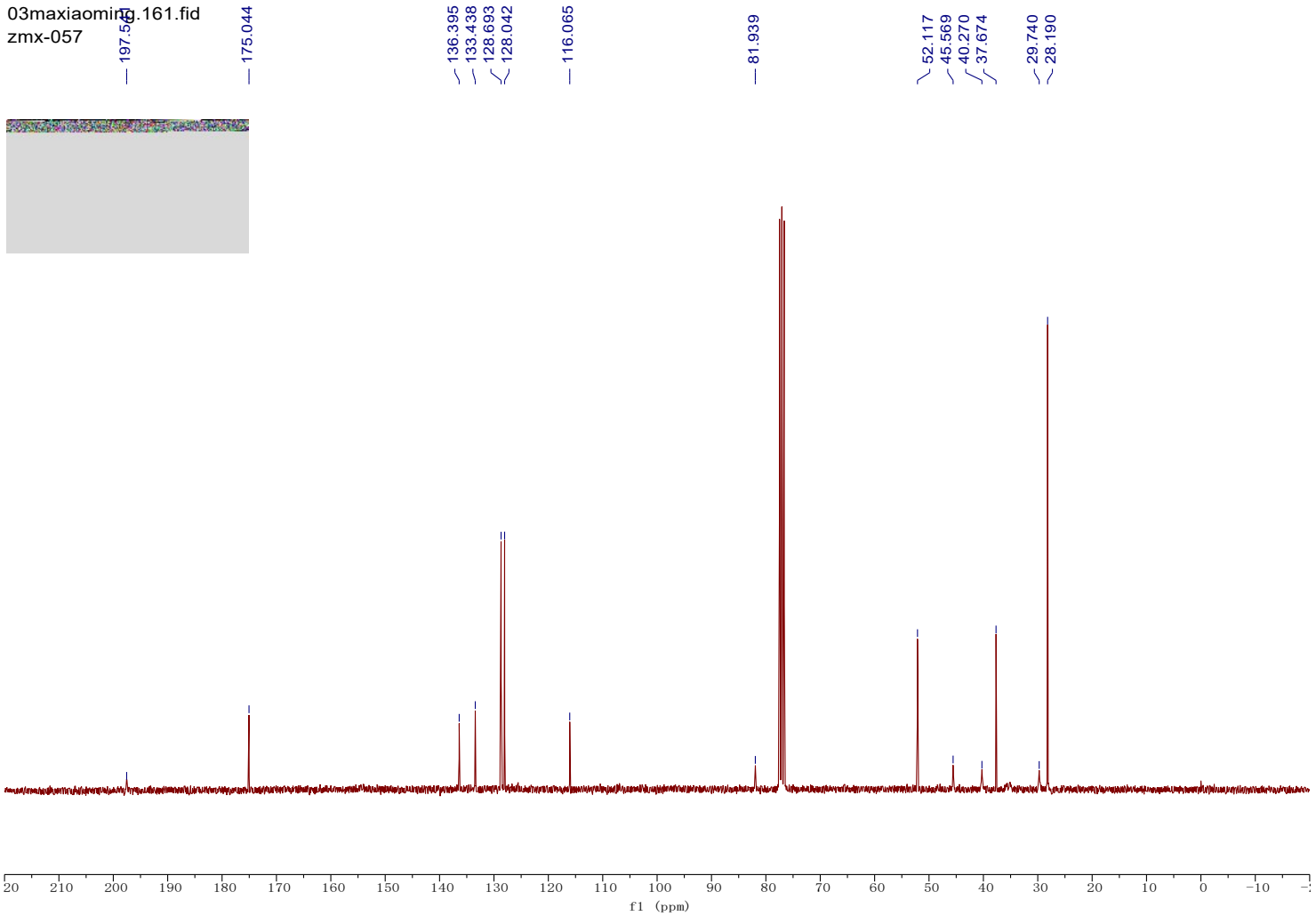
^{1}H NMR Spectrum of Compound 4u (300 MHz, $CDCl_3$)



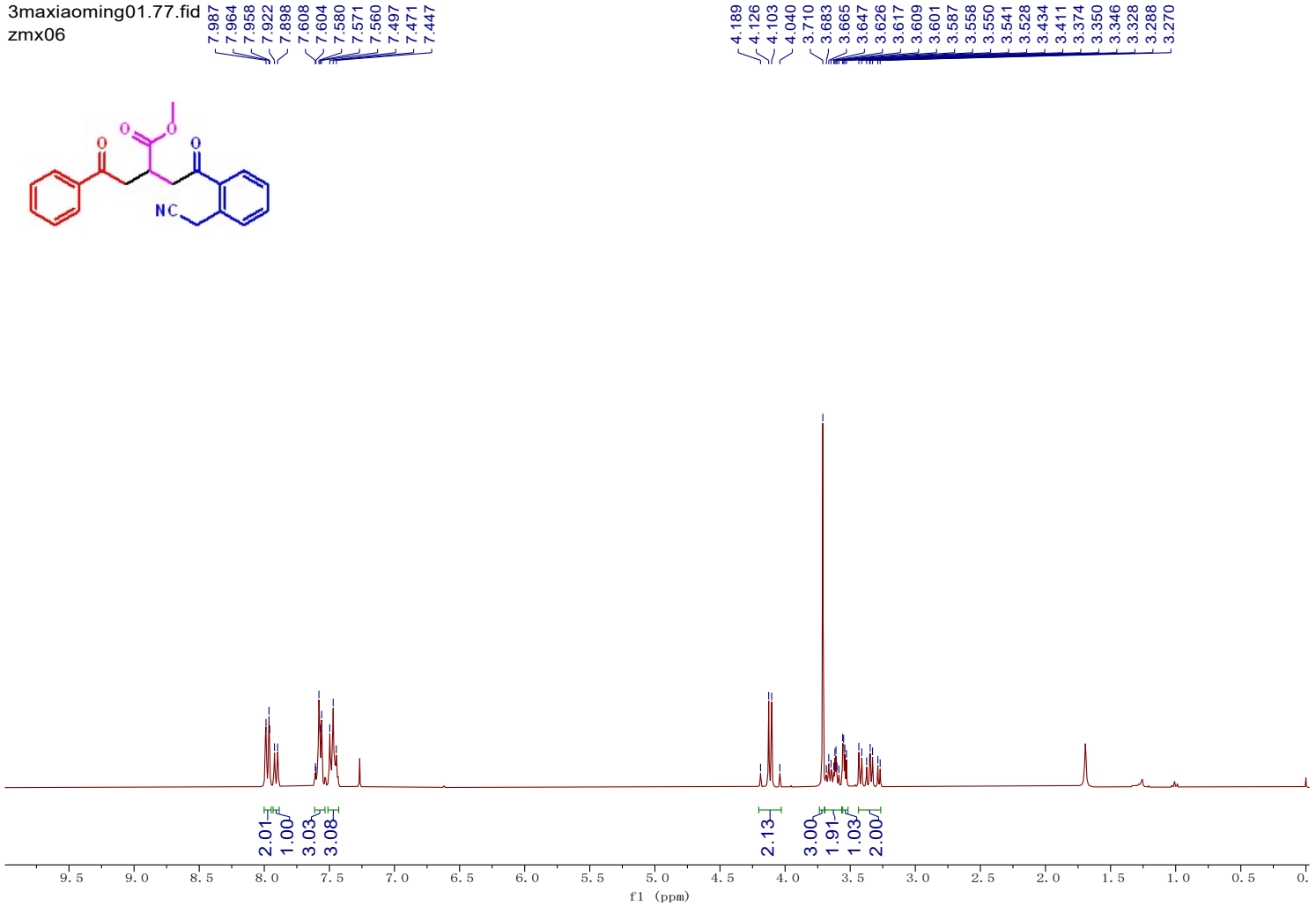
^{13}C NMR Spectrum of Compound 4u (75 MHz, $CDCl_3$)



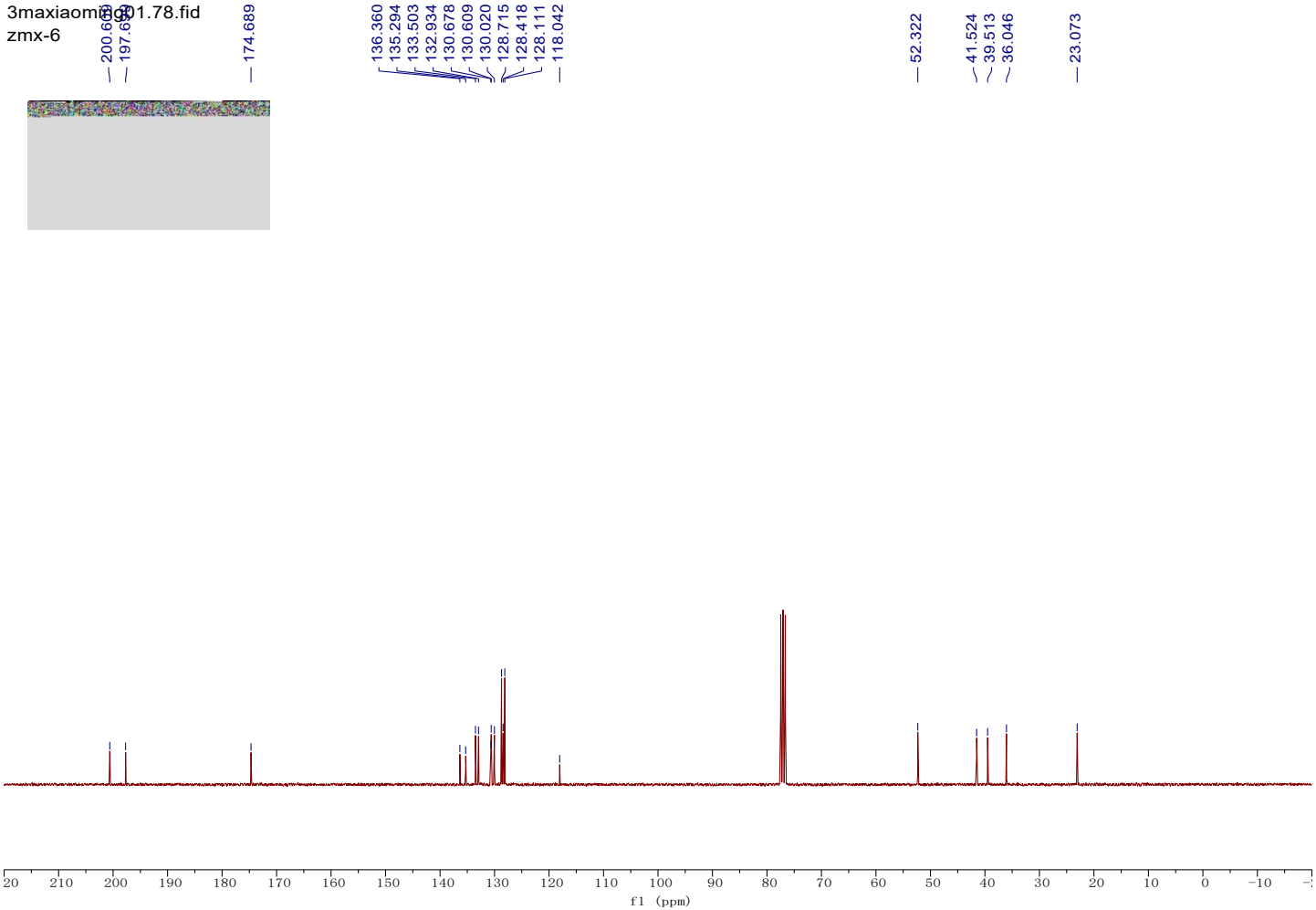
^{1}H NMR Spectrum of Compound 4v (300 MHz, $CDCl_3$)



