Electronic Supplementary Material (ESI) for ChemComm.

NHC-Catalyzed Radical Acylation of Cycloalkylsilyl Peroxides to Access 1,6-, 1,7-, and 1,8-Diketones

Chaolei Liu, Jingyi Wang, Xinlong Liu, Jie Feng, * Ding Du*

State Key Laboratory of Natural Medicines, School of Science, China Pharmaceutical University, Nanjing 210009, P. R. China

Email: 1020162519@cpu.edu.cn (J. Feng); ddmn9999@cpu.edu.cn (D. Du)

Table of Contents

1. General information S2

2. General procedure for the synthesis of products 3..... S2

3. A scale-up synthesis of product 3a S3

4. Coupling of 1,6-diketone 3d with Lenalidoamide.....S3

5. Characterization of the products..... S4

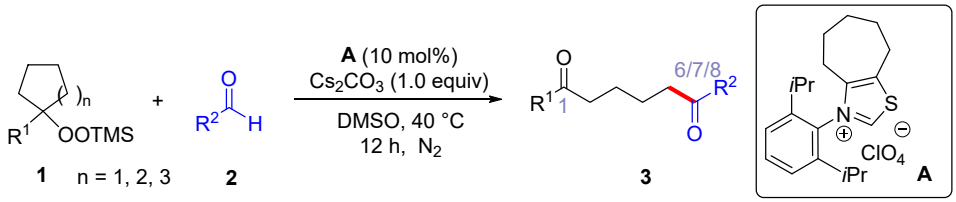
6. Reference..... S16

7. Copies of the NMR spectra..... S17

1. General information

Unless otherwise noted, all reactants or reagents including dry solvents were obtained from commercial suppliers and used as received. All the reactions were conducted using reaction tube (25 mL). The reactions were performed under nitrogen atmosphere. Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F25 plates. Column chromatograph was performed on silica gel 200~300 mesh. ^{1}H,^{13}C and ^{19}F NMR spectra were obtained in $CDCl_3$ using 300 MHz, 400 MHz Varian NMR spectrometer. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual $CDCl_3$ (7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constant in Hertz (Hz). Chemical shifts in ^{13}C NMR spectra are reported in ppm on the δ scale from the central peak of residual $CDCl_3$ (77 ppm). Chemical shifts in ^{19}F NMR are reported in ppm on the δ scale. High-resolution mass spectra were obtained on SCIEX X500B mass spectrometer with ESI source. Aldehydes **2x-y** and cycloalkyl silyl peroxides **1** were synthesized according to reported methods.[1-3]

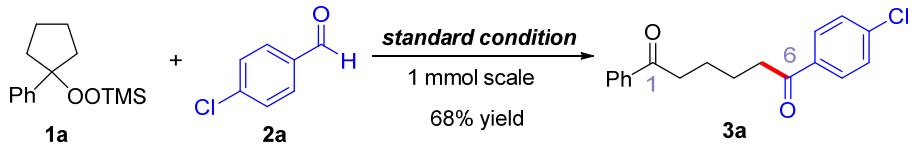
2. General procedure for the synthesis of products 3



1 2 3

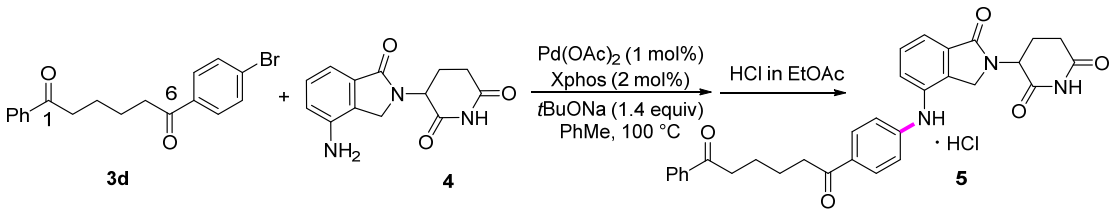
To an oven-dried reaction tube (25 mL) equipped with a Teflon® stir bar and fitted with a rubber septum were added aldehyde **2a** (14 mg, 0.1 mmol), NHC precatalyst **A** (4 mg, 0.01 mmol) and Cs_2CO_3 (32.6 mg, 0.1 mmol) and 25 mg of 4Å MS (molecular sieves). Then, the tube was evacuated and back-filled with nitrogen for three times. Subsequently, dry DMSO (2 mL) and cyclopentyl silyl peroxide **1** (0.3 mmol) were added under the protection of nitrogen. The reaction mixture was stirred at 40 °C (oil bath) for 12 hours. After completion of the reaction, the mixture was poured into 50 mL of water, which was extracted with EtOAc (20 mL×3). The combined organic extractions were washed by saturated brine solution (20 mL), respectively. Then, the organic phase was dried over anhydrous Na_2SO_4, and the solvent was removed under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 20/1) to give the products **3**.

3. A scale-up synthesis of product 3a



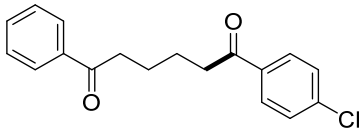
To an oven-dried reaction tube (50 mL) equipped with a Teflon® stir bar and fitted with a rubber septum were added 4-chlorobenzaldehyde **2a** (140 mg, 1 mmol), NHC precatalyst **A** (40 mg, 0.1 mmol), Cs_2CO_3 (326 mg, 1 mmol) and 250 mg of 4Å MS. Then, the tube was evacuated and back-filled with nitrogen for three times. Subsequently, dry DMSO (15 mL) and cyclopentyl silyl peroxide **1a** (750 mg, 3 mmol) were added under the protection of nitrogen. The reaction was stirred at 40℃ (oil bath) for 12 hours. After completion of the reaction, the mixture was poured into 100 mL of water, which was extracted with EtOAc (30 mL×3). The combined organic extractions were washed by saturated brine solution (50 mL), respectively. Then, the organic phase was dried over anhydrous Na_2SO_4, and the solvent was removed under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 20/1) to give the product **3a** as a white solid (204 mg, 68% yield).

4. Coupling of 1,6-diketone 3d with Lenalidoamide

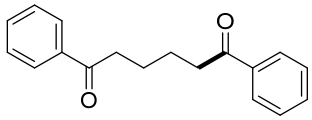


To an oven-dried reaction tube (25 mL) equipped with a Teflon® stir bar and fitted with a rubber septum were added diketone **3d** (25 mg, 0.074 mmol, 1.0 equiv), amine **4** (23 mg, 0.88 mmol, 1.2 equiv), *t*BuONa (9.9 mg, 0.1 mmol, 1.4 equiv), palladium acetate (0.14 mg, 0.00074 mol, 1 mol%), Xphos (0.76 mg, 0.0015 mol, 2 mol%). Then, the tube was evacuated and back-filled with nitrogen for three times. Subsequently, toluene (2 mL) was added to the above mixture under an atmosphere of nitrogen. The reaction was stirred at 100℃ (oil bath) for 12 hours. The reaction mixture was concentrated under reduced pressure and the resulting crude material was purified by column chromatography on silica gel (Methanol/methylene chloride 1/20). Add two drops of HCl (3.0 M in ethyl acetate) solution to the crude substance to obtain the product **5** as a white solid (38 mg, 80% yield).

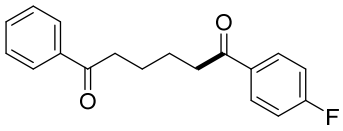
5. Characterization of the products



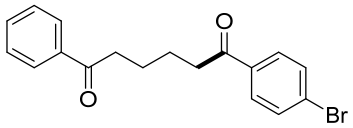
1-(4-chlorophenyl)-6-phenylhexane-1,6-dione (3a). White solid, mp: 137-138℃; 24.6 mg, 82% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3a**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.99 – 7.93 (m, 2H), 7.92 – 7.85 (m, 2H), 7.62 – 7.51 (m, 1H), 7.49 – 7.40 (m, 4H), 3.07 – 2.98 (m, 4H), 7.44 – 7.40 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 198.9, 139.5, 137.1, 135.4, 133.2, 129.6, 129.0, 128.7, 128.1, 38.6, 38.5, 23.9. HRMS (ESI) Calcd. for $C_{18}H_{17}ClO_2Na$ $(M+Na)^+$: 323.0822, found: 323.0809.



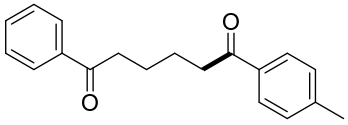
1,6-diphenylhexane-1,6-dione (3b). White solid, mp: 104-105℃; 21.6 mg, 81% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3b**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 7.4 Hz, 4H), 7.56 (t, *J* = 7.3 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 4H), 3.09 – 2.99 (m, 4H), 1.89 – 1.80 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 137.1, 133.1, 128.7, 128.2, 38.5, 24.0. HRMS (ESI) Calcd. for $C_{18}H_{18}O_2Na$ $(M+Na)^+$: 289.1199, found: 289.1215.



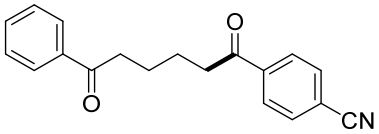
1-(4-fluorophenyl)-6-phenylhexane-1,6-dione (3c). White solid, mp: 132-133℃; 21.9 mg, 77% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3c**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 7.7 Hz, 2H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 3.07 – 2.97 (m, 4H), 1.87 – 1.80 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 198.4, 165.7(d, $^{1}J_{C\text{-}F}$ = 255.5 Hz), 137.0, 133.4(d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 133.0, 130.6 (d, $^{3}J_{C\text{-}F}$ = 9.3 Hz), 128.6, 128.0, 115.7 (d, $^{2}J_{C\text{-}F}$ = 21.9 Hz), 38.38, 38.36, 23.89, 23.86. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.51. HRMS (ESI) Calcd. for $C_{18}H_{17}FO_2Na$ $(M+Na)^+$: 307.1120, found: 307.1105.



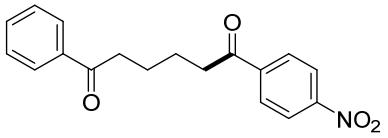
1-(4-bromophenyl)-6-phenylhexane-1,6-dione (3d). White solid, mp: 116-117℃; 25.9 mg, 75% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3d**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 7.7 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 3.08 – 2.96 (m, 4H), 1.86 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 199.1, 137.0, 135.7, 133.2, 132.0, 129.7, 128.7, 128.3, 128.1, 38.53, 38.48, 23.9, 23.9. HRMS (ESI) Calcd. for $C_{18}H_{17}O_2Na$ $(M+Na)^+$:367.0315; 369.0296. found: 367.0343; 369.0284.



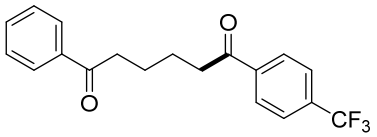
1-phenyl-6-(p-tolyl)hexane-1,6-dione (3e). White solid, mp: 110-111℃; 12.6 mg, 45% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3e**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 7.4 Hz, 2H), 7.86 (d, *J* = 8.1 Hz, 2H), 7.56 (t, *J* = 15.1 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 6.2 Hz, 2H), 3.06 – 2.98 (m, 4H), 2.41 (s, 3H), 1.86 – 1.81 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.2, 199.8, 143.9, 137.1, 134.6, 133.1, 129.4, 128.7, 128.3, 128.2, 38.6, 38.4, 24.2, 24.1, 21.8. HRMS (ESI) Calcd. for $C_{19}H_{20}O_2Na$ $(M+Na)^+$: 303.1372, found: 303.1356.



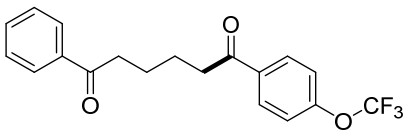
4-(6-oxo-6-phenylhexanoyl)benzonitrile (3f). White solid, mp: 149-150℃; 25.4 mg, 87% yield. The residue was purified by silica gel column chromatography EA:PE = 1:4 (v/v) to afford **3f**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 7.7 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 3.12 – 3.02 (m, 4H), 1.90 – 1.81 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.9, 198.6, 140.0, 137.0, 133.2, 132.6, 128.7, 128.5, 128.1, 118.1, 116.4, 38.9, 38.4, 23.8, 23.7. HRMS (ESI) Calcd. for $C_{19}H_{18}NO_2$ $(M+H)^+$: 292.1318, found: 292.1332.



1-(4-nitrophenyl)-6-phenylhexane-1,6-dione (3g). White solid, mp: 140-141℃; 26.1 mg, 84% yield. The residue was purified by silica gel column chromatography EA:PE = 1:4 (v/v) to afford **3g**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.3 Hz, 2H), 7.97 (d, *J* = 7.5 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 3.15 – 3.01 (m, 4H), 1.94 – 1.80 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.9, 198.4, 150.4, 141.5, 137.0, 133.2, 129.2, 128.8, 128.1, 124.0, 39.2, 38.4, 23.8, 23.7. HRMS (ESI) Calcd. for $C_{18}H_{18}NO_4$ $(M+H)^+$: 312.1213, found: 312.1230.

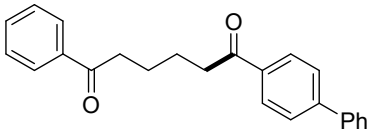


1-phenyl-6-(4-(trifluoromethyl)phenyl)hexane-1,6-dione (3i). White solid, mp: 130-131℃; 29.1 mg, 87% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford 3i. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.1 Hz, 2H), 8.01 – 7.92 (m, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.61 – 7.52 (m, 1H), 7.51 – 7.41 (m, 2H), 3.12 – 3.00 (m, 4H), 1.92 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.0, 199.1, 139.6, 137.0, 134.4 (q, $^{2}J_{C\text{-}F}$ = 32.8 Hz), 133.2, 128.7, 128.5, 128.1, 125.8(q, $^{3}J_{C\text{-}F}$ = 3.7 Hz), 123.7(q, $^{1}J_{C\text{-}F}$ = 273.9 Hz), 38.9, 38.4, 23.83, 23.75. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -63.08. HRMS (ESI) Calcd. for $C_{19}H_{17}F_3NaO_2$ $(M+Na)^+$: 357.1082, found: 357.1073.

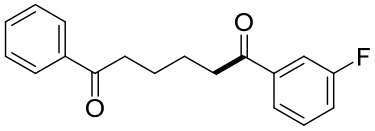


1-phenyl-6-(4-(trifluoromethoxy)phenyl)hexane-1,6-dione (3j). White solid, mp: 108-109℃; 19.3 mg, 55% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3j**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 7.2 Hz, 2H), 7.63 – 7.51 (m, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 3.10 – 2.97 (m, 4H), 1.91 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 198.5, 152.6(q, $^{3}J_{C\text{-}F}$ = 1.8 Hz), 137.0, 135.2, 133.2, 130.2, 128.7, 128.1, 120.5, 120.4(q $^{1}J_{C\text{-}F}$ = 260.0Hz), 38.6, 38.5, 23.89, 23.88. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -57.60. HRMS (ESI) Calcd. for $C_{19}H_{17}F_3NaO_3$

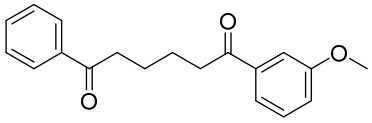
$(M+Na)^+$: 373.1036, found: 373.1022.



1-([1,1'-biphenyl]-4-yl)-6-phenylhexane-1,6-dione (3k). White solid, mp: 139-140℃; 18.5 mg, 54% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3k**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.08 – 8.00 (m, 2H), 8.00 – 7.93 (m, 2H), 7.72 – 7.66 (m, 2H), 7.66 – 7.59 (d, *J* = 7.1 Hz, 2H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.52 – 7.43 (m, 4H), 7.43 – 7.36 (m, 1H), 3.13 – 3.01 (m, 4H), 1.93 – 1.81 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.2, 199.8, 145.8, 140.0, 137.1, 135.8, 133.1, 129.1, 128.8, 128.7, 128.3, 128.2, 127.39, 127.37, 38.6, 38.6, 24.12, 24.06. HRMS (ESI) Calcd. for $C_{24}H_{22}NaO_2$ $(M+Na)^+$: 365.1523, found: 365.1512.

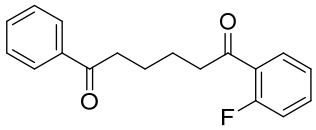


1-(3-fluorophenyl)-6-phenylhexane-1,6-dione (3l). White solid, mp: 84-85℃; 20.2 mg, 71% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3l**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 – 7.93 (m, 2H), 7.76 – 7.71 (m, 1H), 7.67 – 7.61 (m, 1H), 7.60 – 7.52 (m, 1H), 7.50 – 7.44 (m, 2H), 7.44 – 7.40 (m, 1H), 7.30 – 7.20 (m, 1H), 3.08 – 2.99 (m, 4H), 1.87 – 1.80 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 198.8 (d, $^4J_{C\text{-}F}$ = 2.0 Hz), 163.0 (d, $^1J_{C\text{-}F}$ = 252.5 Hz), 139.1(d, $^3J_{C\text{-}F}$ = 6.1 Hz), 137.0, 133.2, 130.4 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 128.7, 128.1, 123.9 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 120.1(d, $^2J_{C\text{-}F}$ = 22.2 Hz), 114.9 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 38.7, 38.5, 23.9, 23.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.88. HRMS (ESI) Calcd. for $C_{18}H_{17}FNaO_2$ $(M+Na)^+$: 307.1121, found: 307.1105.

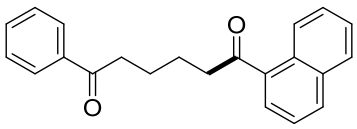


1-(3-methoxyphenyl)-6-phenylhexane-1,6-dione (3m). White solid, mp: 63-64℃; 22.1 mg, 76% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3m**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.00 – 7.93 (m, 2H), 7.59 – 7.52 (m, 2H), 7.51 – 7.46 (m, 3H), 7.46 – 7.42 (m, 1H), 7.15 – 7.07 (m, 1H), 3.86 (s, 3H), 3.09 – 2.99 (m, 4H), 1.88 –

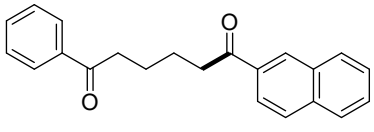
1.78 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.2, 200.0, 159.9, 138.4, 137.0, 133.2, 129.7, 128.7, 128.2, 120.8, 119.6, 112.3, 55.6, 38.7, 38.6, 24.1, 24.0. HRMS (ESI) Calcd. for $C_{19}H_{20}NaO_3$ $(M+Na)^+$: 319.1317, found: 319.1305.



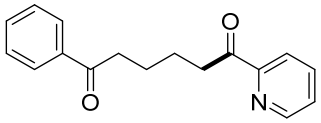
1-(2-fluorophenyl)-6-phenylhexane-1,6-dione (3n). White solid, mp: 91-92℃; 23.0 mg, 81% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3n**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.75 – 7.72 (m, 1H), 7.63 (m, *J* = 9.4 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.30 – 7.22 (m, 2H), 3.04 – 2.98 (m, 4H), 1.86 – 1.80 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.19, 200.18, 151.8 (d, $^1J_{C\text{-}F}$ = 239.4Hz), 137.1, 134.6 (d, $^2J_{C\text{-}F}$ = 13.1 Hz), 133.1, 128.7, 128.2, 124.5 (d, $^3J_{C\text{-}F}$ = 4.0 Hz), 118.7 (d, $^3J_{C\text{-}F}$ = 7.1 Hz), 117.0 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 115.3 (d, $^2J_{C\text{-}F}$ = 19.2 Hz), 38.55, 38.53, 24.04, 24.03. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -108.97. HRMS (ESI) Calcd. for $C_{18}H_{17}FNaO_2$ $(M+Na)^+$: 307.1116, found: 307.1105.



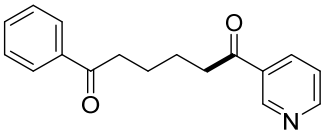
1-(naphthalen-2-yl)-6-phenylhexane-1,6-dione (3o). White solid, mp: 69-70℃; 18.0 mg, 57% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3o**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.33 (s, 1H), 9.33 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 2H), 7.90 (d, *J* = 7.3 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.51 (d, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 3.20 (t, *J* = 7.2 Hz, 2H), 3.03 (t, *J* = 6.7 Hz, 2H), 1.95 – 1.84 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 193.4, 146.8, 136.9, 133.1, 132.0, 131.0, 130.1, 128.63, 128.60, 128.0, 126.9, 125.6, 125.3, 124.1, 77.1, 38.3, 33.8, 30.2, 24.3. HRMS (ESI) Calcd.for $C_{22}H_{21}O_2$ $(M+H)^+$: 317.1548, found: 317.1536.



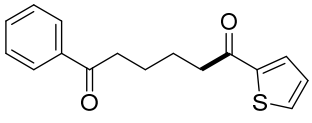
1-(naphthalen-2-yl)-6-phenylhexane-1,6-dione (3p). White solid, mp: 99-100℃; 22.5 mg, 71% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3p**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 (s, 1H), 8.03 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.97 (d, *J* = 7.5 Hz, 3H), 7.92 – 7.85 (t, 2H), 7.63 – 7.53 (m, 3H), 7.46 (t, *J* = 7.8 Hz, 2H), 3.17 (t, *J* = 6.6 Hz, 2H), 3.07 (t, *J* = 6.6 Hz, 2H), 1.94 – 1.85 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.2, 200.1, 137.1, 135.7, 134.4, 133.1, 132.7, 129.8, 129.7, 128.7, 128.6, 128.5, 128.2, 127.9, 126.9, 124.0, 38.64, 38.58, 24.2, 24.1. HRMS (ESI) Calcd.for $C_{22}H_{21}O_2$ $(M+H)^+$: 317.1548, found: 317.1536.



1-phenyl-6-(pyridin-3-yl)hexane-1,6-dione (3q). White solid, mp: 83-84℃; 24.6 mg, 92% yield. The residue was purified by silica gel column chromatography EA:PE = 1:4 (v/v) to afford **3q**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.65 (d, *J* = 4.3 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.95 (d, *J* = 7.6 Hz, 2H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.3 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 3H), 3.28 (t, *J* = 6.3 Hz, 2H), 3.3 (t, *J* = 6.3 Hz, 2H), 1.87 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.8, 200.2, 153.5, 149.0, 137.1, 137.0, 133.0, 128.6, 128.1, 127.2, 121.8, 38.5, 37.5, 24.0, 23.7. HRMS (ESI) Calcd.for $C_{17}H_{18}NO_2$ $(M+H)^+$: 268.1347, found: 268.1332.

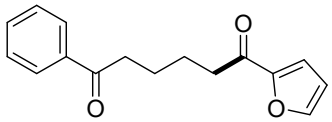


1-phenyl-6-(pyridin-3-yl)hexane-1,6-dione (3r). White solid, mp: 83-84℃; 23.0 mg, 86% yield. The residue was purified by silica gel column chromatography EA:PE = 1:4 (v/v) to afford **3r**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (s, 1H), 8.77 (d, *J* = 5.4 Hz, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.44 – 7.39 (m, 1H), 3.09 – 3.02 (m, 4H), 1.89 – 1.83 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.8, 200.2, 153.5, 149.0, 137.1, 137.0, 133.0, 128.6, 128.1, 127.2, 121.8, 38.5, 37.5, 24.0, 23.7. HRMS (ESI) Calcd.for $C_{17}H_{18}NO_2$ $(M+H)^+$: 268.1347, found: 268.1332.

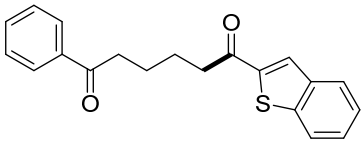


1-phenyl-6-(thiophen-2-yl)hexane-1,6-dione (3s). White solid, mp: 95-96℃; 19.3 mg, 71% yield.

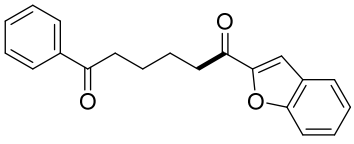
The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3s**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 7.4 Hz, 2H), 7.71 (d, *J* = 3.8 Hz, 1H), 7.62 (d, *J* = 4.9 Hz, 1H), 7.55 (m, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.17 – 7.08 (t, 1H), 3.08 – 3.00 (m, 2H), 3.00 – 2.93 (m, 2H), 1.88 – 1.80 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 193.1, 144.4, 137.0, 133.6, 133.1, 131.9, 128.7, 128.2, 128.1, 39.3, 38.4, 24.4, 24.0. HRMS (ESI) Calcd. for $C_{16}H_{16}NaO_2S$ $(M+Na)^+$:295.0776, found: 295.0763.



