Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Highly Efficient Assembly of Indole Alkaloid Skeleton via Cyclopropanation: Concise Total Synthesis of (±)-Mifiensine

Liqun Shen, Min Zhang, Yi Wu, Yong Qin*

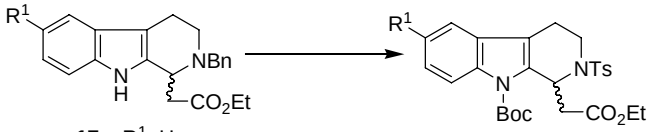
Department of Chemistry of Medicinal Natural Products and Key Laboratory of Drug Targeting, West China School of Pharmacy, and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, P. R. China.

E-mail: Yong Qin (yongqin@scu.edu.cn)

Contents of Supporting Information

General methods

All commercially available reagents were used without further purification. All solvents were dried and distilled before use; THF and Et_2O were distilled from sodium/benzophenone ketyl; dichloromethane and acetonitrile were distilled from calcium hydride; methanol and ethanol were distilled from Mg/I_2; $CHCl_3$ was distilled from P_2O_5. Column chromatography was conducted by using 200-300 mesh silica gel. All new compounds gave satisfactory spectroscopic analyses (IR, ^1H NMR, ^{13}C NMR, HRMS). IR spectra were recorded on a FT IR spectrometer. NMR spectra were recorded on 400/200 MHz NMR spectrometers. HRMS spectra were obtained by the FAB method. Microwave reaction was carried out in MCL-2 microwave reactor (200 mA).



17a, R^1=H
17b, R^1=OMe

5a, R^1=H
5b, R^1=OMe

General procedure for preparation of *N*-Ts tetrahydrocarbolines 5a and 5b

17a[1] (18.40 g, 52.88 mmol) was dissolved in 300 mL of EtOH containing anhydrous HCl (3 M in EtOH, 35 mL, 105 mmol, 2 equiv) and the solution was concentrated. The resultant salts were then hydrogenated in EtOH (450 mL) in the presence of Pd/C (13.2g, 10 mol%, 1 atm of H_2 pressure) at room temperature. After the reaction was continued for 12 h, triethylamine (20 mL) was added to the suspension. The resultant mixture was filtered through Celite. The filtrate was concentrated to give a residue. The residue was used directly for next step.

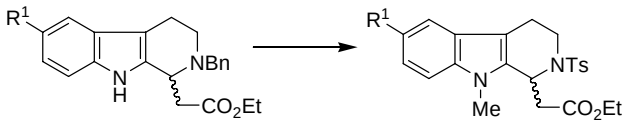
To a solution of the above crude product in CH_2Cl_2 (250 mL) were added triethylamine (11 mL, 78.9 mmol, 1.5 equiv), and *p*-toluenesulfonyl chloride (12 g, 35 mmol, 1.2 equiv). After stirring at room temperature for 2 h, the mixture was diluted with CH_2Cl_2 (500 mL), washed with an aqueous HCl solution (0.1 M, 150 mL × 1) and water (150 mL × 3), dried over magnesium sulfate and concentrated in vacuum to give a residue.

To a solution of the above residue in CH_2Cl_2 (250 mL) were added DMAP (4-dimethylaminopyridine, 0.645 g, 0.1 equiv), TEA (triethylamine, 11 mL, 78.9 mmol, 1.5 equiv), and Boc_2O (di-*tert*-butyl dicarbonate, 12.6 g, 58.33 mmol, 1.1 equiv) sequentially. After stirring at room temperature for 3 h, the mixture was diluted

with CH_2Cl_2 (250 mL), washed with HCl (0.1 M, 200 mL × 1) and water (100 mL × 3), dried over magnesium sulfate and concentrated. The crude residue was purified by column chromatography (20% EtOAc/petroleum) to give **5a** (20.60 g, 75.8% yield) as a colorless solid.

***N*-Ts tetrahydrocarboline 5a:** m.p. 131−133 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.28 (dt, *J* = 7.2, 2.0 Hz, 1H), 7.22 (m, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.12 (dd, *J* = 10.8, 3.6 Hz, 1H), 4.20-4.07 (m, 3H), 3.52 (ddd, *J* = 17.6, 11.6, 6 Hz, 1H), 3.01 (dd, *J* = 14.4, 3.6 Hz, 1H), 2.70 (dd, *J* = 14.4，10.8 Hz, 1H), 2.63-2.47 (m, 2H), 2.51 (s, 3H), 1.76 (s, 9H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.5, 149.7, 143.3, 137.4, 135.6, 132.6, 129.1, 128.5, 126.9, 124.7, 122.8, 117.7, 115.8, 114.8, 85.0, 61.0, 51.0, 40.2, 37.7, 28.3, 21.2, 19.5, 14.1; HRMS ($M+Na^+$) calcd for $C_{27}H_{32}N_2Na_1O_6S_1$ 535.1873, found 535.1864; IR (KBr) 3436, 1725, 1597, 1456 cm^{-1}.

***N*-Ts tetrahydrocarboline 5b:** purified by column chromatography (20% EtOAc/petroleum) in 87% yield, white powder, m.p. 125−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 9.2 Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.87 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.65 (d, *J* = 2.8 Hz, 1H), 6.10 (dd, *J* = 10.8, 3.6 Hz, 1H), 4.17-4.08 (m, 3H), 3.81 (s, 3H), 3.55-3.47 (m, 1H), 3.01 (dd, *J* = 14.4, 3.6 Hz, 1H), 2.69 (dd, *J* = 14.4, 10.4 Hz, 1H), 2.61-5.52 (m, 1H), 2.46 (dd, *J* = 16.4, 5.6 Hz, 1H), 2.21 (s, 3H), 1.75 (s, 9H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.5, 155.9, 149.6, 143.3, 137.3, 133.4, 130.4, 129.3, 129.1, 126.9, 116.4, 114.5, 112.9, 100.8, 84.7, 60.9, 55.7, 51.0, 40.1, 37.7, 28.2, 21.2, 19.5, 14.0; HRMS ($M+Na^+$) calcd for $C_{28}H_{34}N_2Na_1O_7S_1$ 565.1979, found 565.1961; IR (KBr) 1723, 1620, 1462, 1292 cm^{-1}.



General procedure for preparation of *N*-Ts tetrahydrocarbolines 5c and 5d[2]

MeI was added dropwise to a suspension of NaH (1.75 g, 60% dispersion in mineral oil, 43.75 mmol, 1.5 equiv) and **17a** (10.19 g, 29.24 mmol) in DMF (100 mL) at 0 °C. The reaction was warmed to room temperature and stirred for 3 h. The resultant mixture was poured into an ice-cold saturated NH_4Cl solution (200 mL), and

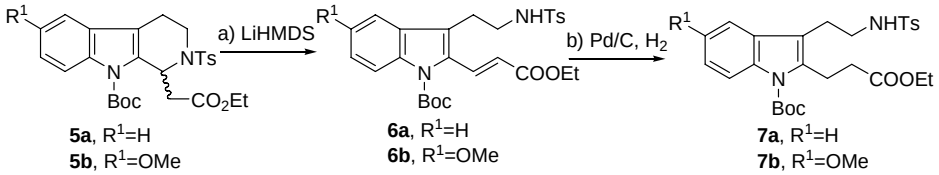
extracted with EtOAC (200 mL × 4). The combined oil layers were washed with brine (200 mL × 3), dried over sodium sulfate and concentrated. The crude residue was dissolved in 100 mL of ethanol containing anhydrous HCl (3 M in EtOH, 30 mL, 90 mmol, 3 equiv), and concentrated. The resultant salts were dissolved in 150 mL of EtOH and then hydrogenated at room temperature under 1 atm of H_2 pressure in the presence of Pd/C (6.2 g, 10 mol%) for 12 h. TEA (10 mL) was added to the suspension and the mixture was filtered through Celite. The filtrate was concentrated to give a residue. The residue was used directly for the next step.

The above residue was dissolved in CH_2Cl_2 (150 mL). TEA (6 mL, 43 mmol, 1.5 equiv) and TsCl (6.7 g, 35 mmol, 1.2 equiv) were added at room temperature to the solution. After being stirred for 2 h, the mixture was diluted with 300 mL of CH_2Cl_2, washed with 0.1 M of HCl (100 mL), water (100 mL × 3), dried over magnesium sulfate and concentrated in vacuum to give a residue. The residue was purified by column chromatography (25% EtOAc/petroleum) to yield **5c** as white foam (10.16 g, 81.5% yield).

***N*-Ts tetrahydrocarboline 5c:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.21 (dt, *J* = 1.2, 8.4 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.08-7.04 (m, 1H), 5.68 (dd, *J* = 9.6 Hz, 1H), 4.23-4.10 (m, 3H), 3.70 (s, 3H), 3.49-3.43 (m, 1H), 2.82 (dd, *J* = 15.2, 9.6 Hz, 1H), 2.72 (dd, *J* = 14.8, 3.6 Hz, 1H) , 2.59-2.56 (m, 2H), 2.26 (s, 3H), 1.3 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.7, 143.2, 137.5, 137.10, 132.6, 129.2, 126.8, 126.1, 121.8, 119.2, 118.1, 108.8, 107.1, 61.1, 49.2, 40.9, 38.9, 29.7, 21.2, 19.7, 14.0; HRMS ($M+Na^+$) calcd for $C_{23}H_{26}N_2Na_1O_4S_1$ 449.1505, found 449.1492; IR (KBr) 1739, 1470, 1282 cm^{-1}.

***N*-Ts tetrahydrocarboline 5d:** purified by column chromatography (25% EtOAc/petroleum) in 82% yield, white powder, m.p. 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.86 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 6.77 (d, *J* = 2 Hz, 1H), 5.66 (dd, *J* = 8.2 Hz, 3.2 Hz, 1H), 4.22-4.10 (m, 3H), 3.82 (s, 3H), 3.67 (s, 3H), 3.50-3.42 (m, 1H), 2.82 (dd, *J* = 15.2, 9.2 Hz, 1H), 2.71 (dd, *J* = 15.2, 3.2 Hz, 1H), 2.56-2.53 (m, 2H), 2.27 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.8, 154.0, 143.3, 137.6, 133.6, 132.5, 129.3, 126.9, 126.5, 111.7, 109.7, 106.8, 100.5, 61.2, 55.9, 49.4, 40.8, 39.0, 29.9, 21.3, 19.9, 14.1; HRMS ($M+Na^+$) calcd for $C_{24}H_{28}N_2Na_1O_5S_1$ 479.1611,

found 479.1610; IR (KBr) 1738, 1620, 1461, 1292 cm^{-1}.



5a, R^1=H
5b, R^1=OMe
6a, R^1=H
6b, R^1=OMe
7a, R^1=H
7b, R^1=OMe

General procedure for preparation of esters 7a and 7b[3]

Lithium hexamethyldisilazide (1 M in THF, 83 mL, 1.5 equiv) was added dropwise to a solution of compound **5** (55.35 mmol) in 250 mL of THF at –40 °C. The reaction solution was stirred for 10 h and then poured into an ice-cold saturated NH_4Cl solution, extracted with EtOAC (200 mL × 3). The combined organic layers were washed with brine (200 mL × 3), dried over magnesium sulfate and concentrated in vacuum to give the crude unsaturated ester **6** as a yellow solid. An analytical sample was obtained by column chromatography purification.

The crude **6** was dissolved in a 1:1 mixture of MeOH/THF (400 mL) and then hydrogenated in the presence of Pd/C (11.7g, 10 mol %) at room temperature under 1 atm of H_2 pressure for 24 h. The suspension was filtered through Celite, the filtrate was concentrated and purified by column chromatography.

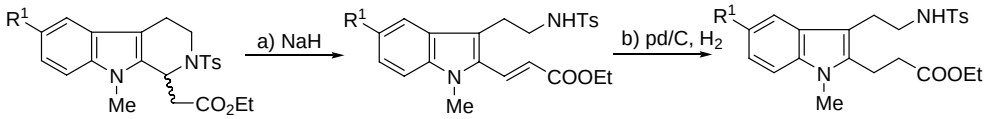
Unsaturated ester 6a: purified by column chromatography (25% EtOAc/petroleum), an off-white solid, m.p. 131–133°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.4, 1H), 7.90 (d, *J* = 16.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.35 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.23(t, *J* = 8.4 Hz, 2H), 6.05 (d, *J* = 16.0 Hz, 1H), 4.54 (N-H, t, *J* = 4.8 Hz, 1H), 4.29 (q, *J* = 6.8 Hz, 2H), 3.25 (q, *J* = 6.8 Hz, 2H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 1.66 (s, 9H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 149.9, 143.3, 136.7, 136.5, 136.0, 132.2, 129.6, 129.2, 127.0, 125.9, 123.2, 120.4, 119.5, 119.2, 115.6, 84.8, 60.7, 42.9, 28.1, 25.6, 21.5, 14.3; HRMS ($M+Na^+$) calcd for $C_{27}H_{32}N_2Na_1O_6S_1$ 535.1873, found 535.1868; IR (KBr) 3286, 1727, 1637, 1560, 1455 cm^{-1}.

Ester 7a: purified by column chromatography (25% EtOAc/petroleum) in 83% yield from **5a**, an off-white solid, m.p. 140–141°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.25 (m, 1H), 7.21-7.16 (m, 3H), 4.59 (N-H, t, *J* = 6.4 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 3.25 (t, *J* = 7.2 Hz, 2H), 3.20 (q, *J* = 6.8 Hz, 2H), 2.92 (t, *J* = 7.2 Hz, 2H), 2.61 (t, *J* = 6.8 Hz, 2H), 2.39 (s, 3H), 1.69 (s, 9H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ

173.0, 150.2, 143.2, 136.6, 136.5, 135.9, 129.5, 129.1, 127.0, 124.0, 122.7, 116.0, 115.7, 115.3, 84.1, 60.6, 42.6, 34.4, 26.2, 24.7, 22.0, 21.5, 14.2; HRMS ($M+Na^+$) calcd for $C_{27}H_{34}N_2Na_1O_6S_1$ 537.2030, found 537.2004; IR (KBr) 3310, 1723, 1711, 1610, 1597, 1474, 1459 cm^{-1}.

Unsaturated ester 6b： purified by column chromatography (25% EtOAc/petroleum), an off-white powder, m.p. 98–100 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.89 (d, *J* = 16 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 6.95 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.00 (d, *J* = 16.4 Hz, 1H), 4.60 (N-H, t, *J* = 6.4 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.22 (q, *J* = 6.8 Hz, 2H), 3.01 (t, *J* = 6.8 Hz, 2H), 2.38 (s, 3H), 1.63 (s, 9H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.4, 156.1, 149.8, 143.3, 136.7, 136.1, 132.6, 131.0, 130.0, 129.5, 126.9, 120.0. 119.4, 116.4, 115.1, 101.2, 84.5, 60.6, 55.6, 42.9, 28.1, 25.7, 21.4, 14.2; HRMS ($M+Na^+$) calcd for $C_{28}H_{34}N_2Na_1O_7S_1$ 565.1979, found 565.1984; IR (KBr) 3294, 1727, 1625, 1480, 1330 cm^{-1}.

Ester 7b: purified by column chromatography (25% EtOAc/petroleum) in 87% yield from **5b**, off-white foam. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* =8.8 Hz, 1H), 6.82 (s, 1H), 4.69 (N-H, t, *J* = 6.4 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 3.23 (t, *J* = 7.2 Hz, 2H), 3.18 (q, *J* = 6.4 Hz, 2H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.61 (t, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 1.67 (s, 9H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.0, 155.8, 150.1, 143.2, 137.0, 136.8, 130.5, 130.0, 129.5, 126.9, 116.5, 115.3, 112.4, 100.8, 83.9, 60.6, 55.6, 42.8, 34.4, 28.1, 24.7, 22.2, 21.4, 14.1; HRMS ($M+Na^+$) calcd for $C_{28}H_{36}N_2Na_1O_7S_1$ 567.2135, found 567.2137; IR (KBr) 3282, 1727, 1610, 1478, 1328 cm^{-1}.



5c, R^1=H
5d, R^1=OMe

6c, R^1=H
6d, R^1=OMe

7c, R^1=H
7d, R^1=OMe

General procedure for preparation of esters 7c and 7d[2]

To a solution of **5c** or **5d** (23.98 mmol) in DMF (100 mL) was added NaH (1.15g, 60% dispersion in mineral oil, 1.2 equiv) at room temperature. After being stirred for 2 h, the mixture was poured into an ice-cold saturated aqueous NH_4Cl solution, extracted with EtOAC (250 mL × 3), the combined organic phases were washed with

brine (200 mL × 3), dried over magnesium sulfate and concentrated to give the crude ester **6** as a yellow solid. An analytical sample was purified by column chromatography.

The crude **6** was dissolved in a 1:1 mixture of MeOH/THF (400 mL) and then hydrogenated in the presence of Pd/C (5.1g, 10 mol %) at room temperature under 1 atm of H_2 pressure for 24 h. The suspension was filtered through Celite, the filtrate was concentrated and purified by column chromatography.

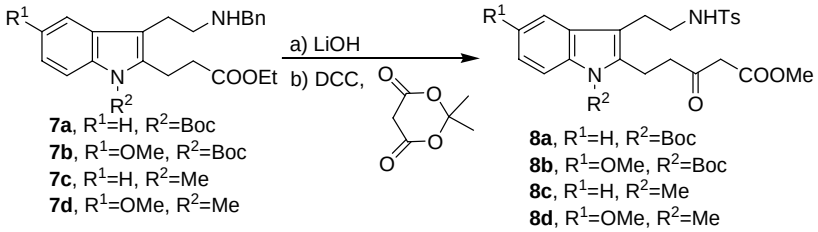
Unsaturated ester 6c: purified by column chromatography (33% EtOAc/petroleum), a yellow solid, m.p. 183−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 16.4 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8 Hz, 1H), 7.32-7.27 (m, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.12-7.08 (m, 1H), 6.27 (d, *J* = 16.4 Hz, 1H), 4.50 (N-H, t, *J* = 6 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.24 (q, *J* = 6.8 Hz, 2H), 3.12 (t, *J* = 6.8 Hz, 2H), 2.40 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.1, 143.2, 138.8, 136.9, 132.1, 131.7, 129.6, 127.2, 127.0, 124.4, 120.1, 119.5, 118.3, 116.2, 109.6, 60.7, 43.4, 31.3, 25.5, 21.5, 14.4; HRMS ($M+Na^+$) calcd for $C_{23}H_{26}N_2Na_1O_4S_1$ 449.1505, found 449.1493; IR (KBr) 3217, 1690, 1628, 1428, 1291 cm^{-1}.

Ester 7c: purified by column chromatography (33% EtOAc/petroleum) in 86% yield from **5c**, colorless foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.24-7.16 (m, 4H), 7.03 (t, *J* = 7.6 Hz, 1H), 4.45 (N-H, t, *J* = 6.0 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.67 (s, 3H), 3.21 (q, *J* = 6.8 Hz, 2H), 3.06 (t, *J* = 8.0 Hz, 2H), 2.95 (t, *J* = 6.8 Hz, 2H), 2.53 (t, *J* =8.0 Hz, 2H), 2.40 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.2, 143.0, 136.8, 136.7, 136.1, 129.5, 127.0, 121.2, 119.1, 117.9, 108.9, 107.2, 60.7, 43.4, 34.3, 29.6, 24.8, 21.4, 19.6, 14.1; HRMS ($M+Na^+$) calcd for $C_{23}H_{28}N_2Na_1O_4S_1$ 451.1662, found 451.1677; IR (KBr) 3283, 1732, 1472, 1266 cm^{-1}.

Unsaturated ester 6d: purified by column chromatography (25% EtOAc/petroleum), a yellow solid, m.p: 139−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 9.6 Hz, 1H), 6.95 (dd, *J* = 7.6, 2.4 Hz, 1H), 6.94 (s, 1H), 6.22 (d, *J* = 12.4 Hz, 1H), 4.66 (N-H, t, *J* = 6.0 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.76 (s, 3H), 3.21 (q, *J* = 6.4 Hz, 2H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.39 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.0, 154.5, 143.2, 136.8, 134.2, 132.0, 129.5, 127.4, 127.0, 117.9, 115.6, 115.4, 110.5, 60.7, 55.7, 43.2, 31.3, 25.5, 21.4, 14.3; HRMS ($M+Na^+$) calcd for

$C_{24}H_{28}N_2Na_1O_5S_1$ 479.1611, found 479.1609; IR (KBr) 3420, 3282, 1706, 1616, 1494, 1292 cm^{-1}.

Ester 7d: purified by column chromatography (25% EtOAc/petroleum) in 85% yield from **5d**, a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.8 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.80 (d, *J* = 2.4 Hz, 1H), 4.43 (N-H, t, *J* = 6.4 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 3.65 (s, 3H), 3.19 (q, *J* = 6.4 Hz, 2H), 3.03 (t, *J* = 8.0 Hz, 2H), 2.93 (t, *J* = 6.4 Hz, 2H), 2.52 (t, *J* = 8.0 Hz, 2H), 2.40 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.2, 154.0, 143.2, 136.8, 132.2, 129.5, 127.3, 127.0, 111.3, 109.7, 106.8, 100.2, 60.8, 55.9, 43.3, 34.4, 29.8, 24.9, 21.5, 19.8, 14.2; HRMS ($M+Na^+$) calcd for $C_{24}H_{30}N_2Na_1O_5S_1$ 481.1768, found 481.1789; IR (KBr) 3283, 1731, 1488, 1266 cm^{-1}.



7a, R^1=H, R^2=Boc
7b, R^1=OMe, R^2=Boc
7c, R^1=H, R^2=Me
7d, R^1=OMe, R^2=Me

8a, R^1=H, R^2=Boc
8b, R^1=OMe, R^2=Boc
8c, R^1=H, R^2=Me
8d, R^1=OMe, R^2=Me

General procedure for preparation of *β*-ketone esters 8a, 8b, 8c, and 8d[4]

To a solution of LiOH–H_2O (3.57 g, 76.5 mmol, 3 equiv) in water (12 mL) was added a mixture of **7** (25.5 mmol) in a 1:1 mixture of THF/MeOH (120 mL). The reaction mixture was stirred at room temperature for 2 h. An aqueous HCl solution (1 M, 150 mL) was added, and extracted with EtOAC (200 mL × 3). The combined extracts were washed with brine (150 mL × 3), dried over magnesium sulfate and concentrated in vacuum to get a white solid which was used directly for next step.

The crude acid was dissolved in CH_2Cl_2 (250 mL). To the solution were added TEA (5.33 mL, 1.5 equiv), DMAP (310 mg, 0.1 equiv), DCC (dicyclohexyl carbodiimide, 5.253 g, 25.5 mmol, 1 equiv), and Meldrum's acid (5.51 g, 38.25 mmol, 1.5 equiv) successively. After being stirred at room temperature for 20 h, the result suspension was filtered. The filtrate was concentrated, and then refluxed in MeOH (100 mL) for 10 h. After removing solvent, the residue was purified by column chromatography.

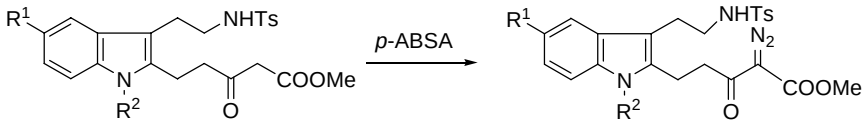
***β*-Ketone ester 8a:** purified by column chromatography (33% EtOAc/petroleum) in 72% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.27-7.25 (m, 1H), 7.23-7.15 (m, 3H), 4.52 (N-H, *J* = 6.0 Hz, 1H), 3.71 (s, 3H), 3.47 (s, 2H), 3.25-3.17 (m, 4H),

2.93-2.88 (m, 4H), 2.35 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.9, 167.6, 150.2, 143.3, 136.8 136.6, 135.8, 129.6, 129.1, 127.0, 124.0, 122.8, 117.9, 115.7, 115.6, 84.2, 52.4, 49.0, 43.1, 42.8, 28.2, 25.6, 21.5, 20.8; HRMS ($M+Na^+$) calcd for $C_{28}H_{34}N_2Na_1O_7S_1$ 565.1979, found 565.1995; IR (neat) 3288, 1726 cm^{-1}.

***β*-Ketone ester 8b**: purified by column chromatography (33% EtOAc/petroleum) in 65% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.2 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 7.6 Hz, 2H), 6.84 (dd, *J* = 10.4, 2.4 Hz, 1H), 6.83 (s, 1H), 4.87 (N-H, *J* = 6.0 Hz, 1H), 3.83 (s, 3H), 3.70 (s, 3H), 3.48 (s, 2H), 3.18 (q, *J* = 6.8 Hz, 2H), 3.14 (t, *J* = 6.8 Hz, 2H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.87 (t, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 1.67 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 202.0, 167.7, 155.9, 150.1, 143.3, 137.2, 136.8, 130.3, 130.0, 129.6, 126.9, 116.5, 115.1, 112.3, 100.8, 84.0, 55.6, 52.4, 49.0, 43.1, 42.7, 28.2, 24.7, 21.5, 20.8; HRMS ($M+Na^+$) calcd for $C_{29}H_{36}N_2Na_1O_8S_1$ 595.2085, found 595.2075; IR (neat) 3286, 1721, 1609, 1478, 1327 cm^{-1}.

***β*-Ketone ester 8c**: purified by column chromatography (33% EtOAc/petroleum) in 63% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.34 (d , *J* = 8.0 Hz, 1H), 7.24 (m, 3H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 4.39 (N-H, t, *J* = 6.4 Hz, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.48 (s, 2H), 3.21 (q, *J* = 6.4 Hz, 2H), 3.04 (t, *J* = 7.6 Hz, 2H), 2.94 (t, *J* = 6.8 Hz, 2H), 2.86 (t, *J* = 7.6 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6, 167.7, 143.3, 136.9, 136.8, 136.5, 129.6, 127.1, 127.0, 121.3, 119.3, 118.0, 109.0, 107.2, 52.5, 49.0, 43.4, 42.9, 29.7, 25.1, 21.5, 18.1; HRMS ($M+Na^+$) calcd for $C_{24}H_{28}N_2Na_1O_5S_1$ 479.1611, found 479.1598; IR (neat) 3292, 3056, 1746, 1717, 1472, 1266 cm^{-1}.

***β*-Ketone ester 8d:** purified by column chromatography (33% EtOAc/petroleum) in 68% yield, off-white powder, m.p. 95–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 4.38 (N-H, t, *J* = 6.4 Hz, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.63 (s, 3H), 3.47 (s, 2H), 3.19 (q, *J* = 6.4 Hz, 2H), 3.01 (t, *J* = 6.8 Hz, 2H), 2.91 (t, *J* = 6.4 Hz, 2H), 2.84 (t, *J* = 6.8 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.8, 167.7, 153.9, 143.2, 137.0, 136.7, 132.2, 129.6, 127.4, 126.9, 111.0, 109.7, 106.7, 100.1, 55.8, 52.4, 48.9, 43.3, 42.8, 29.7, 25.0, 21.4, 18.2; HRMS ($M+Na^+$) calcd for $C_{25}H_{30}N_2Na_1O_6S_1$ 509.1717, found 509.1730; IR (KBr) 3262, 1749, 1711, 1489, 1321 cm^{-1}.



8a, R^1=H, R^2=Boc
8b, R^1=OMe, R^2=Boc
8c, R^1=H, R^2=Me
8d, R^1=OMe, R^2=Me

2a, R^1=H, R^2=Boc
2b, R^1=OMe, R^2=Boc
2c, R^1=H, R^2=Me
2d, R^1=OMe, R^2=Me

General procedure for preparation of *α*-diazo esters 2a, 2b, 2c, and 2d

TEA was added to a solution of **8** (3.798 mmol) and *p*-ABSA (4-acetamidobenzenesulphonyl azide, 1.06 g, 4.42 mmol, 1.1 equiv) in CH_3CN (25 mL). After being stirred at room temperature for 12 h, the reaction mixture was concentrated to one third of the original volume, CH_2Cl_2 (20 mL) was added and filtered. The filtrate was concentrated and purified by column chromatography to give *α*-diazo ester **2**.

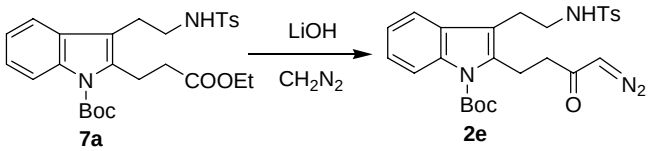
***α*-Diazo ester 2a**: purified by column chromatography (33% EtOAc/petroleum) in 86% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.24 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.19-7.15 (m, 3H), 4.69 (N-H, t, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 3.29 (q, *J* = 7.2 Hz, 2H), 3.24-3.15 (m, 4H), 2.92 (t, *J* = 7.2 Hz, 2H), 2.38 (s, 3H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.6, 160.6, 149.1, 142.1, 135.7, 135.5, 134.9, 128.5, 128.0, 125.9, 122.9, 121.6, 116.9, 114.7, 114.2, 83.0, 75.0, 51.2, 41.8, 39.3, 27.1, 23.6, 20.4, 20.2; HRMS ($M+Na^+$) calcd for $C_{28}H_{32}N_4Na_1O_7S_1$ 591.1884, found 591.1900; IR (KBr) 3289, 2139, 1726, 1653, 1458 cm^{-1}.

***α*-Diazo ester 2b:** purified by column chromatography (33% EtOAc/petroleum) in 89% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.2 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.82 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 6.79 (d, *J* = 2.4 Hz, 1H), 4.78 (N-H, t, *J* = 6.4 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.25 (q, *J* = 7.2 Hz, 2H), 3.22-3.14 (m, 4H), 2.89 (t, *J* = 7.2 Hz, 2H), 2.38 (3, 3H), 1.67 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.6, 161.6, 155.8, 150.1, 143.2, 137.3, 136.7, 130.6, 129.9, 129.5, 126.9, 116.5, 115.1, 112.3, 100.7, 83.9, 76.0, 55.6, 52.2, 42.9, 40.3, 28.2, 24.7, 21.5, 21.3; HRMS ($M+Na^+$) calcd for $C_{29}H_{34}N_4Na_1O_8S_1$ 621.1990, found 621.1989; IR (KBr) 3289, 2140, 1725, 1653, 1479 cm^{-1}.

***α*-Diazo 2c**: purified by column chromatography (33% EtOAc/petroleum) in 83%, off-white powder, m.p. 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.20-7.15 (m, 3H), 7.03

(dt, *J* = 8.0, 1.2 Hz), 4.55 (N-H, t, *J* = 6.4 Hz, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 3.23 (q, *J* = 6.4 Hz, 2H), 3.10-3.06 (m, 4H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 161.5, 142.9, 136.9, 136.8, 136.2, 129.4, 127.0, 126.9, 121.1, 119.1, 117.9, 108.8, 107.3, 76.0, 52.2, 43.4, 39.8, 29.6, 24.8, 21.4, 19.1; HRMS ($M+Na^+$) calcd for $C_{24}H_{26}N_4Na_1O_5S_1$ 505.1516, found 505.1525; IR (KBr) 3254, 3038, 2135, 1717, 1653, 1473 cm^{-1}.

***α*-Diazo ester 2d:** purified by column chromatography (33% EtOAc/petroleum) in 82% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.82 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 4.65 (N-H, t, *J* = 6.0 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.65 (s, 3H), 3.19 (q, *J* = 6.8 Hz, 2H), 3.10-3.01 (m, 4H), 2.93 (t, *J* = 6.8 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 161.5, 153.9, 143.0, 136.8, 132.2, 129.8, 129.5, 127.3, 126.8, 111.1, 109.5, 107.0, 100.3, 76.0, 55.9, 52.2, 43.3, 39.9, 29.7, 24.6, 21.3, 19.1; HRMS ($M+Na^+$) calcd for $C_{25}H_{28}N_4Na_1O_6S_1$ 535.1622, found 535.1619; IR (KBr) 3324, 2140, 1720, 1489, 1322 cm^{-1}.

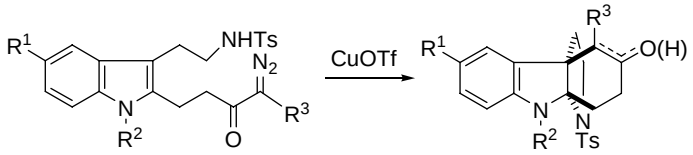


Diazo ketone 2e

To a solution of 7**a** (514 mg, 1 mmol) in THF/MeOH (5 mL/5 mL) was added 1 mL of LiOH solution (1 M, 3 mmol). After being stirred at room temperature for 2 h, the mixture was added HCl solution (1 M, 15 mL), and extracted with EtOAC (50 mL × 3). The combined extracts were washed with brine (50 mL × 3), dried over magnesium sulfate and concentrated in vacuum to give a white solid, which was used without purification for next step.

To a solution of the above crude acid in 10 mL of THF was added TEA (0.14 mL, 1 mmol, 1 equiv) and ethyl chloroformate (0.10 mL, 1.1 mmol, 1.1 equiv) at 0 °C. After 30 min, an ether solution of diazomethane (10 mmol, 10 equiv) was added. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. The reaction mixture was concentrated. The residue was purified by column chromatography (10% EtOAc/petroleum ether) to give **2e** (330 mg, 65%) as yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz,

2H), 7.34 (d, J = 8.0 Hz, 1H), 7.21 (m, 3H), 5.38 (s, 1H), 3.27 (t, J = 7.2 Hz, 2H), 3.18 (q, J = 6.8 Hz, 2H), 2.90 (t, J = 6.4 Hz, 2H), 2.65 (broad s, 2H), 2.38 (s, 3H), 1.69 (s, 9H), ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.3, 150.2, 143.2, 136.7, 135.7, 129.7, 129.5, 129.1, 126.7, 123.9, 122.7, 116.0, 115.9, 115.3, 84.1, 54.8, 42.9, 40.8, 28.2, 24.6, 22.1, 21.5; HRMS (M+Na^+) calcd for $C_{26}H_{30}N_4O_5S_1Na$ 533.1917, found 533.1920; IR (KBr) 3275, 3099, 2105, 1727, 1640, 1458 cm^{-1}.



