

Supporting Information

Assembly of Indoline-2-Carboxylate Embodied Dipeptides via Pd-Catalyzed C(sp²)-H Bond Direct Functionalization

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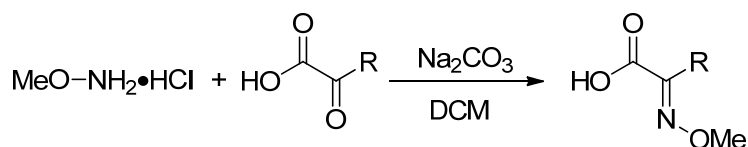
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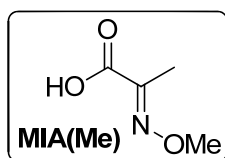
1. Reagents: All commercial materials were used as received unless otherwise noted. DCE was distilled from CaH_2 . $\text{Pd}(\text{OAc})_2$ (98%, Aldrich) and 1-Fluoro-2,4,6-trimethylpyridinium Tetrafluoroborate (>95%, TCI) were used in the Pd-catalyzed reactions. Flash chromatography was performed using 230-400 mesh SiliaFlash® P60 (Silicycle Inc.).

2. Instruments: NMR spectra were recorded on Bruker Ultrashield™ 400 Plus, Agilent Technologies 400/54 Premium Shielded, Agilent Technologies 500/54 Premium Shielded instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet. High resolution ESI mass experiments were operated on a Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS instrument. Optical rotations were obtained on a Jasco P1030 Polarimeter instrument and reported as follows: $[\alpha]_D^{T^\circ\text{C}}$ (c = g/100 mL, solvent).

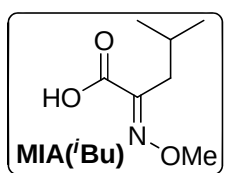
3. General procedure A for preparation of MIA



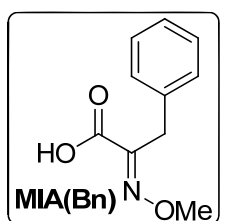
To a solution of methoxyammonium chloride (5.0 g, 0.06 mol, 1.0 eq), and Na_2CO_3 (7.6 g, 0.07 mol, 1.2 eq) in DCM (0.3 M) was added acid (0.06 mol, 1.0 eq) at 0°C . The mixture was stirred at room temperature overnight. Subsequently, the pH of the reaction mixture was adjusted to pH 1 with 4N HCl and the mixture was extracted with DCM. The organic layer was washed with 1N hydrochloric acid and brine, and concentrated. The residue was dried in vacuo to furnish MIA.



White solid (5.06 g, 72%); $R_f = 0.40$, DCM/MeOH = 5:1; ^1H NMR (CD_3OD , 400 MHz): $\delta = 4.01$ (s, 3H), 1.98 (s, 3H); ^{13}C NMR (CD_3OD , 100 MHz): $\delta = 166.3$, 150.2, 63.4, 10.9; ESI-HRMS Calcd for $\text{C}_4\text{H}_6\text{NO}_3\text{Na}_2^+$ [$\text{M}+2\text{Na}^+-\text{H}^+$]: 162.0138; Found: 162.0138.



Light brown liquid (6.11 g, 64%); $R_f = 0.48$, DCM/MeOH = 7:1; ^1H NMR (CD_3OD , 400 MHz): $\delta = 3.99$ (s, 3H), 2.45 (d, $J = 7.2$ Hz, 2H), 2.00-1.92 (m, 1H), 0.90 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (CD_3OD , 100 MHz): $\delta = 166.5$, 153.5, 63.3, 34.5, 27.7, 22.9; ESI-HRMS Calcd for $\text{C}_7\text{H}_{12}\text{NO}_3\text{Na}_2^+$ [$\text{M}+2\text{Na}^+-\text{H}^+$]: 204.0607; Found: 204.0609.



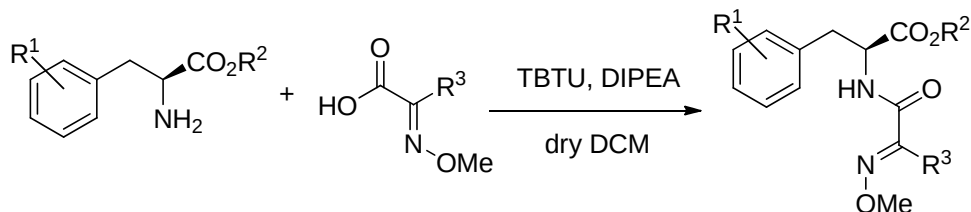
Light yellow solid (7.88 g, 68%); $R_f = 0.54$, DCM/MeOH = 7:1; ^1H NMR (CD_3OD , 400 MHz): $\delta = 7.26$ -7.20 (m, 4H), 7.18-7.14 (m, 1H), 4.03 (s, 3H), 3.88 (s, 2H); ^{13}C NMR (CD_3OD , 100 MHz): $\delta = 166.0$, 152.2, 137.4, 129.8, 129.4, 127.5, 63.6, 31.6; ESI-HRMS Calcd for $\text{C}_{10}\text{H}_{10}\text{NO}_3\text{Na}_2^+$ [$\text{M}+2\text{Na}^+-\text{H}^+$]: 238.0451; Found: 238.0451.

***MIA(H)** was prepared by reacting glyoxylic acid with methoxyamine hydrochloride according to known procedure.¹

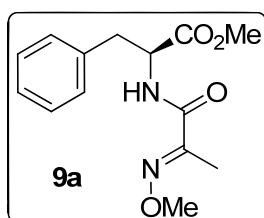
(1) Ahmed A.; Peters N. R.; Fitzgerald M. K.; Watson J. A.; Hoffmann F. M.; Thorson J. S.; *J. Am. Chem. Soc.* **2006**, 128, 14224-14225.

4. Preparation of MIA-phenylalanin-derivates.

4.1 General procedure B for preparation of MIA-phenylalanin-derivates

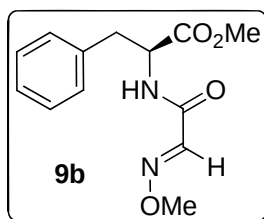


A mixture of acetic acid (1.5 mmol, 1.0 eq), amine (1.8 mmol, 1.2 eq), TBTU (0.58 g, 1.8 mmol, 1.2 eq), and DIPEA (0.66 ml, 3.75 mmol, 2.5 eq) in anhydrous DCM (0.2 M) was stirred at room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with 1N hydrochloric acid and brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography using 10-20% ethyl acetate in hexanes to give the desired amide product.



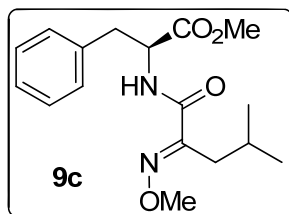
(CHCl₃, *c* = 1.0).

Light yellow oil (350.6 mg, 84%); *R_f* = 0.50, hexane/EtOAc = 3:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.29-7.24 (m, 3H), 7.18-7.13 (m, 3H), 4.92-4.87 (m, 1H), 3.96 (s, 3H), 3.71 (s, 3H), 3.19-3.09 (m, 2H), 1.98 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.8, 162.7, 149.9, 135.9, 129.3, 128.6, 127.2, 62.9, 53.2, 52.3, 38.1, 9.6; ESI-HRMS Calcd for C₁₄H₁₈N₂O₄Na⁺ [M+Na⁺]: 301.1159; Found: 301.1157. [α]_D²⁷ = +29.0



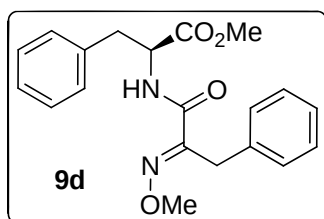
(CHCl₃, *c* = 1.0).

White solid (317.2 mg, 80%); *R_f* = 0.38, hexane/EtOAc = 3:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.36 (s, 1H), 7.31-7.25 (m, 3H), 7.13-7.12 (m, 2H), 6.93 (d, *J* = 7.5 Hz, 1H), 4.95-4.90 (m, 1H), 3.96 (s, 3H), 3.73 (s, 3H), 3.21-3.11 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.7, 161.3, 142.4, 135.8, 129.4, 128.7, 127.3, 63.3, 53.1, 52.5, 38.2; ESI-HRMS Calcd for C₁₃H₁₆N₂O₄Na⁺ [M+Na⁺]: 287.1002; Found: 287.0998. [α]_D²⁷ = +50.0



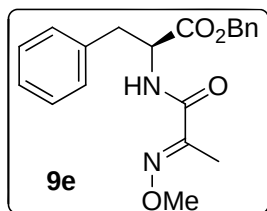
Calcd for C₁₇H₂₅N₂O₄⁺ [M+H⁺]: 321.1809; Found: 321.1807. [α]_D²⁶ = +30.5 (CHCl₃, *c* = 1.0).

Colorless oil (442.1 mg, 92%); *R_f* = 0.54, hexane/EtOAc = 4:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.29-7.22 (m, 3H), 7.17-7.11 (m, 3H), 4.90-4.85 (m, 1H), 3.91 (s, 3H), 3.70 (s, 3H), 3.19-3.08 (m, 2H), 2.44 (d, *J* = 7.4 Hz, 2H), 2.00-1.89 (m, 1H), 0.87 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.8, 162.8, 153.2, 135.9, 129.3, 128.5, 127.1, 62.7, 53.2, 52.3, 38.1, 32.5, 26.5, 22.7, 22.6; ESI-HRMS

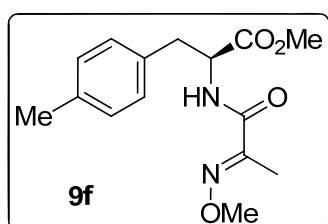


Colorless oil (478.4 mg, 90%); *R_f* = 0.43, hexane/EtOAc = 4:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.25-7.22 (m, 7H), 7.20-7.14 (m, 2H), 7.06-7.04 (m, 2H), 4.90-4.85 (m, 1H), 3.96 (s, 3H), 3.90 (s, 2H), 3.69 (s, 3H), 3.18-3.07 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.7,

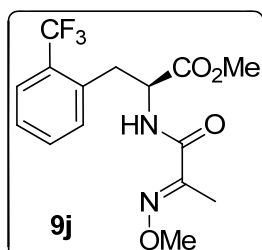
162.3, 151.5, 136.2, 135.8, 129.4, 129.3, 128.6, 128.5, 127.1, 126.5, 63.1, 53.4, 52.4, 38.1, 29.8; ESI-HRMS Calcd for $C_{20}H_{23}N_2O_4^+$ $[M+H]^+$: 355.1652; Found: 355.1649. $[\alpha]_D^{26} = +61.1$ ($CHCl_3$, $c = 1.0$).



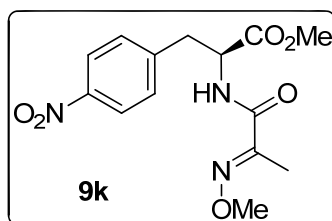
Light yellow oil, (435.9 mg, 82%); $R_f = 0.68$, hexane/EtOAc = 4:1; 1H NMR ($CDCl_3$, 400 MHz): $\delta = 7.33$ -7.31 (m, 3H), 7.27-7.25 (m, 2H), 7.21-7.19 (m, 4H), 7.04-7.02 (m, 2H), 5.13 (d, $J = 29.2$ Hz, 1H), 5.09 (d, $J = 29.2$ Hz, 1H), 4.96-4.91 (m, 1H), 3.90 (s, 3H), 3.16-3.08 (m, 2H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 171.1$, 162.6, 149.9, 135.6, 135.1, 129.3, 128.5, 128.4, 128.3, 126.9, 67.1, 62.8, 53.1, 37.9, 9.5; ESI-HRMS Calcd for $C_{20}H_{23}N_2O_4^+$ $[M+H]^+$: 355.1652; Found: 355.1652. $[\alpha]_D^{27} = -0.9$ ($CHCl_3$, $c = 1.0$).



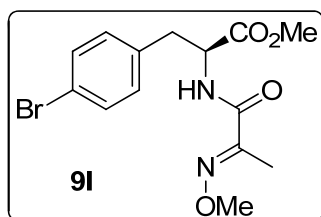
Colorless oil, (377.1 mg, 86%); $R_f = 0.46$, hexane/EtOAc = 3:1; 1H NMR ($CDCl_3$, 400 MHz): $\delta = 7.17$ (d, $J = 8.0$ Hz, 1H), 7.09 (d, $J = 8.0$ Hz, 2H), 7.01 (d, $J = 8.0$ Hz, 2H), 4.88-4.83 (m, 1H), 3.95 (s, 3H), 3.72 (s, 3H), 3.14-3.15 (m, 2H), 2.31 (s, 3H), 1.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 171.9$, 162.7, 150.0, 136.7, 132.7, 129.3, 129.1, 62.9, 53.3, 52.3, 37.7, 21.1, 9.6; ESI-HRMS Calcd for $C_{15}H_{21}N_2O_4^+$ $[M+H]^+$: 293.1496; Found: 293.1493. $[\alpha]_D^{27} = +31.1$ ($CHCl_3$, $c = 1.0$).



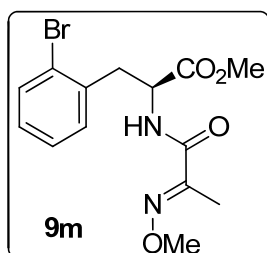
Colorless oil, (405.2 mg, 78%); $R_f = 0.40$, hexane/EtOAc = 4:1; 1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.62$ (d, $J = 8.0$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 1H), 7.39 (d, $J = 8.0$ Hz, 1H), 7.33 (t, $J = 7.7$ Hz, 1H), 7.25 (d, $J = 8.5$ Hz, 1H), 4.93-4.88 (m, 1H), 3.96 (s, 3H), 3.68 (s, 3H), 3.28 (dd, $J = 14.5$, 6.5 Hz, 1H), 3.25 (dd, $J = 14.5$, 6.0 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 171.8$, 162.8, 149.8, 135.1 (q, $J = 1.4$ Hz), 131.9, 131.6, 129.1 (q, $J = 29.6$ Hz), 127.2, 126.2 (q, $J = 5.8$ Hz), 124.1 (q, $J = 272.1$ Hz), 62.9, 53.3, 52.5, 34.9, 9.6; ESI-HRMS Calcd for $C_{15}H_{18}F_3N_2O_4^+$ $[M+H]^+$: 347.1213; Found: 347.1207. $[\alpha]_D^{27} = -20.9$ ($CHCl_3$, $c = 1.0$).



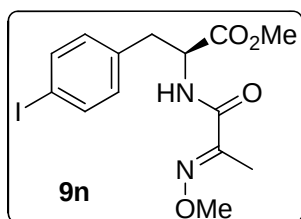
Light yellow solid, (407.4 mg, 84%); $R_f = 0.34$, hexane/EtOAc = 3:1; 1H NMR ($CDCl_3$, 500 MHz): $\delta = 8.15$ (d, $J = 8.5$ Hz, 2H), 7.31 (d, $J = 8.5$ Hz, 2H), 7.21 (d, $J = 8.0$ Hz, 1H), 4.97-4.93 (m, 1H), 3.97 (s, 3H), 3.74 (s, 3H), 3.27 (dd, $J = 14.0$, 8.0 Hz, 1H), 3.24 (dd, $J = 14.0$, 6.5 Hz, 1H), 1.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 171.3$, 162.9, 150.0, 147.4, 143.9, 130.3, 123.8, 63.2, 52.9, 52.8, 38.2, 9.8; ESI-HRMS Calcd for $C_{14}H_{18}N_3O_6^+$ $[M+H]^+$: 324.1190; Found: 324.1189. $[\alpha]_D^{27} = +9.9$ ($CHCl_3$, $c = 1.0$).



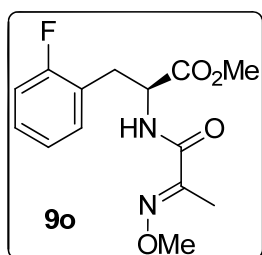
Light yellow solid, (455.4 mg, 85%); $R_f = 0.59$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.39$ (d, $J = 8.4$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 1H), 7.00 (d, $J = 8.4$ Hz, 2H), 4.89-4.84 (m, 1H), 3.95 (s, 3H), 3.70 (s, 3H), 3.14-3.03 (m, 2H), 1.97 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.6, 162.7, 150.0, 135.0, 131.7, 131.0, 121.2, 63.0, 53.0, 52.5, 37.6, 9.7$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{18}\text{BrN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 357.0444; Found: 357.0446. $[\alpha]_{\text{D}}^{27} = +25.7$ (CHCl_3 , $c = 1.0$).



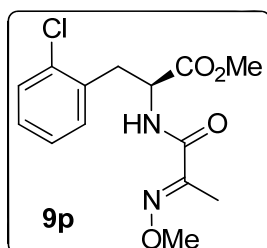
Light yellow solid, (439.4 mg, 82%); $R_f = 0.39$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.51$ (d, $J = 8.0$ Hz, 1H), 7.26-7.23 (m, 1H), 7.21-7.18 (m, 2H), 7.09-7.05 (m, 1H), 4.92-4.87 (m, 1H), 3.94 (s, 3H), 3.68 (s, 3H), 3.27 (dd, $J = 14.0, 6.4$ Hz, 1H), 3.24 (dd, $J = 14.0, 8.0$ Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.8, 162.8, 149.8, 135.9, 132.9, 131.2, 128.8, 127.5, 124.9, 62.9, 52.5, 38.1, 9.6$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{18}\text{BrN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 357.0444; Found: 357.0443. $[\alpha]_{\text{D}}^{27} = -9.6$ (CHCl_3 , $c = 1.0$).



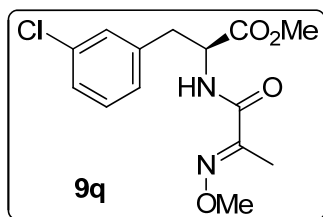
White solid, (460.6 mg, 76%); $R_f = 0.41$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.58$ (d, $J = 8.0$ Hz, 2H), 7.14 (d, $J = 8.0$ Hz, 1H), 6.86 (d, $J = 8.4$ Hz, 2H), 4.88-4.83 (m, 1H), 3.94 (s, 3H), 3.69 (s, 3H), 3.12-3.00 (m, 2H), 1.96 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.5, 162.7, 149.9, 137.6, 135.6, 131.3, 92.7, 63.0, 53.0, 52.5, 37.7, 9.7$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{18}\text{IN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 405.0301; Found: 405.0306. $[\alpha]_{\text{D}}^{27} = +24.4$ (CHCl_3 , $c = 1.0$).



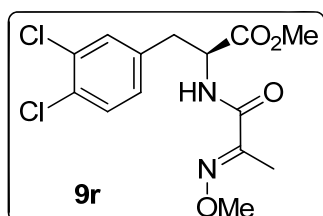
Light yellow oil, (355.6 mg, 80%); $R_f = 0.56$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.23$ -7.17 (m, 2H), 7.15-7.11 (m, 1H), 7.05-6.97 (m, 2H), 4.87-4.82 (m, 1H), 3.93 (s, 3H), 3.69 (s, 3H), 3.22-3.11 (m, 2H), 1.94 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.7, 162.8, 161.4$ (d, $J = 244.0$ Hz), 149.9, 131.6 (d, $J = 4.0$ Hz), 129.1 (d, $J = 8.0$ Hz), 124.2 (d, $J = 4.0$ Hz), 123.0 (d, $J = 16.0$ Hz), 115.4 (d, $J = 22.0$ Hz), 62.9, 52.5, 52.4, 31.6, 9.6; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{17}\text{FN}_2\text{O}_4^+$ $[\text{M}+\text{Na}^+]$: 319.1065; Found: 319.1063. $[\alpha]_{\text{D}}^{27} = +17.9$ (CHCl_3 , $c = 1.0$).



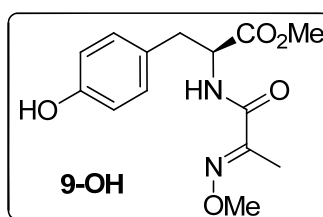
Light yellow oil, (398.7 mg, 85%); $R_f = 0.56$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.34$ -7.31 (m, 1H), 7.25 (d, $J = 8.0$ Hz, 1H), 7.17-7.14 (m, 3H), 4.91-4.86 (m, 1H), 3.94 (s, 3H), 3.68 (s, 3H), 3.27 (dd, $J = 14.0, 6.4$ Hz, 1H), 3.23 (dd, $J = 14.0, 8.0$ Hz, 1H), 1.92 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.8, 162.8, 149.8, 134.5, 134.1, 131.3, 129.6, 128.6, 126.9, 62.9, 52.5, 52.4, 35.7, 9.6$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{18}\text{ClN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 313.0950; Found: 313.0945. $[\alpha]_{\text{D}}^{27} = -5.4$ (CHCl_3 , $c = 1.0$).



Light yellow oil, (379.9 mg, 81%); R_f = 0.59, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 7.21-7.16 (m, 3H), 7.12 (br, 1H), 7.01-6.98 (m, 1H), 4.89-4.84 (m, 1H), 3.95 (s, 3H), 3.70 (s, 3H), 3.14-3.05 (m, 2H), 1.97 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 171.5, 162.7, 149.9, 137.9, 134.3, 129.8, 129.5, 127.5, 127.4, 63.0, 52.9, 52.4, 37.8, 9.6; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{17}\text{ClN}_2\text{O}_4\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 335.0769; Found: 335.0777. $[\alpha]_{\text{D}}^{27}$ = +15.8 (CHCl_3 , c = 1.0).

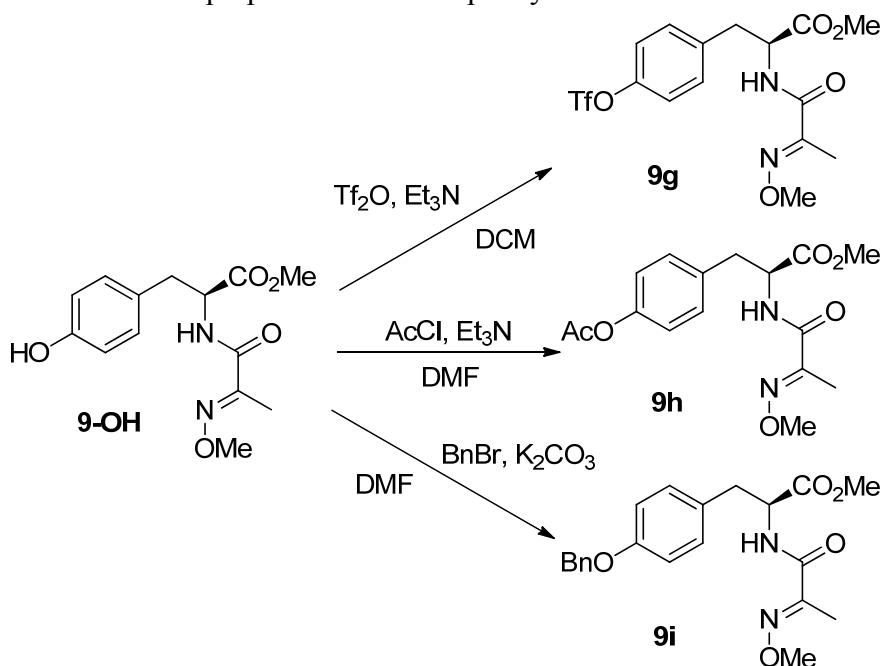


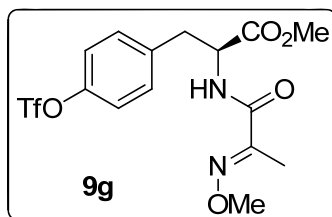
Light yellow oil, (401.1 mg, 77%); R_f = 0.56, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 7.34 (d, J = 8.4 Hz, 1H), 7.22 (d, J = 2.0 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.96 (dd, J = 8.4, 2.0 Hz, 1H), 4.90-4.85 (m, 1H), 3.97 (s, 3H), 3.72 (s, 3H), 3.14-3.03 (m, 2H), 1.98 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 171.4, 162.8, 150.0, 136.3, 132.6, 131.4, 131.4, 130.6, 128.8, 63.1, 52.9, 52.6, 37.3, 9.7; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{17}\text{Cl}_2\text{N}_2\text{O}_4^+$ [$\text{M}+\text{H}^+$]: 347.0560; Found: 347.0559. $[\alpha]_{\text{D}}^{26}$ = +16.2 (CHCl_3 , c = 1.0).



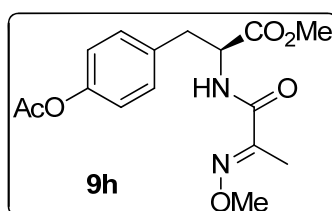
White solid, (331.1 mg, 75%); R_f = 0.44, hexane/EtOAc = 2:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 7.25 (d, J = 7.6 Hz, 1H), 7.03 (s, 1H), 6.95 (d, J = 8.5 Hz, 2H), 6.73 (d, J = 8.6 Hz, 2H), 4.86-4.80 (m, 1H), 3.93 (s, 3H), 3.69 (s, 3H), 3.09-2.99 (m, 2H), 1.96 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 172.1, 163.2, 155.6, 149.8, 130.4, 126.9, 115.7, 63.0, 53.6, 52.5, 37.4, 9.7; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_5^+$ [$\text{M}+\text{H}^+$]: 295.1288; Found: 295.1286. $[\alpha]_{\text{D}}^{27}$ = +30.1 (CHCl_3 , c = 1.0).

4.2 General procedure C for preparation of MIA-phenylalanin-derivates

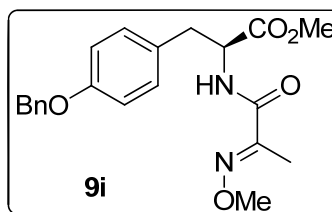




A mixture of **9-OH** (294 mg, 1.0 mmol, 1.0 eq), Tf₂O (0.20 ml, 1.2 mmol, 1.2 eq) and Et₃N (0.28 ml, 2.0 mmol, 2.0 eq) in anhydrous DCM was stirred from 0 °C to room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography using 10% ethyl acetate in hexanes to give the desired amide product as a light yellow solid (400.8 mg, 94%). *R_f* = 0.50, hexane/EtOAc = 4:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.22-7.15 (m, 5H), 4.90-4.85 (m, 1H), 3.93 (s, 3H), 3.69 (s, 3H), 3.21-3.09 (m, 2H), 1.95 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.5, 162.8, 149.9, 148.7, 136.8, 131.2, 121.4, 118.8 (q, *J* = 319.0 Hz), 63.0, 53.0, 52.5, 37.5, 9.6; ESI-HRMS Calcd for C₁₅H₁₈F₃N₂O₇S⁺ [M+H⁺]: 427.0781; Found: 427.0786. [α]_D²⁷ = +14.7 (CHCl₃, *c* = 1.0).

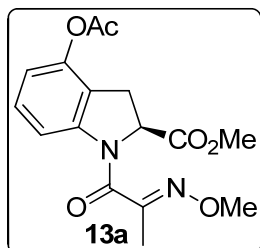


A mixture of **9-OH** (294 mg, 1.0 mmol, 1.0 eq), AcCl (85 μl, 1.2 mmol, 1.2 eq) and Et₃N (0.28 ml, 2.0 mmol, 2.0 eq) in anhydrous DCM was stirred from 0 °C to room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography using 15% ethyl acetate in hexanes to give the desired amide product as colorless oil (302.7 mg, 90%). *R_f* = 0.33, hexane/EtOAc = 2:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.15 (d, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 4.85-4.80 (m, 1H), 3.90 (s, 3H), 3.65 (s, 3H), 3.13-3.04 (m, 2H), 2.21 (s, 3H); 1.93 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.6, 169.2, 162.6, 149.8, 149.7, 133.4, 130.1, 121.6, 62.8, 53.1, 52.3, 37.3, 20.9, 9.5; ESI-HRMS Calcd for C₁₆H₂₀N₂O₆Na⁺ [M+Na⁺]: 359.1213; Found: 359.1211. [α]_D²⁷ = +16.0 (CHCl₃, *c* = 1.0).



A mixture of **9-OH** (294 mg, 1.0 mmol, 1.0 eq), BnBr (0.14 ml, 1.2 mmol, 1.2 eq) and K₂CO₃ (276 mg, 2.0 mmol, 2.0 eq) in anhydrous DMF was stirred at room temperature overnight. Water was added and the mixture was extracted with Ethyl Acetate. The combined organic layers was washed with water and brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography using 10% ethyl acetate in hexanes to give the desired amide product as light yellow oil (361.3 mg, 94%). *R_f* = 0.50, hexane/EtOAc = 4:1; ¹H NMR (CDCl₃, 400 MHz): δ = 7.44-7.32 (m, 5H), 7.19 (d, *J* = 8.1 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.03 (s, 2H), 4.89-4.84 (m, 1H), 3.95 (s, 3H), 3.71 (s, 3H), 3.14-3.15 (m, 2H), 2.00 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 171.8, 162.6, 157.9, 149.9, 136.9, 130.3, 128.6, 128.1, 127.9, 127.4, 114.9, 69.9, 62.9, 53.3, 52.3, 37.3, 9.6; ESI-HRMS Calcd for C₂₁H₂₅N₂O₅⁺ [M+H⁺]: 385.1758; Found: 385.1757. [α]_D²⁷ = +27.3 (CHCl₃, *c* = 1.0).

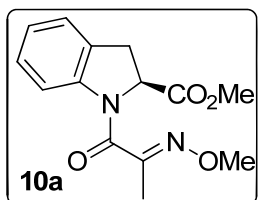
5. Procedure D: Synthesis of acetoxyated product **13a**. A mixture of MIA(Me)-phenylalanin-derivates **9a** (0.5 mmol, 1.0 eq), Pd(OAc)₂ (11.2 mg, 0.05 mmol, 0.1 eq), PhI(OAc)₂ (322.1 mg, 1.0 mmol, 2.0 eq) and Ac₂O (4 mL) in a 10 mL high pressure flask vial was heated at 110 °C for 2 hours. The reaction mixture was cooled to room temperature, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography using 15% ethyl acetate in hexanes to give the indoline product as a white solid.



(53.5 mg, 32% yield); R_f = 0.35, hexane/EtOAc = 2:1; ¹H NMR (CDCl₃, 400 MHz): δ = 8.26 (d, J = 7.6 Hz, 1H), 6.95-6.93 (m, 2H), 5.53 (d, J = 10.0 Hz, 1H), 3.93 (s, 3H), 3.72 (s, 3H), 3.59 (dd, J = 16.8, 11.2 Hz, 1H), 3.20 (d, J = 17.2 Hz, 1H), 2.28 (s, 3H), 2.07 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 172.4, 169.8, 163.4, 152.5, 147.4, 140.9, 130.6, 120.8, 118.6, 117.9, 62.8, 62.6, 52.7, 33.5, 21.2, 11.9; ESI-HRMS Calcd for C₁₆H₁₈N₂O₆Na⁺ [M+Na⁺]: 357.1057; Found: 357.1059. $[\alpha]_D^{27}$ = -21.5

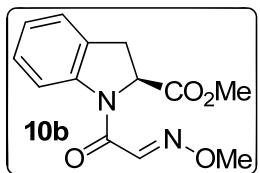
(CHCl₃, c = 0.5).

6. General procedure E: Synthesis of Indoline-2-Carboxylate. A mixture of MIA-phenylalanin-derivates (0.5 mmol, 1.0 eq), Pd(OAc)₂ (5.6 mg, 0.025 mmol, 0.05 eq), F⁺ (1-Fluoro-2,4,6-trimethylpyridinium Tetrafluoroborate) source (170.0 mg, 0.75 mmol, 1.5 eq), dry DMF (48.2 μ l, 1.25 eq) and dry DCE (4 mL) in a 10 mL high pressure flask vial (purged with Ar, sealed with PTFE cap) was heated at 110 °C for 8 hours. The reaction mixture was cooled to room temperature, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography using 10-20% ethyl acetate in hexanes to give the indoline product.



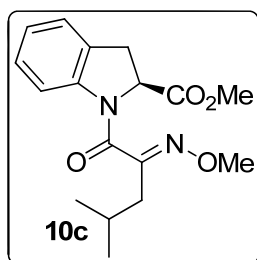
Light yellow solid (121.6 mg, 88% yield); R_f = 0.39, hexane/EtOAc = 2:1; ¹H NMR (CDCl₃, 400 MHz): δ = 8.25 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.8 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 5.50-5.48 (m, 1H), 3.92 (s, 3H), 3.70 (s, 3H), 3.57 (dd, J = 16.4, 11.2 Hz, 1H), 3.21-3.17 (m, 1H), 2.07 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 172.5, 163.5, 152.6, 143.1, 129.2, 127.9, 124.6, 124.1, 117.9, 62.5, 52.6, 33.6, 11.8;

ESI-HRMS Calcd for C₁₄H₁₇N₂O₄⁺ [M+H⁺]: 277.1183; Found: 277.1181. $[\alpha]_D^{27}$ = -69.1 (CHCl₃, c = 1.0).

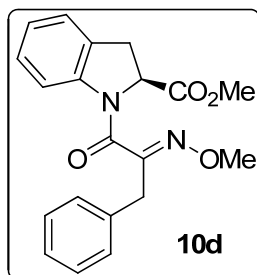


Light yellow solid (102.2 mg, 78% yield); R_f = 0.32, hexane/EtOAc = 2:1; ¹H NMR (CDCl₃, 500 MHz): δ = 8.28 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.25 (t, J = 6.8 Hz, 1H), 7.18 (d, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 5.48 (d, J = 10.5 Hz, 1H), 3.96 (s, 3H), 3.72 (s, 3H), 3.65-3.59 (m, 1H), 3.27-3.24 (m, 1H); ¹³C NMR (CDCl₃, 125 MHz): δ = 172.2, 160.5, 144.6,

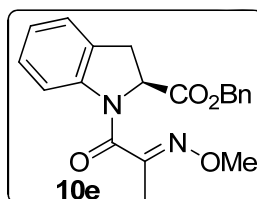
142.8, 129.1, 128.1, 124.9, 124.5, 118.0, 63.1, 61.8, 52.8, 33.8; ESI-HRMS Calcd for C₁₃H₁₅N₂O₄⁺ [M+H⁺]: 263.1026; Found: 263.1023. $[\alpha]_D^{27}$ = -112.8 (CHCl₃, c = 1.0).



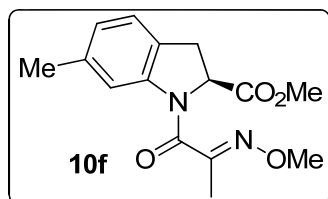
Light yellow oil (132.2 mg, 83% yield); R_f = 0.61, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 500 MHz): δ = 8.25 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 7.5 Hz, 1H), 7.17 (d, J = 7.5 Hz, 1H), 7.06 (t, J = 7.3 Hz, 1H), 5.43 (d, J = 10.5 Hz, 1H), 3.90 (s, 3H), 3.70 (s, 3H), 3.61-3.56 (m, 1H), 3.15 (d, J = 16.0 Hz, 1H), 2.57 (dd, J = 12.5, 7.5 Hz, 1H), 2.55 (dd, J = 12.5, 7.5 Hz, 1H), 2.06-2.01 (m, 1H), 0.92 (d, J = 6.0 Hz, 6H); ^{13}C NMR (CDCl_3 , 125 MHz): δ = 172.6, 163.1, 155.6, 143.4, 129.3, 127.9, 124.6, 124.4, 118.3, 62.8, 62.4, 52.5, 34.4, 34.0, 26.6, 22.9; ESI-HRMS Calcd for $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 319.1652; Found: 319.1649. $[\alpha]_{\text{D}}^{27}$ = -40.8 (CHCl_3 , c = 1.0).



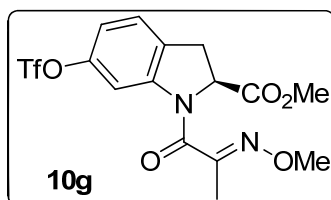
Light yellow solid (151.5 mg, 86% yield); R_f = 0.75, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 8.25 (d, J = 8.4 Hz, 1H), 7.28-7.23 (m, 5H), 7.19-7.12 (m, 2H), 7.04 (t, J = 7.2 Hz, 1H), 5.28 (d, J = 9.6 Hz, 1H), 4.10-3.91 (q and s, 5H), 3.57 (s, 3H), 3.49-3.43 (m, 1H), 3.09 (d, J = 16.0 Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 172.5, 162.6, 153.8, 143.2, 136.0, 129.3, 128.6, 127.9, 126.6, 124.7, 124.4, 118.2, 62.7, 62.6, 52.4, 33.9, 31.6; ESI-HRMS Calcd for $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 353.1496; Found: 353.1491. $[\alpha]_{\text{D}}^{27}$ = -83.3 (CHCl_3 , c = 1.0).



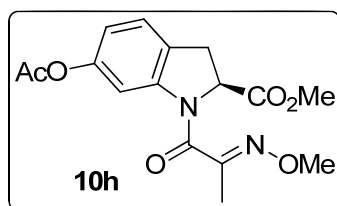
Light yellow solid (135.7 mg, 77% yield); R_f = 0.41, hexane/EtOAc = 2:1; ^1H NMR (CDCl_3 , 500 MHz): δ = 8.30 (d, J = 8.0 Hz, 1H), 7.36-7.34 (m, 3H), 7.29-7.27 (m, 3H), 7.15 (d, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 5.60 (d, J = 8.5 Hz, 1H), 5.17 (s, 2H), 3.82 (s, 3H), 3.60 (dd, J = 16.5, 11.5 Hz, 1H), 3.22 (dd, J = 16.5, 2.5 Hz, 1H), 2.03 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): δ = 171.9, 163.6, 152.7, 143.2, 135.4, 129.1, 128.7, 128.6, 128.3, 128.1, 124.7, 124.5, 118.1, 67.3, 62.6, 62.5, 33.7, 11.9; ESI-HRMS Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_4\text{Na}^+$ $[\text{M}+\text{Na}^+]$: 375.1315; Found: 375.1324. $[\alpha]_{\text{D}}^{27}$ = -60.2 (CHCl_3 , c = 1.0).



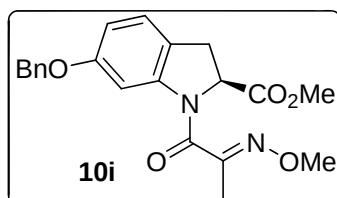
White solid (127.7 mg, 88% yield); R_f = 0.46, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 500 MHz): δ = 8.12 (s, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.88 (d, J = 7.0 Hz, 1H), 5.49 (d, J = 9.5 Hz, 1H), 3.92 (s, 3H), 3.70 (s, 3H), 3.53 (dd, J = 16.0, 11.0 Hz, 1H), 3.15 (d, J = 16.0 Hz, 1H), 2.35 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): δ = 172.6, 163.5, 152.6, 143.2, 137.9, 126.3, 125.4, 124.0, 118.7, 62.9, 62.5, 52.6, 33.4, 21.8, 11.9; ESI-HRMS Calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 291.1339; Found: 291.1338. $[\alpha]_{\text{D}}^{27}$ = -64.0 (CHCl_3 , c = 1.0).



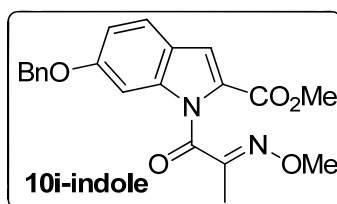
Light yellow oil (180.3 mg, 85% yield); R_f = 0.32, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 8.25 (s, 1H), 7.20 (d, J = 8.0 Hz, 1H), 6.97 (dd, J = 8.0, 1.6 Hz, 1H), 5.59 (d, J = 9.6 Hz, 1H), 3.94 (s, 3H), 3.73 (s, 3H), 3.59 (dd, J = 16.8, 11.2 Hz, 1H), 3.23 (dd, J = 16.8, 2.8 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 172.0, 163.8, 152.3, 149.0, 144.7, 129.4, 125.2, 118.9 (q, J = 319.3 Hz), 117.3, 111.7, 63.3, 62.7, 52.8, 33.1, 11.7; ESI-HRMS Calcd for $\text{C}_{15}\text{H}_{16}\text{F}_3\text{N}_2\text{O}_7\text{S}^+$ $[\text{M}+\text{H}^+]$: 425.0625; Found: 425.0622. $[\alpha]_{\text{D}}^{27}$ = -65.4 (CHCl_3 , c = 1.0).



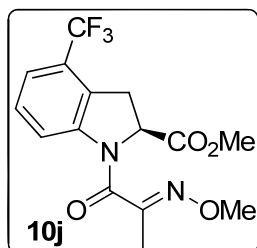
White solid (150.4 mg, 90% yield); R_f = 0.51, hexane/EtOAc = 2:1; ^1H NMR (CDCl_3 , 500 MHz): δ = 8.02 (s, 1H), 7.13 (d, J = 8.5 Hz, 1H), 6.79 (d, J = 7.0 Hz, 1H), 5.55 (d, J = 9.0 Hz, 1H), 3.92 (s, 3H), 3.17 (s, 3H), 3.55 (dd, J = 16.5, 11.0 Hz, 1H), 3.19 (dd, J = 16.5, 2.5 Hz, 1H), 2.27 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): δ = 172.4, 169.6, 163.5, 152.5, 150.4, 144.1, 126.6, 124.5, 117.9, 112.1, 63.2, 62.6, 52.7, 33.2, 21.2, 11.8; ESI-HRMS Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_6\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 357.1057; Found: 357.1059. $[\alpha]_{\text{D}}^{26}$ = -89.2 (CHCl_3 , c = 1.0).



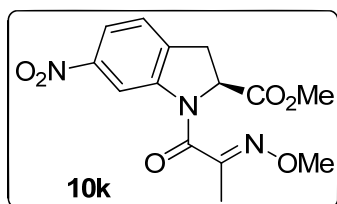
Light yellow solid (124.3 mg, 65% yield); R_f = 0.54, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 500 MHz): δ = 8.08 (s, 1H), 7.45 (d, J = 7.5 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.32 (d, J = 7.3 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.52 (d, J = 9.0 Hz, 1H), 5.08 (s, 2H), 3.94 (s, 3H), 3.72 (s, 3H), 3.52 (dd, J = 16.0, 11.0 Hz, 1H), 3.14 (d, J = 16.0 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): δ = 172.6, 163.6, 158.9, 152.6, 144.3, 137.1, 128.6, 128.0, 127.7, 124.6, 121.3, 112.1, 104.9, 70.4, 63.4, 62.6, 52.6, 33.0, 11.9; ESI-HRMS Calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_5^+$ [$\text{M}+\text{H}^+$]: 383.1601; Found: 383.1595. $[\alpha]_{\text{D}}^{27}$ = -65.8 (CHCl_3 , c = 1.0).



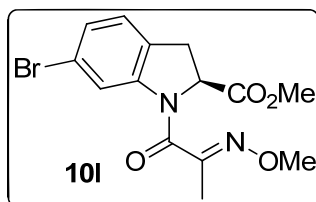
White solid (22.8 mg, 12% yield); R_f = 0.68, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 500 MHz): δ = 7.77 (s, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 7.21 (s, 1H), 7.02 (dd, J = 8.5, 1.5 Hz, 1H), 5.13 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): δ = 165.9, 162.4, 159.5, 153.7, 139.8, 136.8, 130.5, 128.7, 128.2, 127.8, 123.2, 121.5, 116.2, 115.1, 99.1, 70.5, 63.2, 52.3, 11.9; ESI-HRMS Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_5\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 403.1264; Found: 403.1261.



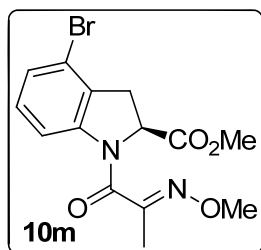
Light yellow solid (148.0 mg, 86% yield); R_f = 0.54, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 8.47 (s, 1H), 7.38-7.30 (m, 2H), 5.57 (d, J = 9.6 Hz, 1H), 3.94 (s, 3H), 3.74 (s, 3H), 3.70-3.66 (m, 1H), 3.38 (d, J = 17.2 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 172.1, 163.8, 152.4, 144.5, 128.7, 127.4, 126.7 (q, J = 32.0 Hz), 124.0 (q, J = 271.0 Hz), 121.3, 121.2, 62.7, 62.6, 52.8, 32.6, 11.8; ESI-HRMS Calcd for $\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_2\text{O}_4\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 367.0876; Found: 367.0878. $[\alpha]_{\text{D}}^{27}$ = -64.6 (CHCl_3 , c = 1.0).



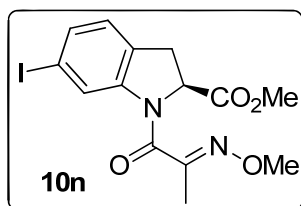
Light yellow solid (86.7 mg, 54% yield); R_f = 0.41, hexane/EtOAc = 2:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 9.06 (s, 1H), 7.94 (dd, J = 8.0, 2.0 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 5.62 (d, J = 10.0 Hz, 1H), 3.94 (s, 3H), 3.65 (s, 3H), 3.69-3.61 (m, 1H), 3.28 (dd, J = 17.6, 2.8 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 171.8, 163.7, 152.3, 148.2, 144.2, 136.5, 124.6, 120.1, 113.0, 63.1, 62.8, 52.9, 33.5, 11.7; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_3\text{O}_6^+$ [$\text{M}+\text{H}^+$]: 322.1034; Found: 322.1030. $[\alpha]_{\text{D}}^{27}$ = -69.3 (CHCl_3 , c = 1.0).



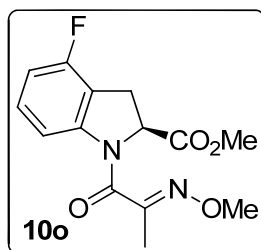
Colorless oil (158.1 mg, 89% yield); $R_f = 0.45$, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.46$ (s, 1H), 7.18 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 5.52 (d, $J = 9.5$ Hz, 1H), 3.93 (s, 3H), 3.71 (s, 3H), 3.51 (dd, $J = 16.5, 11.0$ Hz, 1H), 3.14 (dd, $J = 16.5, 3.0$ Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.3, 163.6, 152.4, 144.4, 128.2, 127.6, 125.5, 121.5, 121.2, 62.9, 62.6, 52.7, 33.3, 11.8$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 355.0288; Found: 355.0287. $[\alpha]_D^{26} = -54.3$ (CHCl_3 , $c = 1.0$).



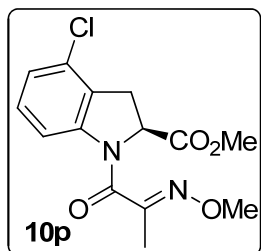
White solid (150.9 mg, 85% yield); $R_f = 0.54$, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.19$ (d, $J = 7.6$ Hz, 1H), 7.19 (d, $J = 7.6$ Hz, 1H), 7.11 (t, $J = 8.0$ Hz, 1H), 5.52 (d, $J = 9.2$ Hz, 1H), 3.92 (s, 3H), 3.73 (s, 3H), 3.51 (dd, $J = 17.2, 11.2$ Hz, 1H), 3.19 (dd, $J = 16.8, 3.2$ Hz, 1H), 2.06 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 172.1, 163.7, 152.4, 144.1, 129.9, 129.7, 127.4, 118.9, 116.7, 62.6, 61.9, 52.7, 35.0, 11.8$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 355.0288; Found: 355.0287. $[\alpha]_D^{27} = -52.0$ (CHCl_3 , $c = 1.0$).



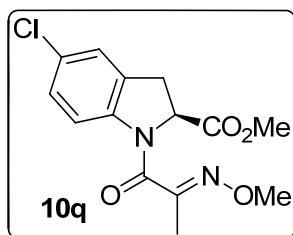
Light yellow solid (166.9 mg, 83% yield); $R_f = 0.41$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.65$ (s, 1H), 7.38 (d, $J = 8.0$ Hz, 1H), 6.90 (d, $J = 8.0$ Hz, 1H), 5.50 (d, $J = 10.0$ Hz, 1H), 3.93 (s, 3H), 3.71 (s, 3H), 3.51 (dd, $J = 16.5, 11.0$ Hz, 1H), 3.14 (dd, $J = 16.5, 2.5$ Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.2, 163.5, 152.4, 144.4, 133.7, 129.1, 126.8, 125.9, 92.7, 62.8, 62.6, 52.7, 33.4, 11.8$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{16}\text{IN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 403.0149; Found: 403.0144. $[\alpha]_D^{27} = -39.0$ (CHCl_3 , $c = 1.0$).



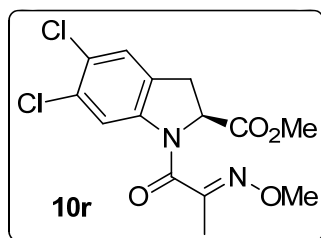
Light yellow solid (117.8 mg, 80% yield); $R_f = 0.50$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.04$ (d, $J = 7.0$ Hz, 1H), 7.22 (q, $J = 7.3$ Hz, 1H), 6.77 (t, $J = 8.5$ Hz, 1H), 5.56 (d, $J = 10.0$ Hz, 1H), 3.93 (s, 3H), 3.73 (s, 3H), 3.55 (dd, $J = 16.5, 11.0$ Hz, 1H), 3.27 (dd, $J = 16.5, 2.5$ Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.2, 163.6, 158.8$ (d, $J = 250.0$ Hz), 157.8, 152.5, 145.5, 129.9 (d, $J = 7.6$ Hz), 115.7 (d, $J = 20.6$ Hz), 113.9, 111.5 (d, $J = 19.5$ Hz), 62.9, 62.6, 52.8, 30.0, 11.8; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{15}\text{FN}_2\text{O}_4\text{Na}^+$ $[\text{M}+\text{Na}^+]$: 317.0908; Found: 317.0907. $[\alpha]_D^{27} = -75.4$ (CHCl_3 , $c = 1.0$).



White solid (127.4 mg, 82% yield); $R_f = 0.57$, hexane/EtOAc = 4:1; ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.15$ (d, $J = 7.0$ Hz, 1H), 7.19 (t, $J = 8.0$ Hz, 1H), 7.04 (d, $J = 8.0$ Hz, 1H), 5.54 (d, $J = 10.0$ Hz, 1H), 3.93 (s, 3H), 3.73 (s, 3H), 3.54 (dd, $J = 17.0, 11.0$ Hz, 1H), 3.24 (dd, $J = 17.0, 2.5$ Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.1, 163.7, 152.4, 144.4, 130.2, 129.6, 127.8, 124.6, 116.2, 62.6, 62.3, 52.8, 33.1, 11.8$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{16}\text{ClN}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 311.0793; Found: 311.0792. $[\alpha]_D^{27} = -63.3$ (CHCl_3 , $c = 1.0$).

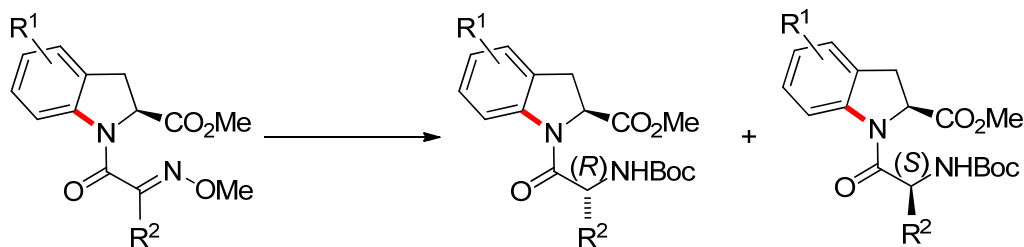


Colorless oil (127.5 mg, 82% yield); $R_f = 0.41$, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.18$ (d, $J = 8.5$ Hz, 1H), 7.19 (d, $J = 8.5$ Hz, 1H), 7.12 (s, 1H), 5.50 (d, $J = 10.5$ Hz, 1H), 3.91 (s, 3H), 3.70 (s, 3H), 3.54 (dd, $J = 16.5, 11.0$ Hz, 1H), 3.16 (dd, $J = 16.5, 2.0$ Hz, 1H), 2.06 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.2, 163.4, 152.4, 141.8, 131.1, 129.5, 127.9, 124.6, 118.8, 62.7, 62.6, 52.7, 33.4, 11.8$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{15}\text{ClN}_2\text{O}_4^+$ $[\text{M}+\text{Na}^+]$: 333.0613; Found: 333.0614. $[\alpha]_D^{27} = -54.7$ (CHCl_3 , $c = 1.0$).

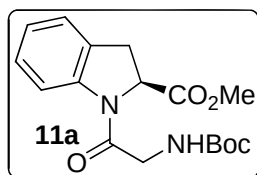


White solid (124.3 mg, 72% yield); $R_f = 0.41$, hexane/EtOAc = 3:1; ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.42$ (s, 1H), 7.23 (s, 1H), 5.54 (d, $J = 10.5$ Hz, 1H), 3.93 (s, 3H), 3.72 (s, 3H), 3.54 (dd, $J = 17.0, 11.0$ Hz, 1H), 3.16 (dd, $J = 16.5, 2.5$ Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.0, 163.5, 152.3, 142.7, 131.8, 129.3, 127.7, 125.8, 119.7, 63.1, 62.7, 52.8, 33.1, 11.8$; ESI-HRMS Calcd for $\text{C}_{14}\text{H}_{15}\text{Cl}_2\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}^+]$: 345.0403; Found: 345.0402. $[\alpha]_D^{27} = -44.7$ (CHCl_3 , $c = 1.0$).

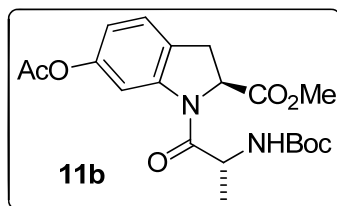
7. General procedure F for hydrogenation of MIA



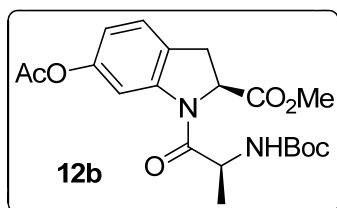
To a solution of indoline product (0.3 mmol, 1.0 eq) and $(\text{Boc})_2\text{O}$ (197 mg, 0.9 mmol, 3.0 eq) in MeOH (0.2 M) was added 10% Raney Ni. The mixture was stirred under H_2 atmosphere (1 atm) at room temperature overnight. After Raney Ni was filtered off, the filtrate was concentrated *in vacuo*.



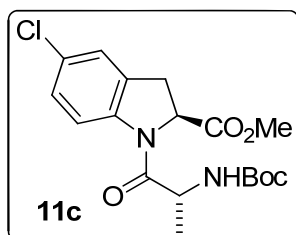
Dipeptide was purified by silica gel flash chromatography using 15-25% ethyl acetate in hexanes to give **11a** as a white solid (93.3 mg, 93% yield); $R_f = 0.57$, hexane/EtOAc = 1:1; (containing a mixture of two amide rotamers) **Major amide rotamer**, ^1H NMR (CDCl_3 , 500 MHz): $\delta = 8.17$ (d, $J = 7.0$ Hz, 1H), 7.24-7.15 (m, 2H), 7.04 (t, $J = 7.3$ Hz, 1H), 5.56-5.51 (br, 1H), 4.93 (d, $J = 9.5$ Hz, 1H), 4.11 (d, $J = 16.0$ Hz, 1H), 3.81 (d, $J = 17.0$ Hz, 1H), 3.75 (s, 3H), 3.59 (t, $J = 13.0$ Hz, 1H), 3.30 (d, $J = 16.0$ Hz, 1H), 1.45 (s, 9H); **Minor amide rotamer**, ^1H NMR (CDCl_3 , 500 MHz): $\delta = 7.24$ -7.15 (m, 3H), 7.04 (t, $J = 7.3$ Hz, 1H), 5.56-5.51 (br, 1H), 5.19 (d, $J = 9.0$ Hz, 1H), 4.41-4.32 (m, 2H), 3.72 (s, 3H), 3.49 (t, $J = 13.5$ Hz, 1H), 3.13 (d, $J = 11.0$ Hz, 1H), 1.45 (s, 9H). **Mixture amide rotamer** ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 171.5, 171.4, 167.4, 155.9, 142.3, 140.0, 130.8, 128.5, 128.2, 125.9, 124.7, 124.5, 124.3, 117.5, 114.2, 80.0, 60.4, 59.8, 53.3, 52.8, 45.2, 43.6, 33.8, 31.7, 28.5$. ESI-HRMS Calcd for $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_5\text{Na}^+$ $[\text{M}+\text{Na}^+]$: 357.1421; Found: 357.1423. $[\alpha]_D^{26} = -82.7$ (CHCl_3 , $c = 1.0$).



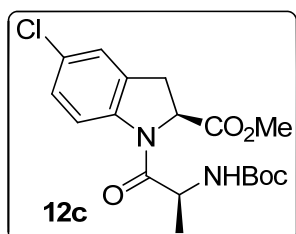
Dipeptide was purified by silica gel flash chromatography using 10-20% ethyl acetate in hexanes to give **11b** as a white solid (78.0 mg, 64% yield); $R_f = 0.34$, hexane/EtOAc = 2:1; (containing a mixture of two amide rotamers, 6:1) **Major amide rotamer**, ^1H NMR (CDCl_3 , 500 MHz): $\delta = 7.95$ (s, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 6.77 (d, $J = 7.5$ Hz, 1H), 5.71 (d, $J = 10.0$ Hz, 1H), 5.11 (d, $J = 8.5$ Hz, 1H), 4.36-4.33 (m, 1H), 3.76 (s, 3H), 3.58 (dd, $J = 16.0, 10.5$ Hz, 1H), 3.31 (d, $J = 16.5$ Hz, 1H), 2.26 (s, 3H), 1.39 (s, 9H), 1.37 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.4, 172.9, 169.7, 155.4, 150.3, 143.3, 127.1, 124.5, 117.8, 112.0, 80.2, 61.3, 53.1, 48.1, 32.9, 28.4, 21.1, 18.1$; ESI-HRMS Calcd for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_7\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 429.1632; Found: 429.1635. $[\alpha]_D^{26} = -7.5$ (CHCl_3 , $c = 1.0$).



Dipeptide was purified by silica gel flash chromatography using 10-20% ethyl acetate in hexanes to give **12b** as a white solid (24.4 mg, 20% yield); $R_f = 0.32$, hexane/EtOAc = 2:1; (containing a mixture of two amide rotamers, 2:1) **Major amide rotamer**, ^1H NMR (CDCl_3 , 500 MHz): $\delta = 7.99$ (s, 1H), 7.14 (d, $J = 8.0$ Hz, 1H), 6.79-6.78 (m, 1H), 5.40 (d, $J = 8.0$ Hz, 1H), 4.97 (d, $J = 10.0$ Hz, 1H), 4.45-4.40 (m, 1H), 3.76 (s, 3H), 3.57 (dd, $J = 16.5, 11.0$ Hz, 1H), 3.32 (d, $J = 16.0$ Hz, 1H), 2.27 (s, 3H), 1.43 (s, 9H), 1.37 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 172.1, 171.3, 169.7, 154.9, 150.5, 143.4, 126.3, 124.7, 117.9, 117.8, 79.8, 61.2, 53.5, 48.7, 33.2, 28.5, 21.2, 19.9$; **Minor amide rotamer**, ^1H NMR (CDCl_3 , 500 MHz): $\delta = 7.17$ (d, $J = 8.0$ Hz, 1H), 6.91 (s, 1H), 6.79-6.78 (m, 1H), 5.50 (d, $J = 8.0$ Hz, 1H), 5.25-5.23 (m, 1H), 4.93-4.90 (m, 1H), 3.72 (s, 3H), 3.45 (dd, $J = 16.5, 11.0$ Hz, 1H), 3.09 (dd, $J = 16.5, 3.5$ Hz, 1H), 3.01 (s, 3H), 1.51 (d, $J = 7.0$ Hz, 3H), 1.43 (s, 9H); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 171.7, 171.3, 169.4, 155.3, 150.8, 140.8, 128.4, 126.1, 117.3, 108.4, 80.0, 61.2, 52.7, 48.7, 30.8, 28.5, 21.3, 18.8$; ESI-HRMS Calcd $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_7\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 429.1632; Found: 429.1648. $[\alpha]_D^{26} = -93.5$ (CHCl_3 , $c = 1.0$).

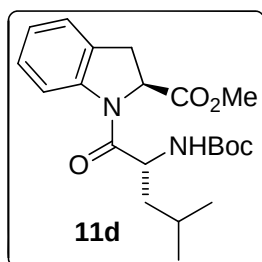


Dipeptide was purified by silica gel flash chromatography using 10-20% ethyl acetate in hexanes to give **11c** as a white solid (75.8 mg, 66% yield); $R_f = 0.35$, hexane/EtOAc = 3:1; (containing a mixture of two amide rotamers, 6:1) **Major amide rotamer**, ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.12$ (d, $J = 8.4$ Hz, 1H), 7.17 (d, $J = 8.8$ Hz, 1H), 7.13 (s, 1H), 5.69 (d, $J = 10.0$ Hz, 1H), 5.15 (d, $J = 7.2$ Hz, 1H), 4.37-4.34 (m, 1H), 3.76 (s, 3H), 3.59 (dd, $J = 16.8, 10.8$ Hz, 1H), 3.30 (d, $J = 16.8$ Hz, 1H), 1.39 (s, 9H), 1.37 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 172.4, 171.8, 155.5, 141.1, 131.6, 129.6, 127.9, 124.7, 118.8, 80.2, 60.8, 53.1, 48.1, 33.1, 28.4, 18.2$; ESI-HRMS Calcd $\text{C}_{18}\text{H}_{23}\text{ClN}_2\text{O}_5\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 405.1188; Found: 405.1187. $[\alpha]_D^{26} = -15.4$ (CHCl_3 , $c = 1.0$).

