Supporting Information

Phase-transfer catalyzed enantioselective α-alkylation of α-acyloxymalonates : construction of chiral α-hydroxy quaternary stereogenic centers

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(1) General Methods

Solvents and Reagents

All reagents bought from commercial sources were used without further purification. Organic solvents were concentrated under reduced pressure using a Büchi rotary evaporator. As the commercially available KOH was a pellet type, solid KOH should be grinded to the powder form for successful reaction and high enantiopurity. 50% w/v aqueous KOH was used as stock solution. Phase-transfer catalysts **(8, 9,** and **11)** were purchased from the commercial source (Wako and Sigma Aldrich). Phase-transfer catalyst **(10)** was prepared according to the reported procedure.[S1]

Chromatography and HPLC

TLC analyses were performed using Merck precoated TLC plate (silica gel 60 GF_{254}, 0.25 mm). Flash column chromatography was carried out using E. Merck Kieselgel 60 (230~400 mesh). Instrument (Hitachi, L-2130) and software (Hitachi, Version LaChrom 8908800-07) were used as HPLC analysis. The values of enantiomeric excess (ee) of chiral products were determined by HPLC using 4.6 mm × 250 mm Daicel Chiralpak AD-H.

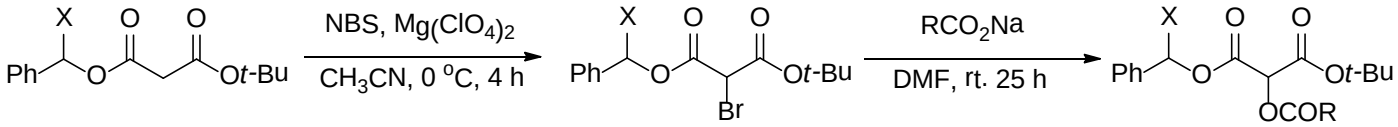
Spectral data

Infrared (IR) spectra were recorded on a JASCO FT/IR-4200 spectrometer. Nuclear magnetic resonance (^{1}H-NMR and ^{13}C-NMR) spectra were measured on JEOL JNM-LA 300 [300 MHz (^{1}H), 75 MHz (^{13}C)] spectrometer, JEOL JNM-GSX 400 [400 MHz (^{1}H), 100 MHz (^{13}C)] spectrometer,

and Bruker AMX 500 [500 MHz (^{1}H), 125 MHz (^{13}C)] spectrometer, using $CHCl_3$-*d* as solvents, and were reported in ppm relative to $CHCl_3$ (δ 7.24) for ^{1}H-NMR and relative to the central $CDCl_3$ (δ 77.23) resonance for ^{13}C-NMR. Coupling constants (*J*) in ^{1}H-NMR are in Hz. Low-resolution mass spectra (LRMS) and high-resolution mass spectra (HRMS) were measured on a JEOL JMS 700, JEOL JMS 600-W spectrometer, or Agilent 6530 Q-TOF (ESI) spectrometer. Melting points were measured on a Büchi B-540 melting point apparatus and were not corrected. Optical rotations were measured on a JASCO polarimeter P-2000 series.

(2) Experimental sections

(A) Procedure for preparation of PTC substrates



1 X = H
2 X = Ph

75 %
80 %

3 X = H
4 X = Ph

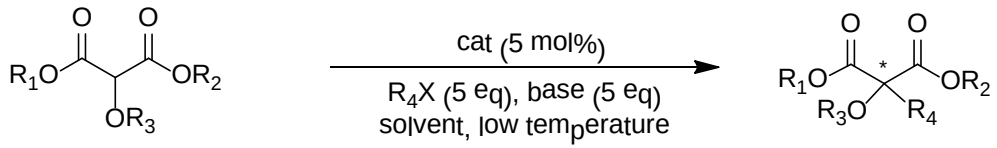
90 - 96 %

5 X = H, R = CH_3
6 X = Ph, R = CH_3
7 X = Ph, R = Ph

Compound **1** and **2** were prepared according to the already reported procedure.[S2] A solution of benzyl *tert*-butyl malonate (**1**, 1 g, 4.0 mmol) in dry

MeCN (40 mL) was added to *N*-bromosuccinimide (853 mg, 4.8 mmol) and magnesium perchlorate (268 mg, 1.2 mmol) at 0 °C under argon atmosphere. The reaction mixture was stirred for 4 hours. After the solvent was removed on a rotary evaporator, the mixture was diluted with EtOAc (200 mL) and washed with brine (150 mL). The organic layers were dried over with anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography (silica gel, hexane : EtOAc = 40 : 1 ~ 20 : 1) to afford 1-benzyl 3-(*tert*-butyl) 2-bromomalonate (**3**) as a colorless oil (987 mg, 75% yield). Sodium acetate (306 mg, 3.74 mmol) was added to a stirred solution of α-bromomalonate (**3**, 820mg, 2.49 mmole) in dry dimethylformamide (25 ml) at room temperature under argon atmosphere. The reaction was stirred until the TLC analysis showed that the reaction was complete. the reaction solvent was evaporated and diluted with EtOAc (200 ml), extracted with brine (100 ml x 2 times), dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography (silica gel, hexanes : EtOAc = 15:1) to afford 1-benzyl 3-(*tert*-butyl) 2-acetoxymalonate (**5**, 698 mg, 91% yield) as a colorless oil. 1-Benzhydryl 3-(*tert*-butyl) 2-bromomalonate (**4**), 1-benzhydryl 3-(*tert*-butyl) 2-acetoxymalonate (**6**), and 1-benzhydryl 3-(*tert*-butyl) 2-(benzoyloxy)malonate (**7**) were synthesized in the same manner described above. Analytic features of the compound **4** was consistent with the known information of the substance.[S3]

(B) Typical experimental procedure for enantioselective phase-transfer catalytic alkylation.



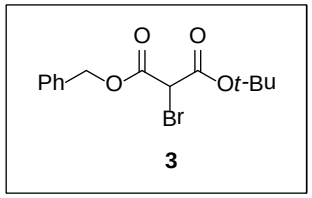
5 R_1= $PhCH_2$, R_2= *t*-Bu, R_3= Ac
6 R_1= Ph_2CH, R_2= *t*-Bu, R_3= Ac
7 R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz

5a, 6a, 7a-n

5a R_1= $PhCH_2$, R_2= *t*-Bu, R_3= Ac, R_4= CH_2CHCH_2
6a R_1= Ph_2CH, R_2= *t*-Bu, R_3= Ac, R_4= CH_2CHCH_2
7a R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= $CH_3(CH_2)_4CH_2$
7b R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= CH_2CHCH_2
7c R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= $CH_2C(CH_3)CH_2$
7d R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= $CH_2C(Br)CH_2$
7e R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= $C_6H_5CH_2$
7f R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 4-Me-$C_6H_4CH_2$
7g R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 4-*t*Bu-$C_6H_4CH_2$
7h R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 3-MeO-$C_6H_4CH_2$
7i R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 3,5-$(MeO)_2$-$C_6H_3CH_2$
7j R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 4-F-$C_6H_4CH_2$
7k R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 4-Cl-$C_6H_4CH_2$
7l R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 4-Br-$C_6H_4CH_2$
7m R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= 4-NO_2-$C_6H_4CH_2$
7n R_1= Ph_2CH, R_2= *t*-Bu, R_3= Bz, R_4= β-naphtyl-CH_2

Allyl bromide (42.1 μL, 0.49 mmol) was added to a solution of -benzyl 3-(*tert*-butyl) 2-acetoxymalonate (**5**, 30 mg, 0.10 mmol) and (*S*,*S*)-3,4,5-trifluorophenyl-NAS bromide (**8**, 4.5 mg, 0.005 mmol) in toluene (324 μL) at room temperature. At the designated low temperature, aqueous 50% w/v aqueous KOH (42.1 μL, 0.49 mmol) was added to the reaction mixture and stirred until the starting material disappeared. After completion of the reaction, the reaction mixture was diluted with ethyl acetate (20ml), washed with brine (10mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel eluting with hexane-EtOAc solution (10:1) to afford **5a** (33.4 mg, 98% yield) as a colorless oil.

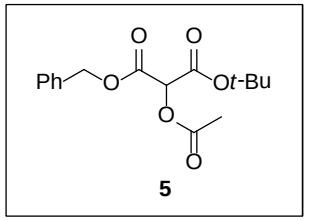
1-Benzyl 3-(*tert*-butyl) 2-bromomalonate (3)



3

Following the procedure **(A)** from the compound **1**, the title molecule **3** was obtained as a colorless oil (75% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.37 ~ 7.35 (m, 5H), 5.22 (s, 2H), 4.77 (s, 1H), 1.39 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 164.7, 163.1, 134.7, 128.64, 128.60, 128.5, 84.4, 68.4, 43.9, 27.6 ppm; IR (KBr) 2981, 2935, 1741, 1456, 1371, 1300, 1257, 1139, 1001, 969, 847, 768, 751, 698 cm^{-1}; HRMS (FAB) calcd for $C_{14}H_{18}BrO_4$ ($[M+H]^+$): 329.0388, found: 329.0383.

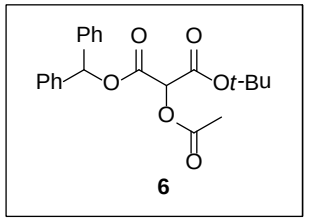
1-Benzyl 3-(*tert*-butyl) 2-acetoxymalonate (5)



5

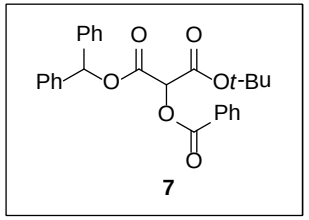
Following the procedure **(A)** from the compound **3**, the title molecule **4** was obtained as a colorless oil (90% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.36 ~ 7.31 (m, 5H), 5.44 (s, 1H), 5.26 (d, *J* = 12.09 Hz, 1H), 5.18 (d, *J* = 12.09 Hz, 1H), 2.19 (s, 3H), 1.37 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.4, 164.6, 163.0, 134.8, 128.58, 128.56, 128.4, 83.9, 72.3, 67.7, 27.7, 20.4 ppm; IR (KBr) 2980, 2939, 1748, 1457, 1371, 1220, 1151, 1100, 1001, 841, 754 cm^{-1}; HRMS (FAB) calcd for $[C_{16}H_{21}O_6]^+$ ($[M+H]^+$): 309.1338, found: 309.1332.

1-Benzhydryl 3-(*tert*-butyl) 2-acetoxymalonate (6)



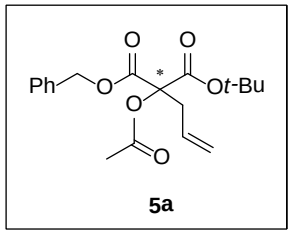
Following the procedure **(A)** from the compound **5**, the title molecule **6** was obtained as a sticky oil (91% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) 7.38 ~ 7.25 (m, 10H), 6.95 (s, 1H), 5.50 (s, 1H), 2.19 (s, 3H), 1.36 (s, 9H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 169.5, 163.8, 163.0, 139.1, 128.55, 128.50, 128.23, 128.21, 127.3, 127.1, 84.0, 78.7, 72.5, 27.7, 20.4 ppm; IR (KBr) 3489, 2980, 1751, 1587, 1496. 1371, 1220, 1150, 1098. 962, 839, 744, 700 cm^{-1}; HRMS (FAB) calcd for $[C_{22}H_{24}O_6]^+$ ($[M+Na]^+$): 407.1471, found: 407.1477.

1-Benzhydryl 3-(*tert*-butyl) 2-(benzoyloxy)malonate (7)



Following the procedure **(A)** from the compound **5** using sodium benzoate, the title molecule **7** was obtained as a white solid (94% yield). mp 98 ^{o}C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.14 ~ 8.11 (m, 2H), 7.60 ~ 7.55 (m, 1H), 7.46 ~ 7.41 (m, 2H), 7.36 ~ 7.23 (m, 10H), 7.01 (s, 1H), 5.78 (s, 1H), 1.40 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.1, 163.8, 163.0, 139.1, 133.7, 130.2, 128.55, 128.49, 128.46, 128.2, 127.3, 127.1, 84.05, 78.7, 72.7, 27.7 ppm; IR (KBr) 2980, 1768, 1734, 1602, 1496, 1453, 1369, 1235, 1119, 1002, 838, 744, 700 cm^{-1}; HRMS (FAB): calcd for $[C_{27}H_{27}O_6]^+$: 447.1808, found: 447.1815.

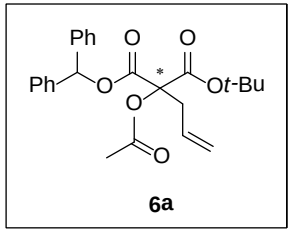
1-Benzyl 3-(*tert*-butyl) 2-acetoxy-2-allylmalonate (5a)



5a

Following the procedure **(B)** from the substrate **5**, the title molecule **5a** was obtained as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.35 ~ 7.29 (m, 5H), 5.76 ~ 5.62 (m, 1H), 5.21 (d, *J* = 12.08 Hz, 1H), 5.15 (d, *J* = 12.08 Hz, 1H), 5.11 ~ 5.05 (m, 2H), 2.99 ~ 2.86 (m, 2H), 2.12 (s, 3H), 1.35 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.3, 166.5, 164.6, 135.1, 130.4, 128.54, 128.48, 128.4, 119.9, 83.4, 82.7, 67.6, 38.5, 27.6, 20.7 ppm; IR (KBr) 2980, 1752, 1457, 1370, 1260, 1229, 1142, 1063, 844, 772 cm^{-1}; HRMS (FAB) calcd for $[C_{19}H_{25}O_6]^+$ ($[M+H]^+$): 349.1651, found: 349.1649; The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralpak AD-H, hexane : 2-propanol = 99 : 1, flow rate = 1.0 ml/min, 23 ℃, λ = 254 nm) retention time; major isomer 11.92 min, minor isomer 13.07 min, 42% ee, $[\alpha]^{20}_D$ = + 4.66 (*c* 1.0, $CHCl_3$).

1-Benzhydryl 3-(*tert*-butyl) 2-acetoxy-2-allylmalonate (6a)

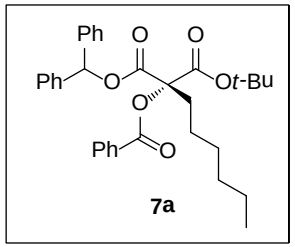


6a

Following the procedure **(B)** from the substrate **6**, the title molecule **6a** was obtained as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.32 ~ 7.27 (m, 10H), 6.92 (s, 1H), 5.67 ~ 5.56 (m, 1H), 5.04 (s, 1H), 5.00 (d, *J* = 8.79 Hz, 1H), 2.99 ~ 2.96 (m, 2H), 2.09 (s, 3H), 1.32 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.3, 165.6, 164.5, 139.3, 139.2, 130.2, 128.44, 128.36, 128.1, 128.0, 127.4, 127.3, 120.0, 83.5, 82.7, 78.5, 38.3, 27.6, 20.7 ppm; IR (KBr) 3033, 2980, 2933, 1751, 1643, 1455, 1370, 1257, 1229, 1142, 1062, 926, 843, 744, 700 cm^{-1}; HRMS (FAB) calcd for $[C_{25}H_{29}NO_6]^+$ ($[M+H]^+$): 425.1964, found: 425.1967; The enantioselectivity was

determined by chiral HPLC analysis (DAICEL Chiralpak AD-H, hexane : 2-propanol = 95 : 5, flow rate = 1.0 ml/min, 23 ℃, λ = 254 nm) retention time ; major isomer 12.94 min, minor isomer14.90 min, 76% ee, $[\alpha]^{20}_{D}$ = + 37.15 (*c* 1.0, $CHCl_3$).

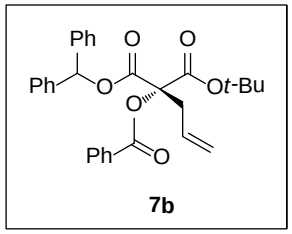
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-hexylmalonate (7a)



7a

Following the procedure **(B)** from the substrate **7** using *n*-iodohexane, the title molecule **7a** was obtained as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.68 Hz, 2H), 7.58 (t, *J* = 7.43 Hz, 1H), 7.45 (d, *J* = 7.70 Hz, 2H), 7.32 ~ 7.24 (m, 10H), 6.99 (s, 1H), 2.42 ~ 2.27 (m, 2H), 1.35 (s, 9H), 1.26 ~ 1.18 (m, 8H), 0.82 (t, *J* = 6.68 Hz, 3H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 166.1, 165.2, 164.8, 139.5, 139.3, 133.3, 130.0, 129.5, 128.42, 128.39, 128.3, 128.1, 127.9, 127.5, 127.2, 83.9, 83.3, 78.3, 34.0, 31.4, 29.7, 29.0, 27.7, 23.2, 22.4, 14.0 ppm; IR (KBr) 2962, 2930, 1752, 1730, 1453, 1370, 1285, 1220, 1143, 772, 700 cm^{-1}; HRMS (CI): calcd for $[C_{33}H_{37}O_6]^+$ ($[M-H]^+$): 529.2590, found: 529.2596; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 95 : 5, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 10.95 min, minor isomer 12.33 min, 75% ee, $[\alpha]^{20}_{D}$ = + 2.64 (*c* 1.0, $CHCl_3$).

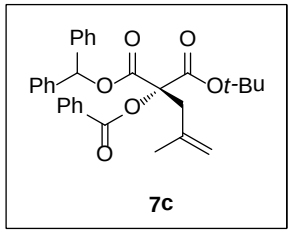
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-allyl-2-(benzoyloxy)malonate (7b)



7b

Following the procedure **(B)** from the substrate **7**, the title molecule **7b** was obtained as a white oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.09 ~ 8.06 (m, 2H), 7.60 ~ 7.55 (m, 1H), 7.46 ~ 7.41 (m, 2H), 7.35 ~ 7.23 (m, 10H), 6.99 (s, 1H), 5.77 ~ 5.64 (m, 1H), 5.08 ~ 5.07 (m, 1H), 5.03 (s, 1H), 3.22 ~ 3.09 (m, 2H), 1.35 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 164.7, 164.5, 139.4, 139.2, 133.4, 130.2, 130.0, 129.4, 128.42, 128.38, 128.3, 128.1, 127.9, 127.5, 127.2, 120.1, 83.6, 83.1, 78.5, 38.3, 27.7 ppm; IR (KBr) 3065, 2980, 1752, 1731, 1644, 1602, 1496, 1395, 1244, 1109, 991, 842, 742 cm^{-1}; HRMS (FAB): calcd for $[C_{30}H_{31}O_6]^+$ ($[M+H]^+$): 487.2121, found: 487.2126; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 9.05 min, minor isomer 11.06 min, 87% ee, $[\alpha]^{20}_{D}$ = + 1.27 (*c* 1.0, $CHCl_3$).

1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(2-methylallyl)malonate (7c)

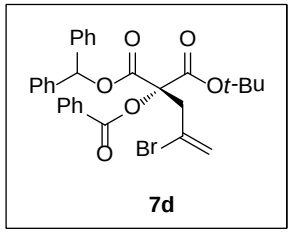


7c

Following the procedure **(B)** from the substrate **7** using 3-bromo-2-methylpropene, the title molecule **7c** was obtained as a white oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.10 ~ 8.07 (m, 2H), 7.61 ~ 7.56 (m, 1H), 7.47 ~ 7.42 (m, 2H), 7.36 ~ 7.22 (m, 10H), 6.99 (s, 1H), 4.76 ~ 4.70 (d, *J* = 15.93 Hz, 2H), 3.19 (s, 2H), 1.68 (s, 3H), 1.33 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 164.71, 164.67, 139.3, 139.2, 139.1, 133.4, 130.0, 129.4, 128.4, 128.3, 128.1, 127.9, 127.5, 127.3, 116.2, 83.54, 83.48, 78.5, 41.0, 27.62, 23.2 ppm; IR (KBr) 3065, 2978, 2854, 2371, 1967, 1868, 1689, 1647, 1601, 1542, 1473, 1395, 954, 759, 648 cm^{-1}; HRMS (FAB):

calcd for $[C_{31}H_{33}O_6]^+$ ($[M+H]^+$): 501.2277, found: 501.2274; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 7.53 min, minor isomer 10.62 min, 91% ee, $[\alpha]^{20}_D$ = + 3.98 (*c* 1.0, $CHCl_3$).

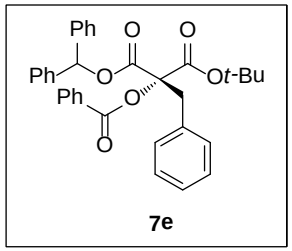
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(2-bromoallyl)malonate (7d)



7d

Following the procedure **(B)** from the substrate **7** using 2,3-bromopropene, the title molecule **7d** was obtained as a white oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.13 ~ 8.10 (m, 2H), 7.62 ~ 7.57 (m, 1H), 7.48 ~ 7.43 (m, 2H), 7.38 ~ 7.24 (m, 10H), 7.01 (s, 1H), 5.54 (s, 1H), 5.43 ~ 5.42 (m, 1H), 3.75 ~ 3.64 (dd, J_1 = 18.21 Hz, J_2 = 15.84 Hz, 2H), 1.33 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.0, 164.7, 163.9, 139.1, 139.0, 133.5, 130.1, 129.2, 128.5, 128.4, 128.3, 128.2, 128.0, 127.5, 127.3, 125.0, 122.1, 84.1, 82.5, 78.8, 43.6, 27.6 ppm; IR (KBr) 2979, 1753, 1729, 1627, 1602, 1496, 1395, 1370, 1289, 1144, 1069, 956, 839, 742, 700 cm^{-1}; HRMS (FAB): calcd for $[C_{30}H_{30}O_6Br]^+$ ($[M+H]^+$): 565.1226, found: 565.1223; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 8.97, minor isomer 14.59, 93% ee, $[\alpha]^{20}_D$ = − 3.89 (*c* 1.0, $CHCl_3$).

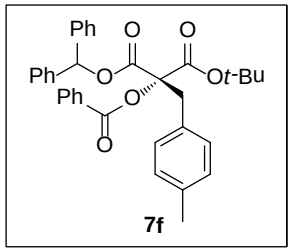
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-benzylmalonate (7e)



7e

Following the procedure **(B)** from the substrate **7** using benzyl bromide, the title molecule **7e** was obtained as a white oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 ~ 7.98 (d, *J* = 7.68 Hz, 2H), 7.59 ~ 7.55 (m, 1H), 7.44 ~ 7.39 (m, 2H), 7.34 ~ 7.19 (m, 10H), 7.17 ~ 7.10 (m, 3H). 7.04 ~ 7.02 (m, 2H), 6.99 (s, 1H), 3.72 (s, 2H), 1.30 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 165.6, 165.0, 164.4, 139.3, 139.1, 134.0, 133.4, 130.2, 130.0, 129.4, 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 127.1, 83.8, 83.6, 78.5, 39.3, 27.6 ppm; IR (KBr) 3064, 3032, 1752, 1727, 1601, 1495, 1453, 1370, 1284, 1108, 1033, 954, 742 cm^{-1}; HRMS (FAB): calcd for $[C_{34}H_{32}O_6Na]^+$ ($[M+Na]^+$): 559.2097, found: 559.2098; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 8.78 min, minor isomer 11.32 min, 91% ee, $[\alpha]^{20}_D$ = + 7.24 (*c* 1.0, $CHCl_3$).

1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(4-methylbenzyl)malonate (7f)

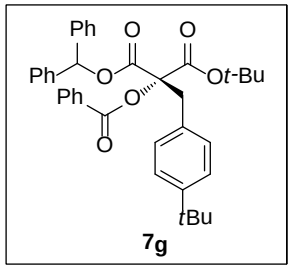


7f

Following the procedure **(B)** from the substrate **7**, using 4-methylbenzyl bromide, the title molecule **7f** was obtained as a colorless oil. ^{1}H-NMR (300 MHz, CDCl3) δ 8.02 ~ 8.00 (d, *J* = 7.32 Hz, 2H), 7.60 ~7.55 (m, 1H), 7.45 ~ 7.40 (m, 2H), 7.33 ~ 7.23 (m, 10H), 6.98 (s, 1H), 6.91 ~ 6.88 (m, 4H), 3.67 (s, 2H), 2.25 (s, 3H), 1.31 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 165.6, 165.0, 164.5, 139.3, 139.2, 136.7, 133.4, 130.9, 130.1, 130.0, 129.5, 128.9, 128.5, 128.4, 128.2, 128.1, 127.8, 127.7,

127.2, 83.9, 83.5, 78.5, 38.9, 27.6, 21.0 ppm; IR (KBr) 3064, 2979, 2310, 1751, 1730, 1602, 1516, 1453, 1370, 1282, 1154, 1110, 955, 842, 712, 700 cm-1; HRMS (FAB): calcd for $[C_{35}H_{35}O_6]^+$ ($[M+H]^+$): 551.2434, found: 551.2445; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 9.03 min, minor isomer 12.37 min, 91% ee, $[\alpha]^{20}_D$ = + 4.13 (*c* 1.0, $CHCl_3$).

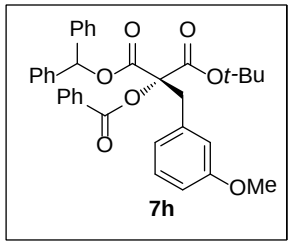
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(4-(*tert*-butyl)benzyl)malonate (7g)



7g

Following the procedure **(B)** from the substrate **7** using 4-(*tert*-butyl)benzyl bromide, the title molecule **7g** was obtained as a white oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 ~ 7.98 (d, *J* = 7.32 Hz, 2H), 7.60 ~ 7.55 (t, *J* = 7.32 Hz, 1H), 7.45 ~ 7.40 (t, *J* = 7.68 Hz, 2H), 7.35 ~ 7.25 (m, 10H), 7.13 ~ 7.08 (d, *J* = 8.25 Hz, 2H), 7.00 ~ 6.97 (m, 3H), 3.68 (s, 2H), 1.29 (s, 9H), 1.24 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 165.8, 165.0, 164.5, 149.9, 139.3, 139.2, 133.3, 131.0, 130.0, 129.9, 129.5, 128.4, 128.4, 128.3, 128.1, 127.9, 127.7, 127.2, 125.1, 83.9, 83.5, 78.5, 38.9, 34.3, 31.3, 27.6 ppm; IR (KBr) 3032, 2962, 1752, 1729, 1602, 1516, 1496, 1394, 1284, 1176, 1108, 1048, 956, 743, 700 cm^{-1}; HRMS (FAB): calcd for $[C_{38}H_{41}O_6]^+$ ($[M+H]^+$): 593.2903, found: 593.2922; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 6.16 min, minor isomer 8.59 min, 91% ee, $[\alpha]^{20}_D$ = + 7.49 (*c* 1.0, $CHCl_3$).

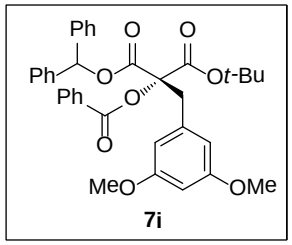
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(3-methoxybenzyl)malonate (7h)



7h

Following the procedure **(B)** from the substrate **7** using 3-methoxybenzyl bromide, the title molecule **7h** was obtained as a white oil.); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.02 ~ 8.00 (d, *J* = 7.68 Hz, 2H), 7.60 ~ 7.55 (t, *J* = 7.32 Hz, 1H), 7.45 ~ 7.40 (t, *J* = 7.68 Hz, 2H), 7.34 ~ 7.23 (m, 10H), 7.06 ~ 7.01 (m, 1H), 6.99 (s, 1H), 6.73 ~ 6.70 (d, *J* = 9.36 Hz, 1H), 6.62 ~ 6.60 (m, 2H), 3.71 (s, 2H), 3.52 (s, 3H), 1.30 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 165.0, 164.4, 159.3, 139.3, 139.2, 135.5, 133.4, 130.0, 129.4, 129.1, 128.5, 128.4, 128.3, 128.1, 127.9, 127.5, 127.2, 122.6, 115.3, 113.4, 83.8, 83.6, 78.5, 54.8, 39.3, 27.6 ppm; IR (KBr) 3032, 2978, 2854, 1752, 1601, 1585, 1454, 1395, 1370, 1264, 1154, 1046, 956, 784, , 699, 649 cm^{-1}; HRMS (FAB): calcd for $[C_{35}H_{34}O_7]^+$ ($[M]^+$): 566.2305, found: 566.2310; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 10.00 min, minor isomer 12.76 min, 93% ee, $[\alpha]^{20}_D$ = + 1.68 (*c* 1.0, $CHCl_3$).

1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(3,5-dimethoxybenzyl)malonate (7i)

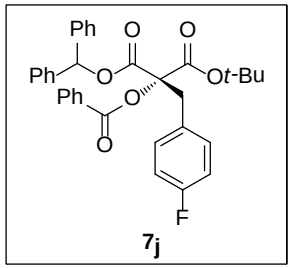


7i

Following the procedure **(B)** from the substrate **7** using 3,5-dimethoxybenzyl bromide, the title molecule **7i** was obtained as a white solid. mp 107 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.03 ~ 8.01 (m, 2H), 7.59 ~ 7.54 (m, 1H), 7.44 ~ 7.19 (m, 12H), 6.99 (s, 1H), 6.28 ~ 6.22 (m, 3H), 3.69 (m, 2H), 3.50 (s, 6H), 1.30 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 164.9, 164.4, 160.4, 139.3, 139.22, 136.21, 133.5, 130.0, 129.5, 128.5, 128.4, 128.3, 128.1, 127.9, 127.4, 127.2, 108.0, 100.0, 83.8, 83.6,

78.5, 55.0, 39.4, 27.6 ppm; IR (KBr) 3064, 3032, 2977, 2321, 1751, 1728, 1598, 1542, 1496, 1395, 1289, 1153, 1108, 1071, 958, 742, 701, 648 cm^{-1}; HRMS (FAB): calcd for $[C_{36}H_{36}O_8]^+$ ($[M]^+$): 596.2410, found: 596.2396; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 11.02 min, minor isomer 14.14 min, 91% ee, $[\alpha]^{20}_D = -5.22$ (*c* 1.0, $CHCl_3$).

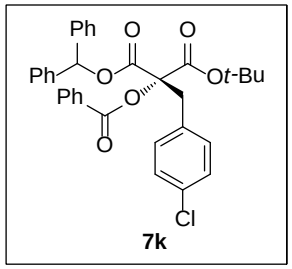
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(4-fluorobenzyl)malonate (7j)



7j

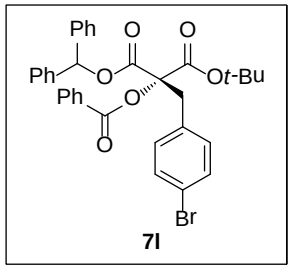
Following the procedure **(B)** from the substrate **7** using 4-fluorobenzyl bromide, the title molecule **7j** was obtained as a pale yellow solid. mp = 112 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 ~ 7.98 (m, 2H), 7.61 ~ 7.57 (m, 1H), 7.46 ~ 7.41 (m, 2H), 7.38 ~ 7.21 (m, 10H), 6.98 (s, 1H), 6.96 ~ 6.92 (m, 2H), 6.82 ~ 6.74 (m, 2H), 3.68 (s, 2H), 1.31 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.4, 164.9, 164.4, 162.1 (d, *J* = 244.0 Hz), 139.2, 139.1, 133.5, 131.7 (d, *J* = 8.0 Hz), 129.9, 129.8 (*d*, J = 3.4 Hz), 129.3, 128.49, 128.47, 128.3, 128.2, 127.9, 127.7, 127.1, 115.0 (d, *J* = 21.1 Hz), 83.8, 83.7, 78.6, 38.5, 27.6 ppm; IR (KBr) 3033, 2962, 1752, 1729, 1602, 1516, 1496, 1453, 1394, 1370, 1284, 1176, 1155, 1108, 956, 843, 700, 647 cm^{-1}; HRMS (FAB): calcd for $[C_{34}H_{32}FO_6]^+$ ($[M+H]^+$): 555.2183, found: 555.2180; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 10.02 min, minor isomer 12.04 min, 85% ee, $[\alpha]^{20}_D = +5.09$ (*c* 1.0, $CHCl_3$).

1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(4-chlorobenzyl)malonate (7k)



Following the procedure **(B)** from the substrate **7** using 4-chlorobenzyl bromide, the title molecule **7k** was obtained as a white solid. mp 145 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 ~ 7.98 (d, *J* = 7.89 Hz, 2H), 7.62 ~ 7.57 (t, *J* = 7.32 Hz, 1H), 7.46 ~ 7.41 (t, *J* = 7.5 Hz, 2H), 7.32 ~ 7.24 (m, 10H), 7.07 ~ 7.05 (d, *J* = 8.04 Hz, 2H), 6.97 (s, 1H), 6.93 ~ 6.90 (d, *J* = 7.89 Hz, 2H), 3.68 (s, 2H), 1.32 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.4, 165.9, 164.4, 139.2, 139.0, 133.6, 133.1, 132.54, 131.49, 129.9, 129.2, 128.5, 128.3, 128.2, 128.0, 127.7, 127.1, 83.8, 83.7, 78.6, 38.6, 27.6 ppm; IR (KBr) 3033, 2979, 1751, 1729, 1648, 1585, 1542, 1409, 1370, 1290, 1045, 910, 814, 712, 700 cm^{-1}; HRMS (FAB): calcd for $[C_{34}H_{32}ClO_6]^+$ ($[M+H]^+$): 571.1887, found: 571.1884; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 9.77 min, minor isomer 12.14 min, 80% ee, $[\alpha]^{20}_{D}$ = + 6.06 (*c* 1.0, $CHCl_3$).

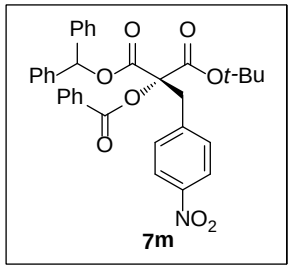
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(4-bromobenzyl)malonate (7l)



Following the procedure **(B)** from the substrate **7** using 4-fluorobenzyl bromide, the title molecule **7l** was obtained as a colorless crystal. mp 64 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 ~ 7.98 (m, 2H), 7.62 ~ 7.56 (m, 1H), 7.50 ~ 7.41 (m, 2H), 7.38 ~ 7.18 (m, 12H), 6.97 (s, 1H), 6.87 ~ 6.82 (m, 2H), 3.66 (s, 2H), 1.32 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.3, 164.9, 164.4, 139.2, 139.0, 133.6, 133.1, 131.8, 131.3, 129.9, 129.2, 128.5, 128.3, 128.2, 128.0, 127.6, 127.1, 121.3, 83.8, 83.6, 78.6,

38.7, 27.6 ppm; IR (KBr) 2930, 2310, 1750, 1730, 1602, 1489, 1452, 1395, 1316, 1176, 1070, 1012, 954, 712, 648 cm^{-1}; HRMS (FAB): calcd for $[C_{34}H_{32}BrO_6]^+$ ($[M+H]^+$): 615.1382, found: 615.1364; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 10.83 min, minor isomer 14.23 min, 86% ee, $[\alpha]^{20}_D$ = + 7.79 (*c* 1.0, $CHCl_3$).

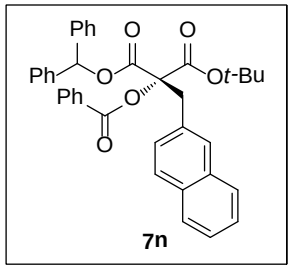
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(4-nitrobenzyl)malonate (7m)



7m

Following the procedure **(B)** from he substrate **7** using 4-nitrobenzyl bromide, the title molecule **7m** was obtained as a white solid. mp 160 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.02 ~ 7.99 (d, *J* = 5.31 Hz, 2H), 7.93 ~ 7.88 (d, *J* = 8.79 Hz, 2H), 7.65 ~ 7.59 (m, 1H), 7.49 ~ 7.43 (m, 2H), 7.33 ~ 7.17 (m, 10H), 7.13 ~ 7.09 (m, 2H), 6.98 (s, 1H), 3.82 (s, 2H), 1.34 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.0, 164.8, 164.2, 147.1, 141.8, 139.0, 138.79, 133.81, 131.0, 129.9, 128.9, 128.6, 128.6, 128.4, 128.3, 128.1, 127.6, 127.1, 123.3, 84.2, 83.3, 78.8, 39.0, 27.6 ppm; IR (KBr) 3614, 2979, 1868, 1731, 1688, 1648, 1603, 1523, 1495, 1453, 1396, 1317, 1284, 1109, 1070, 954, 760, 700 cm^{-1}; HRMS (FAB): calcd for $[C_{34}H_{32}NO_8]^+$ ($[M+H]^+$): 582.2128, found: 582.2140; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 80 : 20, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: minor isomer 13.55 min, major isomer 21.87 min, 81% ee, $[\alpha]^{20}_D$ = − 1.28 (*c* 1.0, $CHCl_3$).

