

Metal-Free Radical Oxidative Alkoxy carbonylation and Imidation of Alkanes

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I. General considerations

All reactions were carried out in oven-dried autoclave tube under a carbon monoxide atmosphere in an autoclave. Cyclohexane and DCE were both dried by activated 4Å molecular sieve. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Thin-layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel. Preparative thin-layer chromatography (PTLC) was InnoChem thin-layer chromatography silica gel plate (GF254-C-C). GC yields were recorded with a Shimadzu GC-2014 gas chromatograph instrument with a FID detector and biphenyl was added as an internal standard. ^1H and ^{13}C NMR data were recorded with Bruker Advanced II (400 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. All chemical shifts are reported relative to tetramethylsilane and *d*-solvent peaks (77.00 ppm, chloroform), respectively. High resolution mass spectra (HRMS) were measured with Waters Micromass GCT Premier instrument and Thermo Fisher Scientific LTQ Orbitrap Elite instrument, the accurate masses were reported for the molecular ion ($[\text{M}]^+$) and the molecular ion + Hydrogen $[\text{M}+\text{H}]^+$.

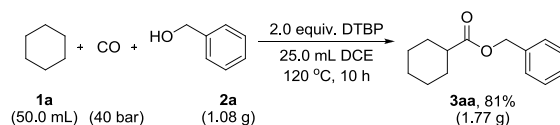
II. Radical oxidative carbonylation reactions

General Procedure A: In an oven-dried autoclave tube equipped with a stir-bar, cyclohexane (2.0 mL) and DCE (1.0 mL) were added to the autoclave tube via a syringe. Then, benzyl alcohol (0.20 mmol), DTBP (72 μL , 0.40 mmol) were added to the autoclave tube. After that, place the autoclave tube in an autoclave, then the autoclave was purged for three times and charged with CO at 40 bar. The reaction mixture was stirred at 120 °C for 10 hours and then cooled to room temperature. Next CO was carefully released. The corresponding reaction mixture was purified by preparative thin-layer chromatography to give the desired product using petroleum ether and ethyl acetate (20:1).

General Procedure B: In an oven-dried autoclave tube equipped with a stir-bar, (trifluoromethyl)benzene (2.0 mL) and DCE (1.0 mL) were added to the autoclave tube via a syringe. Then, benzyl alcohol (0.20 mmol), DTBP (108 μL , 0.60 mmol) were added to the autoclave tube. After that, place the autoclave tube in an autoclave, then the autoclave was purged for three times and charged with CO at 20 bar, C_2H_6 at 40 bar. The reaction mixture was stirred at 120 °C for 10 hours and then cooled to room temperature. Next CO was carefully released. The corresponding reaction mixture was purified by preparative thin-layer chromatography to give the desired product using petroleum ether and ethyl acetate (20:1).

III. Gram scale reaction

In an 150 mL oven-dried autoclave reactor equipped with a stir-bar, cyclohexane (50.0 mL) and DCE (25.0 mL) were added to the autoclave reactor via a syringe. Then, benzyl alcohol (1.08 g, 10.0 mmol), DTBP (3.6 mL, 20.0 mmol) were added to the autoclave reactor. After that, place the autoclave reactor in an autoclave, then the autoclave was purged for three times and charged with CO at 40 bar. The reaction mixture was stirred at 120 °C for 10 hours and then cooled to room temperature. Next CO was carefully released. The corresponding reaction mixture was purified by flash column chromatography on a silica gel to give the desired product using petroleum ether and ethyl acetate (20:1).

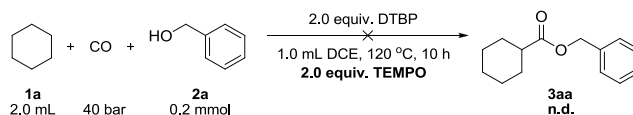


IV. Mechanistic studies

A. Radical scavenger effect studies

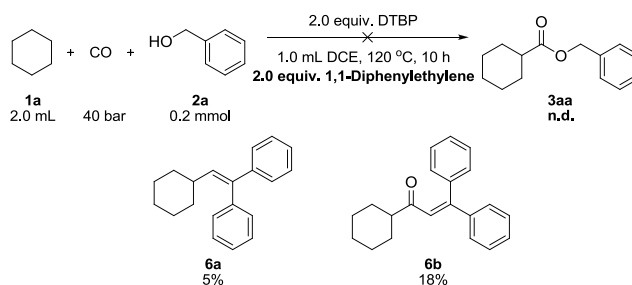
a. Reaction in the presence of TEMPO

A mixture of cyclohexane (2.0 mL), DCE (1.0 mL), benzyl alcohol (0.2 mmol), DTBP (72 μ L, 0.40 mmol) and TEMPO (62.4 mg, 0.4 mmol) were added to an autoclave tube placed in an autoclave. Then the autoclave was purged for three times and charged with CO at 40 bar. The reaction mixture was stirred at 120 $^{\circ}$ C for 10 hours and then cooled to room temperature. Next CO was carefully released. No desired product was observed.

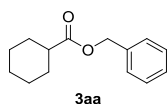


b. Reaction in the presence of 1,1-diphenylethylene

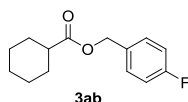
A mixture of cyclohexane (2.0 mL), DCE (1.0 mL), benzyl alcohol (0.2 mmol), DTBP (72 μ L, 0.40 mmol) and 1,1-diphenylethylene (72.0 mg, 0.4 mmol) were added to an autoclave tube placed in an autoclave. Then the autoclave was purged for three times and charged with CO at 40 bar. The reaction mixture was stirred at 120 $^{\circ}$ C for 10 hours and then cooled to room temperature. Next CO was carefully released. No desired product was observed. The yield (based on DTBP) of **6a** and **6b** were determined by 1 H NMR analysis employing diphenyl methane as the internal standard.



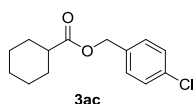
V. Analytical data of products



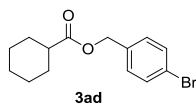
Benzyl cyclohexanecarboxylate (3aa): colorless liquid was obtained with 83% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.29 (m, 5H), 5.11 (s, 2H), 2.35 (tt, J = 11.4, 3.6 Hz, 1H), 1.95-1.91 (m, 2H), 1.77-1.73 (m, 2H), 1.65-1.61 (m, 1H), 1.51-1.41 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.9, 136.3, 128.5, 128.0, 127.9, 65.9, 43.2, 29.0, 25.7, 25.4. HRMS (EI) calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ $[\text{M}]^+$: 218.1307; Found: 218.1303.



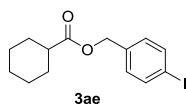
4-Fluorobenzyl cyclohexanecarboxylate (3ab): colorless liquid was obtained with 52% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.30 (m, 2H), 7.07-7.01 (m, 2H), 5.07 (s, 2H), 2.34 (tt, J = 11.2, 3.6 Hz, 1H), 1.94-1.90 (m, 2H), 1.77-1.73 (m, 2H), 1.66-1.62 (m, 1H), 1.49-1.40 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.9, 162.5 (d, $J_{\text{C-F}}$ = 247.5 Hz) 132.1 (d, $J_{\text{C-F}}$ = 3.0 Hz), 129.9 (d, $J_{\text{C-F}}$ = 8.1 Hz), 115.4 (d, $J_{\text{C-F}}$ = 22.2 Hz), 65.2, 43.1, 28.9, 25.7, 25.4. ^{19}F NMR (377 MHz, CDCl_3) δ -114.0. HRMS (ESI) calcd. for $[\text{C}_{14}\text{H}_{17}\text{FO}_2+\text{H}]^+$: 237.1285; Found: 237.1285.



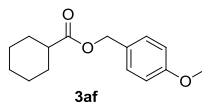
4-Chlorobenzyl cyclohexanecarboxylate (3ac): colorless liquid was obtained with 70% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.34-7.31 (m, 2H), 7.29-7.26 (m, 2H), 5.06 (s, 2H), 2.34 (tt, J = 11.2, 3.6 Hz, 1H), 1.94-1.90 (m, 2H), 1.77-1.72 (m, 2H), 1.66-1.61 (m, 1H), 1.50-1.40 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 134.8, 133.9, 129.3, 128.7, 65.0, 43.1, 29.0, 25.7, 25.4. HRMS (ESI) calcd. for $[\text{C}_{14}\text{H}_{17}\text{ClO}_2+\text{H}]^+$: 253.0990; Found: 253.0992.



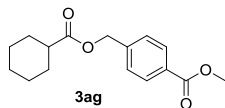
4-Bromobenzyl cyclohexanecarboxylate (3ad): colorless liquid was obtained with 66% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.50-7.46 (m, 2H), 7.23-7.20 (m, 2H), 5.05 (s, 2H), 2.34 (tt, J = 11.4, 3.6 Hz, 1H), 1.94-1.90 (m, 2H), 1.77-1.72 (m, 2H), 1.66-1.61 (m, 1H), 1.50-1.40 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 135.3, 131.6, 129.6, 122.0, 65.0, 43.1, 28.9, 25.7, 25.4. HRMS (EI) calcd for $\text{C}_{14}\text{H}_{17}\text{BrO}_2$ $[\text{M}]^+$: 296.0412; Found: 296.0417.



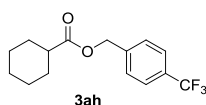
4-Iodobenzyl cyclohexanecarboxylate (3ae): colorless liquid was obtained with 31% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.68 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 5.04 (s, 2H), 2.34 (tt, J = 11.2, 3.6 Hz, 1H), 1.93-1.90 (m, 2H), 1.77-1.73 (m, 2H), 1.66-1.61 (m, 1H), 1.49-1.40 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 137.6, 135.9, 129.8, 93.7, 65.1, 43.1, 28.9, 25.7, 25.4. HRMS (ESI) calcd. for $[\text{C}_{14}\text{H}_{17}\text{IO}_2+\text{H}]^+$: 345.0346; Found: 345.0349.



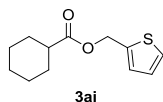
4-Methoxybenzyl cyclohexanecarboxylate (3af): colorless liquid was obtained with 40% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.28 (d, $J = 8.4$ Hz, 2H), 6.88 (d, $J = 8.8$ Hz, 2H), 5.04 (s, 2H), 3.80 (s, 3H), 2.32 (tt, $J = 11.2$, 3.6 Hz, 1H), 1.92-1.89 (m, 2H), 1.76-1.72 (m, 2H), 1.64-1.60 (m, 1H), 1.49-1.39 (m, 2H), 1.31-1.15 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.0, 159.4, 129.8, 128.4, 113.8, 65.7, 55.2, 43.2, 29.0, 25.7, 25.4. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$ $[\text{M}]^+$: 248.1412; Found: 248.1407.



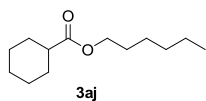
Methyl 4-(cyclohexanecarbonyloxymethyl)benzoate (3ag): colorless liquid was obtained with 63% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 8.03 (d, $J = 8.4$ Hz, 2H), 7.40 (d, $J = 8.4$ Hz, 2H), 5.16 (s, 2H), 3.92 (s, 3H), 2.38 (tt, $J = 11.4$, 3.6 Hz, 1H), 1.96-1.92 (m, 2H), 1.78-1.74 (m, 2H), 1.67-1.63 (m, 1H), 1.52-1.42 (m, 2H), 1.34-1.17 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 166.7, 141.4, 129.8, 129.7, 127.4, 65.1, 52.1, 43.1, 28.9, 25.7, 25.4. HRMS (ESI) calcd. for $[\text{C}_{16}\text{H}_{20}\text{O}_4+\text{H}]^+$: 277.1434; Found: 277.1432.



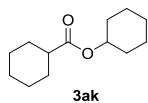
4-(Trifluoromethyl)benzyl cyclohexanecarboxylate (3ah): colorless liquid was obtained with 79% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, $J = 8.0$ Hz, 2H), 7.46 (d, $J = 8.0$ Hz, 2H), 5.16 (s, 2H), 2.38 (tt, $J = 11.2$, 3.6 Hz, 1H), 1.96-1.92 (m, 2H), 1.79-1.75 (m, 2H), 1.67-1.63 (m, 1H), 1.52-1.42 (m, 2H), 1.34-1.17 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 140.3, 130.2 (q, $J_{\text{C-F}} = 32.3$ Hz), 127.9, 125.5 (q, $J_{\text{C-F}} = 4.0$ Hz), 124.0 (q, $J_{\text{C-F}} = 273.0$ Hz), 64.9, 43.1, 29.0, 25.7, 25.4. ^{19}F NMR (377 MHz, CDCl_3) δ -62.6. HRMS (ESI) calcd. for $[\text{C}_{15}\text{H}_{17}\text{F}_3\text{O}_2+\text{H}]^+$: 287.1253; Found: 287.1255.



Thiophen-2-ylmethyl cyclohexanecarboxylate (3ai): colorless liquid was obtained with 66% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.31 (dd, $J = 4.8$, 0.8 Hz, 1H), 7.07 (d, $J = 3.2$ Hz, 1H), 6.98 (dd, $J = 4.8$, 3.2 Hz, 1H), 5.26 (s, 2H), 2.32 (tt, $J = 11.2$, 3.6 Hz, 1H), 1.92-1.89 (m, 2H), 1.76-1.72 (m, 2H), 1.65-1.62 (m, 1H), 1.49-1.39 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 138.3, 127.7, 126.7, 126.6, 60.3, 43.0, 28.9, 25.7, 25.4. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{20}\text{NO}_2\text{S}$ $[\text{M}+[\text{NH}_4]]^+$: 242.1209; Found: 242.1209.

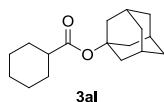


n-Hexyl cyclohexanecarboxylate (3aj): colorless liquid was obtained with 76% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 4.05 (t, $J = 6.8$ Hz, 2H), 2.28 (tt, $J = 11.4$, 3.6 Hz, 1H), 1.92-1.88 (m, 2H), 1.77-1.72 (m, 2H), 1.66-1.58 (m, 3H), 1.49-1.39 (m, 2H), 1.37-1.17 (m, 9H), 0.89 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.2, 64.2, 43.2, 31.4, 29.0, 28.6, 25.7, 25.5, 25.4, 22.5, 13.9. HRMS (ESI) calcd. for $[\text{C}_{13}\text{H}_{24}\text{O}_2+\text{H}]^+$: 213.1849; Found: 213.1852.

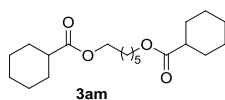


Cyclohexyl cyclohexanecarboxylate (3ak): colorless liquid was obtained with 79% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 4.78-4.72 (m, 1H), 2.26 (tt, $J = 11.2$, 3.6 Hz, 1H), 1.92-1.87 (m, 2H), 1.83-1.60 (m, 7H), 1.56-1.17 (m, 11H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.5, 71.7, 43.3, 31.5, 29.0, 25.7, 25.37, 25.36, 23.5. HRMS (ESI)

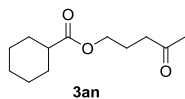
calcd. for $[C_{13}H_{22}O_2+H]^+$: 211.1693; Found: 211.1700.



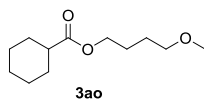
1-Adamantyl cyclohexanecarboxylate (3al): colorless liquid was obtained with 80% isolated yield. 1H NMR (400 MHz, $CDCl_3$) δ 2.21-2.08 (m, 10H), 1.87-1.84 (m, 2H), 1.75-1.59 (m, 9H), 1.43-1.34 (m, 2H), 1.31-1.15 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 79.6, 44.1, 41.3, 36.2, 30.7, 29.1, 25.8, 25.4. HRMS (ESI) calcd. for $[C_{17}H_{26}O_2+H]^+$: 263.2006; Found: 263.1996.



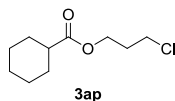
Hexane-1,6-diyl dicyclohexanecarboxylate (3am): colorless liquid was obtained with 79% isolated yield. 1H NMR (400 MHz, $CDCl_3$) δ 4.05 (t, J = 6.6 Hz, 4H), 2.28 (tt, J = 11.4, 3.6 Hz, 2H), 1.91-1.88 (m, 4H), 1.77-1.73 (m, 4H), 1.65-1.61 (m, 6H), 1.48-1.36 (m, 8H), 1.33-1.16 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 64.0, 43.2, 29.0, 28.5, 25.7, 25.6, 25.4. HRMS (ESI) calcd. for $[C_{20}H_{34}O_4+H]^+$: 339.2530; Found: 339.2533.



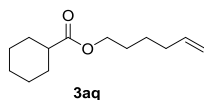
4-Oxopentyl cyclohexanecarboxylate (3an): colorless liquid was obtained with 52% isolated yield. 1H NMR (400 MHz, $CDCl_3$) δ 4.07 (t, J = 6.4 Hz, 2H), 2.52 (t, J = 7.4 Hz, 2H), 2.28 (tt, J = 11.2, 3.6 Hz, 1H), 2.17 (s, 3H), 1.94-1.88 (m, 4H), 1.77-1.73 (m, 2H), 1.66-1.64 (m, 1H), 1.47-1.38 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.8, 176.1, 63.2, 43.2, 39.9, 30.0, 29.0, 25.7, 25.4, 22.8. HRMS (ESI) calcd. for $[C_{12}H_{20}O_3+H]^+$: 213.1485; Found: 213.1486.



4-Methoxybutyl cyclohexanecarboxylate (3ao): colorless liquid was obtained with 79% isolated yield. 1H NMR (400 MHz, $CDCl_3$) δ 4.08 (t, J = 6.2 Hz, 2H), 3.40 (t, J = 6.2 Hz, 2H), 3.34 (s, 3H), 2.29 (tt, J = 11.4, 3.6 Hz, 1H), 1.92-1.88 (m, 2H), 1.77-1.60 (m, 7H), 1.48-1.38 (m, 2H), 1.33-1.16 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 72.2, 63.9, 58.6, 43.2, 29.0, 26.1, 25.7, 25.4. HRMS (ESI) calcd. for $[C_{12}H_{22}O_3+H]^+$: 215.1642; Found: 215.1637.

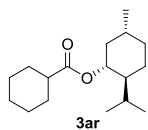


3-Chloropropyl cyclohexanecarboxylate (3ap): colorless liquid was obtained with 73% isolated yield. 1H NMR (400 MHz, $CDCl_3$) δ 4.21 (t, J = 6.2 Hz, 2H), 3.62 (t, J = 6.6 Hz, 2H), 2.30 (tt, J = 11.2, 3.6 Hz, 1H), 2.13-2.06 (m, 2H), 1.92-1.88 (m, 2H), 1.77-1.73 (m, 2H), 1.66-1.62 (m, 1H), 1.49-1.39 (m, 2H), 1.34-1.17 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 60.7, 43.0, 41.1, 31.5, 28.9, 25.6, 25.3. HRMS (EI) calcd for $C_{10}H_{17}ClO_2$ $[M]^+$: 204.0917; Found: 204.0916.

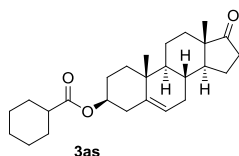


Hex-5-enyl cyclohexanecarboxylate (3aq): colorless liquid was obtained with 50% isolated yield. 1H NMR (400 MHz, $CDCl_3$) δ 5.85-5.75 (m, 1H), 5.04-4.95 (m, 2H), 4.06 (t, J = 6.6 Hz, 2H), 2.29 (tt, J = 11.2, 3.6 Hz, 1H), 2.11-2.06 (m, 2H), 1.92-1.88 (m, 2H), 1.77-1.72 (m, 2H), 1.69-1.60 (m, 3H), 1.49-1.39 (m, 4H), 1.33-1.16 (m, 3H).

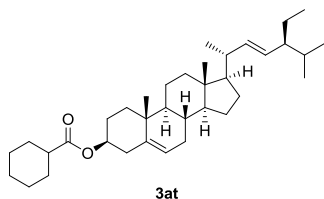
^{13}C NMR (101 MHz, CDCl_3) δ 176.2, 138.4, 114.7, 64.0, 43.2, 33.3, 29.0, 28.1, 25.7, 25.4, 25.2. HRMS (ESI) calcd. for $[\text{C}_{13}\text{H}_{22}\text{O}_2+\text{H}]^+$: 211.1693; Found: 211.1694.



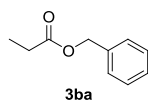
(1S, 2R, 5S)-2-Isopropyl-5-methylcyclohexyl cyclohexanecarboxylate (3ar): colorless liquid was obtained with 68% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 4.65 (td, $J = 10.8, 4.4$ Hz, 1H), 2.26 (tt, $J = 11.2, 3.6$ Hz, 1H), 1.99-1.84 (m, 4H), 1.77-1.61 (m, 5H), 1.55-1.17 (m, 7H), 1.10-1.00 (m, 1H), 0.98-0.81 (m, 8H), 0.75 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.6, 73.5, 47.0, 43.5, 40.9, 34.3, 31.3, 29.1, 28.9, 26.1, 25.8, 25.5, 25.4, 23.3, 22.0, 20.8, 16.1. HRMS (EI) calcd for $\text{C}_{17}\text{H}_{30}\text{O}_2$ $[\text{M}]^+$: 266.2246; Found: 266.2239.



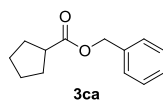
(3S, 8R, 9S, 10R, 13S, 14S)-10, 13-Dimethyl-17-oxo-2, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17-tetradecahydro-1H-cyclopenta [a] phenanthren-3-yl cyclohexanecarboxylate (3as): white solid was obtained with 53% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 5.41-5.40 (m, 1H), 4.64-4.56 (m, 1H), 2.50-2.43 (m, 1H), 2.37-2.22 (m, 3H), 2.16-2.05 (m, 2H), 1.99-1.83 (m, 6H), 1.77-1.38 (m, 11H), 1.34-1.11 (m, 6H), 1.07-1.00 (m, 4H), 0.89 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 221.1, 175.5, 139.9, 121.7, 73.1, 51.6, 50.0, 47.5, 43.3, 38.0, 36.9, 36.7, 35.8, 31.4, 31.3, 30.7, 29.0, 27.6, 25.7, 25.4, 21.8, 20.3, 19.3, 13.5. HRMS (EI) calcd for $\text{C}_{26}\text{H}_{38}\text{O}_3$ $[\text{M}]^+$: 398.2821; Found: 398.2819.



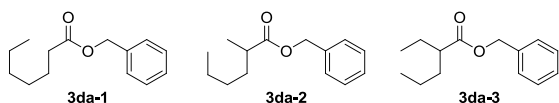
(3S, 8S, 9S, 10R, 13R, 14S, 17R)-17-((2R, 5S, E)-5-ethyl-6-methylhept-3-en-2-yl)-10, 13-dimethyl-2, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl cyclohexanecarboxylate (3at): white solid was obtained with 62% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 5.37-5.36 (m, 1H), 5.15 (dd, $J = 15.2, 8.8$ Hz, 1H), 5.01 (dd, $J = 15.2, 8.8$ Hz, 1H), 4.64-4.56 (m, 1H), 2.34-2.21 (m, 3H), 2.08-1.81 (m, 7H), 1.76-1.61 (m, 4H), 1.59-1.37 (m, 11H), 1.32-0.92 (m, 17H), 0.85-0.79 (m, 9H), 0.69 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 175.6, 139.7, 138.3, 129.2, 122.5, 73.3, 56.7, 55.9, 51.2, 50.0, 43.4, 42.2, 40.5, 39.6, 38.1, 37.0, 36.6, 31.9, 31.8, 29.02, 29.00, 28.9, 27.7, 25.8, 25.43, 25.40, 24.3, 21.2, 21.1, 21.0, 19.3, 19.0, 12.3, 12.0. HRMS (ESI) calcd for $\text{C}_{36}\text{H}_{62}\text{NO}_2$ $[\text{M}+[\text{NH}_4]]^+$: 540.4775; Found: 540.4772.



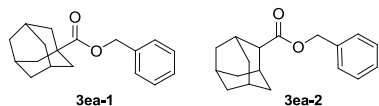
Benzyl propionate (3ba): colorless liquid was obtained with 30% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.37-7.27 (m, 5H), 5.10 (s, 2H), 2.36 (q, $J = 7.6$ Hz, 2H), 1.15 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 174.3, 136.1, 128.5, 128.1, 66.1, 27.6, 9.1. HRMS (EI) calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2$ $[\text{M}]^+$: 164.0837; Found: 164.0841.



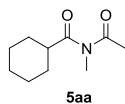
Benzyl cyclopentanecarboxylate (3ca): colorless liquid was obtained with 45% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.39-7.30 (m, 5H), 5.12 (s, 2H), 2.79 (qui, $J = 8.0$ Hz, 1H), 1.95-1.52 (m, 8H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.6, 136.3, 128.5, 128.04, 127.96, 66.0, 43.8, 30.0, 25.8. HRMS (EI) calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$ $[\text{M}]^+$: 204.1150; Found: 204.1149.



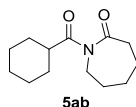
Benzyl heptanoate (3da-1), benzyl 2-methylhexanoate (3da-2), benzyl 2-ethylpentanoate (3da-3): colorless liquid was obtained with 50% total isolated yield. Inseparable mixture of regioisomers 3ga-1:3ga-2:3ga-3 (1:2:1). The ratio was determined by GC analysis. ^1H NMR (400 MHz, CDCl_3) δ 7.39-7.30 (m, 5.0H), 5.13-5.12 (m, 2.0H), 2.53-2.29 (m, 1.3H), 1.72-1.62 (m, 1.6H), 1.60-1.50 (m, 0.9H), 1.31-1.26 (m, 4.0H), 1.16 (d, $J = 7.2$ Hz, 1.5H), 0.90-0.85 (m, 3.7H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.8, 176.3, 136.2, 128.51, 128.48, 128.14, 128.07, 128.06, 128.0, 66.0, 65.93, 65.85, 47.1, 39.5, 34.3, 34.2, 33.5, 31.4, 29.3, 28.8, 25.5, 24.9, 22.6, 22.5, 20.6, 17.0, 14.01, 13.99, 13.9, 11.8. HRMS (EI) calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$ $[\text{M}]^+$: 220.1463; Found: 220.1470.