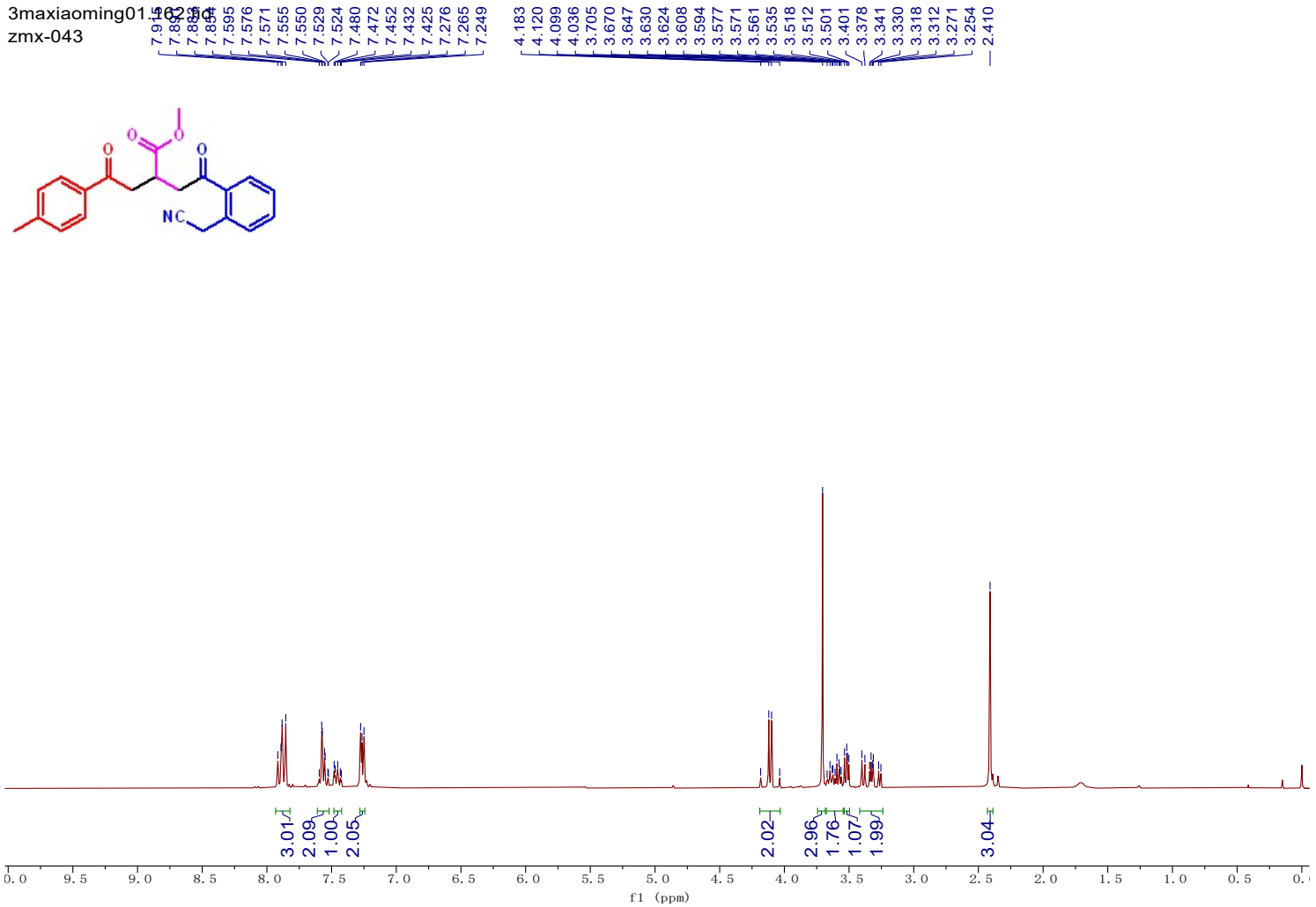
^{13}C NMR Spectrum of Compound 4v (75 MHz, $CDCl_3$)



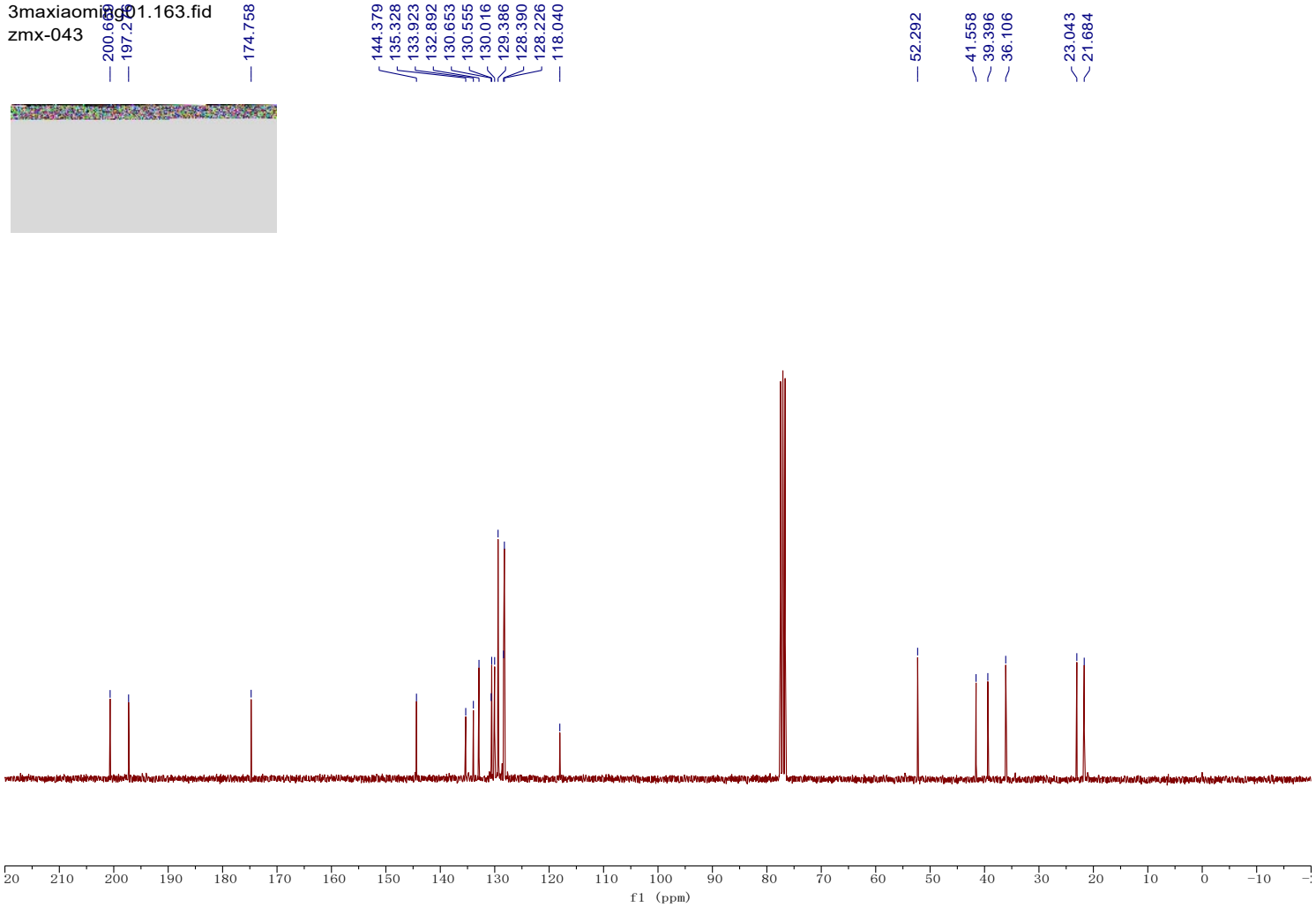
^{1}H NMR Spectrum of Compound 6a (300 MHz, $CDCl_3$)



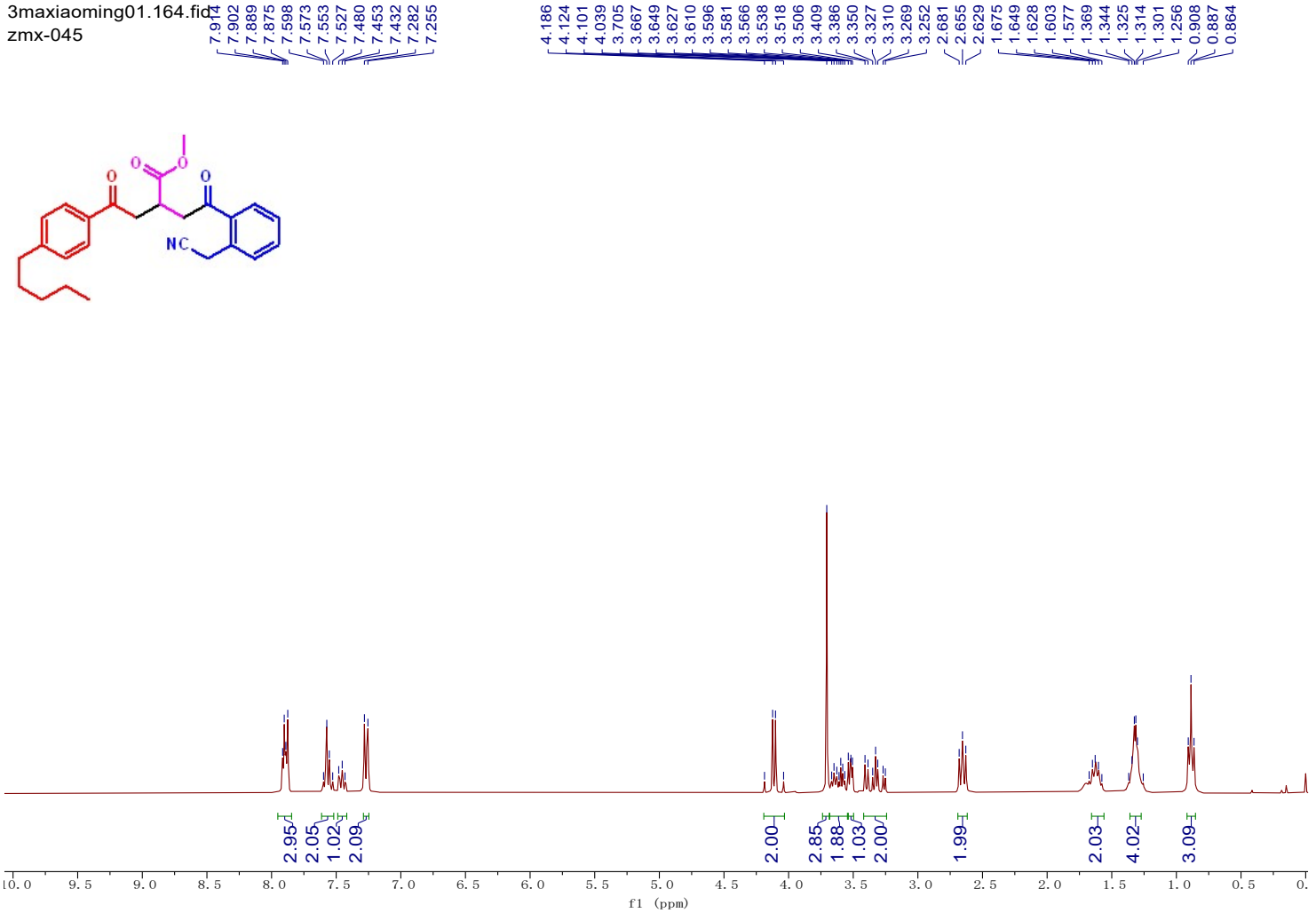
^{13}C NMR Spectrum of Compound 6a (75 MHz, $CDCl_3$)



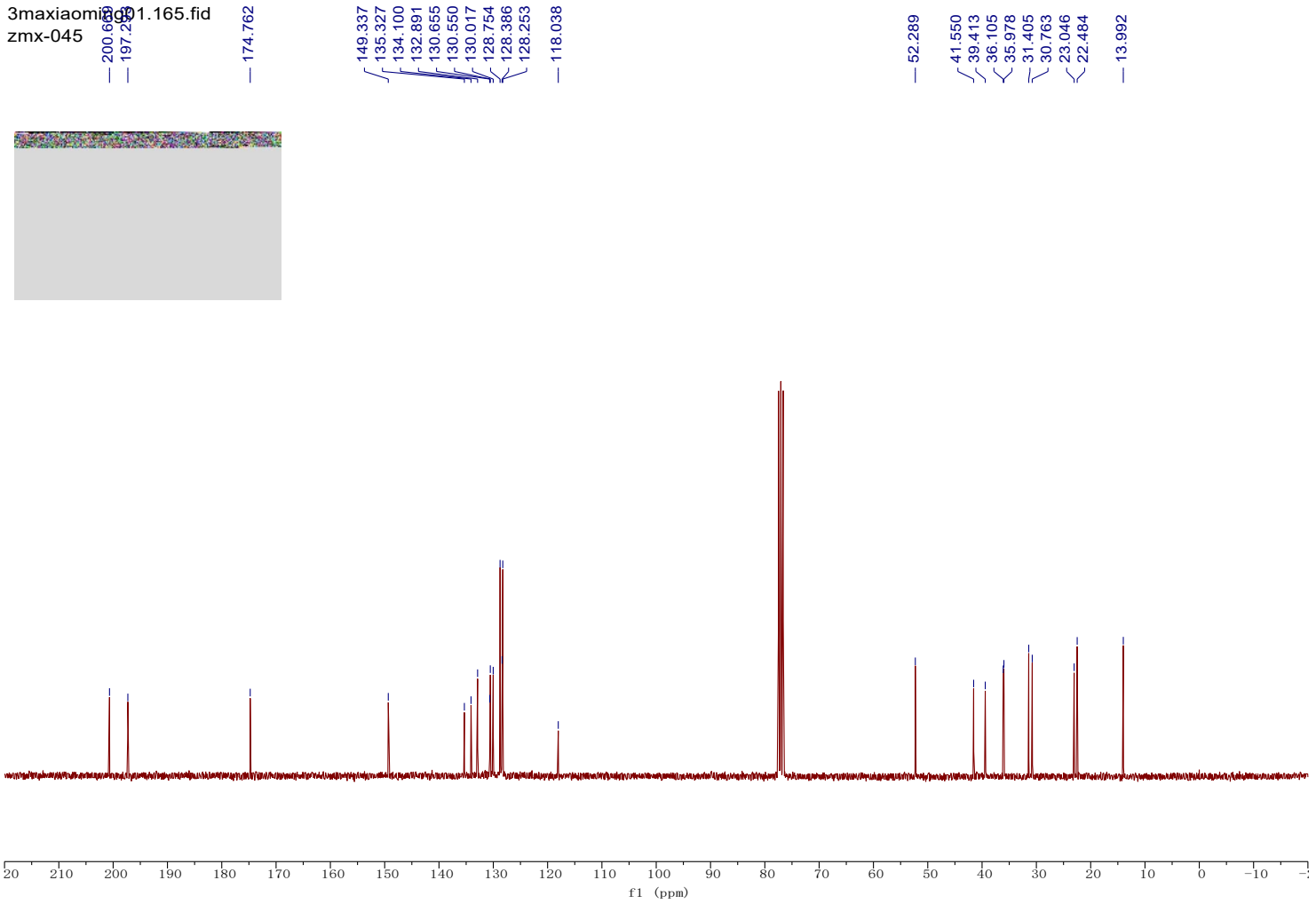
^{1}H NMR Spectrum of Compound 6b (300 MHz, $CDCl_3$)