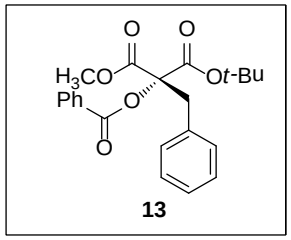
1-Benzhydryl 3-(*tert*-butyl) (*R*)-2-(benzoyloxy)-2-(naphthalen-2-ylmethyl)malonate (7n)



Following the procedure **(B)** from the substrate **7** using 2-(bromomethyl) naphthalene, the title molecule **7n** was obtained as a white oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.02 ~ 8.00 (m, *J* = 7.53 Hz, 2H), 7.76 ~ 7.73 (m, 1H), 7.63 ~ 7.58 (m, 2H), 7.55 ~ 7.16 (m, 17H), 6.98 (s, 1H), 3.88 (s, 2H), 1.31 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 165.6, 165.1, 164.5, 139.3, 139.1, 133.4, 133.2, 132.5, 131.6, 130.0, 129.4, 129.2, 128.5, 128.4, 128.25, 128.18, 127.9, 127.7, 127.6, 127.5, 127.1, 125.9, 125.7, 84.0, 83.7, 78.6, 39.5, 27.6 ppm; IR (KBr) 3648, 2928, 1748, 1689, 1647, 1542, 1489, 1372, 1047, 842, 702 cm^{-1}; HRMS (FAB): calcd for $[C_{38}H_{35}O_6]^+$ ($[M+H]^+$): 587.2434, found: 587.2421; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralpak AD-H, hexane : 2-propanol = 85 : 15, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm) retention time: major isomer 10.68 min, minor isomer 15.57 min, 88% ee, $[\alpha]^{20}_D$ = + 16.56 (*c* 1.0, $CHCl_3$).

(C) Derivatization

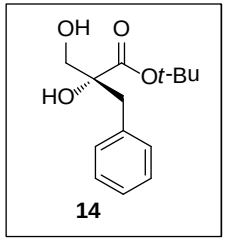
(*R*)-1-Methyl 3-*tert*-butyl 2-(benzoyloxy)-2-benzylmalonate (13)



13

Pd/C (100 mg) was added to a methanolic solution (50 mL) of **7e** (2.6 g, 4.85 mmol) and the reaction mixture was stirred for 1 hr under 1 atm of H_2. The reaction mixture was filtered over a pad of celite to remove Pd/C and the methanol solvent was evaporated in *vacuo* to afford mono-acid (**12**). Without further purification, 2 equiv. of TMS diazomethane (10 mmol) was added to a toluene-CH_3OH (4:1) solution of **12** and the reaction mixture was stirred for 1 hr at 0 °C. After completion of reaction, the mixture was quenched with acetic acid and followed by evaporation. The residue was diluted with EtOAc (100 mL), washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography (silica gel, hexanes: EtOAc = 20:1) to afford **13** (1.86 g, 99% yield) as pale yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.05 ~ 8.03 (d, *J* = 7.14 Hz, 2H), 7.59 ~ 7.54 (t, *J* = 7.2 Hz, 1H), 7.45 ~ 7.40 (t, *J* = 7.6 Hz, 2H), 7.25 ~ 7.23 (m, 5H), 3.78 (s, 3H), 3.66 (s, 2H), 1.42 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 167.2, 165.0, 164.7, 134.2, 133.4, 130.3, 130.0, 129.3, 128.4, 128.2, 127.3, 83.6, 83.5, 52.9, 39.9, 27.7 ppm; IR (KBr) 3064, 3033, 2979, 1755, 1731, 1602, 1584, 1496, 1453, 1438, 1394, 1370, 1285, 1250, 1208, 1155, 1109, 1057, 958, 843, 713 cm^{-1}; HRMS (FAB): calcd for $[C_{22}H_{25}O_6]^+$ ($[M+H]^+$): 385.1651, found: 385.1652; $[\alpha]^{20}_D$ = + 3.46 (*c* 1.0, $CHCl_3$).

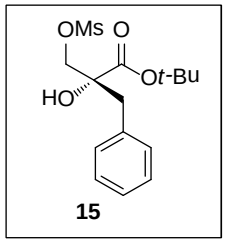
(*R*)-*tert*-Butyl 2-benzyl-2,3-dihydroxypropanoate (14)



14

To a THF solution (20 mL) of **13** (1.02 g, 2.66 mmol) was added a THF solution (3.4 mL) of $LiAl(O\textit{t}\text{-}Bu)_3H$ (13.31 mmol) at −78 °C. The reaction solution was warmed to room temperature and stirred for 5 hours at 60 °C. The reaction was quenched by Rochelle solution (10 mL), diluted with EtOAc (100 mL), washed with brine (50 mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography (silica gel, hexanes: EtOAc = 4:1) to afford **14** (0.62 g, 92% yield) as color less oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.30 ~ 7.19 (m, 5H), 3.85 (d, *J* = 10.98 Hz, 1H), 3.65 (d, *J* = 10.98 Hz, 1H), 2.94 (d, *J* = 13.73 Hz, 1H), 2.88 (d, *J* = 13.73 Hz, 1H), 1.42 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.5, 135.5, 130.4, 128.3, 127.2, 83.6, 78.8, 68.3, 41.2, 28.2 ppm; IR (KBr) 3470, 3032, 2978, 2930, 1728, 1496, 1456, 1395, 1370, 1281, 1220, 1160, 1121, 1035, 938, 845, 773, 701, 673 cm^{-1}; HRMS (FAB): calcd for $[C_{14}H_{21}O_4]^+$ ($[M+H]^+$): 253.1440, found: 253.1444; $[\alpha]^{20}_D$ = − 4.92 (*c* 1.0, $CHCl_3$).

(*R*)-*tert*-Butyl 2-benzyl-2-hydroxy-3-[(methylsulfonyl)oxy]propanoate (15)

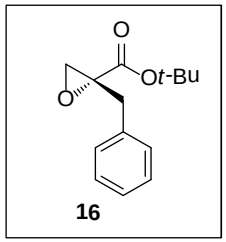


15

To a CH_2Cl_2 solution (6 mL) of **14** (150 mg, 0.59 mmol) was added MsCl (56 μL, 0.72 mmol) and Et_3N (100 μL, 0.72 mmol) at −10 °C. After stirring for 1 hr at −10 °C, the reaction mixture was evaporated and the residue was diluted with EtOAc (30 mL), washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography (silica gel, hexanes: EtOAc = 4:1) to afford **15** (166 mg, 85% yield) as colorless oil. ^{1}H-NMR (300 MHz, CD_3OD) δ 7.29 ~ 7.21 (m, 5H), 4.45 (d, *J* = 9.98 Hz, 1H), 4.18 (d, *J* = 9.98 Hz, 1H), 3.08 (s, 3H), 3.00 (d, *J* = 13.74 Hz, 1H), 2.93 (d, *J* = 13.74 Hz, 1H), 1.41

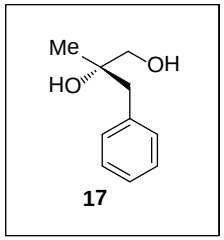
(s, 9H) ppm; ^{13}C-NMR (125 MHz, CD_3OD) δ 172.4, 136.3, 131.6, 129.1, 128.0, 84.1, 78.1, 75.3, 42.3, 37.4, 28.1 ppm; IR (KBr) 3501, 3032, 2978, 2939, 1733, 1496, 1457, 1395, 1359, 1254, 1177, 1134, 993, 967, 837, 793, 741, 702 cm^{-1}; HRMS (FAB): calcd for $[C_{15}H_{23}O_6S]^+$ ($[M+H]^+$): 331.1215, found: 331.1212; $[\alpha]^{20}_D$ = − 3.18 (*c* 1.0, $CHCl_3$).

(*R*)-*tert*-Butyl 2-benzyloxirane-2-carboxylate (16)



To a CH_3CN solution (6 mL) of **14** (118 mg, 0.36 mmol) was added K_2CO_3 (500 mg, 3.6 mmol). The reaction mixture was refluxed for 6 hours. The reaction mixture was diluted with EtOAc (50 mL), washed with brine (10 mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography (silica gel, hexanes: EtOAc = 10:1) to afford **16** (69 mg, 84% yield) as colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.32 ~ 7.19 (m, 5H), 3.33 (d, *J* = 14.85 Hz, 1H), 3.05 (d, *J* = 14.85 Hz, 1H), 3.00 (d, *J* = 5.87 Hz, 1H), 2.67 (d, *J* = 5.87 Hz, 1H), 1.38 (s, 9H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.0, 136.2, 129.8, 128.4, 126.9, 82.5, 57.5, 37.2, 31.1, 27.9 ppm; IR (KBr) 2979, 2932, 1738, 1496, 1456, 1393, 1369, 1304, 1257, 1215, 1157, 1122, 1076, 1032, 939, 846, 771, 736, 700 cm^{-1}; HRMS (FAB): calcd for $[C_{14}H_{19}O_3]^+$ ($[M+H]^+$): 235.1334, found: 235.1330; $[\alpha]^{20}_D$ = + 13.92 (*c* 1.0, $CHCl_3$).

(*S*)-2-Methyl-3-phenylpropane-1,2-diol (17)

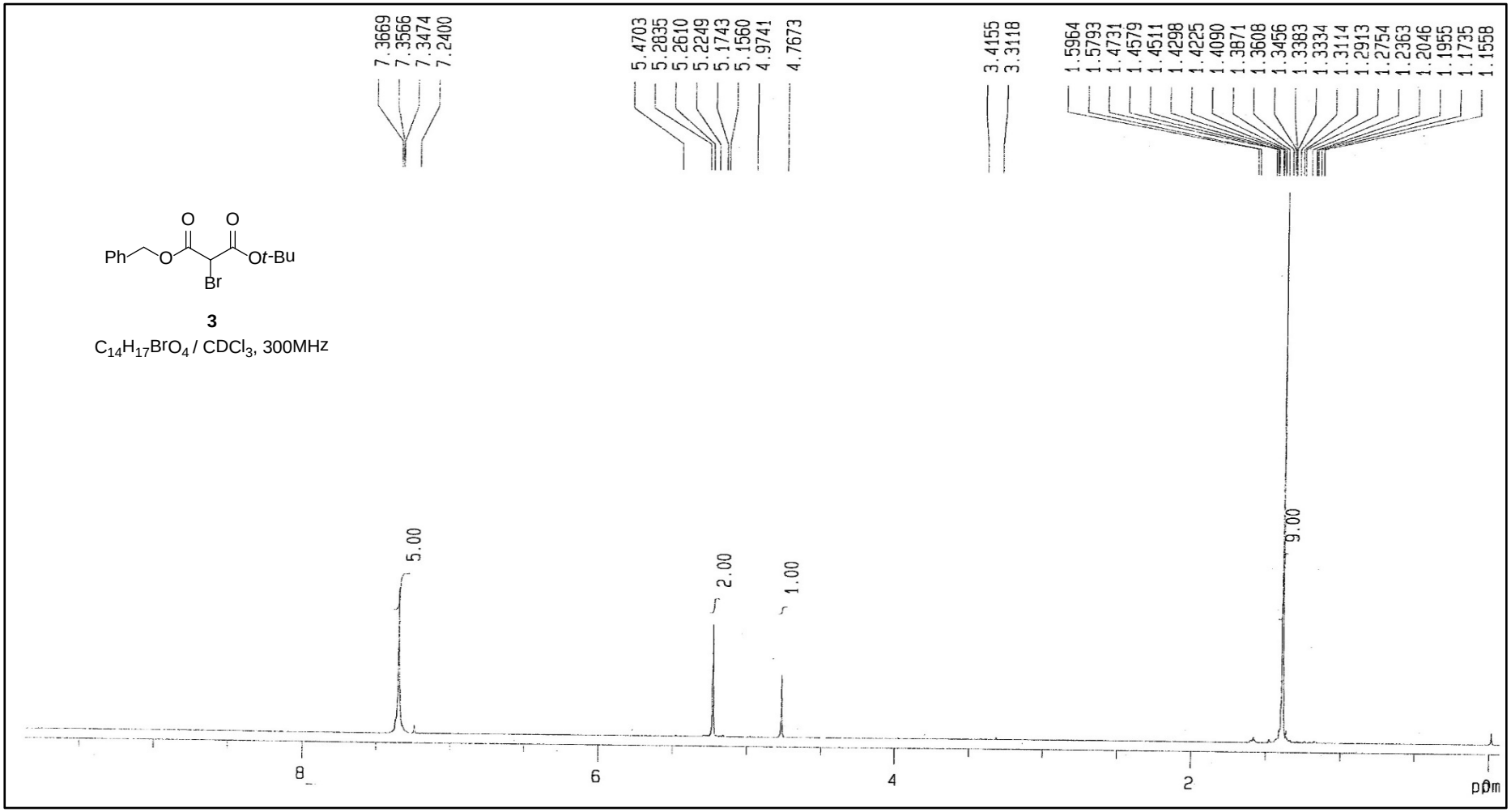


17

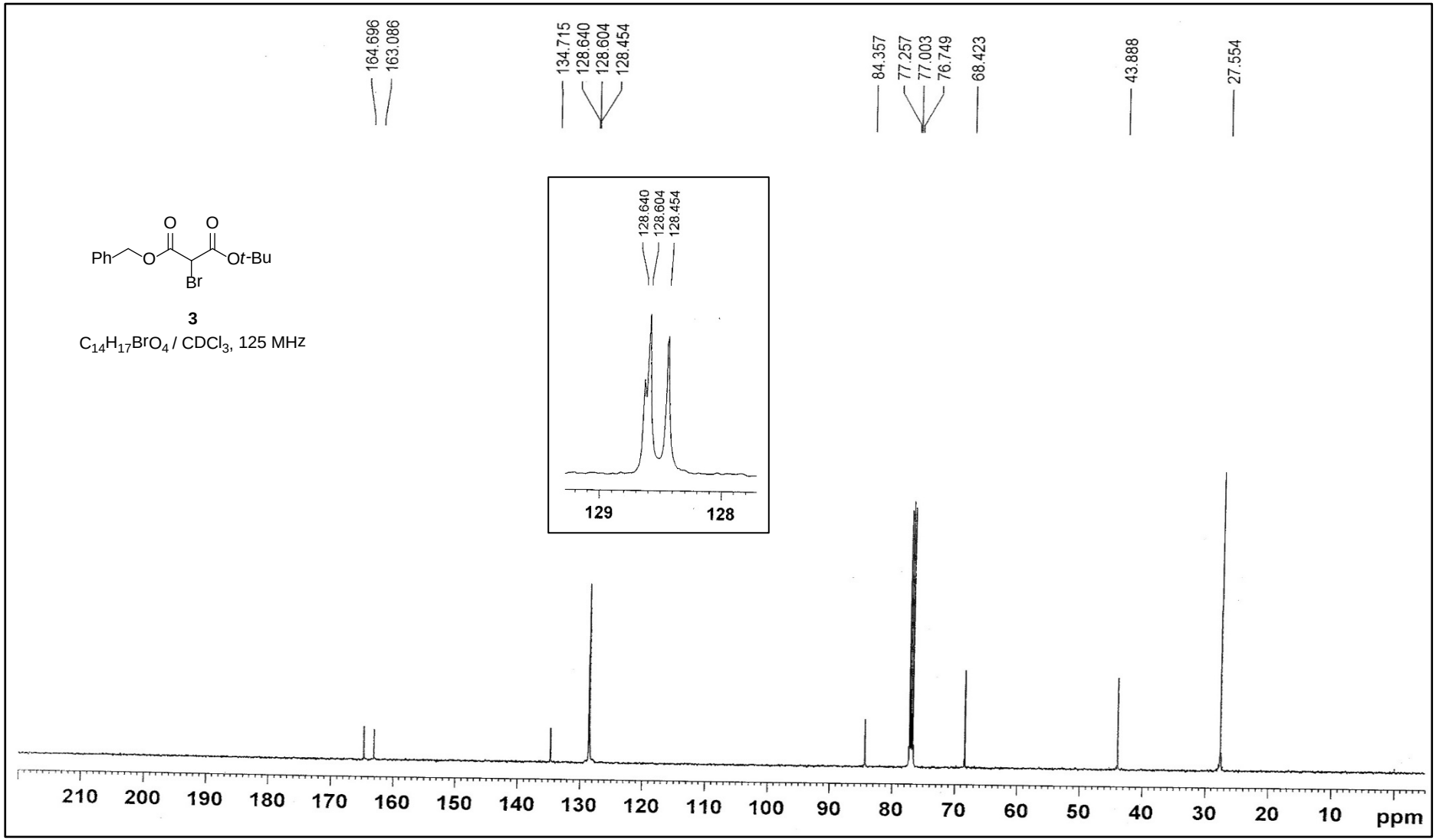
To a THF solution (0.5 mL) of epoxide **16** (9.5 mg, 0.041 mmol) was added a THF solution (0.2 mL) of $LiAlH_4$ (8 mg, 0.2 mmol) at −78 °C. The reaction solution was stirred for 1 hr and gradually raised the temperature to room temperature. The reaction was quenched by Rochelle solution (1 mL), diluted with EtOAc (10 mL), washed with brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concenturated in *vacuo*. The residue was purified by column chromatography (silica gel, hexanes: EtOAc = 1:1) to afford **17** (6.8 mg, 99% yield) as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.35 ~ 7.22 (m, 5H), 3.51 (d, *J* = 10.8 Hz, 1H), 3.44 (d, *J* = 10.8 Hz, 1H), 2.86 (dd, *J* = 13.29 Hz, 1H), 2.79 (dd, *J* = 13.29 Hz, 1H), 1.86 (brs, OH, 1H), 1.61 (brs, OH, 1H), 1.15 (s, 3H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 137.1, 130.6, 128.6, 126.9, 73.1, 69.5, 44.9, 23.9 ppm; The spectral data were exactly same as previously reported data; $[\alpha]_D^{20}$ = –9.6 (*c* 1.0, EtOH 95%); lit[S4](*R*)-**17**, $[\alpha]_D^{20}$ = +11.4 (*c* 1.0, EtOH 95%), 94% ee.

