

## *Supplementary Materials*

### **Importance of the proximity and orientation of ligand-linkage to the design of cinnamate-GW9662 hybrid compounds as covalent PPAR $\gamma$ agonists**

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University, <sup>e</sup>Alliance for Research on the Mediterranean and North Africa, University of

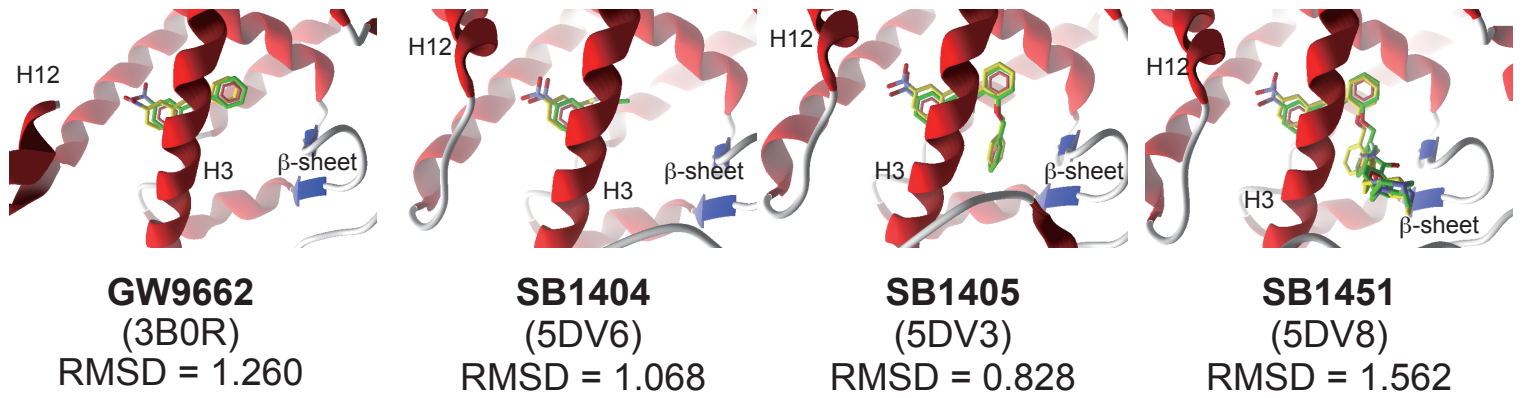
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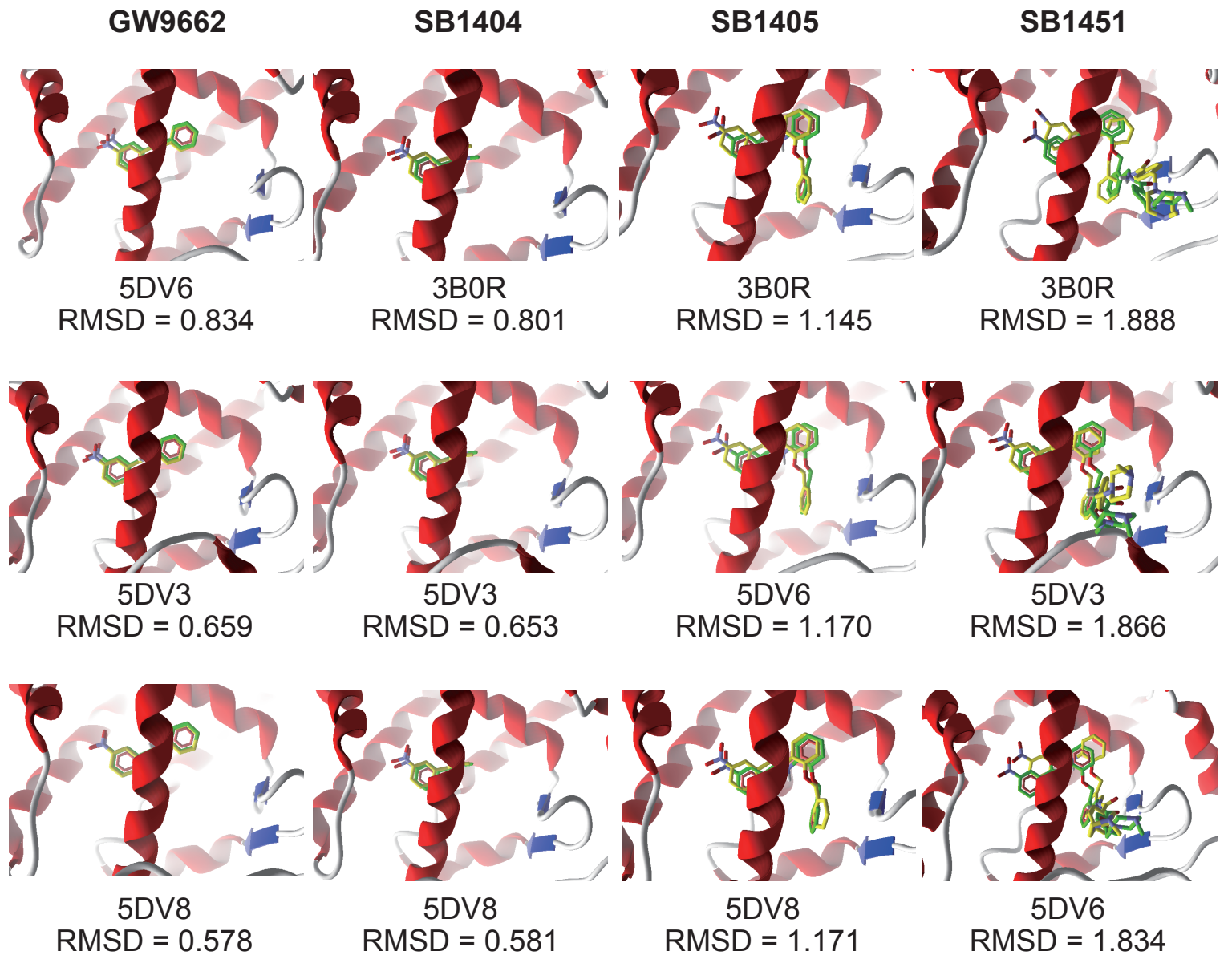
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(A)

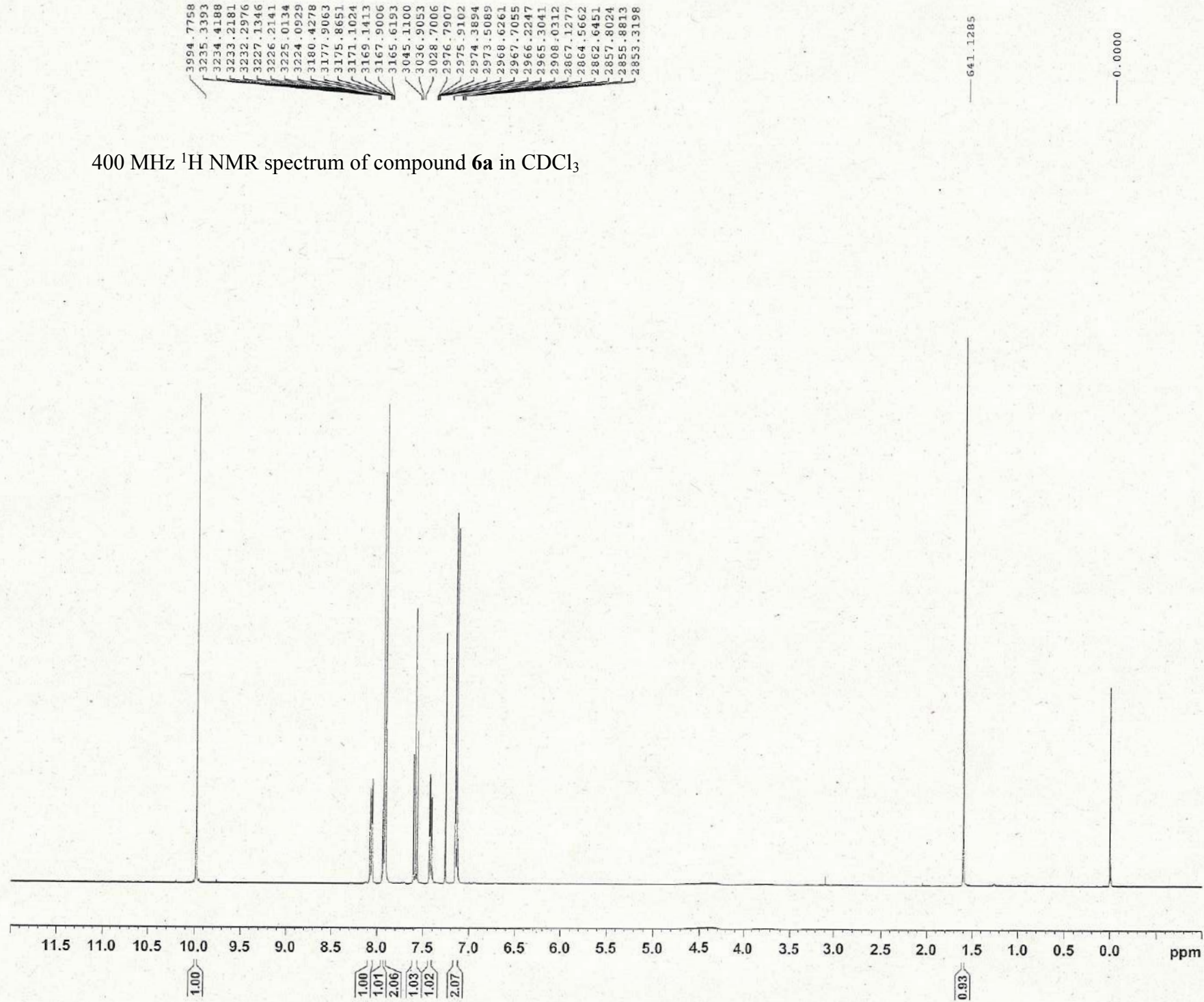


(B)

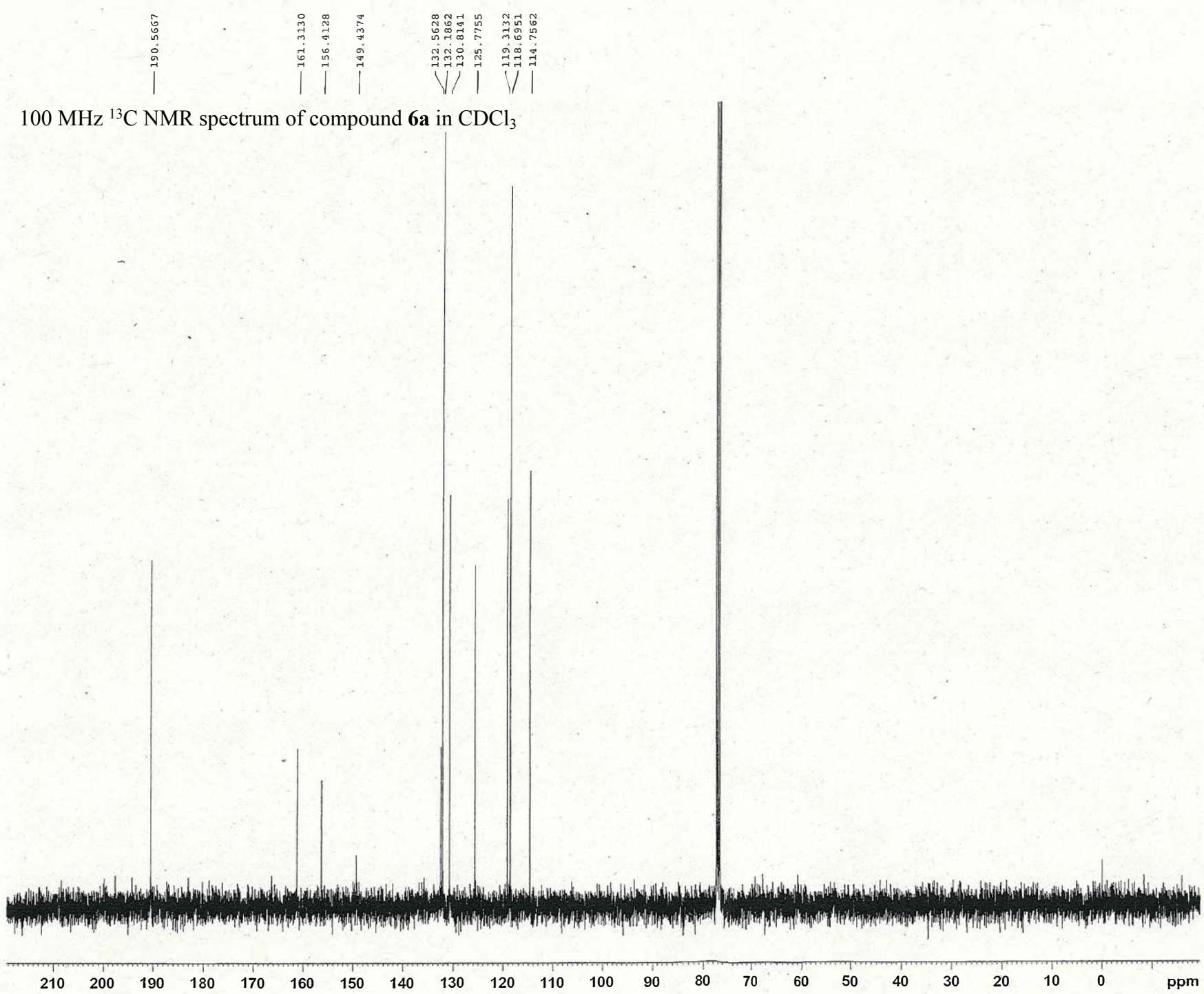


**Supplementary Figure 1.** Validation of docking protocol. (A) The indicated ligands were docked into the original protein crystal structures. The reported binding manners and predicted docking poses were displayed in green and yellow, respectively. (B) The ligands were docked in the crystal structures other than originally reported structural data. The reported binding manners and predicted docking poses were displayed in green and yellow, respectively.

