Supporting Information for

Dual Roles of Ynoates: Desymmetrization of Dicarboxylic Acids using Trialkylamines as alkyl equivalents

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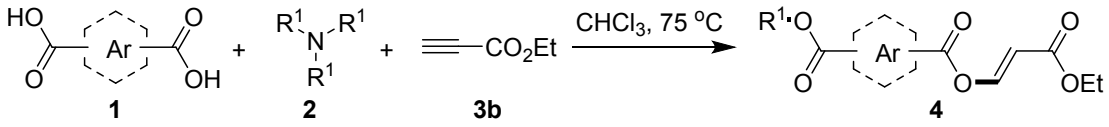
1. General information:

Unless otherwise noted, all commercial reagents were used directly as purchased. All work-up and purification procedures were carried out with reagent-grade solvents that had not been pre-dried under ambient atmosphere. Chloroform was purified and dried according to standard methods prior to use. Thin-layer chromatography (TLC) was performed and Visualization of the compounds was accomplished with UV light (254 nm) or iodine. Flash column chromatography was performed on silica gel (100–200 mesh).

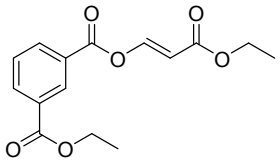
All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III instrument (400 MHz and 100 MHz, respectively). Chemical shifts (δ) are reported in ppm relative to the tetramethylsilane (TMS) signal or residual protio solvent signal. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for ^{13}C NMR is reported in terms of chemical shift (δ, ppm). High resolution mass spectra were obtained on a Shimadzu LCMS-IT-TOF mass spectrometer with an electrospray ionization (ESI) probe.

2. General procedures

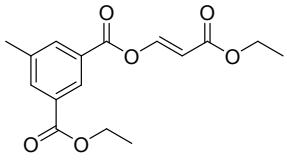
2.1 General procedure for the synthesis of the desired product 4



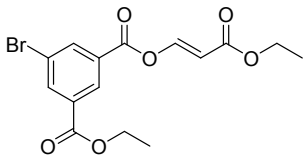
A mixture of aromatic dicarboxylic acid **1** (0.5 mmol), ethyl propiolate **3b** (1.1 mmol) was added a 10 mL tube along with a magnetic stir bar, and then 2 mL dry $CHCl_3$ was add. The tube was stirred and refluxed in oil bath at 75 °C. Subsequently, tertiary amine **2** (0.8 mmol) solved in 1mL $CHCl_3$ was add the tube slowly for 5min. And the tube was stirred again and refluxed at 75 °C for 8 h, the solvent removed under reduced pressure and the residue was loaded on a silica gel column and flashed with 5–10% ethyl acetate in petroleum ether to afford the desired product **4**.



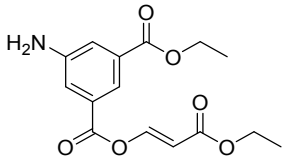
3-ethoxy-3-oxoprop-1-en-1-yl ethyl isophthalate (4a). colorless oil; 112 mg, 77% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.55 (d, *J* = 12.5 Hz, 1H), 8.31 (t, *J* = 7.9 Hz, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 5.96 (d, *J* = 12.5 Hz, 1H), 4.44 (m, 2H), 4.26 (m, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.3, 161.8, 149.5, 135.0, 134.2, 131.3, 128.9, 128.2, 106.9, 77.3, 77.0, 76.7, 61.5, 60.5, 14.2; HRMS (ESI) m/z calcd for $C_{15}H_{16}O_6$ $[M+H]^+$ 293.1020, found 293.1025.



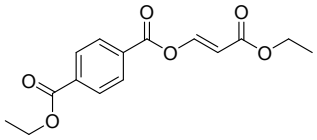
ethoxy-3-oxoprop-1-en-1-yl) 3-ethyl 5-methylisophthalate (4b). colorless oil; 110.9 mg, 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 12.4 Hz, 2H), 8.11 (d, *J* = 9.6 Hz, 2H), 5.96 (d, *J* = 12.5 Hz, 1H), 4.42 (m, 2H), 4.26 (m, 2H), 2.49 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.4, 161.9, 149.5, 139.1, 135.7, 134.7, 131.2, 128.5, 128.0, 106.8, 77.4, 77.0, 76.7, 61.4, 60.5, 21.0, 14.2; HRMS (ESI) m/z calcd for $C_{16}H_{18}O_6$ $[M+H]^+$ 307.1176, found 307.1179.



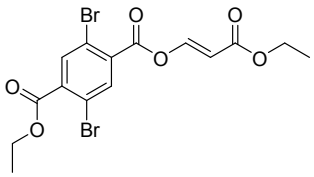
(3-ethoxy-3-oxoprop-1-en-1-yl) 3-ethyl 5-bromoisophthalate (4c). colorless oil; 126.1 mg, 68% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.41 (d, *J* = 12.5 Hz, 1H), 8.32 (d, *J* = 5.9 Hz, 2H), 5.89 (d, *J* = 12.5 Hz, 1H), 4.35 (m, 2H), 4.18 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.0, 160.6, 149.1, 137.8, 136.9, 133.0, 129.9, 129.7, 122.9, 107.4, 77.3, 77.0, 76.7, 62.0, 60.6, 14.2; HRMS (ESI) m/z calcd for $C_{15}H_{15}BrO_6$ $[M+Na]^+$ 392.9944, found 392.9945.



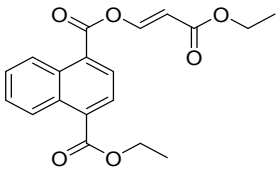
(3-ethoxy-3-oxoprop-1-en-1-yl) 3-ethyl 5-aminoisophthalate (4d). colorless oil; 50.8 mg, 33% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 12.5 Hz, 1H), 8.11 (s, 1H), 7.58 (d, *J* = 16.0 Hz, 2H), 5.93 (d, *J* = 12.5 Hz, 1H), 4.40 (m, 2H), 4.25 (m, 2H), 4.04 (s, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.32 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 165.6, 162.1, 149.6, 147.0, 132.2, 129.0, 121.0, 119.8, 106.7, 77.3, 77.0, 76.7, 61.4, 60.5, 14.2; HRMS (ESI) m/z calcd for $C_{15}H_{15}BrO_6$ $[M+H]^+$ 308.1129, found 308.1129.



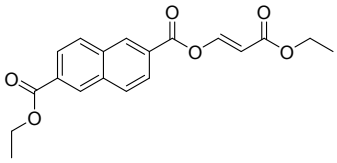
ethoxy-3-oxoprop-1-en-1-yl ethyl terephthalate (4e). yellow soild; m.p.: 100.3–116.6 °C, 108 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 12.5 Hz, 1H), 8.26–8.10 (m, 4H), 5.95 (d, *J* = 12.5 Hz, 1H), 4.43 (m, 2H), 4.26 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.4, 161.8, 149.4, 135.5, 131.3, 130.2, 129.7, 107.0, 77.3, 77.0, 76.7, 61.6, 60.6, 14.2; HRMS (ESI) m/z calcd for $C_{15}H_{16}O_6$ $[M+Na]^+$ 315.0839, found 315.0836 .



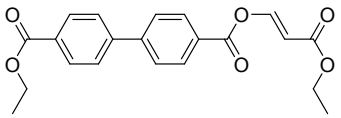
(3-ethoxy-3-oxoprop-1-en-1-yl) 4-ethyl 2,5-dibromoterephthalate (4f). white solid; m.p.: 87.5–91.4 °C， 150.9 mg, 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 12.5 Hz, 1H), 8.09 (s, 1H), 7.99 (s, 1H), 5.88 (d, *J* = 12.5 Hz, 1H), 4.36 (m, 2H), 4.18 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.9, 159.9, 148.9, 137.2, 136.8, 132.4, 121.2, 120.1, 107.9, 77.3, 77.0, 76.7, 62.5, 60.7, 14.1; HRMS (ESI) m/z calcd for $C_{15}H_{14}Br_2O_6$ $[M+Na]^+$ 472.9030, found 472.9036.



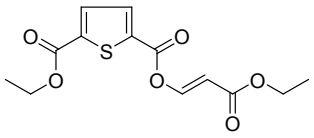
(3-ethoxy-3-oxoprop-1-en-1-yl) 4-ethyl naphthalene-1,4-dicarboxylate (4g). colorless oil; 123.8 mg, 72% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 9.5 Hz, 1H), 8.79 (d, *J* = 9.5 Hz, 1H), 8.63 (d, *J* = 12.5 Hz, 1H), 8.24 (d, *J* = 7.7 Hz, 1H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.74–7.60 (m, 2H), 5.95 (d, *J* = 12.5 Hz, 1H), 4.50 (m, 2H), 4.27 (m, 2H), 1.47 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.8, 166.0, 162.2, 149.6, 133.9, 131.8, 131.3, 129.5, 128.4, 127.9, 127,7, 127.2, 126.1, 125.5, 106.8, 77.4, 77.0, 76.7, 61.7, 60.5, 14.2; HRMS (ESI) m/z calcd for $C_{19}H_{18}O_6$ $[M+H]^+$ 343.1176, found 343.1175.



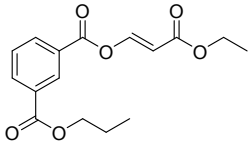
ethoxy-3-oxoprop-1-en-1-yl) 6-ethyl naphthalene-2,6-dicarboxylate (4h). white solid; m.p.: 121.4–121.8 °C, 128.5 mg, 75% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (m, 2H), 8.59 (d, *J* = 12.5 Hz, 1H), 8.22–8.09 (m, 2H), 8.10–7.93 (m, 2H), 5.98 (d, *J* = 12.5 Hz, 1H), 4.47 (m, 2H), 4.27 (m, 2H), 1.46 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 162.3, 149.7, 149.7, 135.1, 134.3, 132.0, 130.6, 130.5, 130.0, 129.7, 126.9, 126.4, 125.8, 106.7, 77.3, 77.0, 76.7, 61.4, 60.6, 14.3; HRMS (ESI) m/z calcd for $C_{19}H_{18}O_6$ $[M+Na]^+$ 365.0996, found 365.1001.



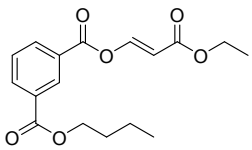
(3-ethoxy-3-oxoprop-1-en-1-yl) 4'-ethyl [1,1'-biphenyl]-4,4'-dicarboxylate (4i). white solid; m.p.: 99.7–100 °C，96.8 mg, 53% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 12.5 Hz, 1H), 8.17 (m, 4H), 7.71 (m, 4H), 5.92 (d, *J* = 12.5 Hz, 1H), 4.41 (m, 2H), 4.25 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 162.2, 149.7, 145.8, 143.7, 130.9, 130.4, 130.2, 127.5, 127.2, 106.5, 77.3, 77.0, 76.7, 61.1, 60.5, 14.2; HRMS (ESI) m/z calcd for $C_{21}H_{20}O_6$ $[M+H]^+$ 369.1333, found 369.1332.



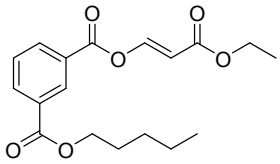
2-(3-ethoxy-3-oxoprop-1-en-1-yl) 5-ethyl thiophene-2,5-dicarboxylate (4j). white solid; m.p.: 48.0–50.1 °C, 93.9 mg, 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 12.5 Hz, 1H), 7.89 (d, *J* = 3.9 Hz, 1H), 7.78 (d, *J* = 3.8 Hz, 1H), 5.90 (d, *J* = 12.5 Hz, 1H), 4.47–4.33 (m, 2H), 4.25 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 161.1, 157.5, 149.0, 141.5, 135.6, 135.0, 133.0, 107.1, 77.2, 76.7, 76.6, 76.2, 62.0, 60.6, 14.2; HRMS (ESI) m/z calcd for $C_{13}H_{14}O_6S$ $[M+Na]^+$ 321.0403, found 321.0400.



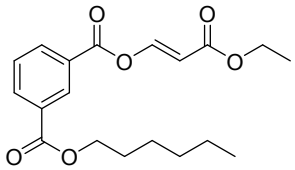
3-ethoxy-3-oxoprop-1-en-1-yl propyl isophthalate (4m). colorless oil; 90 mg, 59% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.54 (d, *J* = 12.5 Hz, 1H), 8.37 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 5.96 (d, *J* = 12.5 Hz, 1H), 4.34 (t, *J* = 6.7 Hz, 2H), 4.26 (m, 2H), 1.83 (m, 2H), 1.34 (m, 3H), 1.05 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.3, 161.8, 149.5, 144.1, 135.0, 134.2, 131.4, 129.0, 128.2, 106.9, 104.0, 77.3, 77.0, 76.7, 67.1, 60.6, 22.0, 14.2, 10.4; HRMS (ESI) m/z calcd for $C_{16}H_{18}O_6$ $[M+H]^+$ 307.1176, found 307.1178.



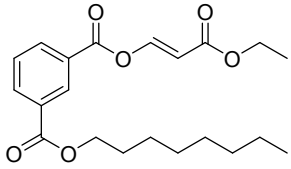
butyl (3-ethoxy-3-oxoprop-1-en-1-yl) isophthalate (4n). colorless oil; 96.1 mg, 60% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.54 (d, *J* = 12.5 Hz, 1H), 8.48–8.21 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 5.96 (d, *J* = 12.5 Hz, 1H), 4.38 (t, *J* = 6.7 Hz, 2H), 4.33–4.18 (m, 2H), 1.86–1.71 (m, 2H), 1.58–1.43 (m, 2H), 1.35 (m, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.4, 161.9, 149.5, 144.1, 135.0, 134.2, 131.4, 131.3, 129.0, 128.2, 107.0, 104.0, 77.3, 77.0, 76.7, 65.4, 60.6, 30.7, 19.2, 14.2, 13.7; HRMS (ESI) m/z calcd for $C_{17}H_{20}O_6$ $[M+H]^+$ 321.1333, found 321.1334.



ethoxy-3-oxoprop-1-en-1-yl pentyl isophthalate (4o). colorless oil; 81 mg, 49% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.55 (d, *J* = 12.5 Hz, 1H), 8.49–8.16 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 5.96 (d, *J* = 12.5 Hz, 1H), 4.37 (t, *J* = 6.8 Hz, 2H), 4.33–4.19 (m, 2H), 1.80 (m, 2H), 1.51–1.26 (m, 7H), 1.01–0.89 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.4, 161.9, 149.5, 135.0, 134.2, 131.4, 131.3, 129.0, 128.2, 107.0, 77.33 (s), 77.0, 76.6, 65.7, 60.6, 28.3, 28.1, 22.3, 14.2, 13.9; HRMS (ESI) m/z calcd for $C_{18}H_{22}O_6$ $[M+Na]^+$ 357.1309, found 357.1307.



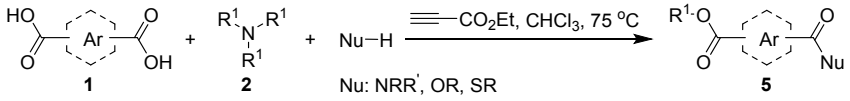
ethoxy-3-oxoprop-1-en-1-yl hexyl isophthalate (4p). colorless oil; 86 mg, 50% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.55 (d, *J* = 12.5 Hz, 1H), 8.48–8.19 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 5.96 (d, *J* = 12.5 Hz, 1H), 4.37 (t, *J* = 6.8 Hz, 2H), 4.26 (m, 2H), 1.88–1.72 (m, 2H), 1.56–1.40 (m, 2H), 1.41–1.27 (m, 7H), 0.91 (t, *J* = 5.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.4, 161.8, 149.5, 135.0, 134.2, 131.4, 131.3, 129.0, 128.2, 107.0, 77.3, 77.0, 76.7, 65.7, 60.6, 31.4, 28.6, 25.6, 22.5, 14.2, 13.9; HRMS (ESI) m/z calcd for $C_{19}H_{24}O_6$ $[M+Na]^+$ 371.1465, found 371.1468.



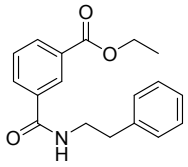
3-ethoxy-3-oxoprop-1-en-1-yl octyl isophthalate (4q). colorless oil; 113.1 mg, 60% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.54 (d, *J* = 12.5 Hz, 1H), 8.47–8.09 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 5.95 (d, *J* = 12.5 Hz, 1H), 4.37 (t, *J* = 6.8 Hz, 2H), 4.31–4.19 (m, 2H), 1.90–1.74 (m, 2H), 1.51–1.41 (m, 2H), 1.35–1.24 (m, 11H), 0.89 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.4, 161.8, 149.5, 135.0, 134.2, 131.4, 131.3, 128.9, 128.2, 107.0, 77.3, 77.0, 76.7, 65.7, 60.6, 31.7, 29.1,

28.6, 25.9, 22.6, 14.2, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{28}O_6$ $[M+Na]^+$ 399.1778, found 399.1781.

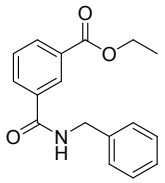
2.2 General procedure for the synthesis of the desired product 5



A mixture of aromatic dicarboxylic acid **1** (0.5 mmol), ethyl propiolate (1.1 mmol) was added a 10 mL tube along with a magnetic stir bar, and then 2 mL dry $CHCl_3$ was add. The tube was stirred and refluxed in oil bath at 75 °C. Subsequently, tertiary amine (0.8 mmol) solved in 1 mL $CHCl_3$ was add the tube slowly for 5 min. And the tube was stirred again and refluxed at 75 °C for 8h. Next the Nu-H (Nu = NRR', OR, SR) was add the tube. And the mixture was heated at 75 °C for another 3h. The solvent removed under reduced pressure and the residue was loaded on a silica gel column and flashed with 10–25% ethyl acetate in petroleum ether to afford the desired product **5**.

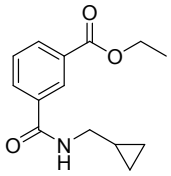


ethyl 3-(phenethylcarbamoyl)benzoate (5Na). white solid; m.p.: 116.8–118.2 °C，92.8 mg, 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.15 (d, *J* = 8.9 Hz, 1H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.34 (m, 2H), 7.25 (t, *J* = 5.9 Hz, 3H), 6.32 (s, 1H), 4.39 (m, 2H), 3.73 (m, 2H), 2.95 (t, *J* = 7.0 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.8, 138.7, 134.9, 132.3, 131.5, 130.8, 128.7, 127.4, 126.6, 77.3, 77.0, 76.7, 61.3, 41.3, 35.7, 14.3; HRMS (ESI) m/z calcd for $C_{18}H_{19}NO_3$ $[M+H]^+$ 298.1438, found 298.1441.

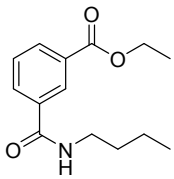


ethyl 3-(benzylcarbamoyl)benzoate (5Nb). white solid; 94.7 mg, 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H),

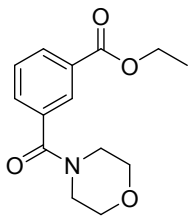
7.51 (t, *J* = 7.8 Hz, 1H), 7.44–7.26 (m, 5H), 6.64 (s, 1H), 4.65 (d, *J* = 5.7 Hz, 2H), 4.38 (m, 2H), 1.45–1.33 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.8, 137.9, 134.7, 132.4, 131.7, 130.9, 128.8, 127.9, 127.6, 77.3, 77.0, 76.7, 61.3, 44.2, 14.2; HRMS (ESI) m/z calcd for $C_{17}H_{17}NO_3$ $[M+H]^+$ 284.1281, found 284.1278.



ethyl 3-((cyclopropylmethyl)carbamoyl)benzoate (5Nc). colorless oil; 66.6 mg, 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 6.45 (s, 1H), 4.41 (m, 2H), 3.46–3.11 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.13–1.00 (m, 1H), 0.64–0.49 (m, 2H), 0.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.9, 135.0, 132.2, 131.7, 130.7, 128.7, 127.5, 77.3, 77.0, 76.7, 61.3, 45.1, 14.3, 10.7, 3.5; HRMS (ESI) m/z calcd for $C_{14}H_{17}NO_3$ $[M+Na]^+$ 270.1101, found 270.1100.

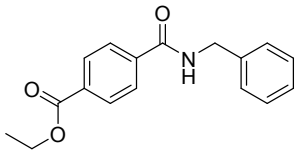


ethyl 3-(butylcarbamoyl)benzoate (5Nd). colorless oil; 75.4 mg, 61% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 6.67 (s, 1H), 4.38 (m, 2H), 3.45 (m, 2H), 1.69–1.53 (m, 2H), 1.40 (m, 5H), 0.94 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 165.9, 135.1, 132.0, 131.5, 130.7, 128.6, 127.6, 77.4, 77.0, 76.7, 61.2, 39.9, 31.6, 20.1, 14.2, 13.7; HRMS (ESI) m/z calcd for $C_{14}H_{19}NO_3$ $[M+H]^+$ 250.1438, found 250.1433.

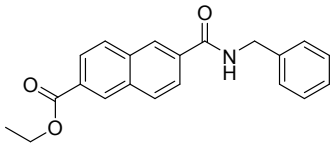


ethyl 3-(morpholine-4-carbonyl)benzoate (5Ne). colorless oil; 83 mg, 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17–7.95 (m, 2H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* =

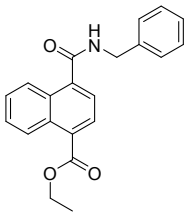
7.7 Hz, 1H), 4.40 (m, 2H), 3.79 (s, 4H), 3.65 (s, 2H), 3.45 (s, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 165.7, 135.6, 131.3, 130.9, 128.7, 128.1, 77.3, 77.2, 76.5, 66.8, 61.3, 14.2.



ethyl 4-(benzylcarbamoyl)benzoate (5Ng). white solid; m.p.: 117.1–119.5 °C，99 mg, 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 4.1 Hz, 5H), 6.74 (s, 1H), 4.63 (d, *J* = 5.7 Hz, 2H), 4.38 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 165.8, 138.2, 137.9, 133.0, 129.7, 128.7, 127.9, 127.6, 127.0, 77.3, 76.7, 61.3, 44.2, 14.2; HRMS (ESI) m/z calcd for $C_{17}H_{17}NO_3$ $[M+H]^+$ 284.1281, found 284.1281 .

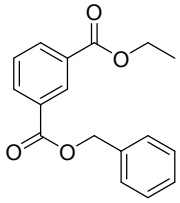


ethyl 6-(benzylcarbamoyl)-2-naphthoate (5Nh). white solid; m.p.: 153.6–154.2 °C，121.5 mg, 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.30 (s, 1H), 8.07 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.92–7.79 (m, 2H), 7.46–7.26 (m, 5H), 6.84 (s, 1H), 4.68 (d, *J* = 5.7 Hz, 2H), 4.43 (m, 2H), 1.44 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 166.4, 138.1, 134.6, 133.7, 130.5), 129.8, 129.3, 129.0, 128.8, 127.9, 127.6, 127.1, 126.1, 124.4, 77.3, 77.0, 76.7, 61.3, 44.3, 14.3; HRMS (ESI) m/z calcd for $C_{21}H_{19}NO_3$ $[M+H]^+$ 334.1438, found 334.1437.

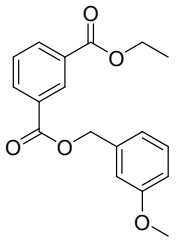


ethyl 4-(benzylcarbamoyl)-1-naphthoate (5Ni). White solid; m.p.: 147.0–147.1 °C，113.2 mg, 68% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.53–7.45 (m, 1H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.37–7.22 (m, 5H), 6.75 (s, 1H), 4.61 (d, *J* = 5.8 Hz, 2H), 4.41 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 165.6,

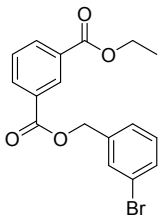
162.1, 149.6, 147.0, 132.2, 129.0, 121.1, 119.8, 106.7, 77.3, 77.0, 76.7, 61.4, 60.5, 14.2; HRMS (ESI) m/z calcd for $C_{21}H_{19}NO_3$ $[M+H]^+$ 334.1438, found 334.1436.



benzyl ethyl isophthalate (5Oa). colorless oil; 102.3 mg, 72% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.23 (m, 2H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.48–7.41 (m, 2H), 7.36 (m, 3H), 5.38 (d, *J* = 4.3 Hz, 2H), 4.39 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 135.8, 133.8, 131.1, 130.5, 128.6, 128.4, 128.1, 77.4, 77.1, 76.8, 67.0, 61.3, 14.3. HRMS (ESI) m/z calcd for $C_{17}H_{16}O_4$ $[M+Na]^+$ 307.0941, found 307.0945.

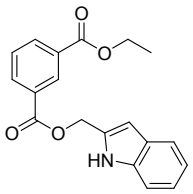


ethyl (3-methoxybenzyl) isophthalate (5Ob). colorless oil; 100.5 mg, 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.25 (t, *J* = 4.7 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.07–6.97 (m, 2H), 6.89 (d, *J* = 8.2 Hz, 1H), 5.37 (s, 2H), 4.40 (m, 2H), 3.82 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.8, 137.3, 133.8, 133.6, 131.0, 130.7, 130.5, 129.7, 128.5, 120.4, 113.7, 77.3, 77.0, 76.7, 66.8, 61.3, 55.2, 14.3; HRMS (ESI) m/z calcd for $C_{18}H_{18}O_5$ $[M+H]^+$ 315.1227, found 315.1226.

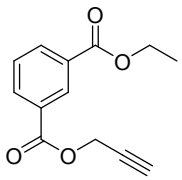


bromobenzyl ethyl isophthalate (5Oc). colorless oil; 130.9 mg, 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.24 (d, *J* = 7.7 Hz, 2H), 7.61 (s, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 7.8 Hz,

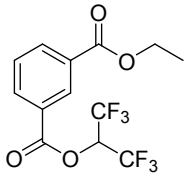
1H), 5.35 (s, 2H), 4.41 (m, 2H), 1.41 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.8, 138.2, 137.9, 133.1, 129.7, 128.8, 127.9, 127.7, 127.0, 77.3, 77.0, 76.7, 61.3, 44.2, 14.2; HRMS (ESI) m/z calcd for $C_{17}H_{15}BrO_4$ $[M+Na]^+$ 385.0046, found 385.0046.



(1H-indol-2-yl)methyl ethyl isophthalate (5Od). colorless oil; 76.9 mg, 48% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.68 (s, 1H), 8.20 (t, J = 6.7 Hz, 2H), 7.60 (d, J = 7.9 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.62 (s, 1H), 5.48 (s, 2H), 4.39 (m, 2H), 1.39 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 165.7, 136.7, 134.1, 133.8, 132.7, 131.0, 130.8, 130.1, 128.6, 127.5, 122.8, 120.9, 120.0, 111.2, 104.2, 77.4, 77.1, 76.8, 61.4, 60.5, 14.3; HRMS (ESI) m/z calcd for $C_{19}H_{17}NO_4$ $[M+H]^+$ 324.1230, found 324.1234.

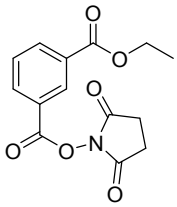


ethyl prop-2-yn-1-yl isophthalate (5Oe). colorless oil; 75.5 mg, 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.37–8.09 (m, 2H), 7.55 (t, J = 7.8 Hz, 1H), 4.96 (s, 2H), 4.42 (m, 2H), 2.58 (s, 1H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 164.9, 134.1, 133.8, 131.0, 130.8, 129.8, 128.6, 77.4, 77.0, 76.7, 75.2, 61.3, 52.6, 14.2; HRMS (ESI) m/z calcd for $C_{13}H_{12}O_4$ $[M+H]^+$ 233.0808, found 233.0808.

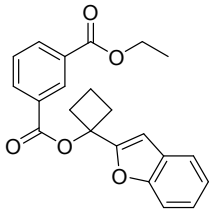


ethyl (1,1,1,3,3,3-hexafluoropropan-2-yl) isophthalate (5Of). colorless oil; 110.2 mg, 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.35 (d, J = 7.8 Hz, 1H), 8.30

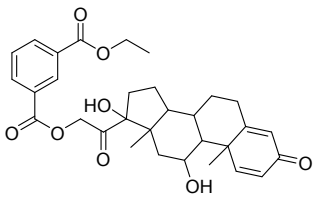
(d, J = 7.8 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 6.05 (quint, J = 6 Hz, 1H), 4.44 (m, 2H), 1.43 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.1. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 162.6, 135.4, 134.2, 131.5, 129.0, 127.2, 124.7-116.3 (q, $J_{C\text{-}F}$ = 279 Hz, 3F), 77.3, 76.9, 76.6, 67.8-66.4 (quint, $J_{C\text{-}C\text{-}F}$ = 35 Hz, CH), 61.6, 14.2; HRMS (ESI) m/z calcd for $C_{13}H_{10}F_6O_4$ $[M+H]^+$ 345.0556, found 345.0554.



2,5-dioxopyrrolidin-1-yl ethyl isophthalate (5Oh). colorless oil; 80.5 mg, 55% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.33 (m, 2H), 7.63 (t, J = 7.8 Hz, 1H), 4.42 (m, 2H), 2.93 (s, 4H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 165.0, 161.2, 135.6, 134.4, 131.4, 129.1, 125.5, 77.4, 77.1, 76.8, 61.6, 25.6, 14.2.

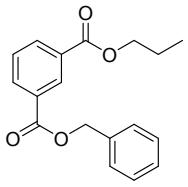


(benzofuran-2-yl)cyclobutyl ethyl isophthalate (5Oi). colorless oil; 63.4 mg, 35% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.36–8.03 (m, 2H), 7.65–7.48 (m, 2H), 7.44 (d, J = 8.3 Hz, 1H), 7.34–7.12 (m, 2H), 6.88 (s, 1H), 4.40 (m, 2H), 3.00–2.87 (m, 2H), 2.88–2.71 (m, 2H), 2.00 (m, 2H), 1.41 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 164.2, 156.7, 154.9, 133.8, 130.8, 128.5, 128.0, 124.3, 122.8, 121.2, 111.3, 104.2, 77.8, 77.3, 77.0, 76.7, 61.3, 34.1, 14.5, 14.3; HRMS (ESI) m/z calcd for $C_{22}H_{20}O_5$ $[M+Na]^+$ 387.1203, found 387.1205.

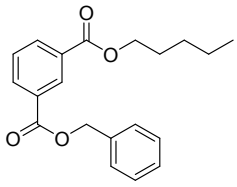


2-(11,17-dihydroxy-10,13-dimethyl-3-oxo-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[a]phenanthren-17-yl)-2-oxoethyl ethyl isophthalate

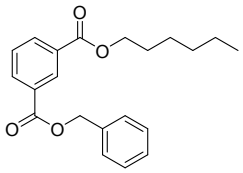
(5Oj). white solid; m.p.: 208.5–209.7 °C, 110.6 mg, 41% yield; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 8.52 (s, 1H), 8.25 (d, *J* = 7.7 Hz, 2H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 10.1 Hz, 1H), 6.18 (d, *J* = 10.1 Hz, 1H), 5.93 (s, 1H), 5.53 (s, 1H), 5.38 (d, *J* = 17.5 Hz, 1H), 5.08 (d, *J* = 17.5 Hz, 1H), 4.79 (d, *J* = 3.7 Hz, 1H), 4.37 (m, 2H), 4.33 (d, *J* = 5.2 Hz, 1H), 2.60–2.43 (m, 3H), 2.30 (d, *J* = 9.9 Hz, 1H), 2.14–1.88 (m, 3H), 1.76 (d, *J* = 12.4 Hz, 1H), 1.66 (m, 2H), 1.58–1.44 (m, 1H), 1.40 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.03 (m, 1H), 0.92 (d, *J* = 13.3 Hz, 1H), 0.84 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 205.5, 185.6, 170.9, 165.3, 164.9, 157.1, 134.2, 130.9, 130.3, 130.1, 127.5, 122.0, 89.1, 69.1, 68.8, 61.7, 55.8, 51.5, 47.6, 44.2, 34.4, 33.6, 31.7, 31.4, 23.9, 21.3, 16.9, 14.5. HRMS (ESI) m/z calcd for $C_{31}H_{36}O_8$ $[M+Na]^+$ 559.2302, found 559.2302.



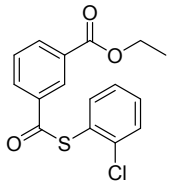
benzyl propyl isophthalate (5Ok). colorless oil; 86.4 mg, 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.24 (t, *J* = 7.2 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 6.9 Hz, 2H), 7.39 (t, *J* = 9.7 Hz, 3H), 5.39 (s, 2H), 4.30 (t, *J* = 6.7 Hz, 2H), 1.80 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 135.8, 133.8, 131.0, 130.7, 128.6, 128.3, 77.4, 77.0, 76.7, 66.9, 22.0, 10.4, 1.0; HRMS (ESI) m/z calcd for $C_{18}H_{18}O_4$ $[M+Na]^+$ 321.1097, found 321.1098.



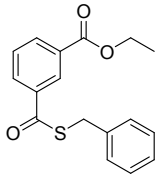
benzyl pentyl isophthalate (5Ol). colorless oil; 108.6 mg, 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.24 (t, *J* = 8.2 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.43–7.29 (m, 3H), 5.40 (s, 2H), 4.34 (t, *J* = 6.7 Hz, 2H), 1.84–1.71 (m, 2H), 1.40 (m, 4H), 0.93 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 135.8, 133.8, 131.0, 130.7, 128.6, 128.3, 77.3, 77.0, 76.7, 67.0, 65.5, 28.3, 28.1, 22.3, 13.9; HRMS (ESI) m/z calcd for $C_{20}H_{22}O_4$ $[M+Na]^+$ 349.1410, found 349.1410.



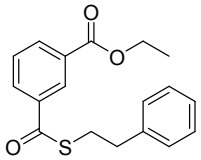
benzyl hexyl isophthalate (5Om). colorless oil; 76.9 mg, 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.24 (t, *J* = 9.5 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 6.7 Hz, 2H), 7.42–7.31 (m, 3H), 5.39 (s, 2H), 4.34 (t, *J* = 6.7 Hz, 2H), 1.76 (m, 2H), 1.49–1.39 (m, 2H), 1.34 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 165.7, 135.8, 133.8, 131.0, 130.8, 130.6, 128.6, 128.3, 77.4, 77.0, 76.7, 67.0, 65.5, 31.4, 28.6, 25.6, 22.5, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{24}O_4$ $[M+Na]^+$ 363.1567, found 363.1569.



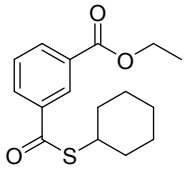
ethyl 3-(((2-chlorophenyl)thio)carbonyl)benzoate (5Sb). colorless oil; 104.5 mg, 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.30 (d, *J* = 9.2 Hz, 1H), 8.21 (d, *J* = 9.6 Hz, 1H), 7.68–7.51 (m, 3H), 7.39 (m, 2H), 4.44 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.6, 165.4, 139.1, 137.5, 136.6, 134.5, 131.4, 130.3, 129.0, 128.6, 127.4, 126.6, 77.3, 77.0, 76.7, 61.5, 14.3; HRMS (ESI) m/z calcd for $C_{16}H_{13}ClO_3S$ $[M+H]^+$ 321.0347, found 321.0346.



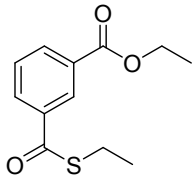
ethyl 3-((benzylthio)carbonyl)benzoate (5Sc). colorless oil; 85.1 mg, 57% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.23 (d, *J* = 1.8 Hz, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.1 Hz, 2H), 7.32 (d, *J* = 6.2 Hz, 2H), 7.25 (m, 1H), 4.44–4.37 (m, 2H), 4.34 (s, 2H), 1.44–1.38 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5, 165.5, 137.0, 134.1, 133.6, 131.2, 129.0, 128.7, 128.3, 127.4, 77.4, 77.0, 76.7, 61.4, 33.5, 14.3; HRMS (ESI) m/z calcd for $C_{17}H_{16}O_3S$ $[M+Na]^+$ 323.0712, found 323.0712.



ethyl 3-((phenethylthio)carbonyl)benzoate (5Sd). colorless oil; 97 mg, 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 8.13 (d, *J* = 3.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.36–7.21 (m, 5H), 4.42 (m, 2H), 3.43–3.23 (m, 2H), 3.08–2.91 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 165.6, 139.9, 137.4, 134.0, 131.1, 128.6, 128.2, 126.6, 77.3, 77.0, 76.7, 61.4, 35.8, 30.6, 14.3; HRMS (ESI) m/z calcd for $C_{18}H_{18}O_3S$ $[M+H]^+$ 315.1049, found 315.1047.

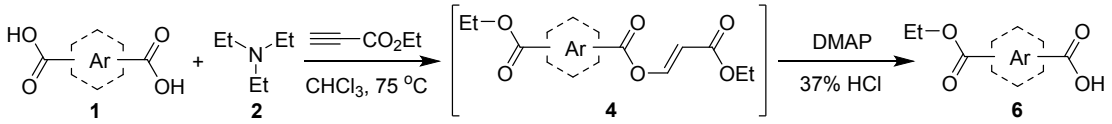


ethyl 3-((cyclohexylthio)carbonyl)benzoate (5Se). colorless oil; 72.6 mg, 50% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.21 (s, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 4.41 (m, 2H), 3.76 (m, 1H), 2.03 (m, 2H), 1.82–1.69 (m, 2H), 1.65 (m, 2H), 1.52 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 165.6, 135.8, 133.8, 133.8, 131.0, 130.8, 130.6, 128.6, 128.6, 128.3, 128.2, 77.4, 77.0, 76.7, 67.0, 65.5, 31.4, 28.6, 25.6, 22.5, 14.0; HRMS (ESI) m/z calcd for $C_{16}H_{20}O_3S$ $[M+H]^+$ 293.1206, found 293.1205.

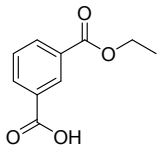


ethyl 3-((ethylthio)carbonyl)benzoate (5Sf). colorless oil; 58.9 mg, 49% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 4.42 (m, 2H), 3.11 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3, 165.6, 137.5, 133.9, 131.1, 128.7, 128.2, 77.3, 77.0, 76.7, 61.3, 23.6, 14.6, 14.2.

