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Supporting information

Microfluidic synthesis of α-ketoesters *via* oxidative coupling of acetophenones with alcohols under metal-free conditions

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General experimental

All general reagents and solvents were commercially available and used as received. ^{1}H and ^{13}C NMR spectra were measured on magnet system 400'54 ascend instrument purchased from Bruker Biospin AG. Chemical data for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvent ($CDCl_3$, 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = penta, dd = doublet of doublets, dt = doublet of triplets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, m = multiplet, br = broad), coupling constant (J) in Hertz (Hz), and integration. ^{13}C NMR were recorded at 125 MHz or 100 MHz and chemical data for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent. Melting points of compounds were recorded with BUCHI (B-545) instrument. Column chromatography was generally performed on Silicycle silica gel (200-300 mesh). Analytical thin-layer chromatography (TLC) was performed on 0.2 mm coated silica gel plates (HSGF 254) and visualized the course of the reactions using a UV light (254 nm or 365 nm).

Microfluidic chip reactor set-ups

Reactions are performed in a Labtrix® Start R2.2 system (Chemtrix BV, NL). This commercially available microreactor system can be fitted with different glass chip reactors, of which in this project a 10.0 µL microreactor chip (Chemtrix *3223* reactor, 3 inlets) was employed. This reactor chip employs staggered oriented ridge (SOR-2) static micromixers to assure fast mixing. Reaction temperatures are controlled via a MTTC1410 temperature controller (Melcor Thermal Solutions, temperature range –20 to 195°C), while the reactor pressure was maintained at 20 bar backpressure via a preset back pressure regulator (Upchurch Scientific). Reactant solutions are injected into the reactor via 1 mL gastight syringes (SGE). Flowrates vary between 0.1 and 40 µL/min, and are controlled via syringe pumps (Chemyx).

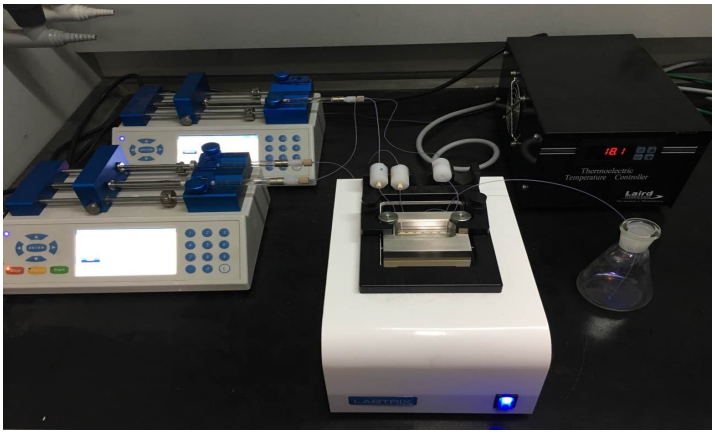


Figure 1 Microfluidic chip reactor for the preparation of α-ketoesters

Scale-up continuous flow reactor system

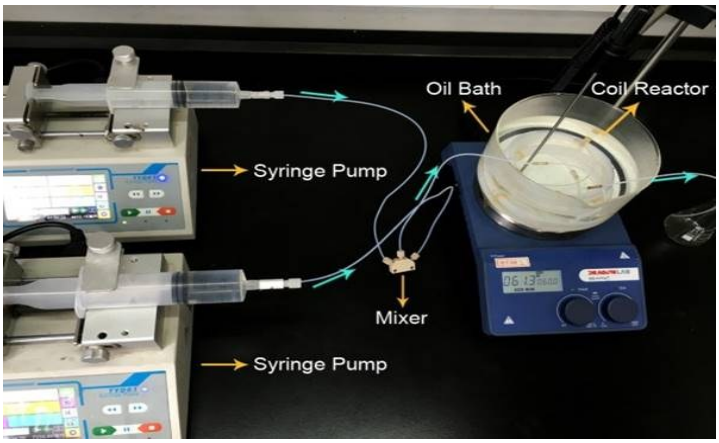
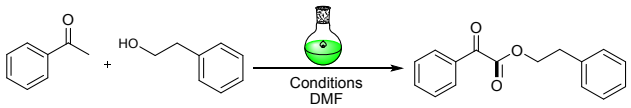


Figure 2 Scale-up continuous flow reactor system[a]

Experimental procedures

2.0 mmol acetophenones **1**, 8.0 mmol alcohols **2**, 0.8 mmol iodine, and 3.0 mmol DBU were dissolved in 3 ml DMF, which was extracted to Syringe A. 8 mmol TBHP (70 wt% in water, 4 eq.) were dissolved in 3 ml DMF, which was extracted to Syringe B. The flow rate of Syringe A and B were both 7.5 μl/min and the residence time was 40s. The temperature of the chip was set in 110 C. The outflow of the reaction mixture was collected, then quenched with saturated $Na_2S_2O_3$ solution and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and solvent was removed under vacuum. And the crude product was purified by flash chromatography on silica gel by gradient elution with ethyl acetate in petroleum (hexane/ethyl acetate 50:1), affording the desired product **3** in good yields (66-90%).

Optimization studies in Batch

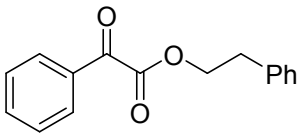


1a 2a 3aa

Entry	Promoter (equiv.)	Oxidant	Base	Temp (℃)	Yield[b] (%)
1	KI (1.0)	TBPB	NaAc	90	12
2	I_2 (1.0)	TBPB	NaAc	90	27
3	TBAI (1.0)	TBPB	NaAc	90	10
4	NIS (1.0)	TBPB	NaAc	90	20
5	I_2 (1.0)	*m*-CPBA	NaAc	90	<10%
6	I_2 (1.0)	TBHP	NaAc	90	34
7	I_2 (1.0)	DTBP	NaAc	90	23
8	I_2 (1.0)	H_2O_2	NaAc	90	No[c]
9	I_2 (1.0)	TBHP	K_2CO_3	90	30
10	I_2 (1.0)	TBHP	Cs_2CO_3	90	18
11	I_2 (1.0)	TBHP	DBU	90	43
12	I_2 (1.0)	TBHP	Pyridine	90	No
13	I_2 (1.0)	TBHP	Et_3N	90	36
14	I_2 (1.0)	TBHP	DBU	80	39
15	I_2 (1.0)	TBHP	DBU	100	44
16	I_2 (1.0)	TBHP	DBU	110	48
17	I_2 (1.0)	TBHP	DBU	120	47
18	I_2 (1.0)	TBHP	DBU	130	45
19	I_2 (0.3)	TBHP	DBU	110	18
20	I_2 (0.5)	TBHP	DBU	110	32
21	I_2 (0.8)	TBHP	DBU	110	46
22	I_2 (1.3)	TBHP	DBU	110	54
23	I_2 (1.5)	TBHP	DBU	110	59
24	I_2 (1.8)	TBHP	DBU	110	58

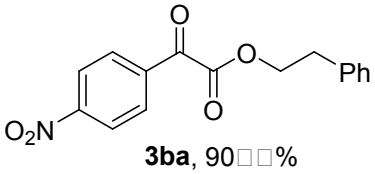
[a]Reaction conditions: 0.5 mmol **1a**, 2.0 mmol **2a**, promoter, 2.0 mmol oxidant and 0.75 mmol base were solved in 3 ml DMF and stirred at 90℃ for 10h in the sealed tube. [b]Yields of the isolated product **3aa**. [c]No reaction.

Analytical data of products 3



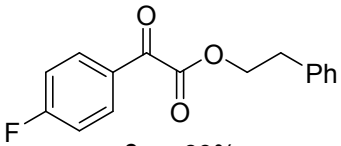
3aa, 86%

Product 3aa: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.72 (m, 2H), 7.58 – 7.53 (m, 1H), 7.40 – 7.35 (m, 2H), 7.27 – 7.17 (m, 5H), 4.54 (t, *J* = 7.0 Hz, 2H), 3.01 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.41, 163.84, 137.06, 135.01, 132.41, 130.15, 129.14, 128.97, 128.81, 126.99, 66.54, 35.05; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{14}O_3$ 277.0835 found 277.0886.



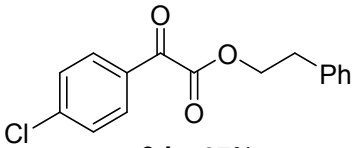
3ba, 90□□%

Product 3ba: Light yellow wax; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.13 (m, 2H), 8.13 – 8.02 (m, 2H), 7.28 – 7.17 (m, 5H), 4.51 (t, *J* = 6.9 Hz, 2H), 3.03 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.72, 150.64, 137.56, 135.76, 130.81, 129.04, 128.79, 126.94, 123.68, 66.45, 35.23; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{13}NO_5$ 322.0686 found 322.0691.



3ca, 89%

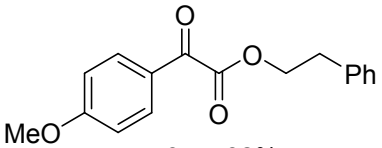
Product 3ca: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.28 – 7.17 (m, 5H), 7.04 (t, *J* = 8.6 Hz, 2H), 4.55 (t, *J* = 6.9 Hz, 2H), 3.02 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.60, 168.17, 165.61, 163.45, 137.04, 133.14 , 133.04, 129.16, 128.85, 127.04, 116.46, 116.24, 66.63, 35.05; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{13}O_3F$ 295.0741 found 295.0742.



3da, 87%

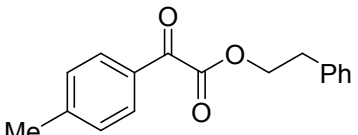
Product 3da: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.22 (dt, *J* = 23.2, 7.5 Hz, 5H), 7.03 (t, *J* = 8.6 Hz, 2H), 4.54 (t, *J* = 6.9 Hz, 2H), 3.01 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.93, 163.23, 141.70, 136.99, 131.53, 130.83, 129.37, 129.14,

128.83, 127.03, 66.67, 35.01; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{13}O_3Cl$ 311.0445 found 311.0477.



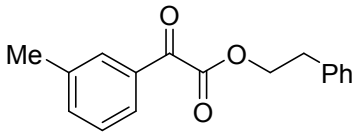
3ea, 82%

Product 3ea: Light yellow wax; ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.84 (dd, *J* = 6.8, 1.8 Hz, 2H), 7.31-7.24 (m, 5H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.60 (t, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 3.08 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 184.7, 164.9, 164.0, 137.0, 132.5, 129.0, 128.6, 126.7, 125.3, 114.1, 66.2, 55.6, 34.9; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{16}O_4$ 307.0932 found 307.0958.



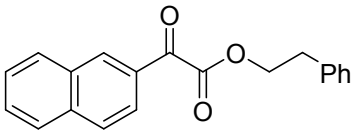
3fa, 80%

Product 3fa: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.24 – 7.14 (m, 7H), 4.51 (t, *J* = 6.9 Hz, 2H), 2.99 (t, *J* = 7.0 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.04, 164.02, 146.32, 137.09, 130.24, 129.67, 129.10, 128.76, 126.93, 66.40, 35.03, 22.00; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{16}O_3$ 291.0992 found 291.0988.



3ga, 79%

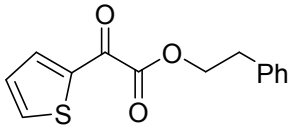
Product 3ga: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.51 (m, 2H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.26 – 7.13 (m, 6H), 4.52 (t, *J* = 7.0 Hz, 2H), 2.99 (t, *J* = 7.0 Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.54, 163.91, 138.82, 137.00, 135.77, 132.36, 130.27, 129.01, 128.76, 128.69, 127.41, 126.87, 66.38, 34.97, 21.27; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{16}O_3$ 291.0992 found 291.0998.



3ha, 84%

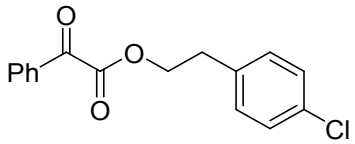
Product 3ha: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.83 – 7.75 (m, 3H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.26-7.15 (m, 5H), 4.59 (t, *J* =

7.0 Hz, 2H), 3.04 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.31, 163.94, 137.17, 136.49, 133.65, 132.36, 130.18, 129.84, 129.69, 129.15, 129.04, 128.83, 128.02, 127.22, 127.02, 124.06, 66.62, 35.12; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{20}H_{16}O_3$ 327.0992 found 327.1008.



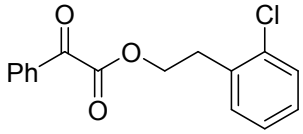
3ia, 73%

Product 3ia: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.26 – 7.14 (m, 5H), 7.06 (t, *J* = 4.4 Hz, 1H), 4.50 (t, *J* = 7.1 Hz, 2H), 3.02 (t, *J* = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.41, 161.69, 139.19, 137.55, 137.39, 137.02, 129.12, 128.80, 128.77, 126.99, 67.03, 34.98; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{14}H_{12}O_3S$ 283.0399 found 283.0391.



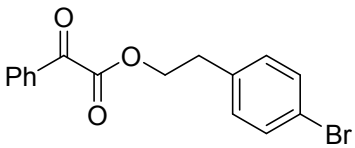
3ab, 76 %

Product 3ab: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 6.7 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 4.52 (t, *J* = 6.8 Hz, 2H), 2.98 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.27, 163.74, 135.62, 135.11, 132.90, 132.38, 130.52, 130.11,129.00, 128.95, 66.13, 34.44; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{13}O_3Cl$ 311.0445 found 311.0454.



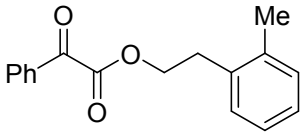
3ac, 78%

Product 3ac: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.78 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.33 – 7.28 (m, 1H), 7.22 – 7.18 (m, 1H), 7.16 – 7.08 (m, 2H), 4.56 (t, *J* = 6.9 Hz, 2H), 3.16 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.20, 163.68, 135.02, 134.73, 134.37, 132.48, 131.48, 130.16, 129.84, 128.97, 128.59, 127.14, 64.86, 32.90; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{13}O_3Cl$ 311.0445 found 311.0460.



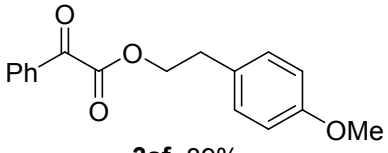
3ad, 80%

Product 3ad: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.74 (m, 2H), 7.69 – 7.61 (m, 1H), 7.53 – 7.38 (m, 4H), 7.19 – 7.05 (m, 2H), 4.60 (ddd, *J* = 9.5, 5.9, 2.4 Hz, 2H), 3.04 (td, *J* = 6.6, 3.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.27, 163.75, 136.15, 135.12, 132.39, 131.93, 130.92, 130.13, 129.02, 120.96, 66.05, 34.5; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{13}O_3Br$ 354.9940 found 354.9964.



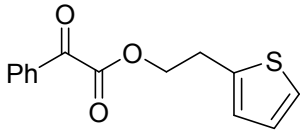
3ae, 88%

Product 3ae: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (t, *J* = 6.2 Hz, 2H), 7.65 (t, *J* = 6.9 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.17 (dd, *J* = 12.4, 5.1 Hz, 4H), 4.59 (t, *J* = 7.0 Hz, 2H), 3.12 (t, *J* = 7.2 Hz, 2H), 2.38 (d, *J* = 4.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.34, 163.79, 136.68, 135.08, 135.00, 132.50, 130.66, 130.18, 129.81, 128.98, 127.17, 126.38, 65.71, 32.35, 19.50; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{16}O_3$ 291.0992 found 291.1001.



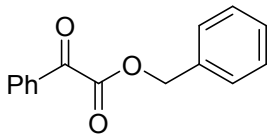
3af, 89%

Product 3af: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.68 – 7.58 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.24 – 7.10 (m, 2H), 6.94 – 6.78 (m, 2H), 4.59 (t, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 3.03 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.44, 163.86, 158.66, 134.98, 132.46, 130.14, 129.04, 128.94, 114.20 , 66.72, 55.36, 34.19; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{16}O_4$ 307.0941 found 307.0949.