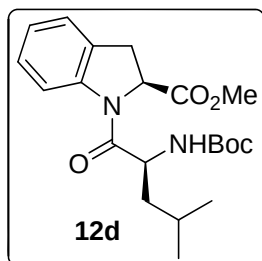


Dipeptide was purified by silica gel flash chromatography using 10-20% ethyl acetate in hexanes to give **12c** as a white solid (24.1 mg, 21% yield); $R_f = 0.32$, hexane/EtOAc = 3:1; (containing a mixture of two amide rotamers, 2:1) **Major amide rotamer**, ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.15$ (d, $J = 8.8$ Hz, 1H), 7.20-7.14 (m, 2H), 5.45-5.39 (m, 1H), 4.96 (d, $J = 8.8$ Hz, 1H), 4.45-4.12 (m, 1H), 3.75 (s, 3H), 3.57 (dd,

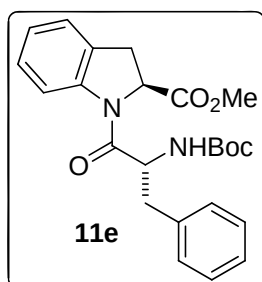
$J = 16.4, 10.4$ Hz, 1H), 3.30 (d, $J = 16.8$ Hz, 1H), 1.42 (s, 9H), 1.37 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.9, 171.1, 154.8, 141.1, 130.7, 129.6, 128.1, 124.7, 118.5, 79.8, 60.7, 53.4, 48.6, 33.4, 28.4, 19.8$; **Minor amide rotamer**, ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.20\text{--}7.14$ (m, 2H), 7.09 (d, $J = 8.4$ Hz, 1H), 5.45–5.39 (m, 1H), 5.25–5.22 (m, 1H), 4.96 (d, $J = 8.8$ Hz, 1H), 3.72 (s, 3H), 3.46 (dd, $J = 16.8, 11.2$ Hz, 1H), 3.08 (dd, $J = 17.2, 3.2$ Hz, 1H), 1.50 (d, $J = 6.8$ Hz, 3H), 1.41 (s, 9H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.6, 171.2, 155.2, 138.8, 133.2, 129.4, 128.2, 126.1, 114.9, 78.0, 60.7, 52.7, 48.4, 31.3, 28.4, 18.7$; ESI-HRMS Calcd $\text{C}_{18}\text{H}_{23}\text{ClN}_2\text{O}_5\text{Na}^+$ $[\text{M}+\text{Na}^+]$: 405.1188; Found: 405.1196. $[\alpha]_{\text{D}}^{26} = -71.1$ (CHCl_3 , $c = 1.0$).



Dipeptide was purified by preparative liquid chromatography using H_2O and MeCN to give **11d** as colorless oil (77.3 mg, 66% yield); $R_f = 0.52$, hexane/EtOAc = 3:1; (containing a mixture of two amide rotamers, 5:1) **Major amide rotamer**, ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.16$ (d, $J = 8.4$ Hz, 1H), 7.23 (t, $J = 7.8$ Hz, 1H), 7.17 (d, $J = 7.2$ Hz, 1H), 7.05 (d, $J = 7.4$ Hz, 1H), 5.67 (d, $J = 10.0$ Hz, 1H), 5.00 (d, $J = 9.2$ Hz, 1H), 4.34 (dt, $J = 9.8, 2.8$ Hz, 1H), 3.75 (s, 3H), 3.63 (dd, $J = 16.4, 11.2$ Hz, 1H), 3.28 (d, $J = 16.4$ Hz, 1H), 1.77–1.46 (m, 3H), 1.40 (s, 9H), 0.94 (d, $J = 6.4$ Hz, 3H), 0.89 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 172.2, 172.1, 155.8, 142.4, 129.7, 127.9, 124.6, 124.5, 118.0, 80.1, 60.5, 52.9, 50.9, 41.2, 33.6, 28.4, 22.5, 23.6, 21.5$; ESI-HRMS Calcd for $\text{C}_{21}\text{H}_{30}\text{N}_2\text{O}_5\text{Na}^+$ $[\text{M}+\text{Na}^+]$: 413.2047; Found: 413.2060. $[\alpha]_{\text{D}}^{26} = -55.6$ (CHCl_3 , $c = 1.0$).

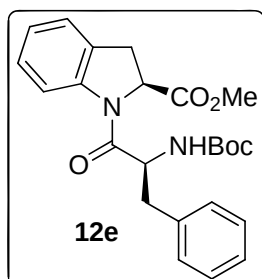


Dipeptide was purified by preparative liquid chromatography using H_2O and MeCN to give **12d** as colorless oil (28.1 mg, 24% yield); $R_f = 0.52$, hexane/EtOAc = 3:1; (containing a mixture of two amide rotamers, 2:1) **Major amide rotamer**, ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.24$ (d, $J = 8.0$ Hz, 1H), 7.31–7.17 (m, 2H), 7.06 (t, $J = 7.4$ Hz, 1H), 5.29–5.27 (m, 1H), 4.96 (d, $J = 10.8$ Hz, 1H), 4.48–4.42 (m, 1H), 3.76 (s, 3H), 3.63 (dd, $J = 16.0, 10.8$ Hz, 1H); 3.34 (d, $J = 16.4$ Hz, 1H), 1.73–1.68 (m, 2H), 1.62–1.56 (m, 1H), 1.43 (s, 9H), 0.98 (d, $J = 6.4$ Hz, 3H), 0.95 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 172.3, 171.5, 155.3, 142.5, 128.8, 128.2, 124.7, 124.5, 117.5, 79.6, 60.5, 52.6, 51.3, 40.9, 33.7, 28.5, 24.8, 23.6, 22.1$; **Minor amide rotamer**, ^1H NMR (CDCl_3 , 400 MHz): $\delta = 7.31\text{--}7.19$ (m, 3H), 7.06 (t, $J = 7.4$ Hz, 1H), 5.29–5.27 (m, 1H), 5.22–5.19 (m, 1H), 5.13–5.08 (m, 1H), 3.73 (s, 3H), 3.48 (dd, $J = 16.0, 10.8$ Hz, 1H); 3.12 (d, $J = 16.4$ Hz, 1H), 1.73–1.68 (m, 2H), 1.62–1.56 (m, 1H), 1.43 (s, 9H), 1.14 (d, $J = 6.4$ Hz, 3H), 0.98 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 172.2, 171.7, 155.8, 140.2, 131.1, 128.2, 125.9, 124.1, 114.2, 79.8, 60.6, 53.4, 51.4, 41.3, 31.4, 28.5, 25.0, 23.7, 21.8$. ESI-HRMS Calcd for $\text{C}_{21}\text{H}_{30}\text{N}_2\text{O}_5\text{Na}^+$ $[\text{M}+\text{Na}^+]$: 413.2047; Found: 413.2048. $[\alpha]_{\text{D}}^{26} = -83.4$ (CHCl_3 , $c = 1.0$).



Dipeptide was purified by preparative liquid chromatography using H_2O and MeCN to give **11e** as a white solid (78.9 mg, 62% yield); $R_f = 0.50$, hexane/EtOAc = 3:1; (containing a mixture of two amide rotamers) **Mixture of amide rotamers** ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.21$ (d, $J = 6.4$ Hz, 1H), 7.49 (d, $J = 6.0$ Hz, 0.4H), 7.31–7.03 (m, 12H), 5.66 (d, $J = 8.0$ Hz, 0.9H), 5.48 (br, 0.7H), 5.07 (d, $J = 7.2$ Hz, 0.9H), 4.93 (d, $J = 8.0$ Hz, 0.4H), 4.58–4.54 (m, 0.9H), 3.69 (s, 4.1H), 3.62 (dd, $J = 12.8, 8.8$ Hz,

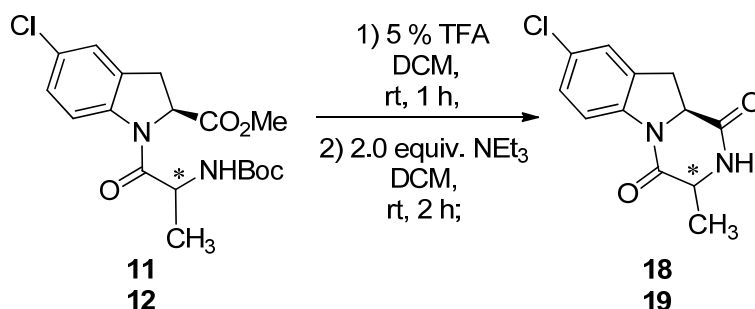
1H); 3.34 (d, $J = 13.2$ Hz, 1H), 3.25 (dd, $J = 11.6, 3.6$ Hz, 1H), 3.16-3.11 (m, 0.5H), 1.73-1.68 (m, 2H), 2.99-2.92 (m, 2.3H), 1.45 (s, 3.8H), 1.32 (s, 9H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 172.1, 171.5, 171.3, 170.3, 155.6, 155.3, 142.4, 140.2, 137.2, 135.9, 131.3, 129.8, 129.5, 129.4, 128.6, 128.3, 128.2, 127.9, 126.8, 125.7, 124.7, 124.5, 124.3, 118.1, 115.5, 80.2, 80.1, 61.3, 60.7, 53.9, 53.3, 53.1, 52.7, 39.9, 38.4$. ESI-HRMS Calcd for $\text{C}_{24}\text{H}_{28}\text{N}_2\text{O}_5\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 447.1890; Found: 447.1891. $[\alpha]_{\text{D}}^{26} = -66.1$ (CHCl_3 , $c = 1.0$).



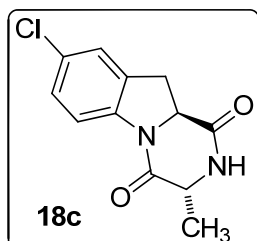
Dipeptide was purified by preparative liquid chromatography using H_2O and MeCN to give **12e** as a white solid (25.4 mg, 20% yield); $R_f = 0.50$, hexane/EtOAc = 3:1; (containing a mixture of two amide rotamers)

Mixture amide rotamer ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.24$ (d, $J = 8.0$ Hz, 1H), 7.31-7.21 (m, 9H), 7.07-7.03 (m, 2.2H), 5.54 (d, $J = 12.0$ Hz, 1H), 5.30 (br, 1H), 4.62-4.56 (m, 1.2H), 4.11 (d, $J = 12.0$ Hz, 1.1H), 3.77 (s, 0.8H), 3.67 (s, 3H), 3.16-2.97 (m, 3.8H), 2.84-2.77 (m, 1.1H), 1.44 (s, 9H), 1.36 (s, 1.7H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 171.3, 170.9, 154.8, 141.6, 136.3, 129.9, 129.6, 129.2, 128.8, 128.6, 128.4, 127.9, 127.2, 127.1, 126.1, 124.8, 124.4, 124.3, 117.8, 114.3, 79.8, 60.7, 60.5, 54.7, 53.3, 52.7, 41.7, 38.4, 32.9, 31.5, 28.5$. ESI-HRMS Calcd for $\text{C}_{24}\text{H}_{28}\text{N}_2\text{O}_5\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 447.1890; Found: 447.1894. $[\alpha]_{\text{D}}^{26} = -83.4$ (CHCl_3 , $c = 1.0$).

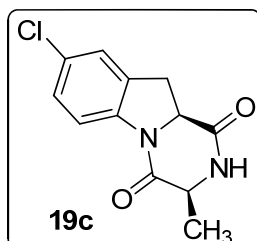
8. General procedure G for Synthesis of cyclic dipeptide product



To a solution of dipeptide product (0.05 mmol, 1.0 eq) in DCM (0.2 M) was added 5% TFA. The mixture was stirred at room temperature for 1h. The solvent was concentrated *in vacuo* and the resulting residue was dissolved in DCM, and was added 2.0 equiv. NEt_3 . The mixture was stirred at room temperature for 2 hours, and purified by silica gel flash chromatography using 30-50% ethyl acetate in hexanes to afford cyclic dipeptide as a white solid in quantitative yields.

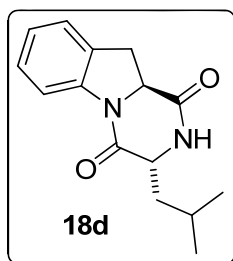


(12.5 mg, quantitative yields); $R_f = 0.33$, EtOAc; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.01$ (d, $J = 8.4$ Hz, 1H), 7.24-7.21 (m, 2H), 7.12 (s, 1H), 4.84 (t, $J = 10.2$ Hz, 1H), 4.21-4.14 (m, 1H), 3.46 (dd, $J = 16.4, 10.4$ Hz, 1H), 3.41 (dd, $J = 16.4, 10.4$ Hz, 1H), 1.59 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 168.6, 165.4, 139.9, 131.3, 130.4, 128.1, 125.3, 117.3, 59.1, 54.1, 31.5, 19.7$; ESI-HRMS Calcd $\text{C}_{12}\text{H}_{11}\text{ClN}_2\text{O}_2\text{Na}^+$ [$\text{M}+\text{Na}^+$]: 273.0401; Found: 273.0402. $[\alpha]_{\text{D}}^{26} = -14.4$ (AcOEt, $c = 0.5$).



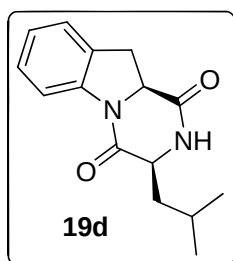
(12.4 mg, quantitative yields); $R_f = 0.35$, EtOAc; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.01$ (d, $J = 8.0$ Hz, 1H), 7.22-7.19 (m, 2H), 6.75 (s, 1H), 4.84 (t, $J = 10.0$ Hz, 1H), 4.26 (q, $J = 6.8$ Hz, 1H), 3.50 (dd, $J = 16.8, 9.6$ Hz, 1H),

3.46 (dd, $J = 16.8, 10.4$ Hz, 1H), 1.56 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 169.5, 165.4, 139.7, 131.4, 130.1, 128.1, 125.3, 116.8, 60.5, 51.8, 30.5, 15.5$; ESI-HRMS Calcd $\text{C}_{12}\text{H}_{11}\text{ClN}_2\text{O}_2\text{Na}^+ [\text{M}+\text{Na}^+]$: 273.0401; Found: 273.0406. $[\alpha]_{\text{D}}^{26} = +1.1$ (AcOEt, $c = 0.5$).



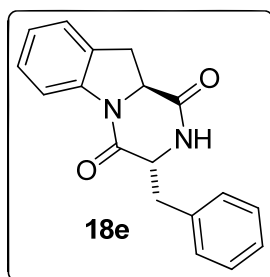
(12.9 mg, quantitative yields); $R_f = 0.34$, hexane/EtOAc = 1:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.09$ (d, $J = 8.0$ Hz, 1H), 7.27-7.23 (m, 2H), 7.10 (t, $J = 7.4$ Hz, 1H), 7.03-7.02 (m, 1H), 4.82 (t, $J = 10.2$ Hz, 1H), 4.10-4.05 (m, 1H), 3.53 (dd, $J = 16.4, 10.4$ Hz, 1H), 3.38 (dd, $J = 16.4, 10.4$ Hz, 1H), 1.87-1.82 (m, 1H), 1.77-1.72 (m, 2H), 1.03 (d, $J = 6.4$ Hz, 3H), 0.99 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 169.1, 165.2, 141.3, 129.3, 128.0, 125.2, 124.9, 116.5, 59.0, 56.9, 42.1, 31.7, 24.8, 23.1, 21.6$.

ESI-HRMS Calcd $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}^+ [\text{M}+\text{Na}^+]$: 281.1260; Found: 281.1260. $[\alpha]_{\text{D}}^{25} = -11.2$ (AcOEt, $c = 0.5$).



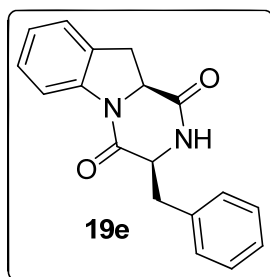
(13.0 mg, quantitative yields); $R_f = 0.40$, hexane/EtOAc = 1:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.09$ (d, $J = 8.0$ Hz, 1H), 7.26-7.23 (m, 2H), 7.09 (t, $J = 7.4$ Hz, 1H), 6.24 (m, 1H), 4.81 (t, $J = 9.8$ Hz, 1H), 4.16-4.13 (m, 1H), 3.62 (dd, $J = 16.8, 9.6$ Hz, 1H), 3.38 (dd, $J = 16.8, 9.6$ Hz, 1H), 2.19-2.12 (m, 1H), 1.88-1.80 (m, 1H), 1.65-1.58 (m, 1H), 1.05 (d, $J = 6.4$ Hz, 3H), 1.00 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 169.8, 165.3, 141.1, 129.5, 128.0, 125.0, 124.9, 116.1, 60.1, 54.0, 38.3, 30.6, 24.9, 23.4, 21.5$.

ESI-HRMS Calcd $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}^+ [\text{M}+\text{Na}^+]$: 281.1260; Found: 281.1264. $[\alpha]_{\text{D}}^{25} = -34.3$ (AcOEt, $c = 0.5$).



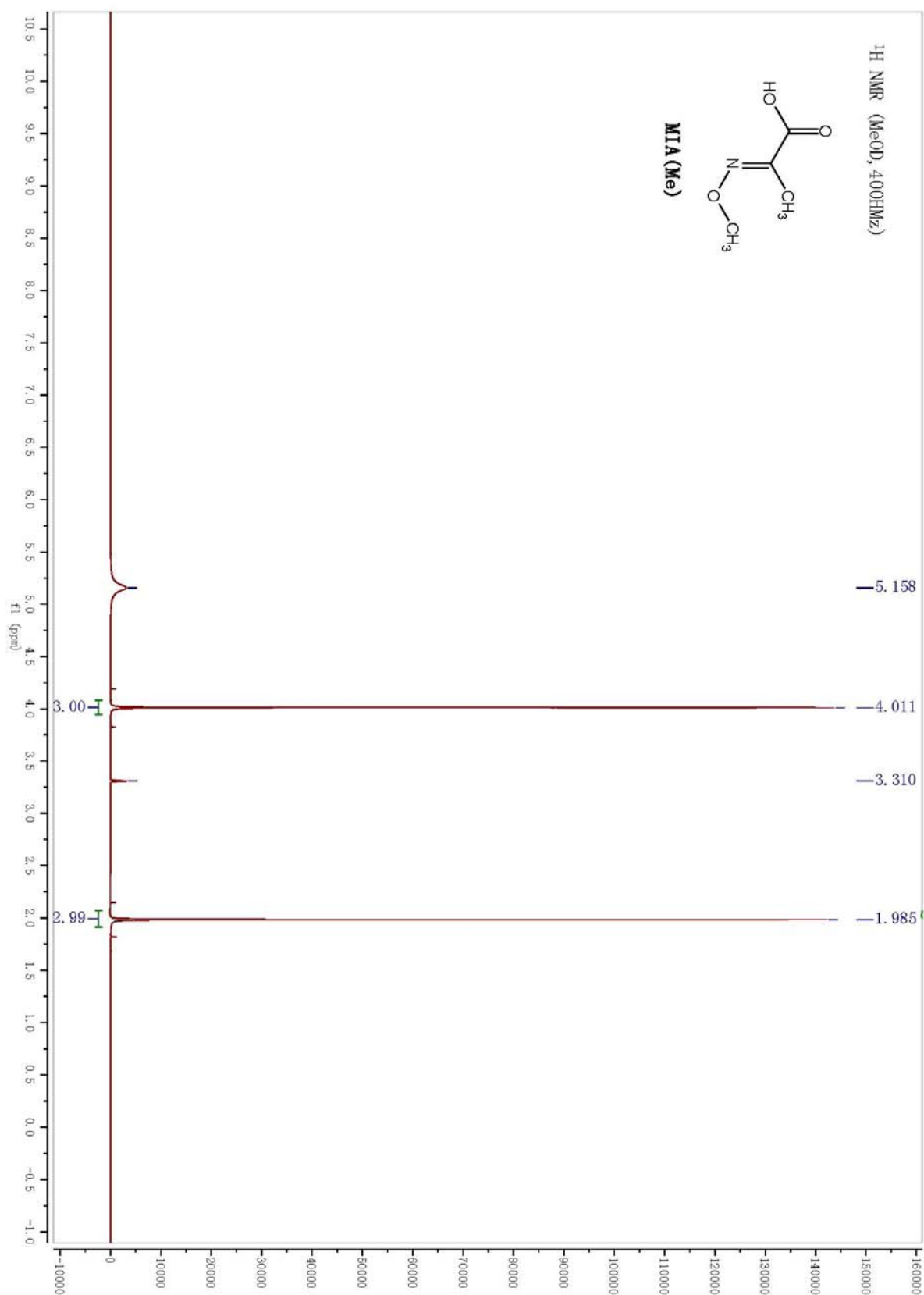
(14.6 mg, quantitative yields); $R_f = 0.28$, hexane/EtOAc = 1:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.15$ (d, $J = 8.0$ Hz, 1H), 7.31-7.25 (m, 6H), 7.21 (d, $J = 7.2$ Hz, 1H), 7.10 (t, $J = 7.4$ Hz, 1H), 6.56-6.48 (br, 1H), 4.39-4.35 (m, 1H), 3.73-3.67 (m, 1H), 3.34-3.26 (m, 2H), 3.19-3.12 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 168.9, 164.0, 141.2, 135.3, 129.9, 129.4, 129.1, 128.0, 127.8, 125.4, 124.9, 116.6, 59.6, 58.9, 40.4, 31.9$. ESI-HRMS Calcd $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2\text{Na}^+ [\text{M}+\text{Na}^+]$: 315.1104; Found: 315.1104.

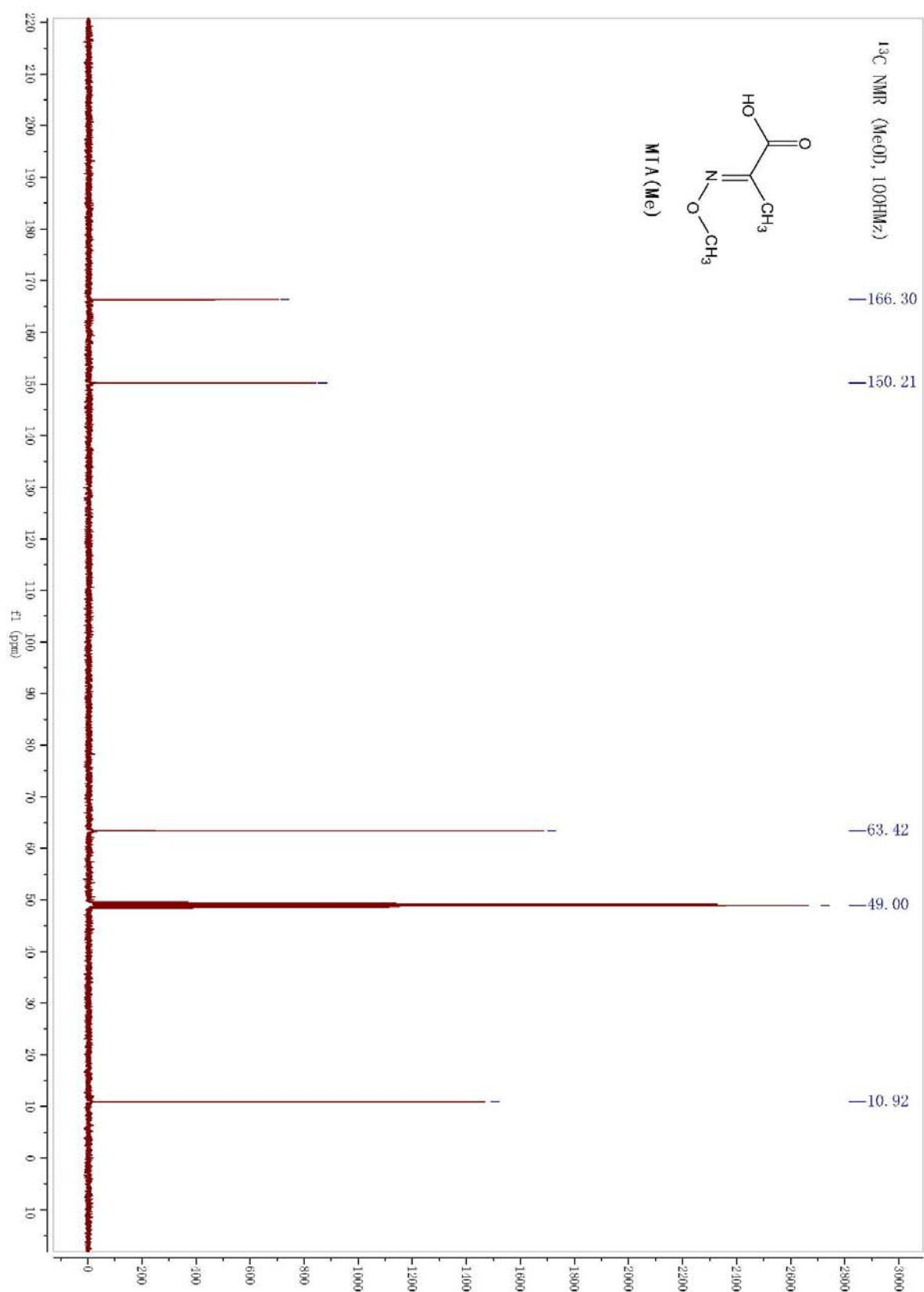
$[\alpha]_{\text{D}}^{25} = +85.3$ (AcOEt, $c = 0.5$).

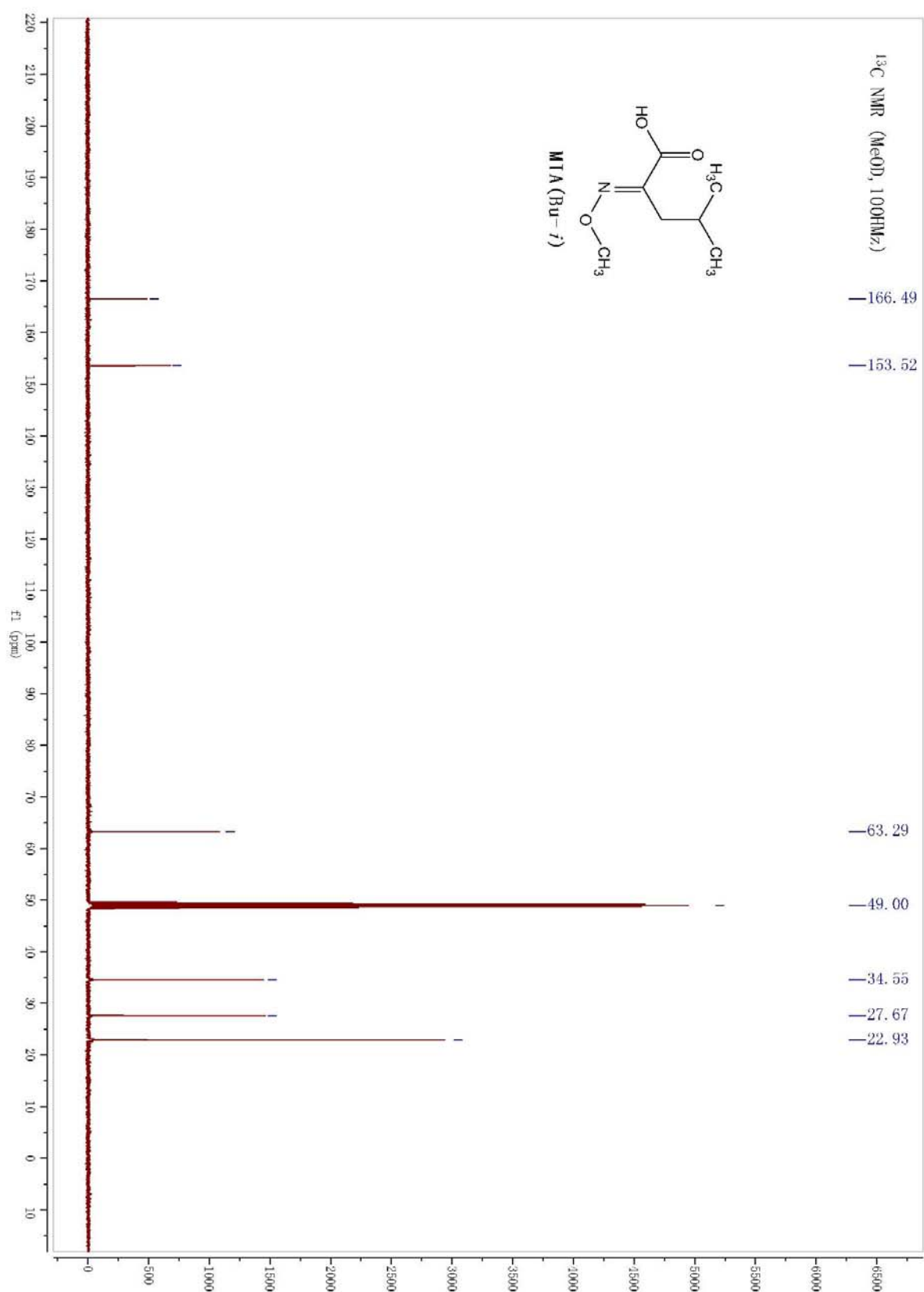


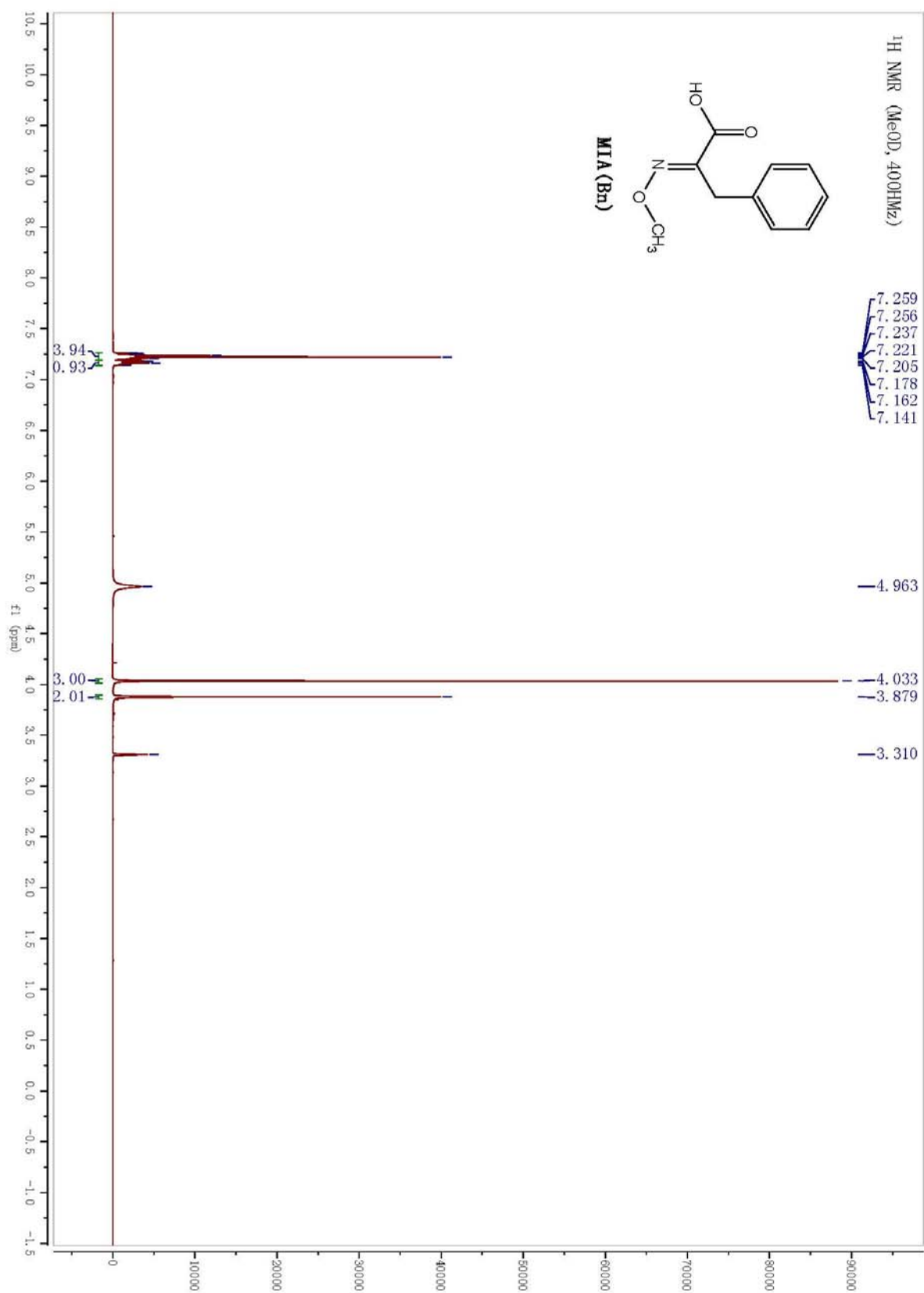
(14.7 mg, quantitative yields); $R_f = 0.33$, hexane/EtOAc = 1:1; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 8.15$ (d, $J = 8.0$ Hz, 1H), 7.40-7.37 (m, 2H), 7.34-7.26 (m, 5H), 7.13 (t, $J = 7.4$ Hz, 1H), 5.73 (s, 1H), 4.80 (t, $J = 9.8$ Hz, 1H), 4.42 (dd, $J = 10.8, 3.6$ Hz, 1H), 3.74 (dd, $J = 14.8, 3.6$ Hz, 1H), 3.61-3.34 (m, 2H), 2.88 (dd, $J = 14.8, 10.8$ Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 169.1, 164.3, 141.1, 135.8, 129.6, 129.2, 128.1, 127.9, 125.2, 125.1, 116.3, 60.3, 56.6, 36.2, 30.1$. ESI-HRMS Calcd $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2\text{Na}^+ [\text{M}+\text{Na}^+]$: 315.1104; Found: 315.1106. $[\alpha]_{\text{D}}^{25} = -115.3$ (AcOEt, $c = 0.25$).