400 MHz  $^1\text{H}$  NMR spectrum of compound **6a** in  $\text{CDCl}_3$

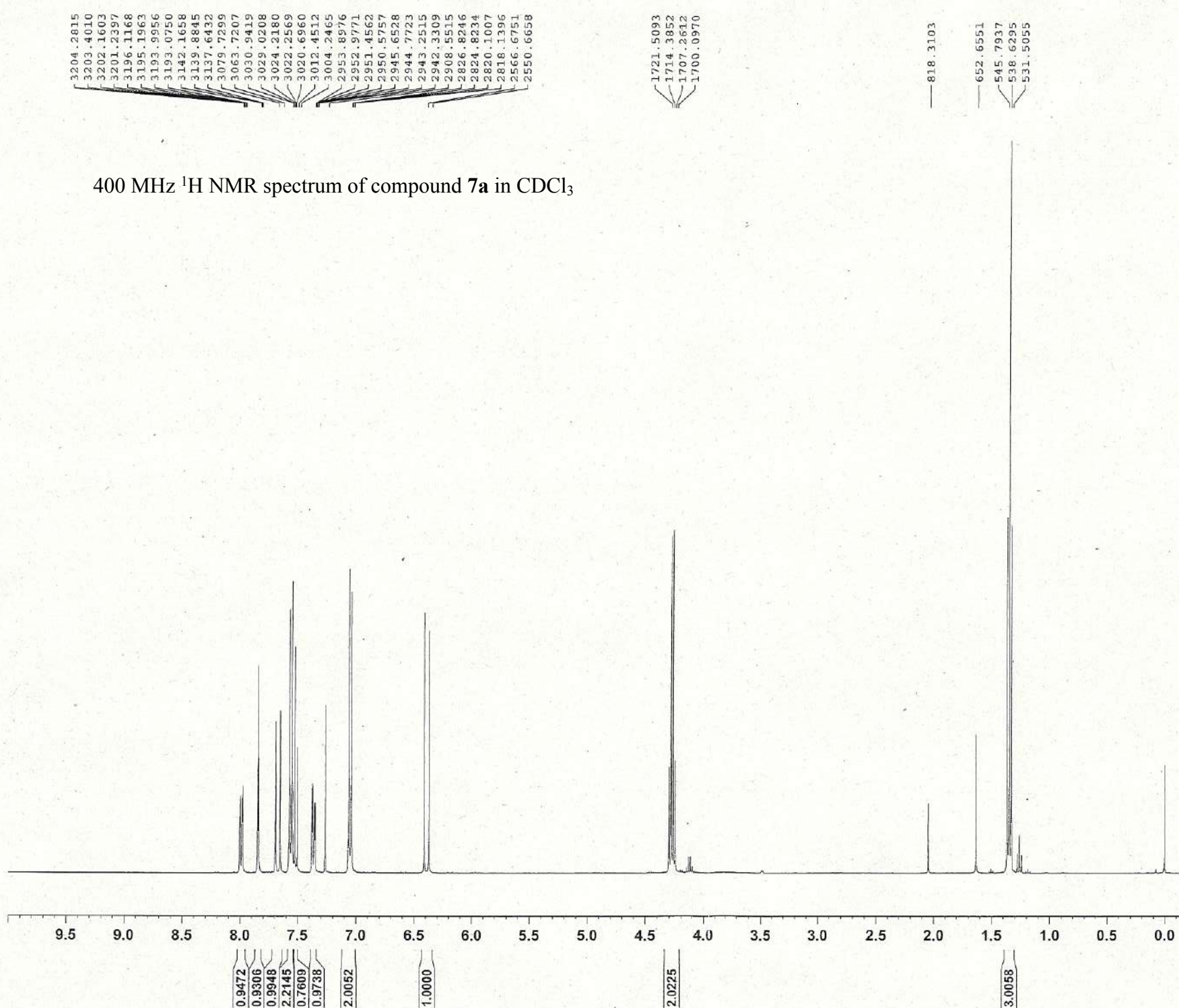


100 MHz  $^{13}\text{C}$  NMR spectrum of compound **6a** in  $\text{CDCl}_3$



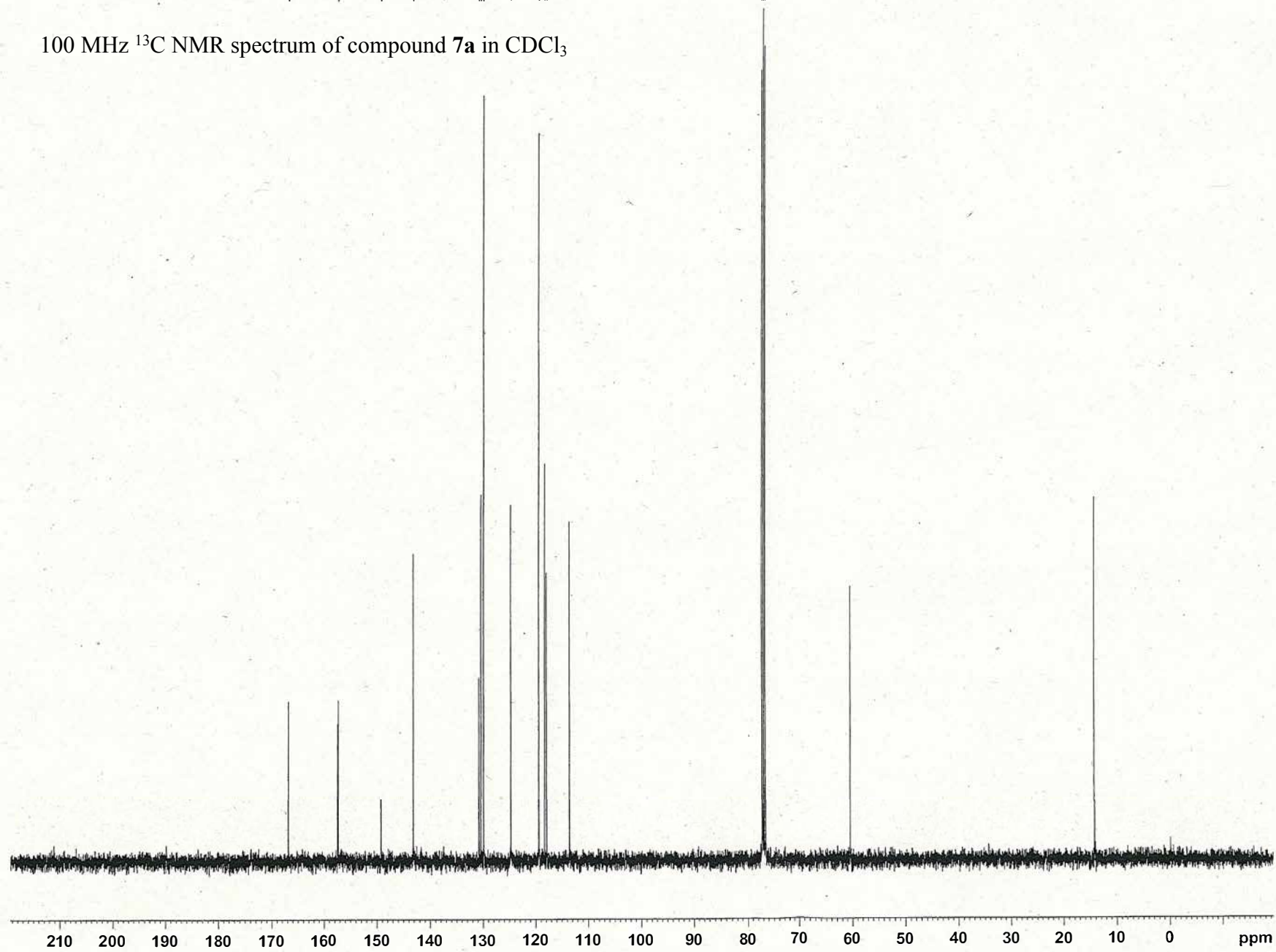


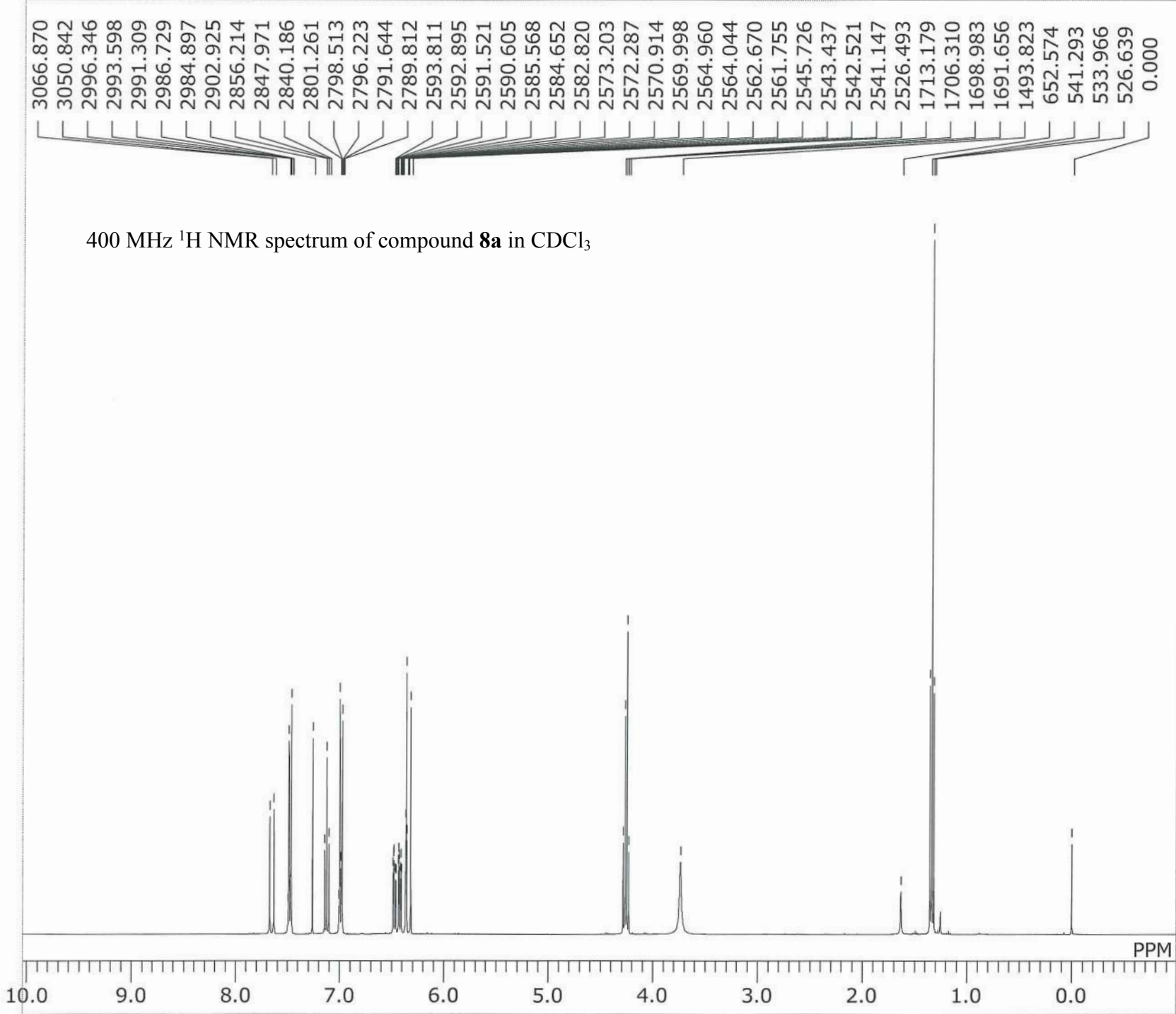
400 MHz  $^1\text{H}$  NMR spectrum of compound **7a** in  $\text{CDCl}_3$



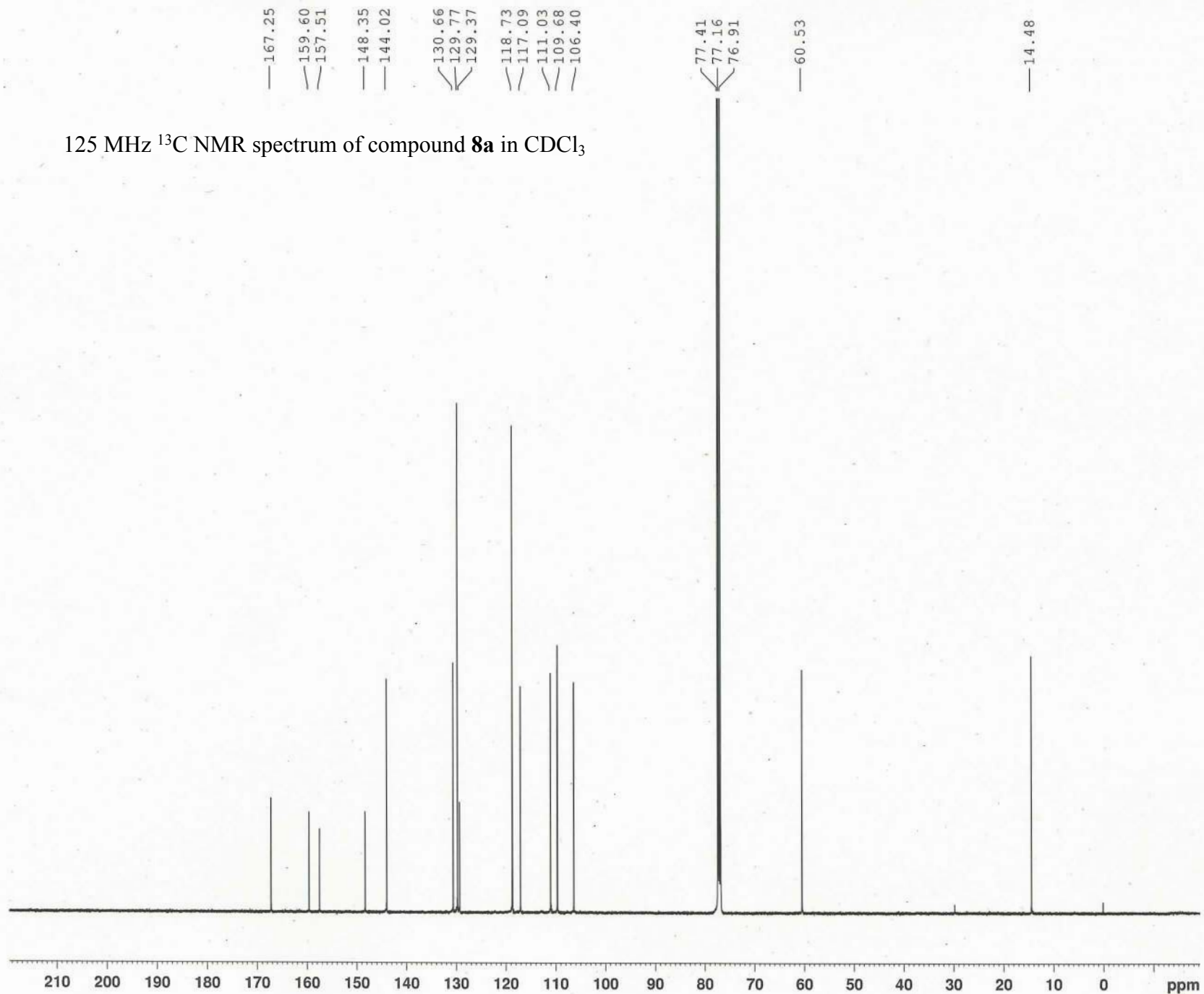
100 MHz  $^{13}\text{C}$  NMR spectrum of compound **7a** in  $\text{CDCl}_3$

166.8641  
157.5110  
157.3894  
149.3266  
143.2559  
130.8916  
130.5049  
129.9948  
124.8190  
119.5061  
118.3677  
118.0275  
113.6421  
77.3174  
77.2025  
76.9997  
76.6818  
60.5288  
14.2964



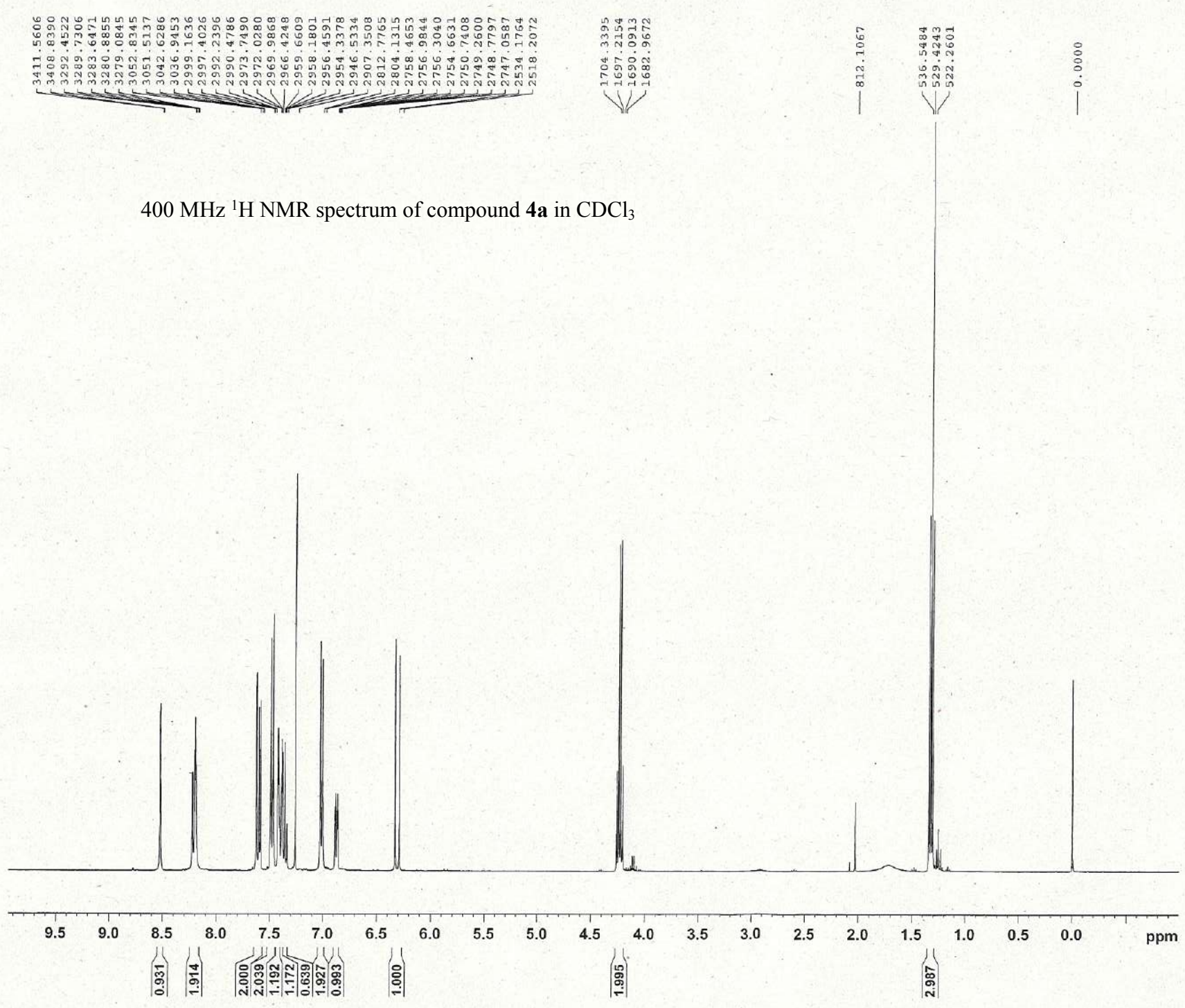


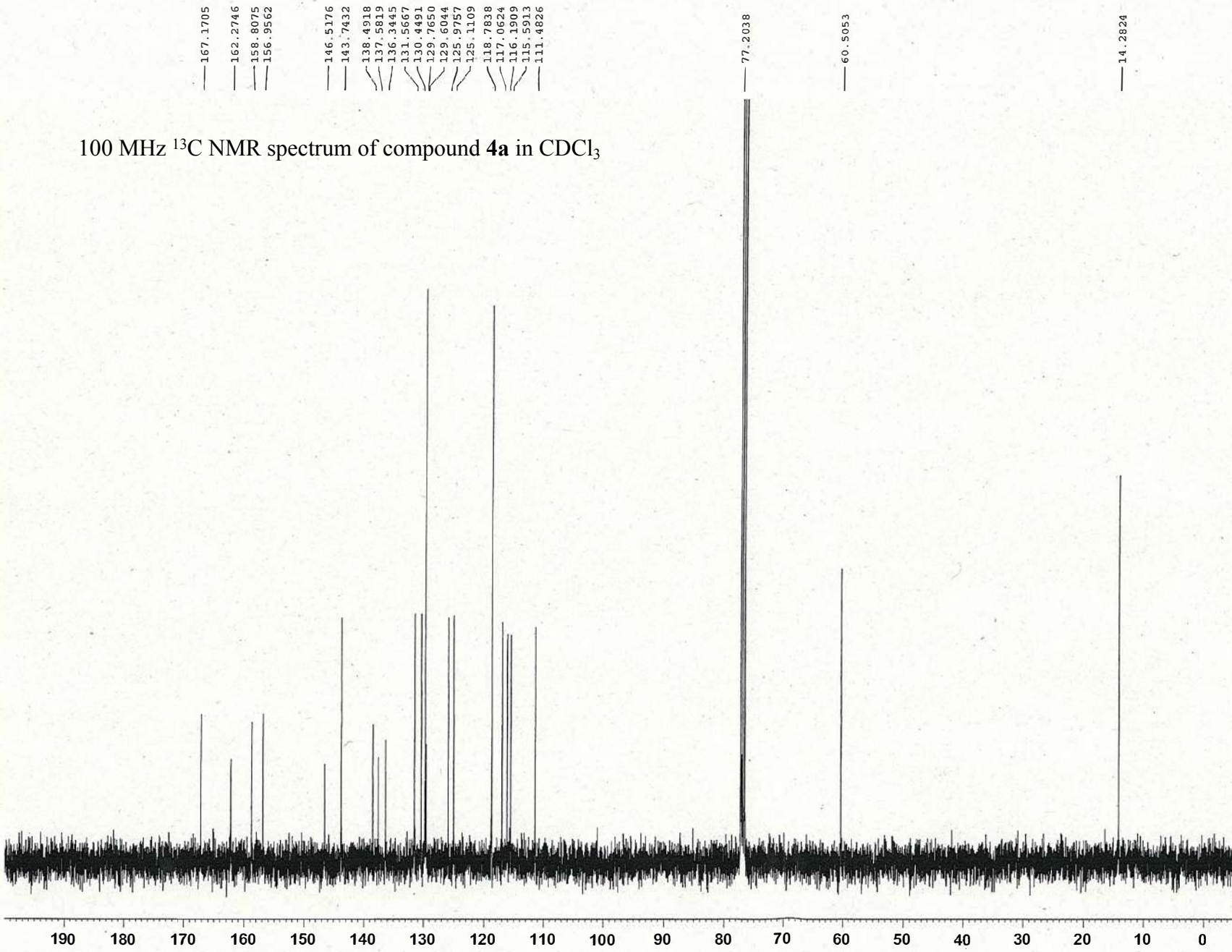
125 MHz  $^{13}\text{C}$  NMR spectrum of compound **8a** in  $\text{CDCl}_3$





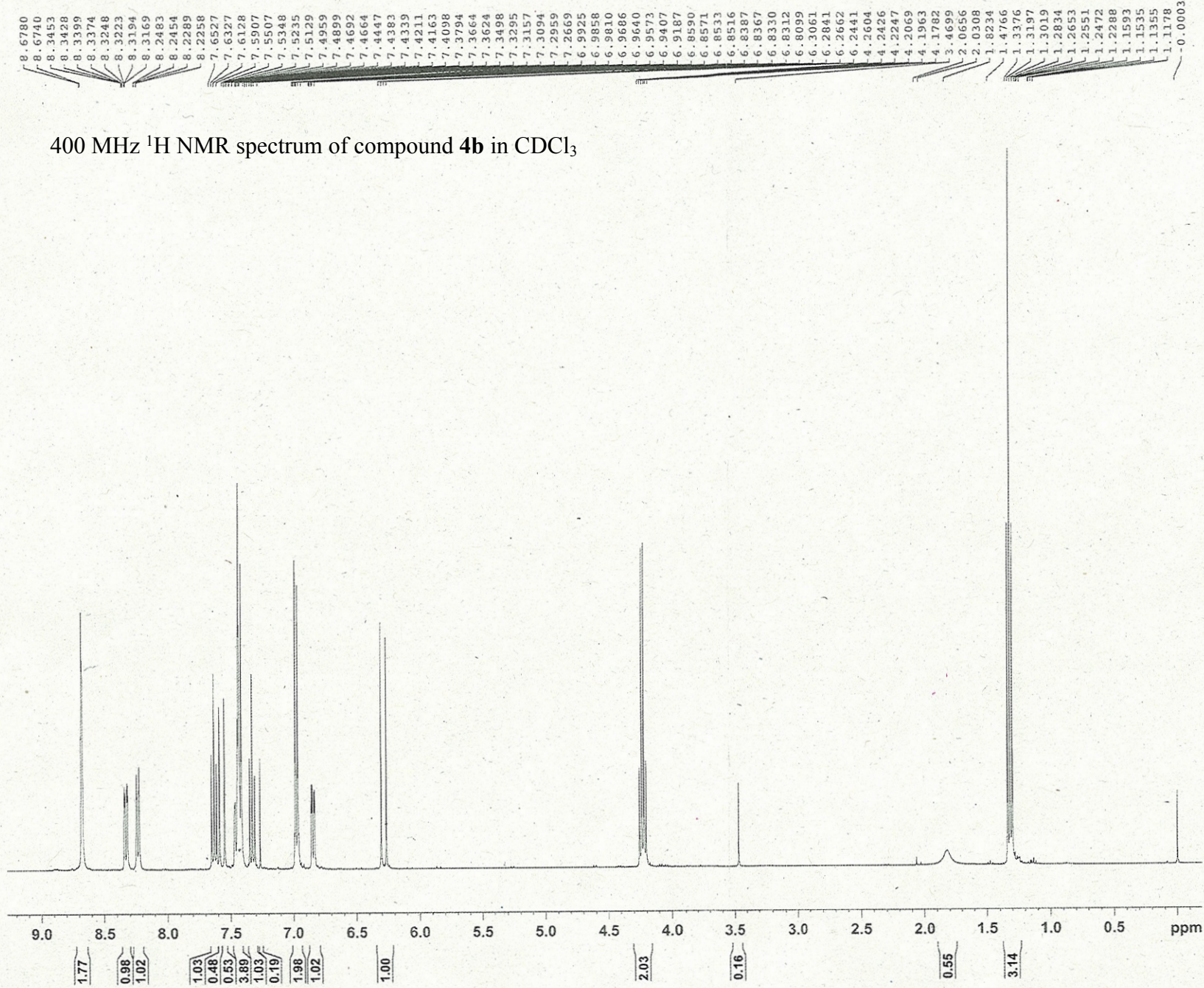
400 MHz  $^1\text{H}$  NMR spectrum of compound **4a** in  $\text{CDCl}_3$



