Palladium-Catalyzed Asymmetric Synthesis of 2-Pyrrolidinones with Quaternary Carbon Stereocenters

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Supplementary Information

I. General

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen or in a glove box under argon.

THF, Et_2O, toluene, and CH_2Cl_2 were purified by passing through neutral alumina columns under nitrogen. MeOH was distilled over Mg turnings under nitrogen. DMF was distilled over CaH_2 under vacuum. Et_3N was distilled over KOH under nitrogen.

Benzyl isocyanate (Wako Chemicals), 4-methoxybenzyl isocyanate (Aldrich), 4-methylbenzyl isocyanate (Aldrich), 4-bromobenzyl isocyanate (Aldrich), 2-furylmethyl isocyanate (Aldrich), 2-chloroethyl isocyanate (Aldrich), ethyl 3-isocyanatopropionate (Aldrich), 4-methoxyphenyl isocyanate (TCI), phenyl isocyanate (TCI), 4-chlorophenyl isocyanate (Aldrich), 4-biphenylacetic acid (Wako Chemicals), 4-(dimethylamino)pyridine (Wako Chemicals), 1-bromo-3,5-dimethylbenzene (TCI), (*S*)-1,1'-binaphthyl-2,2'-diol (Kankyo Kagaku Center), *N*,*N*'-dicyclohexylcarbodiimide (Wako Chemicals), dimethyl carbonate (Aldrich), *tert*-butyl alcohol (Wako Chemicals), thionyl chloride (Wako Chemicals), PCl_3 (Nacalai Tesque), NaH (Kanto Chemical; 60 wt% in mineral oil), $LiAlH_4$ (Wako Chemicals), KOH (Kishida Chemical), TBAF (Aldrich; 1.0 M solution in THF), and *t*-BuLi (Kanto Chemical; 1.65 M solution in pentane) were used as received.

2-(*tert*-Butyldimethylsiloxy)methyl-2-propen-1-yl methanesulfonate,[1] *N*,*N*'-dimethoxy-*N*,*N*'-dimethylsuccinamide,[2] **1a**,[3] **1b**,[4] **1c**,[3] **1d**,[3] **1h**,[3] (*S*,*S*,*S*)-**L1**,[5] (*S*,*S*,*S*)-**L2**,[6] (*S*,*S*,*S*)-**L3**,[7] and $PdCp(\eta^3\text{-}C_3H_5)$[8] were synthesized following the literature procedures.

All other chemicals and solvents were purchased from Aldrich, Wako Chemicals, TCI, or Kanto Chemical and used as received.

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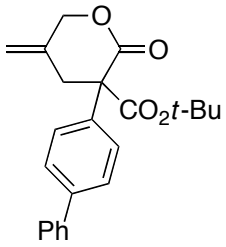
[8] (a) Shaw, B. L. *Proc. Chem. Soc.* **1960**, 247. (b) McClellan, W. R.; Hoehn, H. H.; Cripps, H. N.; Muetterties, E. L.; Howk, B. W. *J. Am. Chem. Soc.* **1961**, *83*, 1601.

II. Synthesis of Substrates and Ligand

Representative Procedure for Substrates 1:
α-*tert*-Butoxycarbonyl-α-(4-biphenyl)-γ-methylidene-δ-valerolactone (1e)



Thionyl chloride (5.50 mL, 75.4 mmol) was added to a suspension of 4-biphenylacetic acid (10.6 g, 49.9 mmol) in MeOH (170 mL) at 0 °C, and the mixture was stirred for 6 h at room temperature. After removal of the volatiles under vacuum, the residue was dissolved in dimethyl carbonate (45 mL). This solution was then added to a suspension of NaH (4.00 g, 100 mmol; 60 wt% in mineral oil) in dimethyl carbonate (15 mL) at 0 °C. The resulting mixture was stirred for 12 h while gradually raising the temperature to room temperature. The reaction was quenched with water and this was extracted with Et_2O. The organic layer was washed with saturated NaCl*aq*, dried over $MgSO_4$, filtered, and concentrated under vacuum. The solid thus obtained was washed with hexane to afford dimethyl 4-biphenylmalonate (CAS 156140-46-4) as a pale yellow solid (12.8 g, 45.0 mmol; 90% yield).

^{1}H NMR ($CDCl_3$): δ 7.61-7.56 (m, 4H), 7.47 (d, $^3J_{HH}$ = 8.3 Hz, 2H), 7.44 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 7.35 (tt, $^3J_{HH}$ = 7.4 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 4.70 (s, 1H), 3.78 (s, 6H).

KOH (13.0 mL, 13.0 mmol; 1.0 M solution in MeOH) was added to a solution of dimethyl 4-biphenylmalonate (4.26 g, 15.0 mmol) in MeOH (15 mL) and the mixture was stirred for 1.5 h at room temperature. The solvent was removed under vacuum and the residue was dissolved in 5% $NaHCO_3$*aq*. This was washed with EtOAc (2 times) and the organic layer was extracted with 5% $NaHCO_3$*aq* (2 times). The combined aqueous layer was acidified with 1 M HCl*aq* and extracted with EtOAc (3 times). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford monomethyl 4-biphenylmalonate as a yellow solid (3.00 g, 11.1 mmol; 74% yield).

^{1}H NMR ($CDCl_3$): δ 7.60 (d, $^3J_{HH}$ = 8.4 Hz, 2H), 7.59-7.55 (m, 2H), 7.47 (d, $^3J_{HH}$ = 8.1 Hz, 2H), 7.44 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 7.36 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 4.71 (s, 1H), 3.82 (s, 3H).

4-(Dimethylamino)pyridine (40.0 mg, 0.327 mmol), *tert*-butyl alcohol (1.20 mL, 12.8 mmol), and *N*,*N*'-dicyclohexylcarbodiimide (2.80 g, 13.6 mmol) were successively added to a solution of monomethyl 4-biphenylmalonate (2.70 g, 9.99 mmol) in CH_2Cl_2 (60 mL) at 0 °C. The resulting mixture was stirred for 1 h while gradually raising the temperature to room temperature, and the precipitate that formed was filtered off through Celite with Et_2O. After removing the solvent under vacuum, the residue was chromatographed on silica gel with EtOAc/hexane = 1/15→1/10 to afford *tert*-butyl methyl 4-biphenylmalonate as a yellow solid (3.04 g, 9.31 mmol; 93% yield).

^{1}H NMR ($CDCl_3$): δ 7.61-7.56 (m, 4H), 7.46 (d, $^3J_{HH}$ = 8.4 Hz, 2H), 7.44 (t, $^3J_{HH}$ = 7.8 Hz, 2H), 7.35 (tt, $^3J_{HH}$ = 7.4 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 4.60 (s, 1H), 3.77 (s, 3H), 1.47 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.1, 167.3, 141.2, 140.8, 132.2, 129.8, 128.9, 127.5, 127.4, 127.3, 82.7, 58.7, 52.8, 28.0.

A solution of *tert*-butyl methyl 4-biphenylmalonate (3.02 g, 9.25 mmol) in THF (16 mL) was added to a suspension of NaH (390 mg, 9.75 mmol; 60 wt% in mineral oil) in THF (5 mL) at 0 °C. The mixture was stirred for 40 min at 0 °C and a solution of 2-(*tert*-

butyldimethylsiloxy)methyl-2-propen-1-yl methanesulfonate (3.00 g, 10.7 mmol) in THF (12 mL) was added to it. DMF (2 mL) was then added to this mixture and it was stirred for 48 h at 55 °C. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with saturated NaCl*aq*, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/15 to afford *tert*-butyl methyl (2-(*tert*-butyldimethylsiloxy)methyl-2-propen-1-yl)(4-biphenyl)malonate as a yellow oil (4.52 g, 8.85 mmol; 96% yield).

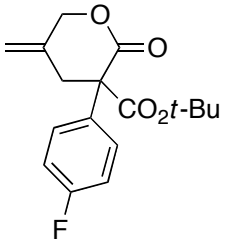
^{1}H NMR ($CDCl_3$): δ 7.61-7.57 (m, 4H), 7.54 (d, $^3J_{HH}$ = 8.6 Hz, 2H), 7.43 (t, $^3J_{HH}$ = 7.7 Hz, 2H), 7.34 (tt, $^3J_{HH}$ = 7.4 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 5.17-5.15 (m, 1H), 4.78-4.76 (m, 1H), 3.82 (bs, 2H), 3.76 (s, 3H), 3.12 (d, $^2J_{HH}$ = 15.5 Hz, 1H), 3.07 (d, $^2J_{HH}$ = 15.5 Hz, 1H), 1.44 (s, 9H), 0.88 (s, 9H), 0.01 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 171.3, 169.2, 143.7, 140.8, 140.3, 135.9, 128.89, 128.88, 127.5, 127.2, 126.7, 113.0, 82.4, 66.5, 62.8, 52.6, 38.5, 27.9, 26.0, 18.5, –5.3.

TBAF (10.0 mL, 1.0 mmol; 1.0 M solution in THF) was added to a solution of *tert*-butyl methyl (2-(*tert*-butyldimethylsiloxy)methyl-2-propen-1-yl)(4-biphenyl)malonate (4.50 g, 8.81 mmol) in THF (28 mL) at –65 °C. The mixture was stirred for 11 h while gradually raising the temperature to –5 °C and the reaction was quenched with water. After extraction with Et_2O, the organic layer was washed with saturated NaCl*aq*, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/7→1/4 and the solid thus obtained was washed with hexane to afford compound **1e** as a white solid (2.25 g, 6.17 mmol; 70% yield).

^{1}H NMR ($CDCl_3$): δ 7.63-7.57 (m, 4H), 7.46-7.40 (m, 4H), 7.35 (tt, $^3J_{HH}$ = 7.4 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 5.15-5.11 (m, 1H), 5.08-5.03 (m, 1H), 4.81 (d, $^2J_{HH}$ = 14.6 Hz, 1H), 4.68 (d, $^2J_{HH}$ = 14.6 Hz, 1H), 3.49 (d, $^2J_{HH}$ = 16.1 Hz, 1H), 3.25 (d, $^2J_{HH}$ = 16.2 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.5, 168.3, 141.1, 140.5, 136.6, 134.6, 128.9, 127.9, 127.7, 127.4, 127.2, 112.2, 83.7, 71.3, 59.8, 36.1, 27.9. HRMS (ESI-TOF) calcd for $C_{23}H_{24}O_4Na$ ($M+Na^+$) 387.1567, found 387.1559.

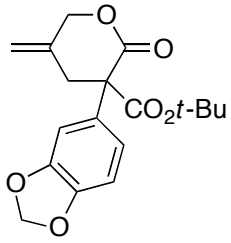
Analytical Data for Other New Substrates:

α-*tert*-Butoxycarbonyl-α-(4-fluorophenyl)-γ-methylidene-δ-valerolactone (1f)



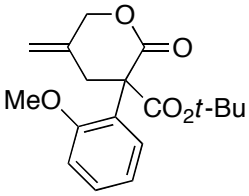
^{1}H NMR ($CDCl_3$): δ 7.34 (dd, $^3J_{HH}$ = 9.0 Hz and $^4J_{HF}$ = 5.1 Hz, 2H), 7.07 (t, ^3J = 8.7 Hz, 2H), 5.13-5.10 (m, 1H), 5.07-5.03 (m, 1H), 4.80 (d, $^2J_{HH}$ = 14.6 Hz, 1H), 4.65 (d, $^2J_{HH}$ = 14.8 Hz, 1H), 3.45 (d, $^2J_{HH}$ = 16.0 Hz, 1H), 3.16 (d, $^2J_{HH}$ = 16.1 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.2, 168.2, 162.6 (d, $^1J_{CF}$ = 248 Hz), 136.4, 131.4 (d, $^4J_{CF}$ = 3.1 Hz), 129.4 (d, $^3J_{CF}$ = 8.3 Hz), 115.6 (d, $^2J_{CF}$ = 21.7 Hz), 112.3, 83.8, 71.3, 59.4, 36.2, 27.8. HRMS (ESI-TOF) calcd for $C_{17}H_{19}FO_4Na$ ($M+Na^+$) 329.1160, found 329.1157.

α-*tert*-Butoxycarbonyl-α-(3,4-methylenedioxyphenyl)-γ-methylidene-δ-valerolactone (1g)



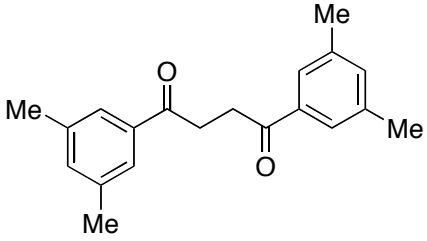
^{1}H NMR ($CDCl_3$): δ 6.85 (dd, $^4J_{HH}$ = 1.3 Hz and $^5J_{HH}$ = 0.9 Hz, 1H), 6.82-6.78 (m, 2H), 5.98-5.96 (m, 2H), 5.12-5.09 (m, 1H), 5.05-5.01 (m, 1H), 4.77 (d, $^2J_{HH}$ = 14.7 Hz, 1H), 4.65 (d, $^2J_{HH}$ = 14.6 Hz, 1H), 3.42 (d, $^2J_{HH}$ = 16.2 Hz, 1H), 3.14 (d, $^2J_{HH}$ = 16.3 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.5, 168.3, 148.1, 147.6, 136.6, 129.1, 120.9, 112.0, 108.4, 108.3, 101.5, 83.6, 71.2, 59.6, 36.0, 27.9. HRMS (ESI-TOF) calcd for $C_{18}H_{20}O_6Na$ ($M+Na^+$) 355.1152, found 355.1148.

α-*tert*-Butoxycarbonyl-α-(2-methoxyphenyl)-γ-methylidene-δ-valerolactone (1i)



^{1}H NMR ($CDCl_3$): δ 7.32-7.27 (m, 1H), 7.11 (dd, $^3J_{HH}$ = 7.9 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 6.95-6.91 (m, 2H), 4.96-4.92 (m, 2H), 4.88-4.80 (m, 2H), 3.82 (s, 3H), 3.38 (d, $^2J_{HH}$ = 15.1 Hz, 1H), 3.21 (d, $^2J_{HH}$ = 15.1 Hz, 1H), 1.47 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.1, 168.4, 157.1, 137.1, 129.4, 127.9, 126.8, 120.9, 112.2, 111.9, 83.0, 72.1, 60.2, 55.7, 36.9, 27.9. HRMS (ESI-TOF) calcd for $C_{18}H_{22}O_5Na$ ($M+Na^+$) 341.1359, found 341.1350.

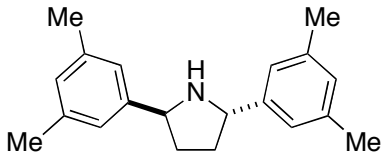
1,4-Bis(3,5-dimethylphenyl)-1,4-butanedione (CAS 860704-61-6)



t-BuLi (15.0 mL, 24.8 mmol; 1.65 M solution in pentane) was added slowly over 9 min to a solution of 1-bromo-3,5-dimethylbenzene (1.65 mL, 12.0 mmol) in Et_2O (12 mL) at –75 °C and the mixture was stirred for 30 min at –75 °C and for 10 min at room temperature. This was cooled to 0 °C and a solution of *N*,*N*'-dimethoxy-*N*,*N*'-dimethylsuccinamide (1.02 g, 4.99 mmol) in THF (10 mL) was added to it. The mixture was stirred for 1 h at 0 °C and for 1 h at room temperature. The reaction was quenched with saturated NH_4Cl*aq* and diluted with H_2O. After extraction with $CHCl_3$, the organic layer was washed with saturated NaCl*aq*, dried over $MgSO_4$, filtered, and concentrated under vacuum. The resulting solid was washed with Et_2O/hexane to afford 1,4-bis(3,5-dimethylphenyl)-1,4-butanedione as a white solid (952 mg, 3.23 mmol; 65% yield).

^{1}H NMR ($CDCl_3$): δ 7.65 (s, 4H), 7.21 (s, 2H), 3.42 (s, 4H), 2.38 (s, 12H). ^{13}C NMR ($CDCl_3$): δ 199.3, 138.3, 137.1, 134.9, 126.1, 32.9, 21.4.

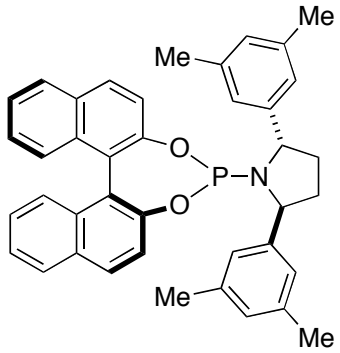
(*S*,*S*)-2,5-Bis(3,5-dimethylphenyl)pyrrolidine (CAS 1269808-63-0)



This was synthesized from 1,4-bis(3,5-dimethylphenyl)-1,4-butanedione, following the literature procedure for (*S*,*S*)-2,5-diphenylpyrrolidine.[9] 44% overall yield. Pale yellow oil. $[\alpha]^{30}_{D}$ –75.4 (*c* 0.90, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ 7.03 (s, 4H), 6.89 (s, 2H), 4.51-4.34 (m, 2H), 2.41-2.32 (m, 2H), 2.33 (s, 12H), 1.95-1.83 (m, 2H), 1.83 (bs, 1H). ^{13}C NMR ($CDCl_3$): δ 146.0, 138.1, 128.6, 124.3, 62.4, 35.7, 21.5.

(*S*,*S*,*S*)-L4



A solution of (*S*,*S*)-2,5-bis(3,5-dimethylphenyl)pyrrolidine (252 mg, 0.902 mmol) and Et_3N (150 μL, 1.08 mmol) in toluene (4.5 mL) was added dropwise over 50 min to a solution of PCl_3 (78.5 μL, 0.900 mmol) in toluene (4.5 mL) at room temperature. The mixture was stirred for 5.5 h at 70 °C and cooled to room temperature. Et_3N (414 μL, 2.97 mmol) was added to it and the mixture was cooled to –75 °C. A solution of (*S*)-1,1'-binaphthyl-2,2'-diol (258 mg, 0.901 mmol) in toluene (3.0 mL) and THF (0.5 mL) was then added to it slowly over 5 min, and the resulting mixture was stirred for 16 h at room temperature. The precipitate was filtered off through Celite with toluene and the solvent was removed under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/15 and the solid thus obtained was washed with hexane to afford compound (*S*,*S*,*S*)-**L4** as a white solid (365 mg, 0.615 mmol; 68% yield). $[\alpha]^{30}_{D}$ +158 (*c* 0.41, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ 7.89-7.84 (m, 2H), 7.73 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.37-7.31 (m, 2H), 7.29 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.24 (d, $^3J_{HH}$ = 8.8 Hz, 1H), 7.18 (t, $^3J_{HH}$ = 7.6 Hz, 1H), 7.16-7.10 (m, 3H), 6.97 (s, 2H), 6.90 (s, 4H), 6.02 (d, $^3J_{HH}$ = 8.8 Hz, 1H), 5.04 (d, $^3J_{HH}$ = 6.8 Hz, 2H), 2.43-2.33 (m, 2H), 2.38 (s, 12H), 1.69-1.59 (m, 2H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ 144.6 (s). HRMS (ESI-TOF) calcd for $C_{40}H_{36}NO_2PNa$ ($M+Na^+$) 616.2367, found 616.2375.

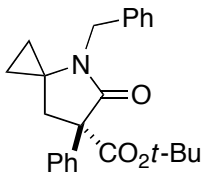
III. Catalytic Reactions

General Procedure for Table 1 (entries 5 and 6), Table 2, and Table 3.

Isocyanate **2** (0.200 mmol) and toluene (0.50 mL) were successively added to a solution of $PdCp(\eta^3\text{-}C_3H_5)$ (2.1 mg, 9.9 μmol), ligand (*S*,*S*,*S*)-**L4** (11.9 mg, 20.0 μmol), and lactone **1** (0.24 mmol) in toluene (0.50 mL), and the resulting solution was stirred for 12 h at 30 °C. The reaction mixture was directly passed through a pad of silica gel with EtOAc and the

[9] Aldous, D. J.; Dutton, W. M.; Steel, P. G. *Tetrahedron: Asymmetry* **2000**, *11*, 2455.

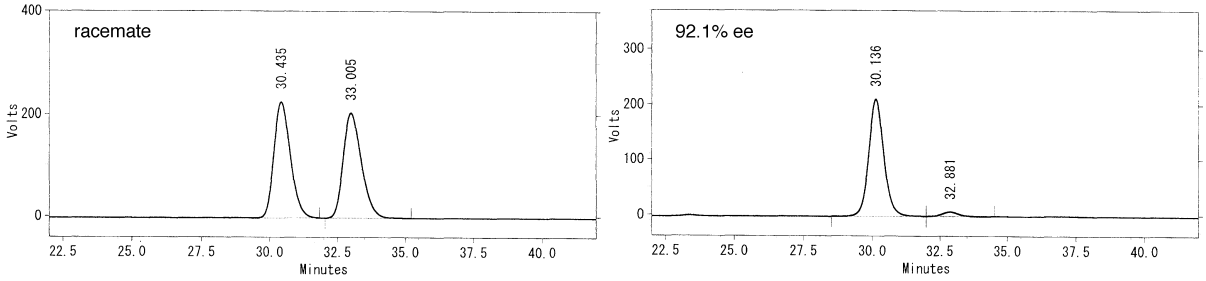
solvent was removed under vacuum. The residue was purified by silica gel preparative TLC to afford compounds **3**/**4**.

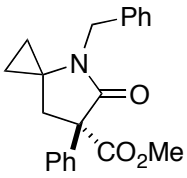


3aa

Table 1, Entry 5. (CAS 1086018-79-2) EtOAc/hexane = 1/3 was used for preparative TLC. Yellow oil. 89% yield (**3aa**/**4aa** = 90/10). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 30.1 min [major enantiomer], 32.9 min [minor enantiomer]. 92% ee. $[\alpha]^{25}_{D}$ +14.2 (*c* 0.88, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.59-7.55 (m, 2H), 7.37 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 7.34-7.21 (m, 6H), 4.48 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.15 (d, $^2J_{HH}$ = 15.8 Hz, 1H), 2.88 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.64 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 1.47 (s, 9H), 0.89 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.71 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.59 (dt, $^2J_{HH}$ = 10.1 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.50 (dt, $^2J_{HH}$ = 10.4 Hz and $^3J_{HH}$ = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.8, 170.2, 138.0, 137.7, 128.6, 128.4, 127.52, 127.48, 127.3, 127.1, 82.4, 61.4, 42.6, 42.1, 40.7, 27.9, 7.8, 6.7.

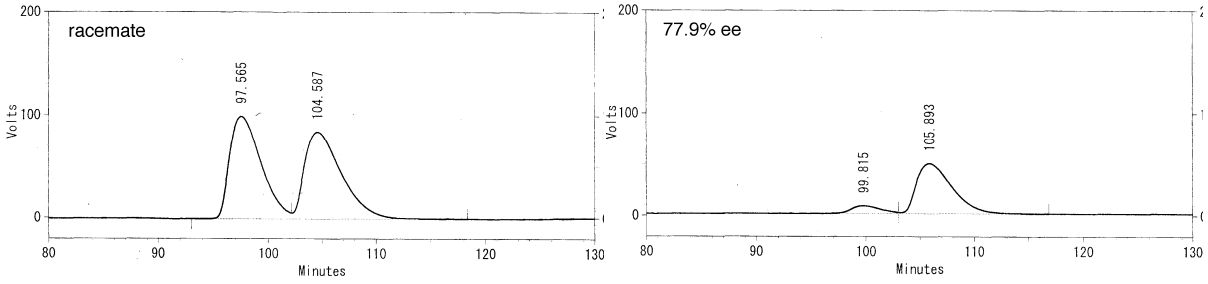


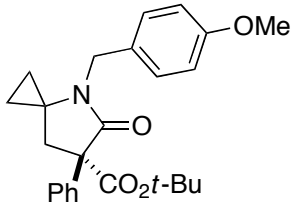


3ba

Table 1, Entry 6. (CAS 1225039-67-7) CH_2Cl_2/EtOAc/hexane = 1/2/6 was used for preparative TLC. Pale yellow oil. 89% yield (**3ba**/**4ba** = 92/8). The ee was determined on two Daicel Chiralcel OD-H columns with hexane/2-propanol = 95/5, flow = 0.5 mL/min. Retention times: 99.8 min [minor enantiomer], 105.9 min [major enantiomer]. 78% ee. $[\alpha]^{30}_{D}$ +19.3 (*c* 0.92, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.55-7.50 (m, 2H), 7.38 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.33-7.27 (m, 3H), 7.26-7.18 (m, 3H), 4.34 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.30 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 3.80 (s, 3H), 3.04 (d, $^2J_{HH}$ = 12.7 Hz, 1H), 2.57 (d, $^2J_{HH}$ = 12.7 Hz, 1H), 0.85-0.76 (m, 2H), 0.66-0.57 (m, 1H), 0.52-0.42 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 171.7, 171.3, 138.1, 137.5, 128.8, 128.7, 127.8, 127.5, 127.4, 127.1, 60.9, 53.3, 42.7, 42.4, 40.7, 7.3, 7.1.

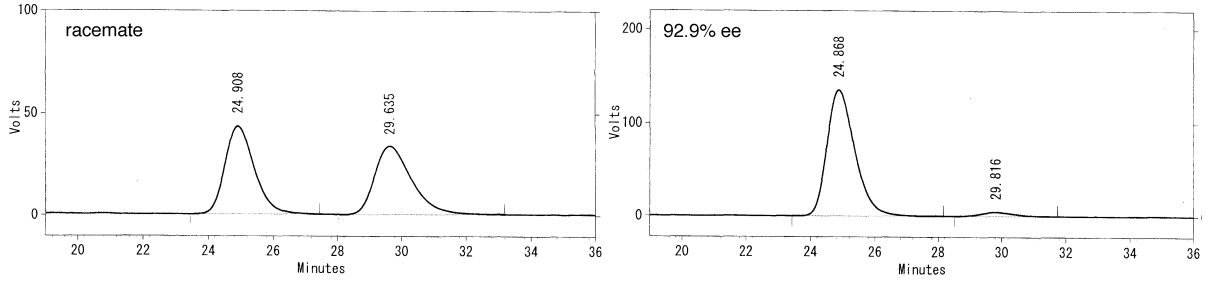


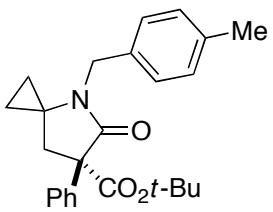


3ab

Table 2, Entry 1. EtOAc/hexane = 1/3 and then hexane/CH_2Cl_2 = 1/4 were used for preparative TLC. Yellow oil. 86% yield (**3ab**/**4ab** = 88/12). The ee was determined on a Daicel Chiralpak AS-H column with hexane/2-propanol = 97/3, flow = 0.8 mL/min. Retention times: 24.9 min [major enantiomer], 29.8 min [minor enantiomer]. 93% ee. $[\alpha]^{25}_D$ +15.9 (*c* 0.86, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.58-7.54 (m, 2H), 7.36 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 7.29 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 7.16 (d, $^3J_{HH}$ = 8.4 Hz, 2H), 6.82 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 4.42 (d, $^2J_{HH}$ = 15.6 Hz, 1H), 4.10 (d, $^2J_{HH}$ = 15.5 Hz, 1H), 3.78 (s, 3H), 2.85 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.61 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 1.46 (s, 9H), 0.90 (dt, $^2J_{HH}$ = 10.7 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.72 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.58 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.49 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.7, 170.2, 158.9, 129.8, 129.7, 128.4, 128.3, 127.5, 127.4, 114.0, 82.3, 61.3, 55.3, 42.11, 42.09, 40.7, 27.9, 7.8, 6.6. HRMS (ESI-TOF) calcd for $C_{25}H_{29}NO_4Na$ ($M+Na^+$) 430.1989, found 430.1988

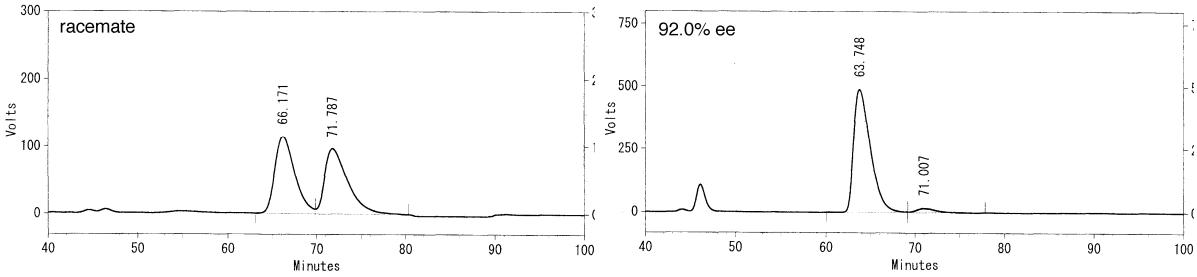


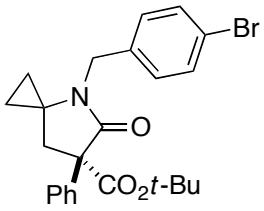


3ac

Table 2, Entry 2. EtOAc/hexane = 1/3 was used for preparative TLC. Pale yellow oil. 92% yield (**3ac**/**4ac** = 89/11). The ee was determined on two Daicel Chiralpak AS-H columns with hexane/2-propanol = 98/2, flow = 0.4 mL/min. Retention times: 63.7 min [major enantiomer], 71.0 min [minor enantiomer]. 92% ee. $[\alpha]^{25}_D$ +12.2 (*c* 0.85, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.59-7.54 (m, 2H), 7.36 (t, $^{3}J_{HH}$ = 7.6 Hz, 2H), 7.29 (tt, $^{3}J_{HH}$ = 7.3 Hz and $^{4}J_{HH}$ = 1.2 Hz, 1H), 7.12 (d, $^{3}J_{HH}$ = 8.2 Hz, 2H), 7.09 (d, $^{3}J_{HH}$ = 8.0 Hz, 2H), 4.44 (d, $^{2}J_{HH}$ = 15.8 Hz, 1H), 4.12 (d, $^{2}J_{HH}$ = 15.6 Hz, 1H), 2.87 (d, $^{2}J_{HH}$ = 12.5 Hz, 1H), 2.62 (d, $^{2}J_{HH}$ = 12.5 Hz, 1H), 2.32 (s, 3H), 1.47 (s, 9H), 0.89 (dt, $^{2}J_{HH}$ = 10.8 Hz and $^{3}J_{HH}$ = 6.3 Hz, 1H), 0.72 (dt, $^{2}J_{HH}$ = 10.8 Hz and $^{3}J_{HH}$ = 6.4 Hz, 1H), 0.58 (dt, $^{2}J_{HH}$ = 10.2 Hz and $^{3}J_{HH}$ = 6.3 Hz, 1H), 0.48 (dt, $^{2}J_{HH}$ = 10.3 Hz and $^{3}J_{HH}$ = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.7, 170.2, 138.1, 136.9, 134.7, 129.3, 128.3, 127.5, 127.4, 127.1, 82.4, 61.4, 42.4, 42.1, 40.7, 27.9, 21.1, 7.8, 6.7. HRMS (ESI-TOF) calcd for $C_{25}H_{29}NO_3Na$ (M+Na^{+}) 414.2040, found 414.2049.

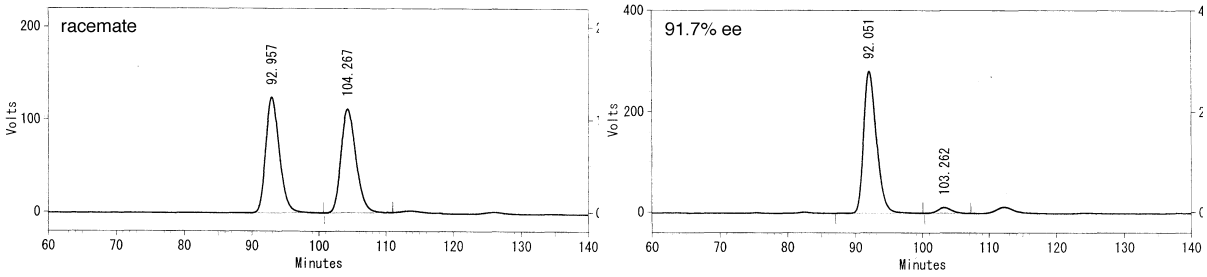


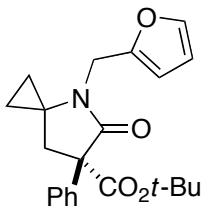


3ad

Table 2, Entry 3. EtOAc/hexane = 1/4 was used for preparative TLC. Yellow oil. 76% yield (**3ad**/**4ad** = 93/7). The ee was determined on two Daicel Chiralcel OD-H columns + a Daicel Chiralcel OF column with hexane/2-propanol = 85/15, flow = 0.3 mL/min. Retention times: 92.1 min [major enantiomer], 103.3 min [minor enantiomer]. 92% ee. $[\alpha]^{30}_{D}$ +11.5 (*c* 1.17, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.58-7.53 (m, 2H), 7.41 (d, $^{3}J_{HH}$ = 8.3 Hz, 2H), 7.37 (t, $^{3}J_{HH}$ = 7.6 Hz, 2H), 7.30 (tt, $^{3}J_{HH}$ = 7.3 Hz and $^{4}J_{HH}$ = 1.2 Hz, 1H), 7.11 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H), 4.40 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H), 4.09 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H), 2.88 (d, $^{2}J_{HH}$ = 12.6 Hz, 1H), 2.64 (d, $^{2}J_{HH}$ = 12.5 Hz, 1H), 1.46 (s, 9H), 0.85 (dt, $^{2}J_{HH}$ = 10.9 Hz and $^{3}J_{HH}$ = 6.5 Hz, 1H), 0.70 (dt, $^{2}J_{HH}$ = 10.9 Hz and $^{3}J_{HH}$ = 6.5 Hz, 1H), 0.61 (dt, $^{2}J_{HH}$ = 10.3 Hz and $^{3}J_{HH}$ = 6.4 Hz, 1H), 0.52 (dt, $^{2}J_{HH}$ = 10.4 Hz and $^{3}J_{HH}$ = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.9, 170.1, 137.8, 136.8, 131.8, 128.9, 128.4, 127.6, 127.5, 121.3, 82.5, 61.3, 42.03, 41.97, 40.7, 28.0, 7.8, 6.7. HRMS (ESI-TOF) calcd for $C_{24}H_{26}BrNO_3Na$ (M+Na^{+}) 478.0988, found 478.0987.

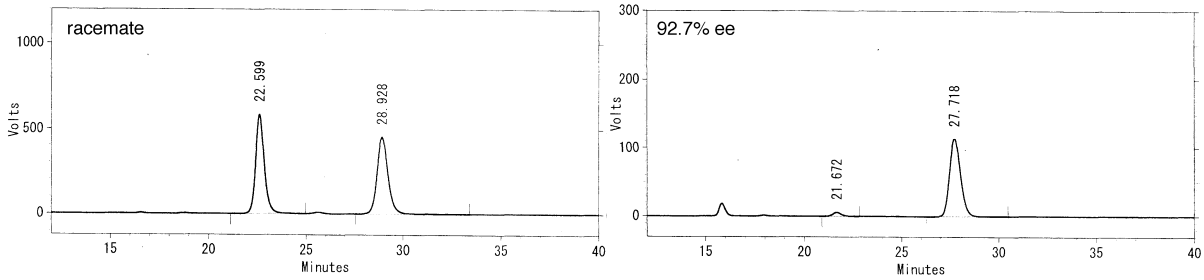


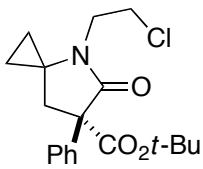


3ae

Table 2, Entry 4. The reaction was conducted with 1.6 equiv of **1a**. MeOH/EtOAc/hexane = 1/2/8 and then EtOAc/hexane/C_6H_6 = 1/5/5 were used for preparative TLC. Yellow oil. 82% yield (**3ae**/**4ae** = 90/10). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 95/5, flow = 0.8 mL/min. Retention times: 21.7 min [minor enantiomer], 27.7 min [major enantiomer]. 93% ee. $[\alpha]^{25}_{D}$ +2.1 (*c* 0.71, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.53-7.48 (m, 2H), 7.34 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 7.30 (dd, $^3J_{HH}$ = 1.8 Hz and $^4J_{HH}$ = 0.7 Hz, 1H), 7.27 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 6.30 (dd, $^3J_{HH}$ = 3.2 and 1.9 Hz, 1H), 6.25 (d, $^3J_{HH}$ = 3.2 Hz, 1H), 4.32 (d, $^2J_{HH}$ = 16.1 Hz, 1H), 4.23 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 2.84 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.58 (d, $^2J_{HH}$ = 12.3 Hz, 1H), 1.42 (s, 9H), 1.01 (dt, $^2J_{HH}$ = 10.9 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 0.87 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 0.66 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.53 (dt, $^2J_{HH}$ = 10.4 Hz and $^3J_{HH}$ = 6.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.4, 170.0, 150.5, 141.8, 138.2, 128.4, 127.47, 127.45, 110.8, 108.2, 82.4, 61.3, 42.2, 40.6, 35.9, 27.9, 7.8, 6.7. HRMS (ESI-TOF) calcd for $C_{22}H_{25}NO_4Na$ (M+Na^+) 390.1676, found 390.1665.