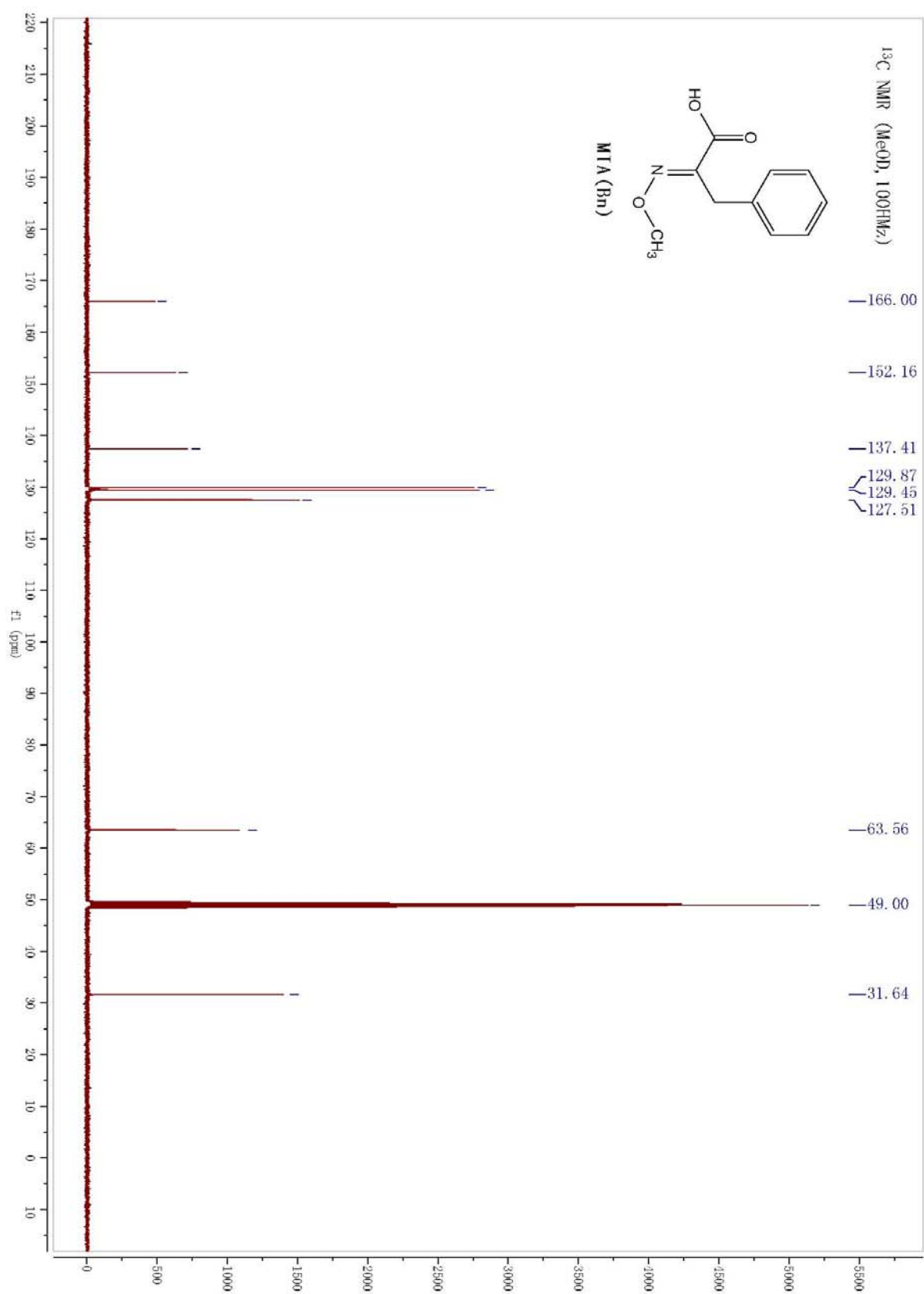
9. Copies of spectra of compounds

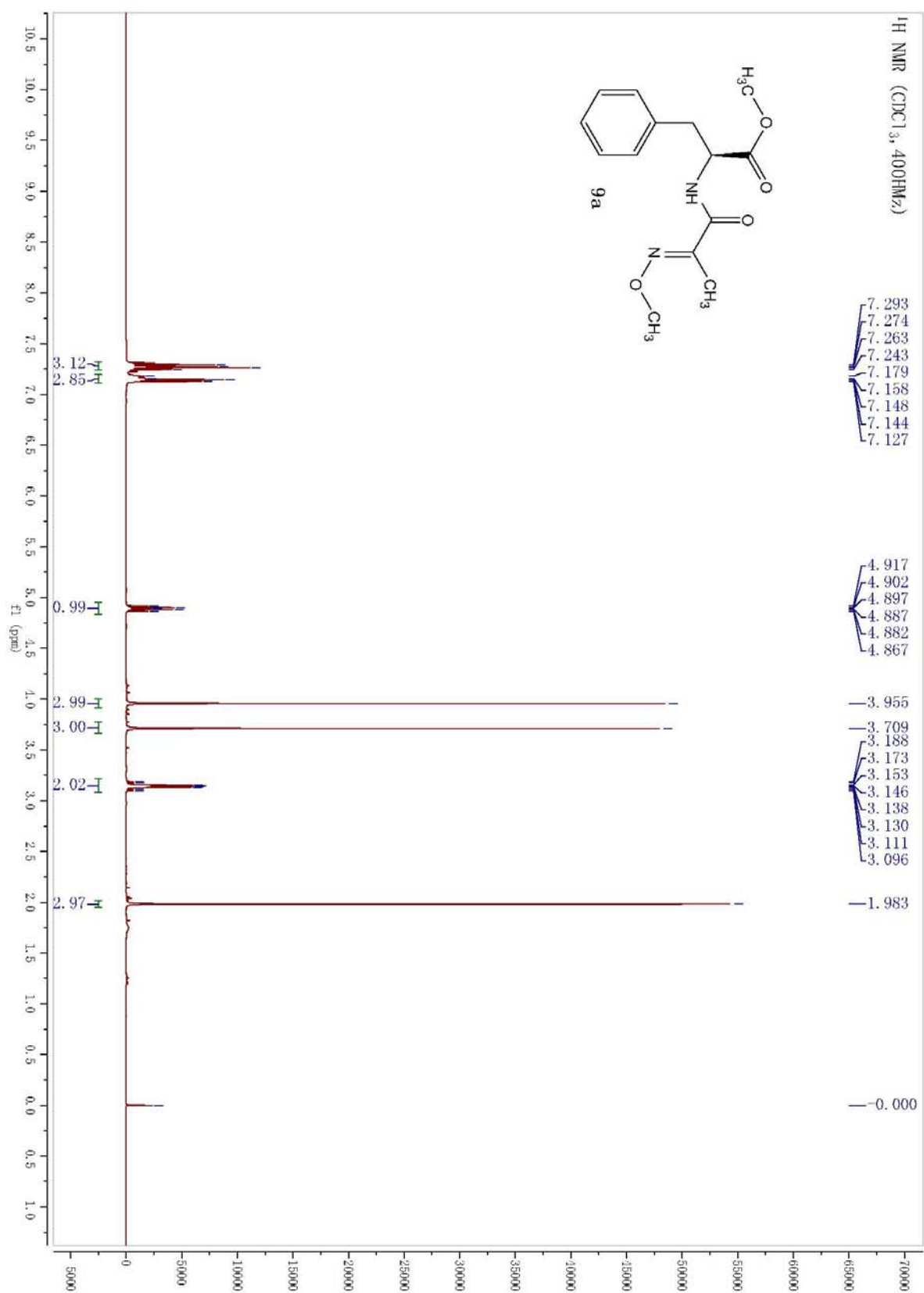


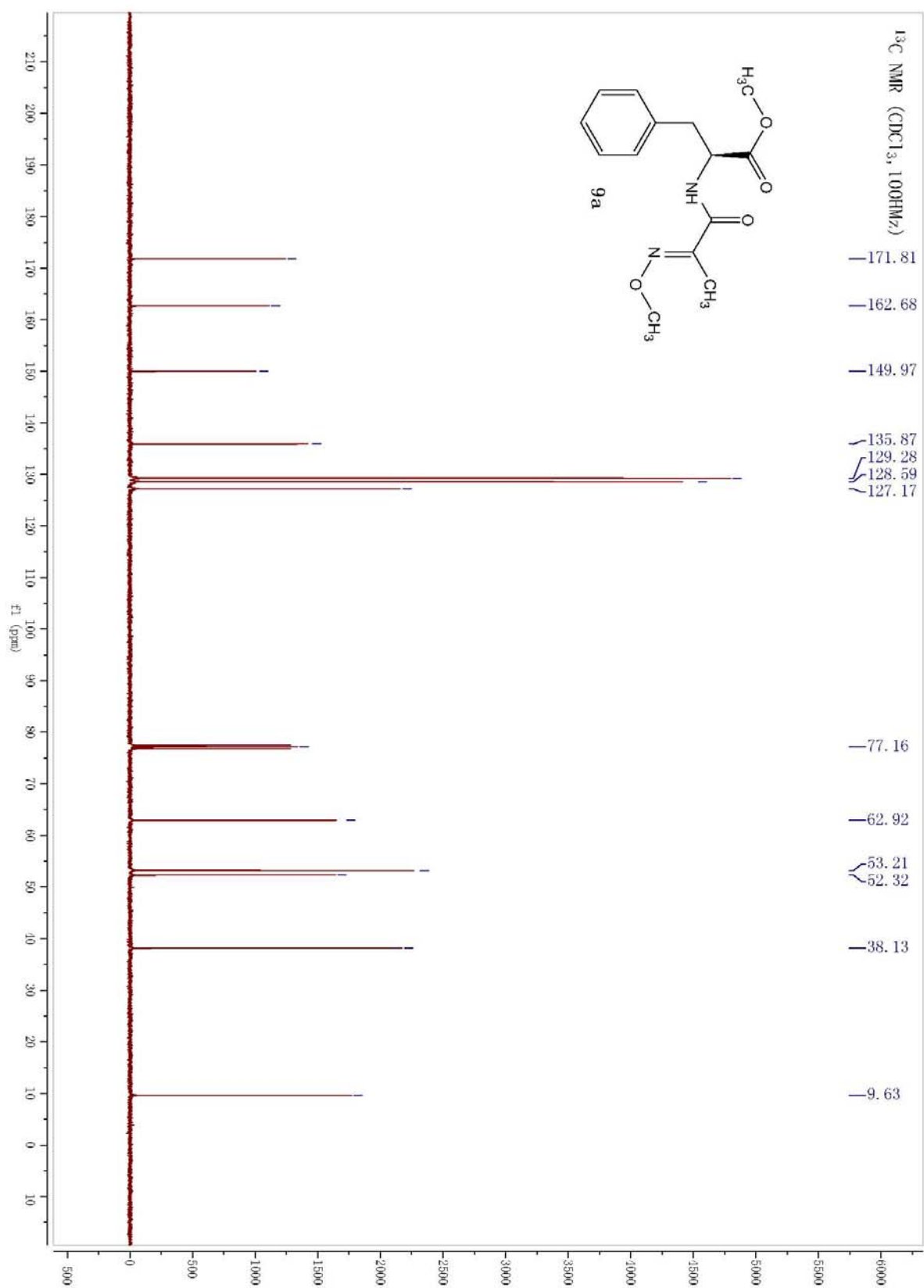


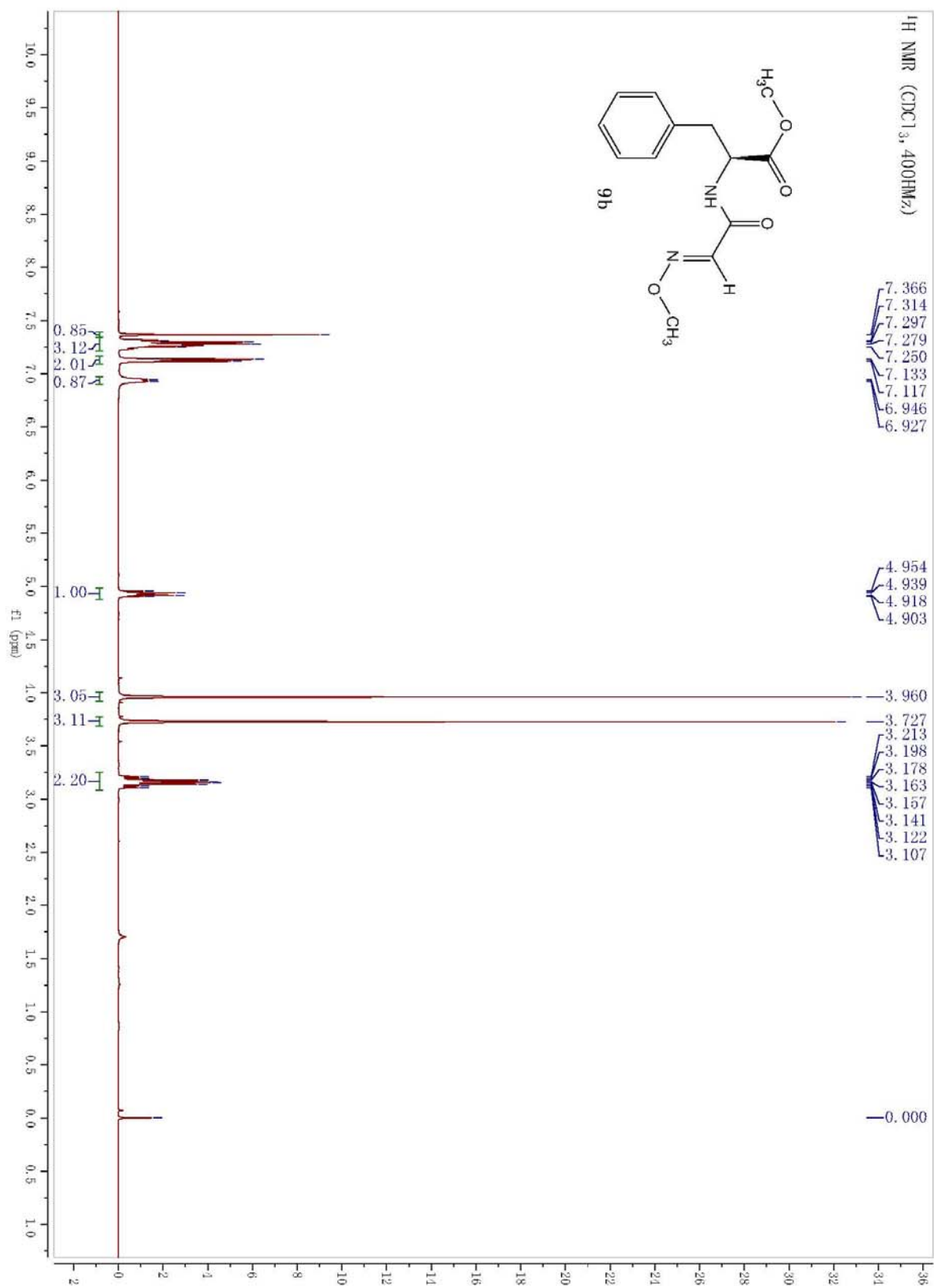


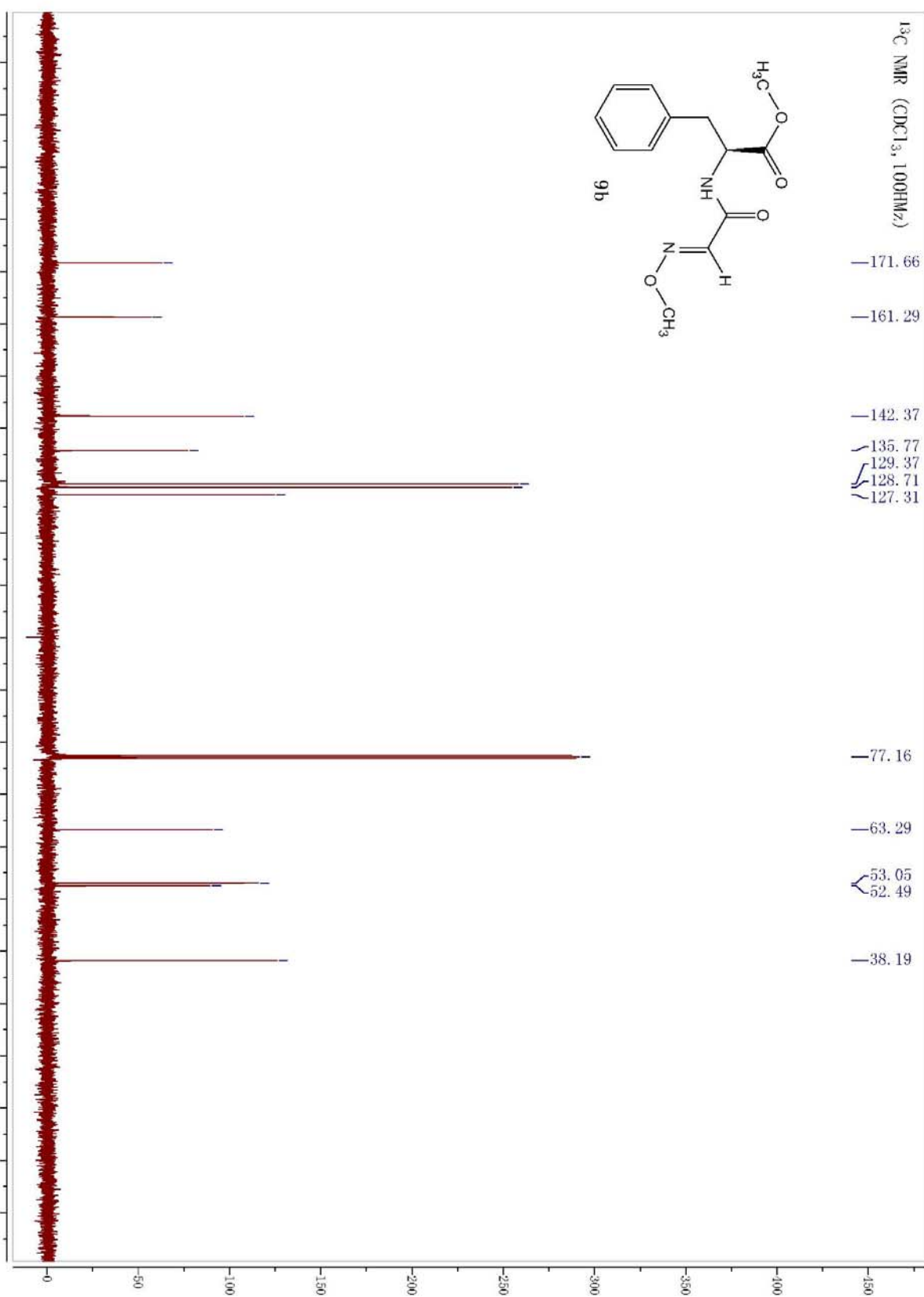


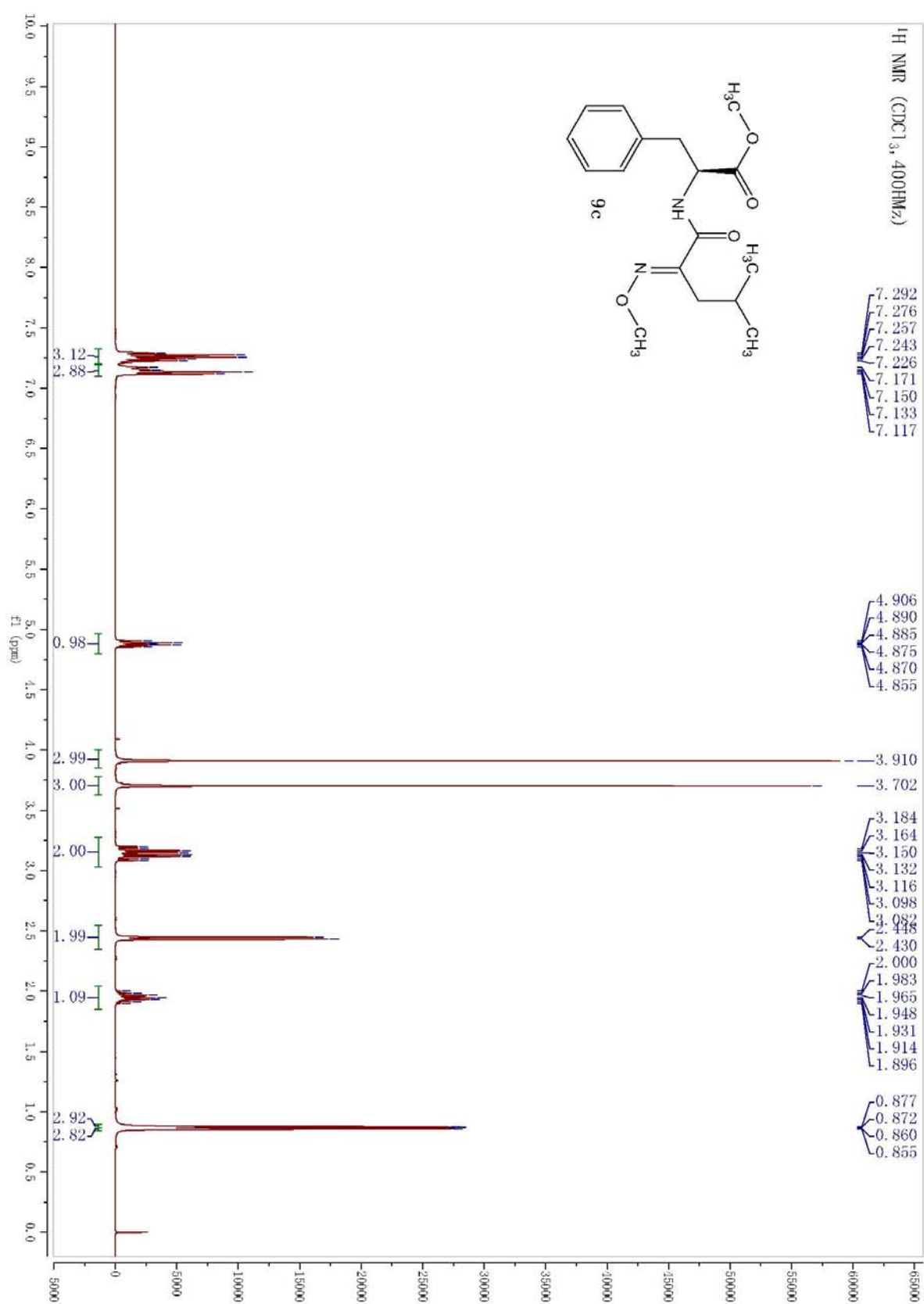


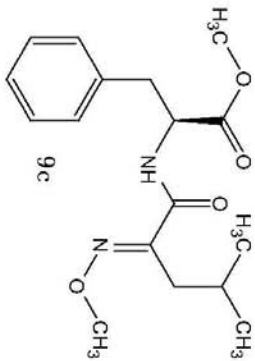


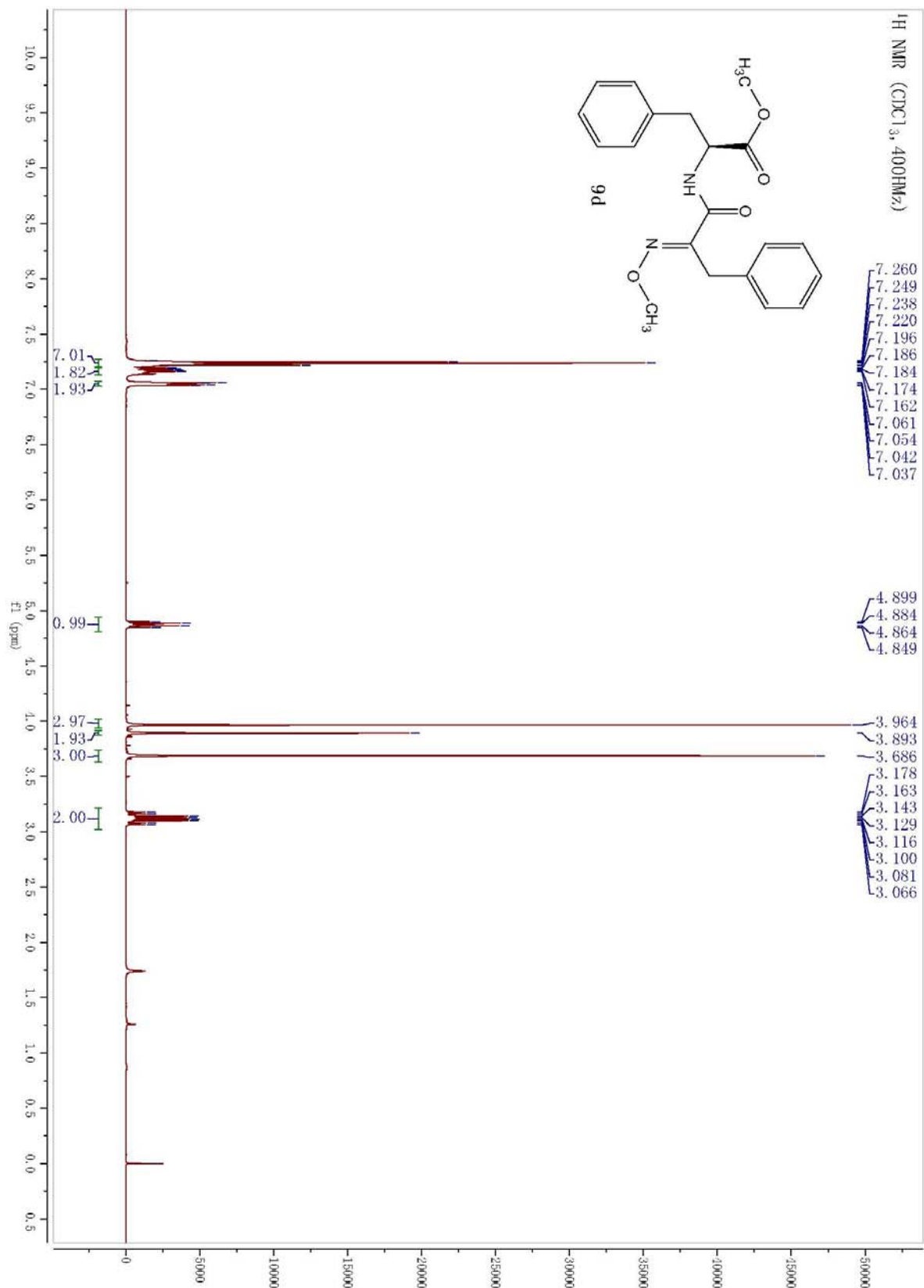


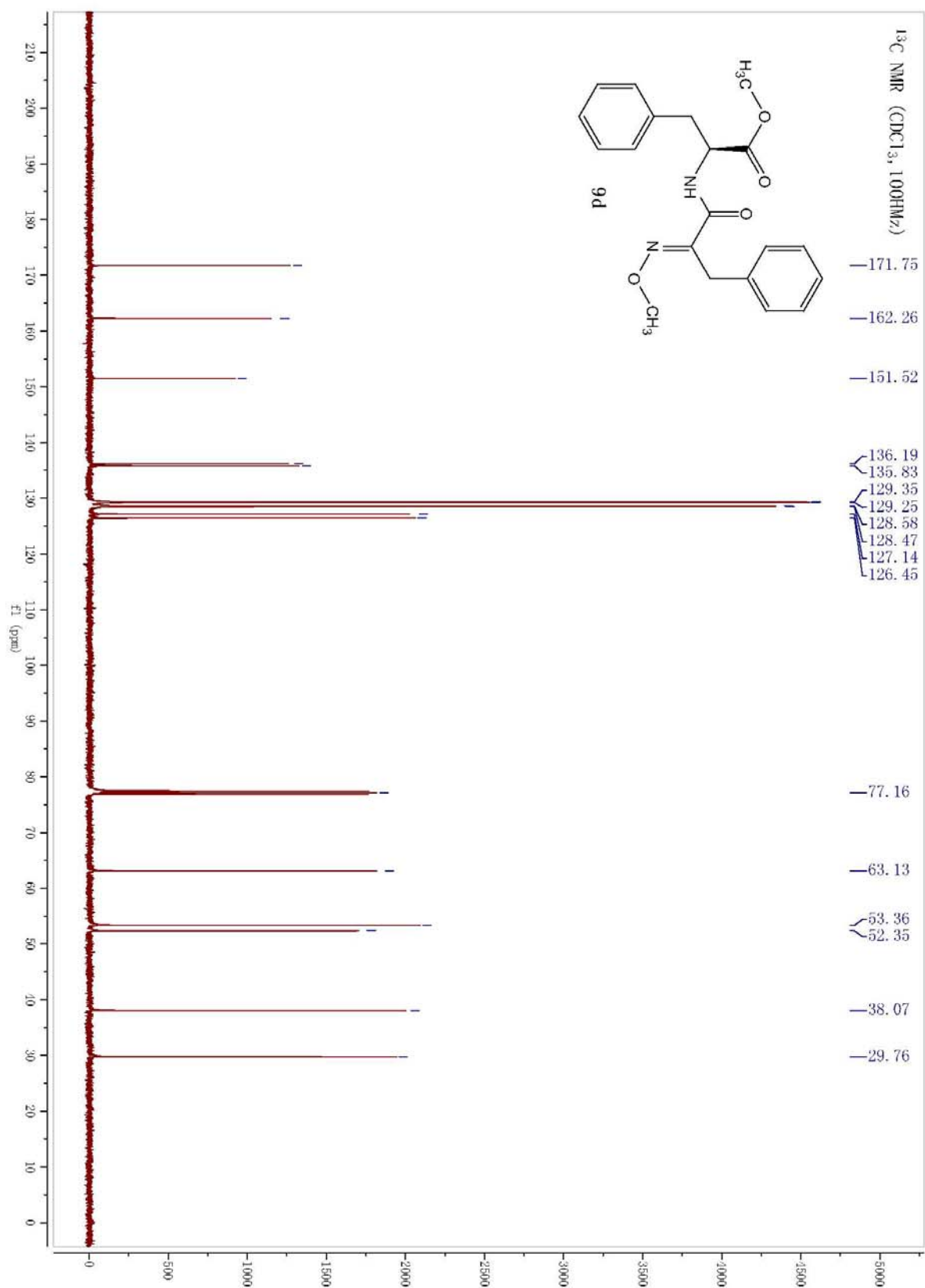


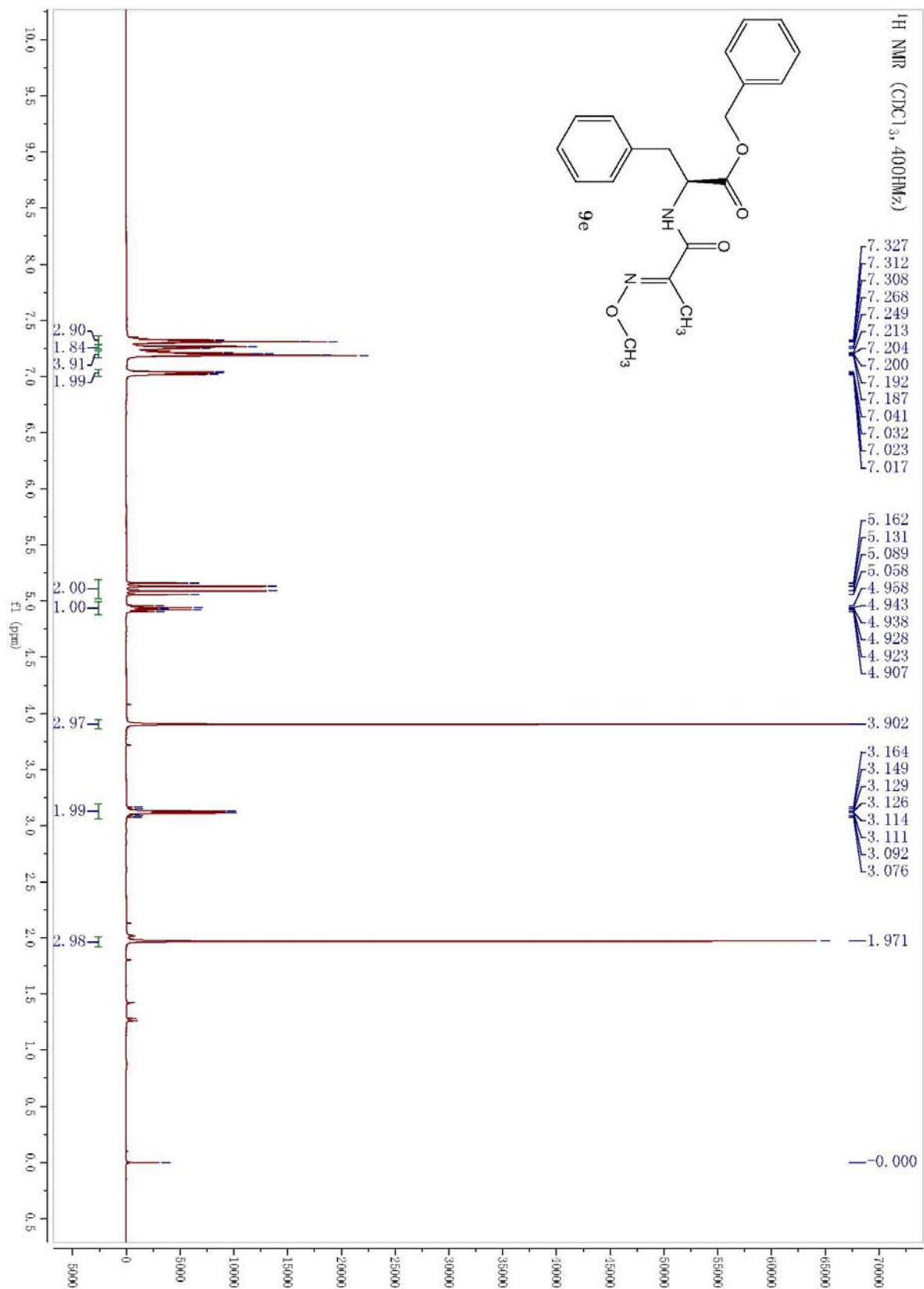


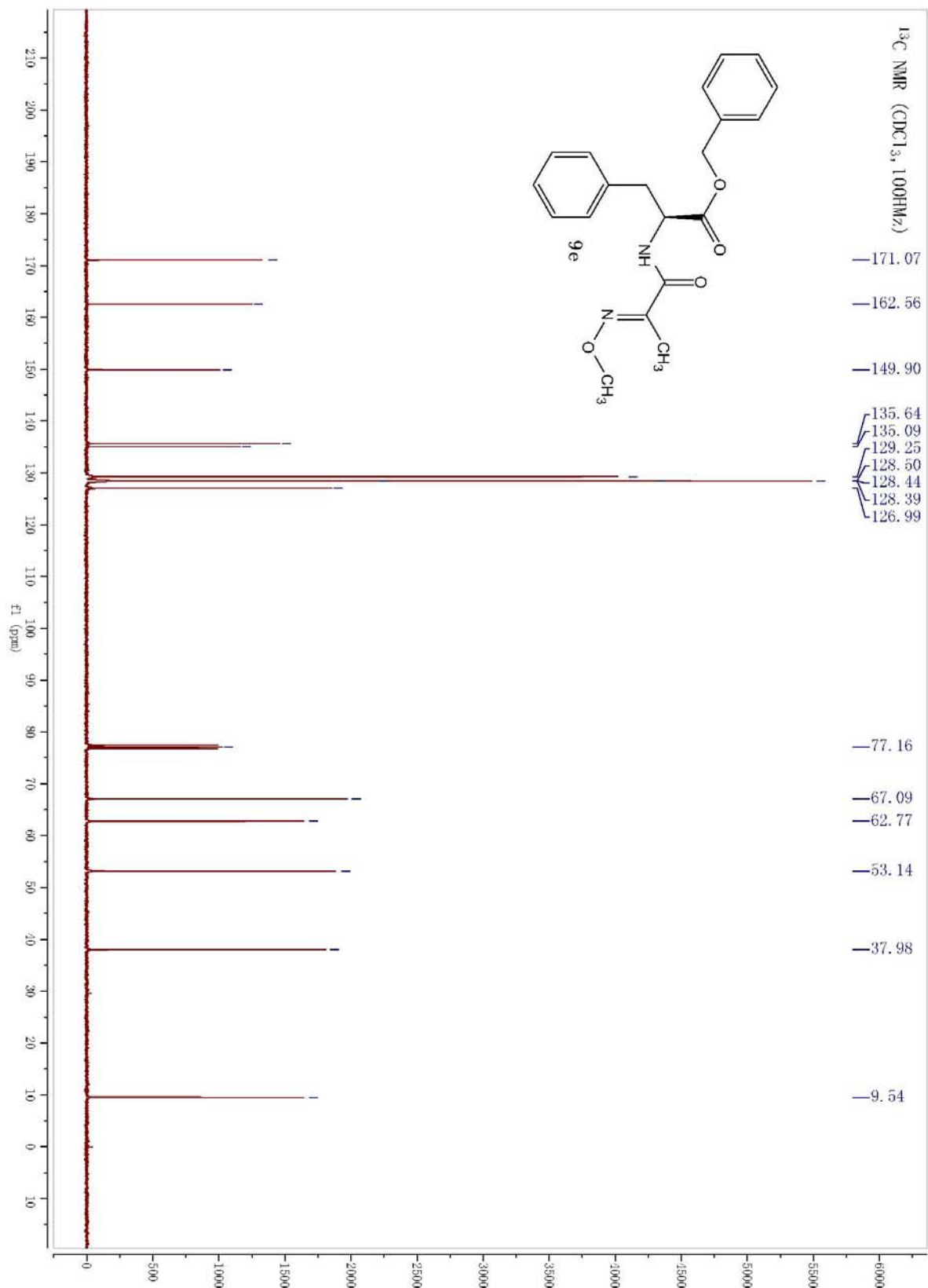


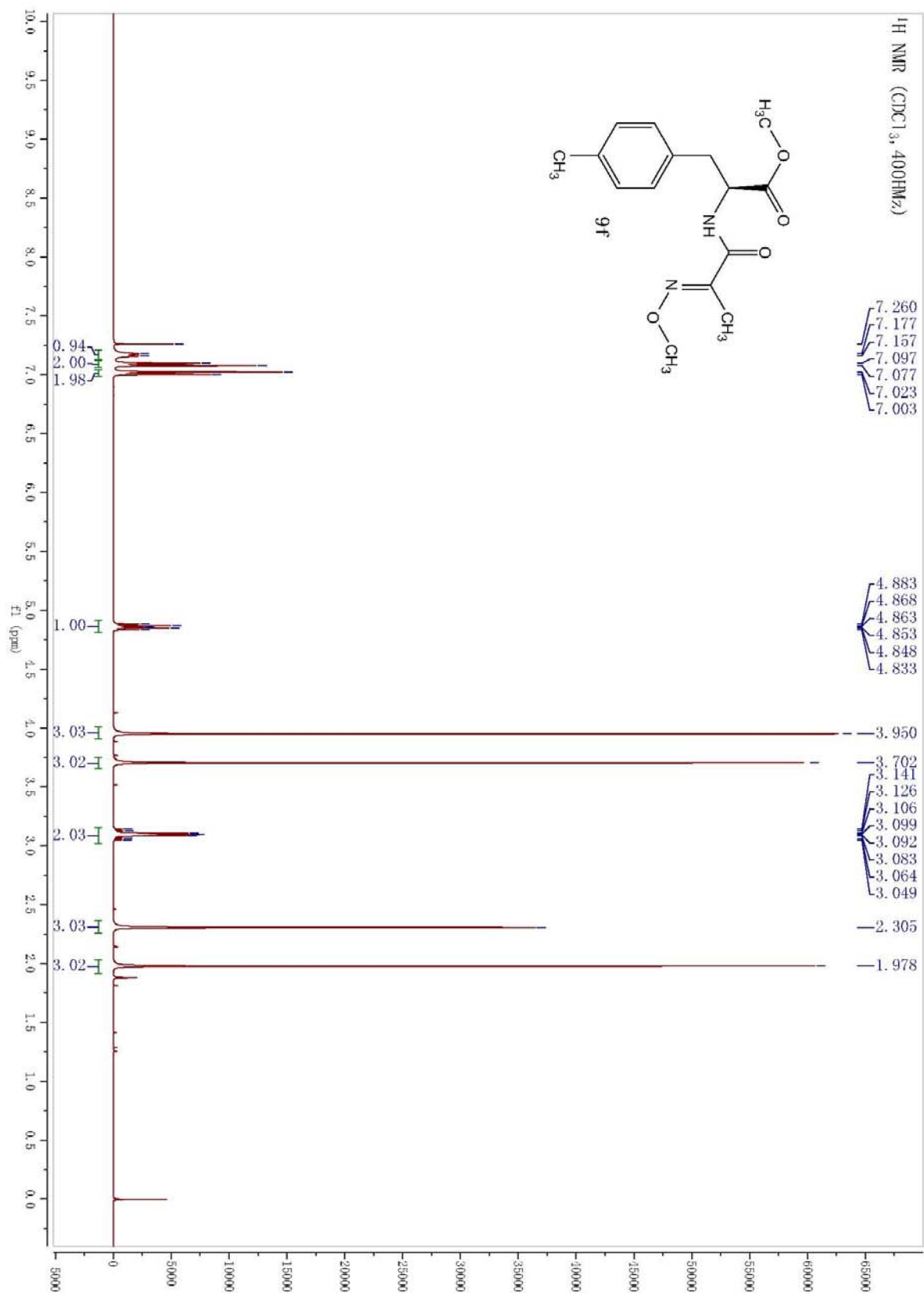


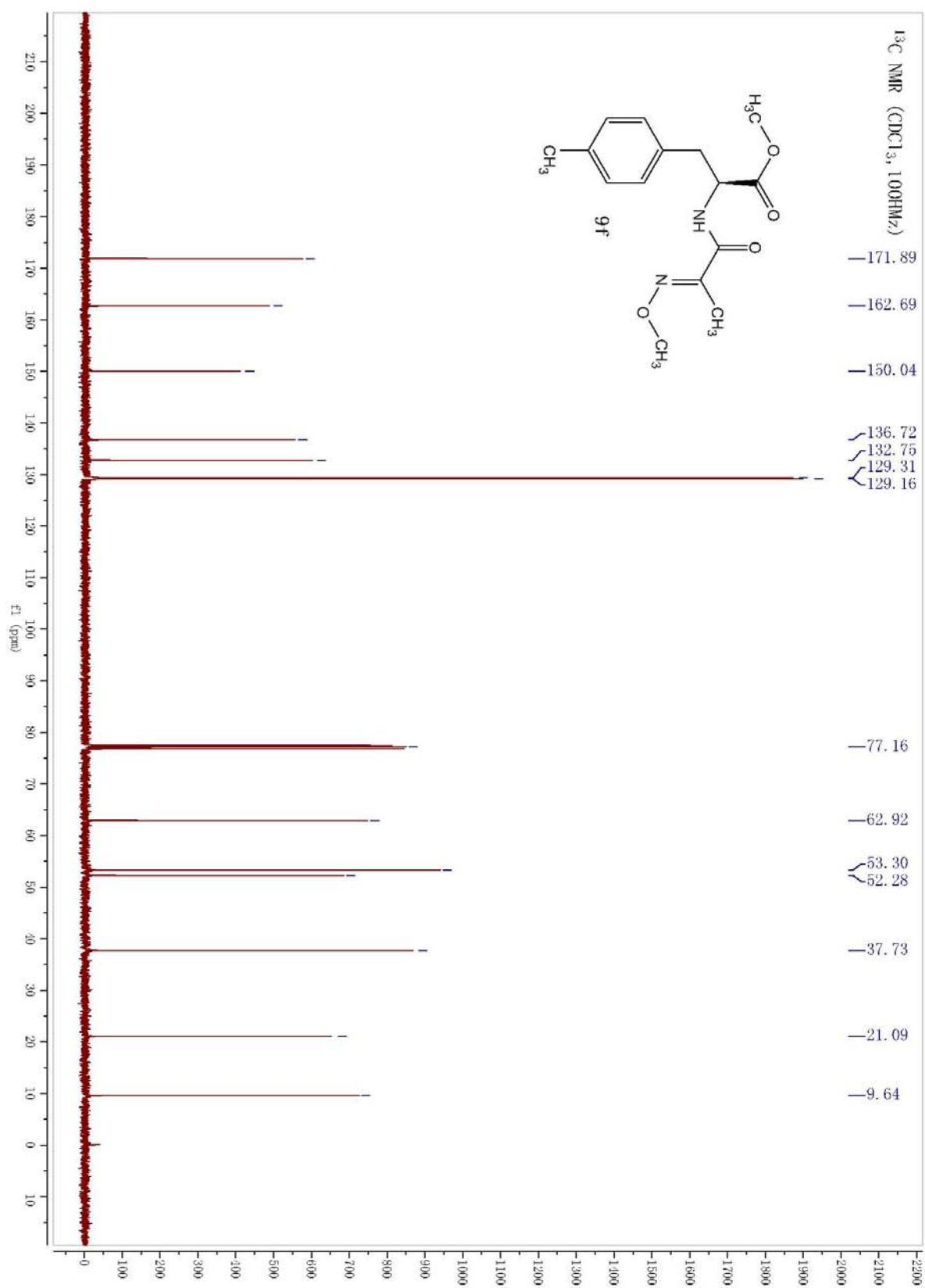


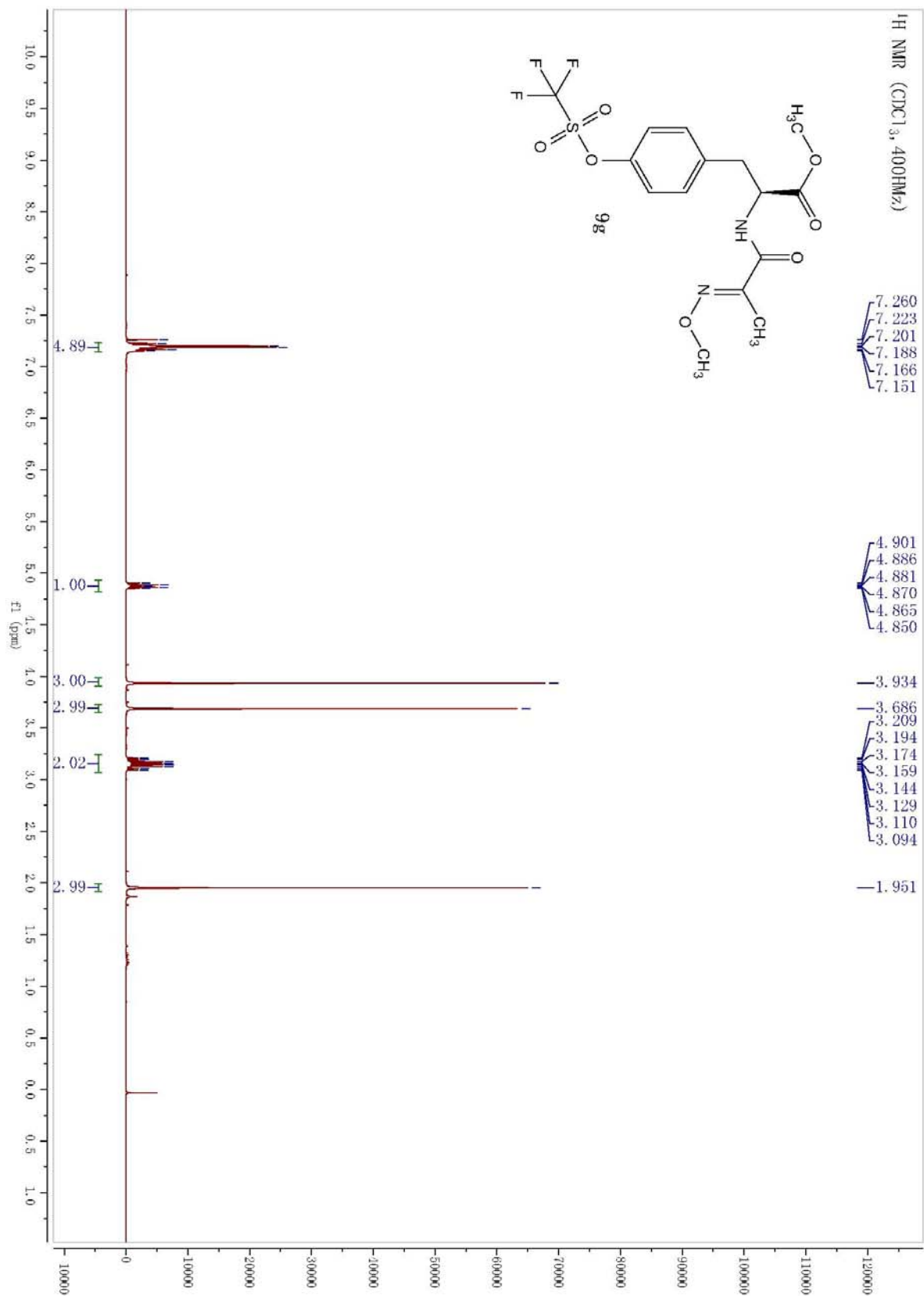


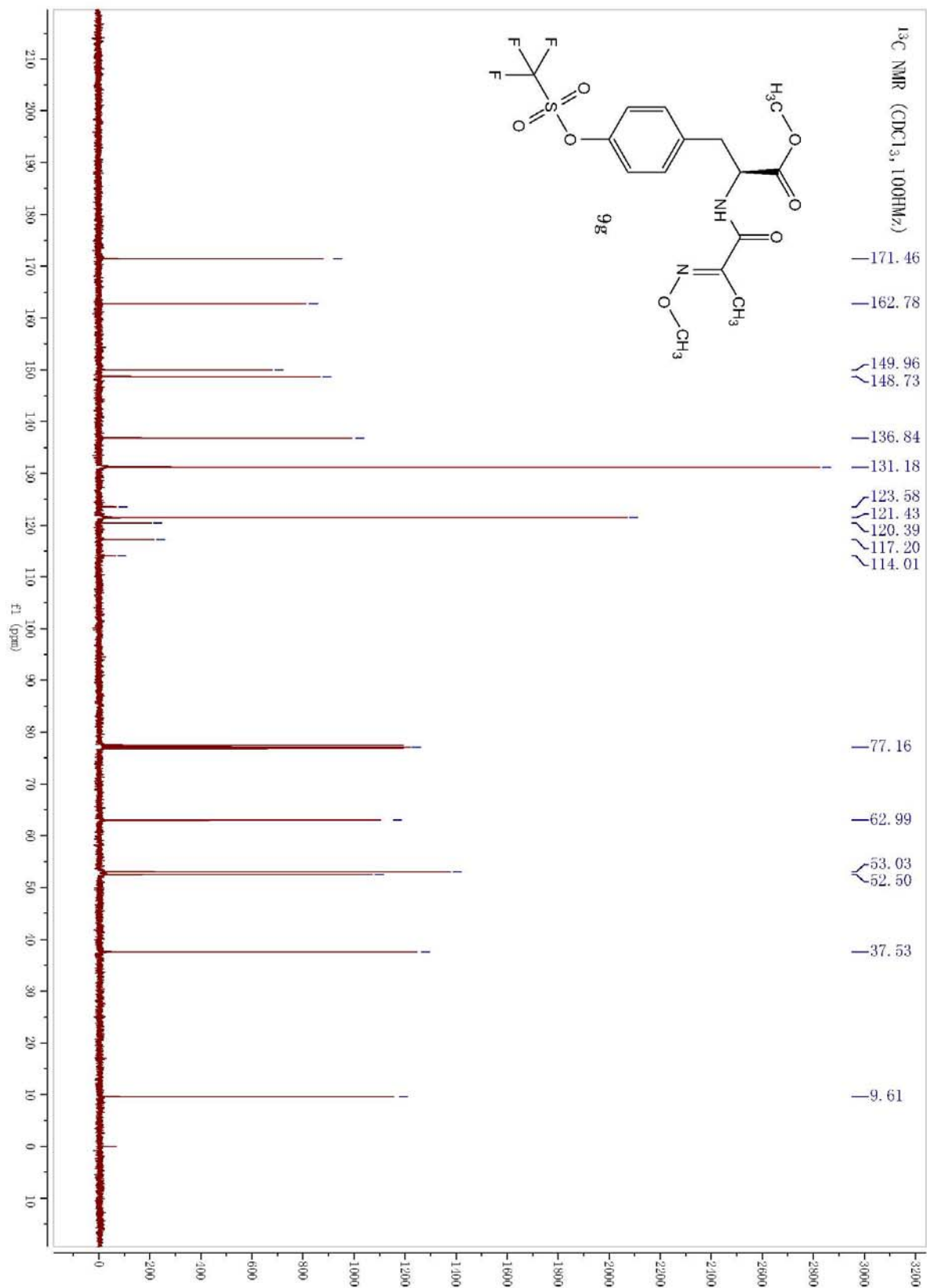


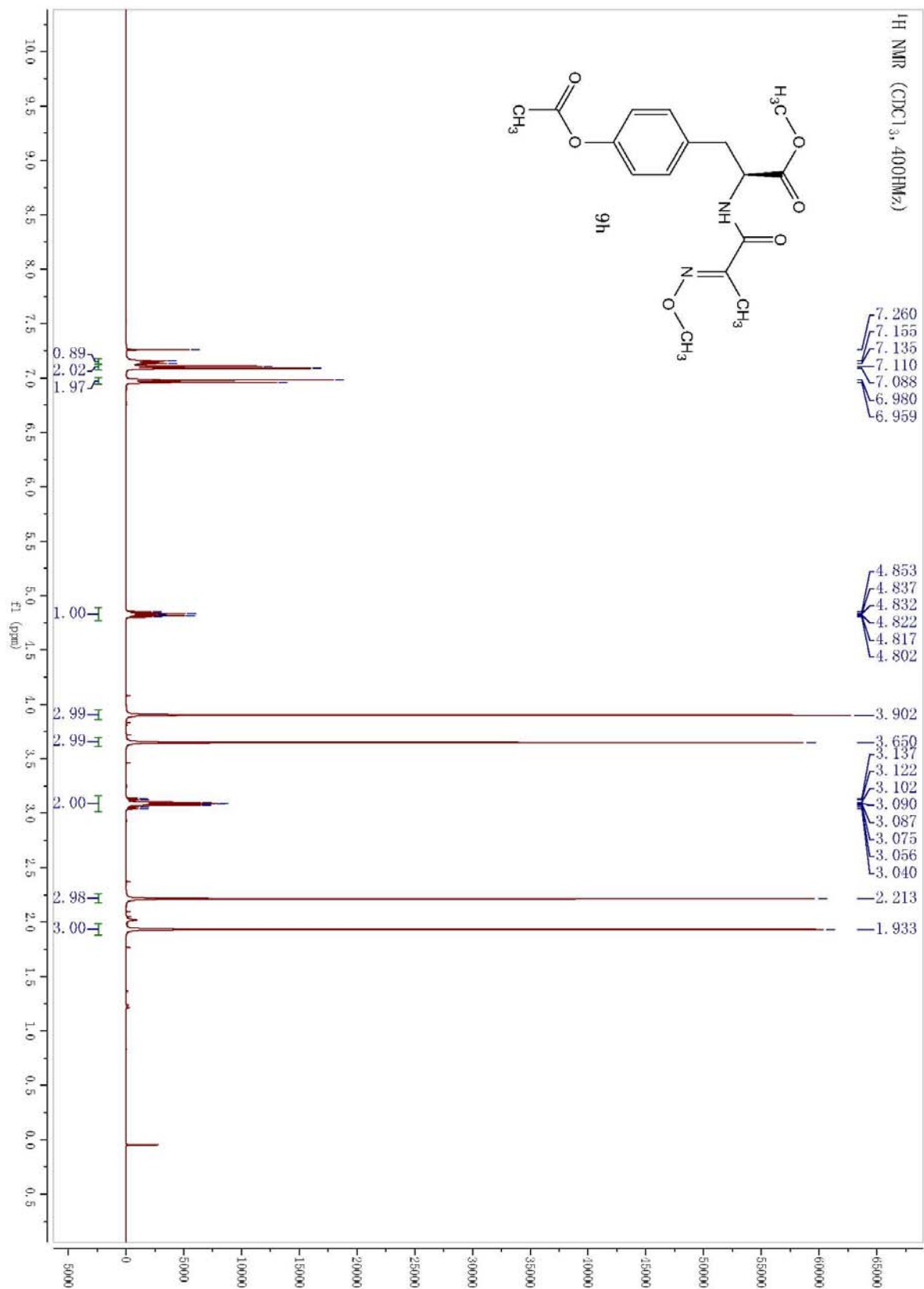


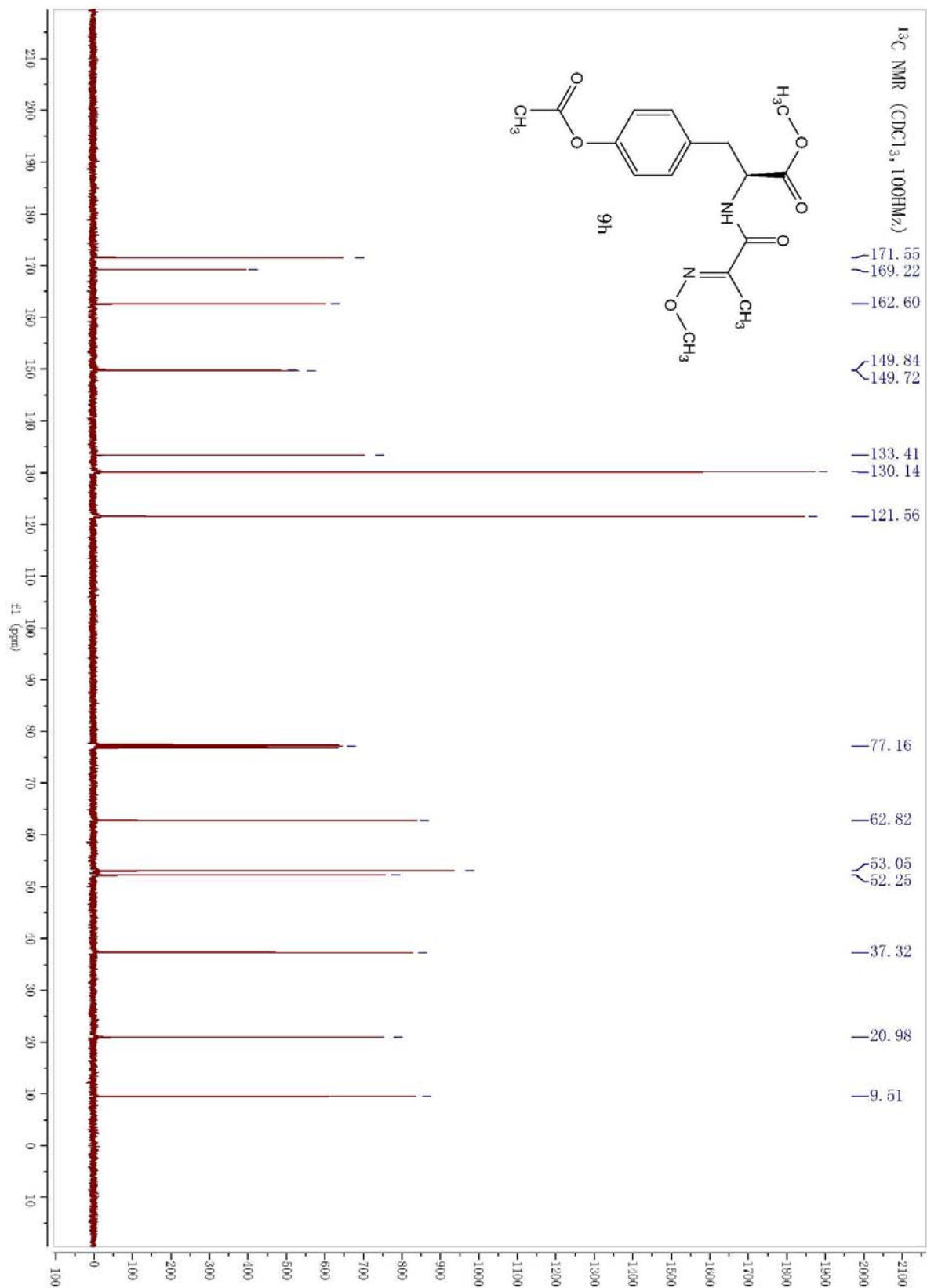


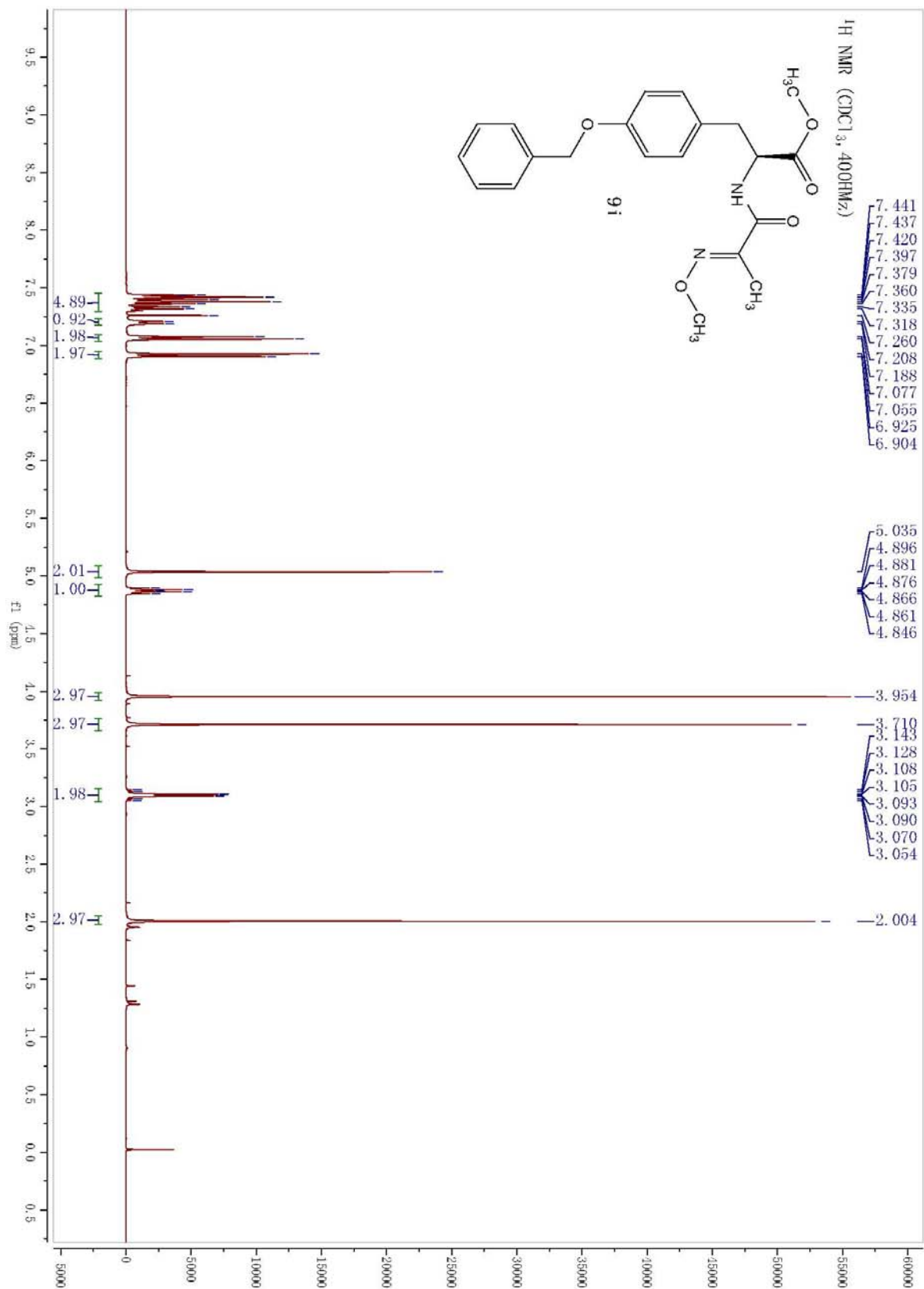




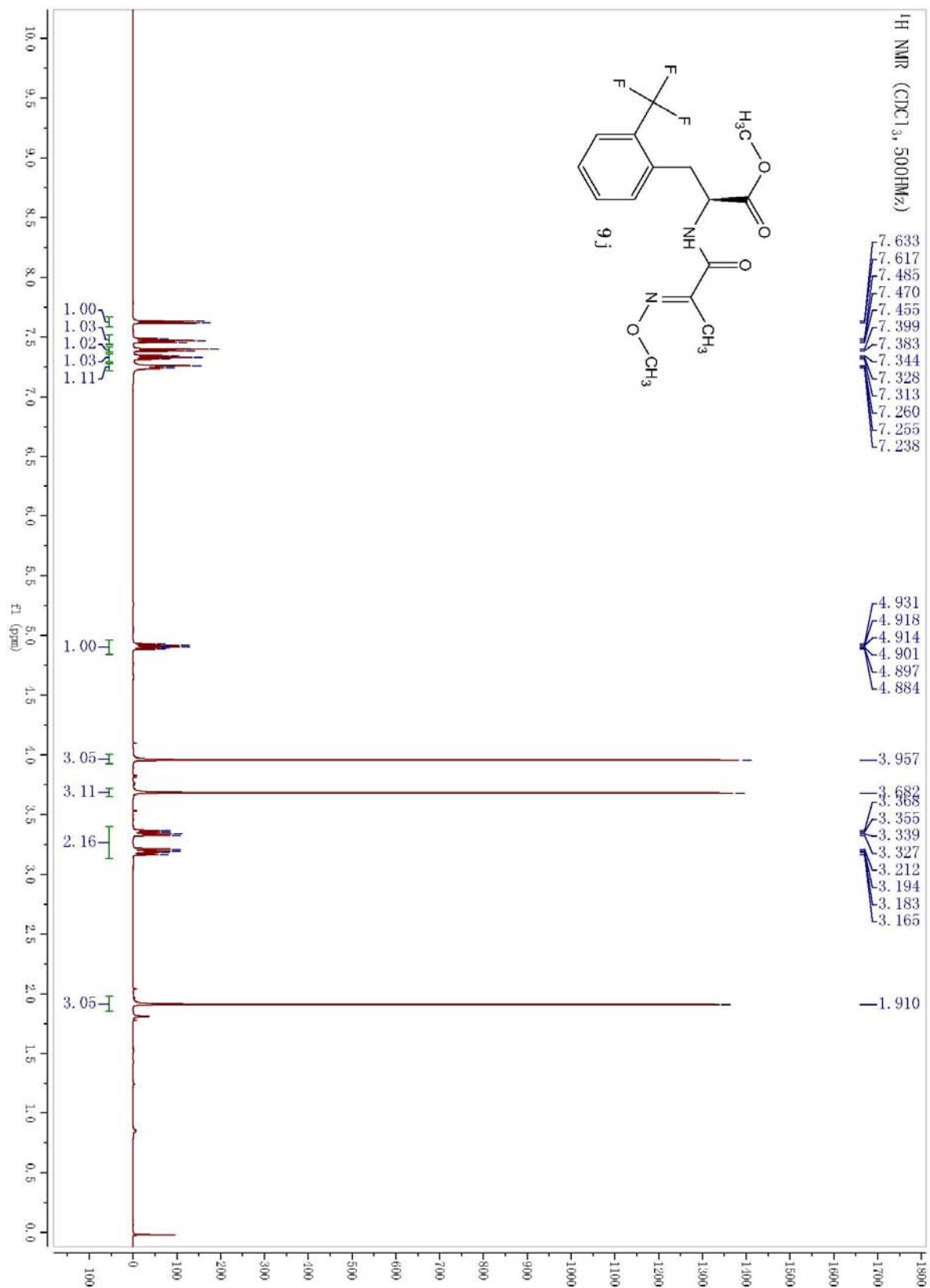


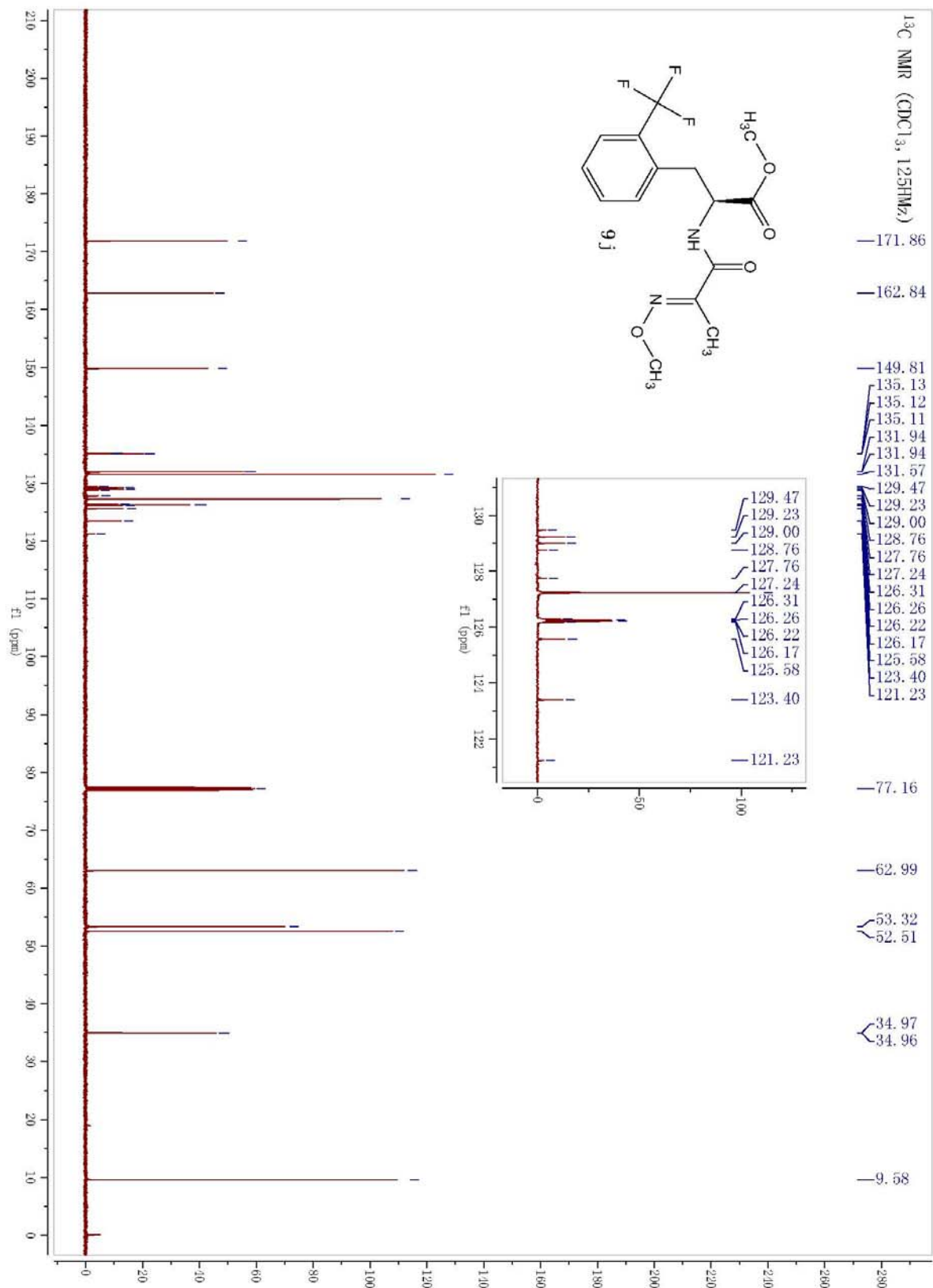


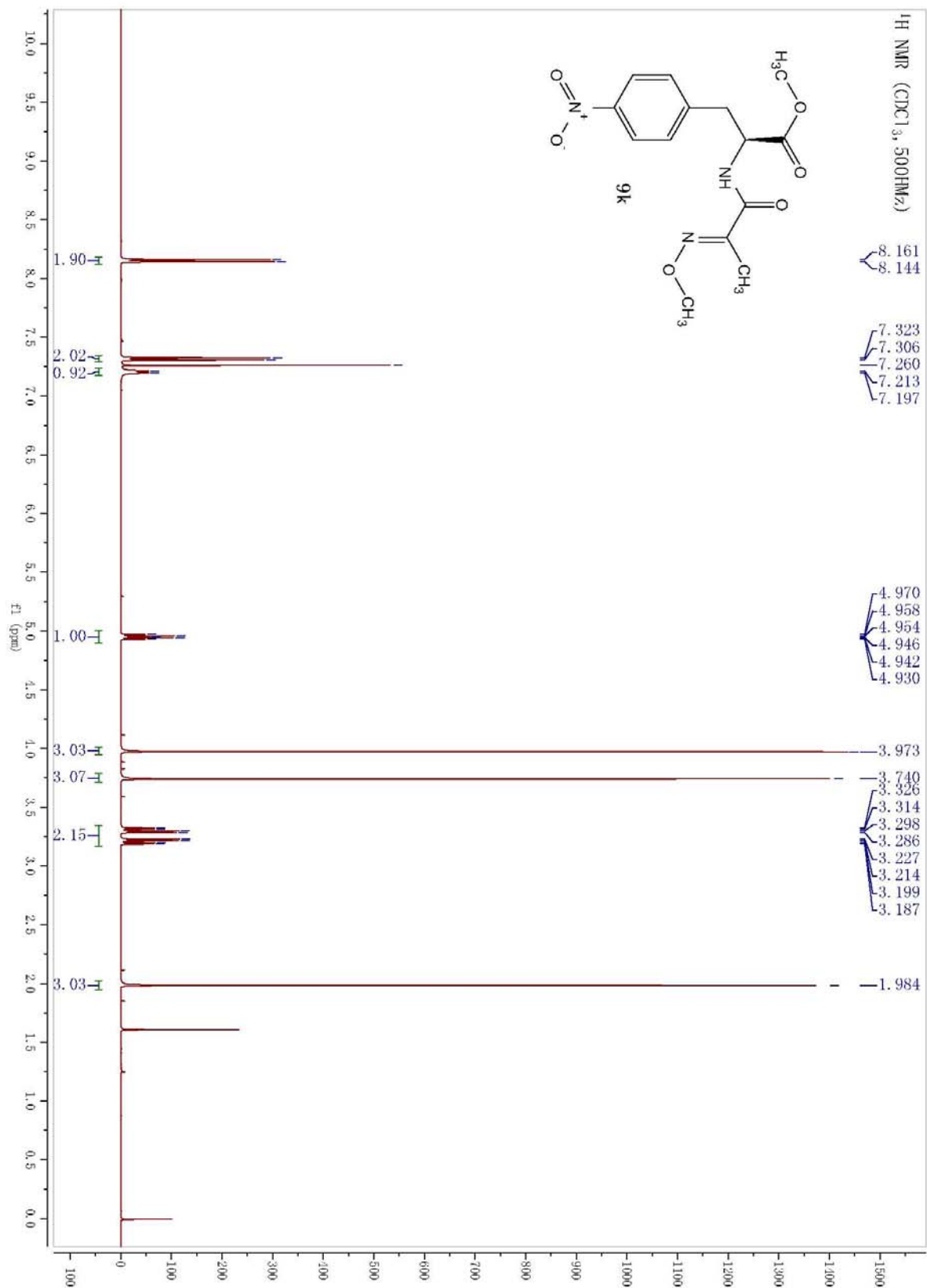


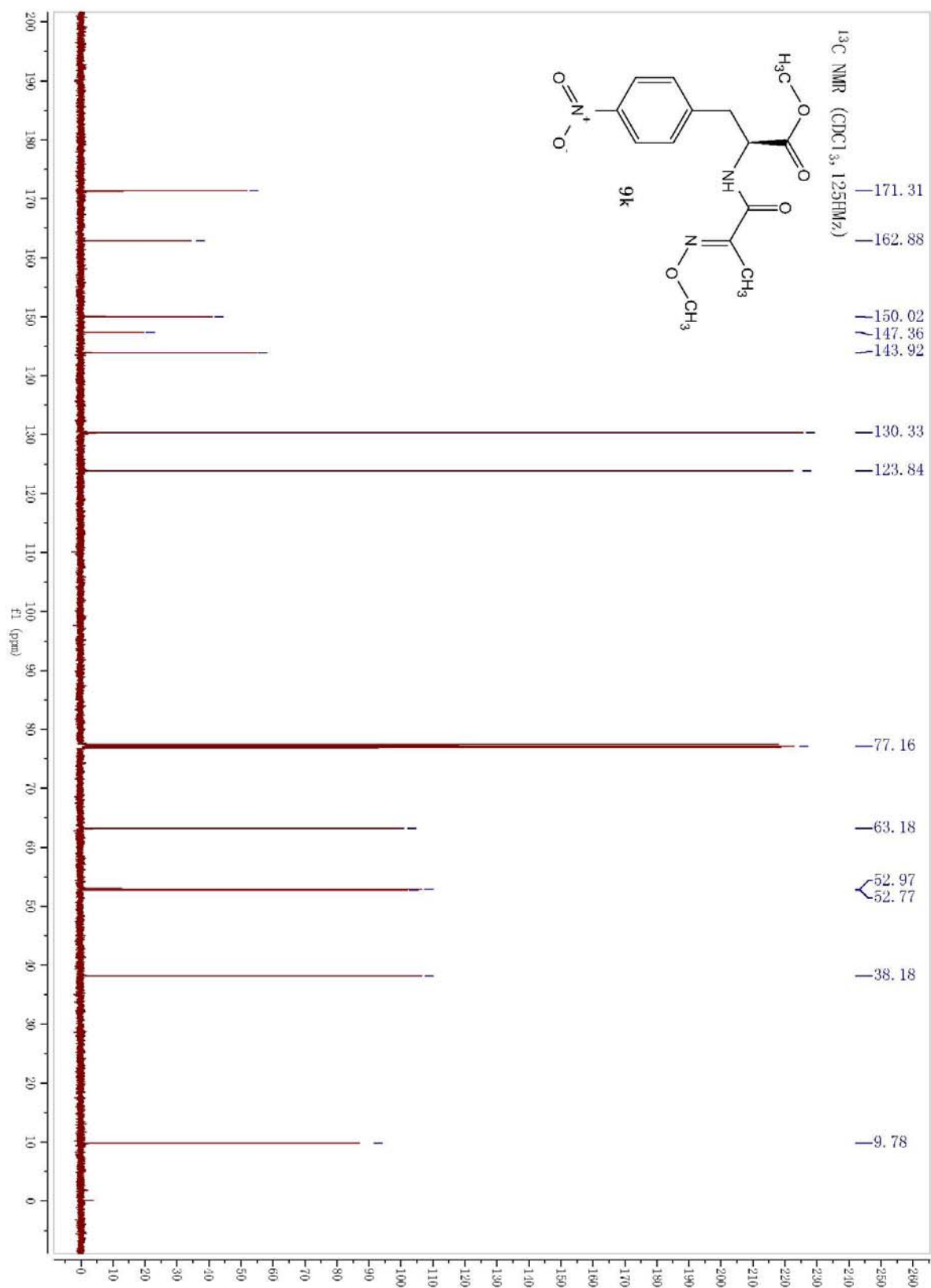