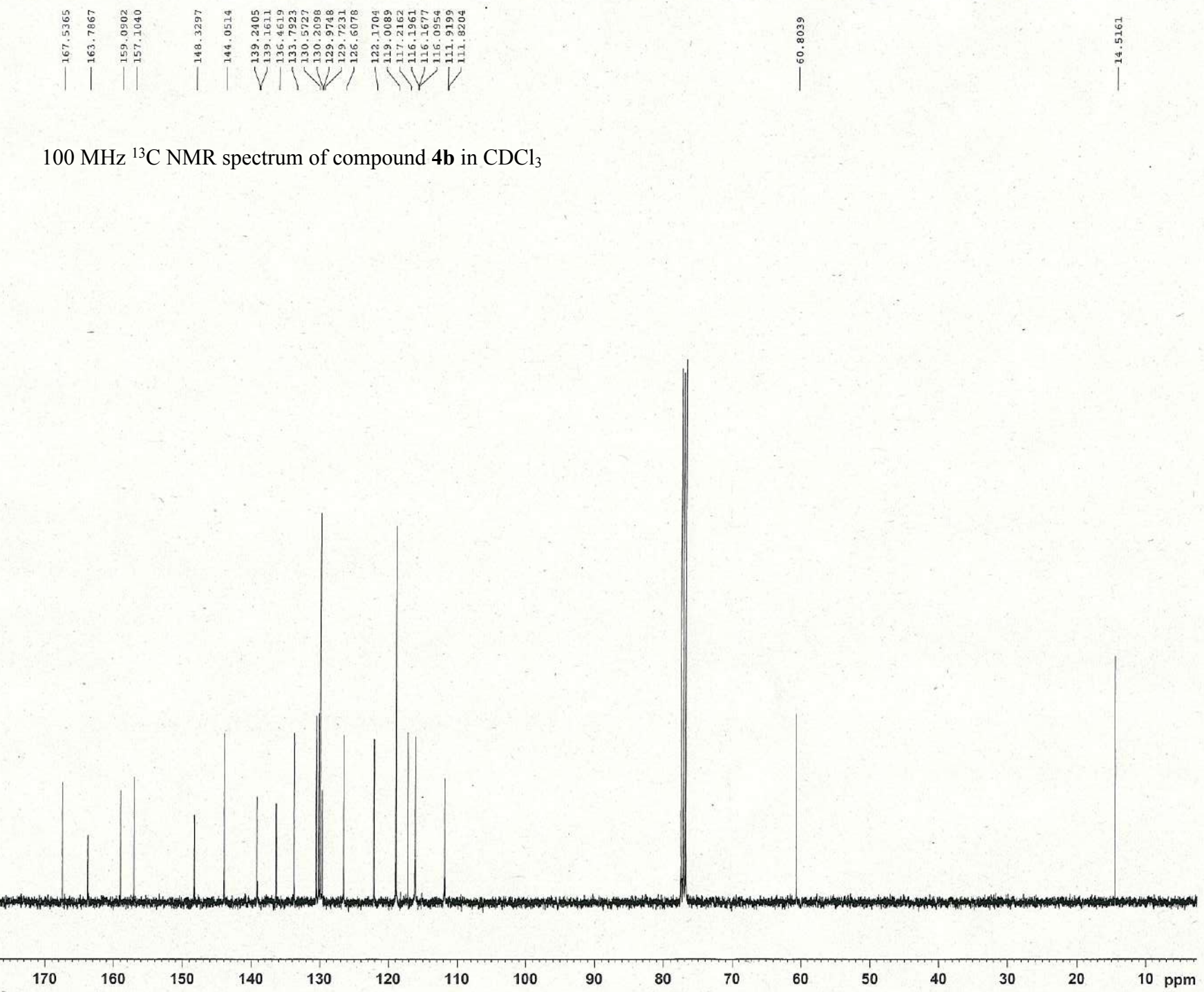




400 MHz  $^1\text{H}$  NMR spectrum of compound **4b** in  $\text{CDCl}_3$

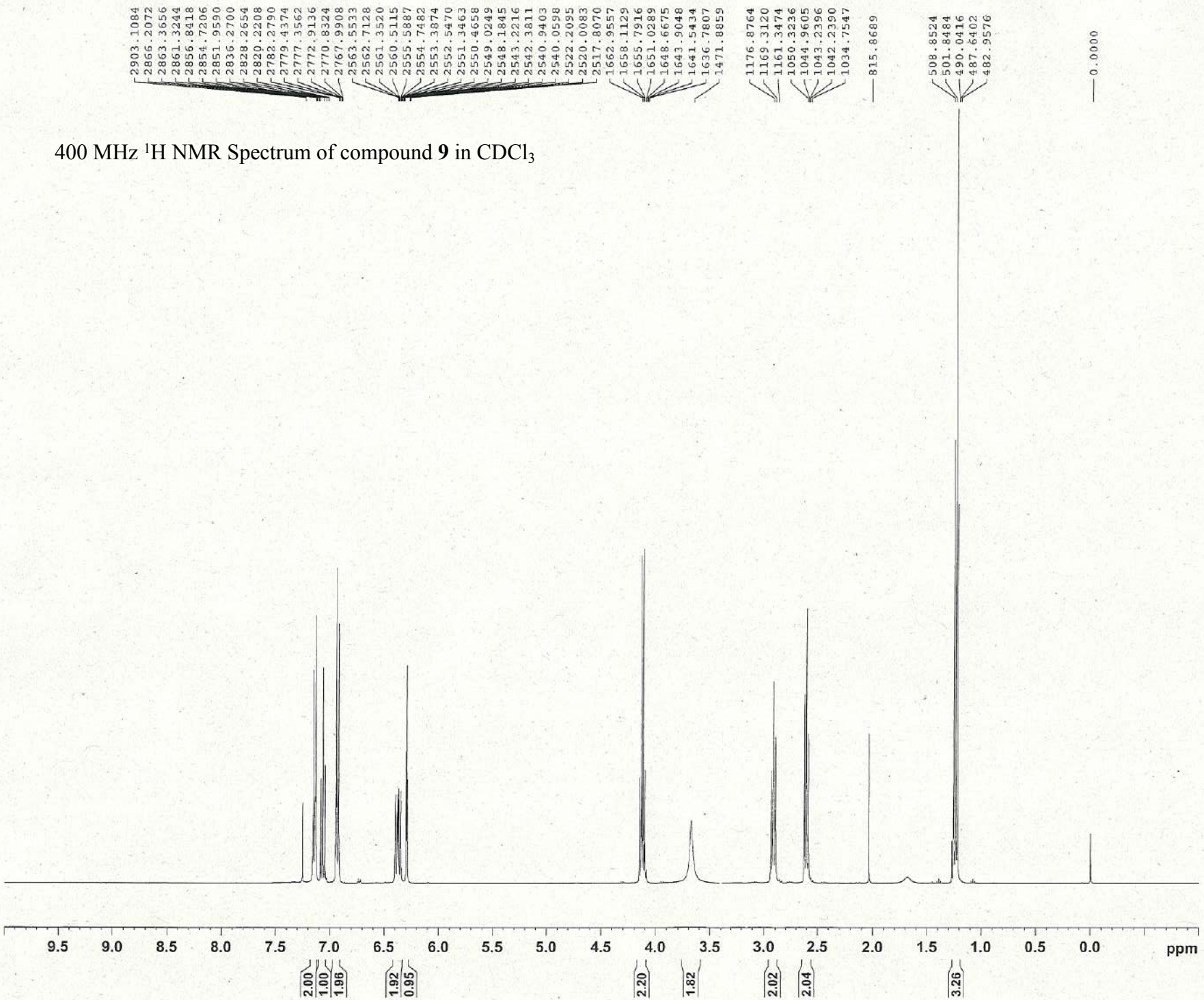


100 MHz  $^{13}\text{C}$  NMR spectrum of compound **4b** in  $\text{CDCl}_3$

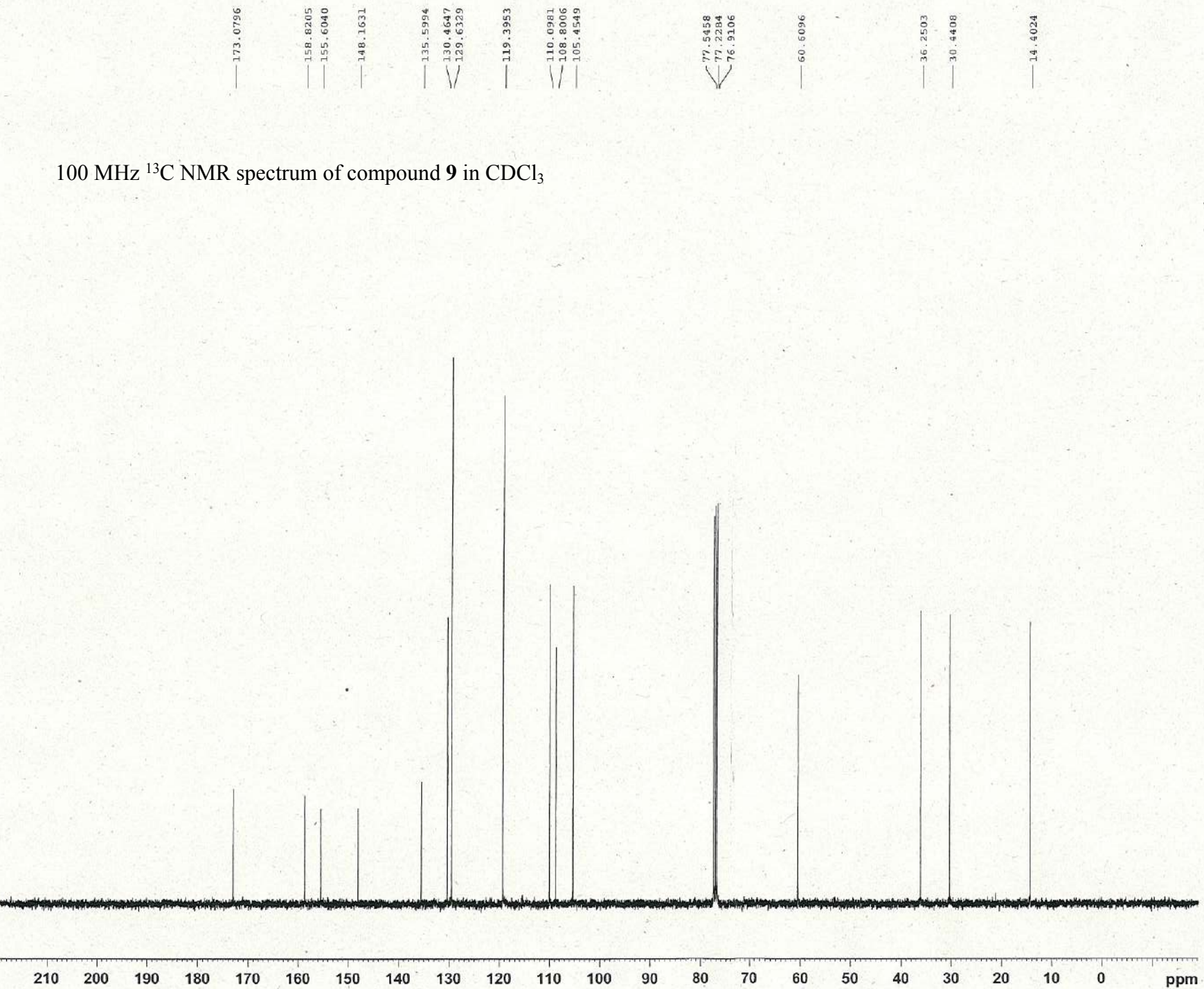




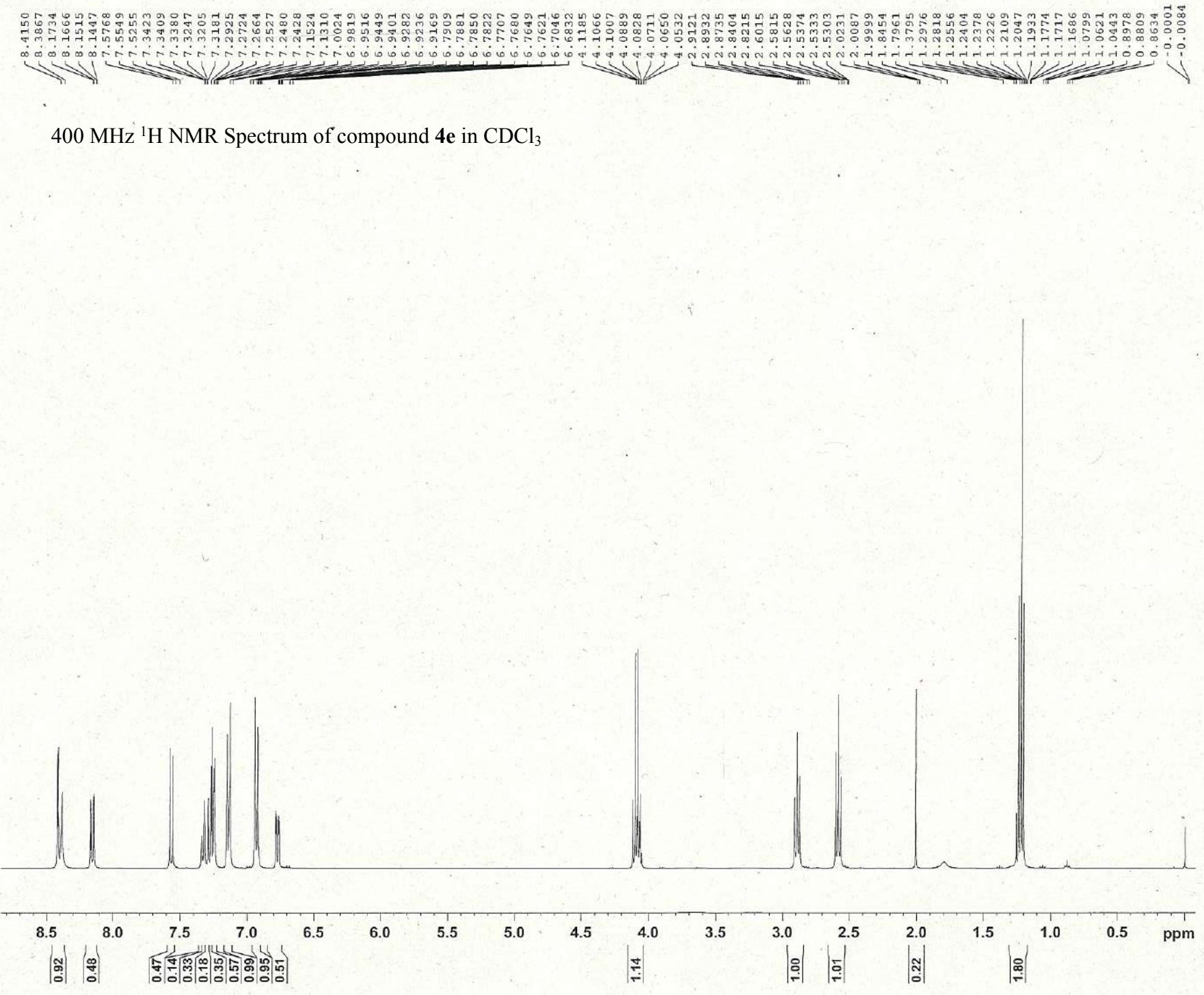
400 MHz  $^1\text{H}$  NMR Spectrum of compound **9** in  $\text{CDCl}_3$