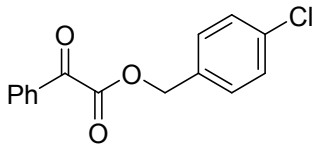
3ag, 65%

Product 3ag: Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.87 (m, 2H), 7.68 – 7.62 (m, 1H), 7.49 (td, *J* = 7.6, 1.7 Hz, 2H), 7.19 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.01 – 6.88 (m, 2H), 4.62 (t, *J* = 6.8 Hz, 2H), 3.31 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.22, 163.70, 138.98, 135.04, 132.44, 130.17, 128.99, 127.18, 126.14, 124.43, 66.21, 29.22; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{14}H_{12}O_3S$ 283.0399 found 283.0417.



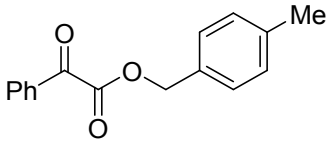
3ah, 84%

Product 3ah: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.53 – 7.33 (m, 7H), 5.42 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.17, 163.77, 135.06, 134.67, 132.56, 130.15, 128.94, 128.87, 67.88; HRMS (TOF) m/z [M + Na]$^{+}$ Calcd for $C_{15}H_{12}O_3$ 263.0679 found 263.0685.



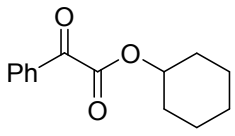
3ai, 81%

Product 3ai: Light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 13.8, 6.5 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.47 – 7.29 (m, 4H), 5.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.92, 163.56, 135.17, 134.94, 133.18, 132.48, 130.15, 130.11, 129.10, 129.07, 66.99; HRMS (TOF) m/z [M + Na]$^{+}$ Calcd for $C_{15}H_{11}O_3Cl$ 297.0829 found 297.0300.



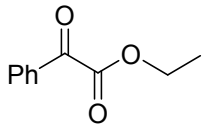
3aj, 87%

Product 3aj: Light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.89 (m, 2H), 7.68 – 7.59 (m, 1H), 7.53 – 7.44 (m, 2H), 7.33 (t, *J* = 10.6 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 5.38 (s, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.27, 163.85, 138.91, 135.03, 132.61, 131.69, 130.16, 129.55, 129.02, 128.91, 67.92, 21.38; HRMS (TOF) m/z [M + Na]$^{+}$ Calcd for $C_{16}H_{14}O_3$ 277.0835 found 277.0845.



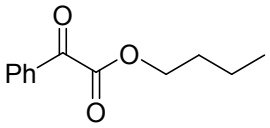
3ak, 80%

Product 3ak: Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 7.76 (m, 2H), 7.74 – 7.56 (m, 1H), 7.54 – 7.40 (m, 2H), 5.09 (ddd, *J* = 13.2, 8.9, 4.0 Hz, 1H), 1.99 (d, *J* = 4.1 Hz, 2H), 1.78 (dd, *J* = 8.7, 4.2 Hz, 2H), 1.65 – 1.51 (m, 3H), 1.47 – 1.27 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.94, 163.80, 134.90, 132.71, 130.07, 129.00, 75.57, 31.57, 25.30, 23.76; HRMS (TOF) m/z [M + Na]$^{+}$ Calcd for $C_{14}H_{16}O_3$ 255.0992 found 255.0998.



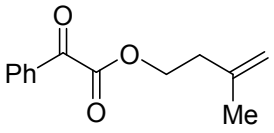
3al, 73%

Product 3al: Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.93 (m, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.56, 163.96, 135.02, 132.62, 130.15, 129.02, 62.46, 14.24; HRMS (TOF) m/z $[M + Na]^+$ Calcd for $C_{10}H_{10}O_3$ 201.0522 found 201.0523.



3am, 76%

Product 3am: Colourless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 4.32 (t, *J* = 6.7 Hz, 2H), 1.73 – 1.64 (m, 2H), 1.43 – 1.32 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.62, 164.13, 134.99, 132.63, 130.11, 129.01, 66.21, 30.59, 19.15, 13.74; HRMS (TOF) m/z $[M + Na]^+$ Calcd for $C_{12}H_{14}O_3$ 229.0835 found 229.0841.



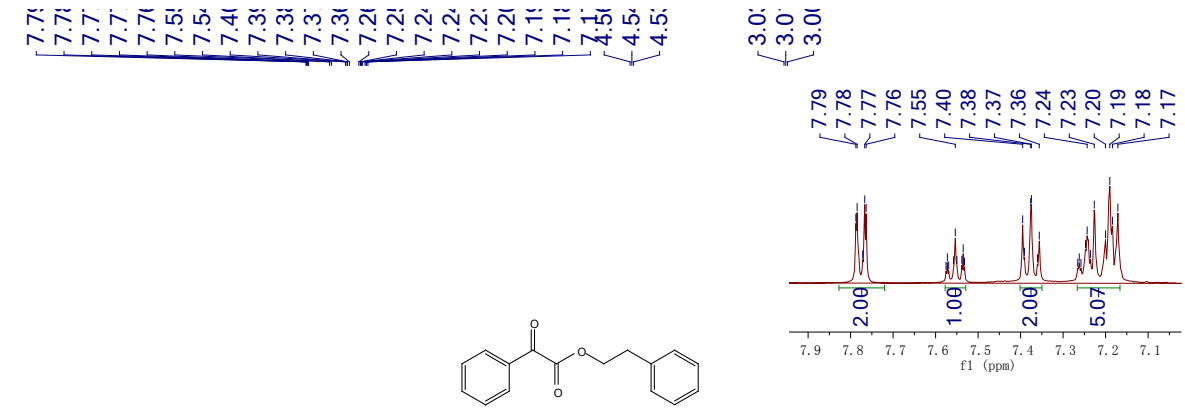
3an, 70%

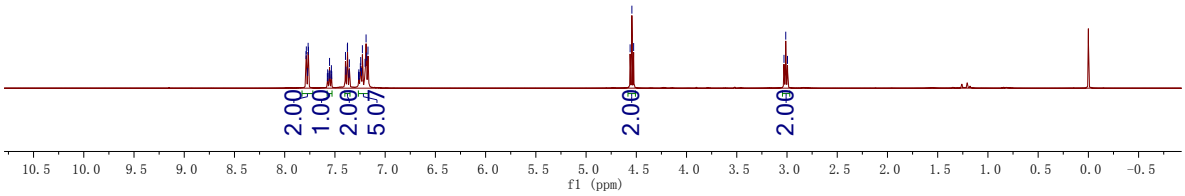
Product 3an: Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 4.78 (s, 1H), 4.72 (s, 1H), 4.44 (t, *J* = 6.9 Hz, 2H), 2.42 (t, *J* = 6.8 Hz, 2H), 1.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.43, 163.92, 141.01, 135.01, 132.55, 130.16, 128.98, 113.13, 64.45, 36.66, 22.54; HRMS (TOF) m/z $[M + Na]^+$ Calcd for $C_{13}H_{14}O_3$ 241.0835 found 241.0834.

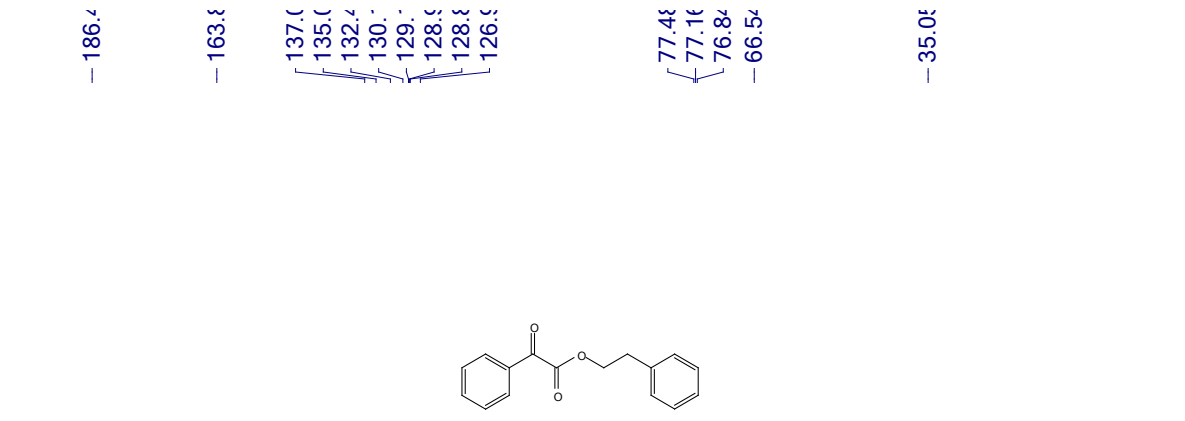
Product 3ao: Light yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.3 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 5.45 (d, *J* = 4.3 Hz, 1H), 4.94 (ddd, *J* = 16.4, 10.5, 4.7 Hz, 1H), 2.50 (d, *J* = 7.7 Hz, 2H), 2.05 – 1.76 (m, 6H), 1.61 – 1.46 (m, 6H), 1.40 – 1.10 (m, 11H), 1.06 – 0.97 (m, 6H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.87 (dd, *J* = 6.6, 2.1 Hz, 6H), 0.69 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 186.68, 163.55, 139.14, 134.81, 132.68, 130.04, 128.92, 123.42, 76.65, 56.78, 56.26, 50.13, 42.41, 39.81, 39.60, 37.97, 37.03, 36.69, 36.27, 35.85, 32.00, 31.94, 28.28, 28.07, 27.73, 24.35, 23.91, 22.86, 22.61, 21.13, 19.34, 18.79, 11.93; HRMS (TOF) m/z $[M + Na]^+$ Calcd for $C_{35}H_{50}O_3$ 541.3652 found 541.3654.

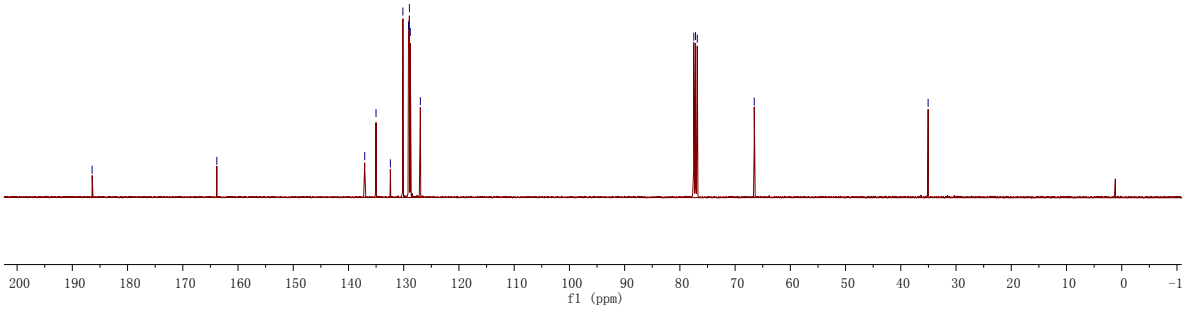
^{1}H NMR and ^{13}C NMR spectra of products 3