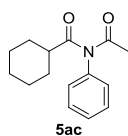
Benzyl 1-adamantanooate (3ea-1), benzyl 2-adamantanooate (3ea-2): colorless liquid was obtained with 77% total isolated yield. Inseparable mixture of regioisomers 3ea-1:3ea-2 (2:1). The ratio was determined by GC analysis. ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.31 (m, 5.0H), 5.15 (s, 0.66H), 5.10 (s, 1.34H), 2.66 (m, 0.33H), 2.37 (m, 0.67H), 2.02-1.68 (m, 14.0H). ^{13}C NMR (101 MHz, CDCl_3) δ 177.5, 174.4, 136.5, 136.4, 128.5, 128.4, 127.99, 127.97, 127.9, 127.6, 65.8, 65.7, 49.6, 40.7, 38.8, 38.1, 37.3, 36.5, 33.5, 29.5, 27.9, 27.42, 27.35. HRMS (EI) calcd for $\text{C}_{18}\text{H}_{22}\text{O}_2$ $[\text{M}]^+$: 270.1620; Found: 270.1626.



N-acetyl-N-methylcyclohexanecarboxamide (5aa): colorless liquid was obtained with 83% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 3.22 (s, 3H), 2.94 (tt, $J = 11.2, 3.2$ Hz, 1H), 2.41 (s, 3H), 1.87-1.80 (m, 4H), 1.72-1.69 (m, 1H), 1.51-1.42 (m, 2H), 1.37-1.18 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 179.6, 173.6, 44.7, 31.6, 29.3, 26.7, 25.7, 25.6. HRMS (ESI) calcd. for $[\text{C}_{10}\text{H}_{17}\text{NO}_2+\text{H}]^+$: 184.1332; Found: 184.1331.

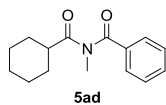


1-(Cyclohexanecarbonyl)azepan-2-one (5ab): colorless liquid was obtained with 86% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 3.86-3.84 (m, 2H), 3.36 (tt, $J = 11.2, 3.2$ Hz, 1H), 2.74-2.71 (m, 2H), 1.89-1.86 (m, 2H), 1.81-1.72 (m, 6H), 1.71-1.63 (m, 3H), 1.46-1.16 (m, 5H). ^{13}C NMR (101 MHz, CDCl_3) δ 180.0, 177.7, 45.3, 43.5, 40.0, 29.7, 29.2, 28.7, 25.9, 25.7, 23.7. HRMS (ESI) calcd. for $[\text{C}_{13}\text{H}_{21}\text{NO}_2+\text{H}]^+$: 224.1645; Found: 224.1646.

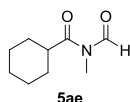


N-acetyl-N-phenylcyclohexanecarboxamide (5ac): colorless liquid was obtained with 76% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 7.49-7.40 (m, 3H), 7.14-7.12 (m, 2H), 2.68 (tt, $J = 11.4, 3.2$ Hz, 1H), 2.32 (s, 3H), 1.85-1.82 (m, 2H), 1.74-1.70 (m, 2H), 1.63-1.60 (m, 1H), 1.52-1.42 (m, 2H), 1.25-1.05 (m, 3H). ^{13}C NMR (101

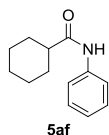
MHz, CDCl₃) δ 179.5, 173.3, 139.2, 129.7, 128.7, 128.6, 44.9, 29.3, 26.9, 25.6, 25.4. HRMS (ESI) calcd. for [C₁₅H₁₉NO₂+H]⁺: 246.1489; Found: 246.1488.



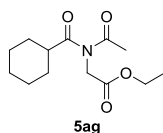
N-(cyclohexanecarbonyl)-N-methylbenzamide (5ad): colorless liquid was obtained with 81% isolated yield. ¹H NMR (400 MHz, CDCl₃) δ 7.64-7.61 (m, 2H), 7.58-7.54 (m, 1H), 7.49-7.46 (m, 2H), 3.21 (s, 3H), 2.78 (tt, *J* = 11.6, 3.2 Hz, 1H), 1.86-1.82 (m, 2H), 1.75-1.69 (m, 2H), 1.65-1.61 (m, 1H), 1.53-1.43 (m, 2H), 1.26-1.07 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 180.5, 174.3, 135.5, 132.3, 128.7, 128.4, 45.1, 34.4, 29.7, 25.7, 25.6. HRMS (ESI) calcd. for [C₁₅H₁₉NO₂+H]⁺: 246.1489; Found: 246.1480.



N-formyl-N-methylcyclohexanecarboxamide (5ae): colorless liquid was obtained with 69% isolated yield. ¹H NMR (400 MHz, CDCl₃) δ 9.28 (s, 1H), 3.11 (s, 3H), 2.71 (tt, *J* = 11.6, 2.8 Hz, 1H), 1.87-1.84 (m, 4H), 1.75-1.72 (m, 1H), 1.64-1.55 (m, 2H), 1.38-1.22 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 177.7, 162.5, 42.7, 29.3, 26.6, 25.53, 25.45. HRMS (ESI) calcd. for [C₉H₁₅NO₂+H]⁺: 170.1176; Found: 170.1174.



N-phenylcyclohexanecarboxamide (5af): white solid was obtained with 70% isolated yield. ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.23 (br, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 2.23 (tt, *J* = 11.8, 3.4 Hz, 1H), 1.97-1.94 (m, 2H), 1.86-1.82 (m, 2H), 1.72-1.69 (m, 1H), 1.59-1.50 (m, 2H), 1.36-1.19 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 174.4, 138.1, 129.0, 124.1, 119.7, 46.6, 29.7, 25.7. HRMS (ESI) calcd. for [C₁₃H₁₇NO+H]⁺: 204.1383; Found: 204.1375.

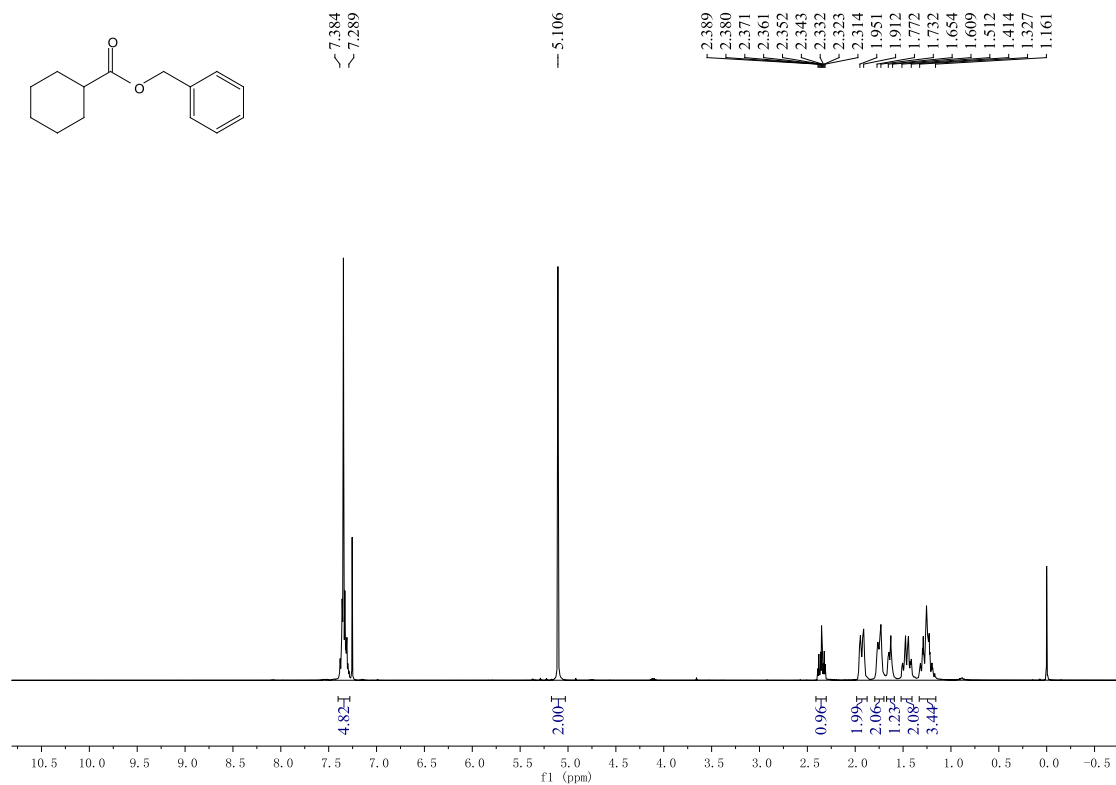


Ethyl 2-(N-acetylcyclohexanecarboxamido)acetate (5ag): colorless liquid was obtained with 44% isolated yield. ¹H NMR (400 MHz, CDCl₃) δ 4.42 (s, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 2.86 (tt, *J* = 11.4, 3.2 Hz, 1H), 2.40 (s, 3H), 1.89-1.85 (m, 2H), 1.83-1.79 (m, 2H), 1.71-1.68 (m, 1H), 1.52-1.43 (m, 2H), 1.31-1.25 (m, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 179.0, 172.9, 168.7, 61.7, 45.9, 44.8, 29.4, 26.2, 25.7, 25.6, 14.1. HRMS (ESI) calcd. for [C₁₃H₂₁NO₄+H]⁺: 256.1543; Found: 256.1534.

