Conversion of α,β-Unsaturated Aldehydes into Saturated Esters: An Umpolung Reaction Catalyzed by Nucleophilic Carbenes

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Supporting Information

General Information. All reactions were carried out under a nitrogen atmosphere in flame-dried glassware with magnetic stirring. THF, Et_2O, CH_2Cl_2, DMF and toluene were purified by passage through a bed of activated alumina.[1] Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.[2] Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain, potassium permangenate, or phosphomolybic acid followed by heating. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Varian Inova 500 (500 MHz) or Mercury 400 (400 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C-NMR spectra were recorded on a Varian Inova 500 (125 MHz) or Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). Mass spectra data were obtained on a Varian 1200 Quadrupole Mass Spectrometer.

3-(4-chlorophenyl)cinnamaldehyde was prepared according to Kirsch.[3] 4-Chloro-cinnamaldehyde was prepared according to a procedure analogous to Moloney.[4] 4-Methoxy-cinnamaldehyde was purchased from Acros Chemical Company and the remaining aldehydes were commercially available from Sigma-Aldrich Chemical Company and purified before use.

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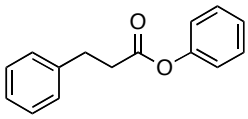
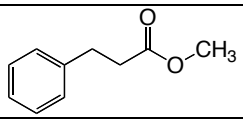
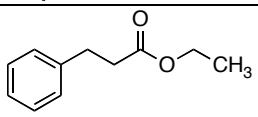
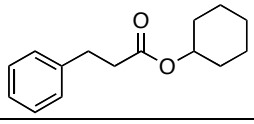
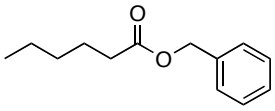
1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.
2. Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals;* 3rd Ed., Pergamon Press, Oxford. 1988.
3. (a) Hess, S.; Kirsch, G. *Synthesis*, **2001**, *5*, 755-758. (b) Kirsch, G.; Prim, D.; Leising, F.; Mignani, G. *J. Heterocycl. Chem.* **1994**, *31*, 1005-1009.
4. Baldwin, J.E.; Turner, S.C.M.; Moloney, M.G. *Tetrahedron*, **1994**, *50*, 9411-9424.

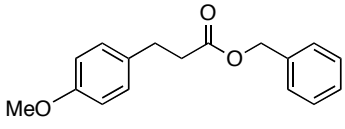
Imidazolium salt **D** was prepared according to Diver and coworkers.[5]

General Procedure for benzimidazolium-catalyzed reaction:
A screw-capped tube was charged with the benzimidazolium salt (11 mg, 0.04 mmol) in a nitrogen-filled dry box. The tube was removed from the box and placed under a positive pressure of nitrogen. The tube was charged with toluene (1.0 mL), DBU (6 μL, 0.04 mmol) and lastly, distilled cinnamaldehyde (104 mg, 0.79 mmol). The reaction mixture was allowed to stir for 5 minutes after which phenol (150mg, 1.6 mmol) in toluene (0.6 ml) was added via syringe followed by the addition of benzyl alcohol (429 mg, 4 mmol). The reaction was heated at 110 °C for 2-6 hours until cinnamaldehyde was consumed (as judged by GC). The reaction was cooled to room temperature, diluted with methylene chloride (20 mL) and washed with water (20 mL). The aqueous layer was washed with methylene chloride (3x30 mL) and the combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography on silica gel.

Known compounds:

Structure	Reference
	Barton, P.; Laws, A.P.; Page, M.I. *J. Chem. Soc. Perkin Trans. 2* 1994, *9*, 2021-2030.
	Rivero, I.A.; Heredia, S.; Ochoa, A. *Synth. Commun*. **2001**, *31*, 2169-2176.
	Kurono, N.; Sugita, K.; Takasugi, S.; Tokuda, M. *Tetrahedron*, **1999**, *55*, 6097-6108.
	Kita, Y.; Akai, S.; Yamamoto, M.; Taniguchi, M.; Tamura, Y. *Synthesis*, **1989**, *4*, 334-337.
	(a) Peterson, P.E.; Stepanian, M. *J. Org. Chem.* **1988**, *53*, 1903-1907.

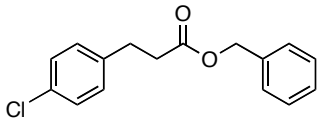
Selected Spectral Data:



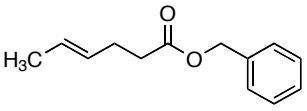
Benzyl 3-(4-methoxyphenyl)propanoate (8): Purified with 10% Et_2O/hexanes yielding 127 mg (76%) of **8** as a light yellow oil. R_f = 0.6 (1:4 Et_2O/hexanes); IR (film) 3448, 3033, 2951, 2835, 1734, 1247 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.30 (m, 5H); 7.10

5. (a) Rivas, F. M.; Riaz, U.; Giessert, A.; Smulik, J. A.; Diver, S. T. *Org. Lett.* **2001**, *3*, 2673-2676. (b) Rivas, F. M.; Giessert, A. J.; Diver, S. T. *J. Org. Chem.* **2002**, *67*, 1708-1711.

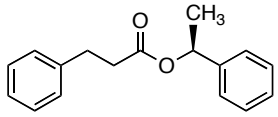
(d, *J* = 7.94, 2H); 6.82 (d, *J* = 7.63, 2H); 5.11 (s, 2H); 3.79 (s, 3H); 2.92 (t, *J* = 7.63, 2H); 2.65 (t, *J* = 7.63, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 158.5, 136.4, 132.9, 129.7, 129.0, 128.7, 128.6, 114.3, 66.7, 55.7, 36.7, 30.6; LRMS (APCI): Mass calculated for $C_{17}H_{18}O_3$ $[M+H]^+$ 271.3. Found 271.4.



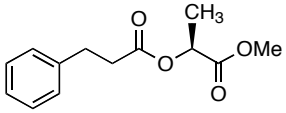
Benzyl 3-(4-chlorophenyl)propanoate (9): Purified with 10% Et_2O/hexanes yielding 118 mg (71%) of **9** as a yellow oil. R_f = 0.75 (1:4 Et_2O/hexanes); IR (film) 3452, 3033, 2949, 1735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.22 (m, 7H); 7.11 (d, *J* = 8.2, 2H); 5.10 (s, 2H); 2.94 (t, *J* = 7.6, 2H); 2.66 (t, *J* = 7.6, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 139.3, 136.2, 132.5, 130.2, 129.1, 128.8, 128.7, 66.8, 36.2, 30.7; LRMS (APCI): Mass calculated for $C_{16}H_{15}ClO_z$ $[M+5H]^+$ 279.7. Found 279.5.



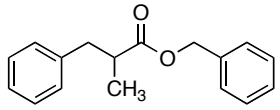
(*E*)-Benzyl hex-4-enoate (11): Purified with 10% Et_2O/hexanes yielding 129 mg (70%) of **11** as a clear oil. R_f = 0.77 (1:4 Et_2O/hexanes); IR (film) 3455, 3040, 2959, 2936, 1736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.32 (m, 5H); 5.50-5.39 (m, 2H); 5.12 (s, 2H); 2.41 (m, 2H); 2.33 (t, *J* = 6.4, 2H); 1.62 (t, *J* = 5.8, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 136.3, 129.3, 128.7, 128.4, 126.5, 66.3, 34.5, 28.1, 22.6, 18.1; LRMS (APCI): Mass calculated for $C_{13}H_{16}O_2$ $[M+H]^+$ 205.2. Found 205.2.



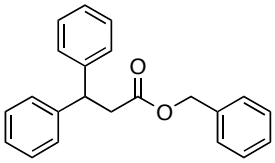
(*S*)-1-Phenylethyl 3-phenylpropanoate (6): Purified with 10% Et_2O/hexanes yielding 155 mg (77%) of **6** as a yellow oil. R_f = 0.70 (1:4 Et_2O/hexanes); IR (film) 3446, 3030, 2981, 2868, 1732, 1248 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.17 (m, 10H); 5.89 (q, *J* = 6.7, 1H); 2.96 (t, *J* = 7.3, 2H); 2.66 (t, *J* = 5.7, 2H); 1.51 (d, *J* = 6.7, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 141.8, 140.7, 129.6, 128.8, 128.7, 128.5, 128.0, 126.4, 126.3, 36.3, 31.1, 22.4; LRMS (ACPI): Mass calculated for $C_{17}H_{18}O_2$ $[M+H]^+$ 255.3. Found 255.4.



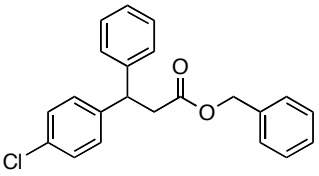
Methyl ester (7): Purified with 10% Et_2O/hexanes yielding 114 mg (61%) of **7** as a light yellow oil. R_f = 0.54 (1:4 Et_2O/hexanes); IR (film) 3463, 3029, 2994, 2951, 1744, 1215 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.20 (m, 5H); 5.10 (q, *J* = 7.0, 1H); 3.74 (s, 3H); 2.98 (t, *J* = 7.9, 2H); 2.75-2.70 (m, 2H); 1.47 (d, *J* = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 171.5, 140.5, 128.7, 128.5, 126.5, 68.7, 52.5, 35.7, 30.9, 17.1; LRMS (APCI): Mass calculated for $C_{13}H_{16}O_4$ $[M+H]^+$ 237.1. Found 237.1.