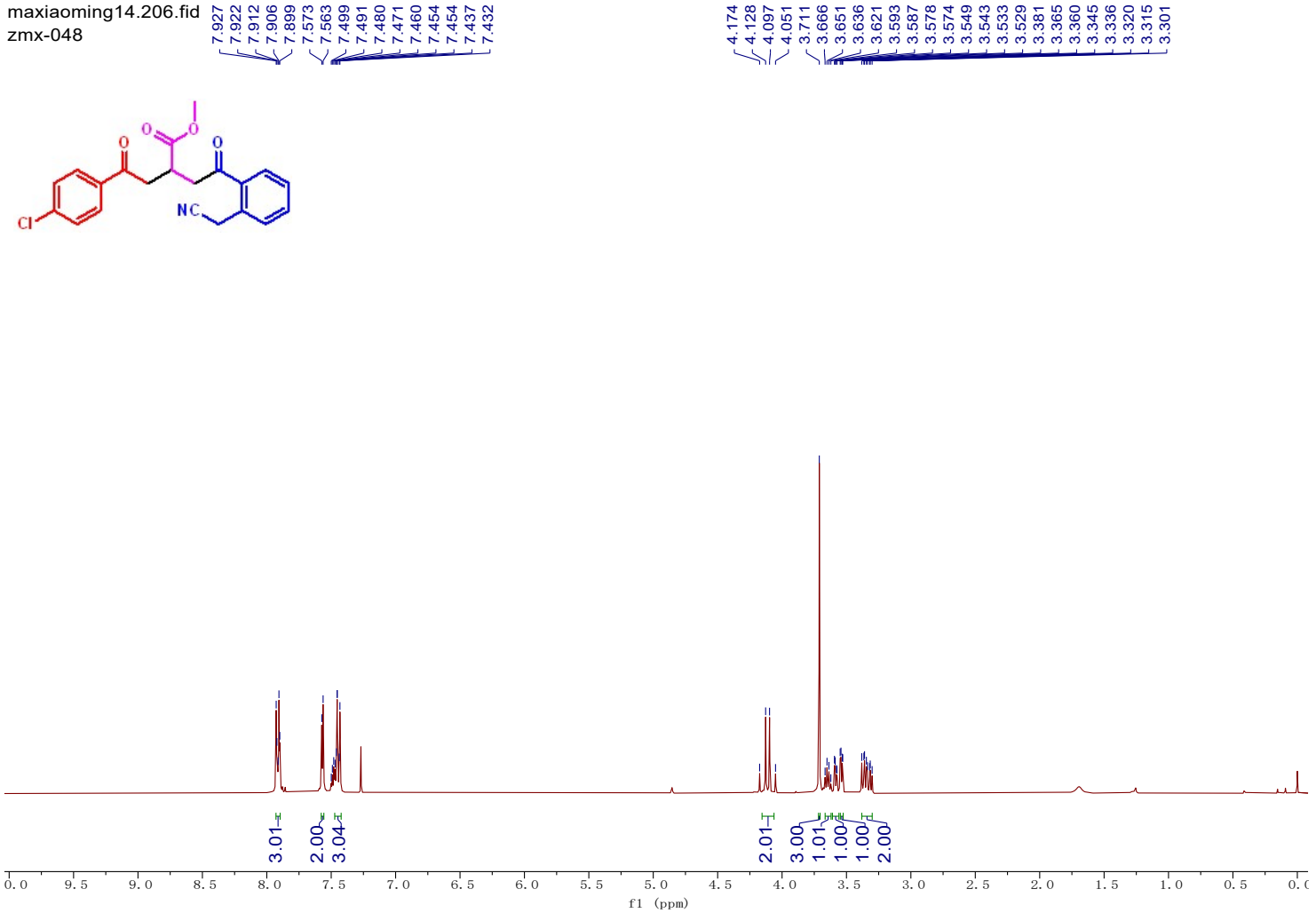
^{13}C NMR Spectrum of Compound 6b (75 MHz, $CDCl_3$)



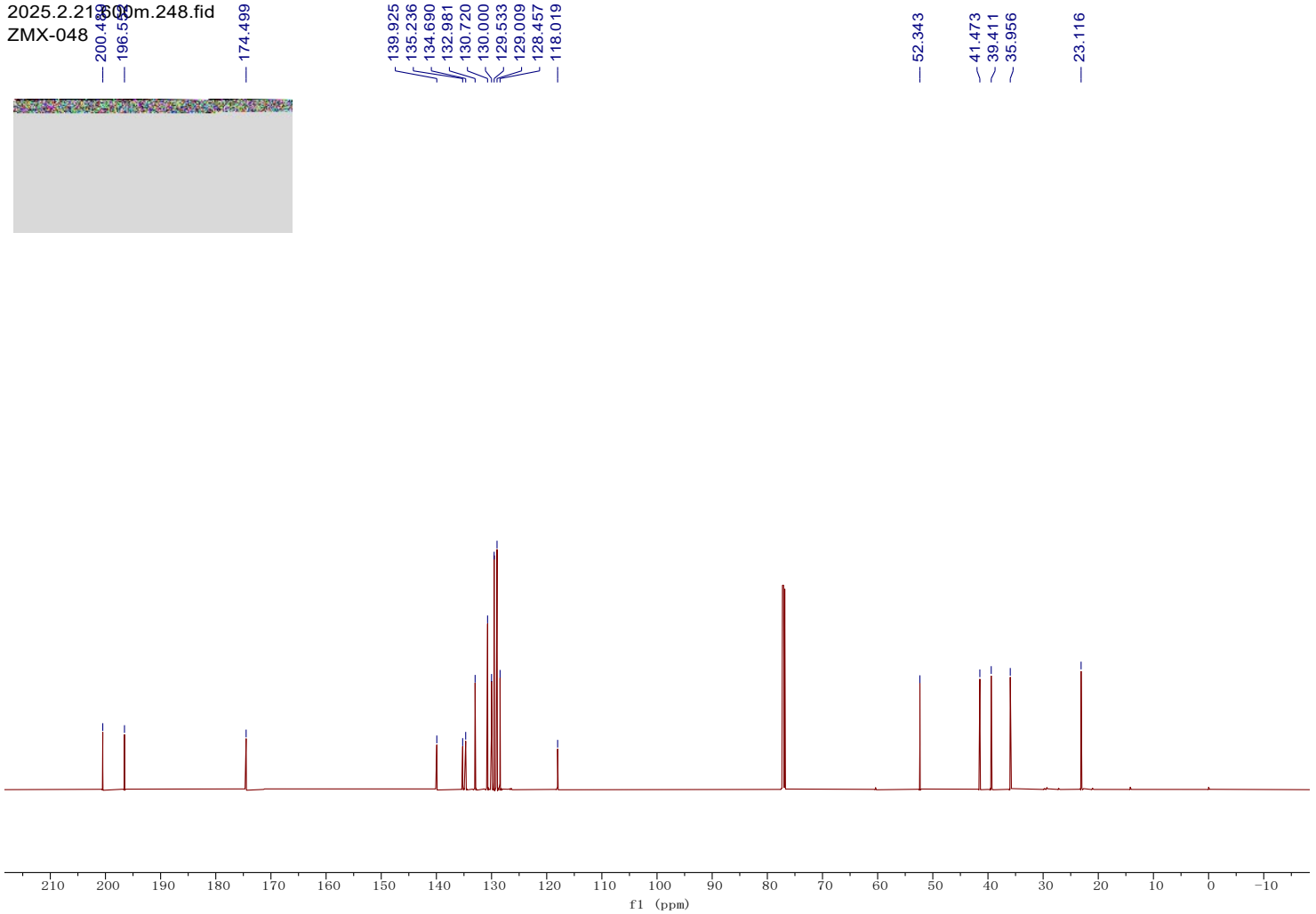
^{1}H NMR Spectrum of Compound 6c (300 MHz, $CDCl_3$)



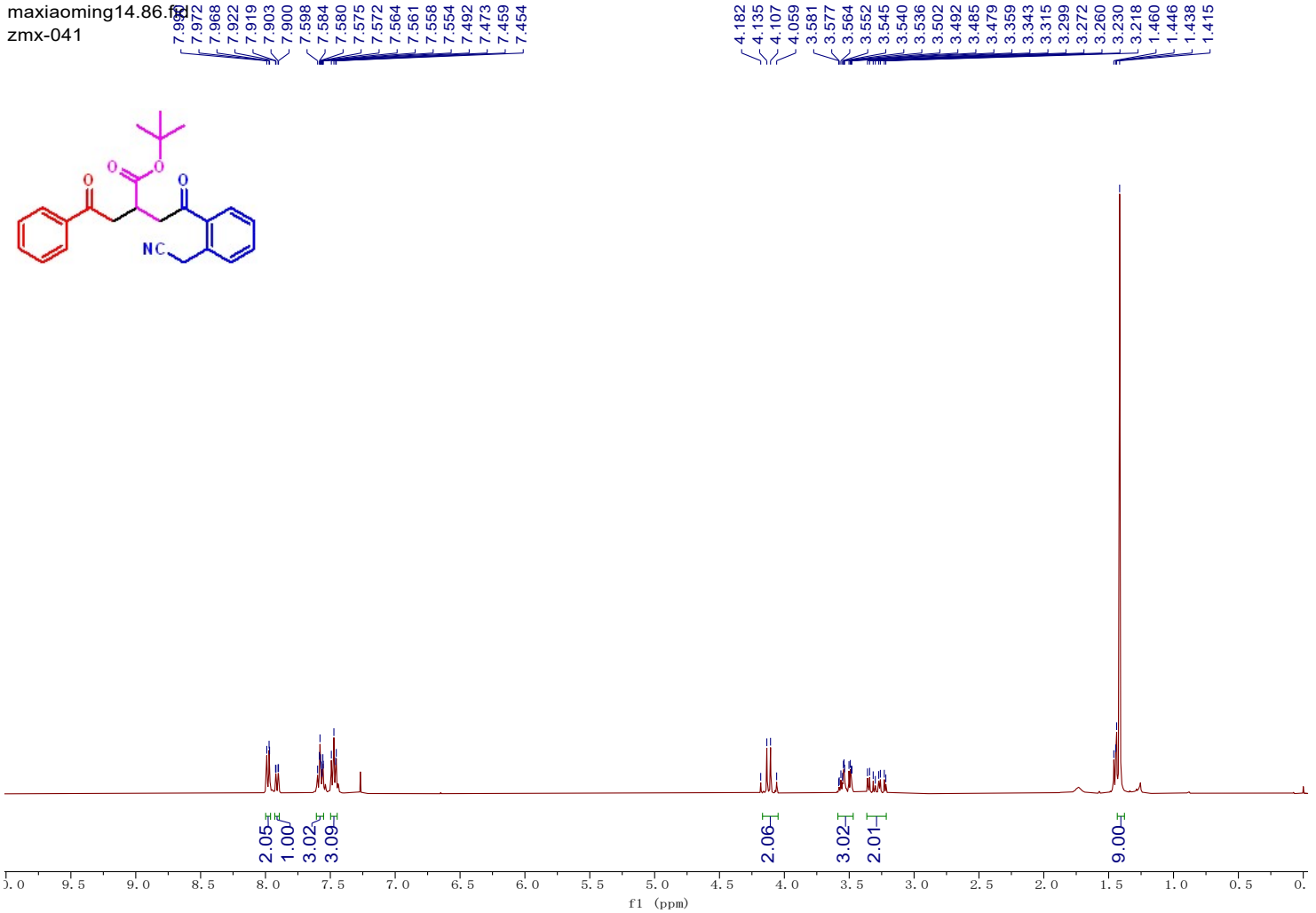
^{13}C NMR Spectrum of Compound 6c (75 MHz, $CDCl_3$)