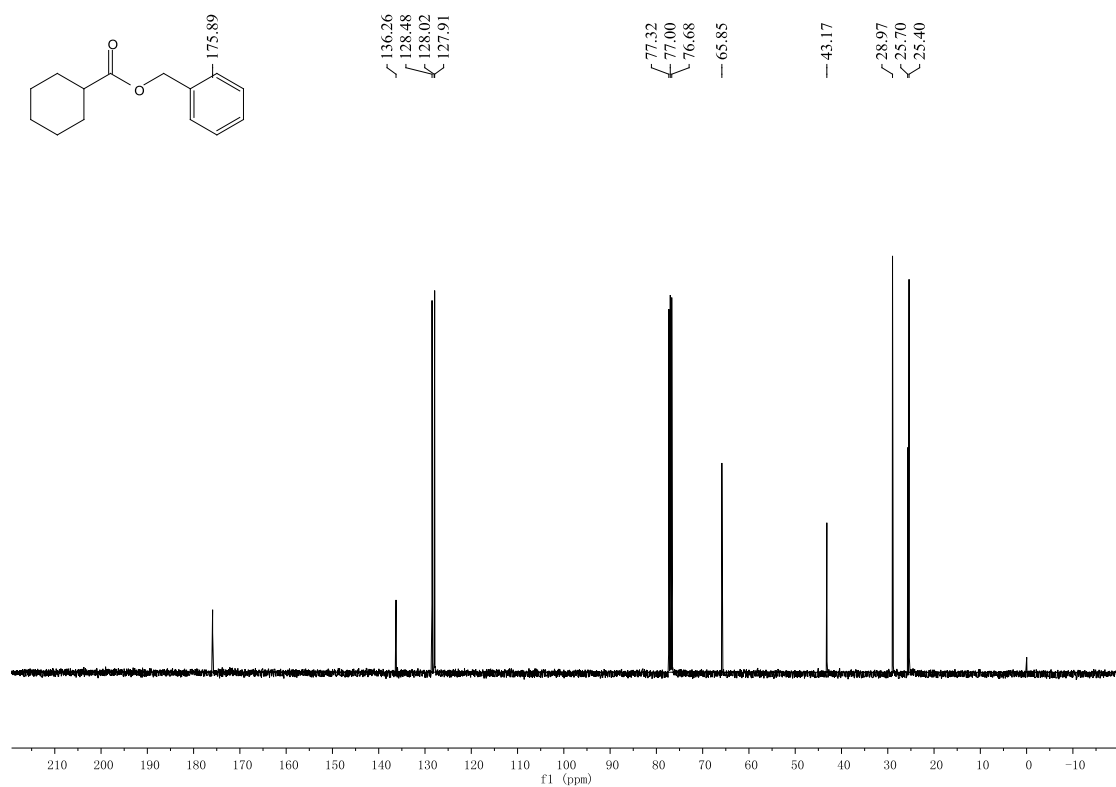
VI. NMR spectra of products

3aa

¹H NMR

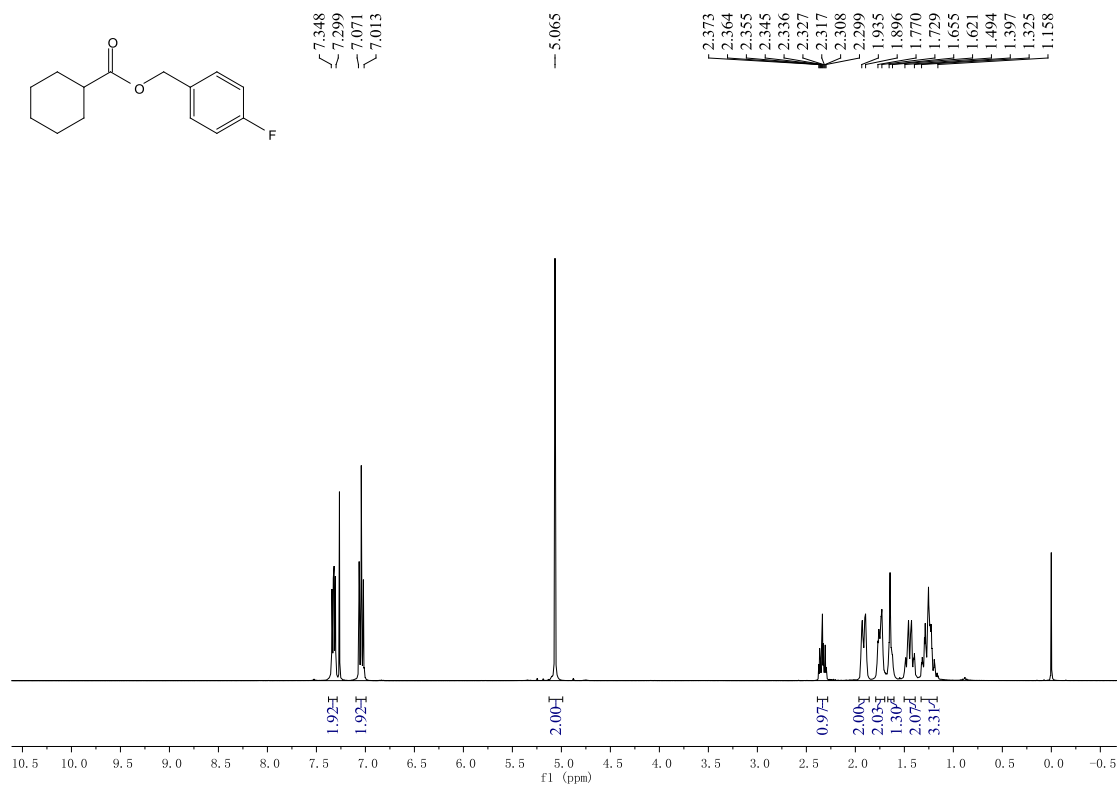


¹³C NMR

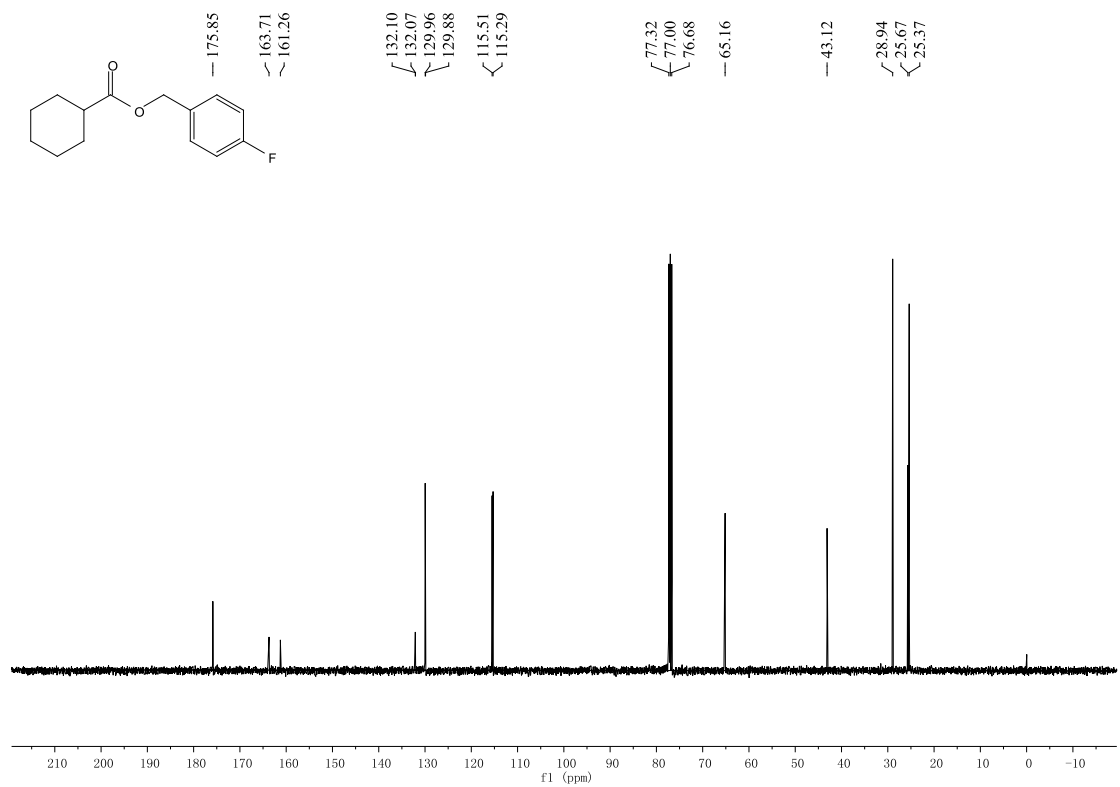


3ab

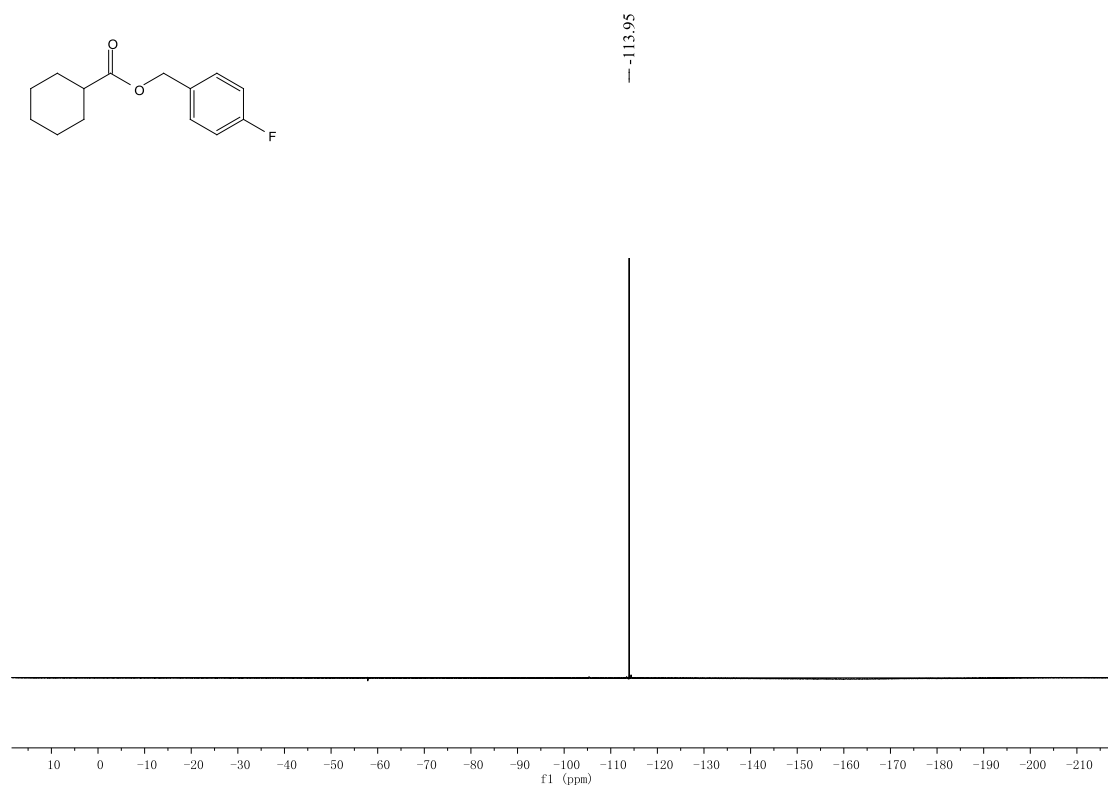
¹H NMR



¹³C NMR

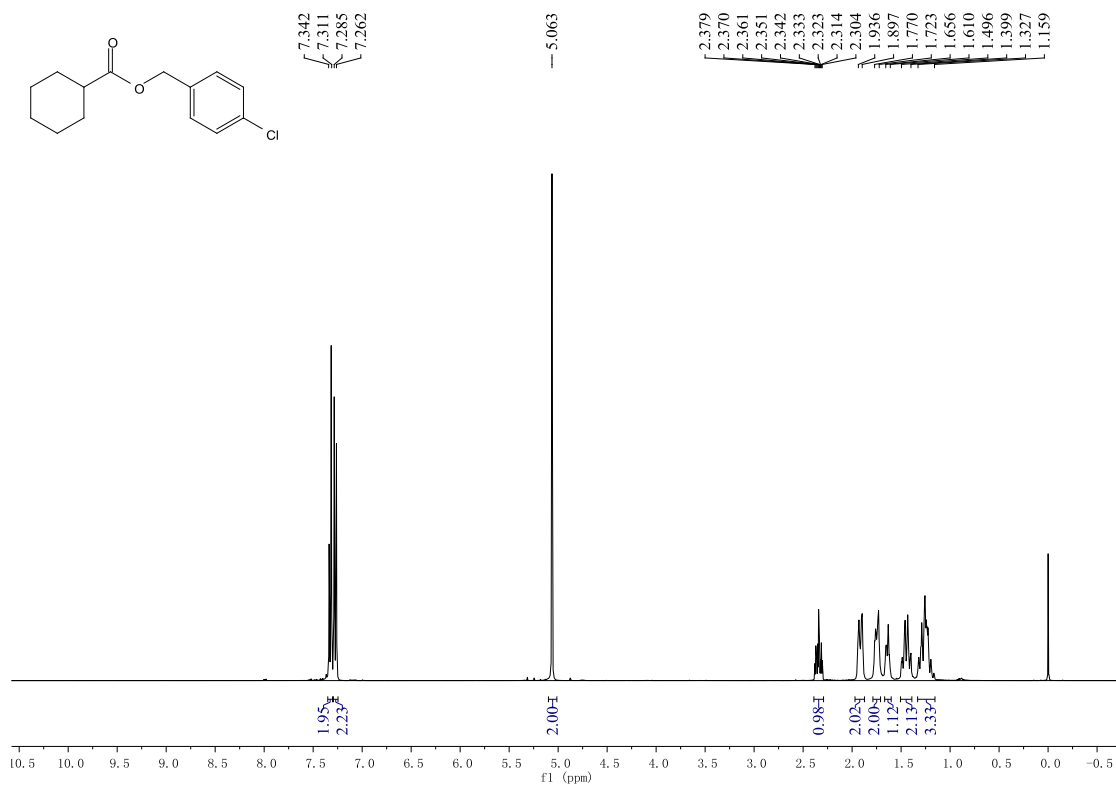


^{19}F NMR

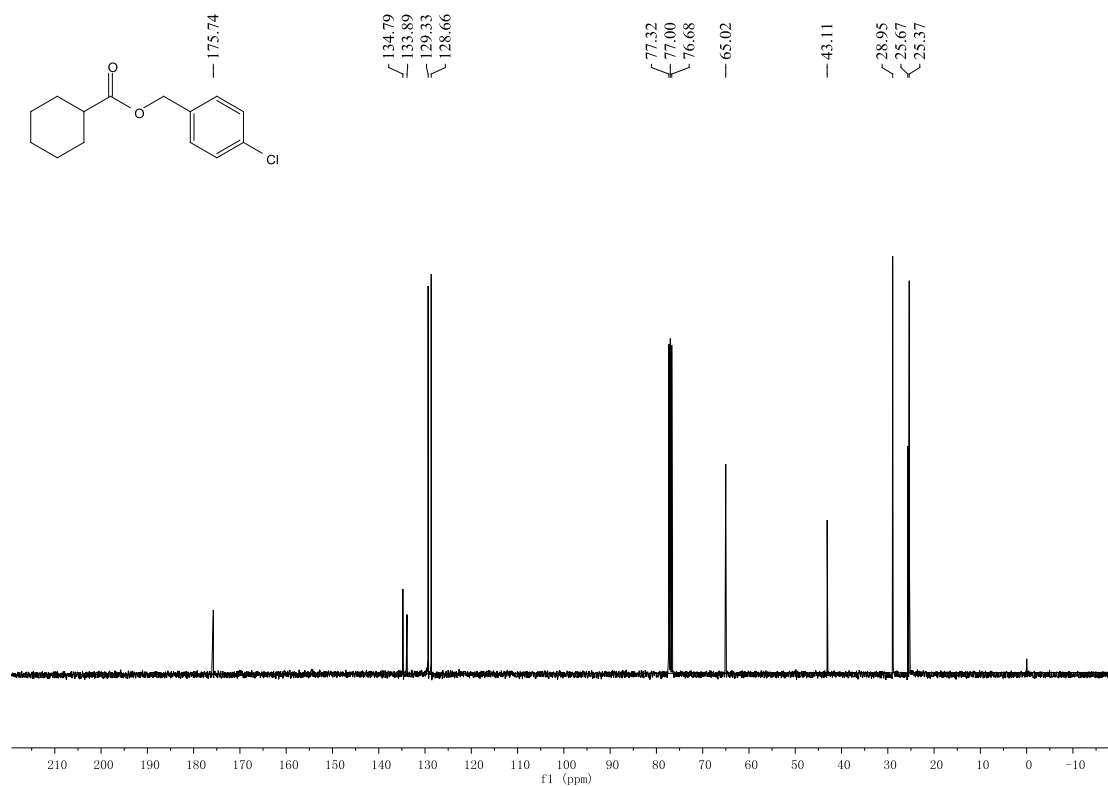


3ac

^1H NMR

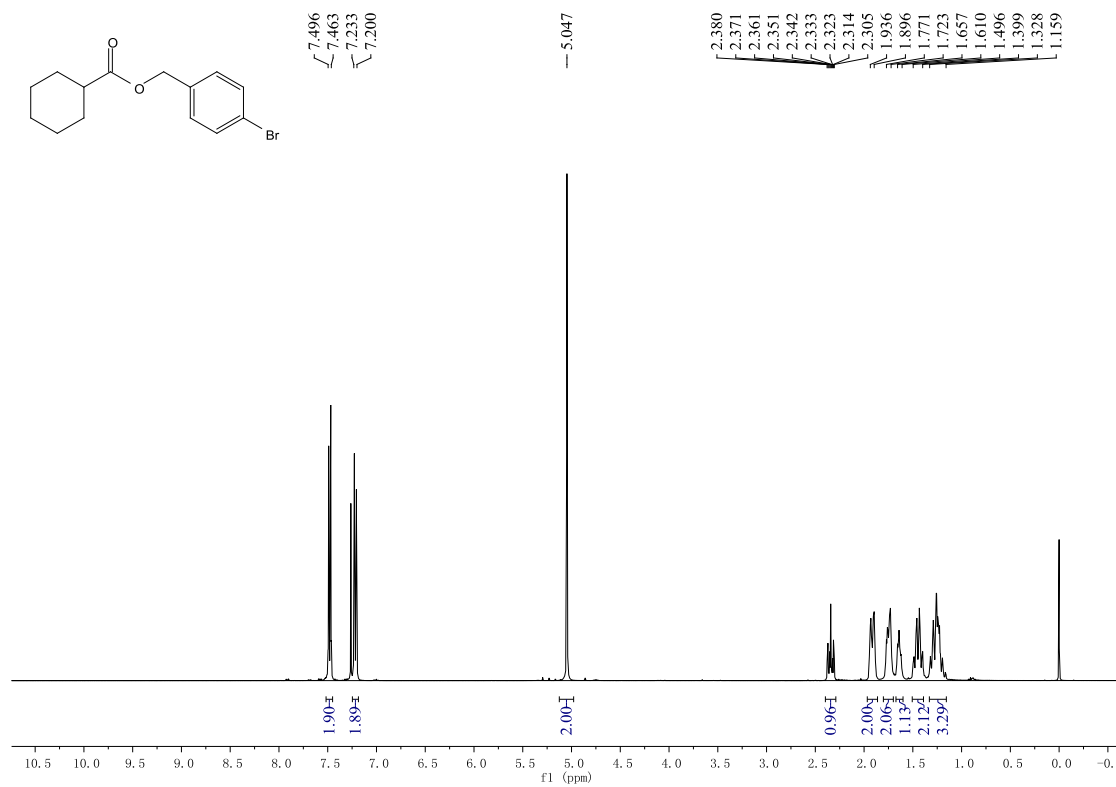


^{13}C NMR

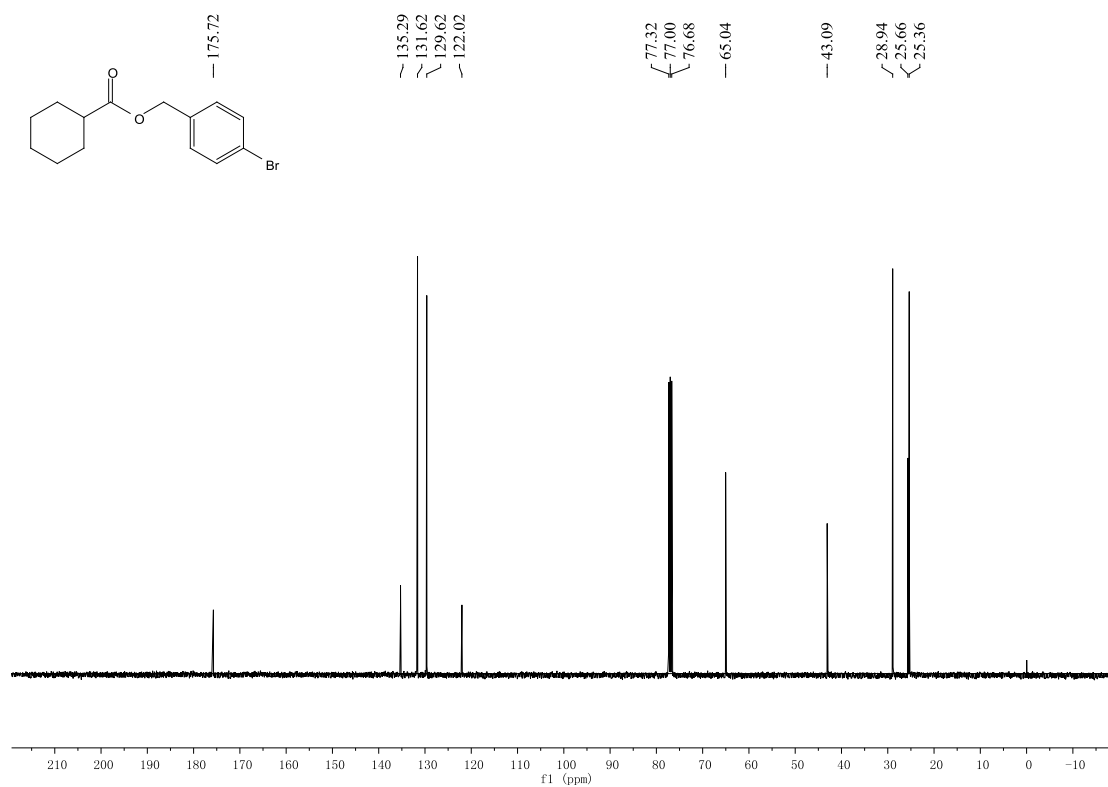


3ad

^1H NMR

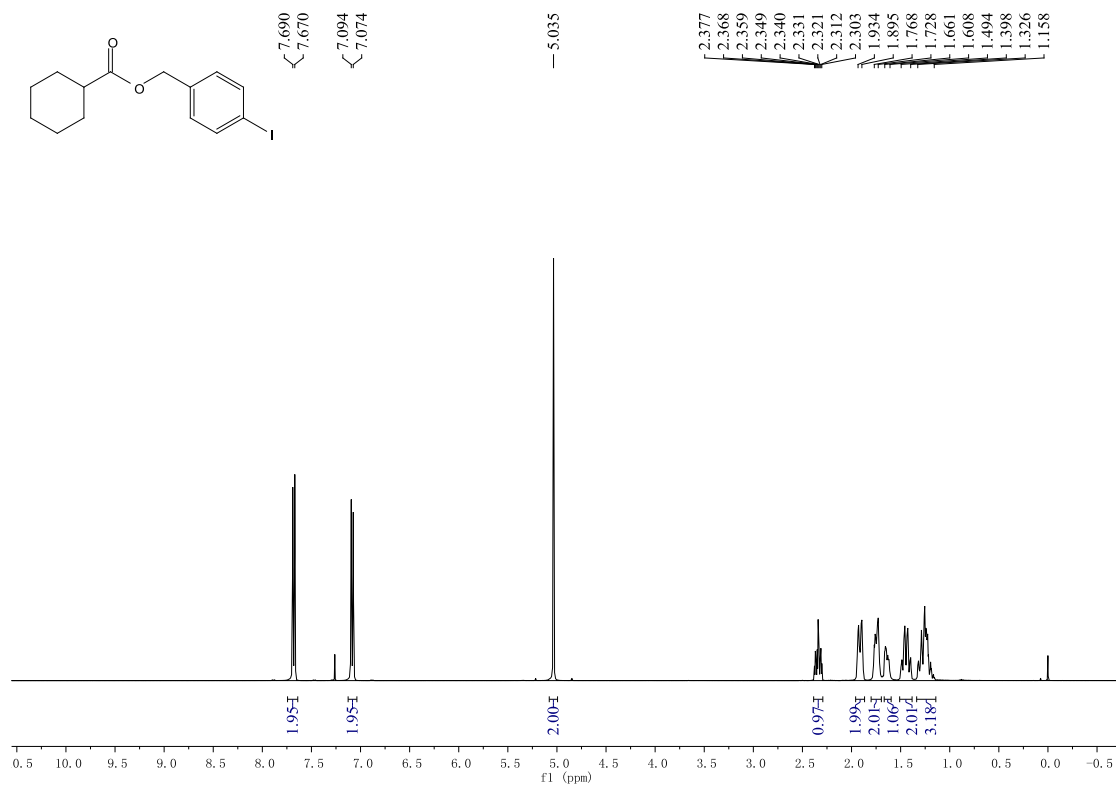


¹³C NMR

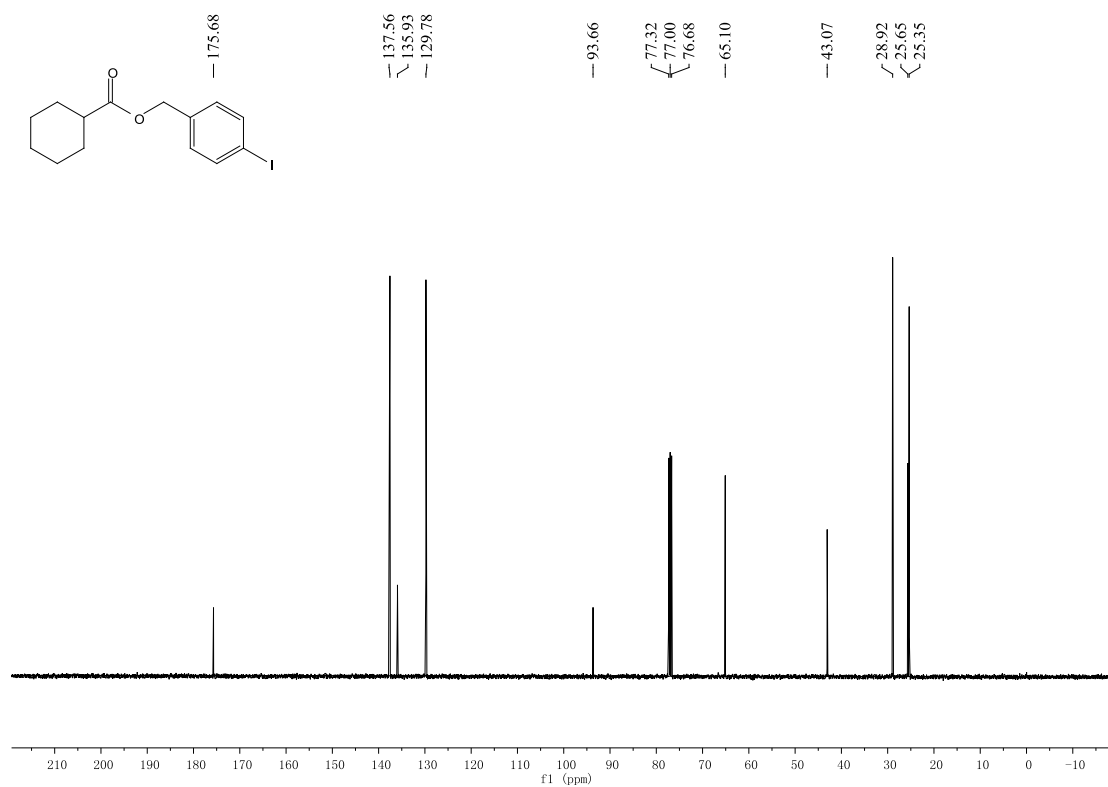


3ae

¹H NMR

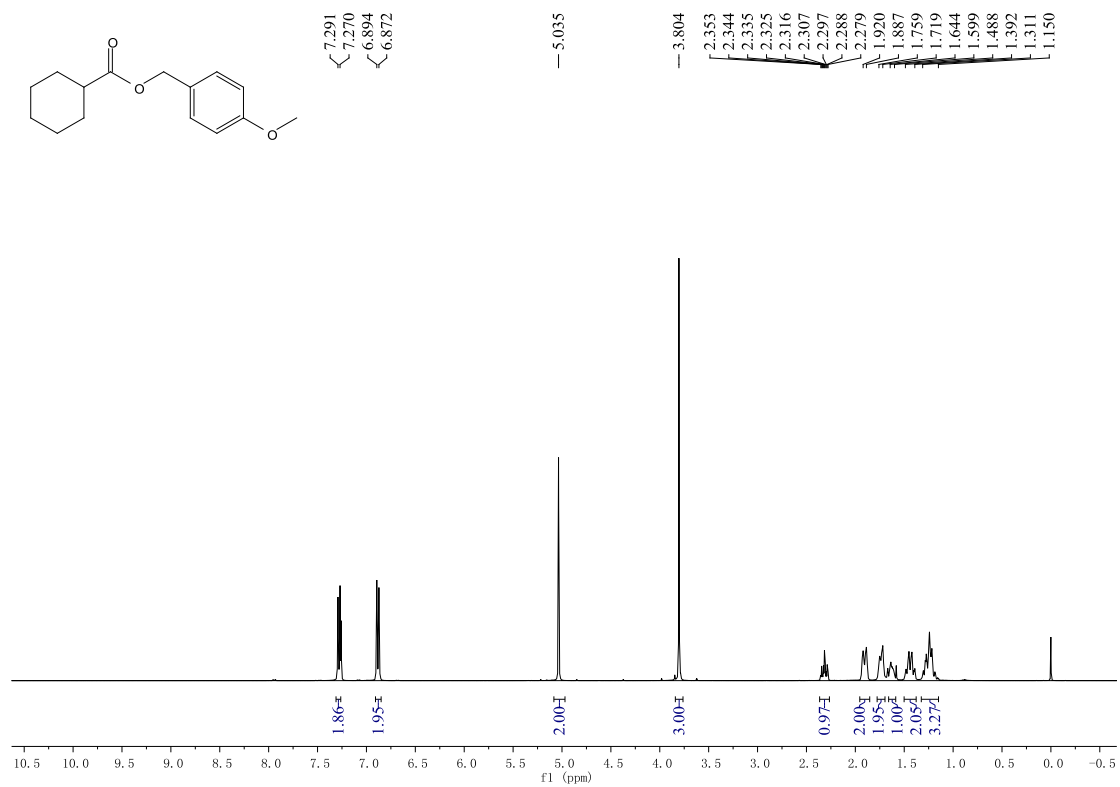


¹³C NMR