(4) ^{1}H & ^{13}C NMR Spectra

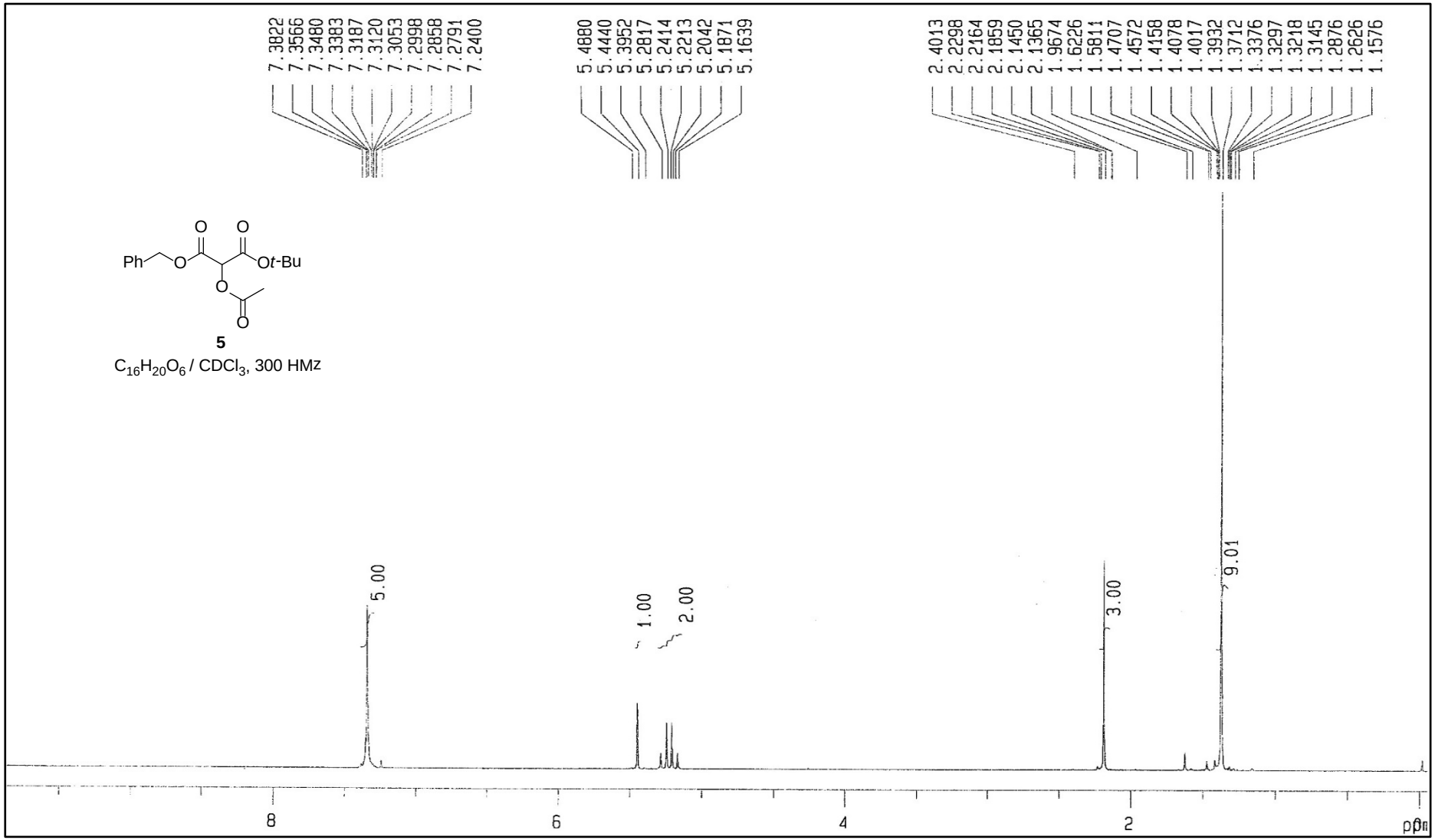
^{1}H-NMR of compound **(3)**



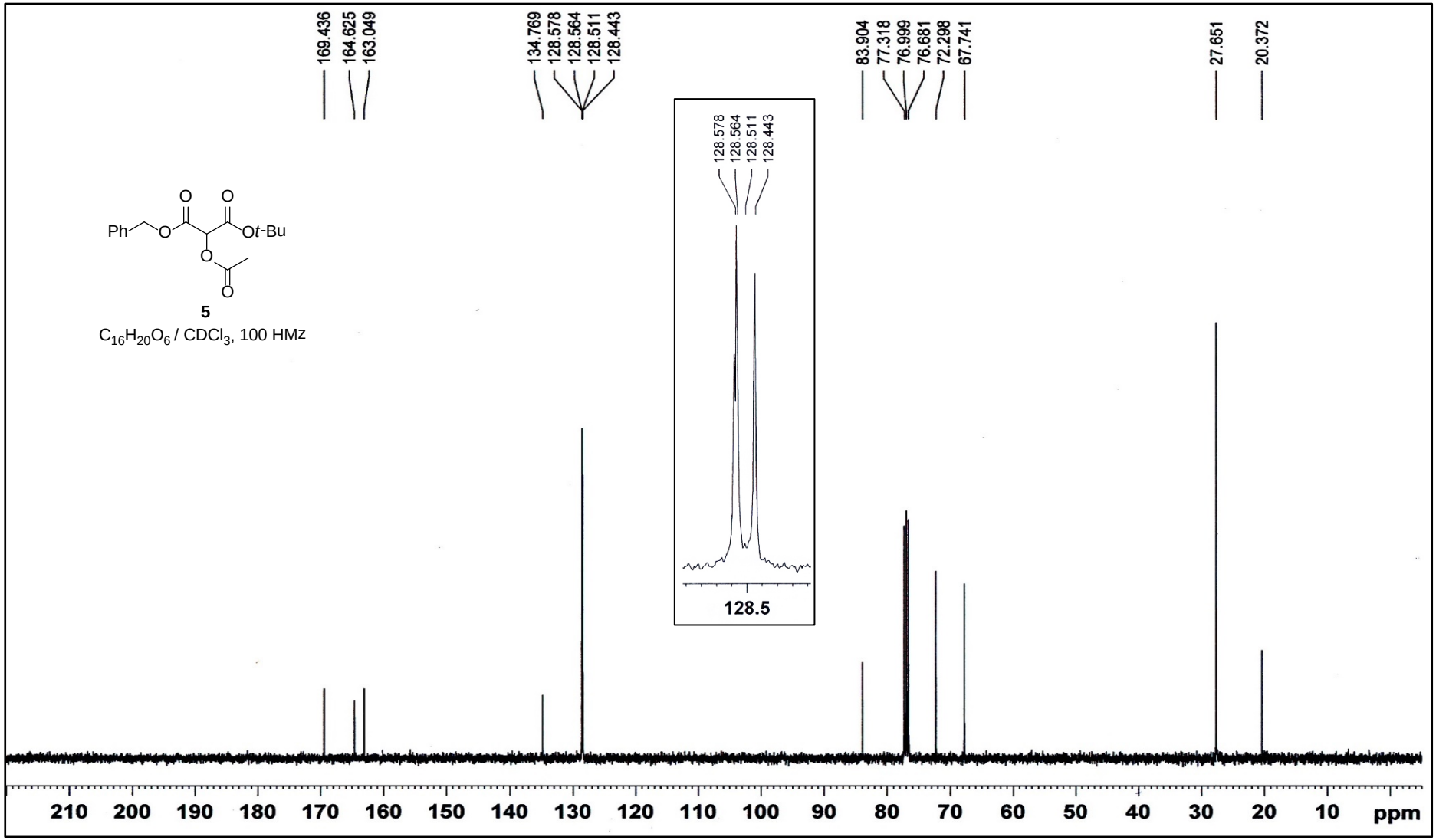
^{13}C-NMR of compound **(3)**



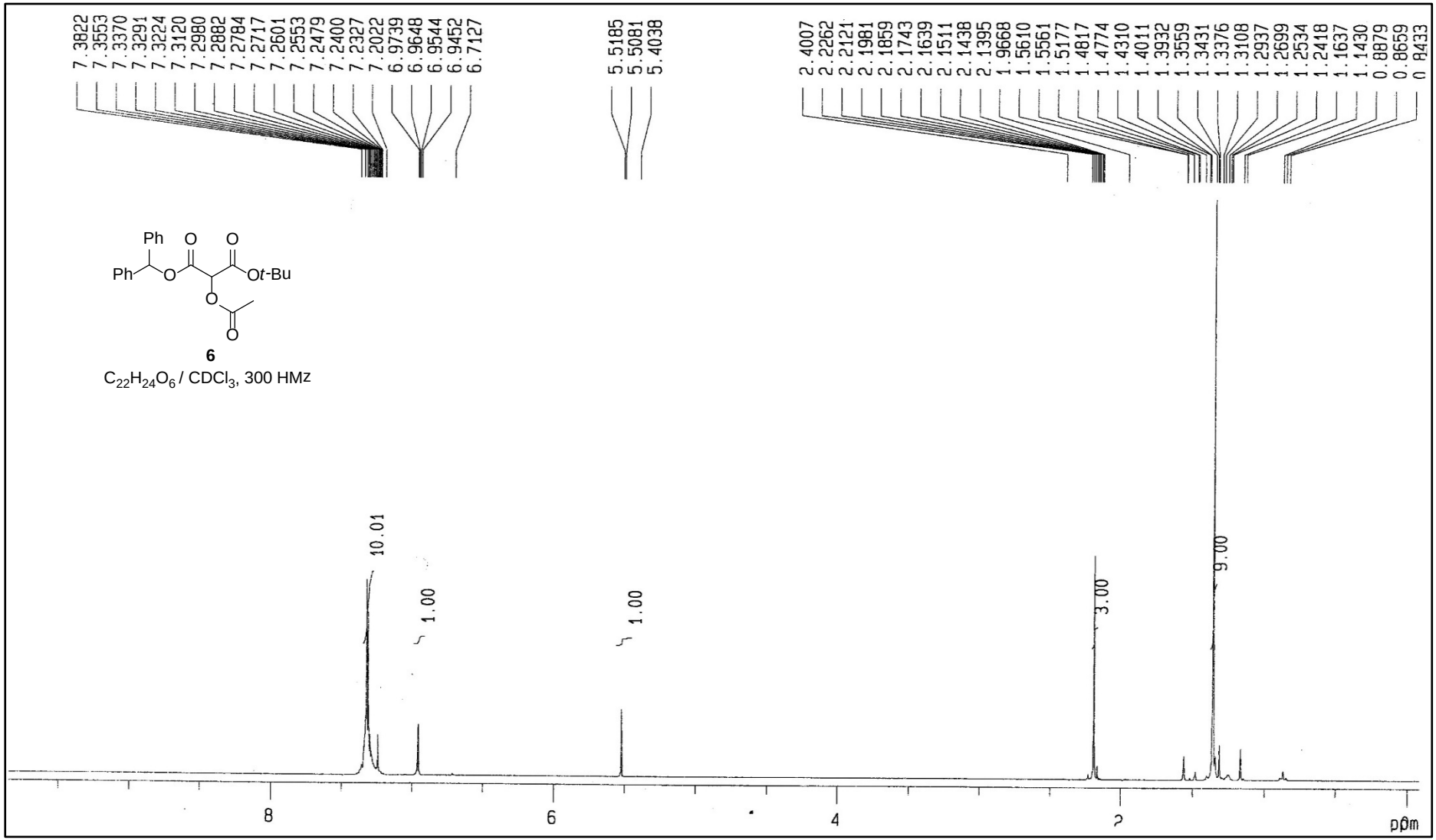
[1]H-NMR of compound **(5)**



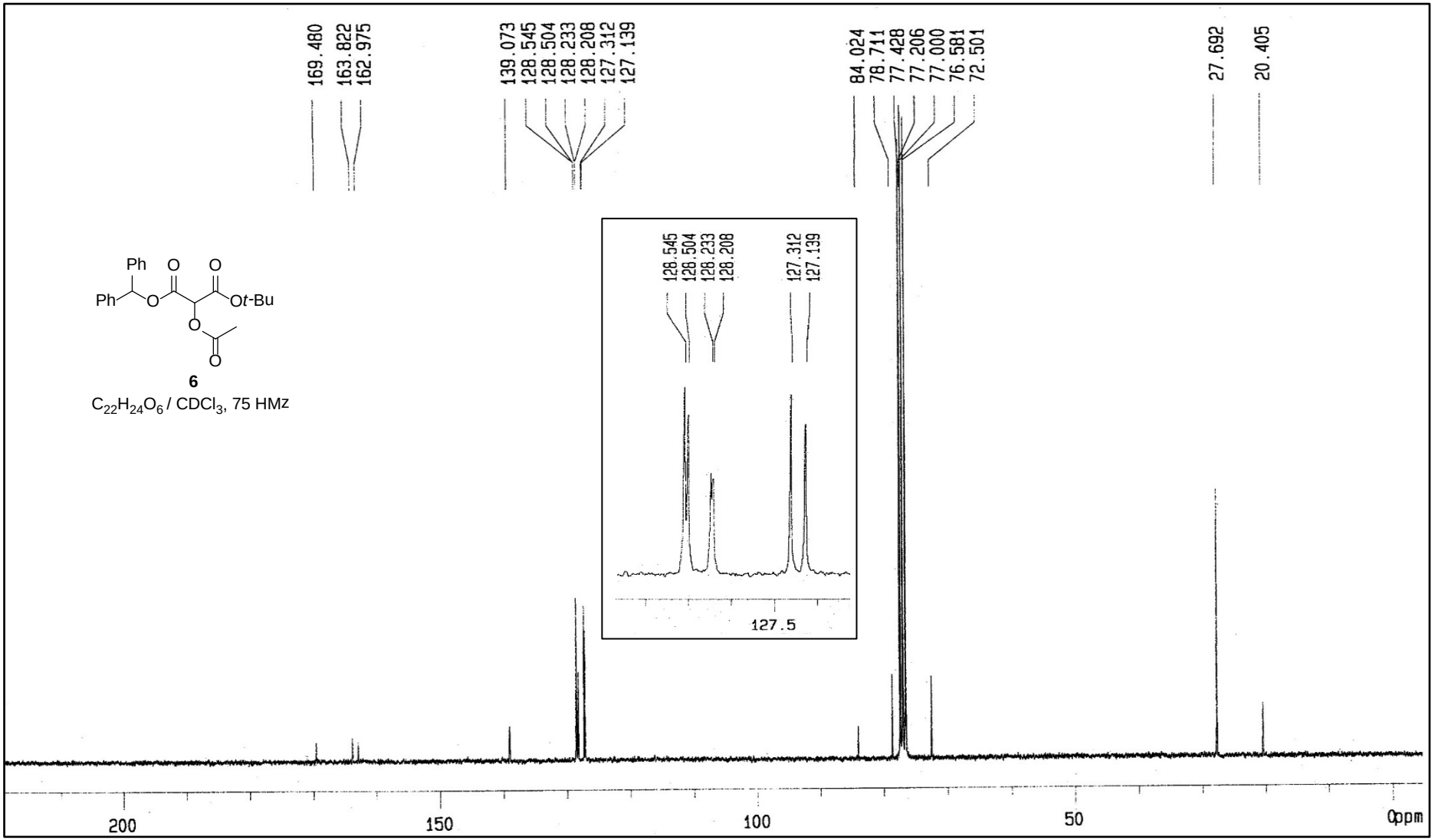
^{13}C-NMR of compound **(5)**



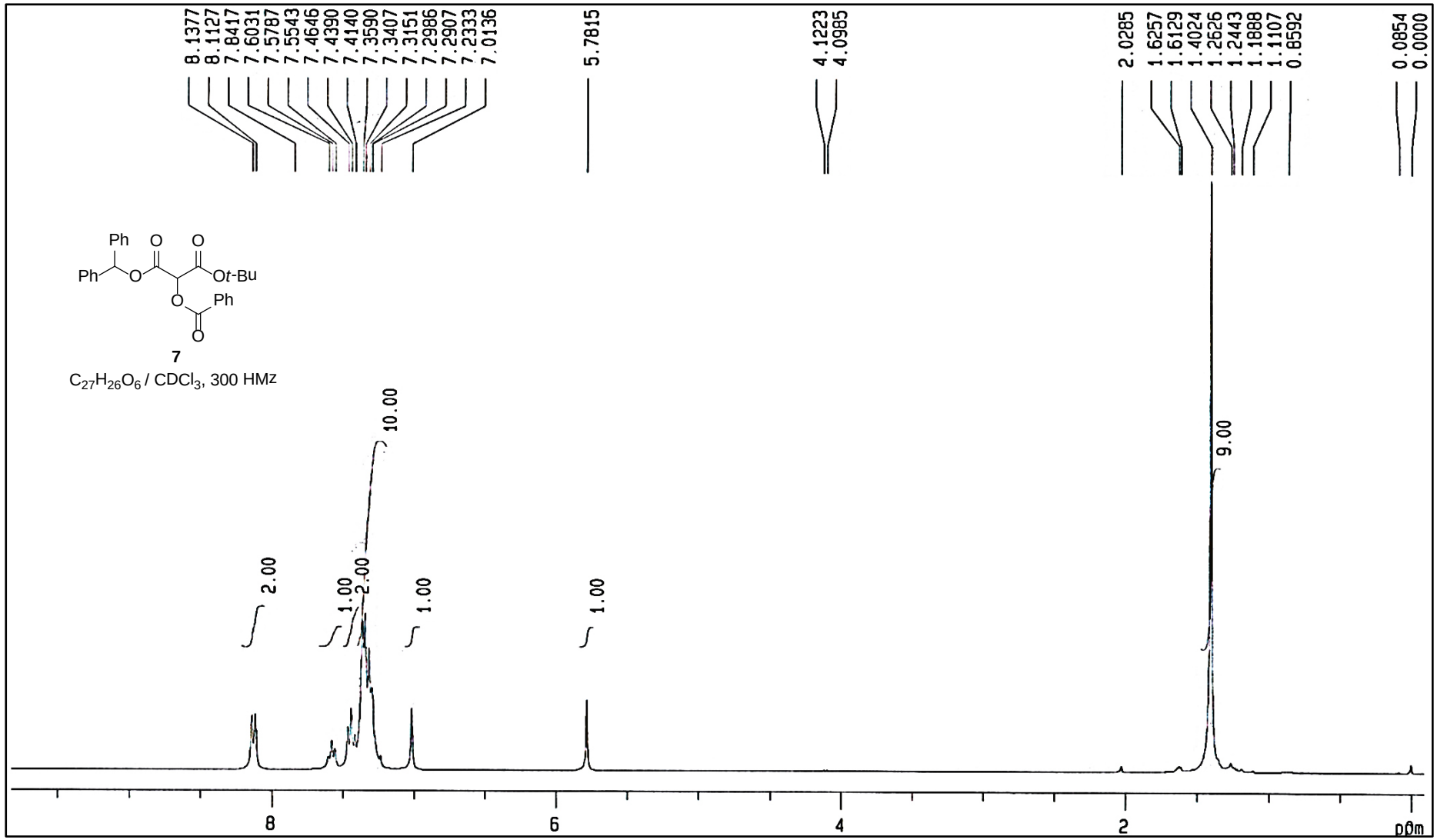
[1]H-NMR of compound **(6)**



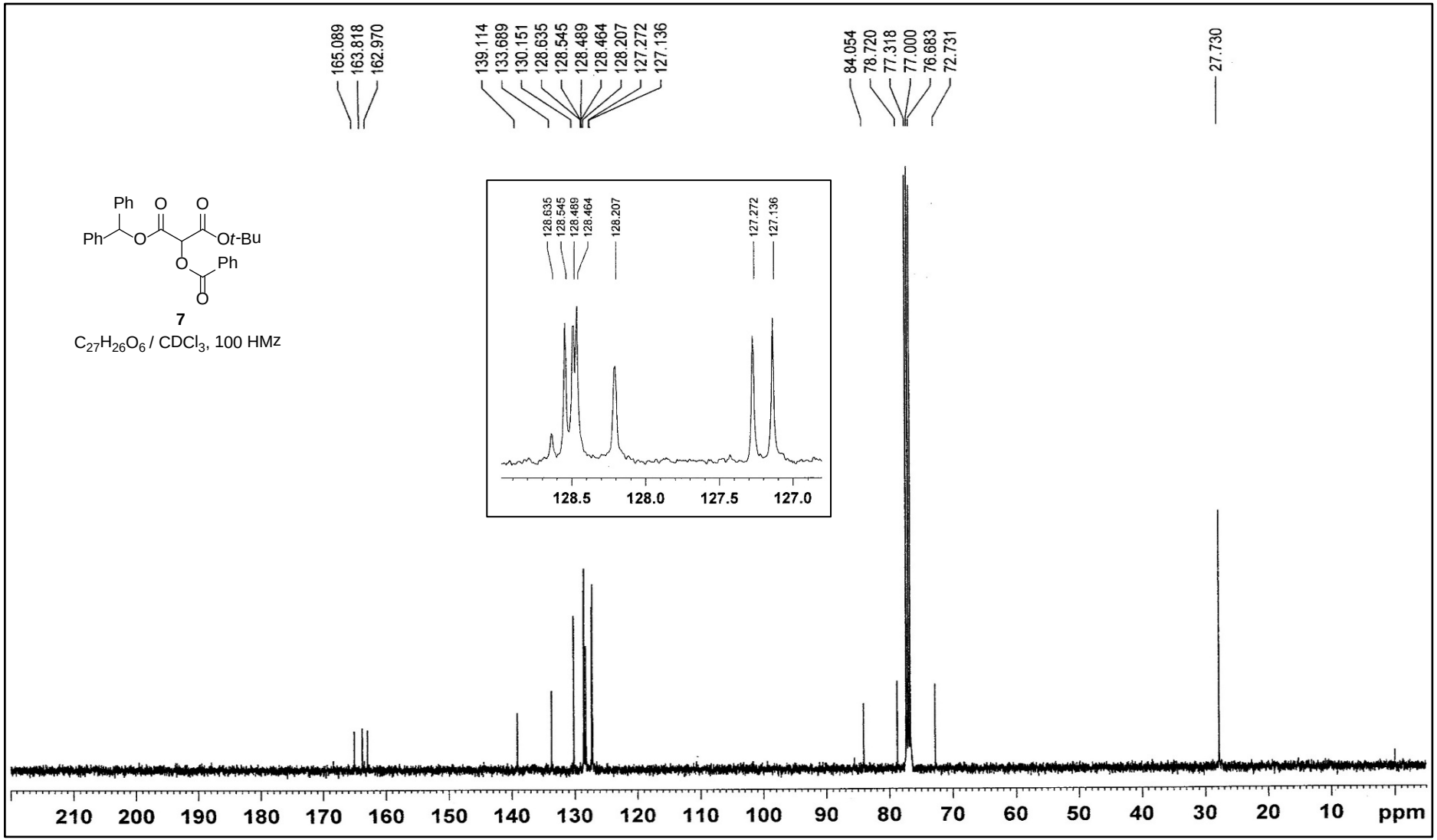
^{13}C-NMR of compound **(6)**



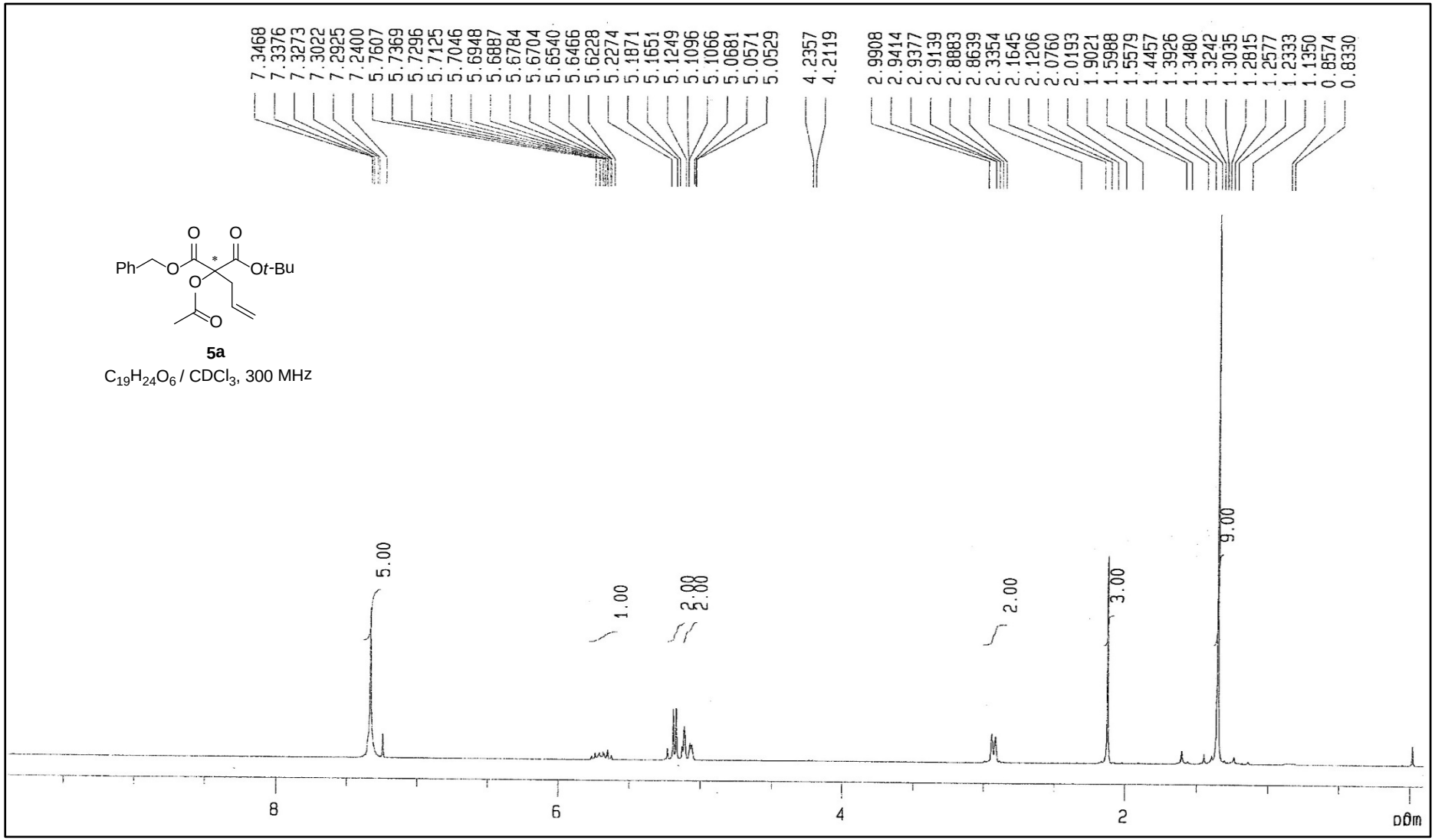
[1]H-NMR of compound **(7)**



^{13}C-NMR of compound **(7)**



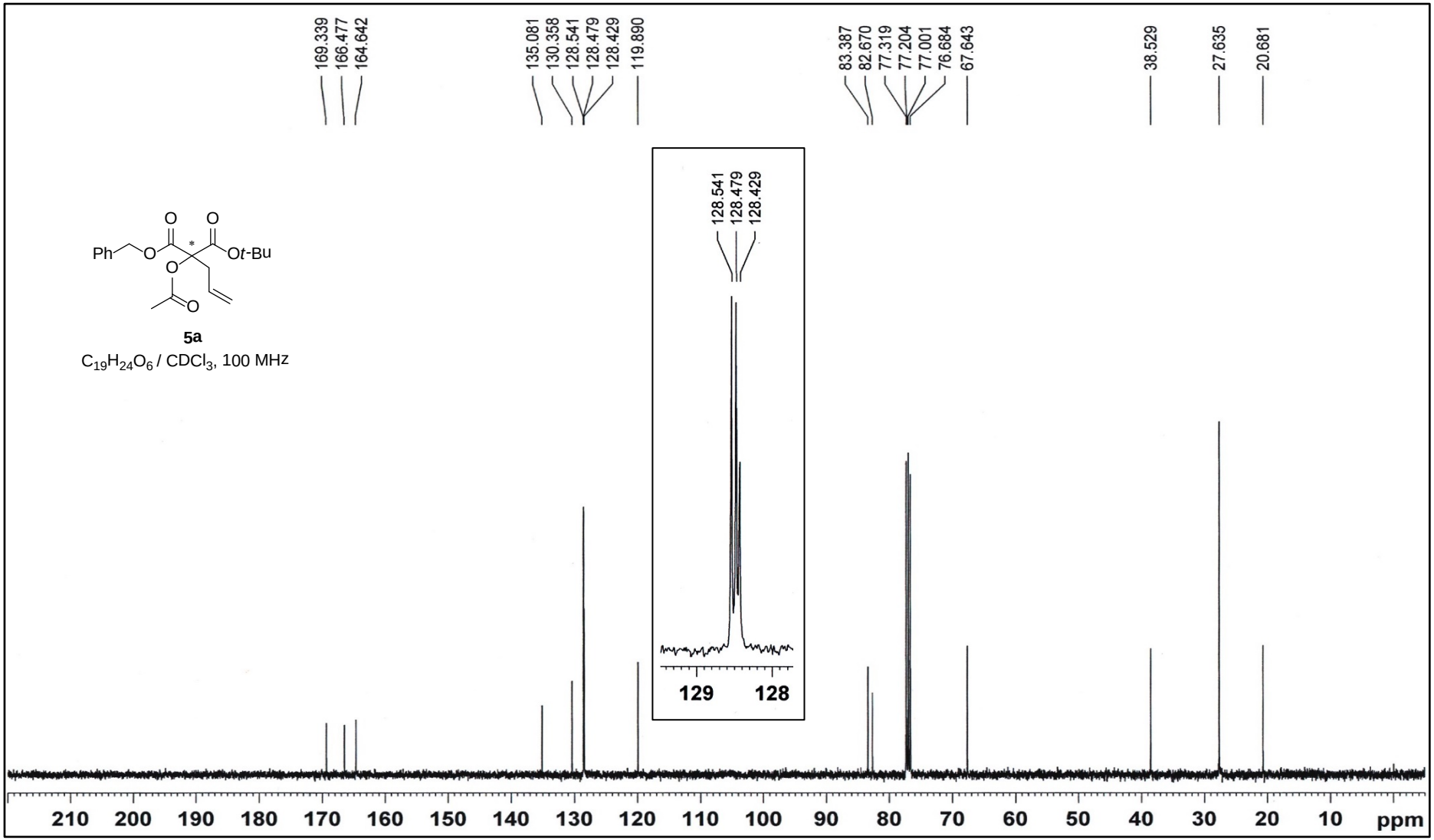
[1]H-NMR of compound **(5a)**



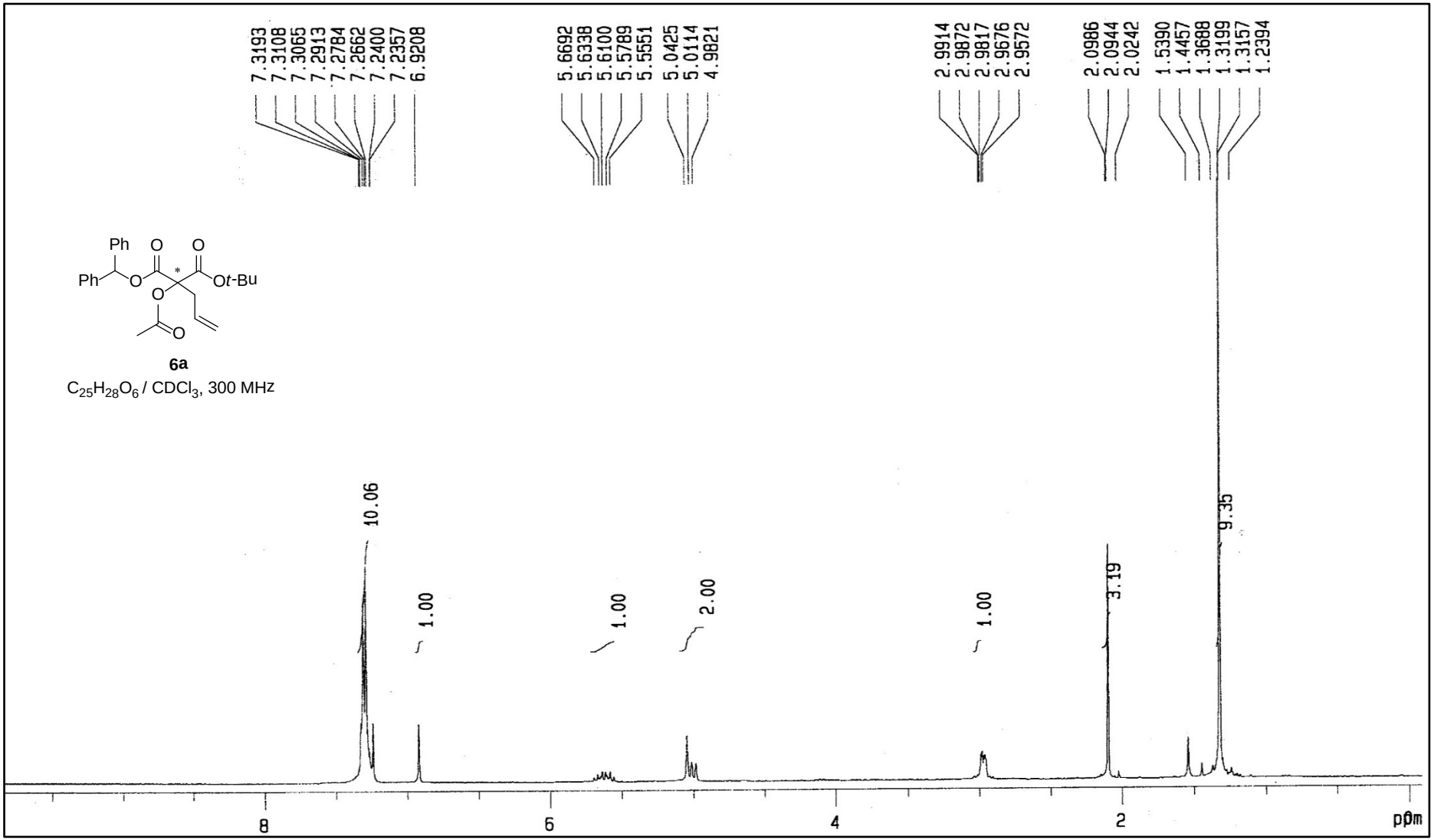
5a

$C_{19}H_{24}O_6$ / $CDCl_3$, 300 MHz

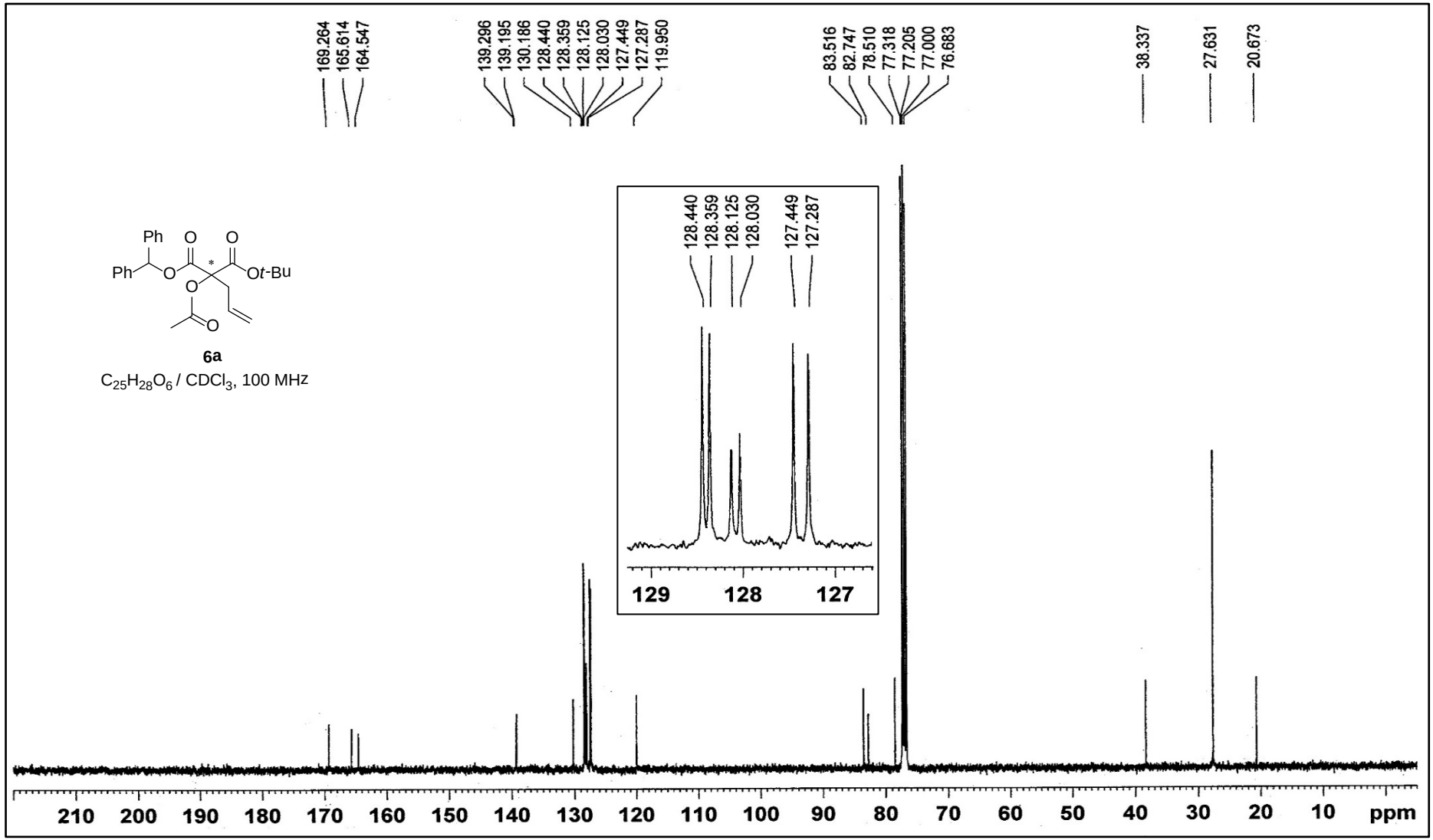
^{13}C-NMR of compound **(5a)**



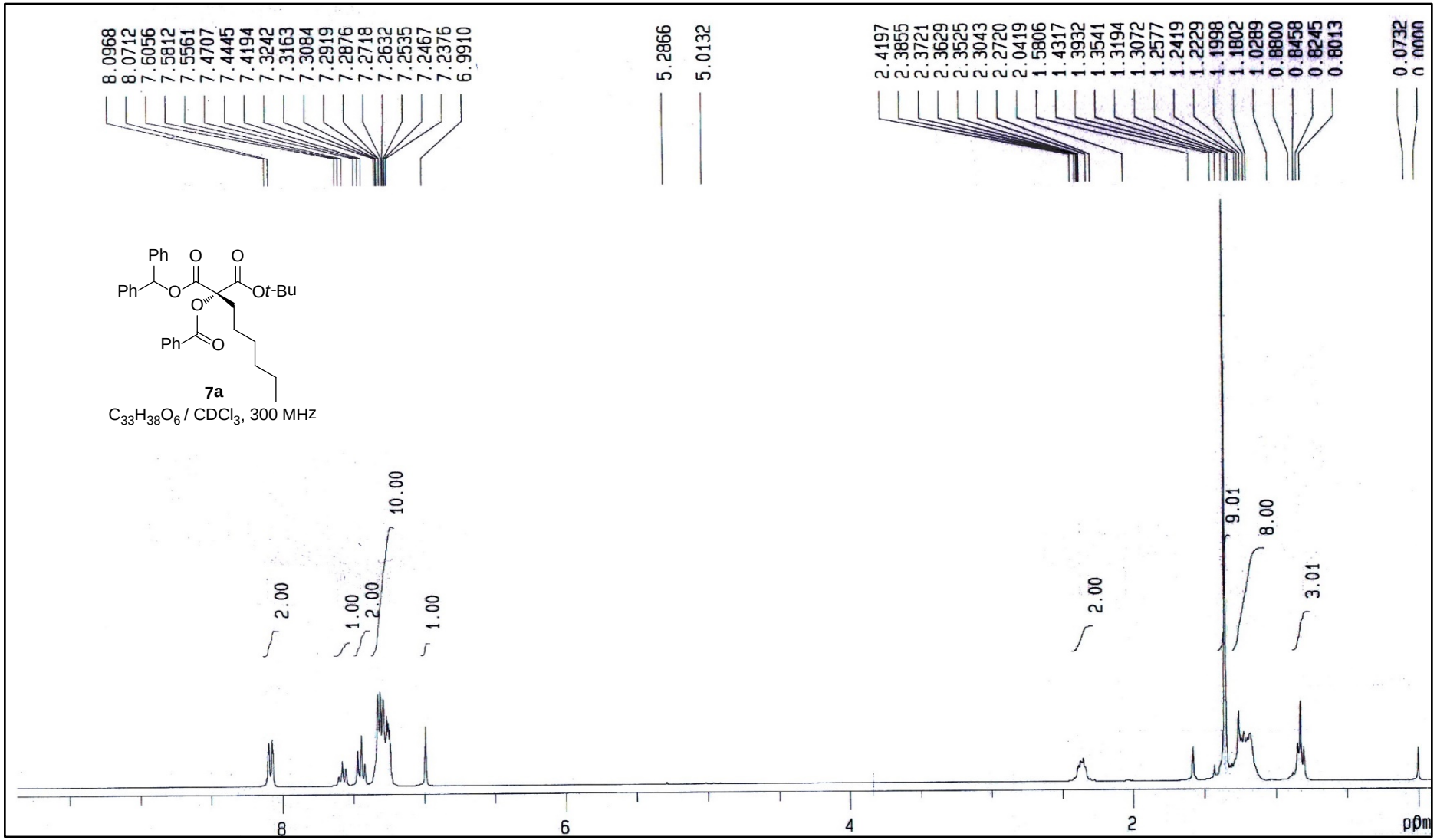
[1]H-NMR of compound **(6a)**



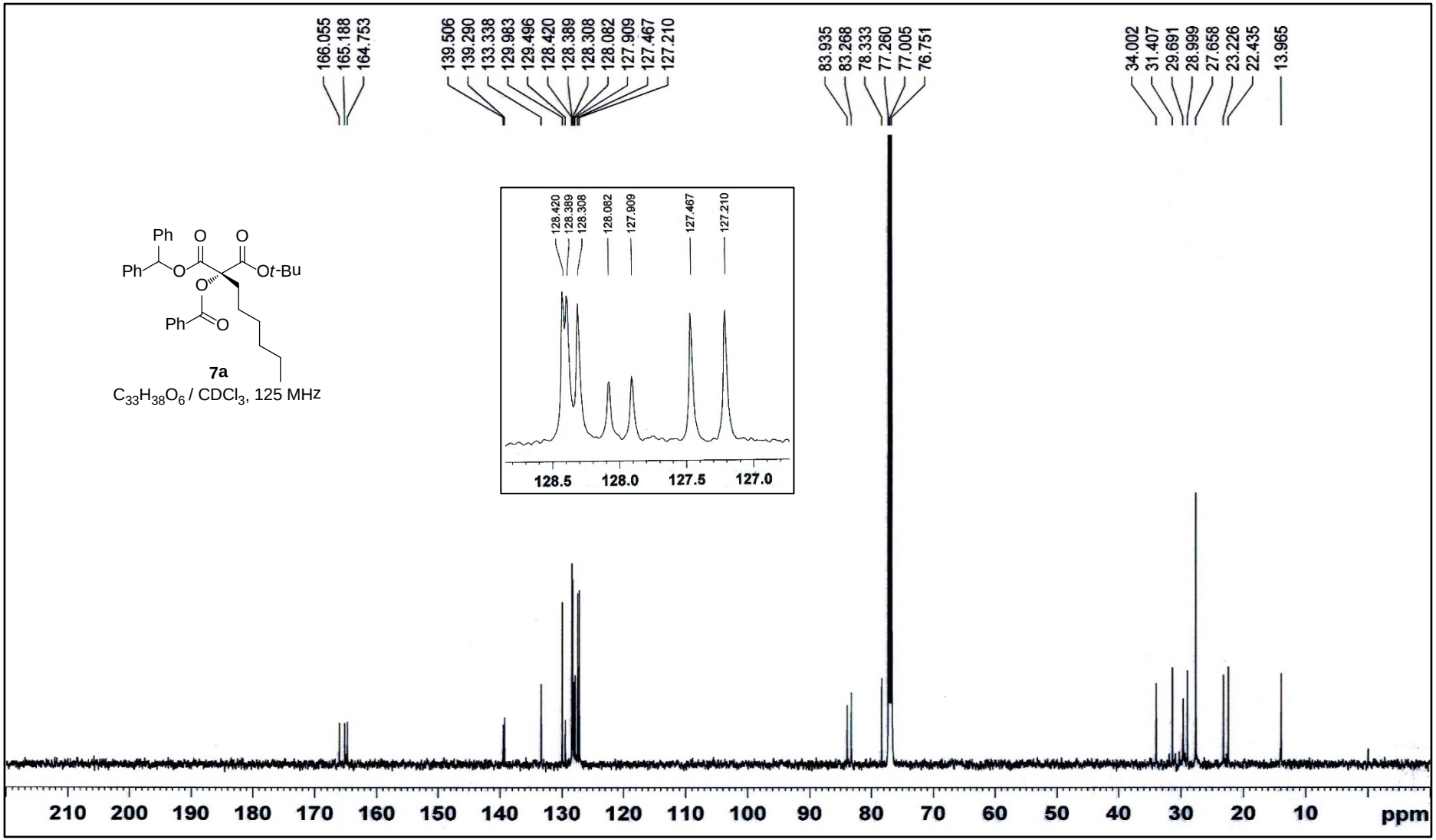
^{13}C-NMR of compound **(6a)**



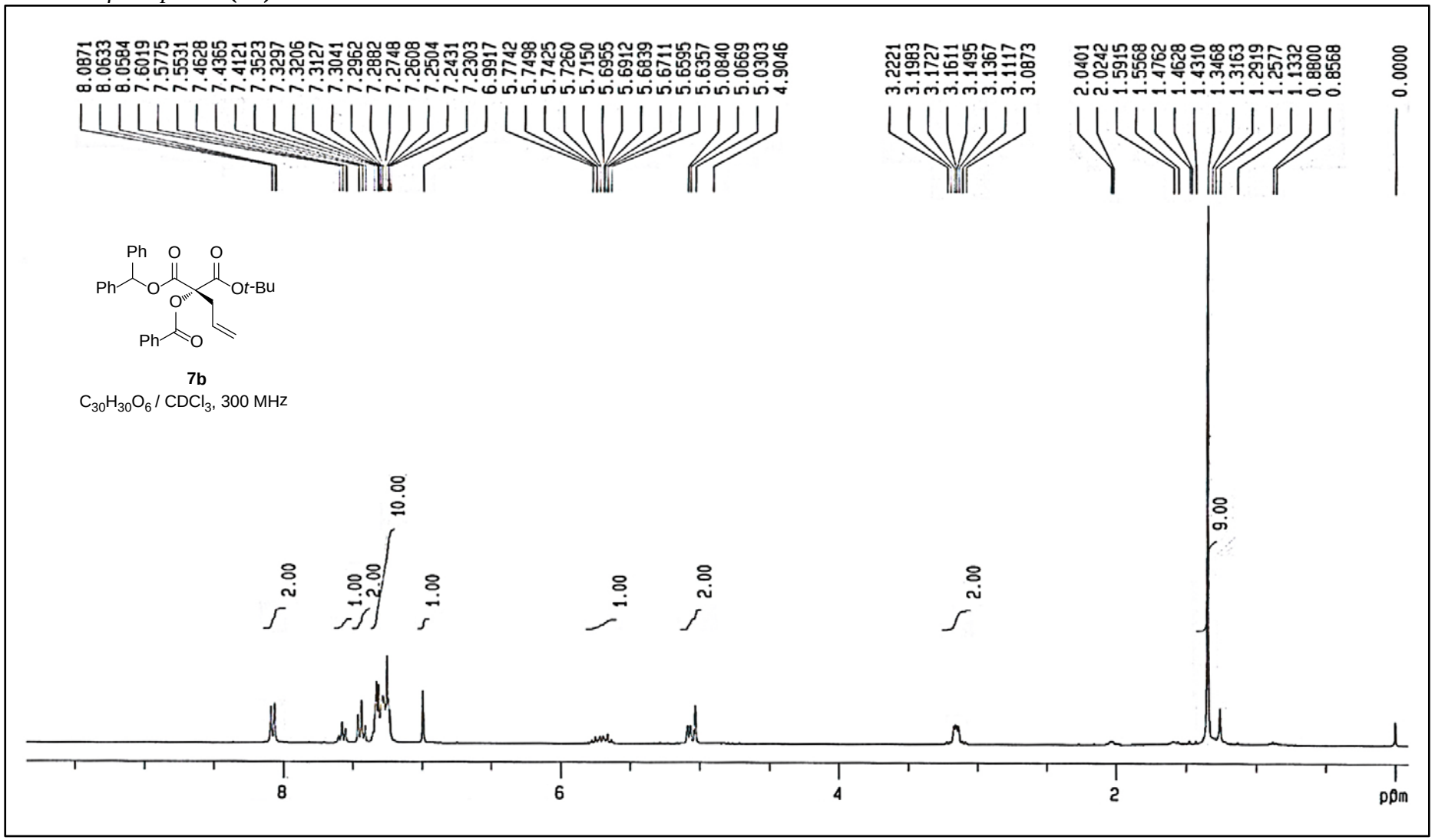
[1]H-NMR of compound **(7a)**



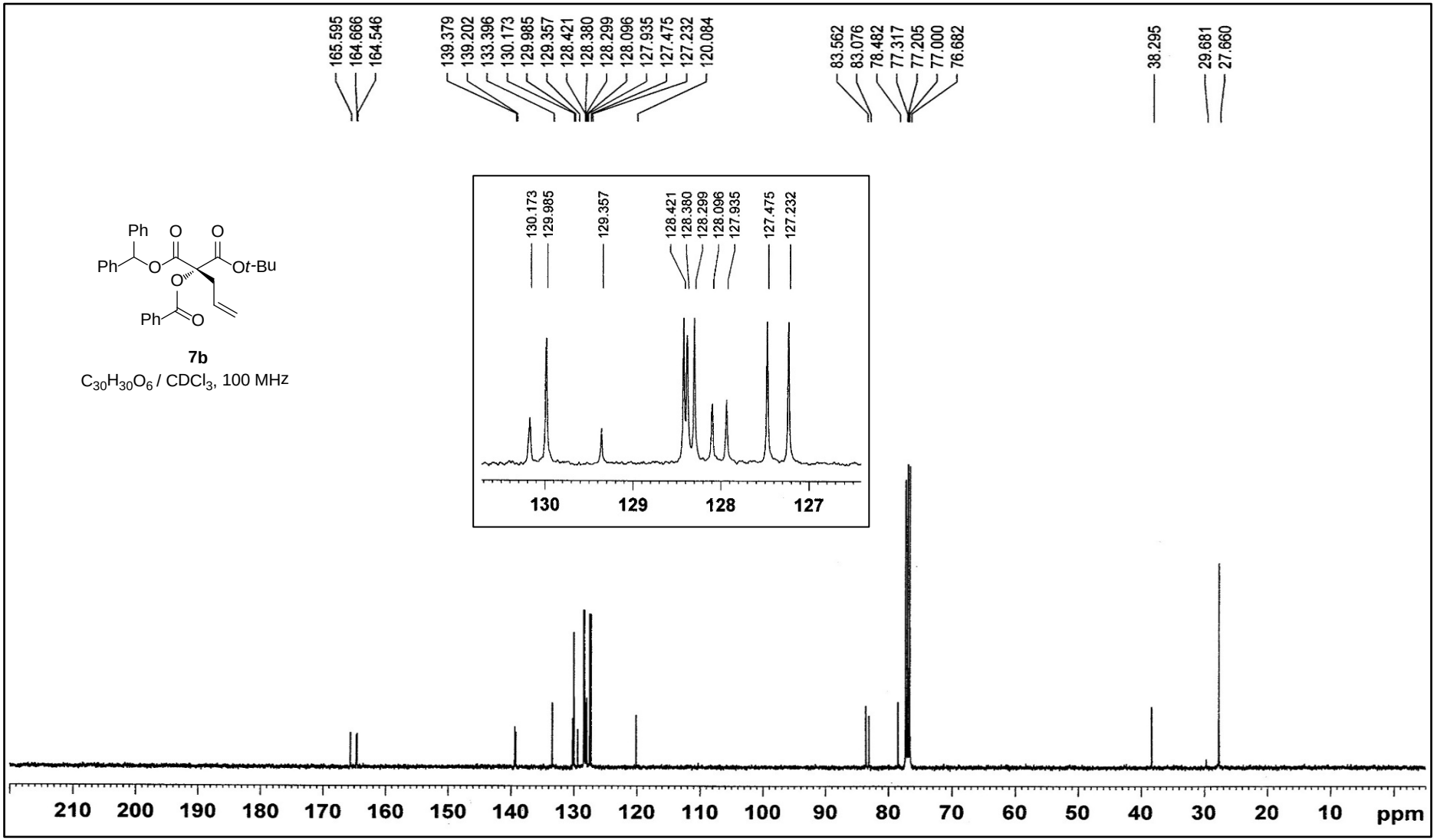
^{13}C-NMR of compound **(7a)**



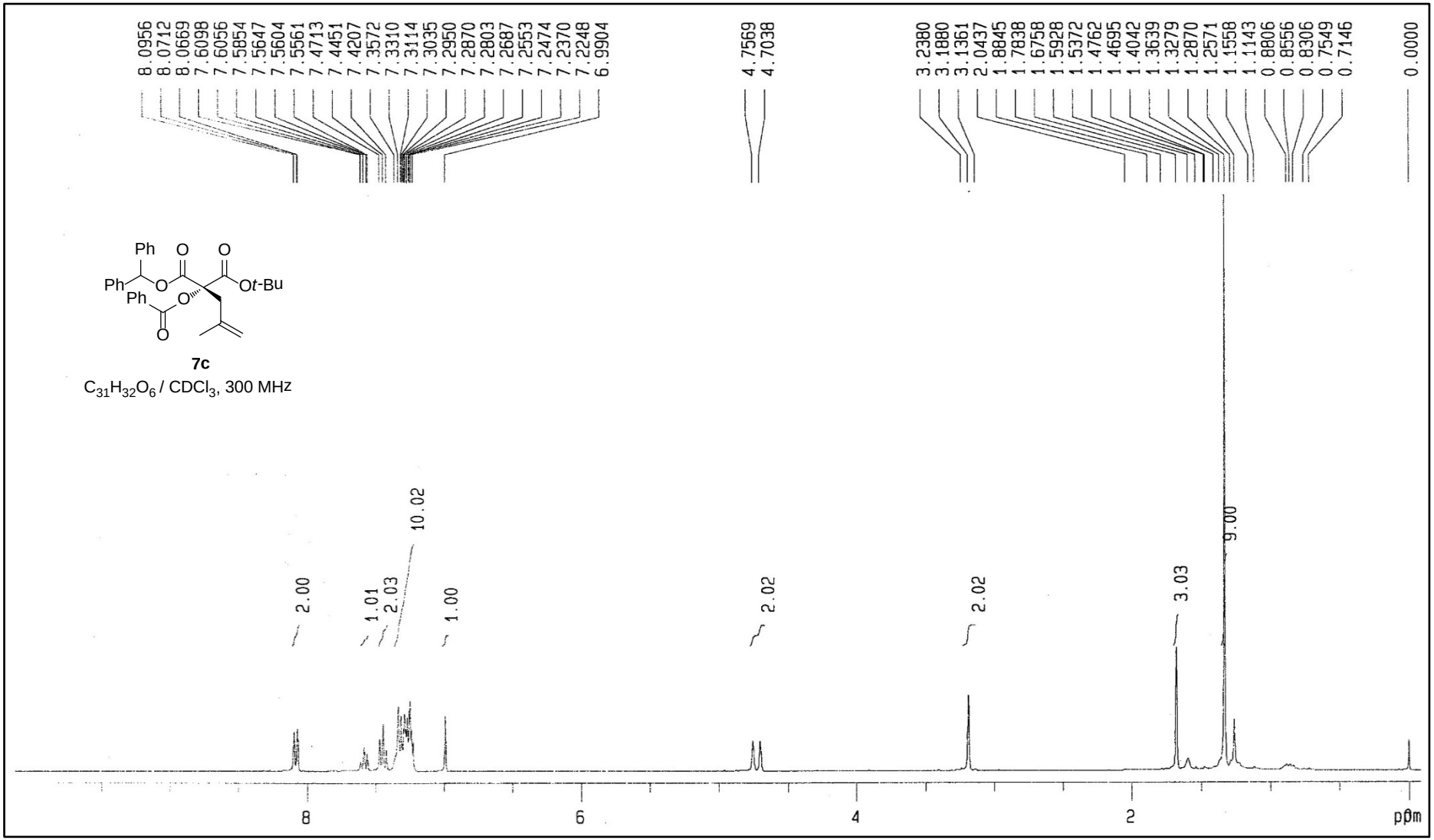
[1]H-NMR of compound **(7b)**



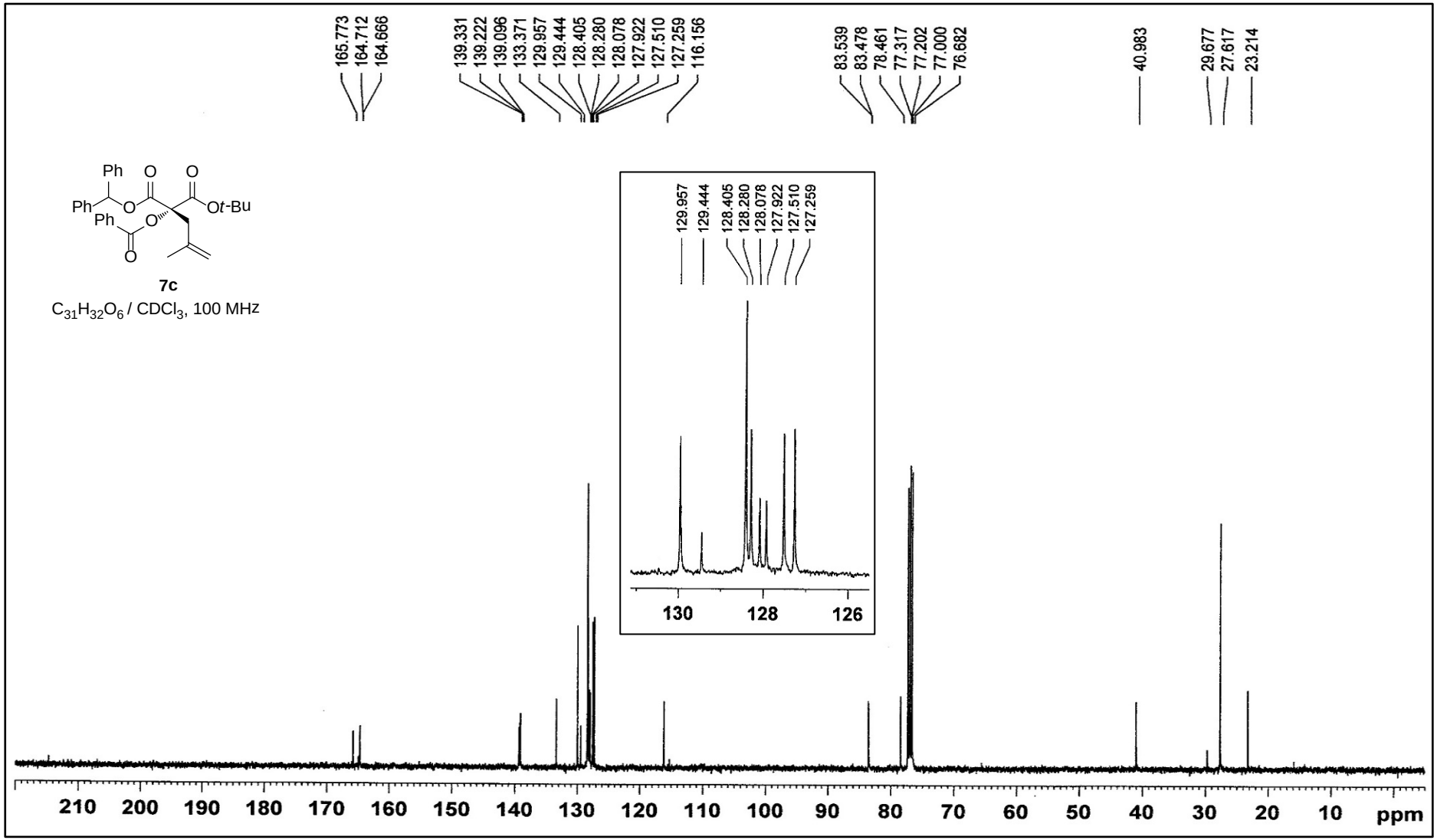
^{13}C-NMR of compound **(7b)**



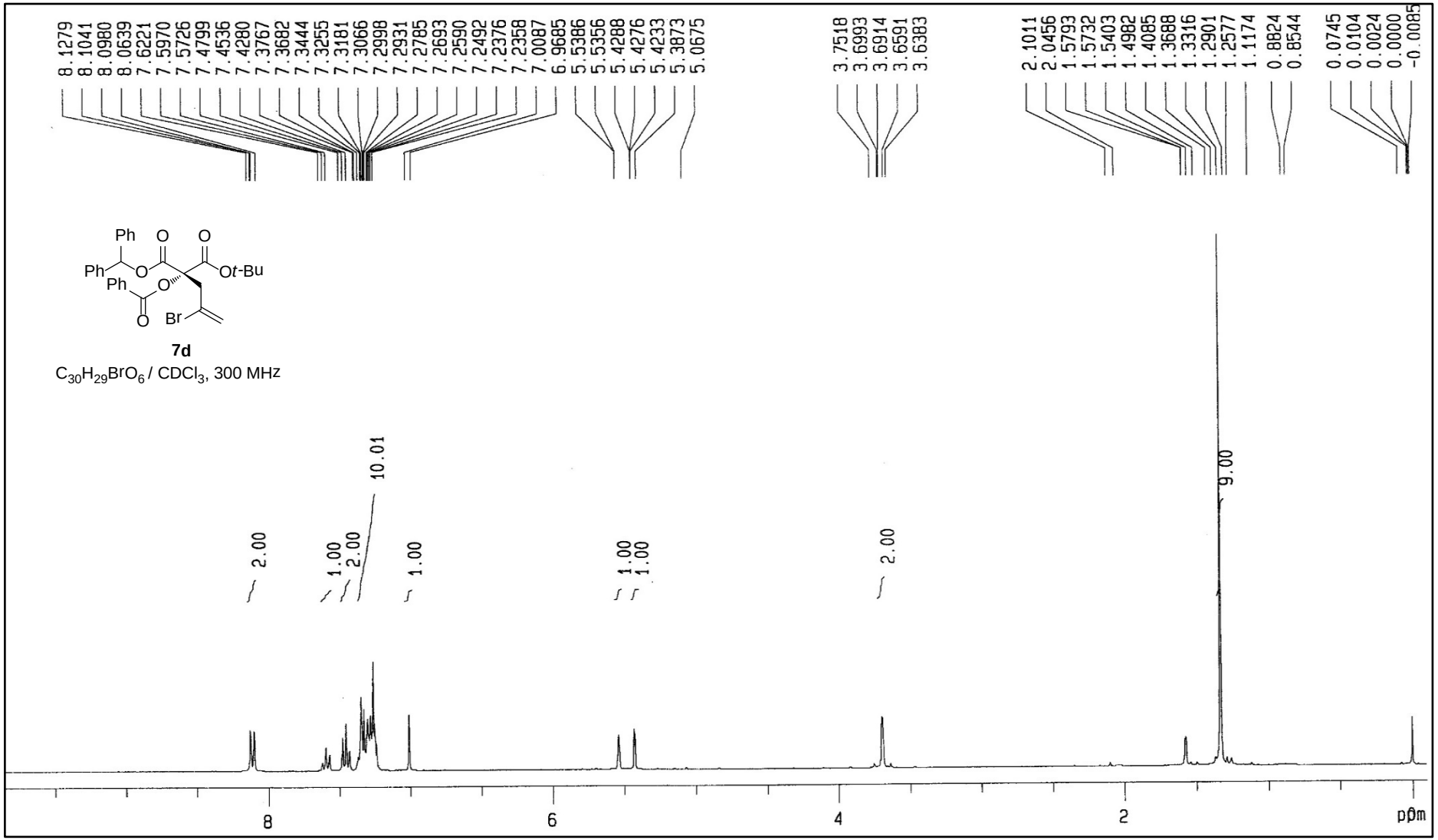
[1]H-NMR of compound **(7c)**