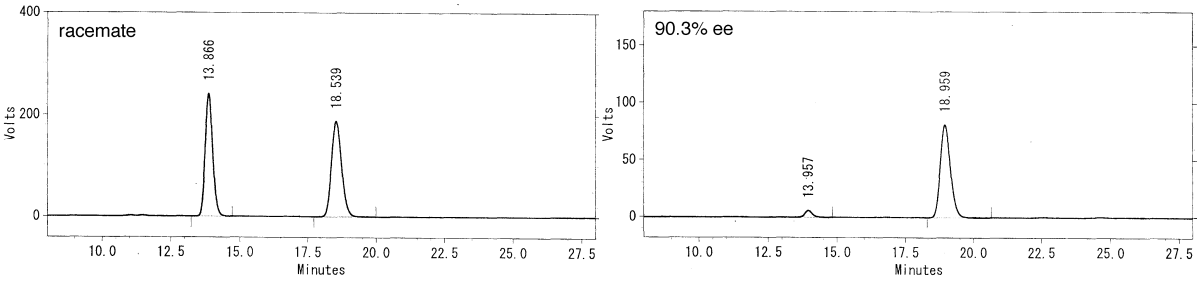


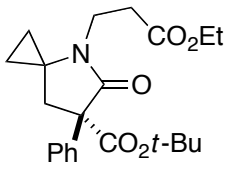
3af

Table 2, Entry 5. The reaction was conducted for 45 h. EtOAc/hexane = 1/3, EtOAc/CH_2Cl_2/hexane = 1/4/12, and then EtOAc/hexane/toluene = 2/5/5 were used for preparative TLC. White solid. 77% yield (**3af**/**4af** = 91/9). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 95/5, flow = 0.8 mL/min. Retention times: 14.0 min [minor enantiomer], 19.0 min [major enantiomer]. 90% ee. $[\alpha]^{25}_{D}$ –2.1 (*c* 0.76, $CHCl_3$). The absolute configuration was determined by X-ray crystallographic analysis after recrystallization from Et_2O.

^{1}H NMR ($CDCl_3$): δ 7.53-7.49 (m, 2H), 7.35 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.29 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 3.62 (t, $^3J_{HH}$ = 6.9 Hz, 2H), 3.30 (dt, $^2J_{HH}$ = 14.5 Hz and $^3J_{HH}$ = 6.8 Hz, 1H), 3.18 (dt, $^2J_{HH}$ = 14.3 Hz and $^3J_{HH}$ = 6.9 Hz, 1H), 2.85 (d, $^2J_{HH}$ = 12.6 Hz, 1H), 2.64 (d, $^2J_{HH}$ = 12.6 Hz, 1H), 1.44 (s, 9H), 0.99-0.90 (m, 2H), 0.83-0.75 (m, 1H), 0.68-0.61 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 171.9, 169.9, 137.9, 128.4, 127.6, 127.4, 82.5, 61.0, 41.9, 41.2, 40.4, 40.2, 27.9, 8.5, 7.4. HRMS (ESI-TOF) calcd for $C_{19}H_{24}ClNO_3Na$ (M+Na^+) 372.1337,

found 372.1334.

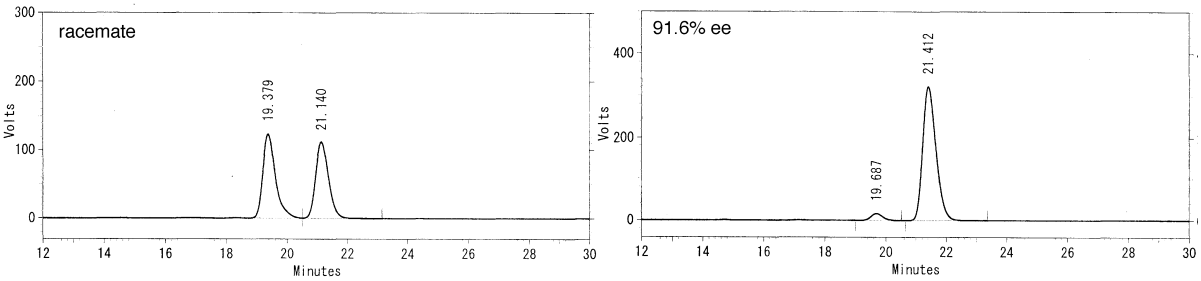


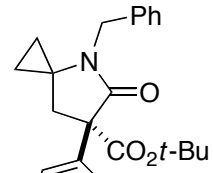


3ag

Table 2, Entry 6. The reaction was conducted with 1.6 equiv of **1a**. EtOAc/hexane = 1/3 and then Et_2O/hexane = 1/3 were used for preparative TLC. Pale yellow oil. 72% yield (**3ag**/**4ag** > 99/1). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 95/5, flow = 0.8 mL/min. Retention times: 19.7 min [minor enantiomer], 21.4 min [major enantiomer]. 92% ee. $[\alpha]^{25}_{D}$ –2.2 (*c* 0.86, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.52-7.46 (m, 2H), 7.33 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.27 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 4.11 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 3.28 (ddd, $^2J_{HH}$ = 14.3 Hz and $^3J_{HH}$ = 8.7 and 6.1 Hz, 1H), 3.15 (ddd, $^2J_{HH}$ = 14.1 Hz and $^3J_{HH}$ = 8.8 and 6.3 Hz, 1H), 2.82 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.62 (ddd, $^2J_{HH}$ = 16.0 Hz and $^3J_{HH}$ = 8.8 and 6.3 Hz, 1H), 2.58 (d, $^2J_{HH}$ = 12.3 Hz, 1H), 2.56 (ddd, $^2J_{HH}$ = 16.1 Hz and $^3J_{HH}$ = 8.7 and 6.1 Hz, 1H), 1.43 (s, 9H), 1.23 (t, $^3J_{HH}$ = 7.1 Hz, 3H), 0.98-0.85 (m, 2H), 0.73 (dt, $^2J_{HH}$ = 10.4 Hz and $^3J_{HH}$ = 6.0 Hz, 1H), 0.59 (dt, $^2J_{HH}$ = 10.4 Hz and $^3J_{HH}$ = 6.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.6, 171.5, 170.1, 138.2, 128.3, 127.44, 127.37, 82.3, 61.0, 60.7, 42.0, 40.0, 35.1, 33.1, 27.9, 14.3, 8.2, 7.1. HRMS (ESI-TOF) calcd for $C_{22}H_{29}NO_5Na$ ($M+Na^+$) 410.1938, found 410.1941.



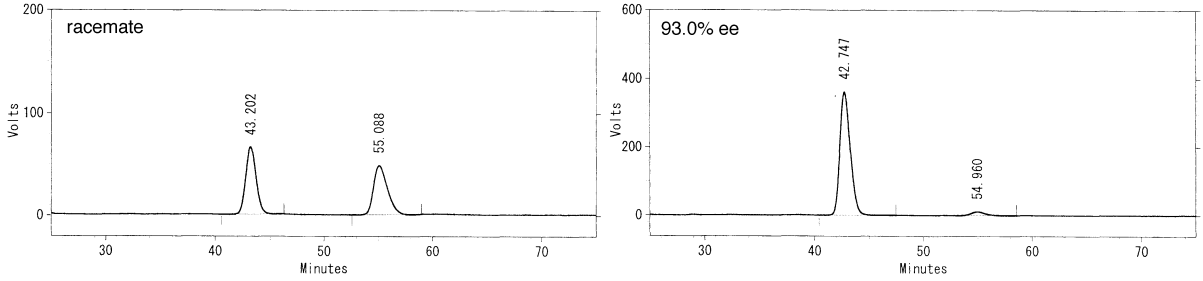


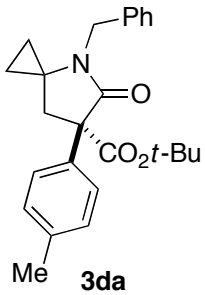
3ca

Table 2, Entry 7. EtOAc/hexane = 1/3 and then hexane/CH_2Cl_2 = 1/4 were used for preparative TLC. Yellow oil. 81% yield (**3ca**/**4ca** = 89/11). The ee was determined on a

Daicel Chiralpak AD-H column with hexane/2-propanol = 90/10, flow = 0.8 mL/min. Retention times: 42.7 min [major enantiomer], 55.0 min [minor enantiomer]. 93% ee. $[\alpha]^{25}_{D}$ +10.6 (*c* 1.03, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.52 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 7.33-7.21 (m, 5H), 6.90 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 4.48 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.13 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 3.81 (s, 3H), 2.85 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.62 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 1.47 (s, 9H), 0.89 (dt, $^2J_{HH}$ = 10.7 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.70 (dt, $^2J_{HH}$ = 10.7 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.58 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.2 Hz, 1H), 0.50 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 172.1, 170.5, 159.0, 137.8, 128.73, 128.71, 128.67, 127.4, 127.2, 113.8, 82.3, 60.6, 55.4, 42.6, 42.0, 40.7, 28.0, 7.8, 6.7. HRMS (ESI-TOF) calcd for $C_{25}H_{29}NO_4Na$ (M+Na$^+$) 430.1989, found 430.1983.

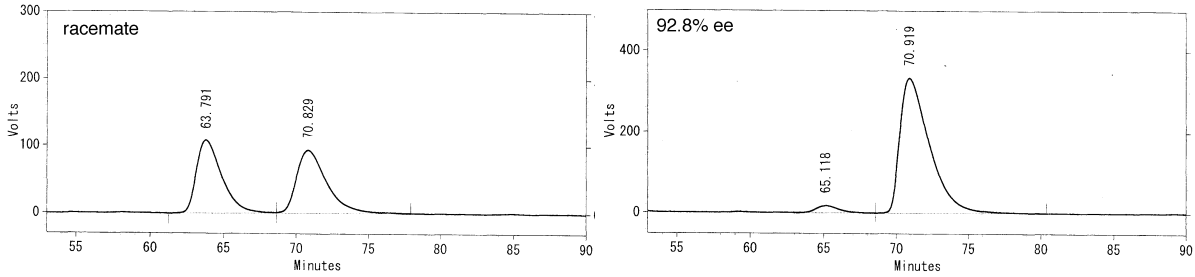


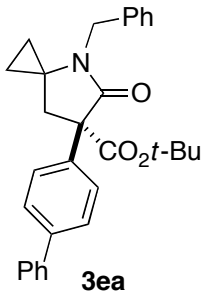


3da

Table 2, Entry 8. EtOAc/hexane = 1/3 was used for preparative TLC. Yellow oil. 83% yield (**3da**/**4da** = 89/11). The ee was determined on two Daicel Chiralpak AS-H columns with hexane/2-propanol = 98/2, flow = 0.4 mL/min. Retention times: 65.1 min [minor enantiomer], 70.9 min [major enantiomer]. 93% ee. $[\alpha]^{25}_{D}$ +5.7 (*c* 1.23, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.46 (d, $^3J_{HH}$ = 8.3 Hz, 2H), 7.32-7.20 (m, 5H), 7.18 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 4.48 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.14 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 2.86 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.63 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.34 (s, 3H), 1.47 (s, 9H), 0.89 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.70 (dt, $^2J_{HH}$ = 10.9 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.58 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.2 Hz, 1H), 0.50 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.9, 170.4, 137.8, 137.1, 134.9, 129.0, 128.6, 127.4, 127.3, 127.1, 82.3, 61.0, 42.5, 42.0, 40.7, 27.9, 21.1, 7.8, 6.6. HRMS (ESI-TOF) calcd for $C_{25}H_{29}NO_3Na$ (M+Na$^+$) 414.2040, found 414.2050.

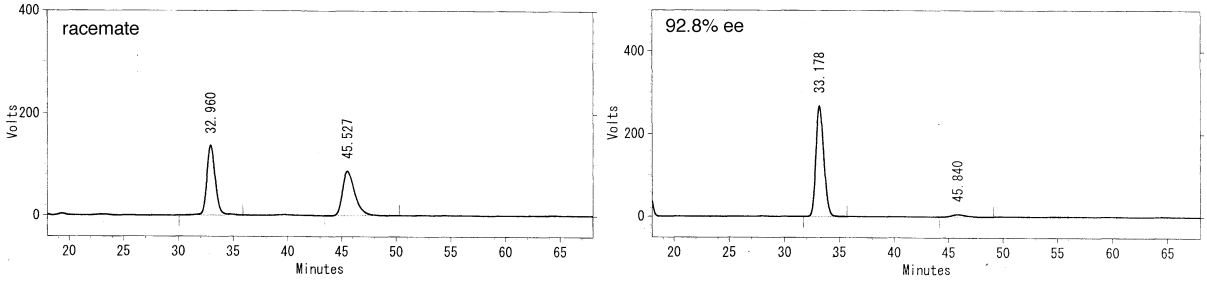


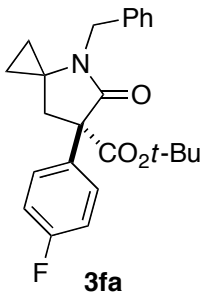


3ea

Table 2, Entry 9. EtOAc/hexane = 1/4 was used for preparative TLC. Brown oil. 93% yield (**3ea**/**4ea** = 92/8). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.8 mL/min. Retention times: 33.2 min [major enantiomer], 45.8 min [minor enantiomer]. 93% ee. $[\alpha]^{25}_{D}$ –11.3 (*c* 0.75, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.66 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 7.63-7.58 (m, 4H), 7.44 (t, $^3J_{HH}$ = 7.7 Hz, 2H), 7.37-7.27 (m, 3H), 7.27-7.22 (m, 3H), 4.51 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.17 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 2.91 (d, $^2J_{HH}$ = 12.6 Hz, 1H), 2.70 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 1.50 (s, 9H), 0.93 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.73 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.61 (dt, $^2J_{HH}$ = 10.4 Hz and $^3J_{HH}$ = 6.2 Hz, 1H), 0.54 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.8, 170.2, 140.9, 140.3, 137.7, 137.0, 128.8, 128.7, 128.0, 127.38, 127.37, 127.2, 127.14, 127.10, 82.6, 61.2, 42.7, 42.0, 40.8, 28.0, 7.9, 6.7. HRMS (ESI-TOF) calcd for $C_{30}H_{31}NO_3Na$ ($M+Na^+$) 476.2196, found 476.2195.



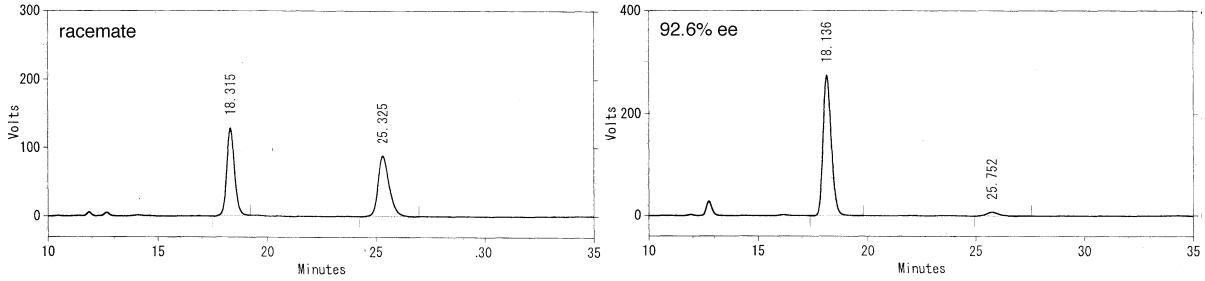


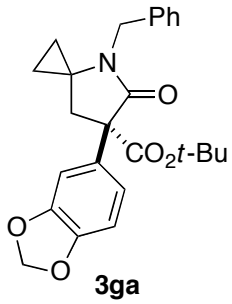
3fa

Table 2, Entry 10. EtOAc/hexane = 1/3 was used for preparative TLC. Yellow oil. 94% yield (**3fa**/**4fa** = 90/10). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.8 mL/min. Retention times: 18.1 min [major

enantiomer], 25.8 min [minor enantiomer]. 93% ee. $[\alpha]^{30}_{D}$ +10.7 (*c* 0.75, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.58 (dd, $^3J_{HH}$ = 8.6 Hz and $^4J_{HF}$ = 5.2 Hz, 2H), 7.33-7.20 (m, 5H), 7.05 (t, ^3J = 8.8 Hz, 2H), 4.48 (d, $^2J_{HH}$ = 15.8 Hz, 1H), 4.14 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 2.86 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.62 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 1.46 (s, 9H), 0.90 (dt, $^2J_{HH}$ = 11.0 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.71 (dt, $^2J_{HH}$ = 10.9 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.59 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.51 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.7, 170.1, 162.2 (d, $^1J_{CF}$ = 246 Hz), 137.6, 133.7 (d, $^4J_{CF}$ = 3.1 Hz), 129.3 (d, $^3J_{CF}$ = 7.7 Hz), 128.7, 127.4, 127.1, 115.1 (d, $^2J_{CF}$ = 21.2 Hz), 82.6, 60.6, 42.6, 42.0, 40.7, 27.9, 7.9, 6.6. HRMS (ESI-TOF) calcd for $C_{24}H_{26}FNO_3Na$ (M+Na$^+$) 418.1789, found 418.1798.

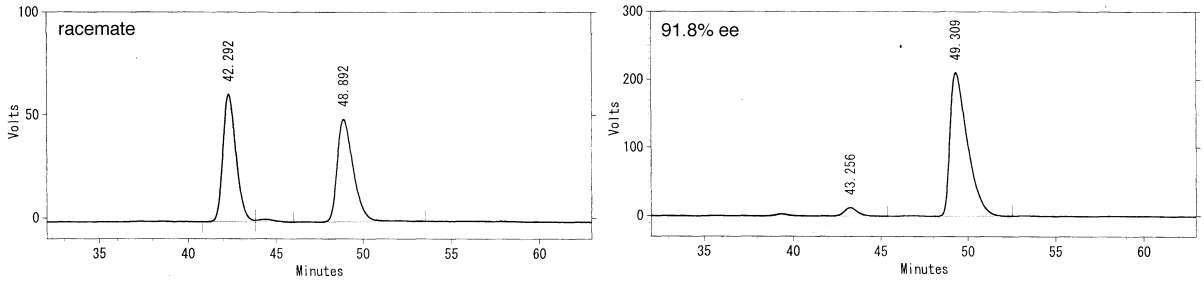


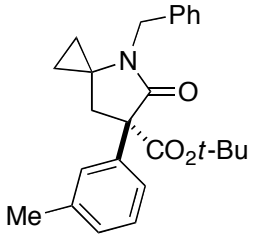


3ga

Table 2, Entry 11. EtOAc/hexane = 1/3 and then EtOAc/CH_2Cl_2/hexane = 1/2/3 were used for preparative TLC. Pale yellow oil. 85% yield (**3ga**/**4ga** = 91/9). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 43.3 min [minor enantiomer], 49.3 min [major enantiomer]. 92% ee. $[\alpha]^{30}_{D}$ –4.3 (*c* 0.80, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.33-7.20 (m, 5H), 7.17 (d, $^4J_{HH}$ = 2.0 Hz, 1H), 7.02 (dd, $^3J_{HH}$ = 8.1 Hz and $^4J_{HH}$ = 1.8 Hz, 1H), 6.79 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 5.954 (d, $^2J_{HH}$ = 1.4 Hz, 1H), 5.947 (d, $^2J_{HH}$ = 1.4 Hz, 1H), 4.47 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.13 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 2.82 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.60 (d, $^2J_{HH}$ = 12.3 Hz, 1H), 1.47 (s, 9H), 0.91 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.1 Hz, 1H), 0.69 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.58 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.1 Hz, 1H), 0.51 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.9, 170.3, 147.7, 147.1, 137.7, 131.7, 128.7, 127.4, 127.2, 120.8, 108.7, 108.1, 101.2, 82.5, 60.9, 42.7, 42.2, 40.7, 28.0, 7.9, 6.6. HRMS (ESI-TOF) calcd for $C_{25}H_{27}NO_5Na$ (M+Na$^+$) 444.1781, found 444.1786.

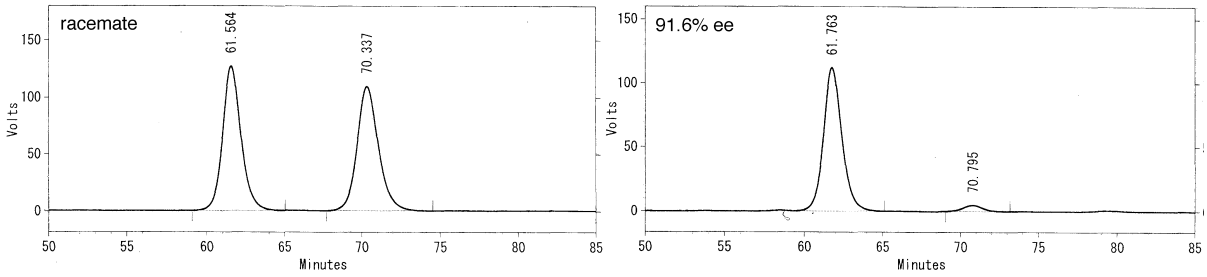


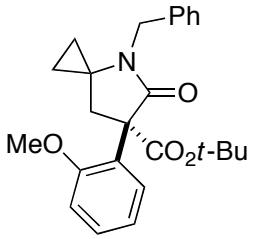


3ha

Table 2, Entry 12. EtOAc/hexane = 1/3 was used for preparative TLC. Yellow oil. 83% yield (**3ha**/**4ha** = 90/10). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 95/5, flow = 0.5 mL/min. Retention times: 61.8 min [major enantiomer], 70.8 min [minor enantiomer]. 92% ee. $[\alpha]^{25}_{D}$ +10.0 (*c* 0.77, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.38 (s, 1H), 7.36-7.32 (m, 2H), 7.31-7.21 (m, 5H), 7.11 (d, $^3J_{HH}$ = 7.4 Hz, 1H), 4.48 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.16 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 2.86 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.63 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.36 (s, 3H), 1.48 (s, 9H), 0.89 (dt, $^2J_{HH}$ = 10.9 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.70 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 0.58 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 0.50 (dt, $^2J_{HH}$ = 10.3 Hz and $^3J_{HH}$ = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.8, 170.3, 138.0, 137.9, 137.8, 128.6, 128.3, 128.23, 128.20, 127.3, 127.2, 124.5, 82.4, 61.4, 42.6, 42.3, 40.7, 27.9, 21.7, 7.8, 6.6. HRMS (ESI-TOF) calcd for $C_{25}H_{29}NO_3Na$ ($M+Na^+$) 414.2040, found 414.2031.



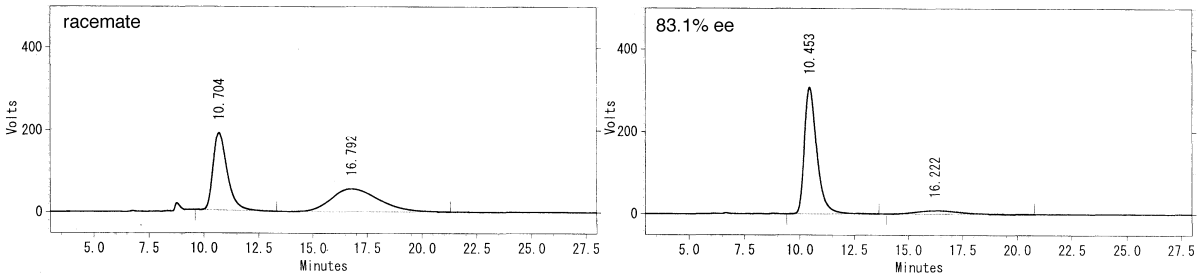


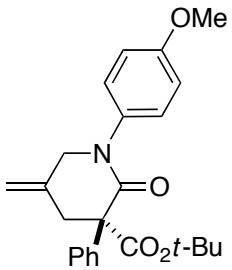
3ia

Table 2, Entry 13. EtOAc/hexane = 1/3 and then EtOAc/hexane/CH_2Cl_2 = 1/4/20 were used for preparative TLC. Yellow oil. 53% yield (**3ia**/**4ia** = 97/3). The ee was determined on a Daicel Chiralcel OJ-H column with hexane/2-propanol = 80/20, flow = 0.5 mL/min. Retention times: 10.5 min [major enantiomer], 16.2 min [minor enantiomer]. 83% ee. $[\alpha]^{25}_{D}$

+104 (*c* 0.85, $CHCl_3$). The absolute configuration was assigned by analogy with Table 2, entry 5.

^{1}H NMR ($CDCl_3$): δ 7.33 (dd, $^3J_{HH}$ = 7.6 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 7.33-7.29 (m, 2H), 7.28-7.22 (m, 4H), 6.92 (td, $^3J_{HH}$ = 7.6 Hz and $^4J_{HH}$ = 1.1 Hz, 1H), 6.88 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 4.46 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 4.24 (d, $^2J_{HH}$ = 15.9 Hz, 1H), 3.79 (s, 3H), 3.27 (d, $^2J_{HH}$ = 12.8 Hz, 1H), 2.17 (d, $^2J_{HH}$ = 12.9 Hz, 1H), 1.44 (s, 9H), 0.85 (dt, $^2J_{HH}$ = 10.9 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 0.67 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 0.54 (dt, $^2J_{HH}$ = 10.2 Hz and $^3J_{HH}$ = 6.6 Hz, 1H), 0.28 (dt, $^2J_{HH}$ = 10.1 Hz and $^3J_{HH}$ = 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 171.9, 169.9, 156.9, 137.8, 129.5, 128.7, 128.5, 127.9, 127.3, 127.1, 120.6, 110.9, 81.4, 60.6, 55.3, 42.6, 41.7, 40.9, 28.0, 7.8, 7.3. HRMS (ESI-TOF) calcd for $C_{25}H_{29}NO_4Na$ (M+Na^+) 430.1989, found 430.1997.



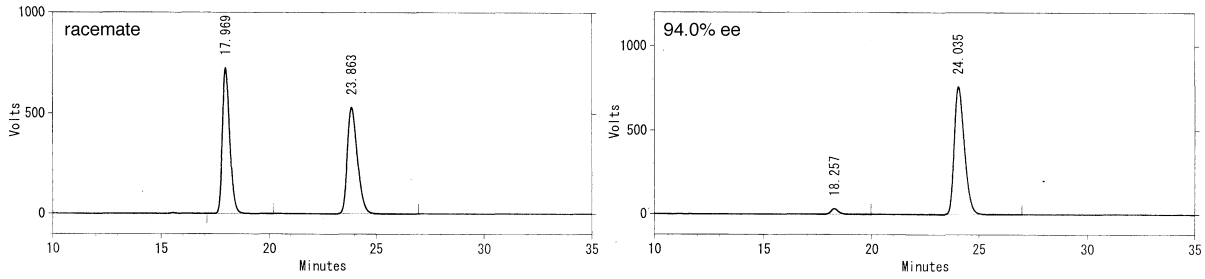


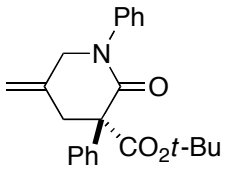
4ah

Table 3, Entry 1. (CAS 1086018-55-4) Et_2O/CH_2Cl_2/hexane = 3/5/10, CH_2Cl_2/EtOAc/hexane = 1/2/6, and then EtOAc/hexane = 1/5 were used for preparative TLC. Pale yellow oil. 89% yield (**3ah**/**4ah** = 6/94). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 18.3 min [minor enantiomer], 24.0 min [major enantiomer]. 94% ee. $[\alpha]^{30}_D$ +31.5 (*c* 1.05, $CHCl_3$). The absolute configuration was determined by comparison of the optical rotation with the literature value.[10]

^{1}H NMR ($CDCl_3$): δ 7.40-7.37 (m, 2H), 7.35 (t, $^3J_{HH}$ = 7.7 Hz, 2H), 7.28 (tt, $^3J_{HH}$ = 7.1 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 7.19 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 6.91 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 4.99 (s, 1H), 4.93 (s, 1H), 4.21 (d, $^2J_{HH}$ = 15.6 Hz, 1H), 4.12 (d, $^2J_{HH}$ = 15.7 Hz, 1H), 3.80 (s, 3H), 3.49 (d, $^2J_{HH}$ = 14.9 Hz, 1H), 3.28 (d, $^2J_{HH}$ = 14.9 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.9, 169.2, 158.4, 137.4, 137.2, 135.5, 128.2, 127.9, 127.5, 127.4, 114.6, 111.9, 82.4, 60.9, 55.7, 55.6, 38.3, 27.9.

[10] Shintani, R.; Park, S.; Shirozu, F.; Murakami, M.; Hayashi, T. *J. Am. Chem. Soc.* **2008**, *130*, 16174.

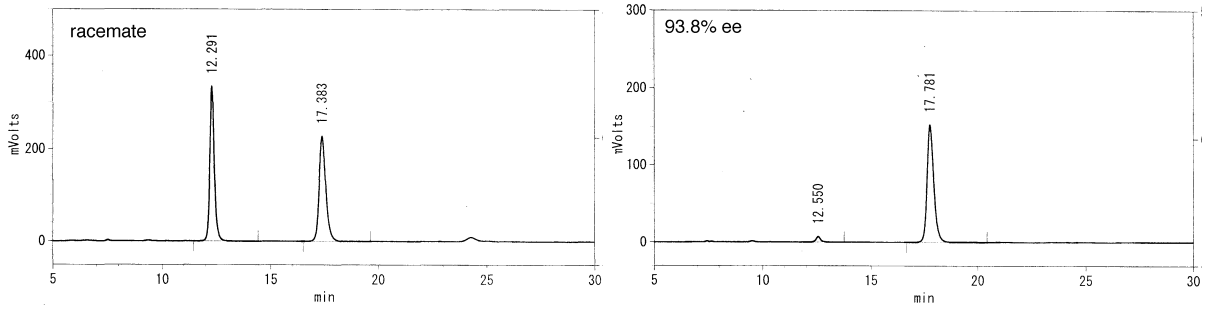


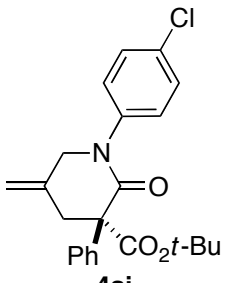


4ai

Table 3, Entry 2. EtOAc/hexane = 1/5 was used for preparative TLC. Pale yellow oil. 89% yield (**3ai**/**4ai** = 1/99). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 12.6 min [minor enantiomer], 17.8 min [major enantiomer]. 94% ee. $[\alpha]^{30}_{D}$ +14.3 (*c* 1.48, $CHCl_3$). The absolute configuration was assigned by analogy with Table 3, entry 1.

^{1}H NMR ($CDCl_3$): δ 7.42-7.33 (m, 6H), 7.31-7.23 (m, 4H), 5.02 (s, 1H), 4.95 (s, 1H), 4.25 (d, $^2J_{HH}$ = 15.6 Hz, 1H), 4.16 (d, $^2J_{HH}$ = 15.6 Hz, 1H), 3.50 (d, $^2J_{HH}$ = 14.8 Hz, 1H), 3.30 (d, $^2J_{HH}$ = 15.0 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.8, 169.1, 142.6, 137.3, 137.1, 129.3, 128.2, 127.8, 127.5, 127.0, 126.2, 112.0, 82.5, 61.0, 55.3, 38.2, 27.9. HRMS (ESI-TOF) calcd for $C_{23}H_{25}NO_3Na$ ($M+Na^+$) 386.1727, found 386.1724.



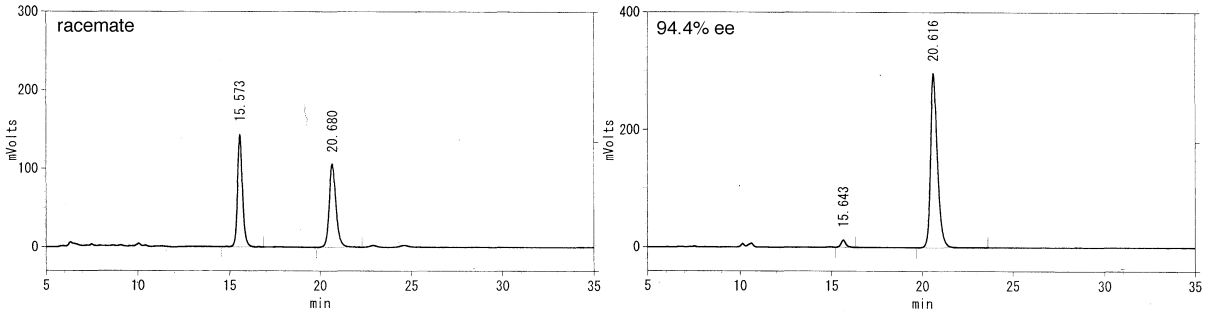


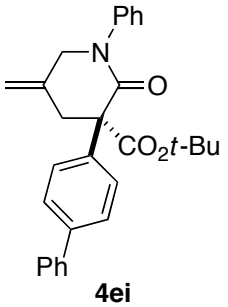
4aj

Table 3, Entry 3. (CAS 1086018-59-8) CH_2Cl_2/EtOAc/hexane = 1/2/20 was used for preparative TLC. Pale yellow oil. 95% yield (**3aj**/**4aj** < 1/99). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 15.6 min [minor enantiomer], 20.6 min [major enantiomer]. 94% ee. $[\alpha]^{25}_{D}$ +23.6 (*c* 0.90, $CHCl_3$). The absolute configuration was determined by comparison of the optical rotation with the literature value.[10]

^{1}H NMR ($CDCl_3$): δ 7.39-7.32 (m, 6H), 7.32-7.27 (m, 1H), 7.23 (d, $^3J_{HH}$ = 8.6 Hz, 2H), 5.03 (s, 1H), 4.97 (s, 1H), 4.22 (d, $^2J_{HH}$ = 15.4 Hz, 1H), 4.15 (d, $^2J_{HH}$ = 15.5 Hz, 1H), 3.47 (d,

$^{2}J_{HH}$ = 14.6 Hz, 1H), 3.30 (d, $^{2}J_{HH}$ = 14.9 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.7, 169.1, 141.0, 136.9, 132.5, 129.3, 128.2, 127.7, 127.6, 127.5, 112.3, 82.5, 61.0, 55.1, 38.1, 27.9.

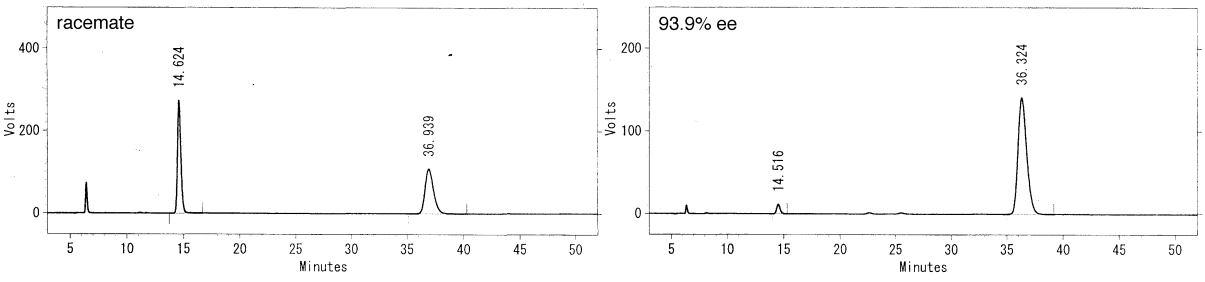


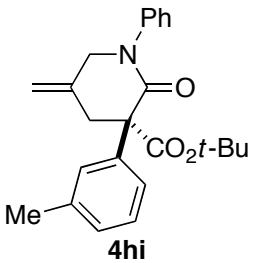


4ei

Table 3, Entry 4. EtOAc/hexane/CH_2Cl_2 = 1/20/60 and then EtOAc/toluene = 1/10 were used for preparative TLC. White solid. 91% yield (**3ei**/**4ei** = 1/99). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.8 mL/min. Retention times: 14.5 min [minor enantiomer], 36.3 min [major enantiomer]. 94% ee. $[\alpha]^{25}_{D}$ +10.2 (*c* 1.10, $CHCl_3$). The absolute configuration was assigned by analogy with Table 3, entry 1.