1-(furan-2-yl)-6-phenylhexane-1,6-dione (3t). White solid, mp: 90-91℃; 20.8 mg, 81% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3t**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 – 7.90 (m, 2H), 7.58 – 7.50 (m, 2H), 7.48 – 7.40 (m, 2H), 7.17 (d, *J* = 3.5 Hz, 1H), 6.51 (dd, *J* = 3.5, 1.6 Hz, 1H), 3.04 – 2.97 (m, 2H), 2.91 – 2.83 (m, 2H), 1.85 – 1.77 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 189.3, 152.8, 146.4, 137.0, 133.1, 128.6, 128.1, 117.1, 112.3, 38.4, 38.3, 23.90, 23.88. HRMS (ESI) Calcd.for $C_{16}H_{16}NaO_3$ $(M+Na)^+$: 279.1006, found: 279.0992.

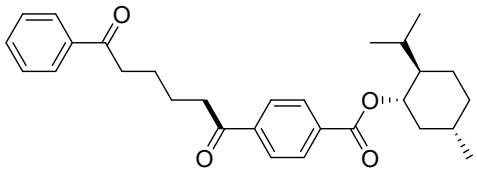


1-(benzo[b]thiophen-2-yl)-6-phenylhexane-1,6-dione (3u). Light yellow solid, mp: 150-151℃; 20.6 mg, 64% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3u**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 – 7.93 (m, 1H), 7.92 – 7.84 (m, 2H), 7.59 – 7.52 (m, 1H), 7.51 – 7.43 (m, 3H), 7.43 – 7.38 (m, 1H), 3.11 – 3.02 (m, 4H), 1.94 – 1.83 (m, 4H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 200.0, 194.6, 143.8, 142.6, 139.2, 137.0, 133.2, 129.1, 128.7, 128.2, 127.5, 126.0, 125.1, 123.1, 39.2, 38.4, 24.4, 24.0. HRMS (ESI) Calcd. for $C_{20}H_{18}NaO_2S$ $(M+Na)^+$: 345.0918, found 345.0925.

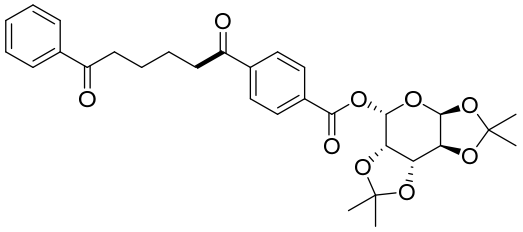


1-(benzofuran-2-yl)-6-phenylhexane-1,6-dione (3v). White solid, mp: 124-125℃; 17.5 mg, 57%

yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3v**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 7.3 Hz, 2H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.50 (s, 1H), 7.48 – 7.41 (m, 3H), 7.30 (t, *J* = 7.5 Hz, 1H), 3.06 – 2.99 (m, 4H), 1.90 – 1.82 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.9, 191.1, 155.6, 152.6, 137.0, 133.0, 128.6, 128.2, 128.1, 127.1, 123.9, 123.3, 112.8, 112.5, 38.8, 38.3, 23.9, 23.8. HRMS (ESI) Calcd. for $C_{20}H_{18}NaO_3$ $(M+Na)^+$: 329.1163, found 329.1148.

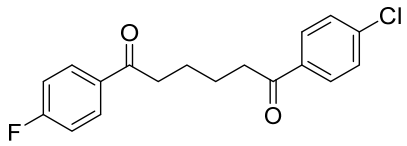


(1S,2R,5S)-2-isopropyl-5-methylcyclohexyl 4-(6-oxo-6-phenylhexanoyl)benzoate (3x). White solid, mp: 105-106℃; 31.8 mg, 71% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3x**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.3 Hz, 2H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.97 – 7.92 (d, 2H), 7.59 – 7.51 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 4.94 (td, *J* = 10.9, 4.4 Hz, 1H), 3.10 – 3.00 (m, 4H), 2.17 – 2.07 (m, 1H), 1.98 – 1.89 (m, 1H), 1.88 – 1.80 (m, 4H), 1.76 – 1.68 (m, 2H), 1.61 – 1.51 (m, 2H), 1.19 – 1.04 (m, 2H), 0.98 – 0.86 (m, 7H), 0.79 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 199.6, 165.3, 140.0, 137.0, 134.6, 133.1, 129.9, 128.7, 128.1, 128.0, 75.5, 47.3, 41.0, 38.9, 38.4, 34.3, 31.5, 26.6, 23.9, 23.8, 23.7, 22.1, 20.8, 16.6. HRMS (ESI) Calcd. for $C_{29}H_{37}NaO_4$ $(M+Na)^+$: 471.2513, found 471.2506.

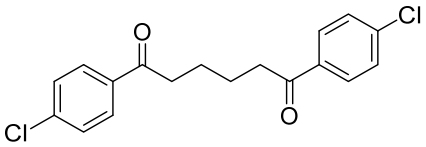


(3aS,5S,5aS,8aS,8bS)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl 4-(6-oxo-6-phenylhexanoyl)benzoate (3y). White solid, mp: 124-125℃; 39.3 mg, 73% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3y**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.95 (d, *J* = 7.3 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 5.56 (d, *J* = 4.9 Hz, 1H), 4.65 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.54 (dd, *J* = 11.6, 4.7 Hz, 1H), 4.45 (dd, *J* = 11.5, 7.7 Hz, 1H), 4.35 (dd,

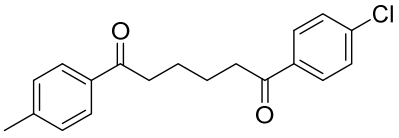
J = 5.0, 2.5 Hz, 1H), 4.32 (dd, *J* = 7.9, 1.6 Hz, 1H), 4.22 – 4.15 (m, 1H), 3.09 – 3.00 (m, 4H), 1.87 – 1.79 (m, 4H), 1.51 (s, 3H), 1.47 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 199.5, 165.7, 140.3, 137.0, 133.8, 133.1, 130.1, 128.7, 128.1, 128.0, 109.8, 108.9, 96.4, 71.2, 70.8, 70.6, 66.2, 64.4, 38.9, 38.4, 26.13, 26.08, 25.1, 24.6, 23.9, 23.8. HRMS (ESI) Calcd. for $C_{30}H_{34}NaO_9$ $(M+Na)^+$: 561.2136, found 561.2095.



1-(4-chlorophenyl)-6-(4-fluorophenyl)hexane-1,6-dione (3aa). White solid, mp: 133-134℃; 23.9 mg, 73% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3aa**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.94 (m, 2H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.13 (t, *J* = 8.6 Hz, 2H), 3.04 – 2.97 (m, 4H), 1.86 – 1.78 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.8, 198.4, 165.8(d, $^1J_{C\text{-}F}$ = 255.5 Hz), 139.5, 135.3, 133.4(d, $^4J_{C\text{-}F}$ = 2.8 Hz), 130.7(d, $^3J_{C\text{-}F}$ = 9.3 Hz), 129.6, 129.0, 115.8(d, $^2J_{C\text{-}F}$ = 21.9 Hz), 38.5, 38.4, 23.9, 23.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.40. HRMS (ESI) Calcd. for $C_{18}H_{18}NaO_2(M+Na)^+$: 341.0724, found: 341.0715.

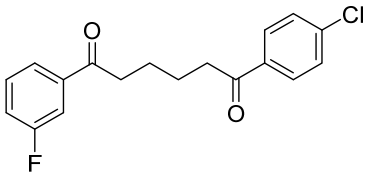


1,6-bis(4-chlorophenyl)hexane-1,6-dione (3ab). White solid, mp: 169-170℃; 28.1 mg, 84% yield. The residue was purified by silica gel column chromatography EA:PE = 1:5 (v/v) to afford **3ab**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (s, 4H), 7.43 (d, *J* = 8.4 Hz, 4H), 3.04 – 2.96 (m, 4H), 1.85 – 1.77 (m, 4H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 198.8, 139.6, 135.3, 129.6, 129.0, 38.5, 23.8. HRMS (ESI) Calcd. for $C_{18}H_{16}ClNaO_2(M+Na)^+$: 357.0432, found: 357.0420.

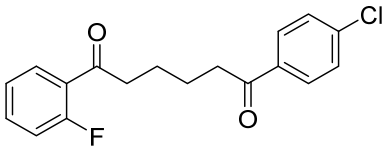


1-(4-chlorophenyl)-6-(p-tolyl)hexane-1,6-dione (3ac). White solid, mp: 148-149℃; 25.1 mg, 80% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to

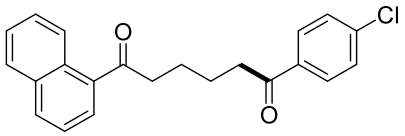
afford **3ac**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.93 – 7.82 (m, 4H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 7.0 Hz, 2H), 3.07 – 2.92 (m, 4H), 2.40 (s, 3H), 1.90 – 1.74 (m, 4H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 199.8, 198.9, 143.9, 139.5, 135.4, 134.6, 129.6, 129.4, 129.0, 128.3, 38.6, 38.4, 24.03, 23.96, 21.8. HRMS (ESI) Calcd. for $C_{19}H_{19}ClNaO_2(M+Na)^+$: 337.0978, found: 337.0966.



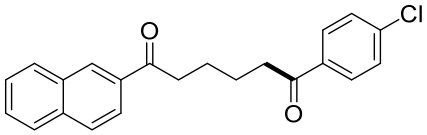
1-(4-chlorophenyl)-6-(3-fluorophenyl)hexane-1,6-dione (3ad). White solid, mp: 115-116℃; 25.8 mg, 81% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3ad**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 9.4 Hz, 1H), 7.48 – 7.40 (m, 3H), 7.30 – 7.20 (m, 2H), 3.05 – 2.98 (m, 4H), 1.86 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.8, 198.7(d, $^{4}J_{C\text{-}F}$ = 2.0 Hz), 163.0(d, $^{1}J_{C\text{-}F}$ = 248.5 Hz), 139.6, 139.1(d, $^{3}J_{C\text{-}F}$ = 5.0 Hz), 135.4, 130.4(d, $^{3}J_{C\text{-}F}$ = 7.1 Hz), 129.6, 129.1, 123.9(d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 120.2(d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 114.9(d, $^{2}J_{C\text{-}F}$ = 22.2 Hz), 38.7, 38.5, 23.84, 23.80. ^{19}F NMR (376 MHz, Chloroform-d) δ -111.85. HRMS (ESI) Calcd. for $C_{18}H_{16}ClFNaO_2(M+Na)^+$: 341.0726, found: 341.0715.



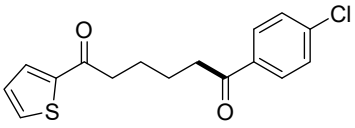
1-(4-chlorophenyl)-6-(2-fluorophenyl)hexane-1,6-dione (3ae). White solid, mp: 119-120℃; 19.4 mg, 81% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3ae**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.92 – 7.87 (m, 2H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.41 – 7.33 (m, 2H), 7.32 – 7.26 (m, 1H), 3.03 – 2.94 (m, 4H), 1.86 – 1.77 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.1, 198.8, 163.0(d, $^{1}J_{C\text{-}F}$= 248.5 Hz), 139.1(d, $^{3}J_{C\text{-}F}$= 7.0 Hz), 137.0, 133.2, 130.4(d, $^{3}J_{C\text{-}F}$= 7.0 Hz), 128.7, 128.2, 123.9(d, $^{4}J_{C\text{-}F}$= 2.0 Hz), 120.2(d, $^{2}J_{C\text{-}F}$= 21.2 Hz), 114.9(d, $^{2}J_{C\text{-}F}$= 22.2 Hz), 38.7, 38.5, 23.9, 23.8. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -108.97. HRMS (ESI) Calcd. for $C_{18}H_{16}ClFNaO_2(M+Na)^+$: 341.0729, found: 341.0715.



1-(4-chlorophenyl)-6-(naphthalen-1-yl)hexane-1,6-dione (3af). White solid, mp: 94-95℃; 29.1 mg, 83% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3af**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.32 (s, 1H), 9.33 (d, *J* = 8.1 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.92 – 7.84 (m, 3H), 7.72 – 7.65 (m, 1H), 7.65 – 7.57 (m, 1H), 7.50 (d, *J* = 7.3 Hz, 1H), 7.45 – 7.38 (m, 2H), 3.19 (t, *J* = 7.0 Hz, 2H), 2.99 (t, *J* = 6.6 Hz, 2H), 1.94 – 1.81 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.8, 193.4, 146.8, 139.6, 136.9, 135.3, 132.1, 131.1, 130.2, 129.5, 129.0, 128.7, 127.0, 125.8, 125.4, 124.2, 38.3, 33.8, 30.3, 24.3. HRMS (ESI) Calcd. For $C_{22}H_{20}ClO_2$ $(M+H)^+$: 351.1153, found: 351.1146.

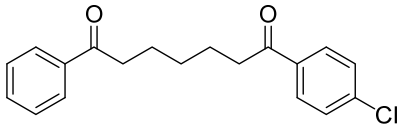


1-(4-chlorophenyl)-6-(naphthalen-2-yl)hexane-1,6-dione (3ag). White solid, mp: 141-142℃; 24.9 mg, 83% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3ag**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (s, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.93 – 7.85 (m, 4H), 7.64 – 7.58 (m, 1H), 7.57 – 7.52 (m, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 3.17 (t, *J* = 6.2 Hz, 2H), 3.03 (t, *J* = 6.1 Hz, 2H), 1.93 – 1.84 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 198.9, 139.6, 135.7, 135.4, 134.4, 132.7, 129.8, 129.7, 129.6, 129.0, 128.59, 128.55, 127.9, 126.9, 124.0, 38.6, 24.1, 24.0. HRMS (ESI) Calcd. For $C_{22}H_{20}ClO_2$ $(M+H)^+$: 351.1157, found:351.1146.

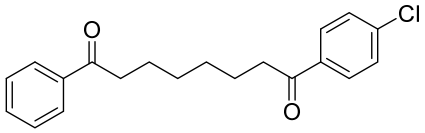


1-(4-chlorophenyl)-6-(thiophen-2-yl)hexane-1,6-dione (3ah). White solid, mp: 96-97℃; 29.6 mg, 73% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3ah**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 3.3 Hz, 1H), 7.62 (d, *J* = 4.8 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.16 – 7.09 (t, *J* = 4.2 Hz, 1H), 3.03 – 2.93 (m, 4H), 1.87 – 1.79 (m, 4H).13C NMR (101 MHz, Chloroform-*d*) δ 198.7, 192.9, 144.3, 139.4, 135.2, 133.5, 131.8, 129.5, 128.9, 128.1, 39.1, 38.3, 24.2, 23.8. HRMS (ESI) Calcd. for

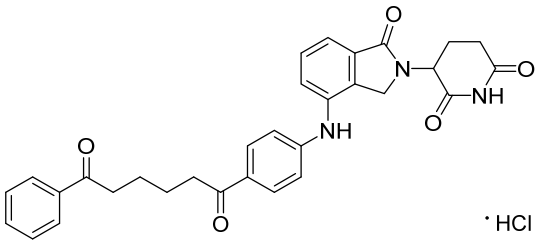
$C_{19}H_{19}ClNaO_2(M+Na)^+$: 329.0383, found: 329.0373.



1-(4-chlorophenyl)-7-phenylheptane-1,7-dione (3ak). Colorless transparent solid, mp: 66-67℃; 20.7 mg, 66% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3ak**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 – 7.93 (m, 2H), 7.92 – 7.86 (m, 2H), 7.59 – 7.52 (m, 1H), 7.49 – 7.40 (m, 4H), 3.03 – 2.92 (m, 4H), 1.84 – 1.73 (m, 4H), 1.53 – 1.43 (m, 2H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 200.4, 199.2, 139.5, 137.1, 135.4, 133.1, 129.6, 129.0, 128.7, 128.2, 38.42, 38.41, 29.0, 24.11, 24.08. HRMS (ESI) Calcd. for $C_{19}H_{19}ClNaO_2$ $(M+Na)^+$: 337.0977, found: 337.0966.



1-(4-chlorophenyl)-8-phenyloctane-1,8-dione (3al). Colorless transparent solid, mp: 111-112℃; 19.7 mg, 61% yield. The residue was purified by silica gel column chromatography EA:PE = 1:20 (v/v) to afford **3al**. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.99 – 7.93 (m, 2H), 7.92 – 7.86 (m, 2H), 7.60 – 7.51 (m, 1H), 7.50 – 7.44 (m, 2H), 7.44 – 7.39 (m, 2H), 3.01 – 2.90 (m, 4H), 1.82 – 1.68 (m, 4H), 1.50 – 1.37 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.5, 199.3, 139.4, 137.2, 135.4, 133.0, 129.6, 129.0, 128.7, 128.2, 38.6, 29.28, 29.27, 24.3, 24.2. HRMS (ESI) Calcd. for $C_{20}H_{21}ClO_2$ $(M+H)^+$: 329.1315, found: 329.1303.



3-(1-oxo-4-((4-(6-oxo-6-phenylhexanoyl)phenyl)amino)isoindolin-2-yl)piperidine-2,6-dione hydrochloride (5). Colorless transparent solid, mp: 294-295℃; The residue was purified by silica gel column chromatography MeOH:DCM = 1:20 (v/v) to afford **5**. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (s, 1H), 7.99 – 7.94 (m, 2H), 7.90 – 7.85 (m, 2H), 7.65 – 7.60 (m, 1H), 7.59 – 7.54 (m, 1H), 7.54 – 7.51 (m, 2H), 7.51 – 7.48 (m, 1H), 7.45 – 7.40 (m, 1H), 7.06 – 7.02 (m, 2H), 5.19 – 5.11 (m,

1H), 4.40 (d, J = 17.4 Hz, 1H), 4.32 (d, J = 17.4 Hz, 1H), 3.11 – 3.03 (m, 2H), 2.98 – 2.93 (m, 2H), 2.64 – 2.55 (m, 1H), 2.42 – 2.30 (m, 1H), 2.05 – 1.93 (m, 2H), 1.69 – 1.63 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 200.1, 199.5, 173.0, 171.3, 169.0, 143.7, 139.9, 136.7, 133.1, 132.8, 132.3, 128.9, 128.7, 128.6, 127.9, 125.6, 118.3, 116.5, 115.1, 110.5, 51.6, 45.6, 38.2, 37.8, 31.3, 23.3, 23.1, 22.8. for $C_{31}H_{29}N_3O_5Na$ $(M+Na)^+$: 546.2007, found: 546.1999.

6. References

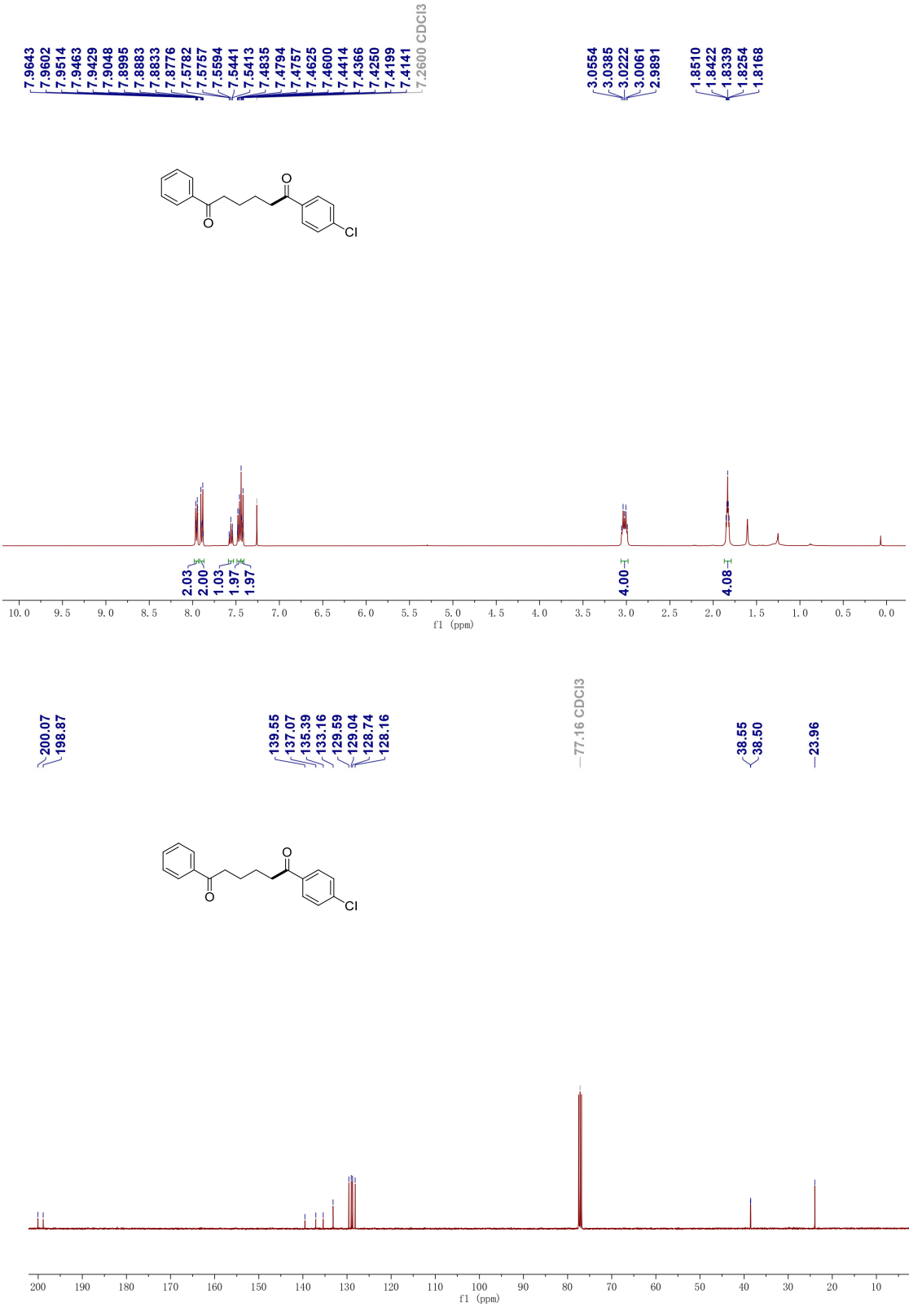
(1) Chen, L.; Lin, C.; Zhang, S.-M.; Zhang, X.-J.; Zhang, J.-M.; Xing, L.-J.; Guo, Y.-G.; Feng, J.; Gao, J.; Du, D. 1,4-Alkylcarbonylation of 1,3-Enynes to Access Tetra-substituted Allenyl Ketones via an NHC-catalyzed Radical Relay. *ACS Catal.*, **2021**, 11, 13363-13373.

(2) Sakamoto, Ryu; Kato, Terumasa; Sakurai, Shunya; Maruoka, Keiji. Copper-Catalyzed C(sp)-C(sp^3) Coupling of Terminal Alkynes with Alkylsilyl Peroxides via a Radical Mechanism. *Org. Lett*. **2018**, 20, 5, 1400–1403.