Benzyl 2-benzylpropanoate (12): Purified with 10% Et_2O/hexanes yielding 150 mg (82%) of **12** as light tan oil. R_f = 0.71 (1:4 EtOAc/hexanes); IR (film) 3448, 3064, 3030, 3974, 2936, 1735, 1245 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.14 (m, 10H); 5.07 (s, 2H); 3.04 (dd, *J* = 13.3, 7.0, 1H); 2.80 (q, *J* = 7.3, 1H); 2.69 (dd, *J* = 13.4, 7.3, 1H); 1.18 (d, *J* = 6.7, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 139.7, 136.5, 129.5, 129.0, 128.8, 128.6, 128.5, 126.8, 66.6. 42.0, 40.2, 17.3; LRMS (APCI): Mass calculated for $C_{17}H_{18}O_2$ $[M+H]^+$ 255.3. Found 255.3.



Benzyl 3,3-diphenylpropanoate (13): Purified with 10% Et_2O/hexanes yielding 113 mg (82%) of **13** as a light yellow oil. R_f = 0.70 (1:4 Et_2O/hexanes); IR (film) 3448, 3061, 3030, 2953, 2921, 1735, 1258 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.14 (m, 15H); 5.02 (s, 2H); 4.56 (t, *J* = 8.2, 1H); 3.12 (d, *J* = 7.9, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 143.8, 136.2, 129.6, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 127.0, 66.8, 47.5, 41.3.



Benzyl 3-(4-chlorophenyl)-3-phenylpropanoate (14): Purified with 60% CH_2Cl_2/hexanes yielding 94 mg (86%) of **14** as a light yellow oil. R_f = 0.85 (5:1 CH_2Cl_2/hexanes); IR (film) 3449, 3030, 2955, 1735, 1254 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31-7.14 (m, 14H); 5.02 (s, 2H); 4.54 (t, *J* = 7.9, 1H); 3.08 (d, *J* = 7.7, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 143.3, 142.2, 136.1, 132.8, 129.5, 129.2, 129.0, 128.7. 128.6, 128.0, 127.2, 114.6, 66.9, 46.9, 41.2.

General Procedure for the Kinetic Resolution of Vinylogous Aldehydes:

A screw-capped tube was charged with the chiral benzimidazolium salt **D** (42 mg, 0.09 mmol) in a nitrogen-filled dry box. The tube was removed from the box and placed under a positive pressure of nitrogen. The tube was charged with toluene (0.6 mL), DBU (14 μL, 0.09 mmol) and lastly, distilled cinnamaldehyde (247 mg, 1.87 mmol). The reaction mixture was allowed to stir for 5 minutes after which 2,6-dimethylphenol (76 mg, 0.62 mmol) in toluene (0.6 ml) was added via syringe followed by the addition of 1-phenylethanol (429 mg, 0.62 mmol) and dodecane (106 mg, 0.62 mmol) that served as an internal standard for GC analysis. The reaction was heated at 80°C 6 days and monitored by standard analytical techniques (GC and HPLC) for % conversion and enantiomeric excess values. Aliquots of the reaction mixture (50 μL) were collected after 24 h, 48 h, 72 h, 96 h, 120 h, and 144 h. Each aliquot was filtered through a small silica gel plug (1:1 EtOAc/hexanes) and analyzed. [6]

[6] Percent conversions were measured by GC integration of the sec-phenethyl alcohol and the dodecane peaks.

Table SI 1. Methods utilized for the determination of enantiomeric exdess.

Entry	Catalyst	ee Assay	Condition	Retention Time of (*S*) isomer (min)	Retention Time of (*S*) isomer (min)
1	D	HPLC Chiralcel OD-H	0.5% IPA/hexane 0.75 mL/min	9.76	11.14

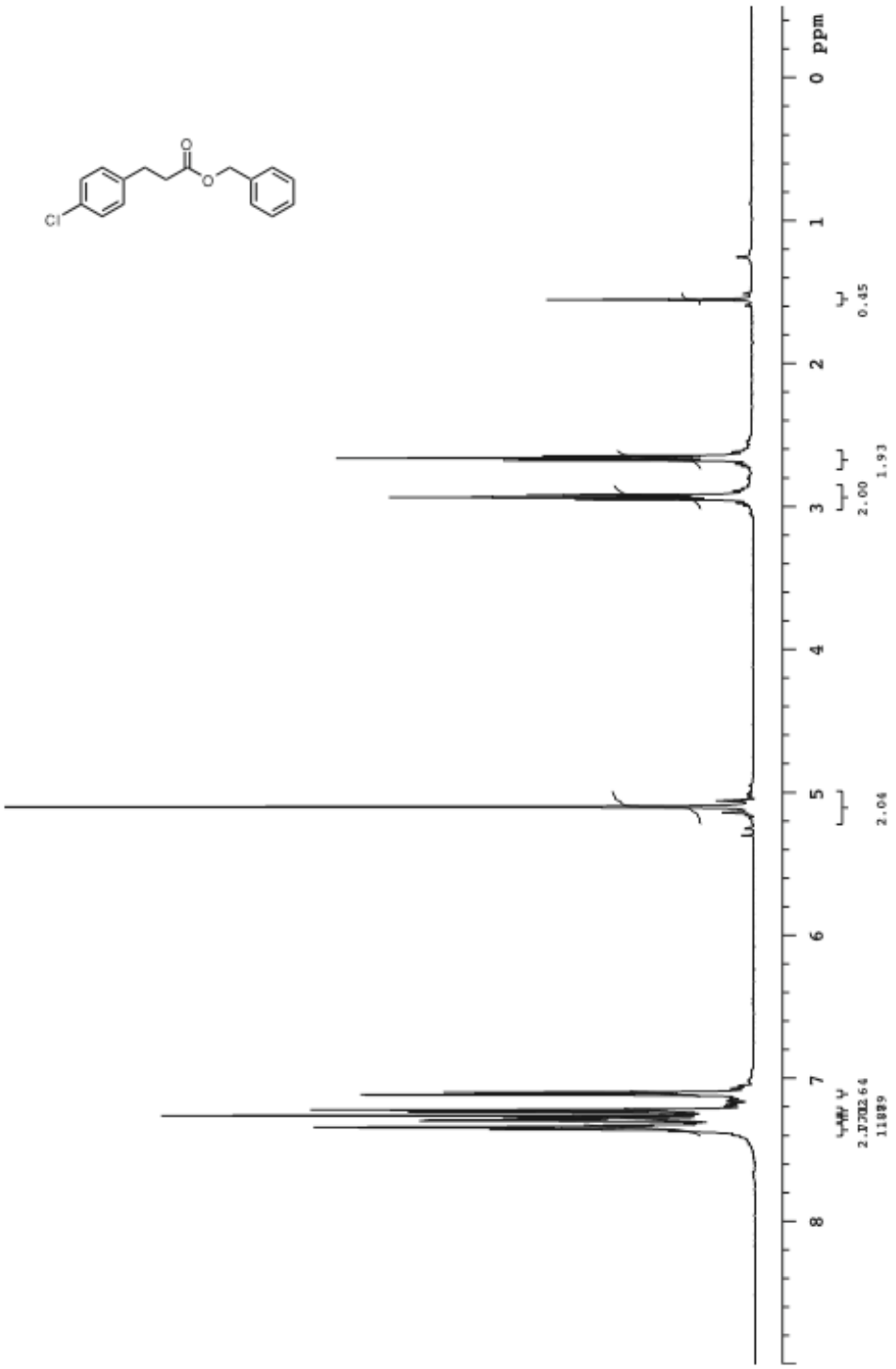
Table SI 2. Methods utilized for the determination of % conversion.

