

Supporting Information

Palladium-catalyzed Ugi-type reaction of 2-iodoanilines with isocyanides and carboxylic acids affording *N*-acyl anthranilamides

Content

1. General	3
2. General Procedure for Synthesis of <i>N</i> -acyl Anthranilamides	4
3. Gram Scale Preparation of 4aaa	22
4. References	23
5. ¹ H, ¹³ C and ¹⁹ F NMR Spectra.....	24
6. X-ray of 4aaa	158

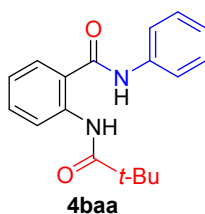
1. General

All reagents and all solvents were used directly as obtained commercially unless otherwise noted. The products were purified by column chromatography with silica gel (pore size 60Å, 200-300 Mesh). ¹H NMR and ¹³C NMR spectra were recorded from solution in CDCl₃ or DMSO on 400 MHz spectrometers using the solvent residual proton signal. The infrared (IR) spectra were acquired as thin films using a universal ATR sampling accessory on a Bruker Vertex 80 FT-IR spectrometer and the absorption frequencies are reported in cm⁻¹ using KBr plates. High-resolution mass analysis was performed using a Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap Mass Spectrometer. 2-Isocyano-1,3-dimethyl benzene (**1a**)¹, isocyanobenzene (**1b**)², 1-isocyano-2-methylbenzene (**1c**)³, 1-(*tert*-butyl)-2-isocyanobenzene (**1d**)⁴, 1-chloro-2-isocyanobenzene (**1e**)⁵, 1-isocyano-2-(trifluoromethyl)benzene (**1f**)⁶, ethyl (*E*)-3-(2-isocyanophenyl)acrylate (**1g**)⁷, 1-bromo-3-isocyanobenzene (**1h**)⁶, 1-isocyano-4-methylbenzene (**1i**)⁵, 1-isocyano-3,5-dimethoxybenzene (**1j**)⁸, 2-isocyano-1-methoxy-4-methylbenzene (**1k**)⁹, 1-chloro-2-isocyano-3-methylbenzene (**1l**)¹, 1-chloro-3-isocyano-2,4-dimethylbenzene (**1m**)⁹, 1-isocyano-naphthalene (**1n**)⁵ were prepared according to literature procedure.

2. General Procedure for Synthesis of *N*-acyl Anthranilamides

Carboxylic acid **3** (0.3 mmol, 1.5 equiv.) and Cs₂CO₃ (0.15 mmol, 0.75 equiv.) were added to a solution of TBAC (0.2 mmol, 1.0 equiv.) in water (0.4 mL). The resulting mixture was stirred at 80 °C for 0.5 h, then cooled down to room temperature (solution A).

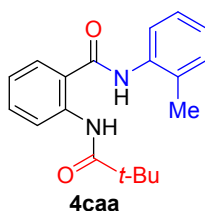
Under Ar atmosphere, Pd(dba)₂ (0.02 mmol, 10 mol %) and BINAP (0.04 mmol, 20 mol %) were added to toluene (1.0 mL). After stirring for 15 min at RT, aniline **2** (0.3 mmol, 1.5 equiv.) was added followed by solution A. The resulting mixture was heated at 100 °C with stirring for 0.5 h by using a heating block before a solution of isocyanide **1** (0.2 mmol, 1.0 equiv.) in toluene (2.0 mL) was added over 2 hours by using a syringe pump. The reaction was further stirred for 0.5 h at 100 °C. The completed reaction was cooled down to RT, quenched with brine (20.0 mL) and extracted with DCM (3 × 20 mL). The combined organic layers were dried (anhydrous MgSO₄), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, petroleum ether/EtOAc).



N-Phenyl-2-pivalamidobenzamide (**4baa**)

Compound **4baa** was prepared following the general procedure using isocyanide **1b** (0.2 mmol, 20.6 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4baa** as a yellow solid (44.5 mg, 75%): m.p.: 226-227 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.84 (s, 1H), 8.62 (s, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 1.31 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.2, 167.4, 139.4, 138.0, 132.3, 129.3, 127.2, 125.0, 123.0, 122.3, 122.2, 120.7, 40.2, 27.8; IR (neat) 3289, 2961, 1652, 1521, 1438, 755 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₈H₂₀N₂NaO₂ [M+Na]⁺: 319.1417; Found 319.1416.

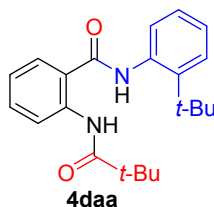
The spectral data match those previously reported^[10].



2-Pivalamido-*N*-(*o*-tolyl)benzamide (**4caa**)

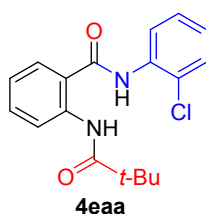
Compound **4caa** was prepared following the general procedure using isocyanide **1c** (0.2 mmol, 23.4 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by

flash column chromatography (silica gel, PE/EA = 5:1) afforded **4caa** as a white solid (49.5 mg, 80%): m.p.: 180-181 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.08 (s, 1H), 8.61 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.19 – 7.13 (m, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 2.32 (s, 3H), 1.29 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.1, 167.7, 140.4, 135.3, 133.0, 131.2, 131.0, 127.1, 126.8, 126.5, 124.4, 122.9, 122.2, 121.3, 40.3, 27.8, 18.1; IR (neat) 2957, 2922, 2856, 1655, 1516, 1439, 754 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₉H₂₂N₂NaO₂ [M+Na]⁺: 333.1573 found 333.1570.



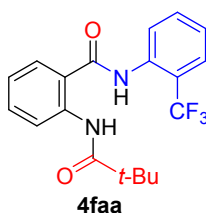
***N*-(2-(*tert*-Butyl)phenyl)-2-pivalamidobenzamide (4daa)**

Compound **4daa** was prepared following the general procedure using isocyanide **1d** (0.2 mmol, 31.9 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4daa** as a white solid (53.5 mg, 76%): m.p.: 188-190 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.12 (s, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 7.84 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.33 – 7.25 (m, 2H), 7.14 (t, *J* = 7.5 Hz, 1H), 1.41 (s, 9H), 1.27 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 178.1, 168.3, 144.8, 140.3, 134.7, 133.0, 129.5, 127.6, 127.3, 127.2, 126.5, 123.0, 122.1, 121.4, 40.3, 35.0, 30.9, 27.7; IR (neat) 2961, 2923, 1656, 1590, 1511, 1437, 756 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₂H₂₈N₂NaO₂ [M+Na]⁺: 375.2043; Found 375.2040.



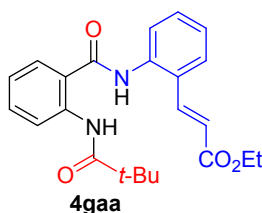
***N*-(2-Chlorophenyl)-2-pivalamidobenzamide (4eaa)**

Compound **4eaa** was prepared following the general procedure using isocyanide **1e** (0.2 mmol, 27.5 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4eaa** as a white solid (54.4 mg, 82%): m.p.: 138-139 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.10 (s, 1H), 8.69 (d, *J* = 8.5 Hz, 1H), 8.44 – 8.37 (m, 2H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.17 – 7.07 (m, 2H), 1.32 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.0, 167.3, 140.7, 134.4, 133.5, 129.4, 128.0, 126.7, 125.6, 124.0, 123.1, 122.2, 122.1, 120.7, 40.4, 27.8; IR (neat) 2957, 2922, 2859, 1662, 1516, 1433, 753 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₈H₁₉ClN₂NaO₂ [M+Na]⁺: 353.1027; Found 353.1023.



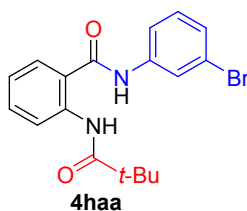
2-Pivalamido-N-(2-(trifluoromethyl)phenyl)benzamide (4faa)

Compound **4faa** was prepared following the general procedure using isocyanide **1f** (0.2 mmol, 34.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4faa** as a white solid (30.7 mg, 42%): m.p.: 152-153 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.02 (s, 1H), 8.69 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 8.16 (s, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.53 (td, *J* = 7.9, 1.2 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.14 (td, *J* = 7.6, 1.0 Hz, 1H), 1.32 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.01, 167.72, 140.84, 135.03, 133.69, 133.25, 126.6 (q, *J*_{C-F} = 5.1 Hz), 126.43, 125.60, 125.4, 124.3 (q, *J*_{C-F} = 273.7 Hz), 123.2, 122.25, 121.6 (q, *J*_{C-F} = 30.3 Hz), 120.47, 40.46, 27.81; ¹⁹F NMR (376 MHz, CDCl₃) δ -60.45 (s, 3F); IR (neat) 2958, 2922, 2858, 1661, 1516, 1318, 759 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₉H₂₀F₃N₂O₂ [M+H]⁺: 365.1471; Found 365.1472.



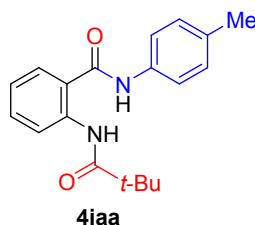
Ethyl (*E*)-3-(2-(2-pivalamidobenzamido)phenyl)acrylate (4gaa)

Compound **4gaa** was prepared following the general procedure using isocyanide **1g** (0.2 mmol, 40.3 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4gaa** as a white solid (49.1 mg, 62%): m.p.: 190-192 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.01 (s, 1H), 8.60 (d, *J* = 8.4 Hz, 1H), 8.13 (s, 1H), 7.83 (d, *J* = 15.9 Hz, 1H), 7.67 (t, *J* = 7.1 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.30 – 1.24 (m, 3H), 1.27 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.1, 168.2, 166.7, 140.6, 139.3, 135.6, 133.3, 131.0, 129.5, 127.7, 127.1, 127.0, 126.2, 123.0, 122.1, 121.4, 120.6, 60.9, 40.4, 27.8, 14.5; IR (neat) 2957, 2925, 2856, 1514, 1440, 1266, 1173, 744 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₃H₂₆N₂NaO₄ [M+Na]⁺: 417.1785; Found 417.1780.



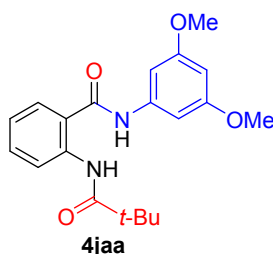
***N*-(3-Bromophenyl)-2-pivalamidobenzamide (4haa)**

Compound **4haa** was prepared following the general procedure using isocyanide **1h** (0.2 mmol, 36.4 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4haa** as a white solid (50.5 mg, 67%): m.p.: 193-194 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.68 (s, 1H), 8.99 – 8.89 (m, 1H), 8.23 – 8.16 (m, 1H), 8.02 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.33 – 7.20 (m, 3H), 6.96 (t, *J* = 7.5 Hz, 1H), 1.32 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 178.4, 167.4, 139.6, 139.1, 132.3, 130.6, 127.8, 127.4, 123.4, 123.2, 122.9, 122.6, 122.2, 119.0, 40.2, 27.8; IR (neat) 2957, 2922, 2859, 1657, 1588, 1520, 751 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₈H₂₀BrN₂O₂ [M+H]⁺: 375.0703; Found 375.0702.



2-Pivalamido-*N*-(*p*-tolyl)benzamide (4iaa)

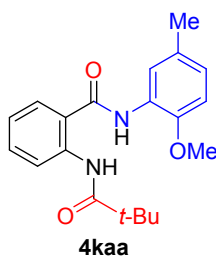
Compound **4iaa** was prepared following the general procedure using isocyanide **1i** (0.2 mmol, 23.4 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4iaa** as a white solid (43.7 mg, 70%): m.p.: 185-187 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.86 (s, 1H), 8.62 (s, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 2.35 (s, 3H), 1.30 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 178.2, 167.4, 139.3, 135.4, 134.7, 132.1, 129.8, 127.2, 123.0, 122.3, 122.2, 120.9, 40.2, 27.8, 21.2; IR (neat) 2957, 2922, 2859, 1657, 1515, 1446, 753 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₉H₂₂N₂NaO₂ [M+Na]⁺: 311.1573; Found 311.1573.



***N*-(3,5-Dimethoxyphenyl)-2-pivalamidobenzamide (4jaa)**

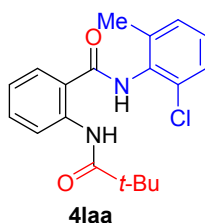
Compound **4jaa** was prepared following the general procedure using isocyanide **1j** (0.2 mmol, 32.6 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4jaa** as a white solid (56.9 mg, 80%): m.p.: 214-215 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.84 (s, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 8.26 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 1.9 Hz, 2H), 6.30 (s, 1H), 3.81 (s, 6H), 1.31 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.2, 167.4, 161.4, 139.7, 139.7, 132.6, 127.0, 123.0, 122.4, 122.1, 99.3, 97.2, 55.7, 40.3, 27.8; IR (neat) 2957, 2922,

2857, 1657, 1453, 1160, 754 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^+$: 379.1628; Found 379.1622.



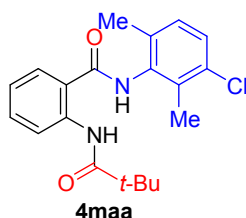
***N*-(2-Methoxy-5-methylphenyl)-2-pivalamidobenzamide (4kaa)**

Compound **4kaa** was prepared following the general procedure using isocyanide **1k** (0.2 mmol, 29.4 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4kaa** as a white solid (64.5 mg, 95%): m.p.: 109-111 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 11.17 (s, 1H), 8.68 (d, $J = 8.4$ Hz, 1H), 8.47 (s, 1H), 8.23 (s, 1H), 7.61 (d, $J = 7.8$ Hz, 1H), 7.49 (t, $J = 7.9$ Hz, 1H), 7.11 (t, $J = 7.6$ Hz, 1H), 6.90 (d, $J = 8.3$ Hz, 1H), 6.80 (d, $J = 8.3$ Hz, 1H), 3.87 (s, 3H), 2.35 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 177.8, 166.9, 146.4, 140.3, 132.7, 130.6, 127.0, 126.6, 124.7, 122.7, 121.7, 121.5, 120.8, 110.0, 56.0, 40.2, 27.6, 21.0; IR (neat) 2960, 2924, 2865, 1683, 1530, 1413, 755 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 341.1860; Found 341.1859.



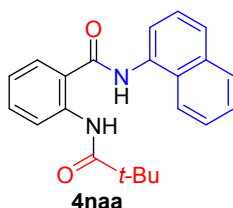
***N*-(2-Chloro-6-methylphenyl)-2-pivalamidobenzamide (4laa)**

Compound **4laa** was prepared following the general procedure using isocyanide **1l** (0.2 mmol, 30.3 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4laa** as a white solid (45.7 mg, 66%): m.p.: 196-197 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 10.99 (s, 1H), 8.62 (t, $J = 6.7$ Hz, 1H), 7.77 (d, $J = 7.7$ Hz, 1H), 7.69 (s, 1H), 7.54 – 7.45 (m, 1H), 7.32 (d, $J = 5.9$ Hz, 1H), 7.22 – 7.17 (m, 2H), 7.15 – 7.08 (m, 1H), 2.32 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 178.1, 167.9, 140.39, 140.37, 138.5, 133.34, 133.32, 132.3, 132.2, 132.12, 132.08, 129.6, 128.7, 127.5, 127.20, 127.16, 123.0, 122.01, 121.98, 120.6, 40.3, 27.8, 19.1; IR (neat) 2957, 2922, 2856, 1657, 1590, 1511, 1441, 760 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 367.1184; Found 367.1175.



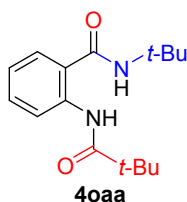
N-(3-Chloro-2,6-dimethylphenyl)-2-pivalamidobenzamide (**4maa**)

Compound **4maa** was prepared following the general procedure using isocyanide **1m** (0.2 mmol, 33.1 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4maa** as a white solid (59.1 mg, 82%): m.p.: 196-197 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.06 (s, 1H), 8.57 (d, *J* = 8.3 Hz, 1H), 7.82 – 7.70 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.14 – 7.03 (m, 2H), 2.29 (s, 3H), 2.24 (s, 3H), 1.23 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.2, 168.1, 140.4, 134.7, 134.6, 134.4, 133.3, 132.8, 128.9, 128.8, 127.0, 123.0, 122.1, 120.5, 40.3, 27.7, 18.6, 15.9; IR (neat) 2958, 2923, 2859, 1657, 1510, 1439, 756 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₃ClN₂NaO₂ [M+Na]⁺: 381.1340; Found 381.1337.



N-(Naphthalen-1-yl)-2-pivalamidobenzamide (**4naa**)

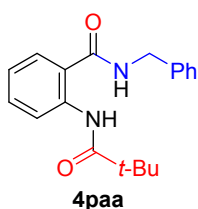
Compound **4naa** was prepared following the general procedure using isocyanide **1n** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4naa** as a white solid (59.9 mg, 86%): m.p.: 206-207 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.06 (s, 1H), 8.65 (d, *J* = 8.3 Hz, 1H), 8.26 (s, 1H), 7.93 – 7.81 (m, 3H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.55 – 7.48 (m, 4H), 7.15 (t, *J* = 7.5 Hz, 1H), 1.27 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 178.1, 168.4, 140.3, 134.4, 133.1, 132.1, 129.0, 128.3, 127.2, 127.0, 126.8, 126.5, 125.8, 123.0, 122.5, 122.2, 121.5, 121.3, 40.3, 27.7. IR (neat) 2956, 2922, 2857, 1511, 1440, 761 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₂H₂₂N₂NaO₂ [M+Na]⁺: 369.1573; Found 369.1570.



N-(*tert*-Butyl)-2-pivalamidobenzamide (**4oaa**)

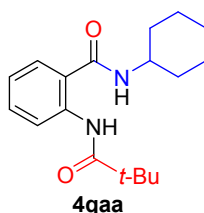
Compound **4oaa** was prepared following the general procedure using isocyanide **1o** (0.2 mmol, 16.6 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by

flash column chromatography (silica gel, PE/EA = 10:1) afforded **4oaa** as a white solid (29.7 mg, 54%): m.p. 180-181 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.93 (s, 1H), 8.48 (d, *J* = 8.3 Hz, 1H), 7.37 (dd, *J* = 19.7, 7.8 Hz, 2H), 6.99 (t, *J* = 7.5 Hz, 1H), 5.99 (s, 1H), 1.44 (s, 9H), 1.28 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 177.8, 169.2, 139.3, 132.0, 126.4, 123.2, 122.7, 121.9, 52.3, 40.2, 28.9, 27.8; IR (neat) 2958, 2922, 2858, 1651, 1518, 1444, 755 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₆H₂₄N₂NaO₂ [M+Na]⁺: 299.1730; Found 299.1729.



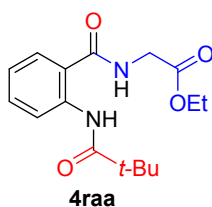
***N*-Benzyl-2-pivalamidobenzamide (4paa)**

Compound **4paa** was prepared following the general procedure using isocyanide **1p** (0.2 mmol, 23.4 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4paa** as a white solid (37.1 mg, 60%): m.p.: 130-131 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.24 (s, 1H), 8.63 (d, *J* = 8.7 Hz, 1H), 7.44 (t, *J* = 6.8 Hz, 2H), 7.38 – 7.27 (m, 5H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.44 (s, 1H), 4.62 (d, *J* = 5.7 Hz, 2H), 1.31 (d, *J* = 4.9 Hz, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.0, 169.2, 140.2, 137.9, 132.8, 129.1, 128.0, 128.0, 126.6, 122.7, 121.8, 120.8, 44.2, 40.4, 27.8; IR (neat) 2961, 1724, 1645, 1515, 1440, 1363, 1290, 754 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₉H₂₃N₂O₂ [M+H]⁺: 311.1754; Found 311.1755.



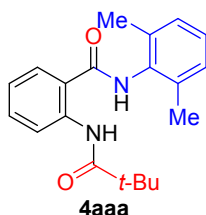
***N*-Cyclohexyl-2-pivalamidobenzamide (4qaa)**

Compound **4qaa** was prepared following the general procedure using isocyanide **1q** (0.2 mmol, 21.8 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4qaa** as a white solid (27.5 mg, 46%): m.p.: 136-137 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.19 (s, 1H), 8.59 (d, *J* = 8.3 Hz, 1H), 7.40 (dd, *J* = 8.1, 3.8 Hz, 2H), 7.01 (td, *J* = 7.6, 0.9 Hz, 1H), 6.03 (d, *J* = 6.4 Hz, 1H), 4.00 – 3.85 (m, 1H), 2.00 (dd, *J* = 12.3, 3.0 Hz, 2H), 1.79 – 1.69 (m, 2H), 1.69 – 1.62 (m, 1H), 1.49 – 1.35 (m, 2H), 1.30 (s, 9H), 1.29 – 1.13 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 178.0, 168.5, 140.1, 132.5, 126.4, 122.6, 121.8, 121.5, 48.9, 40.3, 33.2, 27.8, 25.7, 25.1; IR (neat) 2939, 1640, 1595, 1519, 1440, 754 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₈H₂₇N₂O₂ [M+H]⁺: 303.2067; Found 303.2067.



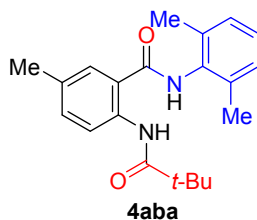
Ethyl (2-pivalamidobenzoyl)glycinate (**4raa**)

Compound **4raa** was prepared following the general procedure using isocyanide **1r** (0.2 mmol, 23.4 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4raa** brown oil (29.6 mg, 48%): ¹H NMR (400 MHz, CDCl₃) δ 11.19 (s, 1H), 8.65 (d, *J* = 8.5 Hz, 1H), 7.54 – 7.50 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.45 (td, *J* = 7.9, 1.2 Hz, 1H), 7.05 (td, *J* = 7.6, 1.0 Hz, 1H), 6.75 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.18 (d, *J* = 5.0 Hz, 2H), 1.33 – 1.30 (s, 9H), 1.30 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 178.0, 169.9, 169.3, 140.5, 133.2, 126.9, 122.7, 121.7, 119.8, 62.0, 42.1, 40.4, 27.8, 14.4; IR (neat) 2938, 1744, 1642, 1520, 1441, 1199, 754 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₆H₂₃N₂O₄ [M+H]⁺: 307.1652; Found 307.1652.



N-(2,6-Dimethylphenyl)-2-pivalamidobenzamide (**4aaa**)

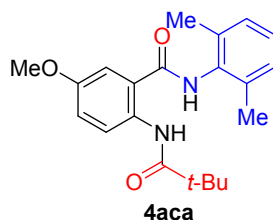
Compound **4aaa** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aaa** as a yellow solid (55.1 mg, 85%): m.p.: 189-191 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.10 (s, 1H), 8.63 (dd, *J* = 8.4, 0.7 Hz, 1H), 7.71 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.59 – 7.41 (m, 2H), 7.21 – 7.07 (m, 4H), 2.27 (s, 6H), 1.25 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.1, 168.0, 140.3, 135.9, 133.4, 133.1, 128.7, 128.2, 126.9, 122.9, 122.0, 120.9, 40.3, 27.8, 18.7; IR (neat) 2957, 2922, 2856, 1655, 1515, 1445 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₄N₂NaO₂ [M+Na]⁺: 347.1730; Found 347.1724.



N-(2,6-Dimethylphenyl)-5-methyl-2-pivalamidobenzamide (**4aba**)

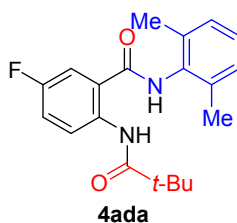
Compound **4aba** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2b** (0.3 mmol, 69.9 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by

flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aba** as a white solid (52.7 mg, 78%): m.p.: 156-157 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.94 (s, 1H), 8.55 – 8.46(m, 1H), 7.48 (s, 1H), 7.42 – 7.27 (m, 2H), 7.19 – 7.08 (m, 3H), 2.37 (s, 3H), 2.28 (s, 6H), 1.26 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 177.9, 168.1, 138.0, 136.0, 133.8, 133.5, 132.5, 128.7, 128.2, 127.0, 122.2, 121.0, 40.28, 27.83, 21.08, 18.66; IR (neat) 2957, 2922, 2856, 1655, 1515, 1445 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₁H₂₇N₂O₂ [M+H]⁺:339.2067; Found 339.2068.



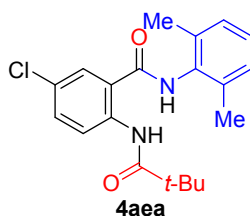
***N*-(2,6-dimethylphenyl)-5-methoxy-2-pivalamidobenzamide (4aca)**

Compound **4aca** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2c** (0.3 mmol, 74.7 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1 to 5:1) afforded **4aca** as a white solid (27.4 mg, 39%): m.p.: 177-179°C; ¹H NMR (400 MHz, CDCl₃) δ 10.68 (s, 1H), 8.53 (d, *J* = 9.1 Hz, 1H), 7.39 (s, 1H), 7.21 (d, *J* = 2.3 Hz, 1H), 7.18 – 7.09 (m, 3H), 7.06 (dd, *J* = 9.1, 2.6 Hz, 1H), 3.84 (s, 3H), 2.27 (s, 6H), 1.25 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 177.7, 167.7, 155.1, 135.9, 133.5, 133.4, 128.7, 128.2, 123.8, 122.7, 117.2, 113.2, 56.0, 40.1, 27.8, 18.6; IR (neat) 2925, 2854, 1726, 1659, 1240, 739 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₁H₂₇N₂O₃ [M+H]⁺:355.2016; Found 355.2015.



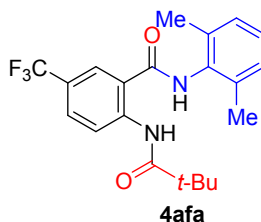
***N*-(2,6-Dimethylphenyl)-5-fluoro-2-pivalamidobenzamide (4ada)**

Compound **4ada** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2d** (0.3 mmol, 71.1 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4ada** as a white solid (51.1 mg, 75%): m.p.: 171-173 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.88 (s, 1H), 8.53 (dd, *J* = 9.1, 5.2 Hz, 1H), 7.69 (s, 1H), 7.40 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.20 – 7.09(m, 4H), 2.26 (s, 6H), 1.23 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.1, 166.9, 157.8 (d, *J*_{C-F} = 245.4 Hz), 136.5, 135.9, 133.3, 128.7, 128.3, 124.0 (d, *J*_{C-F} = 7.1 Hz), 122.4 (d, *J*_{C-F} = 6.1 Hz), 119.6 (d, *J*_{C-F} = 22.2 Hz), 113.6 (d, *J*_{C-F} = 24.2 Hz), 40.2, 27.7, 18.6; ¹⁹F NMR (376 MHz, CDCl₃) δ -118.34 to -118.44 (m, 1F); IR (neat) 2957, 2923, 2858, 1658, 1516, 1460, 771 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₄FN₂O₂ [M+H]⁺:343.1816; Found 343.1816.



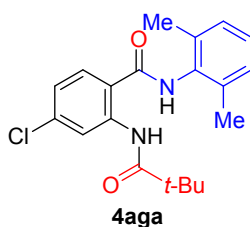
5-Chloro-*N*-(2,6-dimethylphenyl)-2-pivalamidobenzamide (**4aea**)

Compound **4aea** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2e** (0.3 mmol, 76.0 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 15:1 to 10:1) afforded **4aea** as a white solid (41.7 mg, 58%): m.p.: 215-217 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.99 (s, 1H), 8.67 – 8.53 (m, 1H), 7.66 (s, 1H), 7.59 (d, *J* = 23.5 Hz, 1H), 7.49 – 7.39 (m, 1H), 7.21 – 7.09 (m, 3H), 2.27 (s, 6H), 1.24 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.2, 166.9, 139.0, 135.9, 133.2, 132.8, 128.7, 128.4, 127.9, 126.8, 123.5, 122.3, 40.4, 27.7, 18.6; IR (neat) 2924, 1725, 1655, 1264, 748 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₄ClN₂O₂ [M+H]⁺: 359.1521; Found 359.1519.



N-(2,6-Dimethylphenyl)-2-pivalamido-5-(trifluoromethyl)benzamide (**4afa**)

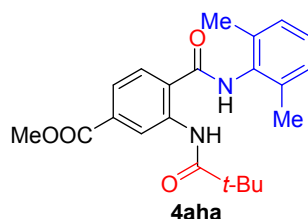
Compound **4afa** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2f** (0.3 mmol, 86.1 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4afa** as a white solid (58.1 mg, 70%): m.p.: 196-197 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.28 (s, 1H), 8.79 (d, *J* = 8.8 Hz, 1H), 7.94 (s, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.66 (s, 1H), 7.22 – 7.10 (m, 3H), 2.28 (s, 6H), 1.25 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.51, 167.05, 143.45, 135.85, 133.10, 129.83 (q, *J*_{C-F} = 4.0 Hz), 128.74, 128.43, 124.7 (q, *J*_{C-F} = 33.3 Hz), 123.96 (q, *J*_{C-F} = 3.0 Hz), 123.94 (q, *J*_{C-F} = 272.7 Hz), 122.03, 120.63, 40.5, 27.6, 18.6; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.06 (s, 3F); IR (neat) 2958, 2921, 2856, 1655, 1516, 1310, 765 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₁H₂₄F₃N₂O₂⁺ [M+H]⁺: 393.1784; Found 393.1781.



4-Chloro-*N*-(2,6-dimethylphenyl)-2-pivalamidobenzamide (**4aga**)

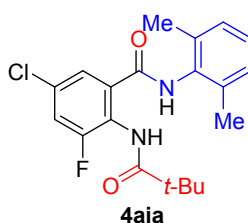
Compound **4aga** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2g** (0.3 mmol, 76.0 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by

flash column chromatography (silica gel, PE/EA = 10:1) afforded **4aga** as a white solid (52.8 mg, 74%): m.p.: 173-175 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.23 (s, 1H), 8.75 (s, 1H), 7.73 – 7.44 (m, 2H), 7.21 – 7.09 (m, 3H), 7.05 (dd, *J* = 8.3, 1.5 Hz, 1H), 2.26 (s, 6H), 1.23 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 178.3, 167.4, 141.4, 139.2, 135.8, 133.2, 128.7, 128.3, 128.0, 122.9, 121.8, 118.8, 40.4, 27.6, 18.6; IR (neat) 2959, 2922, 2858, 1657, 1510, 1434, 773 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₃ClN₂NaO₂ [M+Na]⁺:381.1340; Found 381.1336.



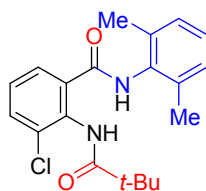
Methyl 4-((2,6-dimethylphenyl)carbamoyl)-3-pivalamidobenzoate (**4aha**)

Compound **4aha** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2h** (0.3 mmol, 83.1 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4aha** as a white solid (55.8 mg, 73%): m.p.: 187-188 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.98 (s, 1H), 9.20 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.95 (d, *J* = 28.0 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.68 – 7.61 (m, 1H), 7.14 (q, *J* = 5.7 Hz, 3H), 3.88 (s, 3H), 2.28 (s, 6H), 1.25 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.2, 167.4, 166.5, 140.2, 135.9, 133.9, 133.3, 128.7, 128.3, 127.1, 124.7, 123.8, 122.9, 52.6, 40.3, 27.7, 18.6; IR (neat) 2938, 1725, 1653, 1578, 1519, 1240, 761 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₂H₂₇N₂O₄ [M+H]⁺:383.1965; Found 383.1964.



5-Chloro-*N*-(2,6-dimethylphenyl)-3-fluoro-2-pivalamidobenzamide (**4aia**)

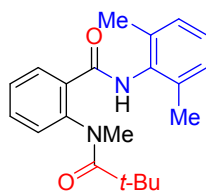
Compound **4aia** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2i** (0.3 mmol, 81.4 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aia** as a white solid (31.7 mg, 42%): m.p.: 219-220 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.79 (s, 1H), 7.65 (s, 1H), 7.45 (s, 1H), 7.28 – 7.24 (m, 1H), 7.12 (q, *J* = 6.2 Hz, 3H), 2.24 (s, 6H), 1.25 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 177.82, 165.07, 157.5 (d, *J*_{C-F} = 258.6 Hz), 135.66, 133.08, 132.4 (d, *J*_{C-F} = 2.0 Hz), 131.8 (d, *J*_{C-F} = 10.1 Hz), 128.66, 128.23, 124.7 (d, *J*_{C-F} = 14.1 Hz), 122.9 (d, *J*_{C-F} = 3.0 Hz), 119.9 (d, *J*_{C-F} = 25.3 Hz), 39.7, 27.7, 18.6; ¹⁹F NMR (376 MHz, CDCl₃) δ -110.46 to -110.54 (m, 1F); IR (neat) 2958, 2921, 2851, 1660, 1508, 1094 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₂ClFN₂NaO₂ [M+Na]⁺: 399.1246; Found 399.1244.



4aja

3-Chloro-*N*-(2,6-dimethylphenyl)-2-pivalamidobenzamide (**4aja**)

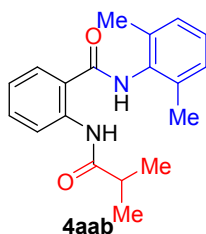
Compound **4aja** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2j** (0.3 mmol, 76.0 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1 to 2:1) afforded **4aja** as a white solid (27.4 mg, 38%): m.p.: 205-206 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.37 (s, 1H), 7.73 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.27 – 7.20 (m, 1H), 7.15 – 7.05 (m, 3H), 2.25 (s, 6H), 1.26 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 178.0, 166.1, 135.6, 134.7, 133.7, 133.5, 133.2, 132.6, 128.6, 127.8, 127.5, 126.4, 39.7, 27.6, 18.7; IR (neat) 2956, 2921, 2854, 1656, 1462, 761 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₂₄ClN₂O₂ [M+H]⁺:359.1521; Found 359.1521.



4aka

N-(2,6-Dimethylphenyl)-2-(*N*-methylpivalamido)benzamide (**4aka**)

Compound **4aka** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2k** (0.3 mmol, 69.9 mg) and carboxylic acid **3a** (0.3 mmol, 30.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1 to 2:1) afforded **4aka** as a white solid (43.9 mg, 65%): m.p.: 185-187 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.95 (s, 2H), 7.51 (td, *J* = 7.6, 1.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.11 – 7.06 (m, 3H), 3.39 (s, 3H), 2.28 (s, 6H), 1.20 (s, 9H); IR (neat) 2962, 2922, 1666, 1625, 1487, 1262, 741 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₁H₂₇N₂O₂ [M+H]⁺:339.2067; Found 339.2072.

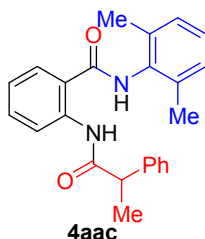


4aab

N-(2,6-Dimethylphenyl)-2-isobutyramidobenzamide (**4aab**)

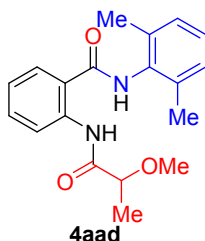
Compound **4aab** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3b** (0.3 mmol, 26.43 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aab** as a white solid (32.3 mg, 52%): m.p. 170-171 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.01 (s, 1H), 8.64 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.57 (s, 1H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.19 – 7.08 (m, 4H), 2.56 – 2.44 (m, 1H),

2.27 (s, 6H), 1.19 (d, $J = 6.9$ Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.4, 168.0, 140.5, 135.8, 133.5, 133.2, 128.7, 128.2, 126.8, 122.9, 122.1, 120.4, 37.4, 19.7, 18.6; IR (neat) 2957, 2922, 2856, 1647, 1513, 1440, 760 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 333.1573; Found 333.1570.



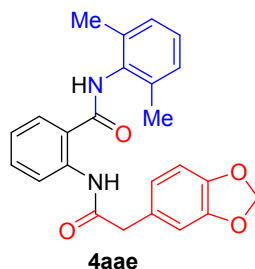
(*RS*)-*N*-(2,6-Dimethylphenyl)-2-(2-phenylpropanamido)benzamide (4aac)

Compound **4aac** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3c** (0.3 mmol, 45.1 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aac** as a colorless oil (48.6 mg, 65%): ^1H NMR (400 MHz, CDCl_3) δ 11.08 (s, 1H), 8.55 (d, $J = 8.4$ Hz, 1H), 7.82 (d, $J = 10.0$ Hz, 1H), 7.68 (d, $J = 7.7$ Hz, 1H), 7.40 (t, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 7.3$ Hz, 2H), 7.28 – 7.24 (m, 2H), 7.22 – 7.10 (m, 4H), 7.04 (t, $J = 7.5$ Hz, 1H), 3.63 (q, $J = 7.0$ Hz, 1H), 2.19 (s, 6H), 1.52 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.2, 167.9, 141.13, 140.05, 135.9, 133.5, 132.9, 128.8, 128.5, 128.0, 127.6, 127.2, 127.0, 123.0, 121.7, 120.6, 48.9, 18.5, 18.4; IR (neat) 2958, 2922, 2855, 1681, 1513, 1440, 760 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 395.1730; Found 395.1729.



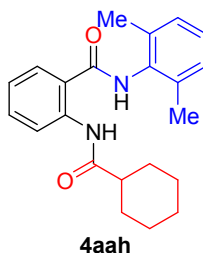
(*RS*)-*N*-(2,6-Dimethylphenyl)-2-(2-methoxypropanamido)benzamide (4aad)

Compound **4aad** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3d** (0.3 mmol, 31.2 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4aad** as a yellow solid (27.5 mg, 41%): m.p. 147-149 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 11.33 (s, 1H), 8.64 (t, $J = 9.5$ Hz, 1H), 7.72 (d, $J = 7.7$ Hz, 1H), 7.54 – 7.47 (m, 1H), 7.40 (s, 1H), 7.19 – 7.07 (m, 4H), 3.84 – 3.74 (m, 1H), 3.39 (d, $J = 7.9$ Hz, 3H), 2.28 (d, $J = 5.0$ Hz, 6H), 1.40 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.0, 167.3, 139.1, 135.9, 133.6, 132.9, 128.6, 128.0, 126.9, 123.5, 122.2, 122.1, 79.2, 58.1, 18.7, 18.6; IR (neat) 2955, 2923, 2856, 1658, 1514, 1444, 760 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{NaO}_3$ $[\text{M}+\text{Na}]^+$: 349.1523; Found 349.1524.



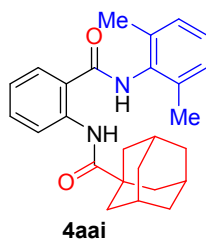
2-(2-(Benzo[*d*][1,3]dioxol-5-yl)acetamido)-*N*-(2,6-dimethylphenyl)benzamide (4aae)

Compound **4aae** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3e** (0.3 mmol, 54.1 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4aae** as a white solid (37.0 mg, 46%): m.p.: 166-168 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.97 (s, 1H), 8.61 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.20 – 7.08 (m, 4H), 6.78 (s, 1H), 6.75 – 6.67 (m, 2H), 5.82 (s, 2H), 3.54 (s, 2H), 2.23 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 170.3, 167.7, 148.2, 147.0, 140.1, 135.9, 133.4, 133.2, 128.6, 128.4, 128.1, 126.8, 123.2, 122.8, 122.0, 120.6, 109.9, 108.7, 101.2, 45.4, 18.6; IR (neat) 2955, 2920, 2853, 1678, 1504, 1449, 1160, 755 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₄H₂₃N₂O₄ [M+H]⁺: 403.1652; Found 403.1653.



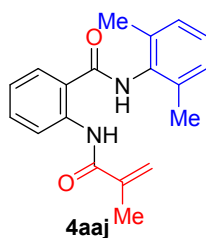
2-(Cyclohexanecarboxamido)-*N*-(2,6-dimethylphenyl)benzamide (4aah)

Compound **4aah** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3h** (0.3 mmol, 38.5 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aah** as a white solid (62.4 mg, 89%): m.p.: 173-175 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.03 (s, 1H), 8.72 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.63 (s, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.27 – 7.14 (m, 4H), 2.34 (s, 6H), 2.33 – 2.24 (m, 1H), 1.98 (d, *J* = 12.0 Hz, 2H), 1.82 (d, *J* = 12.0 Hz, 2H), 1.69 (d, *J* = 12.9 Hz, 1H), 1.54 (t, *J* = 12.0 Hz, 2H), 1.37 – 1.19 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 175.6, 168.0, 140.6, 135.8, 133.5, 133.2, 128.7, 128.2, 126.9, 122.9, 122.1, 120.4, 47.1, 29.8, 25.90, 25.87, 18.6; IR (neat) 2925, 2855, 1764, 1649, 1513, 1440, 1242, 758 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₂H₂₆N₂NaO₂ [M+Na]⁺: 373.1886; Found 373.1878.



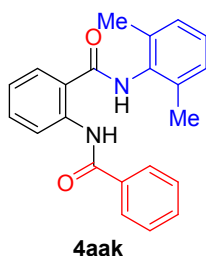
(3*r*,5*r*,7*r*)-*N*-(2-((2,6-Dimethylphenyl)carbamoyl)phenyl)adamantane-1-carboxamide (4aai)

Compound **4aai** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3i** (0.3 mmol, 54.1 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aai** as a yellow oil (79.5 mg, 99%): m.p.: 219-221 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.89 (s, 1H), 8.67 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.35 (s, 1H), 7.20 – 7.09 (m, 4H), 2.30 (s, 6H), 2.04 (s, 3H), 1.95 (s, 6H), 1.71 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 177.7, 168.0, 140.3, 136.0, 133.5, 133.0, 128.7, 128.2, 126.8, 122.9, 122.4, 121.4, 42.3, 39.3, 36.7, 28.4, 18.7; IR (neat) 2913, 2853, 1650, 1513, 1440, 1372, 759 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₆H₃₁N₂O₂ [M+H]⁺: 403.2380; Found 403.2379.



***N*-(2,6-Dimethylphenyl)-2-methacrylamidobenzamide (4aaj)**

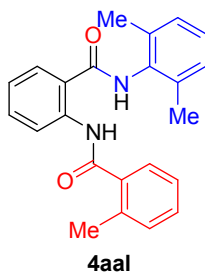
Compound **4aaj** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3j** (0.3 mmol, 25.8 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aaj** as a white solid (45.7 mg, 74%): m.p.: 173-175 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.47 (s, 1H), 8.72 (d, *J* = 8.4 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.59 – 7.40 (m, 2H), 7.22 – 7.05 (m, 4H), 5.91 (s, 1H), 5.43 (s, 1H), 2.27 (s, 6H), 2.02 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.9, 167.1, 140.5, 140.4, 135.8, 133.3, 128.7, 128.2, 126.9, 123.1, 122.0, 121.5, 120.5, 18.8, 18.7. (one carbon missing due to overlap); IR (neat) 2956, 2924, 2856, 1675, 1594, 1515, 1441 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₁₉H₂₀N₂NaO₂ [M+Na]⁺: 331.1417; Found 331.1416.



2-Benzamido-*N*-(2,6-dimethylphenyl)benzamide (4aak)

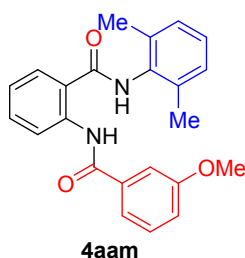
Compound **4aak** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2

mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3k** (0.3 mmol, 36.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aak** as a light white solid (36.6 mg, 53%): m.p.: 206-208 °C; ¹H NMR (400 MHz, CDCl₃) δ 12.00 (s, 1H), 8.86 (d, *J* = 8.4 Hz, 1H), 8.05 – 7.91 (m, 2H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 2H), 7.52 – 7.38 (m, 3H), 7.22 – 7.10 (m, 4H), 2.28 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 165.9, 140.6, 135.9, 134.7, 133.5, 133.4, 132.1, 129.0, 128.7, 128.2, 127.6, 127.0, 123.2, 122.1, 120.4, 18.7; IR (neat) 3271, 2922, 1652, 1511, 1435, 755 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₂H₂₀N₂NaO₂ [M+Na]⁺: 367.1417; Found 367.1415.



***N*-(2,6-Dimethylphenyl)-2-(2-methylbenzamido)benzamide (4aal)**

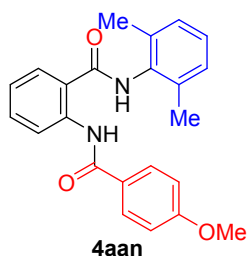
Compound **4aal** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3l** (0.3 mmol, 40.9 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aal** as a light white solid (47.8 mg, 64%): m.p.: 187-189 °C; ¹H NMR (400 MHz, DMSO) δ 11.55 (s, 1H), 10.08 (s, 1H), 8.61 (d, *J* = 8.2 Hz, 1H), 8.06 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.64 (td, *J* = 7.9, 1.2 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.41 – 7.35 (m, 1H), 7.33 – 7.26 (m, 3H), 7.15 – 7.09 (m, 3H) 2.43 (s, 3H), 2.19 (s, 6H); ¹³C NMR (101 MHz, DMSO) δ 167.19, 167.15, 139.2, 136.3, 135.7, 135.5, 134.5, 132.3, 131.1, 130.2, 128.4, 127.8, 126.9, 126.6, 126.0, 123.2, 121.0, 120.7, 19.49, 17.85; IR (neat) 3056, 2983, 1675, 1126, 756 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₃H₂₂N₂O₃ [M+H]⁺: 359.1754; Found 359.1749.



***N*-(2,6-Dimethylphenyl)-2-(3-methoxybenzamido)benzamide (4aam)**

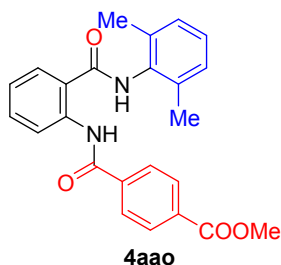
Compound **4aam** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3m** (0.3 mmol, 45.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1 to 3:1) afforded **4aam** as a white solid (48.7 mg, 65%): m.p.: 161-162 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.95 (s, 1H), 8.83 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.19 – 7.10 (m, 4H), 7.02 (dd, *J* = 8.2, 2.0 Hz, 1H), 3.81 (s, 3H), 2.27 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 165.8, 160.2, 140.6, 136.4, 135.9, 133.5, 133.4, 130.0, 128.7, 128.2, 127.0, 123.3,

122.2, 120.6, 119.4, 118.6, 112.8, 55.60, 18.68; IR (neat) 2956, 2922, 2853, 1649, 1514, 1444, 1278, 755 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_2\text{NaO}_3$ $[\text{M}+\text{Na}]^+$: 397.1523; Found 379.1514.



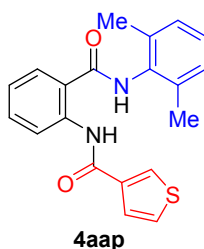
***N*-(2,6-Dimethylphenyl)-2-(4-methoxybenzamido)benzamide (4aan)**

Compound **4aan** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3n** (0.3 mmol, 45.6 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1 to 3:1) afforded **4aan** as a white solid (60.6 mg, 81%); m.p.: 209-210 °C; ^1H NMR (400 MHz, CDCl_3) δ 11.90 (s, 1H), 8.85 (d, $J = 7.8$ Hz, 1H), 8.01 – 7.89 (m, 2H), 7.76 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.65 – 7.53 (m, 1H), 7.50 (s, 1H), 7.21 – 7.09 (m, 4H), 6.97 – 6.81 (m, 2H), 3.82 (s, 3H), 2.28 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 168.2, 165.5, 162.7, 140.7, 135.9, 133.5, 133.3, 129.5, 128.6, 128.1, 127.1, 127.0, 122.9, 121.9, 120.2, 114.1, 55.6, 18.7; IR (neat) 2956, 2922, 2854, 1648, 1509, 1411, 761 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_2\text{NaO}_3$ $[\text{M}+\text{Na}]^+$: 397.1523; Found 397.1517.



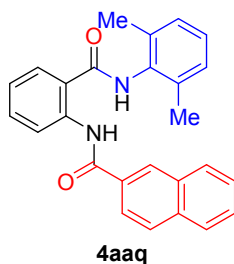
Methyl 4-((2-((2,6-dimethylphenyl)carbamoyl)phenyl)carbamoyl)benzoate (4aao)

Compound **4aao** was prepared following the general procedure using isocyanide **1a** (0.3 mmol, 39.4 mg), aniline **2a** (0.45 mmol, 98.6 mg) and carboxylic acid **3o** (0.3 mmol, 81.1 mg). Purification on a Biotage prep-HPLC with UV detector and Biotage[®] Sfar C-18 D-Duo 100Å, 30 μm (CV 17 mL, Capacity 100-1000 mg) to afforded **4aap** as a white solid (33.5 mg, 28%); m.p.: 250-251 °C; ^1H NMR (400 MHz, CDCl_3) δ 12.15 (s, 1H), 8.87 (d, $J = 8.4$ Hz, 1H), 8.06 (dd, $J = 22.8, 8.4$ Hz, 4H), 7.79 (d, $J = 7.8$ Hz, 1H), 7.60 (t, $J = 7.9$ Hz, 1H), 7.55 (s, 1H), 7.23 – 7.09 (m, 4H), 3.91 (s, 3H), 2.28 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 168.1, 166.6, 164.9, 140.6, 138.7, 135.9, 133.6, 133.3, 133.2, 130.2, 128.8, 128.3, 127.7, 127.0, 123.6, 122.2, 120.4, 52.6, 18.7; IR (neat) 2953, 2923, 2851, 1726, 1649, 1440, 1281, 757 cm^{-1} ; HRMS(ESI) m/z : Calcd for $\text{C}_{24}\text{H}_{23}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 403.1652; Found 403.1651.



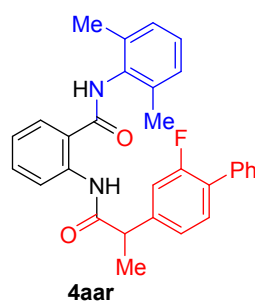
***N*-(2-((2,6-Dimethylphenyl)carbamoyl)phenyl)thiophene-3-carboxamide (4aap)**

Compound **4aap** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3p** (0.3 mmol, 38.4 mg). Purification by flash column chromatography (silica gel, PE/EA = 10:1) afforded **4aap** as a yellow solid (23.1 mg, 33%): m.p.: 235-237 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.93 (s, 1H), 8.84 (d, *J* = 8.4 Hz, 1H), 8.04 (s, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 6.0 Hz, 2H), 7.51 (s, 1H), 7.31 – 7.27 (m, 1H), 7.21 – 7.11 (m, 4H), 2.29 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 161.5, 140.8, 138.4, 135.9, 133.51, 133.46, 129.7, 128.7, 128.2, 127.0, 126.8, 126.7, 123.1, 121.9, 119.9, 18.7; IR (neat) 2957, 2921, 2852, 1675, 1511, 1443, 760, cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₀H₁₈N₂NaO₂S [M+Na]⁺: 373.0981; Found 373.0977.