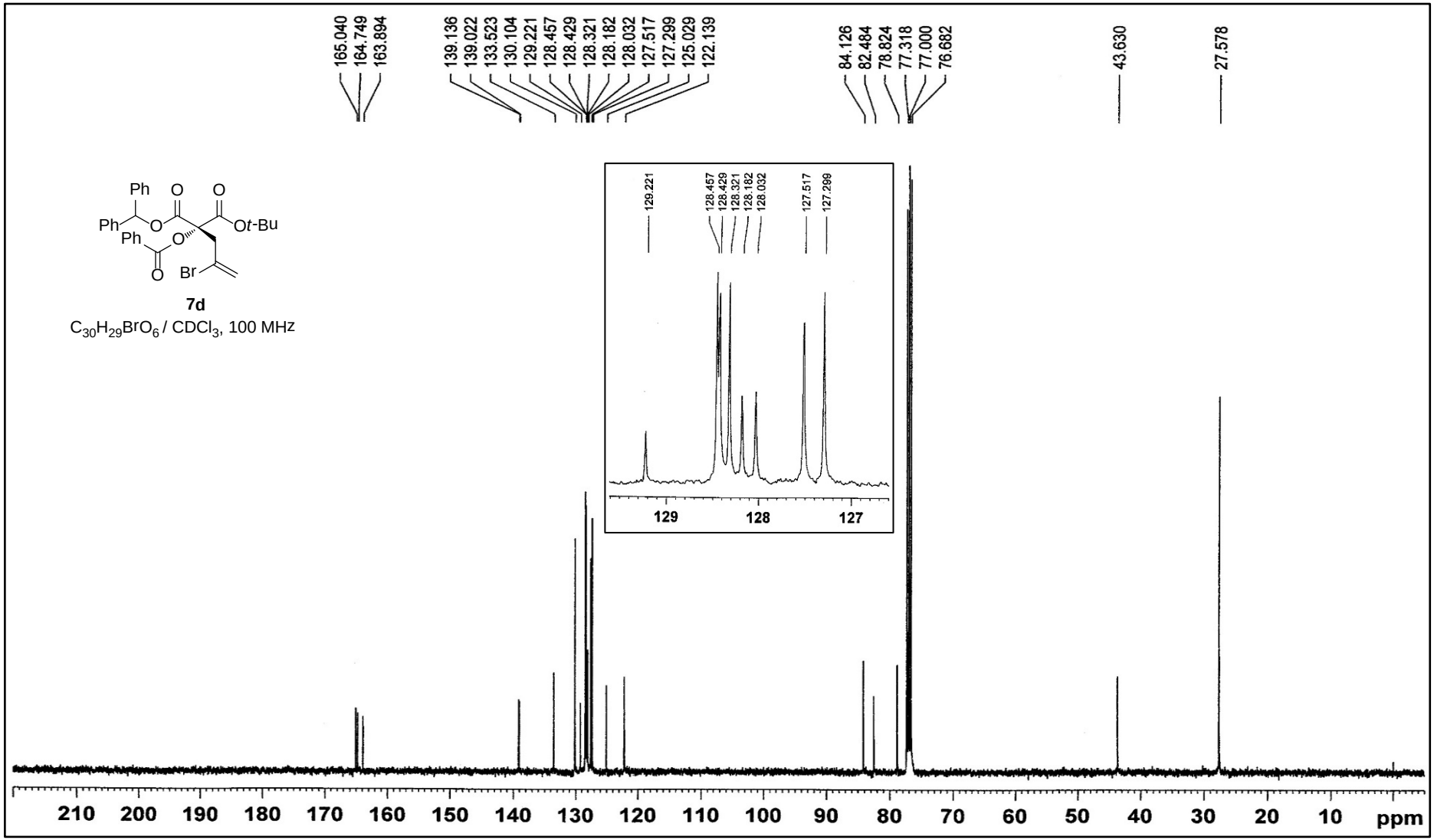
^{13}C-NMR of compound **(7c)**



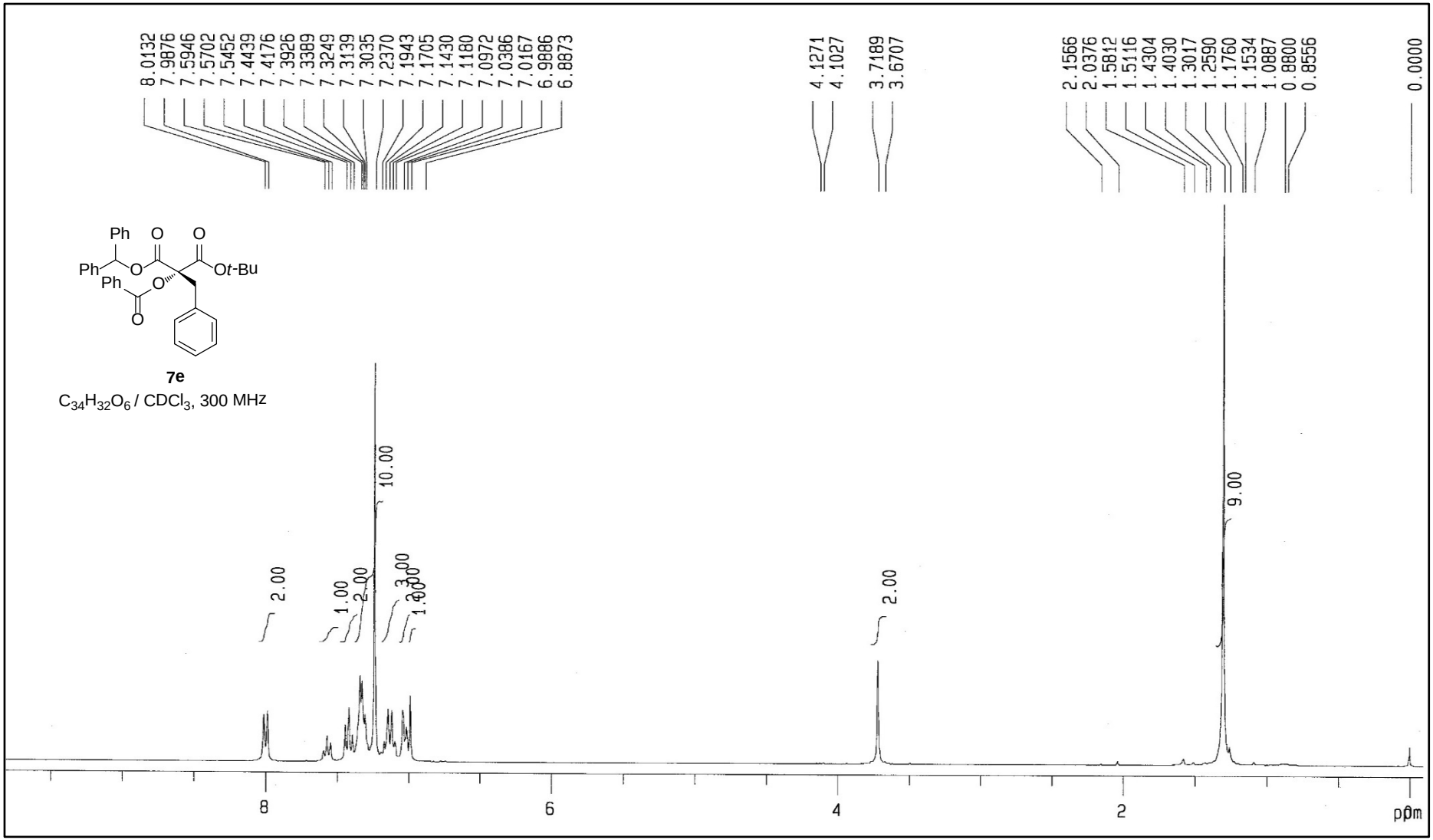
[1]H-NMR of compound **(7d)**



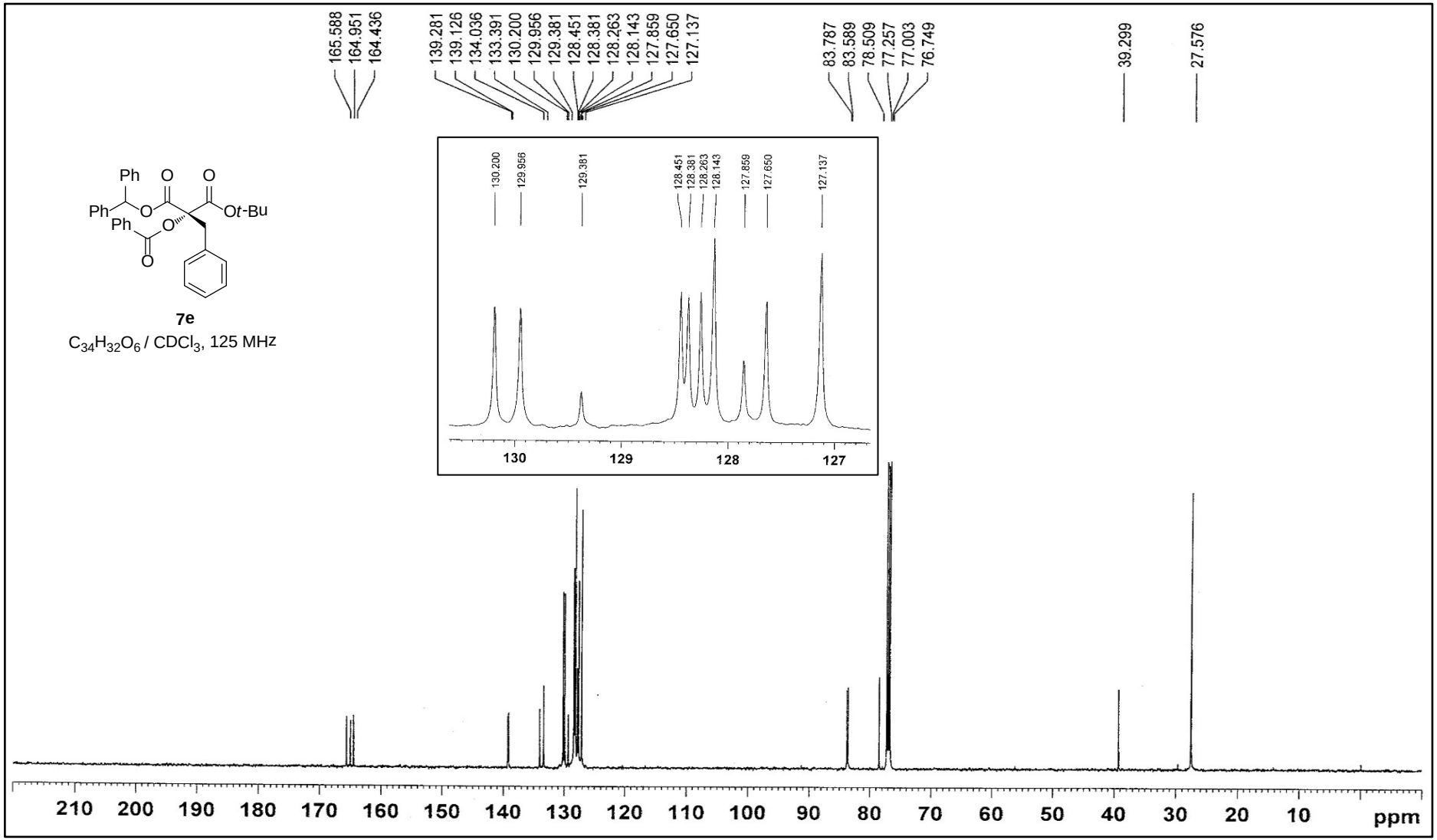
^{13}C-NMR of compound **(7d)**



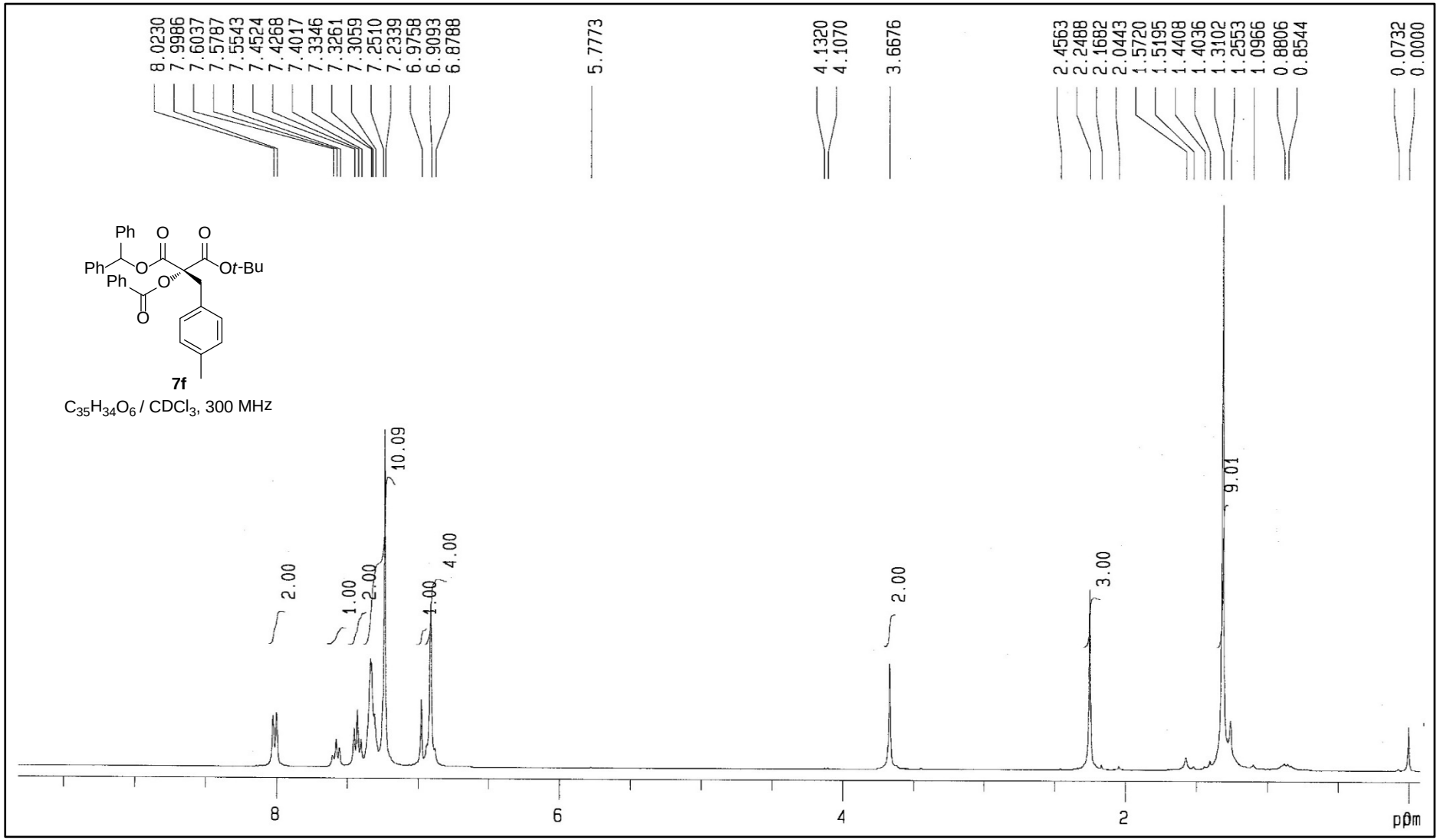
[1]H-NMR of compound **(7e)**



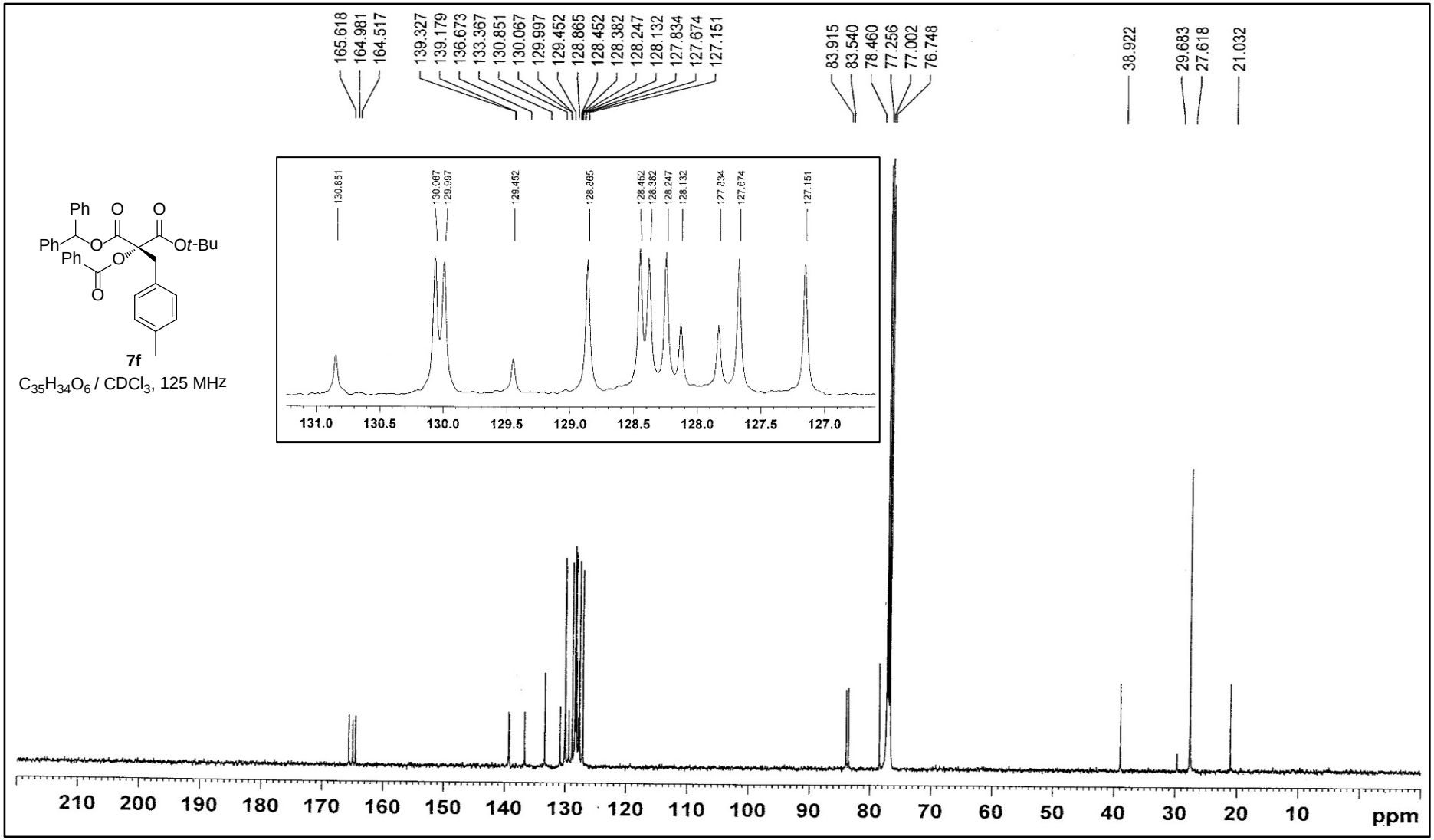
^{13}C-NMR of compound **(7e)**



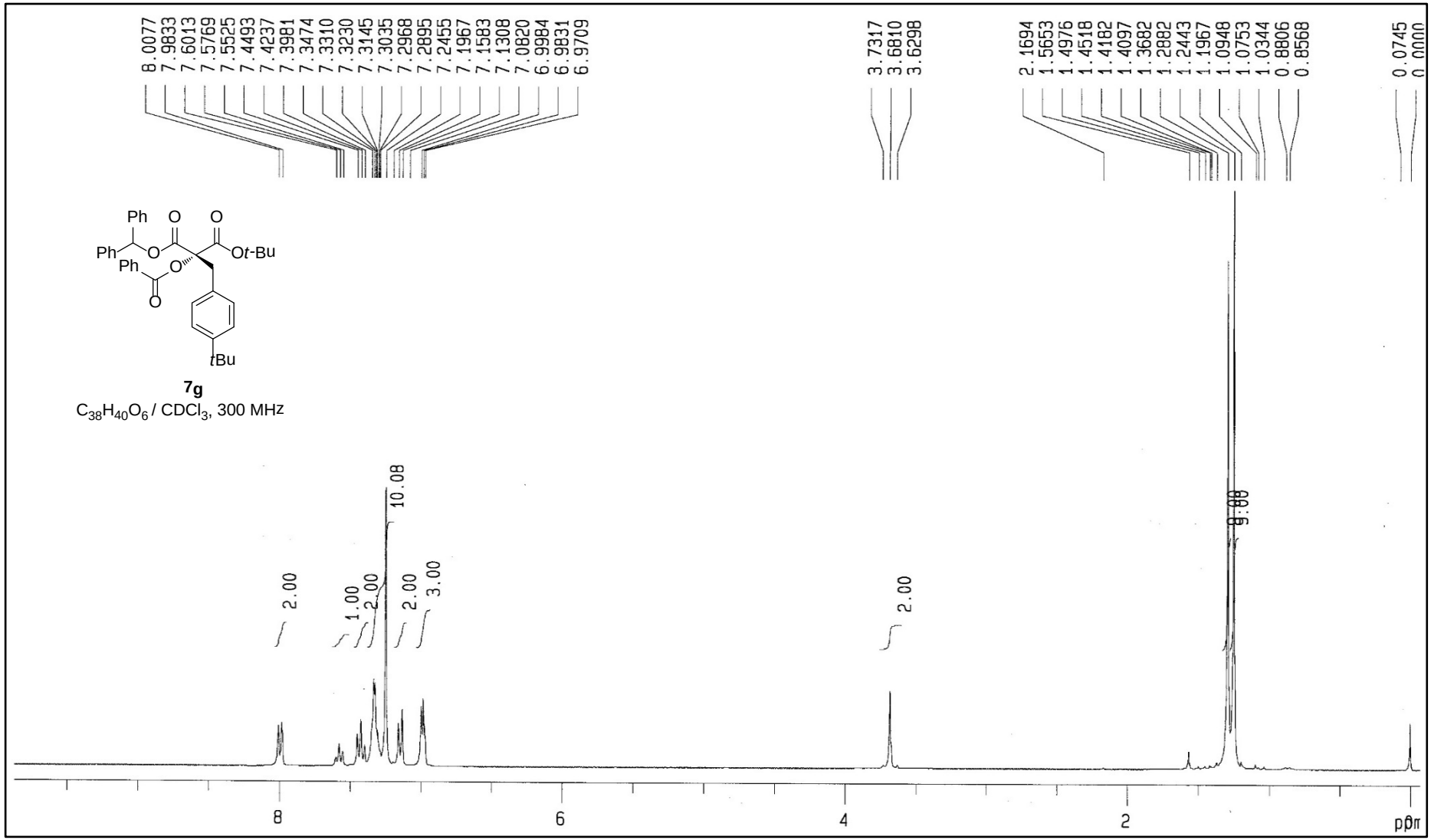
[1]H-NMR of compound **(7f)**



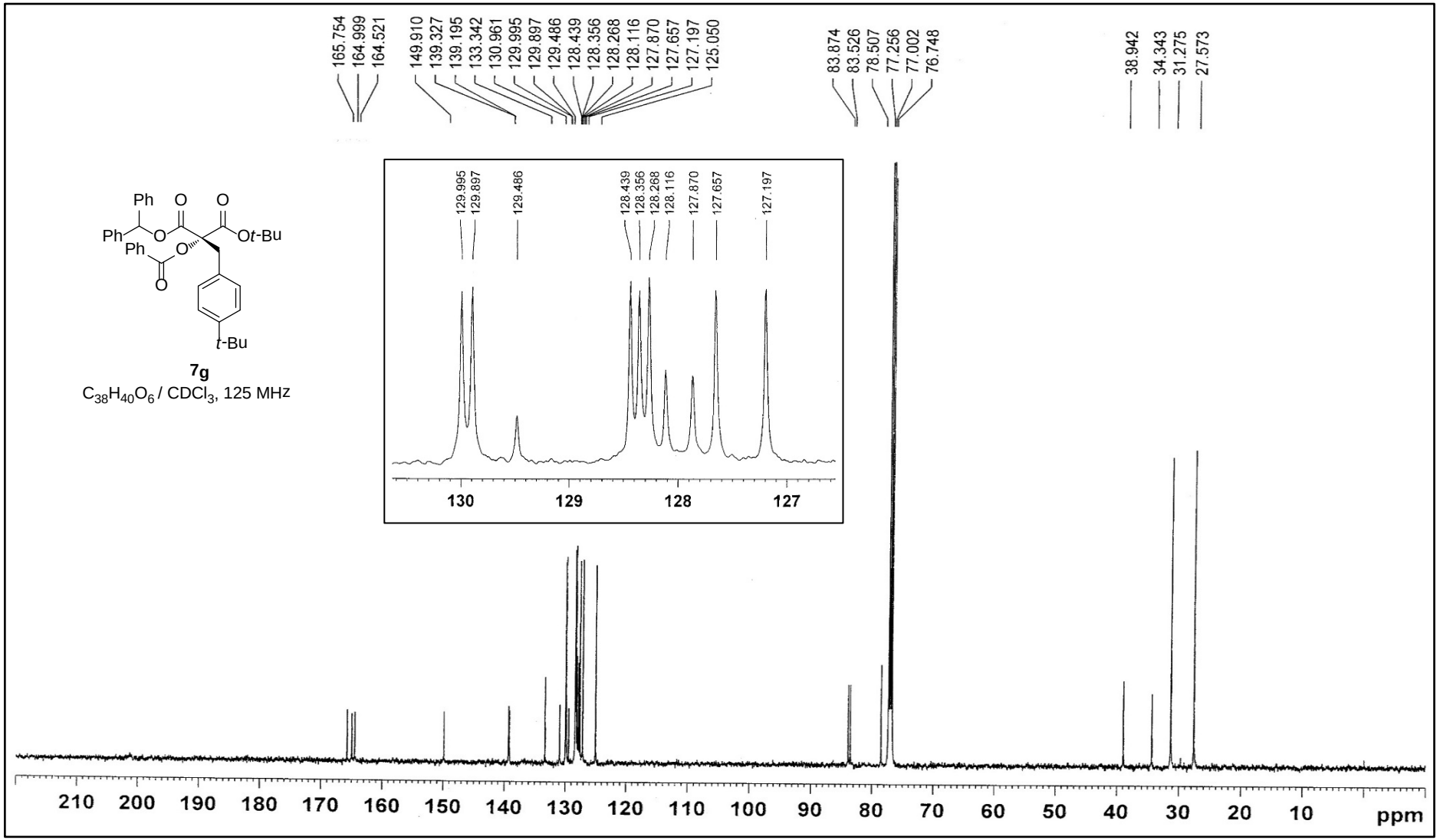
^{13}C-NMR of compound **(7f)**



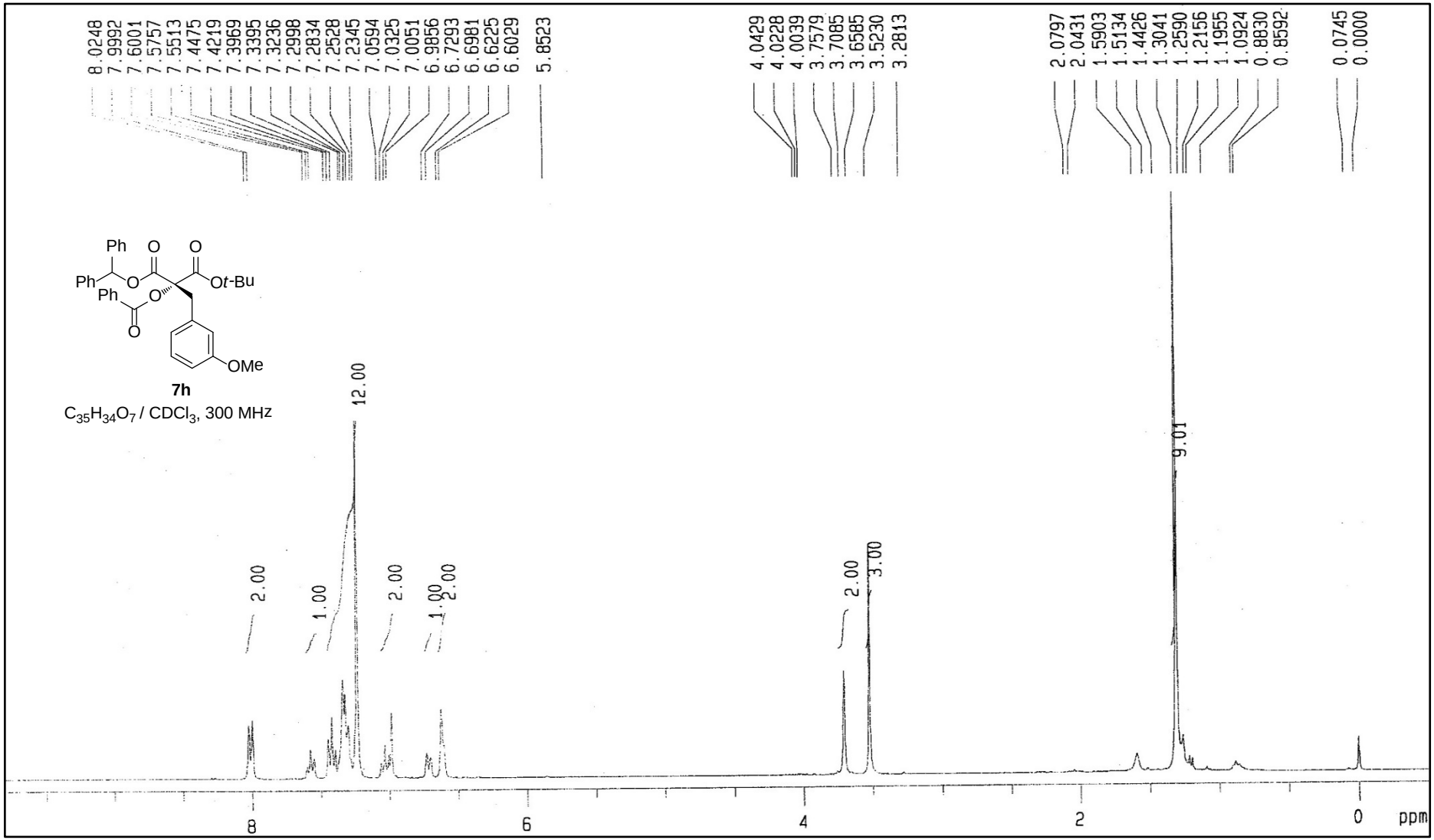
[1]H-NMR of compound **(7g)**



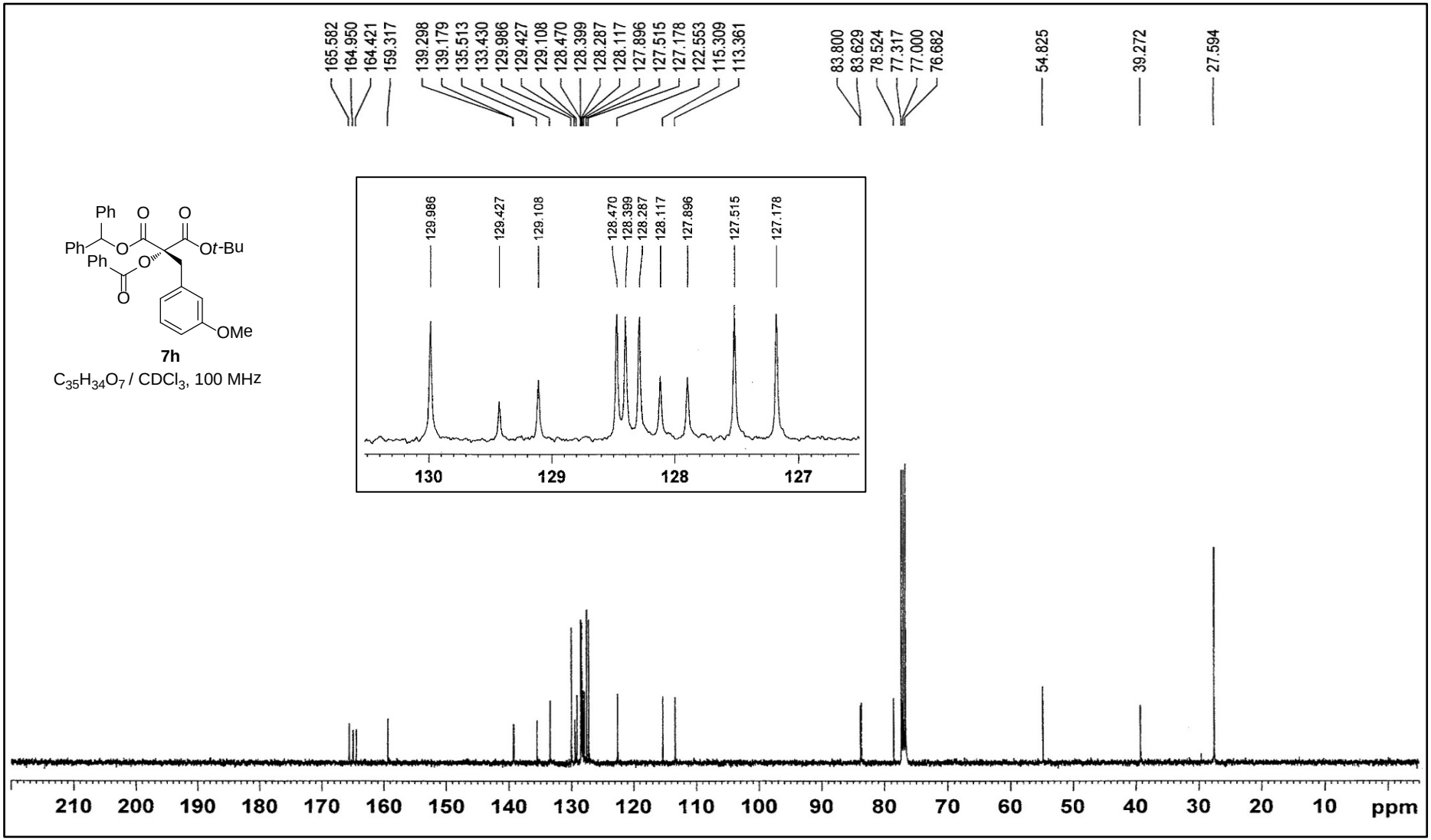
^{13}C-NMR of compound **(7g)**



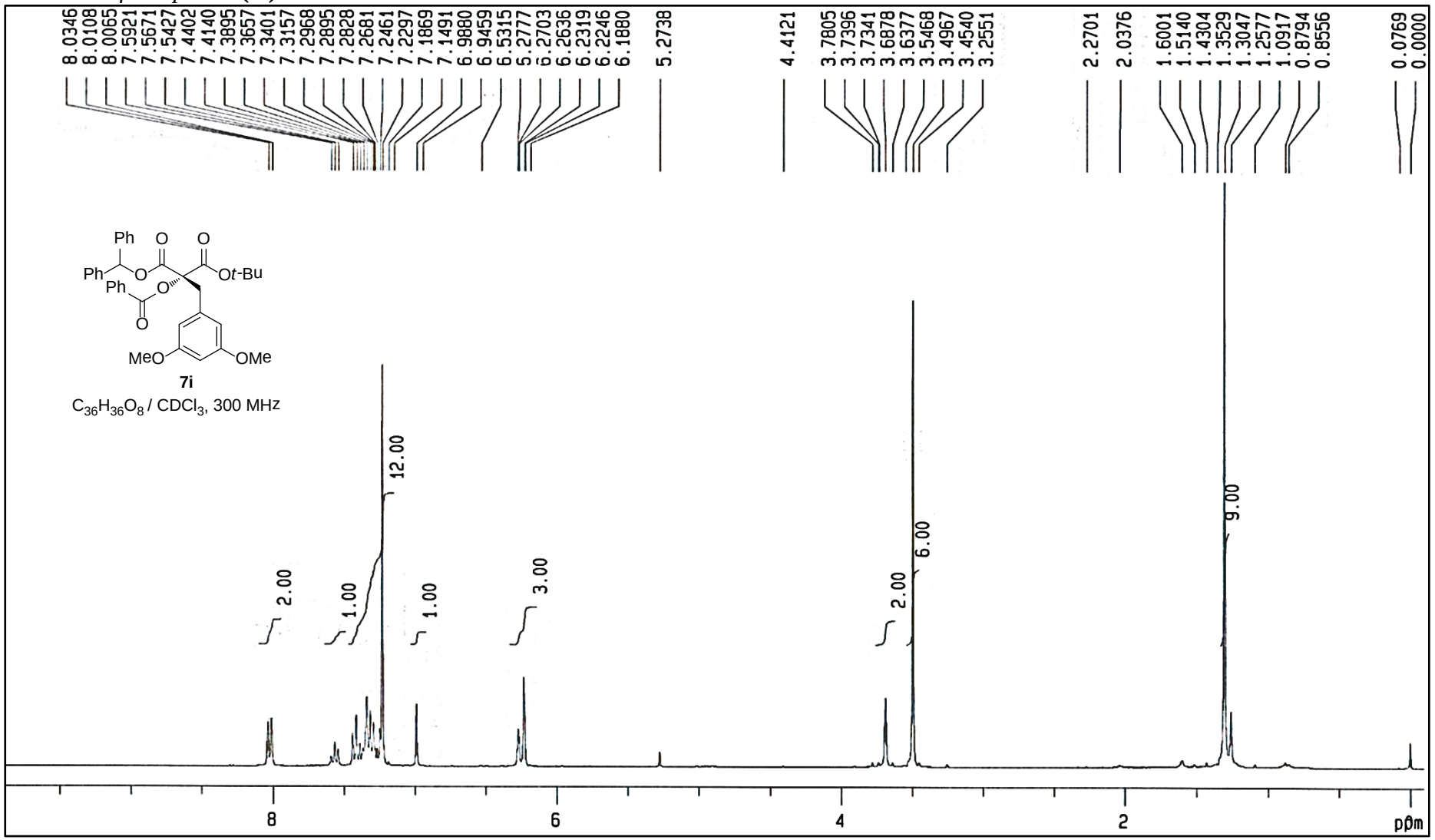
[1]H-NMR of compound **(7h)**



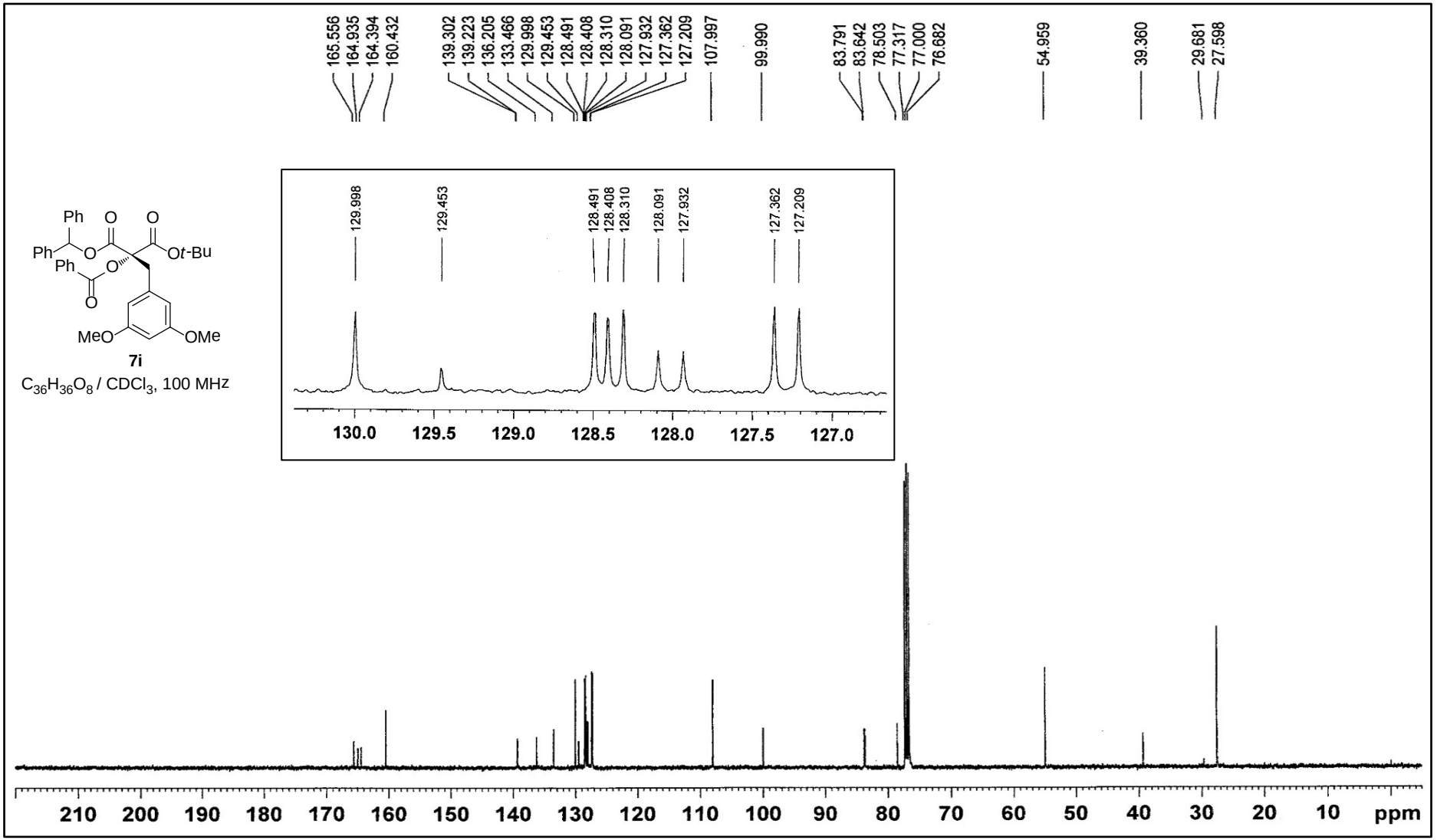
^{13}C-NMR of compound **(7h)**



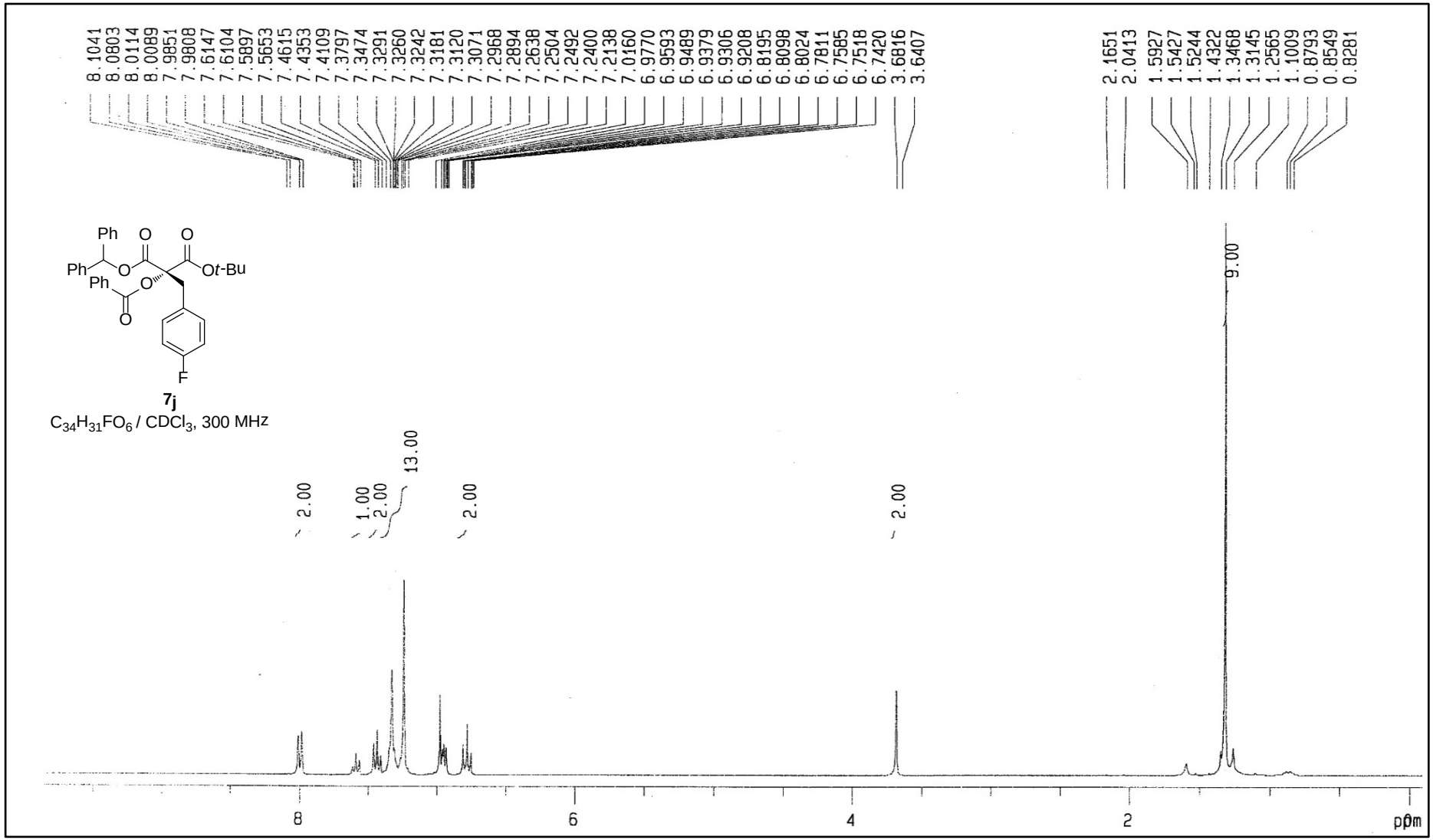
[1]H-NMR of compound **(7i)**



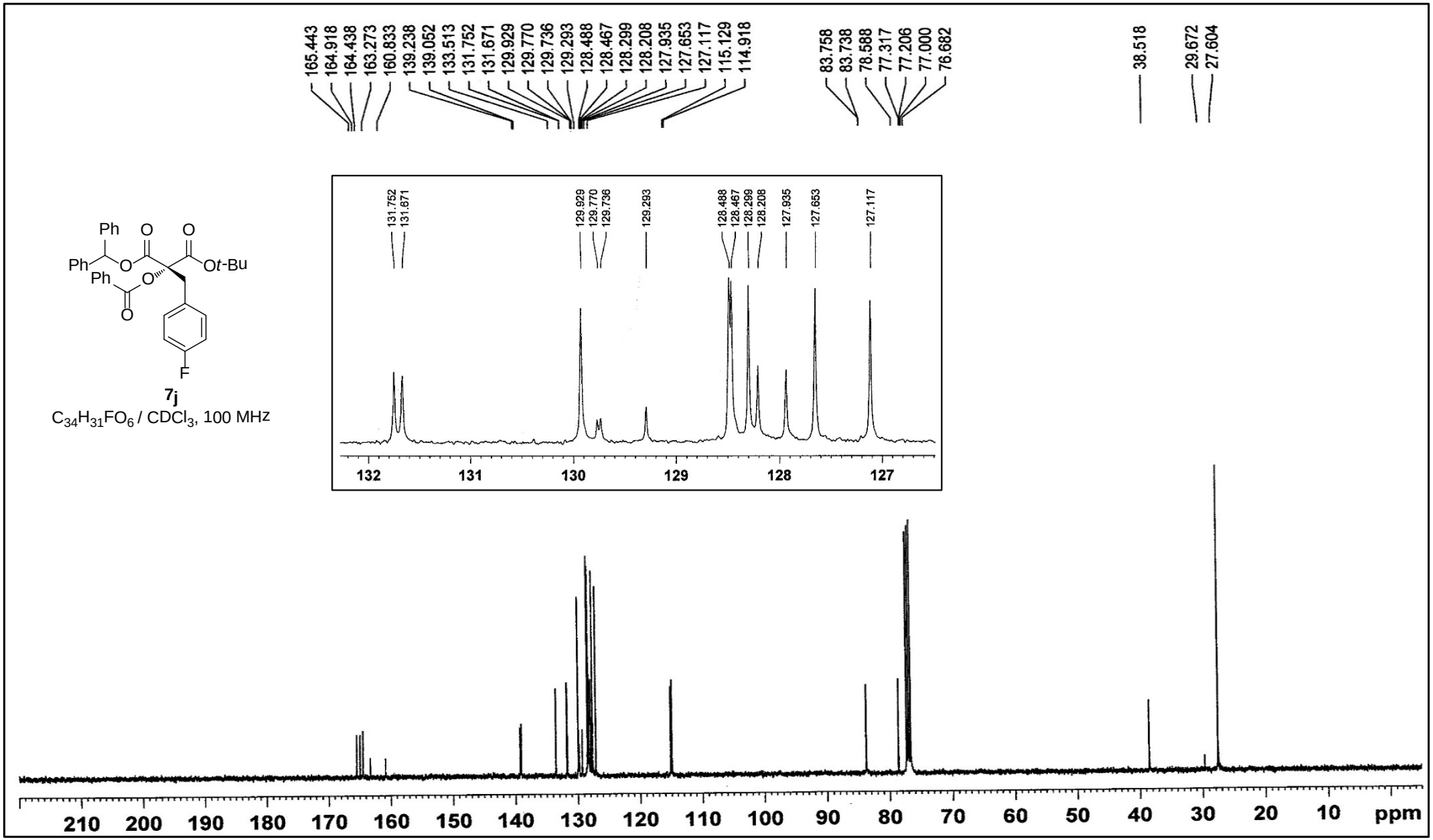
^{13}C-NMR of compound **(7i)**



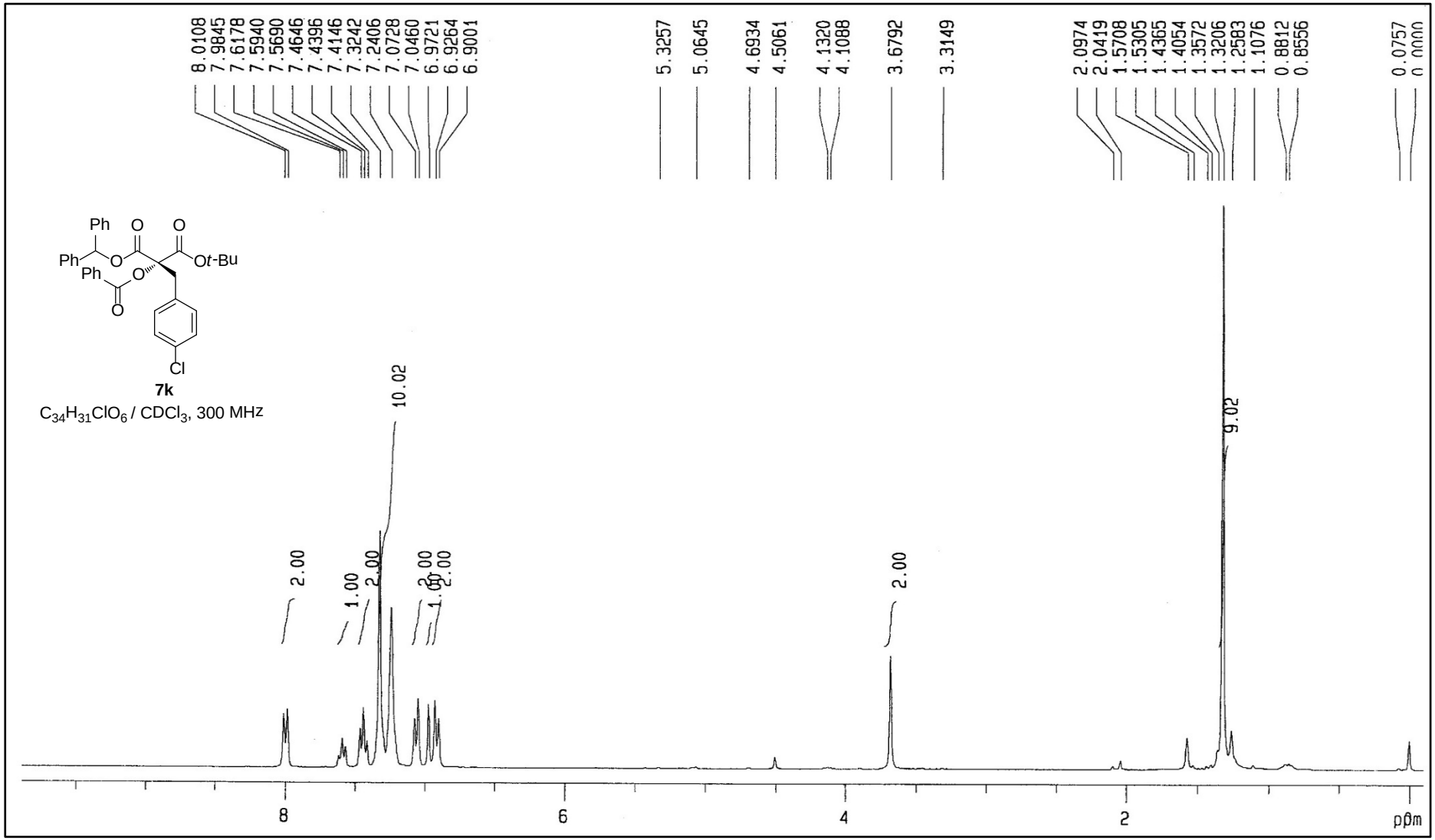
[1]H-NMR of compound **(7j)**



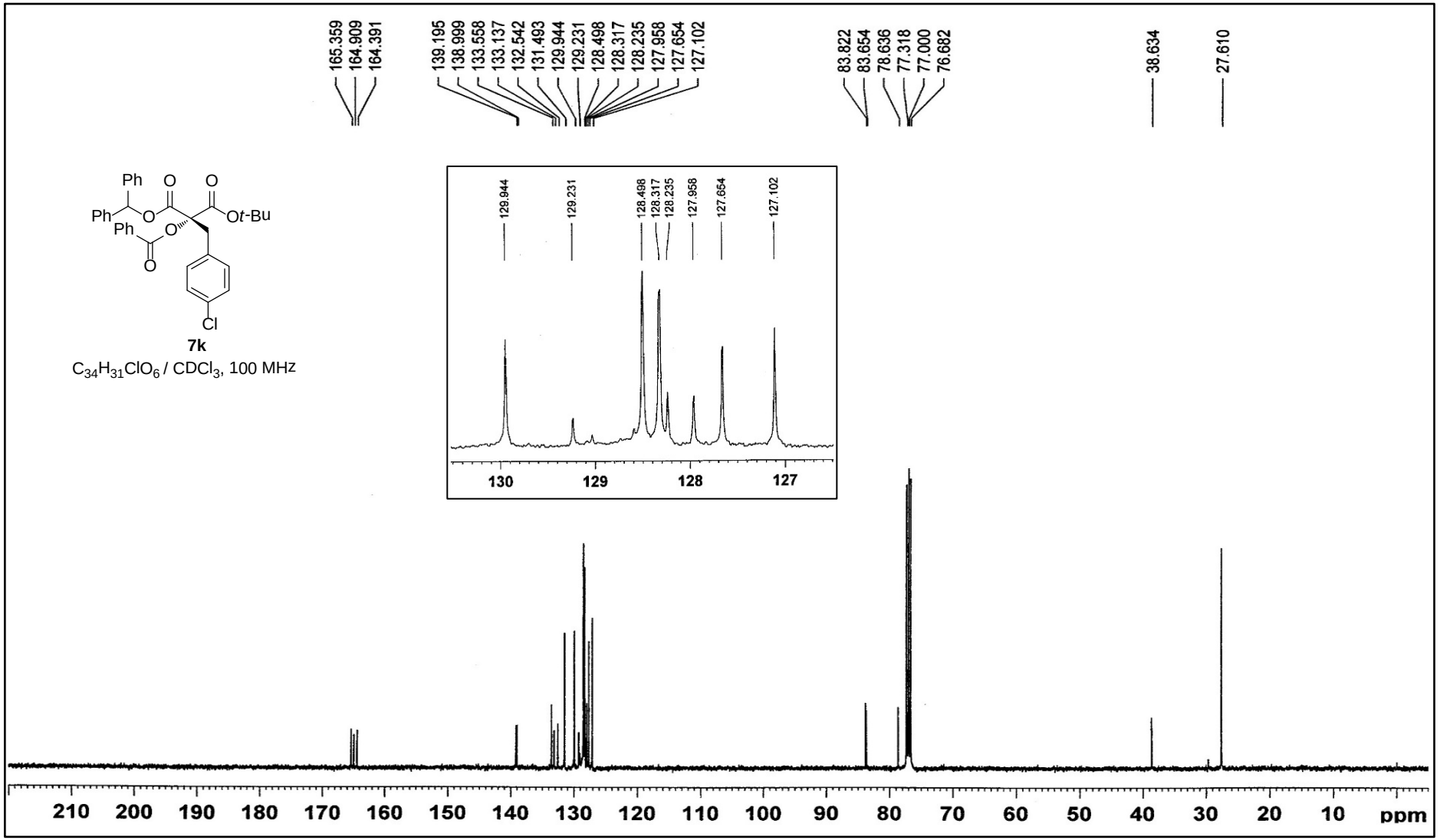
^{13}C-NMR of compound **(7j)**



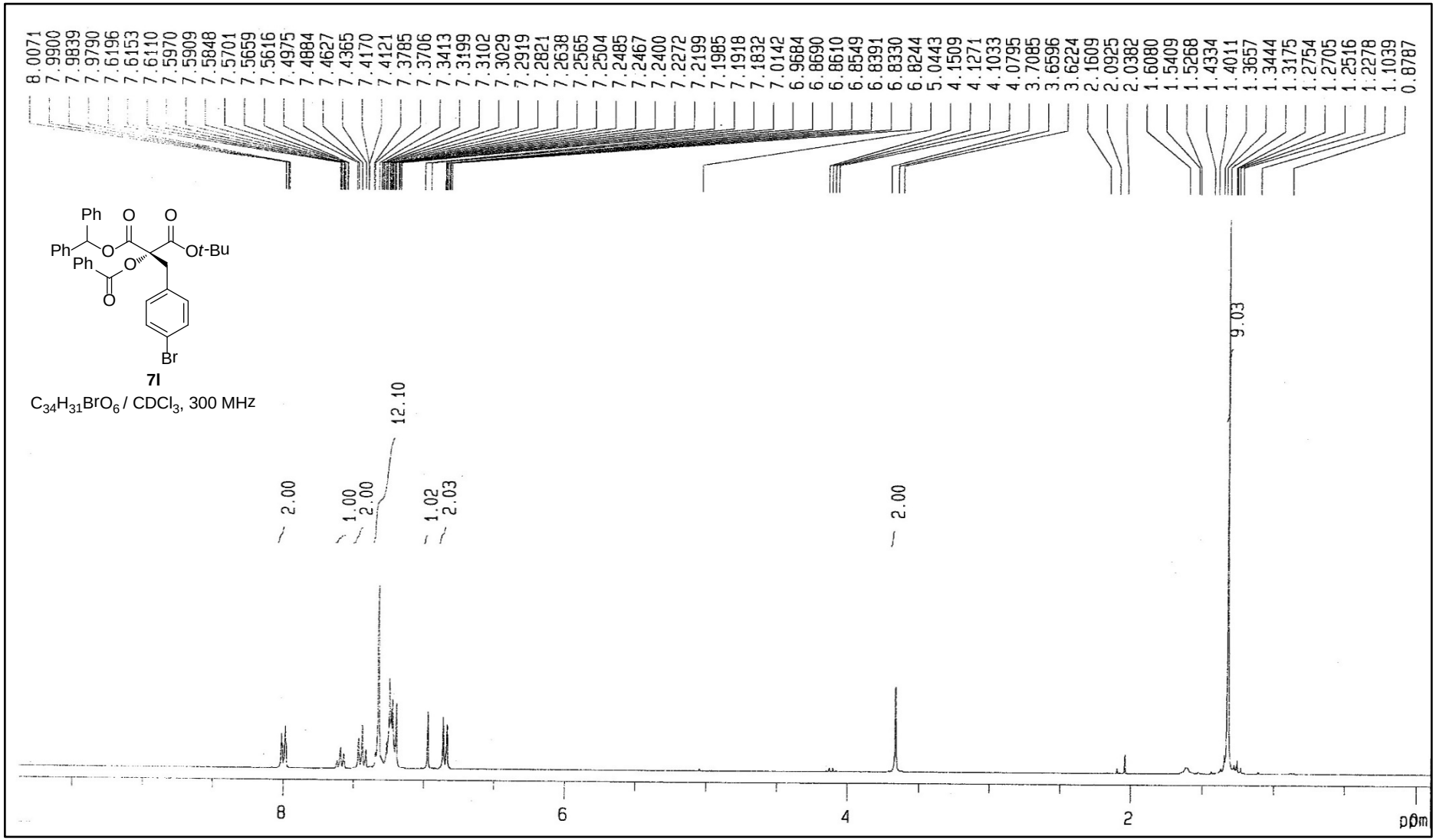
[1]H-NMR of compound **(7k)**



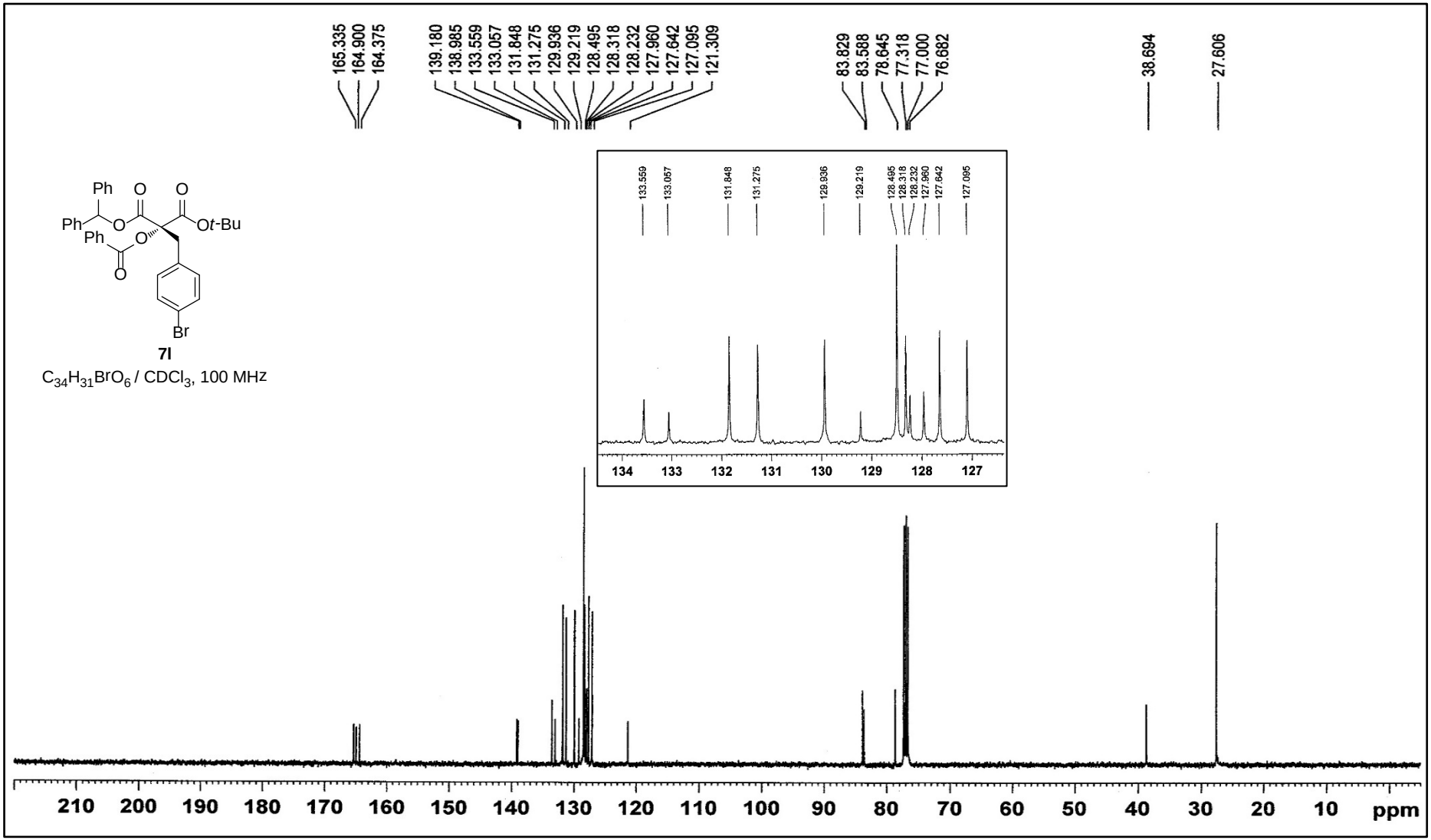
^{13}C-NMR of compound **(7k)**



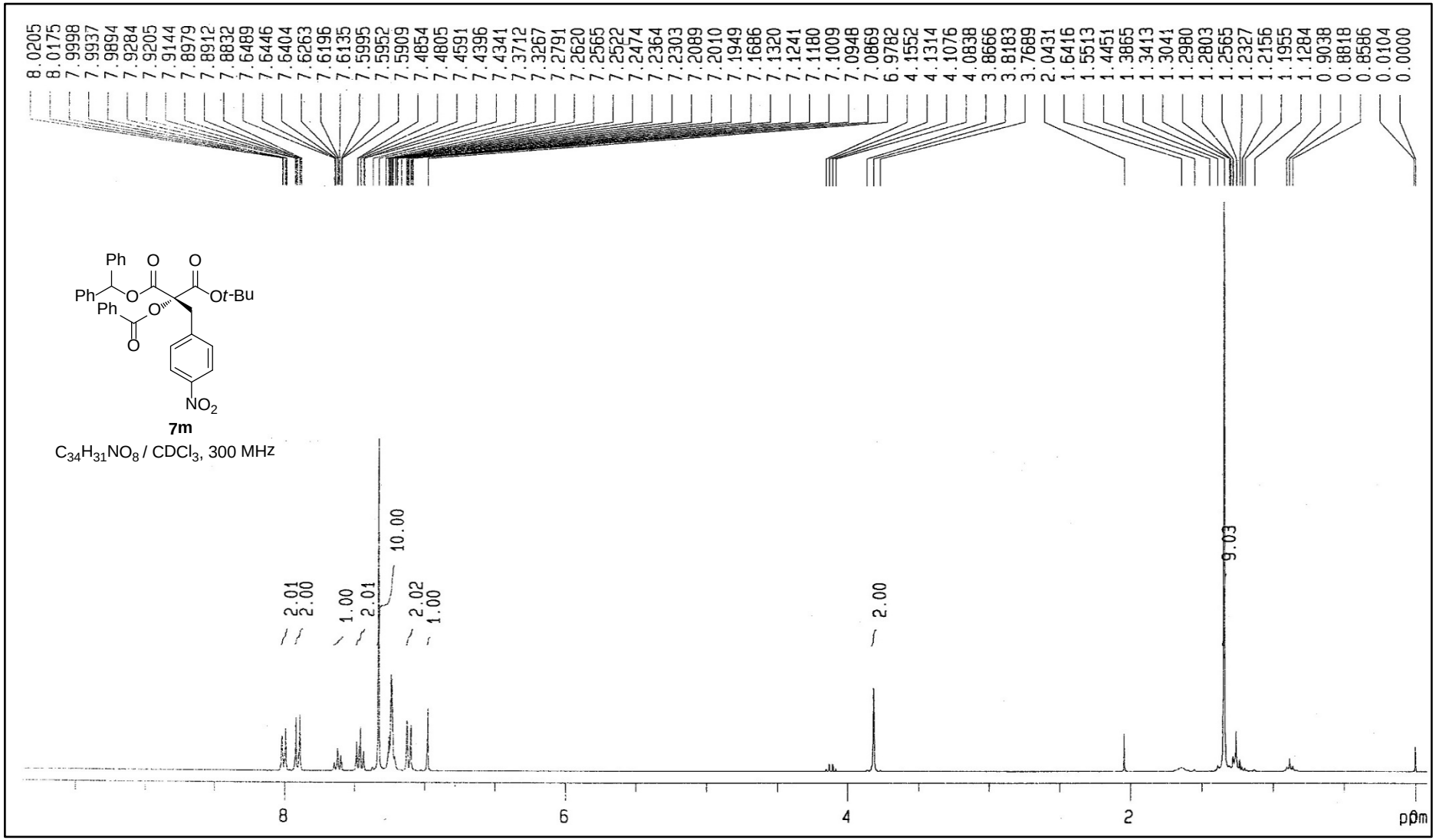
[1]H-NMR of compound **(7l)**



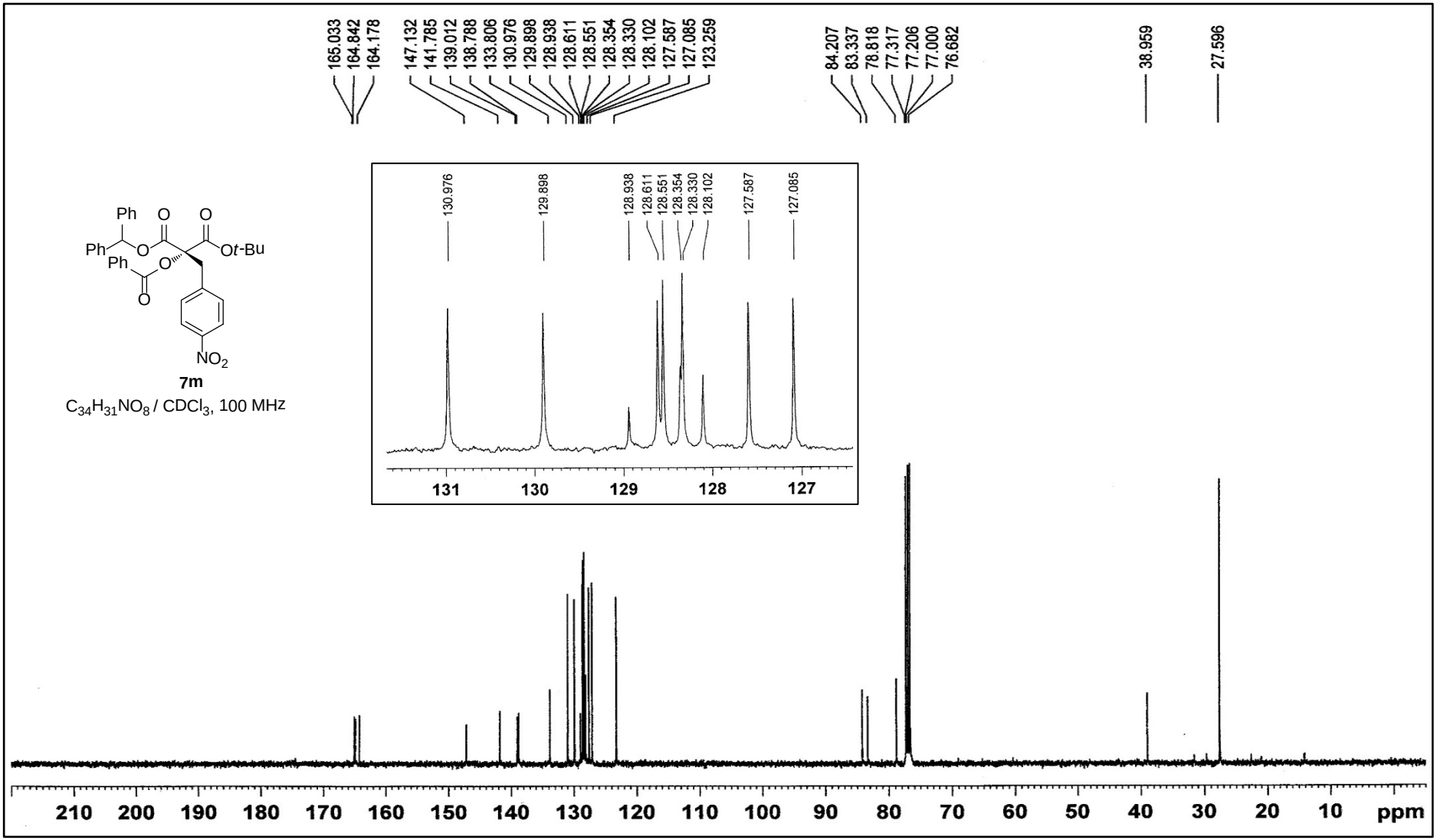