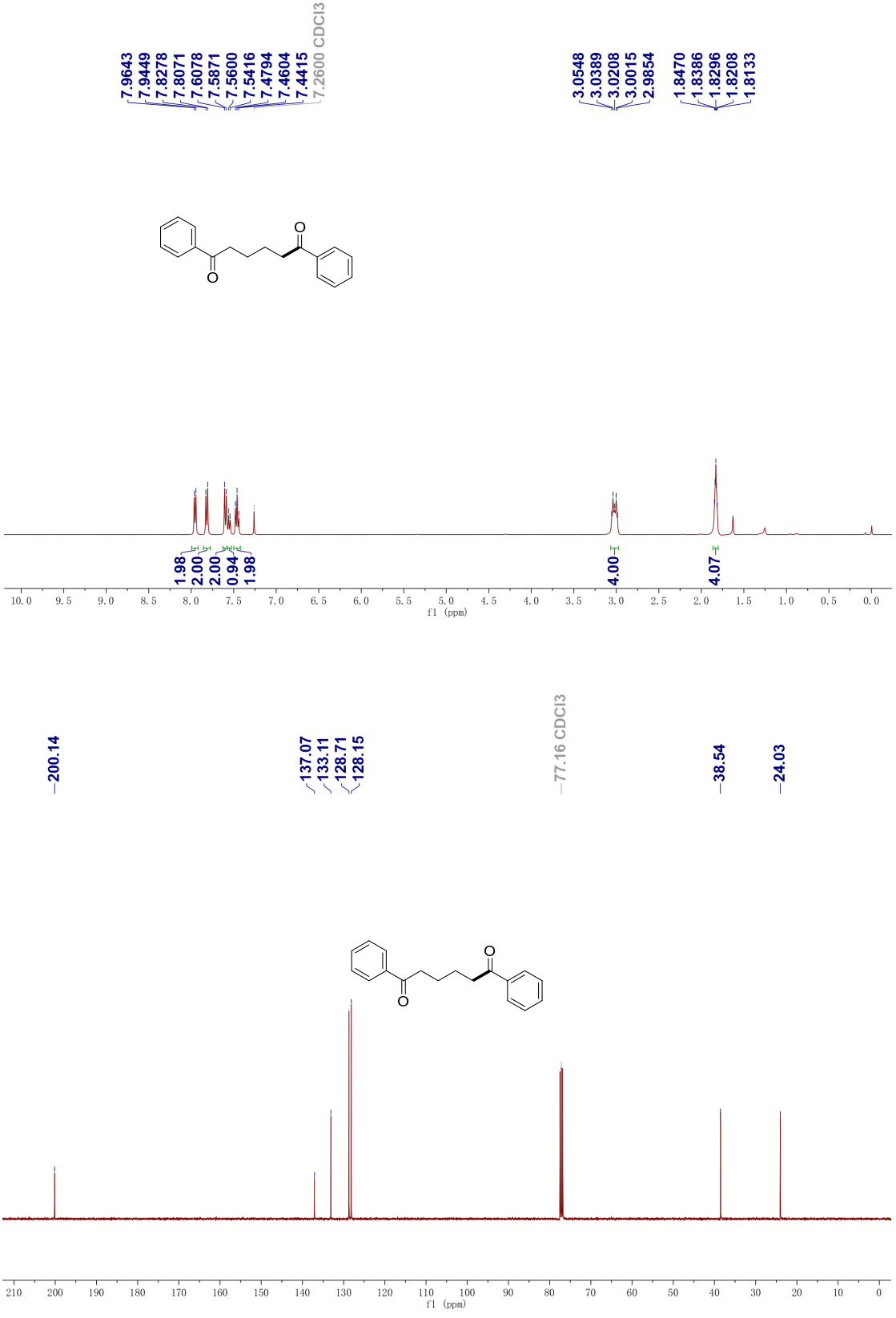
(3) Weiping Xu, Yan Liu, Terumasa Kato, and Keiji Maruoka. The Formation of C–C or C–N Bonds via the Copper-Catalyzed Coupling of Alkylsilyl Peroxides and Organosilicon C ompounds: A Route to Perfluoroalkylation.%*Org. Lett*. **2021**, 23, 5, 1809–1813.

7. Copies of the NMR spectra

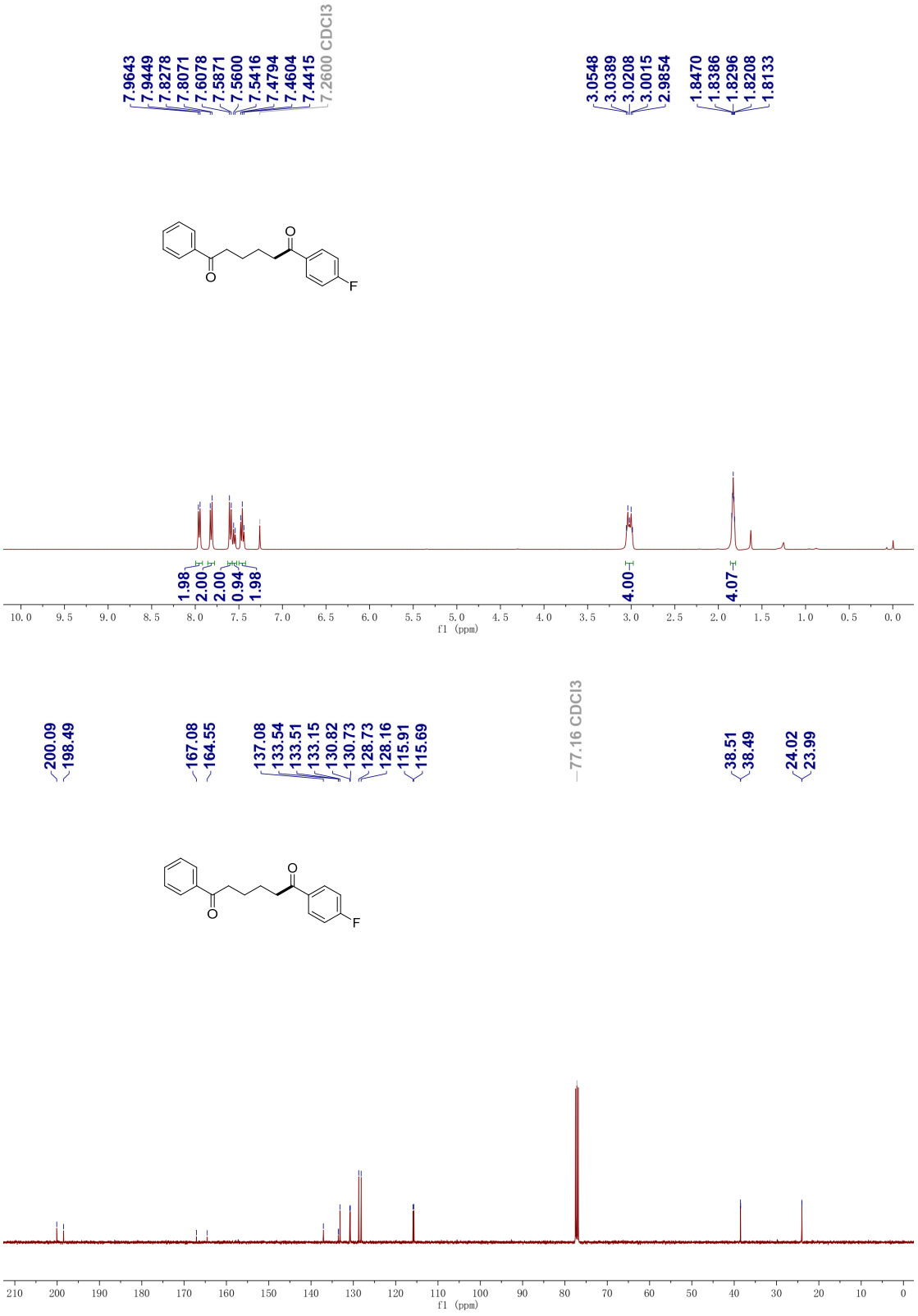
3a. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



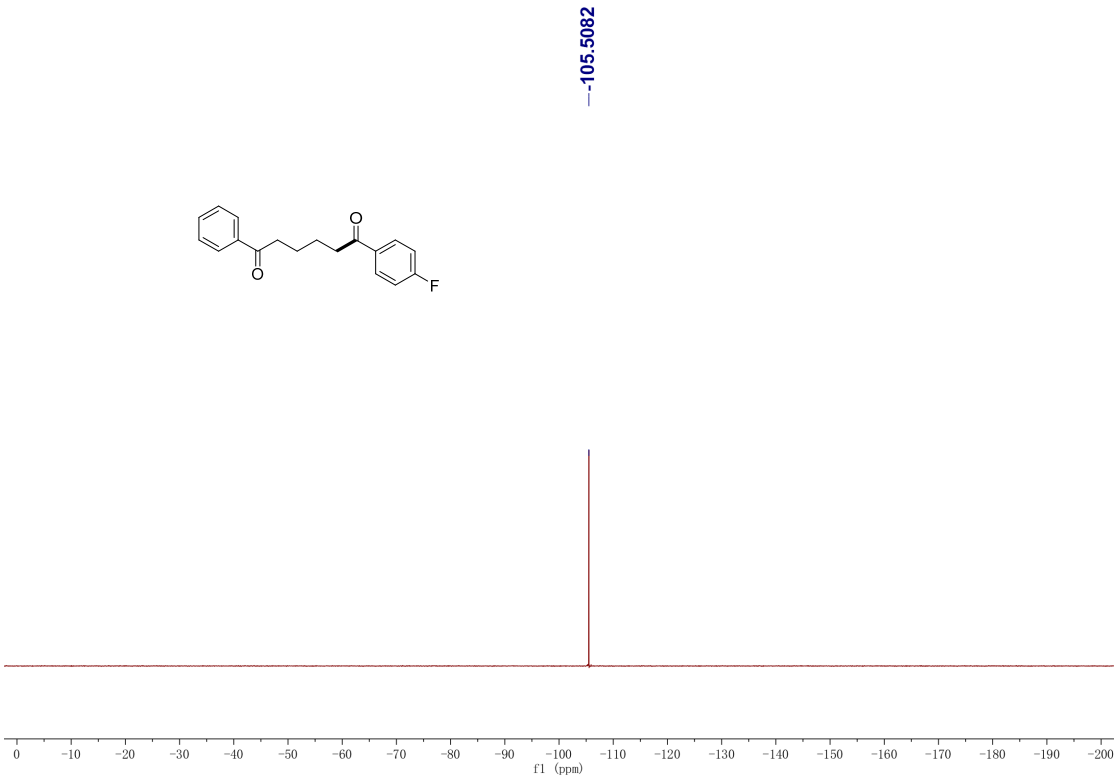
3b. ^{1}H NMR (400 MHz, Chloroform-*d*) /^{13}C NMR (101 MHz, Chloroform-*d*)



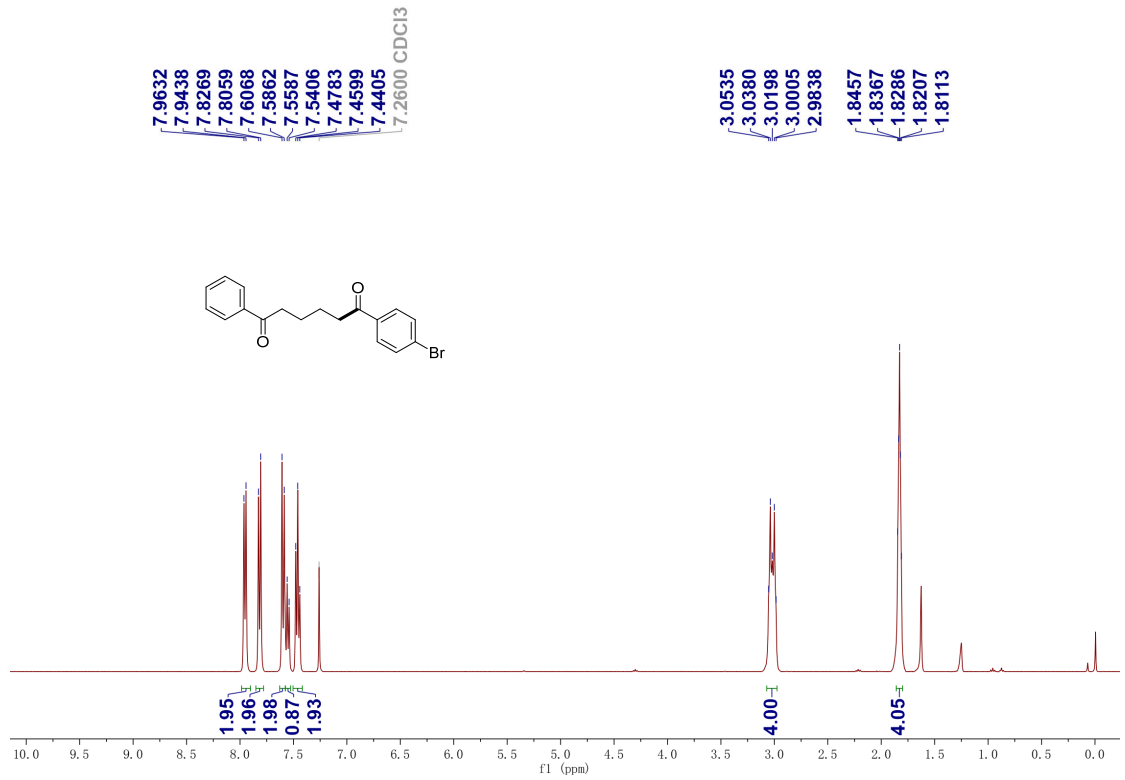
3c. ^{1}H NMR (300 MHz, Chloroform-d) /^{13}C NMR (101 MHz, Chloroform-*d*)

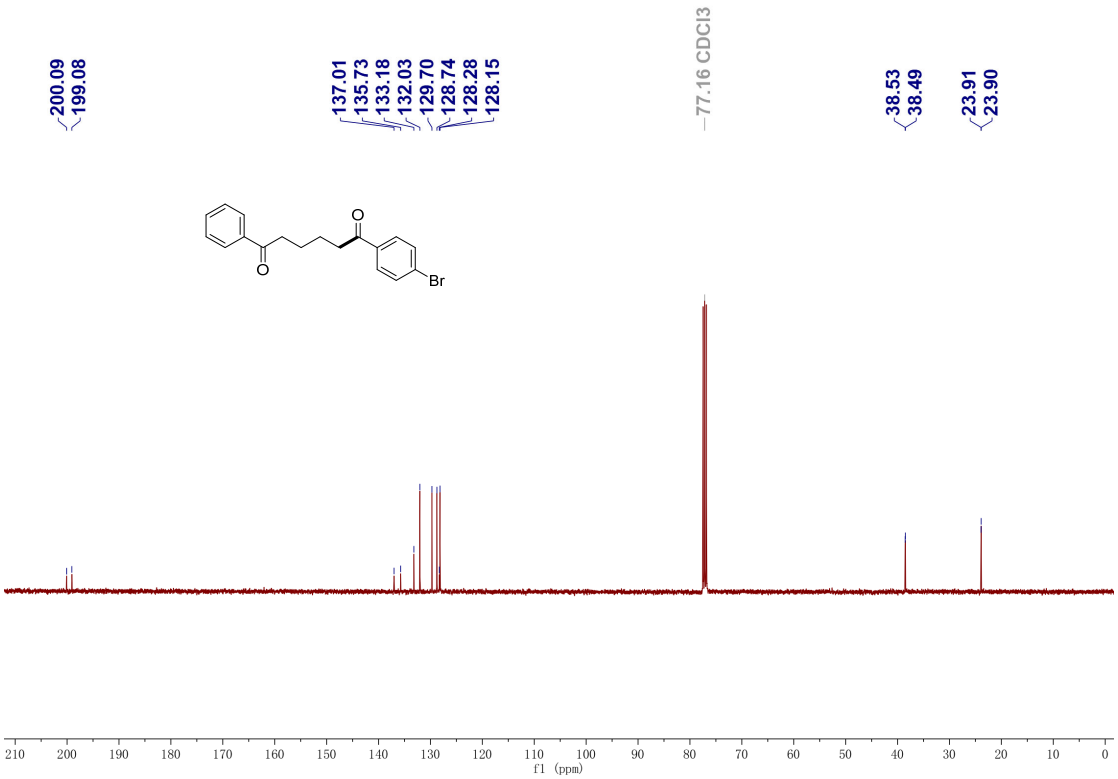


3c. ^{19}F NMR (376 MHz, Chloroform-*d*).

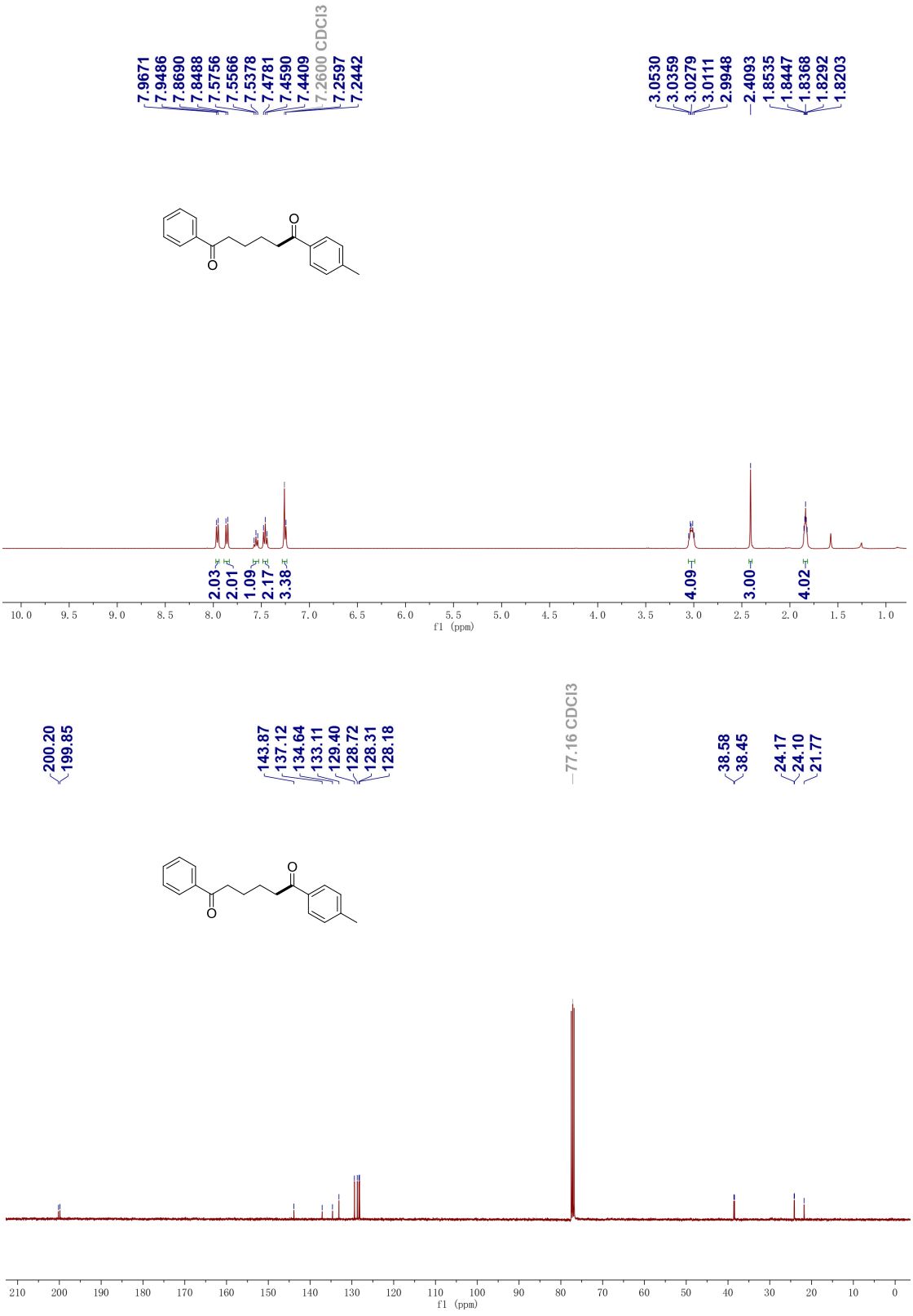


3d. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)

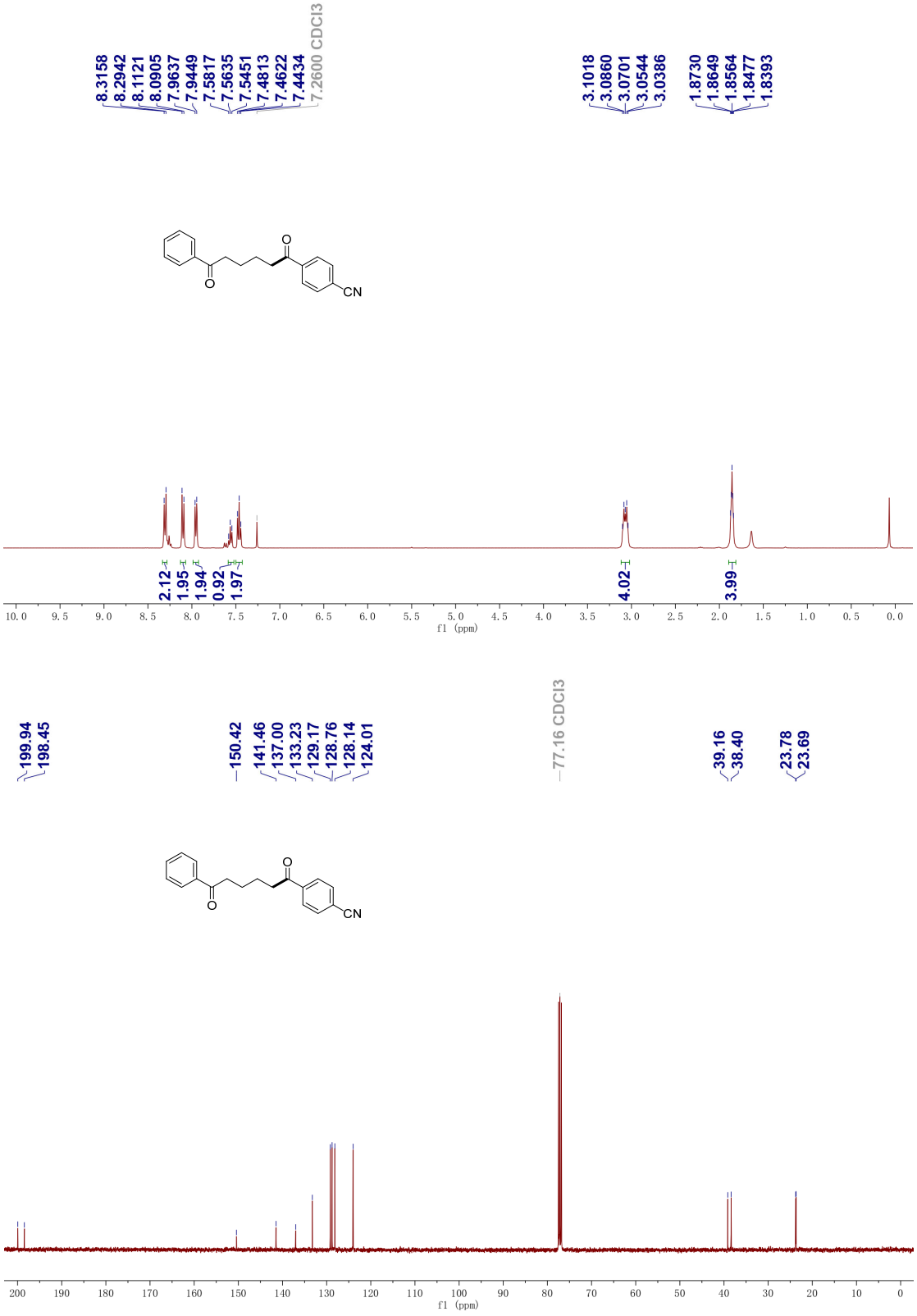




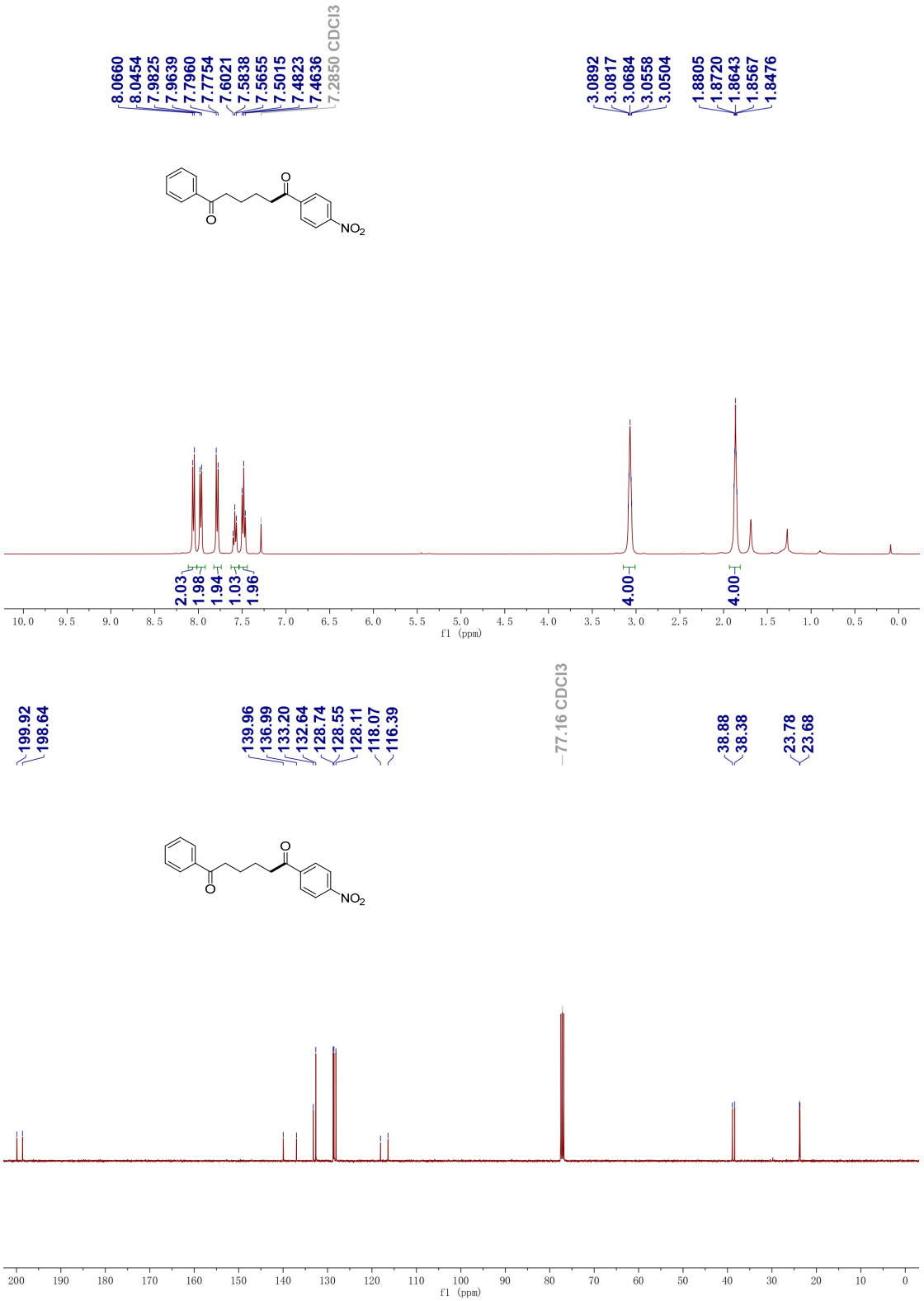
3e. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