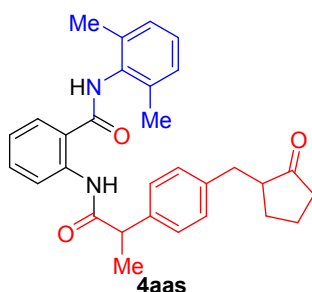
***N*-(2-((2,6-Dimethylphenyl)carbamoyl)phenyl)-2-naphthamide (4aaq)**

Compound **4aaq** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3q** (0.3 mmol, 51.7 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aaq** as a white solid (42.9 mg, 54%): m.p.: 195-197 °C; ¹H NMR (400 MHz, CDCl₃) δ 12.09 (s, 1H), 8.91 (d, *J* = 8.4 Hz, 1H), 8.52 (s, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.86 (dd, *J* = 15.5, 8.3 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.57 – 7.47 (m, 3H), 7.23 – 7.11 (m, 4H), 2.30 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 166.0, 140.7, 135.9, 135.2, 133.5, 133.4, 133.0, 132.1, 129.7, 128.9, 128.7, 128.2, 128.0, 127.9, 126.9, 126.8, 123.9, 123.3, 122.4, 120.7, 18.7 (one carbon missing due to overlap); IR (neat) 2955, 2922, 2856, 1661, 1511, 1438, 1318, 763 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₂₆H₂₃N₂O₂ [M+H]⁺: 395.1754; Found 395.1755.



(*RS*)-*N*-(2,6-Dimethylphenyl)-2-(2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanamido)benzamide (4aar)

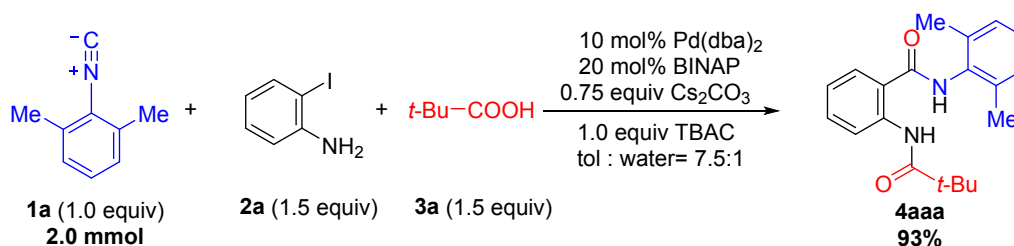
Compound **4aar** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3r** (0.3 mmol, 73.3 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1) afforded **4aar** as a white solid (53.7 mg, 58%): m.p.: 127-128 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.16 (s, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.53 – 7.43 (m, 4H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.22 – 7.08 (m, 6H), 3.70 (q, *J* = 7.1 Hz, 1H), 2.21 (s, 6H), 1.58 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 172.7, 167.8, 160.0 (d, *J*_{C-F} = 249.5 Hz), 142.6 (d, *J*_{C-F} = 7.1 Hz), 140.2, 135.9, 133.4, 133.3, 131.14, 131.11, 129.18, 129.16, 128.7, 128.6, 128.2, 128.1 (d, *J*_{C-F} = 14.1 Hz), 127.8, 126.8, 123.8 (d, *J*_{C-F} = 3.0 Hz), 123.2, 122.0, 120.5, 115.4 (d, *J*_{C-F} = 23.2 Hz), 48.5, 18.6, 18.4; ¹⁹F NMR (376 MHz, CDCl₃) δ -117.25 to -117.46 (m, 1F); IR (neat) 3956, 2922, 2854, 1665, 1513, 1441, 763 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₃₀H₂₈FN₂O₂ [M+H]⁺: 467.2129; Found 467.2130.



***N*-(2,6-Dimethylphenyl)-2-(2-(4-((2-oxocyclopentyl)methyl)phenyl)propanamido)benzamide (4aas)**

Compound **4aas** was prepared following the general procedure using isocyanide **1a** (0.2 mmol, 26.2 mg), aniline **2a** (0.3 mmol, 65.7 mg) and carboxylic acid **3s** (0.3 mmol, 73.9 mg). Purification by flash column chromatography (silica gel, PE/EA = 5:1 to 3:1) afforded **4aas** as a colorless oil (59.9 mg, 64%): ¹H NMR (400 MHz, CDCl₃) δ 10.99 (s, 1H), 8.59 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 10.9 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.20 – 7.07 (m, 4H), 7.05 (d, *J* = 7.8 Hz, 2H), 3.63 (q, *J* = 7.0 Hz, 1H), 3.06 (dd, *J* = 13.9, 3.7 Hz, 1H), 2.43 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.33 – 2.23 (m, 2H), 2.21 (s, 6H), 2.12 – 1.97 (m, 2H), 1.95 – 1.84 (m, 1H), 1.68 (m, 1H), 1.52 (d, *J* = 7.0 Hz, 3H), 1.50 – 1.39 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 220.4, 173.4, 167.8, 140.2, 139.1, 139.0, 135.9, 133.5, 133.0, 129.4, 128.6, 128.1, 127.8, 126.9, 123.0, 121.9, 120.7, 51.2, 48.6, 38.3, 35.4, 29.4, 20.7, 18.6, 18.5; IR (neat) 2957, 2923, 2858, 1735, 1512, 1440, 761 cm⁻¹; HRMS(ESI) *m/z*: Calcd for C₃₀H₃₂N₂NaO₃ [M+Na]⁺: 491.2305; Found 491.2300.

3. Gram Scale Preparation of 4aaa



Pivalic acid **3a** (306.4 mg, 3.0 mmol, 1.5 equiv.) and Cs₂CO₃ (488.7 mg, 1.5 mmol, 0.75 equiv.) were added to a solution of TBAC (555.8 g, 2.0 mmol, 1.0 equiv.) in water (4.0 mL). The resulting mixture was stirred at 80 °C for 0.5 h, then cooled down to room temperature (Solution A).

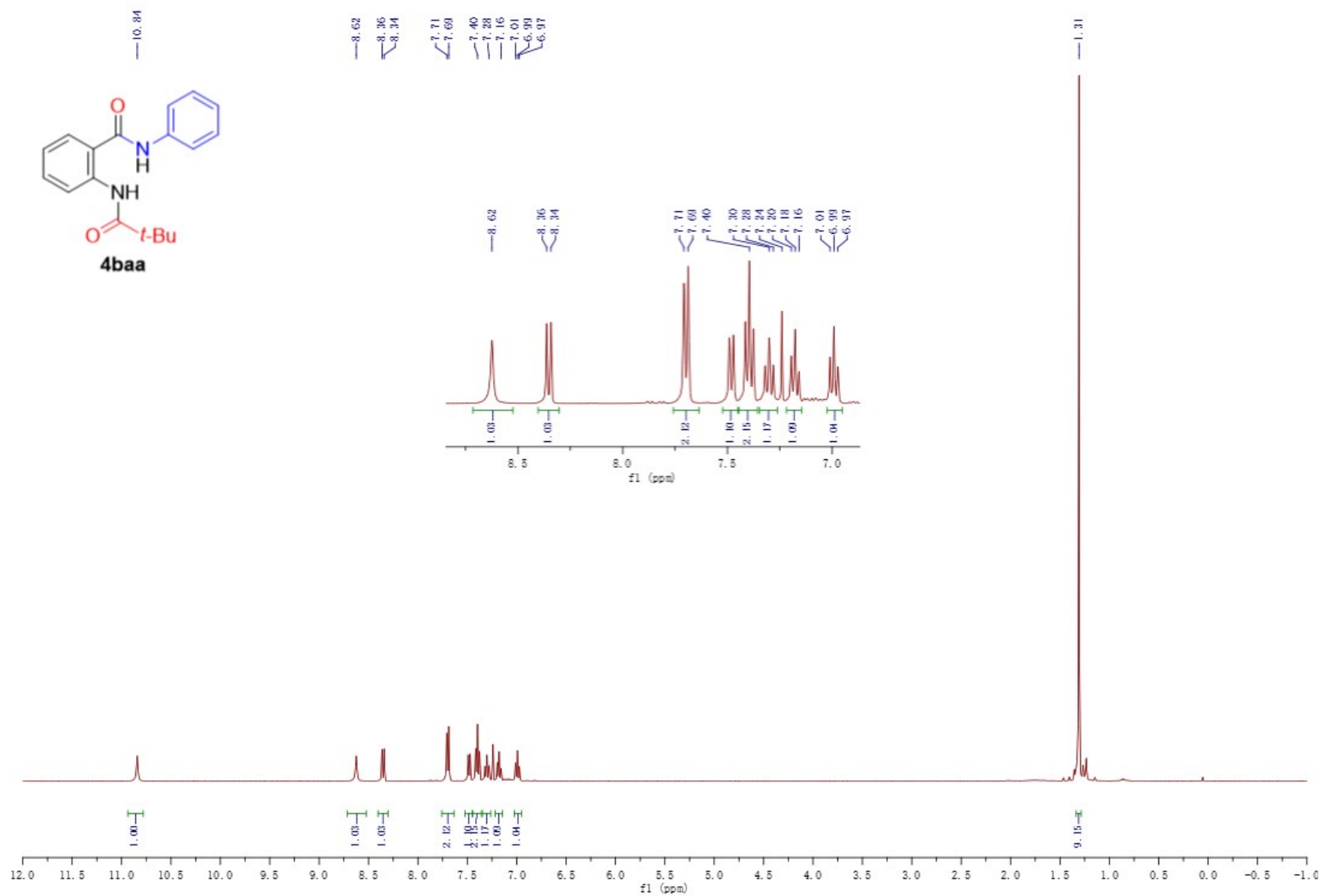
Under Ar atmosphere, to a 50 mL round flask were added Pd(dba)₂ (115.0 mg, 0.2 mmol, 10mol%) and BINAP (249.1 mg, 0.6 mmol, 20mol%) and toluene (10.0 mL). After stirring for 15 min at RT, 2-iodoaniline **2a** (657.1 mg, 3.0 mmol, 1.5 equiv.) was added followed by solution A. The resulting mixture was heated at 100 °C with stirring for 0.5 h by using an oil bath before a solution of 2-isocyanato-1,3-dimethylbenzene **1a** (262.4 mg, 2.0 mmol, 1.0 equiv.) in toluene (20.0 mL) was added over 2 hours by using a syringe pump. The reaction mixture was further stirred for 0.5 h at 100 °C.

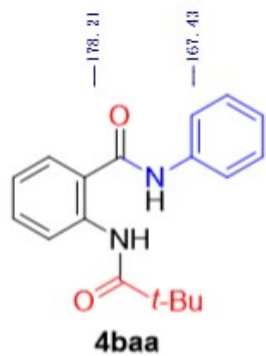
The completed reaction was cooled down to RT, quenched with sat. NaCl (50 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were dried (anhydrous MgSO₄), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 15:1, v/v) to afford **4aaa** (586.8 mg, 90%).

4. References

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5. ^1H , ^{13}C and ^{19}F NMR Spectra

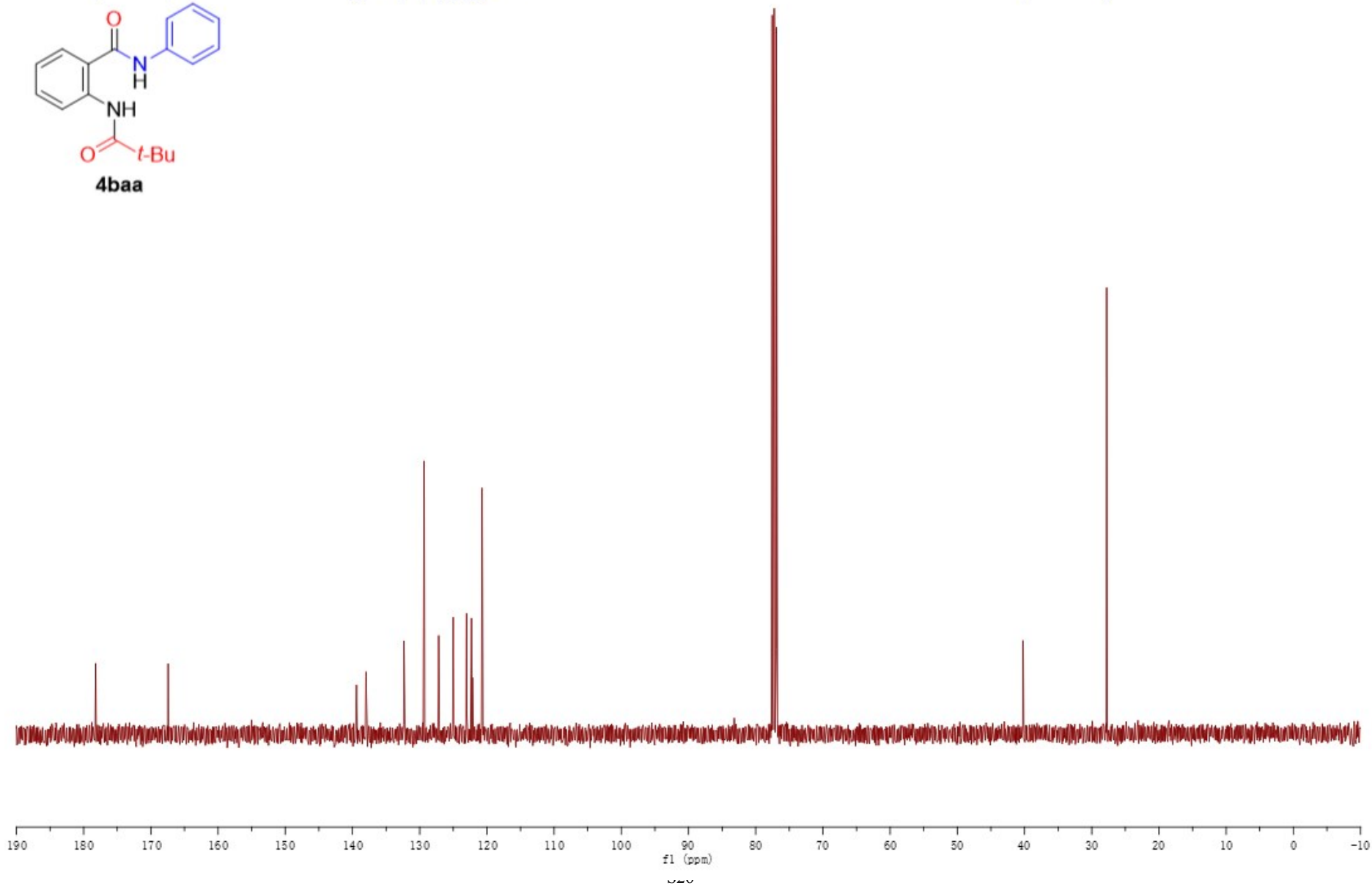


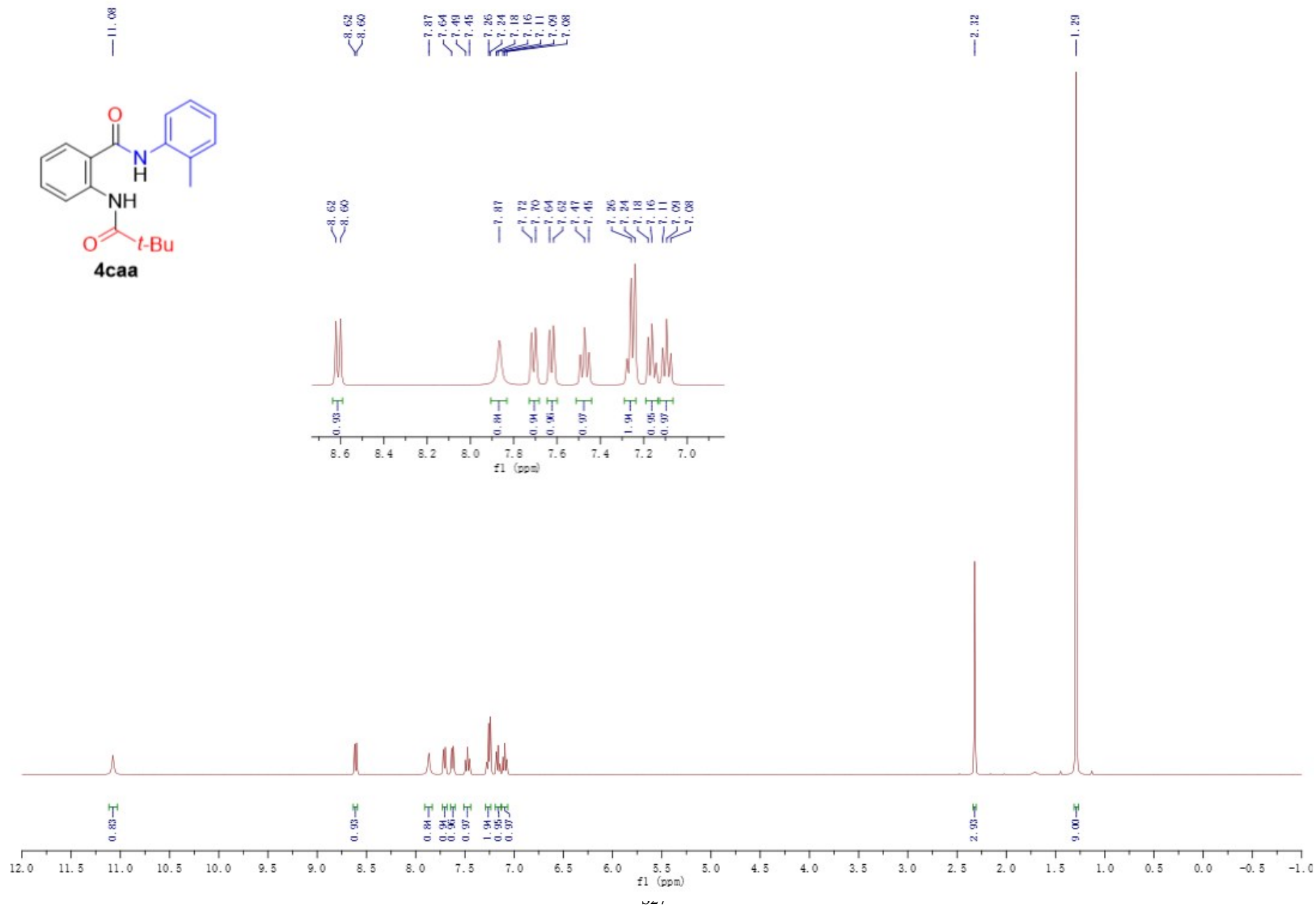
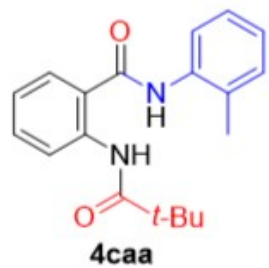


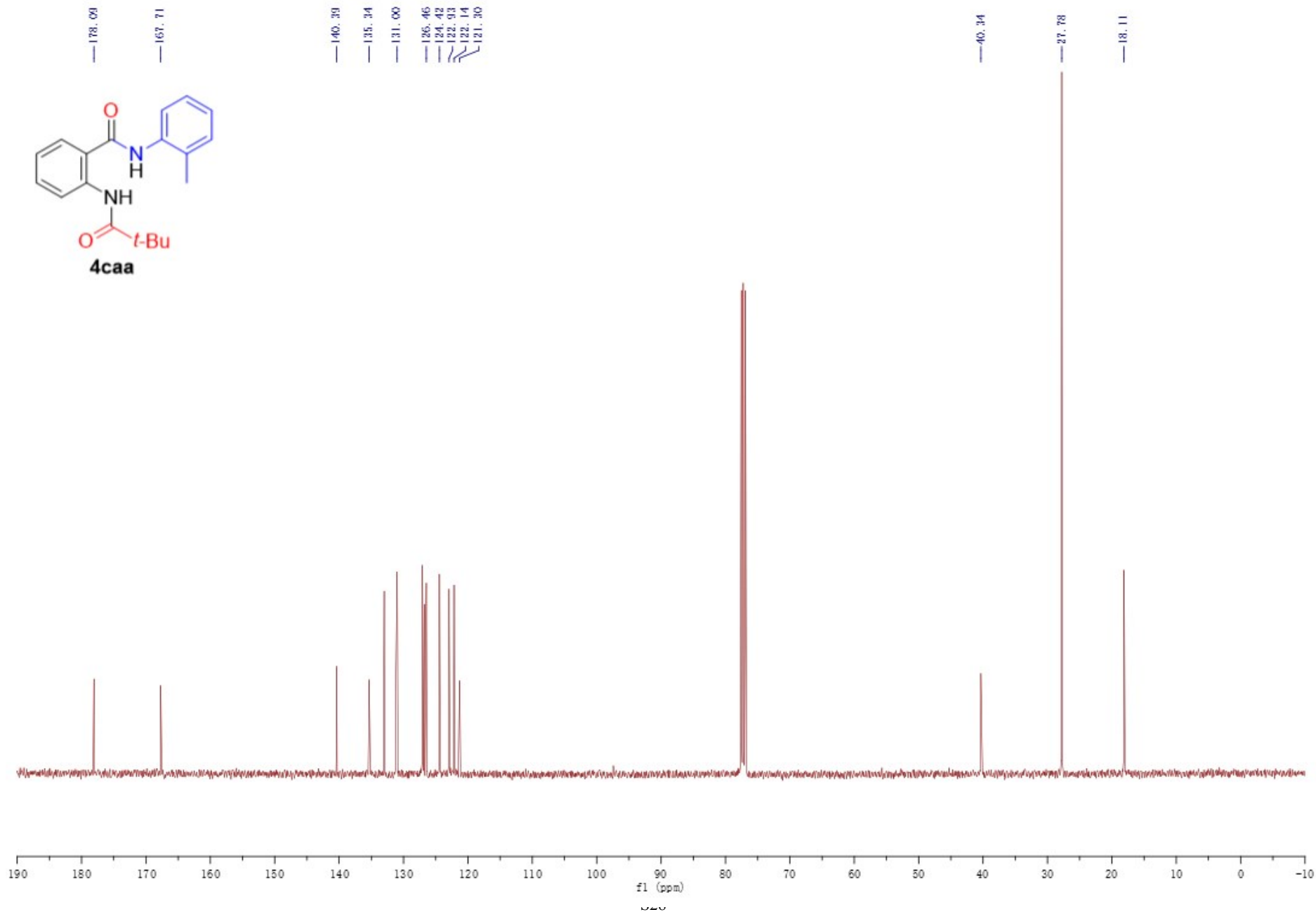
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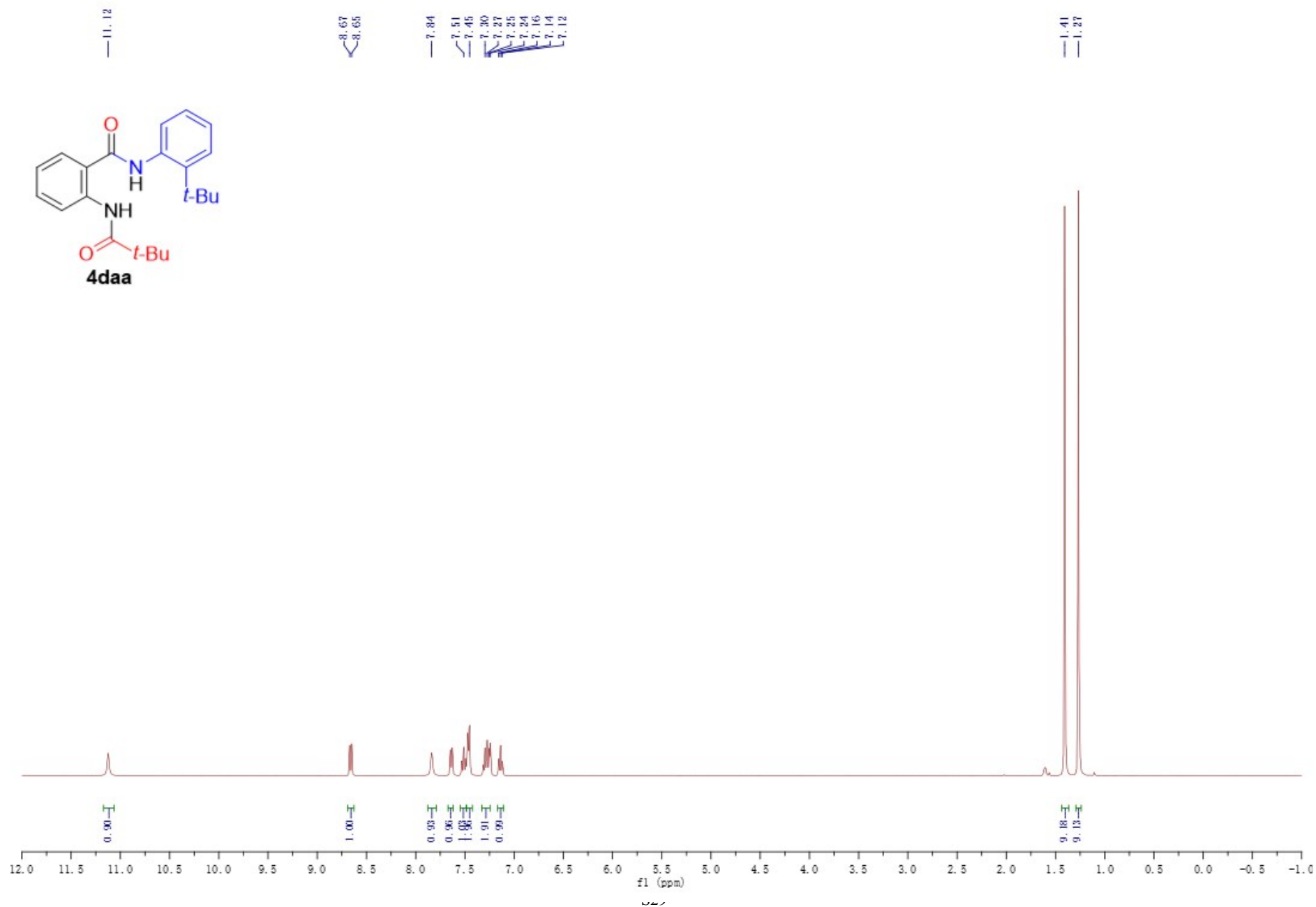
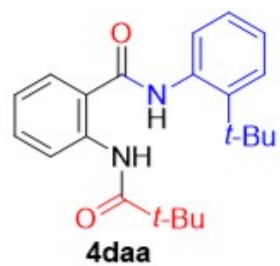
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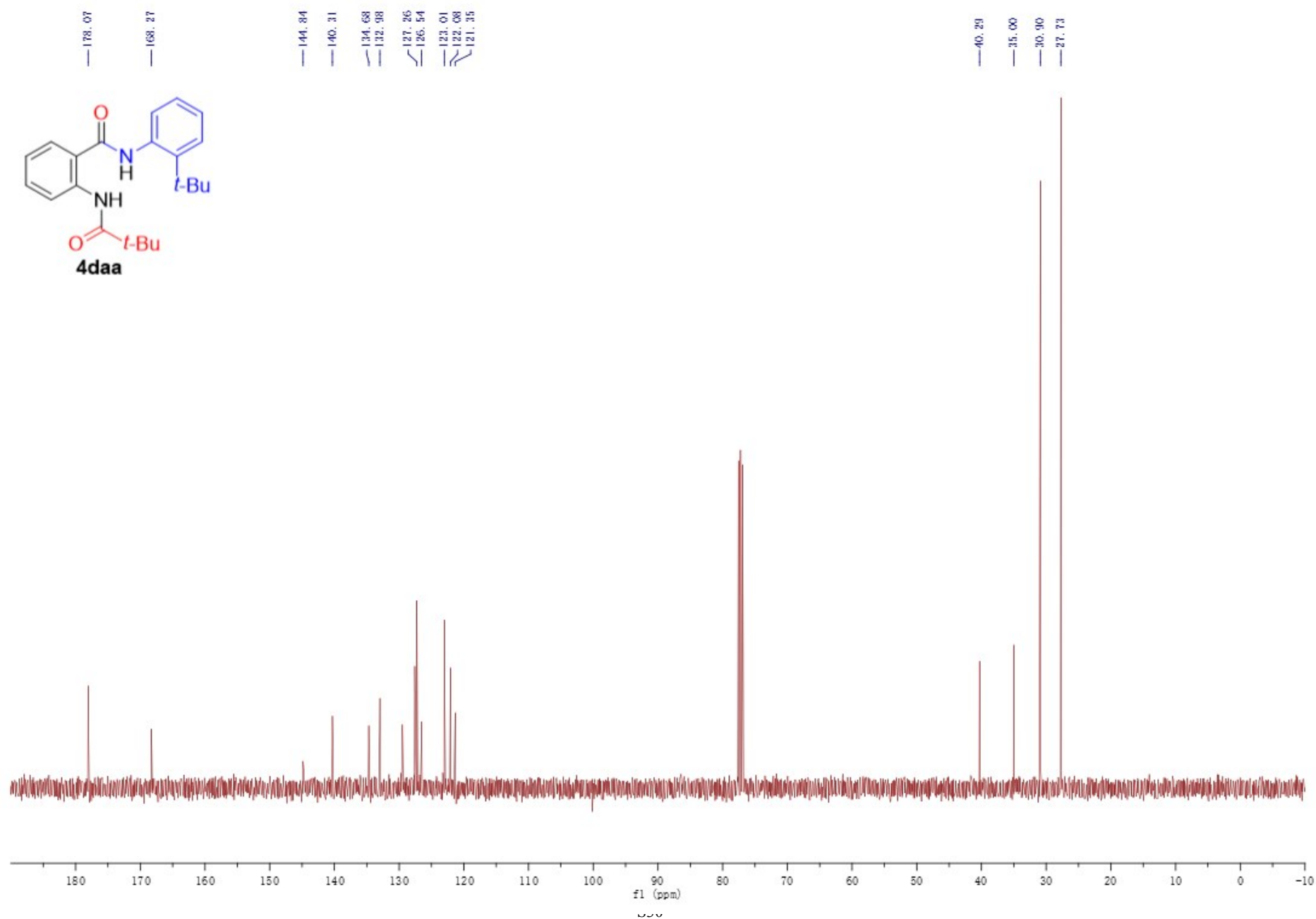
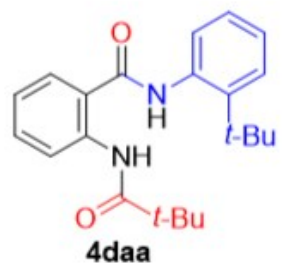
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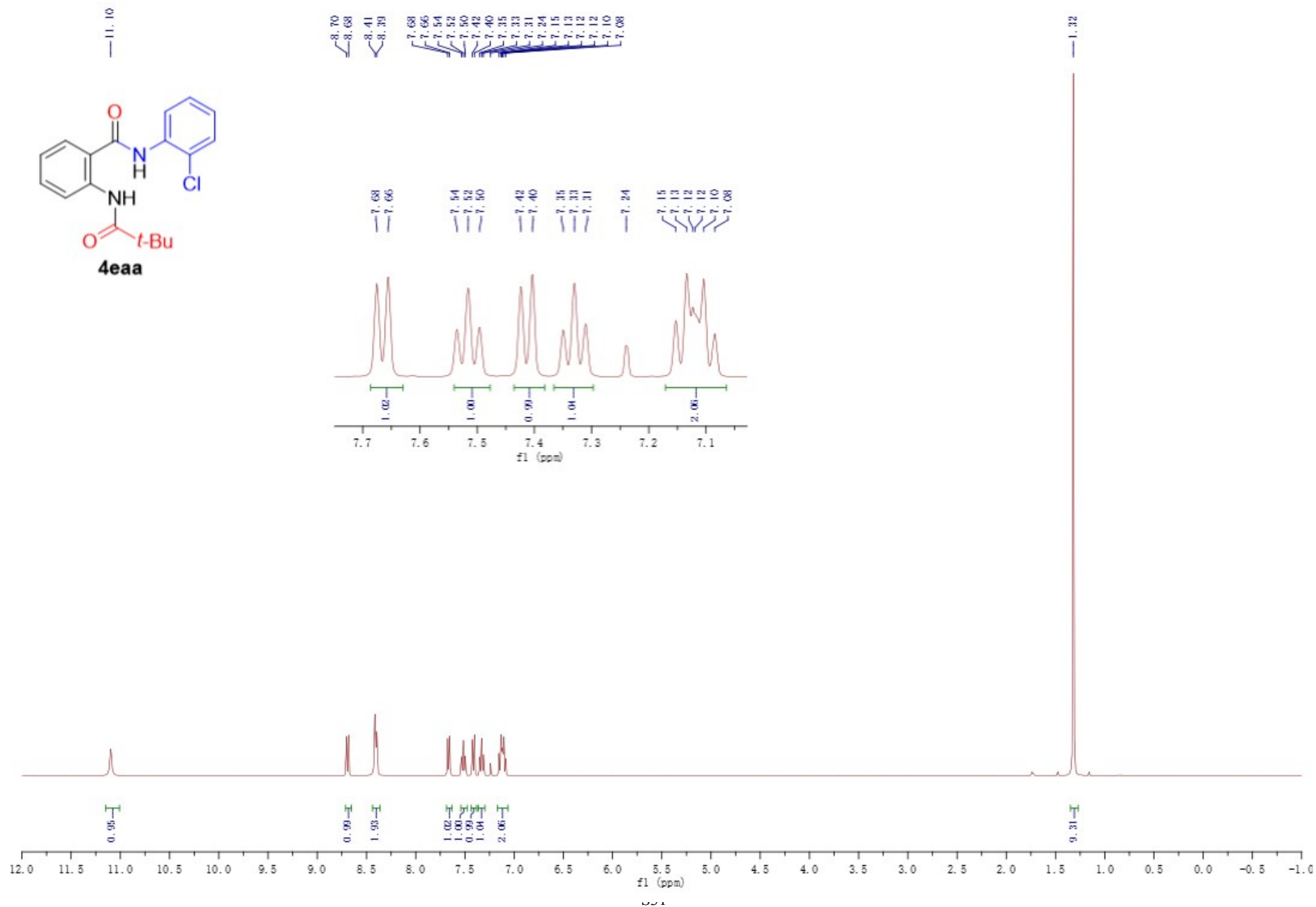
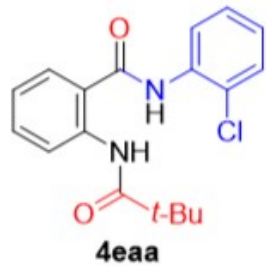


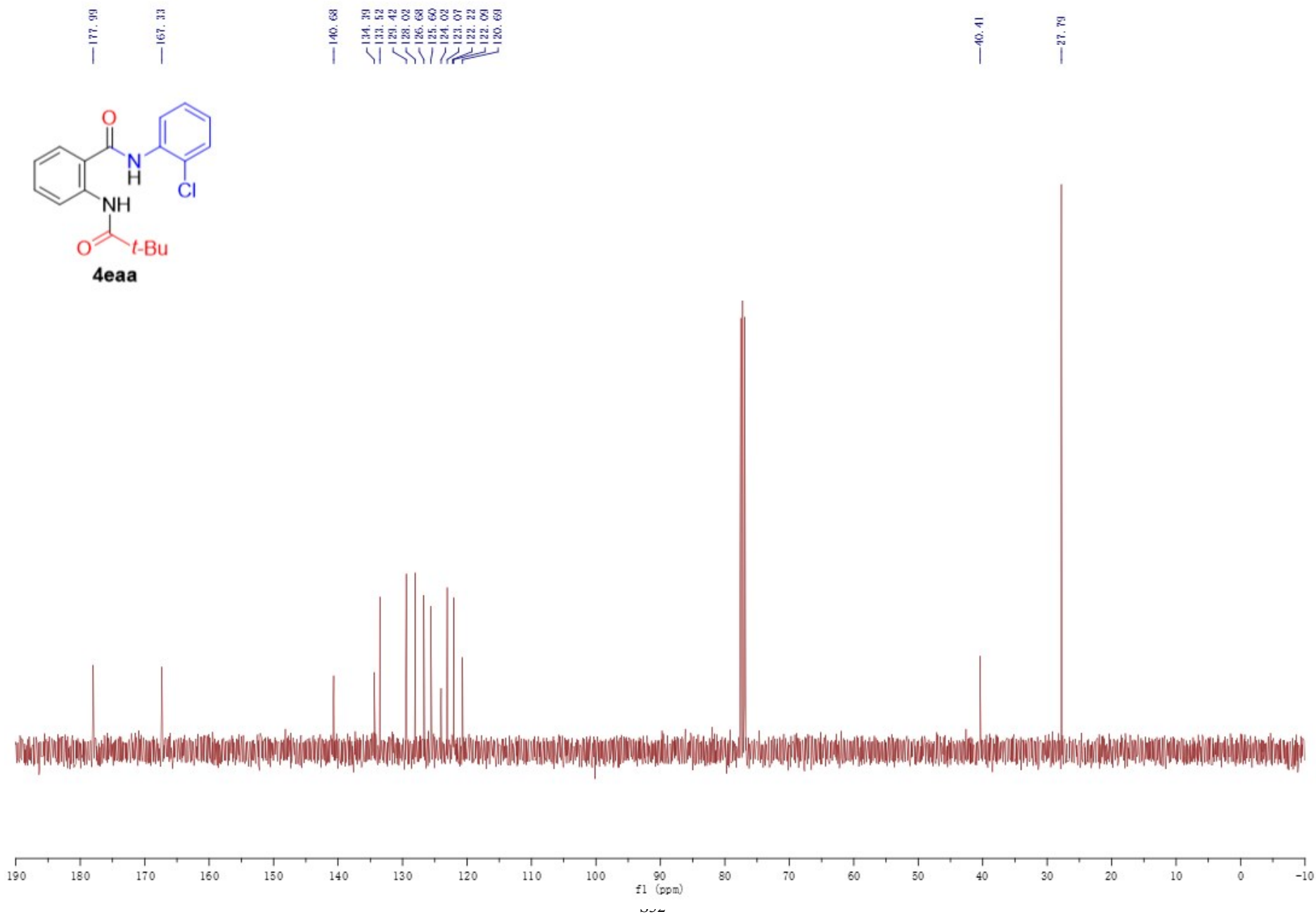


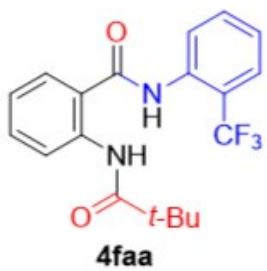






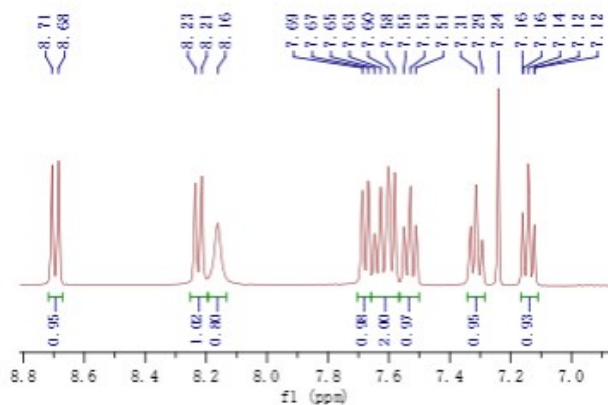




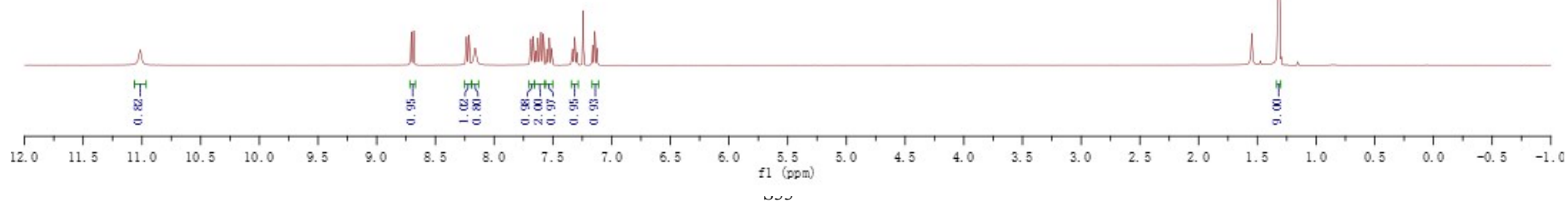


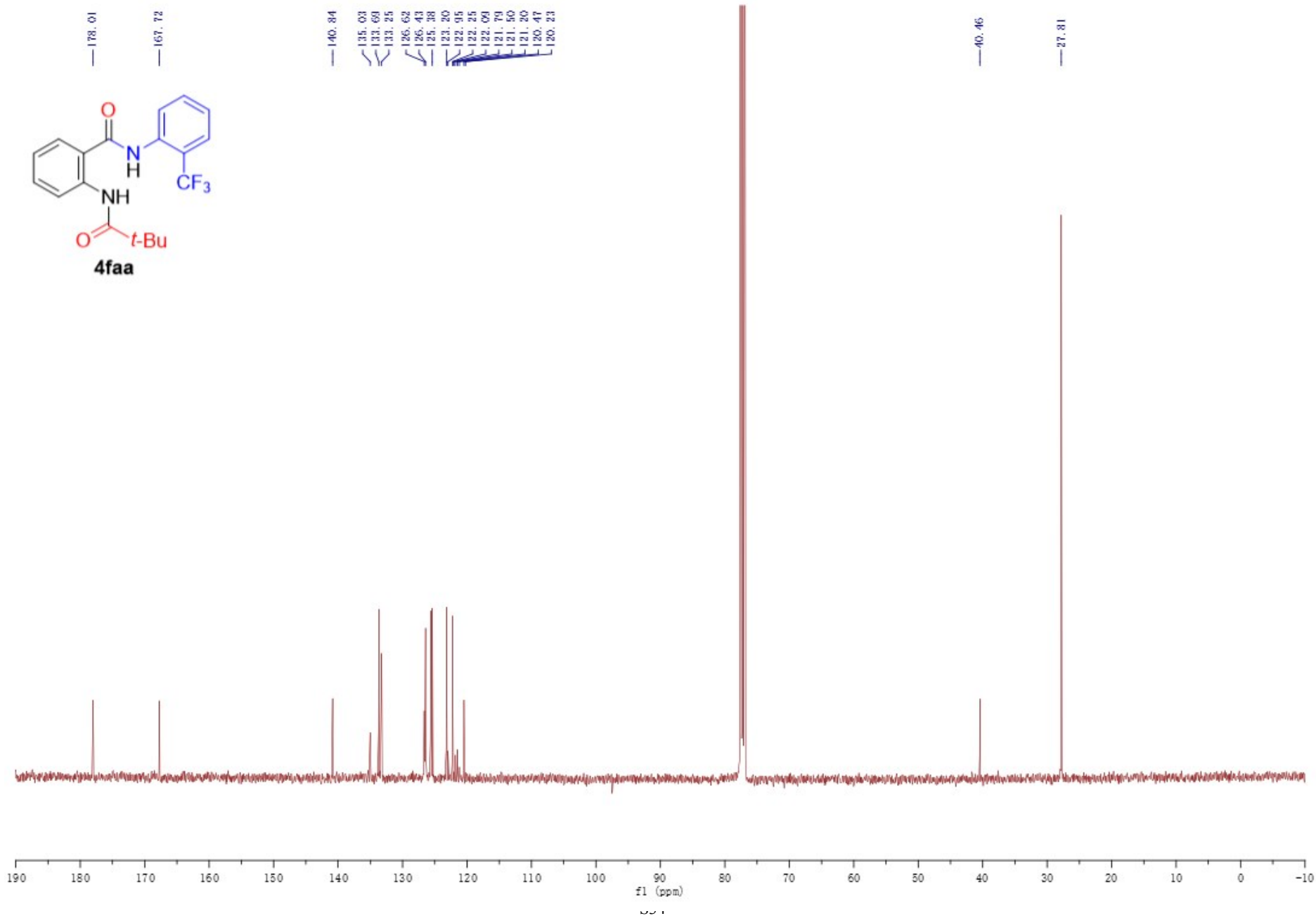
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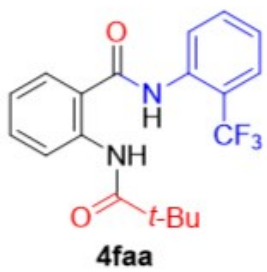
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 7.12



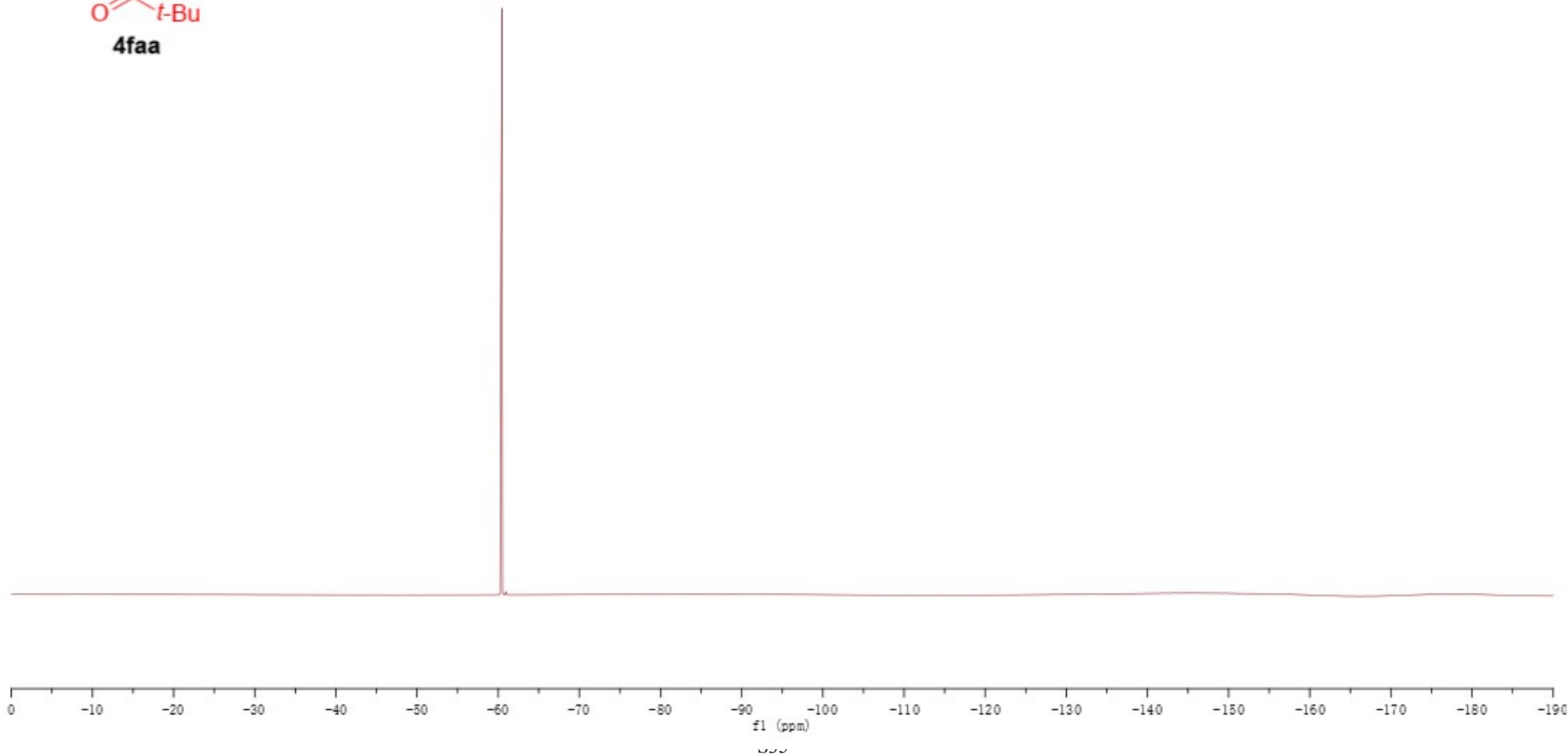
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— 1.32

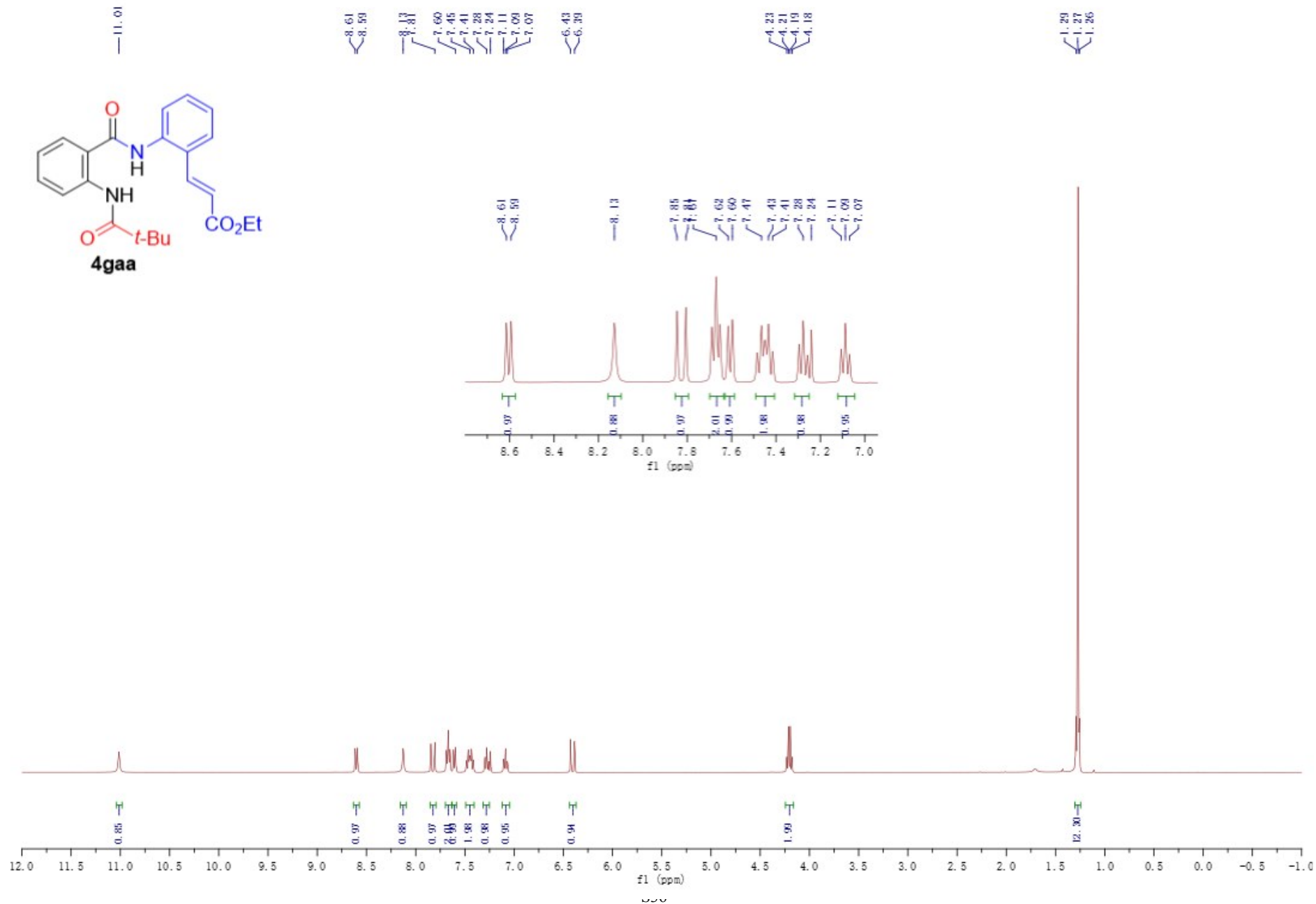
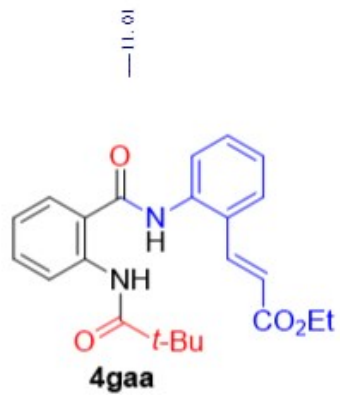