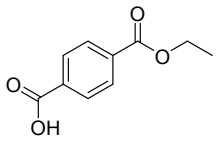
2.3 General procedure for the synthesis of (ethoxycarbonyl)benzoic acid 6



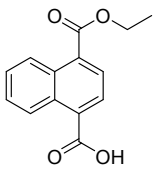
A mixture of aromatic dicarboxylic acid **1** (0.5 mmol), ethyl propiolate (1.1 mmol) was added a 10 mL tube along with a magnetic stir bar, and then 2mL dry $CHCl_3$ was add. The tube was stirred and refluxed in oil bath at 75°C. Subsequently, triethylamine (0.8 mmol) solved in 1mL $CHCl_3$ was add the tube slowly for 5min. And the tube was stirred again and refluxed at 75 °C for 8 h, Next DMAP (0.9 mmol) was add the tube and the mixture was heated at 75 °C for 5 h. Then 0.3 g 37% HCl solution, 2 mL H_2O and 40 mol% $Bu_4N^+Br^-$ were add the tube in sequence. The tube was sealed and stirred at room temperature for 10 h. The solution was extracted with CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was loaded on a silica gel column and flashed with 5-10% methanol in dichloromethane to afford the desired product **6**.



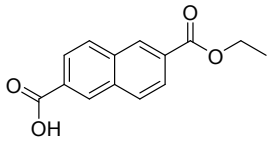
3-(ethoxycarbonyl)benzoic acid (6a). white solid; m.p.: 127.6–128.9 °C, 73.8 mg, 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.31 (d, *J* = 7.8 Hz, 2H), 7.58 (t, *J* = 7.8 Hz, 1H), 4.43 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 134.6, 134.2, 131.2, 128.7, 77.3, 77.0, 76.7, 61.4, 14.3.



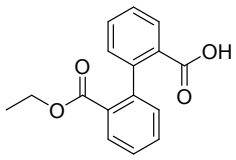
4-(ethoxycarbonyl)benzoic acid (6b). white solid; 168.4–171.0 °C, 71.6 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (m, 4H), 4.42 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 165.7, 135.0, 132.9, 130.1, 129.6, 77.3, 77.0, 76.6, 61.5, 14.2.



4-(ethoxycarbonyl)-1-naphthoic acid (6c). white solid; 234.5–235.6 °C, 87.1 mg, 71% yield; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 8.80 (m, 1H), 8.67 (m, 1H), 8.10 (m, 2H), 7.72 (m, 2H), 4.44 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 168.8, 167.1, 133.0, 131.8, 131.0, 128.2, 126.3, 125.9, 61.8, 40.6, 40.3, 40.2, 40.1, 40.0, 39.8, 39.6, 39.4, 14.5; HRMS (ESI) m/z calcd for $C_{14}H_{12}O_4$ $[M+H]^+$ 245.0808, found 245.0812.

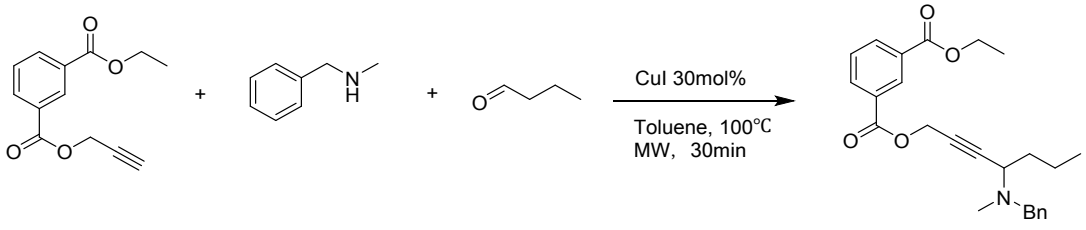


6-(ethoxycarbonyl)-2-naphthoic acid (6d). white solid; m.p.: 233.2–234.4 °C, 91.7 mg, 75% yield; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 8.65 (s, 2H), 8.20 (d, *J* = 8.5 Hz, 2H), 8.03 (m, 2H), 4.38 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 167.5, 166.0, 134.5, 130.6, 130.2, 129.6, 126.4, 125.9, 61.5, 40.6, 40.2, 39.9, 39.9, 39.6, 39.3, 39.3, 14.6.



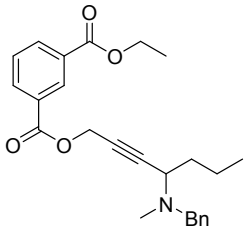
2'-(ethoxycarbonyl)-[1,1'-biphenyl]-2-carboxylic acid (6e). white solid; m.p.: 89.3–90.7 °C, 81 mg, 60% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.52 (m, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 2H), 4.05 (m, 2H), 0.99 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 167.5, 143.6, 142.6, 131.8, 131.3, 130.2, 129.8, 128.8, 127.2, 77.3, 77.0, 76.7, 60.8, 13.6.

2.4 Synthesis of compound 7a



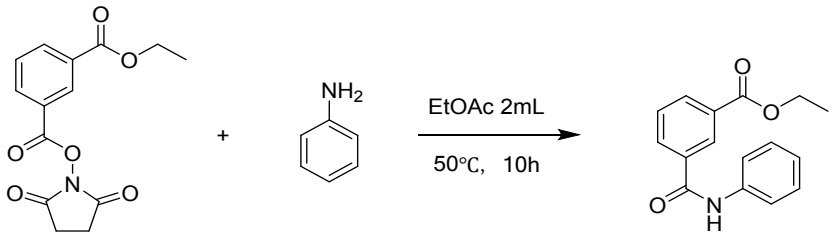
A mixture of ethyl prop-2-yn-1-yl isophthalate **5Oe** (0.93 mmol), *N*-methyl-1-phenylmethanamine (0.74 mmol), butyraldehyde (0.62 mmol) was added a

microwave vial along with a magnetic stir bar, then CuI (30 mol%) and Toluene (1 mL) was added. The reaction vessel was sealed and irradiated in the cavity of Biotage microwave reactor at a ceiling temperature of 100 °C and a maximum power of 100 W for 30 min. The resulting reaction mixture was loaded on a silica gel column and flashed with 4−10% ethyl acetate in petroleum ether to afford the desired product **7a**, a yellow oil.

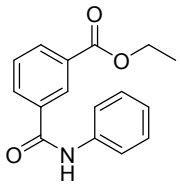


(benzyl(methyl)amino)hept-2-yn-1-yl ethyl isophthalate (7a). yellow oil; 187.5mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.26 (t, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.40–7.09 (m, 5H), 5.04 (s, 2H), 4.41 (m, 2H), 3.67 (d, *J* = 13.2 Hz, 1H), 3.45 (m, 2H), 2.21 (s, 3H), 1.66 (m, 2H), 1.47 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 165.1, 139.2, 134.0, 133.8, 131.0, 130.8, 130.2, 128.9, 128.6, 128.2, 126.9, 85.3, 79.1, 77.4, 77.1, 76.8, 61.3, 59.1, 55.1, 53.3, 37.6, 35.6, 19.6, 14.3, 13.7; HRMS (ESI) m/z calcd for $C_{25}H_{29}NO_4$ $[M+H]^+$ 408.2169, found 408.2166

2.5 Synthesis of compound 5Nf

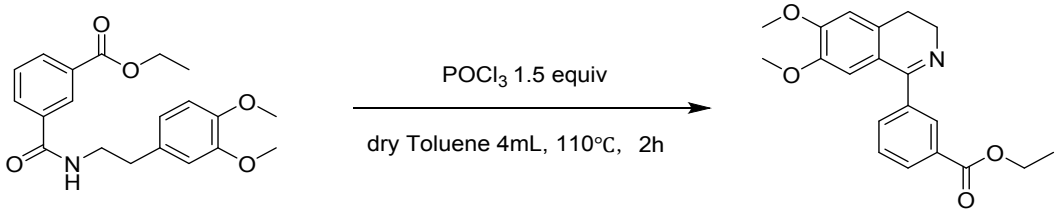


A mixture of 2,5-dioxopyrrolidin-1-yl ethyl isophthalate **5Oh** (0.29 mmol), aniline (0.87 mmol) was added a 10 mL tube along with a magnetic stir bar, and then 2mL EtOAc was add. The tube was stirred and refluxed in oil bath at 50 °C. The solvent removed under reduced pressure and the residue was loaded on a silica gel column and flashed with 10–25% ethyl acetate in petroleum ether to afford the desired product **5Nf**, a white solid.

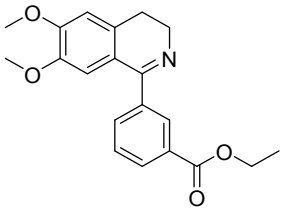


ethyl 3-(phenylcarbamoyl)benzoate (5Nf). White solid; m.p.: 119.8–120.0 °C, 54 mg, 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.19 (d, *J* = 10.4 Hz, 1H), 8.10 (d, *J* = 9.2 Hz, 2H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 4.40 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 164.8, 137.7, 135.2, 132.6, 131.9, 130.9, 129.0, 127.5, 124.8, 120.4, 77.3, 77.0, 76.7, 61.5, 14.3;

2.6 Synthesis of compound 7b



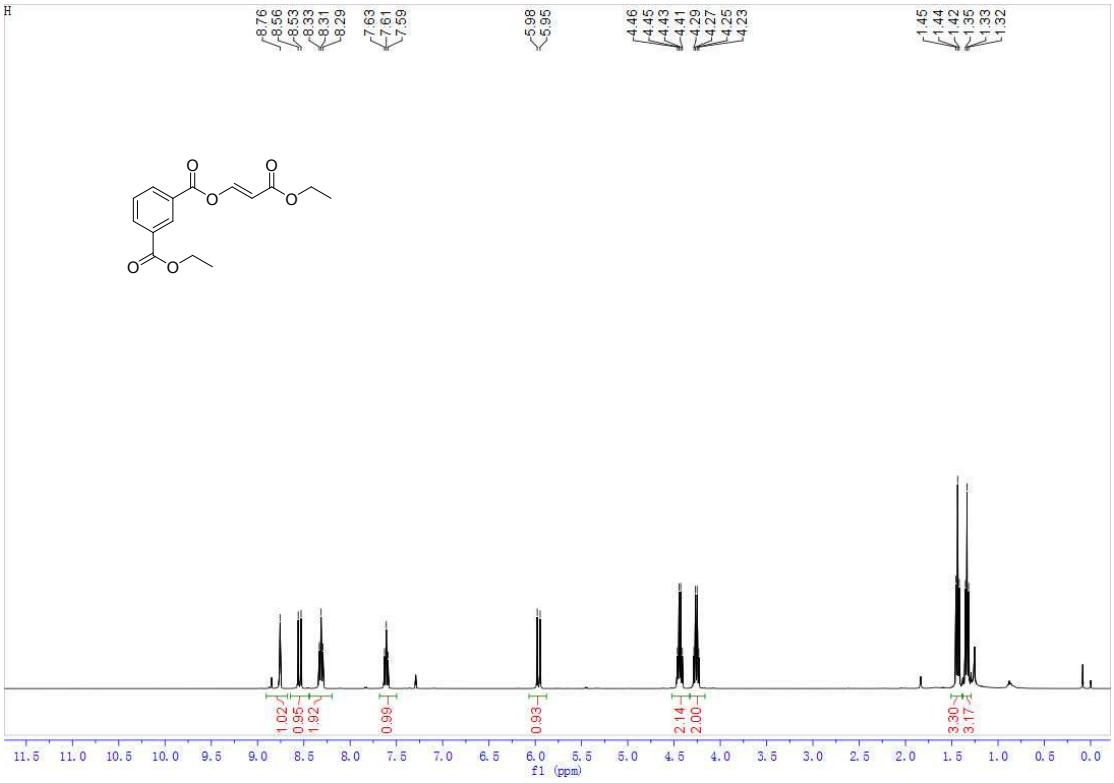
ethyl 3-((3,4-dimethoxyphenethyl)carbamoyl)benzoate (0.49 mmol), 3 mL dry toluene was added a 10 mL tube along with a magnetic stir bar, and then $POCl_3$ (1.5 equiv) was add the tube slowly. The tube was stirred and refluxed in oil bath at 110 °C for 2 h. The solvent removed under reduced pressure and the residue was loaded on a silica gel column and flashed with 10–25% ethyl acetate in petroleum ether to afford the desired product **7b**, a yellow oil.

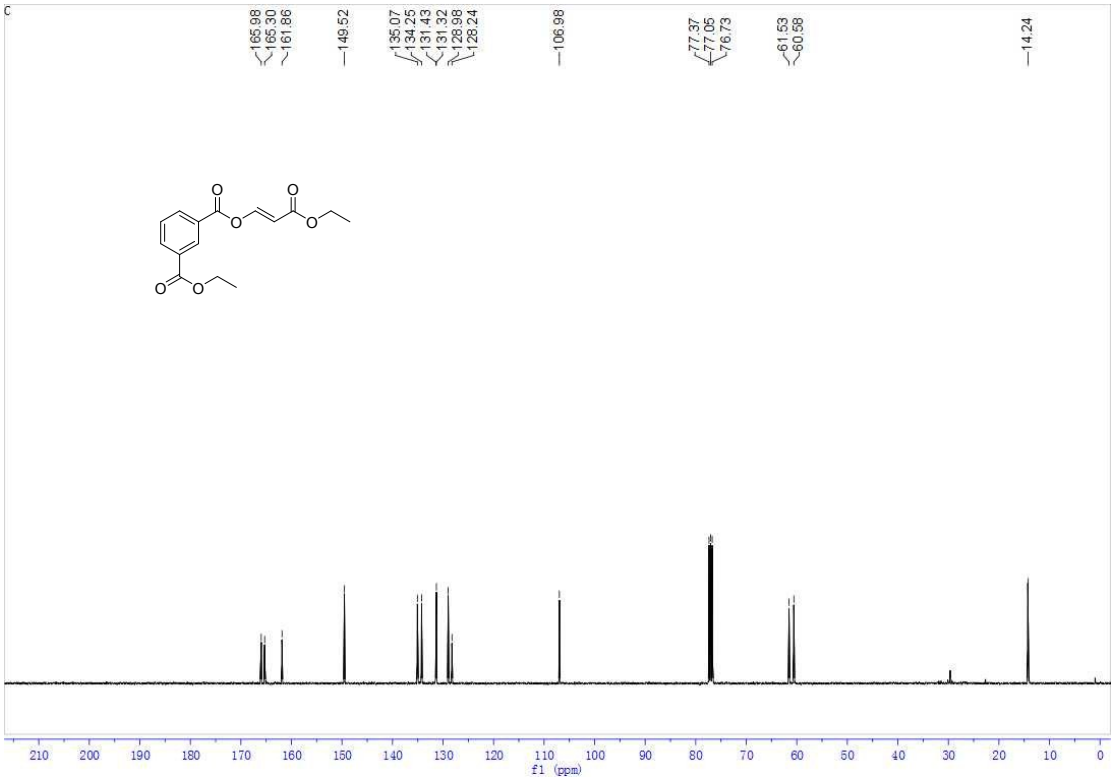


ethyl 3-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)benzoate (7b). yellow oil; 100.3 mg, 60% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 6.7 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 6.82 (s, 1H), 6.75 (s, 1H), 4.49–4.27 (m, 2H), 3.96 (s, 3H), 3.88–3.80 (m, 2H), 3.73 (s, 3H), 2.84–2.67 (m, 2H), 1.39 (t, *J* =

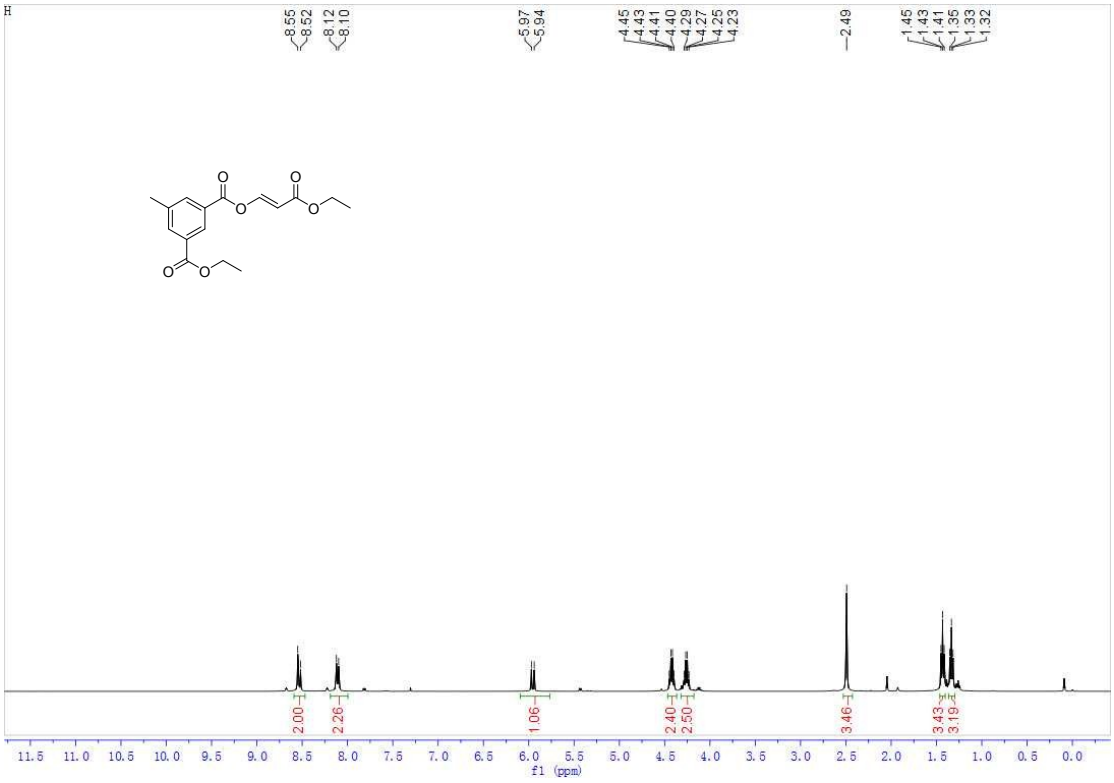
7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 165.8, 151.1, 147.2, 139.3, 132.9, 132.5, 130.5, 130.3, 129.7, 128.2, 121.1, 111.3, 110.4, 77.5, 77.2, 77.0, 60.9, 56.0, 47.6, 25.8, 14.2; HRMS (ESI) m/z calcd for $C_{20}H_{21}NO_4$ $[M+H]^+$ 340.1543, found 340.1544.

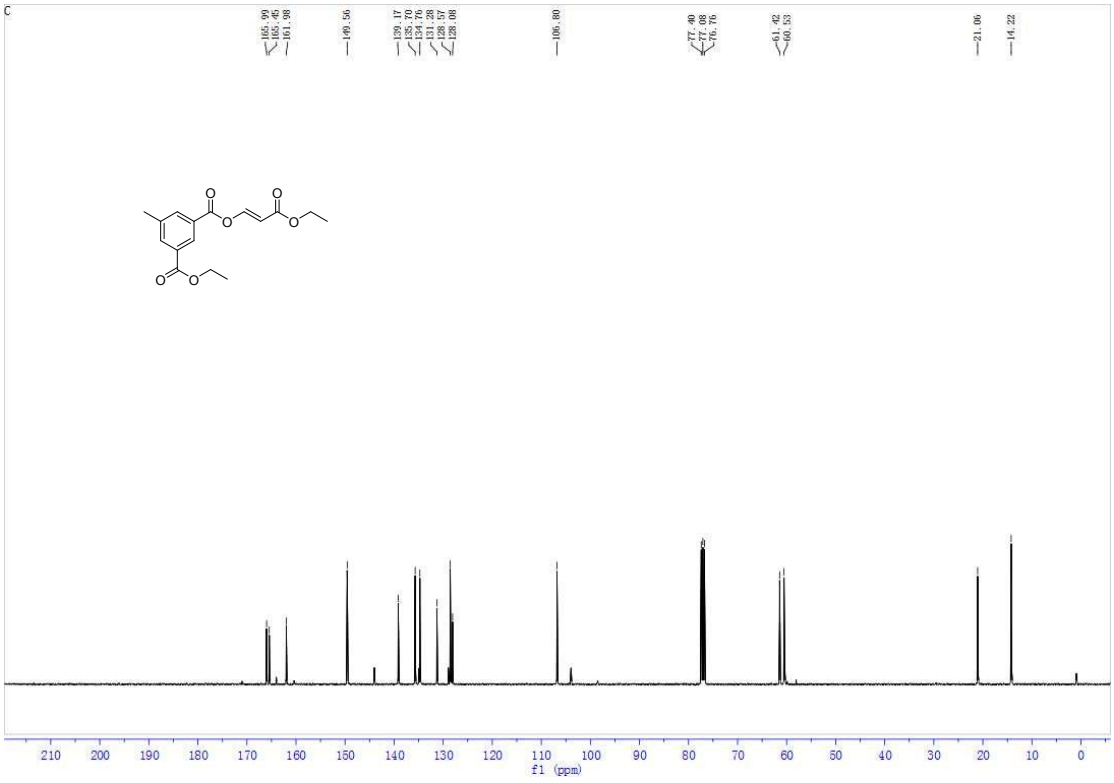
3-ethoxy-3-oxoprop-1-en-1-yl ethyl isophthalate (4a)



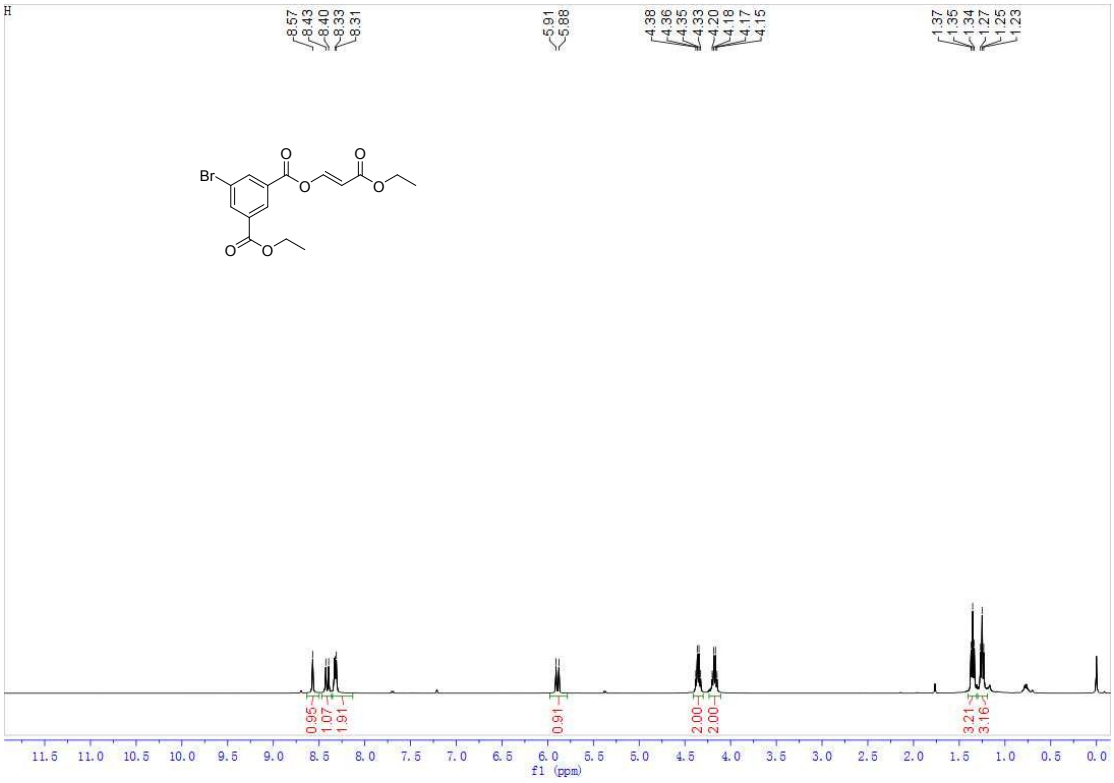


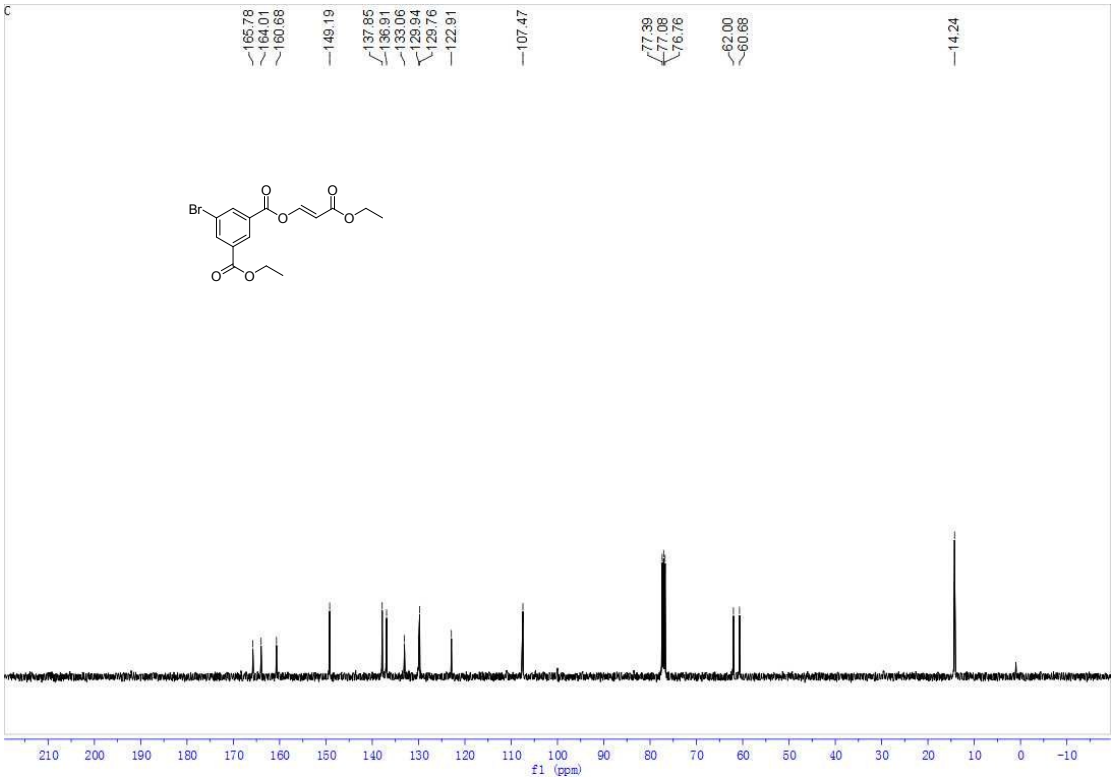
(3-ethoxy-3-oxoprop-1-en-1-yl) 3-ethyl 5-methylisophthalate (4b)



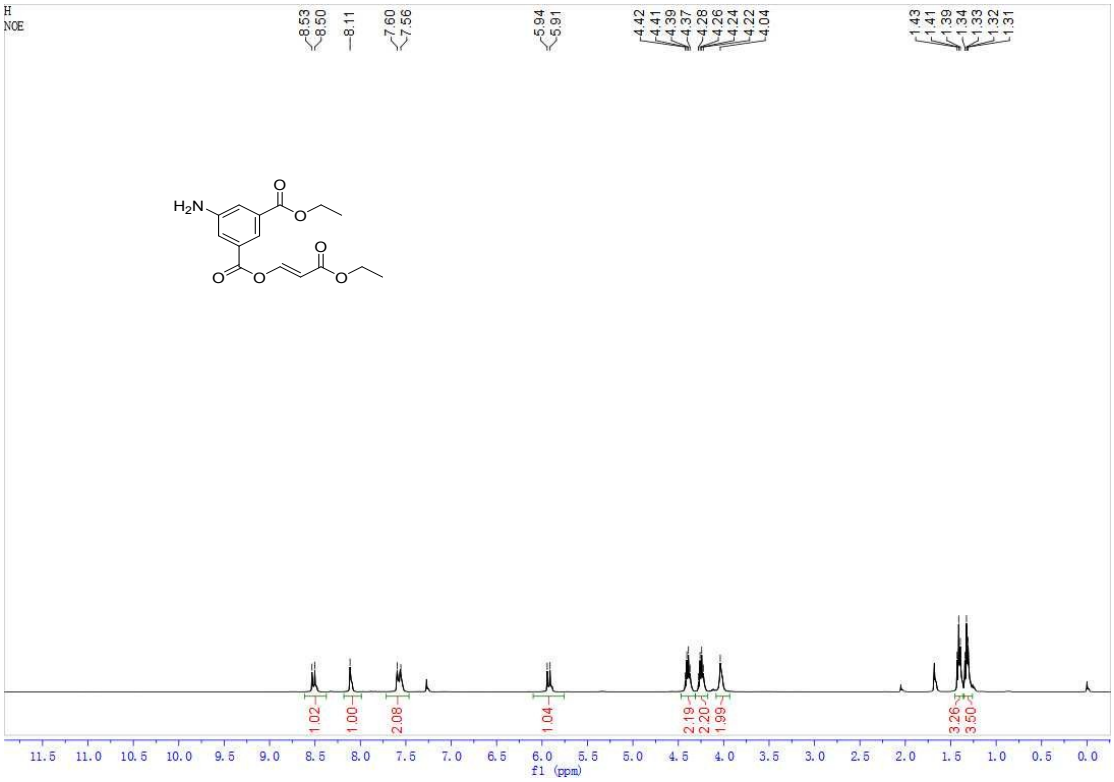


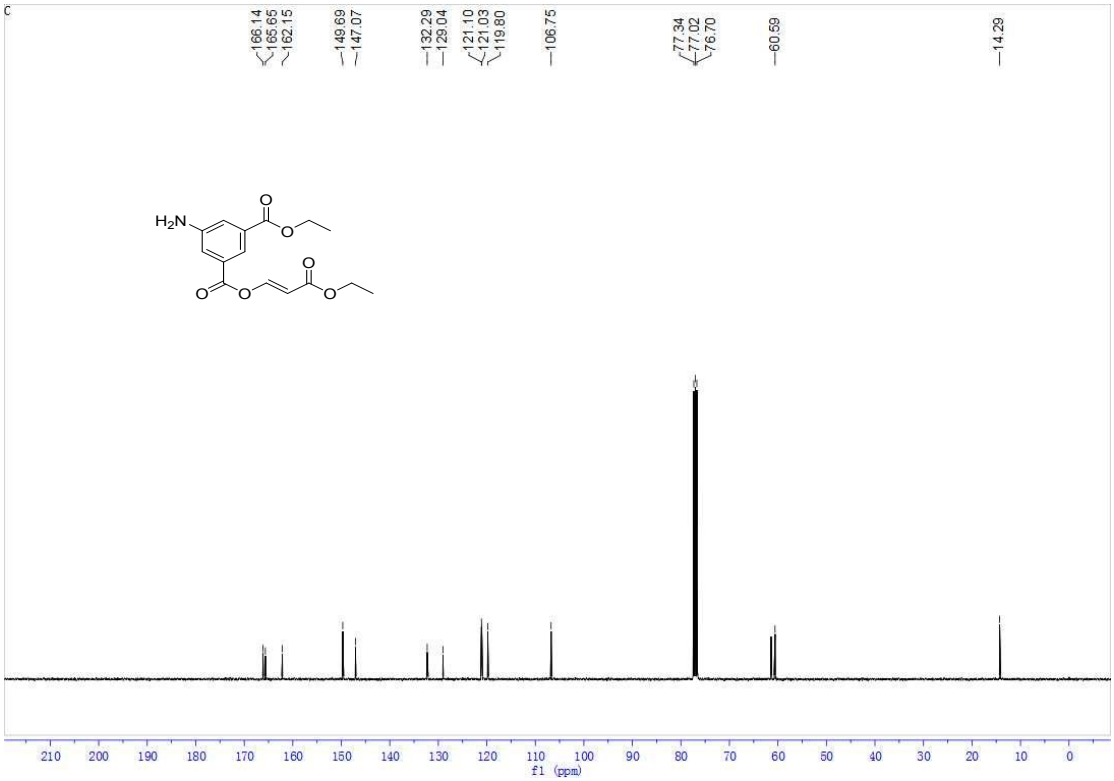
(3-ethoxy-3-oxoprop-1-en-1-yl) 3-ethyl 5-bromoisophthalate (4c)



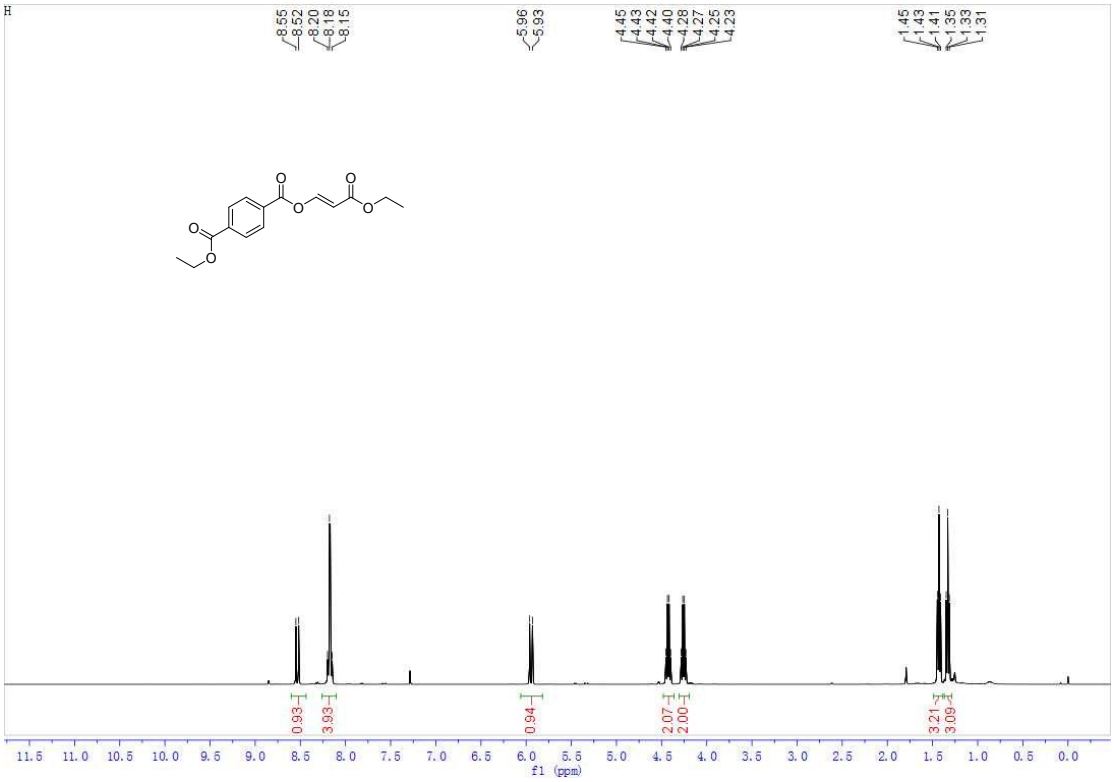


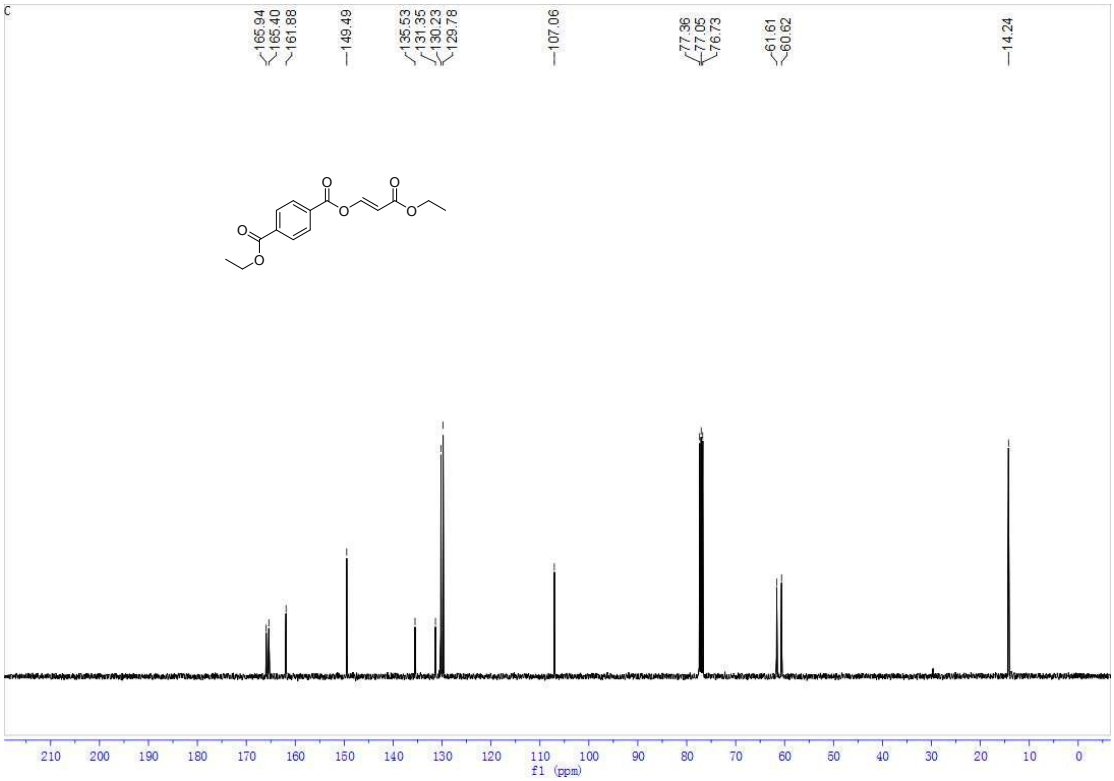
(3-ethoxy-3-oxoprop-1-en-1-yl) 3-ethyl 5-aminoisophthalate (4d)



