Solvent- or Temperature-Controlled Diastereoselective Aldol Reaction of Methyl Phenylacetate

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Supporting Information

Contents

General Information:

All reactions were performed under an inert atmosphere. Dichloromethane, carbon tetrachloride, and pentane were freshly distilled from calcium hydride. Diethyl ether was distilled from

sodium/benzophenone. All other chemicals were purchased from Aldrich Chemical Co. and used without further purification, unless otherwise noted. Reaction-flasks were dried in oven at 100 ^{o}C for 12 h. Flash column chromatography was performed using silica gel (100-200 mesh, Sorbent technologies) with hexane-ethyl acetate mixture as eluent. TLC analysis was performed using glass-backed, Thin-Layer Silica Gel chromatography plates (Dynamic Absorbent Inc., 200 μm thickness, F-254 Indicator). ^{1}H and ^{13}C NMR spectra were recorded on Varian ASM 300 MHz spectrometer. Chemical shift (δ) values are reported in parts per million, and are referenced to tetramethylsilane. Data are reported as: δ value (multiplicity, *J*-value, integration, where s=singlet, d=doublet, t=triplet, m=multiplet, br=broad).

Phenylacetic acid and methyl phenylacetate (**3**) were purchased from Aldrich Chemical Co; isopropyl phenylacetate[1] (**4**) and *t*-butyl phenylacetate[2] (**5**) were prepared according to literature procedures. Diastereomeric ratios (*syn*:*anti* ratios) were determined by either ^{1}H NMR or GC analysis (for compounds **7j** and **7k**) of the crude reaction mixture. Varian 430-GC was used for recording gas chromatograms and specific conditions are discussed as a part of characterization of compounds.

Procedure for the preparation of dicyclohexylborane (Chx_2BH)[3]

An oven-dried, 250 mL round-bottom flask with a charged magnetic stirrer bar was equipped with an air-tight, rubber septum and flushed with nitrogen gas. This was followed by the introduction of 8.2 g (100 mmol) of cyclohexene. Anhydrous diethyl ether (35 mL) was added, and the flask was cooled to 0 ^{o}C. 3.85 g (50 mmol) of borane-methyl sulfide complex was slowly added at this temperature. A white, solid compound was formed. Finally, 12 mL of diethyl ether was added. The mixture was stirred throughout the entire addition process, and continued thereafter for 3 additional hours at 0 ^{o}C. The solid was allowed to settle, and the supernatant solvent was then removed via cannula. The compound was then washed with (2 × 10 mL) of cold ether under nitrogen. Finally, it was dried under high vacuum to obtain free flowing powder and stored under nitrogen at 0 ^{o}C.

1 . Kazemi, F.; Kiasat, A. R.; Mombaini, B.; Chamran, S. *Phosphorus, Sulfur, and Silicon* **2004**, *179*, 1187.
2 . Harker, W. R. R.; Carswell, E. L.; Carbery, D. R. *Org. Lett.* **2010**, *12*, 3712.
3 . Slight modification of reported procedure. See: (a) Inoue, T.; Liu, *J*.-F.; Buske, D. C.; Abiko, A. *J. Org. Chem.* **2002**, *67*, 5250. (b) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975; pp 28-29.

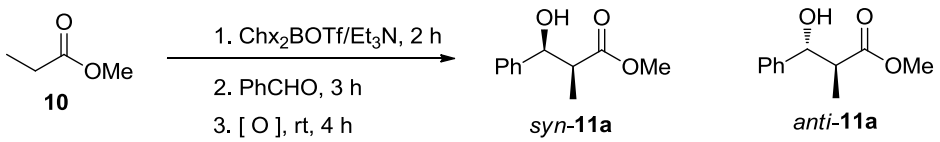
General Procedure for the *Anti*-Selective Aldol Reaction

Freshly-prepared dicyclohexylborane (Chx_2BH) (0.267 g, 1.5 mmol) was transferred to a 50 mL round-bottom flask and suspended in 3 mL dichloromethane. Trifluoromethanesulfonic acid (TfOH) (0.15 mL, 1.69 mmol) was then added dropwise at 0 ^oC. The reaction mixture was stirred at room temperature for 1 h followed by cooling to -78 ^oC. Methyl phenylacetate (0.150 g, 1 mmol), dissolved in 1 mL dichloromethane, was slowly added to the cooled reaction mixture. Triethylamine (0.30 mL, 2.2 mmol) was then added dropwise to the reaction mixture and stirred for 2 h at -78 ^oC. Aldehyde (1.5 mmol) was added dropwise to the solution of enolate and stirred for 3 h at the same temperature (-78 ^oC). The reaction was quenched by addition of *p*H 7 buffer solution (2 mL). The mixture was diluted with MeOH (2 mL) followed by slow addition of 30% hydrogen peroxide (2 mL) and stirred for 4 h at room temperature. Organic layer was separated and aqueous layer was washed with dichloromethane (3 × 10 mL). Combined organic layers were then washed with saturated brine solution (5 mL), dried over anhydrous Na_2SO_4, filtered, concentrated *in vacuo* and purified by silica gel column chromatography to obtain pure *anti*-aldol product.

General Procedure for the *Syn*-Selective Aldol Reaction

Freshly-prepared dicyclohexylborane (Chx_2BH) (0.267 g, 1.5 mmol) was transferred to a 50 mL round-bottom flask and suspended in 3 mL dichloromethane. Trifluoromethanesulfonic acid (TfOH) (0.15 mL, 1.69 mmol) was then added dropwise at 0 ^oC. The reaction mixture was stirred at room temperature for 1 h. Methyl phenylacetate (0.150 g, 1 mmol), dissolved in 1 mL dichloromethane, was slowly added to the reaction mixture. *N*, *N*-diisopropylethylamine (0.38 mL, 2.2 mmol) was then added dropwise to the reaction mixture and stirred for 2 h at room temperature. Aldehyde (1.5 mmol) was added dropwise to the solution of enolate and stirred for 3 h at the same temperature (RT). The reaction was quenched by addition of *p*H 7 buffer solution (2 mL). The mixture was diluted with MeOH (2 mL) followed by slow addition of 30% hydrogen peroxide (2 mL) and stirred for 4 h at room temperature. Organic layer was separated and aqueous layer was washed with dichloromethane (3 × 10 mL). Combined organic layers were then washed with saturated brine solution (5 mL), dried over anhydrous Na_2SO_4, filtered, concentrated *in vacuo* and purified by silica gel column chromatography to obtain pure *syn*-aldol product.

Effect of Temperature or Solvent on Diastereoselectivity of Aldol Reaction of Methyl Propanoate (10)

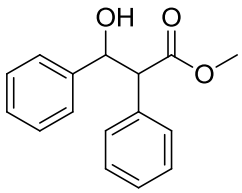


Freshly-prepared dicyclohexylborane (Chx_2BH) (0.267 g, 1.5 mmol) was transferred to a 50 mL round-bottom flask and suspended in 3 mL solvent. Trifluoromethanesulfonic acid (TfOH) (0.15 mL, 1.69 mmol) was then added dropwise at 0 ^oC. The reaction mixture was stirred at room temperature for 1 h followed by cooling to 0 ^oC (Cooling is not required in case of room temperature enolization and aldolization). Methyl Propanoate (0.088 g, 1 mmol), dissolved in 1 mL solvent, was slowly added to the reaction mixture. Triethylamine (0.30 mL, 2.2 mmol) was then added dropwise to the reaction mixture and stirred for 2 h at the enolization temperature. Aldehyde (1.5 mmol) was added dropwise to the solution of enolate and stirred for 3 h at the aldolization temperature. The reaction was quenched by addition of *p*H 7 buffer solution (2 mL). The mixture was diluted with MeOH (2 mL) followed by slow addition of 30% hydrogen peroxide (2 mL) and stirred for 4 h at room temperature. Organic layer was separated and aqueous layer was washed with dichloromethane (3 × 10 mL). Combined organic layers were then washed with saturated brine solution (5 mL), dried over anhydrous Na_2SO_4, filtered, concentrated *in vacuo* and purified by silica gel column chromatography to obtain pure *syn*-aldol product (**11a**). ^1H NMR analysis of crude reaction mixture showed that *syn*-aldol product was formed as the predominant product at both temperatures (0 ^oC and rt) and solvents (CH_2Cl_2 and Pentane). No temperature and solvent effect on the diastereoselectivity was observed for the aldol reaction of methyl propanoate. Results are summarized in the following table.

Entry	Enolization conditions	Aldolization conditions	Solvent	Yield (%)	*syn:anti*
1	0 ^oC	0 ^oC	CH_2Cl_2	87	90:10
2	0 ^oC	0 ^oC	Pentane	77	91:09
3	rt	rt	Pentane	69	85:15
4	rt	rt	CH_2Cl_2	78	85:15

Characterization of the compounds:

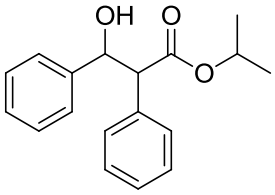
Methyl 3-hydroxy-2,3-diphenylpropanoate (7a)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.35 – 7.25 (m, 10H), 5.30 (dd, *J* = 1.8, 7.5 Hz, 1H), 3.88 (d, *J* = 7.5 Hz, 1H), 3.53 (s, 3H), 2.59 (d, *J* = 2.4 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.0, 140.9, 134.8, 129.3, 128.8, 128.4, 128.1, 126.7, 75.1, 59.7, 52.2. **HRMS-EI** $C_{16}H_{16}O_3$ calc. 256.1099, found 256.1105.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.16 – 7.04 (m, 10H), 5.16 (dd, *J* = 3.9, 9.3 Hz, 1H), 3.86 (d, *J* = 9.3 Hz, 1H), 3.68 (s, 3H), 3.37 (d, *J* = 4.2 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 174.0 , 140.8, 135.2, 128.6, 128.5, 128.1, 127.8, 127.6, 126.7, 76.6, 59.9, 52.3. **HRMS-EI** $C_{16}H_{16}O_3$ calc. 256.1099, found 256.1103.

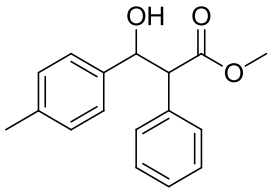
Isopropyl 3-hydroxy-2,3-diphenylpropanoate (8a)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.35 – 7.26 (m, 10H), 5.19 (d, *J* = 8.1 Hz, 1H), 4.84 – 4.76 (m, 1H), 3.81(d, *J* = 8.1 Hz, 1H), 2.64 (br, 1H), 1.00 (d, *J* = 6.3 Hz, 3H), 0.91 (d, *J* = 6.3, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 171.7, 141.0, 135.2, 129.1, 128.6, 128.2, 128.0, 127.8, 127.0, 75.5, 68.3, 60.0, 21.4. **HRMS-EI** $C_{18}H_{20}O_3$ calc. 284.1412, found 284.1401.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.19 – 7.07 (m, 10H), 5.17 – 5.04 (m, 2H), 3.83 (d, *J* = 9.0 Hz, 1H), 3.30 (d, *J* = 4.2 Hz, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.1, 141.0, 135.6, 128.6, 128.5, 128.1, 127.8, 127.4, 126.7, 76.7, 68.8, 60.1, 21.8, 21.5. **HRMS-EI** $C_{18}H_{20}O_3$ calc. 284.1412, found 284.1399.

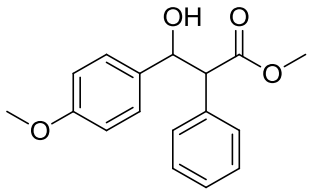
Methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (7b)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.36 – 7.30 (m, 5H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 5.25 (dd, *J* = 2.1, 7.8 Hz, 1H), 3.87 (d, *J* = 7.8 Hz, 1H), 3.52 (s, 3H), 2.45 (d, *J* = 2.1 Hz, 1H), 2.32 (s, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 172.8, 138.0, 137.7, 135.0, 129.2, 129.1, 128.7, 128.0, 126.6, 75.0, 59.8, 52.1, 21.3. **HRMS-EI** $C_{17}H_{18}O_3$ calc. 270.1256, found 270.1265.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** 7.17 – 7.06 (m, 5H), 6.96 (s, 4H), 5.13 (dd, *J* = 3.6, 9.6 Hz, 1H), 3.86 (d, *J* = 9.3 Hz, 1H), 3.67 (s, 3H), 3.27 (d, *J* = 3.6 Hz, 1H), 2.22 (s, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 174.0, 137.9, 137.4, 135.3, 128.8, 128.6, 128.5, 127.5, 126.6, 76.4, 59.9, 52.3, 21.1. **HRMS-EI** $C_{17}H_{18}O_3$ calc. 270.1256, found 270.1263.

Methyl 3-hydroxy-3-(4-methoxyphenyl)-2-phenylpropanoate (7c)

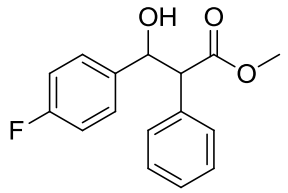


***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.37 -7.32 (m, 5H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.24 (dd, *J* = 1.8, 8.1 Hz, 1H), 3.86 (d, *J* = 7.8 Hz, 1H), 3.79 (s, 3H), 3.53 (s, 3H),

2.45 (d, *J* = 2.4 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 172.9, 159.4, 135.0, 133.2, 129.2, 128.8, 128.0, 113.8, 74.8, 59.9, 55.4, 52.1. **HRMS-EI** $C_{17}H_{18}O_4$ calc. 286.1205, found 286.1211.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.19 -7.16 (m, 3H), 7.09 -7.06 (m, 2H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 5.13 (d, *J* = 9.3 Hz, 1H), 3.86 (d, *J* = 9.6 Hz, 1H), 3.71 (s, 6H), 3.16 (br, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 174.1, 159.1, 135.3 133.0, 128.6, 128.6, 127.9, 127.6, 113.5, 76.3, 60.0, 55.2, 52.4. **HRMS-EI** $C_{17}H_{18}O_4$ calc. 286.1205, found 286.1215.

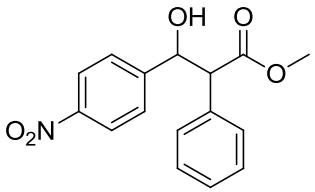
Methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (7d)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.30 (s, 5H), 7.23 (dd, *J* = 5.4 Hz, 8.7 Hz, 2H), 6.96 (t, *J* = 8.7, 2H), 5.23 (d, *J* = 7.5 Hz, 1H), 3.80 (d, *J* = 7.5 Hz, 1H), 3.51 (s, 3H), 2.77 (br, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 172.9, 162.4 (d, $J_{C\text{-}F}$ = 244.5 Hz), 136.7, 134.5, 129.2, 128.7, 128.5, 128.4, 128.1, 115.1 (d, $J_{C\text{-}F}$ = 21.2 Hz), 74.4, 59.7, 52.2. **HRMS-EI** $C_{16}H_{15}FO_3$ calc. 274.1005, found 274.1014.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.15 (t, *J* = 3.6 Hz, 3H), 7.05 – 7.00 (m, 4H), 6.82 (t, *J* = 8.7 Hz, 2H), 5.15 (dd, *J* = 3.9, 9.9 Hz, 1H), 3.80 (d, *J* = 9.6 Hz, 1H), 3.67 (s, 3H), 3.58 (d, *J* = 3.9 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ 174.0, 162.3 (d, $J_{C\text{-}F}$ = 244.4 Hz), 136.6, 135.0, 128.7, 128.4, 127.8, 115.0 (d, $J_{C\text{-}F}$ = 20.9 Hz), 76.0, 60.2, 52.5. **HRMS-EI** $C_{16}H_{15}FO_3$ calc. 274.1005, found 274.1012

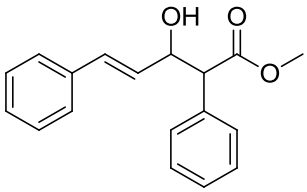
Methyl 3-hydroxy-3-(4-nitrophenyl)-2-phenylpropanoate (7e)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 8.11 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.30 – 7.26 (m, 3H), 7.23 – 7.19 (m, 2H), 5.42 (d, *J* = 6.3 Hz, 1H), 3.84 (d, *J* = 6.3 Hz, 1 H), 3.59 (s, 3H), 3.27 (br, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.0, 148.1, 147.4, 133.4, 129.3, 128.7, 128.3, 127.5, 123.4, 73.8, 58.8, 52.4. **HRMS-EI** $C_{16}H_{15}NO_5$ calc. 301.0950, found 301.0956.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.98 (d, *J* = 8.7 Hz, 2H), 7.22 – 7.17 (m, 5H), 7.06 – 7.02 (m, 2H), 5.30 (dd, *J* = 3.3, 9.6 Hz, 1H), 3.99 (d, *J* = 3.9 Hz), 3.82 (d, *J* = 9.6 Hz, 1H), 3.69 (s, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.5, 148.2, 147.2, 134.2, 128.8, 128.4, 128.0, 127.5, 123.1, 75.5, 59.8, 52.5. **HRMS-EI** $C_{16}H_{15}NO_5$ calc. 301.0950, found 301.0958.

(*E*)-methyl 3-hydroxy-2,5-diphenylpent-4-enoate (7f)

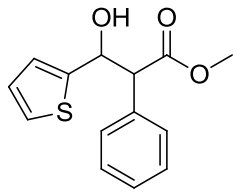


***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.39 – 7.23 (m, 10H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 6.9, 15.9 Hz, 1H), 4.85 (td, *J* = 0.9, 7.2 Hz, 1H), 3.77 (d, *J* = 7.5, 1H), 3.64 (s, 3H), 2.50 (br, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 172.9, 136.6, 134.8, 132.4, 129.2, 128.9, 128.6, 128.4, 128.1, 127.9, 126.7, 73.9, 58.2, 52.3. **HRMS-EI** $C_{18}H_{18}O_3$ calc. 282.1256, found 282.1260.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.30 – 7.14 (m, 10H), 6.50 (dd, *J* = 0.9, 15.9 Hz, 1H), 5.99 (dd, *J* = 6, 15.9 Hz, 1H), 4.86 (dd, *J* = 7.2, 8.7 Hz, 1H), 3.74 (d, *J* = 9.0 Hz, 1H), 3.68 (s,

3H), 3.29 (br, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.7, 136.6, 135.3, 131.6, 128.8, 128.7, 128.5, 127.9, 127.7, 126.5, 74.1, 58.6, 52.3. **HRMS-EI** $C_{18}H_{18}O_3$ calc. 282.1256, found 282.1265. Diastereomeric ratio of **7f** was determined by measuring peak area of methyl protons.

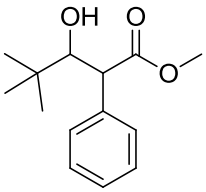
Methyl 3-hydroxy-2-phenyl-3-(thiophen-2-yl)propanoate (7g)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.40 – 7.29 (m, 5H), 7.22 -7.20 (m, 1H), 6.98 – 6.90 (m, 2H), 5.53 (dd, *J* = 2.4, 8.1 Hz, 1H), 3.92 (d, *J* = 8.1 Hz, 1H), 3.54 (s, 3H), 2.69 (d, *J* = 3 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 172.5, 144.6, 134.7, 129.1, 128.8, 128.2, 126.6, 125.1, 124.9, 71.2, 60.2, 52.2. **HRMS-EI** $C_{14}H_{14}O_3S$ calc. 262.0664, found 262.0654.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.25 -7.15 (m, 5H), 7.12 (dd, *J* = 0.6, 5.1 Hz, 1H), 6.74 (dd, *J* = 3.3, 5.1 Hz, 1H), 6.57 – 6.55 (m, 1H), 5.45 (dd, *J* = 4.2, 9.0 Hz, 1H), 3.93 (d, *J* = 9.3 Hz, 1H), 3.68 (s, 3H), 3.61 (d, *J* = 4.5 Hz, 1H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.6, 144.6, 135.1, 128.6, 128.6, 127.8, 126.4, 125.0, 72.5, 60.1, 52.4. $C_{14}H_{14}O_3S$ calc. 262.0664, found 262.0656.

Methyl 3-hydroxy-4,4-dimethyl-2-phenylpentanoate (7h)

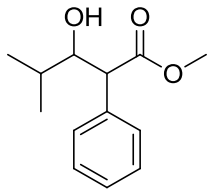


***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.44 – 7.25 (m, 5H), 4.02 (dd, *J* = 3, 7.5 Hz, 1 H), 3.75 (d, *J* = 7.8 Hz, 1H), 3.62 (s, 3H), 1.96 (d, *J* = 3.3 Hz, 1H), 0.91 (s, 9H); **^{13}C NMR (75 MHz,**

$CDCl_3$): δ 174.2, 136.2, 129.6, 128.9, 127.9, 78.6, 53.8, 52.2, 35.7, 26.3. **HRMS-EI** $C_{14}H_{20}O_3$ calc. 236.1412, found 236.1420.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.45 – 7.23 (m, 5H), 3.89 -3.86 (m, 2H), 3.68 – 3.63 (m, 1H), 3.67 (s, 3H), 0.89 (s, 9H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 175.0, 138.0, 128.8, 128.5, 127.6, 82.1, 52.3, 51.4, 36.3, 26.5. **HRMS-EI** $C_{14}H_{20}O_3$ calc. 236.1412, found 236.1423.

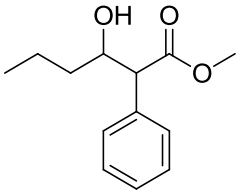
Methyl 3-hydroxy-4-methyl-2-phenylpentanoate (7i)



***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.42 – 7.25 (m, 5H), 3.95 (t, *J* = 6.3 Hz, 1H), 3.73 (d, *J* = 6.9 Hz, 1H), 3.64 (s, 9H), 2.33 (s, 1H), 1.67 -1.54 (m, 1H), 0.97 (dd, *J* = 4.2, 6.6 Hz, 6H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.9, 135.5, 129.4, 128.7, 127.8, 77.0, 54.8, 52.1, 30.8, 19.9, 16.7. $C_{13}H_{18}O_3$ calc. 222.1256, found 222.1266.

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.34 – 7.26 (m, 5H), 4.10 – 4.04 (m, 1H), 3.73 (d, *J* = 9.3 Hz, 1H), 3.68 (s, 3H), 2.61 (d, *J* = 5.4 Hz, 1H), 1.50 - 1.38 (m, 1H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 174.5, 136.2, 129.0, 128.5, 127.8, 77.4, 55.9, 52.3, 29.2, 20.4, 14.6. $C_{13}H_{18}O_3$ calc. 222.1256, found 222.1268.

Methyl 3-hydroxy-2-phenylhexanoate (7j)

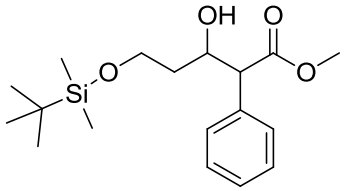


***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.37 – 7.25 (m, 5H), 4.23 – 4.15 (m, 1H), 3.66 (s, 3H), 3.57 (d, *J* = 6.3 Hz, 1H), 2.43 (d, *J* = 2.4 Hz, 1H), 1.55 – 1.34 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8, 135.2, 129.3, 128.7, 127.8, 72.0, 57.3, 52.1, 36.7, 19.1, 14.0. **HRMS-EI** $C_{13}H_{18}O_3$ calc. 222.1256, found 222.1267. Diastereomeric ratio was determined by using Varian 430-GC (FactorFour™:Capillary column VF-1ms, 15m 0.25mm 0.25µm, 60 °C-200 °C , flow rate - 3.0 mL/min., concentration = 20 µg/mL in CH_2Cl_2, Minor peak at 18.2 min. and major peak at 18.9 min.)

***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.35 – 7.24 (m, 5H), 4.24 -4.14 (m, 1H), 3.67 (s, 3H), 3.59 (d, *J* = 9.3 Hz, 1H), 3.03 (br, 1H), 1.56 – 1.20 (m, 4H), 0.81 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 174.3, 136.3, 128.9, 128.4, 127.7, 73.1, 58.8, 52.2, 36.1, 18.6, 13.9. **HRMS-EI** $C_{13}H_{18}O_3$ calc. 222.1256, found 222.1269. Diastereomeric ratio was determined by using Varian 430-GC (FactorFour™:Capillary column VF-1ms, 15m 0.25mm 0.25µm, 60 °C-200 °C , flow rate - 3.0 mL/min., concentration = 20 µg/mL in CH_2Cl_2, Major peak at 18.1 min. and minor peak at 19.2 min.)

Methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (7k)

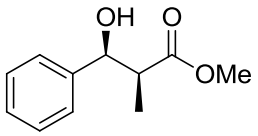


***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.41 – 7.25 (m, 5H), 4.47 – 4.40 (m, 1H), 3.91 – 3.78 (m, 2H), 3.66 (d, *J* = 7.2 Hz, 1H), 3.66 (s, 3H), 3.43 (d, 2.4 Hz, 1H), 1.76 – 1.58 (m, 2H), 0.89 (s, 9H), 0.06 (s, 6H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.4, 135.7, 129.2, 128.7, 127.7, 71.9, 61.9, 57.6, 52.2, 36.5, 26.0, 18.3, -5.4. **HRMS-EI** $C_{18}H_{30}O_4Si$ calc. 338.1913, found 338.1918. Diastereomeric ratio was determined by using Varian 430-GC (CP-Chirasil-Dex CB Varian Capillary column, 25m 0.32mm 0.25µm, 80 °C-200 °C , flow rate - 3.0 mL/min., concentration = 200 µg/mL in CH_2Cl_2, Minor peak at 43.2 min. and major peak at 44.3 min.)

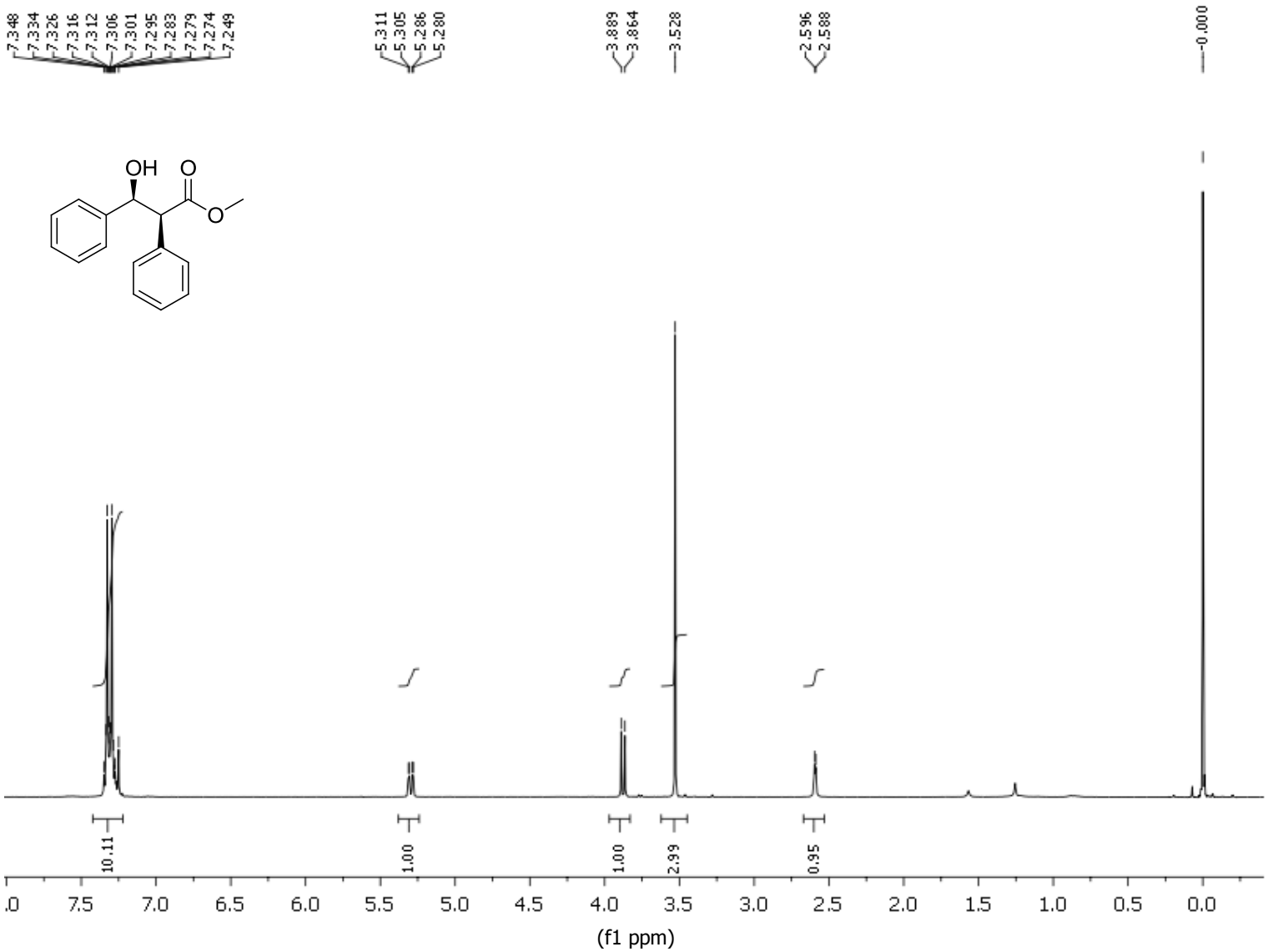
***Anti*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.34 – 7.23 (m, 5H), 4.49 – 4.41 (m, 1H), 3.93 (d, *J* = 2.7 Hz, 1H), 3.83 – 3.71 (m, 2H), 3.69 (s, 3H), 3.62 (d, *J* = 9.6 Hz, 1H), 1.57 – 1.38 (m, 2H), 0.88 (s,

9H), 0.04 (d, *J* = 3.9 Hz, 6H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 173.7, 136.0, 128.9, 128.6, 127.8, 73.7, 62.2, 58.9, 52.2, 35.3, 26.0, 18.2, -5.5. **HRMS-EI** $C_{18}H_{30}O_4Si$ calc. 338.1913, found 338.1925. Diastereomeric ratio was determined by using Varian 430-GC (CP-Chirasil-Dex CB Varian Capillary column, 25m 0.32mm 0.25µm, 80 ^{o}C-200 ^{o}C , flow rate - 3.0 mL/min., concentration = 200 µg/mL in CH_2Cl_2, Major peak at 43.2 min. and minor peak at 44.3 min.)