Product 3aa

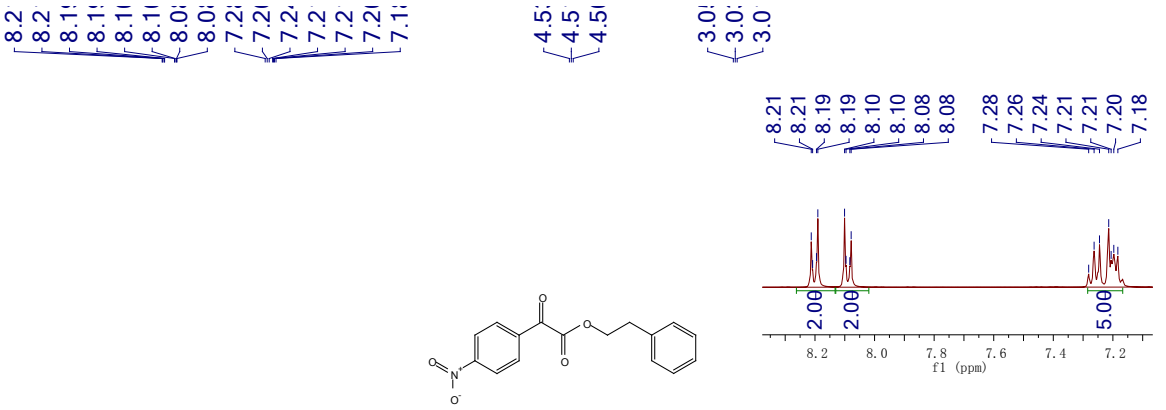


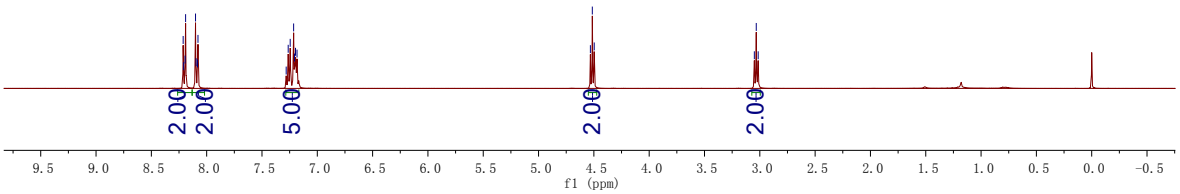


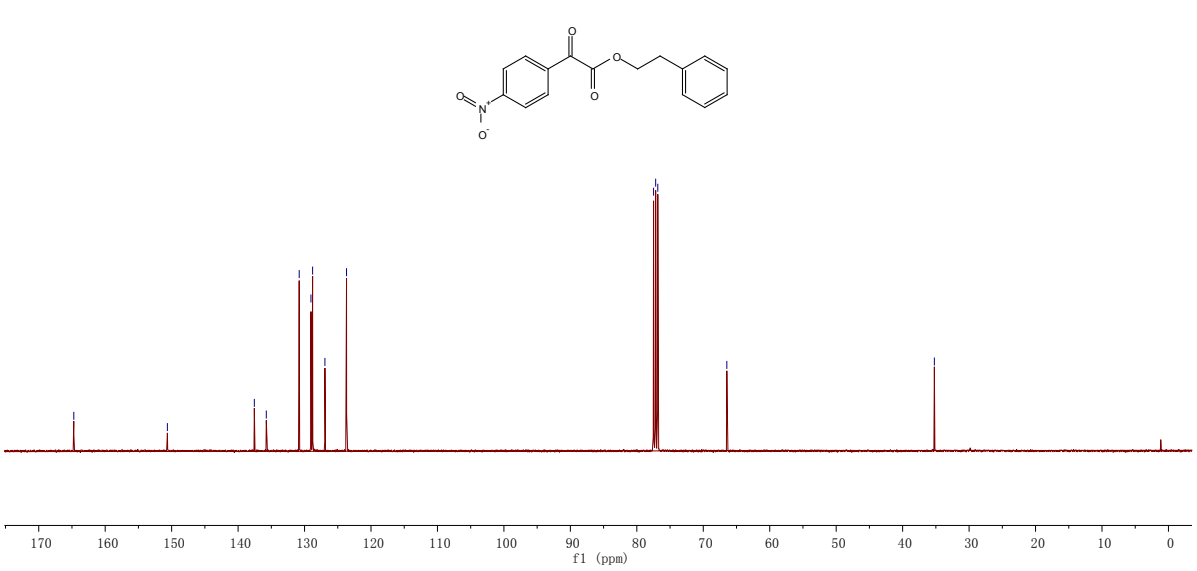




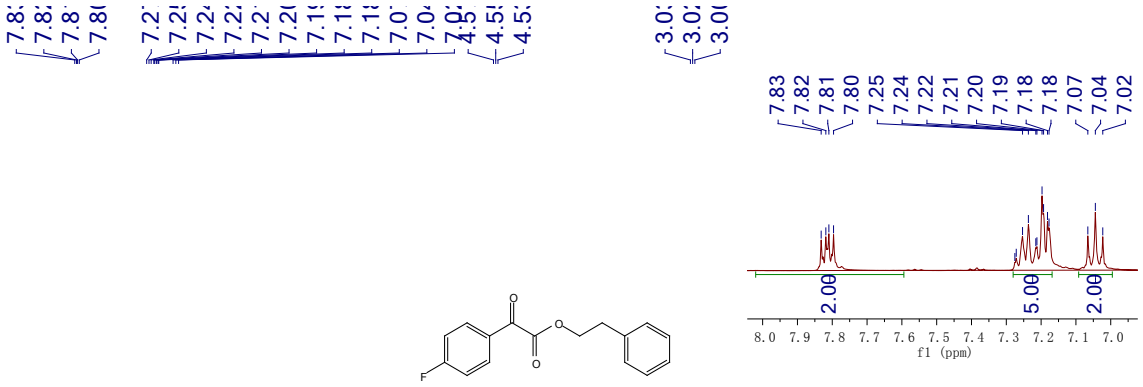
Product 3ba







Product 3ca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7.25
7.24
7.22
7.21
7.20
7.19
7.18
7.18
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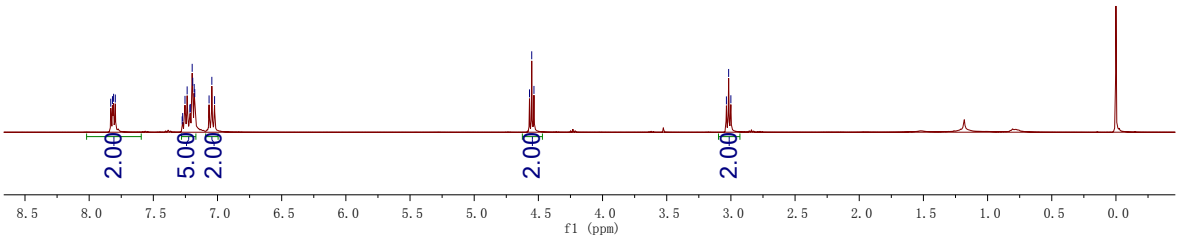
7.02
2.00
5.00
2.00
f1 (ppm)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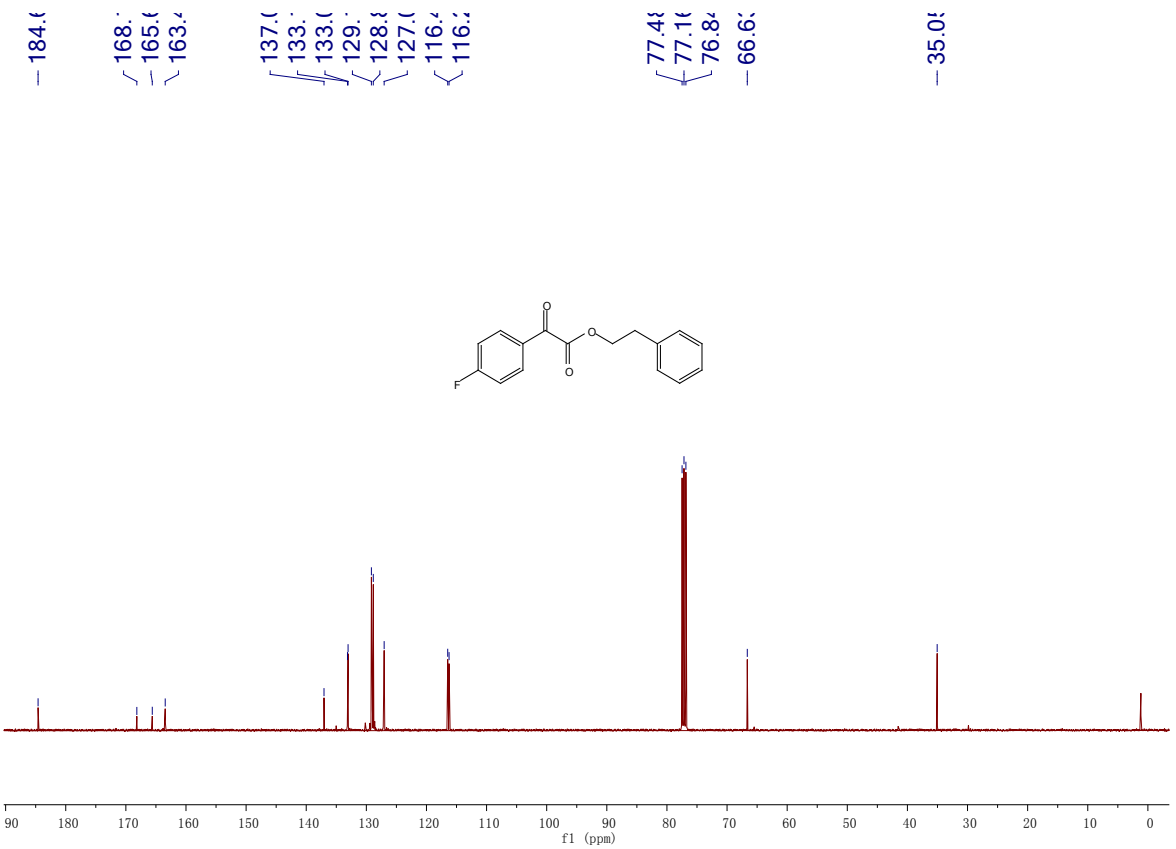
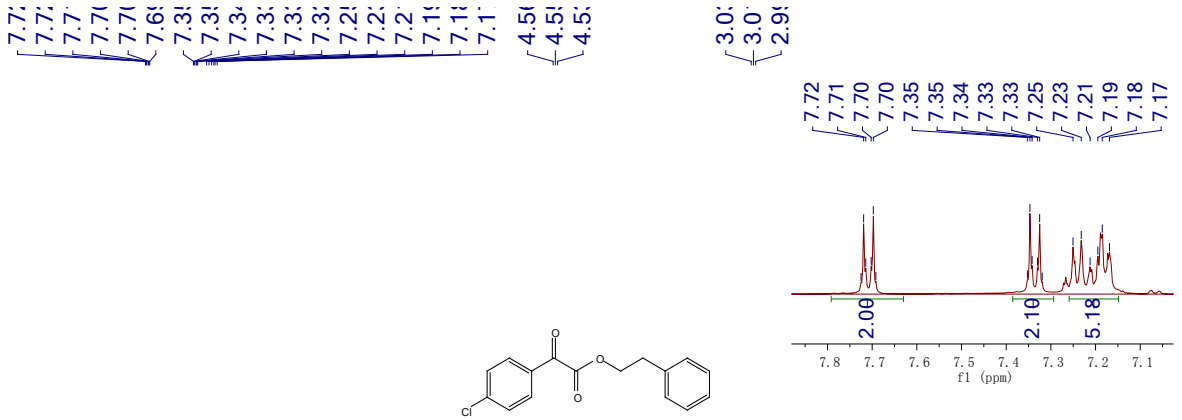
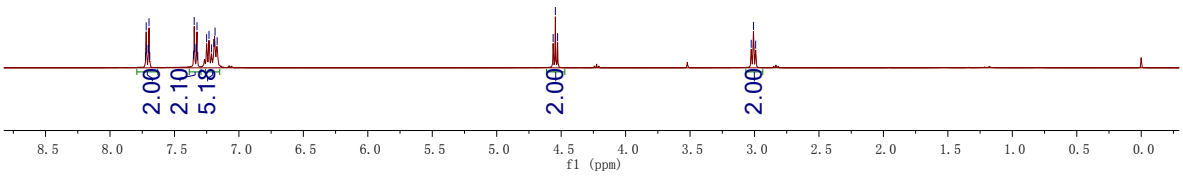
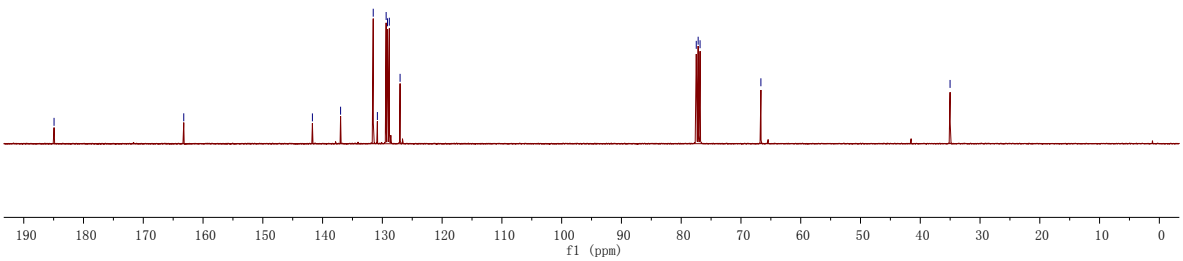
5.00
2.00
2.00
2.00
f1 (ppm)


184.
168.
165.
163.
137.
133.
133.
129.
128.
127.
116.
116.
77.4
77.1
76.8
66.6
35.0
f1 (ppm)