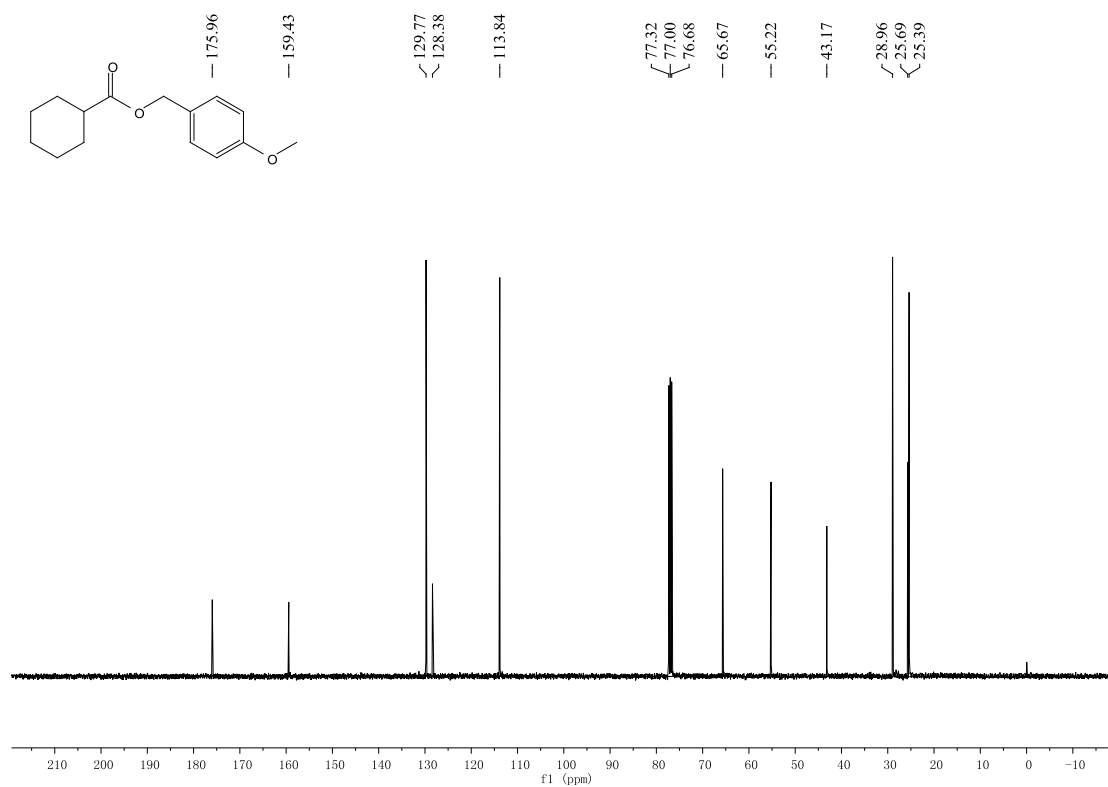


3af

¹H NMR

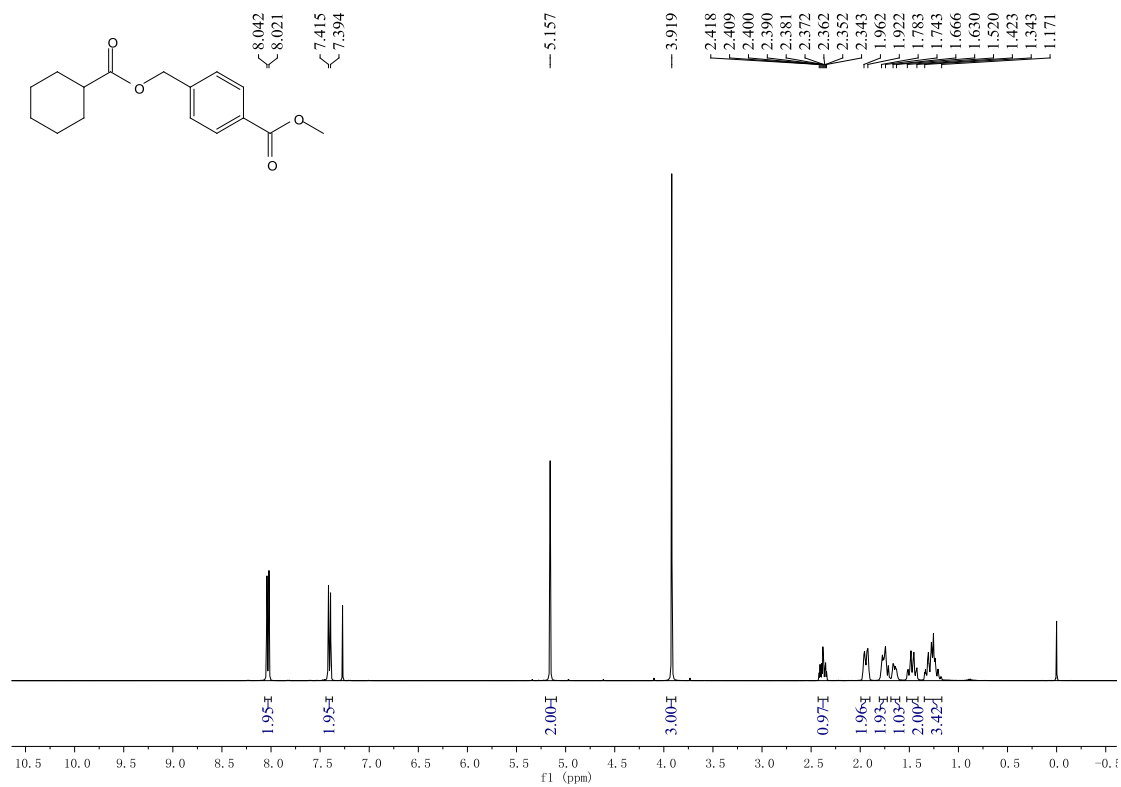


¹³C NMR

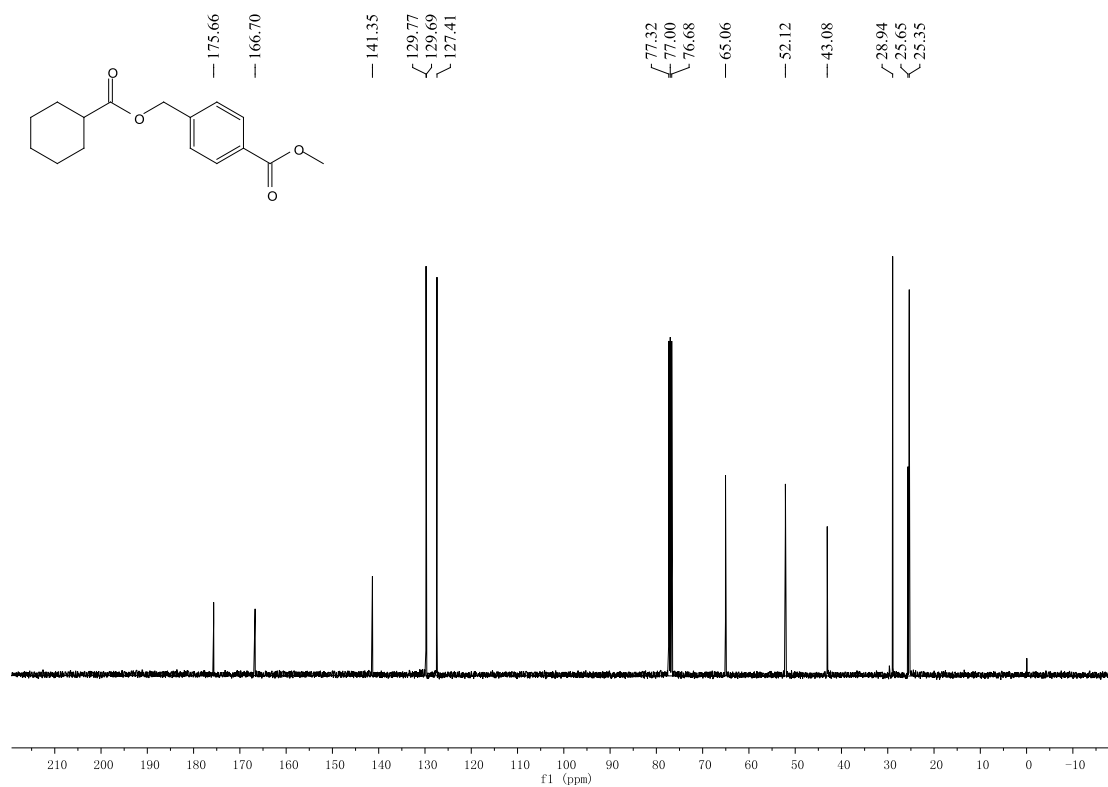


3ag

¹H NMR

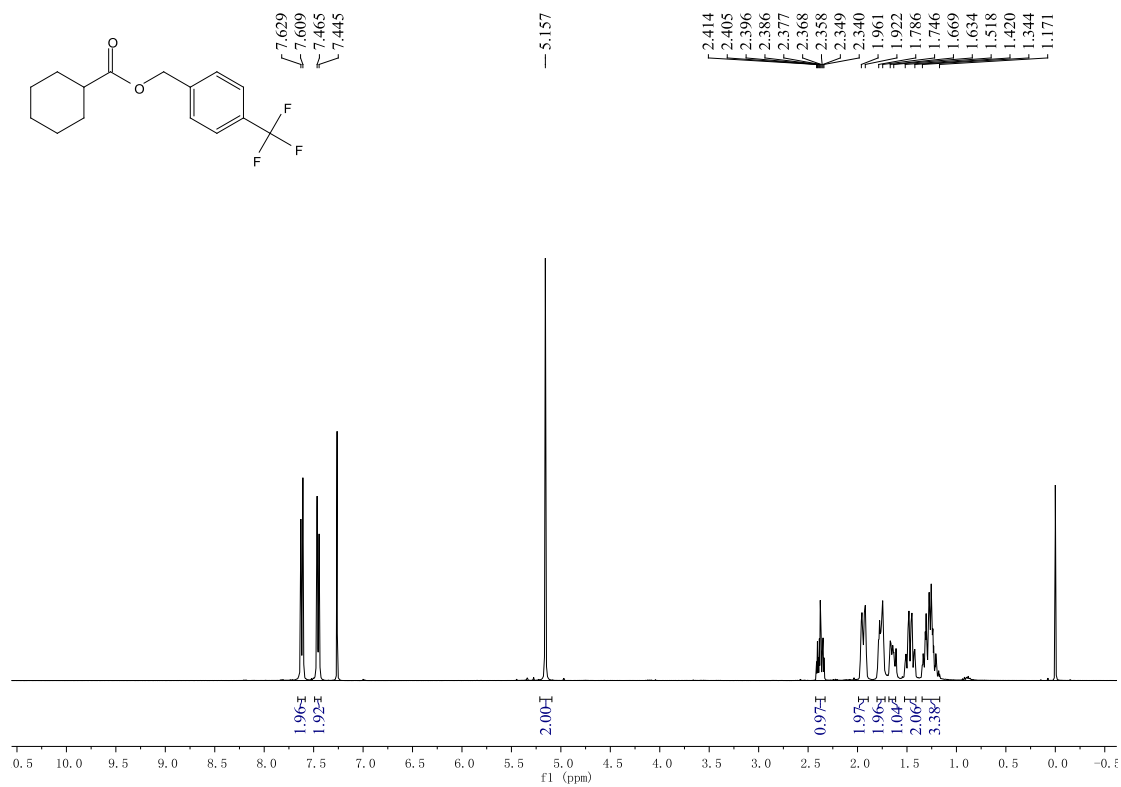


¹³C NMR

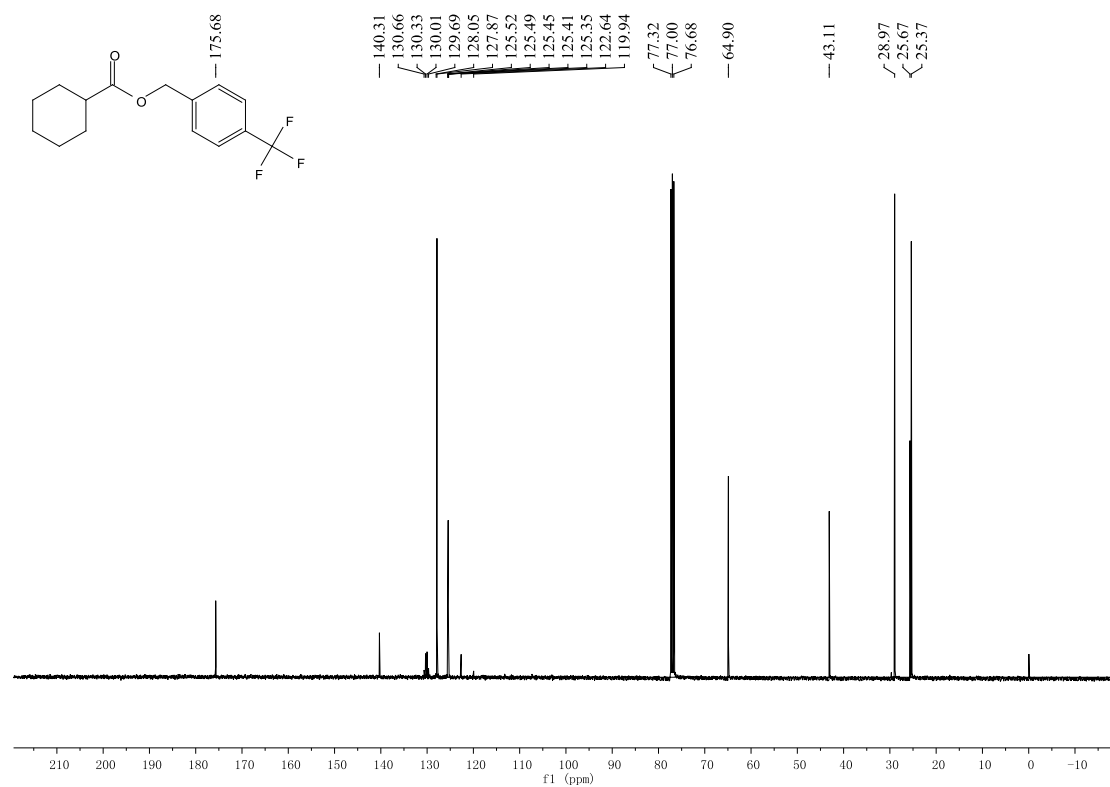


3ah

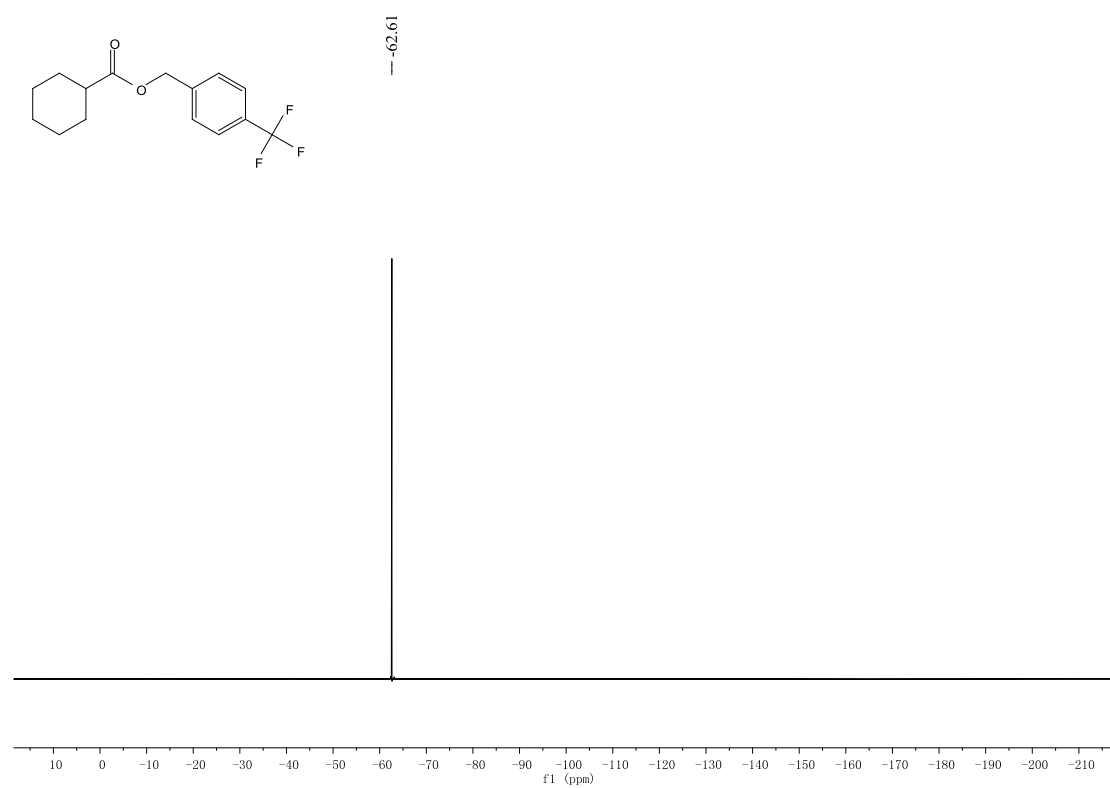
¹H NMR



¹³C NMR

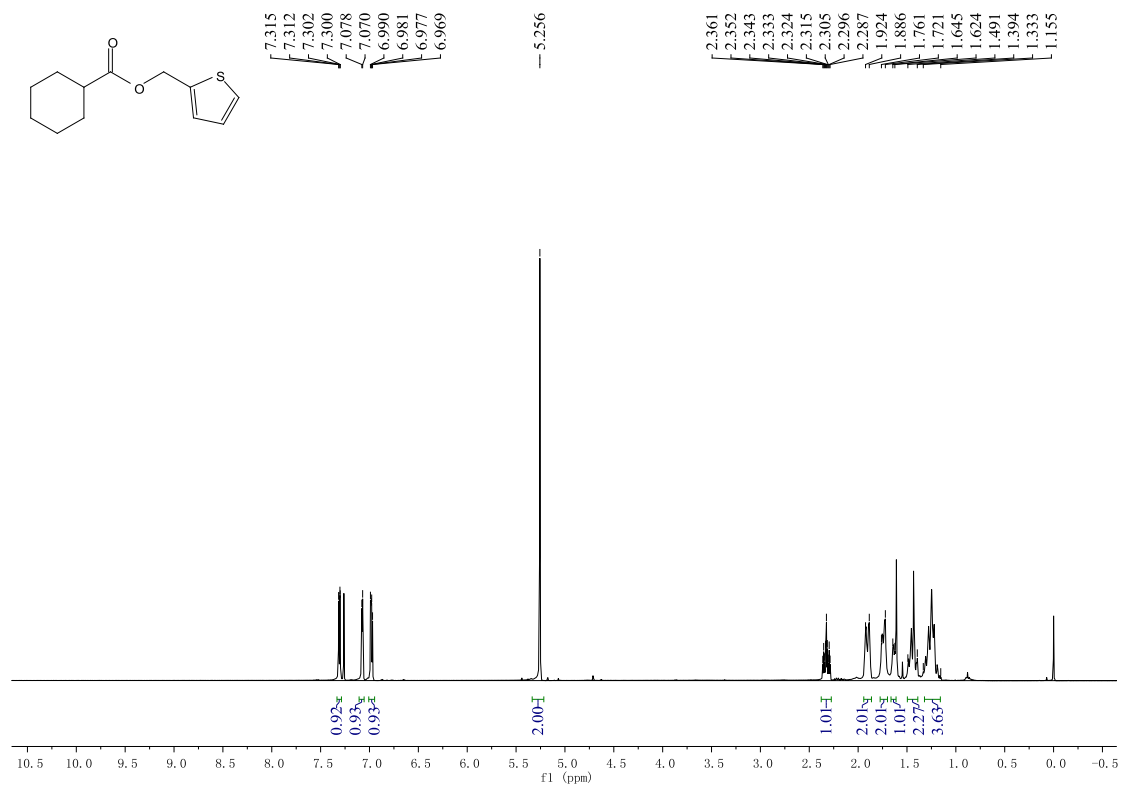


¹⁹F NMR

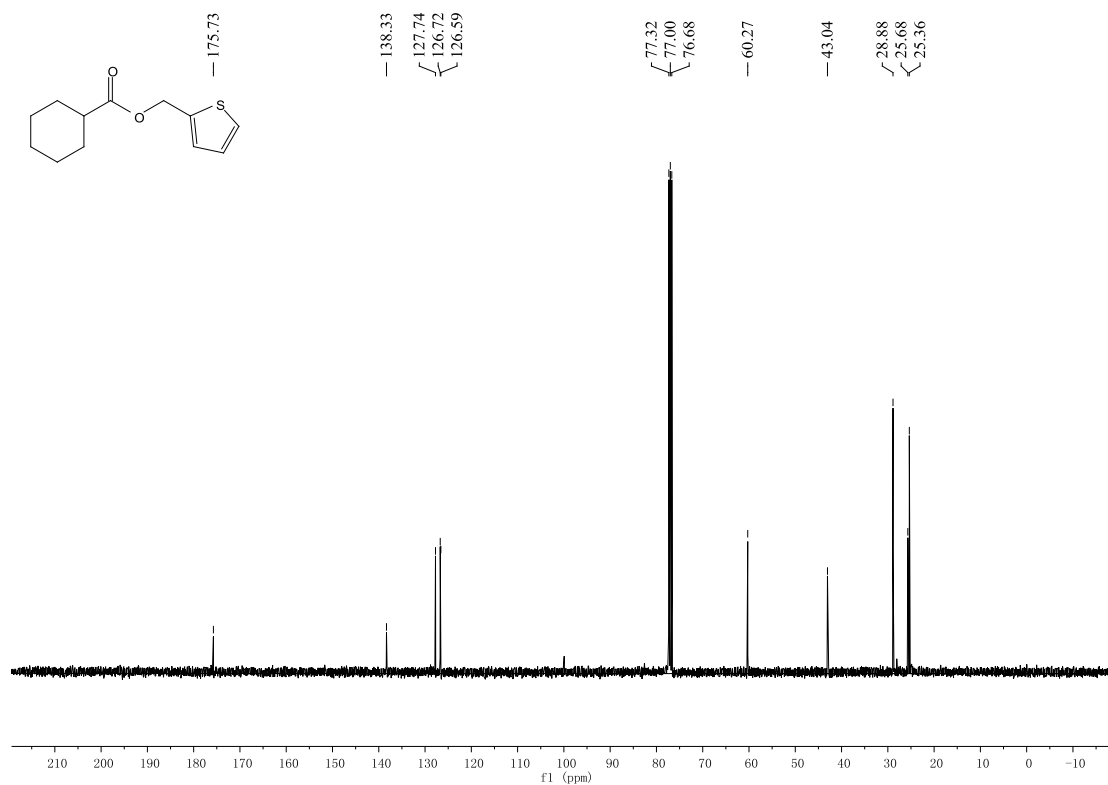


3ai

¹H NMR

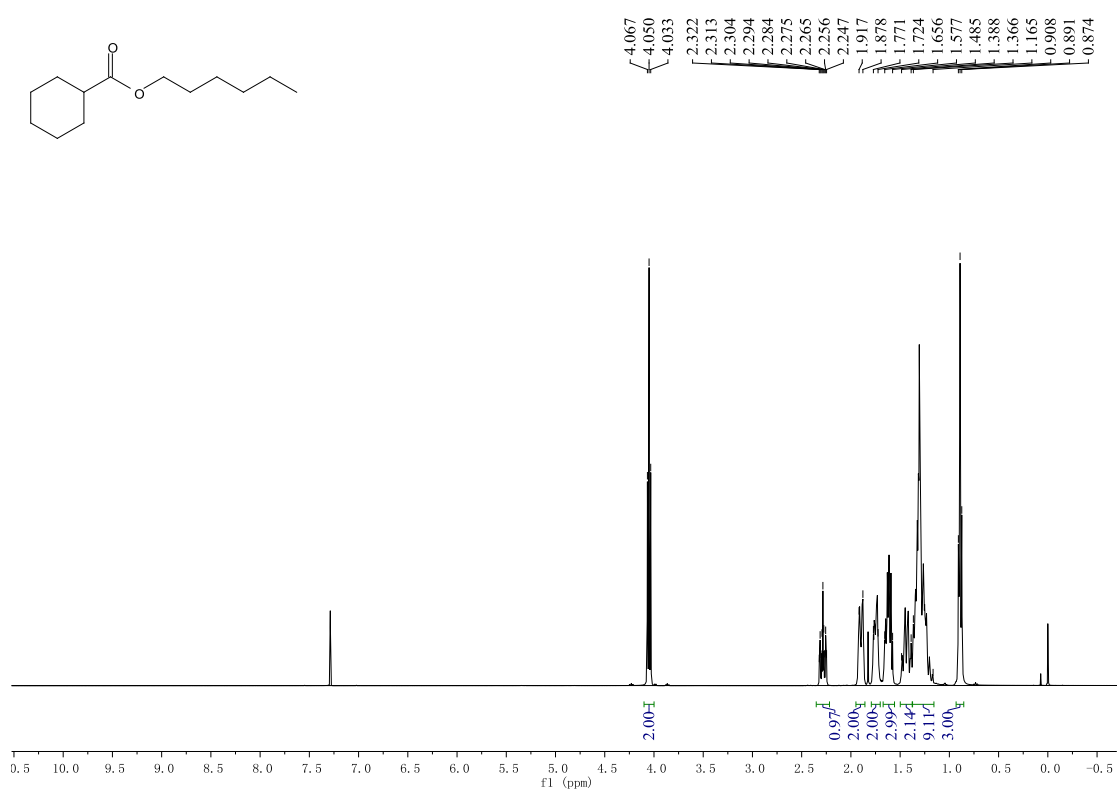


¹³C NMR

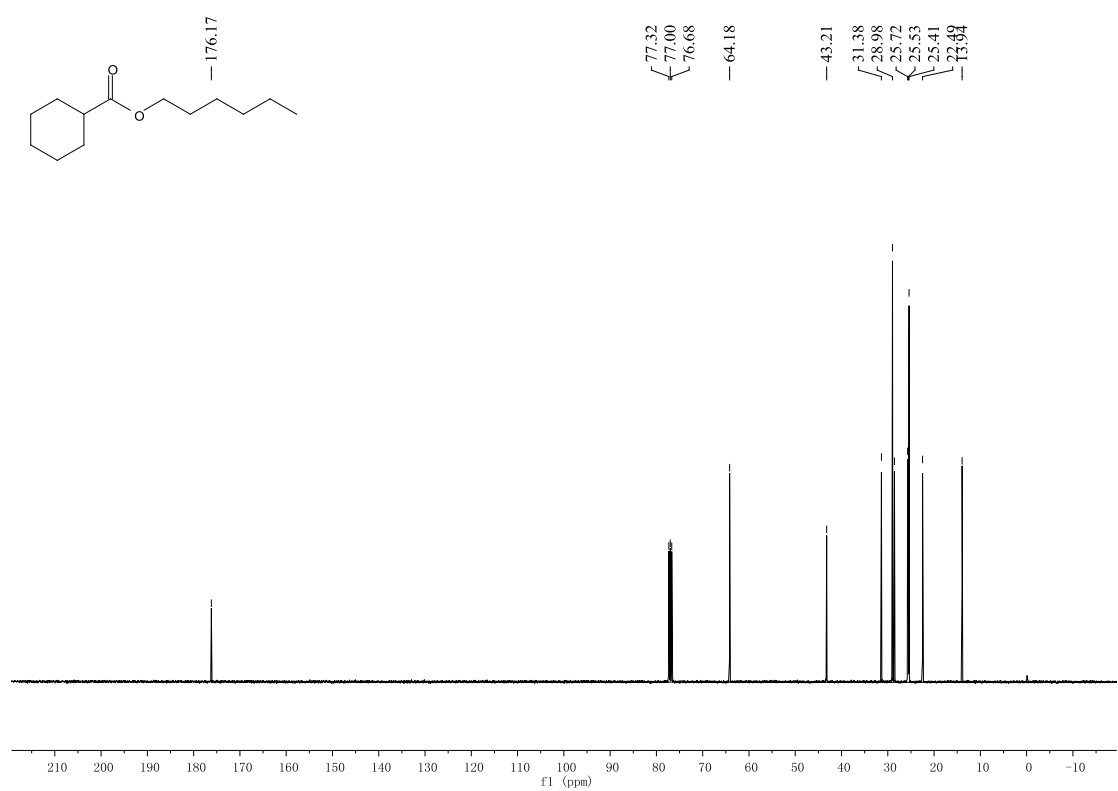


3aj

¹H NMR

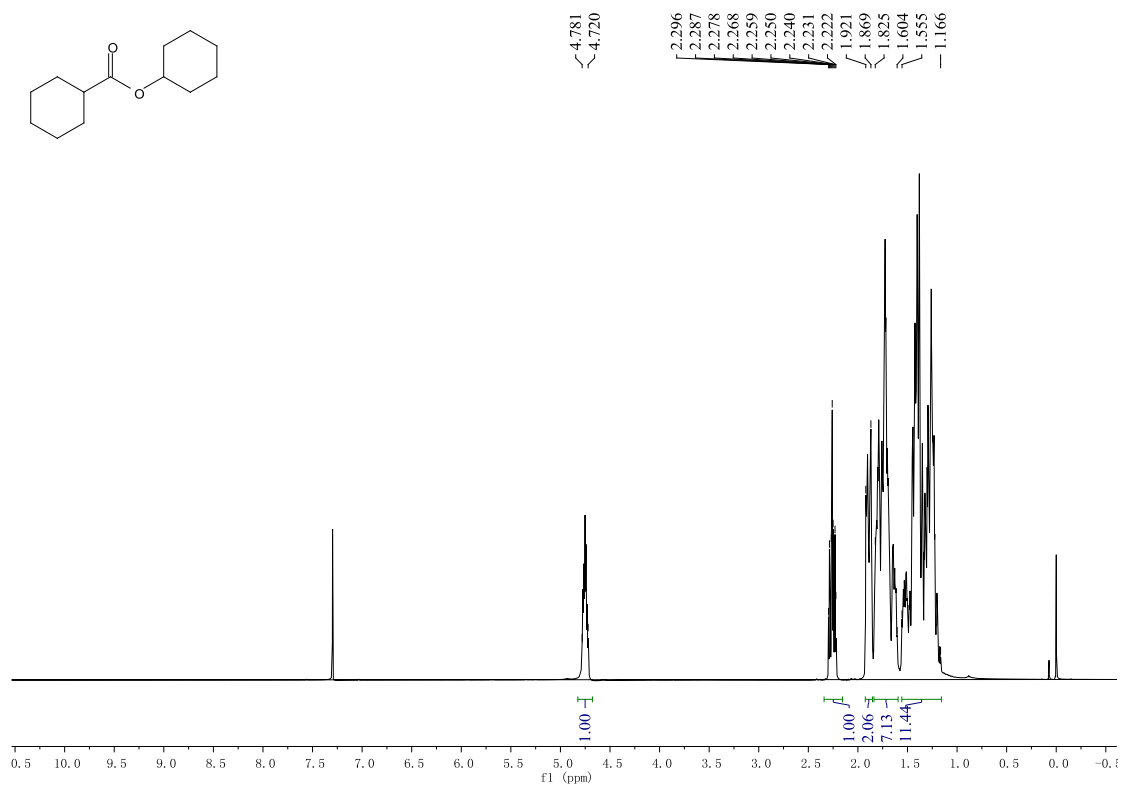


¹³C NMR

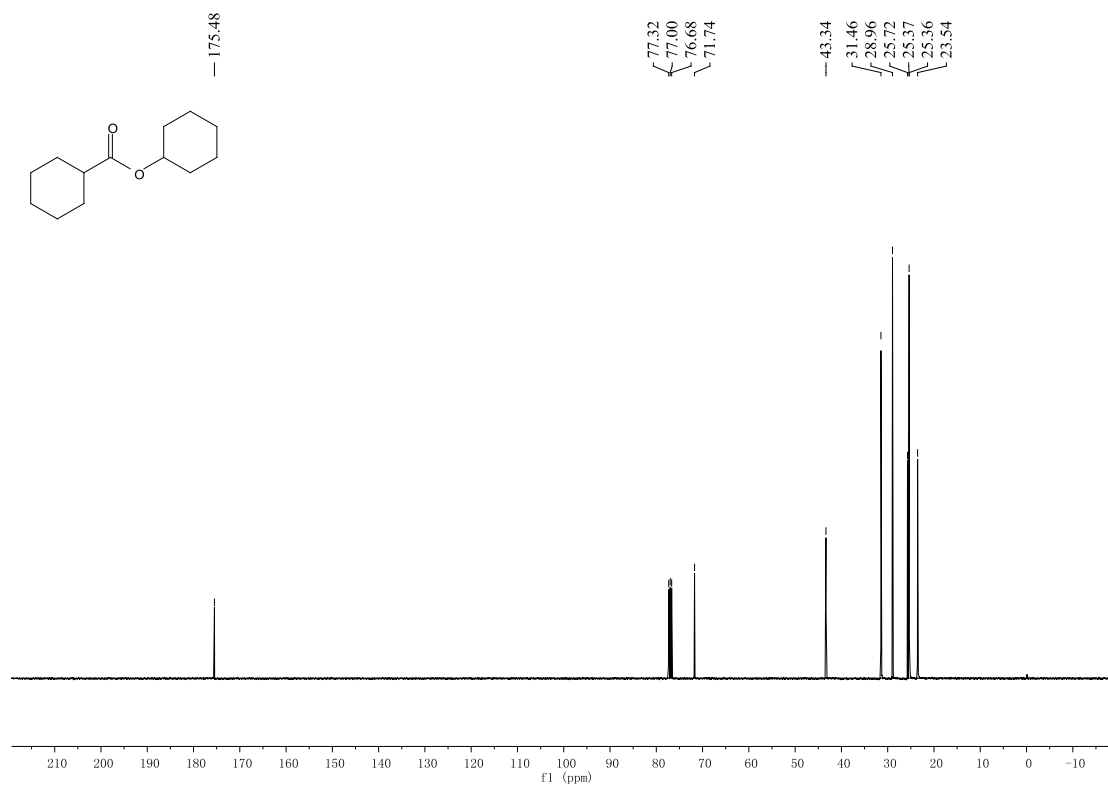