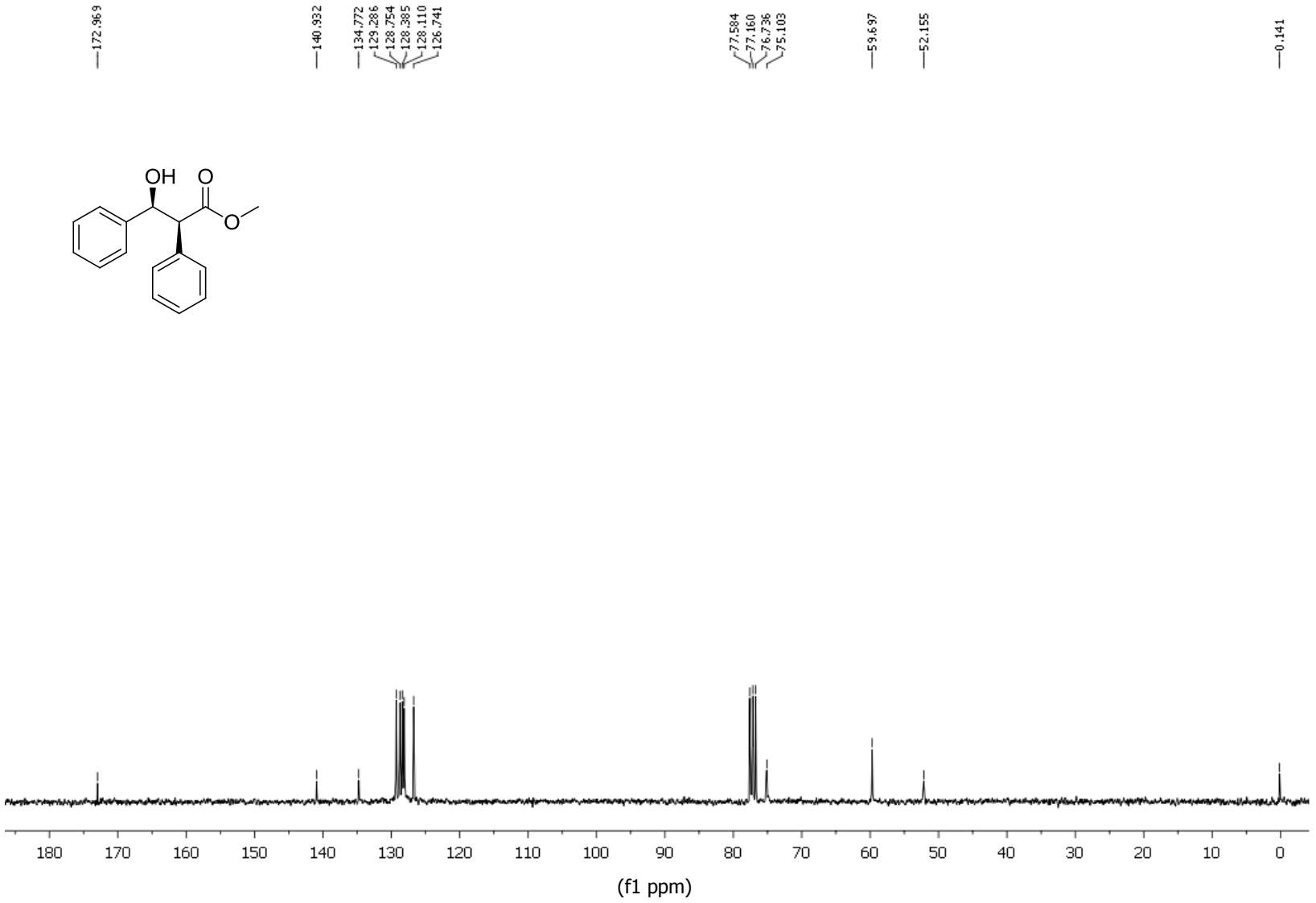
Methyl 3-hydroxy-2-methyl-3-phenylpropanoate (11a)



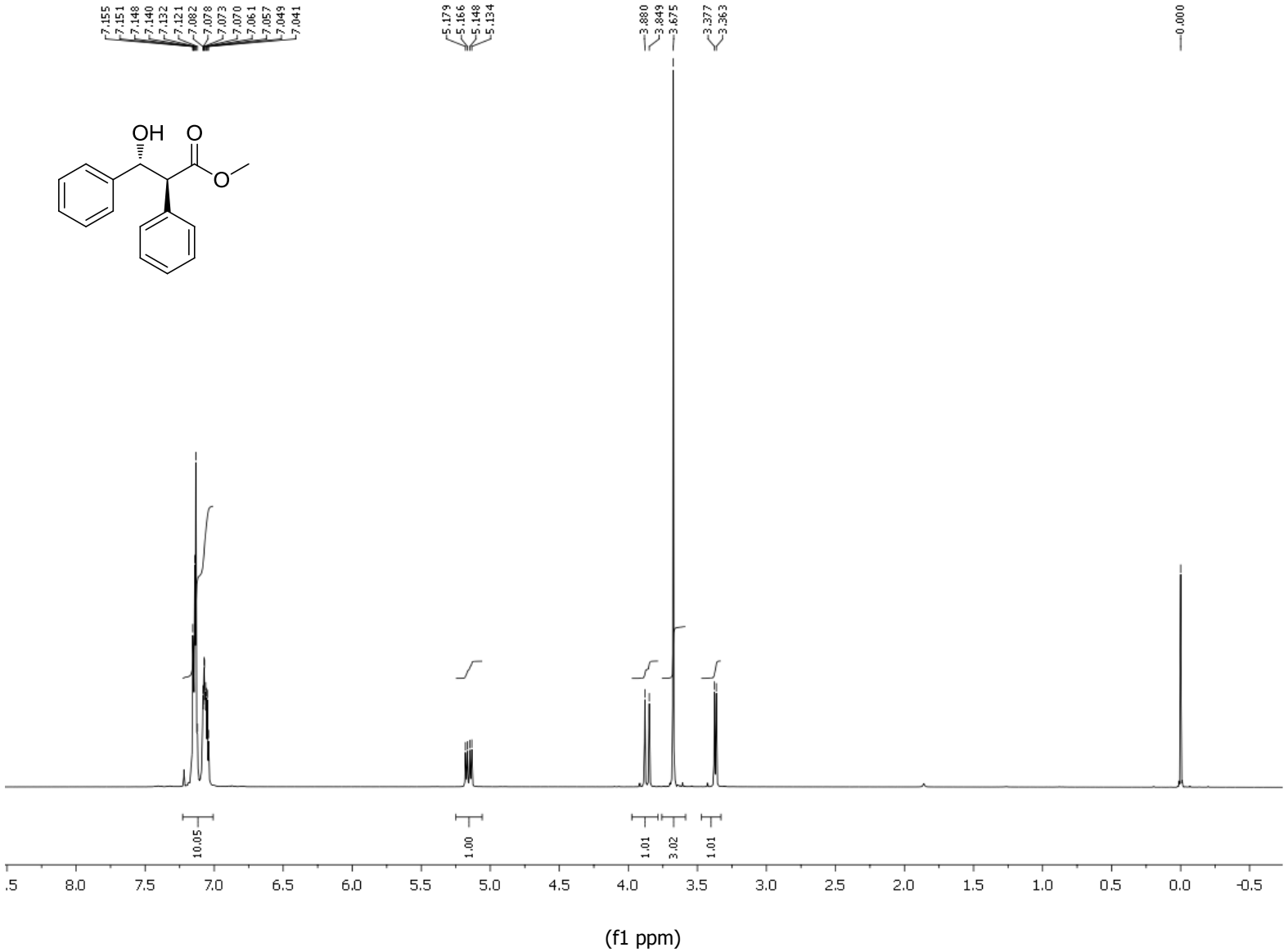
***Syn*: ^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.32 – 7.24 (m, 5H), 5.05 (d, *J* = 4.2 Hz, 1H), 3.62 (s, 1H), 3.18 (br, 1H), 2.81 – 2.72 (m, 1H), 1.11 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 176.1, 141.6, 128.2, 127.5, 126.0, 73.7, 51.9, 46.6, 10.9. **HRMS-EI** $C_{11}H_{14}O_3$ calc. 194.0943, found 194.0925.



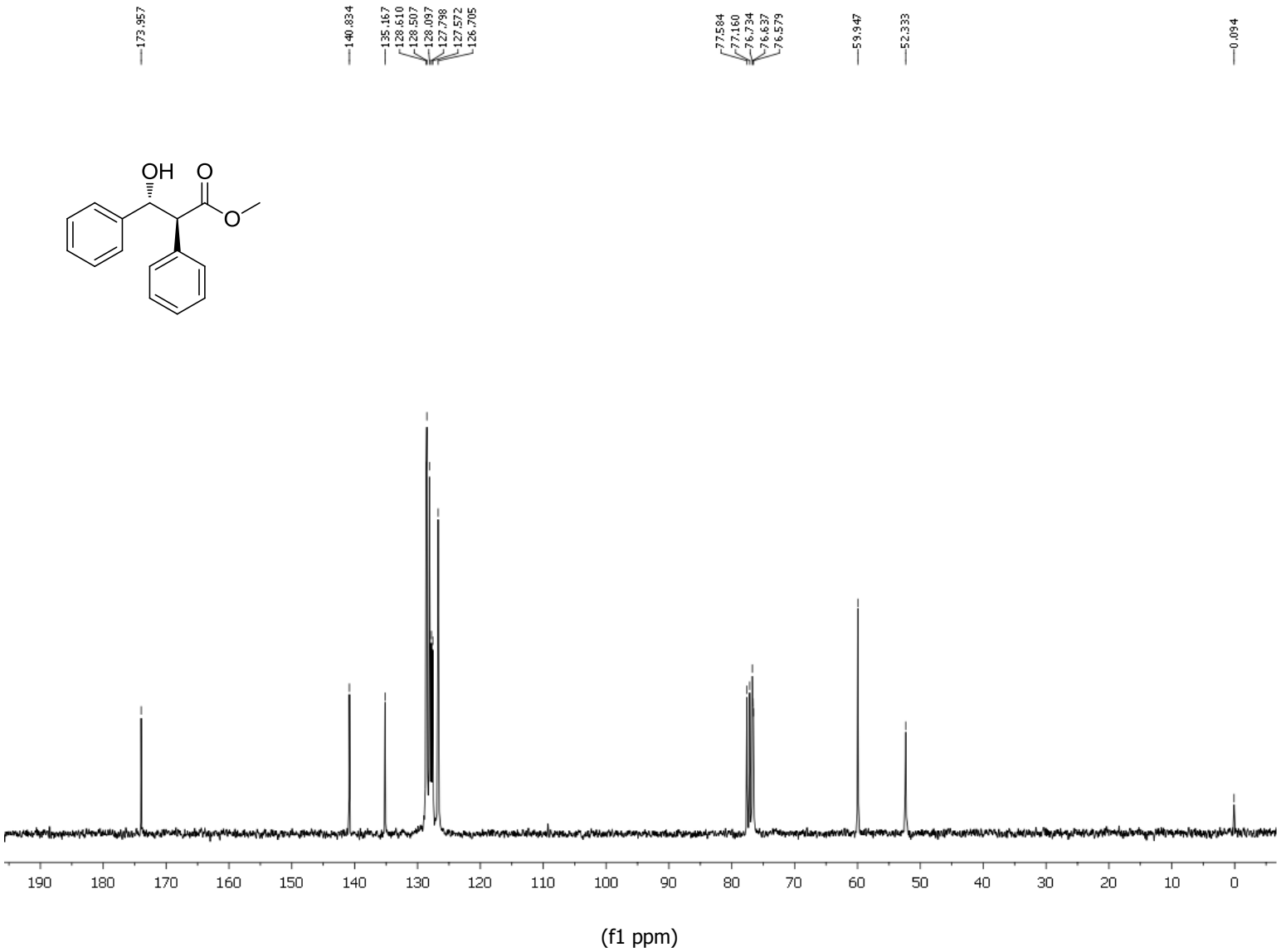
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-2,3-diphenylpropanoate (**7a**)



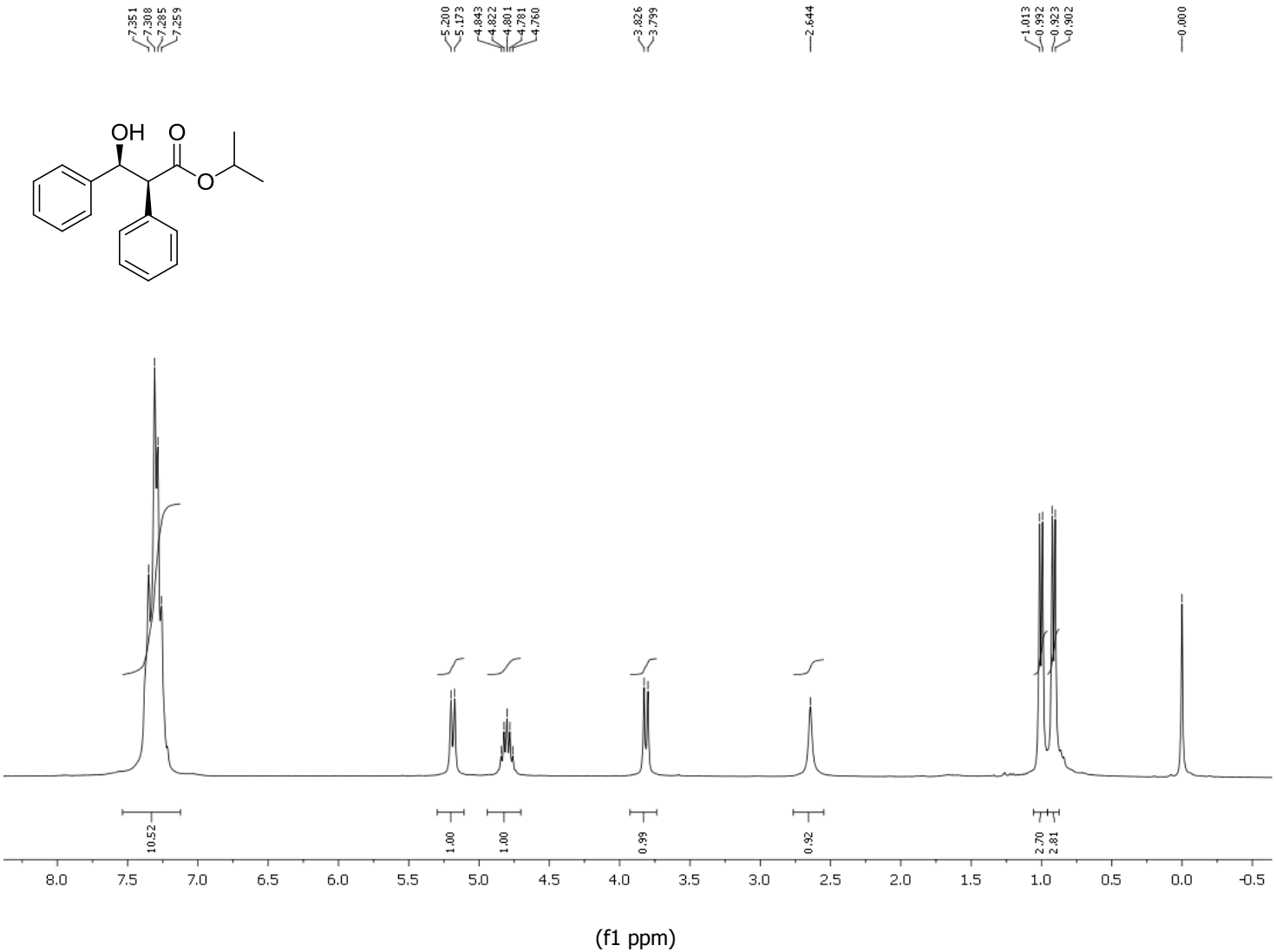
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-2,3-diphenylpropanoate (**7a**)



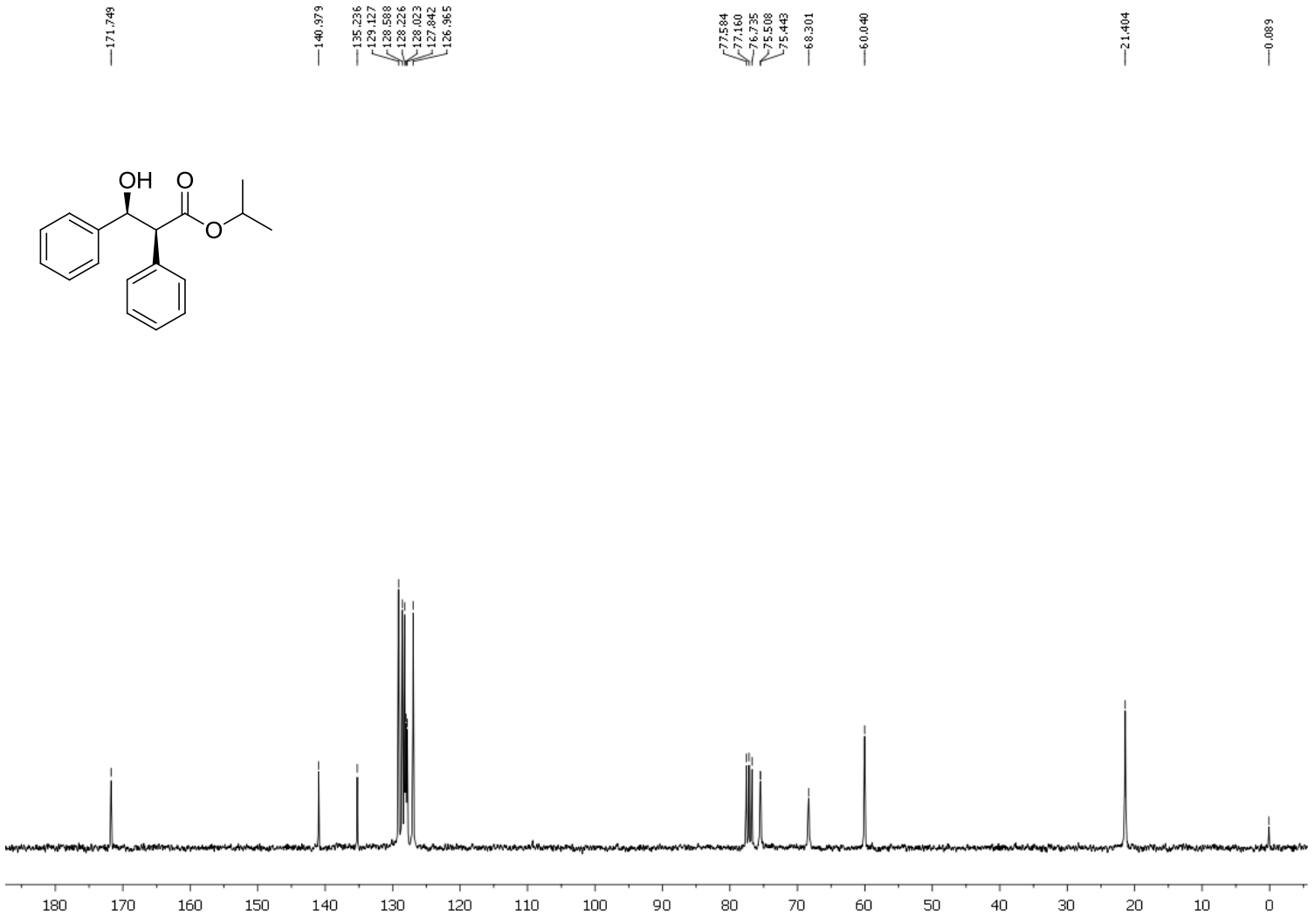
^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-2,3-diphenylpropanoate (**7a**)



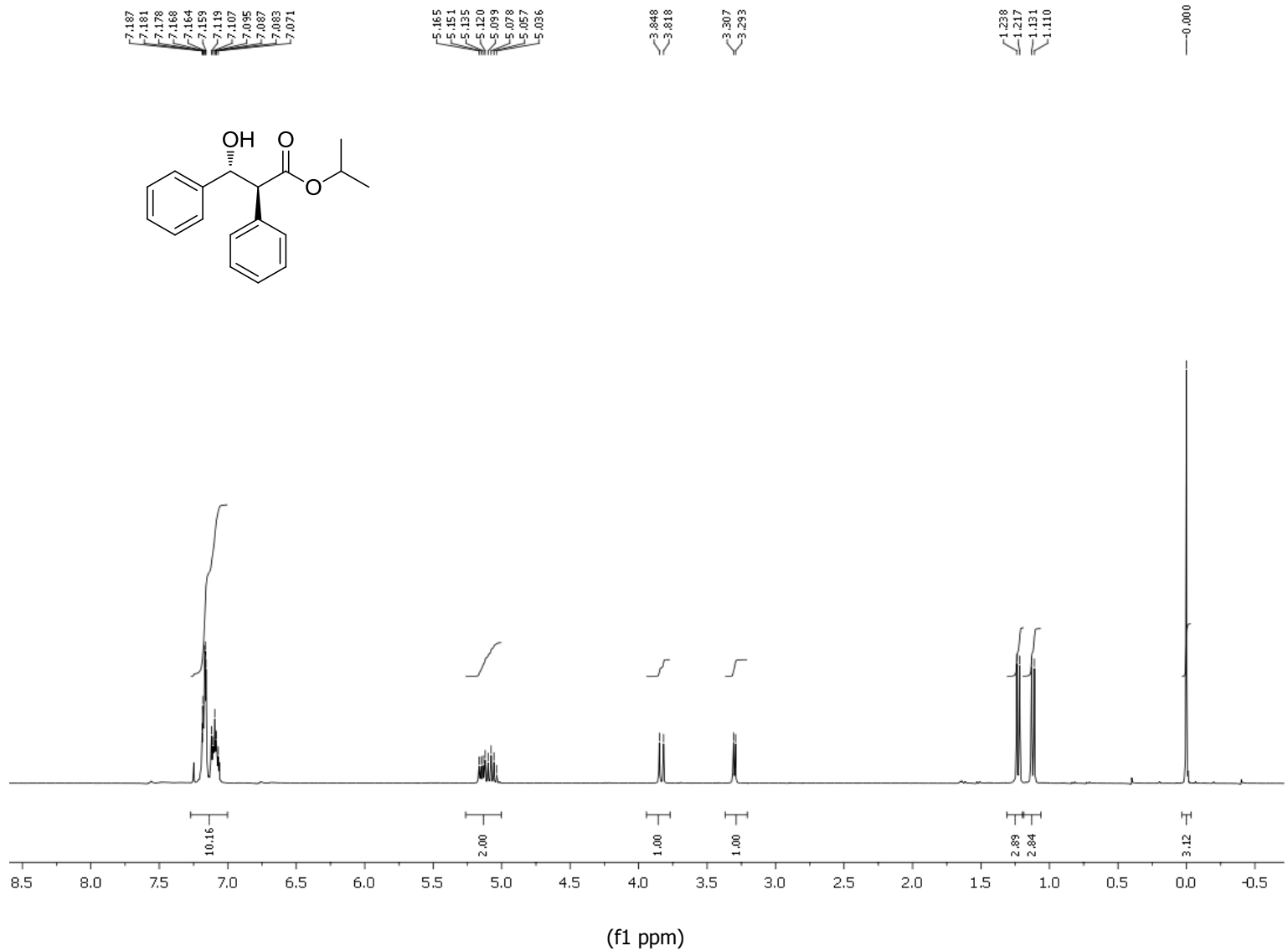
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-2,3-diphenylpropanoate (**7a**)



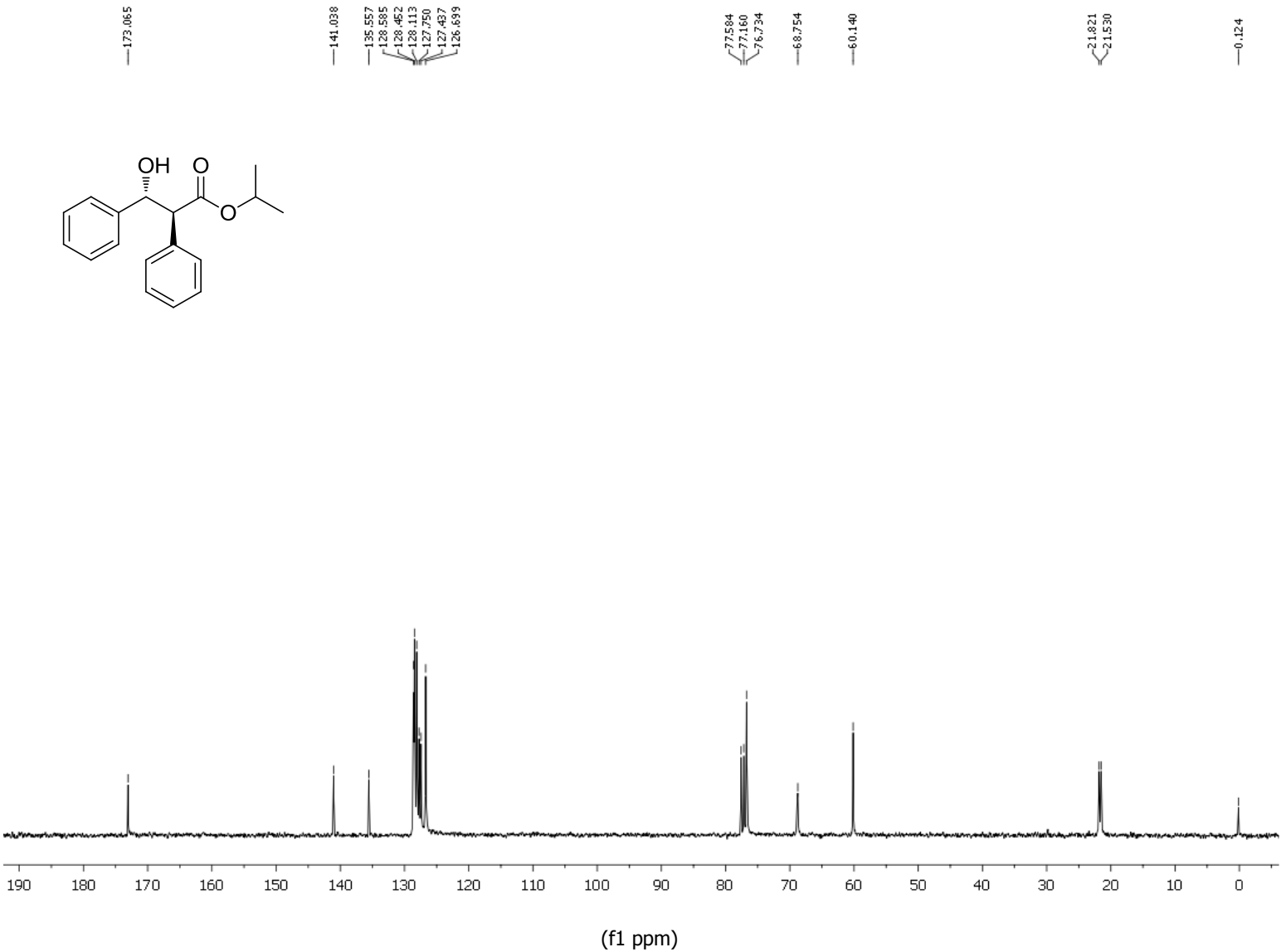
^{1}H NMR spectrum of *syn*-isopropyl 3-hydroxy-2,3-diphenylpropanoate (**8a**)



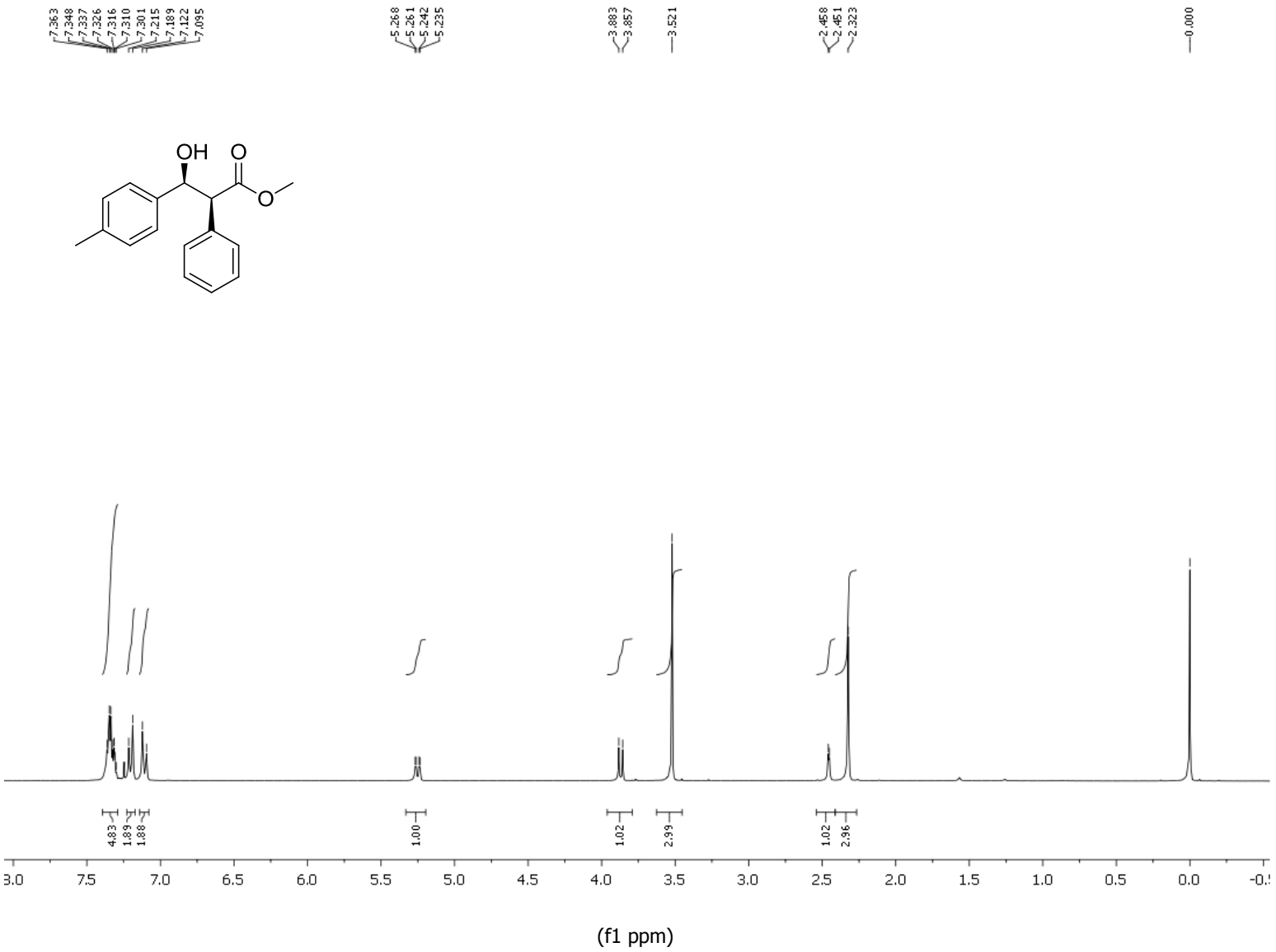
^{13}C NMR spectrum of *syn*-isopropyl 3-hydroxy-2,3-diphenylpropanoate (**8a**)



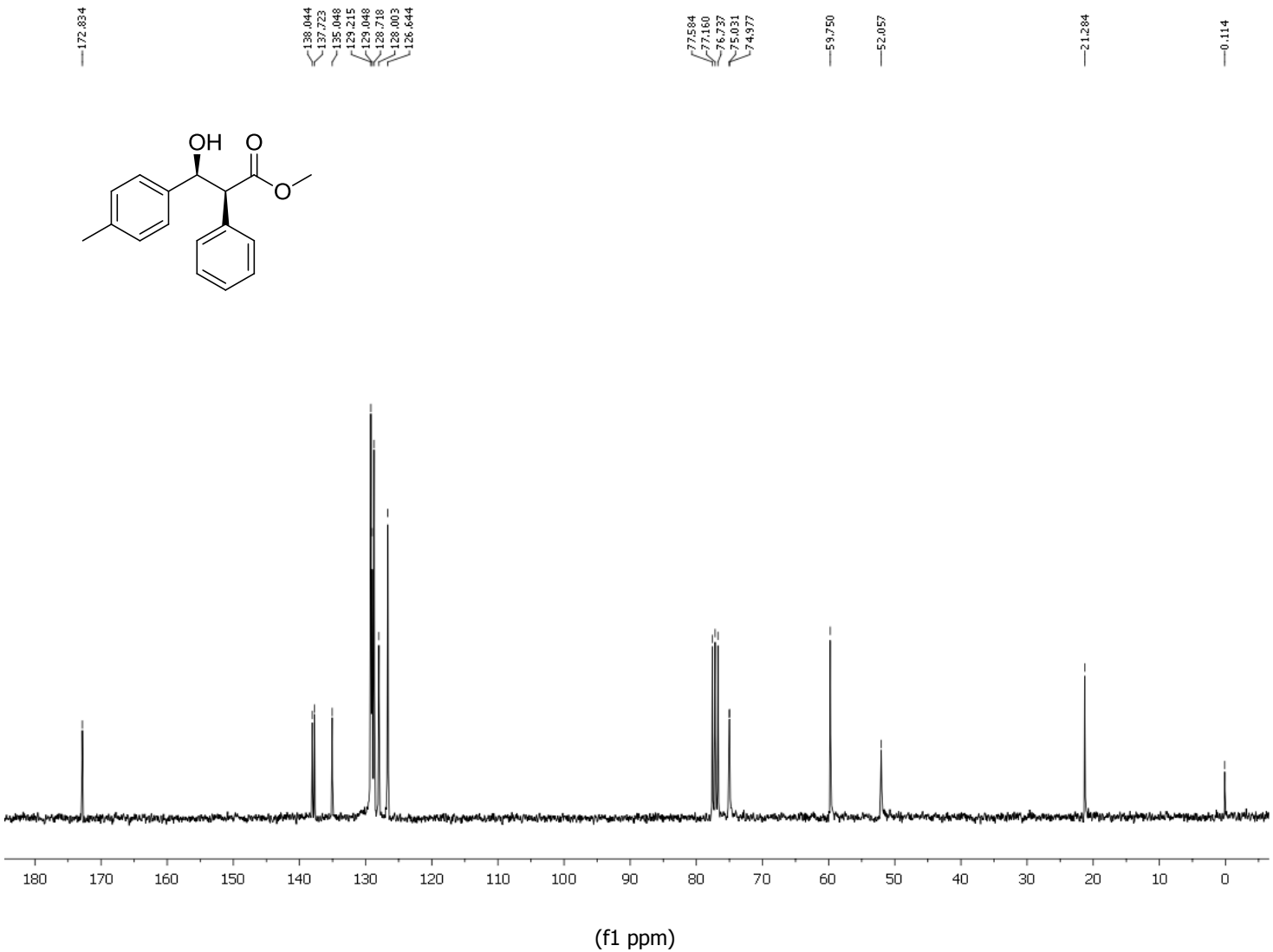
^{1}H NMR spectrum of *anti*-isopropyl 3-hydroxy-2,3-diphenylpropanoate (**8a**)