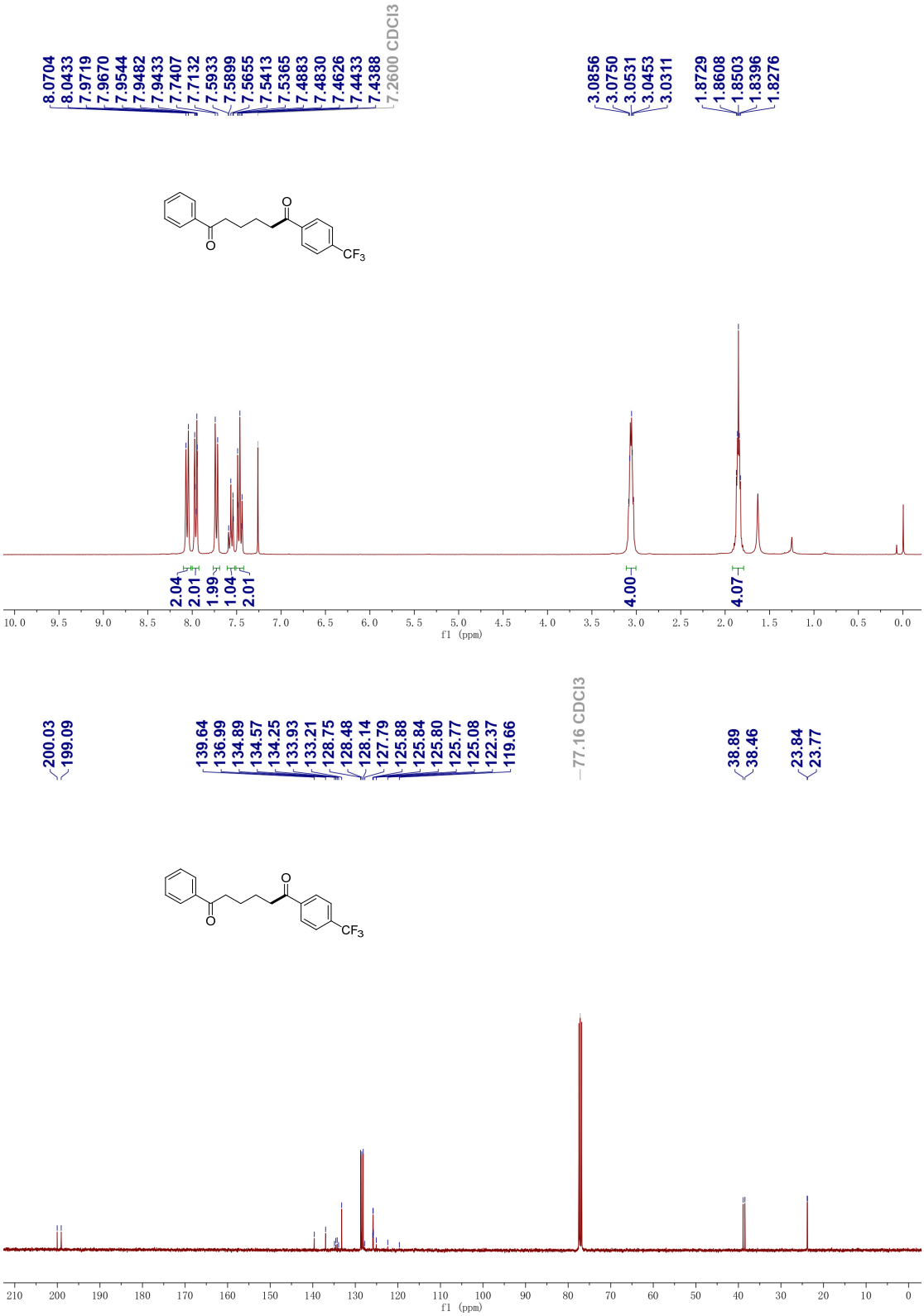
3f. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



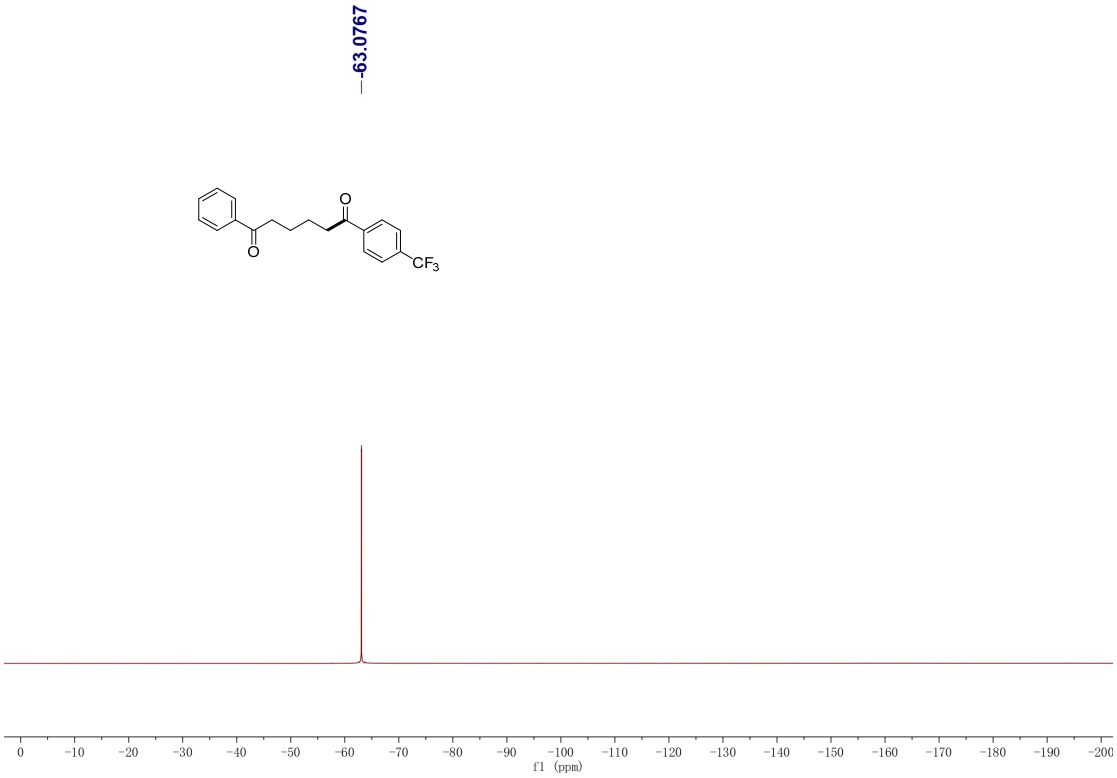
3g. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



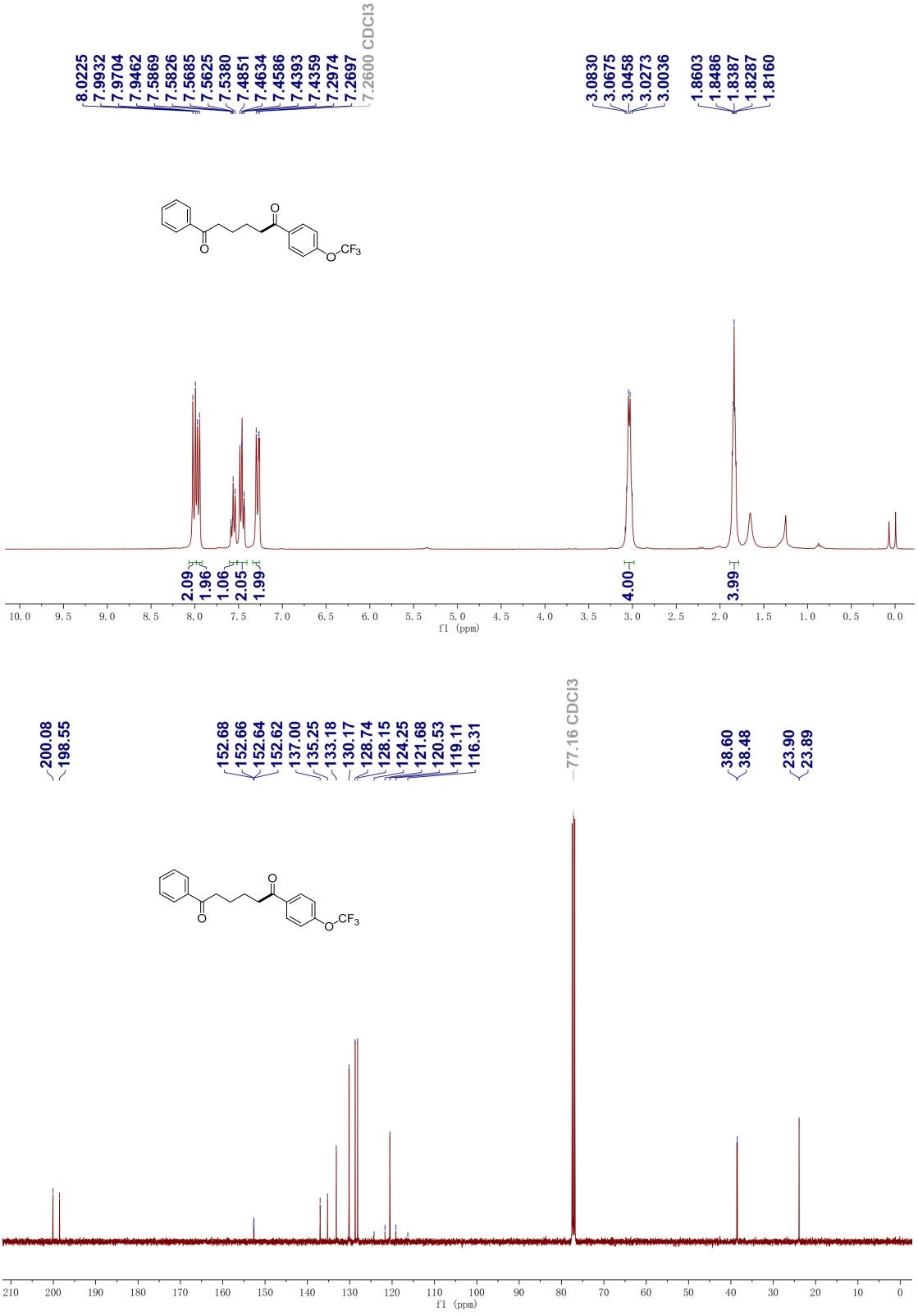
3i. ^{1}H NMR (300 MHz, Chloroform-*d*) /^{13}C NMR (101 MHz, Chloroform-*d*)



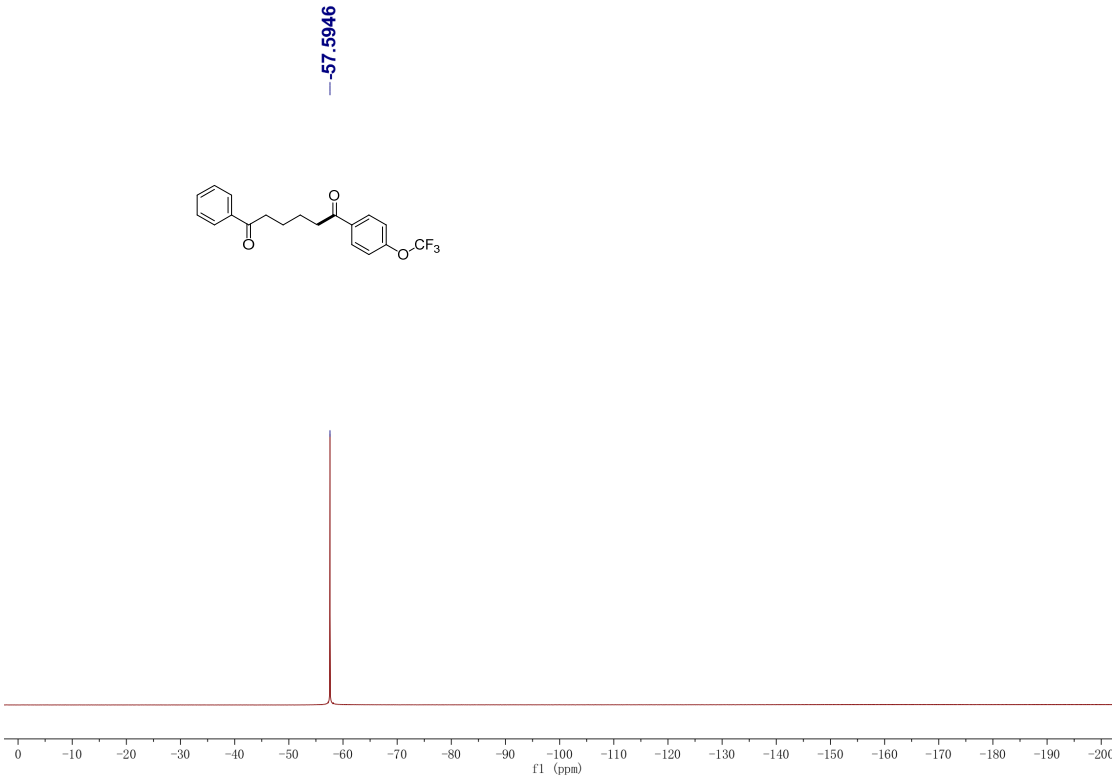
3i. ^{19}F NMR (282 MHz, Chloroform-*d*)



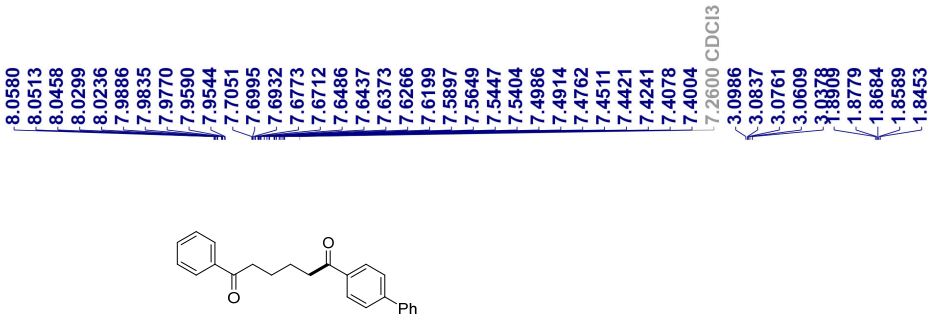
3j. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)

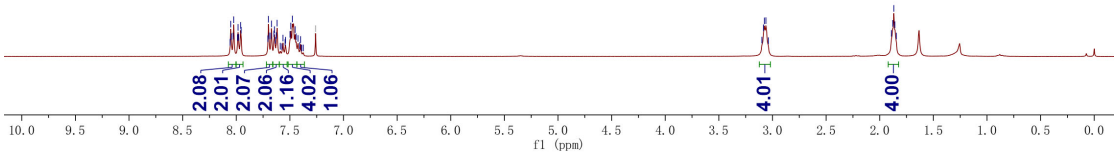


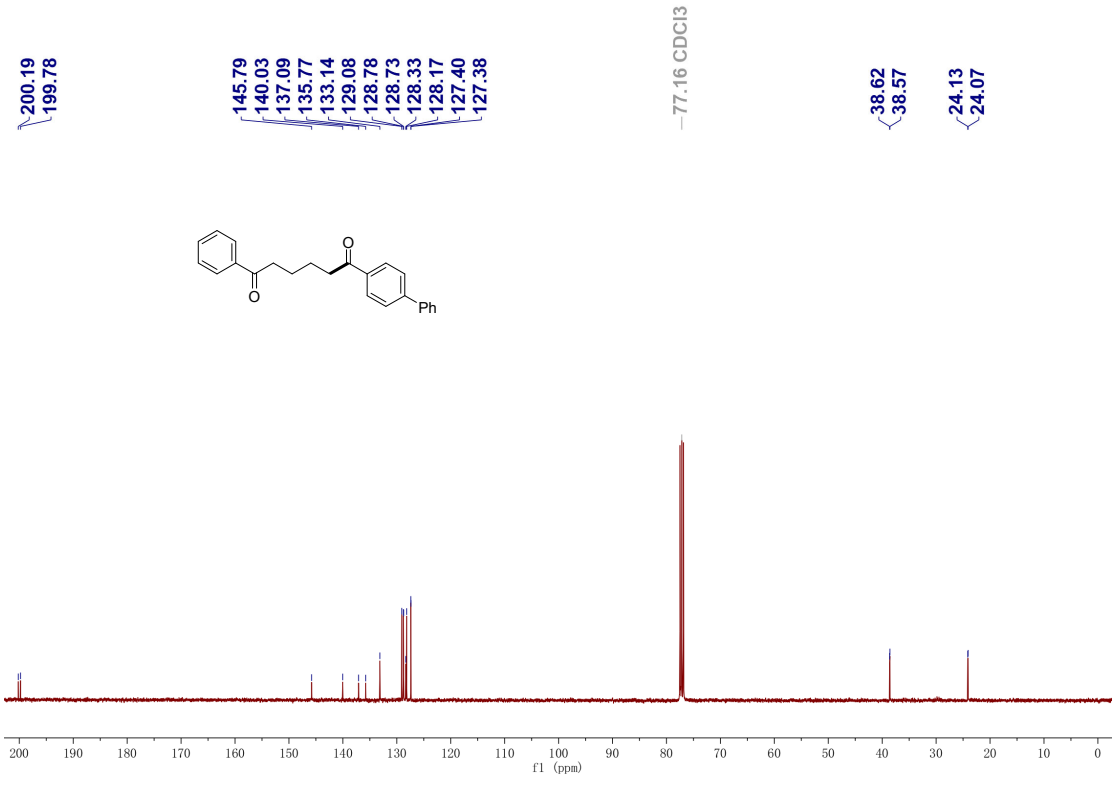
3j. ^{19}F NMR (282 MHz, Chloroform-*d*)



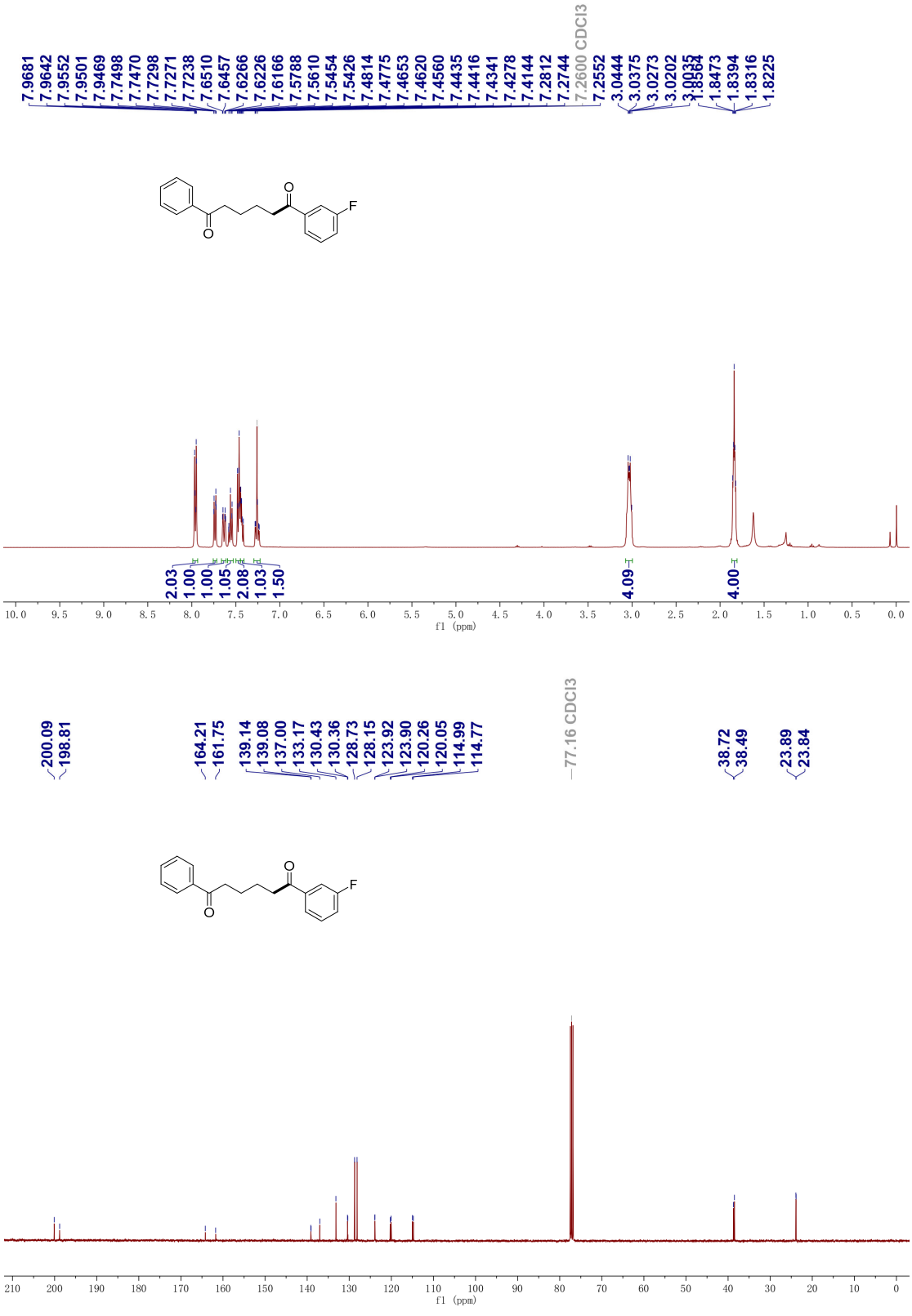
3k. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