3ak

¹H NMR

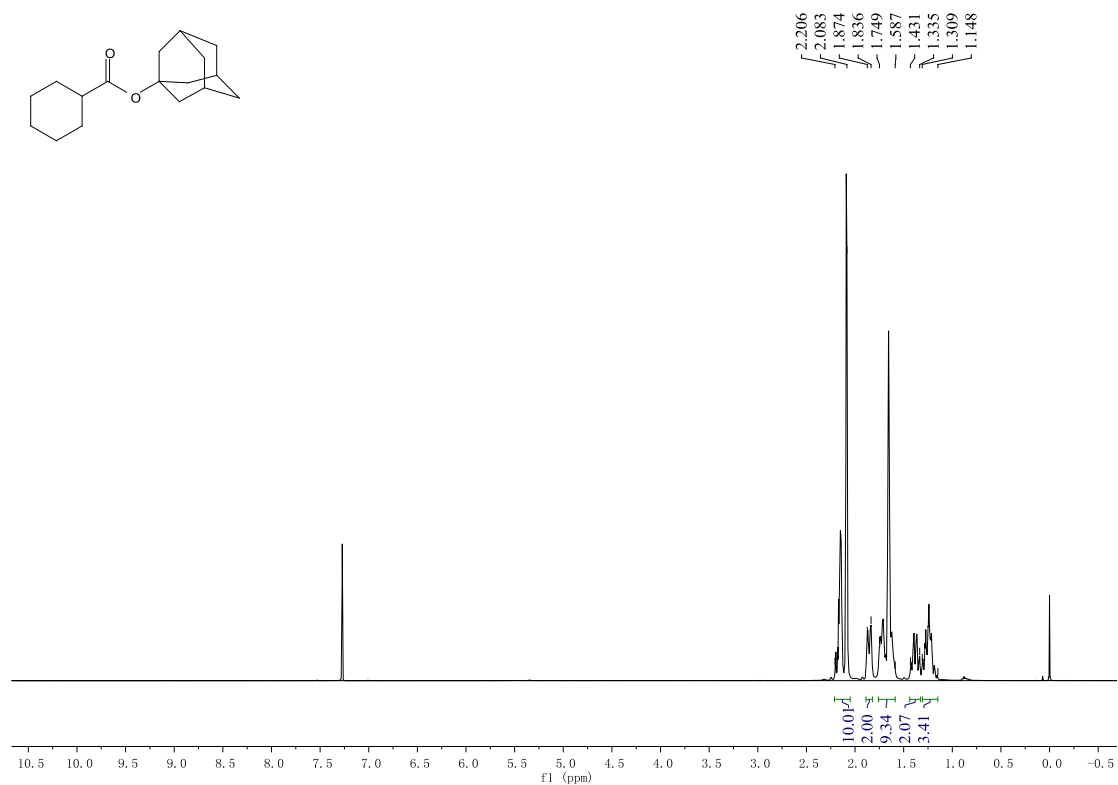


¹³C NMR

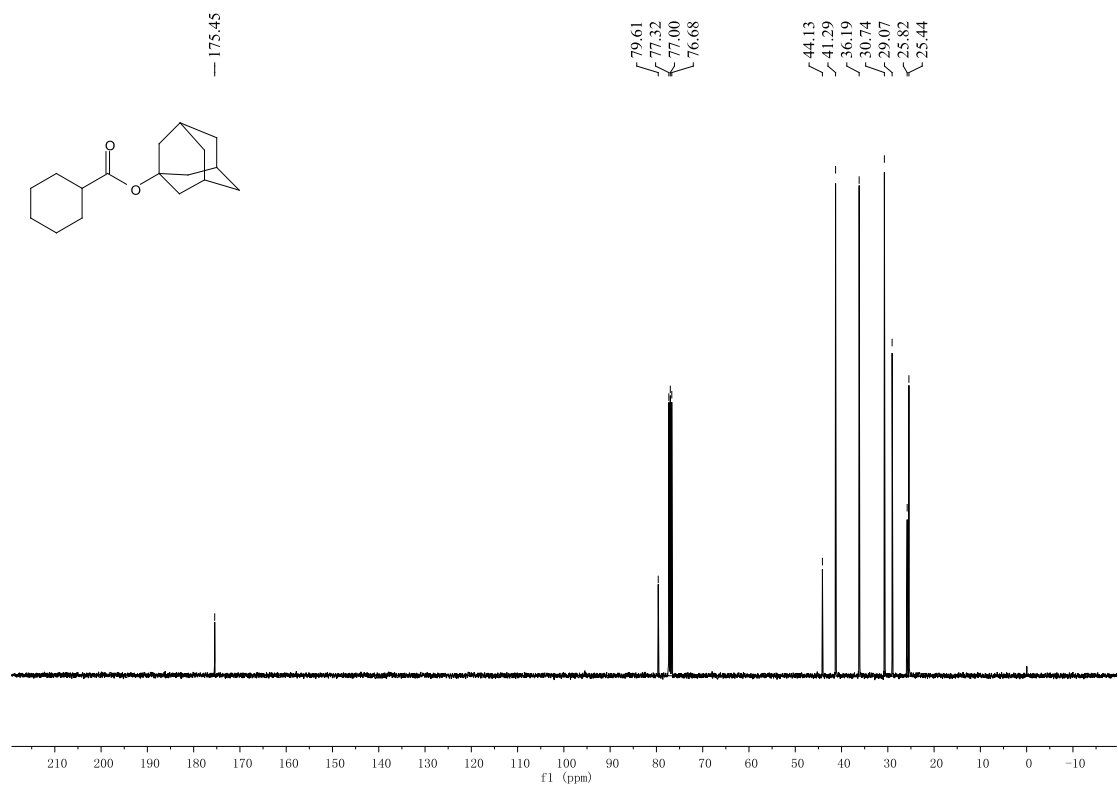


3al

¹H NMR

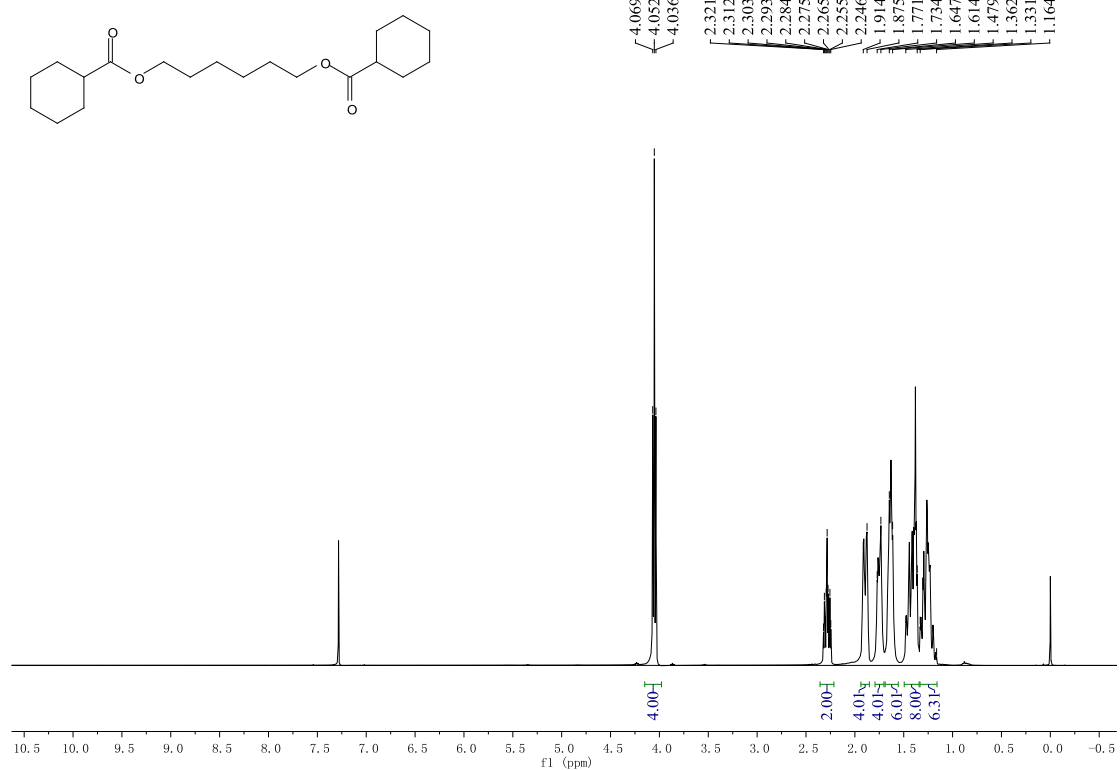


¹³C NMR

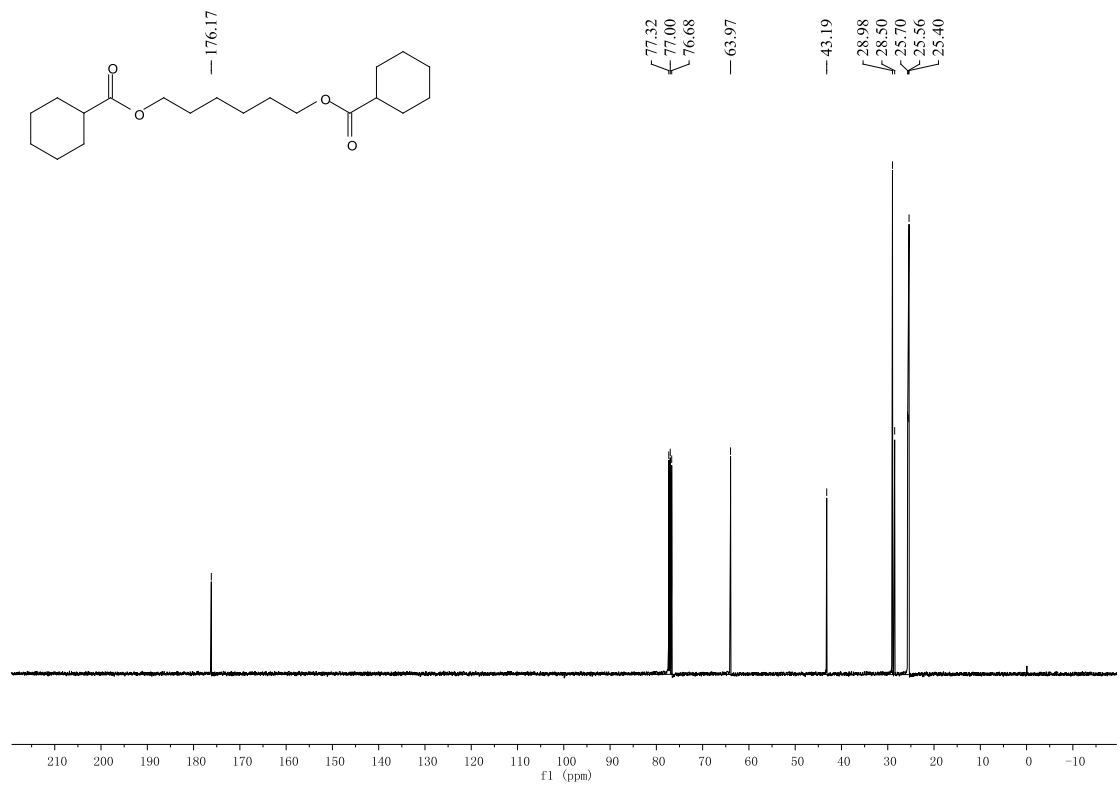


3am

¹H NMR

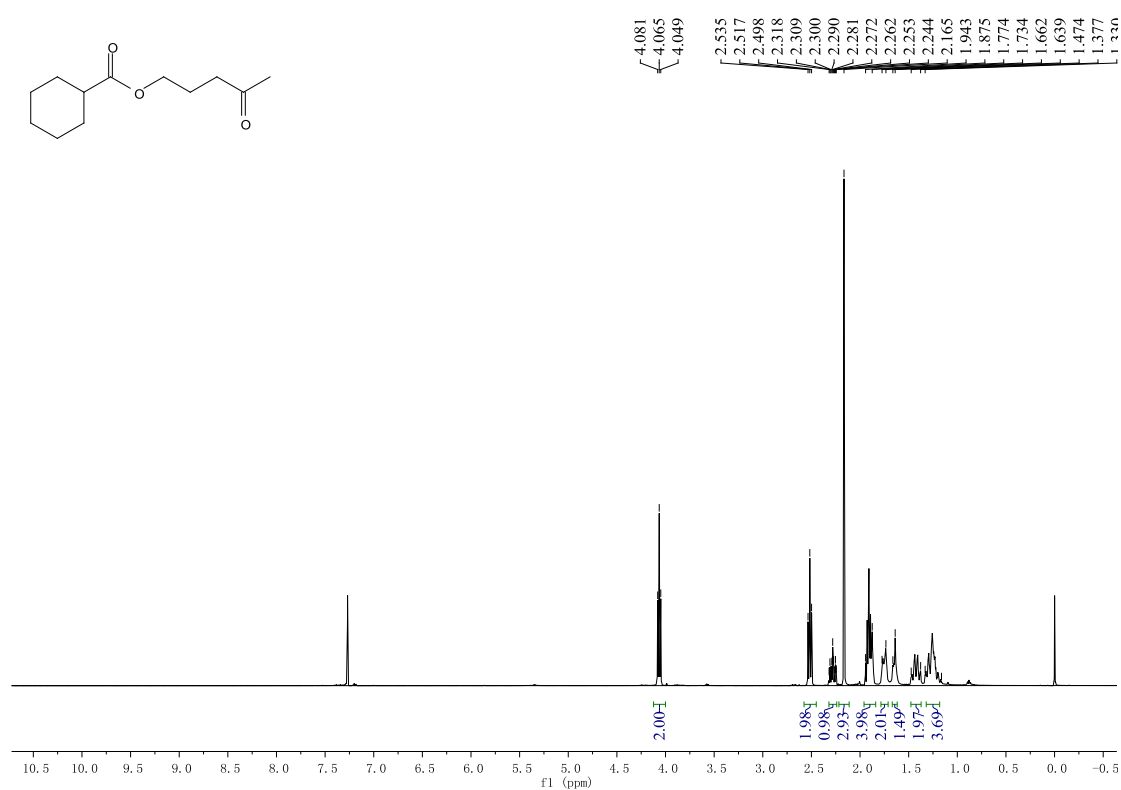


¹³C NMR

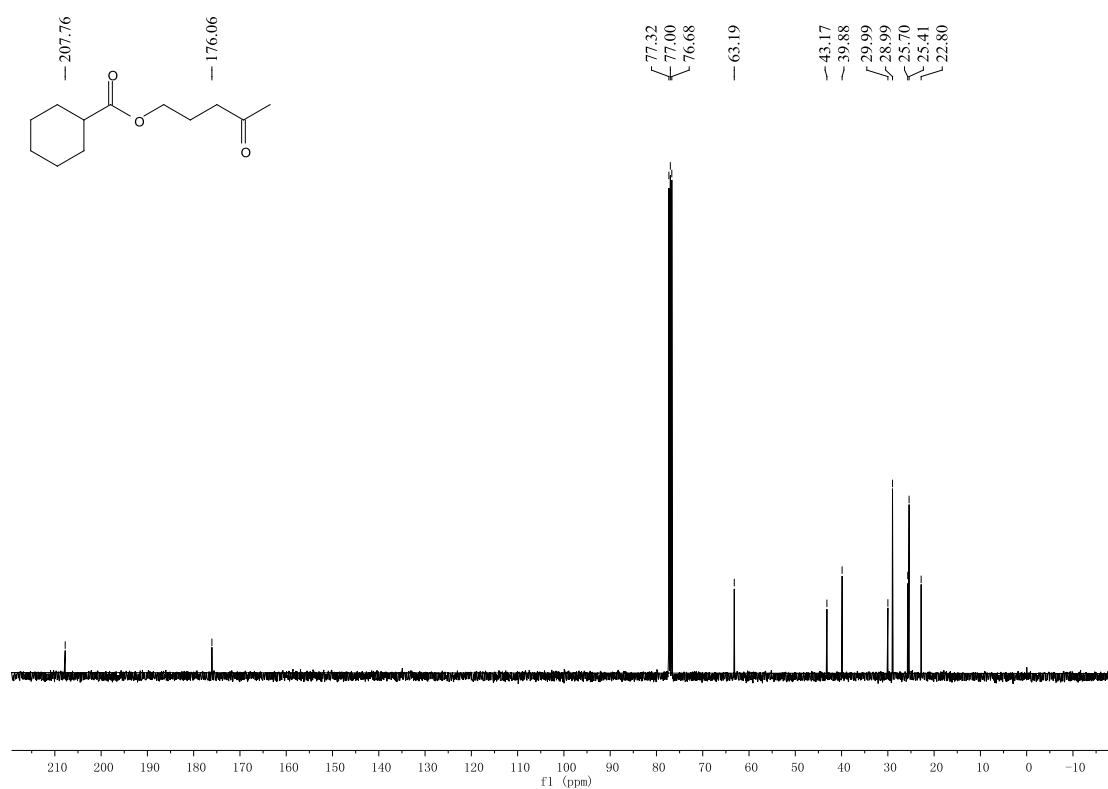


3an

¹H NMR

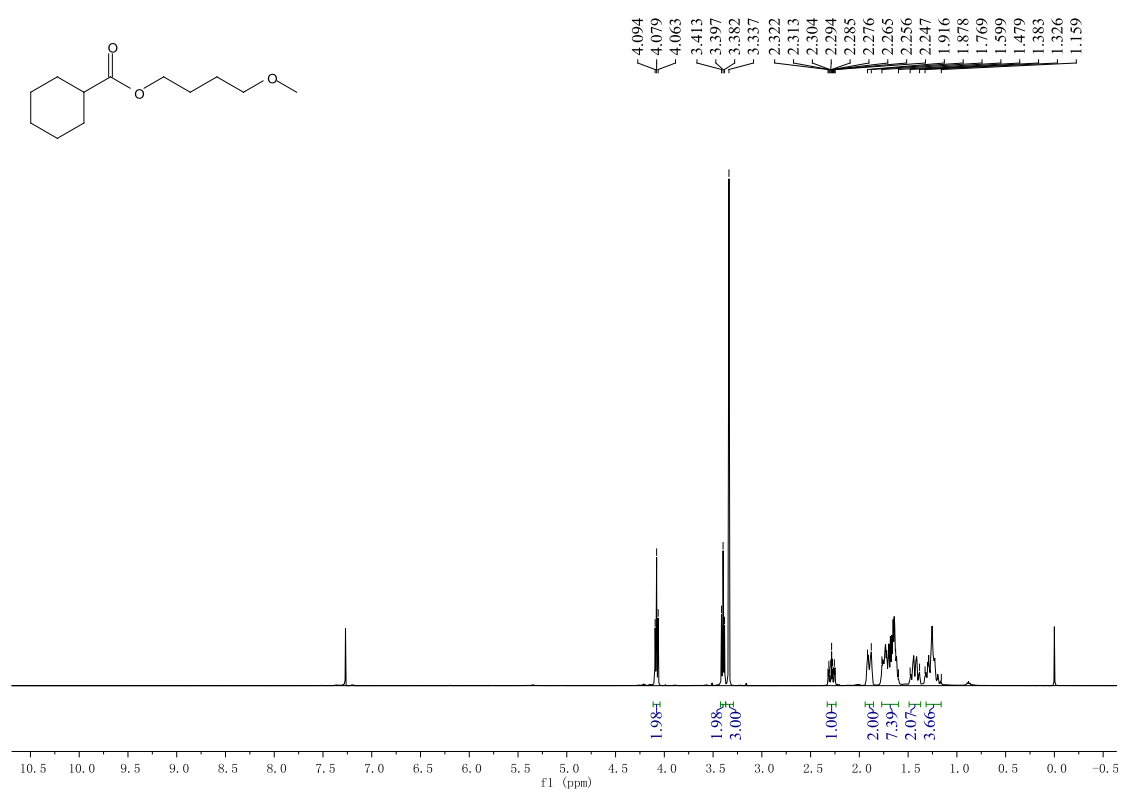


¹³C NMR

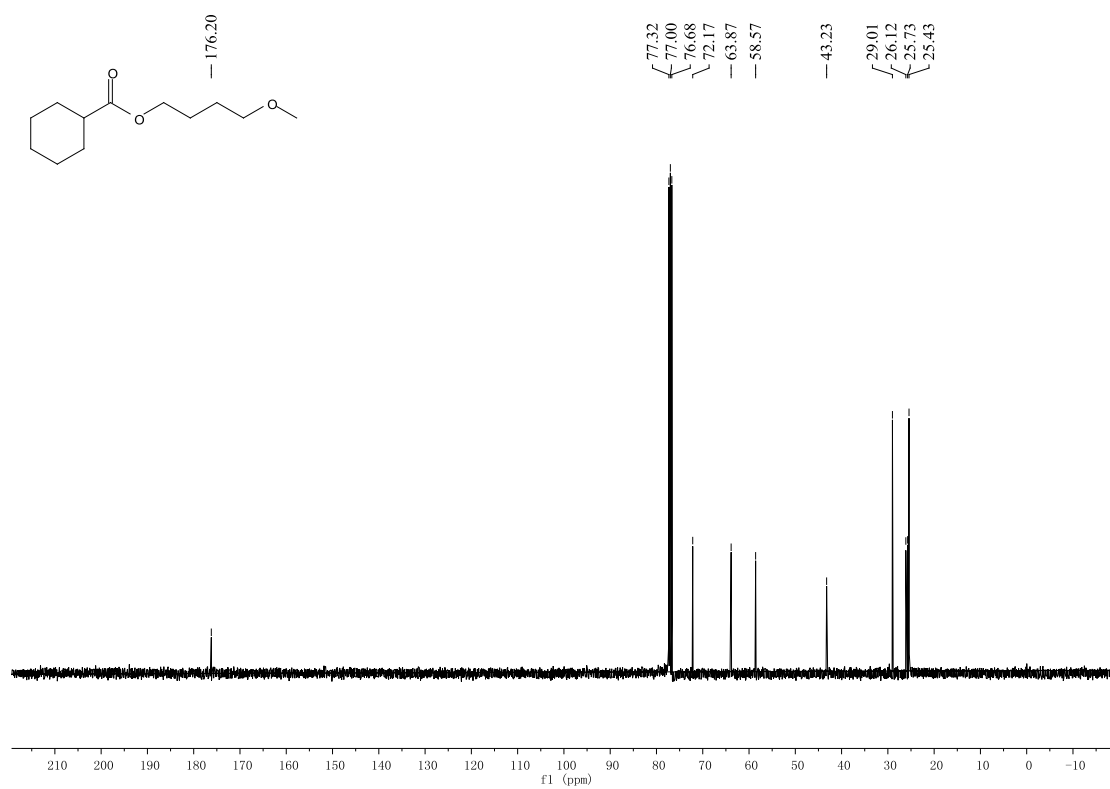


3ao

¹H NMR

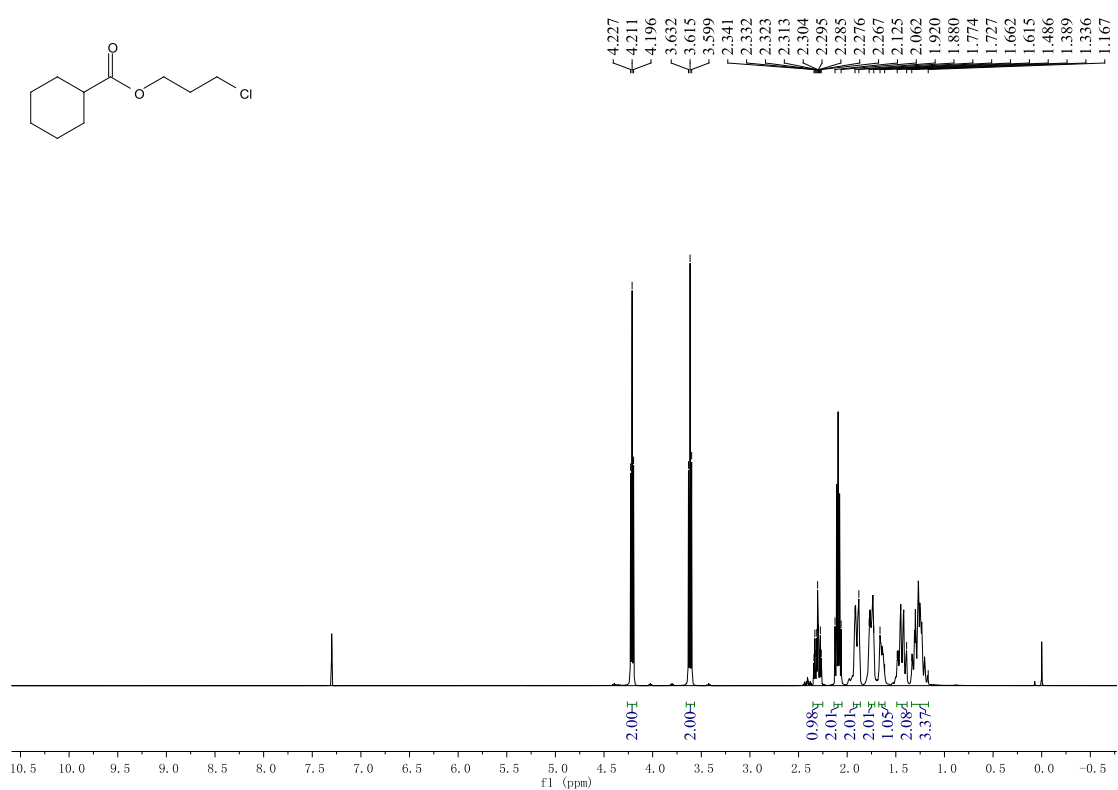


¹³C NMR

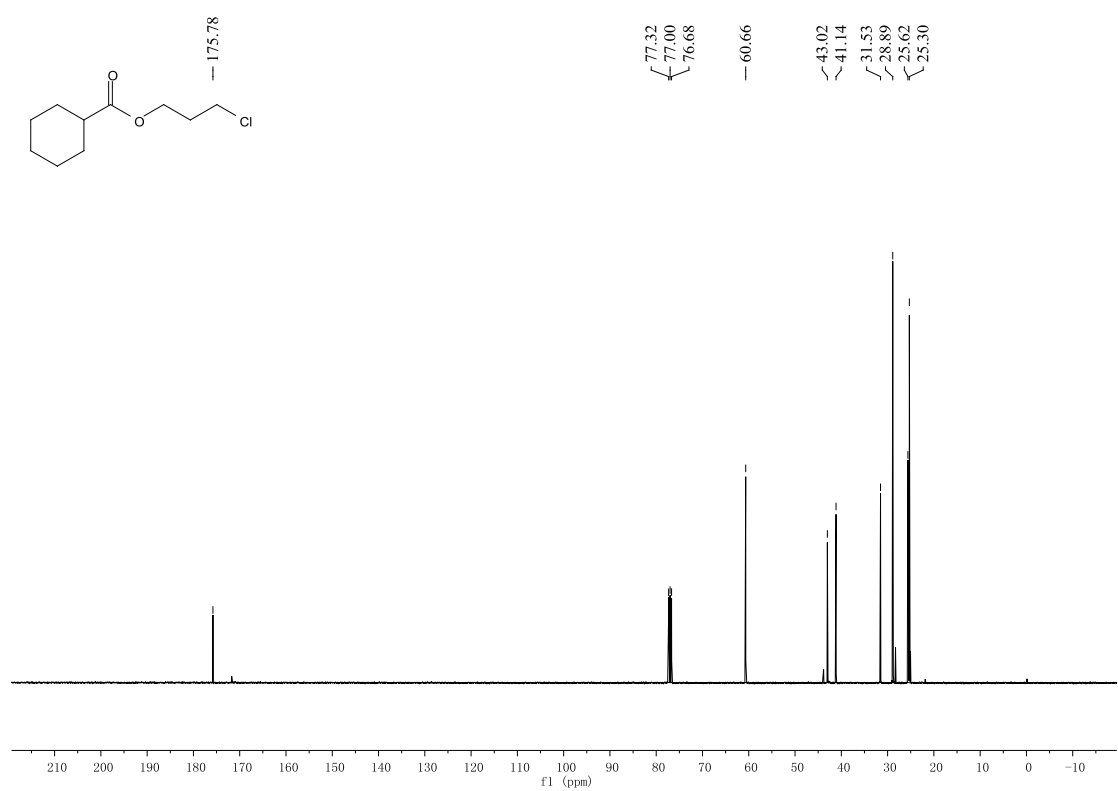


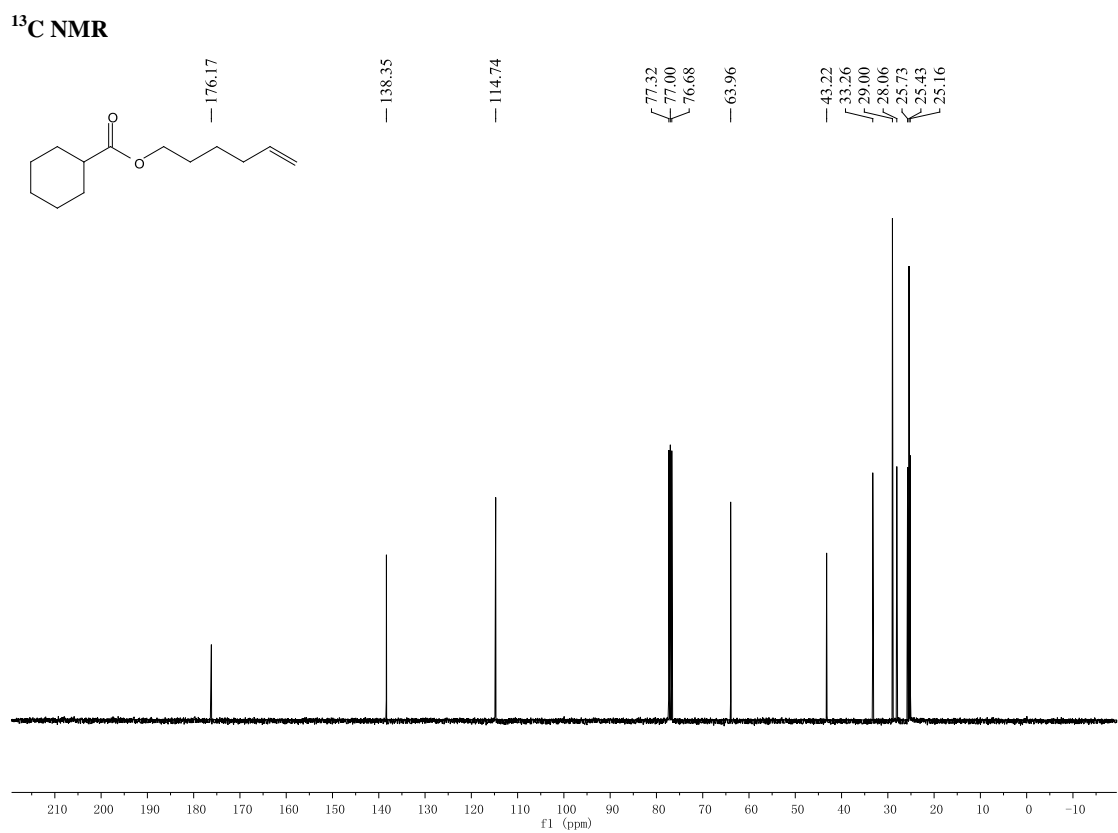
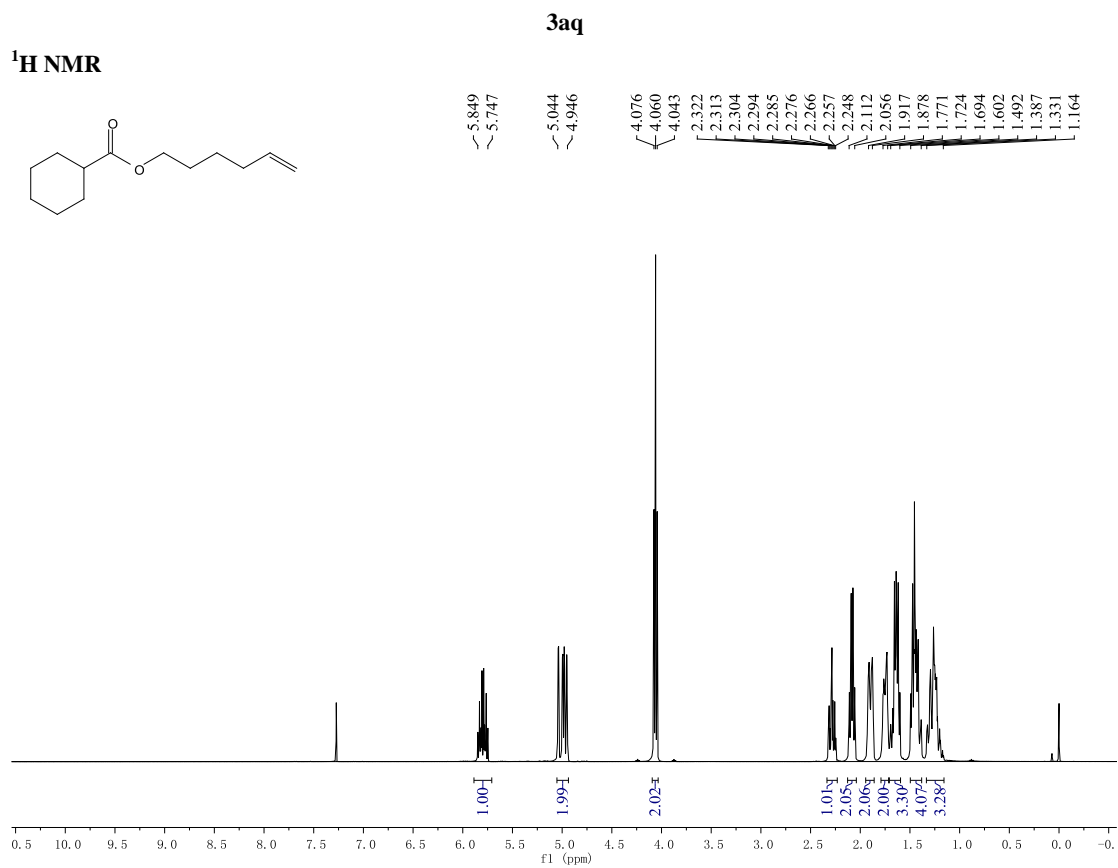
3ap