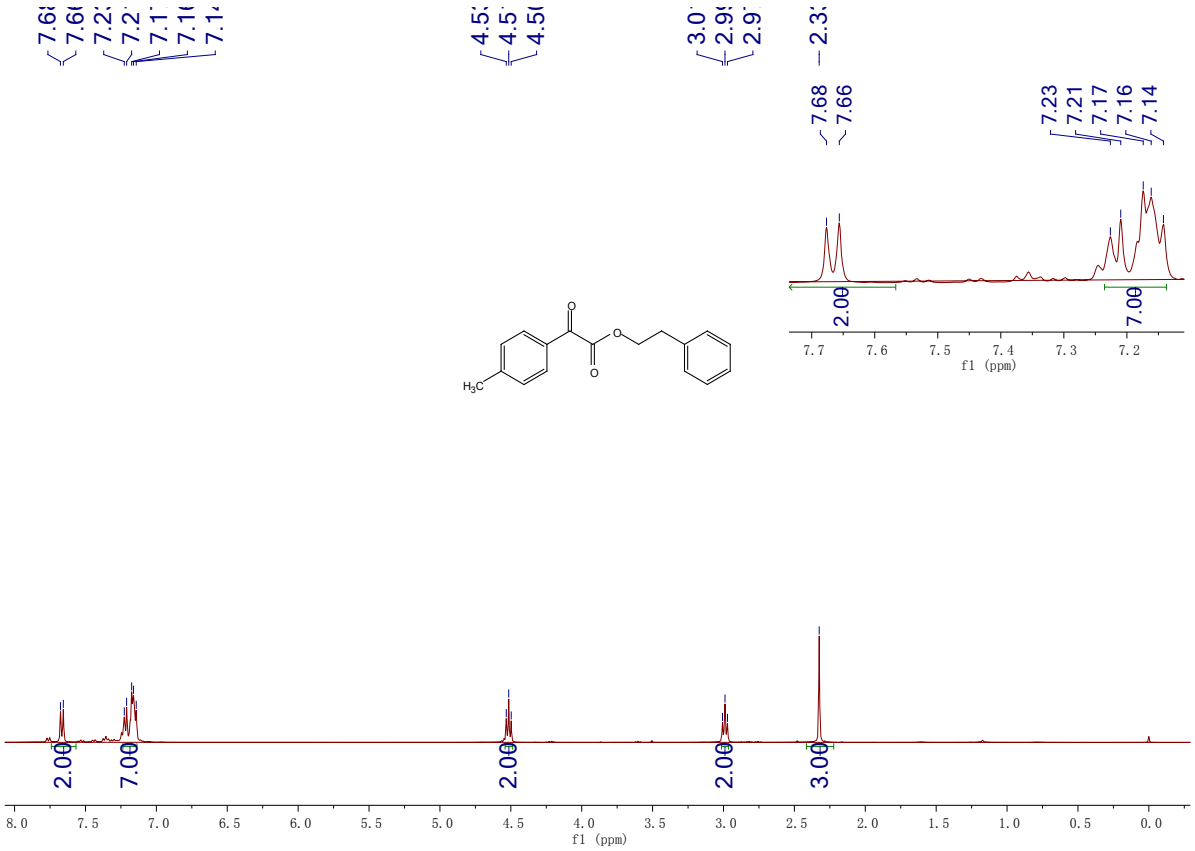
Product 3da

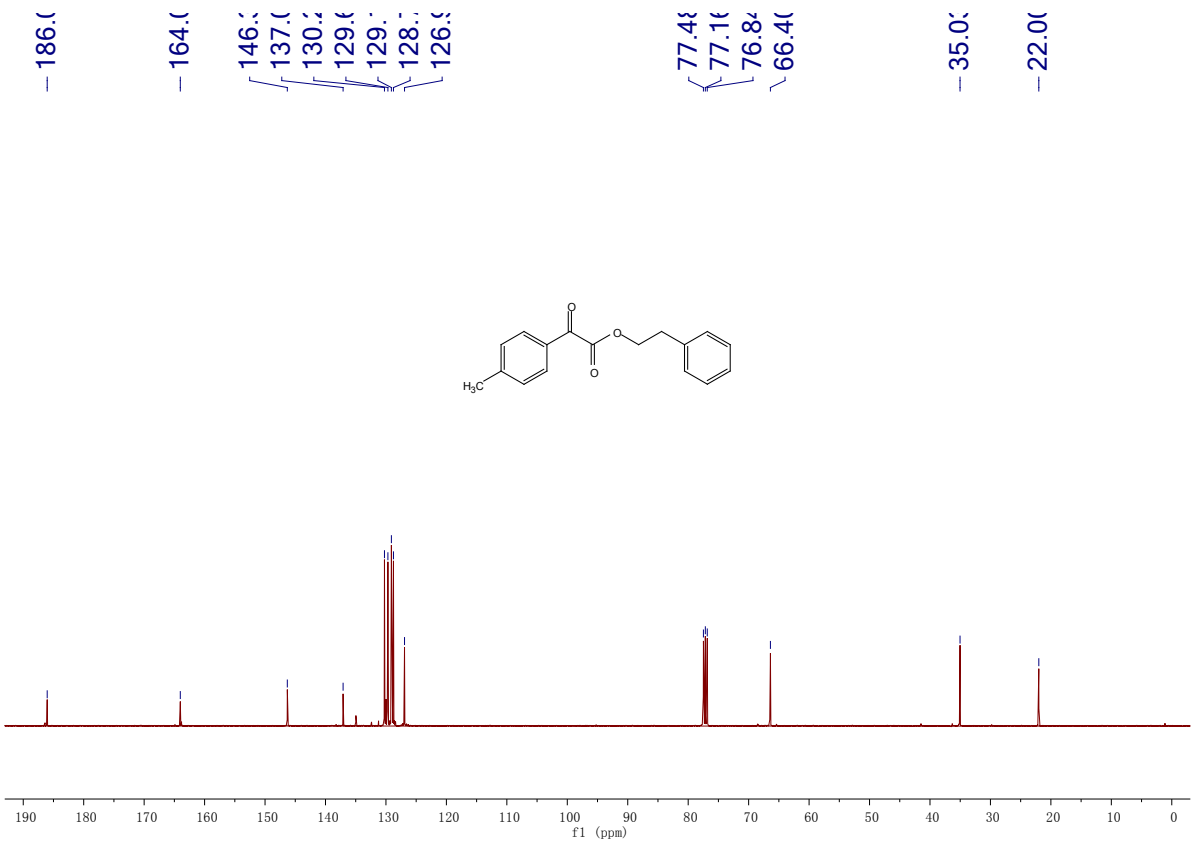




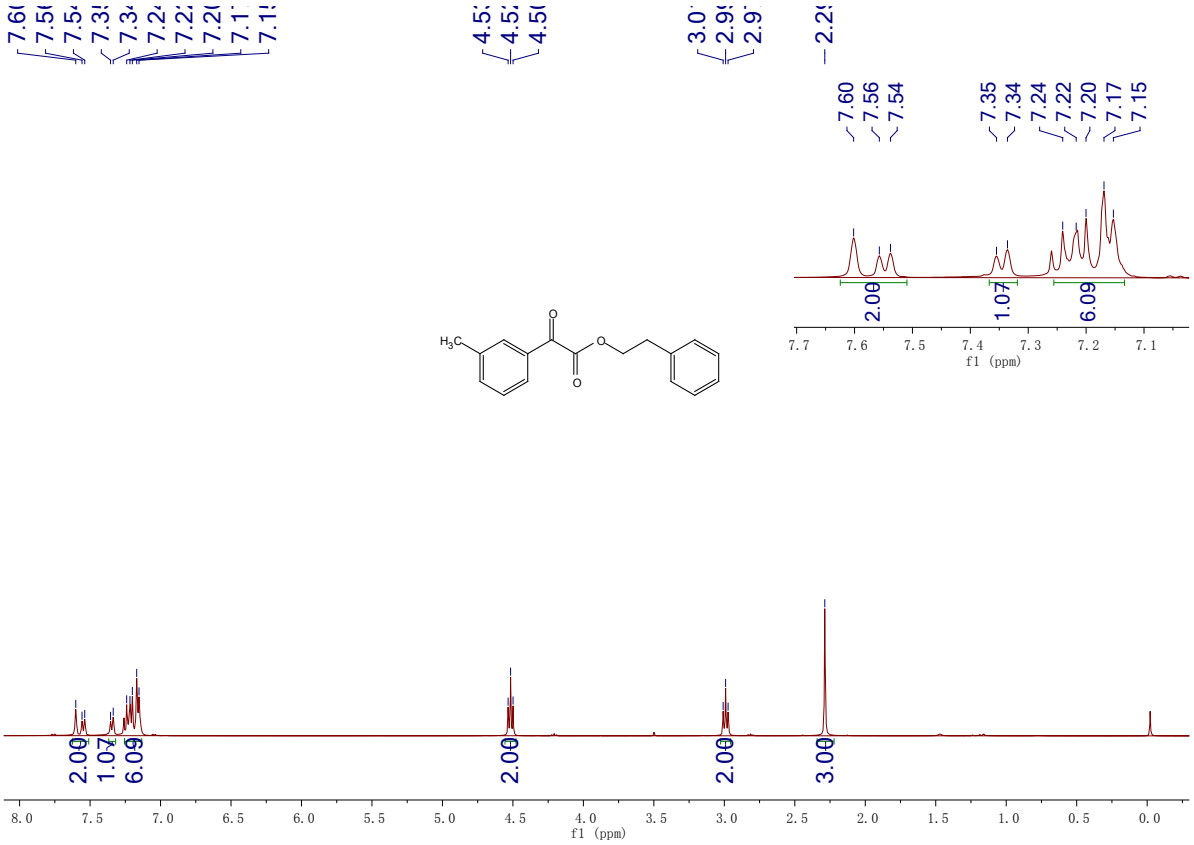


Product 3fa





Product 3ga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7.54
7.35
7.34
7.24
7.22
7.20
7.17
7.15
2.00
1.07
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f1 (ppm)
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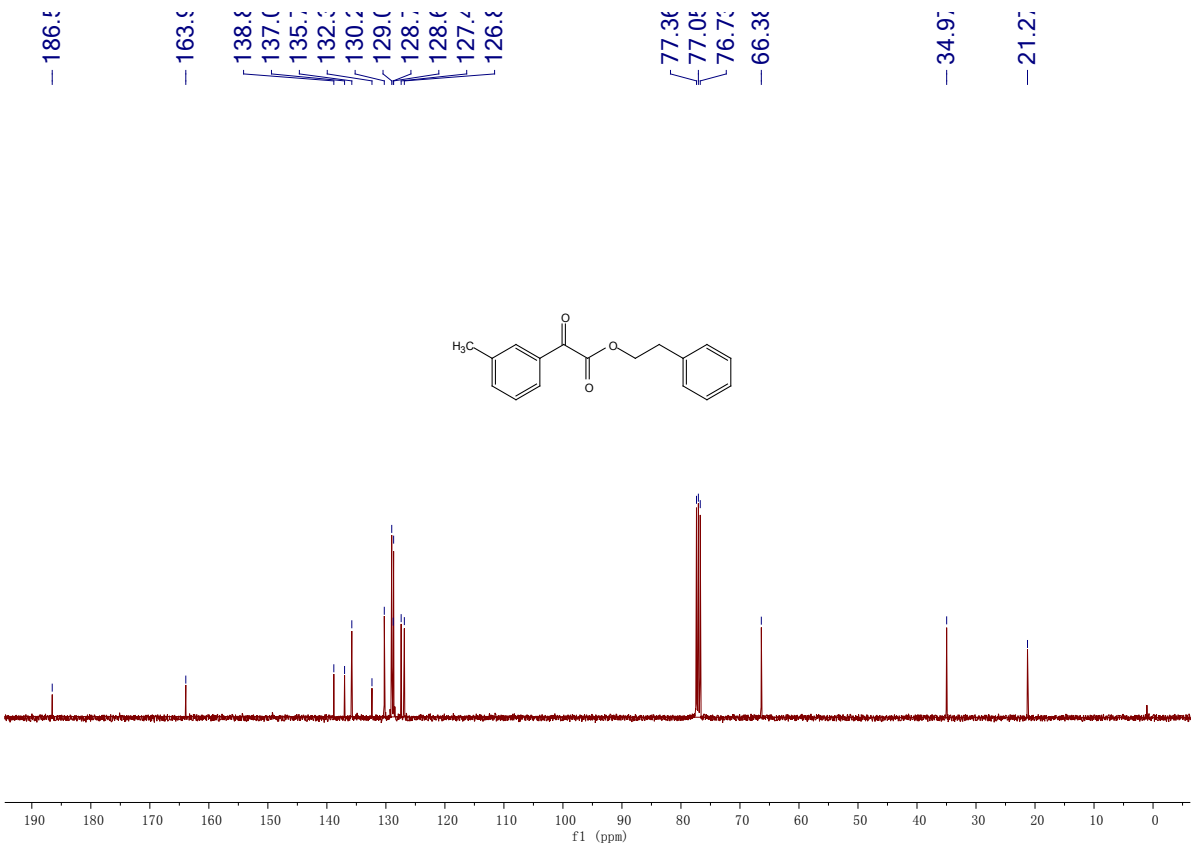
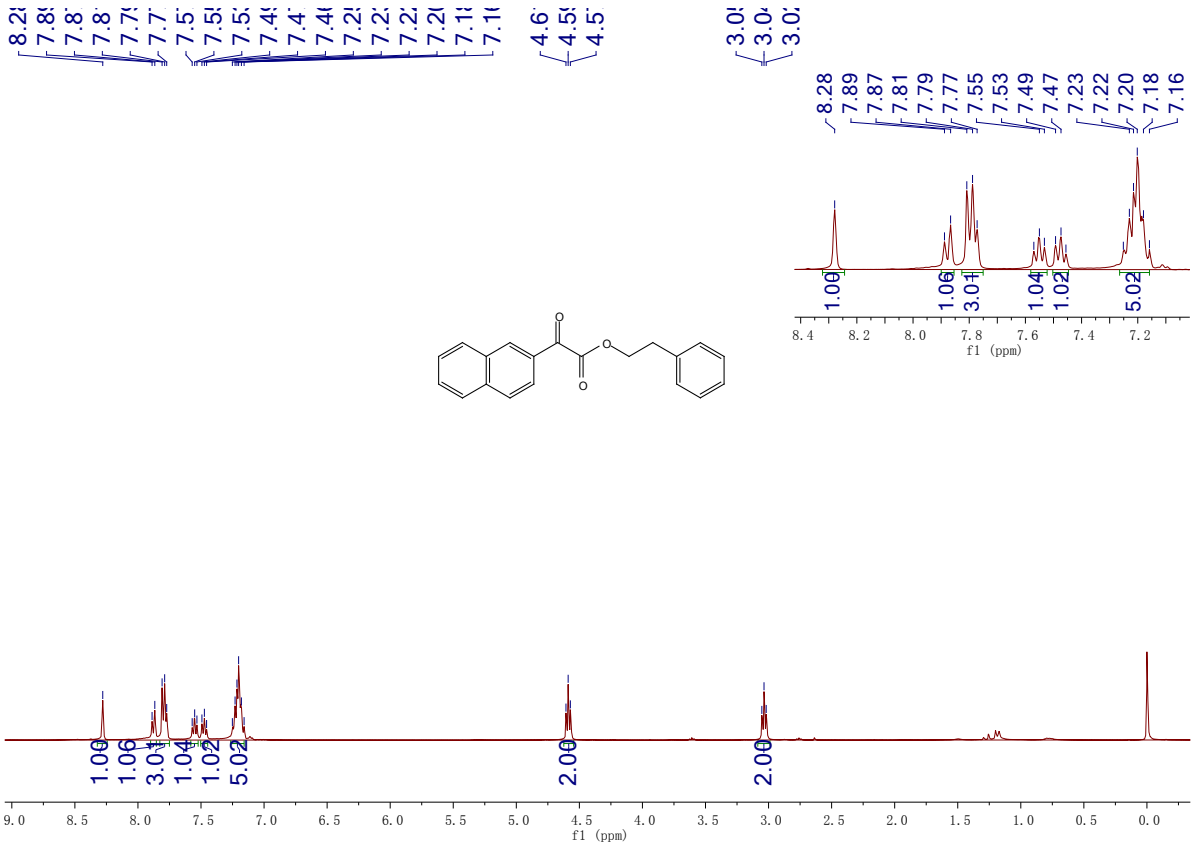
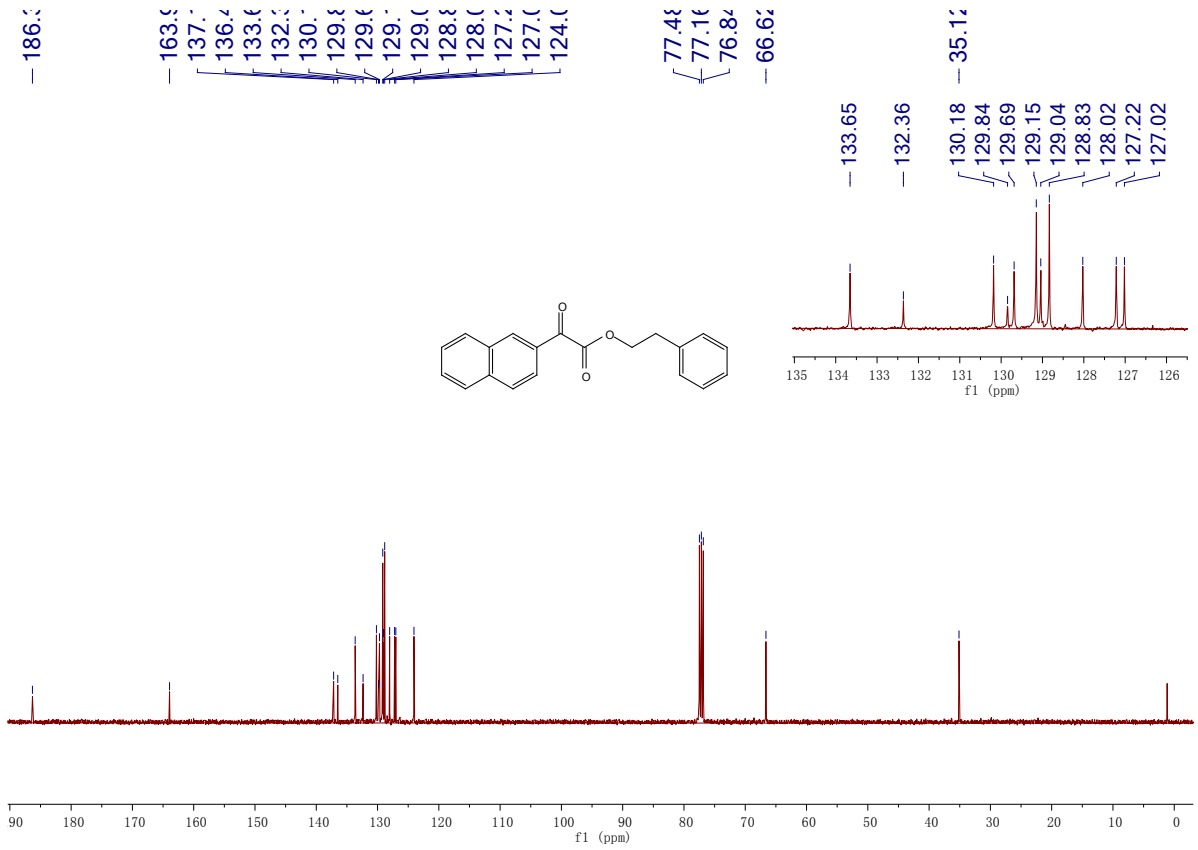
6.09
2.00
2.00
3.00
f1 (ppm)



Product 3ha

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129.84
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129.04
128.83
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127.22
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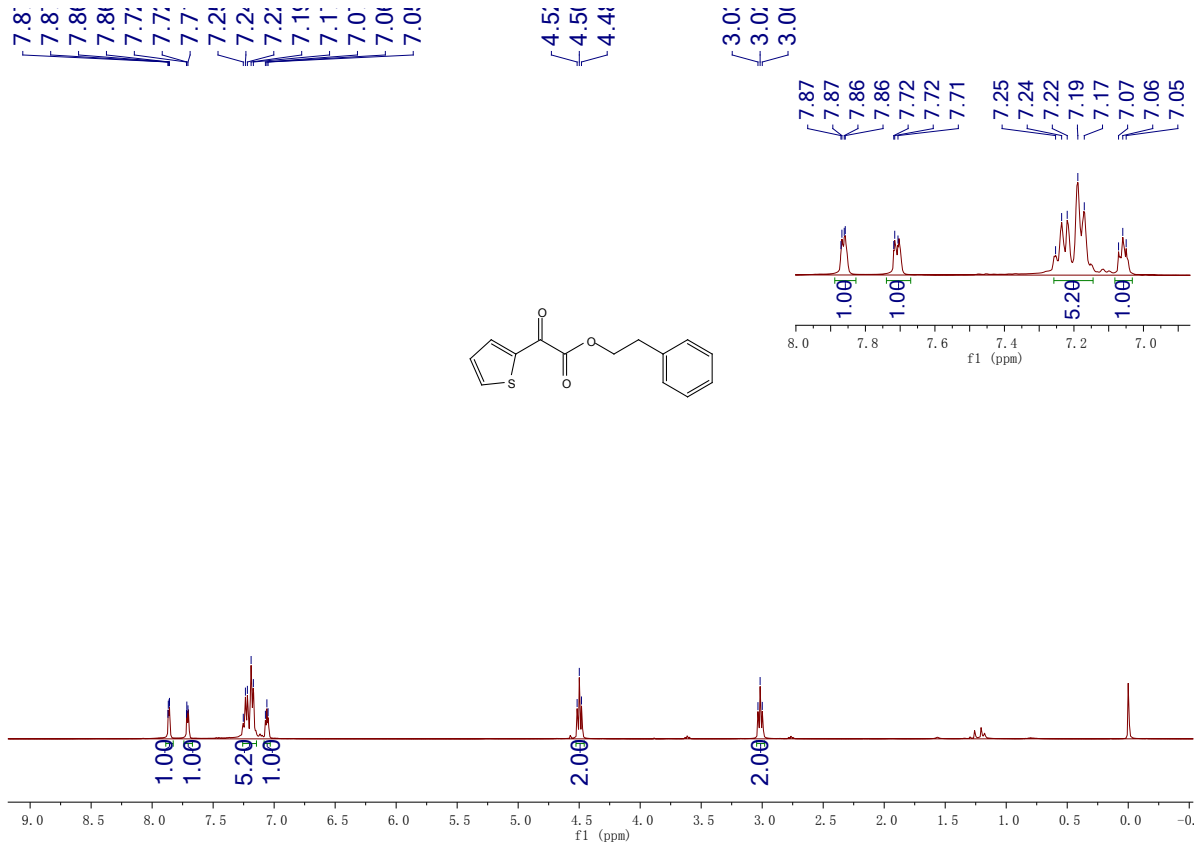
76.84
66.62
35.12
f1 (ppm)