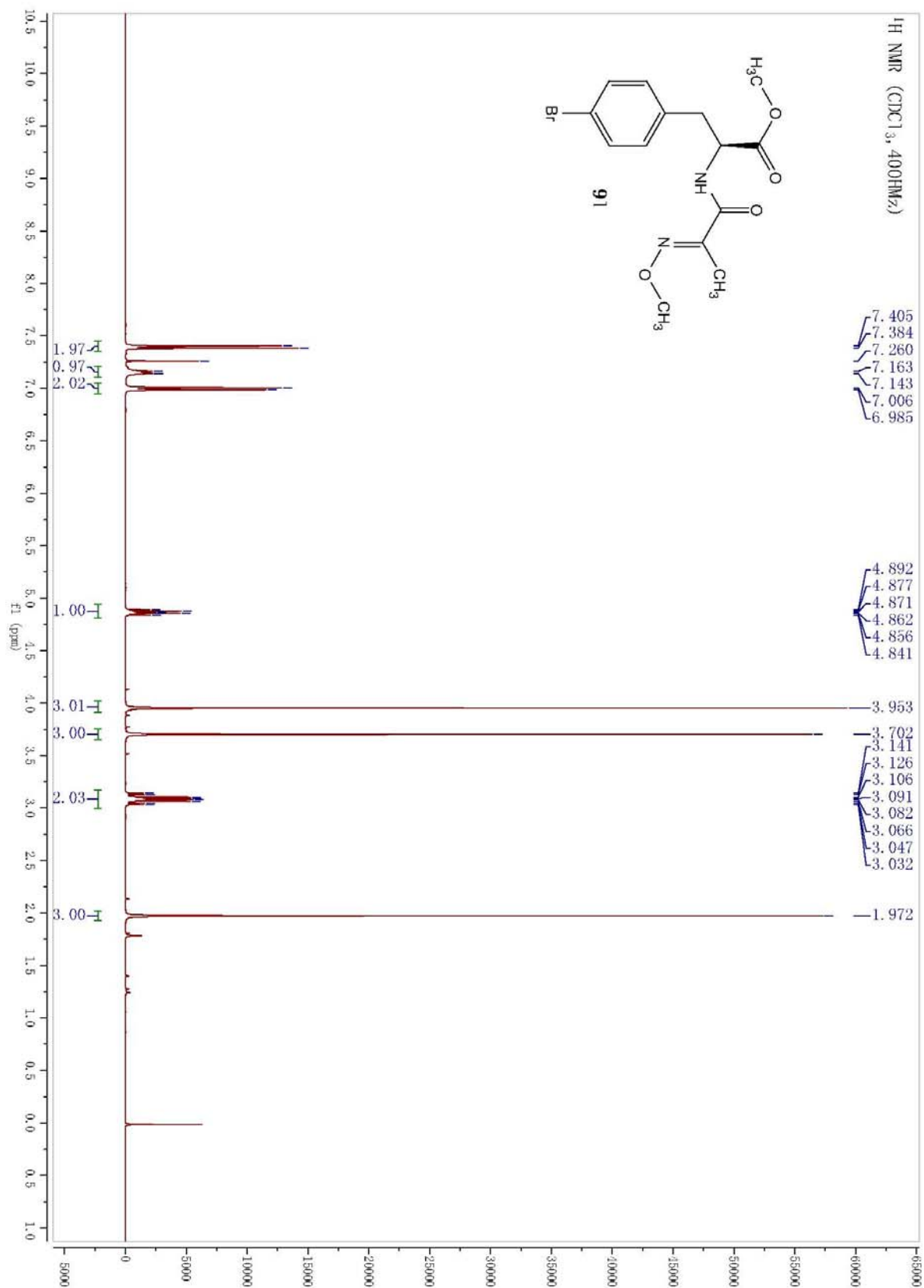


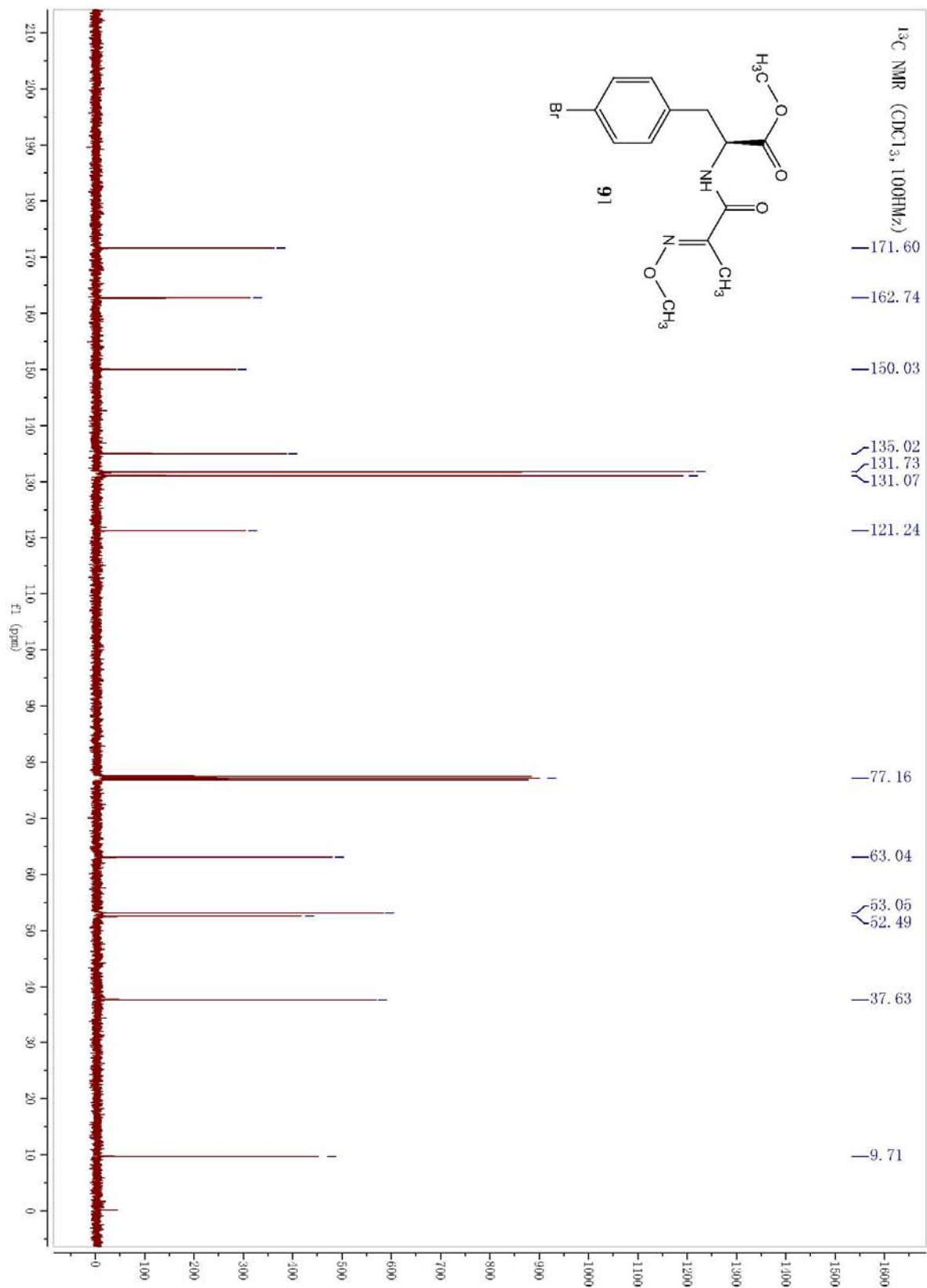


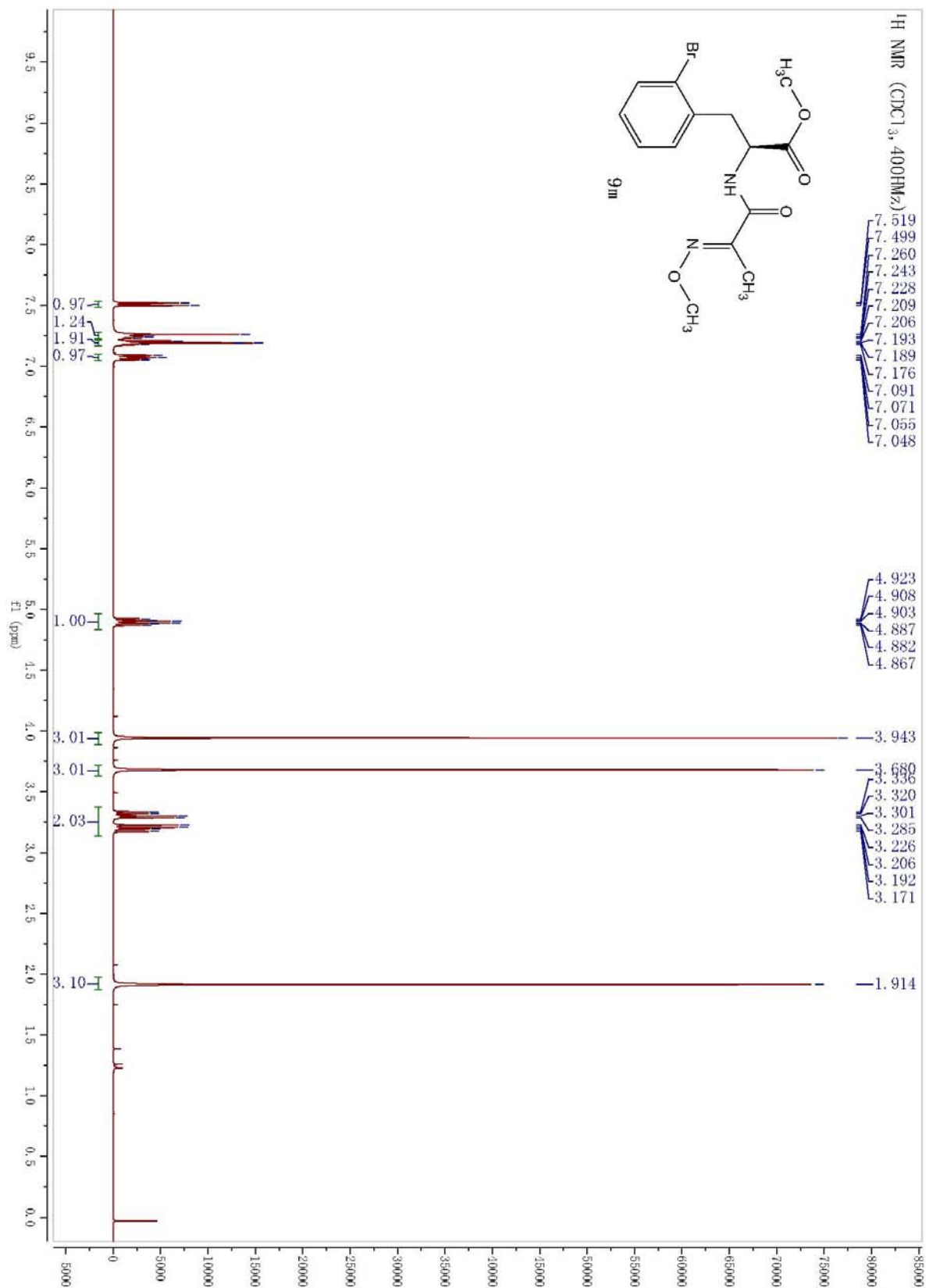


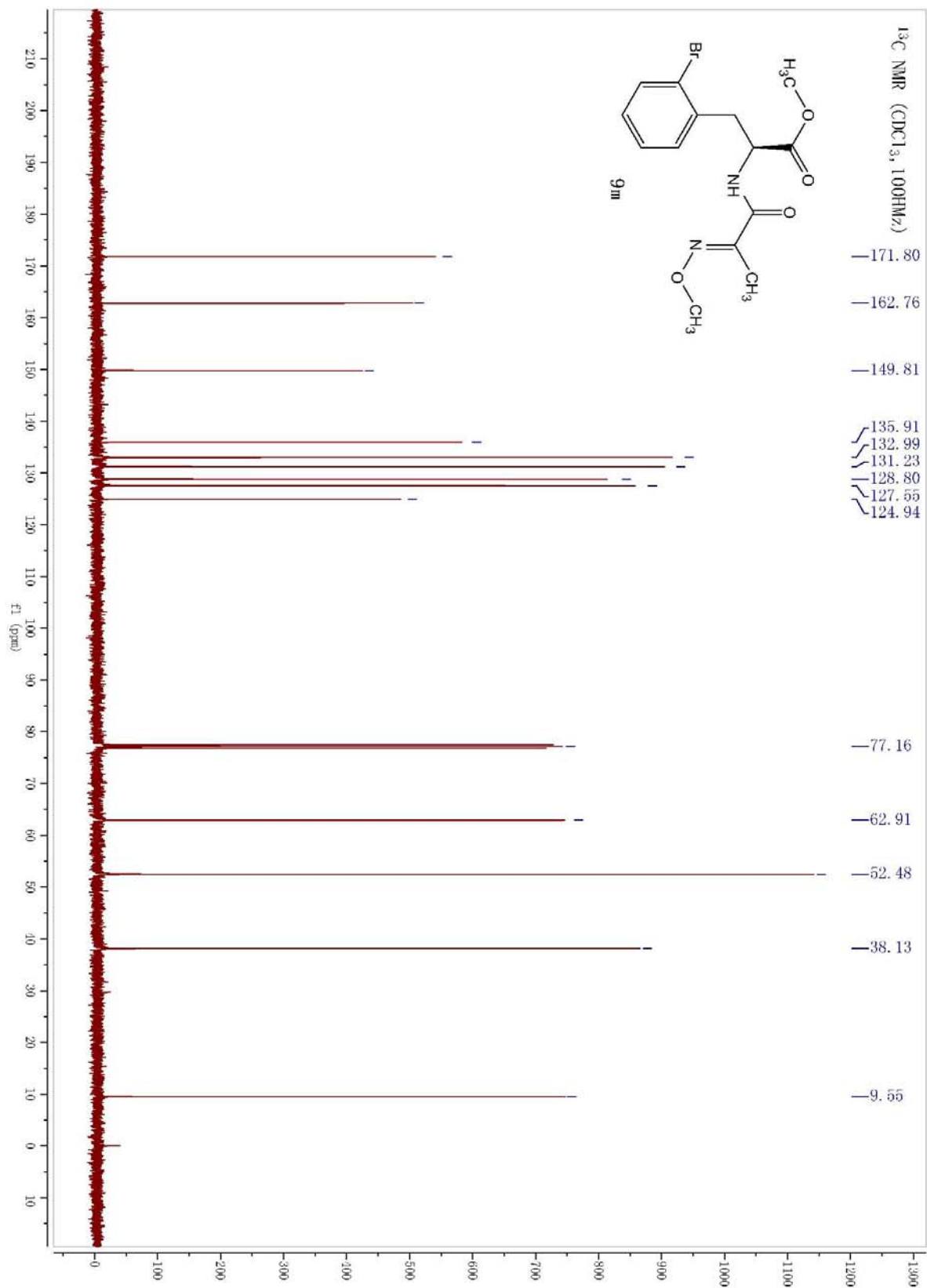


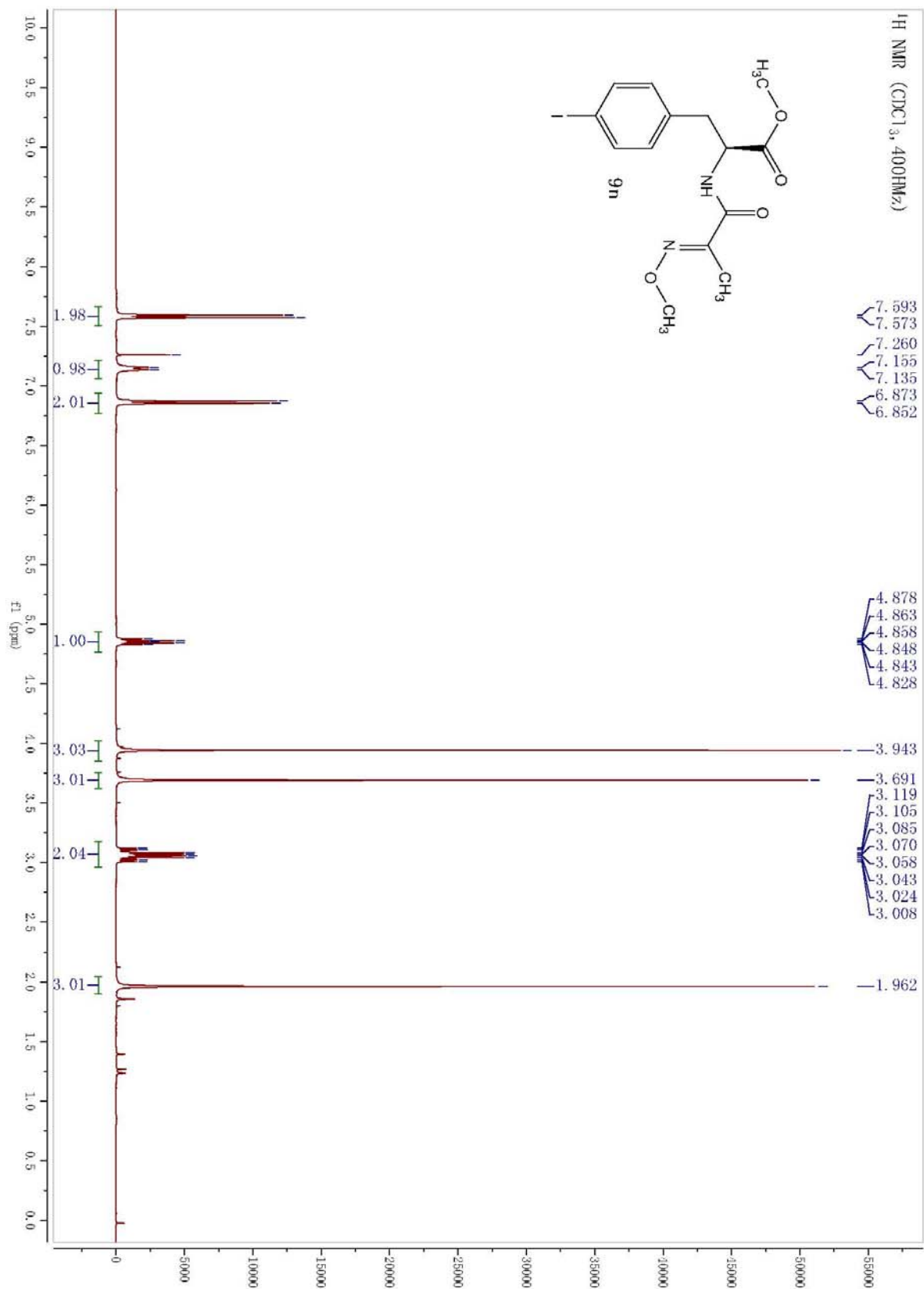


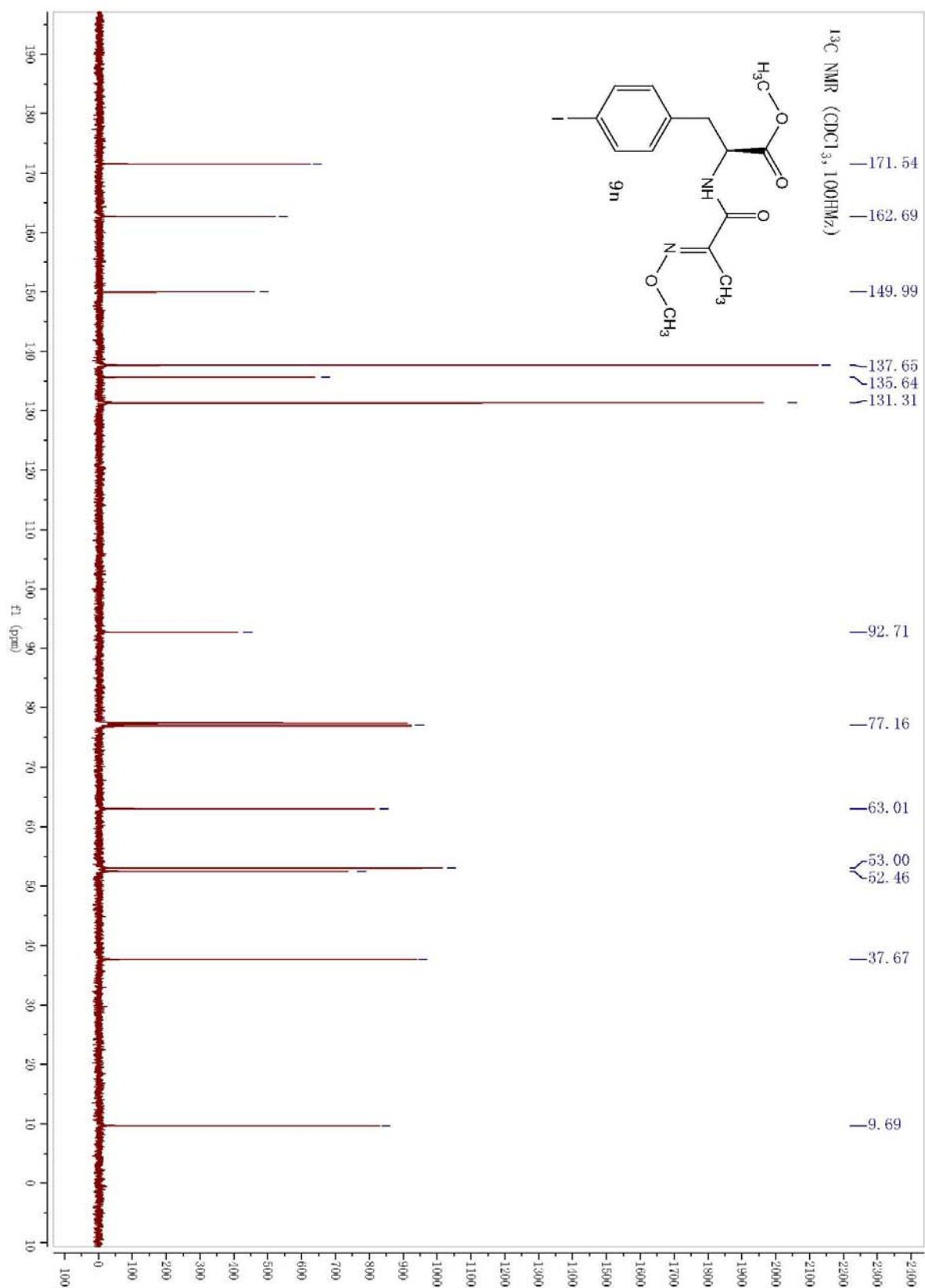


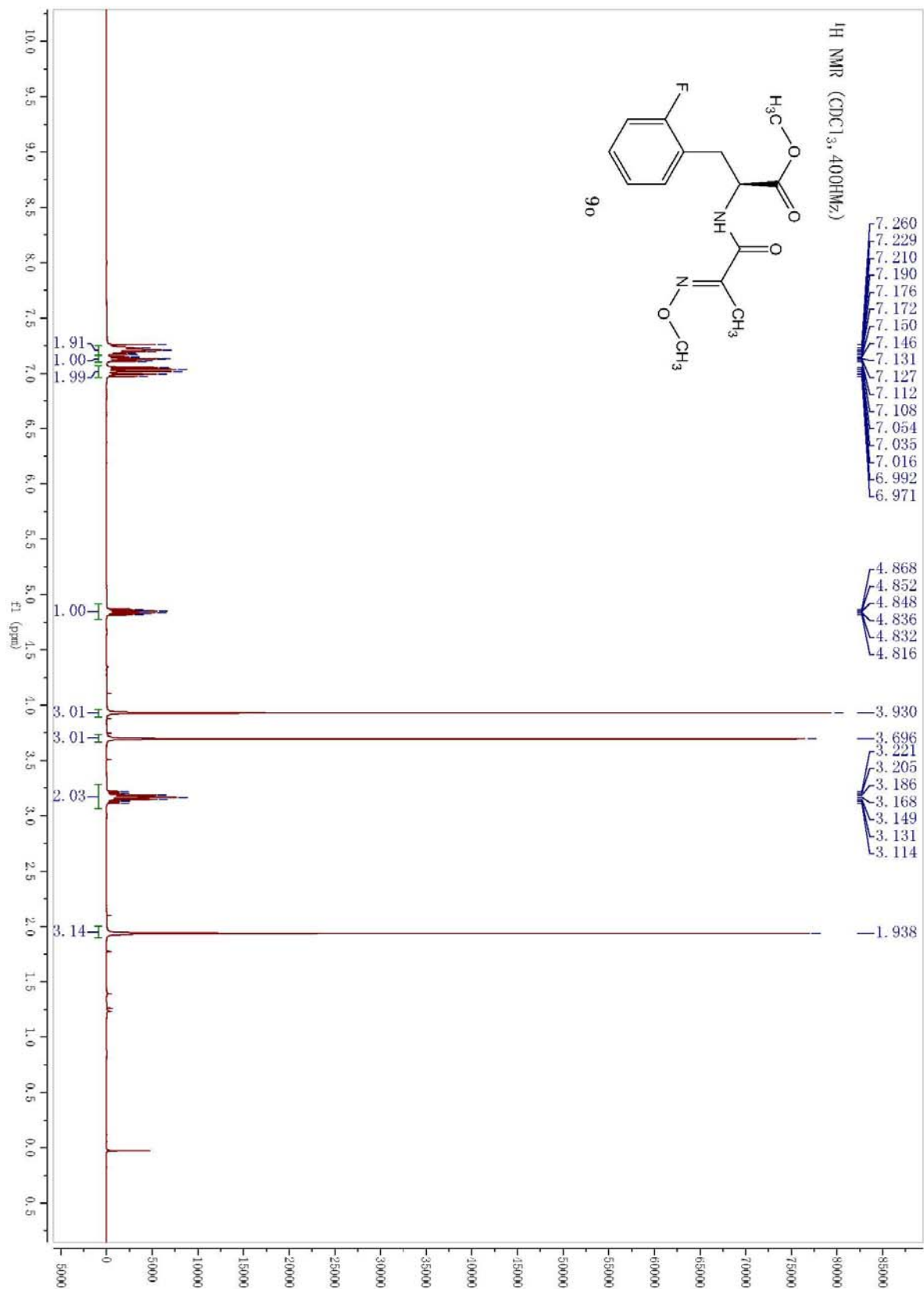


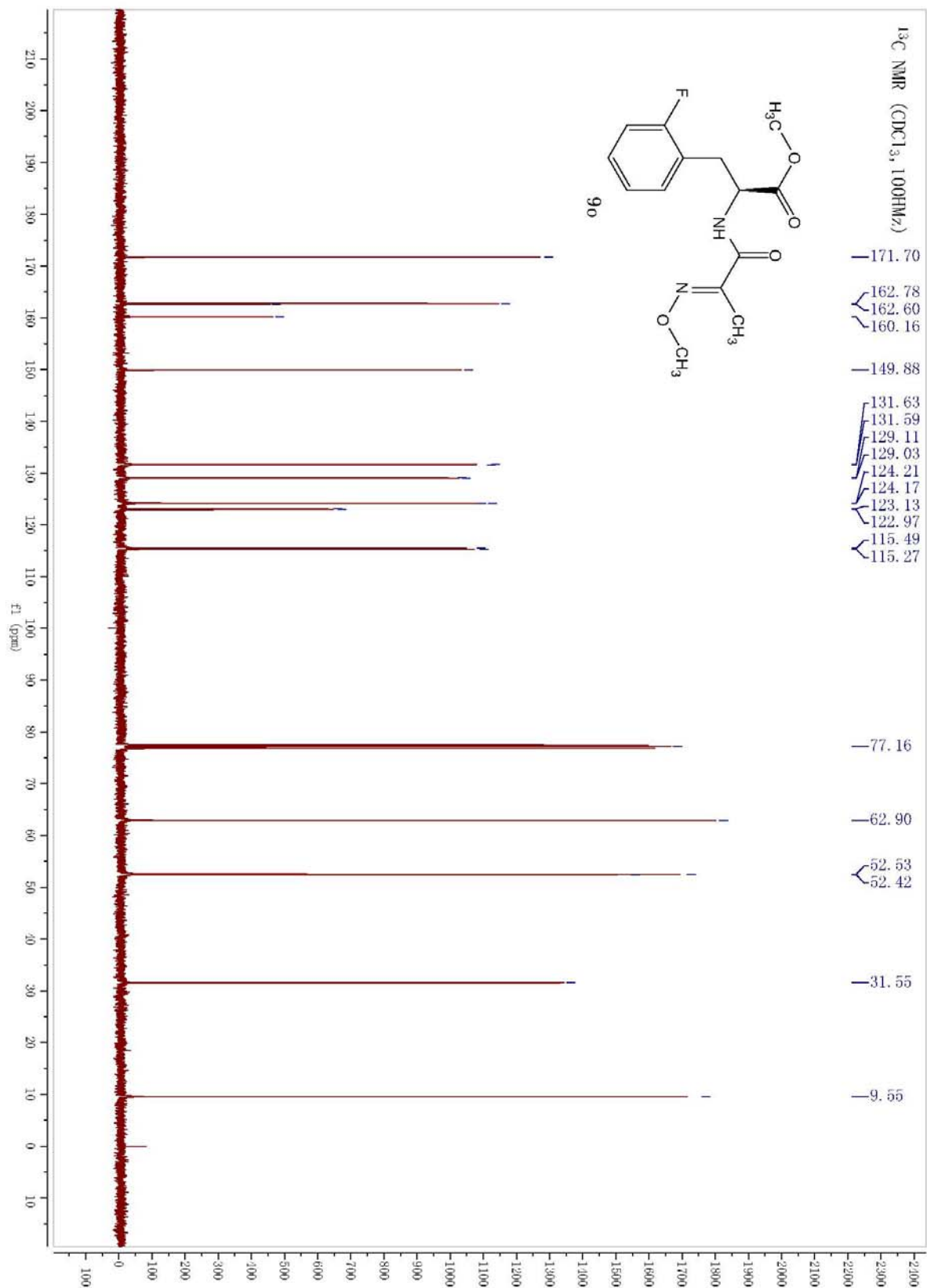


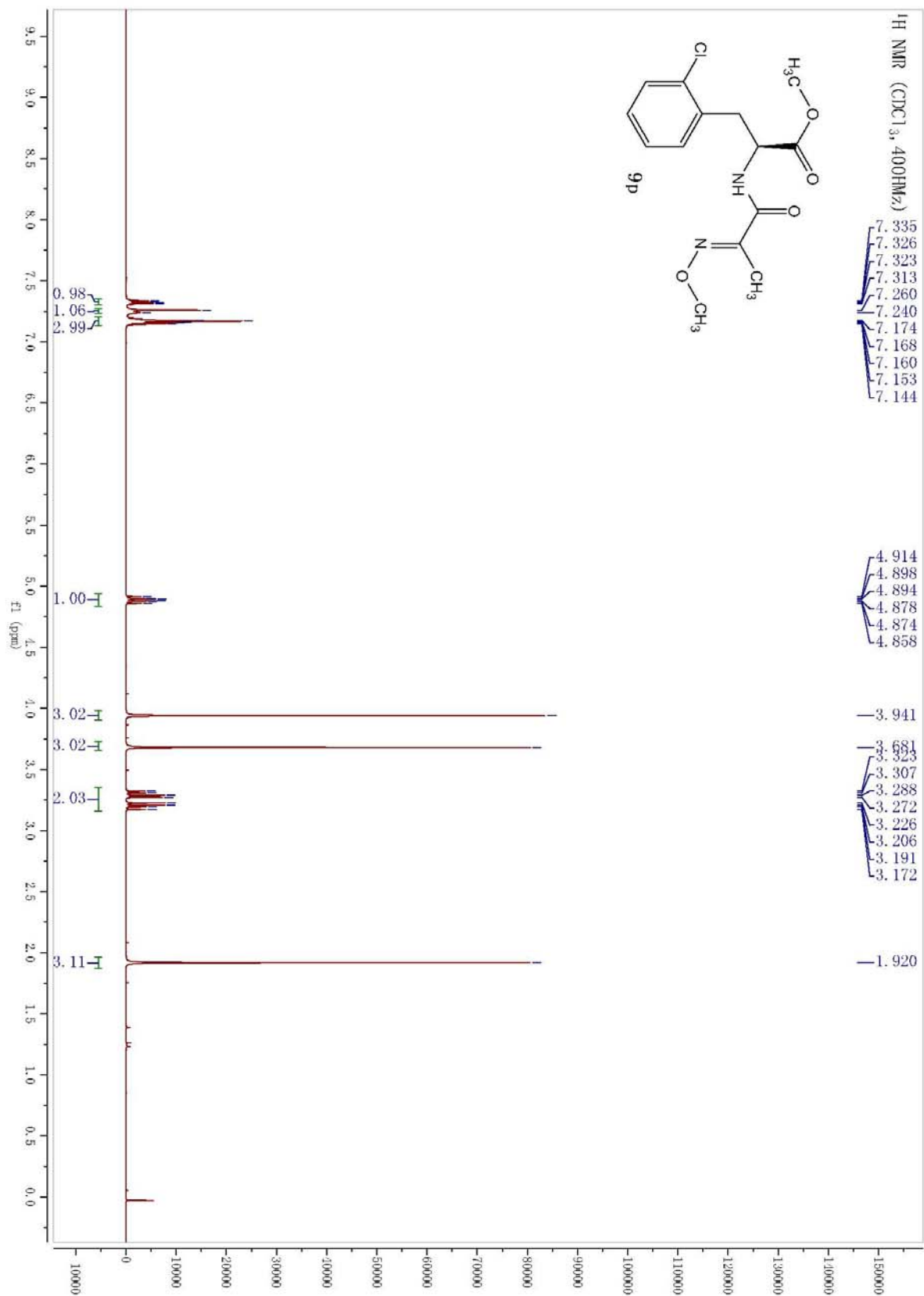


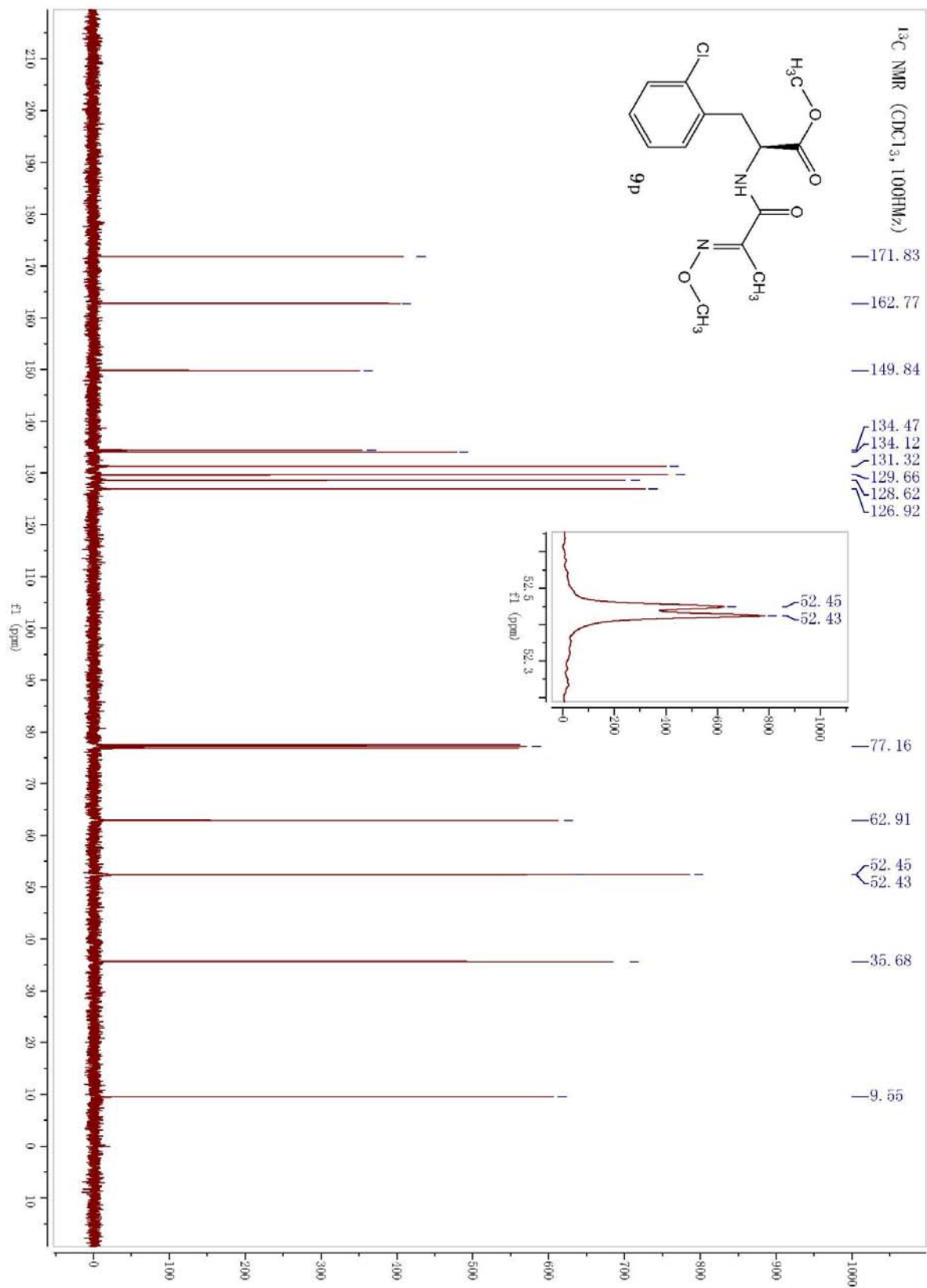


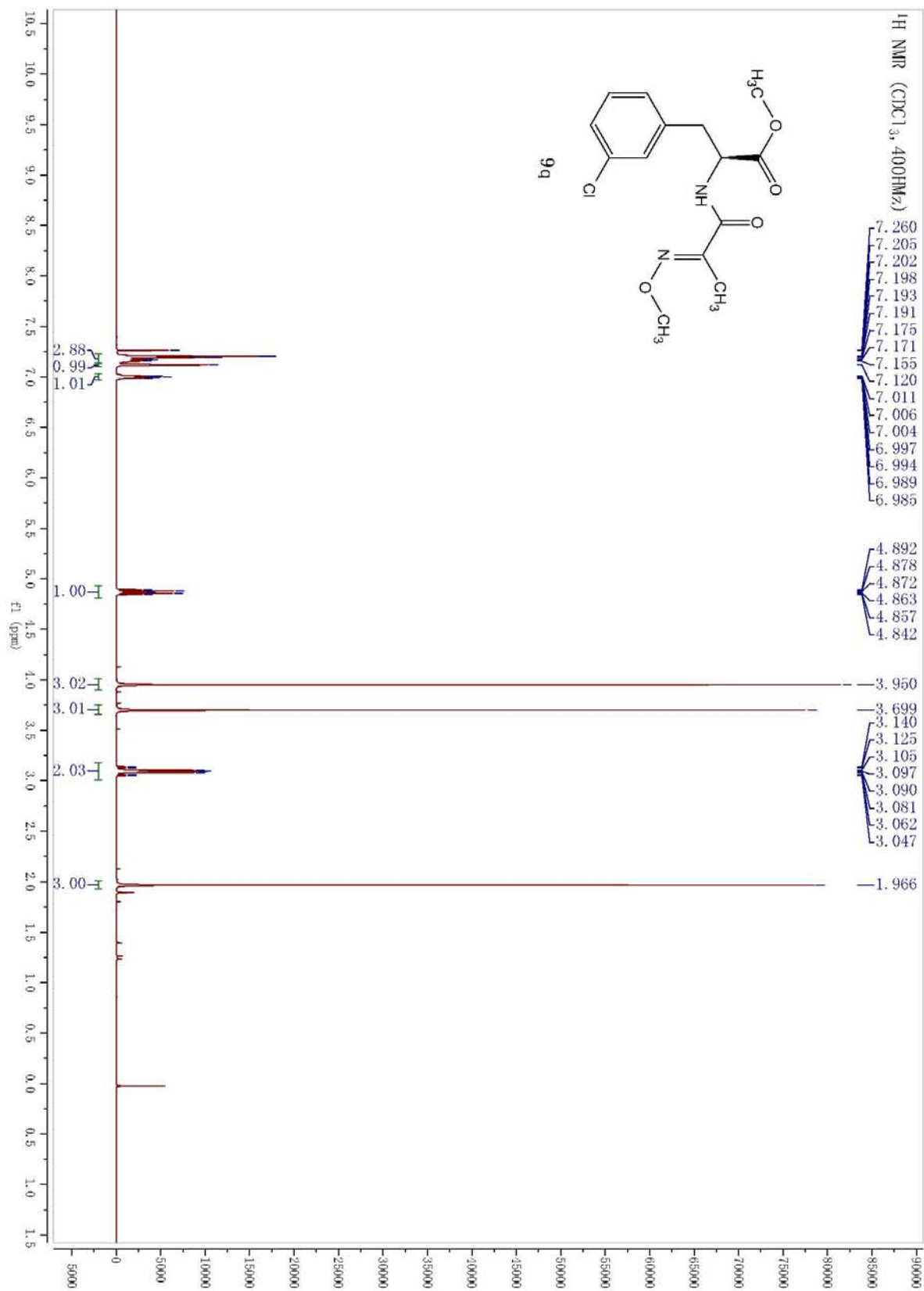


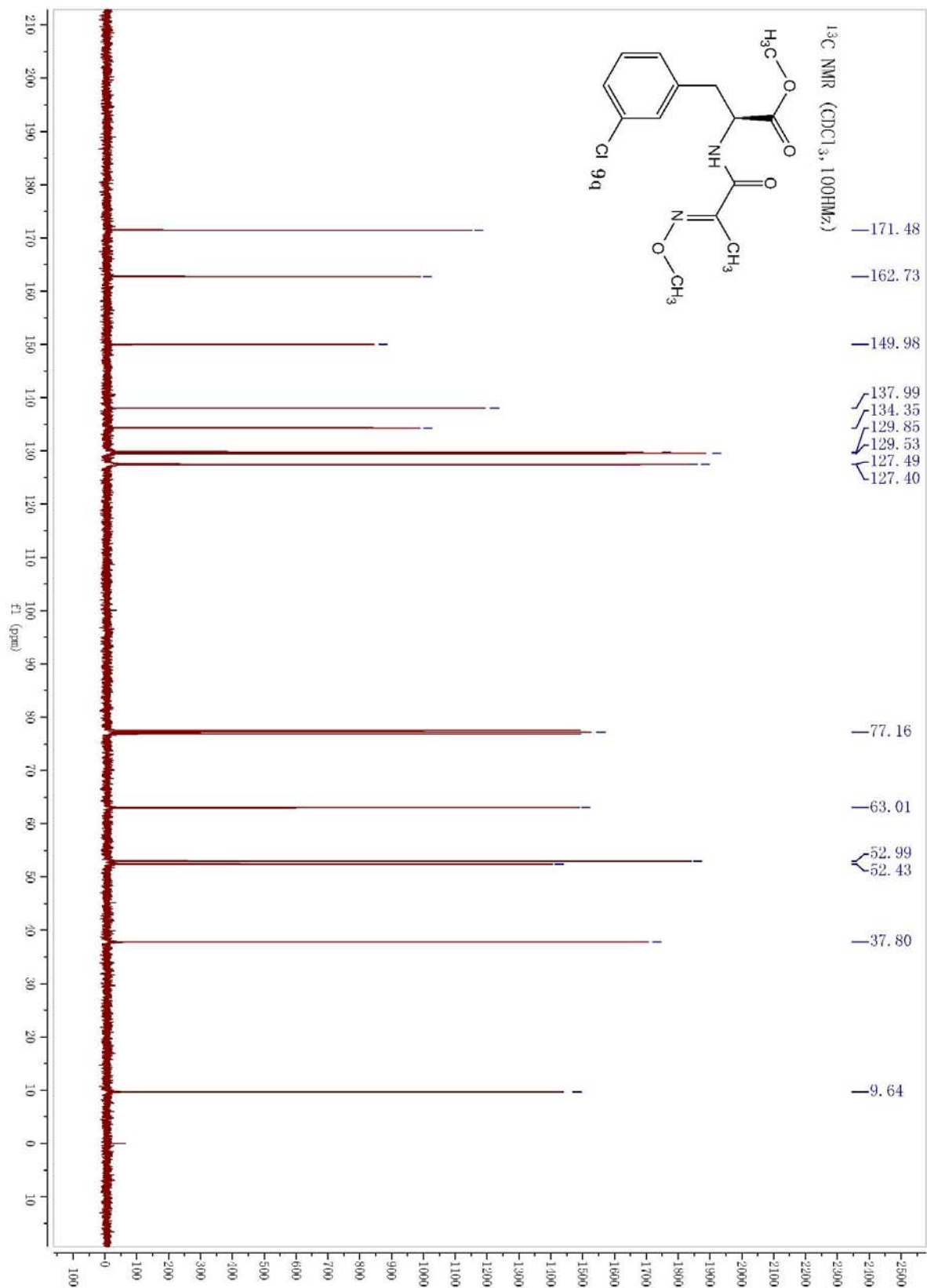


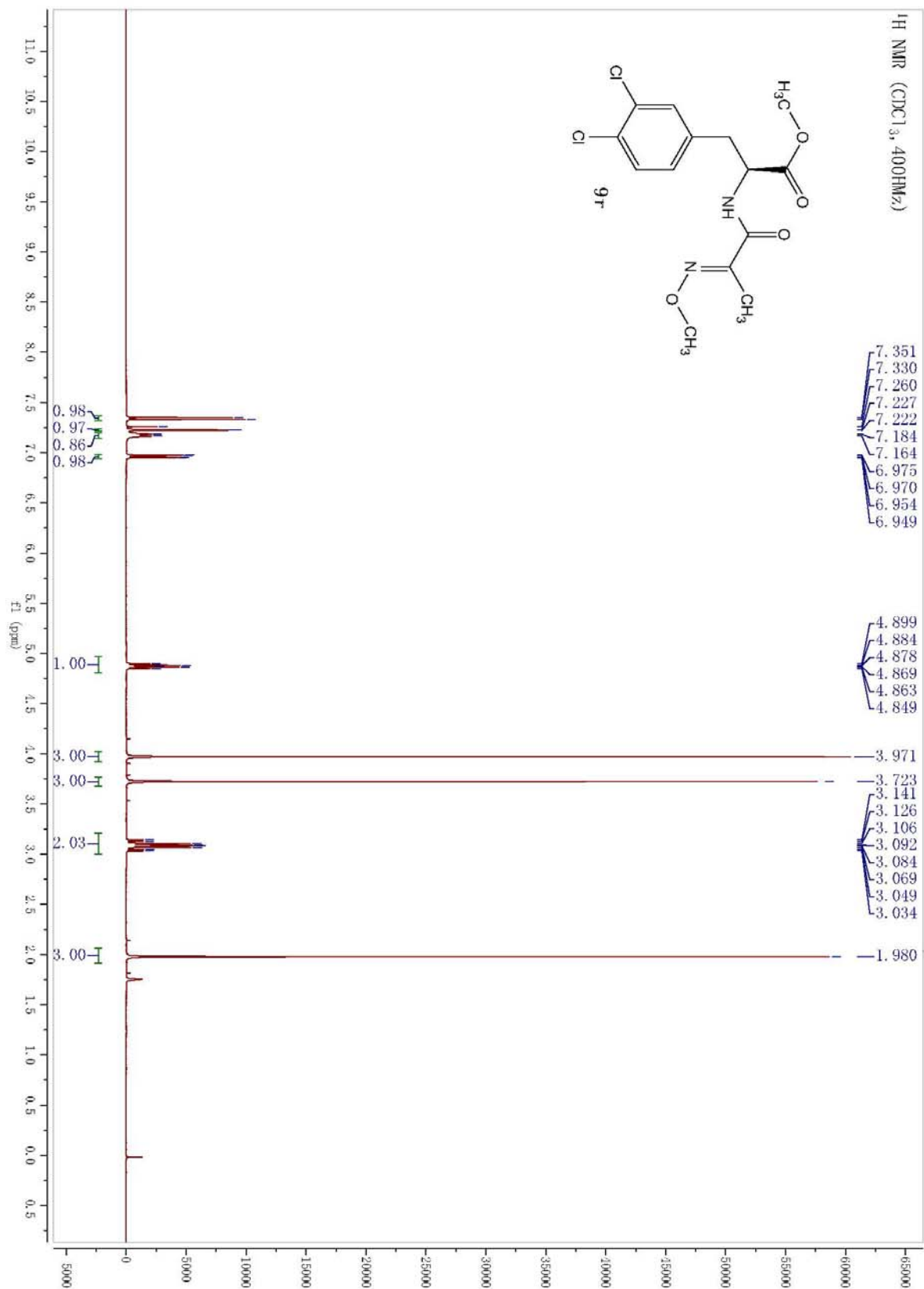


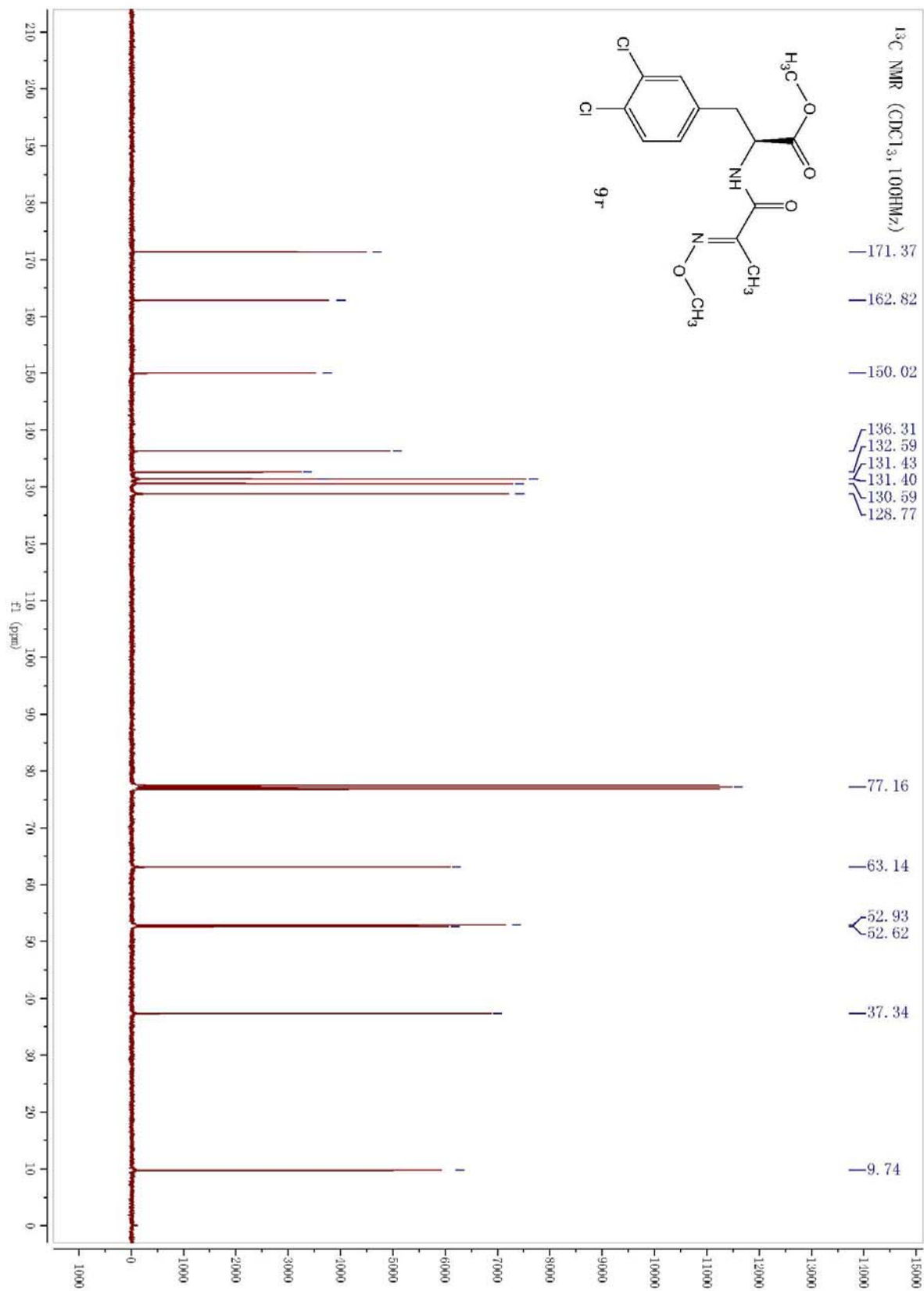


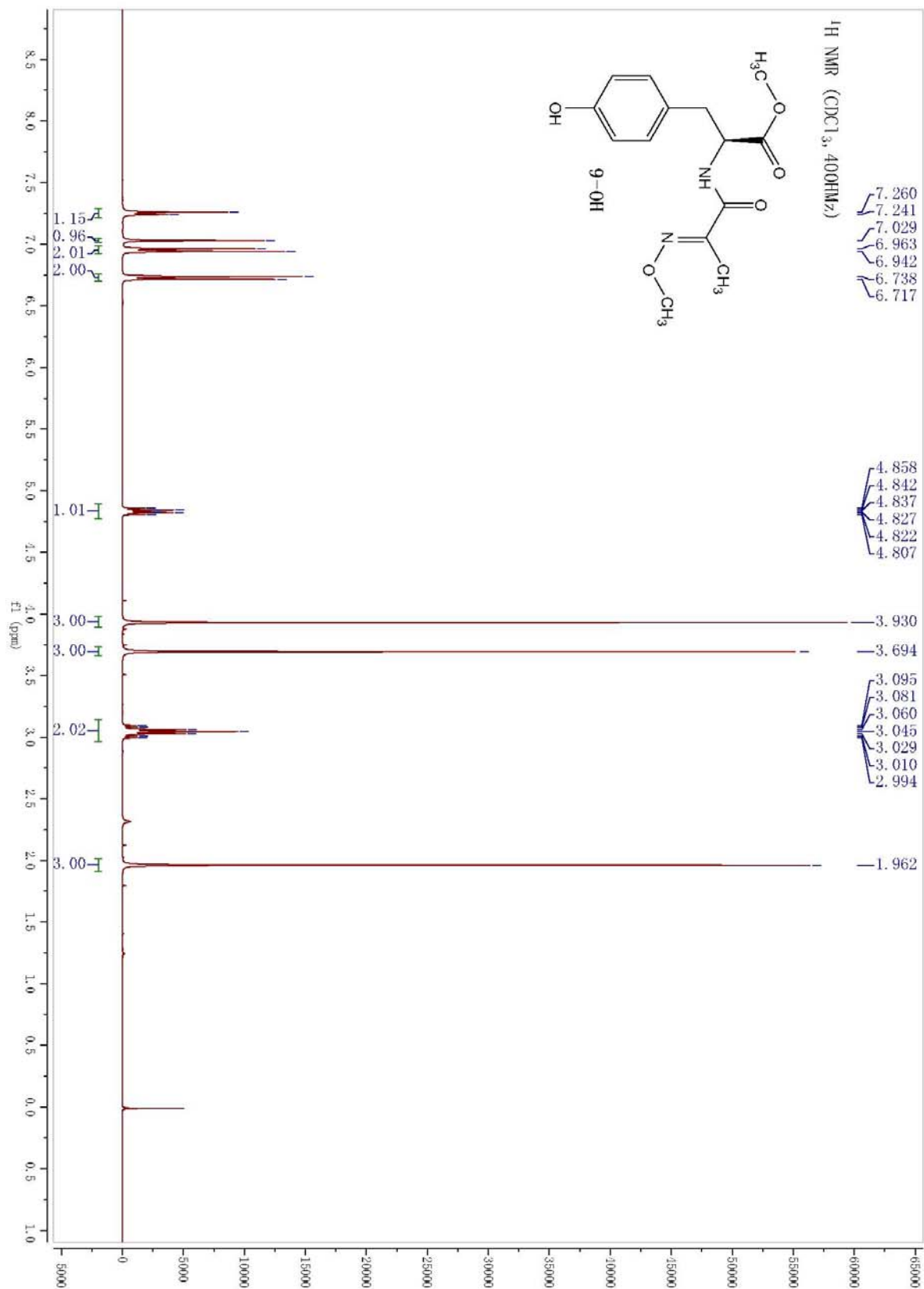


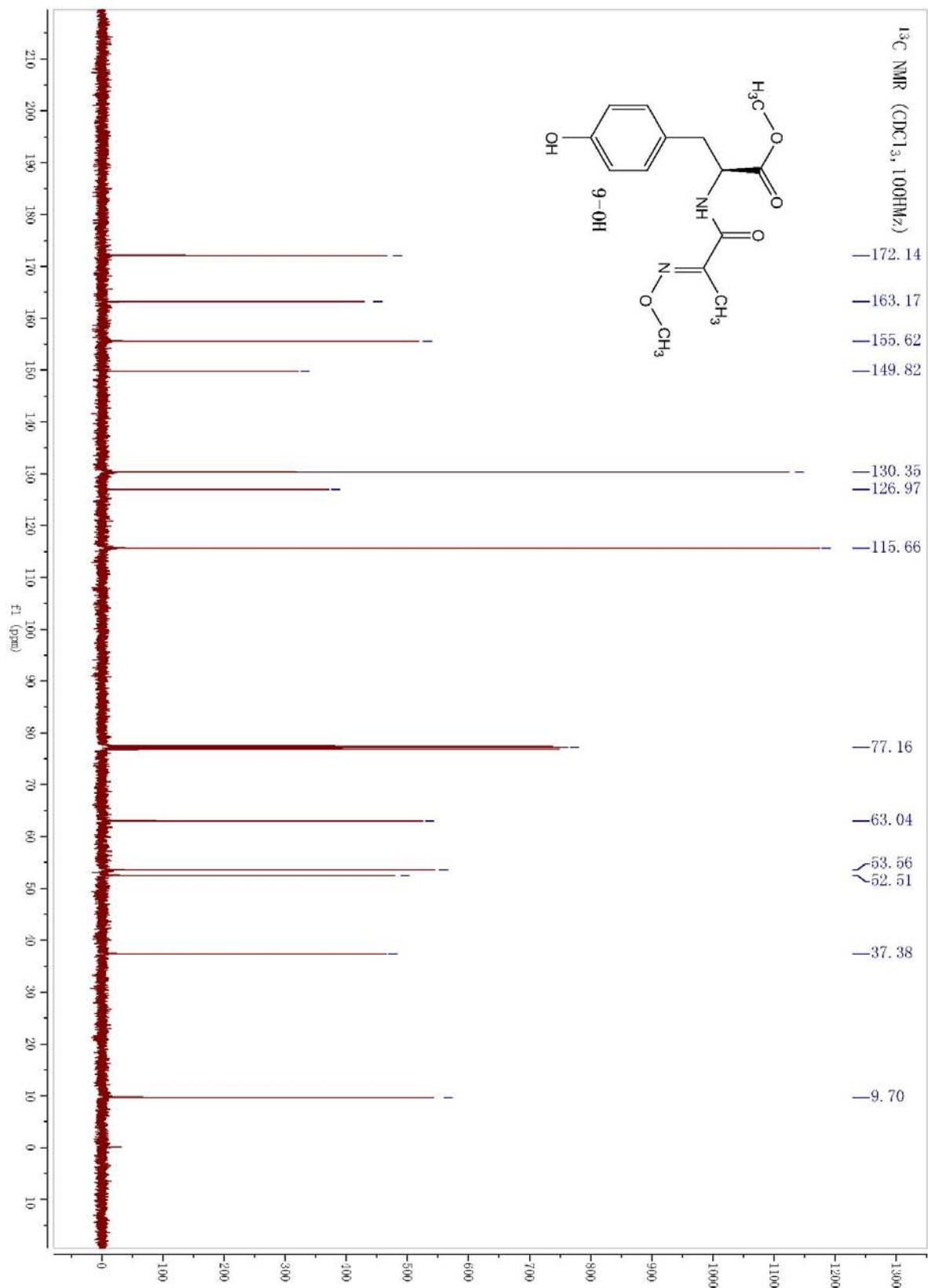


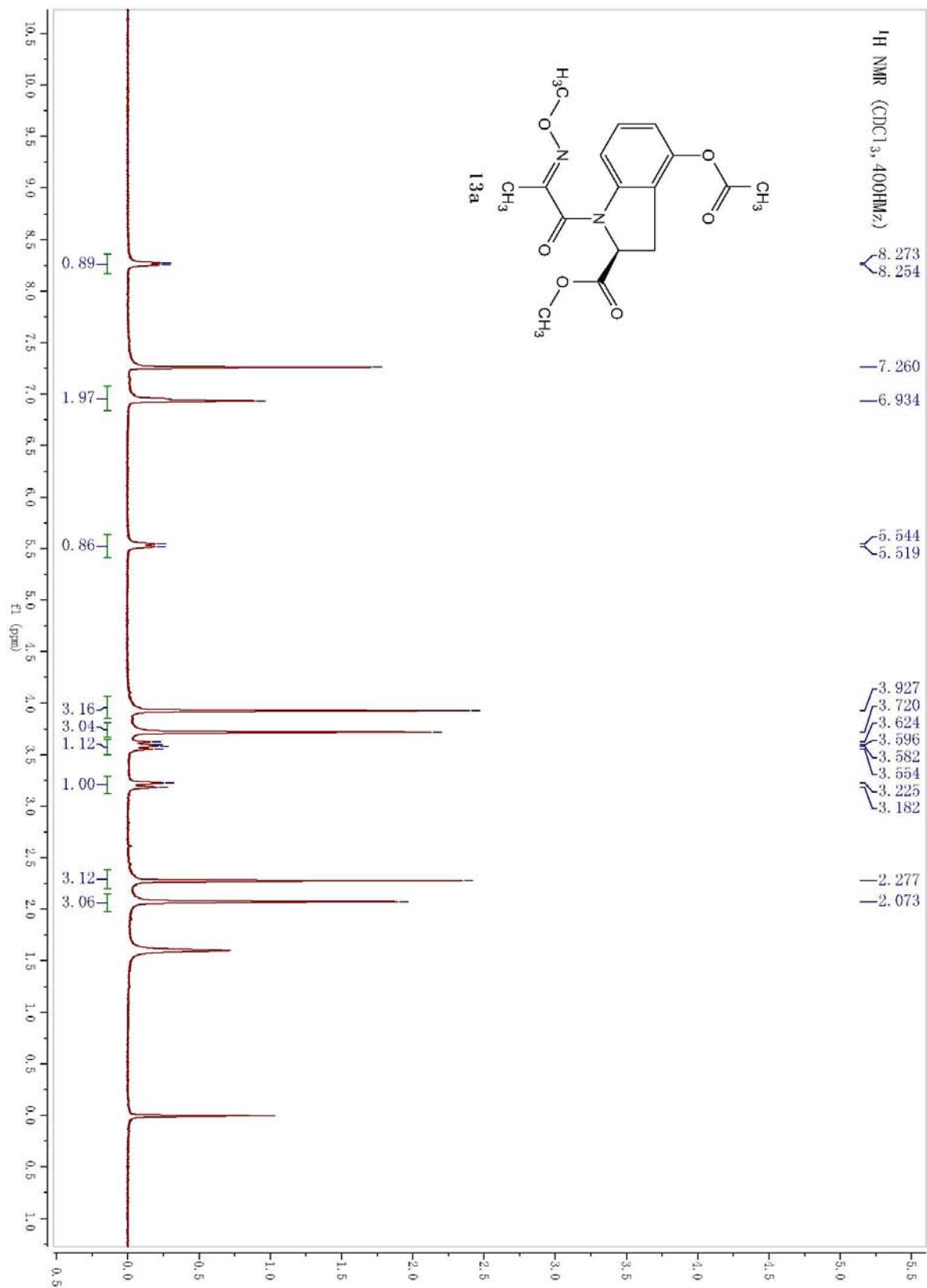


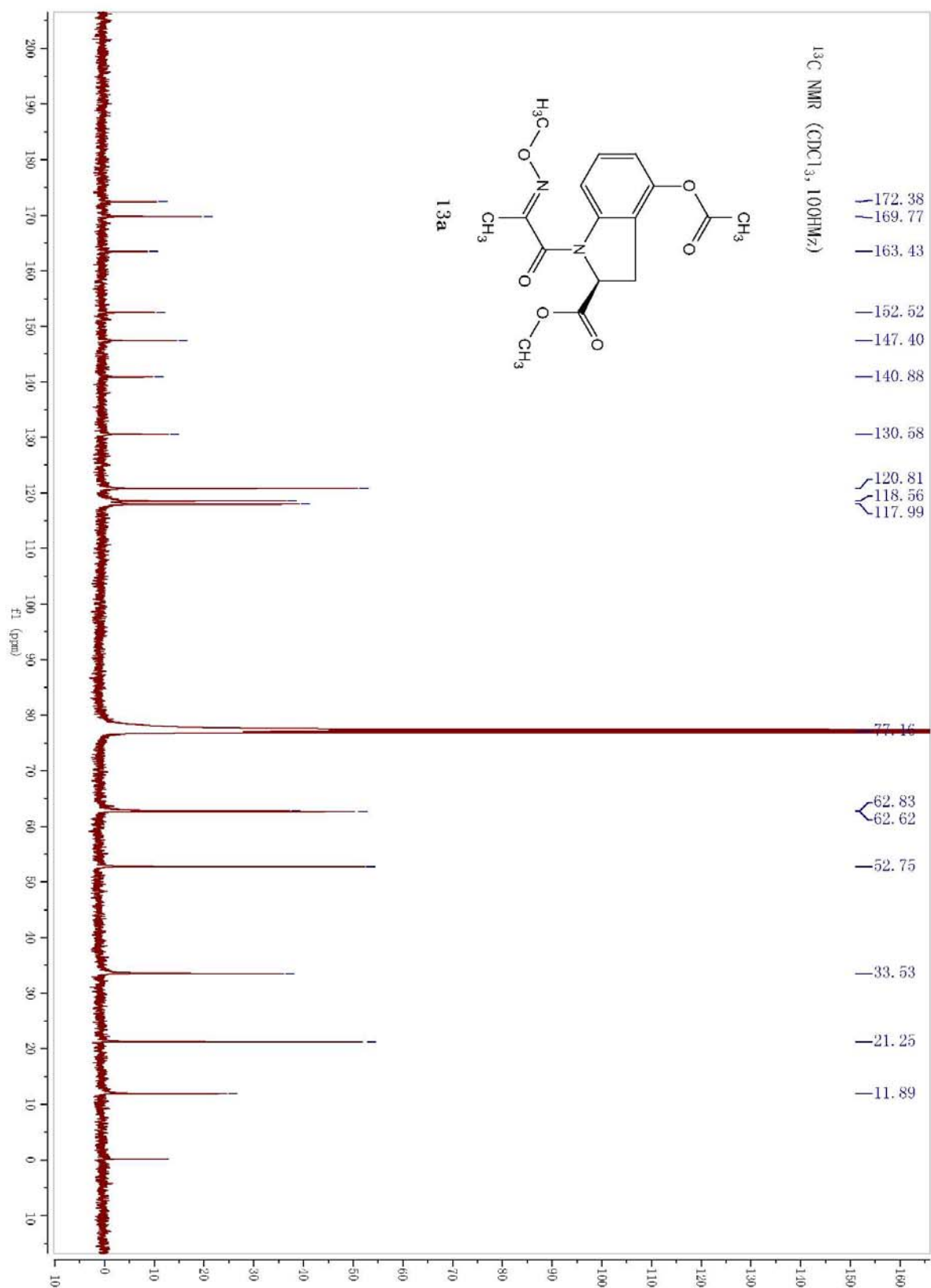


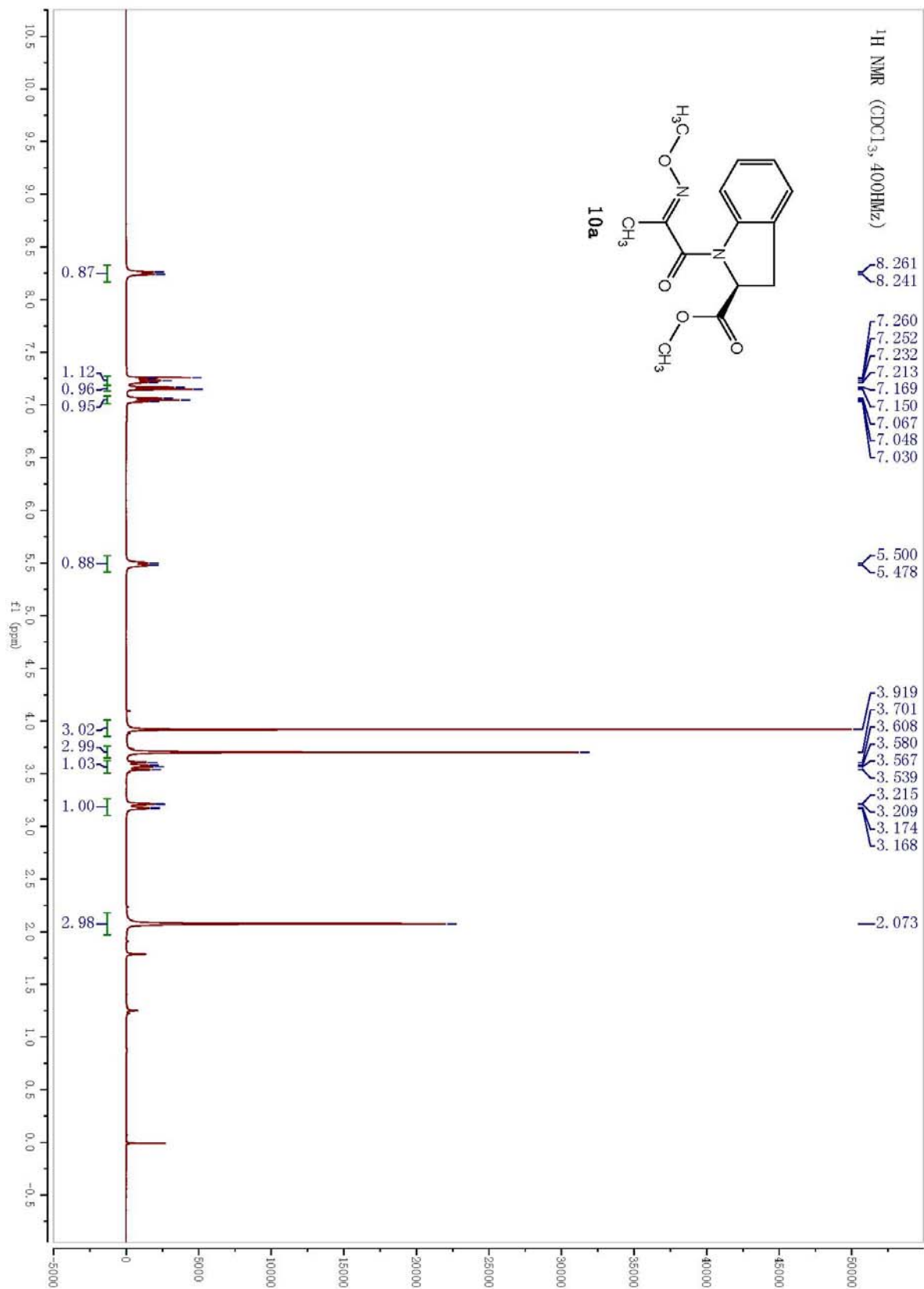


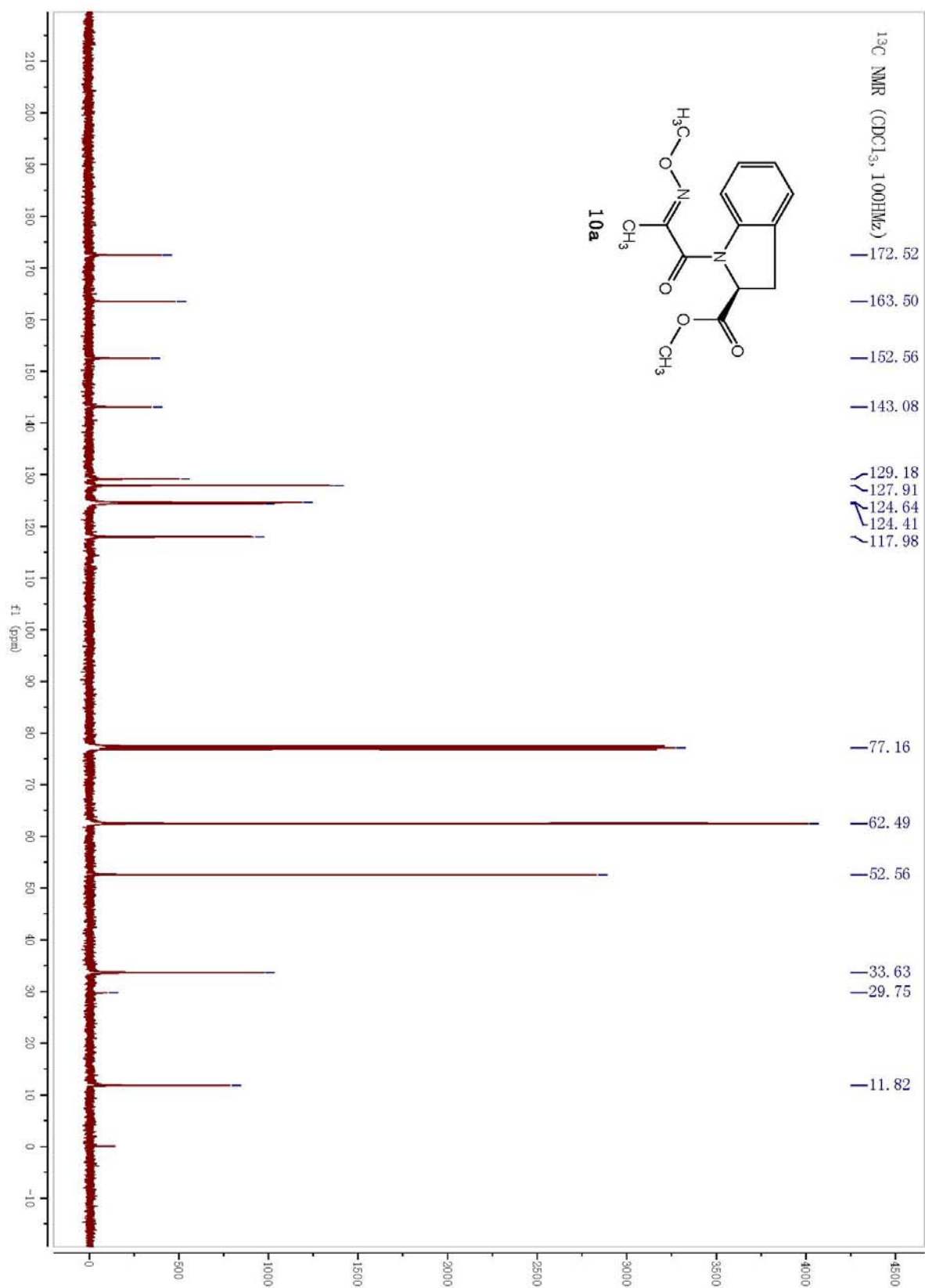




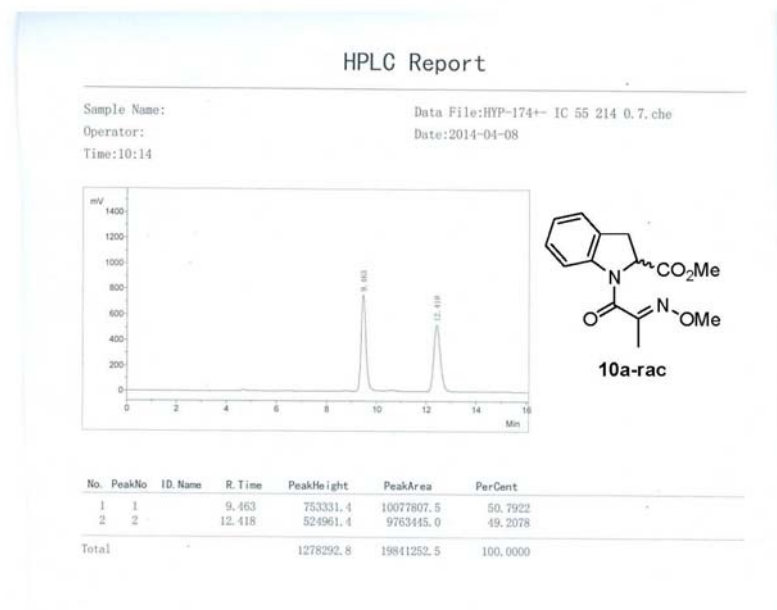
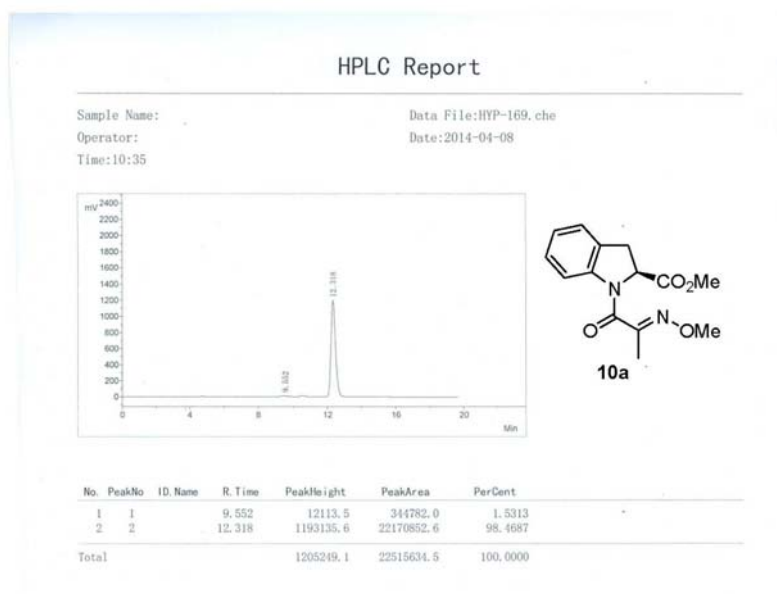