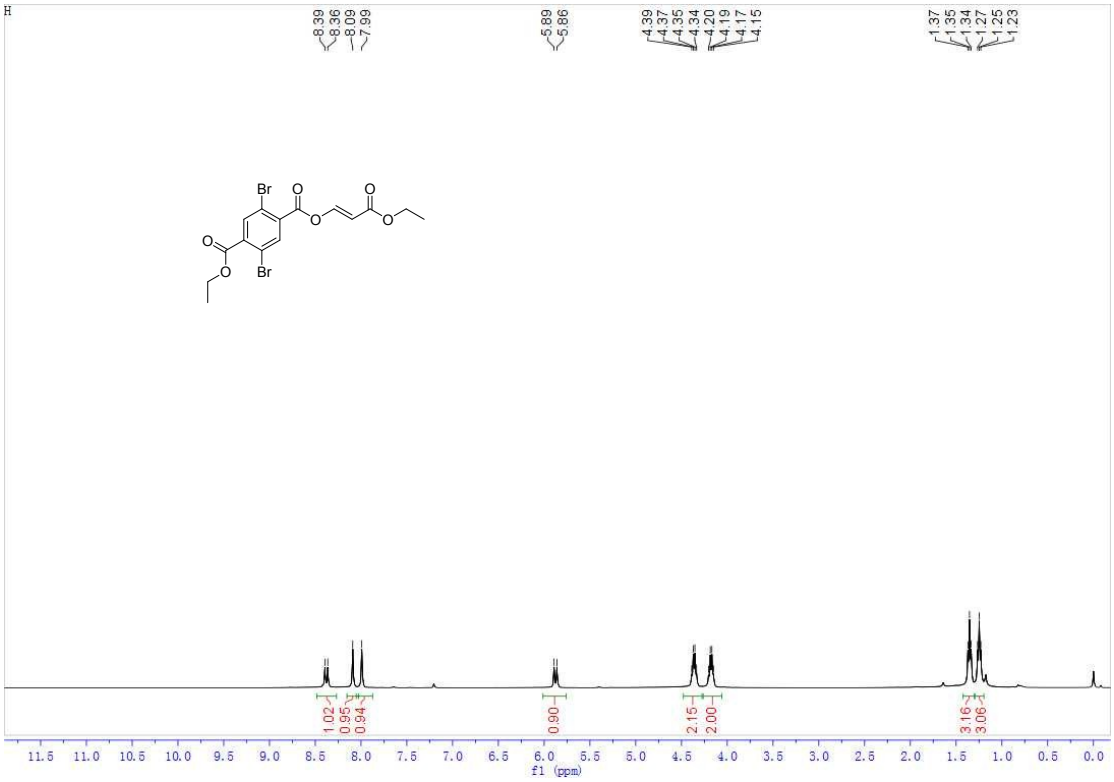


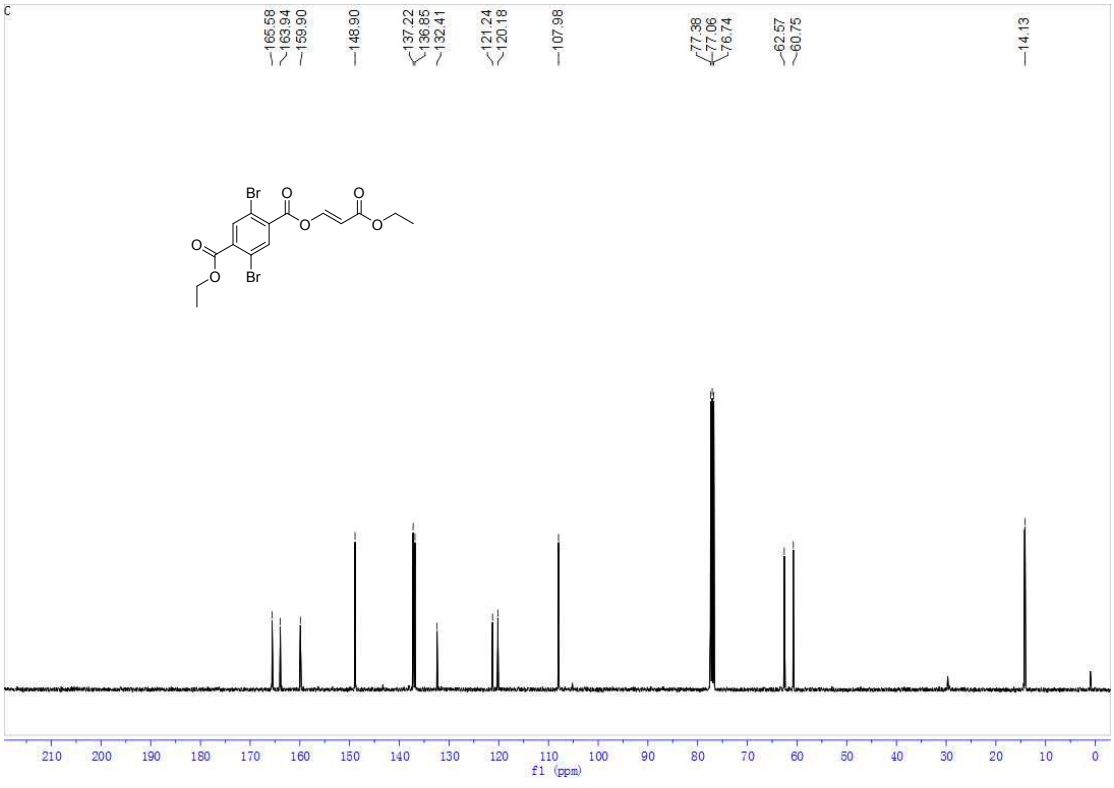
ethoxy-3-oxoprop-1-en-1-yl ethyl terephthalate (4e)



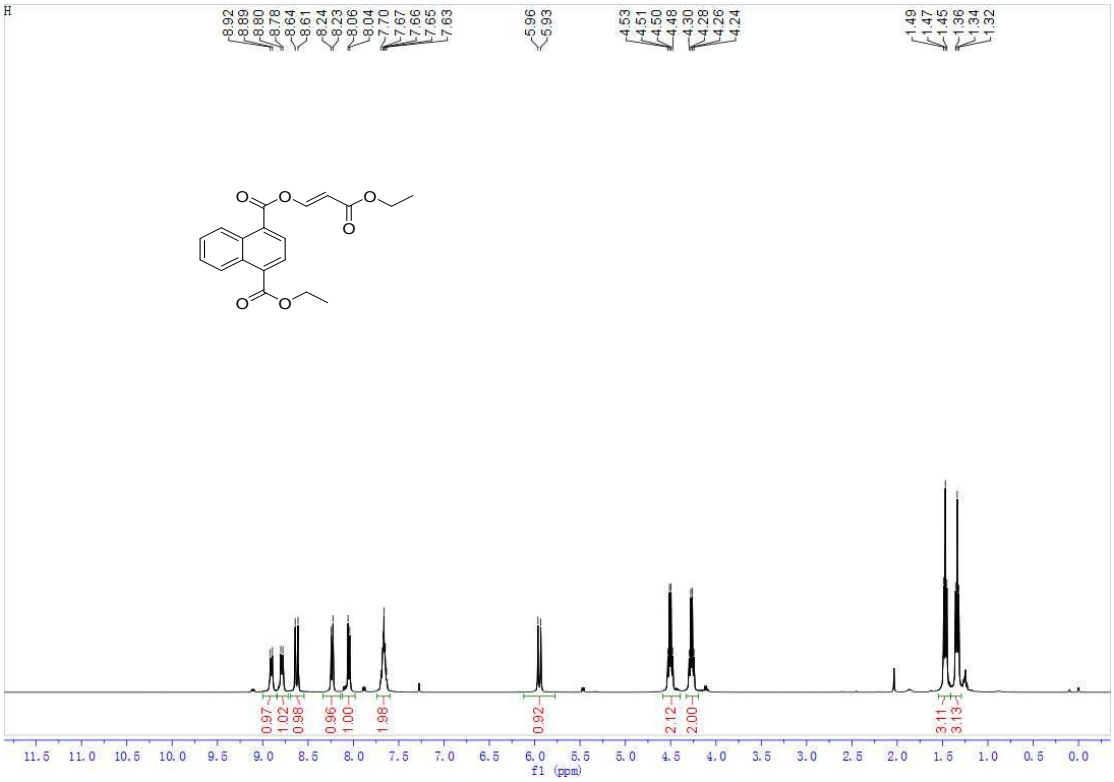


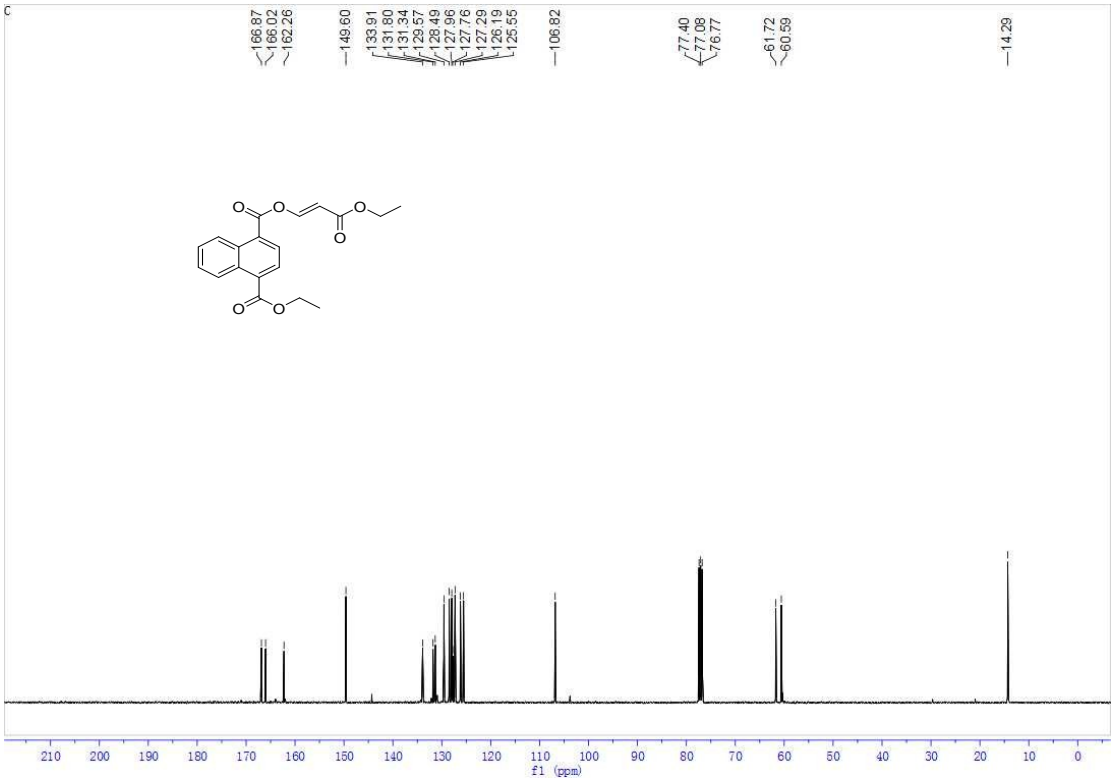
(3-ethoxy-3-oxoprop-1-en-1-yl) 4-ethyl 2,5-dibromoterephthalate (4f)



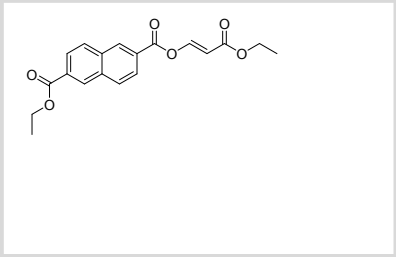


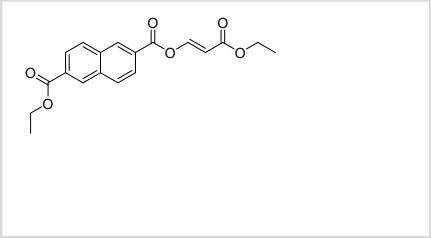
(3-ethoxy-3-oxoprop-1-en-1-yl) 4-ethyl naphthalene-1,4-dicarboxylate (4g)



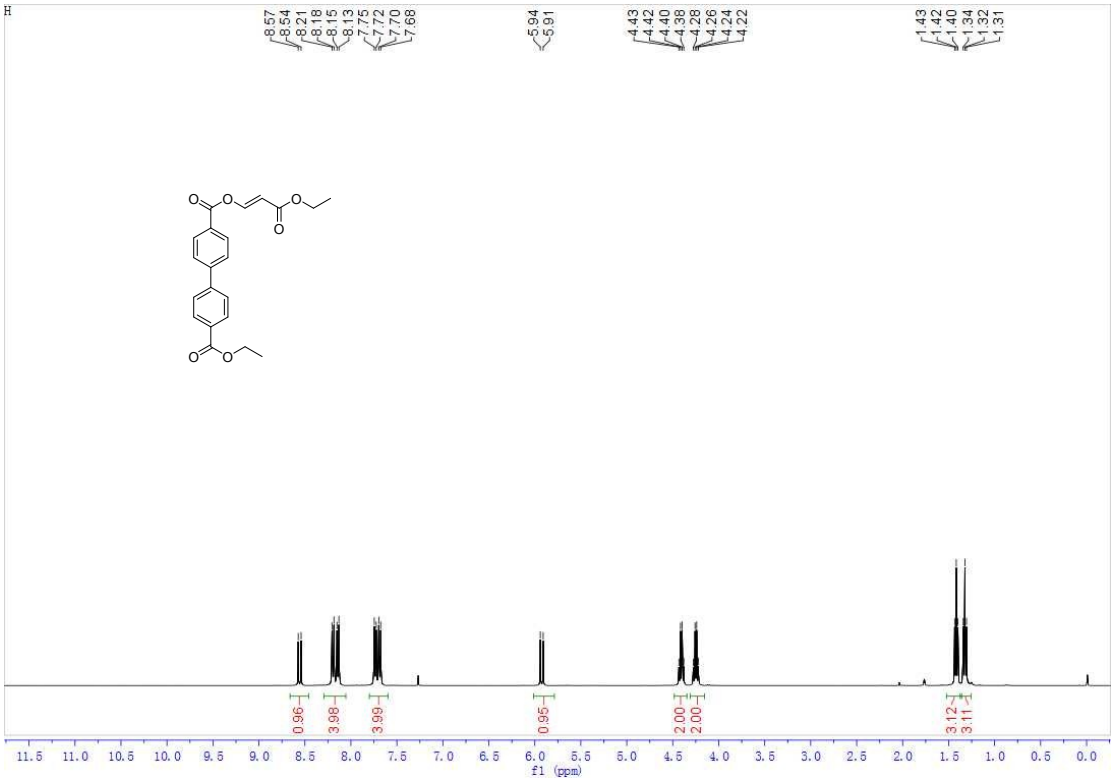


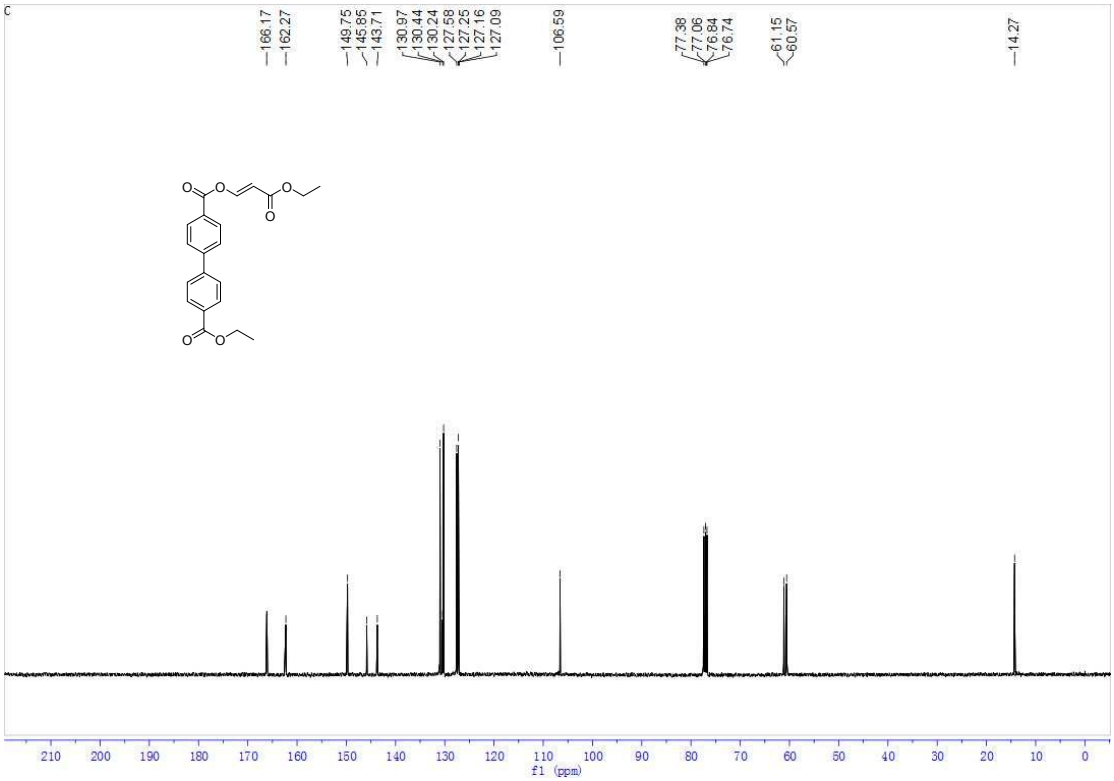
(3-ethoxy-3-oxoprop-1-en-1-yl) 6-ethyl naphthalene-2,6-dicarboxylate (4h)



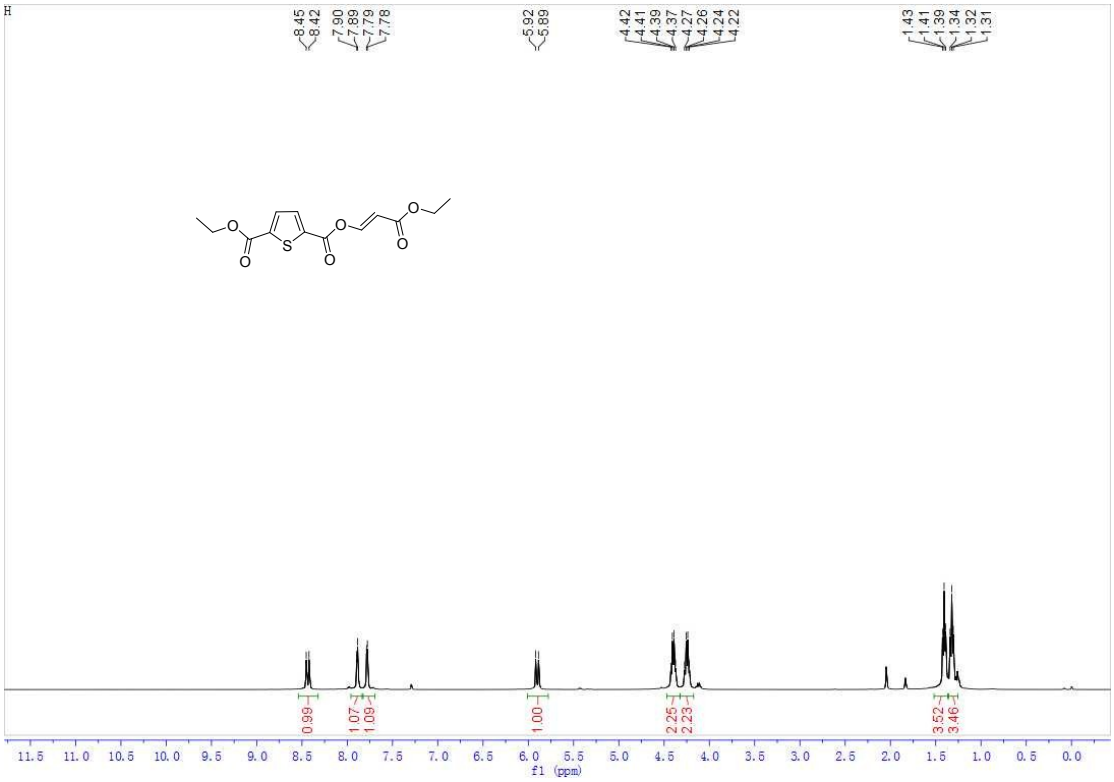


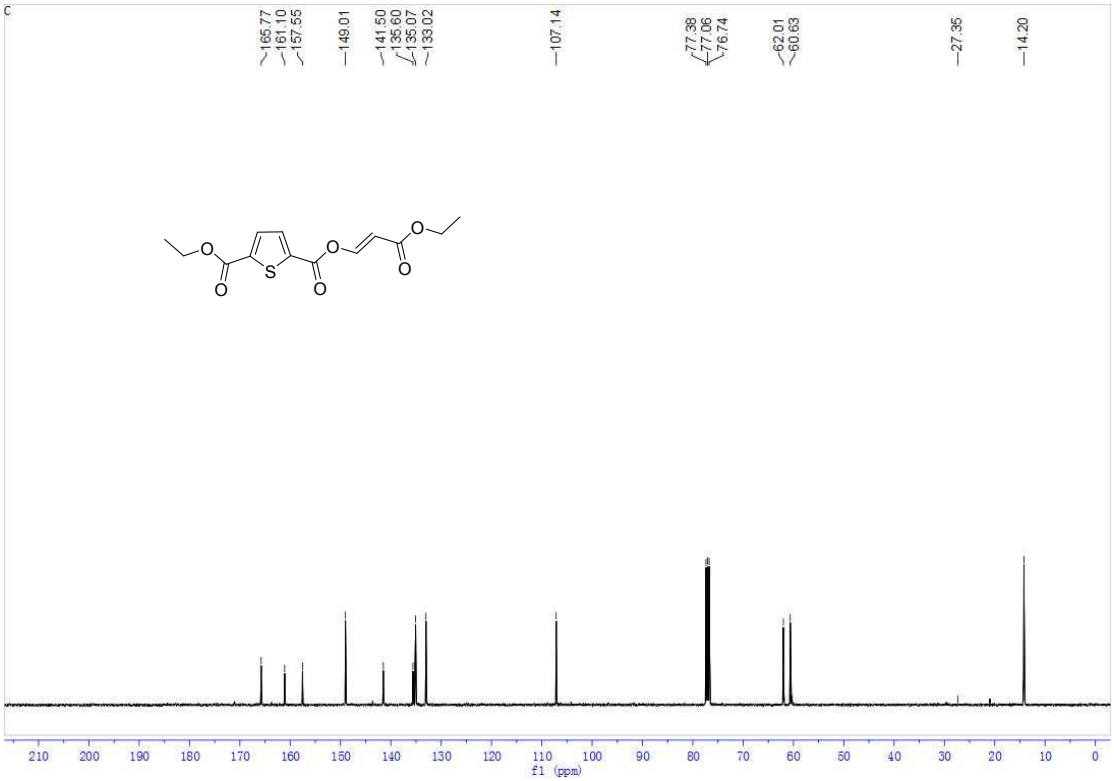
(3-ethoxy-3-oxoprop-1-en-1-yl) 4'-ethyl [1,1'-biphenyl]-4,4'-dicarboxylate (4i)



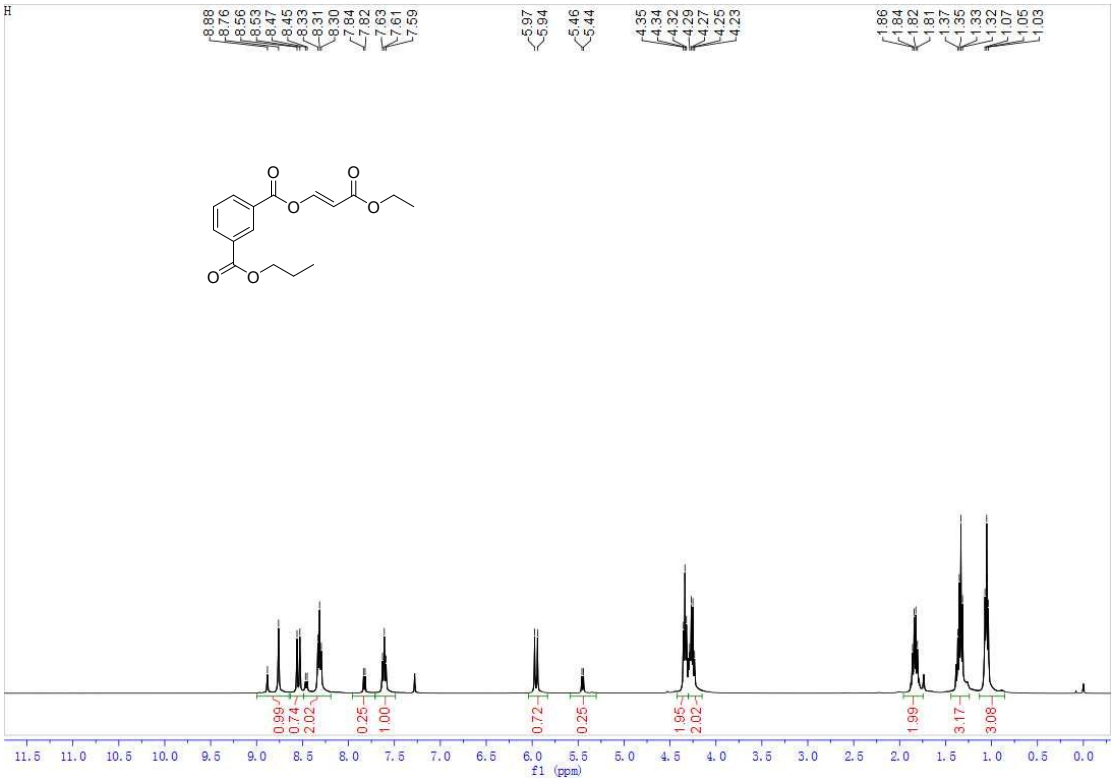


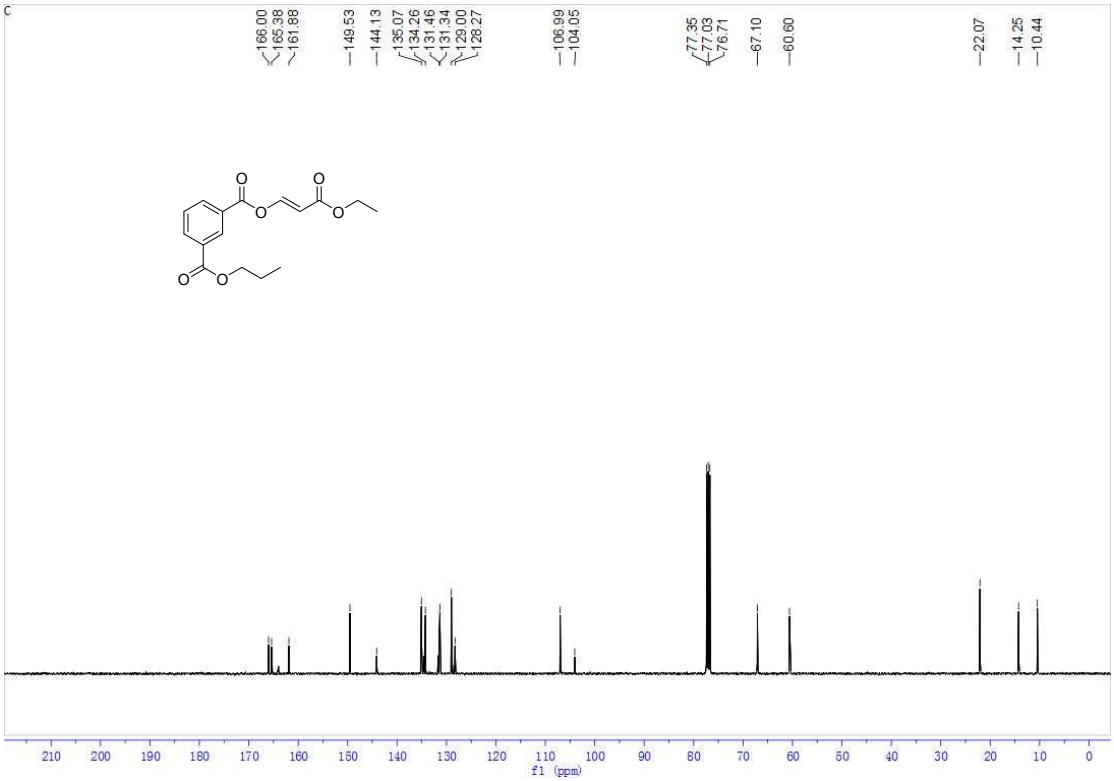
2-(3-ethoxy-3-oxoprop-1-en-1-yl) 5-ethyl thiophene-2,5-dicarboxylate (4j)



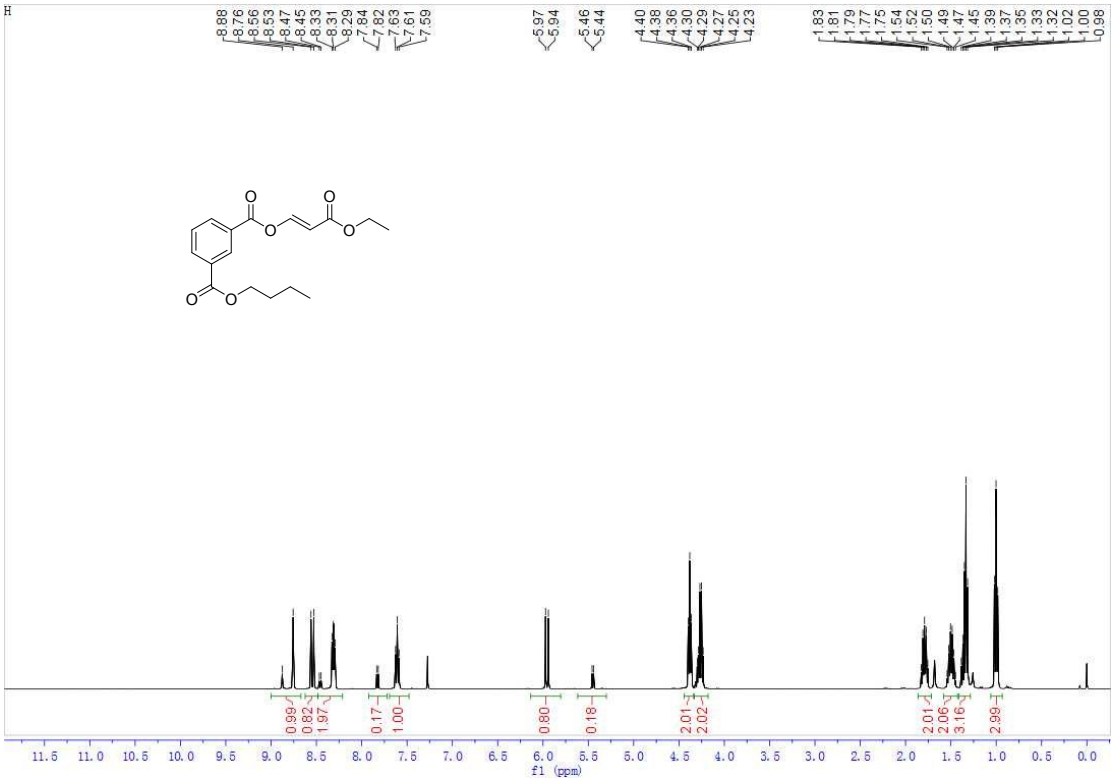


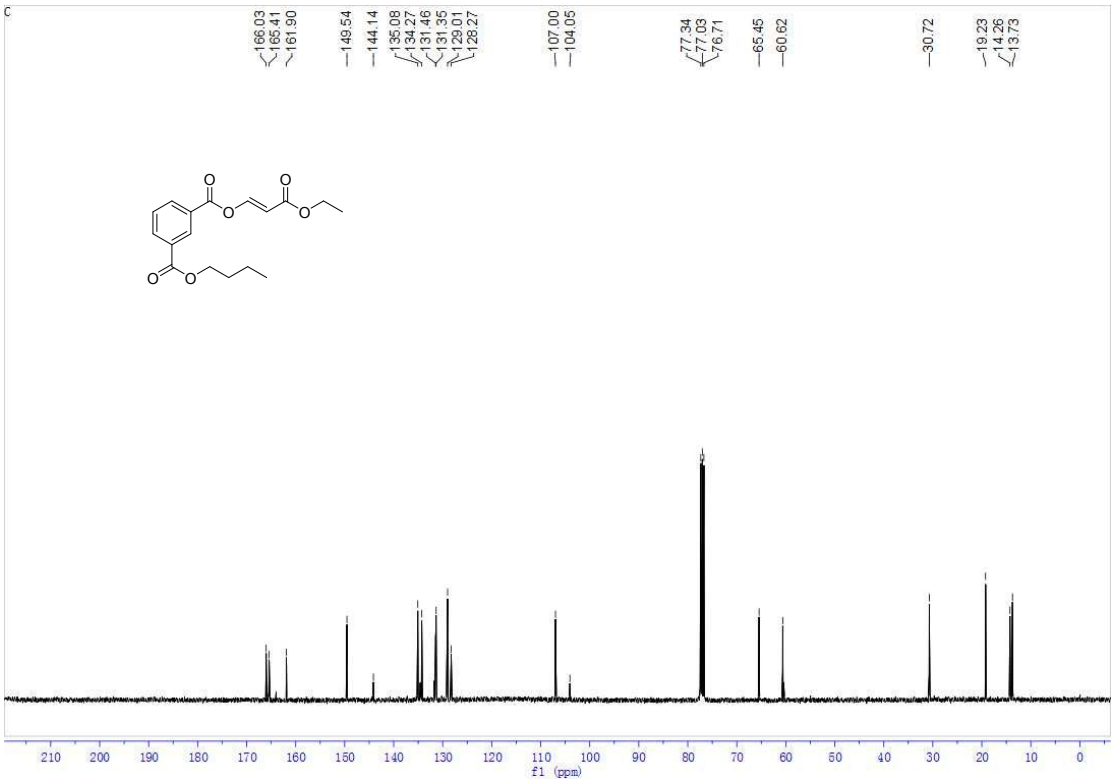
3-ethoxy-3-oxoprop-1-en-1-yl propyl isophthalate (4m)



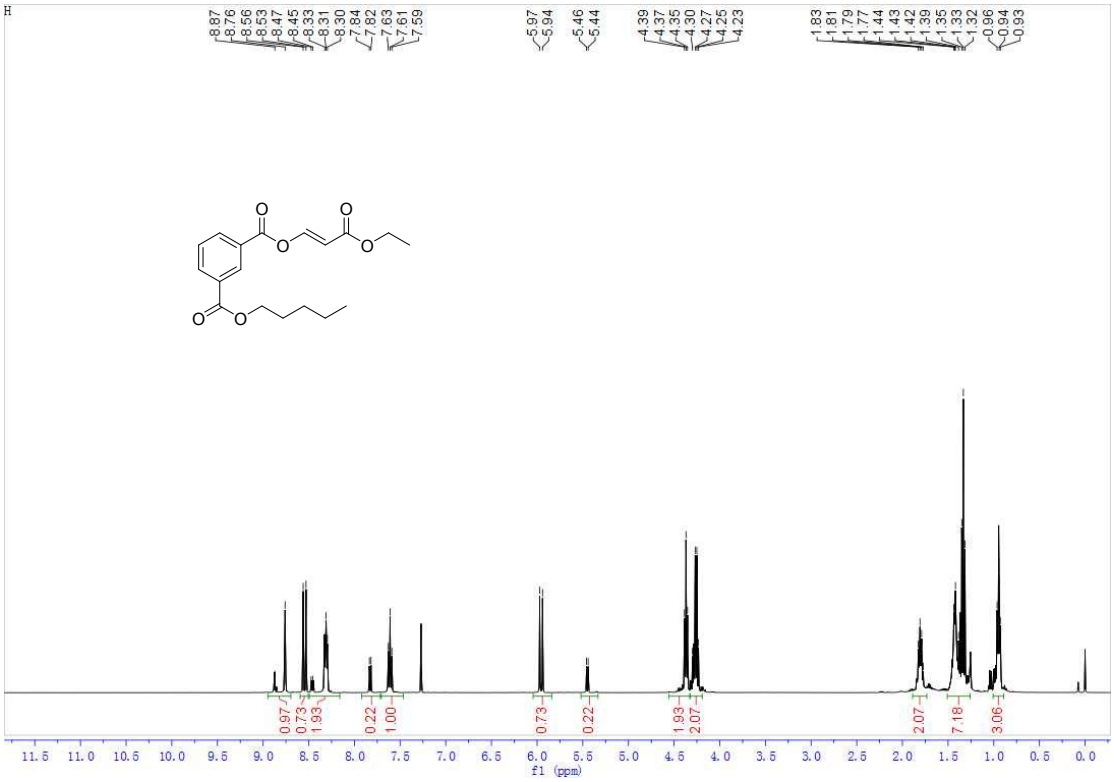


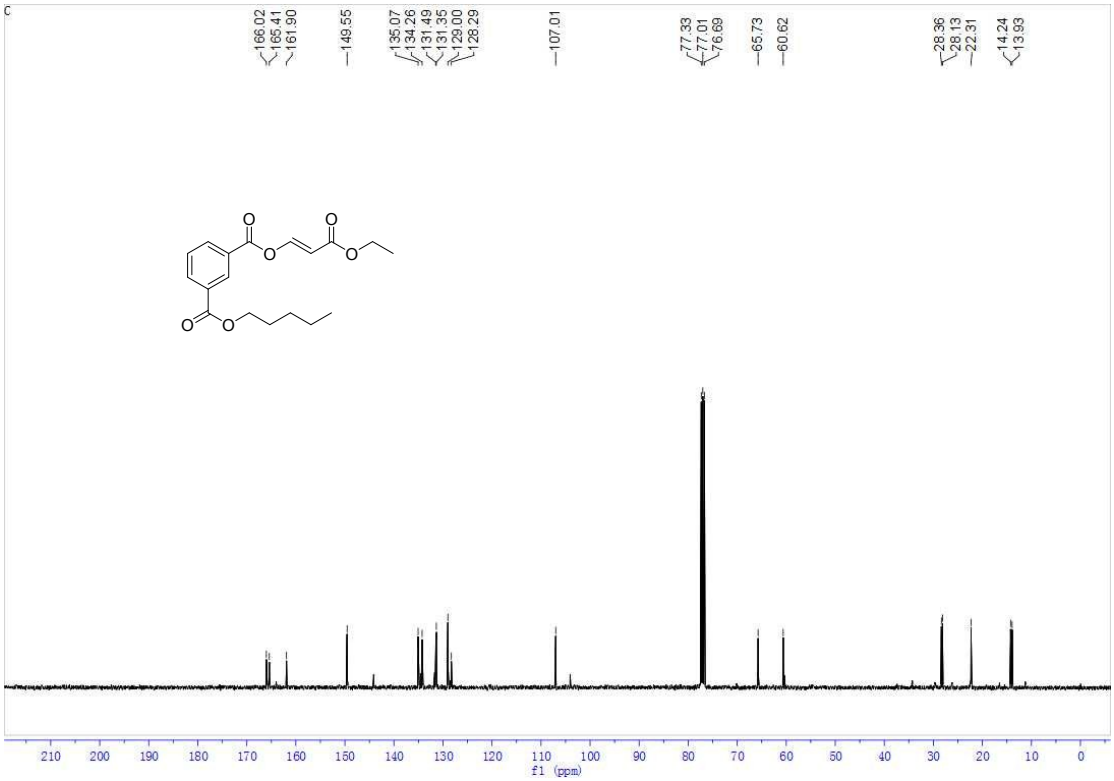
butyl (3-ethoxy-3-oxoprop-1-en-1-yl) isophthalate (4n)