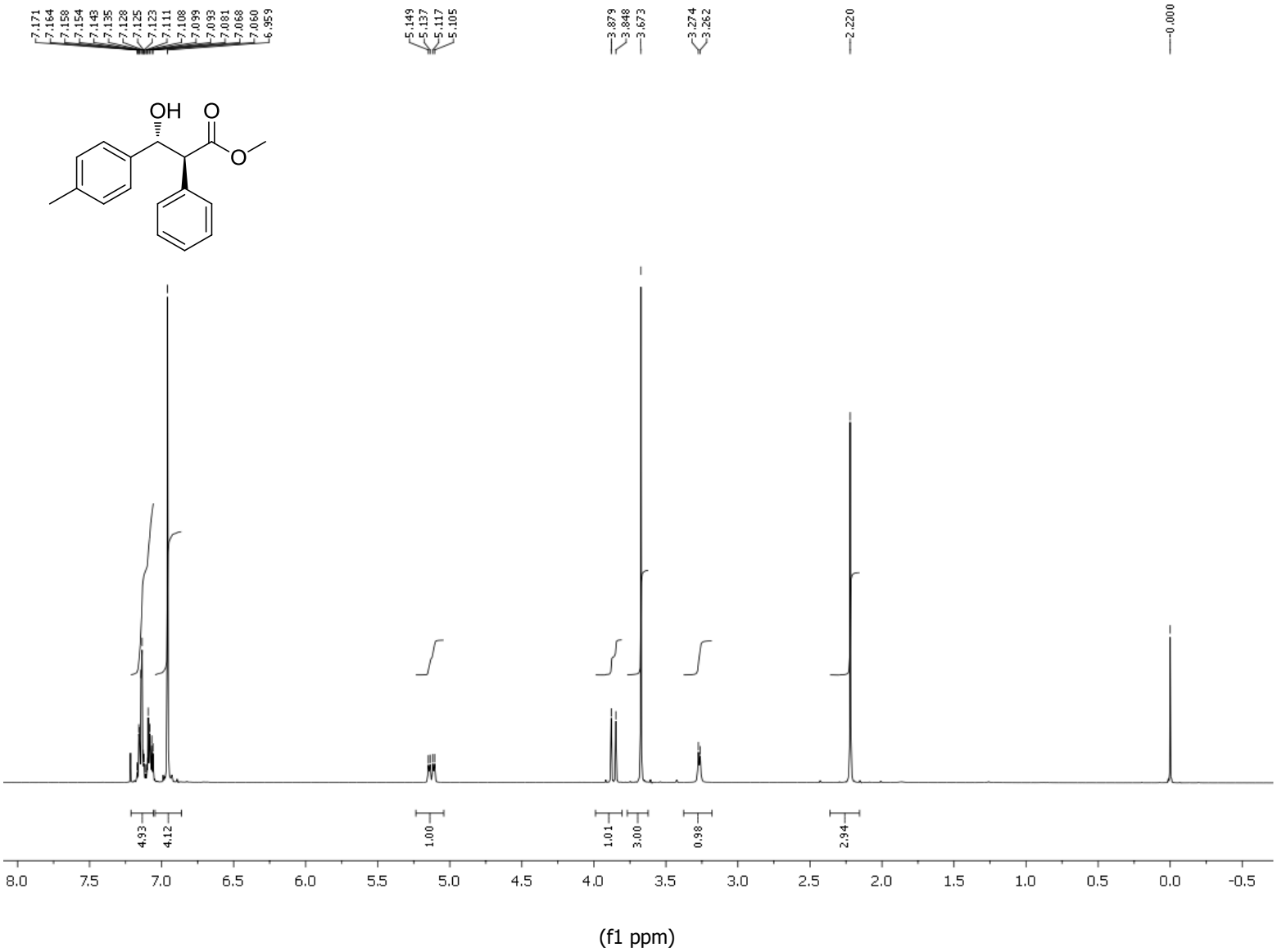
^{13}C NMR spectrum of *anti*-isopropyl 3-hydroxy-2,3-diphenylpropanoate (**8a)**



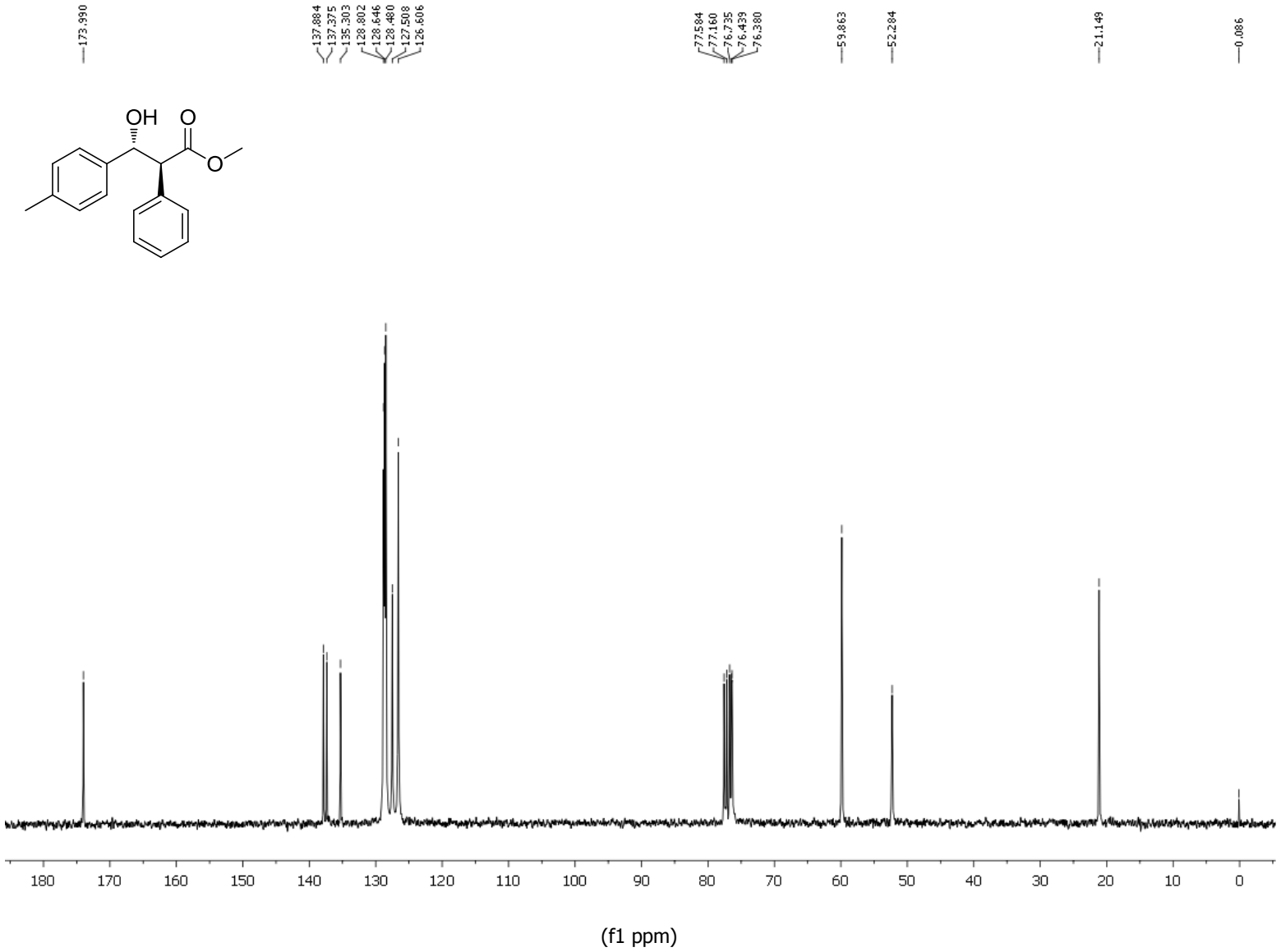
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (**7b**)



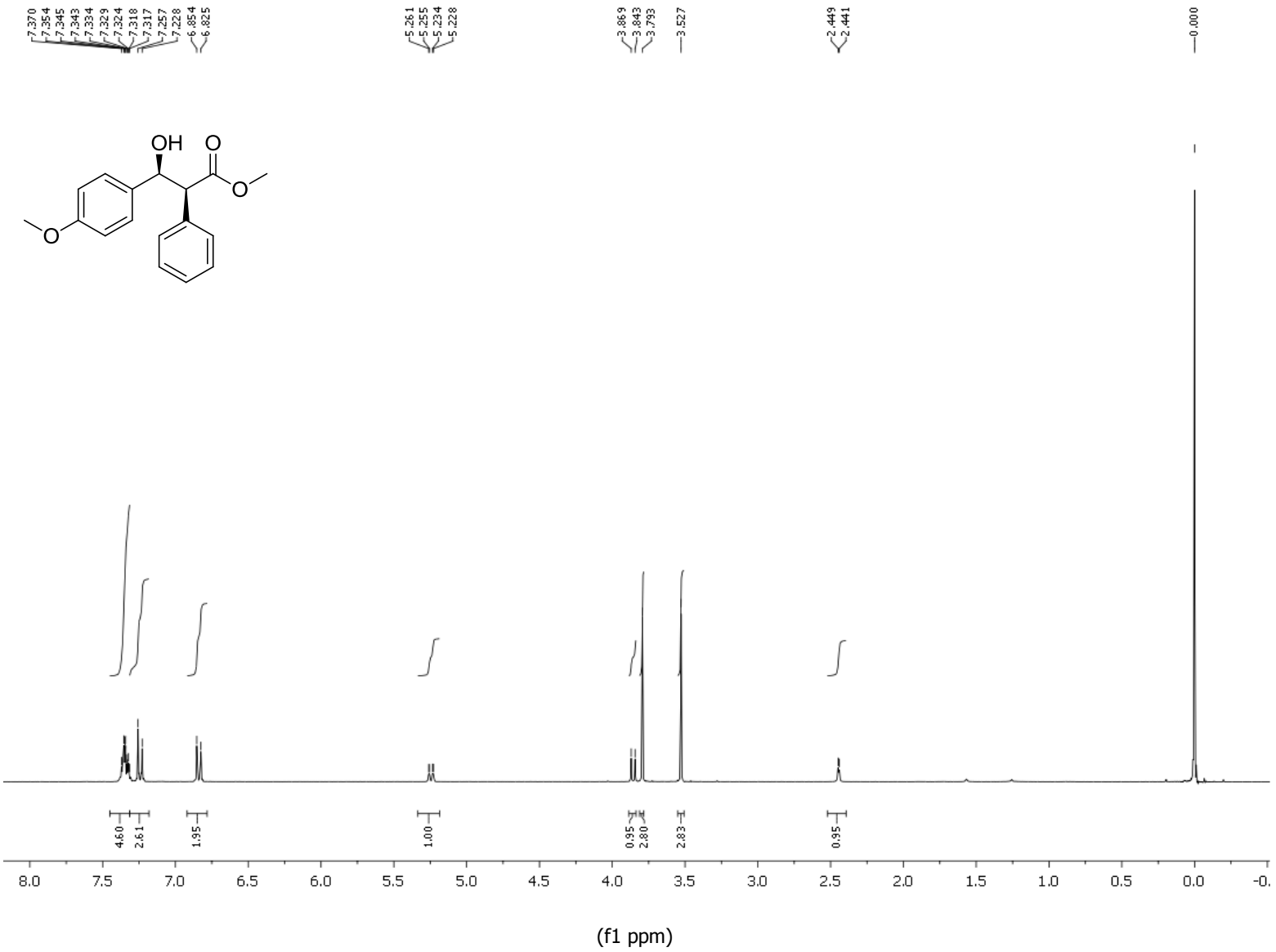
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (**7b**)



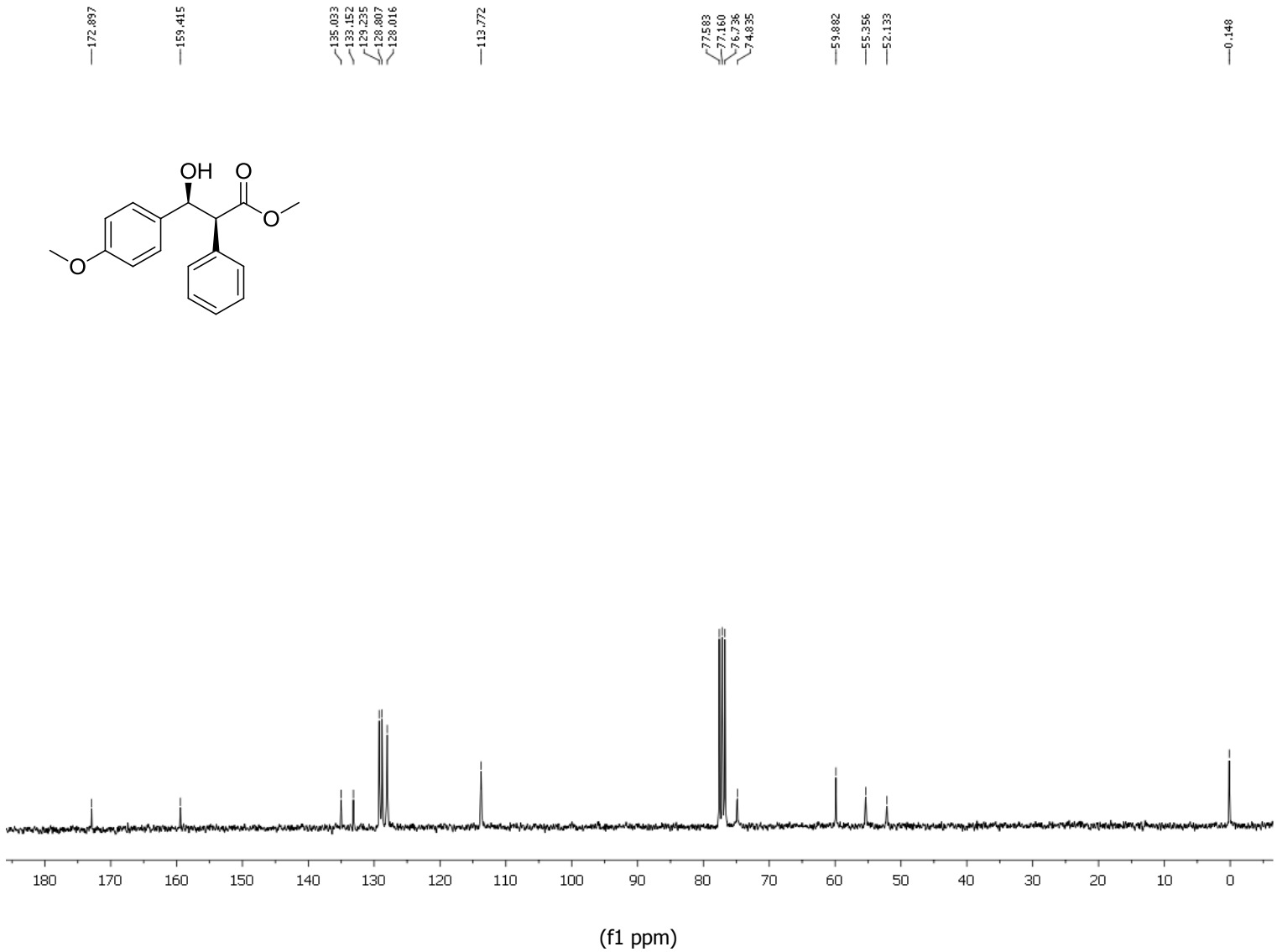
^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (**7b**)



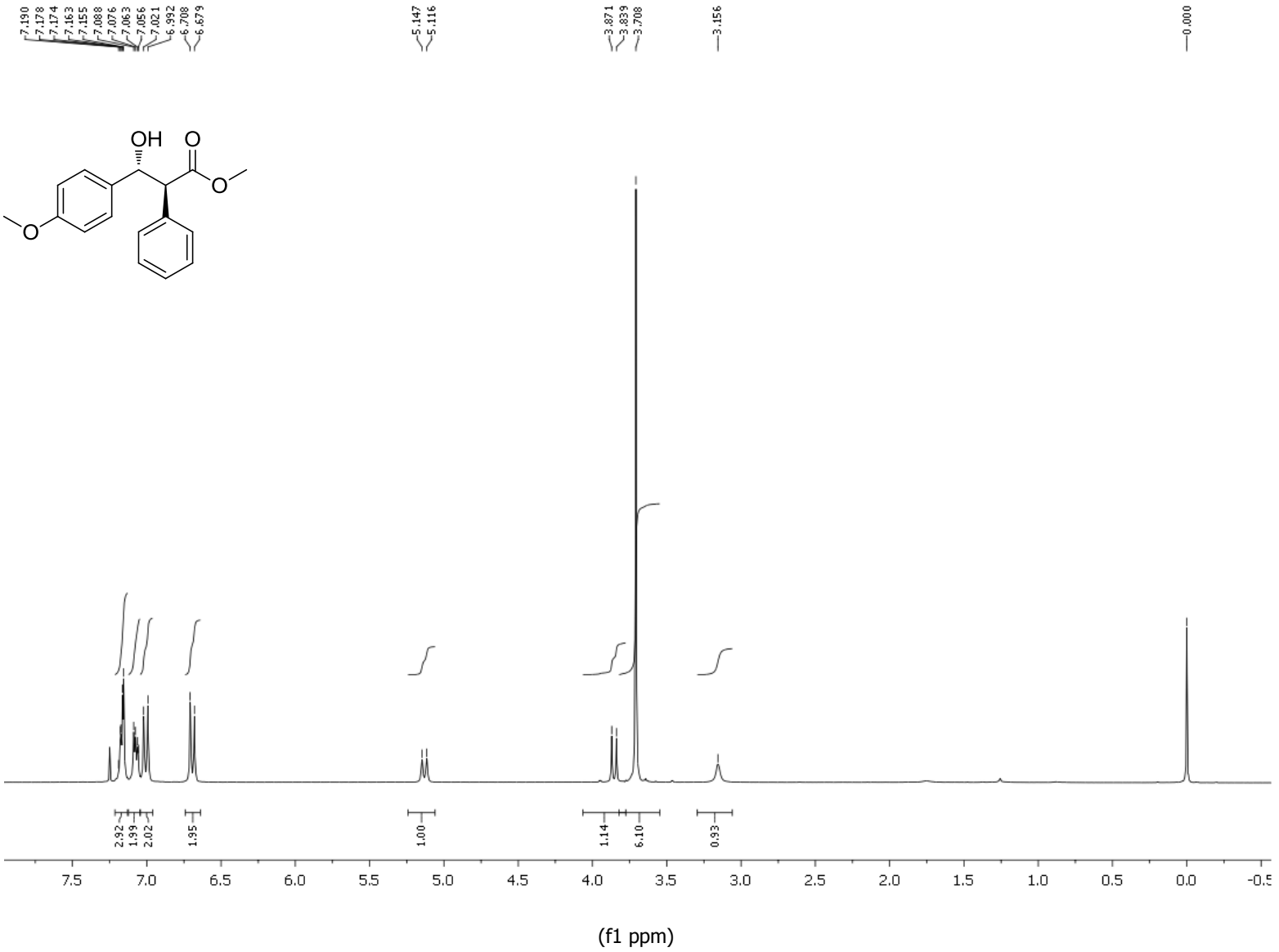
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (**7b**)



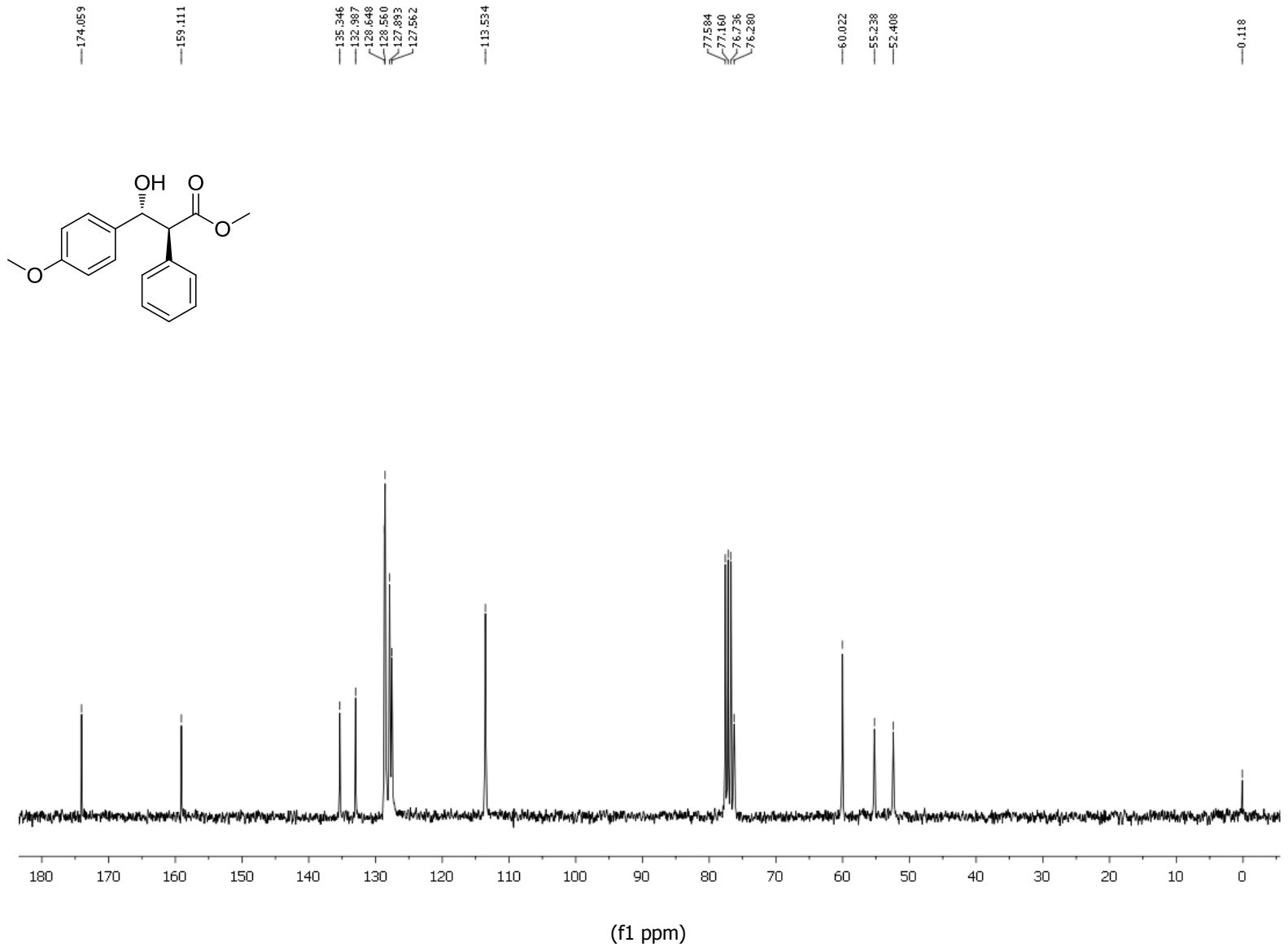
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy -3-(4-methoxyphenyl)-2-phenypropanoate (**7c**)



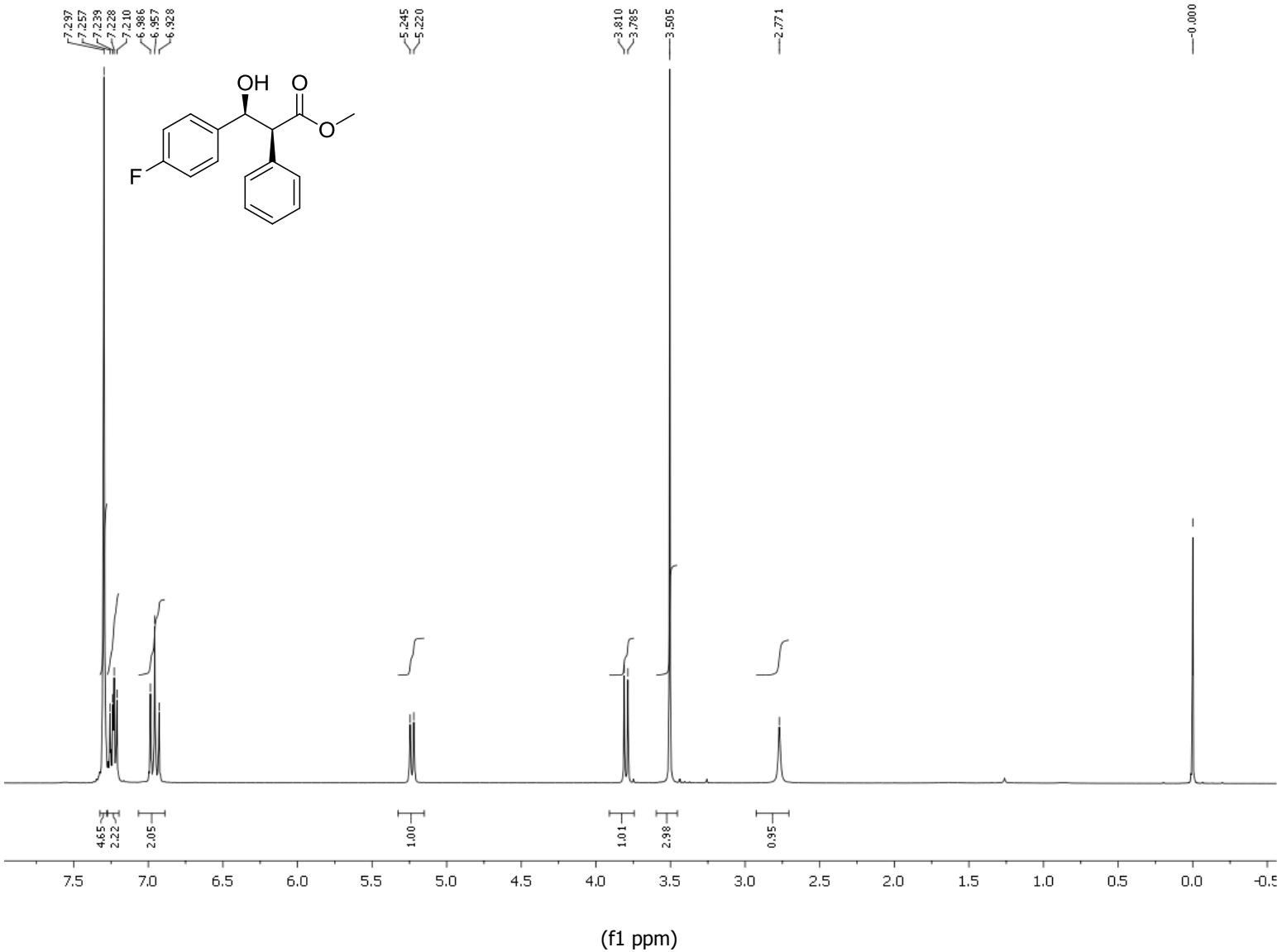
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-3-(4-methoxyphenyl)-2-phenylpropanoate (**7c**)



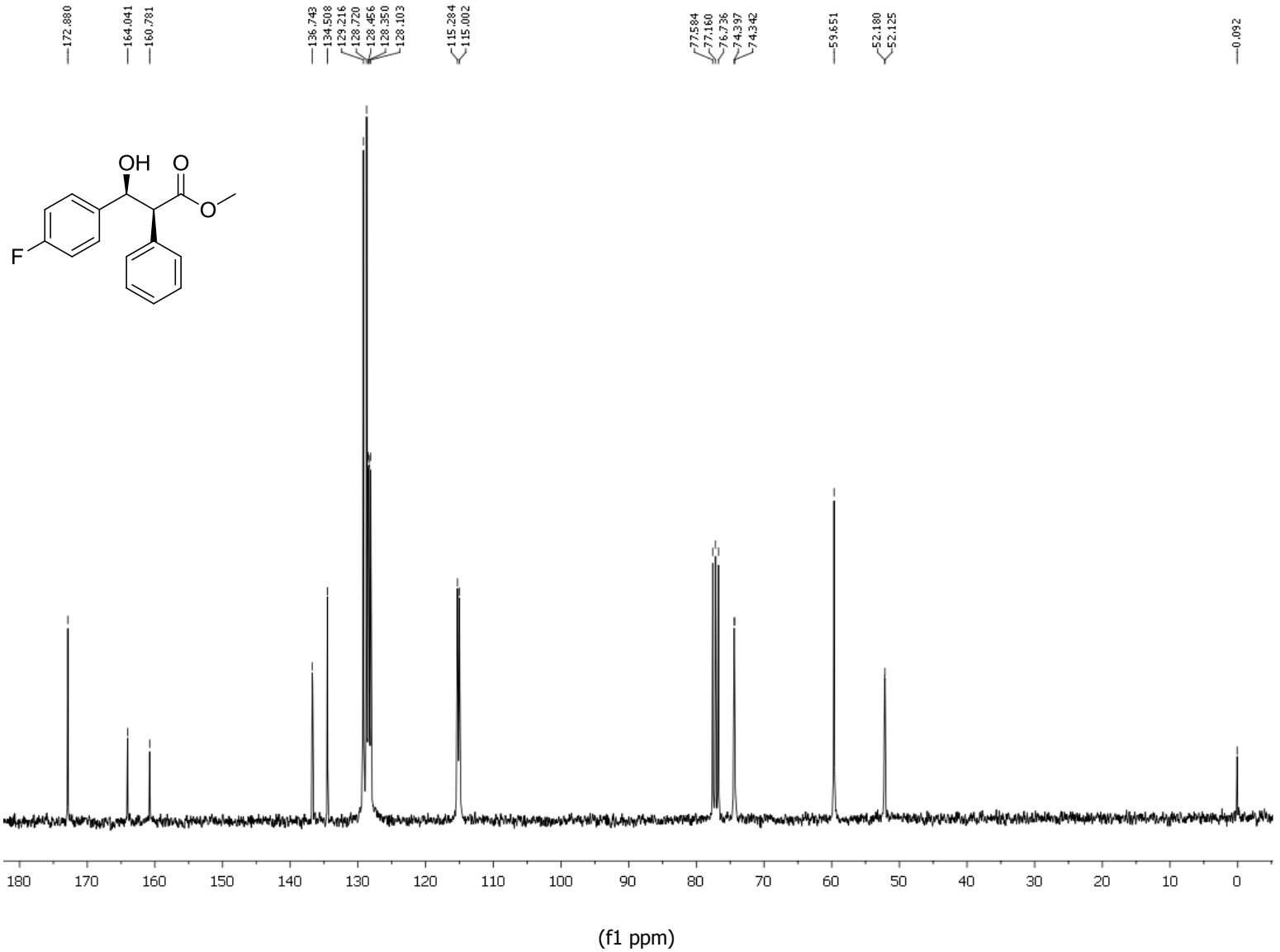
^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-3-(4-methoxyphenyl)-2-phenylpropanoate (**7c**)