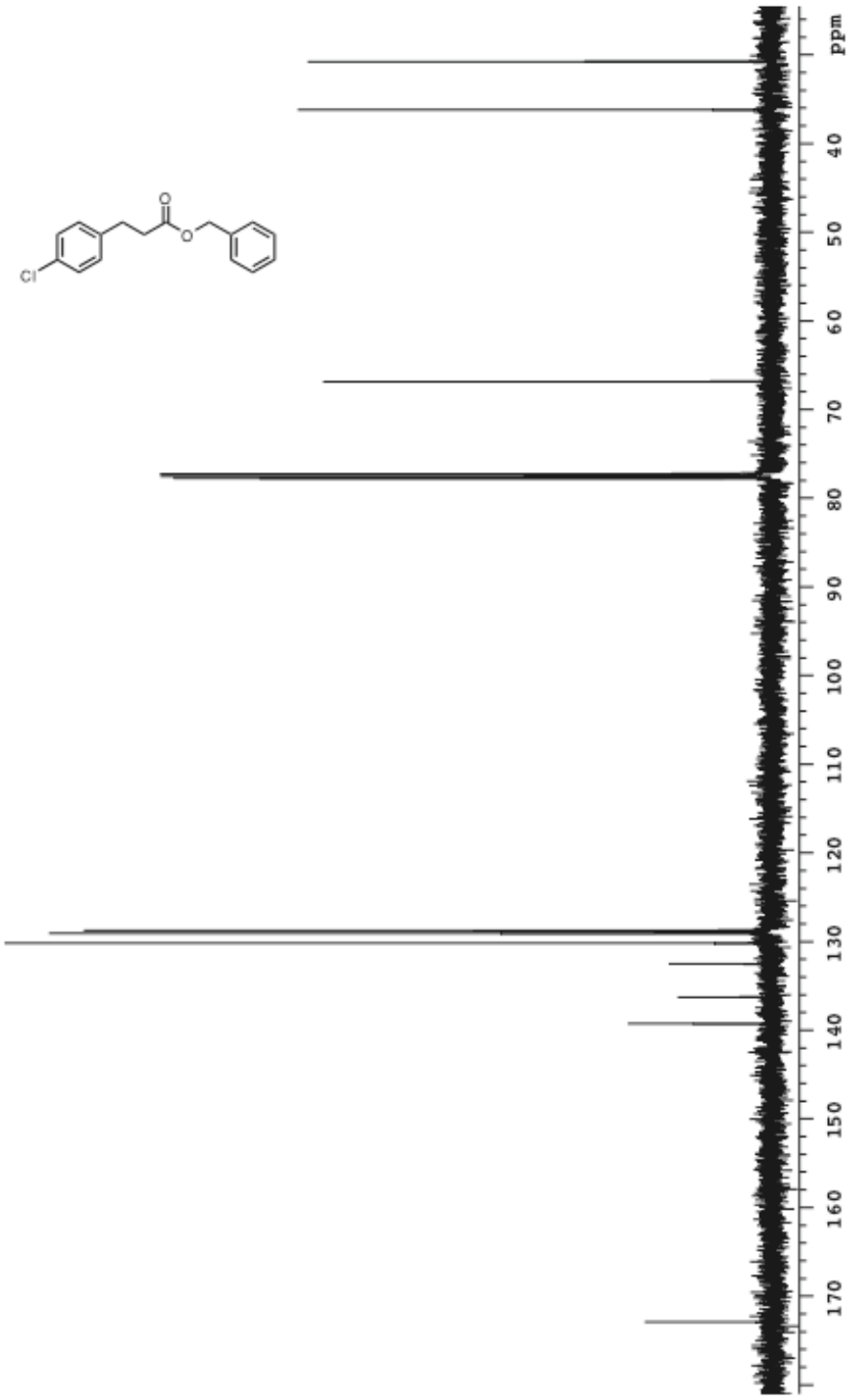
Entry	Catalyst	GC Conditions	Retention Time of sec-phenethyl alcohol (min)	Retention Time of dodecane (min)
1	D	70 ^{o}C, 1 min; 35 ^{o}C/min to 285 ^{o}C; 285 ^{o}C, 3 min	4.44	5.39

Table SI 3. Selected Experimental Data for the Deternination of Conversion, Enantiomeric Excess, and Selectivity (s).

Entry	Catalyst	time (h)	% conversion	Measured % ee	s
1	D	54	32.4	34.2	8.25
		76	33.2	32.3	7.08
		100	38.7	25.3	2.93
		124	40.1	24.2	2.66
		150	41.0	28.9	3.15

