Asymmetric Retro Claisen Reaction by Synergistic Chiral Primary Amine/Palladium-Catalysis

Yanfang Han, [†,‡] Long Zhang, [§] and Sanzhong Luo[*,§]

[†]Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

[‡]School of Chemical Science, University of Chinese Academy of Sciences, Beijing 100490, China

[§]Center of Basic Molecular Science, Department of Chemistry, Tsinghua University, Beijing, 100084, China

Supporting Information

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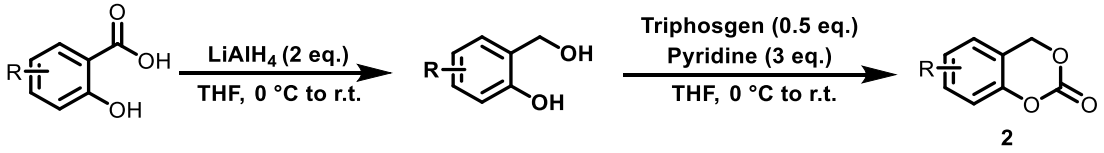
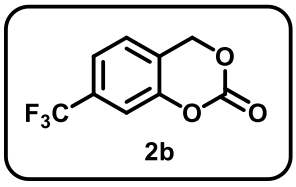
General Information: All commercial reagents were used without further purification unless otherwise indicated. ^{1}H NMR and ^{13}C NMR spectra were measured on Bruker UltraShield 300 MHz, 400MHz or 500MHz spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CDCl_3$ at 7.26 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm). ^{1}H NMR data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, td = triplet of doublet, dt = doublet of triplet, dd = doublet of doublet), coupling constants (Hz), and integration. Infrared Spectroscopy was conducted on Thermo Fisher Nicolet 6700. HRMS were recorded using electrospray ionization (ESI), Atmospheric Pressure Chemical Ionization (APCI) and Electron Impact (EI) mass spectrometer. Silica gel (300 – 400 mesh) was used for column chromatography. The enantiomeric excesses were determined by HPLC analysis on Chiral Daicel Chiralpak AS-H, AD-H, OD-H and OJ-H columns. Optical rotation were measured on a commercial polarimeter and reported as follows: $[\alpha]_D^{25}$ (c = g/100 mL, solvent).

Materials: The PdCp(allyl) was prepared according to literature report.[1] The corresponding *β*-diketons **1a**, **1d-h** and **1k-l** were prepared by alkylation of the corresponding *α*-unsubstituted *β*-diketons with alkyl iodide or alkyl bromine.[2] **1b** was prepared according to literature precedent.[3] **1c** was prepared according to literature procedure.[4] **1i** was prepared according to literature procedure.[5] **1j** was prepared according to literature procedure.[6] Cyclic *β*-diketons **1m-o** were prepared according to literature precedent.[7] **1p-q** were prepared according to literature precedent.[8] **1r** was prepared according to literature report.[9]

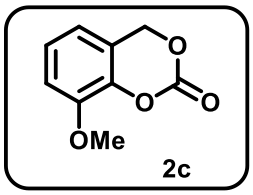
A modified experimental procedure for the preparation of salicylic carbonate **2**[10] from readily available salicylic acid is described below.



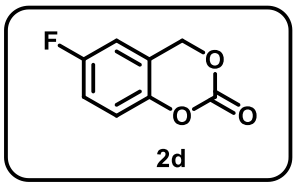
A solution of substituted salicylic acid (1equiv, 50 mmol) in THF was added dropwise to a stirred suspension of lithium aluminium hydride (2 equiv) in dry THF at 0 ºC. The reaction was stirred for 3-5 h at room temperature. After completion, the mixture was quenched with a little amount of water carefully at 0℃. The reaction mixture was acidified with 5% hydrochloric acid to pH = 4~5, and extracted with EtOAc three times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The obtained crude product salicylic alcohol was directly used for the following step without further purification. To a solution of this crude product salicylic alcohol (100 mmol) and pyridine (3 equiv) in THF (300 ml), a solution of triphosgene (0.5 equiv) in toluene was added dropwise at 0℃ and the reaction mixture was stirred overnight at room temperature. After the reaction was completed by TLC, the mixture was quenched with 75ml of 2.5% HCl at 0℃ and extracted with EtOAc. The organic phase was separated and washed with brine to neutral. The solution was dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica to afford the corresponding crude product and recrystallized twice from diethyl ether to give the pure carbonate **2**.



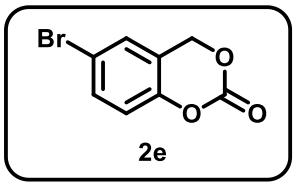
2b: obtained as white crystal (8.0 g) in 73% yield by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.9 Hz, 1H), 7.39 (s, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 5.47 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 145.7, 132.8 (q, *J* = 33.7 Hz), 125.3, 123.16 (q, *J* = 272.6 Hz), 122.3, 121.6, 113.81 (q, *J* = 3.9 Hz), 68.1. IR (thin film, cm^{-1}) 3006, 2989, 2959, 1783, 1637, 1599, 1518, 1462, 1434, 1395, 1327, 1275, 1265, 1242, 1216, 1160, 1125, 1064, 949, 885, 828, 802, 751, 730, 707, 648,626, 598. HRMS (APCI) calcd for $C_9H_6O_3F_3^+$: 219.0264, found 219.0265.



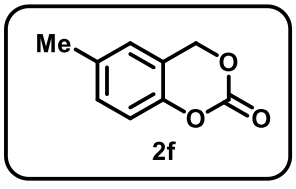
2c: obtained as white solid (5.0 g) in 56% yield by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 5.39 (s, 2H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 146.7, 138.7, 125.7, 118.9, 115.5, 112.7, 68.5, 56.3. IR (thin film, cm^{-1}) 3007, 2989, 2946, 2845, 1869, 1770, 1628, 1594, 1494, 1461, 1442, 1393, 1325, 1277, 1261, 1241, 1220, 1192, 1157, 1192, 1157, 1097, 1057, 1007, 956, 915, 765, 750, 703, 591, 524, 434. HRMS (ESI) calcd for $C_9H_8O_4Na^+$: 203.0315, found 203.0316.



2d: obtained as white crystal (5.2 g) in 62% yield by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.00 (m, 2H), 6.91 (d, *J* = 6.9 Hz, 1H), 5.39 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5 (d, *J* = 245.7 Hz), 145.4 (d, *J* = 2.6 Hz), 119.2 (d, *J* = 8.3 Hz), 117.9 (d, *J* = 8.5 Hz), 116.9 (d, *J* = 23.9 Hz), 111.4 (d, *J* = 25.4 Hz), 68.0 (d, *J* = 1.9 Hz). IR (thin film, cm^{-1}) 3056, 3006, 2924, 2854, 1784, 1496, 1474, 1448, 1382, 1275, 1264, 1226, 1163, 1103, 1050, 951, 914, 870, 819, 802, 764, 748, 701, 685, 598, 555, 481, 443, 423. HRMS (APCI) calcd for $C_8H_6O_3F^+$: 169.0295, found 169.0296.

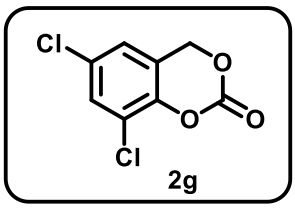


2e: obtained as white solid (5.1 g) in 45% yield by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.32 (d, *J* = 1.9 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 1H), 5.37 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 146.1, 133.1, 127.4, 119.7, 118.1, 67.8. IR (thin film, cm^{-1}) 3069, 3034, 2954, 2926, 1763, 1585, 1482, 1463, 1437, 1376, 1266, 1247, 1225, 1162, 1128, 1060, 883, 868, 839, 828, 750, 703, 638, 560, 537, 512, 466, 432. HRMS (APCI) calcd for $C_8H_6O_3Br^+$: 228.9495, found 228.9494.



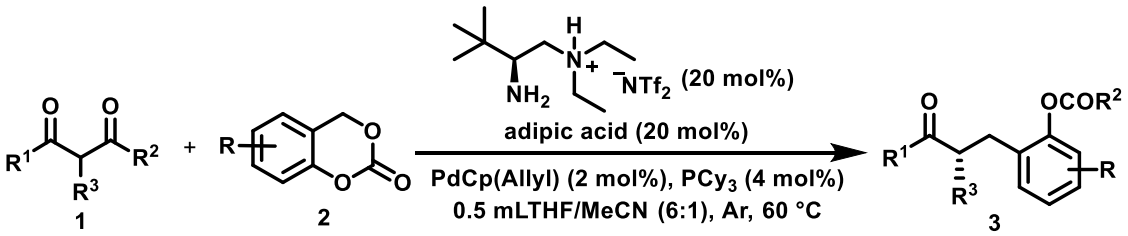
2f: obtained as white crystal (3.8 g) in 46% yield by using 1:5 (v/v) ethyl acetate/petroleum ether as eluent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.0 Hz, 1H), 7.06 – 6.87 (m, 2H), 5.37 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$)

δ 147.3, 135.3, 130.5, 124.6, 117.4, 116.0, 68.6, 21.0. IR (thin film, cm^{-1}) 3006, 2989, 1769, 1754, 1625, 1608, 1502, 1462, 1432, 1381, 1275, 1265, 1227, 1178, 1149, 1129, 1059, 913, 896, 820, 750, 703, 685, 596, 556, 543. HRMS (APCI) calcd for $C_9H_9O_3^+$: 165.0546, found 165.0546.



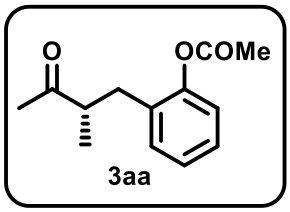
2g: obtained as white solid (6.0 g) in 55% yield by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.09 (s, 1H), 5.37 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 144.3, 130.8, 130.6, 122.8, 120.6 , 67.9. IR (thin film, cm^{-1}) 3085, 2954, 2891, 1781, 1607, 1588, 1457, 1424, 1376, 1263, 1229, 1143, 1097, 1057, 1009, 952, 916, 863, 837, 792, 758, 705, 691, 568, 549, 519, 488. HRMS (APCI) calcd for $C_8H_5O_3Cl_2^+$: 218.9616, found 218.9606.

General procedure of the catalytic reactions

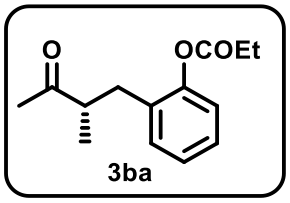


General procedure: To a flame-dried Schlenk tube equipped with a magnetic stir bar was added chiral primary amine catalyst (20 mol%), adipic acid (20 mol%), PdCp(allyl) (2 mol%), and PCy_3 (4 mol%), then a mixture solution of 1,3-diketones **1** (0.1 mmol) and the carbonates **2** (0.2 mmol) in 0.5 mL anhydrous THF/MeCN (6/1) was added via syringe under Ar. After degassing 3 times by a standard freeze-thaw operation, the reaction was conducted at 60 ℃ for 48 h or 72 h. Solvent was removed and purification by silica gel column to give the desired product **3** as a colorless oil.

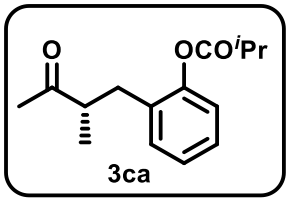
Products **3aa-3da**, **3fa-3la**, **3oa**, **3pa**, **3p'a**, **3ab** were known.[11] Products **3ra** was also known.[12] For chiral compounds, absolute configuration was determined by comparing HPLC analysis and optical rotation with previous reported literature. [11]



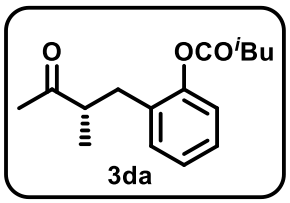
3aa: obtained as colorless oil (15.8 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 72% yield, 94% *ee*. $[\alpha]_D^{22}$ = +25.4 (c = 0.79, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 2% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 205 nm, retention time: 11.72 min (major), 14.97 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (qdd, *J* = 8.6, 6.9, 3.2 Hz, 3H), 7.03 (dd, *J* = 7.9, 1.0 Hz, 1H), 2.93 (dd, *J* = 13.7, 6.7 Hz, 1H), 2.86 – 2.74 (m, 1H), 2.47 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.33 (s, 3H), 2.09 (s, 3H), 1.09 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9, 169.5, 149.2, 131.7, 131.1, 127.7, 126.2, 122.7, 47.5, 33.4, 29.0, 21.1, 16.6.



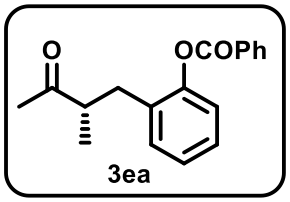
3ba: obtained as colorless oil (17.4 mg) with general procedure by using 1:15 (v/v) ethyl acetate/petroleum ether as eluent. 74% yield, 96% *ee*. $[\alpha]_D^{22}$ = +25.1 (c = 0.87, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 206 nm, retention time: 6.78 min (major), 7.86 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.13 (m, 3H), 7.03 (dd, *J* = 7.9, 0.9 Hz, 1H), 2.92 (dd, *J* = 13.6, 6.7 Hz, 1H), 2.85 – 2.75 (m, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.47 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.08 (s, 3H), 1.29 (t, *J* = 7.6 Hz, 3H), 1.08 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9, 173.0, 149.2, 131.7, 131.1, 127.7, 126.1, 122.7, 47.5, 33.4, 29.0, 27.9, 16.6, 9.4.



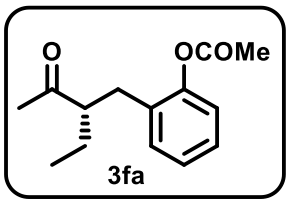
3ca: obtained as colorless oil (10.7 mg) with general procedure by using 1:15 (v/v) ethyl acetate/petroleum ether as eluent. 43% yield, 97% *ee*. $[\alpha]_D^{22}$ = +19.1 (c = 0.53, $CHCl_3$). HPLC analysis: Daicel Chiralpak OJ-H*2, 3% *iso*-propanol/hexane, flow rate = 0.5 mL/min, λ = 205 nm, retention time: 34.55 min (major), 37.77 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (dtd, *J* = 14.6, 13.2, 6.9 Hz, 3H), 7.00 (d, *J* = 8.0 Hz, 1H), 2.85 (ddt, *J* = 20.1, 14.0, 6.9 Hz, 3H), 2.48 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.07 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 6H), 1.08 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9, 175.6, 149.3, 131.7, 131.2, 127.7, 126.0, 122.6, 47.4, 34.4, 33.3, 29.1, 19.2, 16.6.



3da: obtained as colorless oil (19.3 mg) with general procedure by using 1:15 (v/v) ethyl acetate/petroleum ether as eluent. 74% yield, 96% *ee*. $[\alpha]_D^{22}$ = +19.8 (c = 0.97, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H*2, 5% *iso*-propanol/hexane, flow rate =0.5 mL/min, λ = 205 nm, retention time: 19.43 min (major), 21.20 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.12 (m, 3H), 7.05 – 6.99 (m, 1H), 2.91 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.87 – 2.76 (m, 1H), 2.49 (dd, *J* = 14.8, 7.3 Hz, 3H), 2.30 (d, *J* = 6.7 Hz, 1H), 2.08 (s, 3H), 1.08 (dd, *J* = 6.8, 1.9 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9, 171.6, 149.3, 131.7, 131.1, 127.7, 126.1, 122.7, 47.4, 43.4, 33.4, 29.0, 25.9, 22.6, 16.6.

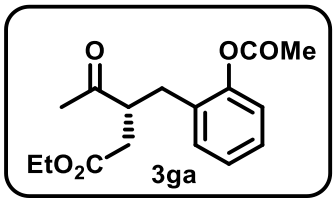


3ea: obtained as colorless oil (16.7 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 59% yield, 77% *ee*. $[\alpha]_D^{25}$ = +13.7 (c = 0.83, $CHCl_3$). HPLC analysis: Daicel Chiralpak AD-H*2, 2% *iso*-propanol/hexane, flow rate = 0.5 mL/min, λ = 201 nm, retention time: 57.65 min (major), 59.62 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.4 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.30 (dd, *J* = 12.0, 4.7 Hz, 1H), 7.25 – 7.14 (m, 3H), 2.99 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.85 (dd, *J* = 14.1, 7.0 Hz, 1H), 2.55 (dd, *J* = 13.7, 7.8 Hz, 1H), 2.01 (s, 3H), 1.06 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.8, 165.2, 149.5, 133.9, 132.0, 131.3, 130.3, 129.5, 128.9, 127.8, 126.3, 122.8, 47.6, 33.5, 29.0, 16.5. IR (thin film, cm^{-1})3057, 3005, 2988, 2926, 2854, 1716, 1676, 1597, 1582, 1489, 1450, 1422, 1358, 1328, 1275, 1263, 1215, 1172, 1115, 1080, 1063, 1024, 978, 951, 896, 848, 764, 749, 704, 592, 539, 449. HRMS (ESI) calcd for $C_{18}H_{18}O_3Na^+$: 305.1148, found 305.1148.

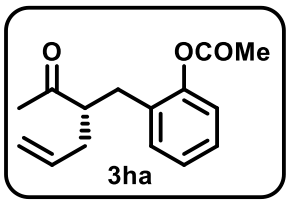


3fa: obtained as colorless oil (16.9 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 72% yield, 97% *ee*. $[\alpha]_D^{22}$ = +33.0 (c = 0.84, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 206 nm, retention time: 7.10 min (major), 7.87 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.12 (m, 3H), 7.06 – 6.99 (m, 1H), 2.81 (dd, *J* = 13.2, 8.1 Hz, 1H), 2.72 (dt, *J* = 7.7, 5.7 Hz, 1H), 2.60 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.34 (s, 3H), 2.01 (s, 3H), 1.72 – 1.59 (m, 1H), 1.57 – 1.44 (m,

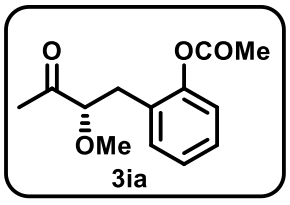
1H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.1, 169.6, 149.1, 131.8, 131.1, 127.7, 126.2, 122.7, 54.7, 31.8, 30.4, 24.9, 21.1, 11.8.



3ga: obtained as colorless oil (22.0 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 75% yield, 93% *ee*. $[\alpha]_D^{22}$ = +71.9 (c = 1.10, $CHCl_3$). HPLC analysis: Daicel Chiralpak OD-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 205 nm, retention time: 16.40 min (major), 13.88 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 1H), 7.18 (dd, *J* = 5.1, 1.9 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 3.30 – 3.20 (m, 1H), 2.83 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.73 (dd, *J* = 17.1, 9.6 Hz, 1H), 2.55 (dd, *J* = 13.7, 8.1 Hz, 1H), 2.36 (s, 3H), 2.31 (dd, *J* = 17.3, 12.6 Hz, 1H), 2.11 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.6, 172.2, 169.5, 149.2, 131.1, 130.4, 128.2, 126.4, 122.9, 60.8, 48.2, 35.6, 32.4, 30.5, 21.1, 14.2.

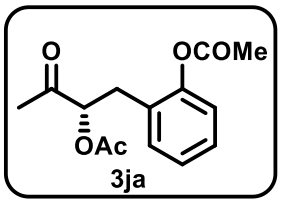


3ha: obtained as colorless oil (20.6 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 84% yield, 97% *ee*. $[\alpha]_D^{22}$ = +9.14 (c = 1.03, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 205 nm, retention time: 7.38 min (major), 8.05 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (dd, *J* = 8.0, 0.8 Hz, 1H), 5.72 (ddt, *J* = 17.3, 10.3, 7.1 Hz, 1H), 5.08 (dd, *J* = 12.6, 5.9 Hz, 2H), 2.83 (ddd, *J* = 19.2, 10.4, 5.0 Hz, 2H), 2.64 (dd, *J* = 12.8, 4.9 Hz, 1H), 2.40 – 2.30 (m, 4H), 2.23 – 2.13 (m, 1H), 1.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.3, 169.5, 149.1, 135.1, 131.6, 131.2, 127.8, 126.3, 122.7, 117.6, 52.7, 36.1, 31.7, 30.7, 21.1.

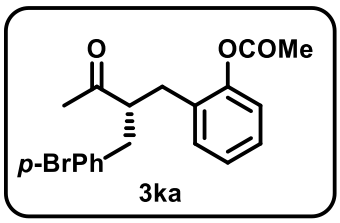


3ia: obtained as colorless oil (21.3 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 90% yield, 91% *ee*. $[\alpha]_D^{25}$ = -45.9 (c = 0.70, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H*2, 3% *iso*-propanol/hexane, flow rate = 0.6 mL/min, λ = 204 nm, retention time: 28.15 min (major), 29.23 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 3.74 (dd, *J* = 8.2, 4.5 Hz, 1H), 3.27 (s, 3H), 2.89 (dd, *J* = 14.1, 4.4 Hz, 1H), 2.80 (dd, *J* = 14.1, 8.3 Hz, 1H), 2.34 (s, 3H),

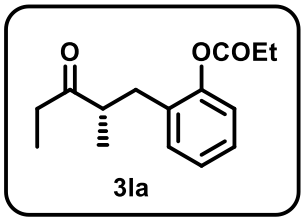
2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.8, 169.5, 149.3, 131.6, 129.4, 128.1, 126.1, 122.7, 87.4, 58.7, 33.1, 25.8, 21.1.



3ja: obtained as colorless oil (26.0 mg) with general procedure by using 1:5 (v/v) ethyl acetate/petroleum ether as eluent. 99% yield, 93% *ee*. $[\alpha]_D^{25}$ = -2.1 (c = 0.58, $CHCl_3$). HPLC analysis: Daicel Chiralpak OJ-H, 20% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 208 nm, retention time: 11.73 min (major), 12.85 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 3H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 7.9 Hz, 1H), 5.18 (dd, *J* = 8.2, 5.1 Hz, 1H), 3.06 (dd, *J* = 14.3, 5.0 Hz, 1H), 2.94 (dd, *J* = 14.3, 8.3 Hz, 1H), 2.35 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.3, 170.5, 169.4, 149.4, 131.4, 128.5, 128.1, 126.3, 122.8, 78.2, 31.3, 27.0, 21.1, 20.7.

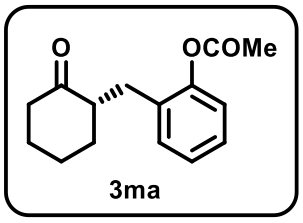


3ka: obtained as colorless oil (26.5 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 71% yield, 96% *ee*. $[\alpha]_D^{22}$ = -9.2 (c = 1.32, $CHCl_3$). HPLC analysis: Daicel Chiralpak OJ-H, 20% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 205 nm, retention time: 12.70 min (major), 37.77 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.25 – 7.20 (m, 1H), 7.19 – 7.11 (m, 2H), 7.06 – 6.98 (m, 3H), 3.10 – 2.98 (m, 1H), 2.84 (ddd, *J* = 20.0, 13.6, 8.5 Hz, 2H), 2.61 (ddd, *J* = 13.5, 5.9, 4.3 Hz, 2H), 2.19 (s, 3H), 1.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 169.5, 149.0, 138.4, 131.8, 131.2, 130.8, 128.0, 126.4, 122.8, 120.5, 54.8, 37.6, 32.5, 31.7, 20.9.



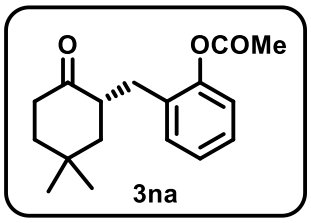
3la: obtained as colorless oil (7.3 mg) with general procedure by using 1:15 (v/v) ethyl acetate/petroleum ether as eluent. 29% yield, 88% *ee*. $[\alpha]_D^{22}$ = +27.82 (c = 0.36, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H*2, 5% *iso*-propanol/hexane, flow rate = 0.5 mL/min, λ = 205 nm, retention time: 18.76 min (major), 20.83 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.11 (m, 3H), 7.03 (d, *J* = 7.9 Hz, 1H), 2.89 (dd, *J* = 13.3, 7.1 Hz, 1H), 2.85 – 2.76 (m, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.53 – 2.36 (m, 2H), 2.24 (dq, *J* = 17.8, 7.2 Hz, 1H), 1.30 (t, *J* = 7.6 Hz,

3H), 1.07 (d, *J* = 6.9 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.9, 131.2, 127.7, 126.1, 122.7, 46.5, 35.4, 33.8, 27.9, 17.0, 9.4, 7.7.



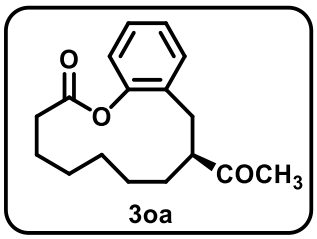
3ma

3ma: obtained as colorless oil (16.8 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 68% yield, 87% *ee*. $[\alpha]_D^{25}$ = +1.8 (c = 0.84, $CHCl_3$). HPLC analysis: Daicel Chiralpak OD-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 206 nm, retention time: 10.17 min (major), 8.68 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 7.7 Hz, 1H), 3.18 (dd, *J* = 14.1, 4.5 Hz, 1H), 2.51 (dd, *J* = 10.4, 6.0 Hz, 1H), 2.43 (d, *J* = 13.7 Hz, 1H), 2.38 – 2.26 (m, 5H), 2.10 – 1.97 (m, 2H), 1.87 – 1.78 (m, 1H), 1.74 – 1.51 (m, 3H), 1.35 (ddd, *J* = 25.0, 12.4, 3.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.3, 169.6, 149.3, 132.4, 131.3, 127.4, 126.1, 122.6, 51.4, 42.2, 33.8, 29.8, 28.1, 25.3, 21.1. IR (thin film, cm^{-1}) 3006, 2989, 2930, 2857, 1755, 1689, 1588, 1489, 1457, 1369, 1275, 1262, 1242, 1210, 1171, 1148, 1111, 1036, 982, 941, 909, 890, 858, 828, 750, 659, 609, 551, 442. HRMS (ESI) calcd for $C_{15}H_{18}O_3Na^+$: 269.1148, found 269.1138.



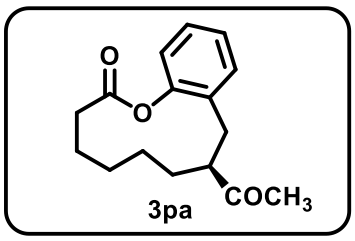
3na

3na: obtained as colorless oil (16.6 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 60% yield, 76% *ee*. $[\alpha]_D^{28}$ = +29.6 (c = 0.83, $CHCl_3$). HPLC analysis: Daicel Chiralpak OD-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 206 nm, retention time: 9.55 min (major), 7.92 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.4 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 3.20 (dd, *J* = 14.2, 5.0 Hz, 1H), 2.68 (td, *J* = 13.2, 5.4 Hz, 1H), 2.48 (td, *J* = 14.0, 6.4 Hz, 1H), 2.33 – 2.21 (m, 5H), 1.76 – 1.59 (m, 3H), 1.34 (t, *J* = 13.2 Hz, 1H), 1.12 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.7, 169.6, 149.3, 132.5, 131.3, 127.4, 126.1, 122.5, 46.7, 40.3, 38.5, 31.5, 31.0, 29.8, 24.4, 21.1. IR (thin film, cm^{-1}) 2957, 2925, 2854, 1759, 1708, 1489, 1451, 1369, 1275, 1263, 1209, 1172, 1116, 1043, 1010, 945, 916, 827, 764, 749 ,703, 548, 527, 484, 450. HRMS (ESI) calcd for $C_{17}H_{23}O_3^+$: 275.1642, found 275.1638.



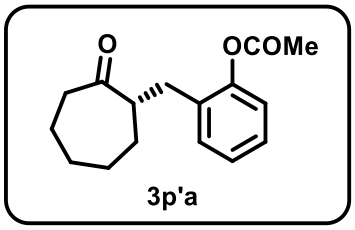
3oa

3oa: obtained as colorless oil (19.5 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 71% yield, 97% *ee*. $[\alpha]_D^{25}$ = +21.1 (c = 0.98, $CHCl_3$). HPLC analysis: Daicel Chiralpak OD-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 205 nm, retention time: 21.34 min (major), 20.10 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (td, *J* = 5.5, 2.7 Hz, 2H), 7.16 – 7.05 (m, 1H), 7.05 – 6.96 (m, 1H), 2.98 – 2.86 (m, 1H), 2.85 – 2.69 (m, 3H), 2.48 (ddd, *J* = 14.5, 10.4, 2.2 Hz, 1H), 2.15 – 2.02 (m, 1H), 1.98 (s, 3H), 1.88 (ddd, *J* = 14.8, 7.7, 5.1 Hz, 1H), 1.70 (ddd, *J* = 20.9, 11.9, 6.8 Hz, 2H), 1.56 – 1.40 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 173.4, 149.2, 132.9, 131.9, 127.6, 126.1, 122.7, 51.9, 35.4, 30.2, 29.1, 28.2, 24.9, 23.3, 22.5.



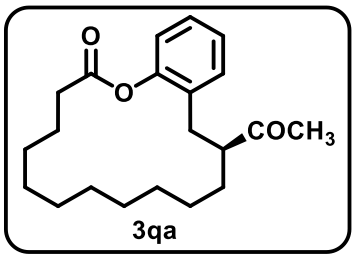
3pa

3pa: obtained as colorless oil (8.2 mg) with general procedure by using 1:10 (v/v) ethyl acetate/petroleum ether as eluent. 32% yield, 99% *ee*. $[\alpha]_D^{25}$ = +57.2 (c = 0.55, $CHCl_3$). HPLC analysis: Daicel Chiralpak OJ-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 203 nm, retention time: 25.95 min (major), 24.44 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 2H), 7.18 – 7.07 (m, 2H), 2.96 (dd, *J* = 13.8, 7.7 Hz, 1H), 2.85 (dd, *J* = 13.8, 2.5 Hz, 1H), 2.81 – 2.71 (m, 1H), 2.65 (dt, *J* = 14.2, 5.1 Hz, 1H), 2.60 – 2.51 (m, 1H), 2.13 – 1.99 (m, 4H), 1.88 – 1.74 (m, 2H), 1.69 – 1.42 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.7, 171.7, 148.7, 133.6, 131.5, 127.5, 126.1, 122.7, 52.6, 32.8, 29.7, 29.3, 28.4, 24.3, 22.8, 21.5.

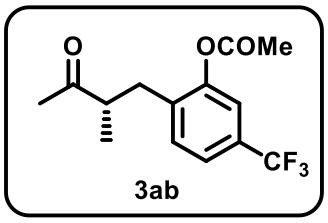


3p'a

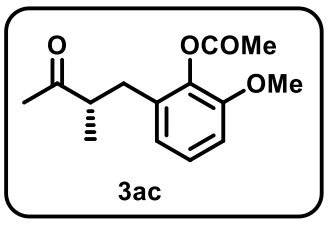
3p'a: obtained as colorless oil (6.1 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 24% yield, 83% *ee*. $[\alpha]_D^{25}$ = +36.3 (c = 0.41, $CHCl_3$). HPLC analysis: Daicel Chiralpak OD-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 206 nm, retention time: 9.06 min (major), 8.39 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.12 (m, 3H), 7.02 (d, *J* = 7.8 Hz, 1H), 3.02 (dd, *J* = 14.0, 5.6 Hz, 1H), 2.83 – 2.72 (m, 1H), 2.48 (dd, *J* = 12.8, 7.5 Hz, 3H), 2.33 (s, 3H), 1.88 – 1.72 (m, 4H), 1.62 (dd, *J* = 10.7, 5.6 Hz, 1H), 1.41 – 1.29 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.3, 169.6, 149.4, 132.2, 131.3, 127.6, 126.1, 122.7, 52.4, 43.2, 32.3, 30.6, 29.5, 28.7, 24.5, 21.1.



3qa: obtained as colorless oil (18.3 mg) with general procedure by using 1:20 (v/v) ethyl acetate/petroleum ether as eluent. 55% yield, 99% *ee*. $[\alpha]_D^{28}$ = -1.1 (c = 0.92, $CHCl_3$). HPLC analysis: Daicel Chiralpak OD-H*2, 2% *iso*-propanol/hexane, flow rate = 0.6 mL/min, λ = 204 nm, retention time: 24.19 min (major), 25.05 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 1H), 7.10 (d, *J* = 4.4 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 1H), 2.85 (dt, *J* = 12.0, 6.1 Hz, 1H), 2.80 – 2.71 (m, 2H), 2.68 – 2.54 (m, 2H), 1.94 (s, 3H), 1.91 – 1.76 (m, 2H), 1.69 – 1.59 (m, 1H), 1.55 – 1.28 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.6, 172.5, 149.2, 131.8, 130.8, 127.6, 126.1, 122.6, 52.4, 33.9, 32.3, 31.6, 31.2, 29.9, 27.3, 27.0, 26.2, 25.9, 25.7, 25.5, 24.1. IR (thin film, cm^{-1}) 3055, 2930, 2858, 1754, 1710, 1489, 1453, 1353, 1264, 1214, 1171, 1128, 1103, 896, 732, 703. HRMS (ESI) calcd for $C_{21}H_{31}O_3^+$: 331.2268, found 331.2258.

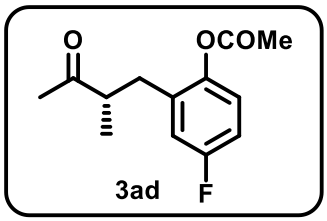


3ab: obtained as colorless oil (14.9 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 52% yield, 94% *ee*. $[\alpha]_D^{22}$ = +7.7 (c = 0.99, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 3% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 202 nm, retention time: 6.91 min (major), 9.38 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 2H), 3.00 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.86 – 2.76 (m, 1H), 2.52 (dd, *J* = 13.8, 7.3 Hz, 1H), 2.35 (s, 3H), 2.11 (s, 3H), 1.12 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.10, 169.05, 149.17, 136.23, 131.67, 130.12 (q, *J* = 33.2 Hz), 123.65 (q, *J* = 272.2 Hz), 122.92 (dd, *J* = 7.0, 3.4 Hz), 120.10 (dd, *J* = 7.3, 3.6 Hz), 47.21, 32.98, 28.90, 20.98, 16.78.

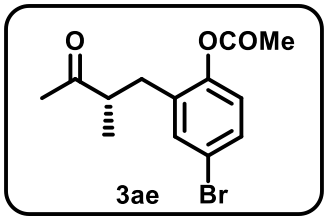


3ac: obtained as colorless oil (8.3 mg) with general procedure by using 1:6 (v/v) ethyl acetate/petroleum ether as eluent. 33% yield, 97% *ee*. $[\alpha]_D^{25}$ = +34.8 (c = 0.55, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 204 nm, retention time: 9.33 min (major), 10.54 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, *J* = 8.0 Hz, 1H), 6.80 (dd, *J* = 23.9, 7.8 Hz, 2H), 3.81 (s, 3H), 2.92 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.85 – 2.71 (m, 1H), 2.47 (dd, *J* = 13.6, 7.7 Hz, 1H), 2.34 (s, 3H), 2.09 (s, 3H), 1.08 (d, *J* =

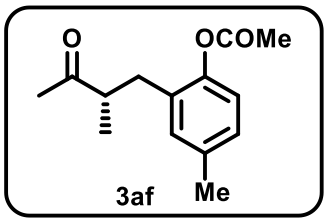
7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.0, 168.9, 151.4, 138.6, 133.3, 126.4, 122.5, 110.6, 56.1, 47.4, 33.3, 29.0, 20.7, 16.6. IR (thin film, cm^{-1}) 3055, 3006,2988, 1761, 1712, 1478, 1459, 1440, 1369, 1275, 1264, 1214, 1191, 1174, 1084, 1011, 897, 764, 748, 732, 703. HRMS (ESI) calcd for $C_{14}H_{18}O_4Na^+$: 273.1097, found 273.1097.



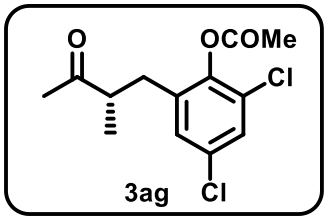
3ad: obtained as colorless oil (13.7 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 58% yield, 97% *ee*. $[\alpha]_D^{25}$ = +2.2 (c = 0.69, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H, 5% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 206 nm, retention time: 9.43 min (major), 10.83 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 – 6.96 (m, 1H), 6.96 – 6.87 (m, 2H), 2.92 (dd, *J* = 13.8, 6.7 Hz, 1H), 2.84 – 2.73 (m, 1H), 2.46 (d, *J* = 7.4 Hz, 1H), 2.32 (s, 3H), 2.11 (s, 3H), 1.10 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.29, 169.55, 160.24 (d, *J* = 244.6 Hz), 145.01, 133.93 (d, *J* = 7.7 Hz), 123.96 (d, *J* = 8.8 Hz), 117.42 (d, *J* = 23.1 Hz), 114.36 (d, *J* = 23.3 Hz), 47.28, 33.13, 28.95, 21.01, 16.69. IR (thin film, cm^{-1}) 2929, 2856, 1761, 1712, 1621, 1594, 1493, 1459, 1424, 1369, 1265, 1208, 1174, 1012, 961, 907, 879, 823, 733, 703, 499. HRMS (ESI) calcd for $C_{13}H_{15}O_3FNa^+$: 261.0897, found 261.0897.



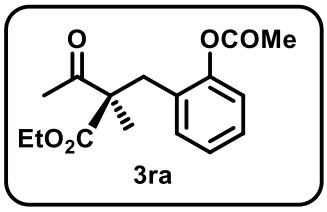
3ae: obtained as colorless oil (24.9 mg) with general procedure by using 1:6 (v/v) ethyl acetate/petroleum ether as eluent. 83% yield, 96% *ee*. $[\alpha]_D^{30}$ = +3.78 (c = 1.24, $CHCl_3$). HPLC analysis: Daicel Chiralpak OJ-H, 10% *iso*-propanol/hexane, flow rate = 1.0 mL/min, λ = 204 nm, retention time: 14.07 min (major), 12.40 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 2H), 6.97 – 6.88 (m, 1H), 2.92 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.82 – 2.72 (m, 1H), 2.42 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.32 (s, 3H), 2.12 (s, 3H), 1.10 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.2, 169.2, 148.2, 134.2, 133.8, 130.7, 124.4, 119.2, 47.4, 32.9, 28.9, 21.0, 16.6. IR (thin film, cm^{-1}) 3005, 2958, 2925, 2855, 2252, 1763, 1714, 1481, 1459, 1370,1275, 1264, 1205, 1168, 1119, 1064, 908, 764, 749, 731. HRMS (ESI) calcd for $C_{13}H_{15}BrO_3Na^+$: 321.0102, found 321.0089.