2a, R^1=H, R^2=Boc, R^3=COOMe
2b, R^1=OMe, R^2=Boc, R^3=COOMe
2c, R^1=H, R^2=Me, R^3=COOMe
2d, R^1=OMe, R^2=Me, R^3=COOMe
2e, R^1=H, R^2=Boc, R^3=H

1a, R^1=H, R^2=Boc, R^3=COOMe
1b, R^1=OMe, R^2=Boc, R^3=COOMe
1c, R^1=H, R^2=Me, R^3=COOMe
1d, R^1=OMe, R^2=Me, R^3=COOMe
1e, R^1=H, R^2=Boc, R^3=H

General procedure for the CuOTf-catalyzed one-pot cascade reaction of 2a–e to generate tetracyclic 1a–e

To a suspension of CuOTf–benzene complex (0.022 g, 0.044 mmol) in 10 mL of CH_2Cl_2 was added a solution of diazo compound **2** (0.88 mmol) in CH_2Cl_2 (30 mL) via an injector at room temperature. The mixture was stirred for 12 h and concentrated. The crude residue was purified by column chromatography to give tetracyclic **1**.

Enol ester 1a: purified by column chromatography (20% EtOAc/petroleum) in 50% yield, off-white solid, m.p. 159–161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.63 (O-H, s, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 7.2, 1H), 7.21 (br, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.94 (t, J = 8.0 Hz, 1H), 6.87 (dt, J = 8.0, 1.2 Hz, 1H) 3.83 (s, 3H), 3.79 (m, 2H), 3.03-2.97 (m, 2H), 2.64-2.55 (m, 1H), 2.41-2.34 (m, 1H), 2.37 (s, 3H), 2.24-2.15 (m, 1H), 2.07-1.99 (m ,1H), 1.62 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 172.8, 172.0, 142.6, 141.8, 137.5, 131.9, 129.1, 127.9, 126.6, 124.0, 123.0, 117.9, 100.0, 91.4, 82.4, 57.4, 51.2, 49.2, 32.6, 29.1, 28.2, 28.0, 21.3; HRMS (M+Na^+) calcd for $C_{28}H_{32}N_2Na_1O_7S_1$ 563.1822, found 563.1796; IR (KBr) 3447, 1703, 1662, 1477 cm^{-1}.

Enol ester 1b: purified by column chromatography (20% EtOAc/petroleum) in 52% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.65 (O-H, s, 1H), 7.44 (d, J = 7.6 Hz, 2H), 7.11 (d, J = 8.4, 2H), 7.08-6.91 (br, 1H), 6.90 (s, 1H), 6.48 (d, J = 8.8 Hz, 1H), 3.85 (s, 3H), 3.82-3.70 (m, 2H), 3.72 (s, 3H), 3.01-2.92 (m, 2H), 2.61-2.55 (m, 1H), 2.40-2.34 (m, 1H), 2.37 (s, 3H), 2.23-2.15 (m, 1H), 2.05-2.02 (m, 1H), 1.61 (s,

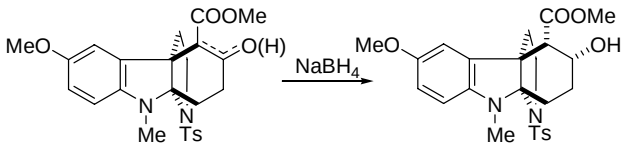
9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.0, 172.1, 155.6, 151.2, 142.6, 137.3, 135.2, 133.3, 129.1, 126.9, 126.6, 118.4, 112.4, 110.5, 99.9, 91.5, 82.2, 57.4, 55.5, 51.3, 49.1, 32.6, 28.2, 28.0, 21.4; HRMS ($M+Na^+$) calcd for $C_{29}H_{34}N_2Na_1O_8S_1$ 593.1928, found 593.1935; IR (KBr) 3446, 1713, 1653, 1602, 1491, 1224 cm^{-1}.

Ester 1c: purified by column chromatography (17% EtOAc/petroleum) in 81% yield as an inseparable ketone-enol isomers mixture in a 1:30 ratio, off-white foam. ^{1}H NMR of the major enol ester isomer (400 MHz, $CDCl_3$) δ 12.76 (O-H, s, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.66 (t, *J* = 7.6 Hz, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 3.86 (s, 3H), 3.58-3.53 (m, 1H), 3.33-3.29 (m, 1H), 3.06-2.99 (m, 2H), 2.96 (s, 3H), 2.52-2.29 (m, 2H), 2.14-2.03 (m, 2H); ^{13}C NMR of the major enol ester isomer (50 MHz, $CDCl_3$) δ 173.4, 172.6, 149.4, 142.8, 137.9, 130.4, 129.4, 128.7, 126.6, 123.8, 118.0, 106.5, 101.2, 94.9, 57.4, 51.3, 49.3, 34.8, 29.4, 27.8, 26.4, 21.4; HRMS ($M+Na^+$) calcd for $C_{24}H_{26}N_2Na_1O_5S_1$ 477.1455, found 477.1433; IR (KBr) 3446, 1700, 1645, 1607, 1490, 1318, 1235 cm^{-1}.

Ester 1d: purified by column chromatography (17% EtOAc/petroleum) in 82% yield as an inseparable mixture of ketone-enol isomers in a 1:5 ratio, off-white foam. ^{1}H NMR of the major enol ester isomer (400 MHz, $CDCl_3$) δ 12.75 (OH, S, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 2.8 Hz, 1H), 6.67 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.24 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 3.73 (s, 3H), 3.54 (t, *J* = 8.4 Hz, 1H), 3.28 (m, 1H), 3.02-2.87 (m, 2H), 2.92 (s, 3H), 2.55-2.44 (m, 1H), 2.37 (s, 3H), 2.34-2.28 (m, 1H), 2.11-2.02 (m, 2H); ^{13}C NMR of the major enol ester isomer (100 MHz, $CDCl_3$) δ 173.6, 172.4, 153.1, 143.7, 142.7, 136.6, 131.7, 129.3, 126.6, 112.5, 112.1, 106.2, 100.8, 95.5, 57.4, 55.9, 51.2, 49.0, 34.5 29.6, 27.8, 26.4, 21.3; HRMS ($M+Na^+$) calcd for $C_{25}H_{28}N_2Na_1O_6S_1$ 507.1560, found 507.1542; IR (KBr) 3445, 1735, 1645, 1496, 1319, 1218 cm^{-1}.

Ketone 1e: purified by column chromatography (30% EtOAc/petroleum) in 42% yield, off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* =8.0Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 6.8 Hz, 1H), 7.00 (t, *J* = 8.0 Hz, 1H), 3.84 (t, *J* = 8.0 Hz, 1H), 3.29-3.22 (m, 1H), 3.19-3.12 (m, 1H), 2.95 (ddd, *J* = 16.8, 11.2, 5.2 Hz, 1H), 2.72 (q, *J* = 16 Hz, 2H), 2.52-2.44 (m, 1H), 2.41 (s, 3H), 2.37-2.29 (m, 1H), 2.17 (dd, *J* = 12.4, 5.2 Hz, 1H), 2.08-2.00 (m, 1H), 1.57 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 209.2, 152.1, 143.6, 142.6, 136.5, 133.0, 129.7, 129.3, 127.4, 124.4, 122.7, 117.3, 90.7, 83.3, 59.4, 49.1, 48.9, 37.6, 35.3, 31.1, 26.8, 22.0; HRMS ($M+Na^+$) calcd for $C_{26}H_{30}N_2O_5SNa$ 505.1768, found:

505.1777; IR (KBr) 1719, 1599 cm^{-1}.

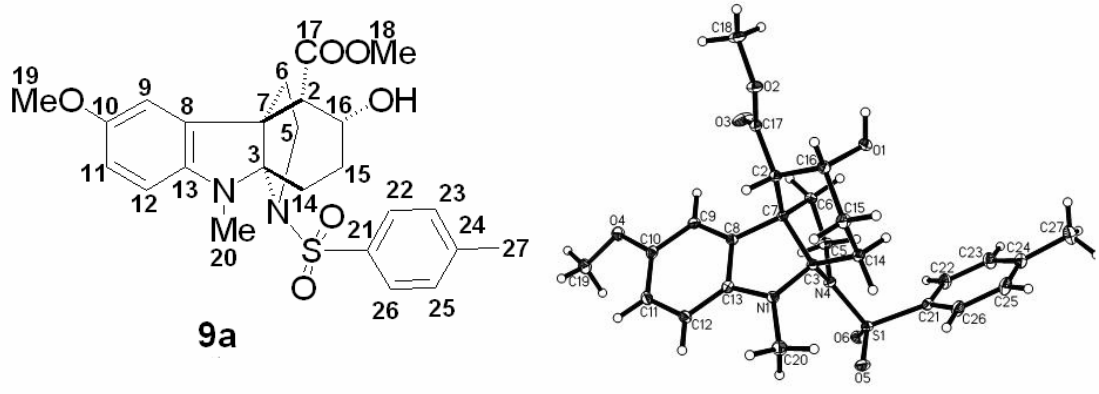


1a, ketone:enol = 1: 5 **9a**

***β*-Hydroxy ester 9a**

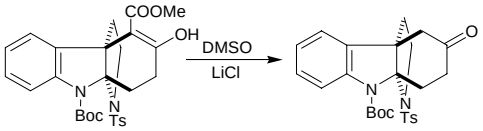
To a solution of **9a** (500 mg, 1.0 mmol) in a 50:1 mixture of THF/MeOH (20 mL) was added $NaBH_4$ (120 mg, 3.1 mmol, 3 equiv) in portions over a period of 3 h at −5 °C. The reaction was stirred for an additional 3 h at −5 °C and quenched with acetone (2 mL). The mixture was diluted with EtOAC (50 mL), washed with brine (20 mL × 3), dried over magnesium sulfate and concentrated to give a residue. The residue was purified by column chromatography (30% EtOAc/petroleum) to afford **9a** (382 mg, 76% yield) as off-white powder and other isomers in less than 10% yield. A colorless crystal of **9a** for the X-ray analysis (CCDC-663298) was obtained by recrystallization from EtOH, m.p. 168–170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 6.66 (dd, J = 7.2, 2.8 Hz, 1H), 6.65 (s, 1H), 6.25 (d, J = 7.2 Hz), 4.20 (d, J = 2.4 Hz, 1H), 3.73 (s, 3H), 3.73 (s, 3H), 3.49 (t, J = 8.0 Hz, 1H), 3.22 (O-H, s, 1H), 2.98 (s, 3H), 2.95-2.77 (m, 3H), 2.48-2.39 (m, 2H), 2.34 (s, 3H), 2.28 (d, J = 2.4 Hz, 1H), 1.92 (dq, J = 8.8, 3.6 Hz, 1H), 1.51 (t, J = 14 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 152.6, 142.7, 142.4, 138.1, 133.6, 129.2, 126.6, 112.8, 110.7, 107.3, 95.4, 65.6, 56.2, 56.0, 51.8, 51.7, 48.1, 29.8, 28.7, 28.3, 23.9, 21.3; HRMS ($M+H^+$) calcd for $C_{25}H_{31}N_2O_6S_1$ 487.1897, found 487.1917; IR (KBr) 3459, 1737, 1599, 1493, 1283 cm^{-1}.

ORTEP Drawing and Relative Stereochemistry of 9a



CCDC 663298 contains the supplementary crystallographic data for this paper. These

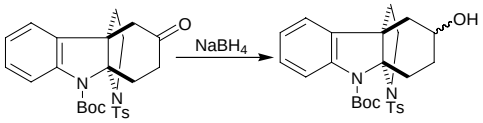
data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



1a **1e**

Decarboxylation of tetracyclic 1a yielding ketone 1e

A mixture of **1a** (2.100 g, 3.7 mmol), water (133 μL, 7.4 mmol, 2 equiv), LiCl (0.310 g, 7.4 mmol, 2 equiv) in DMSO (15 mL) was heated to 130 °C for 7 h. After cooling to room temperature, the mixture was diluted with EtOAc (100 mL), washed with brine (50 mL× 3), dried over magnesium sulfate and concentrated to give a residue. The residue was purified by column chromatography (30% EtOAc/petroleum) to yield **1e** (1.55 g, 87% yield) as off-white foam. ^{1}H NMR and ^{13}C NMR spectra were identical to that of the sample obtained by the cascade reaction of **2e**.



1e **10a** **10b**

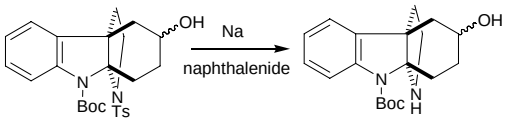
Alcohol 10a and 10b

To a solution of ketone **1e** (1.012 g, 2.1 mmol) in CH_3OH (30 mL) was added $NaBH_4$ (0.079 g, 2.1 mmol, 1 equiv) in one portion at room temperature. After being stirred for 30 min, the reaction was quenched with acetone (1 mL), diluted with EtOAc (100 mL), washed with brine (50 mL × 3), dried over magnesium sulfate and concentrated to give a 7:4 mixture of diastereomers **10a** and **10b** (0.984 g, 98% yield) as colorless foam. Analytical samples of **10a** and **10b** were obtained by chromatography (40% EtOAc/petroleum).

10a (less polar)**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 2 H), 6.97 (m, 2H), 6.89 (t, *J* = 7.4 Hz, 1H), 3.96 (t, *J* = 7.6 Hz, 1H), 3.65 (t, *J* = 7.6 Hz, 1H), 3.57 (dt, *J* = 14.8, 3.6 Hz, 1H), 2.90-2.84 (m, 1H), 2.79-2.71 (m, 1H), 2.39-2.31 (m, 1H), 2.35 (s, 3H), 2.19 (q, *J* = 6.4 Hz, 1H), 2.03 (dd, *J* = 14.8, 4.0 Hz, 1H) 1.78-1.66 (m, 2H), 1.62 (s, 9H); 1.50 (dd, *J* = 14.8, 4.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.1, 142.4, 141.4, 137.7, 136.0, 129.0 127.5, 126.7, 123.3, 120.9, 117.8, 90.6 82.0, 64.6, 55.2, 47.9, 40.2, 31.5, 29.5, 28.2,

27.0, 21.3; HRMS (M+Na^+) calcd for $C_{26}H_{32}N_2O_5SNa$ 507.1924, found 507.1938; IR (KBr) 3446, 1700, 1600, 1558, 1478, 759 cm^{-1}.

10b (more polar**):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.96-6.87 (m, 3H), 3.89-3.84 (m, 2H), 3.66 (d, *J* = 8.0 Hz, 1H), 2.96-2.89 (m, 1H), 2.34 (s, 3H), 2.32-2.28 (m, 1H), 2.20-2.14 (m, 2H), 1.96-1.93 (m, 1H), 1.88-1.79 (m, 1H), 1.64 (s, 9H), 1.42-1.38 (m, 1H), 1.27-1.21 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.0, 142.5, 141.0, 137.3, 135.6, 129.1, 127.5, 126.6, 123.4, 120.3, 116.2, 90.6, 82.1, 66.5, 57.3, 47.5, 42.6, 32.2, 31.7, 26.8, 26.2, 21.3; HRMS (M+Na^+) calcd for $C_{26}H_{32}N_2O_5SNa$ 507.1924, found 507.1938; IR (KBr) 3446, 1700, 1600, 1558, 1478, 759 cm^{-1}.



10a
10b

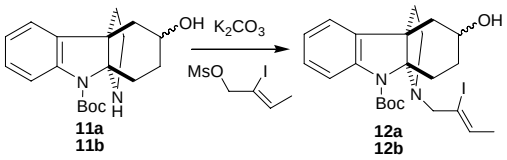
11a
11b

Amines 11a and 11b

To a solution of naphthalene (641 mg, 5.0 mmol) in THF (25 mL) was added metal sodium (115.5 mg, 5.0 mmol). The mixture was stirred at room temperature for 2 h to yield a deep-blue sodium-naphthalenide solution (0.2 M). The fresh-prepared Sodium-naphthalenide solution was added slowly to a solution of a mixture of **10a** and **10b** (0.200 g, 0.41 mmol) in THF (5 ml) at −78 °C until the color of reaction mixture maintained unchanged blue (about 21 mL, 10 equiv was used). After being stirred at −78 °C for 1 h, water (1 mL) was added. The resultant mixture was warmed to room temperature and diluted with EtOAc (50 mL), washed with brine (20 mL × 3), dried over sodium sulfate and concentrated. The crude residue was purified by column chromatography (60% EtOAc/petroleum) to afford **11a** (0.083 g, 61%) and **11b** (0.047 g, 34% yield) as colorless foam.

11a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (br d, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 5.07 (m, 1H), 3.57 (ddd, *J* = 17.8, 10.8, 5.6 Hz, 1H), 3.13 (m, 1H), 2.88 (q, *J* = 8.4 Hz, 1H), 2.31 (dd, *J* = 14.2, 6.0 Hz, 1H), 2.26 (s, 1H), 2.10-2.00 (m, 4H), 1.88-1.83 (m, 1H), 1.60 (s, 9H), 1.51-1.43 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.3, 135.2, 127.6, 125.0, 122.7, 122.1, 115.0, 91.6, 81.4, 66.9, 51.5, 43.2, 40.7, 32.2, 28.6, 26.3, 23.4; HRMS (M+H^+) calcd for $C_{19}H_{27}N_2O_3$ 331.2016, found 331.2018; IR (neat) 3460, 3053, 1683, 1482, 1458 cm^{-1}.

11b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (br d, 1H), 7.19-7.14 (m, 2H), 6.98 (t, *J* = 7.6 Hz, 1H), 5.13 (m, 1H), 4.14 (m, 1H), 3.02 (dt, *J* = 9.2, 2 Hz, 1H), 2.86 (q, *J* = 8.4 Hz, 1H), 2.21 (dd, *J* = 14.2, 6.0 Hz, 1H), 2.14-2.10 (m, 2H), 2.09-1.95 (m, 4H), 1.85 (ddd, *J* = 11.0, 6.2, 2.0 Hz, 1H), 1.60 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.2, 136.9, 135.2, 127.9, 125.0, 122.9, 114.9, 91.0, 81.5, 65.7, 51.4, 42.6, 40.0, 32.2, 28.6, 26.3, 23.4; HRMS ($M+H^+$) calcd for $C_{19}H_{27}N_2O_3$ 331.2016, found 331.2018; IR (neat) 3460, 3053, 1683, 1482, 1458 cm^{-1}.



11a
11b

12a
12b

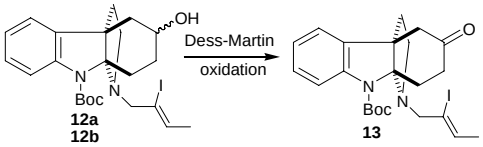
General procedure for preparation of 12a and 12b

A mixture of **11a** (0.102 g, 0.30 mmol), (*Z*)-2-iodo-2-butenyl mesylate[5] (0.251 g, 0.91mmol, 3 equiv) and K_2CO_3 (0.166 g, 1.20 mmol, 4 equiv) in CH_3CN (5 mL) was heated to 70 °C. After 24 h, the mixture was filtered. The filtrate was diluted with EtOAc (40 mL), washed with brine (20 mL × 3), dried over sodium sulfate and concentrated. The crude residue was purified by column chromatography (15% EtOAc/petroleum) give **12a** (0.127 g, 82% yield) as colorless foam.

12a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.14 (m, 2H), 6.96 (t, *J* = 7.2 Hz, 1H), 5.81 (q, *J* = 6.4 Hz, 1H), 4.13 (d, *J* = 14.4 Hz,1H), 3.70 (m, 1H), 3.55 (d, *J* = 14.4 Hz,1H), 2.86 (ddd, *J* = 10.6, 7.0, 2.8 Hz, 1H), 2.46 (m, 2H), 2.21 (m, 2H), 2.01 (m, 1H), 1.86 (m, 3H), 1.78 (d, *J* = 6.4 Hz, 3H), 1.72 (m, 1H), 1.65 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.3, 142.5, 135.6 130.1, 127.7, 122.5, 122.0, 115.6, 111.8, 92.4, 81.3, 66.2, 60.4, 55.8, 47.9, 40.8, 38.8, 29.3, 28.5, 27.6, 21.6; HRMS ($M+H^+$) calcd for $C_{23}H_{32}IN_2O_3$ 511.1452, found 511.1463; IR (neat) 3386, 3048, 1697, 1600, 1480, 1458, 1367 cm^{-1}.

12b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* =8.0Hz, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 5.72 (t, *J* = 6.4 Hz, 1H), 4.17 (m, 1H), 4.12 (d, *J* = 14.4 Hz, 1H), 3.38 (d, *J* = 14.4 Hz, 1H), 2.71 (t, *J* = 7.2 Hz, 1H), 2.48 (ddd, *J* = 14.4, 6.0, 3.6 Hz, 1H), 2.36-2.22 (m, 3H), 2.19-2.12 (m, 1H), 1.96-1.89 (m, 1H), 1.83-1.79 (m, 1H), 1.72 (d, *J* = 6.4 Hz, 3H), 1.65-1.61 (m, 1H), 1.56 (s, 9H), 1.51-1.42 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 153.1, 142.6, 136.6 130.3, 127.8, 122.9, 122.2, 115.6, 111.8, 91.2, 81.4, 65.0, 60.1, 55.1, 47.3, 40.1, 38.3, 29.0, 28.5, 26.7 ,

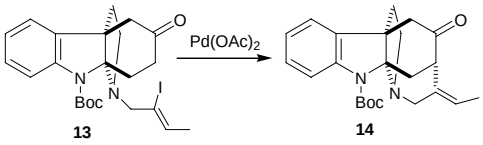
21.6; HRMS (M+H$^+$) calcd for $C_{23}H_{32}IN_2O_3$ 511.1452, found 511.1463; IR (neat) 3386, 3048, 1697, 1600, 1480, 1458, 1367 cm^{-1}.



12a
12b **13**

General procedure for oxidation of alcohol 12 to ketone 13

To a solution of **12a** (0.102 g, 0.20 mmol) in CH_2Cl_2 (5 mL) was added Dess-Martin reagent (82.4 mg, 0.20 mmol, 1 equiv) in one portion at room temperature. After 30 min, the suspension was diluted with ether (30 mL) and washed sequentially with 10% aqueous $Na_2S_2O_3$ (10 mL × 1), saturated $NaHCO_3$ (10 mL × 1) and brine (10 mL × 2). The combined organic phases were dried over sodium sulfate and concentrated. The crude residue was purified by column chromatography (10% EtOAc/petroleum) to give **13** (0.090 mg, 90%) as off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.16 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.03 (m, 2H), 5.78 (q, *J* = 6.4 Hz, 1H), 4.38 (d, *J* = 14.0 Hz, 1H), 3.29 (d, *J* = 14.0 Hz, 1H), 3.14 (dt, *J* = 14.6, 4.4 Hz, 1H), 2.90-2.68 (m, 4H), 2.34 (dt, *J* = 19.2, 4 Hz, 1H), 2.24-2.16 (m, 2H), 1.93 (dd, *J* = 12.0, 4.4 Hz, 1H), 1.85-1.80 (m, 1H), 1.77 (d, *J* = 6.4 Hz, 3H), 1.60 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.0, 152.9, 143.0, 134.6, 131.1, 128.3, 123.2, 122.7, 115.8, 111.1, 90.2, 81.9, 59.7, 56.4, 48.7, 46.7, 38.5, 35.6, 29.7, 28.4, 21.7; HRMS (M+Na$^+$) calcd for $C_{23}H_{29}I_1N_2O_3Na$ 531.1115, found 531.1110; IR (KBr) 1720, 1699, 1602, 1486 cm^{-1}.

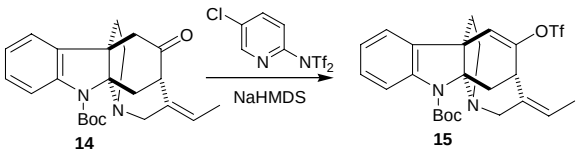


13 **14**

Pentacycle ketone 14

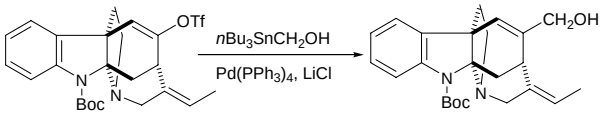
A mixture of ketone **13** (50 mg, 0.1 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.05 equiv), Bu_4NBr (32 mg, 0.1 mmol, 1 equiv), PPh_3 (13 mg, 0.05 mmol, 0.5 equiv) and K_2CO_3 (55.2 mg, 0.4 mmol, 4 equiv) in a 10:1 mixture of DMF/H_2O (3 mL) was degassed with nitrogen gas for 20 min. The mixture was then heated to 70 °C for 12 h. After cooled to room temperature, the mixture was diluted with EtOAc (100 mL), washed with brine (50 mL × 3), dried over sodium sulfate and concentrated. The

residue was purified by column chromatography (10% EtOAc/petroleum) to yield **14** (22 mg, 60%) as off-white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (br s, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 5.54 (q, *J* = 6.8 Hz, 1H), 4.40 (br s, 1H), 3.49 (br s, 1H), 3.19-3.10 (m, 2H), 2.96-2.92 (m, 2H), 2.81-2.74 (m, 2H), 2.21 (d, *J* = 11.6 Hz, 1H), 2.05-1.94 (m, 2H), 1.81 (d, *J* = 6.8 Hz, 3H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 208.1, 152.8, 143.9, 135.1, 128.6, 128.5, 123.9, 123.1, 123.0, 116.2, 89.7, 81.1, 56.6, 53.6, 48.4, 48.2, 44.3, 37.4, 35.2, 28.4, 14.8; HRMS ($M+H^+$) calcd for $C_{23}H_{29}N_2O_3$ 381.2173, found 381.2181; IR (neat) 1702, 1602, 1481, 1368 cm^{-1}.



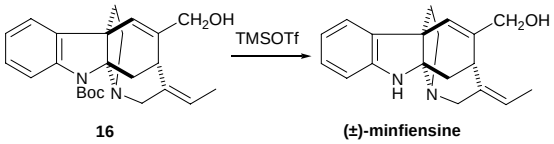
Enol triflate 15

NaHMDS (1 M solution in THF, 132 μL, 0.132 mmol, 2 equiv) was added dropwise via an injector to a solution of **14** (25 mg, 0.066 mmol) in THF (3 mL) at −78 °C. After 20 min, a solution of Comins' reagent[6] (52 mg, 0.132 mmol, 2 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 20 min and then quenched by adding saturated NH_4Cl solution (5 mL). The resultant mixture was diluted with EtOAC (50 mL) and washed with brine (20 mL × 3), dried over magnesium sulfate and concentrated in vacuum to yield a residue. The residue was purified by column chromatography (7% EtOAc/petroleum) to afford **15** (30 mg, 88% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.42 (br, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 7.2 Hz, 1H), 5.87 (s, 2H), 5.53 (q, *J* = 6.8 Hz, 1H), 4.36-4.10 (br, 1H), 3.49 (s, 1H), 3.19 (t, *J* = 7.6 Hz, 1H), 3.09 (d, *J* = 14 Hz, 1H), 2.86-2.64 (m, 2H), 2.07-1.99 (m, 2H), 1.94 (m, 2H), 1.75 (d, *J* = 6.8 Hz, 3H), 1.62 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.7, 139.8, 132.9, 131.1, 128.5, 123.1, 122.3, 122.1, 121.7, 115.6, 115.4, 109.0, 90.4, 81.6, 56.0, 52.2, 51.6, 37.8, 34.6, 28.7, 27.6, 14.0; HRMS ($M+H^+$) calcd for $C_{24}H_{28}F_3N_2O_5S_1$ 513.1666, found 513.1674; IR (neat) 1702, 1382, 1211, 1140 cm^{-1}.



Allyl alcohol 16

A mixture of **15** (30 mg, 0.058 mmol), tri-*n*-butylstannylmethanol[7] (75mg, 0.23 mmol, 4 equiv), LiCl (100 mg, 2.35mmol, 40 equiv) and $Pd(PPh_3)_4$ (6.7 mg, 0.1 equiv) in degassed dioxane (4 mL) was irradiated under microwave (200 mA) for 1 h and then concentrated under reduced pressure. The residue was purified by flash chromatography (30% EtOAc/petroleum) to give **4** (17 mg, 85% yield) as off-white powder. ^{1}H NMR (400 MHz, C_6D_6, 60 °C) δ 8.17 (br s, 1H), 7.21-7.16 (m, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 5.61 (s, 2H), 5.15 (q, *J* = 6.8 Hz, 1H), 4.42 (d, *J* = 14.8 Hz, 1H), 3.84 (q, *J* = 13.6 Hz, 2H), 3.21 (s, 1H), 3.01-2.95 (m, 2H), 2.65 (d, *J* = 12 Hz, 1H), 2.57-2.50 (m, 1H), 1.95-1.87 (m, 1H), 1.63-1.48 (m, 5H), 1.52 (s, 9H); ^{13}C NMR (50 MHz, C6D6, 23°C) δ 153.0, 144.3, 141.1, 137.6, 133.9, 128.3, 122.9, 122.1, 121.0, 119.3, 116.1, 91.9, 80.6, 65.4, 55.8, 52.9, 38.3, 30.7, 28.7, 27.8, 14.4; HRMS ($M+H^+$) calcd for $C_{24}H_{31}N_2O_3$ 395.2329, found 395.2308; IR (KBr) 3228, 1694, 1480, 1369, 1252, 1165 cm^{-1}.



(±)-Minfiensine

TMSOTf (44 μL, 0.24 mmol, 4.5 equiv) was added dropwise to a solution of **16 (**21 mg, 0.053 mmol) in CH_2Cl_2 (4 mL) via an injector at 0 °C. After 10 min, the reaction was quenched with saturated $NaHCO_3$ solution (5 mL). The organic layer was separated, and the water layer was extracted with CH_2Cl_2 (5 mL × 2). The combined organic layers were washed with saturated $NaHCO_3$ solution (10 mL× 2), dried over sodium sulfate and concentrated. The residue was purified by preparative TLC (10% MeOH/CH_2Cl_2), and then passing through a short column of silica gel using CH_3CN (containing 1% NH_4OH) as eluent to give (±)-minfiensine (13 mg, 83% yield) as off-white powder. The synthetic sample has identical ^{1}H and ^{13}C NMR spectra to that of the natural minfiensine provided by Prof. G. Massiot and a synthetic sample provided by Prof. L. E. Overman. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.2 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.71 (d, *J* = 7.2 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 6.04

(s, 1H), 5.39 (q, J = 6.8 Hz, 1H), 4.10 (s, 2H), 3.89 (N-H, br s, 1H), 3.68 (d, J = 15.2 Hz, 1H), 3.43 (s, 1H), 3.30 (ddd, J = 11.2, 7.2, 5.2 Hz, 1H), 3.16 (d, J = 14.8, 1H), 2.65 (dt, J = 10.0, 7.6 Hz, 1H), 2.04 (m, 2H), 1.94 (m, 2H), 1.72 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 140.9, 135.7, 133.5, 127.7, 124.7, 122.6, 119.4, 118.5, 109.8, 90.1, 65.6, 55.4, 53.8, 53.3, 38.4, 32.1, 31.4, 13.7; HRMS ($M+H^+$) calcd for $C_{19}H_{23}N_2O_1$ 295.1805, found 295.1805.

References:

Ref. 6a in main text: M. S. Baliga, G. C. Jagetia, J. N. Ulloor, M. P. Baliga, P. Venkatesh, R. Reddy, K. V. N. M. Rao, B. S. Baliga, S. Devi, S. K. Raju, V. Veeresh, T. K. Reddy, K. L. Bairy, *Toxicology Lett*. **2004**, *151*, 317.

[1] a) S. P. Chavan, P. Sharma, R. Sivappa, U. R. Kalkote, *Tetrahedron Lett*. **2006**, *47*, 9301; b) A. Boumendjel, J. M. Nuzillard, G. Massiot, *Tetrahedron Lett*. **1999,** *40*, 9033.

[2] P. D. Bailey, S. P. Hollinshead, *Tetrahedron Lett*. **1987,** *28*, 2879.