Selected NMR Spectra

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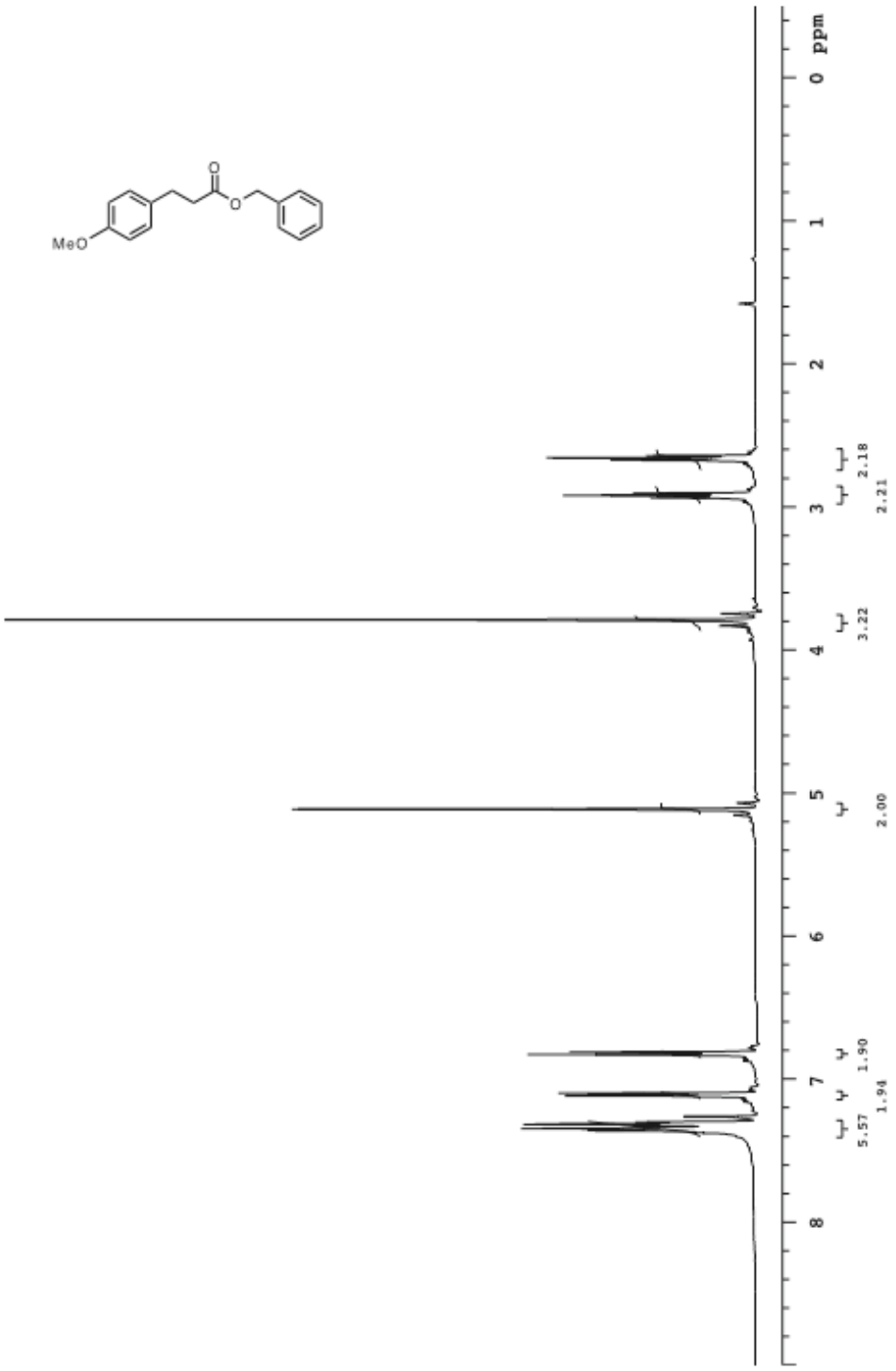
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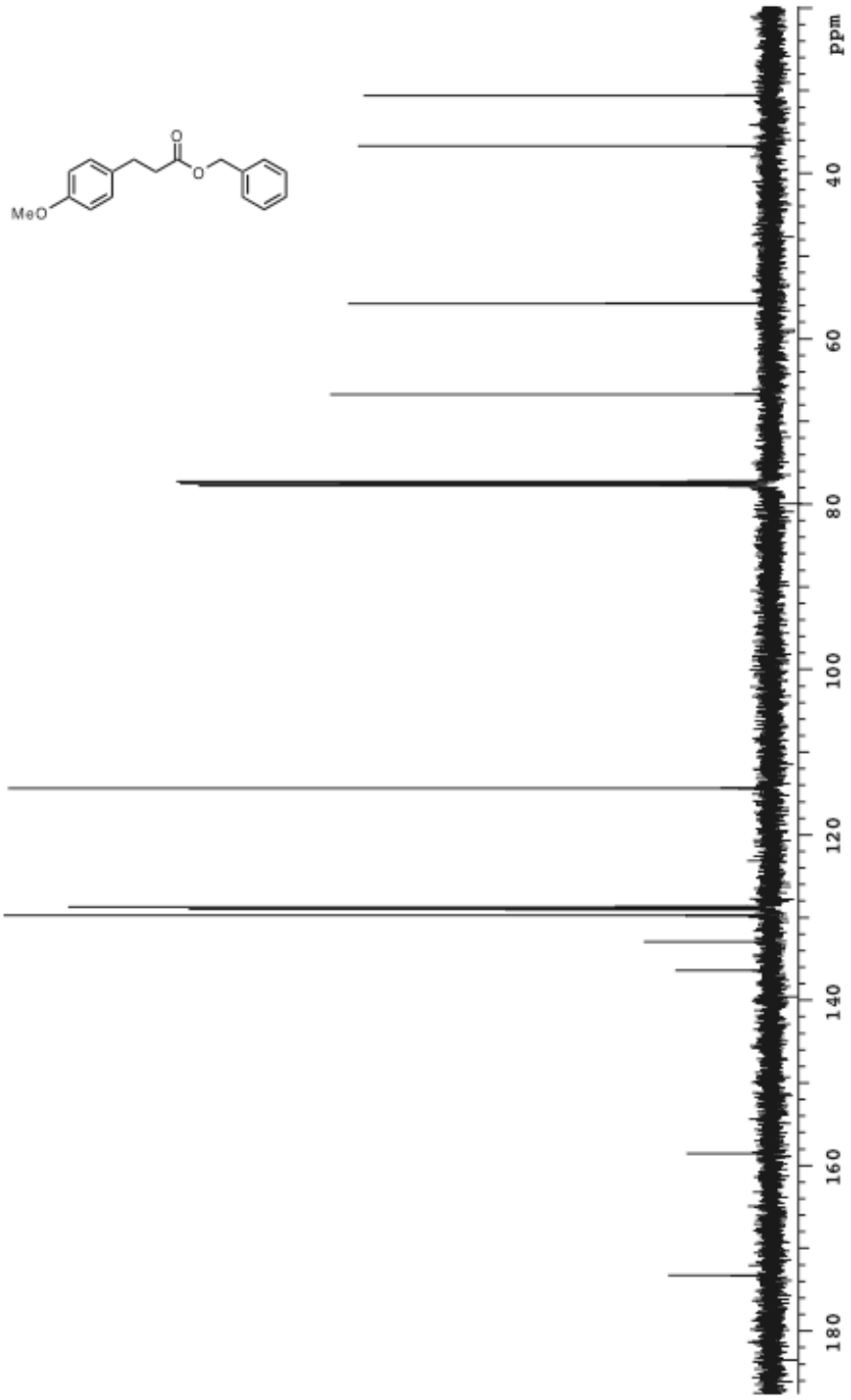
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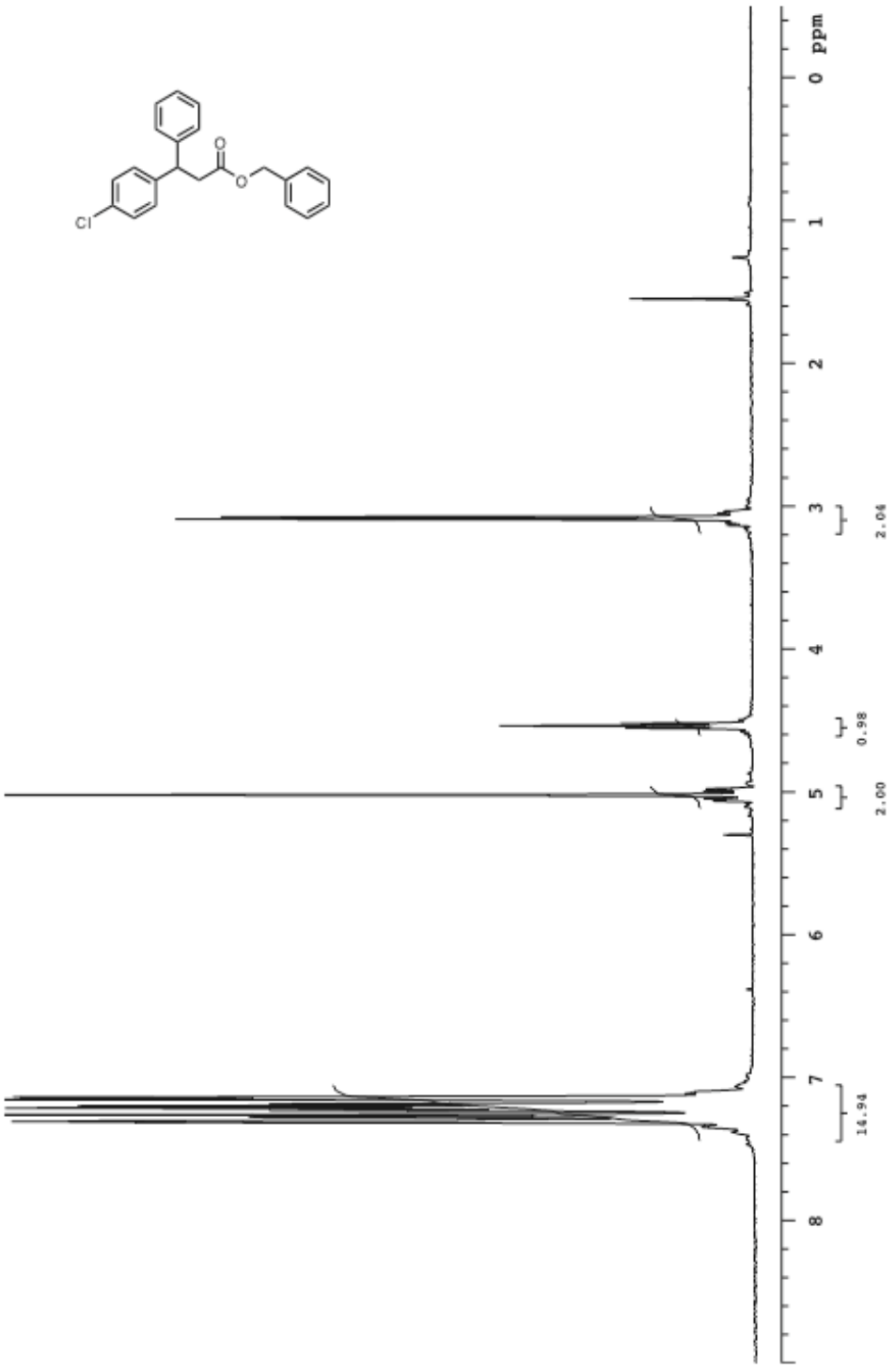