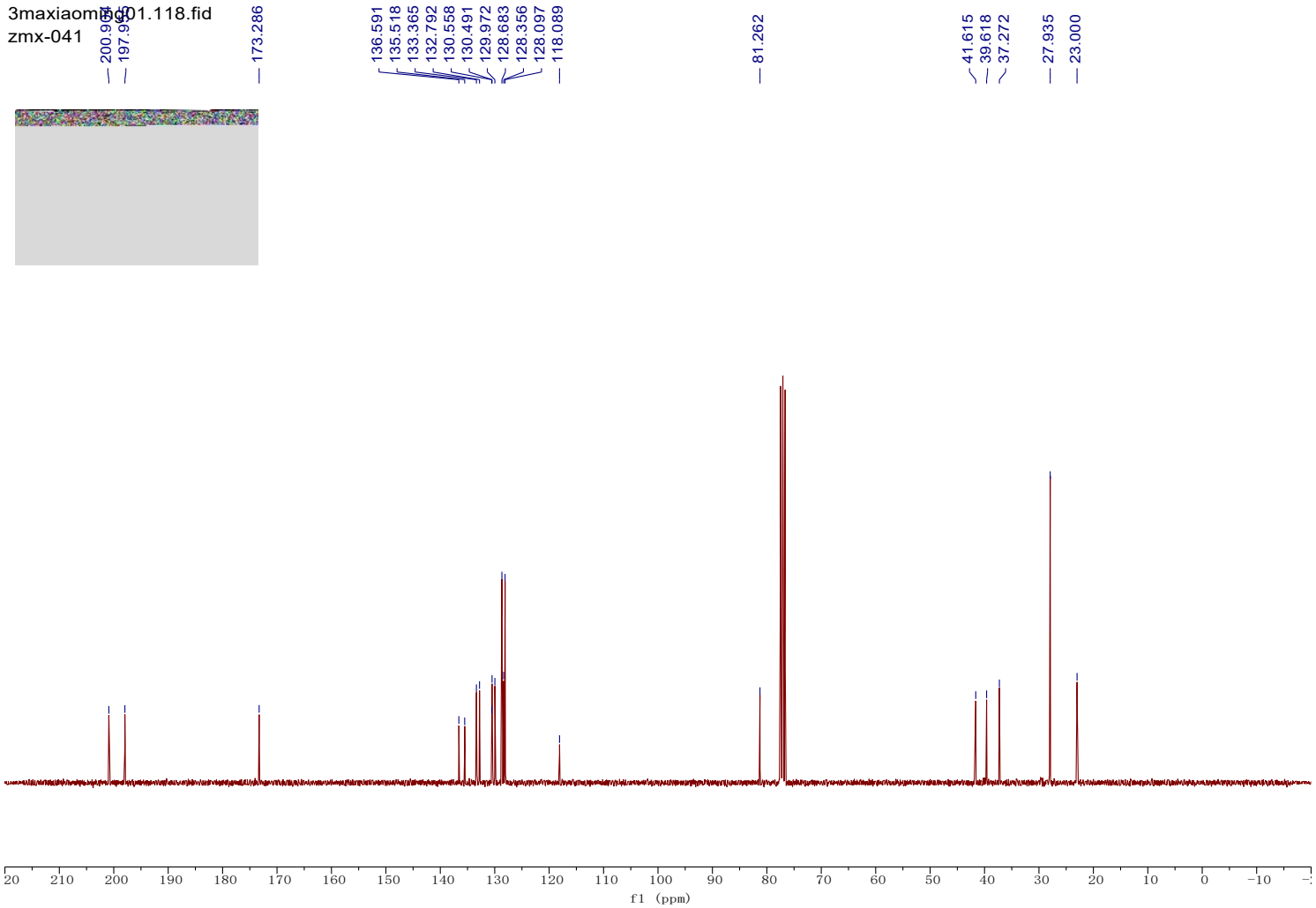
^{1}H NMR Spectrum of Compound 6d (400 MHz, $CDCl_3$)



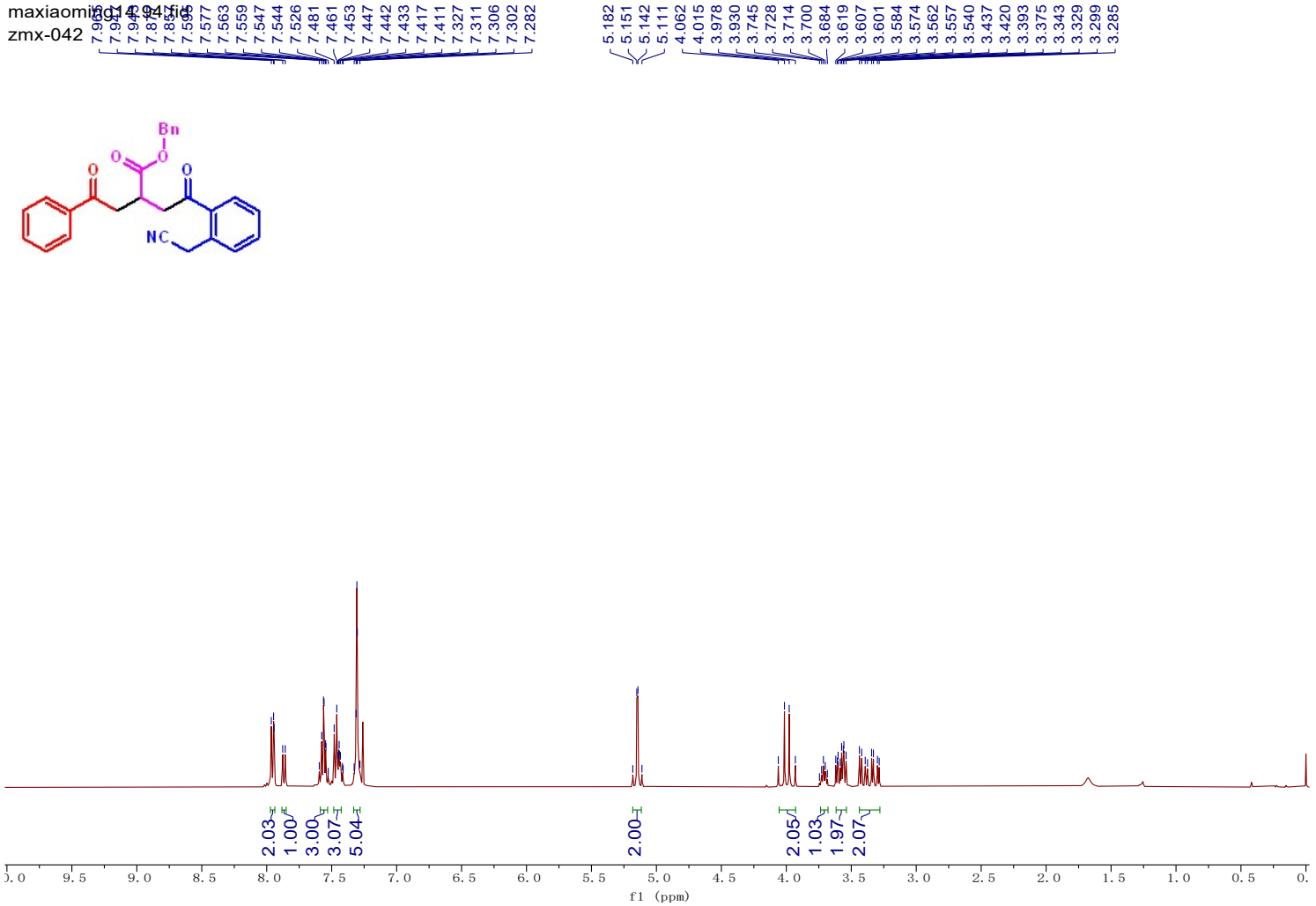
^{13}C NMR Spectrum of Compound 6d (151 MHz, $CDCl_3$)



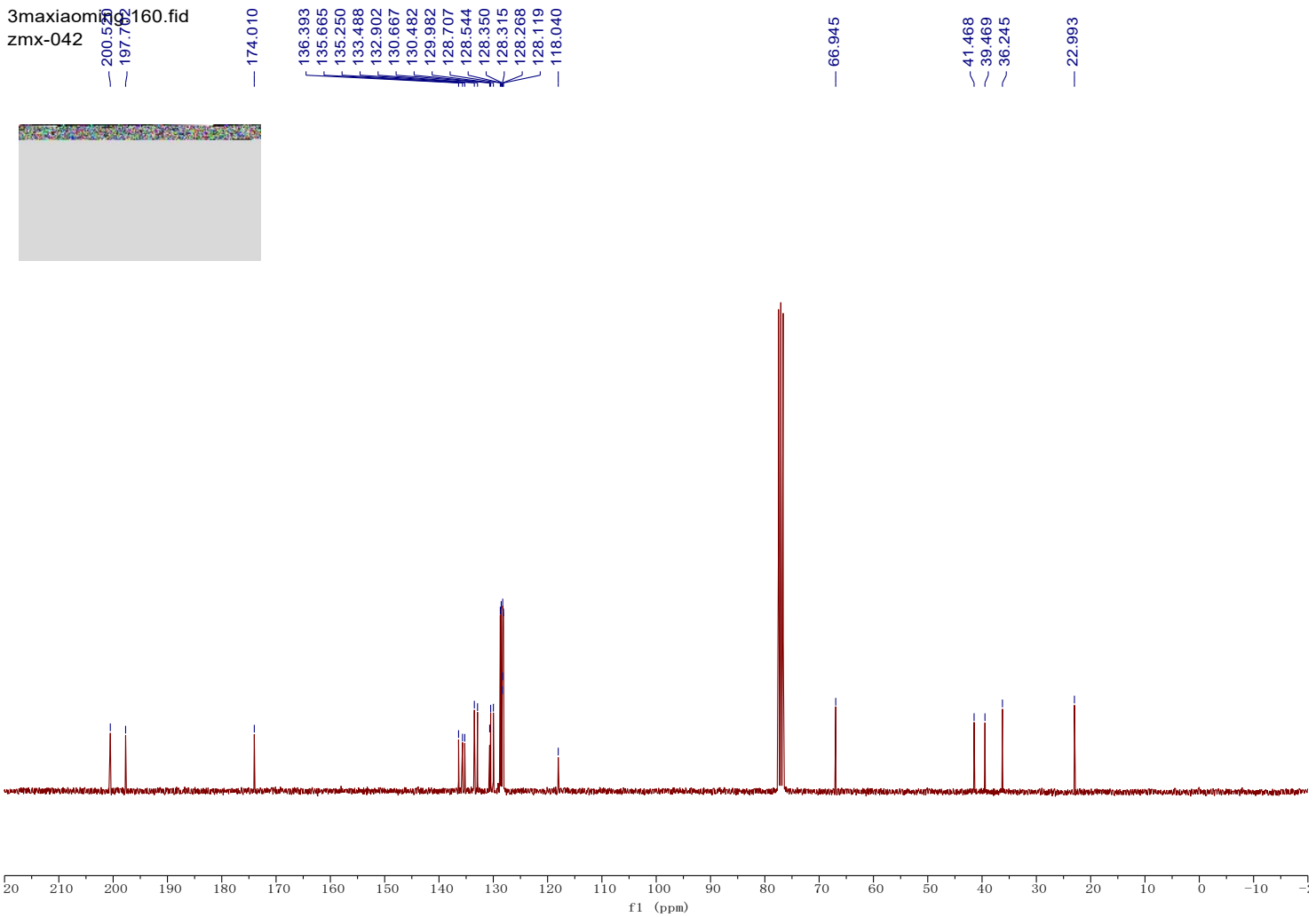
^{1}H NMR Spectrum of Compound 6e (400 MHz, $CDCl_3$)



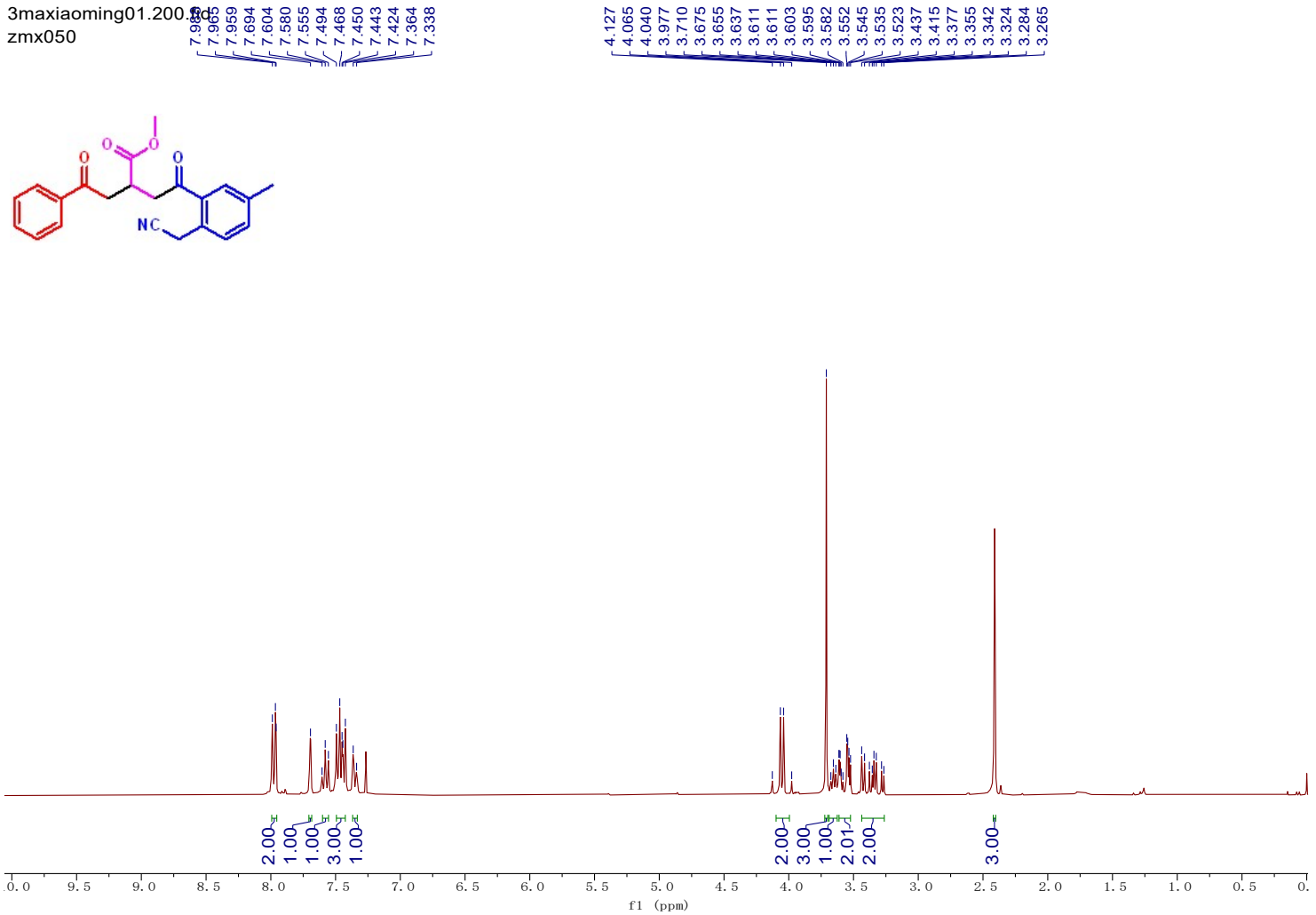
^{13}C NMR Spectrum of Compound 6e (75 MHz, $CDCl_3$)