^{1}H NMR ($CDCl_3$): δ 7.64-7.56 (m, 4H), 7.48 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H), 7.46-7.38 (m, 4H), 7.34 (tt, $^{3}J_{HH}$ = 7.3 Hz and $^{4}J_{HH}$ = 1.1 Hz, 1H), 7.32-7.24 (m, 3H), 5.07 (s, 1H), 4.99 (s, 1H), 4.28 (d, $^{2}J_{HH}$ = 15.6 Hz, 1H), 4.22 (d, $^{2}J_{HH}$ = 15.7 Hz, 1H), 3.53 (d, $^{2}J_{HH}$ = 14.9 Hz, 1H), 3.35 (d, $^{2}J_{HH}$ = 14.8 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.9, 169.0, 142.6, 140.8, 140.3, 137.3, 136.1, 129.3, 128.8, 128.3, 127.4, 127.2, 127.1, 126.9, 126.2, 112.2, 82.6, 60.7, 55.4, 38.2, 28.0. HRMS (ESI-TOF) calcd for $C_{29}H_{29}NO_3Na$ (M+Na$^+$) 462.2040, found 462.2037.

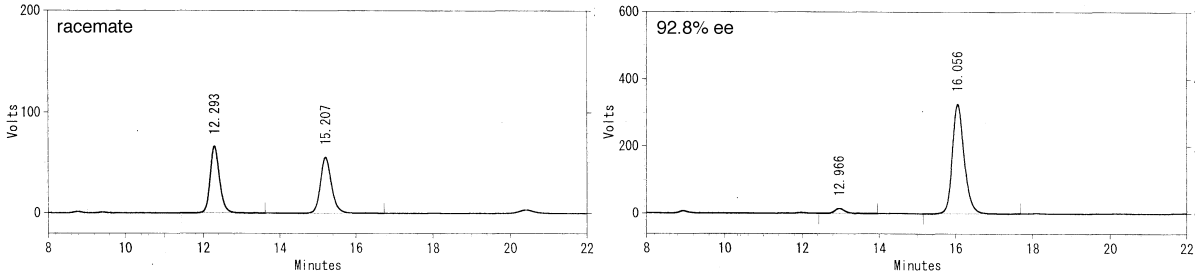




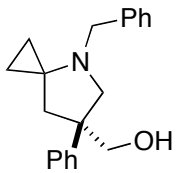
4hi

Table 3, Entry 5. EtOAc/hexane = 1/3 was used for preparative TLC. Pale yellow oil. 91% yield (**3hi**/**4hi** = 1/99). The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 13.0 min [minor enantiomer], 16.1 min [major enantiomer]. 93% ee. $[\alpha]^{25}_{D}$ +7.5 (*c* 1.06, $CHCl_3$). The absolute configuration was assigned by analogy with Table 3, entry 1.

^{1}H NMR ($CDCl_3$): δ 7.42-7.36 (m, 2H), 7.31-7.22 (m, 4H), 7.22-7.16 (m, 2H), 7.10 (d, $^3J_{HH}$ = 7.3 Hz, 1H), 5.02 (s, 1H), 4.95 (s, 1H), 4.24 (d, $^2J_{HH}$ = 15.6 Hz, 1H), 4.18 (d, $^2J_{HH}$ = 15.6 Hz, 1H), 3.47 (d, $^2J_{HH}$ = 15.0 Hz, 1H), 3.30 (d, $^2J_{HH}$ = 14.9 Hz, 1H), 2.35 (s, 3H), 1.46 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.9, 169.1, 142.6, 137.6, 137.4, 136.9, 129.2, 128.6, 128.3, 128.1, 127.0, 126.2, 124.8, 111.9, 82.4, 60.9, 55.3, 38.2, 27.9, 21.7. HRMS (ESI-TOF) calcd for $C_{24}H_{27}NO_3Na$ ($M+Na^+$) 400.1883, found 400.1876.



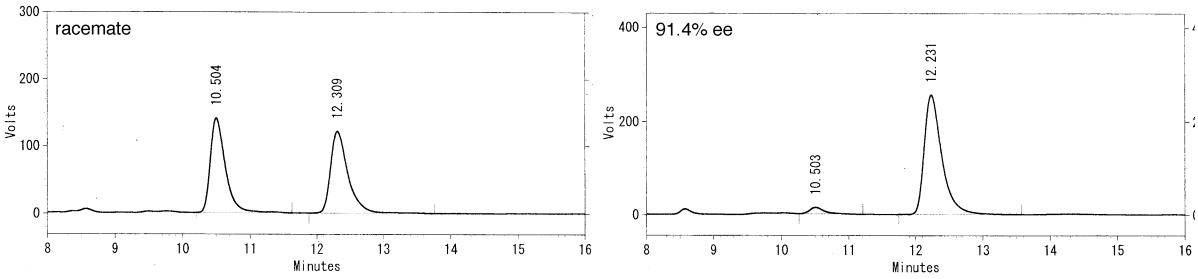
Procedure for Equation 1.



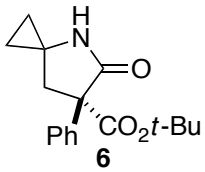
5

A solution of compound **3aa** (111 mg, 0.266 mmol of **3aa**; **3aa**/**4aa** = 93/7, 92% ee) in Et_2O (5.0 mL) was added to a suspension of $LiAlH_4$ (109 mg, 2.87 mmol) in Et_2O (1.0 mL) at –30 °C, and the mixture was stirred for 72 h h at –20 °C. The reaction mixture was cooled to –50 °C and slowly quenched with saturated NaCl*aq*. After extraction with CH_2Cl_2, the organic layer was washed with saturated NaCl*aq*, dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/5→1/4 to afford compound **5** as a pale yellow oil (68.1 mg, 0.232 mmol; 87% yield). The ee was determined on a Daicel Chiralpak AS-H column with hexane/2-propanol = 85/15, flow = 0.5 mL/min. Retention times: 10.5 min [minor enantiomer], 12.3 min [major enantiomer]. 91% ee. $[\alpha]^{25}_{D}$ +147 (*c* 1.10, CH_2Cl_2).

^{1}H NMR (C_6D_6): δ 7.25 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.19 (t, $^3J_{HH}$ = 7.6 Hz, 2H), 7.13-7.05 (m, 3H), 7.03 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.4 Hz, 1H), 6.90-6.86 (m, 2H), 3.71 (d, $^2J_{HH}$ = 10.1 Hz, 1H), 3.63 (dd, $^2J_{HH}$ = 10.1 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 3.24 (d, $^2J_{HH}$ = 8.9 Hz, 1H), 3.16 (d, $^2J_{HH}$ = 13.0 Hz, 1H), 2.76 (d, $^2J_{HH}$ = 13.0 Hz, 1H), 2.70 (dd, $^2J_{HH}$ = 8.9 Hz and $^4J_{HH}$ = 1.1 Hz, 1H), 2.47 (d, $^2J_{HH}$ = 12.4 Hz, 1H), 2.10 (d, $^2J_{HH}$ = 12.6 Hz, 1H), 1.46-1.16 (m, 1H), 0.75 (dt, $^2J_{HH}$ = 10.7 Hz and $^3J_{HH}$ = 5.9 Hz, 1H), 0.62 (dt, $^2J_{HH}$ = 10.8 Hz and $^3J_{HH}$ = 6.1 Hz, 1H), 0.49 (dt, $^2J_{HH}$ = 10.1 Hz and $^3J_{HH}$ = 6.0 Hz, 1H), 0.03 (dt, $^2J_{HH}$ = 10.0 Hz and $^3J_{HH}$ = 6.0 Hz, 1H). ^{13}C NMR (C_6D_6): δ 145.9, 139.7, 128.8, 128.7, 128.5, 127.4, 127.1, 126.4, 74.1, 62.9, 53.9, 49.8, 46.5, 44.3, 7.3, 7.0. HRMS (ESI-TOF) calcd for $C_{20}H_{24}NO$ ($M+H^+$) 294.1852, found 294.1851.



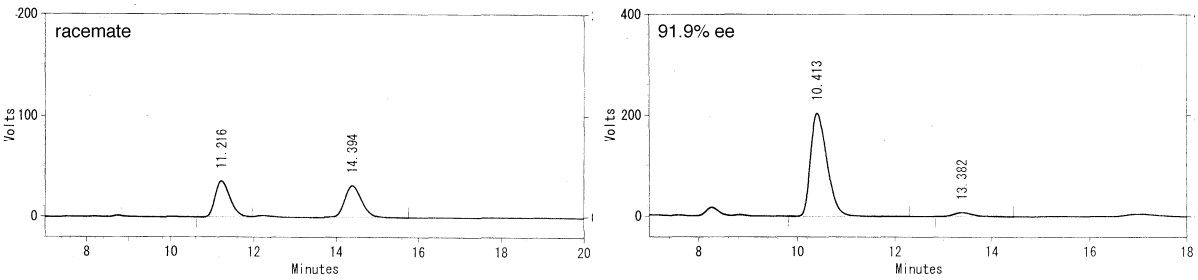
Procedure for Equation 2.



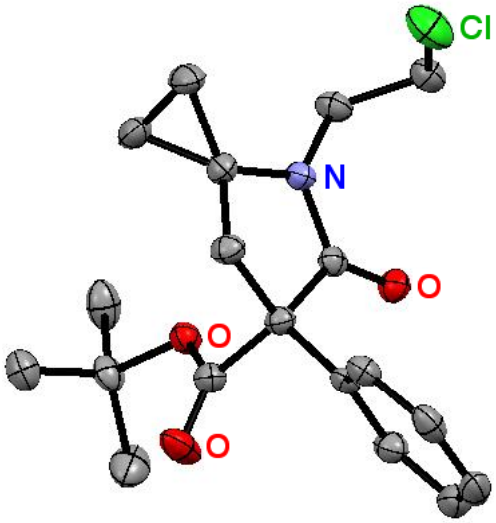
6

A solution of compound **3ag** (76.2 mg, 0.197 mmol; 92% ee) in THF (1.50 mL) was added to a suspension of NaH (15.7 mg, 0.393 mmol; 60 wt% in mineral oil) in THF (0.50 mL) at 0 °C, and the mixture was stirred for 5 h at 50 °C. The reaction mixture was diluted with Et_2O and quenched with H_2O. After extraction with Et_2O, the organic layer was washed with saturated NaCl*aq*, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel preparative TLC with EtOAc/hexane = 1/2 to afford compound **6** as a white solid (52.6 mg, 0.184 mmol; 93% yield). The ee was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 80/20, flow = 0.5 mL/min. Retention times: 10.4 min [major enantiomer], 13.4 min [minor enantiomer]. 92% ee. $[\alpha]^{25}_D$ +3.9 (*c* 1.11, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ 7.52-7.47 (m, 2H), 7.37-7.32 (m, 2H), 7.28 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 6.37 (bs, 1H), 2.91 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.65 (d, $^2J_{HH}$ = 12.7 Hz, 1H), 1.46 (s, 9H), 0.86-0.76 (m, 3H), 0.70-0.61 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 174.2, 170.0, 138.4, 128.4, 127.44, 127.38, 82.4, 62.6, 42.9, 36.8, 27.9, 11.4, 9.8. HRMS (ESI-TOF) calcd for $C_{17}H_{21}NO_3Na$ ($M+Na^+$) 310.1414, found 310.1419.



IV. X-ray Crystal Structure of (*S*)-3af



Data Collection

A colorless Et_2O solution of (*S*)-**3af** was prepared at room temperature. Crystals suitable for X-ray analysis were obtained by slow evaporation of the solvent at room temperature.

A colorless prism crystal of $C_{19}H_{24}ClNO_3$ having approximate dimensions of 0.50 x 0.40 x 0.20 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Cu-Kα radiation.

Indexing was performed from 3 oscillations that were exposed for 15 seconds. The crystal-to-detector distance was 127.40 mm.

Cell constants and an orientation matrix for data collection corresponded to a primitive monoclinic cell with dimensions:

a = 8.71555(18) Å
b = 8.71796(19) Å β = 104.9876(14)°
c = 12.4456(3) Å
V = 913.47(3) Å^3

For Z = 2 and F.W. = 349.86, the calculated density is 1.272 g/cm^3. Based on the systematic absences of:

0k0: k ± 2n

packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

$P2_1$ (#4)

The data were collected at a temperature of –180 ± 1 °C to a maximum 2θ value of 136.4°. A total of 30 oscillation images were collected. A sweep of data was done using ω scans from 80.0 to 260.0° in 30.0° step, at χ = 54.0° and ϕ = 0.0°. The exposure rate was 10.0 [sec./°]. A second sweep was performed using ω scans from 80.0 to 260.0° in 30.0° step, at χ = 54.0° and ϕ = 90.0°. The exposure rate was 10.0 [sec./°]. Another sweep was performed using ω scans from 80.0 to 260.0° in 30.0° step, at χ = 54.0° and ϕ = 180.0°. The exposure

rate was 10.0 [sec./°]. Another sweep was performed using ω scans from 80.0 to 260.0° in 30.0° step, at χ = 54.0° and ϕ = 270.0°. The exposure rate was 10.0 [sec./°]. Another sweep was performed using ω scans from 80.0 to 260.0° in 30.0° step, at χ = 0.0° and ϕ = 0.0°. The exposure rate was 10.0 [sec./°]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 9740 reflections that were collected, 3224 were unique (R_{int} = 0.057).

The linear absorption coefficient, μ, for Cu-Kα radiation is 19.823 cm^{-1}. An empirical absorption correction was applied which resulted in transmission factors ranging from 0.564 to 0.673. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[11] and expanded using Fourier techniques.[12] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement[13] on F^2 was based on 3224 observed reflections and 219 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma \; ||Fo| - |Fc|| \; / \; \Sigma \; |Fo| = 0.0404$$

$$wR2 = [\Sigma \; w \; (Fo^2 - Fc^2)^2 \; / \; \Sigma \; w \; (Fo^2)^2]^{1/2} = 0.1020$$

The standard deviation of an observation of unit weight[14] was 1.04. A Chebychev polynomial weighting scheme was used.[15] The maximum and minimum peaks on the final difference Fourier map corresponded to 0.19 and –0.25 $e^-/Å^3$, respectively. The absolute structure was deduced based on Flack parameter, 0.040(15), refined using 1446 Friedel pairs.[16]

Neutral atom scattering factors were taken from Cromer and Waber.[17] Anomalous dispersion effects were included in Fcalc;[18] the values for Δf' and Δf" were those of Creagh

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[11] SIR92: Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, *27*, 435.

[12] DIRDIF99: Beurskens, P. T.; Admiraal, G.; Beurskens, G.; Bosman, W. P.; de Gelder, R.; Israel, R.; Smits, J. M. M. The DIRDIF-99 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands (1999).

[13] Least Squares function minimized: (SHELXL97)

$\Sigma w(F_o^2 - F_c^2)^2$ where w = Least Squares weights.

[14] Standard deviation of an observation of unit weight:

$[\Sigma w(F_o^2 - F_c^2)^2/(N_o - N_v)]^{1/2}$

where: N_o = number of observations, N_v = number of variables

[15] Carruthers, J. R.; Watkin, D. J. *Acta Crystallogr.* **1979**, *A35*, 698.

[16] Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876.

[17] Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

[18] Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, *17*, 781.

and McAuley.[19] The values for the mass attenuation coefficients are those of Creagh and Hubbell.[20] All calculations were performed using the CrystalStructure[21] crystallographic software package except for refinement, which was performed using SHELXL-97.[22]

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 892796). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

[19] Creagh, D. C.; McAuley, W. J. "International Tables for Crystallography", Vol C, (A. J. C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219–222 (1992).
[20] Creagh, D. C.; Hubbell, J. H. "International Tables for Crystallography", Vol C, (A. J. C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200–206 (1992).
[21] CrystalStructure 3.8: Crystal Structure Analysis Package, Rigaku and Rigaku Americas (2000-2007). 9009 New Trails Dr. The Woodlands TX 77381 USA.
[22] SHELXL97: Sheldrick, G. M. (1997).

Experimental Details

A. Crystal Data

Empirical Formula	$C_{19}H_{24}ClNO_3$
Formula Weight	349.86
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.40 X 0.20 mm
Crystal System	monoclinic
Lattice Type	Primitive
Indexing Images	3 oscillations @ 15.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 8.71555(18) Å b = 8.71796(19) Å c = 12.4456(3) Å β = 104.9876(14)° V = 913.46(3) $Å^3$
Space Group	$P2_1$ (#4)
Z value	2
D_{calc}	1.272 g/cm^3
F_{000}	372.00
μ(CuKα)	19.823 cm^{-1}

B. Intensity Measurements

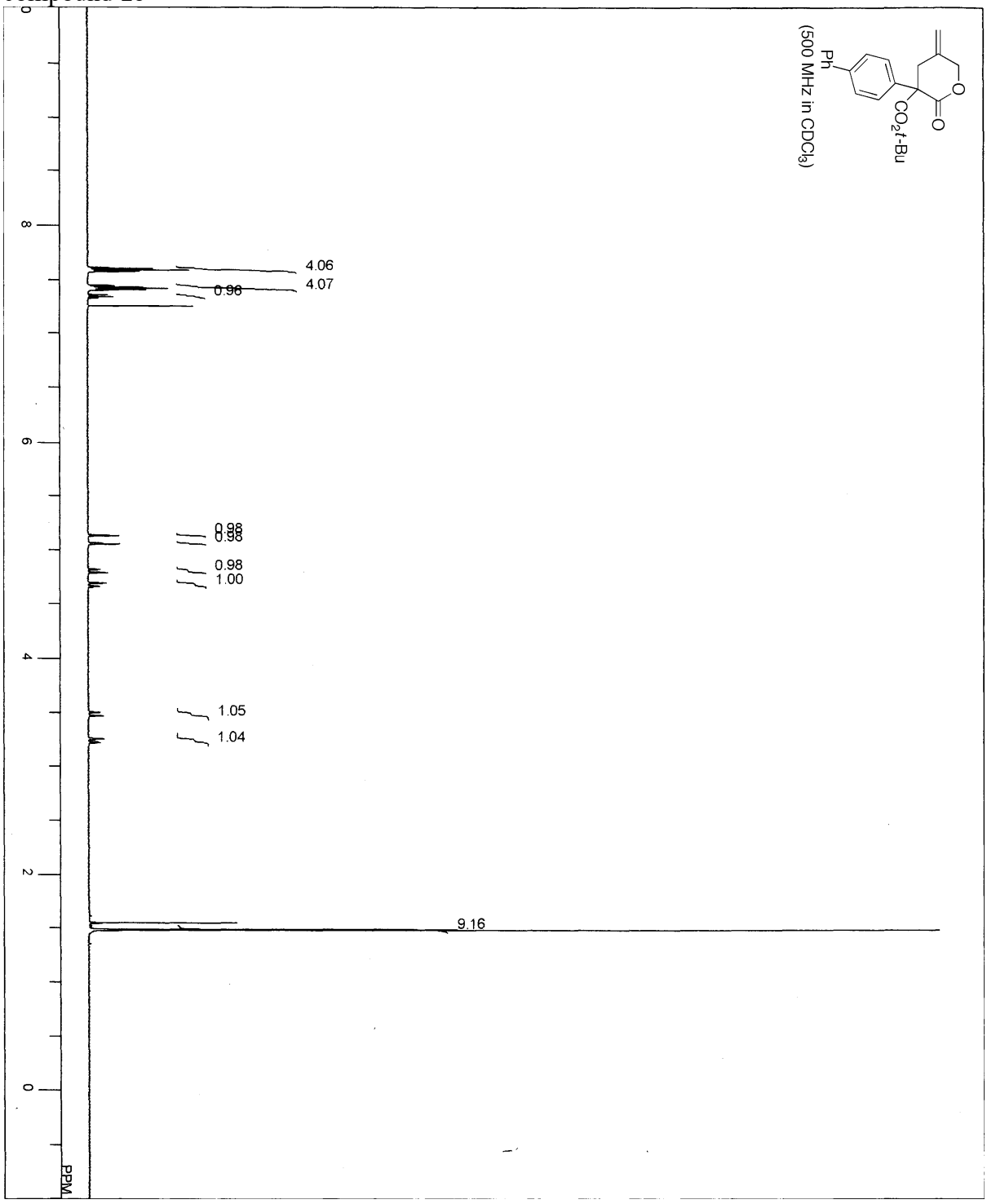
Diffractometer	Rigaku RAXIS-RAPID
Radiation	CuKα (λ = 1.54187 Å) graphite monochromated
Detector Aperture	460 mm x 256 mm
Data Images	30 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=0.0, ϕ=0.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4°
No. of Reflections Measured	Total: 9740 Unique: 3224 (R_{int} = 0.057) Friedel pairs: 1446
Corrections	Lorentz-polarization Absorption (trans. factors: 0.564 - 0.673)

C. Structure Solution and Refinement

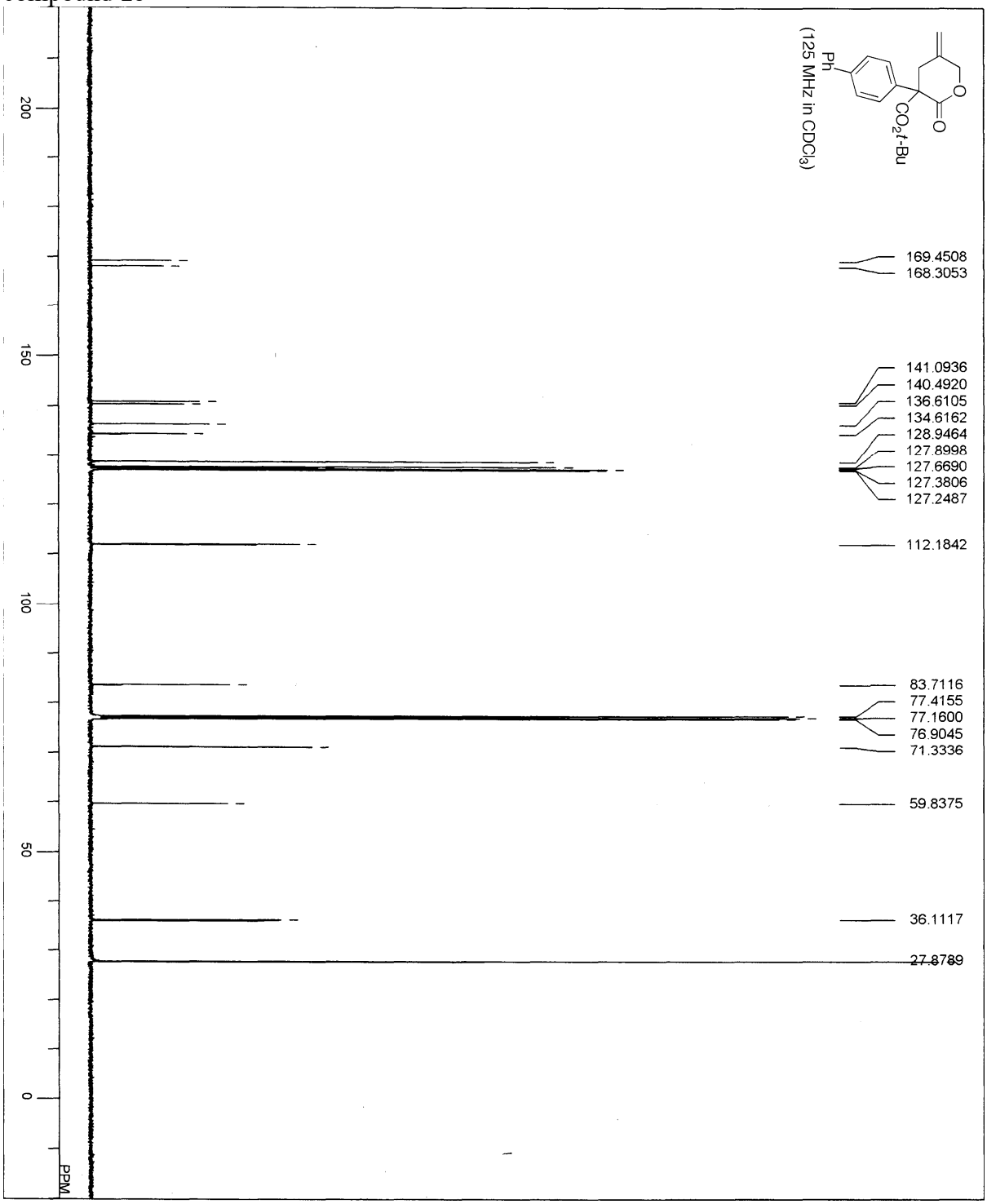
Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/[\sigma^2(Fo^2)+(0.0535P)^2+0.0256P]$ where $P = (Max(Fo^2,0)+2Fc^2)/3$
$2\theta_{max}$ cutoff	136.4°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3224
No. Variables	219
Reflection/Parameter Ratio	14.72
Residuals: R1 (I>2.00σ(I))	0.0404
Residuals: R (All reflections)	0.0459
Residuals: wR2 (All reflections)	0.1020
Goodness of Fit Indicator	1.036
Flack Parameter	0.040(15)
Max Shift/Error in Final Cycle	0.004
Maximum peak in Final Diff. Map	0.19 $e^-/Å^3$
Minimum peak in Final Diff. Map	–0.25 $e^-/Å^3$

V. ^{1}H and ^{13}C NMR Spectra

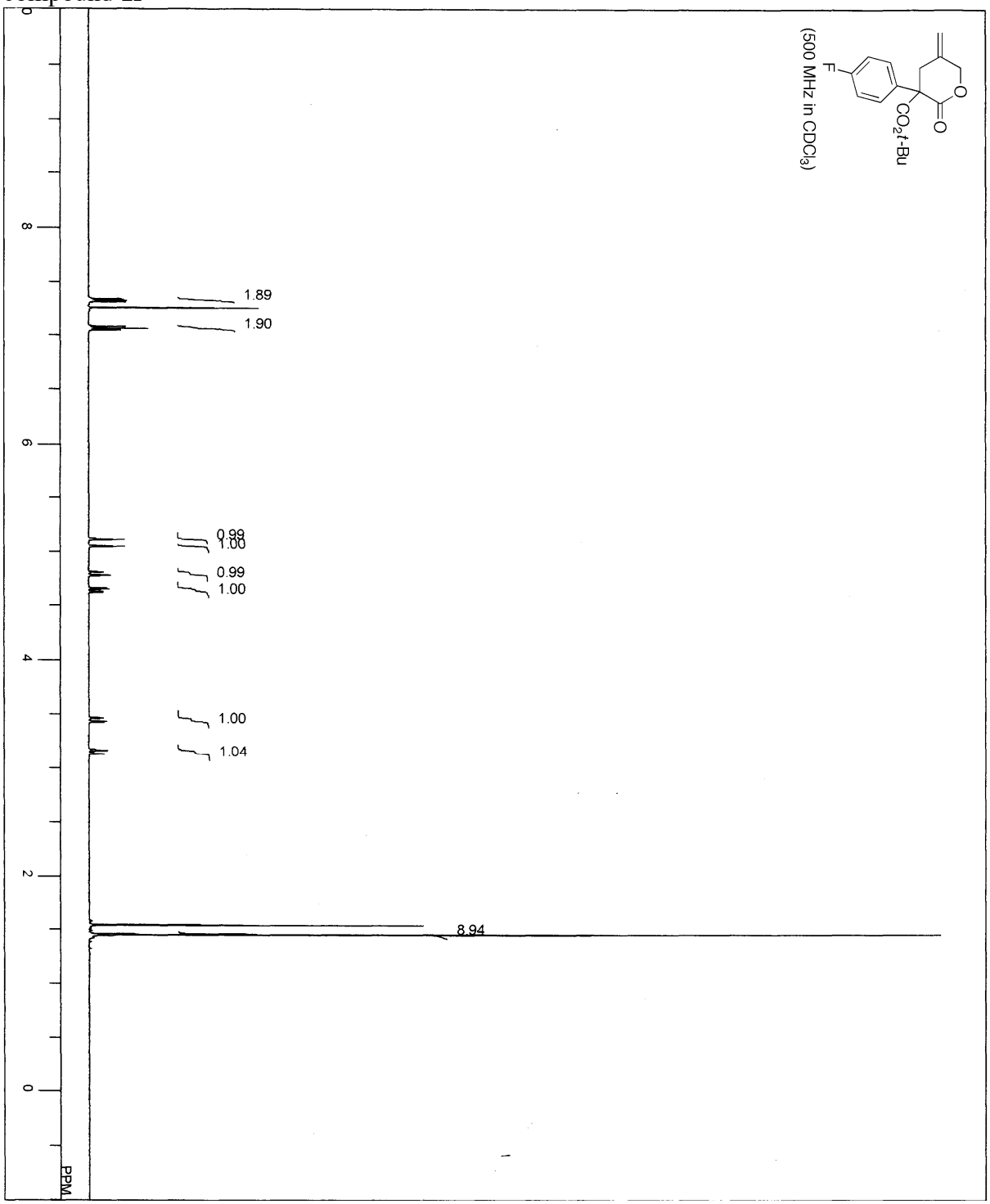
compound **1e**



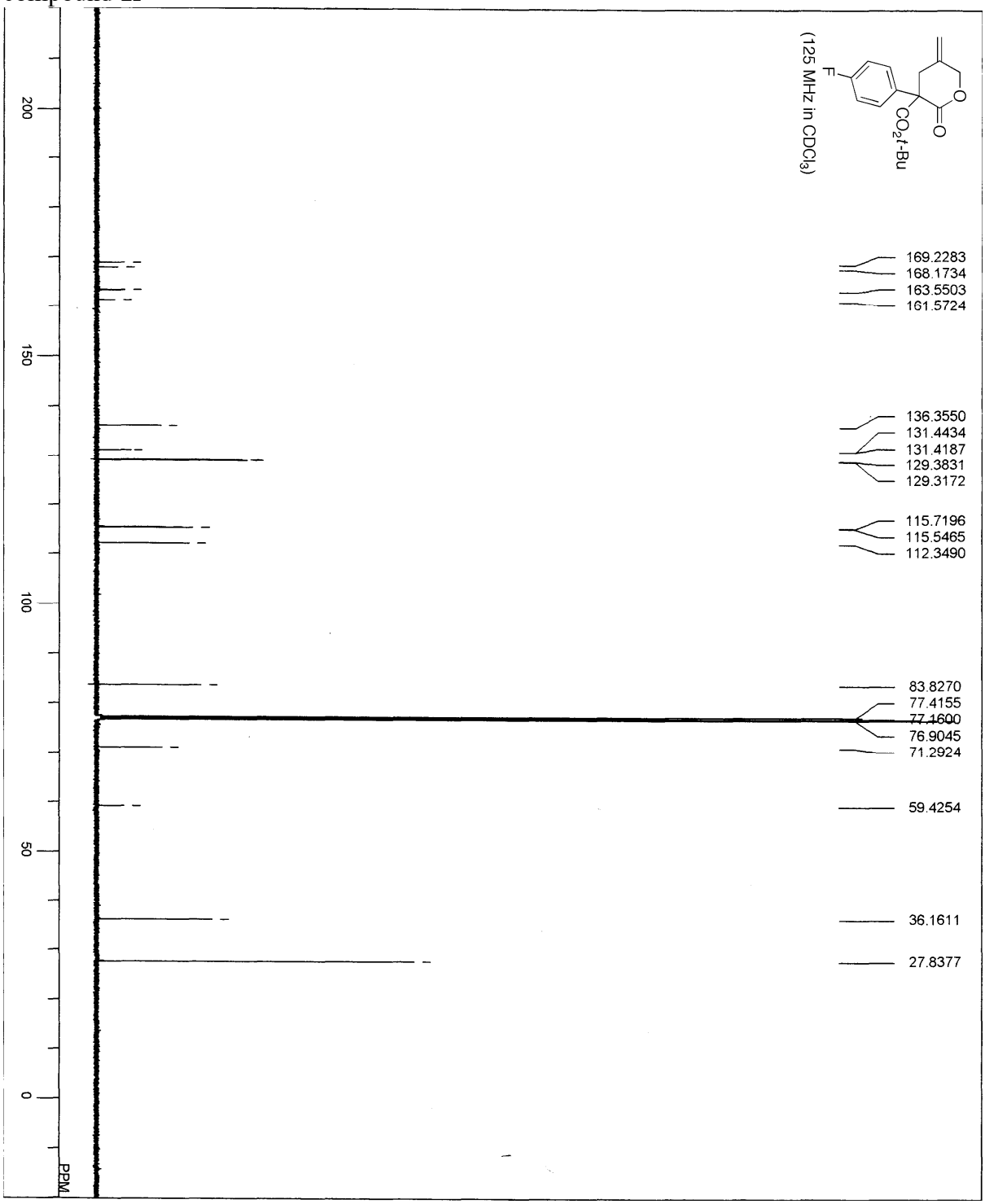
compound **1e**


(125 MHz in CDCl3)
Ph
CO2t-Bu
O
O
169.4508
168.3053
141.0936
140.4920
136.6105
134.6162
128.9464
127.8998
127.6690
127.3806
127.2487
112.1842
83.7116
77.4155
77.1600
76.9045
71.3336
59.8375
36.1117
27.8789
200
150
100
50
0
PPM

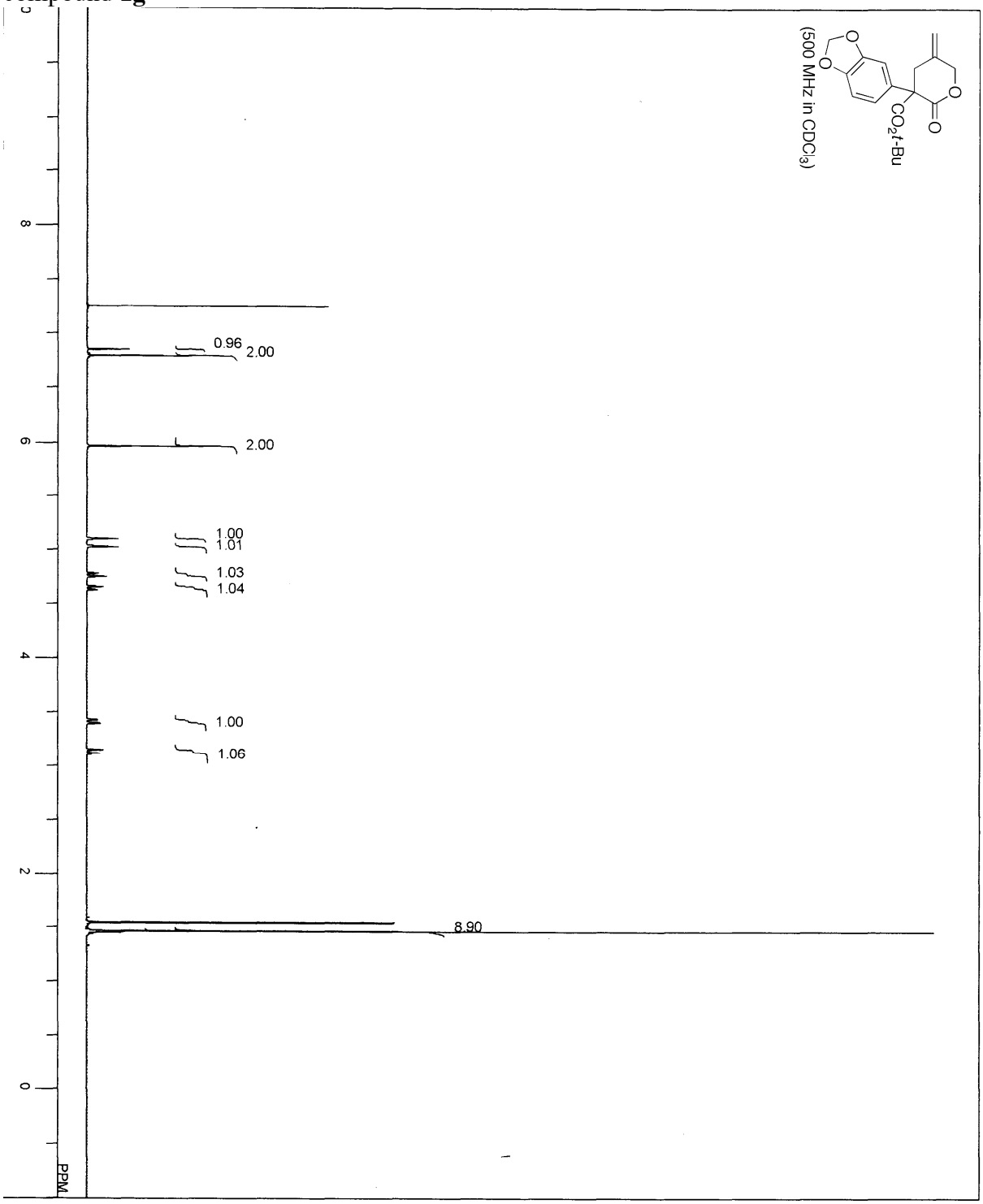
compound **1f**


(500 MHz in CDCl3)
F
CO2t-Bu
O
O
1.89
1.90
0.99
1.00
0.99
1.00
1.00
1.04
8.94
PPM