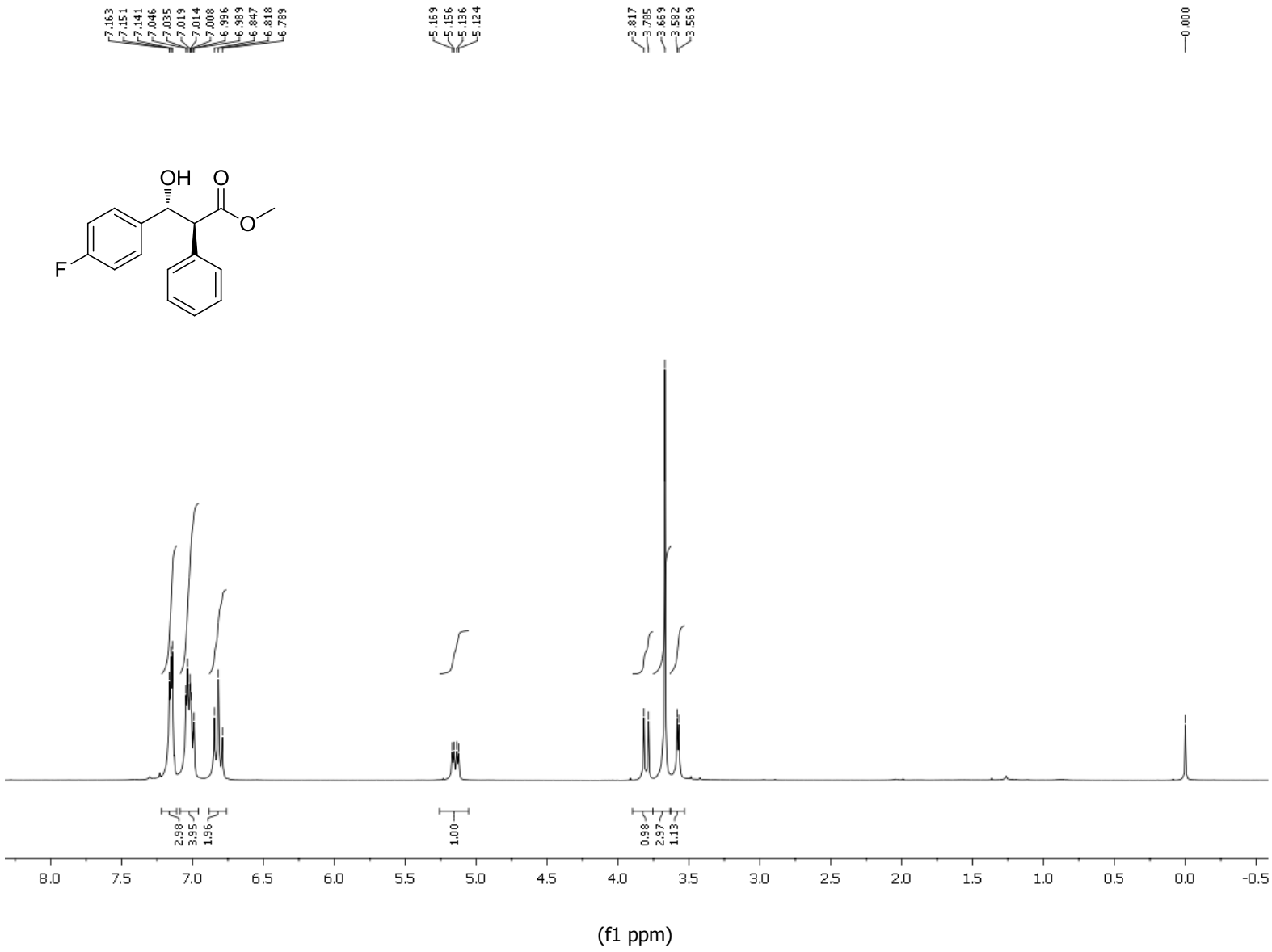
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-3-(4-methoxyphenyl)-2-phenypropanoate (**7c**)



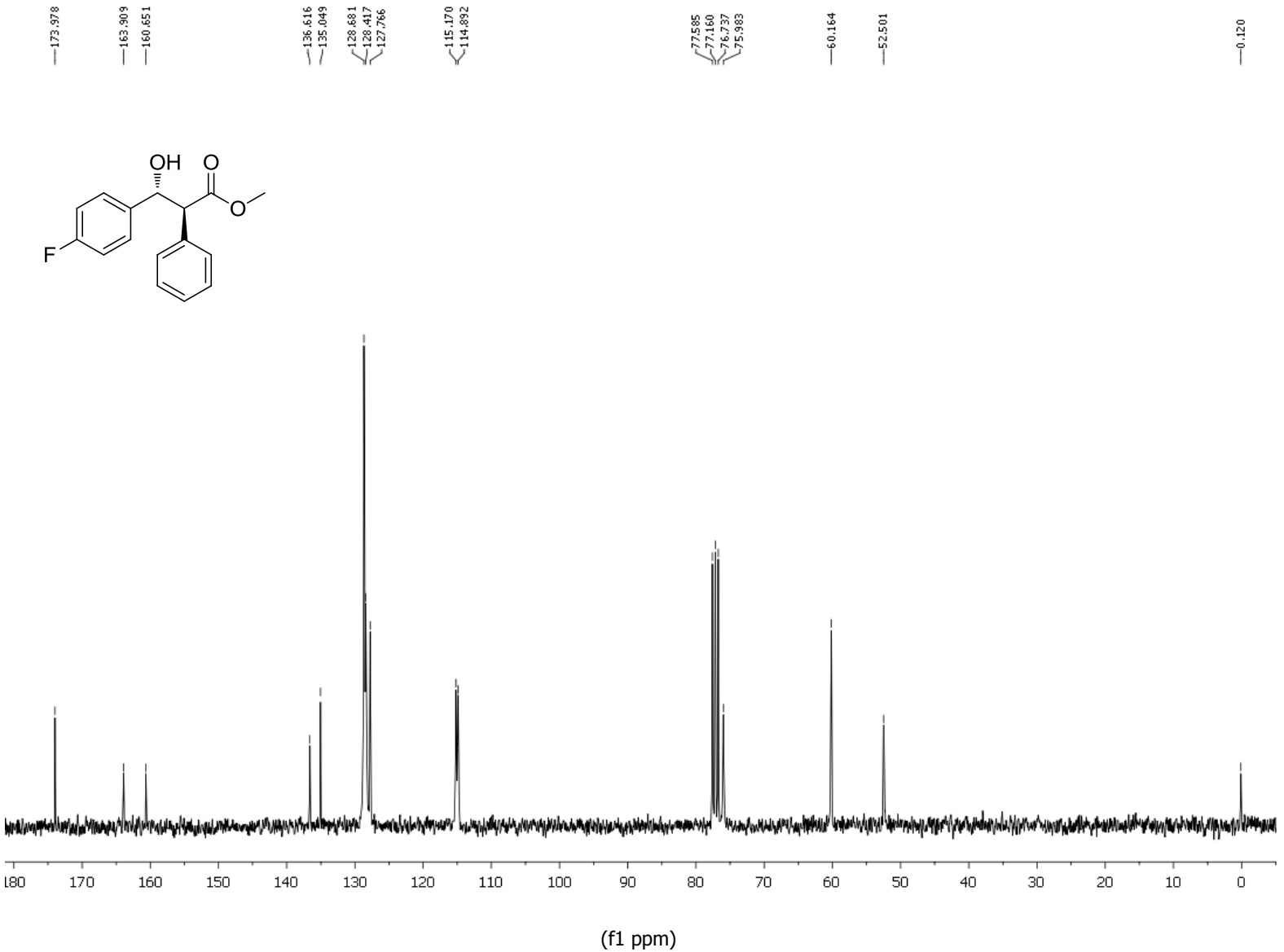
^{1}H NMR spectrum of *syn*-methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (**7d**)



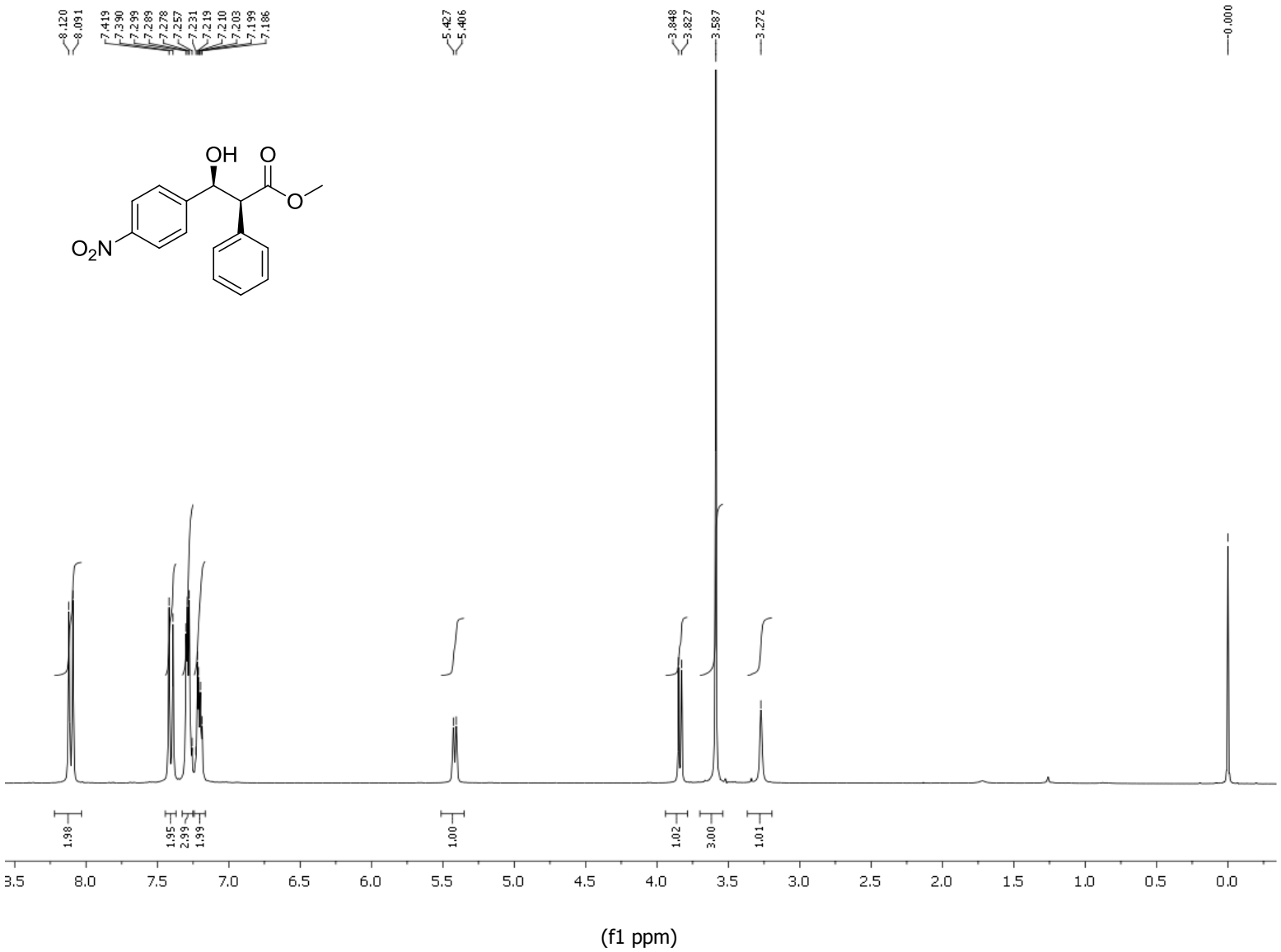
^{13}C NMR spectrum of *syn*-methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (**7d**)



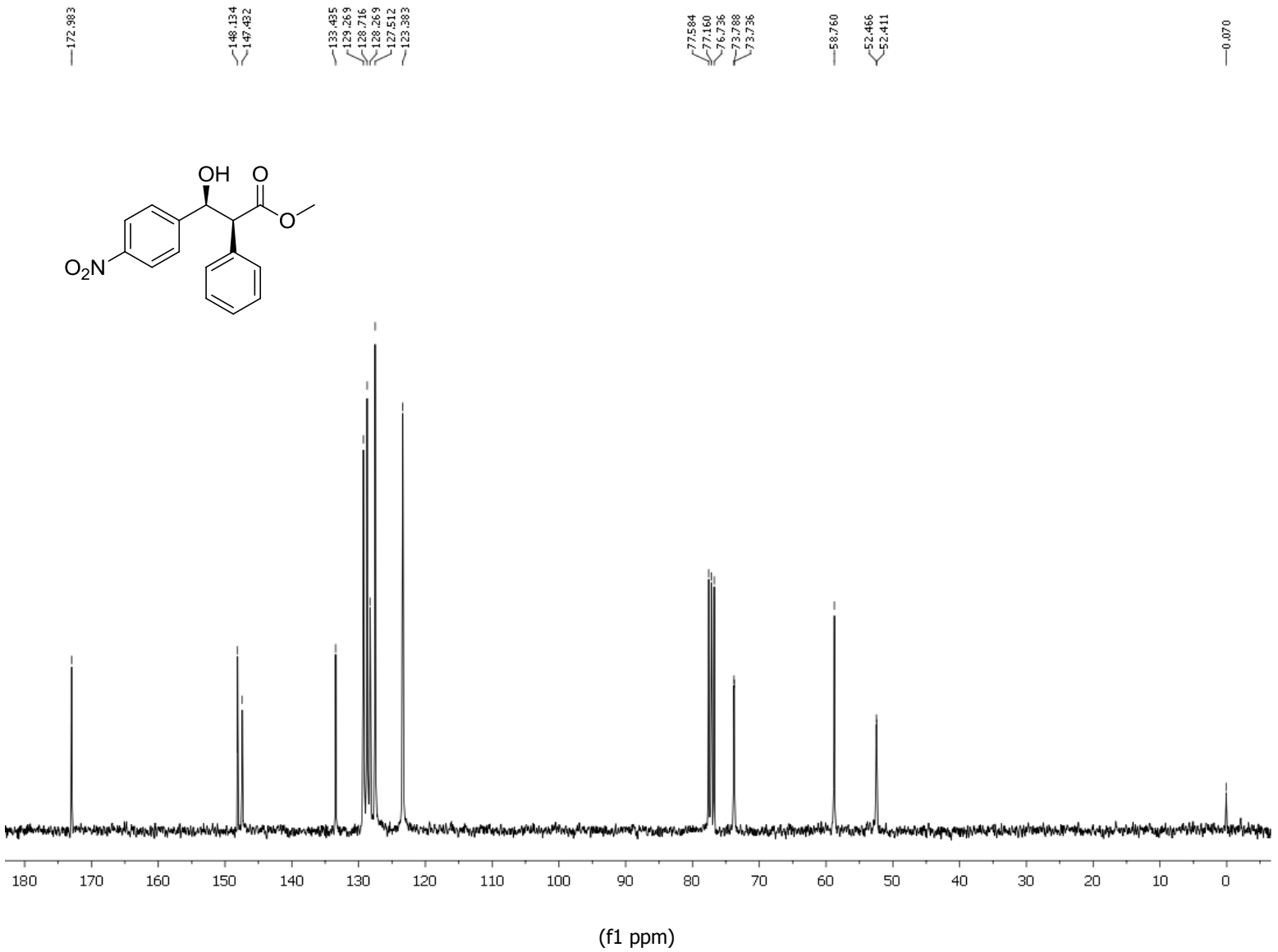
^{1}H NMR spectrum of *anti*-methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (**7d**)



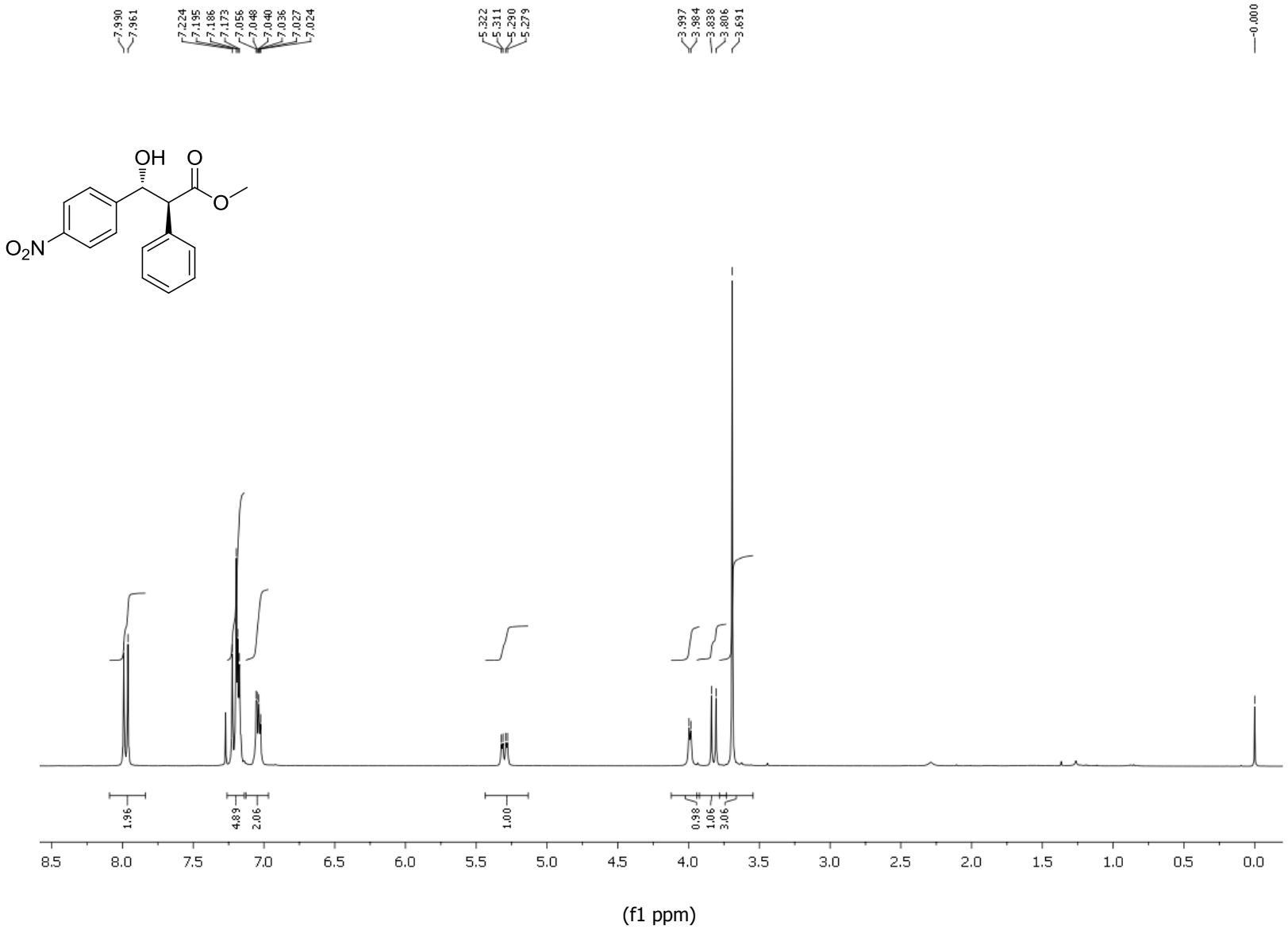
^{13}C NMR spectrum of *anti*-methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (**7d**)



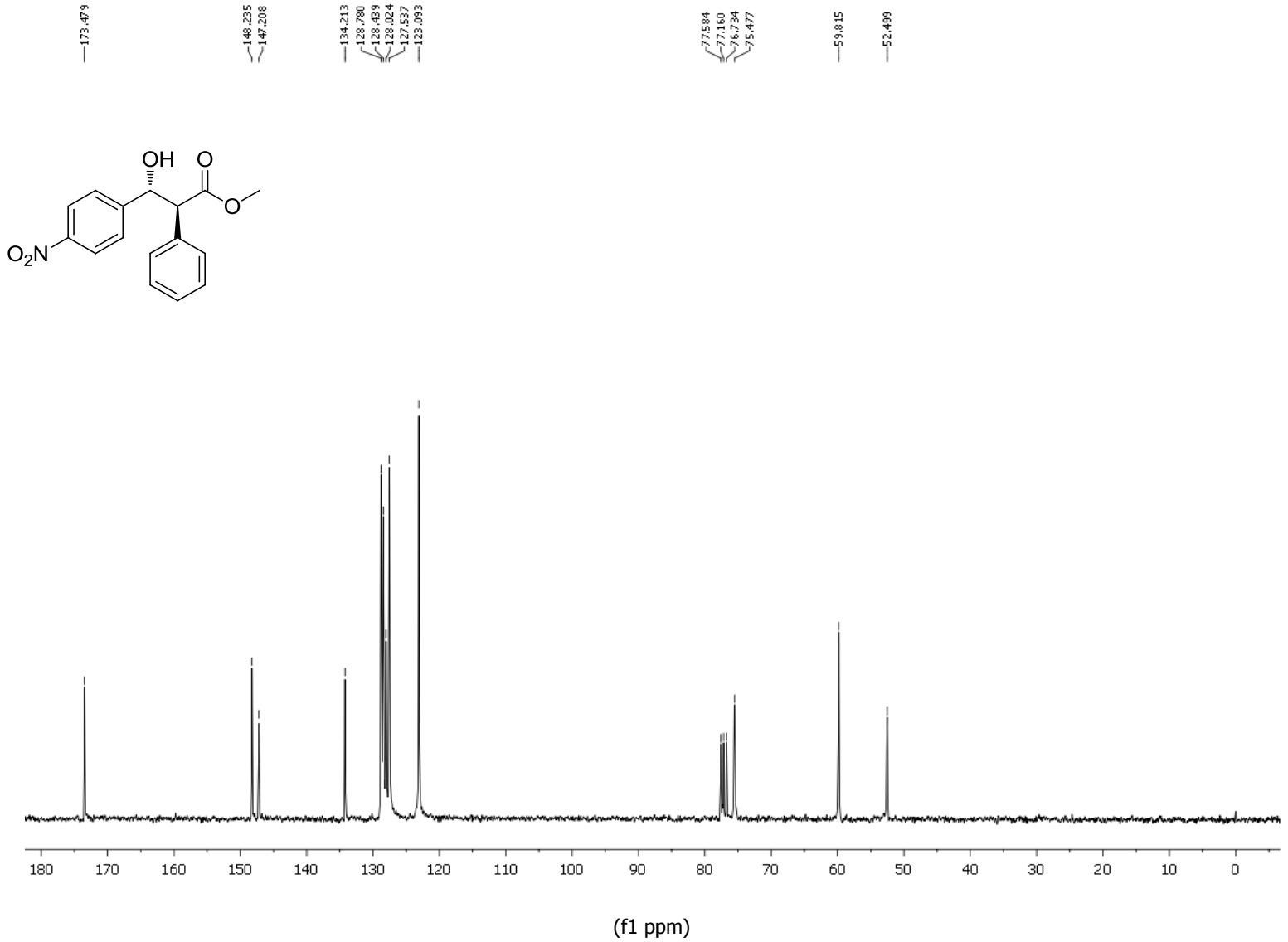
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-3-(4-nitrophenyl)-2-phenylpropanoate (**7e**)



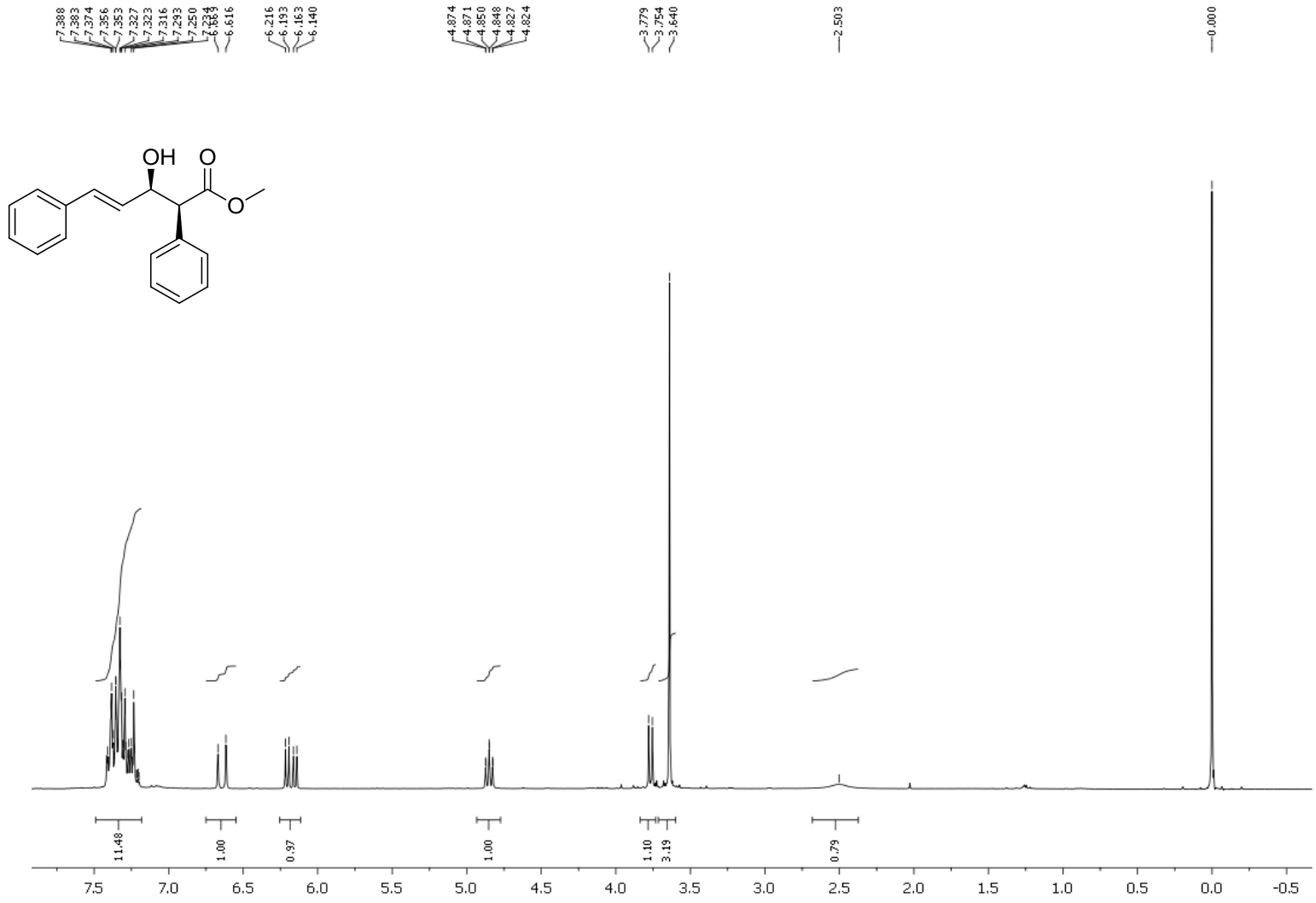
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-3-(4-nitrophenyl)-2-phenylpropanoate (**7e**)



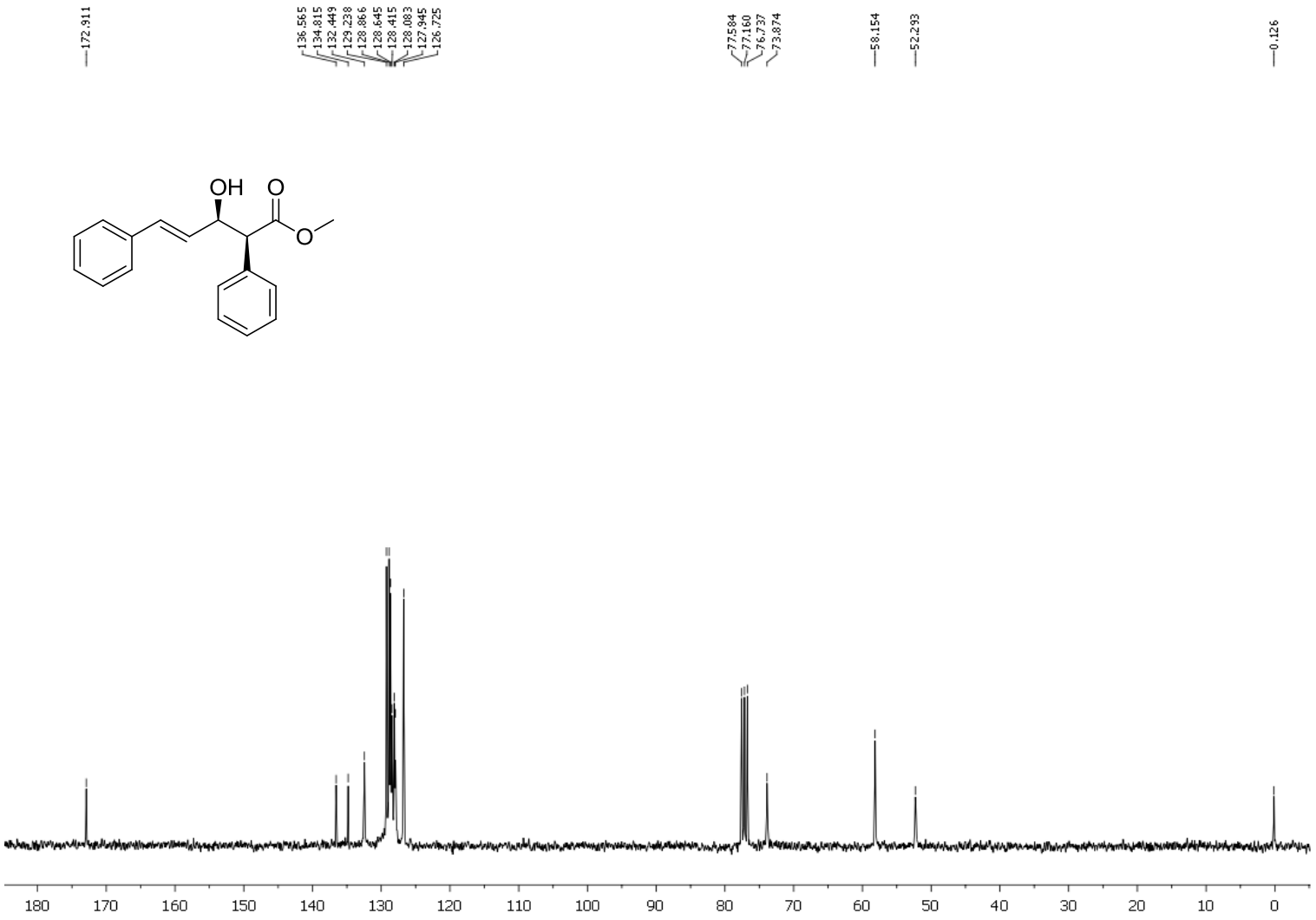
^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-3-(4-nitrophenyl)-2-phenylpropanoate (**7e**)



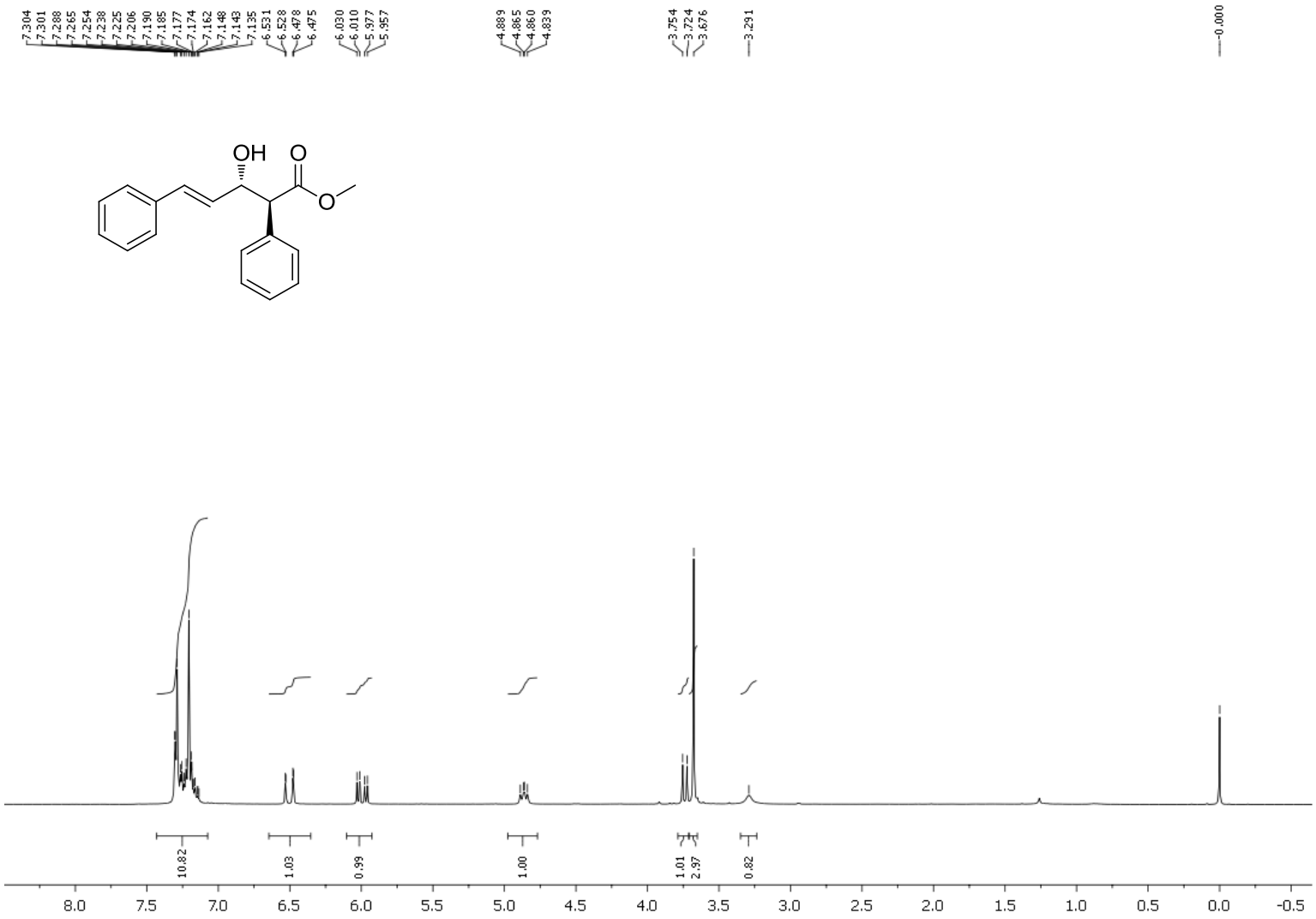
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-3-(4-nitrophenyl)-2-phenypropanoate (**7e**)