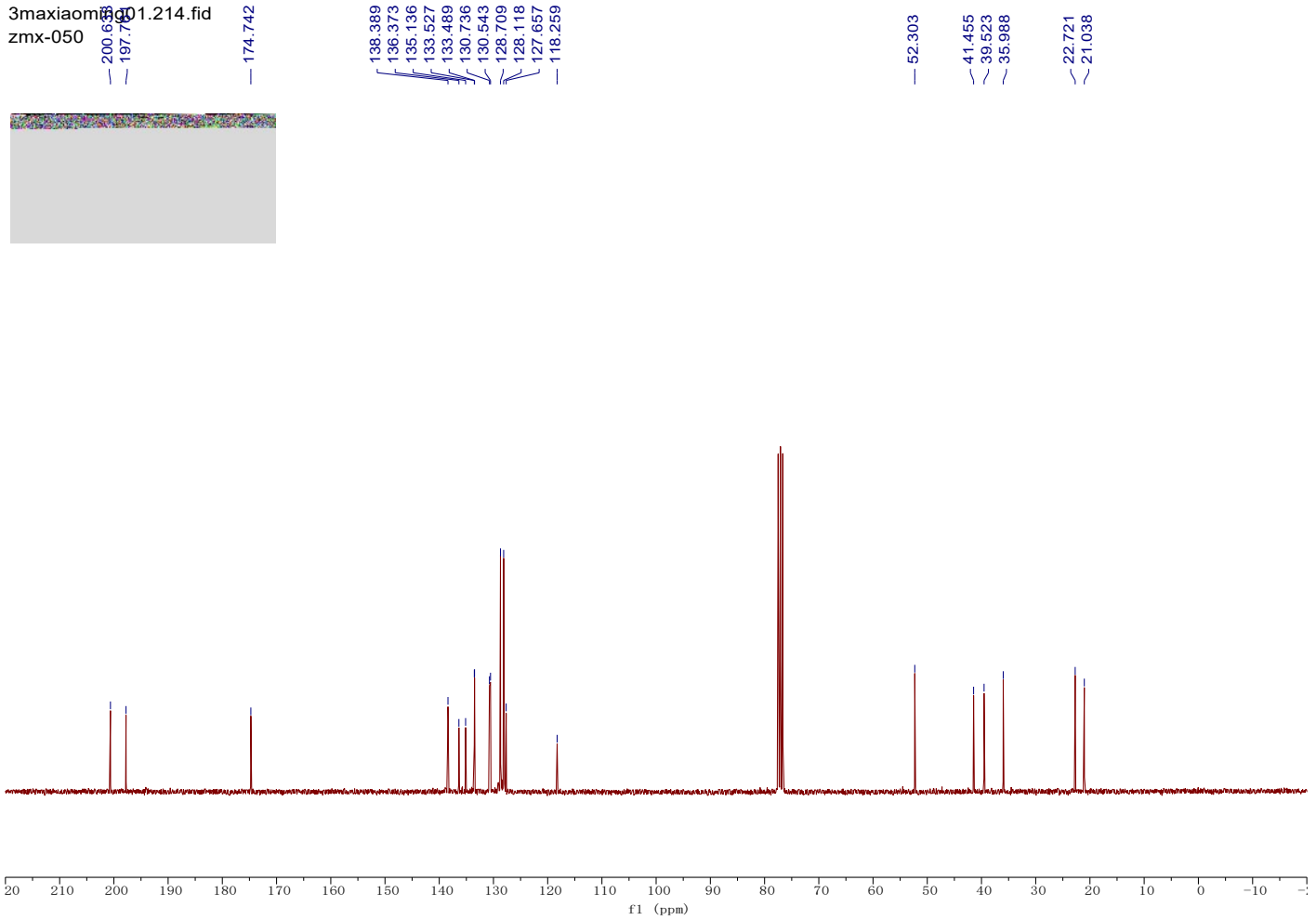
^{1}H NMR Spectrum of Compound 6f (400 MHz, $CDCl_3$)



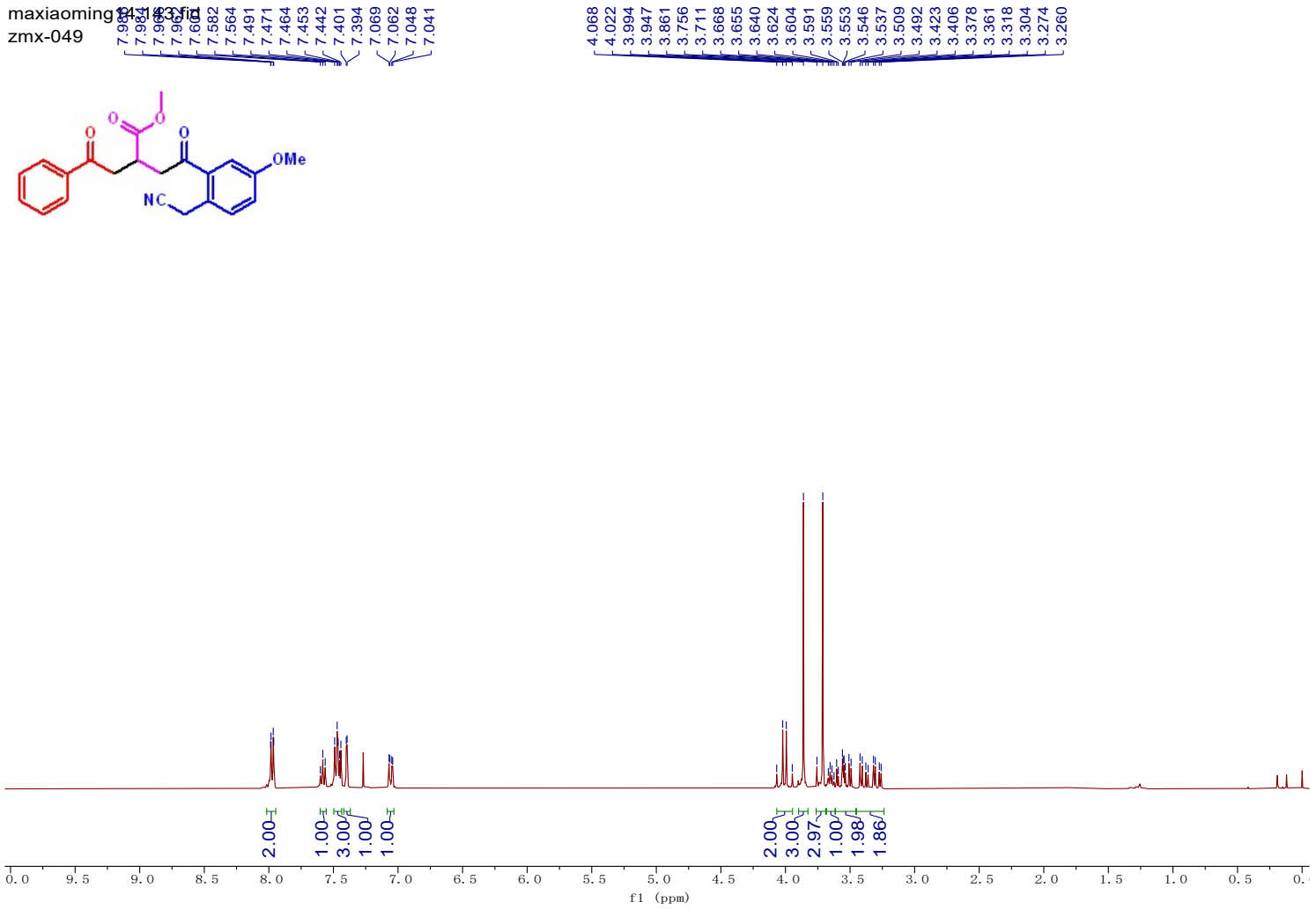
^{13}C NMR Spectrum of Compound 6f (75 MHz, $CDCl_3$)



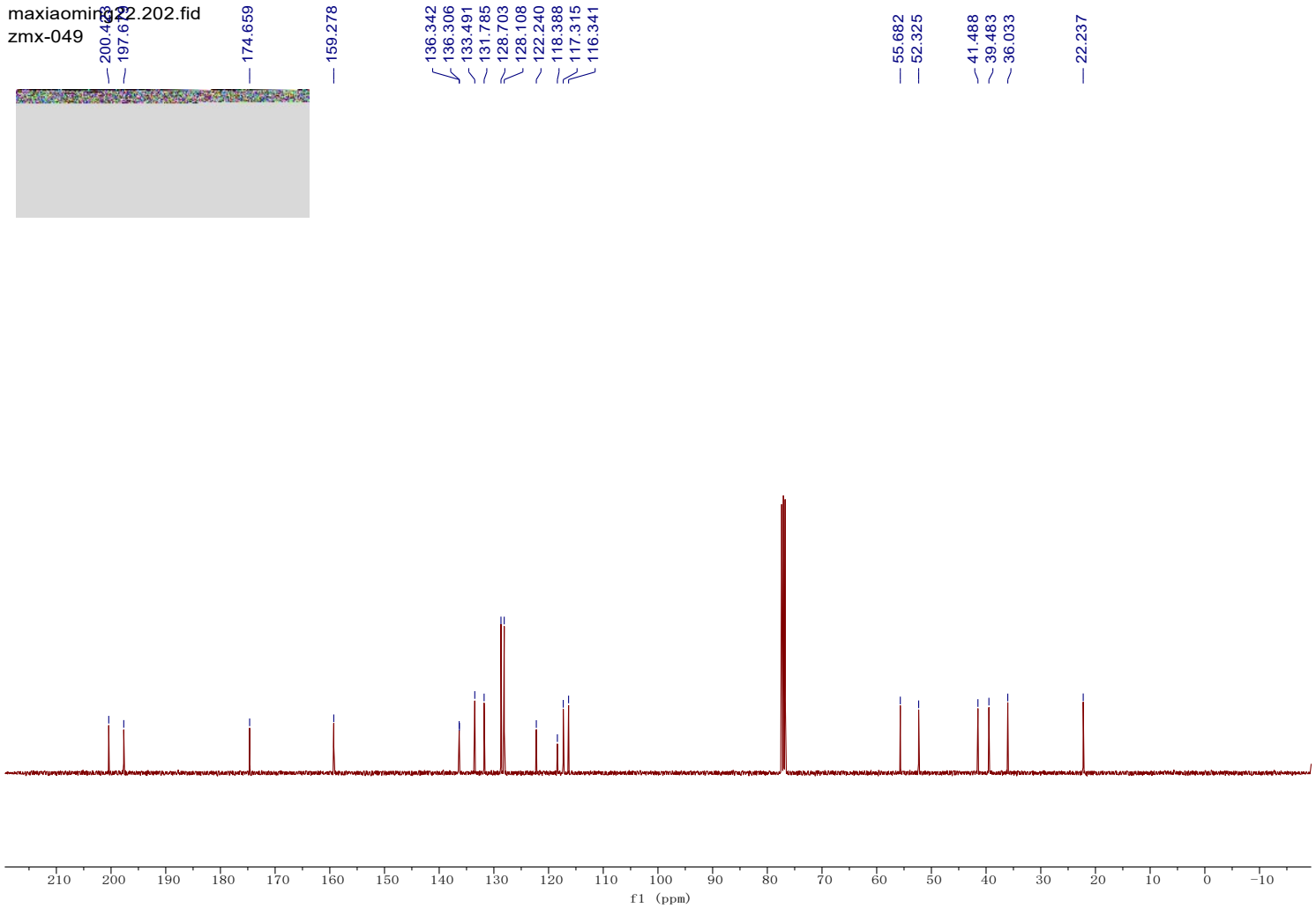
^{1}H NMR Spectrum of Compound 6g (300 MHz, $CDCl_3$)