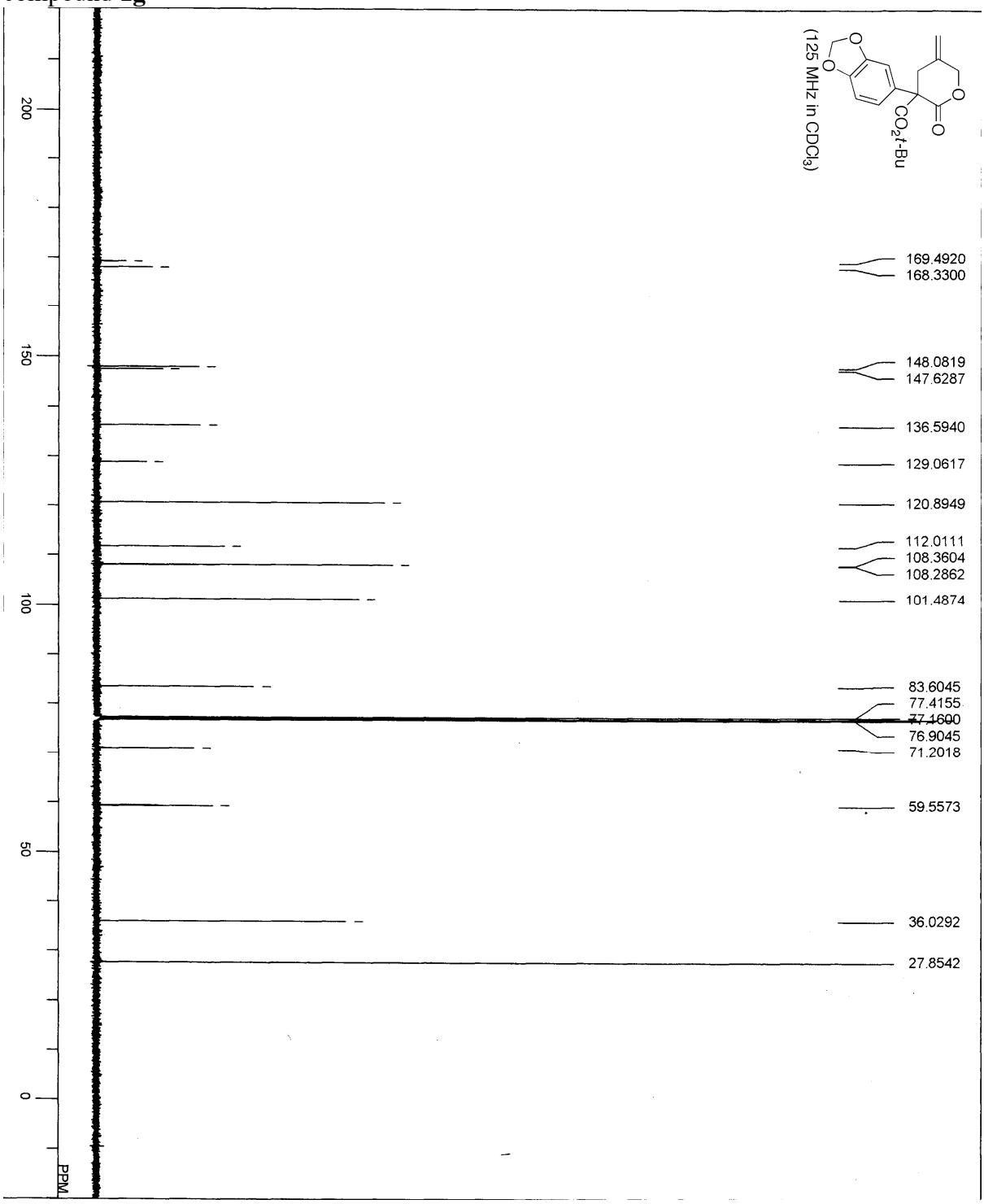
compound **1f**


(125 MHz in CDCl3)
F
CO2t-Bu
O
O
169.2283
168.1734
163.5503
161.5724
136.3550
131.4434
131.4187
129.3831
129.3172
115.7196
115.5465
112.3490
83.8270
77.4155
77.1600
76.9045
71.2924
59.4254
36.1611
27.8377
200
150
100
50
0
PPM

compound **1g**


(500 MHz in CDCl3)
CO2t-Bu
0.96
2.00
2.00
1.00
1.01
1.03
1.04
1.00
1.06
8.90
PPM

compound **1g**


(125 MHz in CDCl3)
CO2t-Bu
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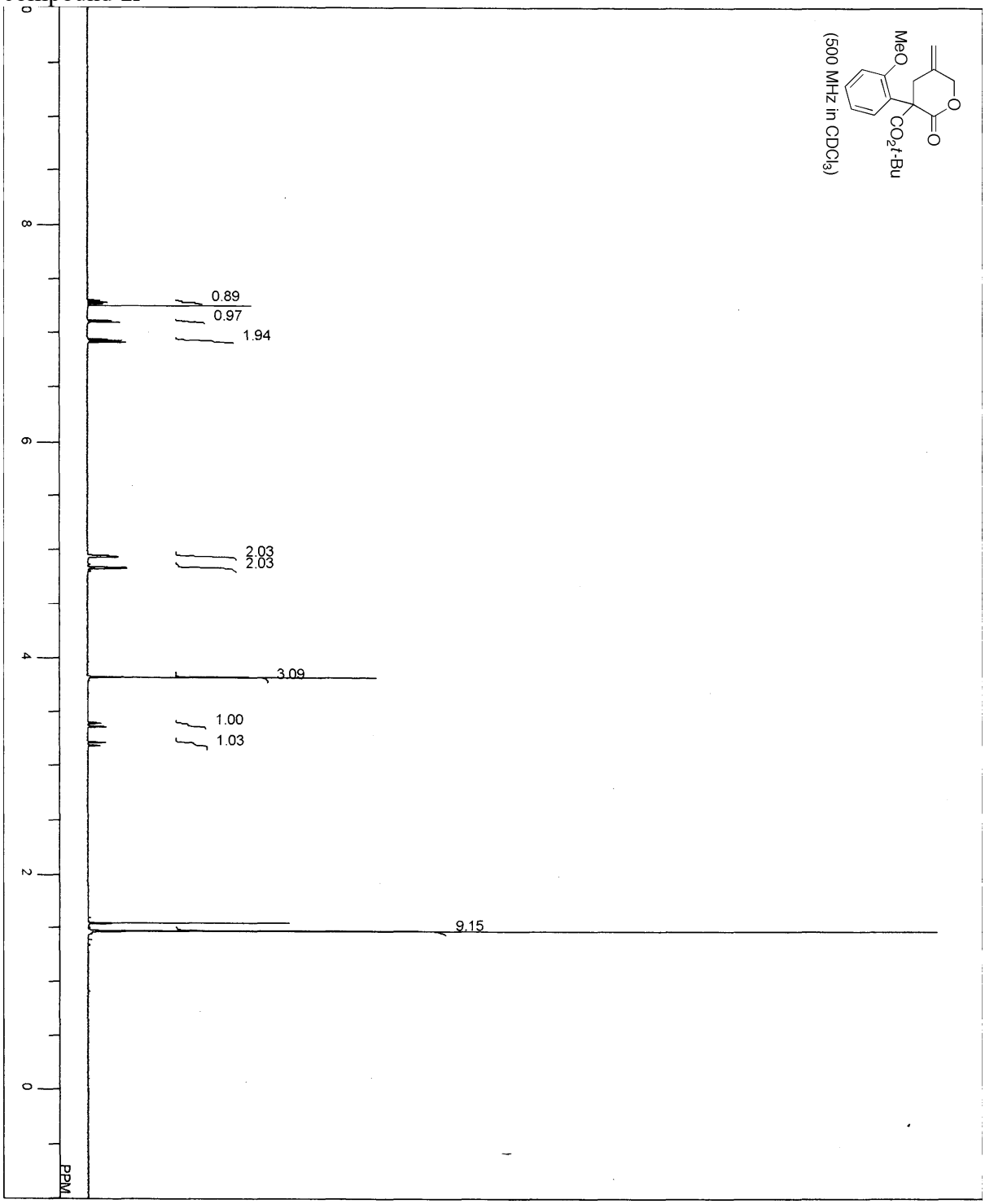
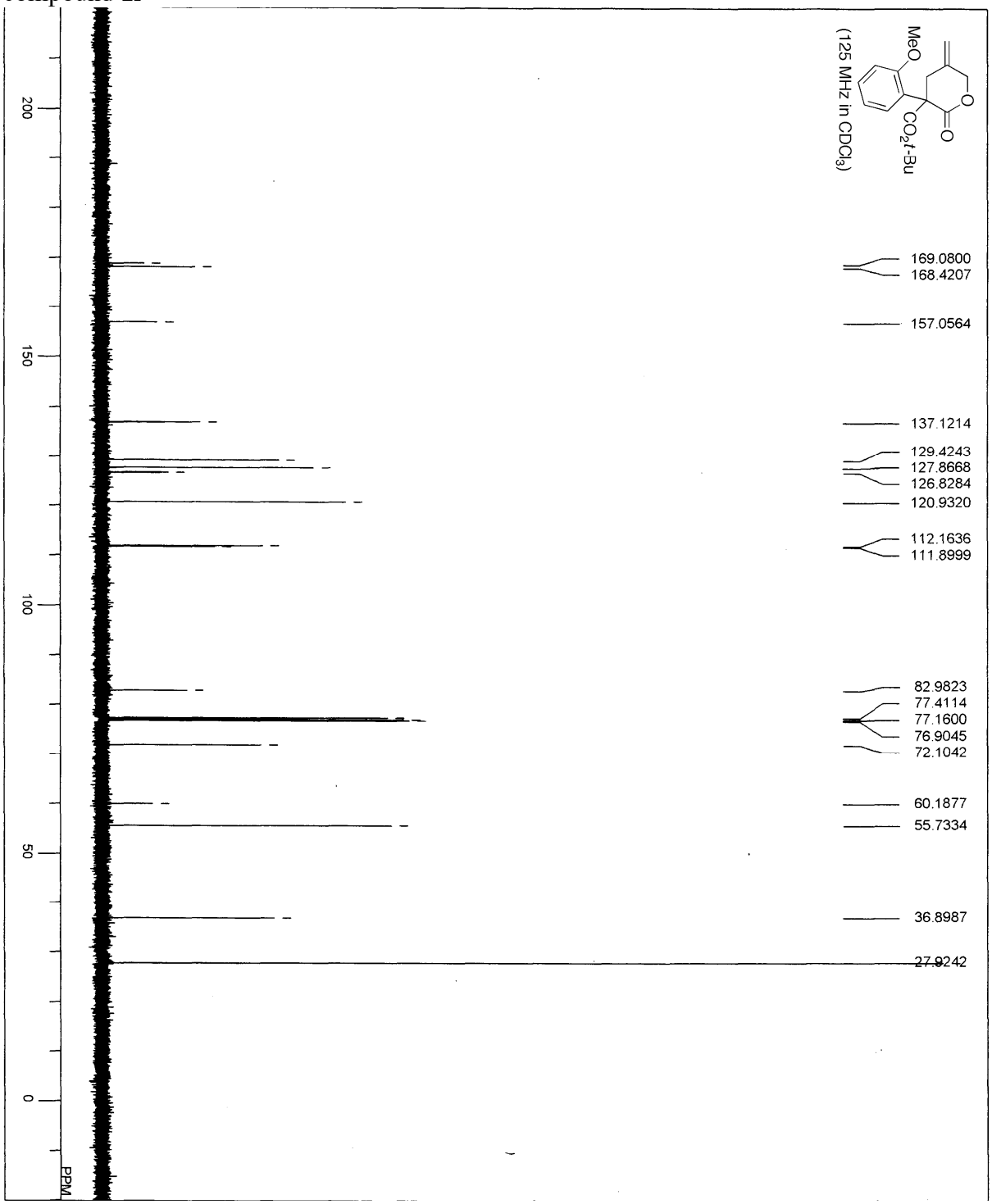
168.3300
148.0819
147.6287
136.5940
129.0617
120.8949
112.0111
108.3604
108.2862
101.4874
83.6045
77.4155
77.1600
76.9045
71.2018
59.5573
36.0292
27.8542
200
150
100
50
0
PPM

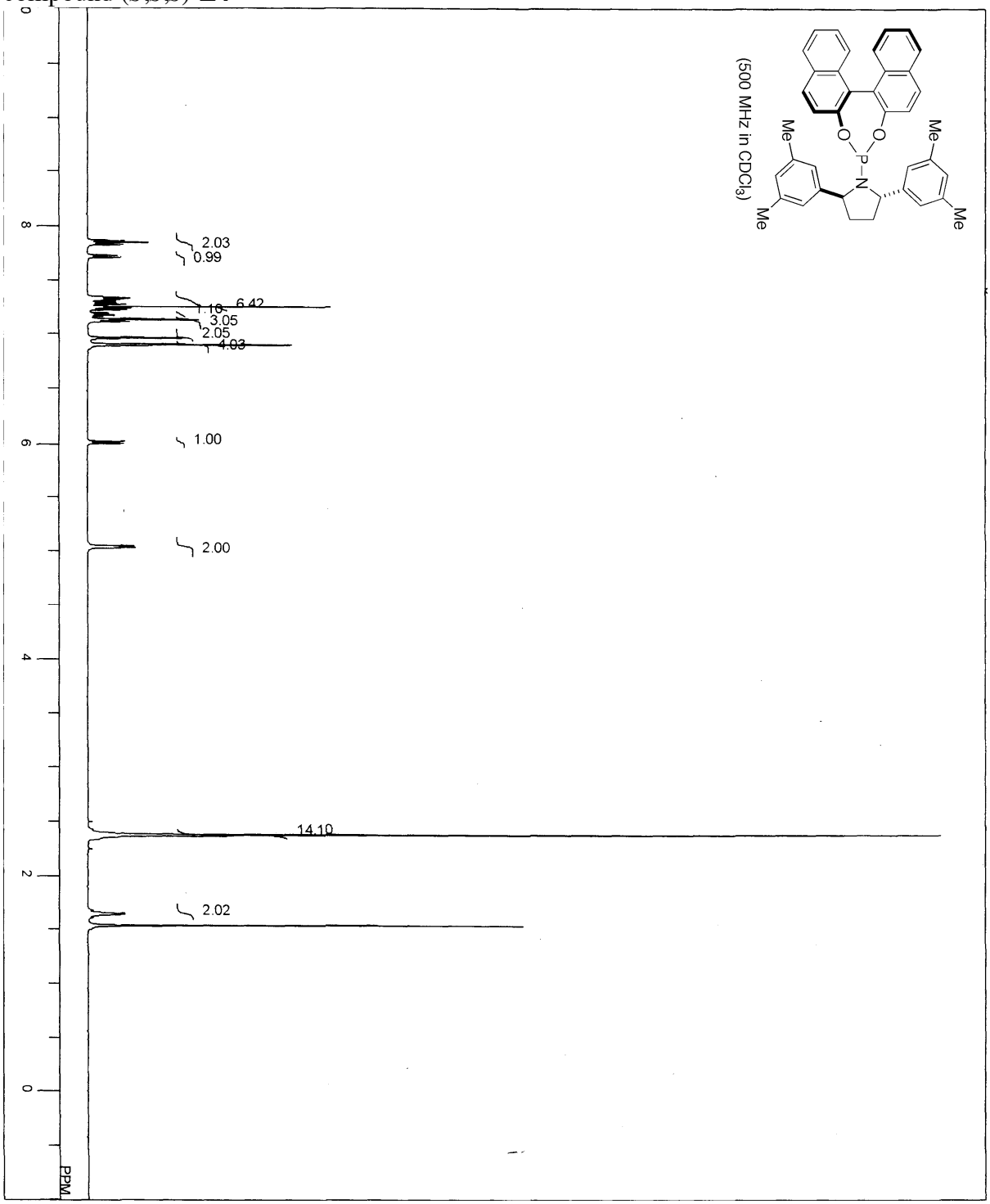
compound **1i**


(500 MHz in CDCl3)
MeO
CO2t-Bu
O
O
0.89
0.97
1.94
2.03
2.03
3.09
1.00
1.03
9.15
PPM

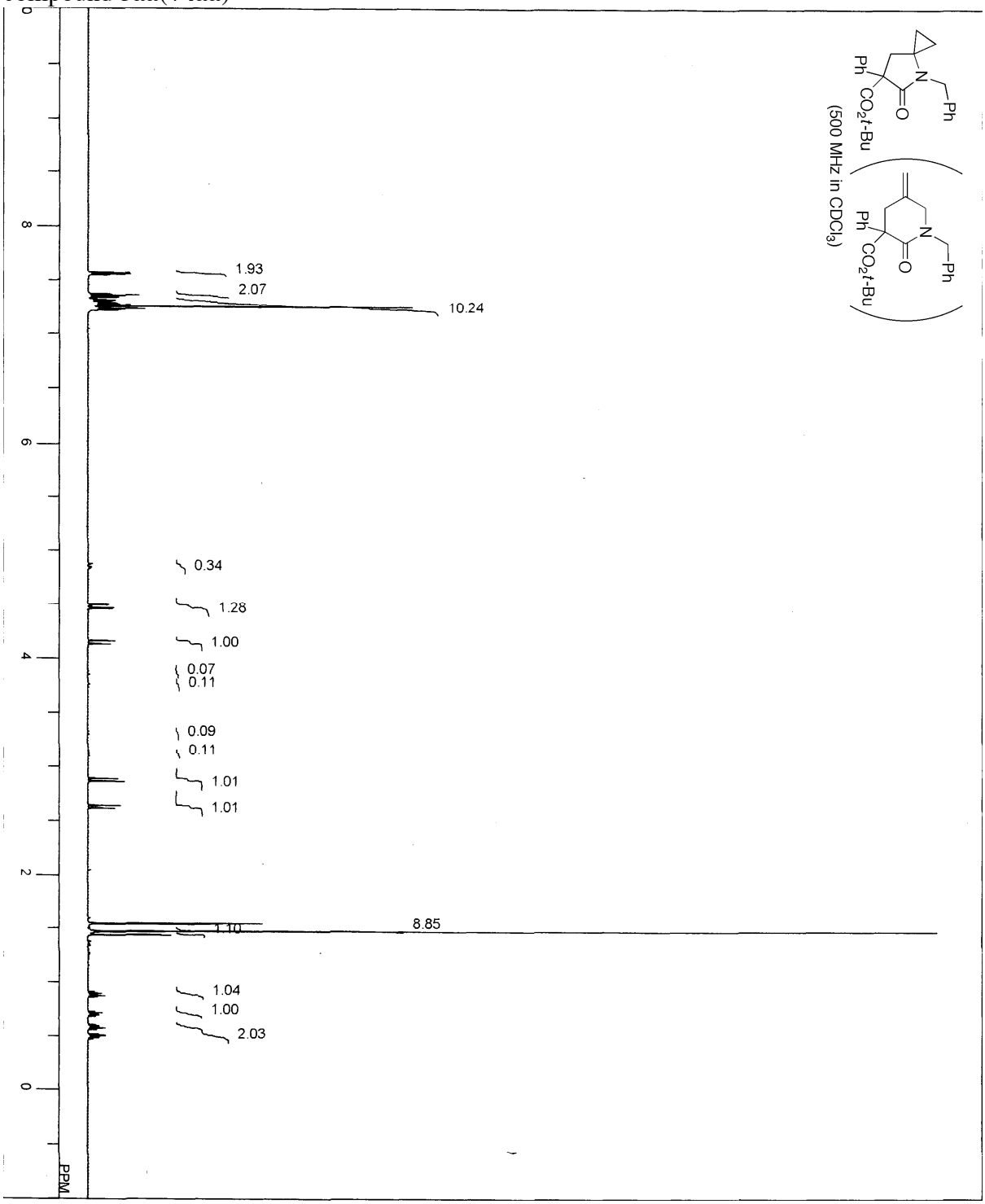
compound **1i**


(125 MHz in CDCl3)
MeO
CO2t-Bu
O
O
169.0800
168.4207
157.0564
137.1214
129.4243
127.8668
126.8284
120.9320
112.1636
111.8999
82.9823
77.4114
77.1600
76.9045
72.1042
60.1877
55.7334
36.8987
27.9242
200
150
100
50
0
PPM

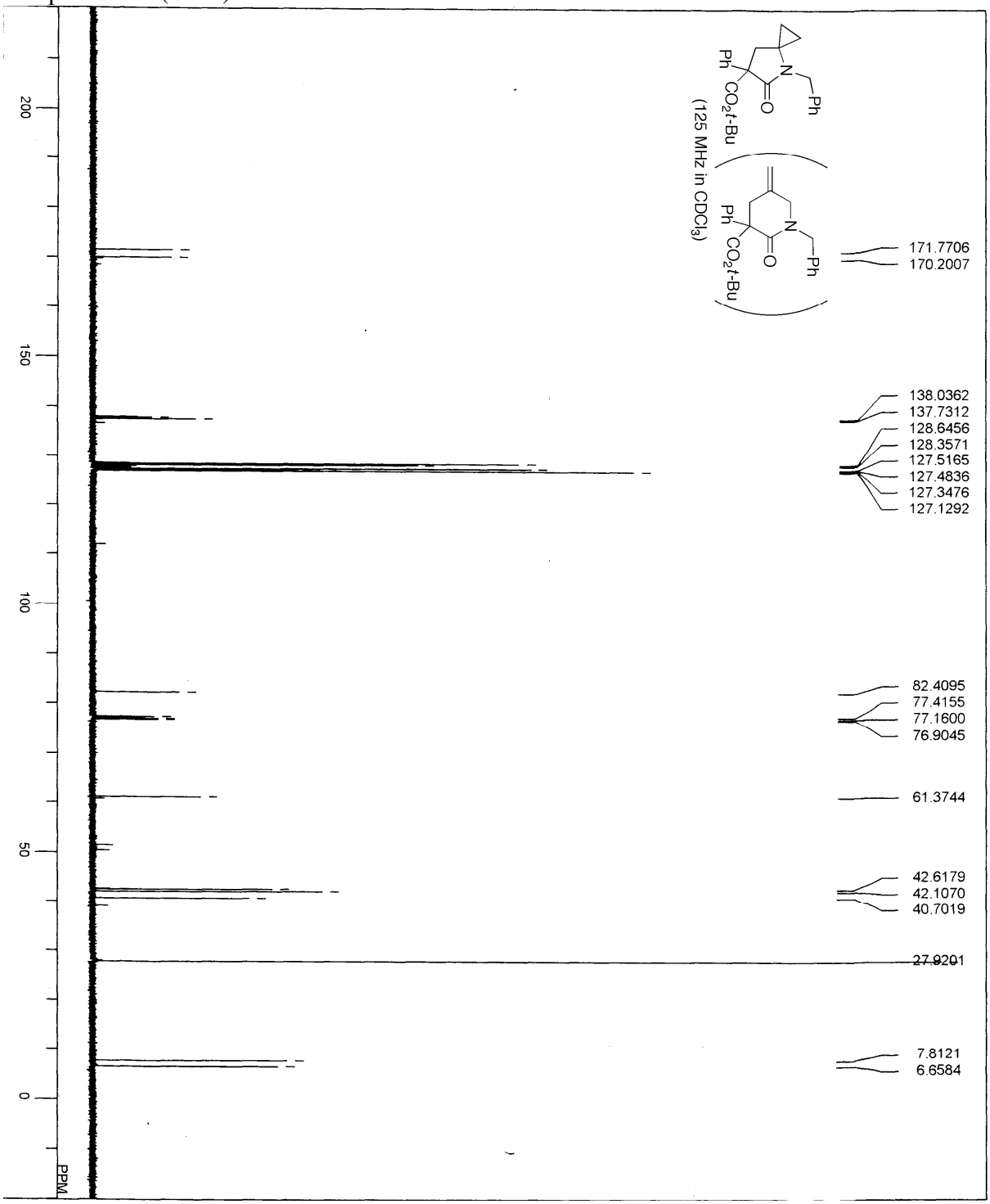
compound (*S*,*S*,*S*)-**L4**



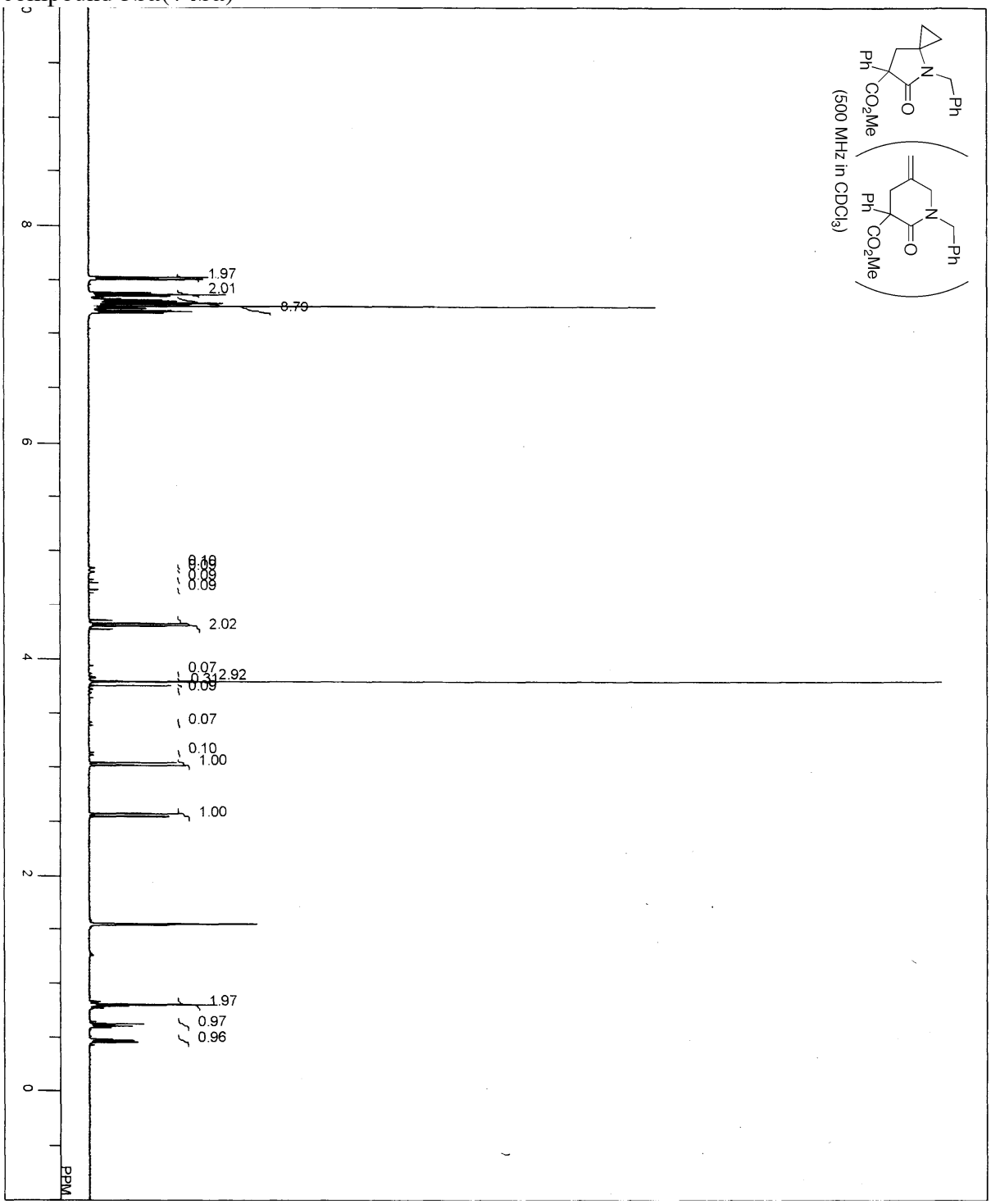
compound **3aa**(+**4aa**)



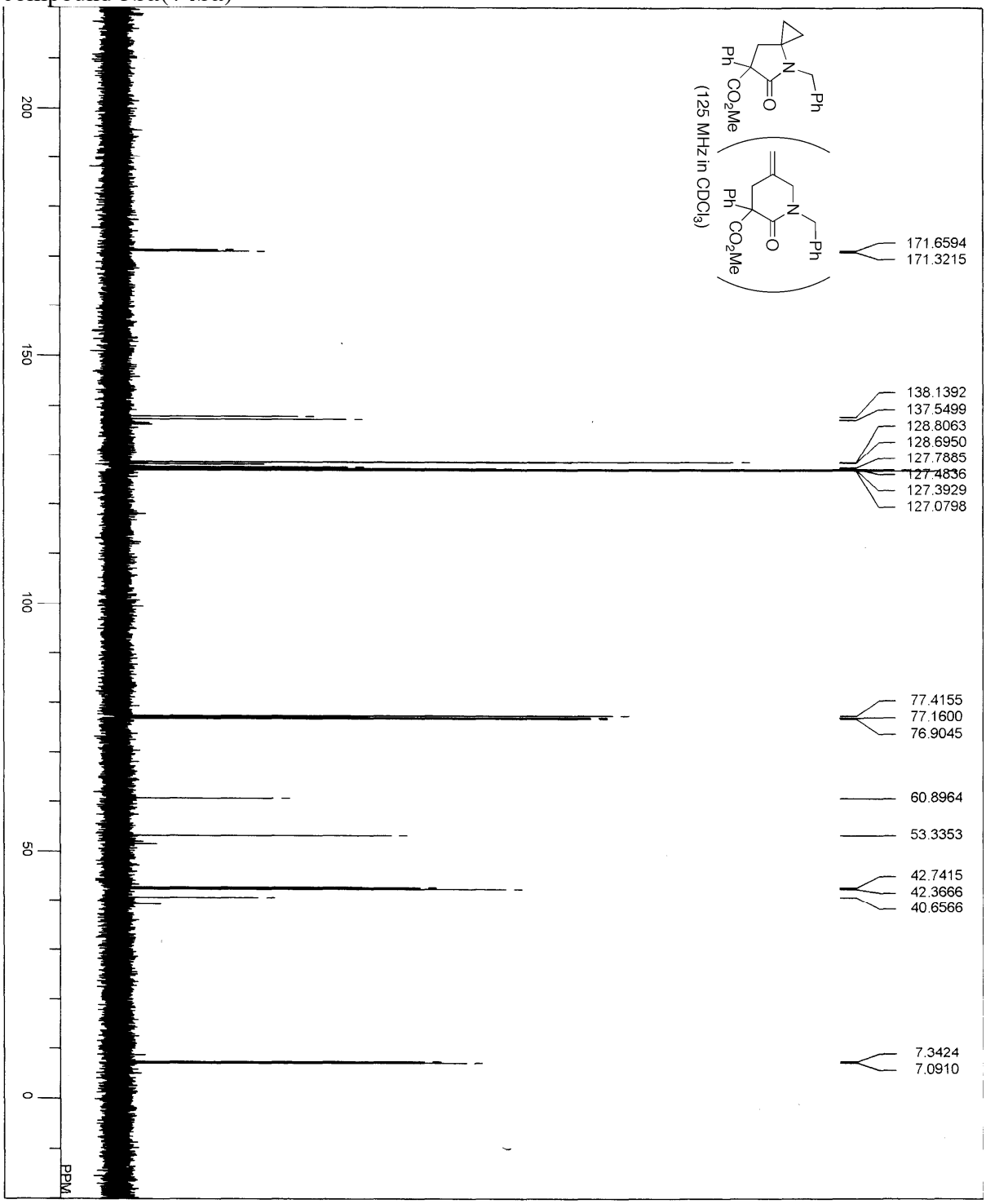
compound **3aa**(+**4aa**)



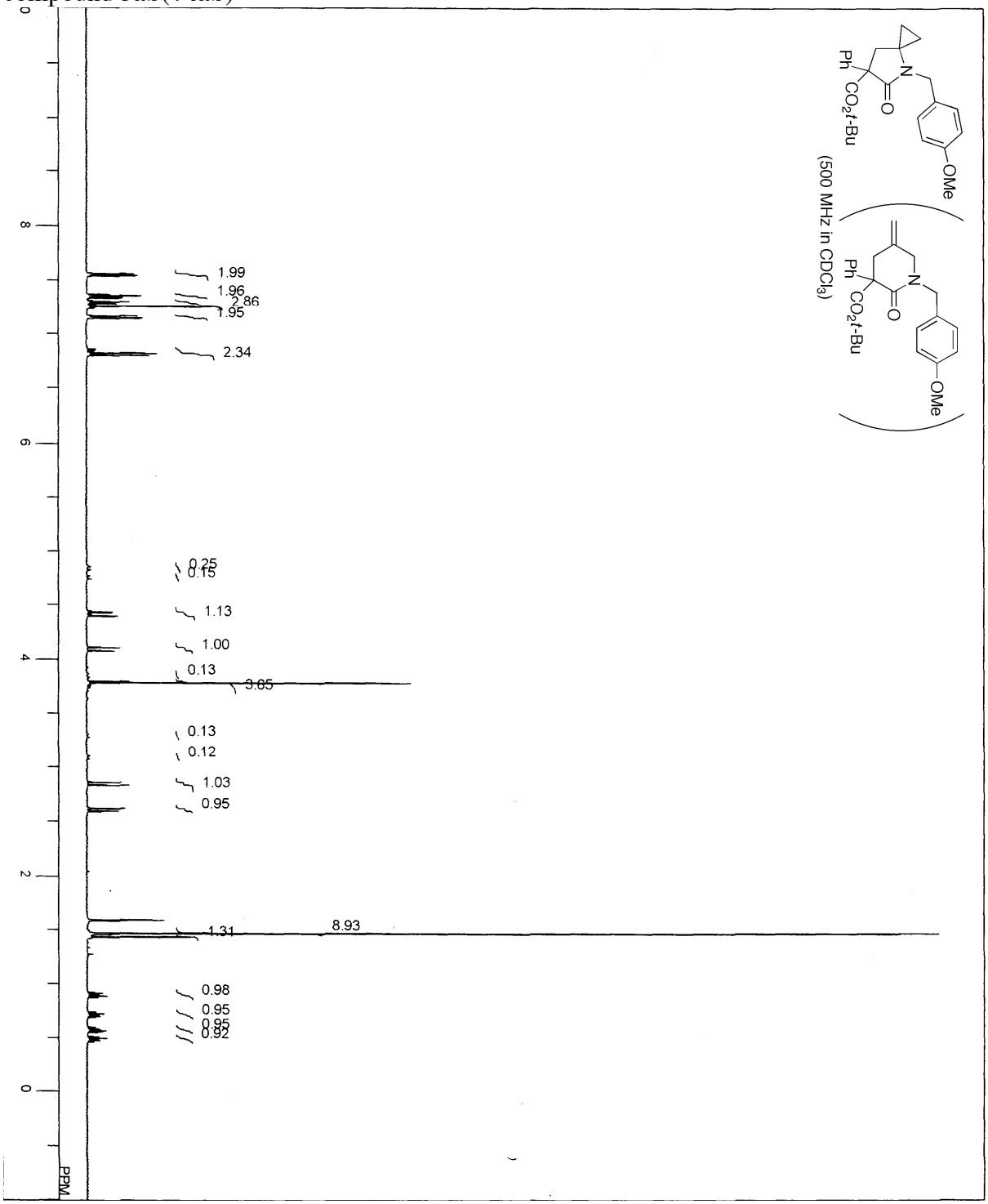
compound **3ba**(+**4ba**)