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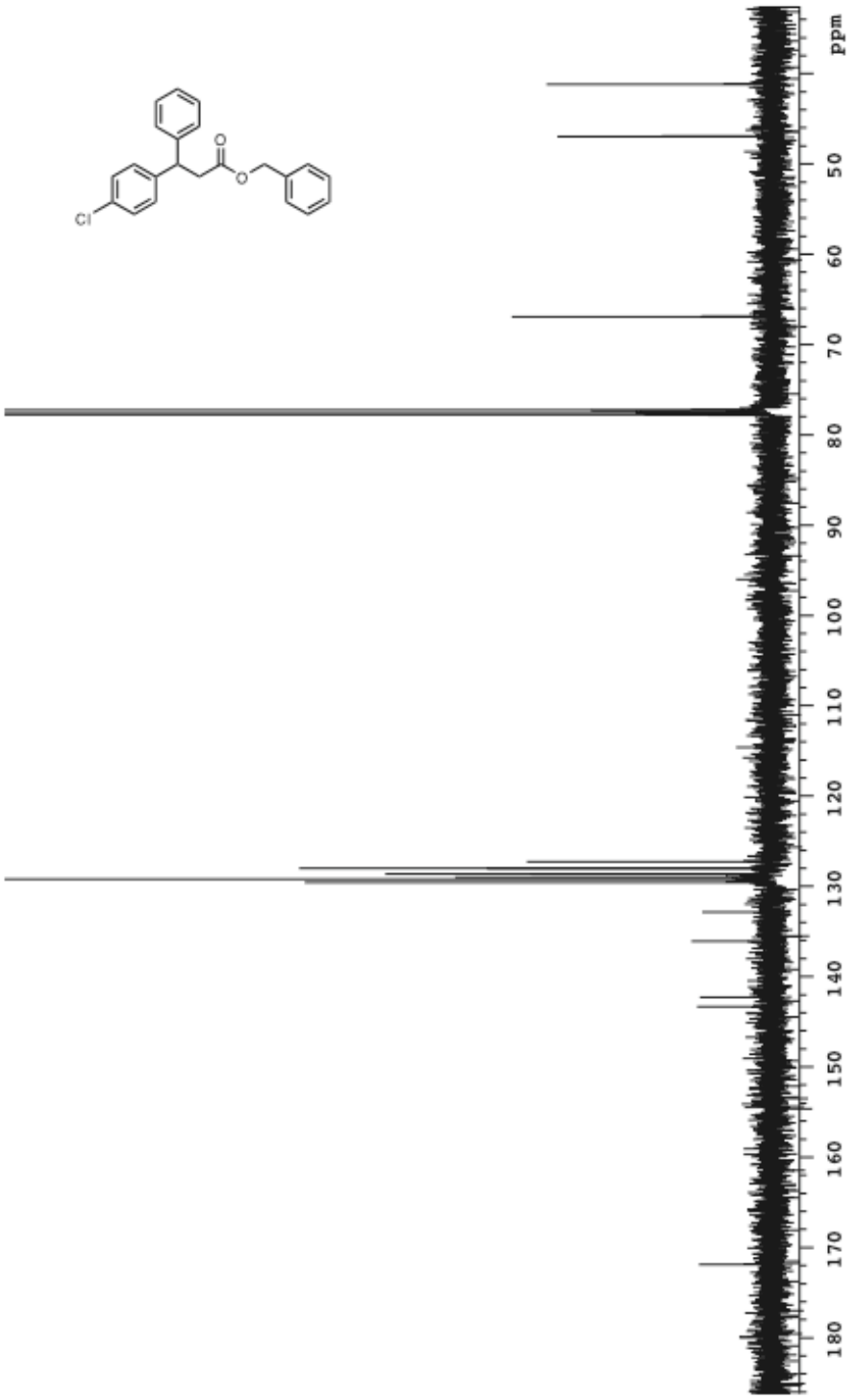
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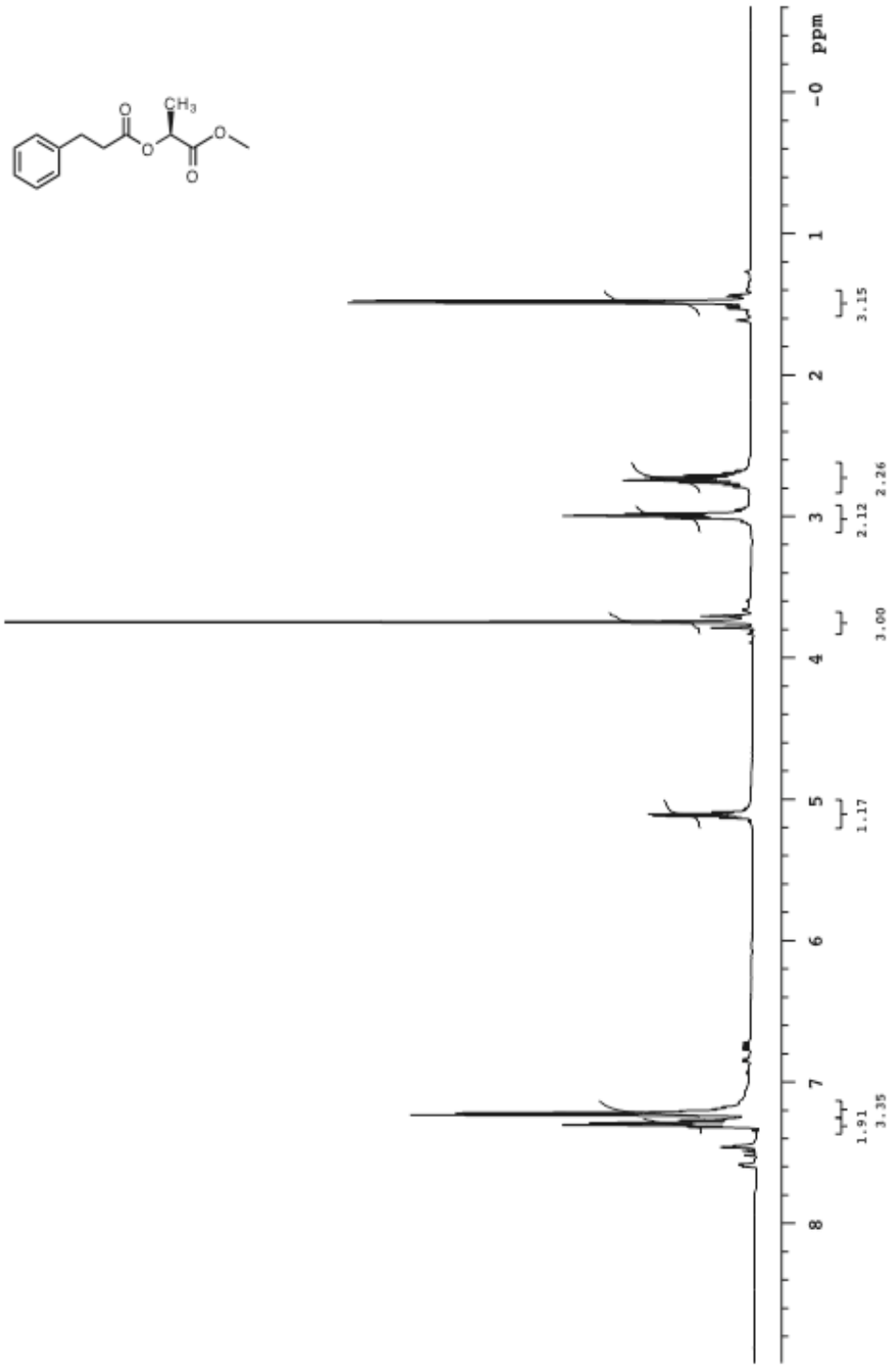
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