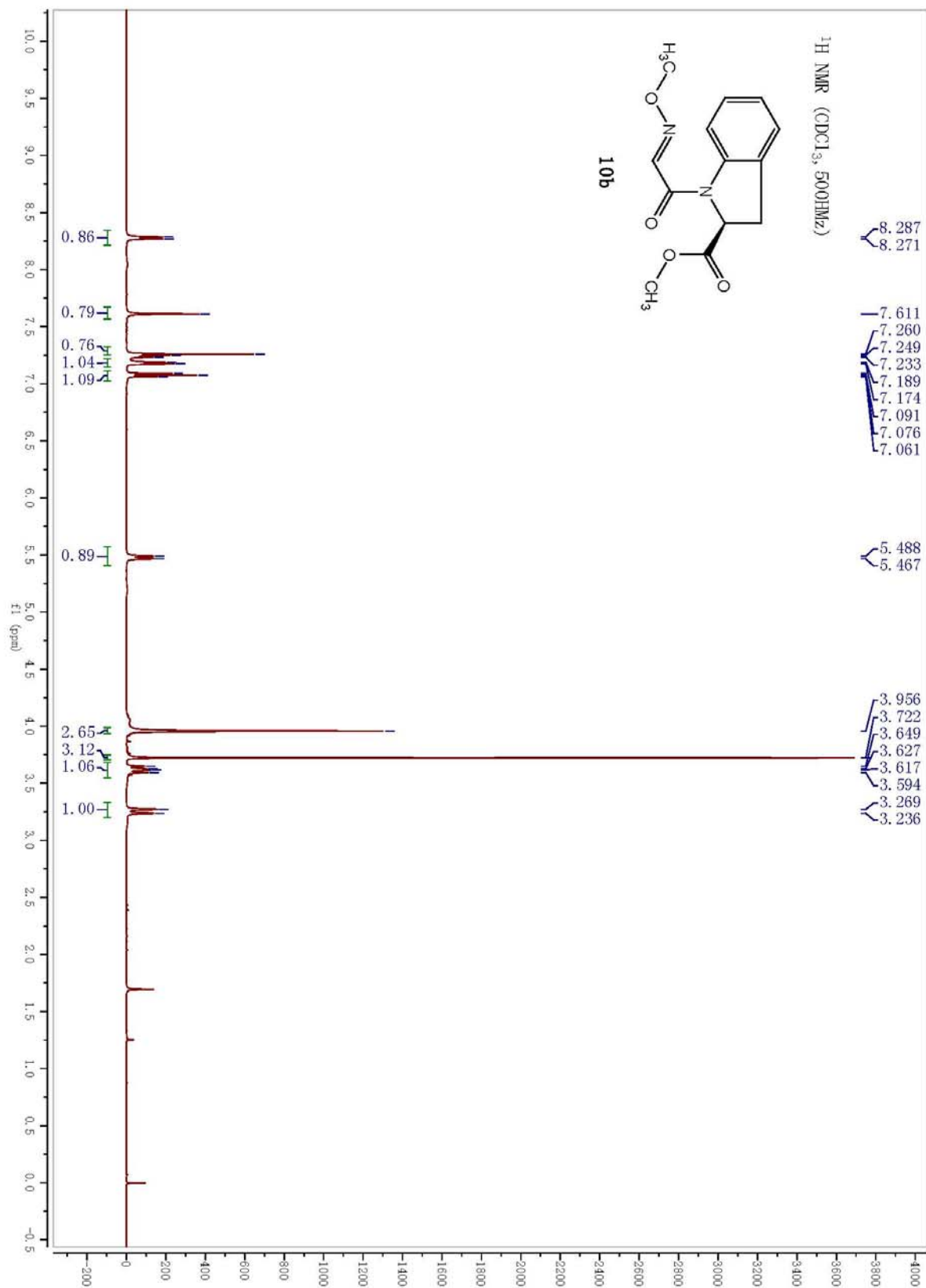


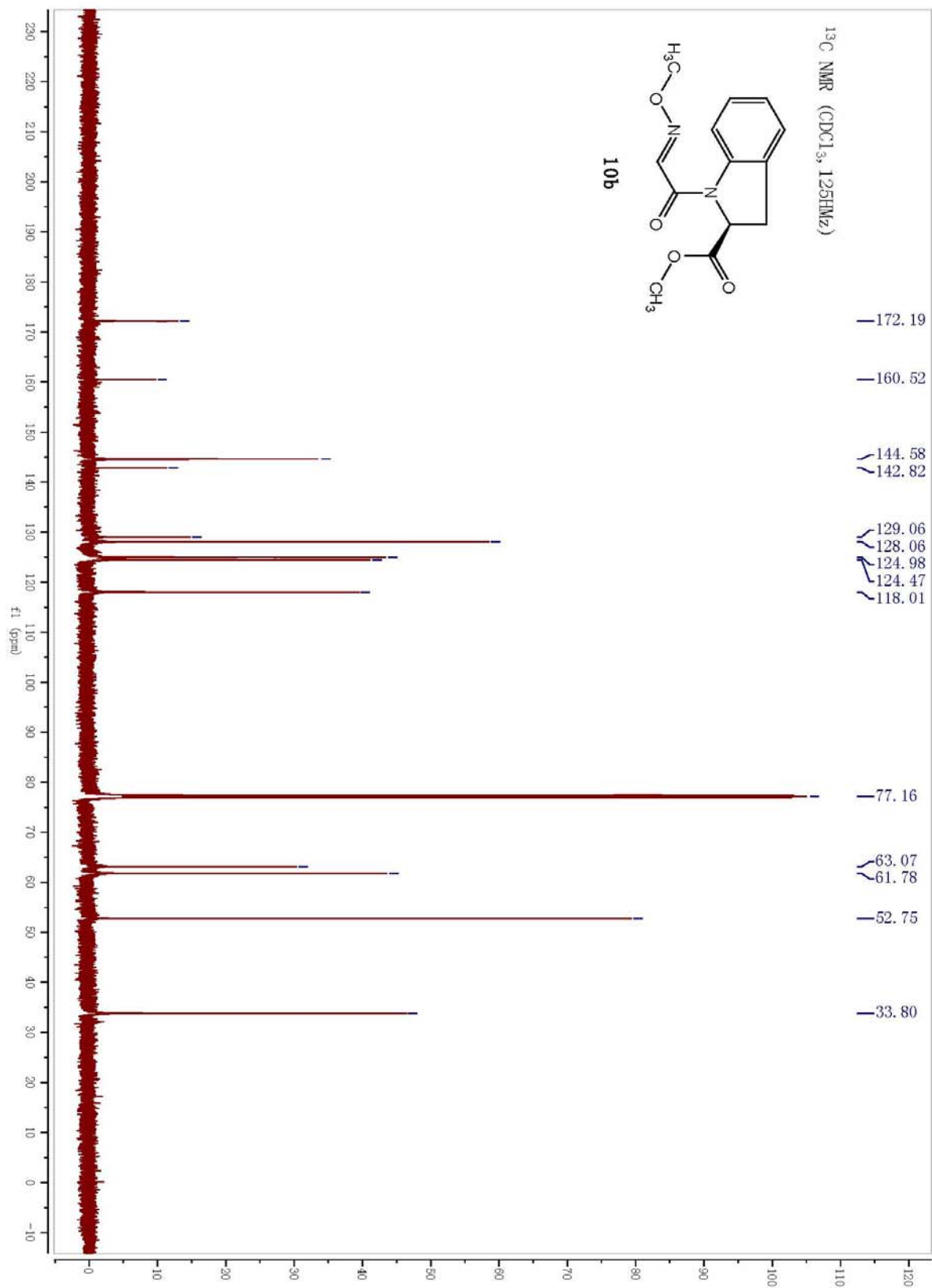


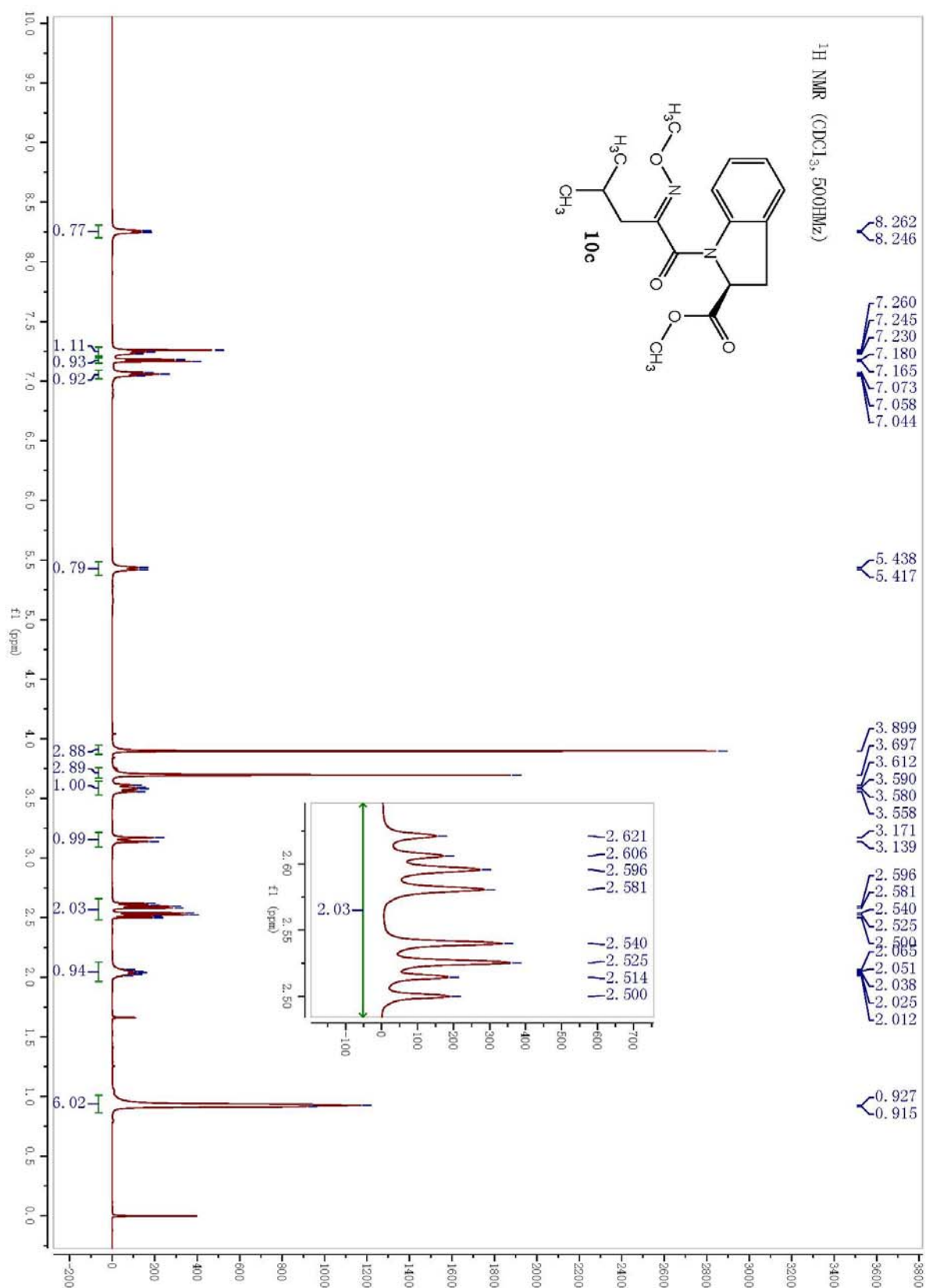


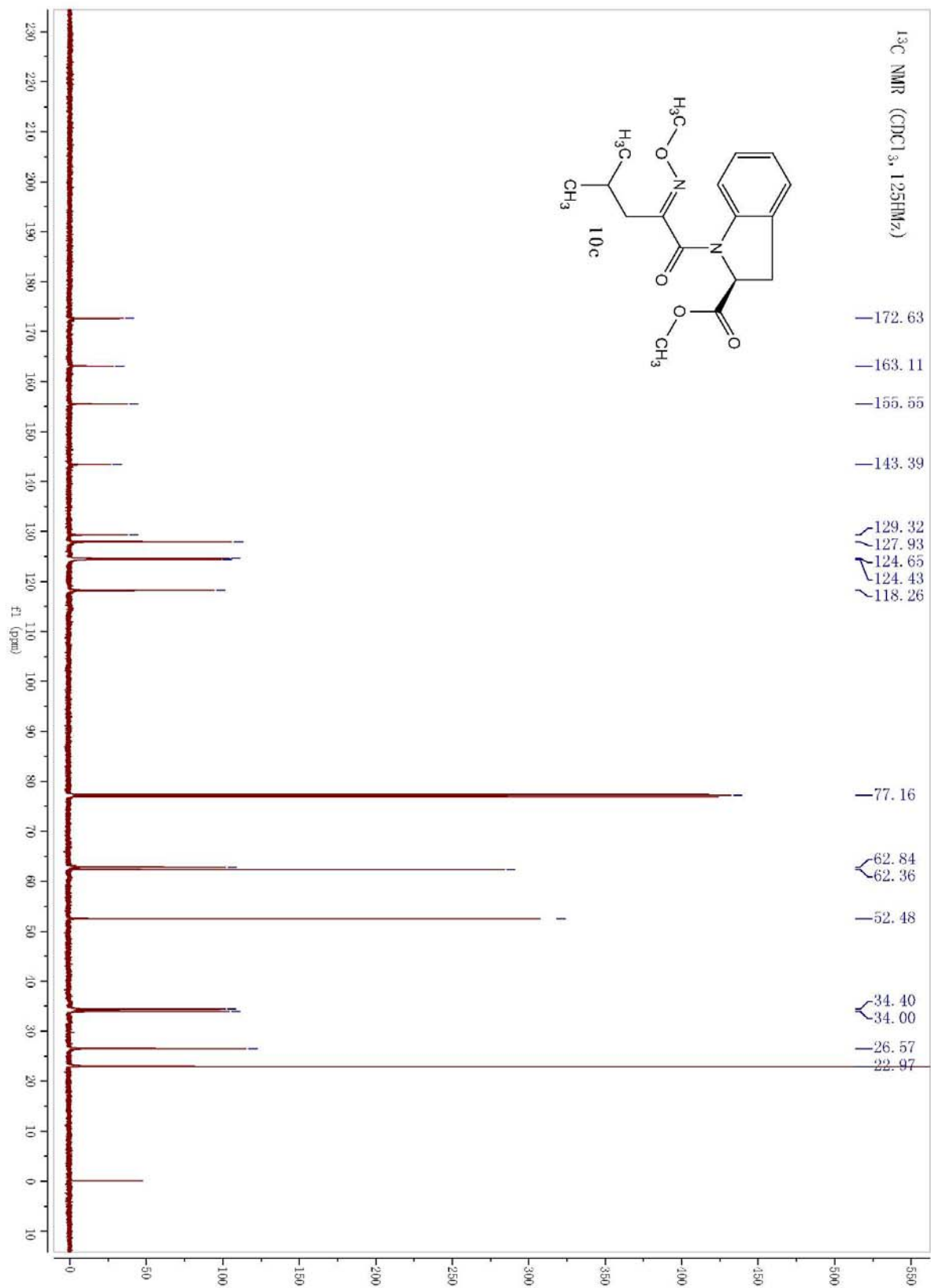
Racemic and optically active **10a** were analyzed with HPLC [CHIRALPAK IC (0.46*25cm, 5 μ m) column, hexan/isopropanol = 50/50, 0.7 mL/min, 214 nm] to determine retention time and enantiomeric excesses. **10a**, ee = 97%.