3af: obtained as colorless oil (21.1 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 90% yield, 96% *ee*. $[\alpha]_D^{22}$ = +20.8 (c = 1.02, $CHCl_3$). HPLC analysis: Daicel Chiralpak AS-H*2, 2% *iso*-propanol/hexane, flow rate = 0.5 mL/min, λ = 202 nm, retention time: 34.21 min (major), 37.43 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (dd, *J* = 13.7, 5.5 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 1H), 2.89 (dd, *J* = 13.5, 6.5 Hz, 1H), 2.79 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.42 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.31 (d, *J* = 3.1 Hz, 6H), 2.10 (s, 3H), 1.08 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.0, 169.8, 146.9, 135.8, 131.6, 131.3, 128.3, 122.3, 47.5, 33.4, 29.0, 21.1, 21.0, 16.6. IR (thin film, cm^{-1}) 2973, 2926, 1758, 1711, 1497, 1458, 1424, 1368, 1265, 1214, 1191, 1118, 1011, 908, 825, 734, 703. HRMS (ESI) calcd for $C_{14}H_{18}O_3Na^+$: 257.1148, found 257.1148.



3ag: obtained as colorless oil (19.3 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 67% yield, 89% *ee*. $[\alpha]_D^{22}$ = +1.45 (c = 0.96, $CHCl_3$). HPLC analysis: Daicel Chiralpak OJ-H, 2% *iso*-propanol/hexane, flow rate = 0.5 mL/min, λ = 205 nm, retention time: 28.60 min (major), 25.79 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 2.3 Hz, 1H), 7.12 (d, *J* = 2.2 Hz, 1H), 2.94 (dd, *J* = 13.9, 6.7 Hz, 1H), 2.82 – 2.71 (m, 1H), 2.42 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.37 (s, 3H), 2.13 (s, 3H), 1.11 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.8, 168.1, 144.6, 136.0, 131.8, 129.4, 128.6, 128.3, 77.5, 77.2, 76.8, 47.1, 33.3, 28.9 20.5, 16.9. IR (thin film, cm^{-1}) 3078, 2972, 2930, 2855, 1767, 1712, 1591, 1571, 1454, 1402, 1368, 1265, 1195, 1155, 1110, 1045, 1009, 900, 859, 846, 780, 734, 704, 612, 559, 515. HRMS (ESI) calcd for $C_{13}H_{14}O_3Cl_2Na^+$: 311.0212, found 311.0202.



3ra: obtained as colorless oil (21.0 mg) with general procedure by using 1:8 (v/v) ethyl acetate/petroleum ether as eluent. 72% yield, > 99% *ee*. $[\alpha]_D^{28}$ = +35.1 (c = 1.05, $CHCl_3$). HPLC analysis: Daicel Chiralpak AD-H*2, 10% *iso*-propanol/hexane, flow rate = 0.2 mL/min, λ = 205 nm, retention time: 62.41 min (major), 60.94 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 1H), 7.15 (t, *J* = 7.4 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 1H), 4.19 (ddd, *J* = 10.8, 6.7, 3.5 Hz, 2H),

3.13 (q, *J* = 14.2 Hz, 2H), 2.30 (s, 3H), 2.16 (s, 3H), 1.27 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.3, 172.6, 169.3, 149.8, 132.0, 128.7, 128.2, 126.0, 122.6, 61.7, 60.6, 34.2, 26.6, 21.2, 19.1, 14.1.

General procedure for the Small-scale experiment: To a flame-dried Schlenk tube equipped with a magnetic stir bar was added chiral primary amine catalyst (10 mol%), adipic acid (10 mol%), PdCp(allyl) (1 mol%), and PCy_3 (2 mol%), then a mixture solution of 1,3-diketones **1a** (1 mmol) and salicyl carbonates **2f** (2 mmol) in 4.5 mL anhydrous THF/MeCN (6/1) was added via syringe under Ar. After degassing 3 times by a standard freeze-thaw operation, the reaction was conducted at 60℃ for 72 h. The solvent was removed and purification by silica gel column (ethyl acetate/petroleum = 1:8) to afford the desired product **3af** (180 mg, 75% yield, 97% ee) as a colorless oil. The enantiometric excess was determined by HPLC (AS-H).

General procedure for the Gram-scale experiment: To a flame-dried Schlenk tube equipped with a magnetic stir bar was added chiral primary amine catalyst (20 mol%), adipic acid (20 mol%), PdCp(allyl) (2 mol%), and PCy_3 (4 mol%), then a mixture solution of 1,3-diketones **1a** (7 mmol) and salicyl carbonates **2b** (14 mmol) in 35 mL anhydrous THF/MeCN (6/1) was added via syringe under Ar. After degassing 3 times by a standard freeze-thaw operation, the reaction was conducted at 60℃ for 68 h. The solvent was removed and purification by silica gel column (ethyl acetate/petroleum = 1:8) to afford the desired product **3af** (1.42g, 70% yield, 89% ee) as a colorless oil. The enantiometric excess was determined by HPLC (AS-H).

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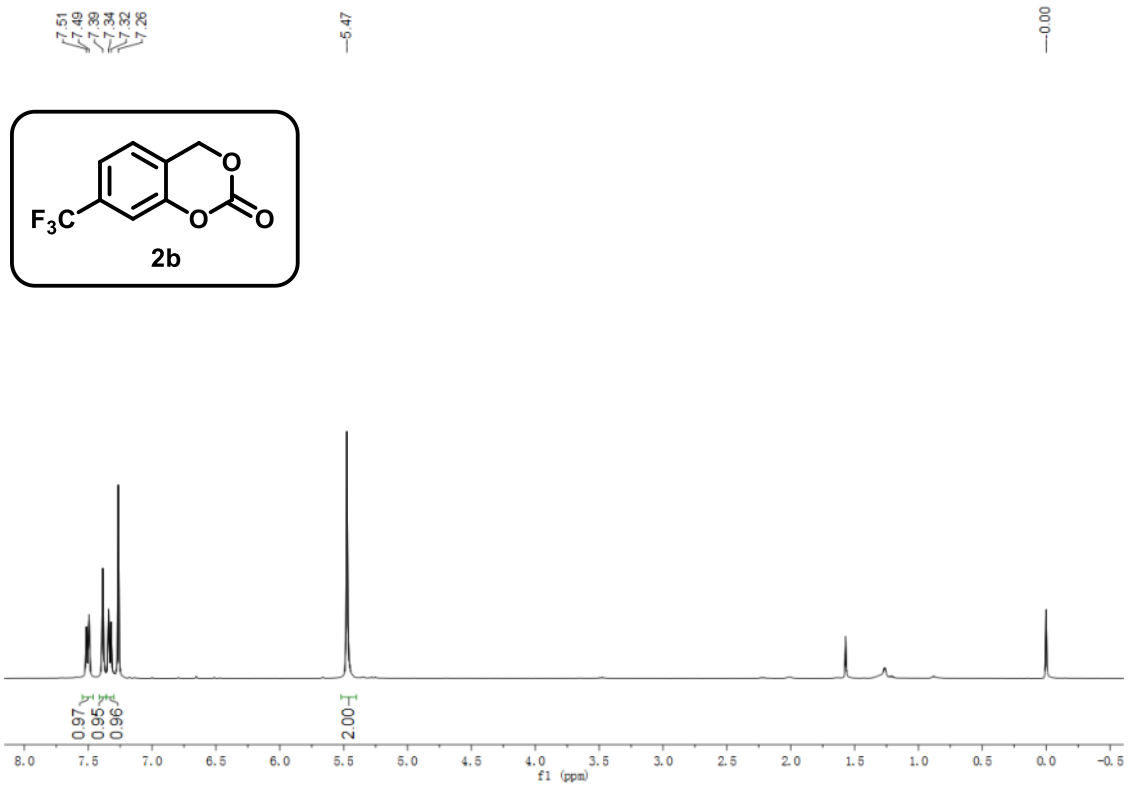
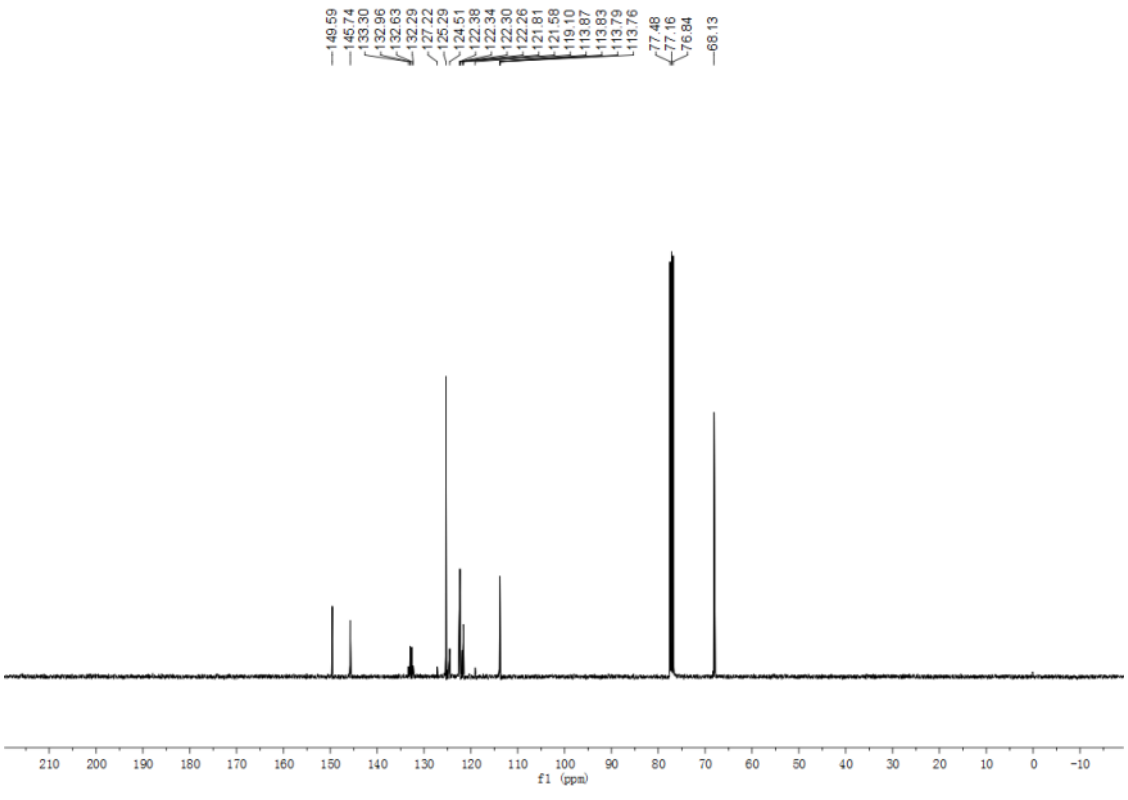
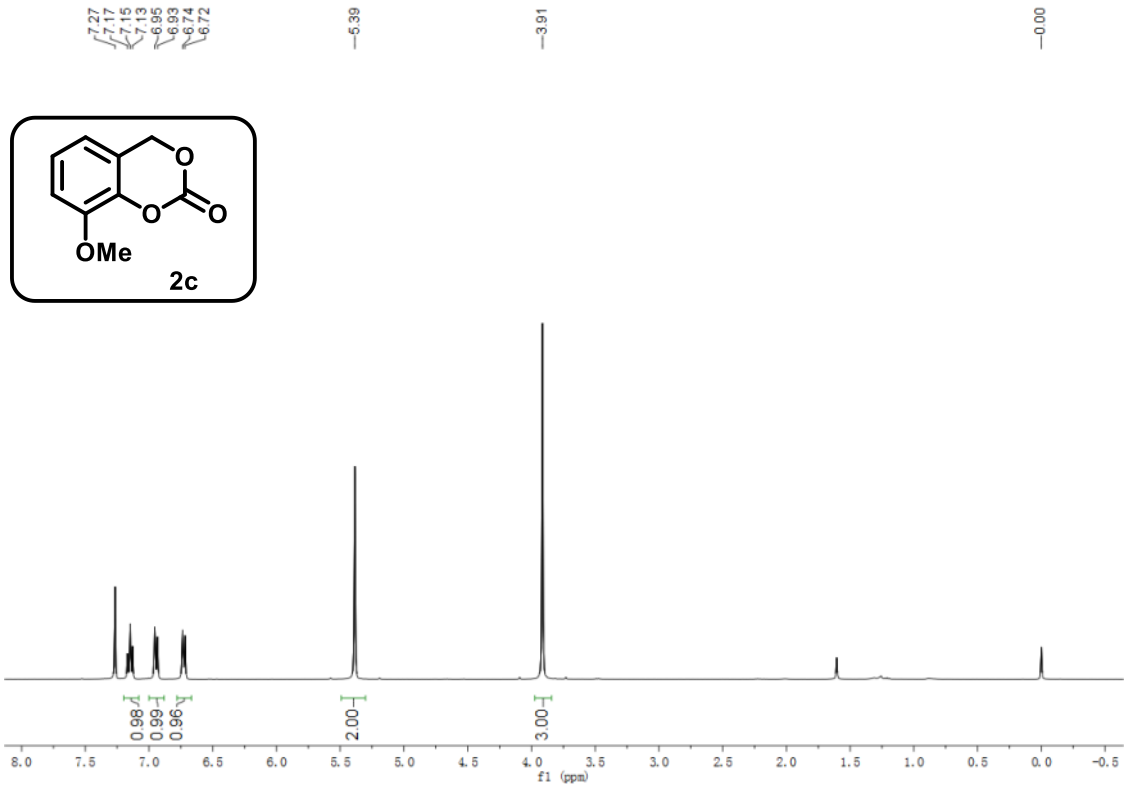
NMR spectral for new substrates



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3.00
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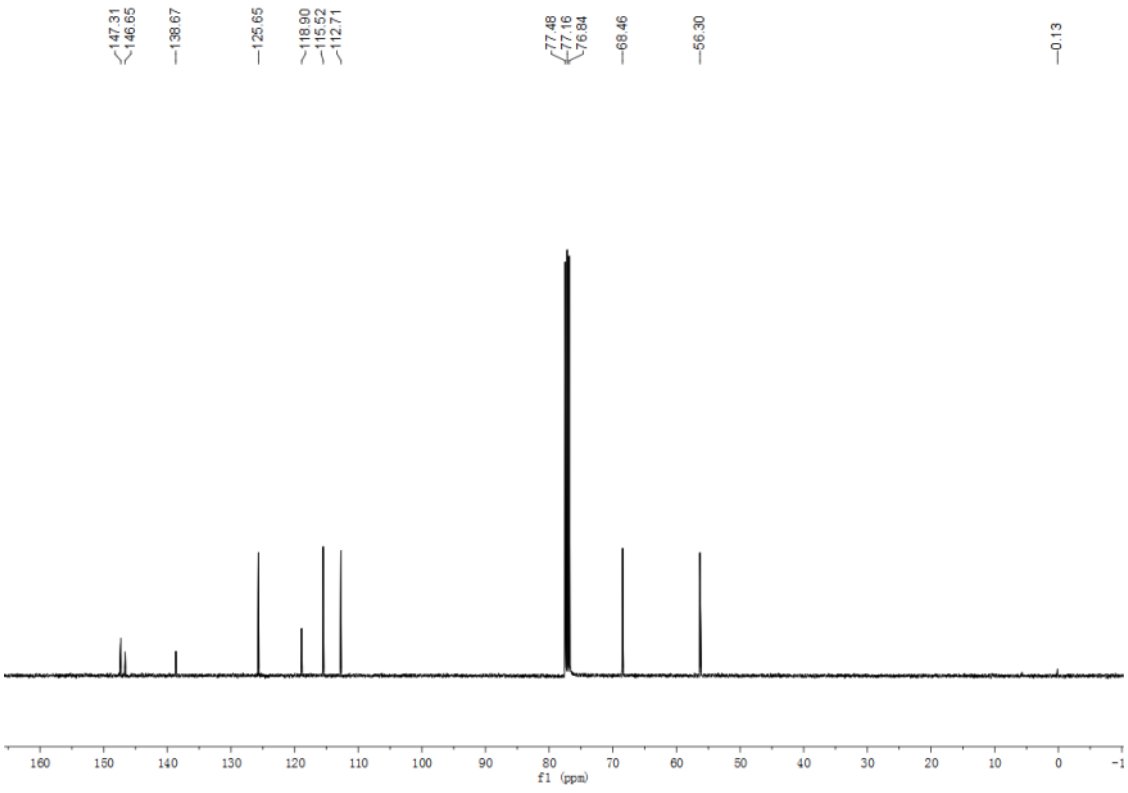
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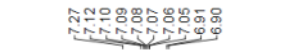
f1 (ppm)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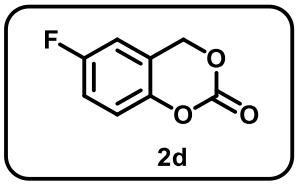
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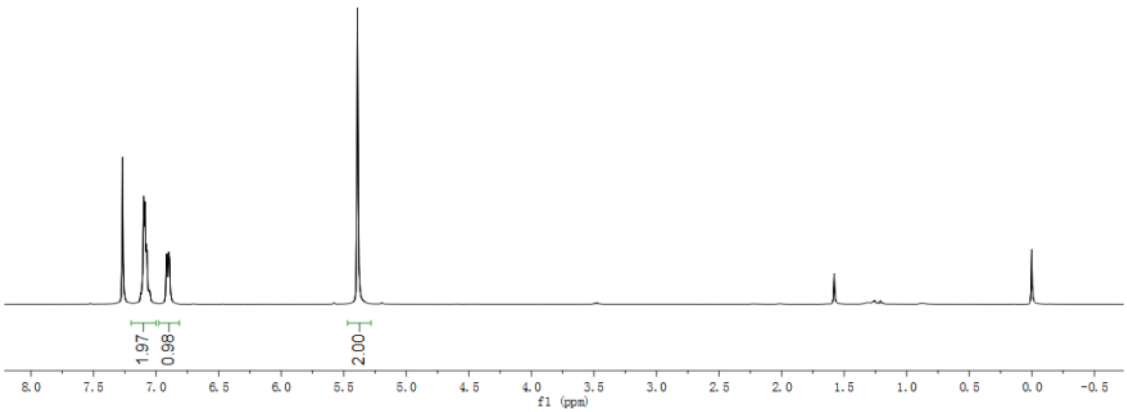
O
O
2d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3.0
2.5
2.0
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0.5
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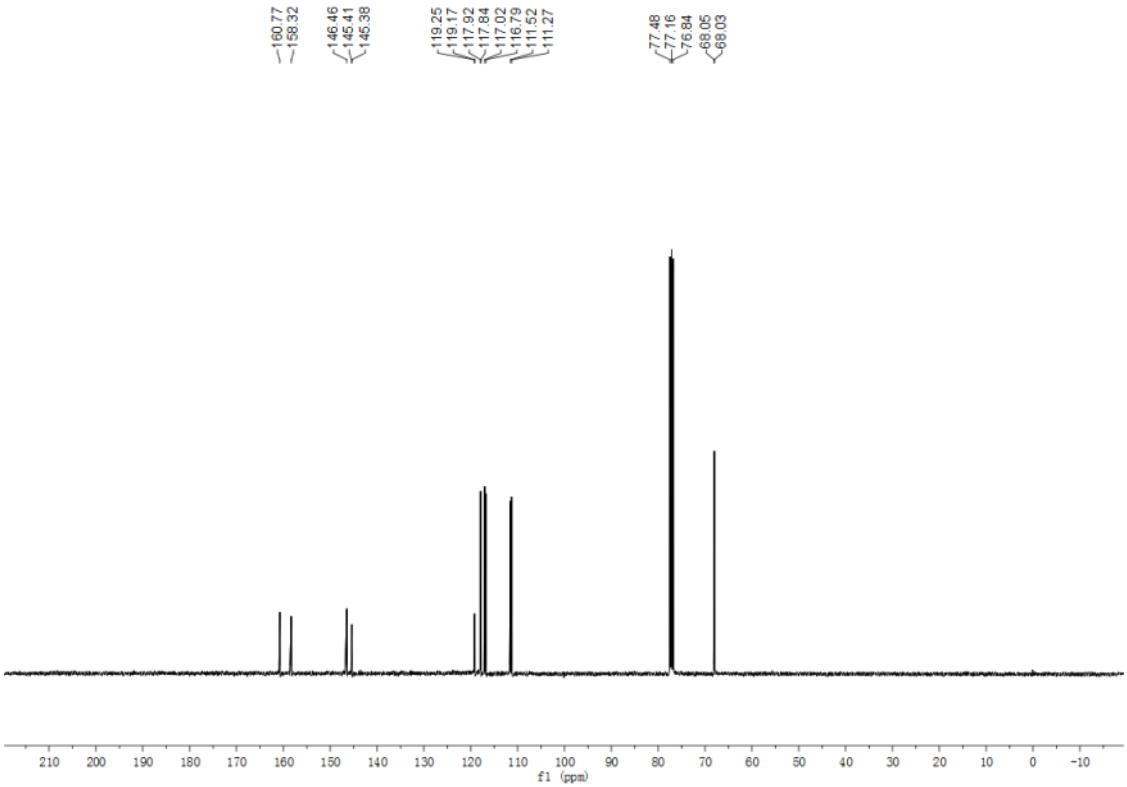
-0.5
f1 (ppm)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68.05
68.03
210
200
190
180
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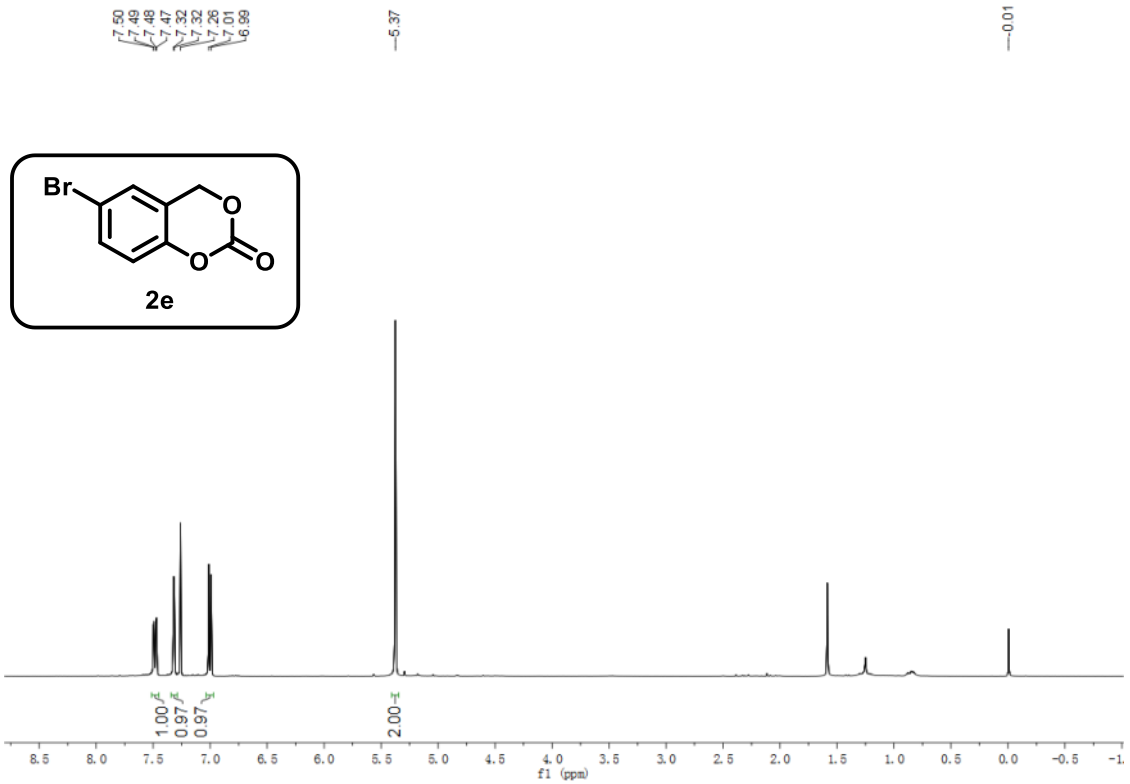
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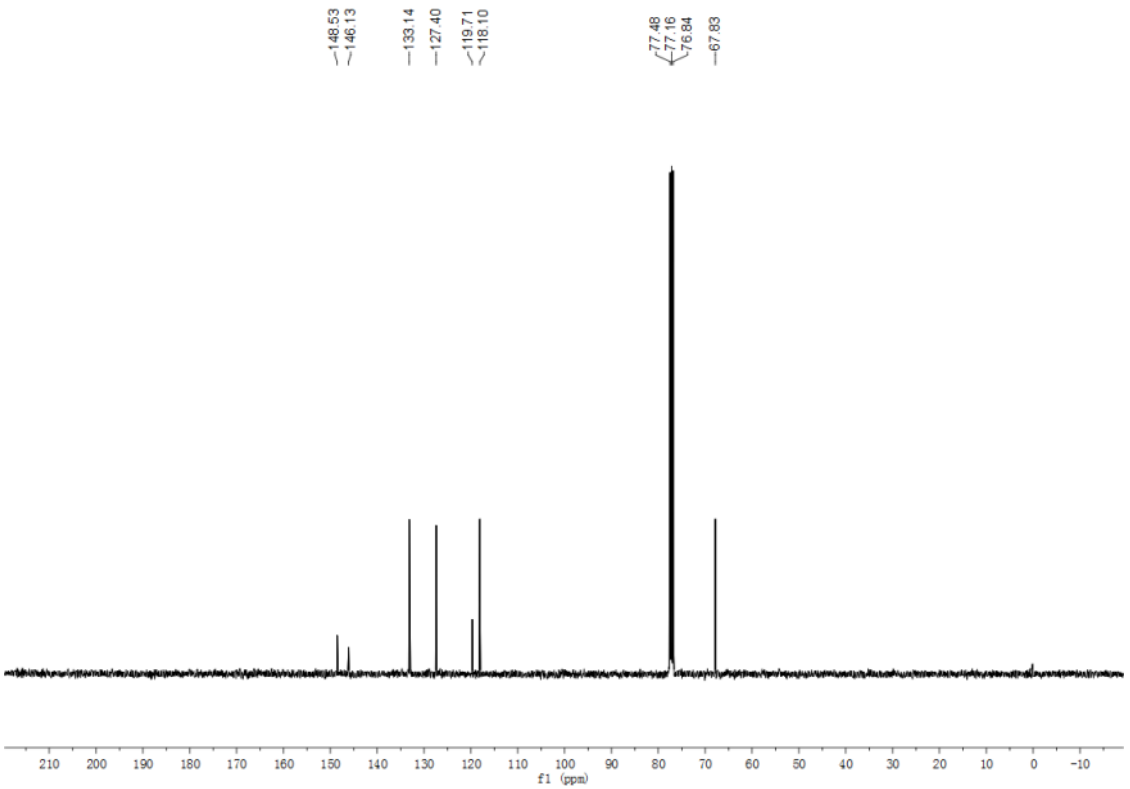
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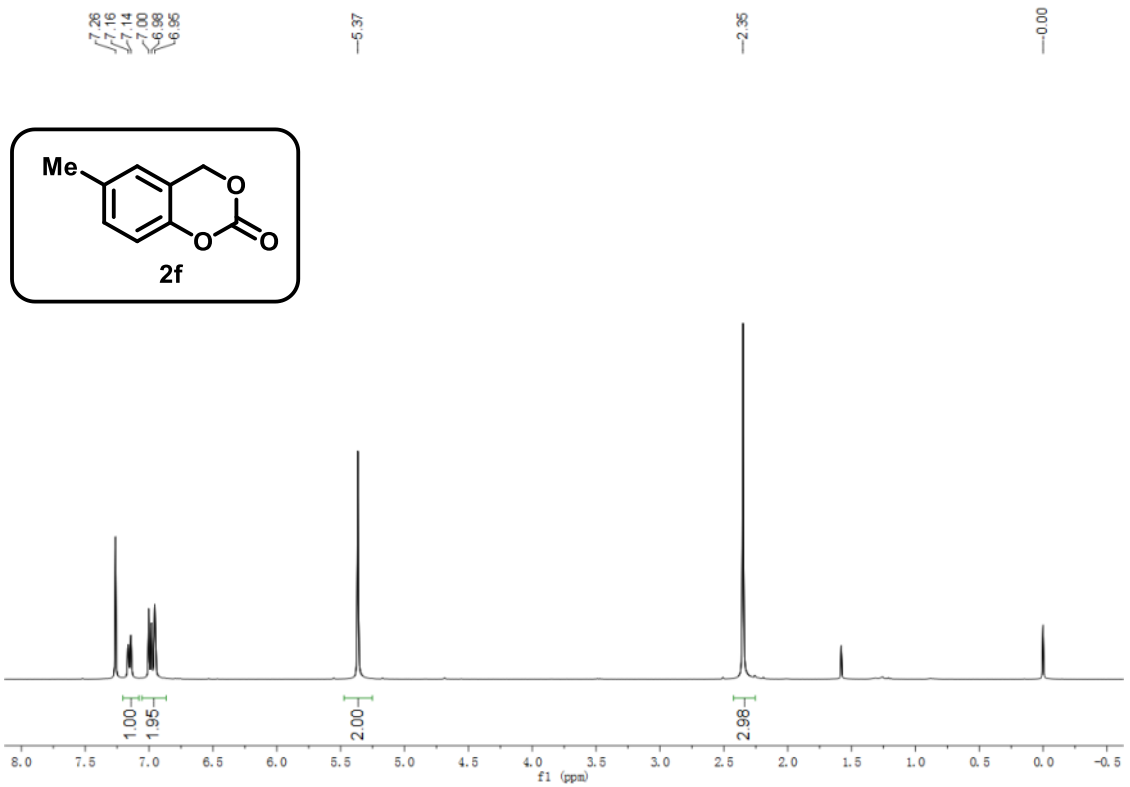
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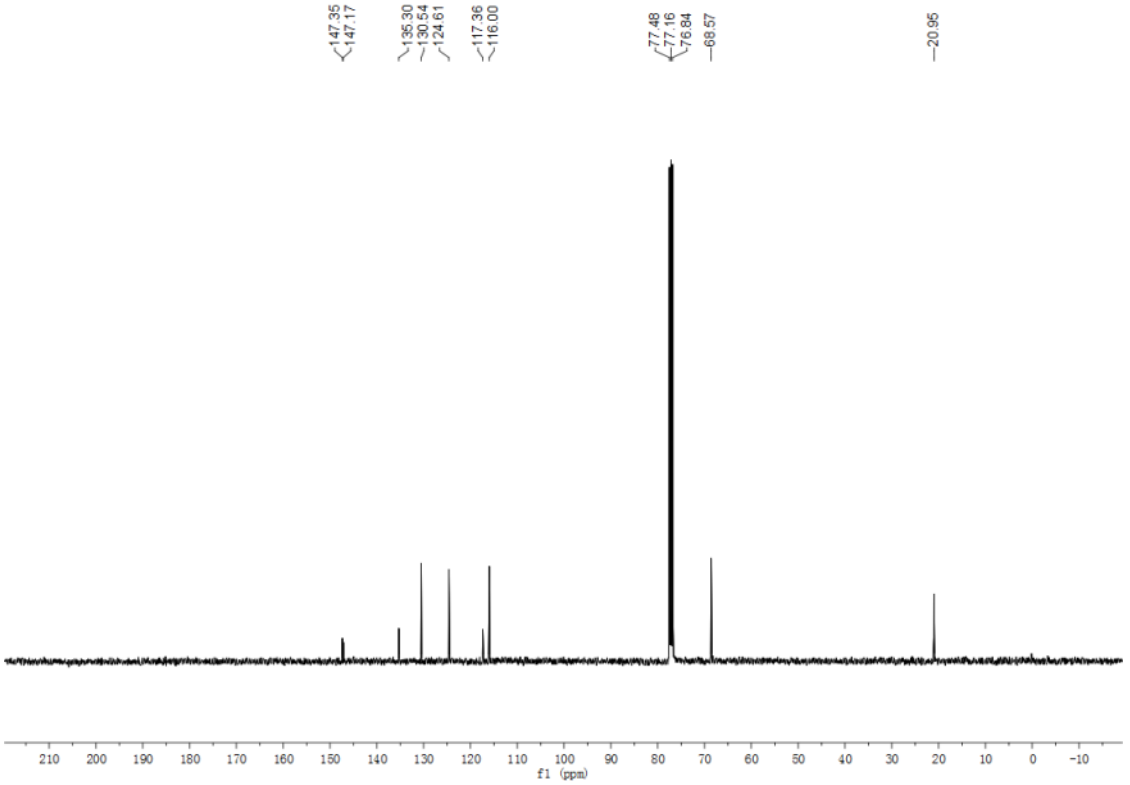
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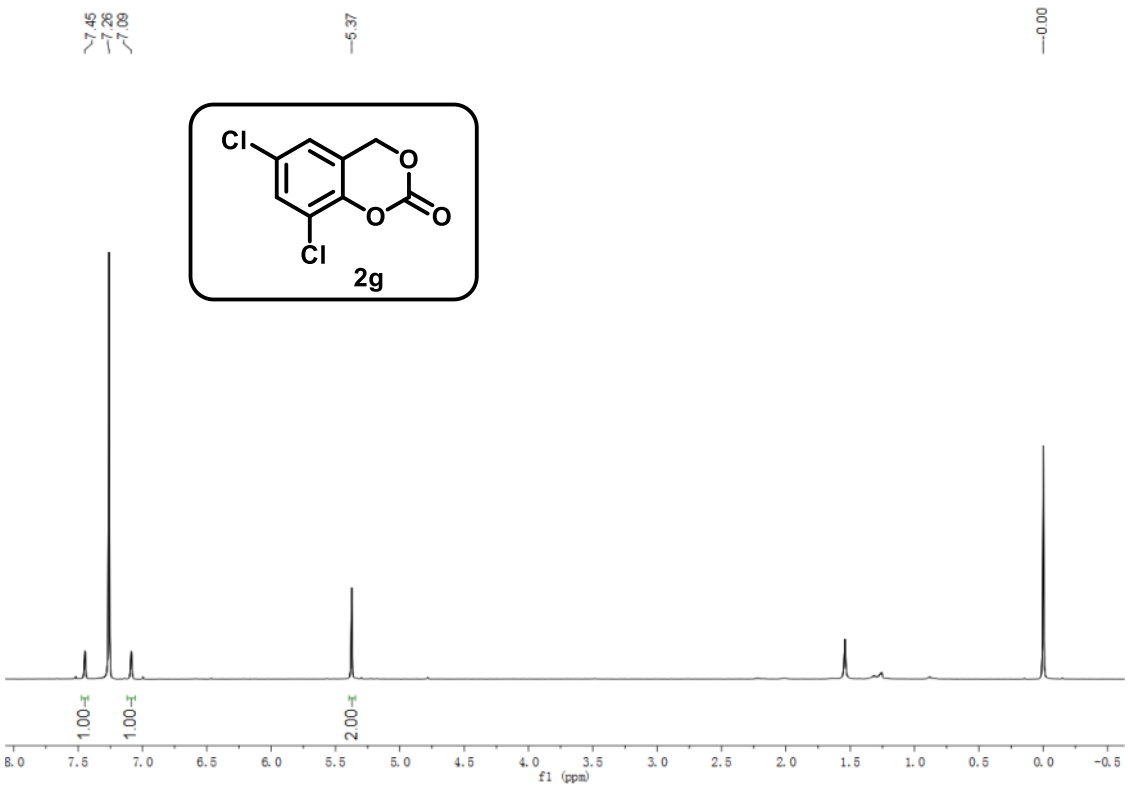
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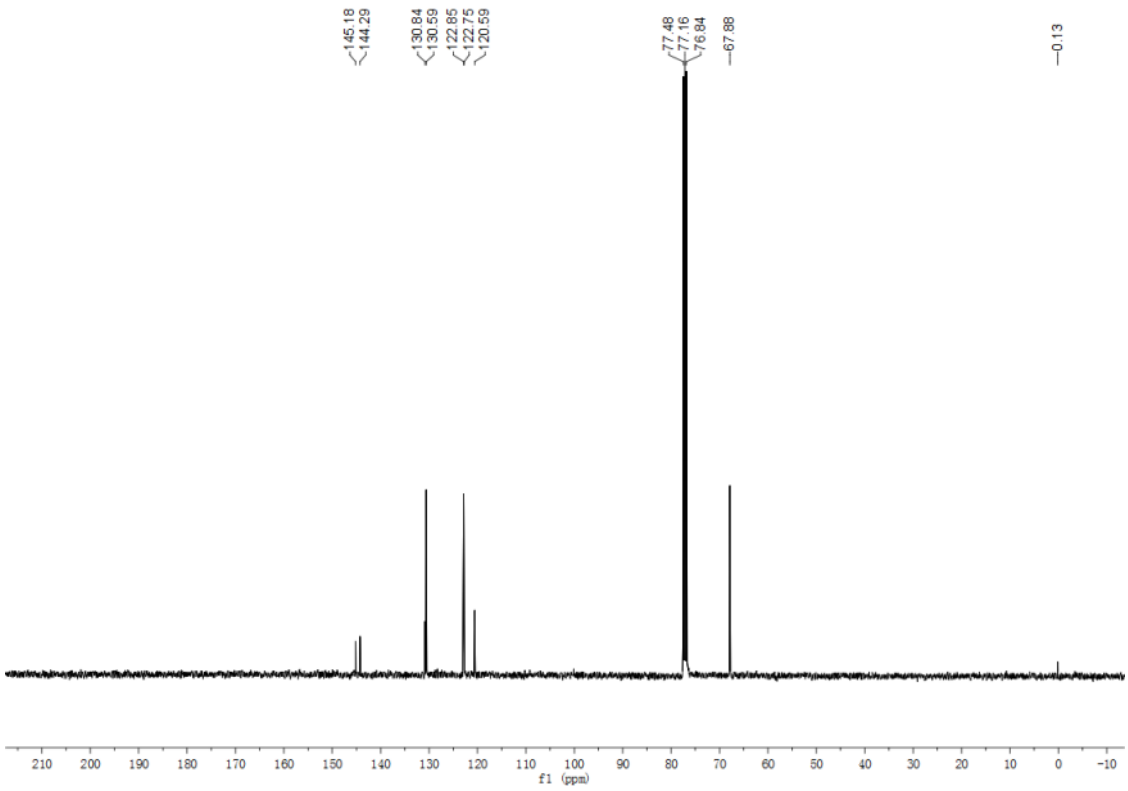
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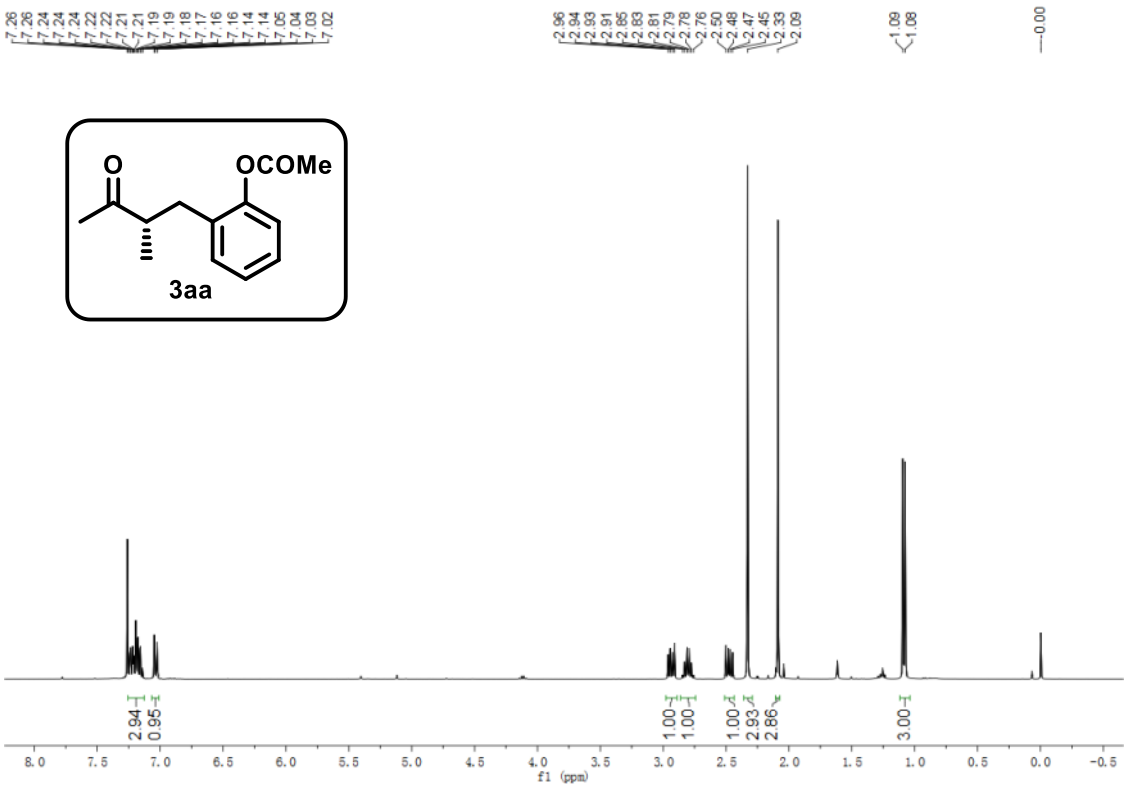
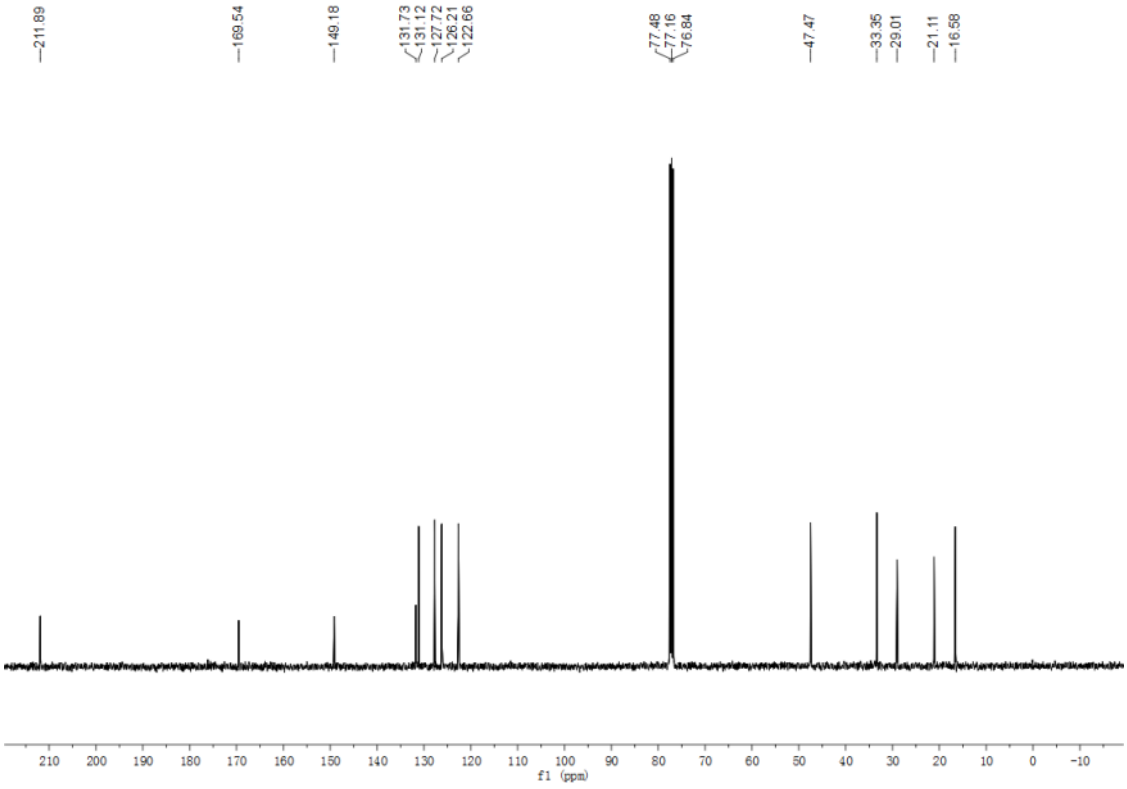
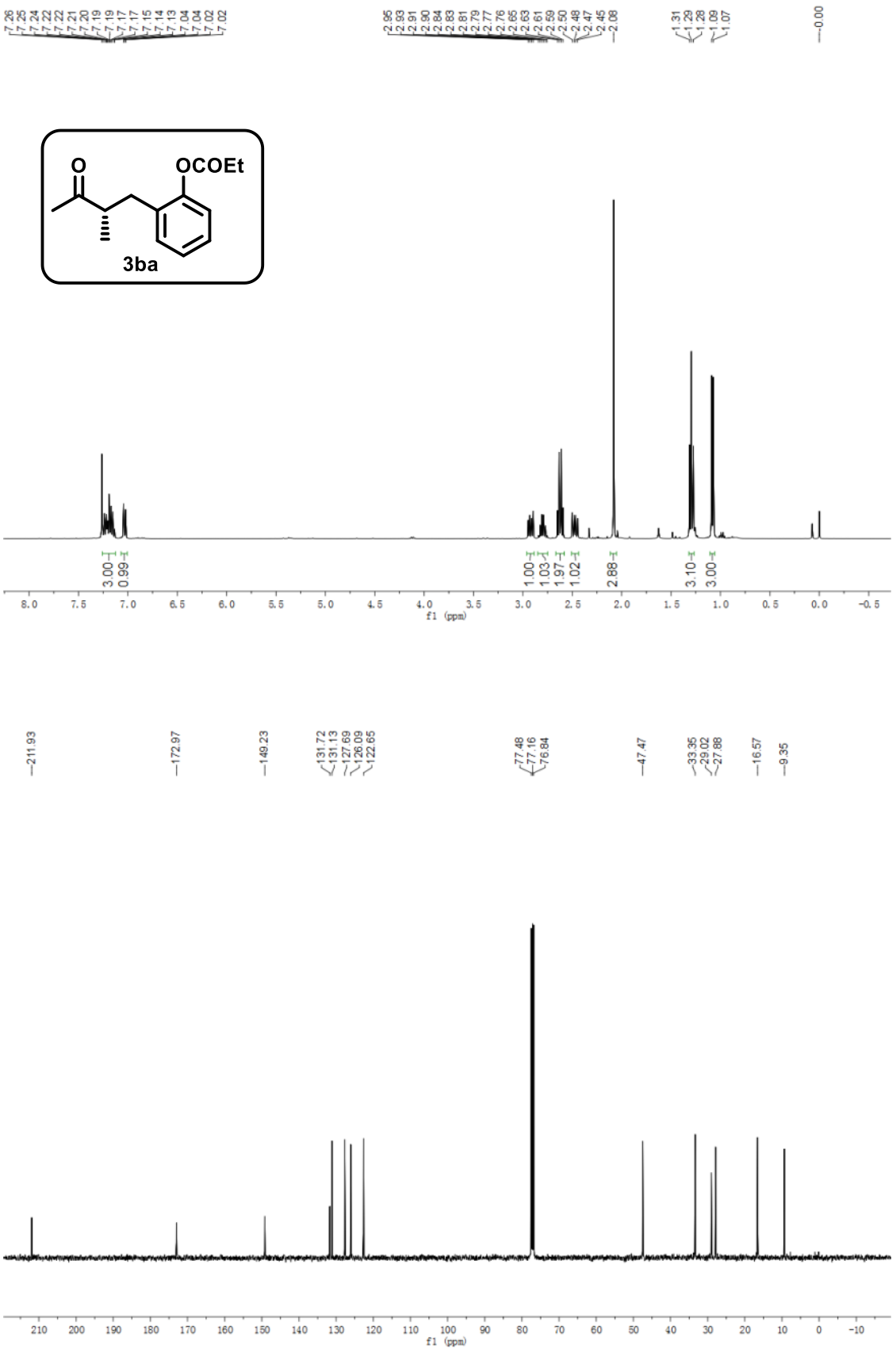
f1 (ppm)