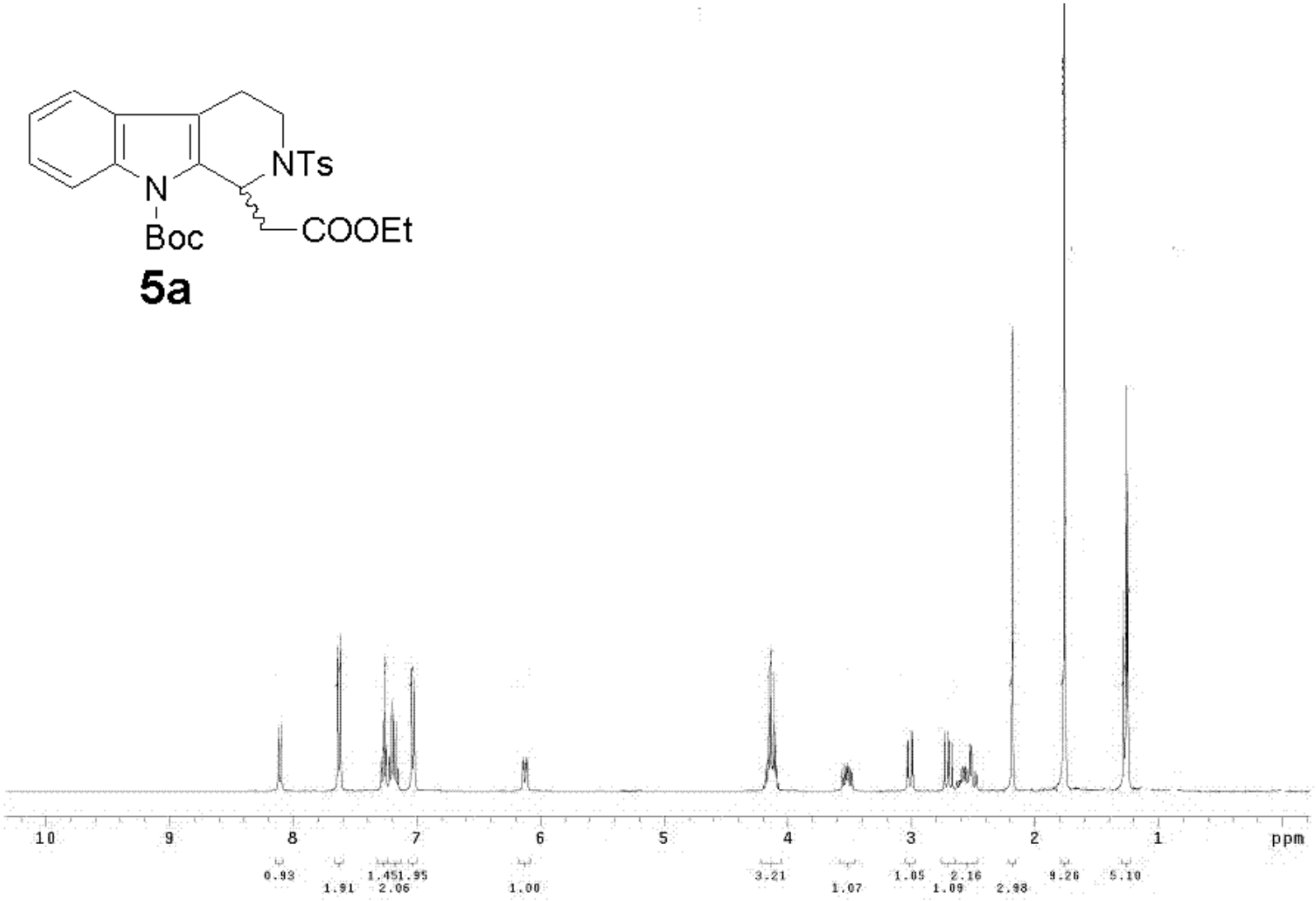
[3] Large amounts of Boc-deprotection product was obtained when NaH was used as a base.

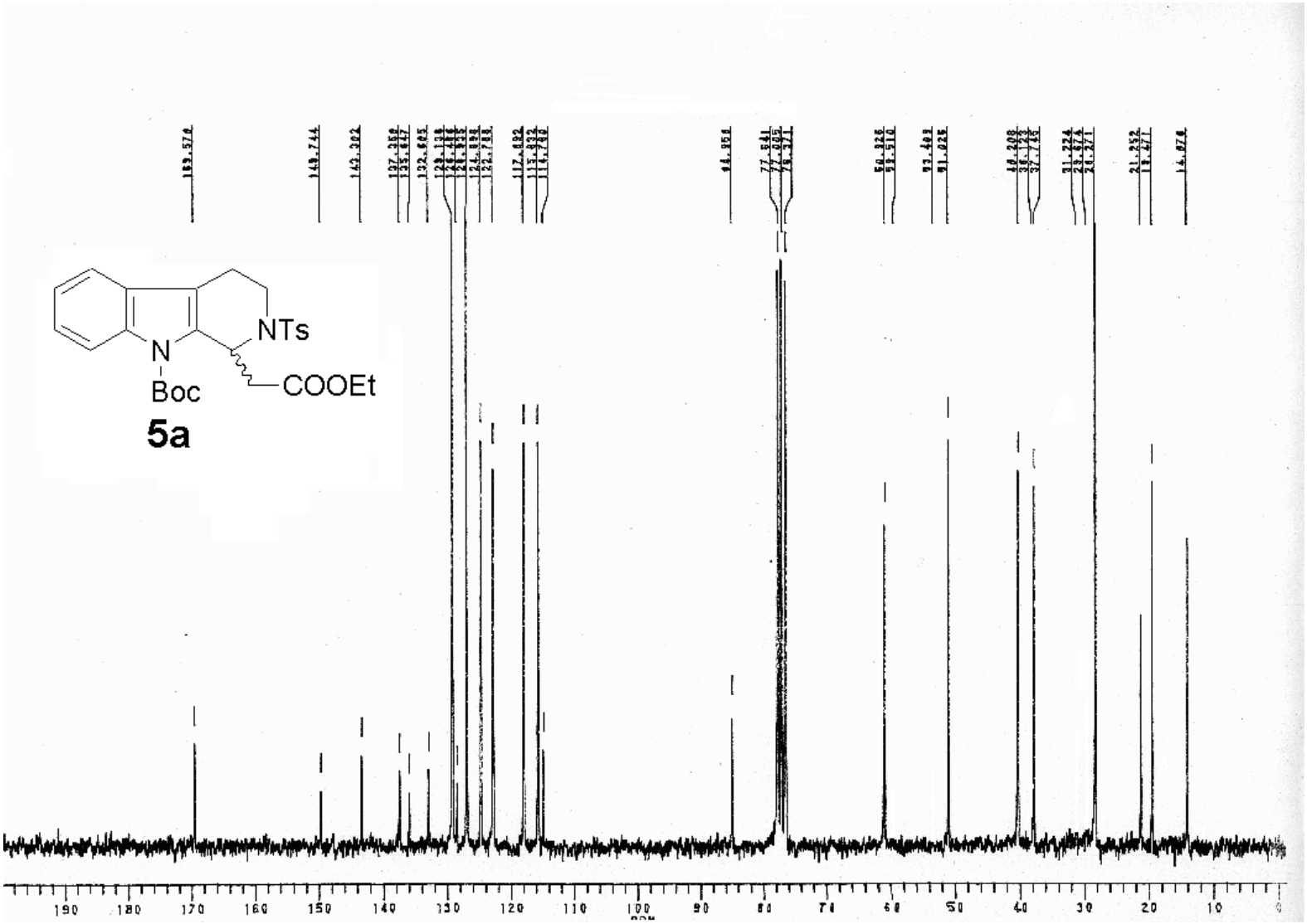
[4] M. Smrcina, P. Majer, E. Majerová, T. A. Guerassina, M. A. Eissenstat, *Tetrahedron* **1997**, *53,* 12867.

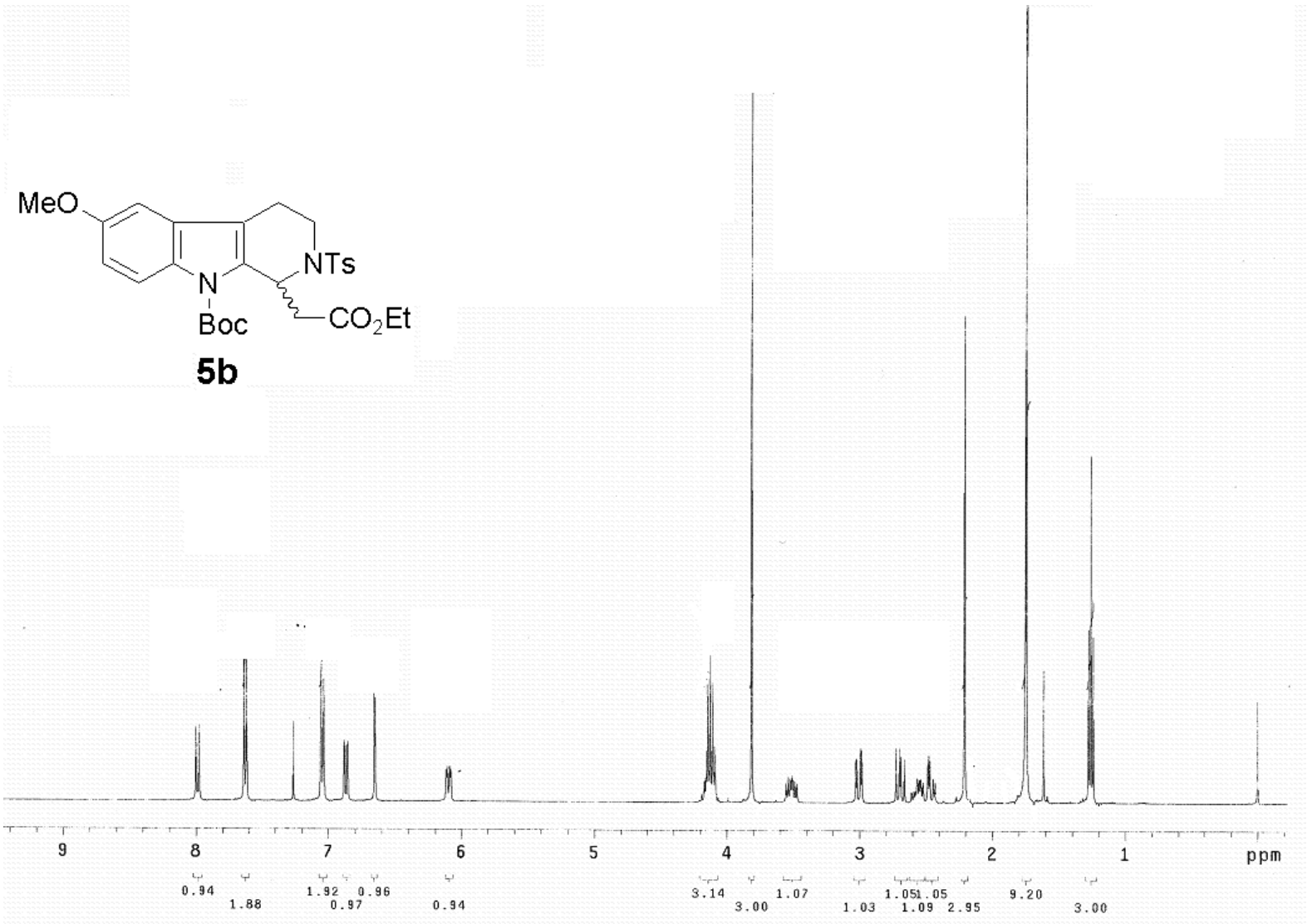
[5] (*Z*)-2-iodo-2-butenyl mesylate was prepared through mesylation of the butenyl alcohol. P. Gamez, C. Ariente, J. Goré, B. Cazes, *Tetrahedron* **1998**, *54*, 14825.

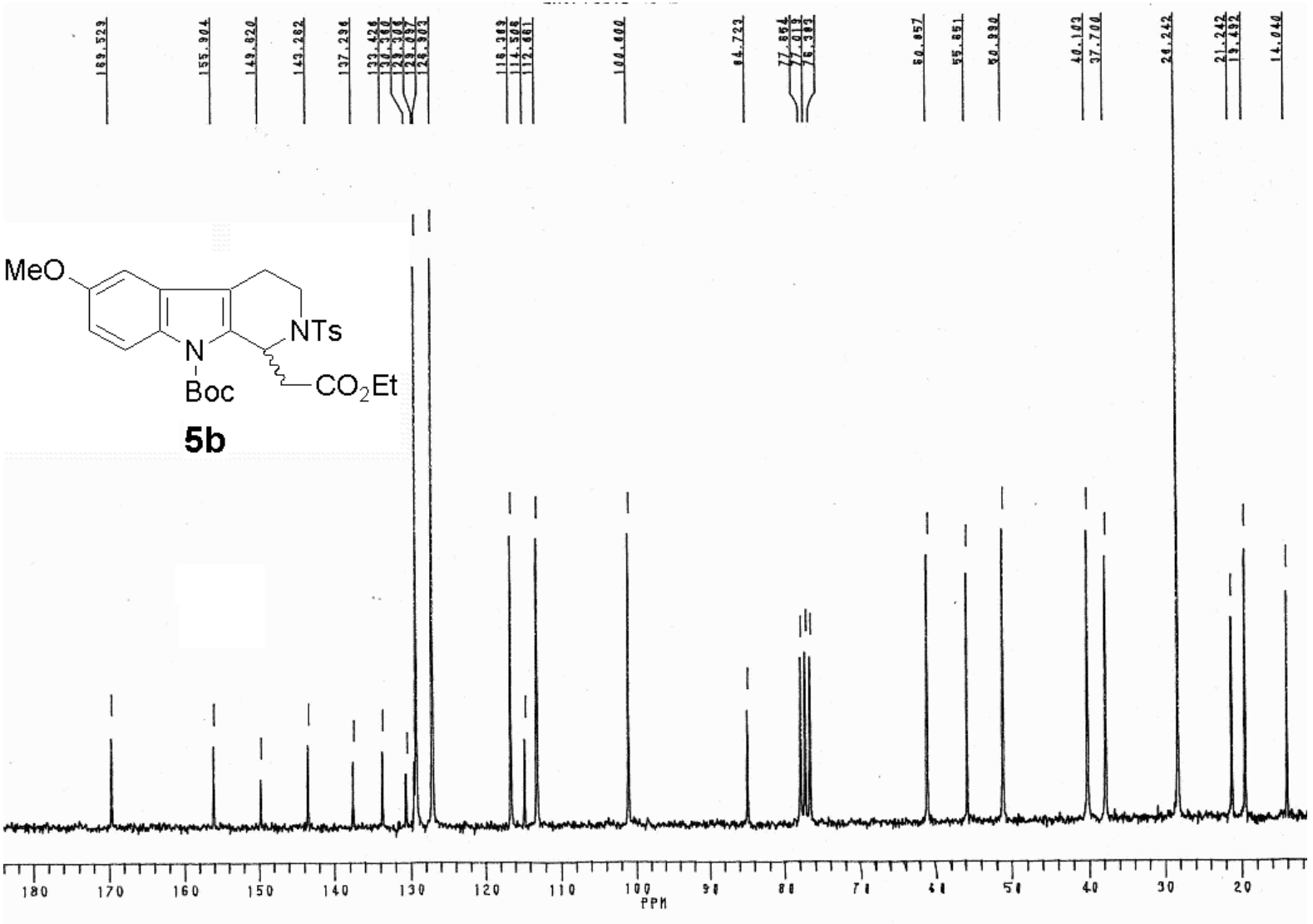
[6] D. L. Comins, A. Dehghani, *Tetrahedron Lett.* **1992**, *33*, 6299.

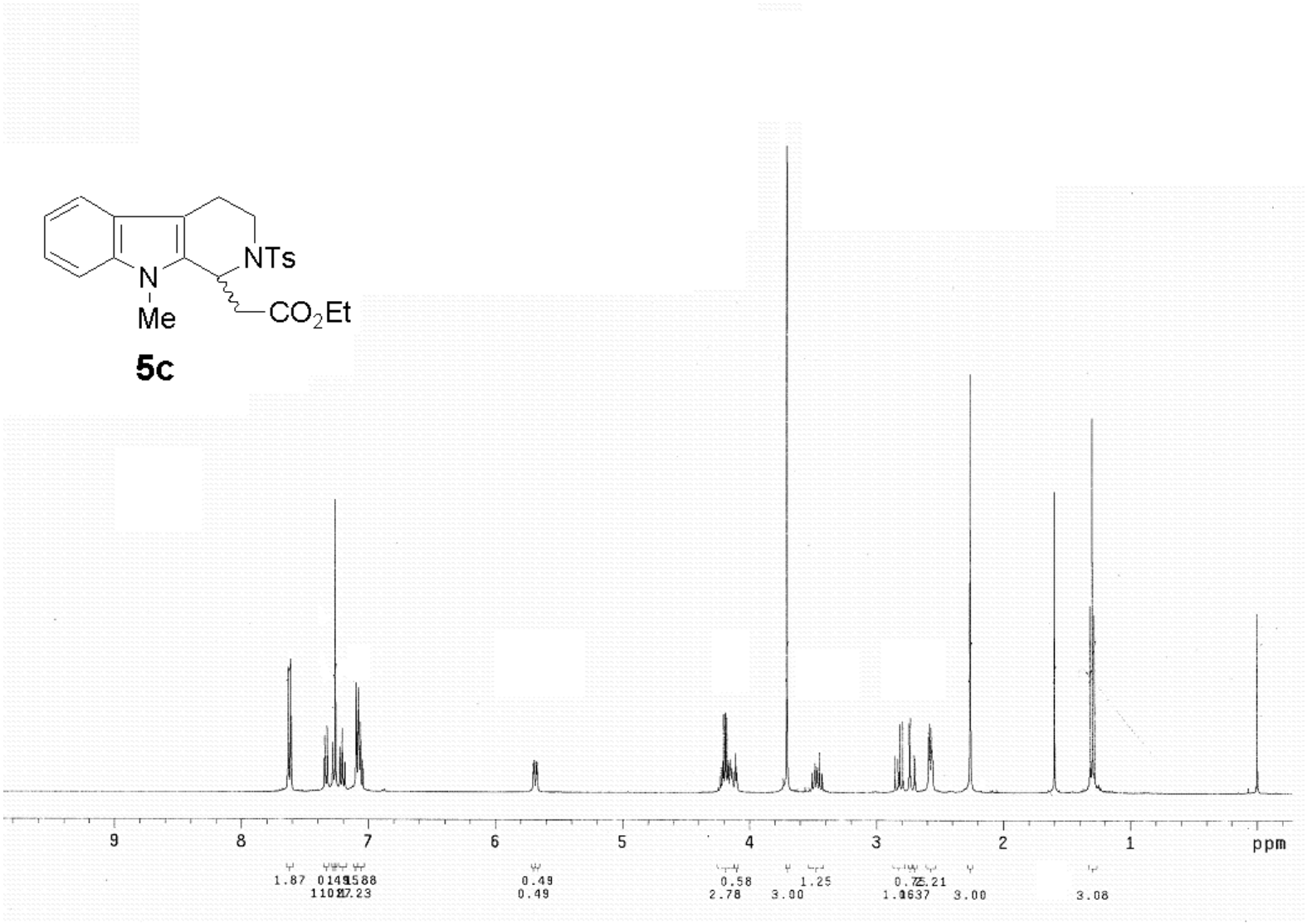
[7] R. L. Danheiser, K. R. Romines, H. Koyama, S. K. Gee, C. R. Johnson, J. R. Medich, *Org. Syn*. **1993**, *71,* 133.

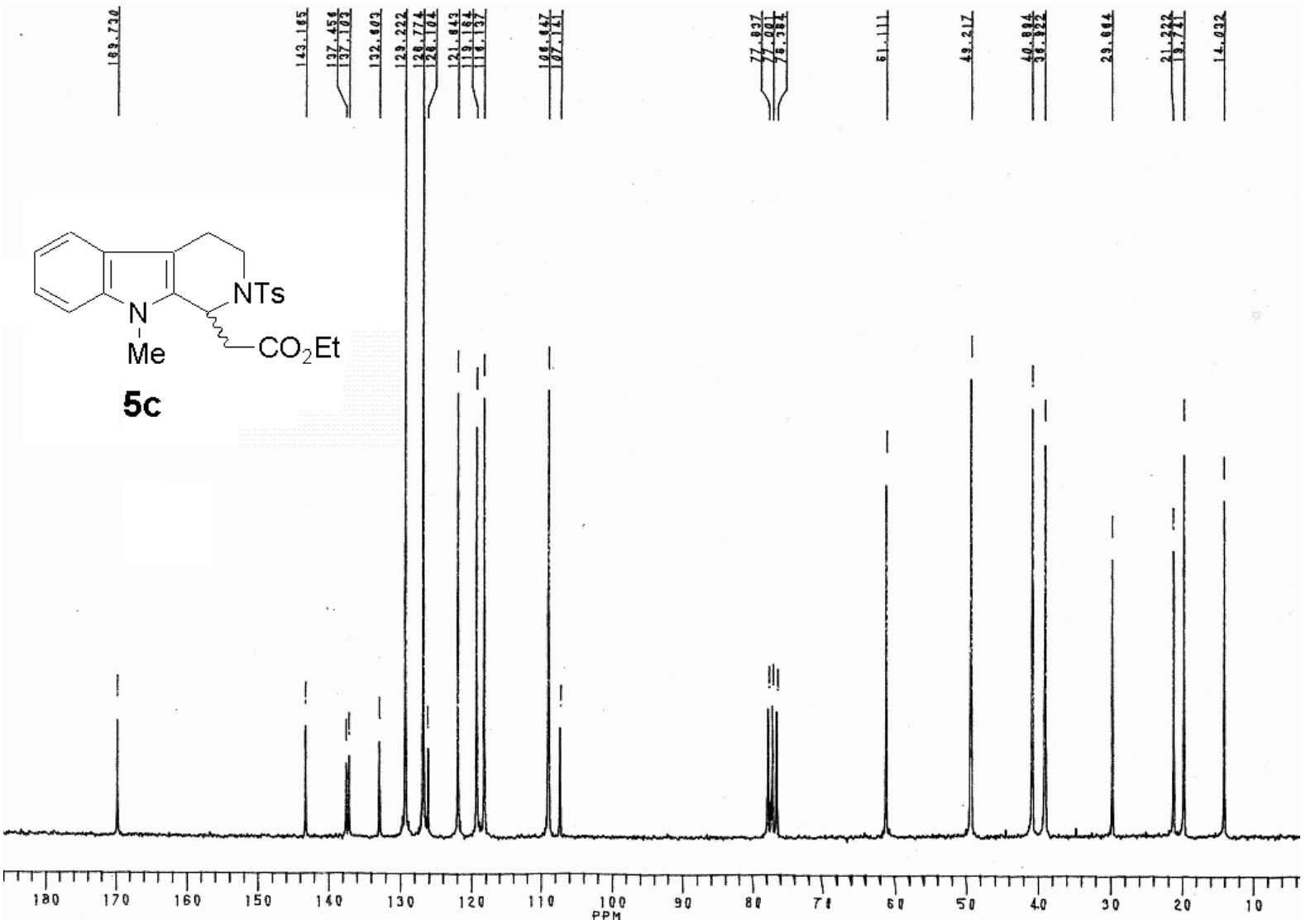

NTs
N
Boc
COOEt
5a
10
9
8
7
6
5
4
3
2
1
ppm
0.93
1.91
1.45
1.95
2.06
1.00
3.21
1.07
1.05
2.16
1.09
2.98
9.26
5.10

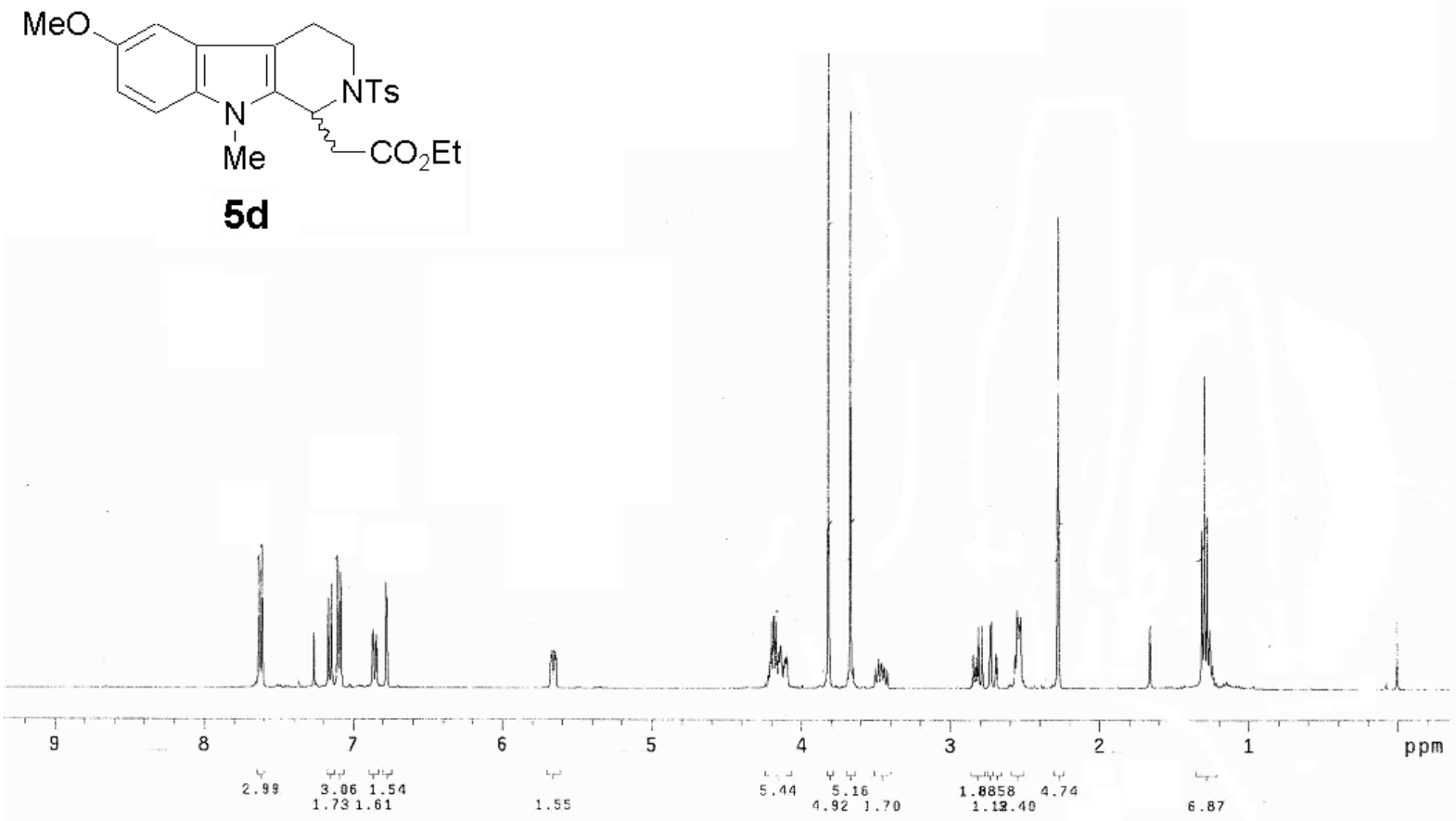

NTs
N
Boc
COOEt
5a

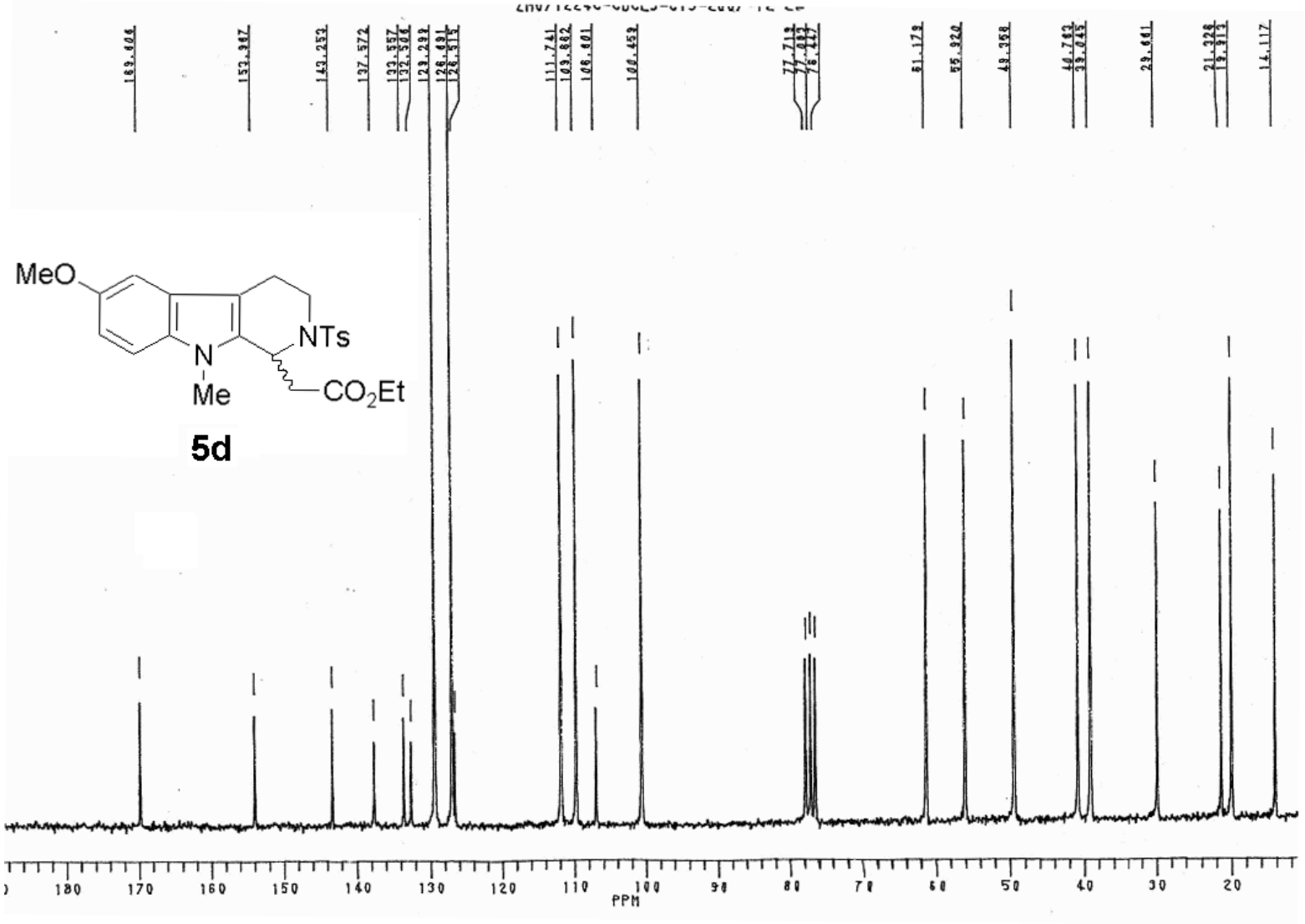

MeO
NTs
N
Boc
CO2Et
5b
9
8
7
6
5
4
3
2
1
ppm
0.94
1.88
1.92
0.96
0.97
0.94
3.14
3.00
1.07
1.03
1.05
1.05
1.09
2.95
9.20
3.00

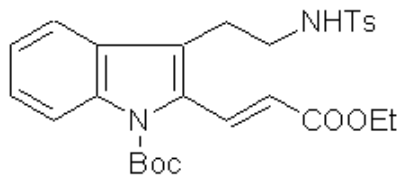

MeO
NTs
N
Boc
CO2Et
5b
PPM


NTs
N
Me
CO2Et
5c
9
8
7
6
5
4
3
2
1
ppm
1.87
0.49
0.49
0.58
2.78
1.25
3.00
3.00
3.08


NTs
N
Me
CO2Et
5c
PPM

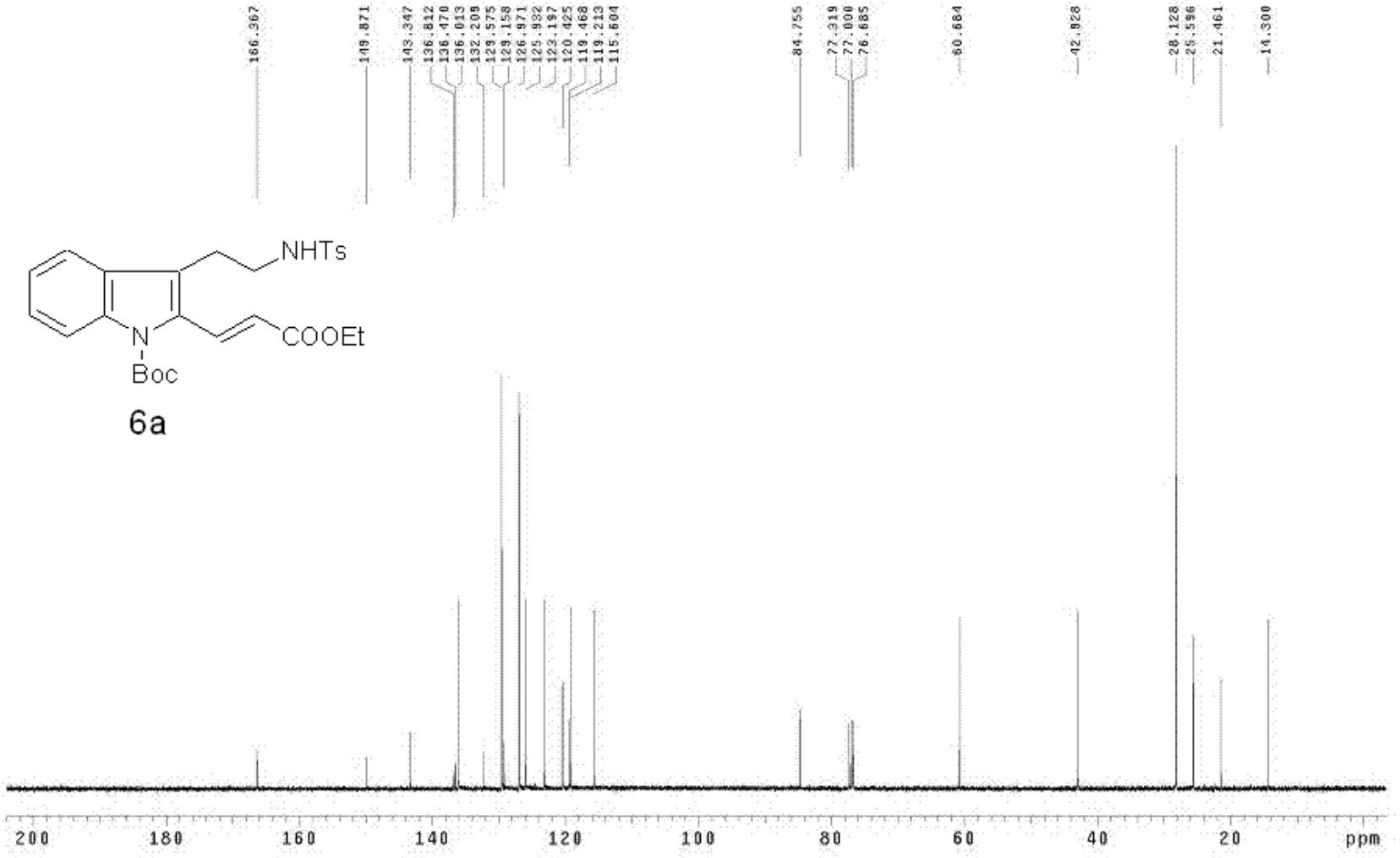

MeO
NTs
N
Me
CO2Et
5d
9
8
7
6
5
4
3
2
1
ppm
2.99
3.06
1.54
1.73
1.61
1.55
5.44
5.16
4.92
1.70
1.8858
4.74
1.12
2.40
6.87

