Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers

Cu-Catalyzed Practical Approach to *α*-Ketoesters under Air: An Efficient Aerobic Oxidative Dehydrogenative Coupling of Alcohols and *α*-Carbonyl Aldehydes

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Supporting Information

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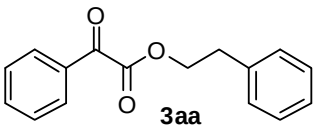
General Remarks.

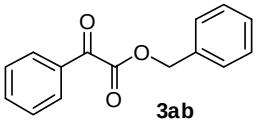
All manipulations were conducted with test tube.[1]H-NMR spectra were recorded on Bruker AVIII-400 spectrometers. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ as an internal standard. [13]C-NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.00 ppm). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

Analytical data for compounds **3**



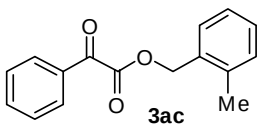
3aa

1): **Phenethyl 2-oxo-*2*-phenylacetate**.[1] Typical procedure: Mix CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) and 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) in toluene (2 mL) under Air (1 atm). The reaction mixture was stirred at 90 °C for 18 h. After cooling down to room temperature and concentrating in vacuum, the residue was purified by flash chromatography on a short silica gel (eluent: petroleum ether/ethyl acetate = 40:1) to afford 56 mg (88%) of **3aa**. **3aa**: colourless liquid; [1]H NMR ($CDCl_3$, 400 MHz): δ = 7.85 (d, *J* = 7.2 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.33-7.24 (m, 5H), 4.61 (t, *J* = 6.8 Hz, 2H), 3.08 (t, *J* = 6.8 Hz, 2H); [13]C NMR ($CDCl_3$, 100 MHz): δ = 186.2, 163.7, 136.9, 134.8, 132.2, 129.9, 128.9, 128.8, 128.6, 126.8, 66.3, 34.8 ppm; IR (neat): ν = 2993.7, 1779.6, 1689.0, 1373.8, 1053.4 cm^{-1}; MW (ESI): $(M + Na)^+$ 277.08.



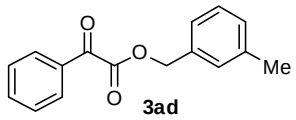
3ab

2): **Benzyl 2-oxo-2-phenylacetate**.[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and phenylmethanol **2b** (40.6 mg, 0.75 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 48 mg (80%) of **3ab**. **3ab**: colorless liquid; [1]H NMR ($CDCl_3$, 400 MHz): δ = 7.96 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.49-7.42 (m, 4H), 7.41-7.33 (m, 3H), 5.41 (s, 2H); [13]C NMR ($CDCl_3$, 100 MHz): δ = 186.0, 163.6, 134.9, 134.5, 132.3, 130.0, 128.8, 128.7, 128.69, 128.5, 67.7 ppm; IR (neat): ν = 3466.6, 2957.8, 1739.5, 1686.4, 1452.3 cm^{-1}; MW (ESI): $(M + Na)^+$ 263.07.



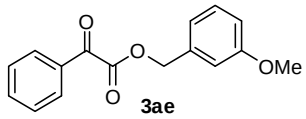
3ac

3): **2-Methylbenzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and *o*-tolylmethanol **2c** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 50 mg (79%) of **3ac**. **3ac**: colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.95 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.29-7.19 (m, 3H), 5.43 (s, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.1, 163.7, 137.2, 134.9, 132.5, 132.4, 130.5, 129.9, 129.7, 129.1, 128.9, 126.1, 66.1, 18.9 ppm; IR (neat): ν = 2925.8, 1735.4, 1685.2, 1196.0, 1173.1 cm^{-1}; MW (ESI): $(M + Na)^+$ 277.08.



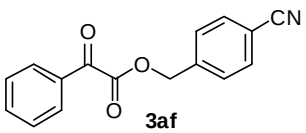
3ad

4): **3-Methylbenzyl 2-oxo-2-phenylacetate**.[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and *m*-tolylmethanol **2d** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 45 mg (71%) of **3ad**. **3ad**: colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.97 (d, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.29-7.22 (m, 3H), 7.17 (d, *J* = 6.8 Hz, 1H), 5.37 (s, 2H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.1, 163.7, 138.4, 134.9, 134.4, 132.4, 130.0, 129.5, 129.3, 128.8, 128.6, 125.6, 67.8, 21.3 ppm; IR (neat): ν = 2924.1, 1736.8, 1687.4, 1244.5, 687.5 cm^{-1}; MW (ESI): $(M + Na)^+$ 277.08.



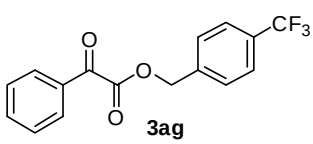
3ae

5) **3-Methoxybenzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and (3-methoxyphenyl)methanol **2e** (52 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 54 mg (80%) of **3ae**. **3ae**: yellow wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98-7.95 (m, 2H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.32-7.24 (m, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.97 (s, 1H), 6.91-6.88 (m, 1H), 5.38 (s, 2H), 3.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.0, 163.5, 159.8, 135.9, 134.9, 132.3, 130.0, 129.8, 128.9, 120.6, 114.4, 113.8, 67.5, 55.2 ppm; IR (neat): ν = 2924.3, 1735.6, 1686.4, 1596.2, 687.1 cm^{-1}; MW (ESI): $(M + Na)^+$ 293.08.



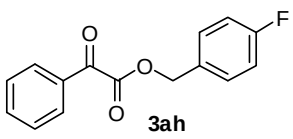
3af

6）**4-Cyanobenzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and 4-(hydroxymethyl)benzonitrile **2f** (50 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 53 mg (80%) of **3af**. **3af**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, *J* = 7.2 Hz, 2H), 7.70-7.65 (m, 3H), 7.56-7.49 (m, 4H), 5.46 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 185.4, 163.0, 139.6, 135.2, 132.5, 132.1, 129.9, 128.9, 128.5, 118.3, 112.5, 66.2 ppm; IR (neat): ν = 3071.5, 2223.9, 1745.0, 1452.5, 994.1 cm^{-1}; MW (ESI): $(M + Na)^+$ 288.06.



3ag

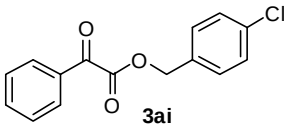
7) **4-(Trifluoromethyl)benzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and (4-(trifluoromethyl)phenyl)methanol **2g** (66 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 55 mg (71%) of **3ag**. **3ag**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (d, *J* = 7.6 Hz, 2H), 7.68-7.64 (m, 3H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 8.0 Hz, 2H), 5.46 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 185.6, 163.3, 138.5, 135.1, 132.3, 131.4, 131.0, 130.7, 130.4, 130.0, 129.0, 128.5, 125.8, 125.73, 125.68, 125.65, 125.2, 122.5, 66.6 ppm; IR (neat): ν = 3449.9, 3063.2, 1736.5, 1688.6, 1329.9, 837.9 cm^{-1}; MW (ESI): $(M + Na)^+$ 331.06.



3ah

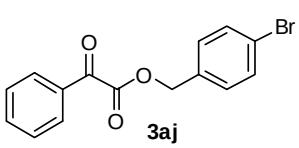
8）**4-Fluorobenzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and (4-fluorophenyl)methanol **2h** (47.6 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 44.2 mg (68%) of **3ah**. **3ah**: colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.96 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.50-7.41 (m, 4H), 7.07 (t, *J* = 8.4 Hz, 2H), 5.37 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 185.9, 163.5, 162.9 (d, *J* = 246.4 Hz), 135.0, 132.3, 130.7, 130.6, 130.4, 130.38, 130.0, 128.9, 115.7 (d, *J* = 21.5 Hz), 67.0 ppm; IR (neat): ν = 3436.0,

2921.1, 1737.8, 1689.4, 1196.8 cm^{-1}; MW (ESI): $(M + Na)^+$ 281.06.



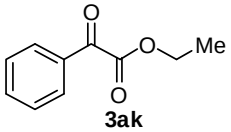
3ai

9） **4-Chlorobenzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and (4-chlorophenyl)methanol **2i** (53.3 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 50 mg (73%) of **3ai**. **3ai**: yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.96 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.39-7.34 (m, 4H), 5.37 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 185.8, 163.4, 135.0, 134.7, 133.0, 132.3, 129.96, 129.94, 129.0, 128.9, 66.8 ppm; IR (neat): ν = 3064.1, 1736.9, 1689.2, 1200.7, 688.0 cm^{-1}; MW (ESI): $(M + Na)^+$ 297.03.



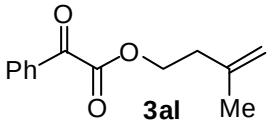
3aj

10） **4-Bromobenzyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and (4-bromophenyl)methanol **2j** (66.3 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 59 mg (74%) of **3aj**. **3aj**: yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.96 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.52-7.47 (m, 4H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.35 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 185.7, 163.3, 135.0, 133.5, 132.3, 131.9, 130.2, 130.0, 129.0, 122.9, 66.8 ppm; IR (neat): ν = 3062.5, 1736.9, 1688.7, 1201.8, 821.8 cm^{-1}; MW (ESI): $(M + Na)^+$ 340.98.



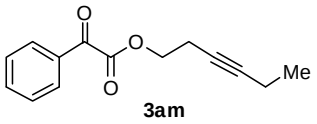
3ak

11): **Ethyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and ethanol **2k** (17.3 mg, 0.375 mmol) in toluene (1.5 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 29.4 mg (66%) of **3ak**. **3ak**: colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.01 (d, *J* = 7.2 Hz, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 4.46 (q, *J* = 7.0 Hz, 2H), 1.43 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.4, 163.8, 134.9, 132.5, 130.0, 128.9, 62.3, 14.1 ppm; IR (neat): ν = 2927.8, 1737.1, 1688.2, 1200.4, 687.4 cm^{-1}; MW (ESI): $(M + Na)^+$ 201.05.



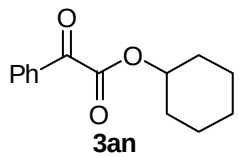
3al

12): **3-Methylbut-3-enyl 2-oxo-2-phenylacetate.** The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and 3-methylbut-3-en-1-ol **2l** (32.3 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 44 mg (81%) of **3al**. **3al**: colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.01 (d, *J* = 3.6 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 4.86 (s, 1H), 4.80 (s, 1H), 4.52 (t, *J* = 7.0 Hz, 2H), 2.50 (t, *J* = 7.0 hz, 2H), 1.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.3, 163.8, 140.8, 134.9, 132.4, 130.0, 128.8, 113.0, 64.3, 36.5, 22.3 ppm; IR (neat): ν = 2933.0, 1737.7, 1690.0, 1197.4, 987.4 cm^{-1}; HRMS m/z (ESI) calcd for $C_{13}H_{14}NaO_3$ $(M + Na)^+$ 241.0835, found 241.0831.



3am

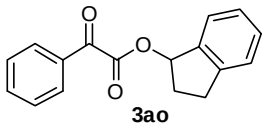
13）**Hex-3-ynyl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and hex-3-yn-1-ol **2m** (36.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 24 mg (42%) of **3am**. **3am**: white liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.04 (d, *J* = 6.8 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 4.46 (t, *J* = 6.8 Hz, 2H), 2.68-2.63 (m, 2H), 2.20-2.14 (m, 2H), 1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.1, 163.6, 134.9, 132.4, 130.1, 128.9, 84.0, 74.1, 64.3, 19.2, 14.0, 12.3 ppm; IR (neat): ν = 3468.0, 2975.3, 1913.4, 1739.0, 1689.9, 1195.8 cm^{-1}; MW (ESI): $(M + Na)^+$ 253.08.



3an

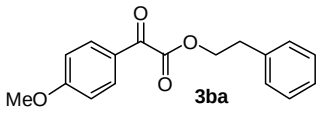
14): **Cyclohexyl 2-oxo-2-phenylacetate.** The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and cyclohexanol **2n** (47.6 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, , afforded 45.6 mg (78%) of **3an**. **3an**: colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 5.13-5.06 (m, 1H), 2.03-1.99 (m, 2H), 1.82-1.76 (m, 2H), 1.65-1.56 (m, 3H), 1.48-1.25 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.8, 163.6, 134.7, 132.5, 129.9, 128.8, 75.4, 31.4, 25.1, 23.6

ppm; IR (neat): ν = 2938.8, 1732.1, 1690.5, 1203.3, 989.3 cm^{-1}; HRMS m/z (ESI) calcd for $C_{14}H_{16}NaO_3$ $(M + Na)^+$ 255.0992, found 255.0986.



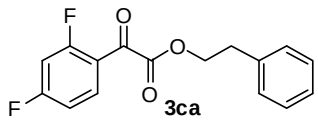
3ao

15）**2,3-Dihydro-*1H*-inden-1-yl 2-oxo-2-phenylacetate.** The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and 2,3-dihydro-1*H*-inden-1-ol **2o** (50.3 mg, 0.375 mmol) in toluene (1.5 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 33 mg (50%) of **3ao**. **3ao**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.94 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.35-7.24 (m, 3H), 6.51 (q, *J* = 3.2 Hz, 1H), 3.22-3.13 (m, 1H), 2.98-2.90 (m, 1H), 2.65-2.55 (m, 1H), 2.35-2.27 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.4, 164.0, 144.8, 139.7, 134.8, 132.5, 129.9, 129.5, 128.8, 126.9, 125.8, 124.9, 80.8, 32.0, 30.2 ppm; IR (neat): ν = 2926.9, 1732.5, 1688.0, 1199.2, 985.5 cm^{-1}; HRMS m/z (ESI) calcd for $C_{17}H_{14}NaO_3$ $(M + Na)^+$ 289.0835, found 289.0846.



3ba

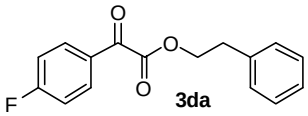
16): **phenethyl 2-(4-methoxyphenyl)-2-oxoacetate**.[1] The reaction of CuBr (3.6 mg, 0.025 mmol)，pyridine (10.0 mg, 0.125 mmol), 2-(4-methoxyphenyl)-2-oxoacetaldehyde hydrate **1b** (45.5 mg, 0.25 mmol) and 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 51 mg (72%) of **3ba**. **3ba**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.84 (dd, J_1 = 6.8 Hz, J_2 = 1.8 Hz, 2H), 7.31-7.24 (m, 5H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.60 (t, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 3.08 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 184.7, 164.9, 164.0, 137.0, 132.5, 129.0, 128.6, 126.7, 125.3, 114.1, 66.2, 55.6, 34.9 ppm; IR (neat): ν = 2956.4, 1769.9, 1709.5, 1605.2, 1247.8 cm^{-1}; MW (ESI): $(M + Na)^+$ 307.09.



3ca

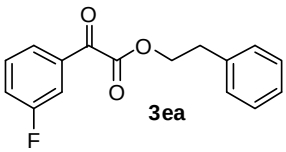
17) **phenethyl 2-(2,4-difluorophenyl)-2-oxoacetate**. The reaction of CuBr (3.6 mg, 0.025 mmol)，pyridine (10.0 mg, 0.125 mmol), 2-(2,4-difluorophenyl)-2-oxoacetaldehyde hydrate **1c** (47 mg, 0.25 mmol) and 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 55 mg (76%) of **3ca**. **3ca**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ =

7.93-7.87 (m, 1H), 7.32-7.22 (m, 5H), 7.03-6.98 (m, 1H), 6.89-6.84 (m, 1H), 4.57 (t, J = 7.2 Hz, 2H), 3.06 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 182.4, 167.1 (dd, J_1 = 259 Hz, J_2 = 12 Hz), 163.7, 163.6 (dd, J_1 = 259 Hz, J_2 = 13 Hz), 136.8, 133.0 (dd, J_1 = 11 Hz, J_2 = 3 Hz), 128.9, 128.6, 126.8, 118.4 (dd, J_1 = 11 Hz, J_2 = 4 Hz), 122.8 (dd, J_1 = 22 Hz, J_2 = 3 Hz), 105.0 (t, J = 26 Hz), 66.7, 34.7 ppm; IR (neat): ν = 3030.5, 1749.7, 1611.4, 1498.4, 996.4cm^{-1}; HRMS m/z (ESI) calcd for $C_{16}H_{12}F_2NaO_3$ $(M + Na)^+$ 313.0647, found 313.0650.



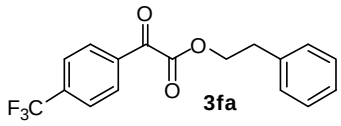
3da

18): **phenethyl 2-(4-fluorophenyl)-2-oxoacetate**.[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-(4-fluorophenyl)-2-oxoacetaldehyde hydrate **1d** (42.5 mg, 0.25 mmol) and 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 53 mg (78%) of **3da**. **3da**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.91-7.87 (m, 2H), 7.34-7.24 (m, 5H), 7.13-7.09 (m, 2H), 4.62 (t, J = 7.0 Hz, 2H), 3.09 (t, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 184.4, 166.7 (d, J = 256 Hz), 163.3, 136.9, 132.9 (d, J = 10 Hz), 129.0, 128.9, 128.8, 128.7, 126.9, 116.2 (d, J = 22.2 Hz), 66.4, 34.9 ppm; IR (neat): ν = 3466.4, 2924.5, 1738.8, 1686.2, 1597.4, 993.6 cm^{-1}; MW (ESI): $(M + Na)^+$ 295.07.



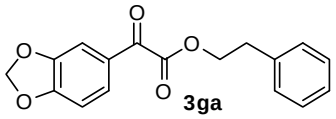
3ea

19) **phenethyl 2-(3-fluorophenyl)-2-oxoacetate**. The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-(3-fluorophenyl)-2-oxoacetaldehyde hydrate **1e** (42.5 mg, 0.25 mmol) and 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 52 mg (76%) of **3ea**. **3ea**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64-7.59 (m, 2H), 7.45-7.39 (m, 1H), 7.35-7.24 (m, 6H), 4.62 (t, J = 7.0 Hz, 2H), 3.09 (t, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 184.8 (d, J = 2.2 Hz), 162.9, 162.6 (d, J = 248 Hz), 136.8, 134.35, 134.3, 130.6, 130.5, 128.9, 128.7, 126.9, 126.0, 125.98, 122.1, 121.9, 116.5, 116.3, 66.6, 34.9 ppm; IR (neat): ν = 3030.1, 1737.6, 1693.5, 1235.3, 1143.4 cm^{-1}; HRMS m/z (ESI) calcd for $C_{16}H_{13}FNaO_3$ $(M + Na)^+$ 295.0741, found 295.0738.