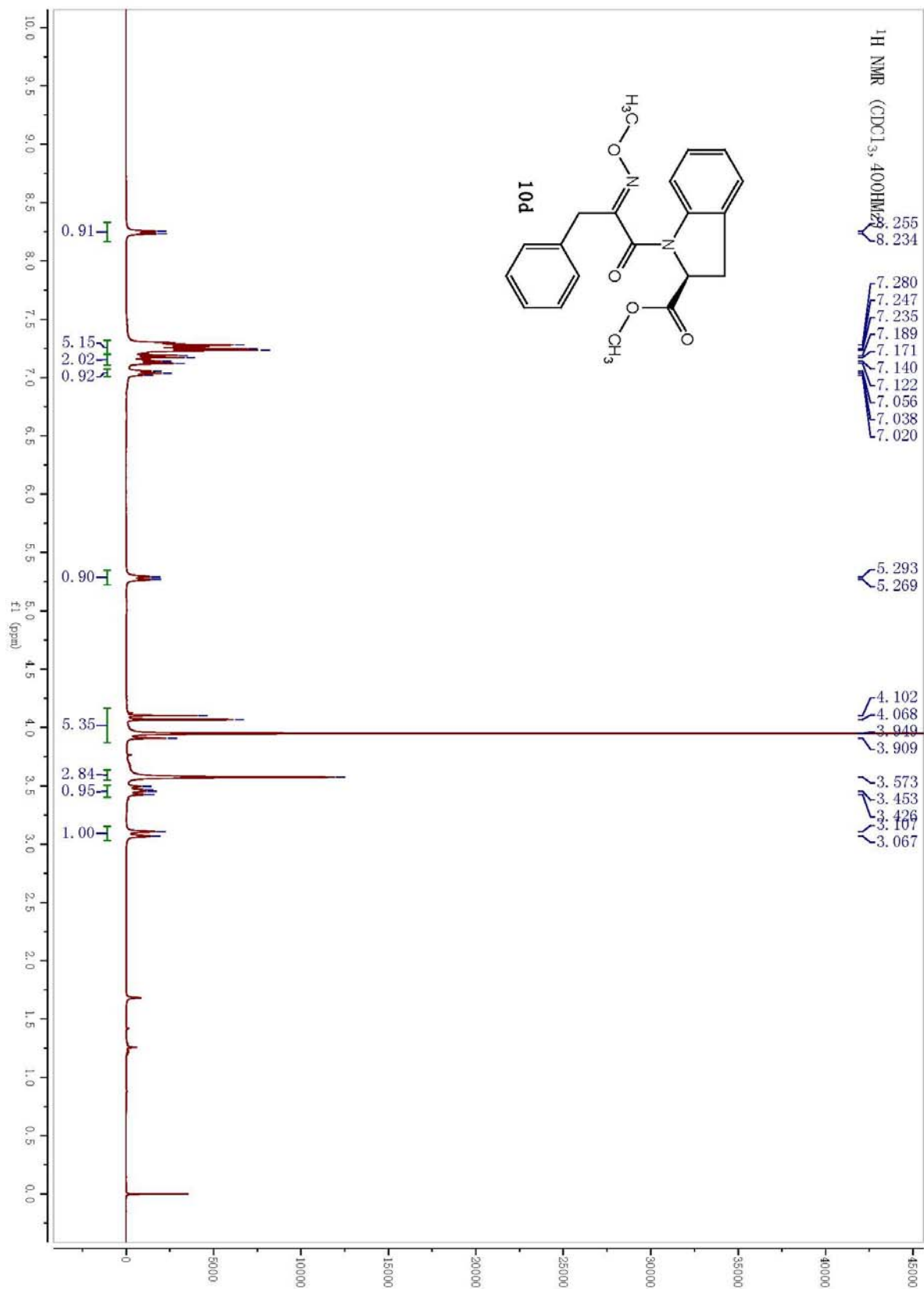


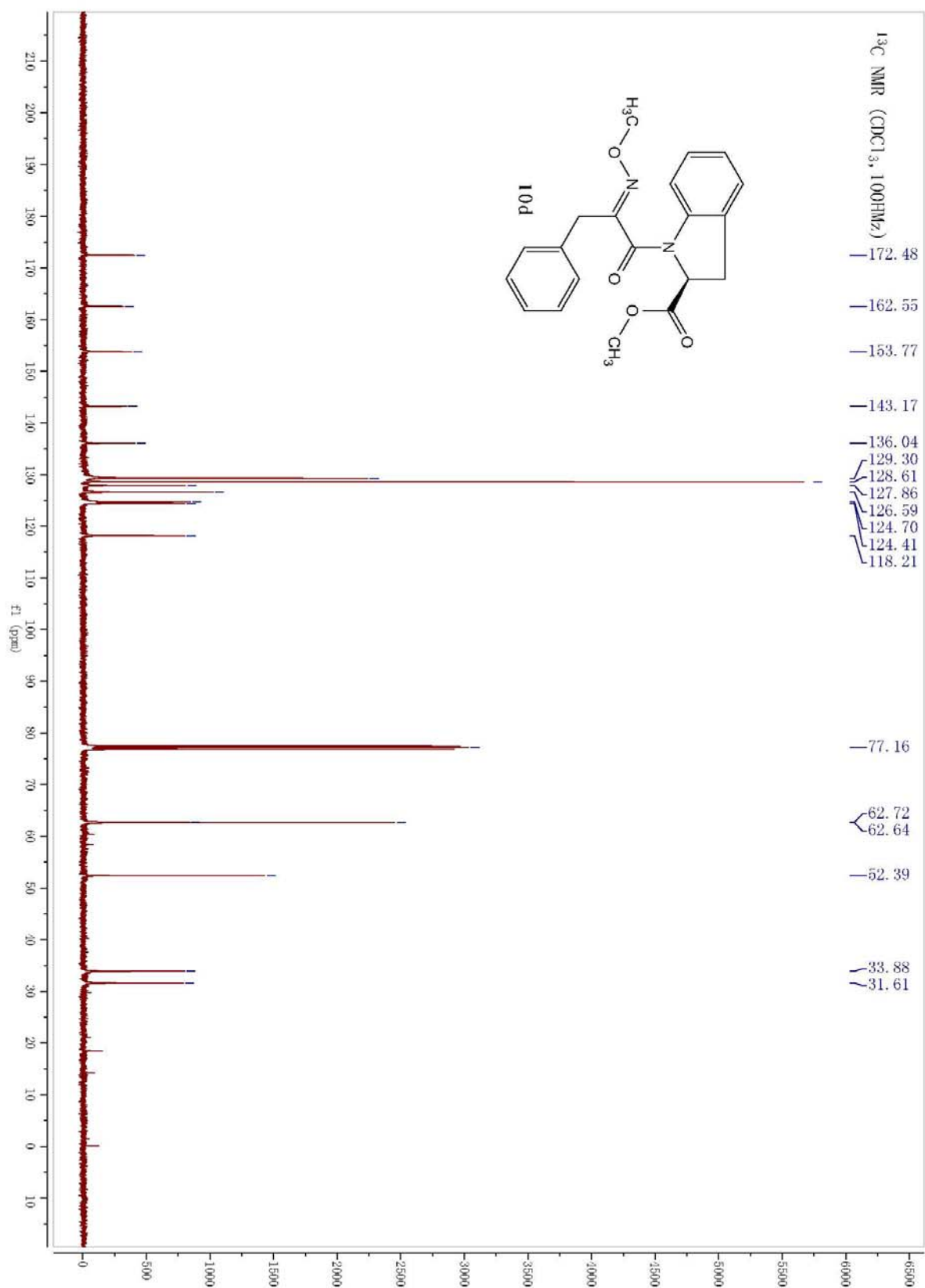


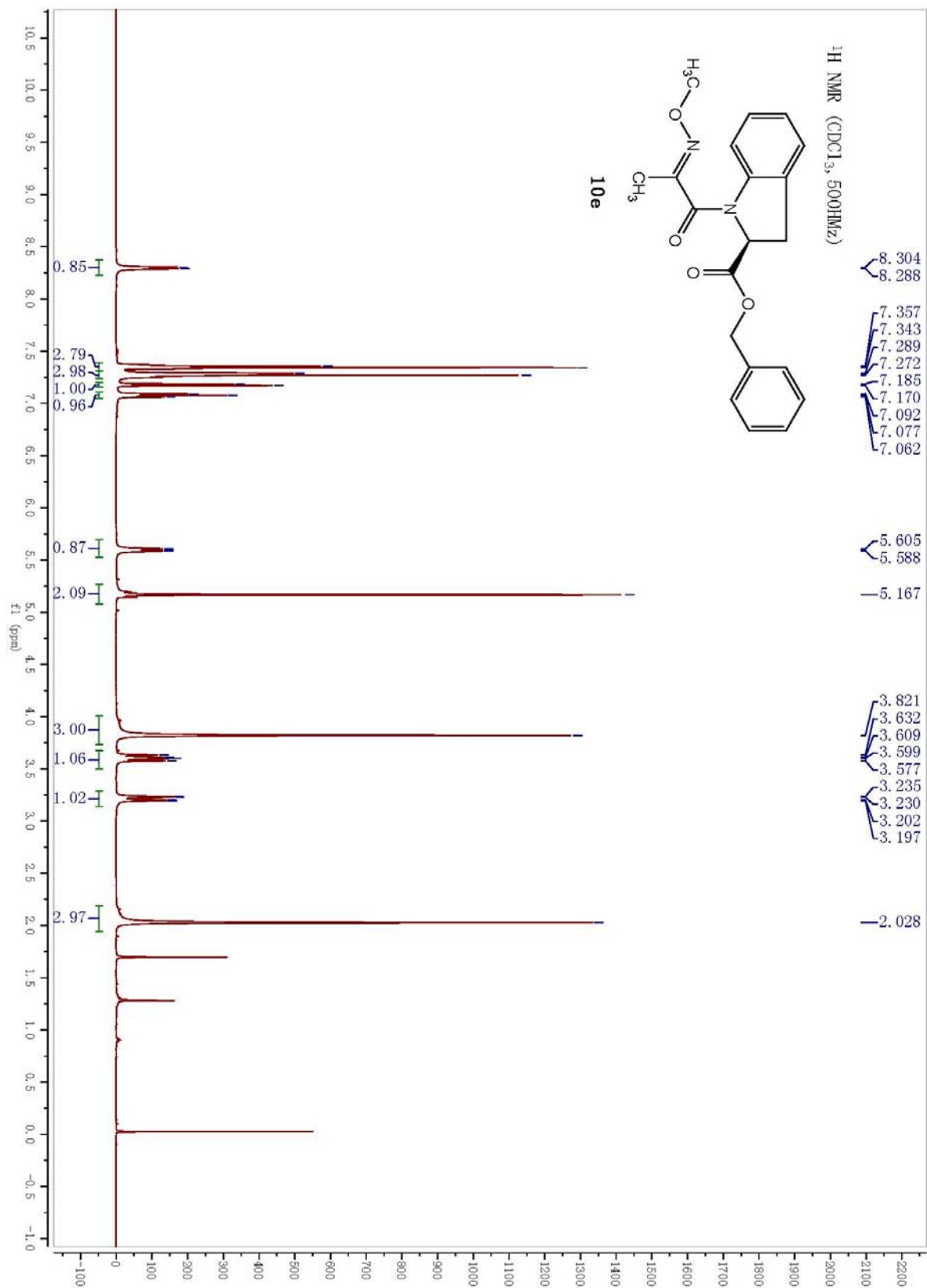


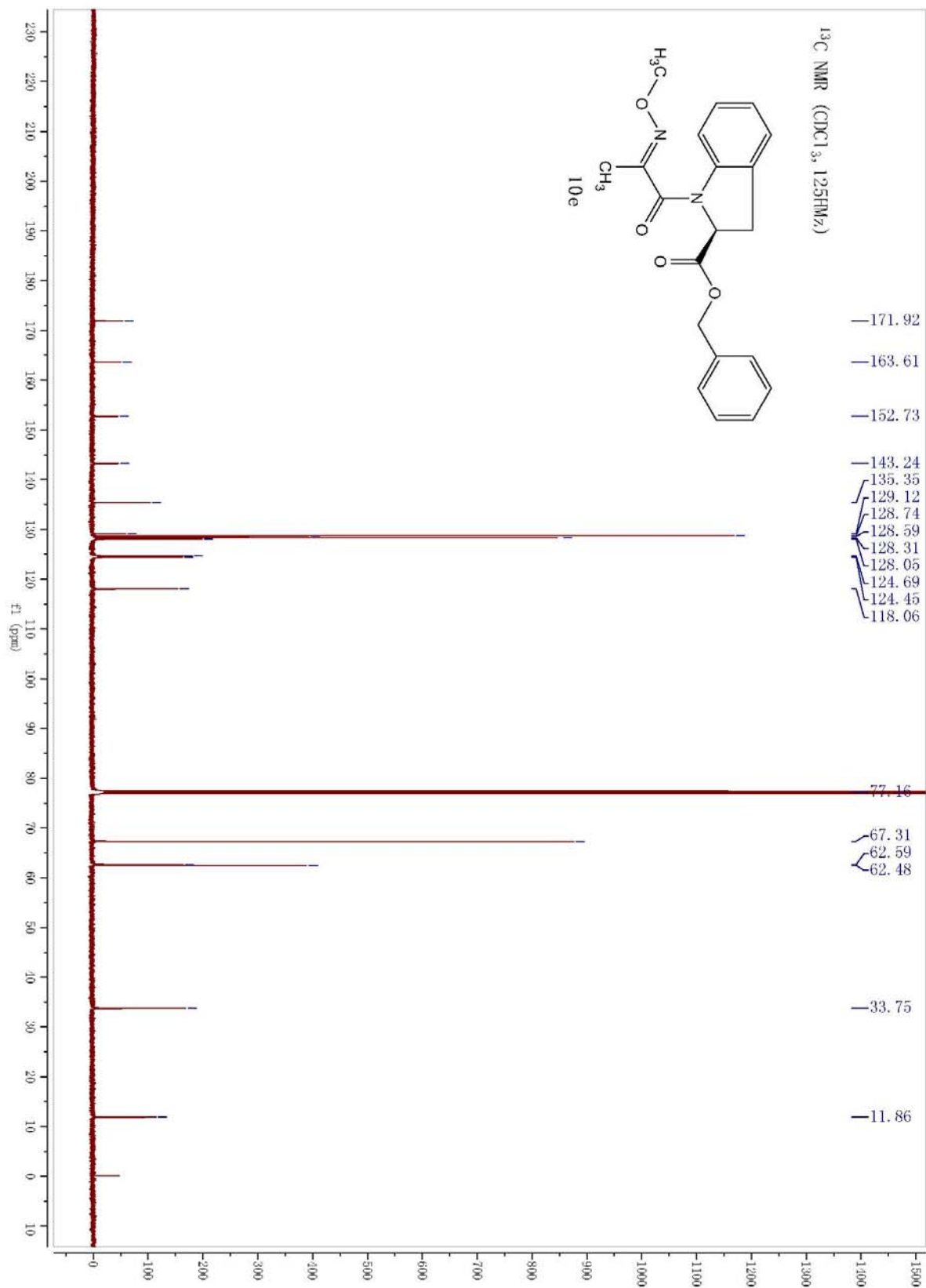


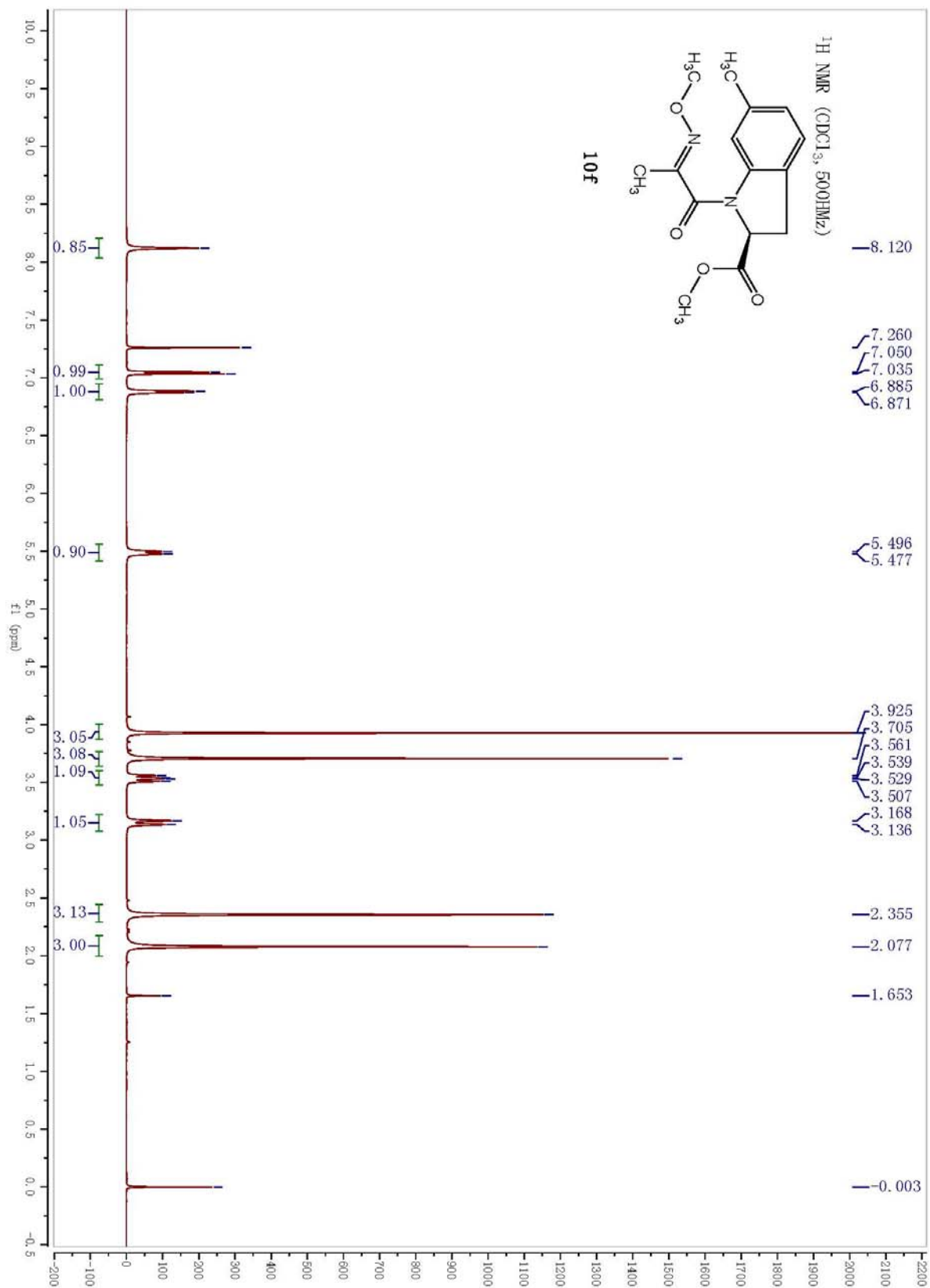


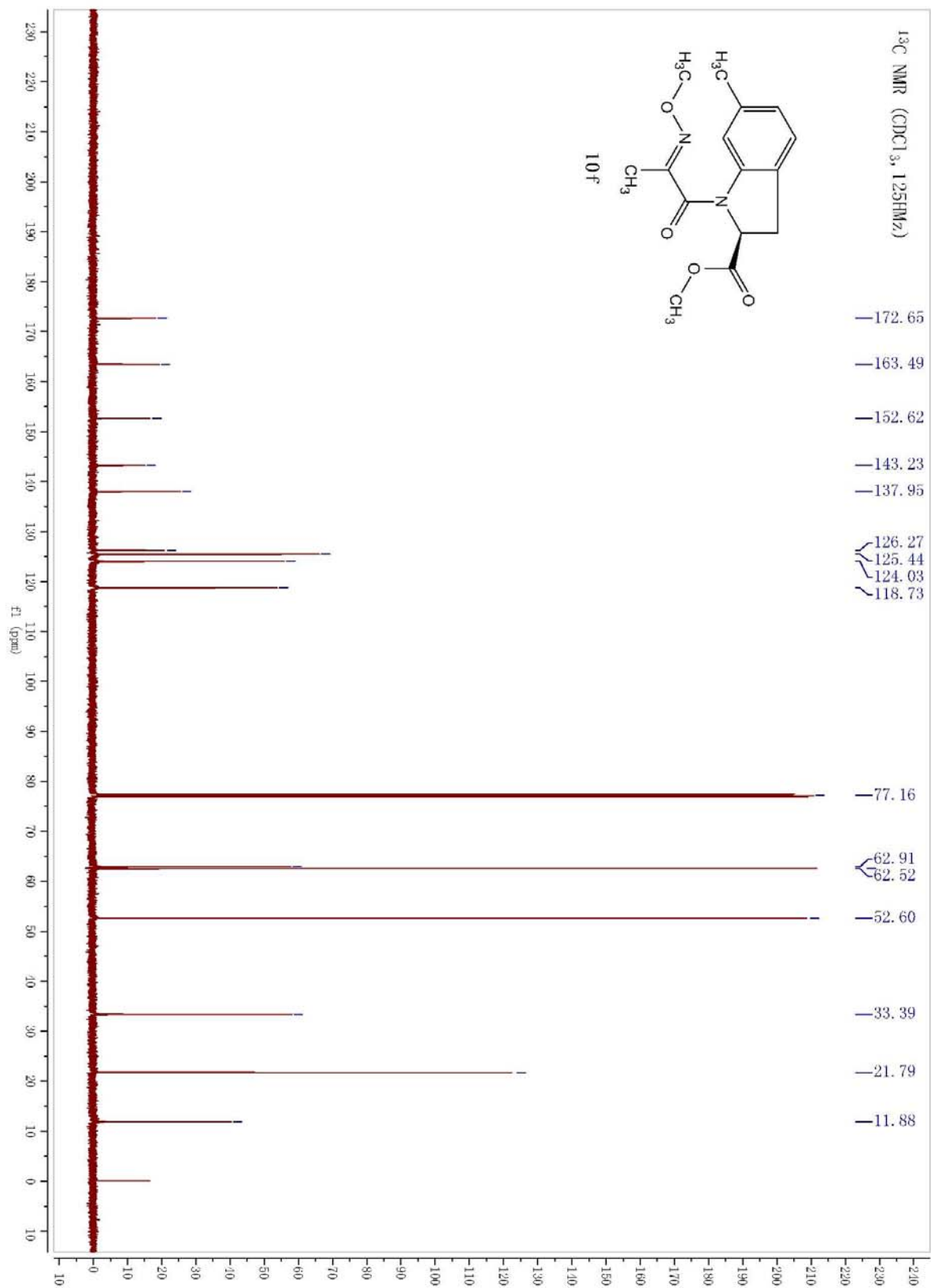


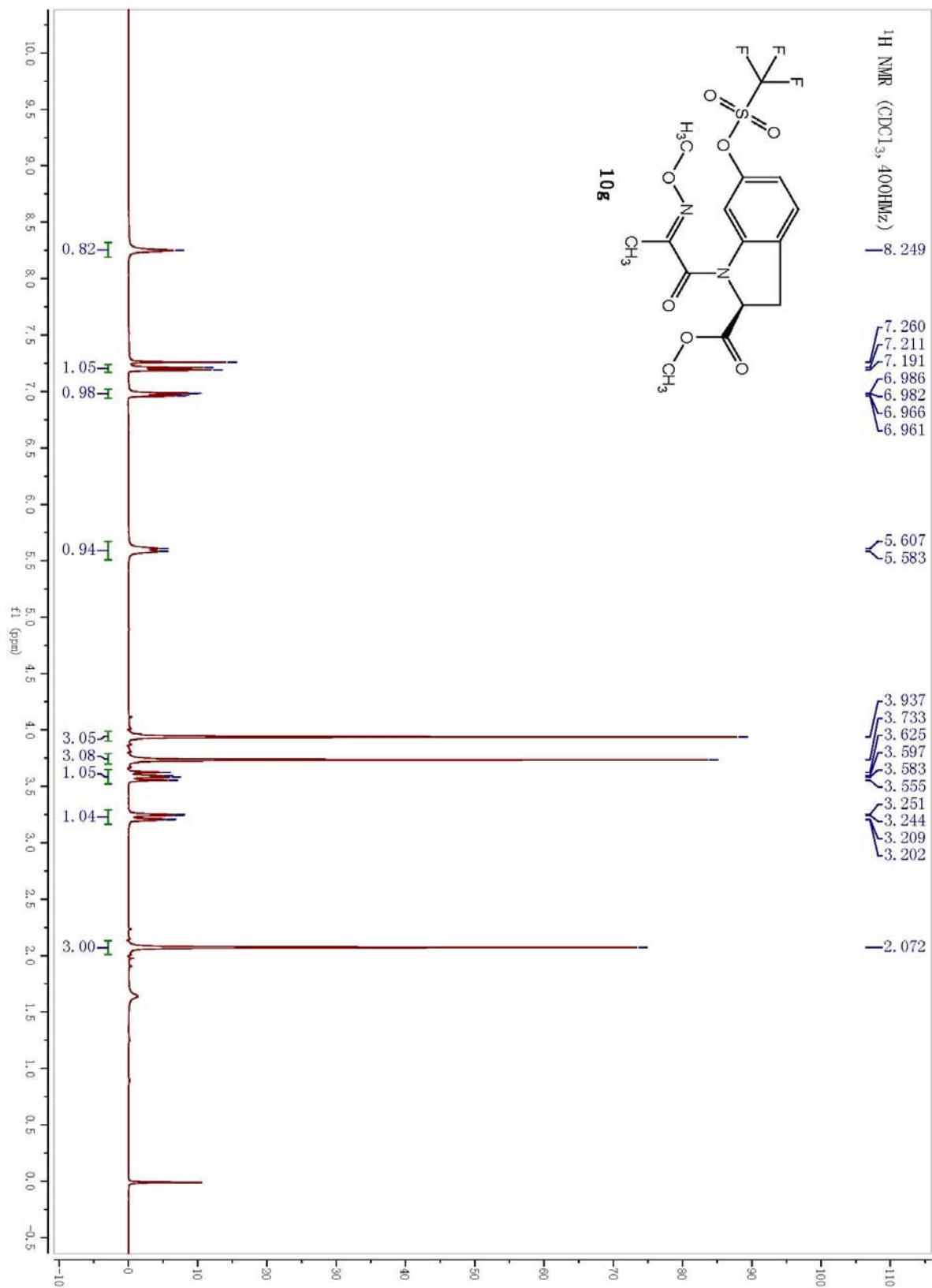


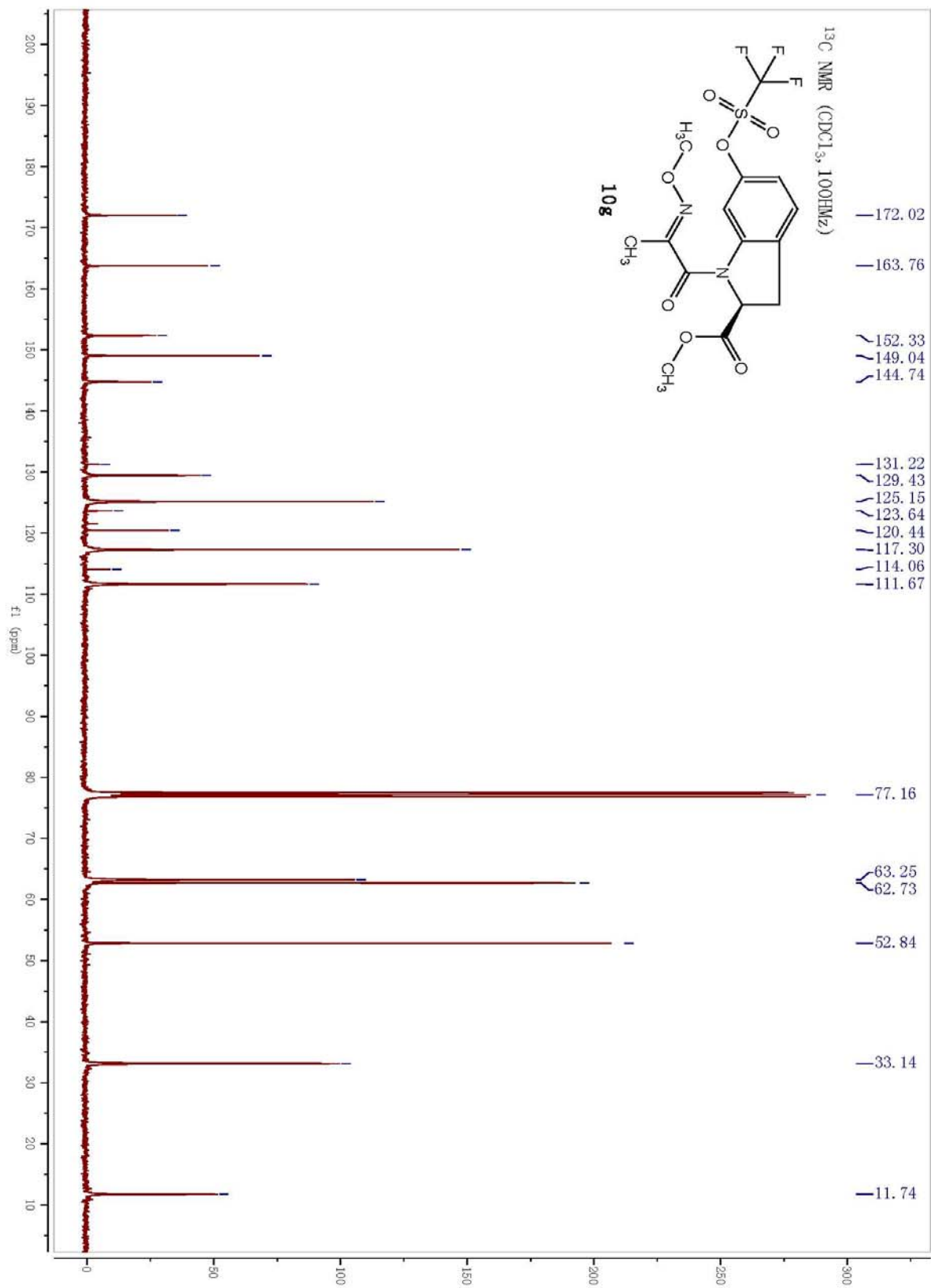


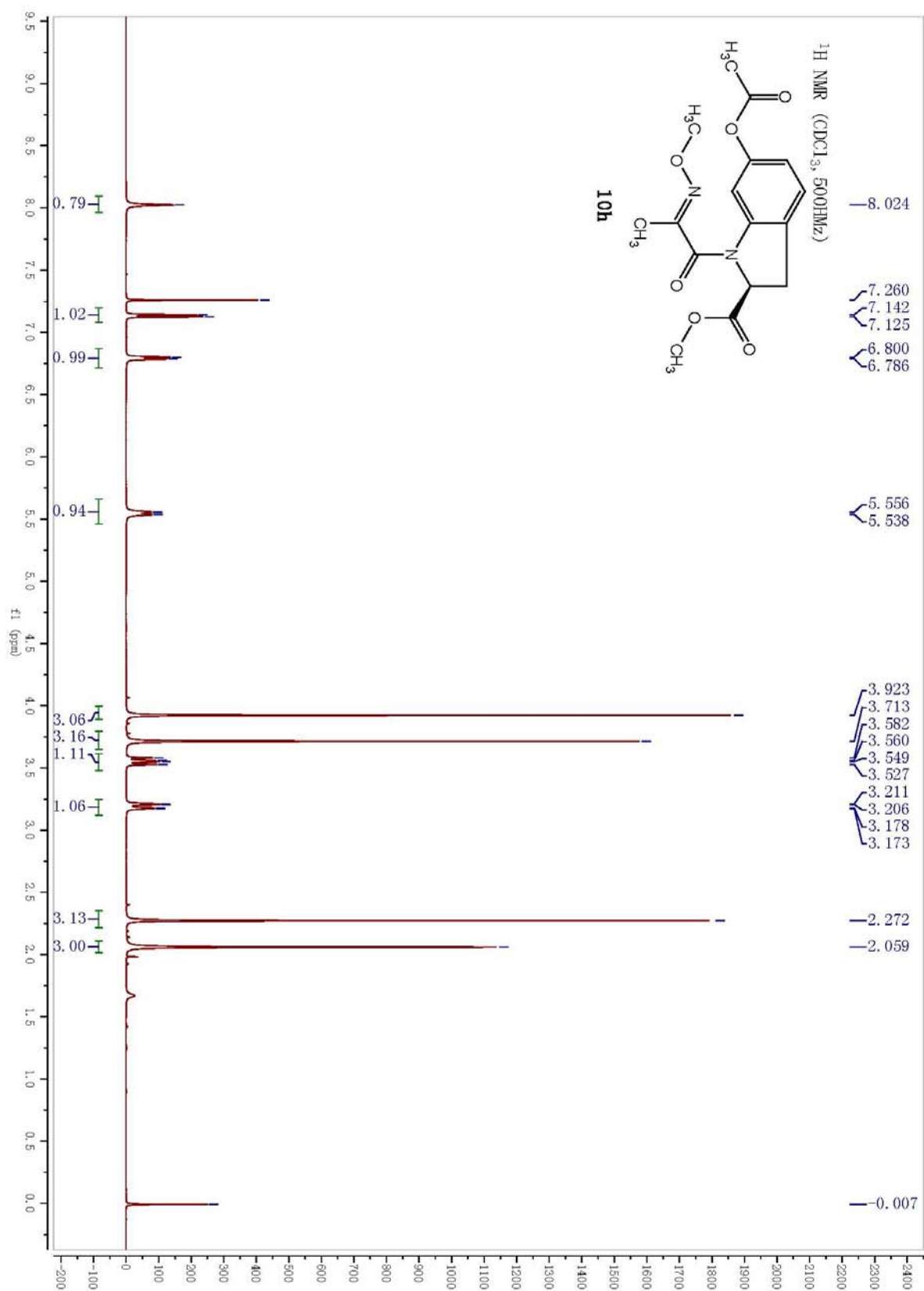


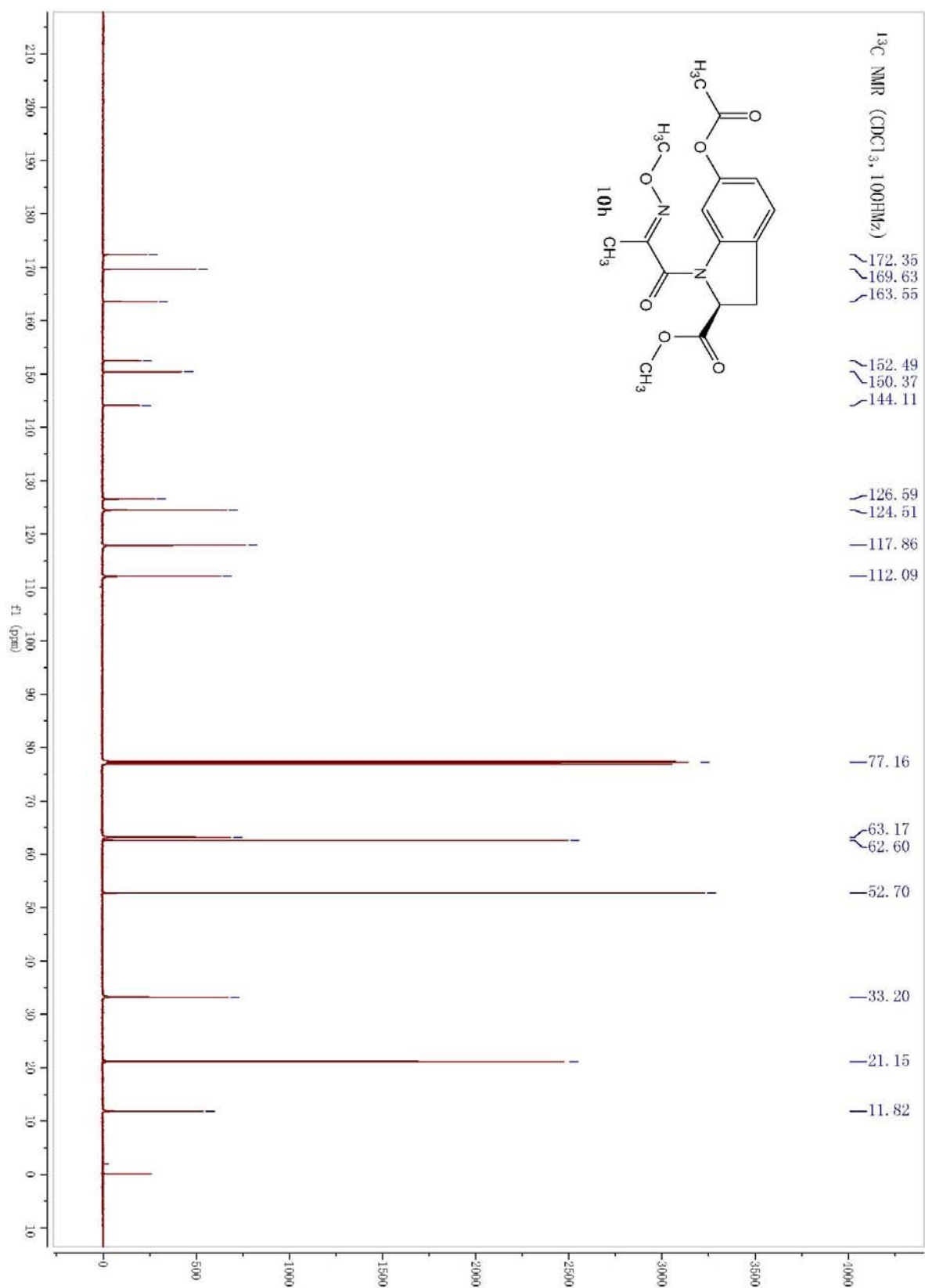


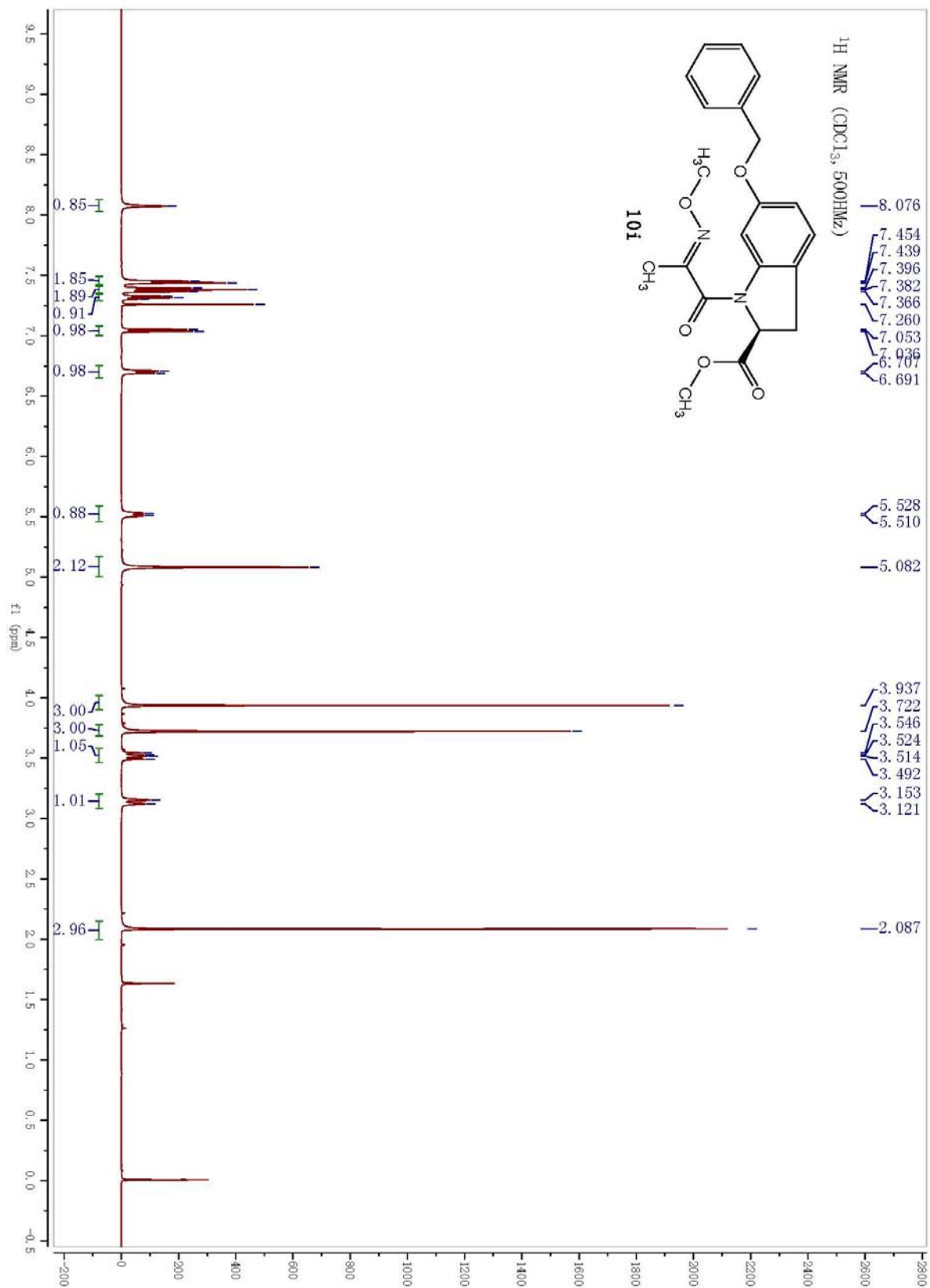


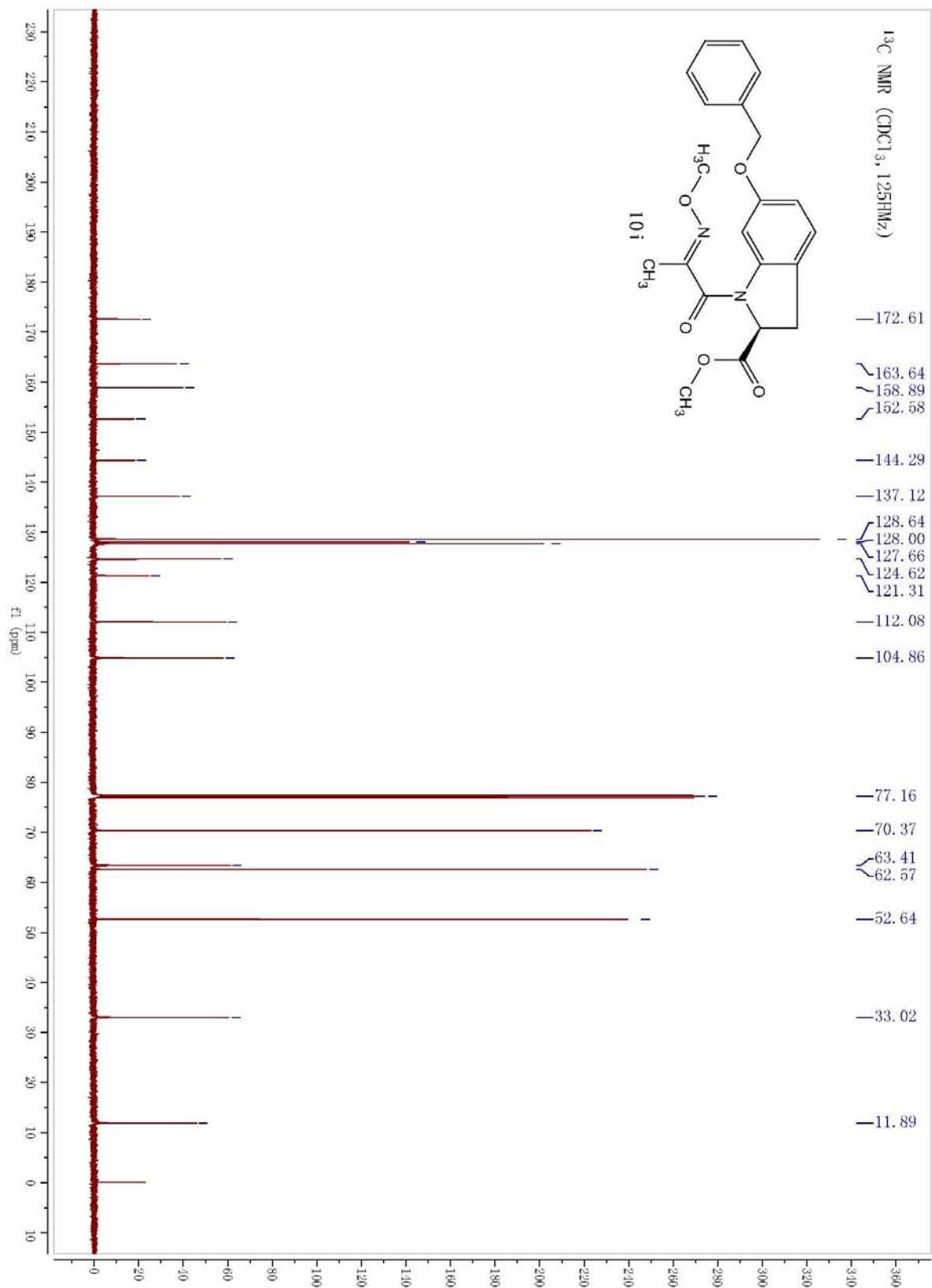


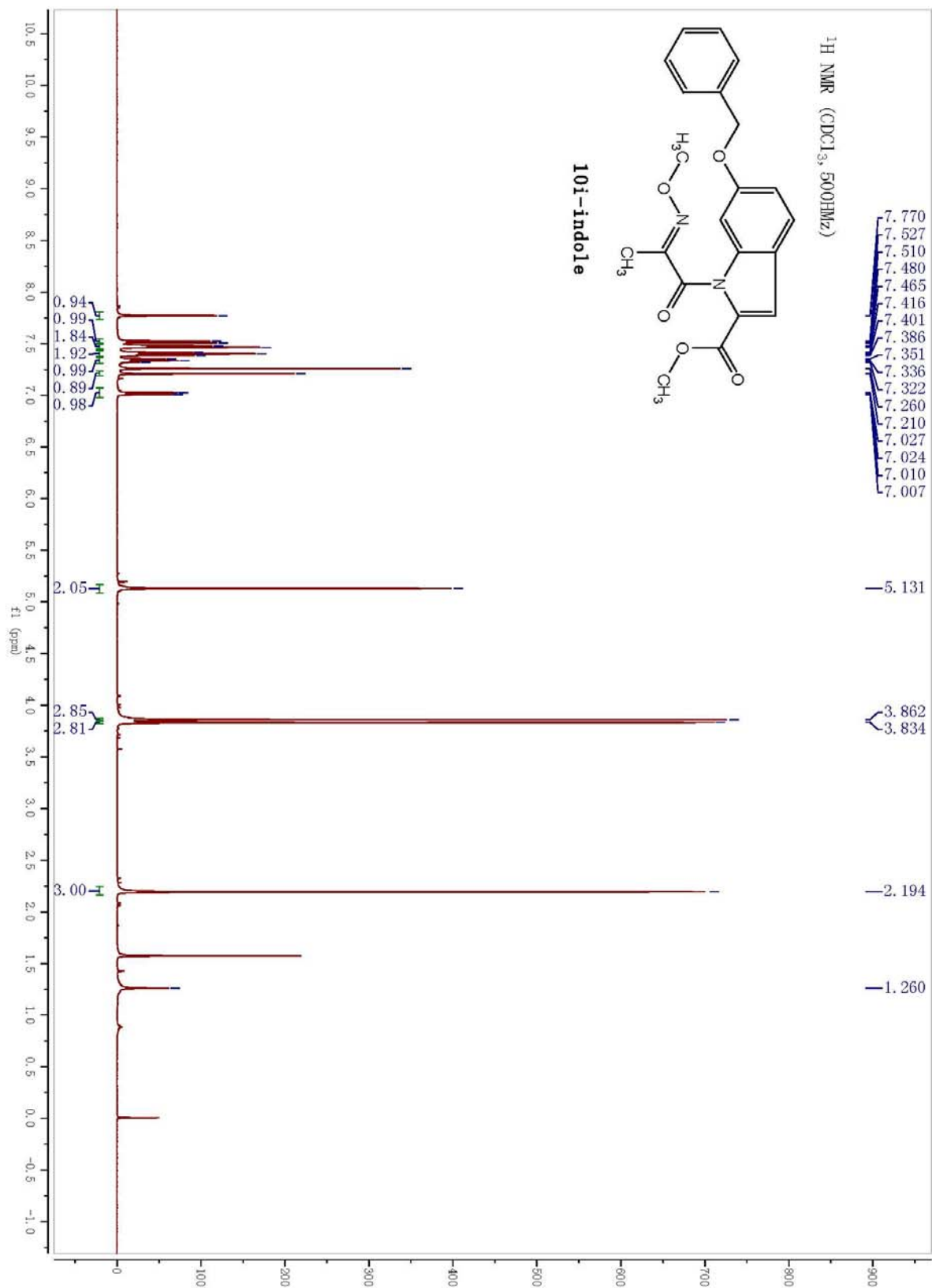


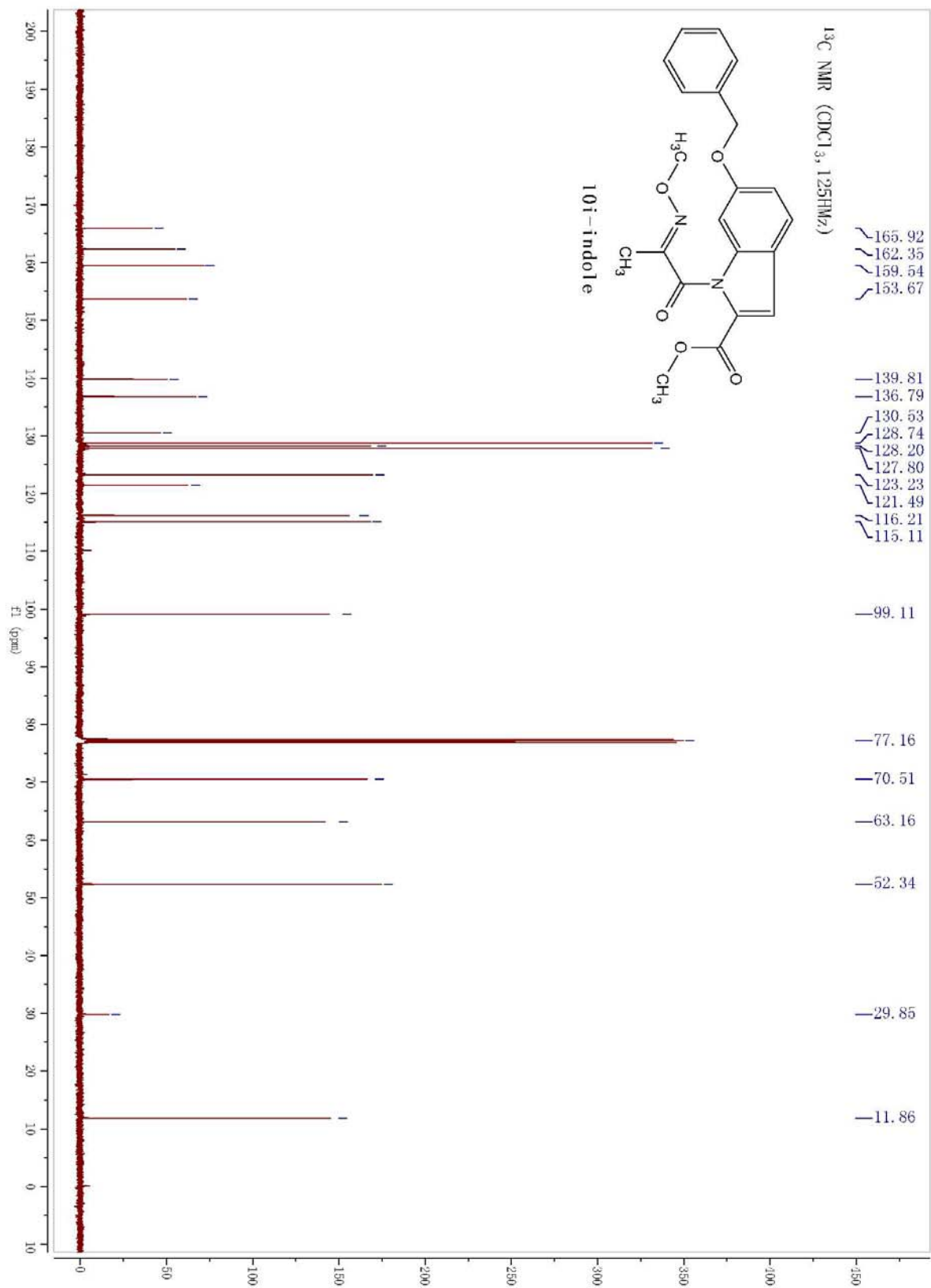


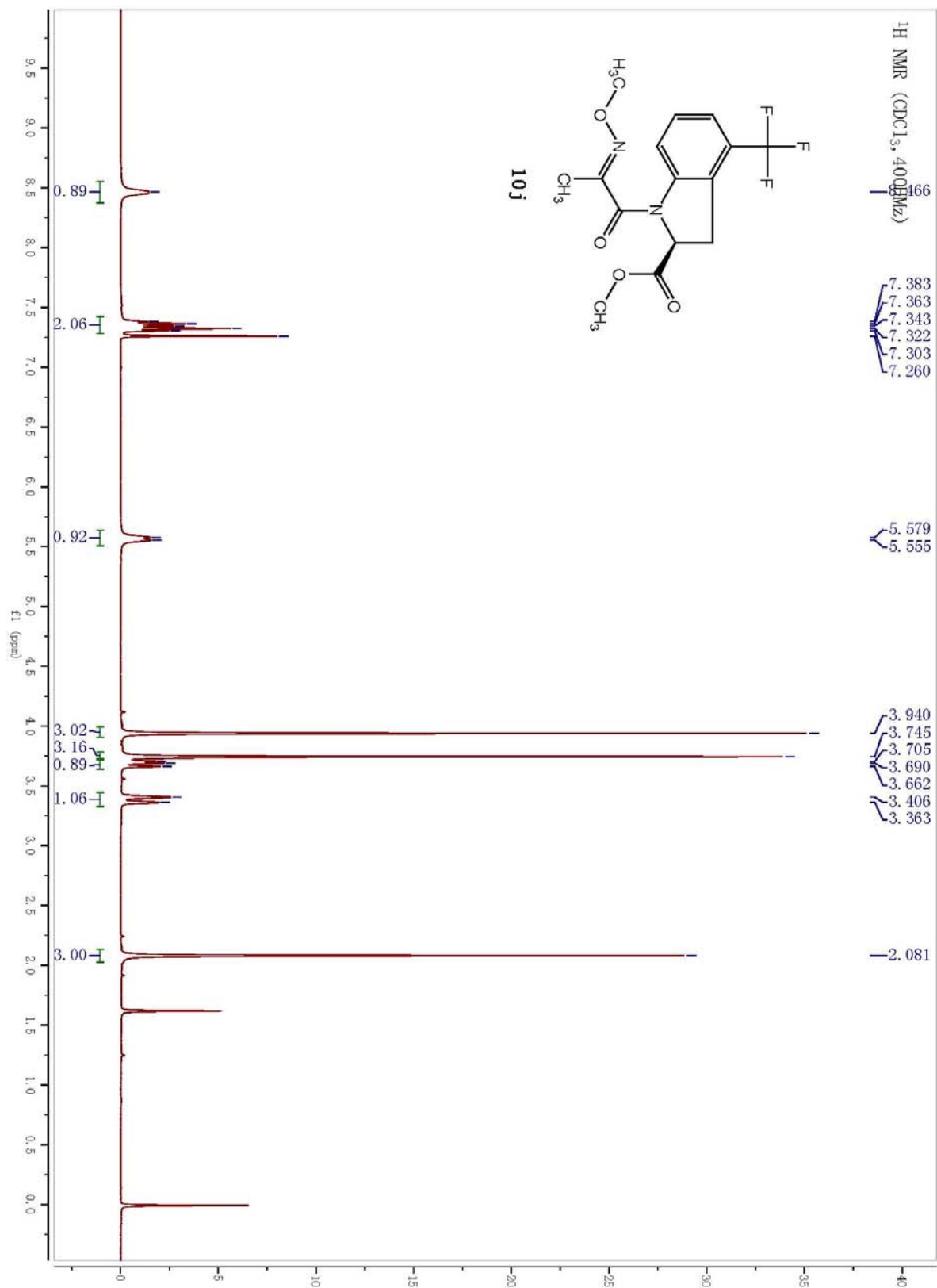


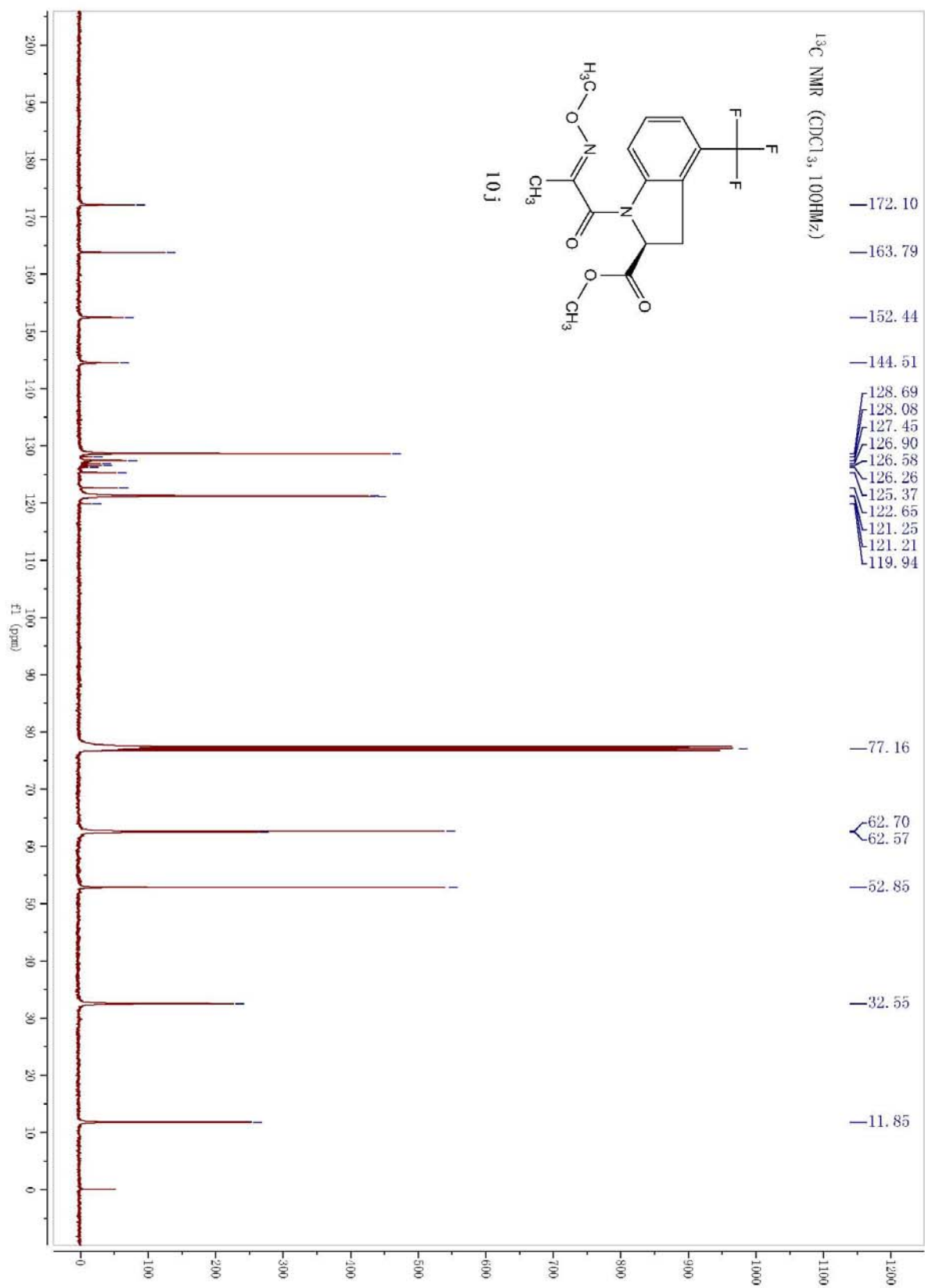


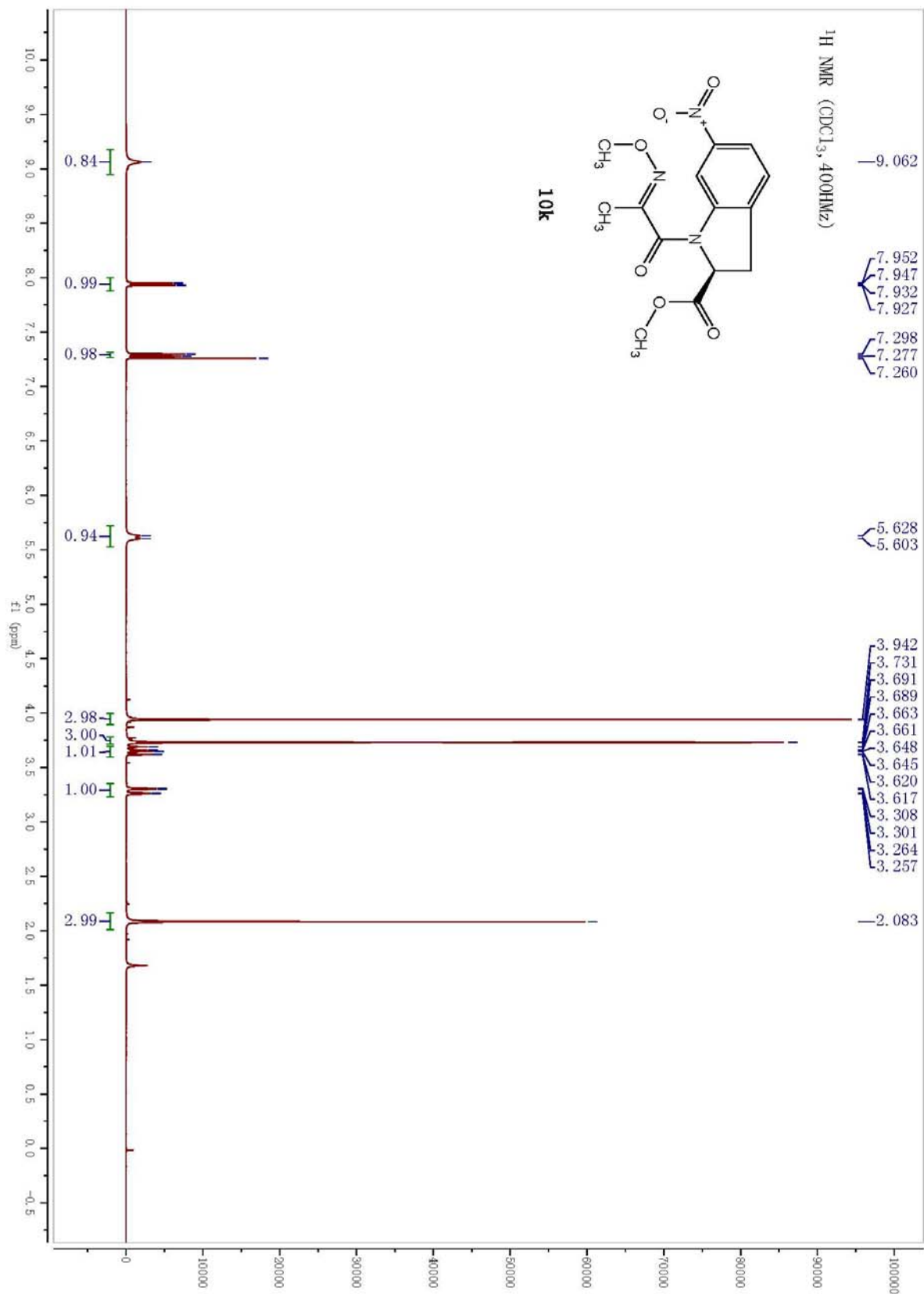


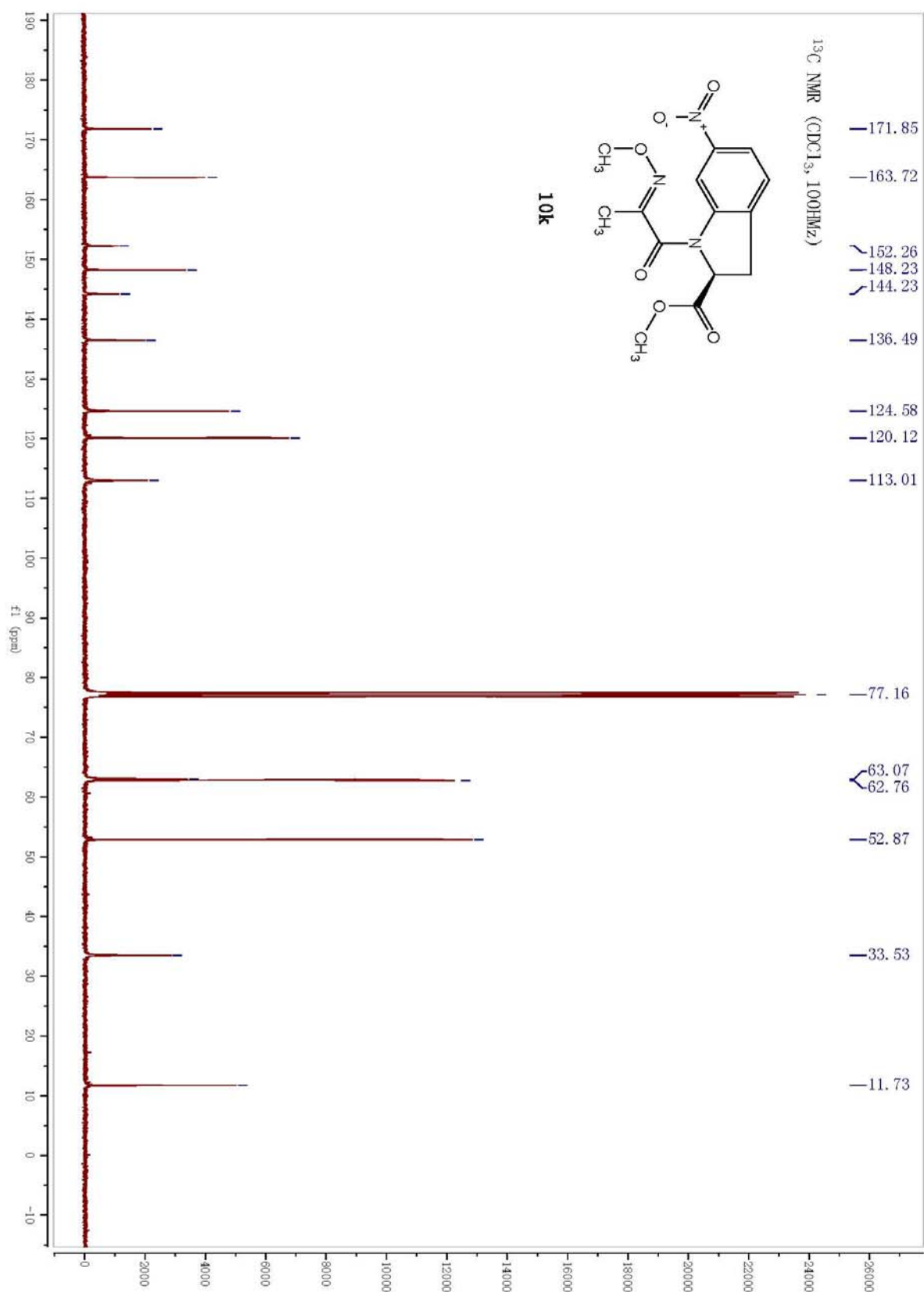


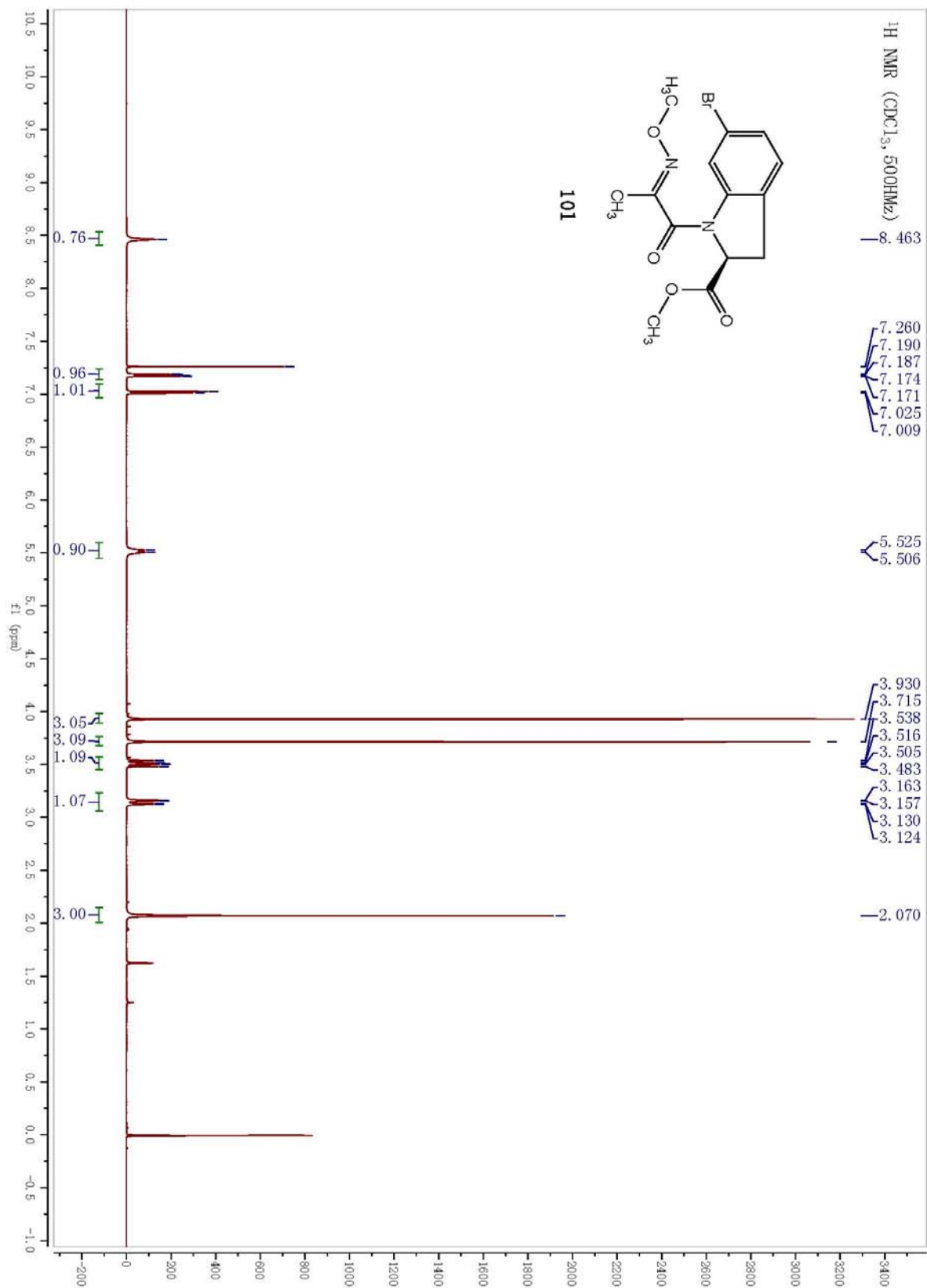


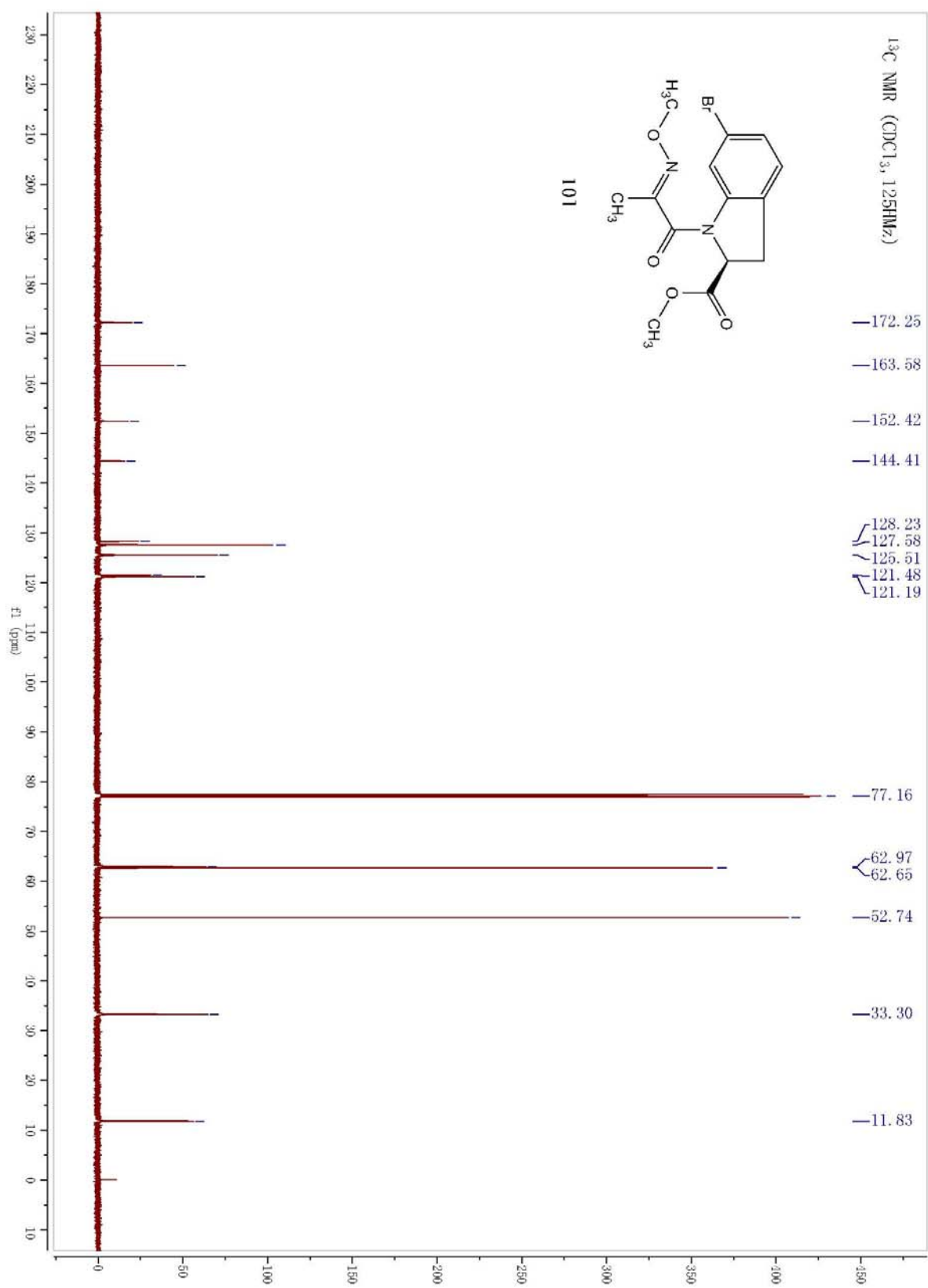


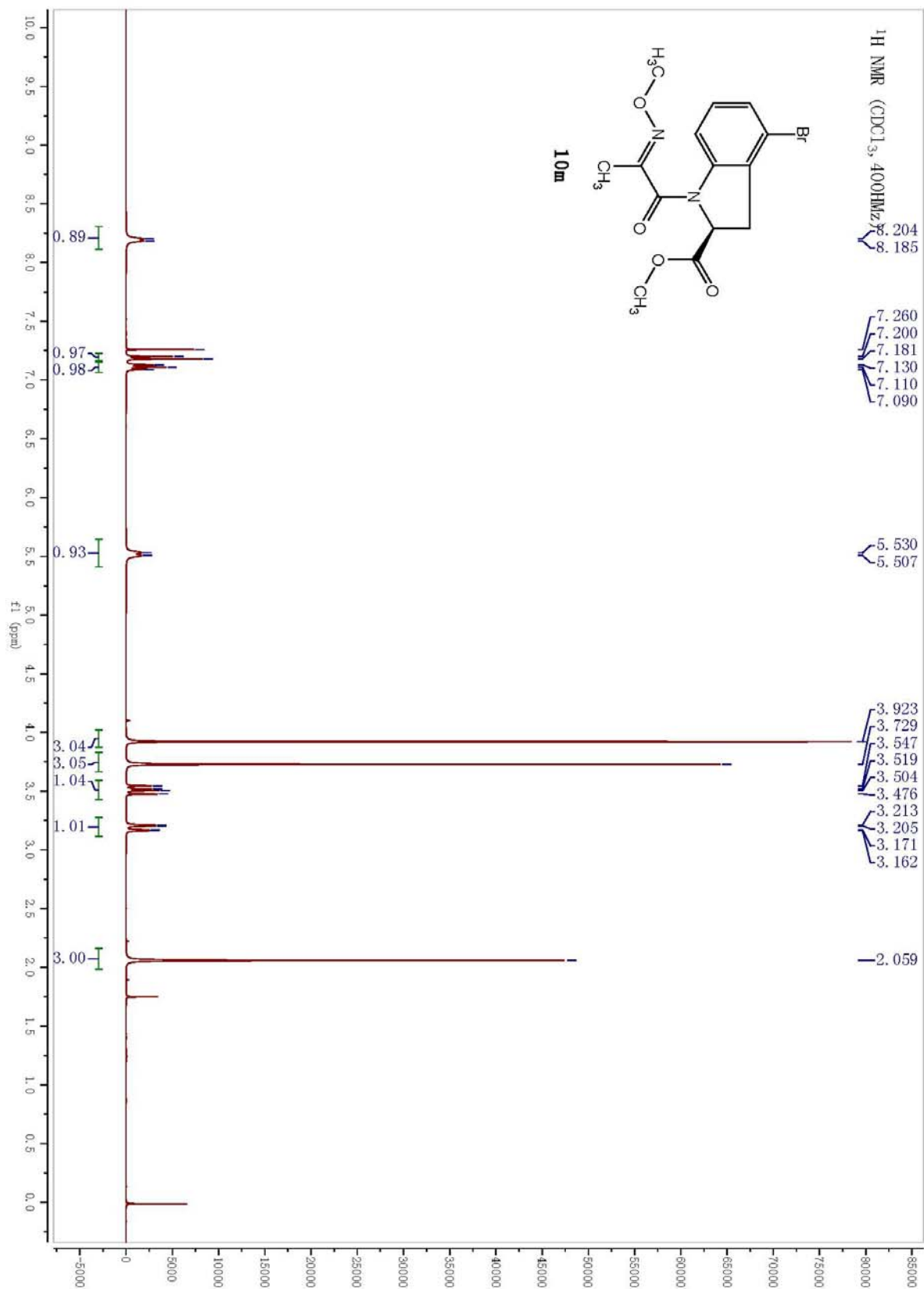


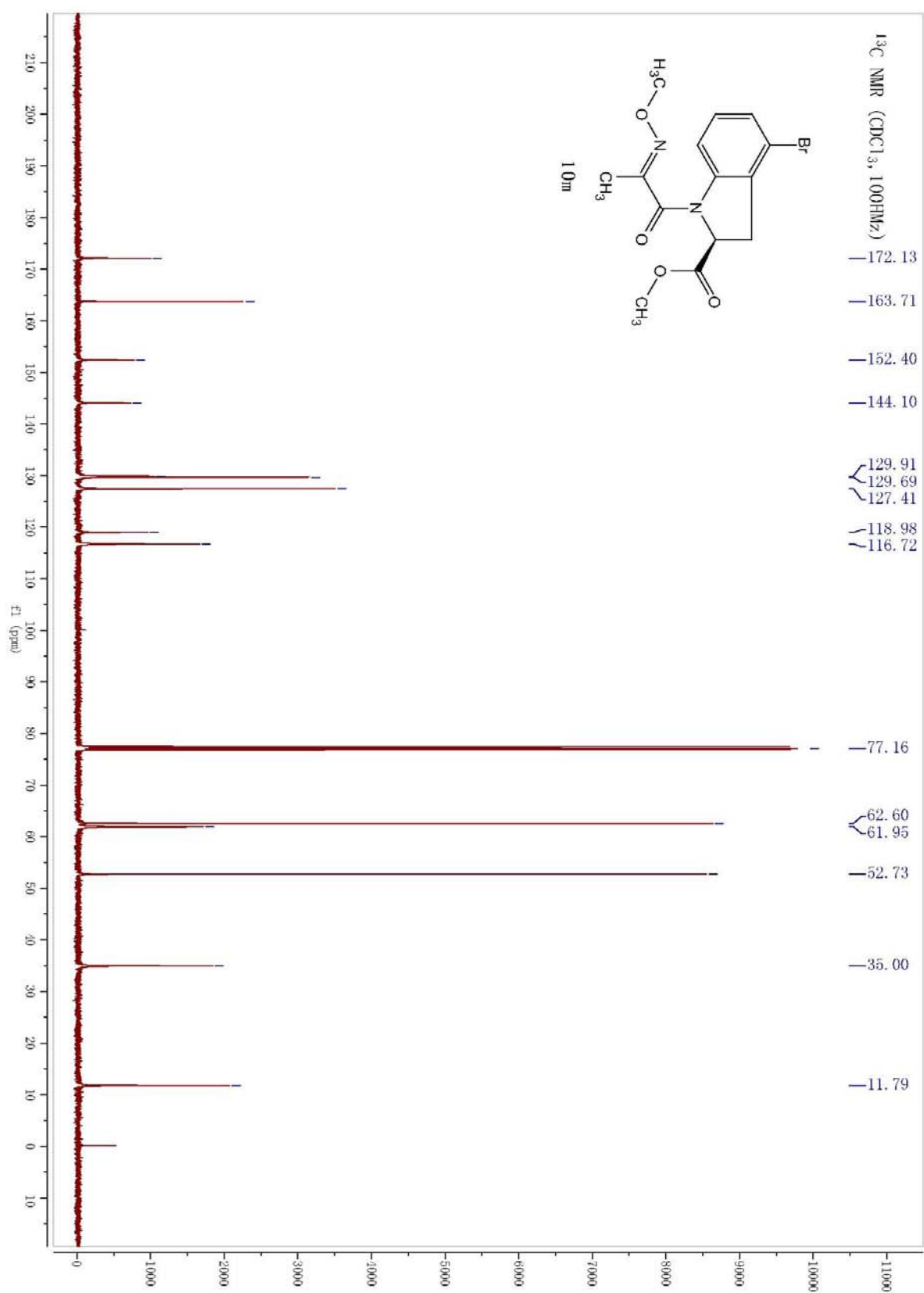


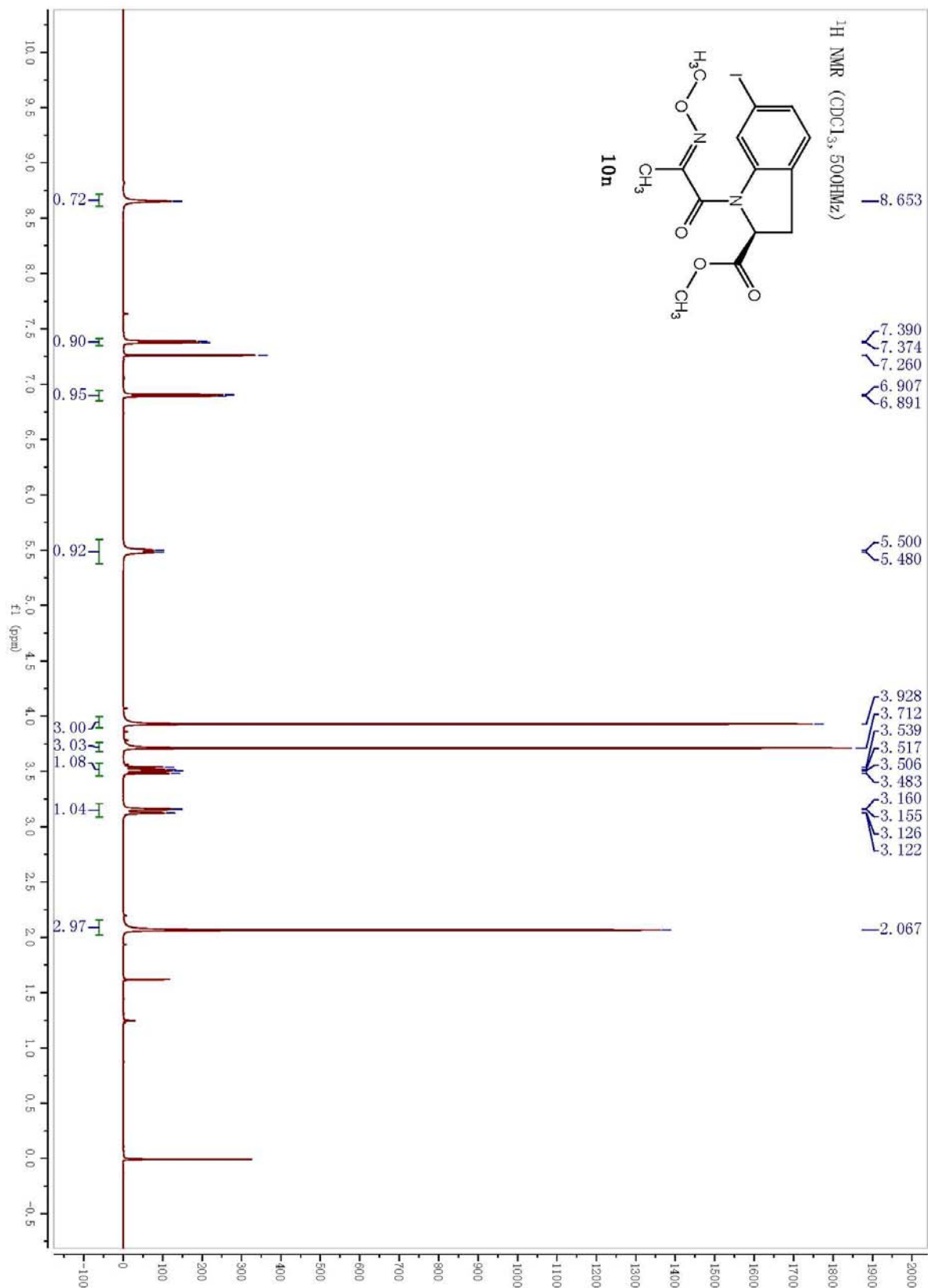


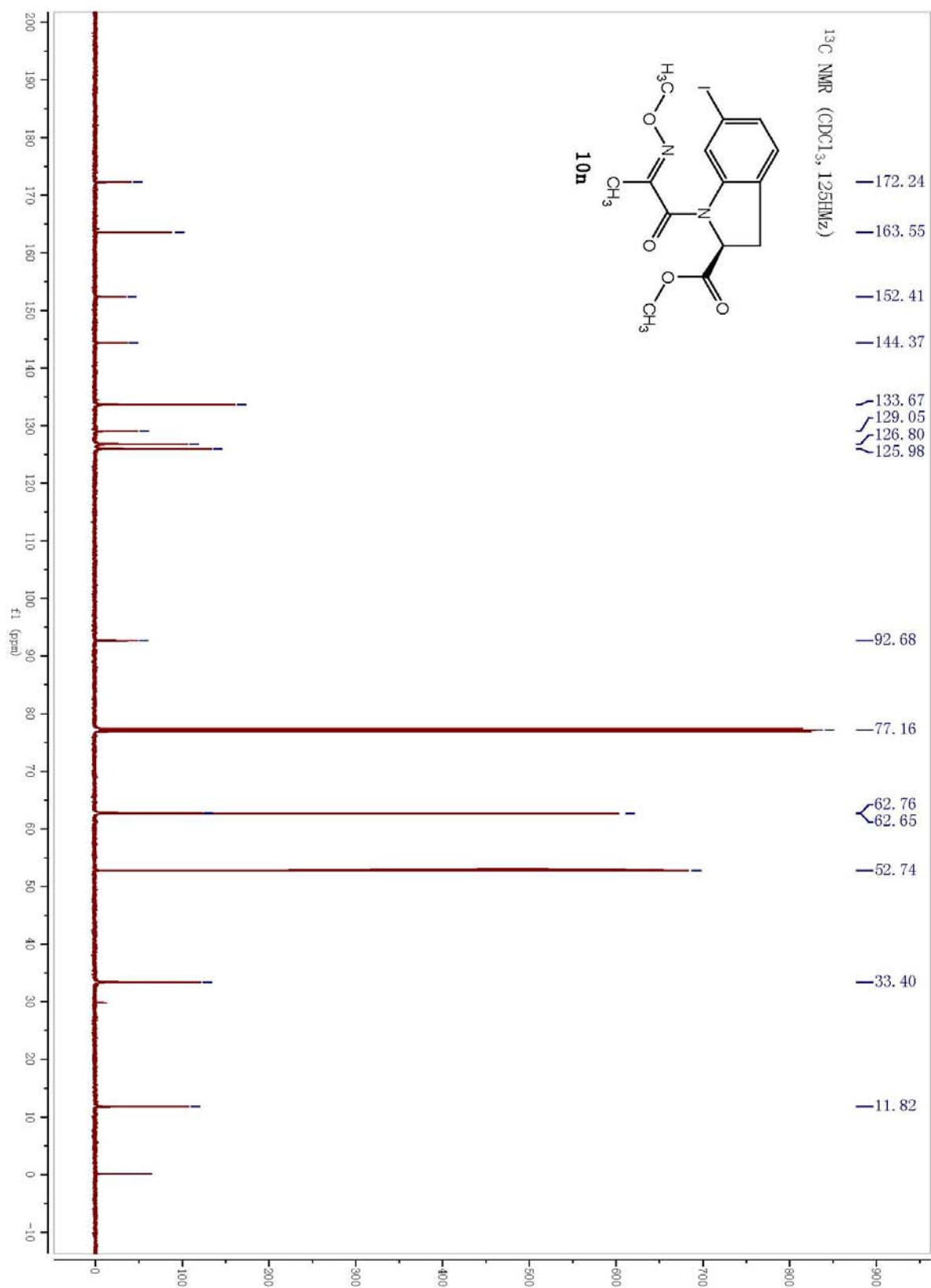


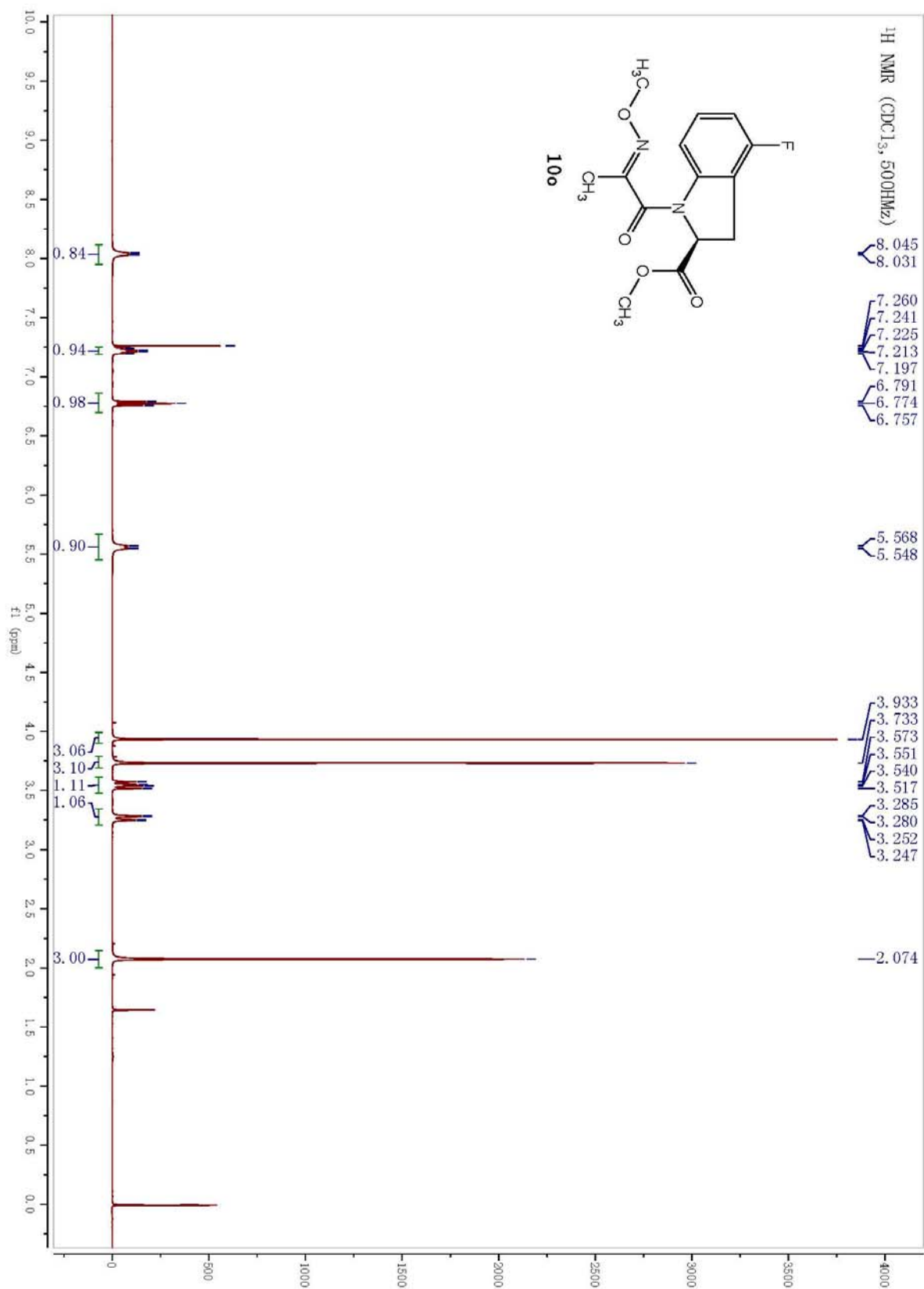


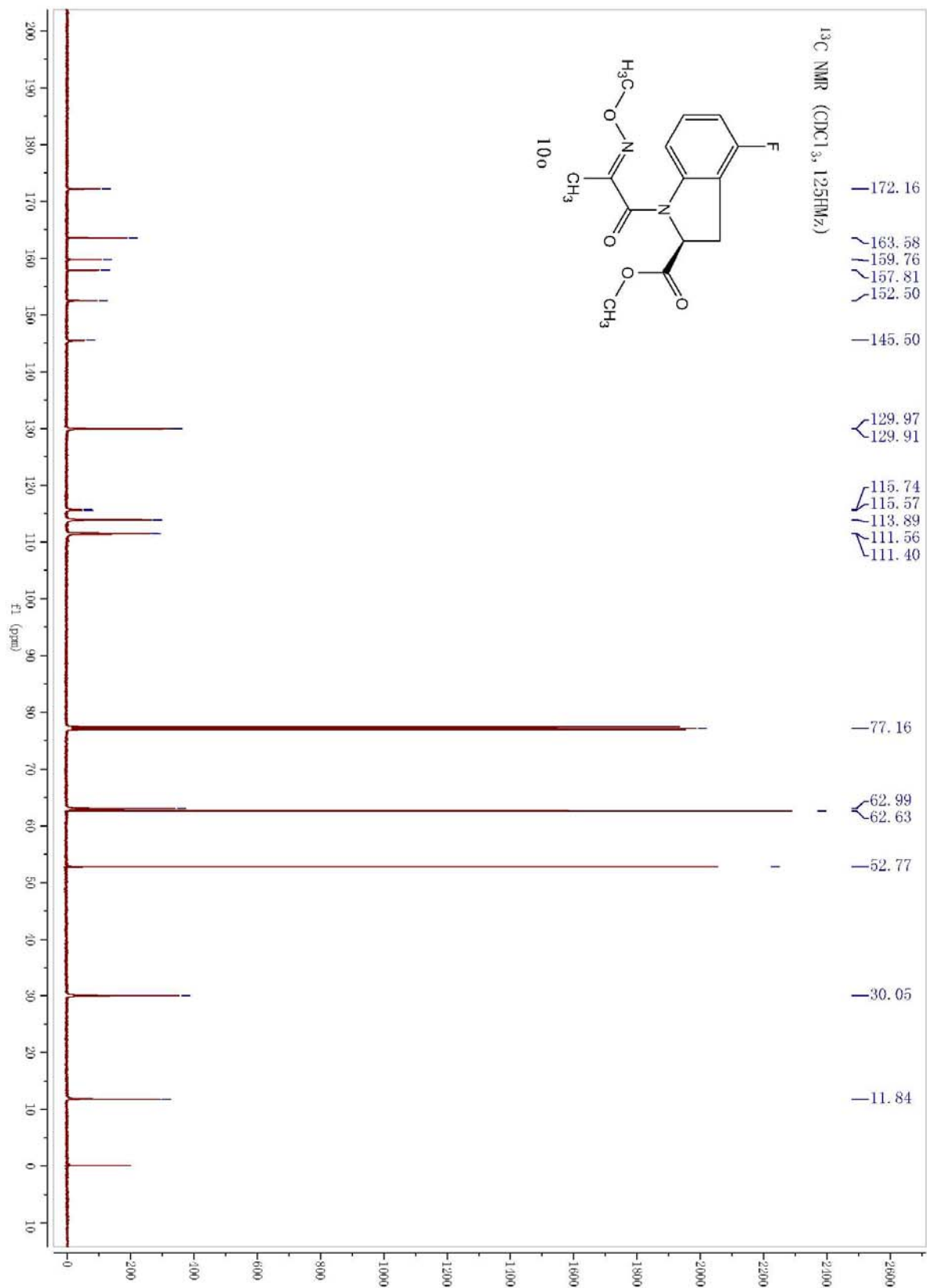


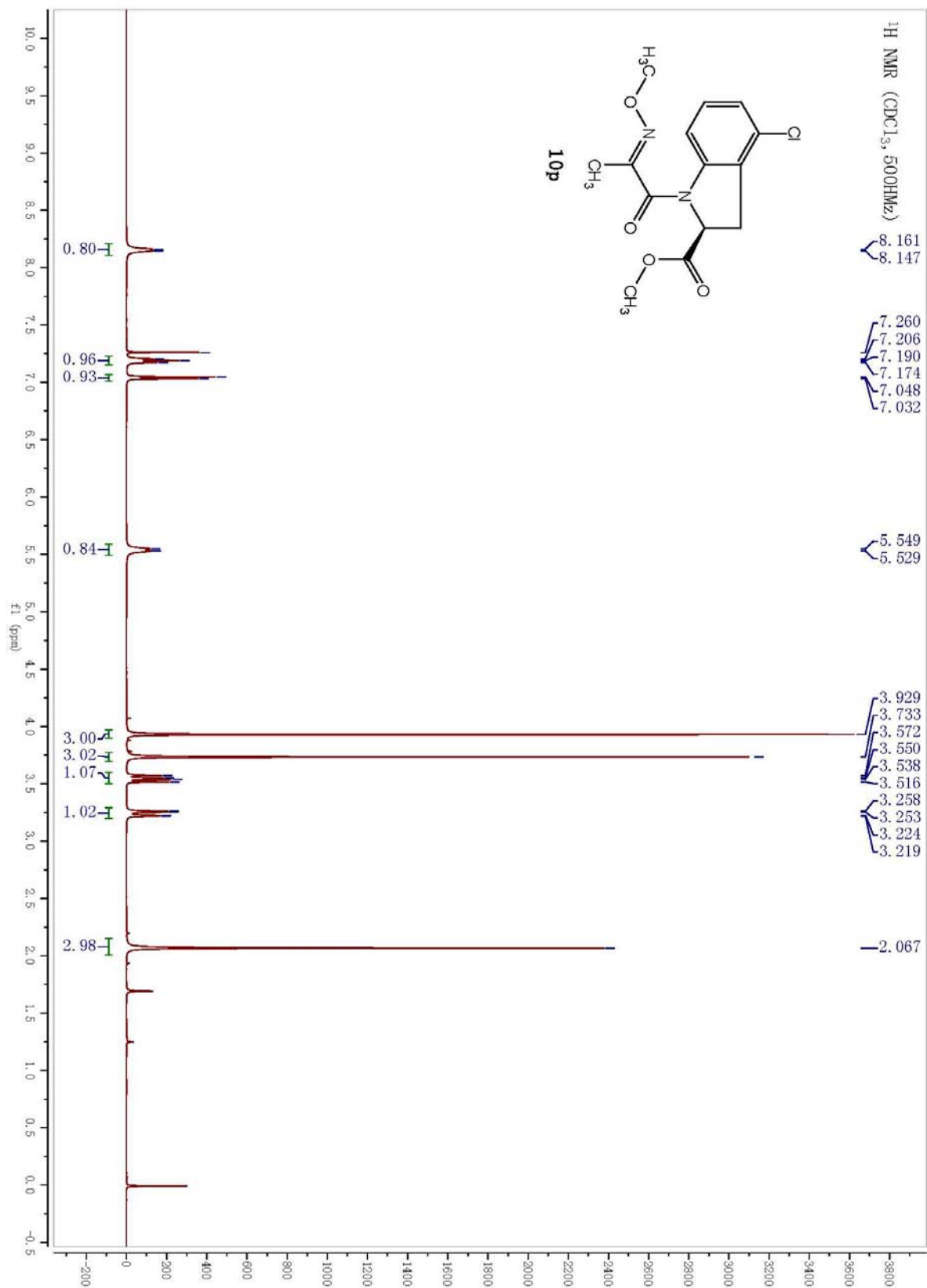


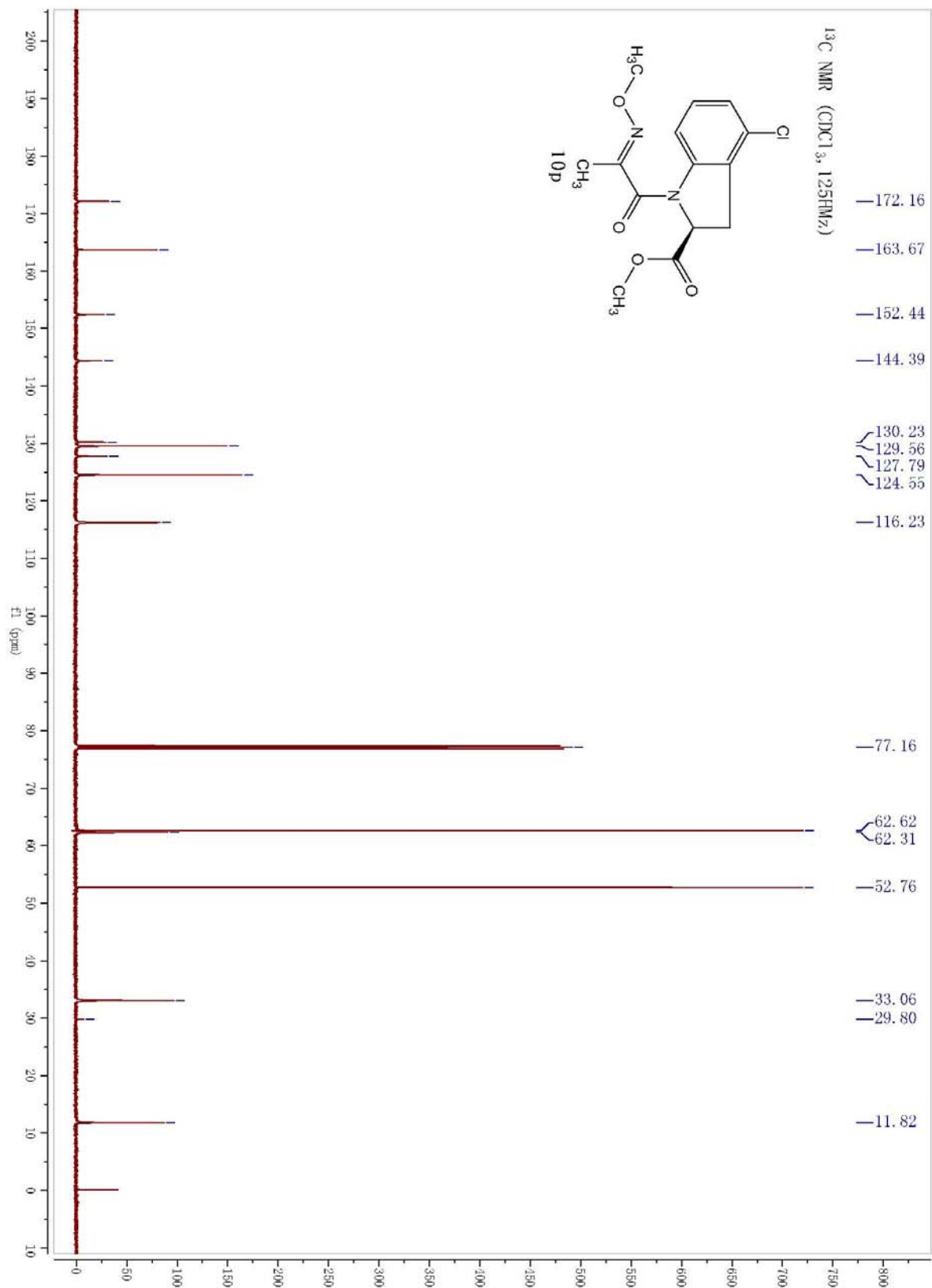


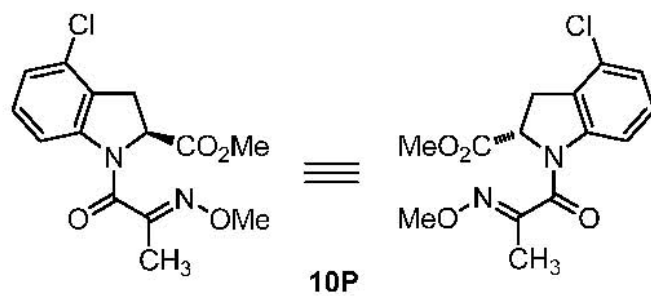
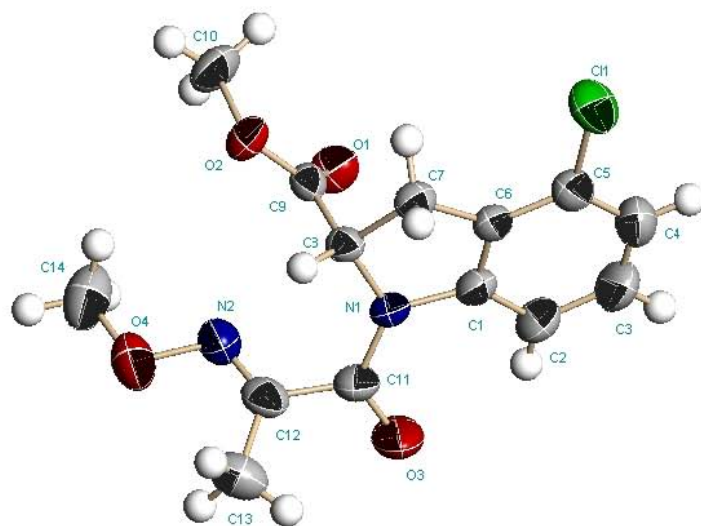