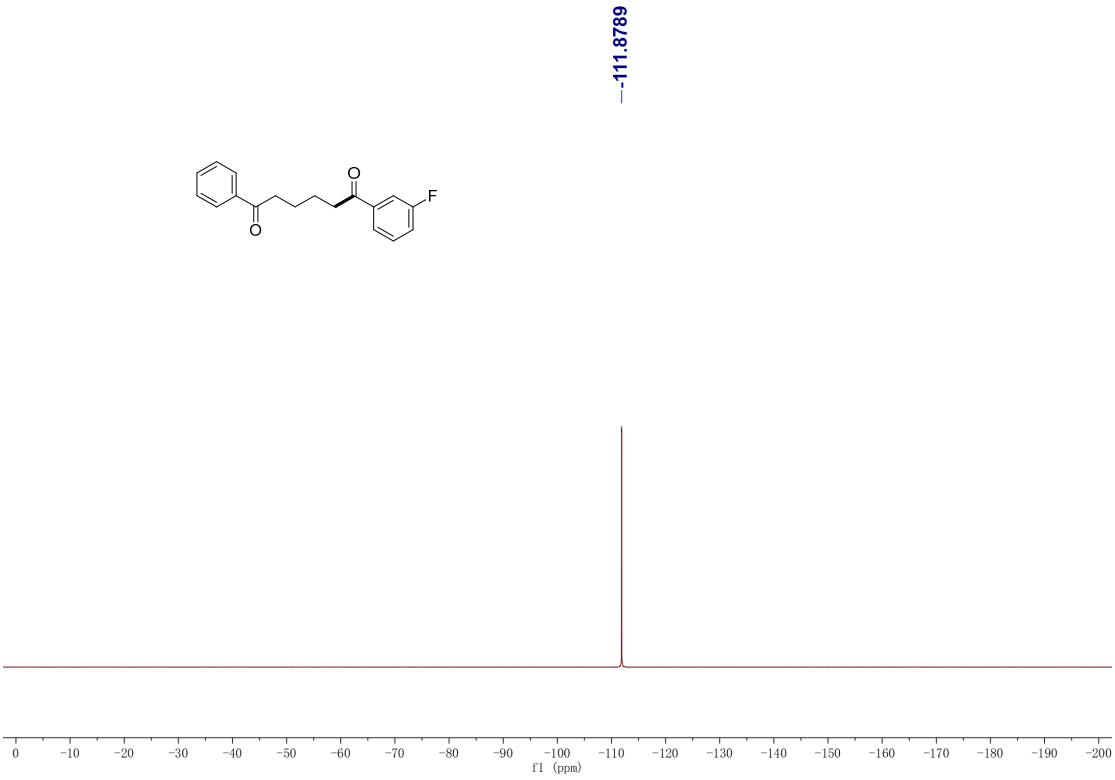




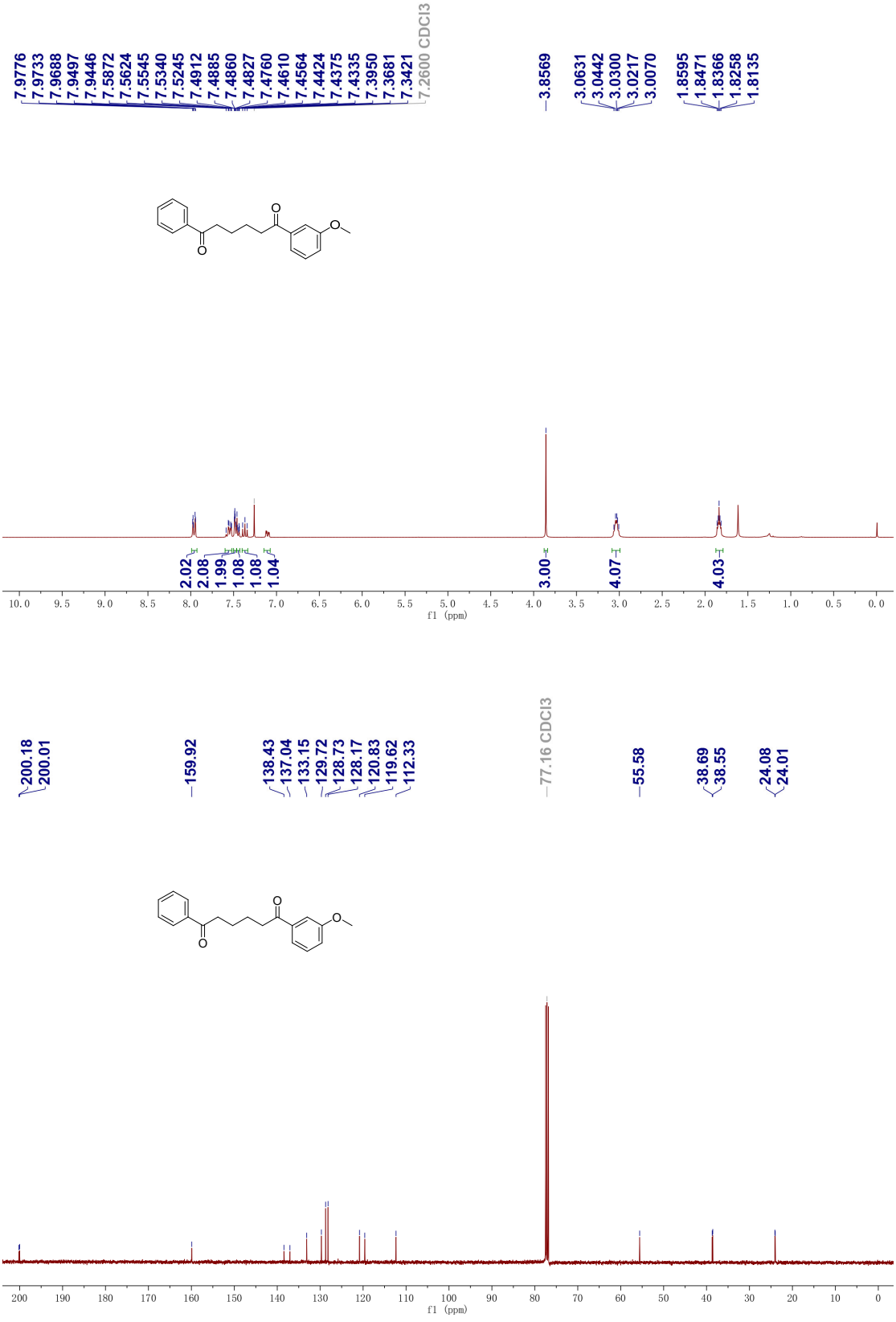
3l. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



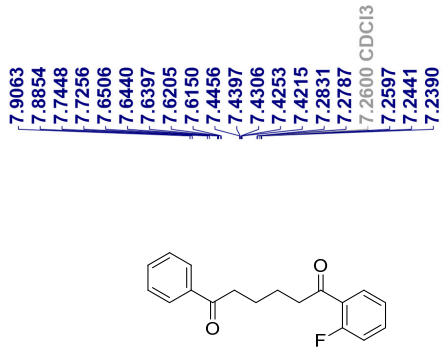
3l. ^{19}F NMR (376 MHz, Chloroform-*d*)

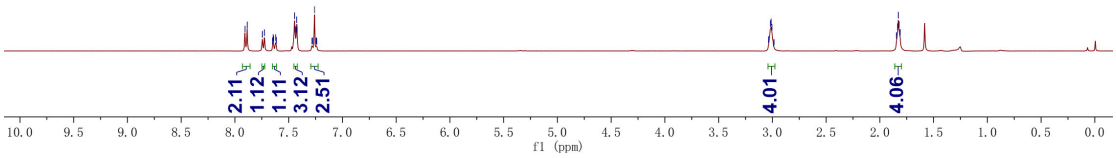


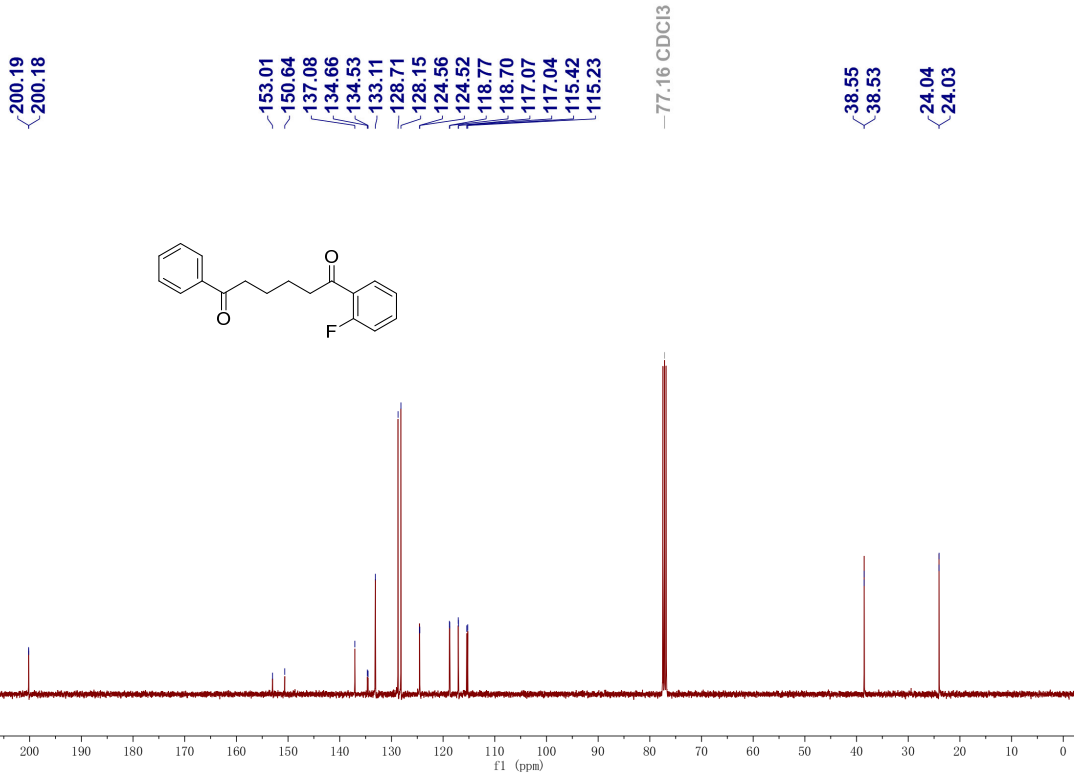
3m. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



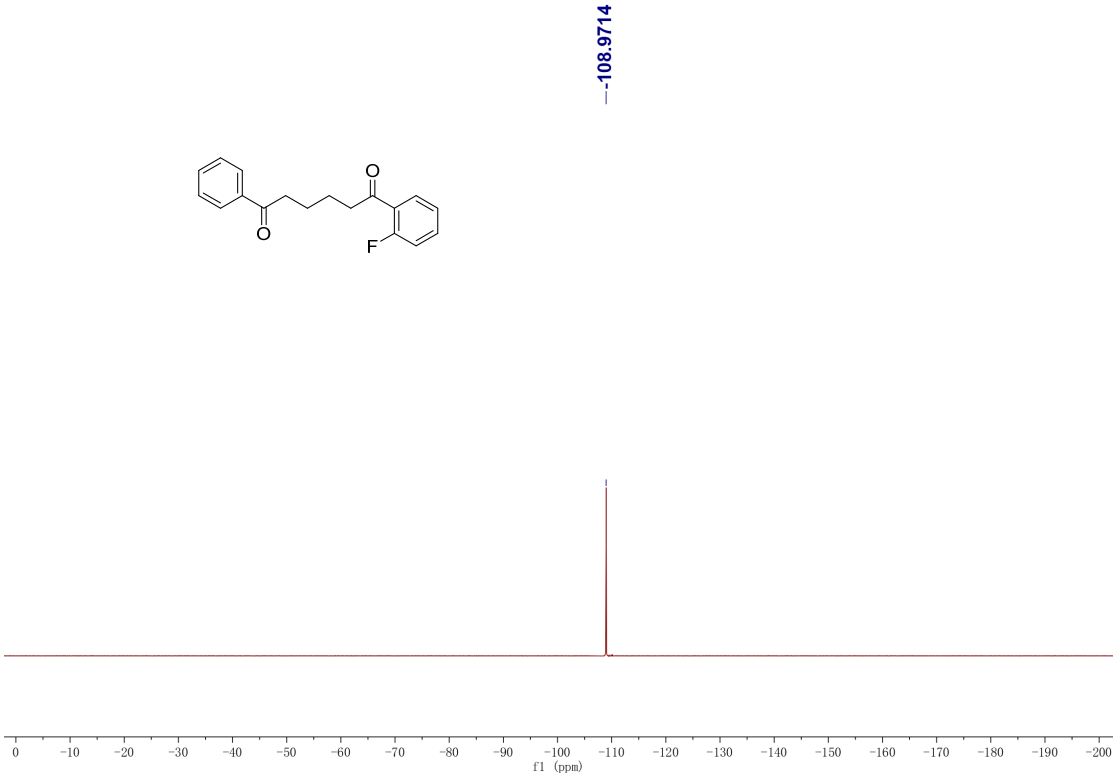
3n. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



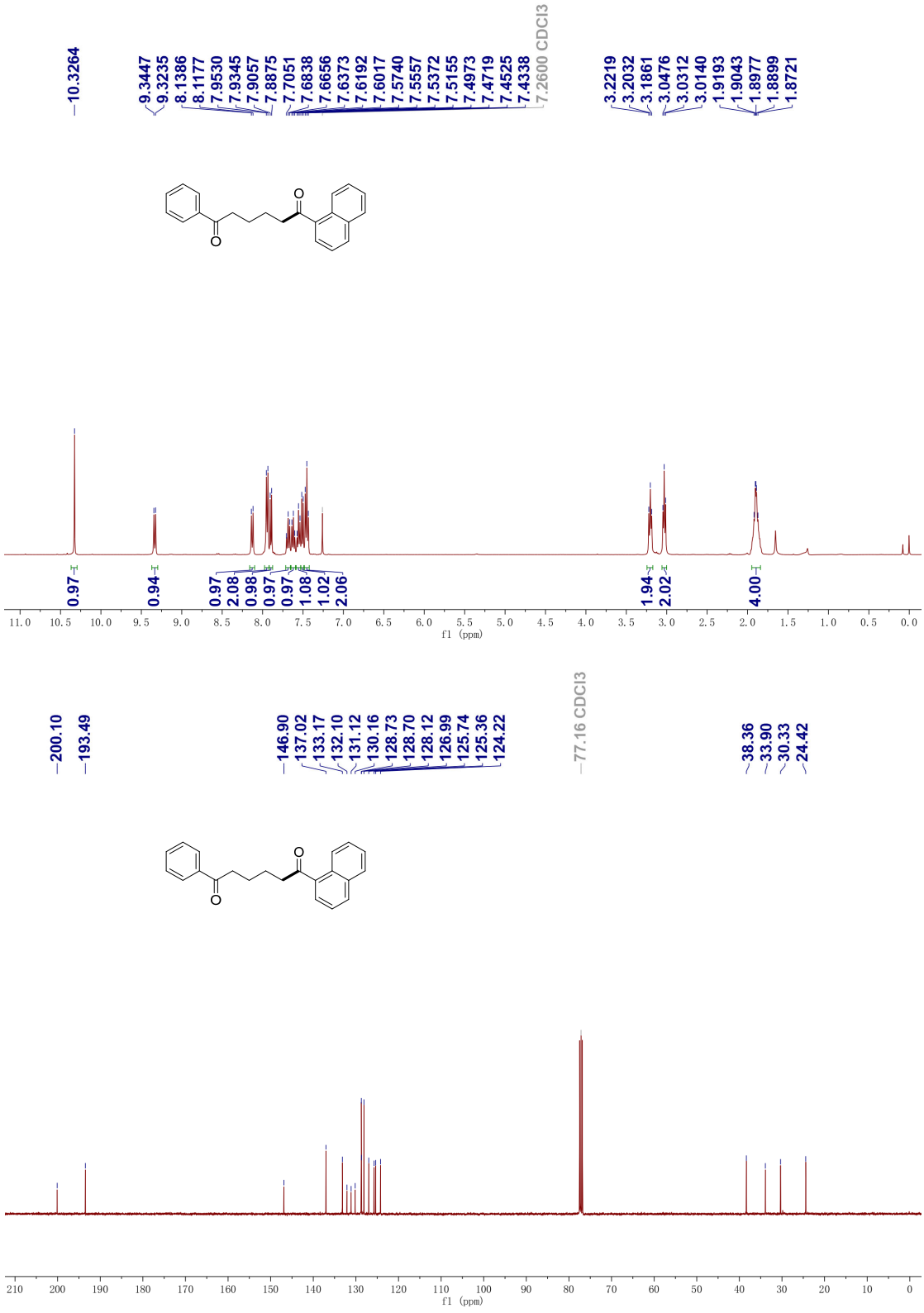




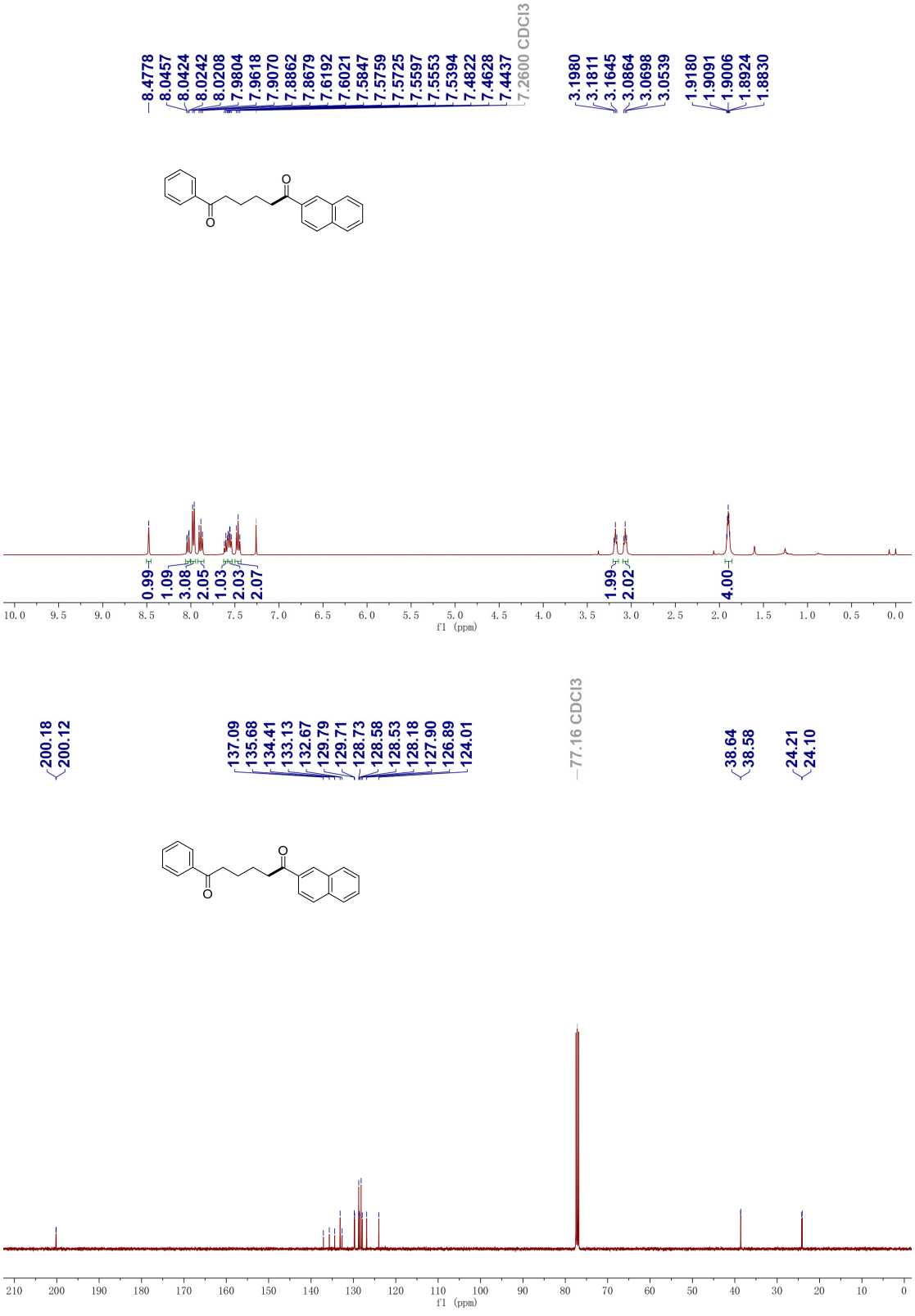
3n. ^{19}F NMR (282 MHz, Chloroform-*d*)



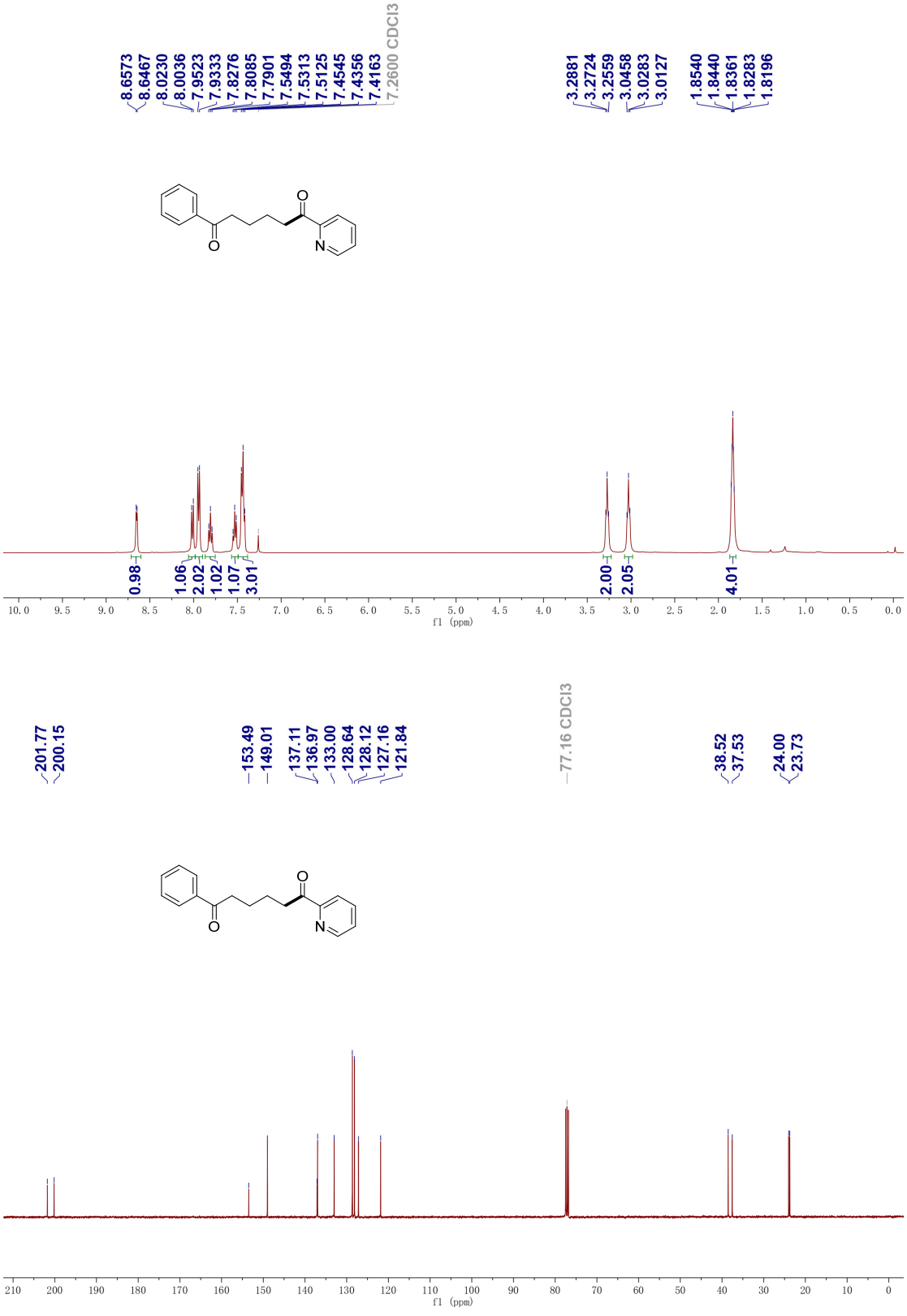
3o. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