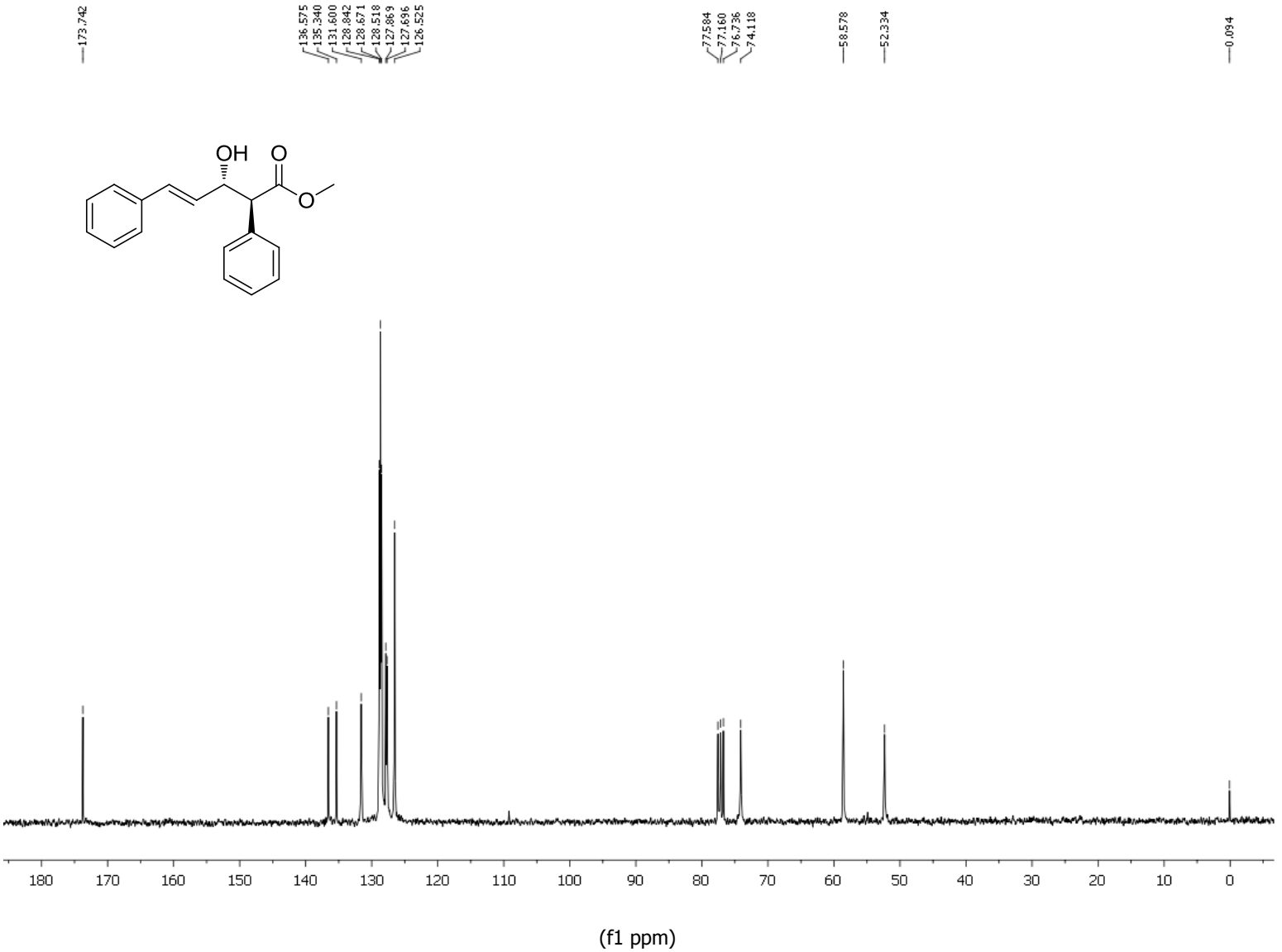
^{1}H NMR spectrum of *syn*-(*E*)-methyl 3-hydroxy-2,5-diphenylpent-4-enoate (**7f**)



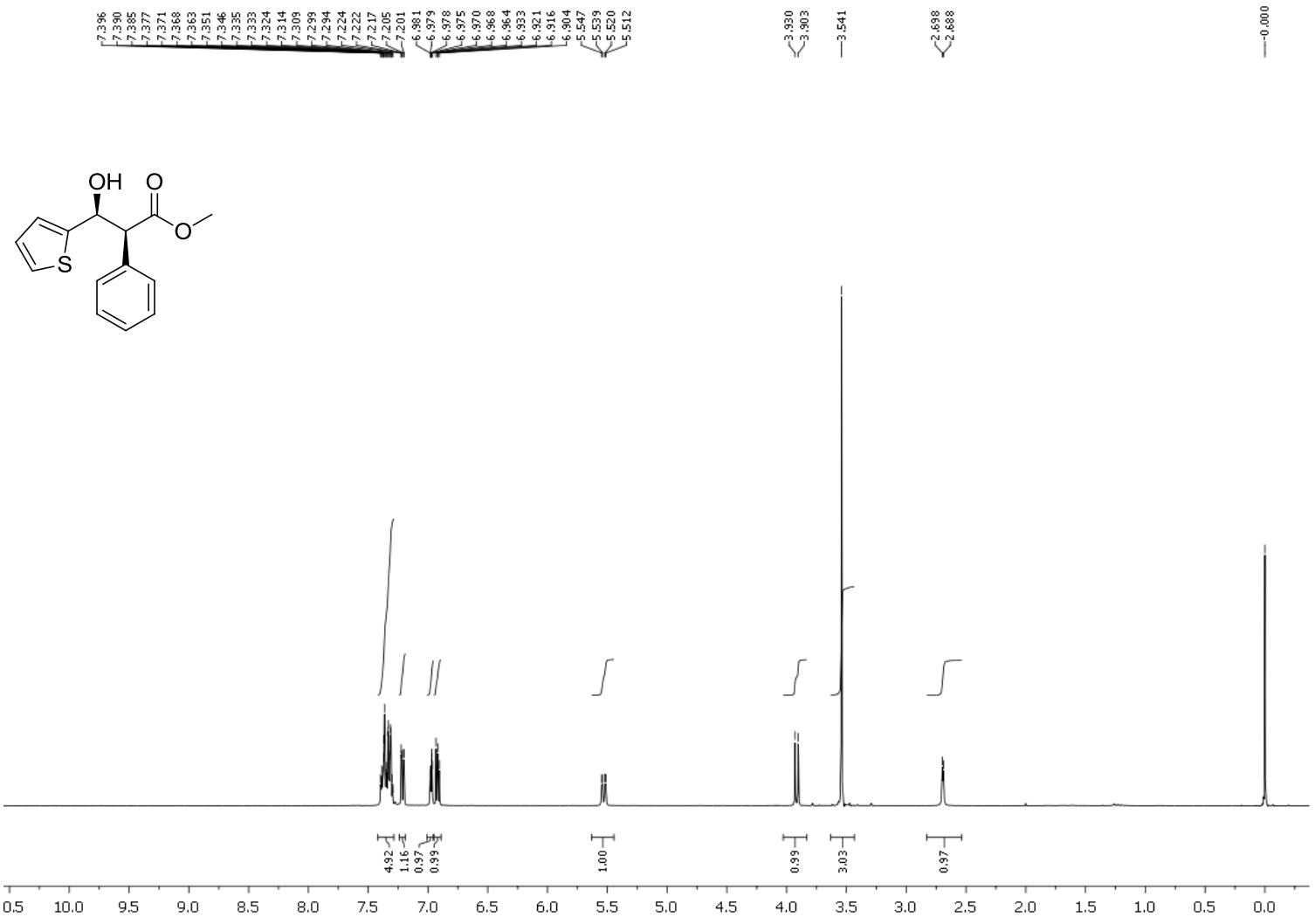
^{13}C NMR spectrum of *syn*-(*E*)-methyl 3-hydroxy-2,5-diphenylpent-4-enoate (**7f**)



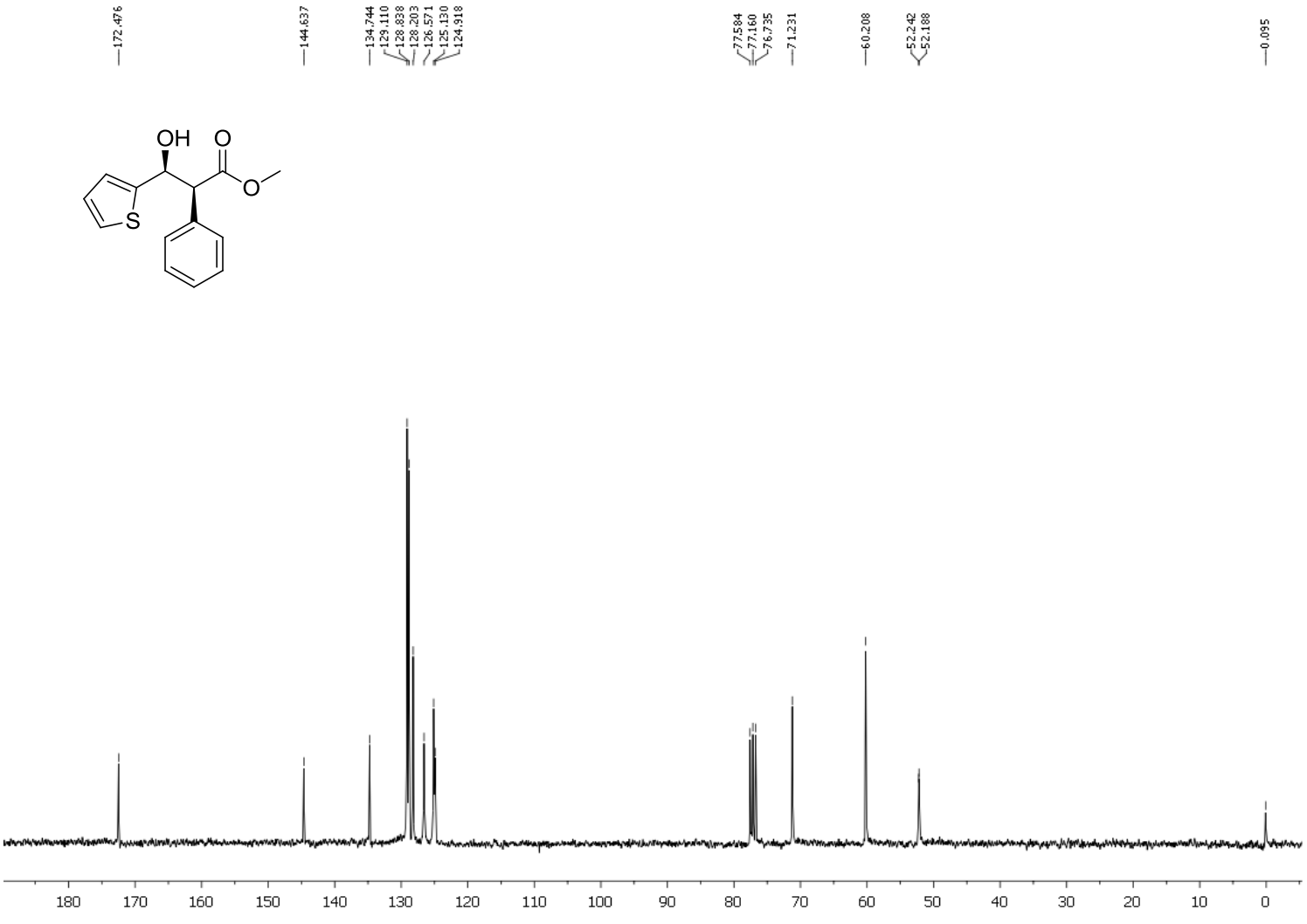
^{1}H NMR spectrum of *anti*-(*E*)-methyl 3-hydroxy-2,5-diphenylpent-4-enoate (**7f**)



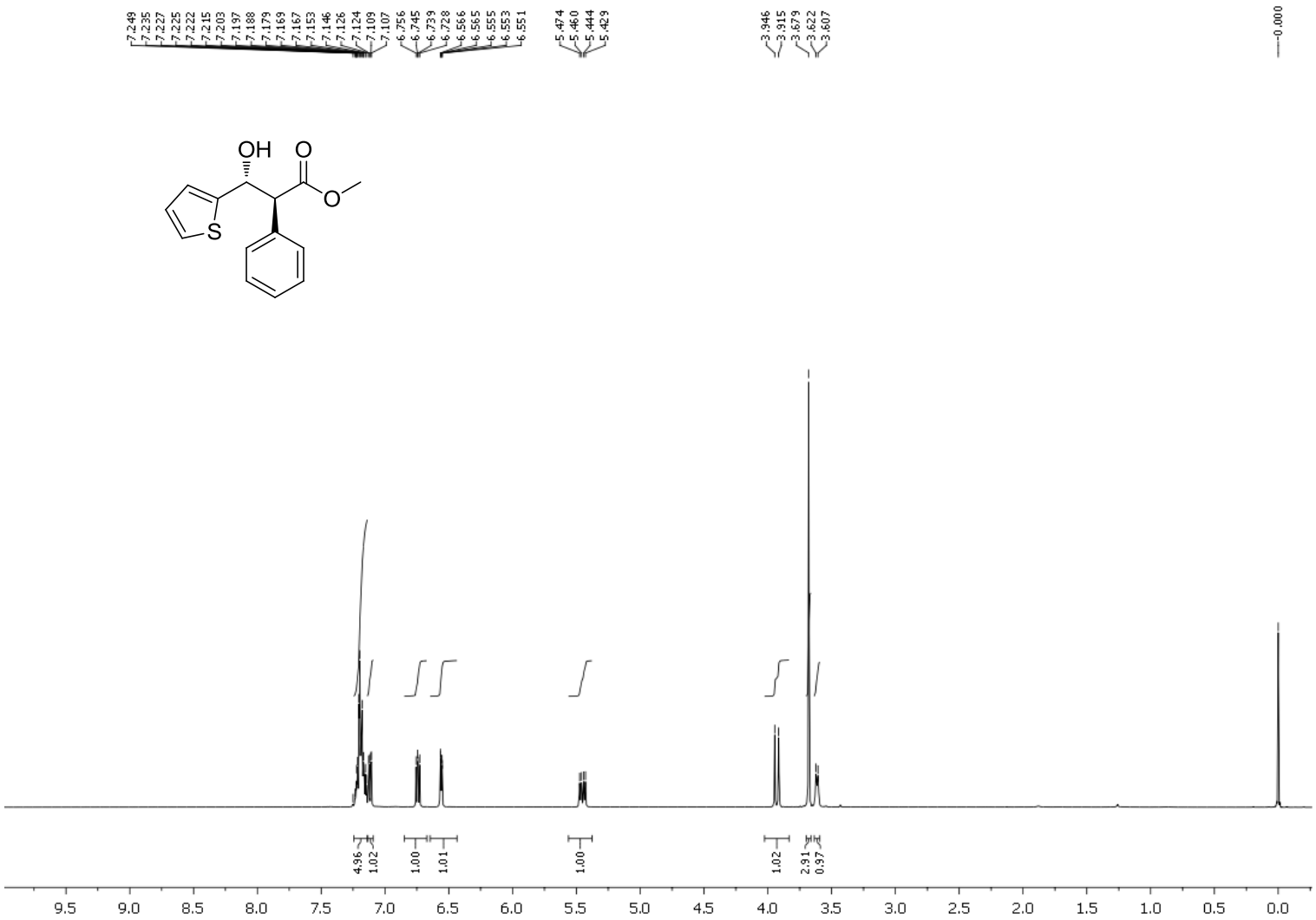
^{13}C NMR spectrum of *anti*-(*E*)-methyl 3-hydroxy-2,5-diphenylpent-4-enoate (**7f**)



^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-2-phenyl-3-(thiophen-2-yl)propanoate (**7g**)

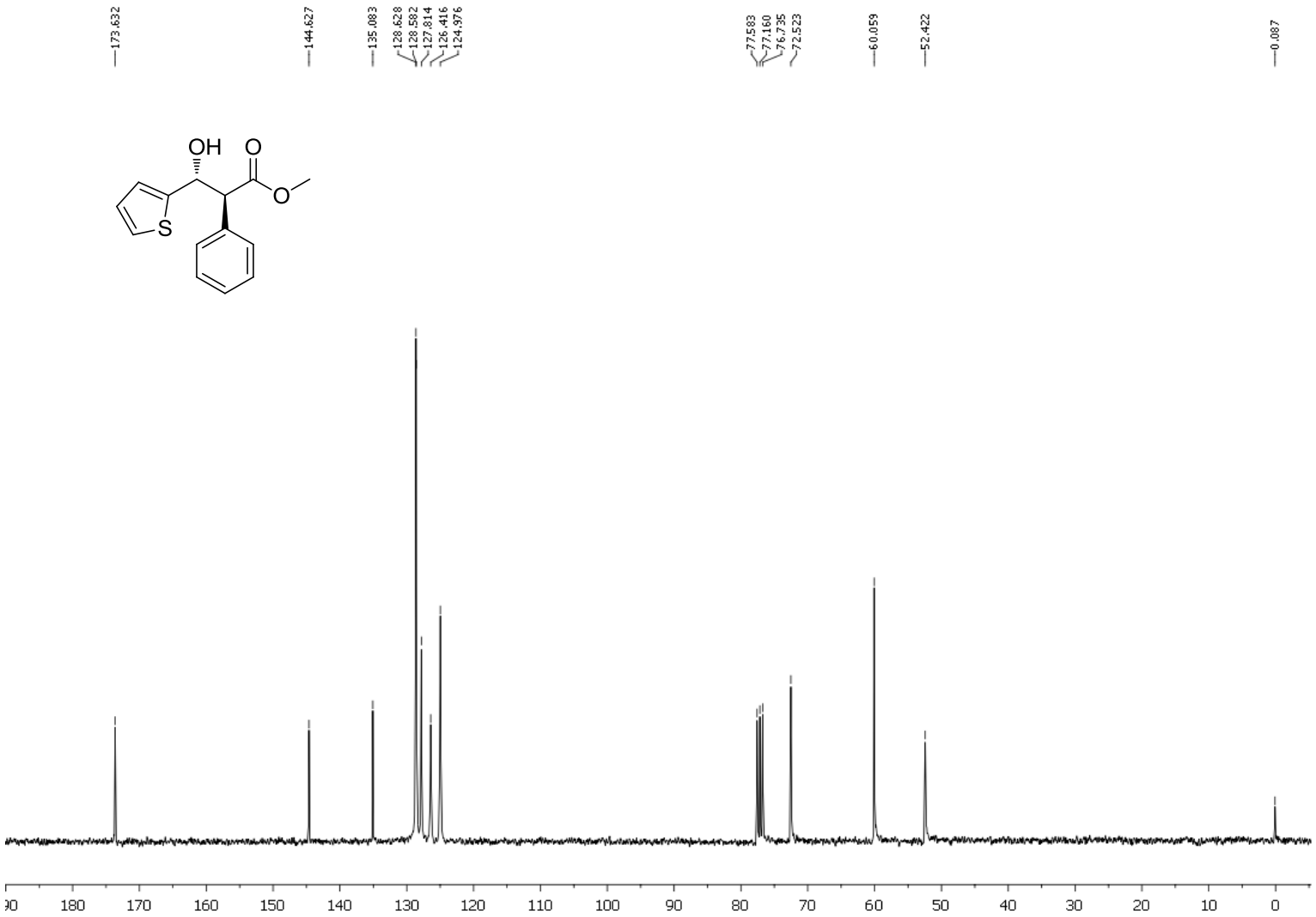


^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-2-phenyl-3-(thiophen-2-yl)propanoate (**7g**)

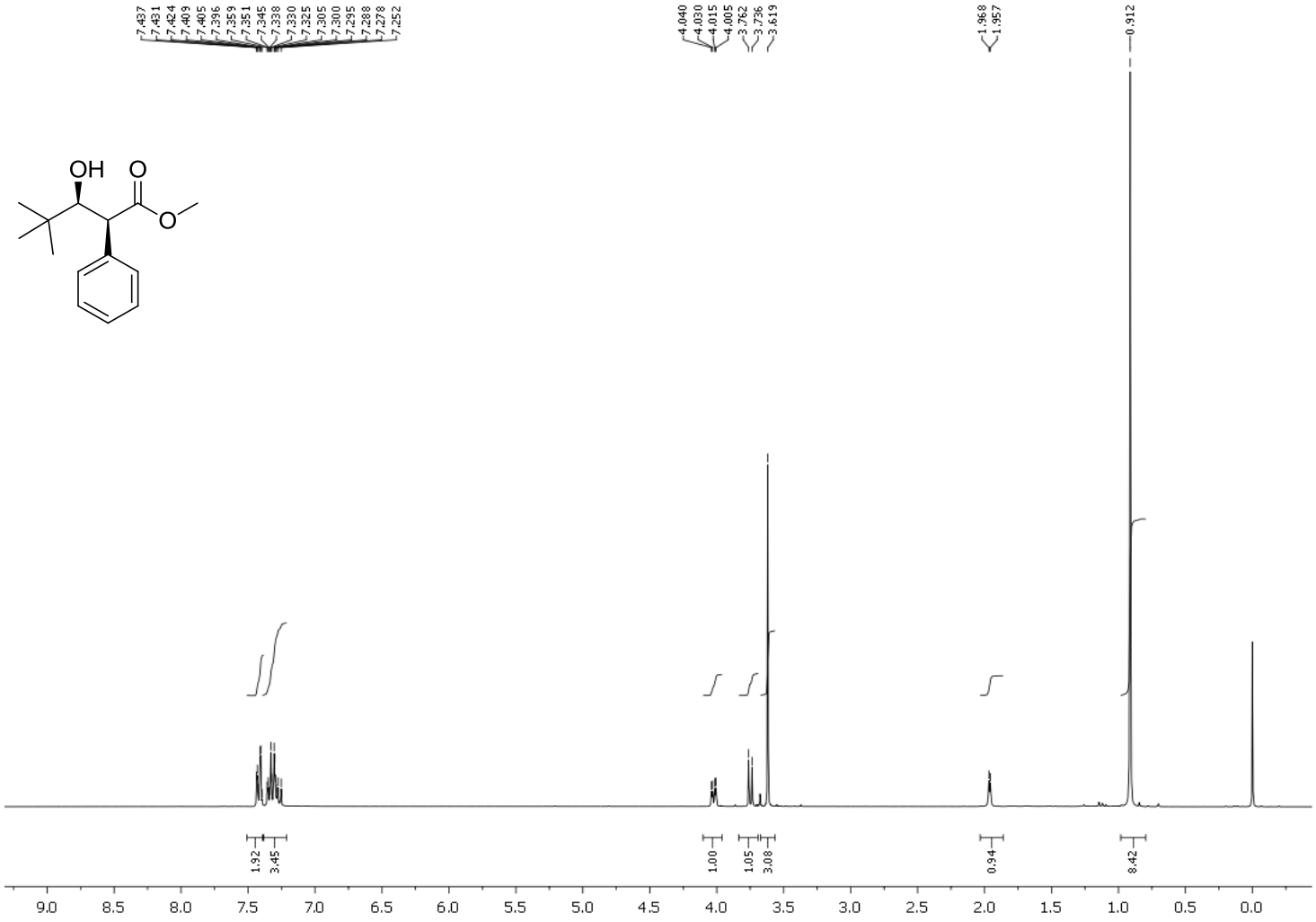


(f1 ppm)

^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-2-phenyl-3-(thiophen-2-yl)propanoate (**7g**)

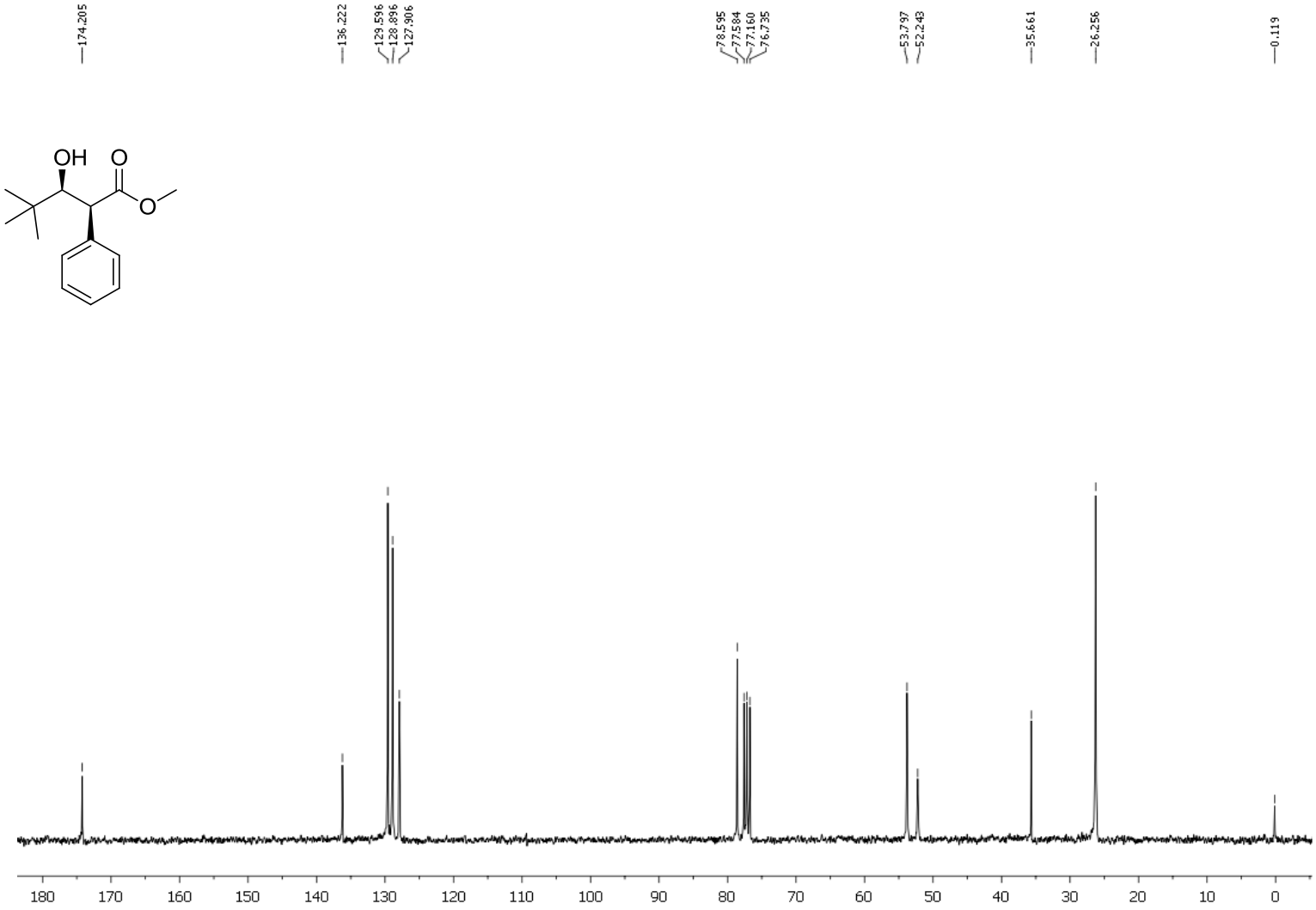


^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-2-phenyl-3-(thiophen-2-yl)propanoate (**7g**)

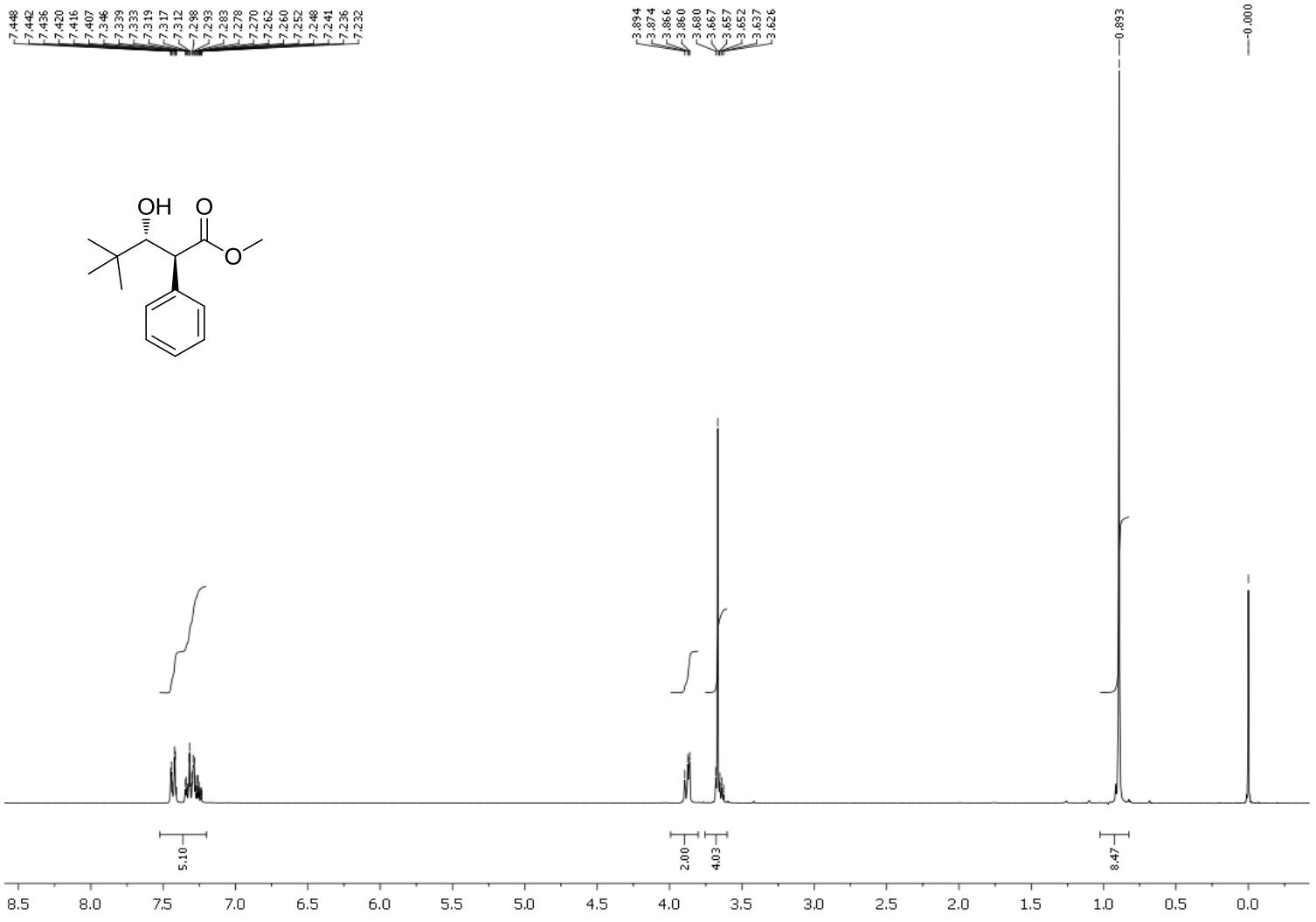


(f1 ppm)