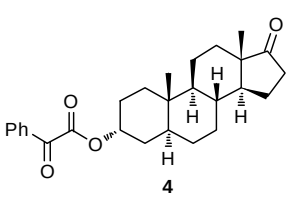
3fa

20): **phenethyl 2-oxo-2-(4-(trifluoromethyl)phenyl)acetate**.[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-(4-(trifluoromethyl)phenyl)acetaldehyde hydrate **1f** (55 mg, 0.25 mmol) and 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 59 mg (73%) of **3fa**. **3fa**: yellow wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.96 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.35-7.25 (m, 5H), 4.65 (t, *J* = 7.0 Hz, 2H), 3.10 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 184.9, 162.7, 136.8, 135.9, 135.6, 135.1, 130.4, 129.0, 128.7, 126.9, 125.9, 125.8, 125.79, 125.76, 124.6, 121.9, 66.7, 34.9 ppm; IR (neat): ν = 2925.0, 1740.5, 1692.1, 1334.3, 702.0 cm^{-1}; MW (ESI): $(M + Na)^+$ 345.07.



3ga

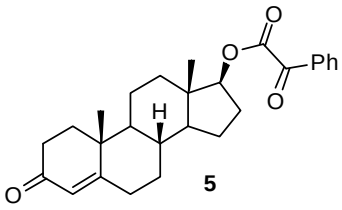
21) **phenethyl 2-(benzo[*d*][1,3]dioxol-5-yl)-2-oxoacetate**. The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-(benzo[*d*][1,3]dioxol-5-yl)-2-oxoacetaldehyde hydrate **1g** (49 mg, 0.25 mmol) and 2-phenylethanol **2a** (45.8 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 59 mg (79%) of **3ga**. **3ga**: white wax; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.39-7.37 (m, 2H), 7.33-7.29 (m, 2H), 7.27-7.24 (m, 3H), 6.81-6.79 (m, 1H), 6.05 (s, 2H), 4.59 (t, *J* = 7.0 Hz, 2H), 3.07 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 184.4, 163.8, 153.5, 148.4, 136.9, 128.9, 128.6, 127.9, 127.0, 126.8, 108.5, 108.2, 102.2, 66.3, 34.9 ppm; IR (neat): ν = 3450.0, 2926.4, 1736.5, 1599.1, 988.3 cm^{-1}; HRMS m/z (ESI) calcd for $C_{17}H_{14}NaO_5$ $(M + Na)^+$ 321.0733, found 321.0731.



4

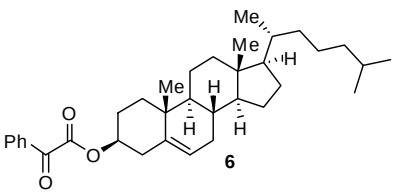
22) **(3R,5S,8R,9S,10S,13S,14S)-10,13-dimethyl-17-oxohexadecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-oxo-2-phenylacetate.**[1] The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and androsterone (109 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 75 mg (74%) of **4**. **4**: white solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, *J* = 7.6 Hz, 2H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 5.38 (s, 1H), 2.46-2.39 (m, 1H), 2.10-1.92 (m, 3H), 1.80-1.77 (m, 3H),

1.66-1.51 (m, 6H), 1.32-1.21 (m, 7H), 1.03-0.98 (m, 1H), 0.85-0.79 (m, 7H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 221.2, 186.8, 163.7, 134.8, 132.5, 129.9, 128.9, 73.0, 54.0, 51.3, 47.7, 39.8, 35.9, 35.8, 34.9, 32.7, 32.6, 31.4, 30.6, 27.9, 26.1, 21.7, 20.0, 13.8, 11.3 ppm; IR (neat): ν = 2926.2, 1757.0, 1672.1, 1243.5, 1047.9 cm^{-1}; MW (ESI): $(M + NH_4)^+$ 440.28; $[\alpha]_D^{21}$ = 64 (c = 0.1, ethyl acetate).



5

22) **(8R,10R,13S,17S)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl 2-oxo-2-phenylacetate.** The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and (8R,10R,13S,17S)-17-hydroxy-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3(2H)-one (108.2 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 66 mg (63%) of **5**. **5**: white solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, *J* = 7.2 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 5.74 (s, 1H), 4.95-4.90 (m, 1H), 2.48-2.26 (m, 5H), 2.07-2.01 (m, 1H), 1.93-1.85 (m, 2H), 1.79-1.49 (m, 5H), 1.45-1.38 (m, 2H), 1.30-1.26 (m, 1H), 1.24 (s, 3H), 1.20-0.94 (m, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.3, 186.6, 170.6, 164.1, 134.8, 132.4, 129.9, 128.9, 124.0, 84.5, 53.6, 50.1, 42.9, 38.5, 36.6, 35.6, 35.3, 33.9, 32.6, 31.4, 27.3, 23.5, 20.4, 17.3, 12.0 ppm; IR (neat): ν = 2952.7, 1734.2, 1672.6, 1244.7, 1004.8 cm^{-1}; HRMS m/z (ESI) calcd for $C_{27}H_{33}O_4$ $(M + H)^+$ 421.2373, found 421.2370; $[\alpha]_D^{21}$ = 95 (c = 0.1, ethyl acetate).

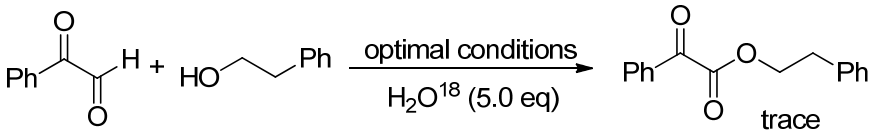


6

24) **(3R,5S,8R,9S,10S,13S,14S)-10,13-dimethyl-17-oxohexadecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-oxo-2-phenylacetate.** The reaction of CuBr (3.6 mg, 0.025 mmol), pyridine (10.0 mg, 0.125 mmol), 2-oxo-2-phenylacetaldehyde hydrate **1a** (38 mg, 0.25 mmol) and cholesterol (145 mg, 0.375 mmol) in toluene (2 mL), at 90 °C, under Air (1 atm), for 18 h, afforded 91 mg (70%) of **6**. **6**: white solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, *J* = 8.4 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 2H), 5.45 (d, *J* = 4.0 Hz, 1H), 4.98-4.90 (m,

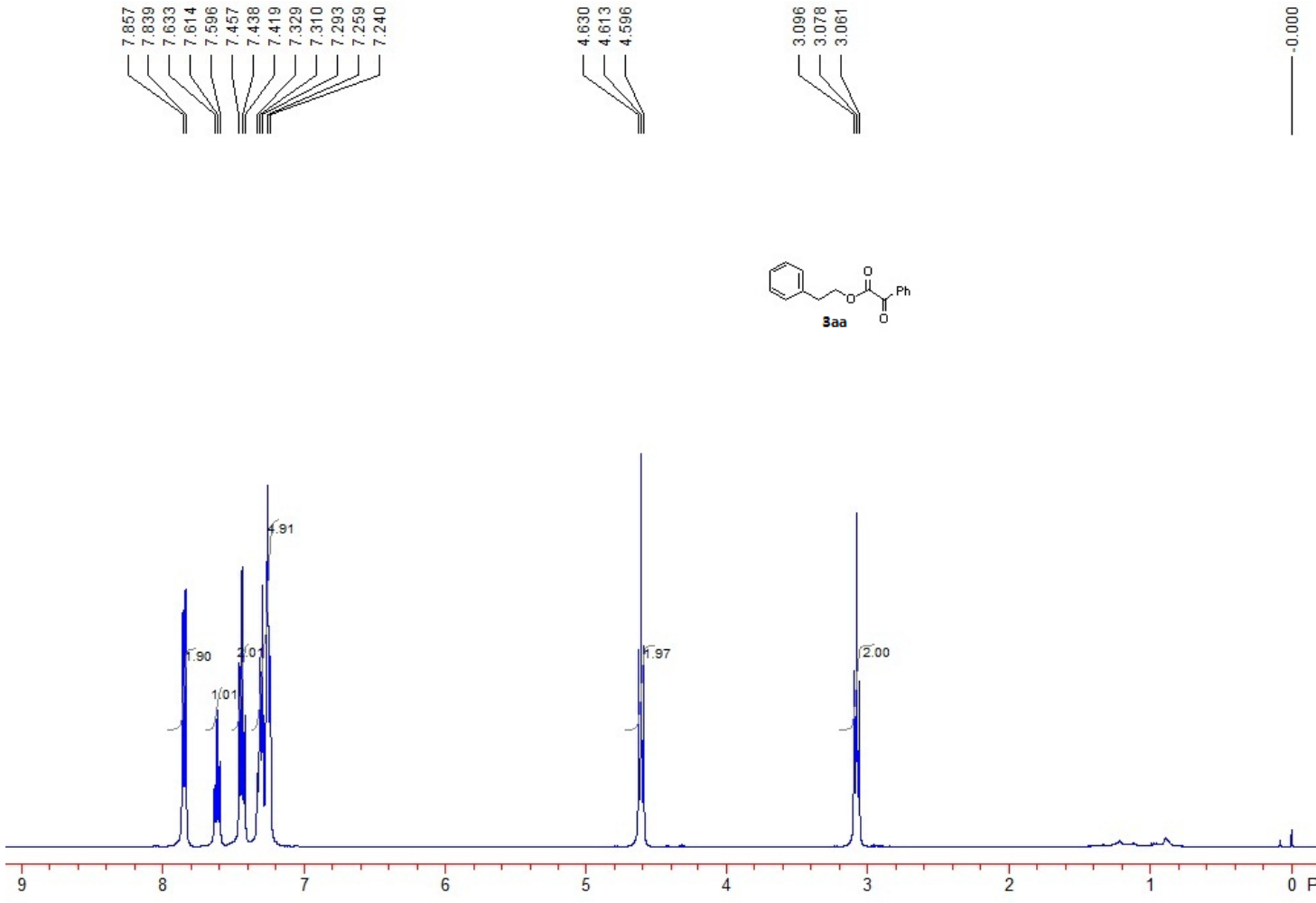
1H), 2.50 (d, *J* = 8.0 Hz, 2H), 2.04-1.72 (m, 6H), 1.60-1.43 (m, 6H), 1.30-1.08 (m, 11H), 1.04-0.96 (m, 6H), 0.88-0.85 (m, 9H), 0.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ =186.7, 163.5, 139.0, 134.8, 132.5, 130.0, 128.9, 123.4, 76.6, 56.7, 56.1, 50.0, 42.3, 39.7, 39.5, 37.9, 36.9, 36.6, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.6, 24.3, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8 ppm; IR (neat): ν = 3453.1, 2922.5, 1714.3, 1451.9, 1209.8 cm^{-1}; HRMS m/z (ESI) calcd for $C_{35}H_{50}NaO_3$ (M + Na)$^+$ 541.3652, found 541.3654. $[\alpha]_D^{21}$ = -9 (c = 0.1, ethyl acetate).

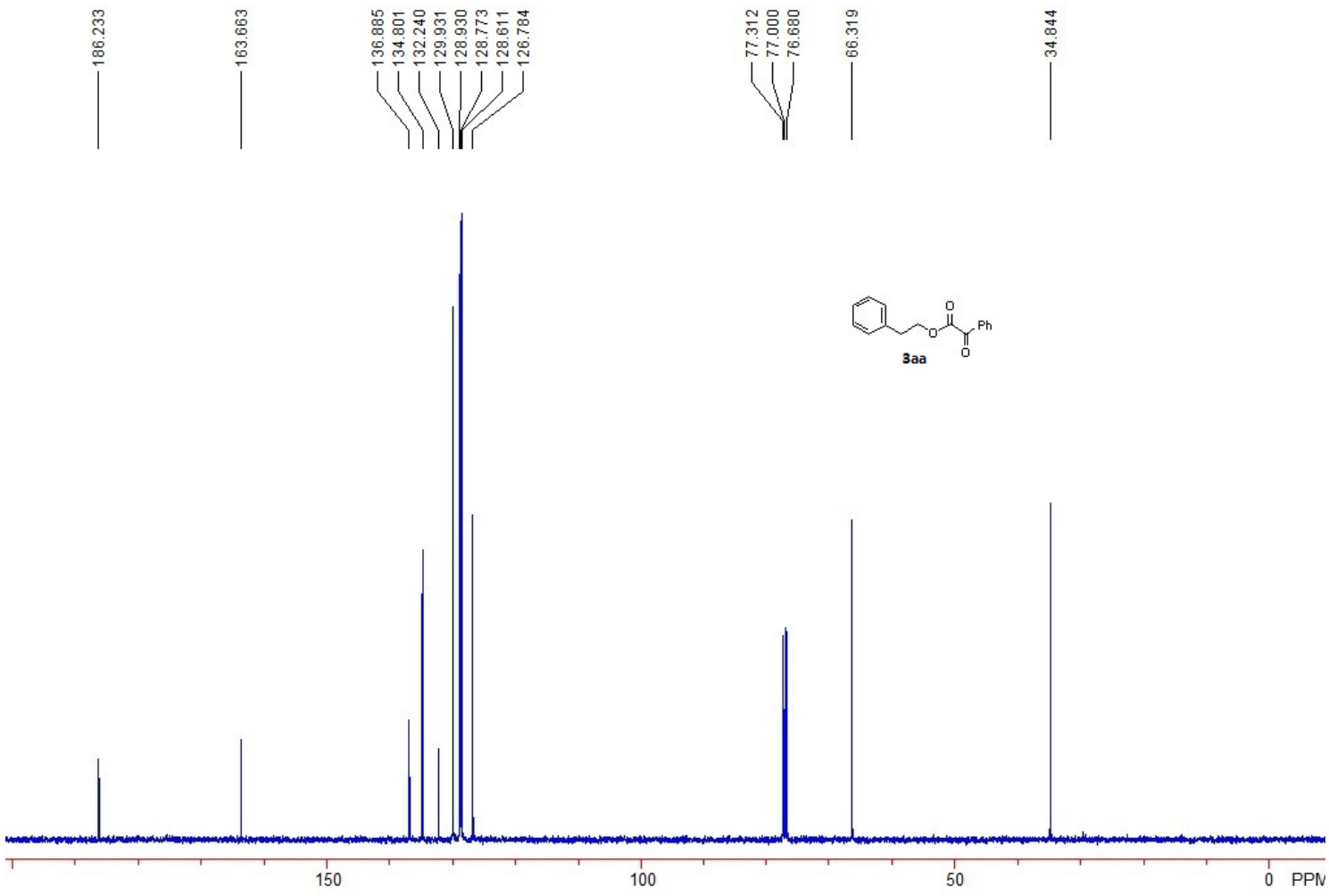
Mechanistic study:

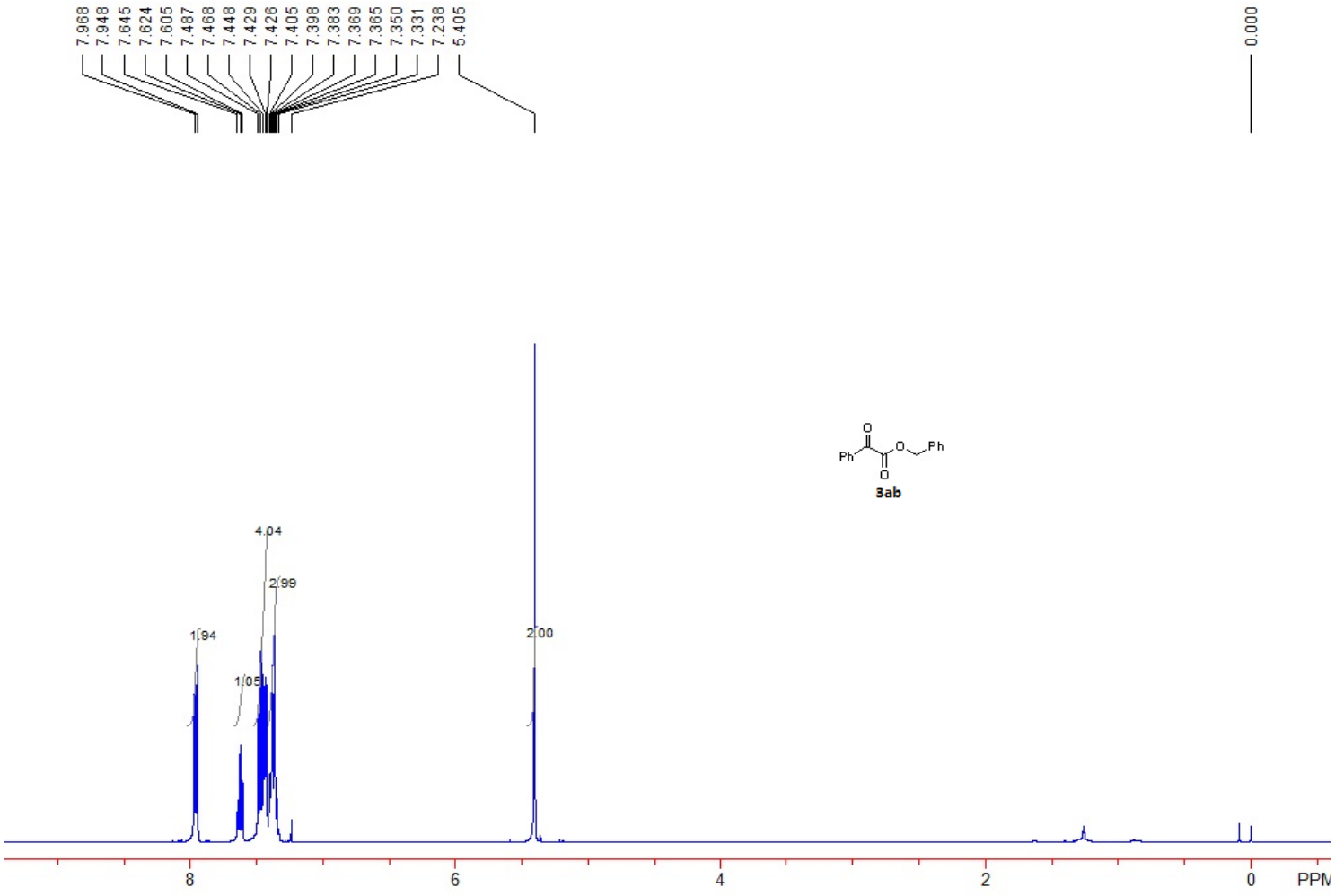


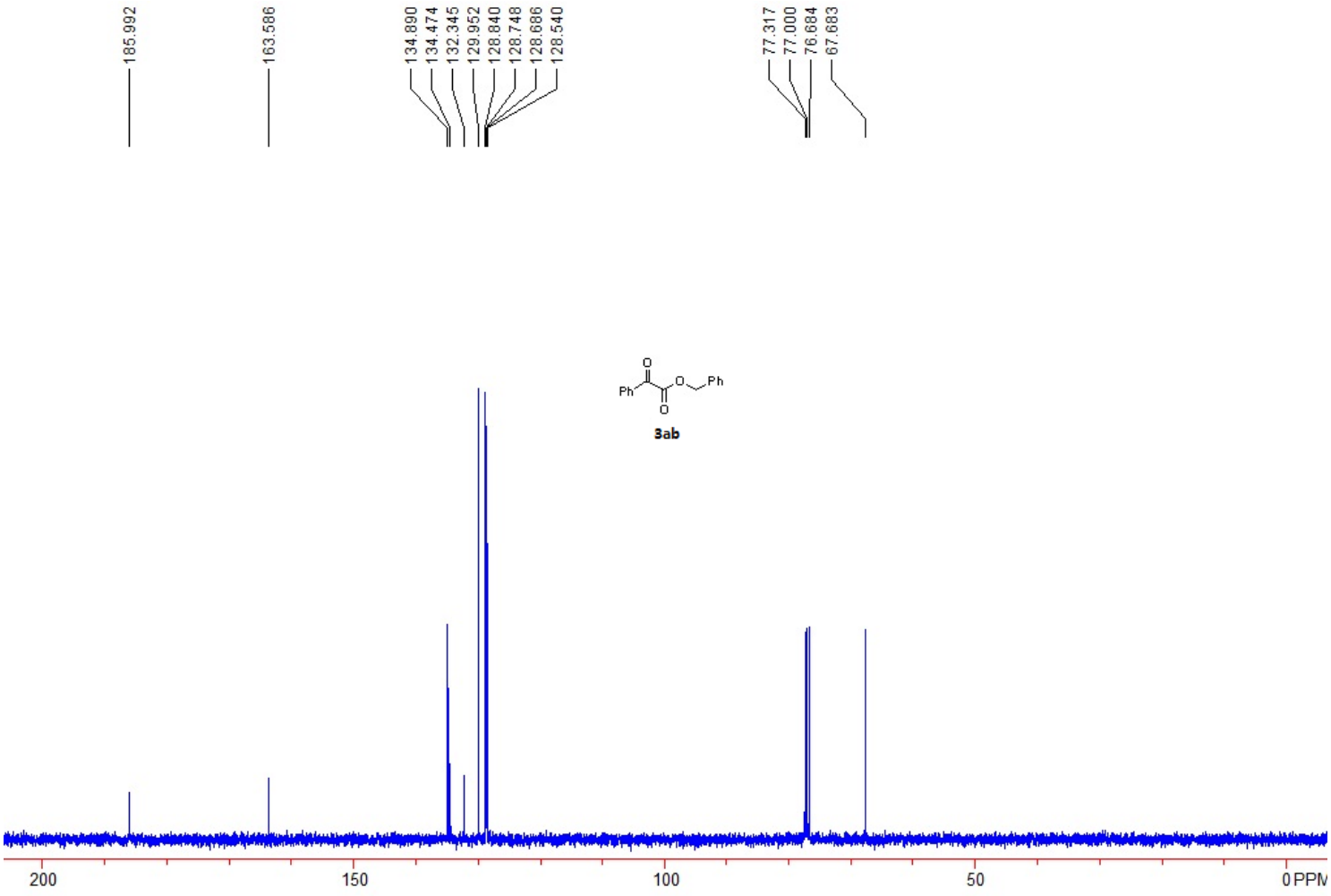
Reference:

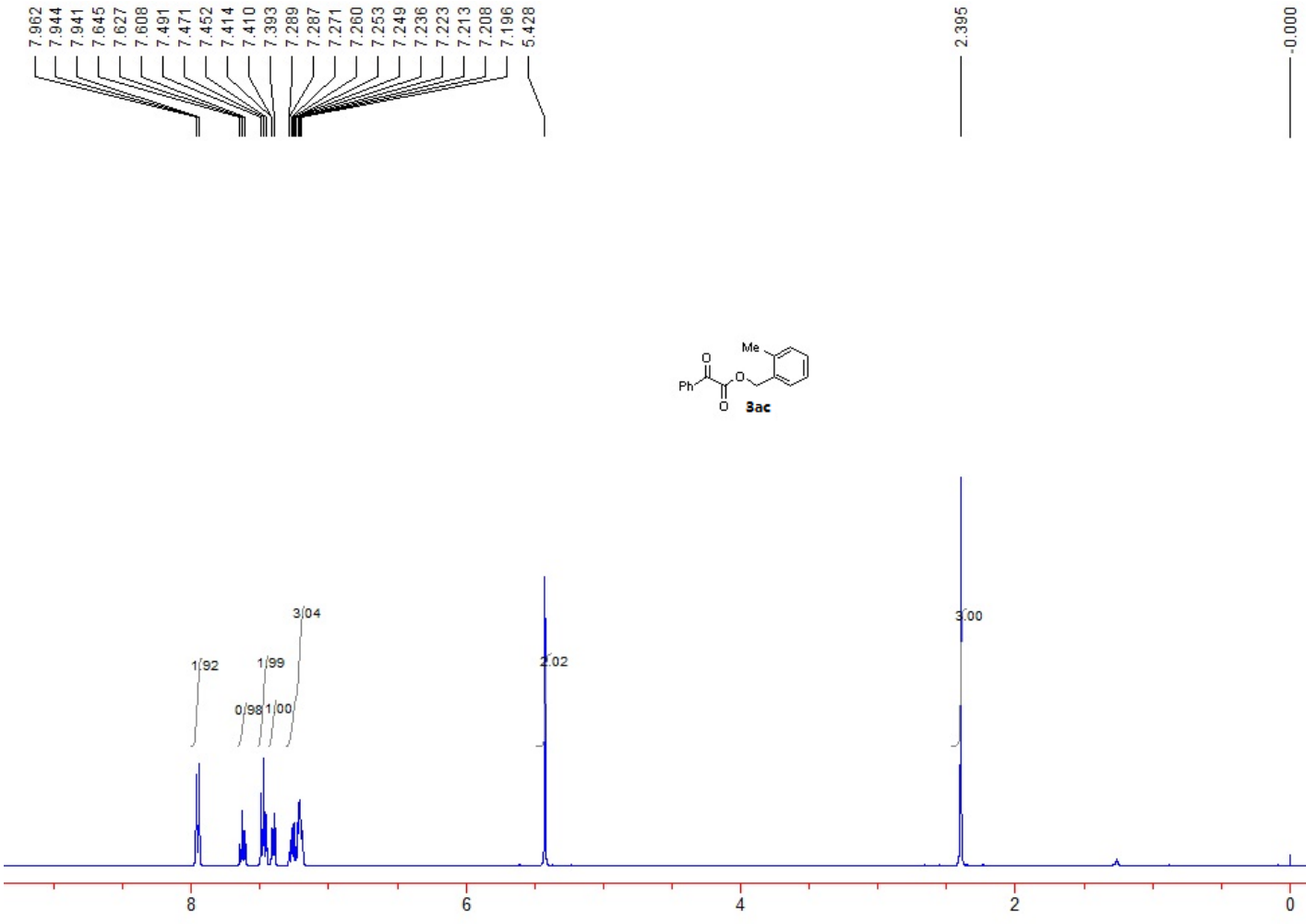
1. C. Zhang, P. Feng and N. Jiao, *J. Am. Chem. Soc.* 2013, **135**, 15257.