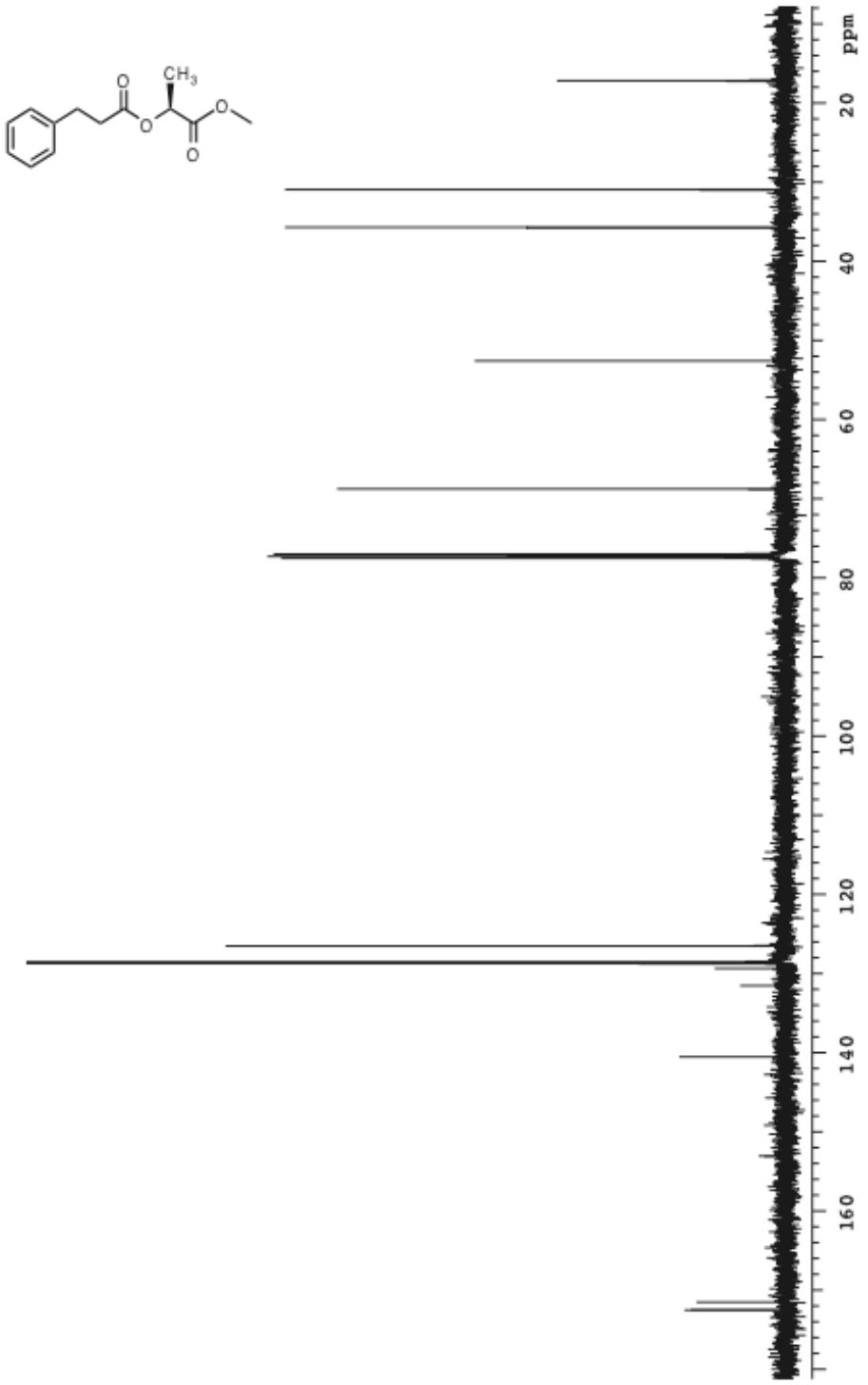
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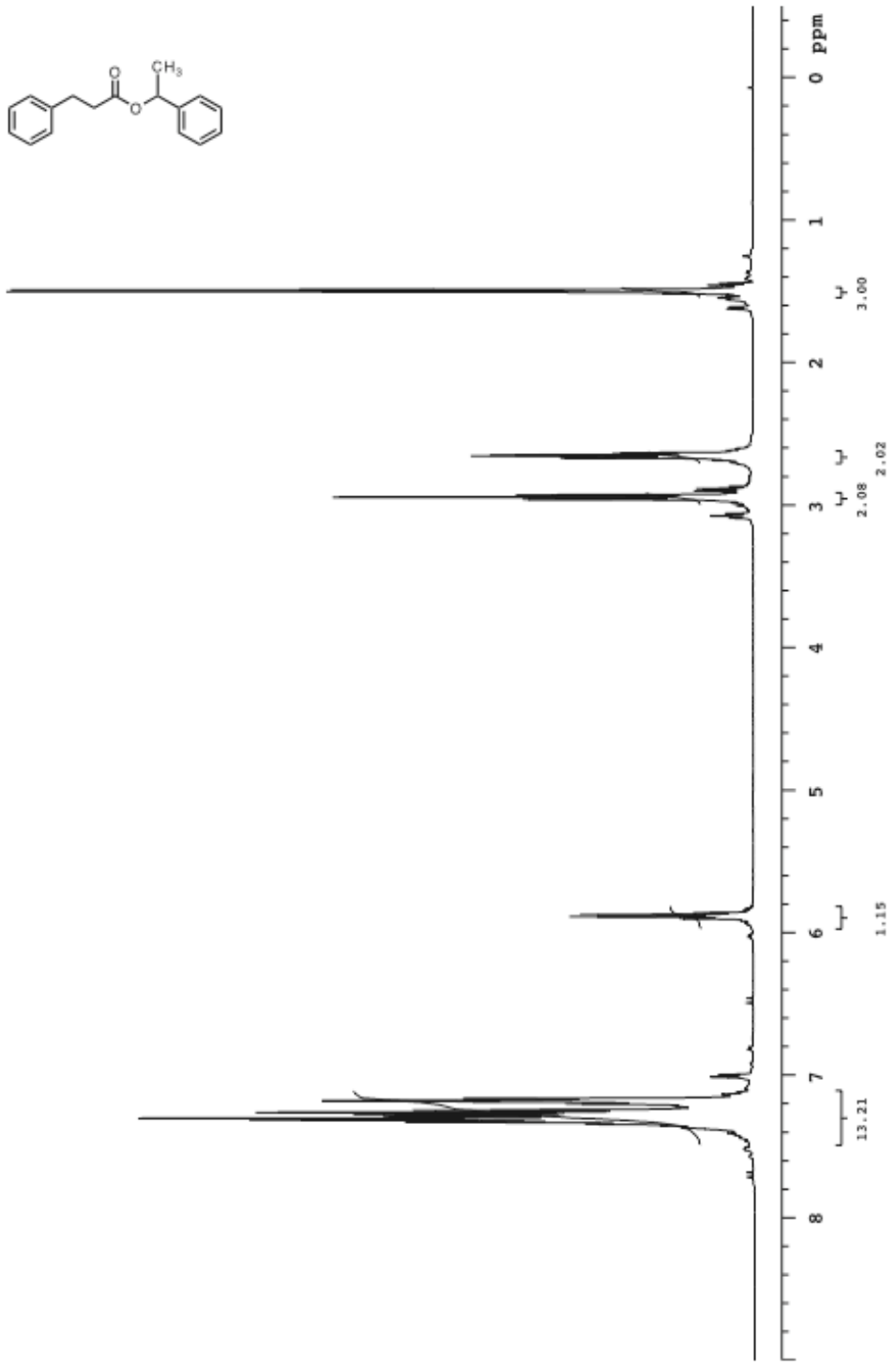
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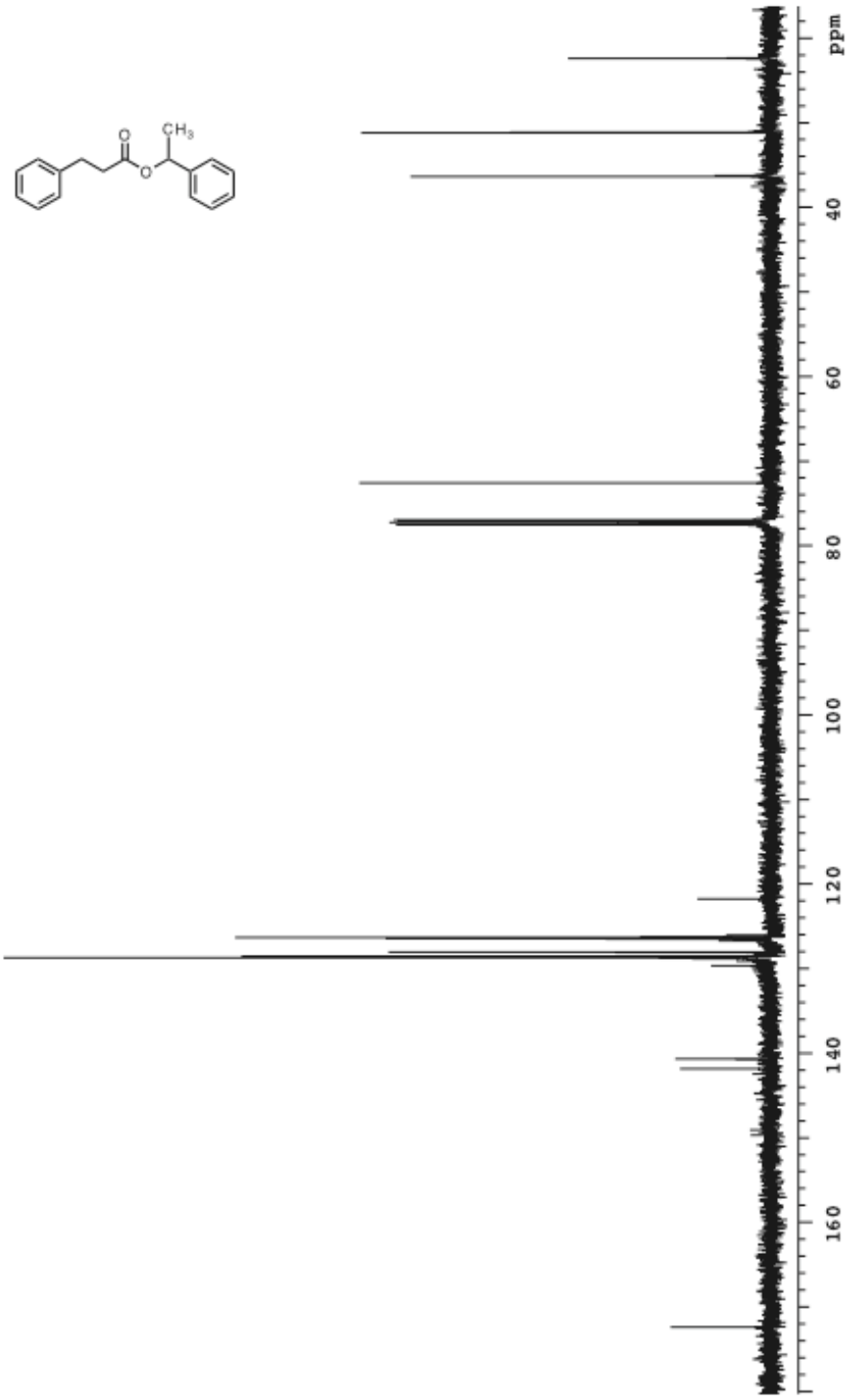