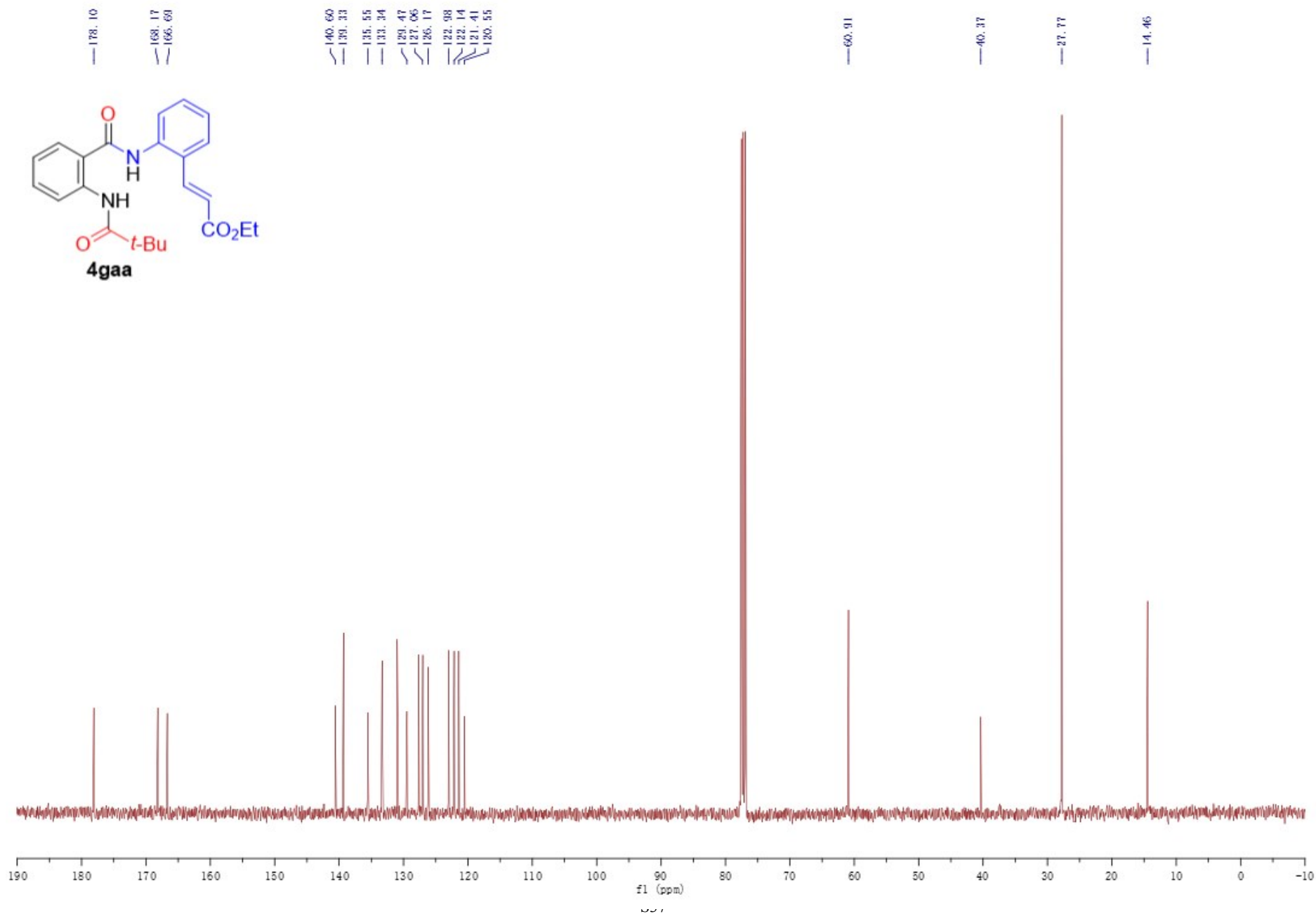
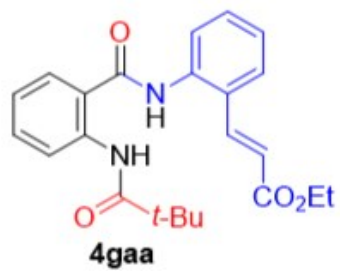


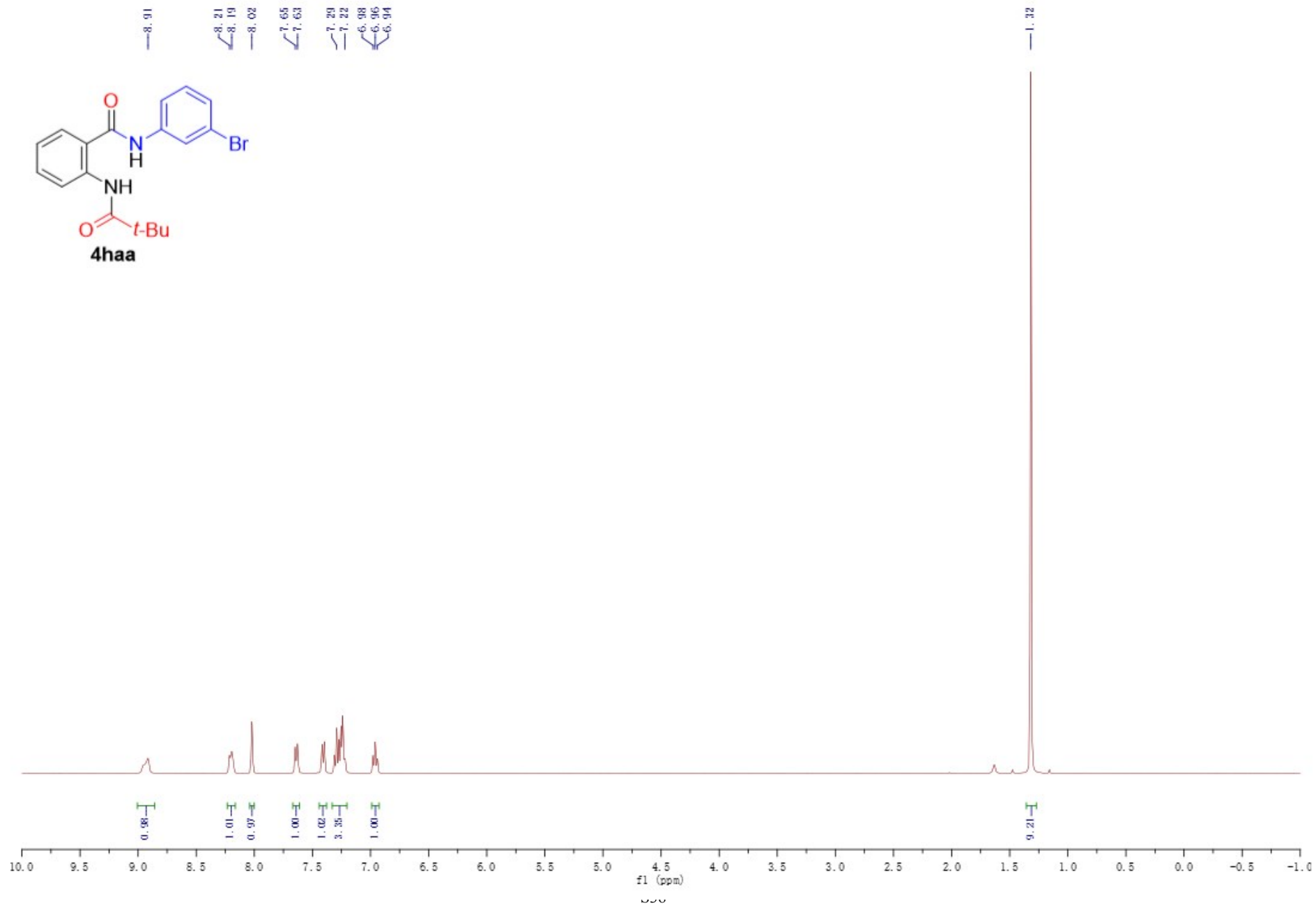
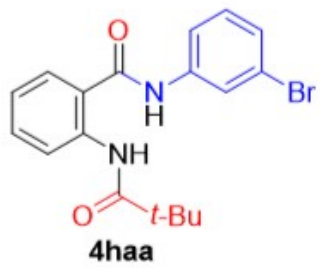


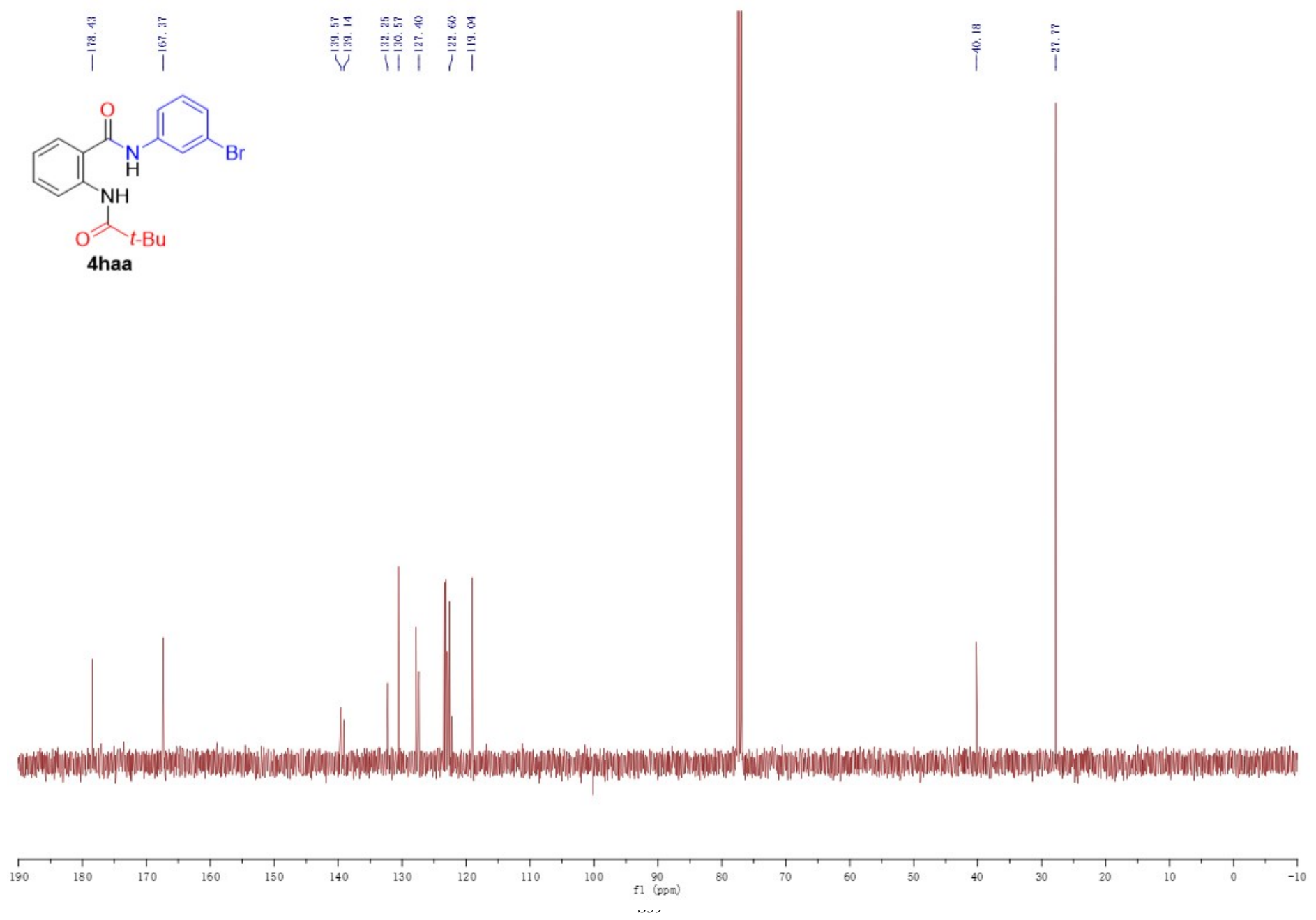
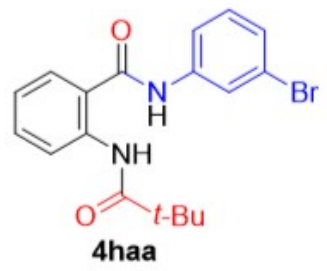
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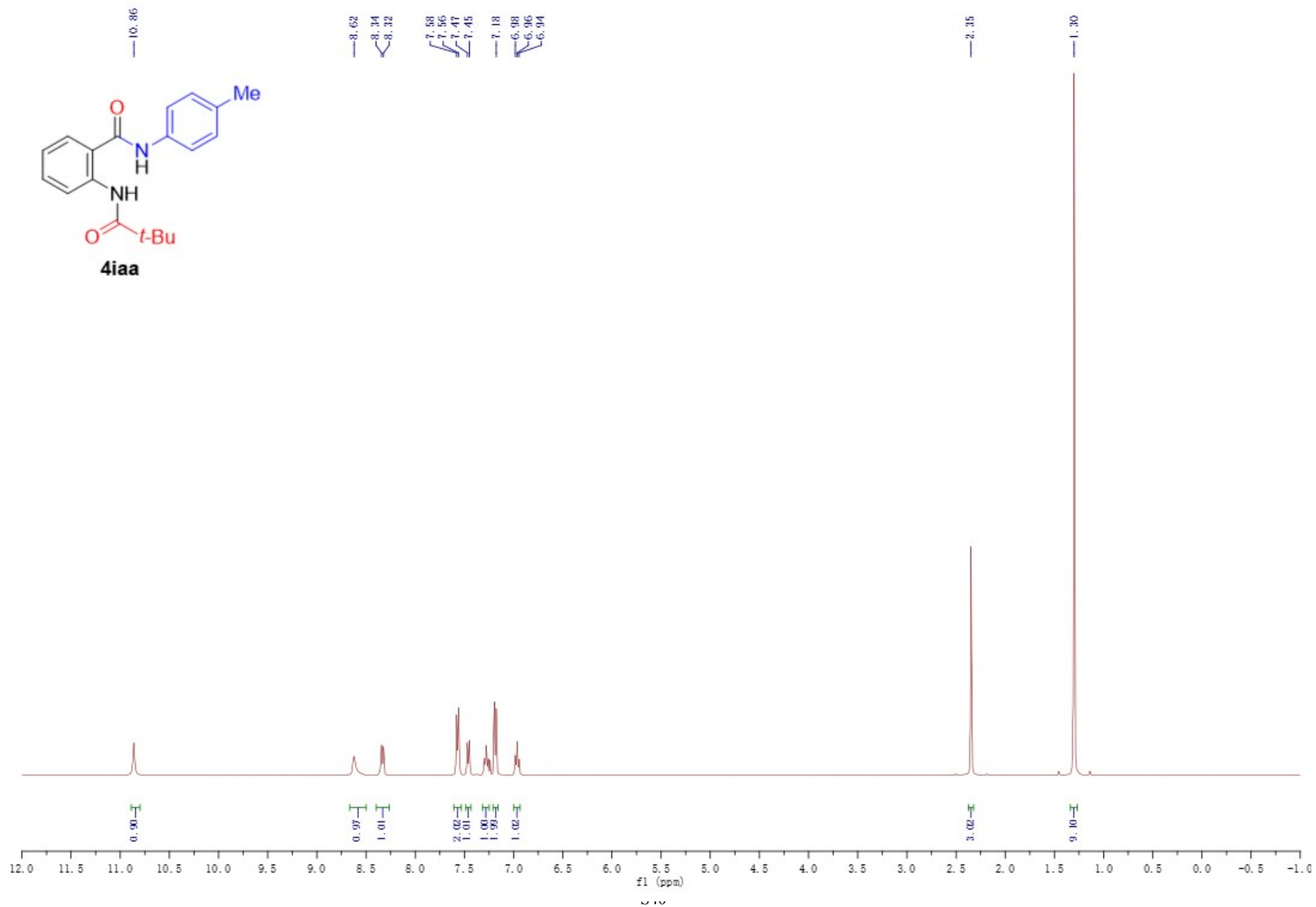
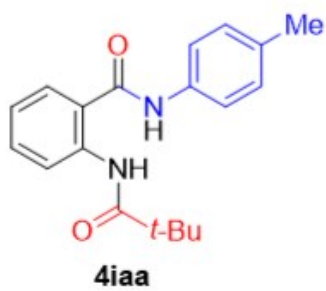


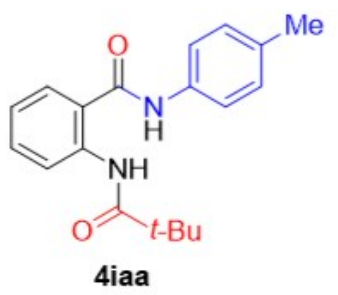






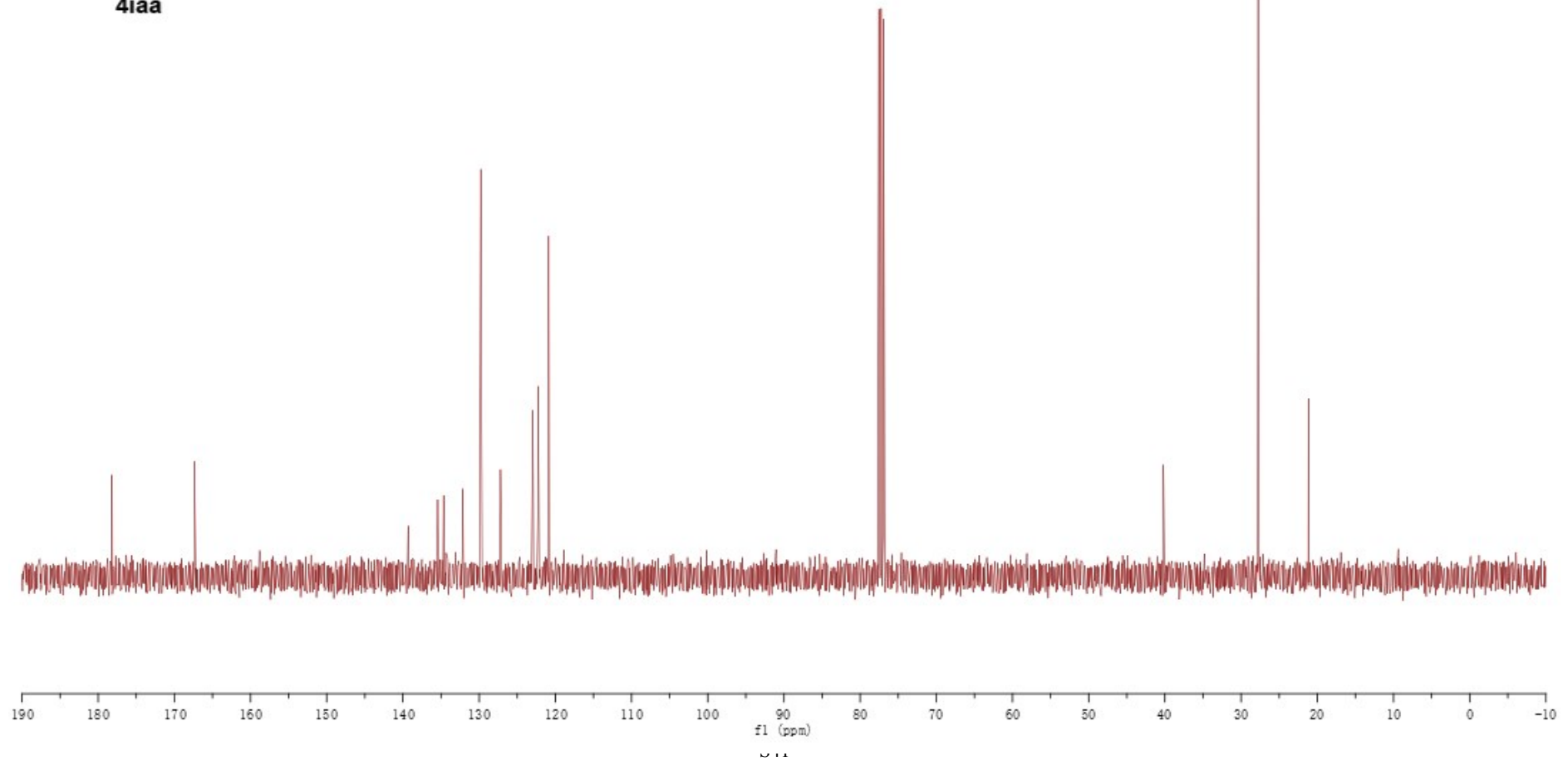


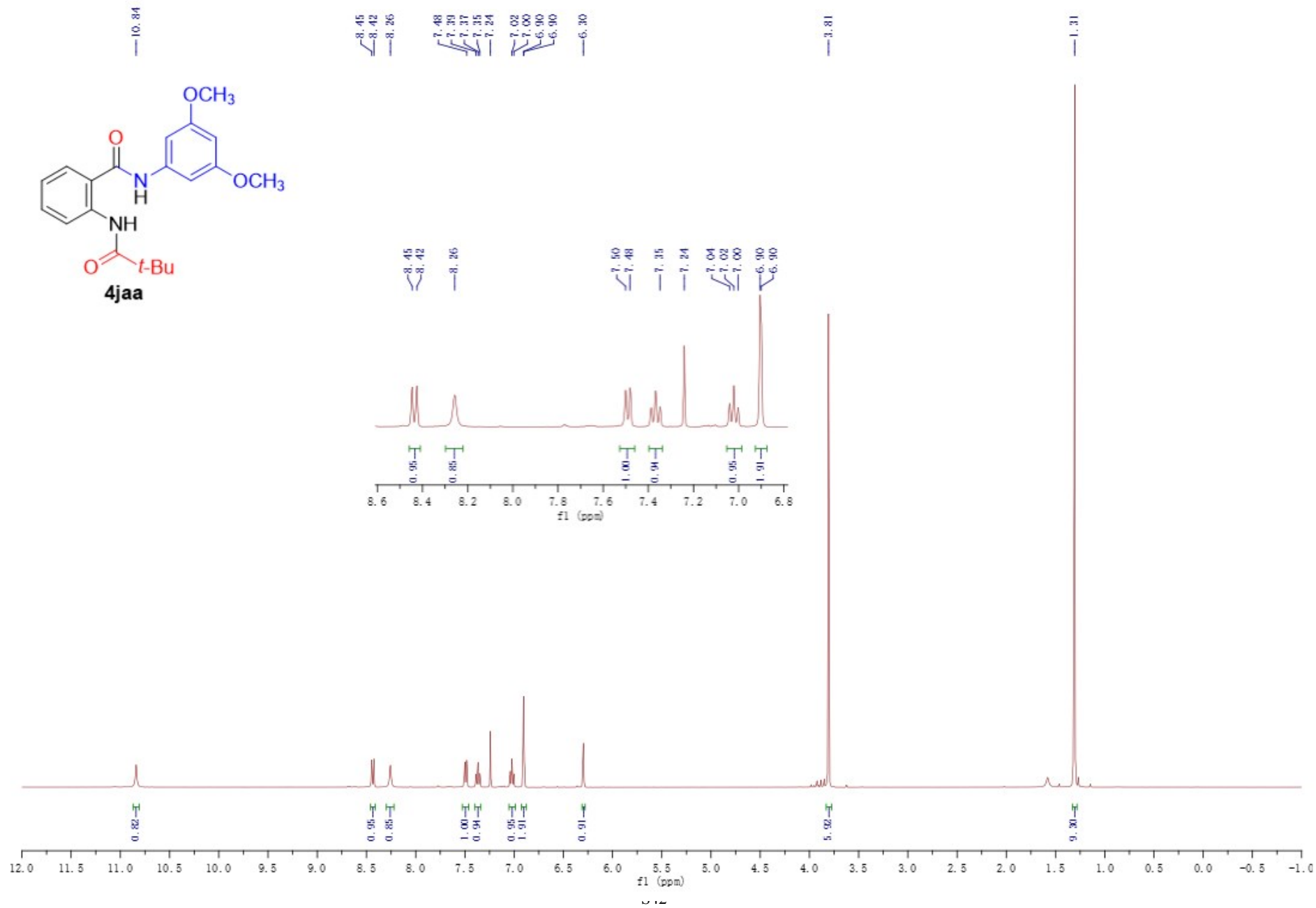
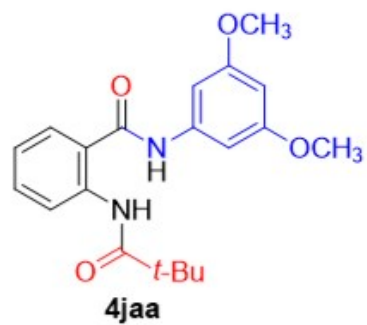


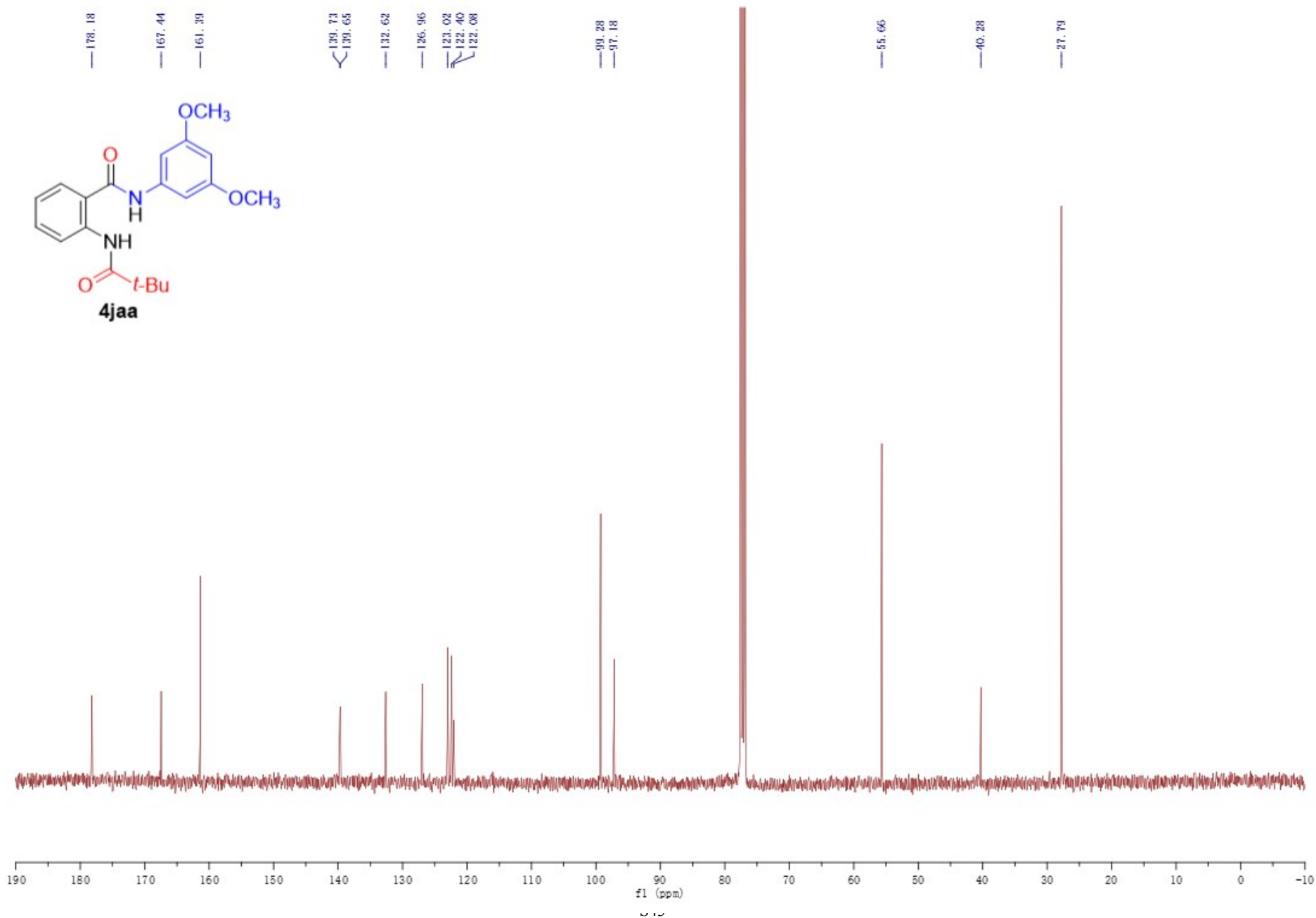


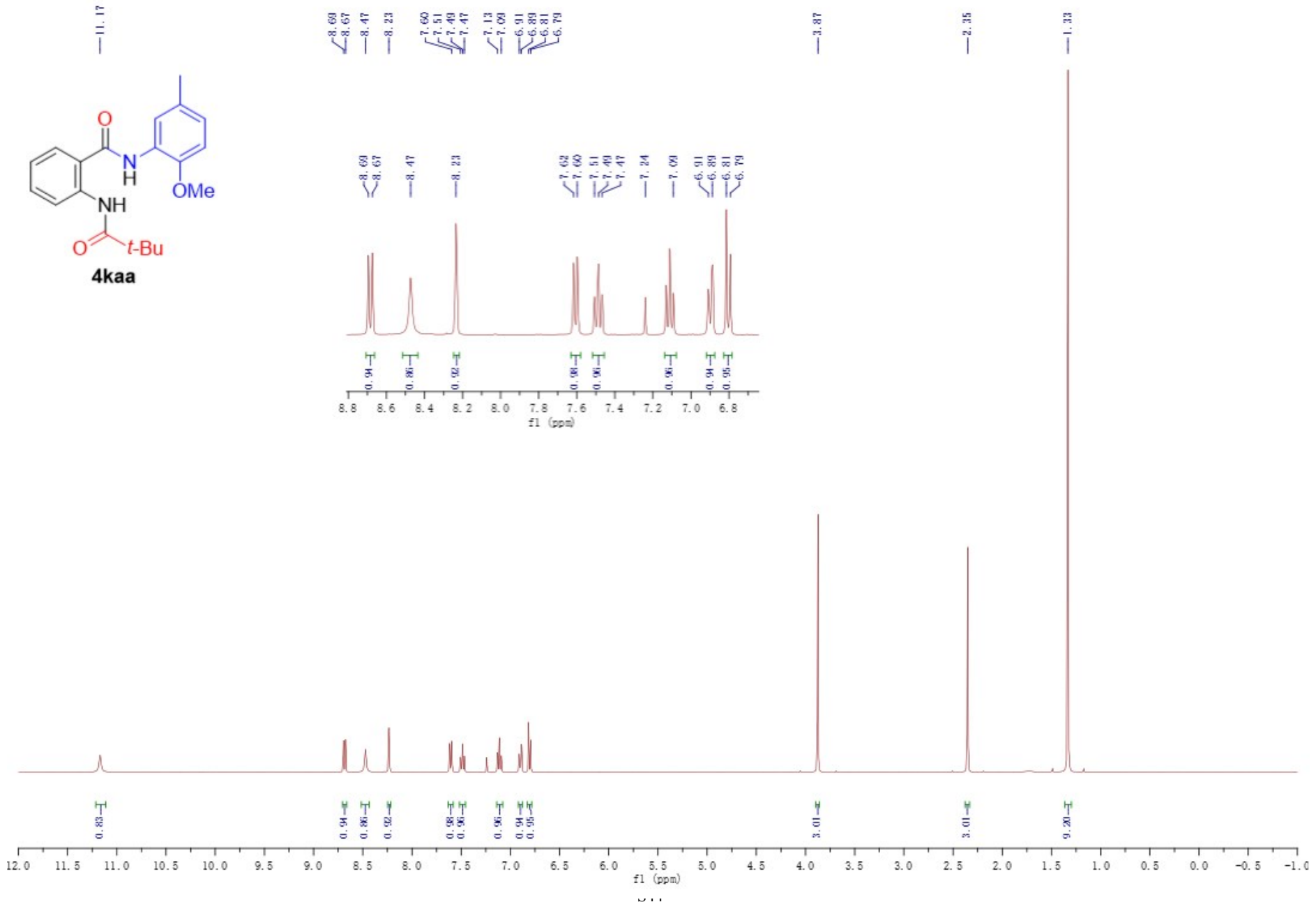
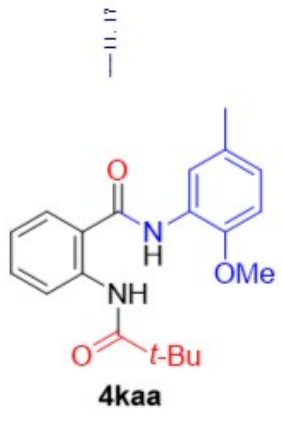
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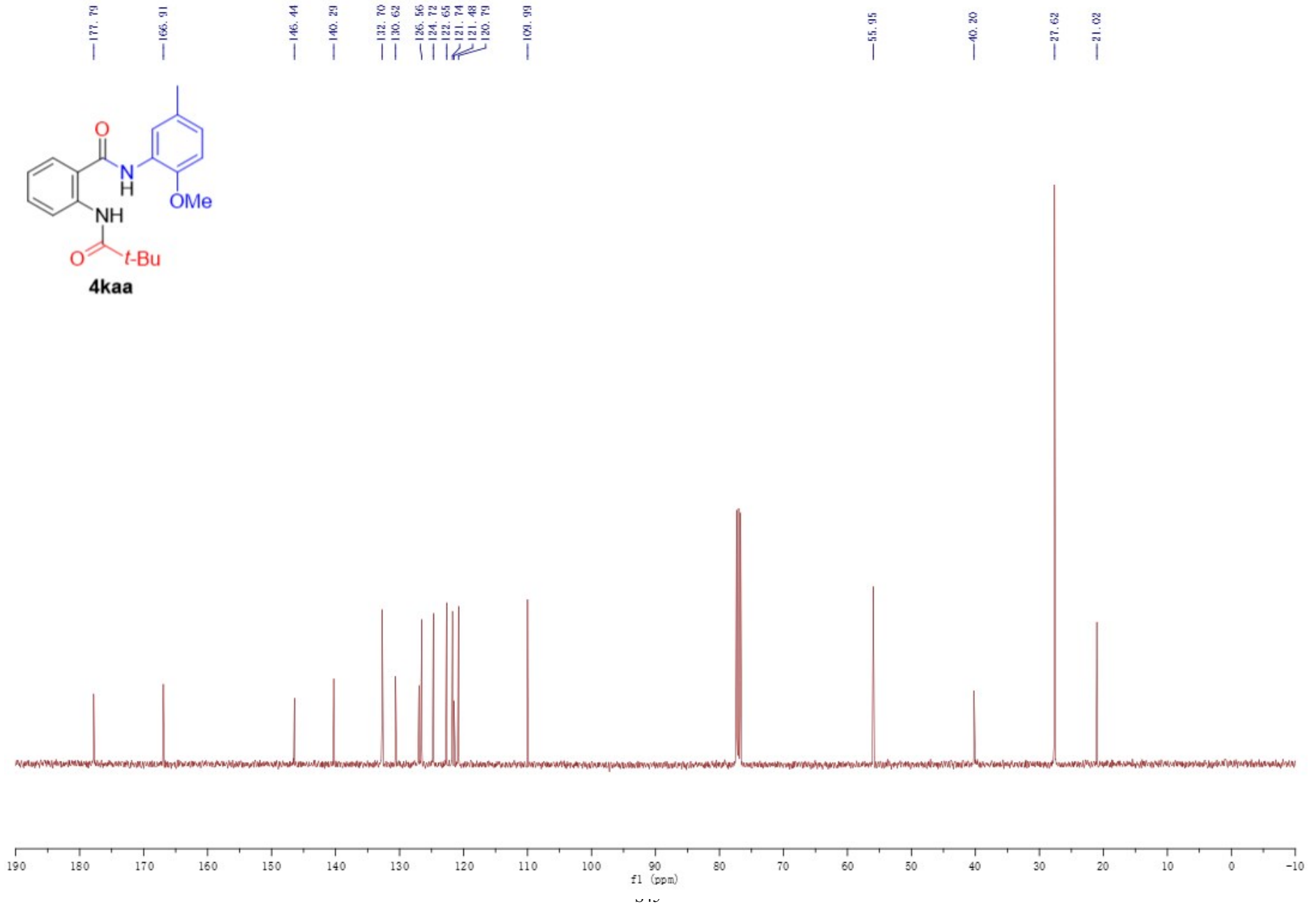
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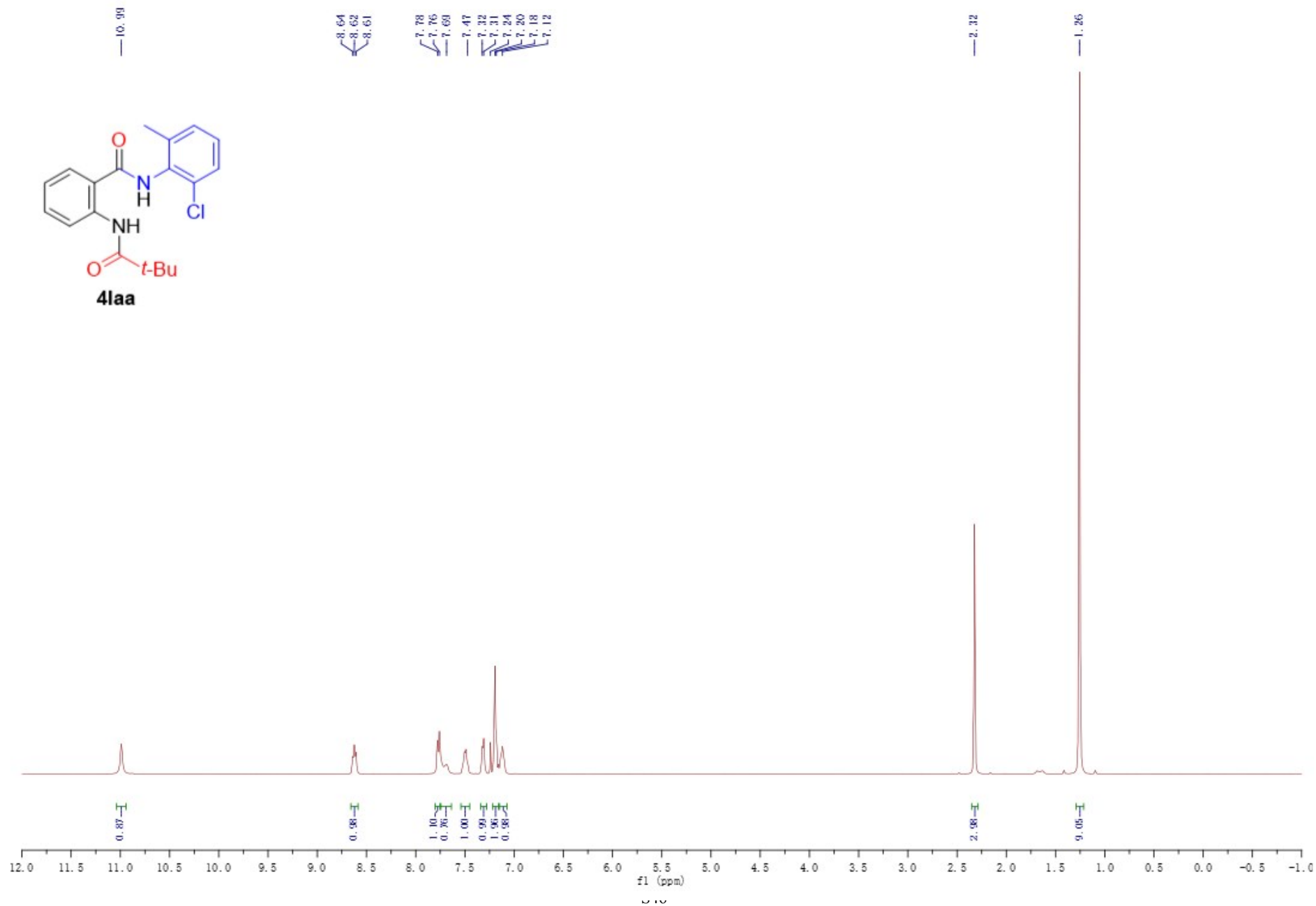
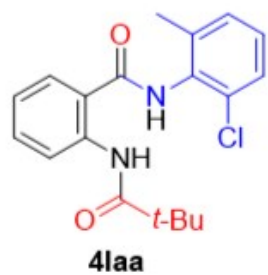


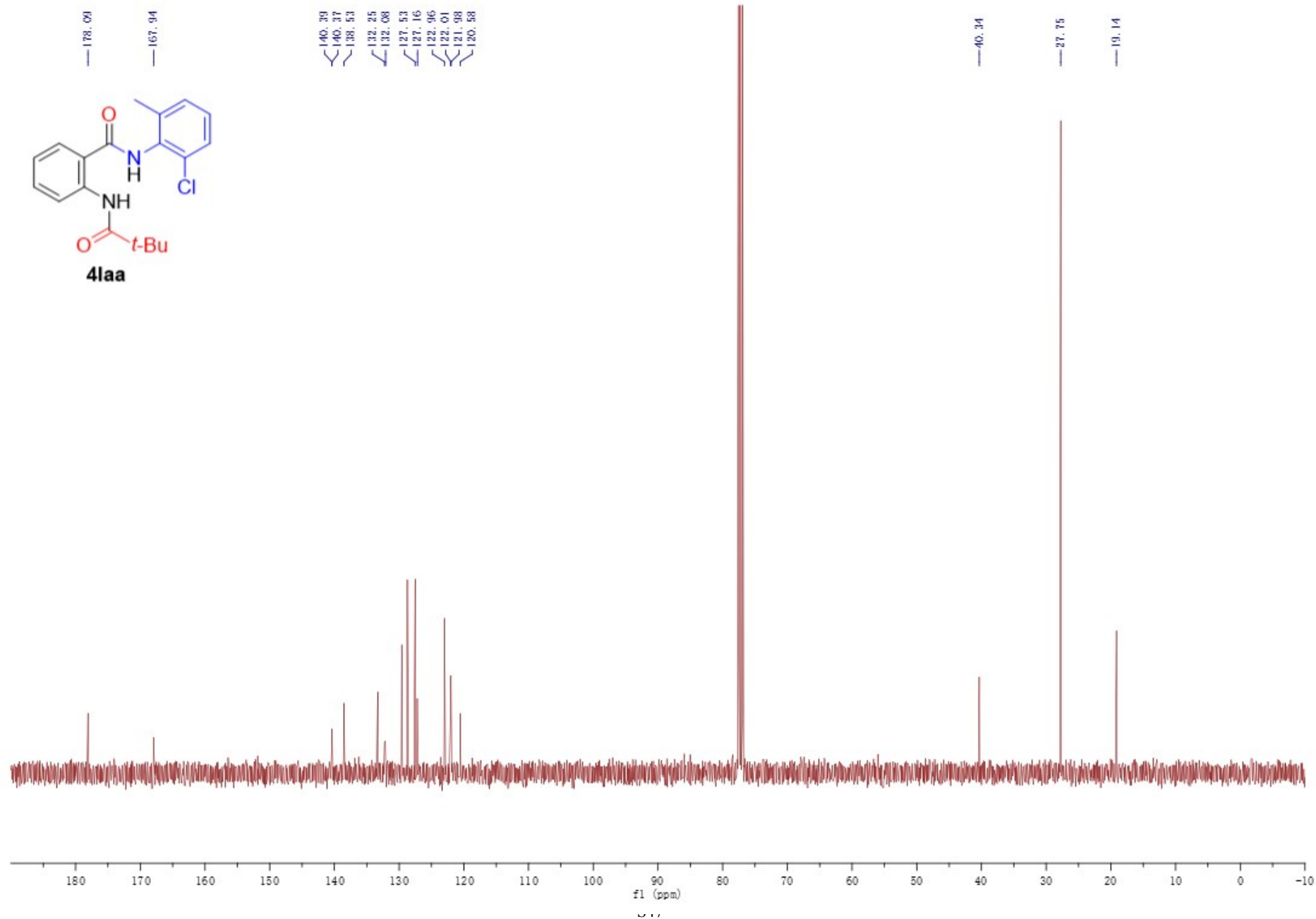
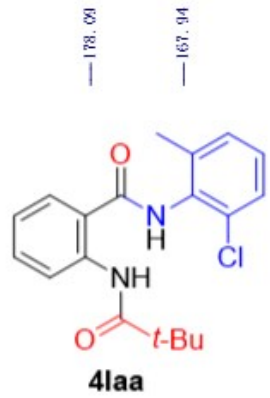


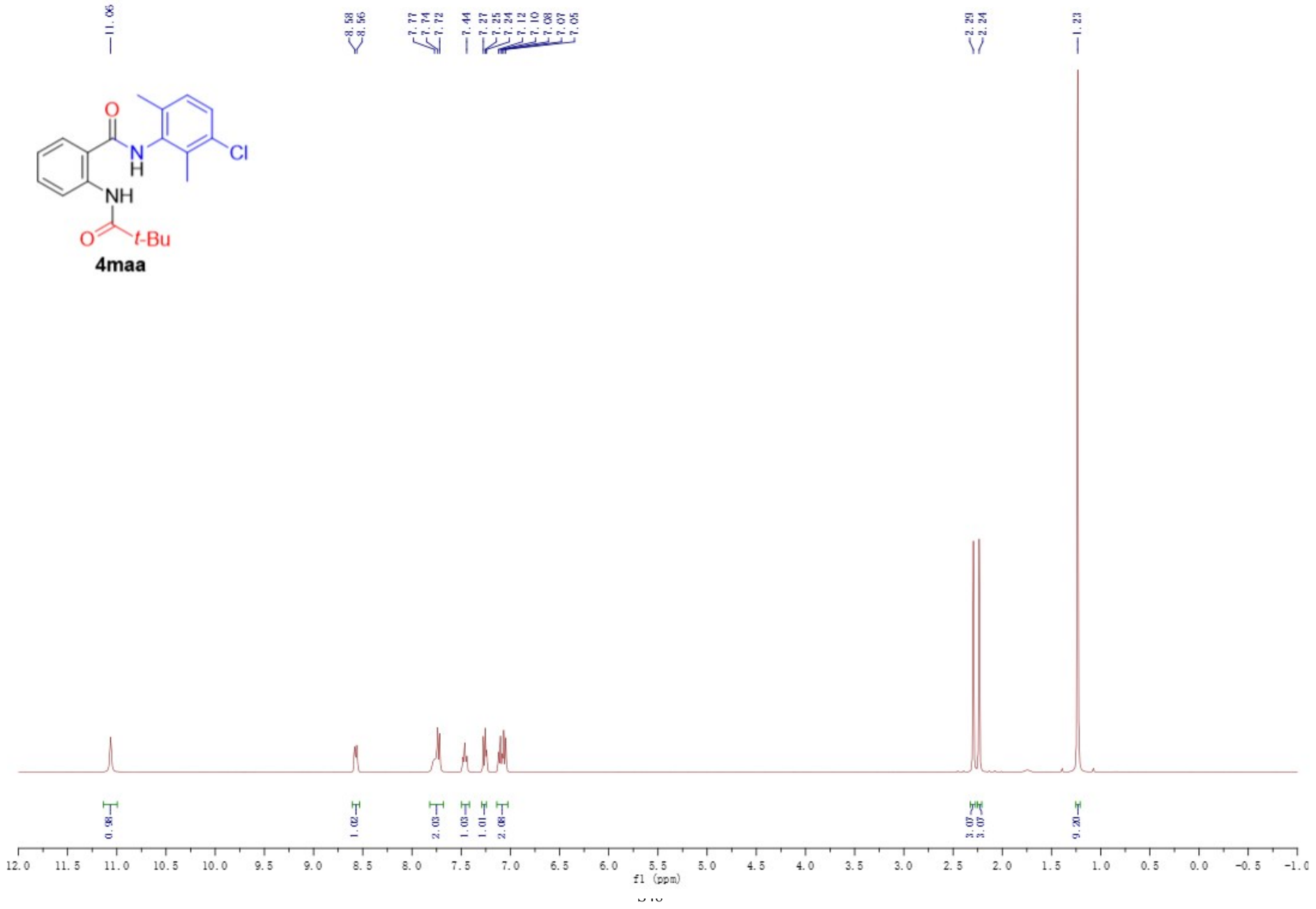
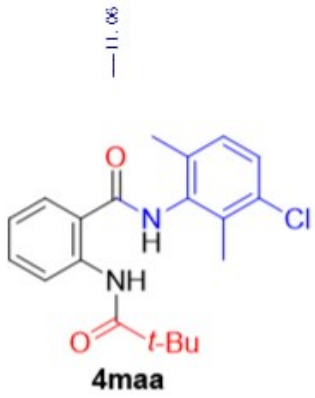