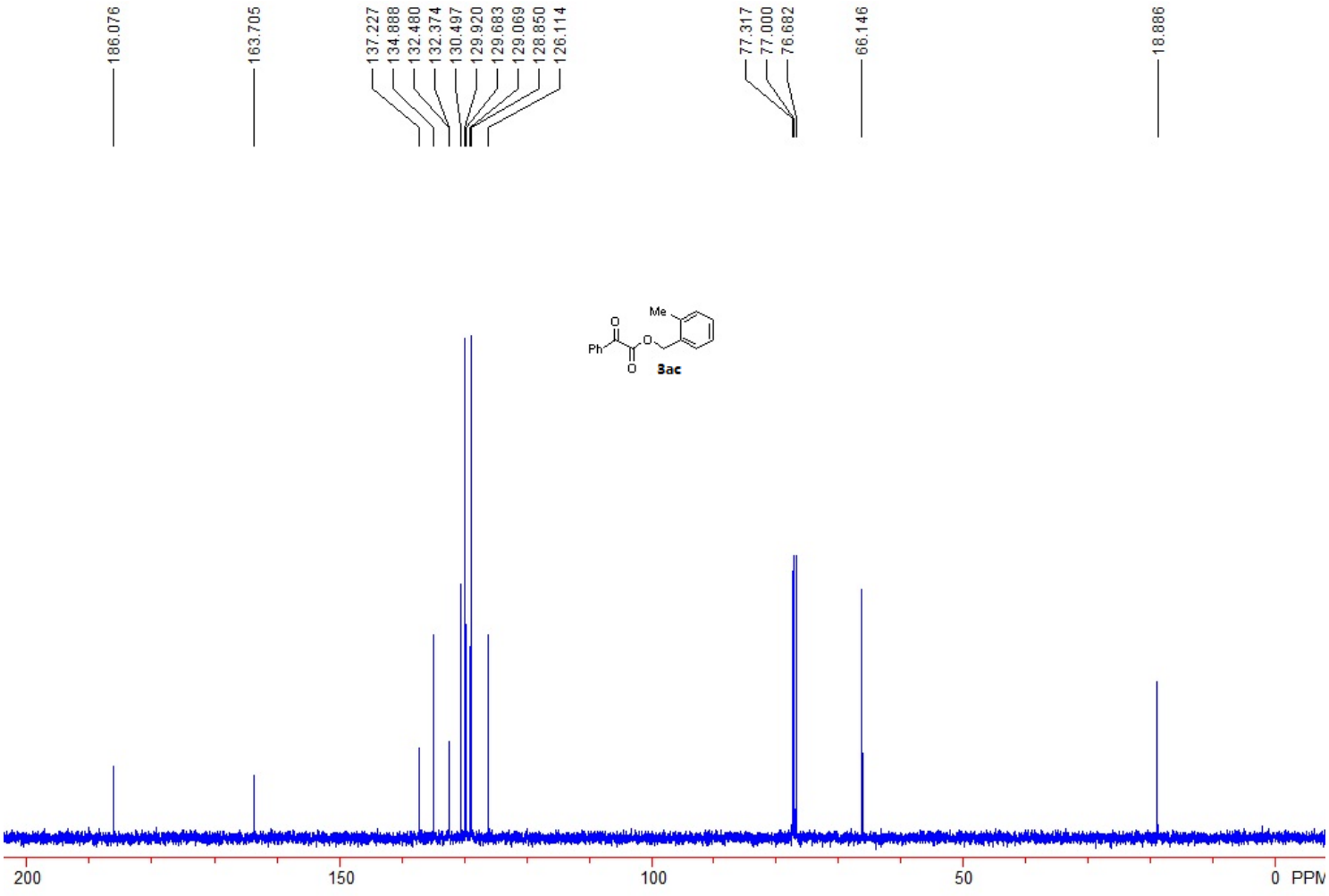


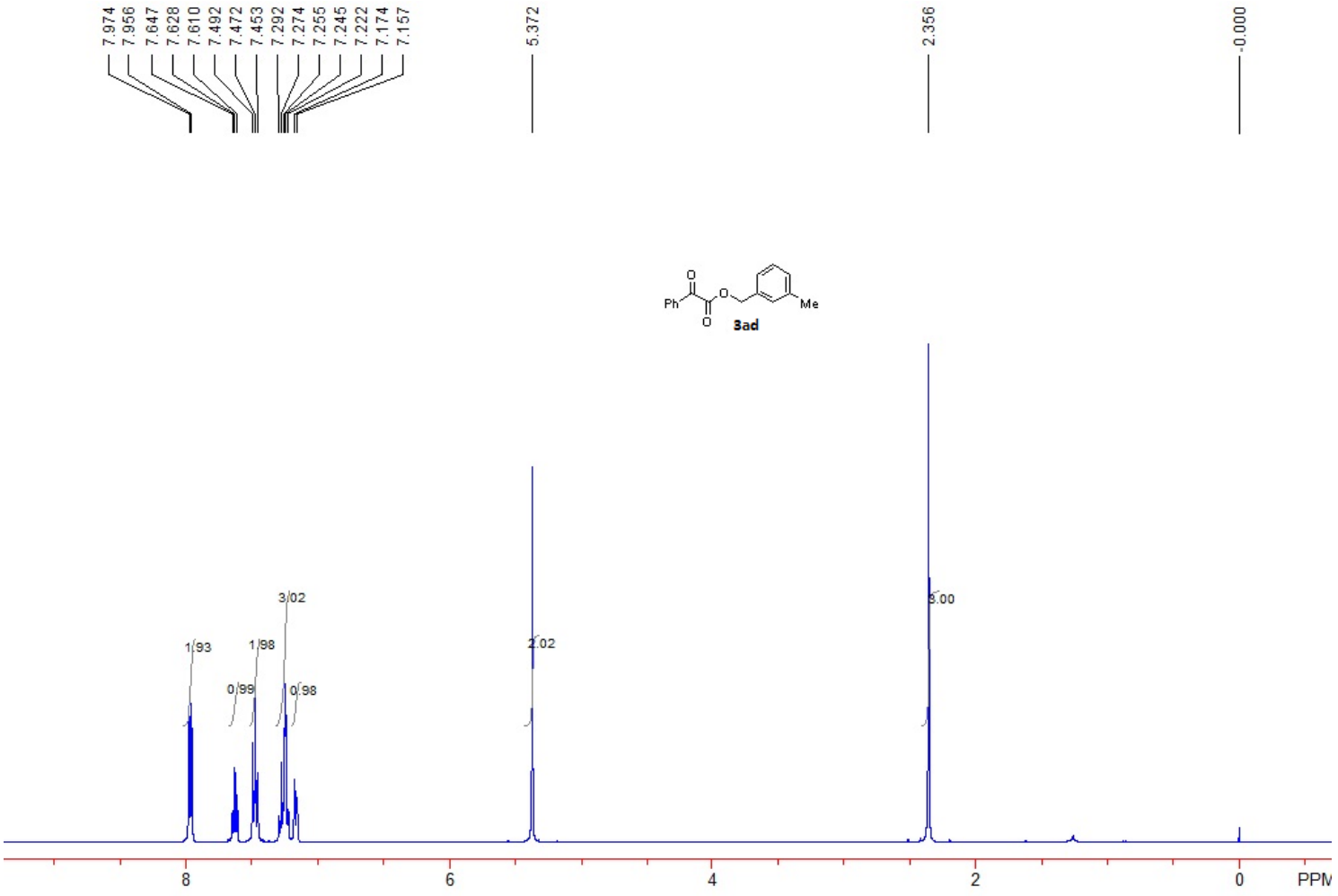


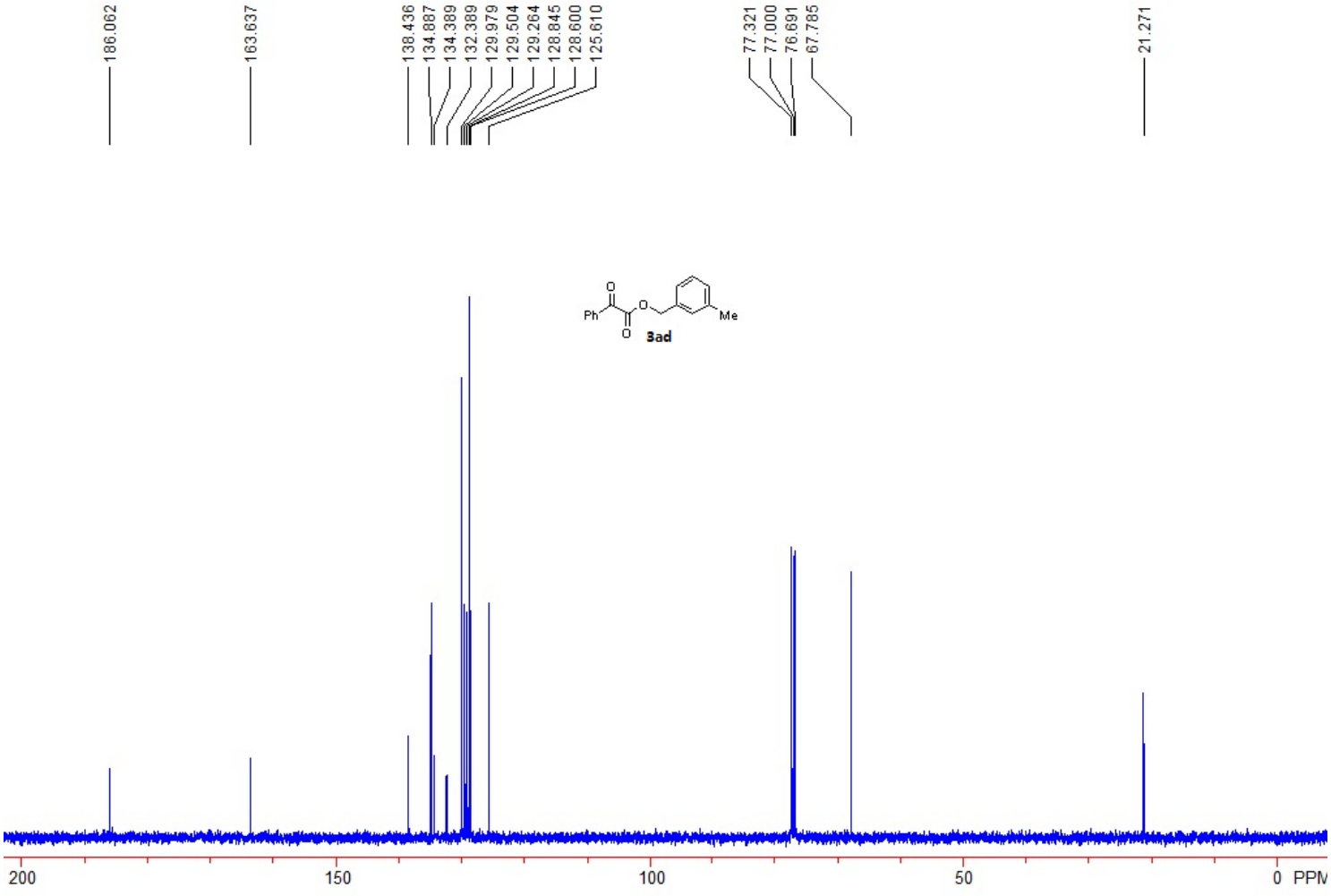


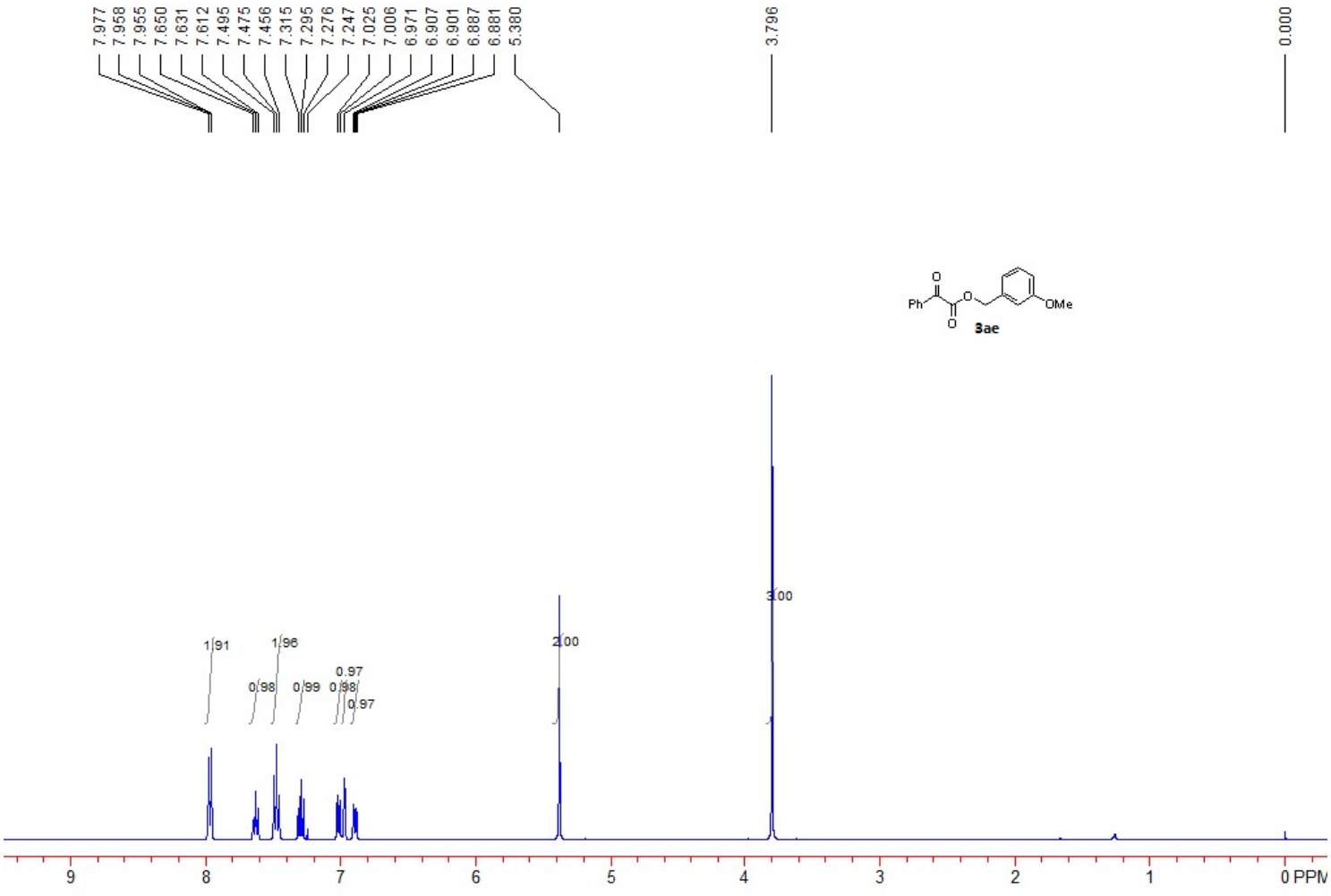


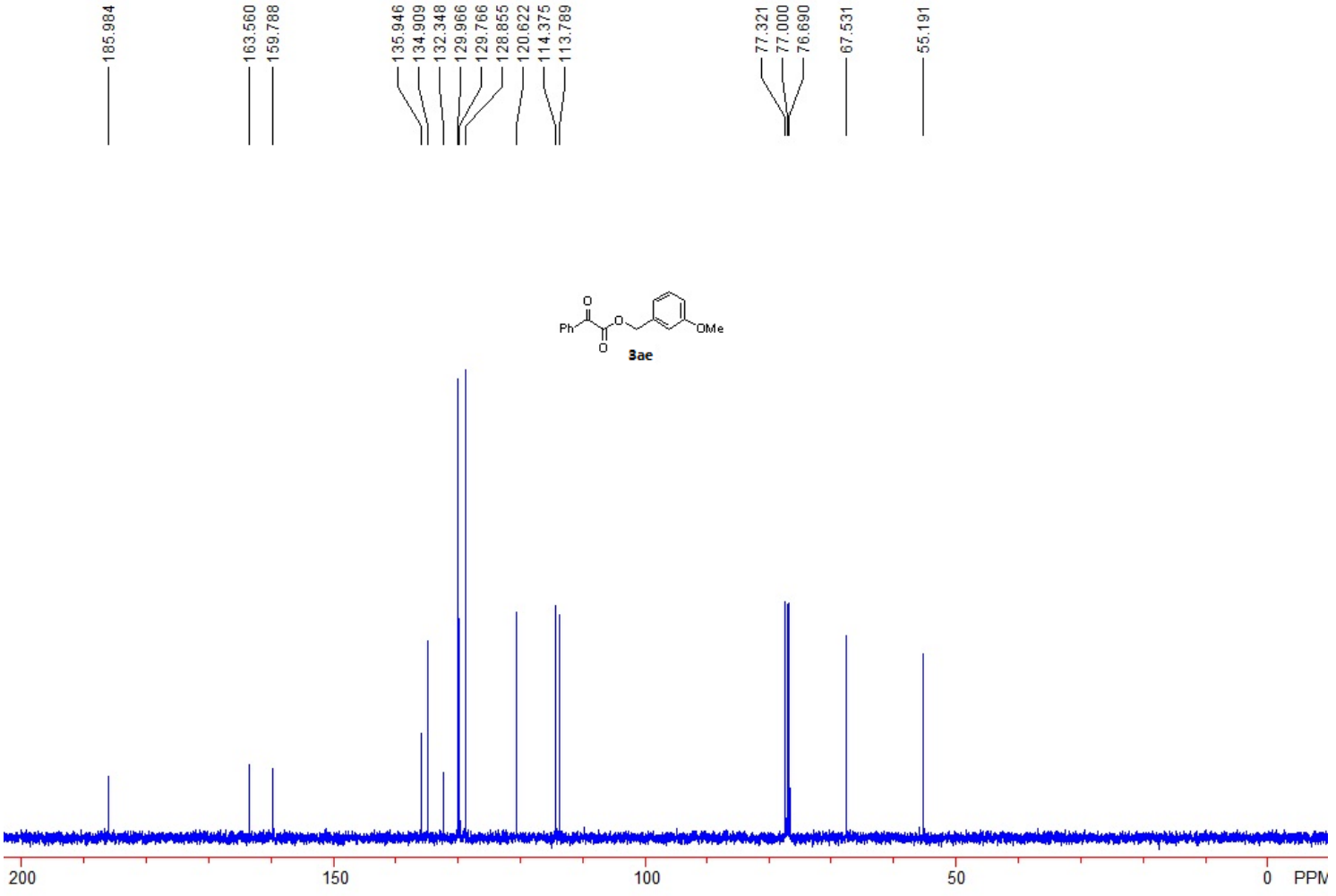


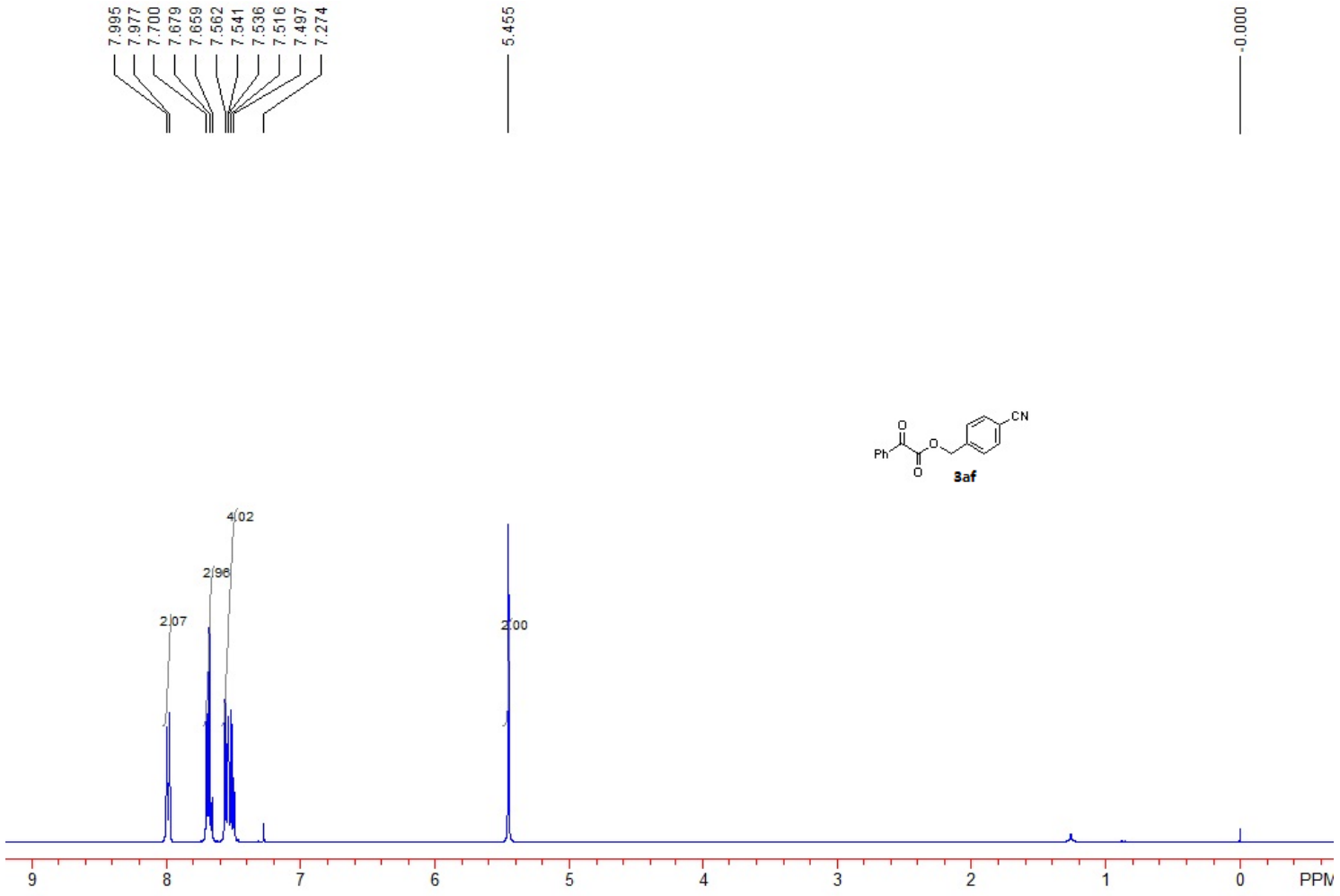


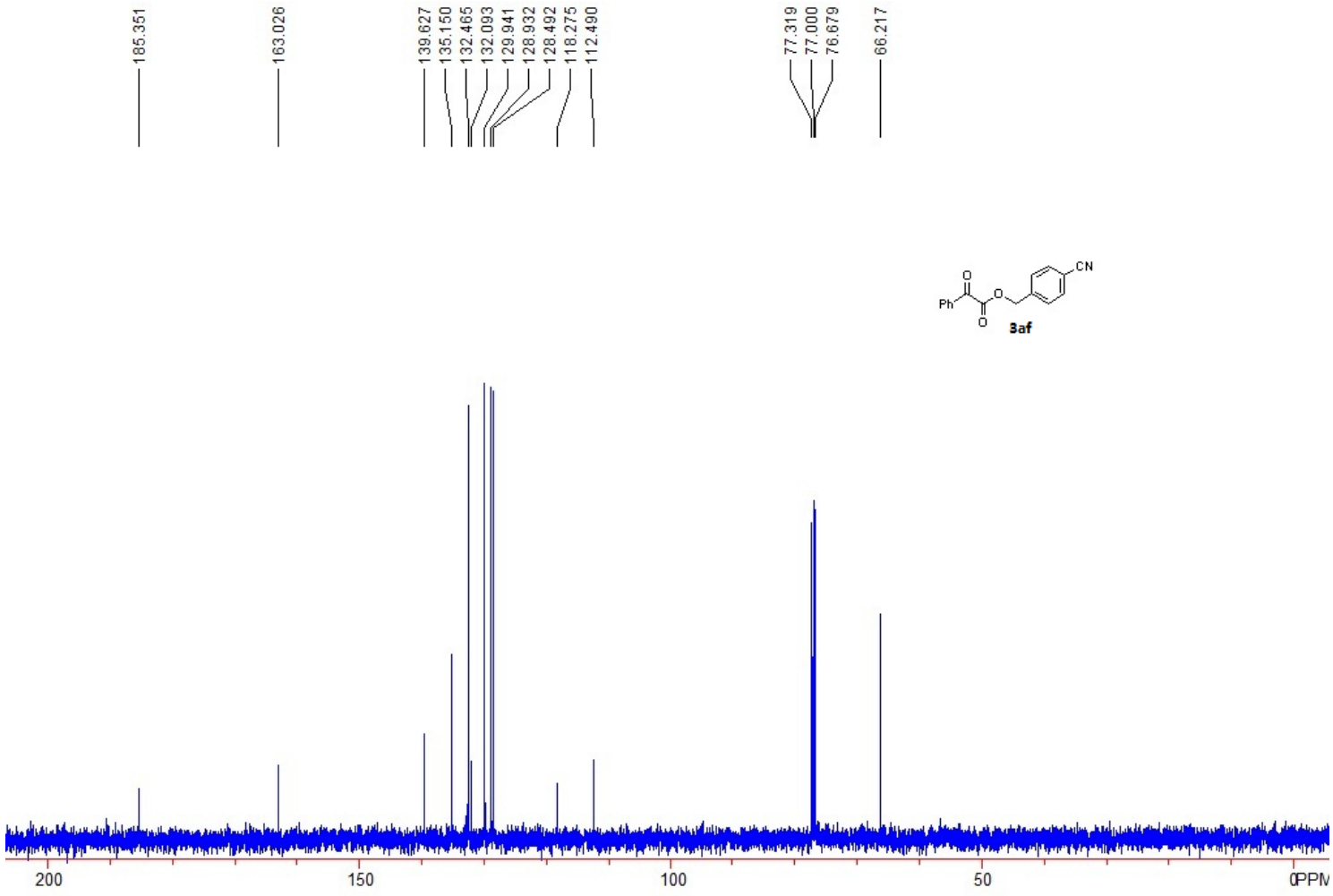