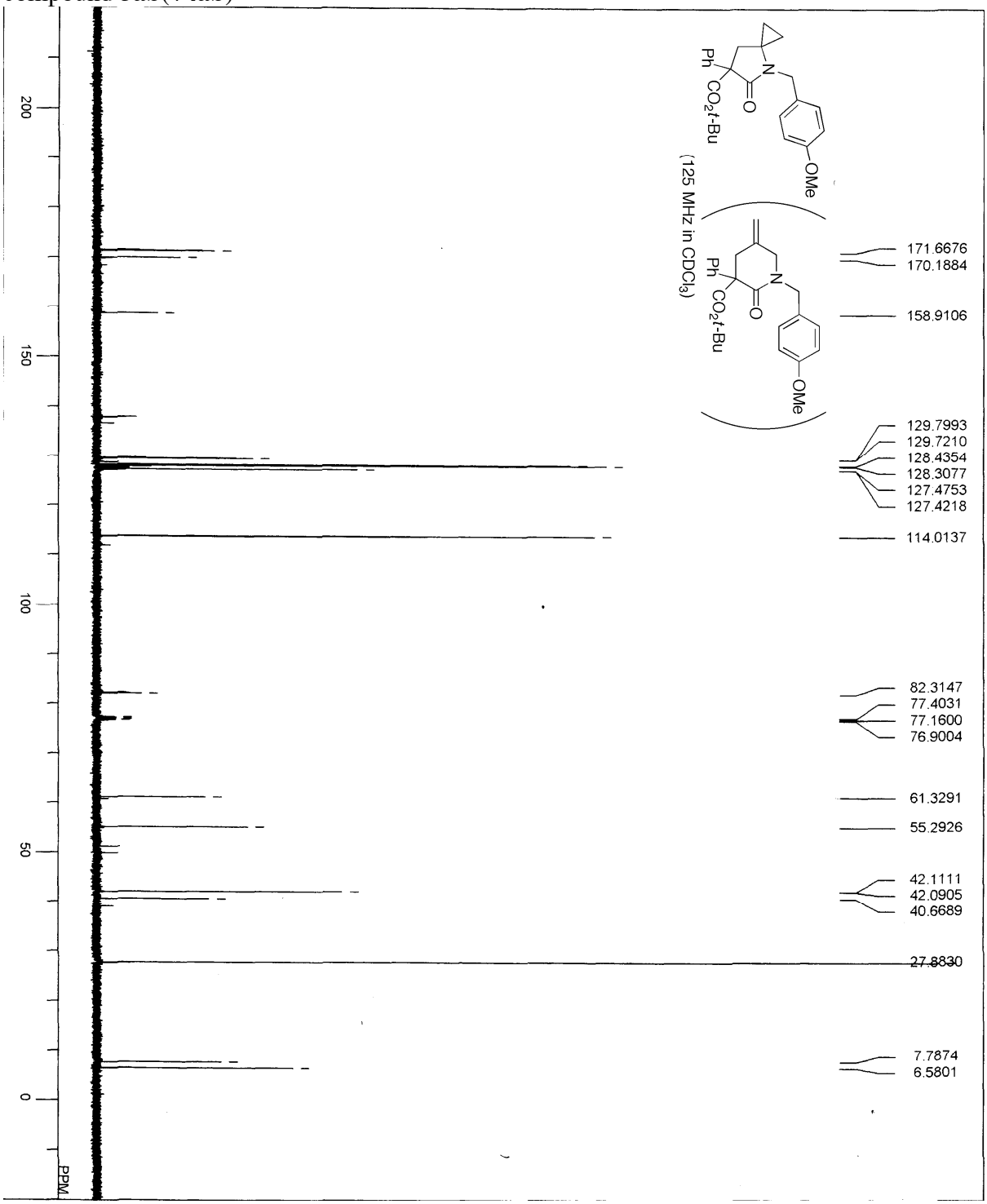
compound **3ba**(+**4ba**)



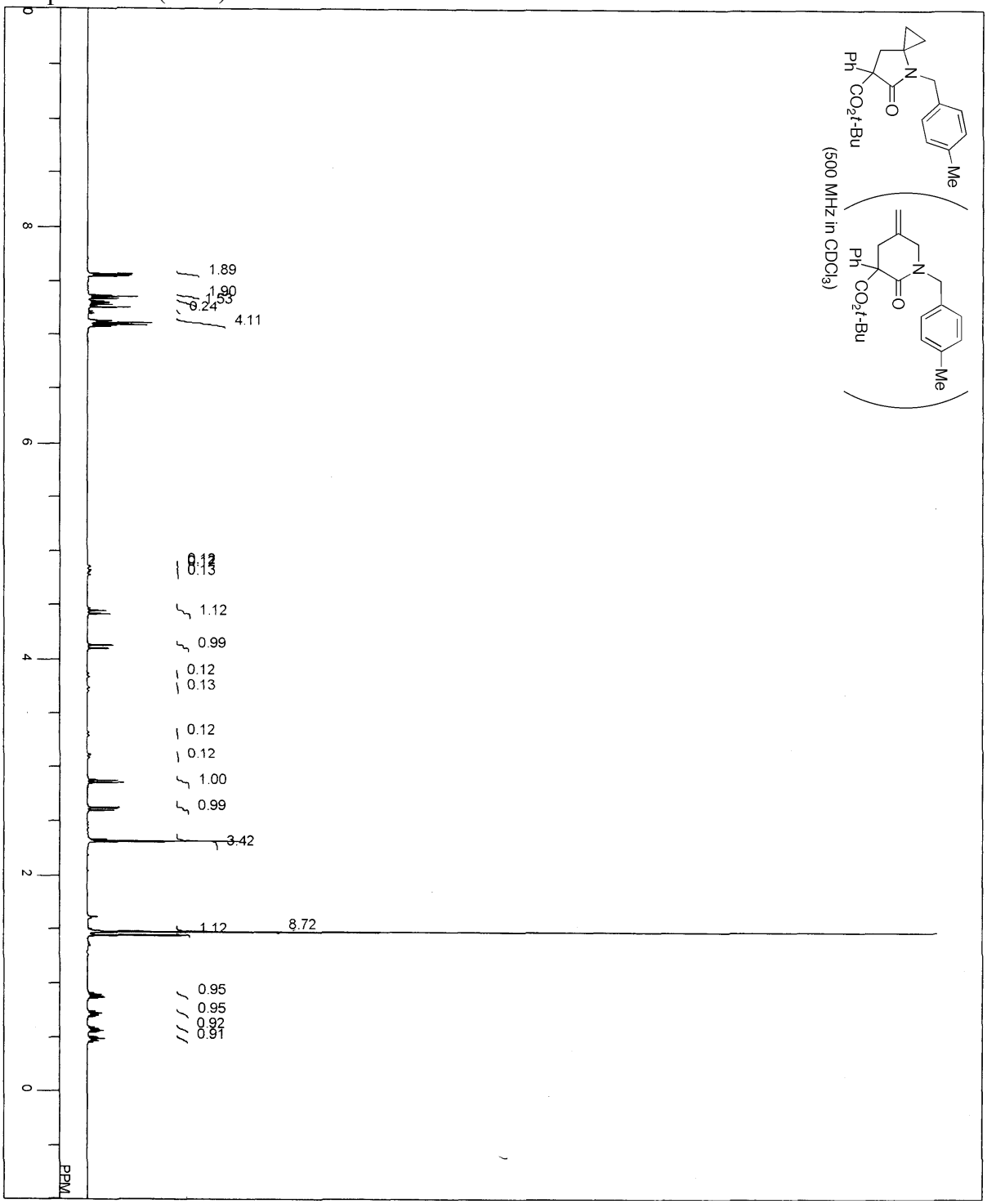
compound **3ab**(+**4ab**)



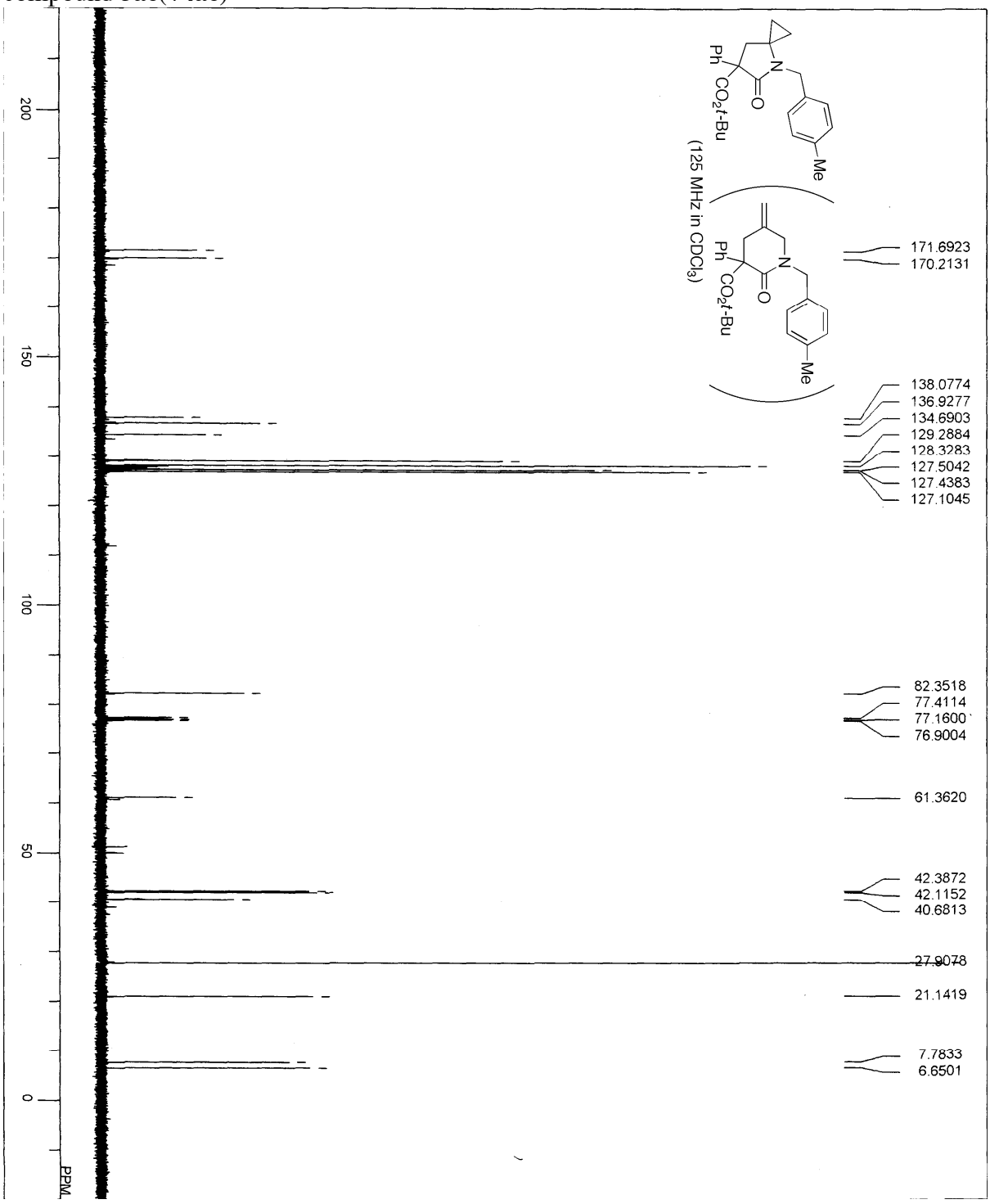
compound **3ab**(+**4ab**)



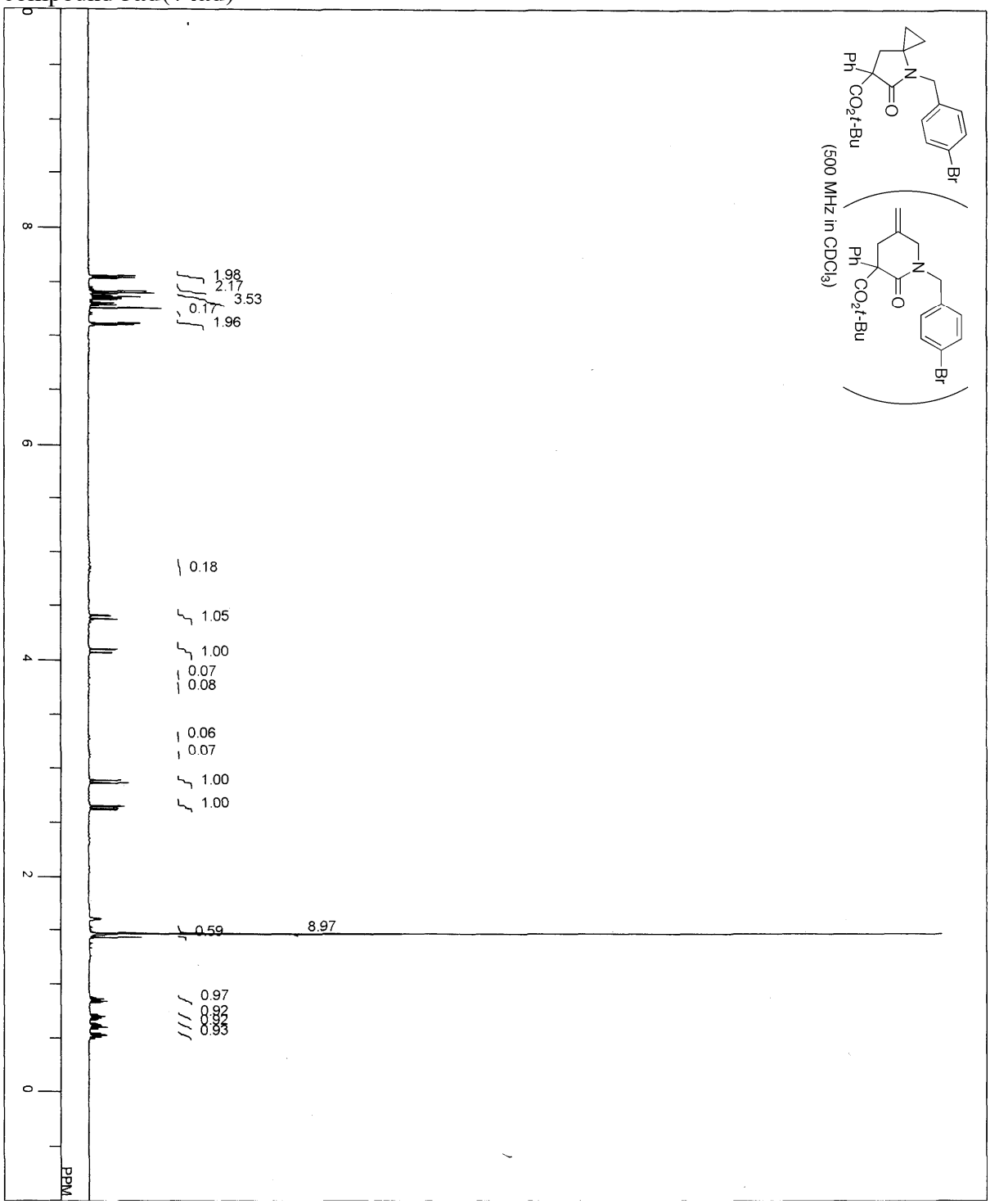
compound **3ac**(+**4ac**)



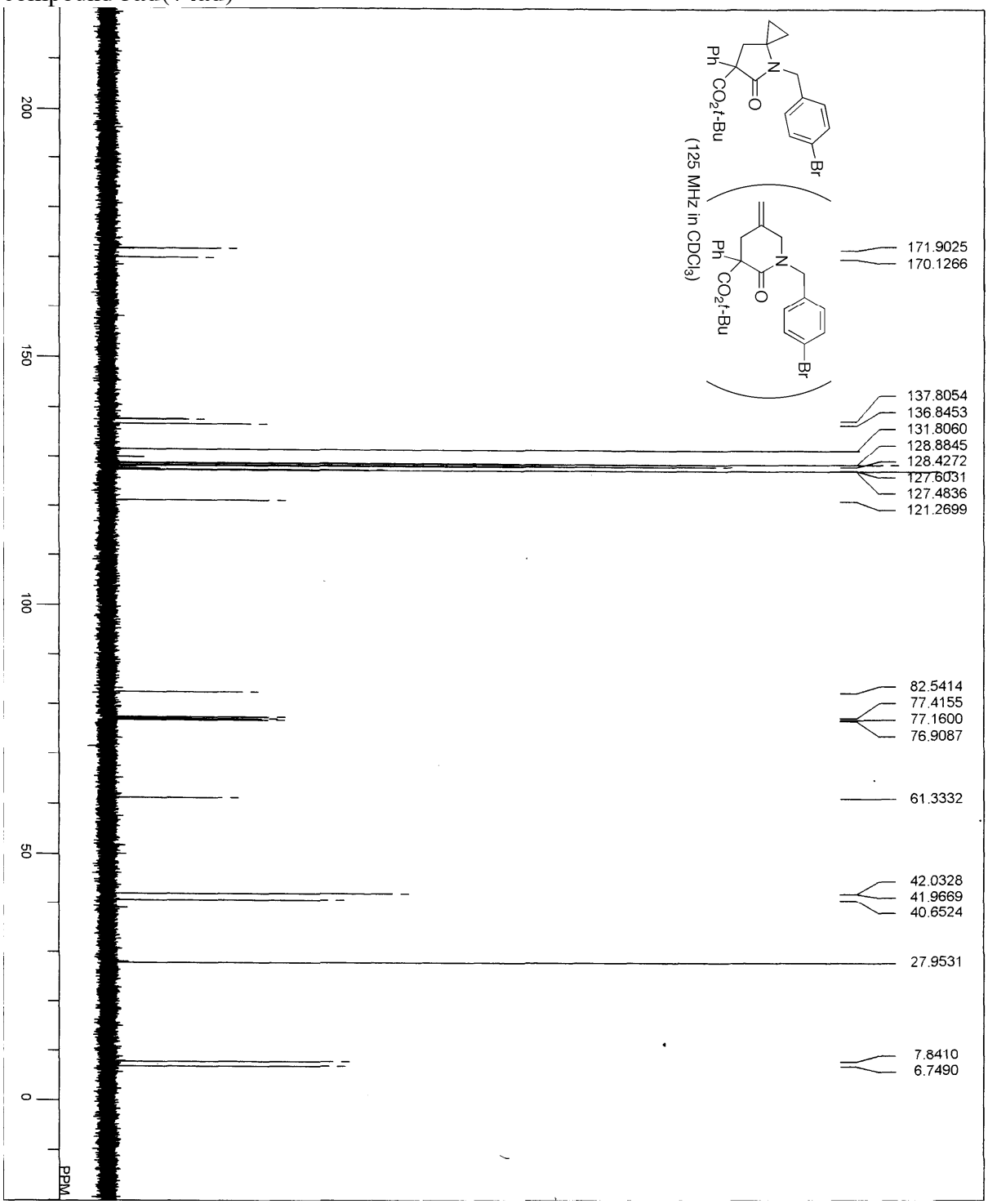
compound **3ac**(+**4ac**)



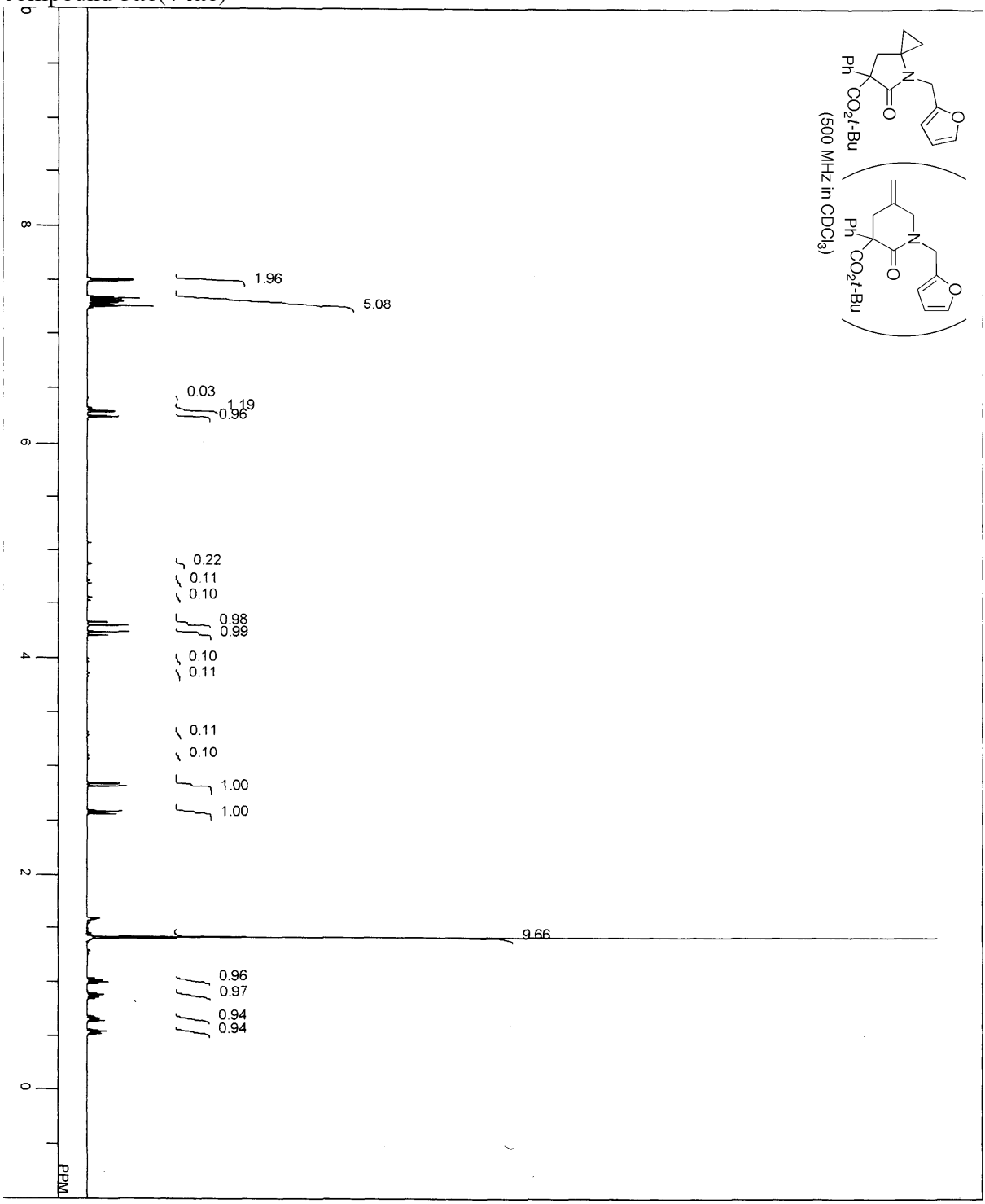
compound **3ad**(+**4ad**)



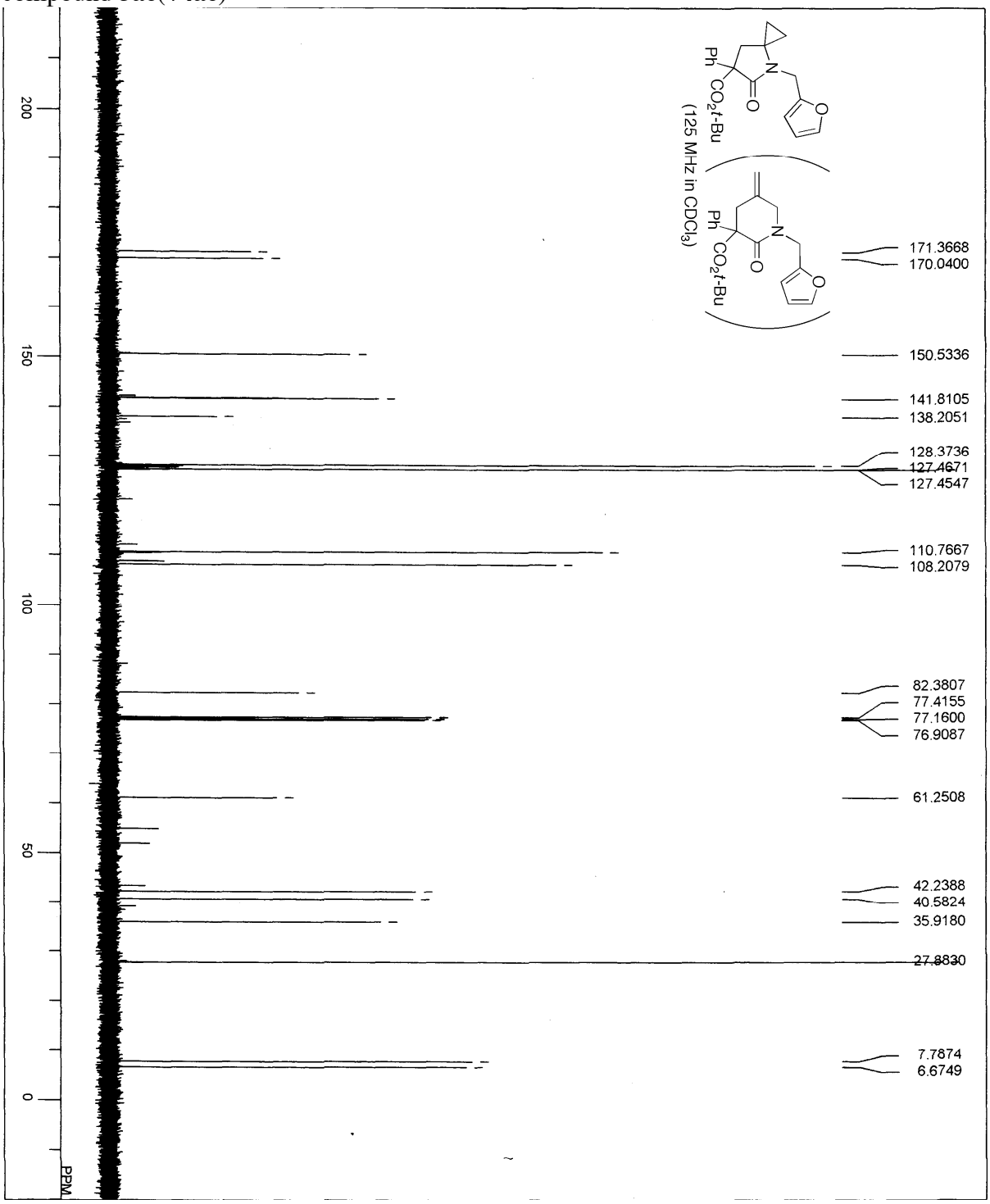
compound **3ad**(+**4ad**)



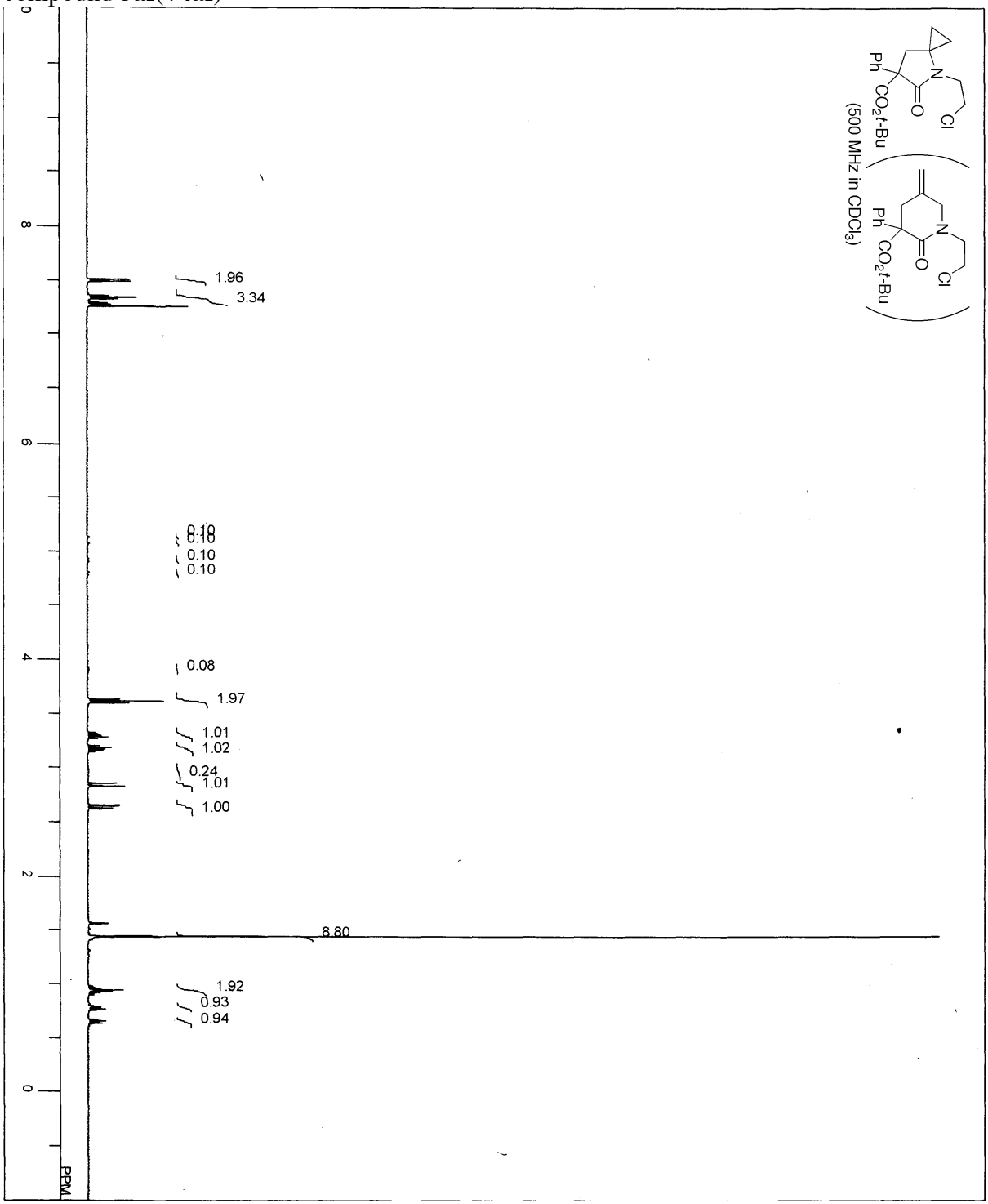
compound **3ae**(+**4ae**)



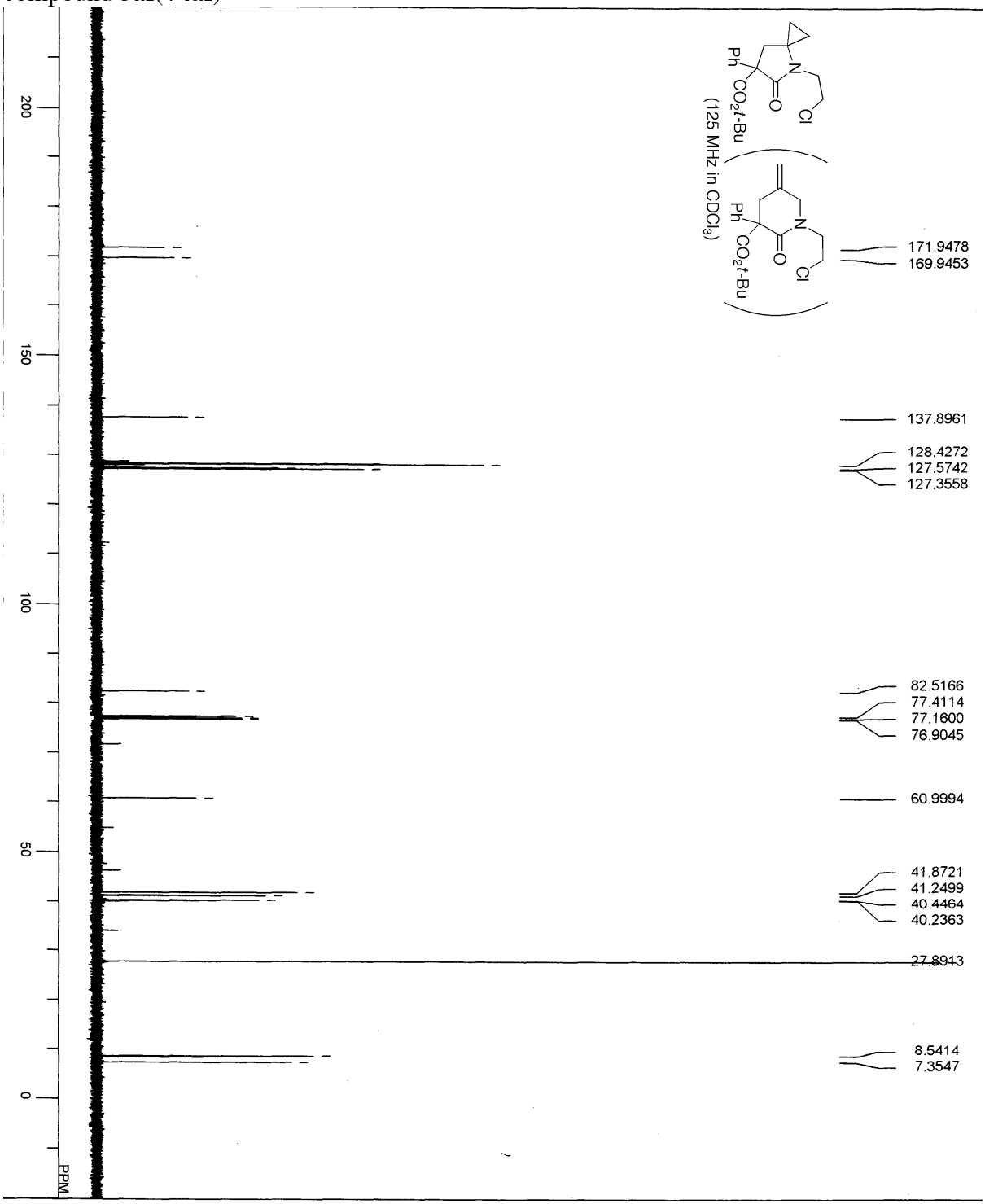
compound **3ae**(+**4ae**)



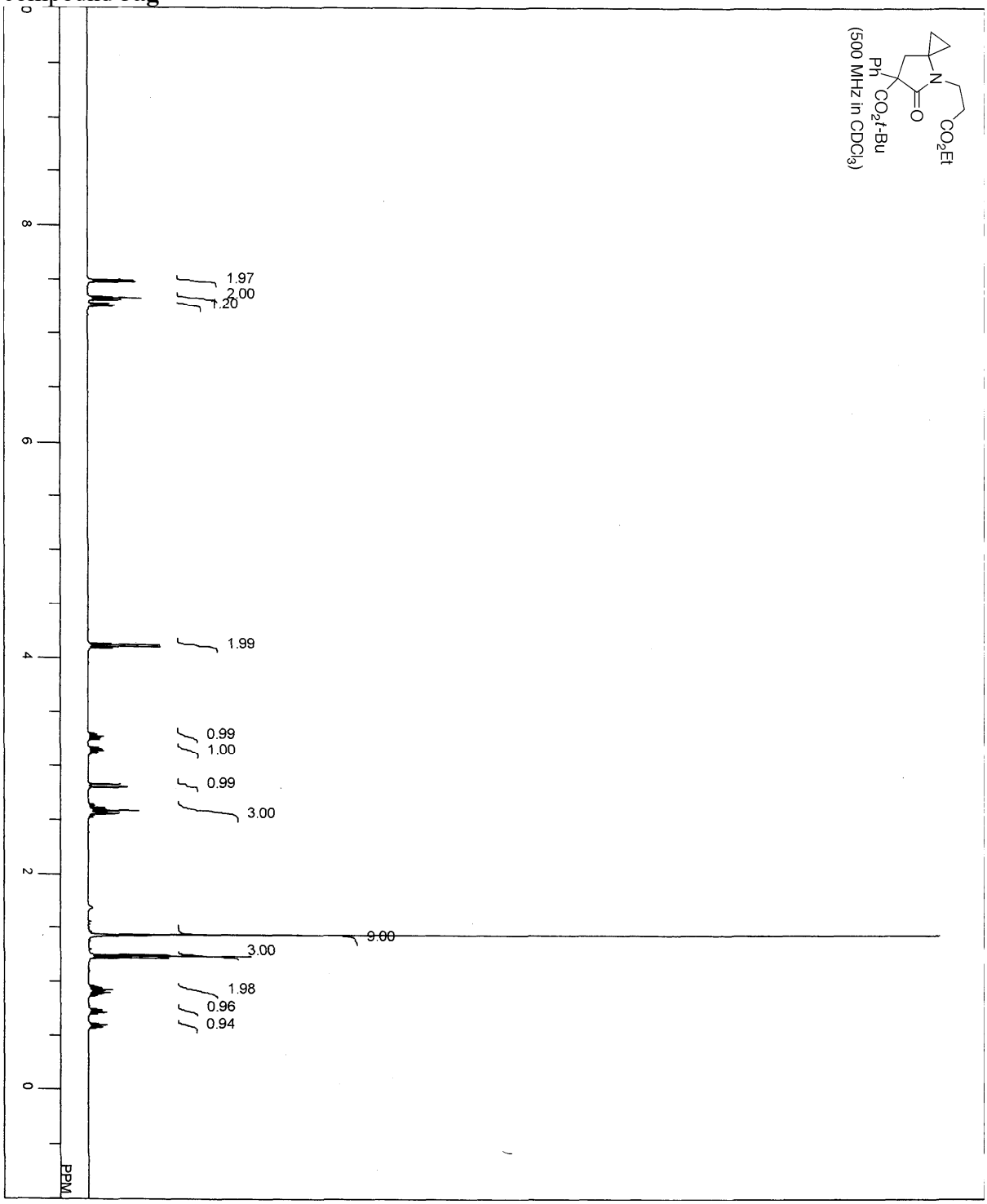
compound **3af**(+**4af**)