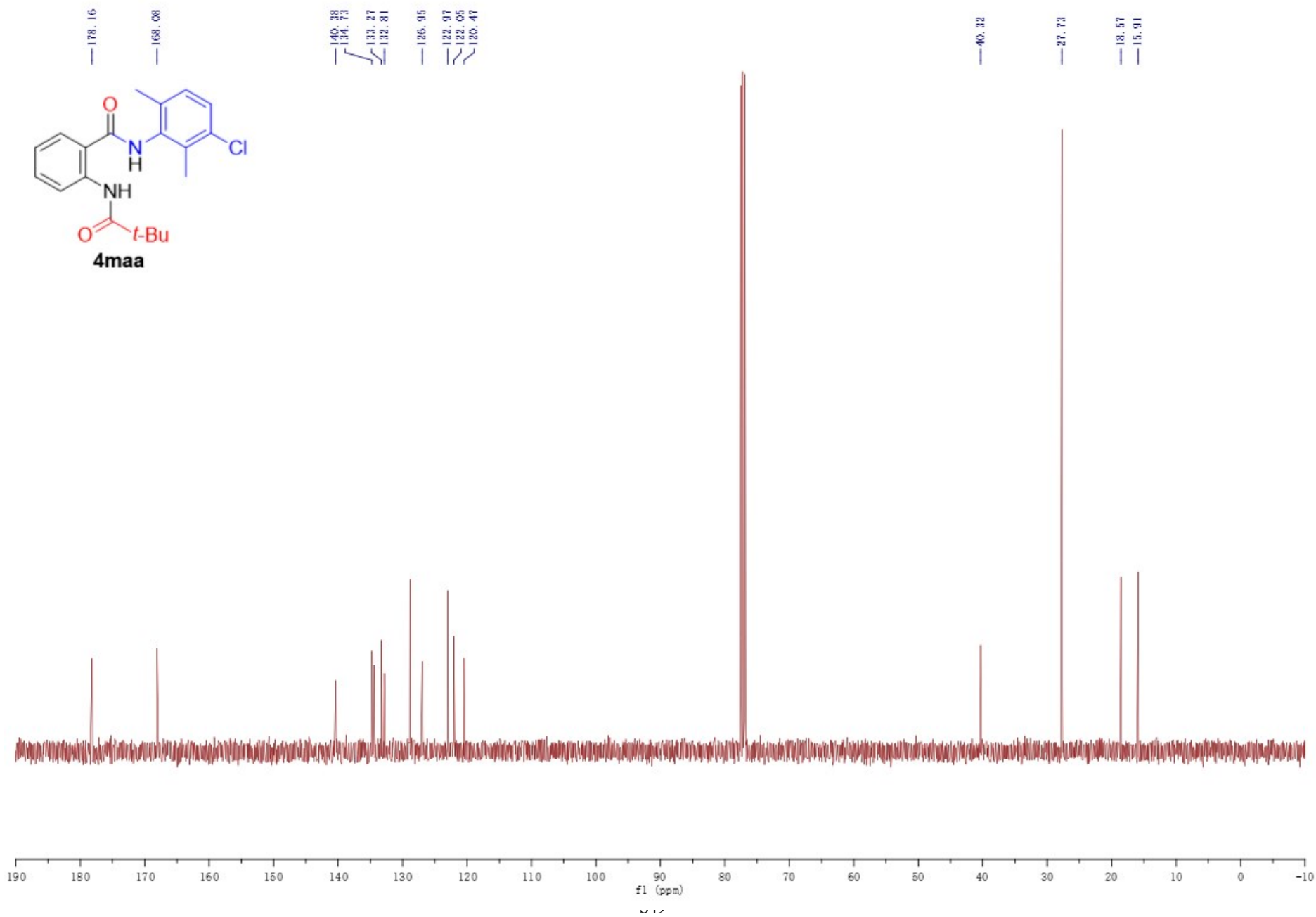


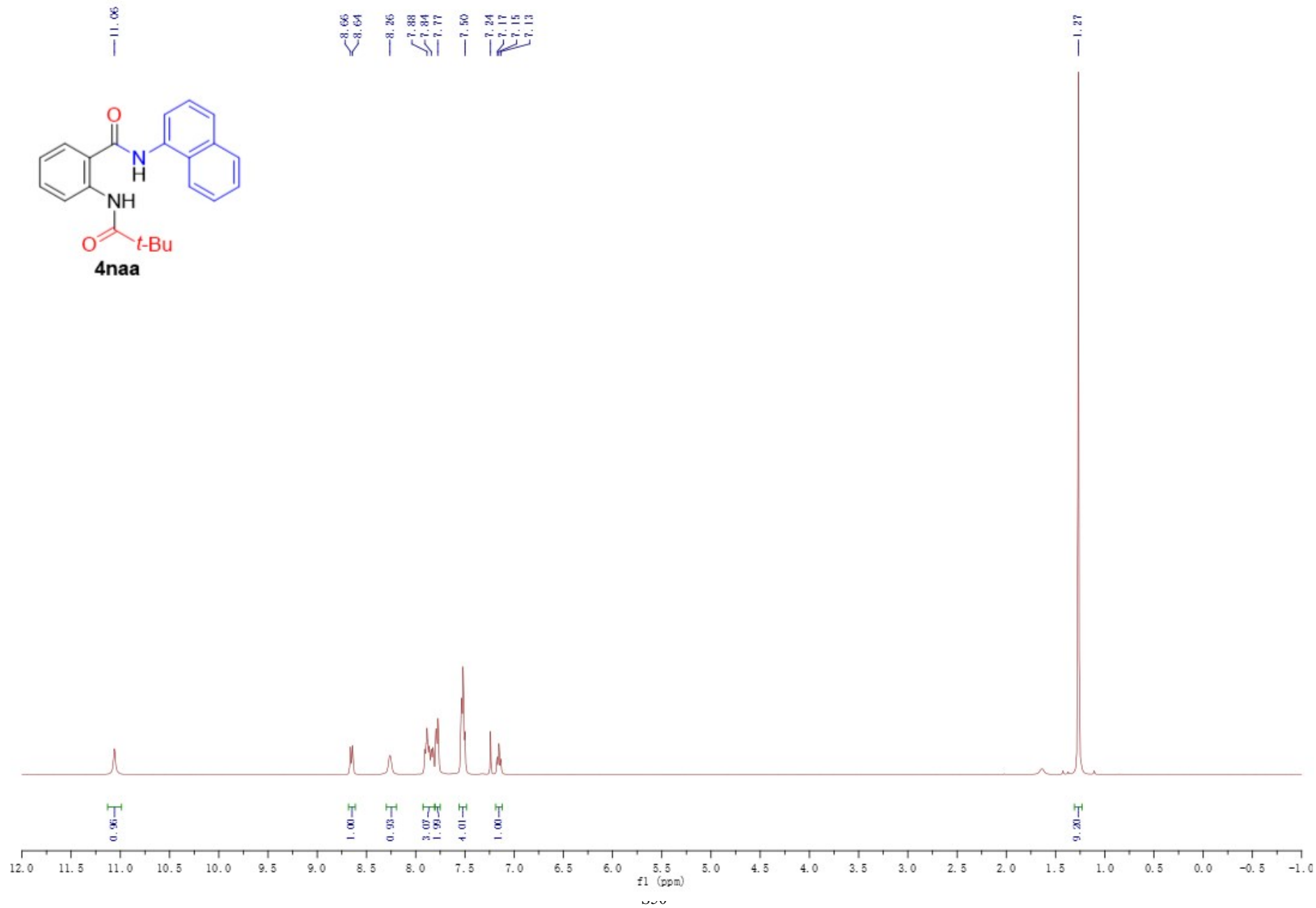
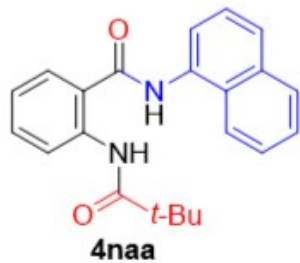


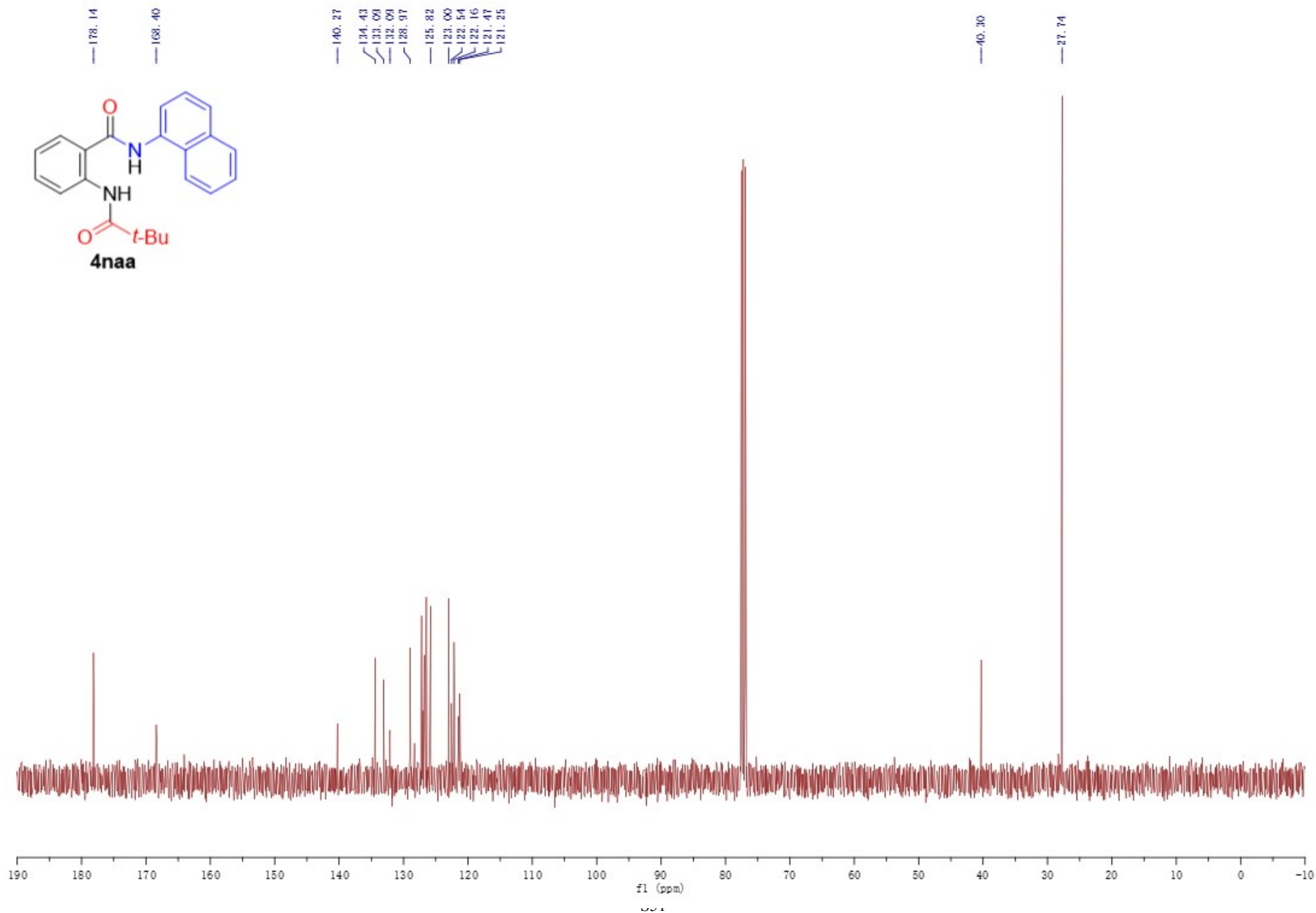
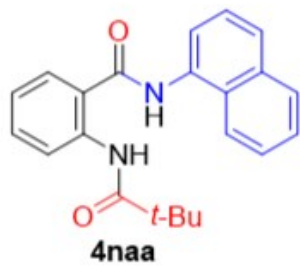


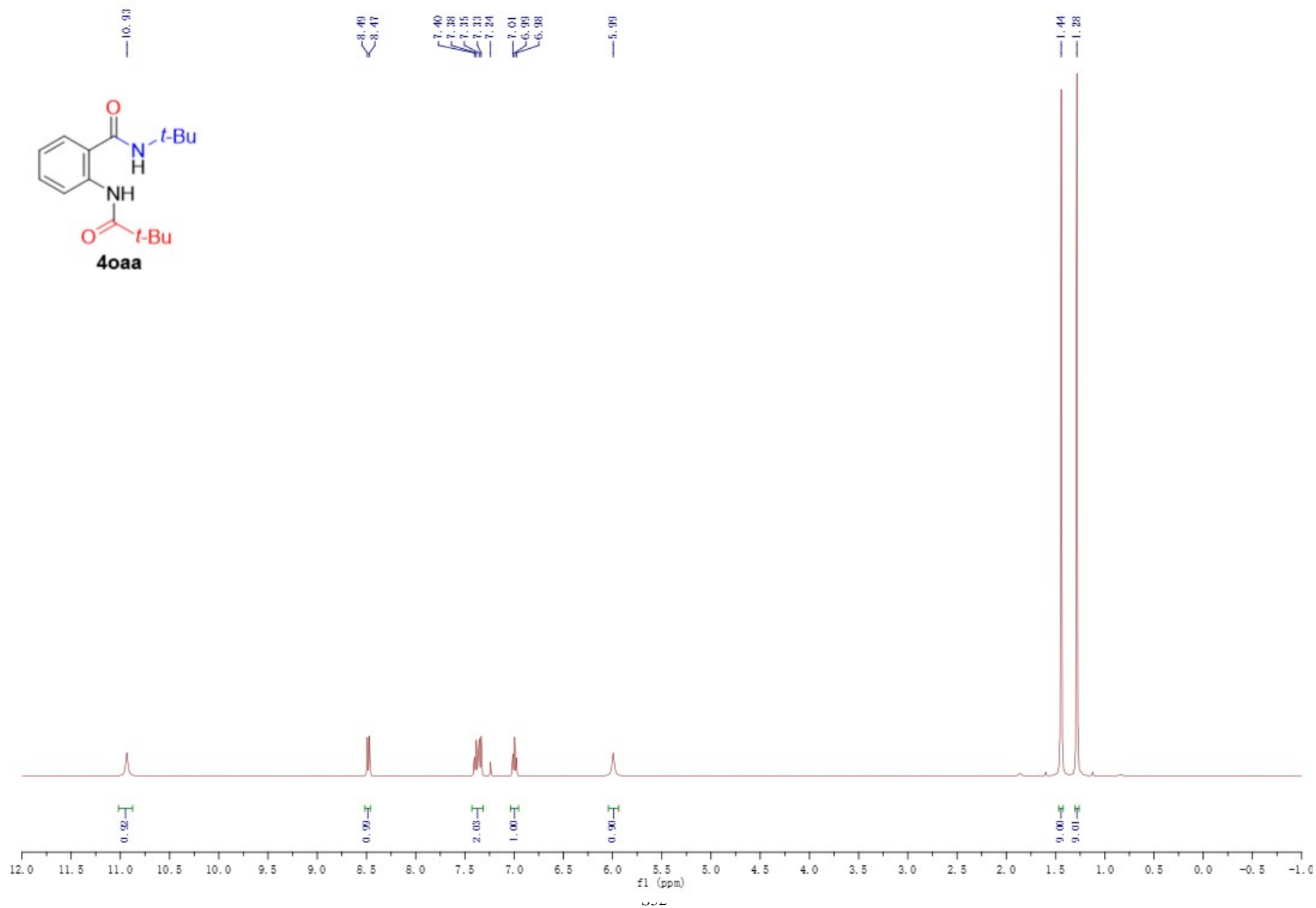


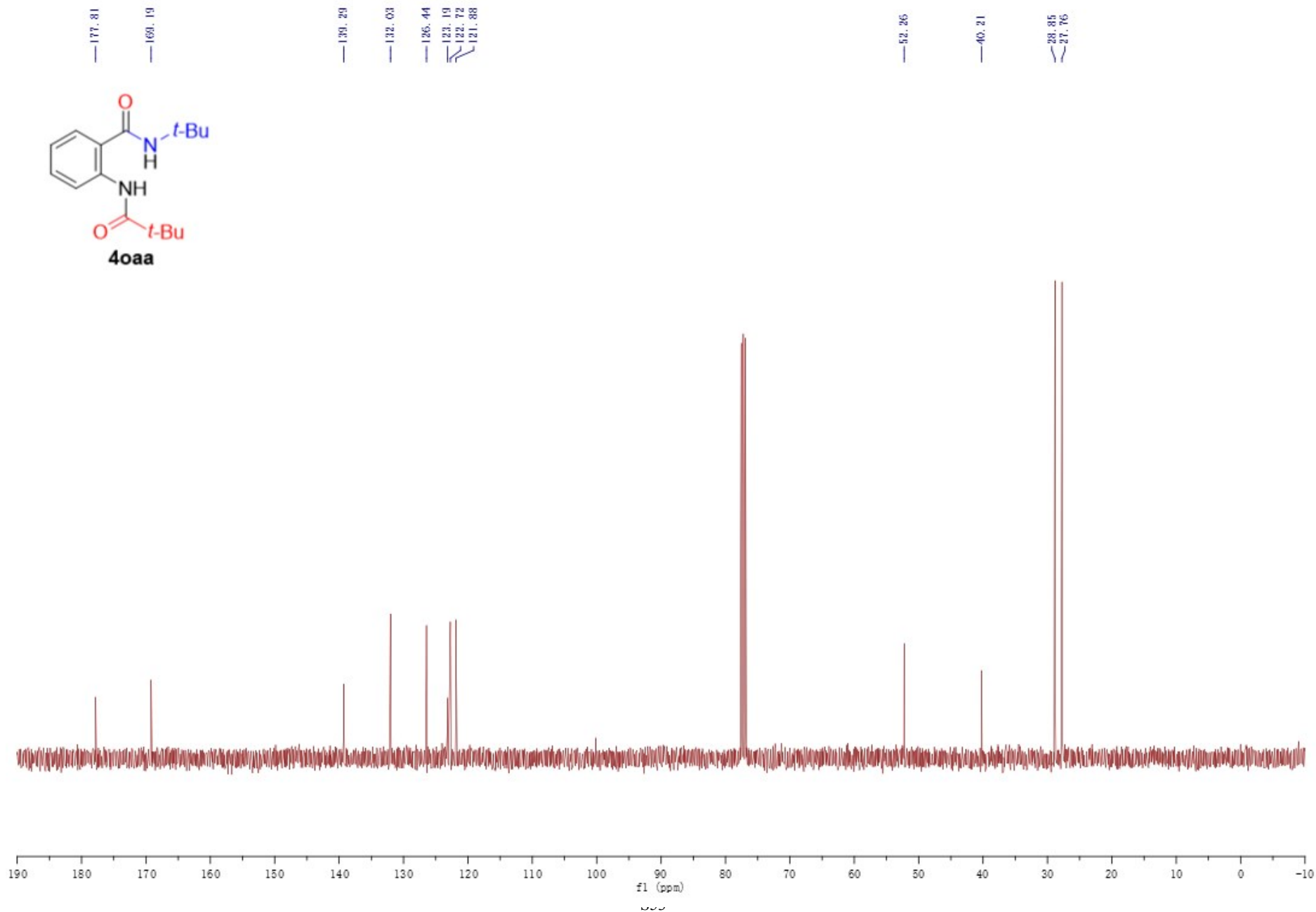
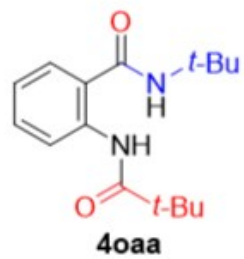


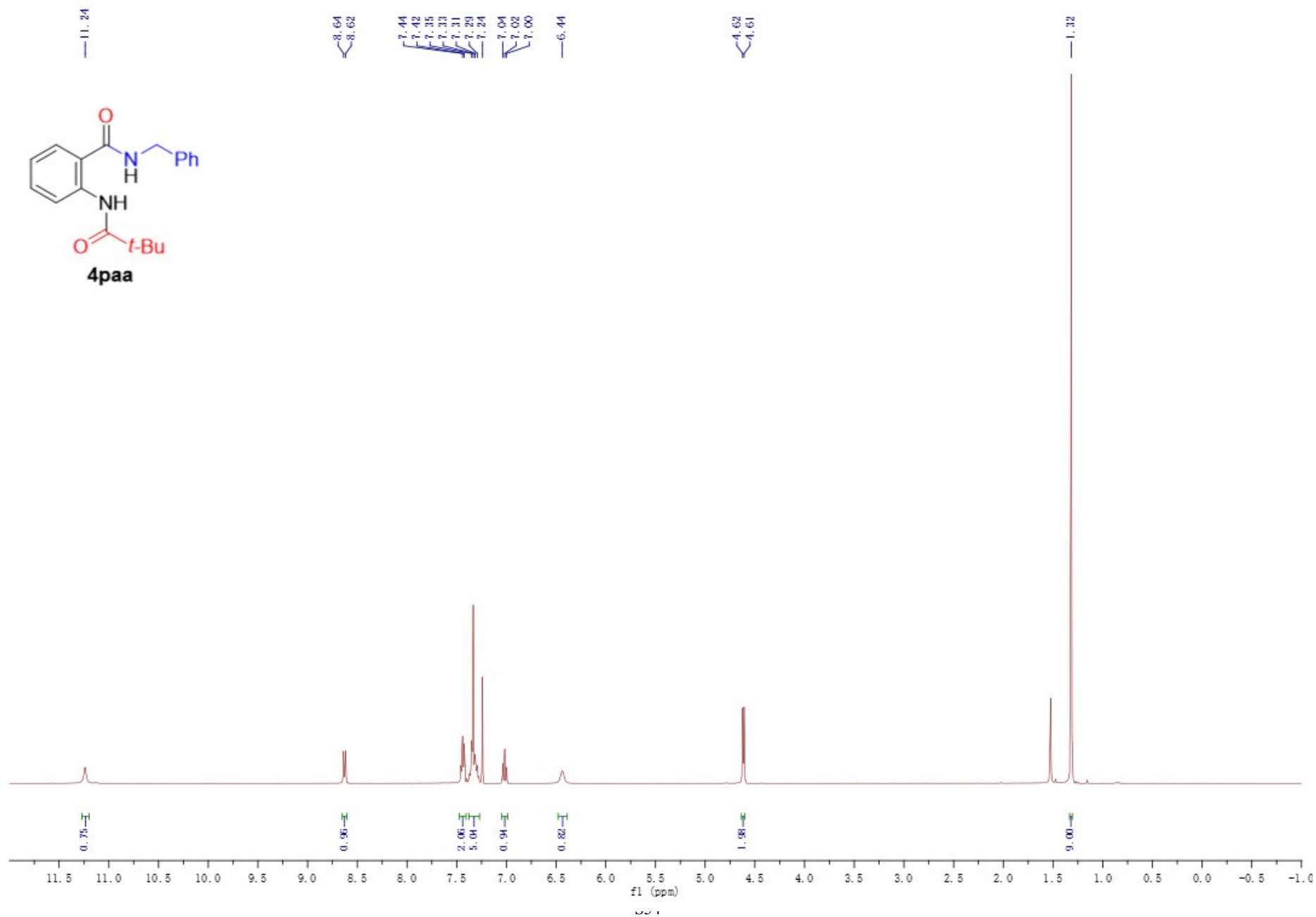
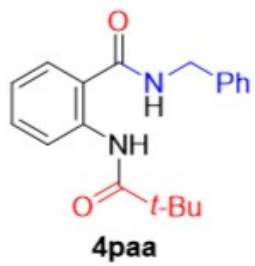


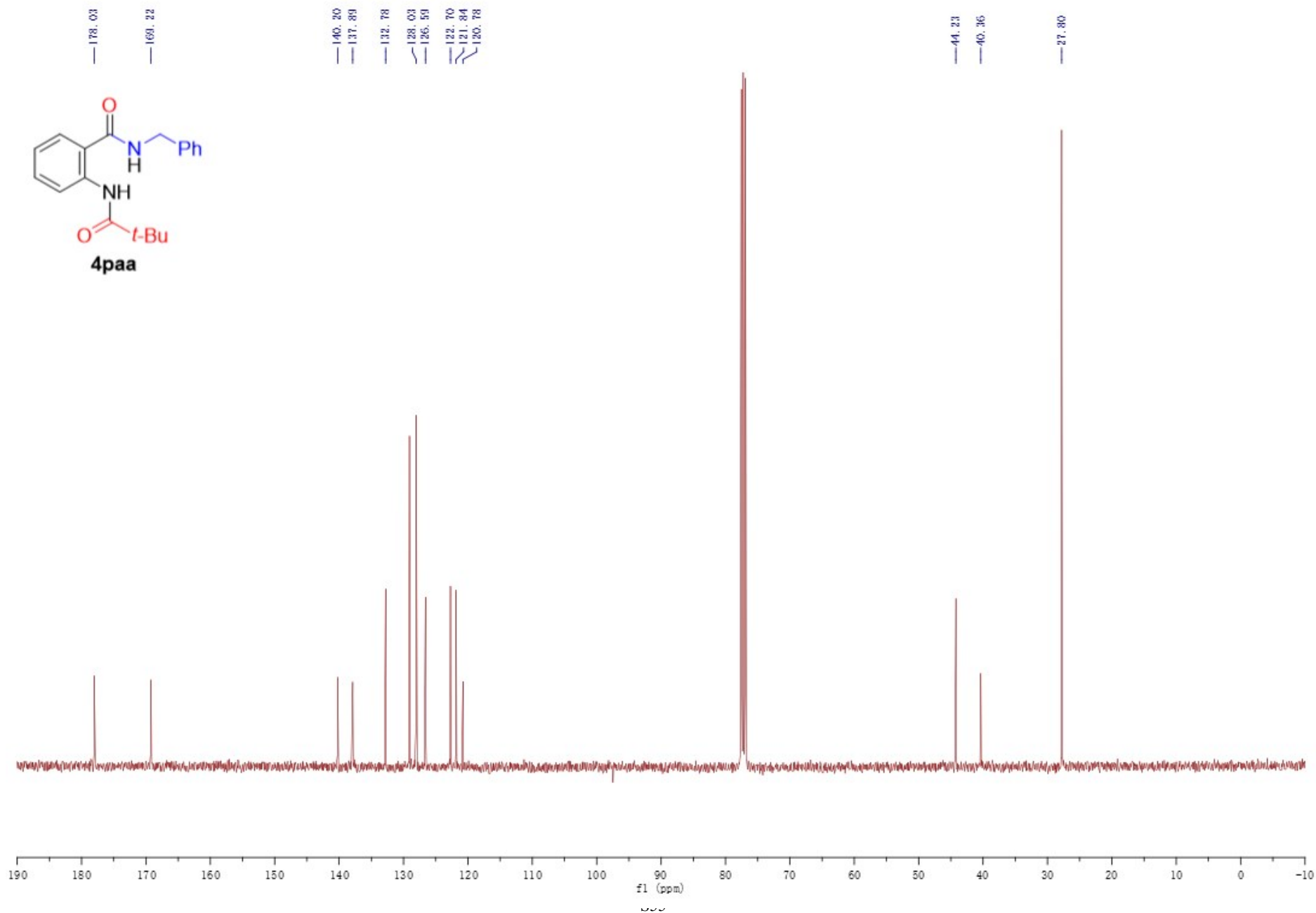
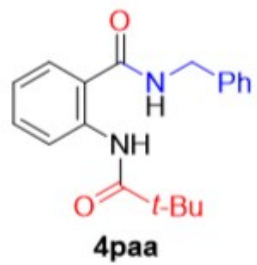


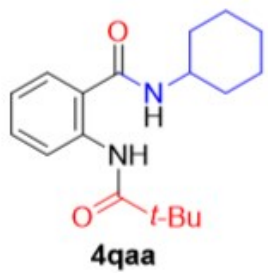










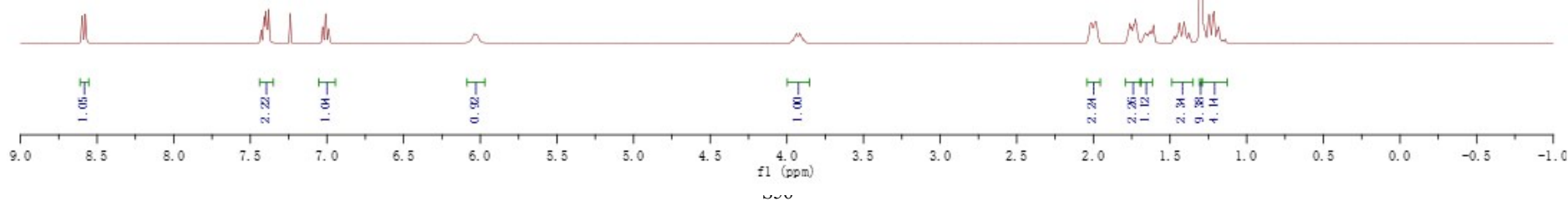
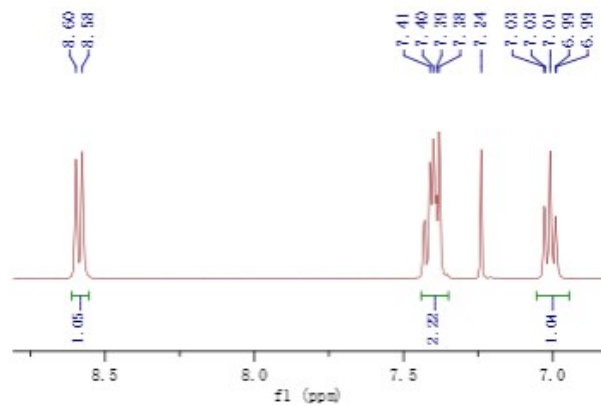


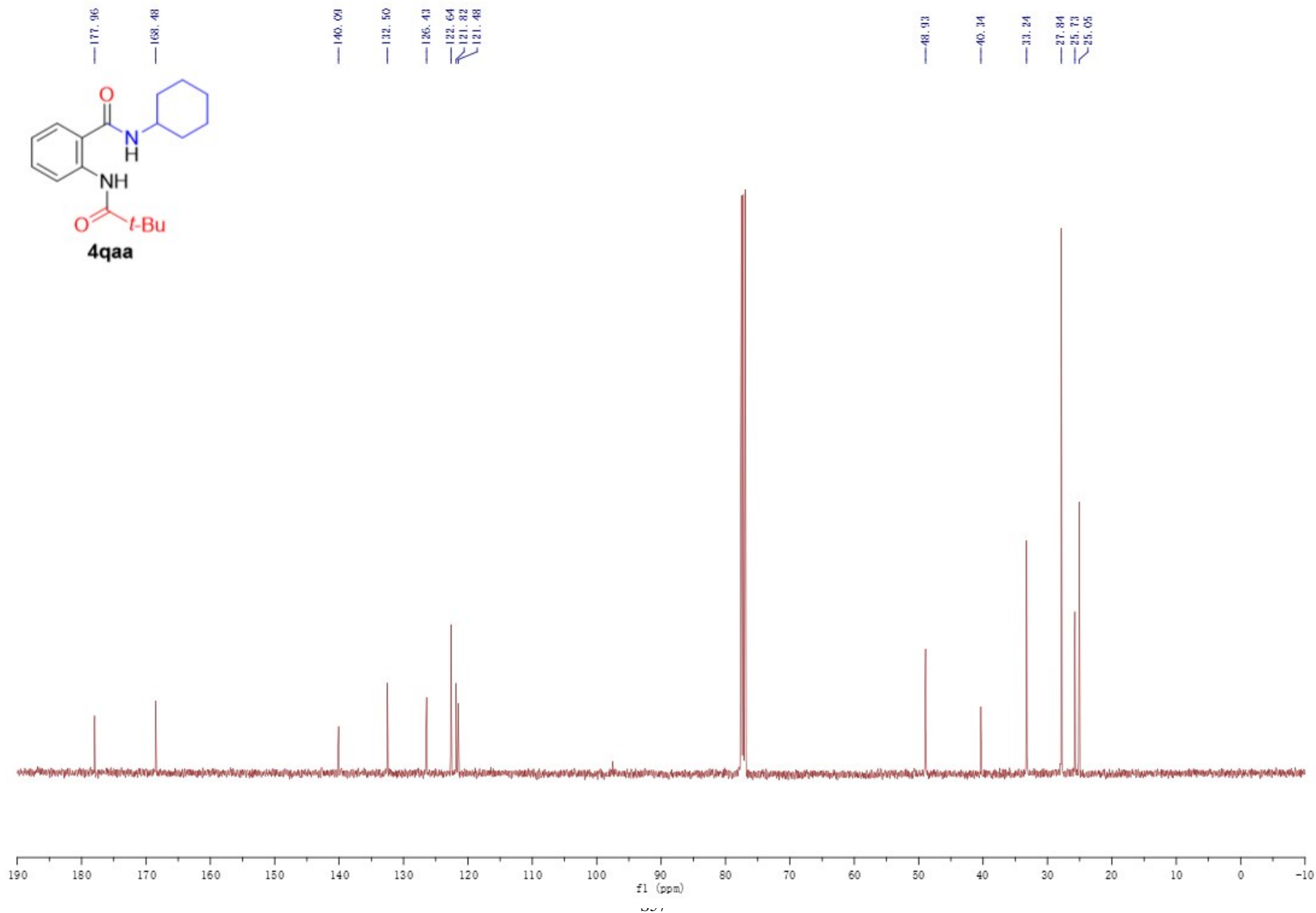
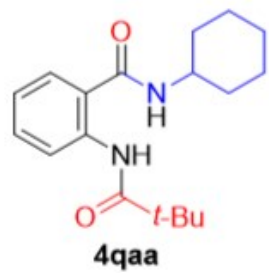
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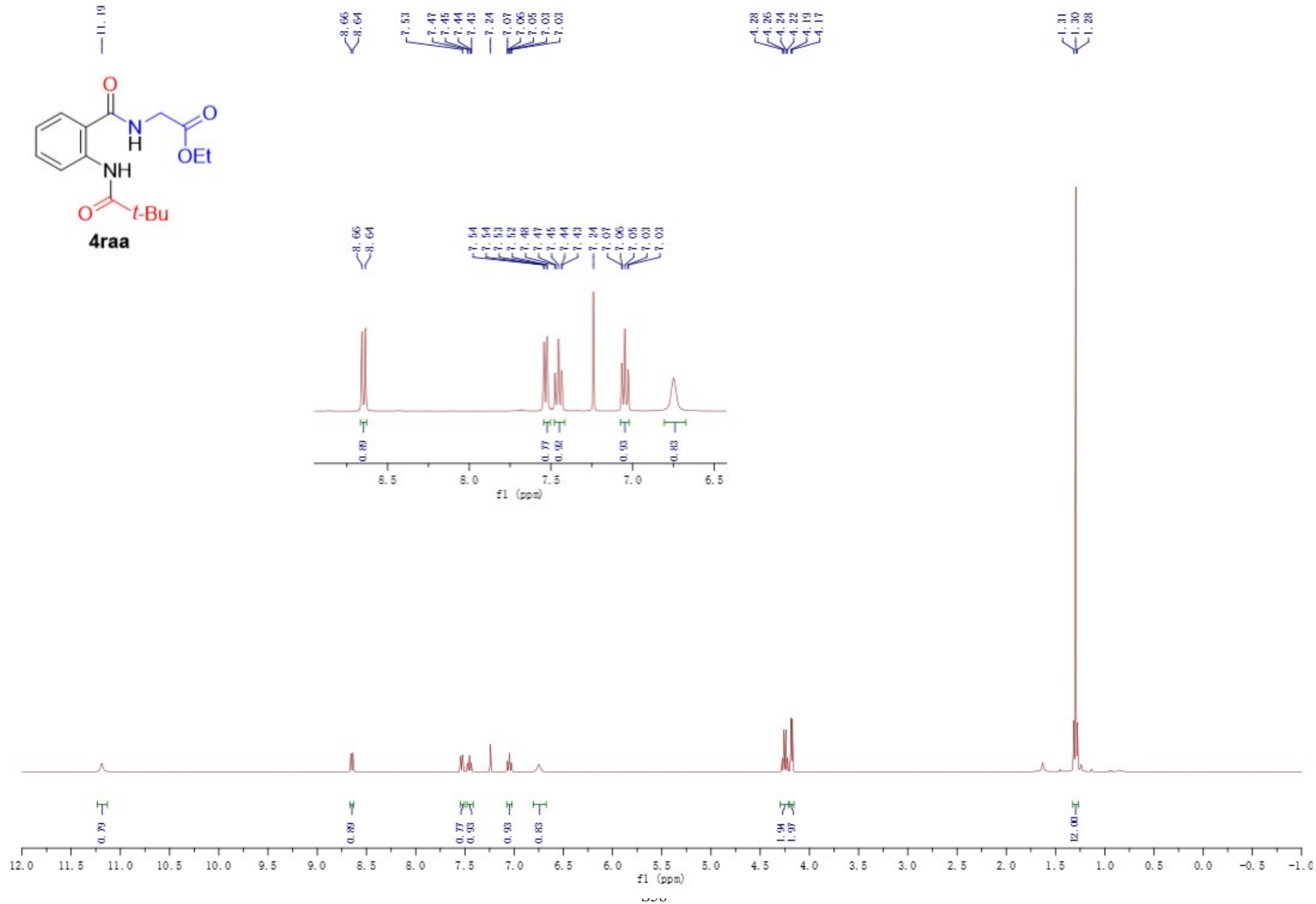
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6.99

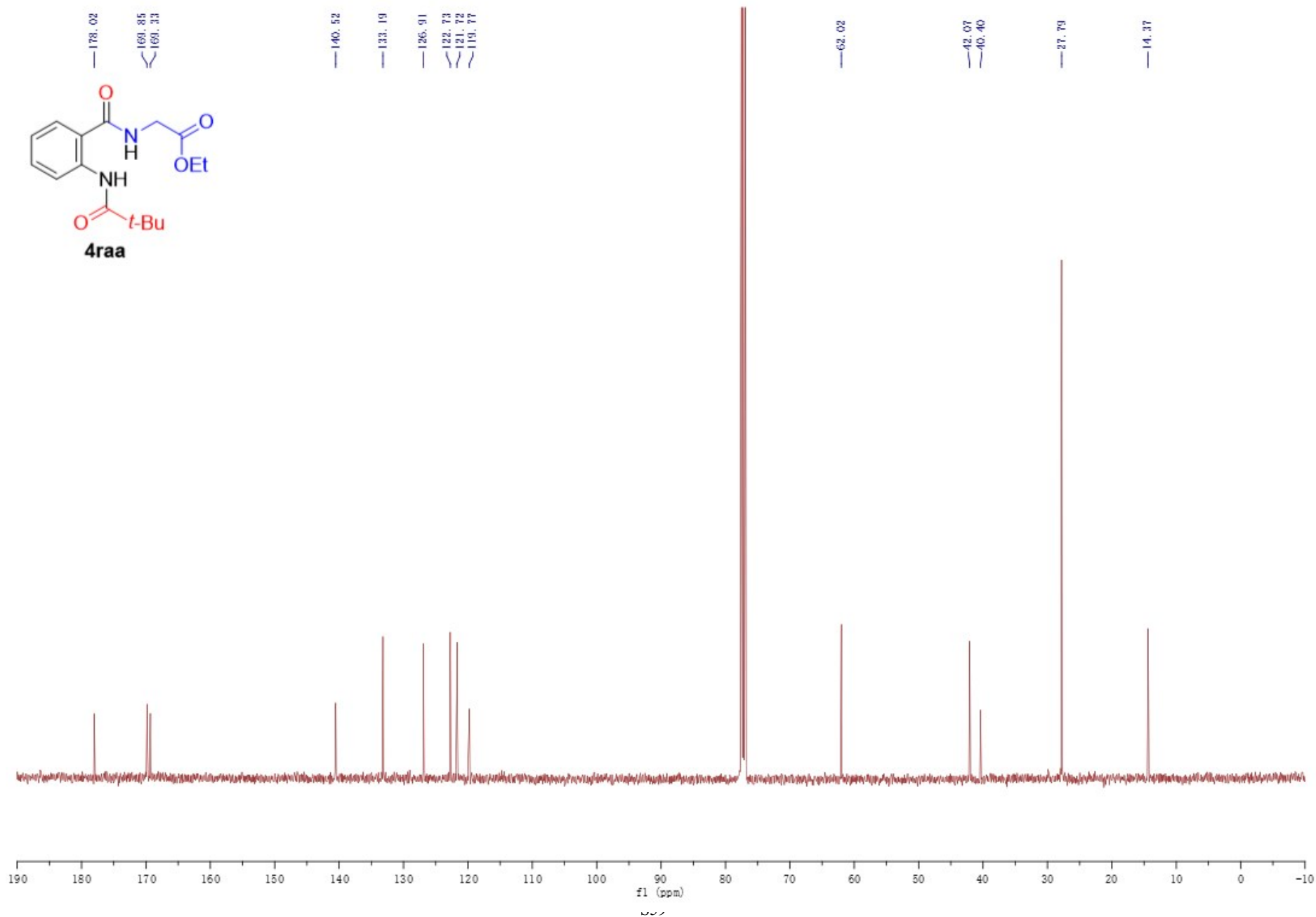
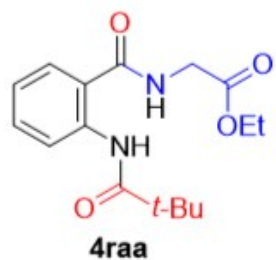
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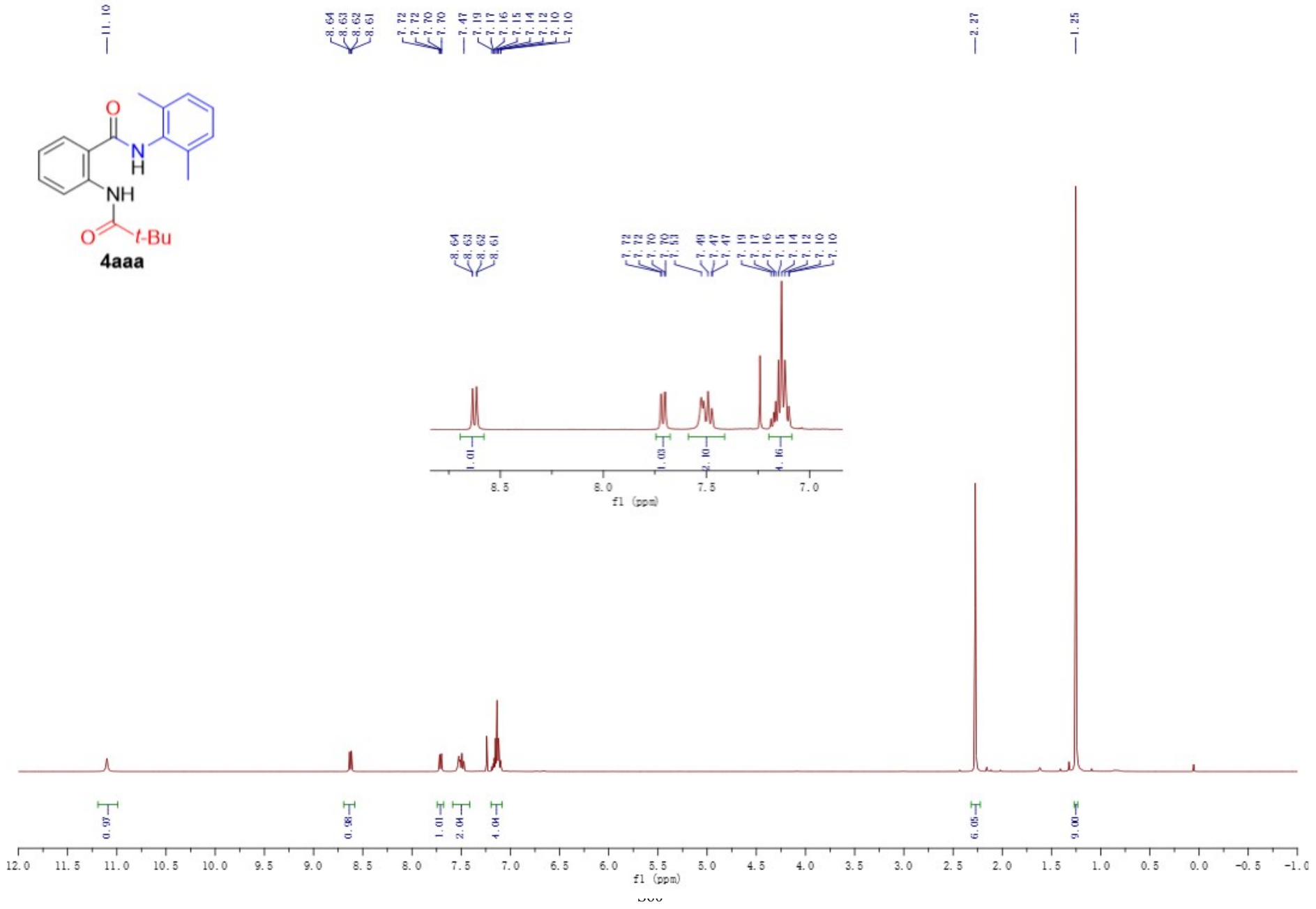
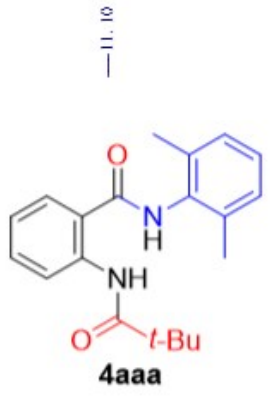
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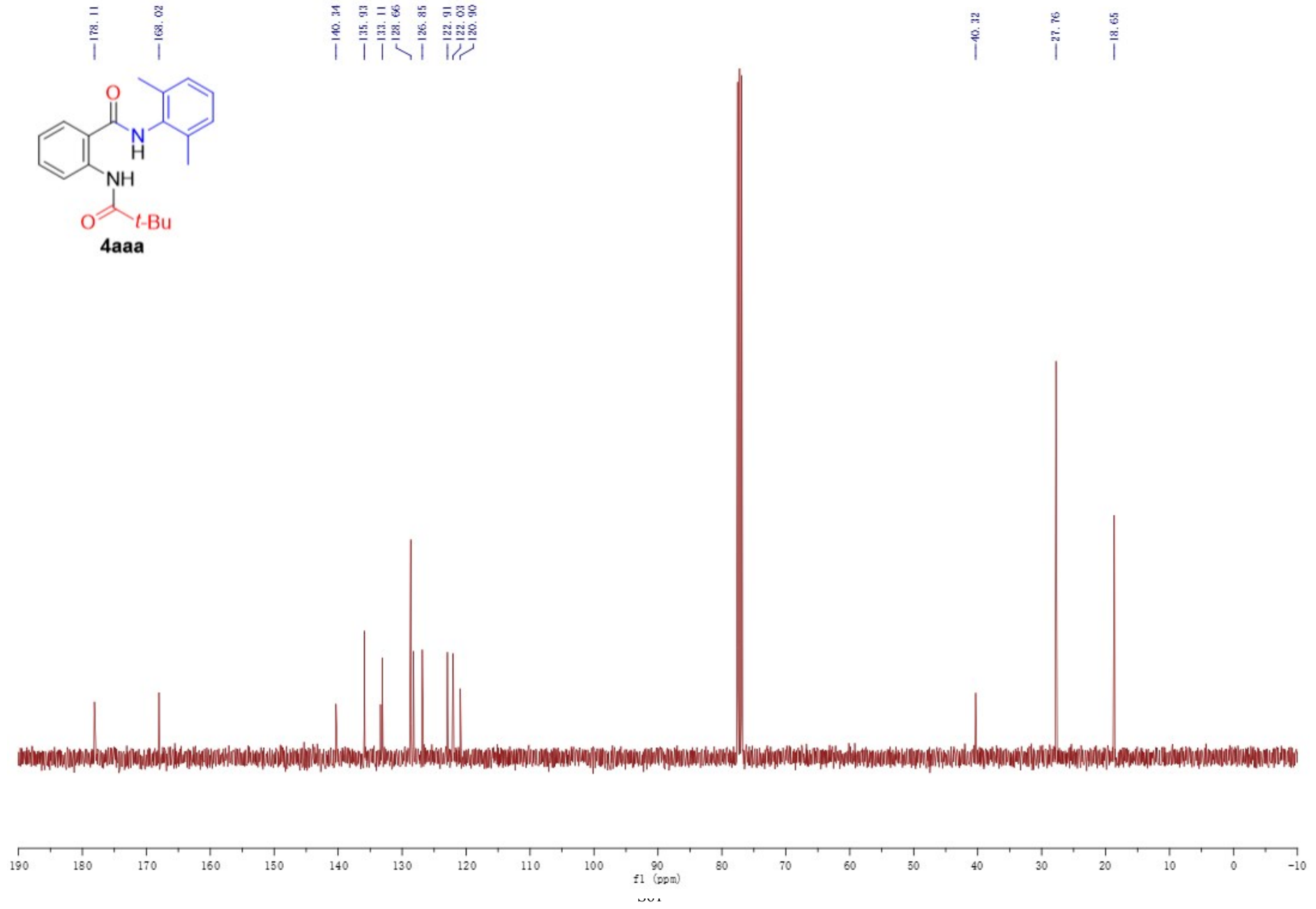
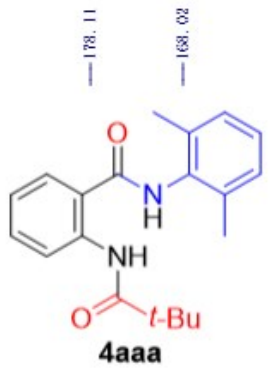


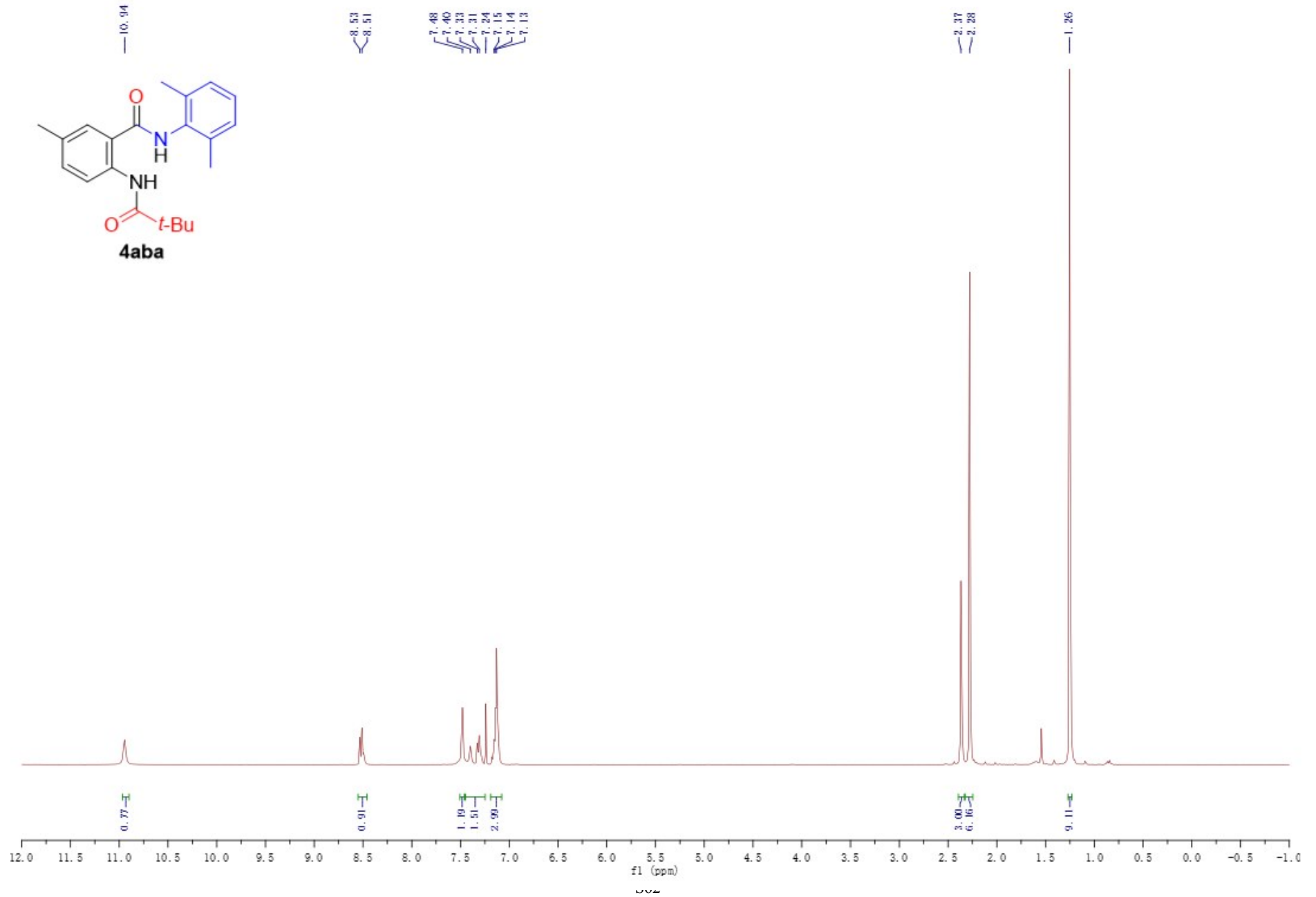
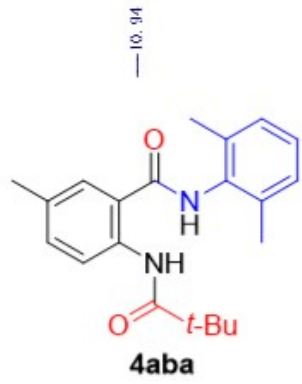