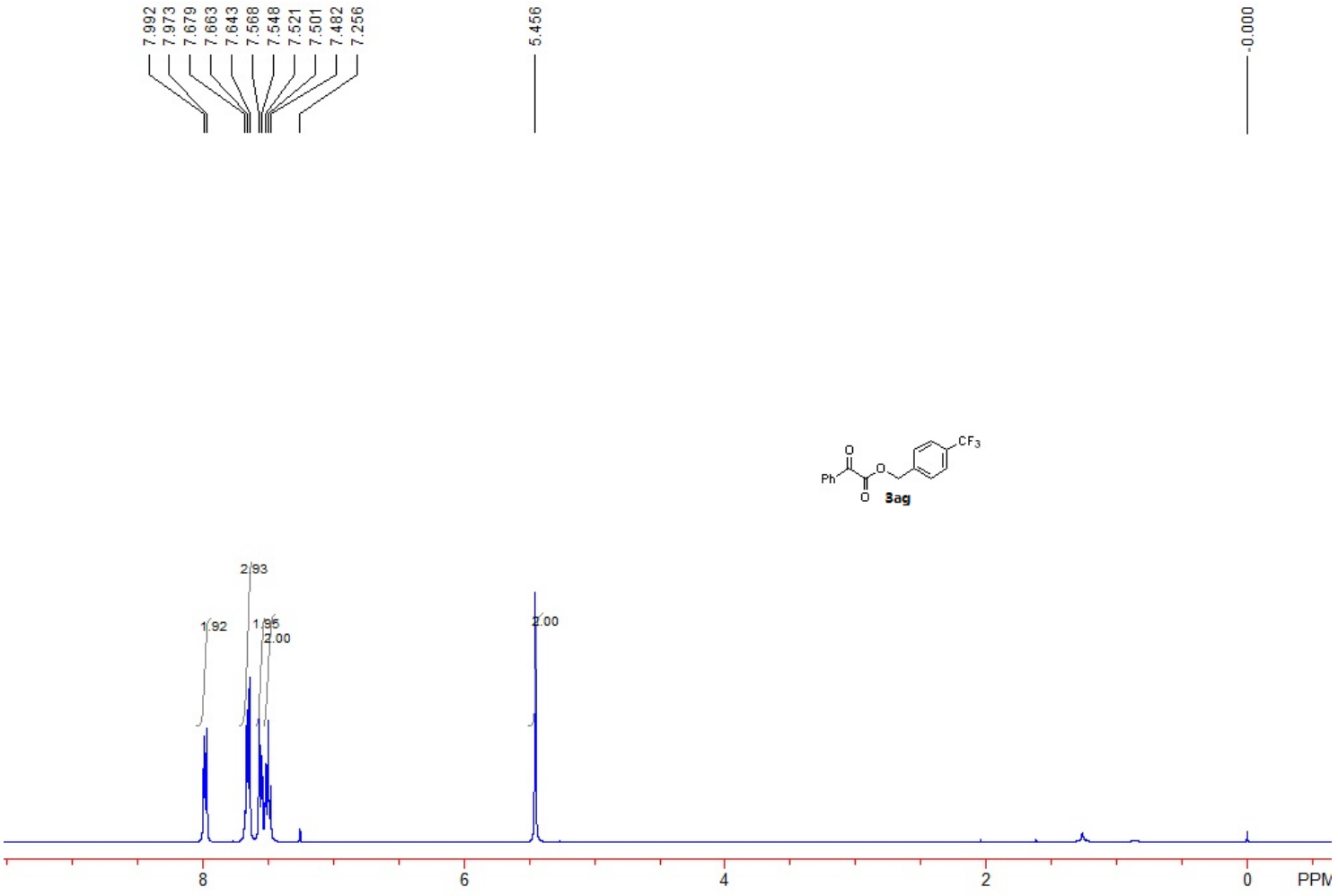


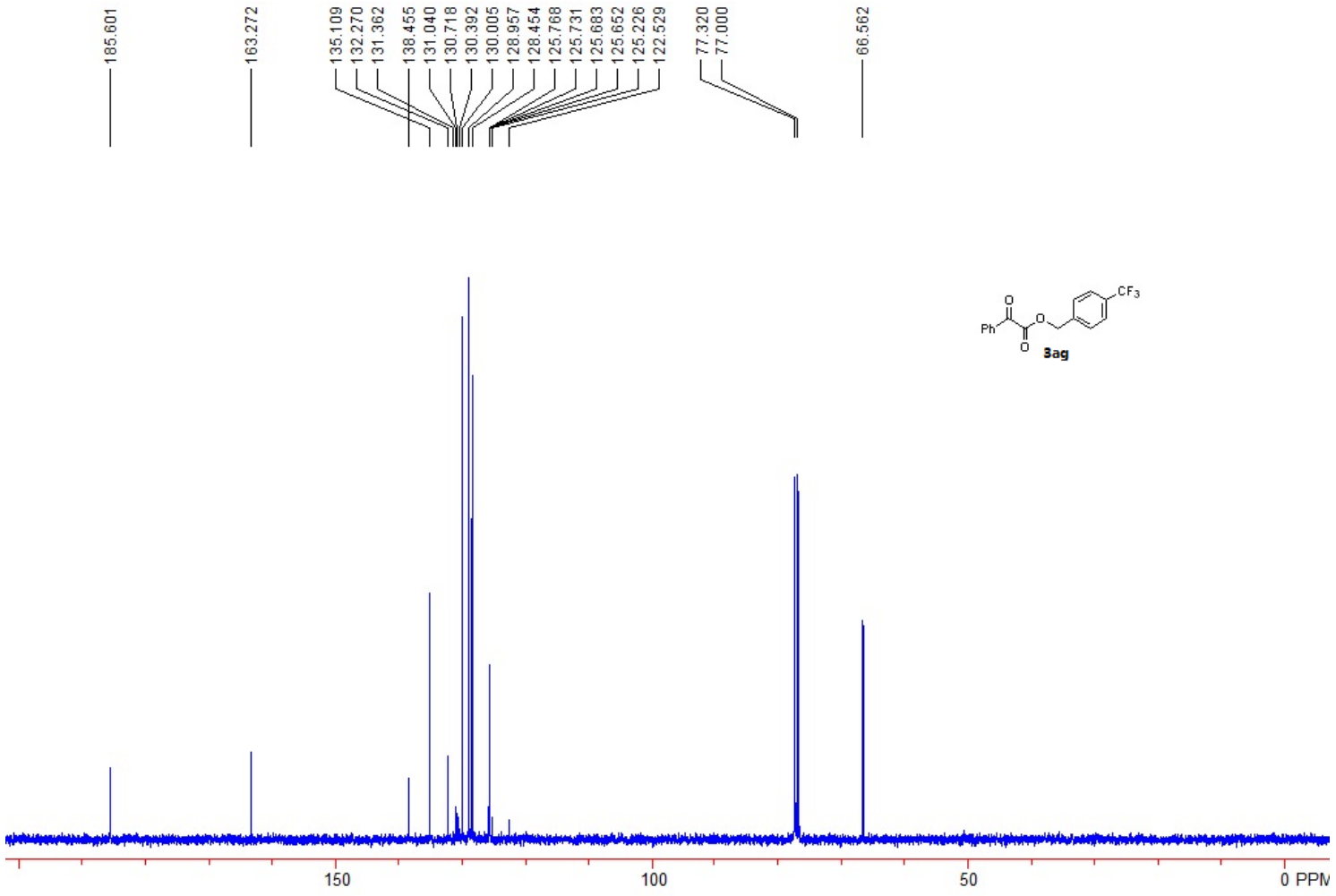


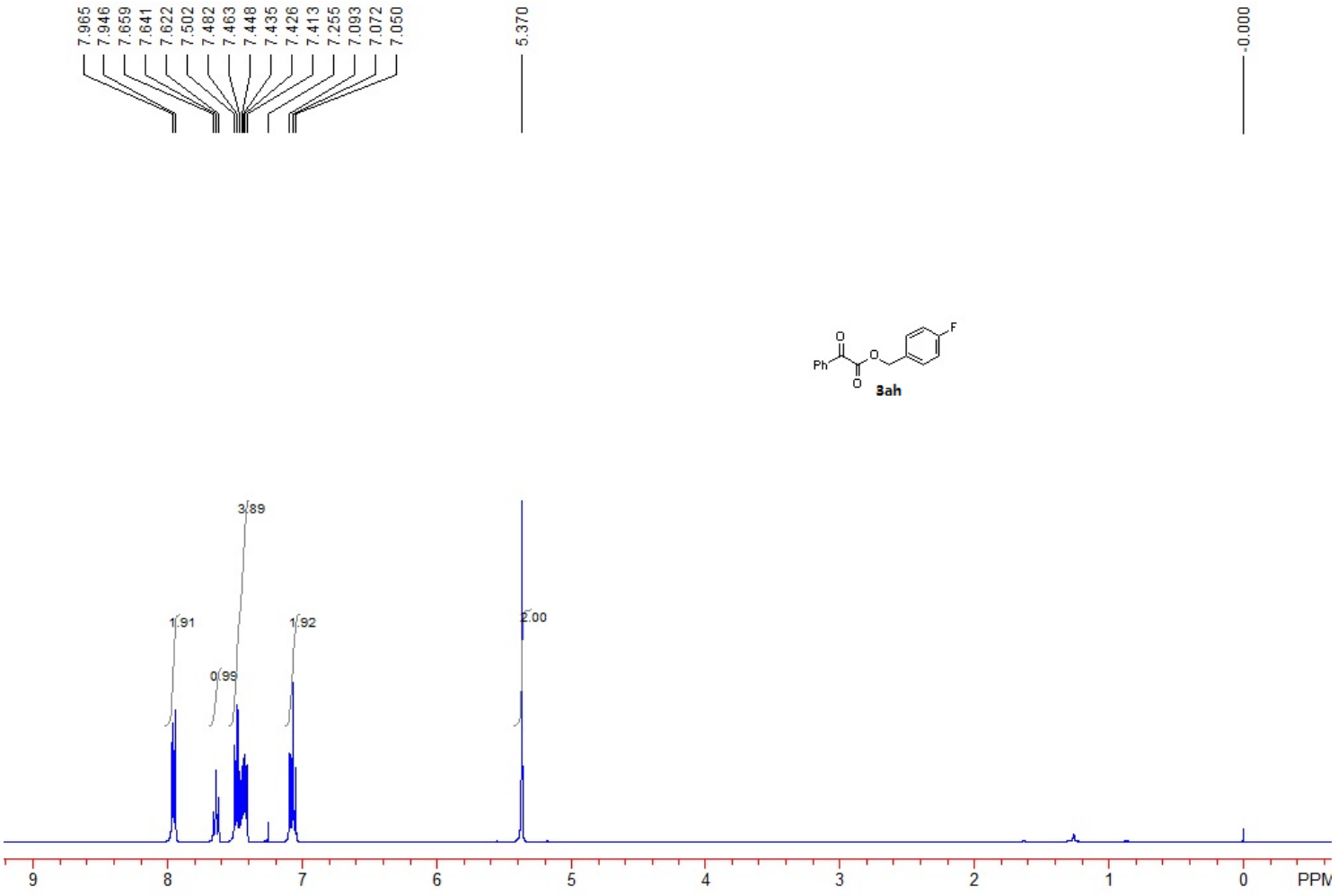


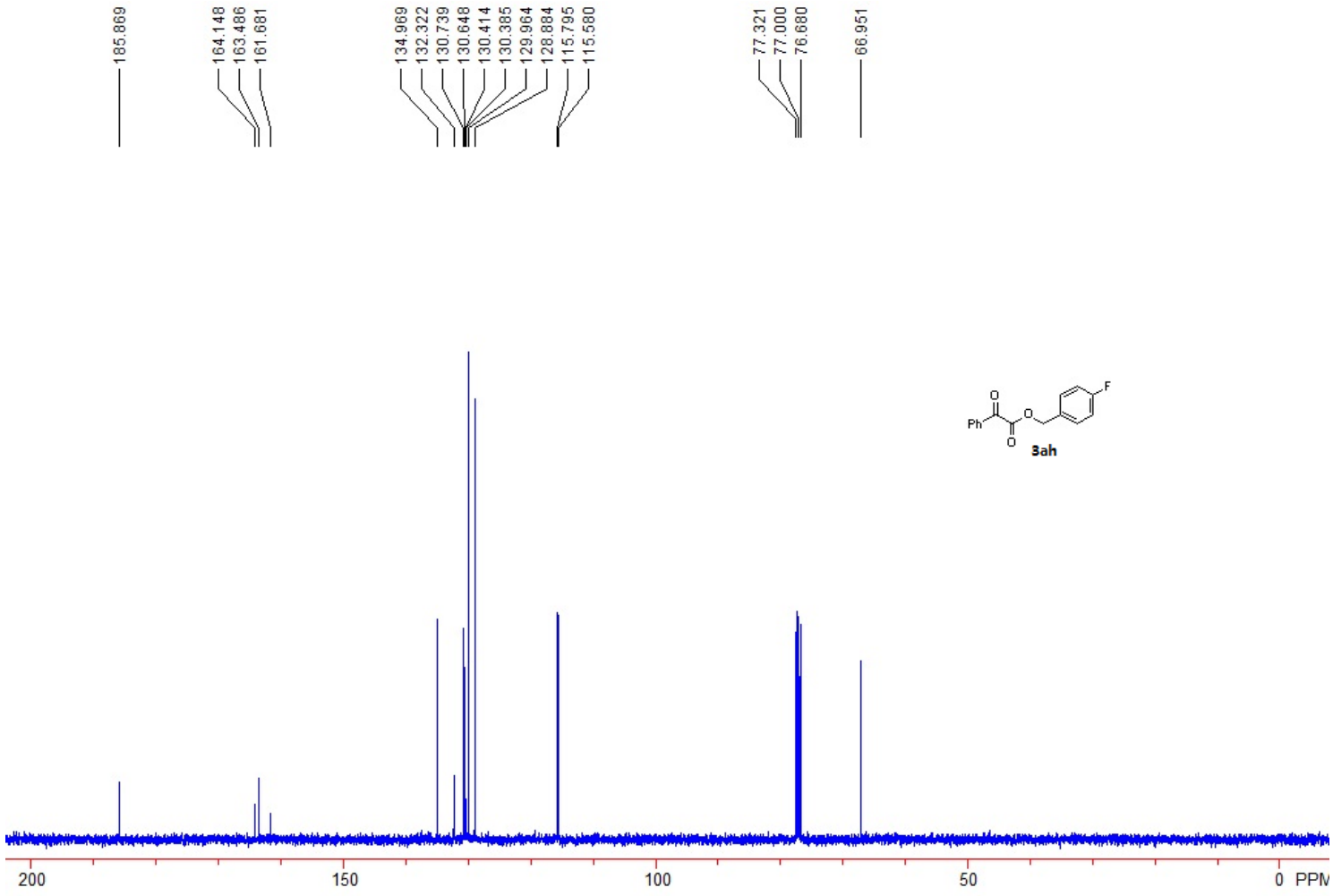


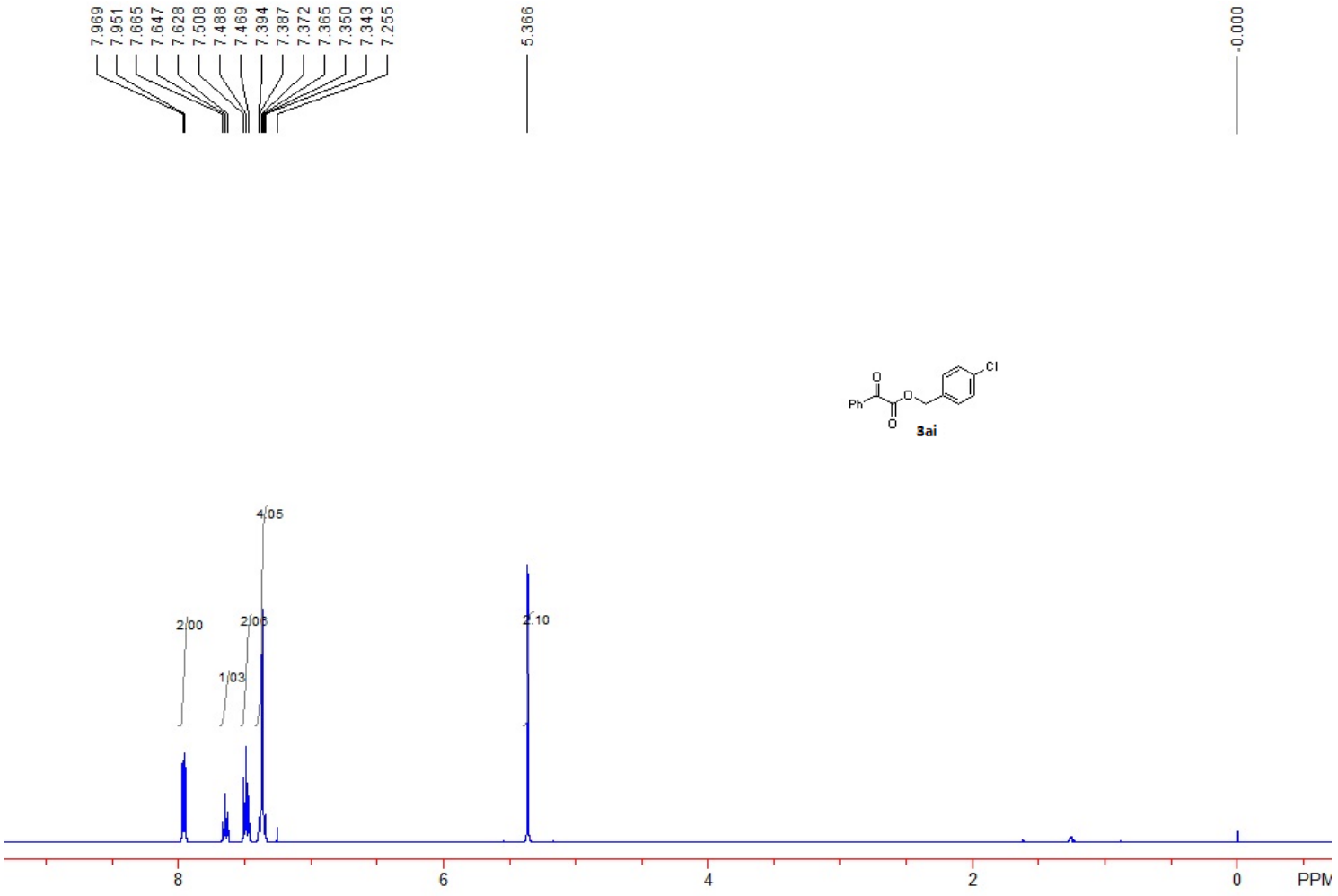


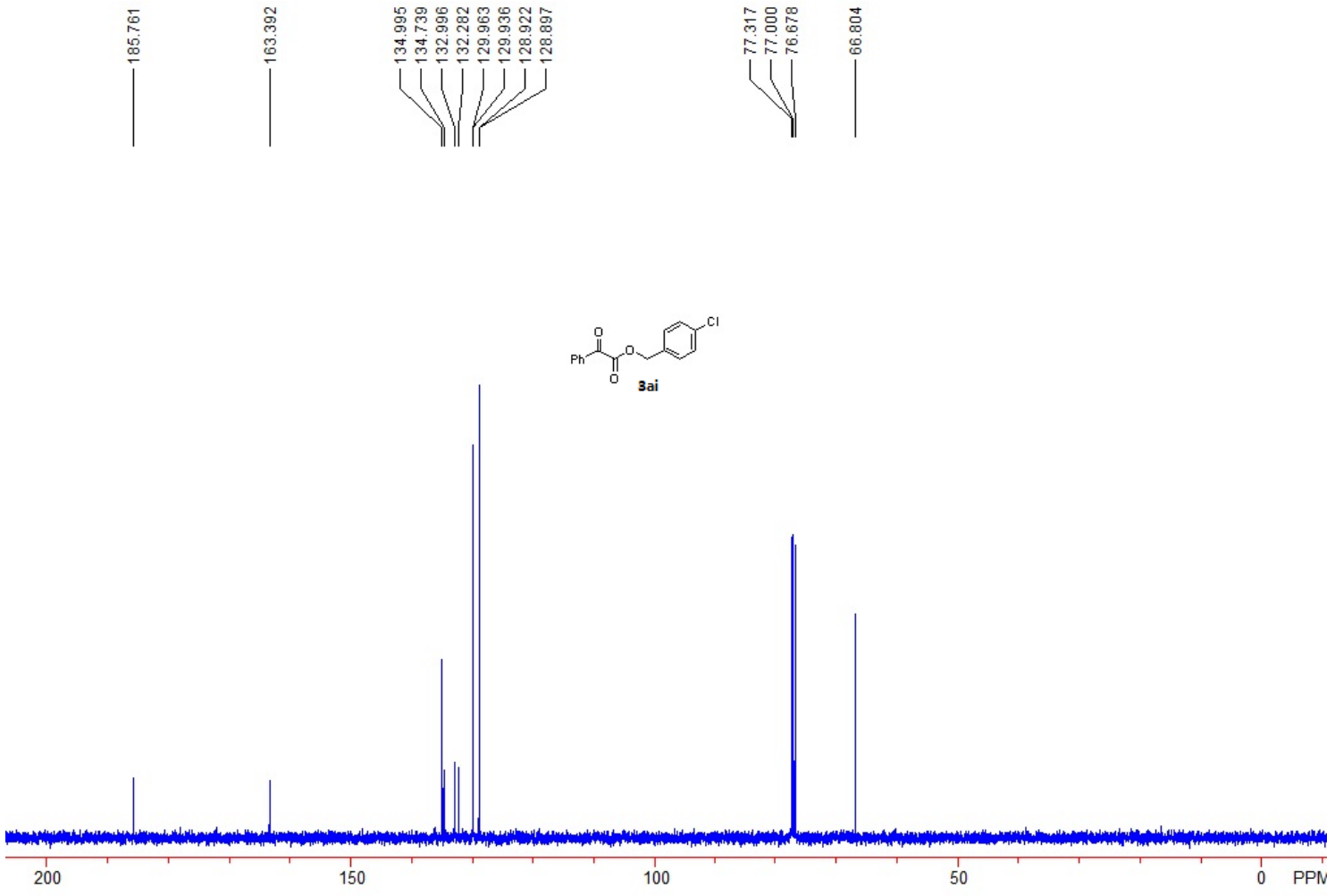


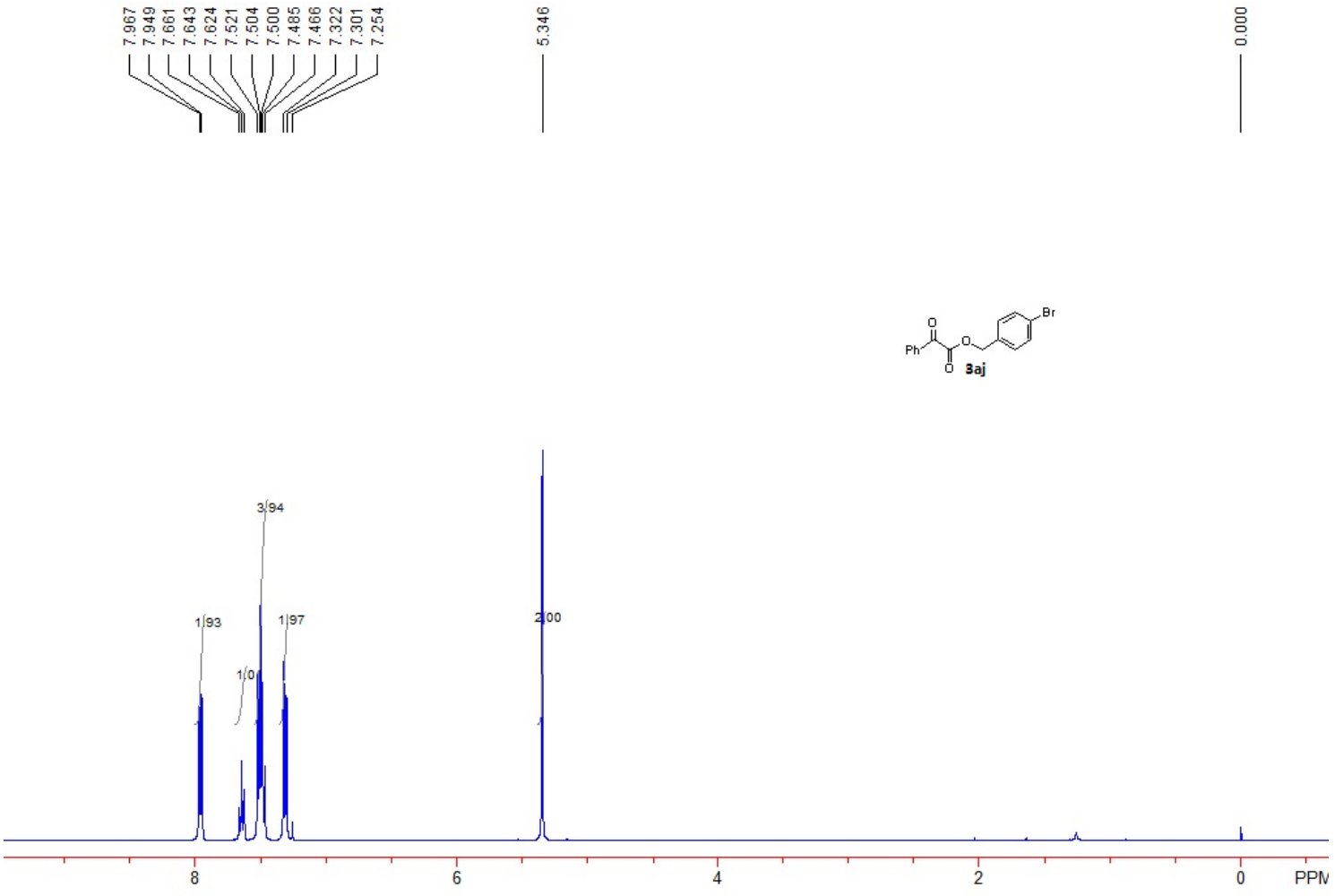