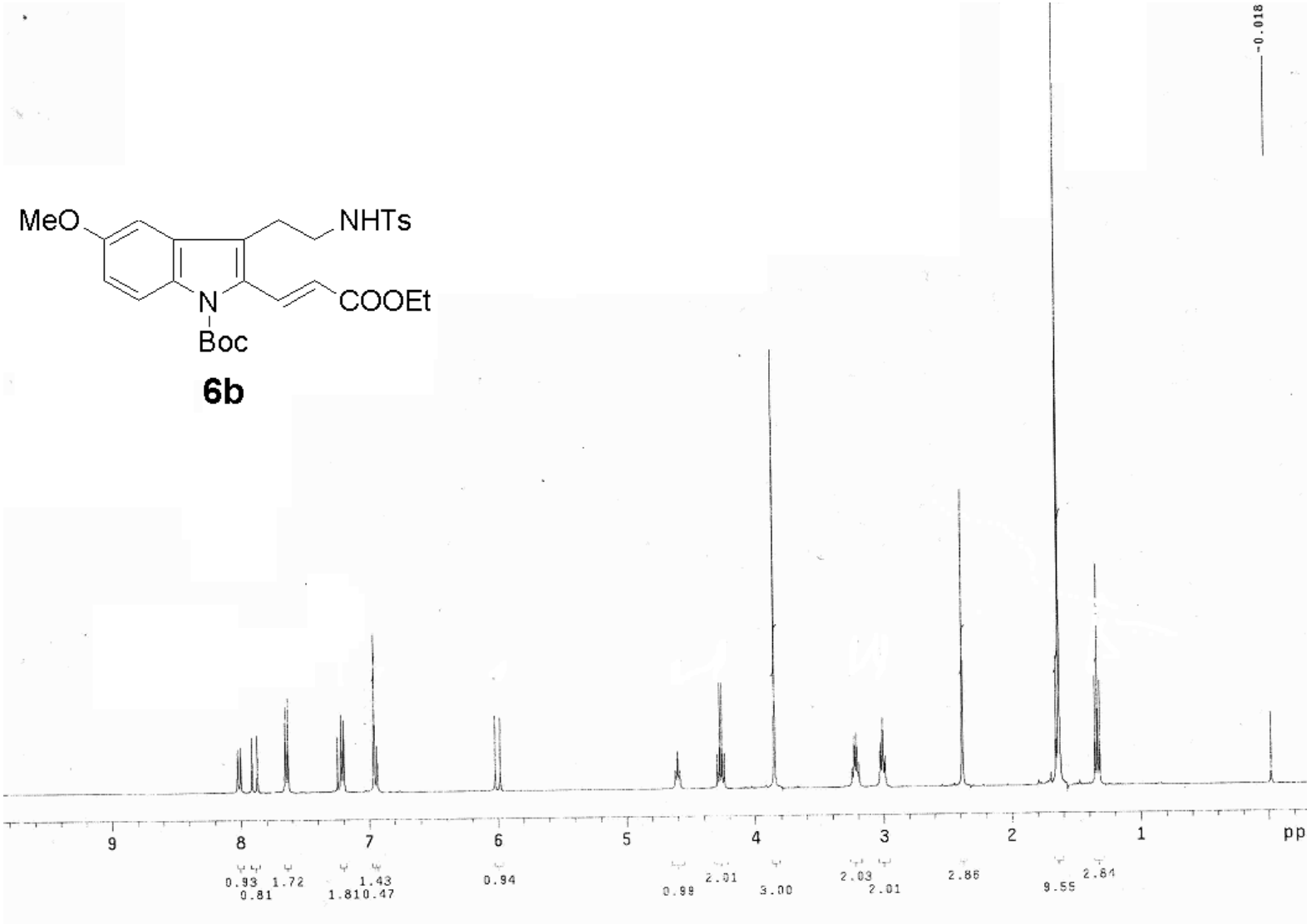

MeO
NTs
N
Me
CO2Et
5d
PPM

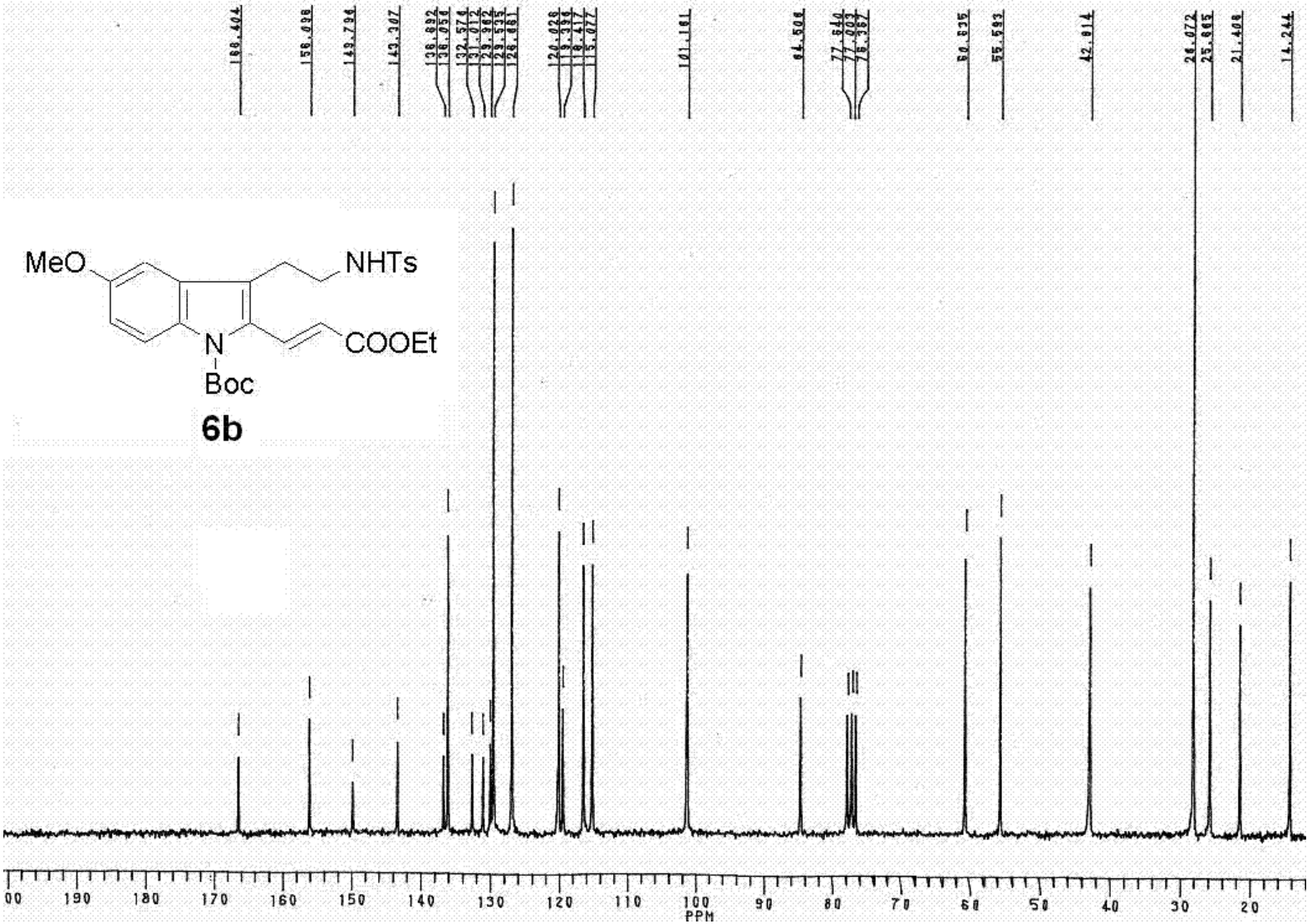

NHTs
COOEt
N
Boc

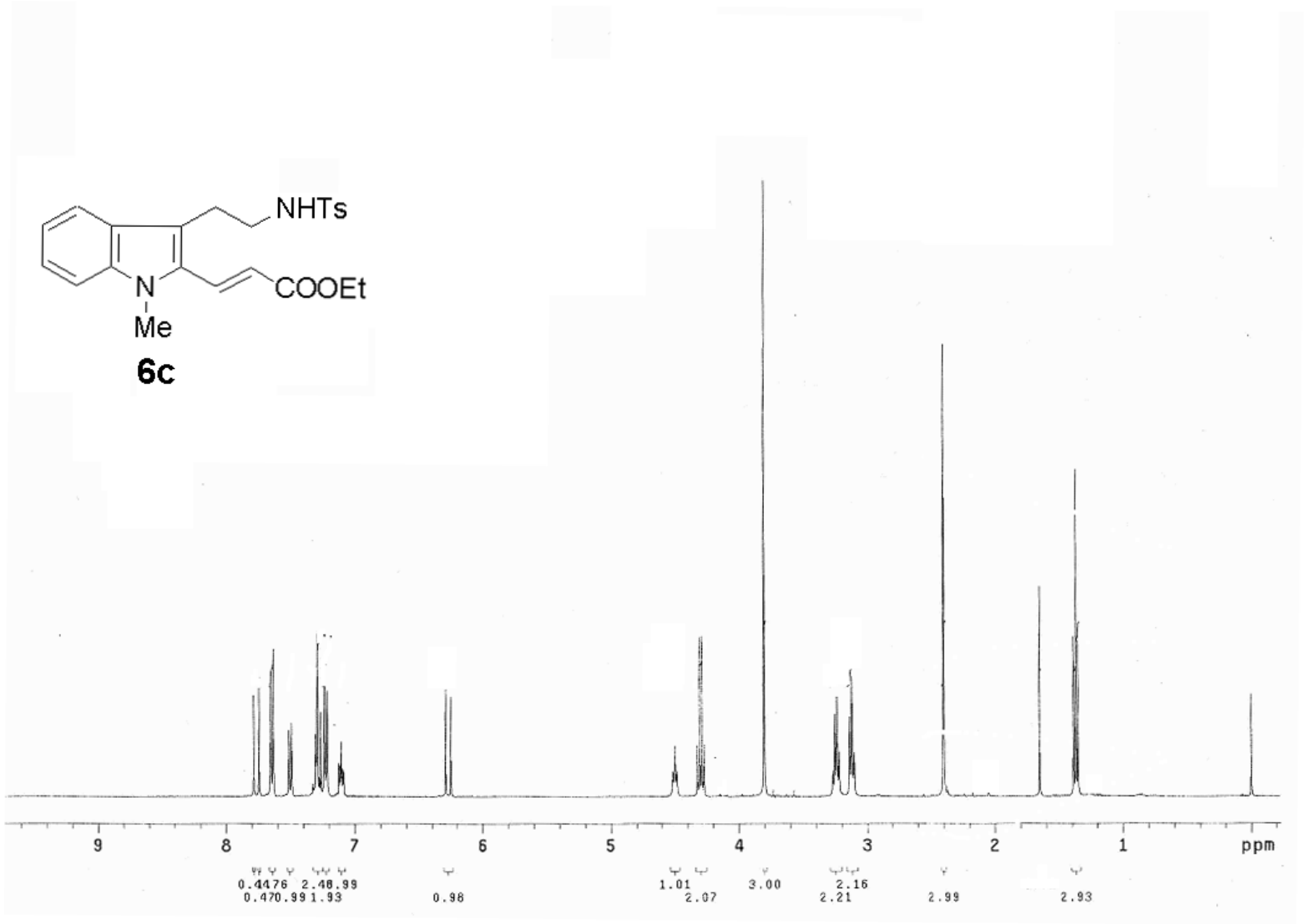
6a

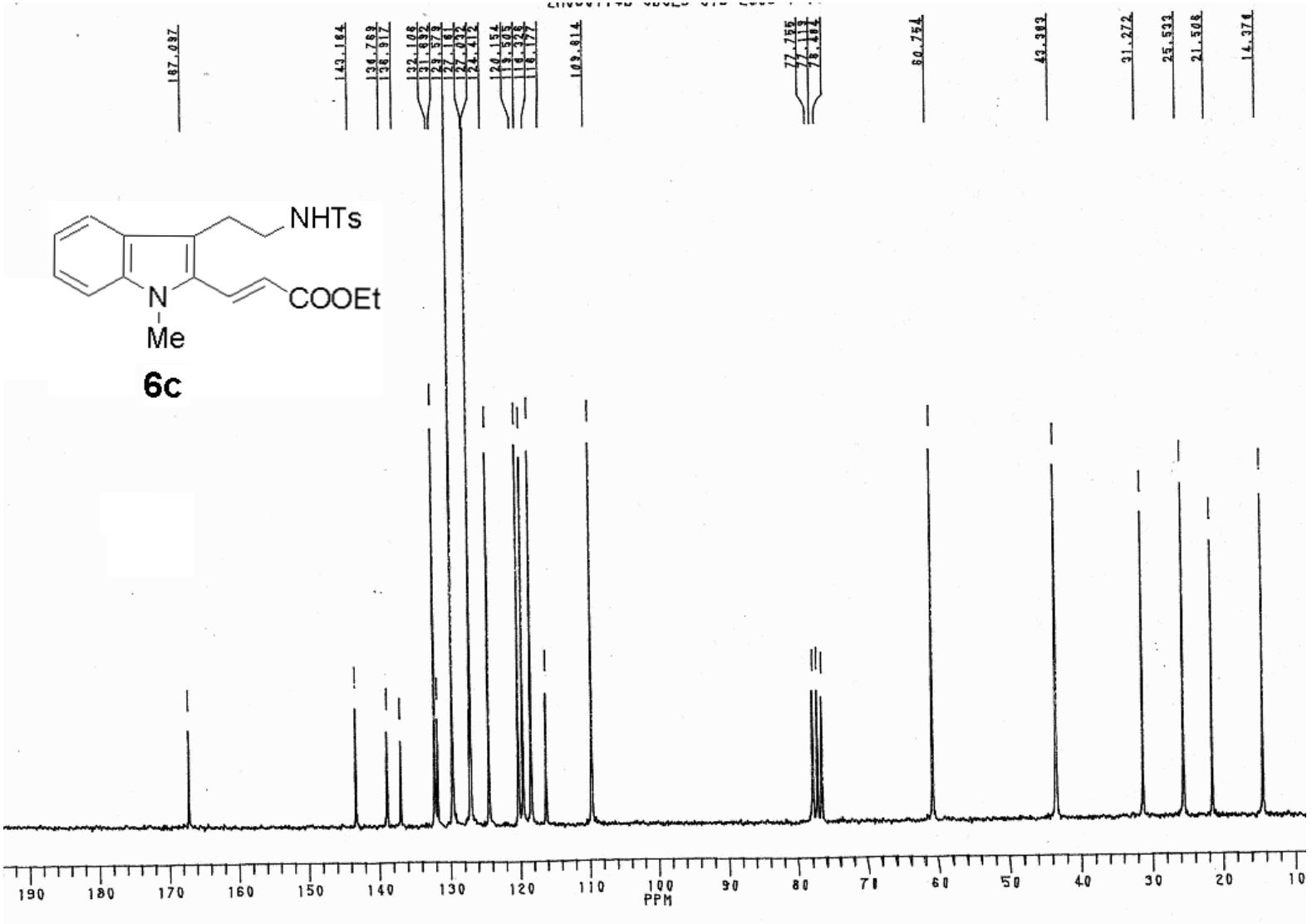
10
9
8
7
6
5
4
3
2
1
ppm
0.45
0.40
0.86
0.51
0.49
1.20
0.46
0.47
0.96
1.00
0.99
1.40
4.86
1.34

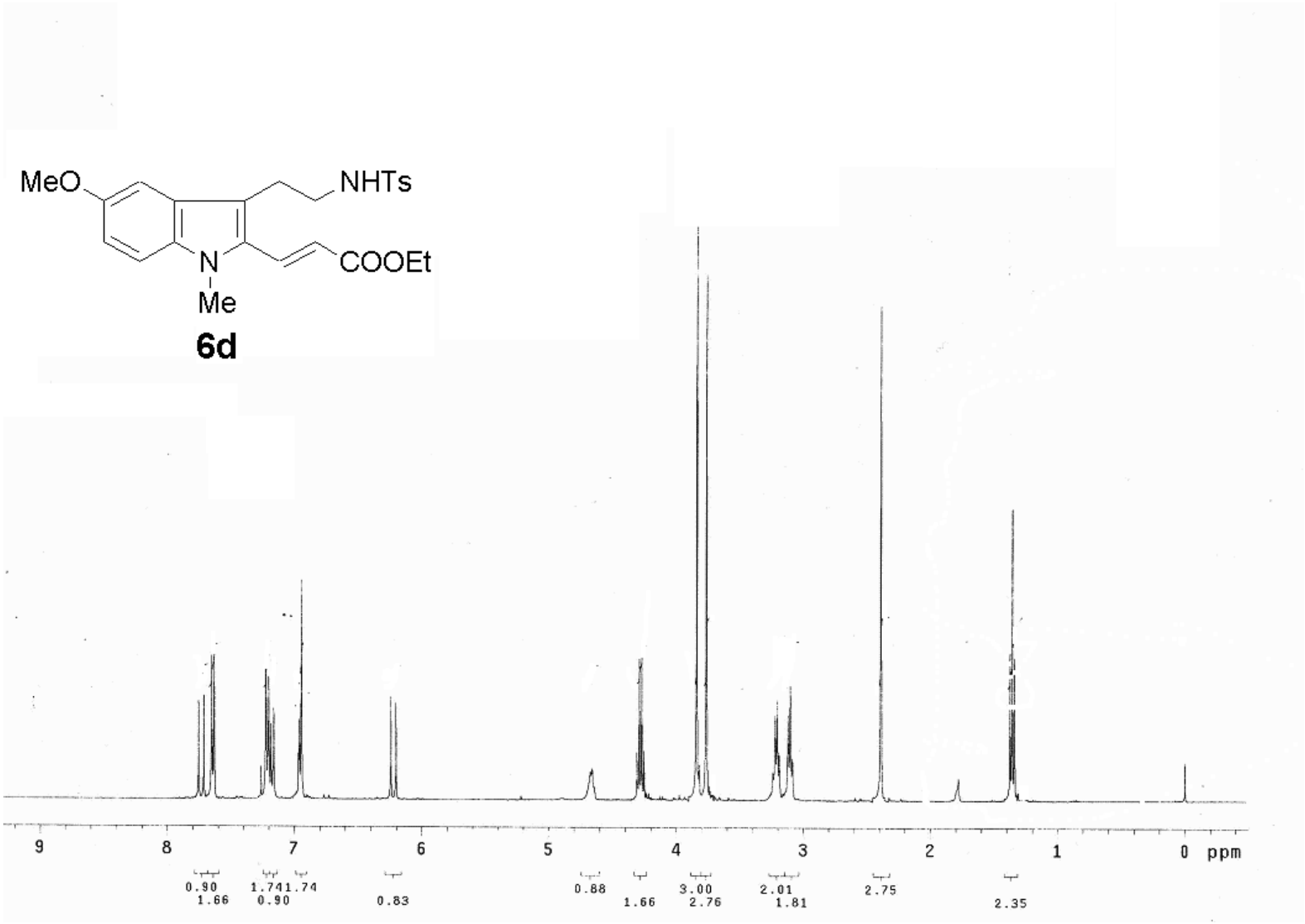

166.367
149.871
143.347
136.812
136.470
136.013
132.209
129.575
129.158
126.971
125.932
123.197
120.425
119.468
119.213
115.604
84.755
77.319
77.000
76.685
60.684
42.928
28.128
25.596
21.461
14.300
NHTs
COOEt
N
Boc
6a
200
180
160
140
120
100
80
60
40
20
ppm

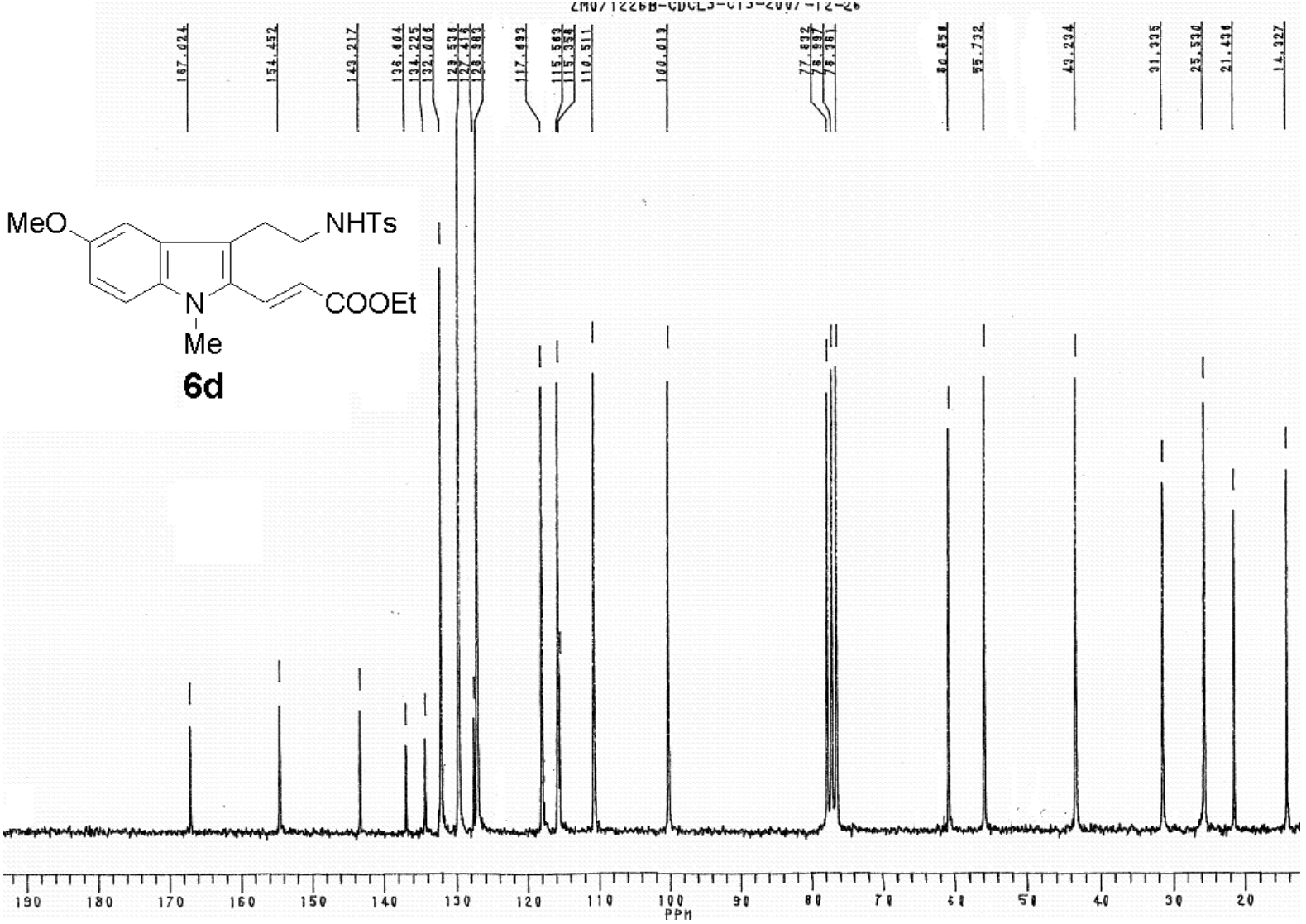

MeO
NHTs
N
Boc
COOEt
6b
-0.018
9
8
7
6
5
4
3
2
1
pp
0.93
0.81
1.72
1.43
1.81
0.47
0.94
0.99
2.01
3.00
2.03
2.01
2.86
9.55
2.84

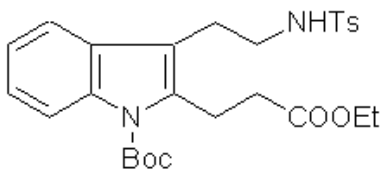

MeO
NHTs
N
Boc
COOEt
6b
PPM


NHTs
N
Me
COOEt
6c
9
8
7
6
5
4
3
2
1
ppm
0.4476 2.48 .99
0.470.99 1.93
0.98
1.01
2.07
3.00
2.16
2.21
2.99
2.93


NHTs
COOEt
N
Me
6c
187.037
143.184
136.789
136.917
132.108
131.892
131.374
127.155
127.032
124.412
120.154
119.303
118.343
110.177
109.814
77.255
77.113
76.482
60.754
43.383
31.272
25.533
21.508
14.374
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM

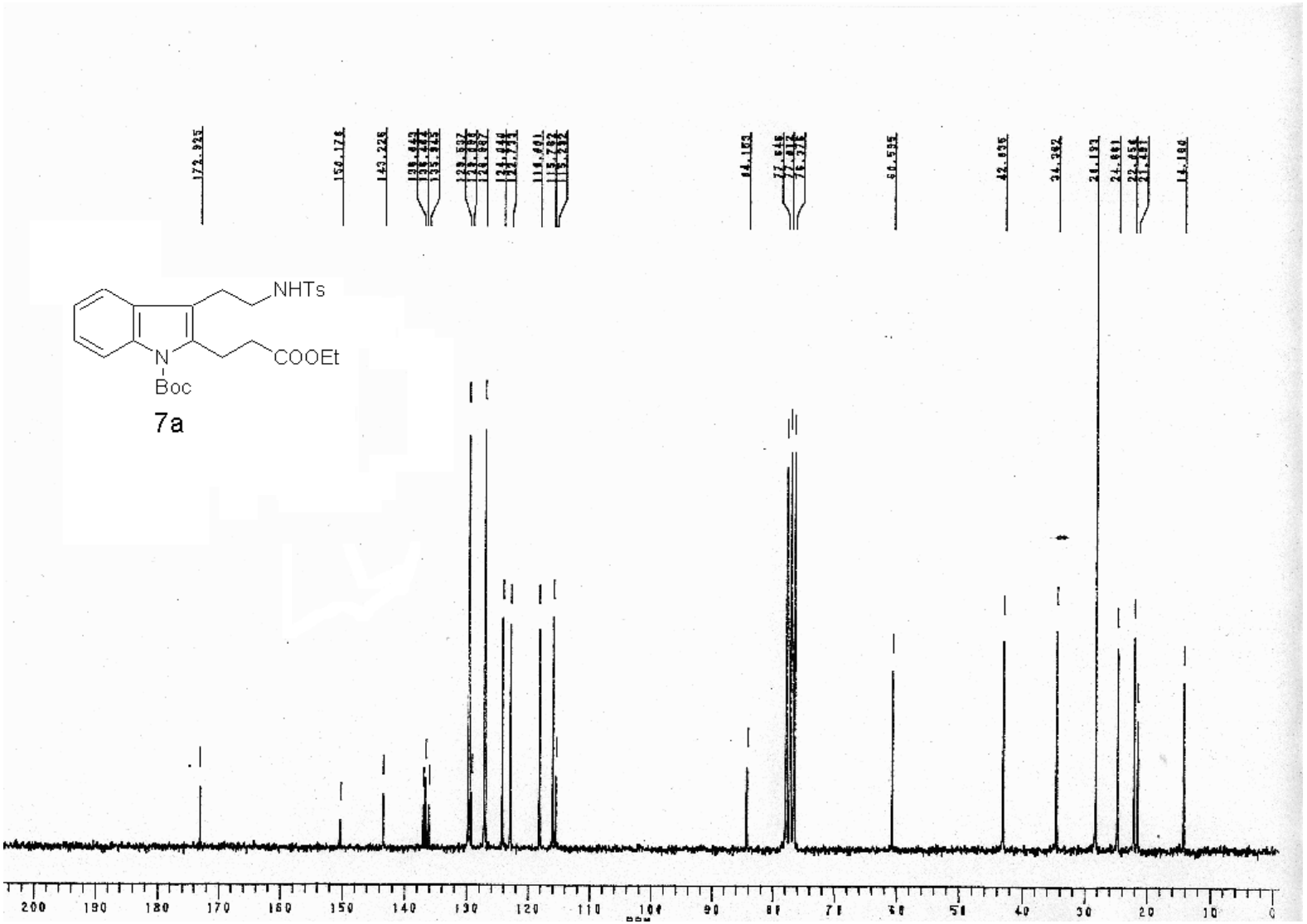

MeO
NHTs
N
Me
COOEt
6d
9
8
7
6
5
4
3
2
1
0
ppm
0.90
1.66
1.74
1.74
0.90
0.83
0.88
1.66
3.00
2.76
2.01
1.81
2.75
2.35

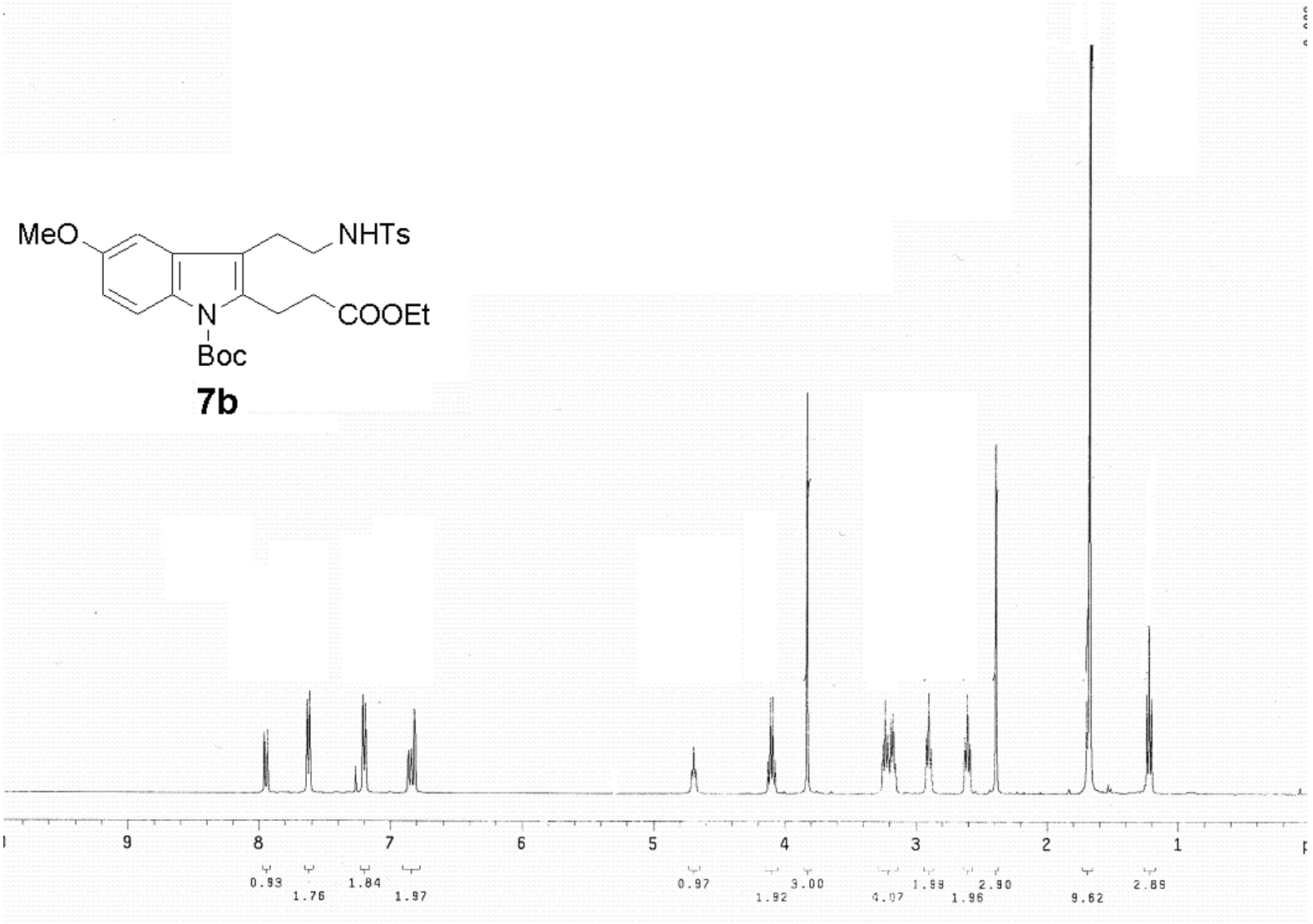

MeO
NHTs
N
COOEt
Me
6d
187.024
154.452
149.217
136.464
134.225
132.004
123.534
127.418
126.383
117.492
115.563
115.358
110.511
100.013
77.832
77.507
77.181
50.654
55.732
43.234
31.235
25.530
21.434
14.327
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
PPM