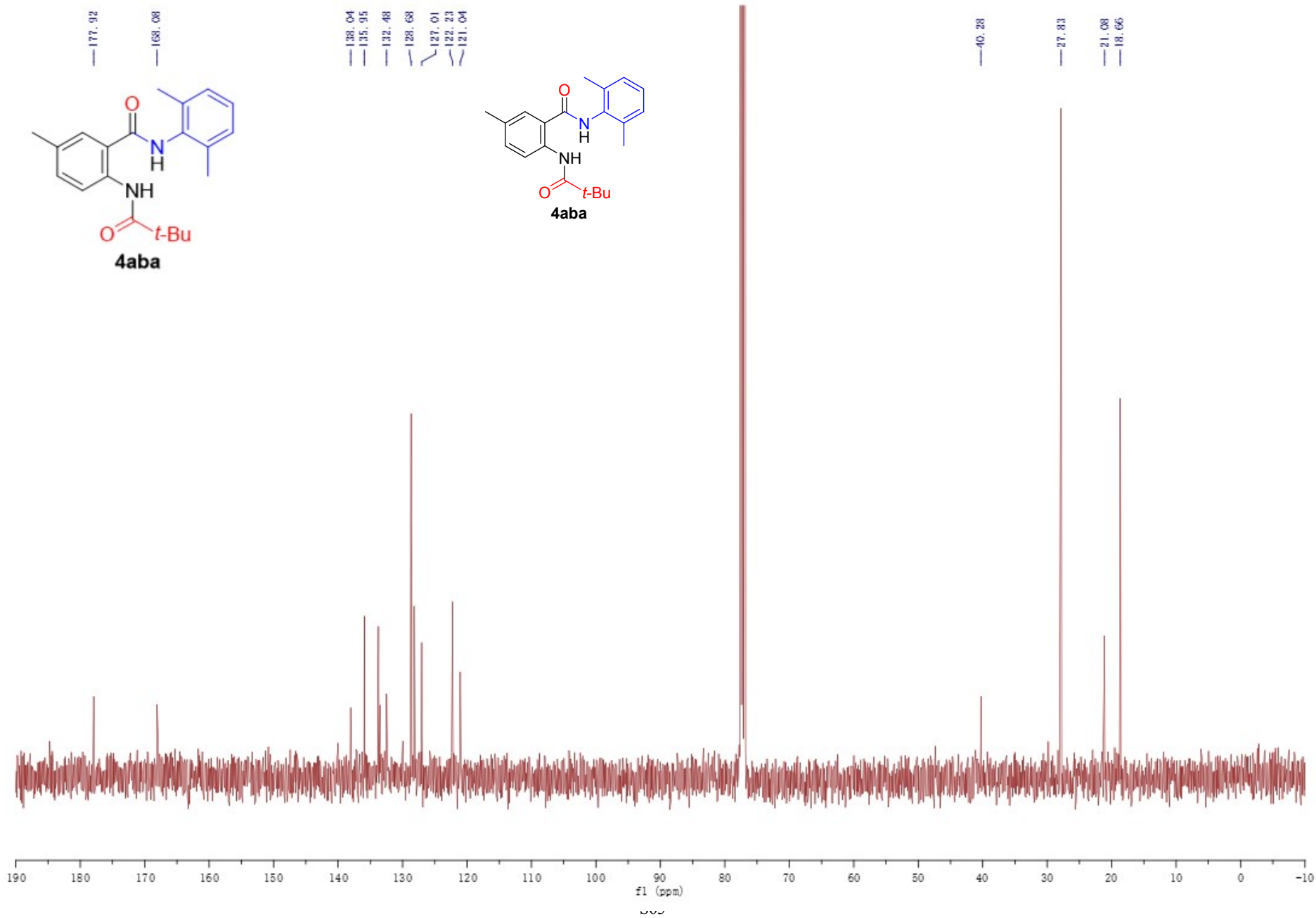


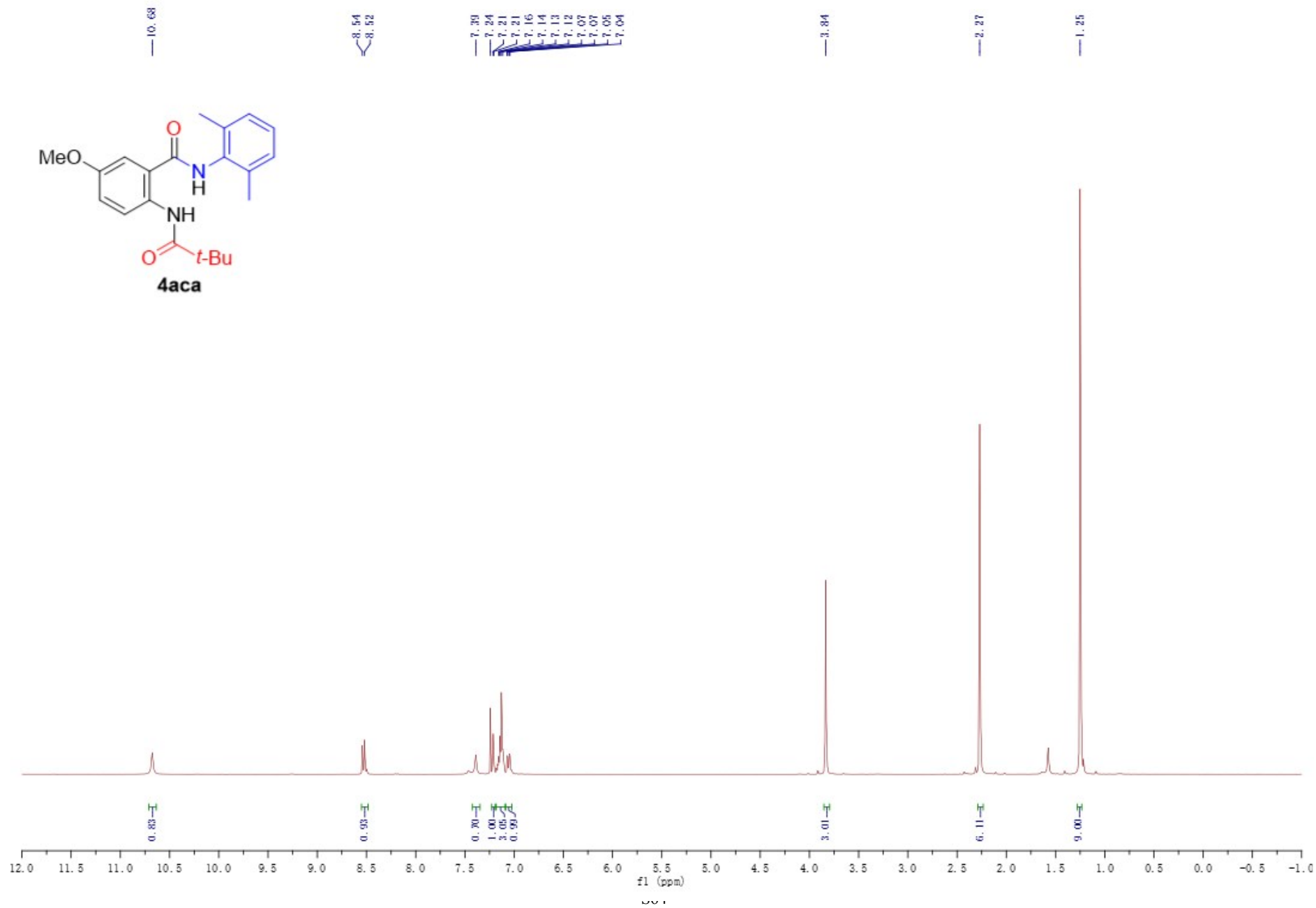
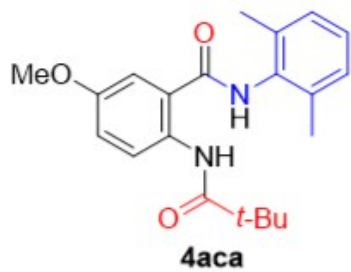


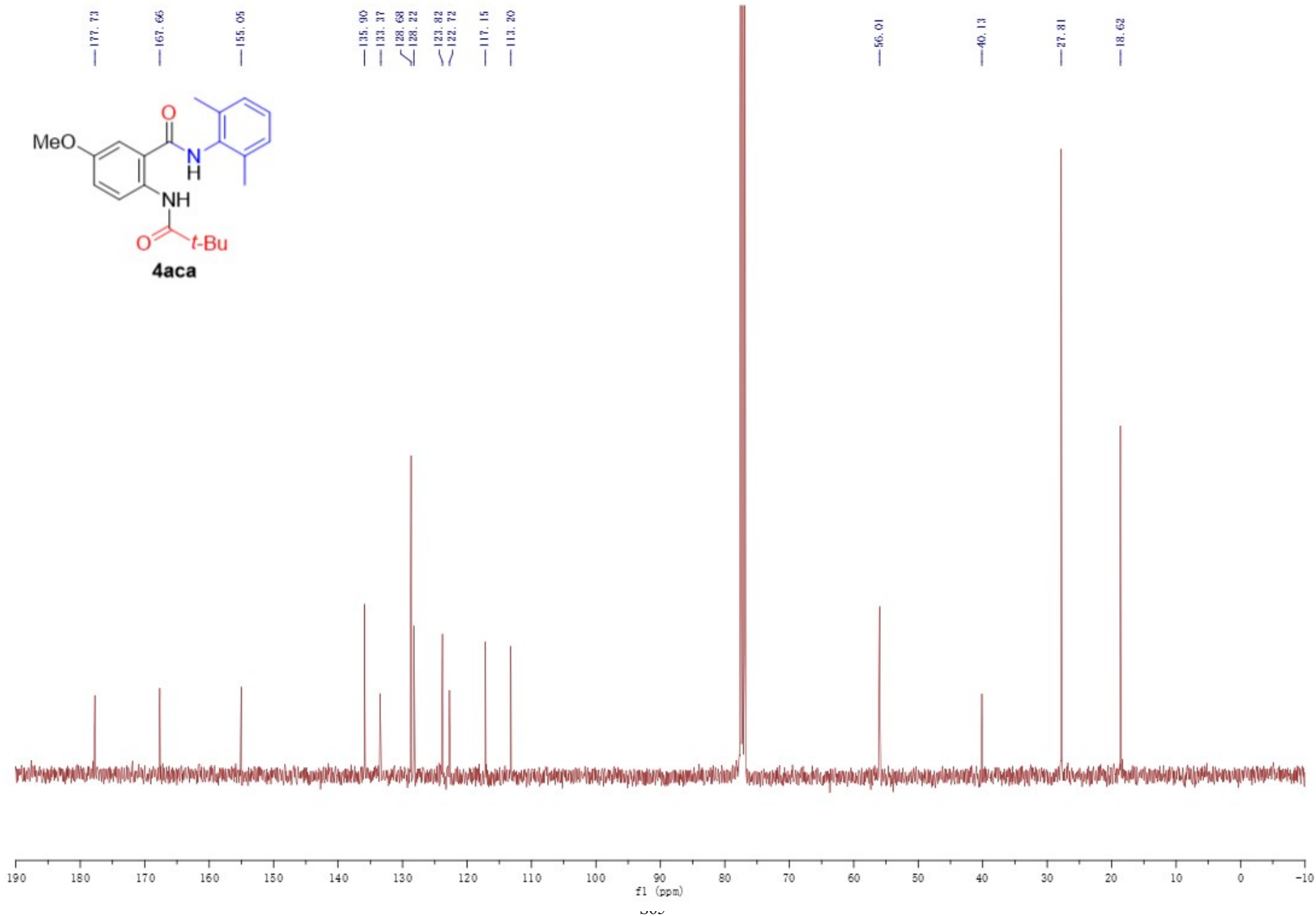


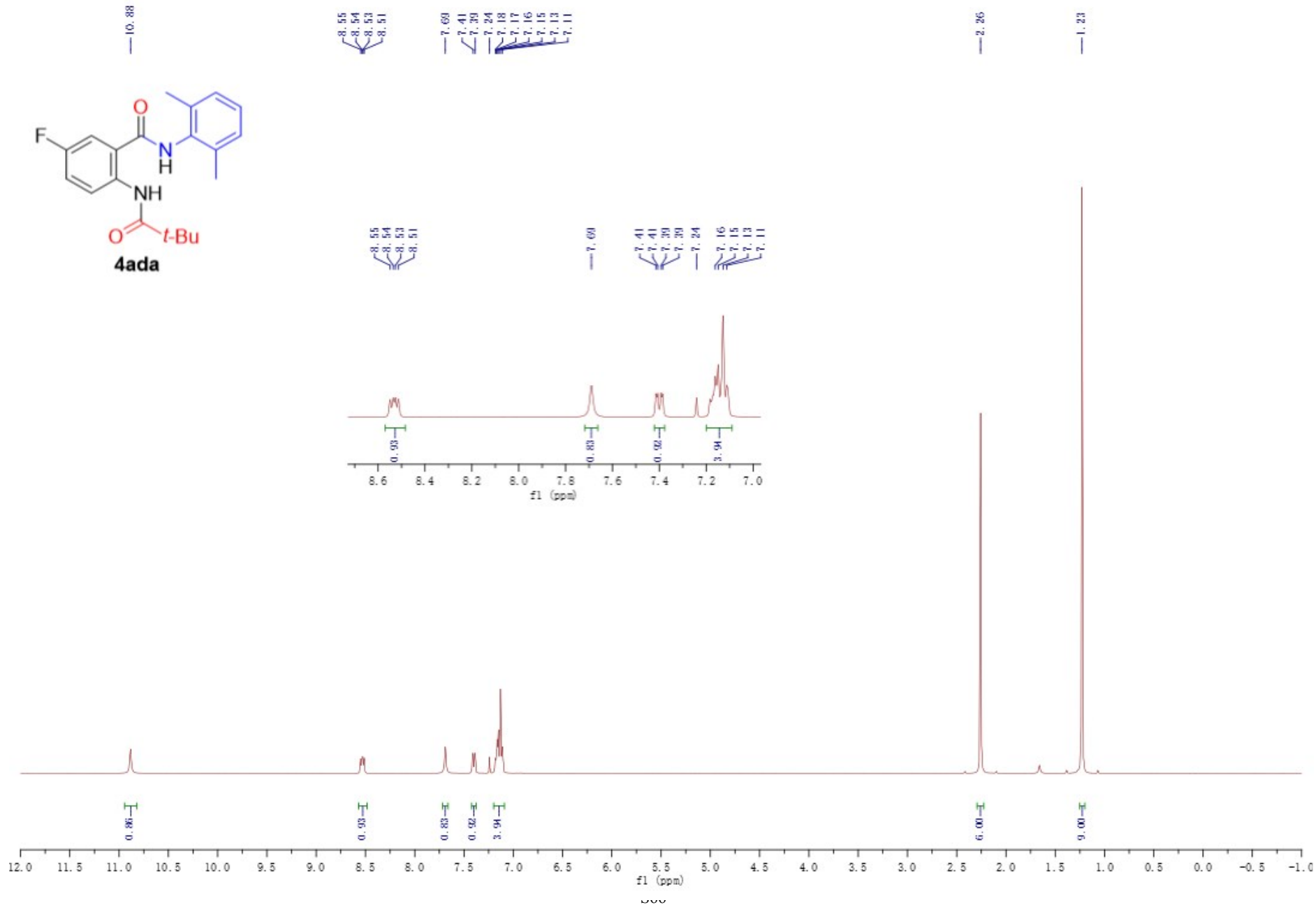
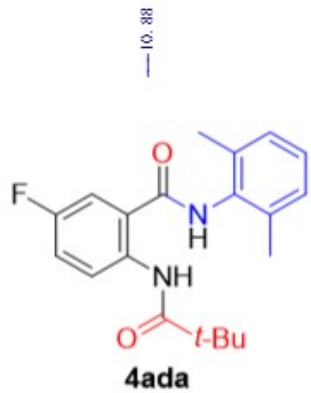


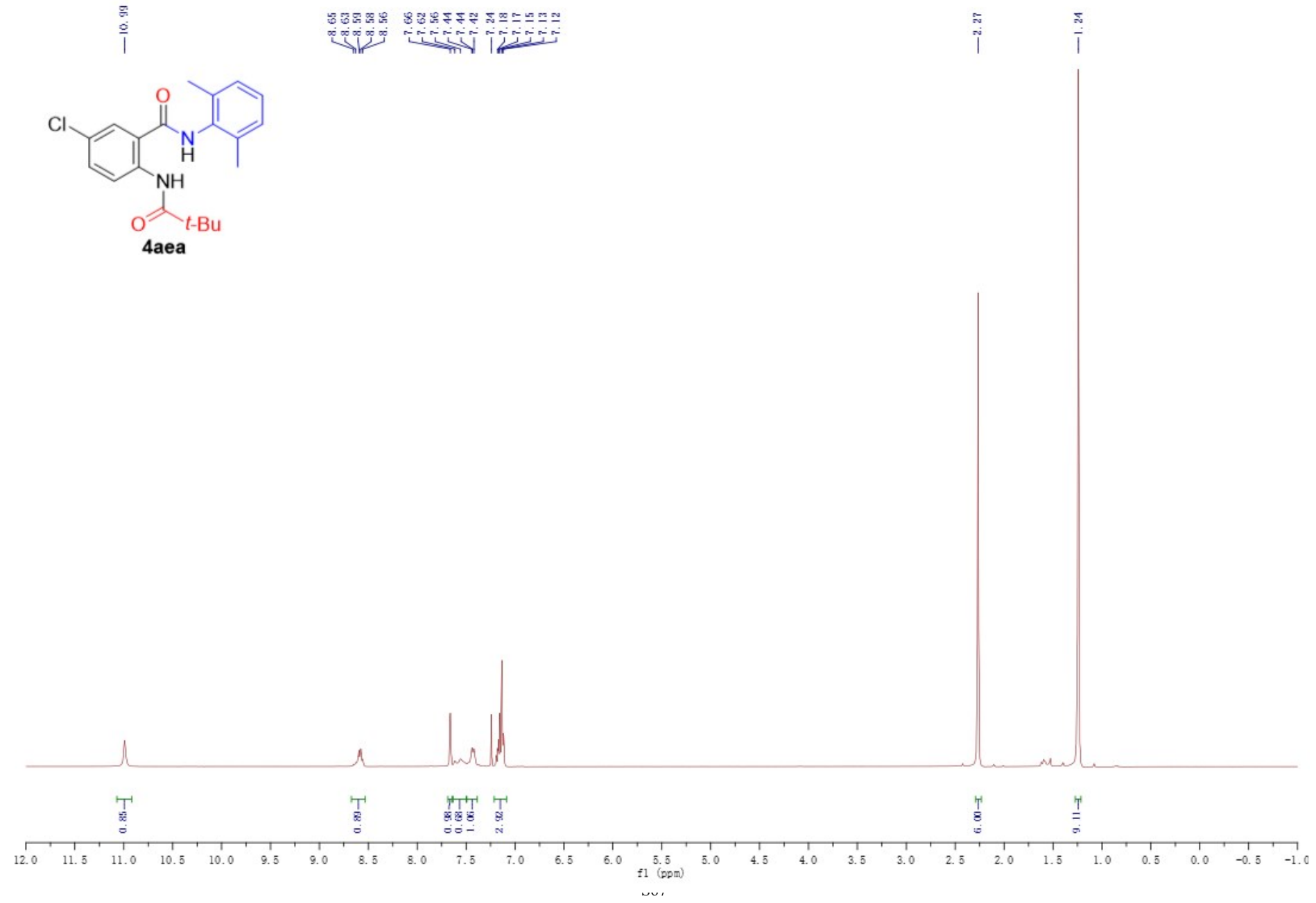
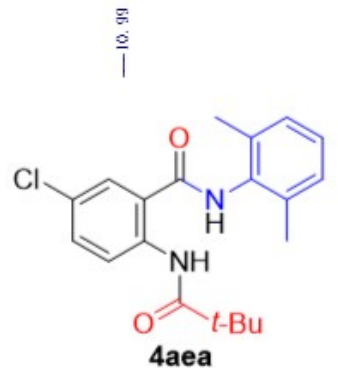


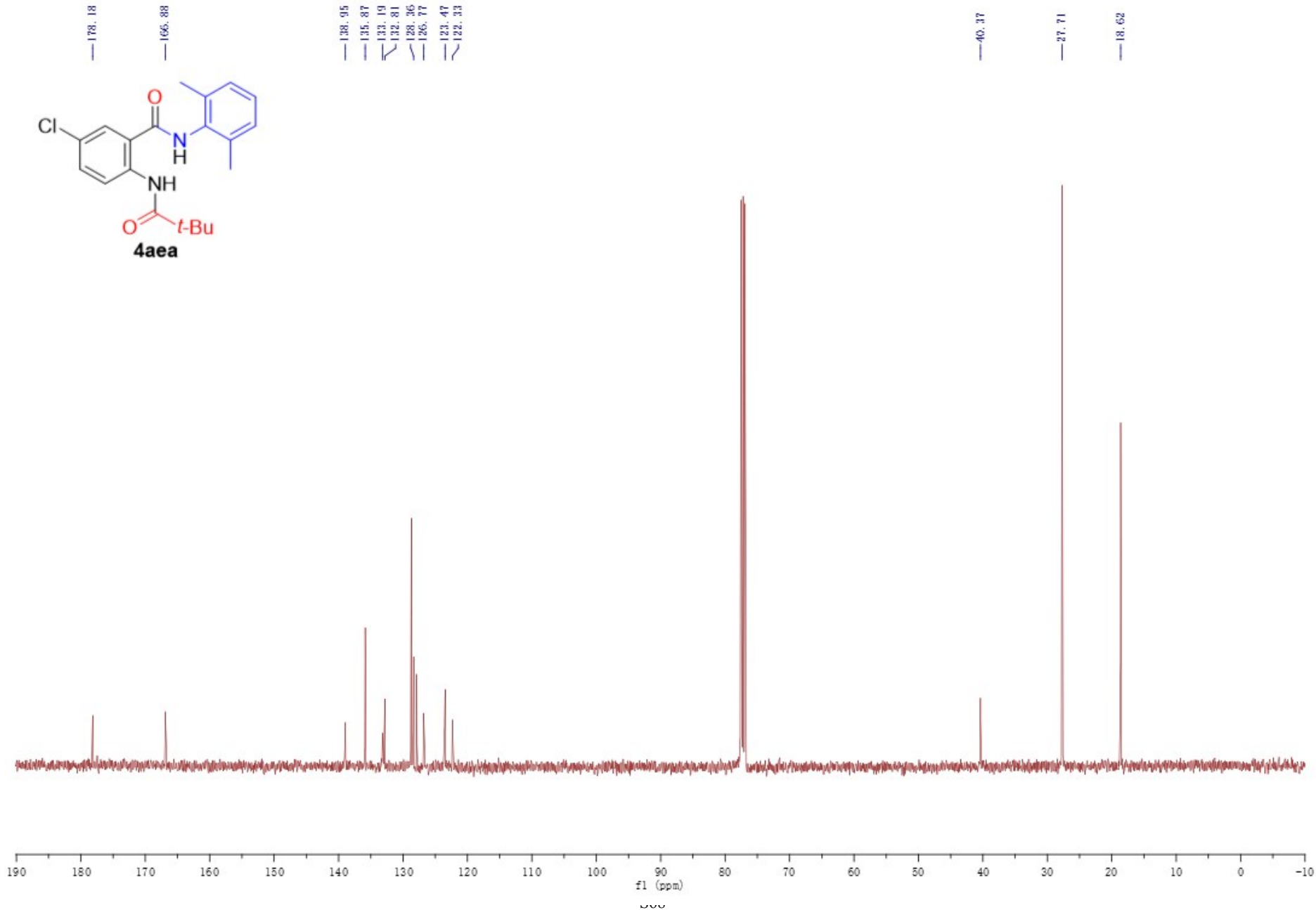
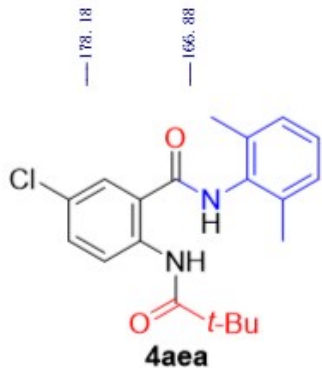


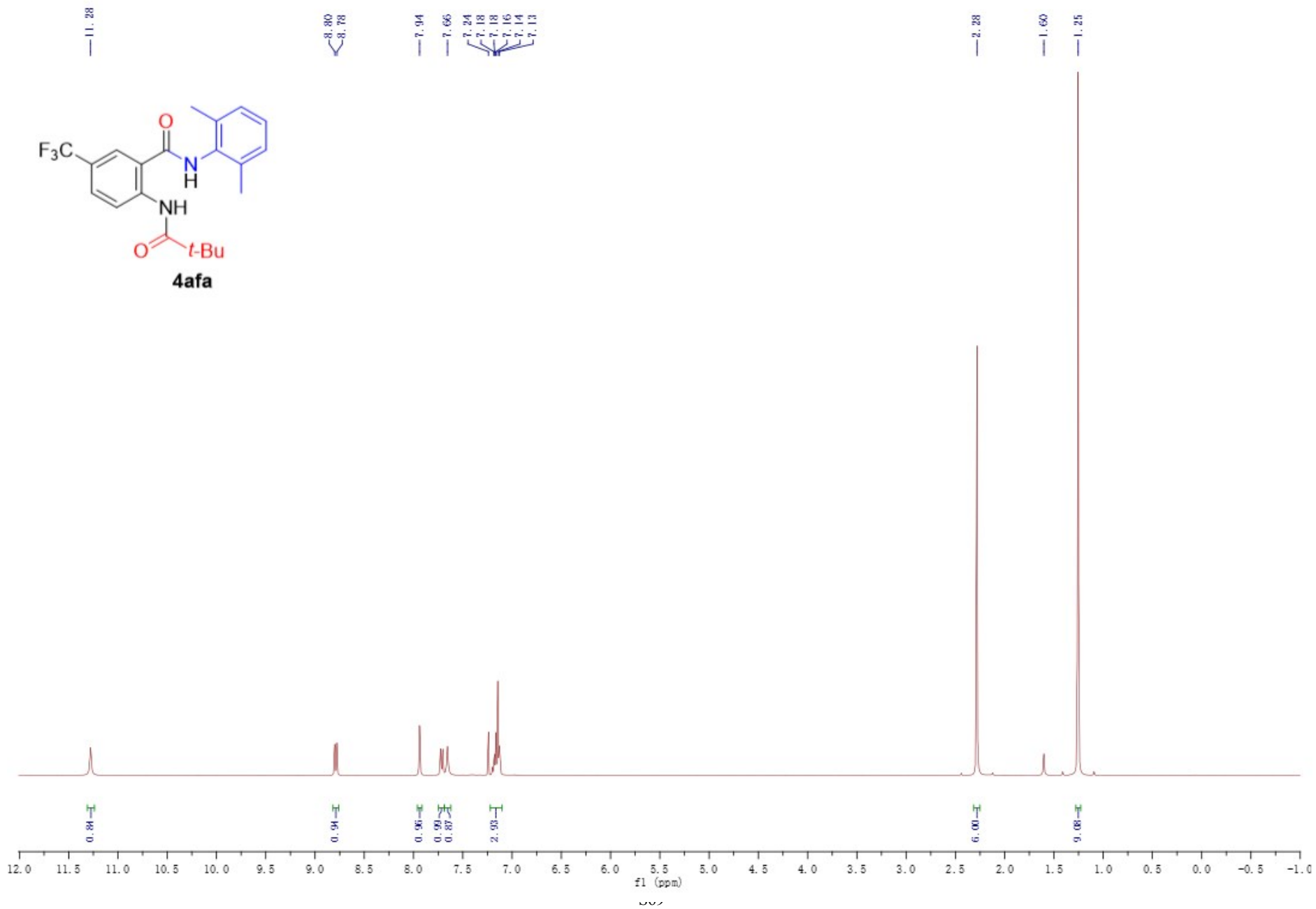
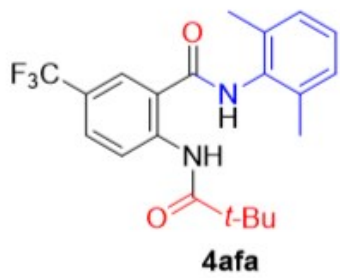


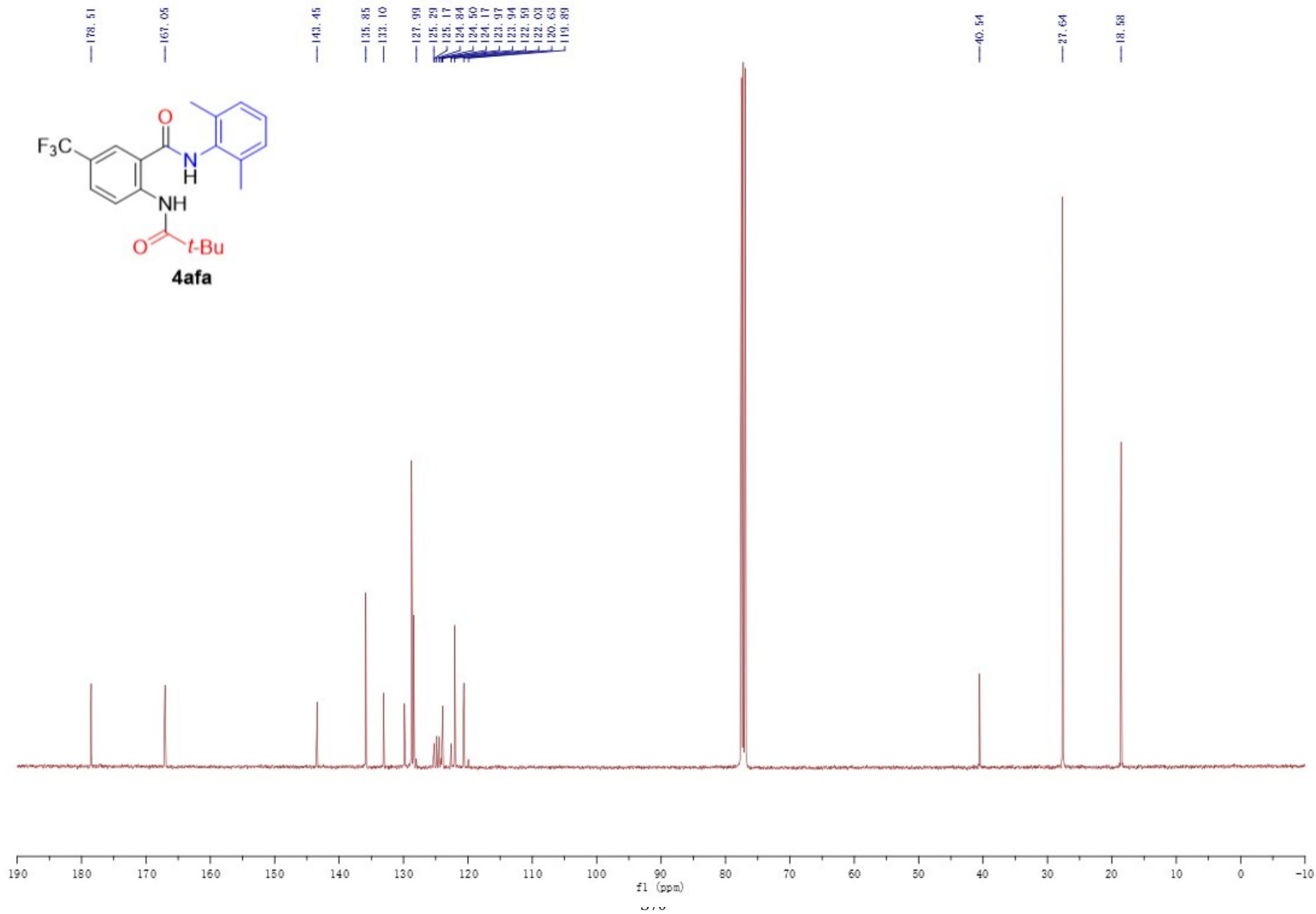


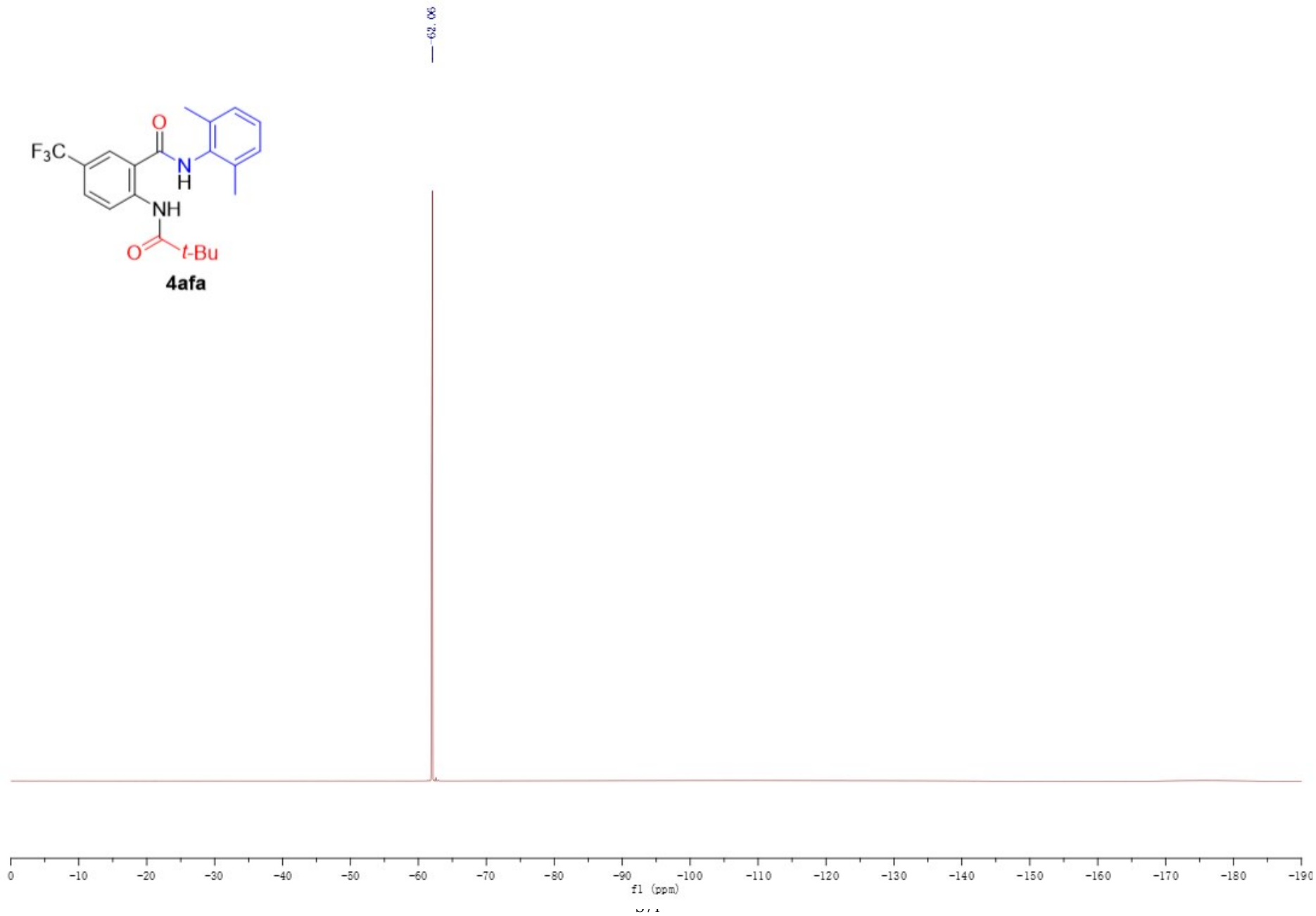
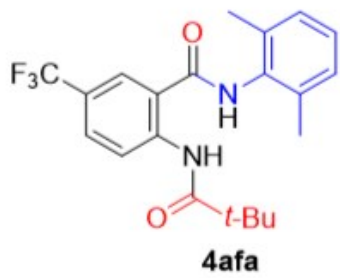


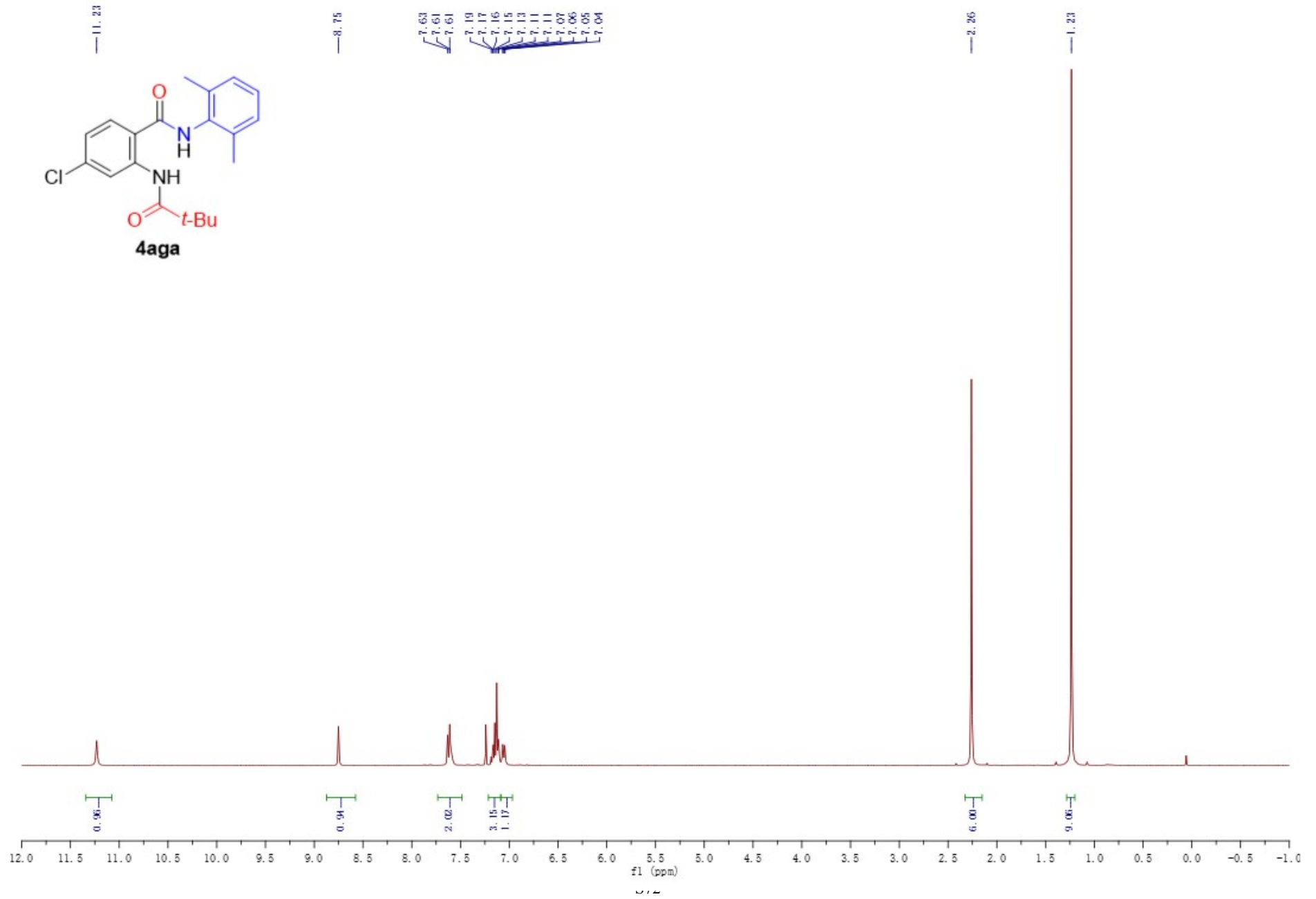
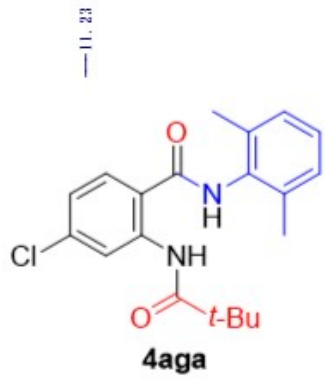


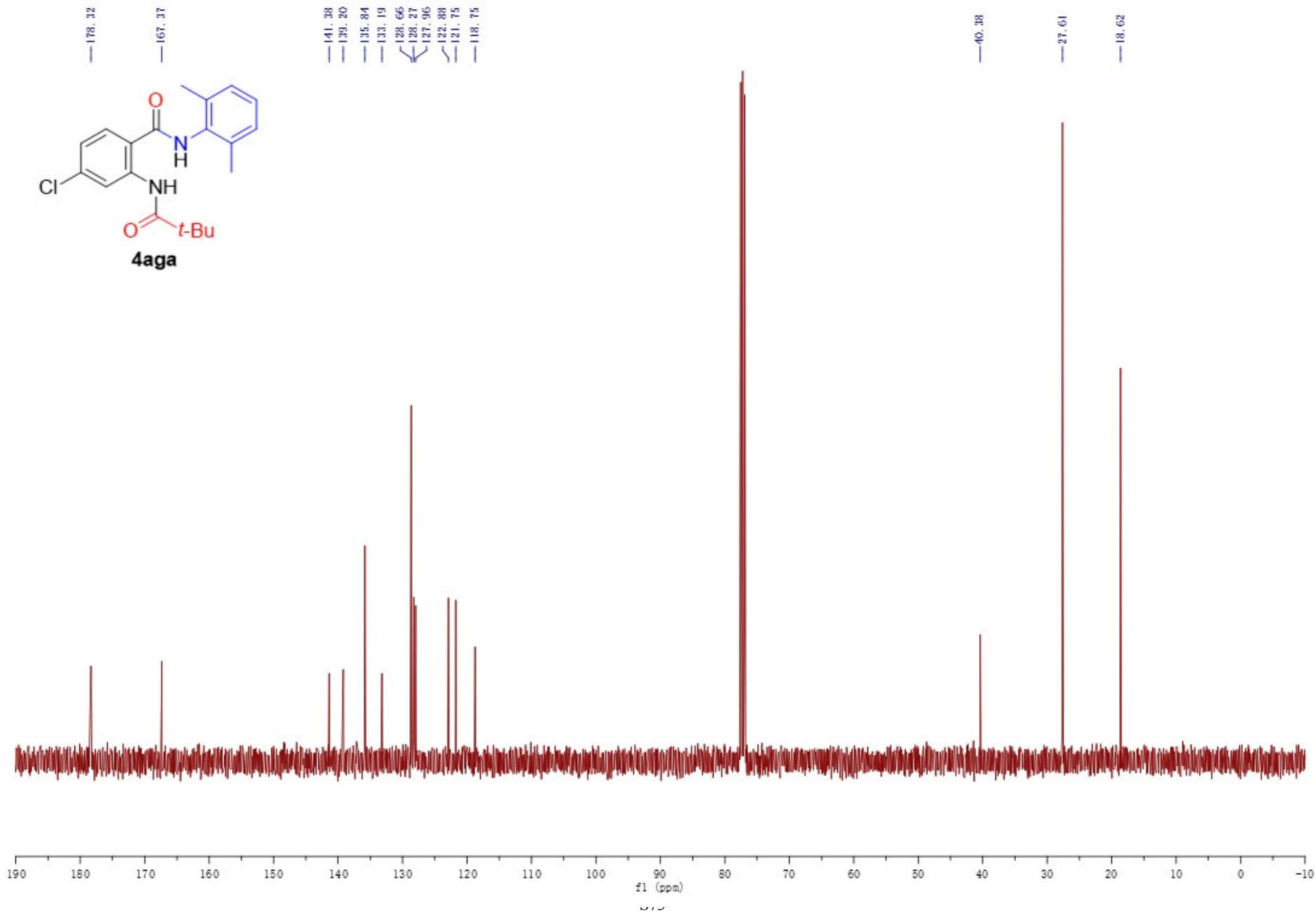
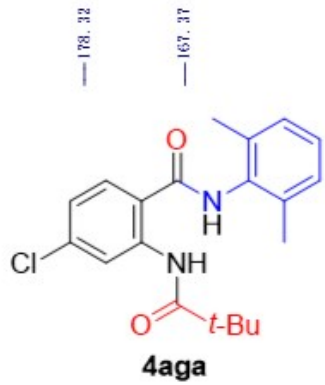


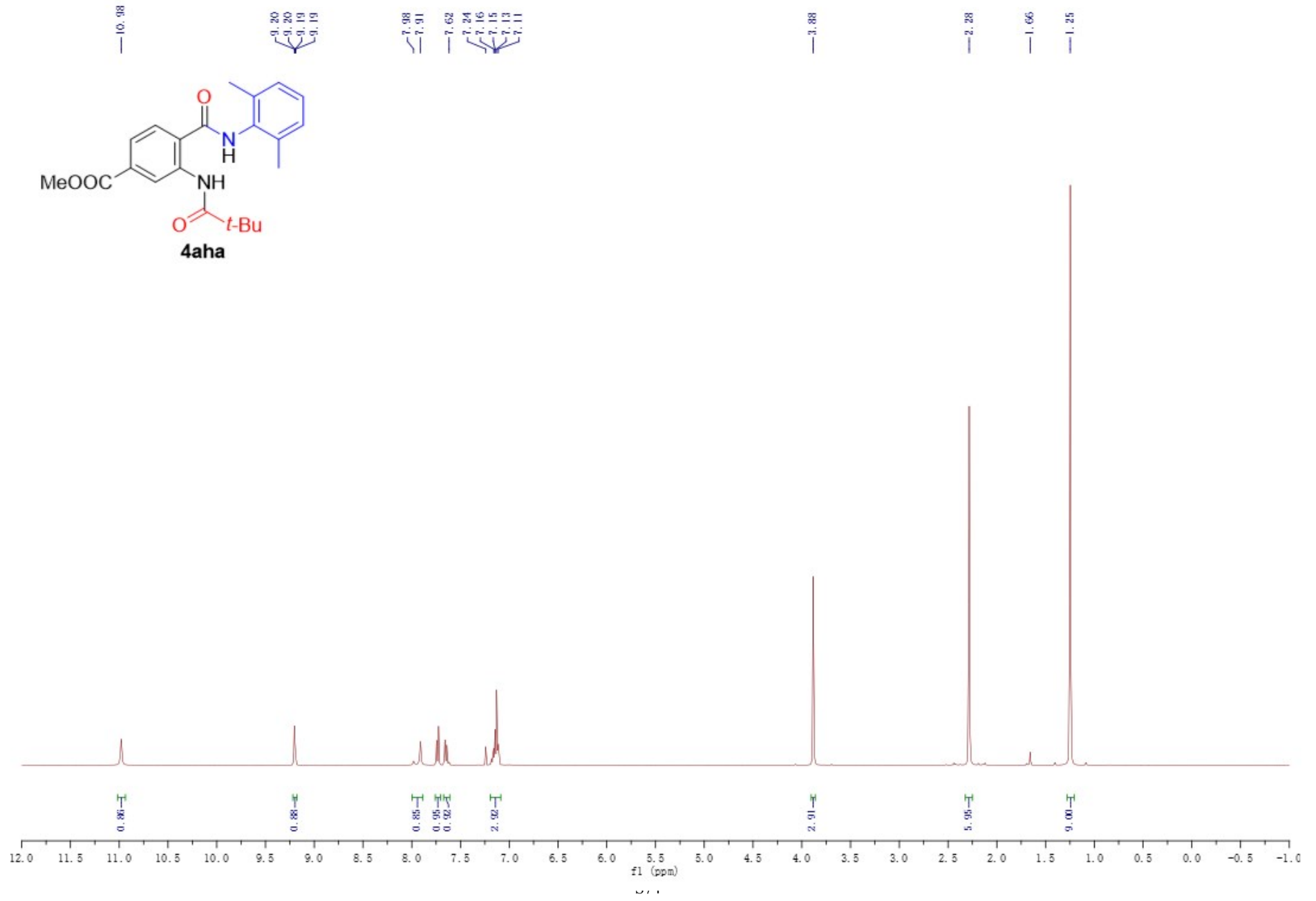
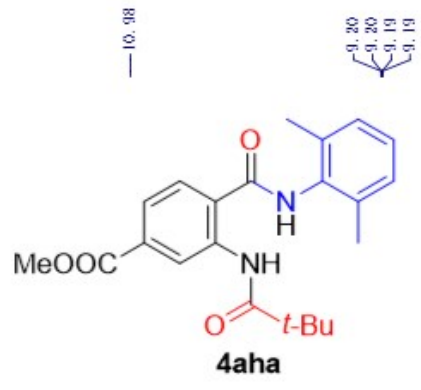