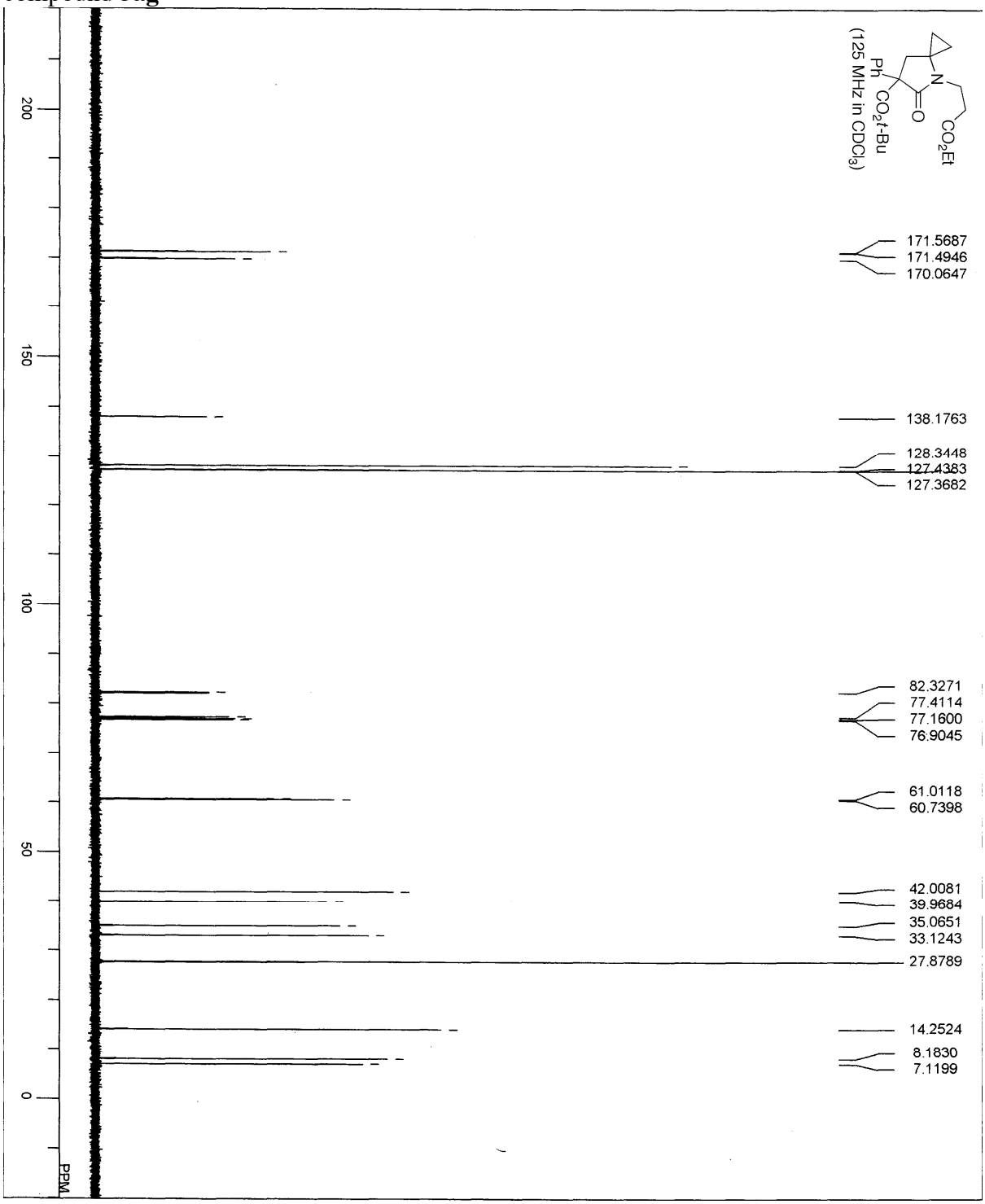
compound **3af**(+**4af**)



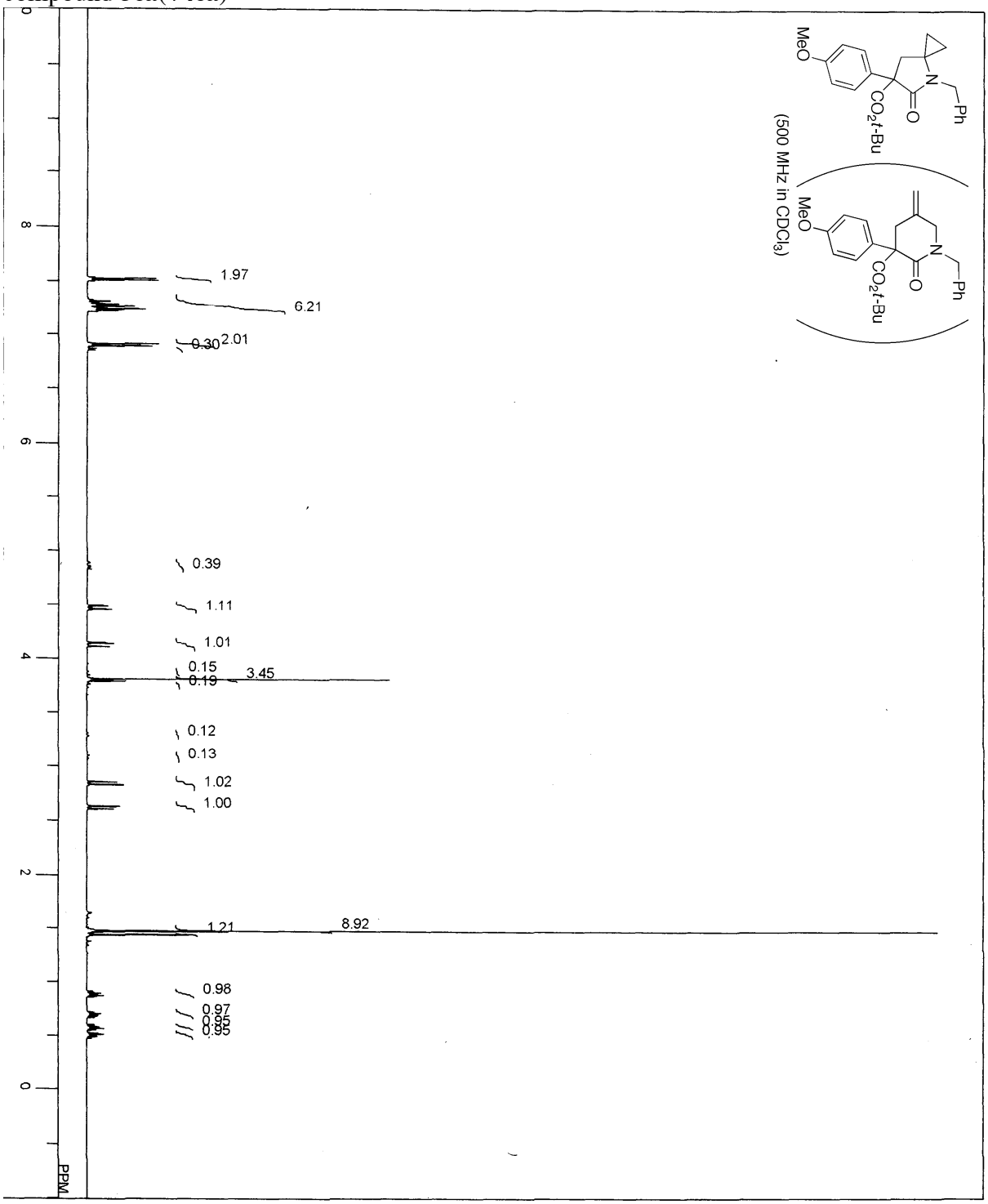
compound **3ag**



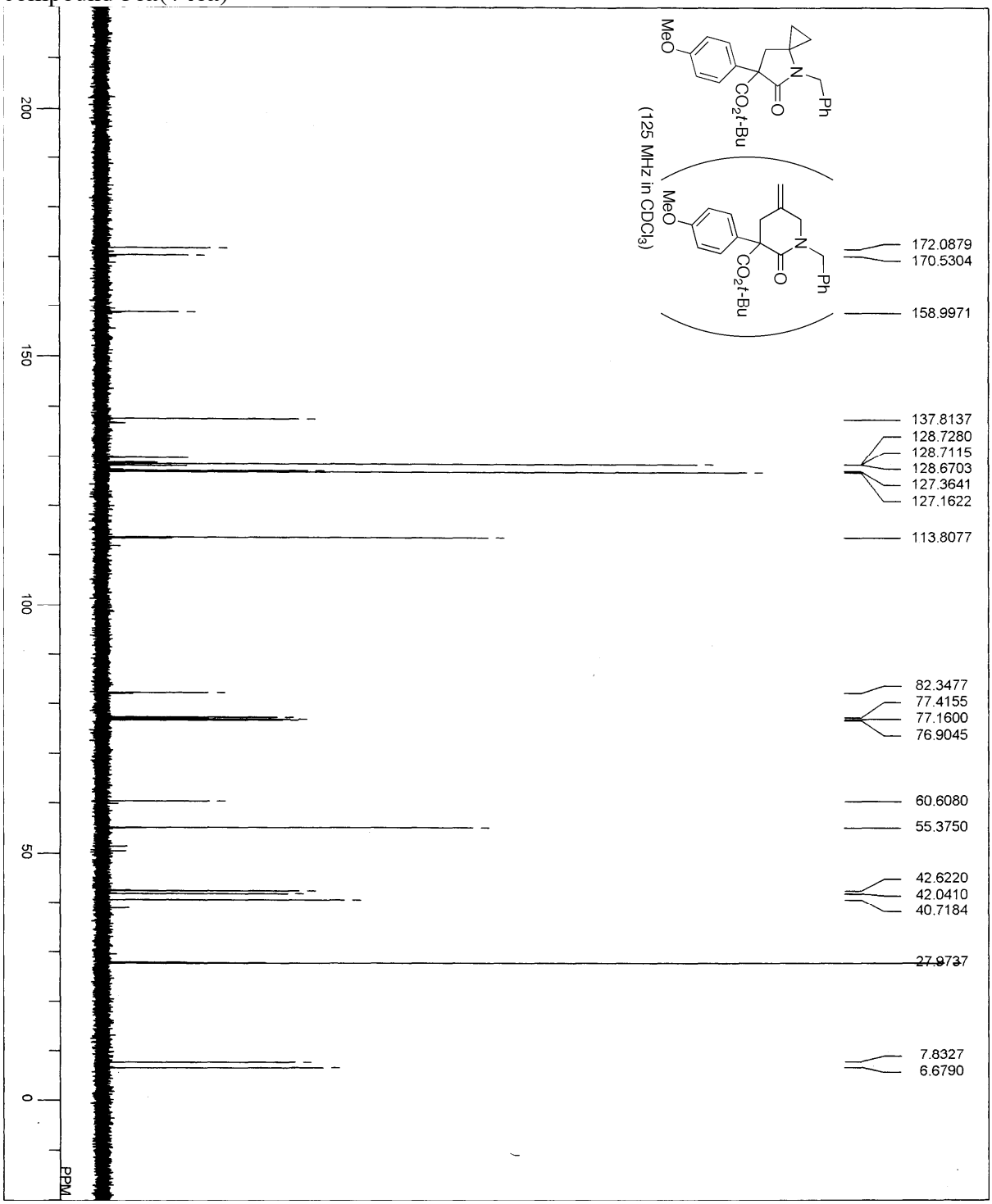
compound **3ag**



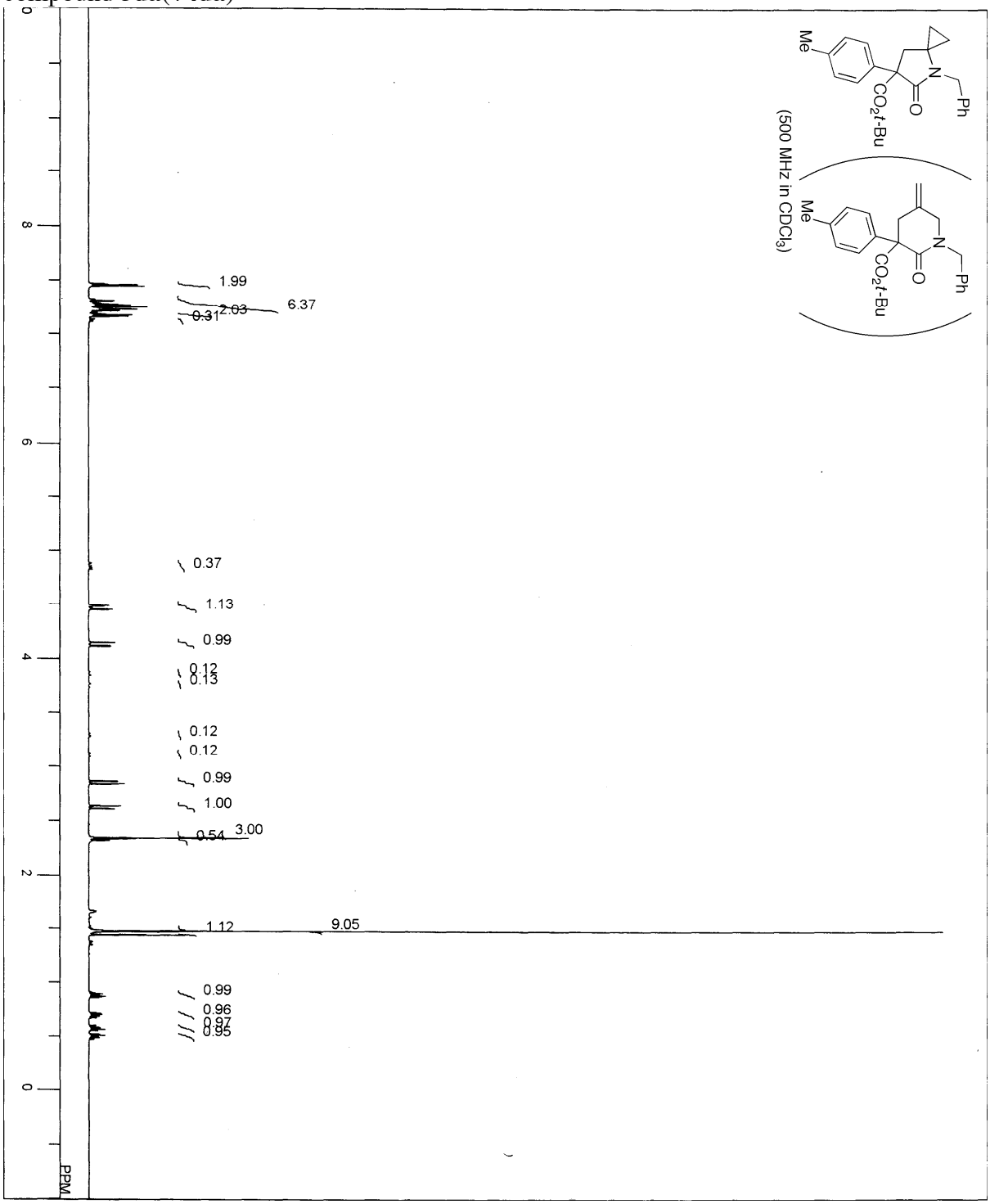
compound **3ca**(+**4ca**)



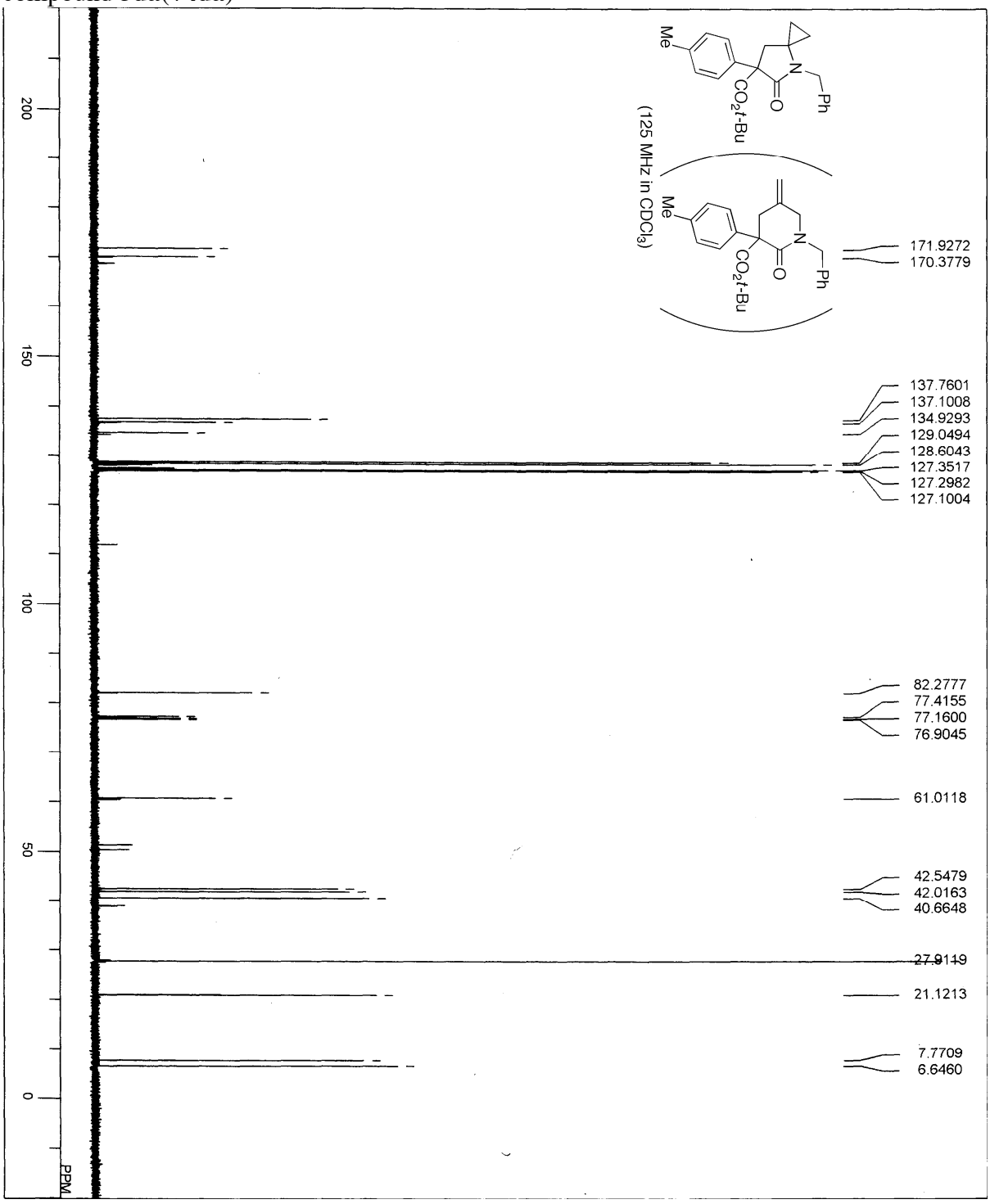
compound **3ca**(+**4ca**)



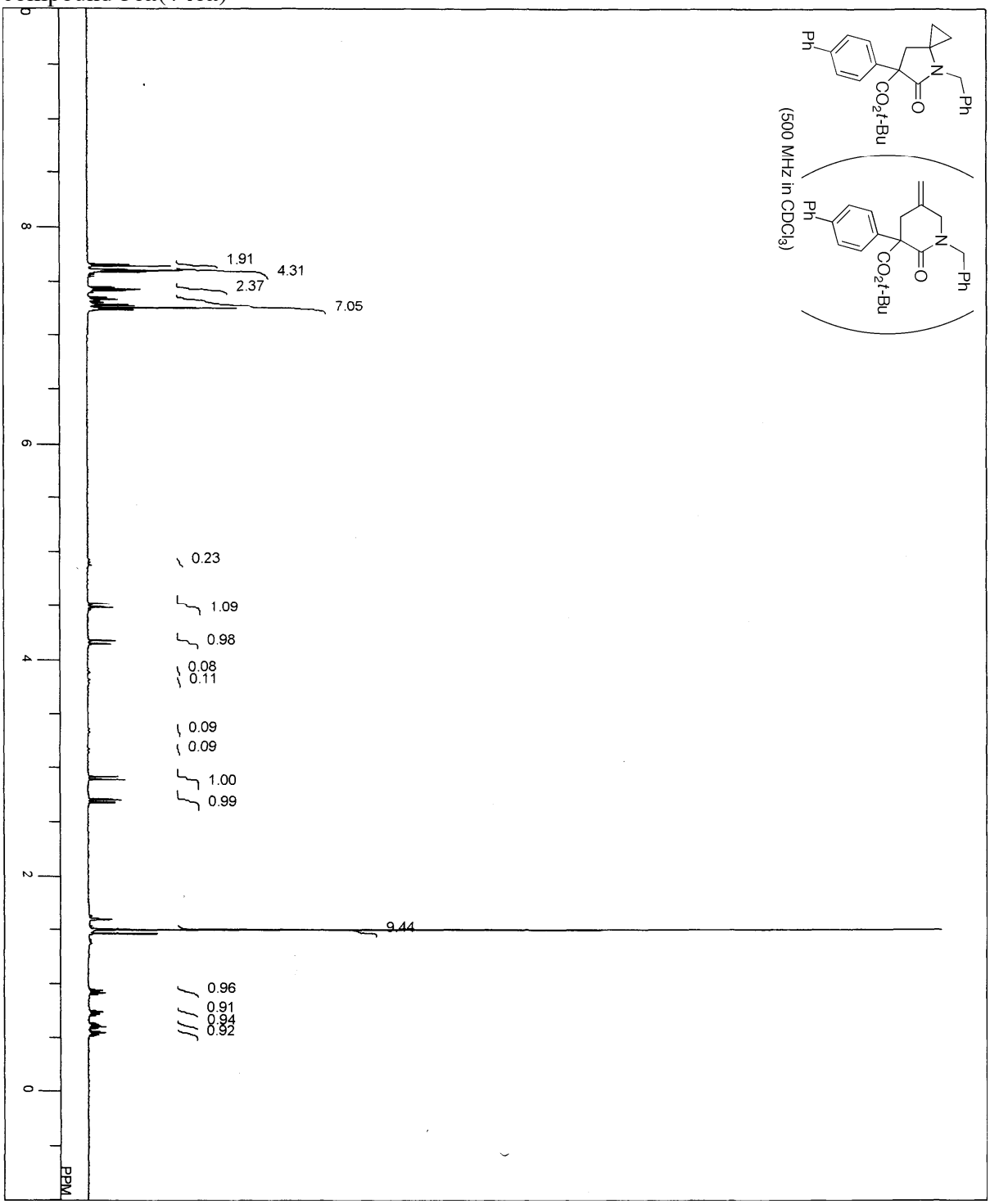
compound **3da**(+**4da**)



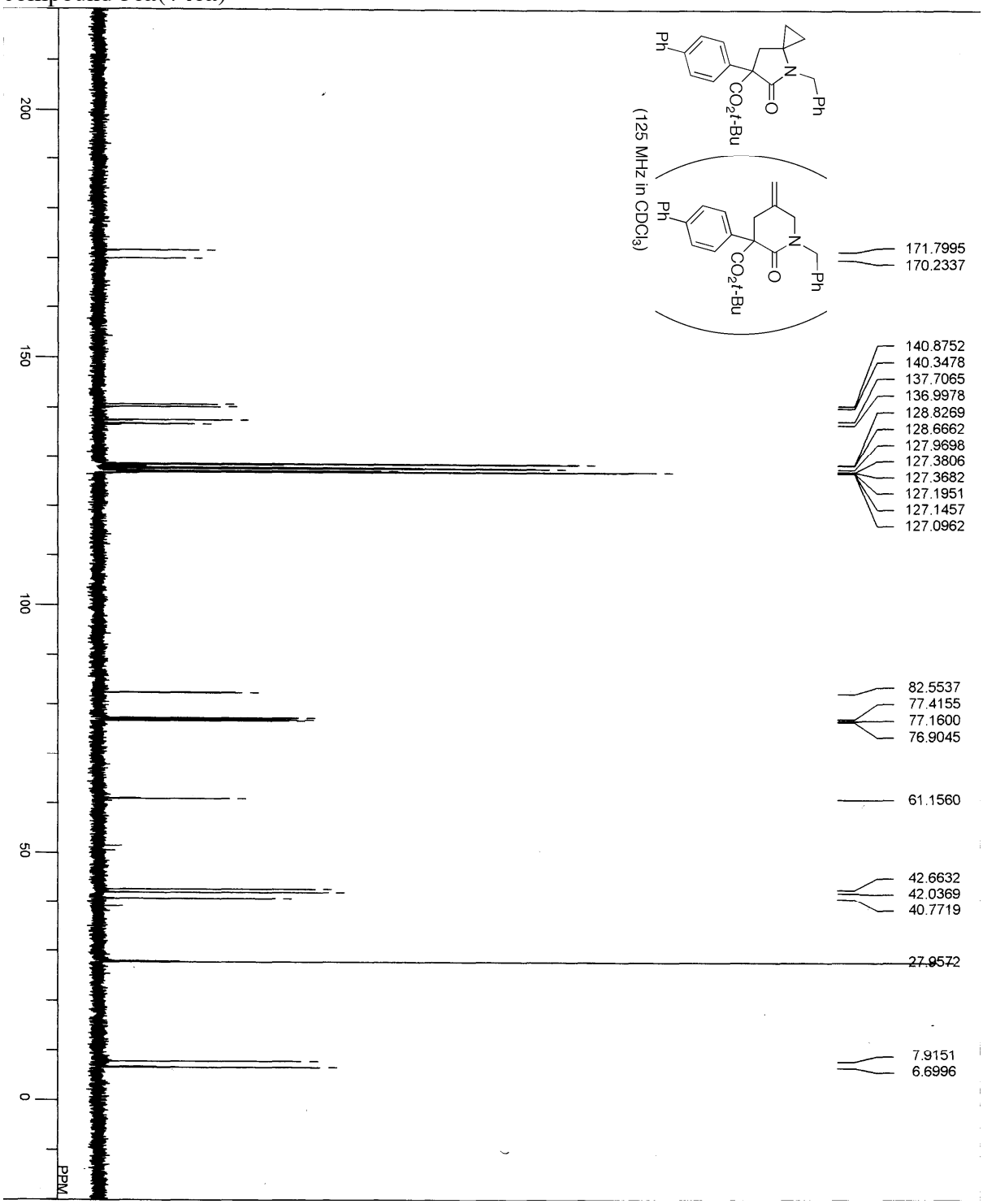
compound **3da**(+**4da**)



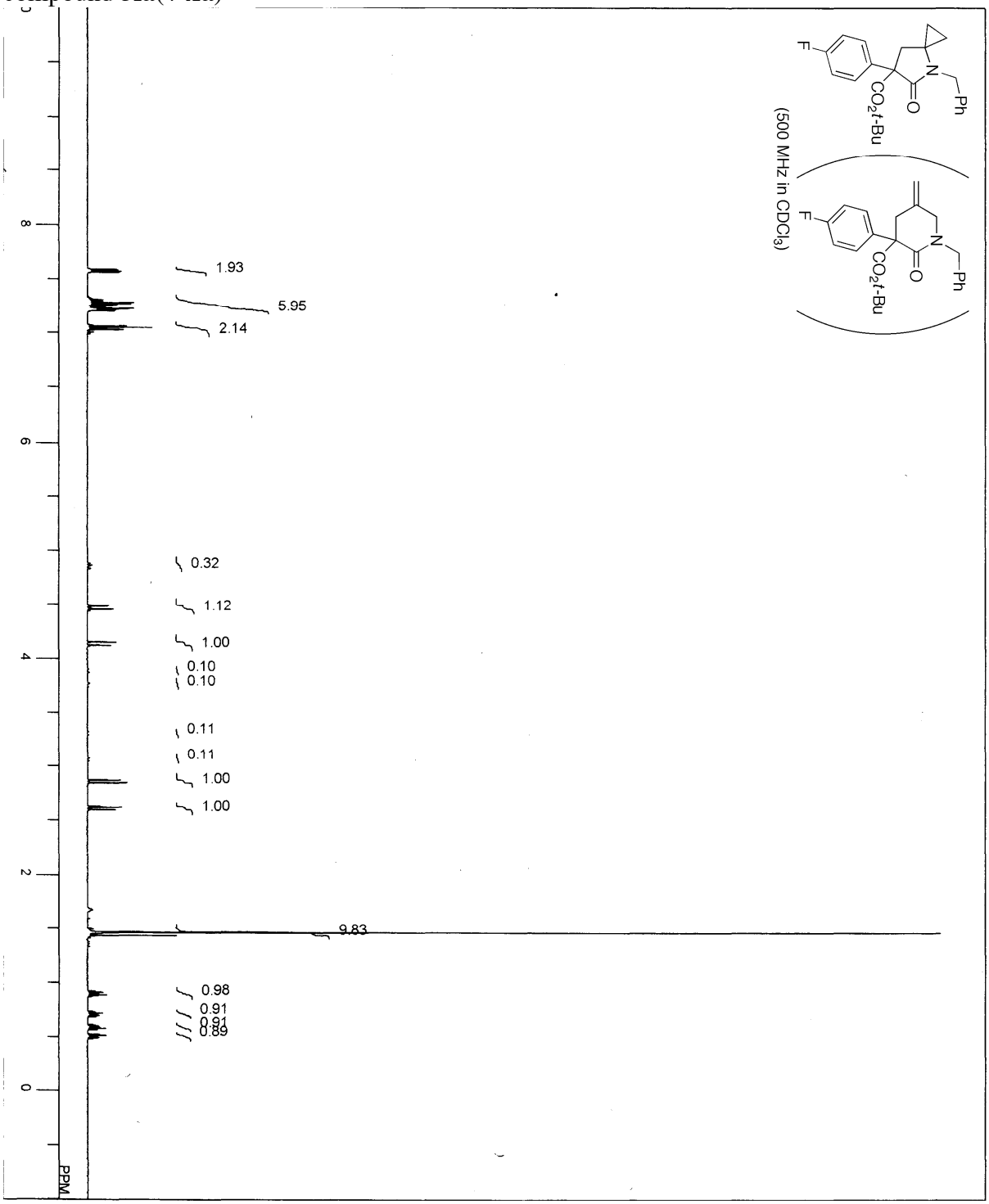
compound **3ea**(+**4ea**)



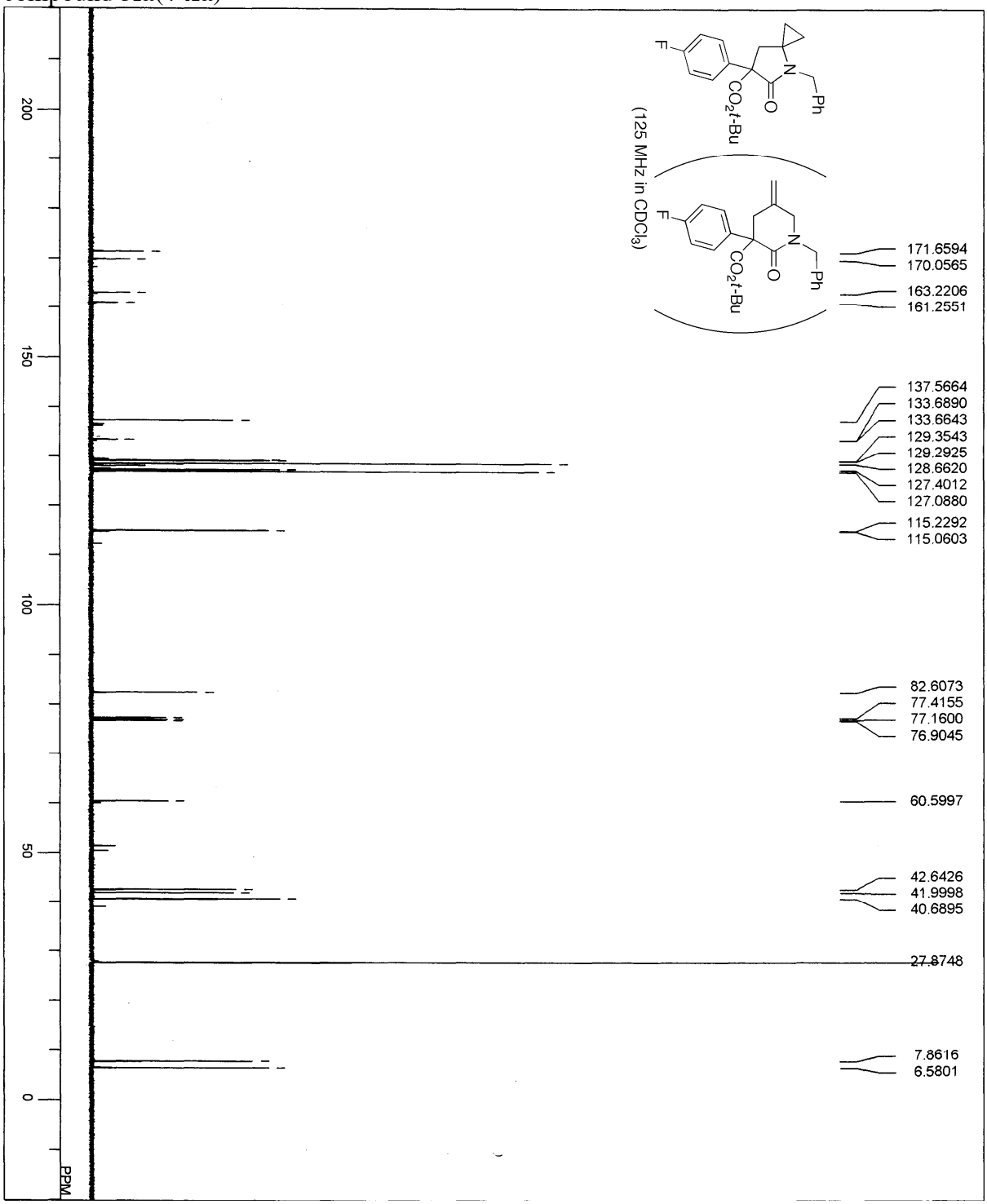
compound **3ea**(+**4ea**)



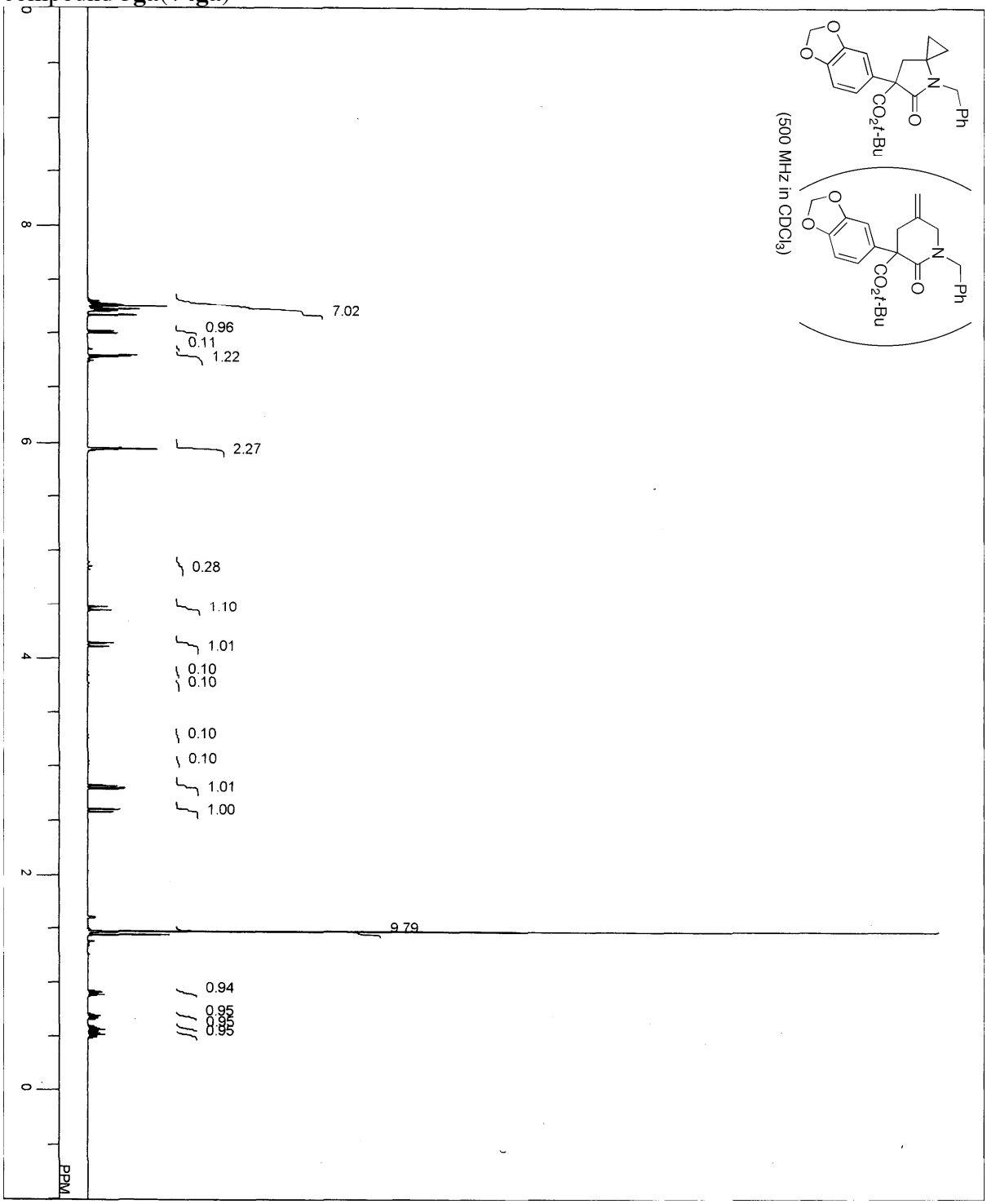
compound **3fa**(+**4fa**)