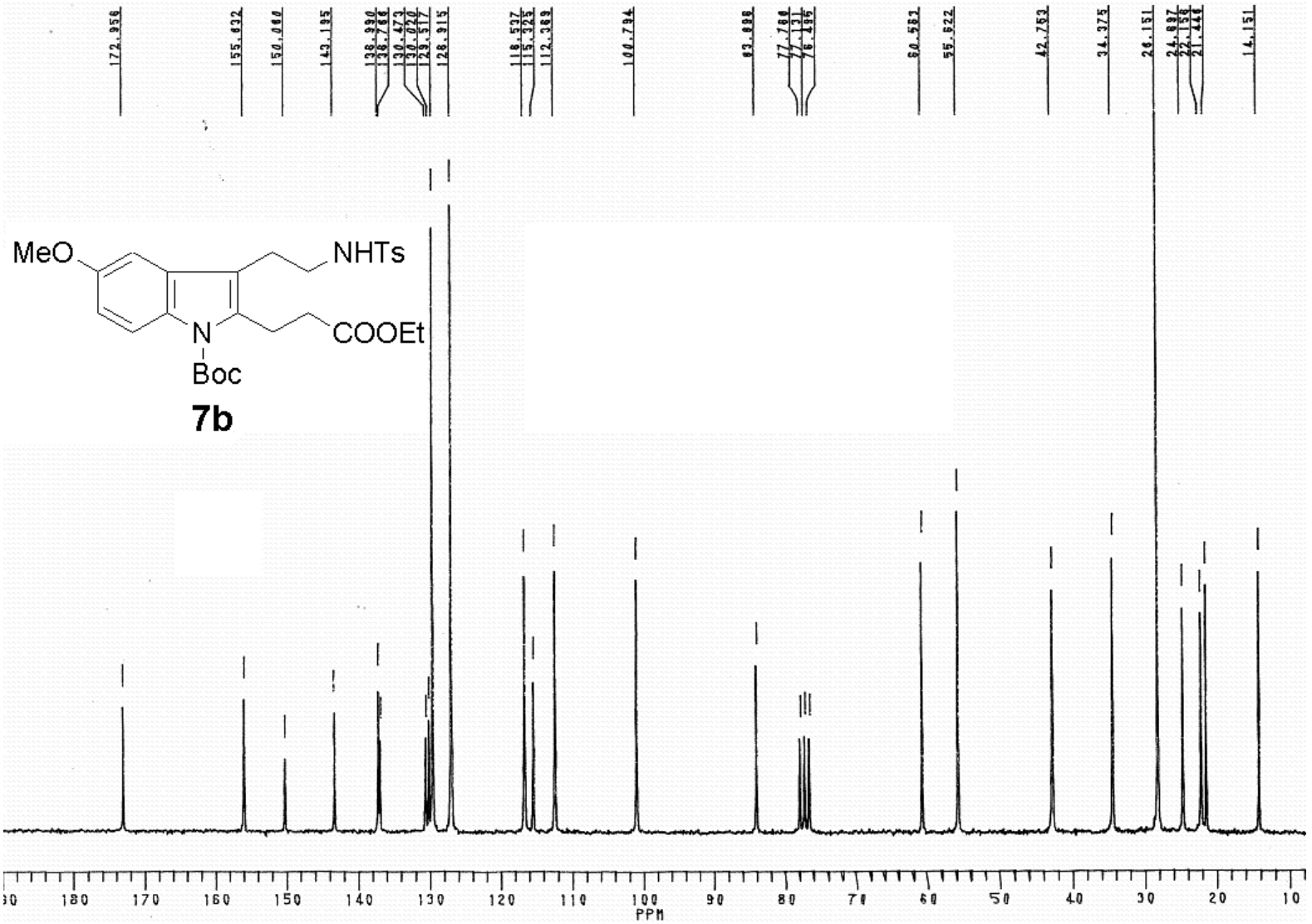

NHTs
N
Boc
COOEt

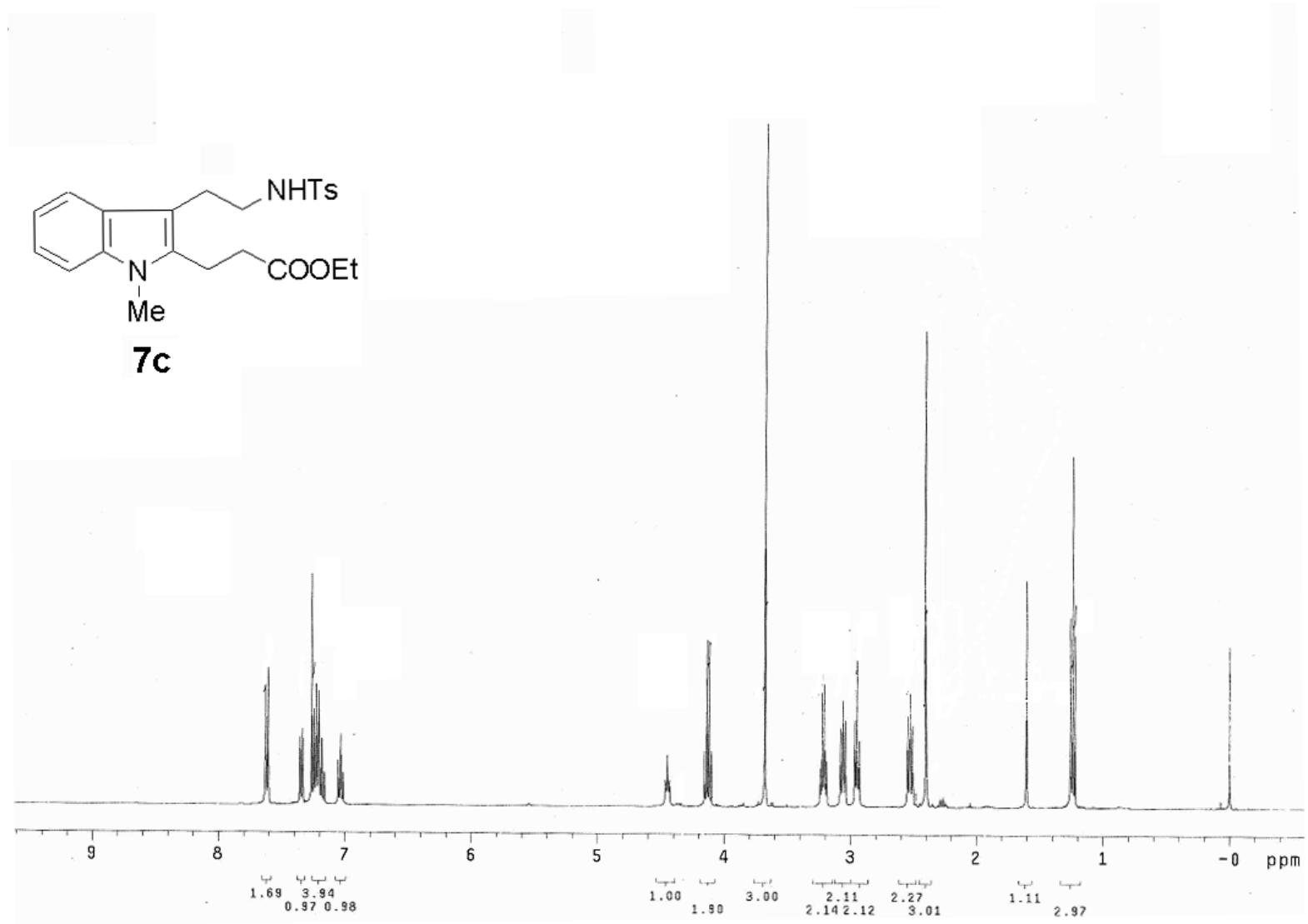
7a

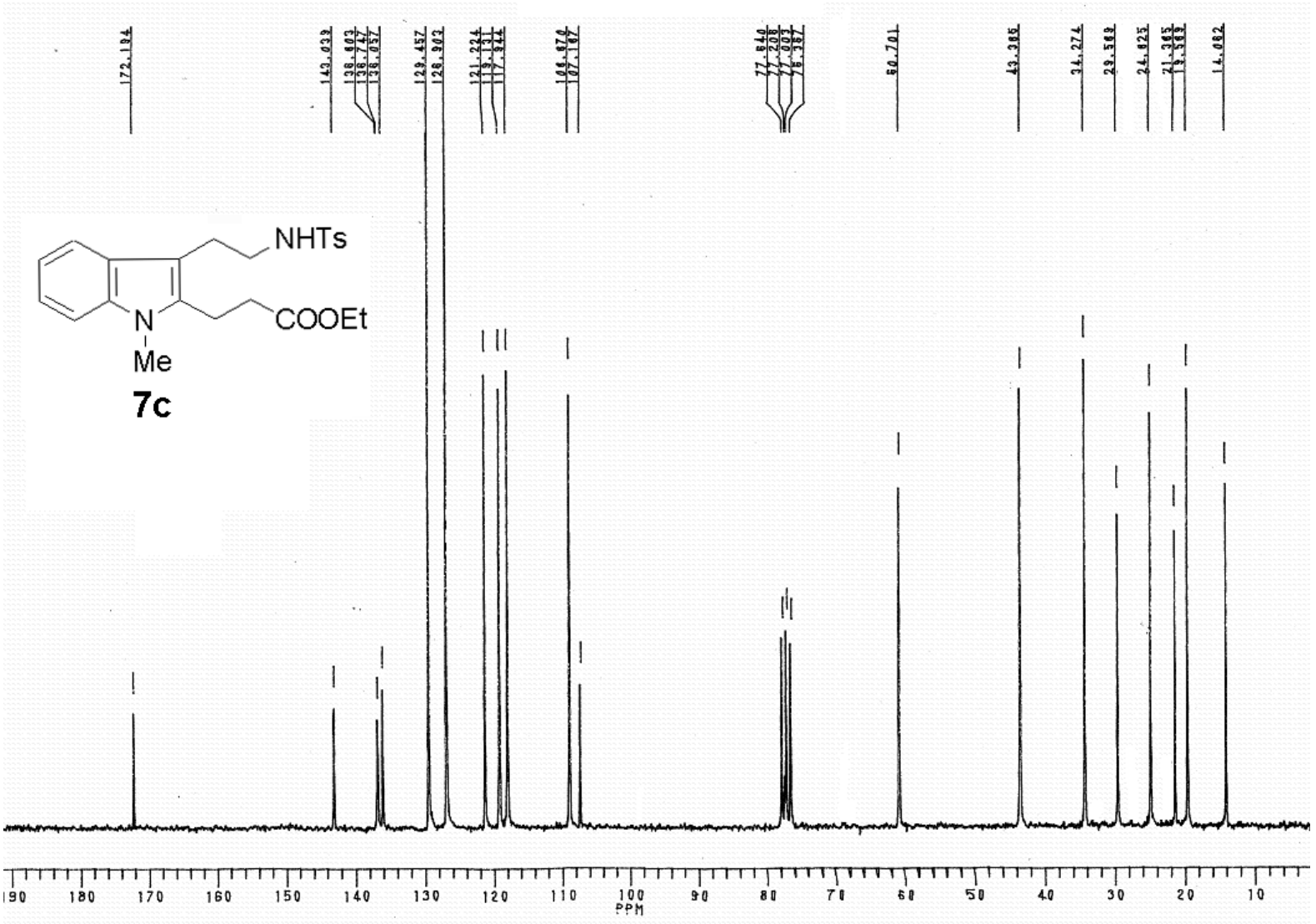
10
9
8
7
6
5
4
3
2
1
ppm
0.94
1.77
1.59
1.00
2.01
4.25
2.07
2.08
2.97
9.18
2.92

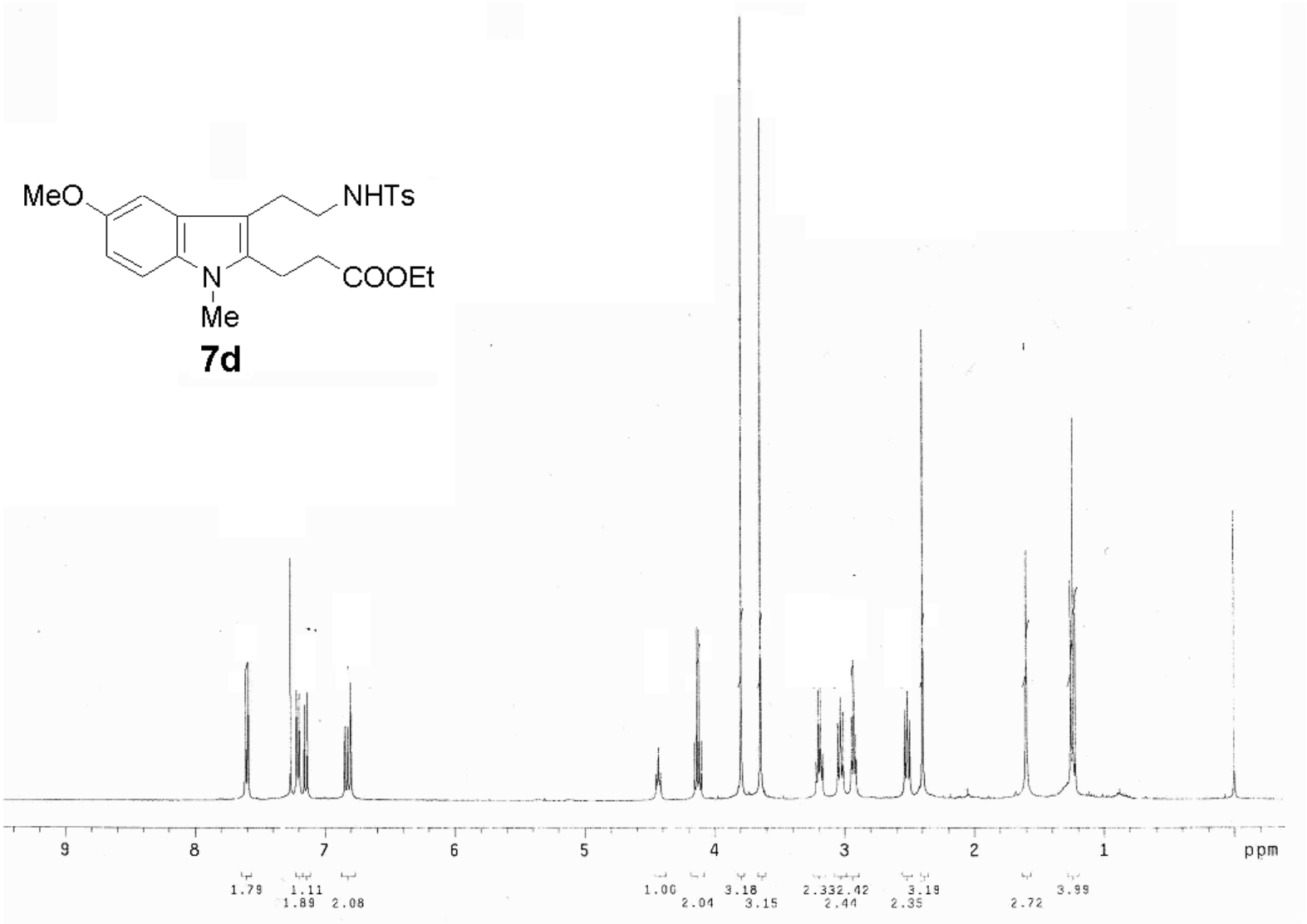

NHTs
COOEt
N
Boc
7a

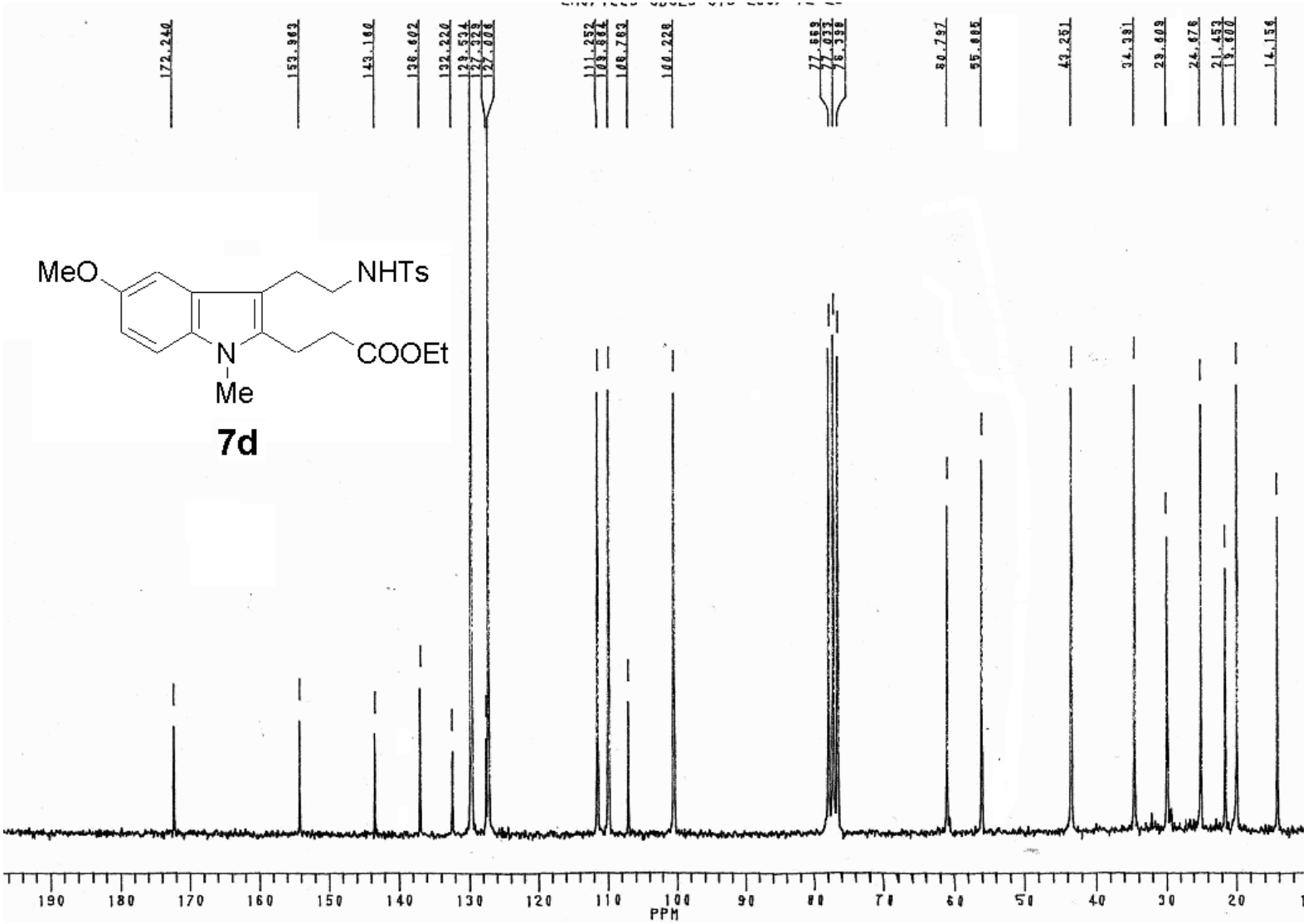

MeO
NHTs
N
COOEt
Boc
7b
9
8
7
6
5
4
3
2
1
0.93
1.76
1.84
1.97
0.97
1.92
3.00
4.07
1.98
1.96
2.90
9.62
2.89

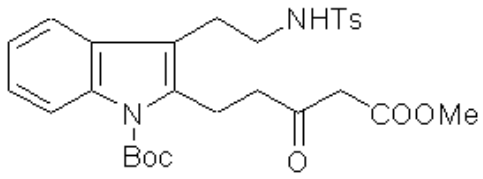

MeO
NHTs
N
COOEt
Boc
7b
PPM


NHTs
COOEt
N
Me
7c
9
8
7
6
5
4
3
2
1
-0
ppm
1.69
3.94
0.97
0.98
1.00
1.90
3.00
2.11
2.14
2.12
2.27
3.01
1.11
2.97


172.184
143.033
138.603
136.747
136.057
129.457
128.902
121.224
119.131
117.342
106.674
107.167
77.640
77.208
76.987
76.387
60.701
43.386
34.274
29.588
24.825
21.365
13.569
14.082
NHTs
COOEt
N
Me
7c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM

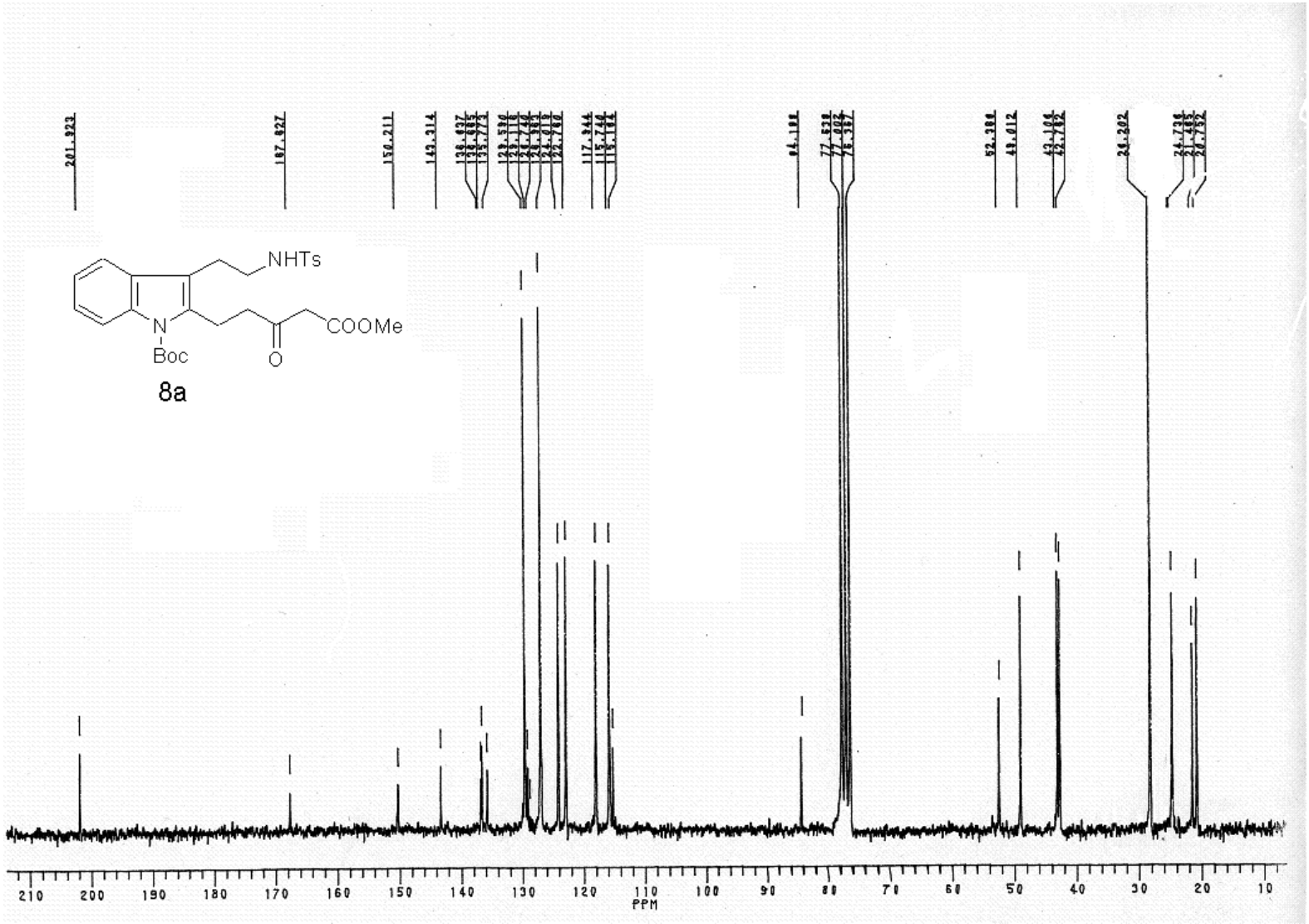

MeO
NHTs
N
Me
COOEt
7d
9
8
7
6
5
4
3
2
1
ppm
1.79
1.11
1.89
2.08
1.00
2.04
3.18
3.15
2.33
2.42
2.44
3.19
2.35
2.72
3.99

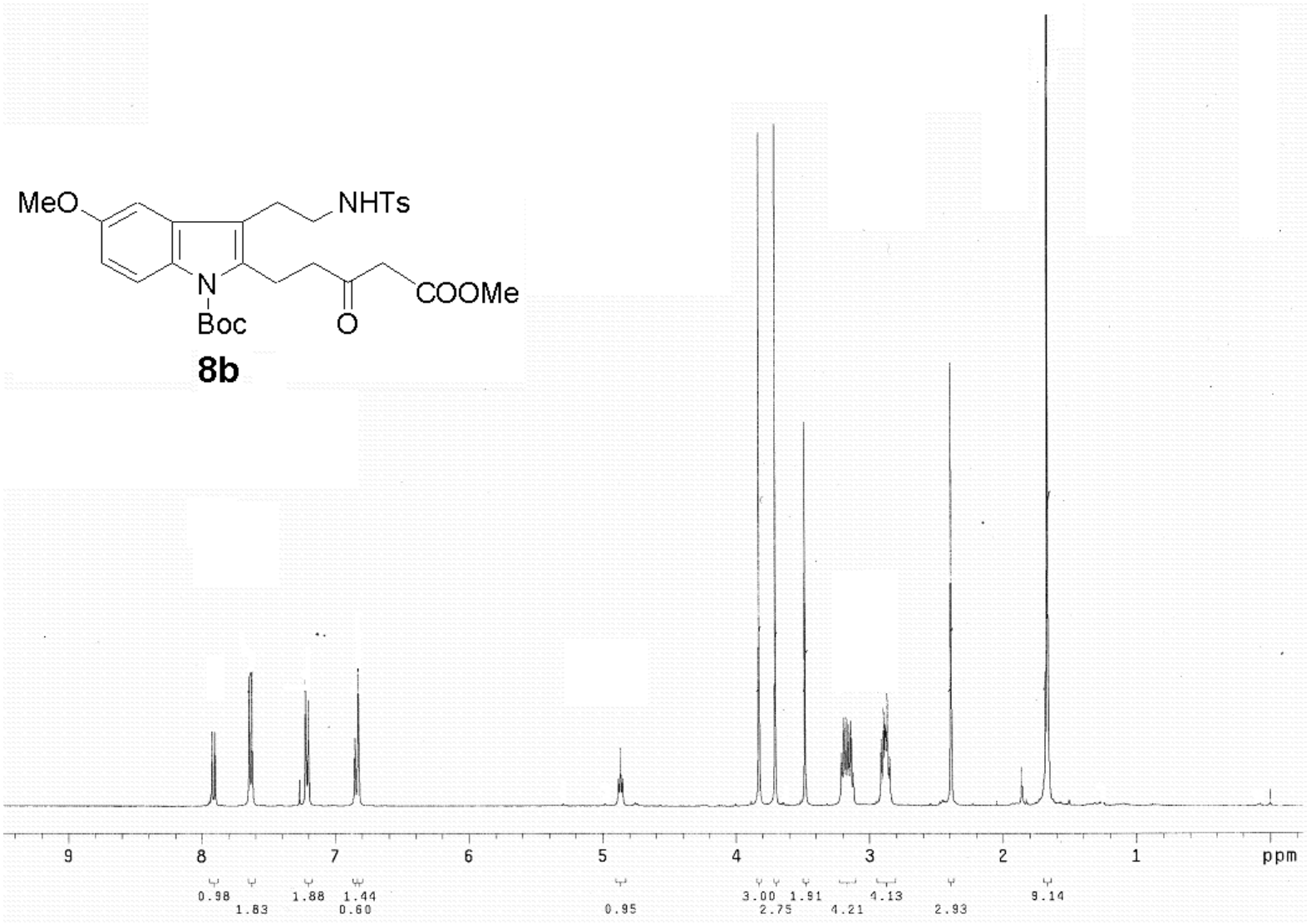

MeO
NHTs
N
Me
COOEt
7d
172.240
159.963
143.140
136.602
132.224
129.534
127.329
127.004
111.252
103.882
108.763
100.228
77.663
77.033
76.398
80.797
55.885
43.251
34.381
29.609
26.678
21.453
19.600
14.154
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
PPM