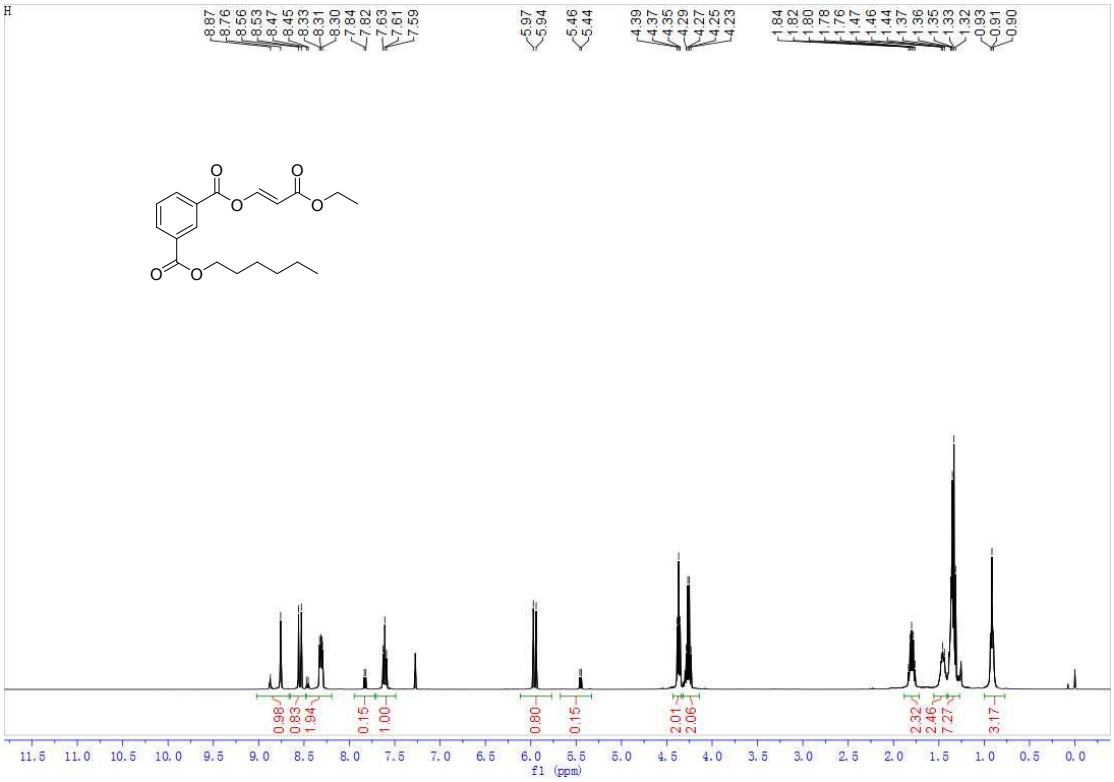


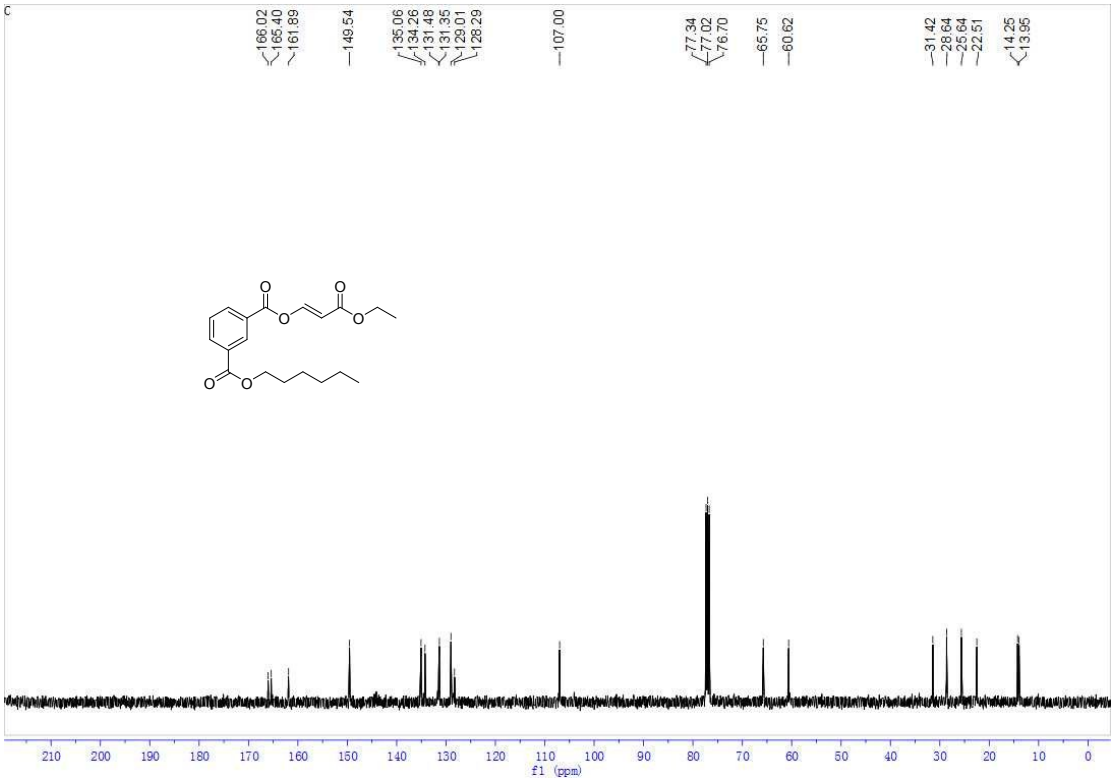
3-ethoxy-3-oxoprop-1-en-1-yl pentyl isophthalate (4o)



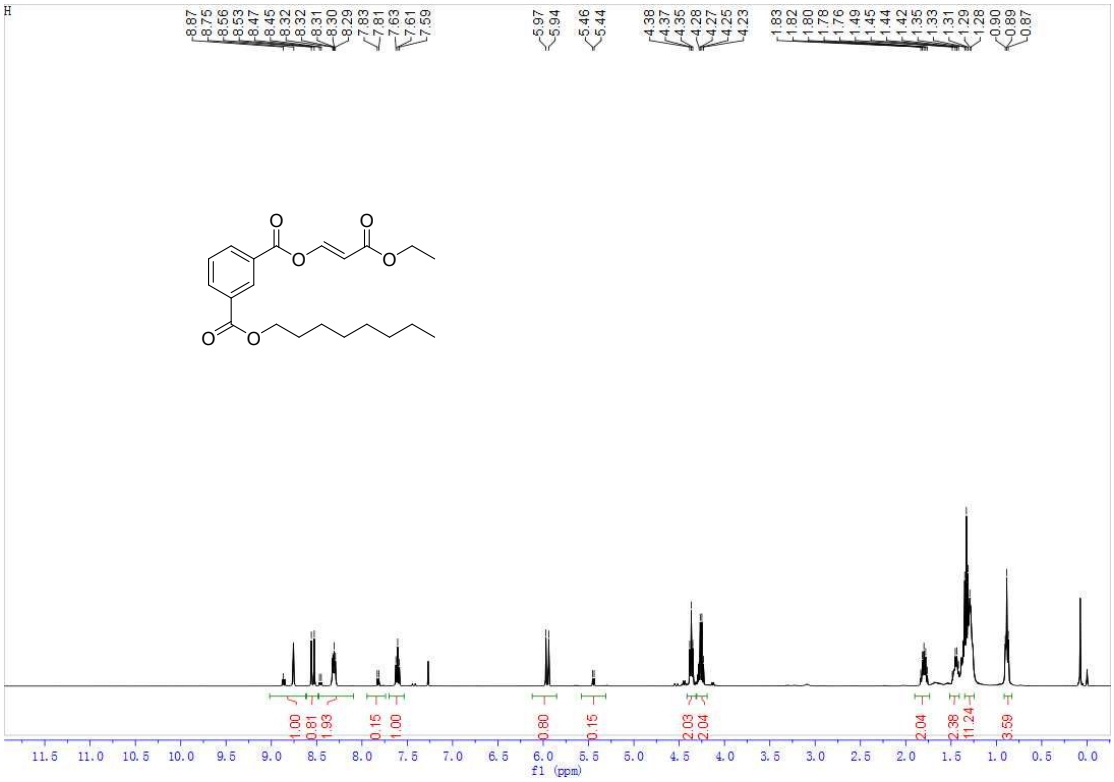


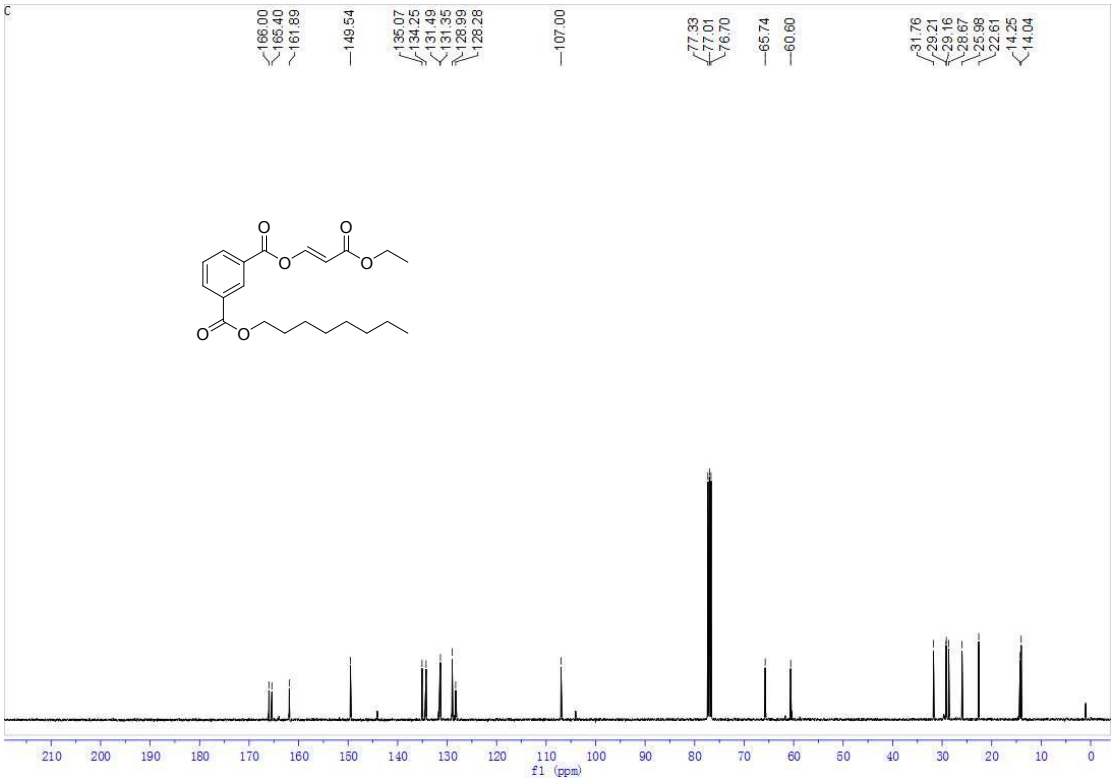
ethoxy-3-oxoprop-1-en-1-yl hexyl isophthalate (4p)



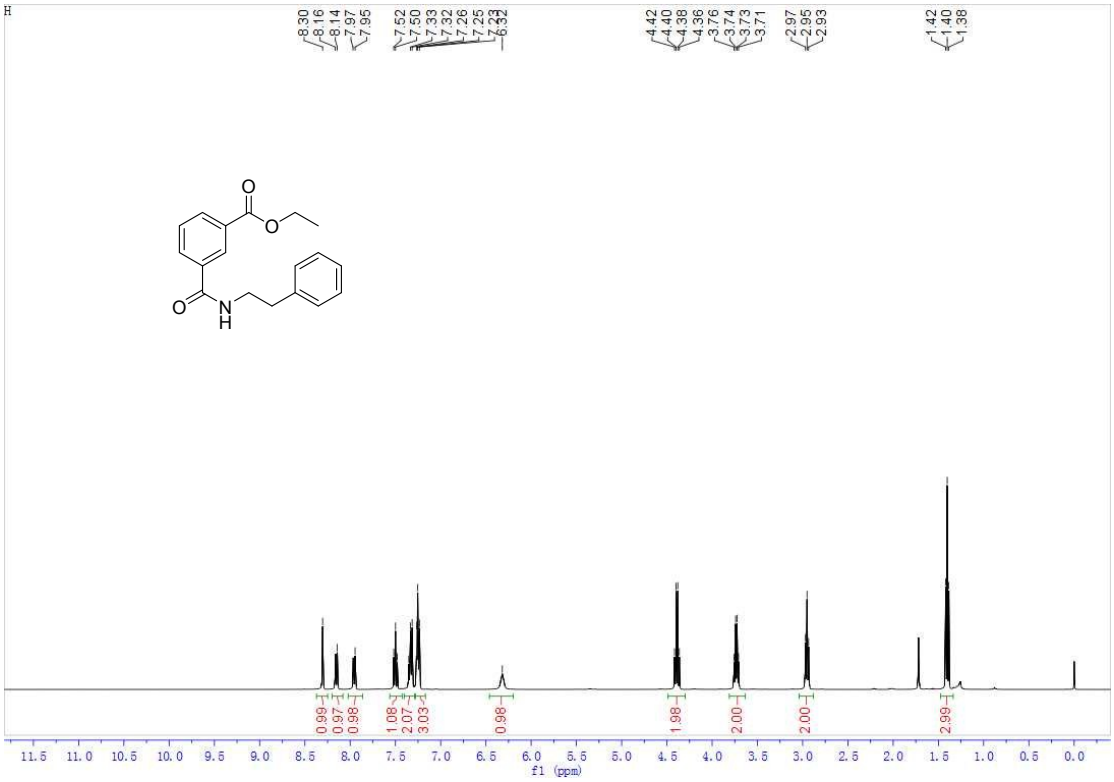


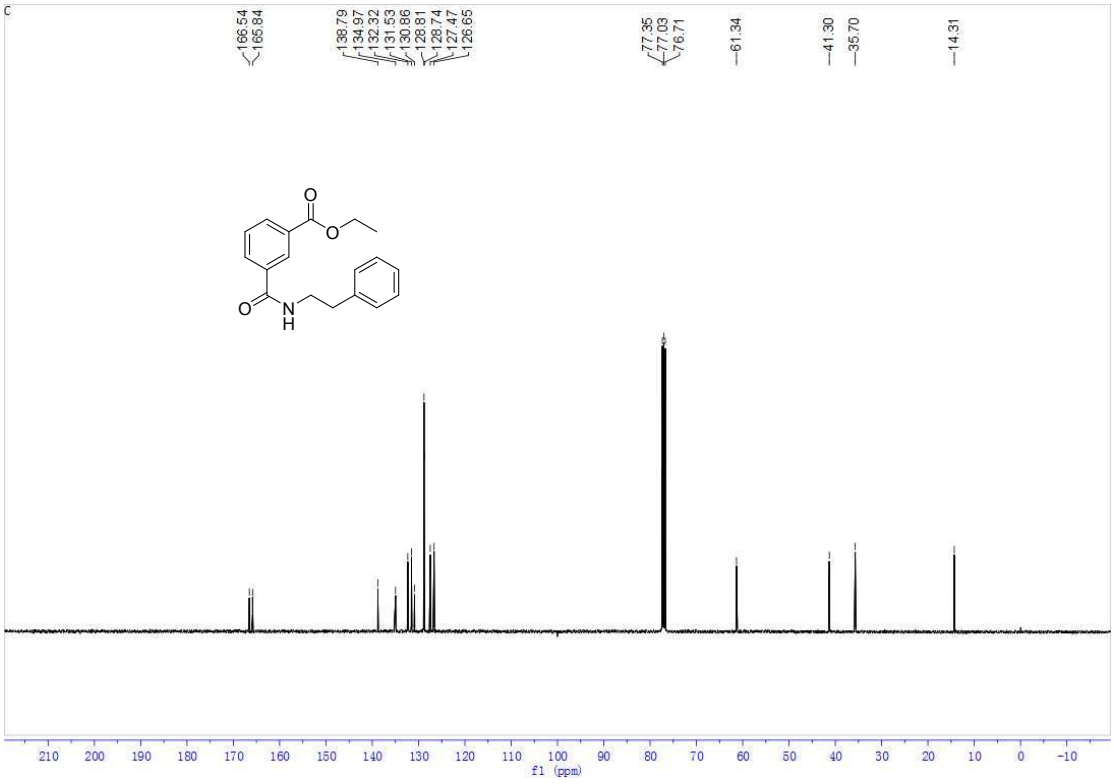
3-ethoxy-3-oxoprop-1-en-1-yl octyl isophthalate (4q)



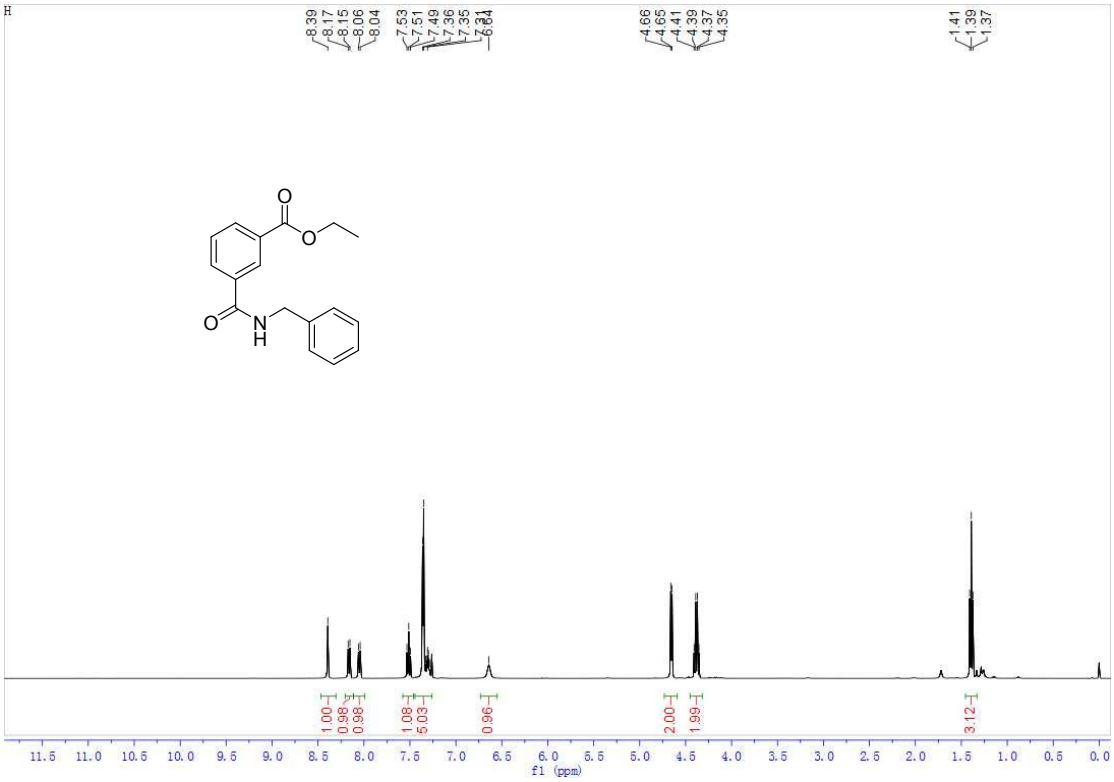


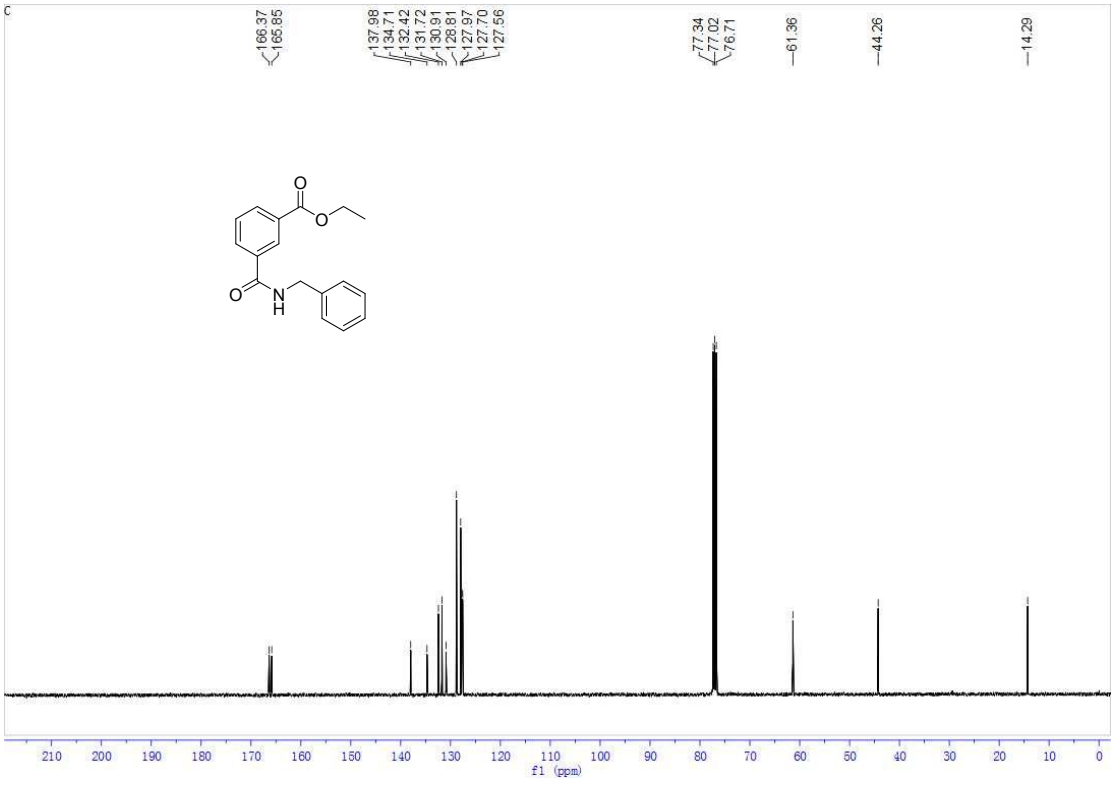
ethyl 3-(phenethylcarbamoyl)benzoate (5Na)



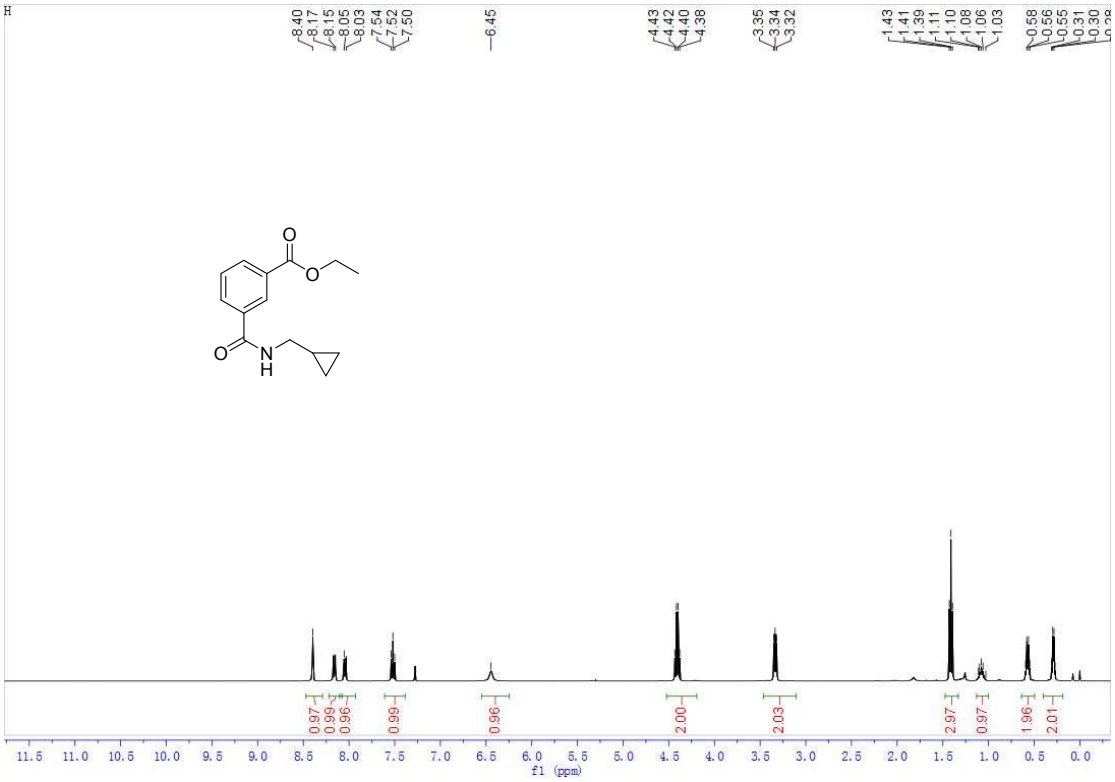


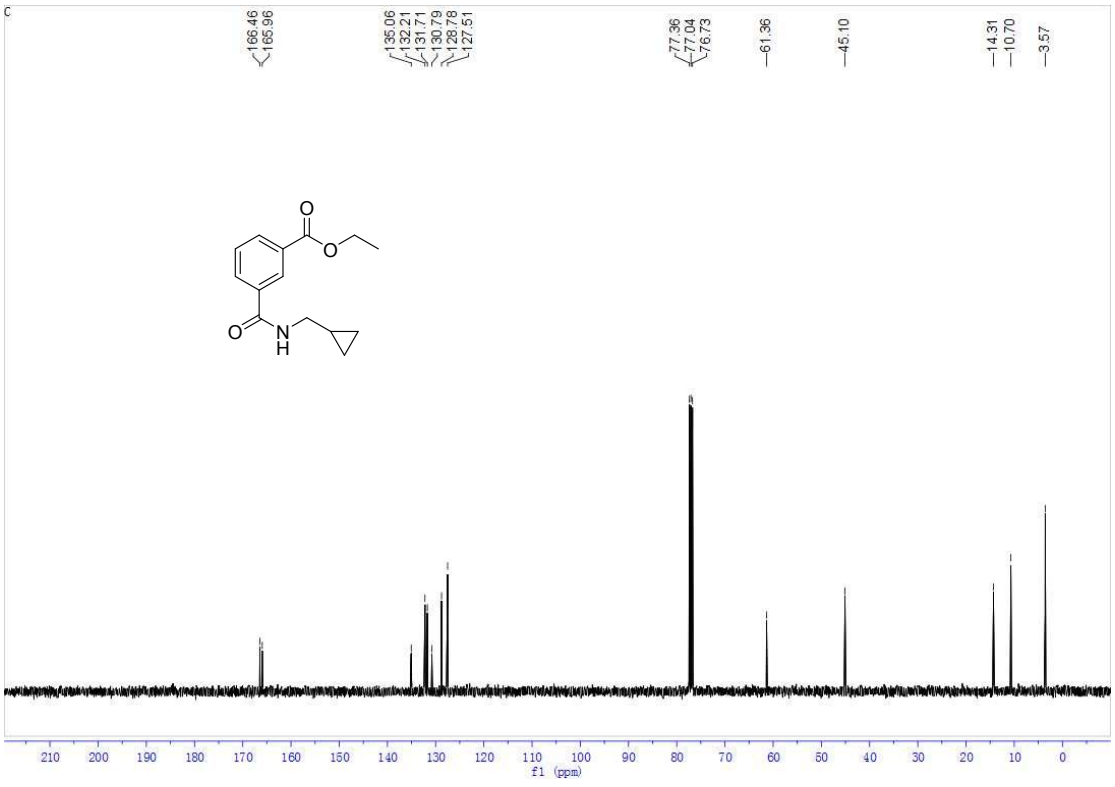
ethyl 3-(benzylcarbamoyl)benzoate (5Nb)



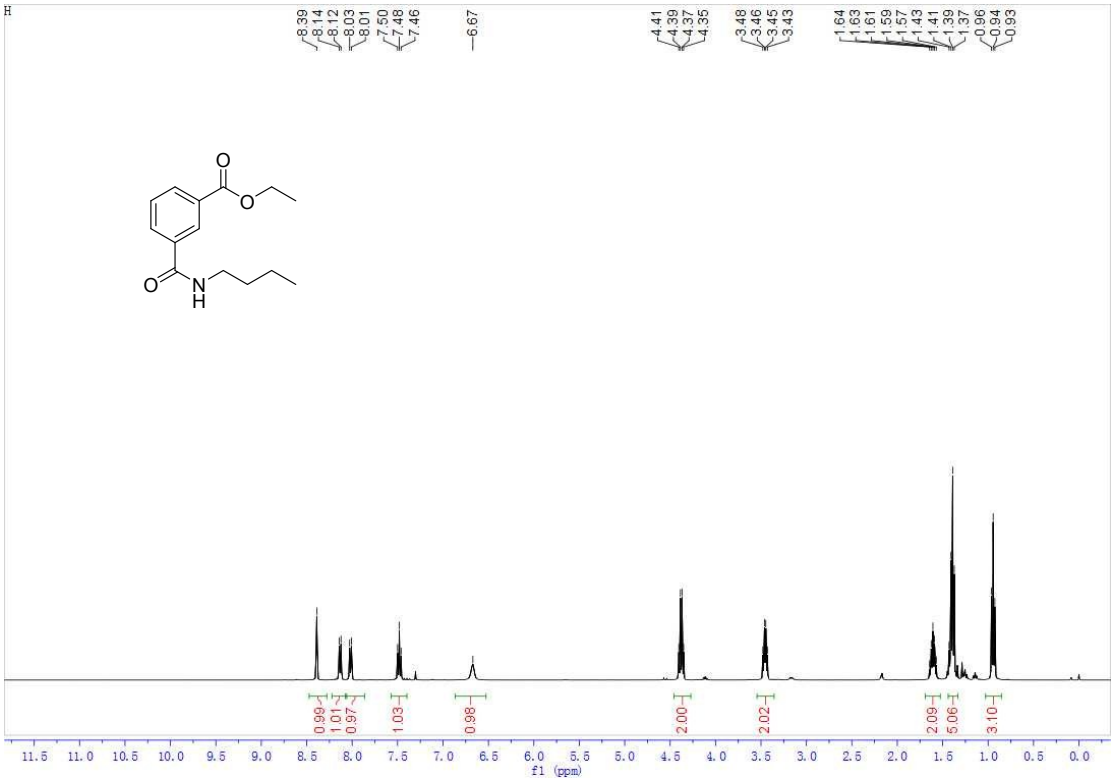


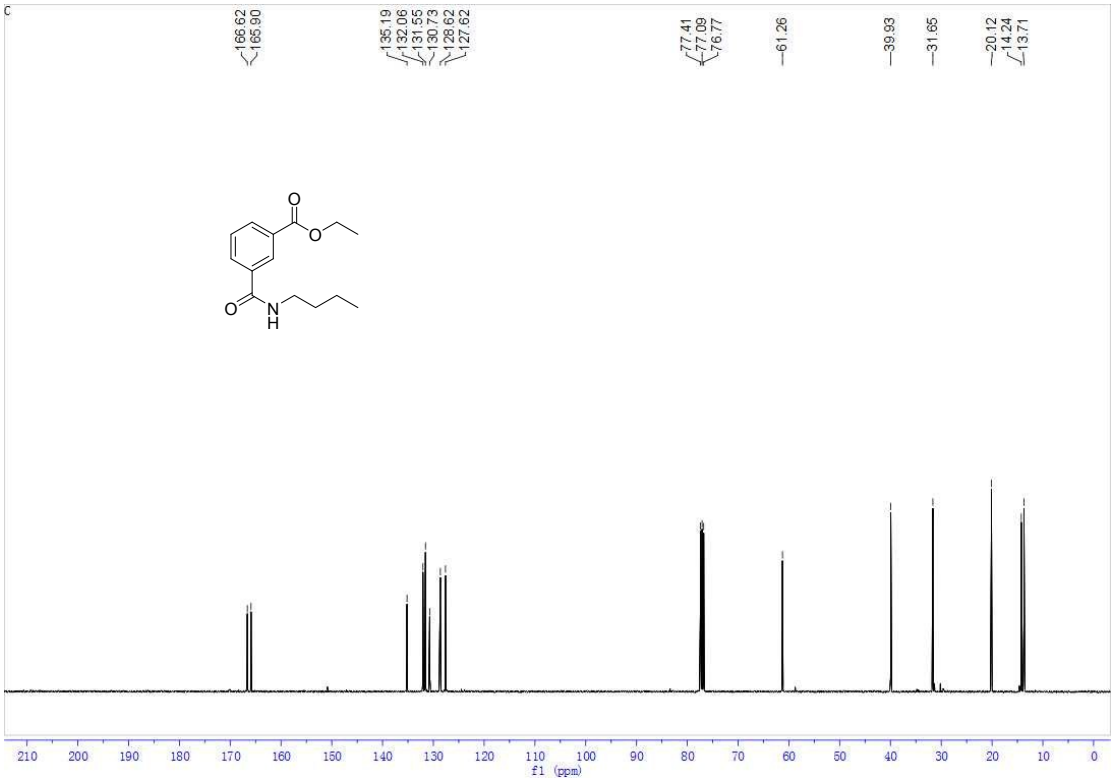
ethyl 3-((cyclopropylmethyl)carbamoyl)benzoate (5Nc)



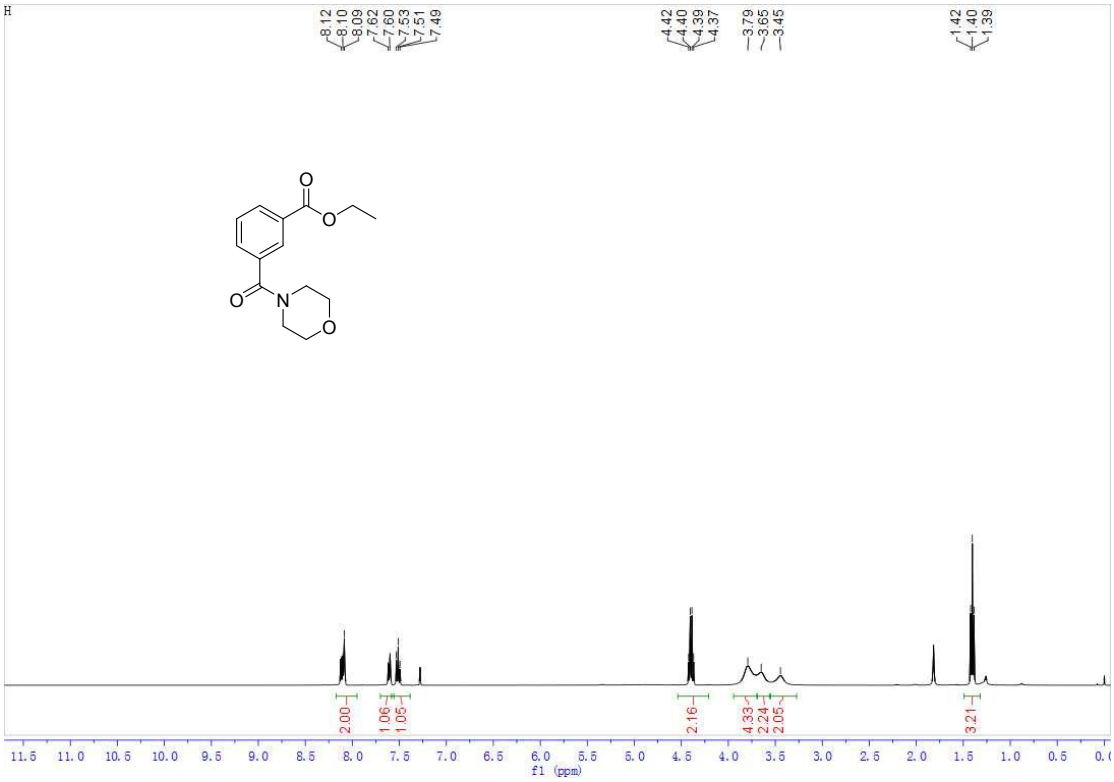


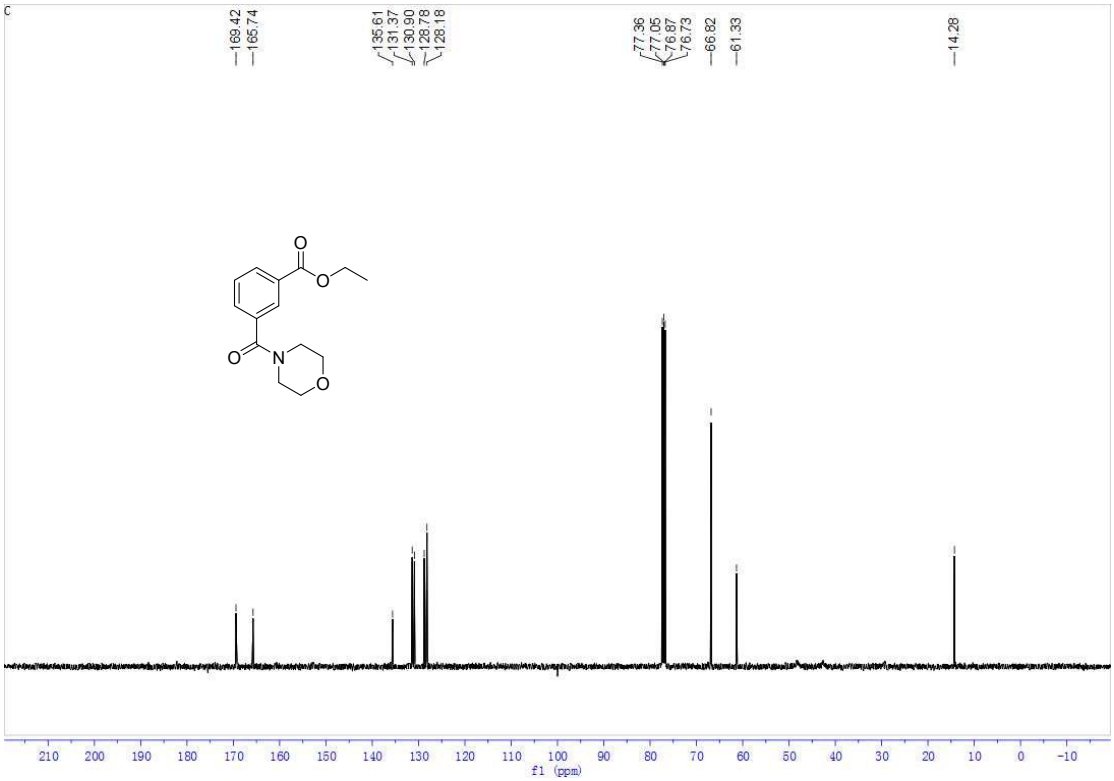
ethyl 3-(butylcarbamoyl)benzoate (5Nd)