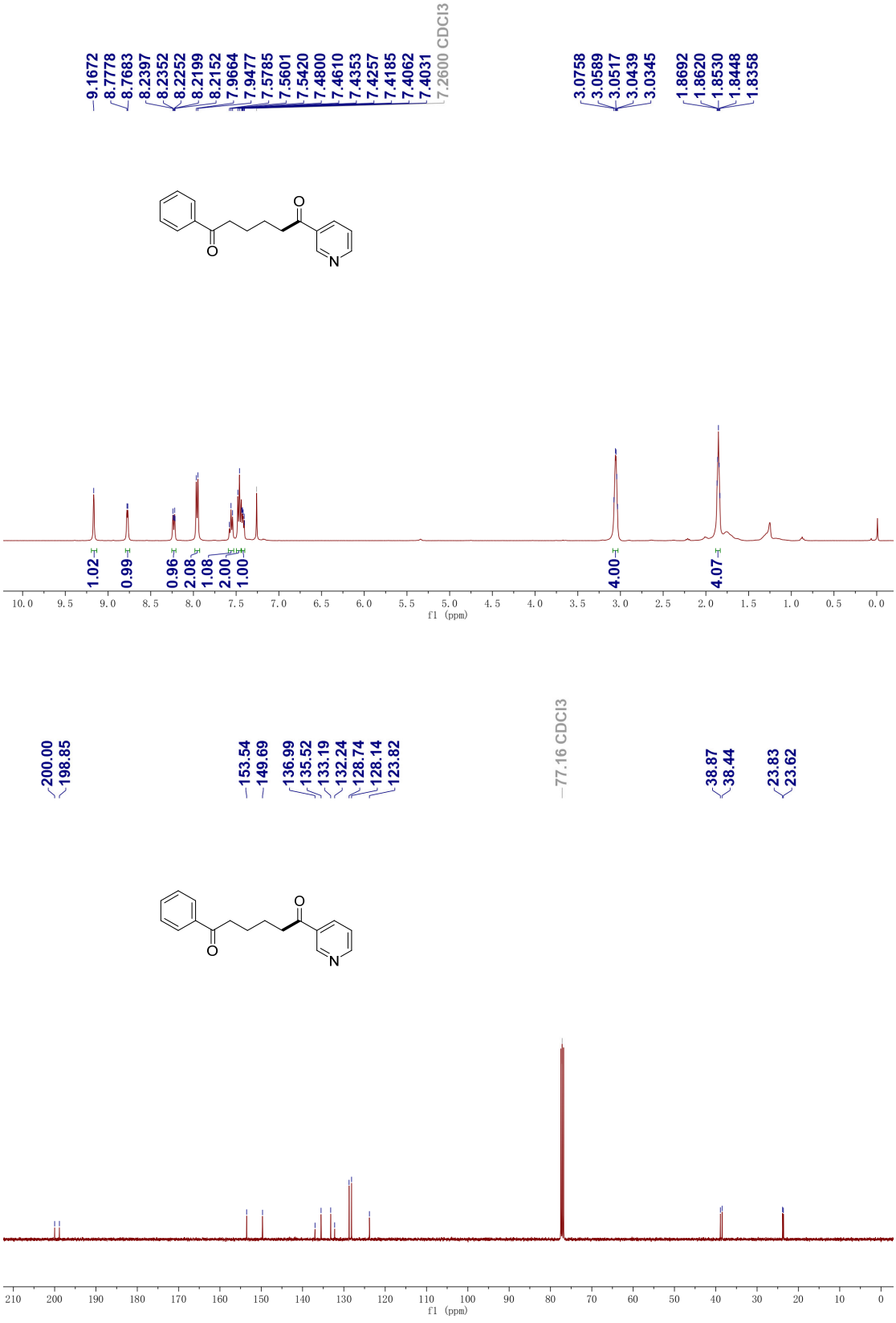
3p. **^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).**



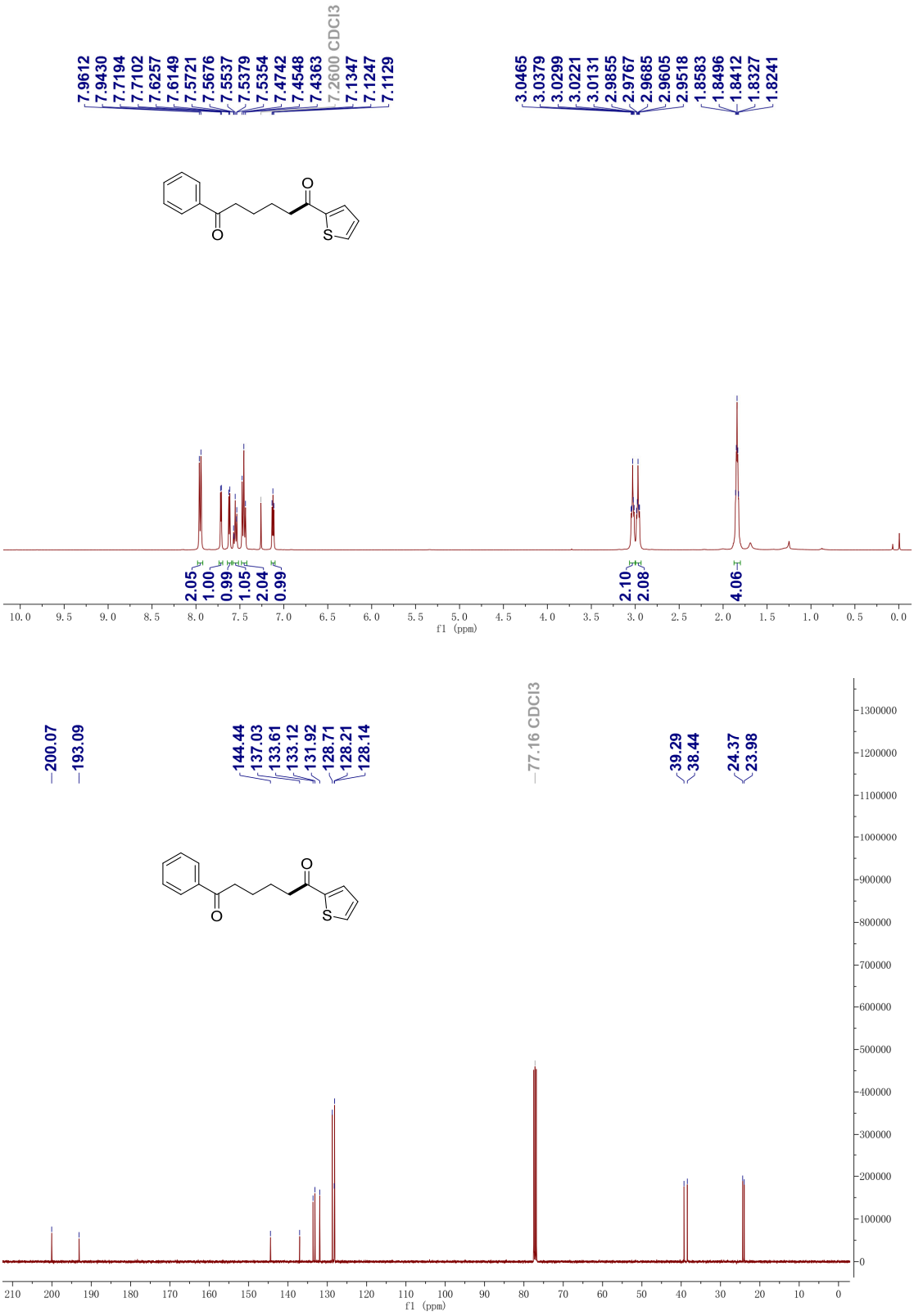
3q. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



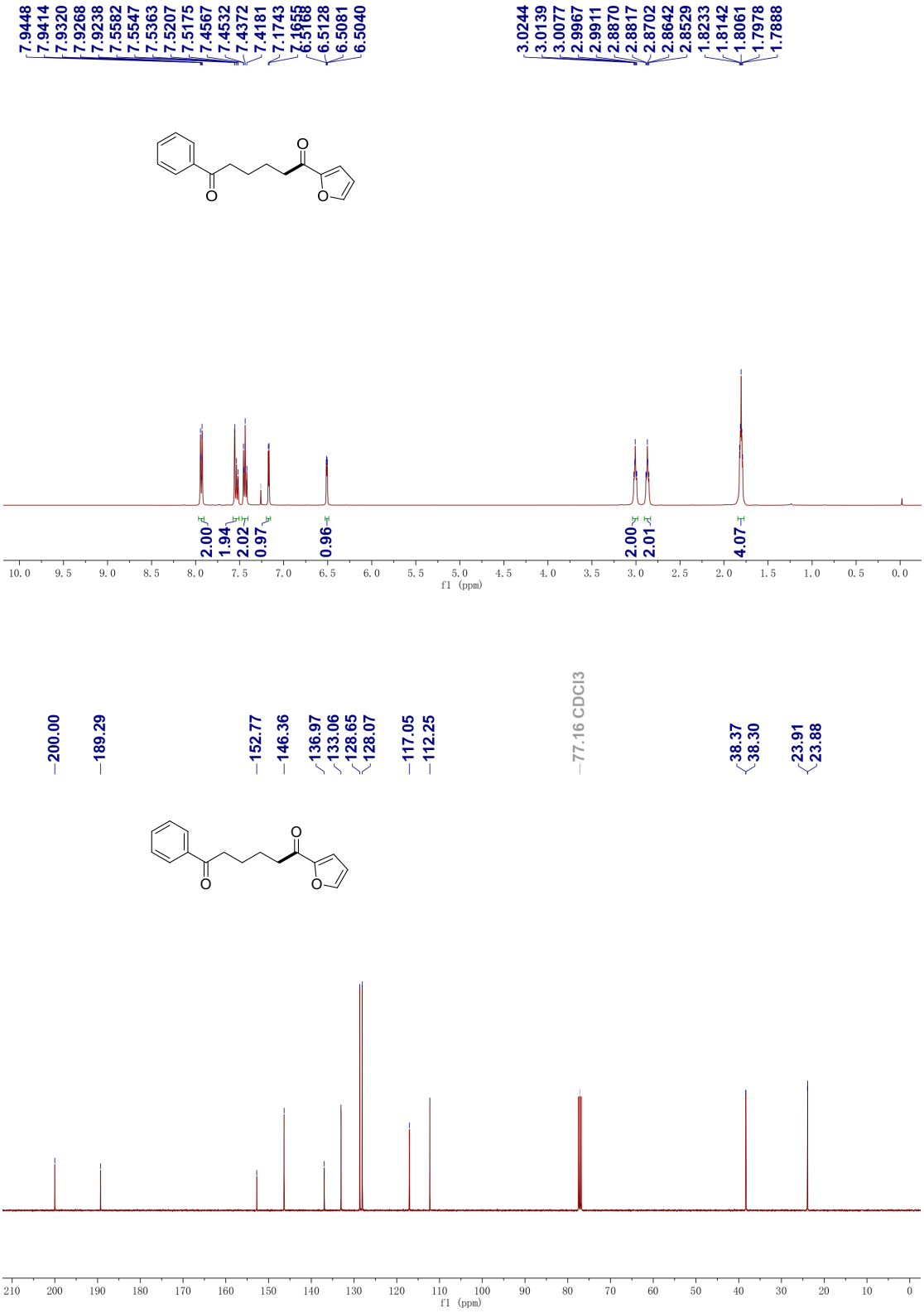
3r. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



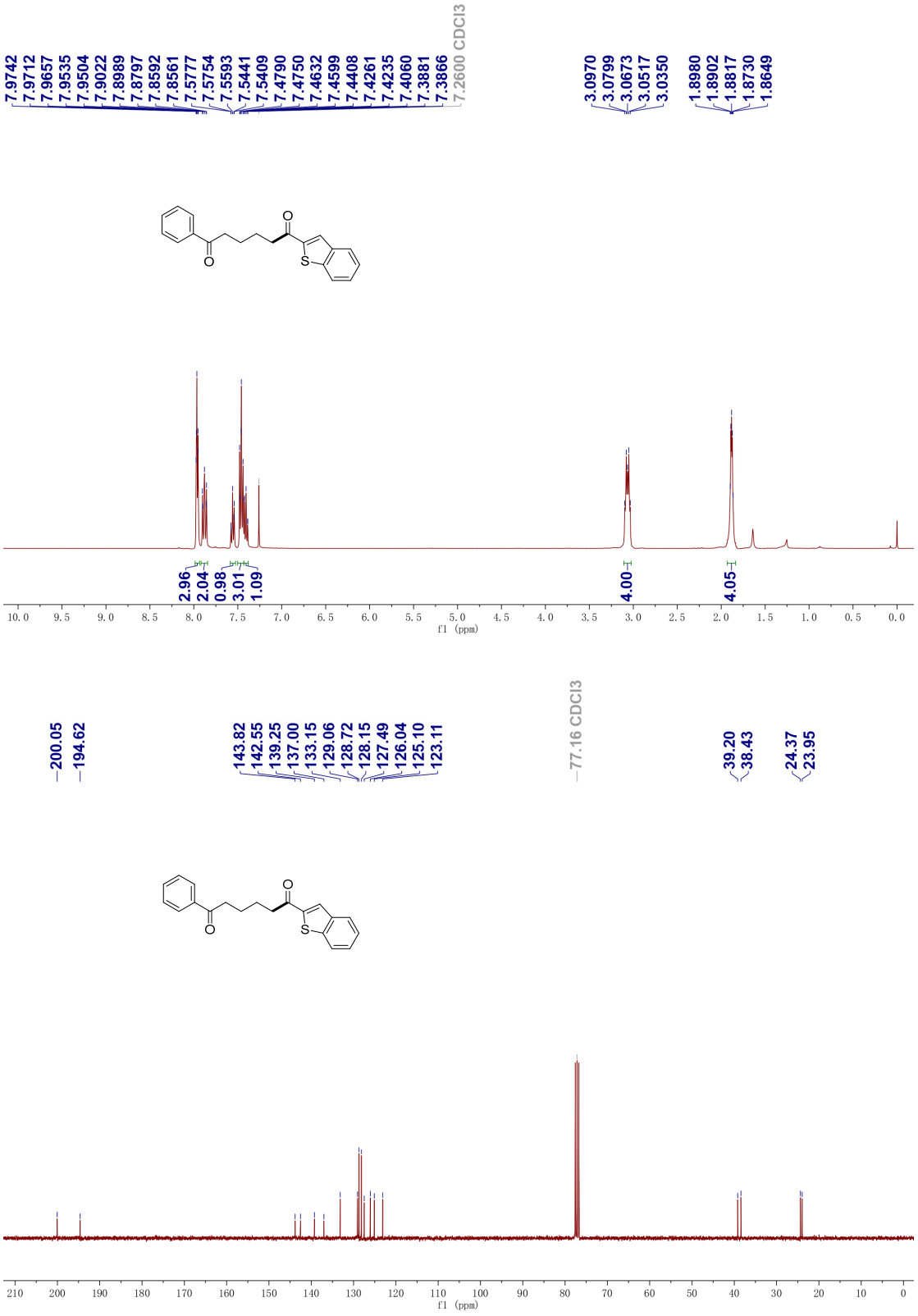
3s. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



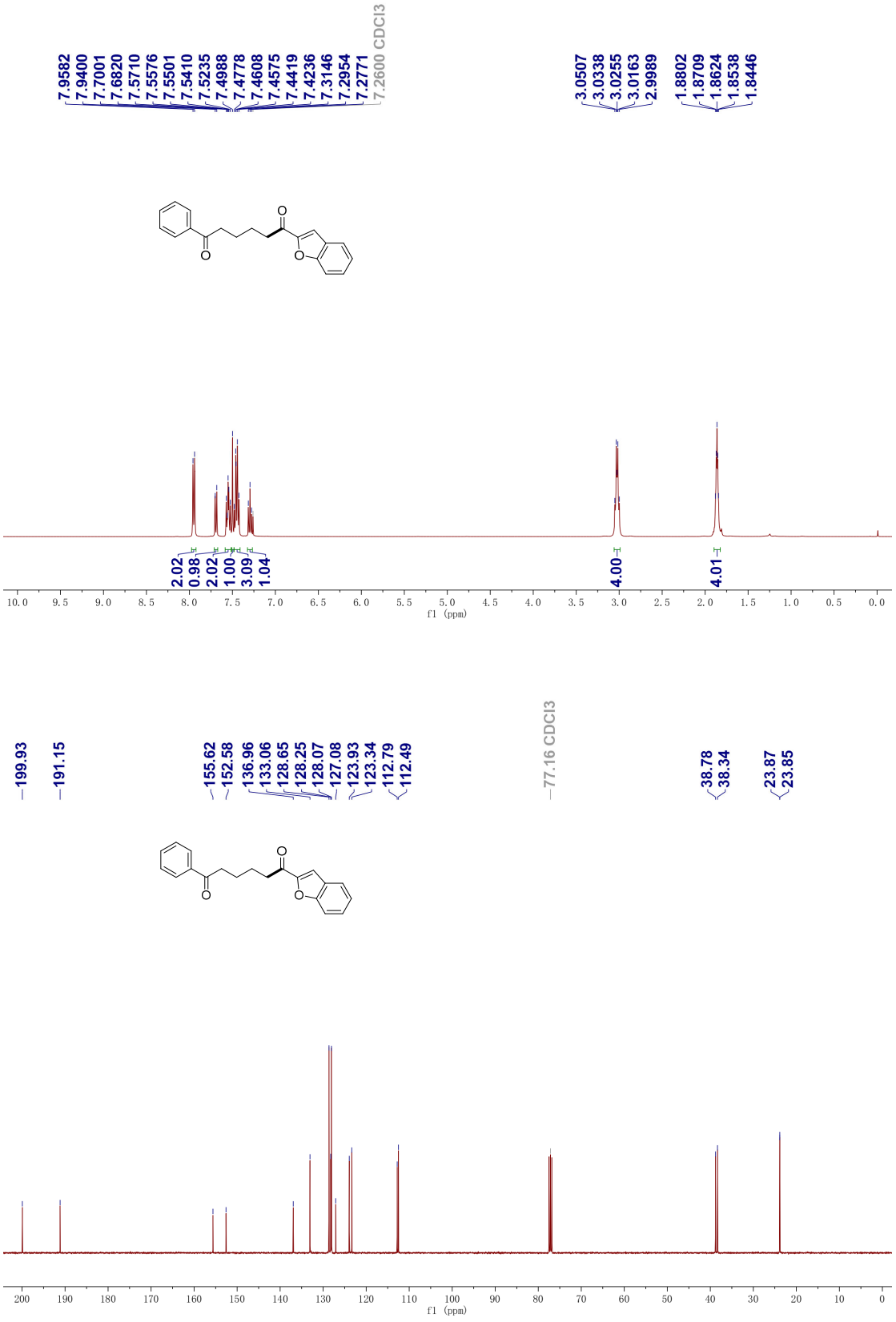
3t. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



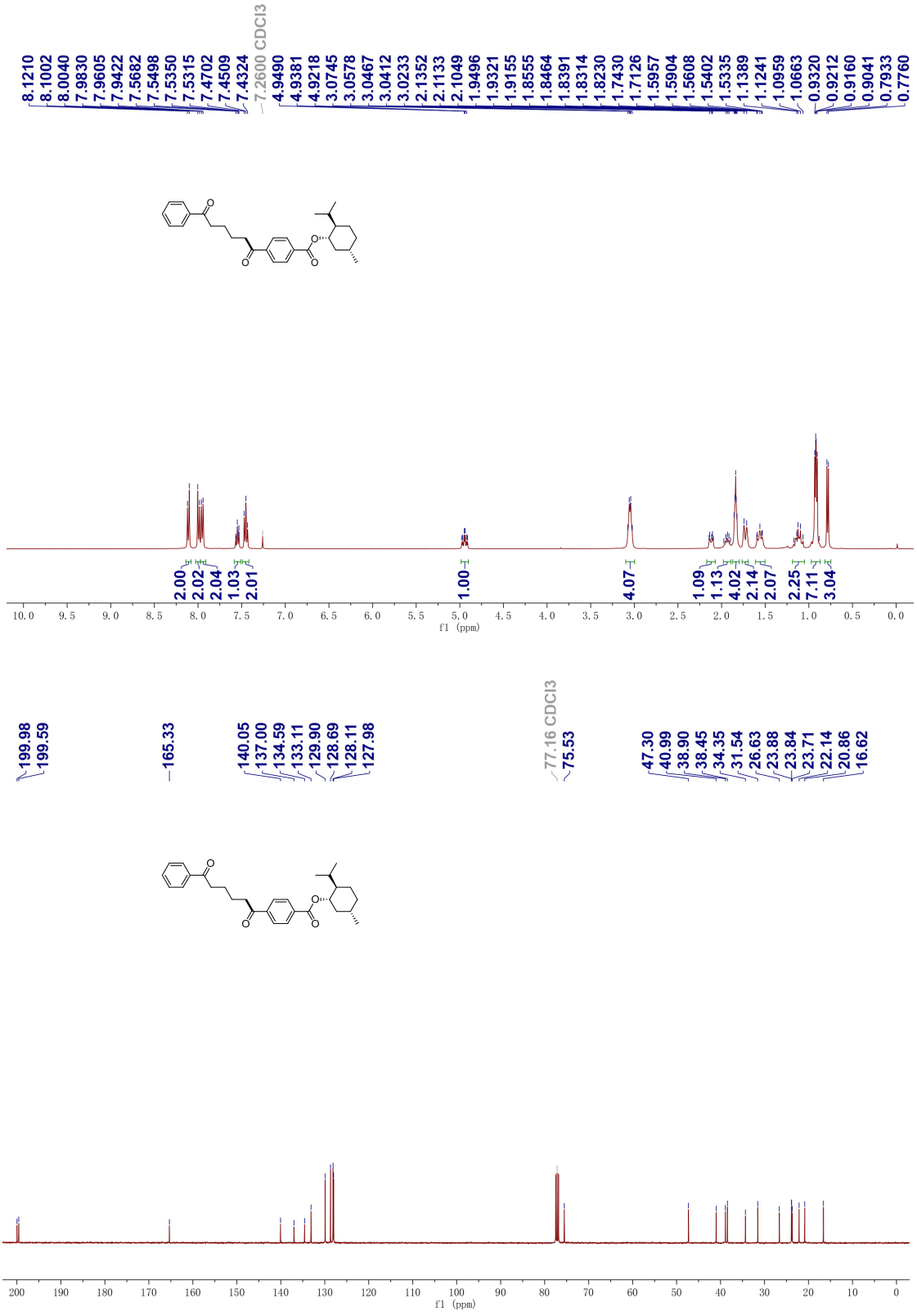
3u. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (75 MHz, Chloroform-*d*)