100 MHz  $^{13}\text{C}$  NMR spectrum of compound **9** in  $\text{CDCl}_3$

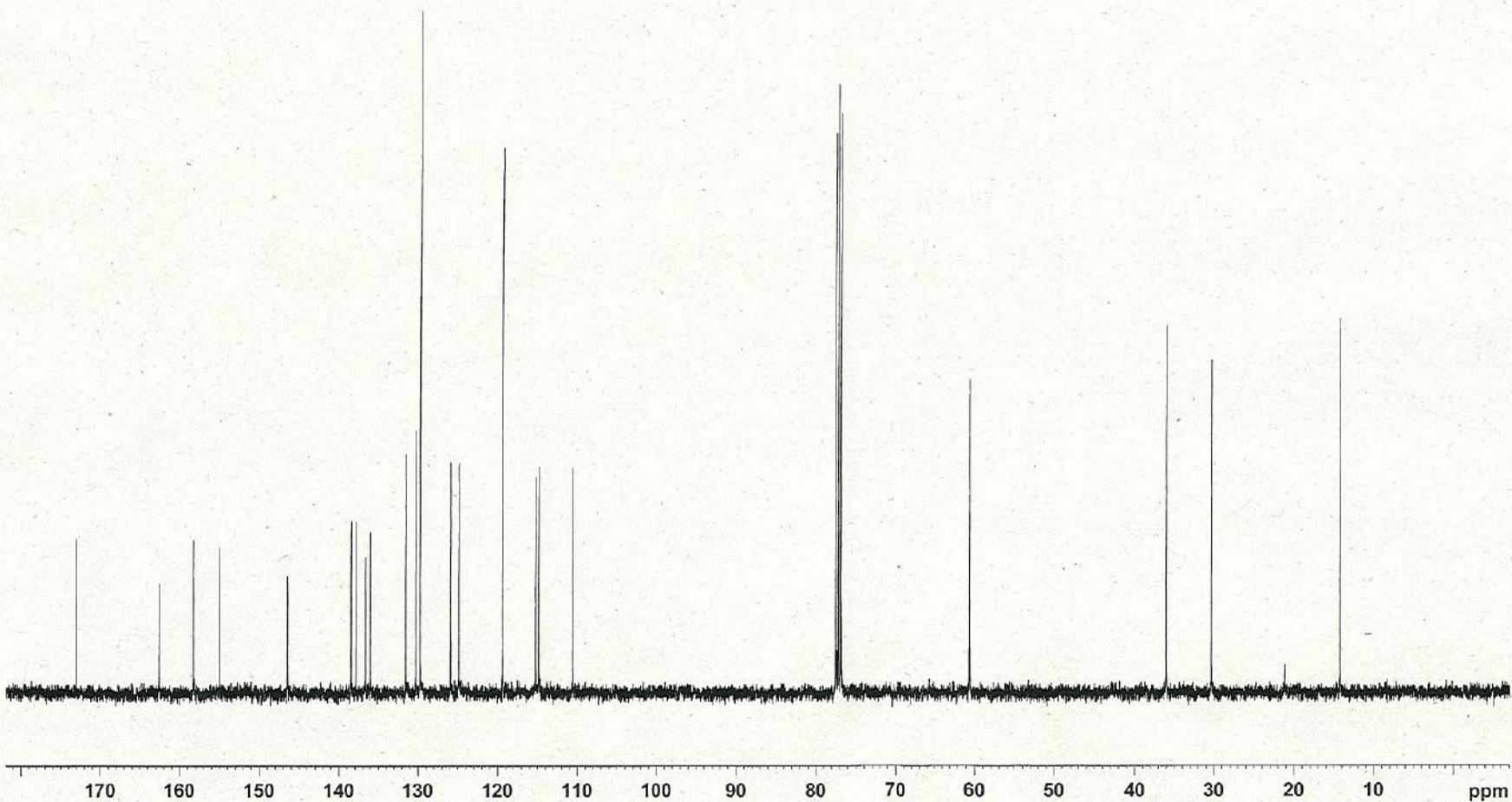






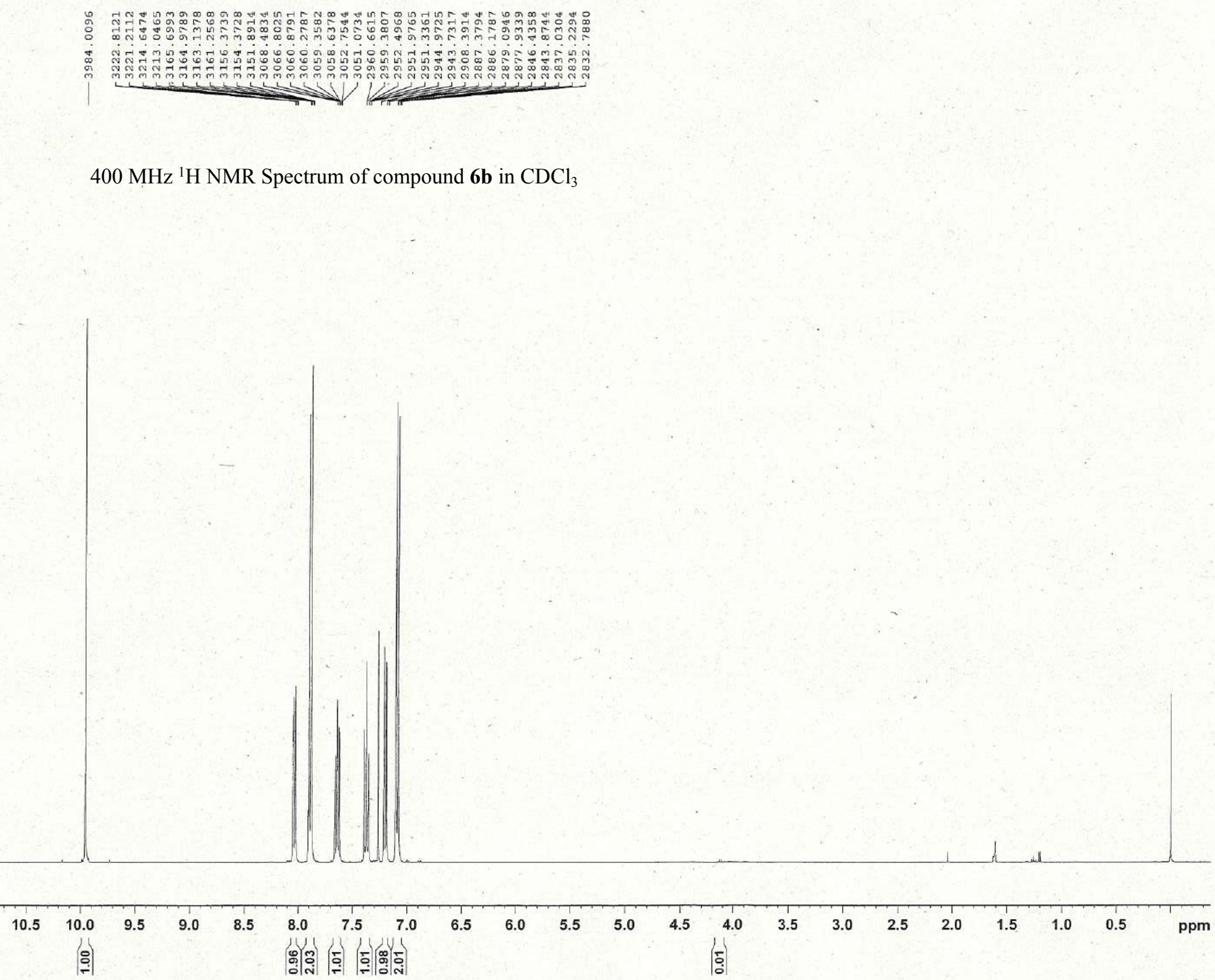
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— 158.3345  
— 155.0887  
— 146.5283  
138.5317  
137.9282  
136.7117  
136.0712  
131.6261  
130.3485  
129.7930  
125.9727  
124.9698  
— 119.4735  
115.3255  
114.9302  
— 110.6847  
77.5461  
77.4298  
77.2282  
76.9101  
60.6677  
60.6106  
— 36.1008  
— 30.3588  
— 21.1802  
— 14.3507

100 MHz  $^{13}\text{C}$  NMR spectrum of compound **4e** in  $\text{CDCl}_3$

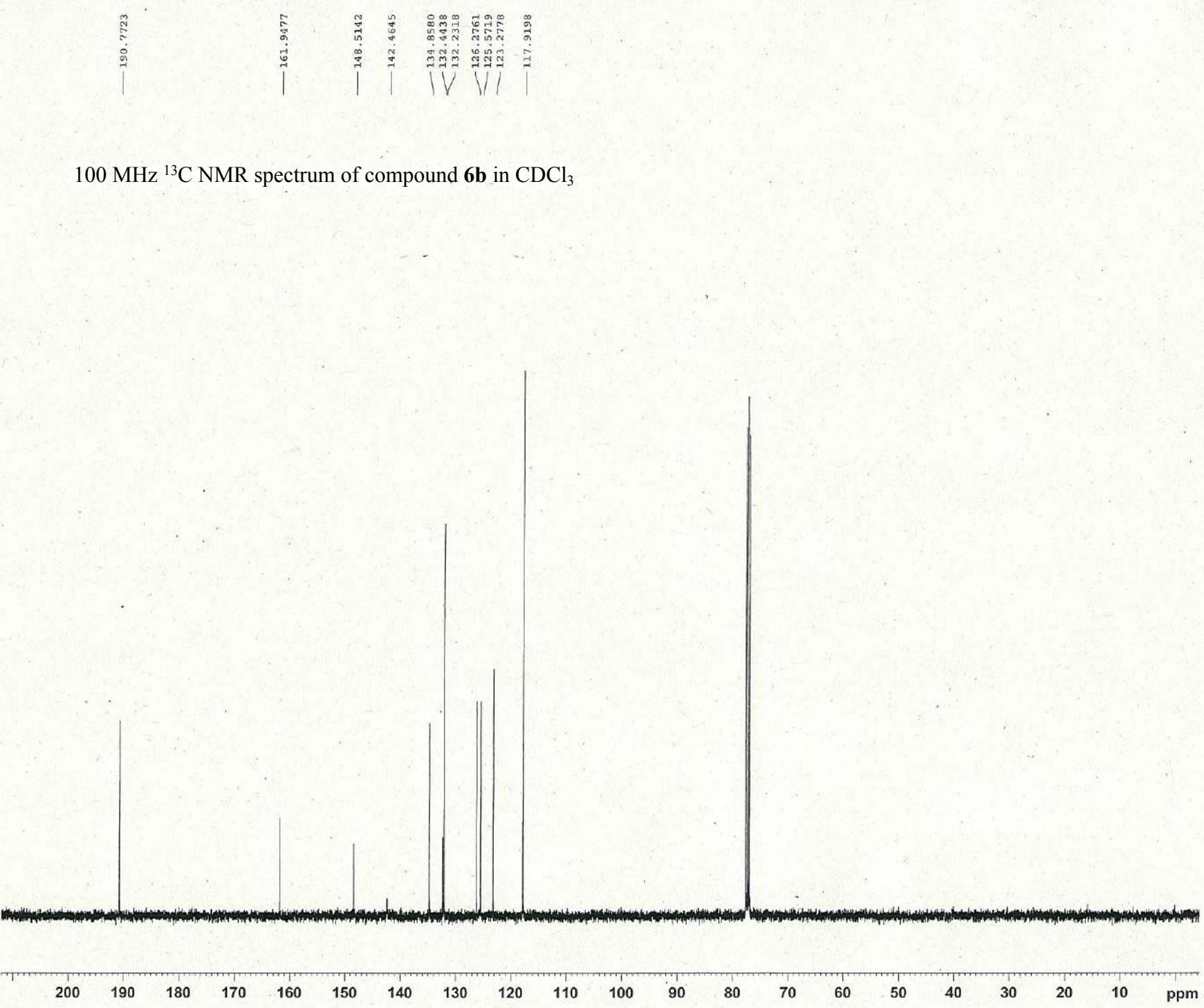




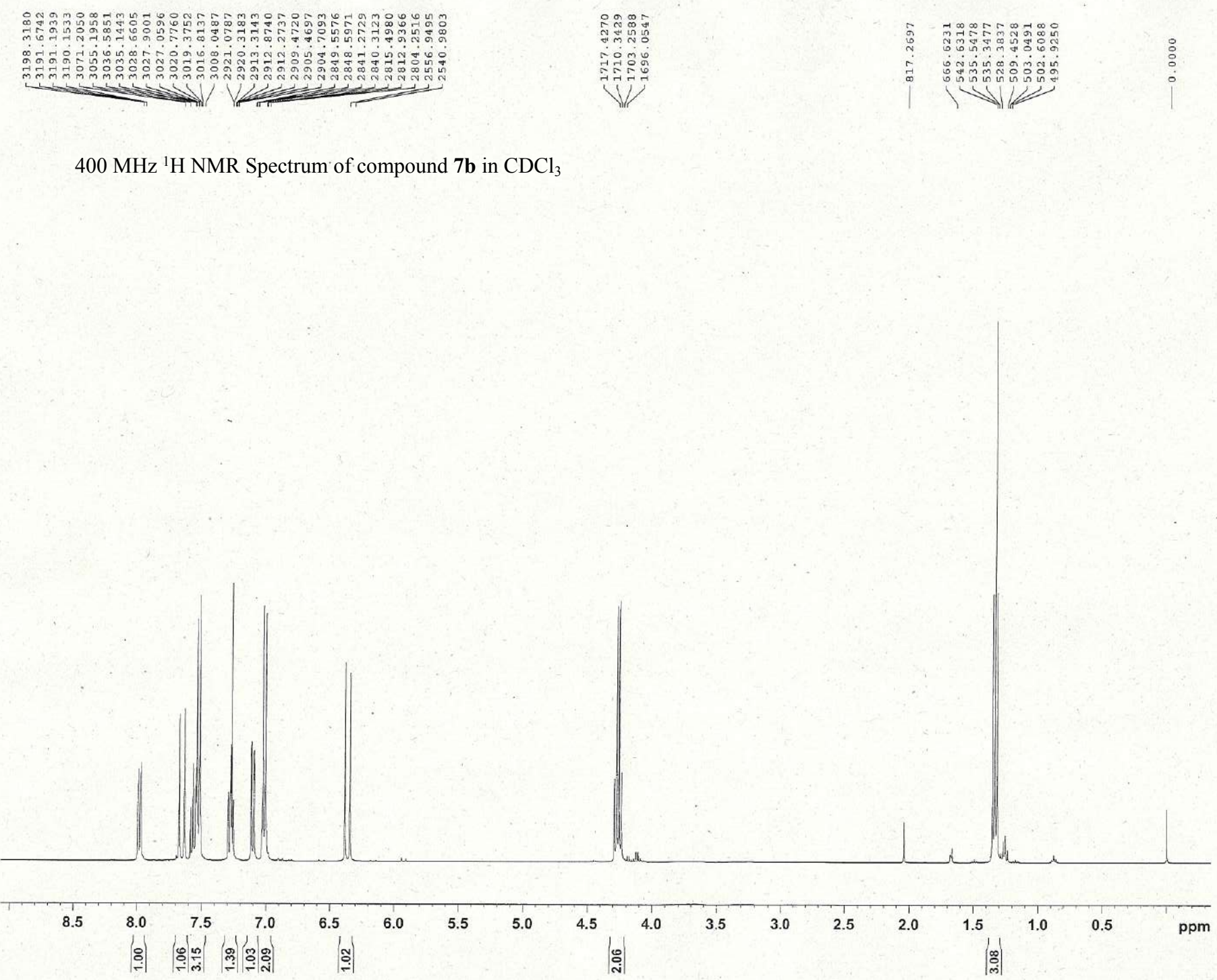
400 MHz  $^1\text{H}$  NMR Spectrum of compound **6b** in  $\text{CDCl}_3$