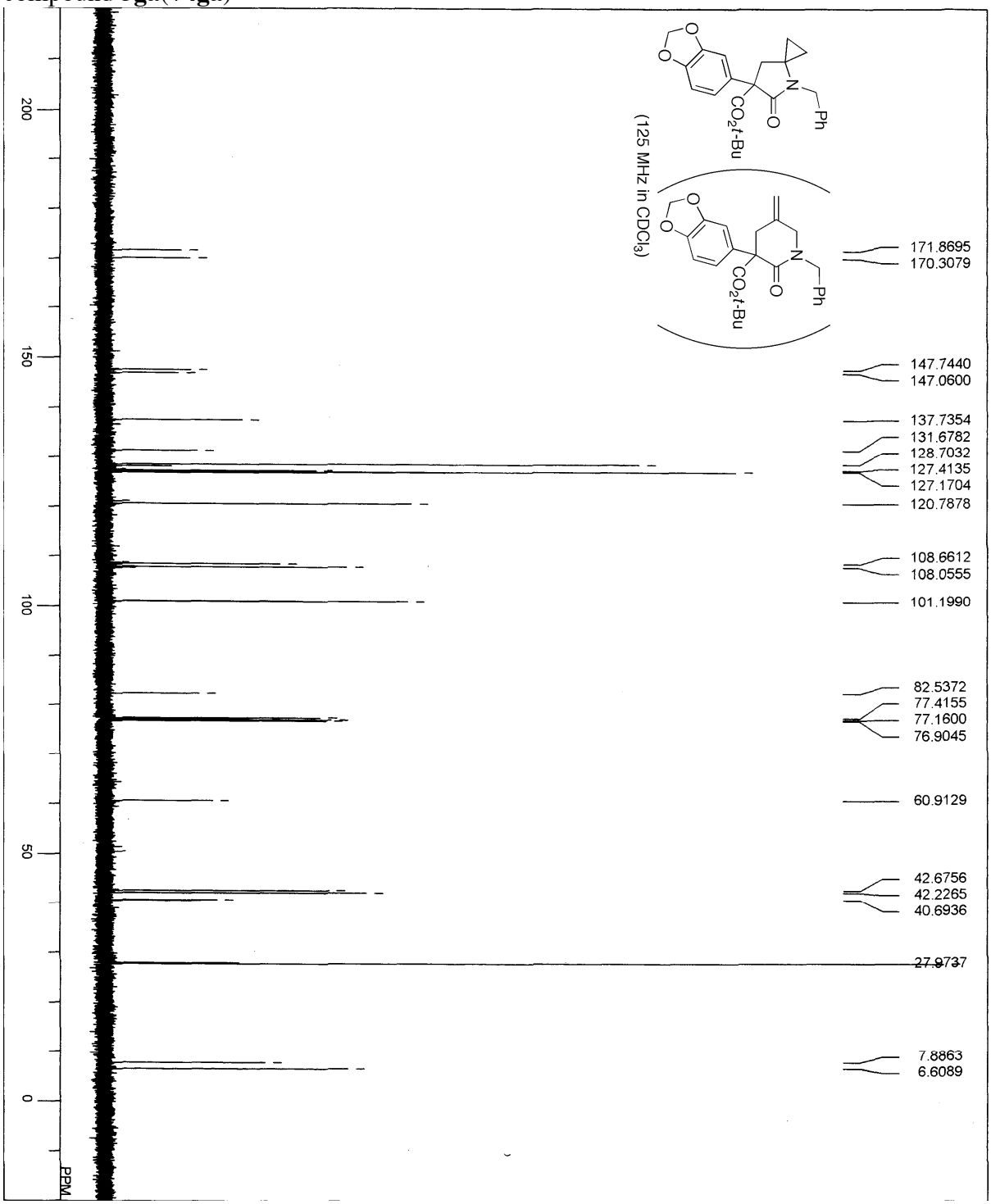
compound **3fa**(+**4fa**)



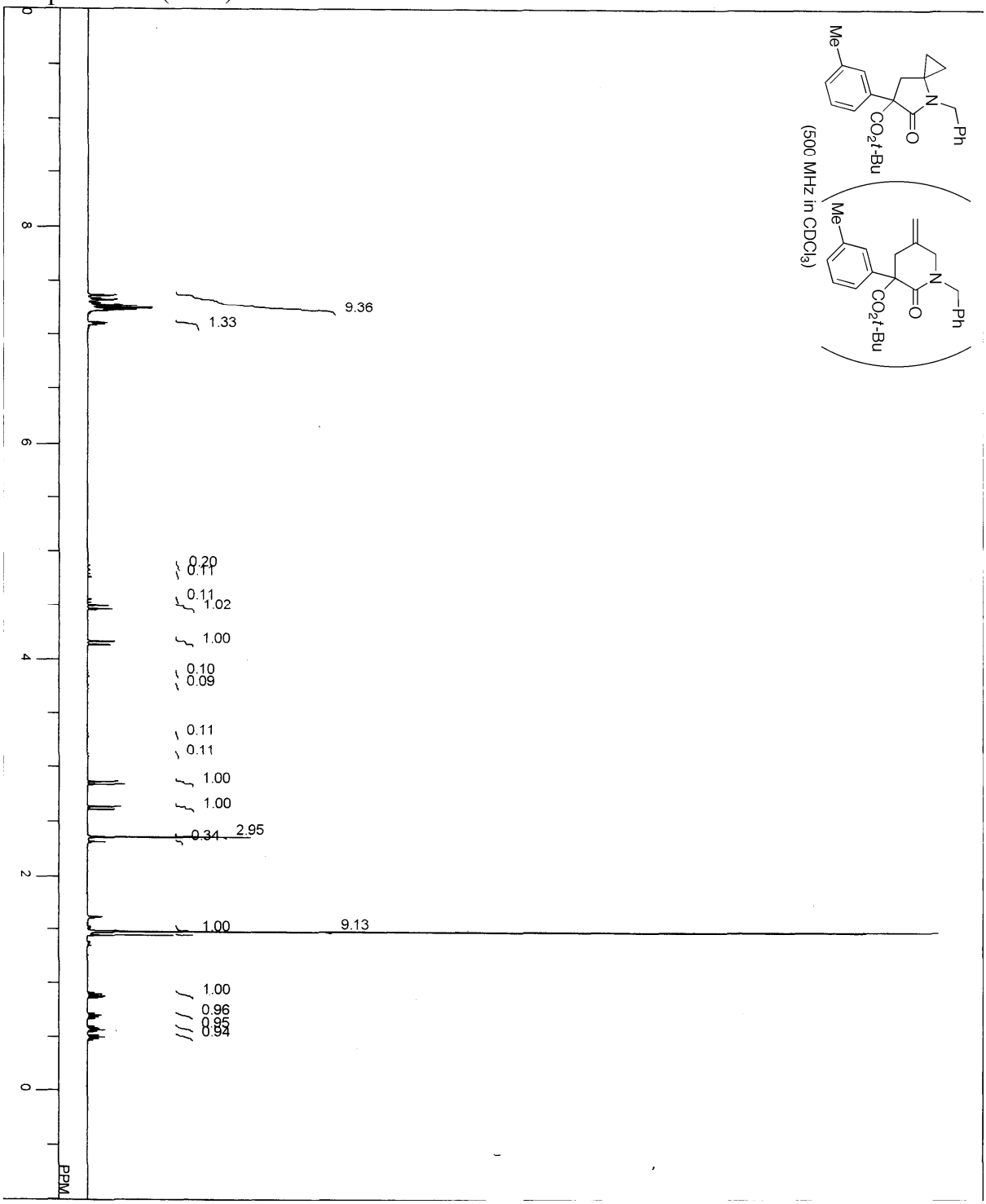
compound **3ga**(+**4ga**)



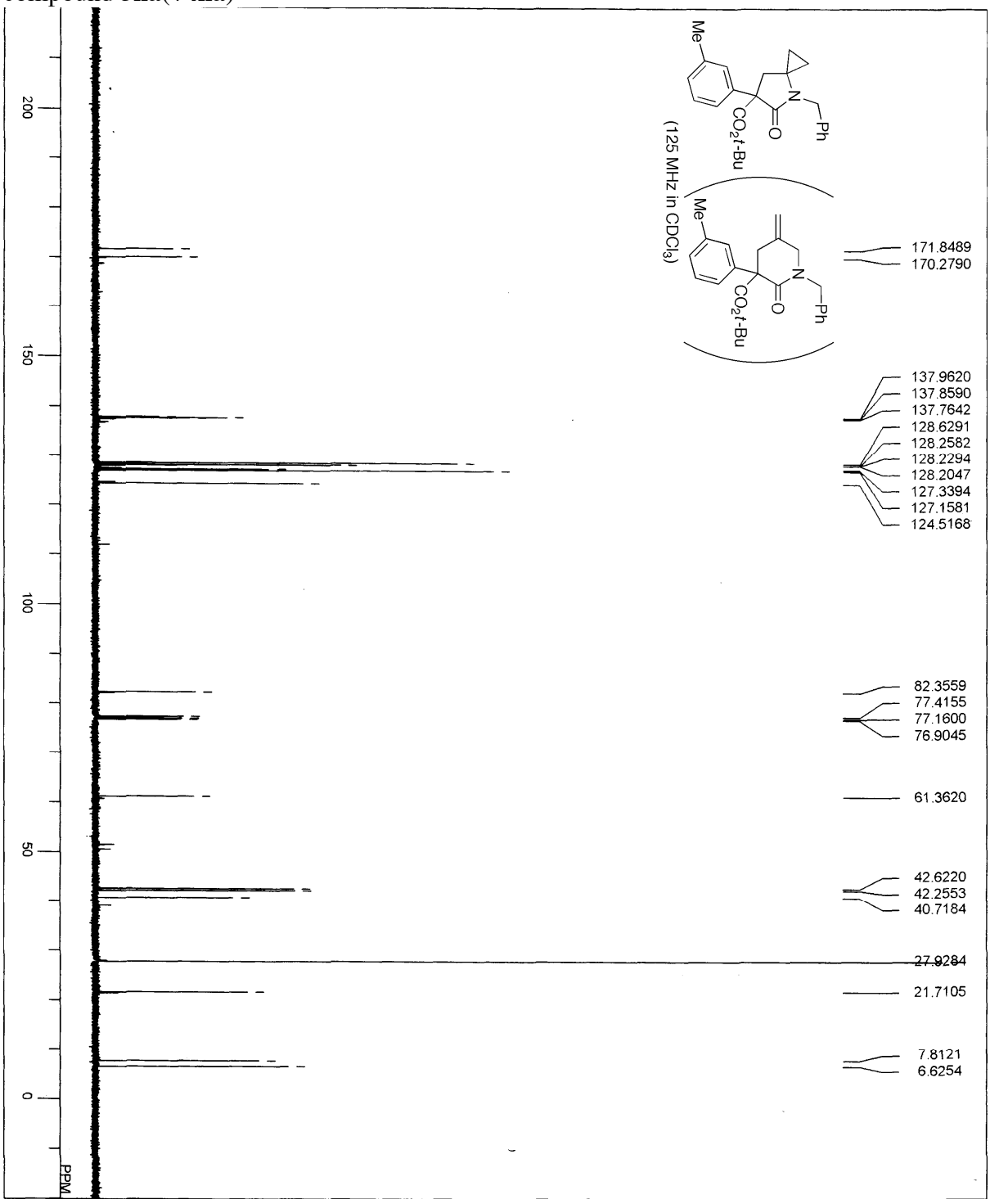
compound **3ga**(+**4ga**)



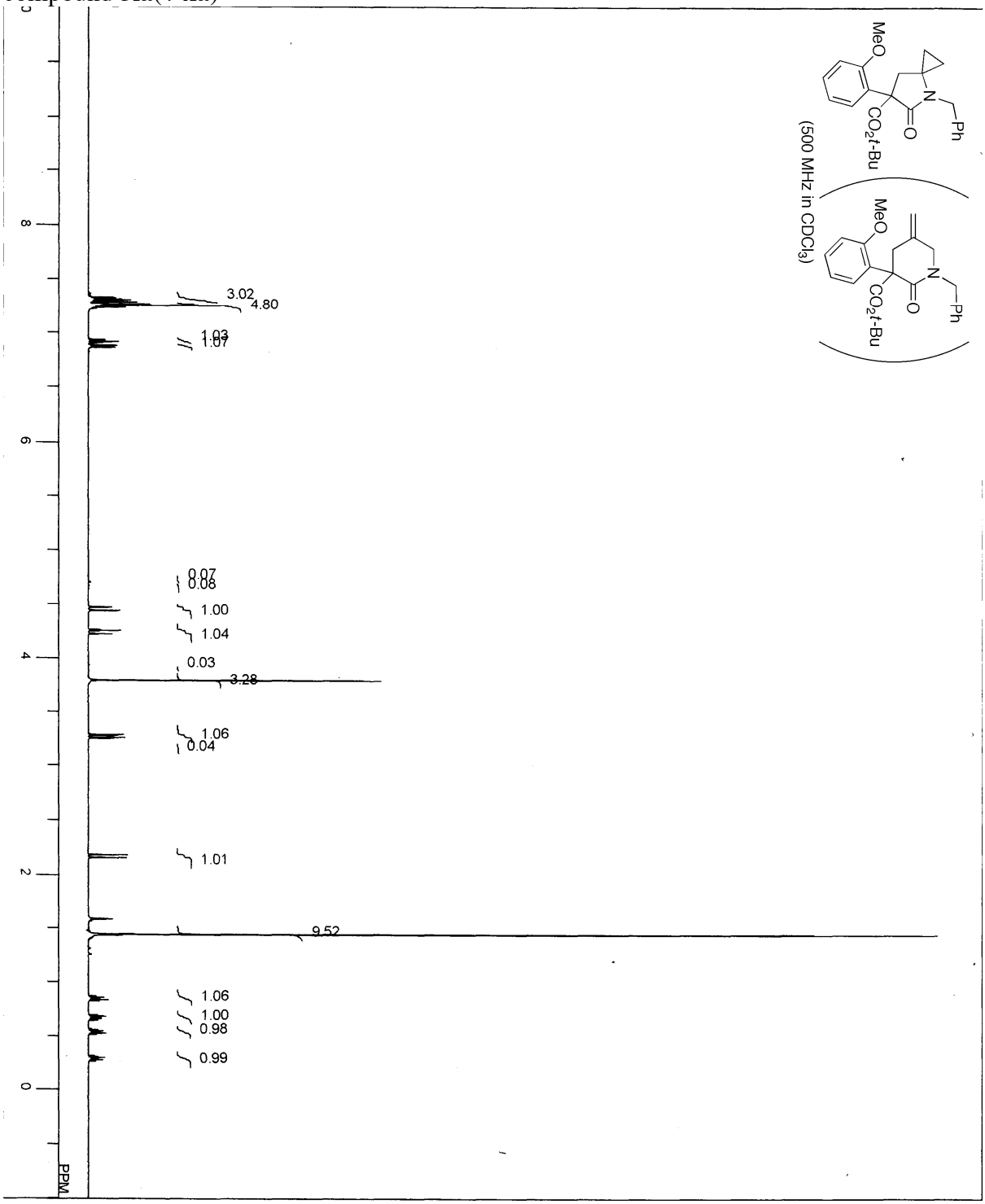
compound **3ha**(+**4ha**)



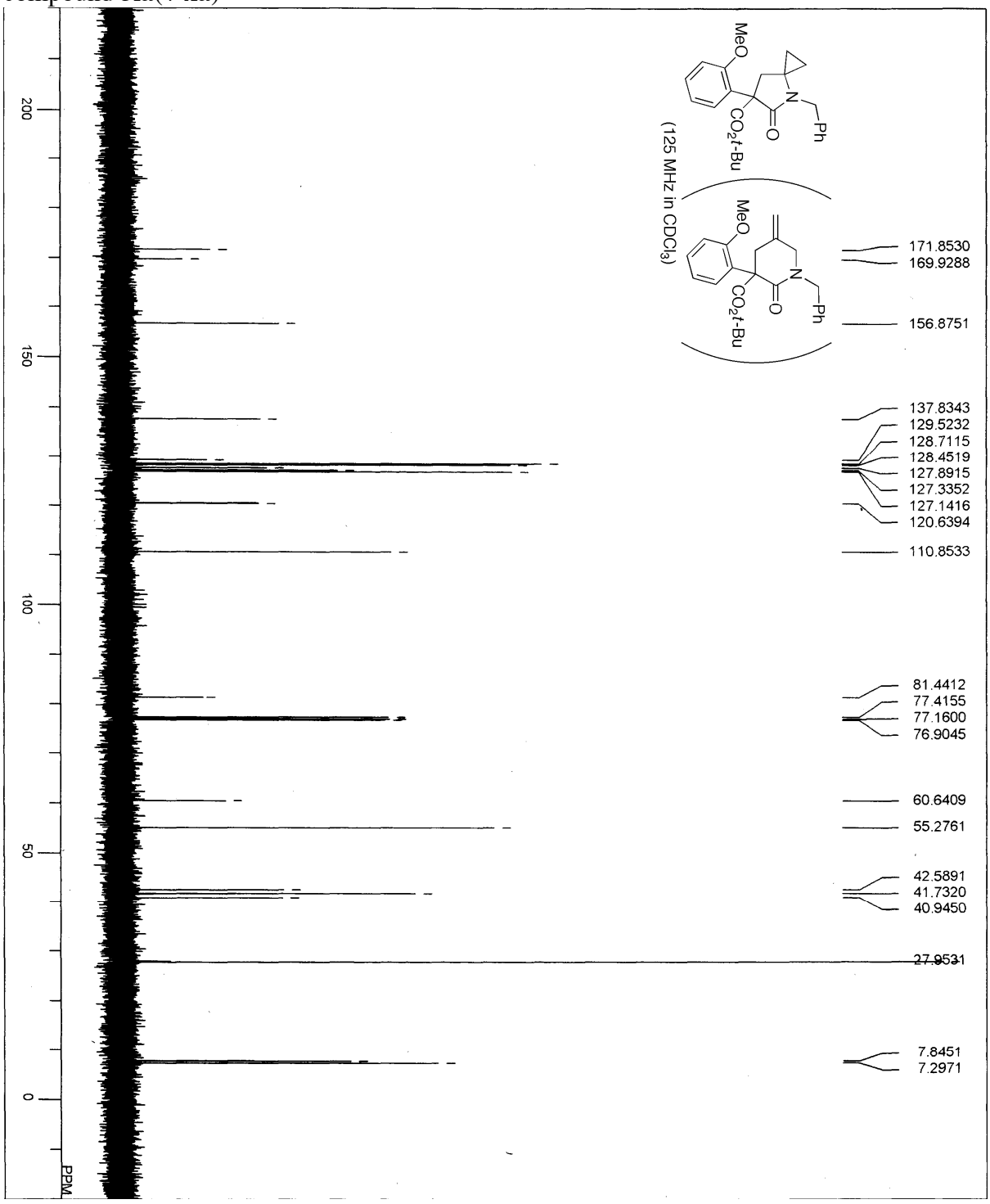
compound **3ha**(+**4ha**)



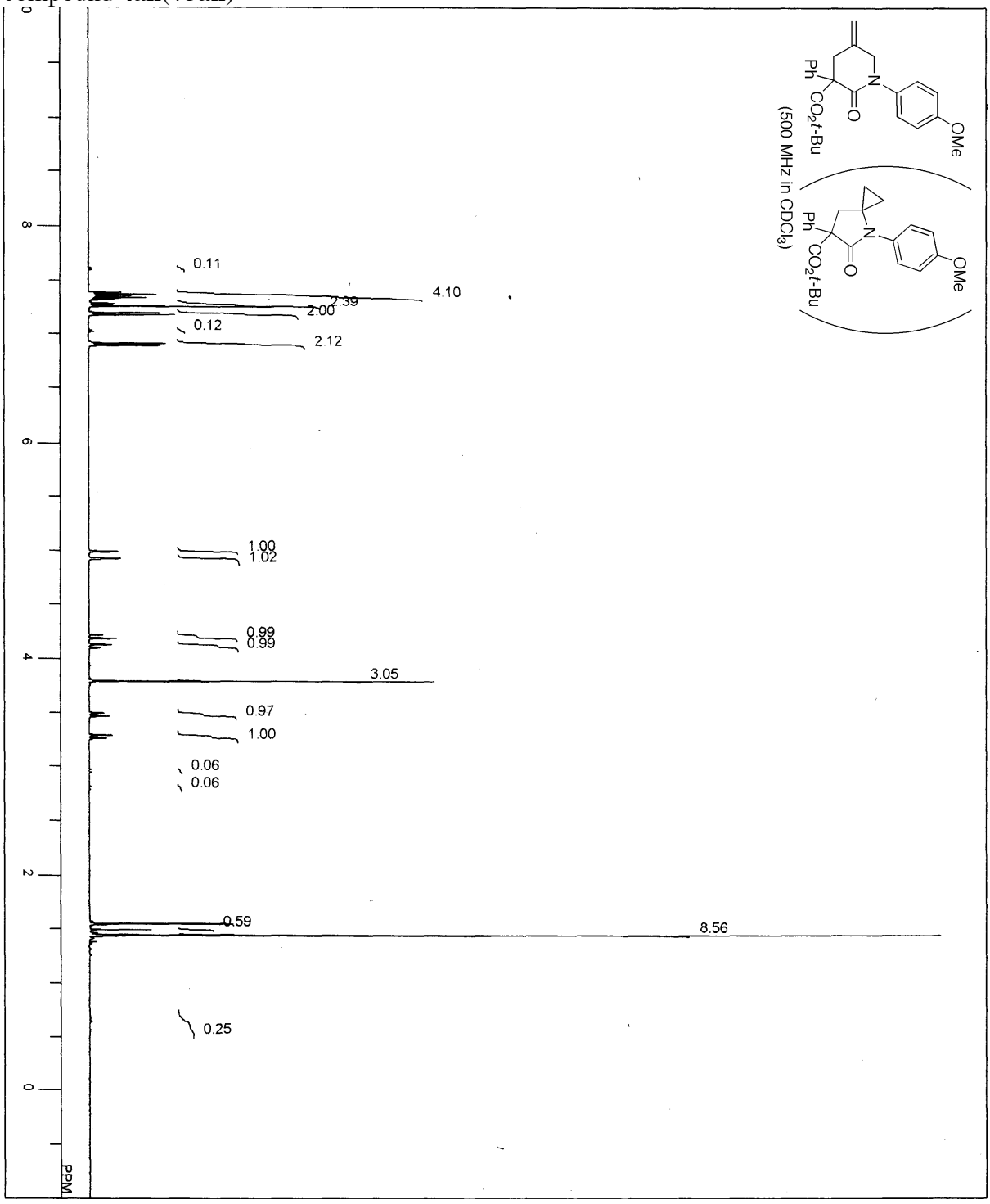
compound **3ia**(+**4ia**)



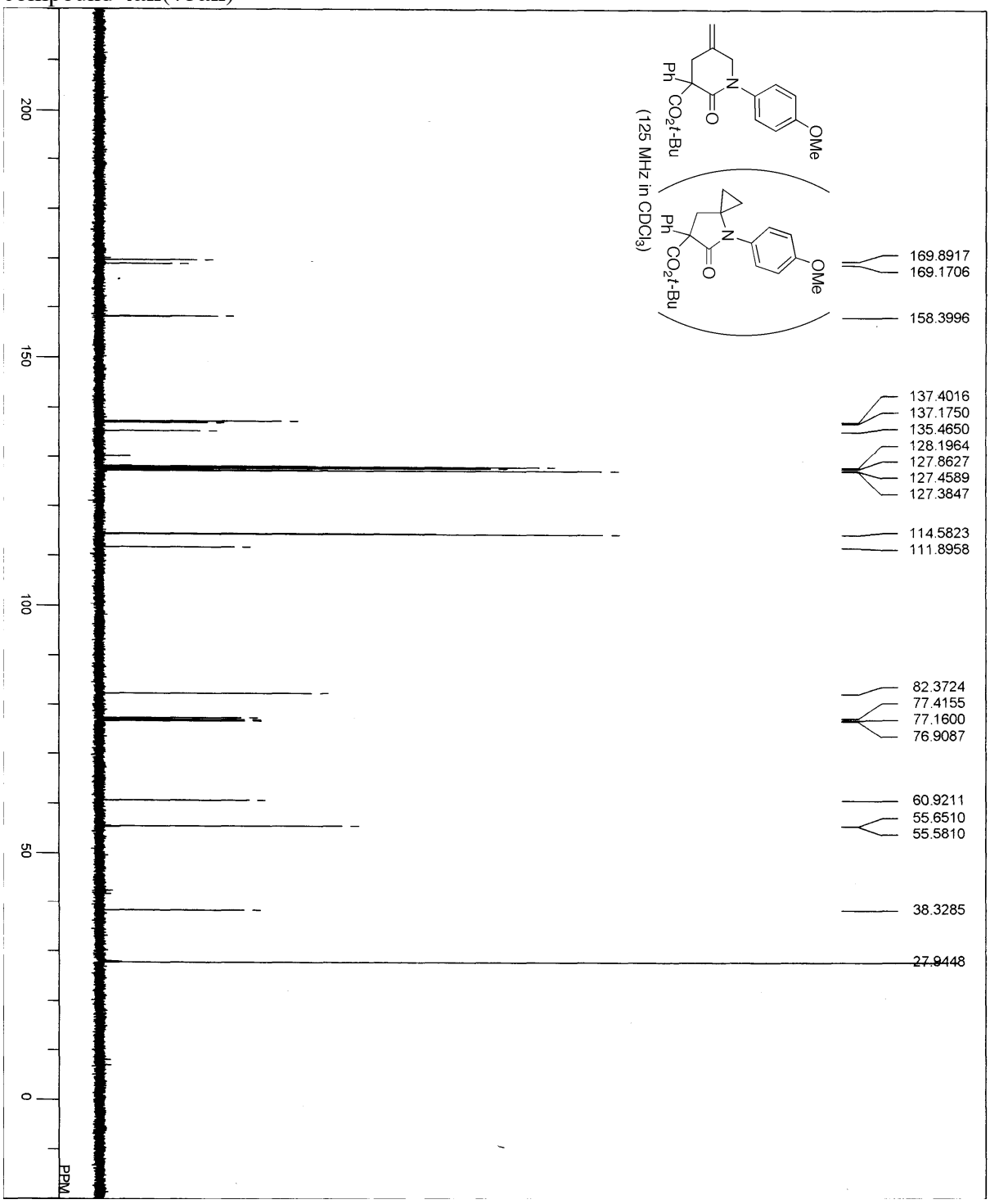
compound **3ia**(+**4ia**)



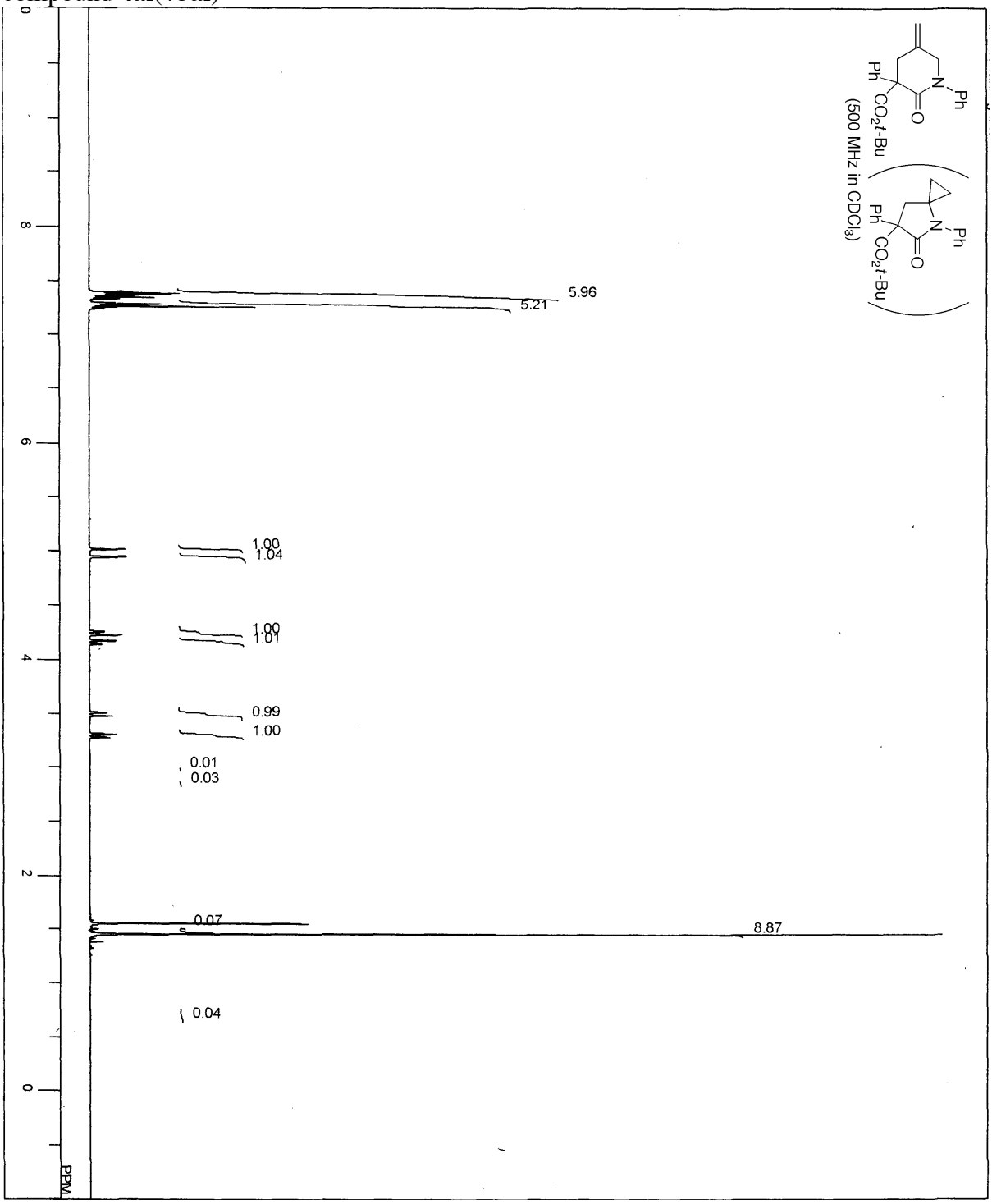
compound **4ah**(+**3ah**)



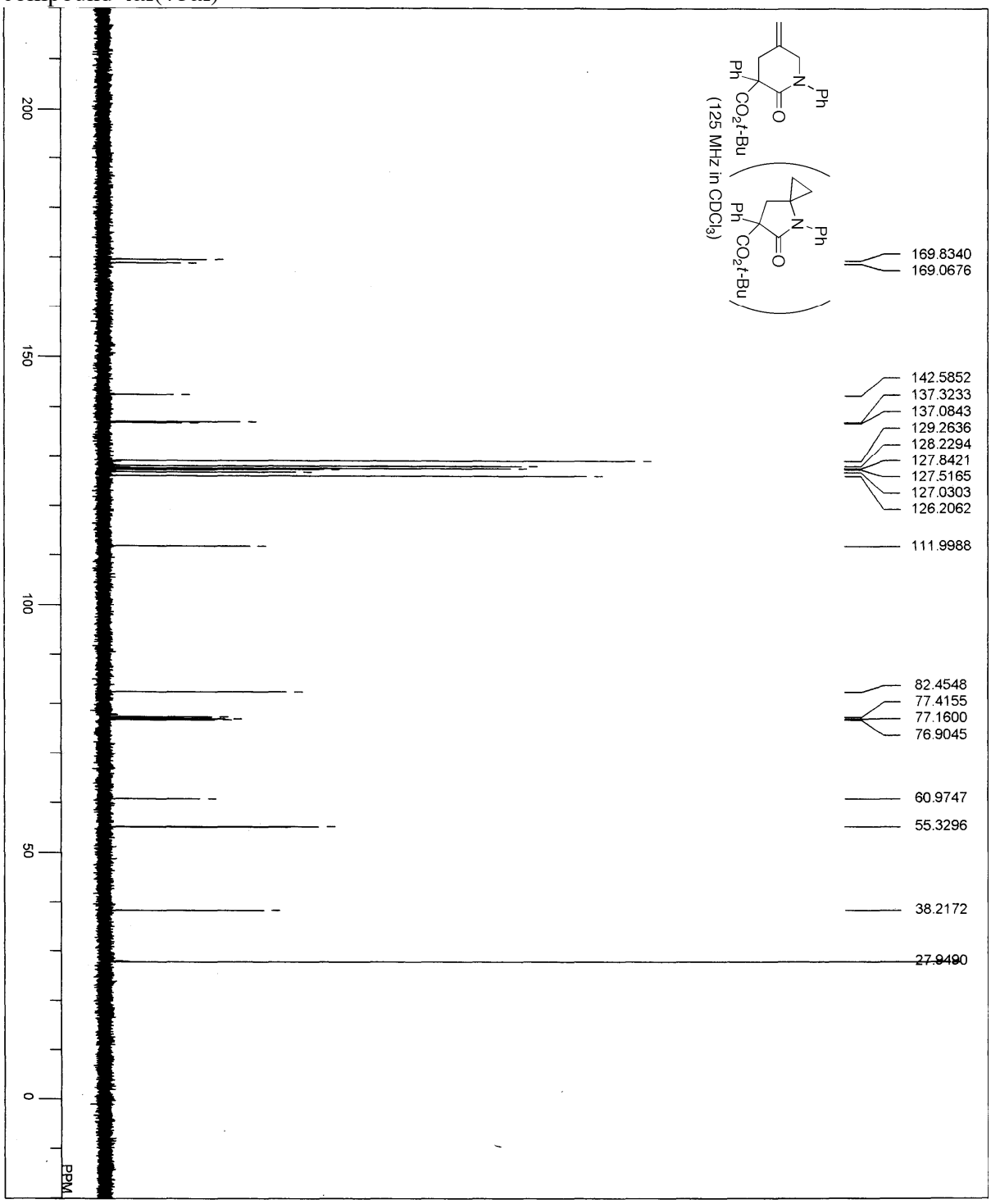
compound **4ah**(+**3ah**)



compound **4ai**(+**3ai**)



compound **4ai**(+**3ai**)