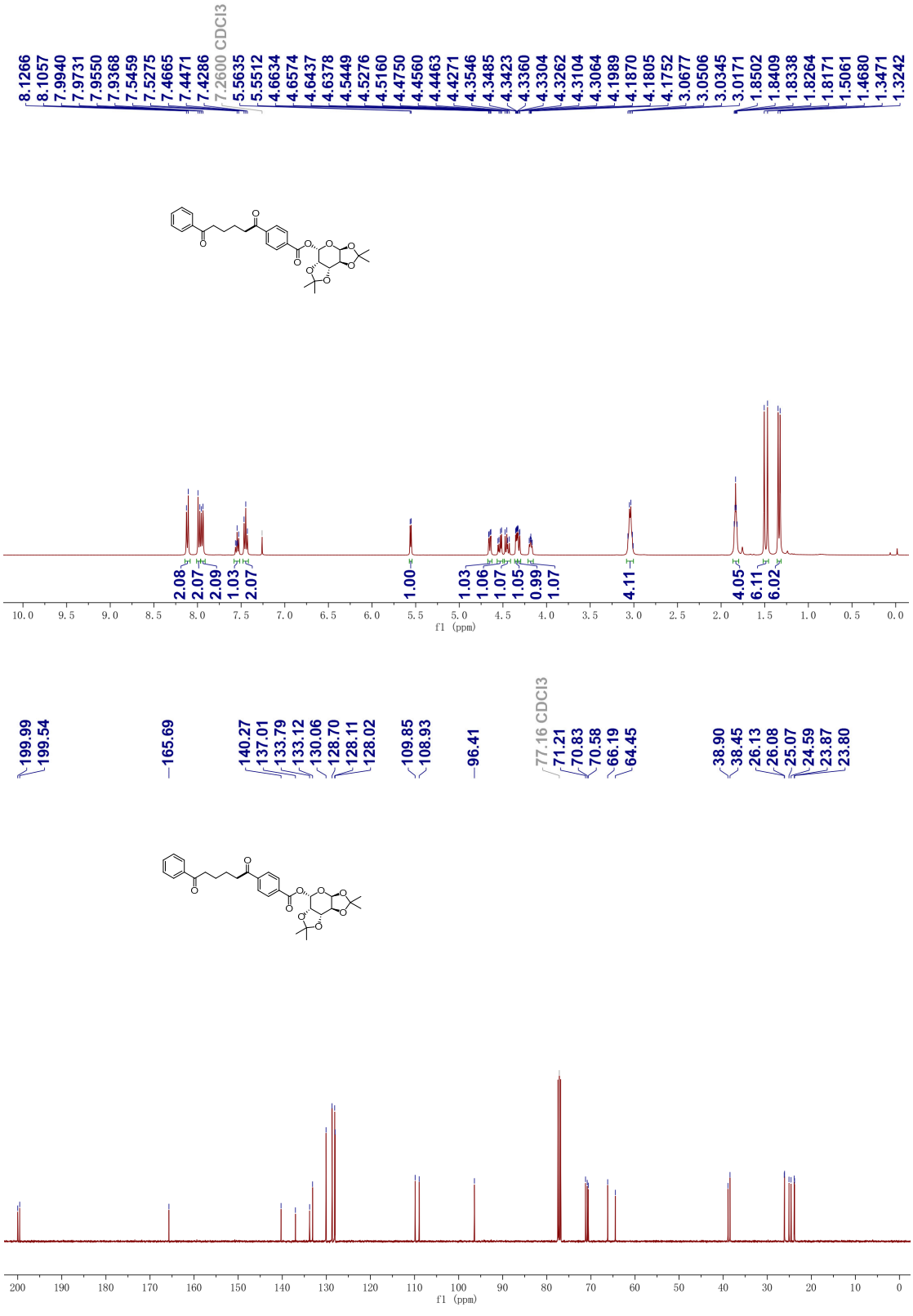
3v. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



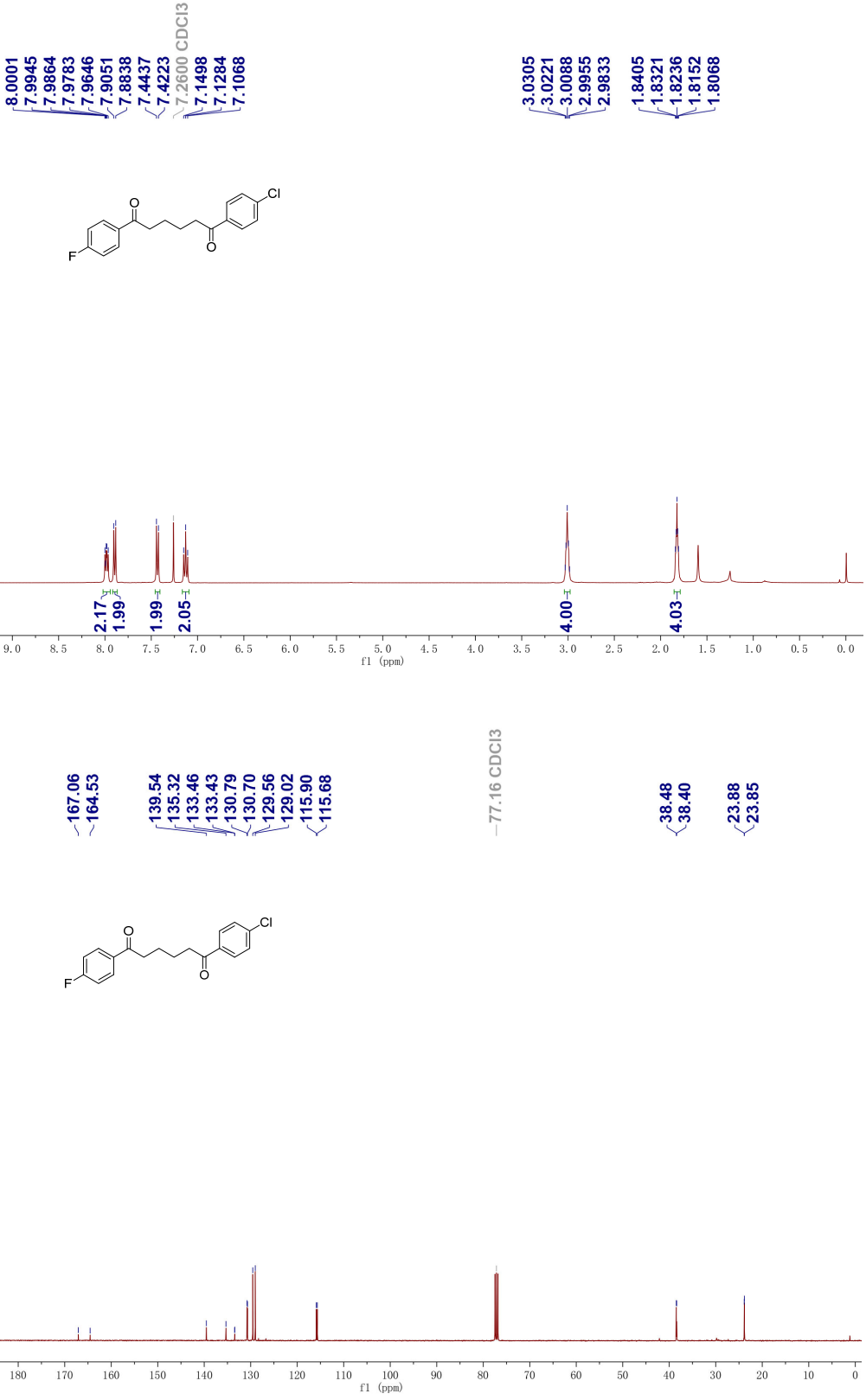
3x. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



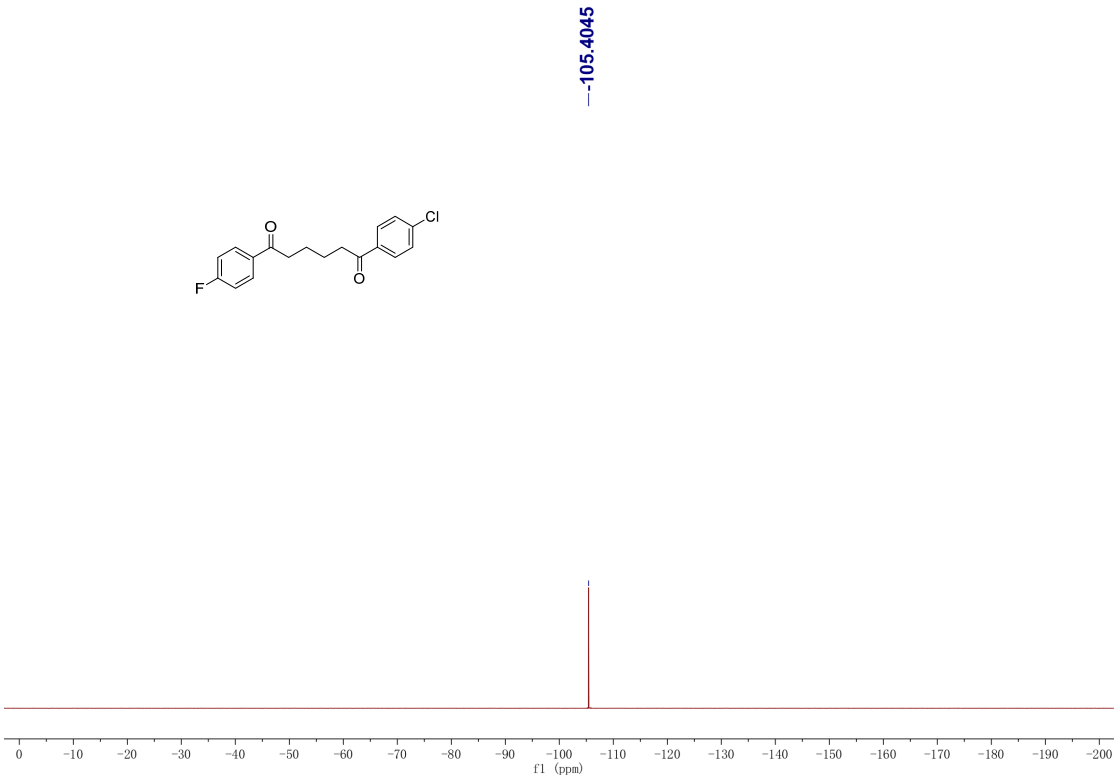
3y. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).



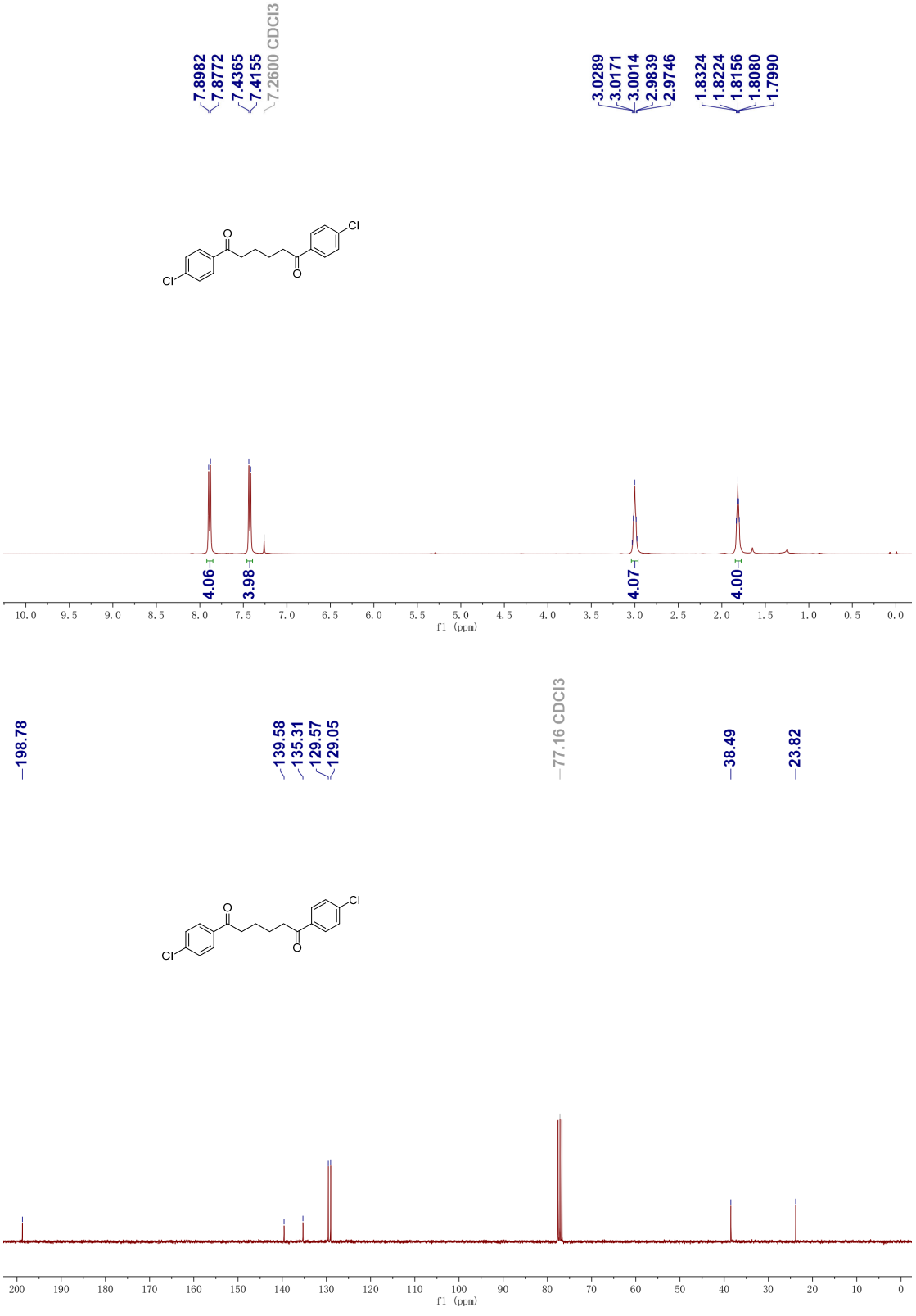
3aa. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



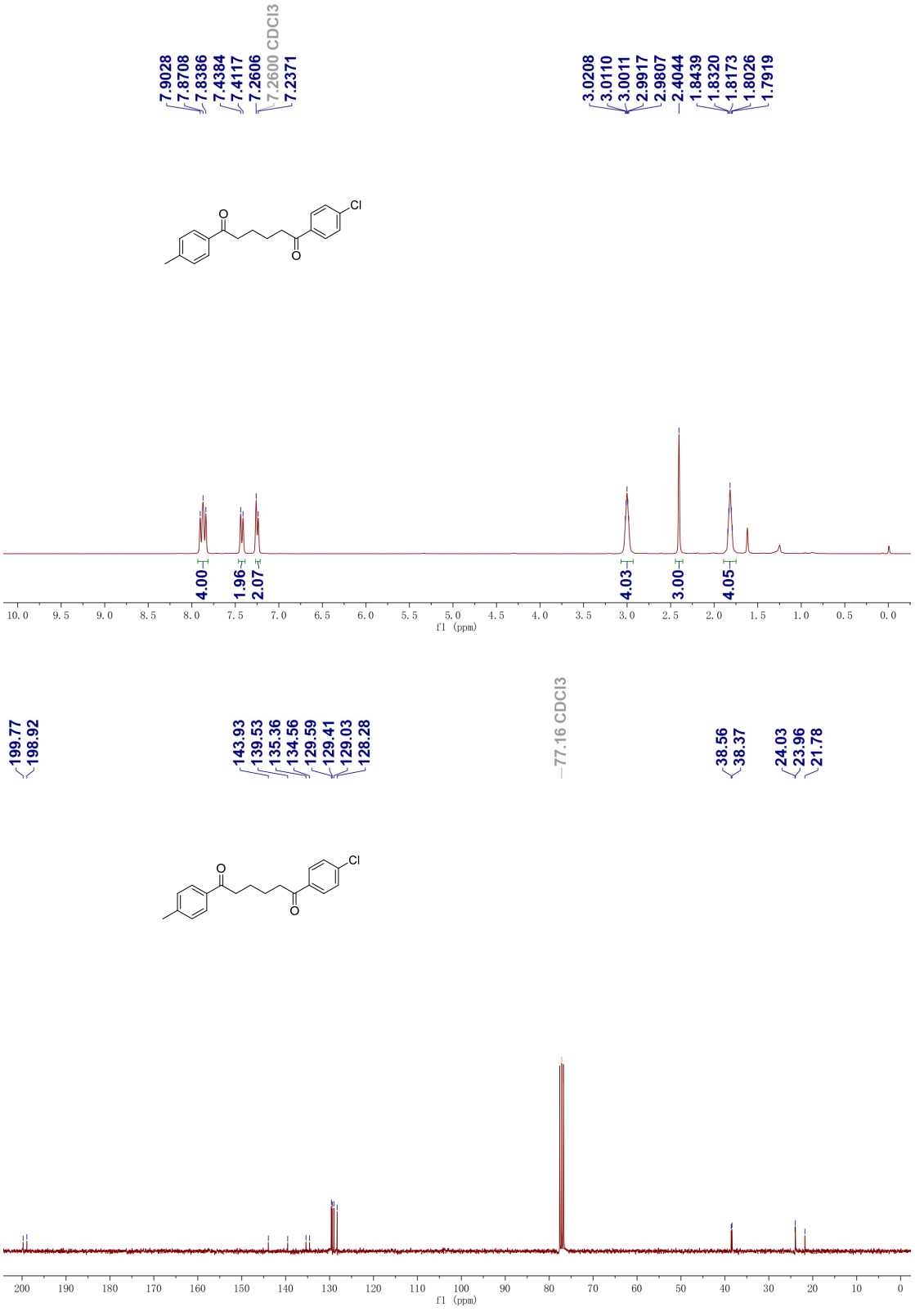
3aa. ^{19}F NMR (376 MHz, Chloroform-*d*)



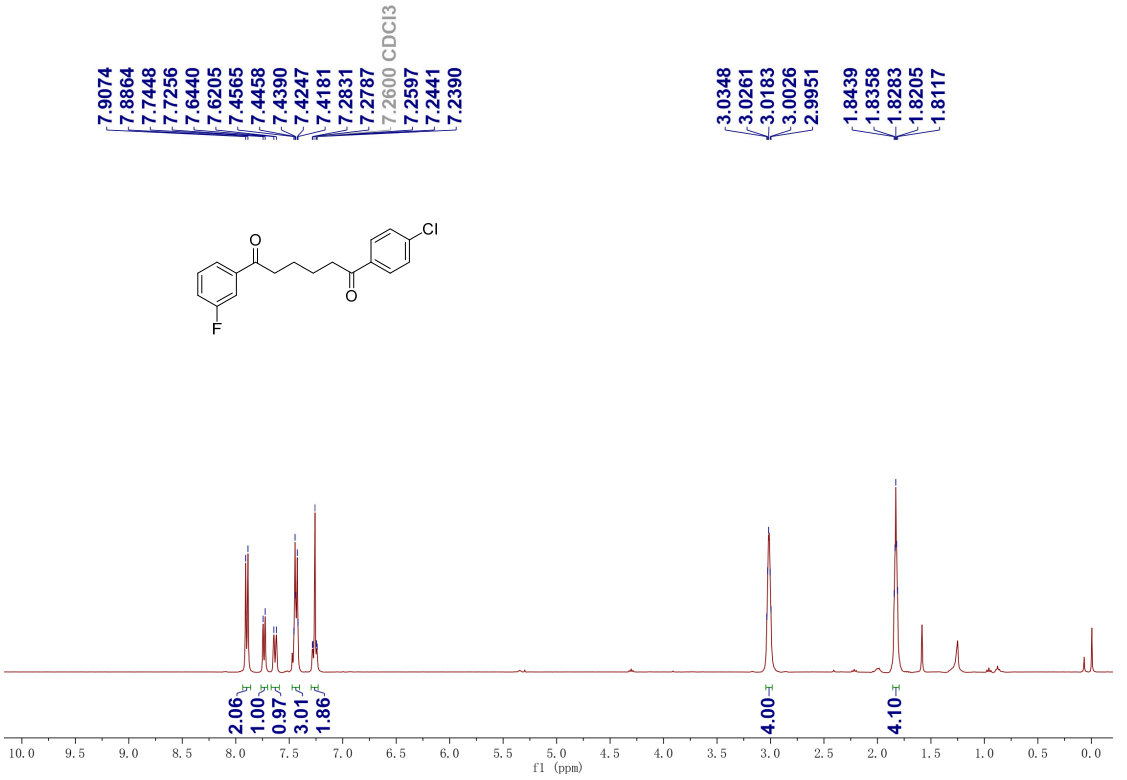
3ab. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (75 MHz, Chloroform-*d*).

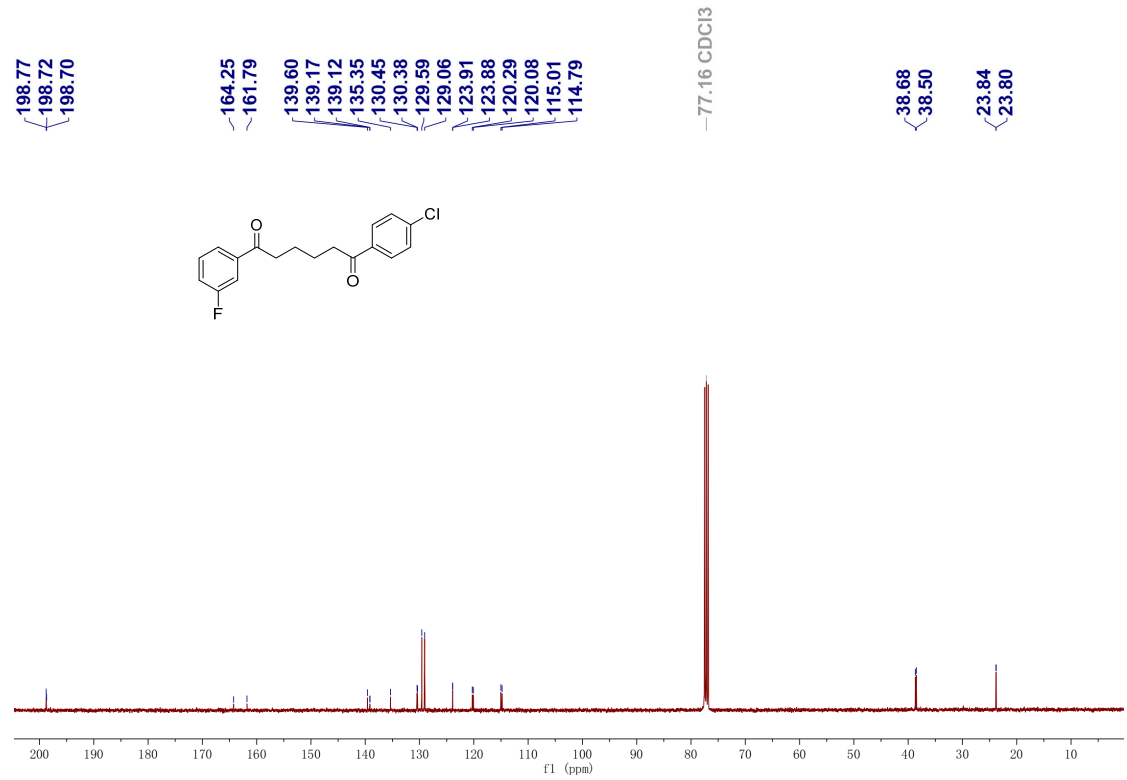


3ac. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (75 MHz, Chloroform-*d*).

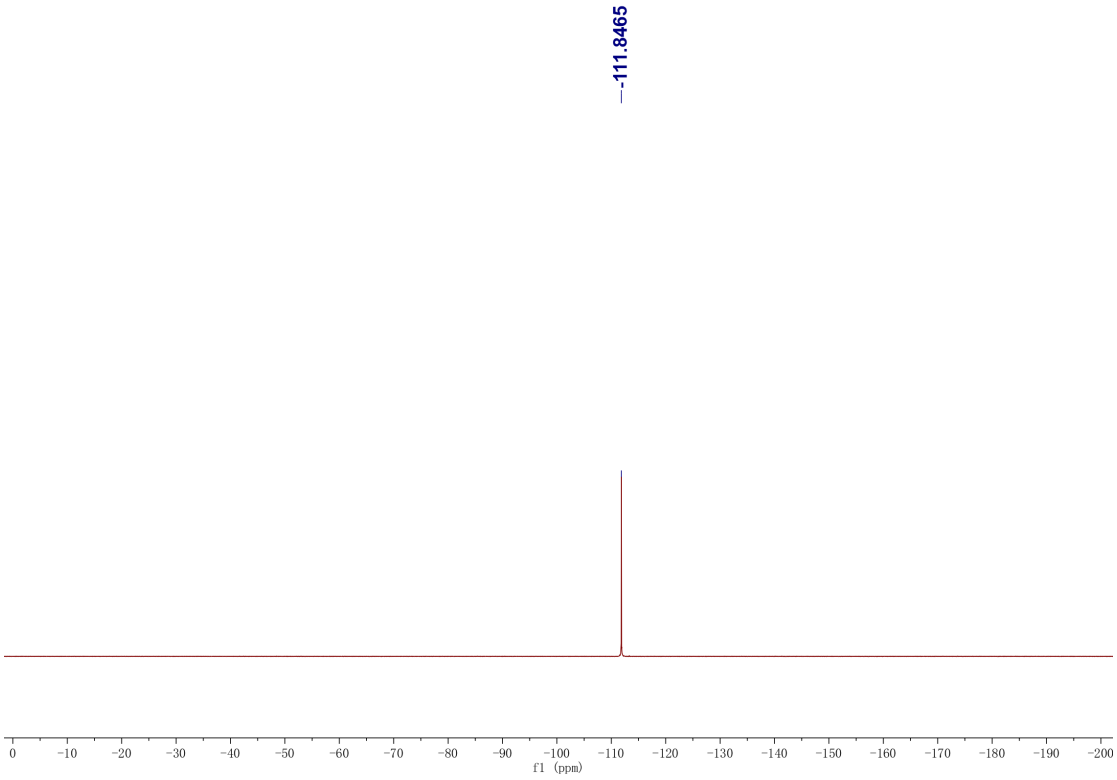


3ad. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).