100 MHz  $^{13}\text{C}$  NMR spectrum of compound **6b** in  $\text{CDCl}_3$

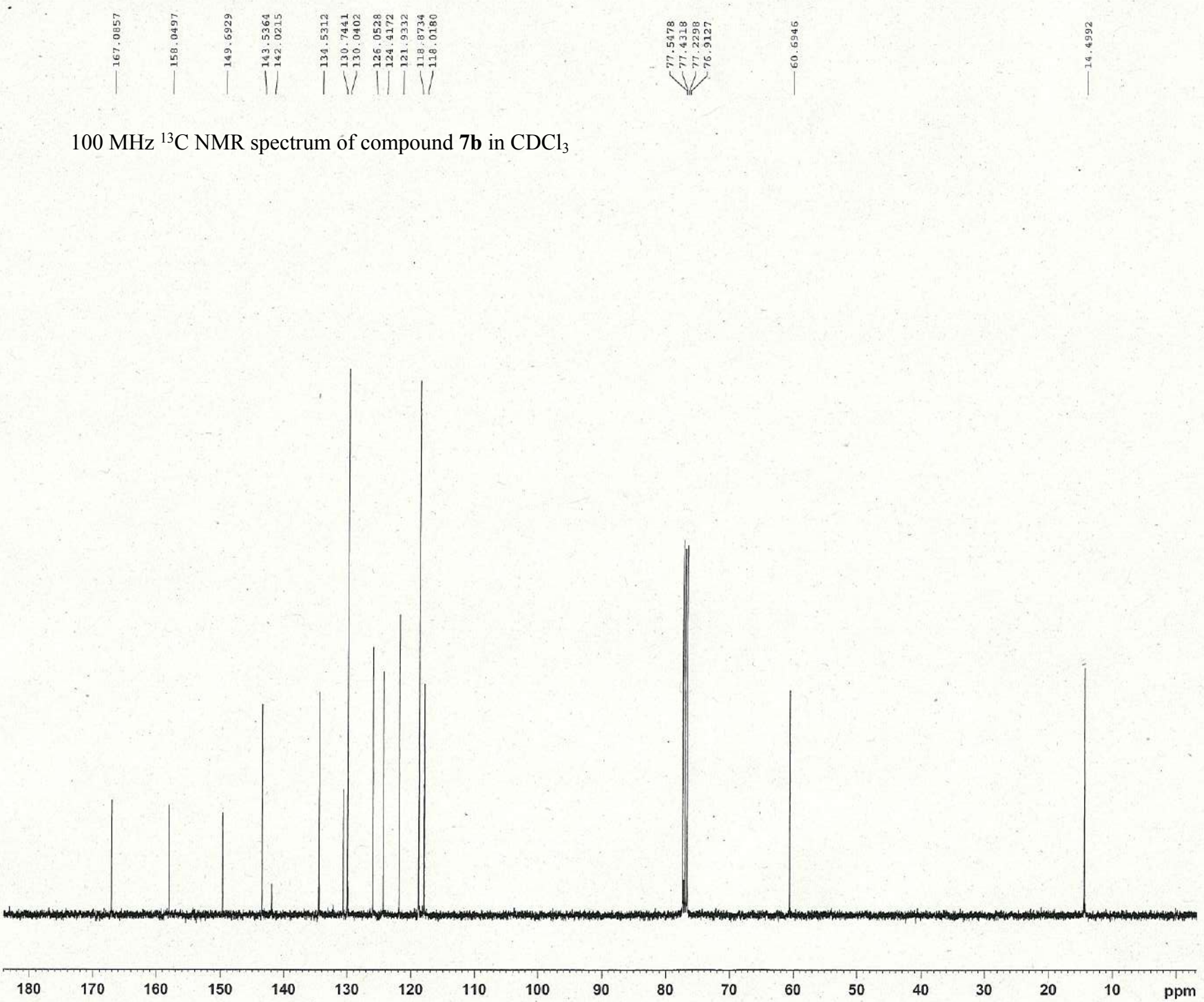


400 MHz  $^1\text{H}$  NMR Spectrum of compound **7b** in  $\text{CDCl}_3$



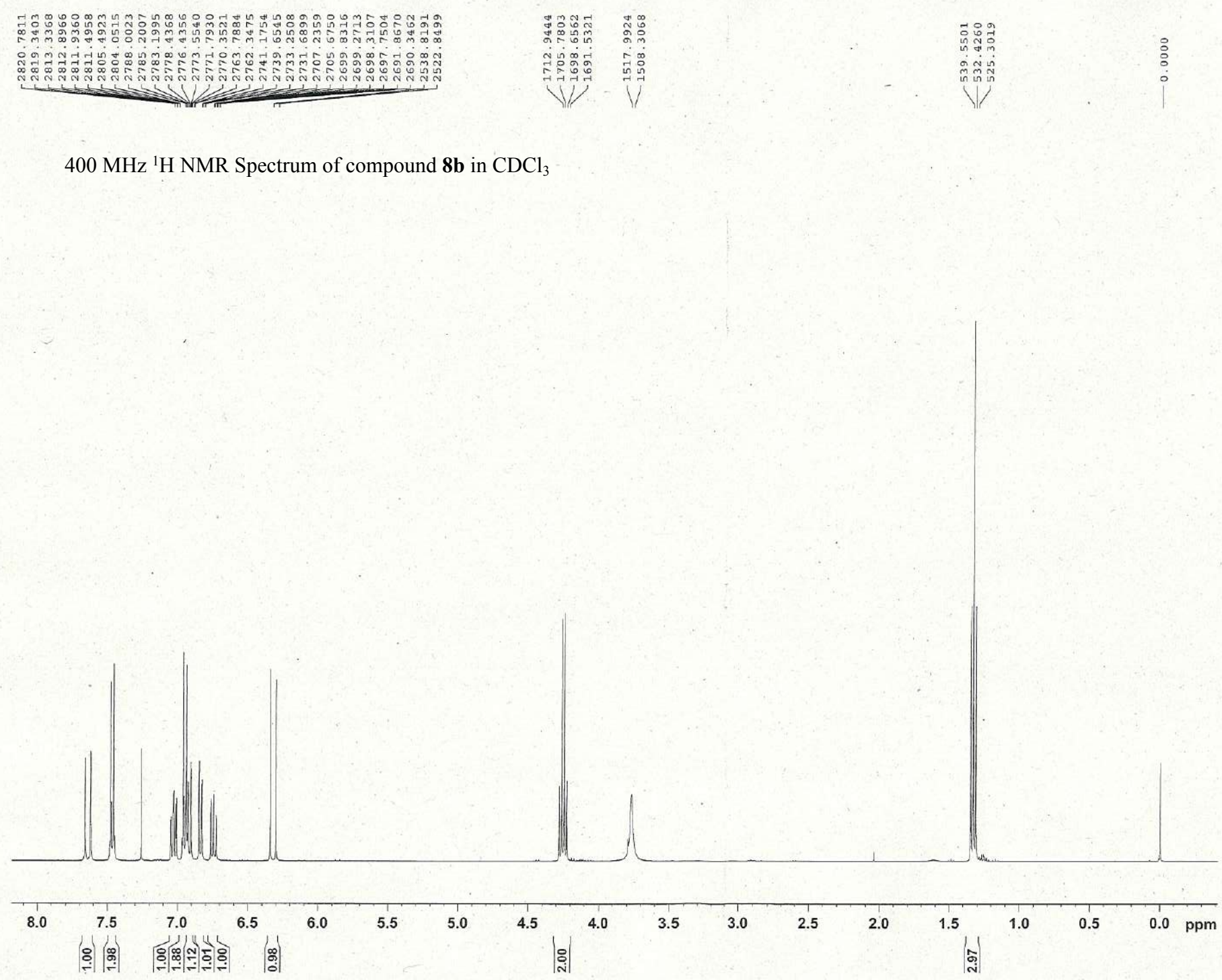


100 MHz  $^{13}\text{C}$  NMR spectrum of compound **7b** in  $\text{CDCl}_3$

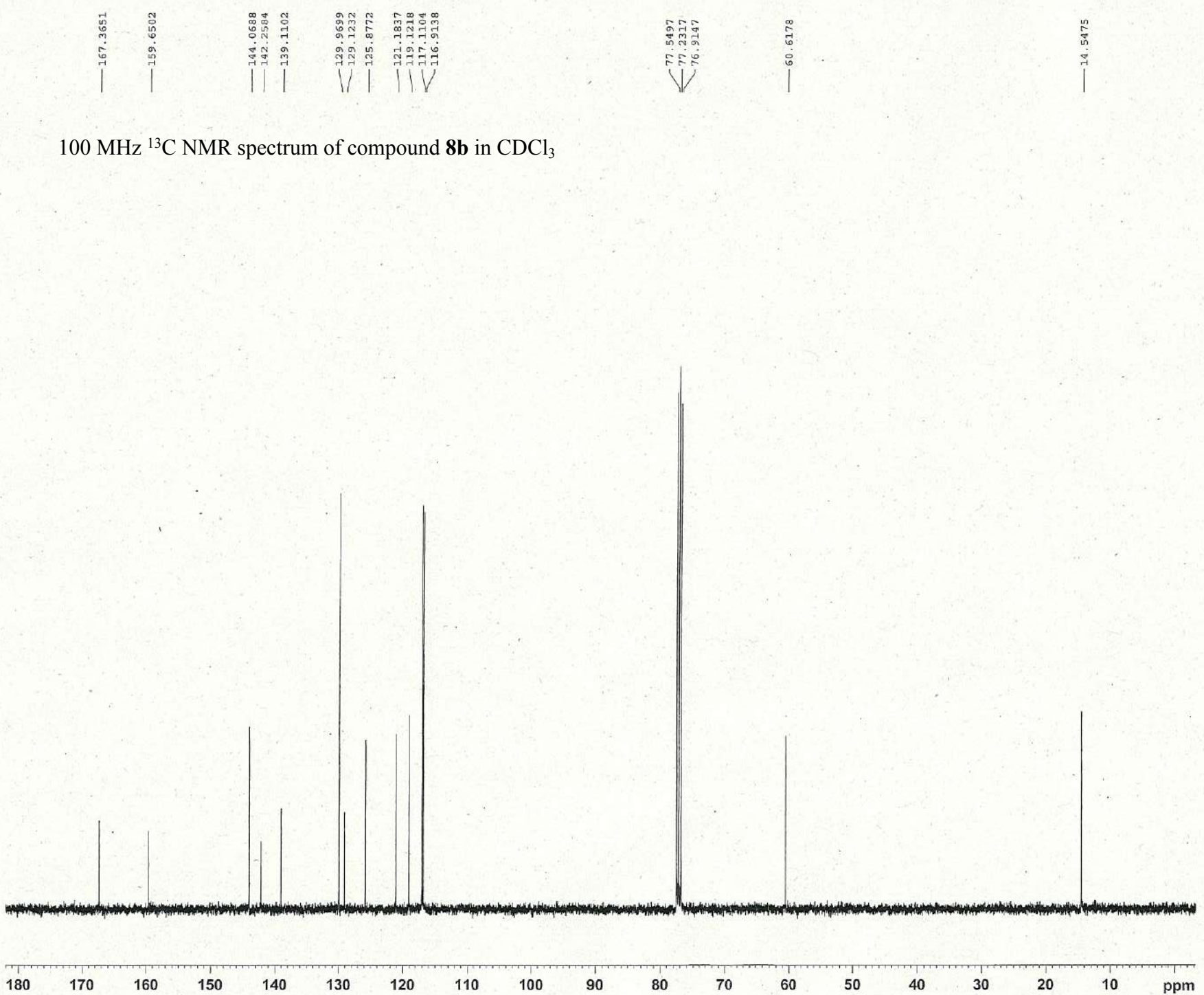


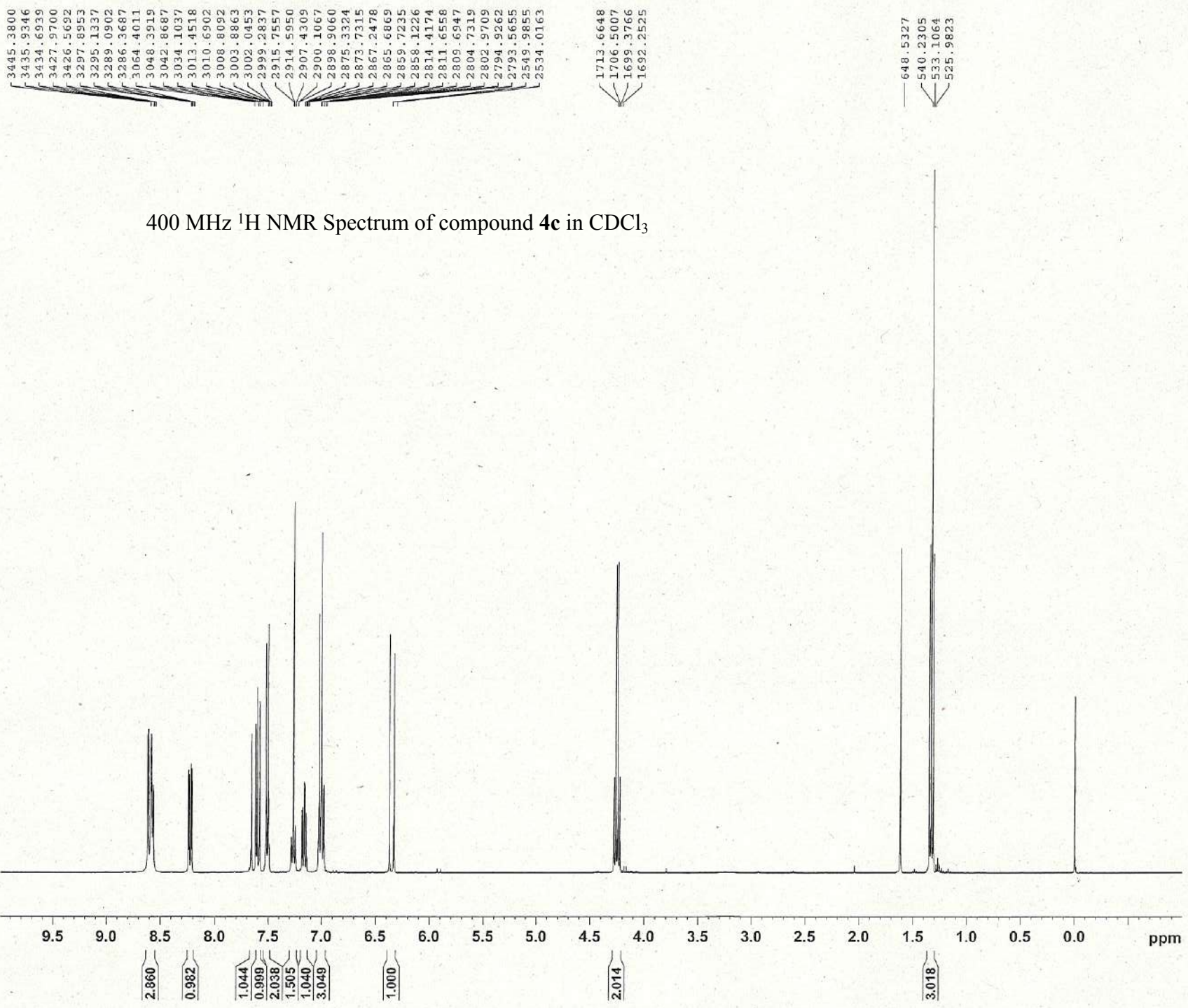


400 MHz  $^1\text{H}$  NMR Spectrum of compound **8b** in  $\text{CDCl}_3$



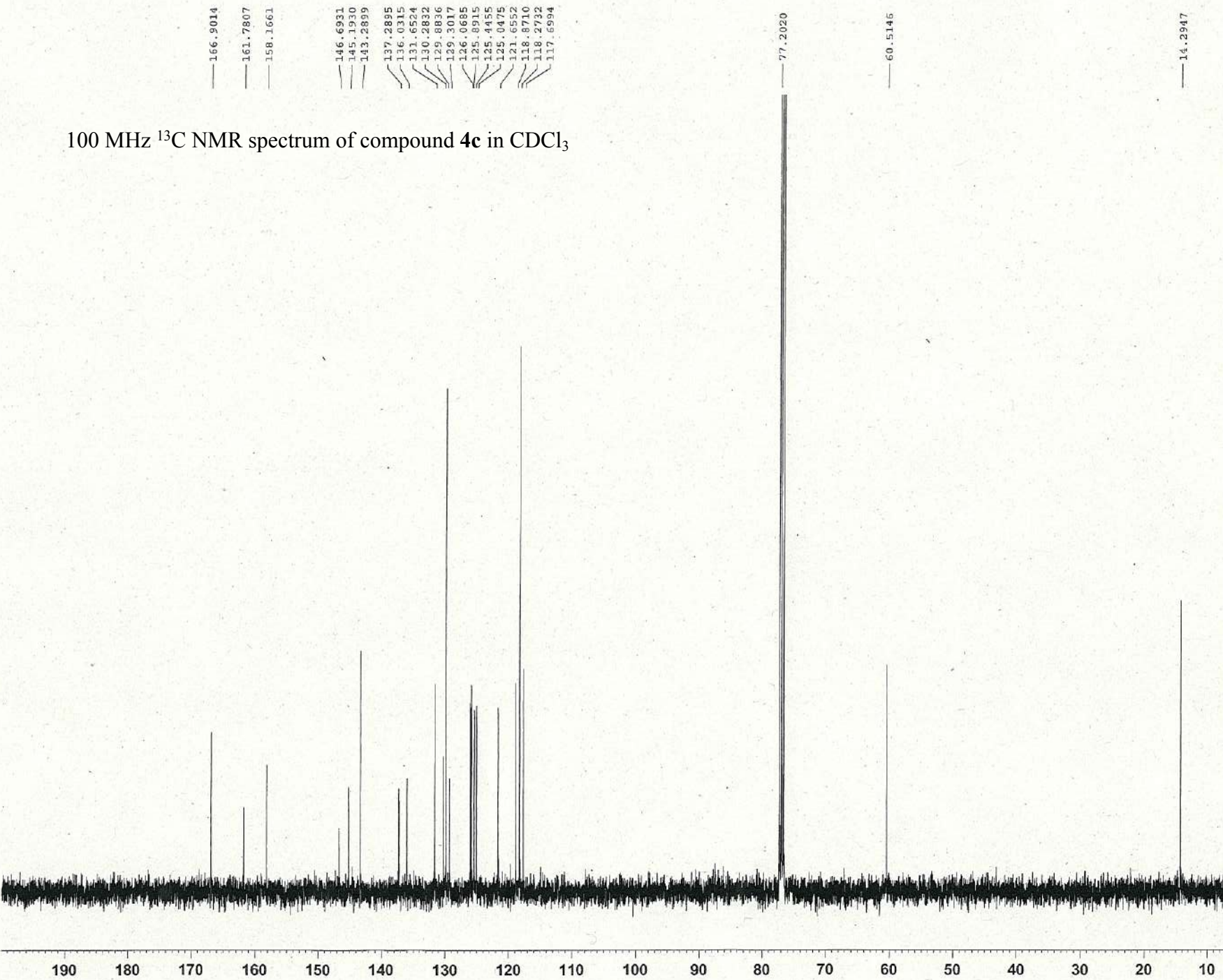
100 MHz  $^{13}\text{C}$  NMR spectrum of compound **8b** in  $\text{CDCl}_3$