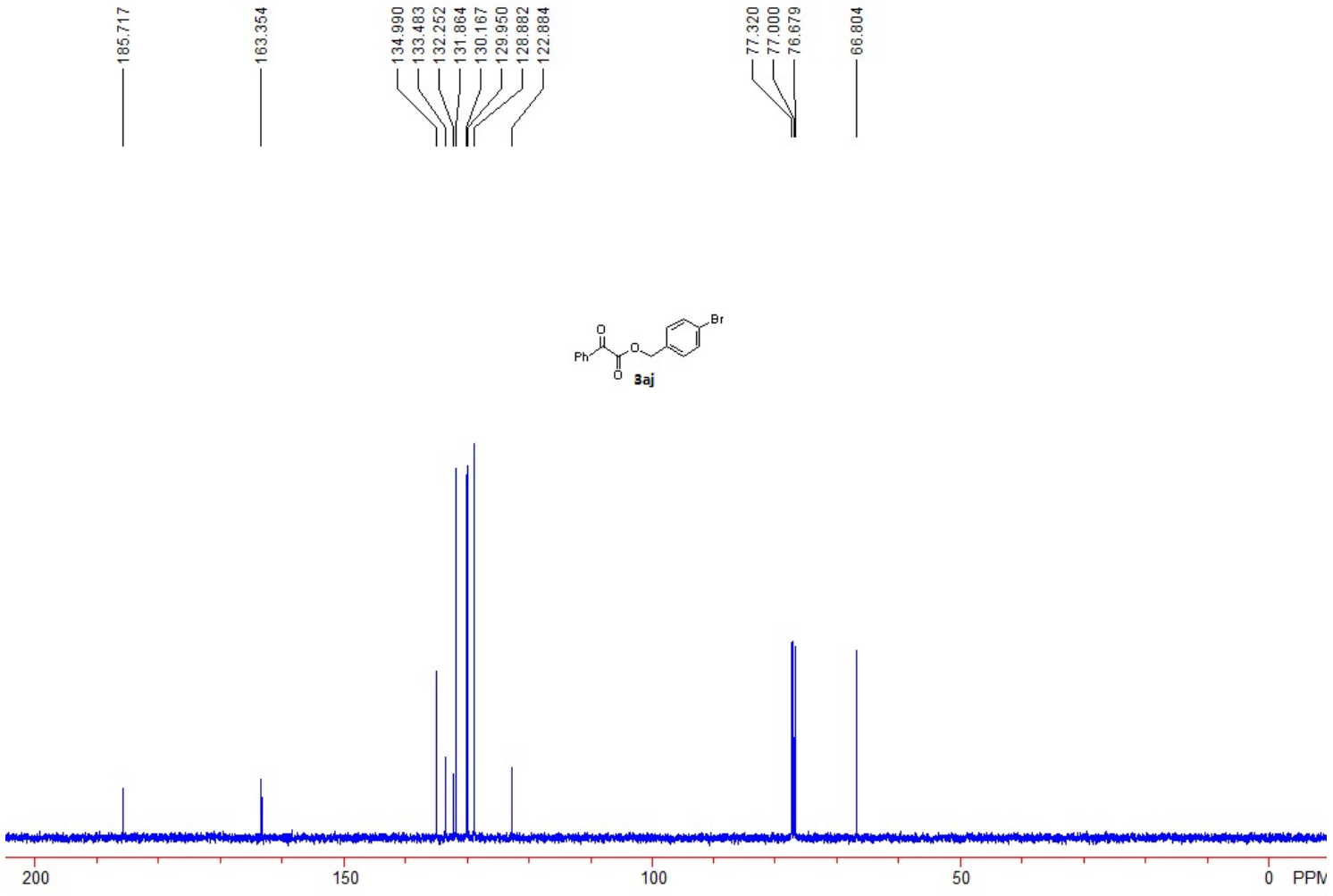


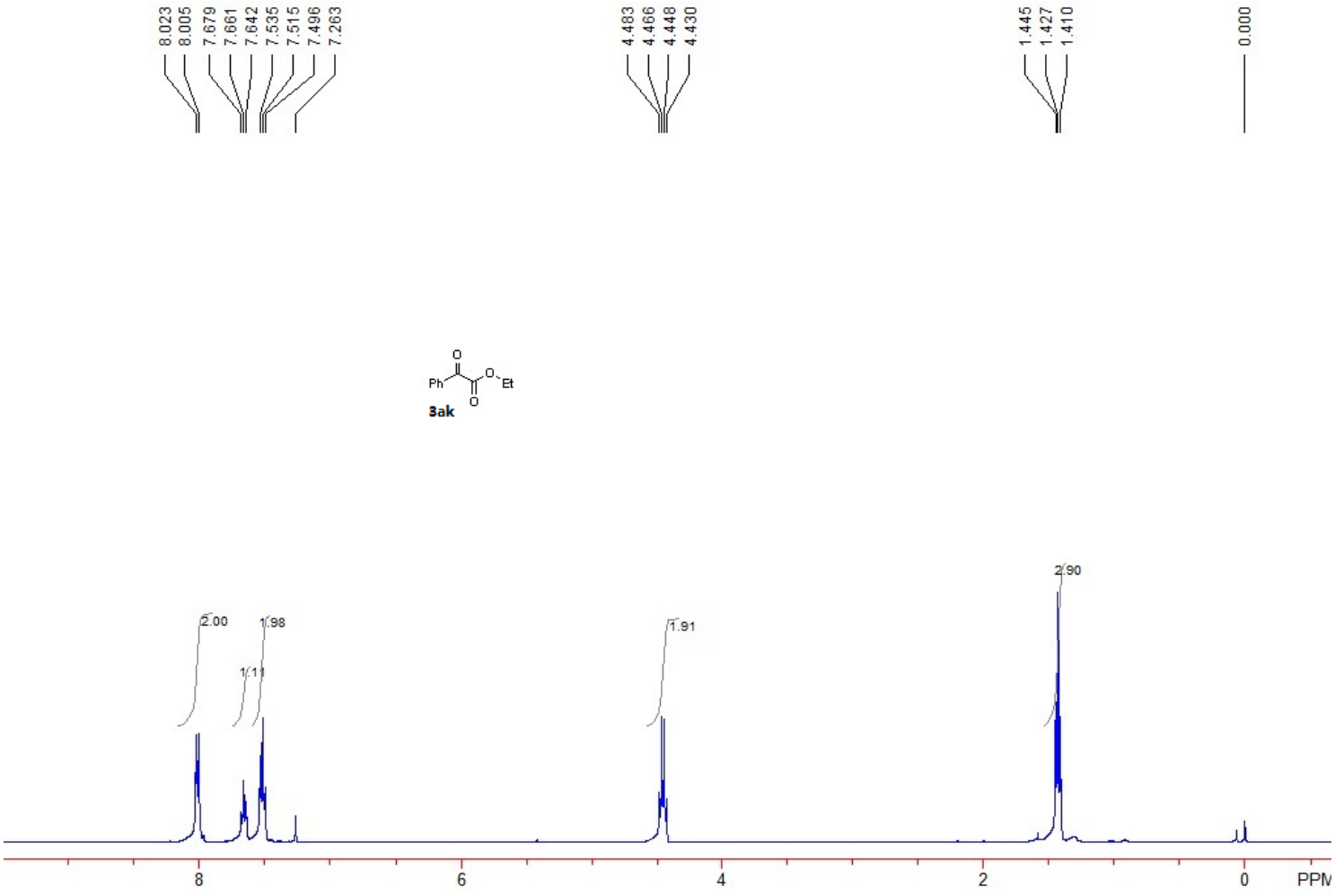


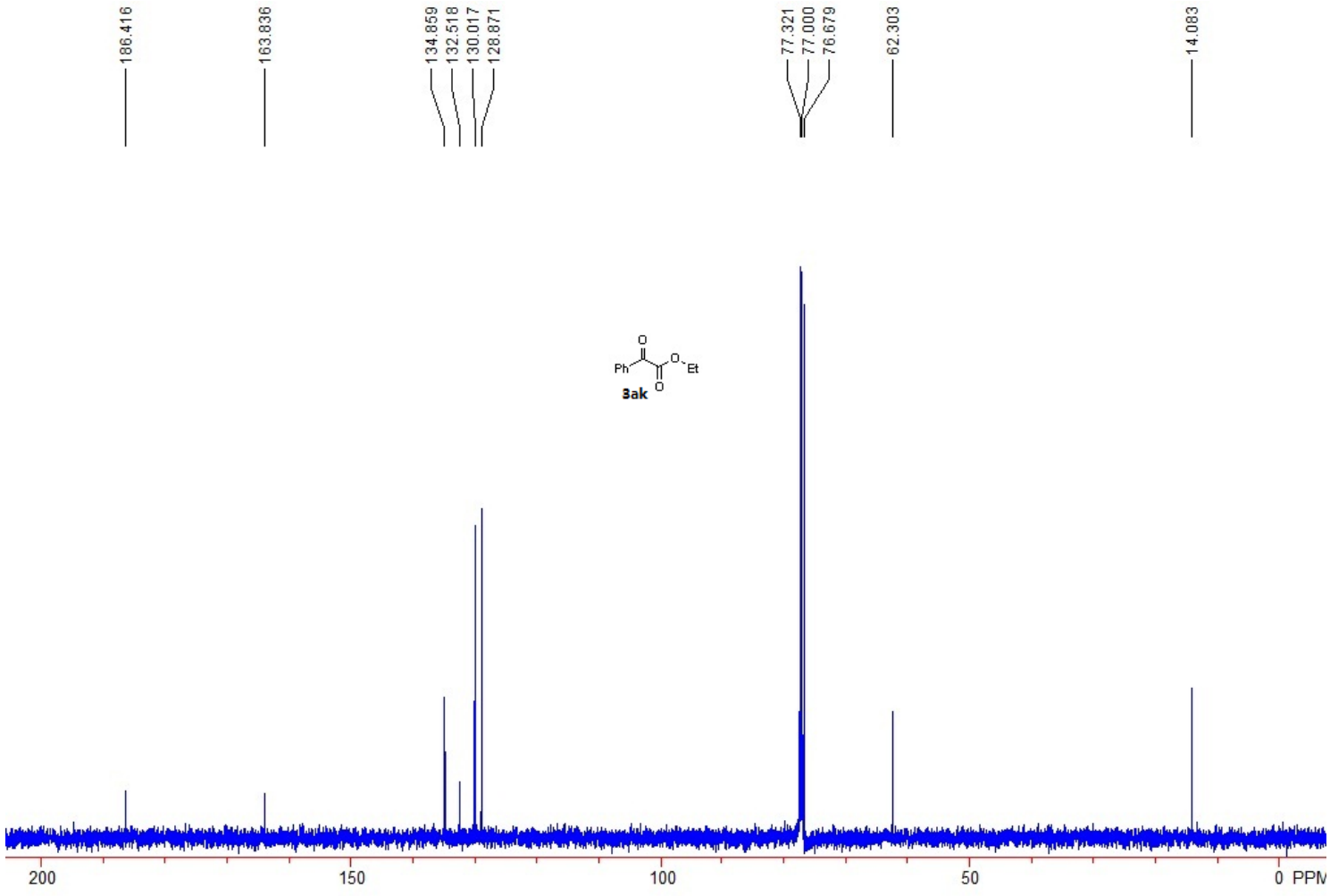


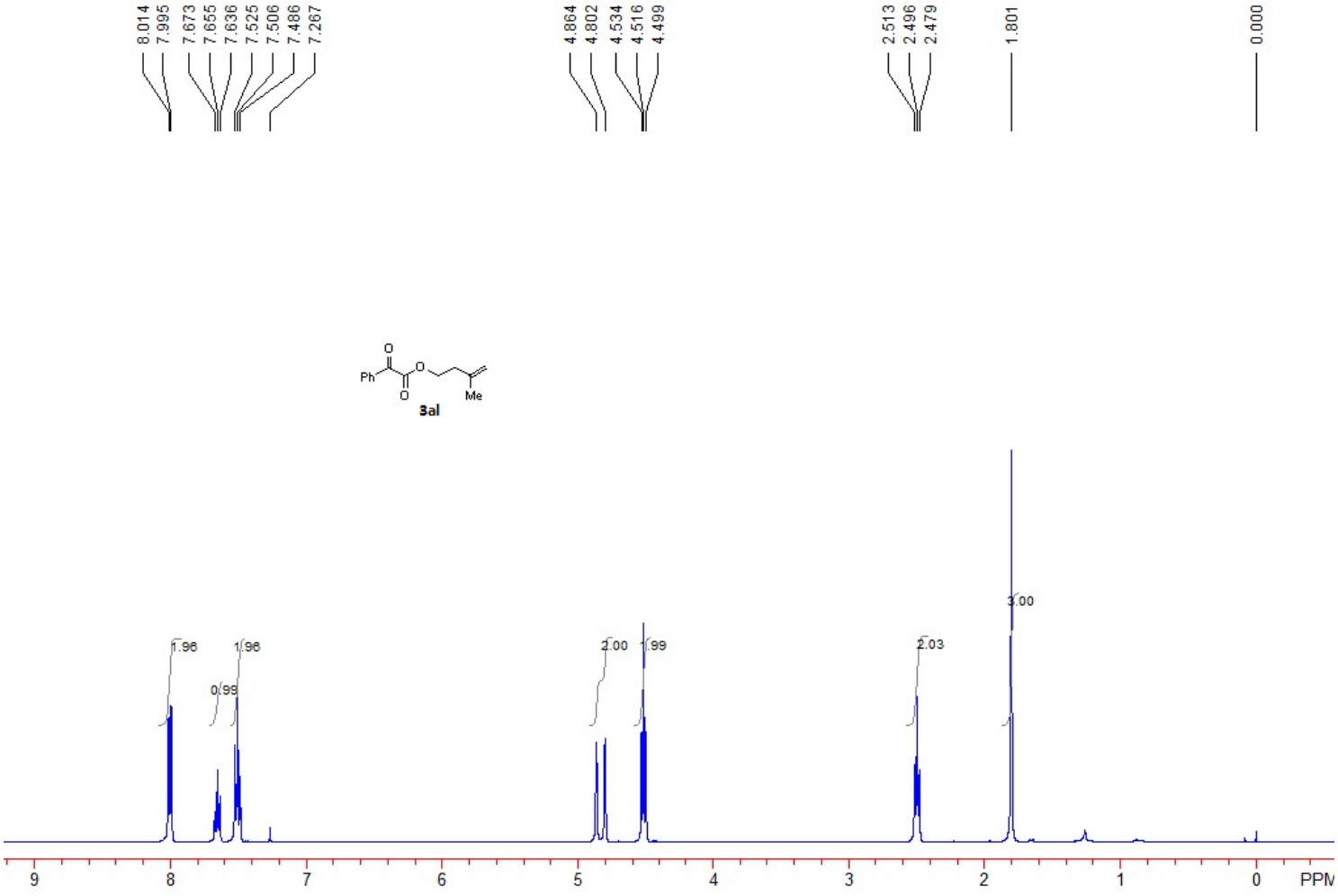


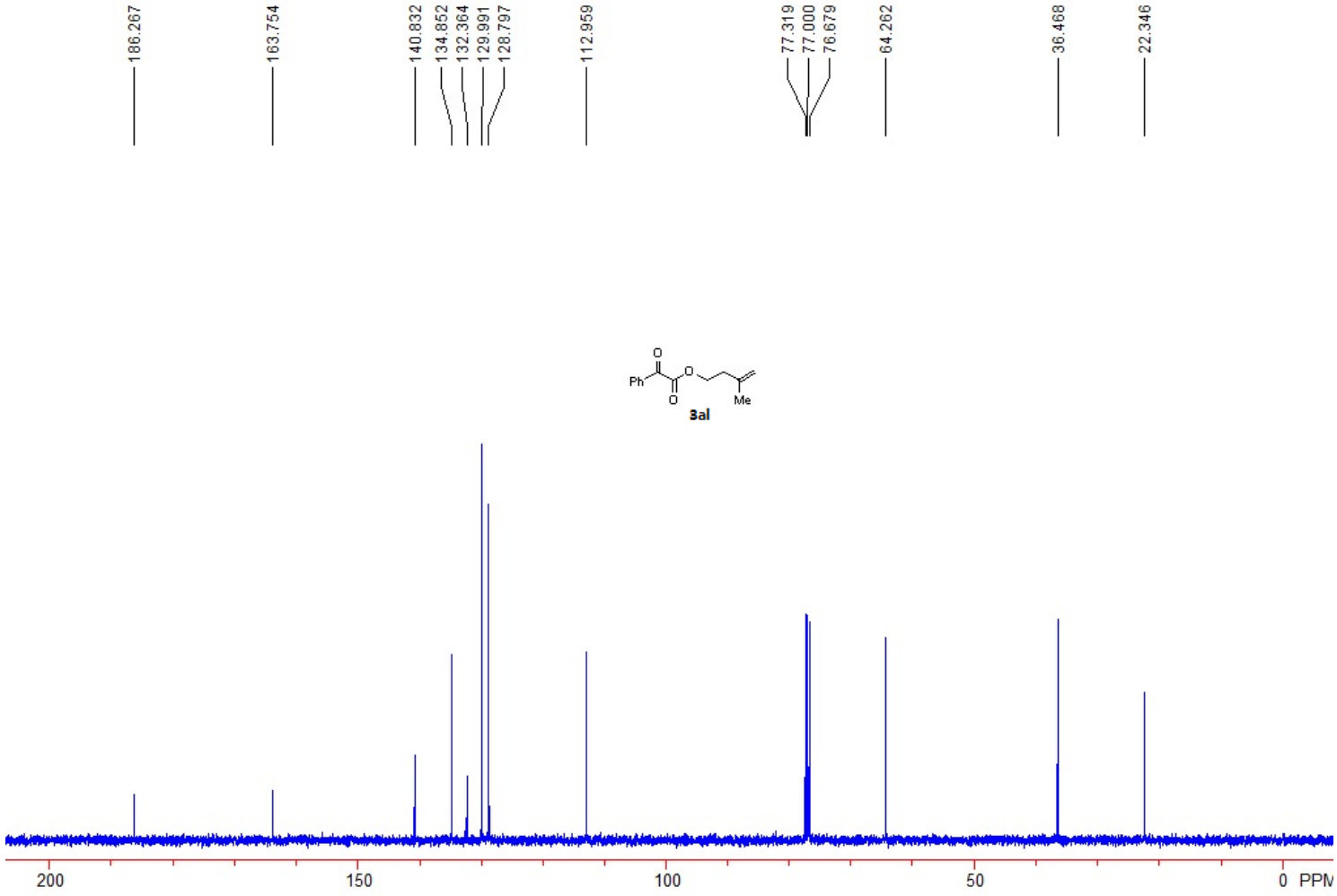


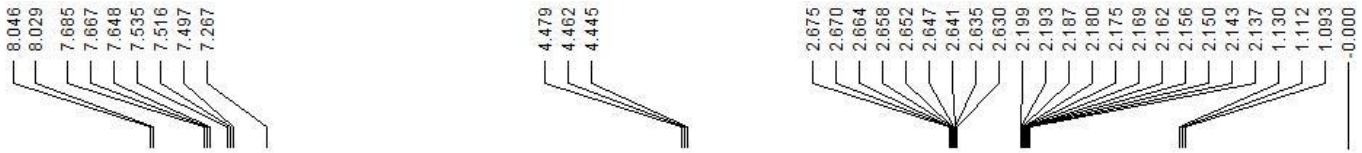


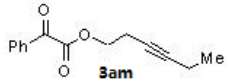