¹H NMR

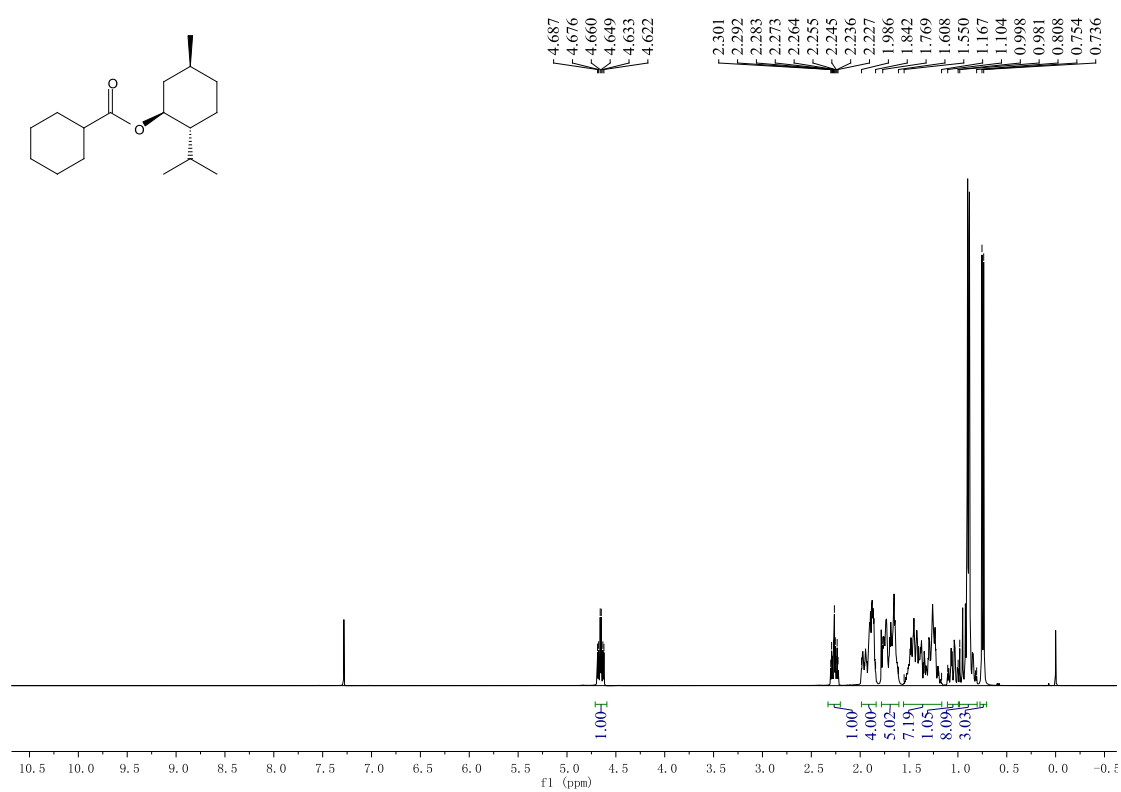


¹³C NMR

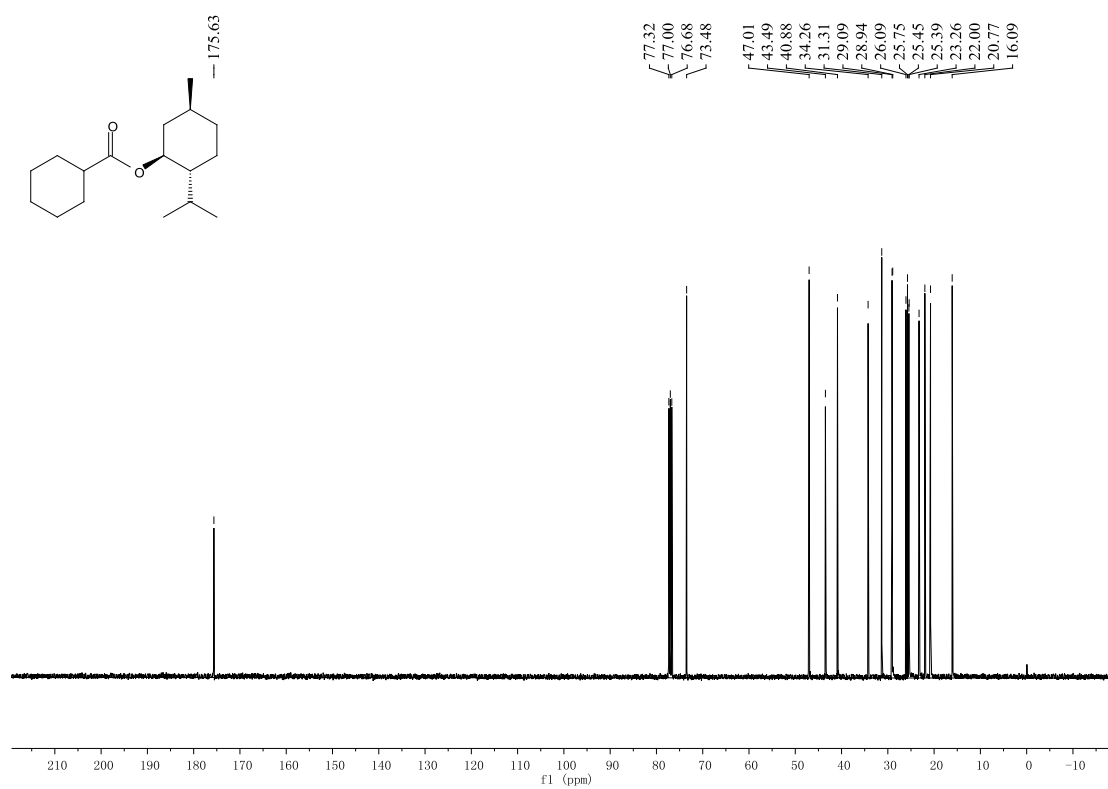




¹H NMR

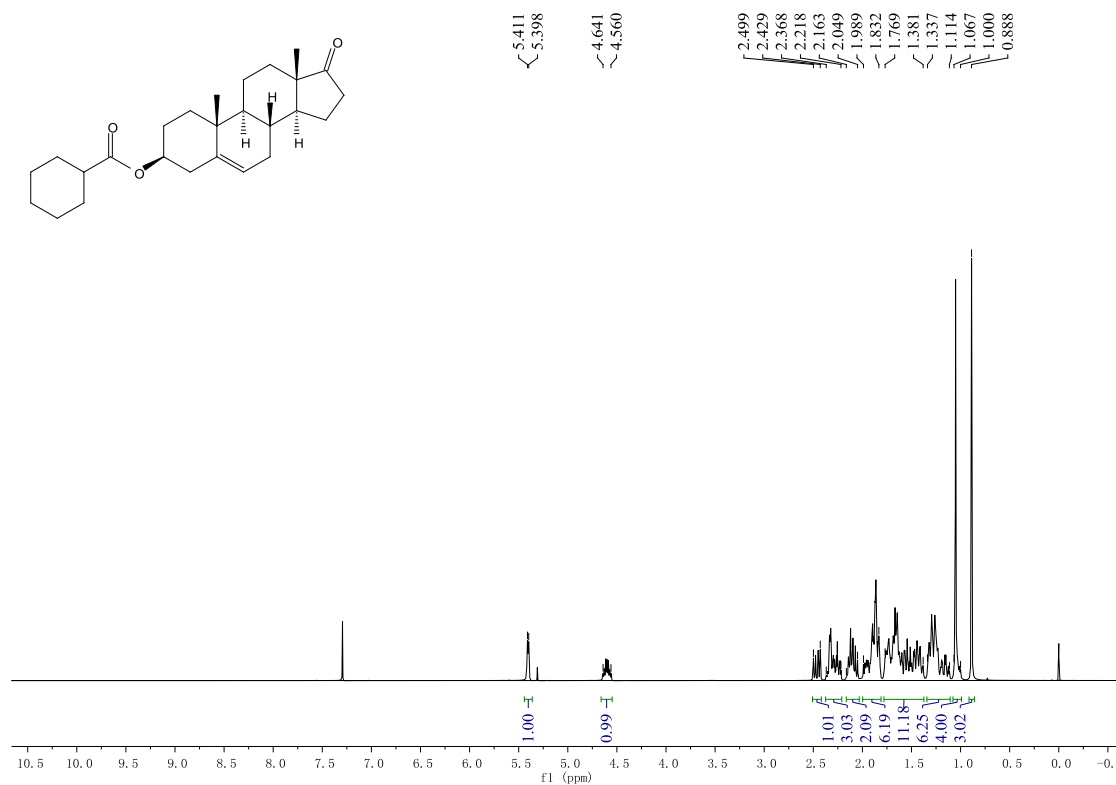


¹³C NMR

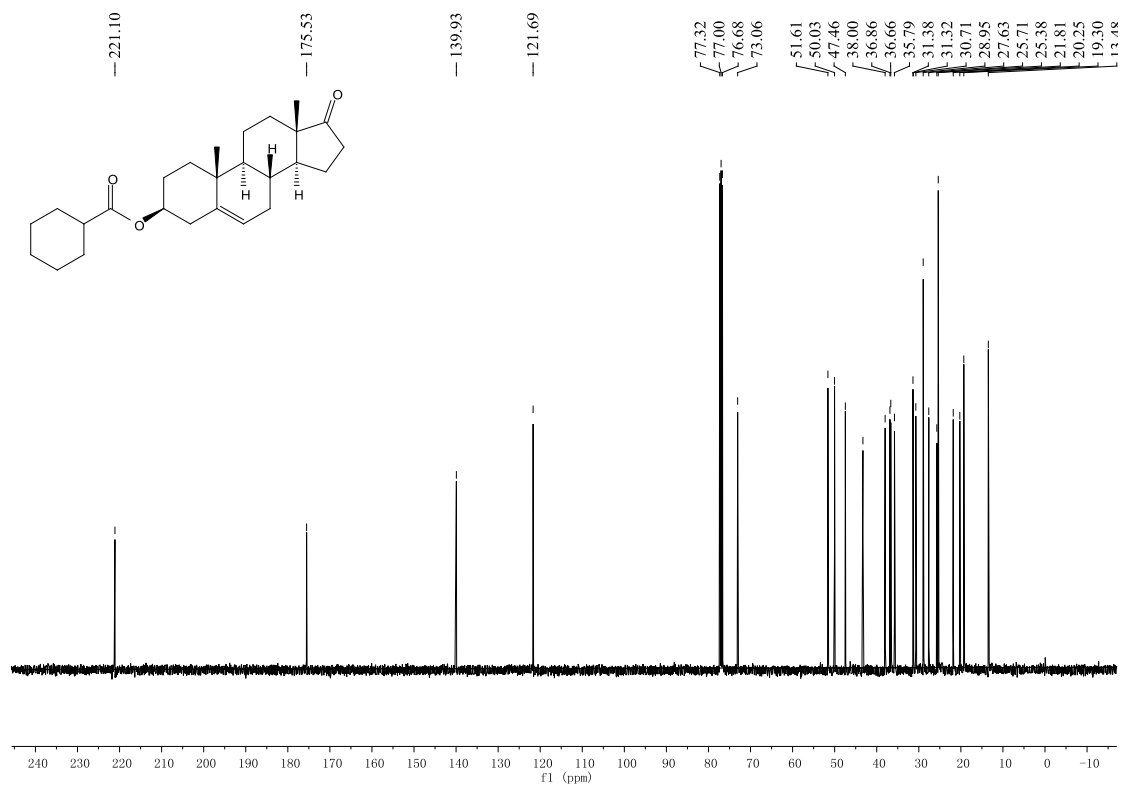


3as

¹H NMR

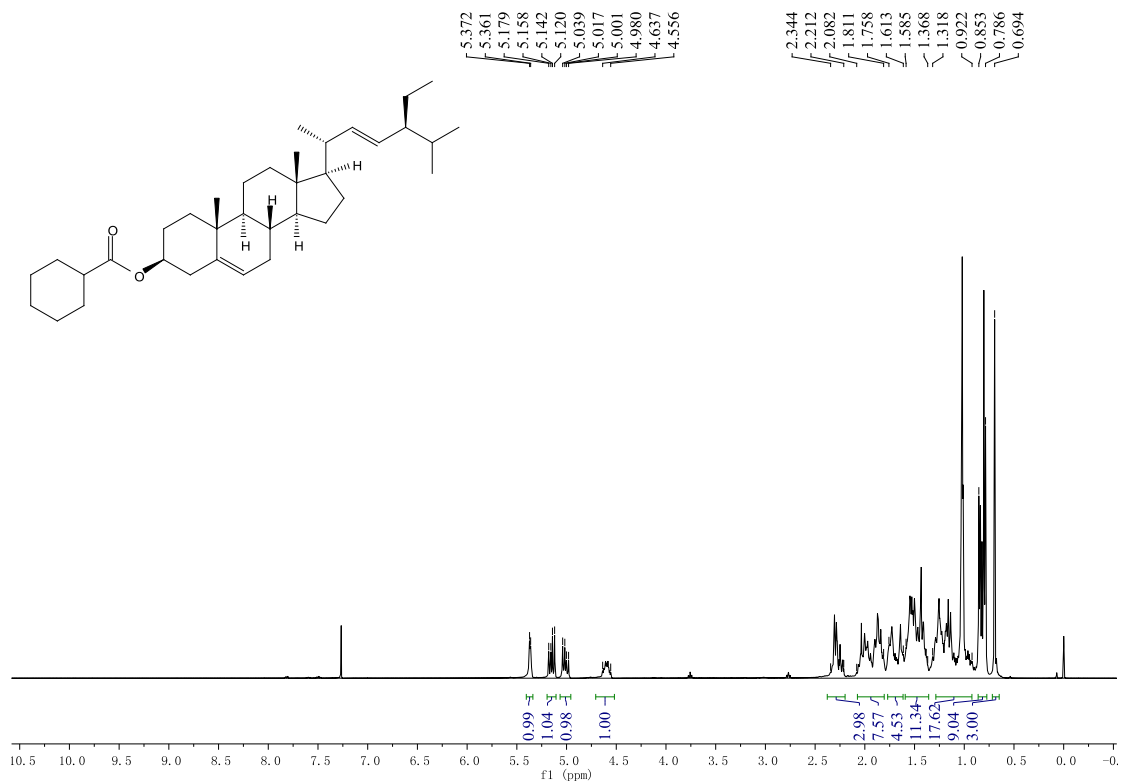


¹³C NMR

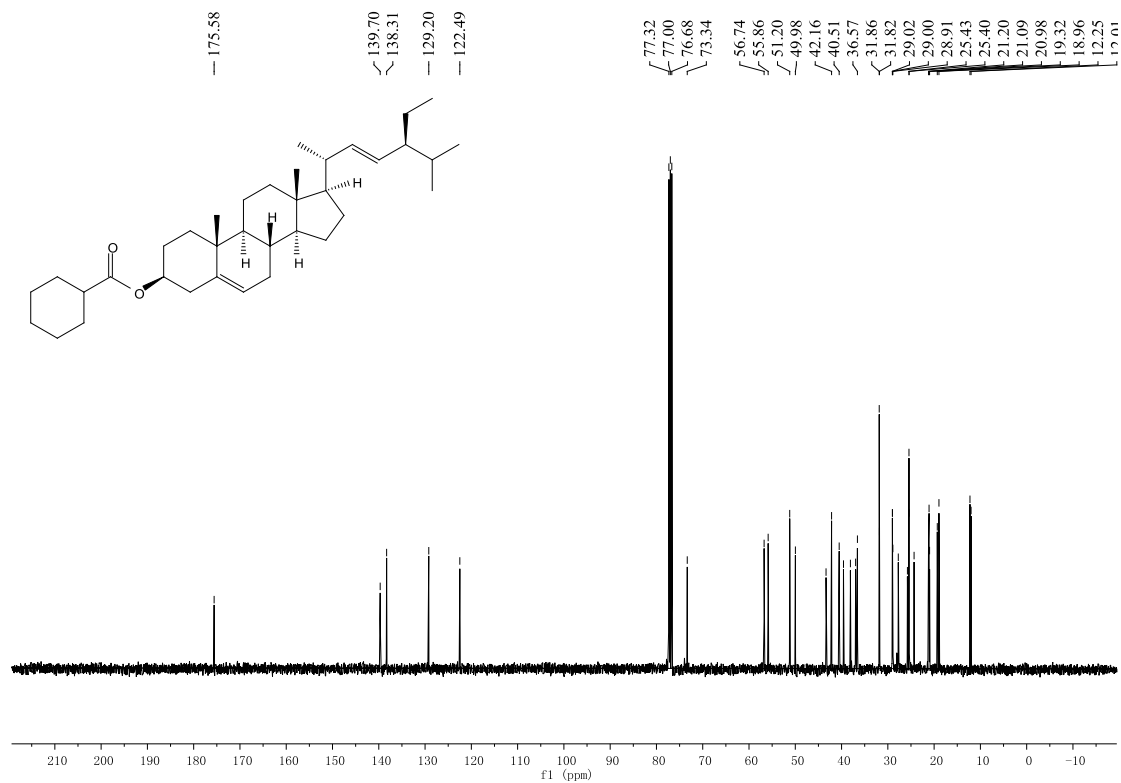


3at

¹H NMR

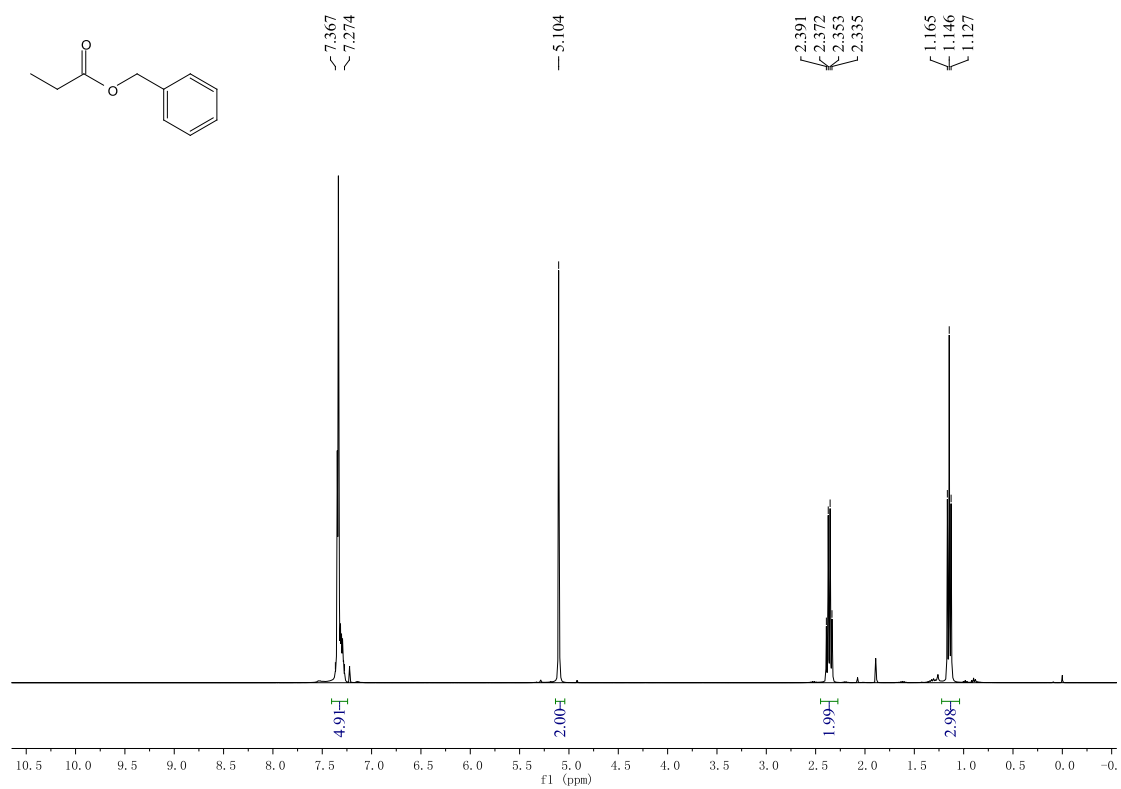


¹³C NMR

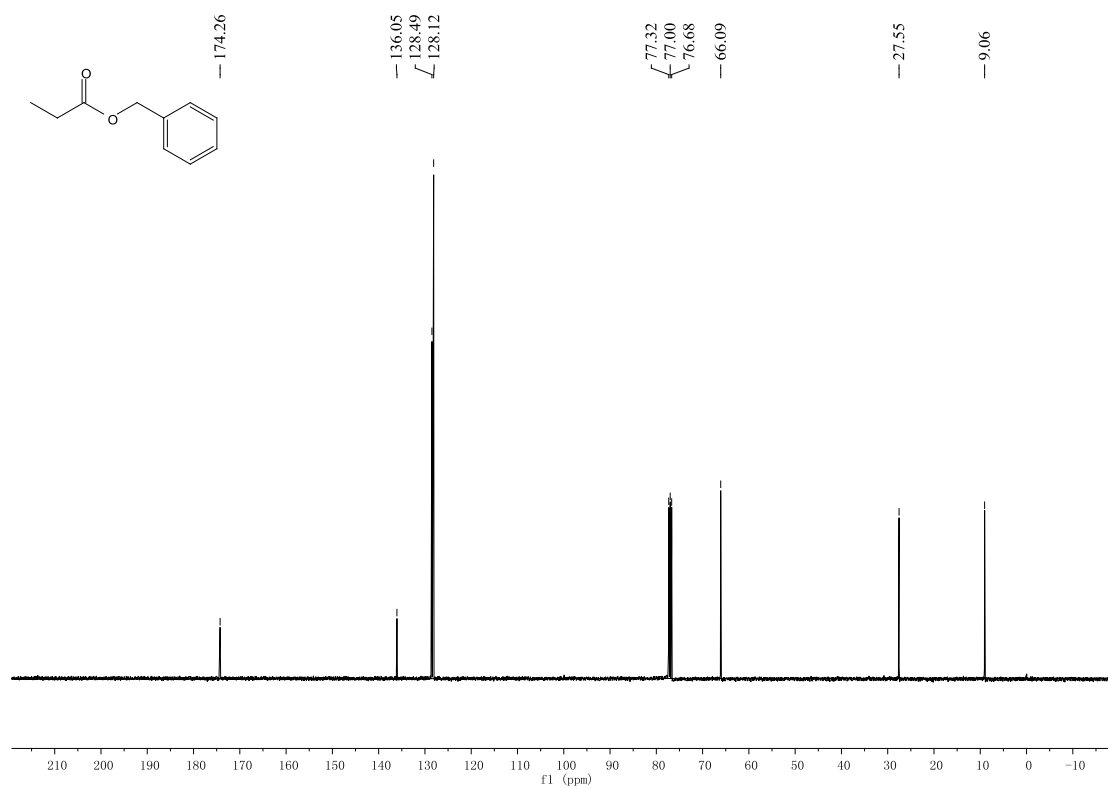


3ba

¹H NMR

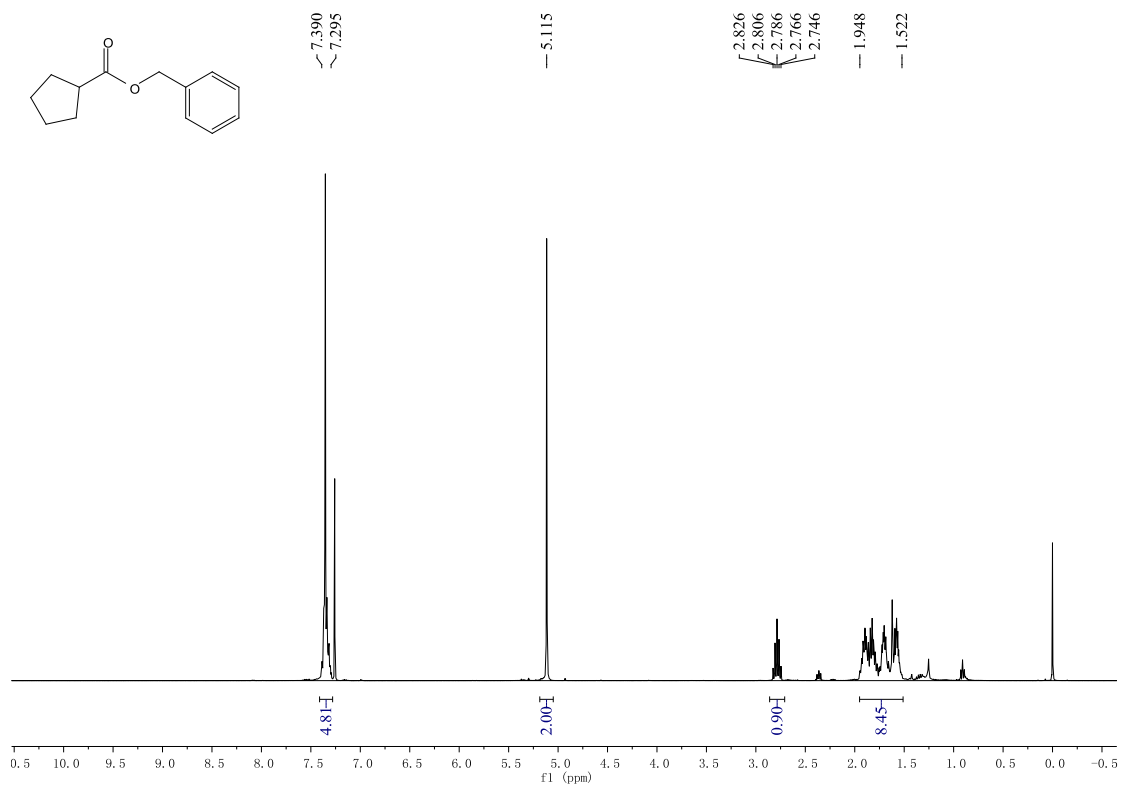


¹³C NMR