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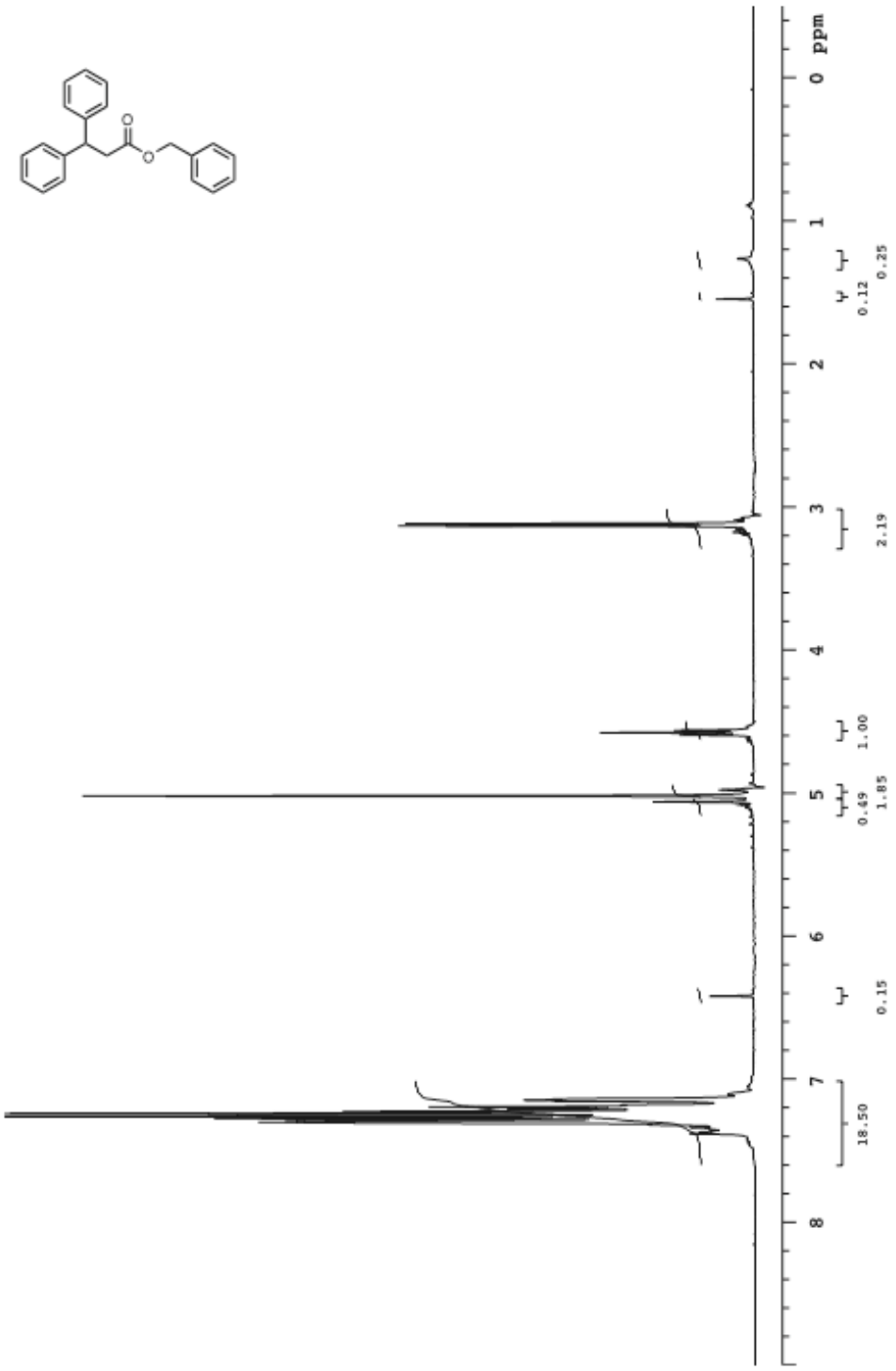
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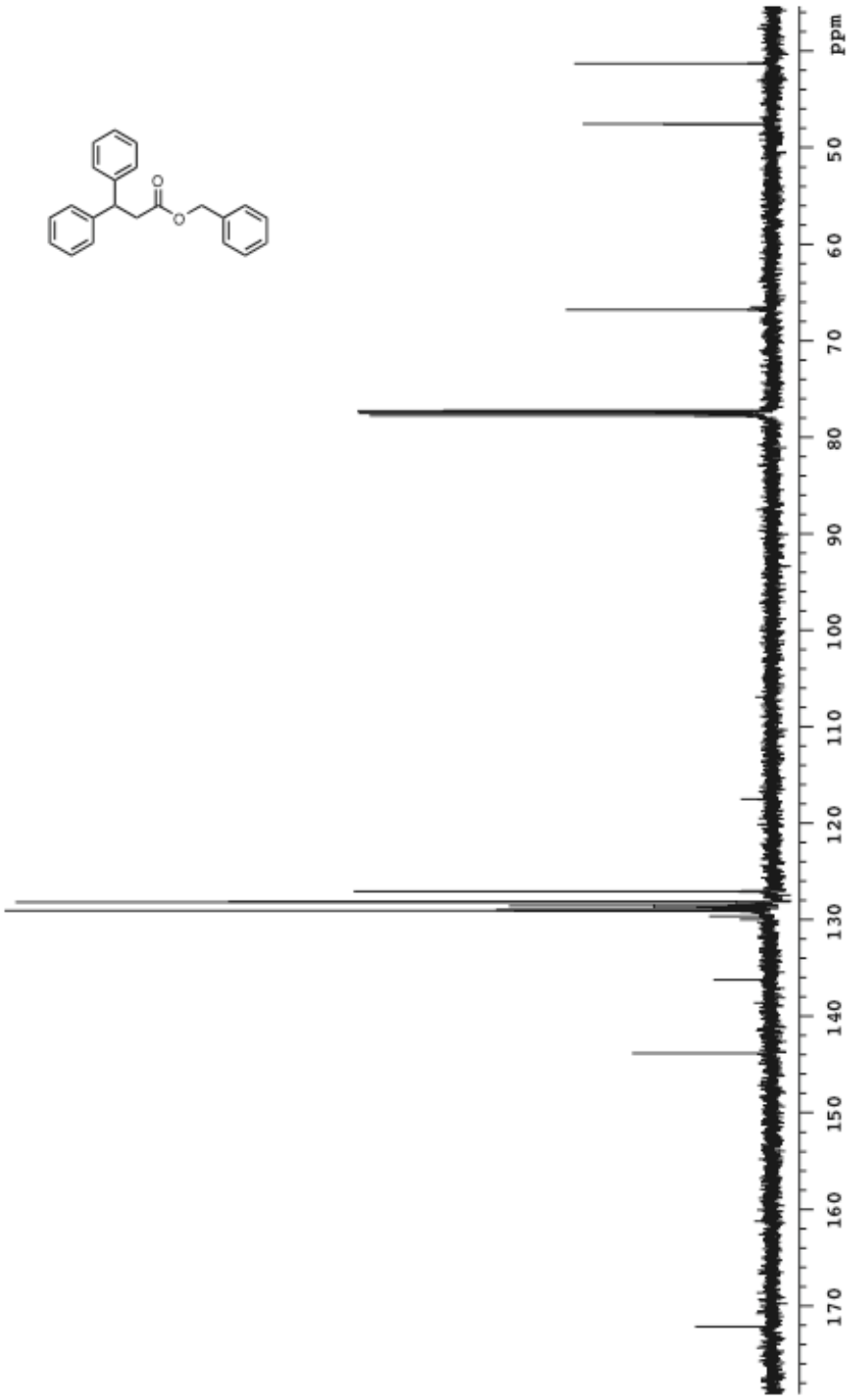
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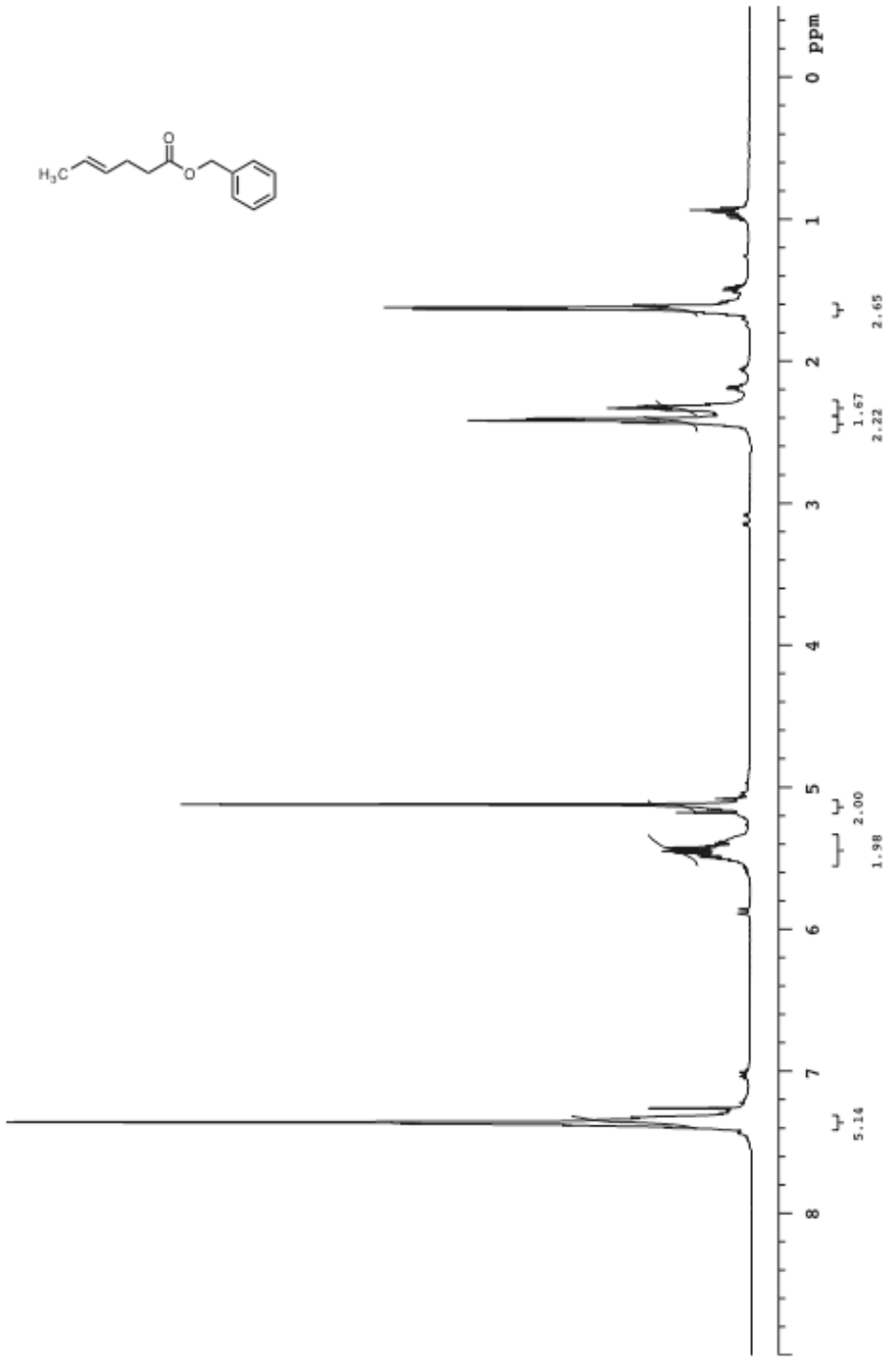
160
170