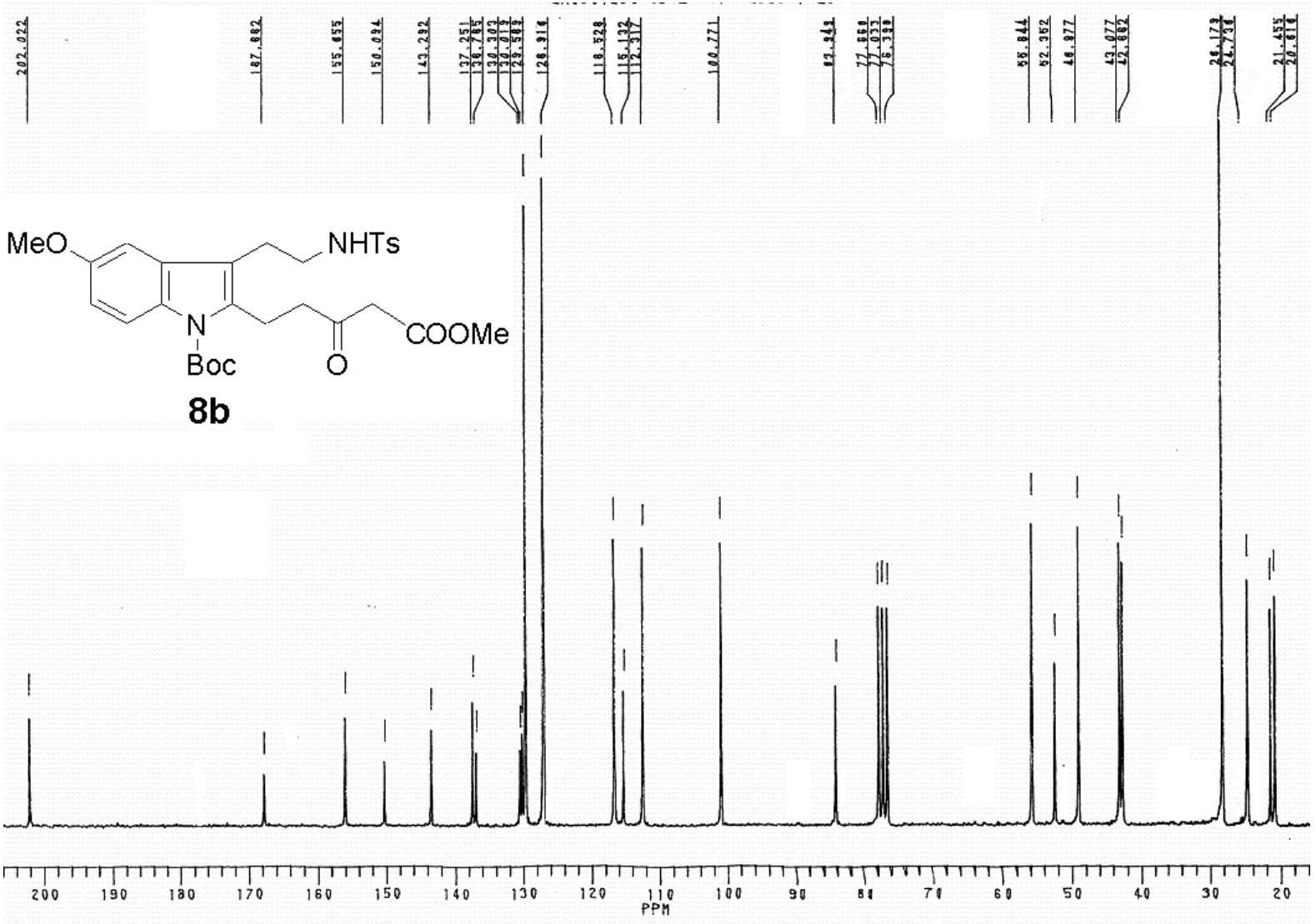

NHTs
N
Boc
O
COOMe

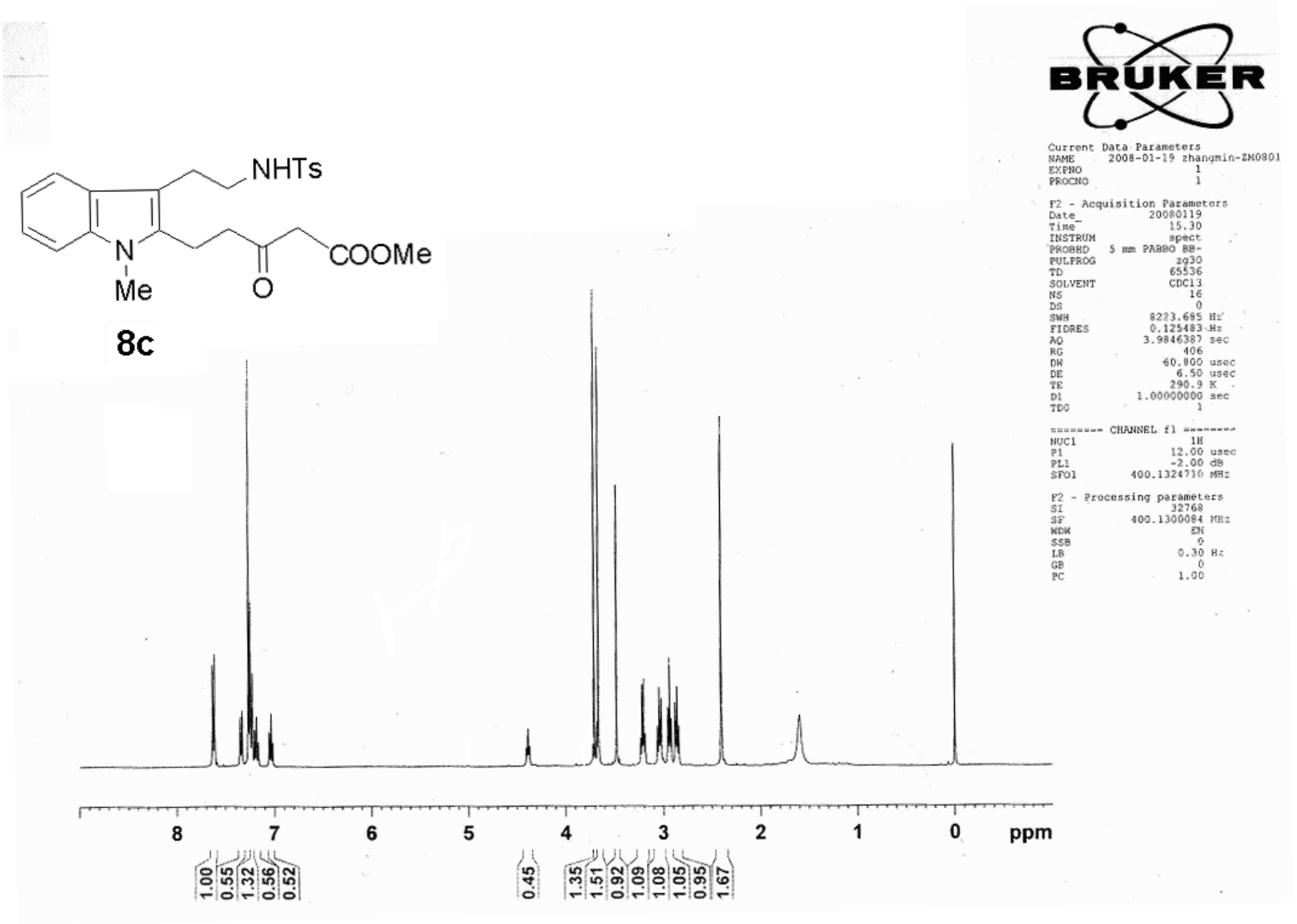
8a

10
9
8
7
6
5
4
3
2
1
ppm
1.05
2.20
1.32
5.76
1.00
2.86
2.08
4.52
4.38
3.23
10.58


NHTs
N
Boc
COOMe
O
8a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM

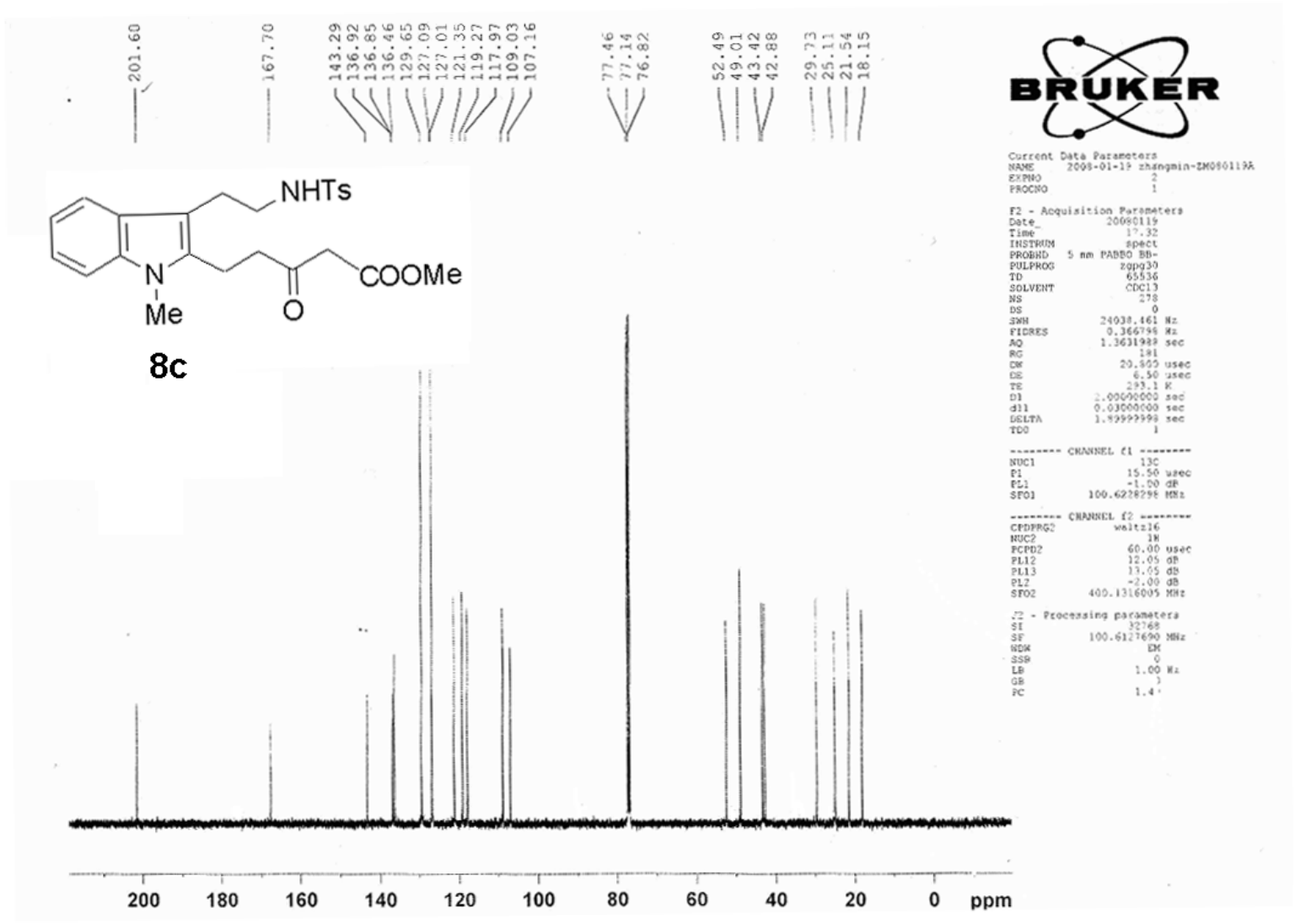

MeO
NHTs
N
Boc
O
COOMe
8b
9
8
7
6
5
4
3
2
1
ppm
0.98
1.83
1.88
1.44
0.60
0.95
3.00
2.75
1.91
4.21
4.13
2.93
9.14