NMR spectral for new products



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1.07
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1.03
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1.02
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3.00
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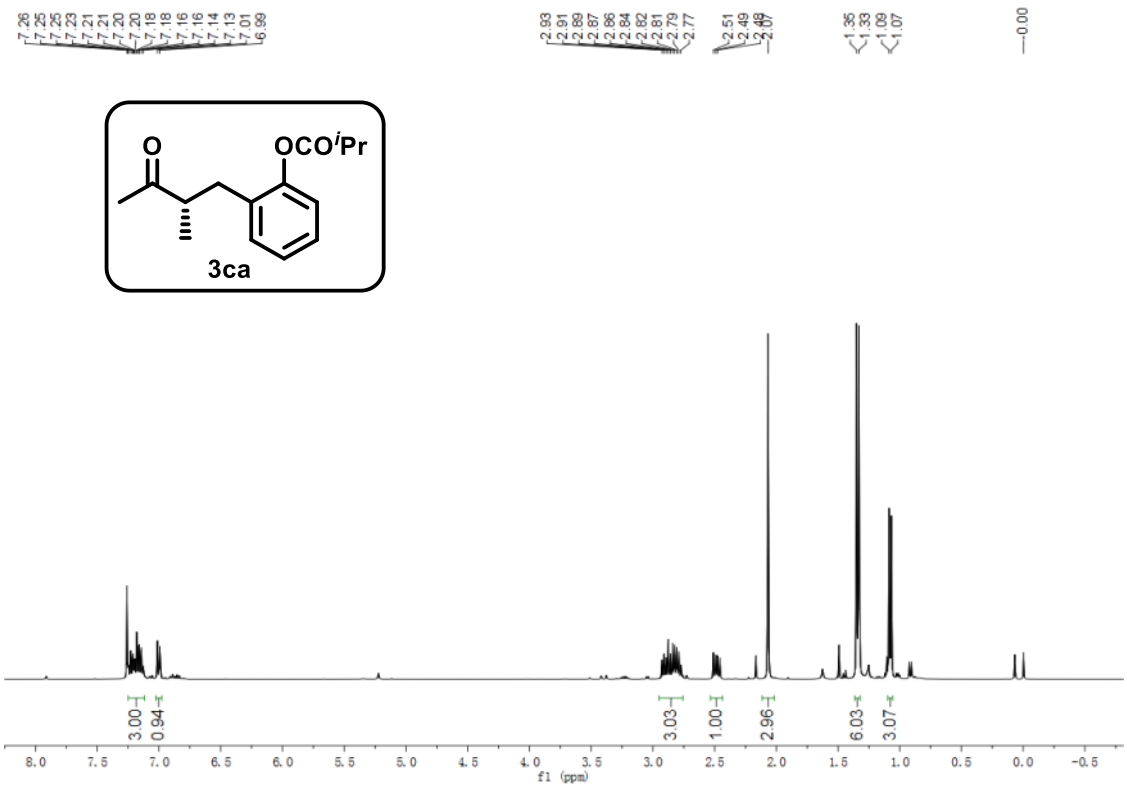
9.35
f1 (ppm)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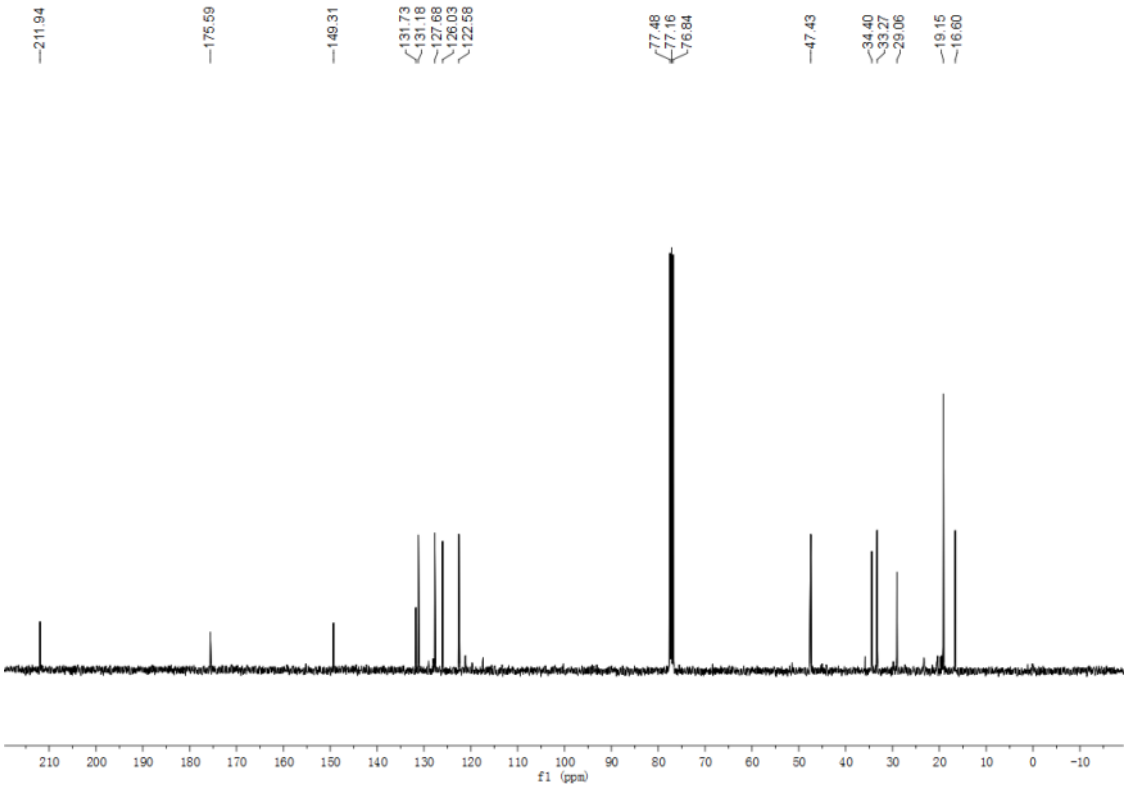
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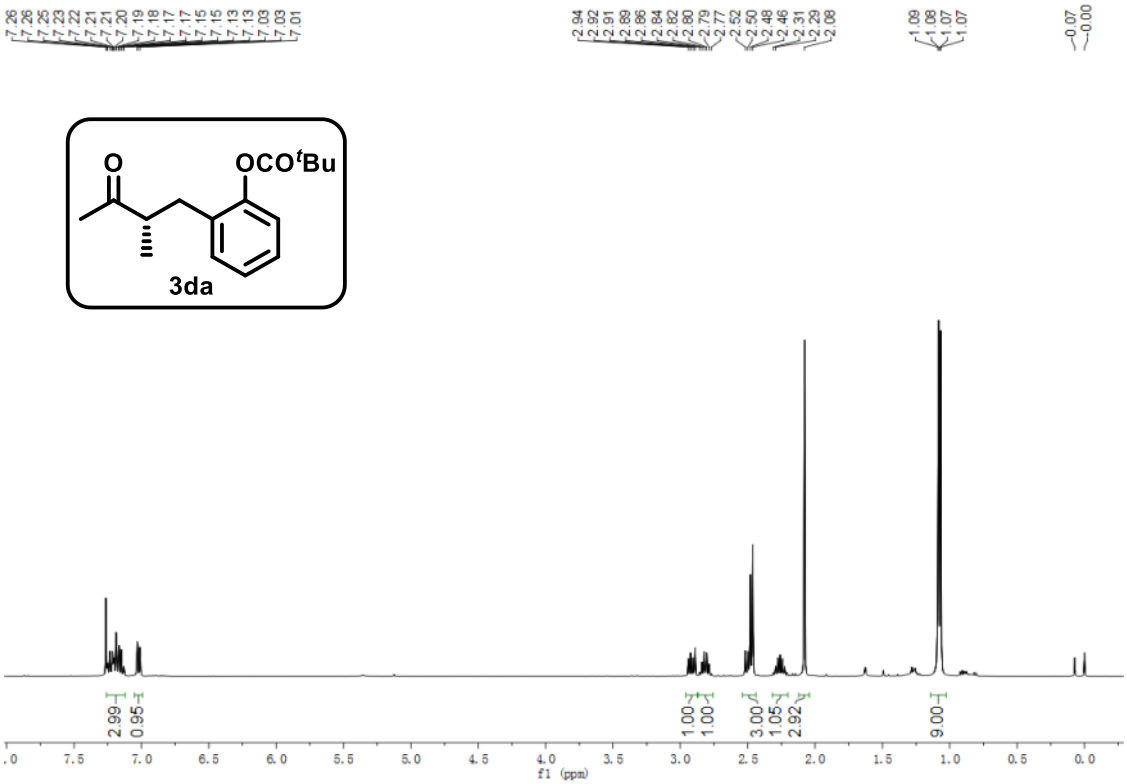
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7.15
7.15
7.13
7.13
7.03
7.03
7.01
2.94
2.92
2.91
2.89
2.86
2.84
2.82
2.80
2.79
2.77
2.52
2.50
2.48
2.46
2.31
2.29
2.08
1.09
1.08
1.07
1.07
0.07
0.00
O
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1.00
1.00
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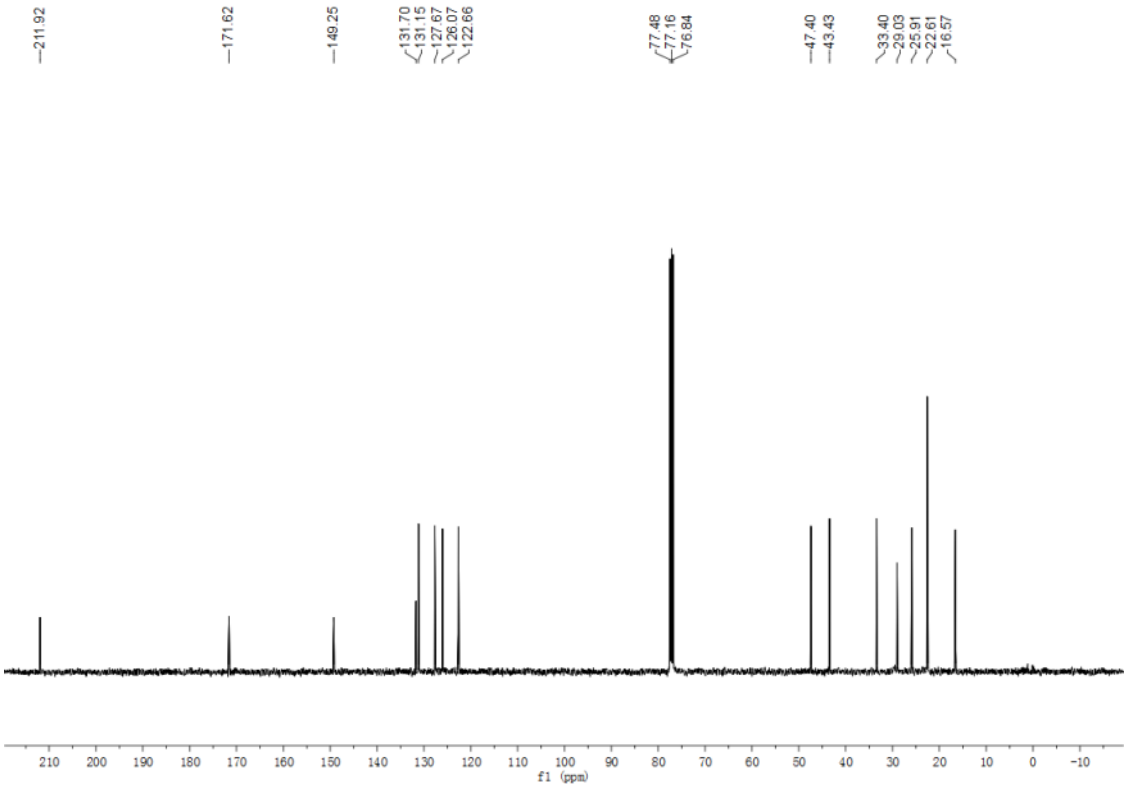
f1 (ppm)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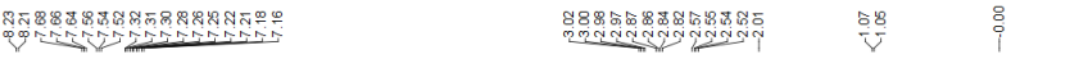
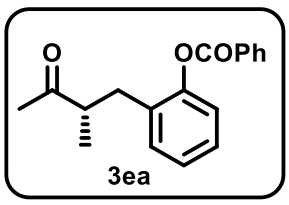
f1 (ppm)




O
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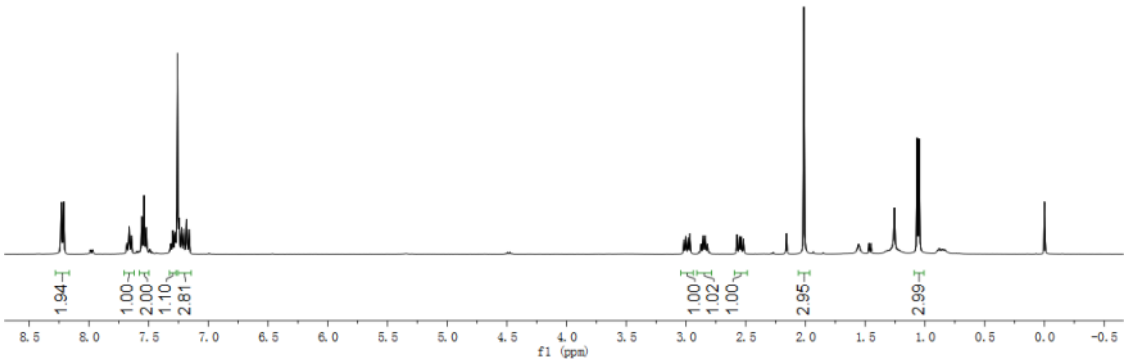
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1.00
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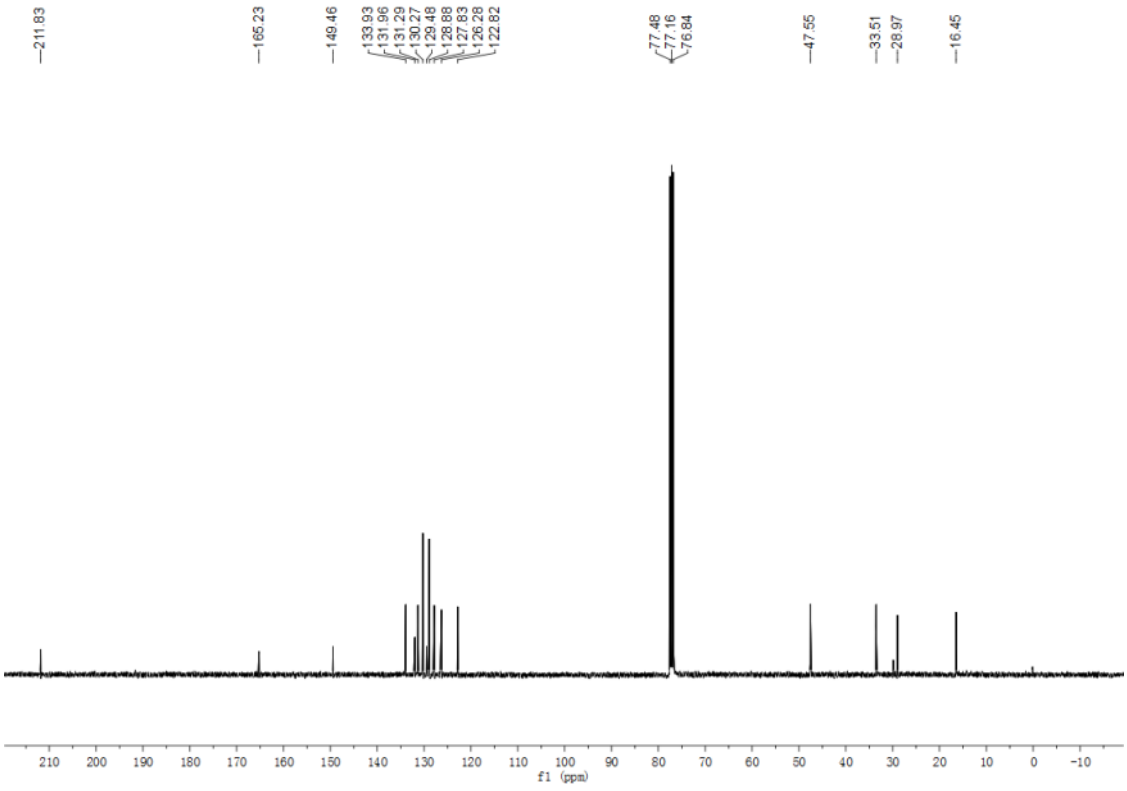
f1 (ppm)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47.55
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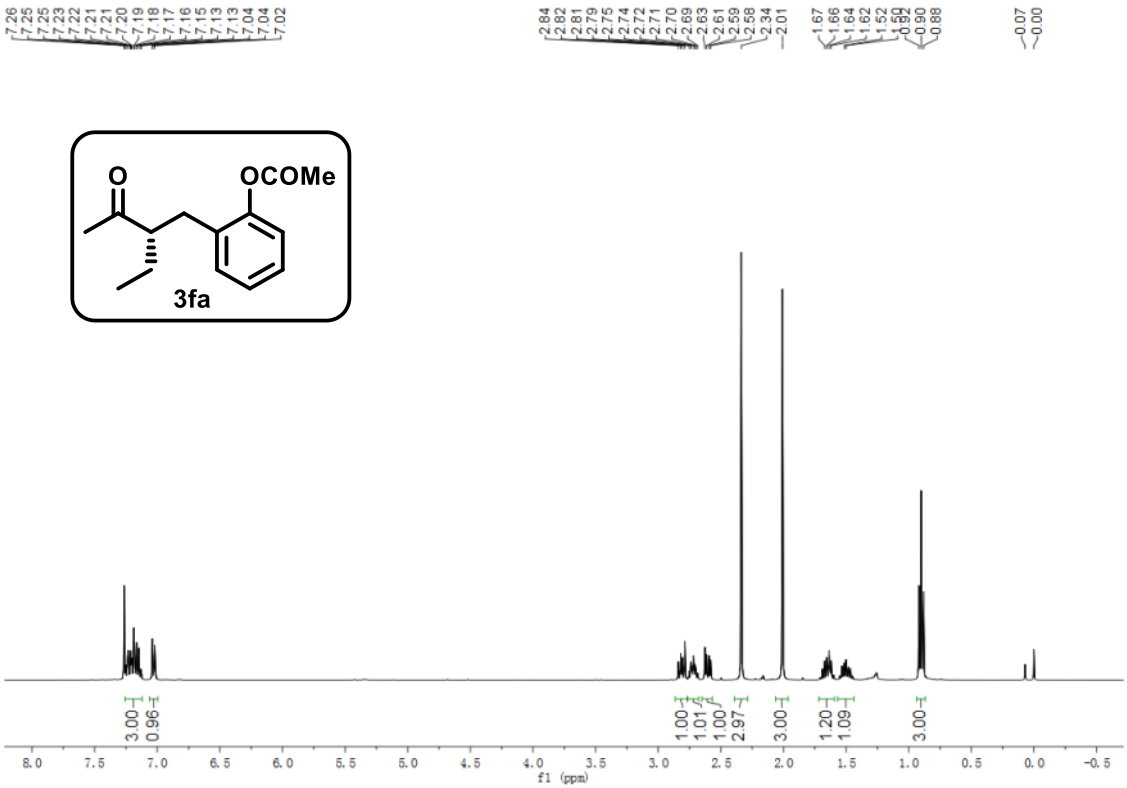
f1 (ppm)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7.04
7.04
7.02
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2.63
2.61
2.59
2.58
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1.64
1.62
1.52
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0.90
0.88
0.07
0.00
O
OCOMe
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1.00
2.97
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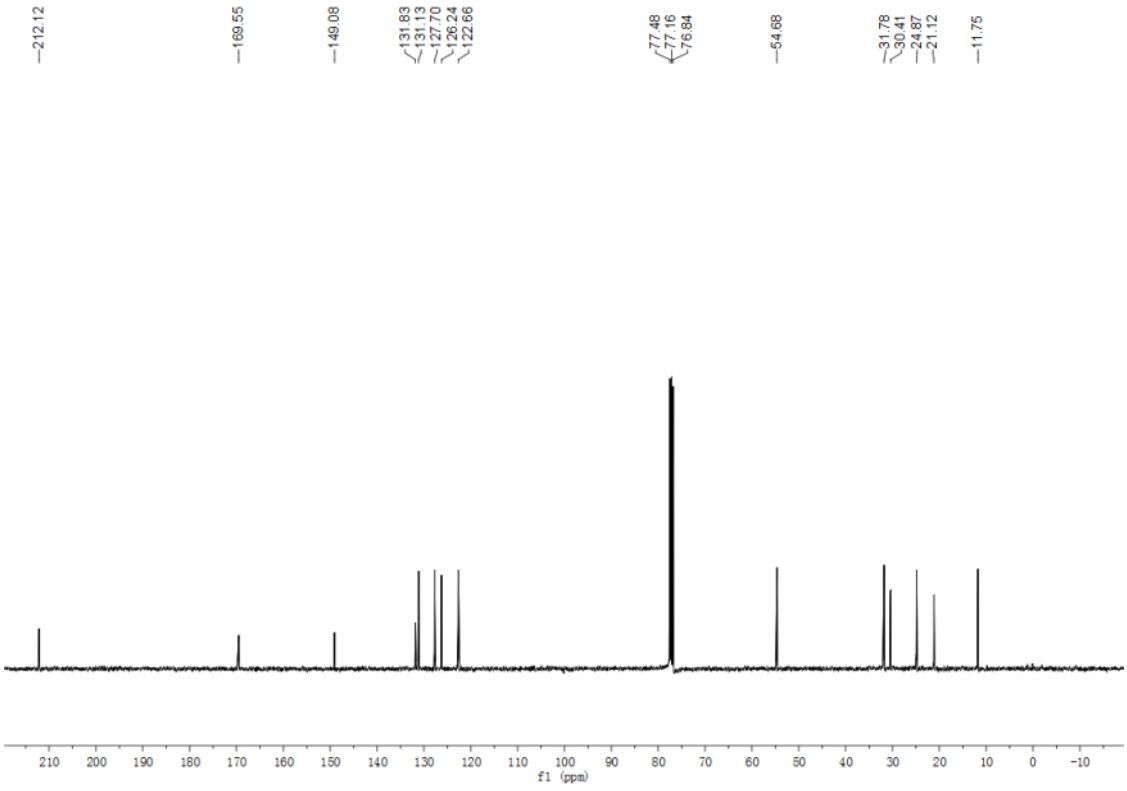
1.20
1.09
3.00
f1 (ppm)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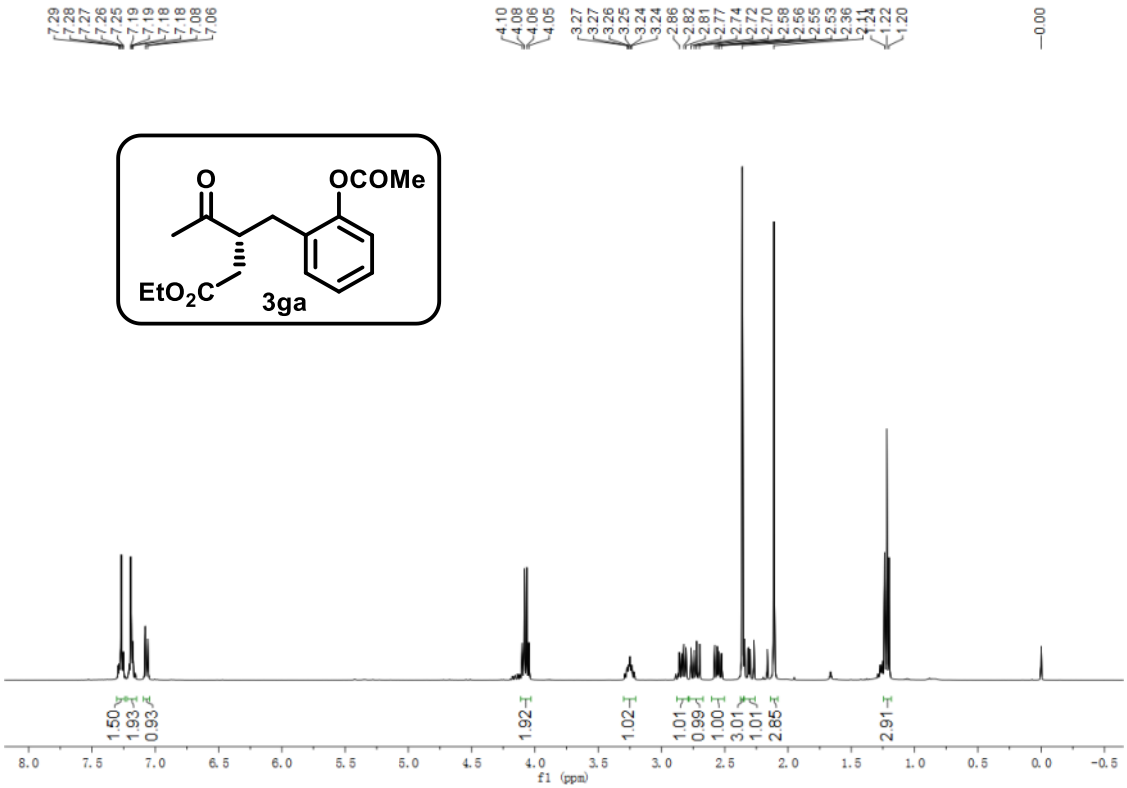
24.87
21.12
11.75
f1 (ppm)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7.18
7.08
7.06
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4.08
4.06
4.05
3.27
3.27
3.26
3.25
3.24
3.24
2.86
2.82
2.81
2.77
2.74
2.72
2.70
2.58
2.56
2.55
2.53
2.36
2.11
1.24
1.22
1.20
0.00
O
OCOMe
EtO2C
3ga
1.50
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0.99
1.00
3.01
1.01
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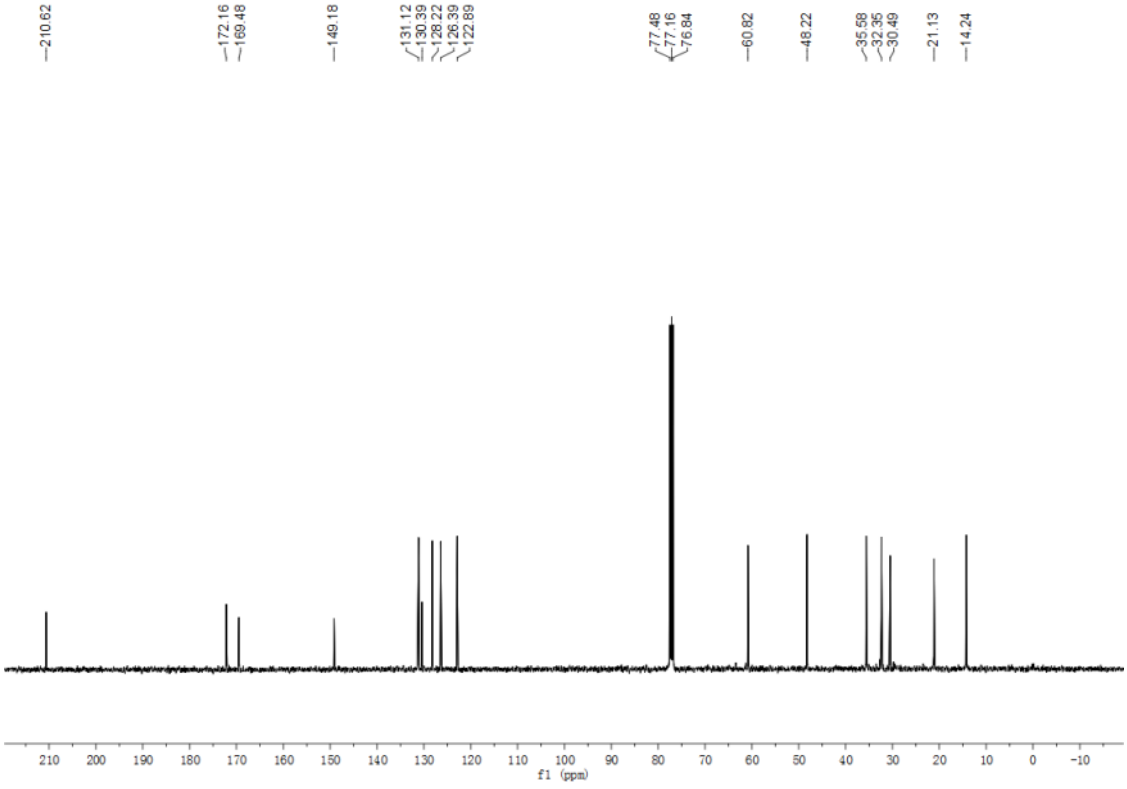
2.91
f1 (ppm)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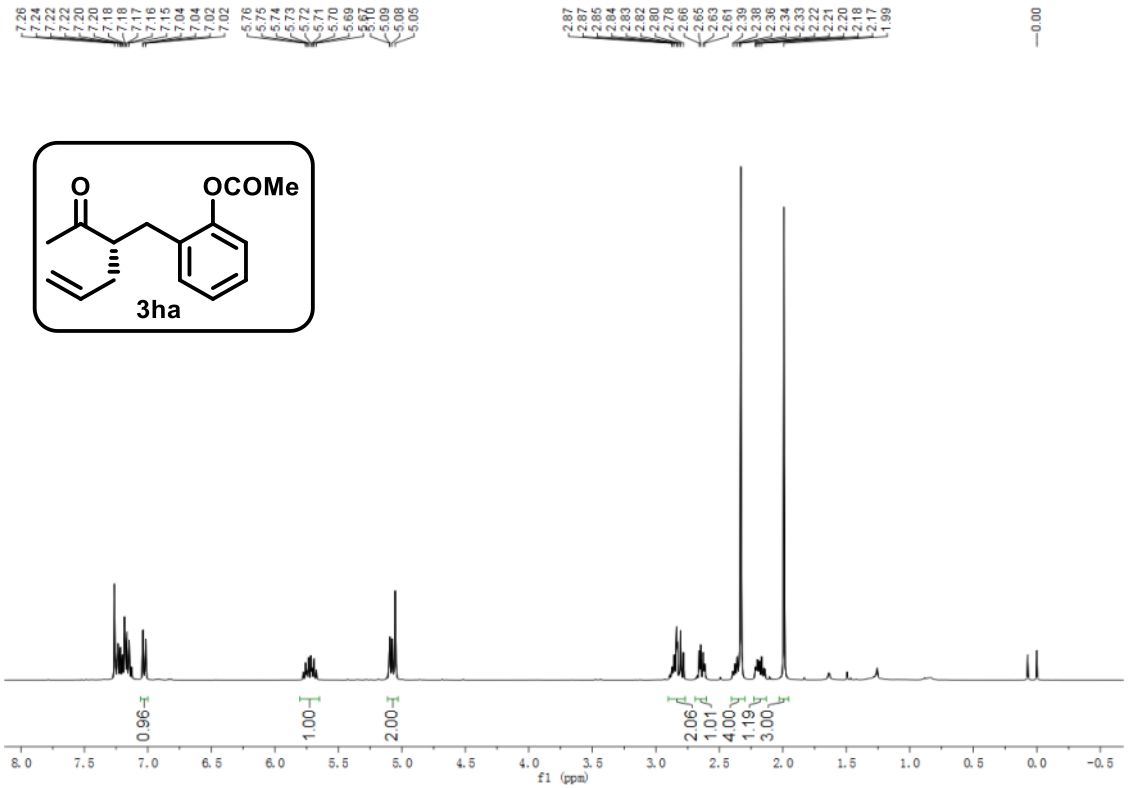
32.35
30.49
21.13
14.24
f1 (ppm)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7.17
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7.15
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7.04
7.02
7.02
5.76
5.75
5.74
5.73
5.72
5.71
5.70
5.69
5.67
5.67
5.09
5.08
5.05
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2.87
2.85
2.84
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2.36
2.34
2.33
2.22
2.21
2.20
2.18
2.17
1.99
0.00
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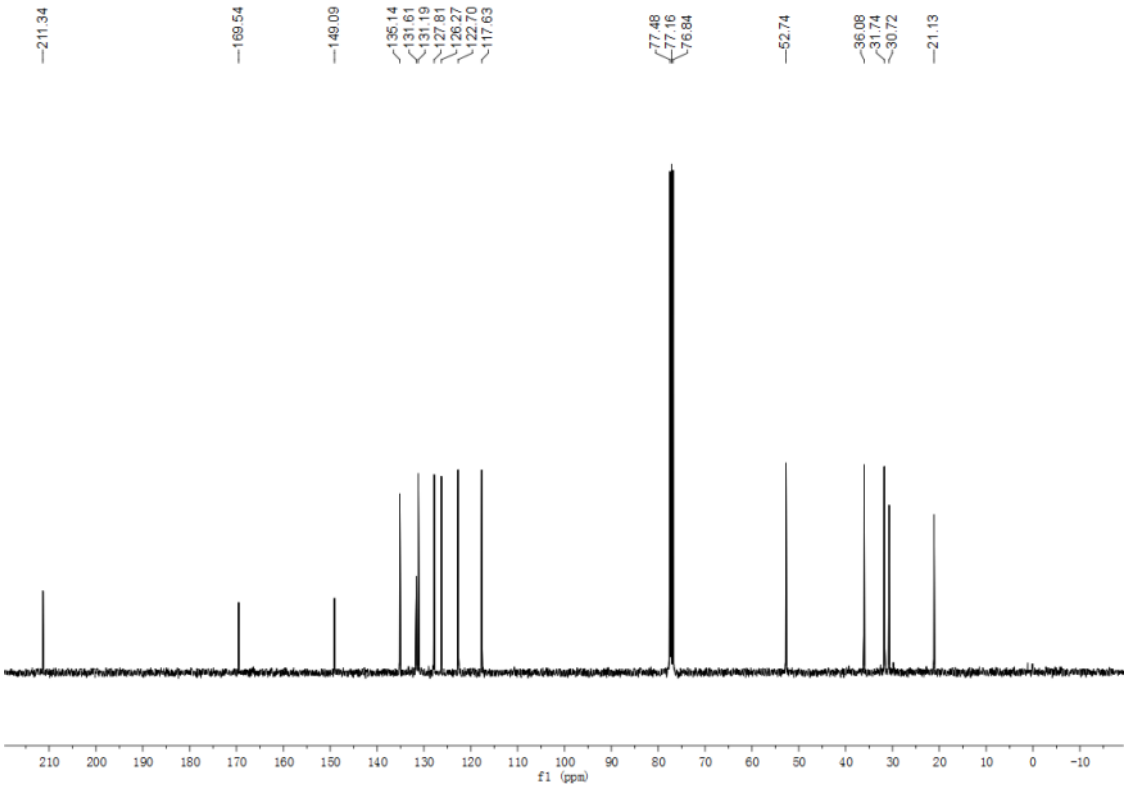
2.06
1.01
4.00
1.19
3.00
f1 (ppm)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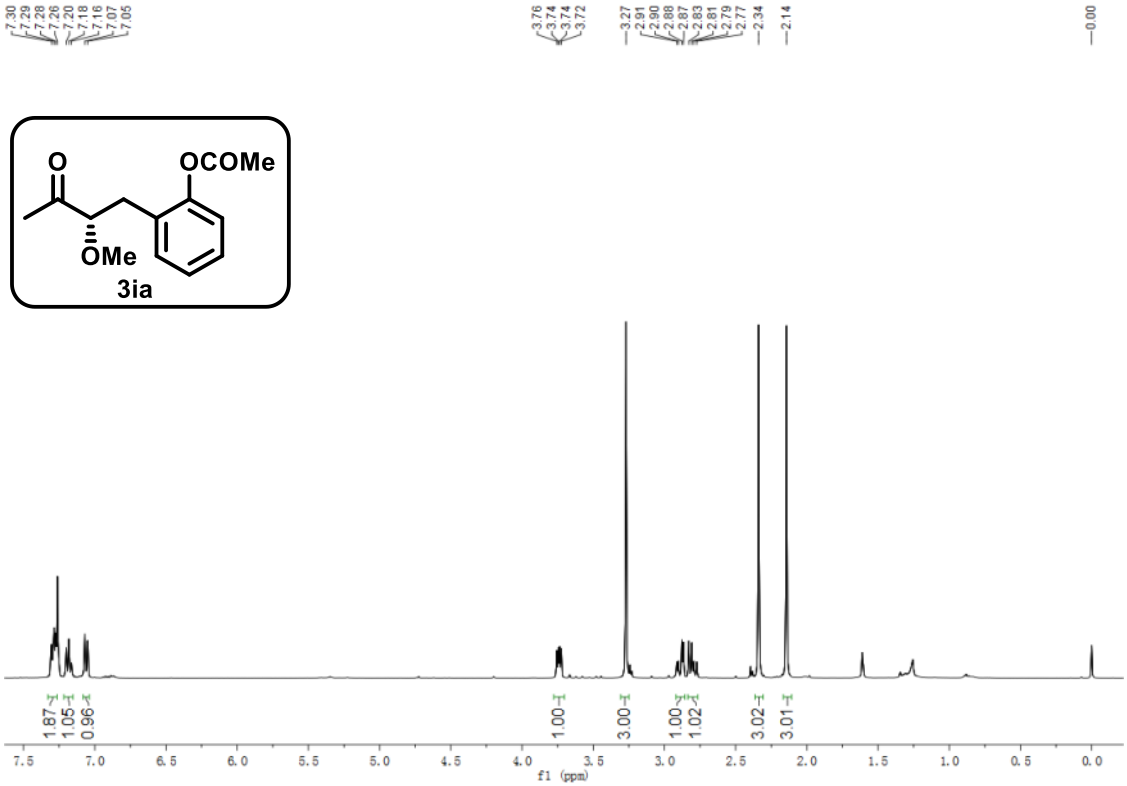
36.08
31.74
30.72
21.13
f1 (ppm)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3.72
3.27
2.91
2.90
2.88
2.87
2.83
2.81
2.79
2.77
2.34
2.14
0.00
O
OCOMe
OMe
3ia
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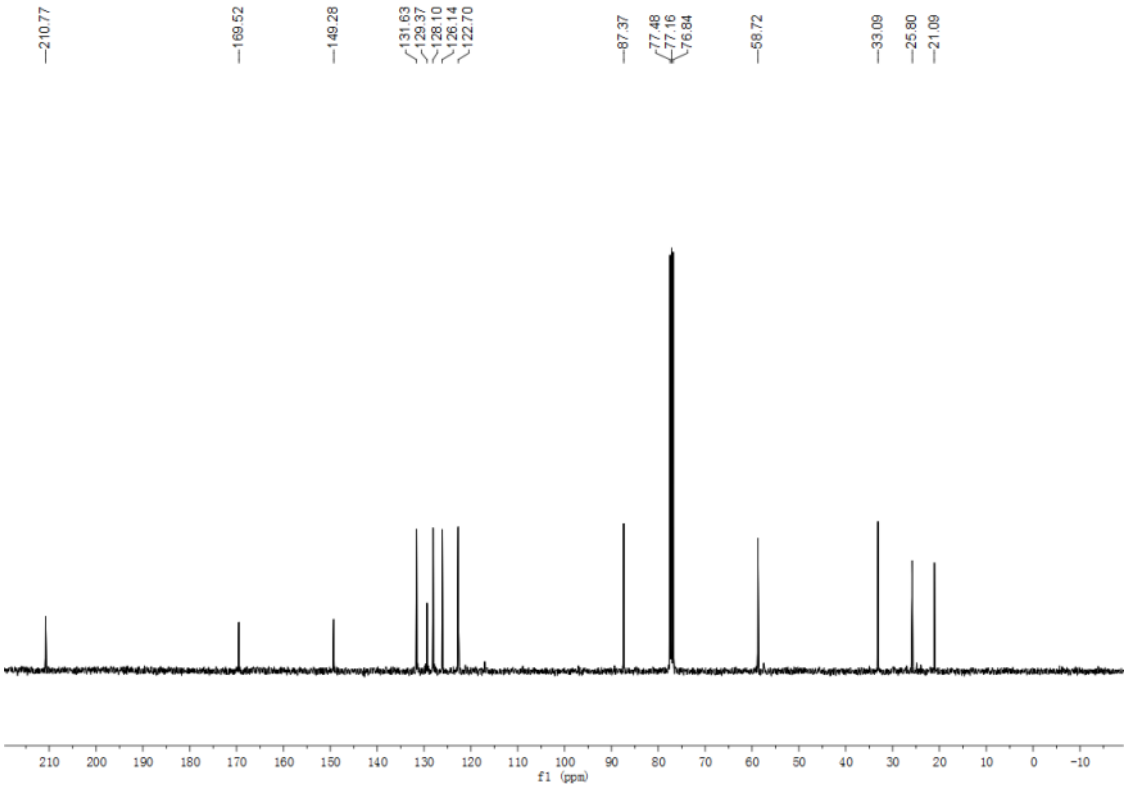
1.05
0.96
1.00
3.00
1.00
1.02
3.02
3.01
f1 (ppm)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76.84
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33.09
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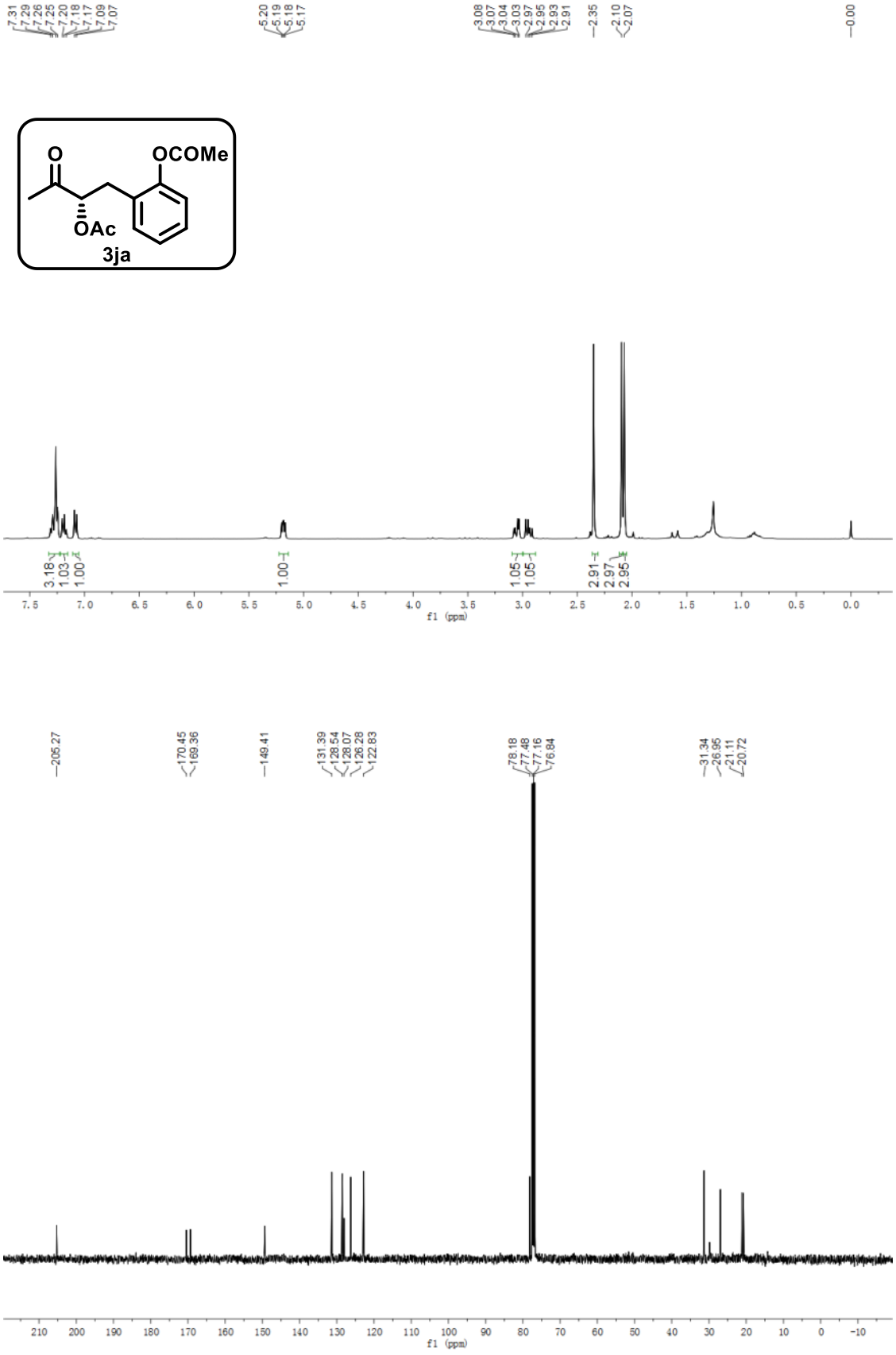
21.09
f1 (ppm)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5.20
5.19
5.18
5.17
3.08
3.07
3.04
3.03
2.97
2.95
2.93
2.91
2.35
2.10
2.07
0.00
O
OCOMe
OAc
3ja
3.18
1.03
1.00
1.00
1.05
1.05
2.91
2.97
2.95
f1 (ppm)
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170.45
169.36
149.41
131.39
128.54
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77.48
77.16
76.84
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26.95
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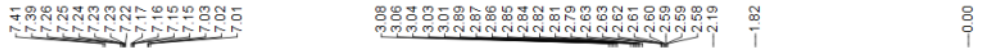
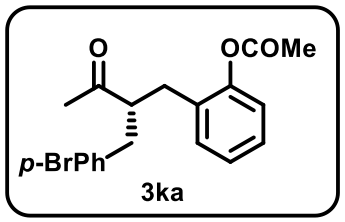
20.72
f1 (ppm)