^{13}C-NMR of compound **(7l)**



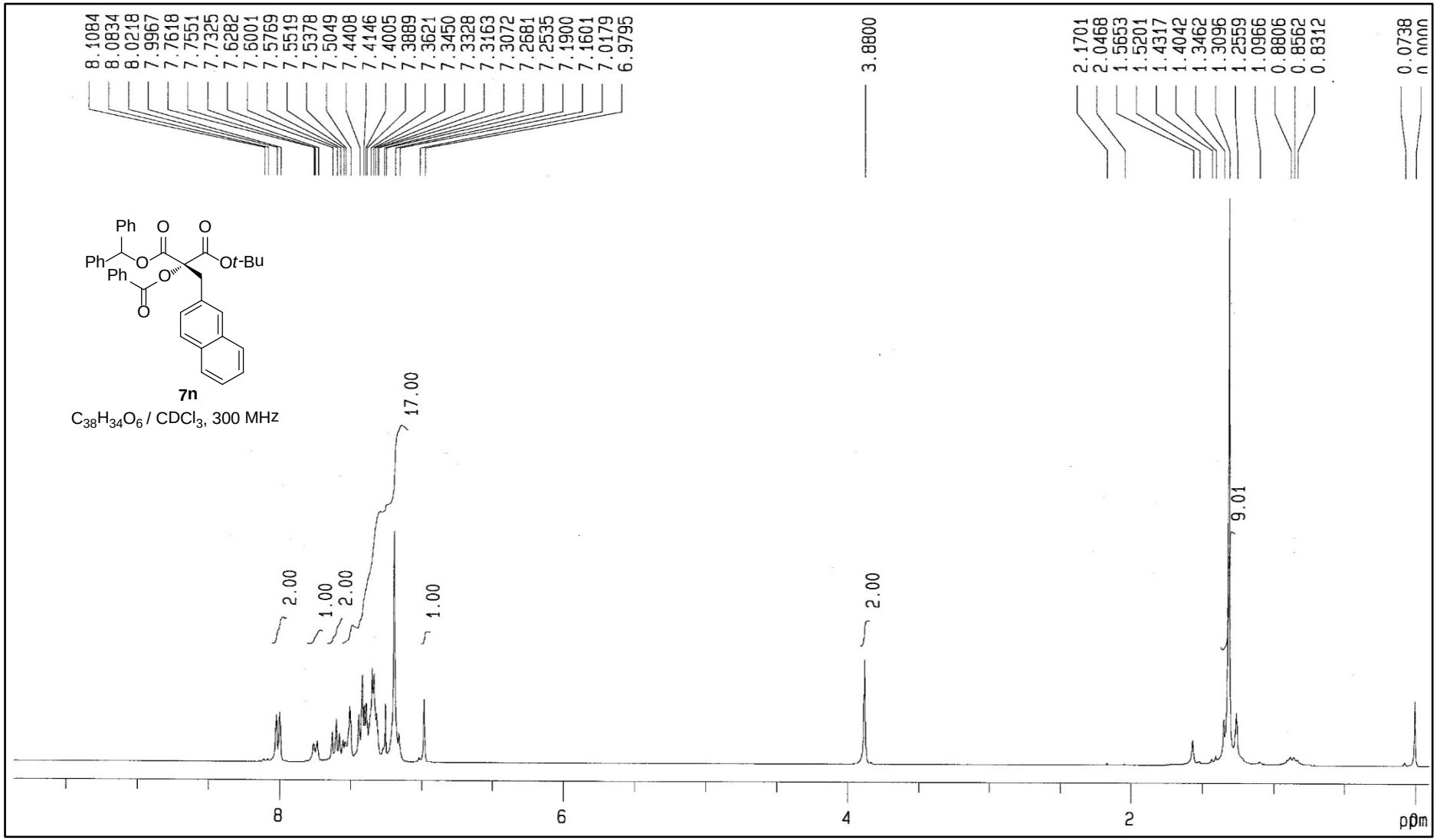
[1]H-NMR of compound **(7m)**



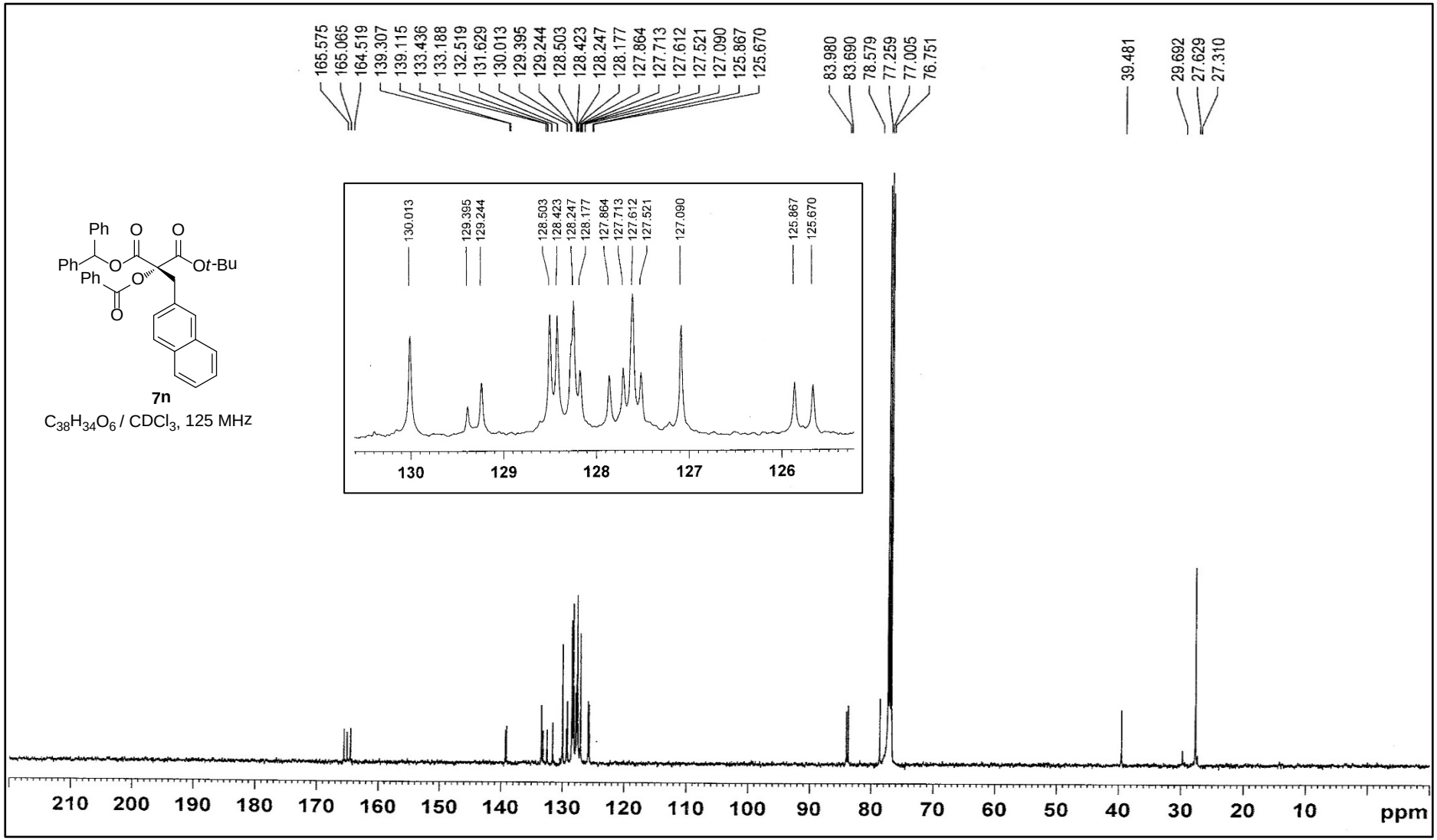
^{13}C-NMR of compound **(7m)**



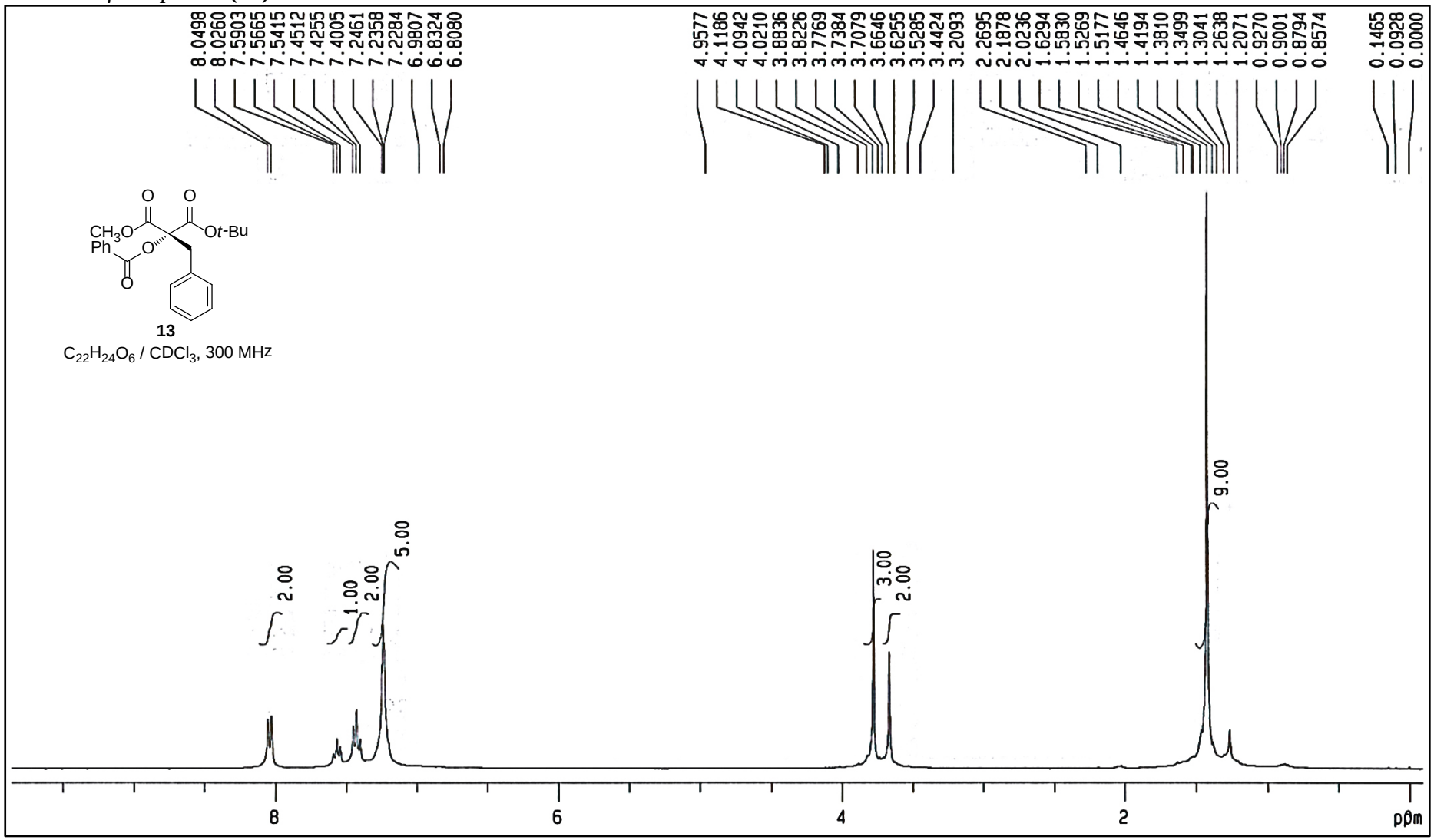
[1]H-NMR of compound **(7n)**



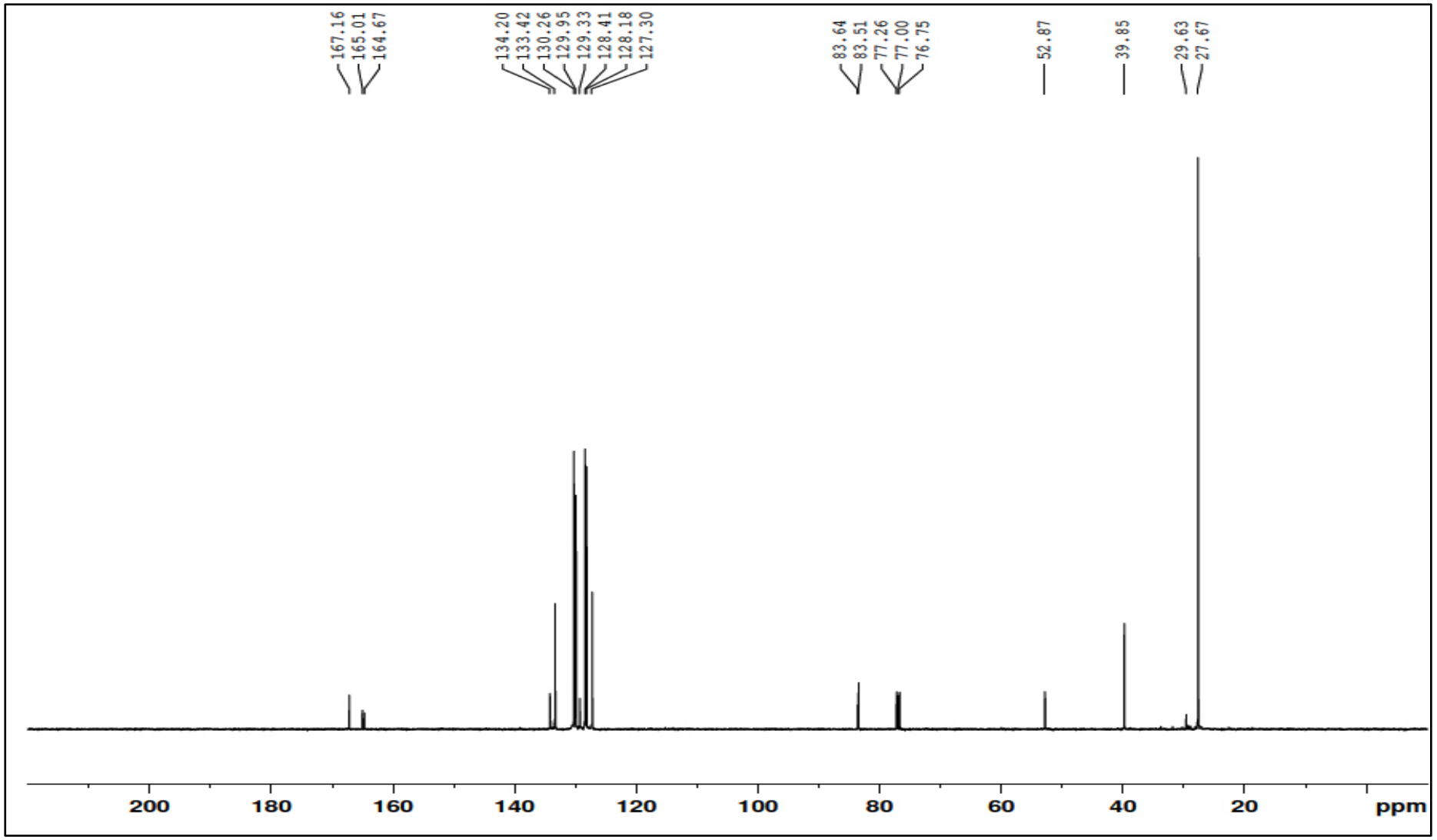
^{13}C-NMR of compound **(7n)**



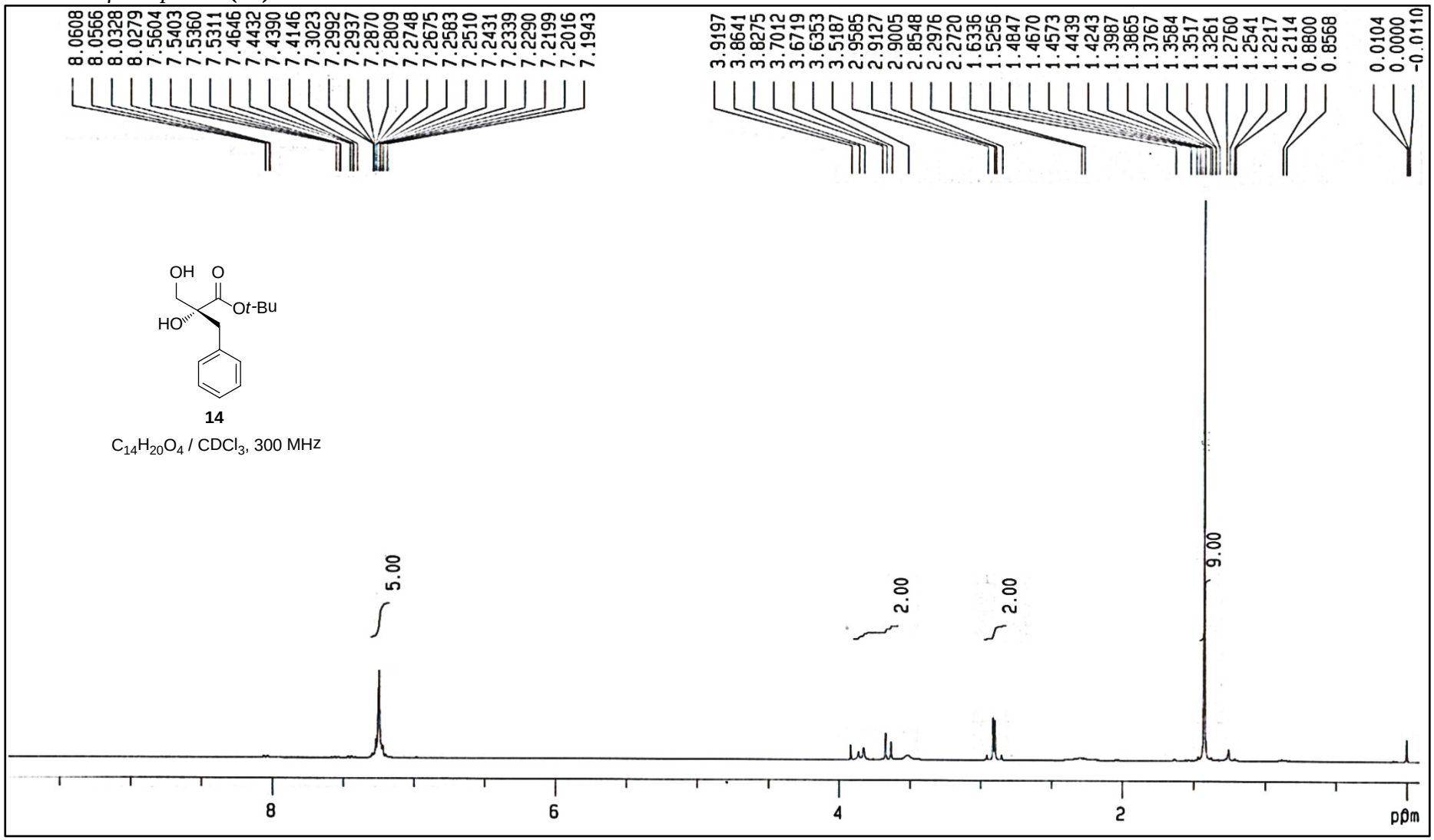
[1]H-NMR of compound **(13)**



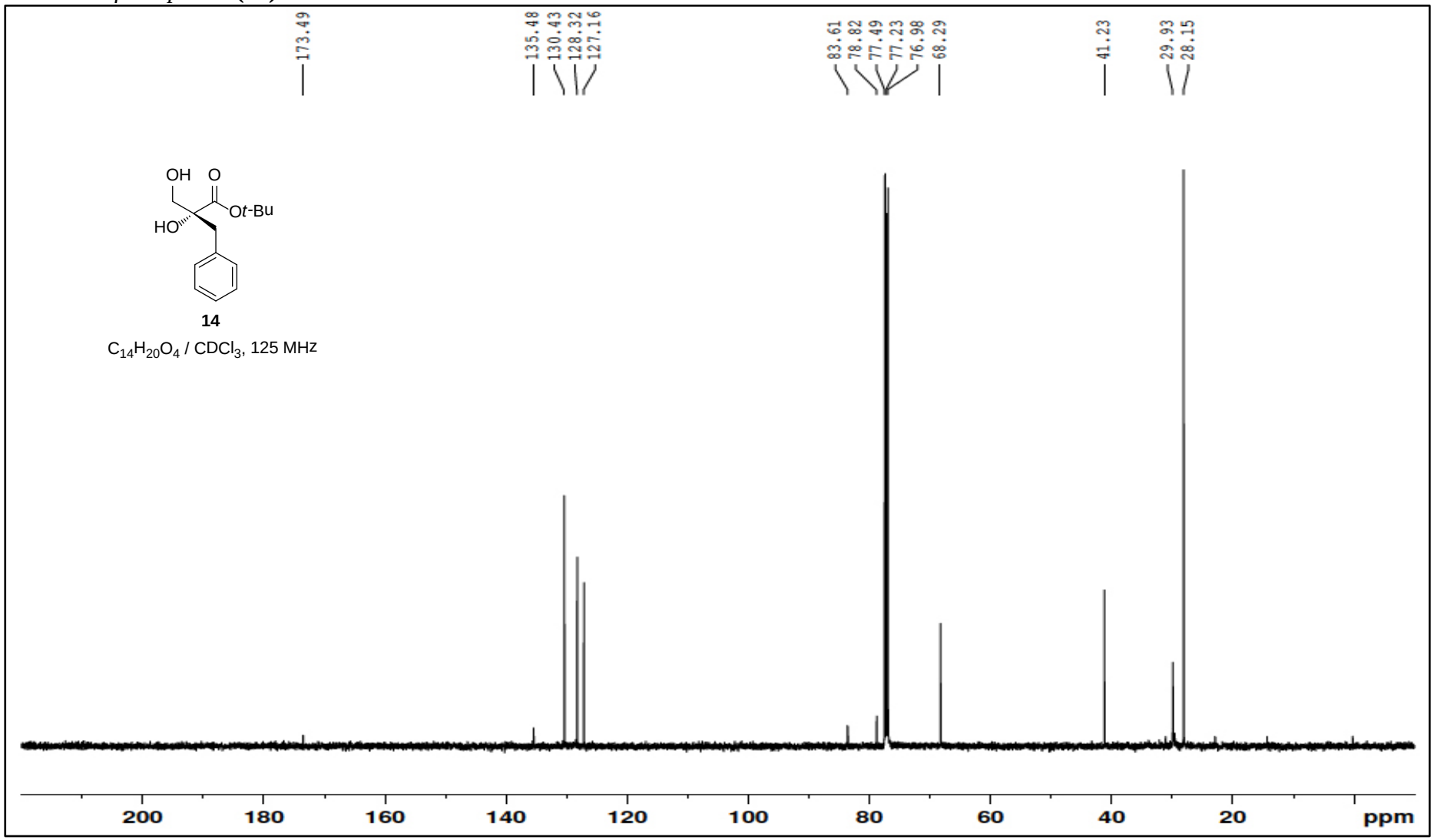
^{13}C-NMR of compound **(13)**



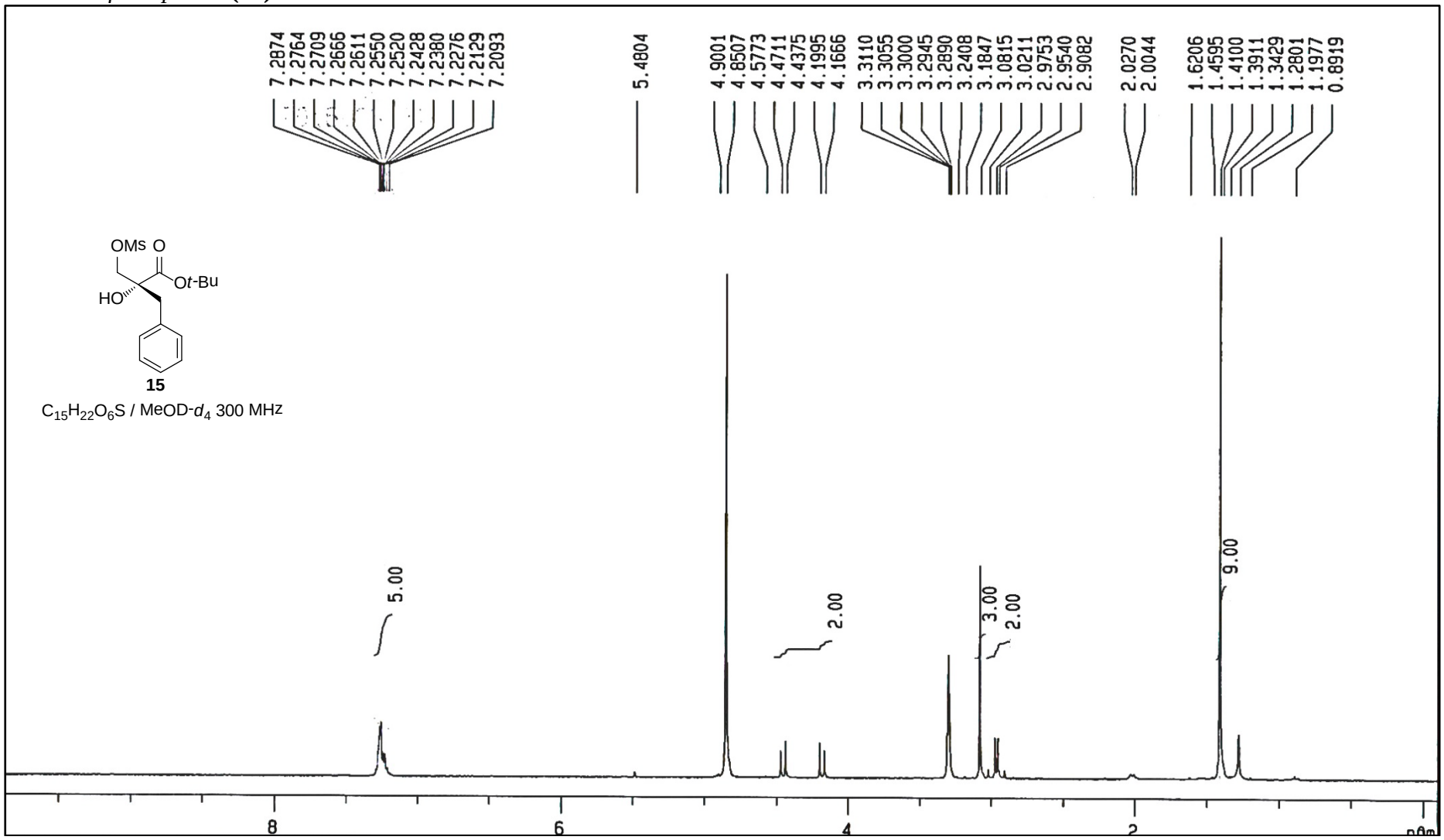
[1]H-NMR of compound **(14)**



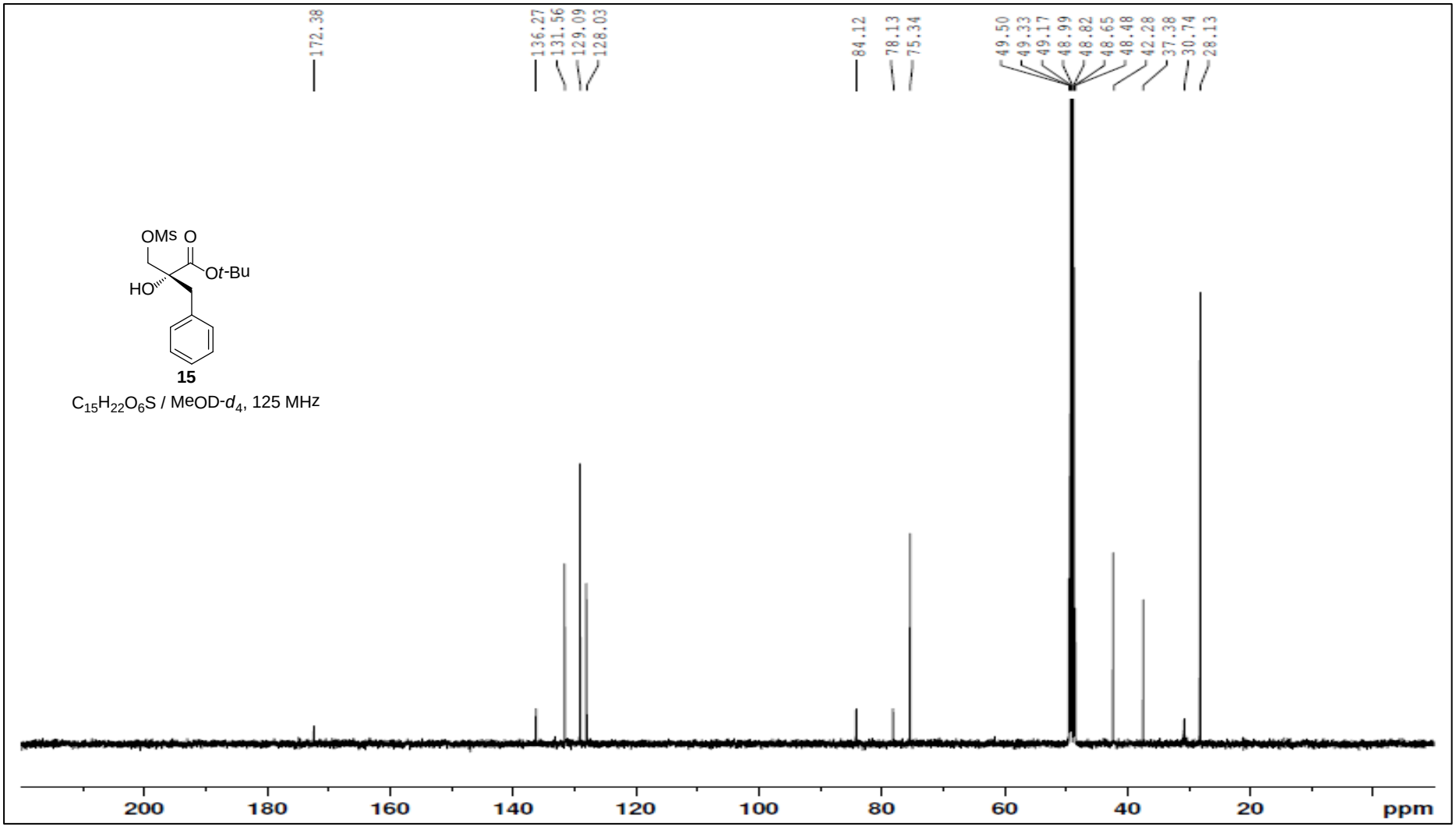
^{13}C-NMR of compound **(14)**



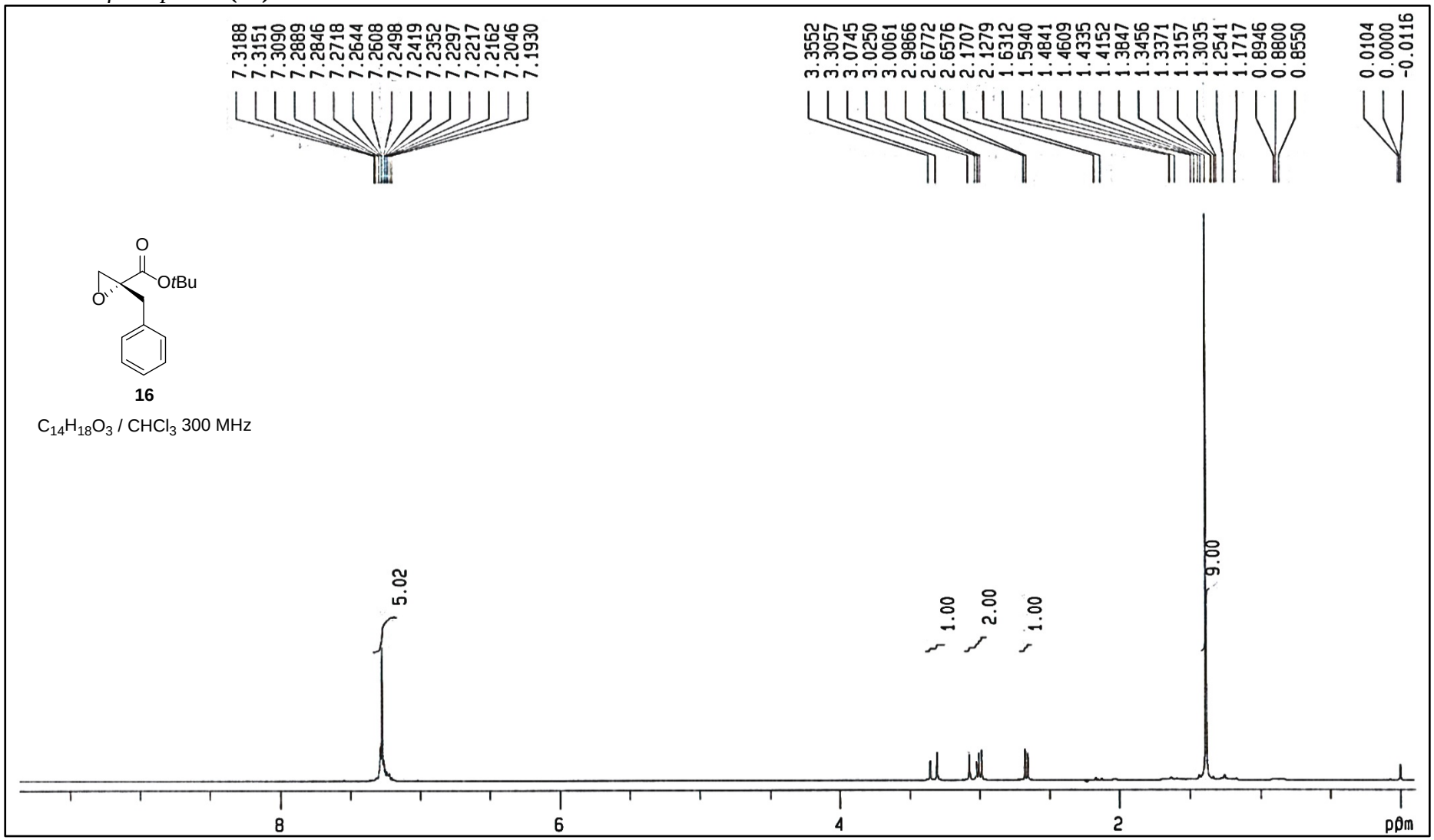
[1]H-NMR of compound **(15)**



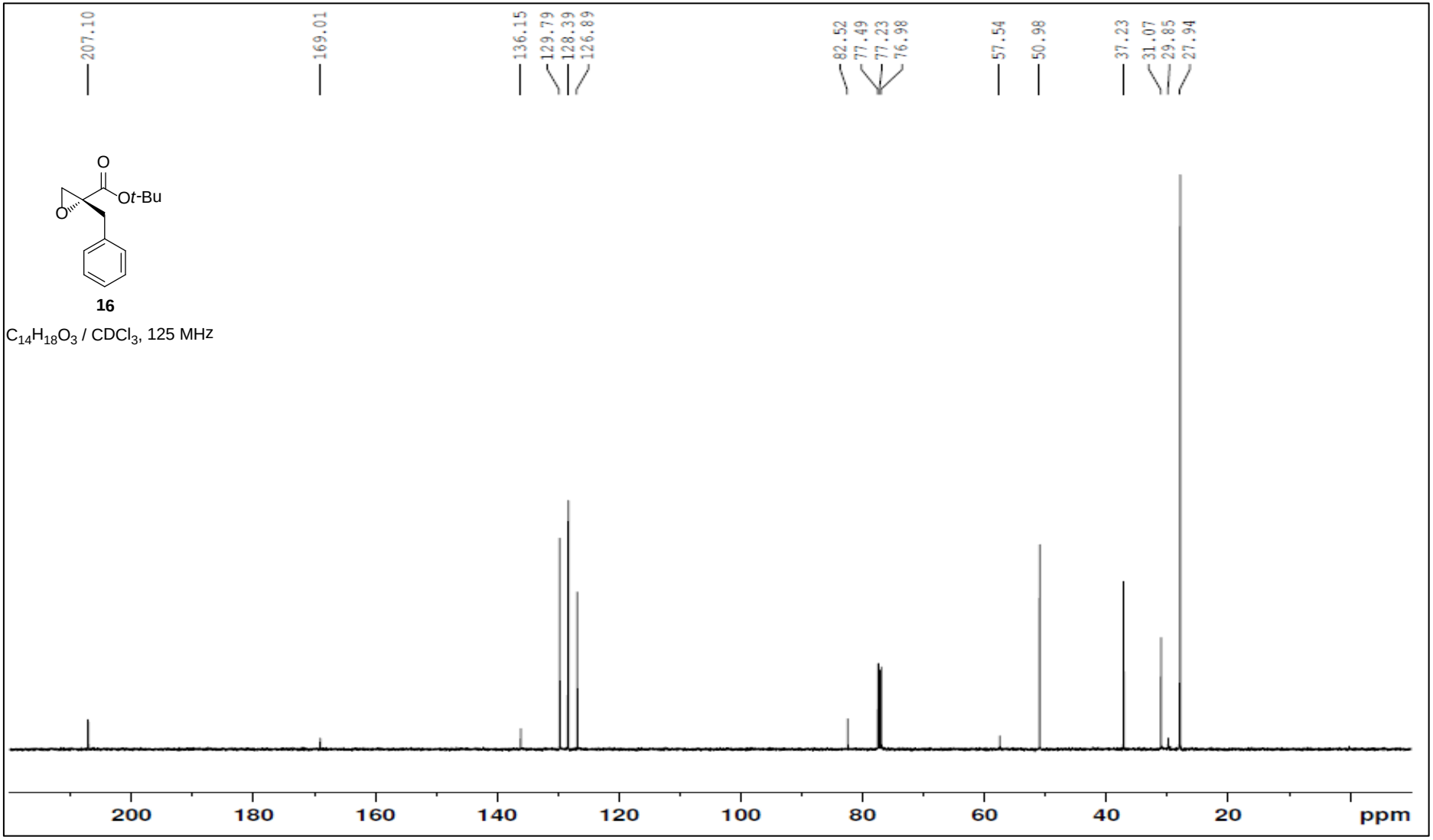
^{13}C-NMR of compound **(15)**



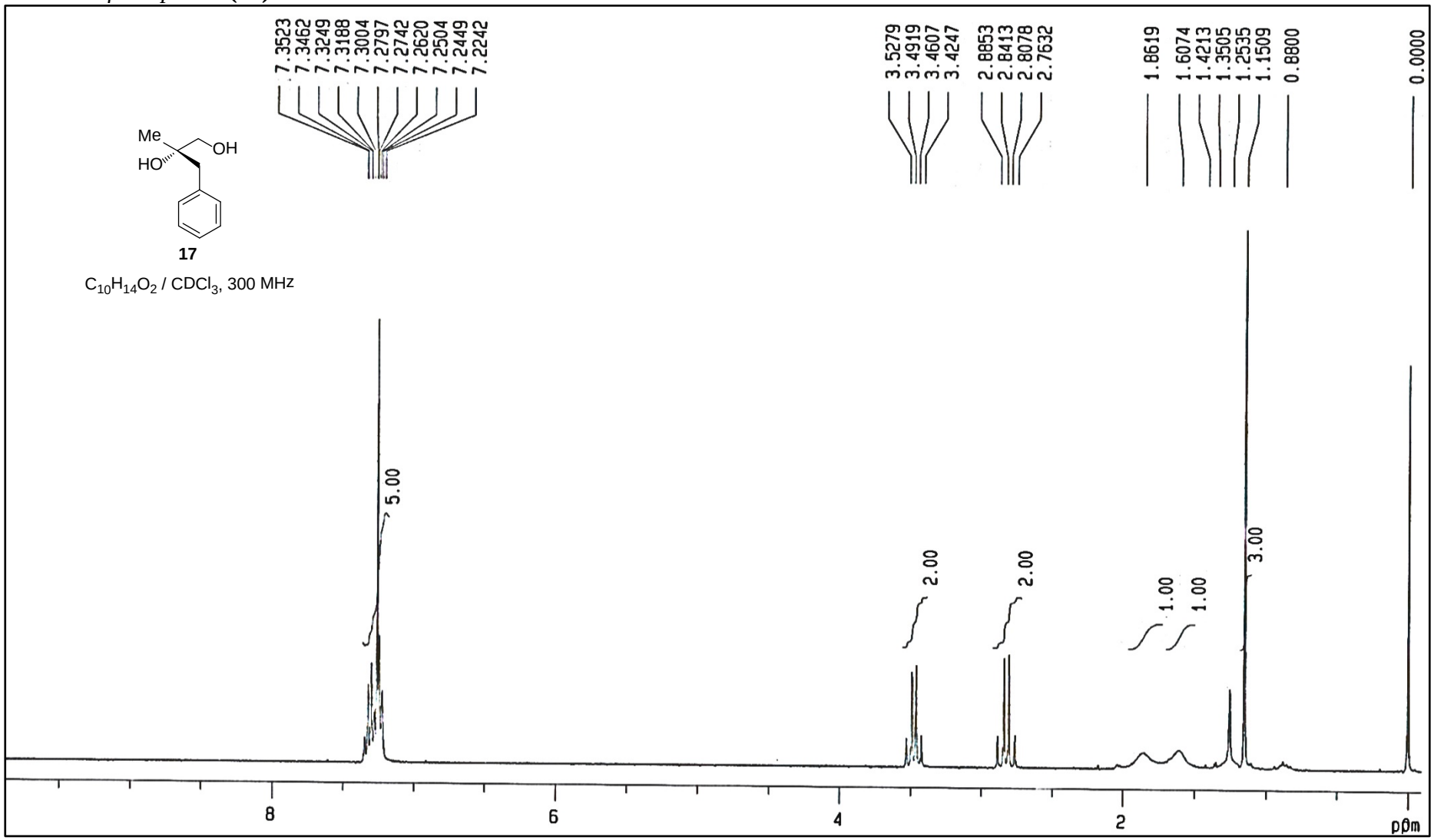
[1]H-NMR of compound **(16)**



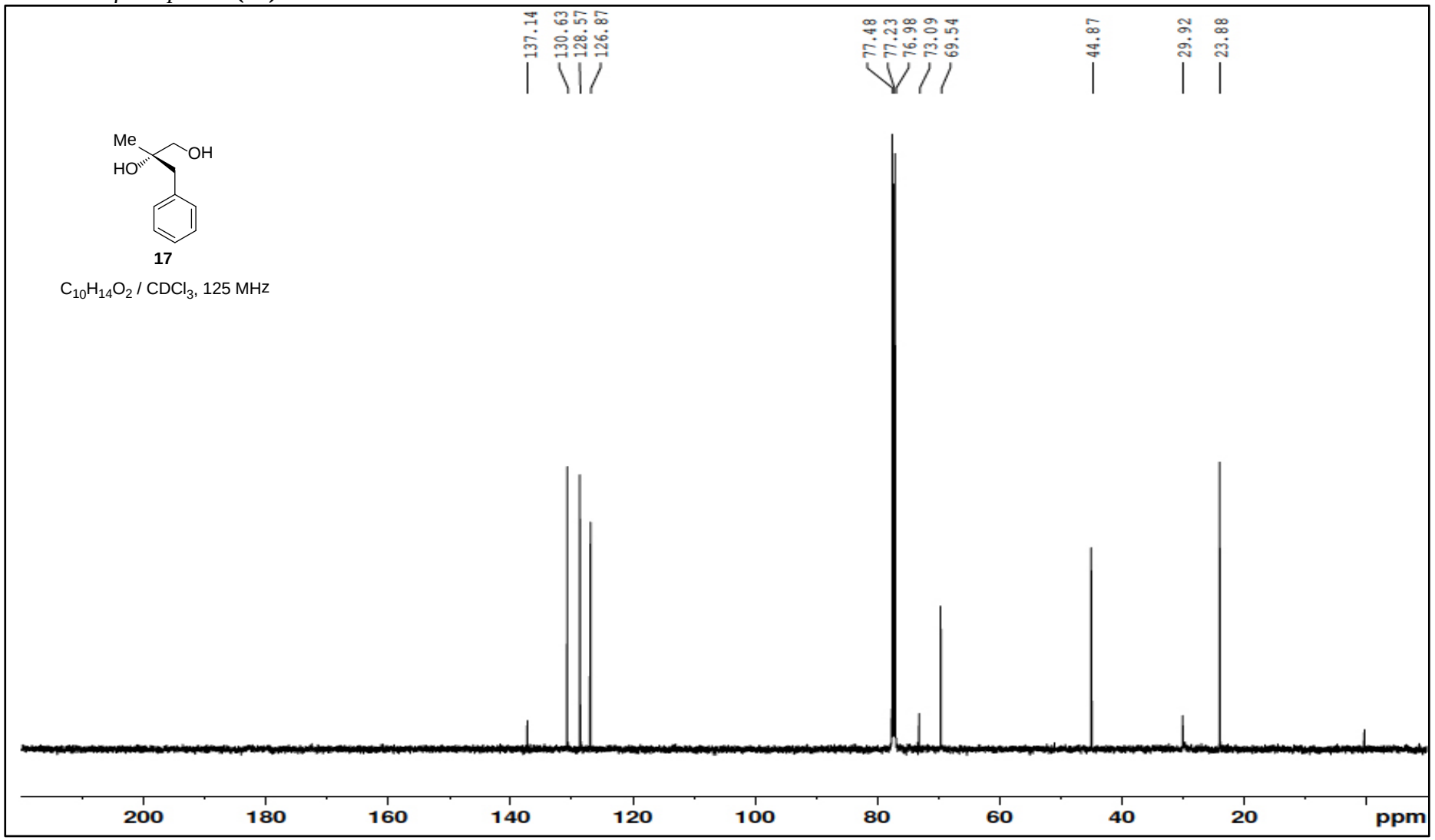
^{13}C-NMR of compound **(16)**



[1]H-NMR of compound **(17)**



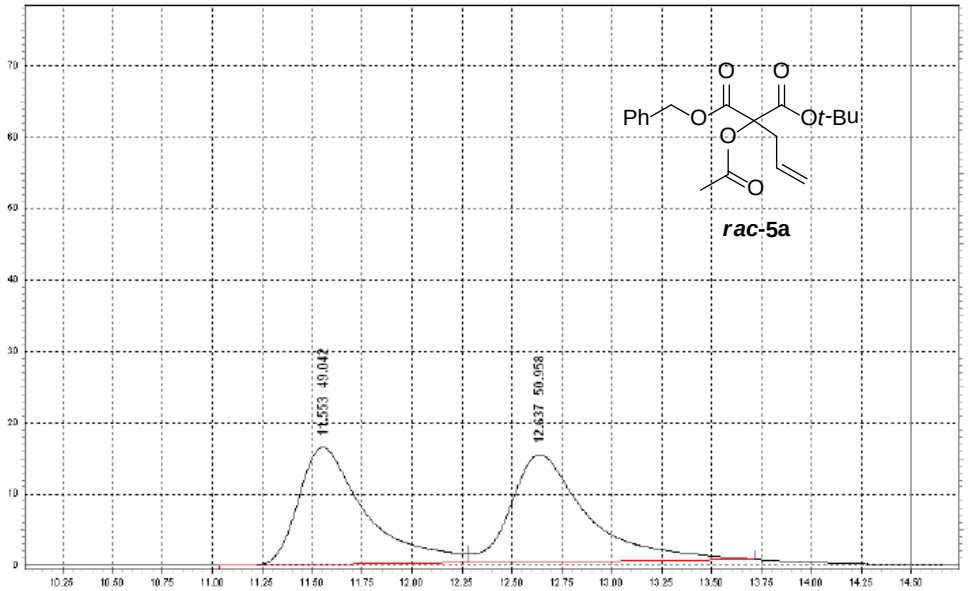
^{13}C-NMR of compound **(17)**



(4) Chiral HPLC spectra

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 99 : 1,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-5a**

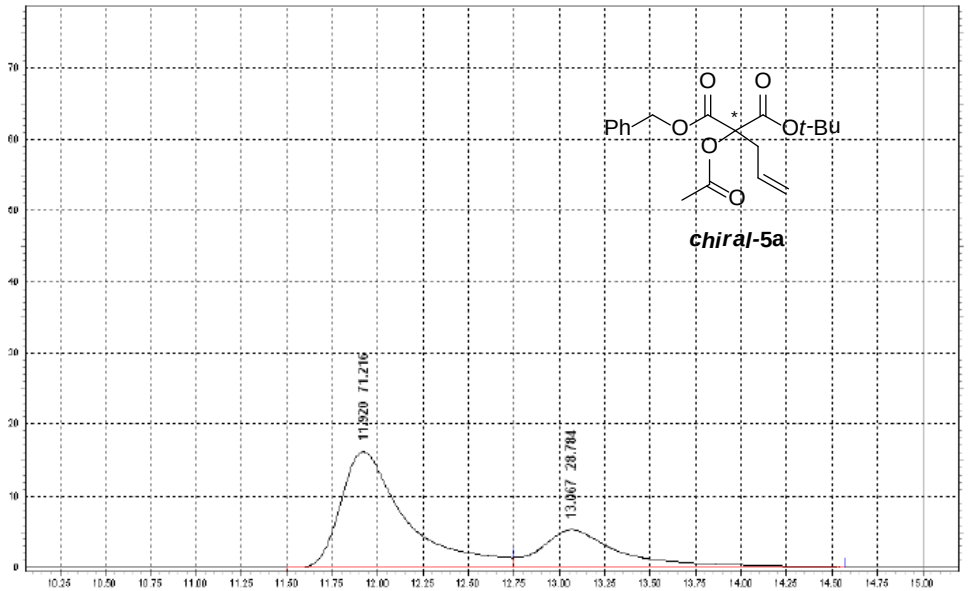


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	11.553	1519599	49.042	mm
2	12.637	1578952	50.958	mm