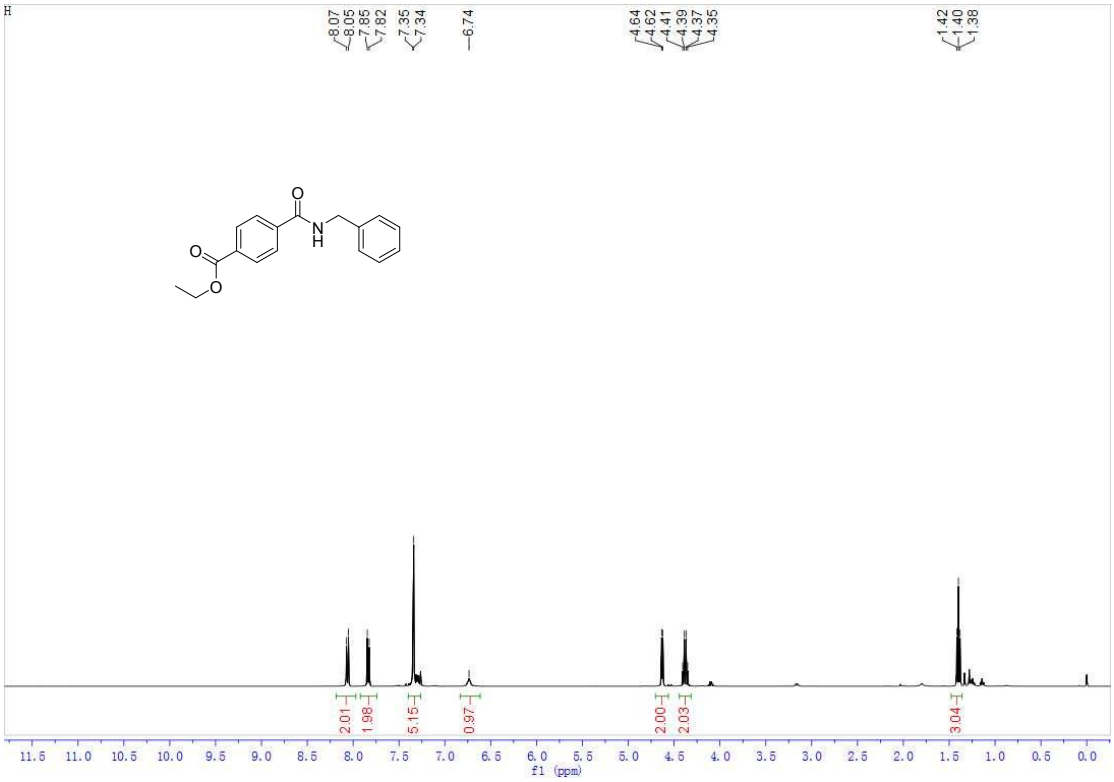


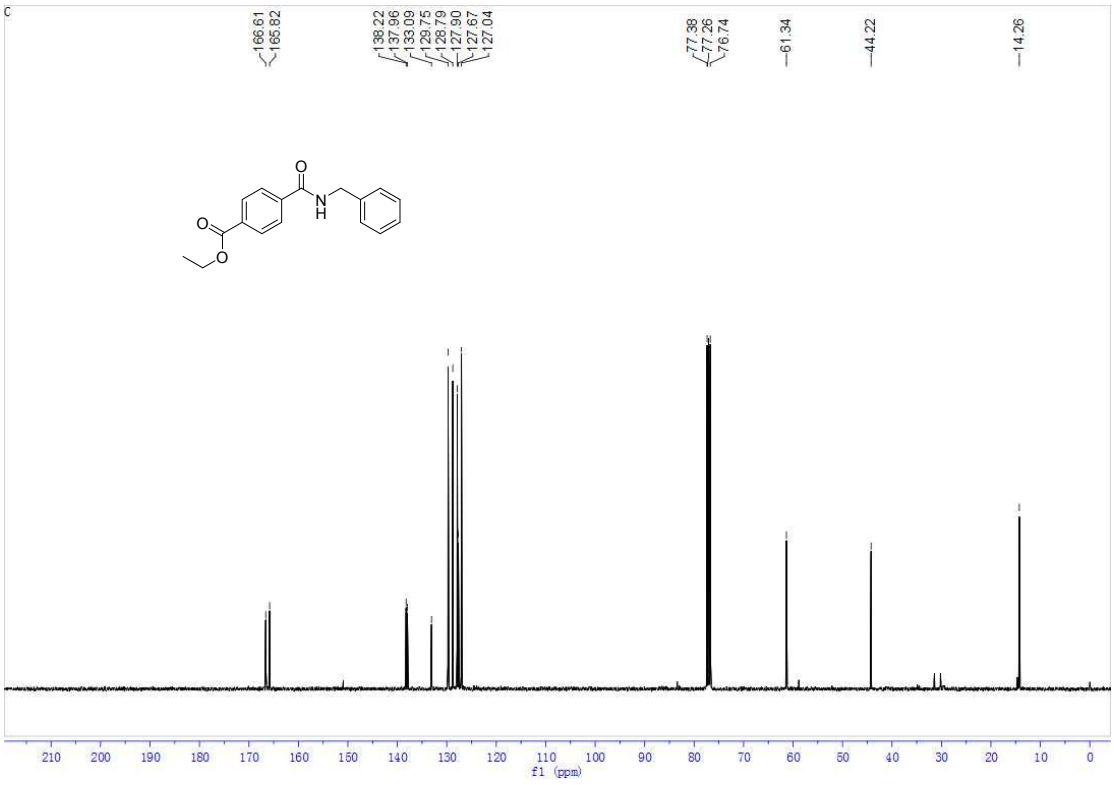
ethyl 3-(morpholine-4-carbonyl)benzoate (5Ne)



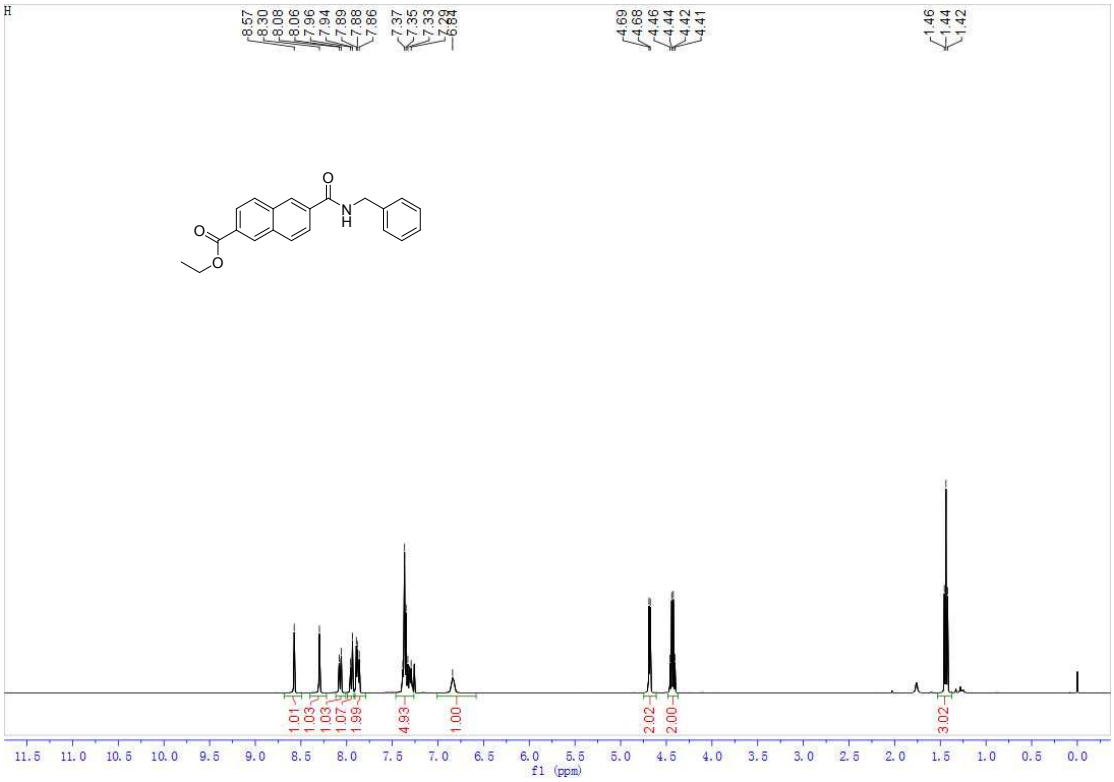


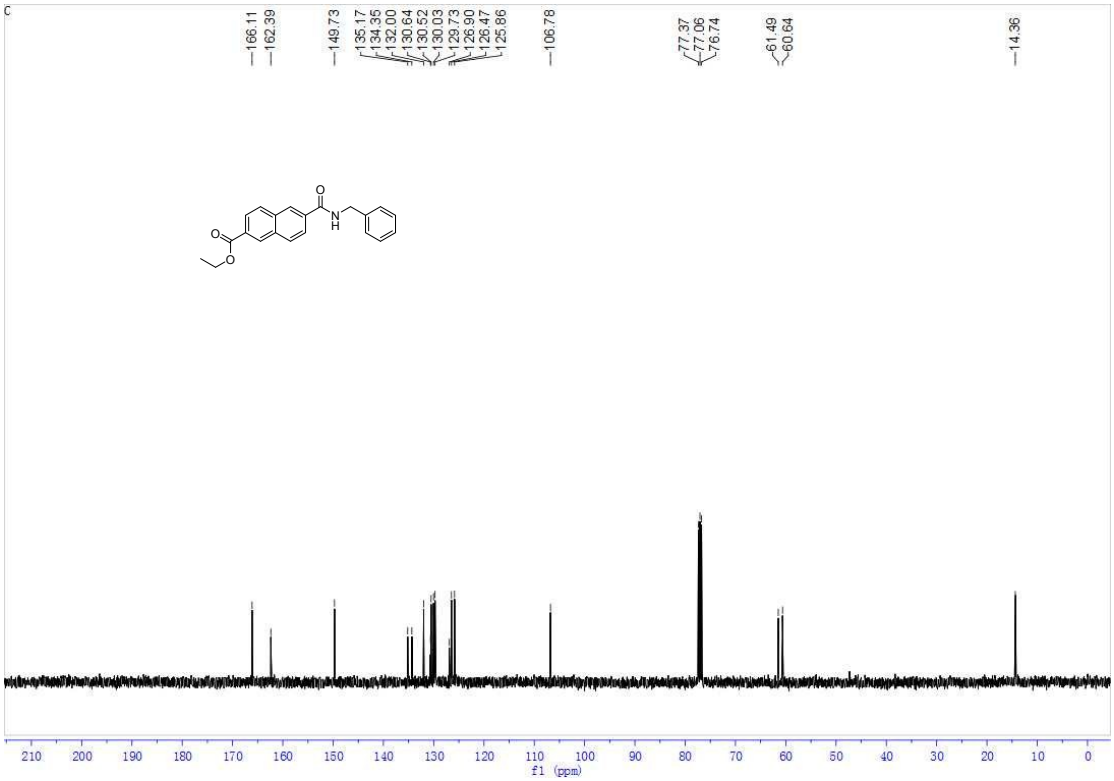
ethyl 4-(benzylcarbamoyl)benzoate (5Nf)



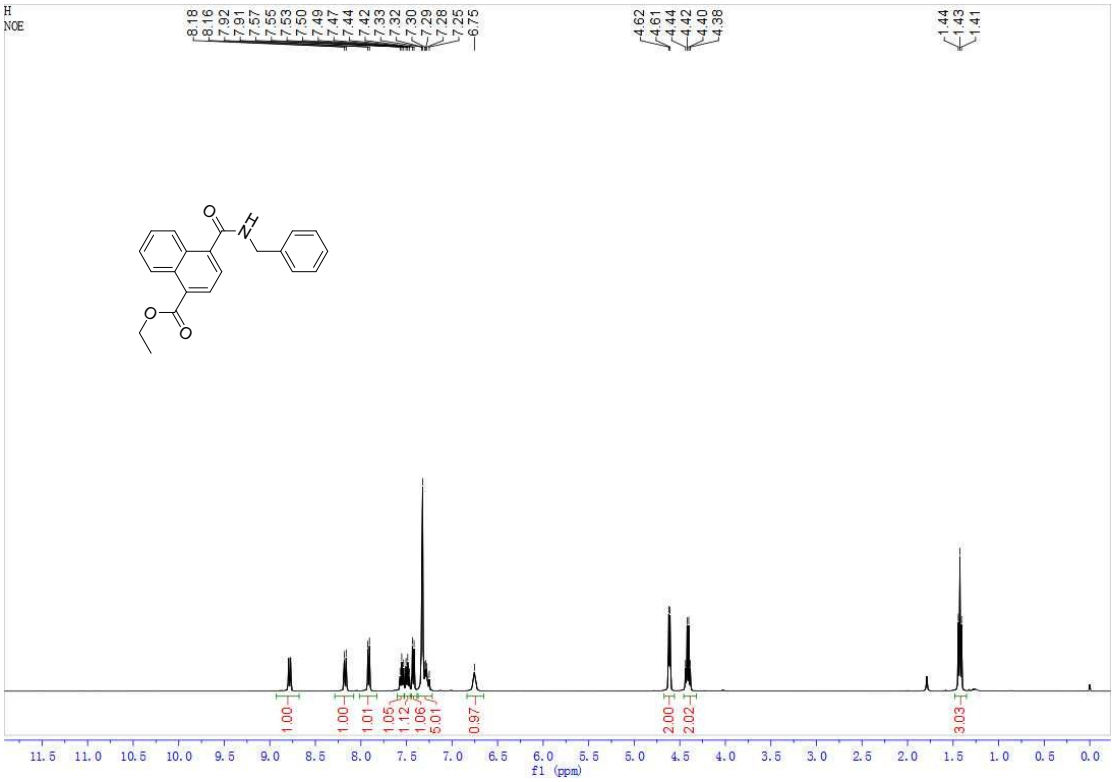


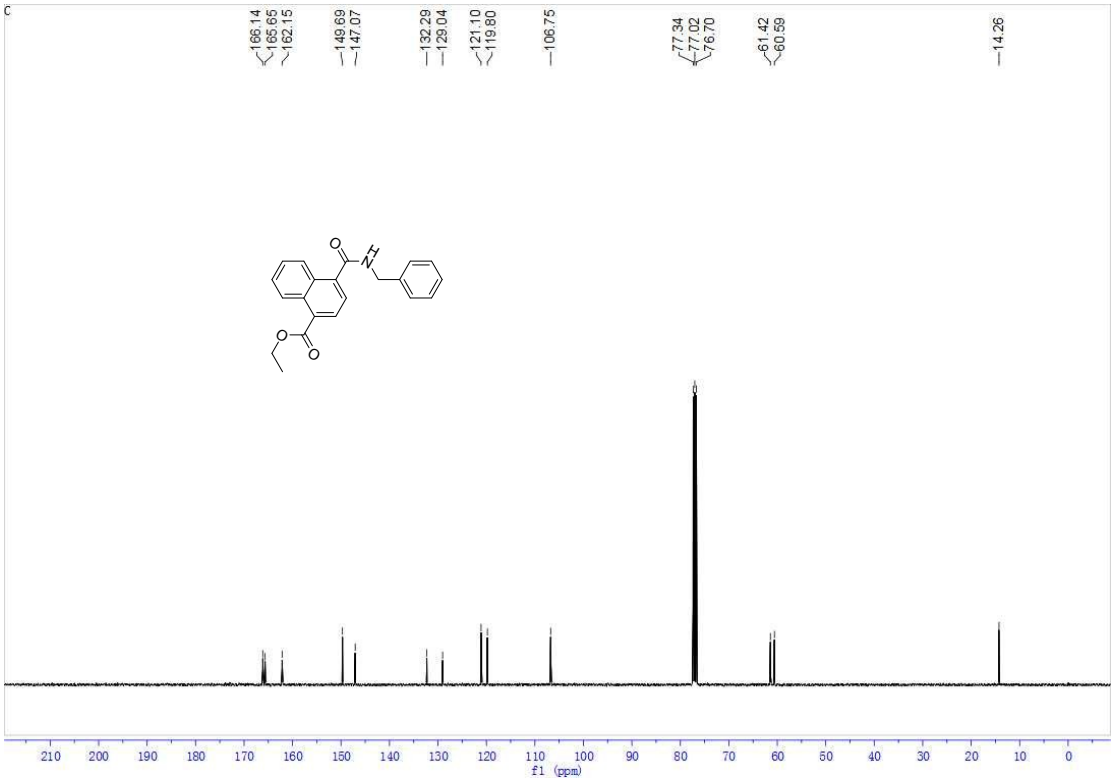
ethyl 6-(benzylcarbamoyl)-2-naphthoate (5Ng)



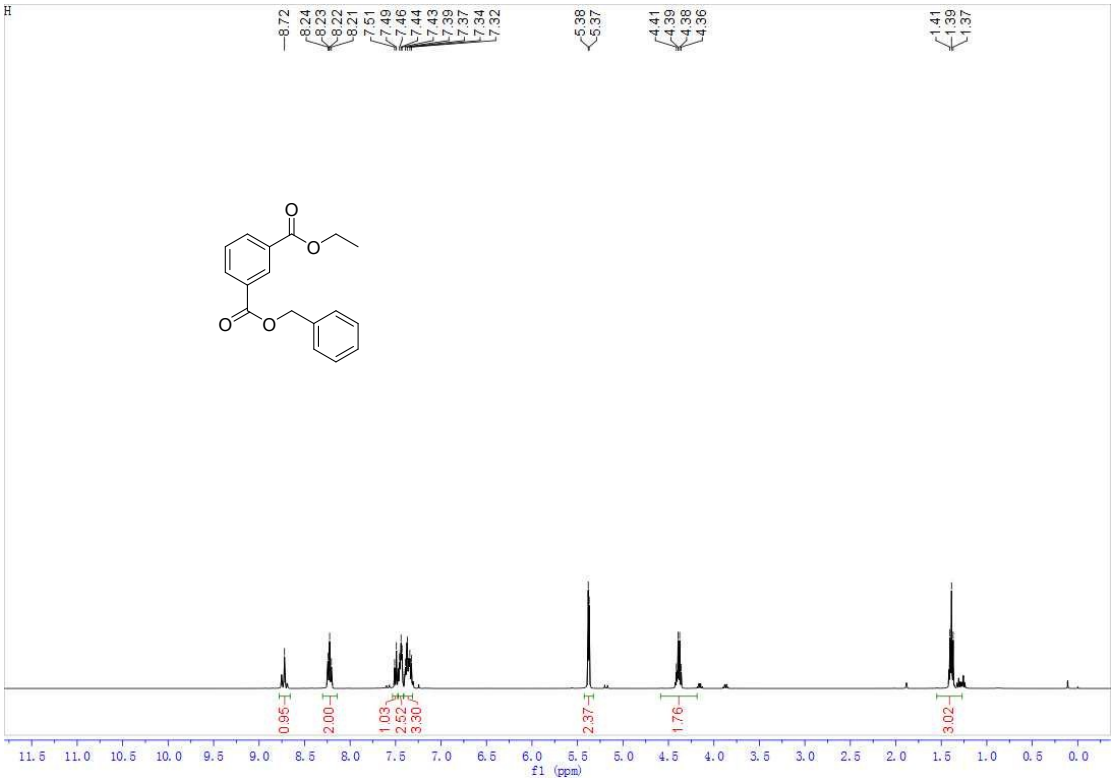


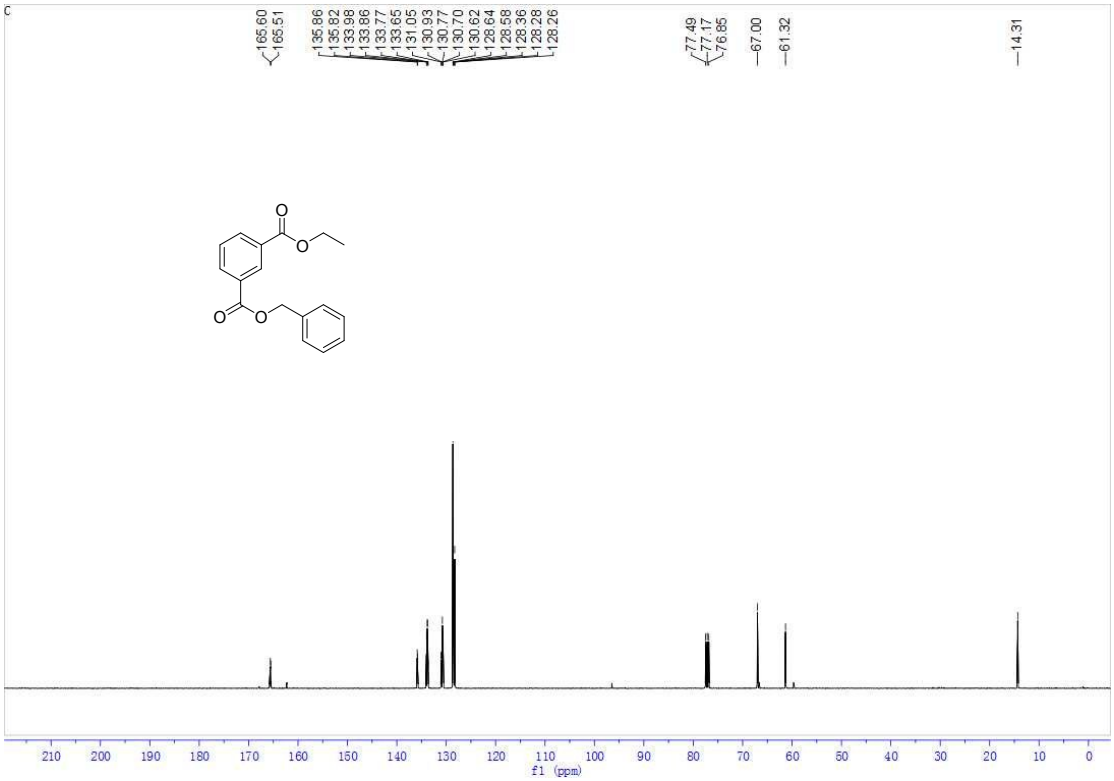
ethyl 4-(benzylcarbamoyl)-1-naphthoate (5Nh)



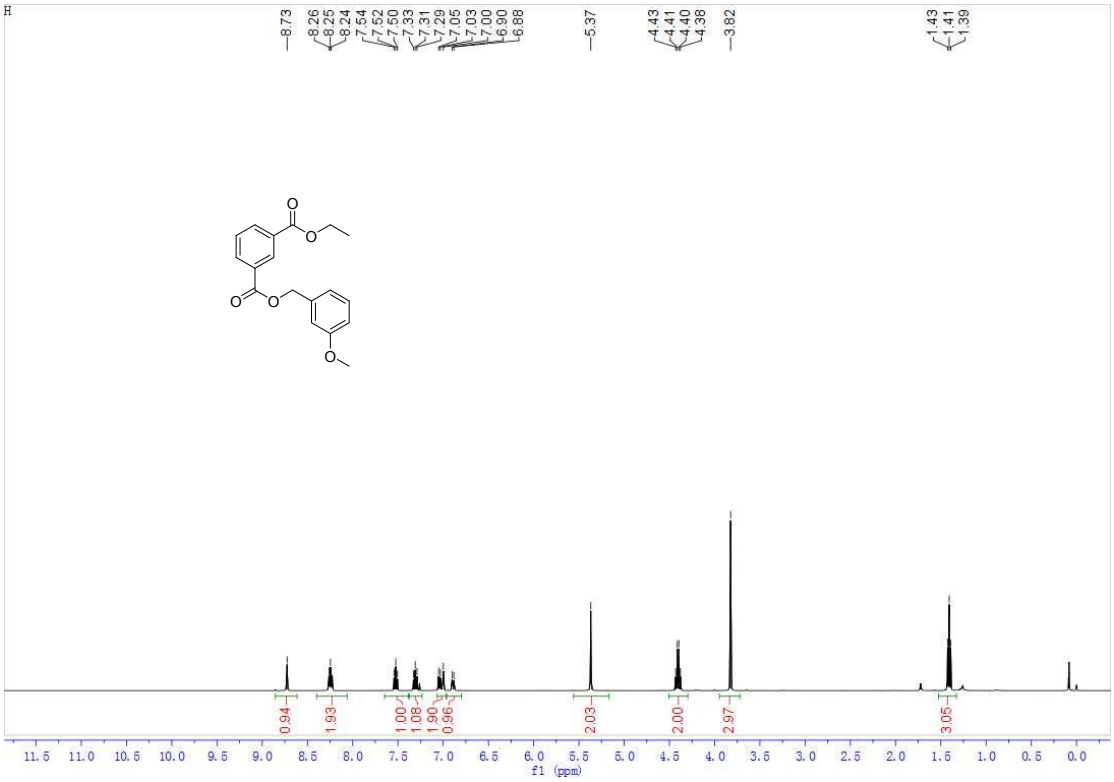


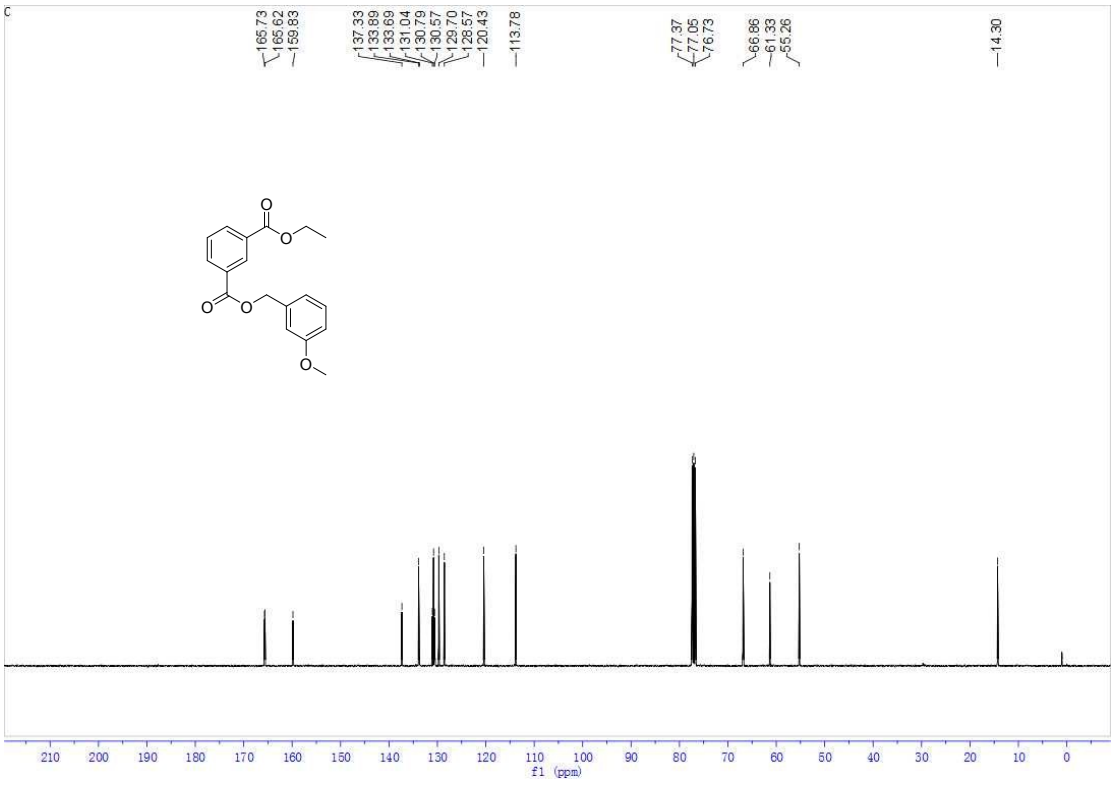
benzyl ethyl isophthalate (5Oa)



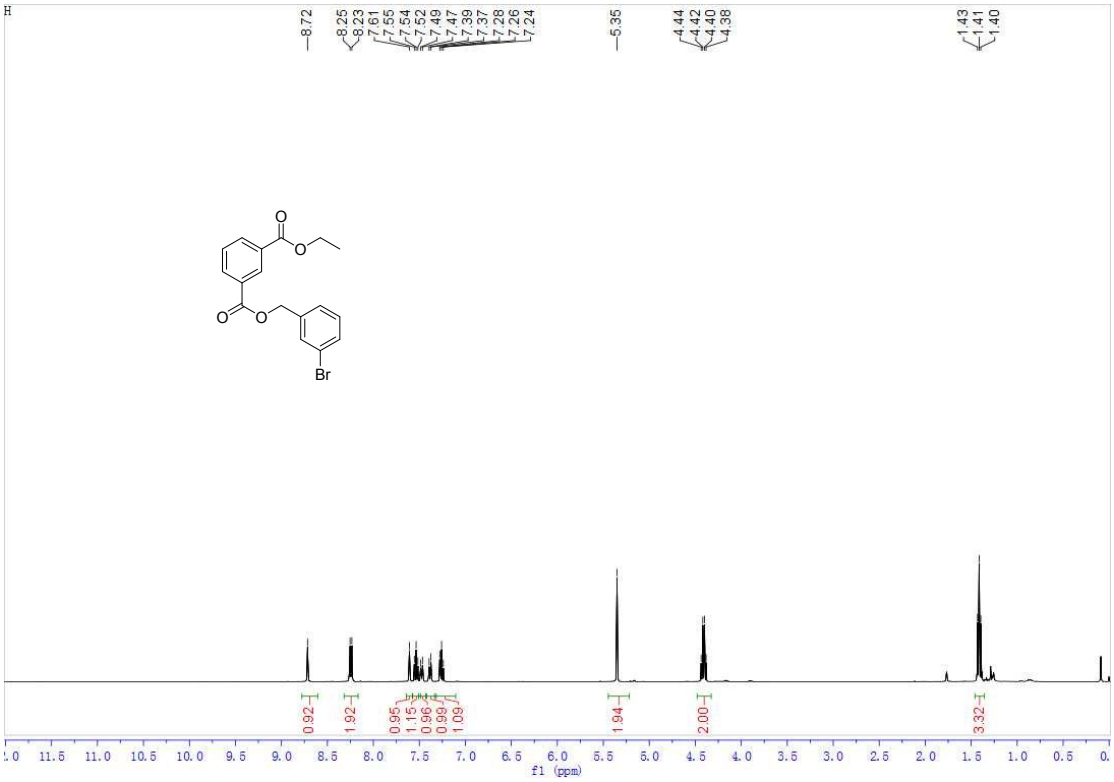


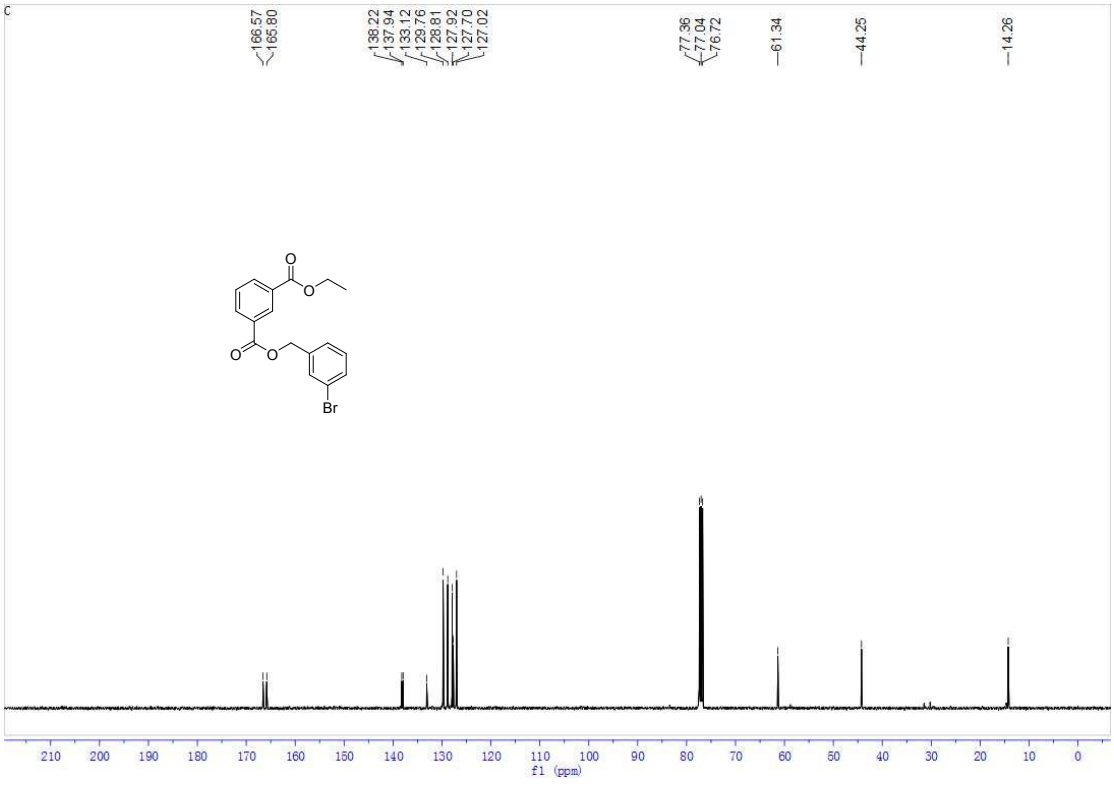
ethyl (3-methoxybenzyl) isophthalate (5Ob)



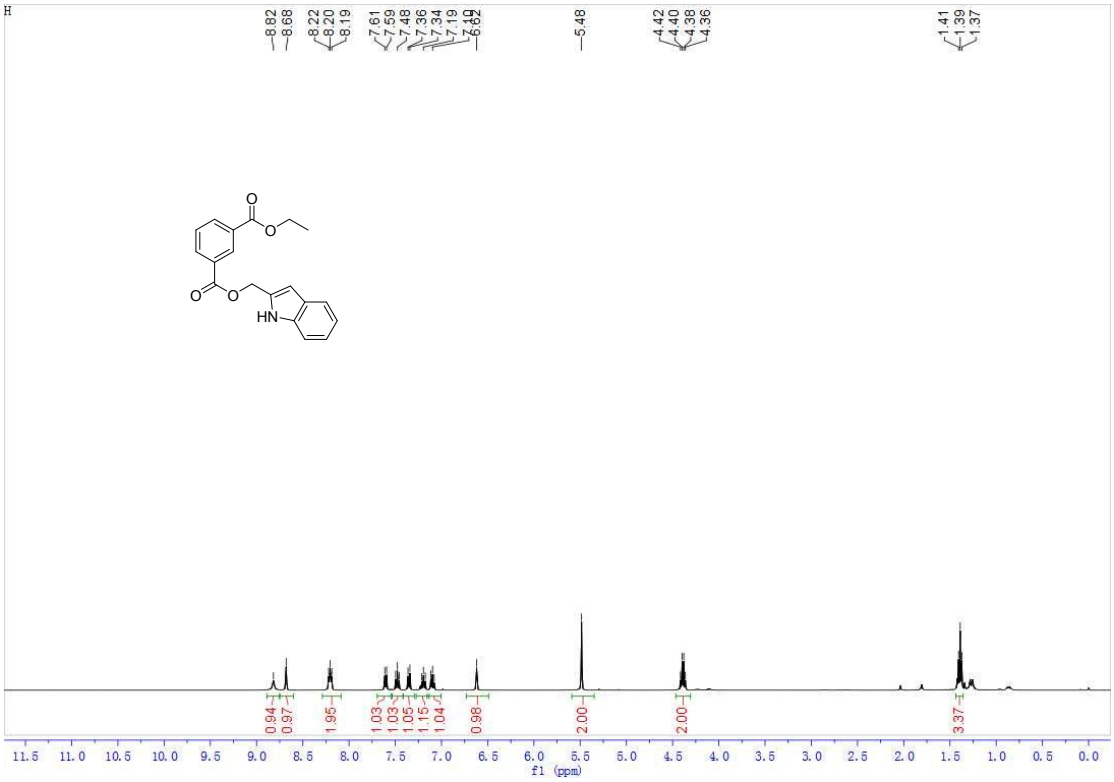


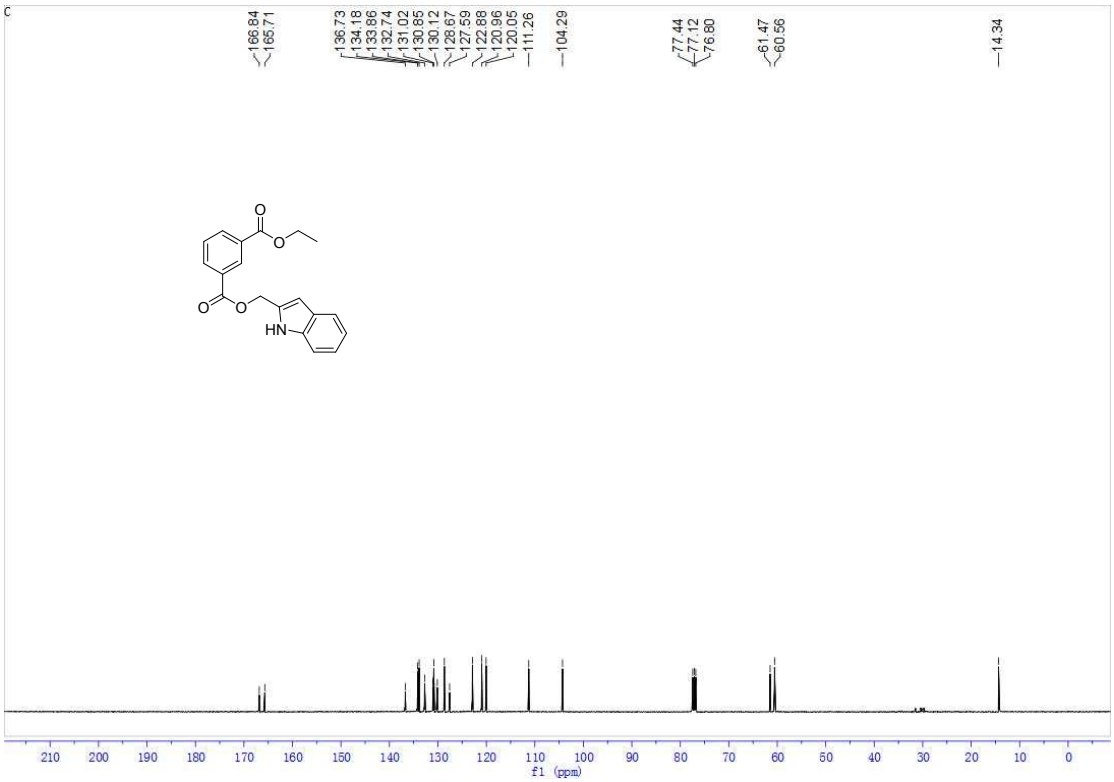
bromobenzyl ethyl isophthalate (5Oc)