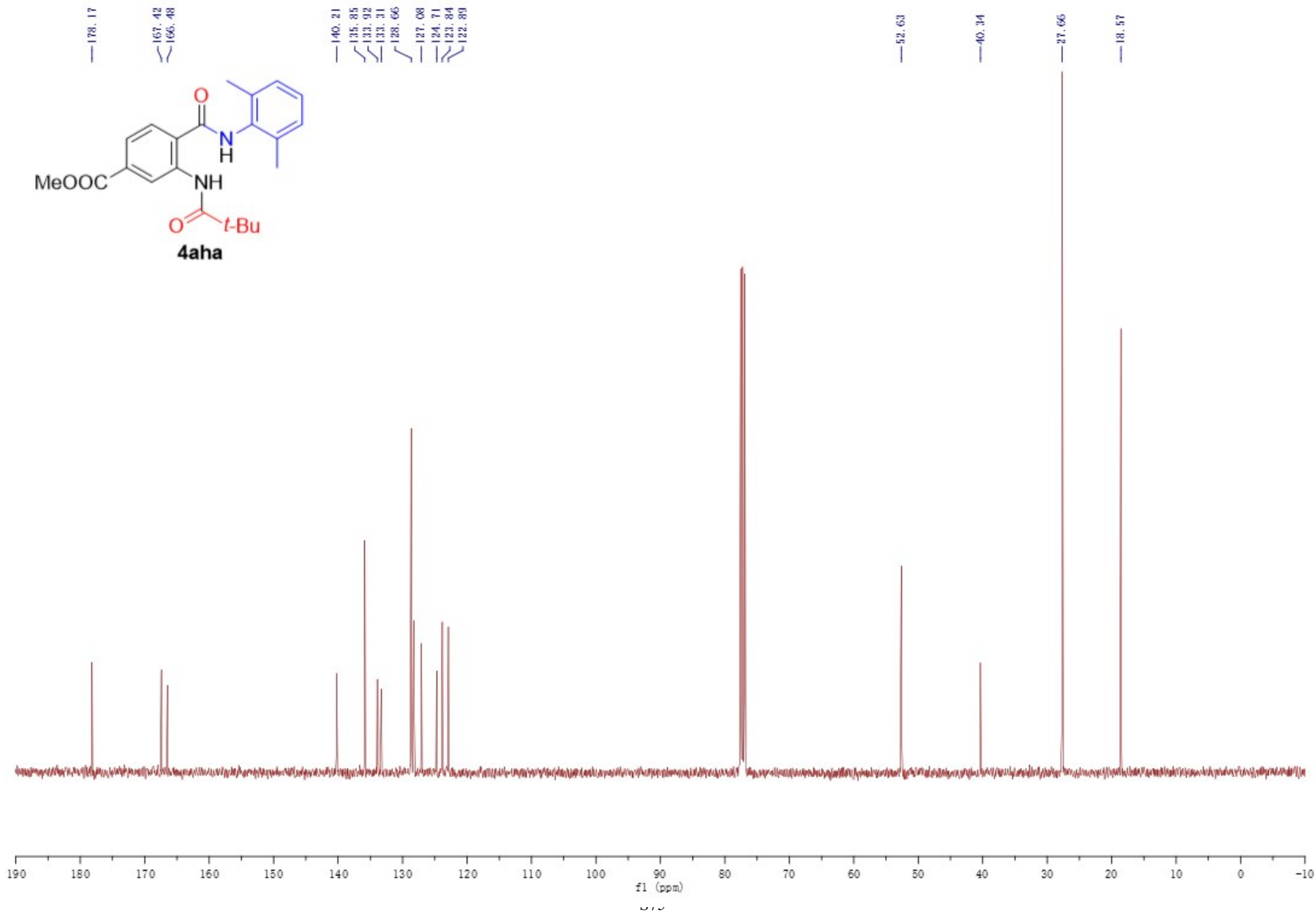


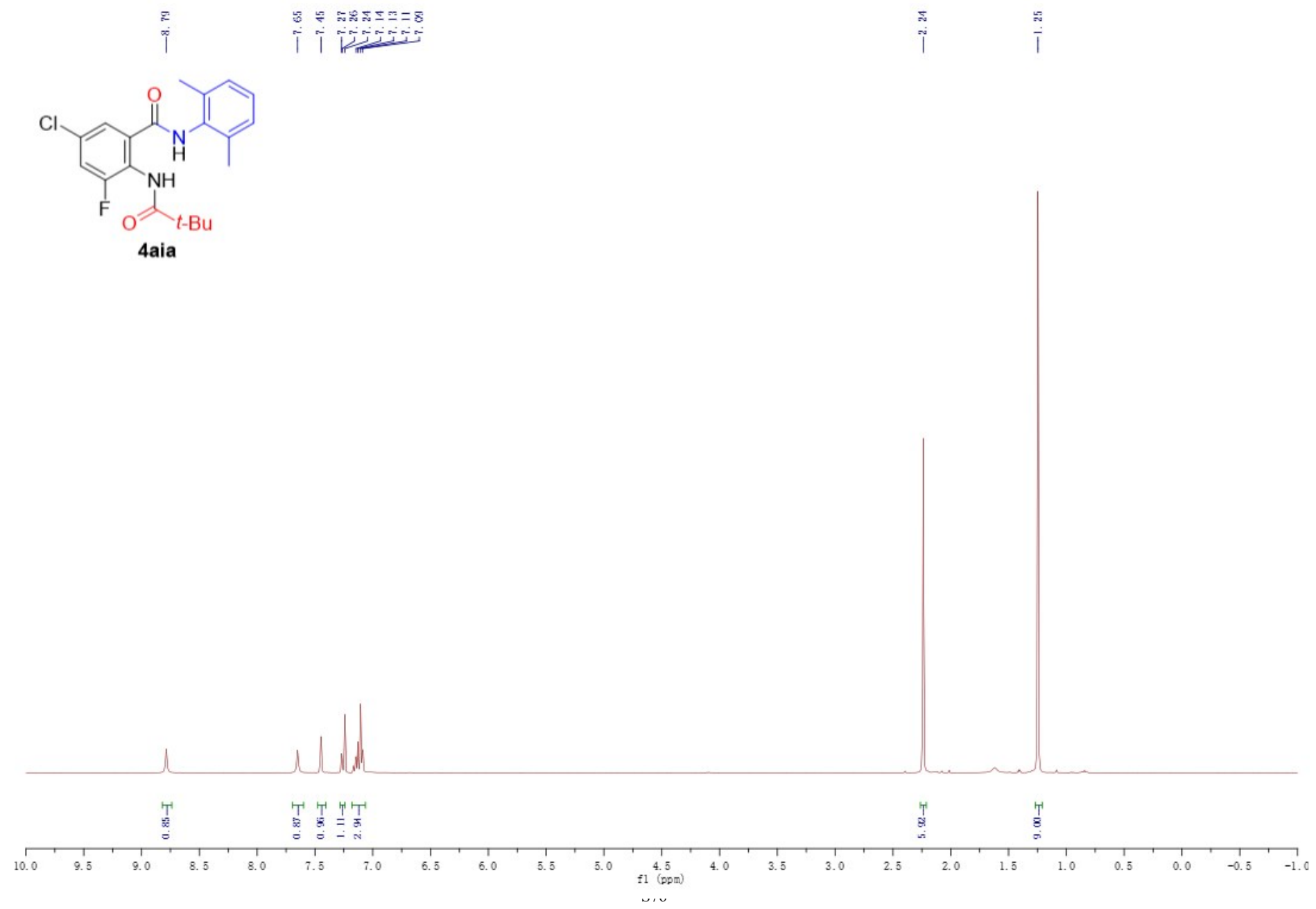
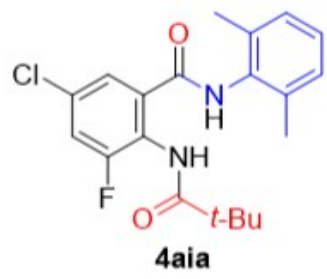


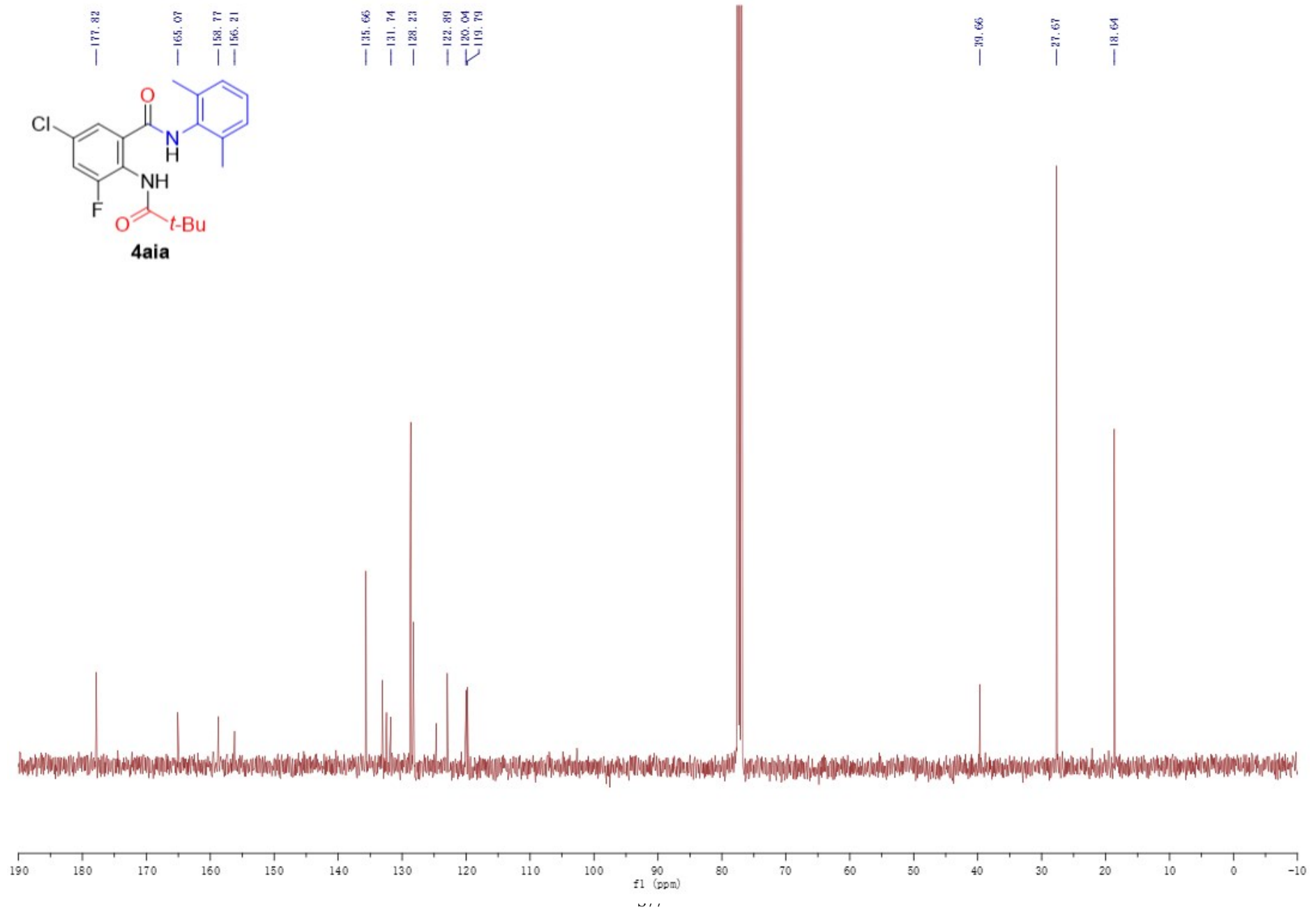
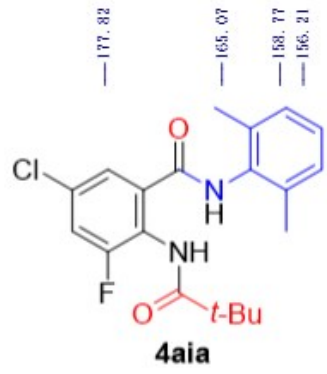


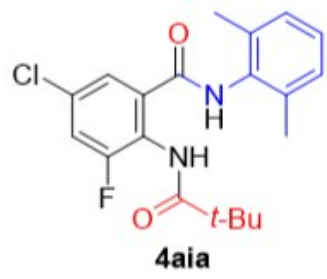




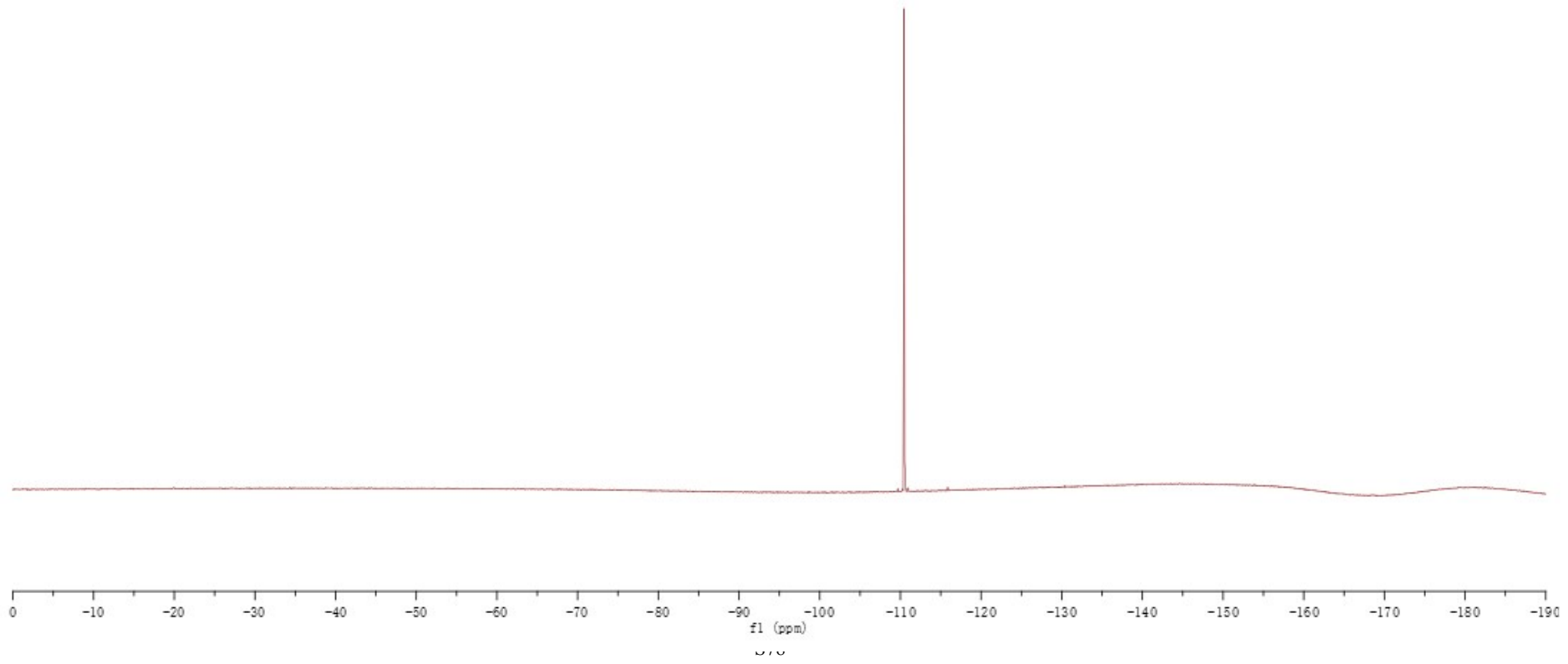


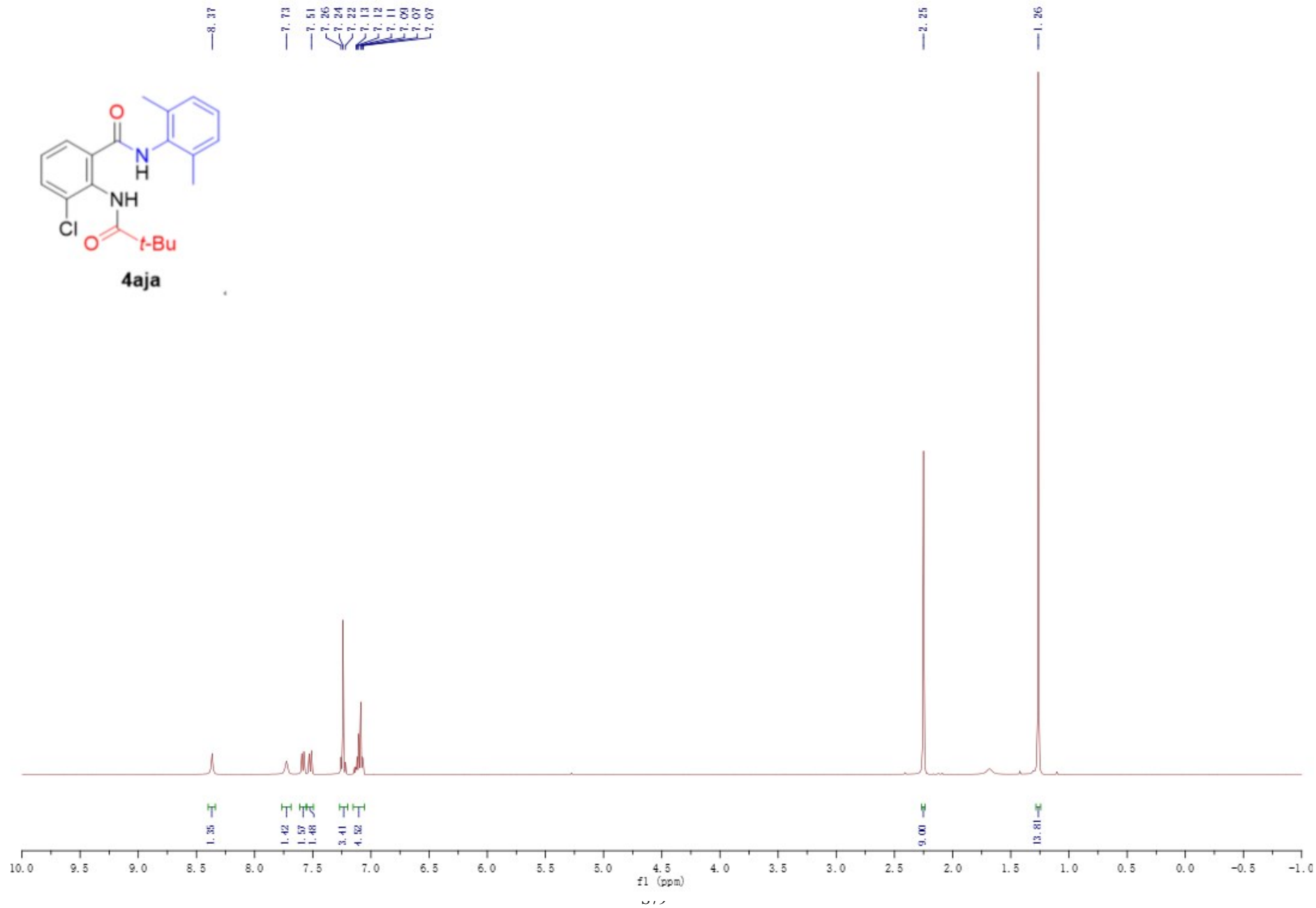
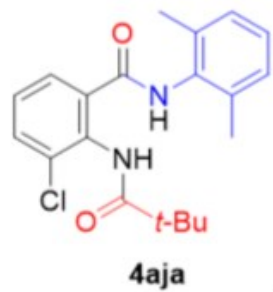


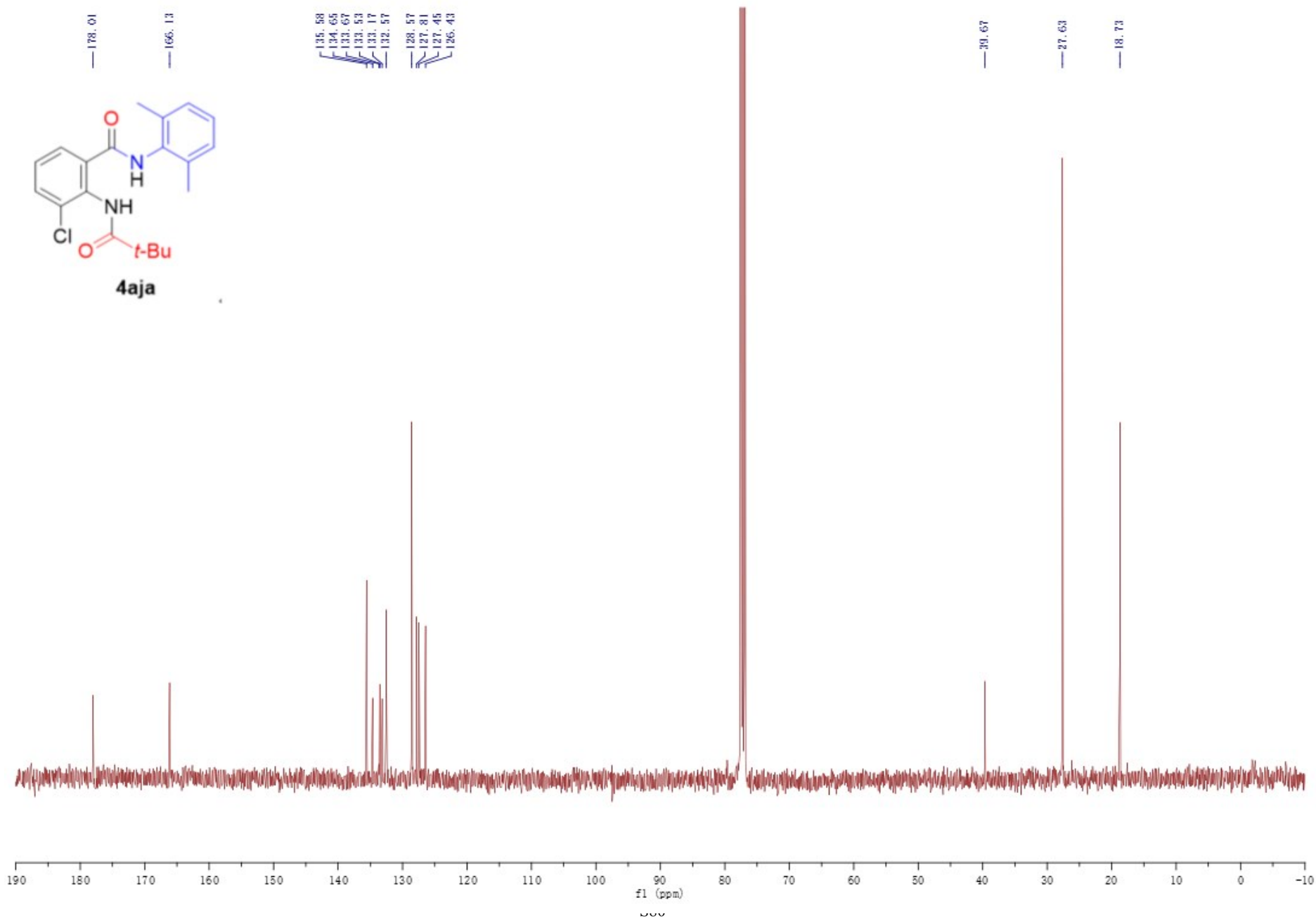


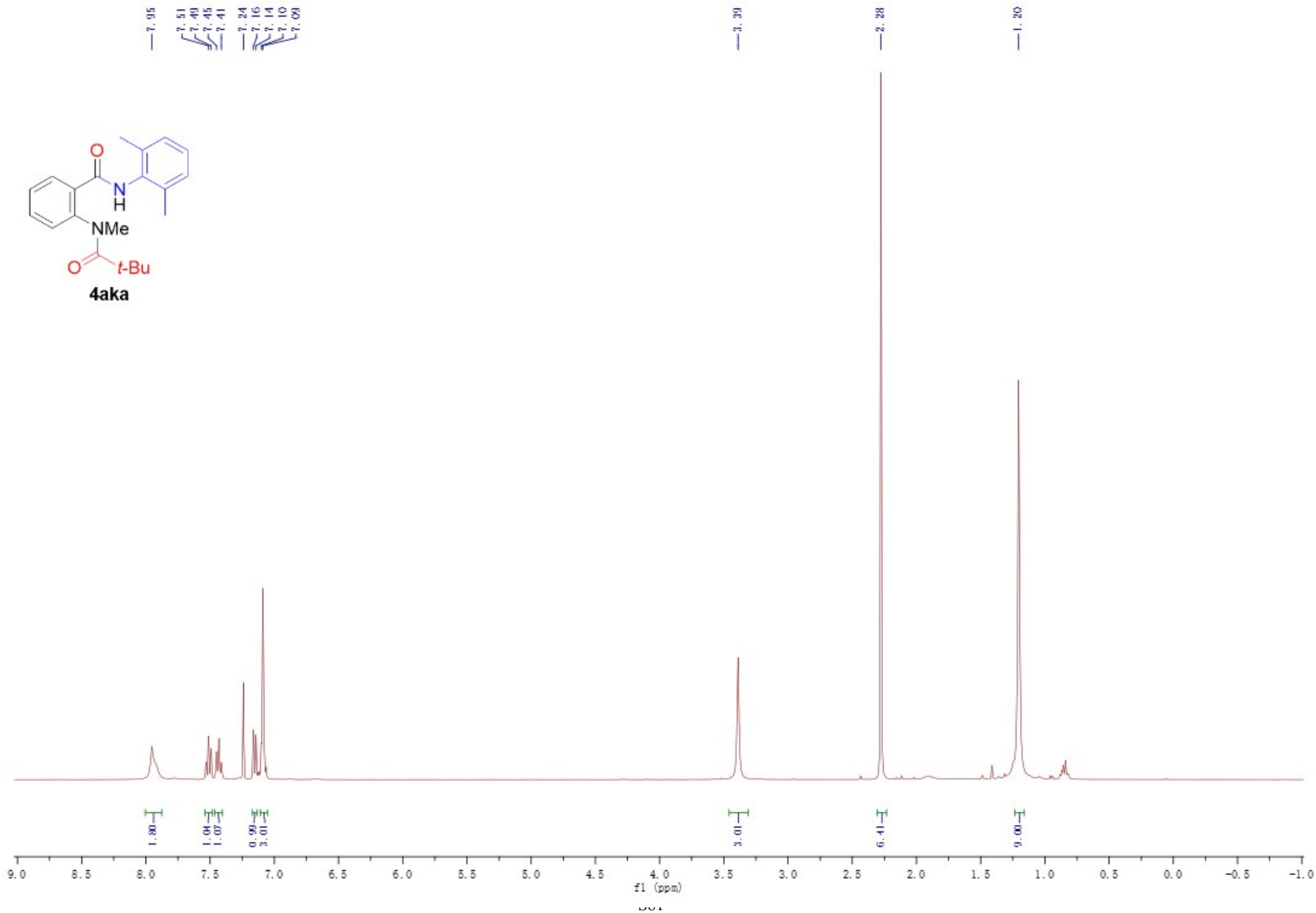


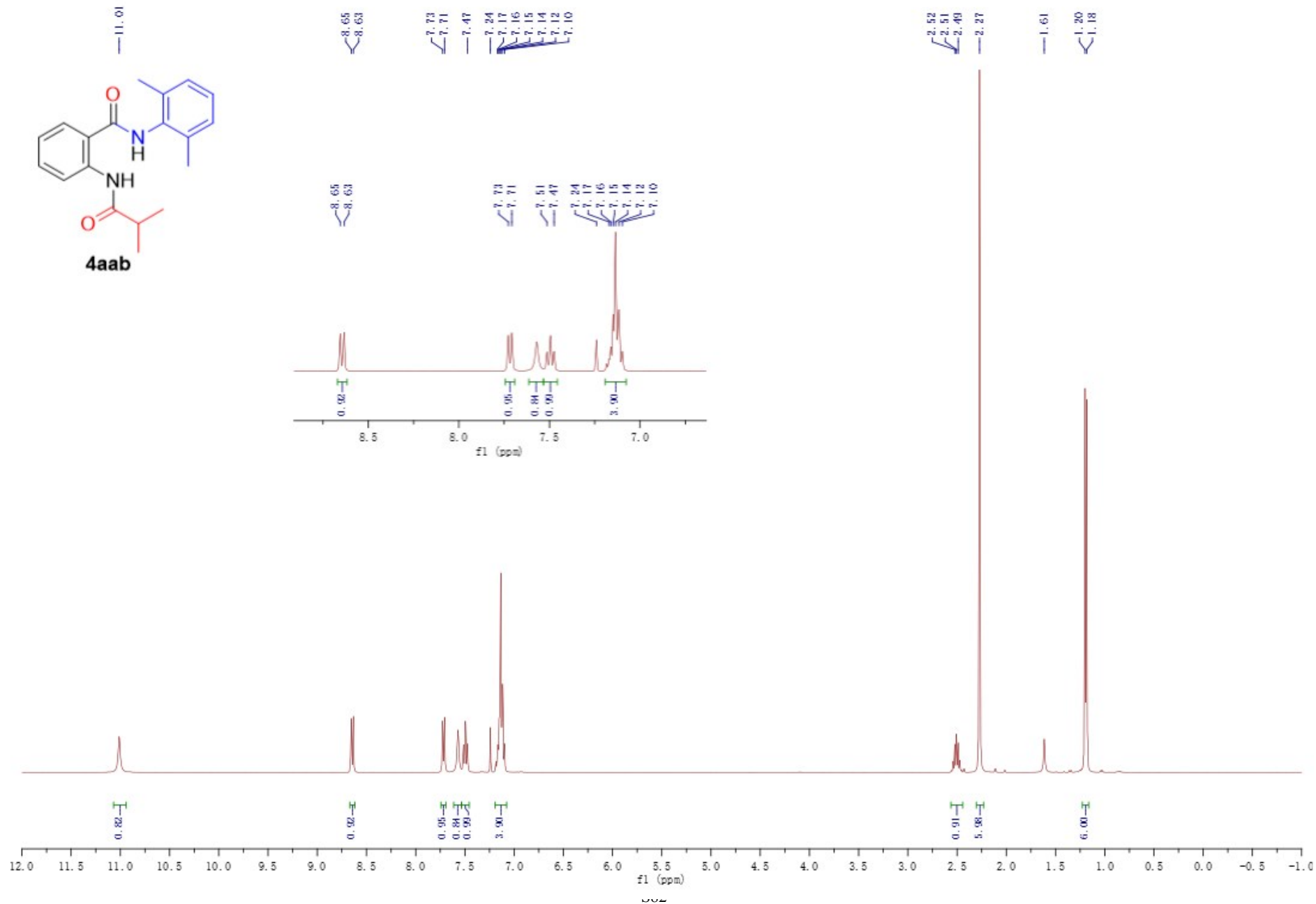
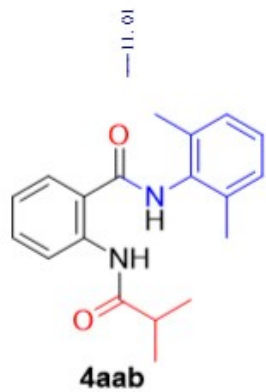
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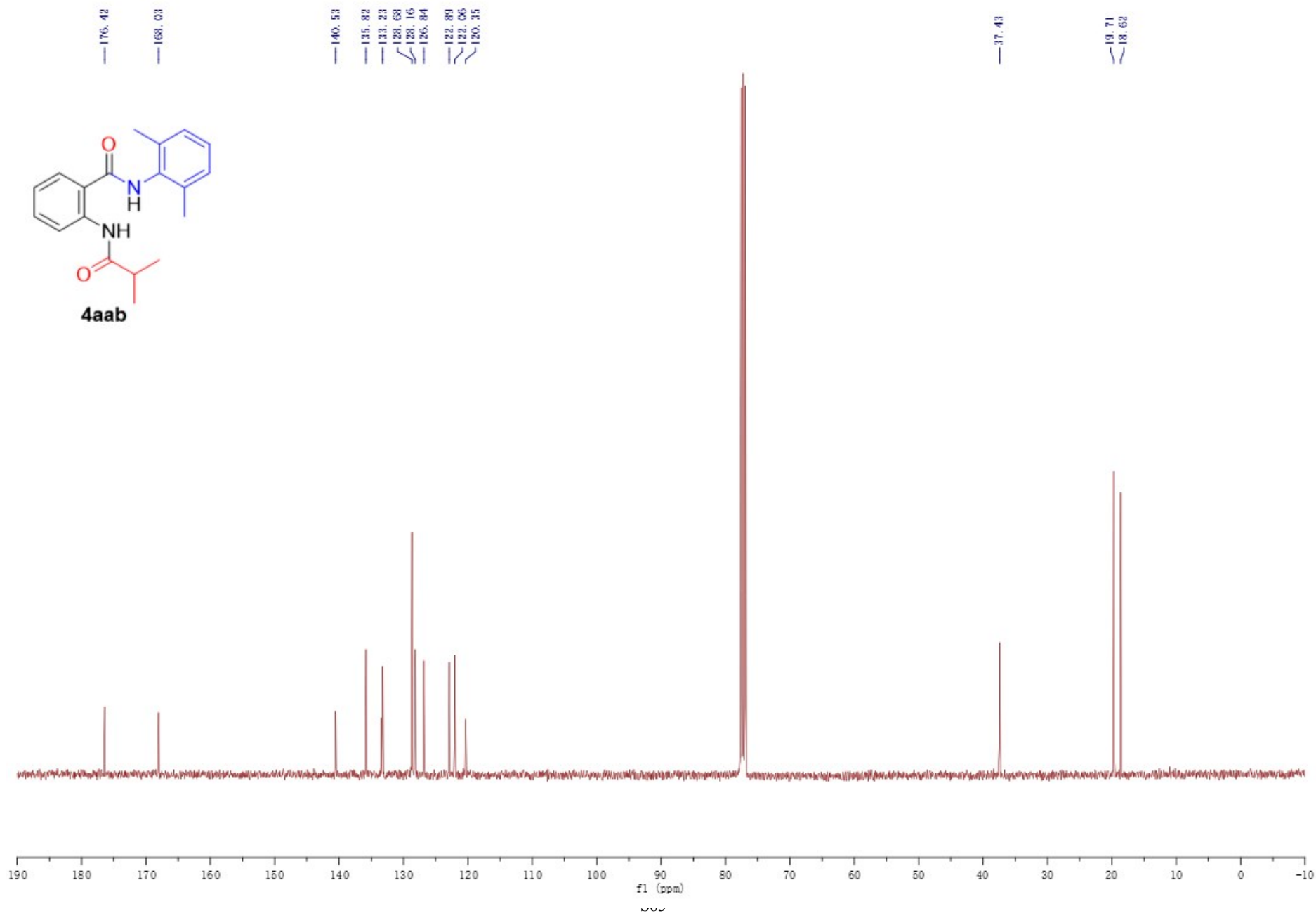
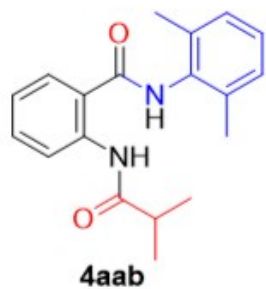


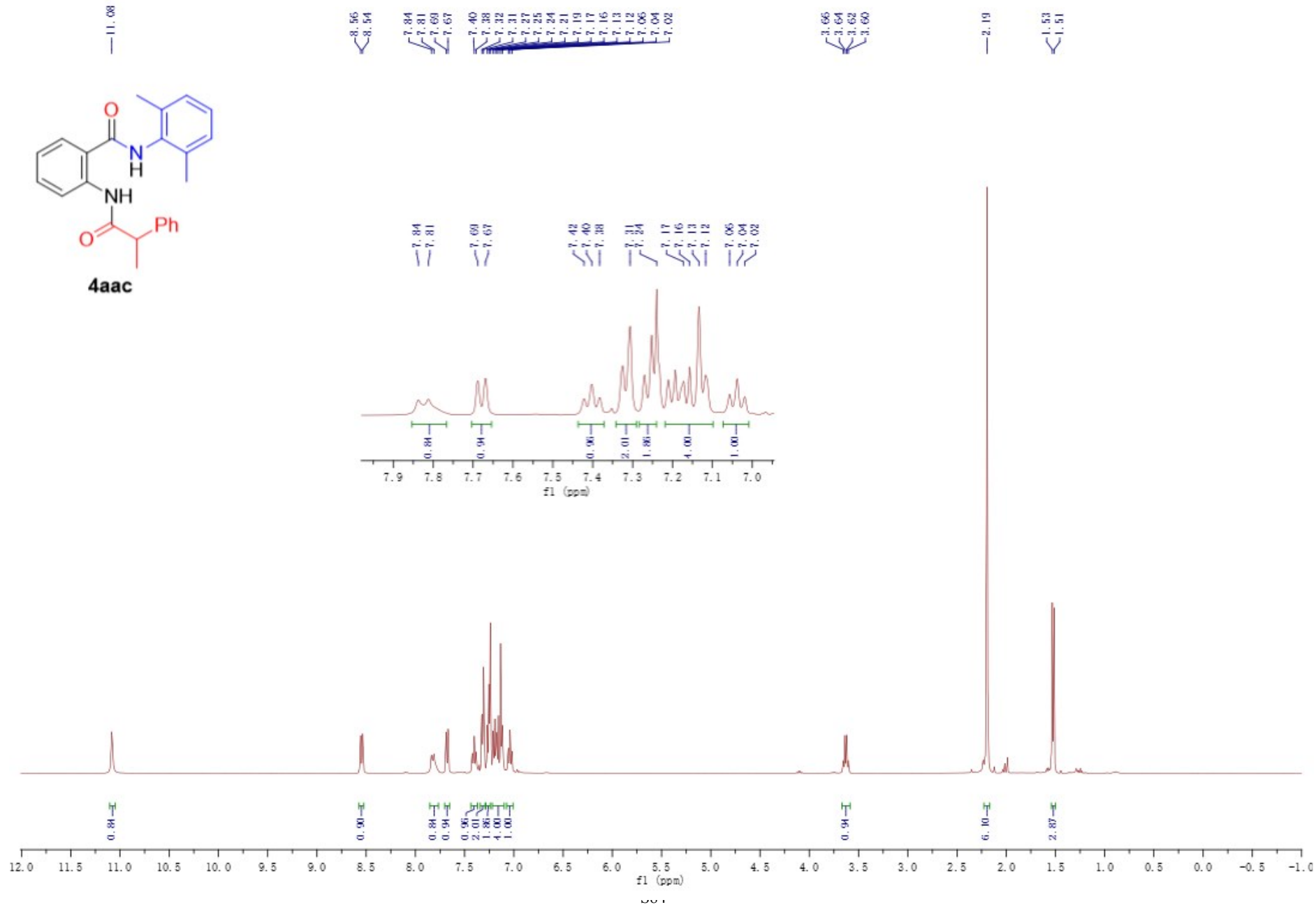
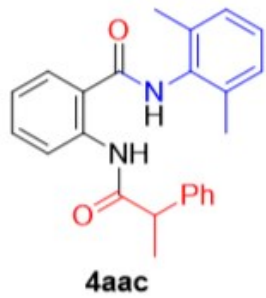


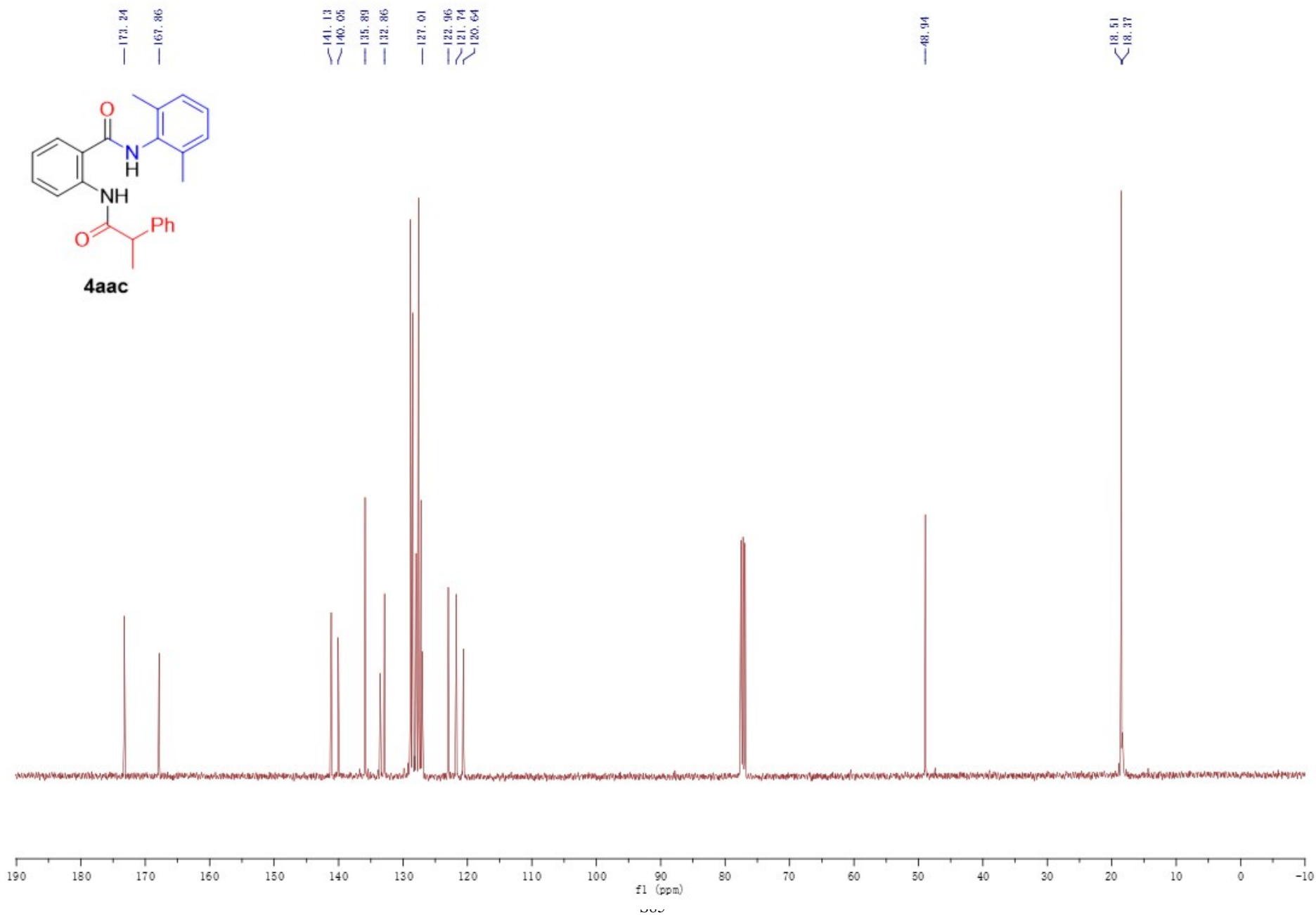


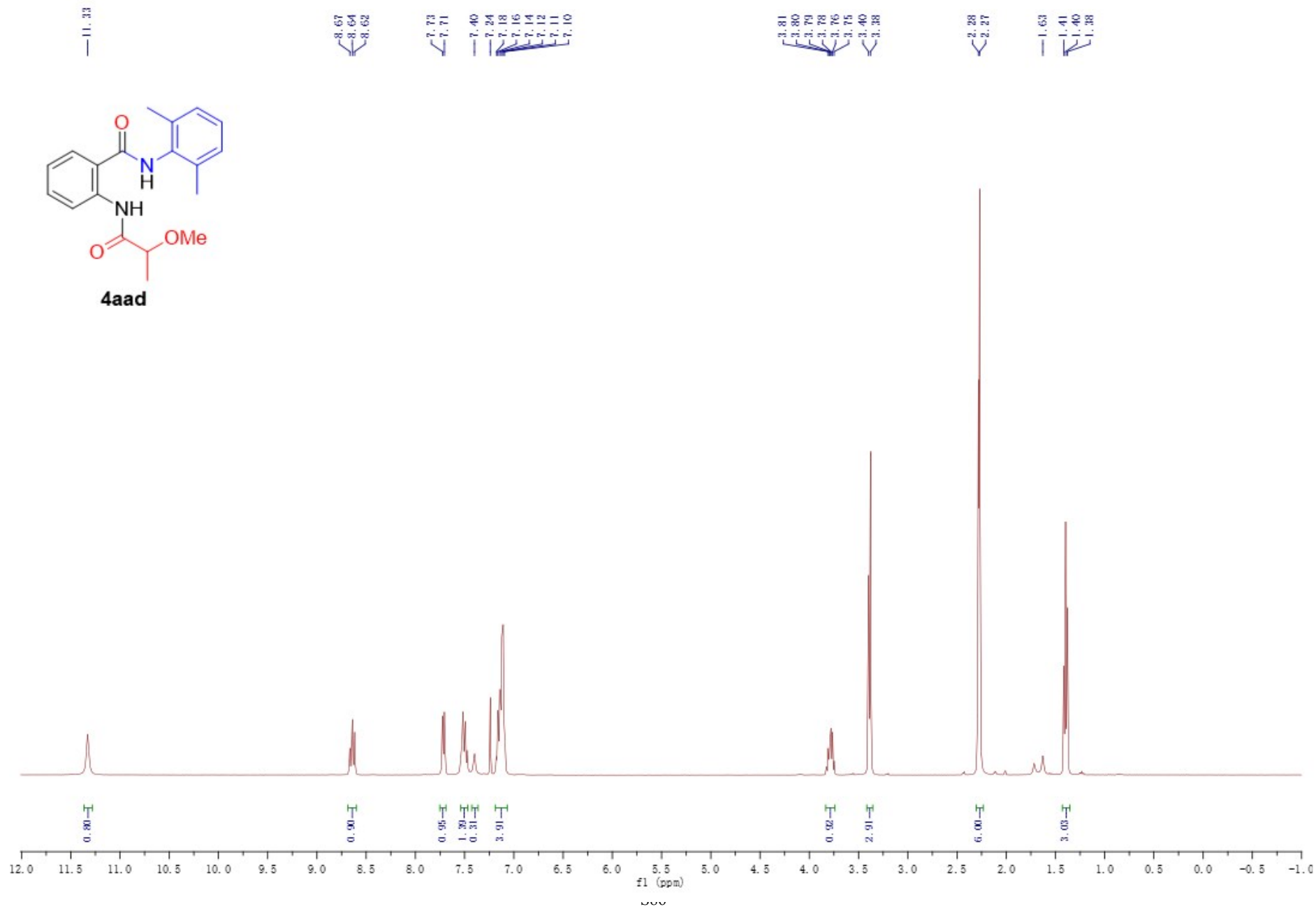
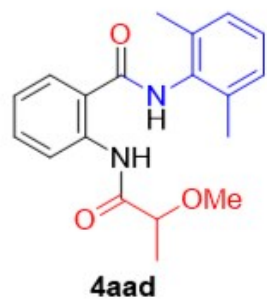


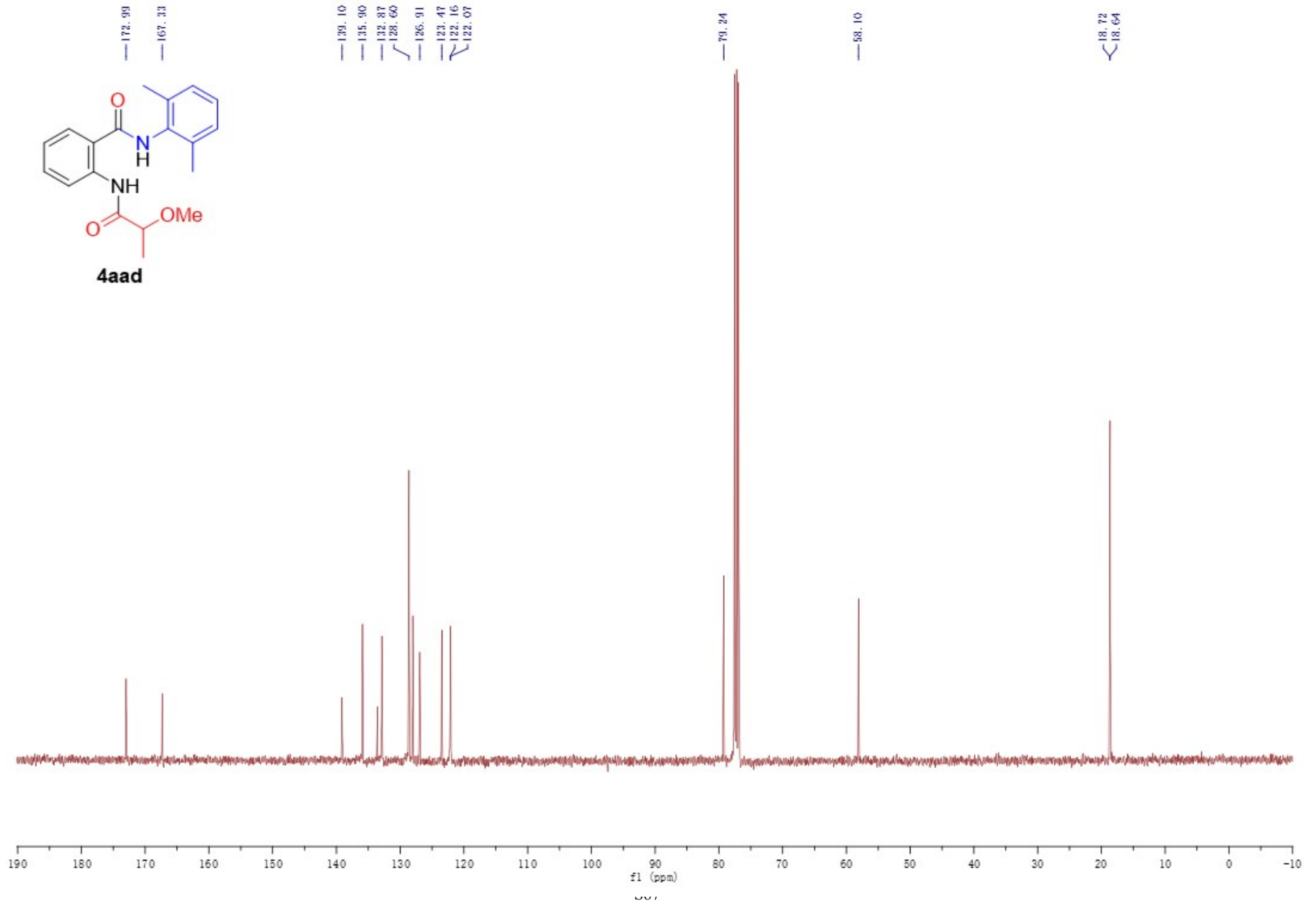


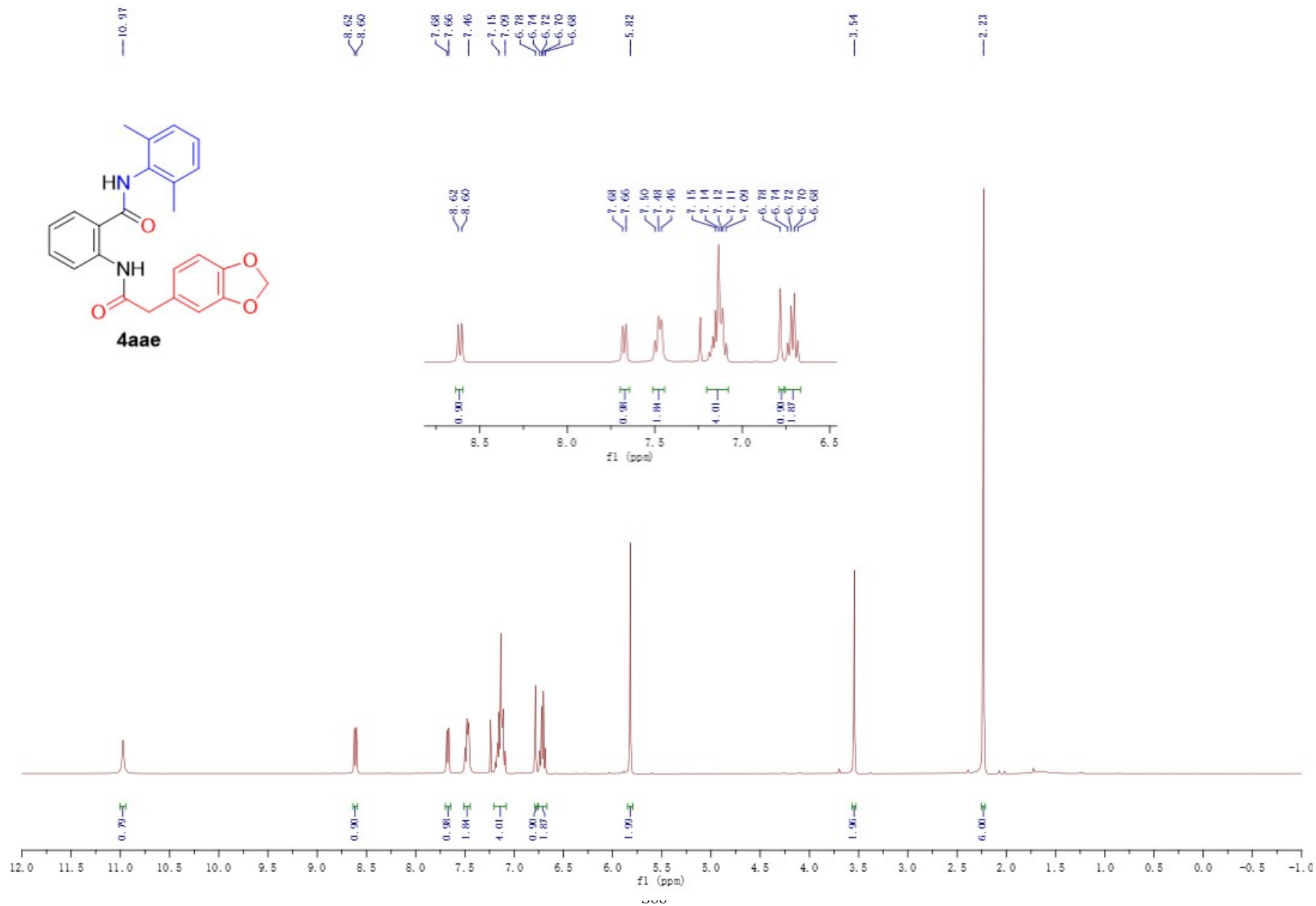
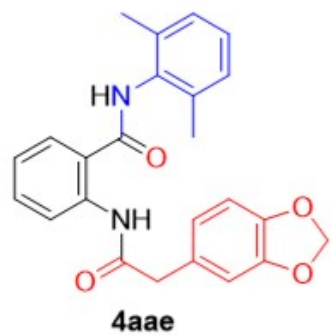