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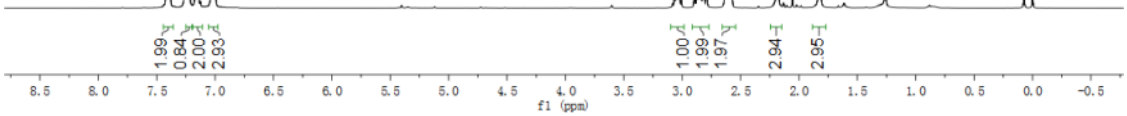
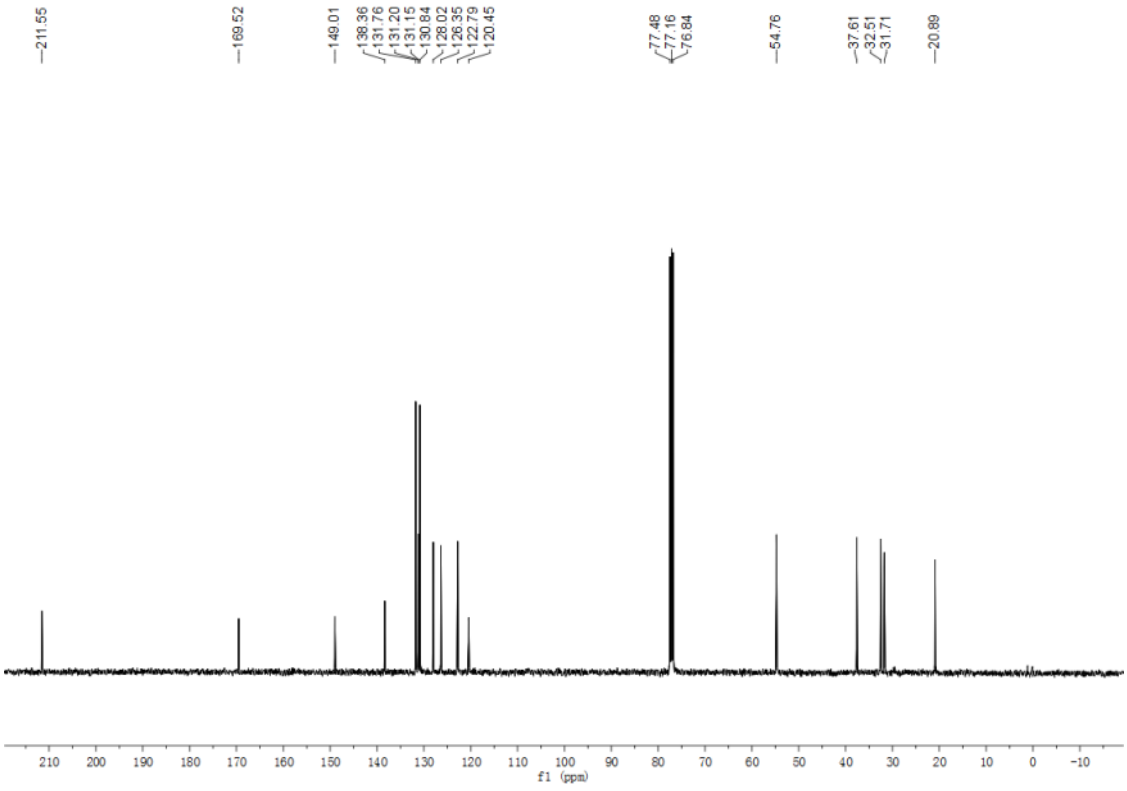
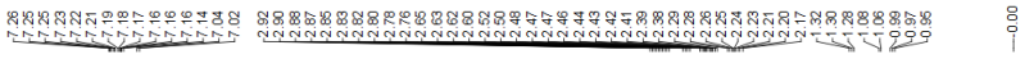
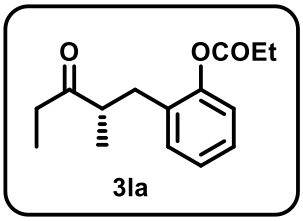
p-BrPh
3ka

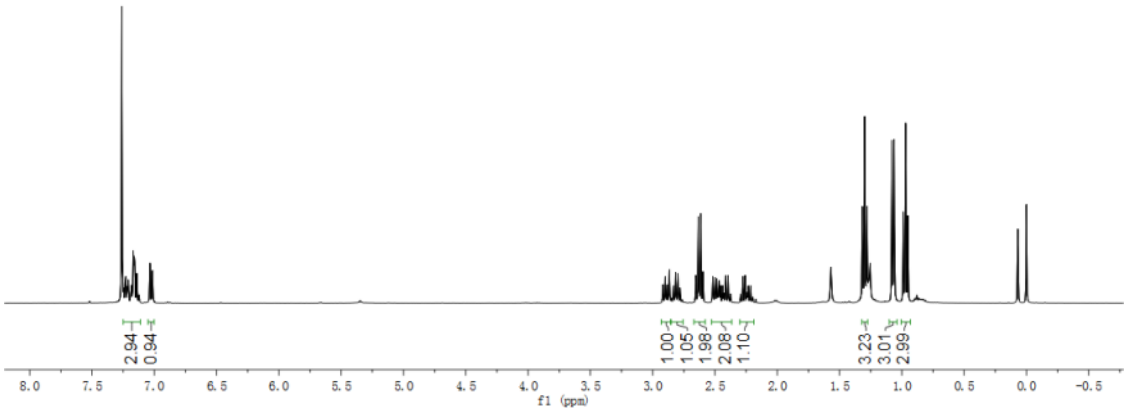







O
OCOEt

3la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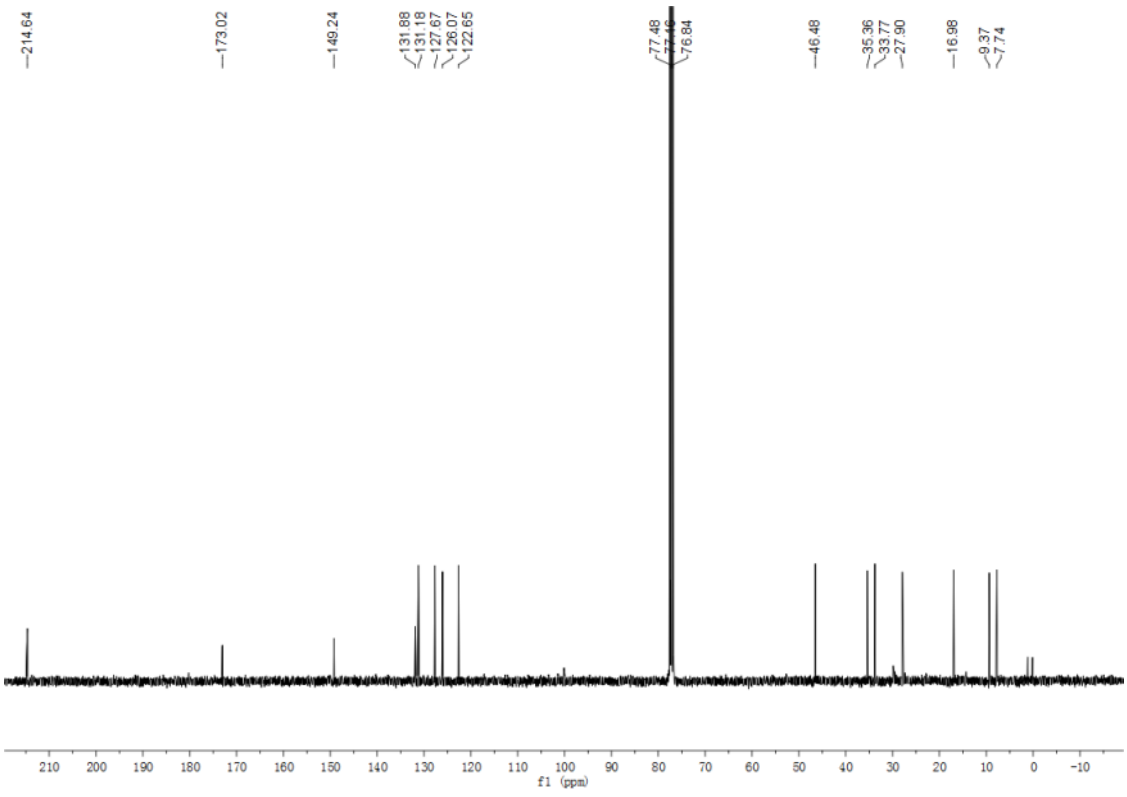
1.10
3.23
3.01
2.99
f1 (ppm)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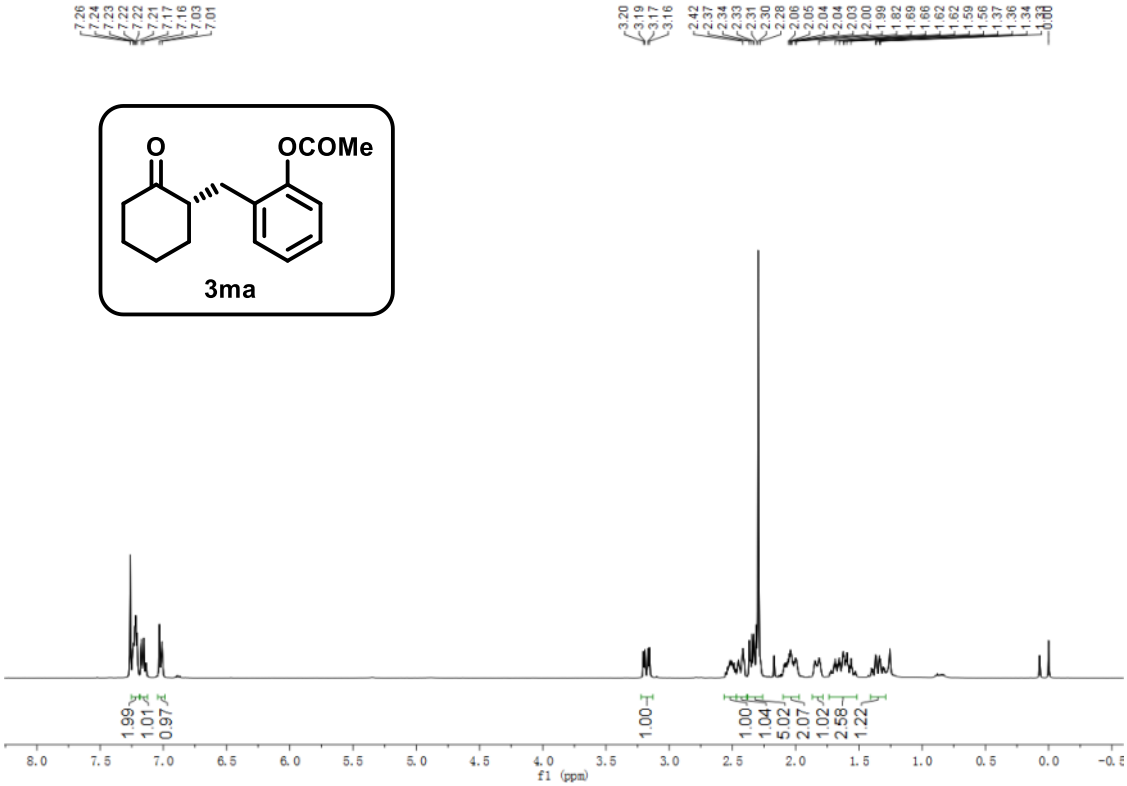
16.98
9.37
7.74
f1 (ppm)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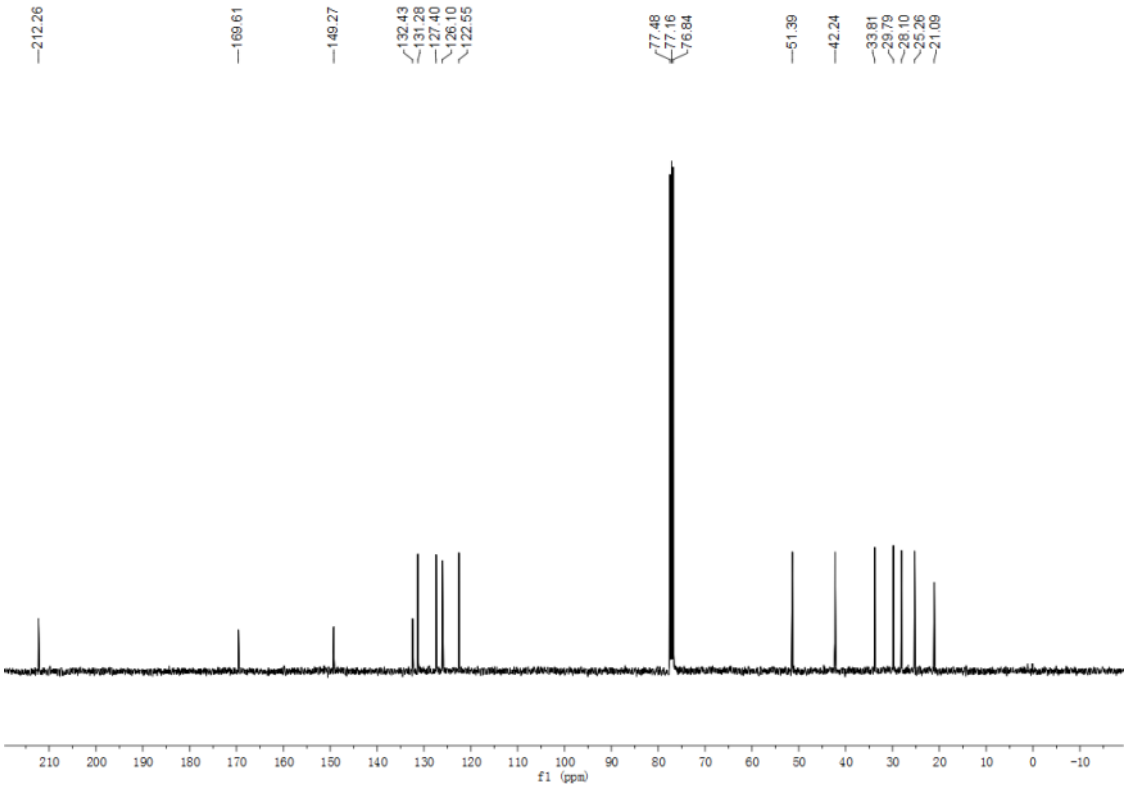
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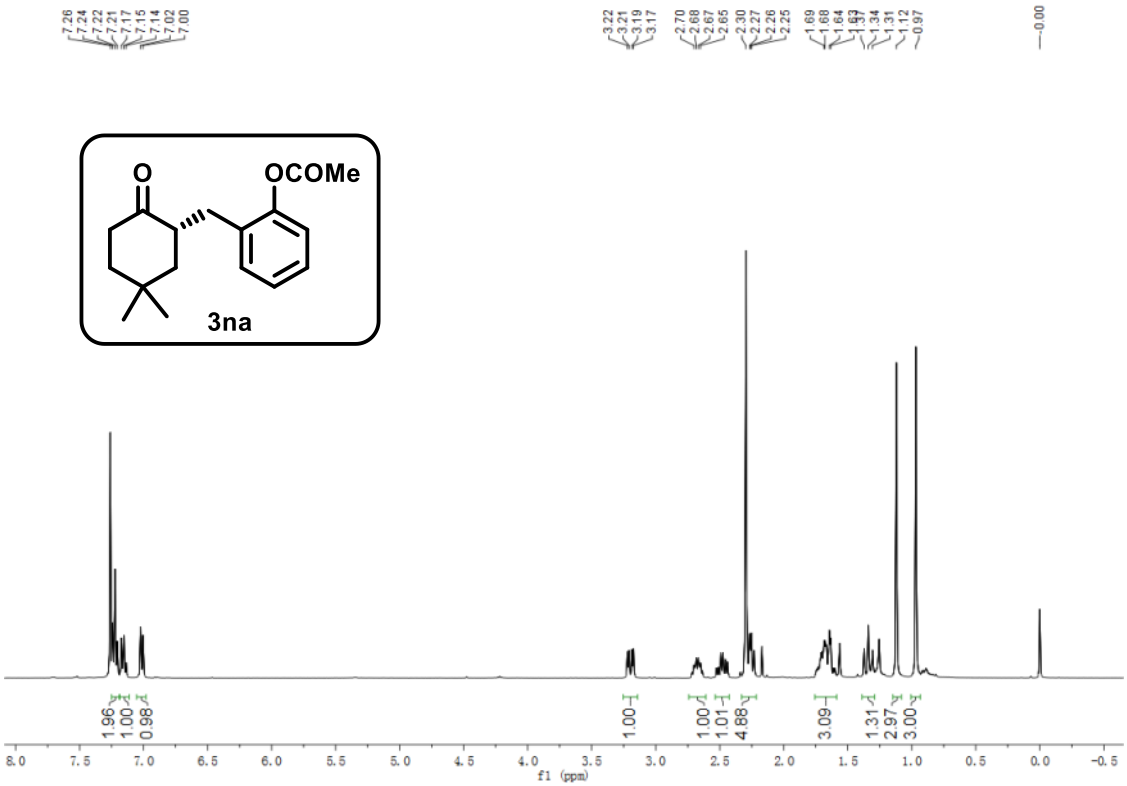
29.79
28.10
25.26
21.09
f1 (ppm)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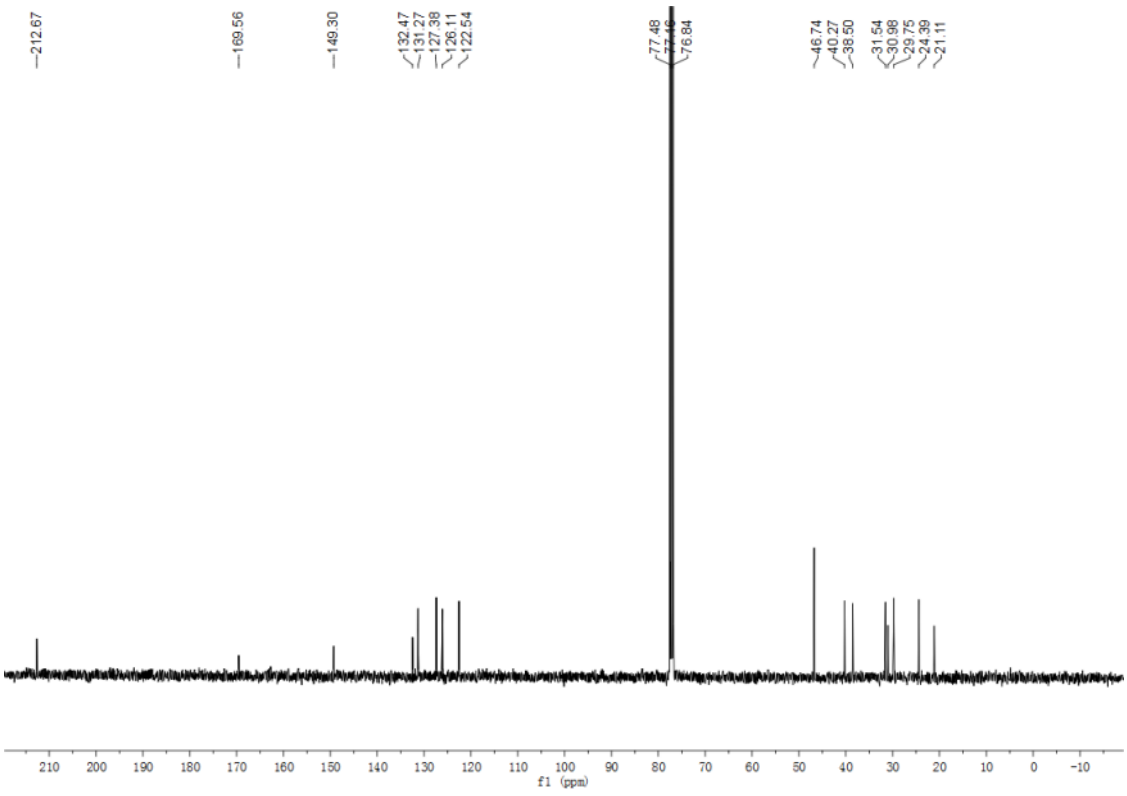
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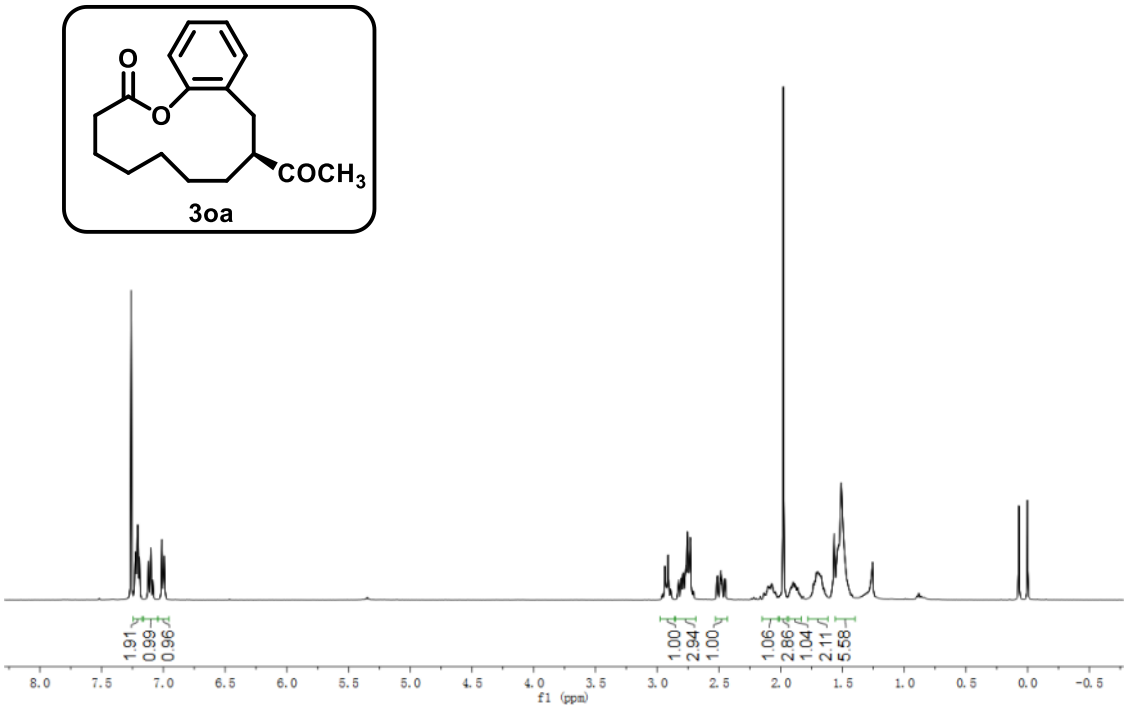
O
O
COCH3
3oa
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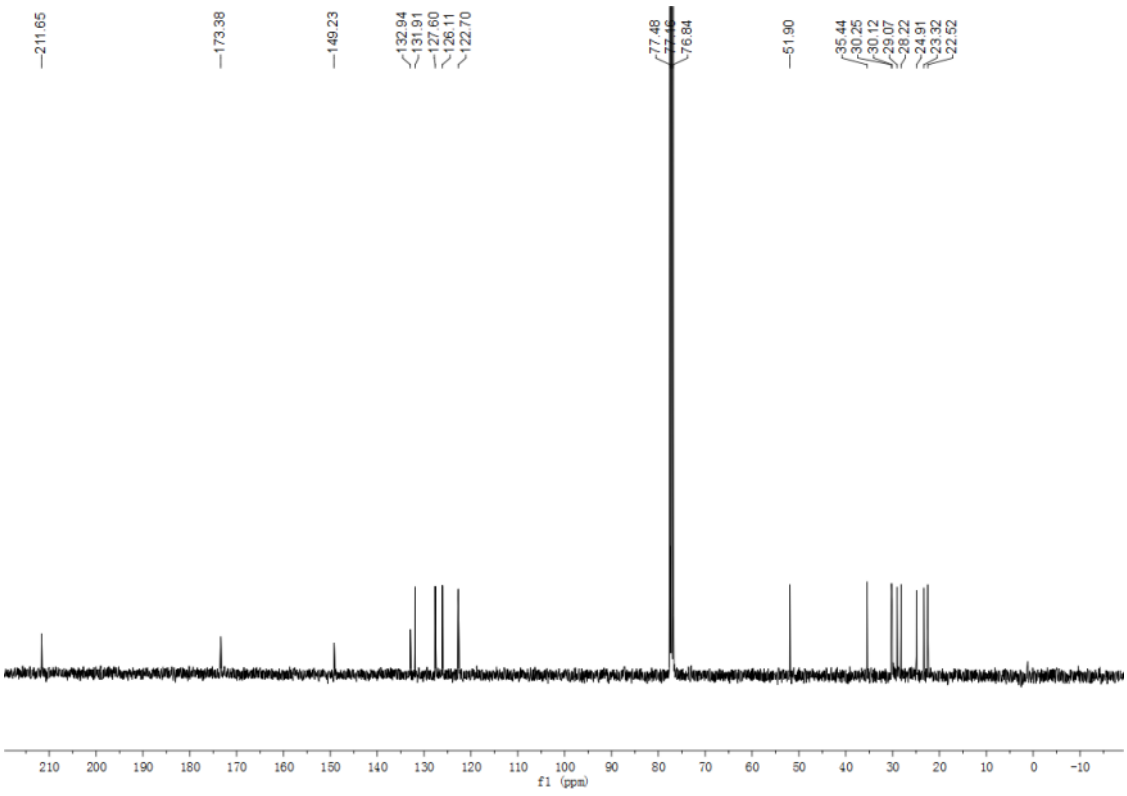
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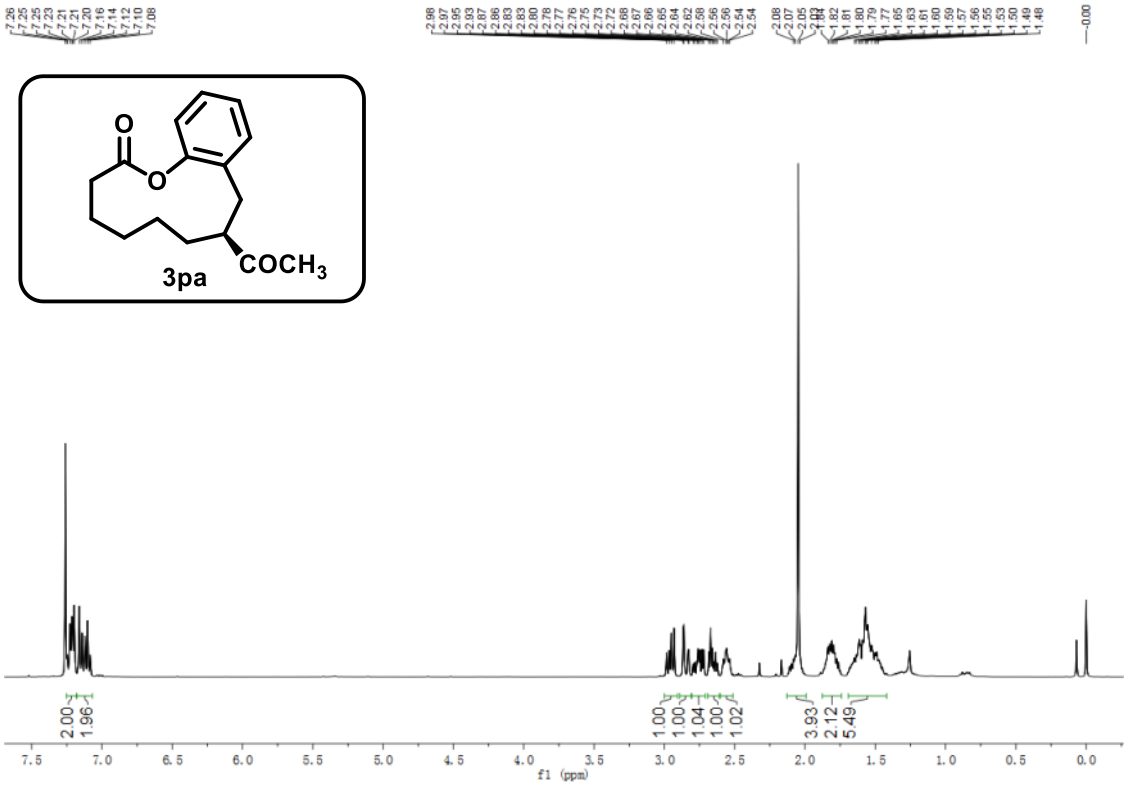
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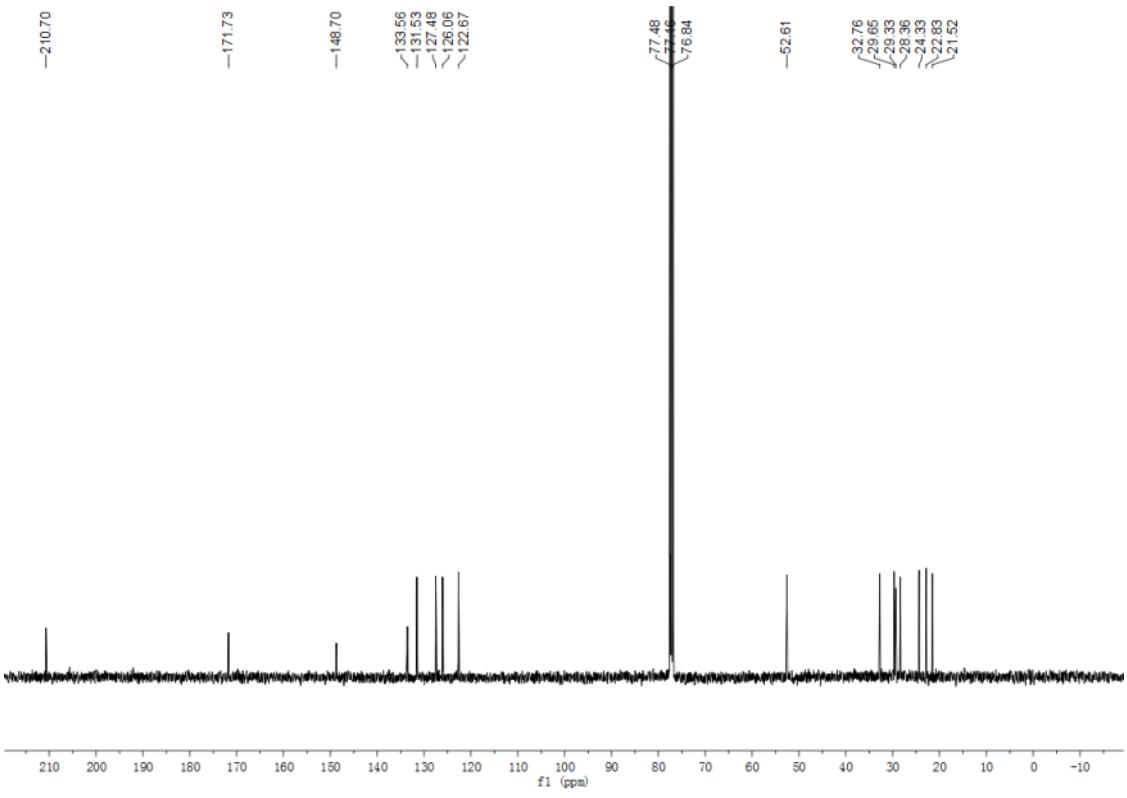
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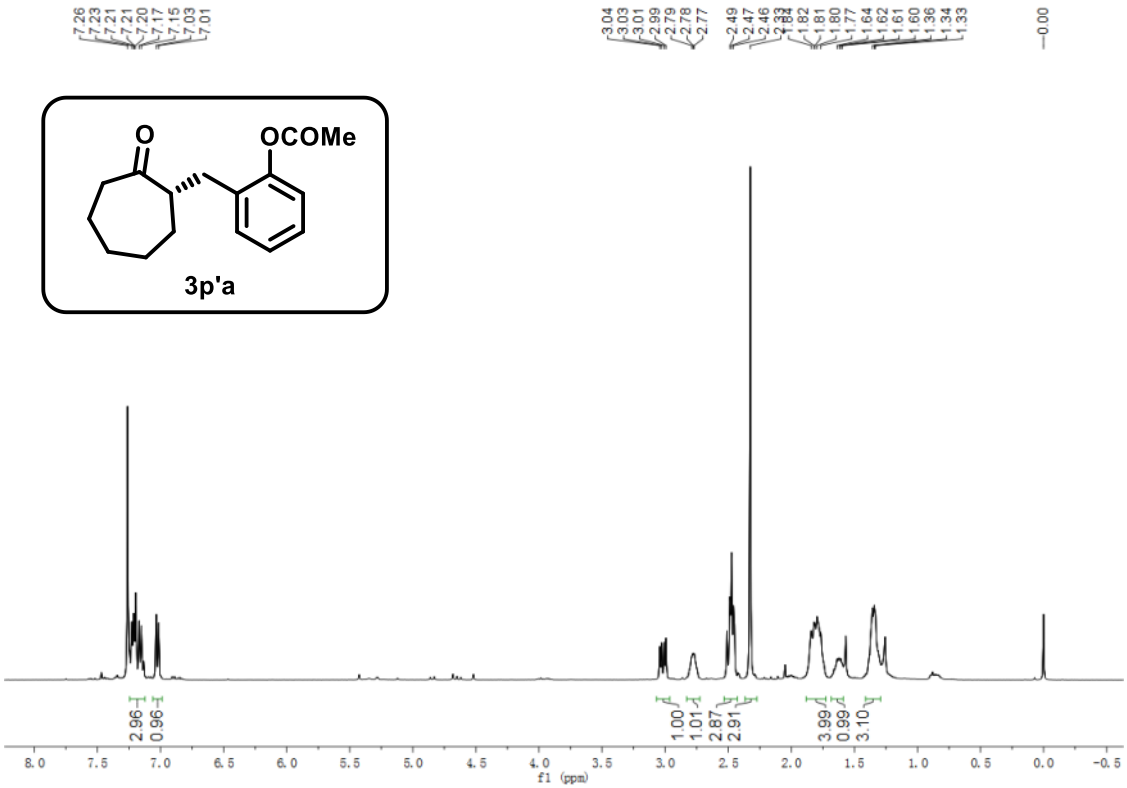
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7.01
3.04
3.03
3.01
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2.79
2.78
2.77
2.49
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1.80
1.77
1.64
1.62
1.61
1.60
1.36
1.34
1.33
0.00
O
OCOMe
3p'a
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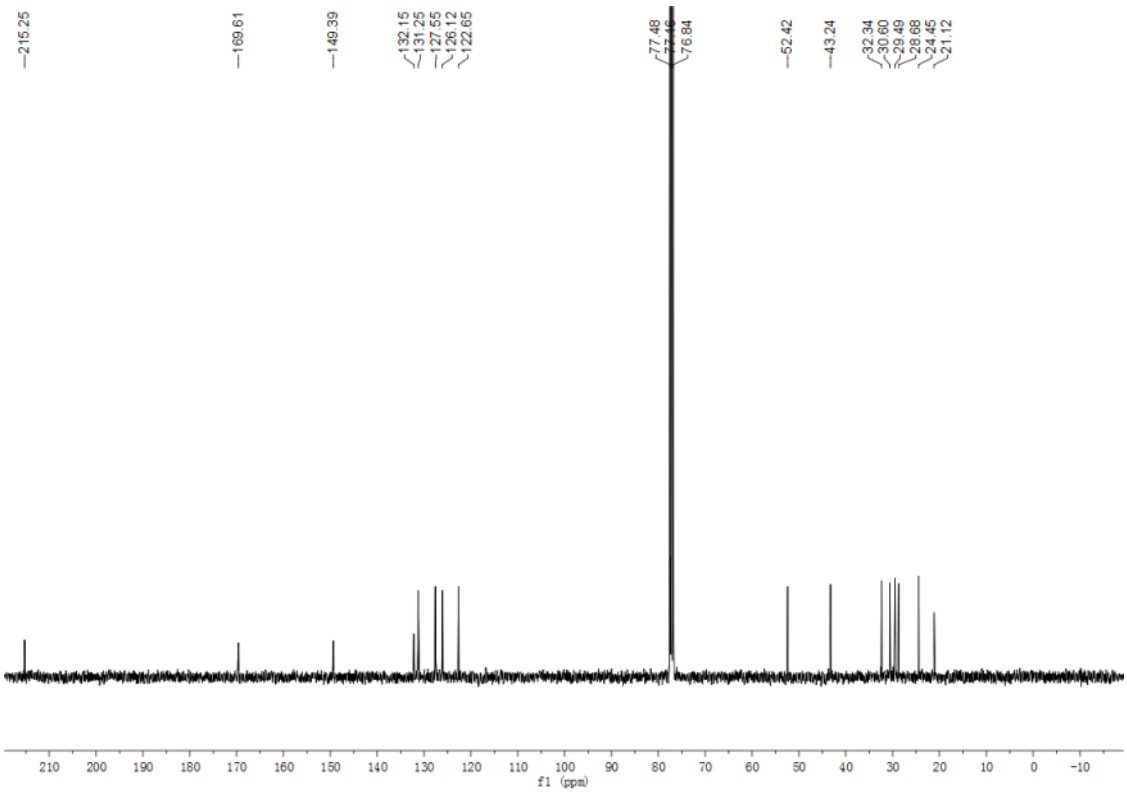
1.00
1.01
2.87
2.91
3.99
0.99
3.10
f1 (ppm)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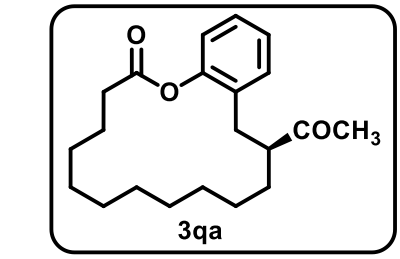
30.60
29.49
28.68
24.45
21.12
f1 (ppm)