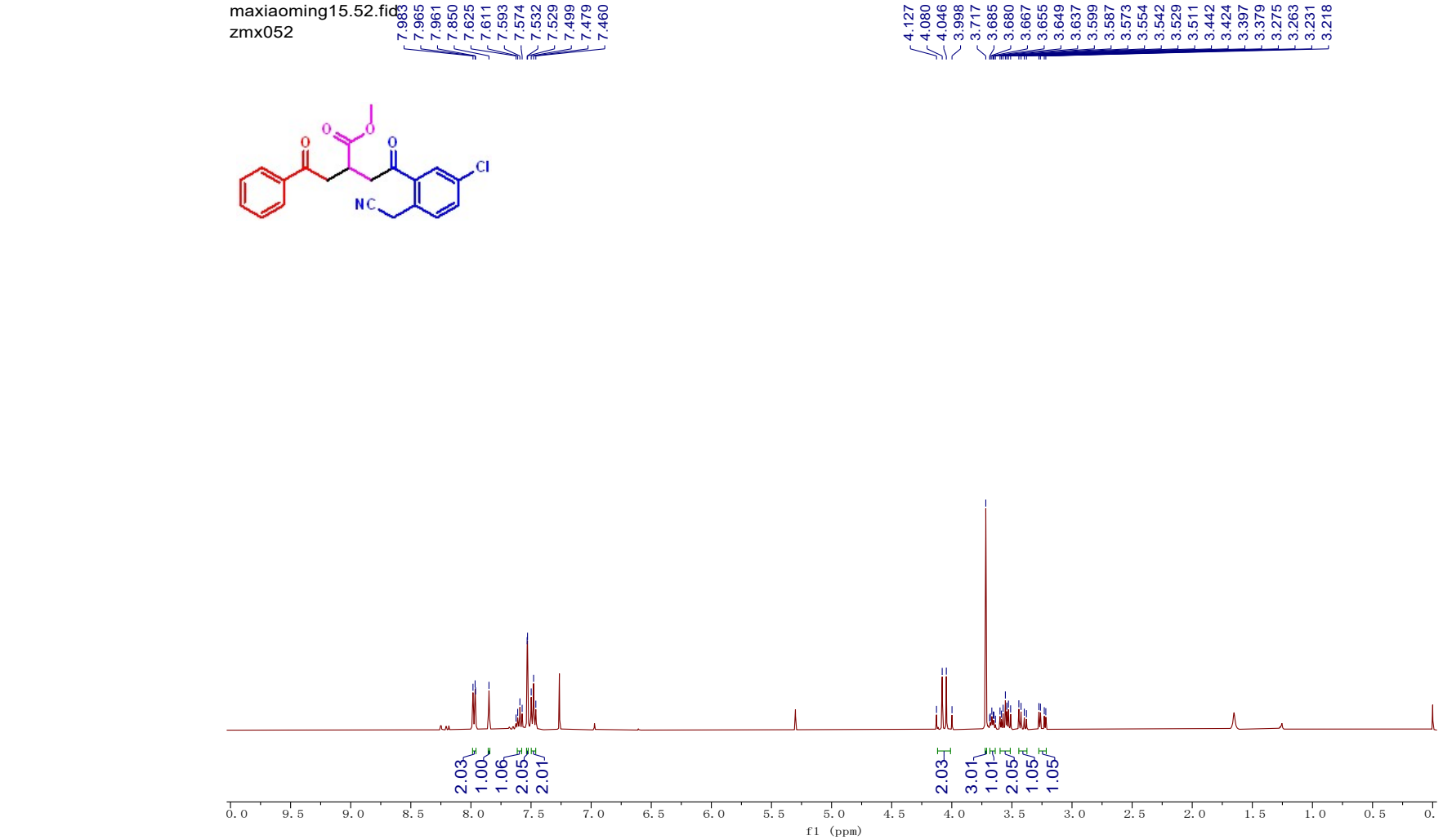
^{13}C NMR Spectrum of Compound 6g (75 MHz, $CDCl_3$)



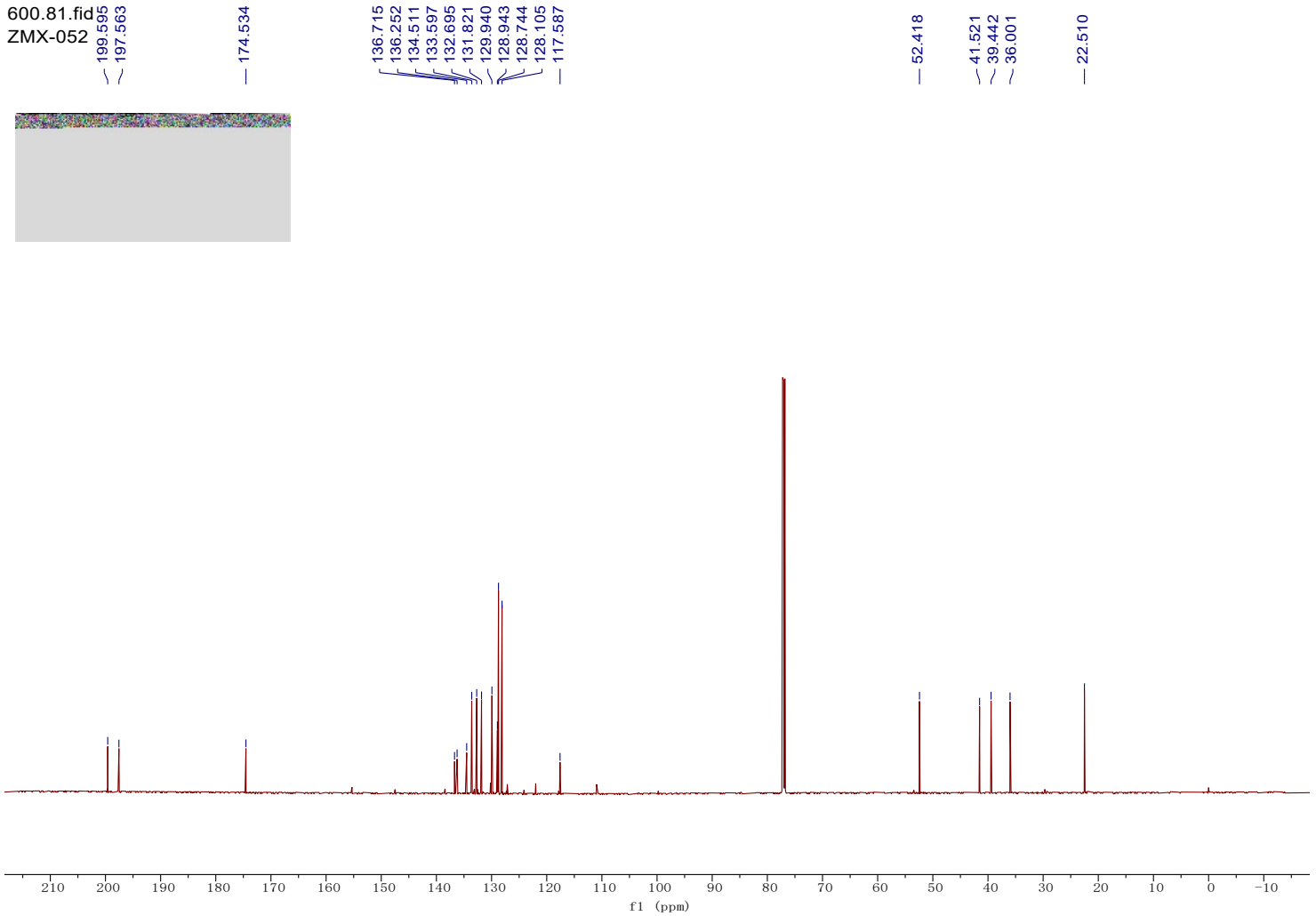
^{1}H NMR Spectrum of Compound 6h (400 MHz, $CDCl_3$)



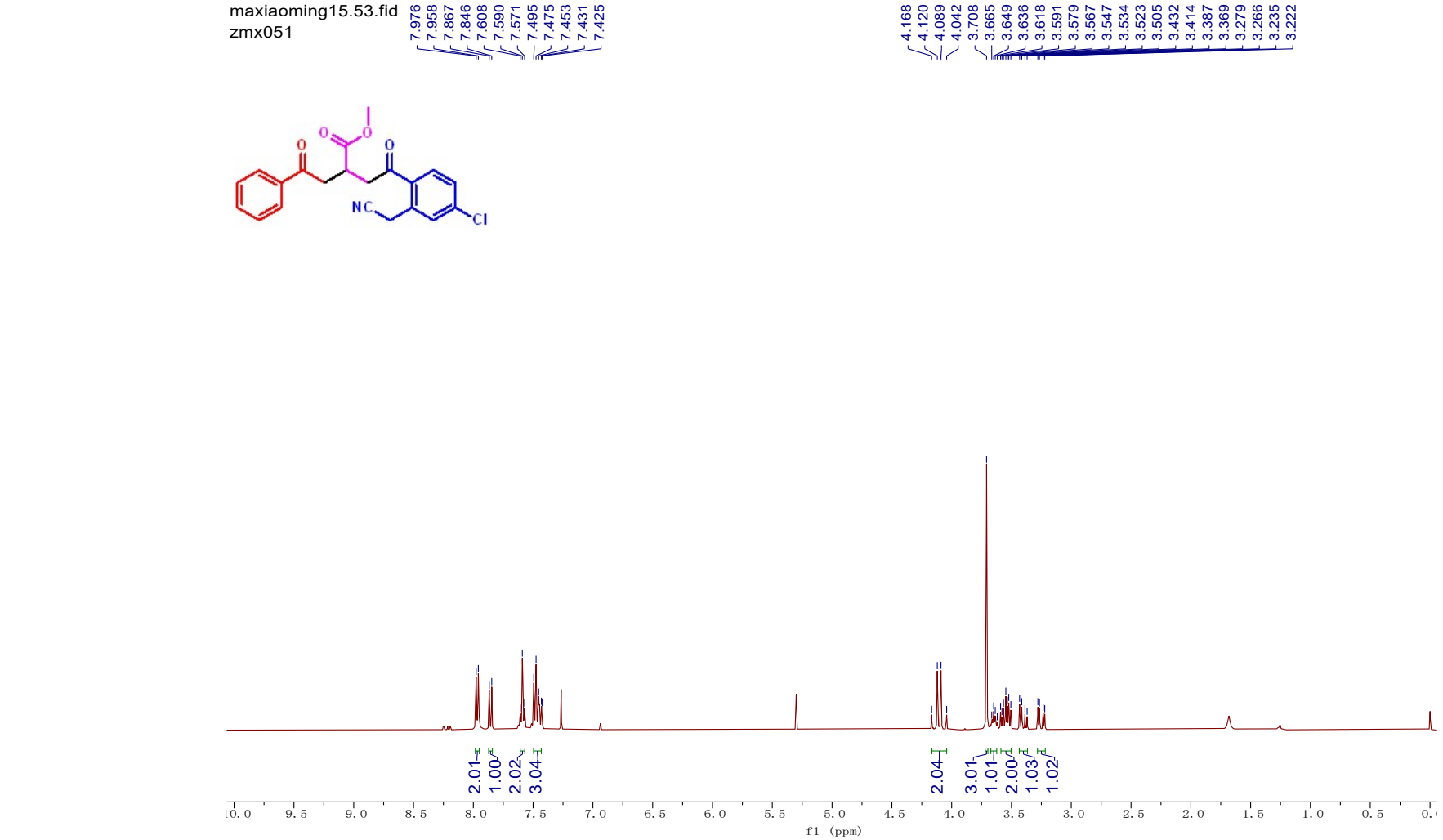
^{13}C NMR Spectrum of Compound 6h (100 MHz, $CDCl_3$)