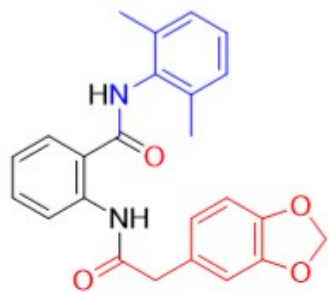




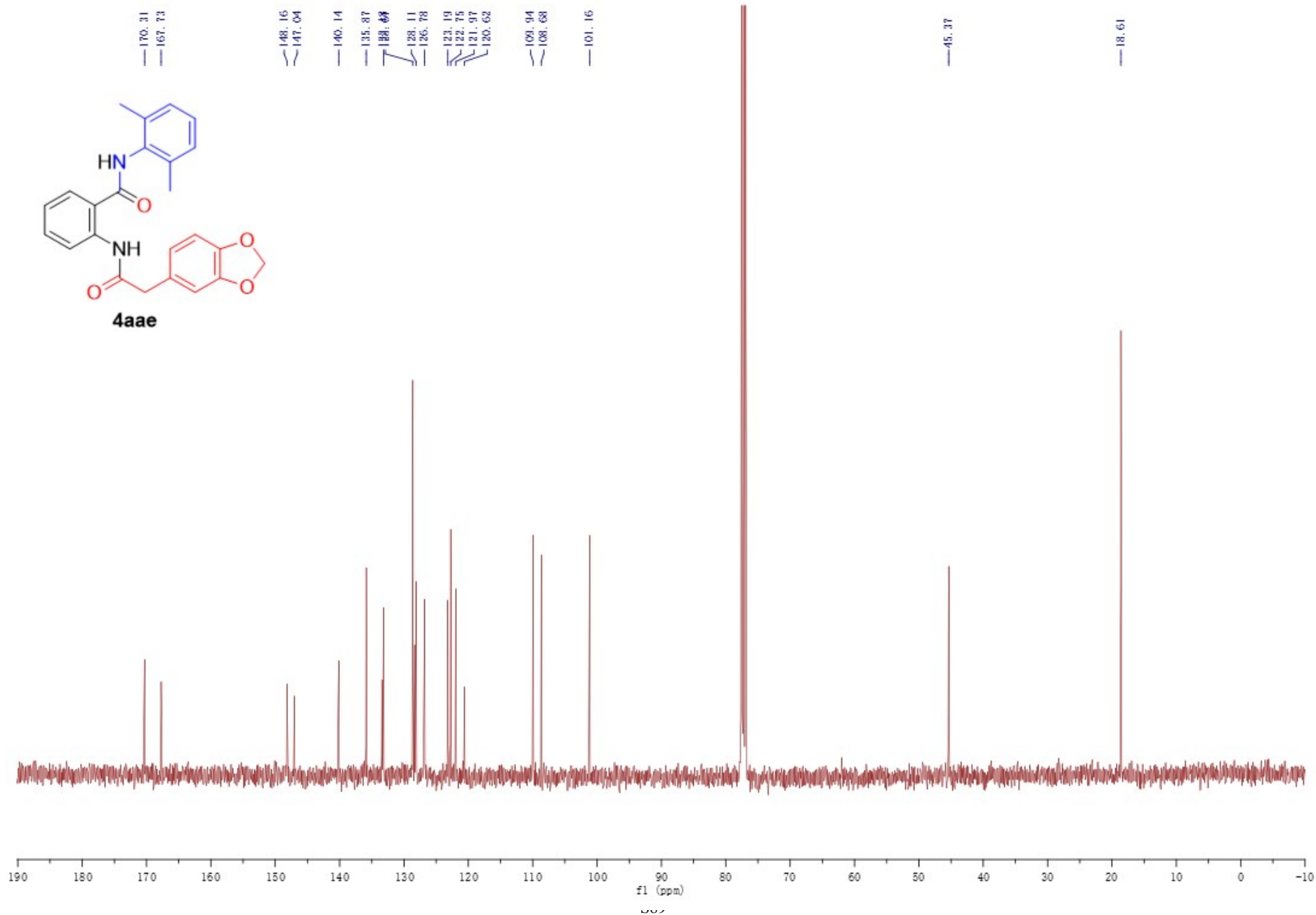


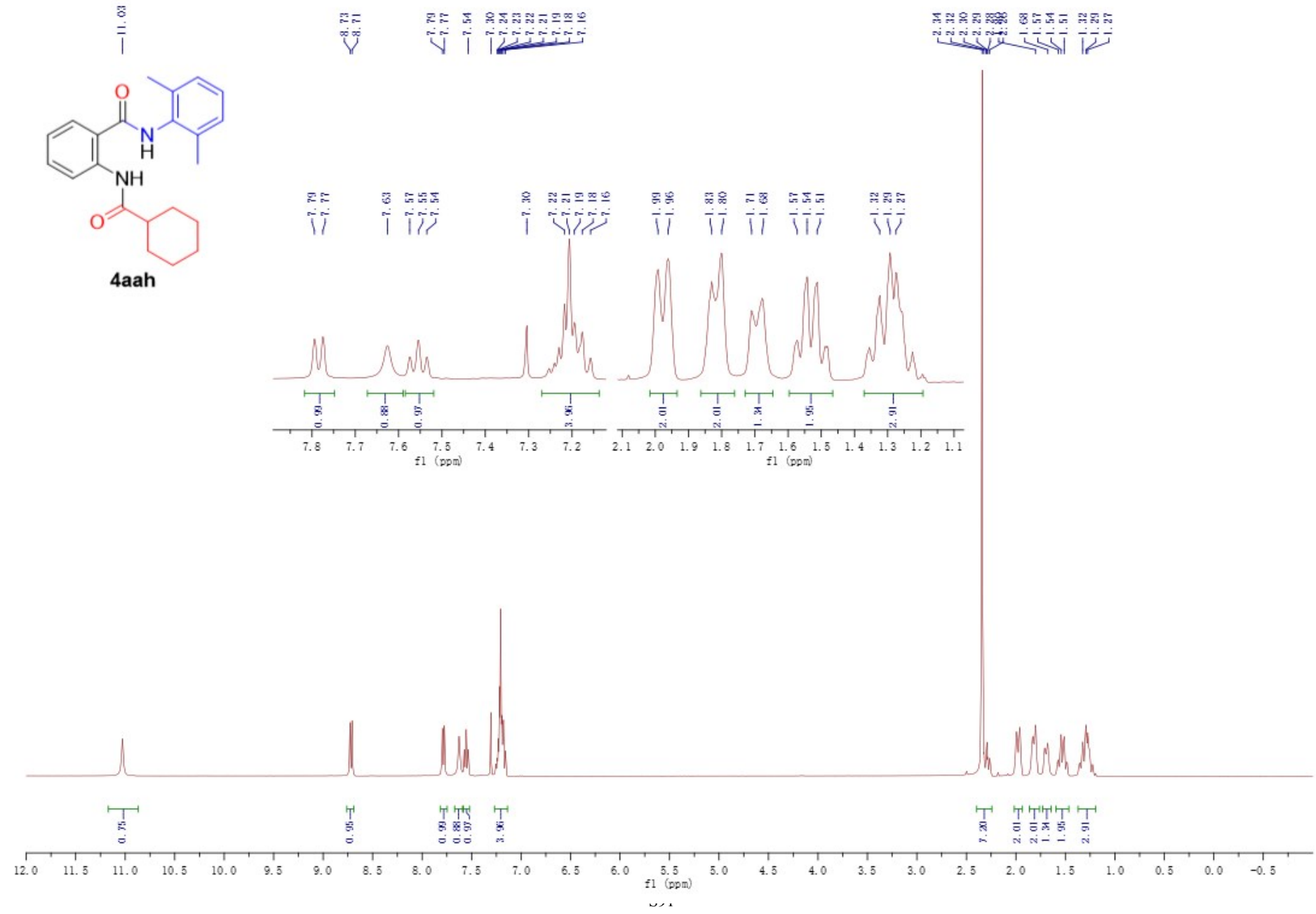
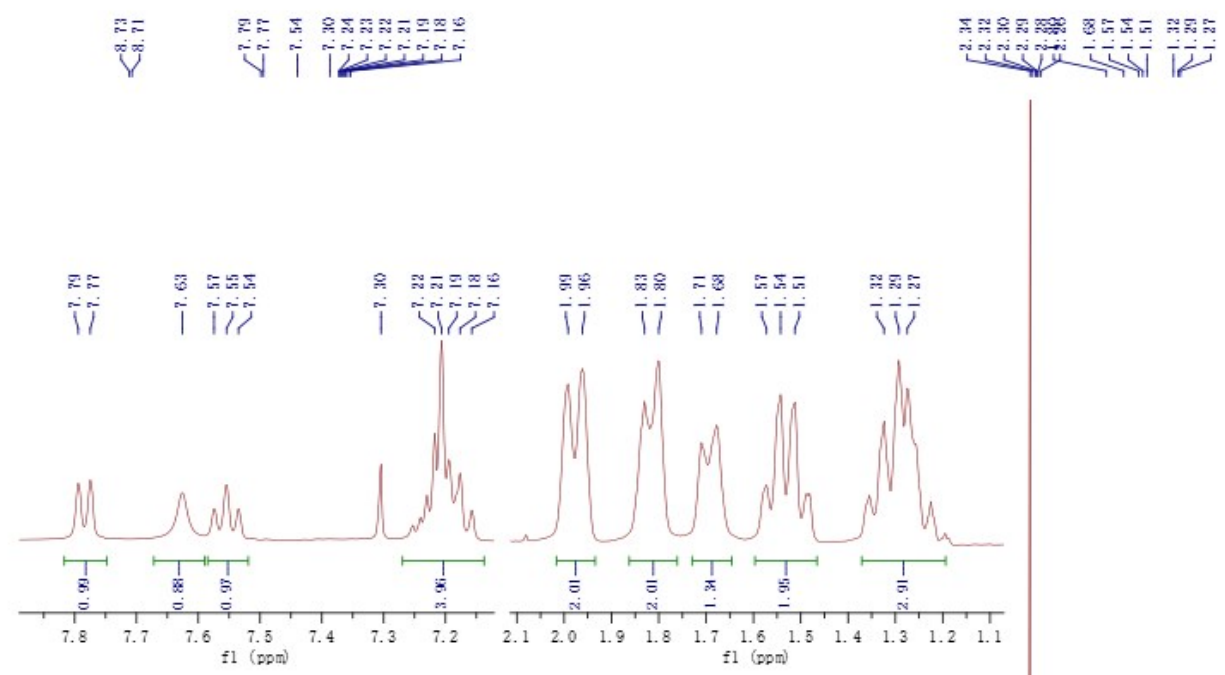
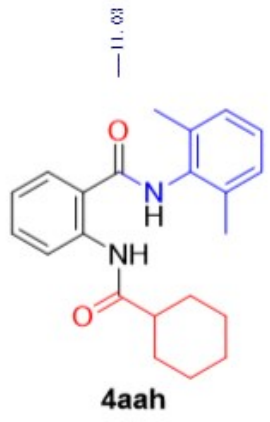


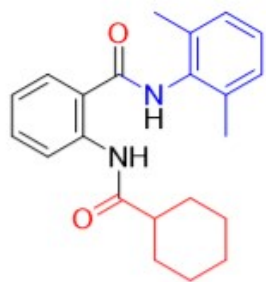




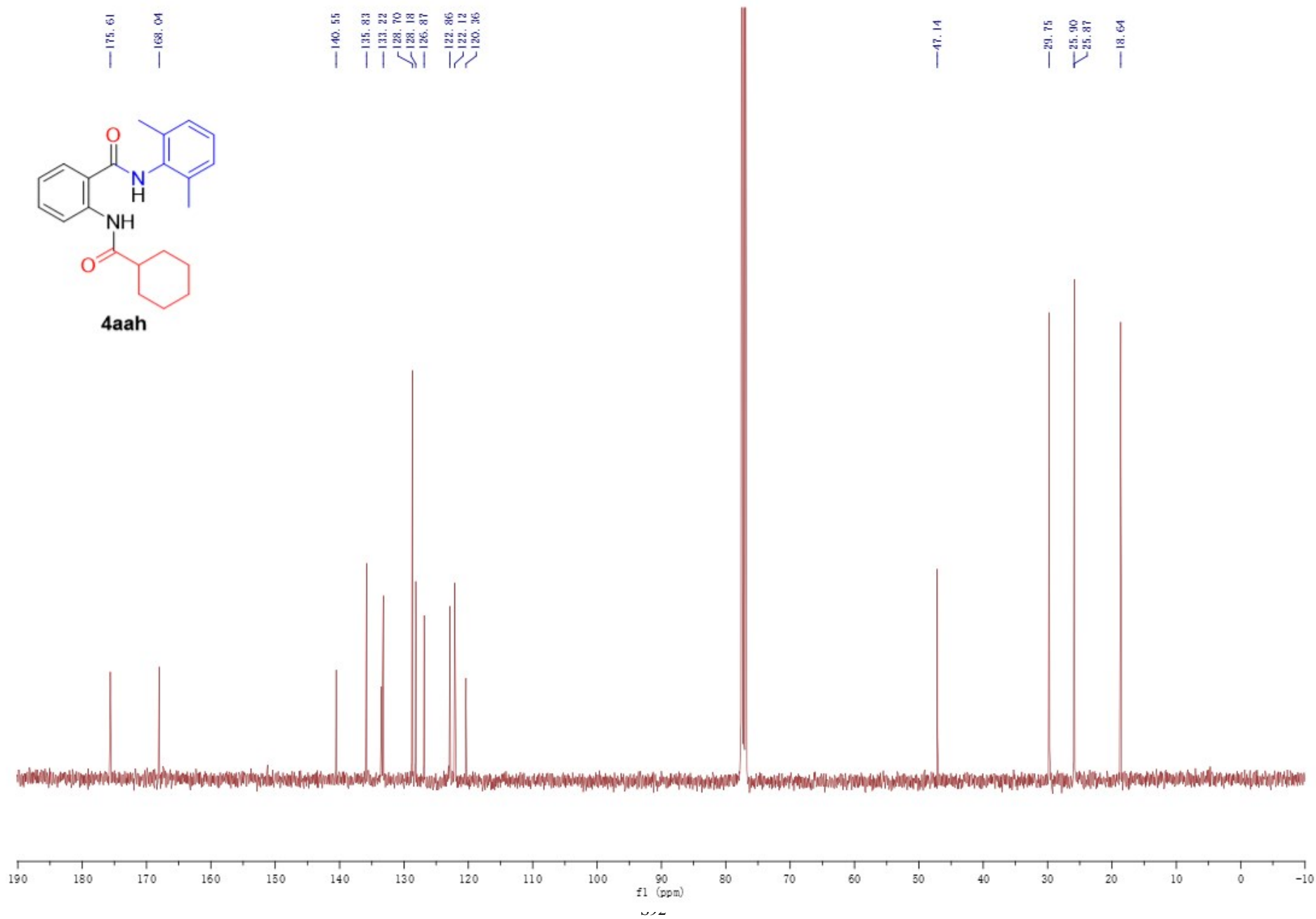
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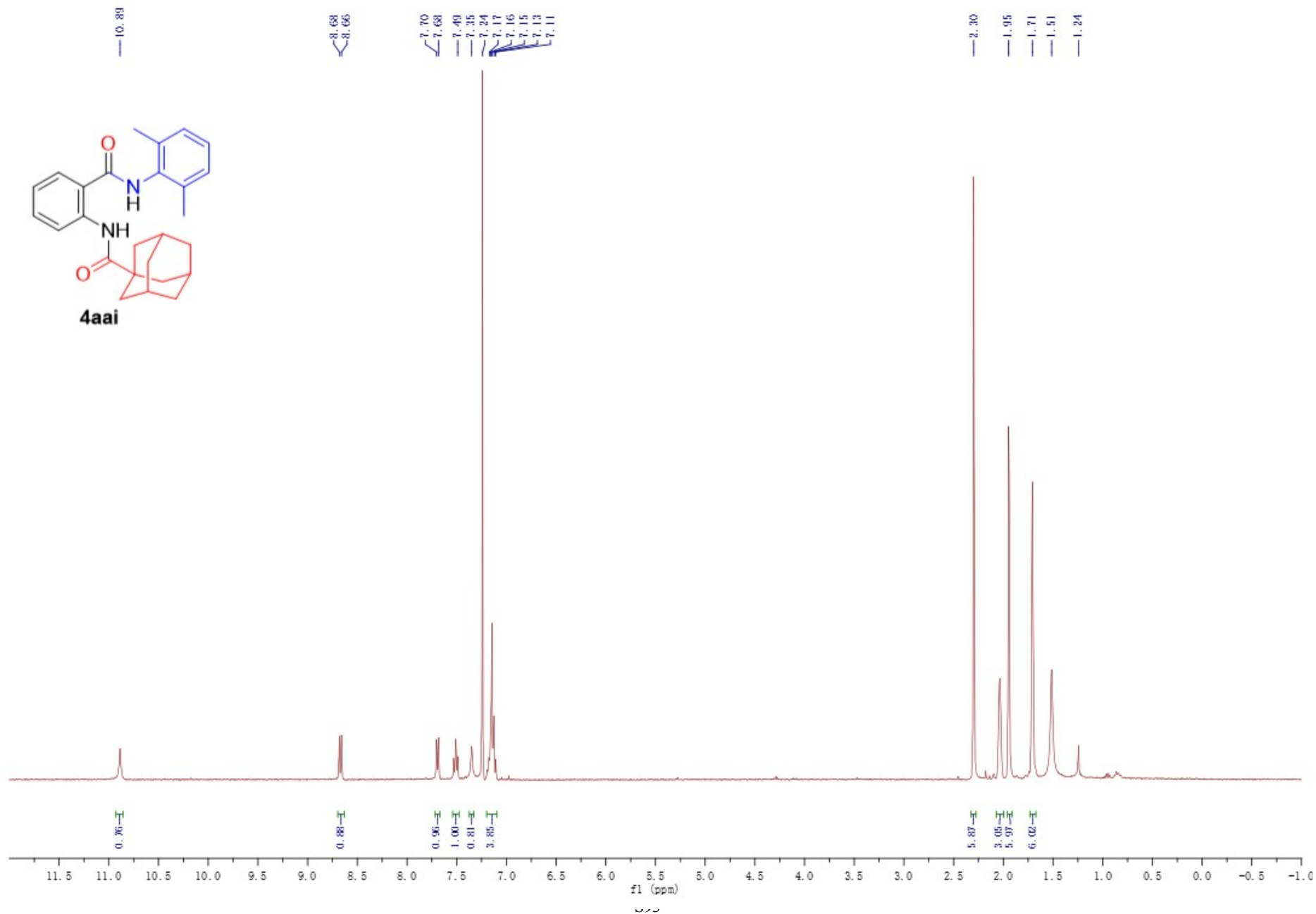
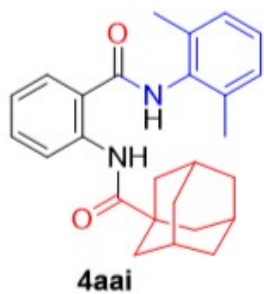


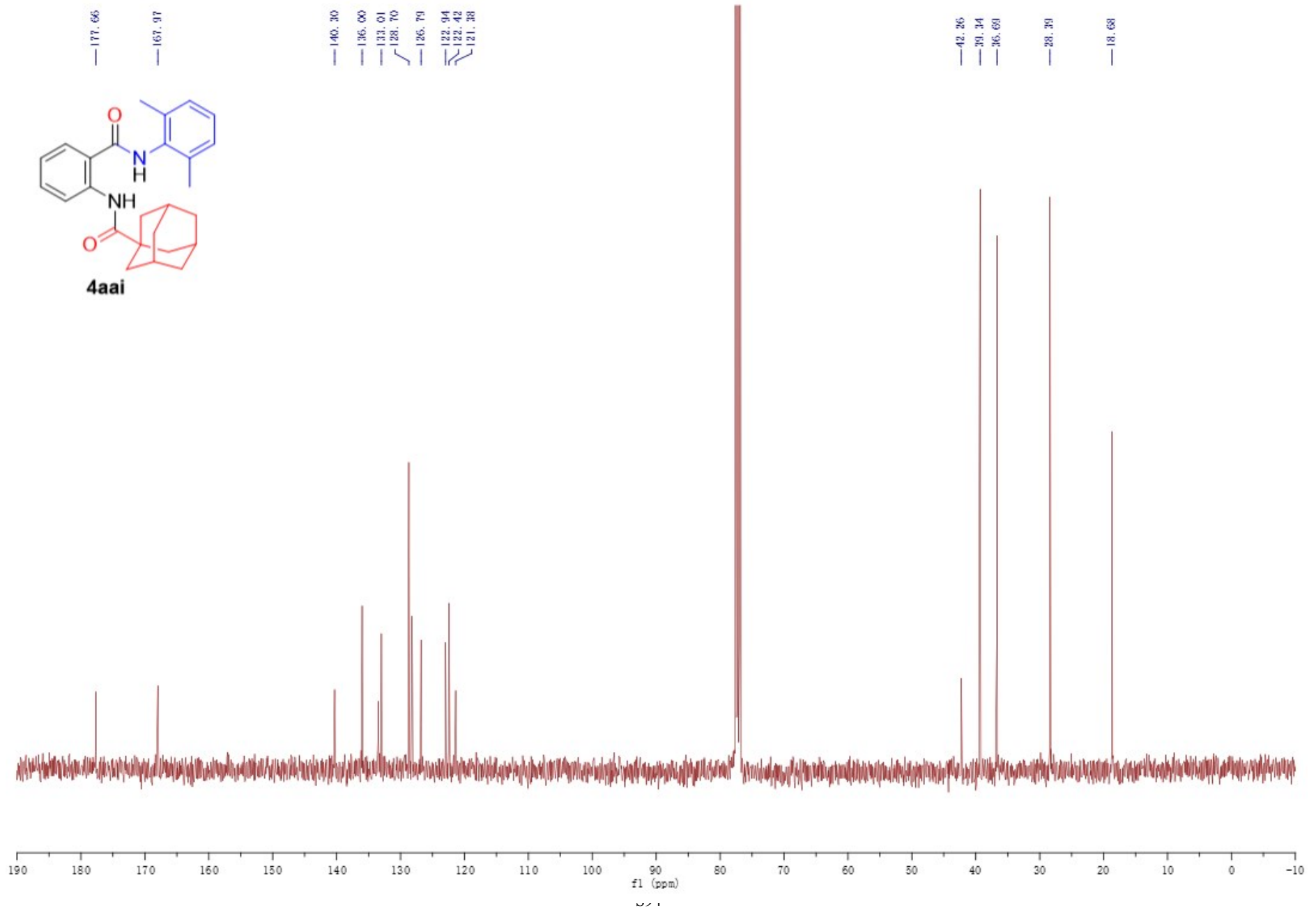
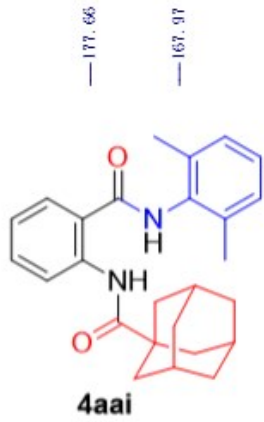


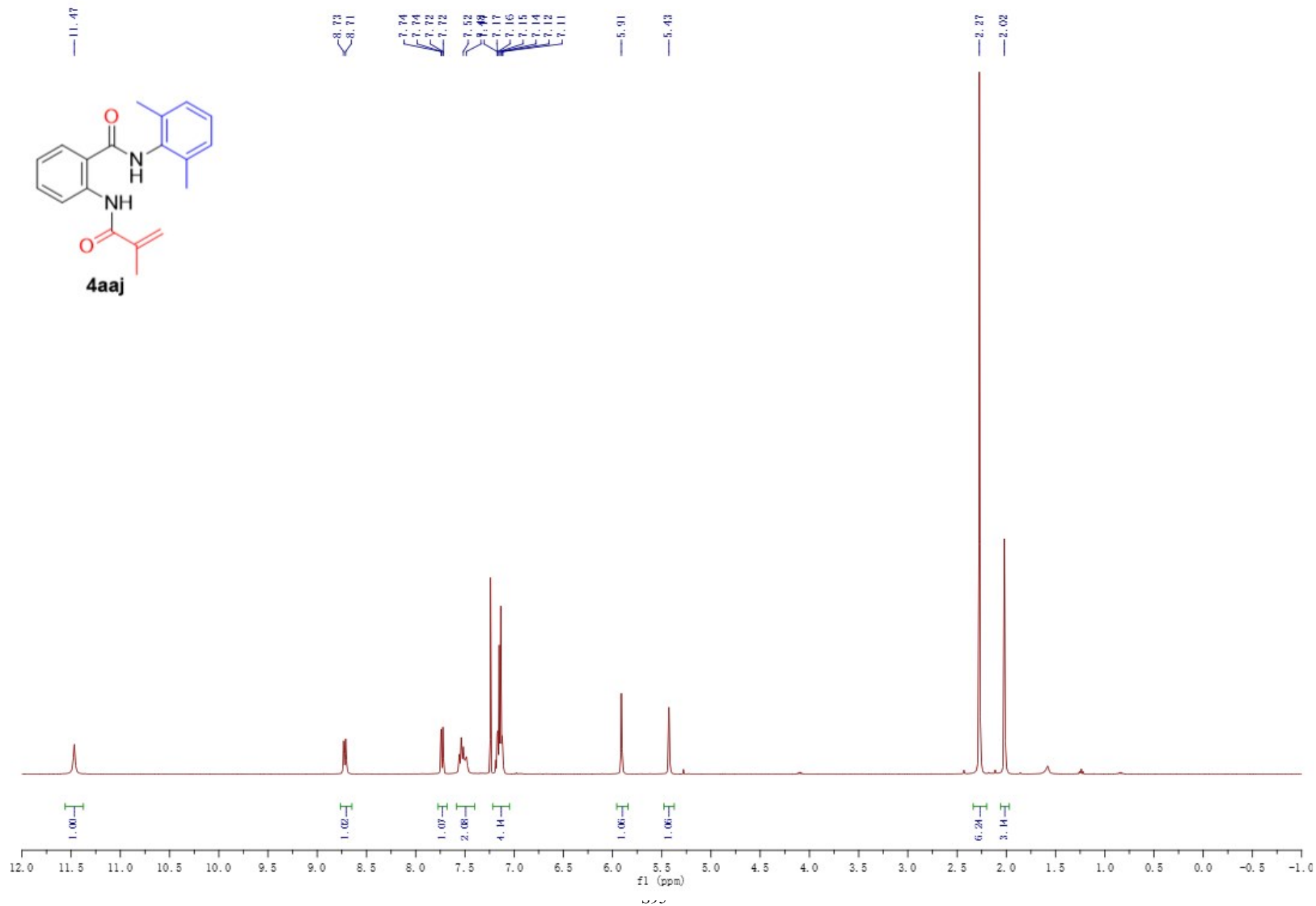
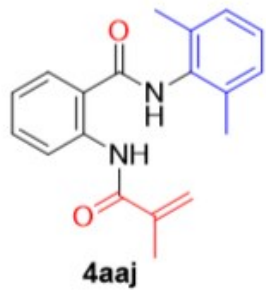


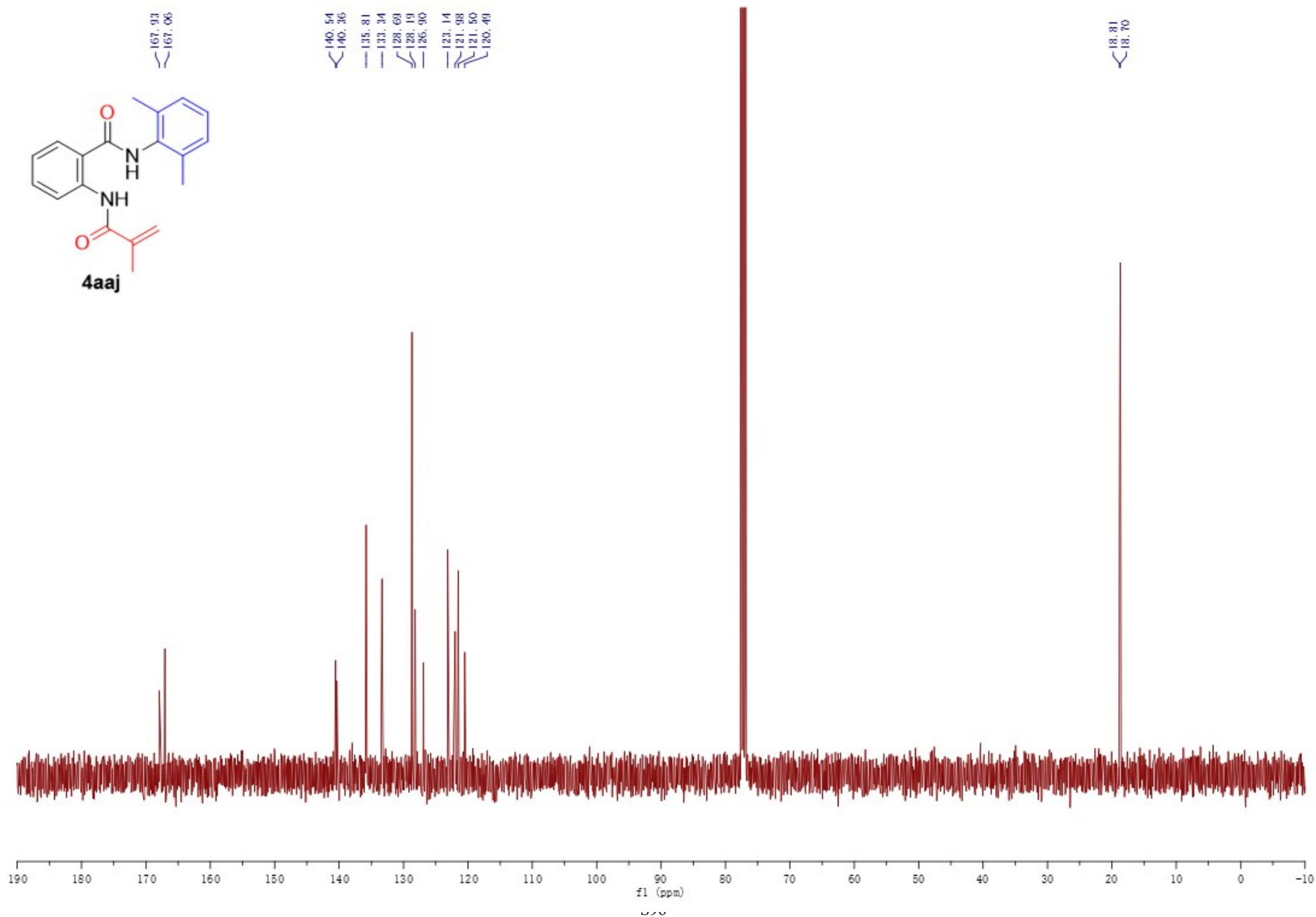
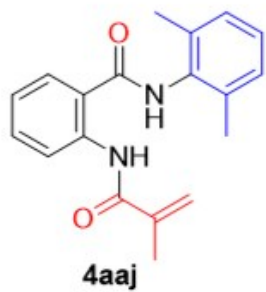
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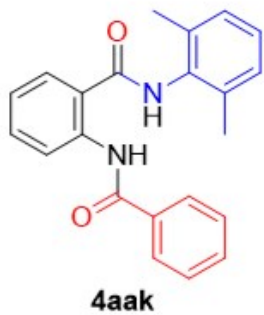










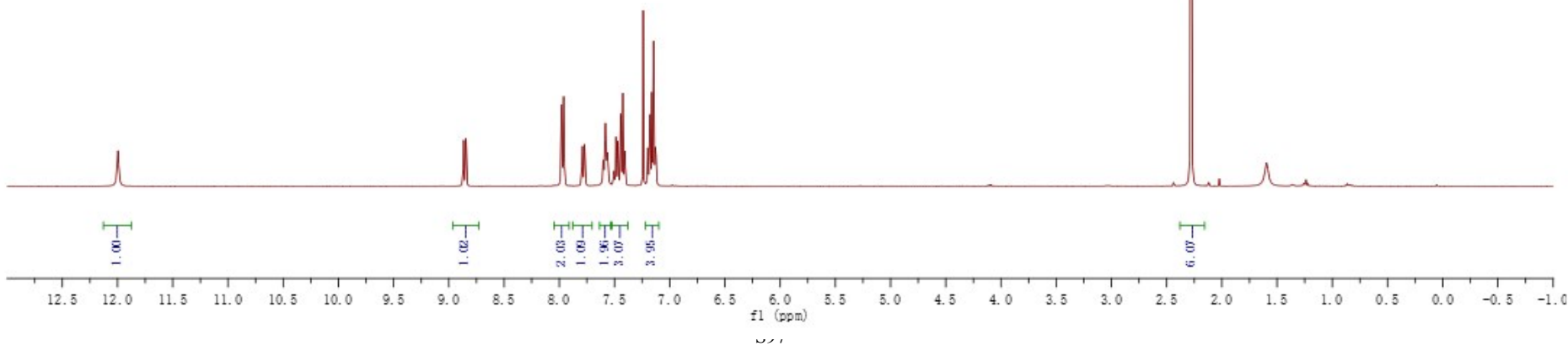
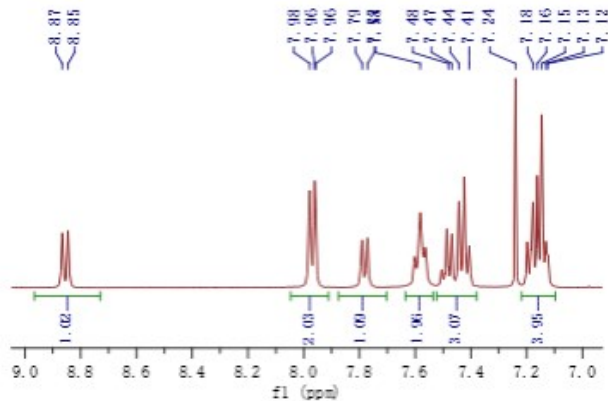


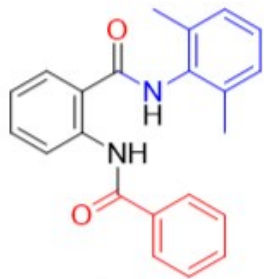
12.00

8.87
8.85

7.98
7.96
7.77
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7.24
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7.19
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7.16
7.15
7.13
7.12

2.28



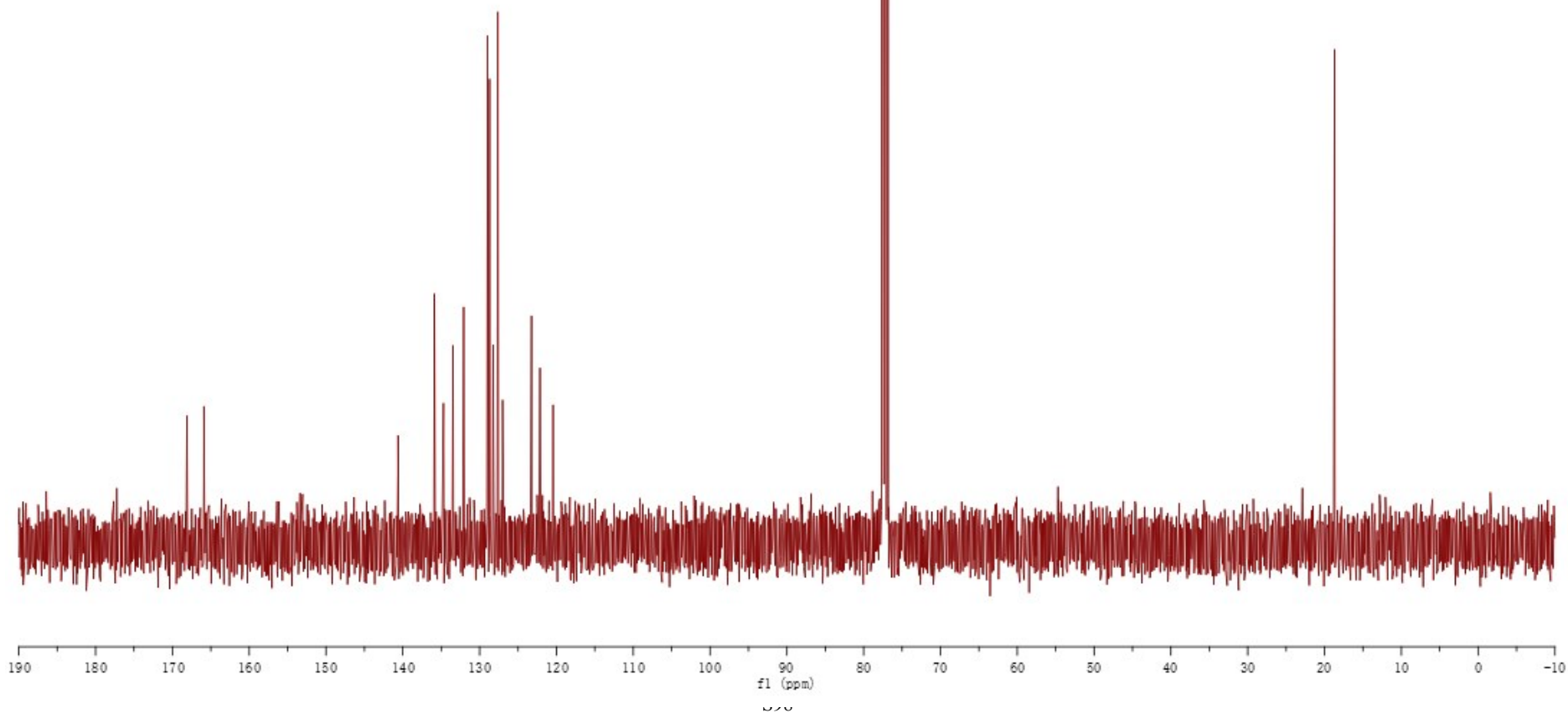


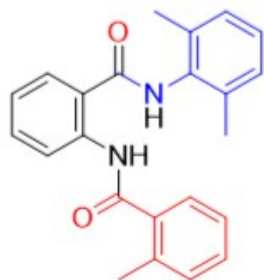
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168.12
165.90

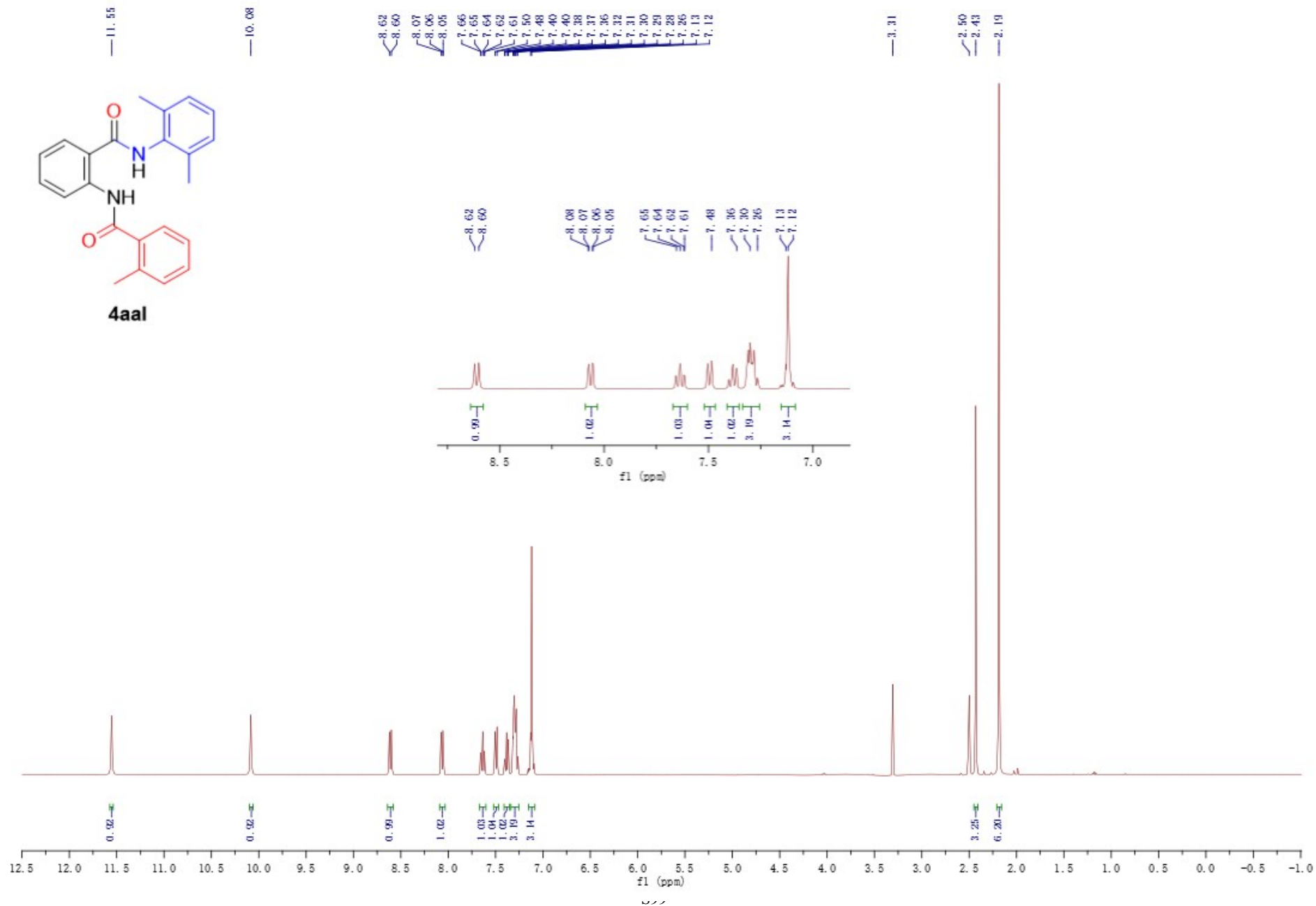
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120.44

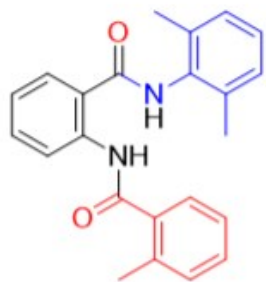
18.71





4aai



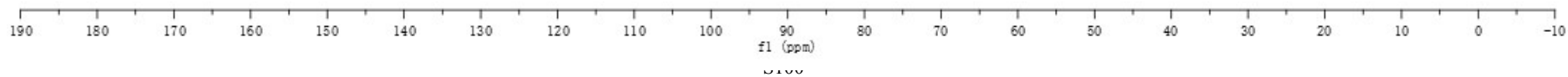


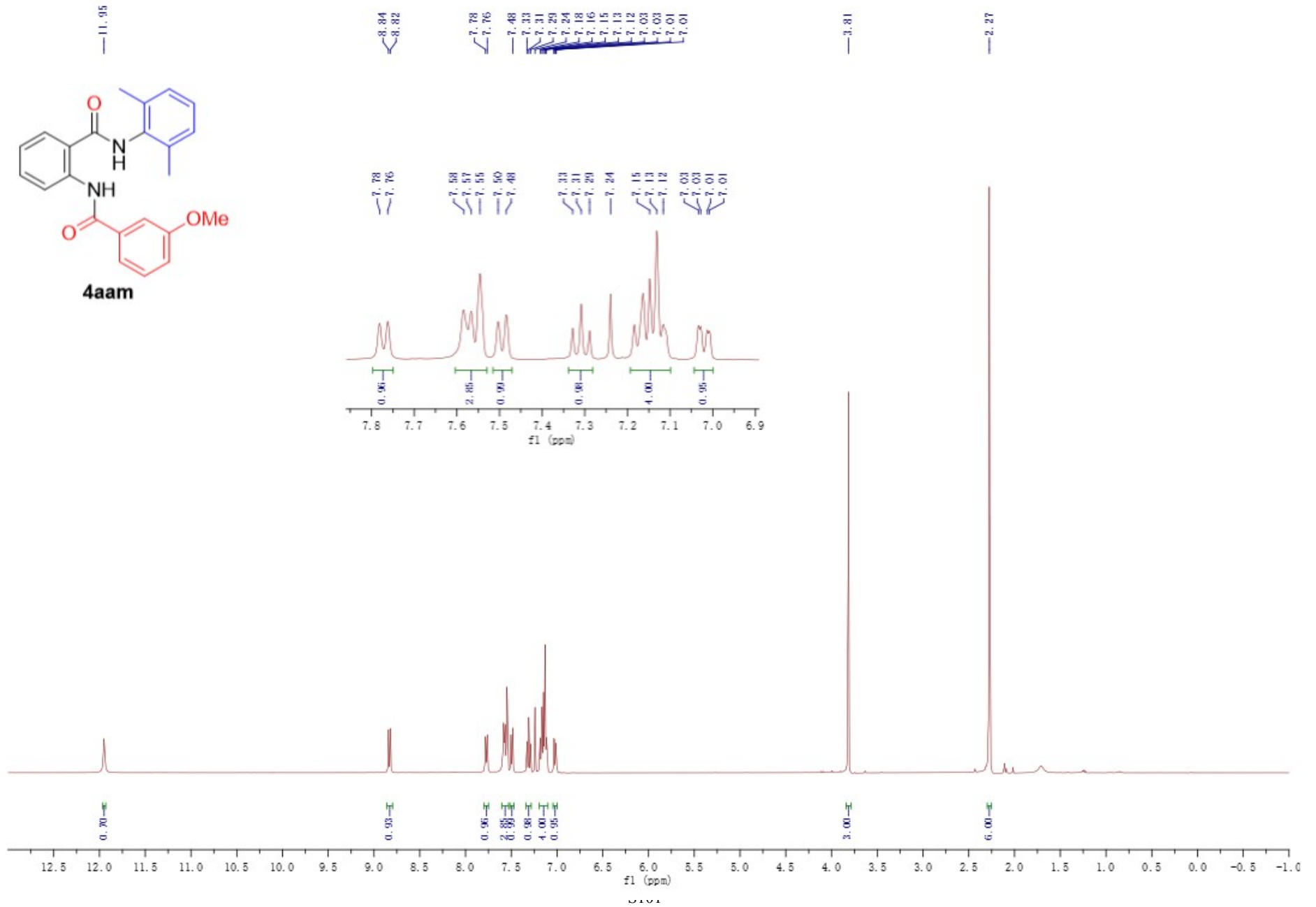
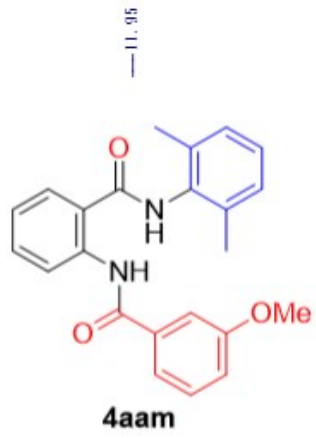
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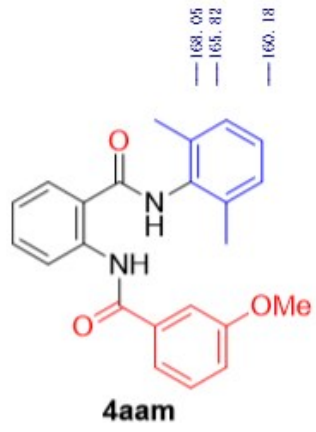
167.19
167.15

139.18
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131.07
128.44
126.93
126.00
123.15
120.99
120.69

19.49
17.85





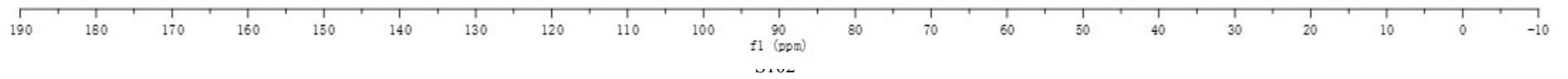


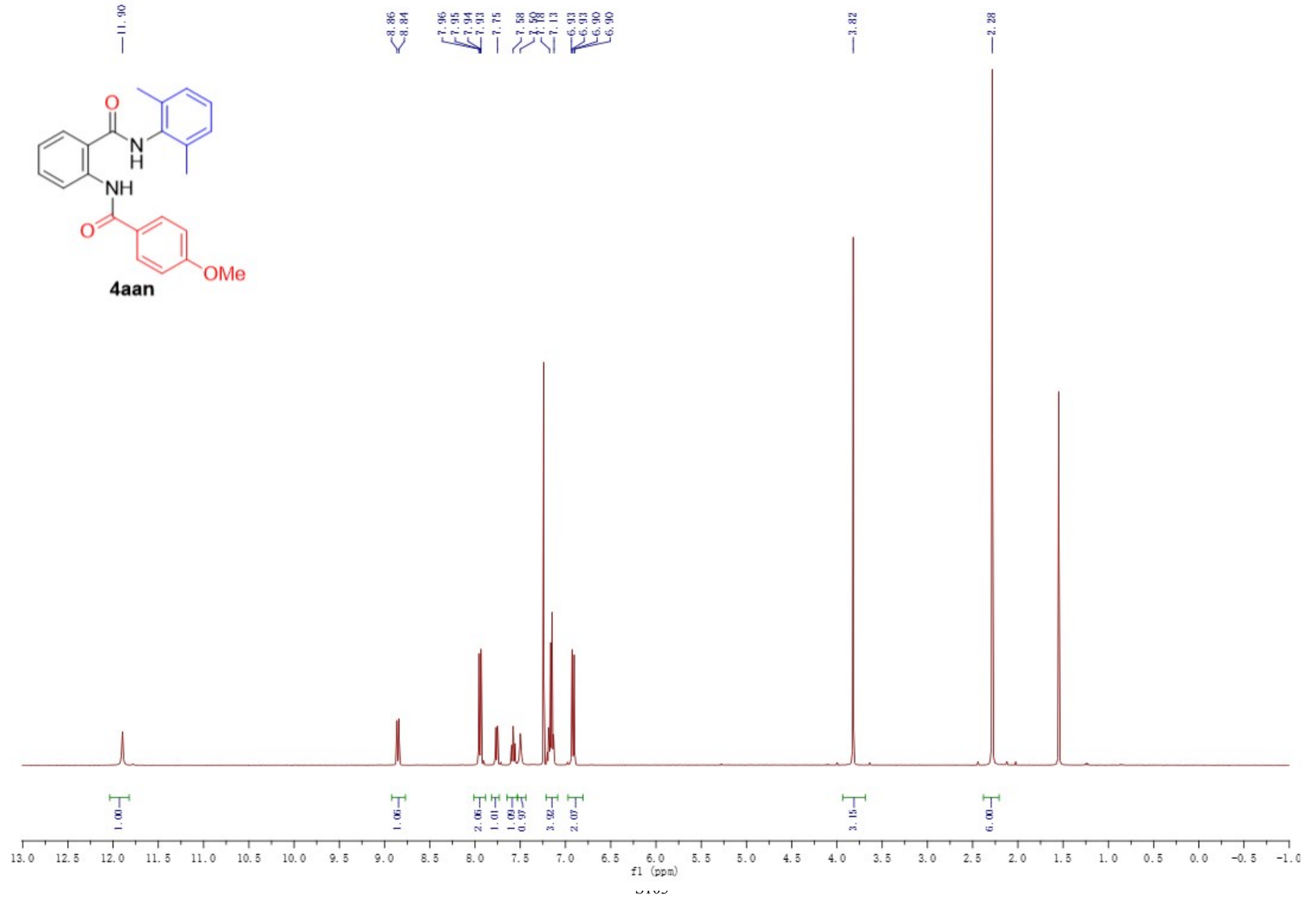
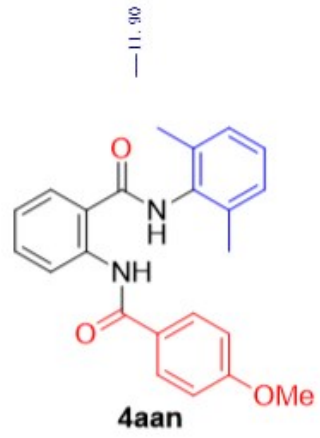
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165.82
160.18