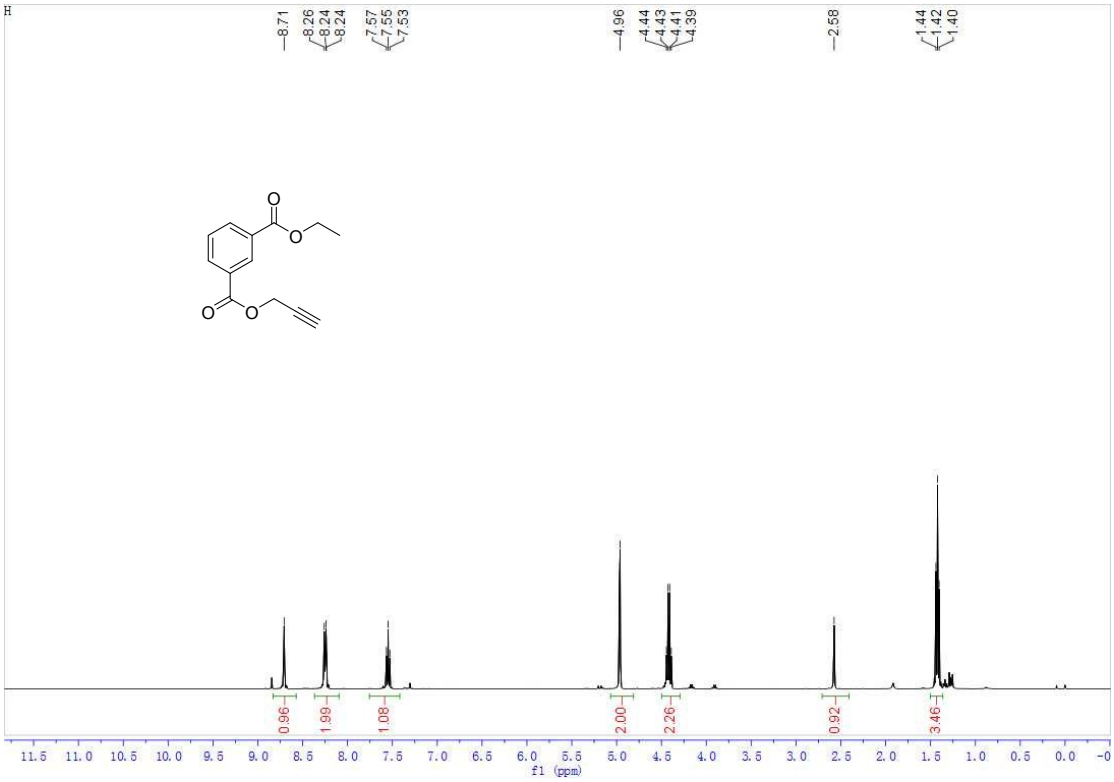


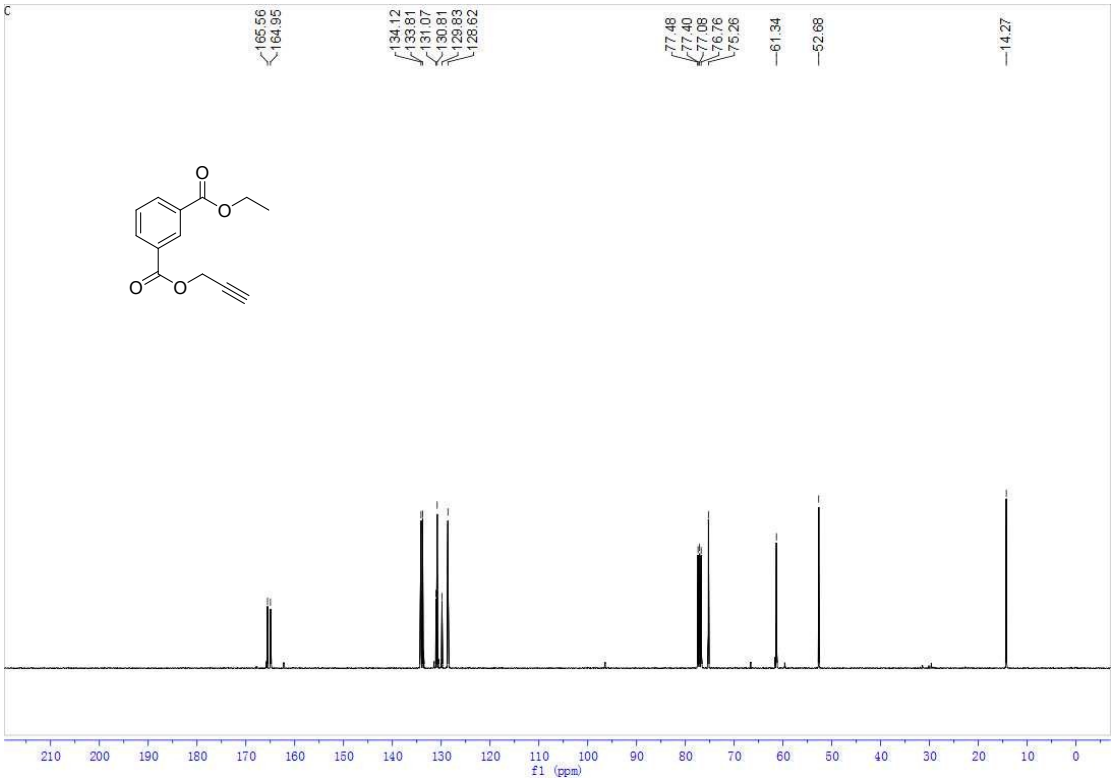
(1H-indol-2-yl)methyl ethyl isophthalate (5Od)



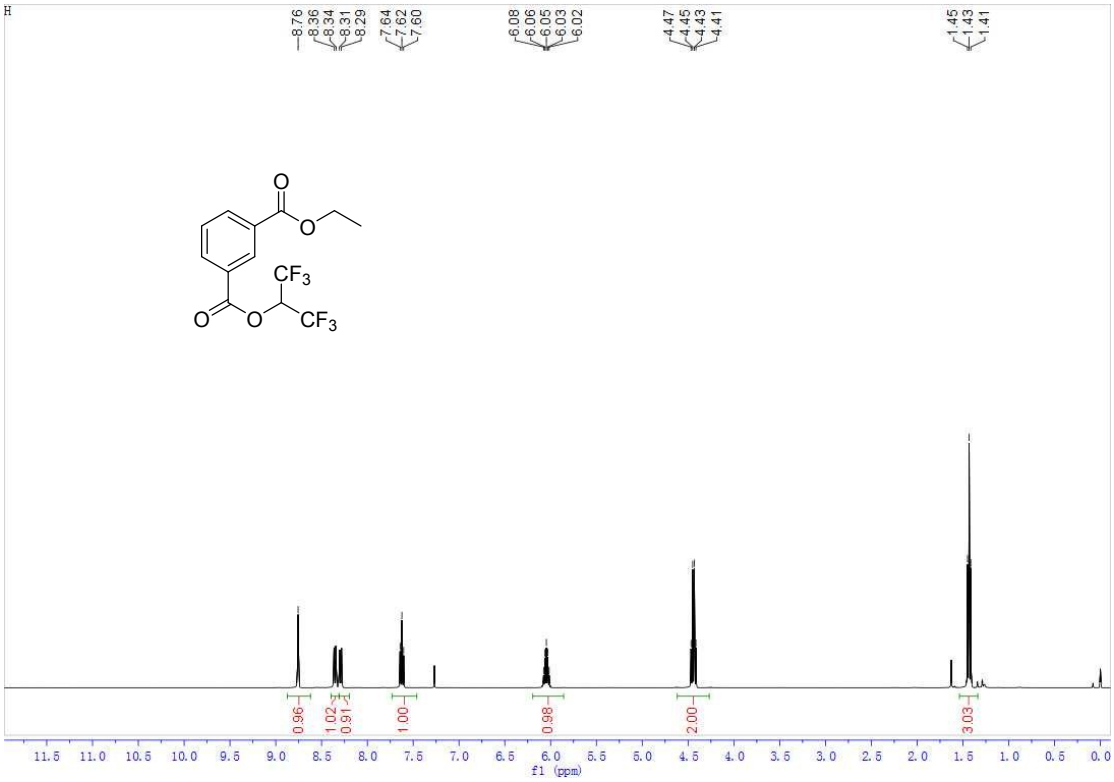


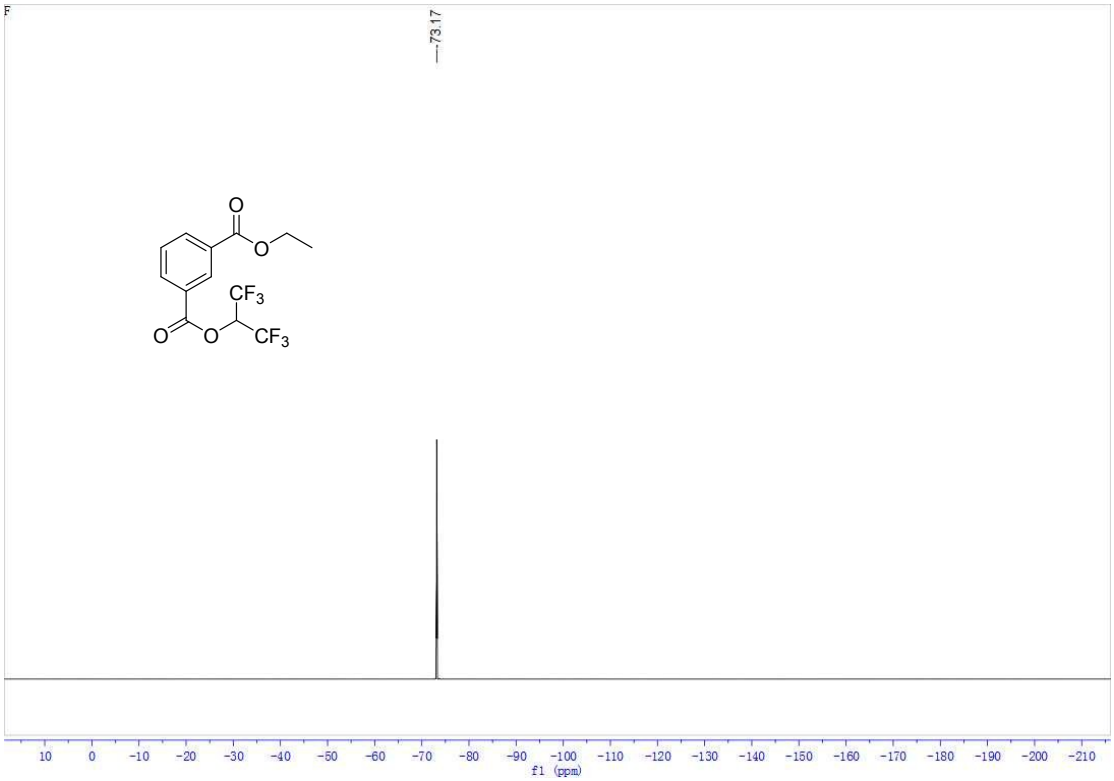
ethyl prop-2-yn-1-yl isophthalate (5Oe)

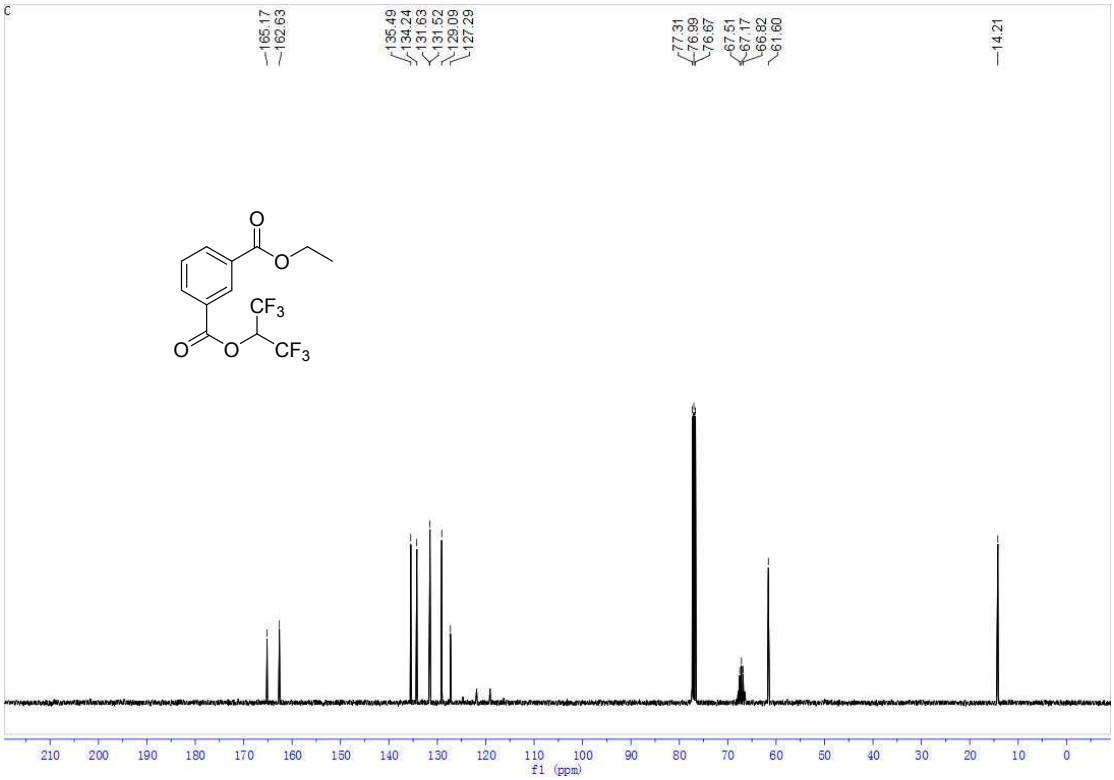




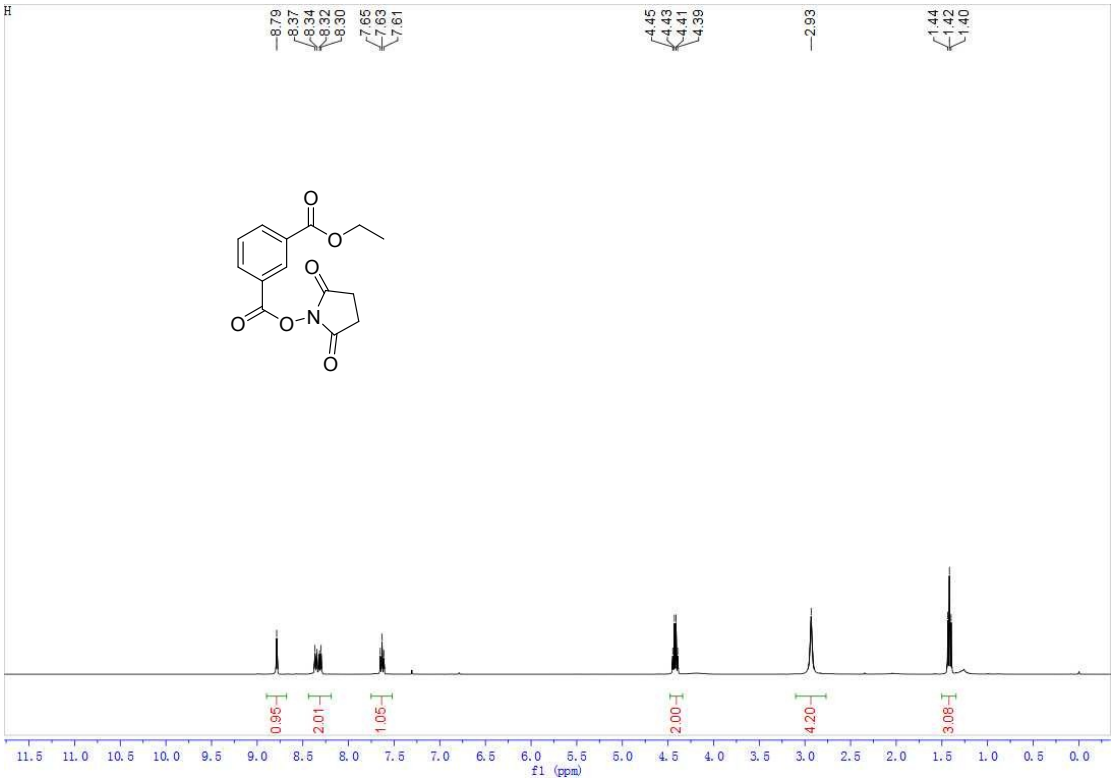
ethyl (1,1,1,3,3,3-hexafluoropropan-2-yl) isophthalate (5Of)

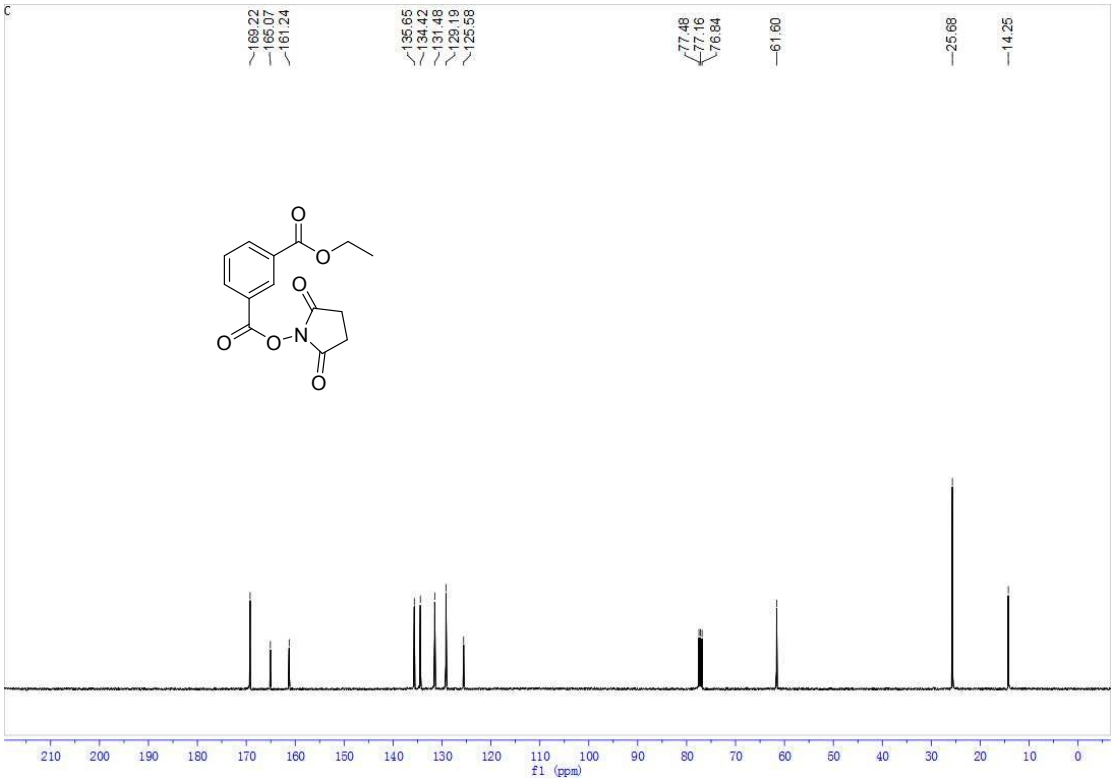




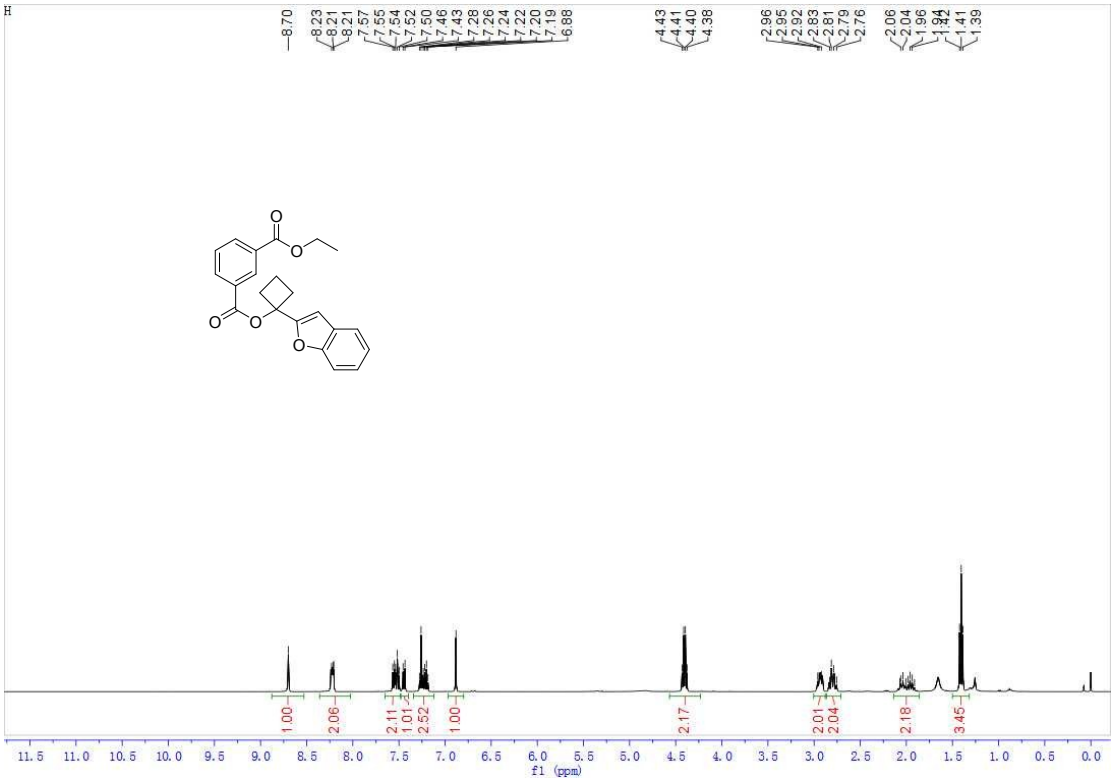

C
165.17
162.63
135.49
134.24
131.63
131.52
129.09
127.29
77.31
76.99
76.67
67.51
67.17
66.82
61.60
14.21
O
O
CF3
O
O
CF3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

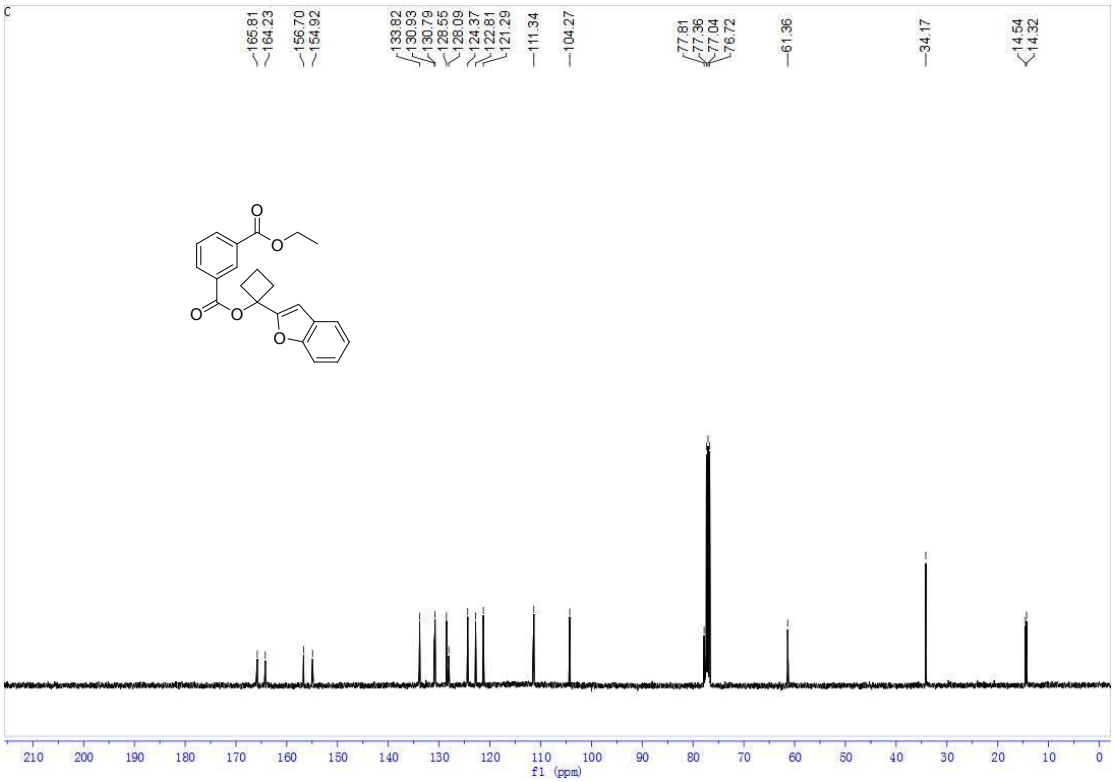
2,5-dioxopyrrolidin-1-yl ethyl isophthalate (5Oh)



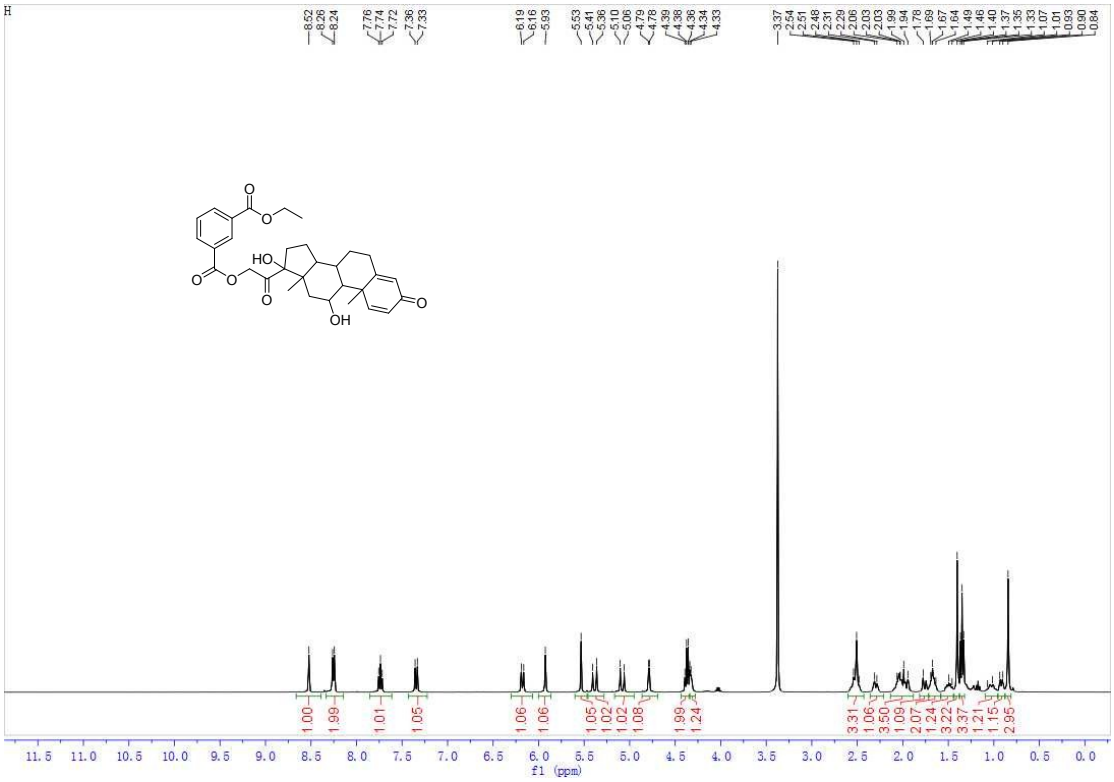


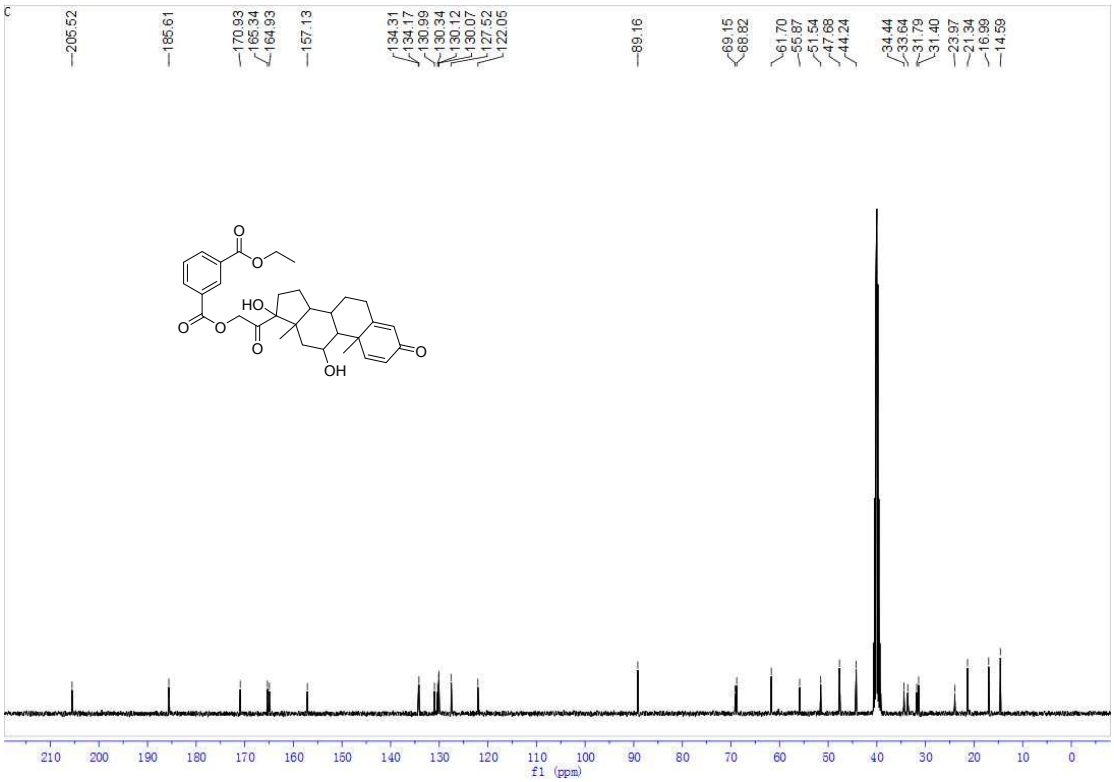
(benzofuran-2-yl)cyclobutyl ethyl isophthalate (5Oi)



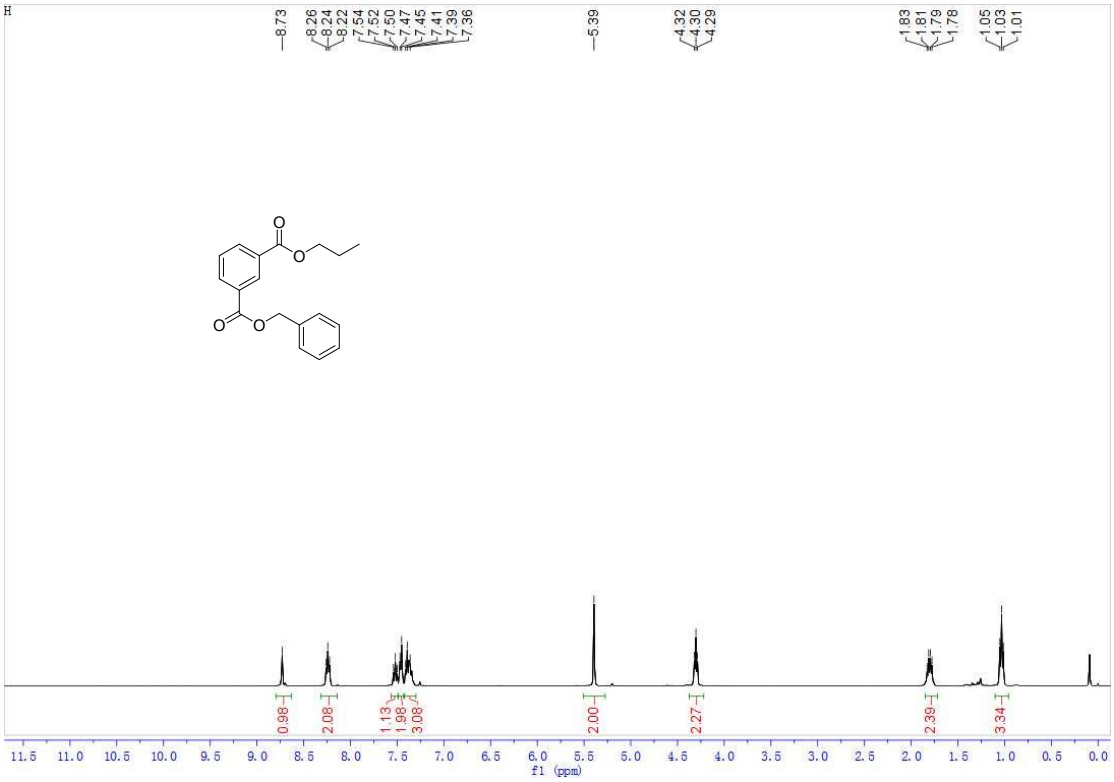


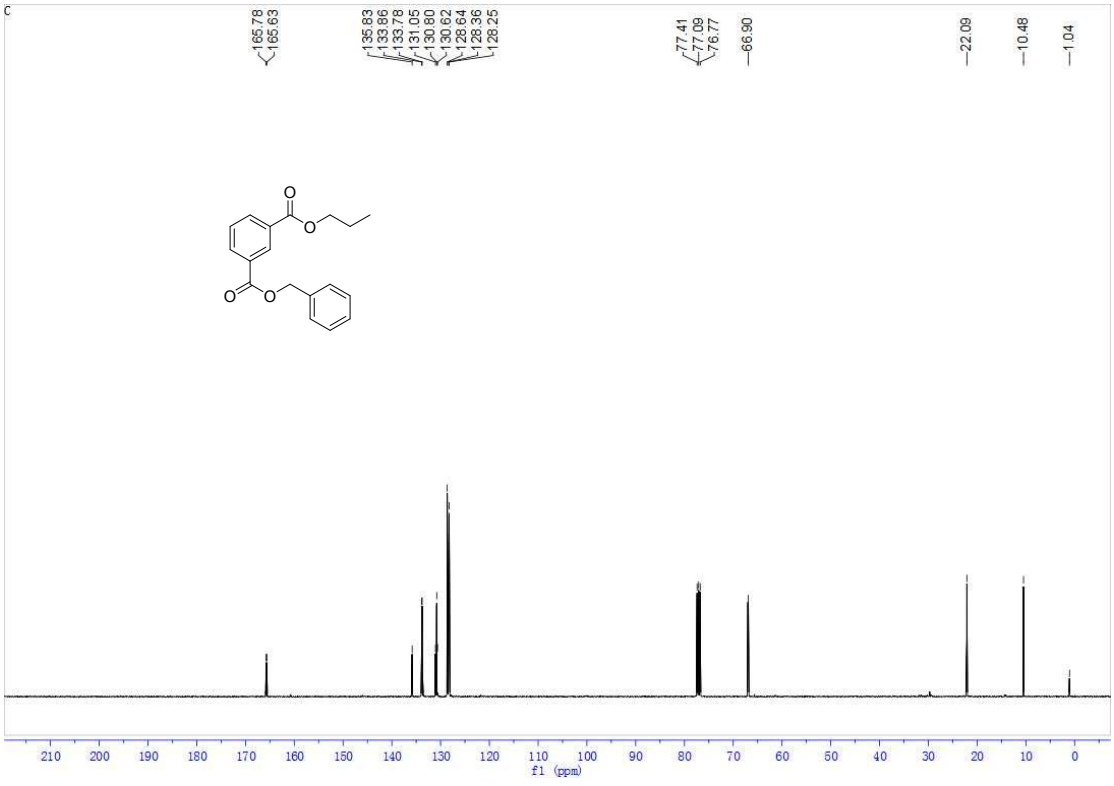
2-(11,17-dihydroxy-10,13-dimethyl-3-oxo-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[a]phenanthren-17-yl)-2-oxoethyl ethyl isophthalate (5Oj)