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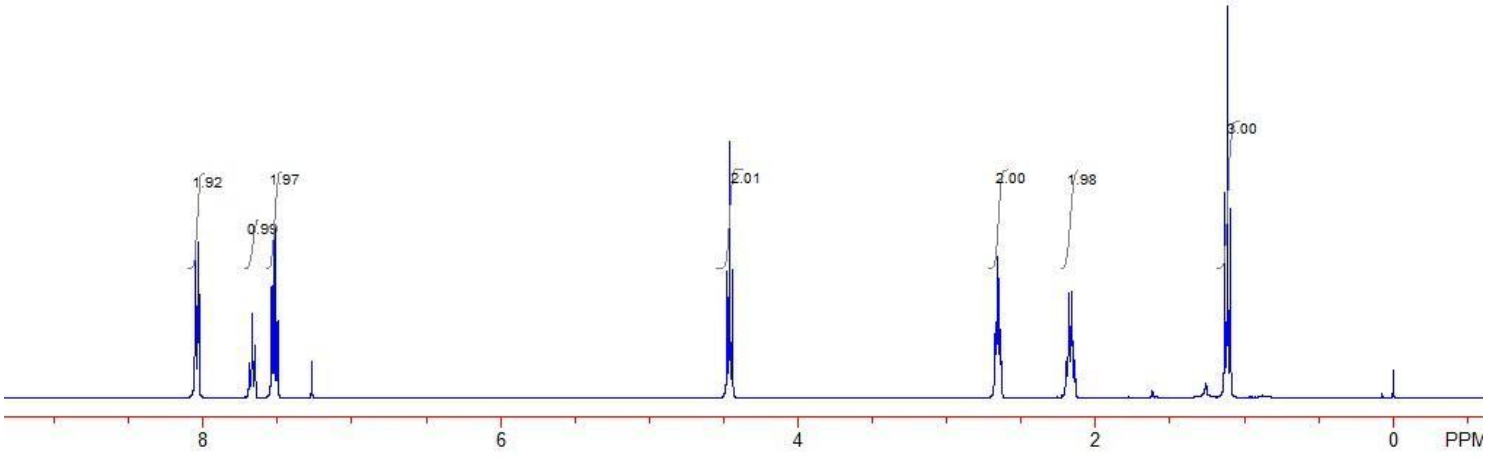

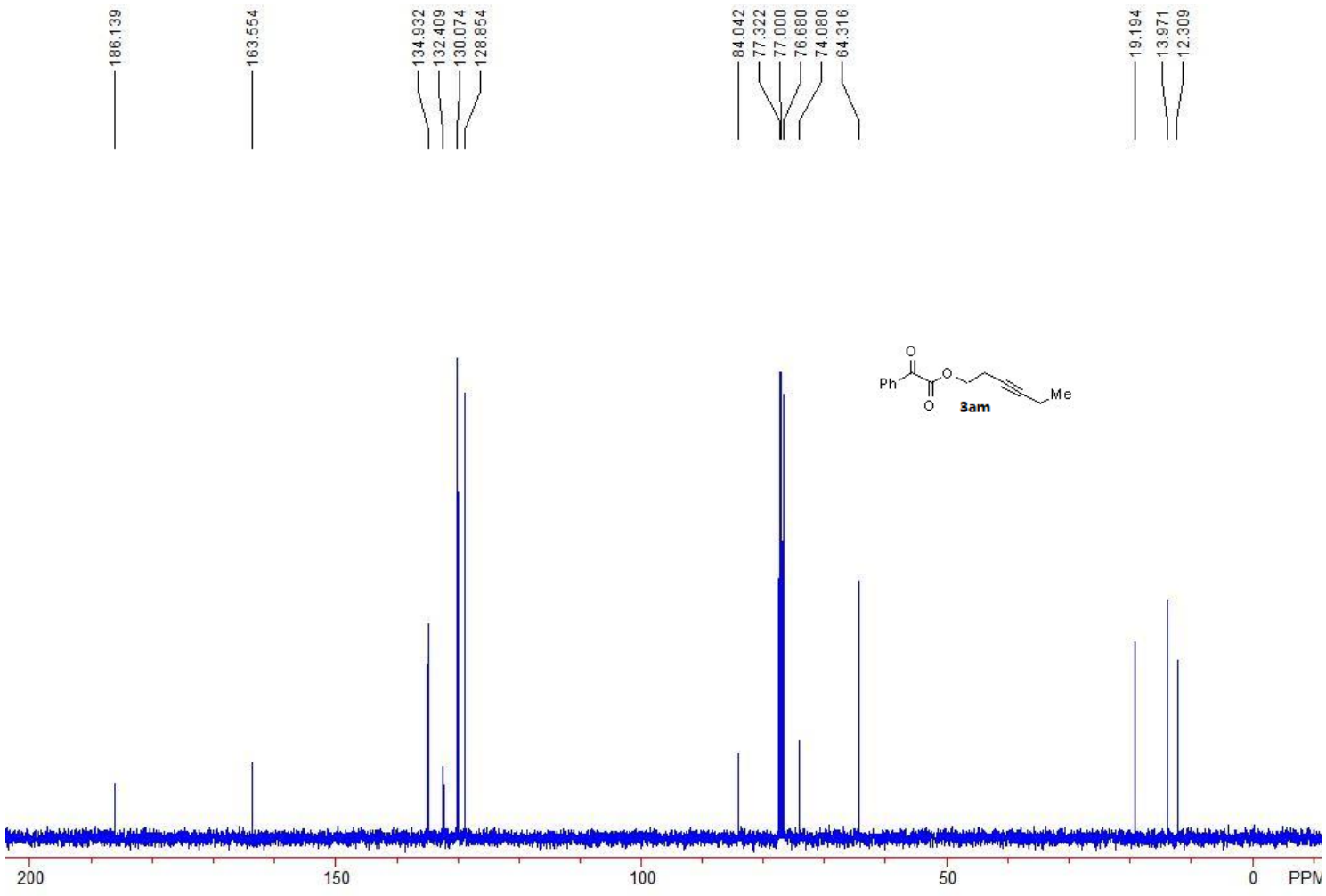

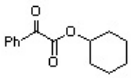

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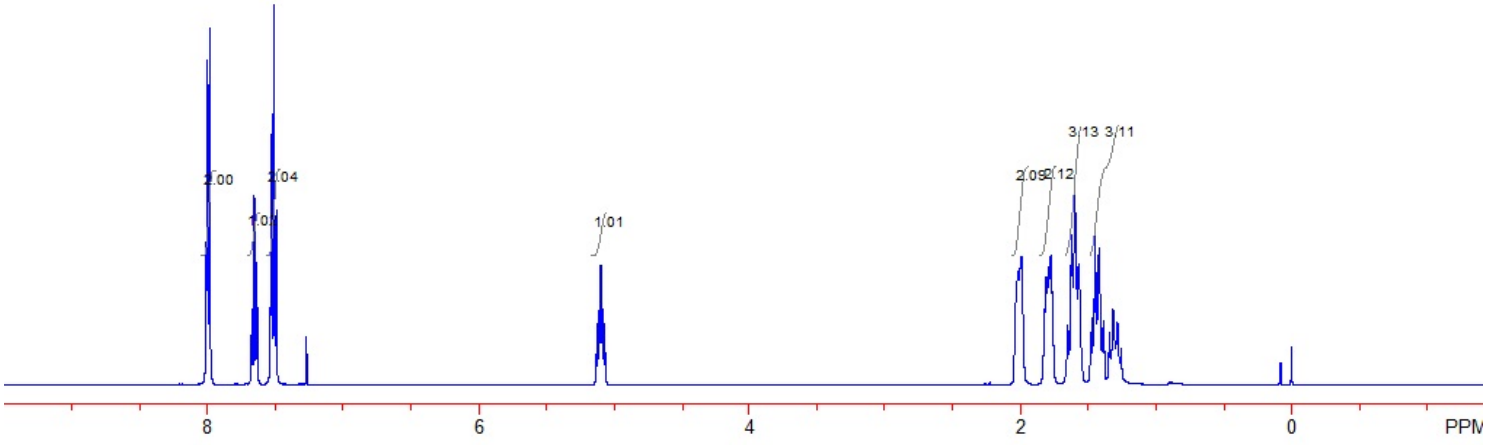