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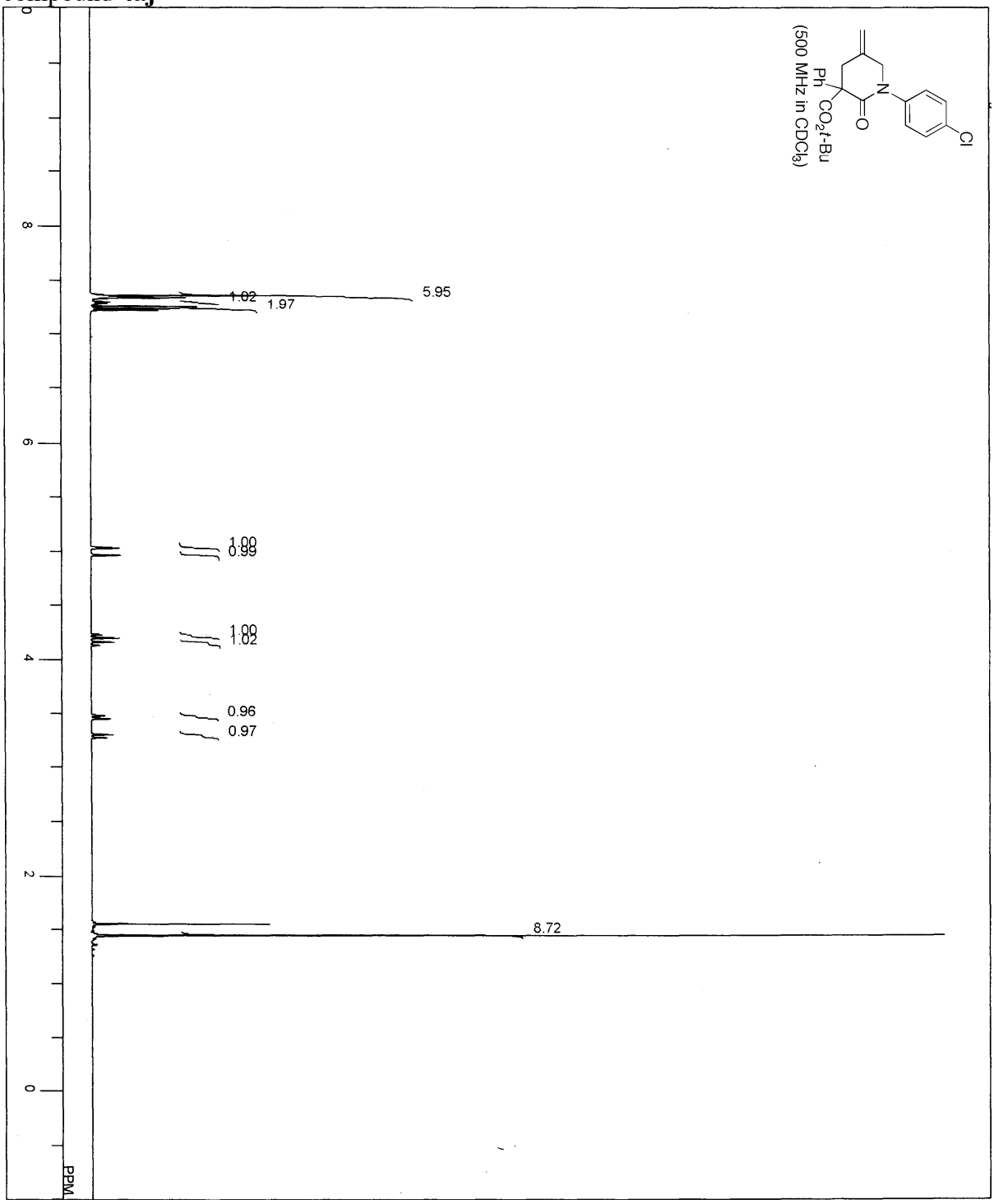
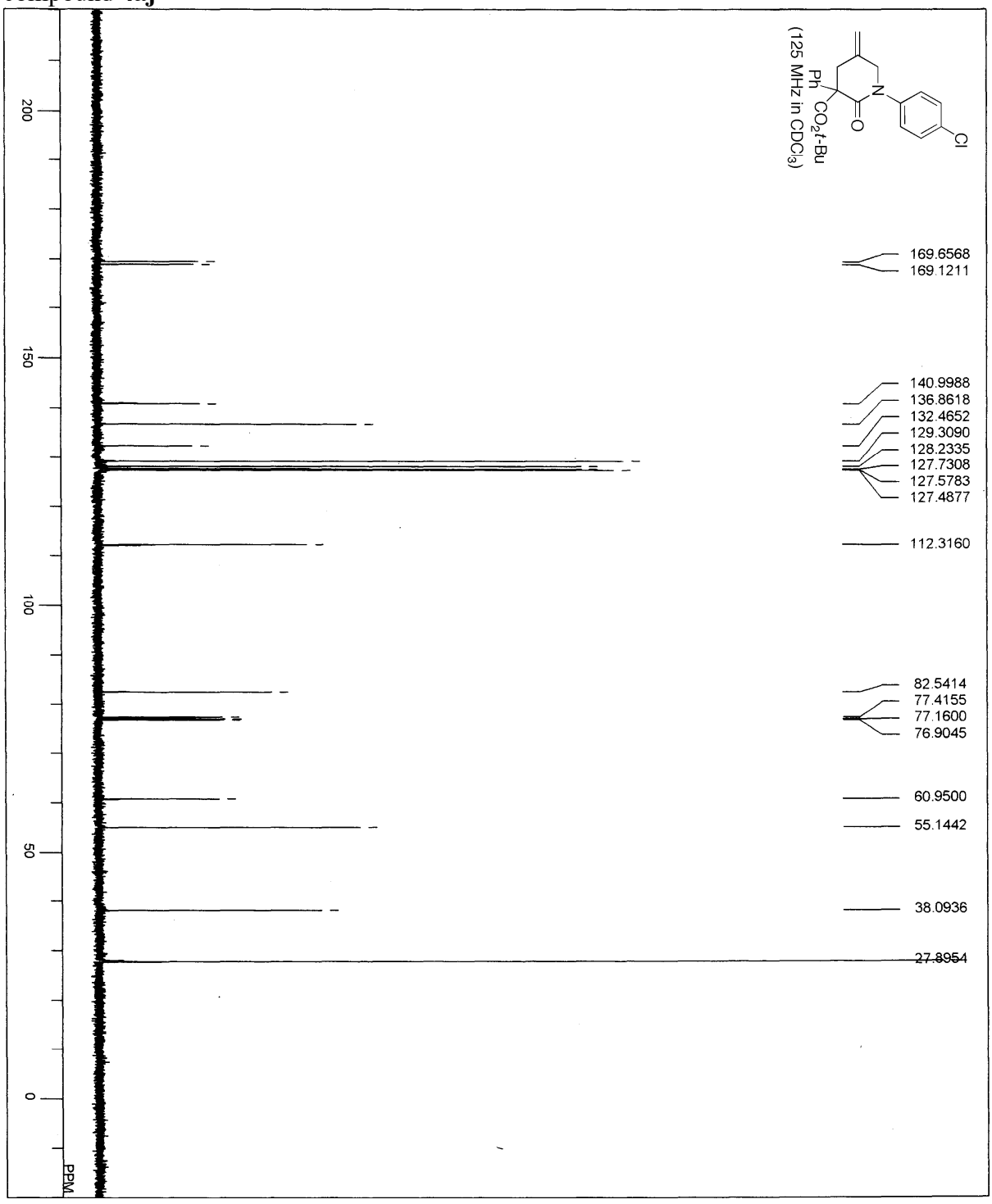
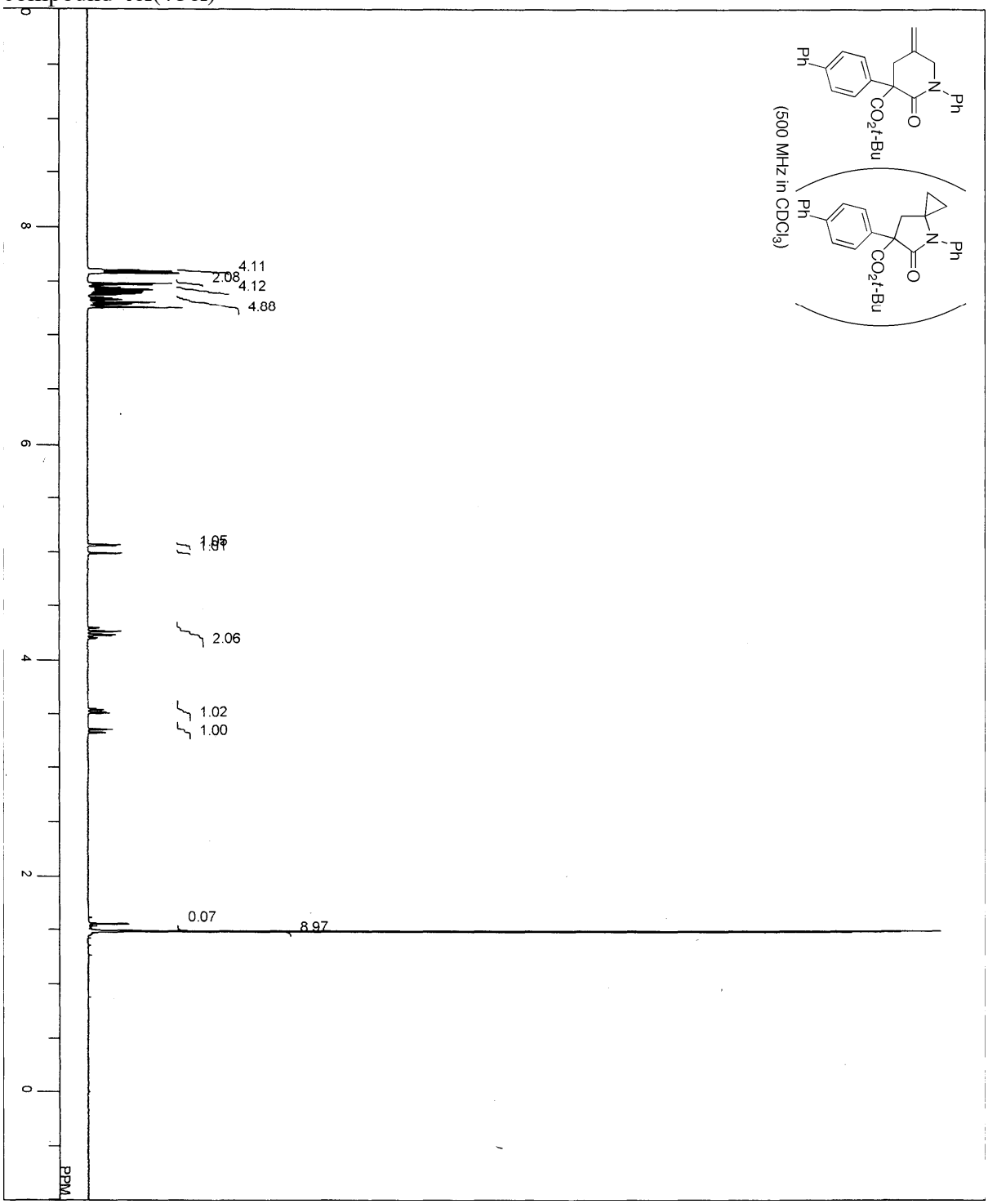


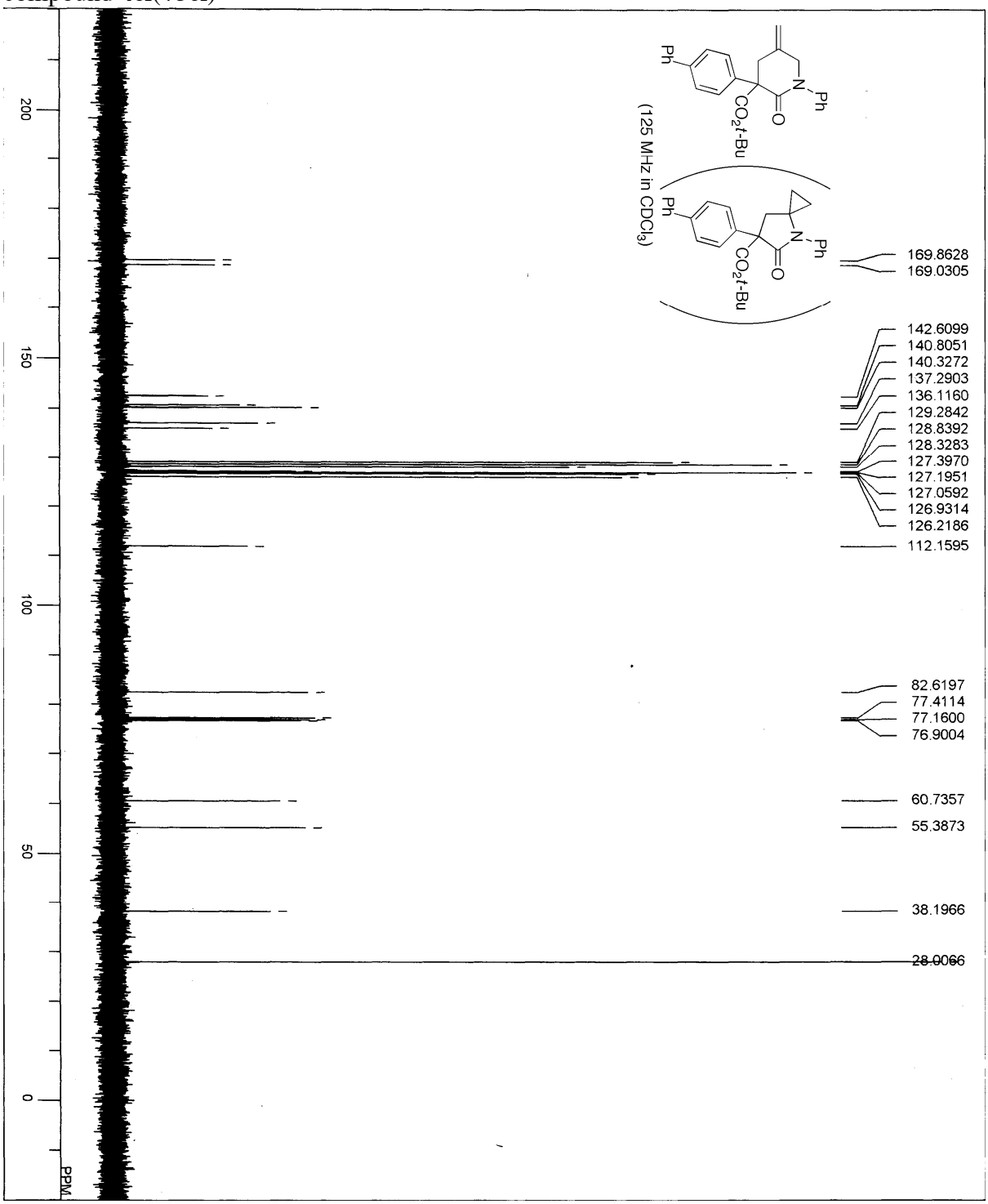
compound **4aj**



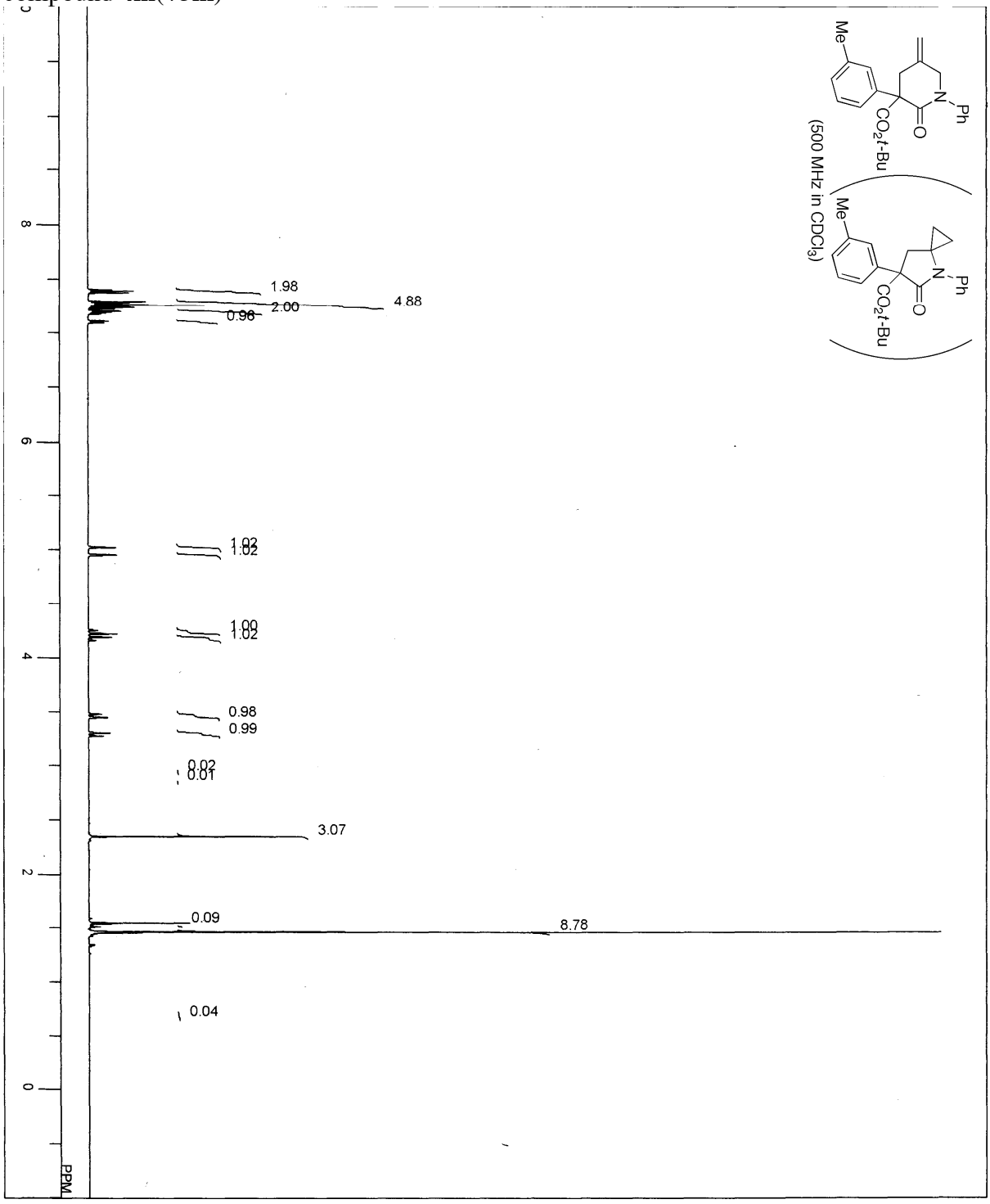
compound **4ei**(+**3ei**)



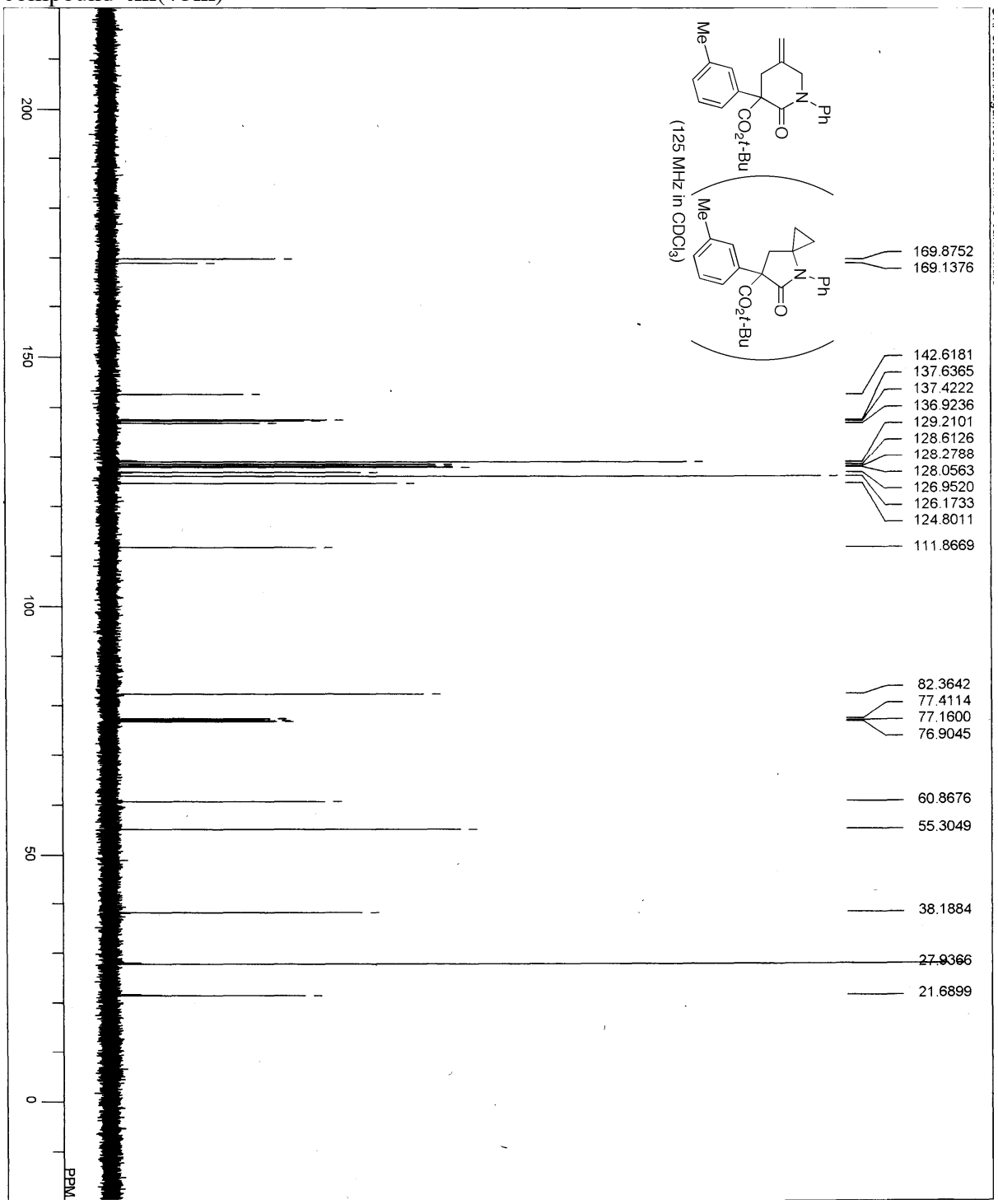
compound **4ei**(+**3ei**)



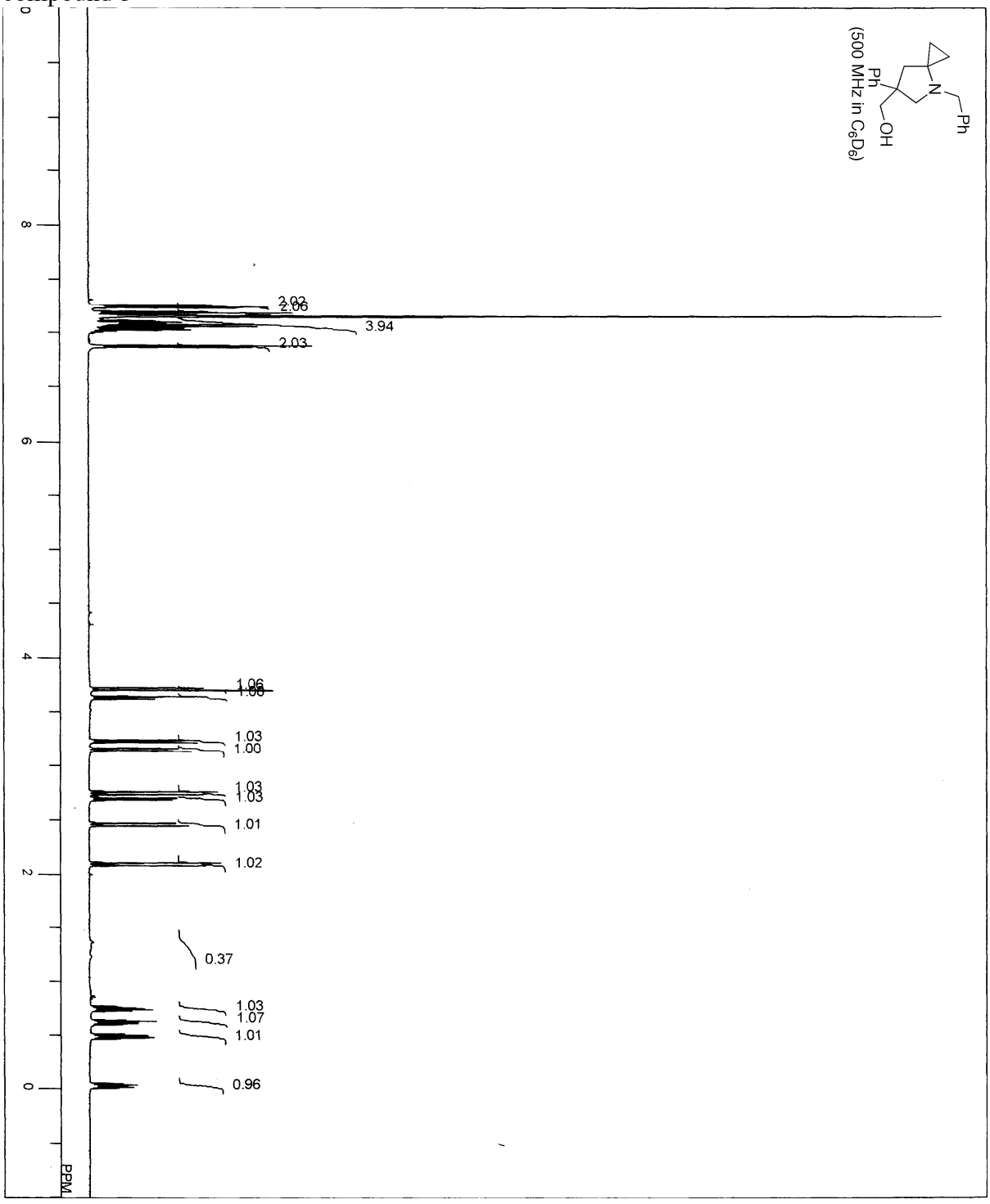
compound **4hi**(+**3hi**)



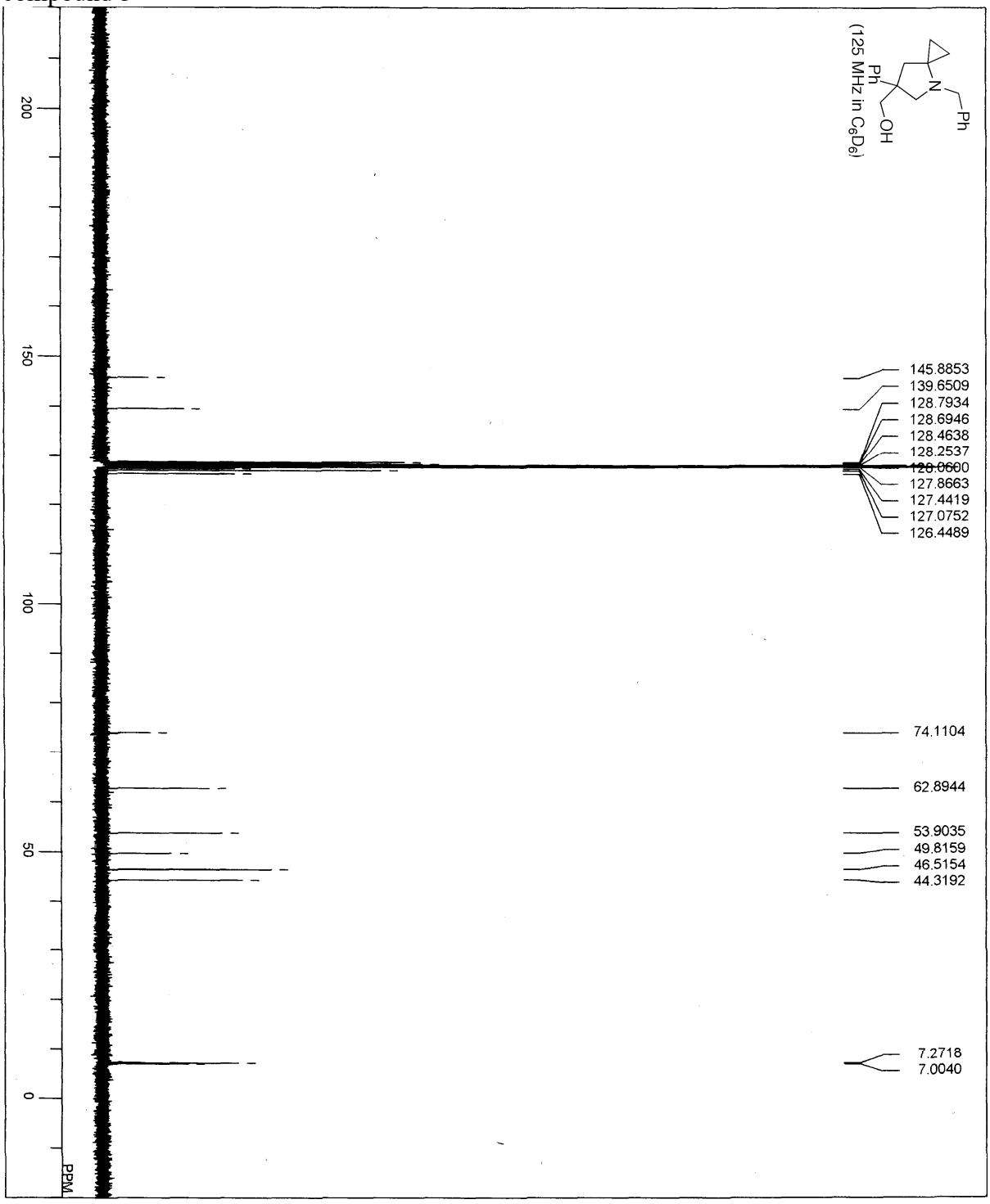
compound **4hi**(+**3hi**)



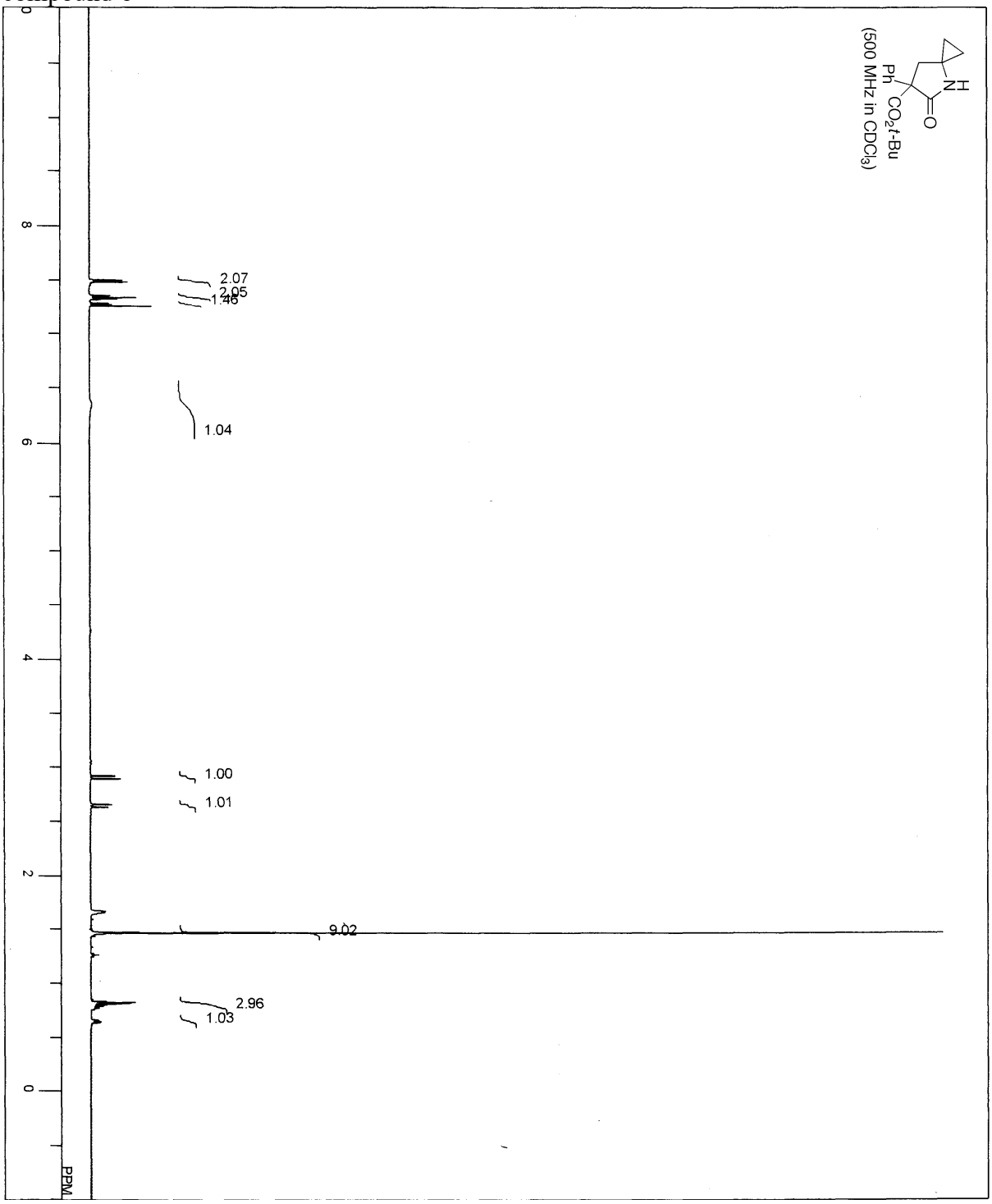
compound **5**


Ph
N
Ph
OH
(500 MHz in C6D6)
2.02
2.06
3.94
2.03
1.06
1.08
1.03
1.00
1.03
1.03
1.01
1.02
0.37
1.03
1.07
1.01
0.96
PPM

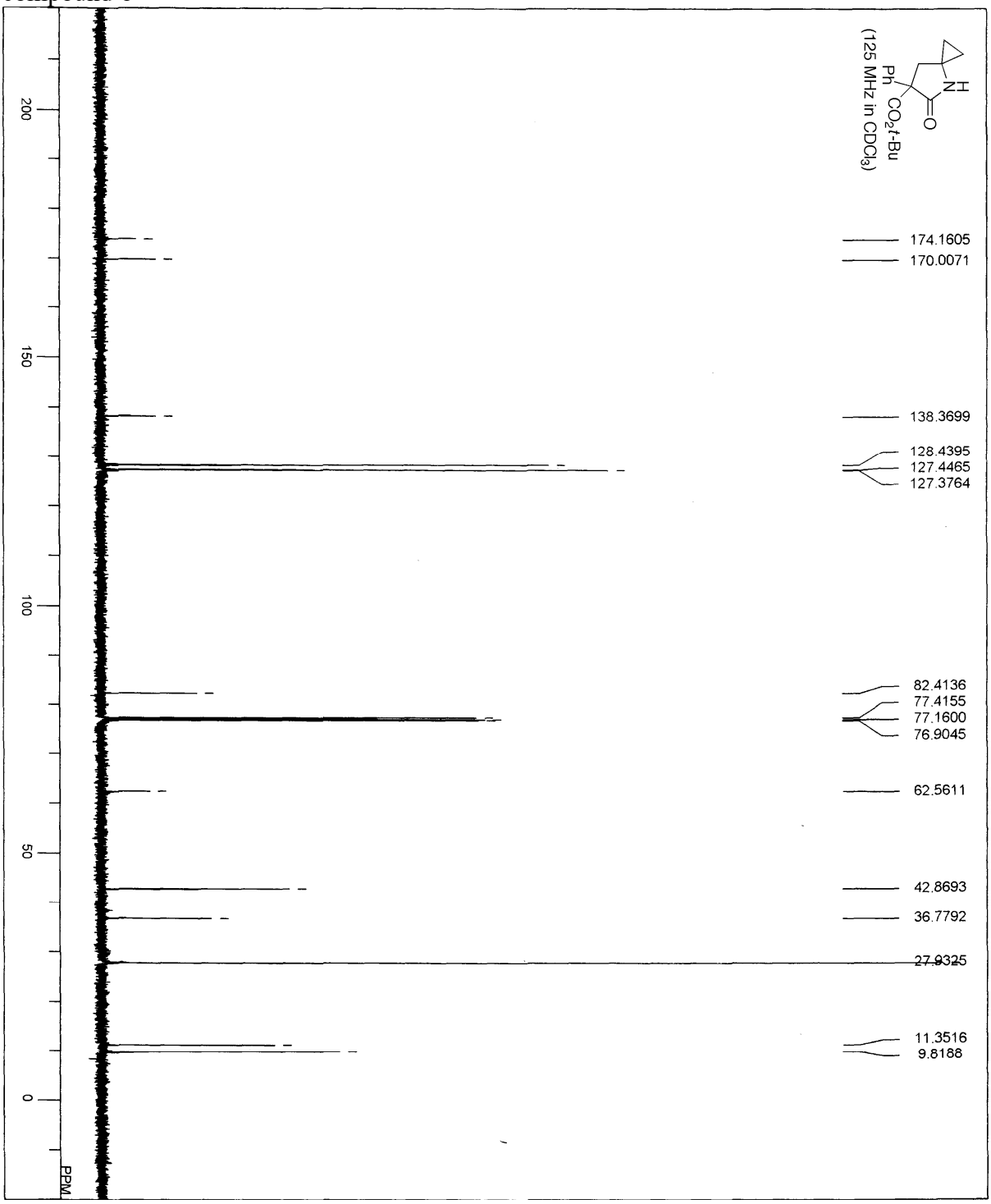
compound **5**


(125 MHz in C_6D_6)
Ph
OH
N
Ph
145.8853
139.6509
128.7934
128.6946
128.4638
128.2537
128.0660
127.8663
127.4419
127.0752
126.4489
74.1104
62.8944
53.9035
49.8159
46.5154
44.3192
7.2718
7.0040
200
150
100
50
0
PPM

compound **6**


(500 MHz in CDCl3)
Ph
CO2t-Bu
H
N
O
2.07
2.05
1.46
1.04
1.00
1.01
9.02
2.96
1.03
PPM

compound **6**


(125 MHz in CDCl3)
Ph
CO2t-Bu
H
N
O
174.1605
170.0071
138.3699
128.4395
127.4465
127.3764
82.4136
77.4155
77.1600
76.9045
62.5611
42.8693
36.7792
27.9325
11.3516
9.8188
200
150
100
50
0
PPM