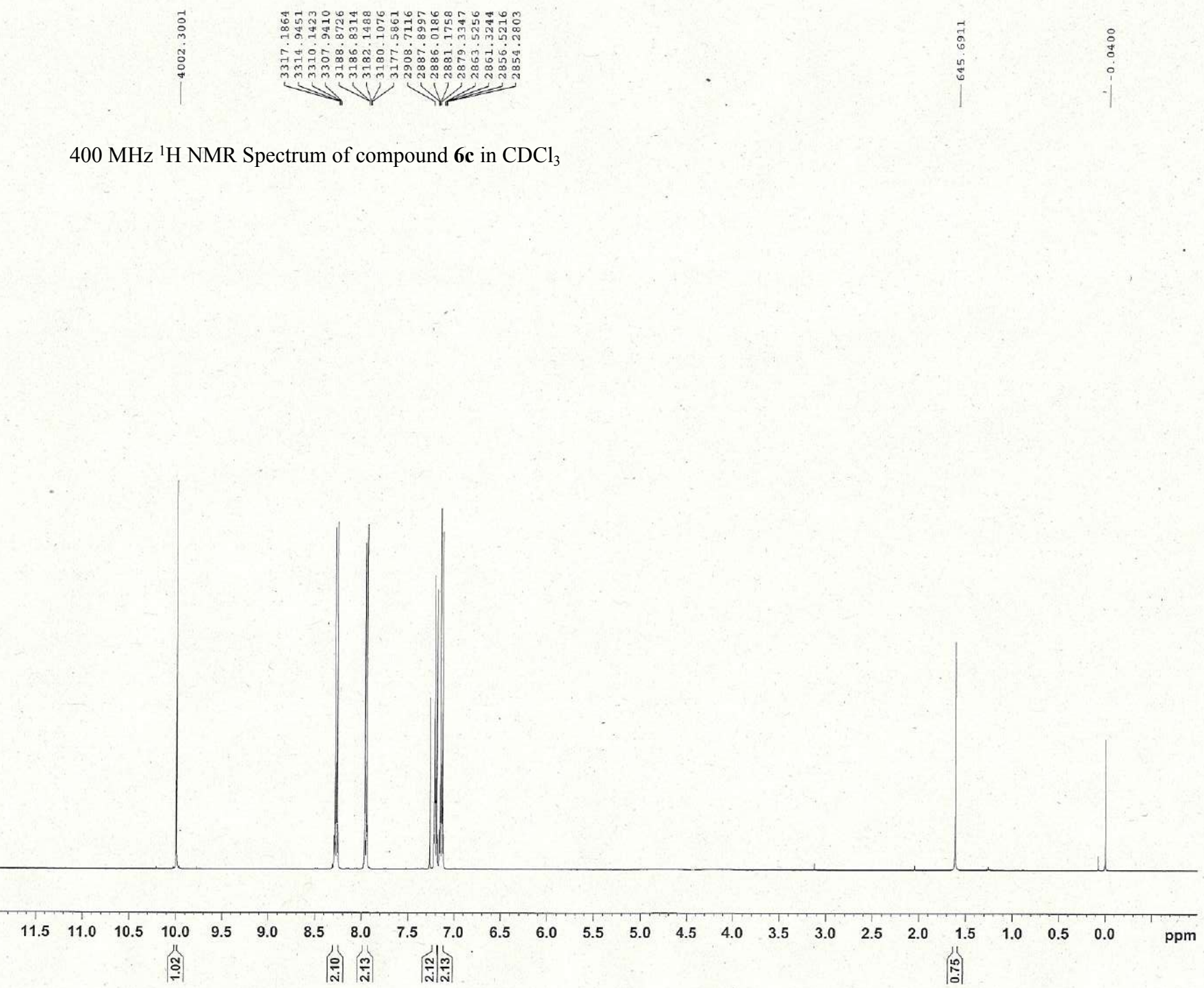


100 MHz  $^{13}\text{C}$  NMR spectrum of compound **4c** in  $\text{CDCl}_3$

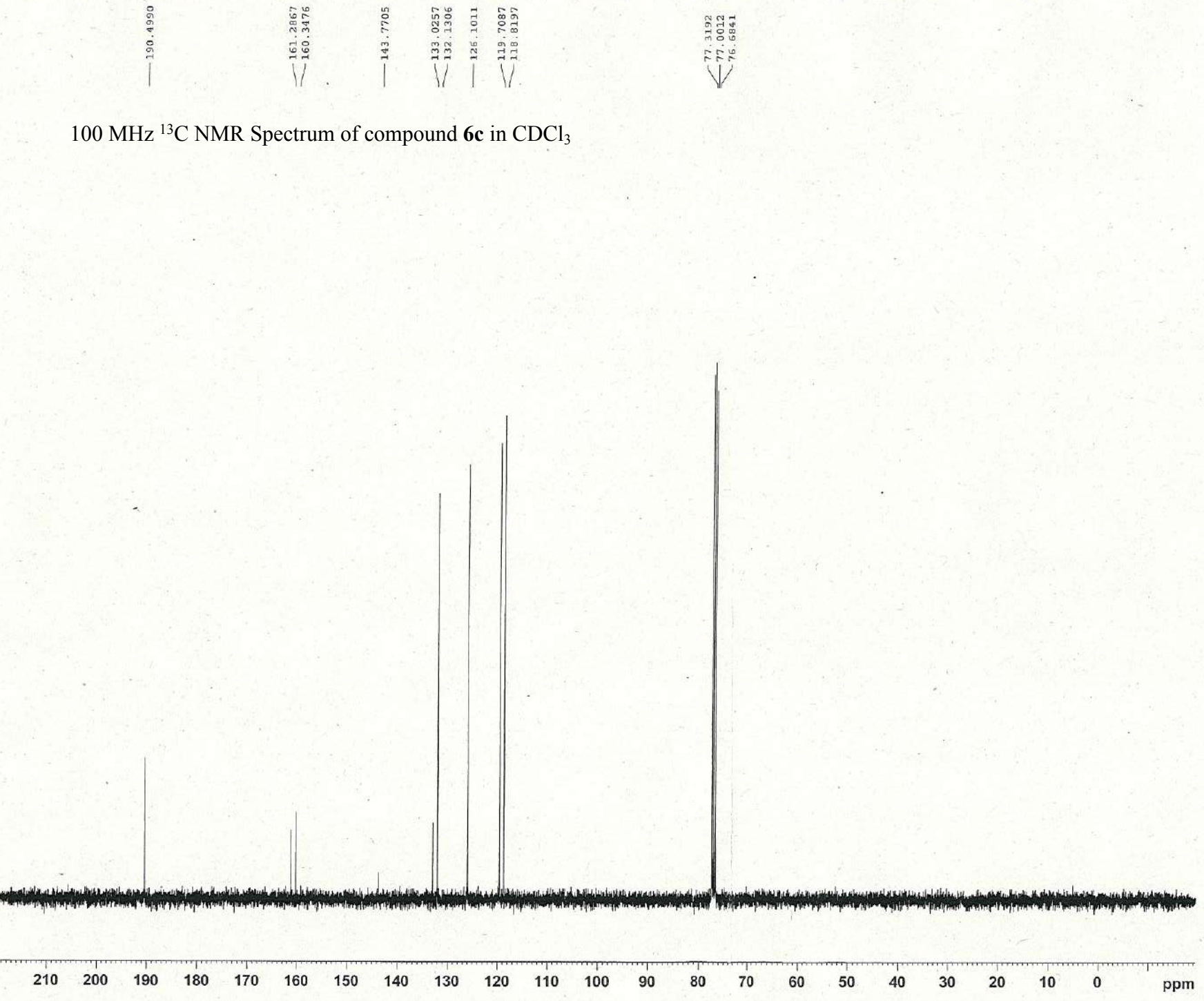




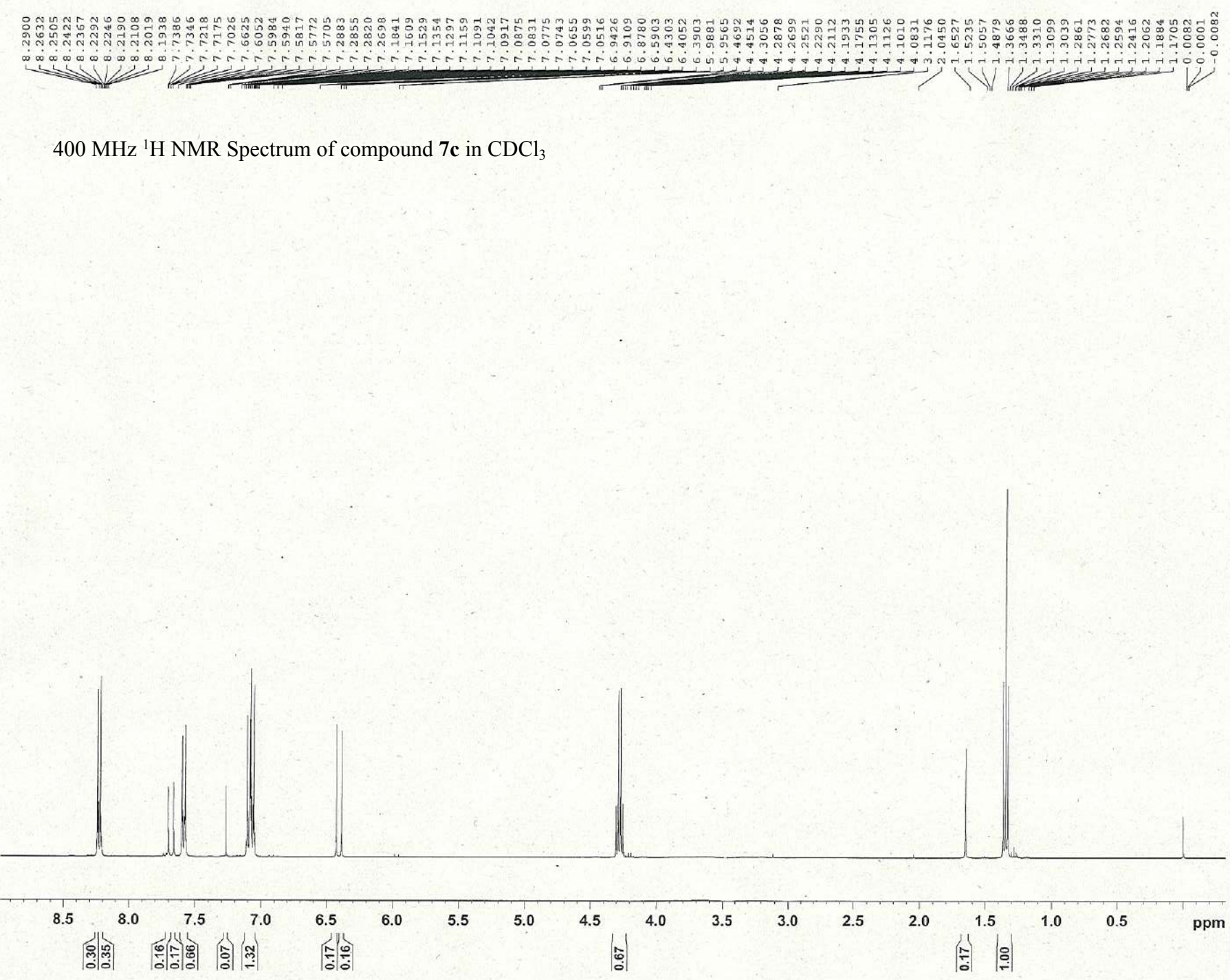
400 MHz  $^1\text{H}$  NMR Spectrum of compound **6c** in  $\text{CDCl}_3$



100 MHz  $^{13}\text{C}$  NMR Spectrum of compound **6c** in  $\text{CDCl}_3$

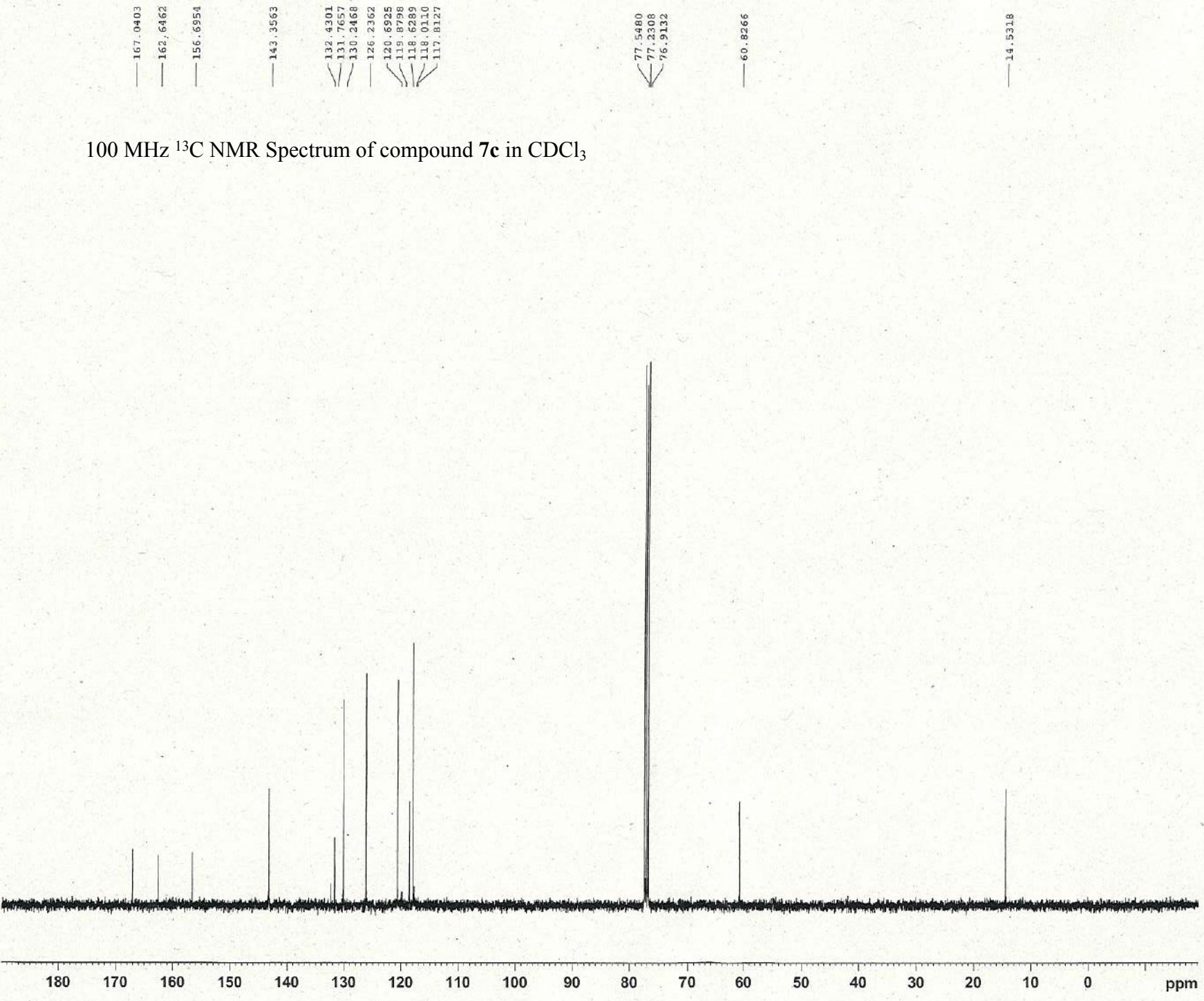


400 MHz  $^1\text{H}$  NMR Spectrum of compound **7c** in  $\text{CDCl}_3$

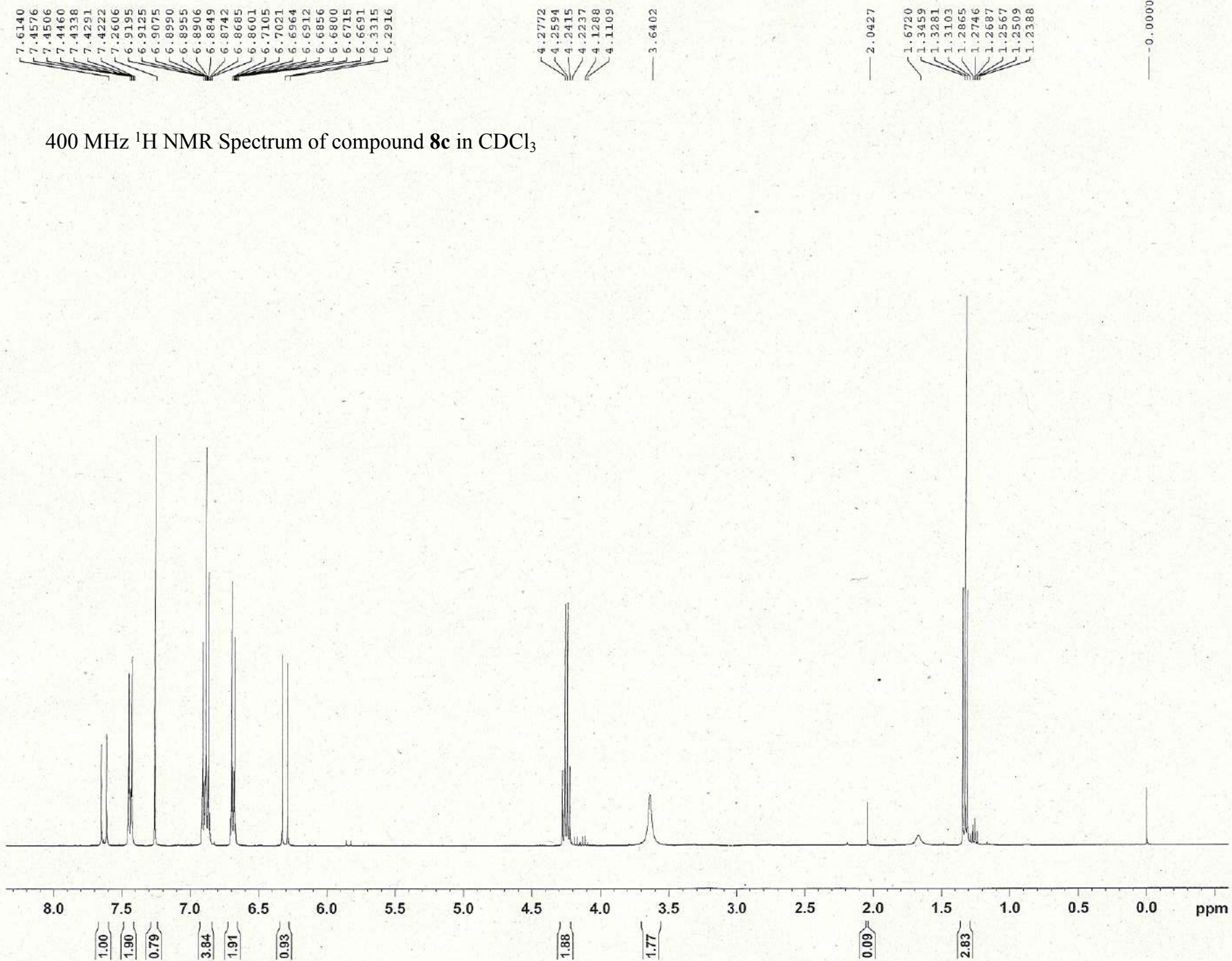




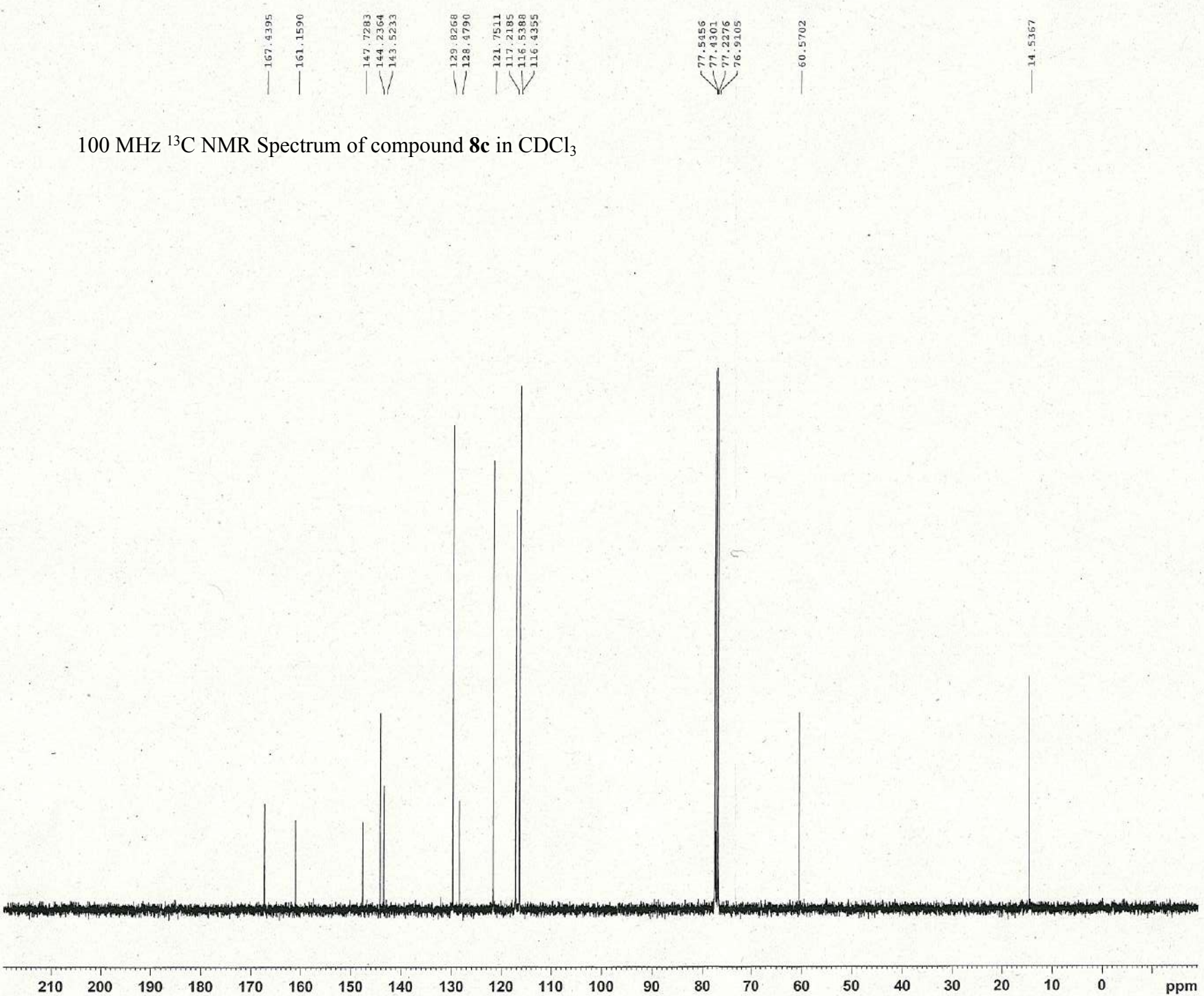
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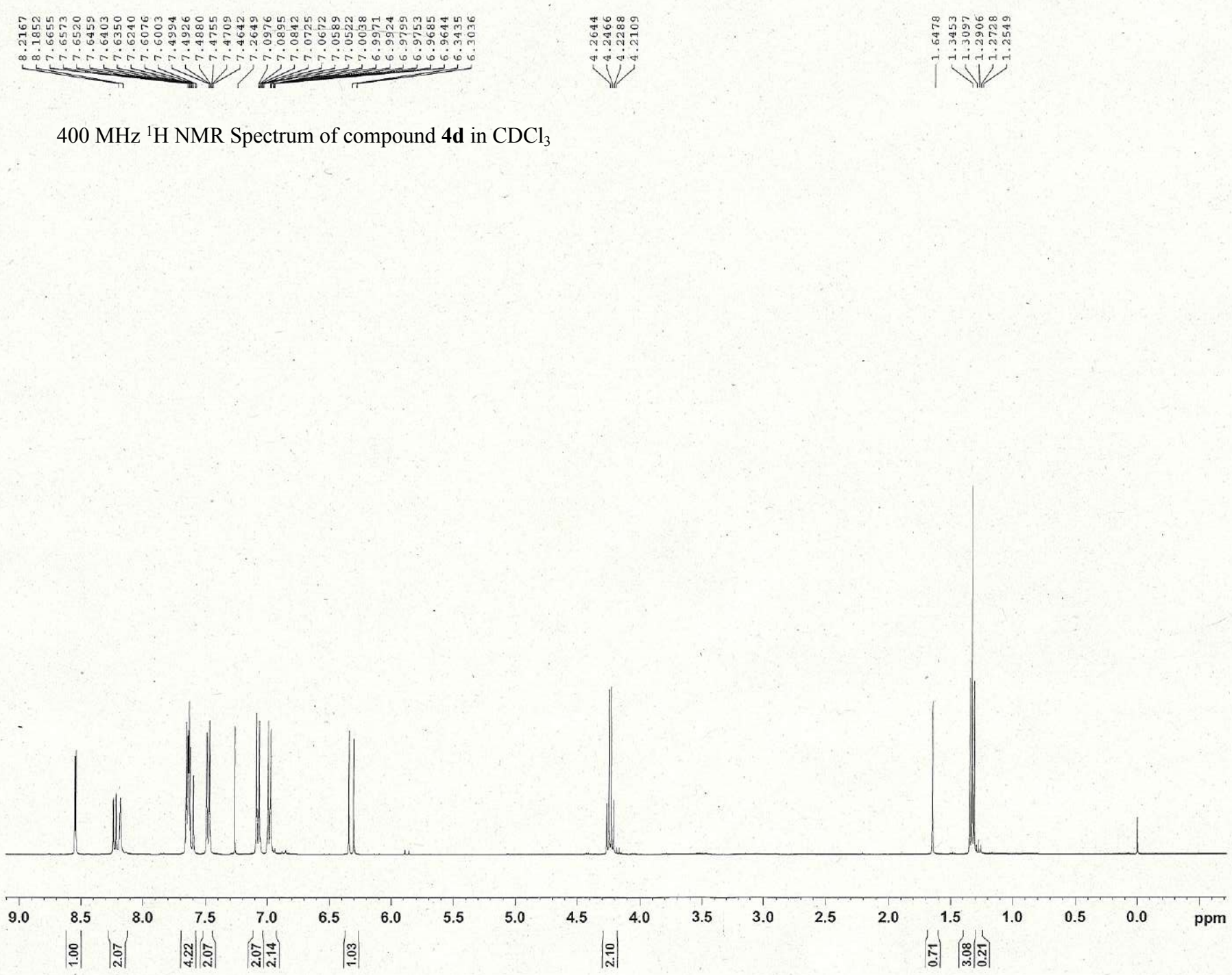
400 MHz  $^1\text{H}$  NMR Spectrum of compound **8c** in  $\text{CDCl}_3$