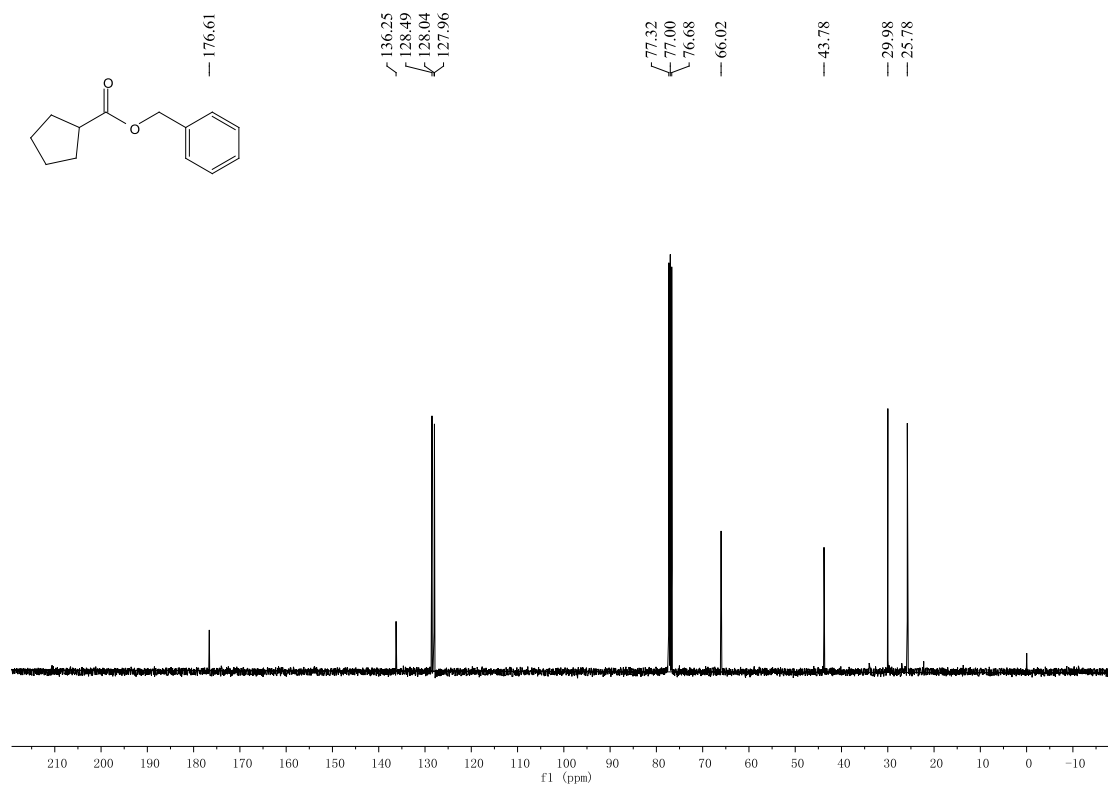


3ca

¹H NMR

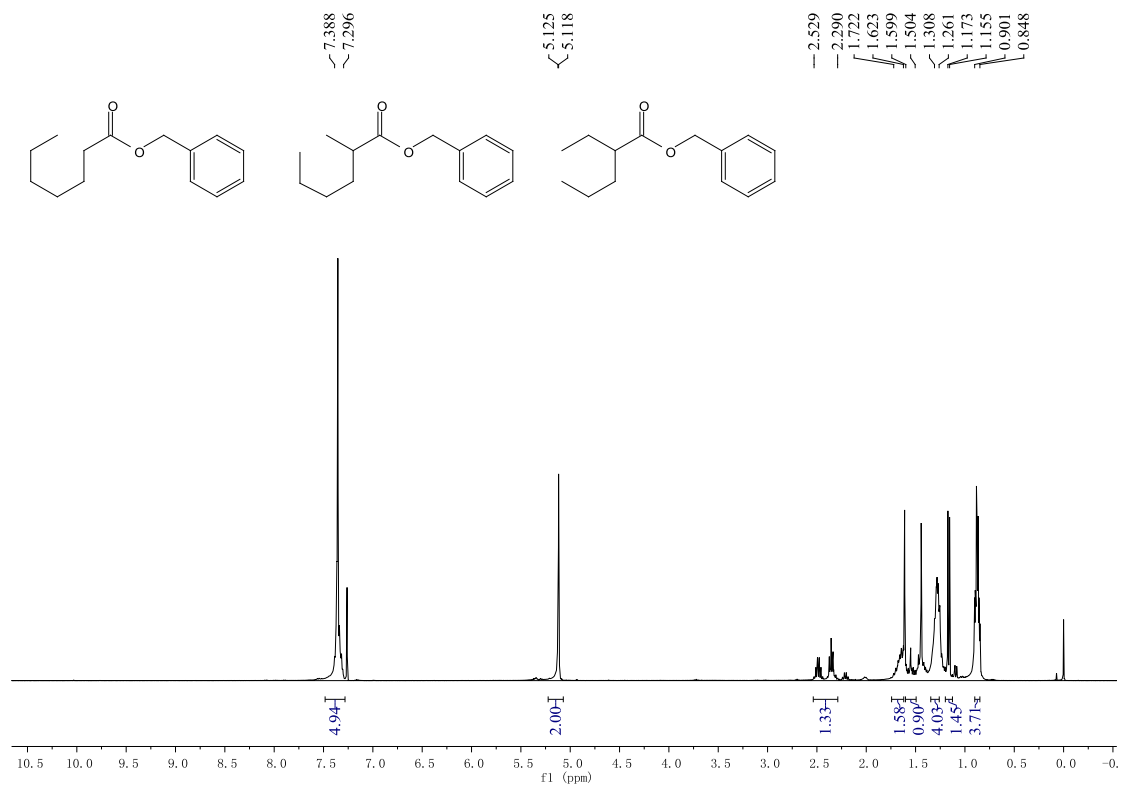


¹³C NMR

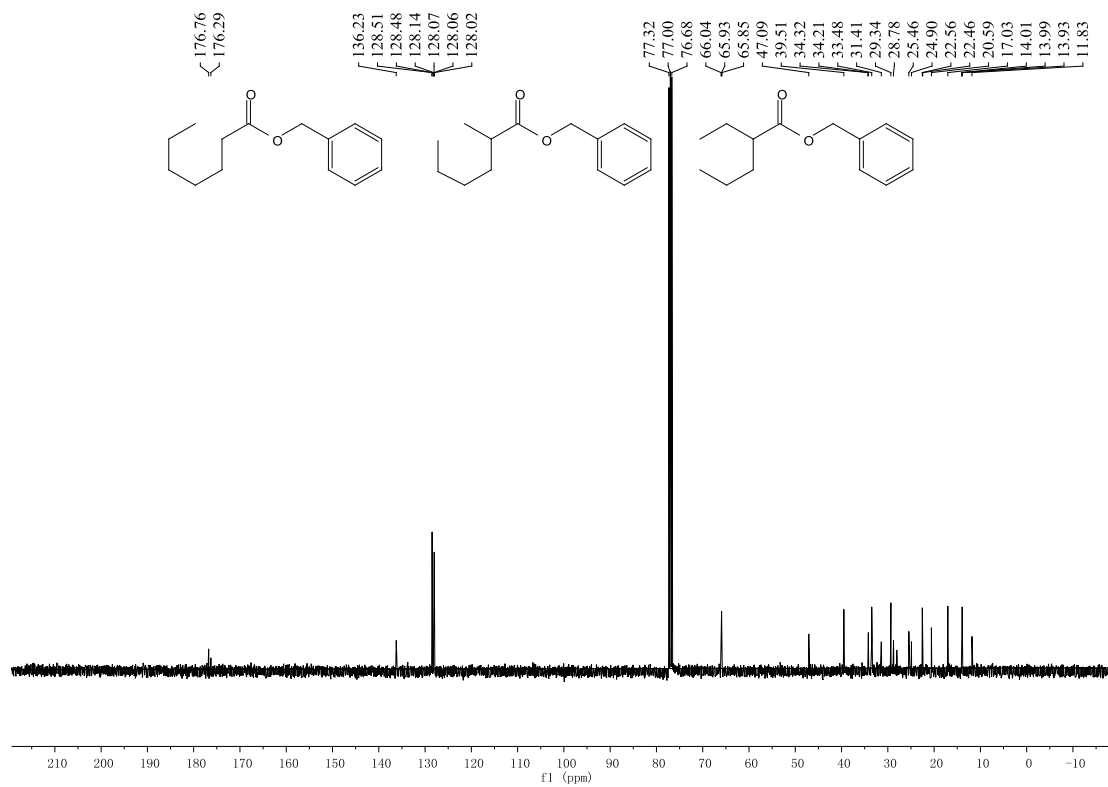


3da

¹H NMR

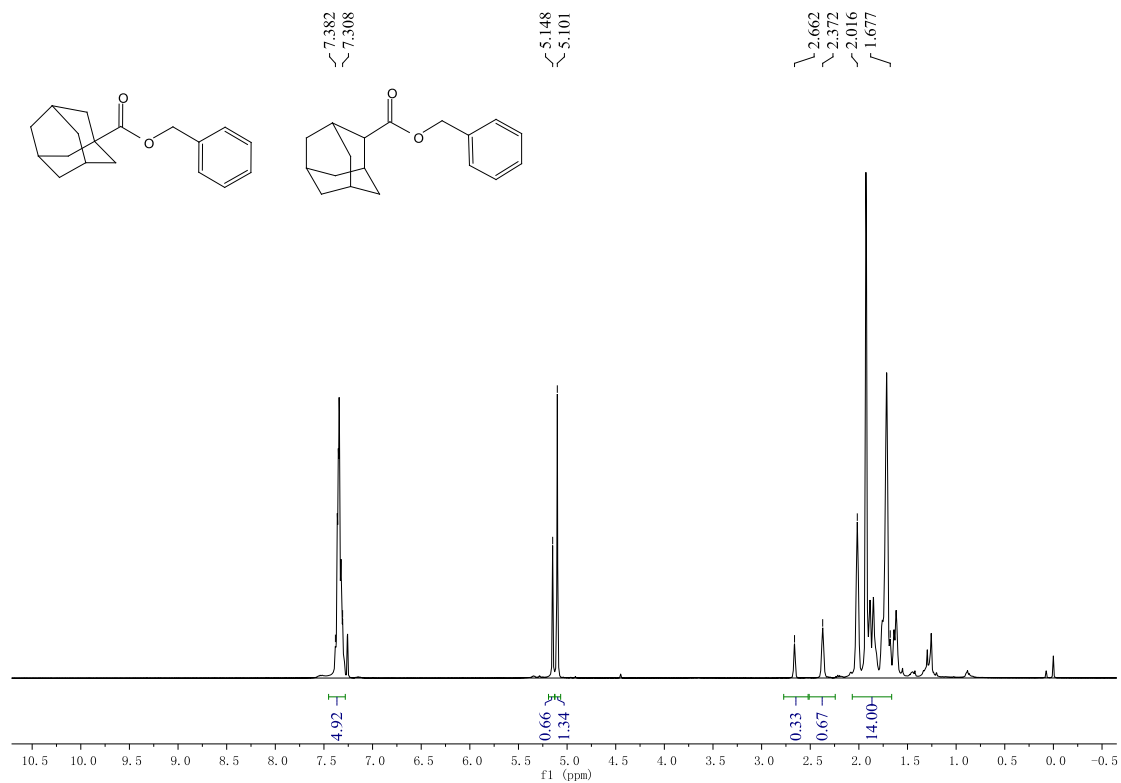


¹³C NMR

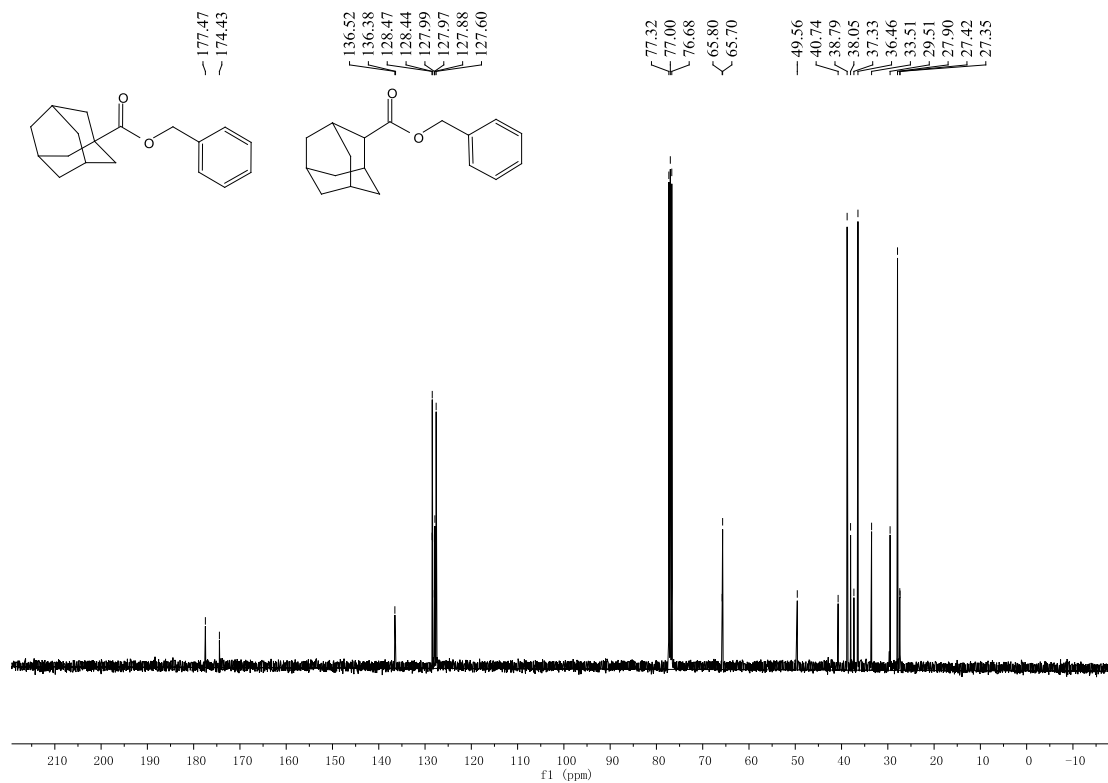


3ea

¹H NMR

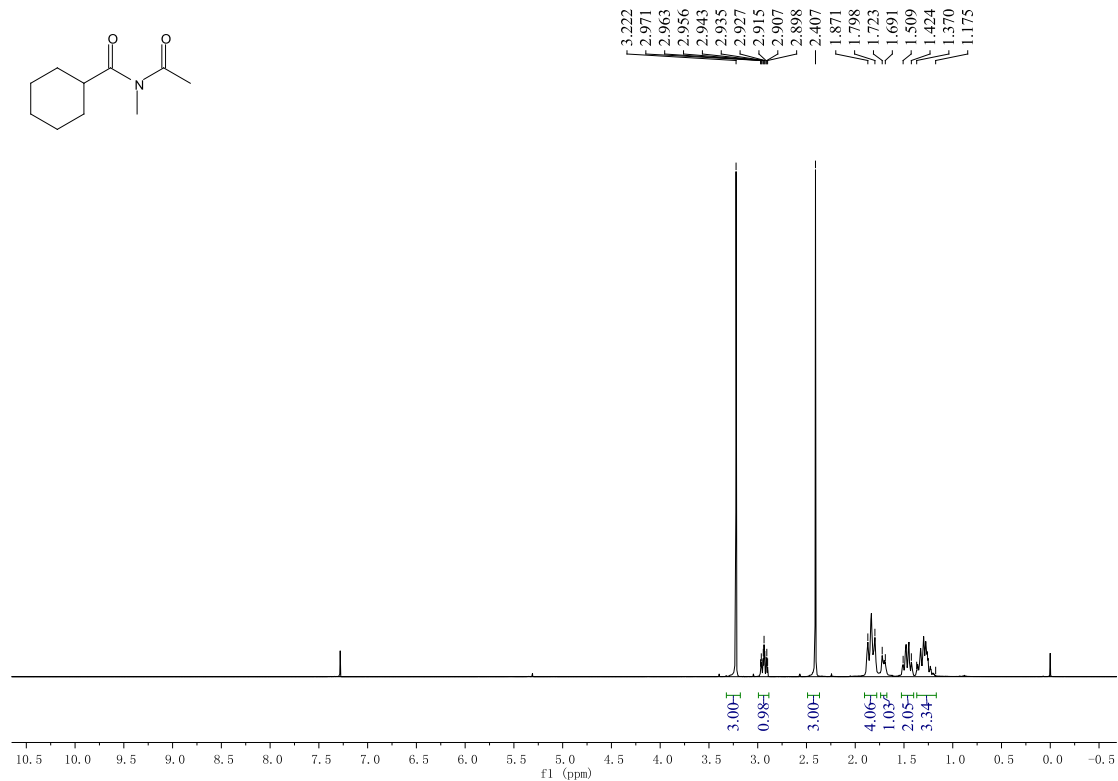


¹³C NMR

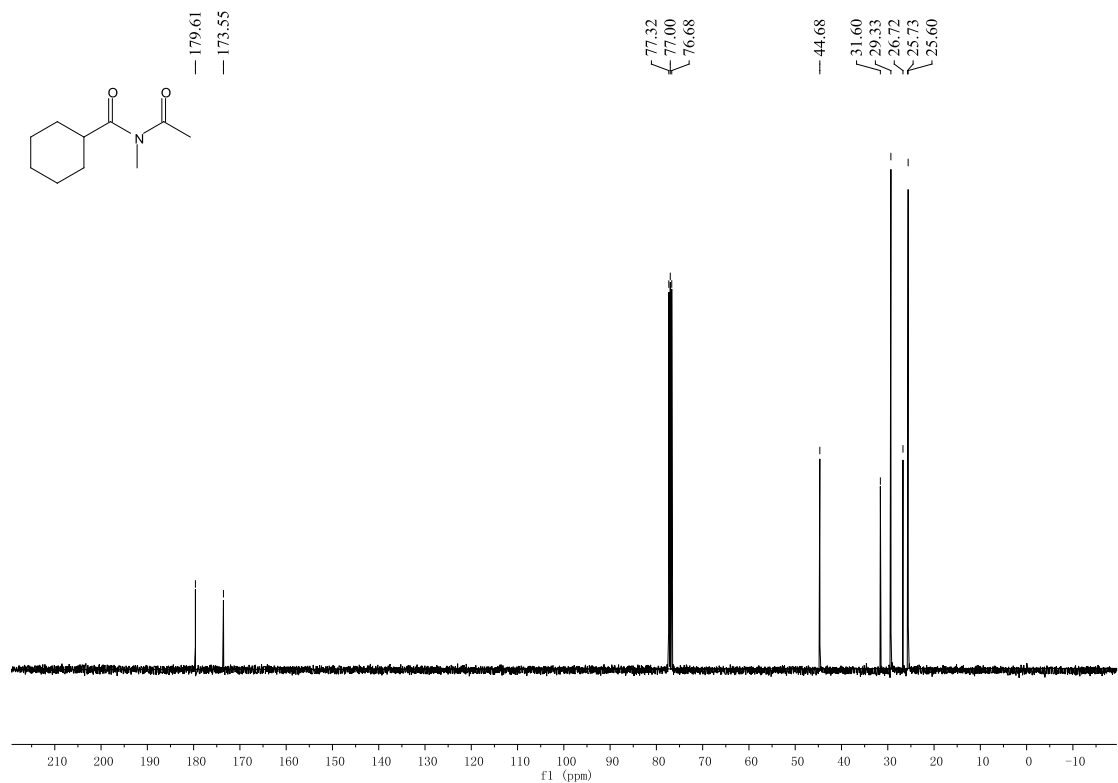


5aa

¹H NMR

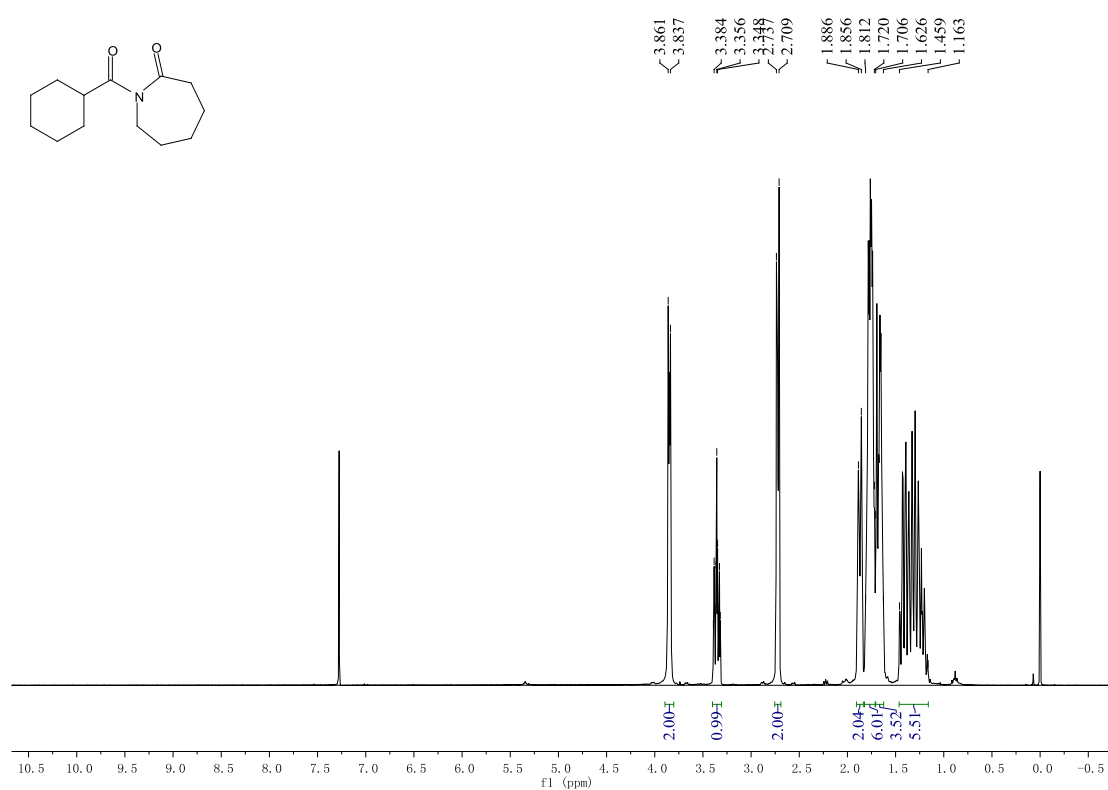


¹³C NMR

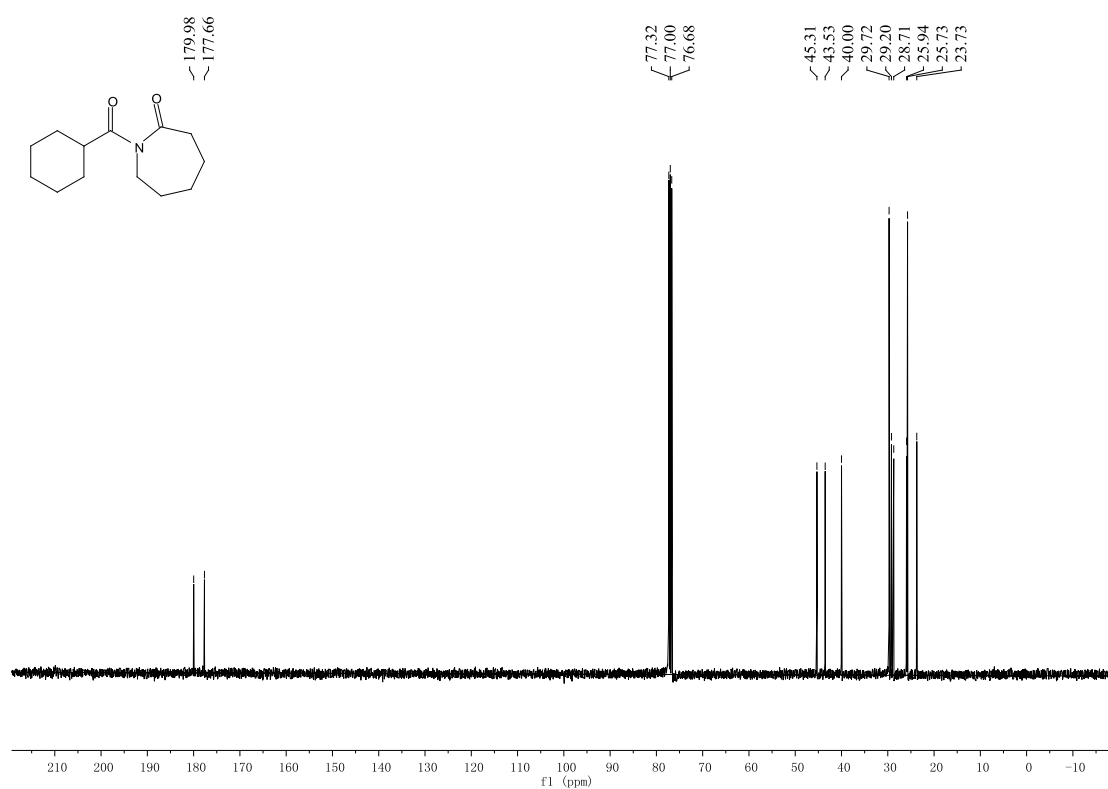


5ab

¹H NMR