O
O
COCH3

3qa

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1.82
1.93
2.69
1.95
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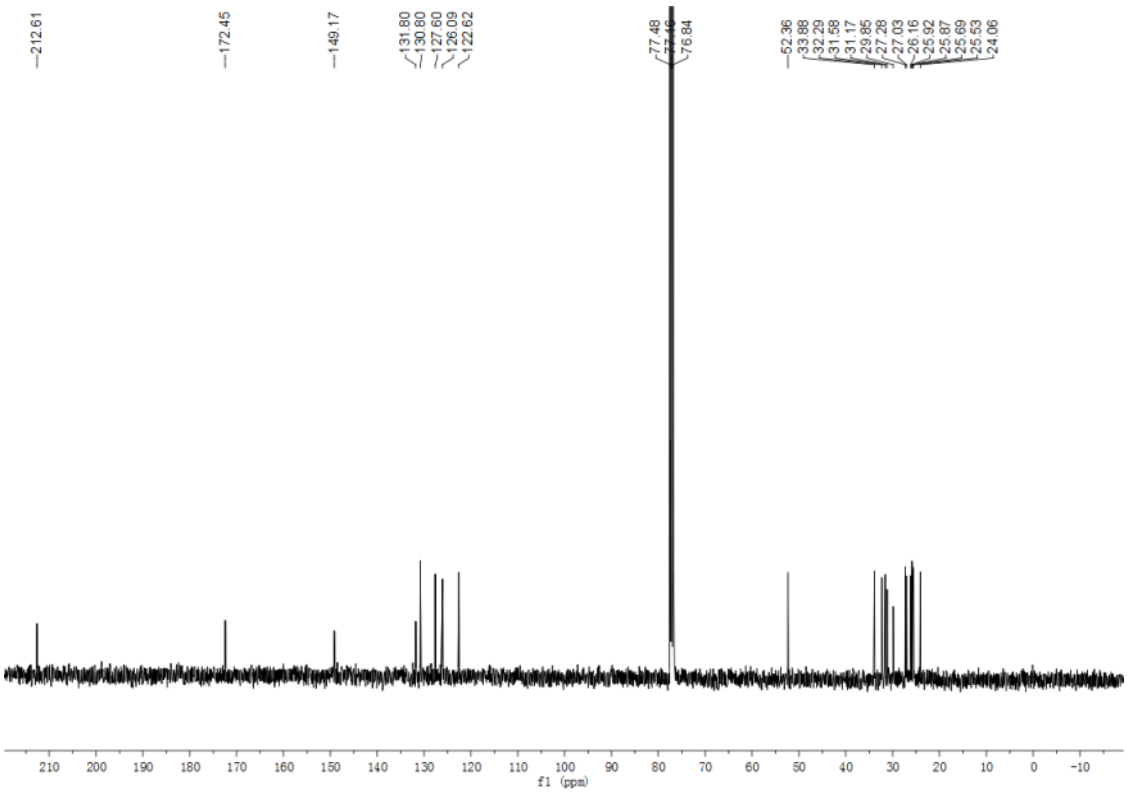
15.02
f1 (ppm)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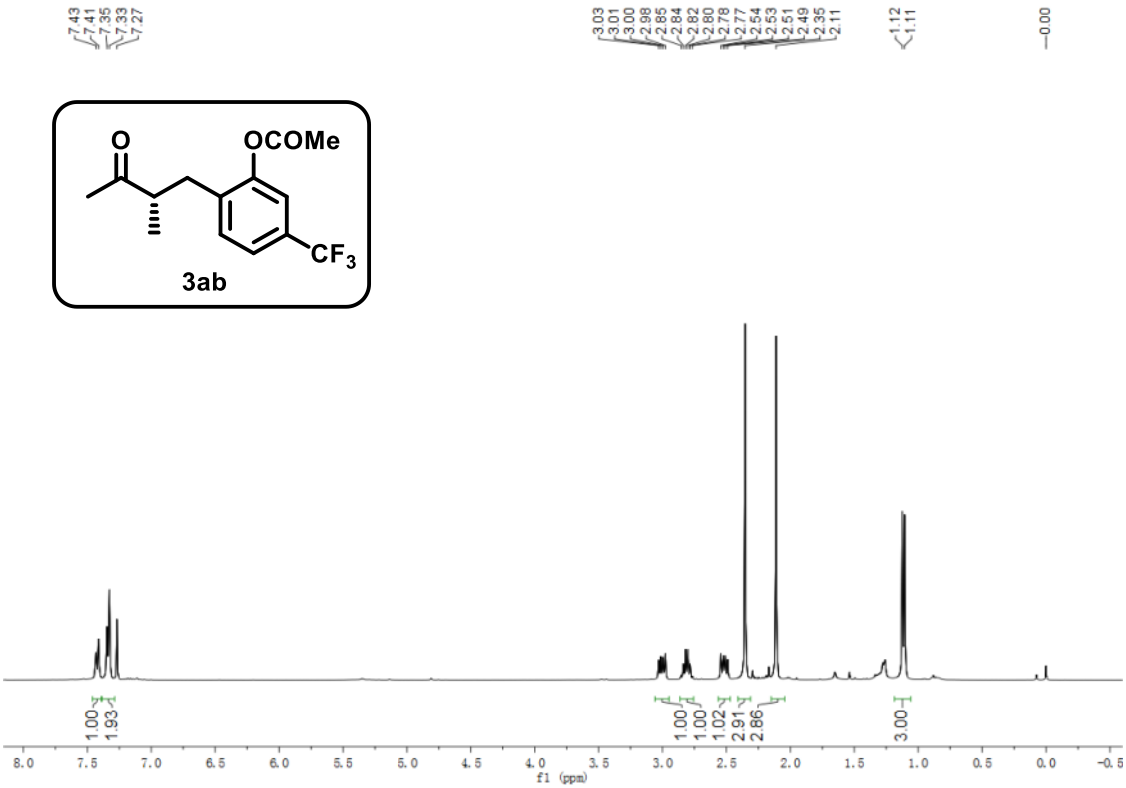
33.88
32.29
31.58
31.17
29.85
27.28
27.03
26.16
25.92
25.87
25.69
25.53
24.06
f1 (ppm)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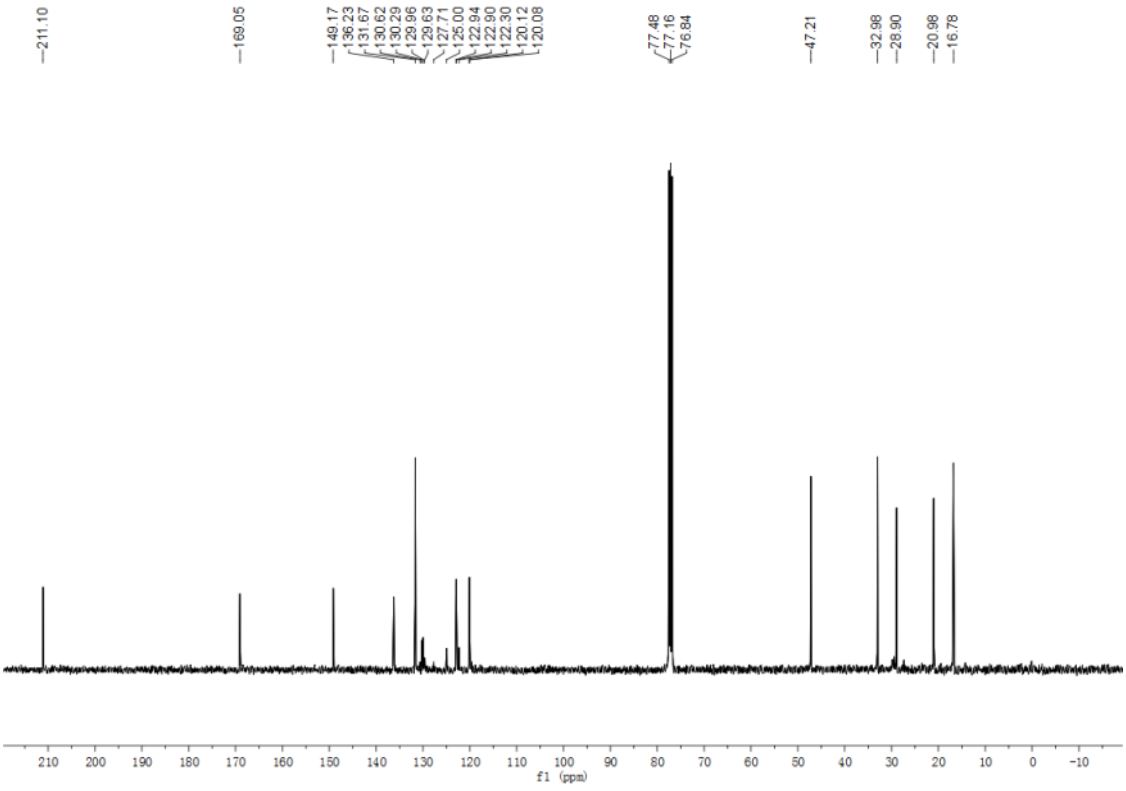
7.41
7.35
7.33
7.27
3.03
3.01
3.00
2.98
2.85
2.84
2.82
2.80
2.78
2.77
2.54
2.53
2.51
2.49
2.35
2.11
1.12
1.11
0.00
O
OCOMe
CF3
3ab
1.00
1.93
1.00
1.00
1.02
2.91
2.86
3.00
f1 (ppm)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149.17
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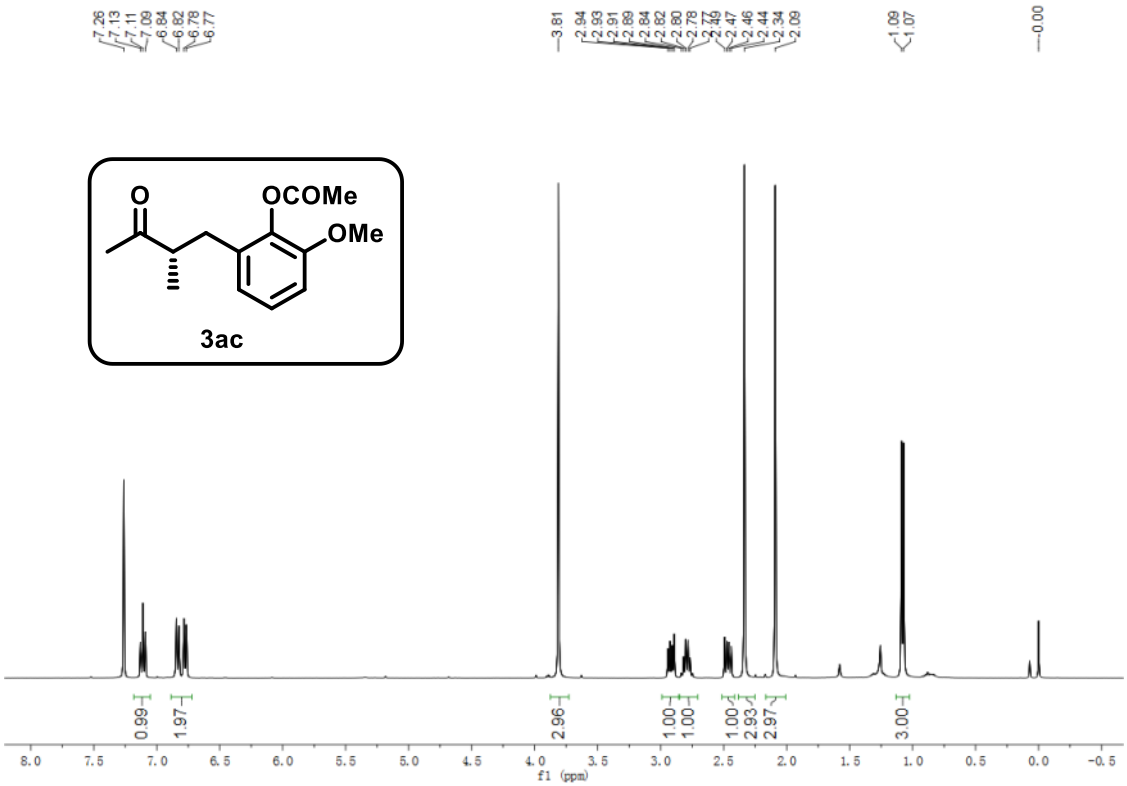
131.67
130.62
130.29
129.96
129.63
127.71
125.00
122.94
122.90
122.30
120.12
120.08
77.48
77.16
76.84
47.21
32.98
28.90
20.98
16.78
f1 (ppm)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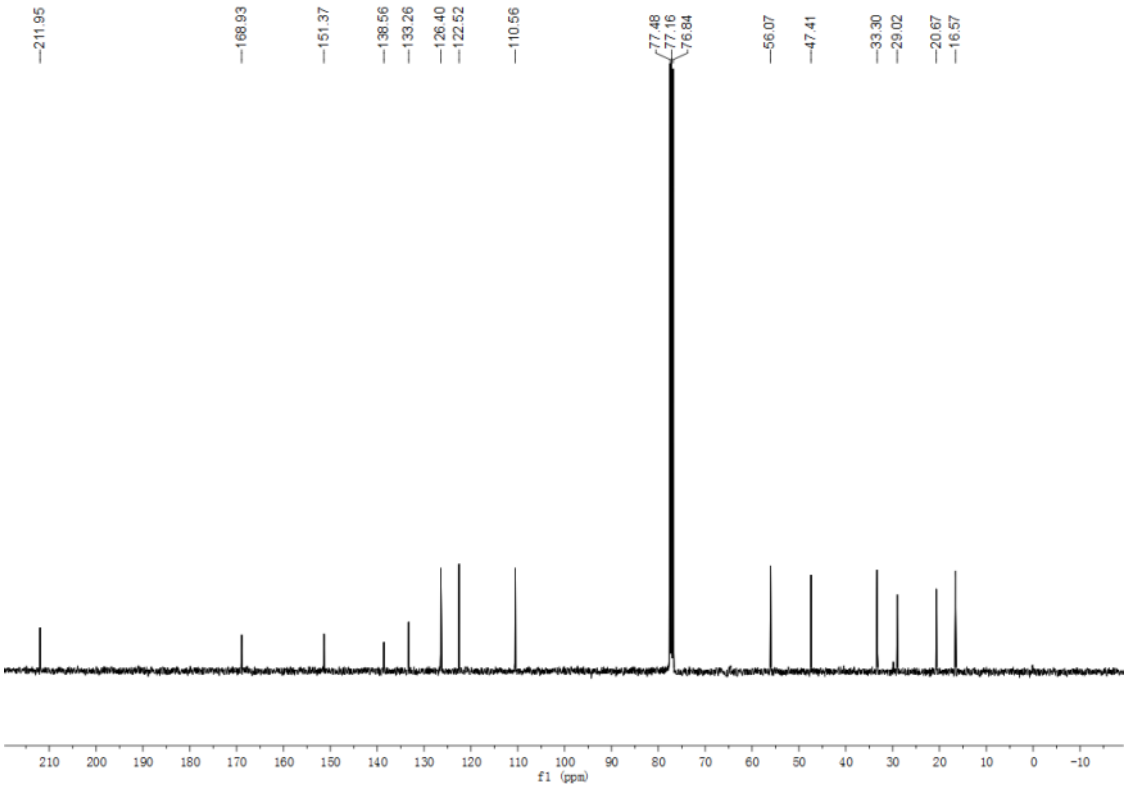
7.13
7.11
7.09
6.84
6.82
6.78
6.77
3.81
2.94
2.93
2.91
2.89
2.84
2.82
2.80
2.78
2.47
2.46
2.44
2.34
2.09
1.09
1.07
0.00
O
OCOMe
OMe
3ac
0.99
1.97
2.96
1.00
1.00
1.00
2.93
2.97
3.00
f1 (ppm)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151.37
138.56
133.26
126.40
122.52
110.56
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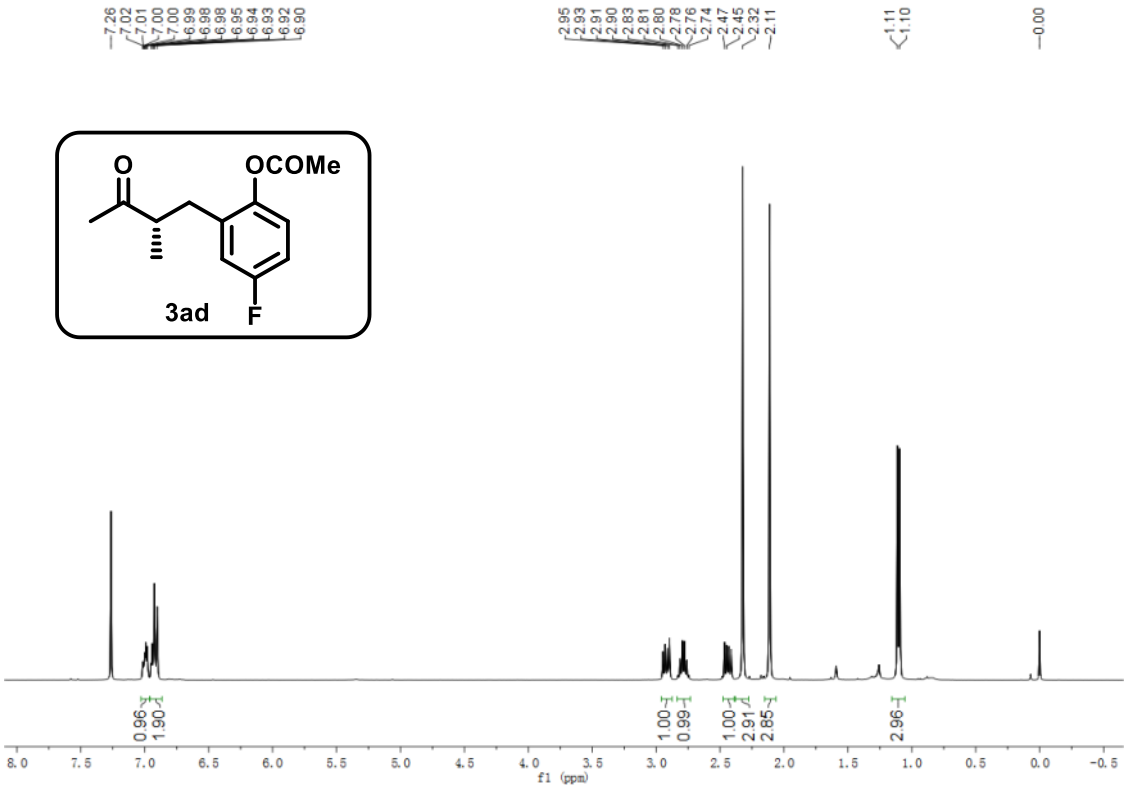
77.16
76.84
56.07
47.41
33.30
29.02
20.67
16.57
f1 (ppm)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7.01
7.00
7.00
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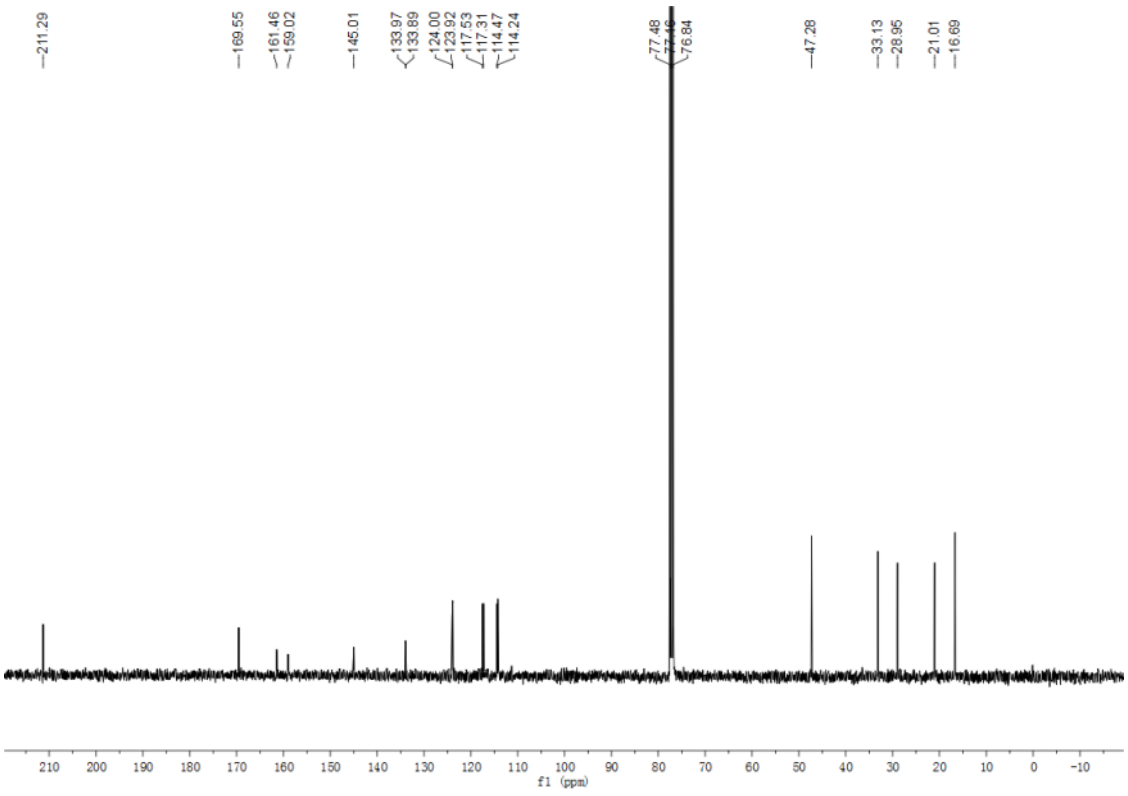
6.98
6.98
6.95
6.94
6.93
6.92
6.90
2.95
2.93
2.91
2.90
2.83
2.81
2.80
2.78
2.76
2.74
2.47
2.45
2.32
2.11
1.11
1.10
0.00
O
OCOMe
3ad
F
0.96
1.90
1.00
0.99
1.00
2.91
2.85
2.96
f1 (ppm)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124.00
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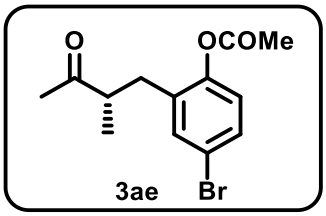
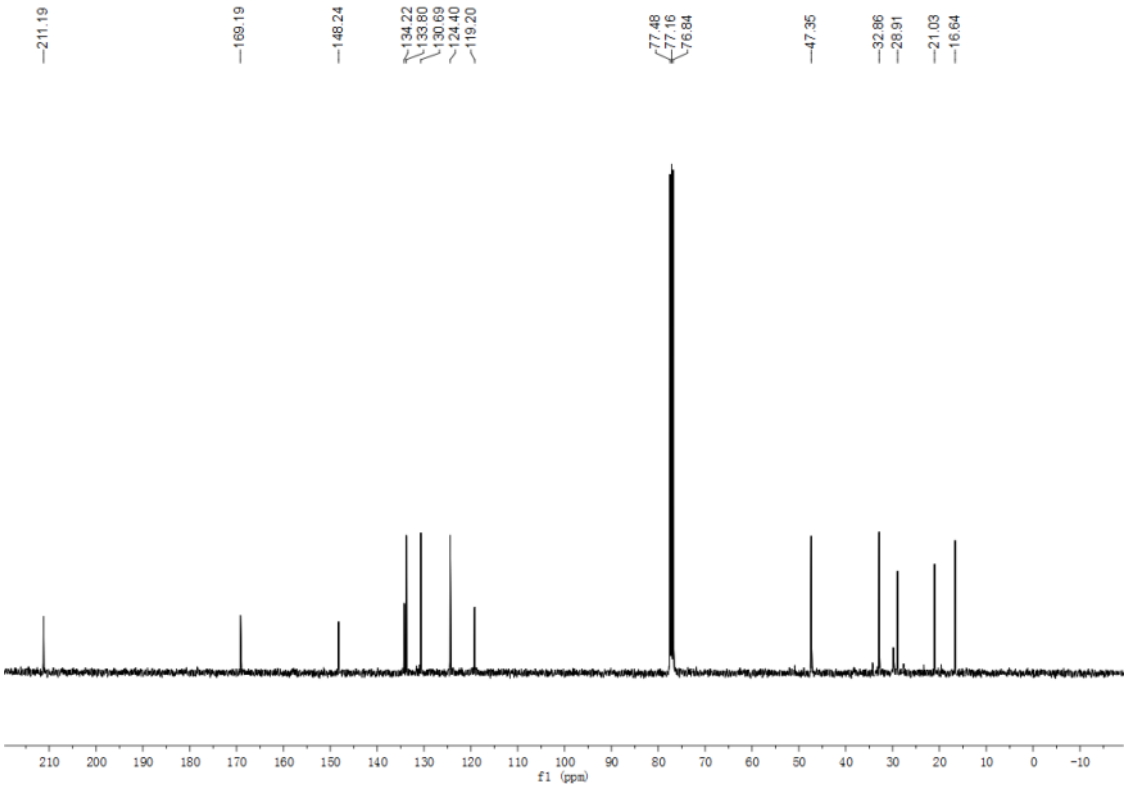
76.84
47.28
33.13
28.95
21.01
16.69
f1 (ppm)