100 MHz  $^{13}\text{C}$  NMR Spectrum of compound **8c** in  $\text{CDCl}_3$







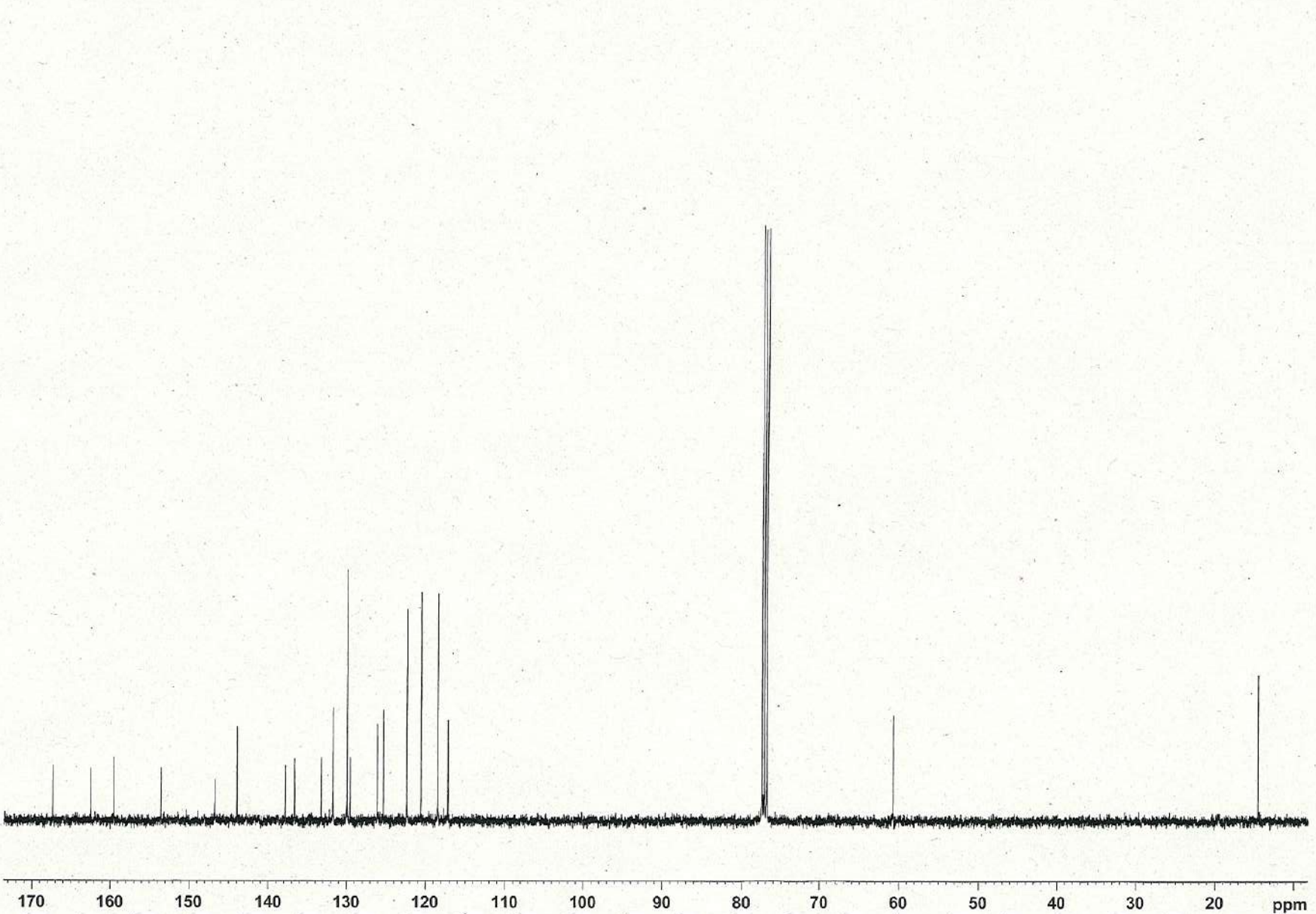
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159.5707  
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131.7799  
129.9762  
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120.6452  
118.4869  
117.2012

77.4329

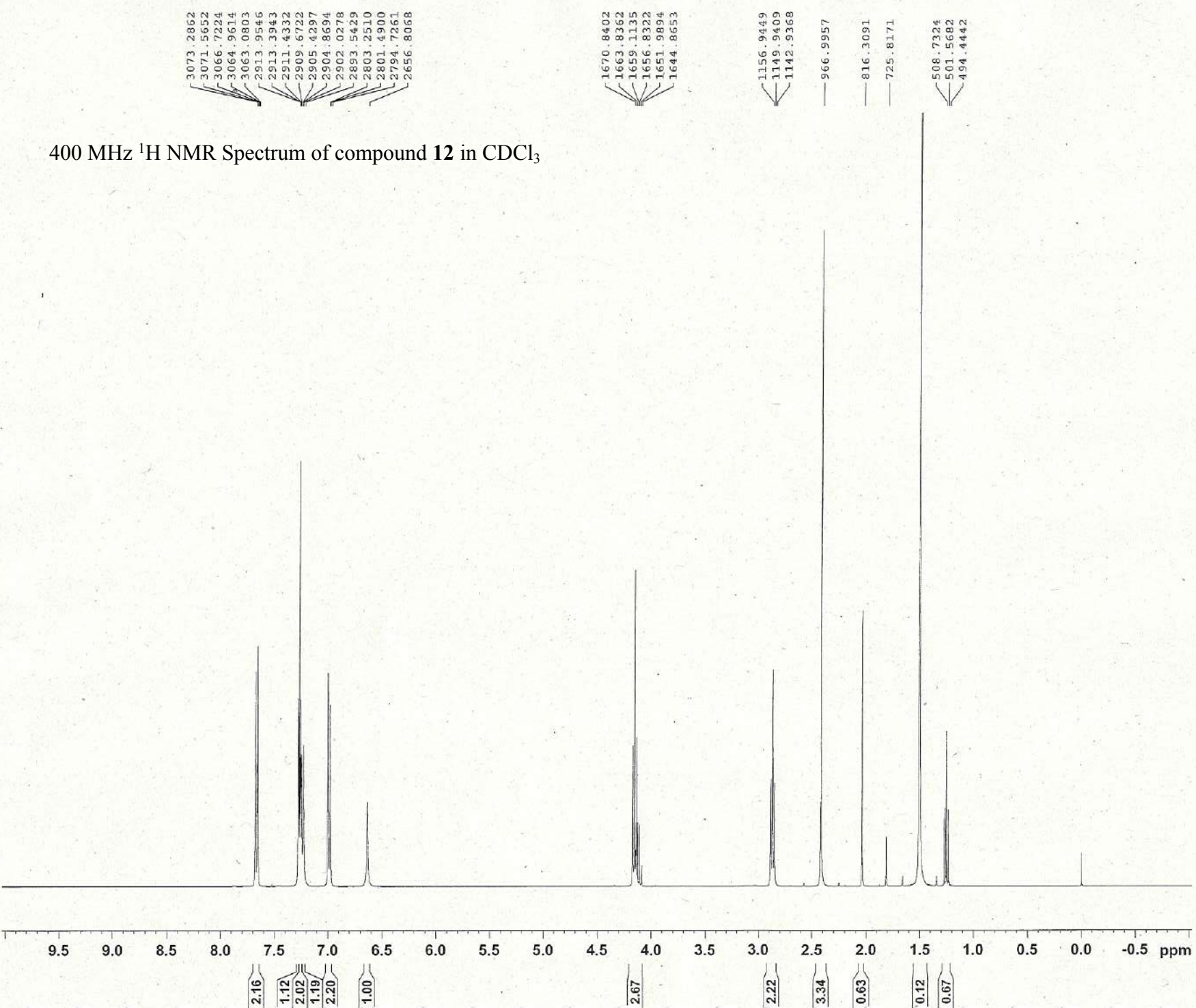
60.7118

14.5158

100 MHz  $^{13}\text{C}$  NMR Spectrum of compound **4d** in  $\text{CDCl}_3$

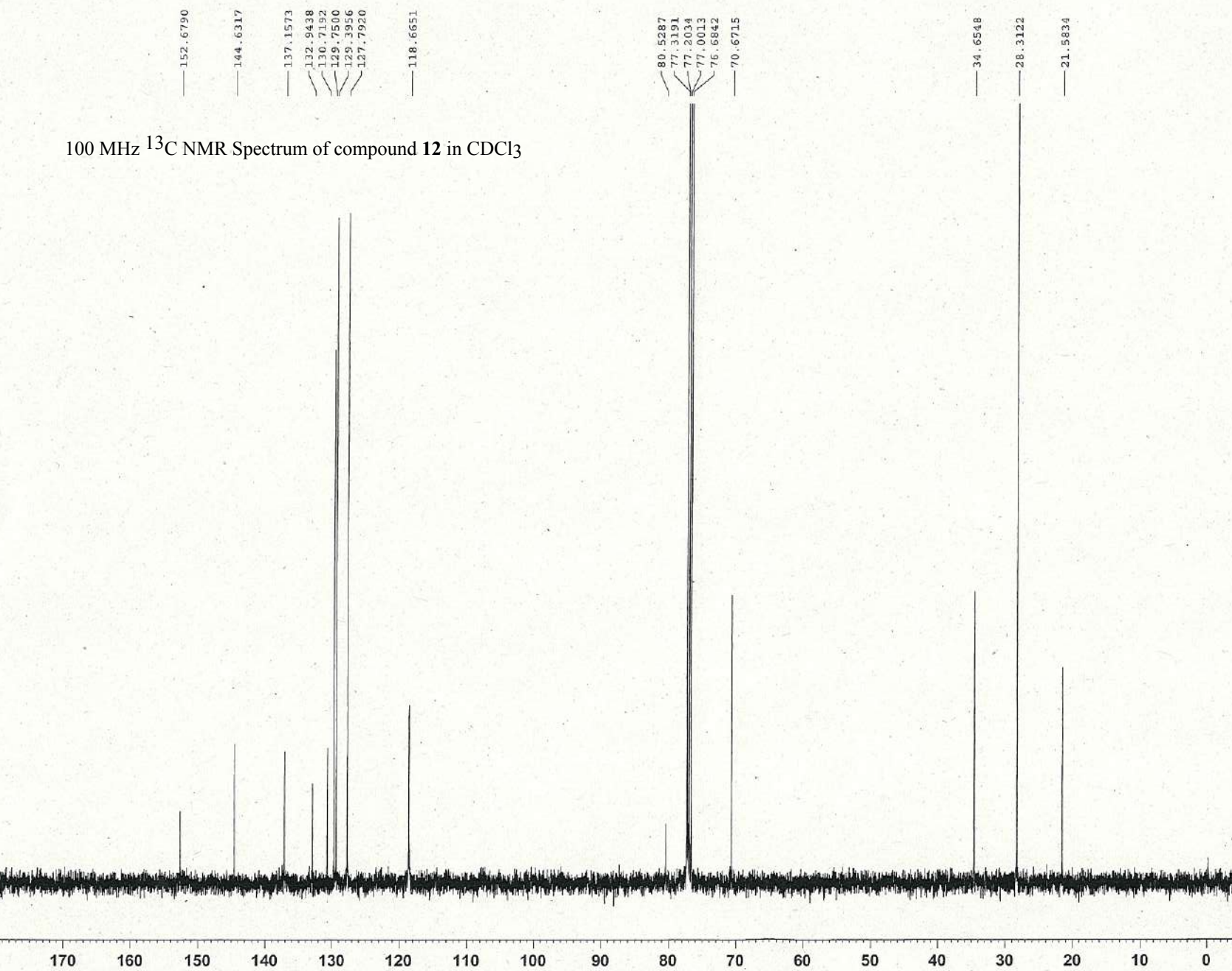


400 MHz  $^1\text{H}$  NMR Spectrum of compound **12** in  $\text{CDCl}_3$

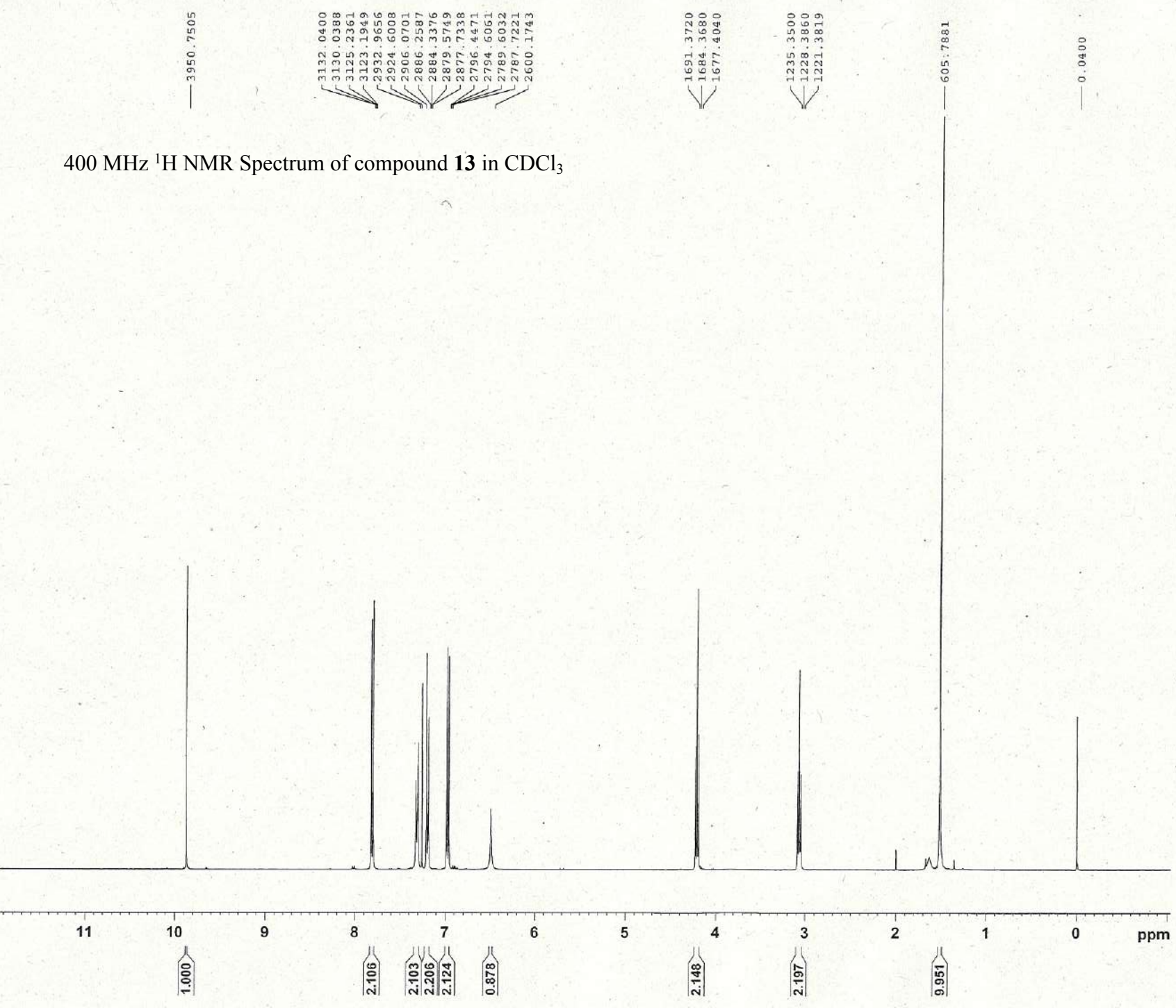




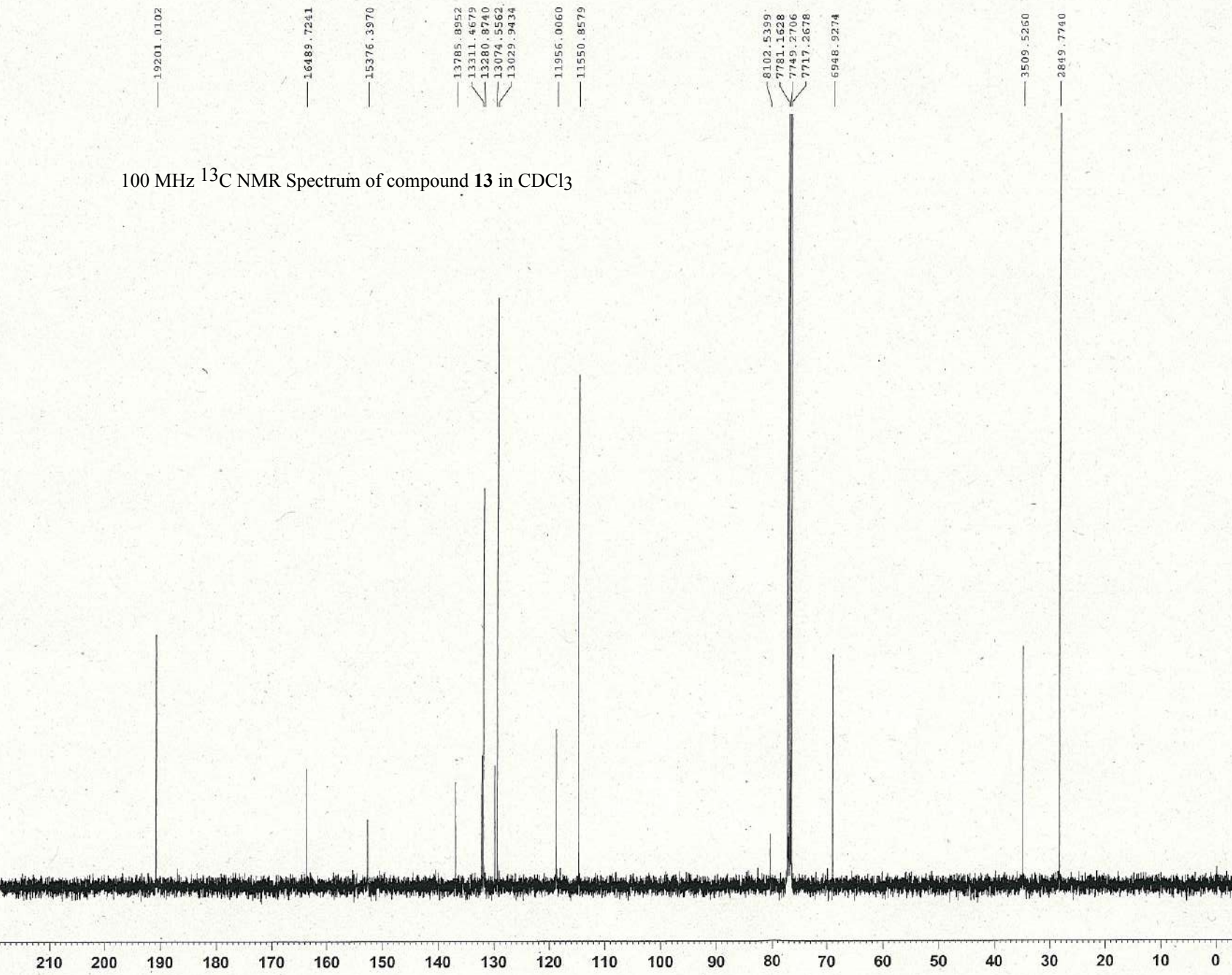
100 MHz  $^{13}\text{C}$  NMR Spectrum of compound 12 in  $\text{CDCl}_3$