H3C
O
O
0 ppm
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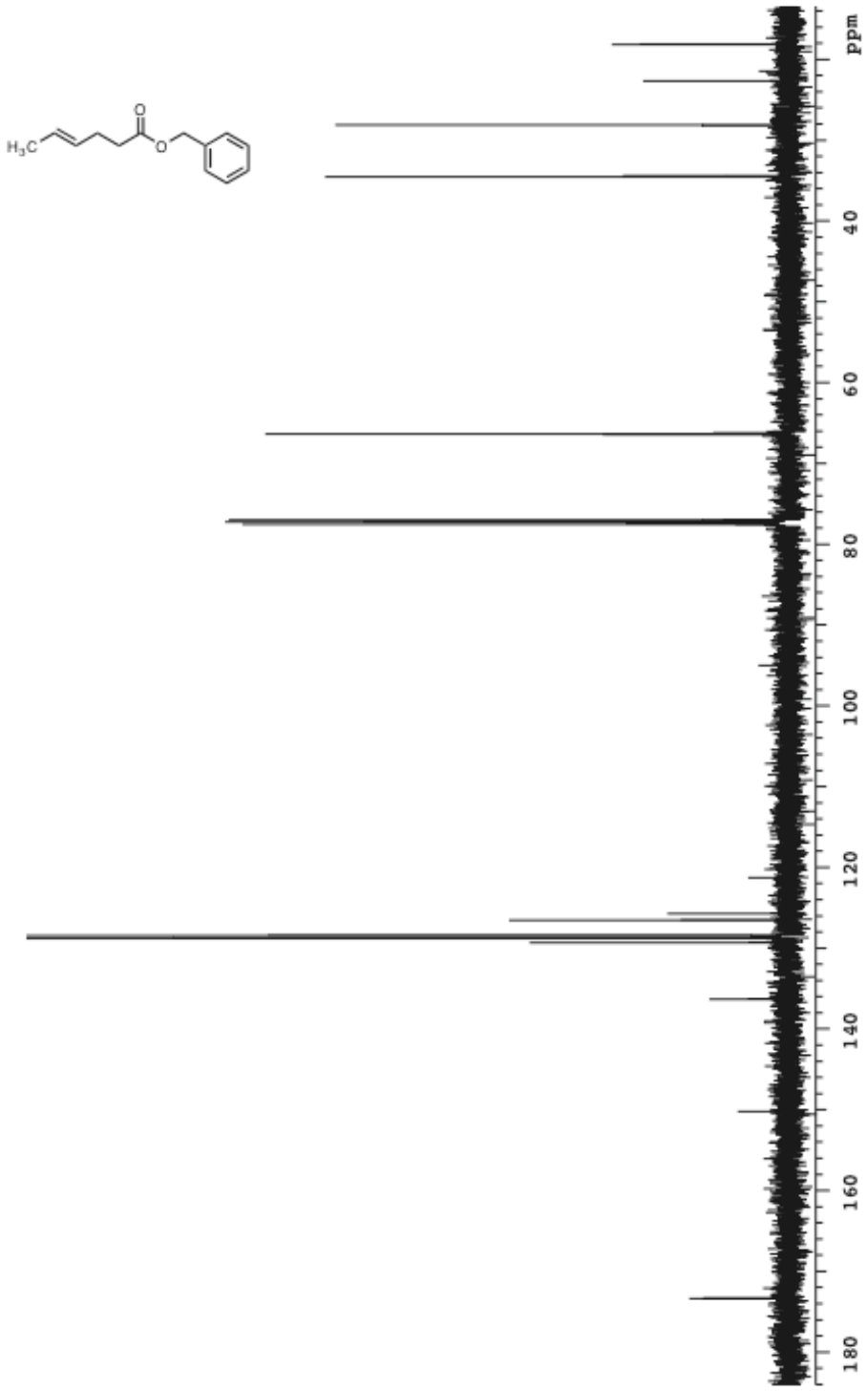
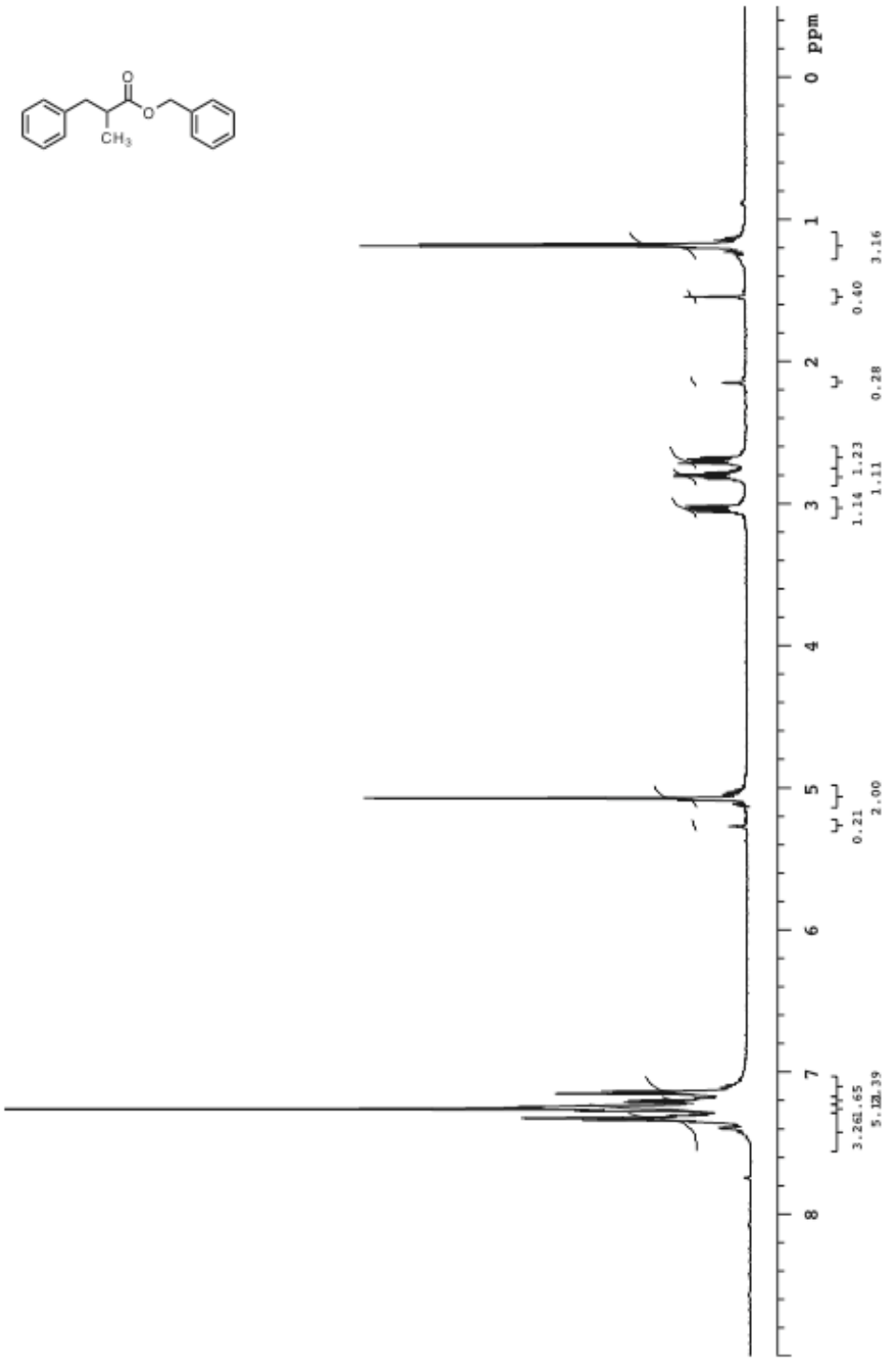
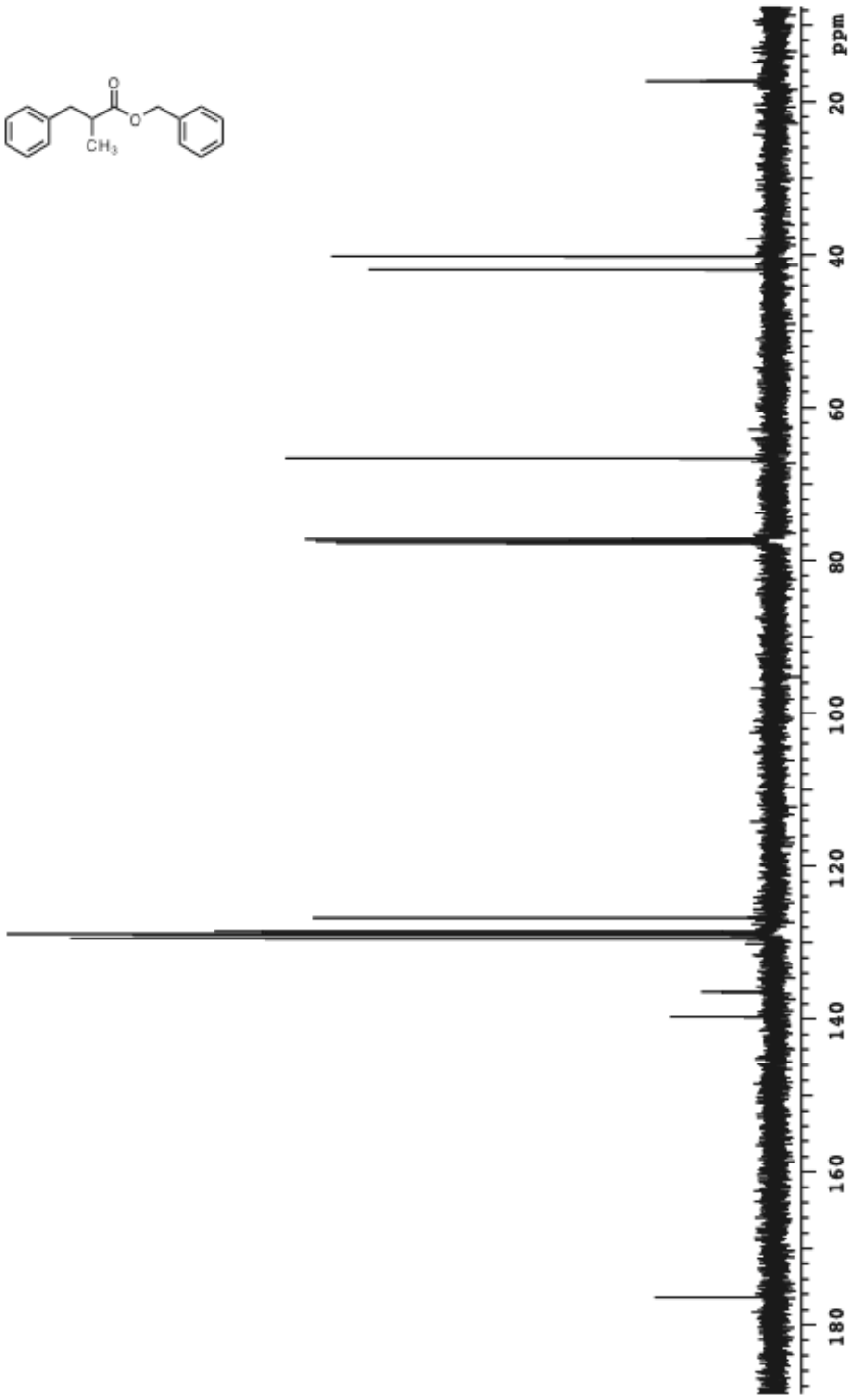
2
3
4
5
6
7
8
5.14
2.00
1.98
1.67
2.22
2.65


ppm
40
60
80
100
120
140
160
180


O
O
CH3
0 ppm
1
2
3
4
5
6
7
8
1.14 1.23
1.11
0.21
2.00
3.16
0.40
0.28


O
O
CH3
ppm
20
40
60
80
100
120
140
160
180