O
OCOMe
3ae
Br

7.36
7.36
7.35
7.34
7.34
6.84
6.83
6.82
2.94
2.93
2.91
2.89
2.82
2.80
2.78
2.77
2.75
2.73
2.45
2.43
2.42
2.40
2.32
2.12
1.11
1.09
0.00
1.97
0.98
1.00
1.08
1.02
2.98
3.00
3.01
f1 (ppm)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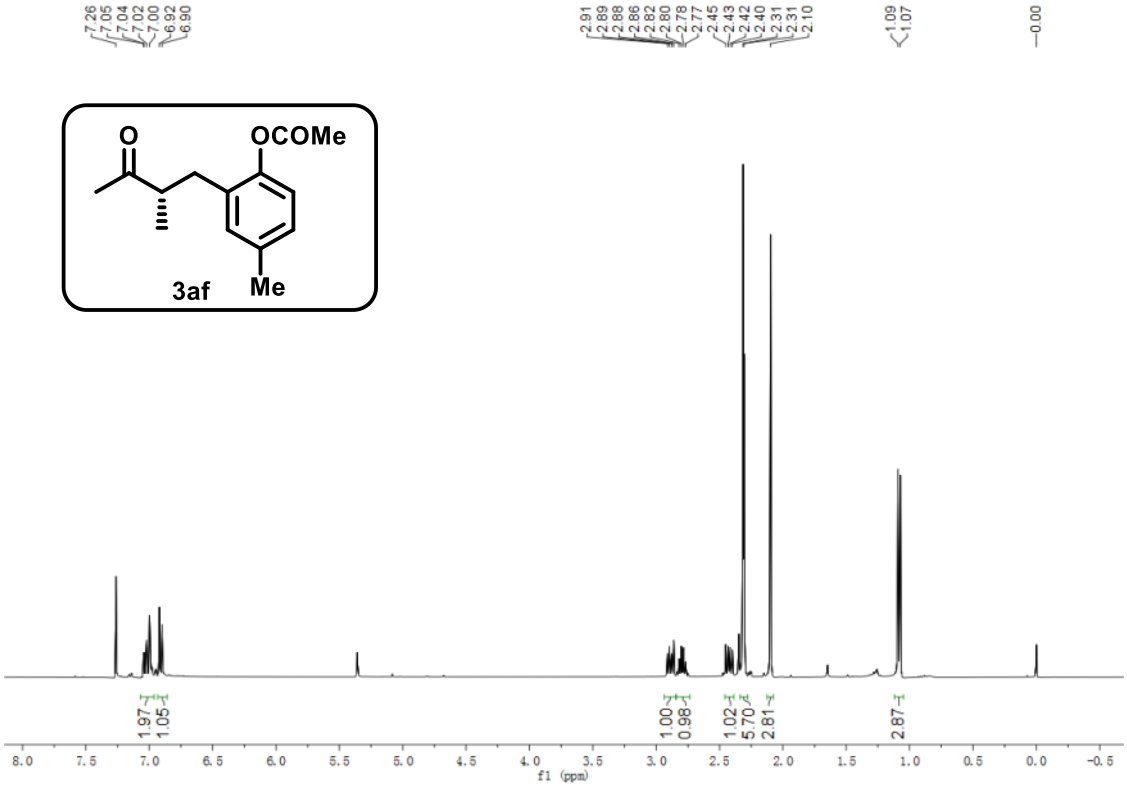
47.35
32.86
28.91
21.03
16.64
f1 (ppm)


7.26
7.05
7.04
7.02
7.00
6.92
6.90
2.91
2.89
2.88
2.86
2.82
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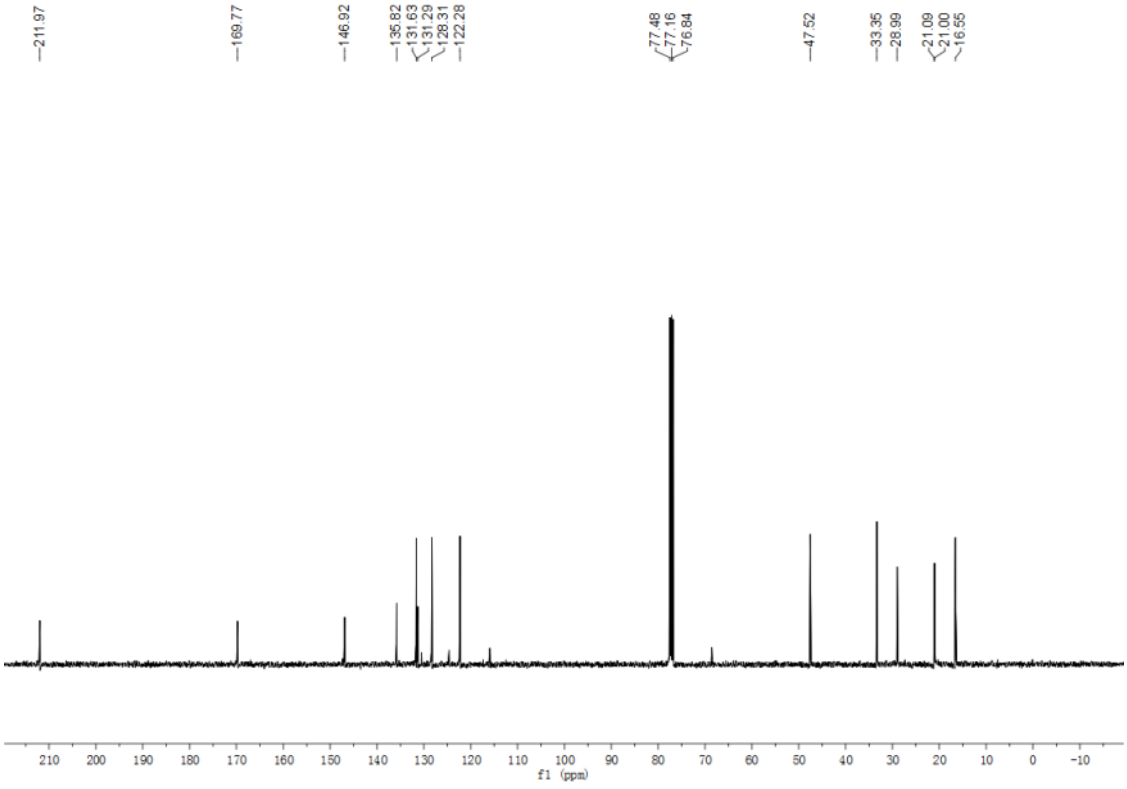
2.78
2.77
2.45
2.43
2.42
2.40
2.31
2.31
2.10
1.09
1.07
0.00
O
OCOMe
3af
Me
1.97
1.05
1.00
0.98
1.02
5.70
2.81
2.87
f1 (ppm)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131.29
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122.28
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77.16
76.84
47.52
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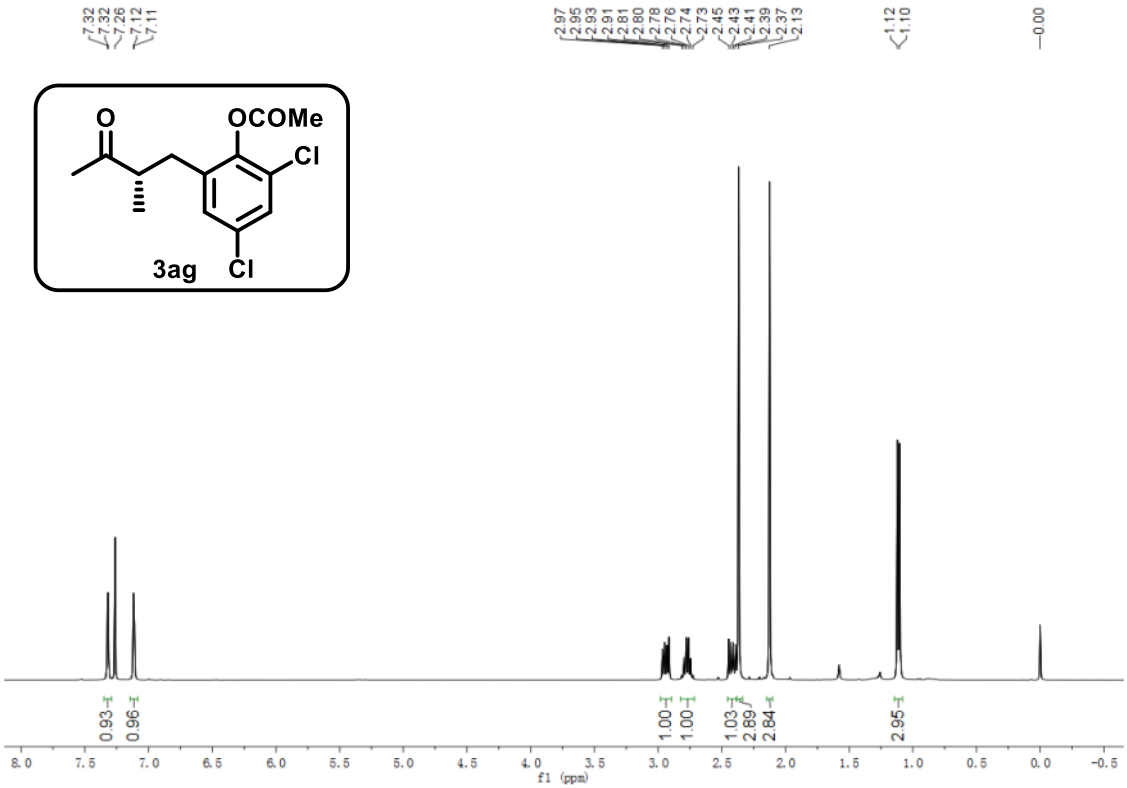
28.99
21.09
21.00
16.55
f1 (ppm)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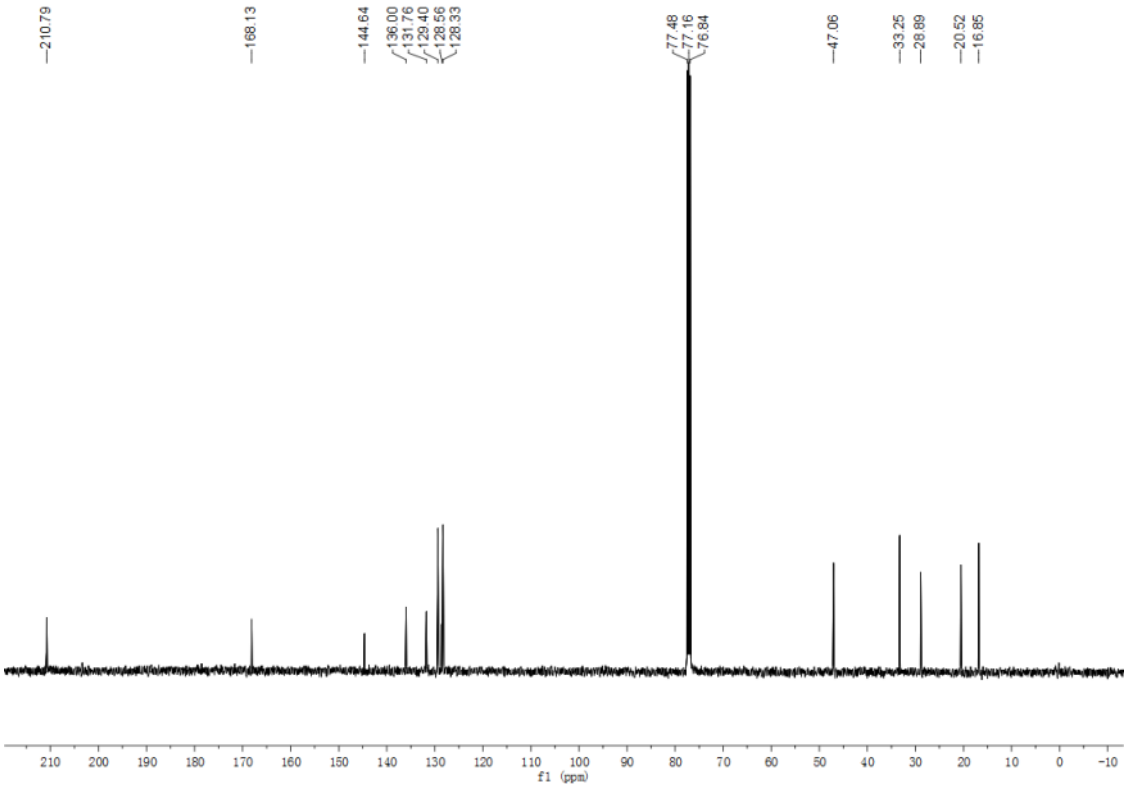
7.12
7.11
2.97
2.95
2.93
2.91
2.81
2.80
2.78
2.76
2.74
2.73
2.45
2.43
2.41
2.39
2.37
2.13
1.12
1.10
0.00
O
OCOMe
Cl
3ag
Cl
0.93
0.96
1.00
1.00
1.03
2.89
2.84
2.95
f1 (ppm)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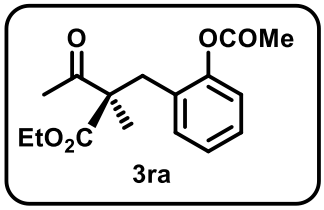
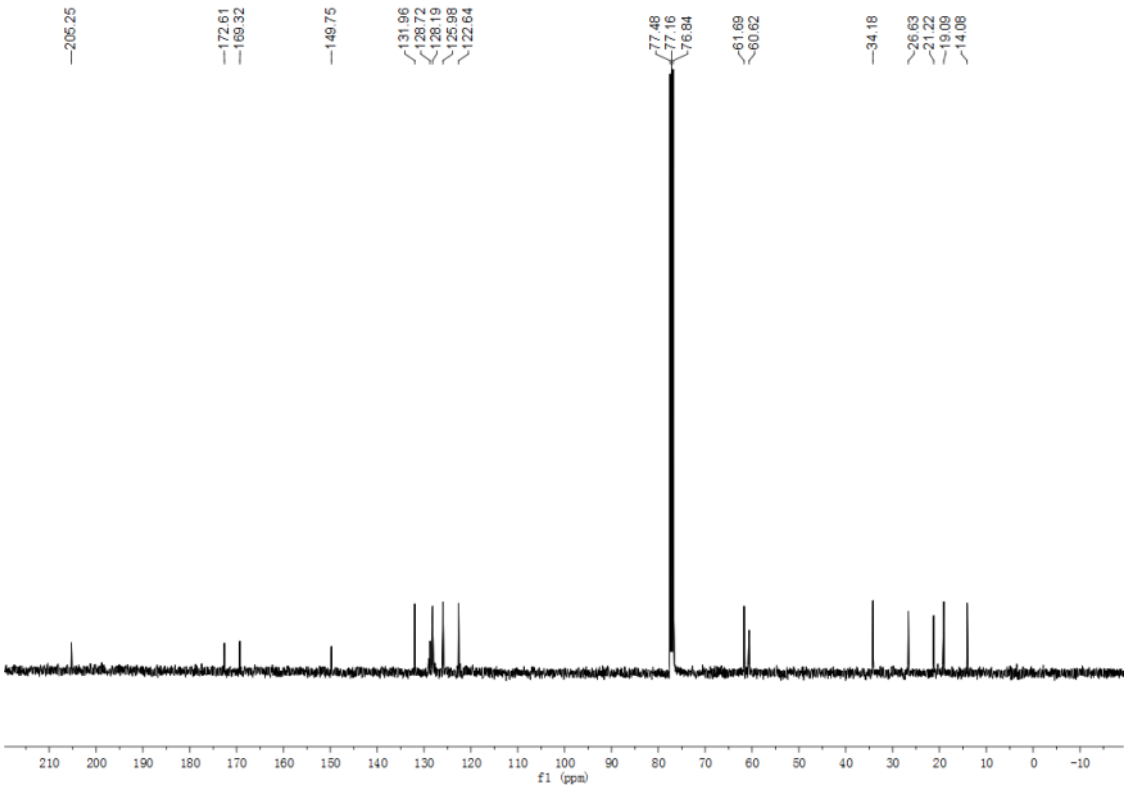
77.16
76.84
47.06
33.25
28.89
20.52
16.85
f1 (ppm)


O
OCOMe
EtO2C

3ra

7.26
7.25
7.23
7.23
7.17
7.15
7.13
7.05
7.03
4.22
4.21
4.21
4.20
4.19
4.18
4.17
4.16
3.18
3.15
3.11
3.08
2.30
2.16
1.27
1.26
1.24
1.22
0.00
0.82
1.95
0.95
2.00
2.00
2.99
2.98
2.98
3.19
f1 (ppm)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172.61
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125.98
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77.48
77.16
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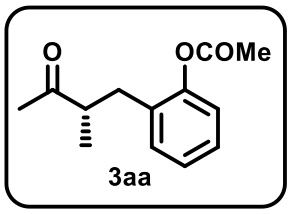
61.69
60.62
34.18
26.63
21.22
19.09
14.08
f1 (ppm)

HPLC charts



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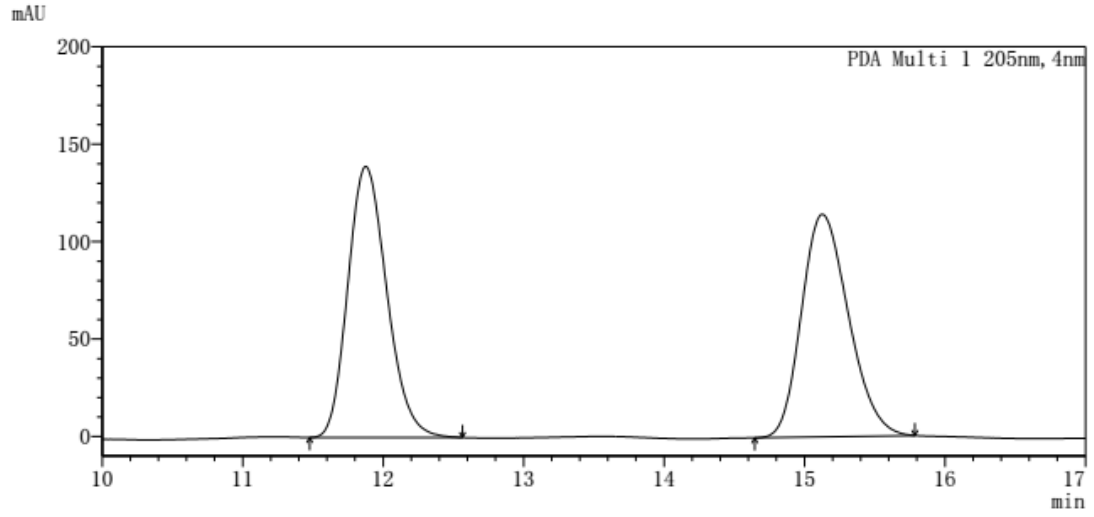

<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	11.876	139140	2688956	50.290
2	15.127	114258	2657909	49.710

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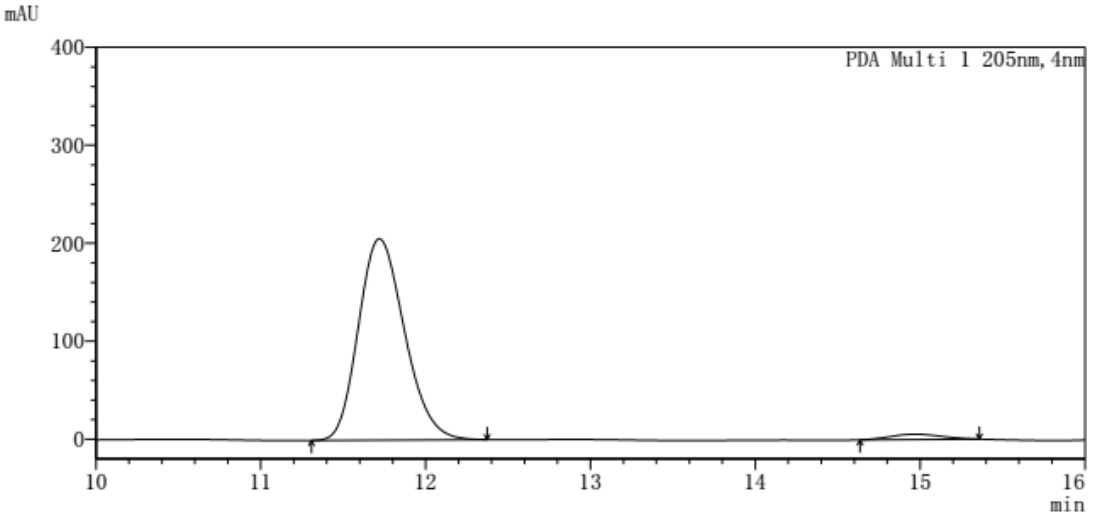
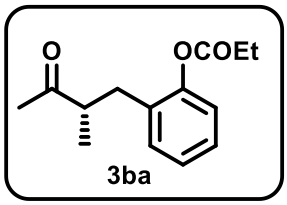


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	11.719	205601	3997704	97.151
2	14.970	5467	117219	2.849



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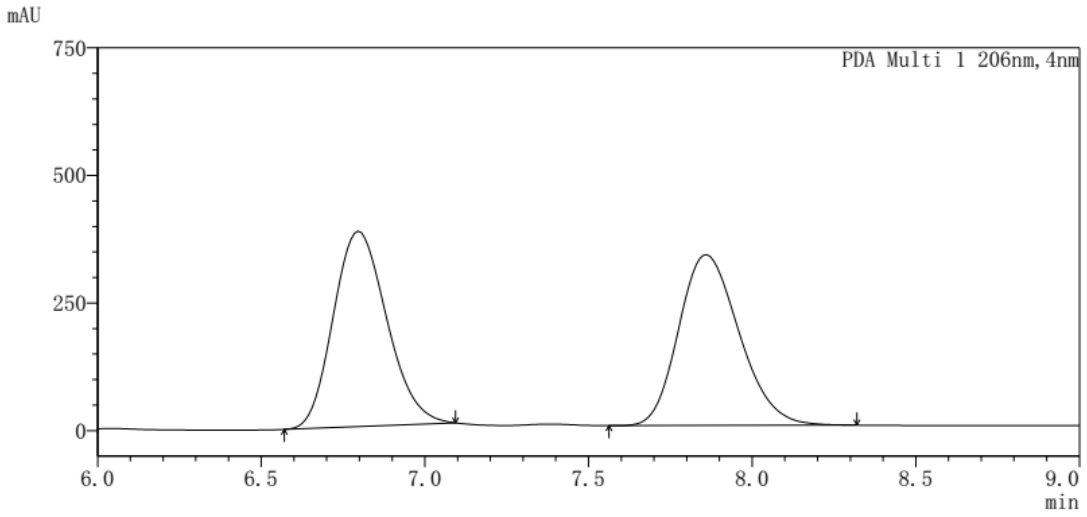

<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	6.796	383052	4362860	50.307
2	7.859	334766	4309593	49.693

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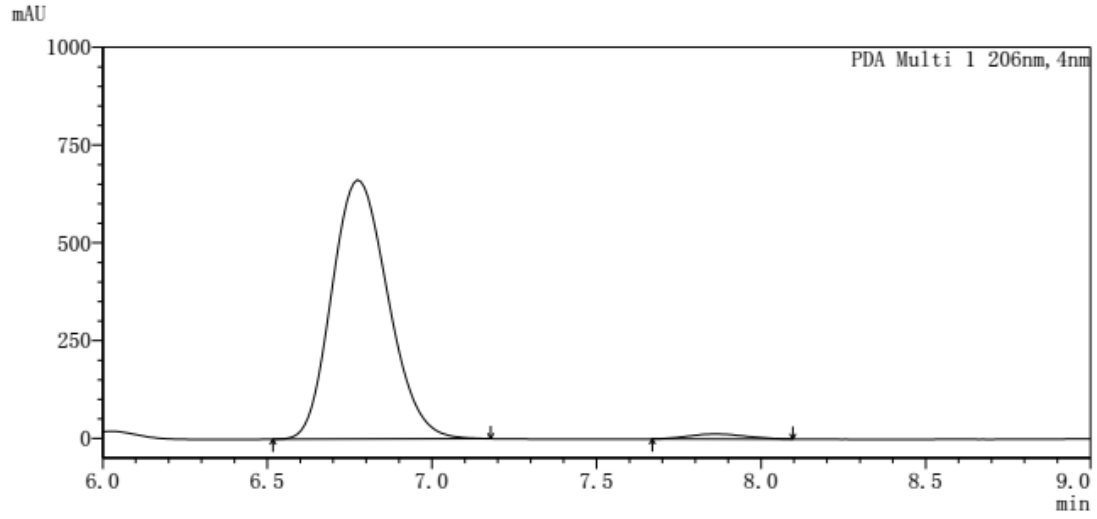
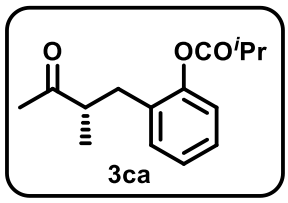


<Peak Results>

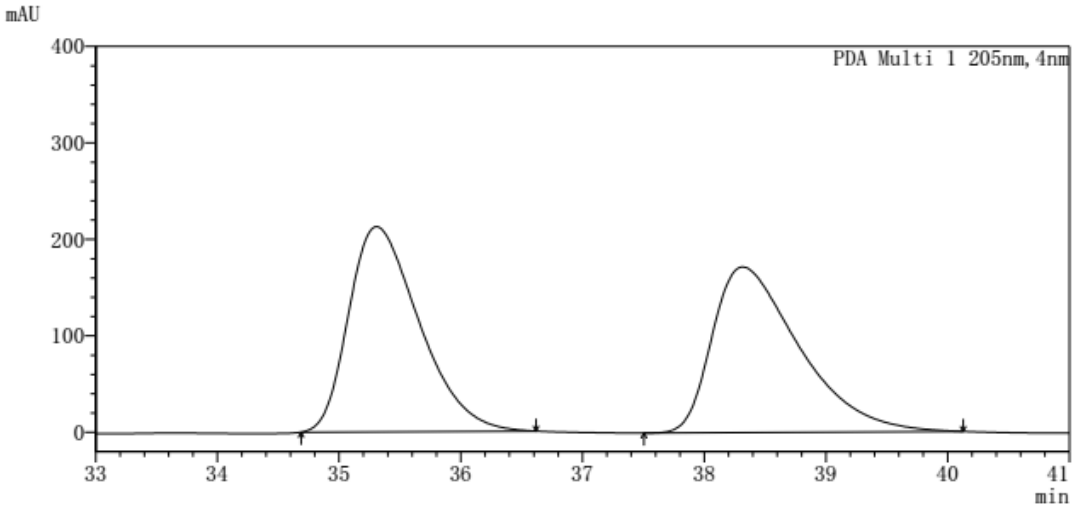
PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	6.775	662140	7867794	98.087
2	7.861	12796	153442	1.913



3ca

<Chromatogram>



<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	35.307	212652	8585580	50.128
2	38.317	171723	8541666	49.872

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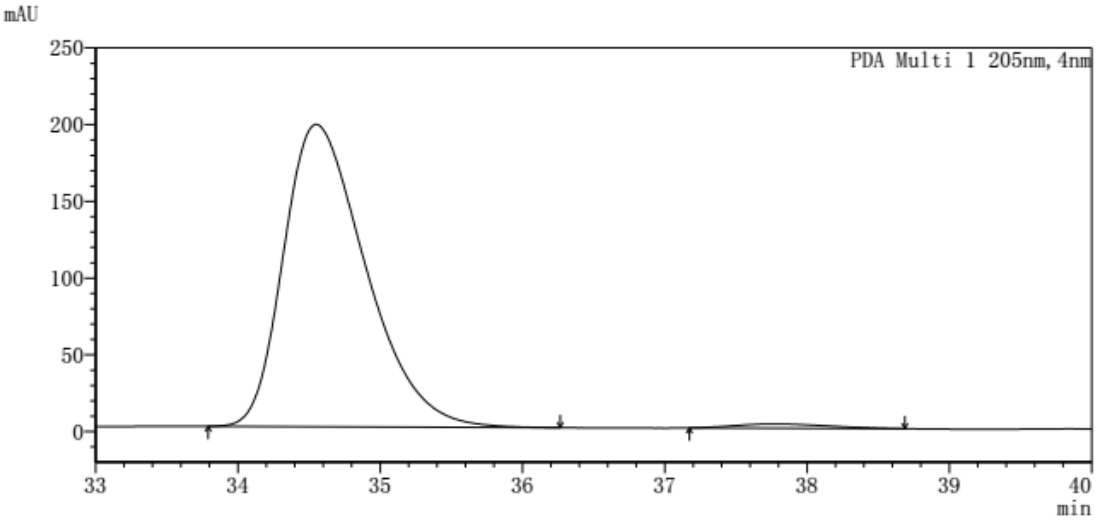
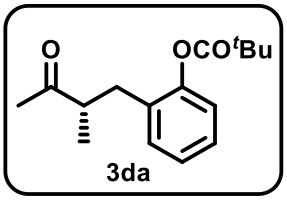


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	34.551	197096	7922223	98.466
2	37.768	2745	123451	1.534



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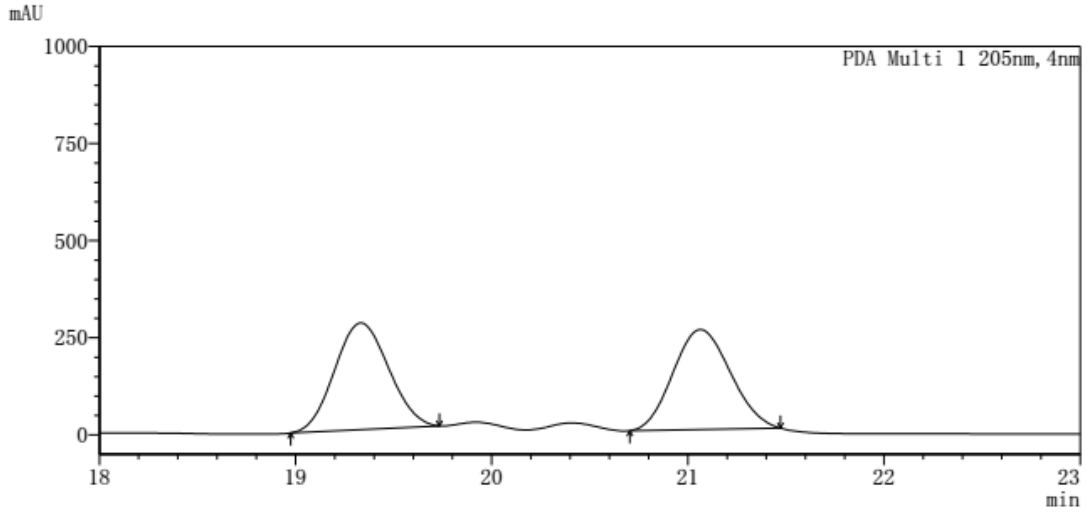

<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	19.333	274498	5255866	50.115
2	21.064	257277	5231673	49.885

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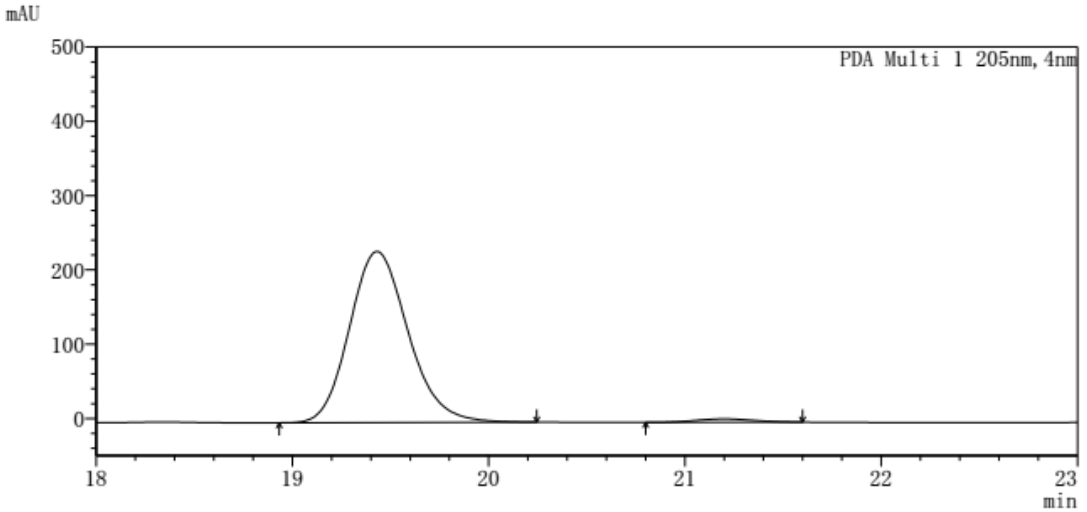
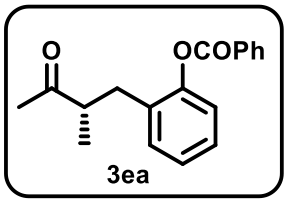


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	19.431	230217	4783859	98.085
2	21.197	4580	93400	1.915



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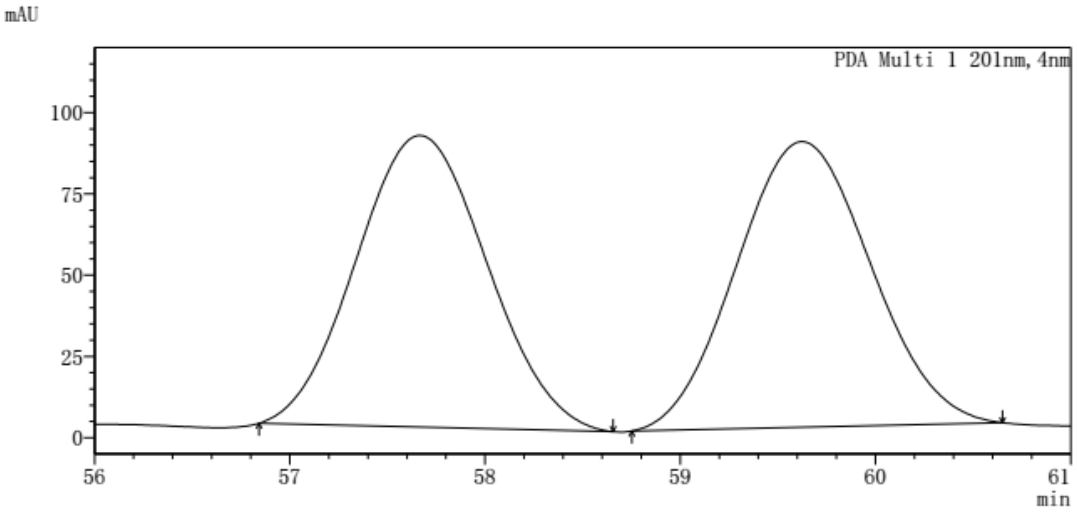
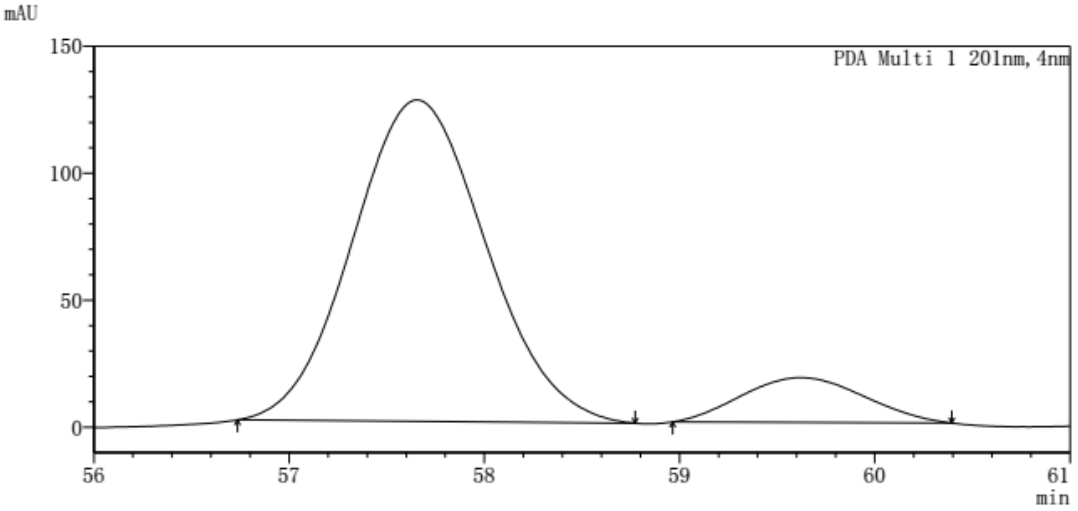


<Peak Results>

PDA Ch1 201nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	57.665	89702	4172706	49.841
2	59.625	87881	4199305	50.159

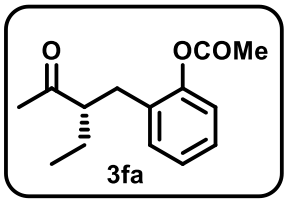
<Chromatogram>



<Peak Results>

PDA Ch1 201nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	57.653	126613	6009482	88.648
2	59.621	17624	769542	11.352



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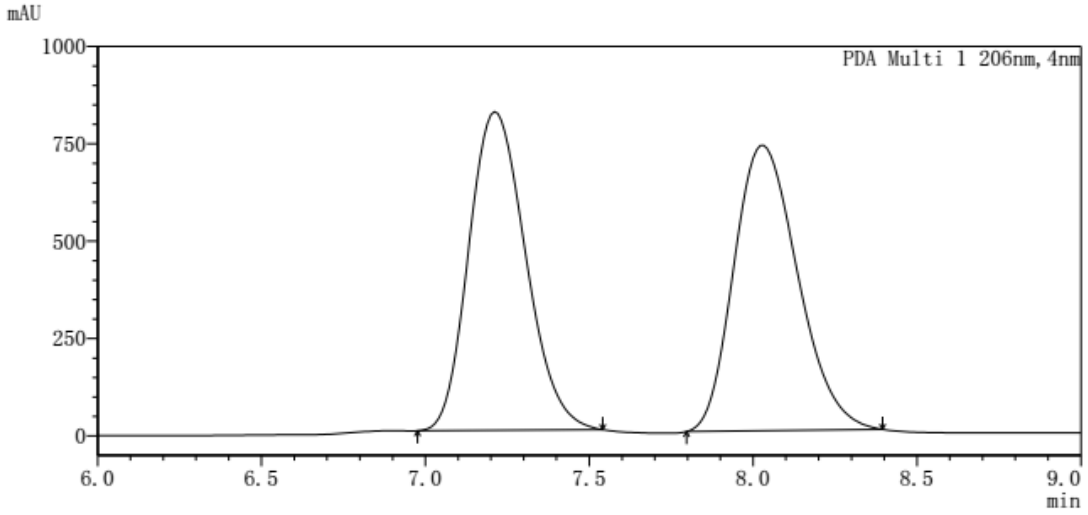
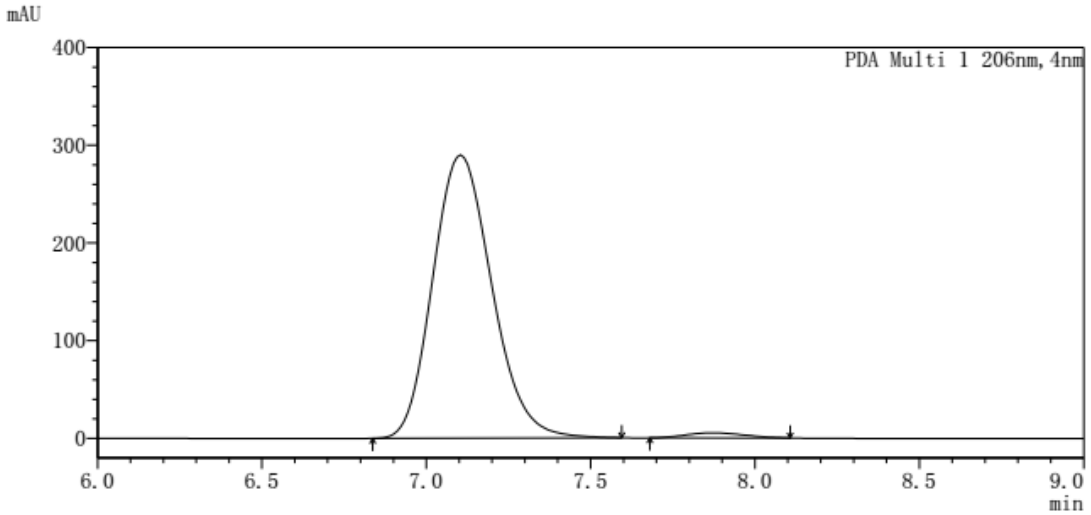