Product 3ia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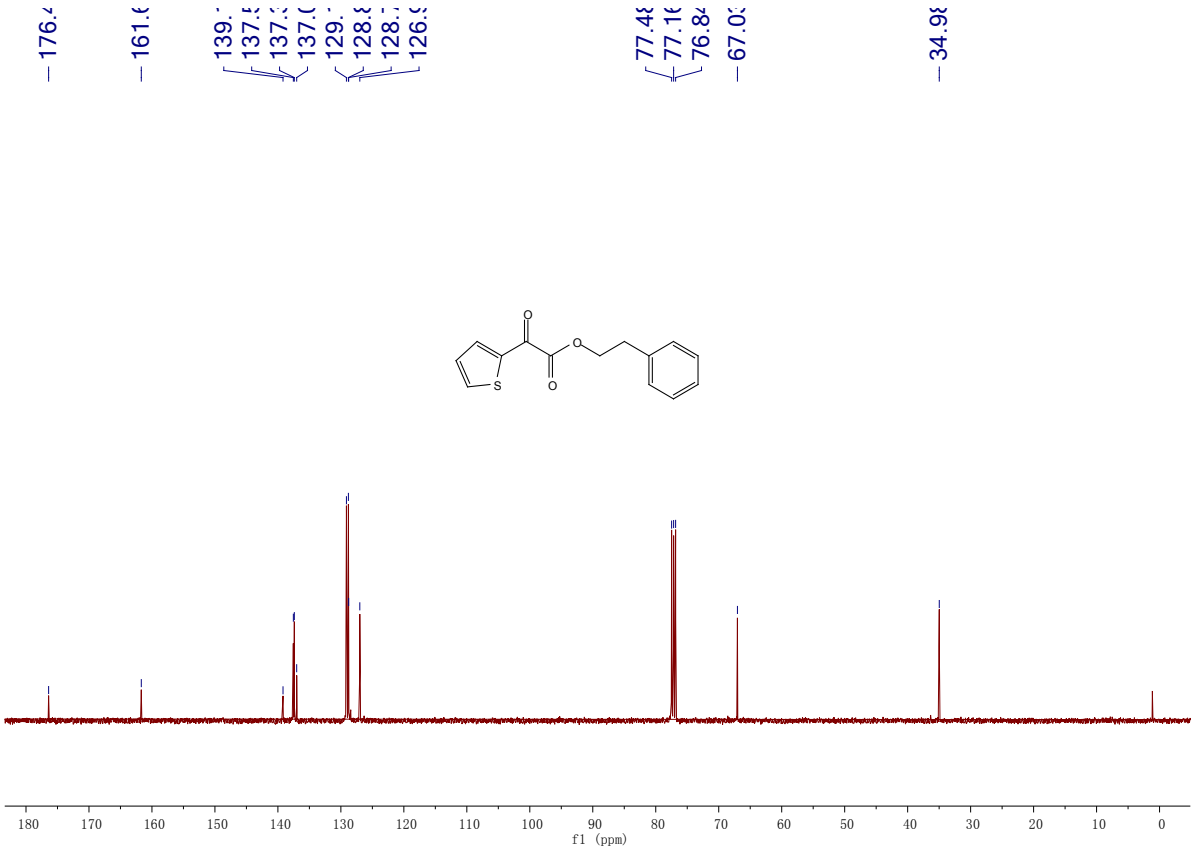
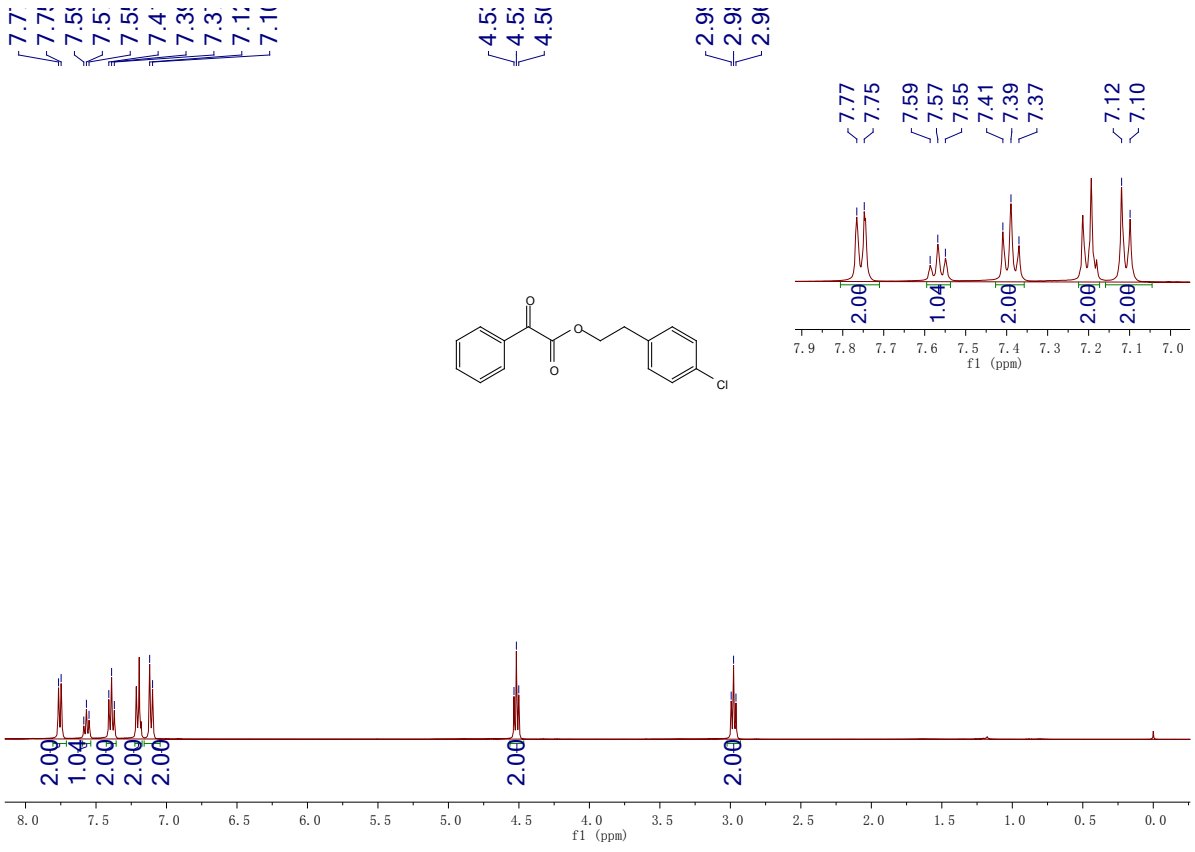
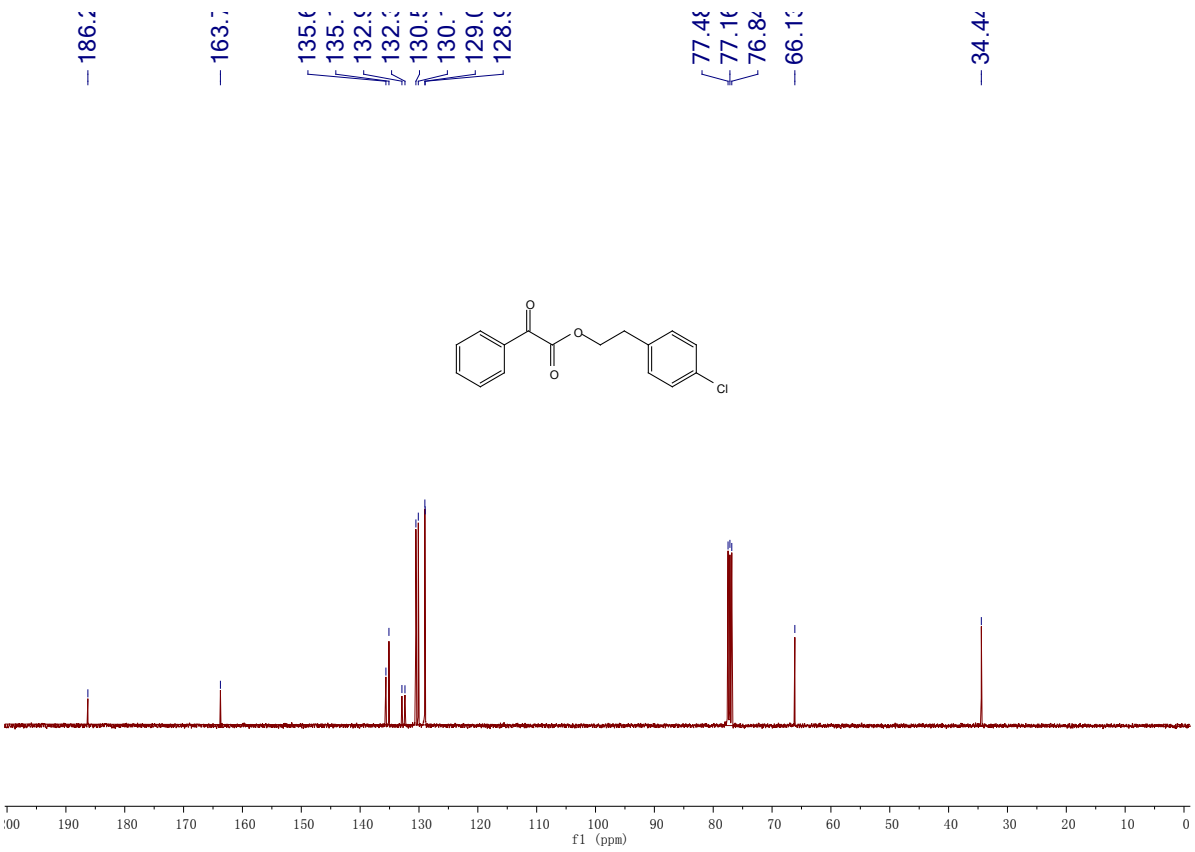
7.24
7.22
7.19
7.17
7.07
7.06
7.05
4.52
4.51
4.48
3.03
3.02
3.01
1.00
1.00
5.20
1.00
2.00
2.00
f1 (ppm)

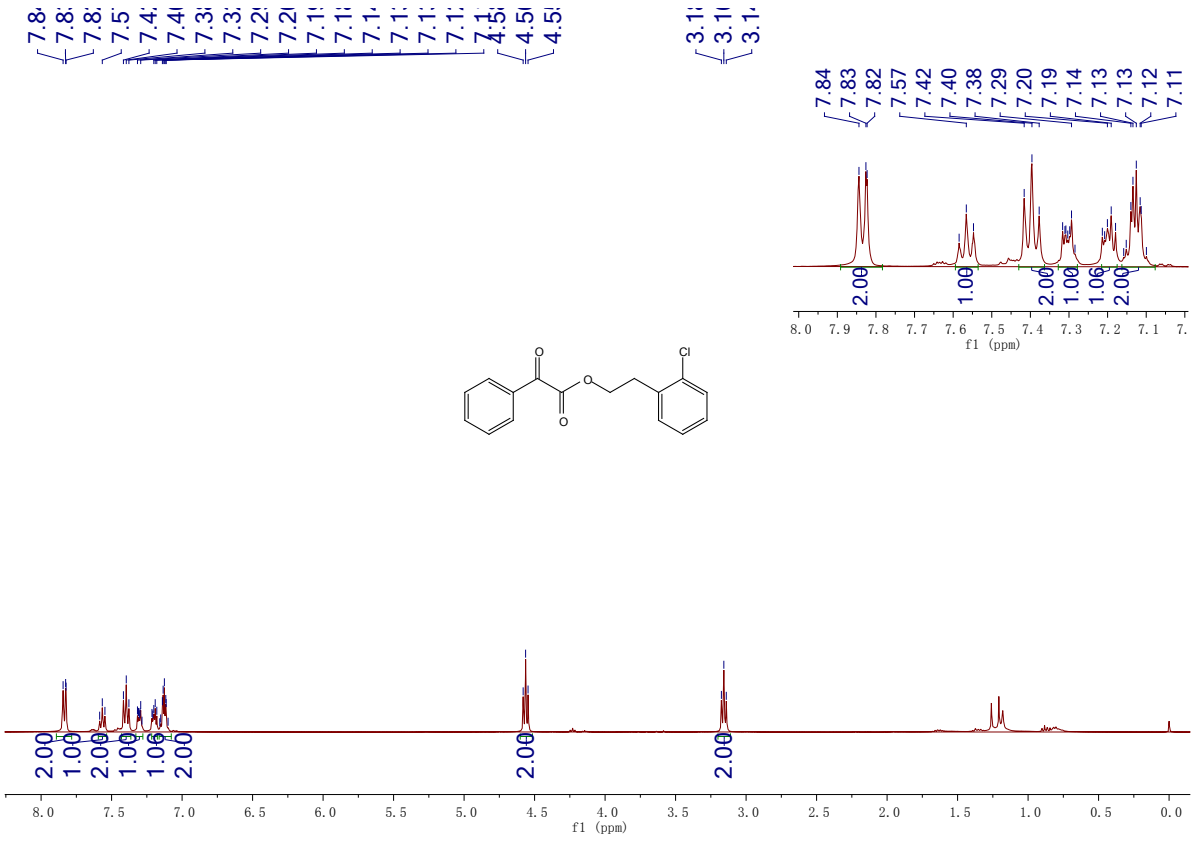


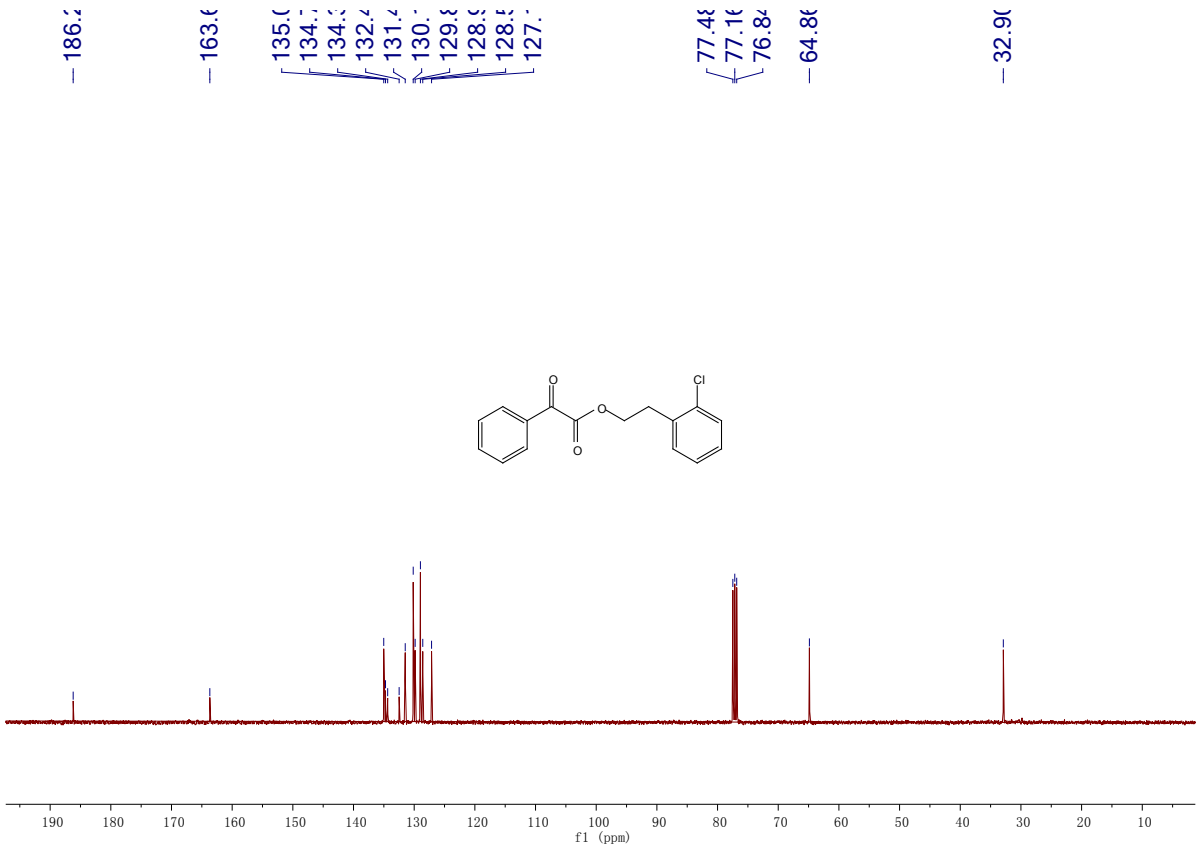
Product 3ab



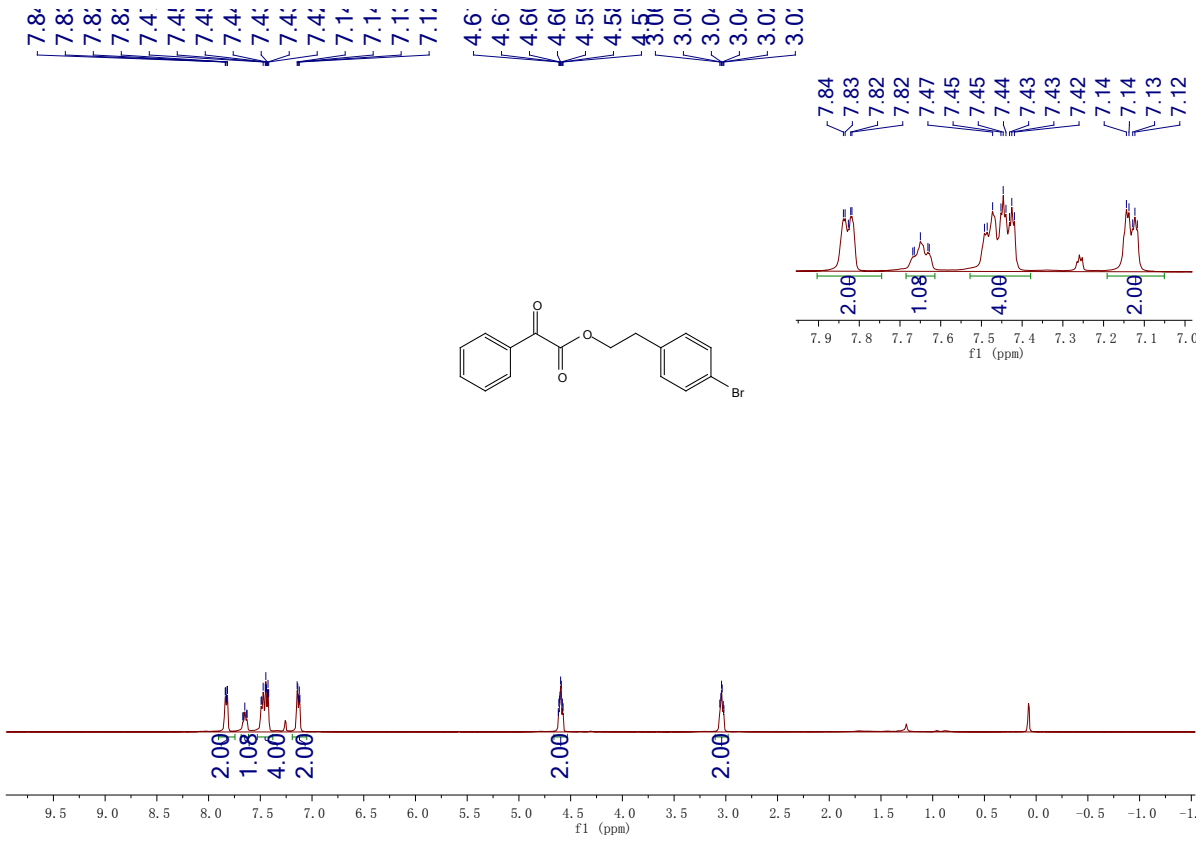


Product 3ac




— 186.
— 163.
135.
134.
134.
132.
131.
130.
129.
128.
128.
127.
77.4
77.1
76.8
— 64.8
— 32.9
O
Cl
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