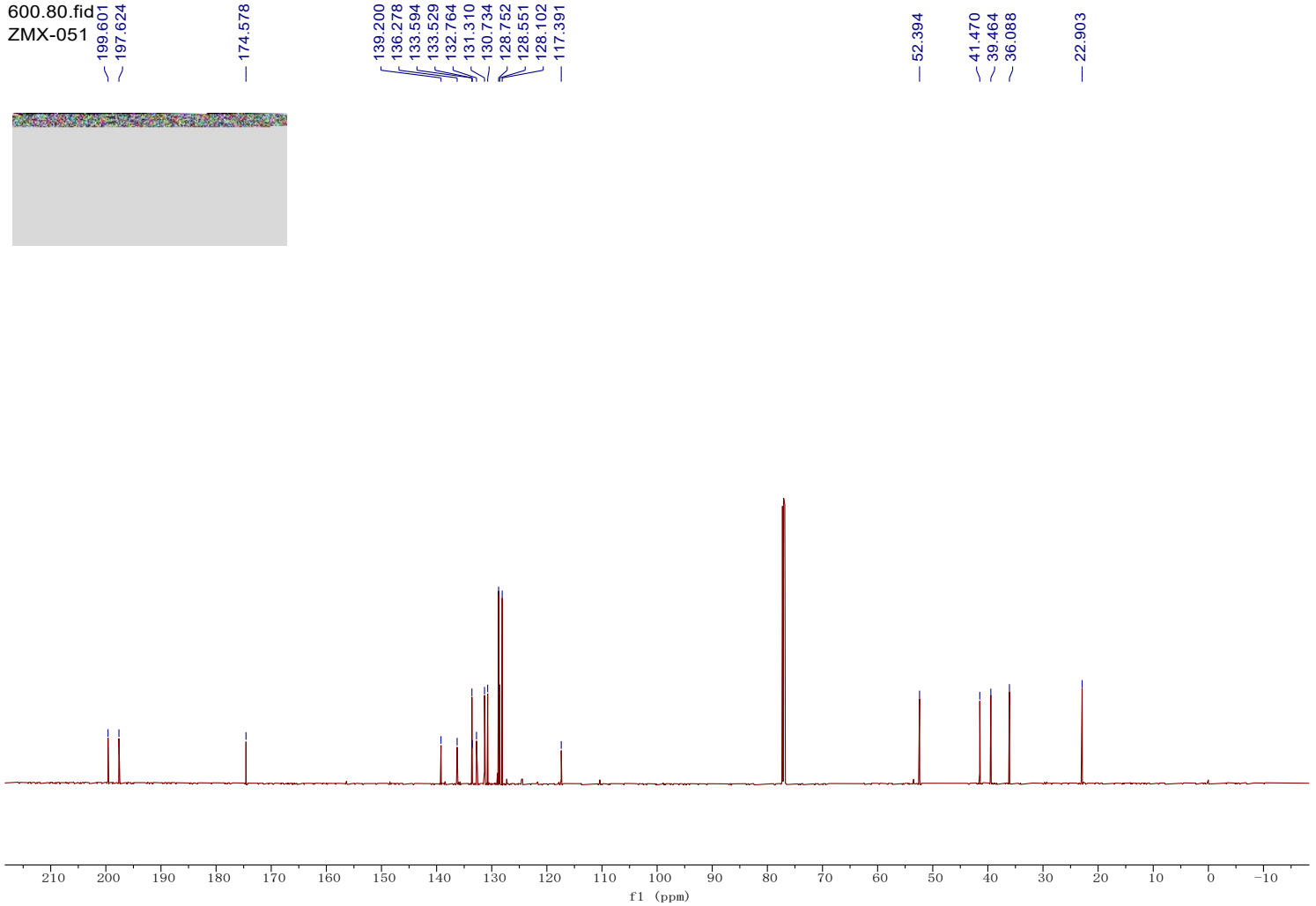
^{1}H NMR Spectrum of Compound 6i (400 MHz, $CDCl_3$)



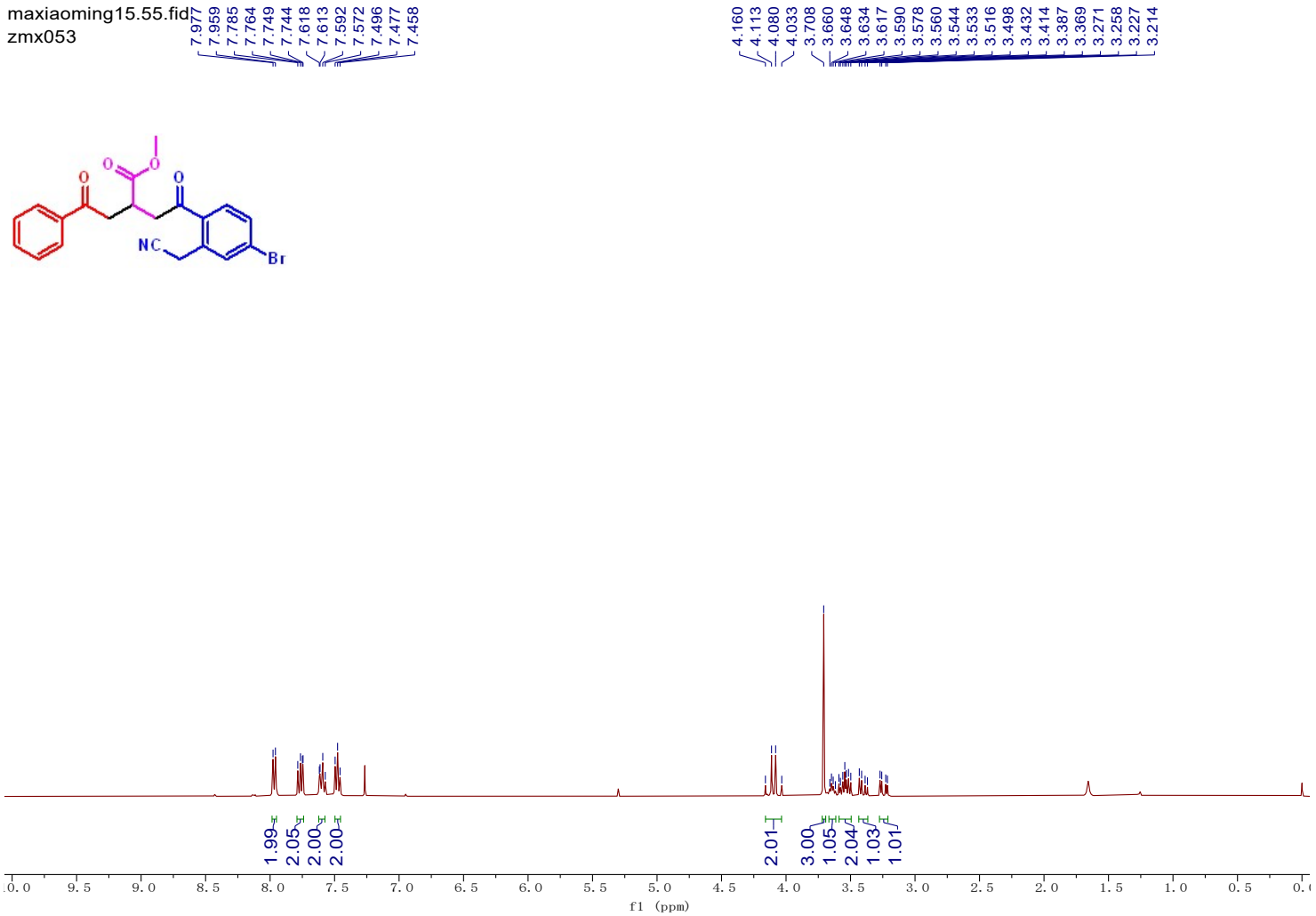
^{13}C NMR Spectrum of Compound 6i (151 MHz, $CDCl_3$)



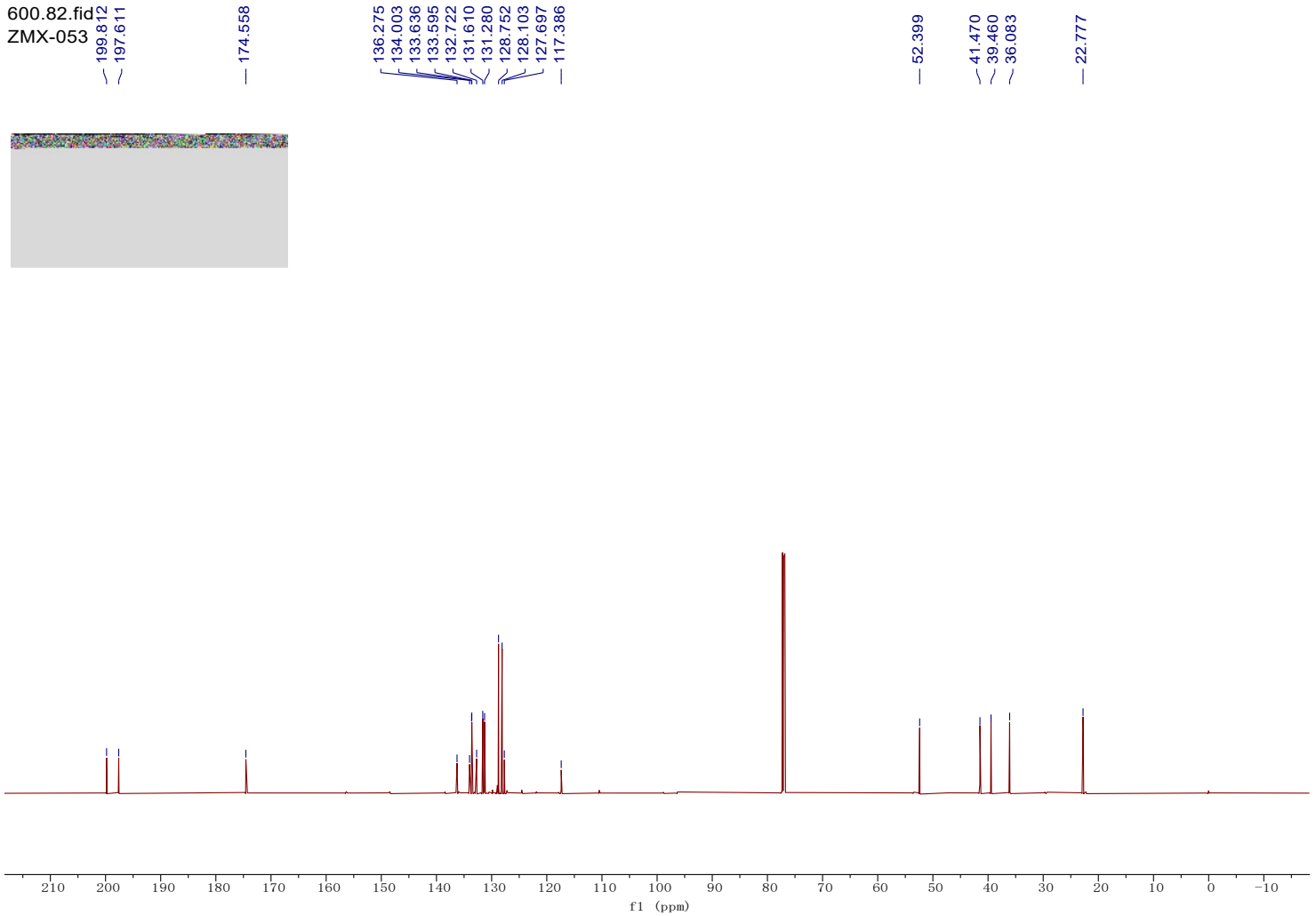
^{1}H NMR Spectrum of Compound 6j (400 MHz, $CDCl_3$)



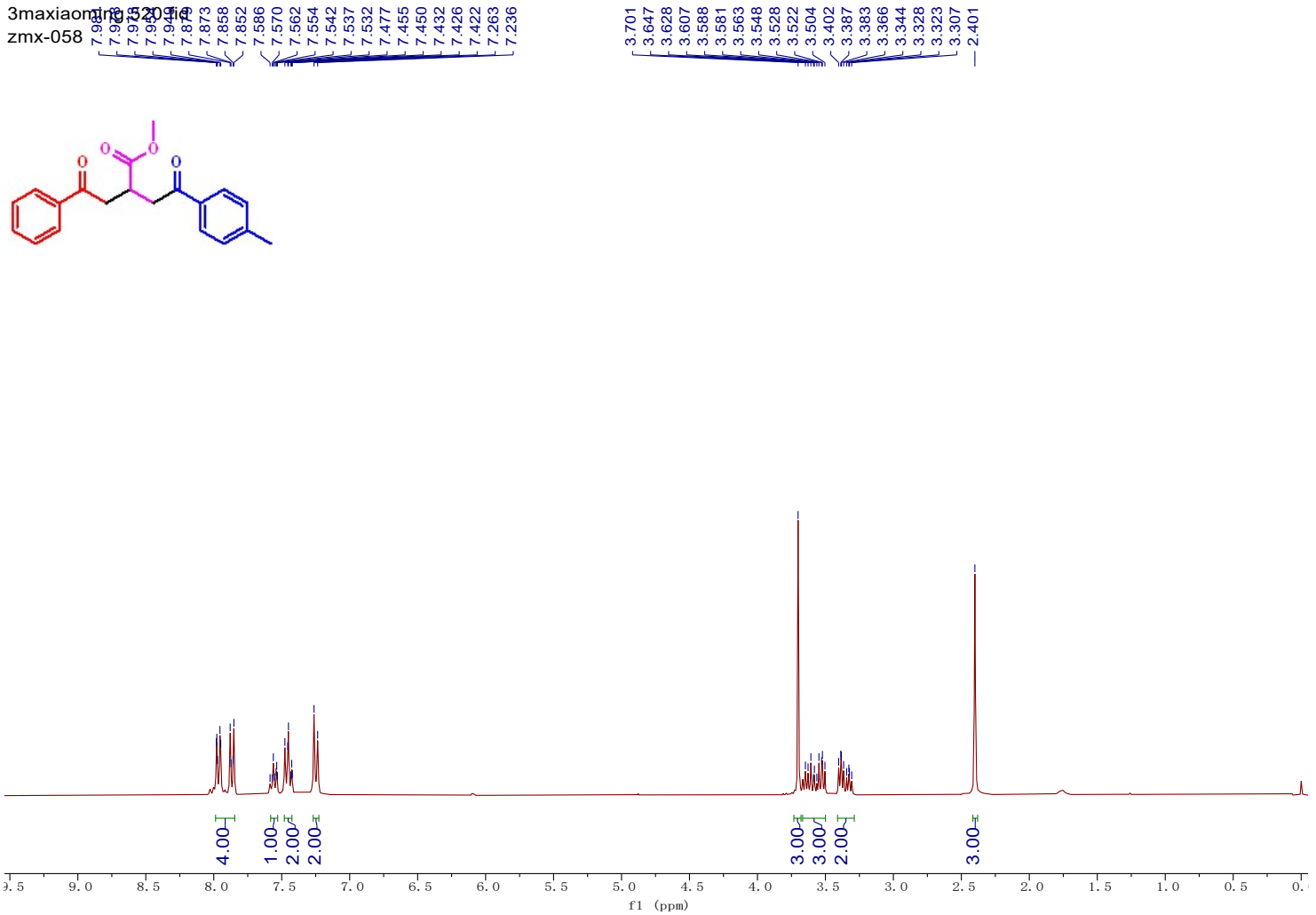
^{13}C NMR Spectrum of Compound 6j (151 MHz, $CDCl_3$)