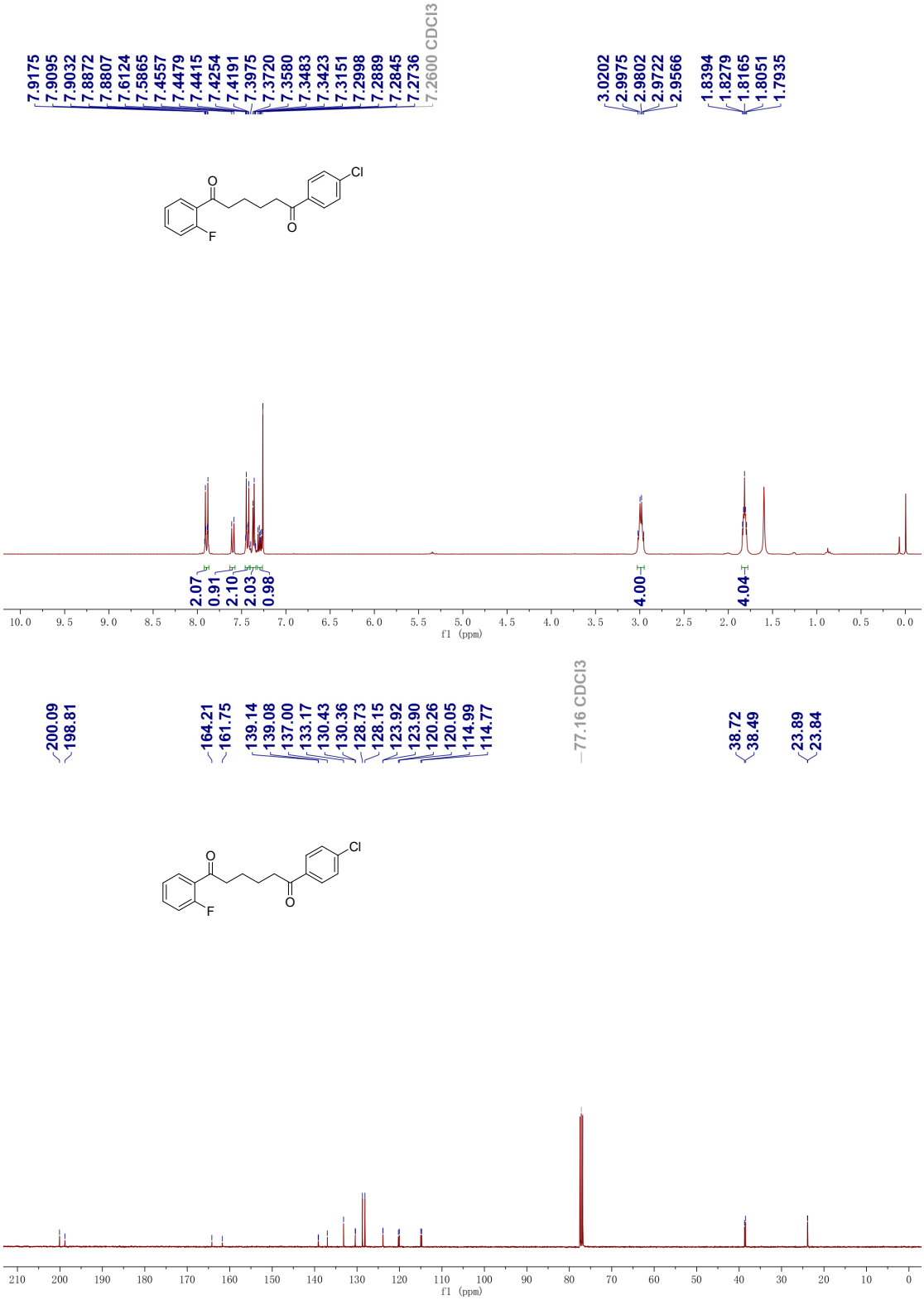




3ad. ^{19}F NMR (376 MHz, Chloroform-*d*)

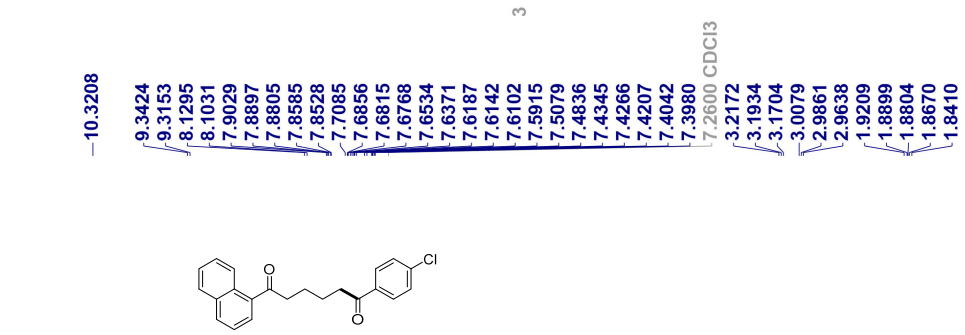


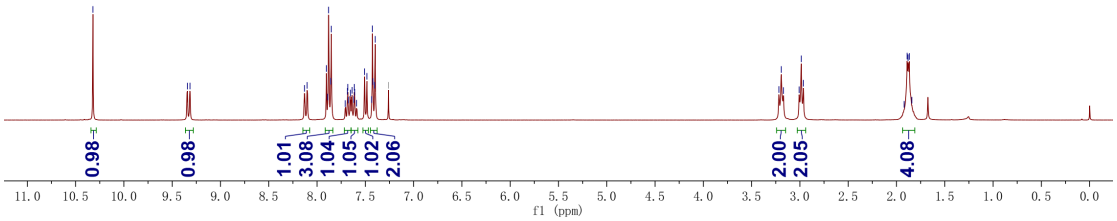
3ae. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*).

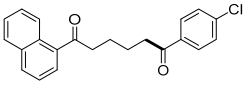


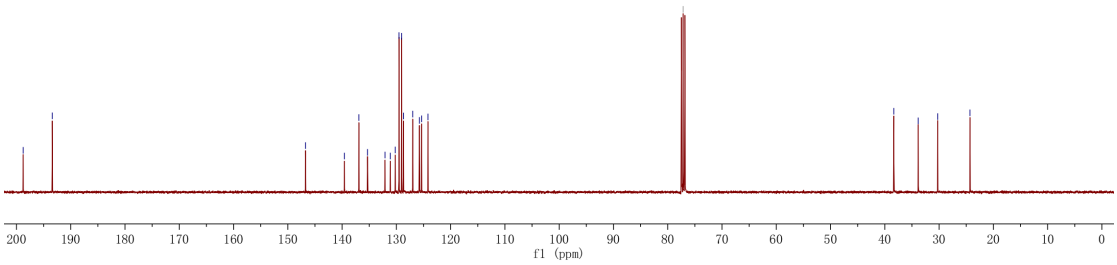
3ae. ^{19}F NMR (376 MHz, Chloroform-*d*)

3af. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)

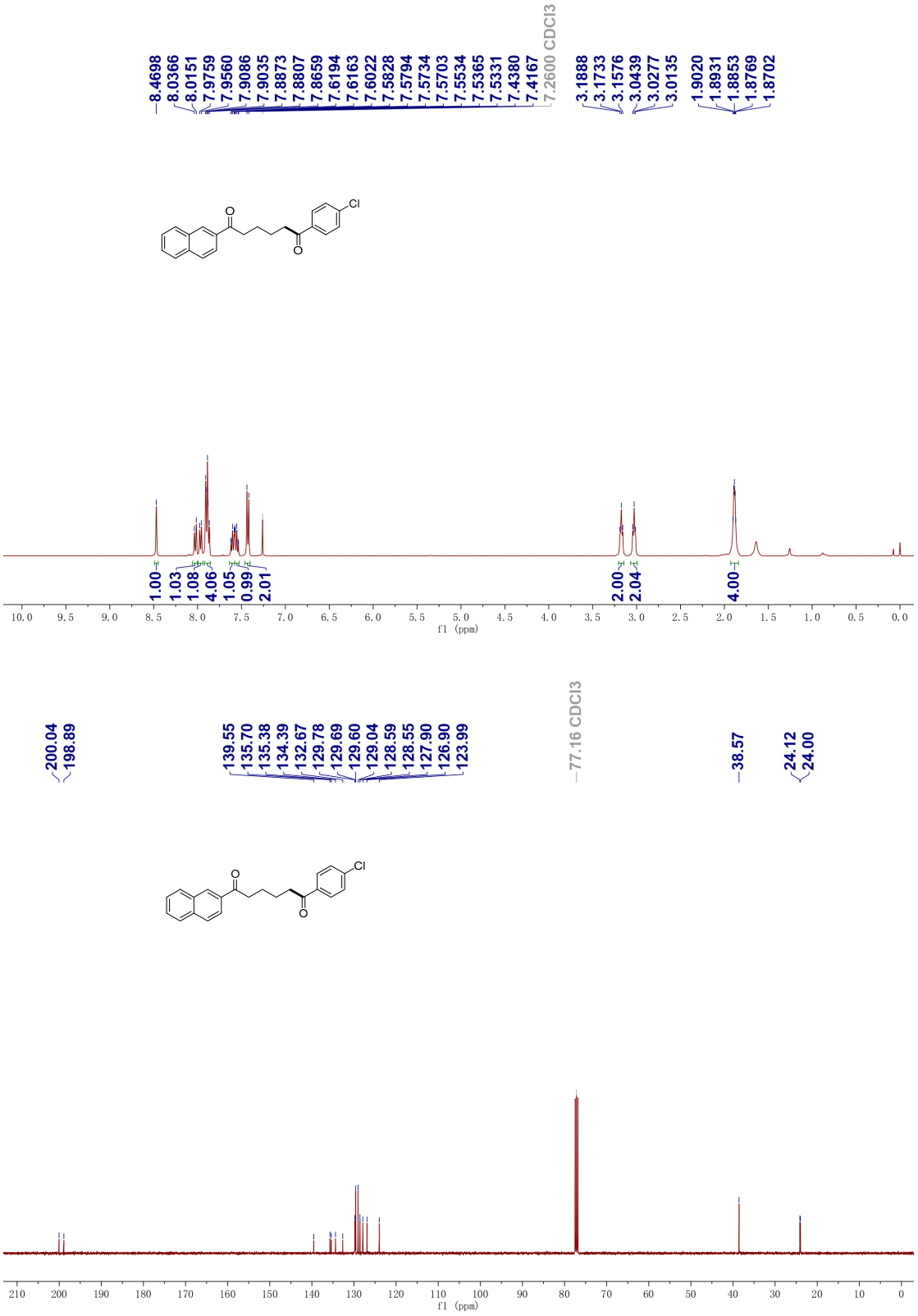




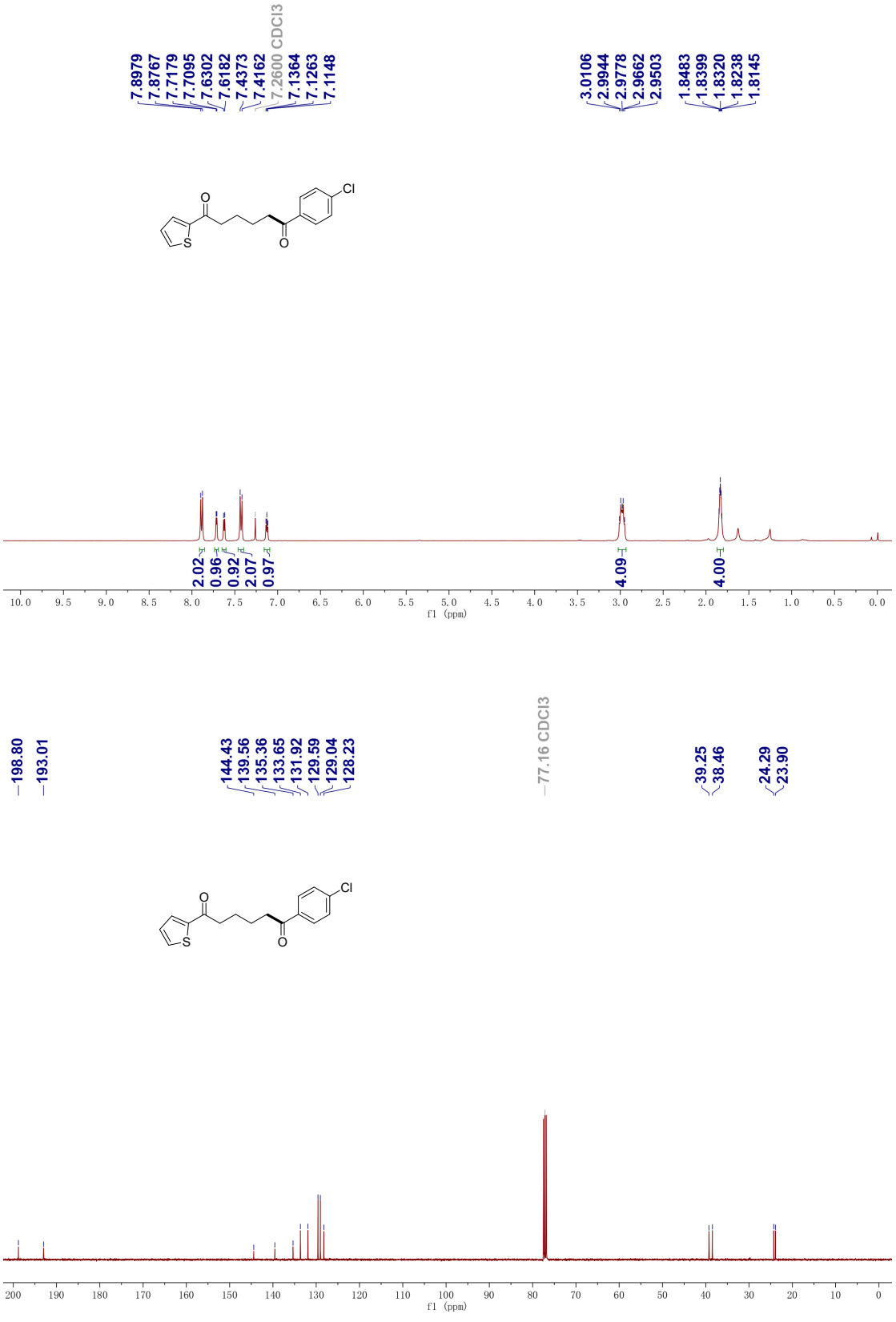




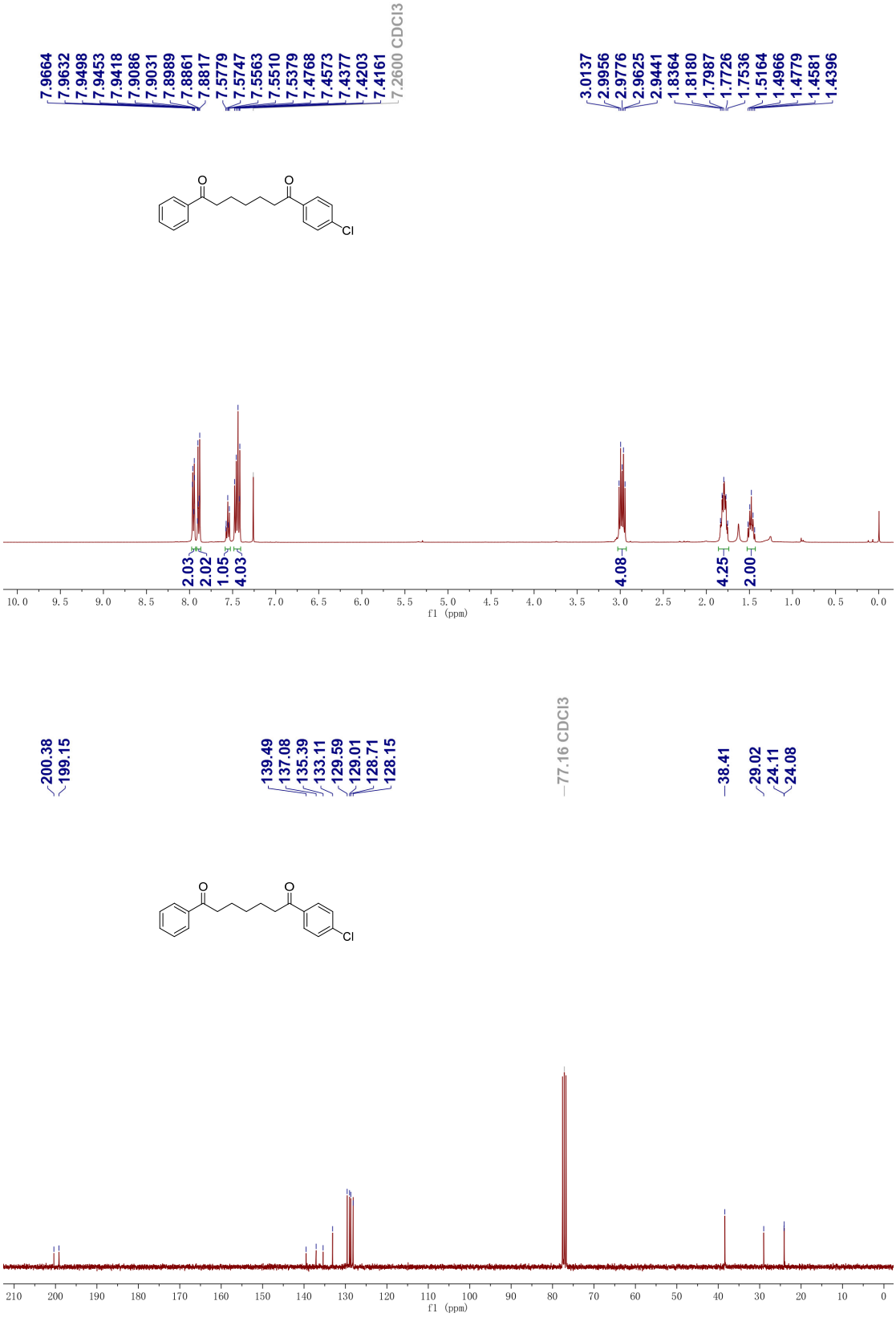
3ag. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)



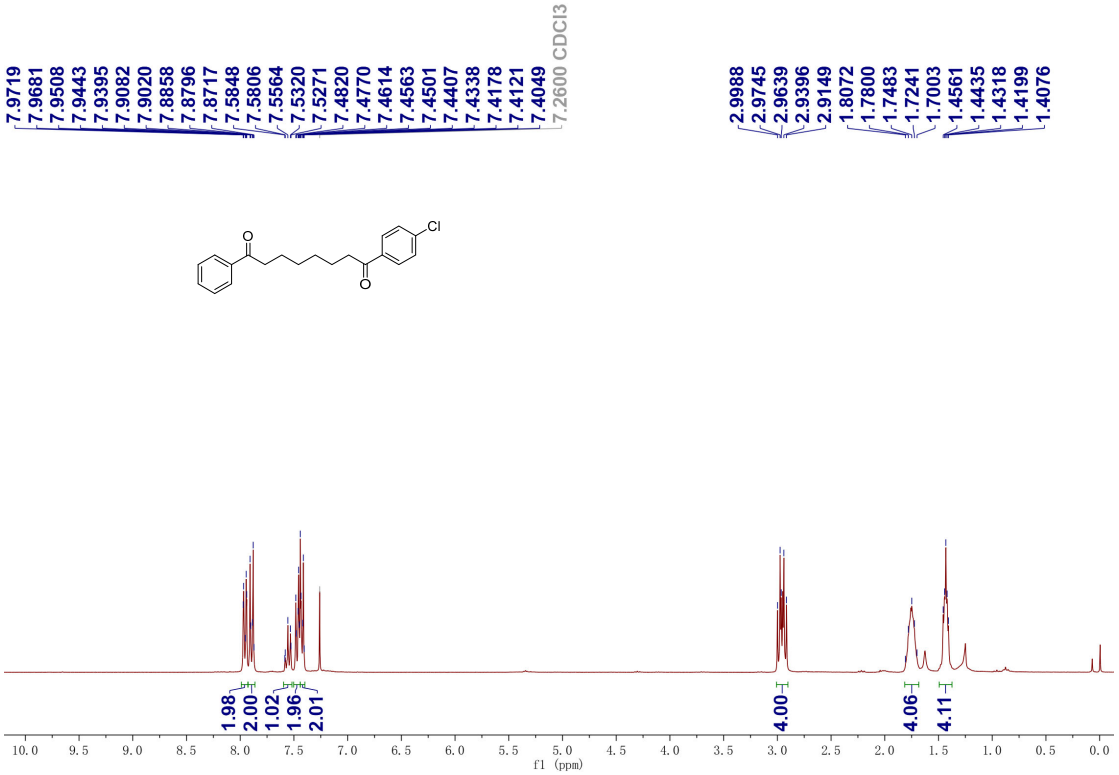
3ai. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)

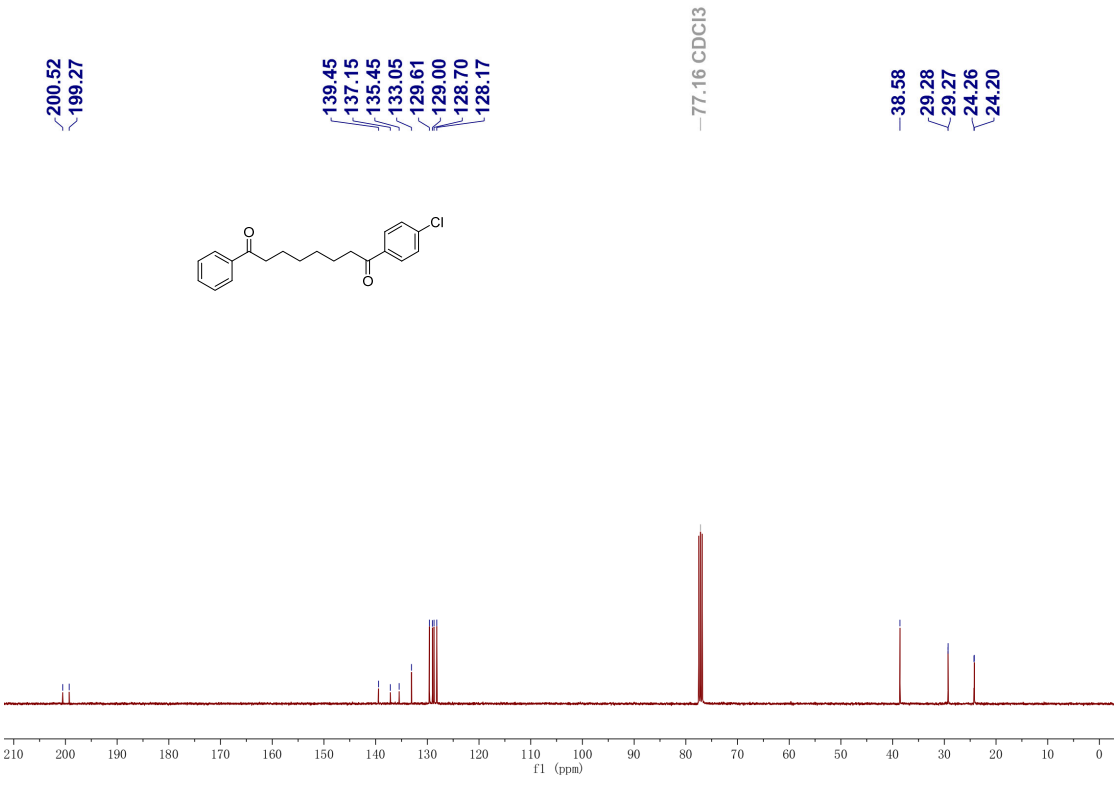


3ak. ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C NMR (75 MHz, Chloroform-*d*)



3al. ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C NMR (101 MHz, Chloroform-*d*)





5. ^{1}H NMR (400 MHz, DMSO)/ ^{13}C NMR (101 MHz, DMSO)