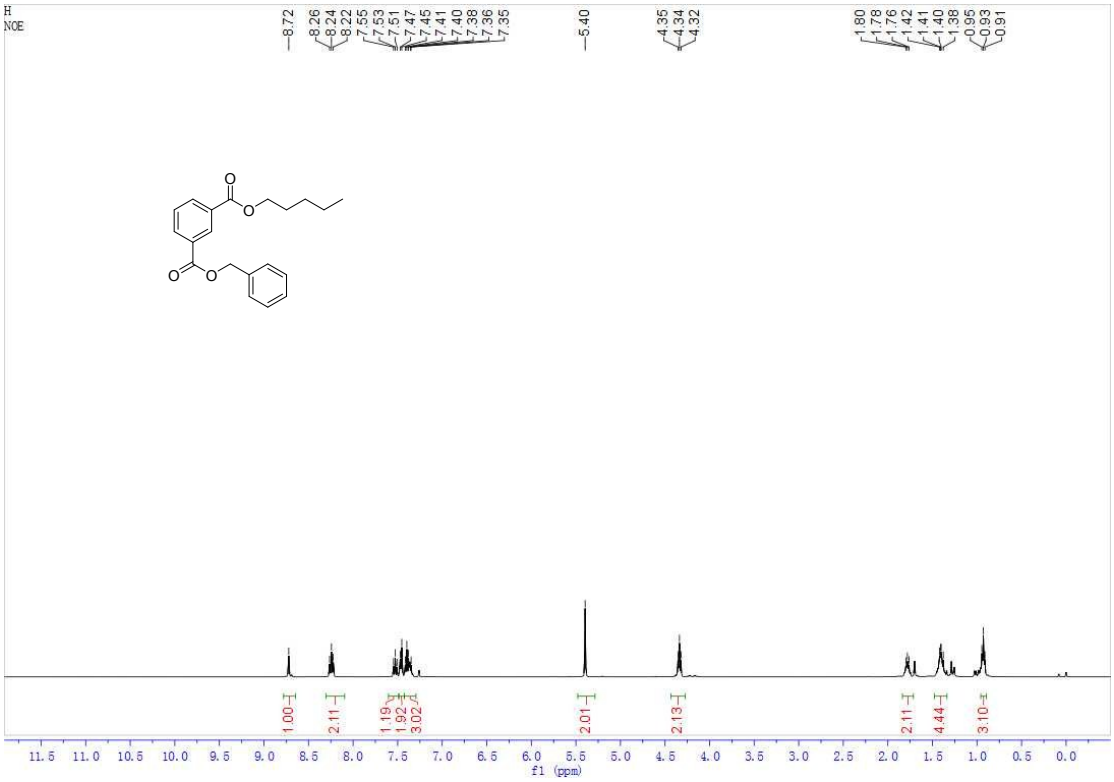


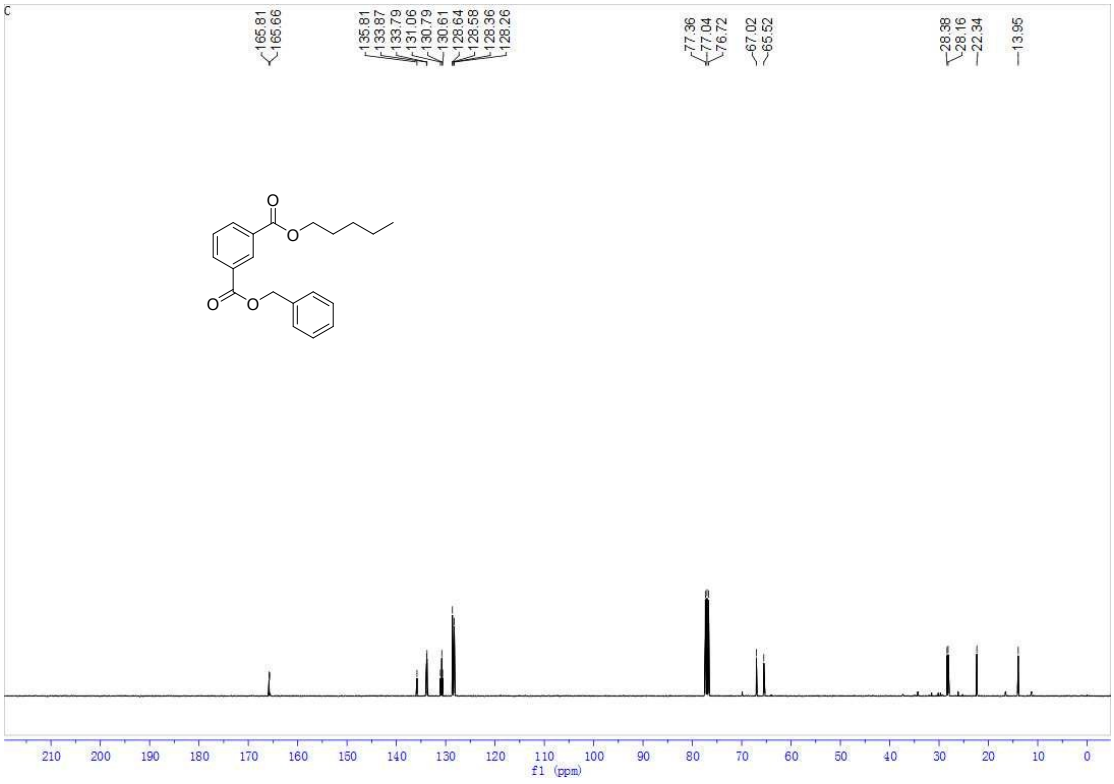
benzyl propyl isophthalate (5Ok)



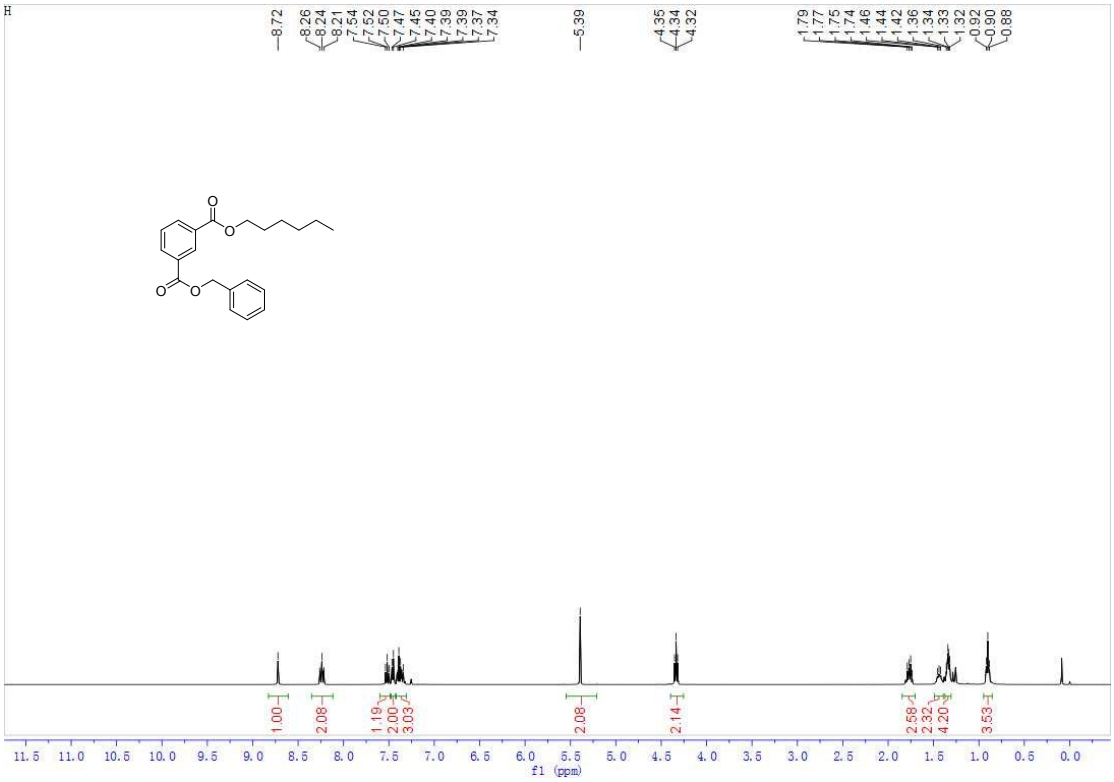


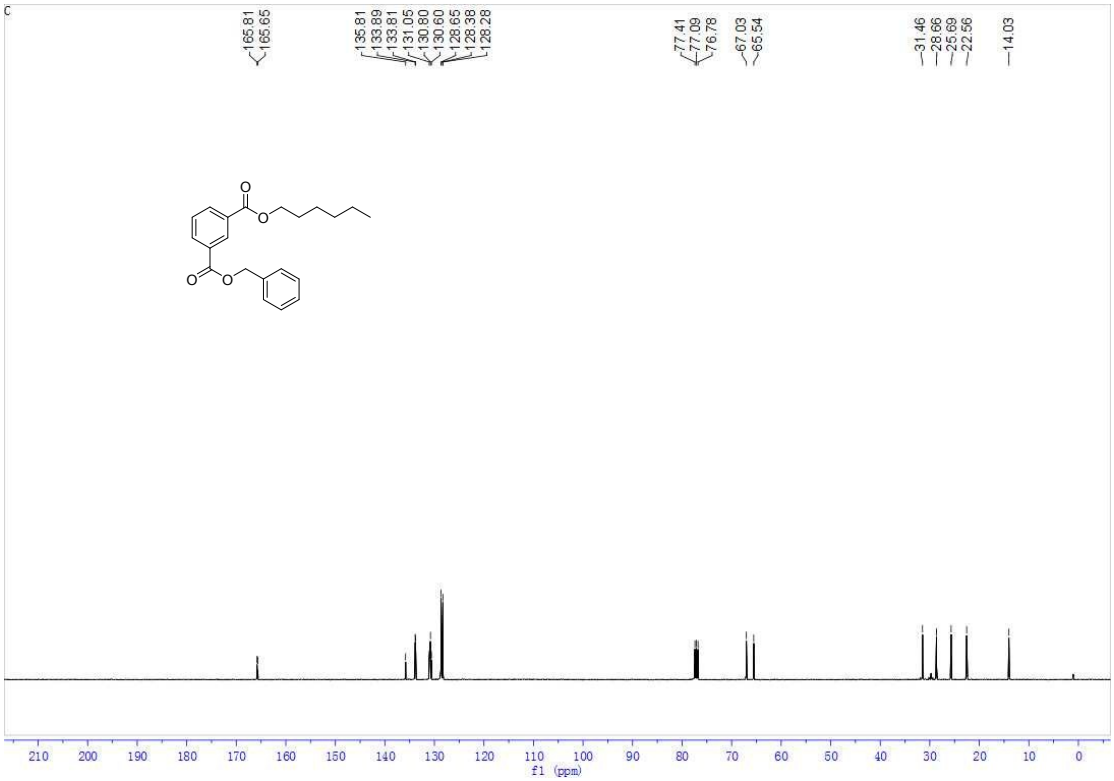
benzyl pentyl isophthalate (5Ol)



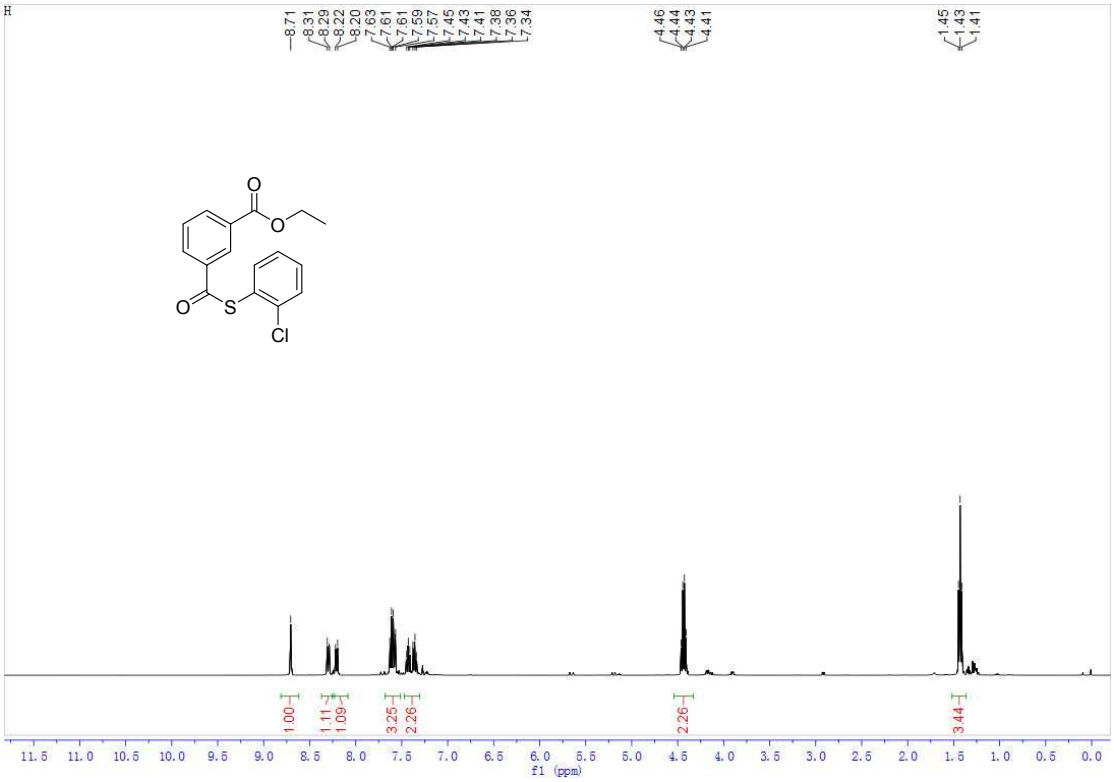


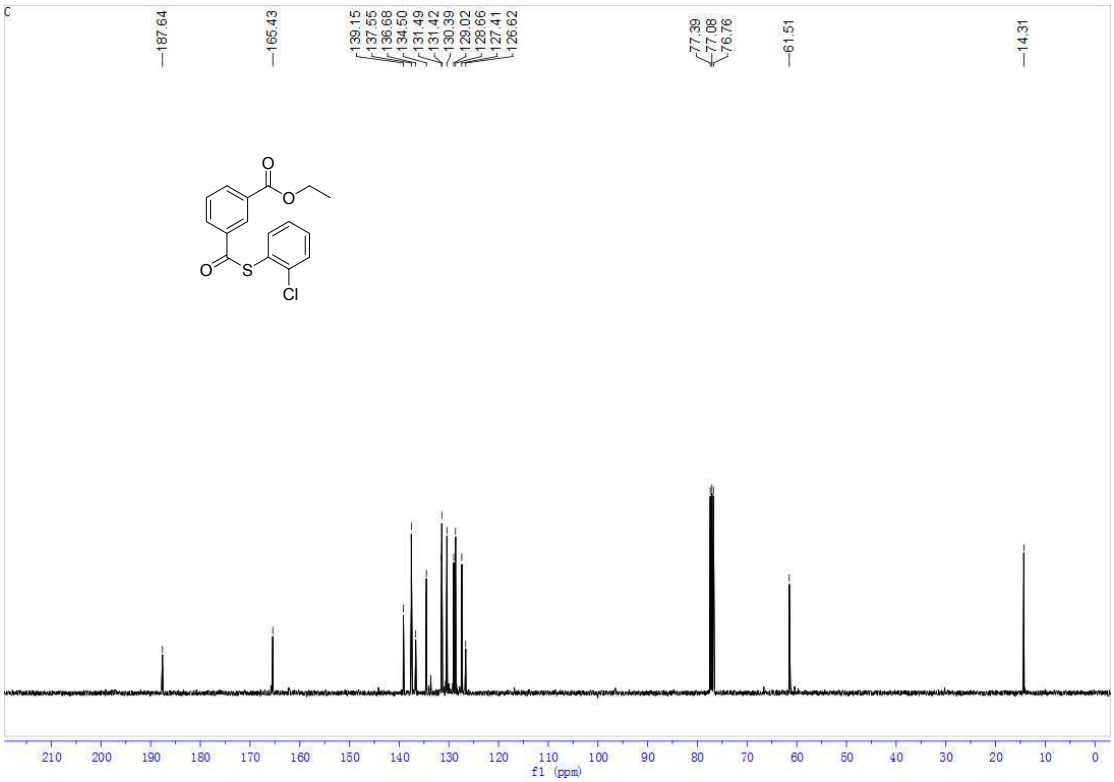
benzyl hexyl isophthalate (5Om)



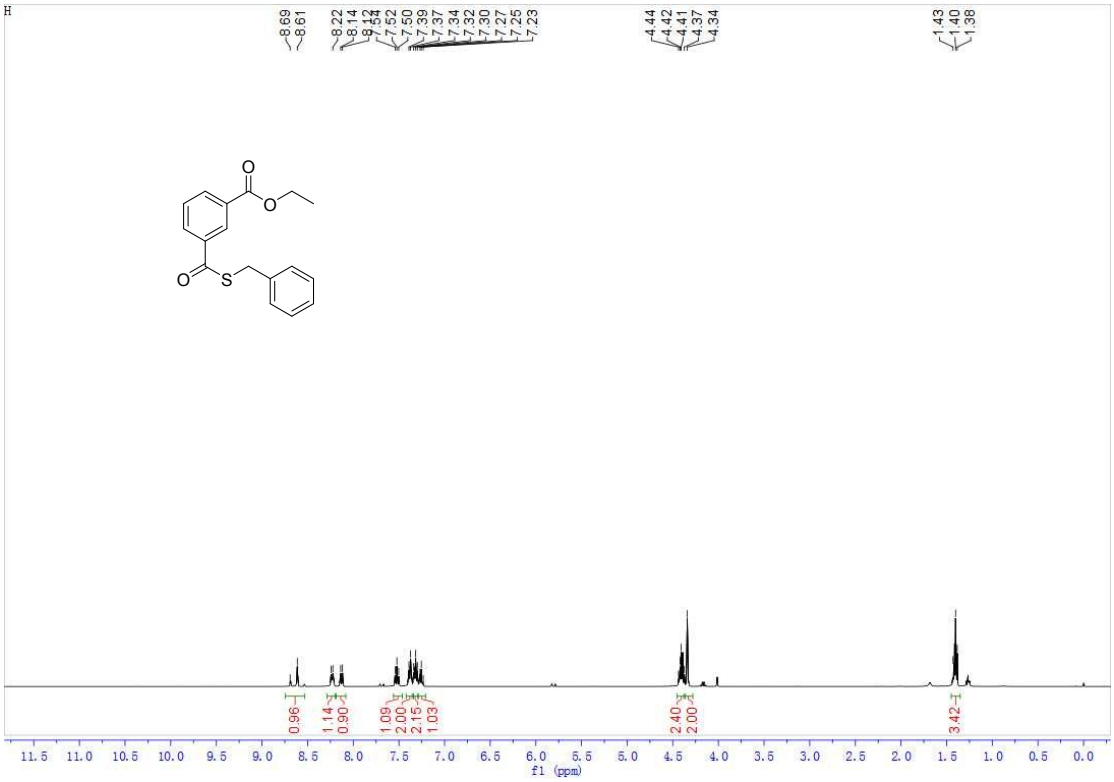


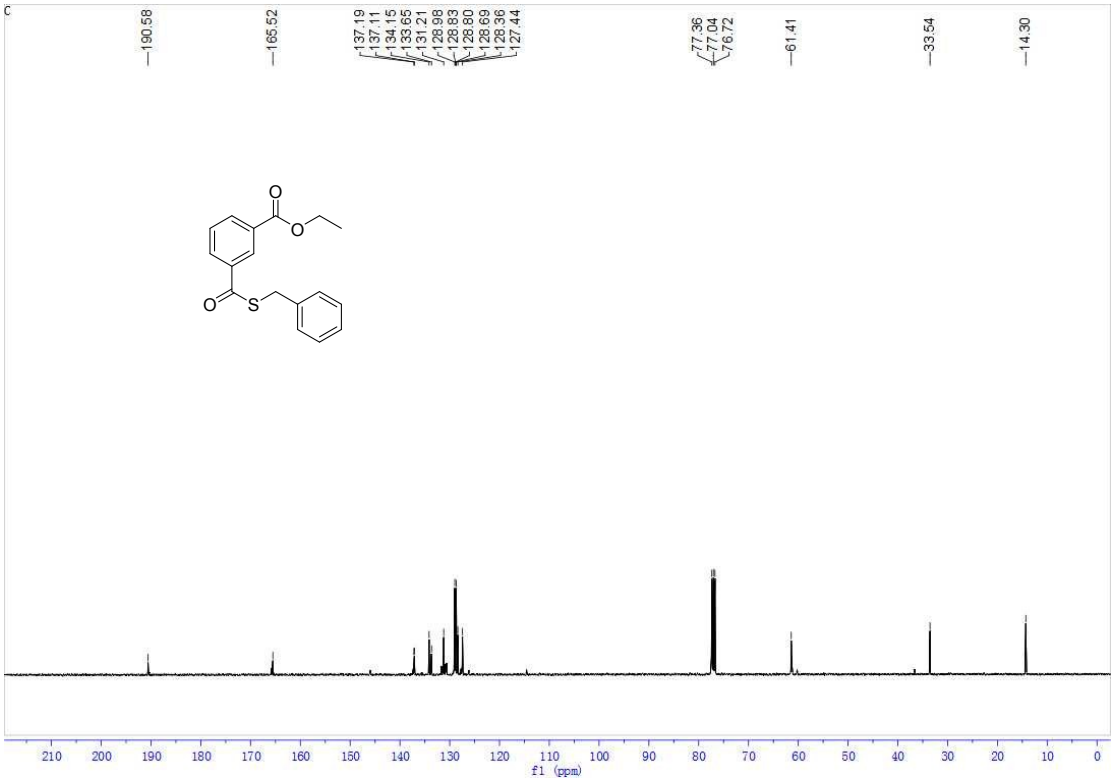
ethyl 3-(((2-chlorophenyl)thio)carbonyl)benzoate (5Sb)



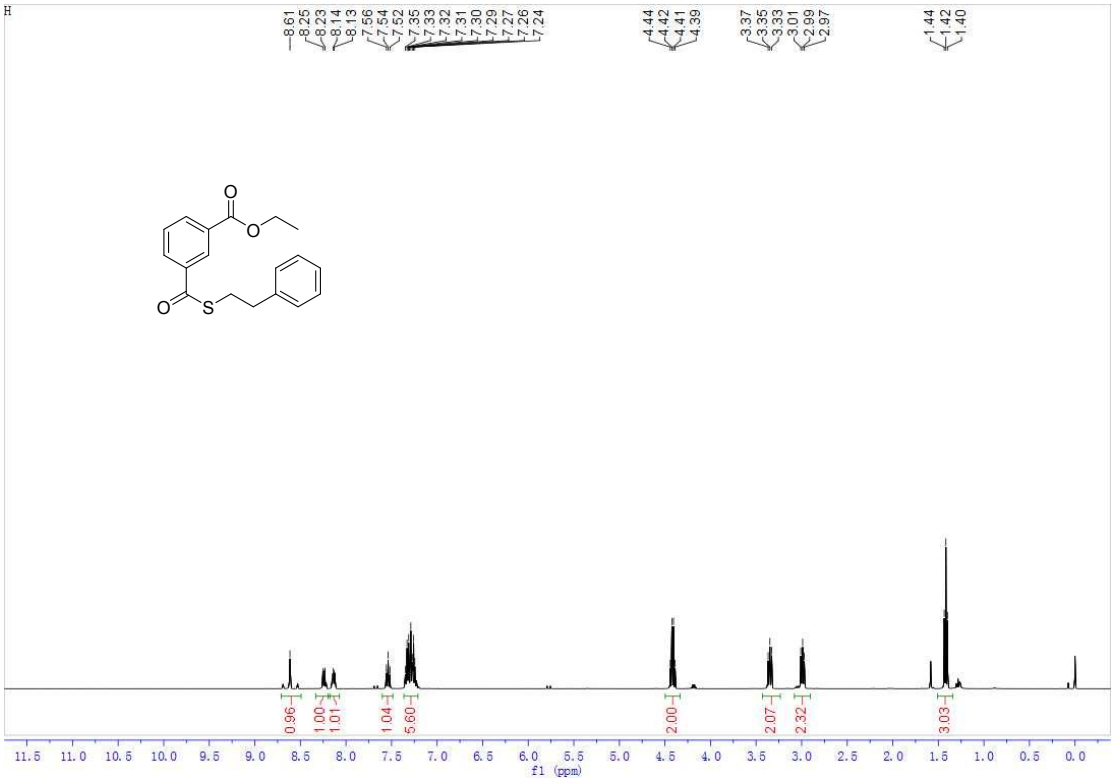


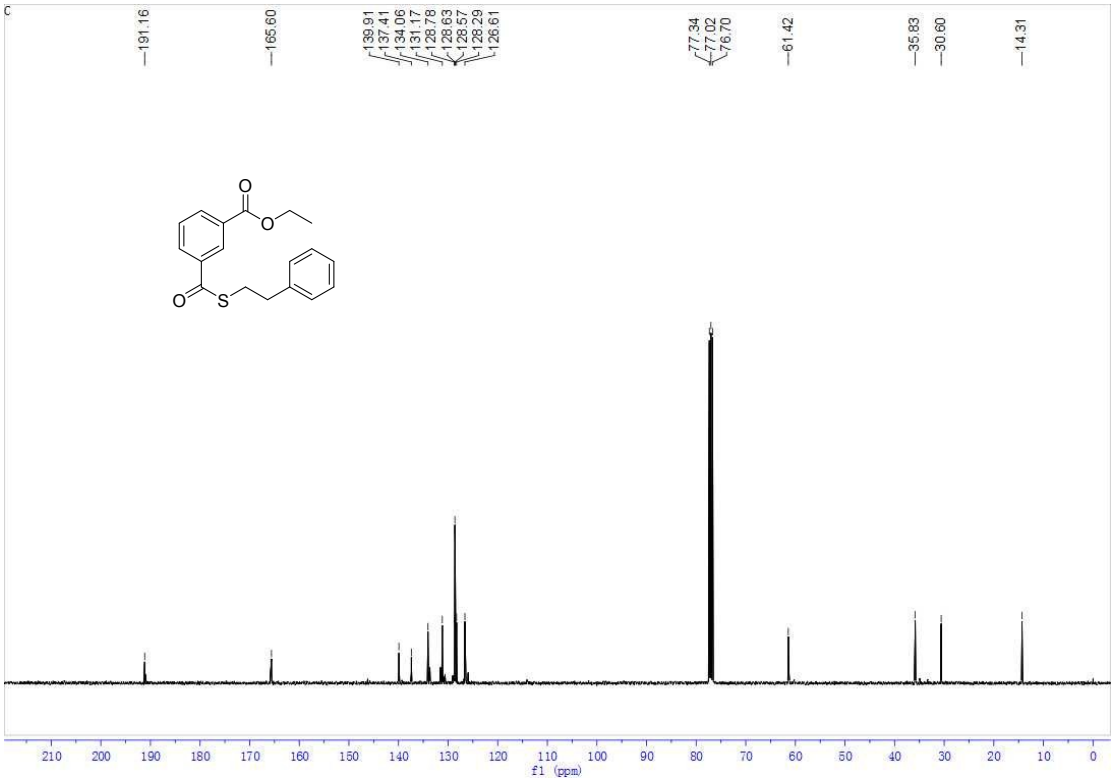
ethyl 3-((benzylthio)carbonyl)benzoate (5Sc)



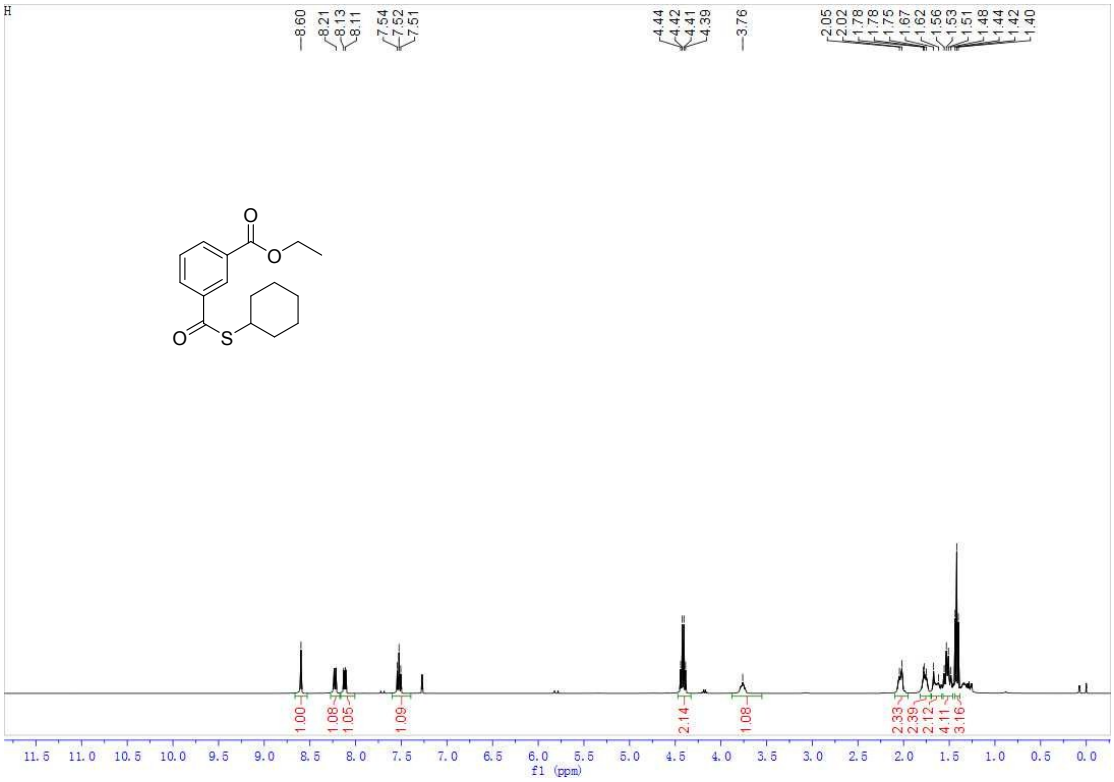


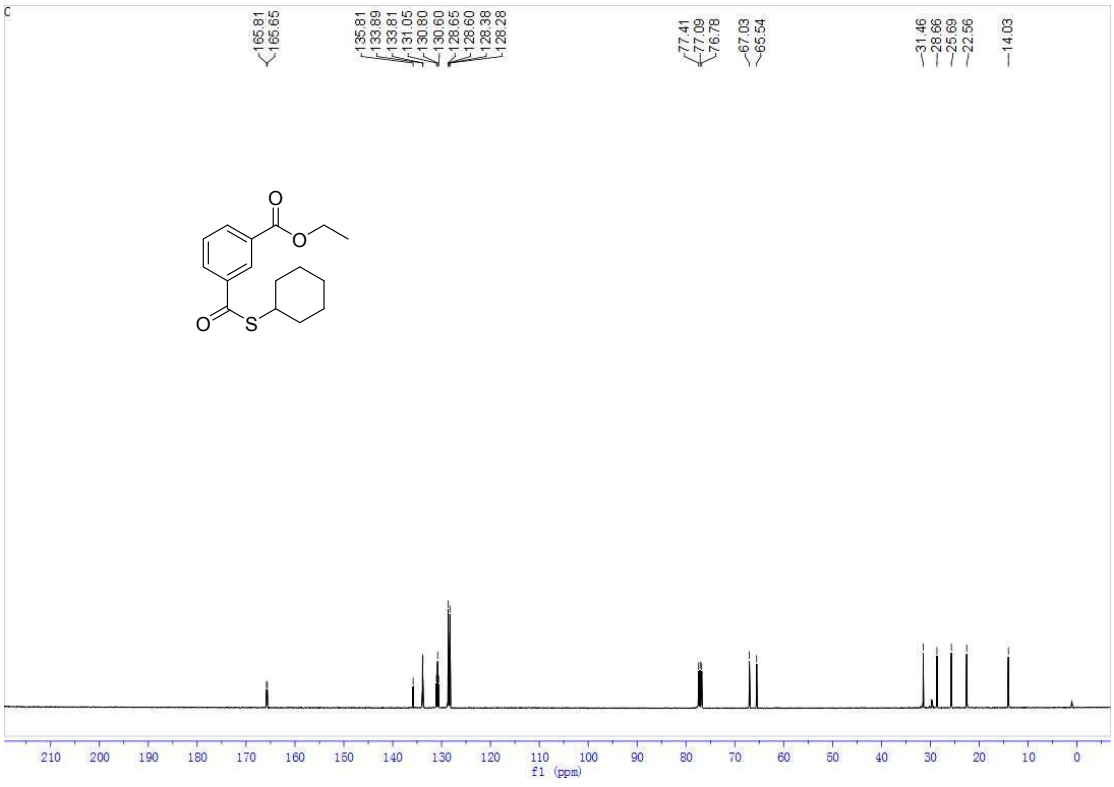
ethyl 3-((phenethylthio)carbonyl)benzoate (5Sd)



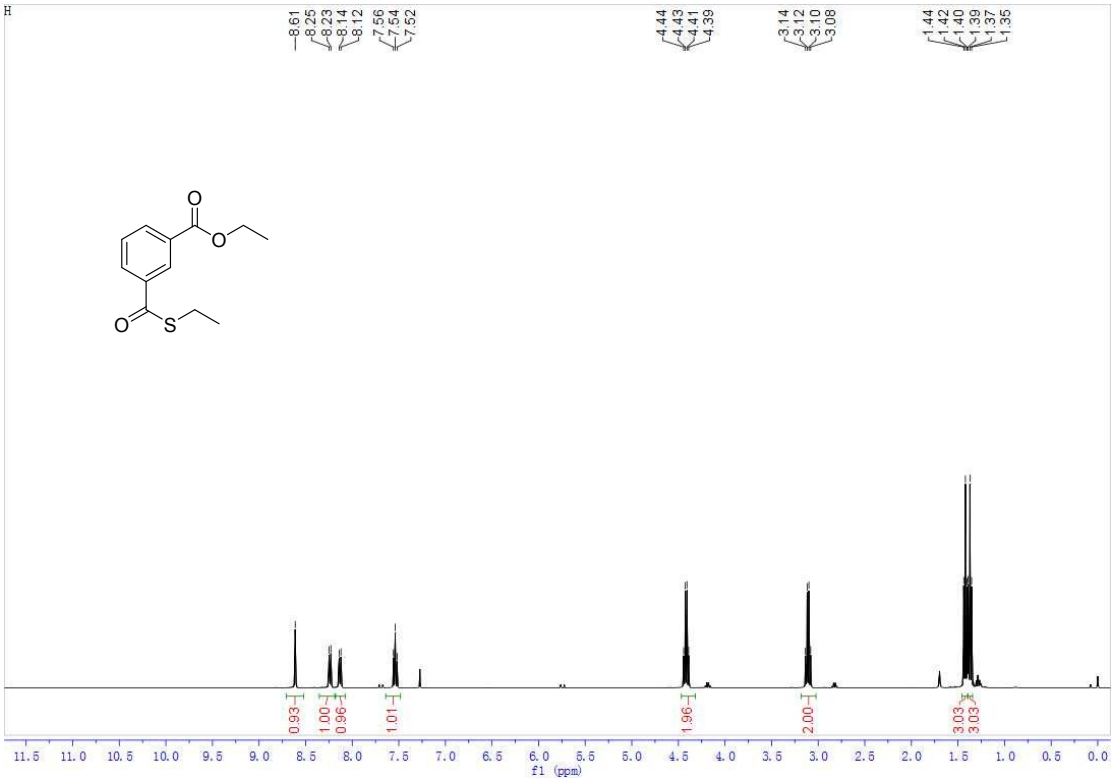


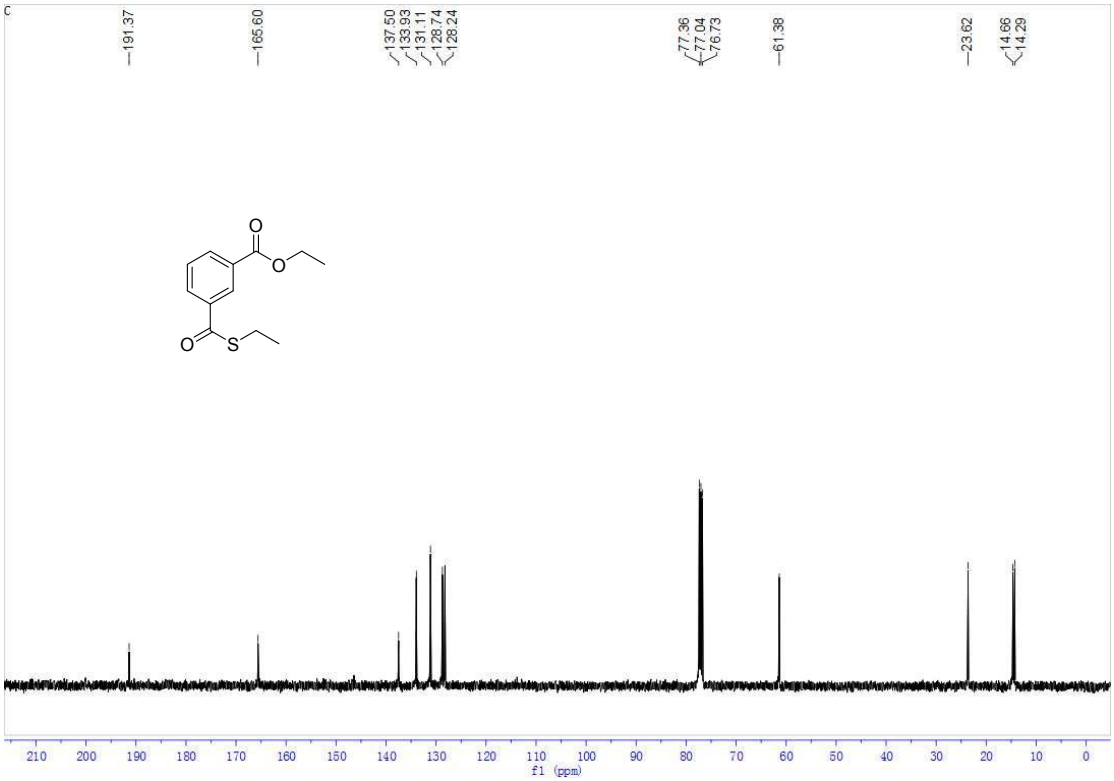
ethyl 3-((cyclohexylthio)carbonyl)benzoate (5Se)