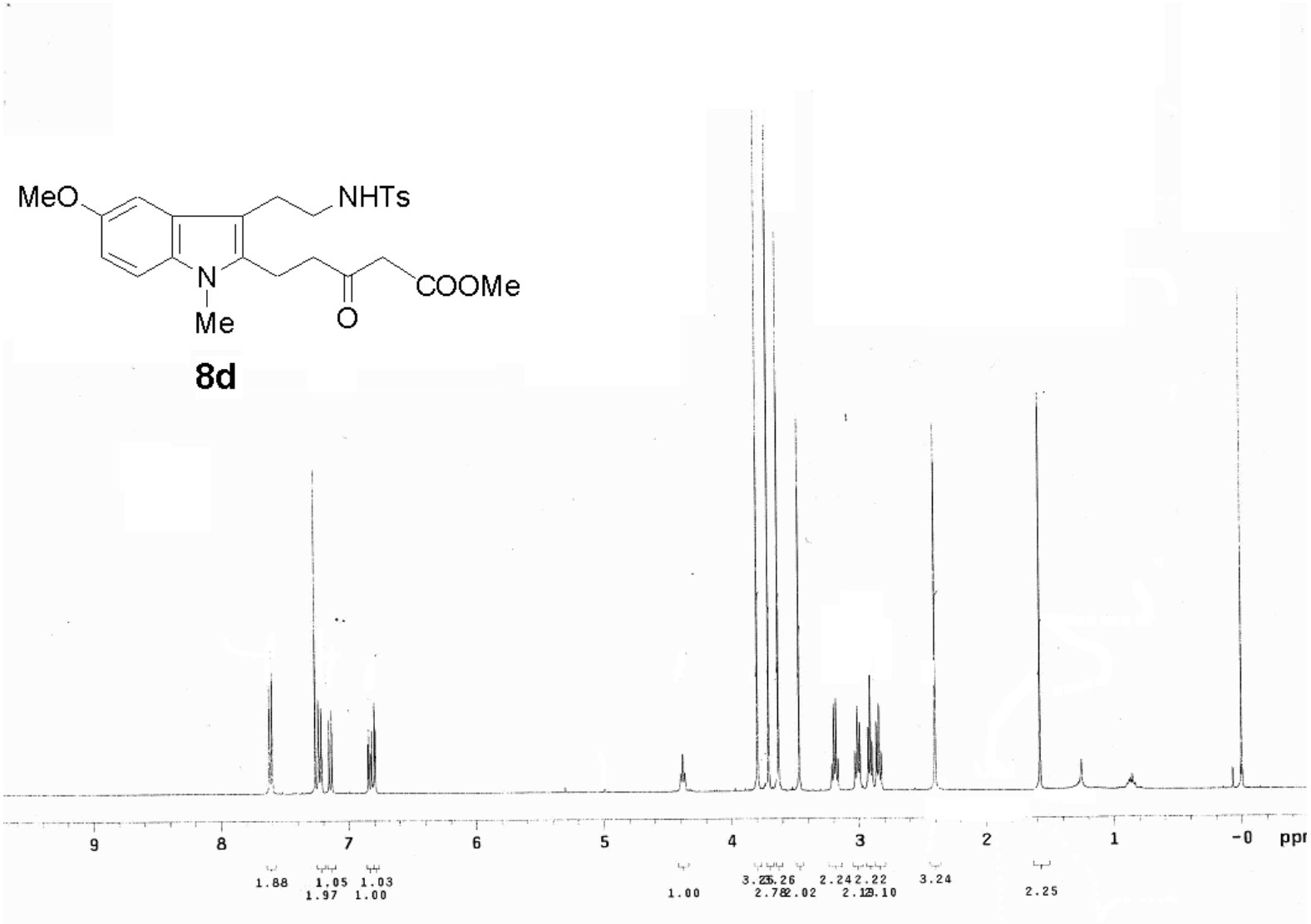

MeO
NHTs
N
Boc
O
COOMe
8b
PPM

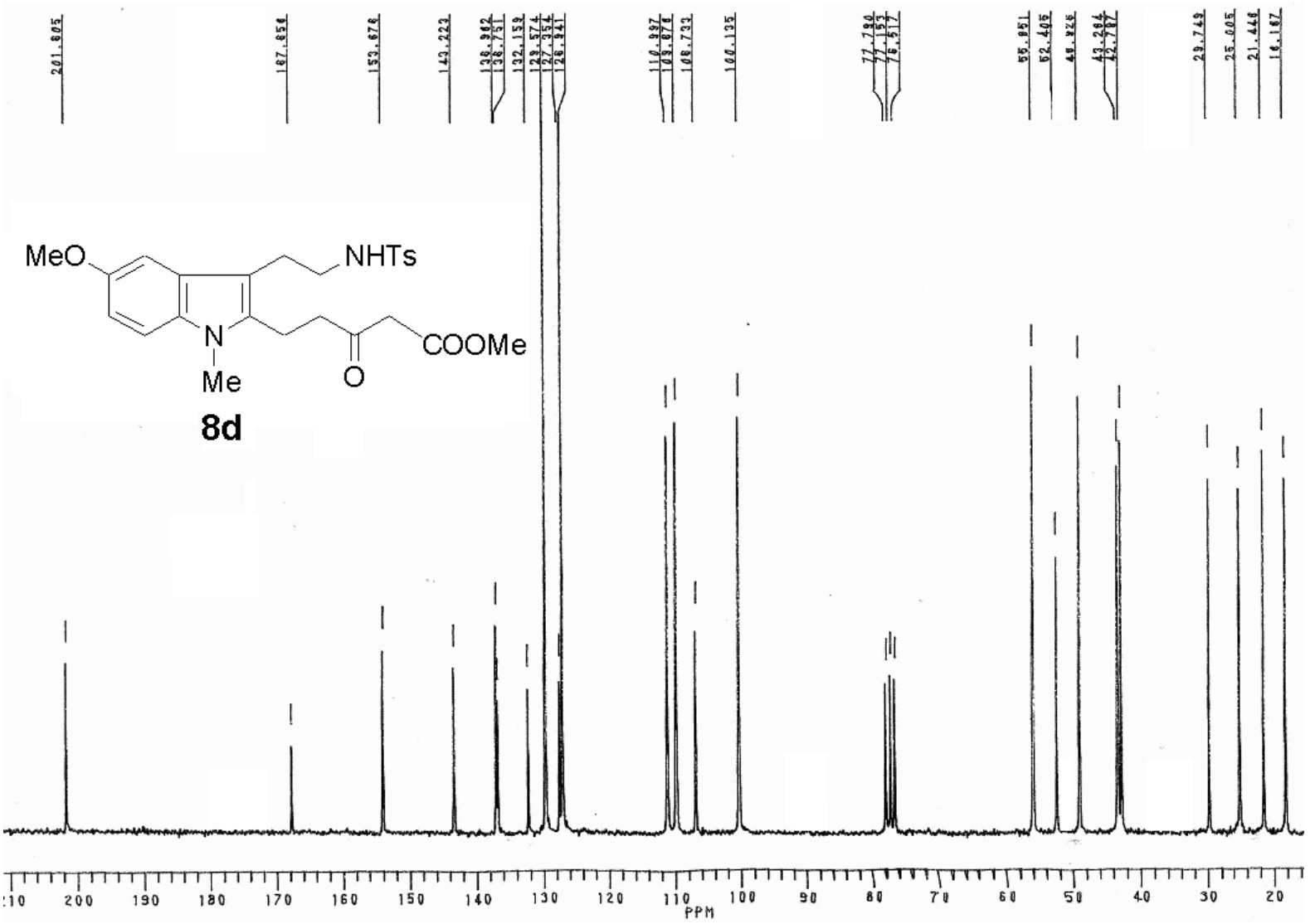


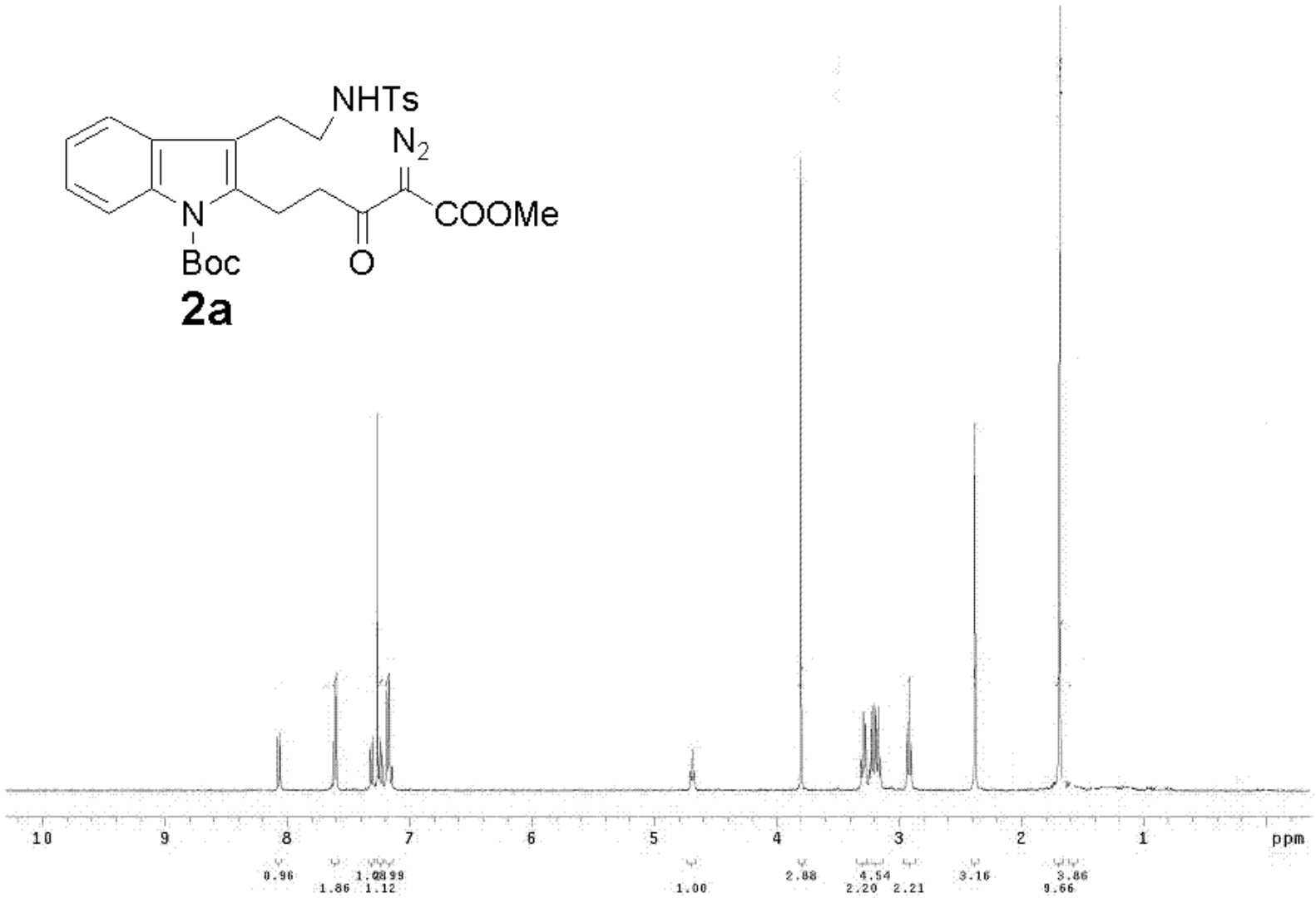
BRUKER

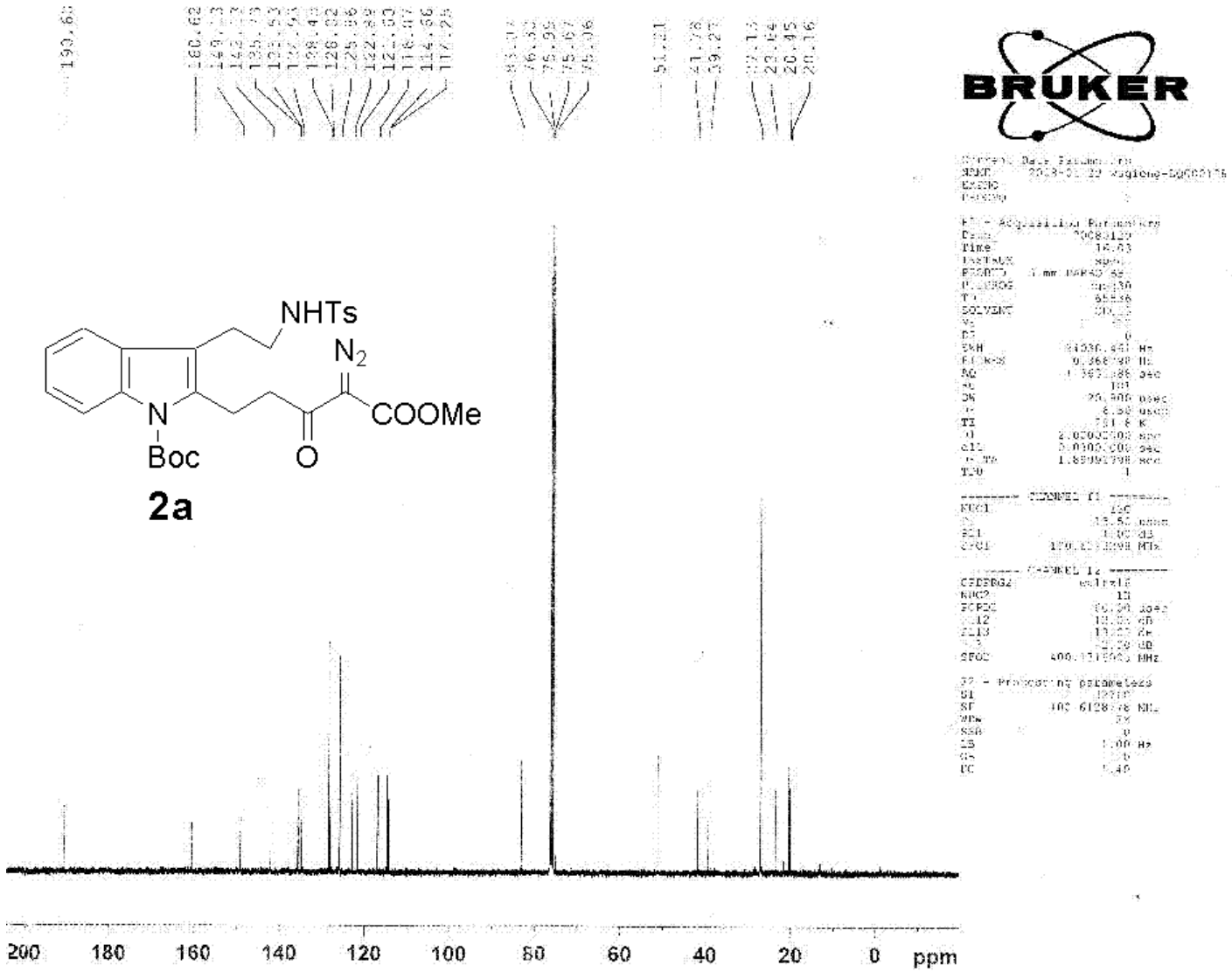
```
Current Data Parameters
NAME      2008-01-19 zhangmin-ZM0801
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_            20080119
Time                15.30
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9846387 sec
RG                   406
DW                60.800 usec
DE                 6.50 usec
TE                290.9 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -2.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF           400.1300084 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

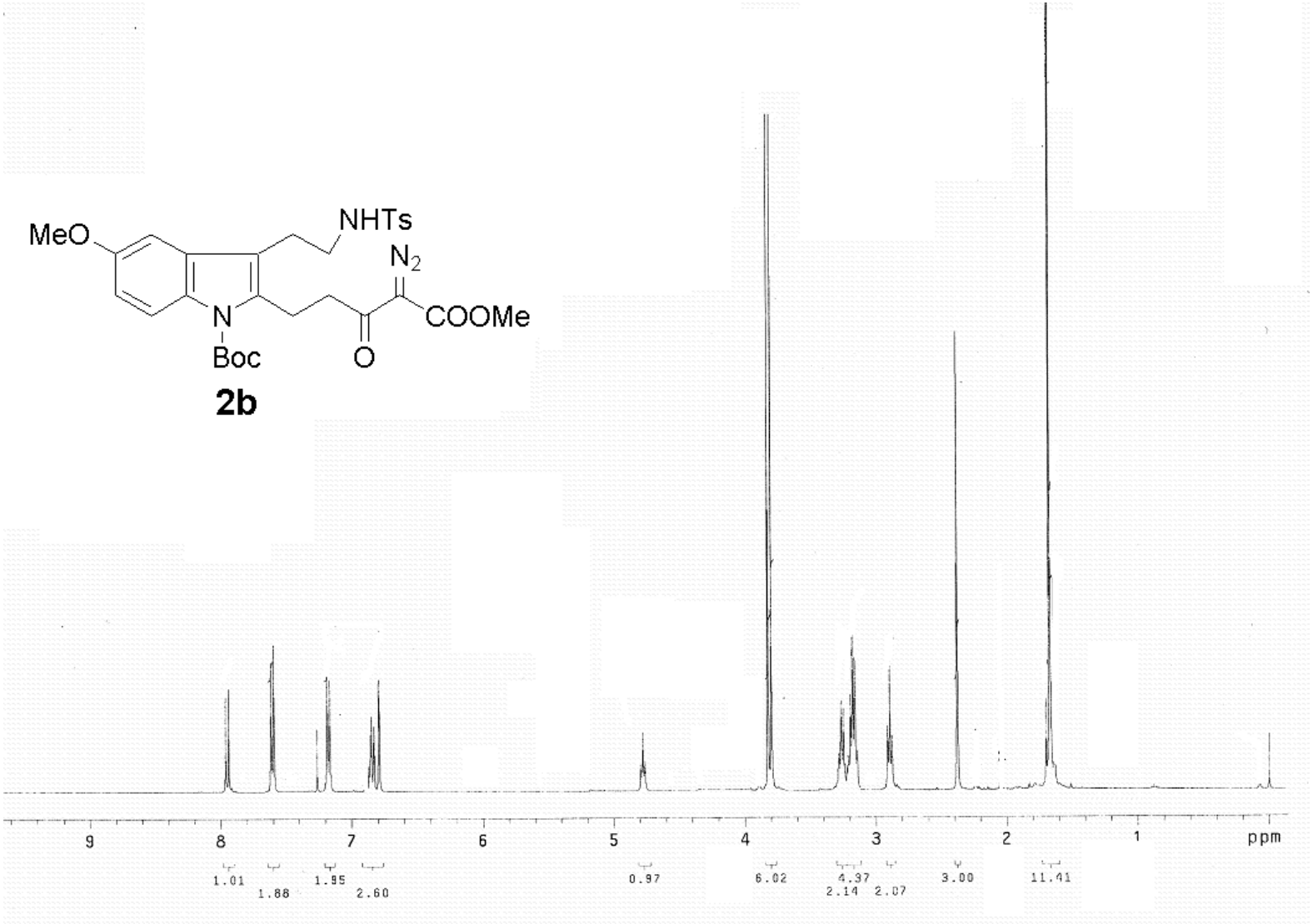

201.60
167.70
143.29
136.92
136.85
136.46
129.65
127.09
127.01
121.35
119.27
117.97
109.03
107.16
77.46
77.14
76.82
52.49
49.01
43.42
42.88
29.73
25.11
21.54
18.15
NHTs
N
Me
O
COOMe
8c
BRUKER
Current Data Parameters
NAME 2008-01-19 zhangmin-ZM080119A
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080119
Time 17.32
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zppg30
TD 65536
SOLVENT CDCl3
NS 278
DS 0
SWH 24038.461 Hz
FIDRES 0.366796 Hz
AQ 1.3631989 sec
RG 181
DW 20.800 usec
DE 6.50 usec
TE 293.1 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.99999998 sec
TD0 1
-------- CHANNEL f1 --------
NUC1 13C
P1 15.50 usec
PL1 -1.00 dB
SFO1 100.6228298 MHz
-------- CHANNEL f2 --------
CPDPRG2 waltz16
NUC2 1H
PCPD2 60.00 usec
PL12 12.05 dB
PL13 11.65 dB
PL2 -2.00 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.4
200
180
160
140
120
100
80
60
40
20
0
ppm

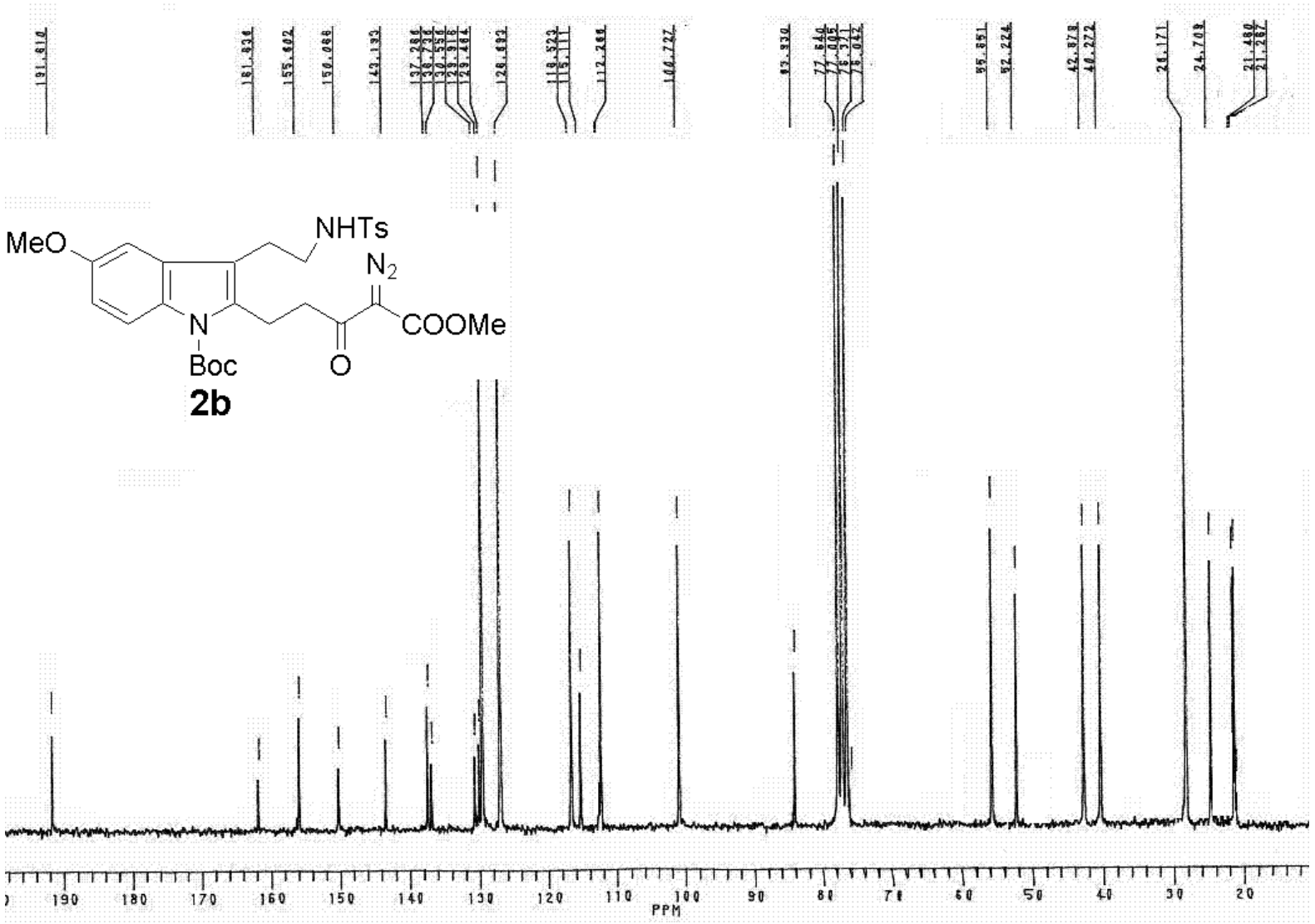

MeO
NHTs
N
Me
O
COOMe
8d
9
8
7
6
5
4
3
2
1
-0
ppm
1.88
1.05
1.97
1.03
1.00
1.00
3.25
2.78
5.26
2.02
2.24
2.12
2.22
3.10
3.24
2.25

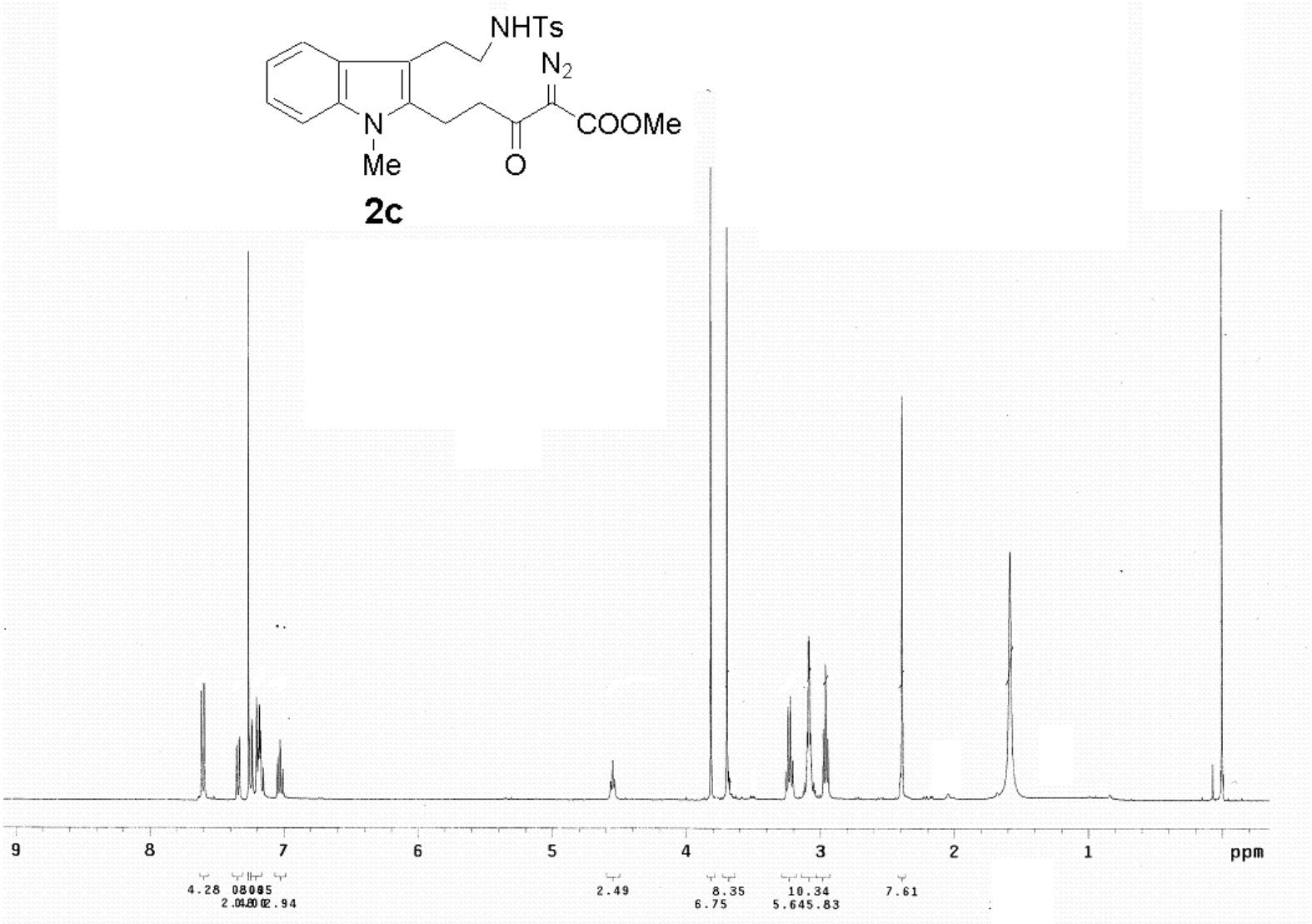

MeO
NHTs
N
Me
O
COOMe
8d
PPM

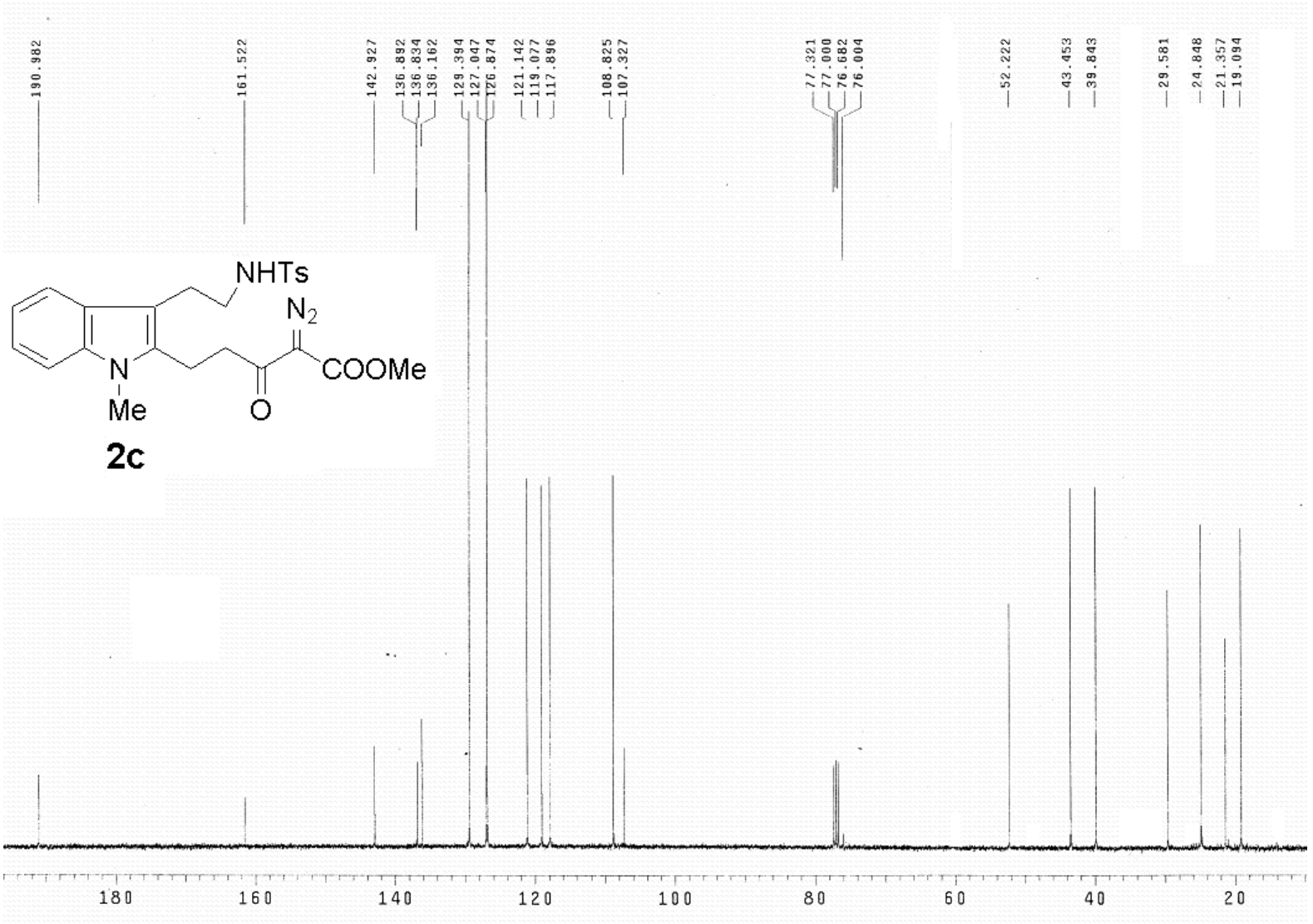

NHTs
N2
COOMe
N
Boc
O
2a
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.86
1.12
1.00
2.88
4.54
2.20
2.21
3.16
3.86
9.66

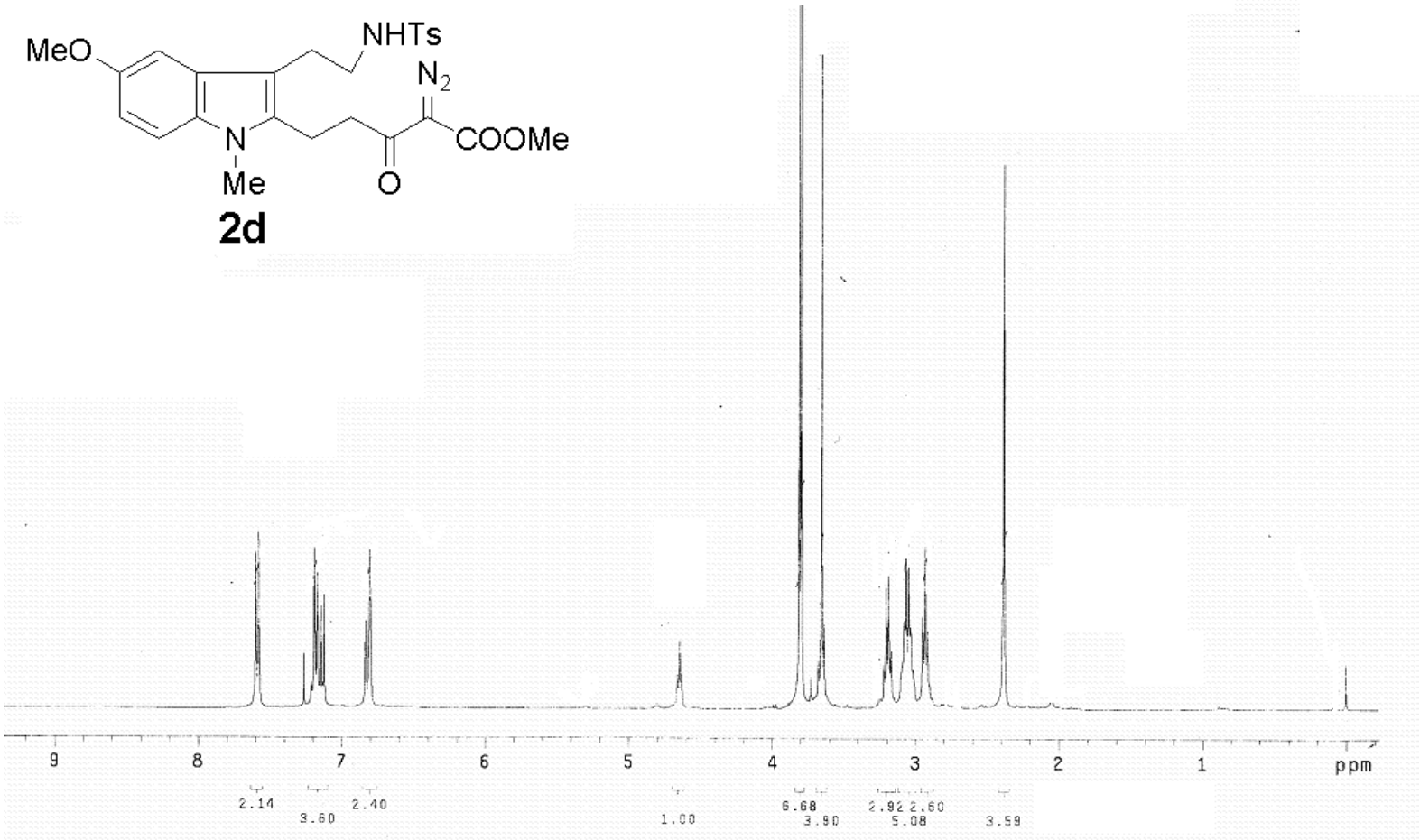

NHTs
N2
COOMe
N
Boc
O
2a
200
180