<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	7.212	818256	9881622	49.794
2	8.028	733106	9963260	50.206

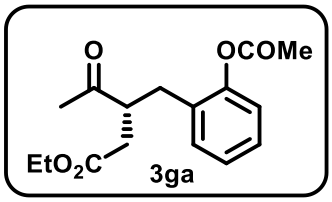
<Chromatogram>



<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	7.103	289876	3626082	98.258
2	7.874	5219	64275	1.742



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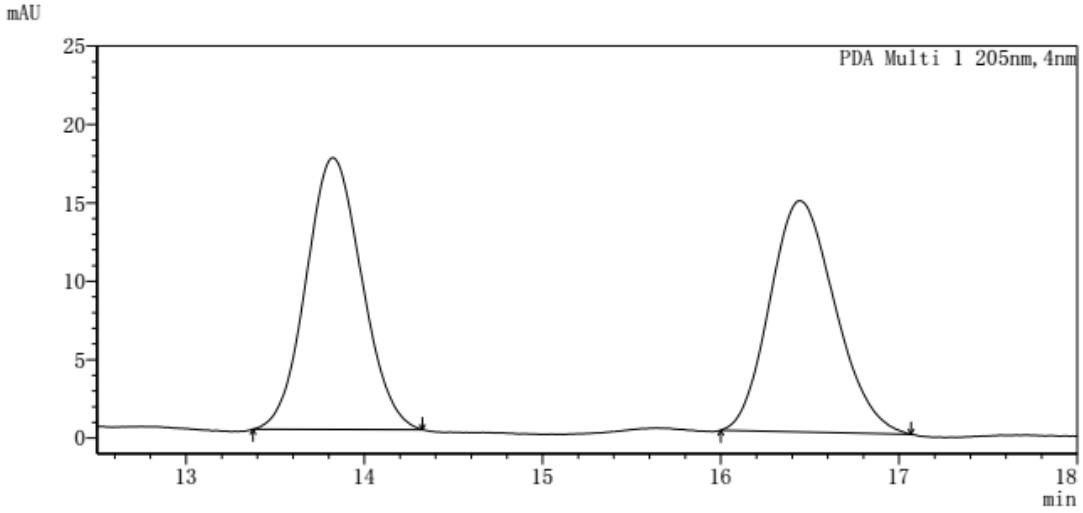
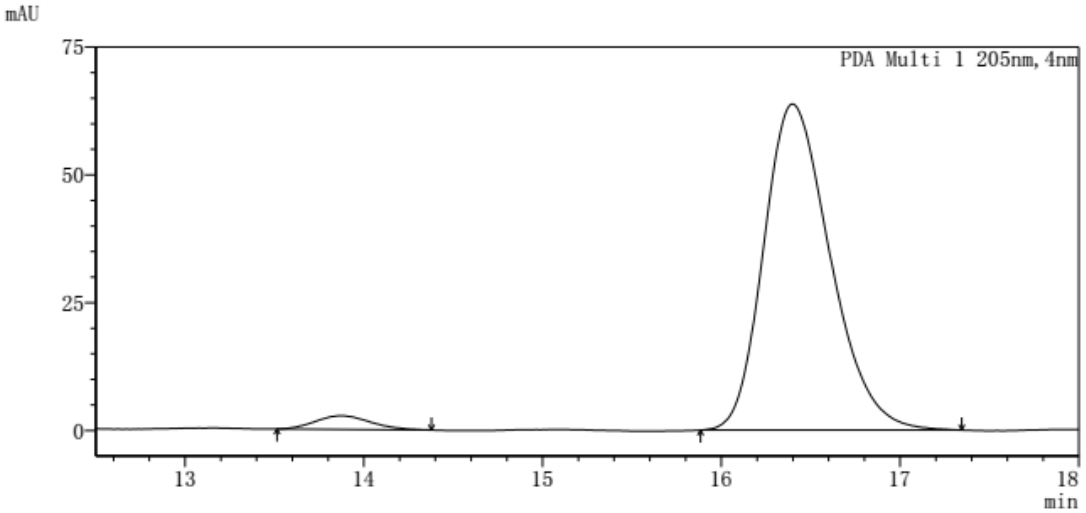


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	13.824	17339	376244	50.082
2	16.442	14744	375009	49.918

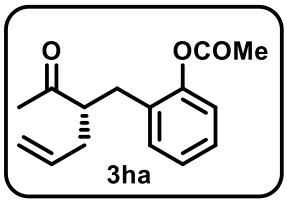
<Chromatogram>



<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	13.877	2669	57359	3.353
2	16.398	63817	1653202	96.647



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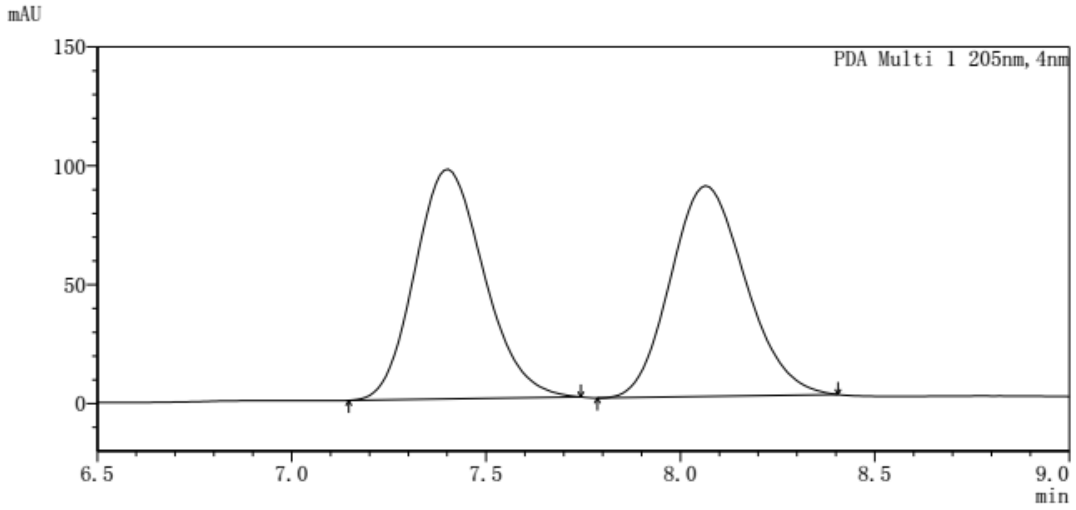
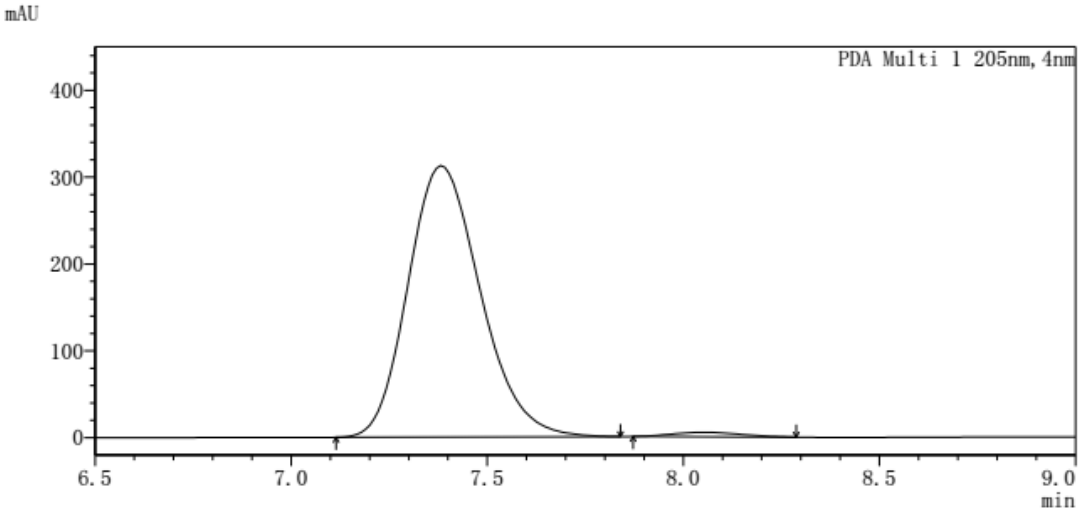


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	7.400	96589	1200766	50.237
2	8.065	88552	1189428	49.763

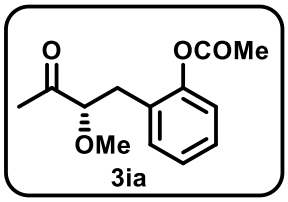
<Chromatogram>



<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	7.382	312563	4011409	98.488
2	8.052	5097	61577	1.512



3ia

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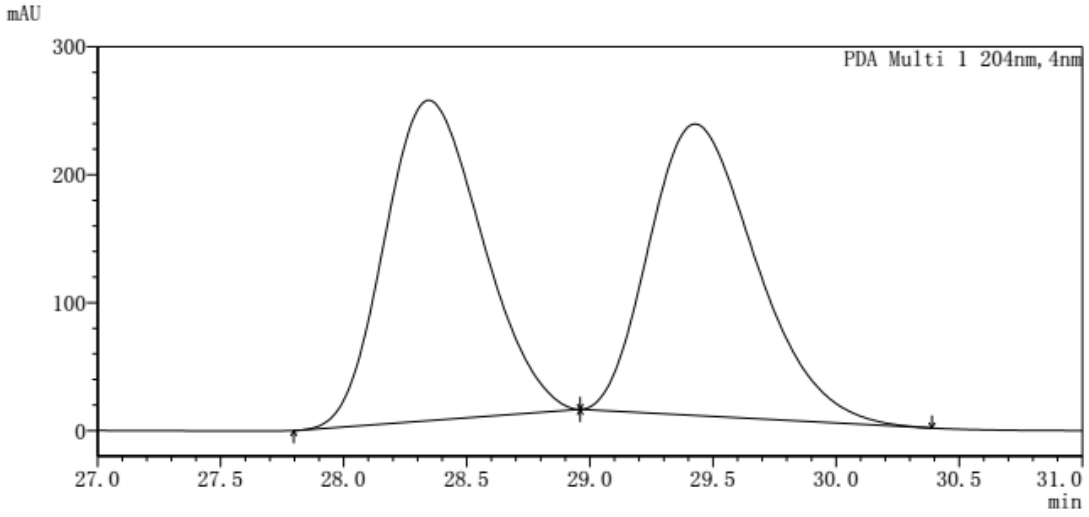
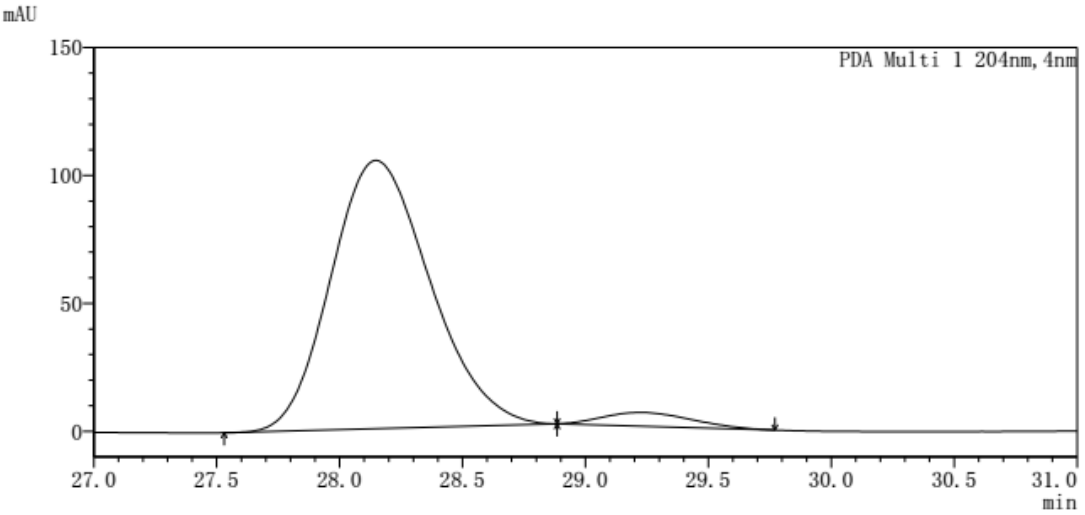


<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	28.345	250388	6896593	50.093
2	29.427	227924	6871115	49.907

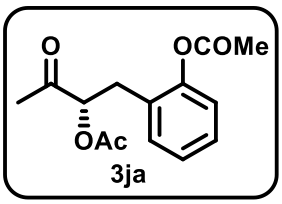
<Chromatogram>



<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	28.148	104894	2942830	95.639
2	29.226	5360	134177	4.361



3ja

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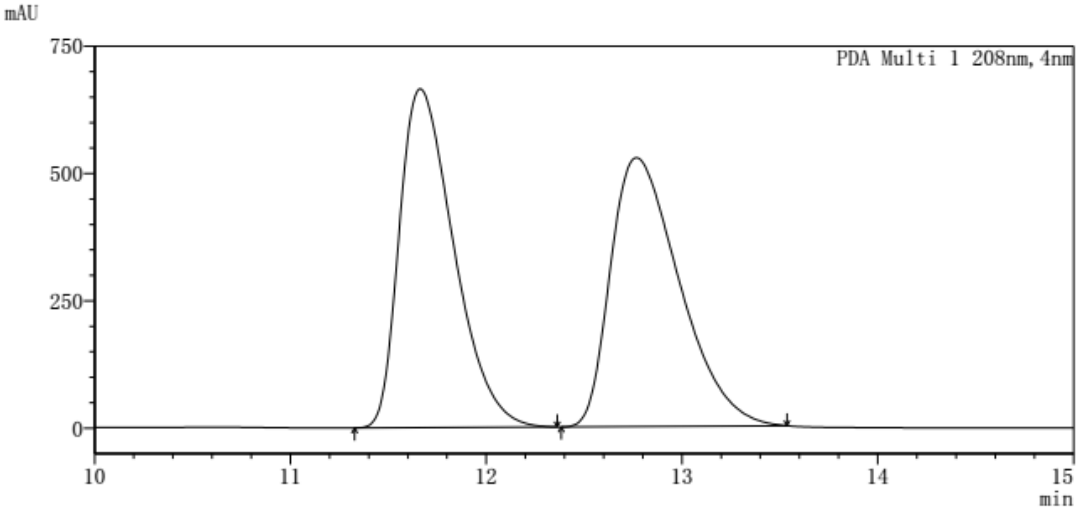

<Peak Results>

PDA Ch1 208nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	11.663	665604	12876272	49.888
2	12.768	528408	12934083	50.112

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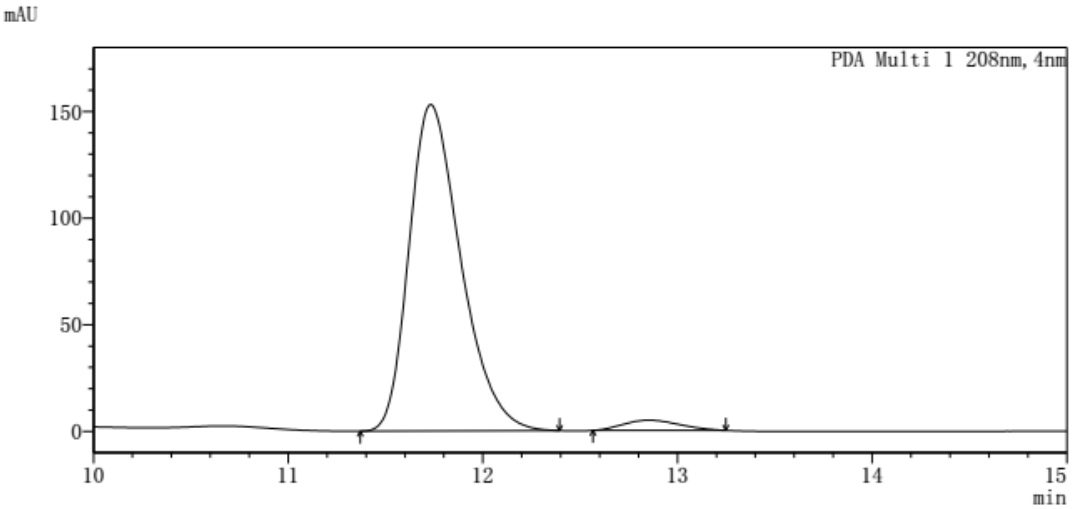
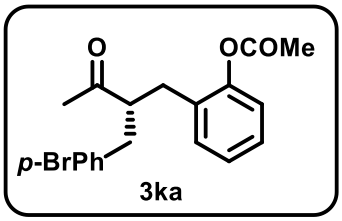


<Peak Results>

PDA Ch1 208nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	11.733	153182	2834174	96.700
2	12.849	4807	96710	3.300



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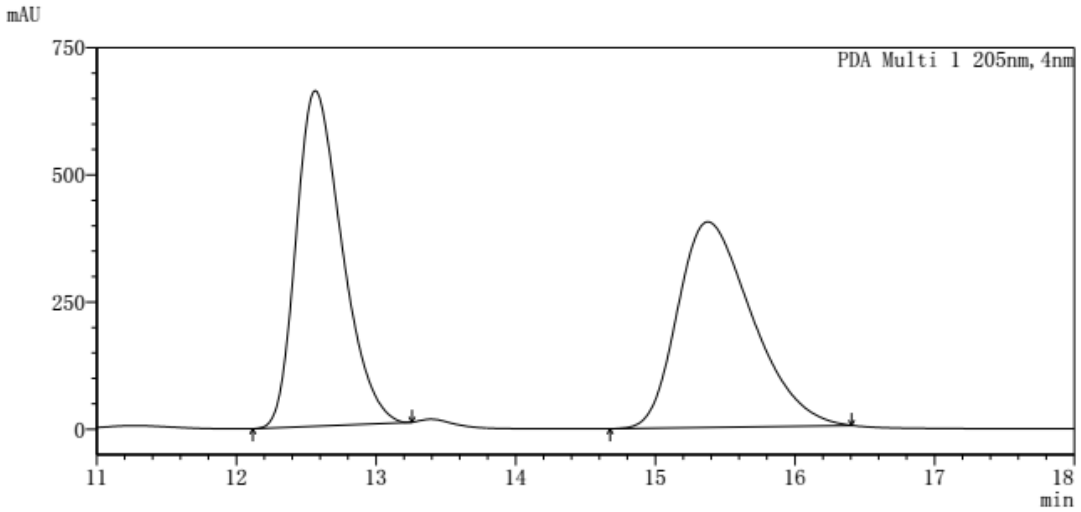

<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	12.565	660010	15064262	50.075
2	15.376	404327	15018975	49.925

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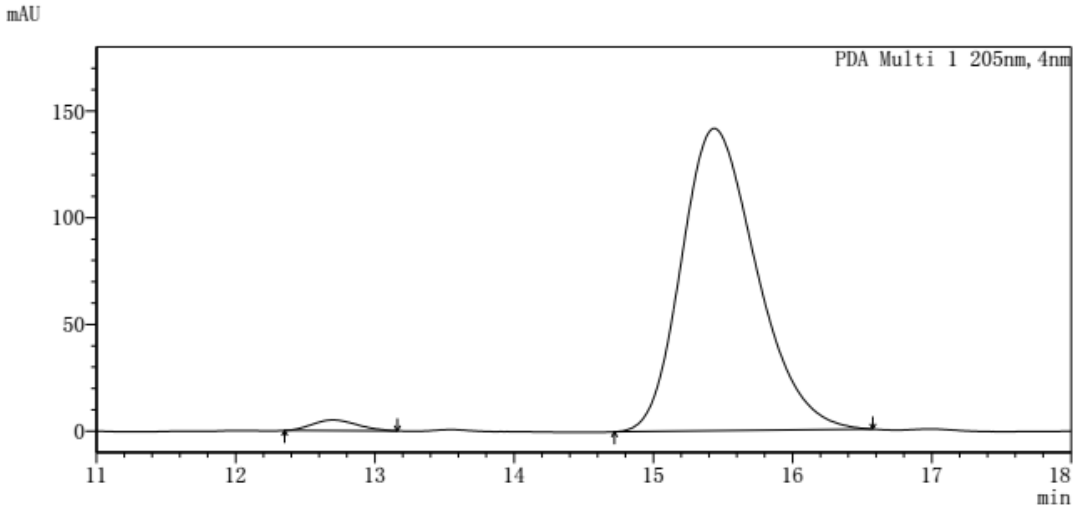
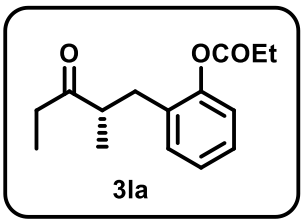


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	12.701	4990	111878	2.062
2	15.437	141723	5314520	97.938



3la

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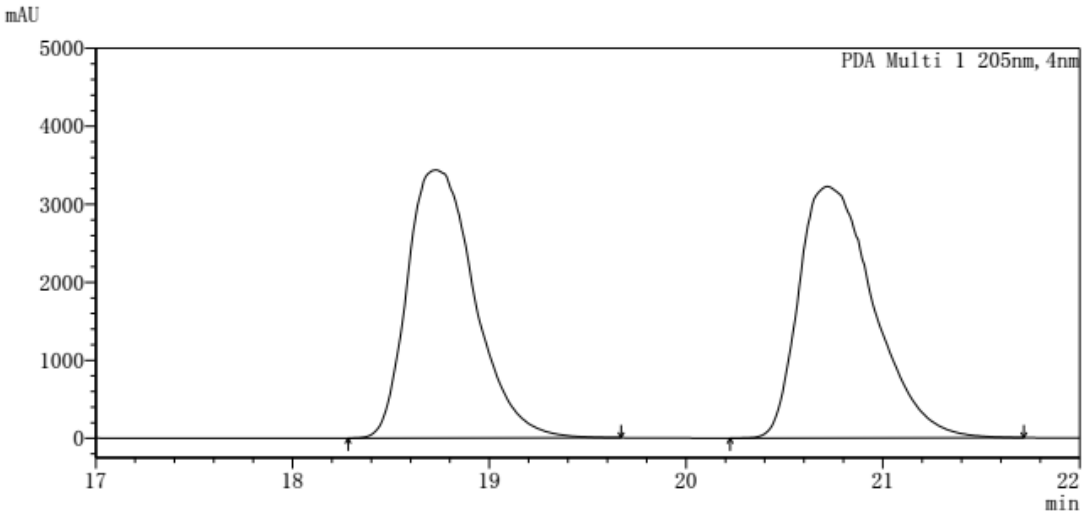

<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	18.727	3435189	81937755	48.942
2	20.717	3223865	85481227	51.058

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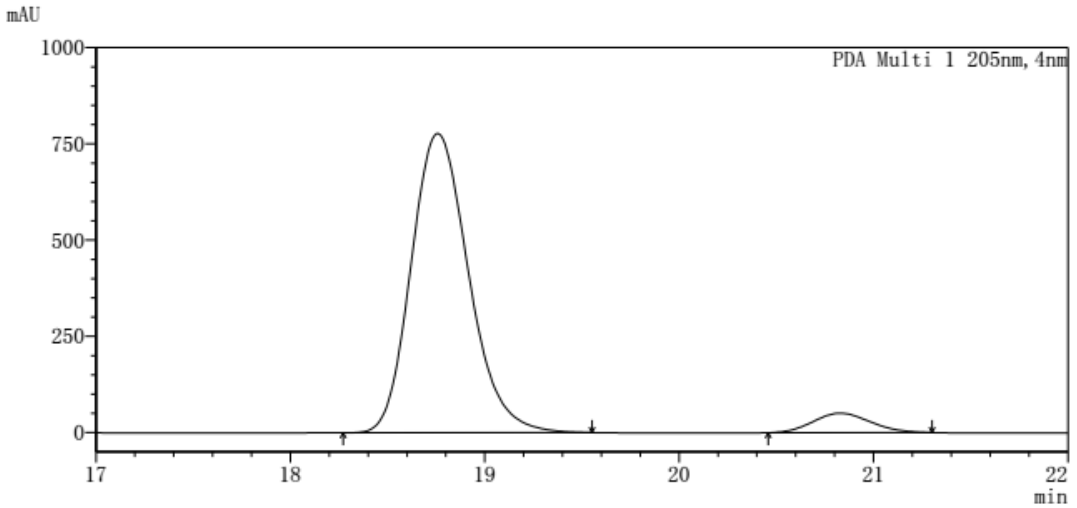
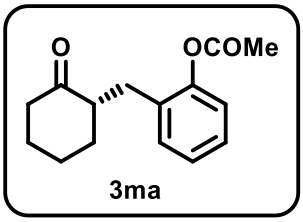


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	18.757	777324	15985538	93.890
2	20.830	50500	1040253	6.110



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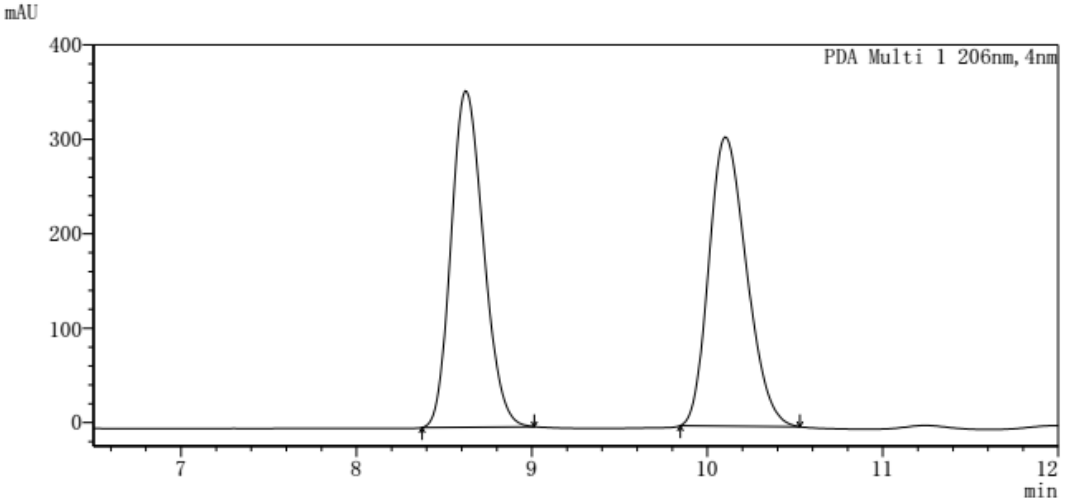
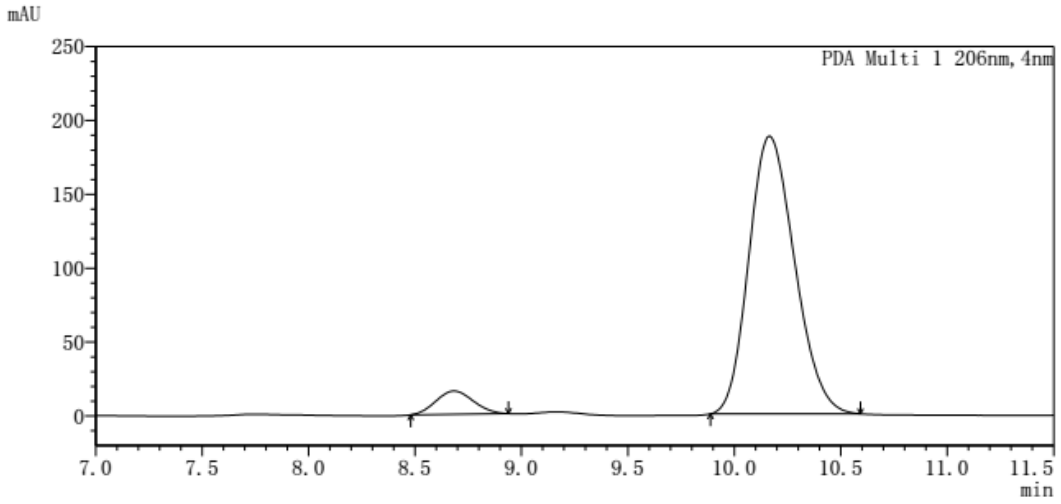


<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	8.623	356056	4568864	50.001
2	10.103	306164	4568590	49.999

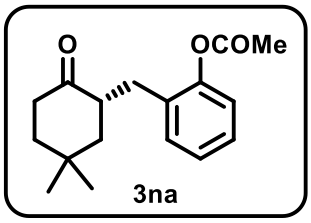
<Chromatogram>



<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	8.683	15816	192917	6.414
2	10.165	188152	2814869	93.586



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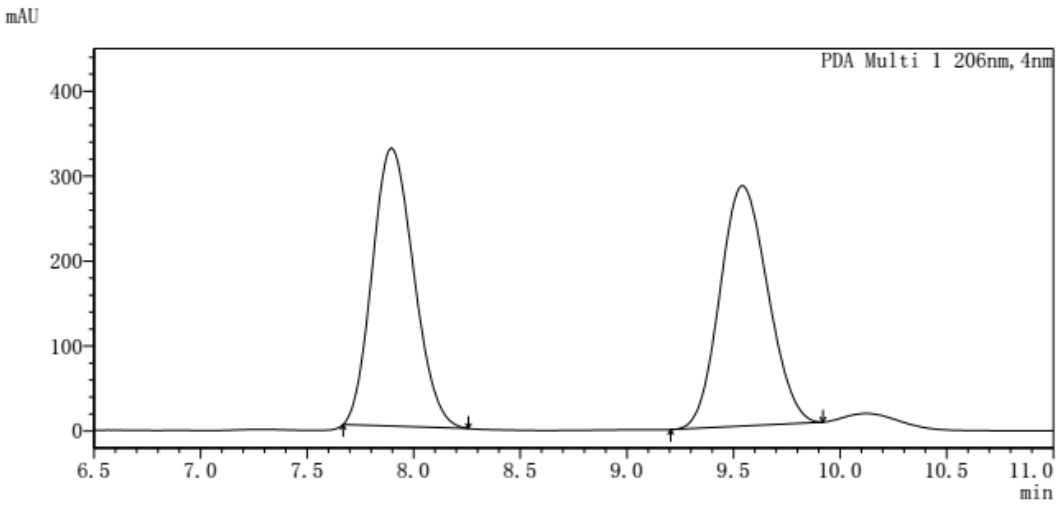
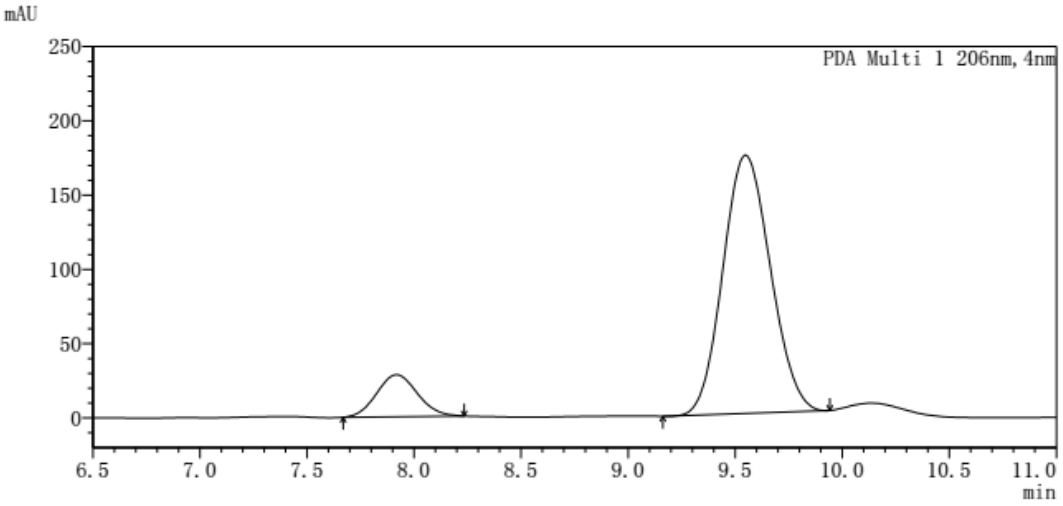


<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	7.896	327336	4424754	50.035
2	9.542	282551	4418543	49.965

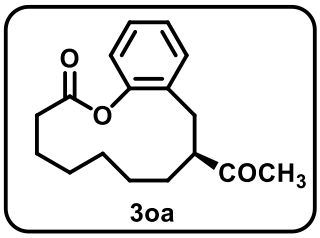
<Chromatogram>



<Peak Results>

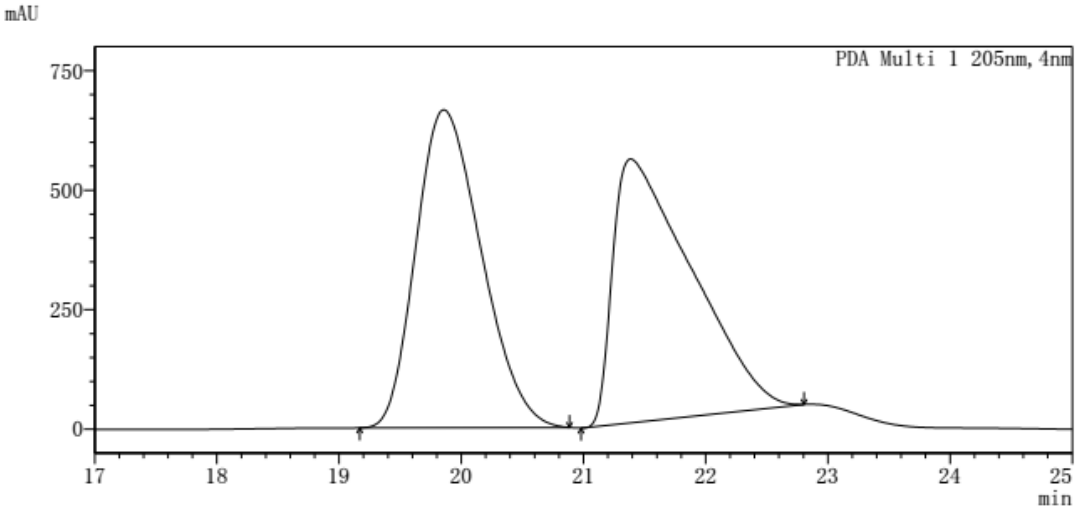
PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	7.918	28263	374921	12.248
2	9.548	173943	2686064	87.752



3oa

<Chromatogram>

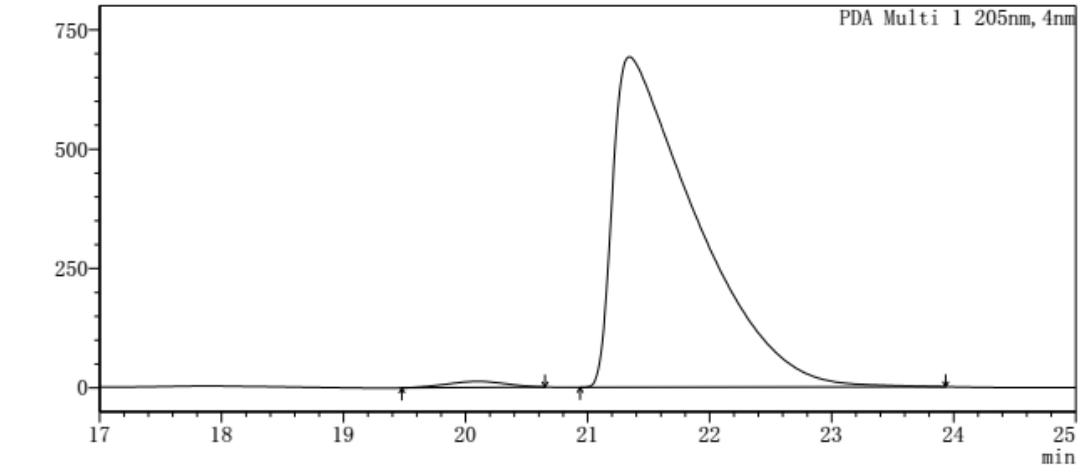


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	19.857	664791	24792182	50.113
2	21.386	551629	24680240	49.887

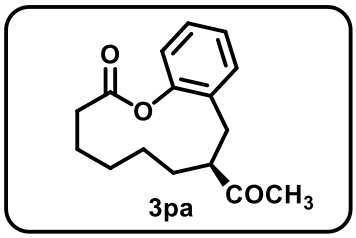
<Chromatogram>



<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	20.101	12700	429242	1.291
2	21.343	692027	32818887	98.709