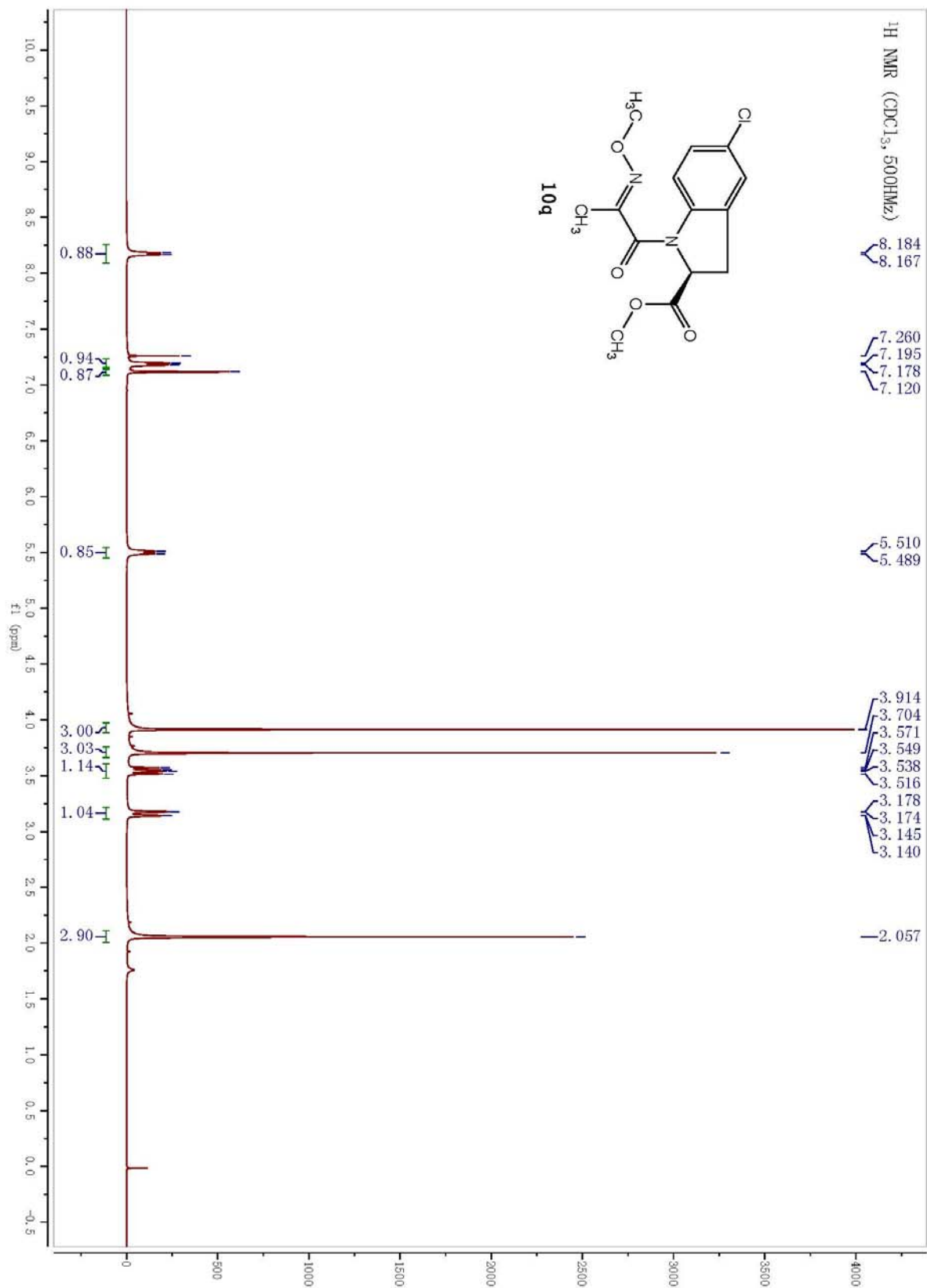


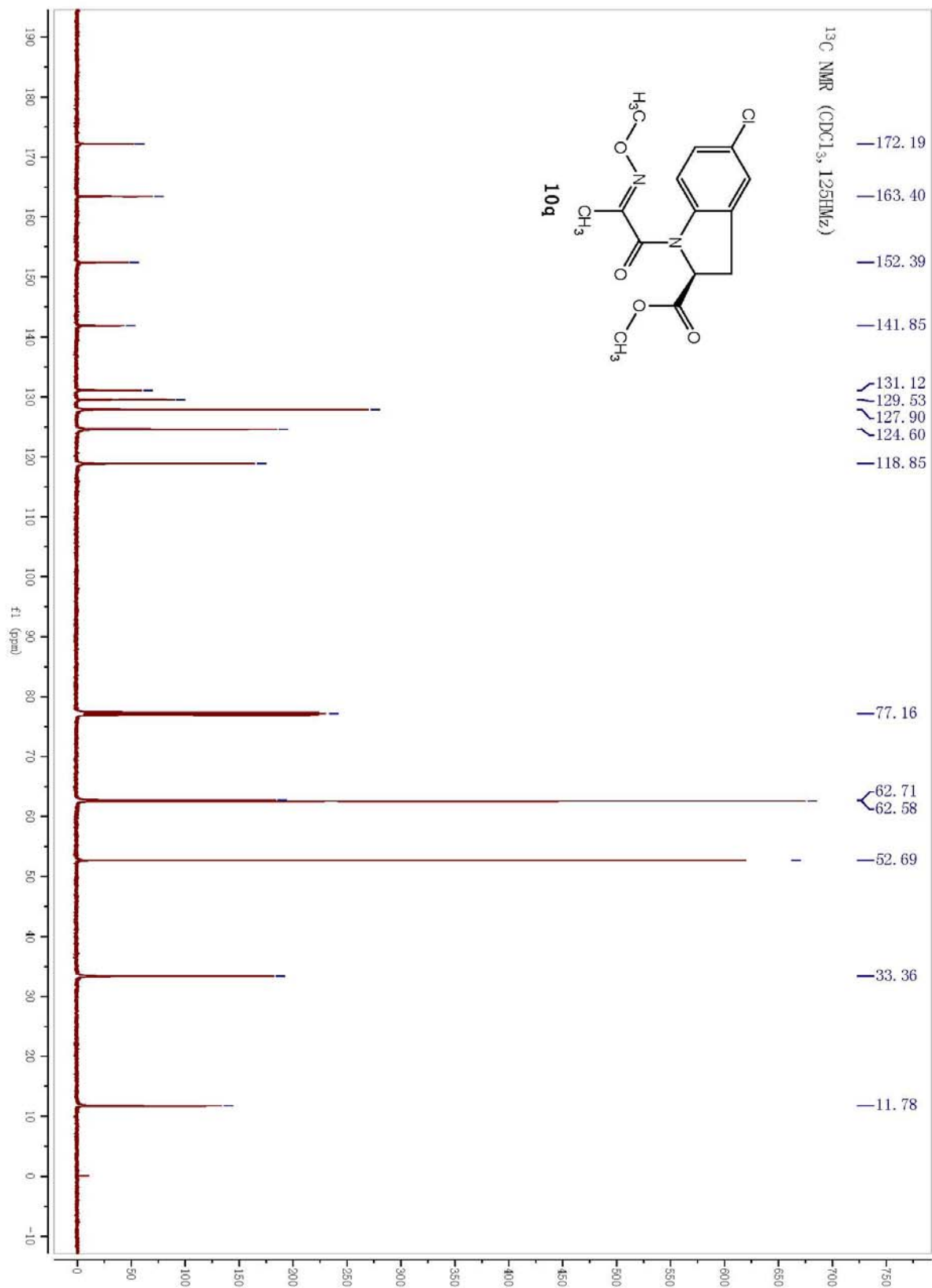


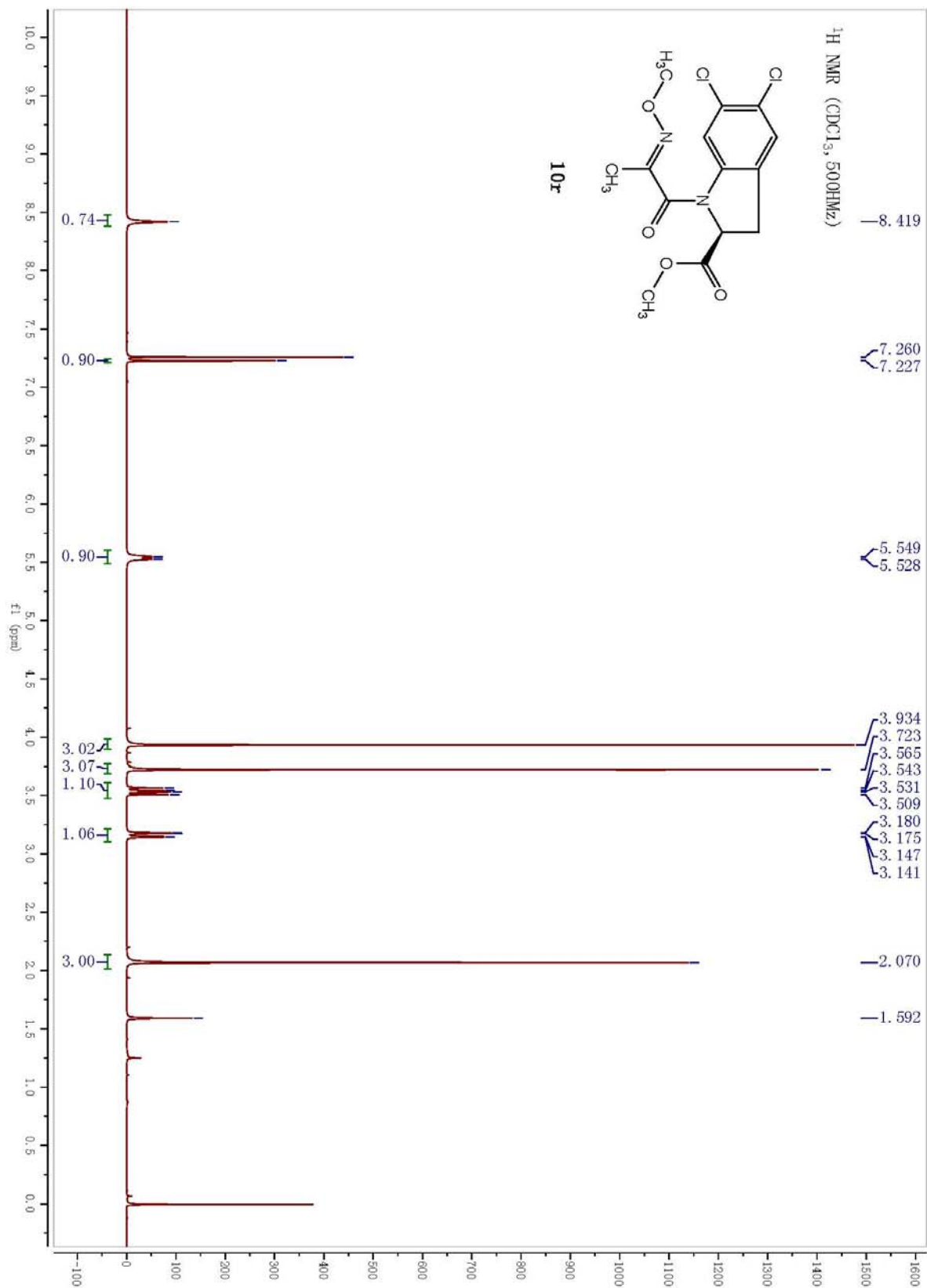


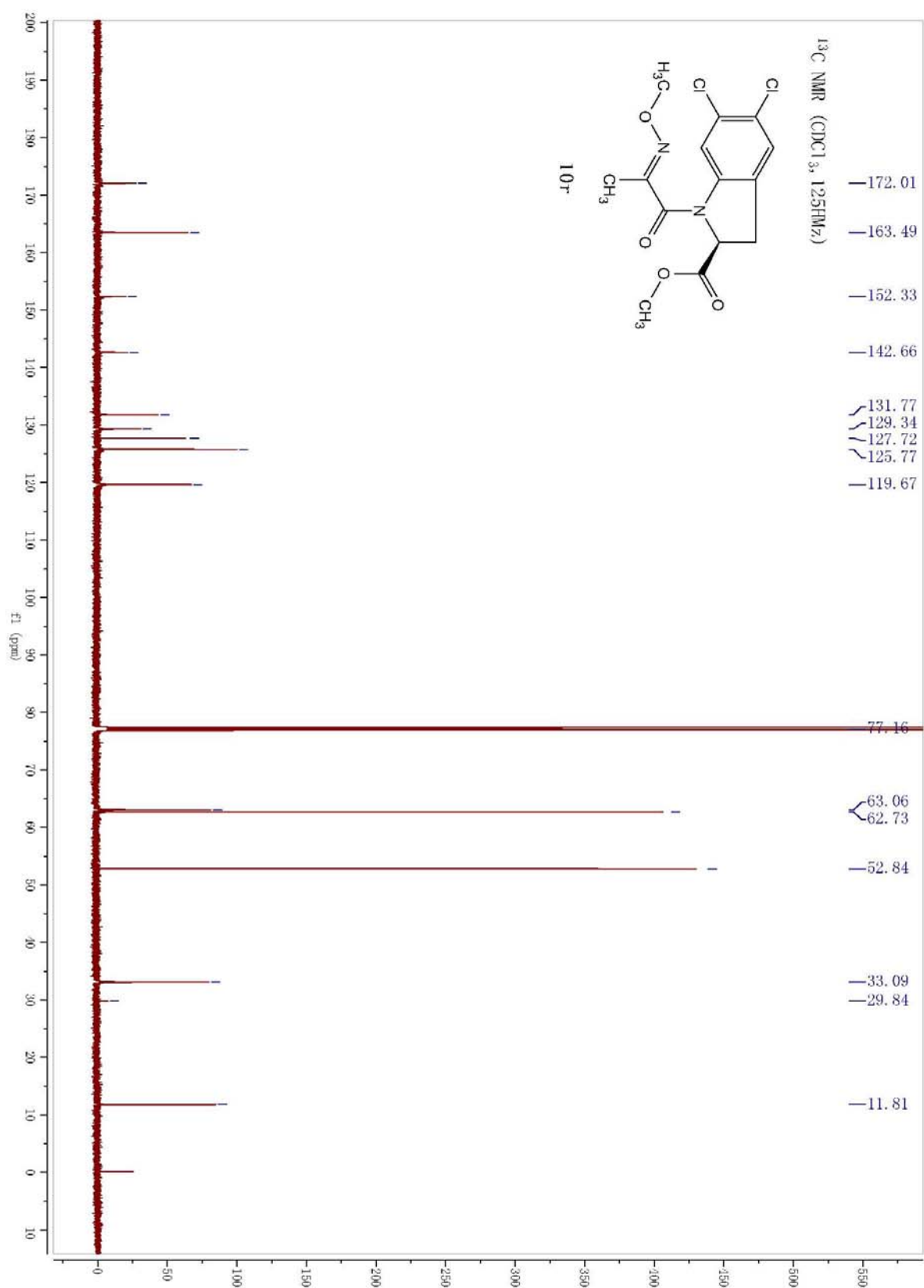


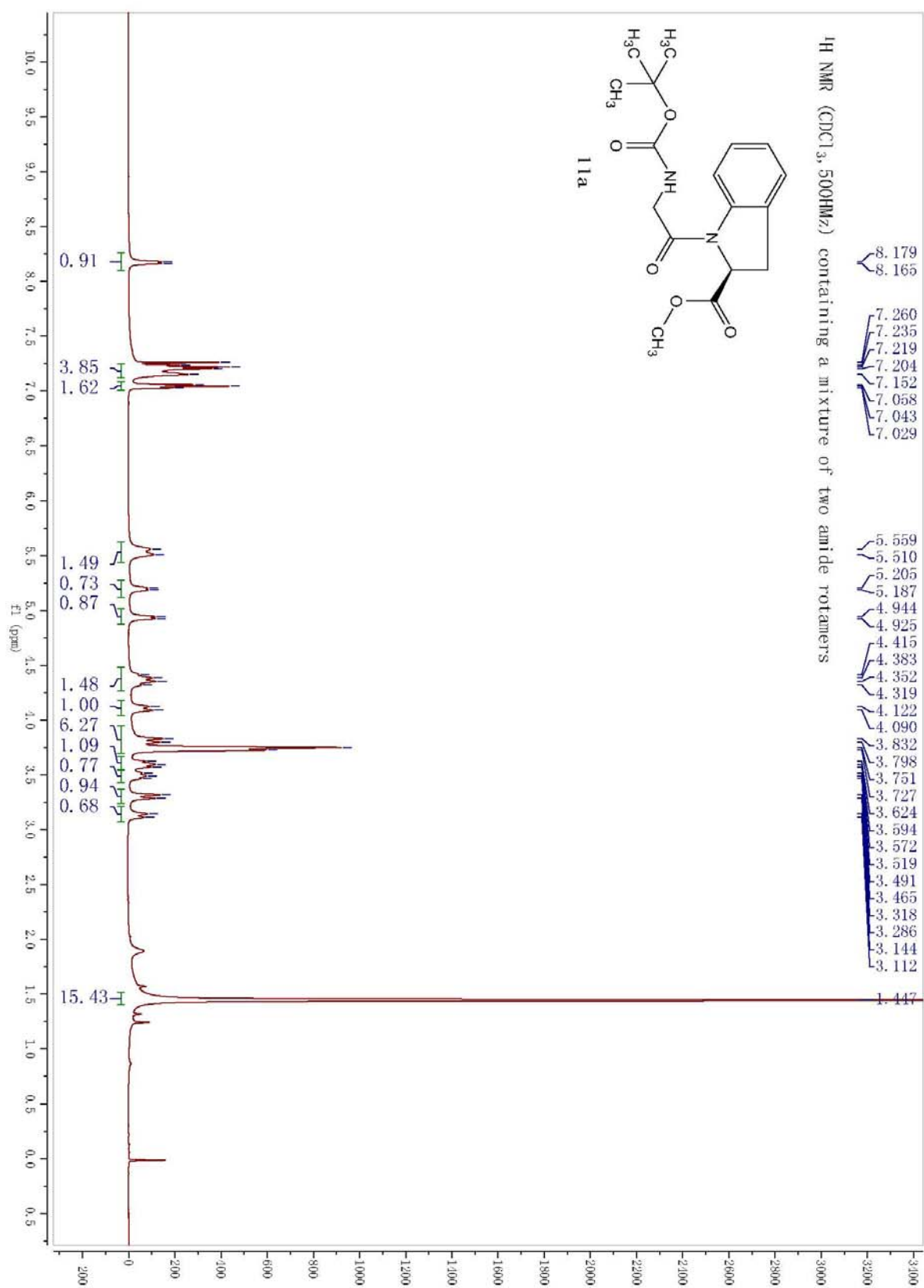




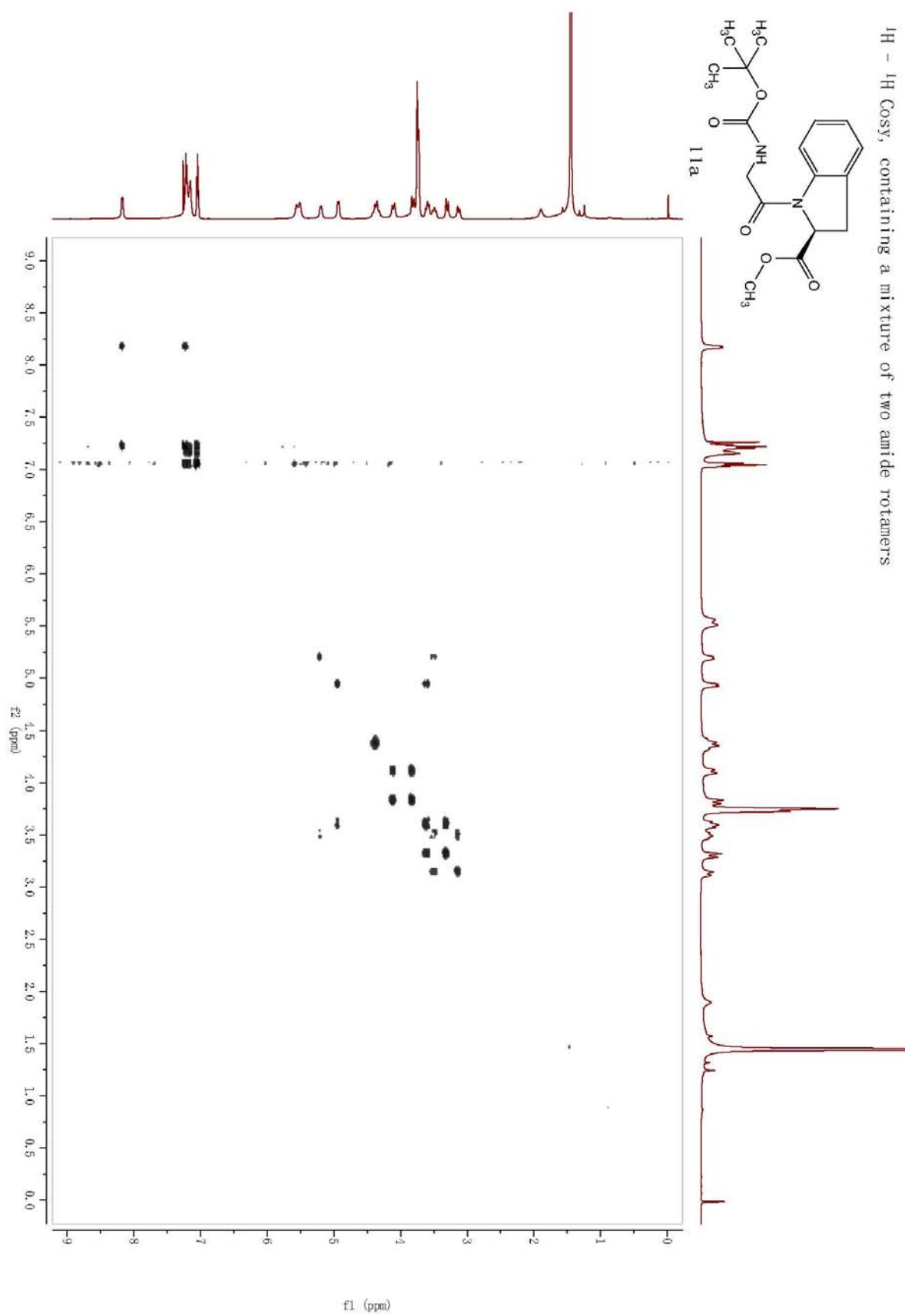
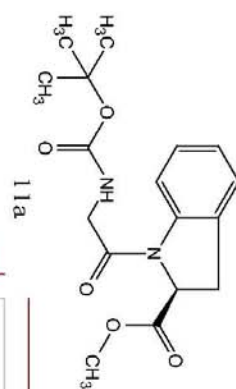


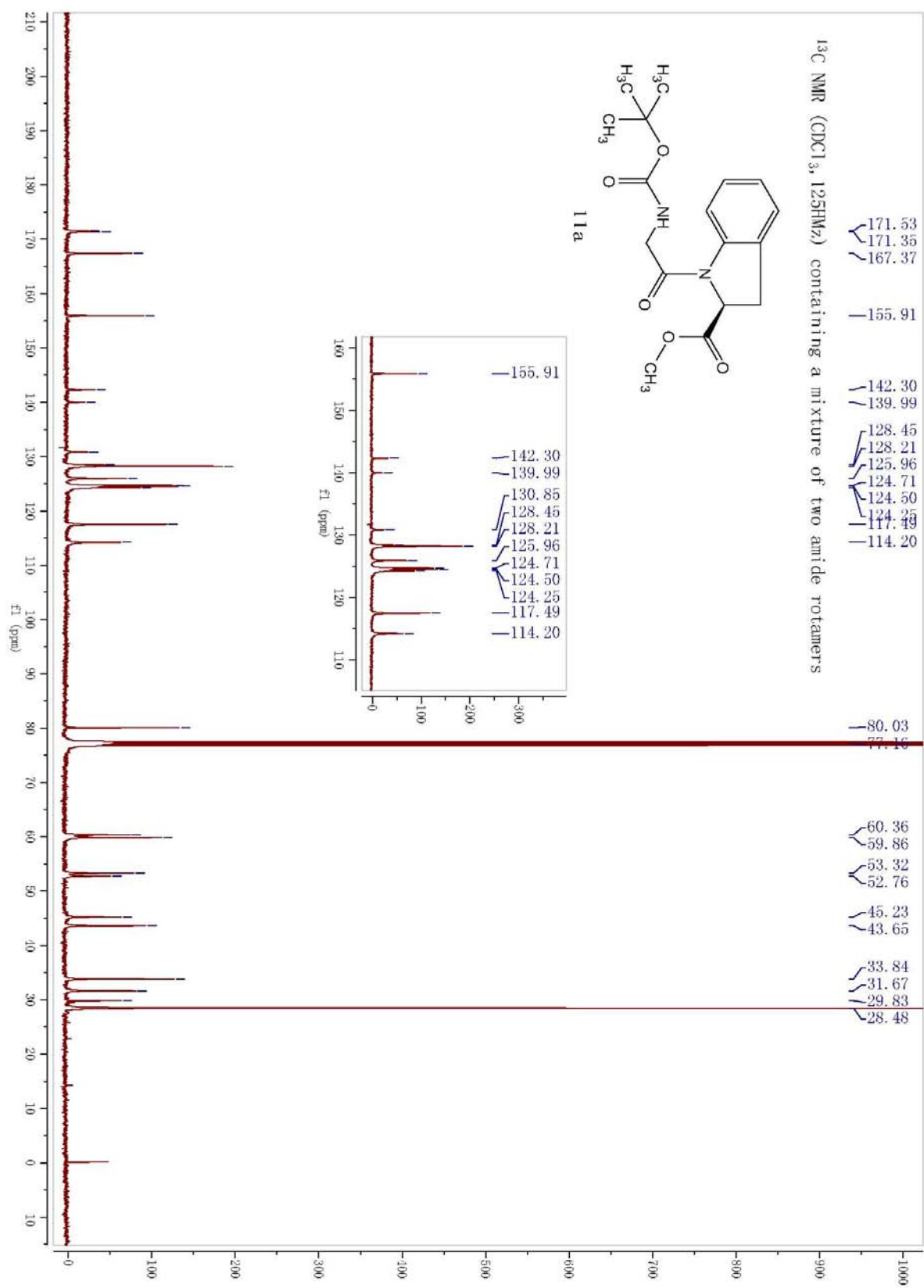


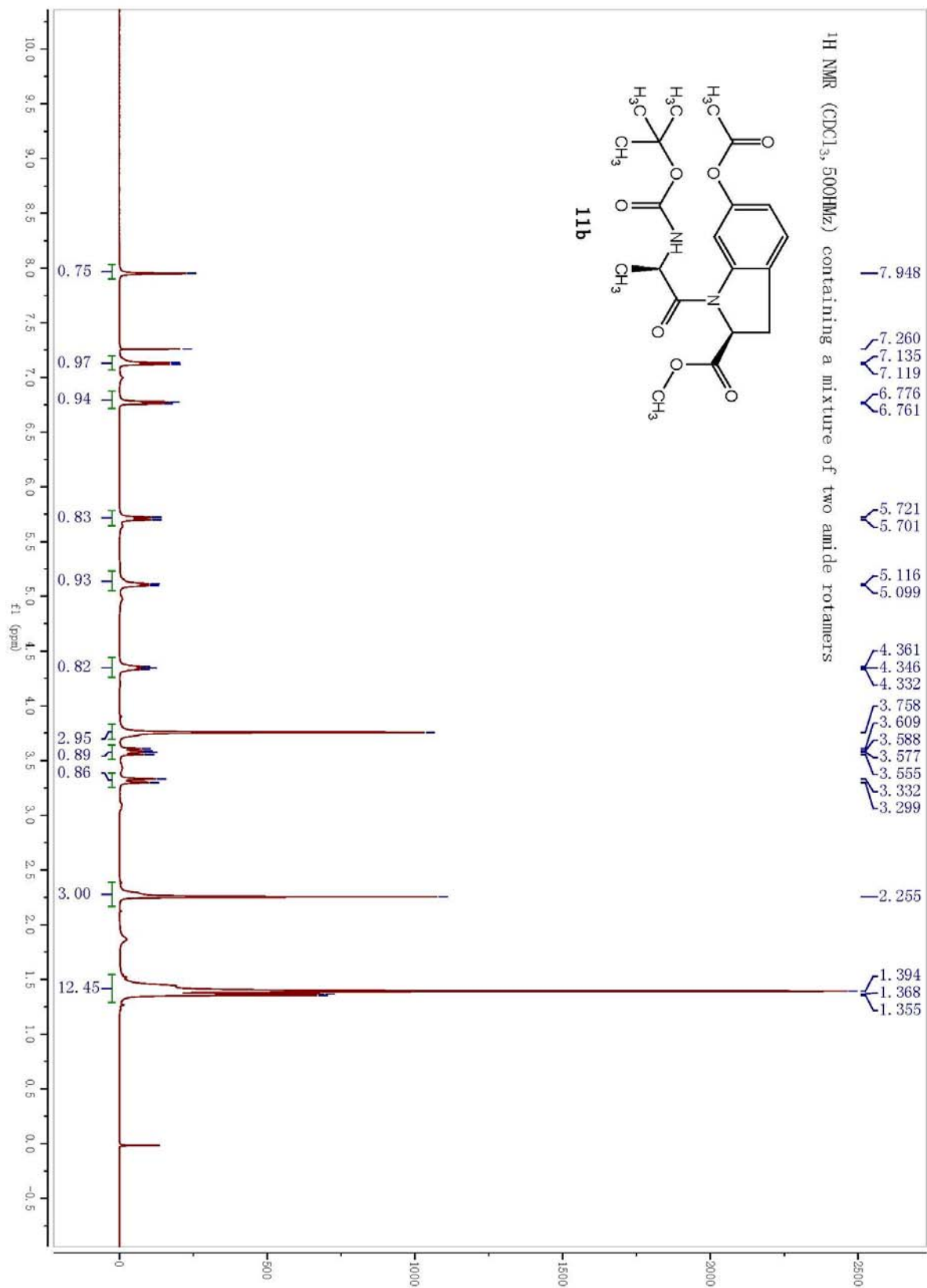


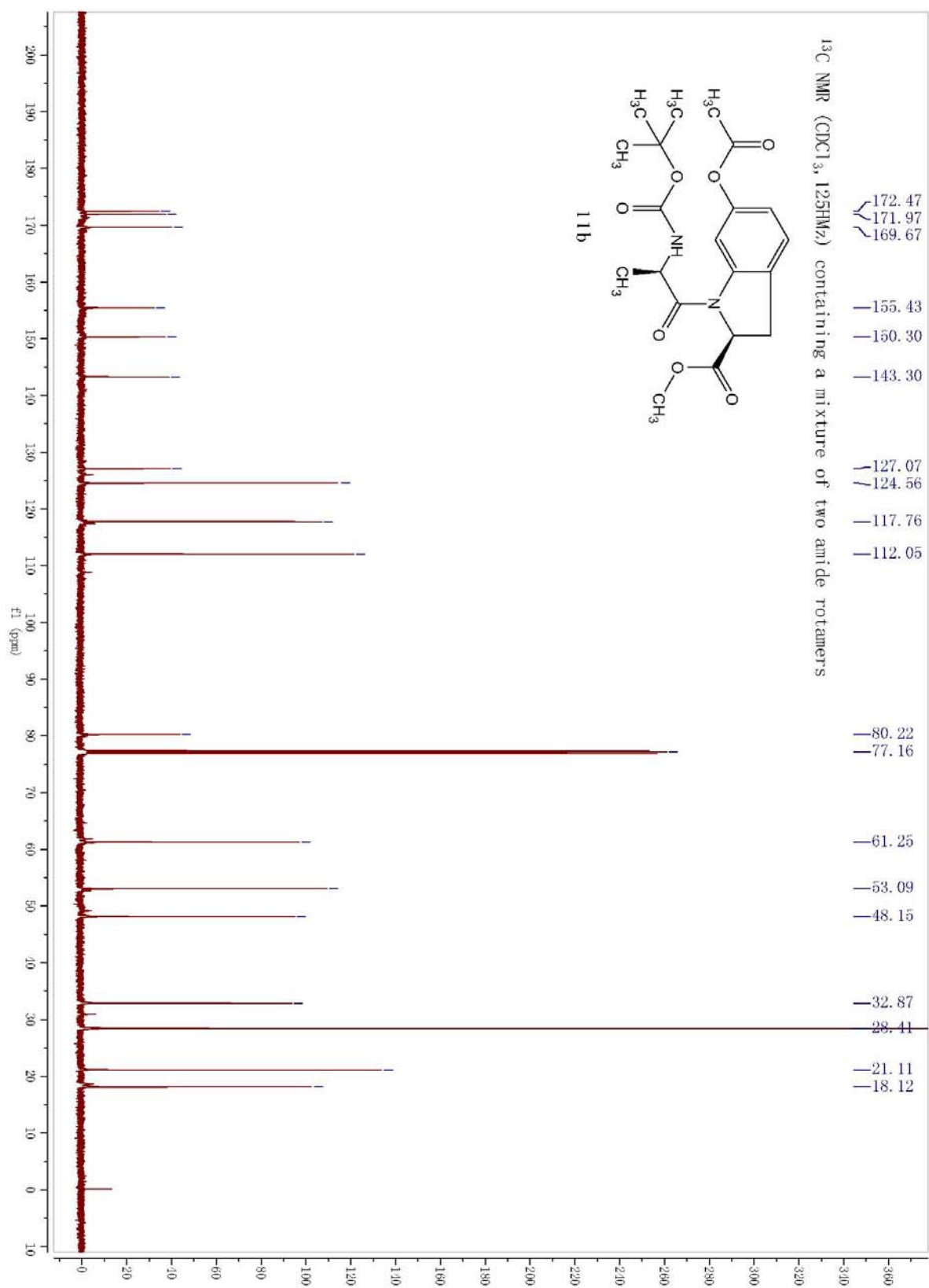


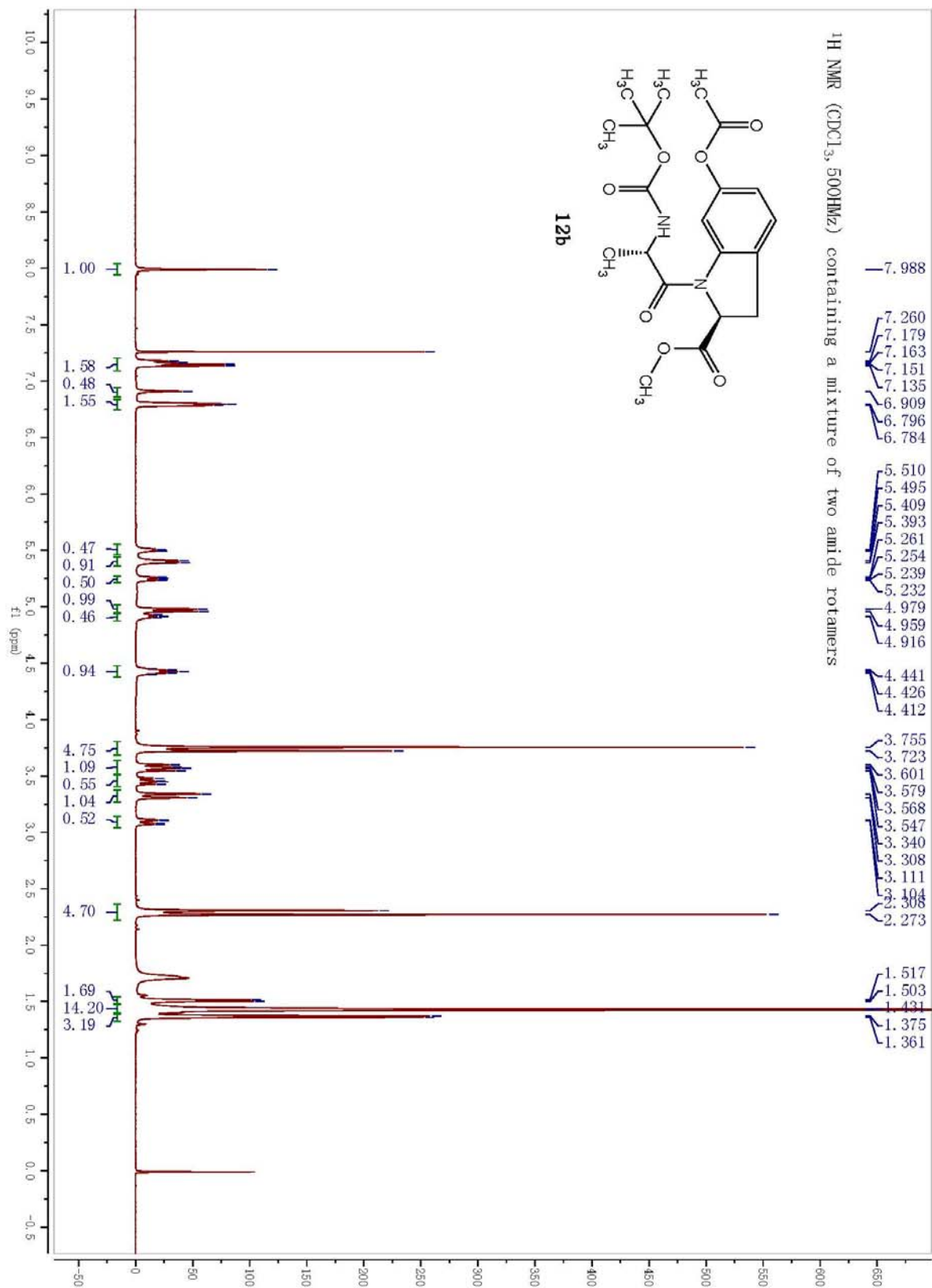
¹H - ¹H Cosy, containing a mixture of two amide rotamers