400 MHz  $^1\text{H}$  NMR Spectrum of compound **13** in  $\text{CDCl}_3$

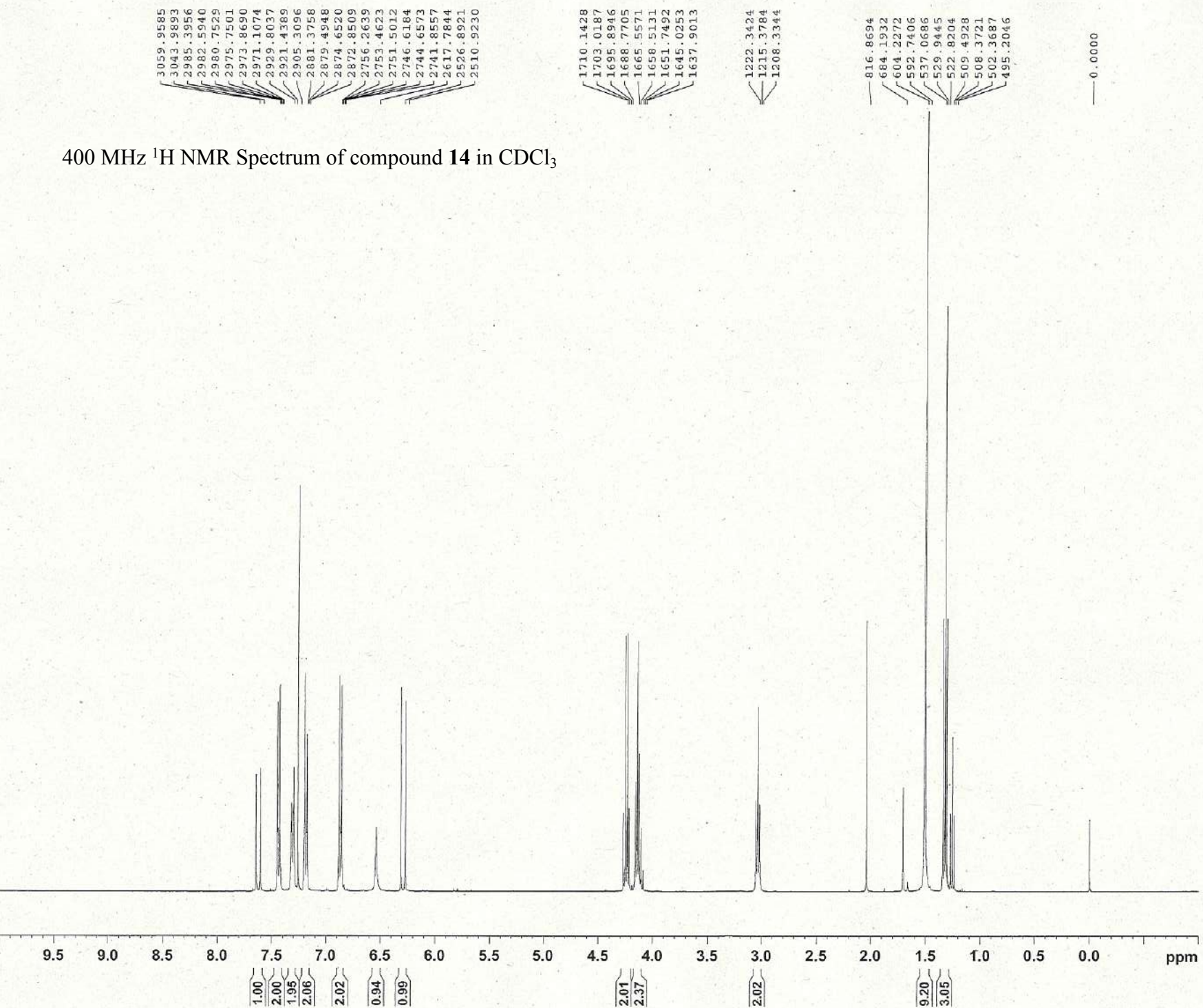


100 MHz  $^{13}\text{C}$  NMR Spectrum of compound **13** in  $\text{CDCl}_3$

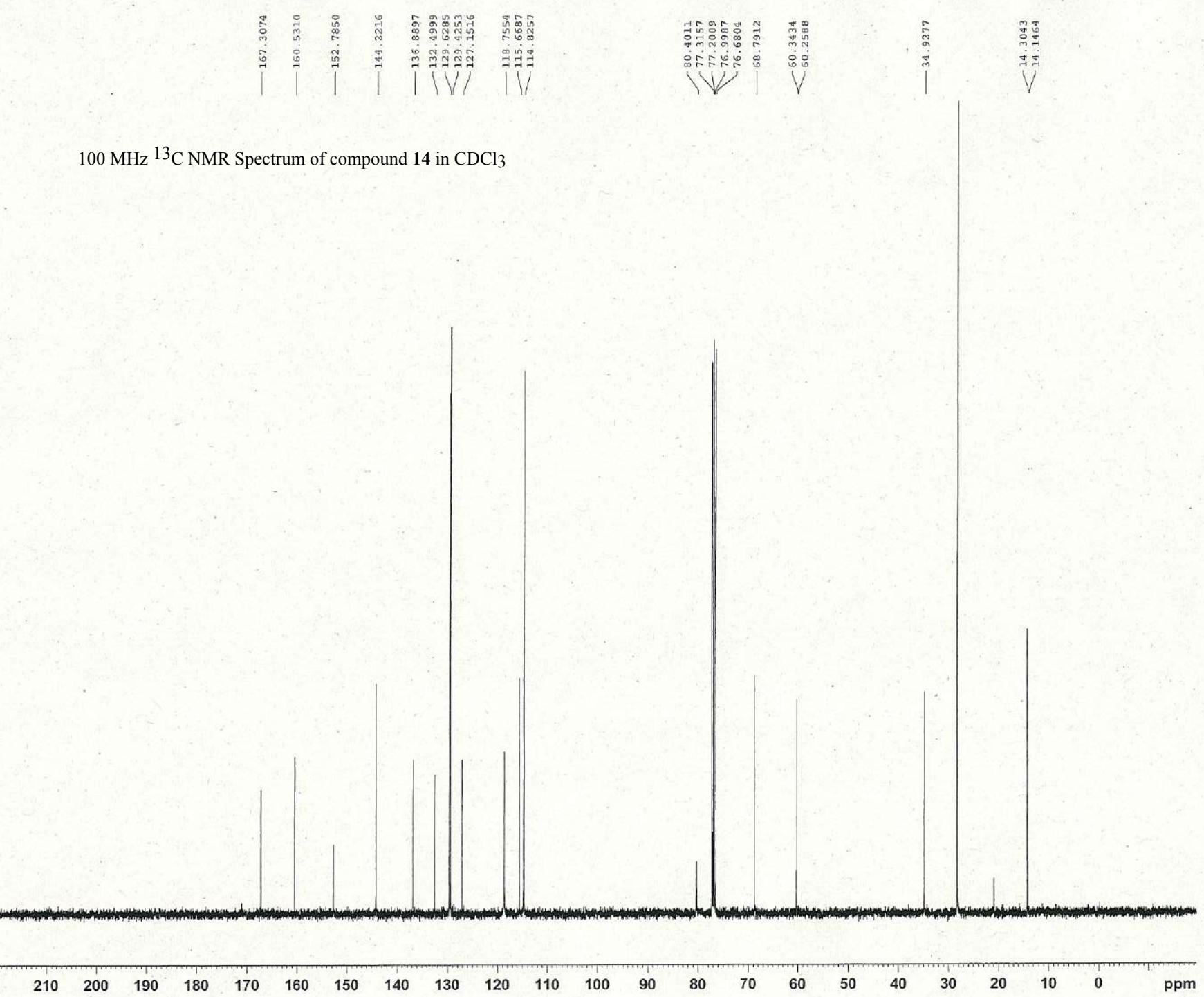




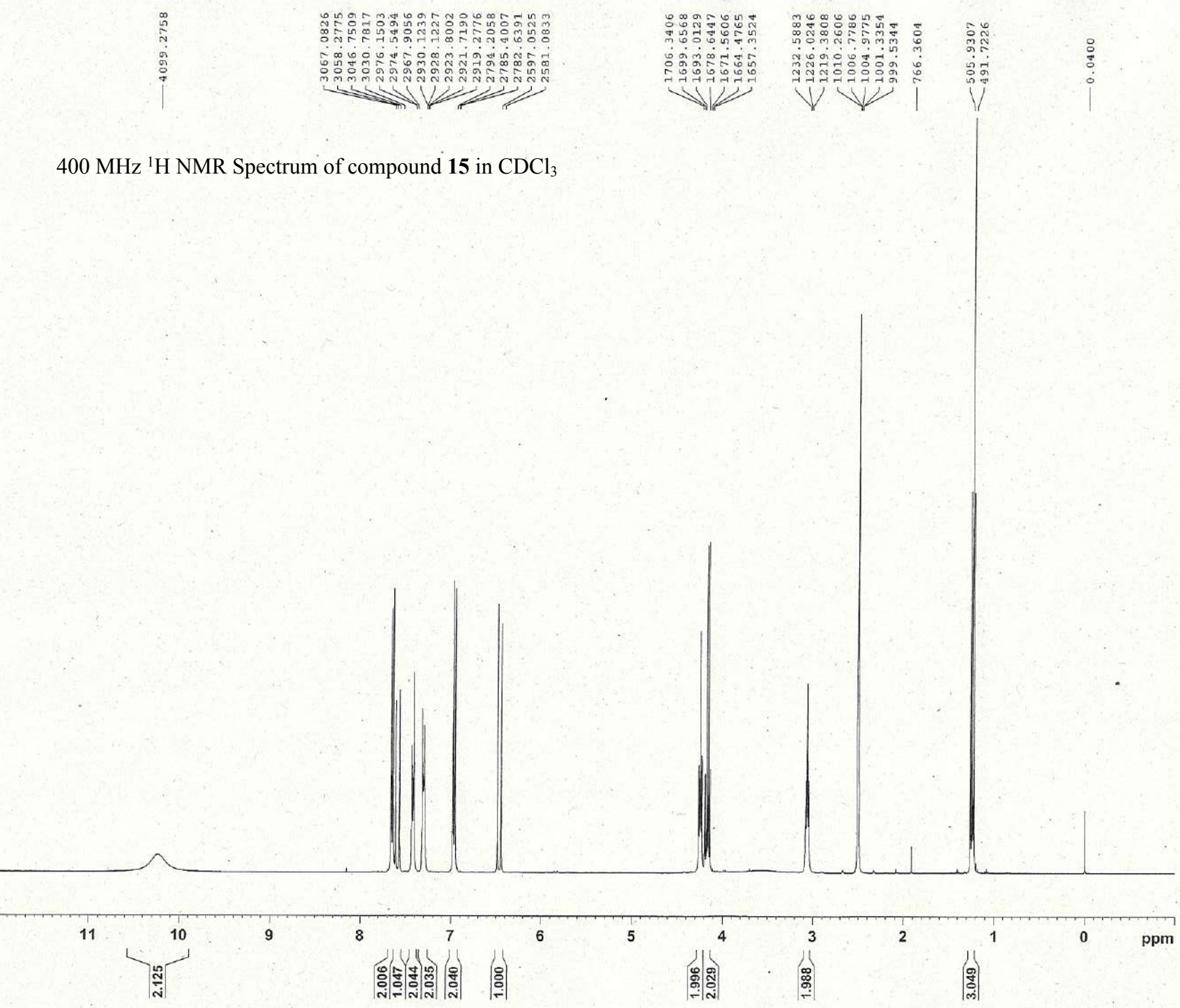
400 MHz  $^1\text{H}$  NMR Spectrum of compound **14** in  $\text{CDCl}_3$



100 MHz  $^{13}\text{C}$  NMR Spectrum of compound **14** in  $\text{CDCl}_3$

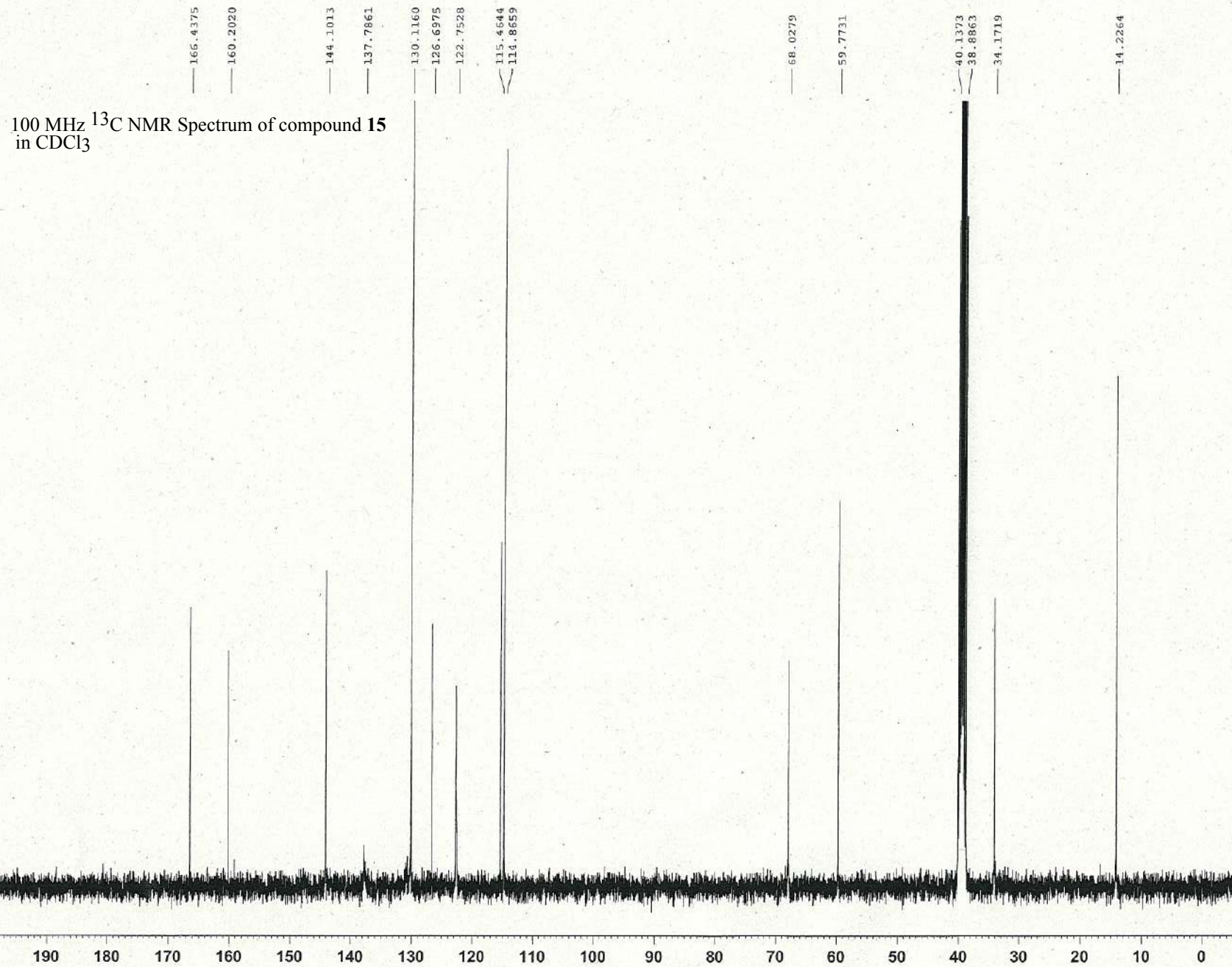


400 MHz  $^1\text{H}$  NMR Spectrum of compound **15** in  $\text{CDCl}_3$





100 MHz  $^{13}\text{C}$  NMR Spectrum of compound **15**  
in  $\text{CDCl}_3$



3402.6755  
3399.9539  
3299.3361  
3278.6042  
3275.8826  
3269.8392  
3267.0776  
3043.2289  
3039.6269  
3035.6646  
3030.8218  
3027.2197  
2981.7136  
2979.0721  
2970.3070  
2922.8397  
2914.3949  
2906.8305  
2759.5459  
2750.8209  
2513.4845  
2497.5153

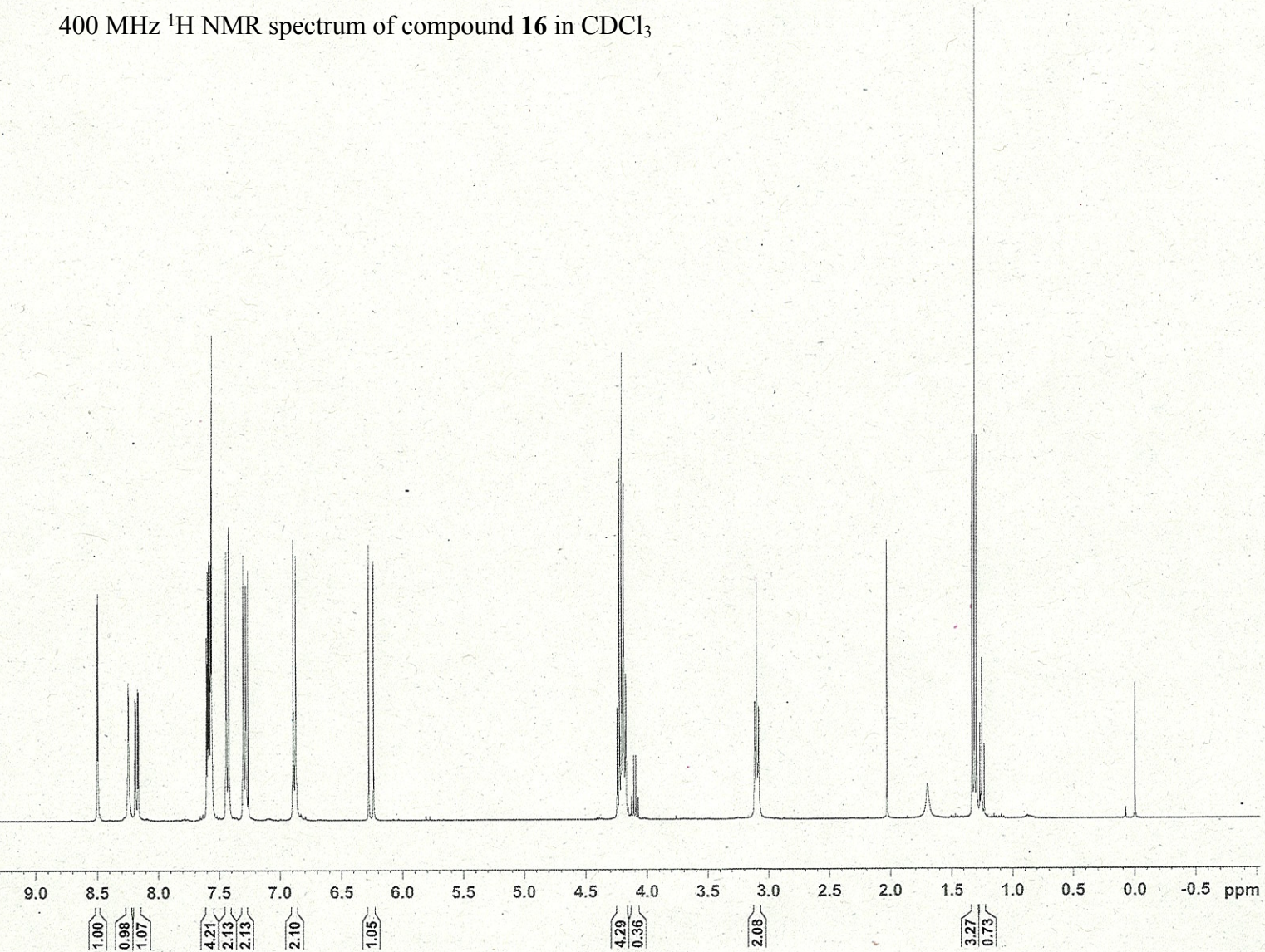
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1684.6882  
1678.2445  
1671.5606  
1652.5097  
1645.3856  
1638.2215  
1631.0974

1246.6364  
1239.8726  
1233.1087

811.8266  
680.4711  
532.5060  
525.3819  
518.2578  
513.9754  
506.9313  
502.3287  
499.8072  
492.6831

0.0000

400 MHz  $^1\text{H}$  NMR spectrum of compound **16** in  $\text{CDCl}_3$





100 MHz  $^{13}\text{C}$  NMR spectrum of compound **16** in  $\text{CDCl}_3$