Totals		3098551	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 99 : 1,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-5a**

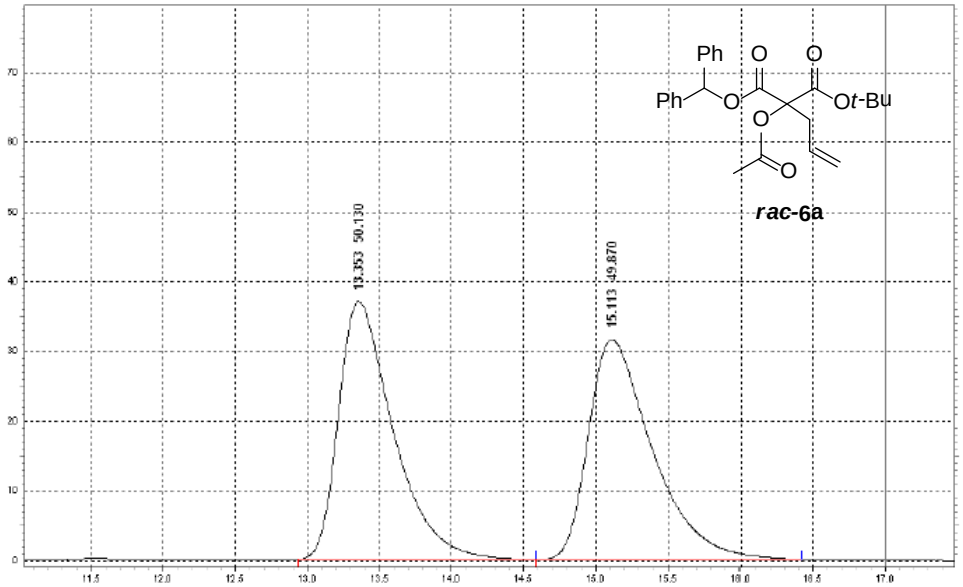


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	11.920	1610686	71.216	BV
2	13.067	651015	28.784	VI
Totals		2261701	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 95 : 5,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-6a**

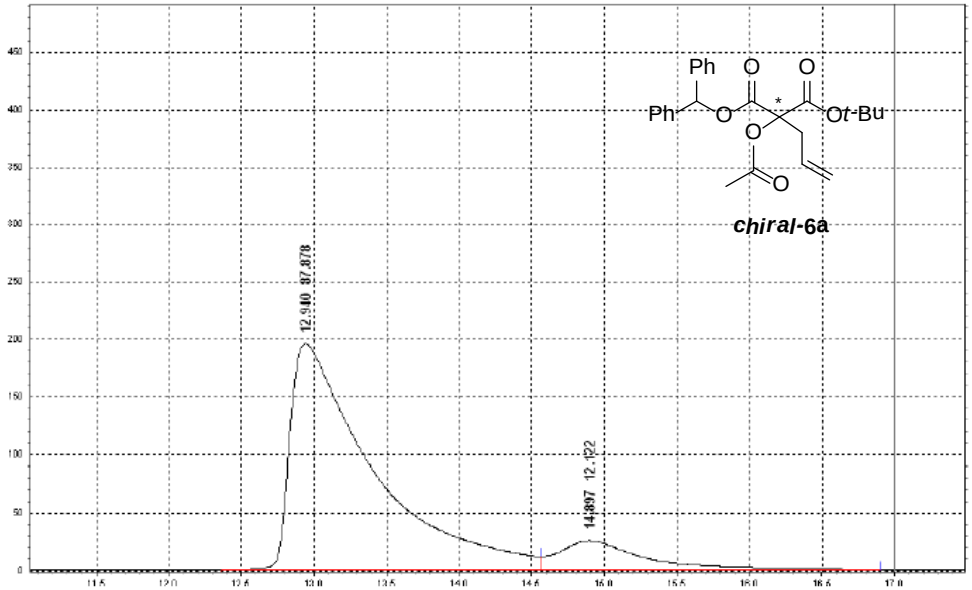


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	13.353	3905932	50.130	IB
2	15.113	3885694	49.870	BI
Totals		7791626	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 95 : 5,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-6a**

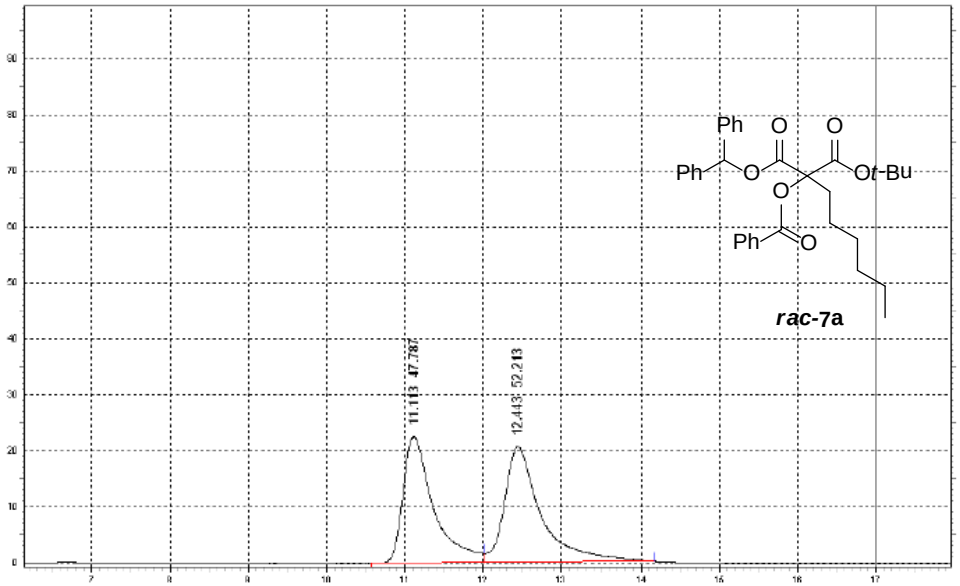


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	12.940	31092667	87.878	mm
2	14.897	4288770	12.122	mm
Totals		35381437	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7a**

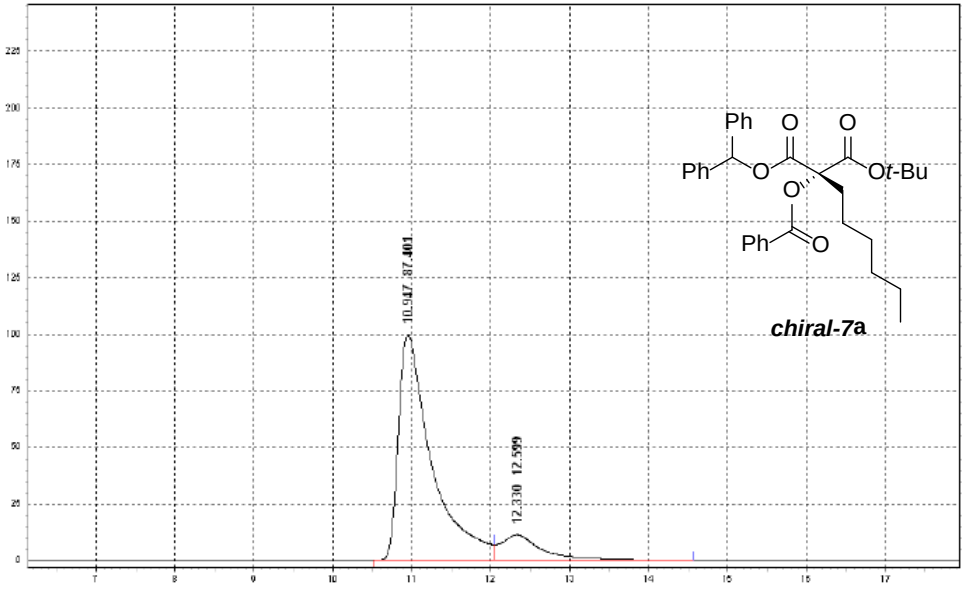


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	11.113	2448202	47.787	mm
2	12.443	2674948	52.213	mm
Totals		5123150	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7a**

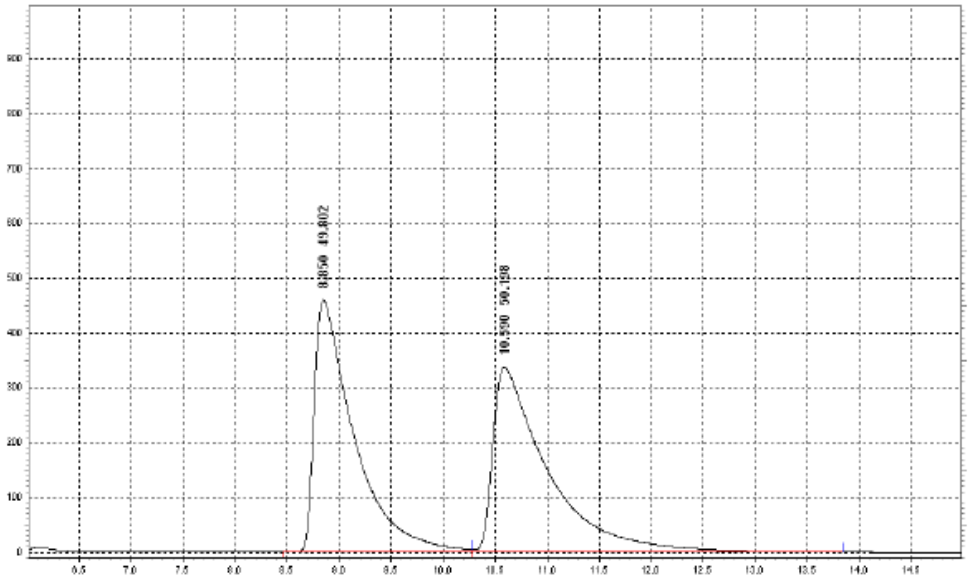


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.947	11687617	87.401	BV
2	12.330	1684859	12.599	VI
Totals		13372476	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7b**