Product 3ad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7.4
7.1
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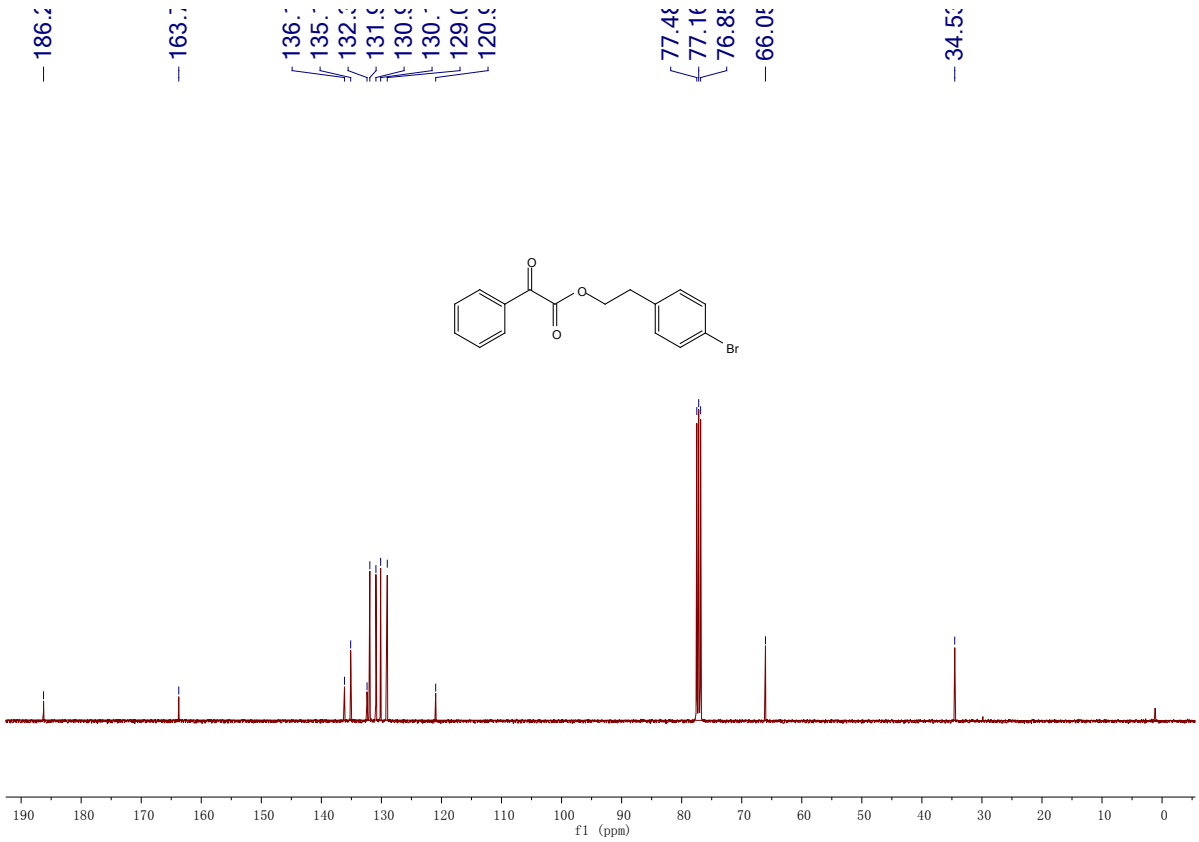
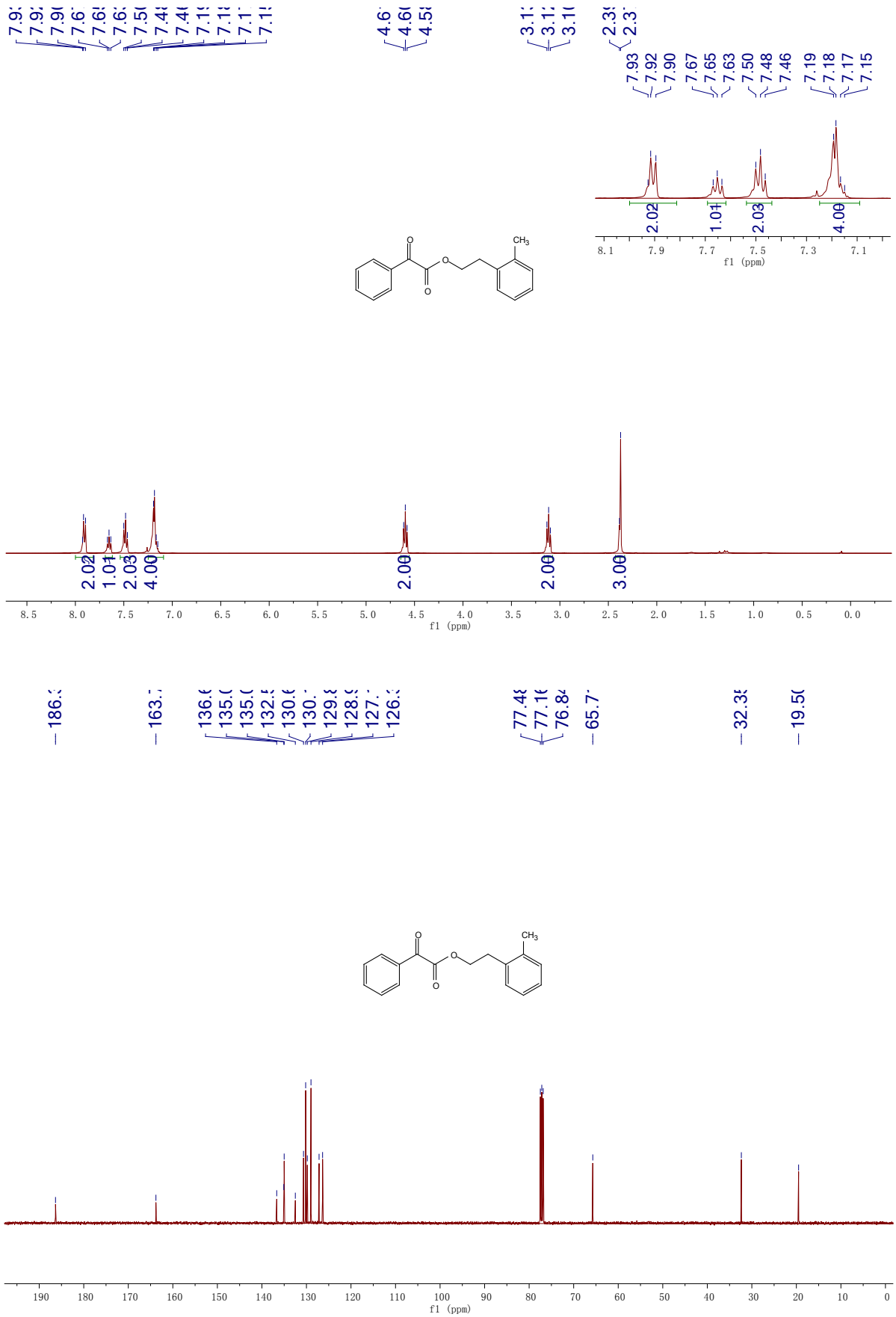
7.1
7.1
4.6
4.6
4.6
4.6
4.5
4.5
4.5
3.0
3.0
3.0
3.0
3.0
3.0
7.84
7.83
7.82
7.82
7.47
7.45
7.45
7.44
7.43
7.43
7.42
7.14
7.14
7.13
7.12
2.00
1.08
4.00
2.00
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
O
O
O
Br
2.00
1.08
4.00
2.00
2.00
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)


186.
163.
136.
135.
132.
131.
130.
130.
129.
120.
77.48
77.16
76.85
66.05
34.52
O
O
O
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Product 3ae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7.92
7.90
7.67
7.65
7.63
7.50
7.48
7.46
7.19
7.18
7.17
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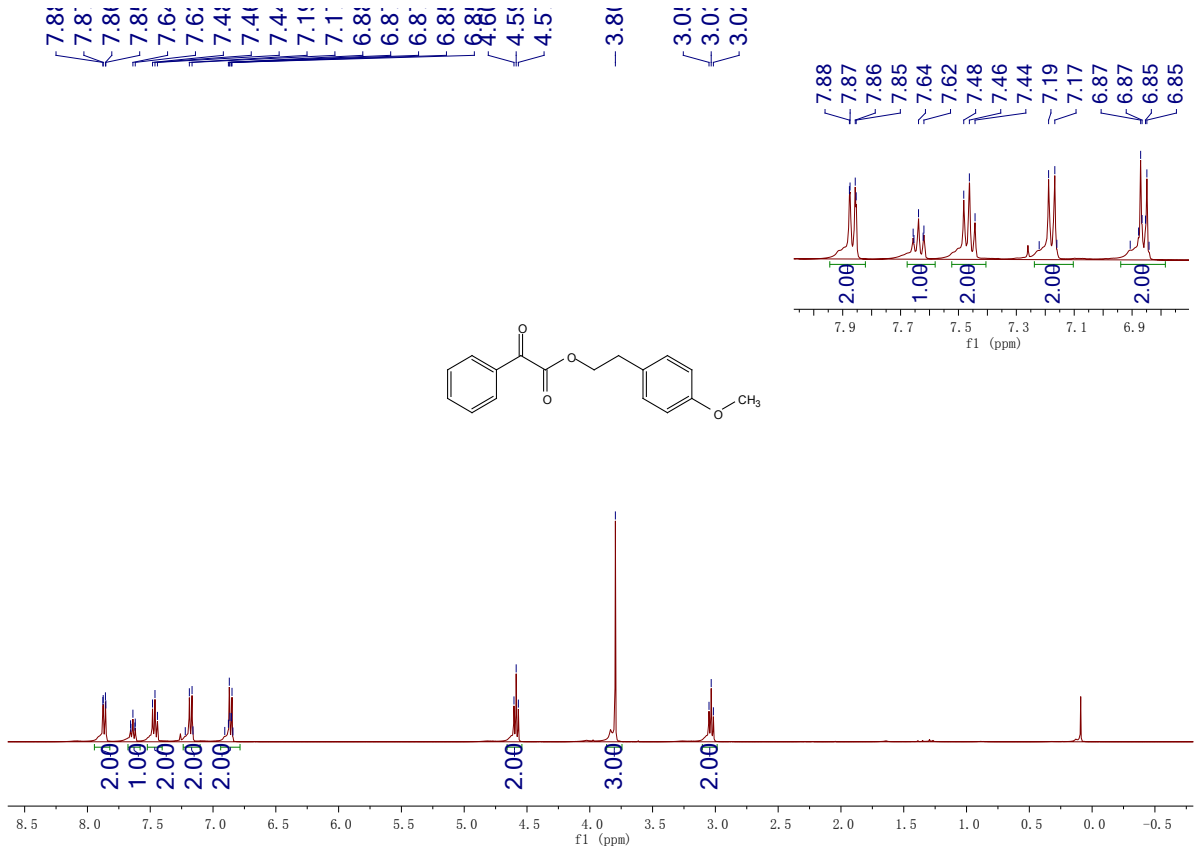
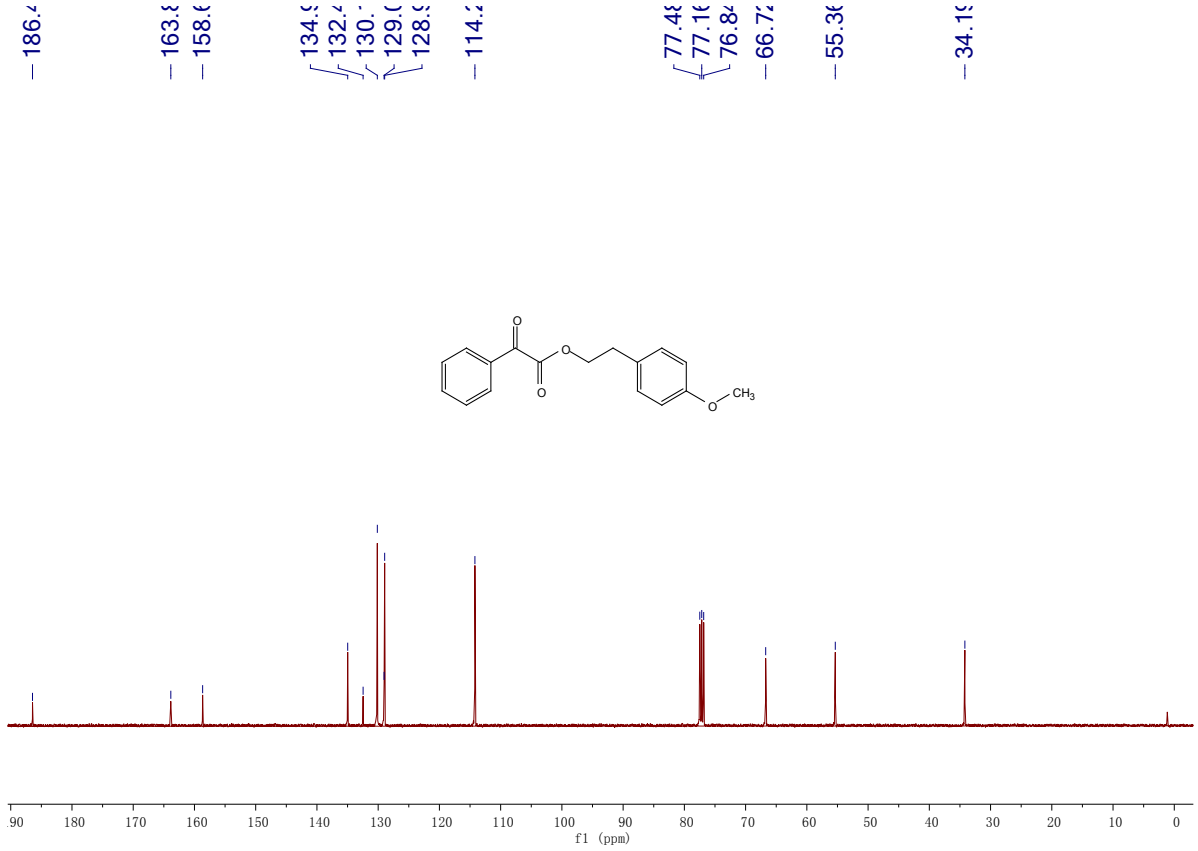
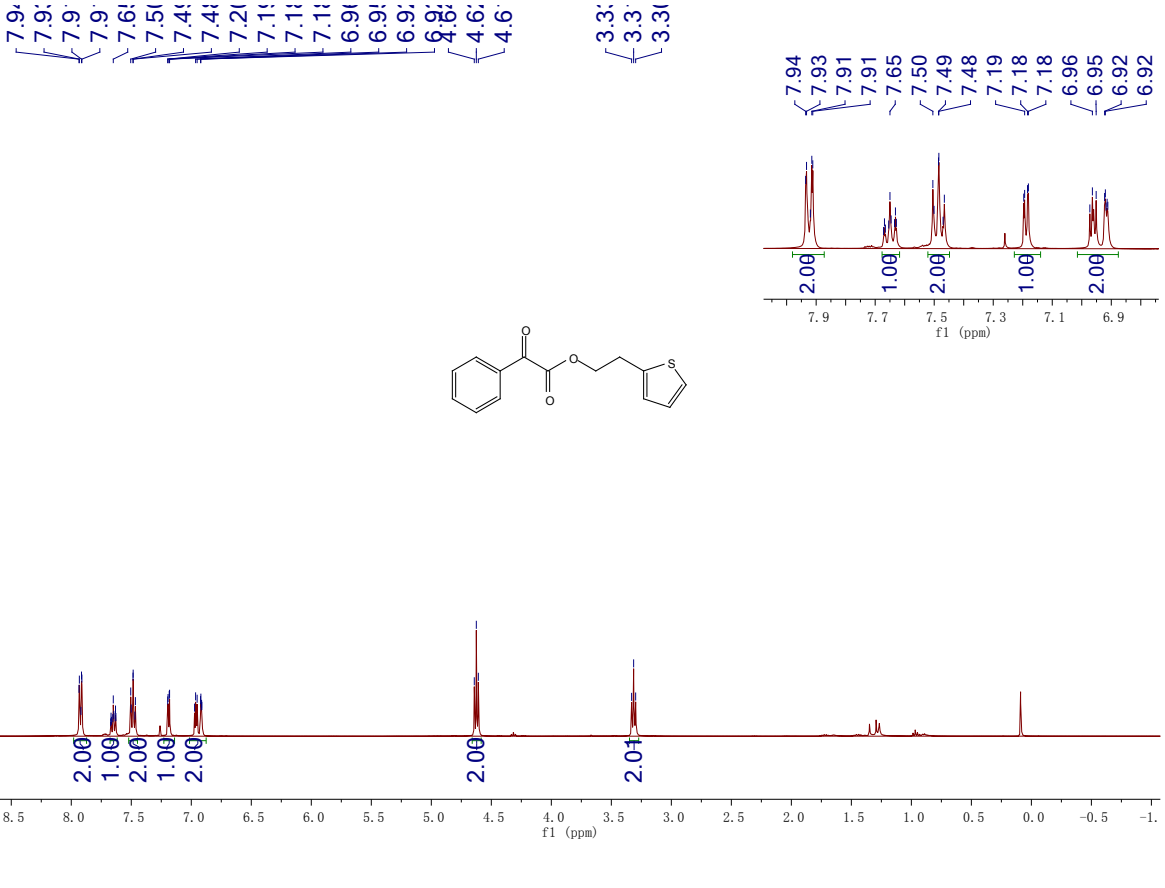
4.60
4.58
3.13
3.12
3.10
2.38
2.37
2.02
1.01
2.03
4.00
2.00
2.00
3.00
f1 (ppm)
CH3
O
O
O
186.4
163.7
136.6
135.0
135.0
132.5
130.6
130.1
129.8
128.9
127.1
126.3
77.48
77.16
76.84
65.77
32.35
19.50
f1 (ppm)