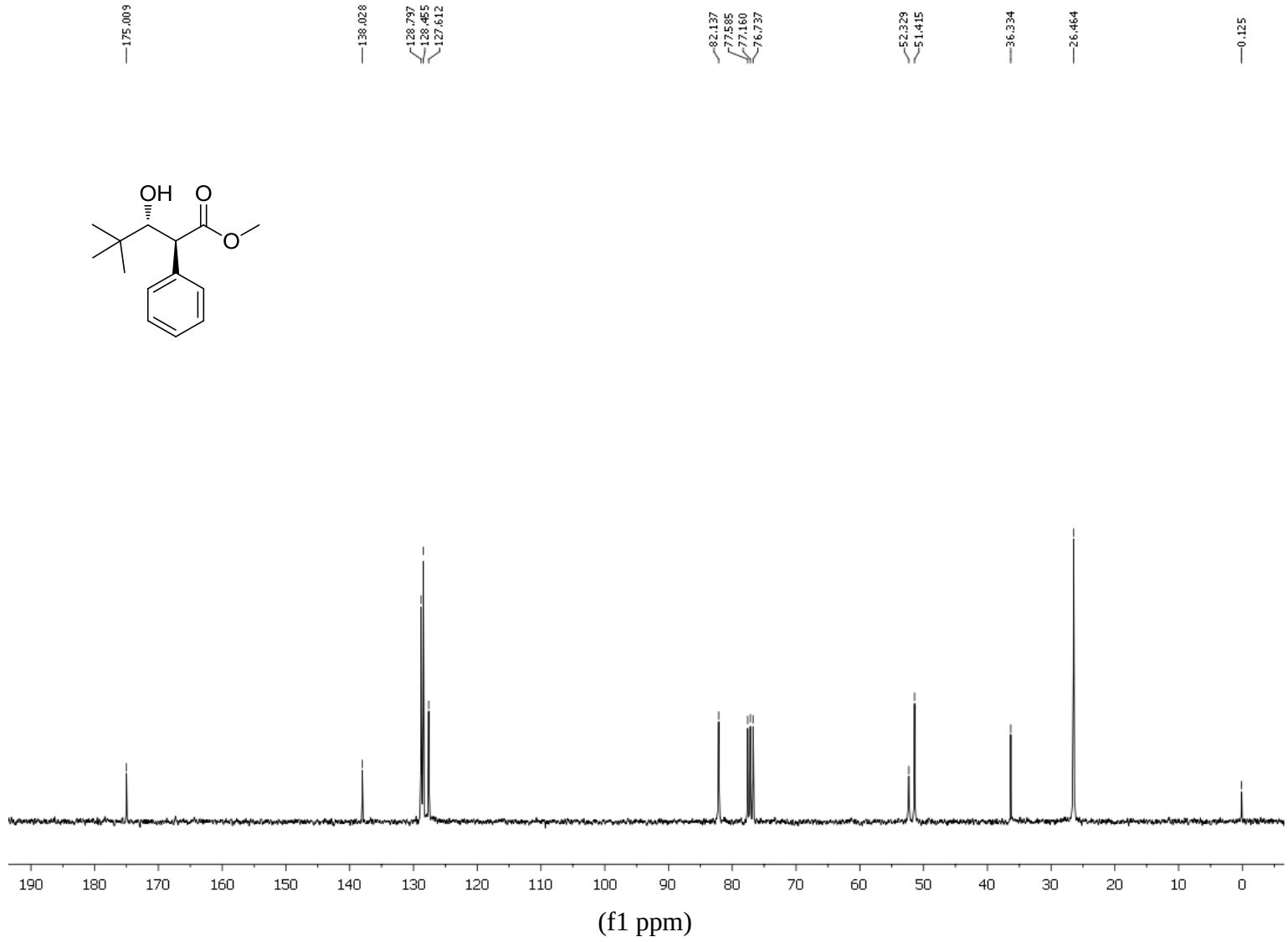
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-4,4-dimethyl-2-phenylpentanoate (**7h**)



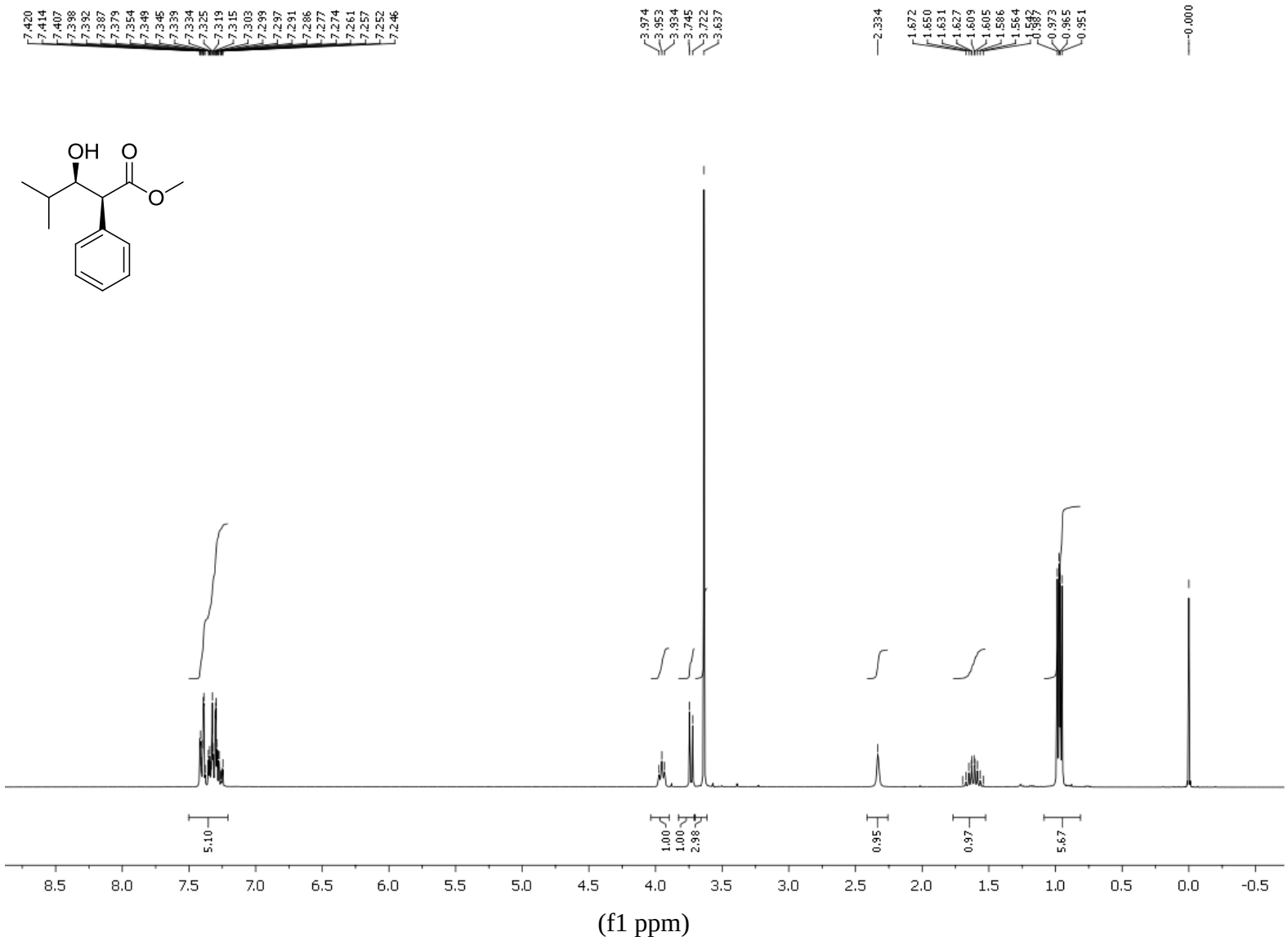
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-4,4-dimethyl-2-phenylpentanoate (**7h**)



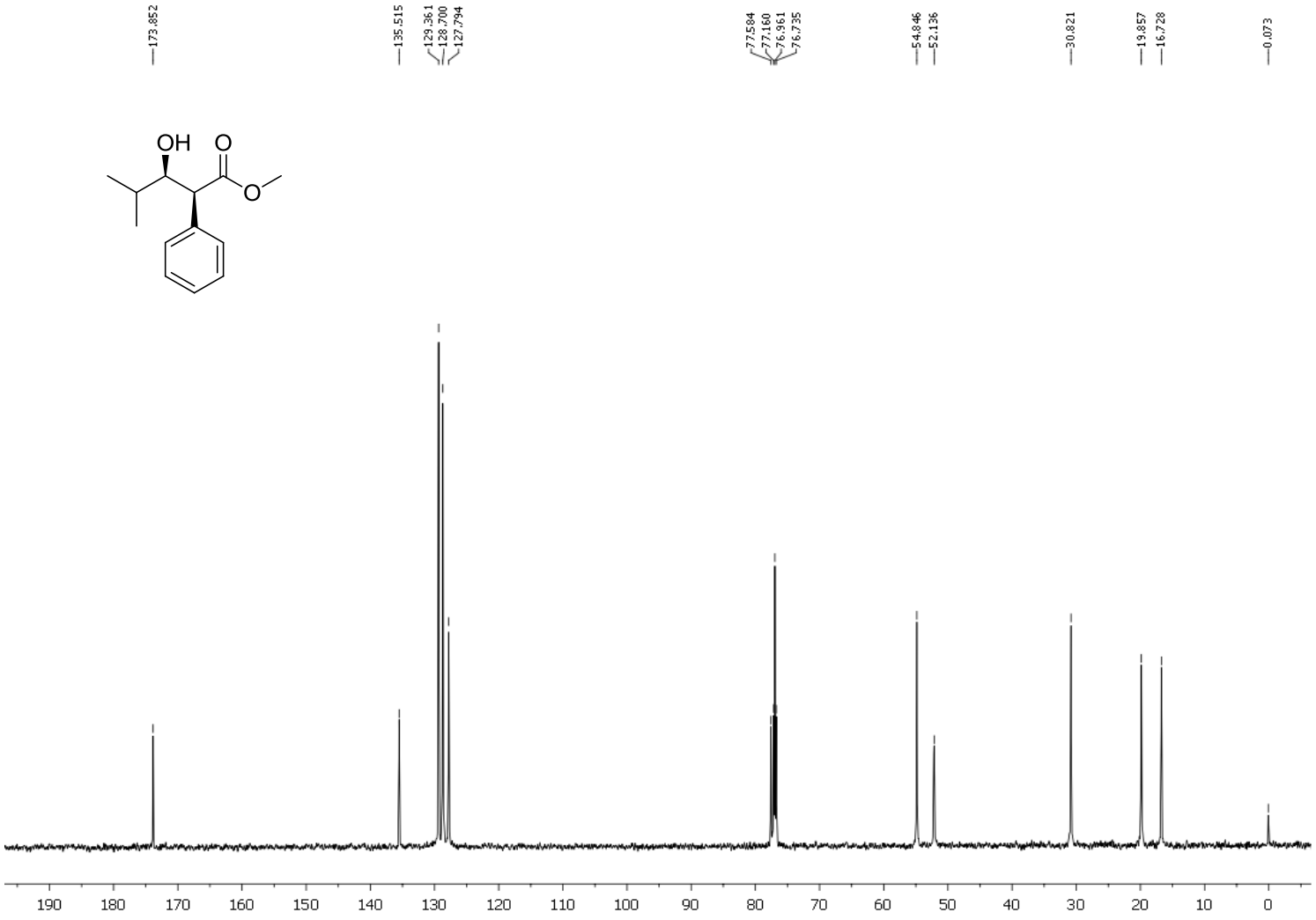
^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-4,4-dimethyl-2-phenylpentanoate (**7h**)



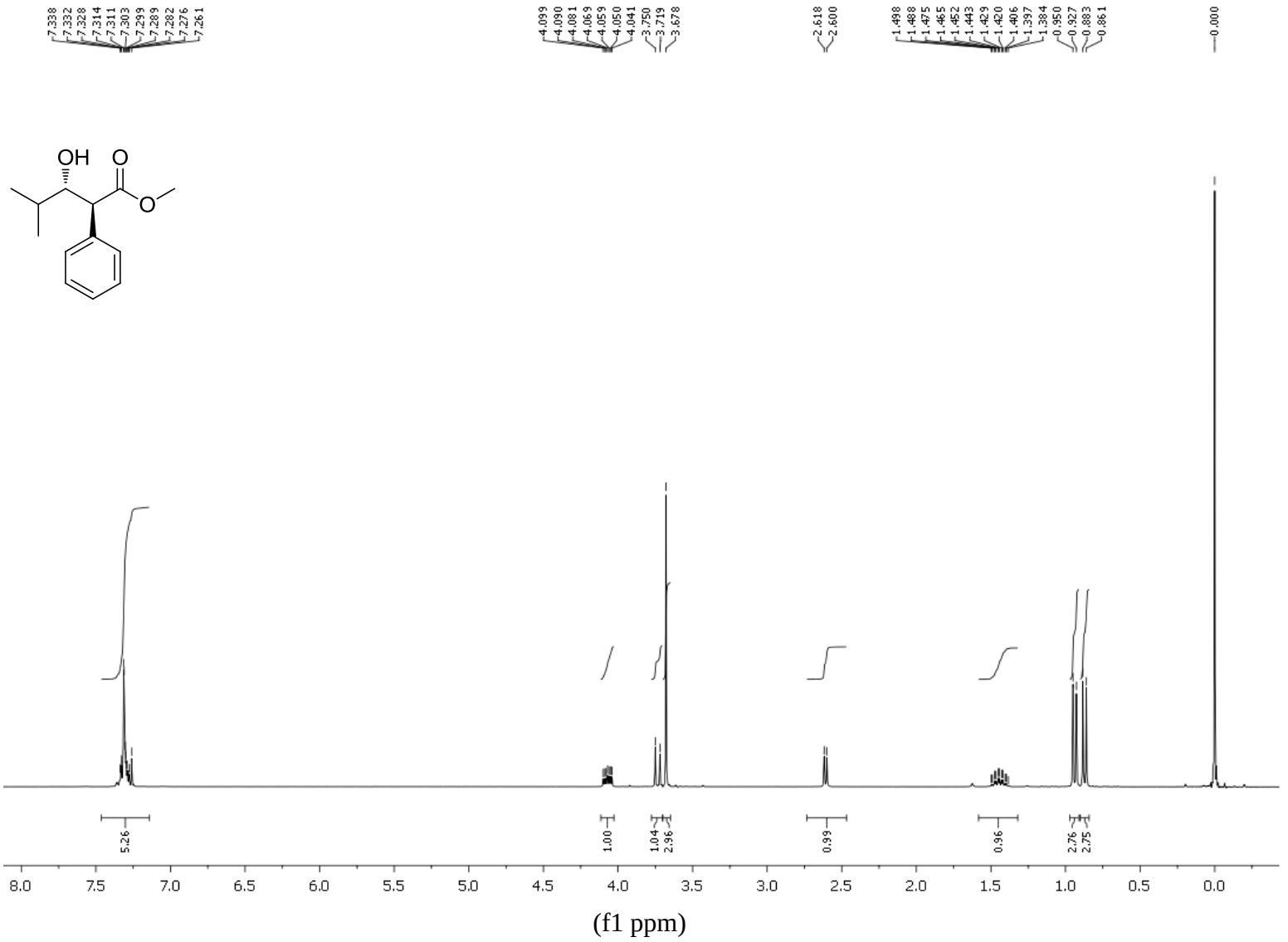
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-4,4-dimethyl-2-phenylpentanoate (**7h**)



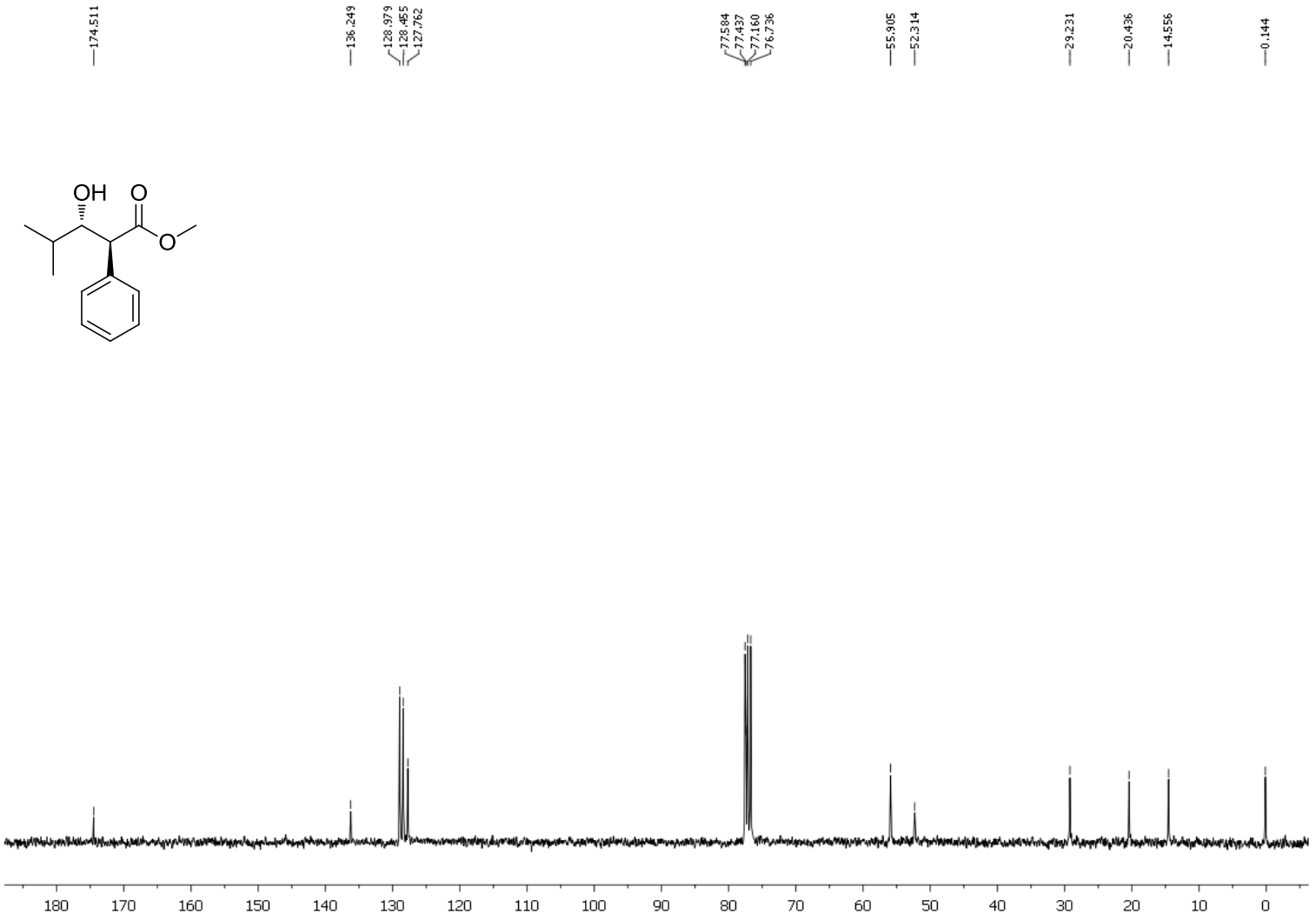
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-4-methyl-2-phenylpentanoate (**7i**)



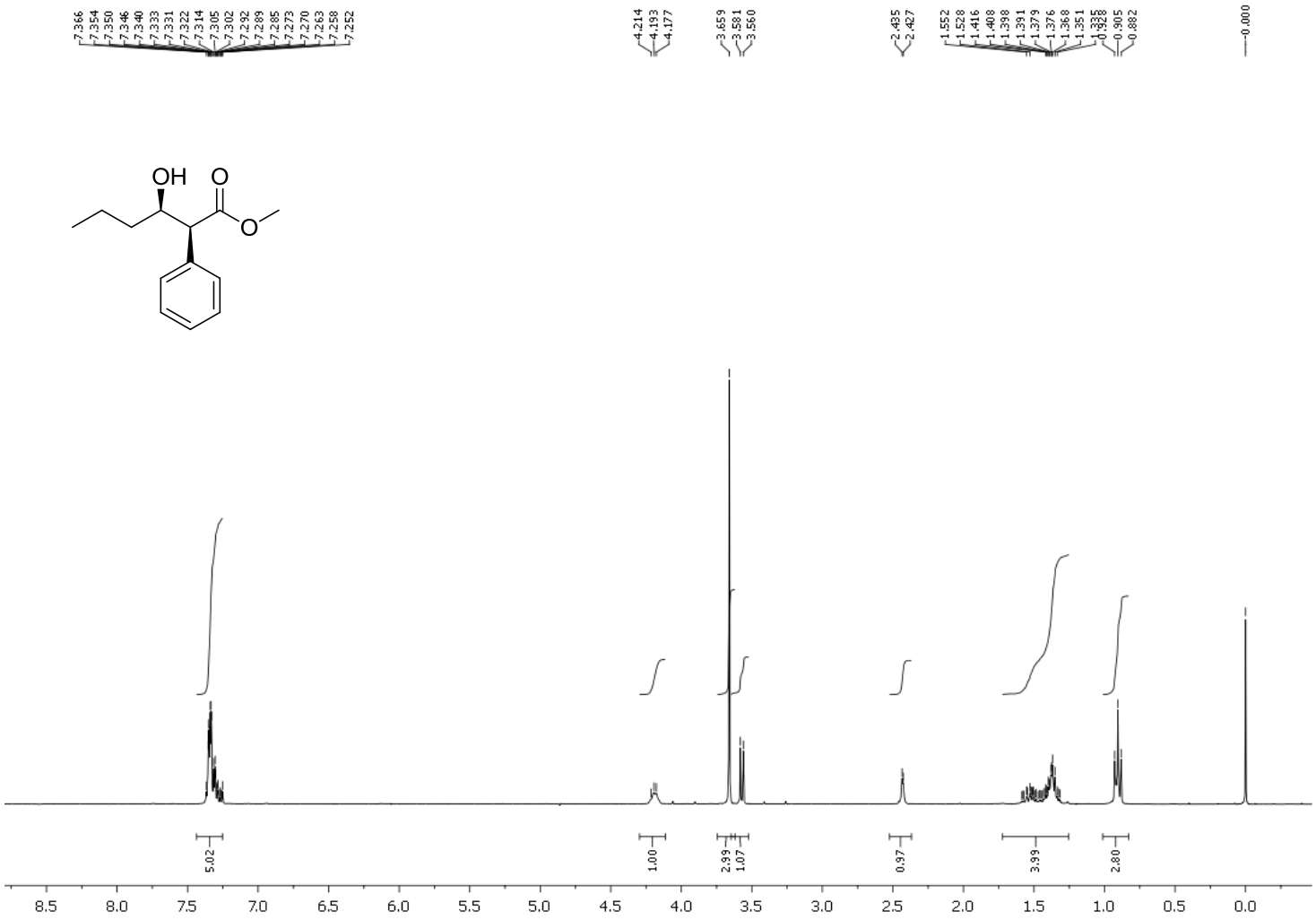
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-4-methyl-2-phenylpentanoate (**7i**)



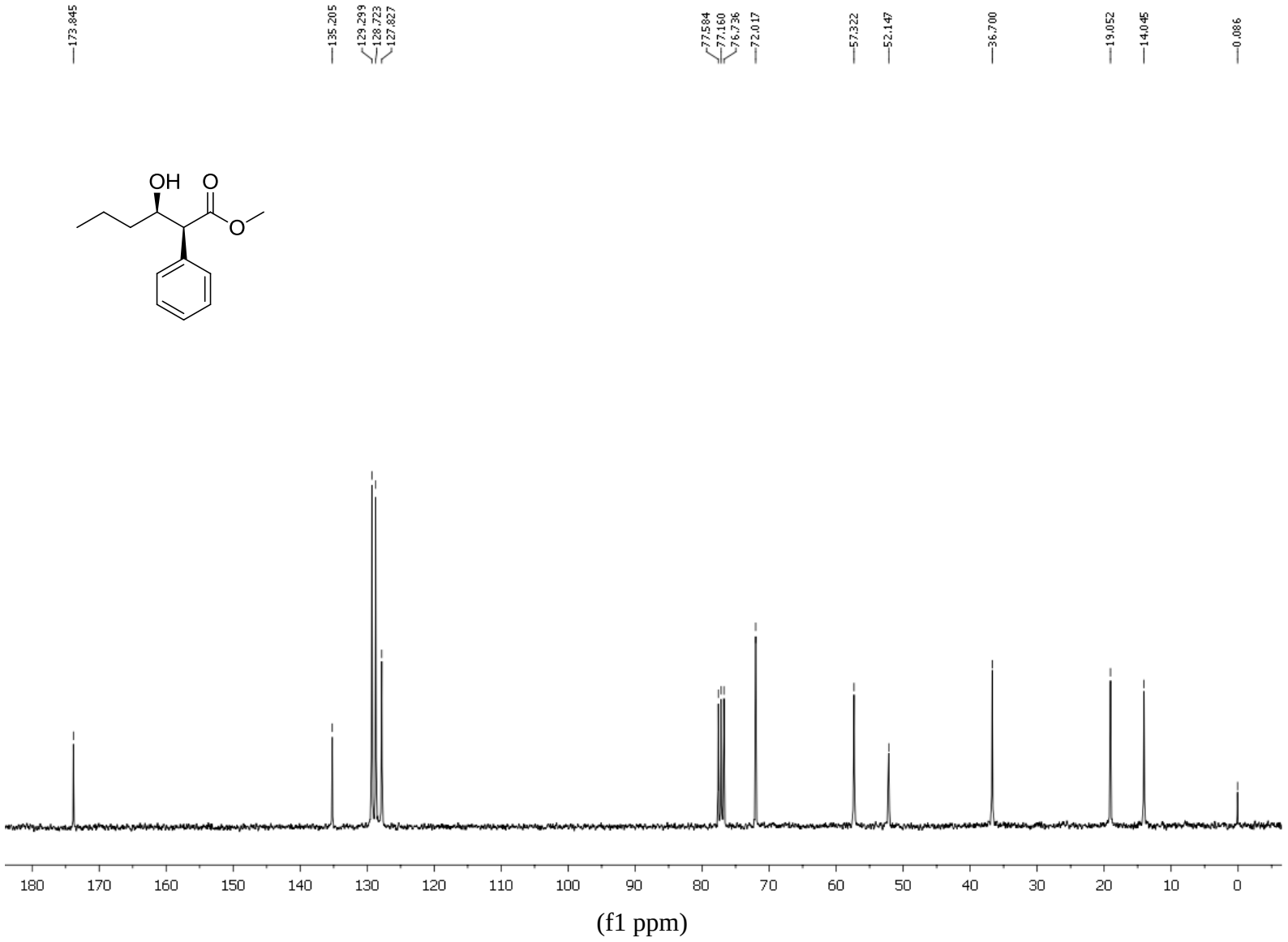
^{1}H NMR spectrum of *anti*-methyl 3-hydroxy-4-methyl-2-phenylpentanoate (**7i**)



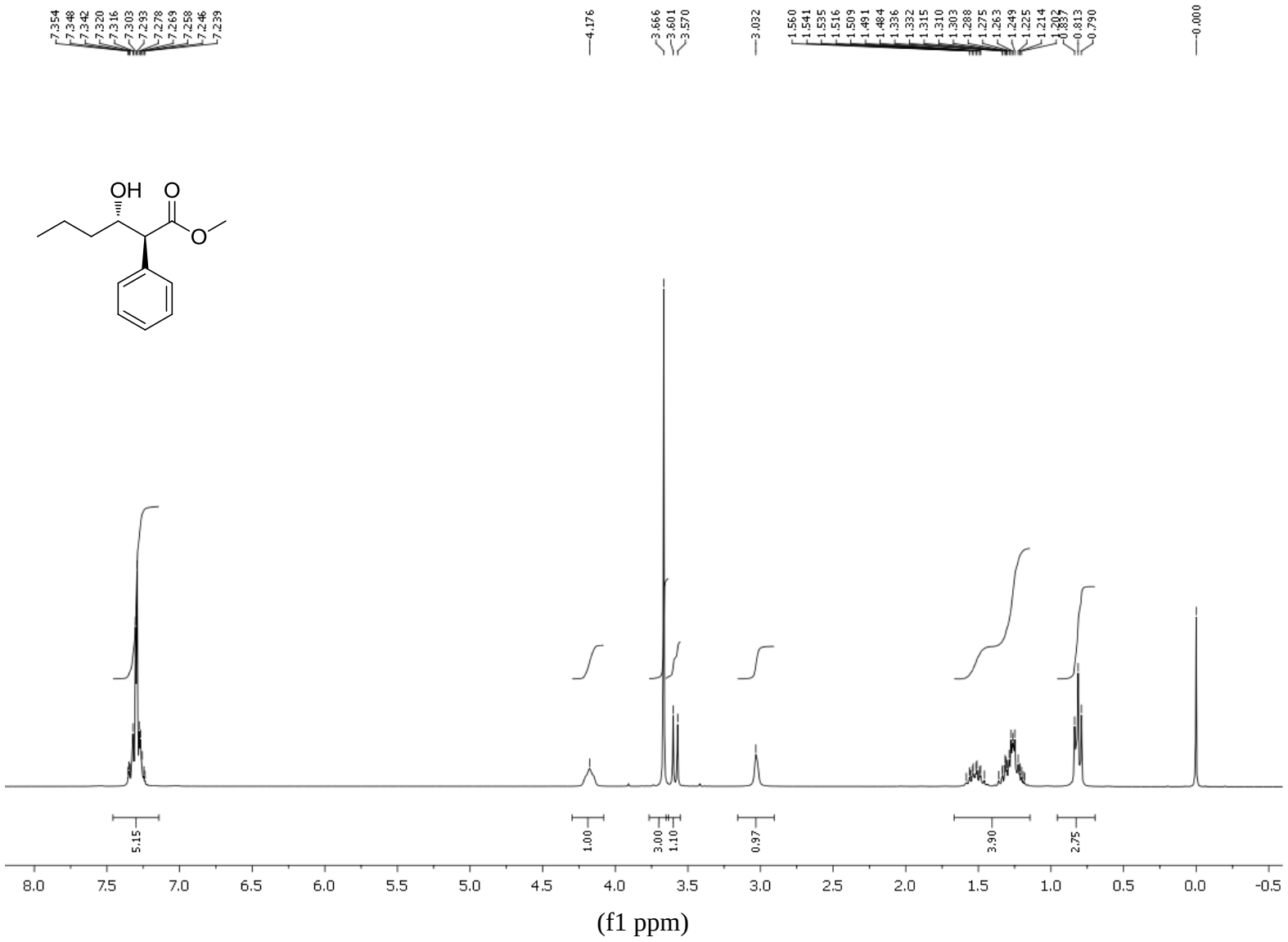
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-4-methyl-2-phenylpentanoate (**7i**)