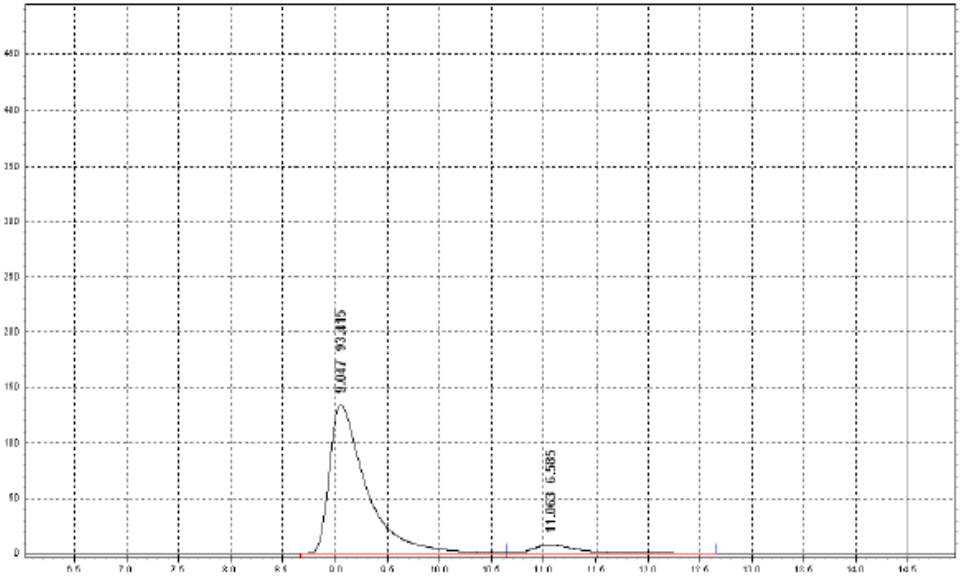


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	8.850	48687467	49.802	BV
2	10.590	49074712	50.198	VI
Totals		97762179	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7b**

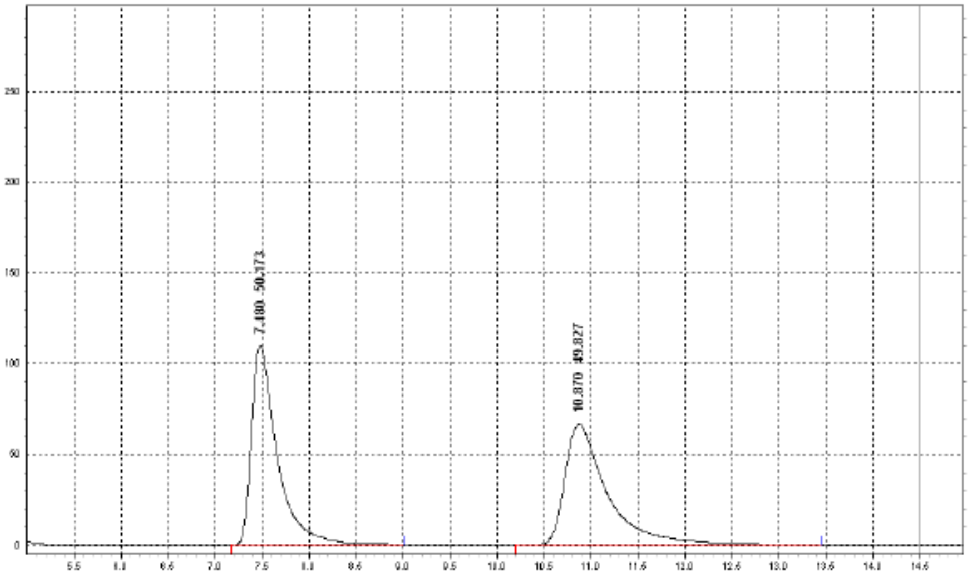


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	9.047	13176343	93.415	BV
2	11.063	928826	6.585	VI
Totals		14105169	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7c**

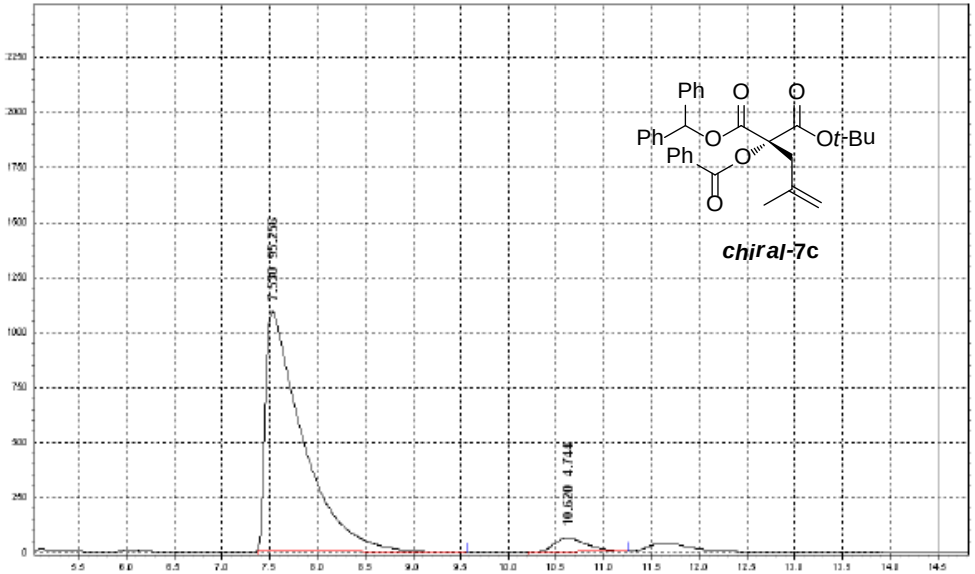


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	7.480	8431110	50.173	II
2	10.870	8373060	49.827	BI
Totals		16804170	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7c**

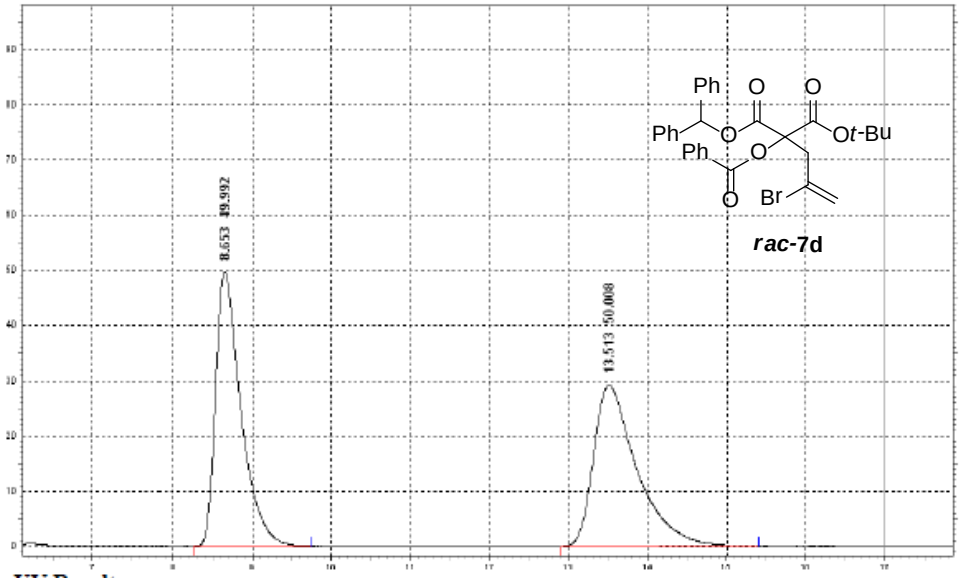


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	7.530	117974523	95.256	mm
2	10.620	5875165	4.744	BI
Totals		123849688	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7d**

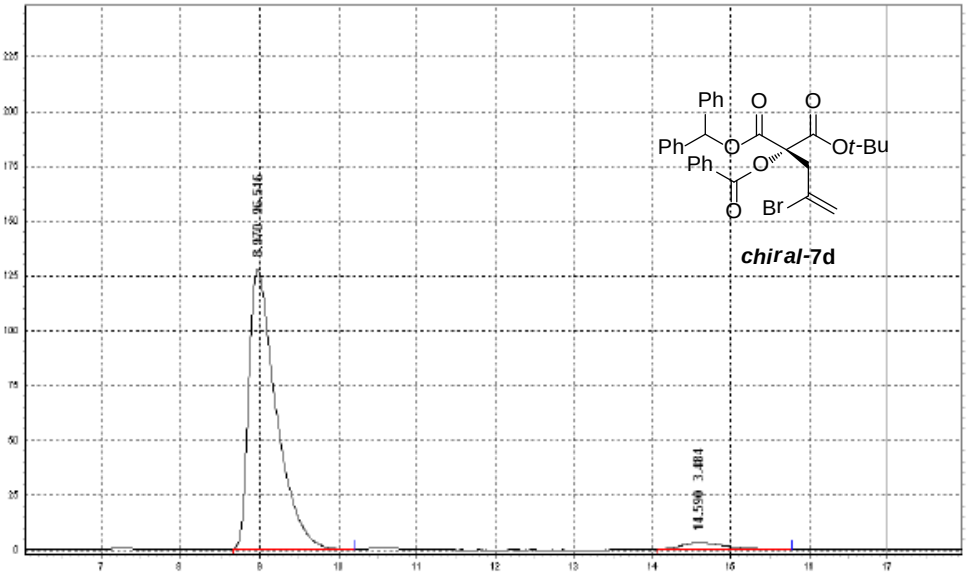


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	8.653	4418495	49.992	BI
2	13.513	4419836	50.008	II
Totals		8838331	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7d**

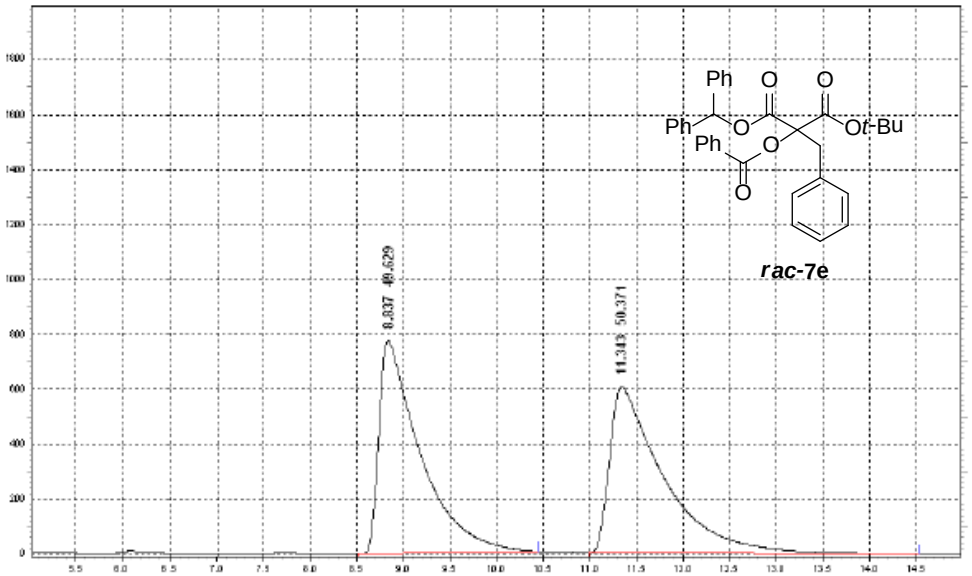


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	8.970	12330872	96.516	IB
2	14.590	445142	3.484	BB
Totals		12776014	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7e**