Product 3af

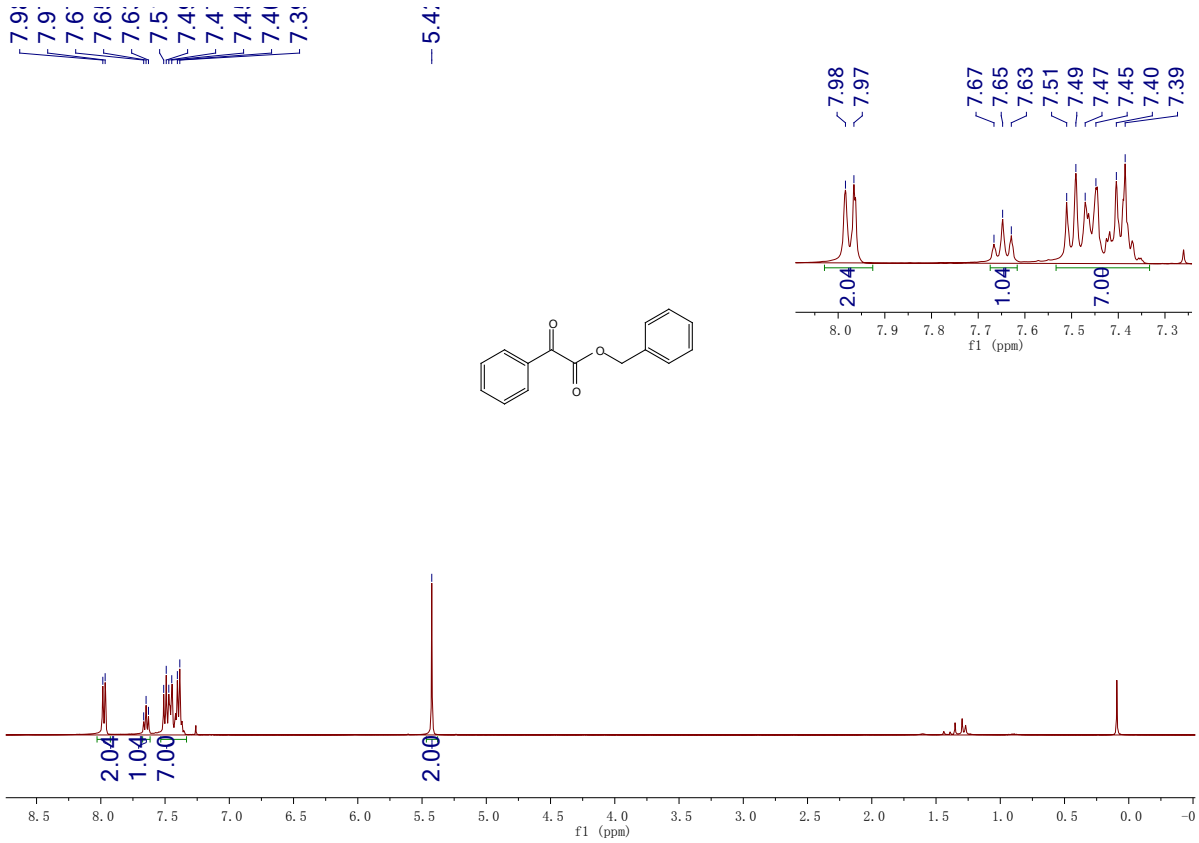




Product 3ag



Product 3ah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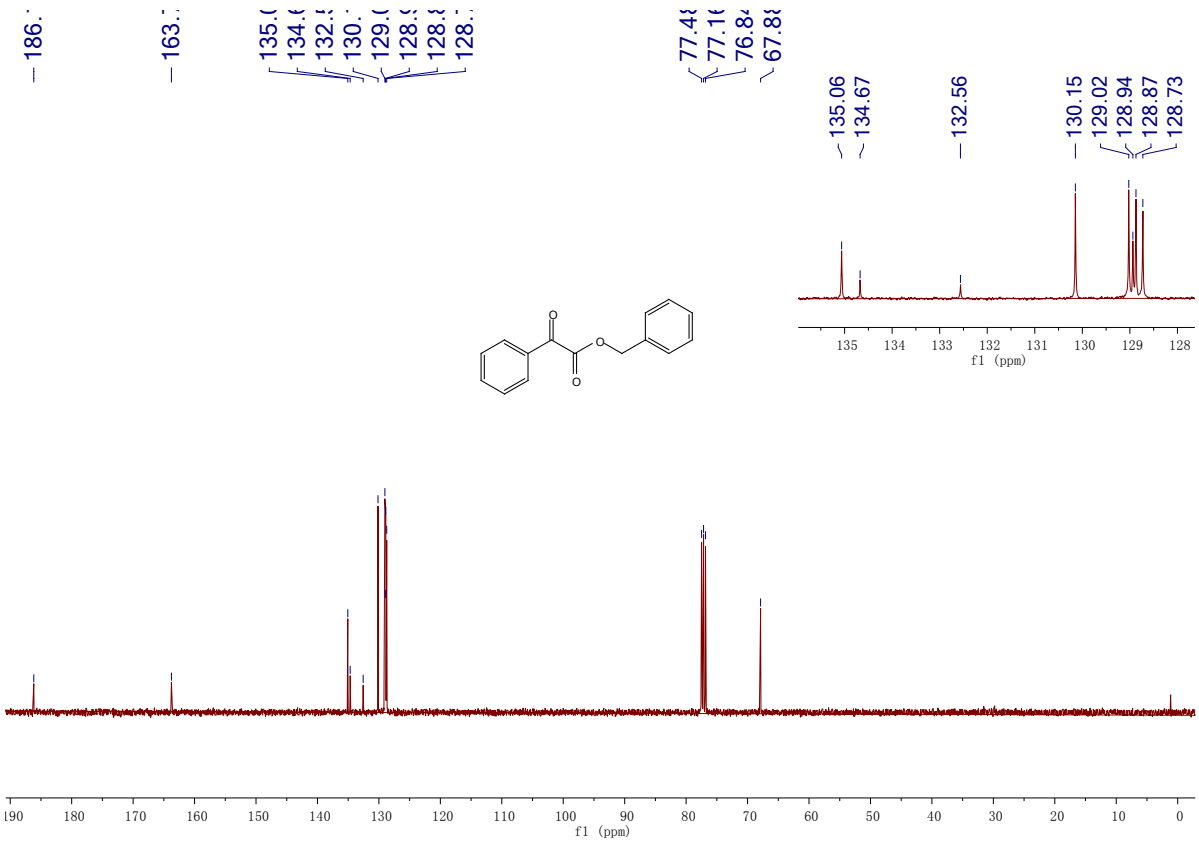
7.97
7.67
7.65
7.63
7.51
7.49
7.47
7.45
7.40
7.39
2.04
1.04
7.00
2.00
f1 (ppm)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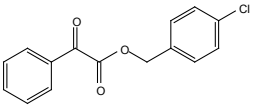
134.67
132.56
130.15
129.02
128.94
128.87
128.73
77.48
77.16
76.84
67.88
f1 (ppm)

Product 3ai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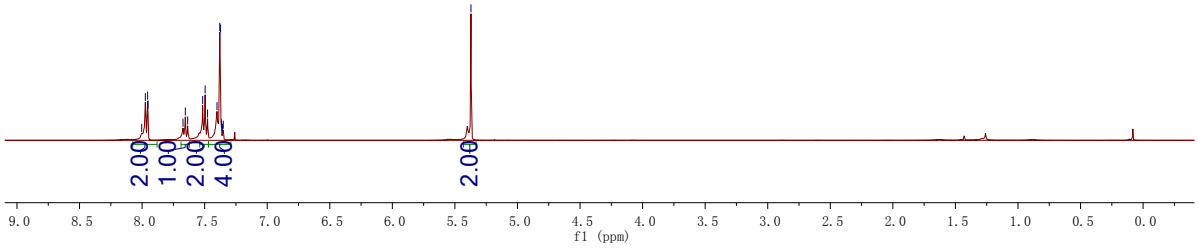
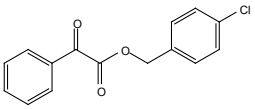
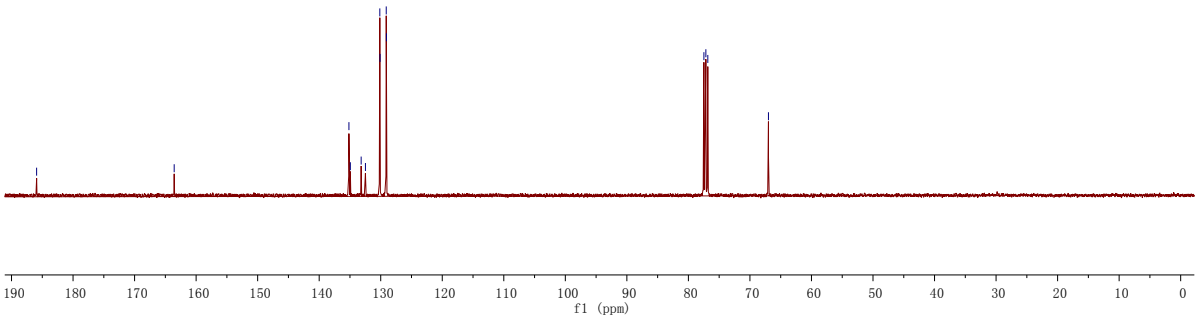
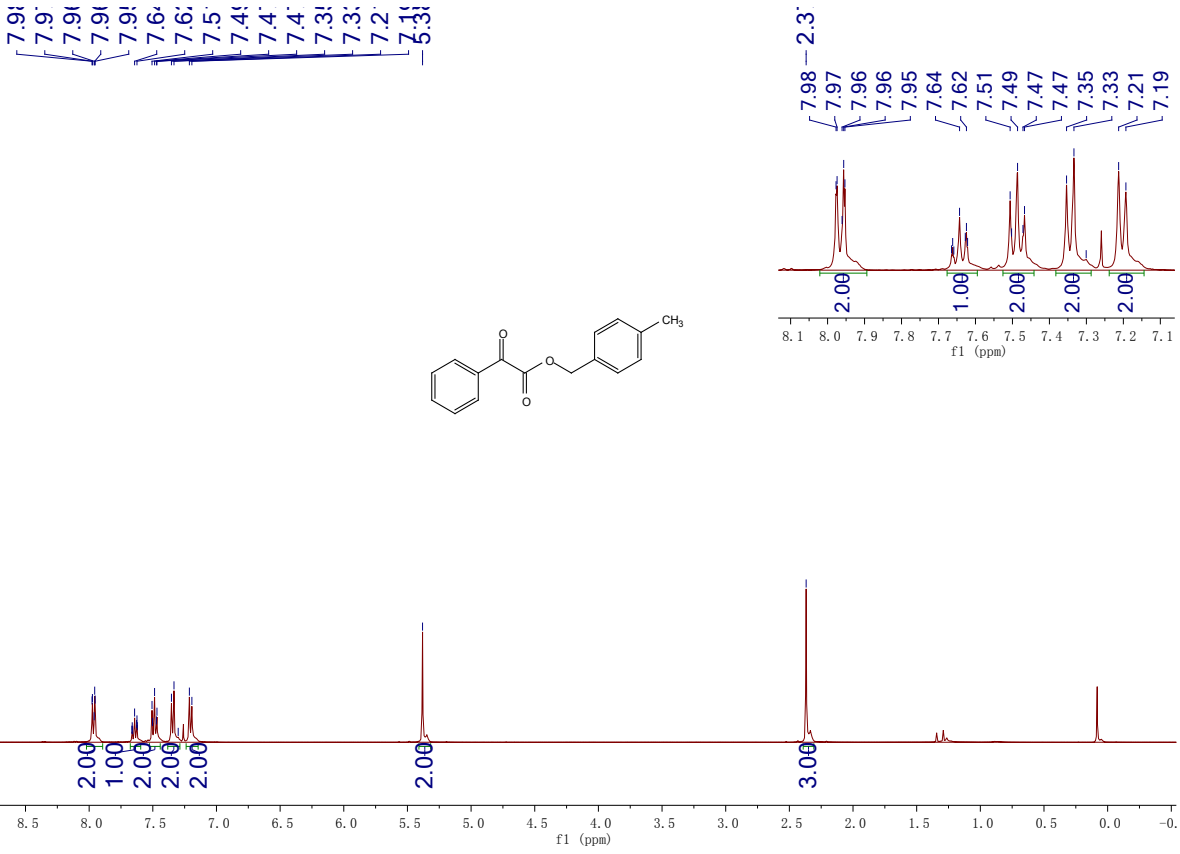
O
O
Cl