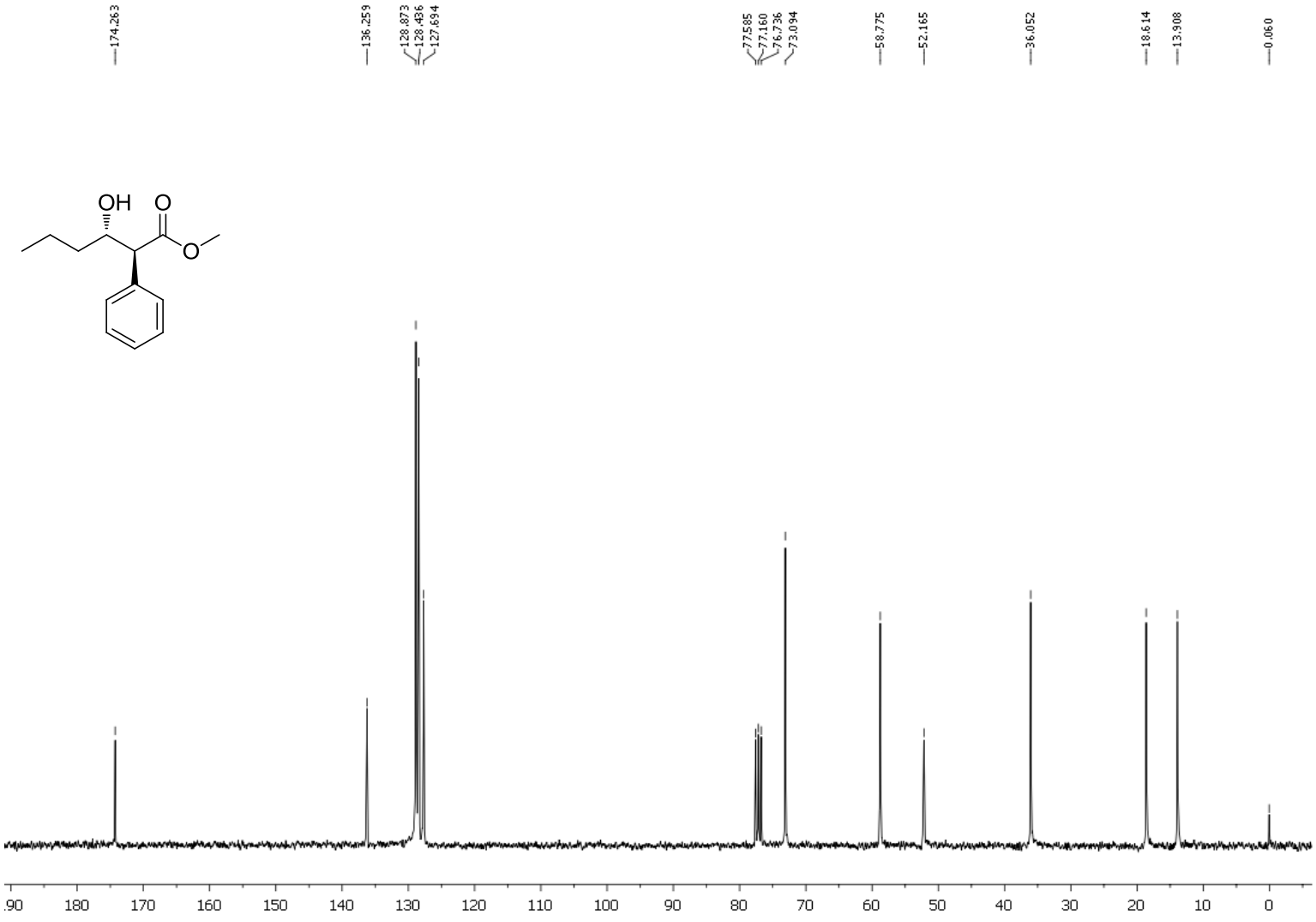
^{1}H NMR spectrum of *syn*-methyl 3-hydroxy-2-phenylhexanoate (**7j**)



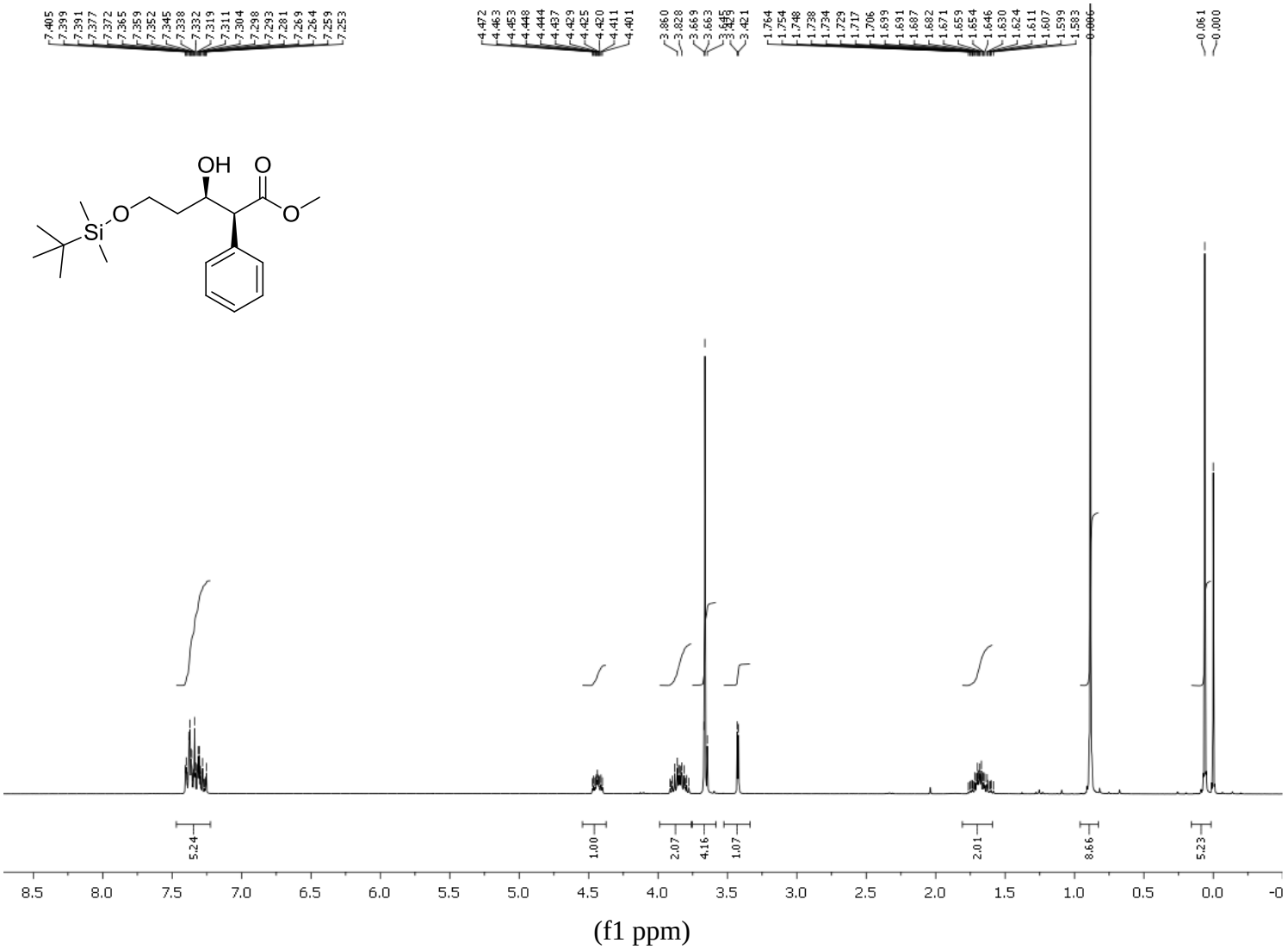
^{13}C NMR spectrum of *syn*-methyl 3-hydroxy-2-phenylhexanoate (**7j**)



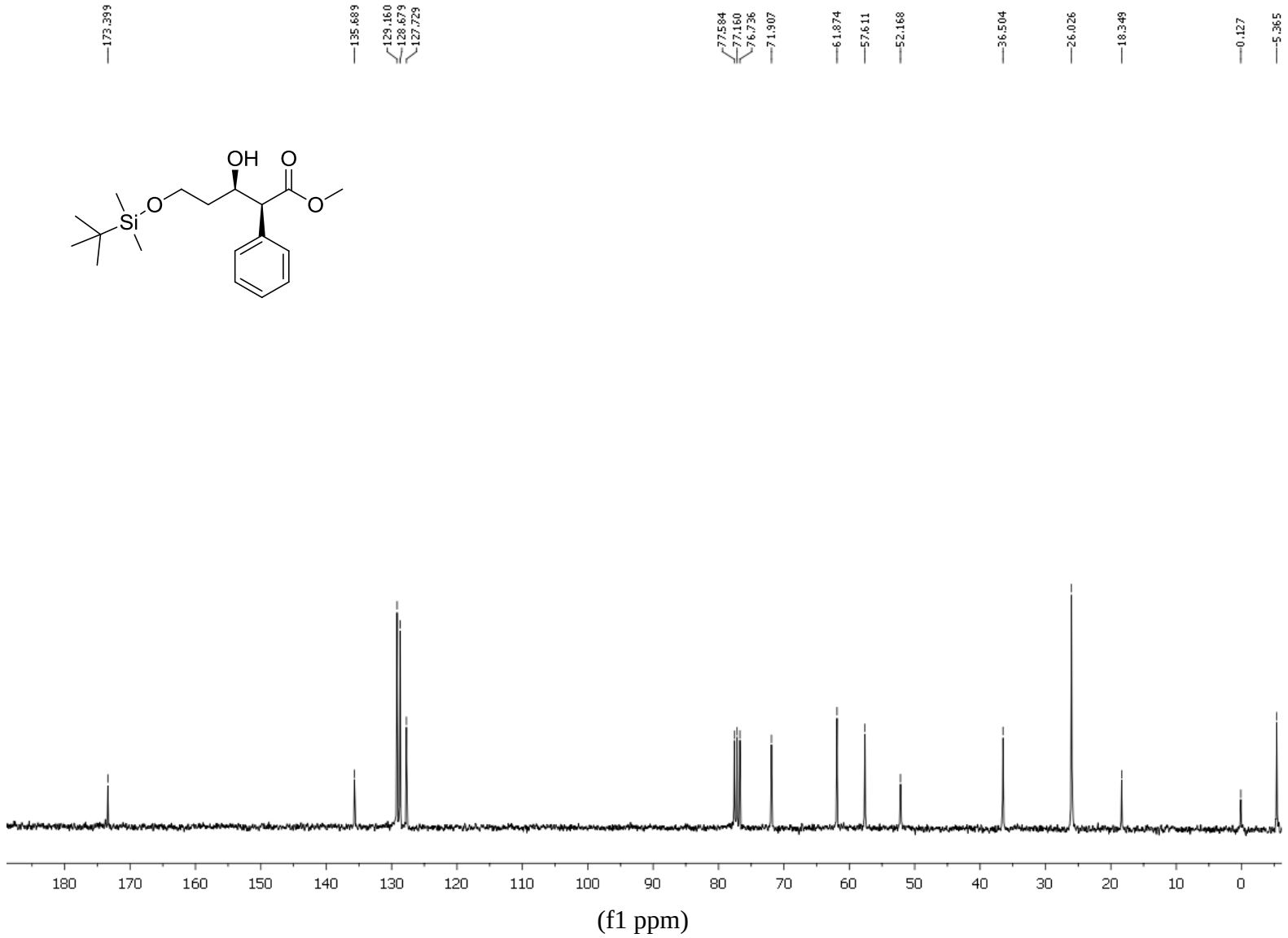
^{1}H spectrum of *anti*-methyl 3-hydroxy-2-phenylhexanoate (**7j**)



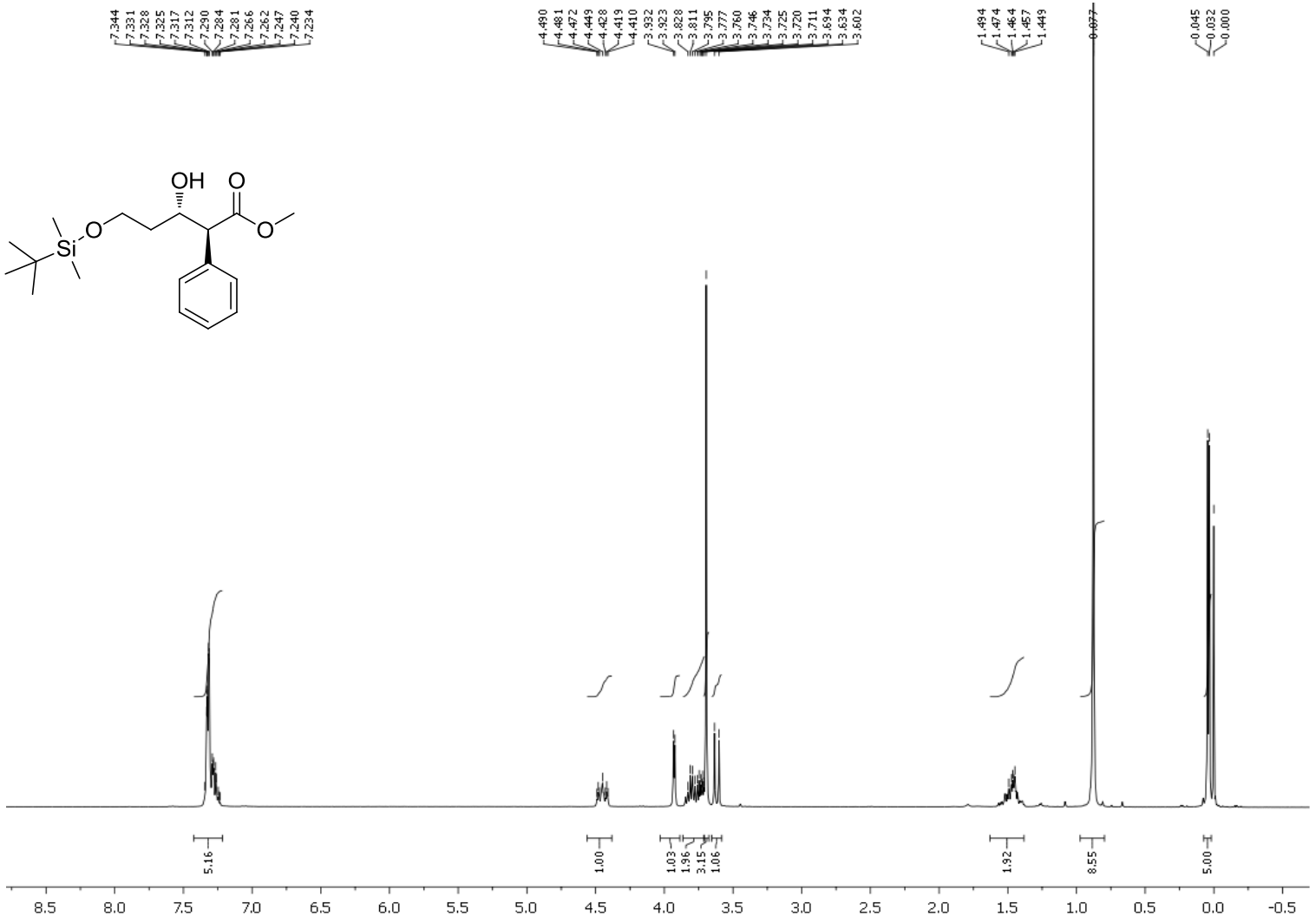
^{13}C NMR spectrum of *anti*-methyl 3-hydroxy-2-phenylhexanoate (**7j**)



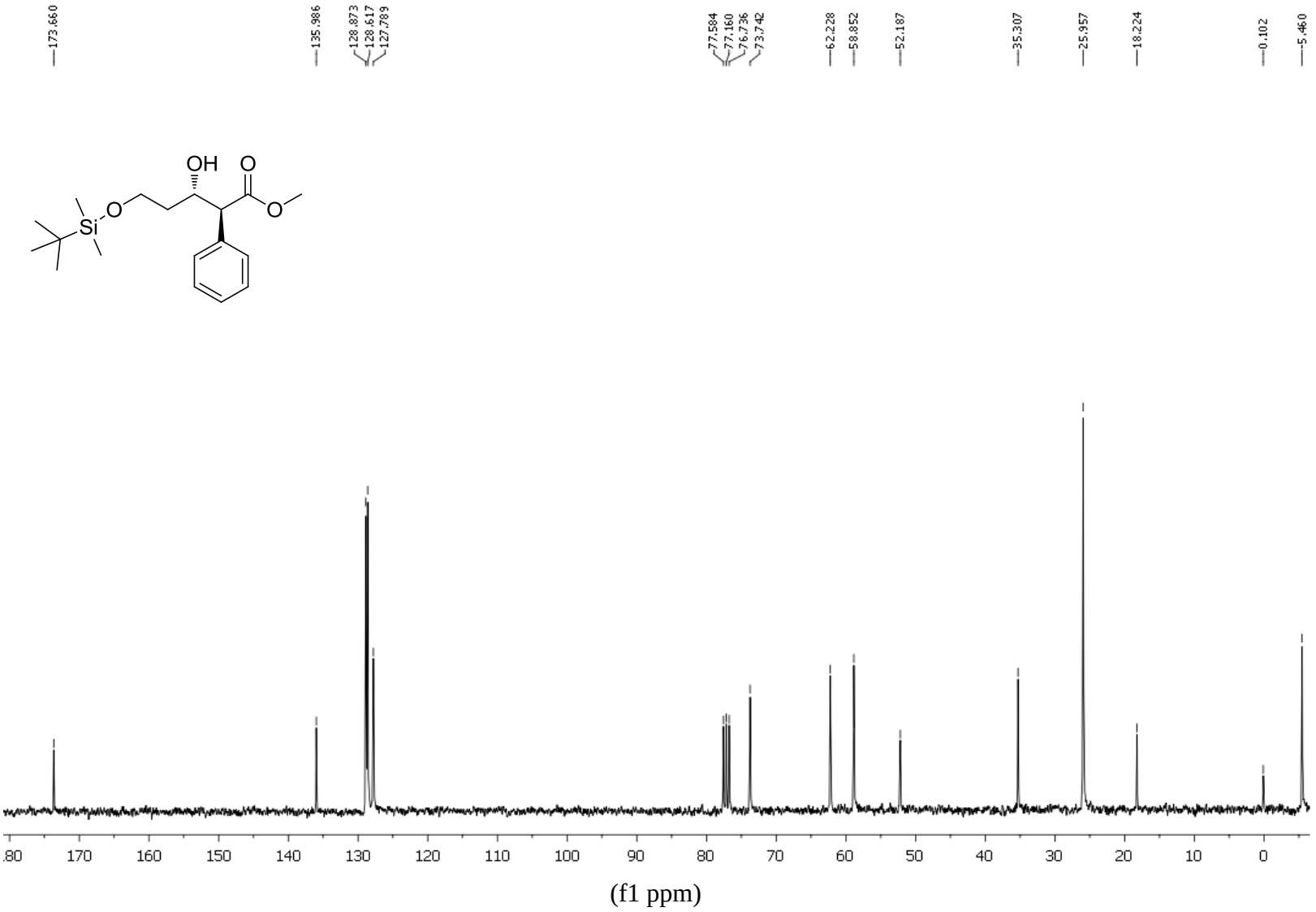
^{1}H NMR spectrum of *syn*-methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (**7k**)



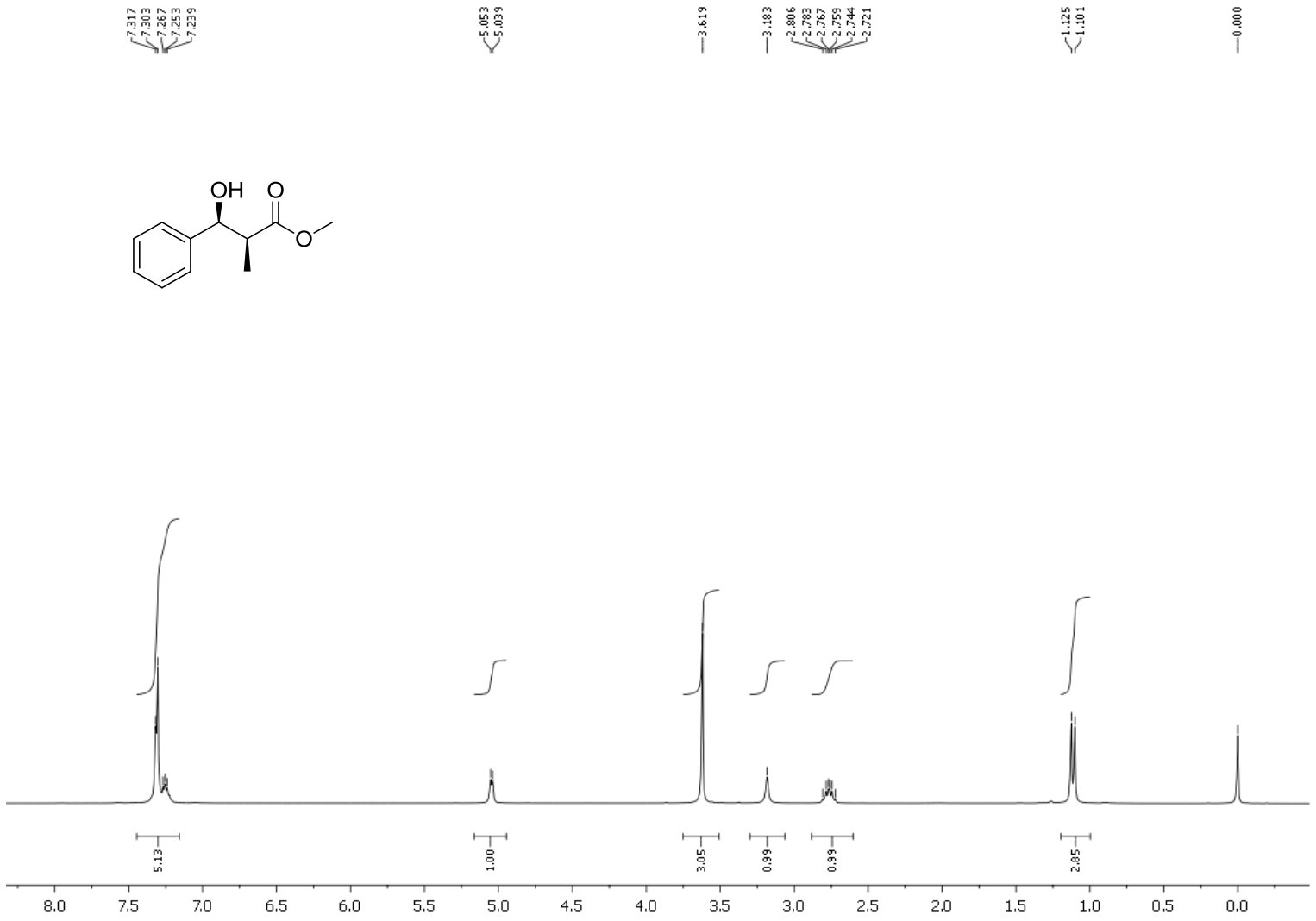
^{13}CNMR spectrum of *syn*-methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (**7k**)



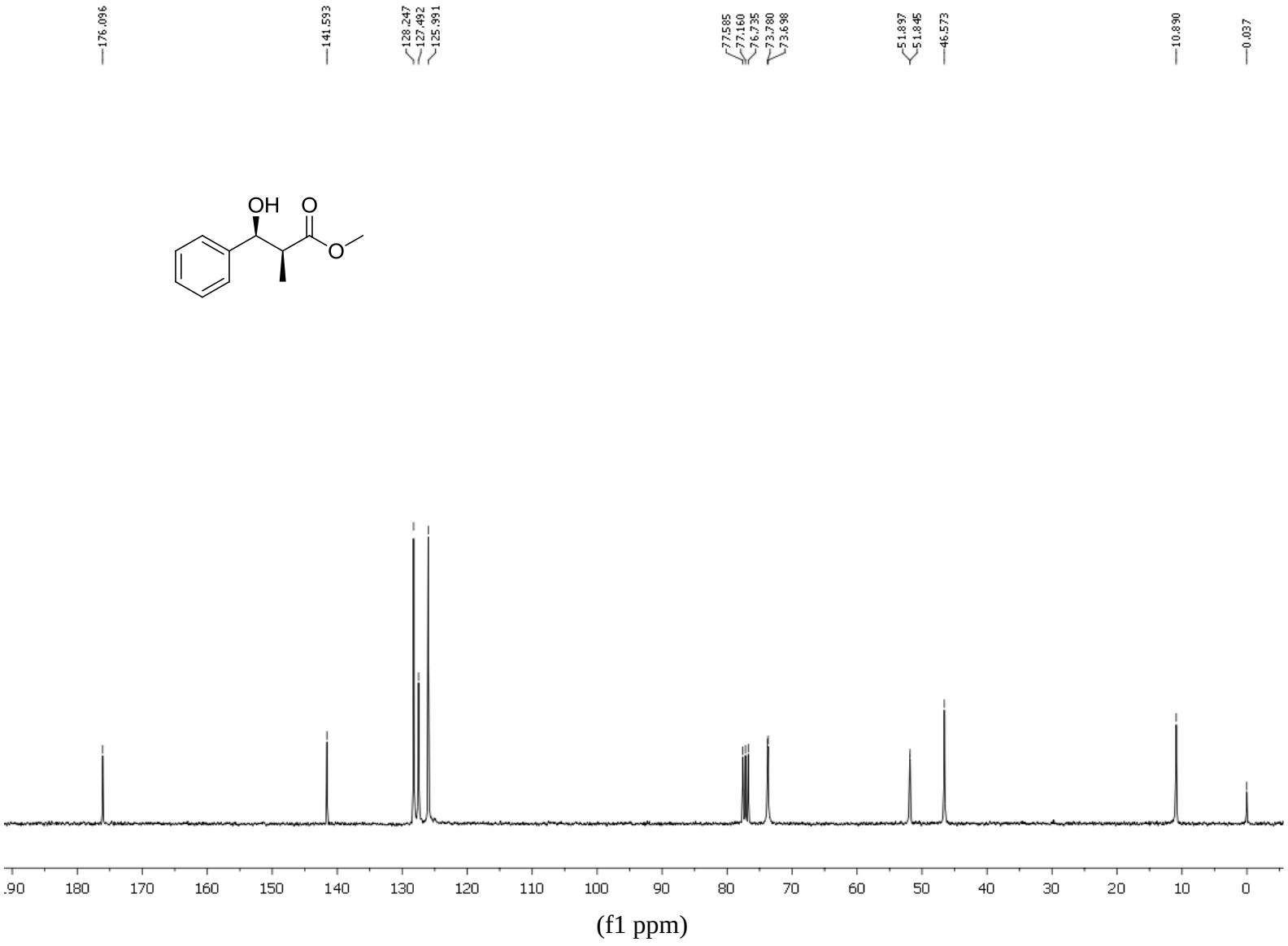
^{1}H NMR spectrum of *anti*-methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (**7k**)



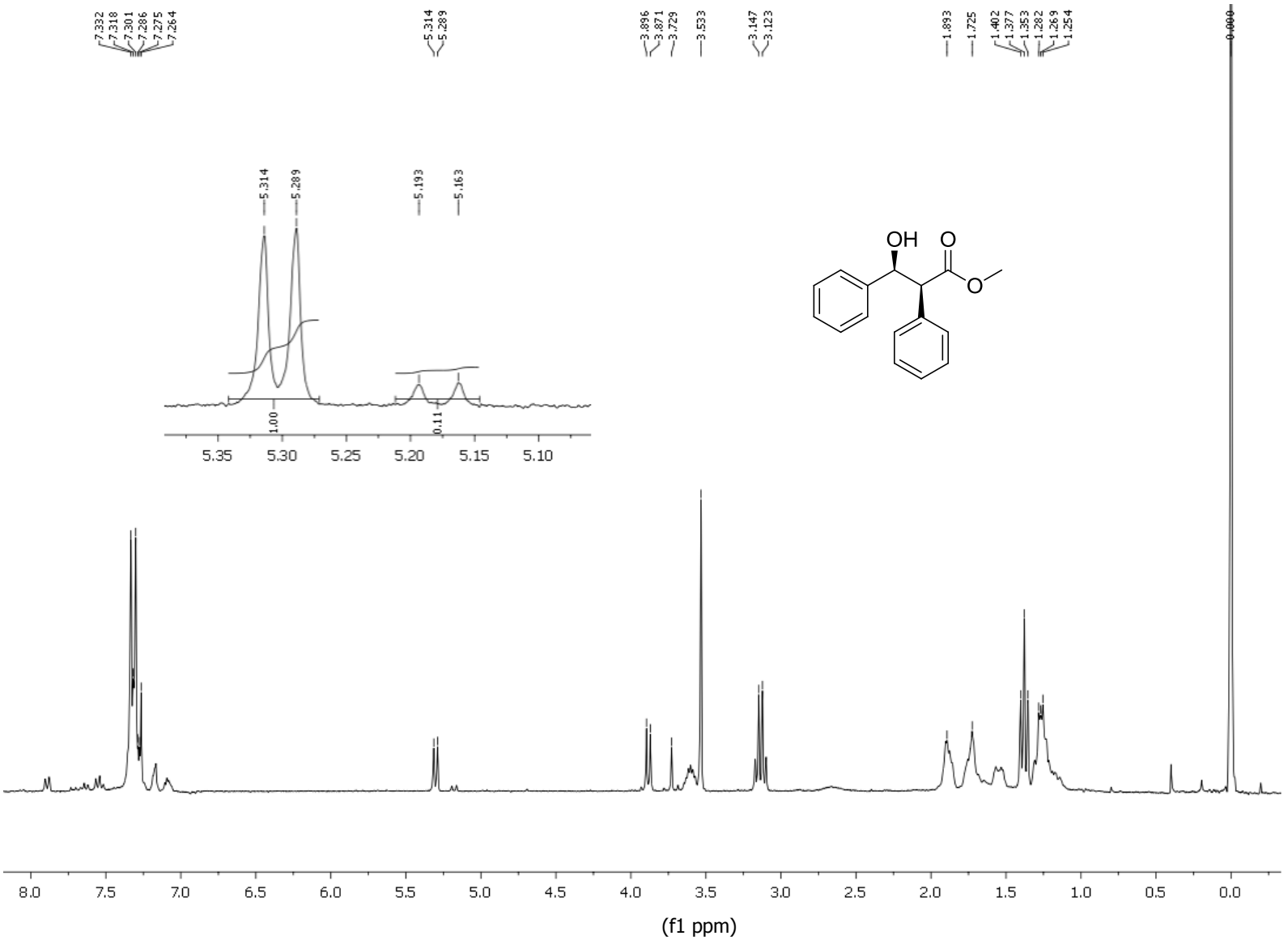
^{13}CNMR spectrum of *anti*-methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (**7k**)



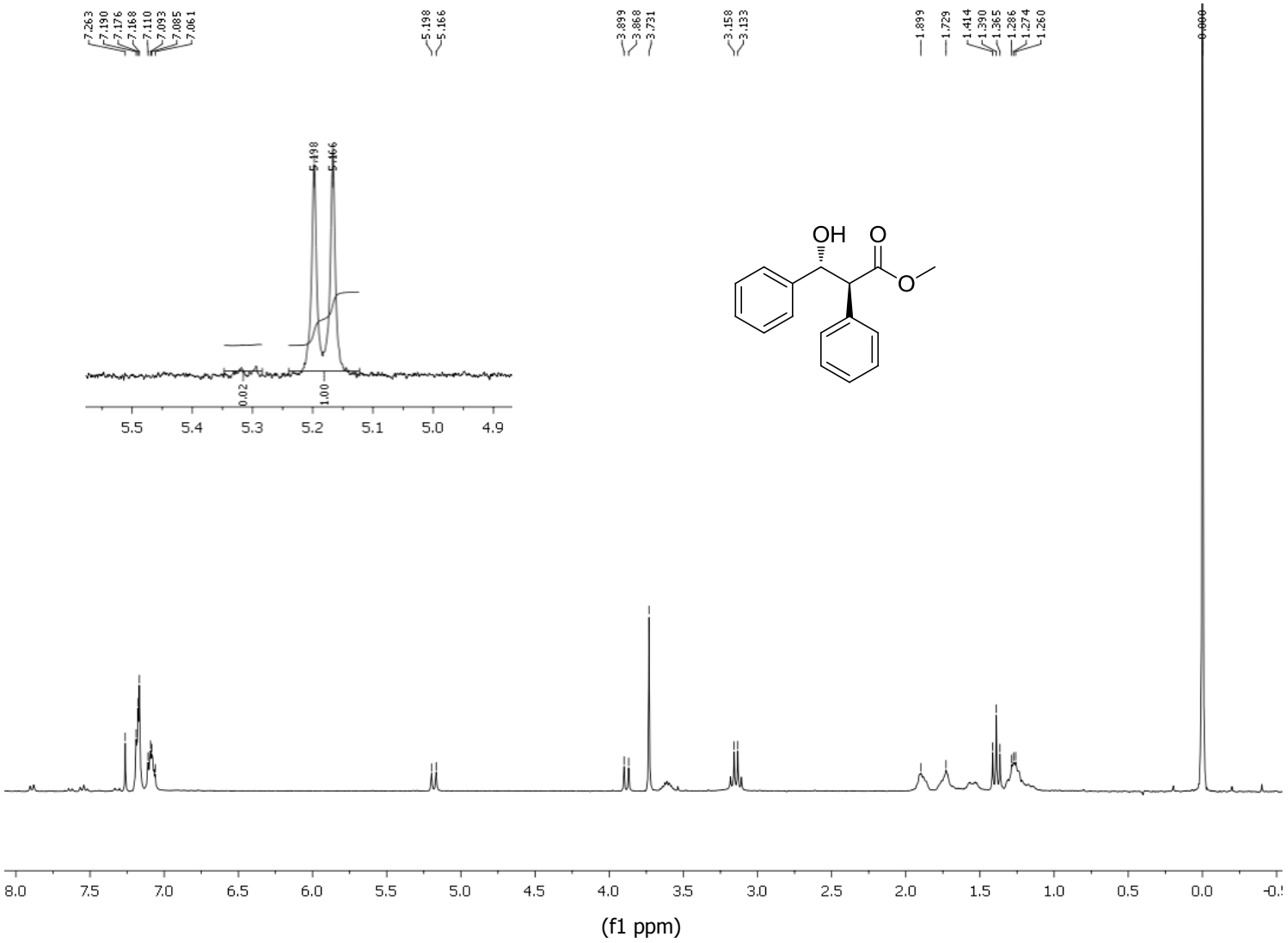
^{1}H NMR spectrum of *syn*-Methyl 3-hydroxy-2-methyl-3-phenylpropanoate (**11a**)