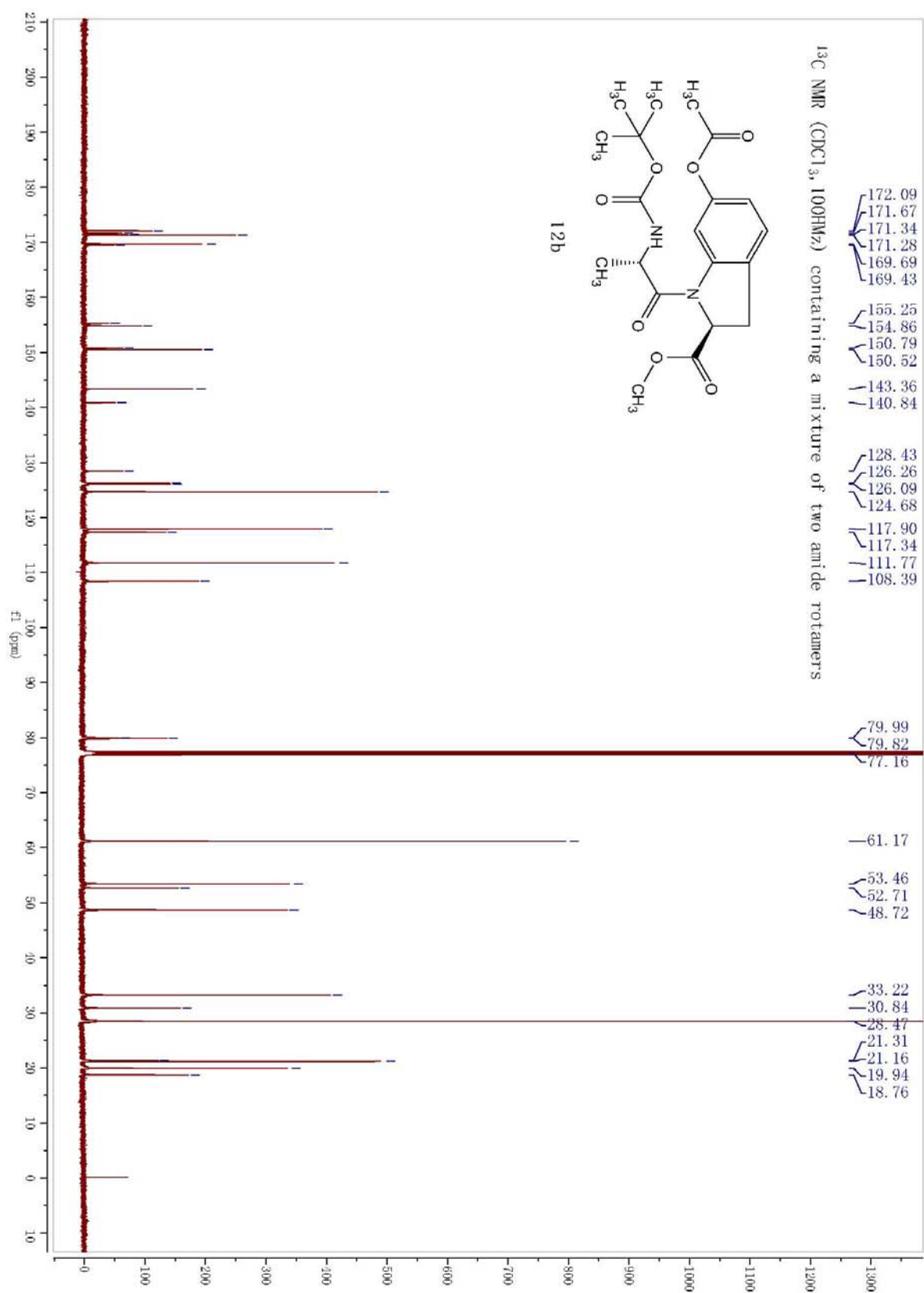


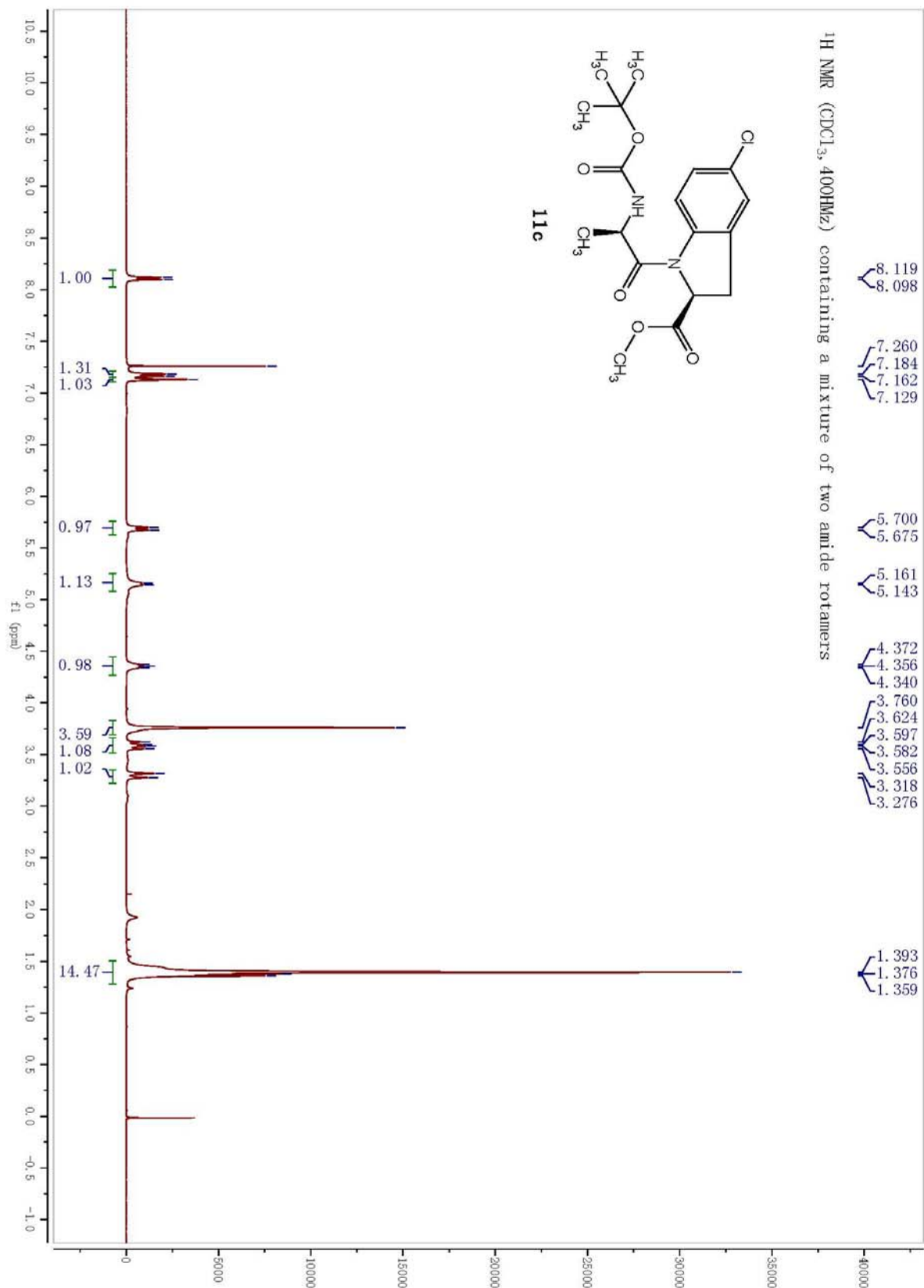


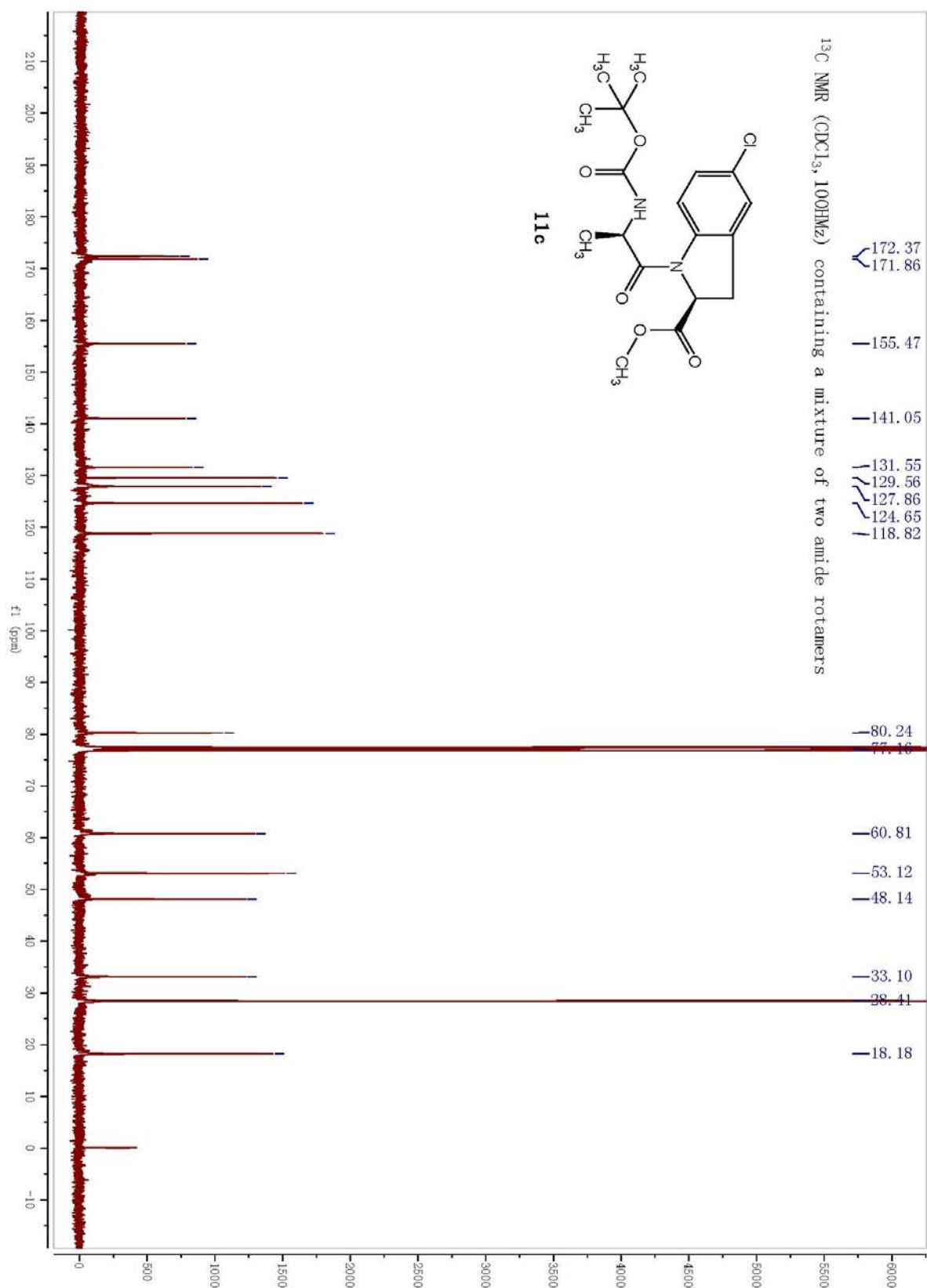


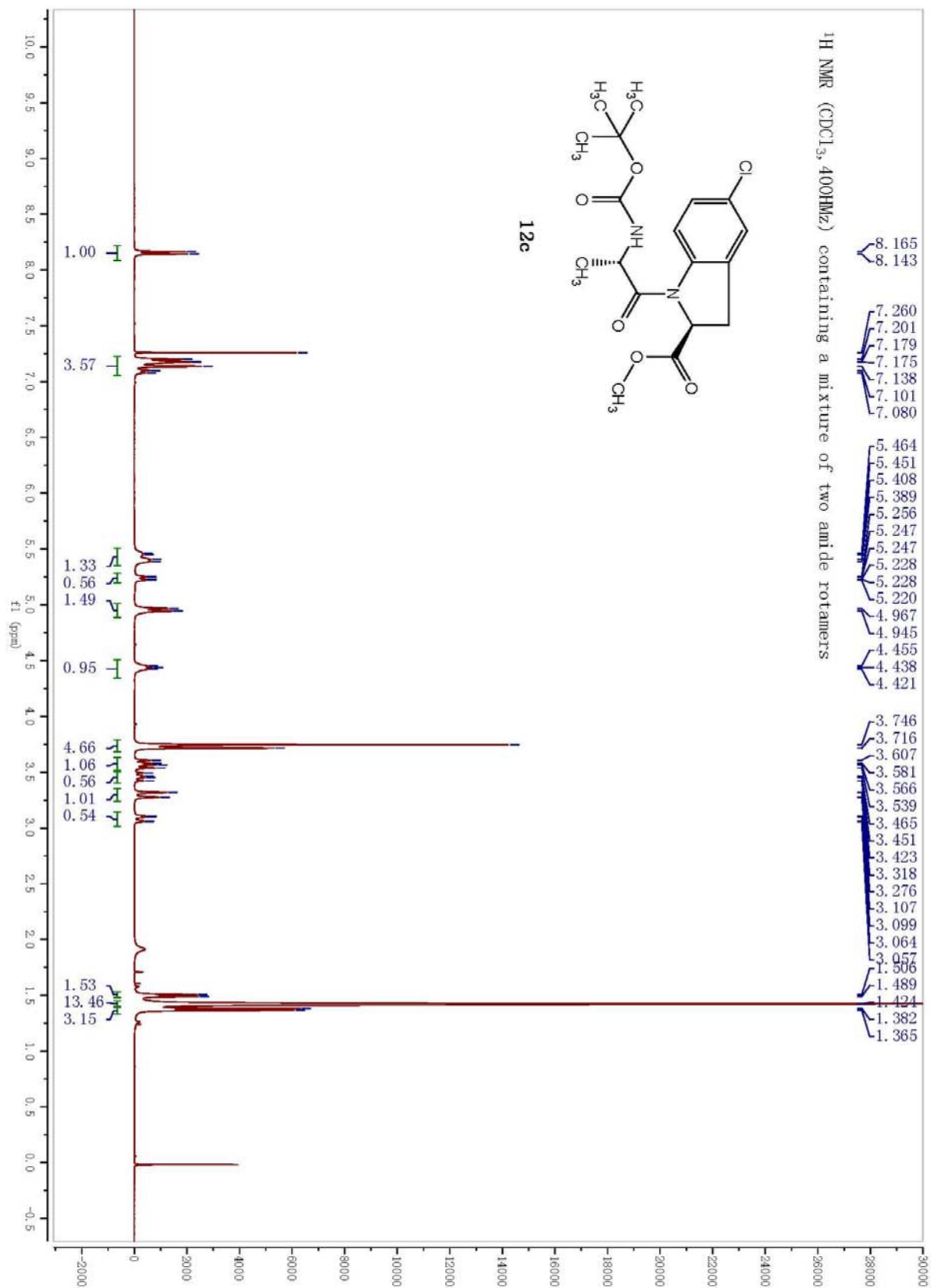


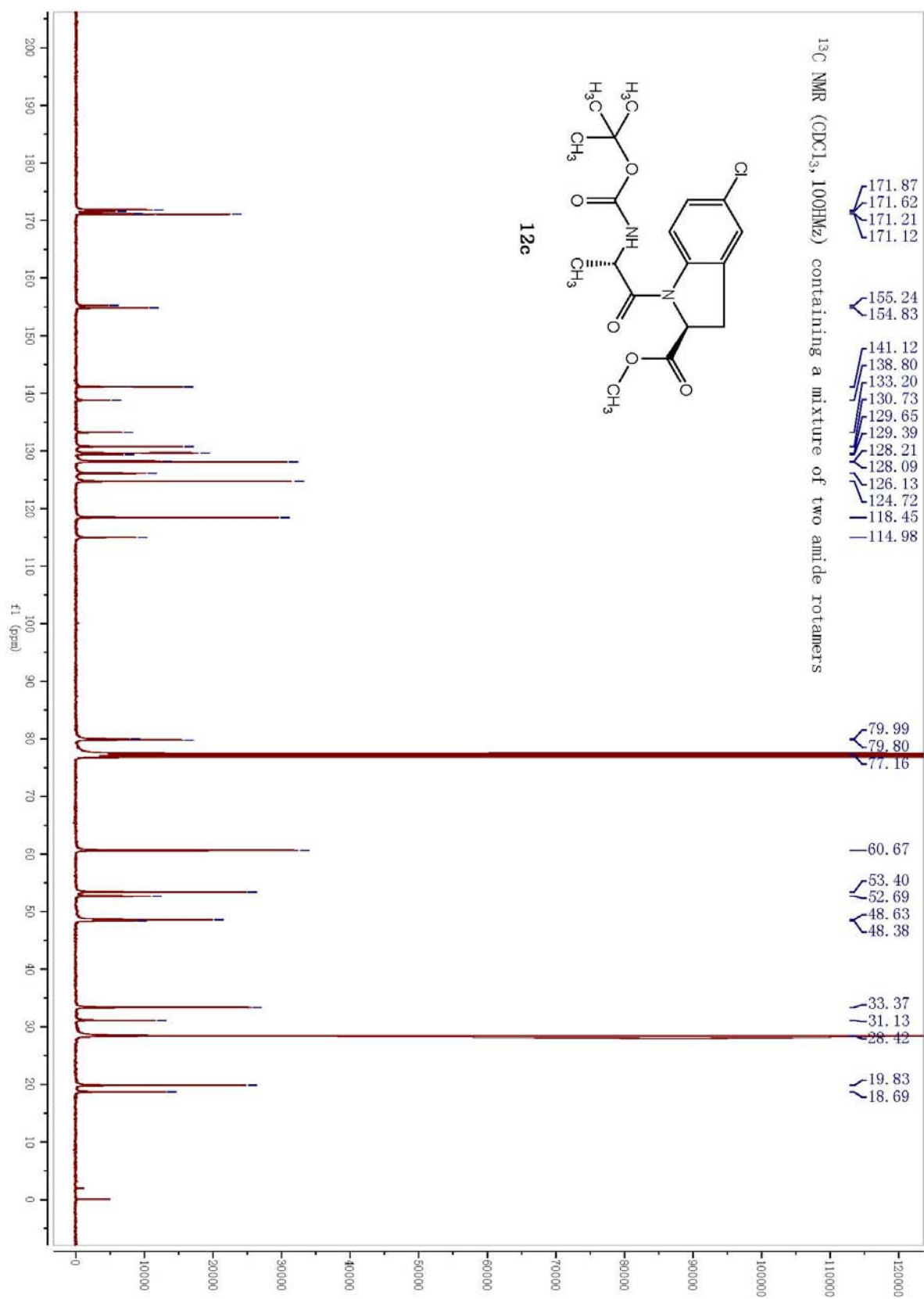


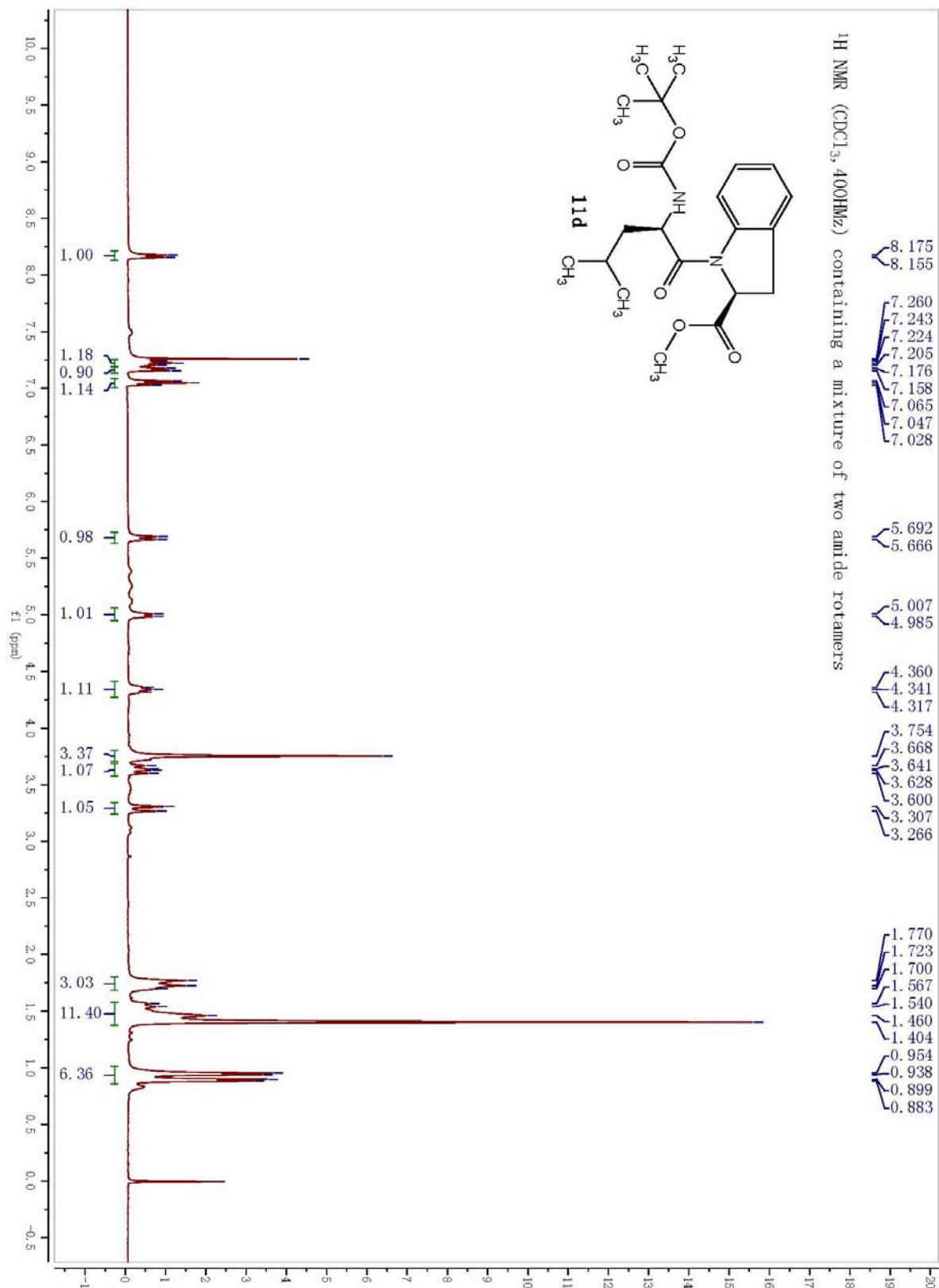


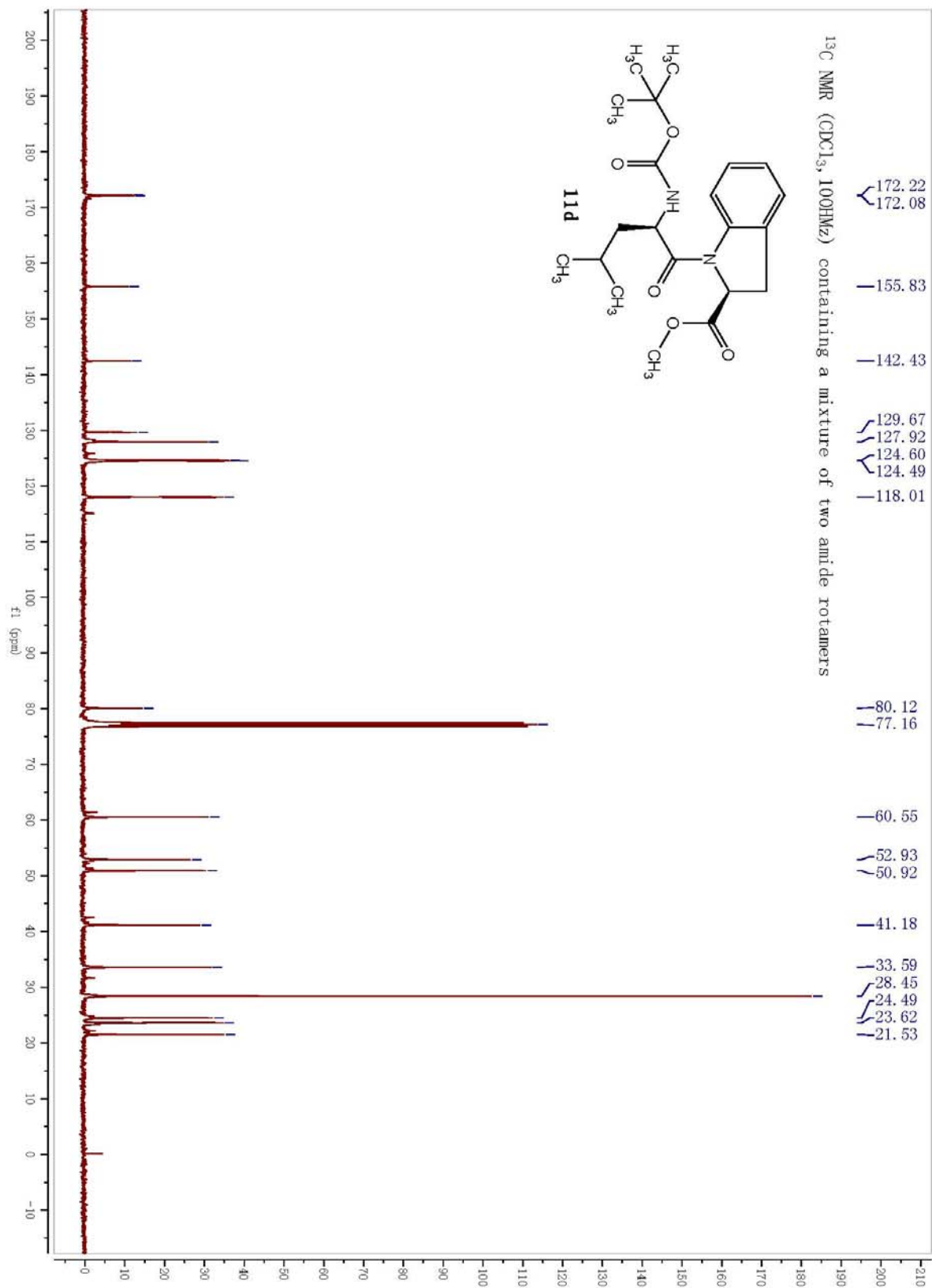


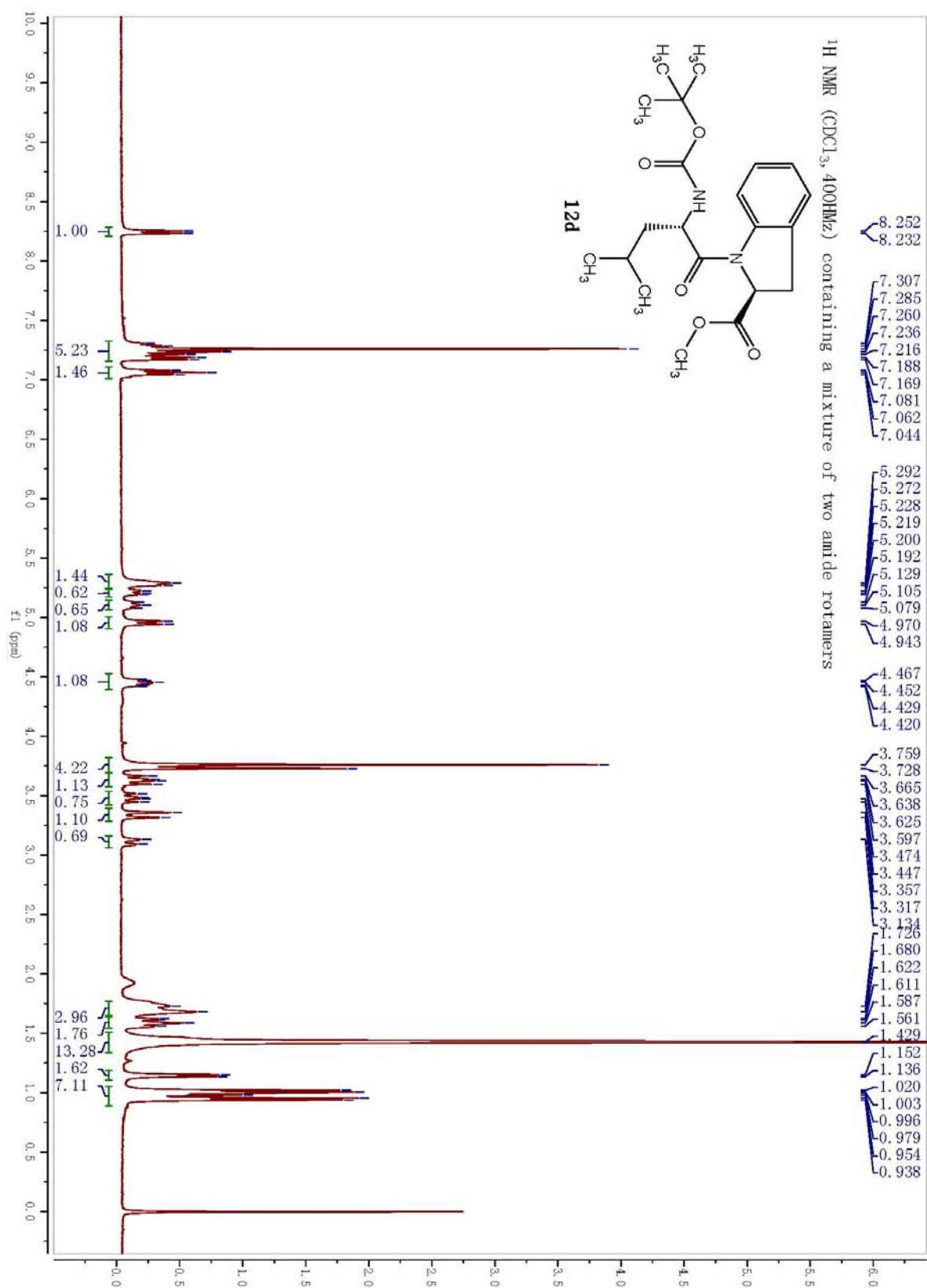


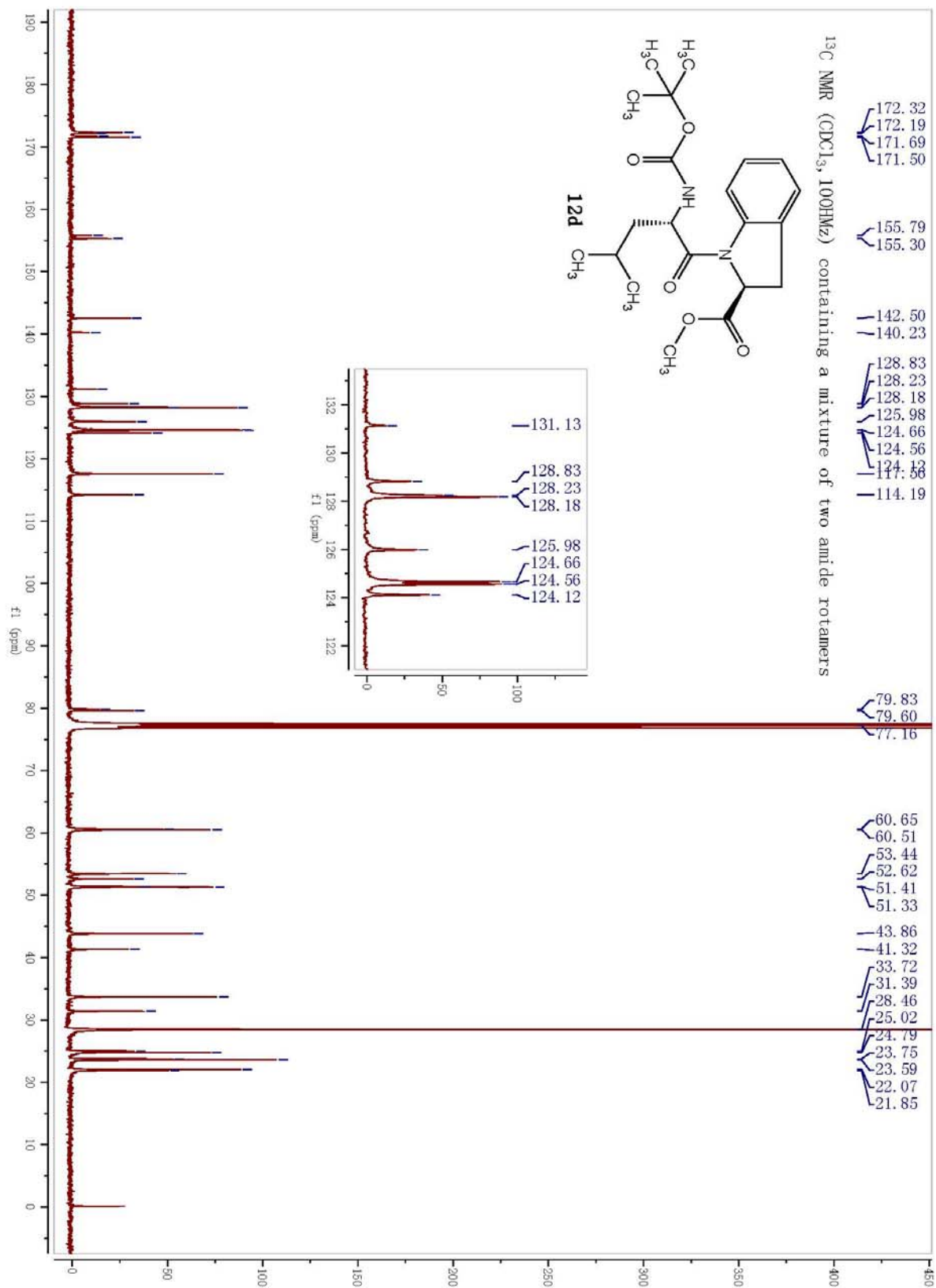


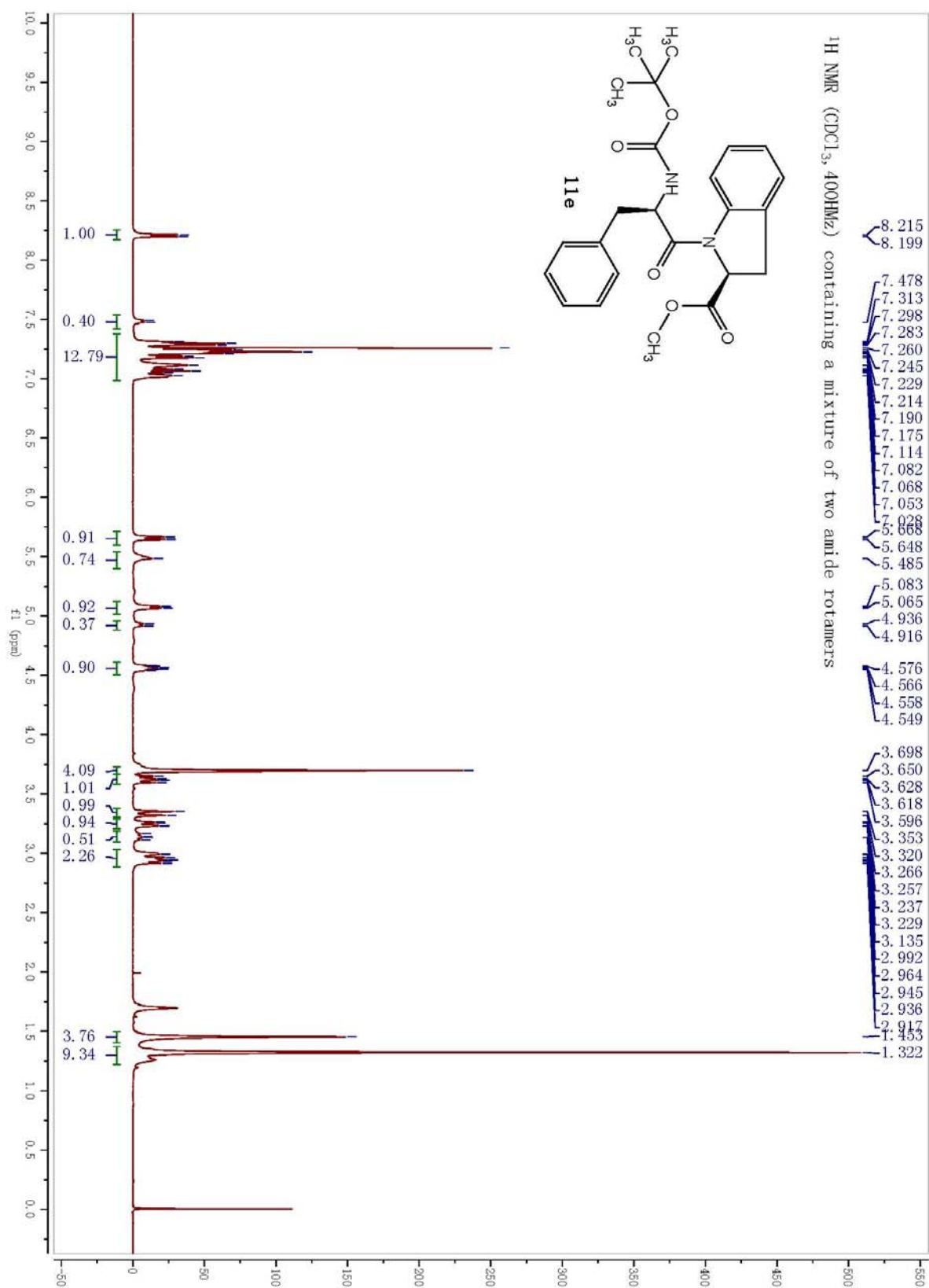


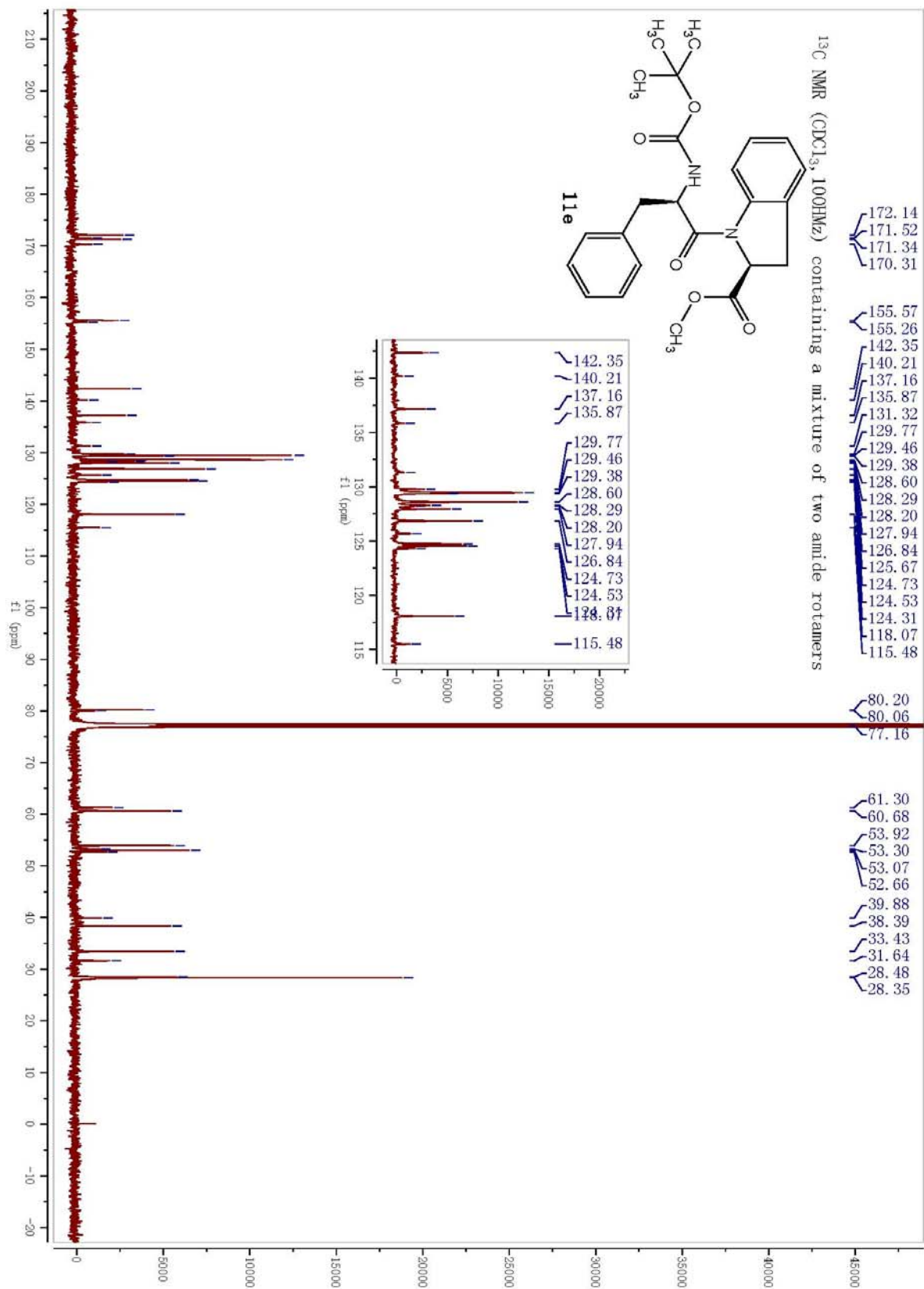


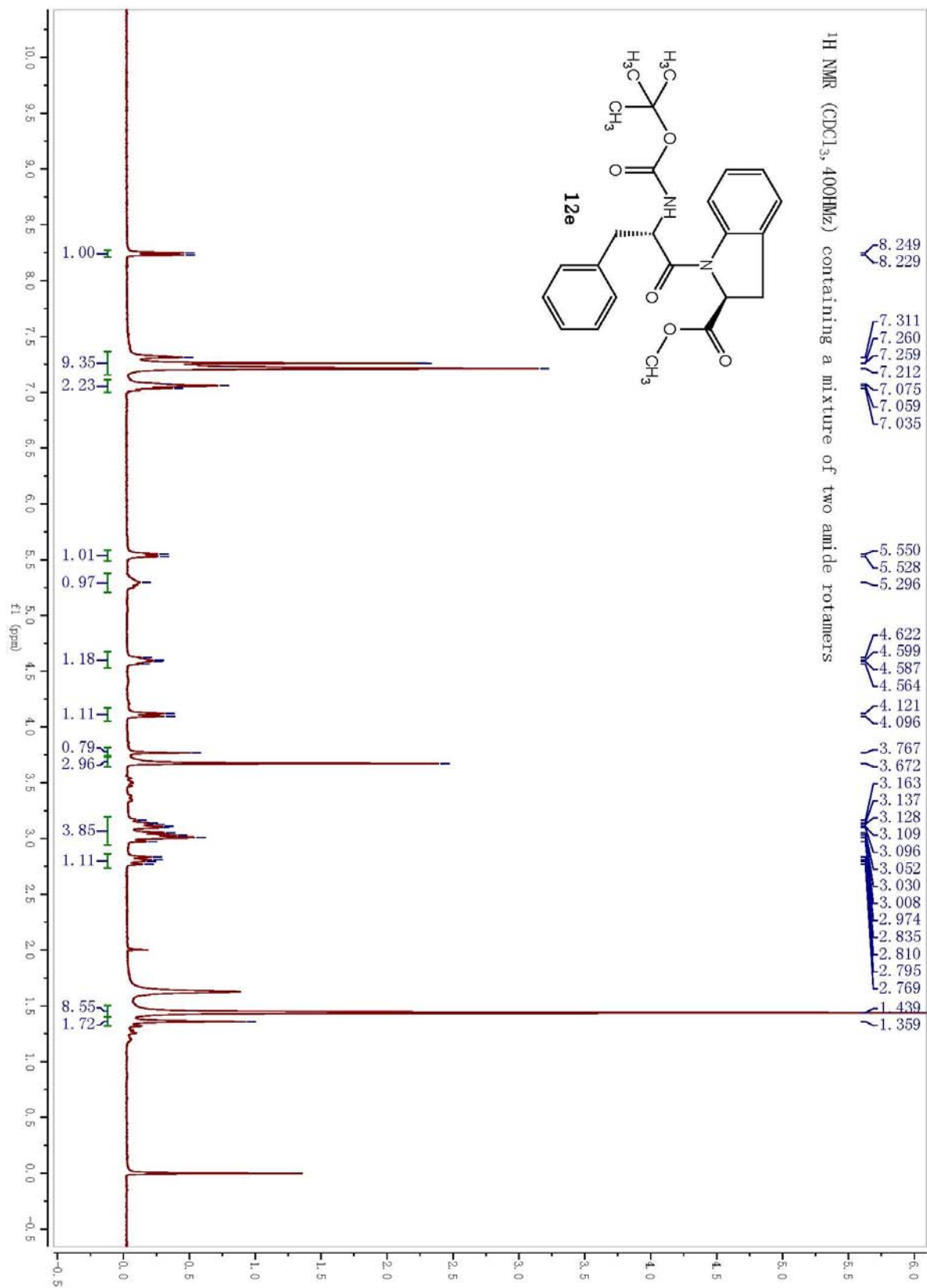


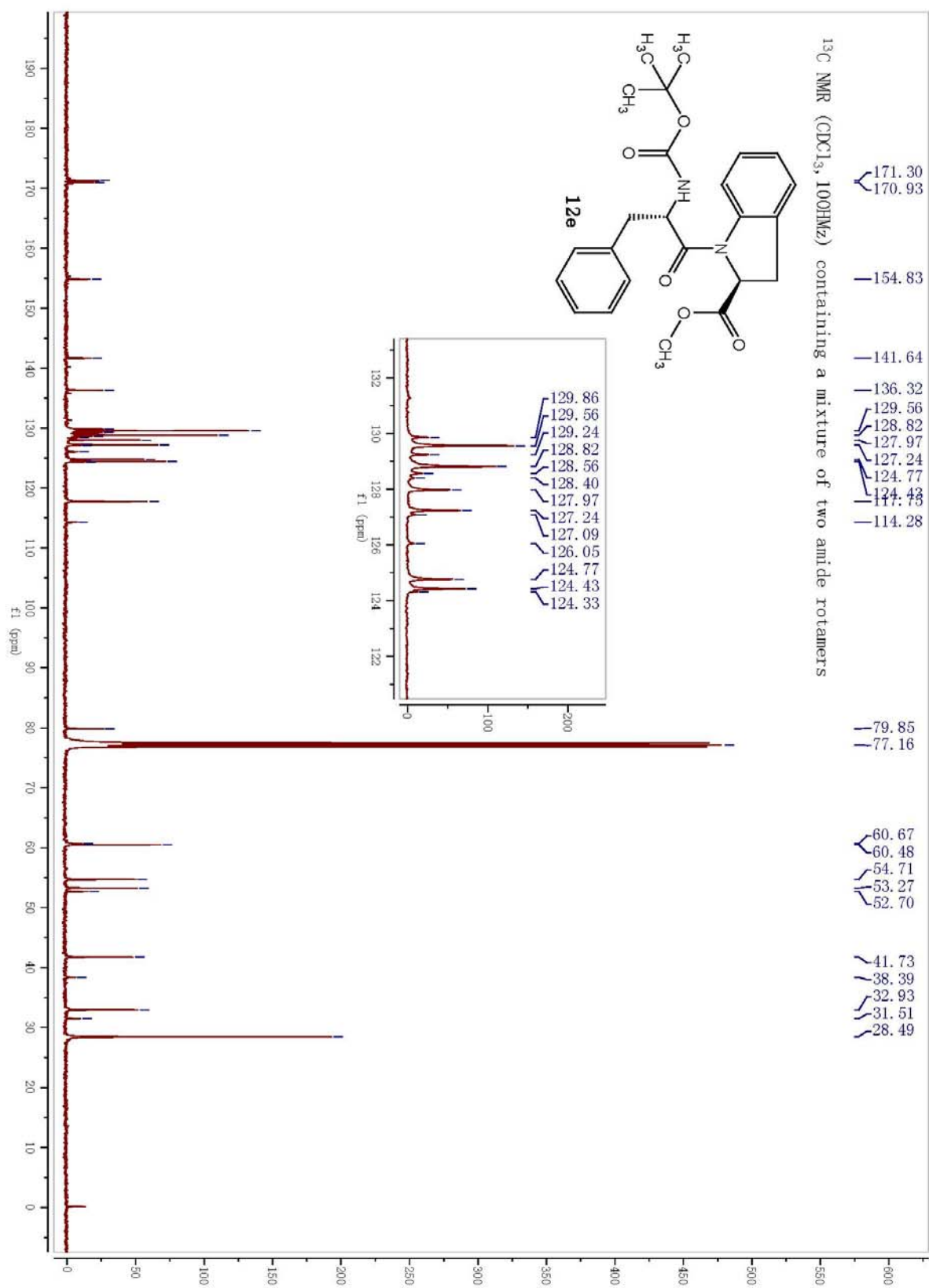


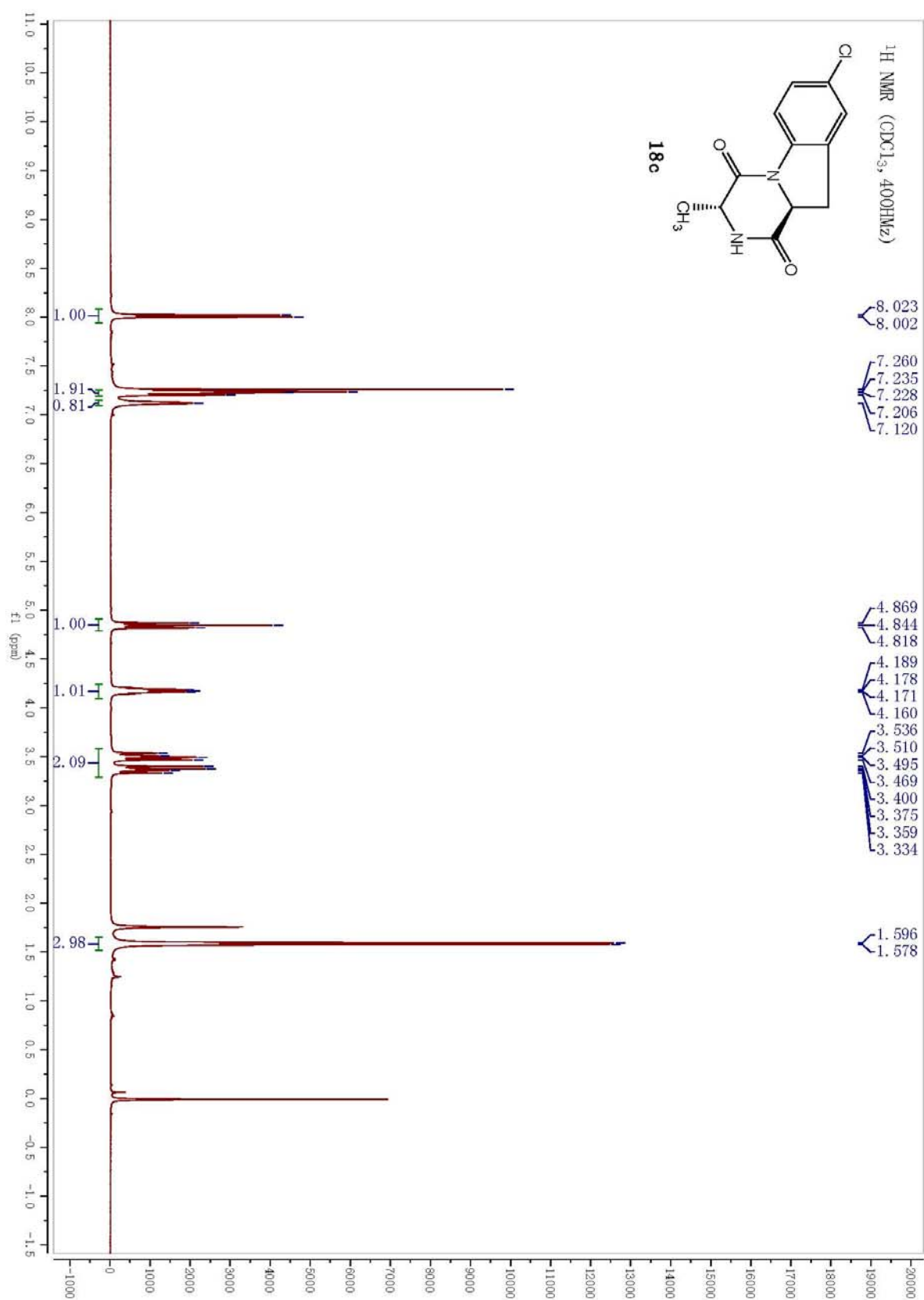


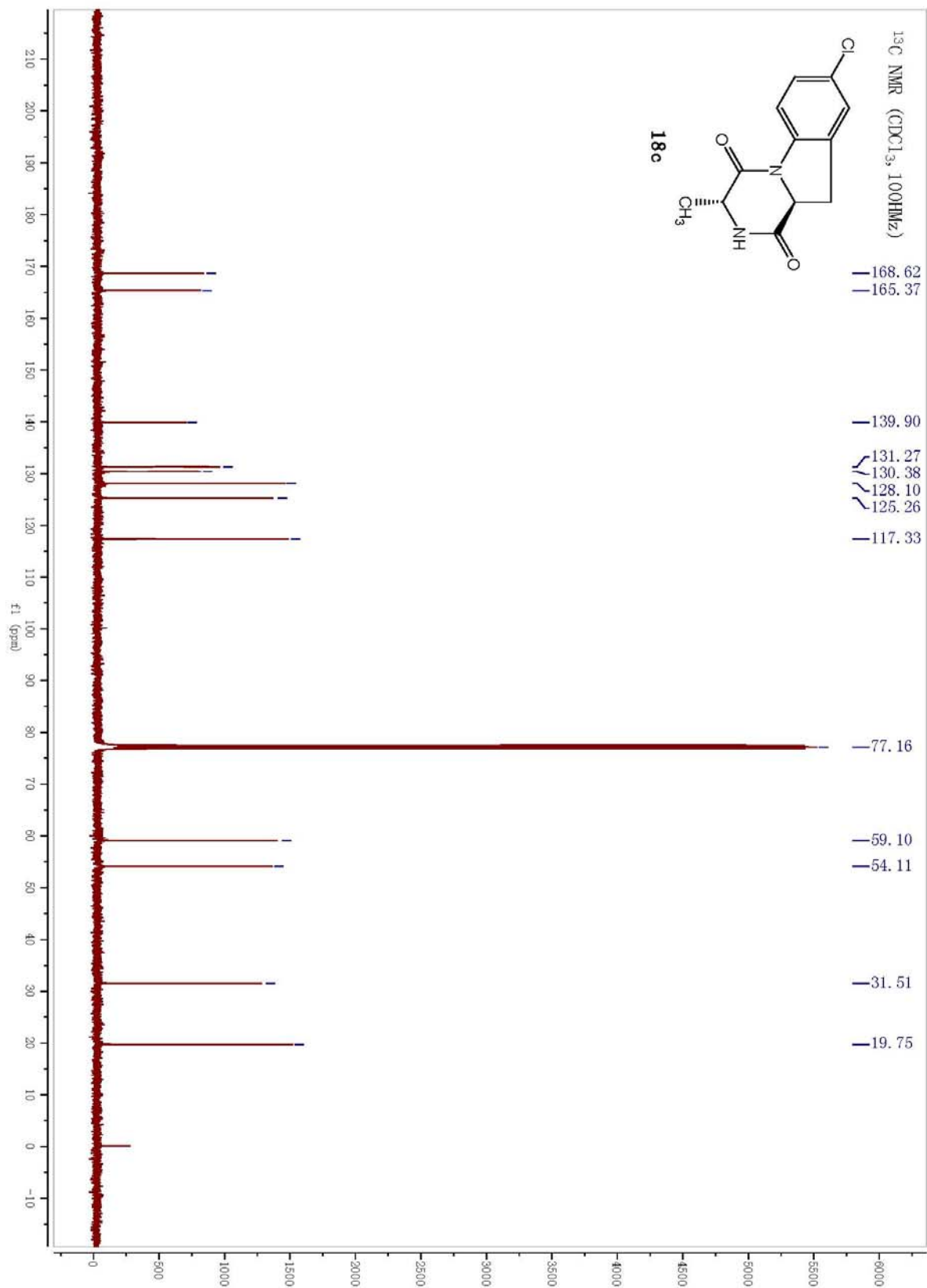


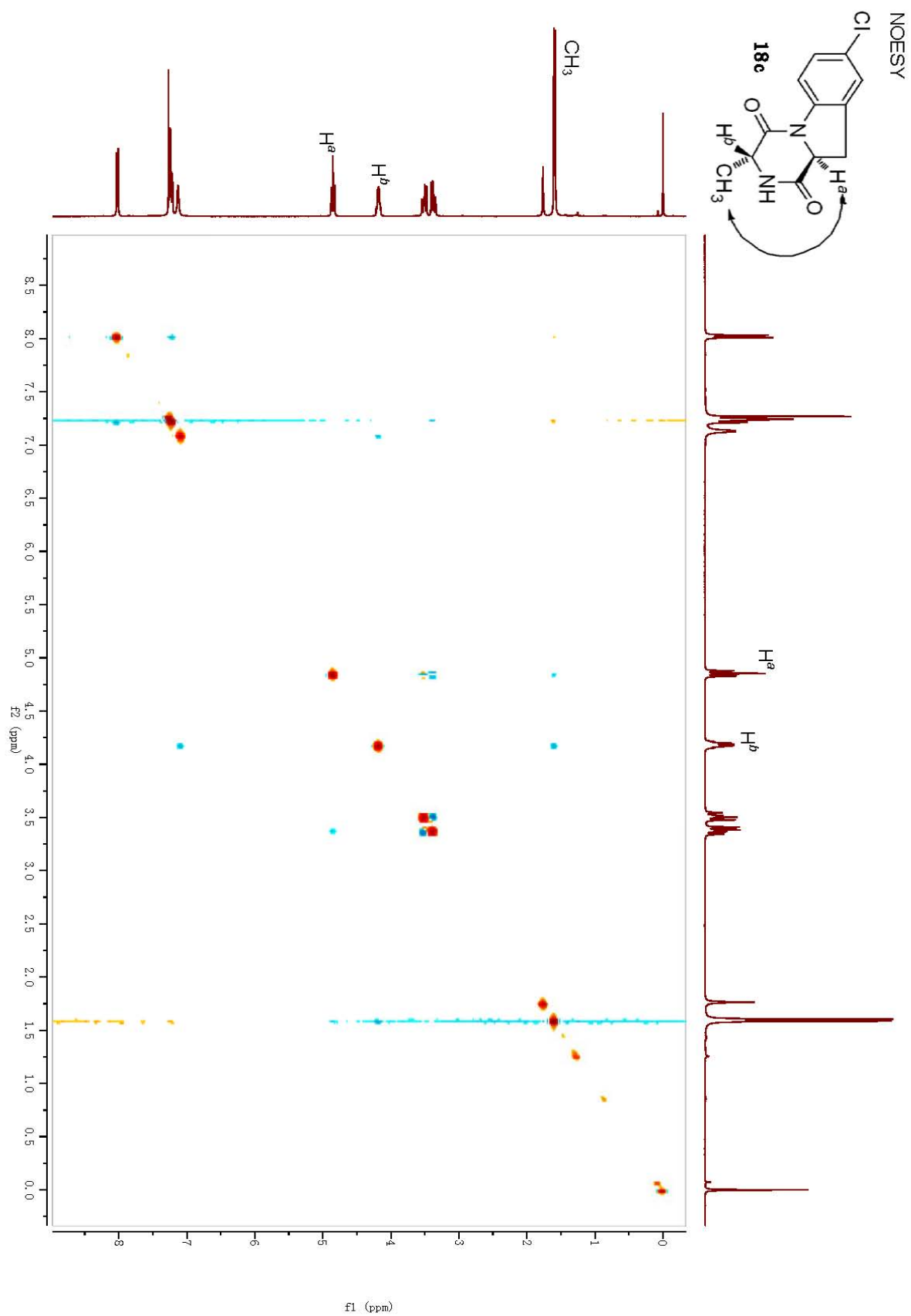


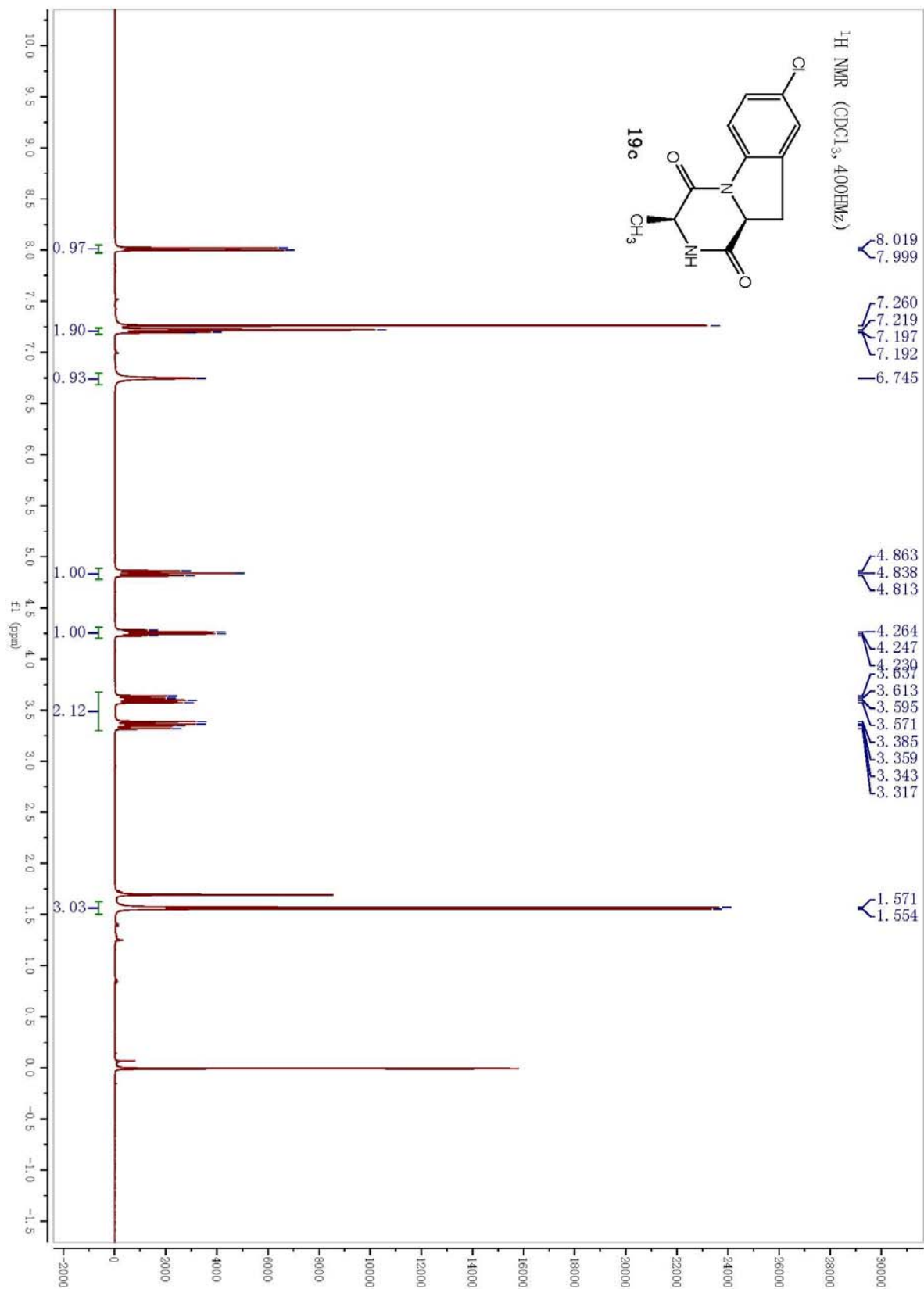


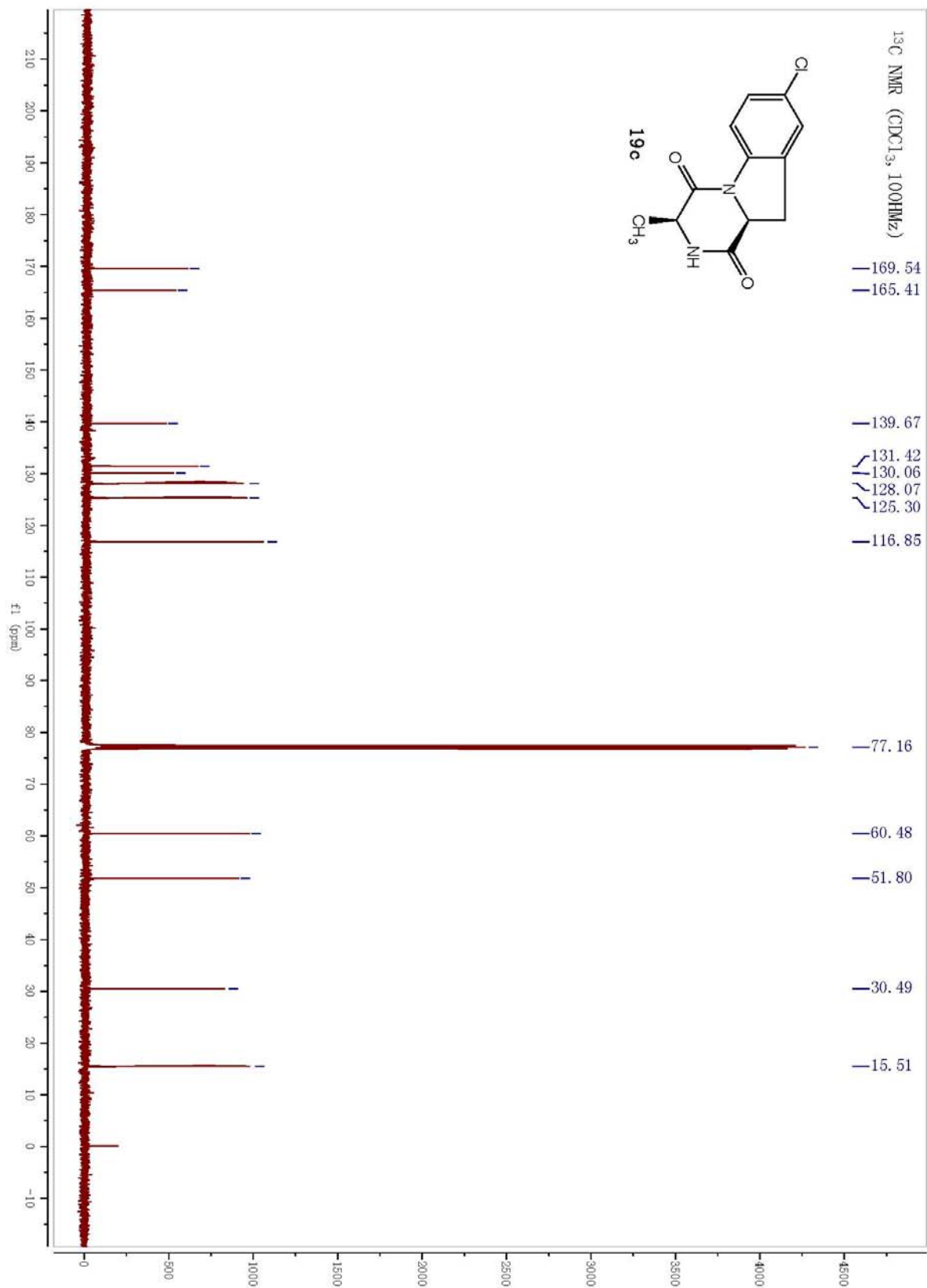


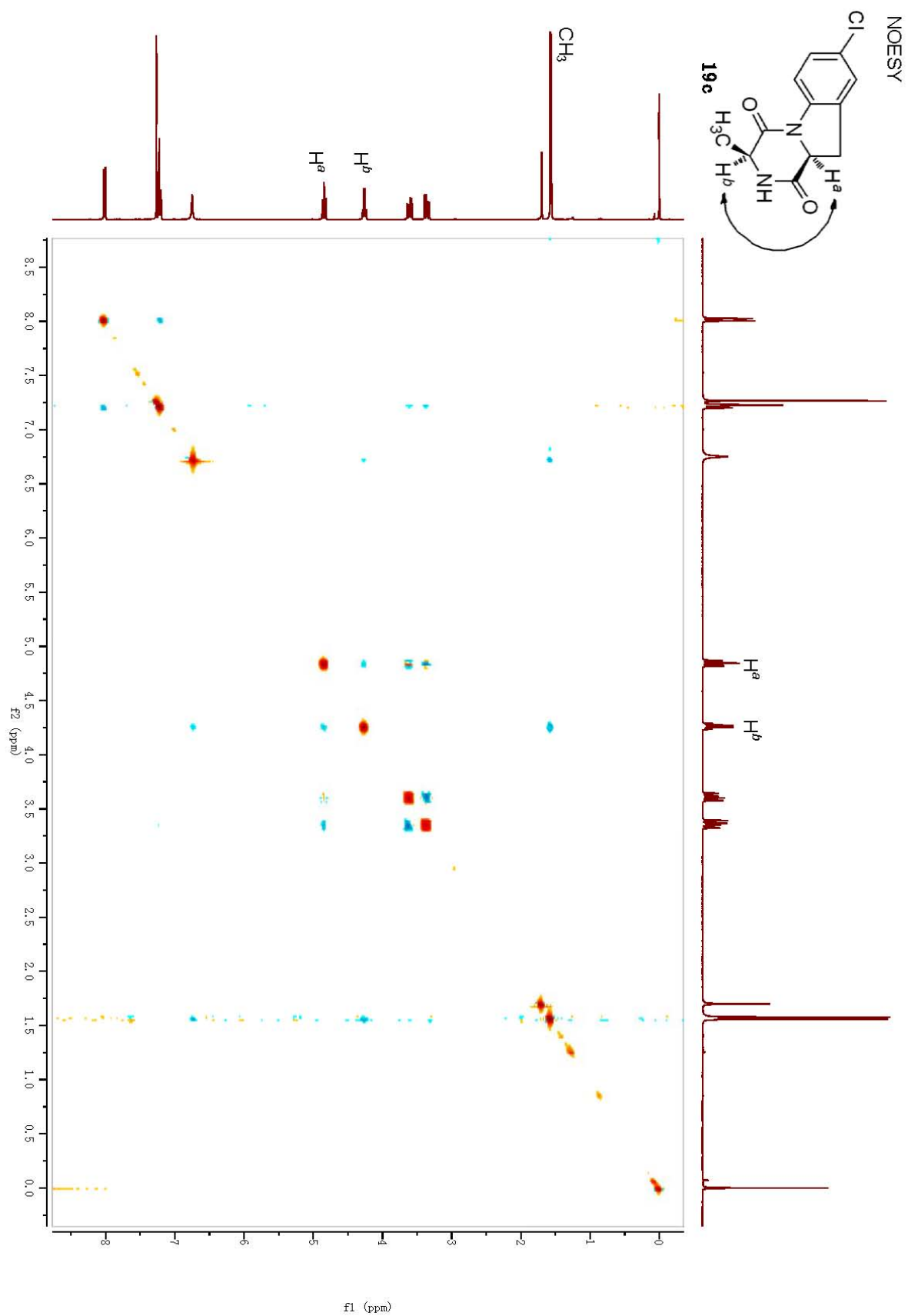


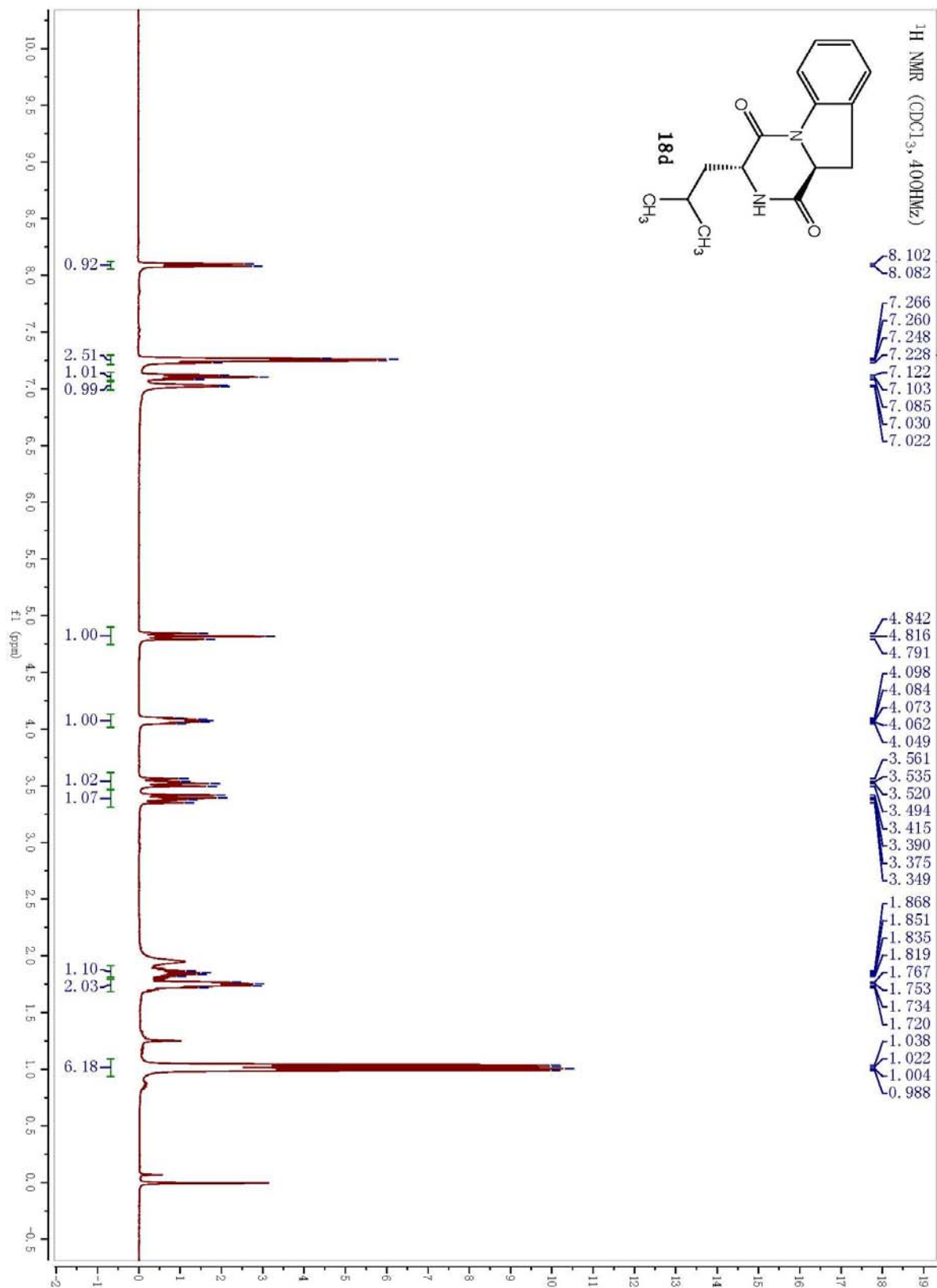


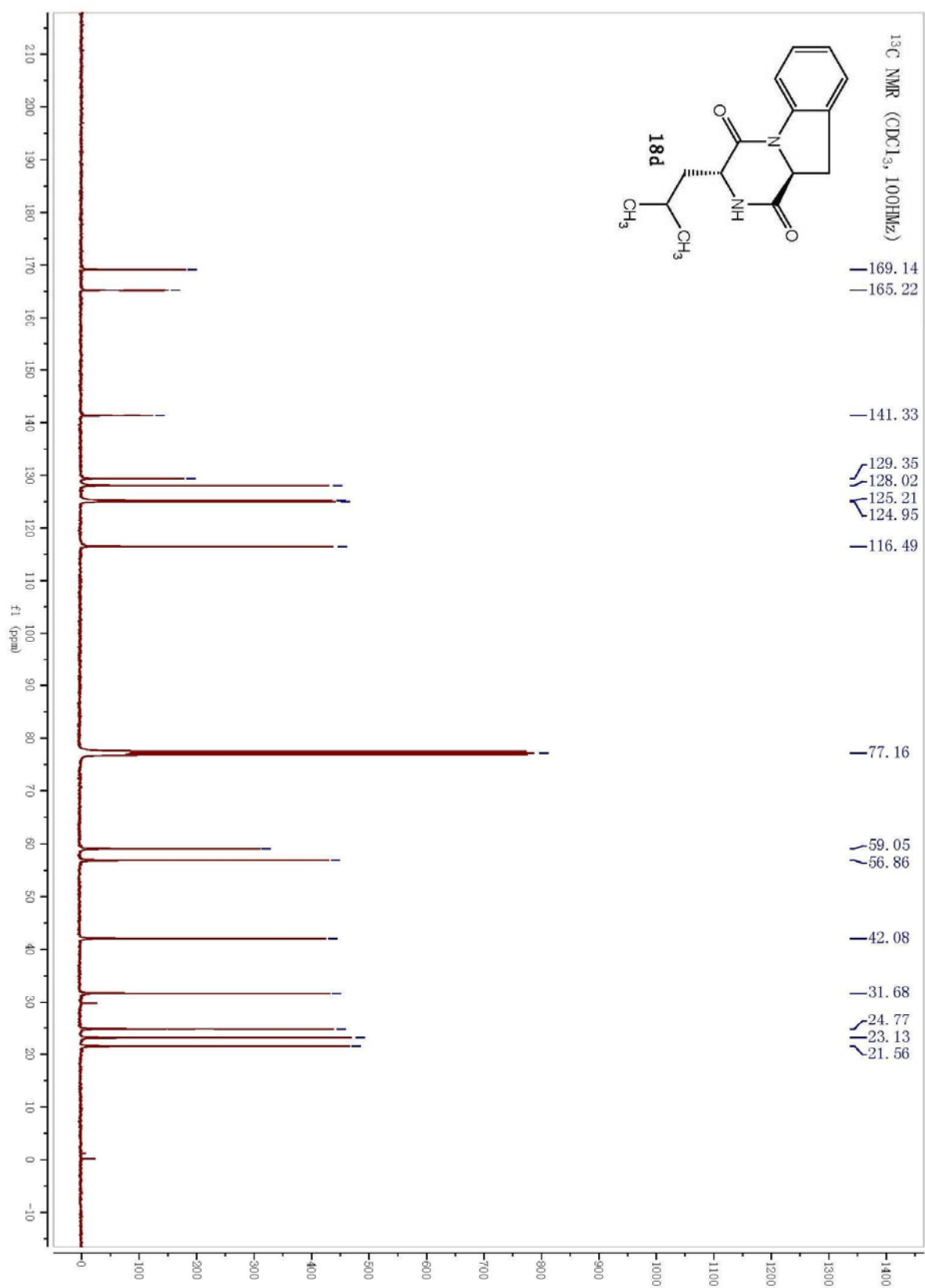












NOESY