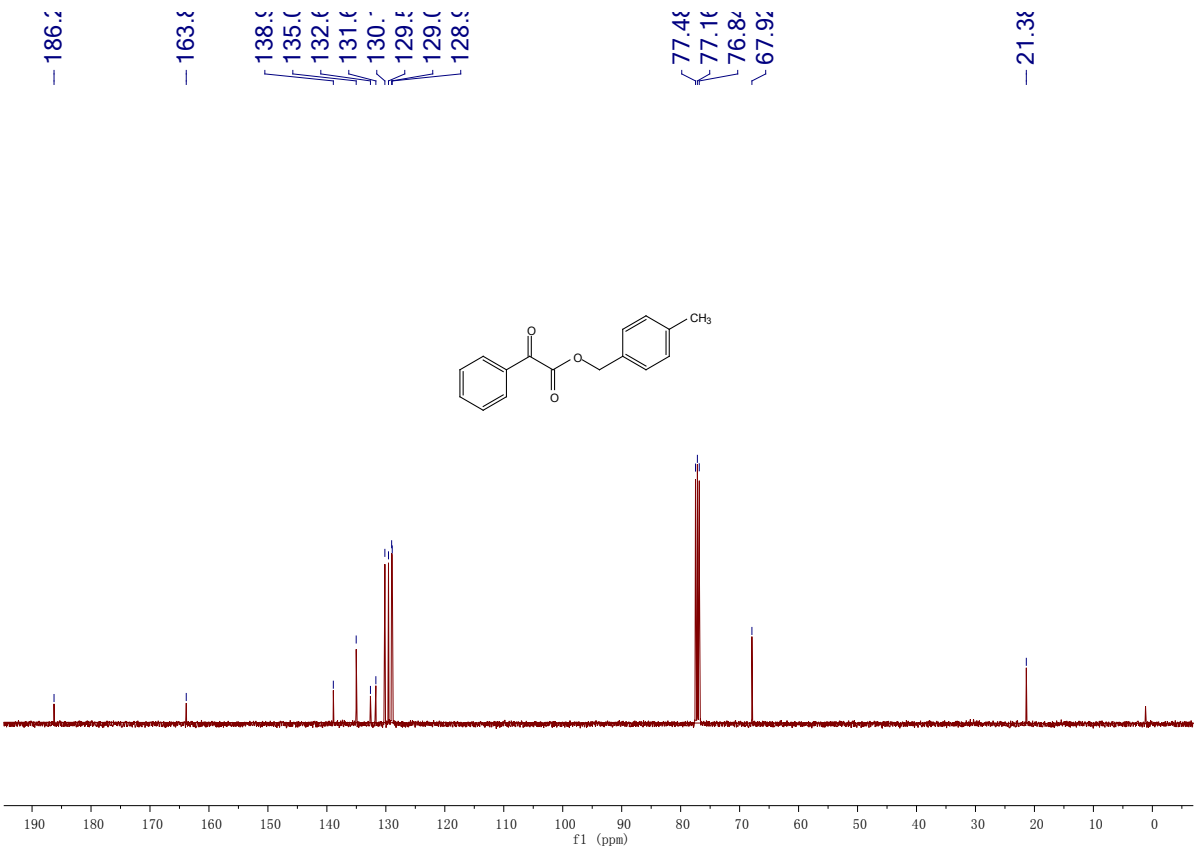

2.00
1.00
2.00
4.00
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O
O
O
Cl

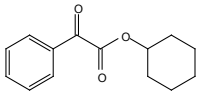

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

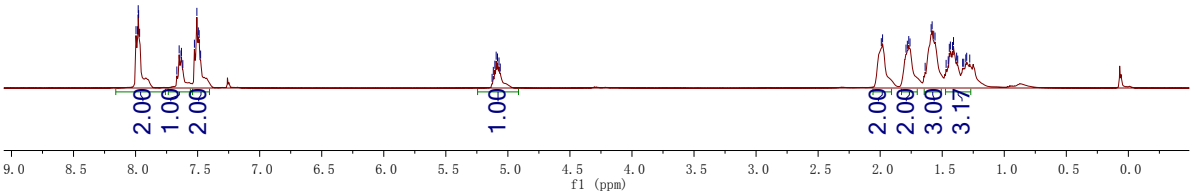
Product 3aj

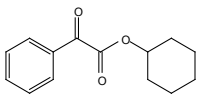


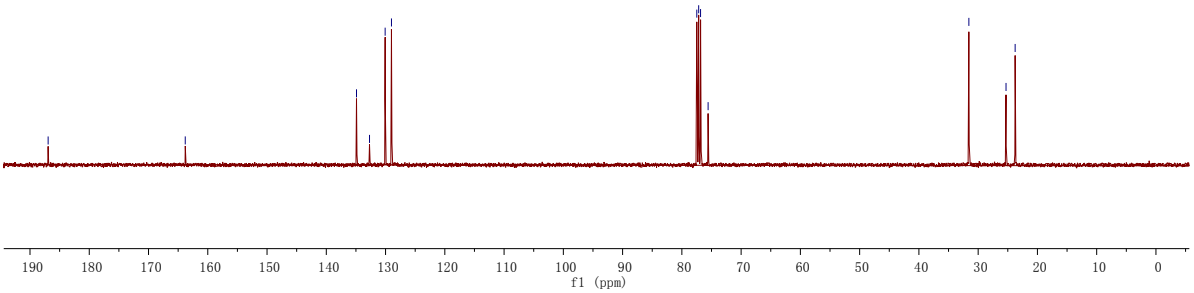


Product 3ak

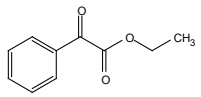


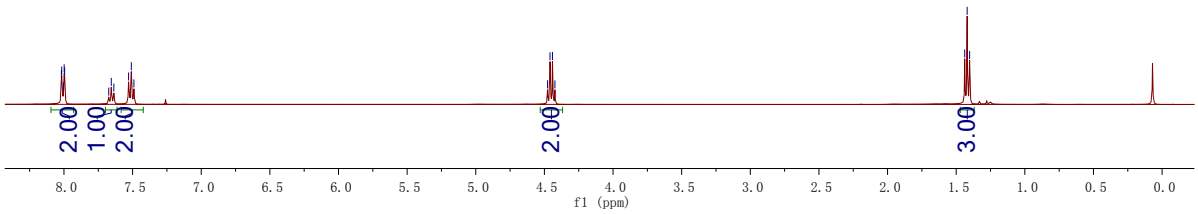


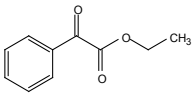


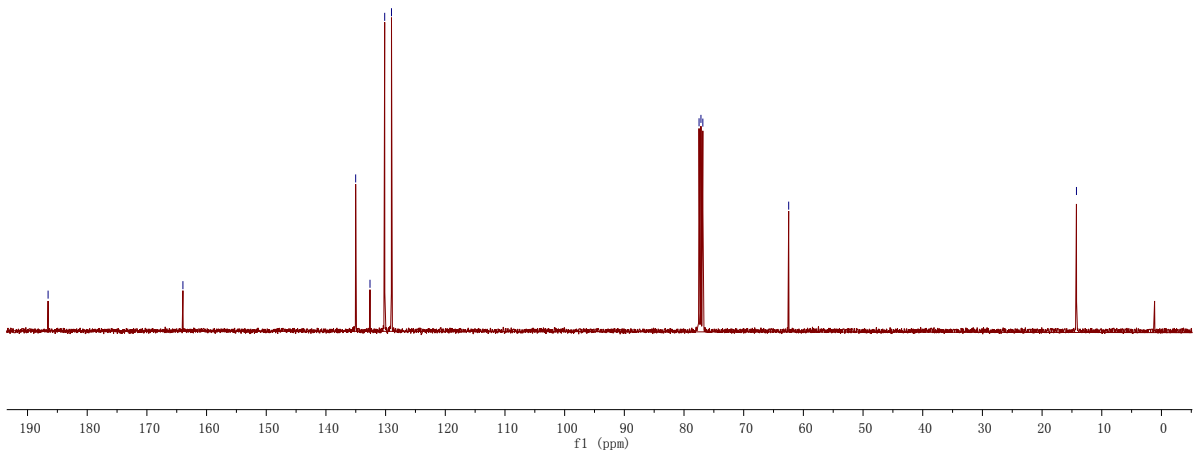


Product 3al

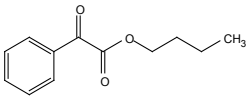


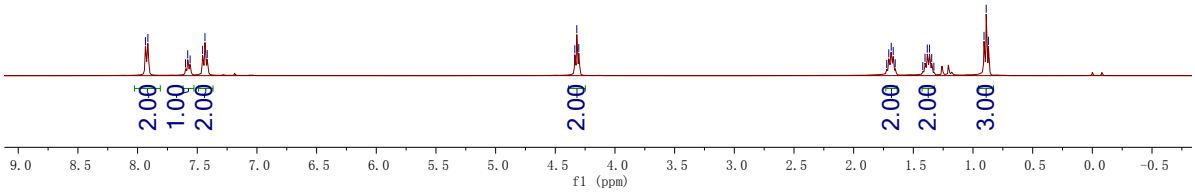


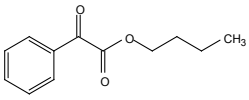


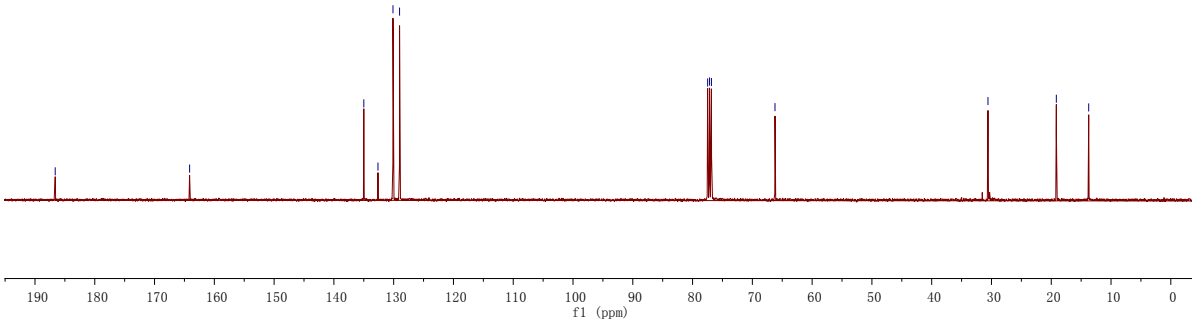


Product 3am

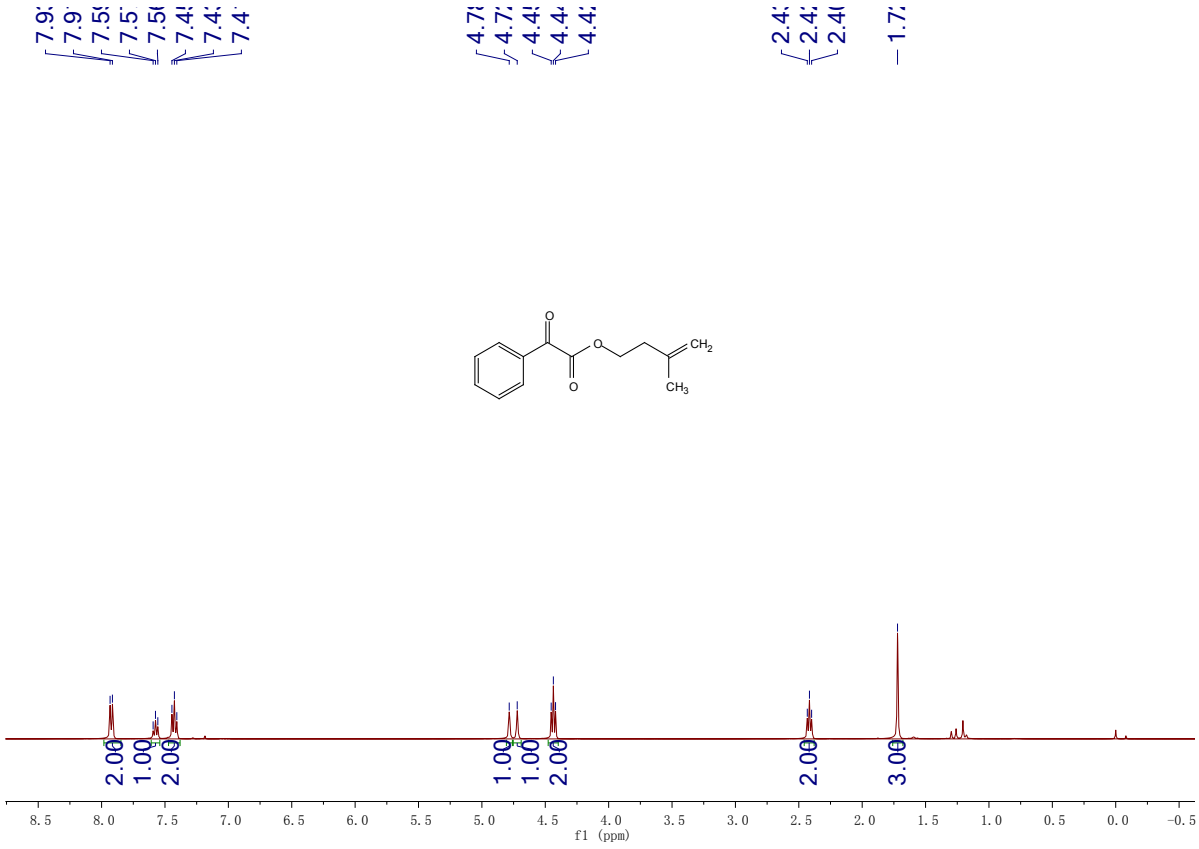


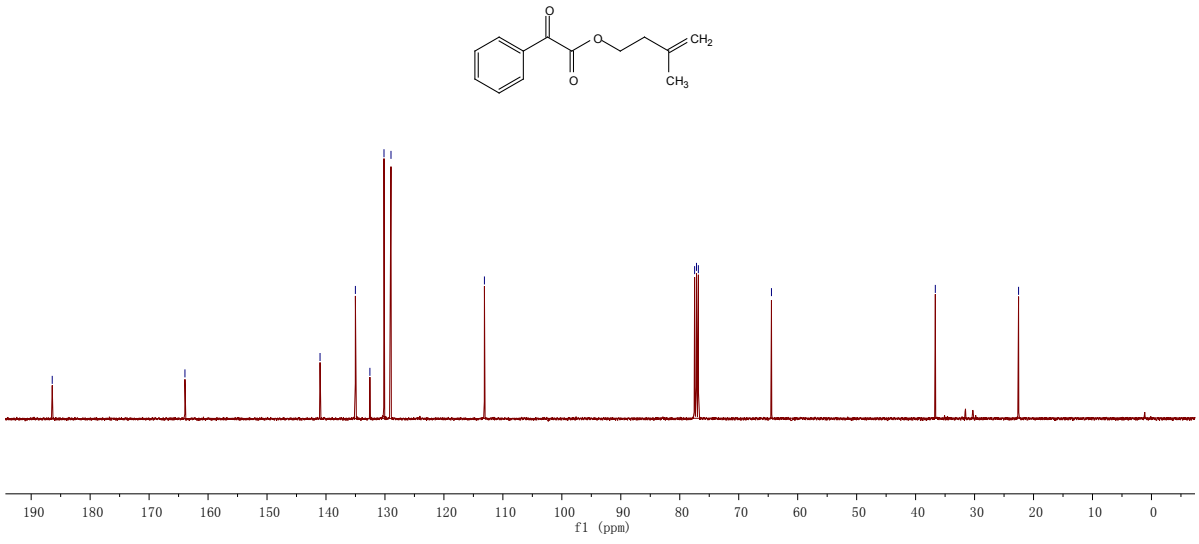






Product 3an


O
O
O
CH2
CH3
2.00
1.00
2.00
1.00
1.00
2.00
2.00
3.00
f1 (ppm)


O
O
O
CH2
CH3
f1 (ppm)

Product 3ao