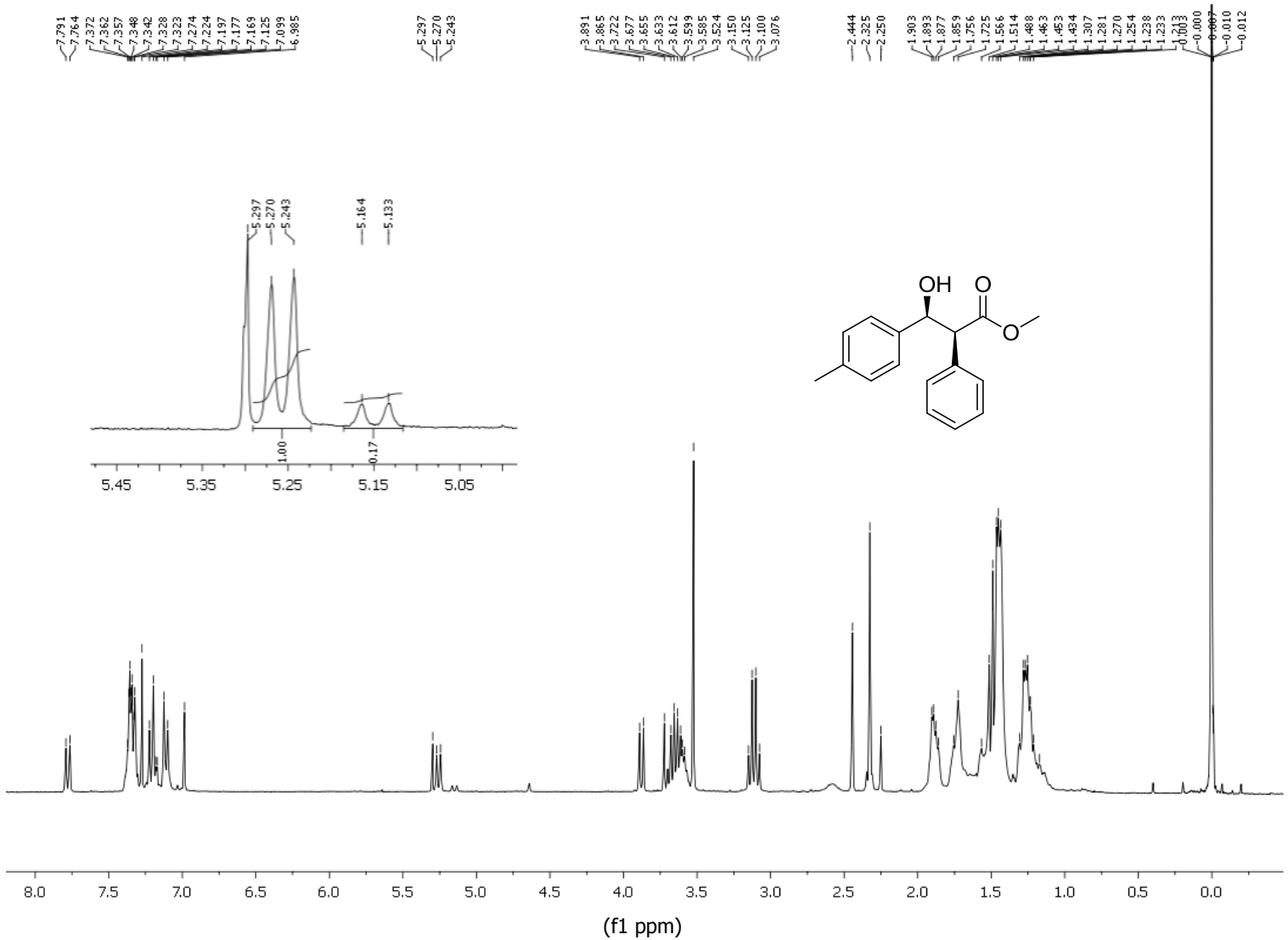
^{13}C NMR spectrum of *syn*-Methyl 3-hydroxy-2-methyl-3-phenylpropanoate (**11a**)



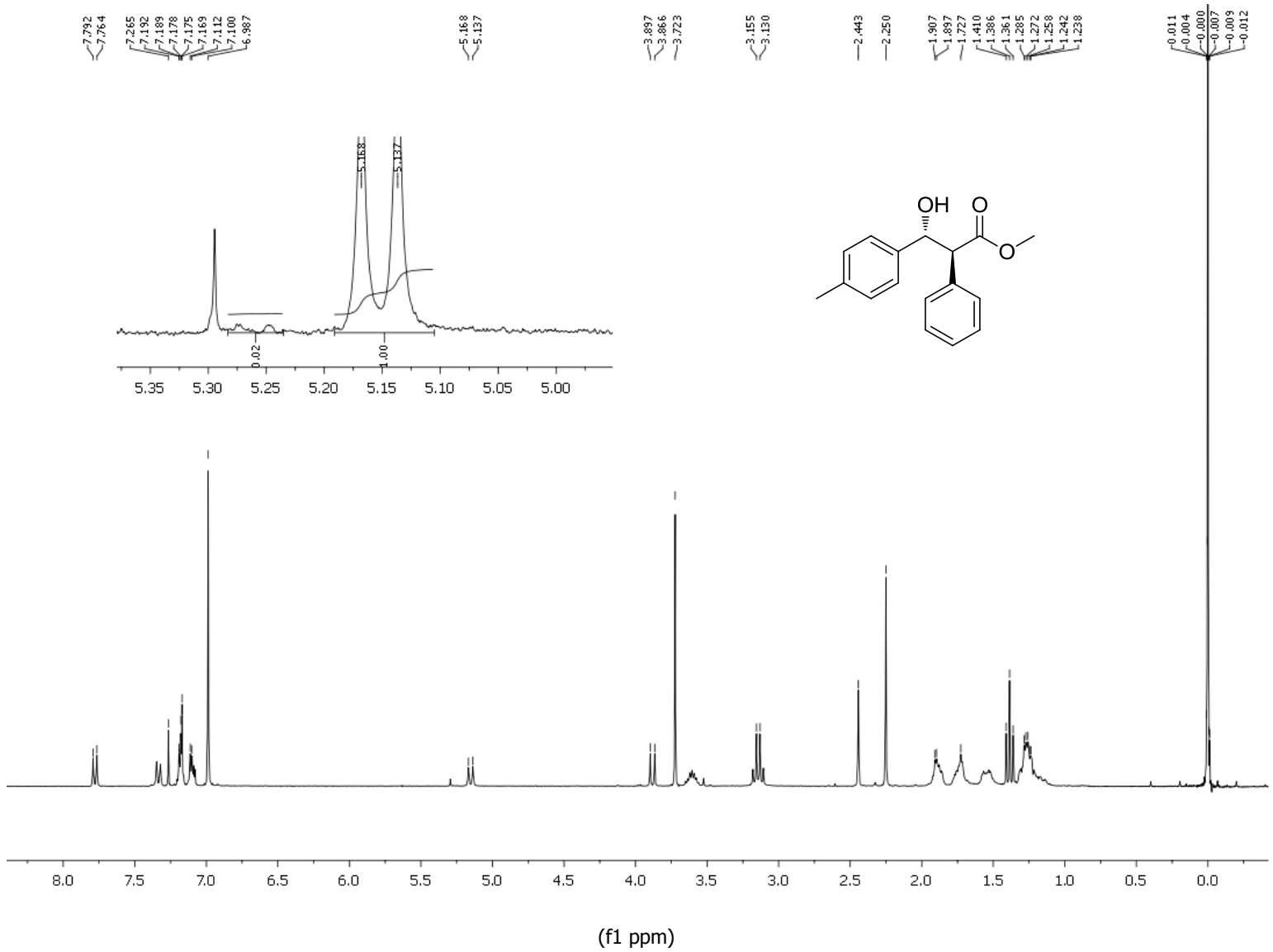
^{1}H NMR spectrum of crude reaction mixture of *syn*-methyl 3-hydroxy-2,3-diphenylpropanoate (**7a**)



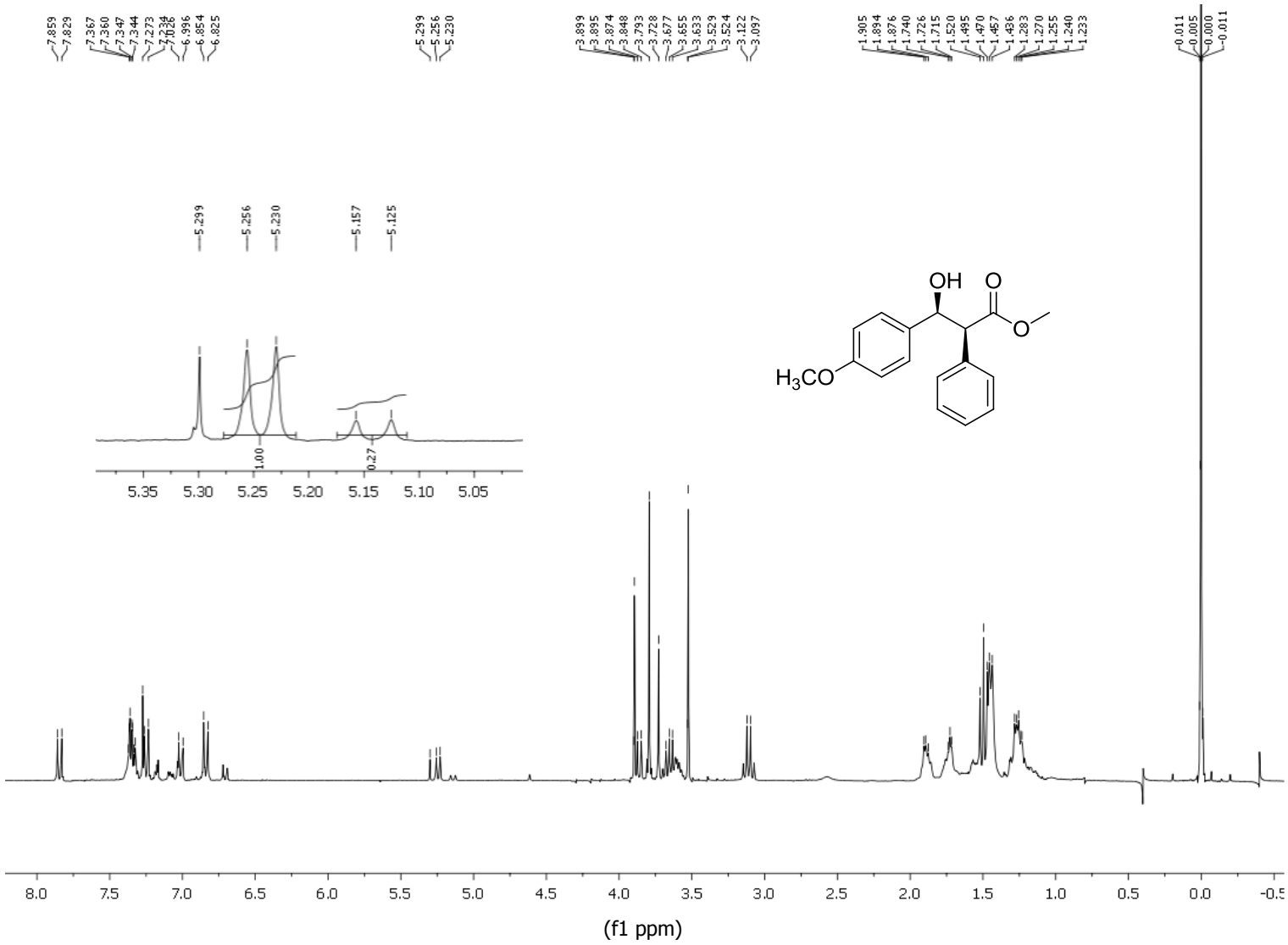
^{1}H NMR spectrum of crude reaction mixture of *anti*-methyl 3-hydroxy-2,3-diphenylpropanoate (**7a**)



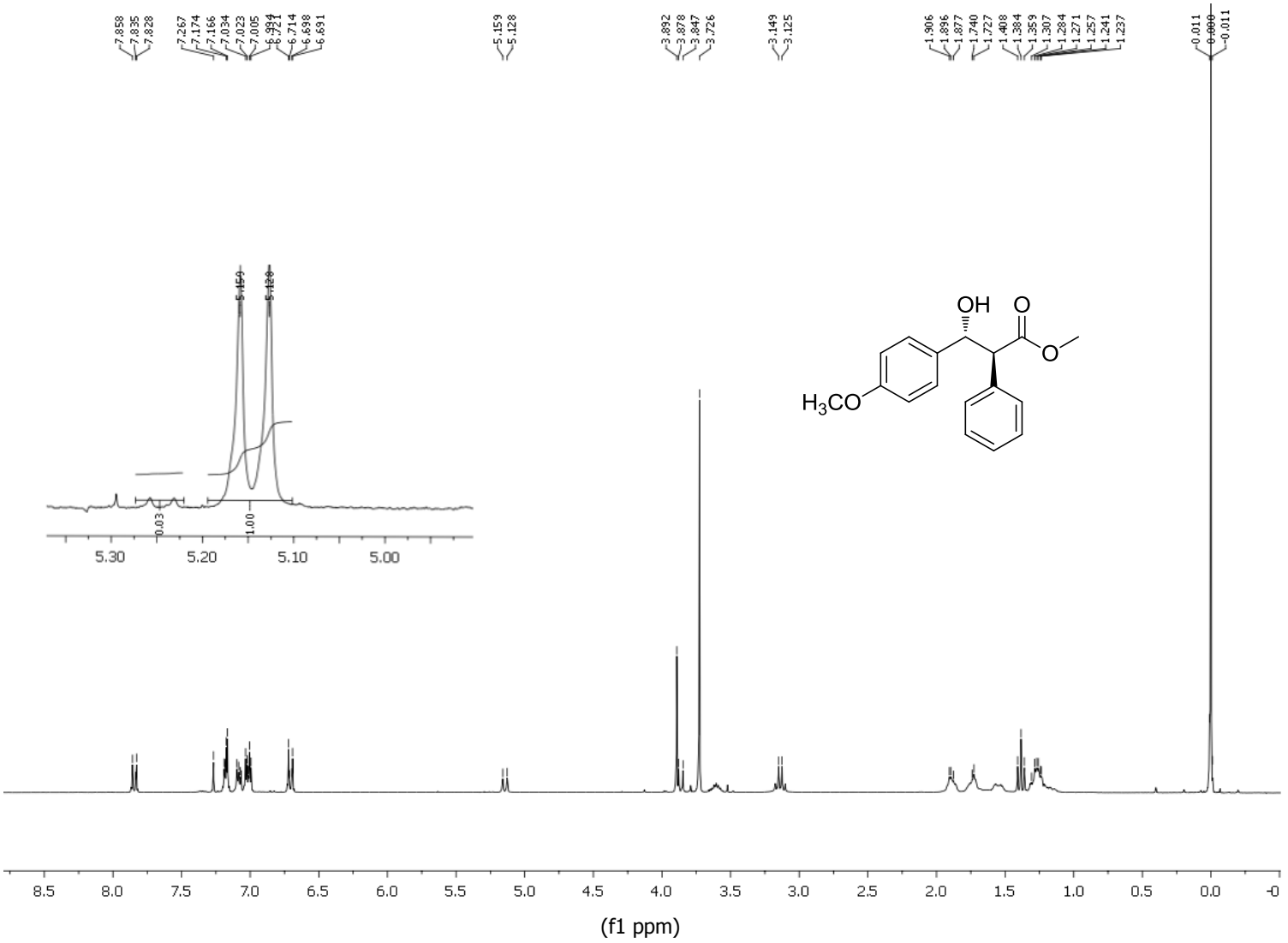
^{1}H NMR spectrum of crude reaction mixture of *syn*-methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (**7b**)



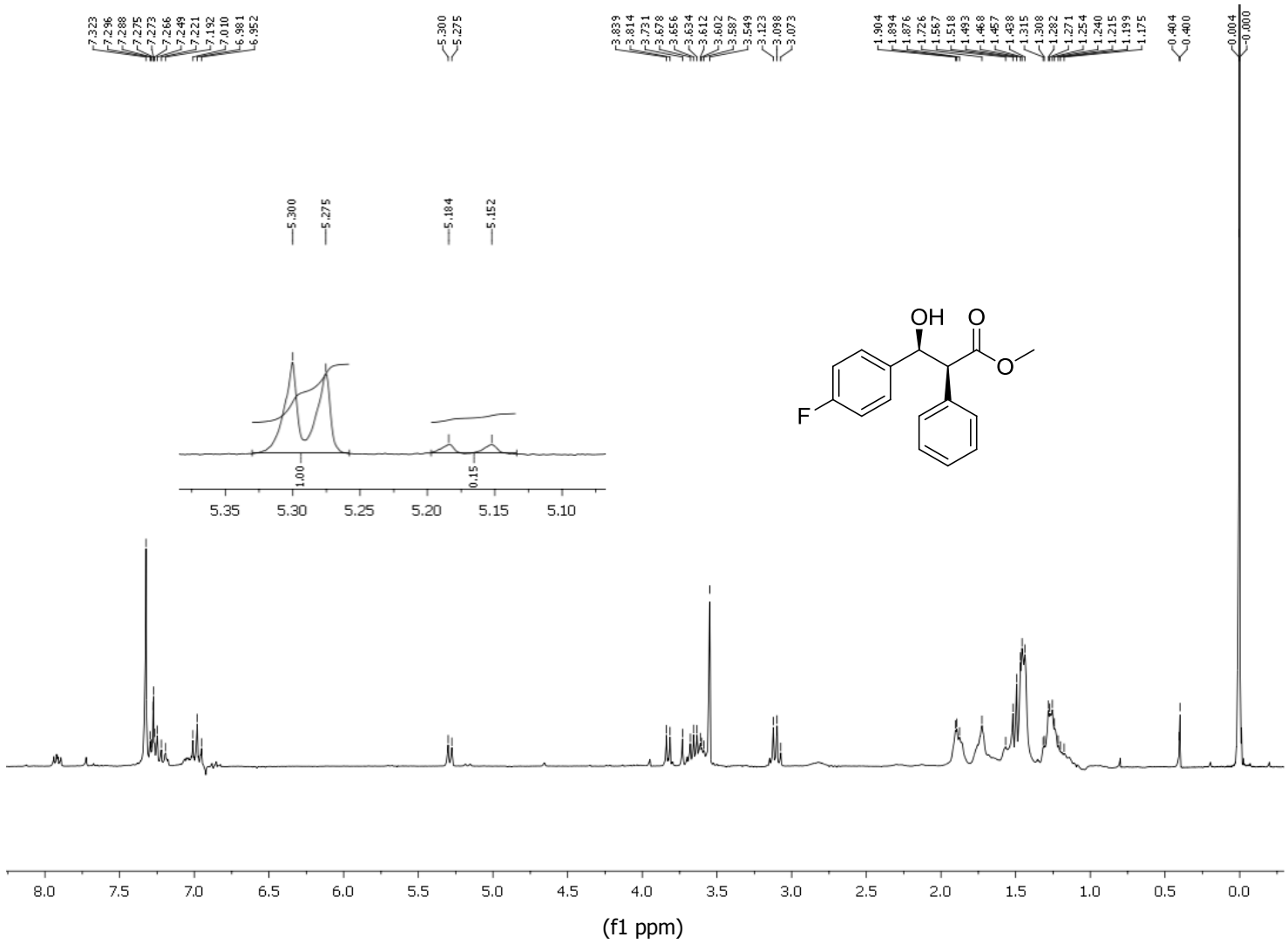
^{1}H NMR spectrum of crude reaction mixture of *anti*-methyl 3-hydroxy-2-pheny-3-(*p*-tolyl)propanoate (**7b**)



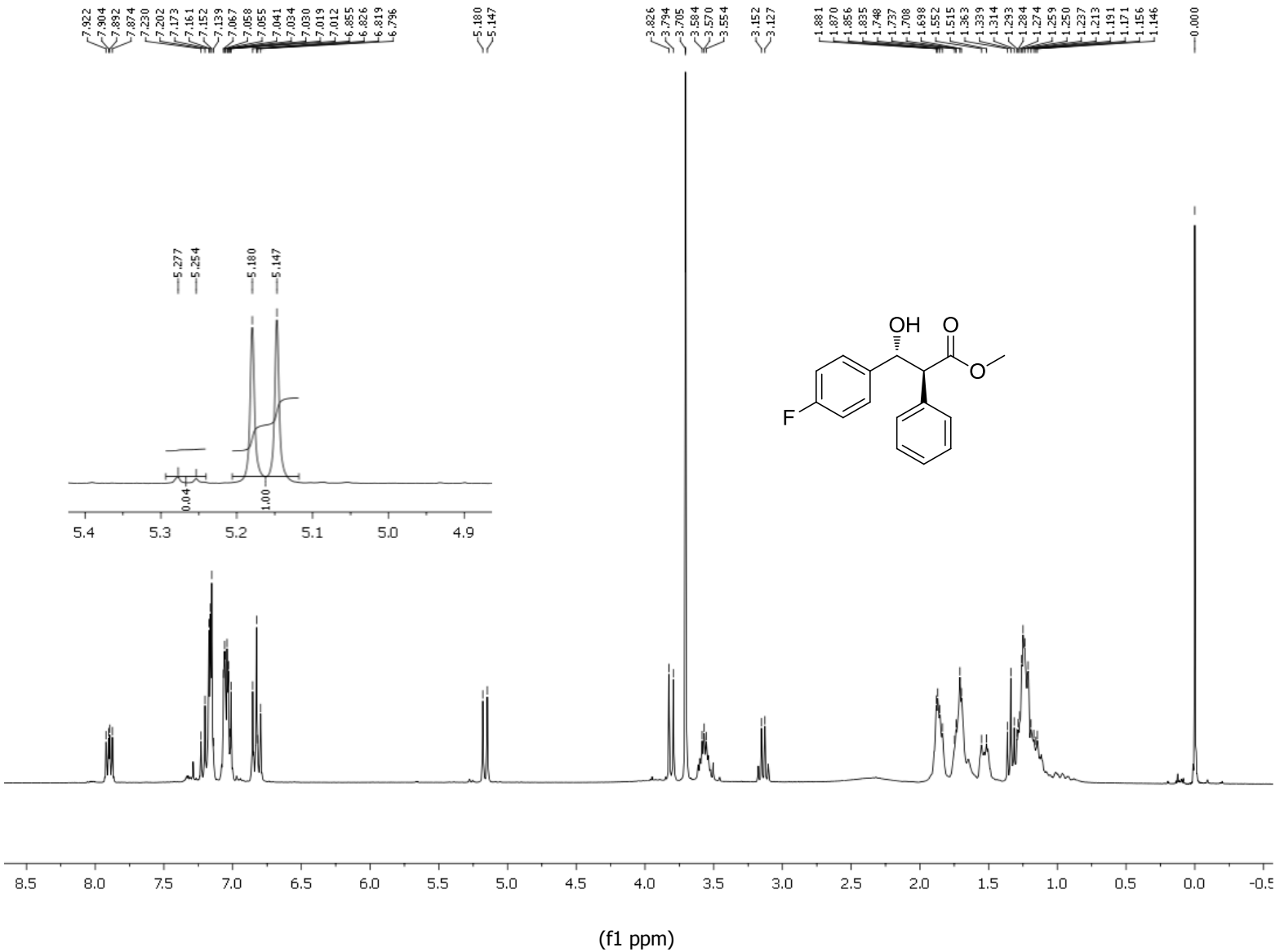
^{1}H NMR spectrum of crude reaction mixture of *syn*-methyl 3-hydroxy -3-(4-methoxyphenyl)-2-phenypropanoate (**7c**)



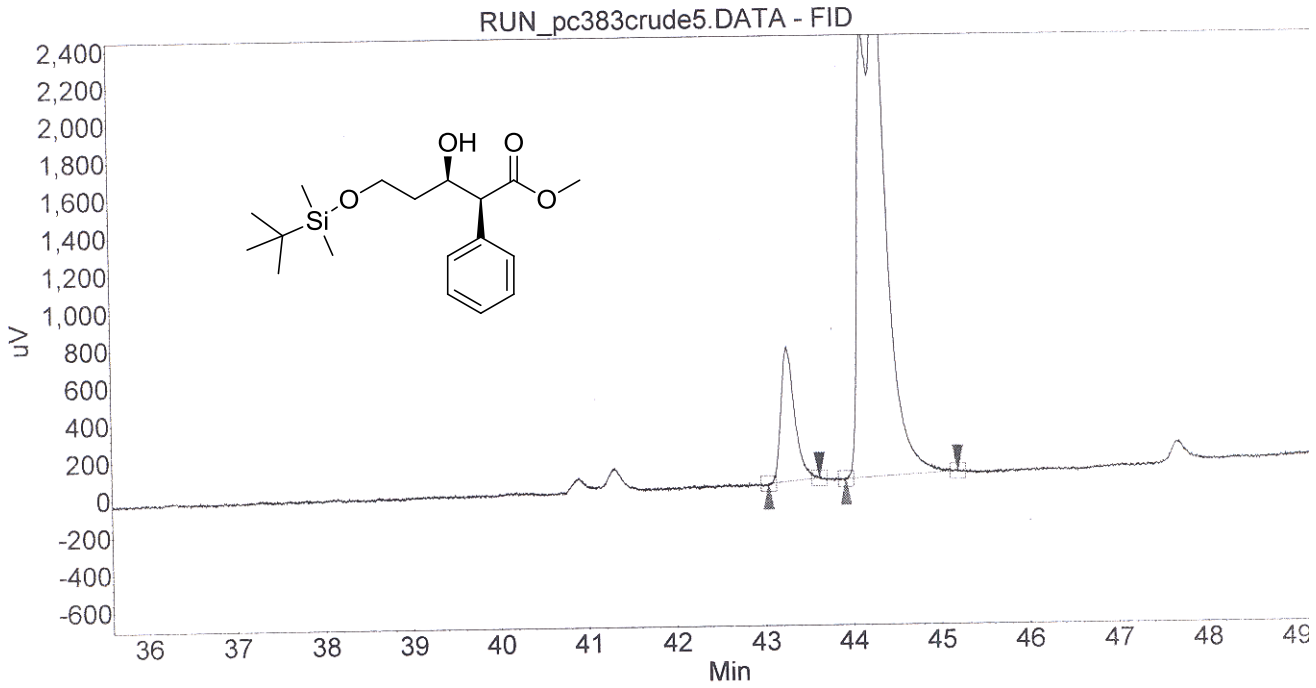
^{1}H NMR spectrum of crude reaction mixture of *anti*-methyl 3-hydroxy -3-(4-methoxyphenyl)-2-phenypropanoate (**7c**)



^{1}H NMR spectrum of crude reaction mixture of *syn*-methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (**7d**)



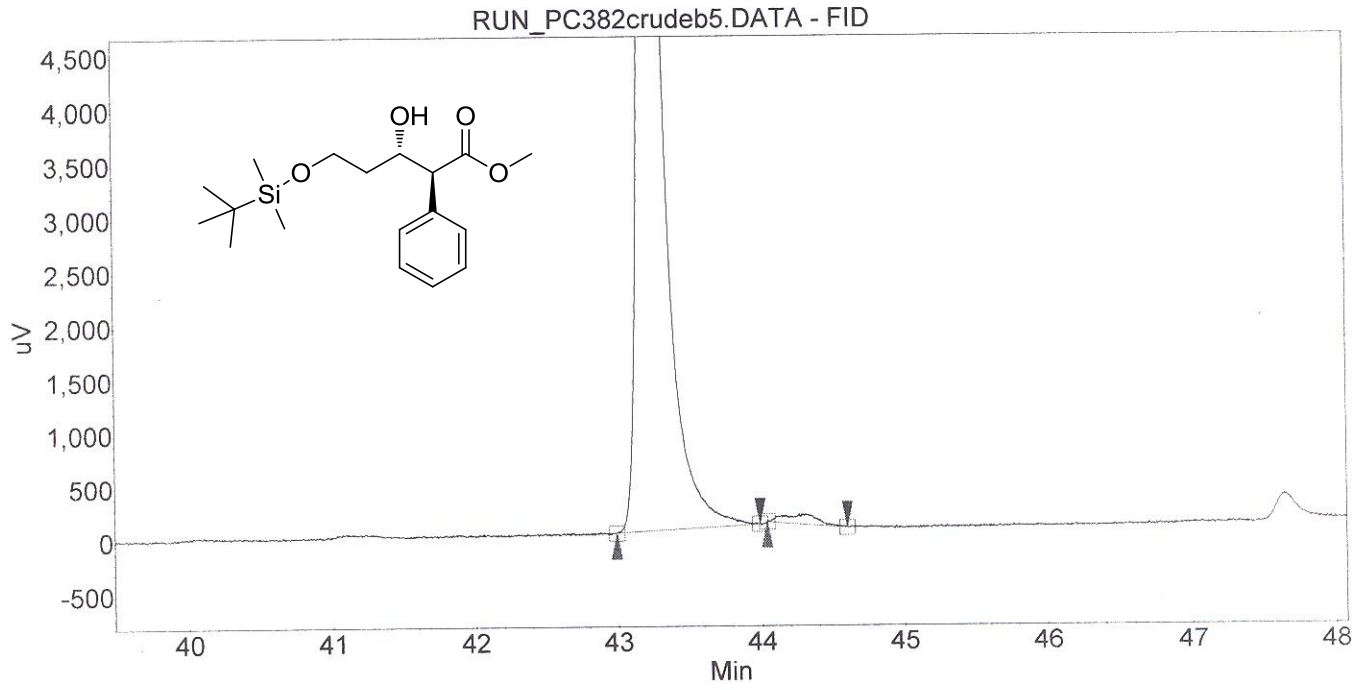
^{1}H NMR spectrum of crude reaction mixture of *anti*-methyl 3-(4-fluorophenyl)-3-hydroxy-2-phenylpropanoate (**7d**)



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [uV]	Area [uV.Min]	Area % [%]
1	UNKNOWN	43.27	11.82	719.2	128.1	11.822
2	UNKNOWN	44.33	88.18	2850.1	955.5	88.178
Total			100.00	3569.2	1083.6	100.000

Chromatogram of *syn*-methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (**7k**)



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [uV]	Area [uV.Min]	Area % [%]
1	UNKNOWN	43.24	98.76	10348.5	1912.8	98.758
2	UNKNOWN	44.31	1.24	94.3	24.1	1.242
Total			100.00	10442.8	1936.8	100.000

Chromatogram of *anti*-methyl 5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-phenylpentanoate (**7k**)