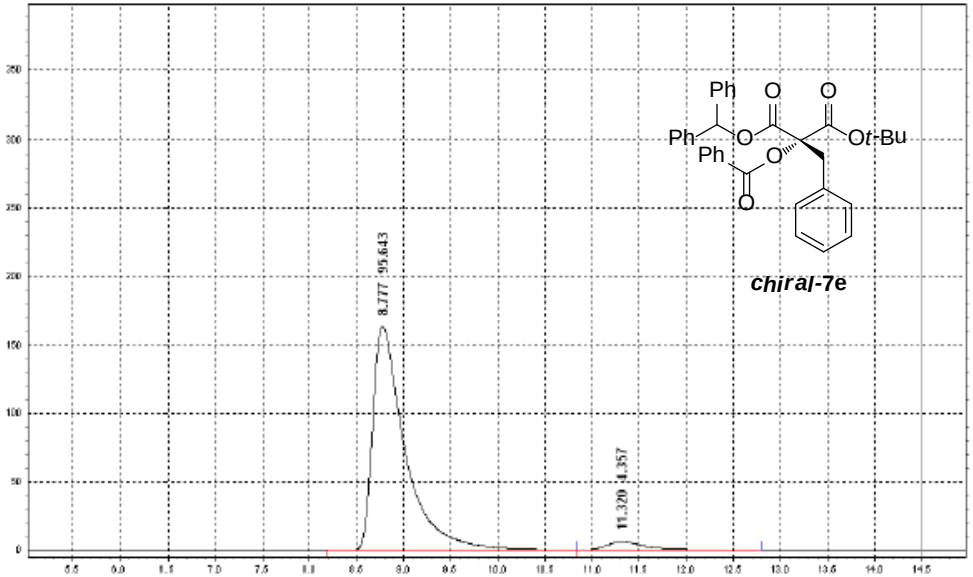


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	8.837	94795089	49.629	II
2	11.343	96211603	50.371	II
Totals		191006692	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7e**

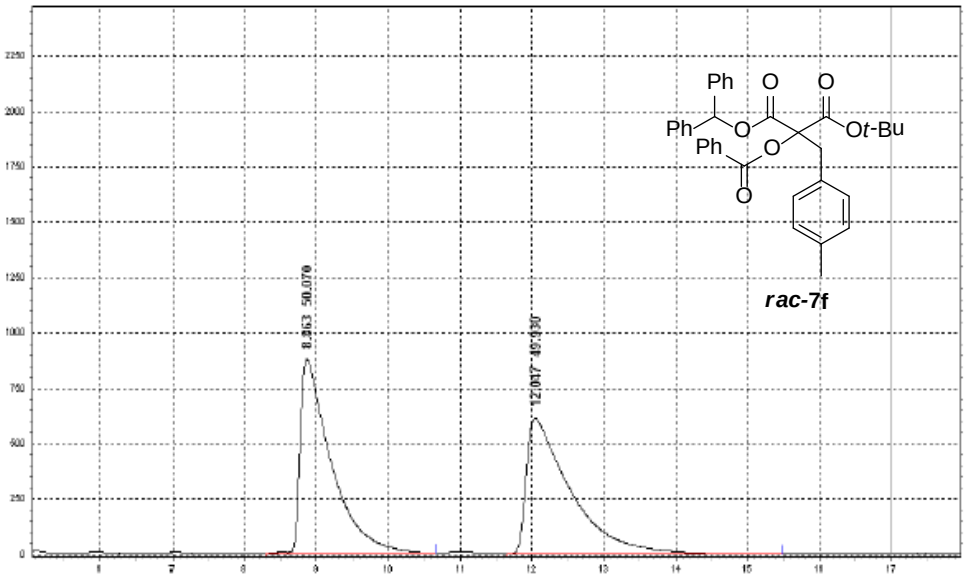


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	8.777	15679265	95.643	BV
2	11.320	714317	4.357	VI
Totals		16393582	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7f**

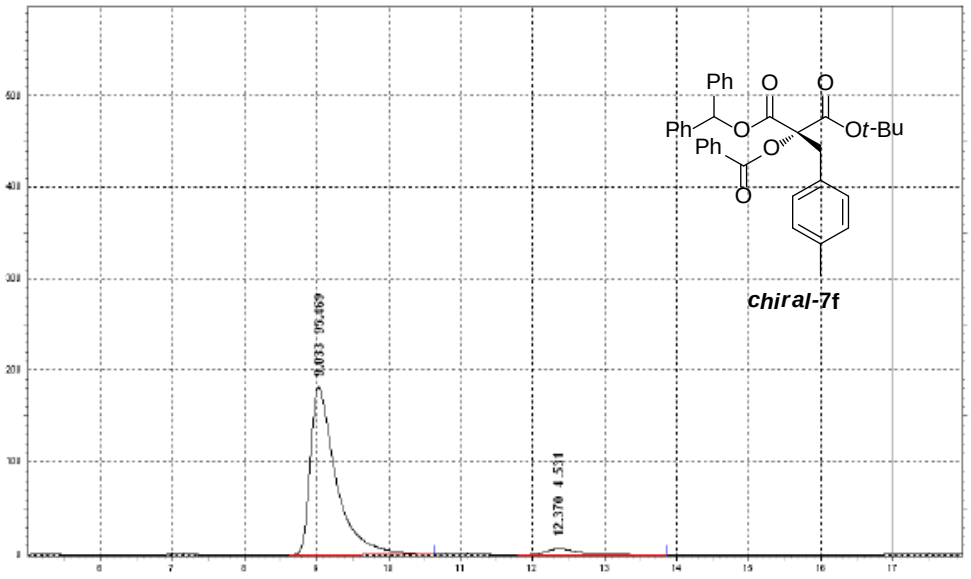


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	8.863	104653034	50.070	mm
2	12.047	104358549	49.930	II
Totals		209011583	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7f**

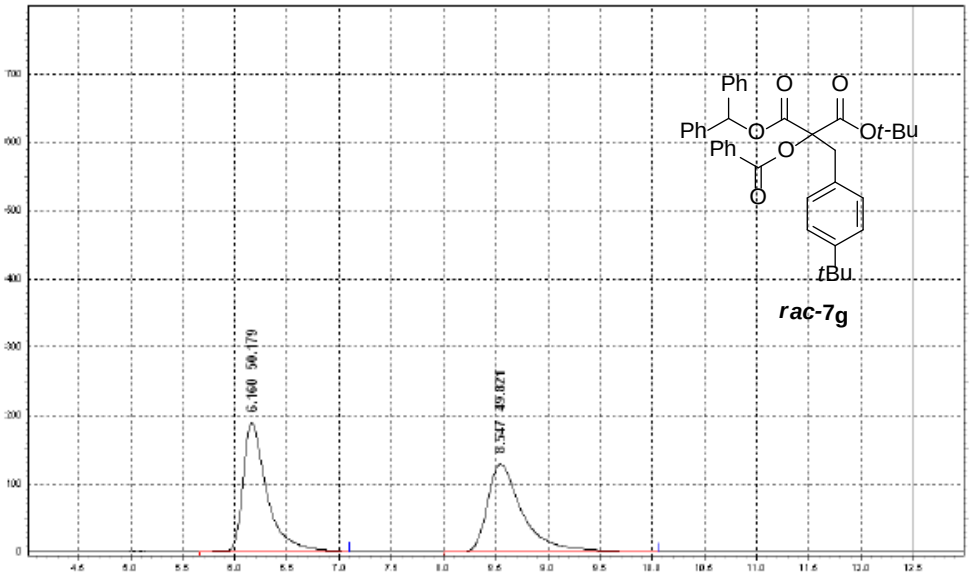


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	9.033	18022487	95.469	BB
2	12.370	855342	4.531	BI
Totals		18877829	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7g**

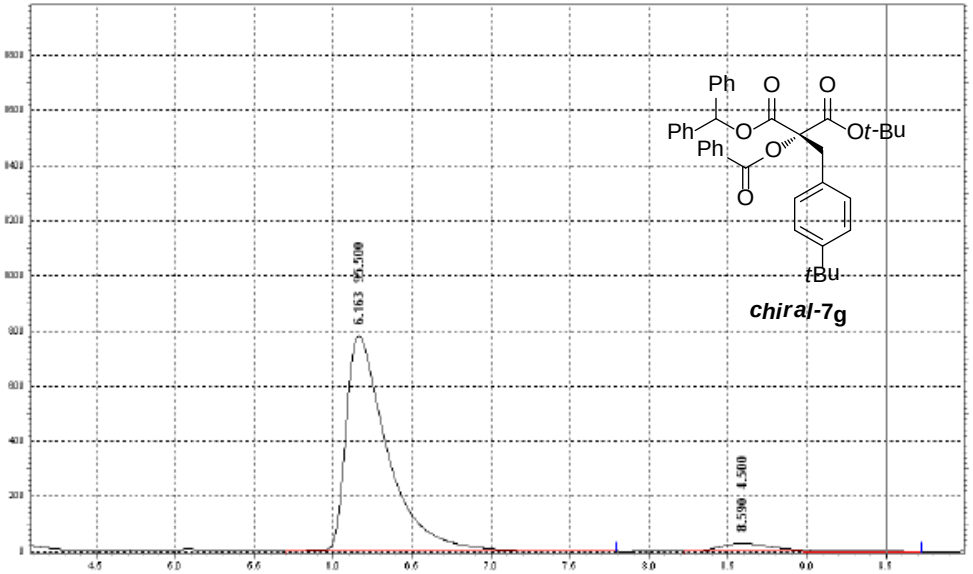


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	6.160	12096393	50.179	II
2	8.547	12010069	49.821	BI
Totals		24106462	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7g**

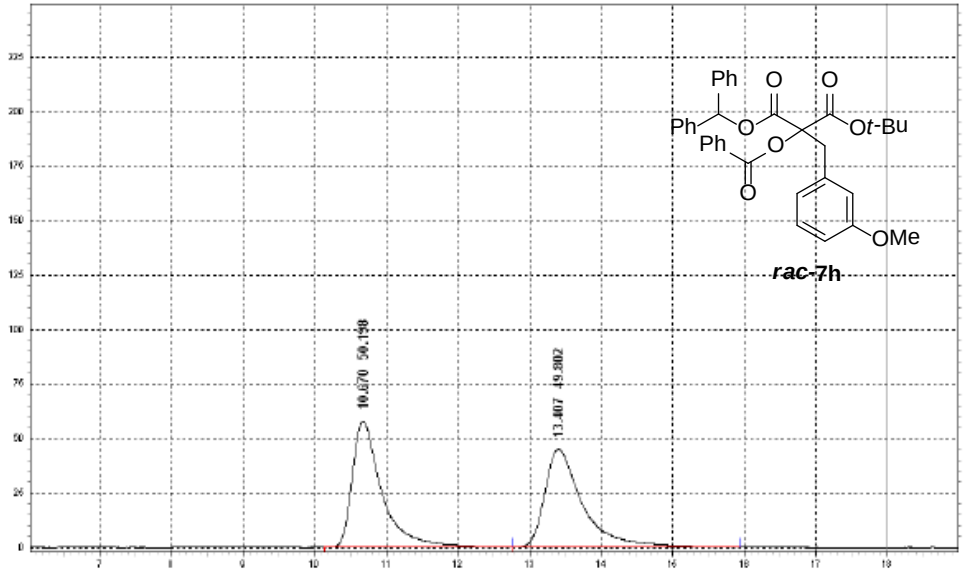


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	6.163	56826301	95.500	BI
2	8.590	2677981	4.500	II
Totals		59504282	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7h**

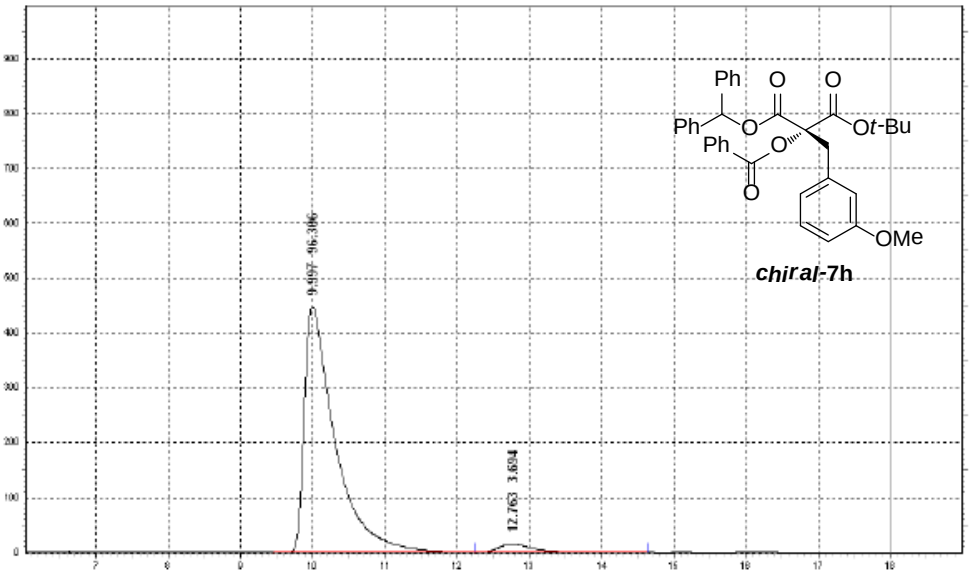


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.670	6645743	50.198	BV
2	13.407	6593233	49.802	VI
Totals		13238976	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7h**

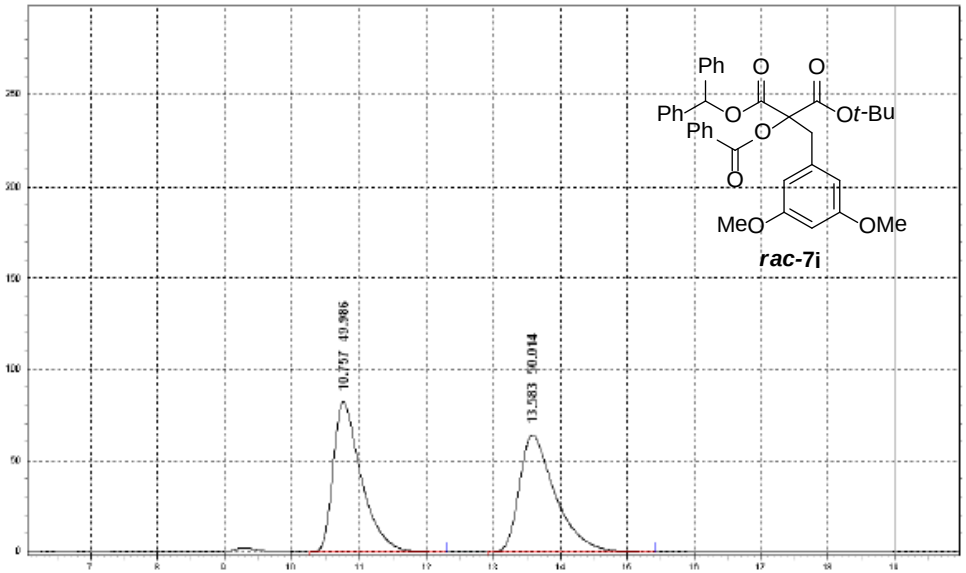


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	9.997	52886748	96.306	BV
2	12.763	2028532	3.694	VI
Totals		54915280	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7i**

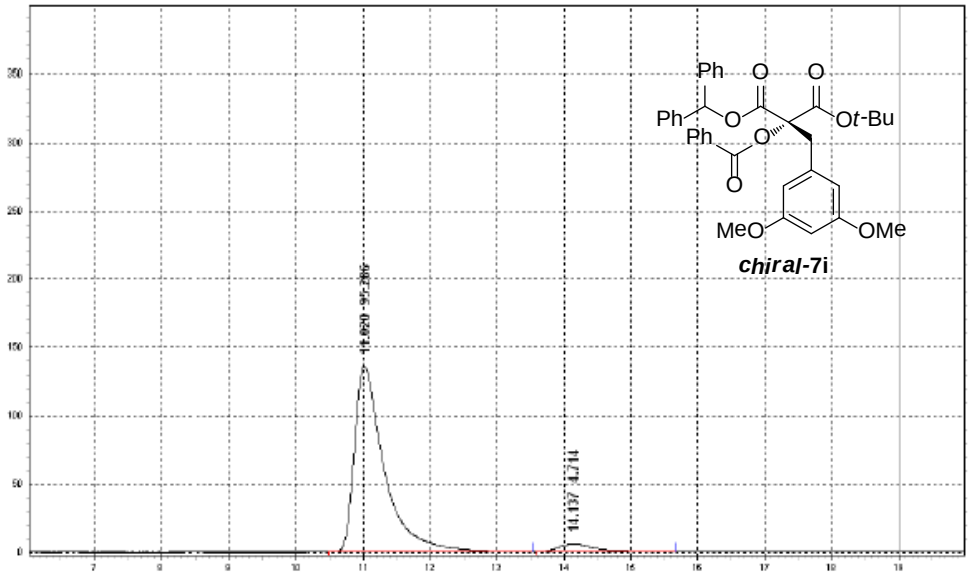


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.757	9553904	49.986	II
2	13.583	9559082	50.014	II
Totals		19112986	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7i**

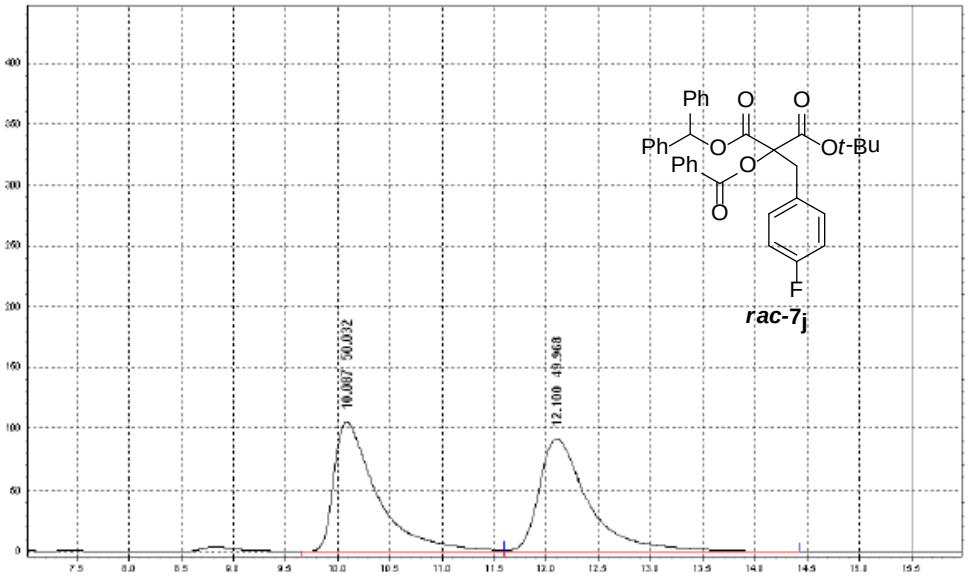


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	11.020	16910565	95.286	BB
2	14.137	836556	4.714	mm
Totals		1774712111	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7j**



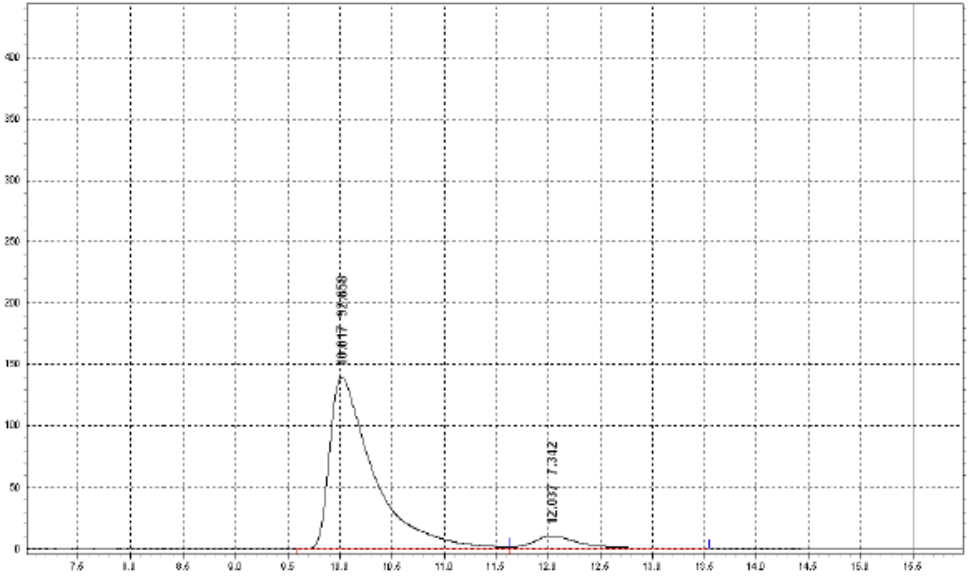
***rac*-7$_j$**

UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.087	11959106	50.032	BV
2	12.100	11943698	49.968	VI
Totals		23902804	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7j**

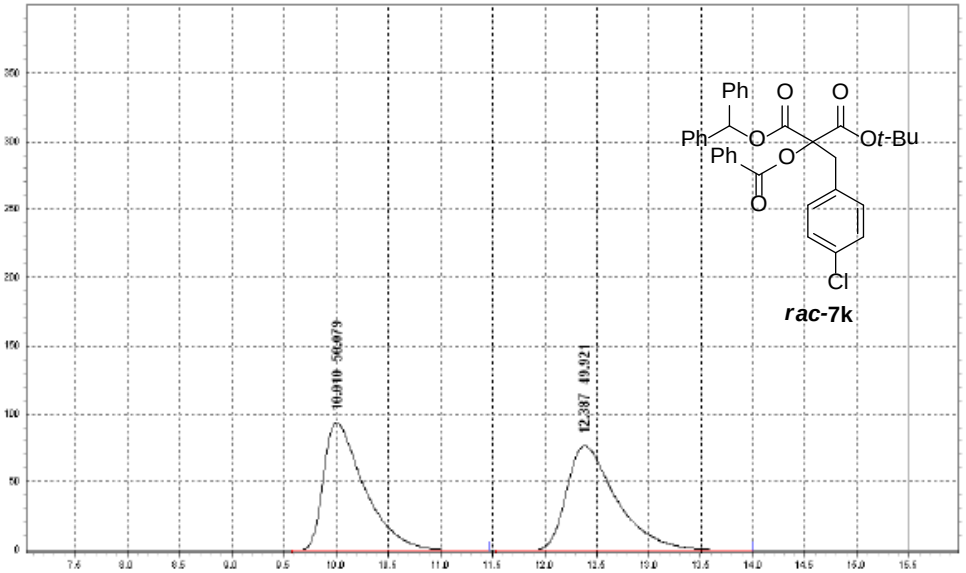


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.017	16332477	92.658	IV
2	12.037	1294175	7.342	VI
Totals		17626652	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7k**

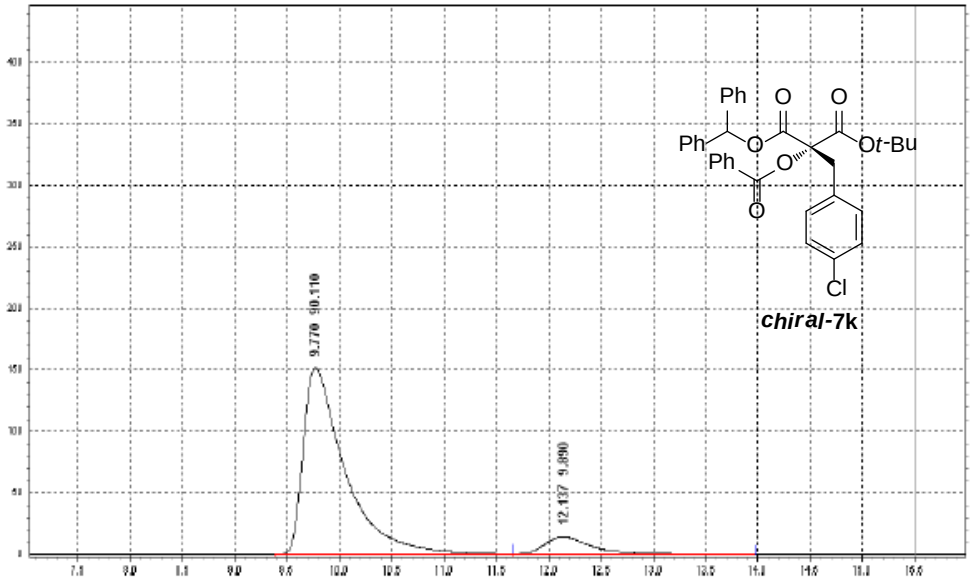


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.010	10198026	50.079	IB
2	12.387	10165832	49.921	BI
Totals		20363858	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7k**

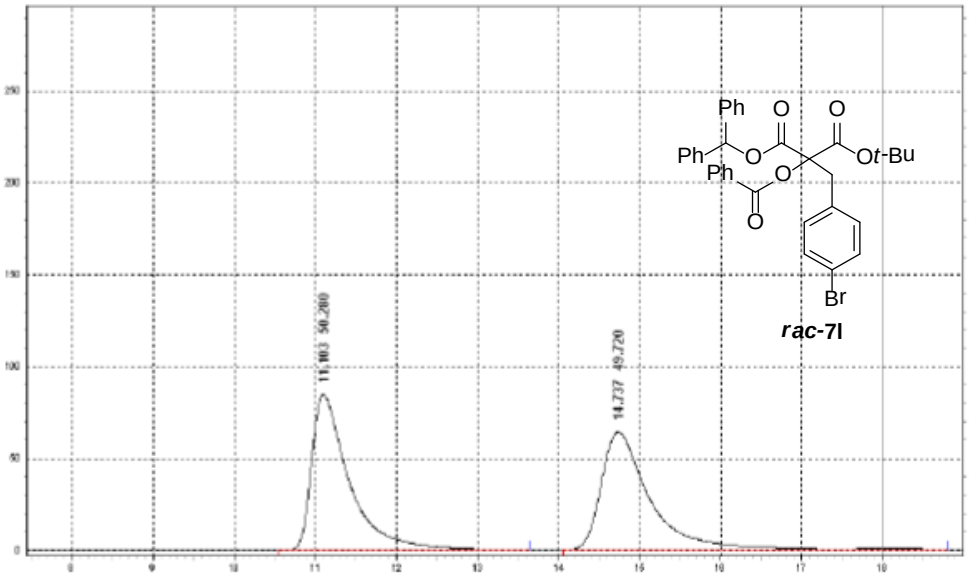


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	9.770	16868384	90.110	IV
2	12.137	1851401	9.890	VI
Totals		18719785	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7l**



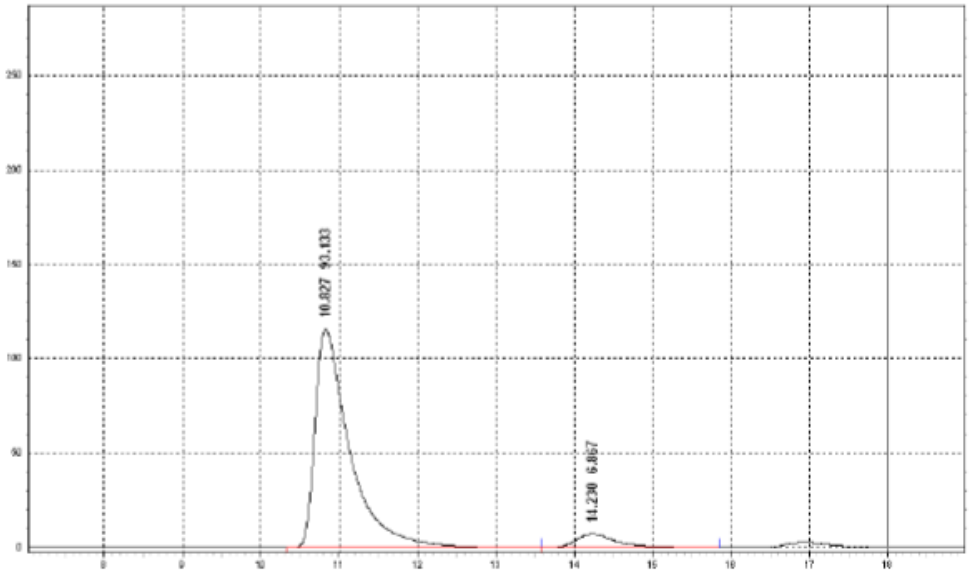
***rac*-7l**

UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	11.103	10806953	50.280	BI
2	14.737	10686722	49.720	mm
Totals		21493675	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7l**

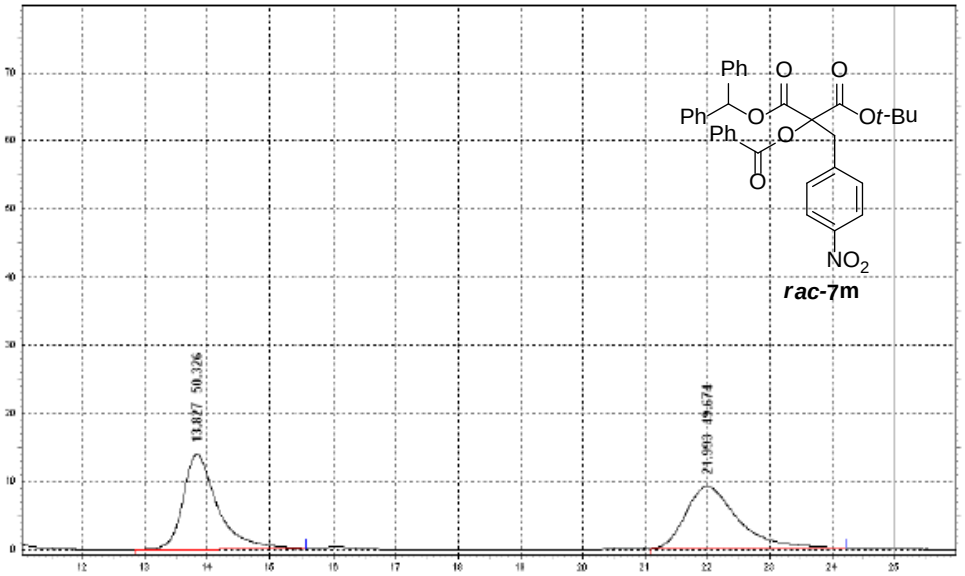


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.827	14128280	93.133	IB
2	14.230	1041734	6.867	BI
Totals		15170014	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 80 : 20,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7m**

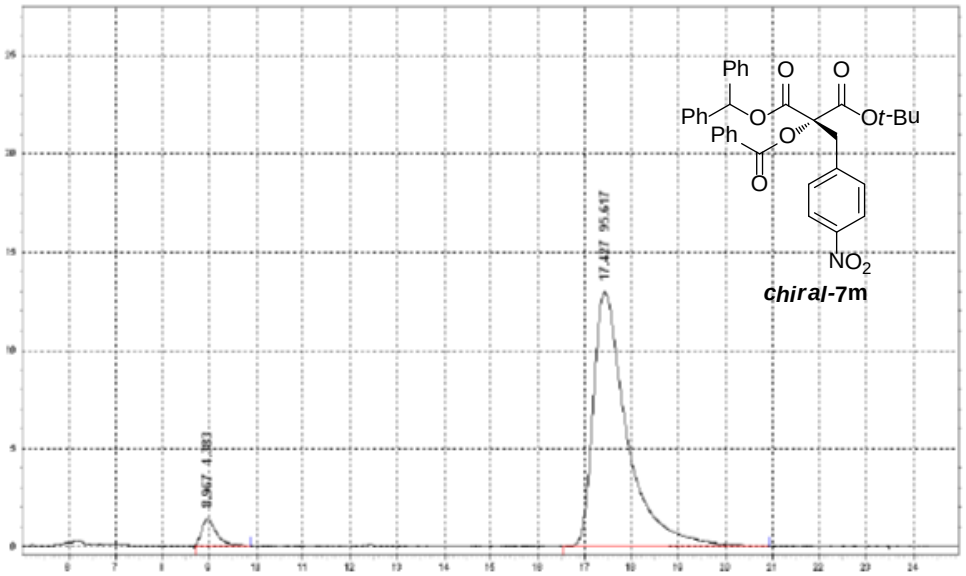


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	13.827	2116158	50.326	II
2	21.993	2088727	49.674	II
Totals		4204885	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 80 : 20,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7m**

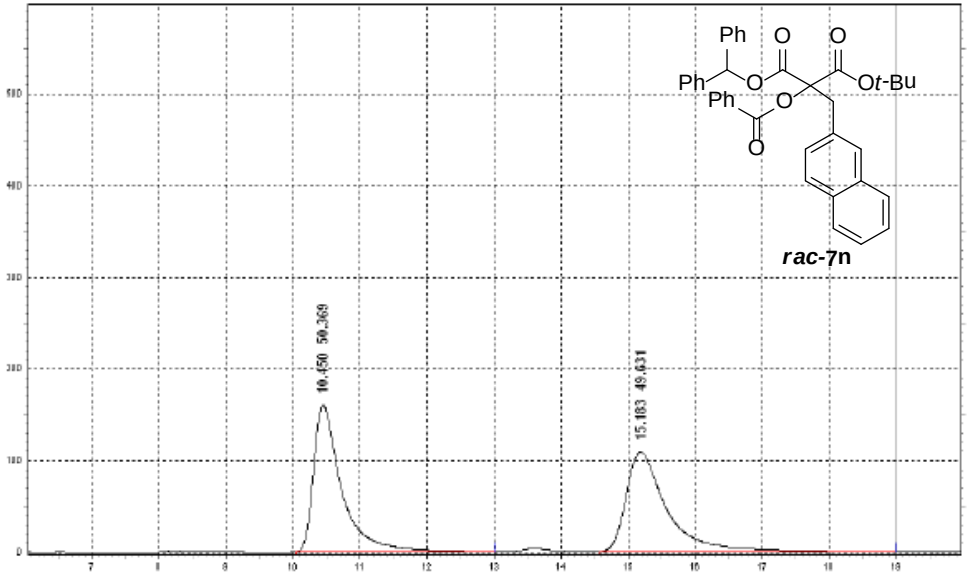


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	13.547	96123991	90.635	BB
2	21.870	9932412	9.365	II
Totals		106056403	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **rac-7n**

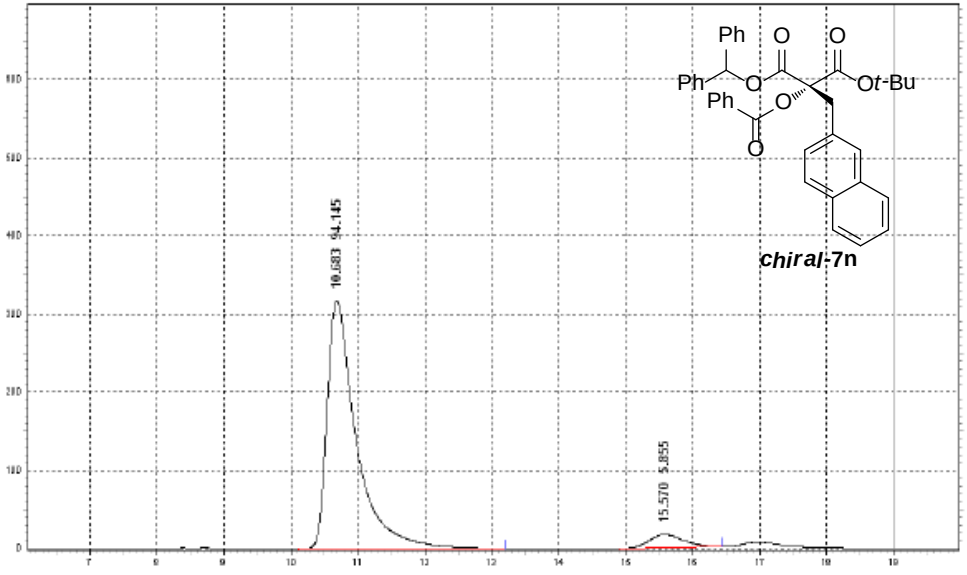


UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.450	18563642	50.369	II
2	15.183	18291531	49.631	II
Totals		36855173	100.000	

Area Percent Report

Instrument Name: L-2000
Software Version: Version LaChrom 8908800-07
Acquisition Method: Diacel Chiralpak AD-H, Hexane : 2-Propanol = 85 : 15,
λ =254nm, flow rate = 1mL/min
Sample ID: **chiral-7n**



UV Results

Name	Retention Time	Area	Area Percent	Integration Codes
1	10.683	38160932	94.145	II
2	15.570	2373226	5.855	II
Totals			100.000	

(6) References

S1. Lygo, B.; Crosby, J.; Lowdon, T. R.; Wainwright, P. G. *Tetrahedron* **2001**, *57*, 2391.

S2. Ha, M. W.; Lee, M.; Choi, S.; Kim, S.; Hong, S.; Park, Y.; Kim, M.-h.; Kim, T.-S.; Lee, J.; Lee, J. K.; Park, H.–g. **2015**, *80*, 3270.

S3. Hong, S.; Kim, M.; Jung, M,; Ha, M. W.; Lee, M.; Park, Y.; Kim, M.-h.; Kim, T.-S.; Lee, J.; Park, H.–g. **2014**, *12*, 1510.

S4. Shoba, V. M.; Thacker, N. C.; Bochat, A. J.; Takacs, J. M. *Angew. Chem., Int. Ed*. 2016, **55**, 1465