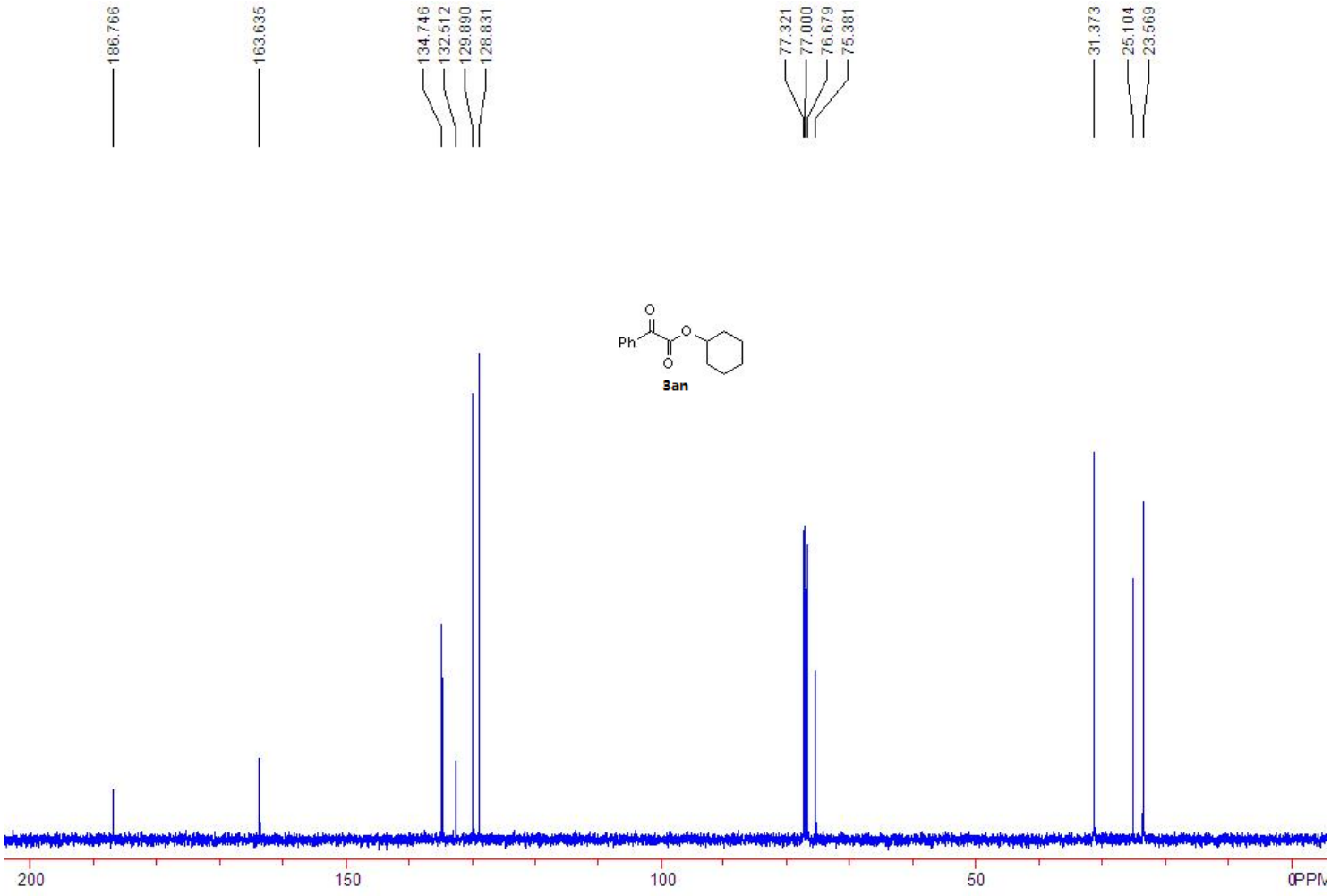

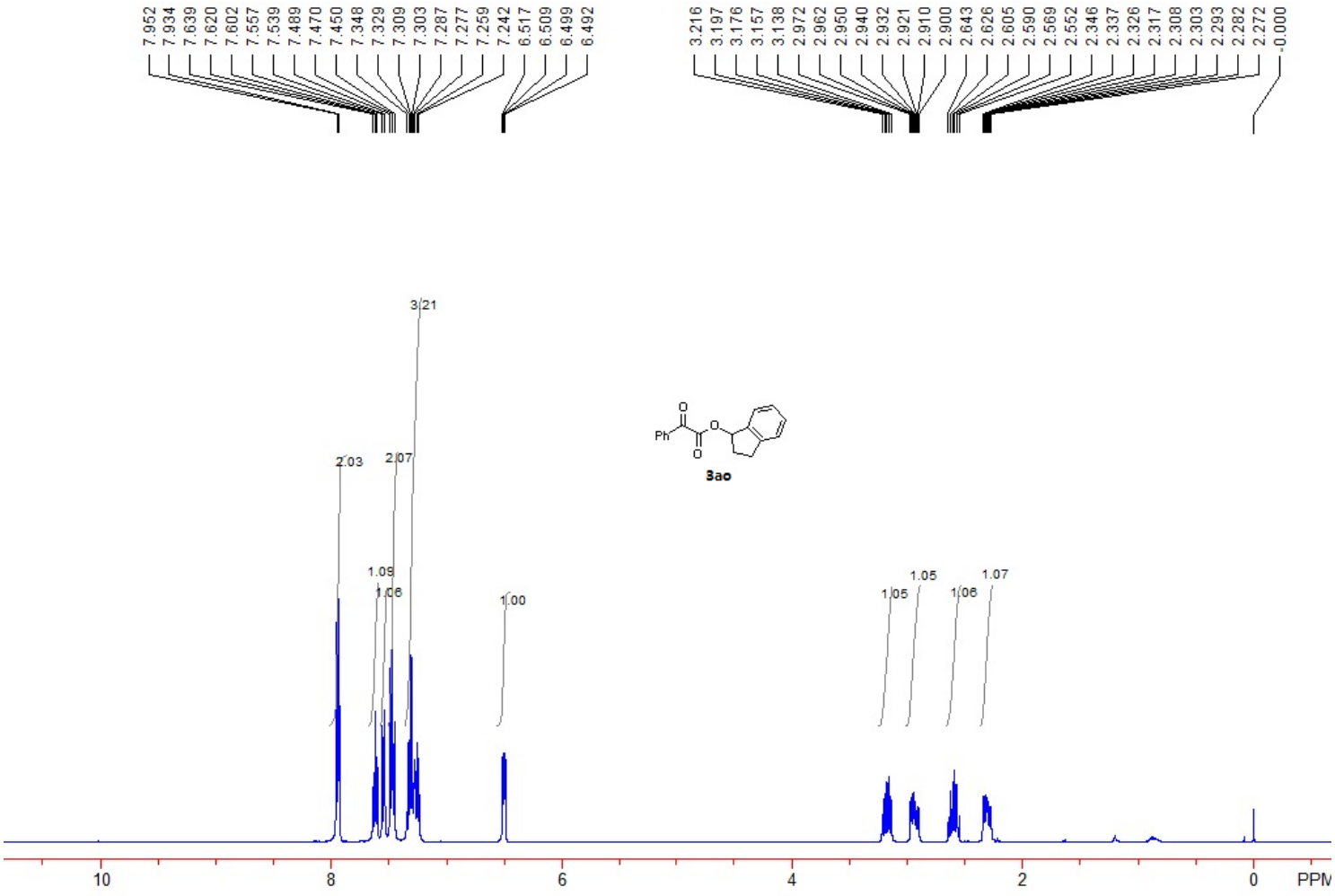

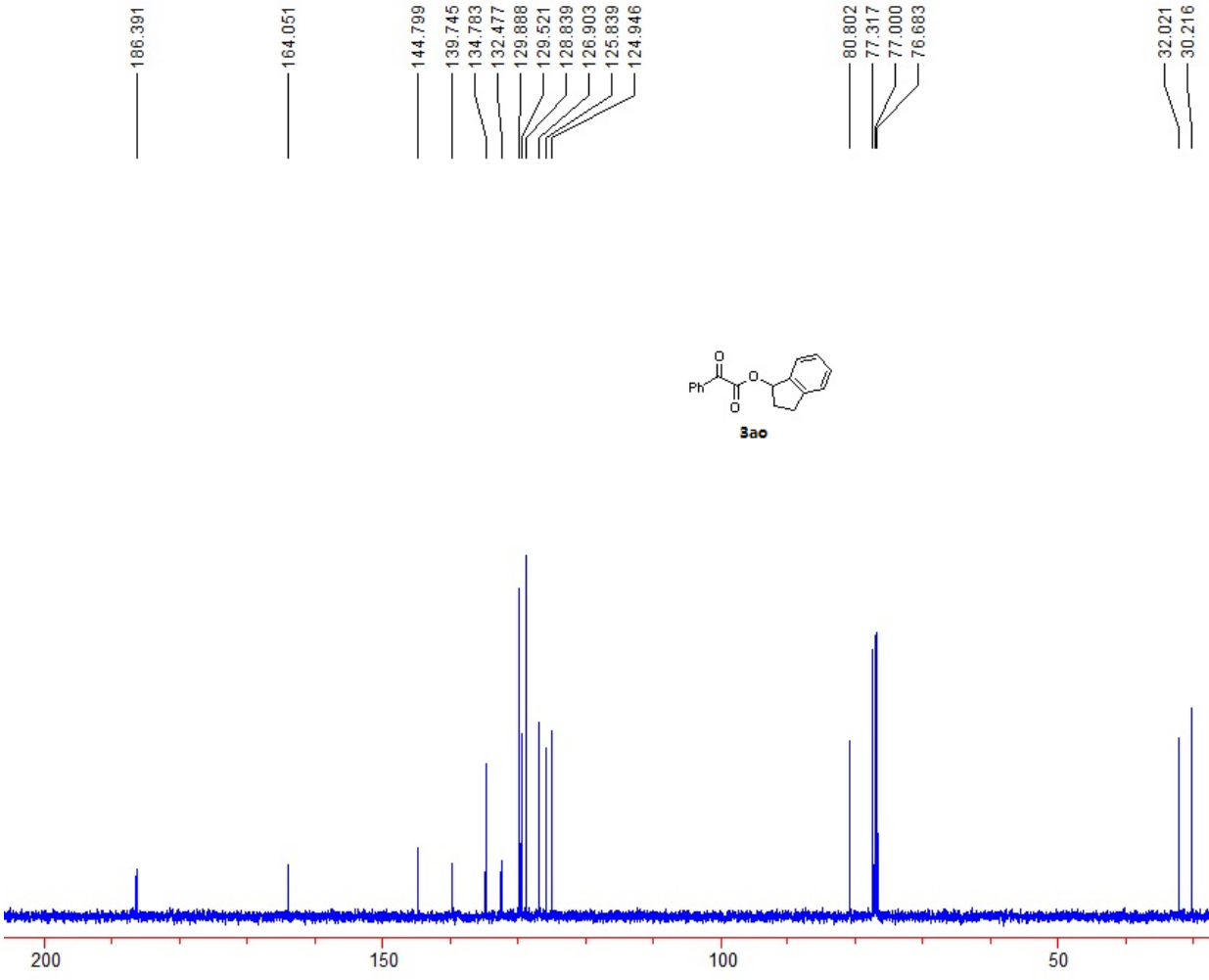

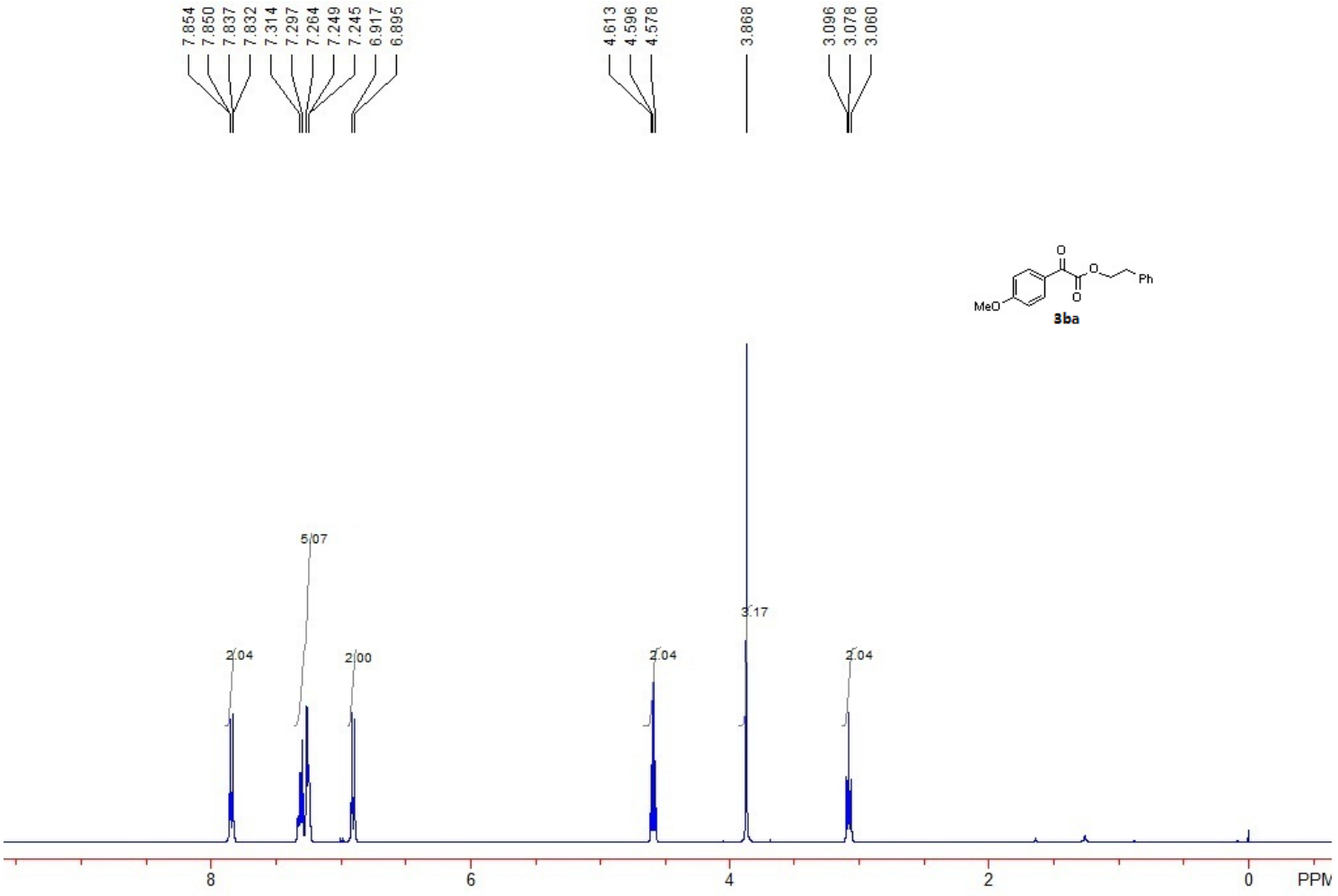

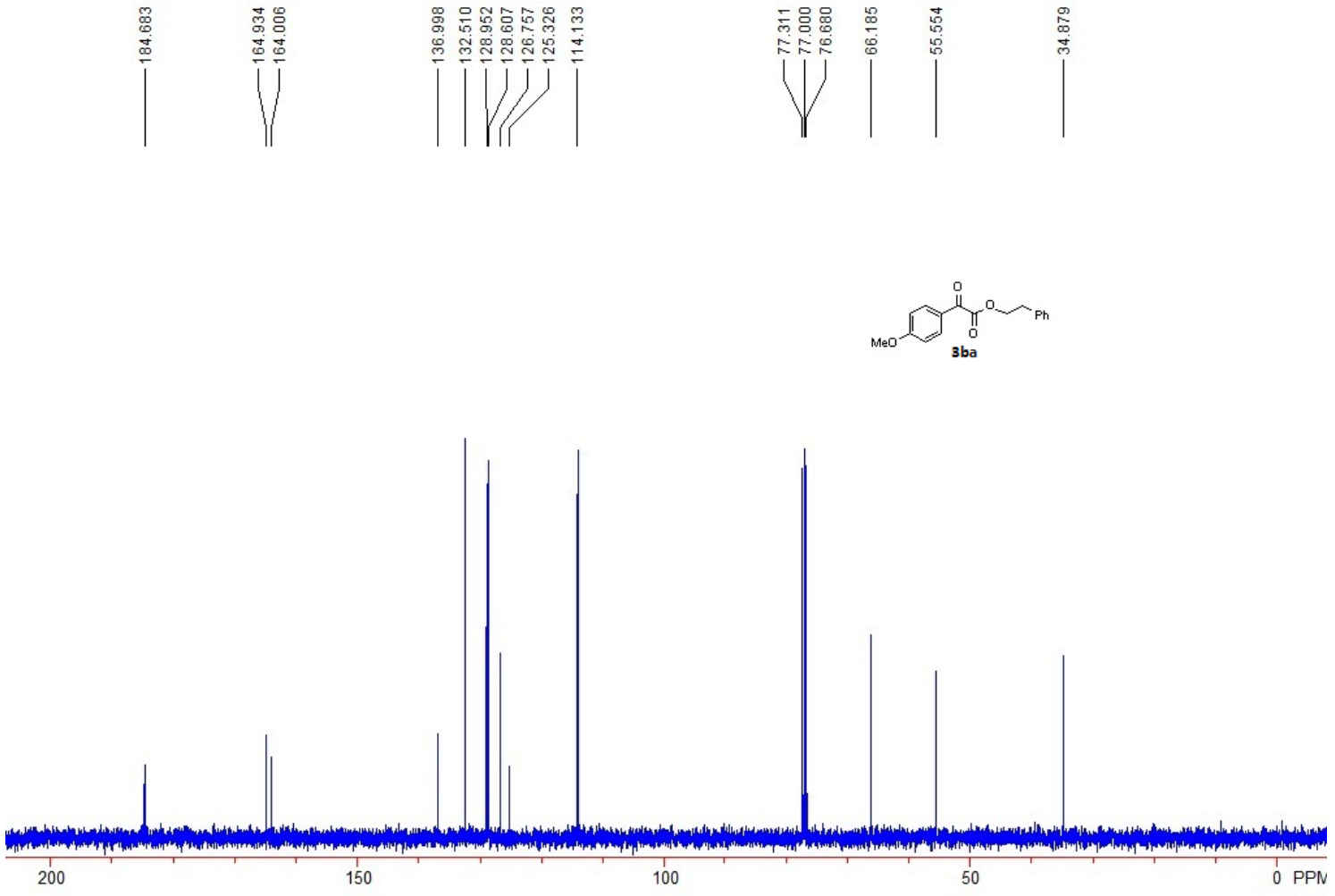

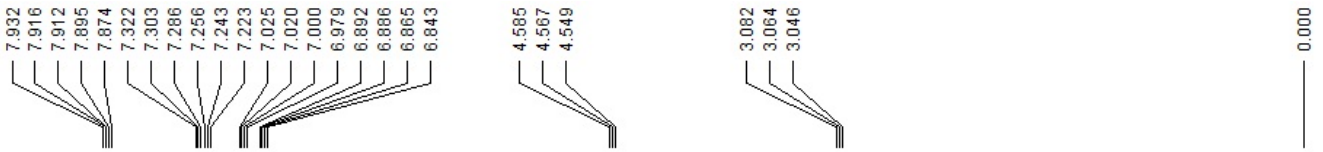

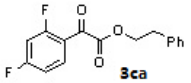

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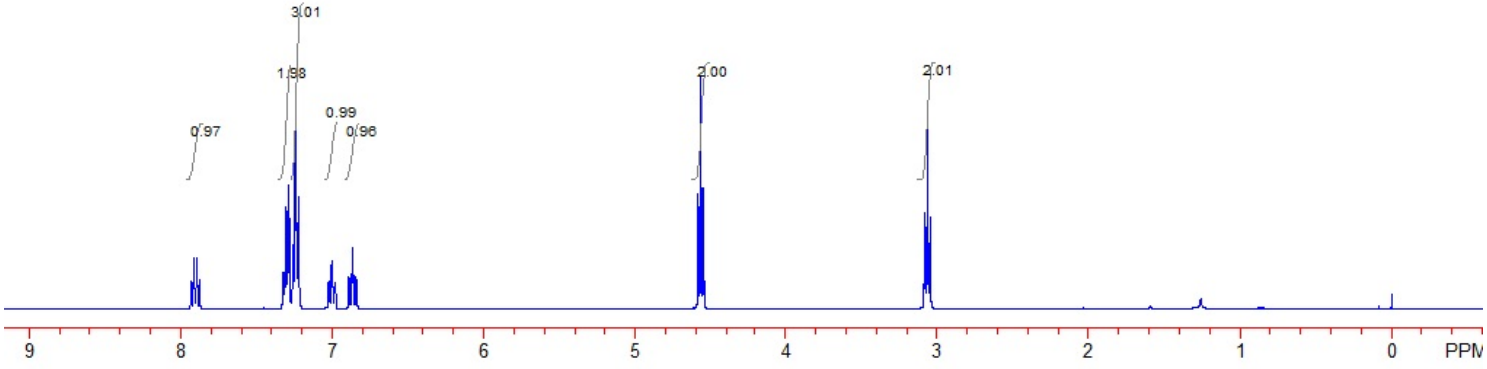

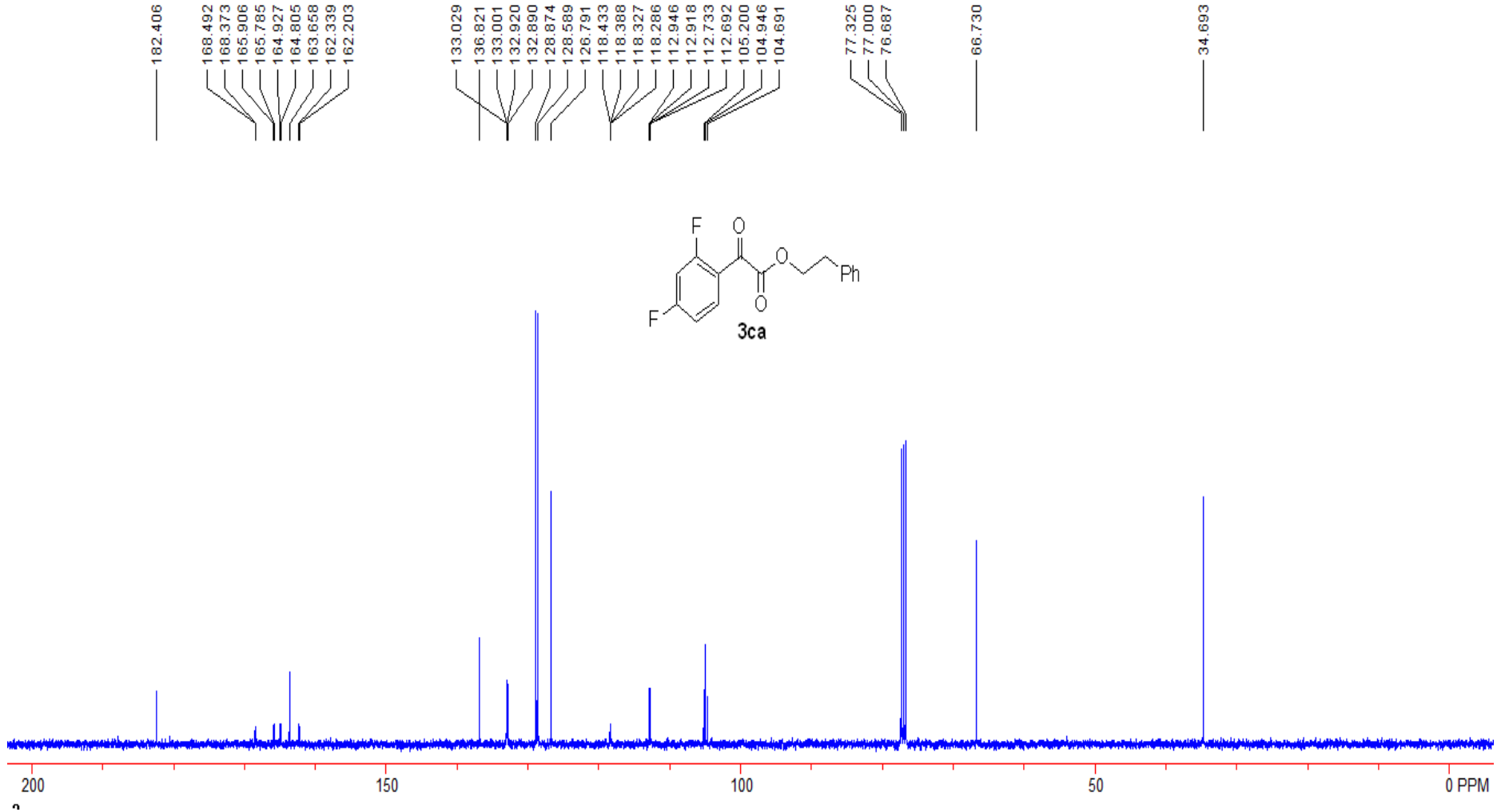

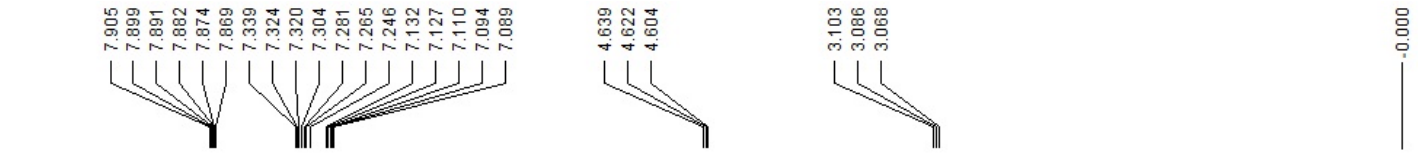

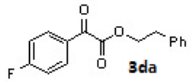

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