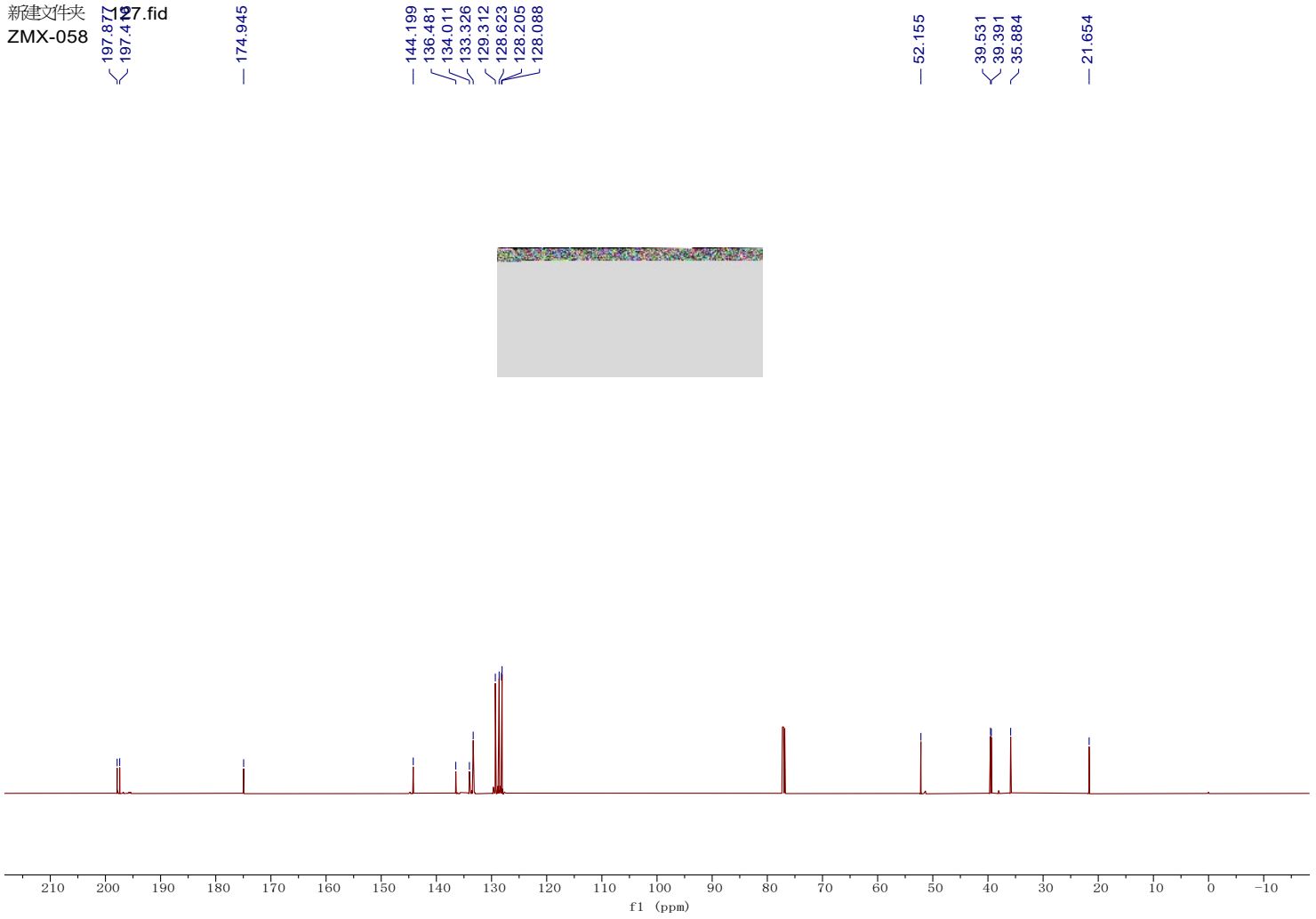
^{1}H NMR Spectrum of Compound 6k (400 MHz, $CDCl_3$)



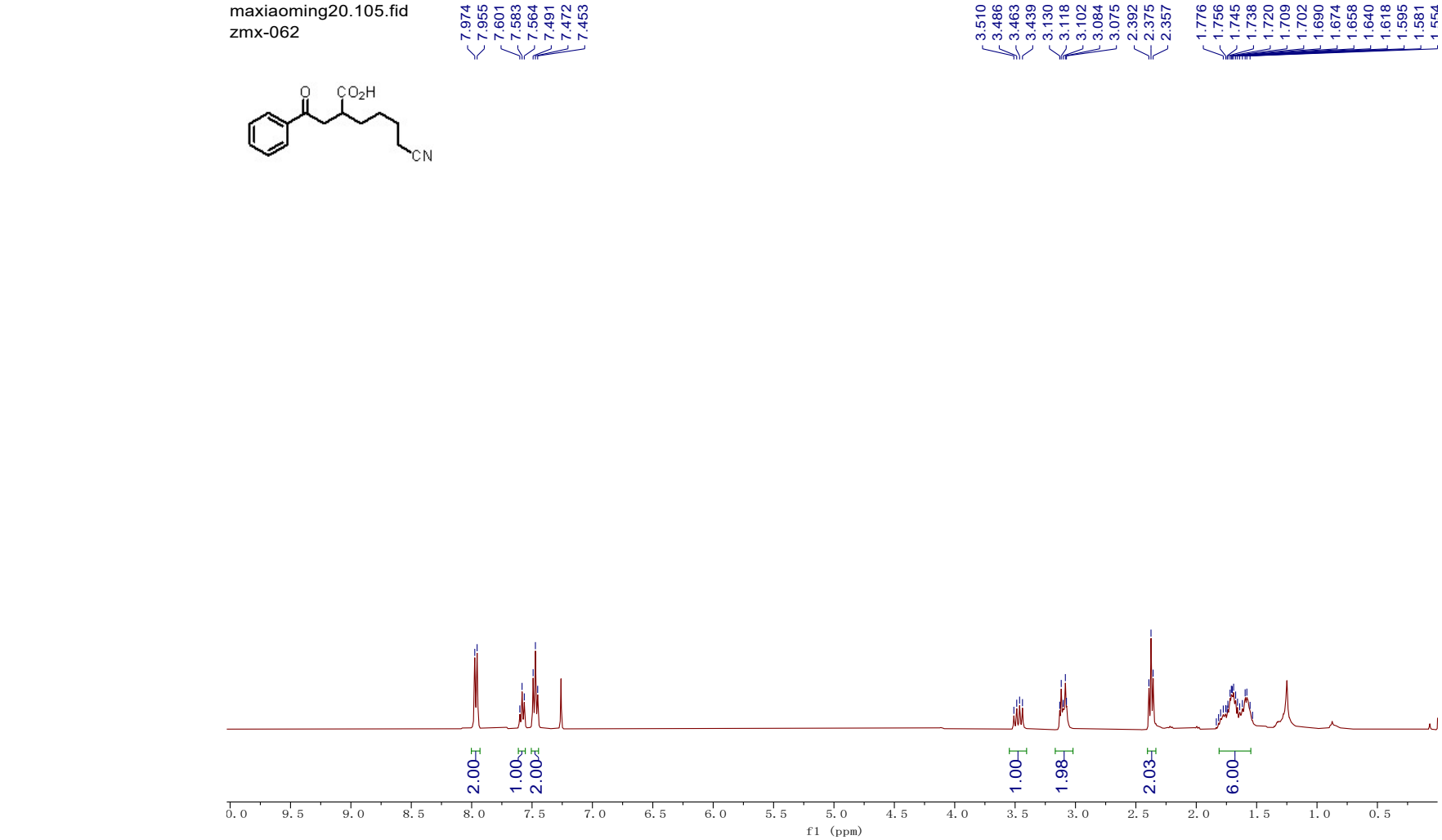
^{13}C NMR Spectrum of Compound 6k (151 MHz, $CDCl_3$)



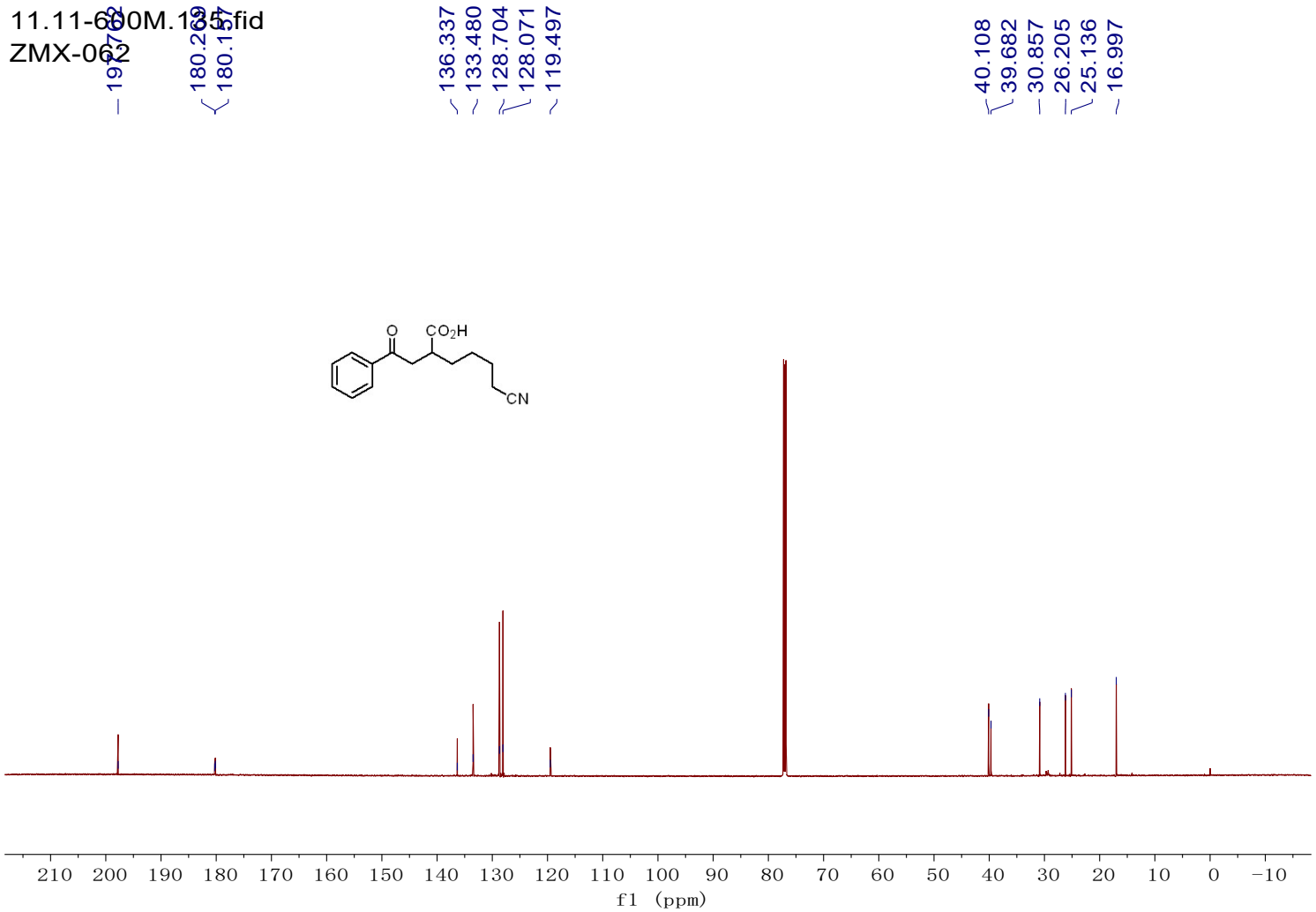
^{1}H NMR Spectrum of Compound 8 (300 MHz, $CDCl_3$)



^{13}C NMR Spectrum of Compound 8 (151 MHz, $CDCl_3$)



^{1}H NMR Spectrum of Compound 9 (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of Compound 9 (151 MHz, $CDCl_3$)