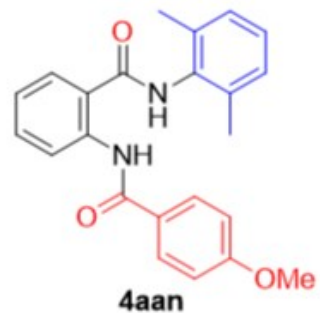
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122.16
120.60
119.39
118.62
112.84

55.60

18.68





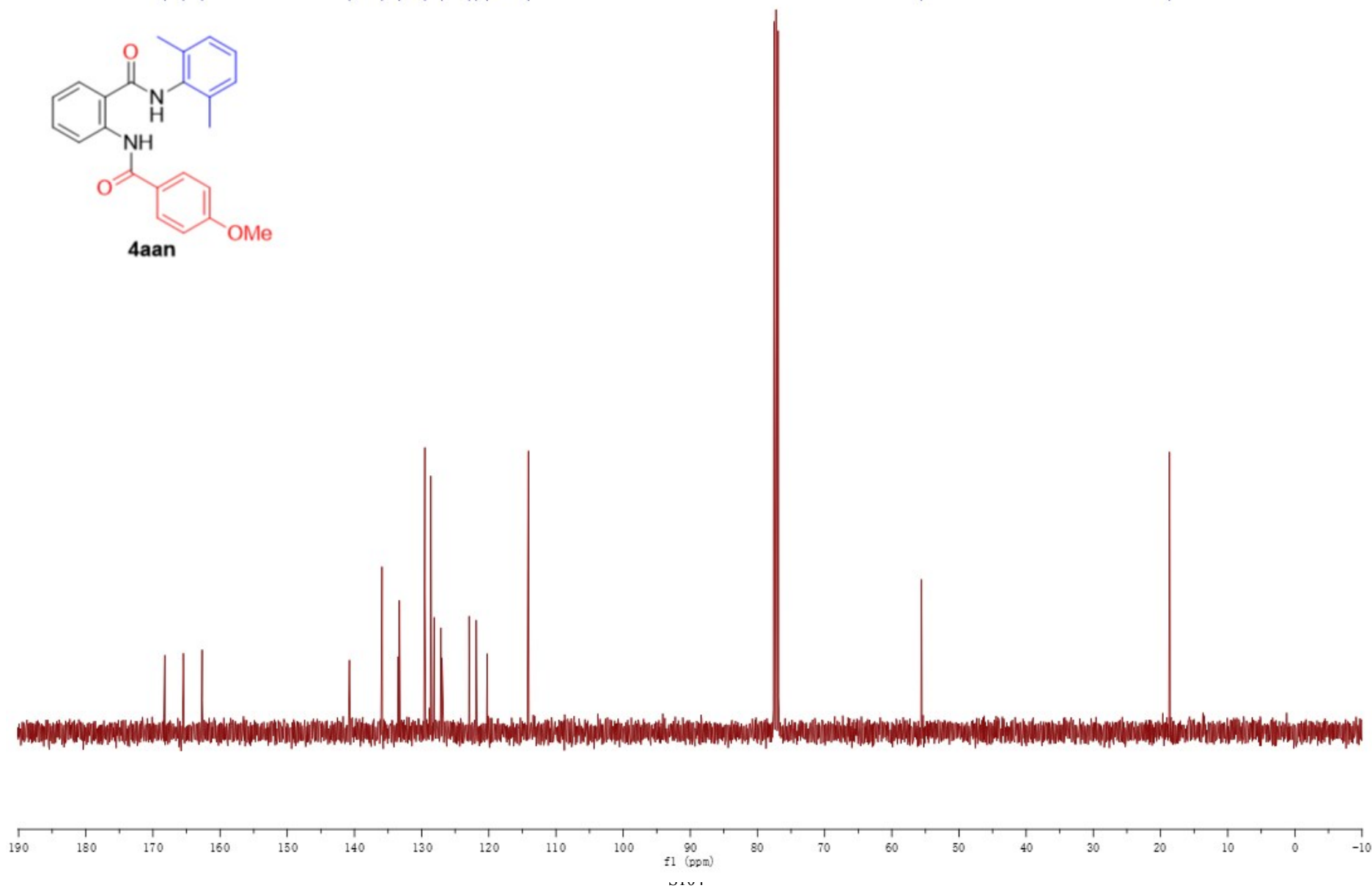


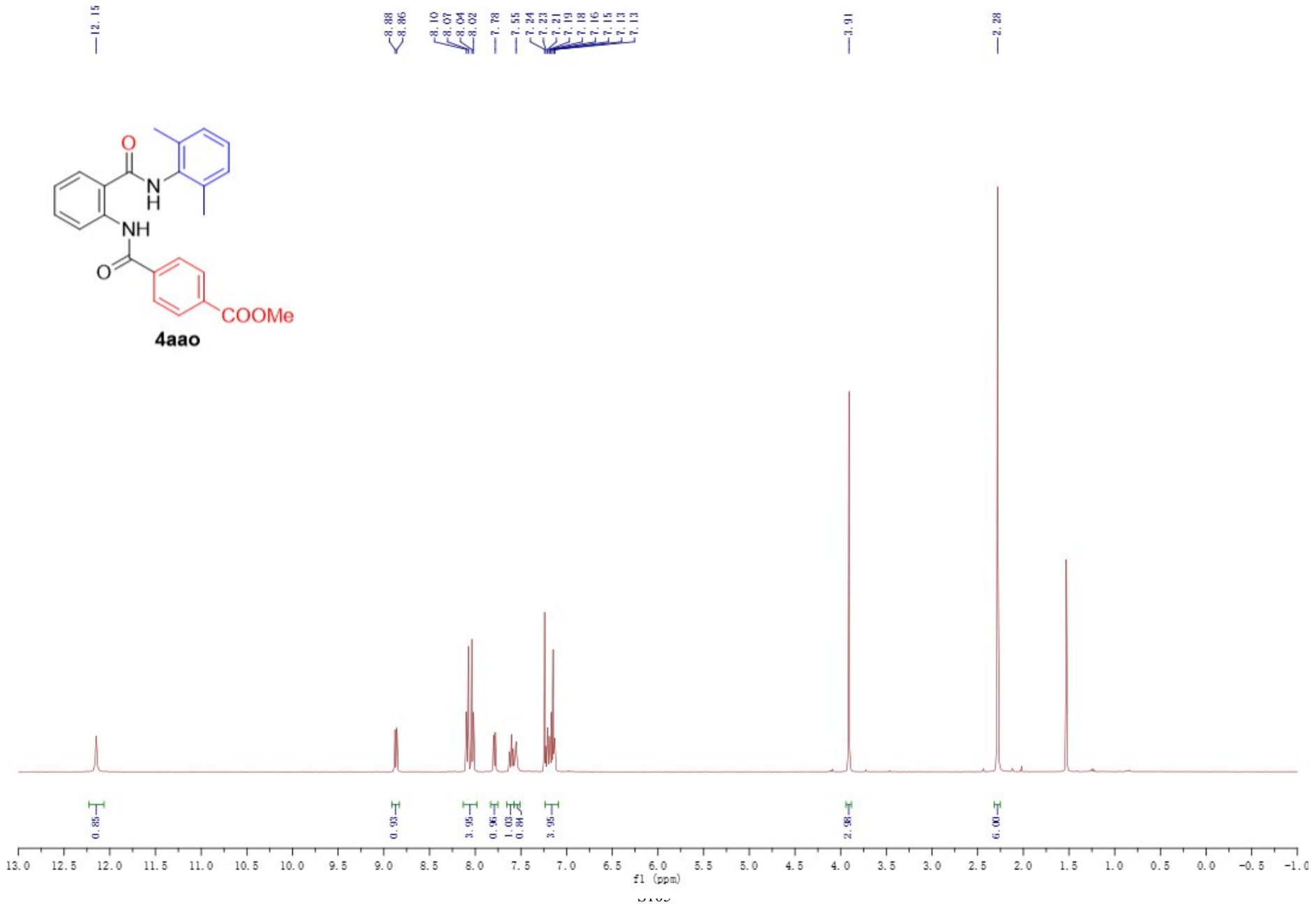
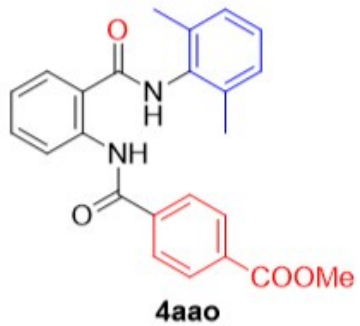
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165.47
162.67

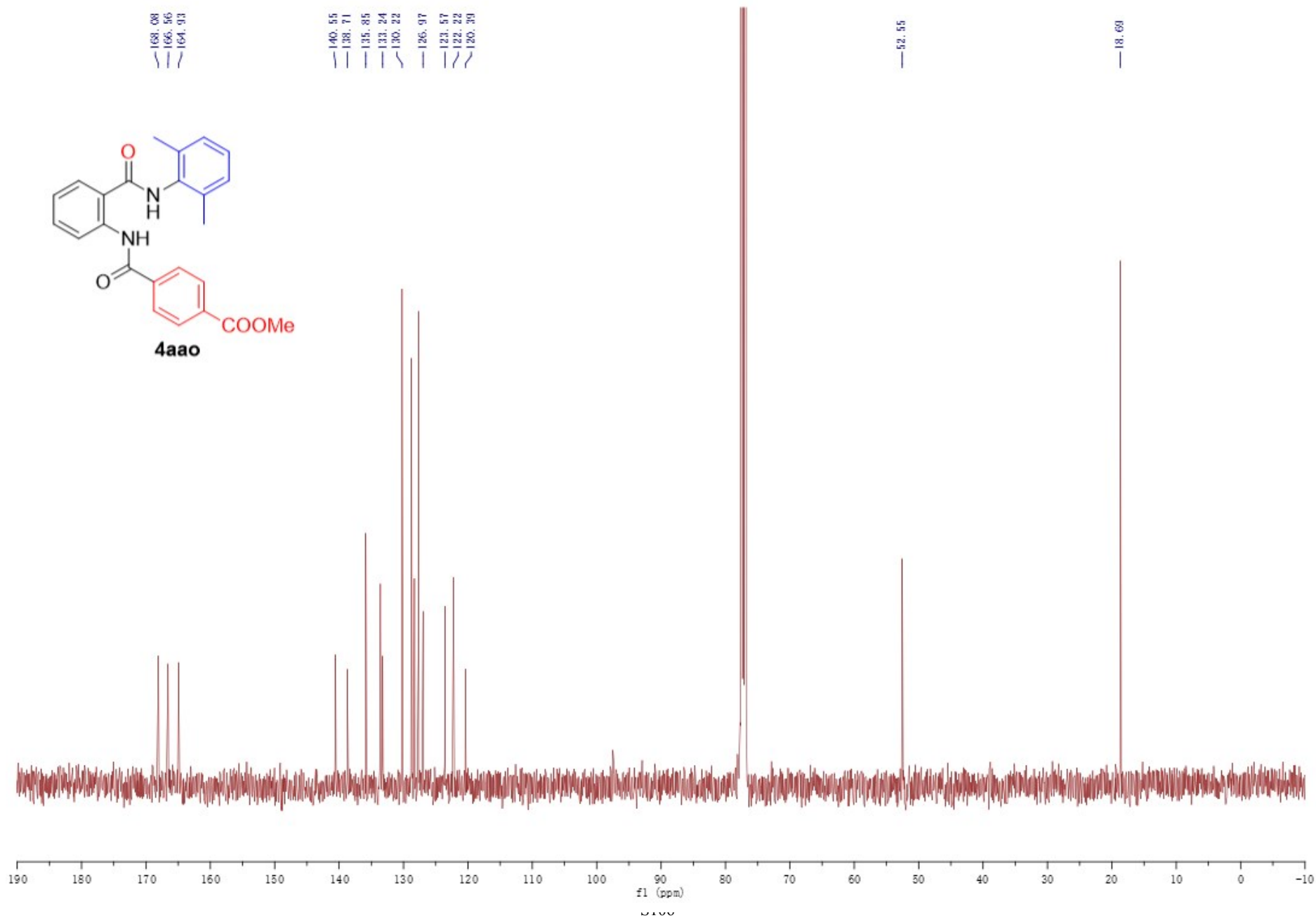
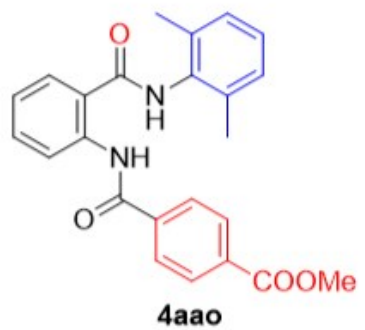
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121.88
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114.10

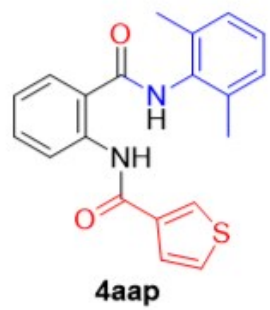
55.88

18.67

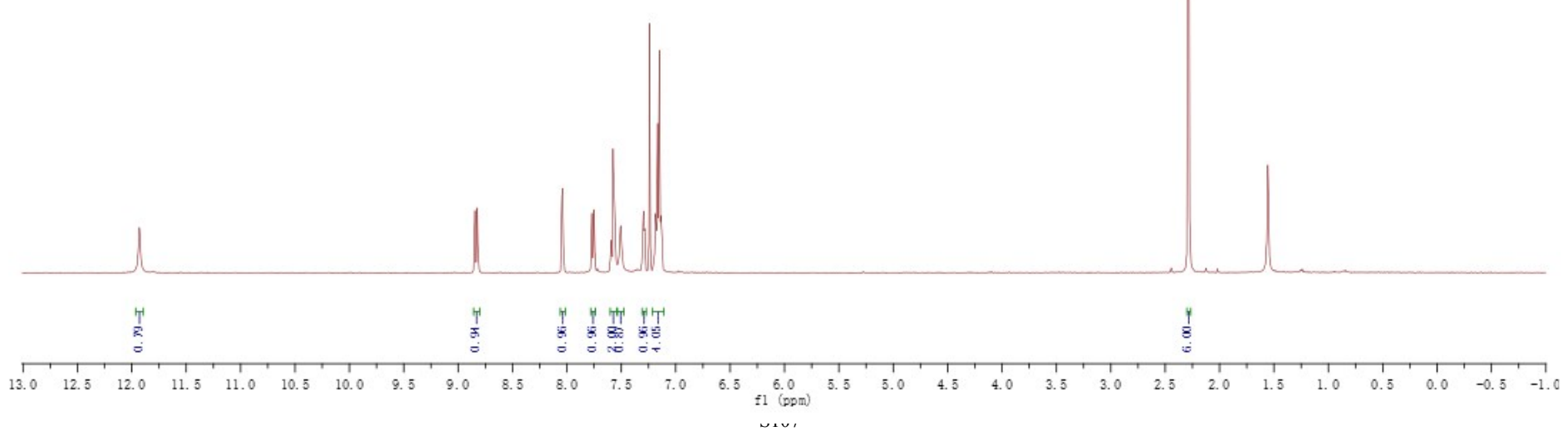
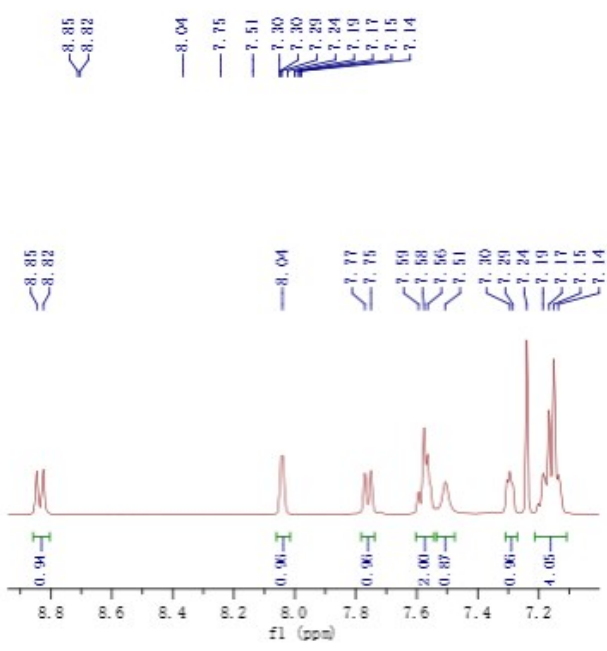


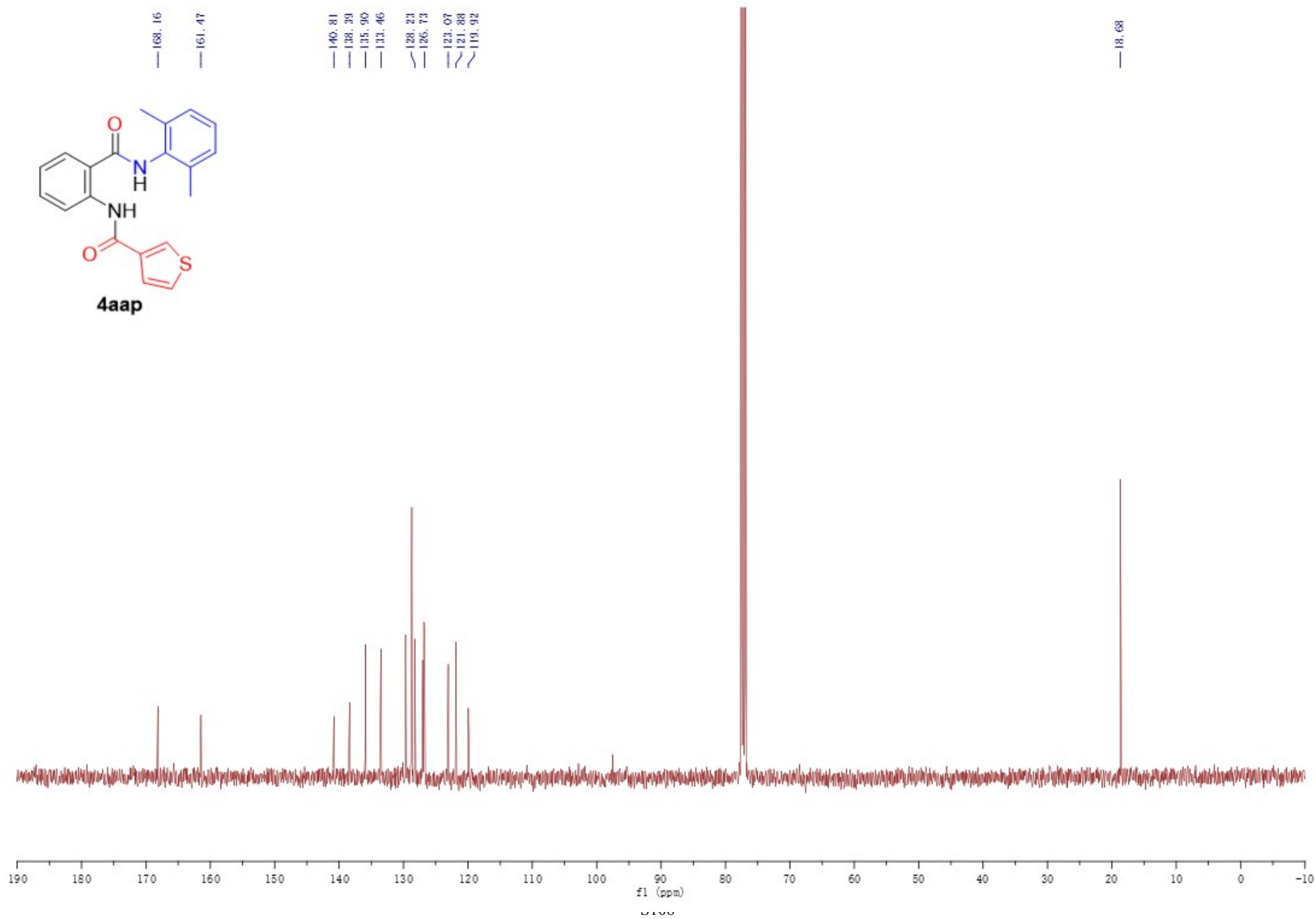
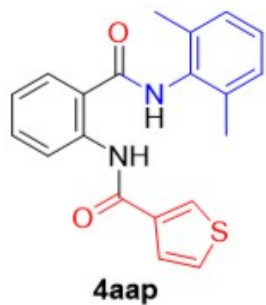


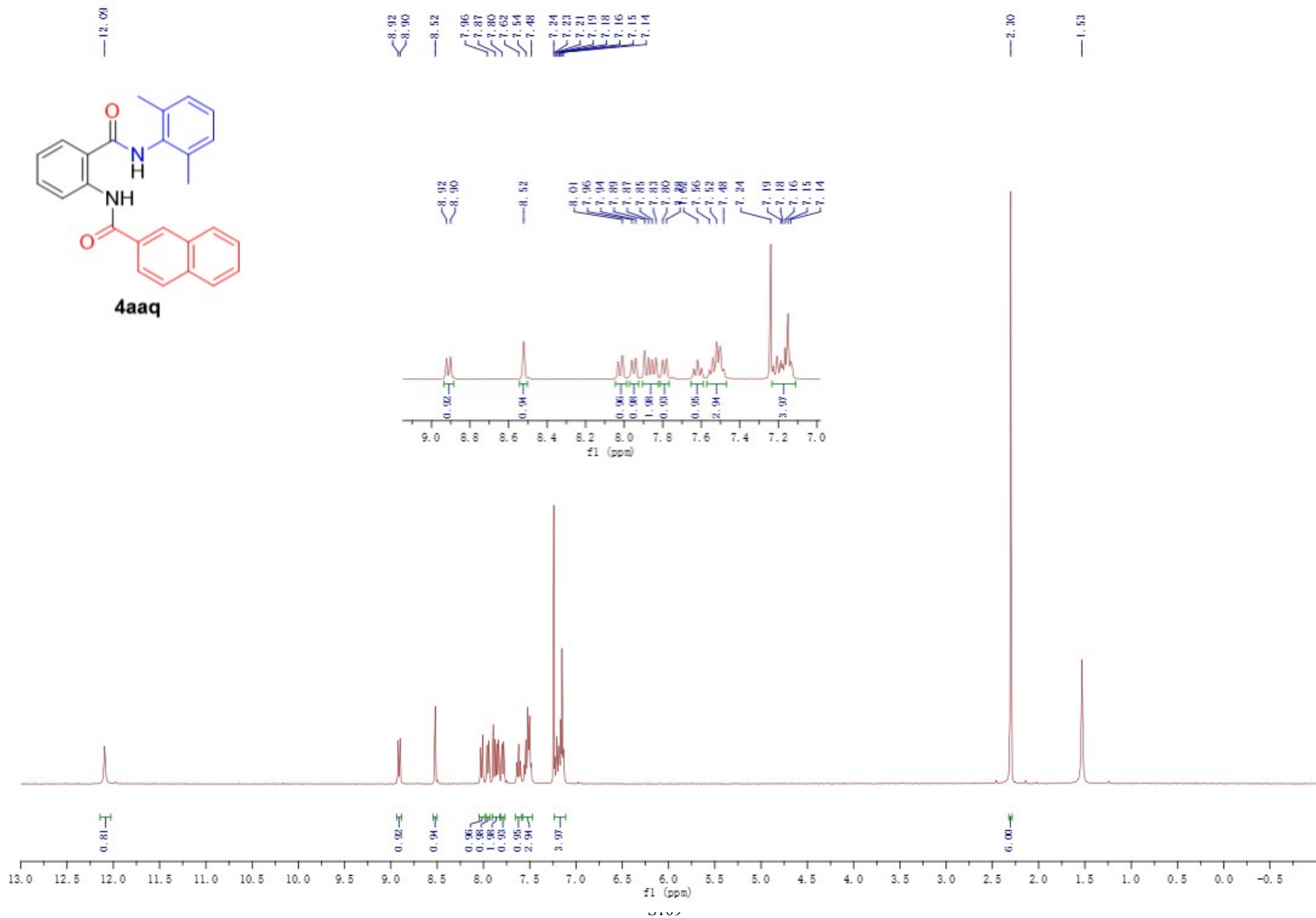
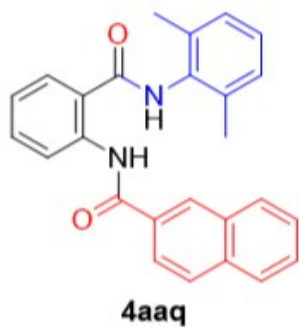


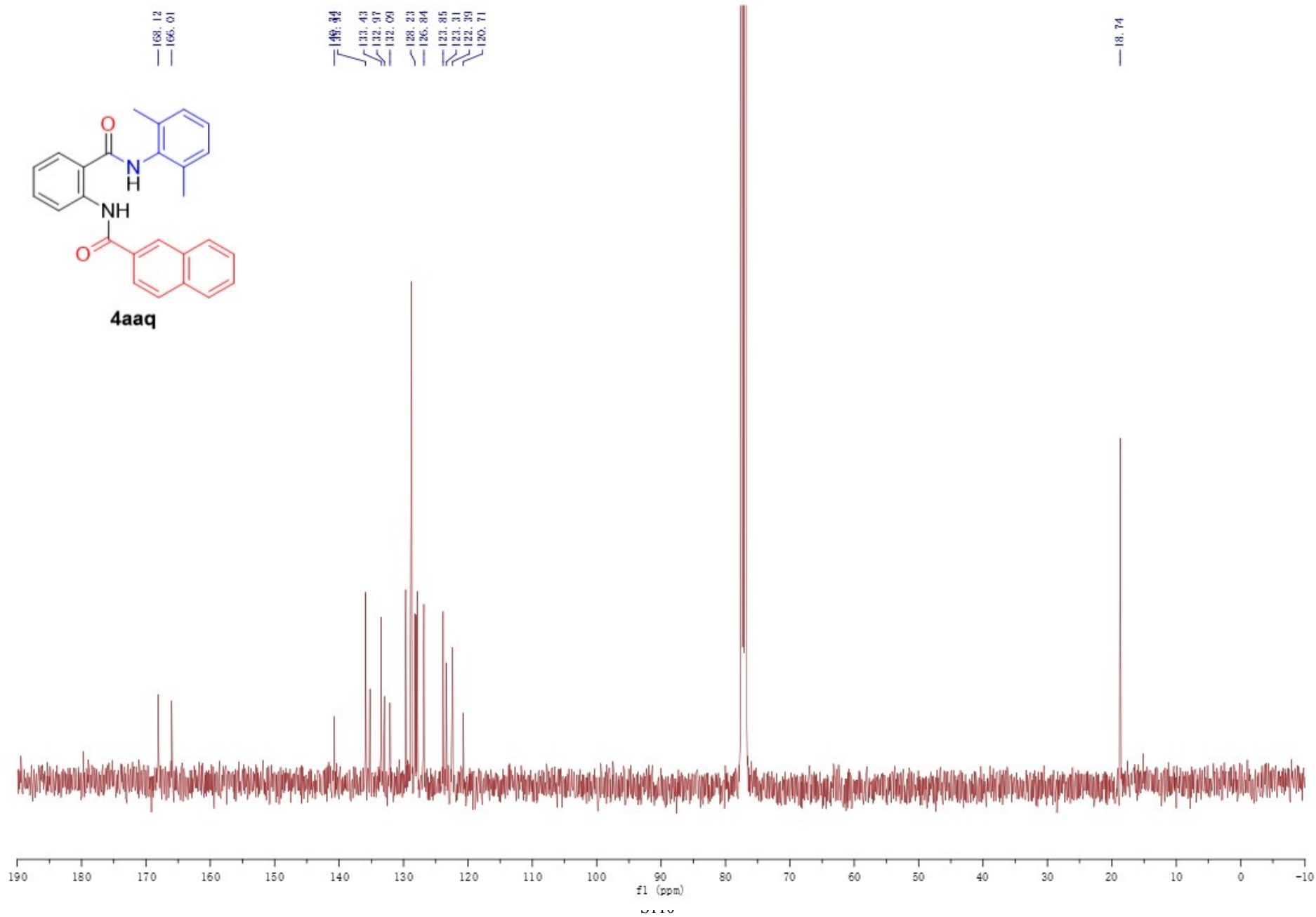


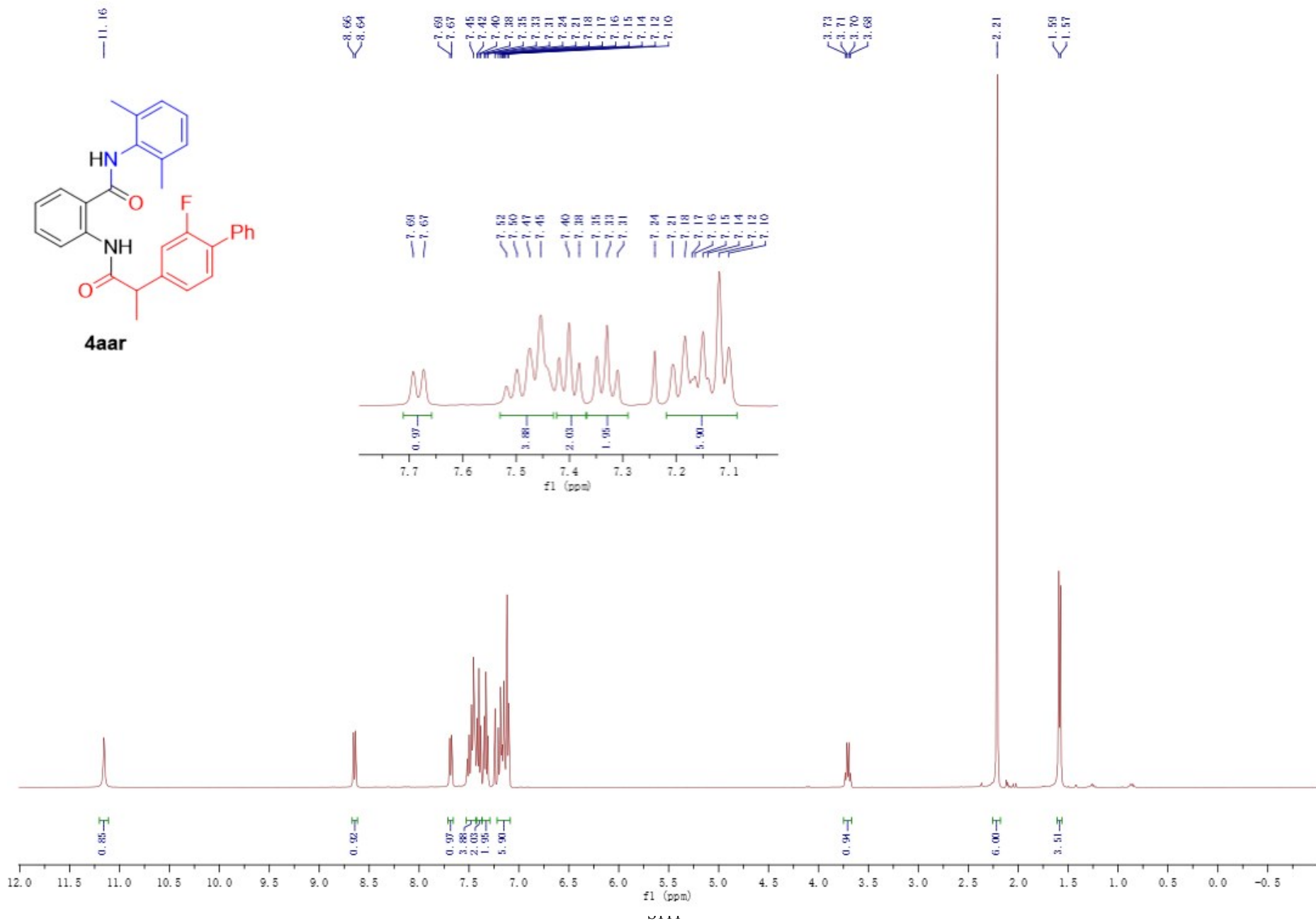
11.93

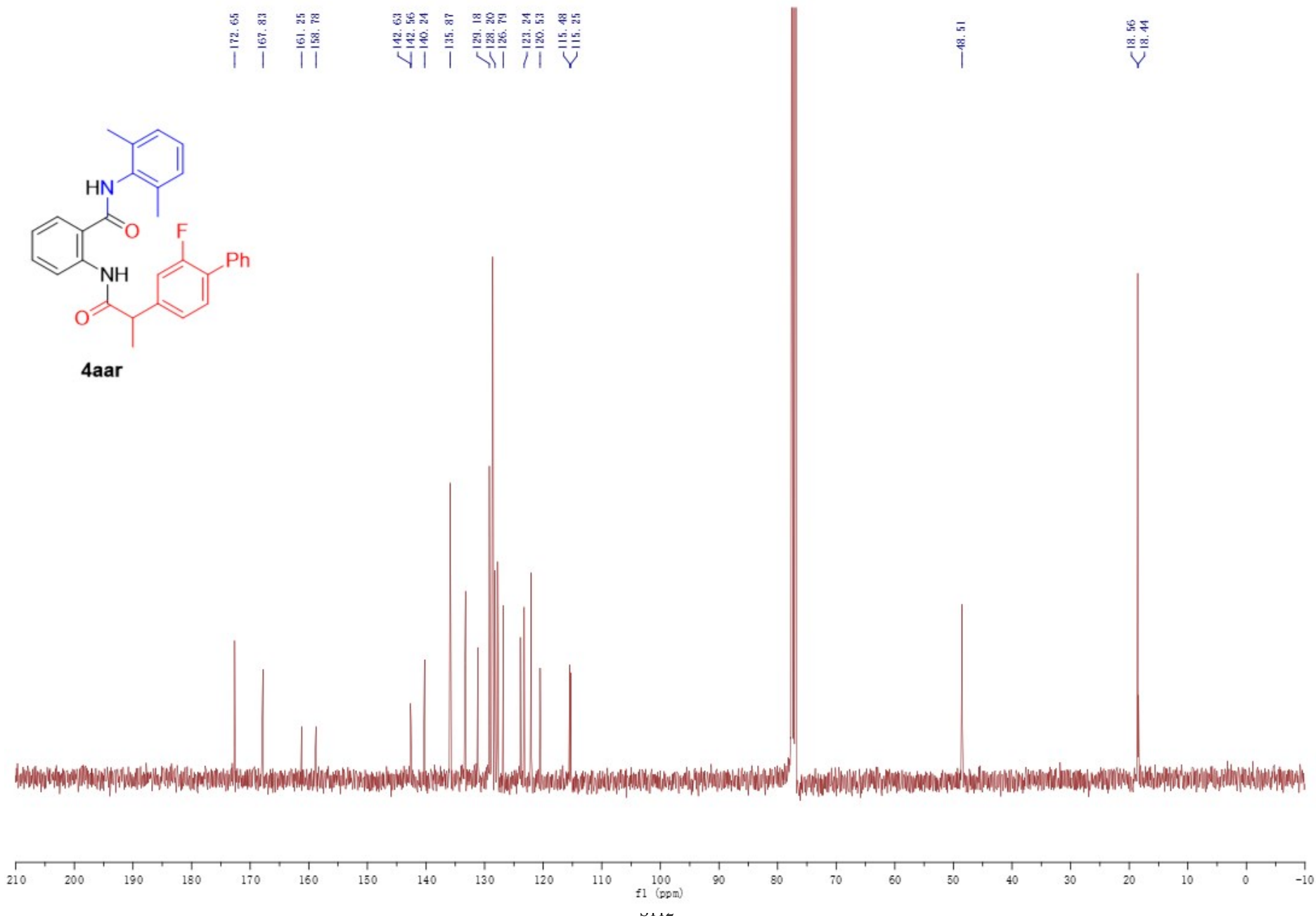


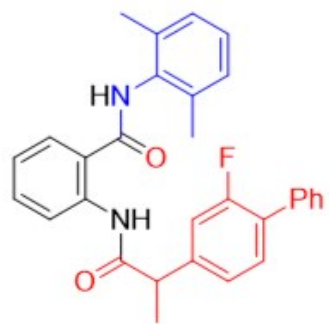






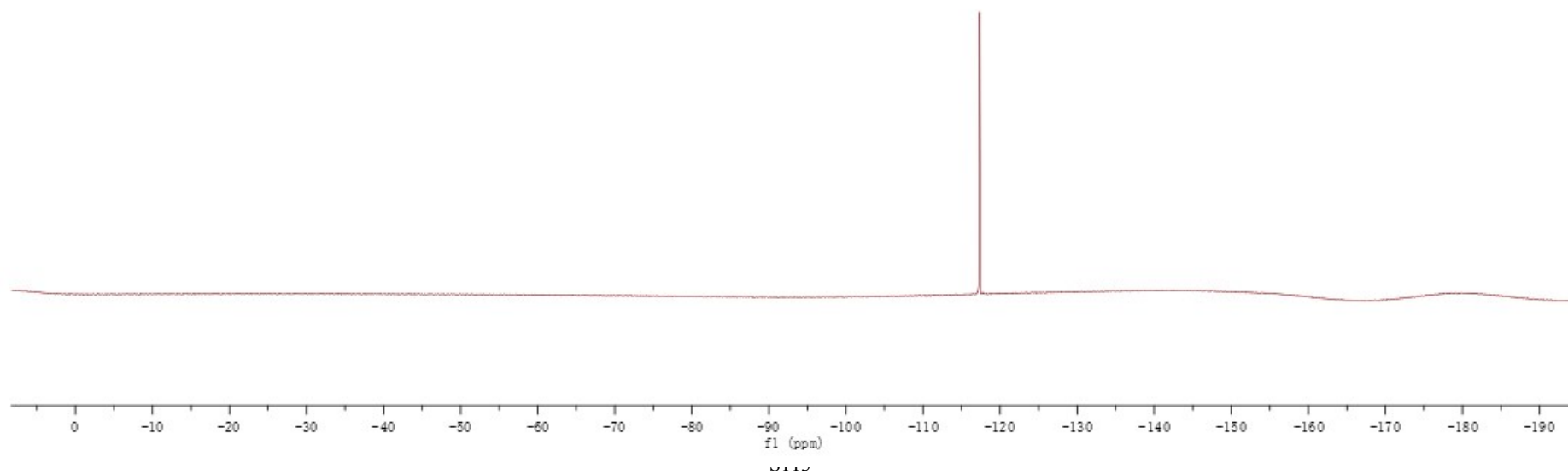


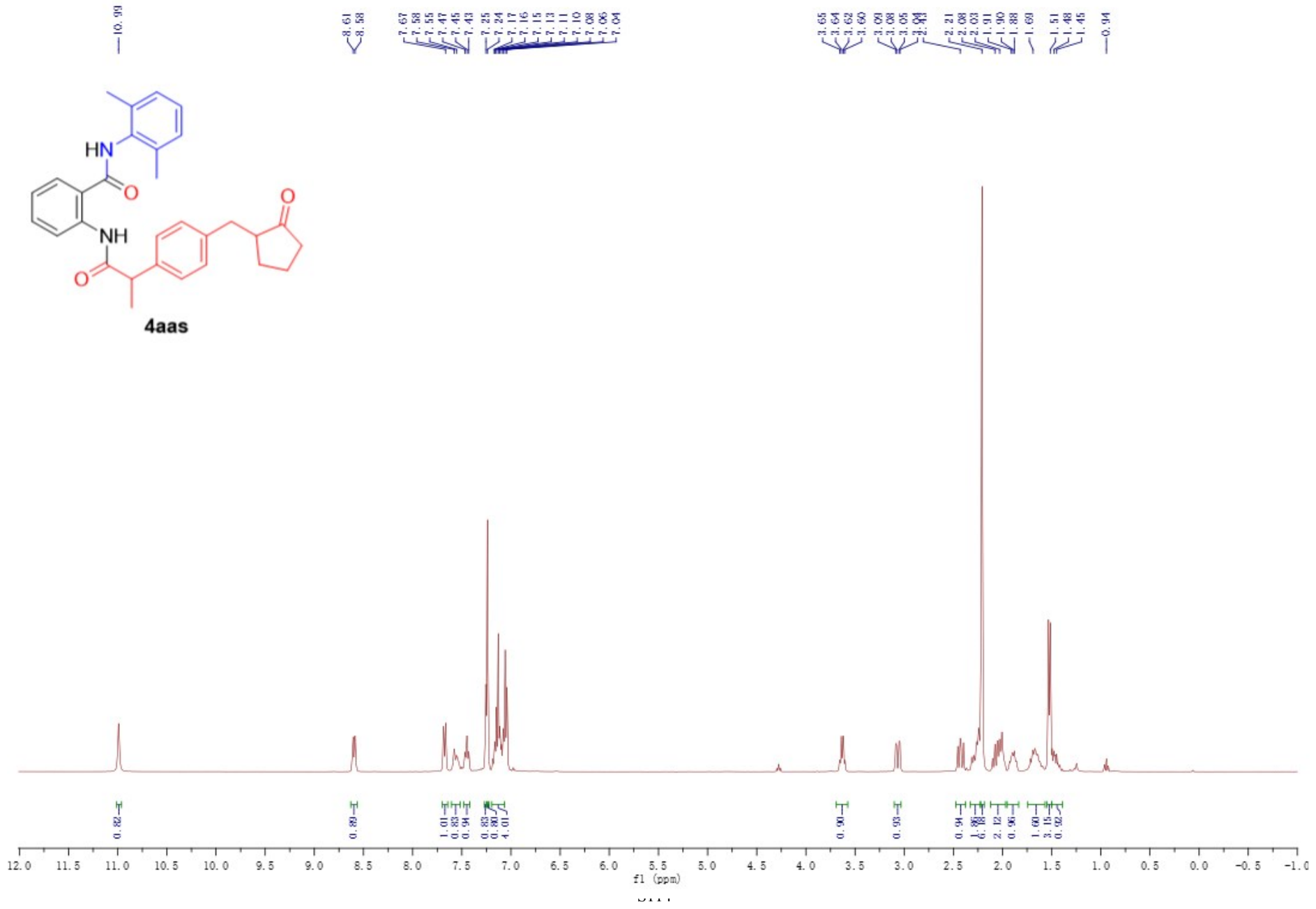




4aar

117.32
117.35
117.37





220.42

173.43

167.79

140.20

139.06

138.95

135.89

133.94

133.94

136.85

123.03

121.94

120.68

51.15

48.60

38.33

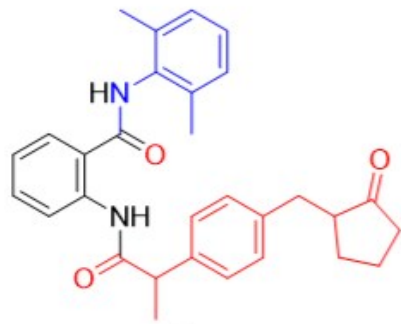
35.41

29.37

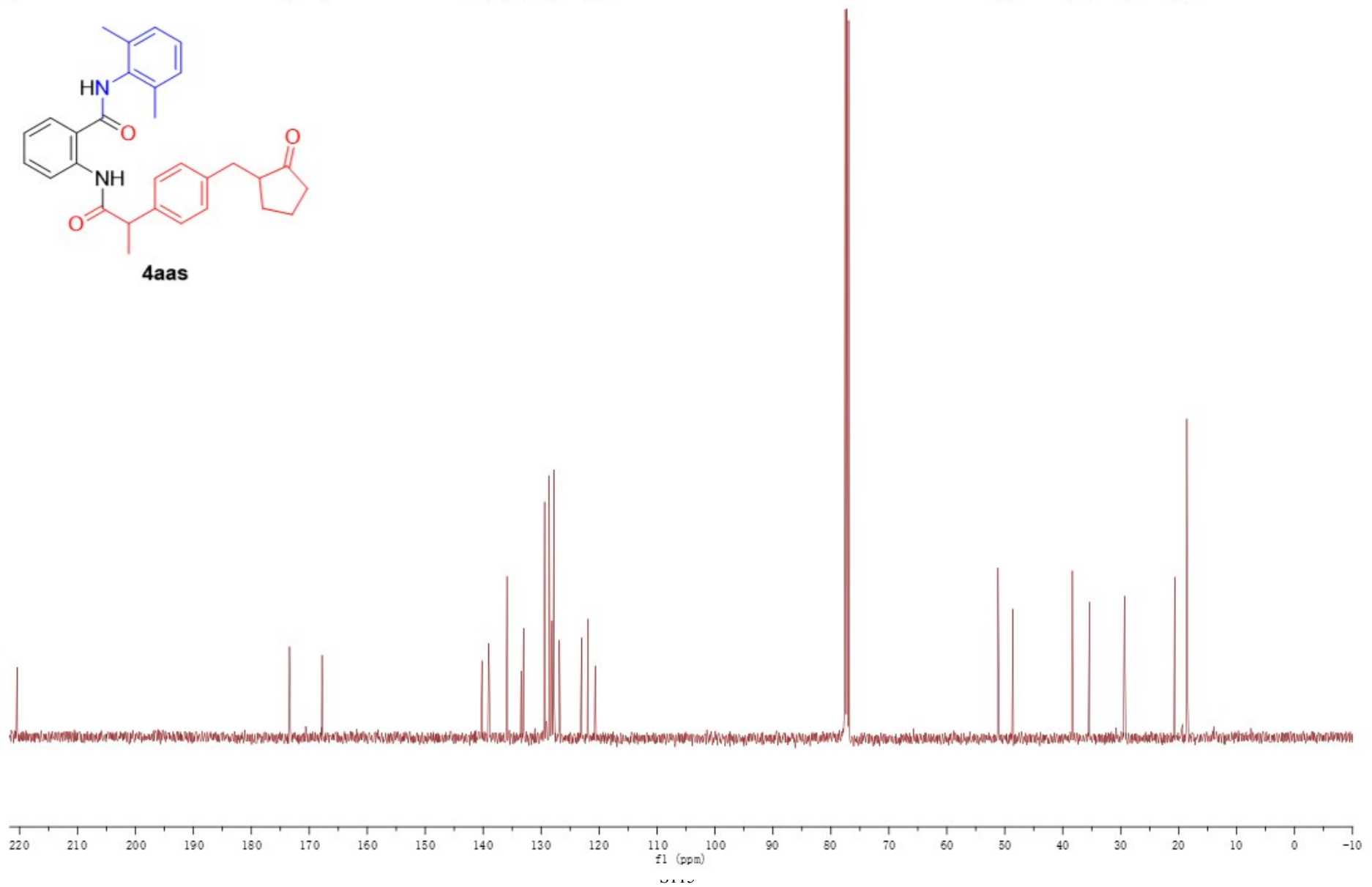
20.67

18.59

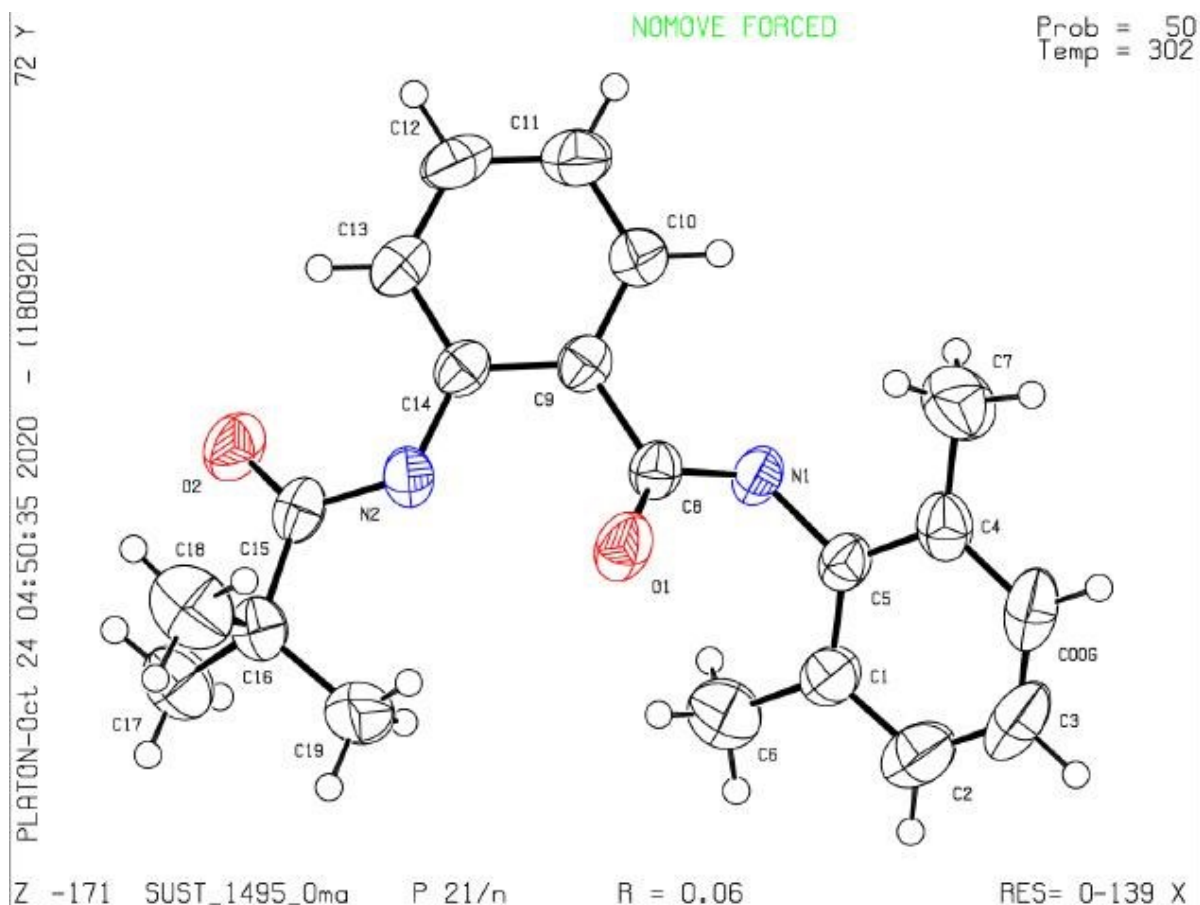
18.47



4aas



6. X-ray of 4aaa



Bond precision: C-C = 0.0042 Å

Wavelength=0.71073

Cell: a=13.135(2) b=10.7195(17) c=13.166(2)
 alpha=90 beta=102.281(10) gamma=90
 Temperature: 302 K

	Calculated	Reported
Volume	1811.4(5)	1811.4(5)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C20 H22 N2 O2	?
Sum formula	C20 H22 N2 O2	C20 H22 N2 O2
Mr	322.40	322.39
Dx, g cm ⁻³	1.182	1.182
Z	4	4
Mu (mm ⁻¹)	0.077	0.077
F000	688.0	688.0
F000'	688.28	
h,k,lmax	17,13,17	17,13,17
Nref	4196	4138
Tmin,Tmax	0.989,0.990	
Tmin'	0.989	

Correction method= Not given

Data completeness= 0.986

Theta(max)= 27.607

R(reflections)= 0.0621(1734)

wR2(reflections)= 0.1964(4138)

S = 1.014

Npar= 223