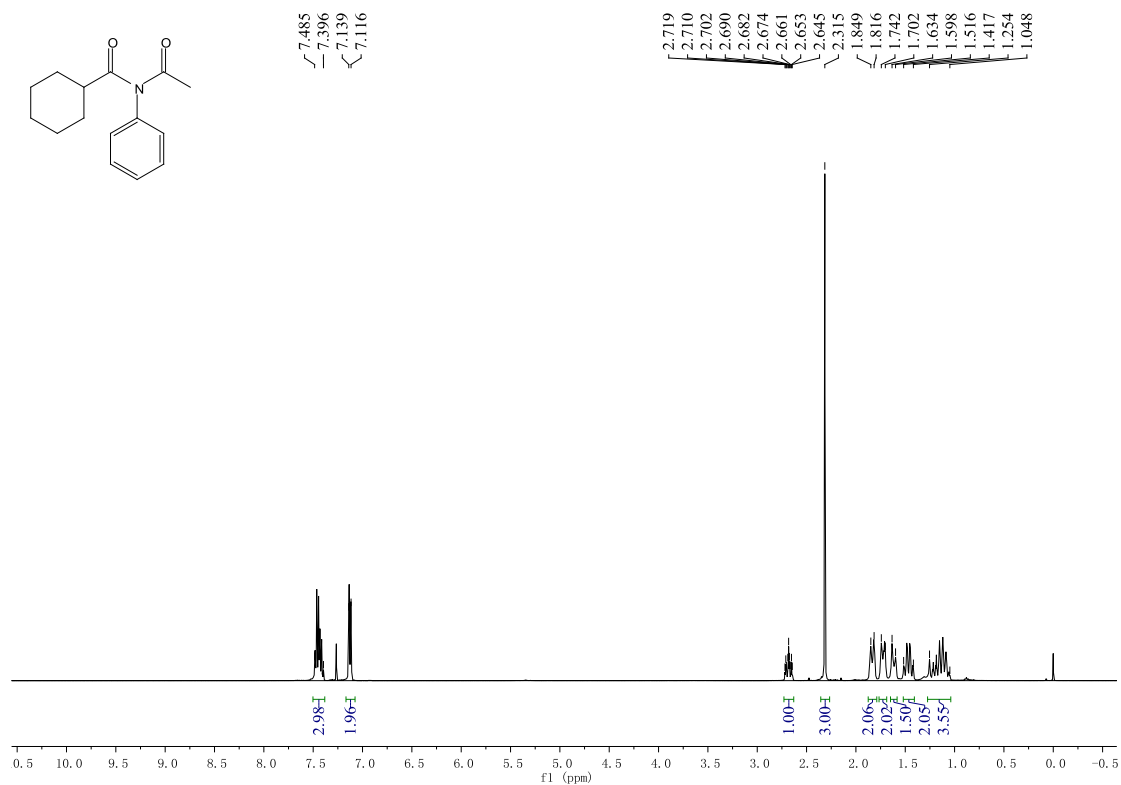


¹³C NMR

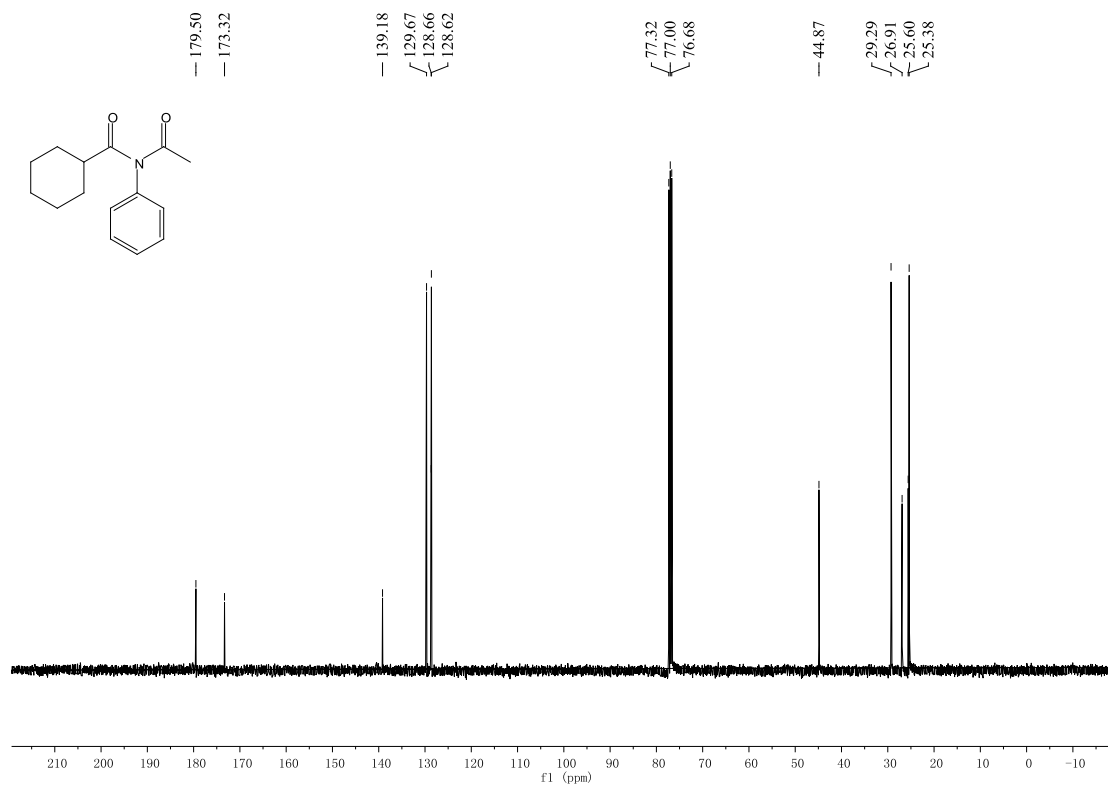


5ac

¹H NMR

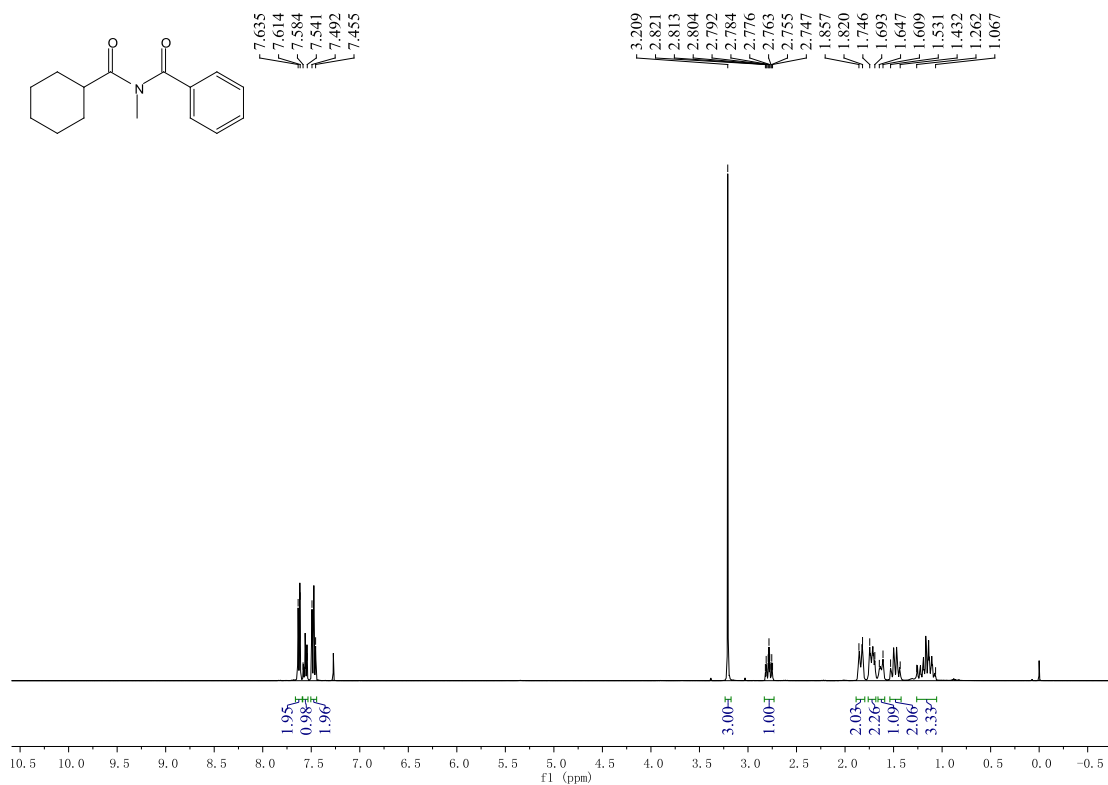


¹³C NMR

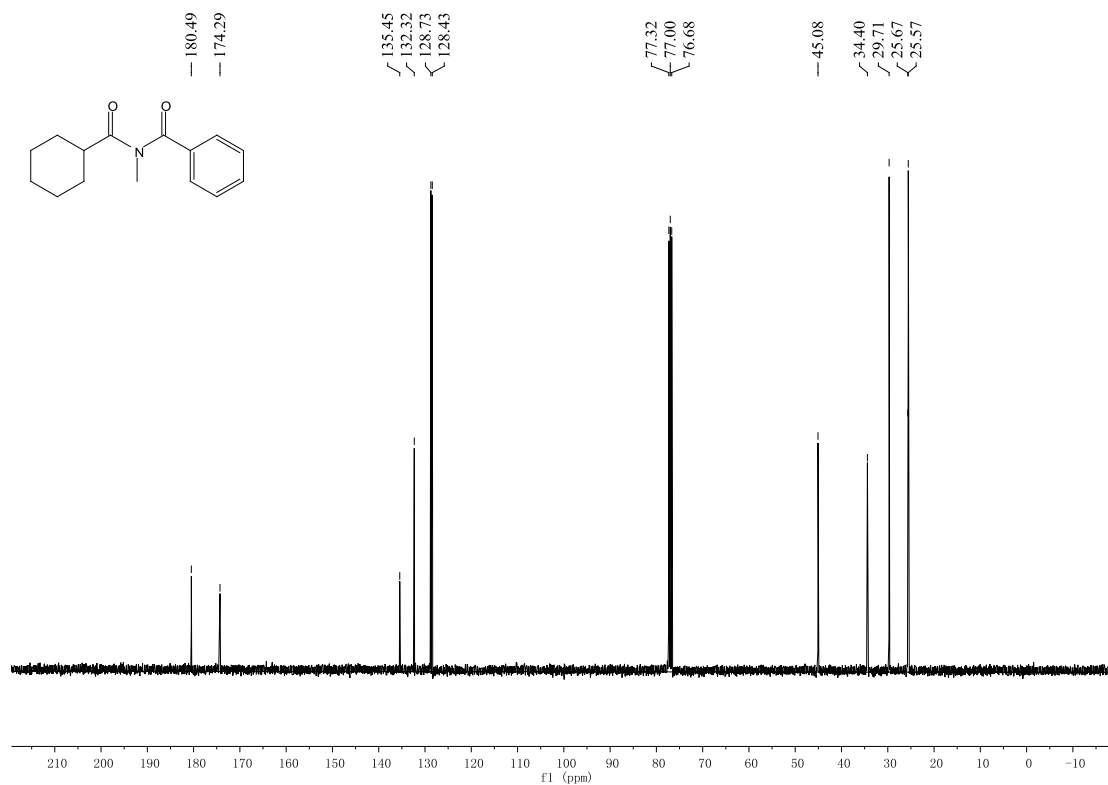


5ad

¹H NMR

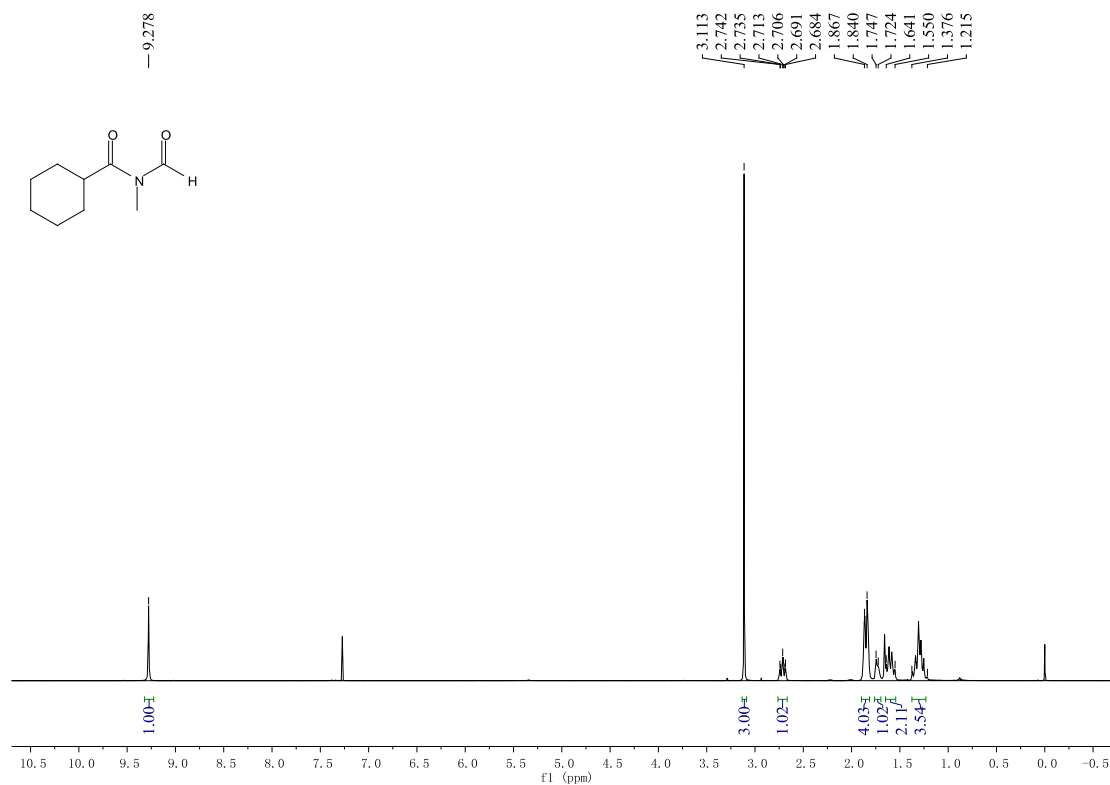


¹³C NMR

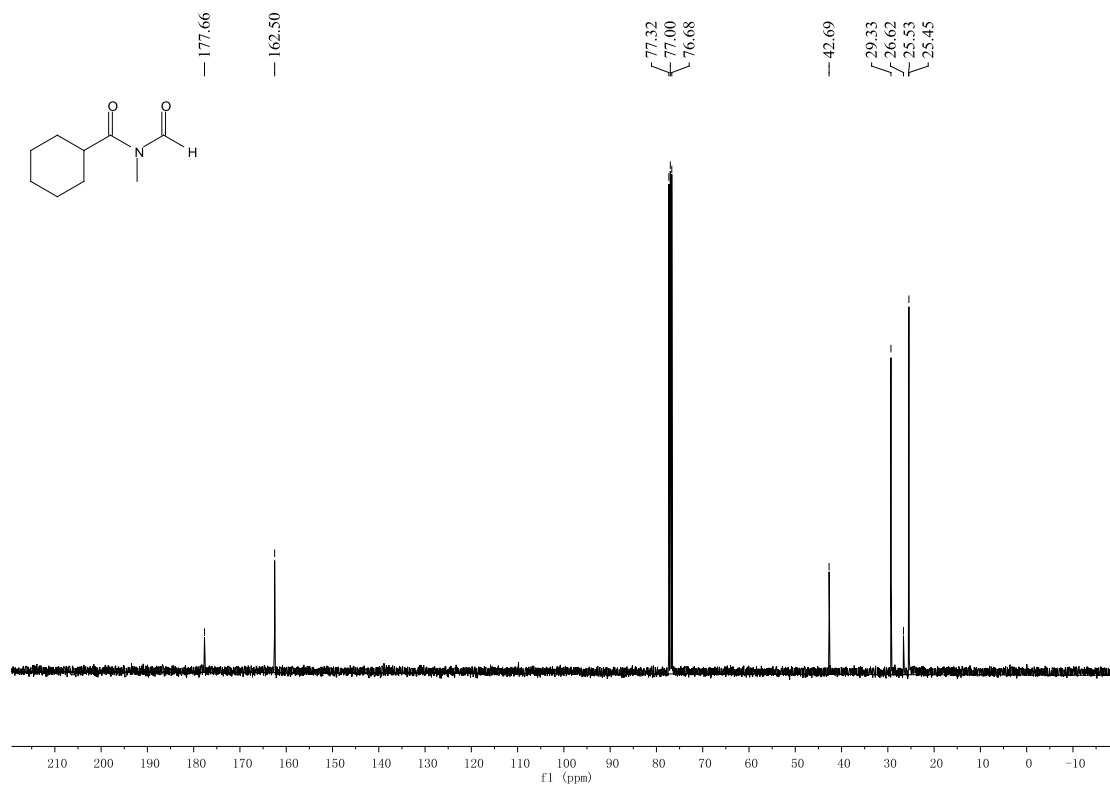


5ae

¹H NMR

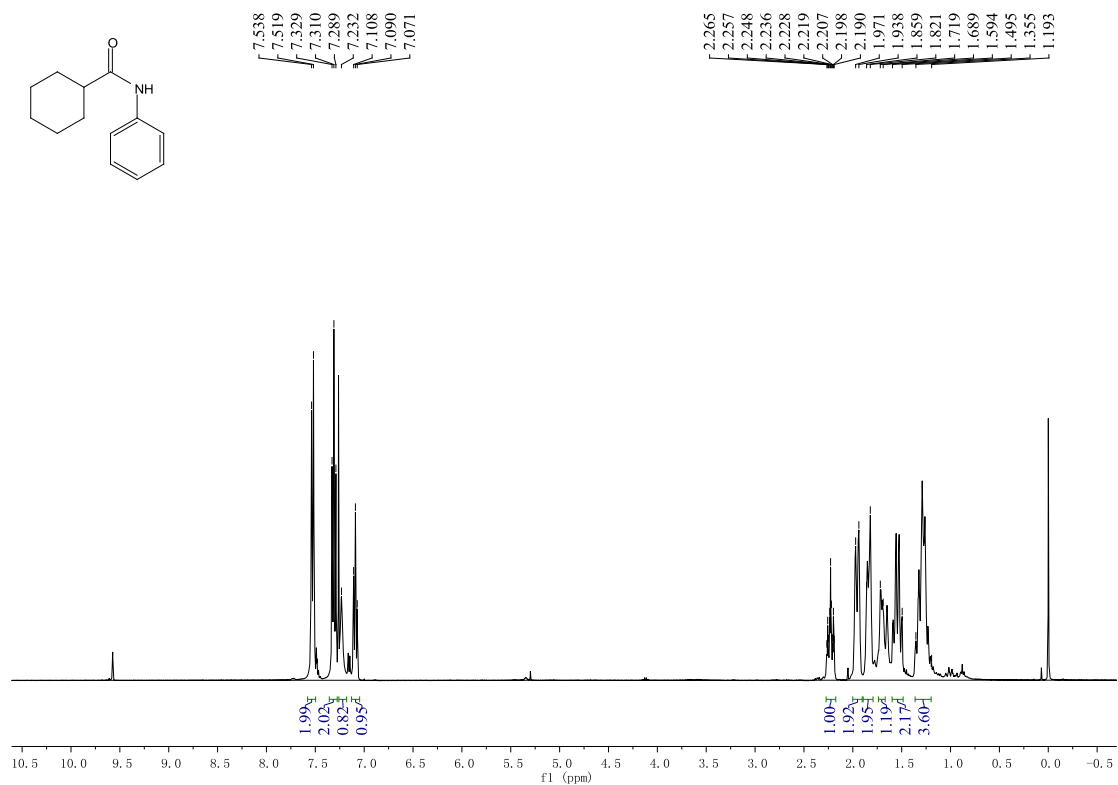


¹³C NMR

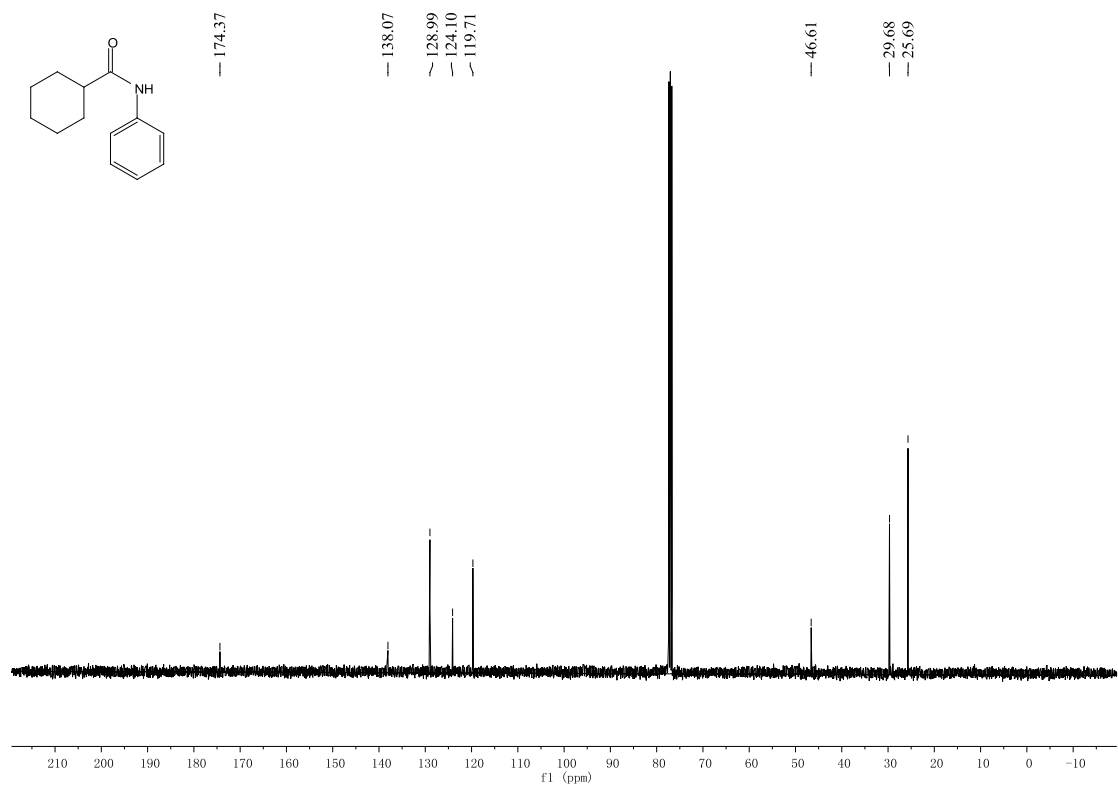


5af

¹H NMR

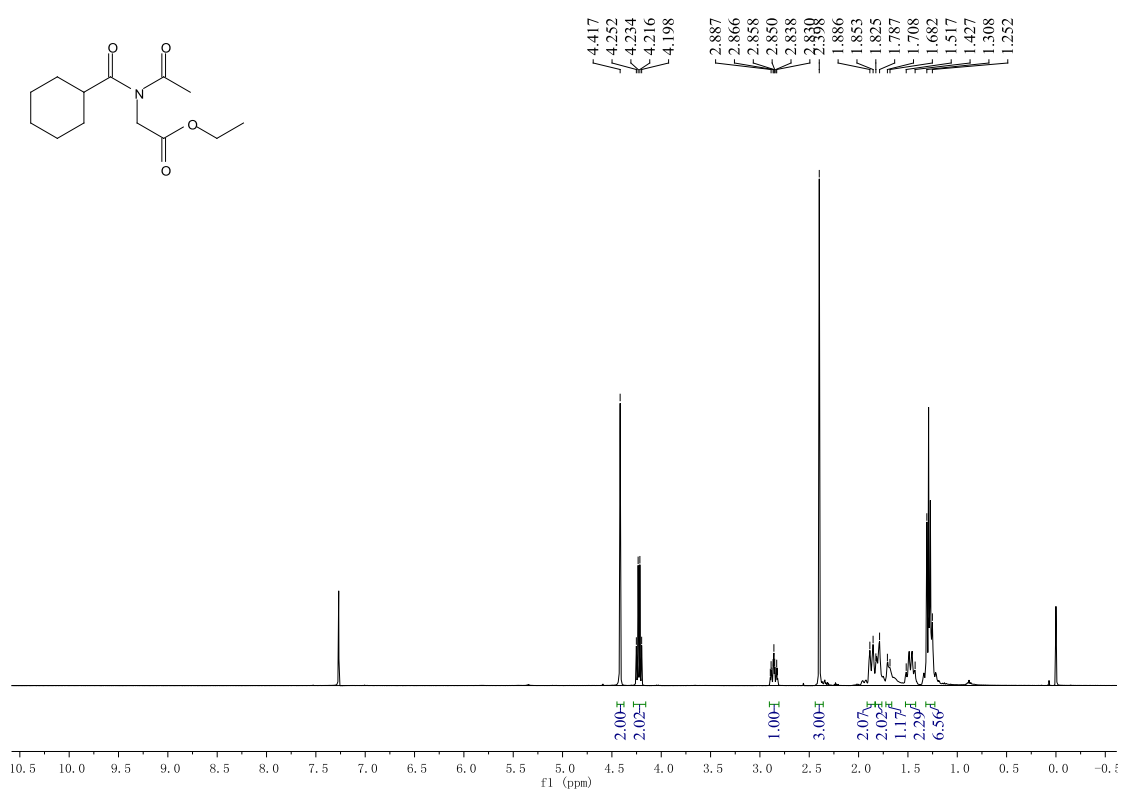


¹³C NMR



5ag

¹H NMR



¹³C NMR