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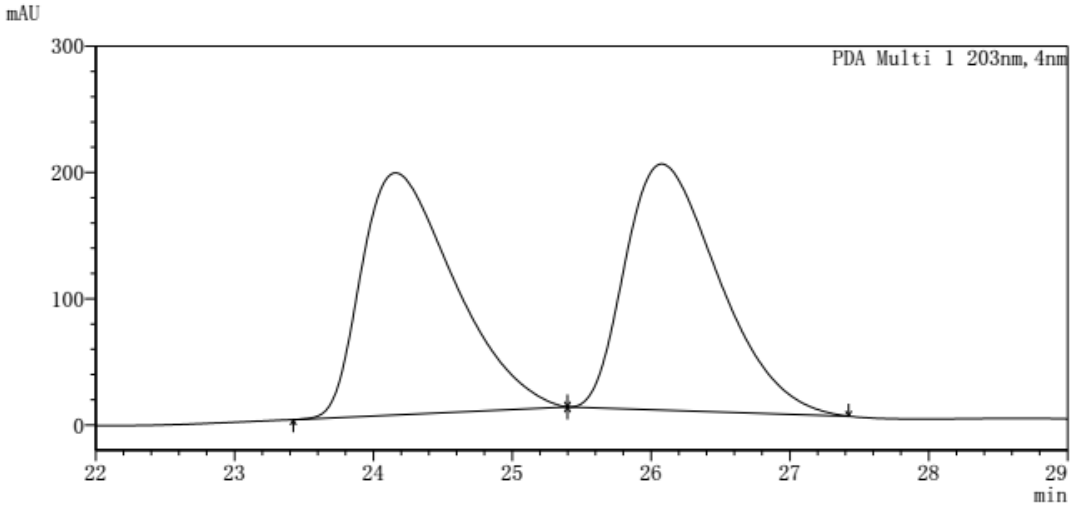
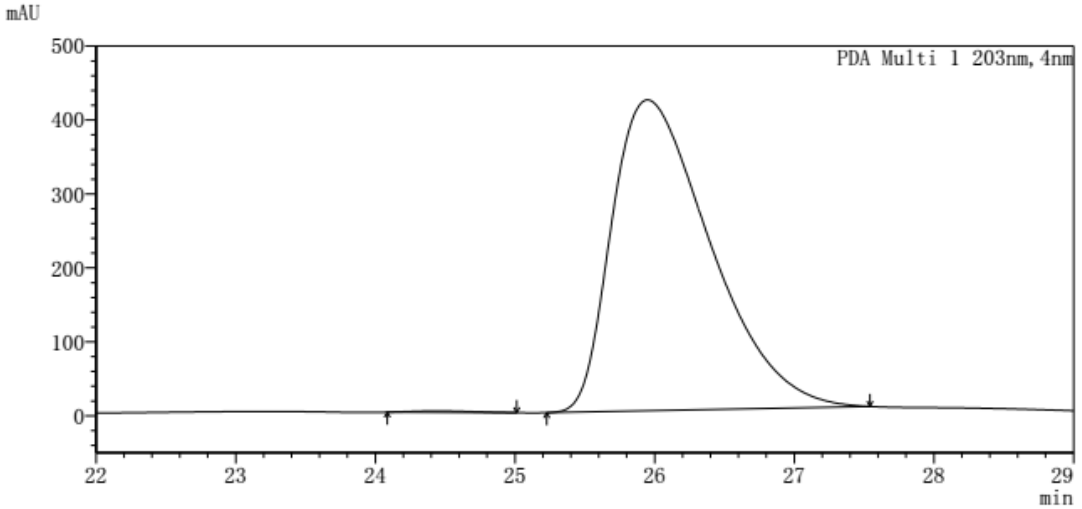


<Peak Results>

PDA Ch1 203nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	24.160	191642	8953587	49.433
2	26.076	194856	9159162	50.567

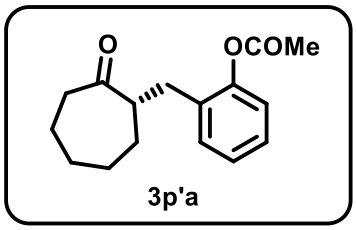
<Chromatogram>



<Peak Results>

PDA Ch1 203nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	24.441	1855	56865	0.274
2	25.948	420345	20674453	99.726



3p'a

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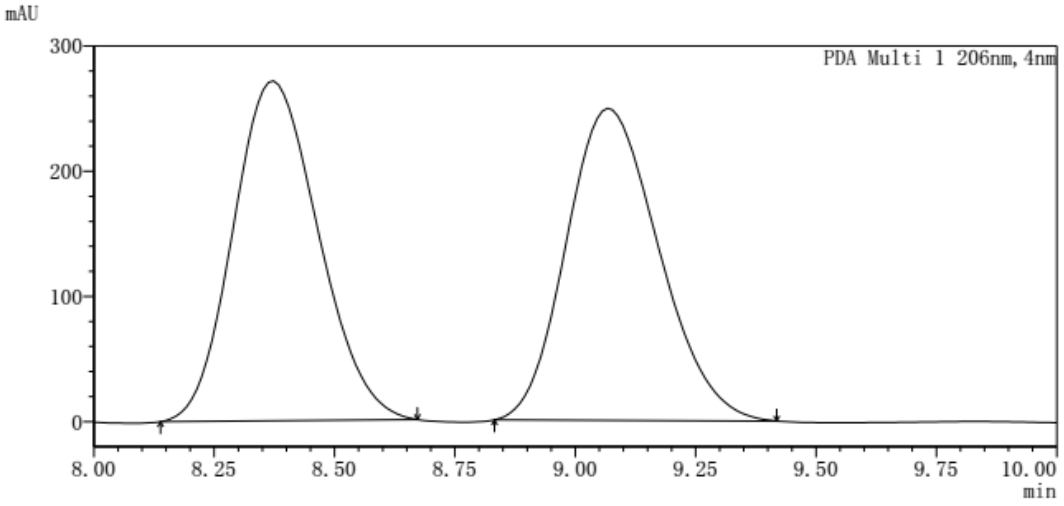
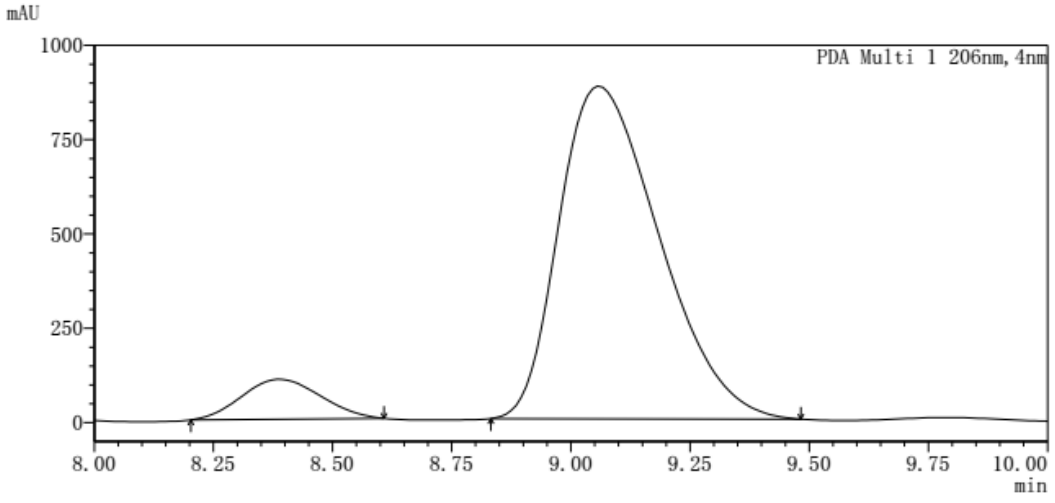


<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	8.371	271504	3343885	50.076
2	9.068	249281	3333777	49.924

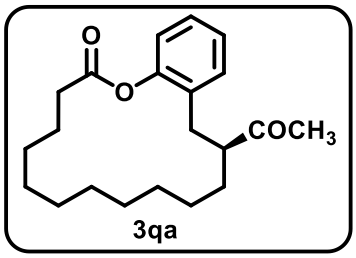
<Chromatogram>



<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	8.388	105744	1217197	8.617
2	9.058	881878	12908950	91.383



3qa

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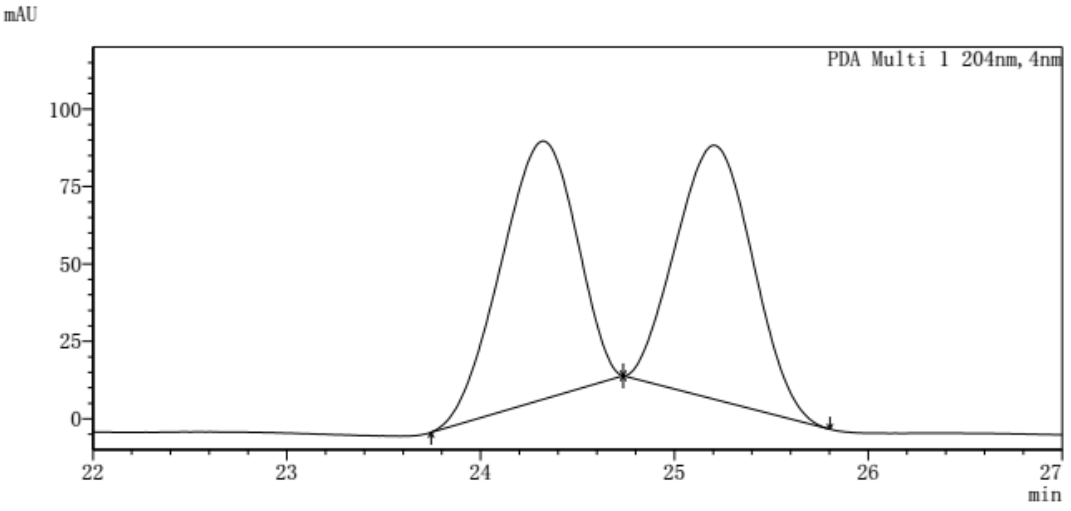
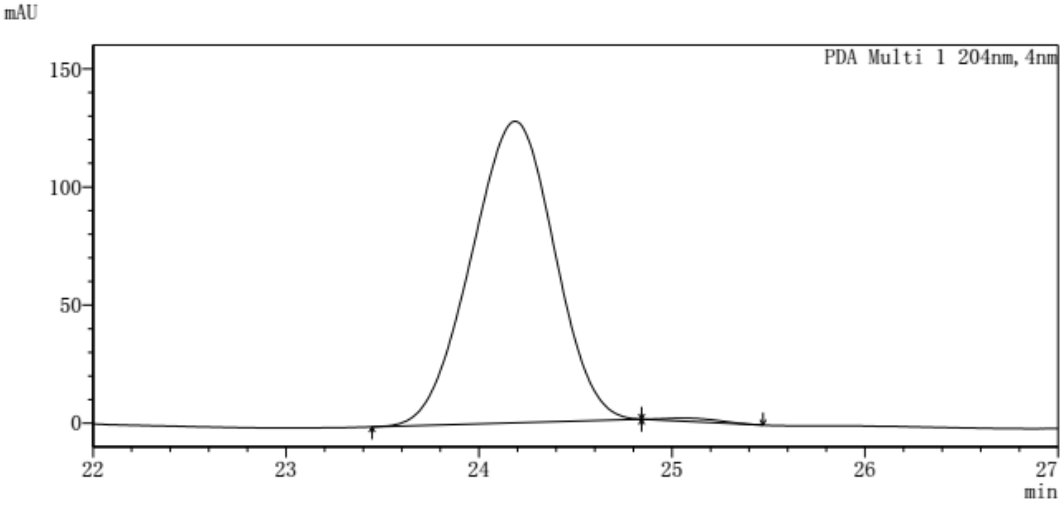


<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	24.323	83382	2266726	50.025
2	25.204	82014	2264426	49.975

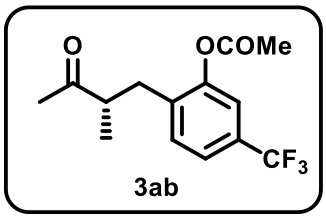
<Chromatogram>



<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	24.187	127566	3825134	99.319
2	25.049	1269	26212	0.681



3ab

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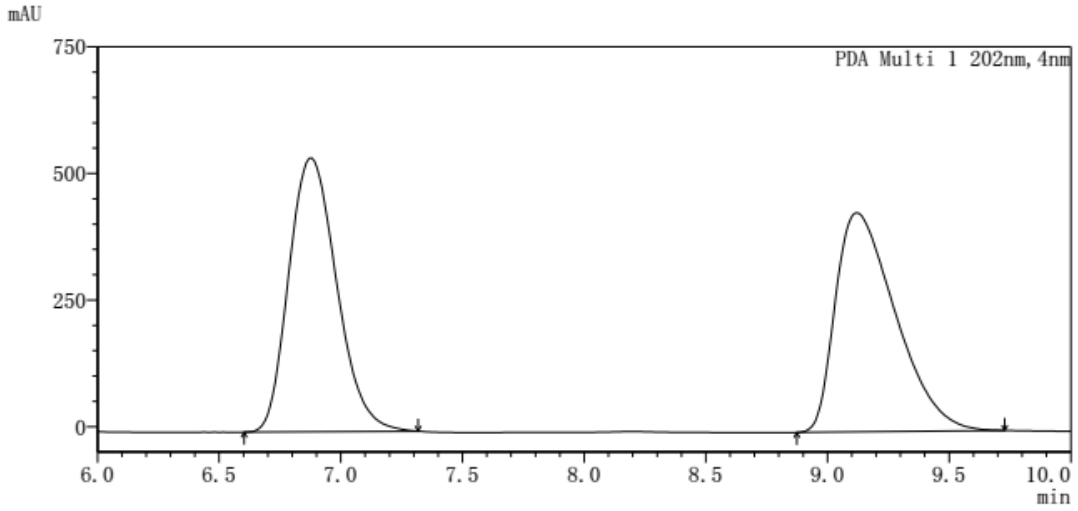
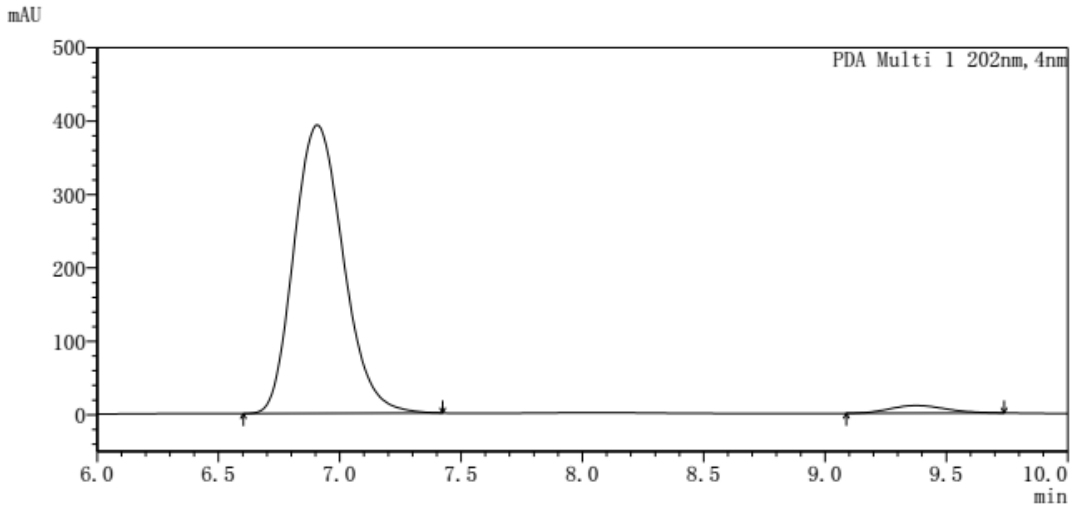


<Peak Results>

PDA Ch1 202nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	6.876	540865	7406375	49.907
2	9.120	432953	7434027	50.093

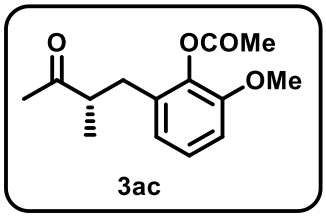
<Chromatogram>



<Peak Results>

PDA Ch1 202nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	6.907	392597	5553919	97.031
2	9.376	10454	169923	2.969



3ac

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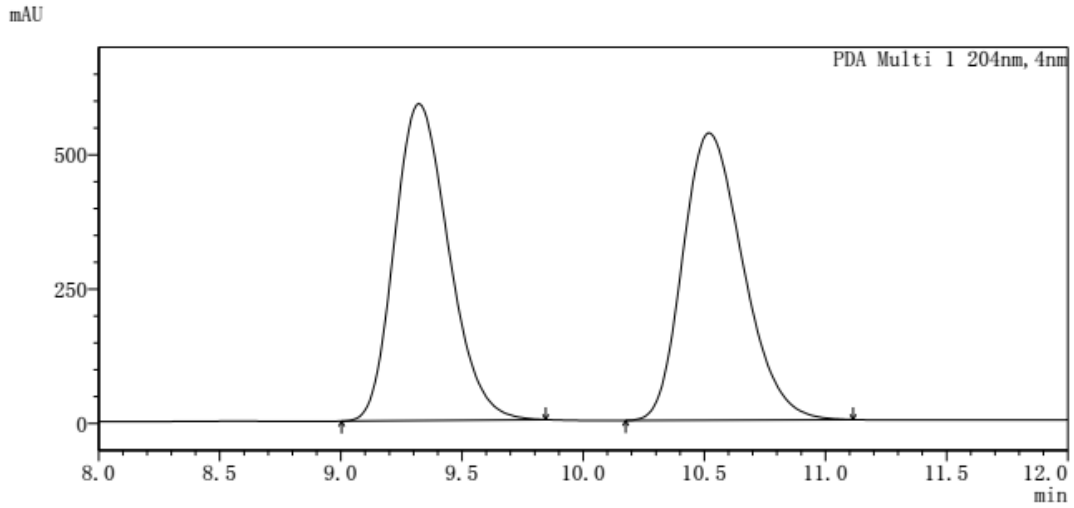
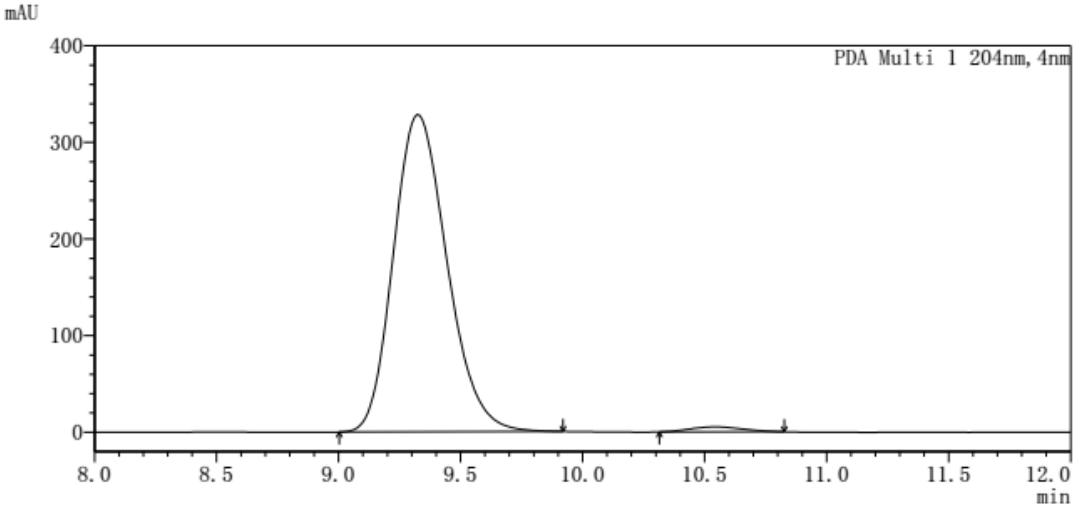


<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	9.322	589776	9187552	49.794
2	10.520	534410	9263641	50.206

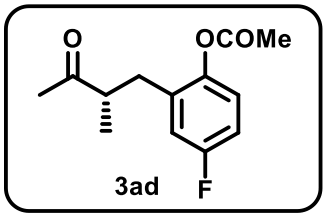
<Chromatogram>



<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	9.325	328490	5016708	98.503
2	10.542	5087	76231	1.497



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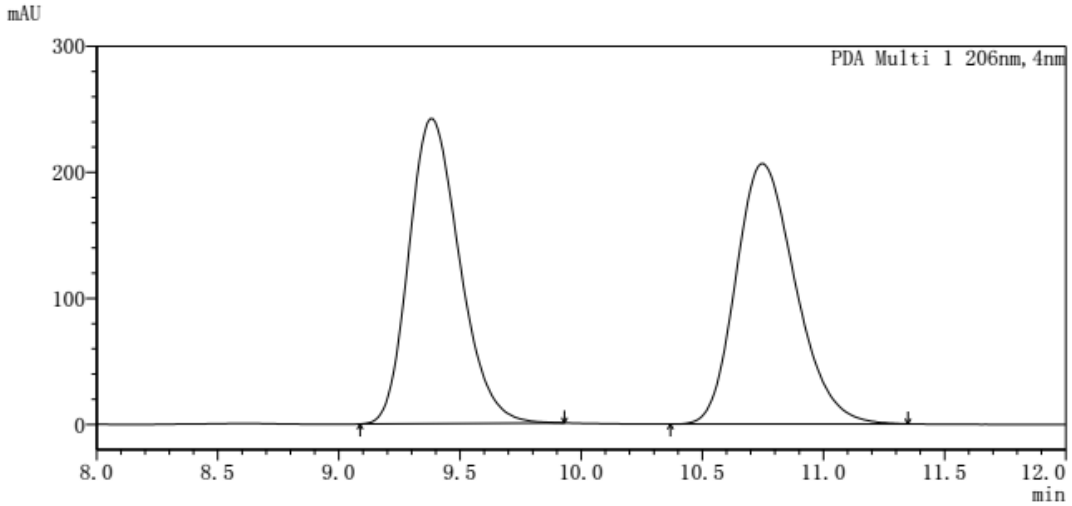
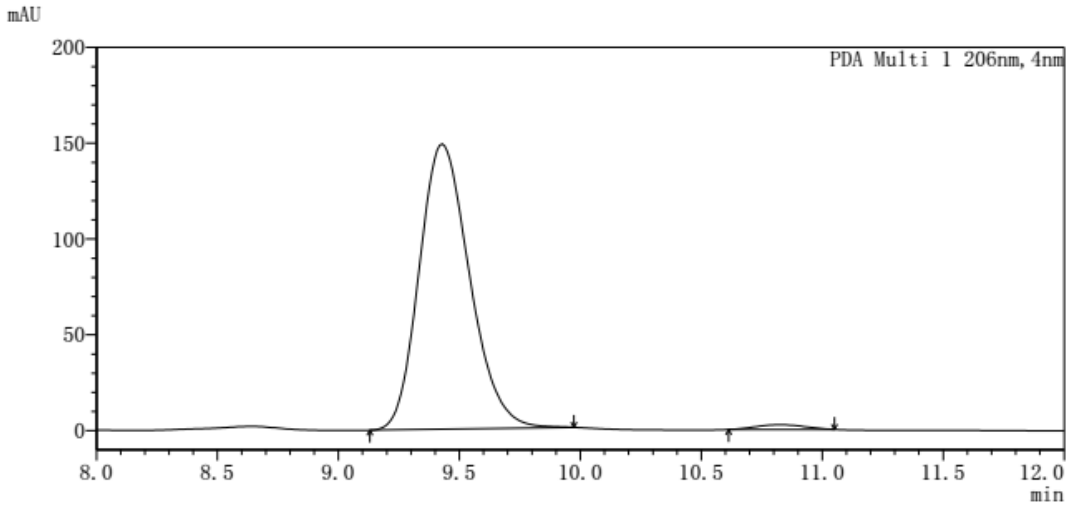


<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	9.382	242063	3527985	49.914
2	10.748	206662	3540121	50.086

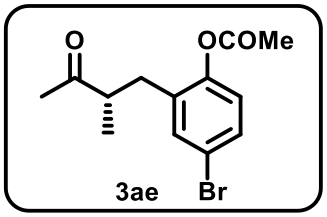
<Chromatogram>



<Peak Results>

PDA Ch1 206nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	9.428	148884	2158761	98.430
2	10.825	2469	34431	1.570



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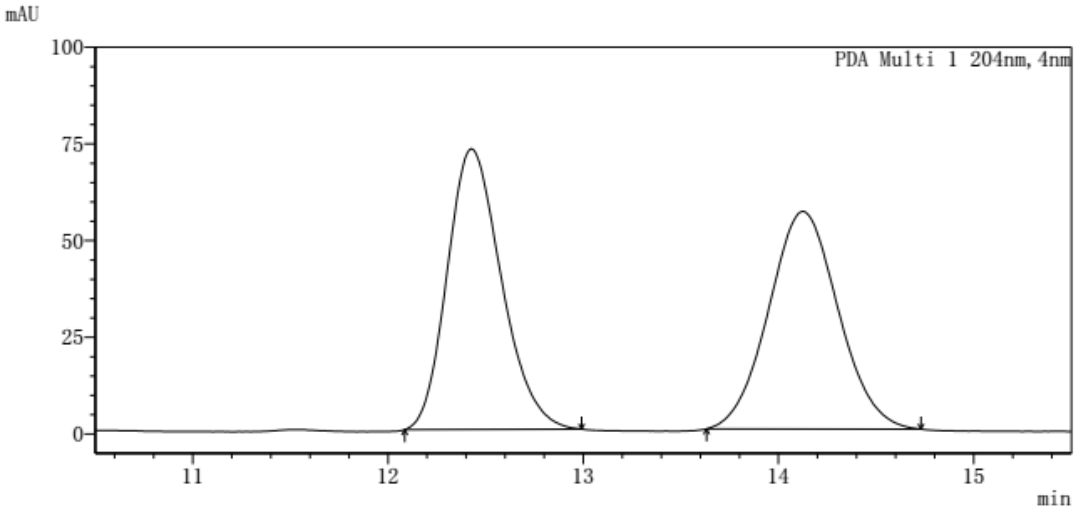
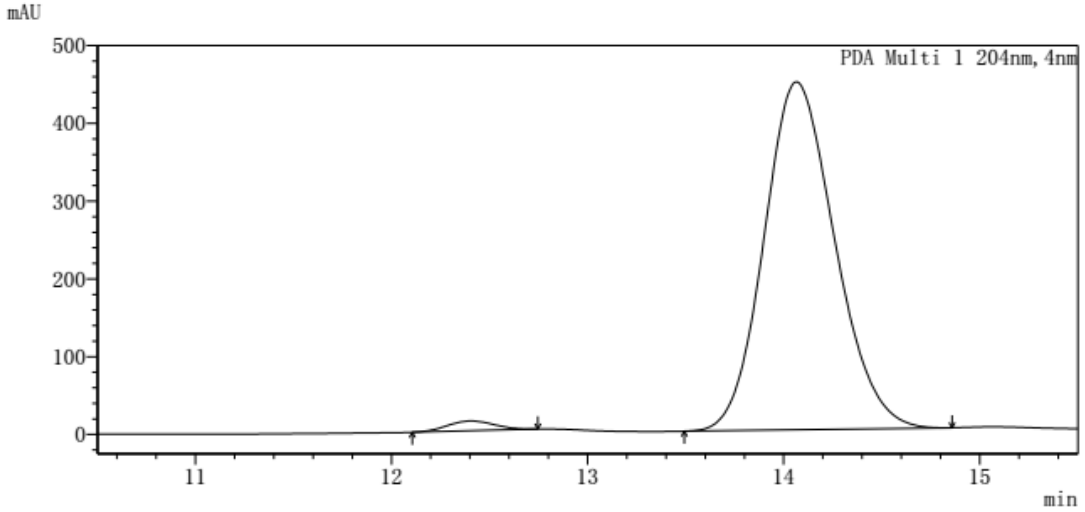


<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	12.428	72590	1401112	50.093
2	14.125	56273	1395910	49.907

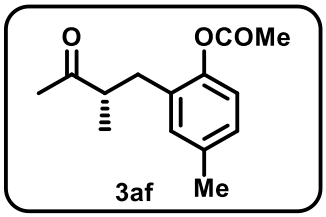
<Chromatogram>



<Peak Results>

PDA Ch1 204nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	12.404	12672	212523	1.856
2	14.065	447287	11239841	98.144



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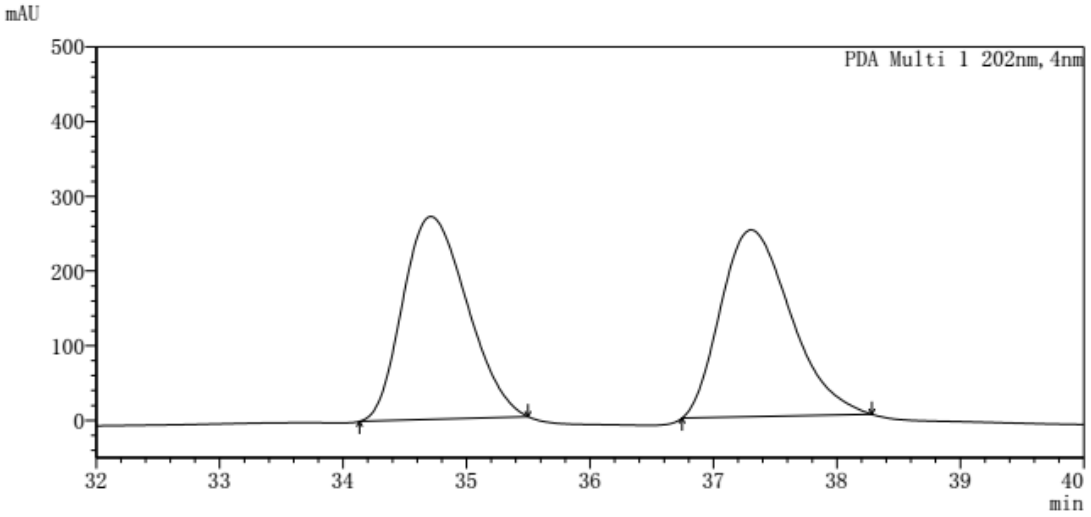
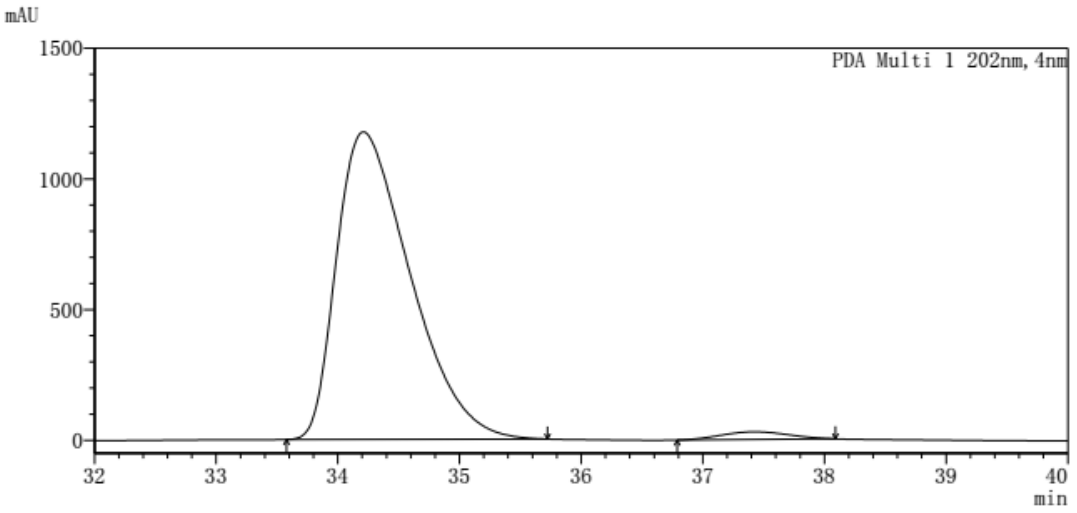


<Peak Results>

PDA Ch1 202nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	34.710	271705	9863472	49.906
2	37.305	250134	9900679	50.094

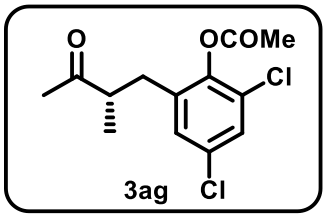
<Chromatogram>



<Peak Results>

PDA Ch1 202nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	34.210	1176724	49656736	97.789
2	37.427	29203	1122729	2.211



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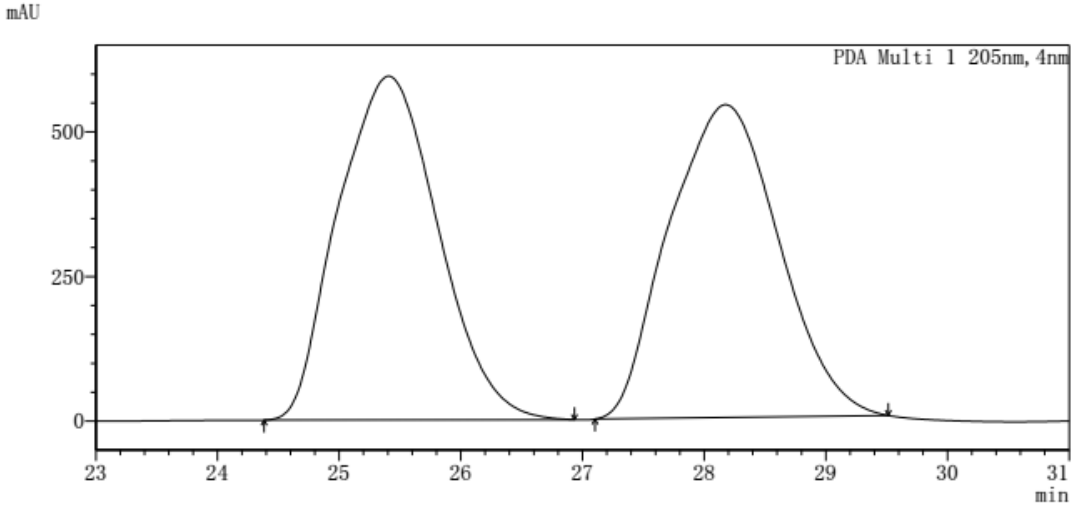
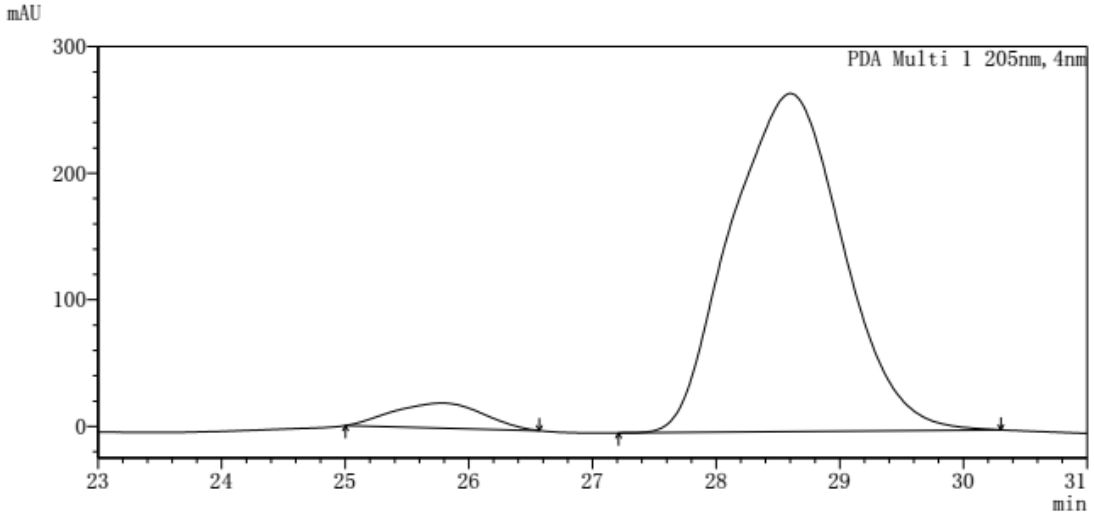


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	25.406	594464	34071315	50.042
2	28.178	540845	34013918	49.958

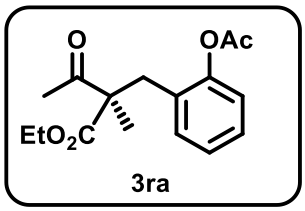
<Chromatogram>



<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	25.785	19764	995415	5.583
2	28.600	267086	16834696	94.417



3ra

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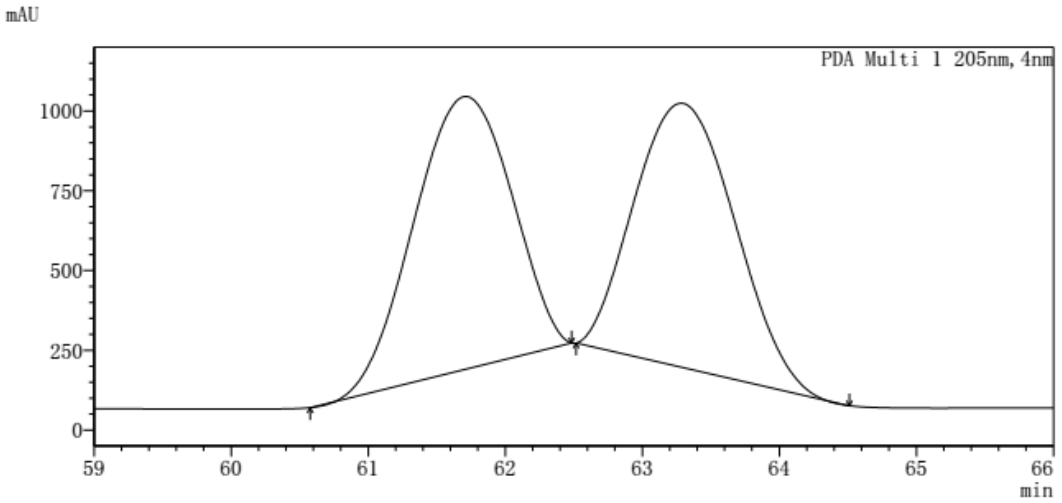
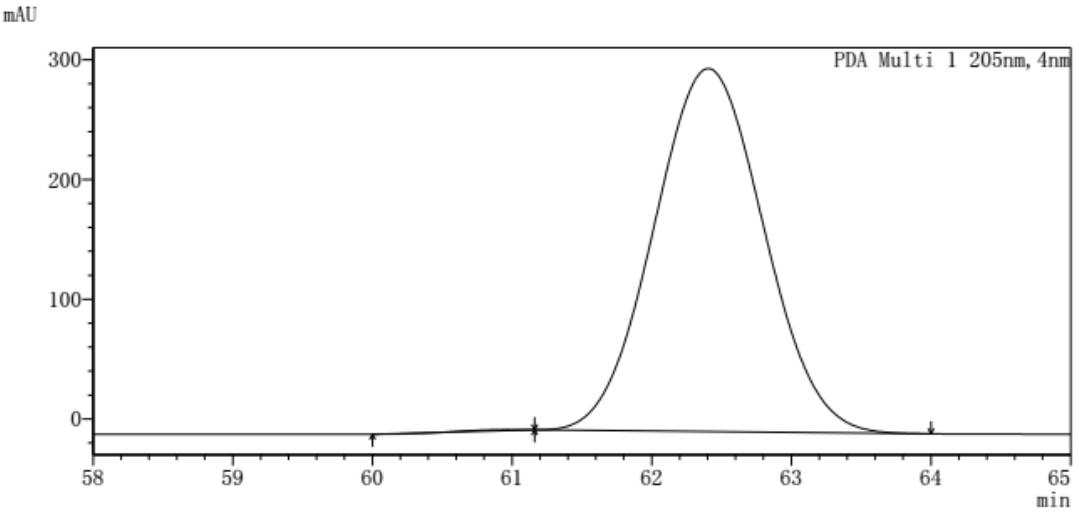


<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	61.712	854990	42480829	50.075
2	63.285	827526	42354071	49.925

<Chromatogram>



<Peak Results>

PDA Ch1 205nm

Index	Time/min	Height/mAU	Quantity/Area	Area %/%
1	60.939	908	19552	0.118
2	62.406	303273	16610874	99.882