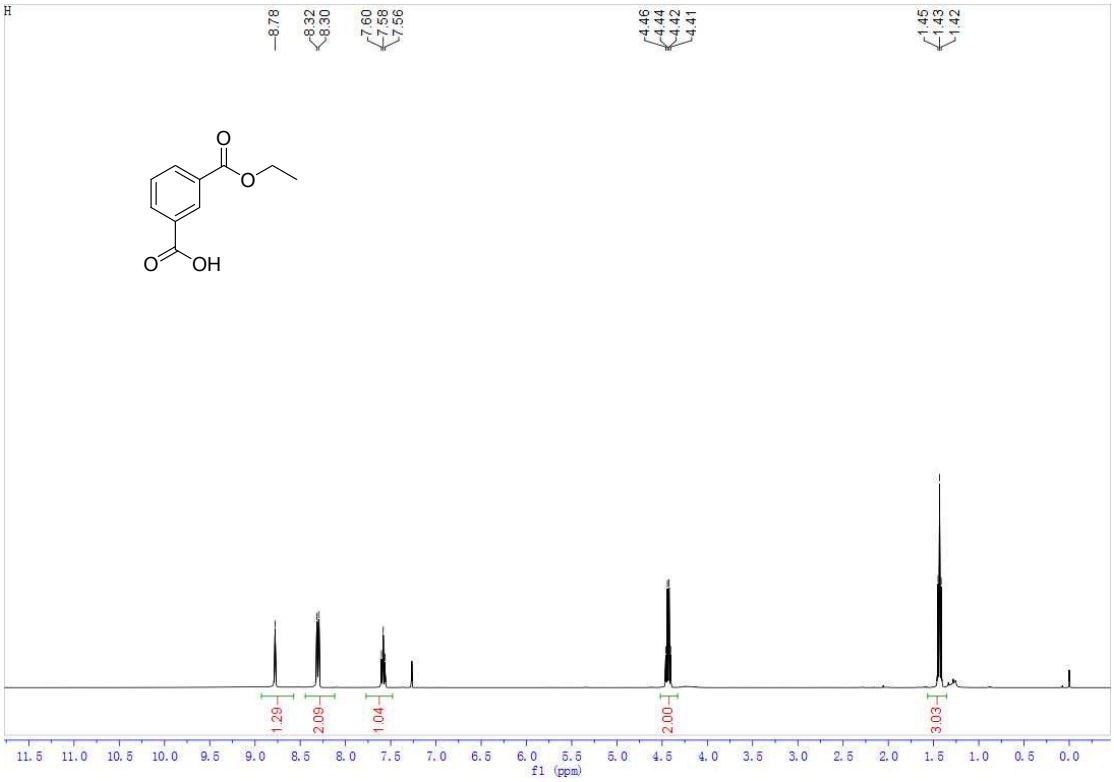


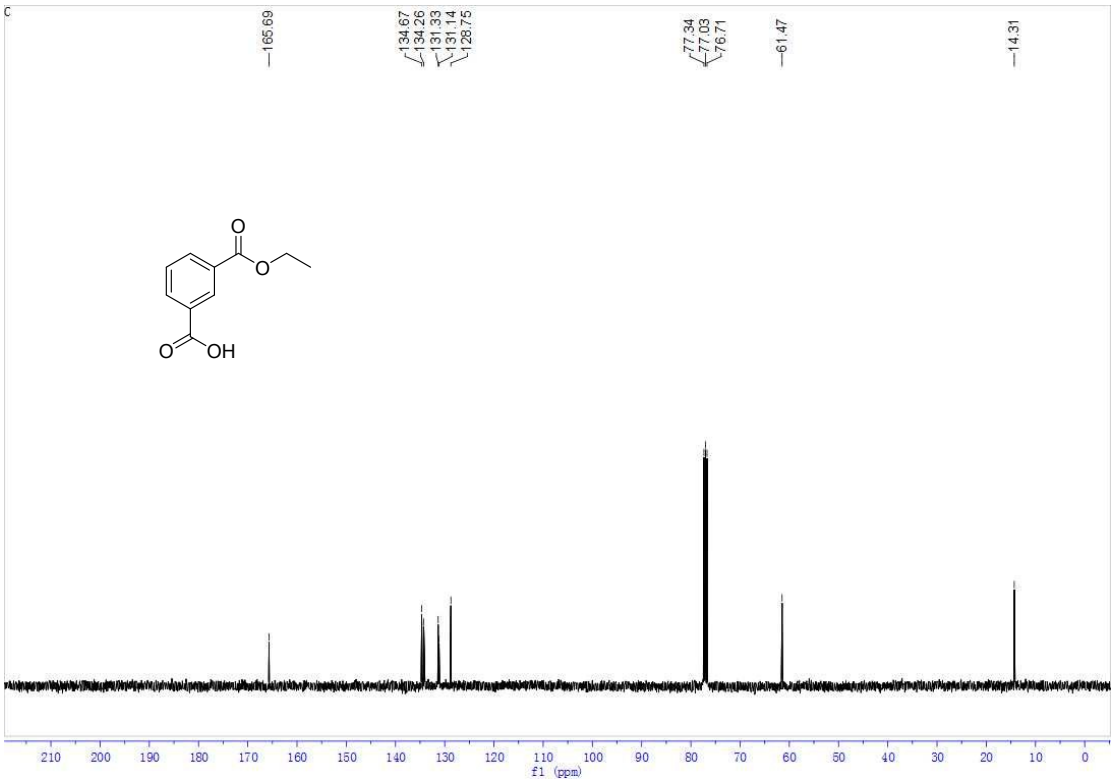
ethyl 3-((ethylthio)carbonyl)benzoate (5Sf)



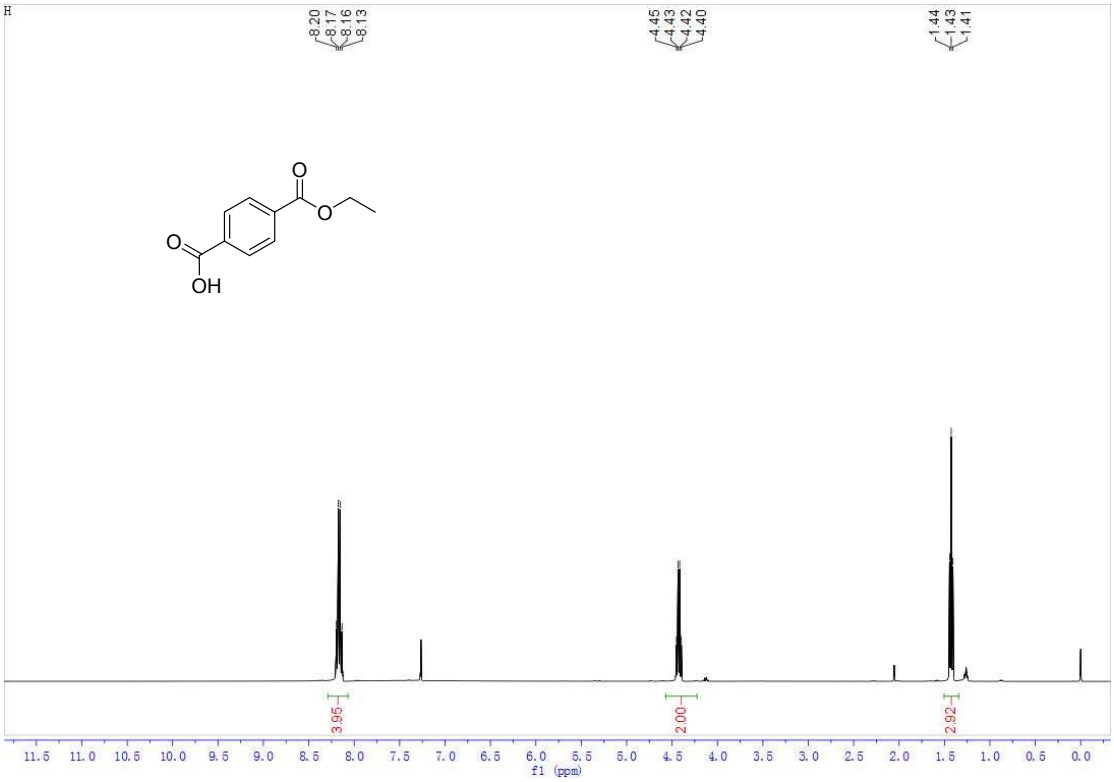


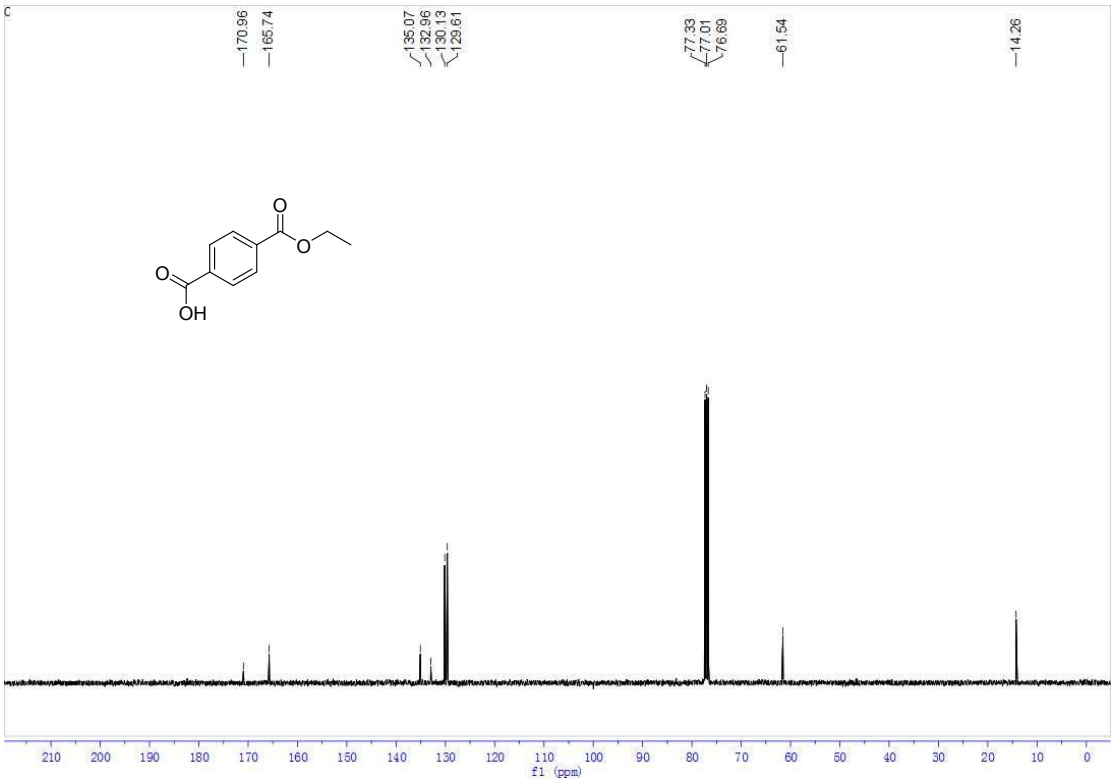
3-(ethoxycarbonyl)benzoic acid (6a)



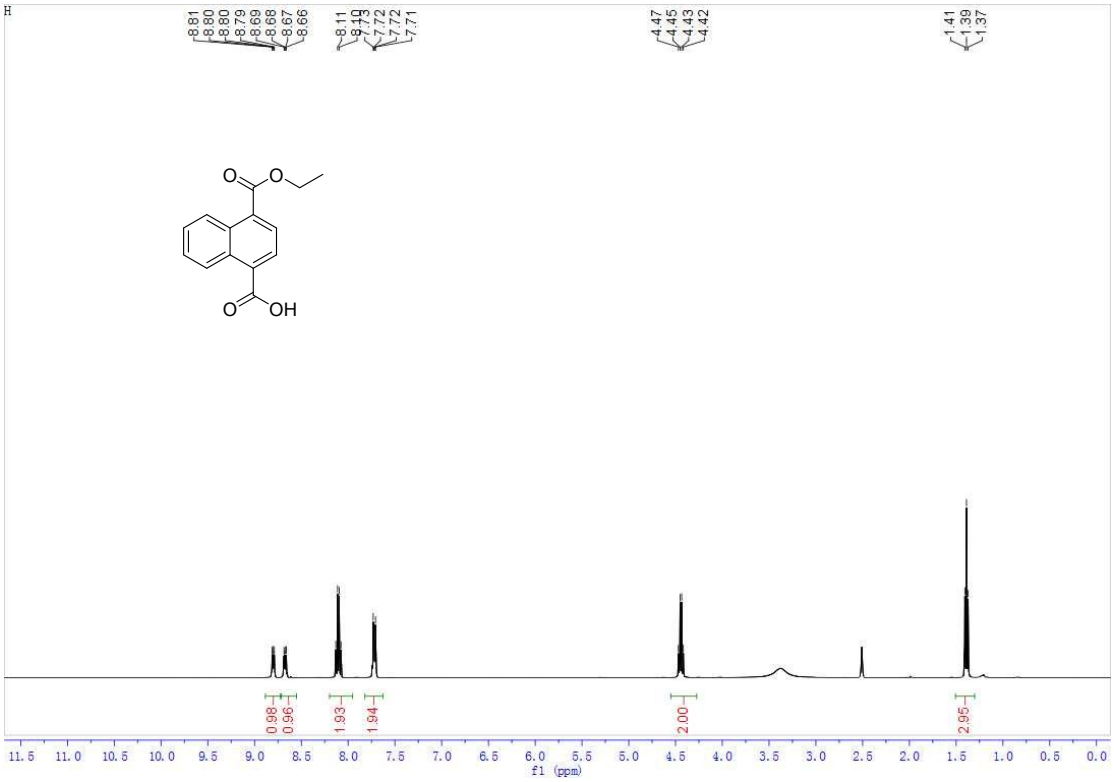


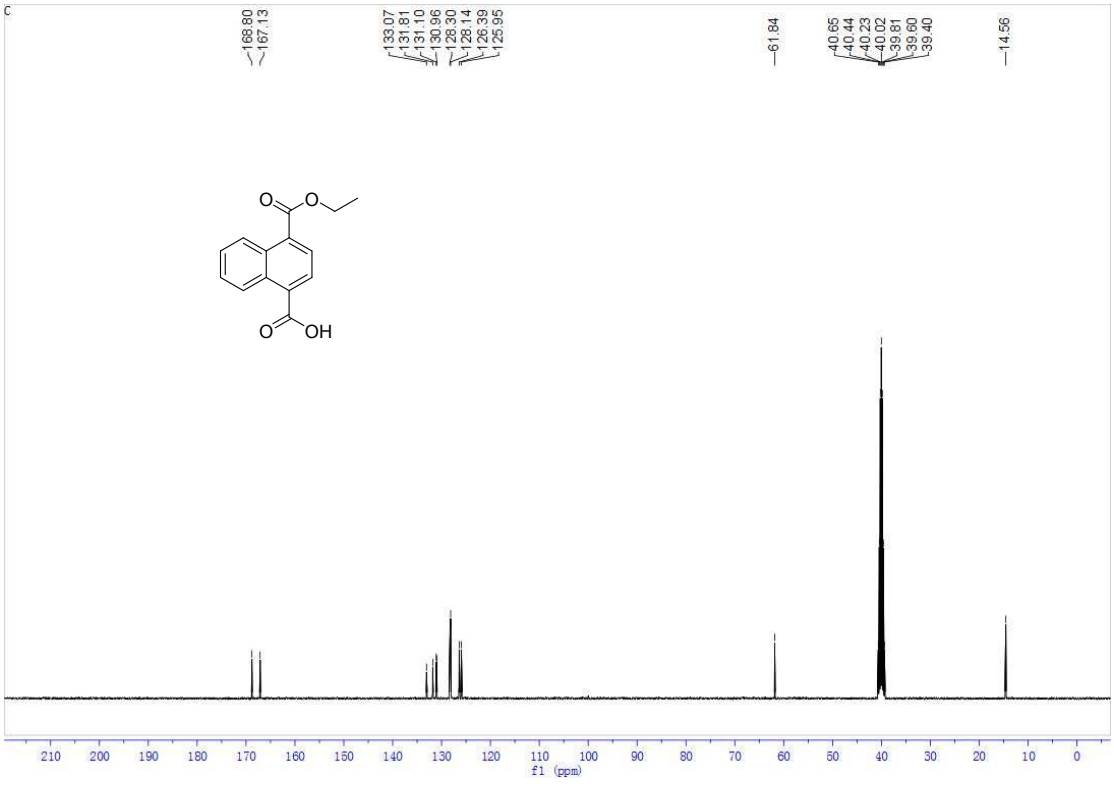
4-(ethoxycarbonyl)benzoic acid (6b)



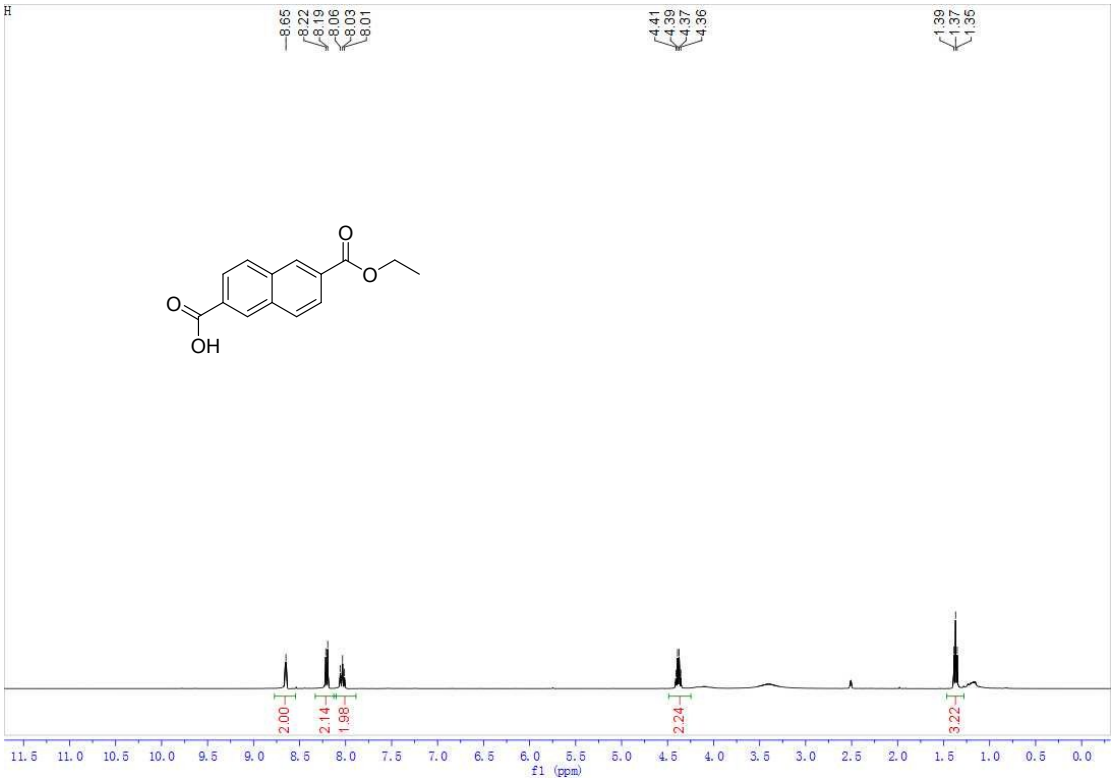


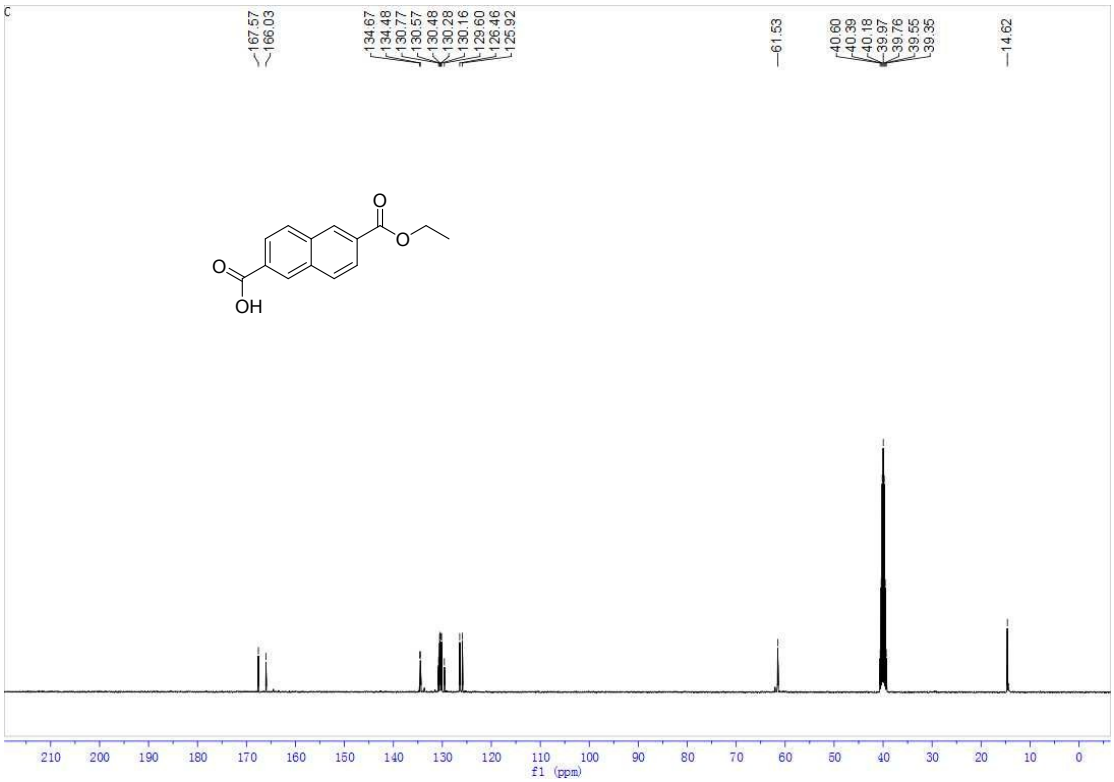
4-(ethoxycarbonyl)-1-naphthoic acid (6c)



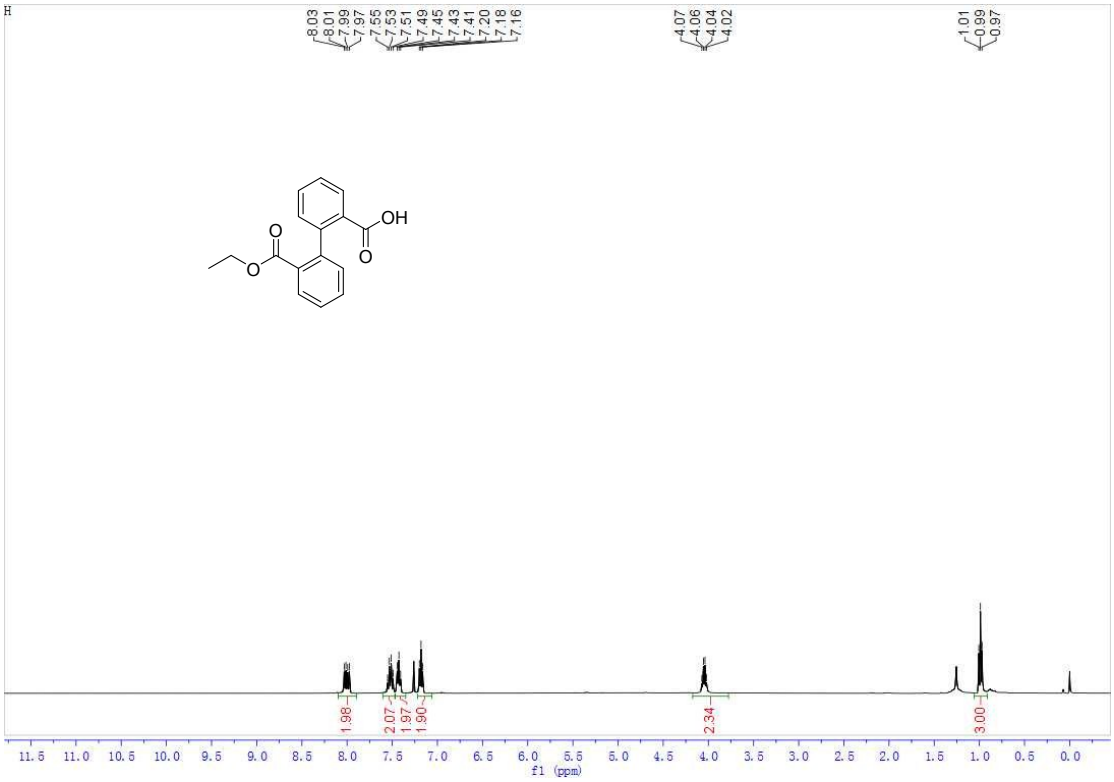


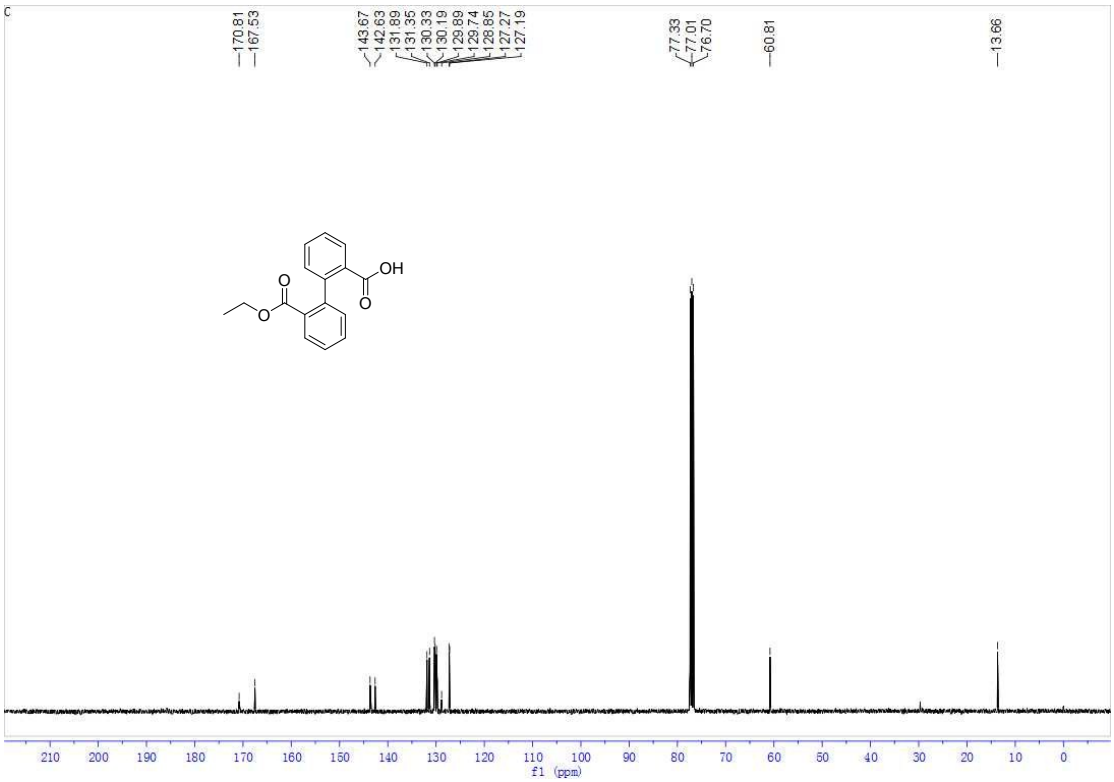
6-(ethoxycarbonyl)-2-naphthoic acid (6d)



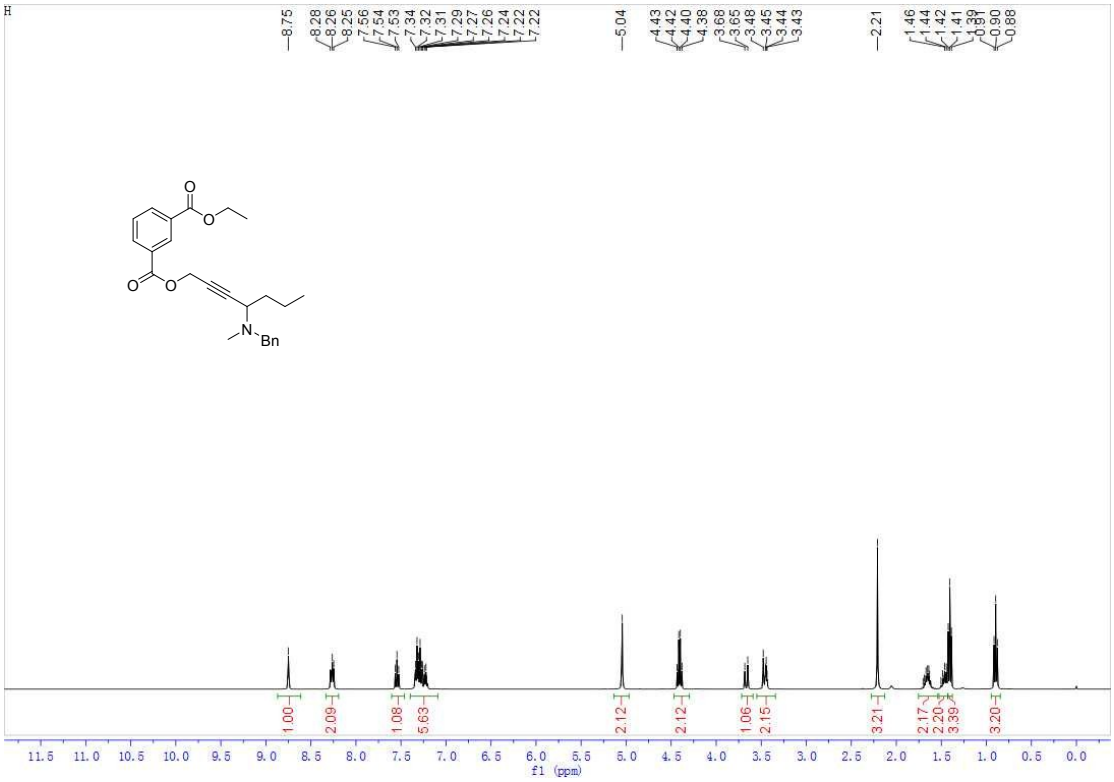


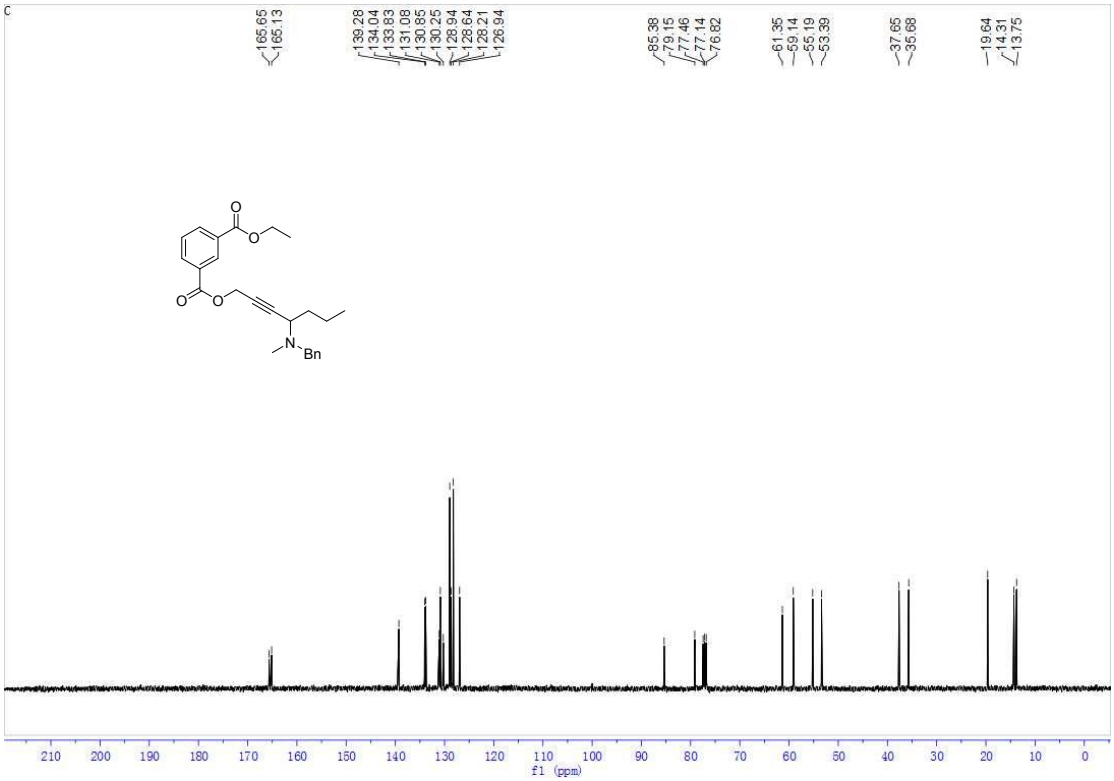
2'-(ethoxycarbonyl)-[1,1'-biphenyl]-2-carboxylic acid (6e)



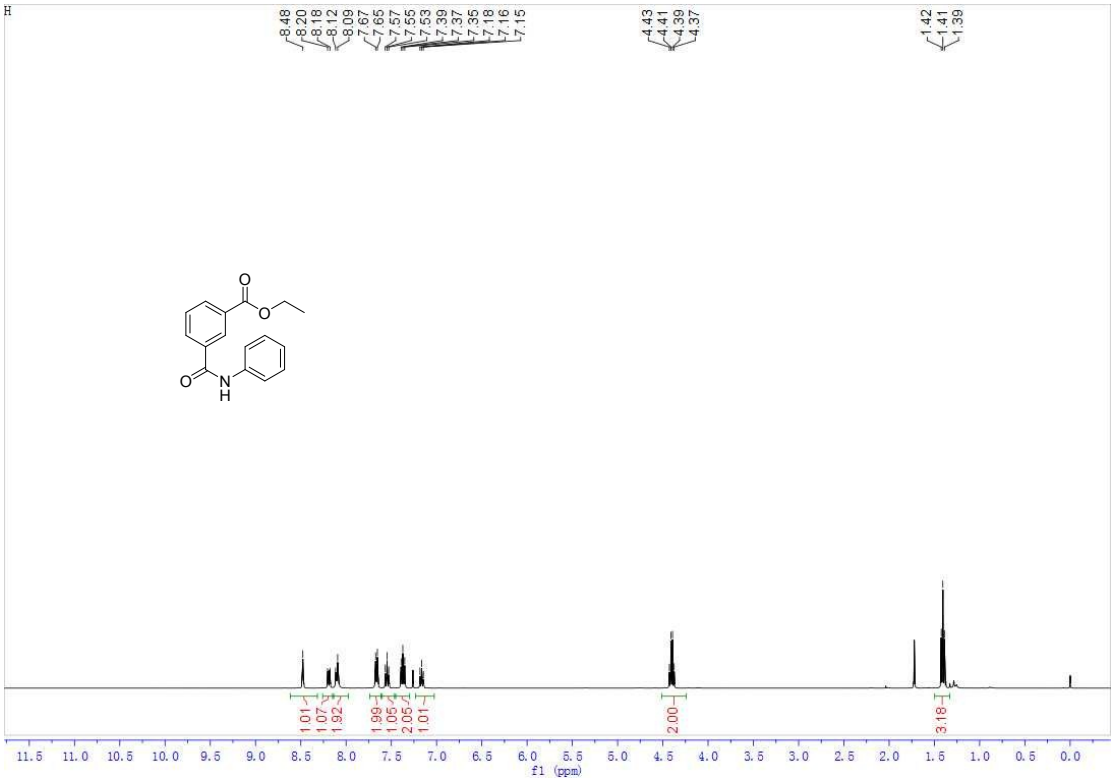


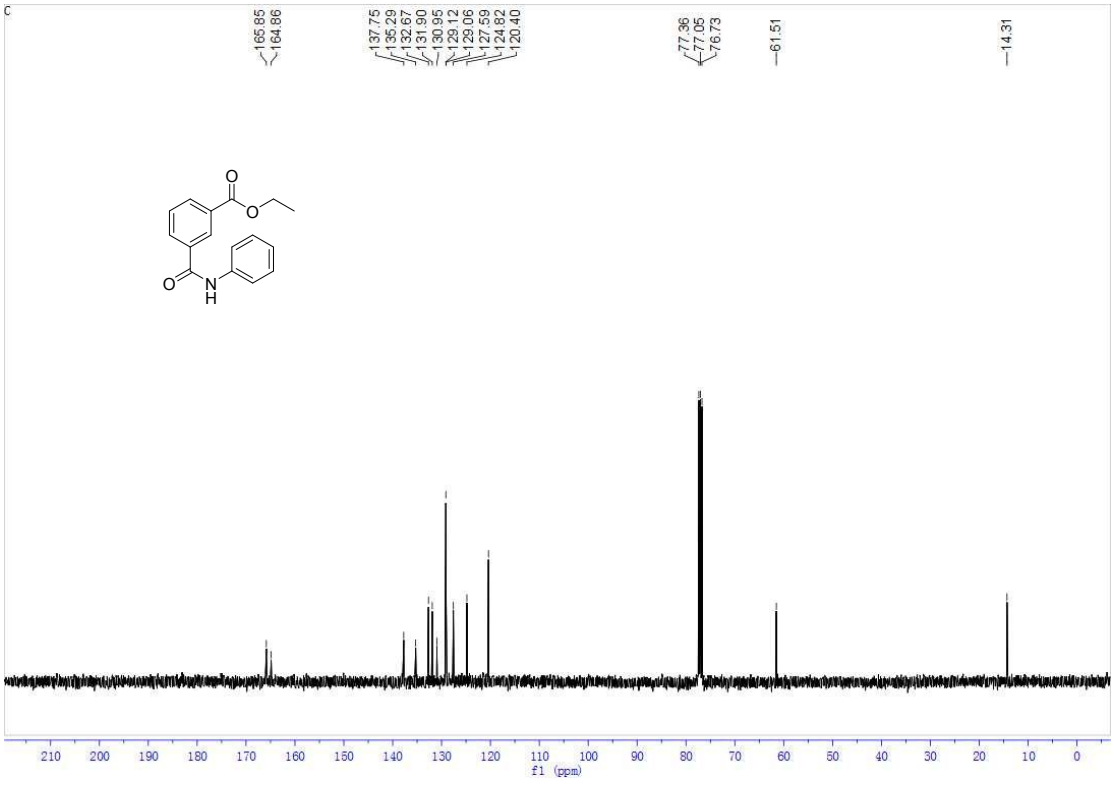
4-(benzyl(methyl)amino)hept-2-yn-1-yl ethyl isophthalate (7a)





ethyl 3-(phenylcarbamoyl)benzoate (7b)





ethyl 3-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)benzoate (7c)