160
140
120
100
80
60
40
20
0
ppm

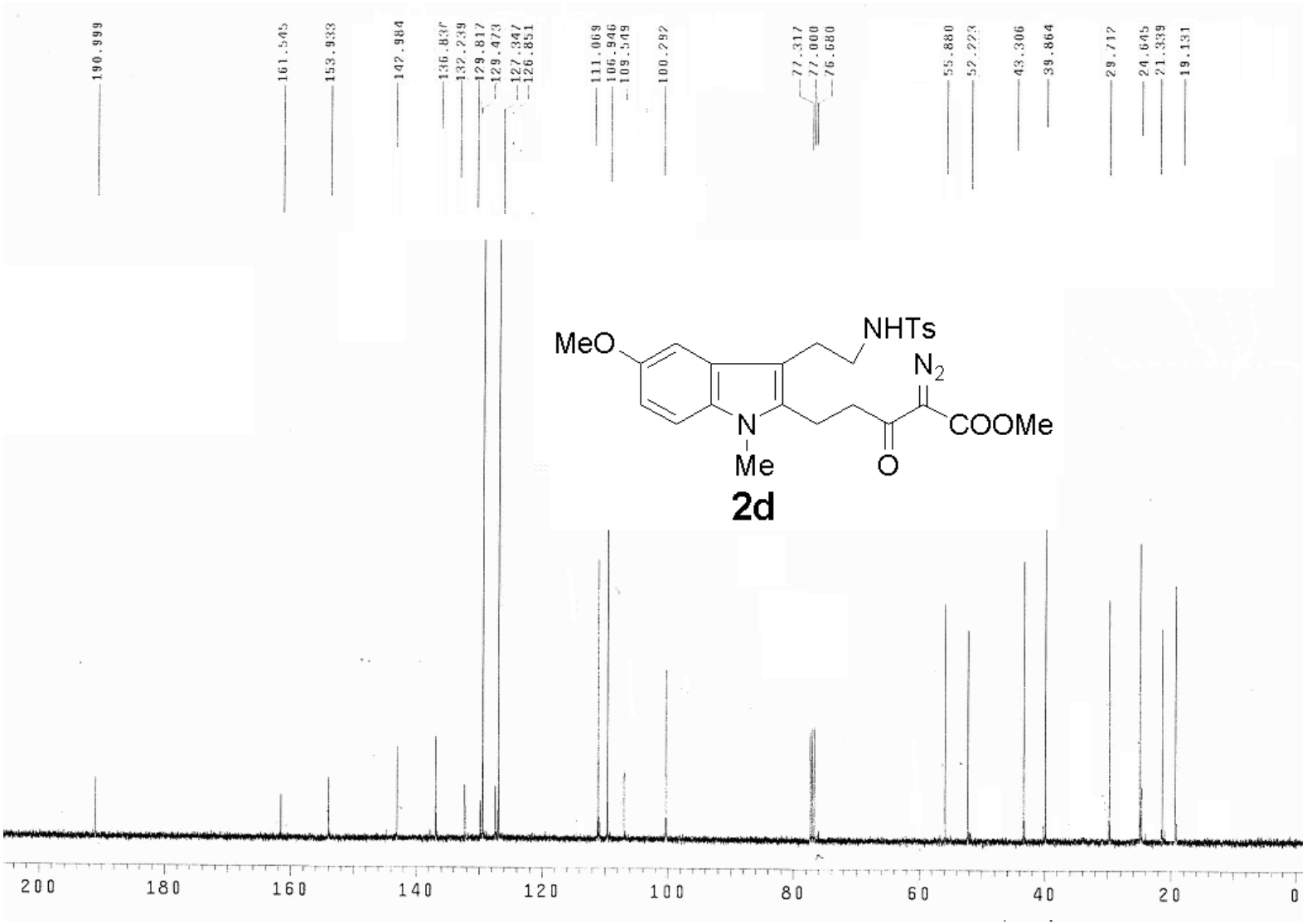

MeO
NHTs
N2
N
Boc
O
COOMe
2b
9
8
7
6
5
4
3
2
1
ppm
1.01
1.88
1.85
2.60
0.97
6.02
4.97
2.14
2.07
3.00
11.41

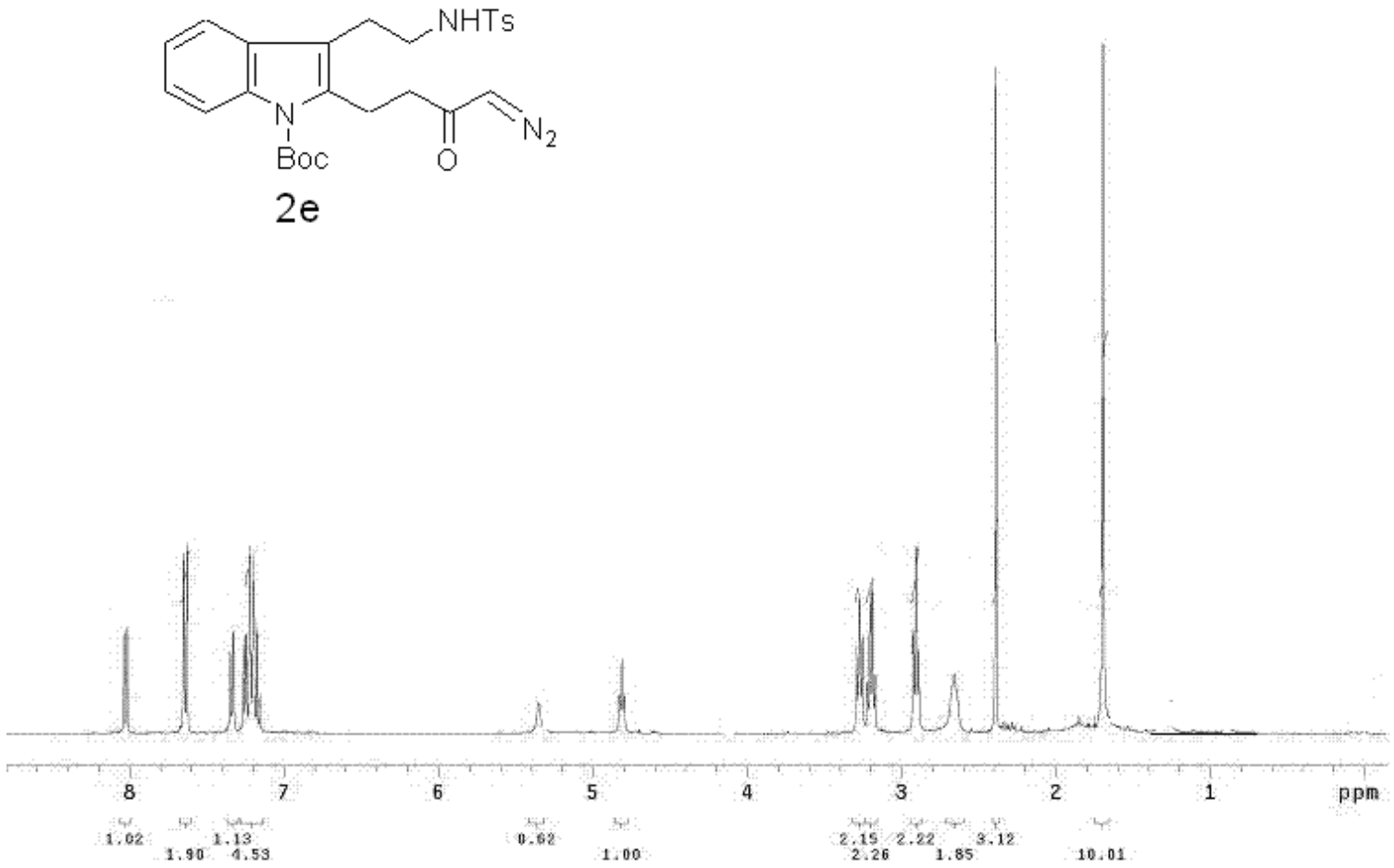

MeO
NHTs
N2
N
COOMe
Boc
O
2b
PPM

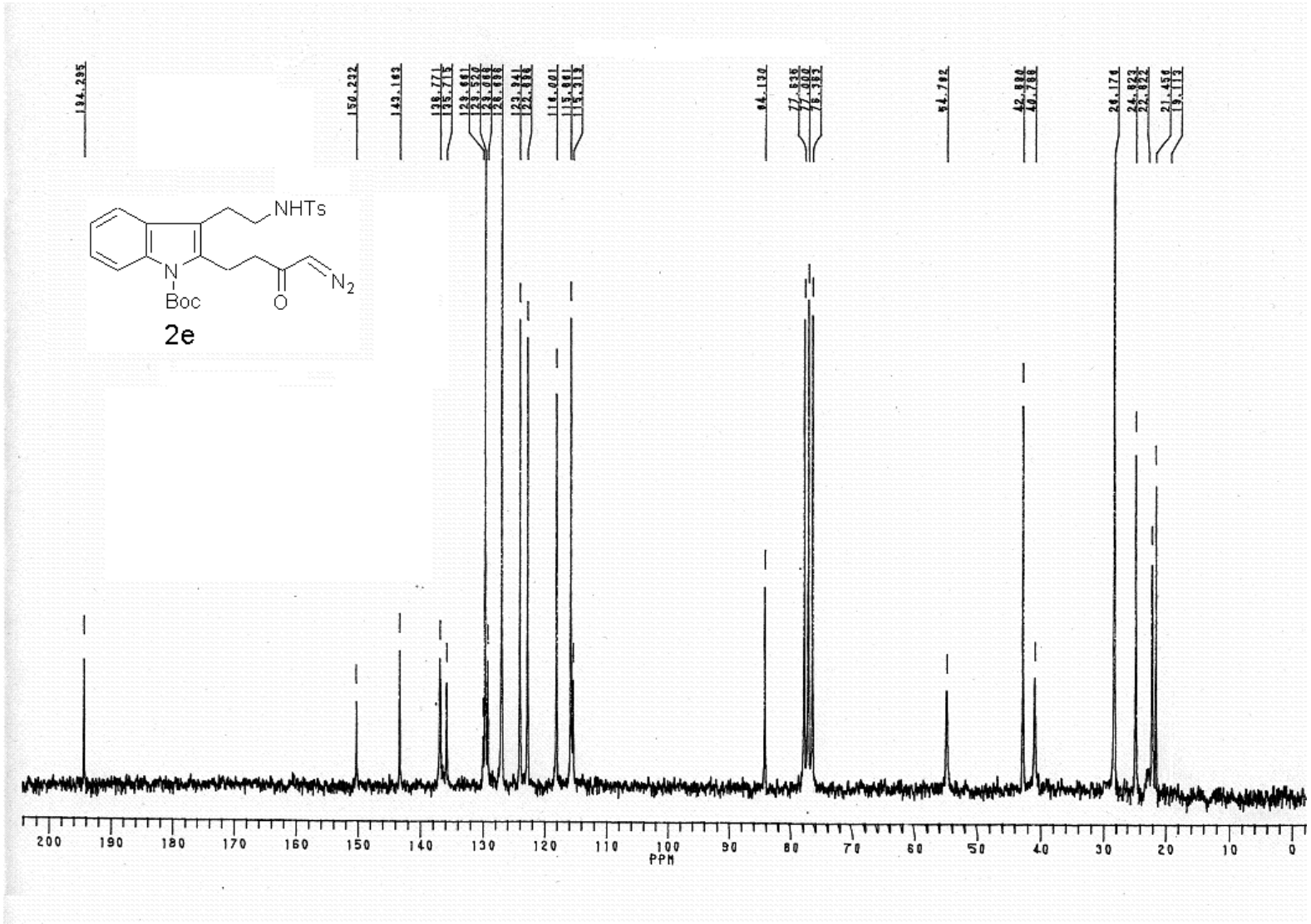

NHTs
N2
COOMe
N
Me
O
2c
9
8
7
6
5
4
3
2
1
ppm
4.28
2.49
8.35
6.75
10.34
5.64
5.83
7.61


190.982
161.522
142.927
136.892
136.834
136.162
129.394
127.047
126.874
121.142
119.077
117.896
108.825
107.327
77.321
77.000
76.682
76.004
52.222
43.453
39.843
29.581
24.848
21.357
19.094
NHTs
N2
COOMe
N
Me
O
2c
180
160
140
120
100
80
60
40
20

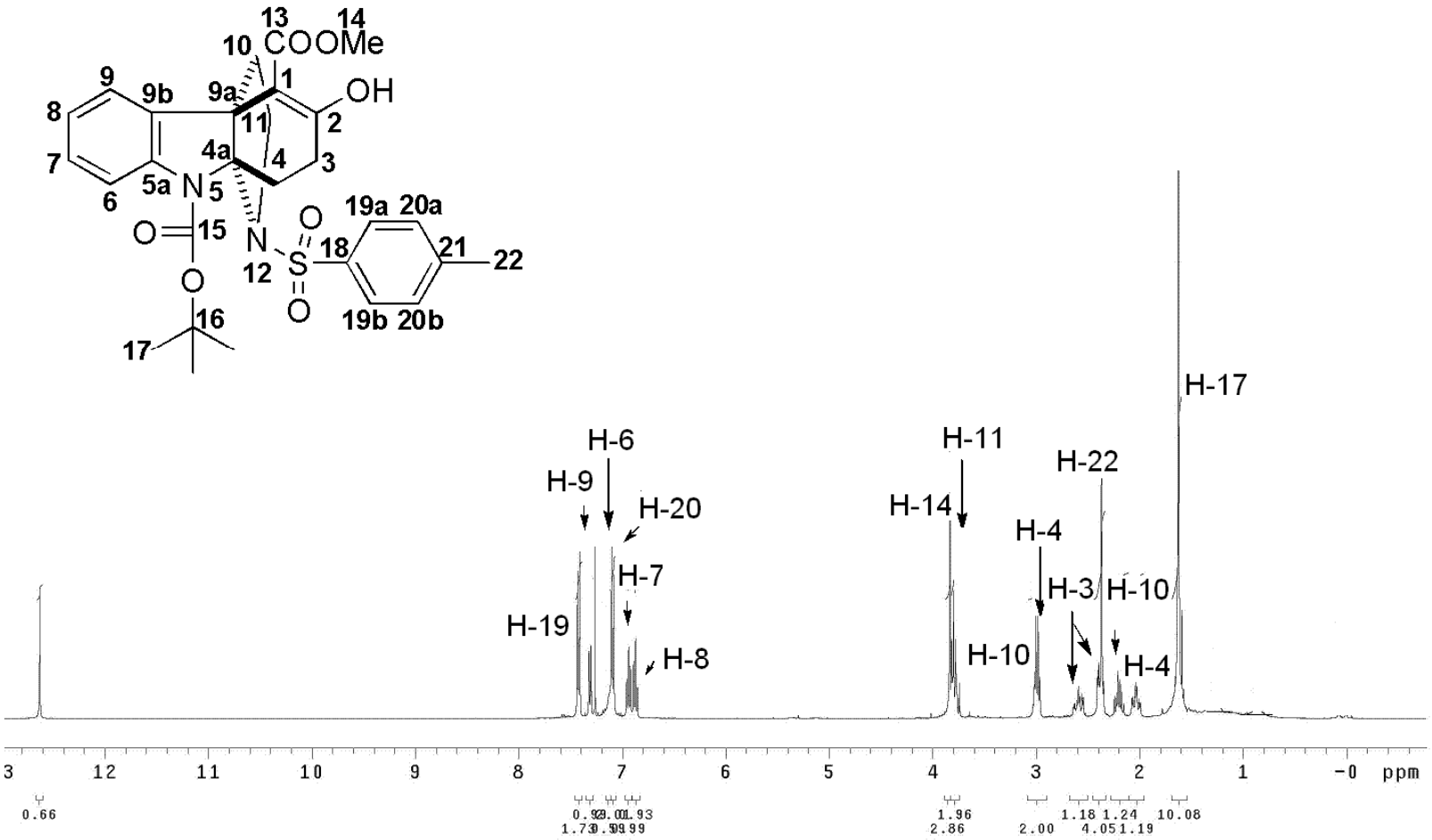

MeO
NHTs
N2
N
Me
O
COOMe
2d
9
8
7
6
5
4
3
2
1
ppm
2.14
3.60
2.40
1.00
6.68
3.50
2.92
5.08
2.60
3.59


190.999
161.545
153.933
142.984
136.838
132.239
129.817
129.473
127.347
126.851
111.069
106.946
100.292
77.317
77.000
76.680
55.880
52.223
43.306
39.864
29.717
24.645
21.339
19.131
MeO
NHTs
N2
N
Me
O
COOMe
2d
200
180
160
140
120
100
80
60
40
20
0

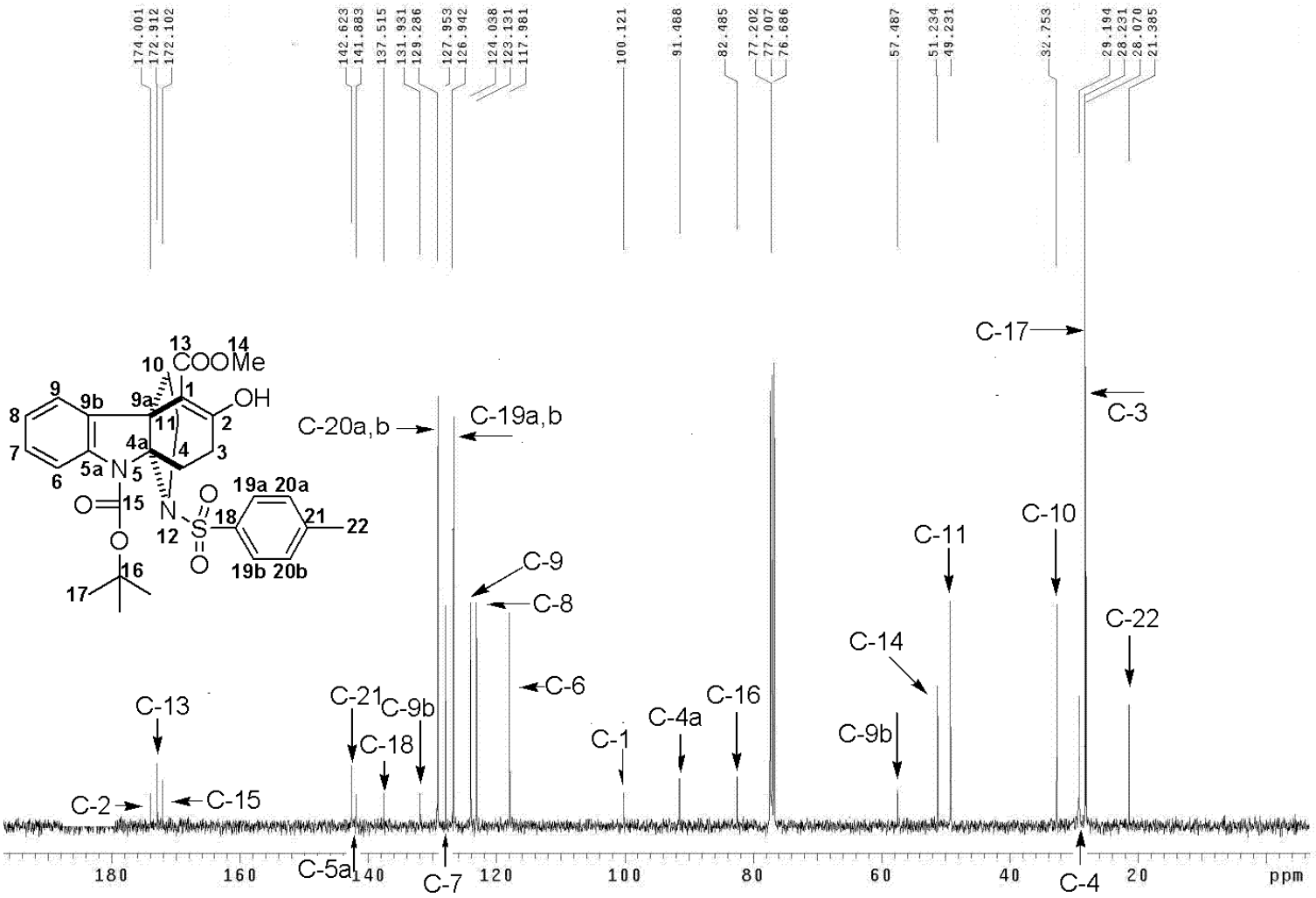

NHTs
N
Boc
O
N2
2e
8
7
6
5
4
3
2
1
ppm
1.02
1.90
1.13
4.53
0.62
1.00
2.15
2.26
2.22
1.85
3.12
10.01


NHTs
N
Boc
O
N_2
2e
PPM

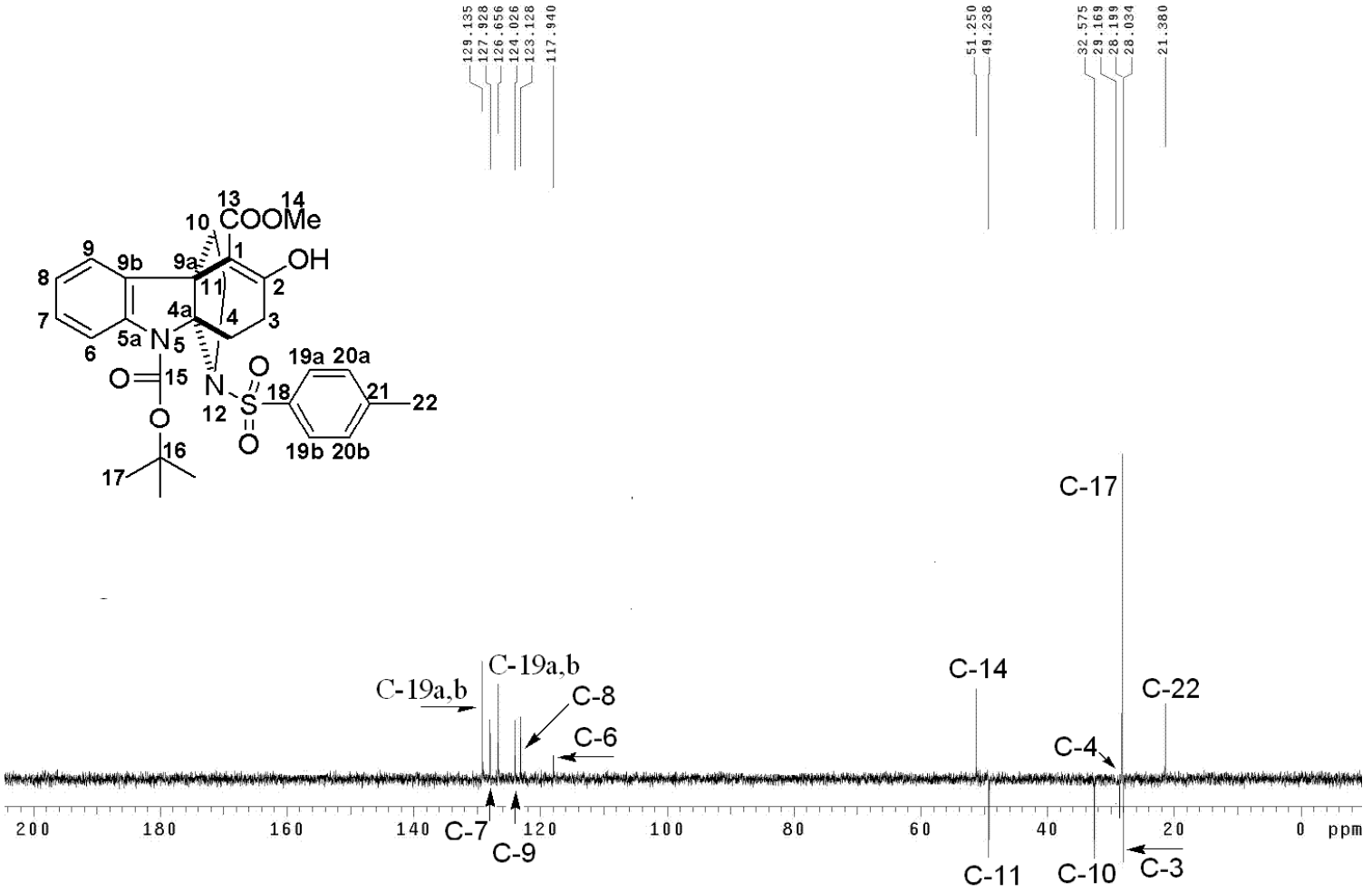
^{1}HNMR Spectrum of Enol Ester 1a

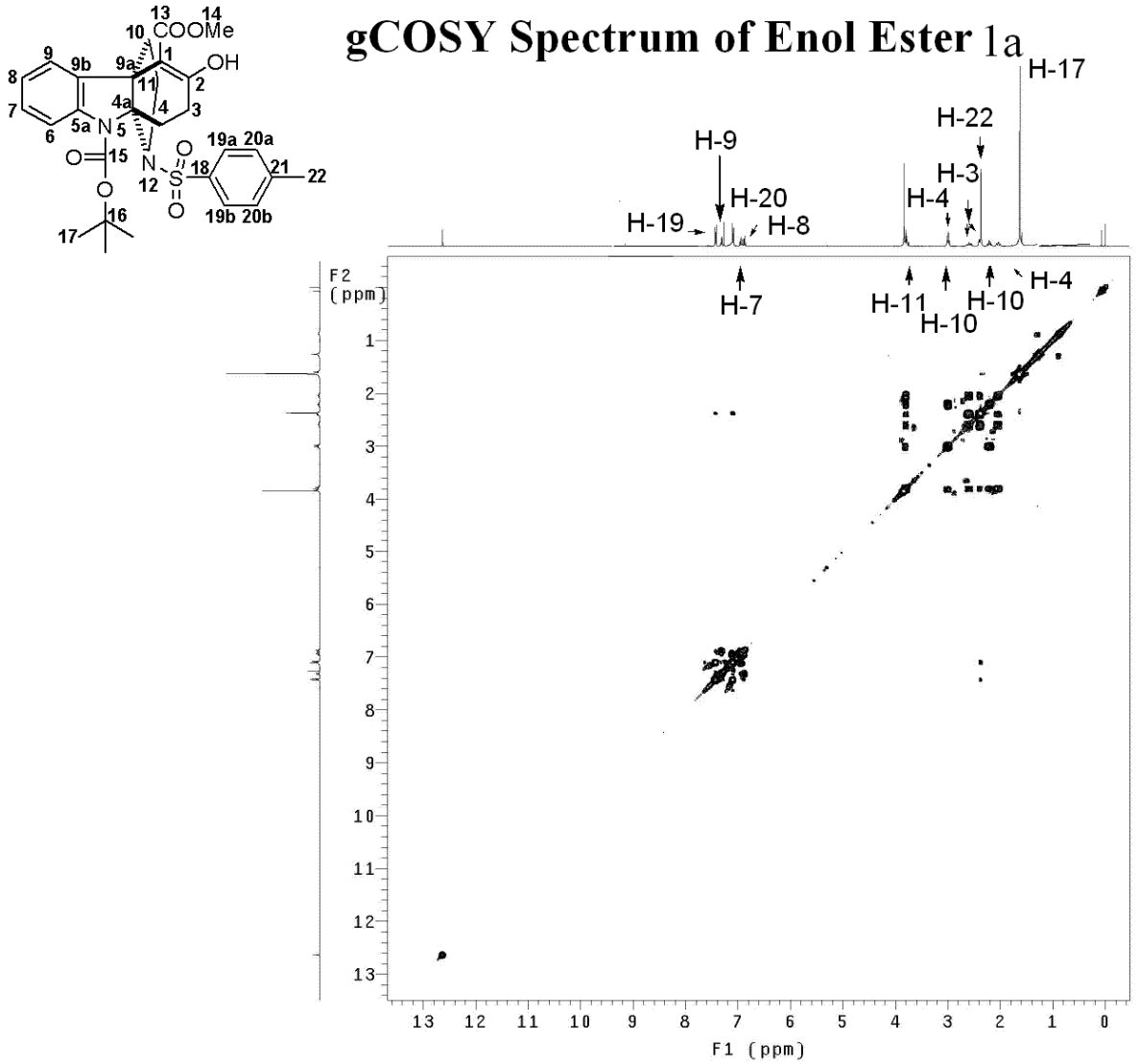


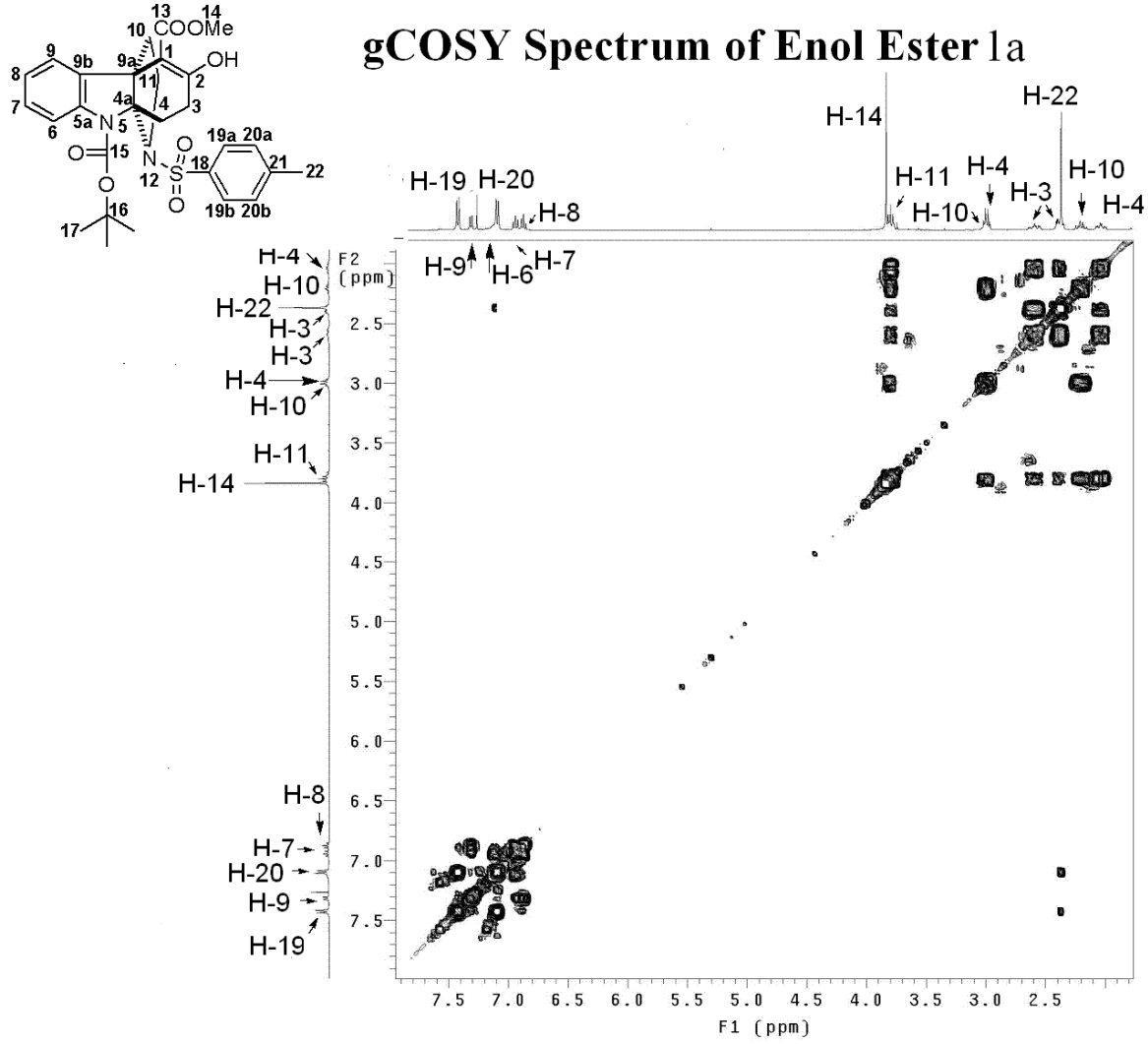
^{13}CNMR Spectrum of Enol Ester 1a



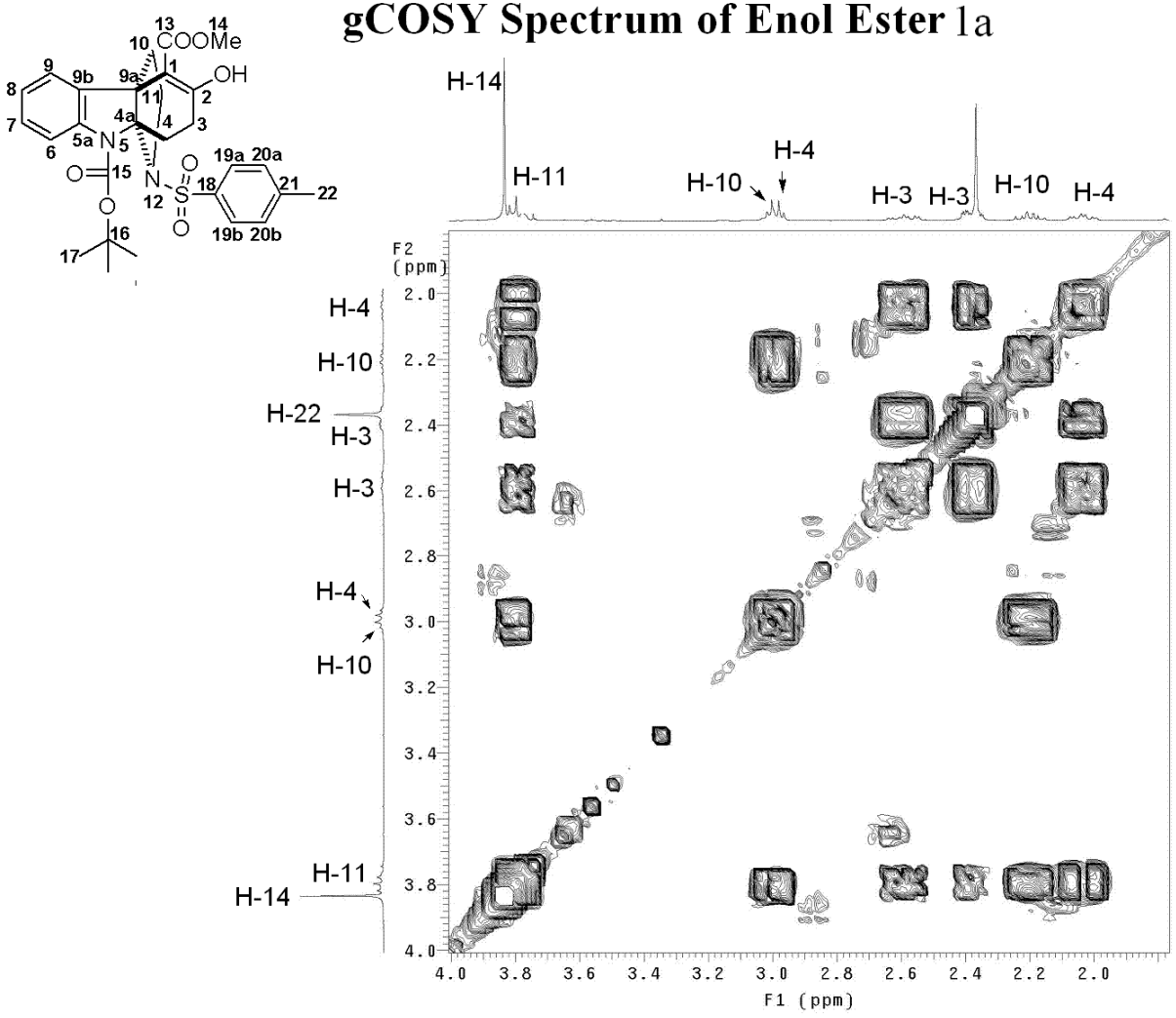
DEPT Spectrum of Enol Ester 1a



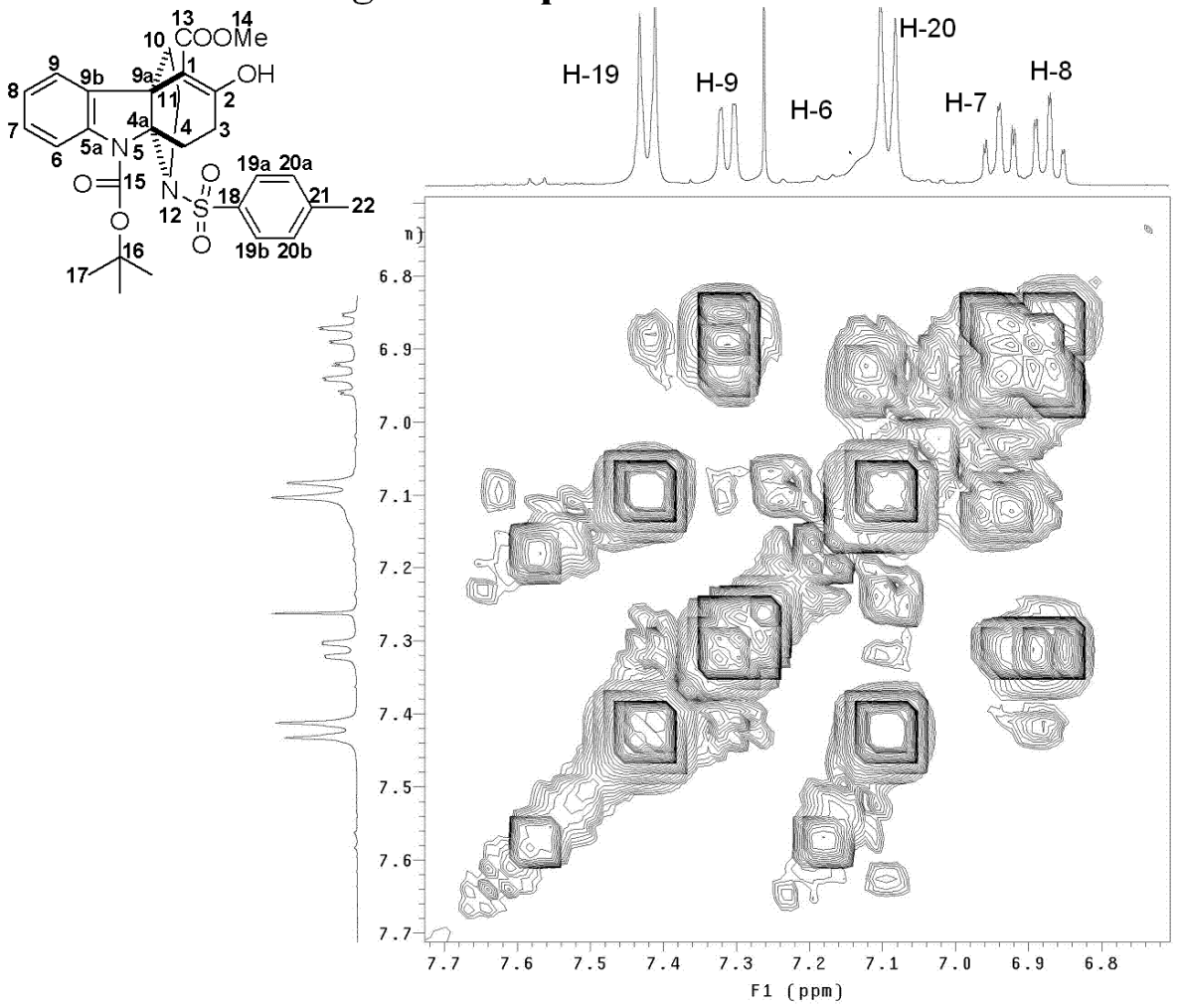

gCOSY Spectrum of Enol Ester 1a
H-17
H-22
H-9
H-3
H-4
H-20
H-19
H-8
H-7
H-11
H-10
H-10
H-4
F2 (ppm)
F1 (ppm)


gCOSY Spectrum of Enol Ester 1a
COOMe
OH
H-14
H-22
H-19 H-20
H-8
H-11
H-4
H-3
H-10
H-4
H-9
H-6
H-7
H-10
H-22
H-3
H-3
H-4
H-10
H-11
H-14
H-8
H-7
H-20
H-9
H-19
F2 (ppm)
F1 (ppm)

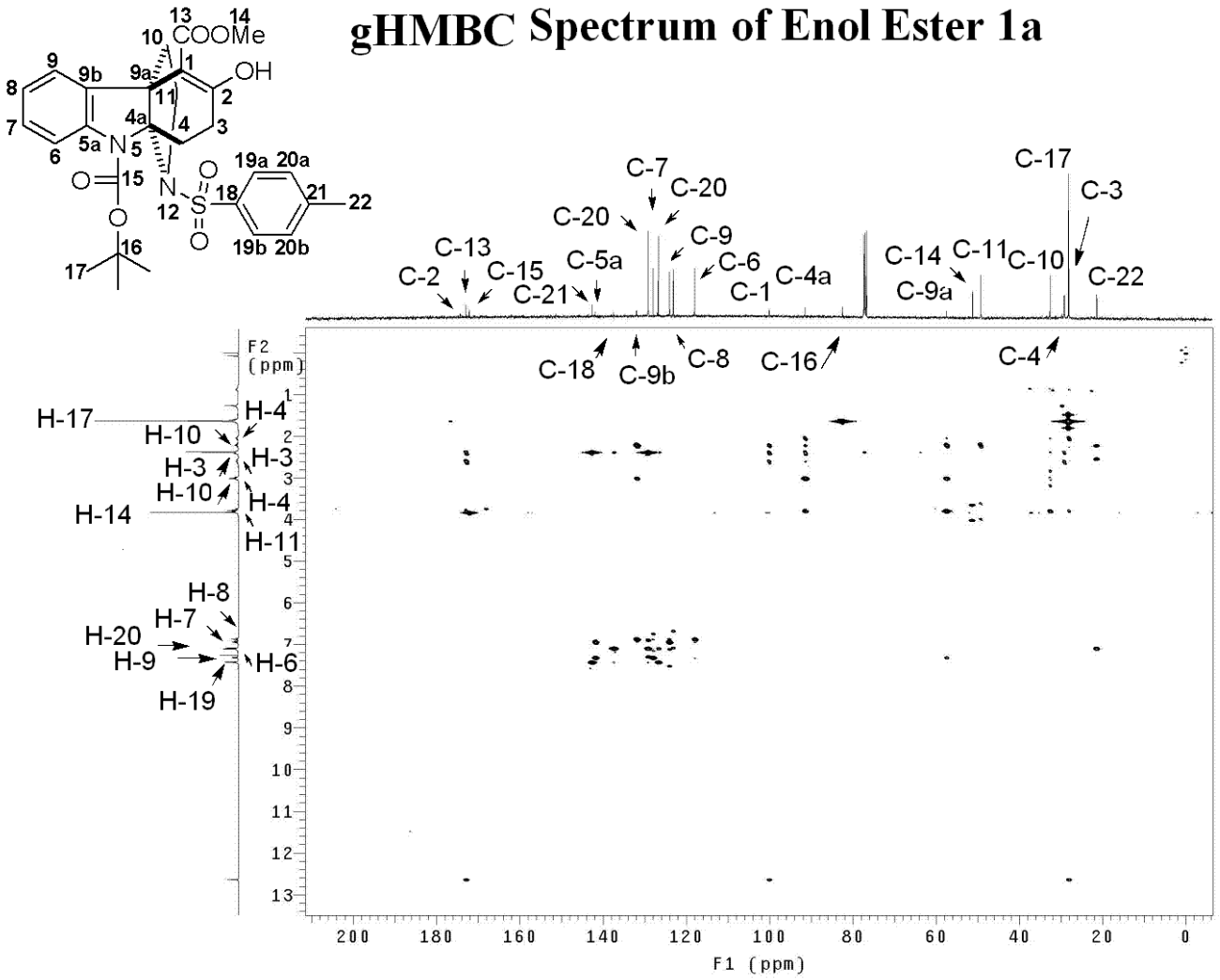
gCOSY Spectrum of Enol Ester 1a



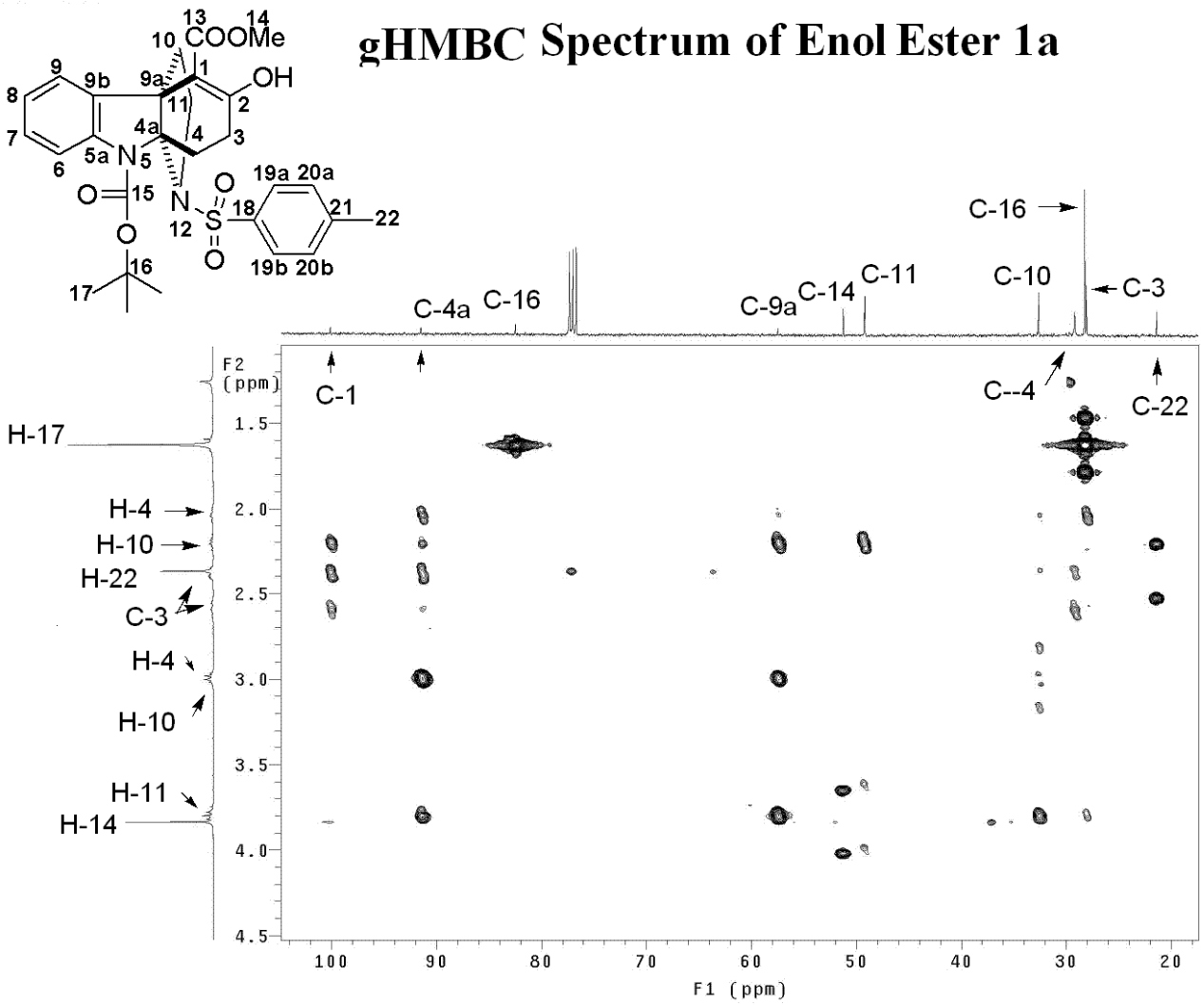
gCOSY Spectrum of Enol Ester 1a



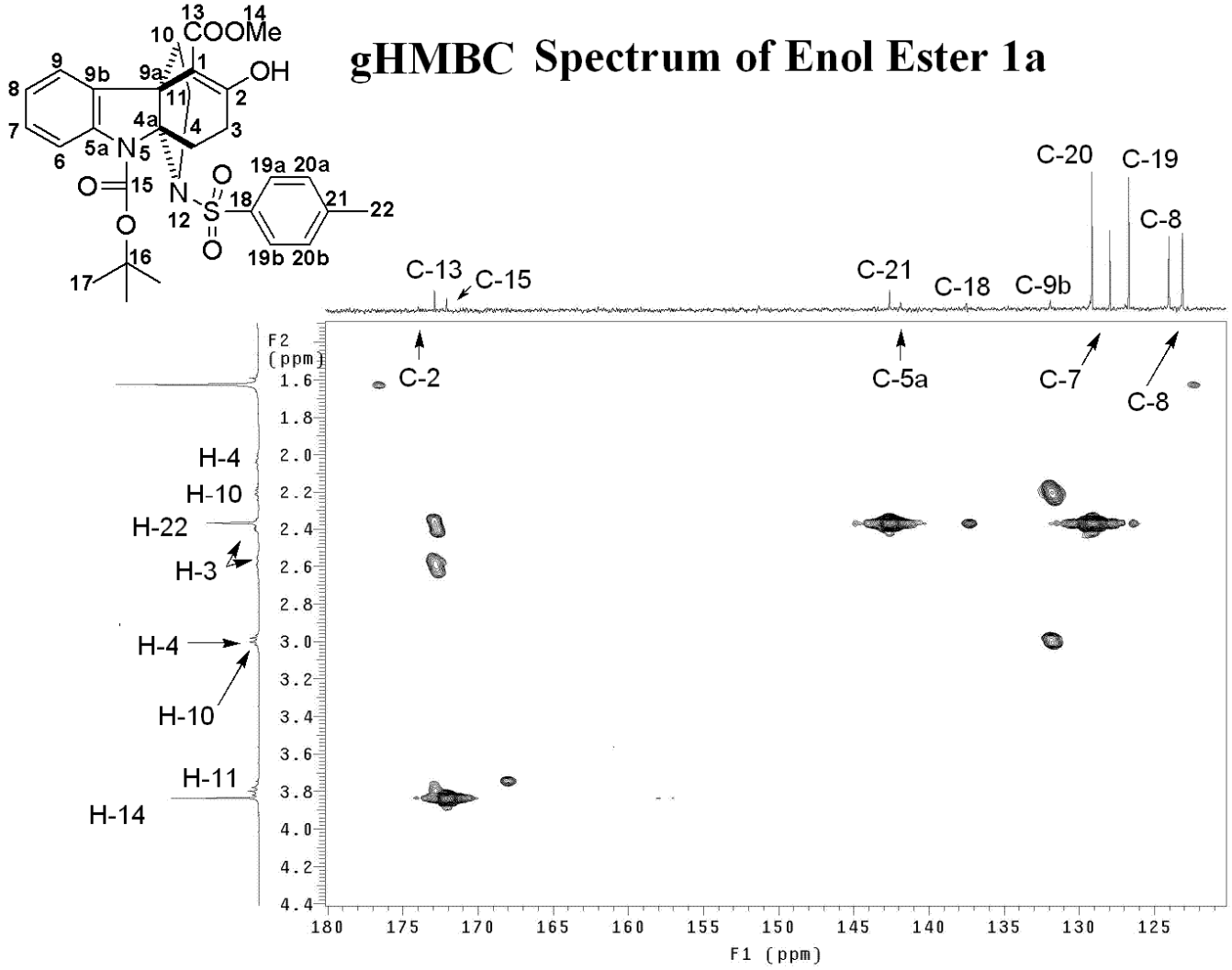
gHMBC Spectrum of Enol Ester 1a



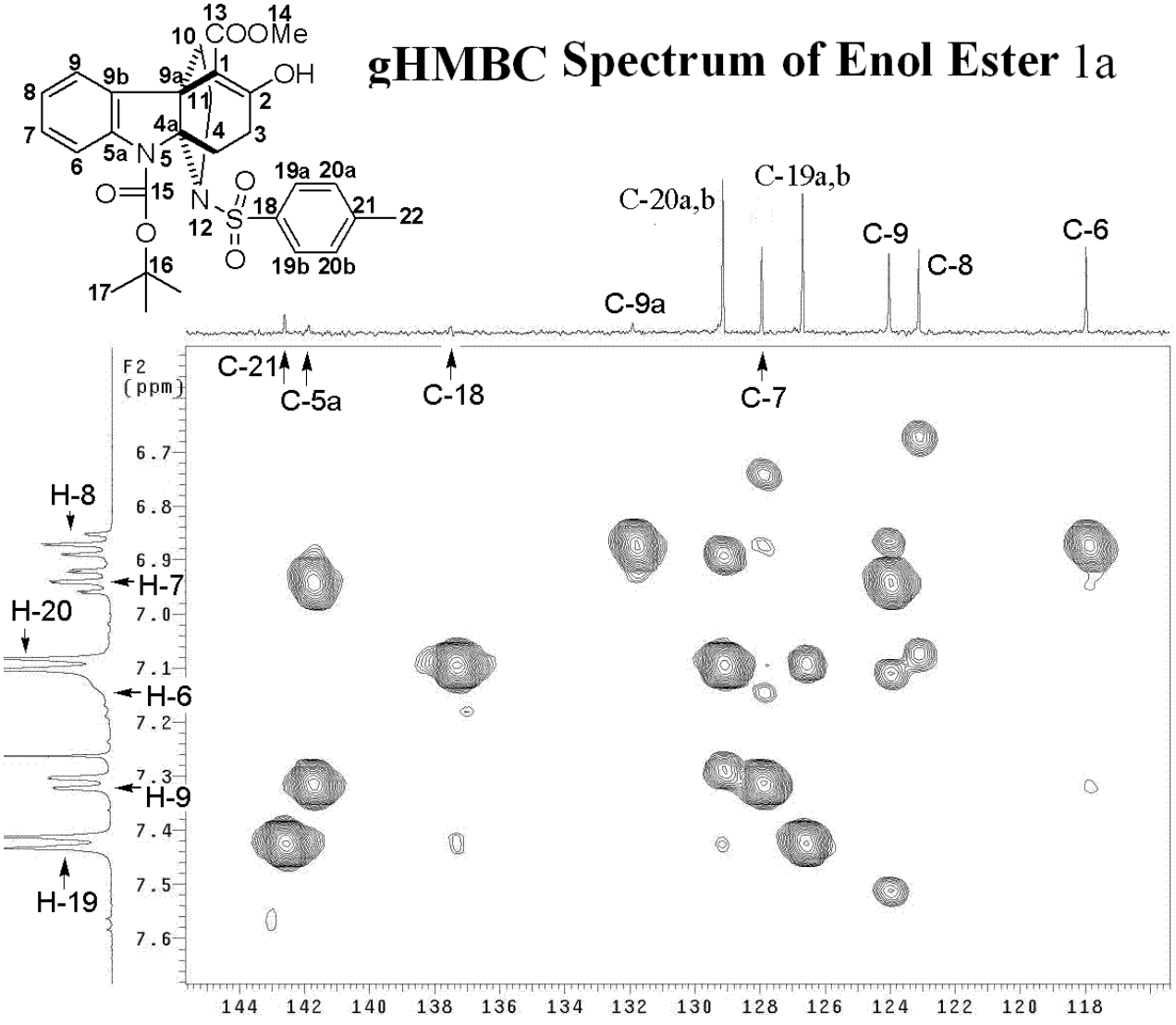
gHMBC Spectrum of Enol Ester 1a

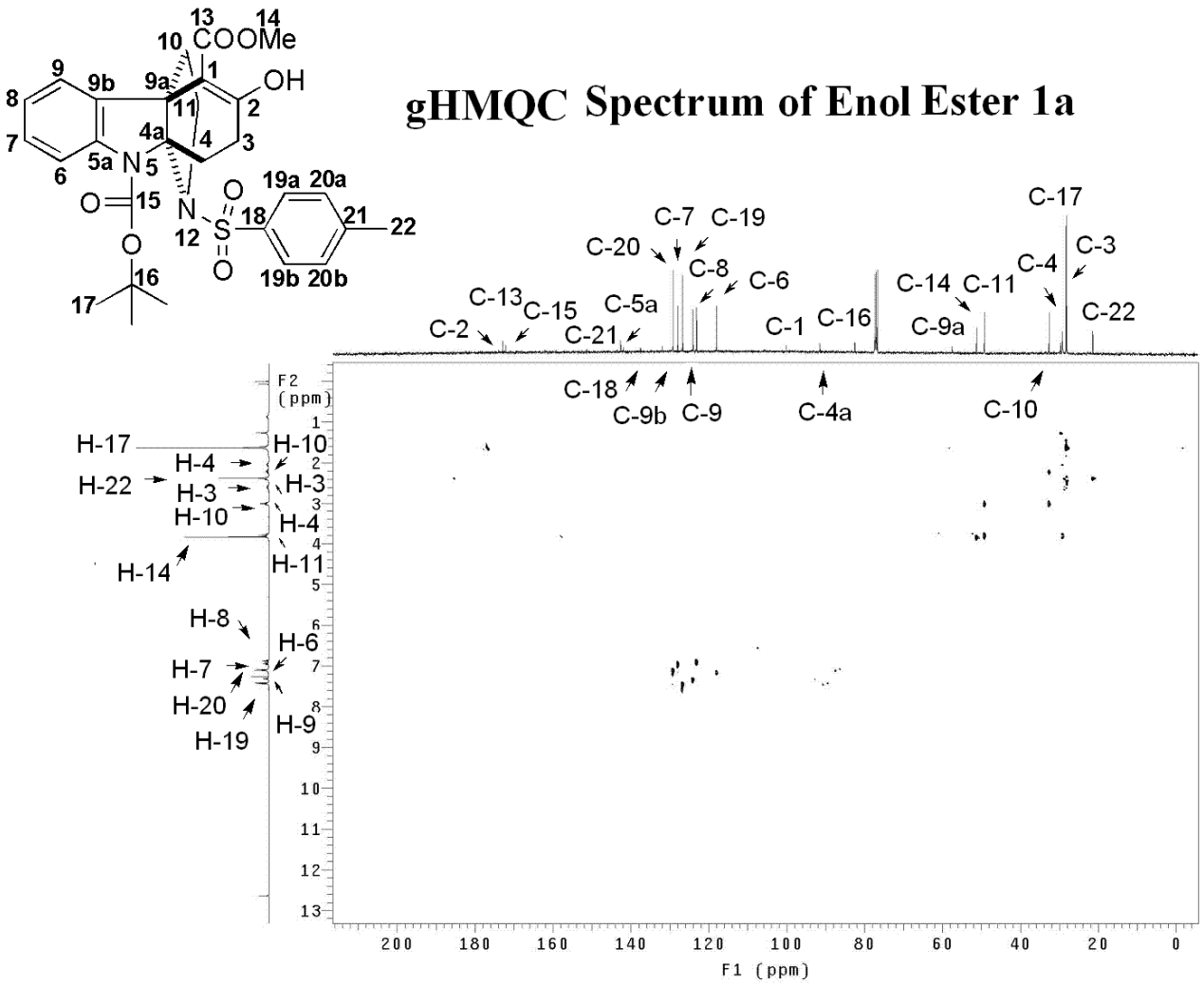


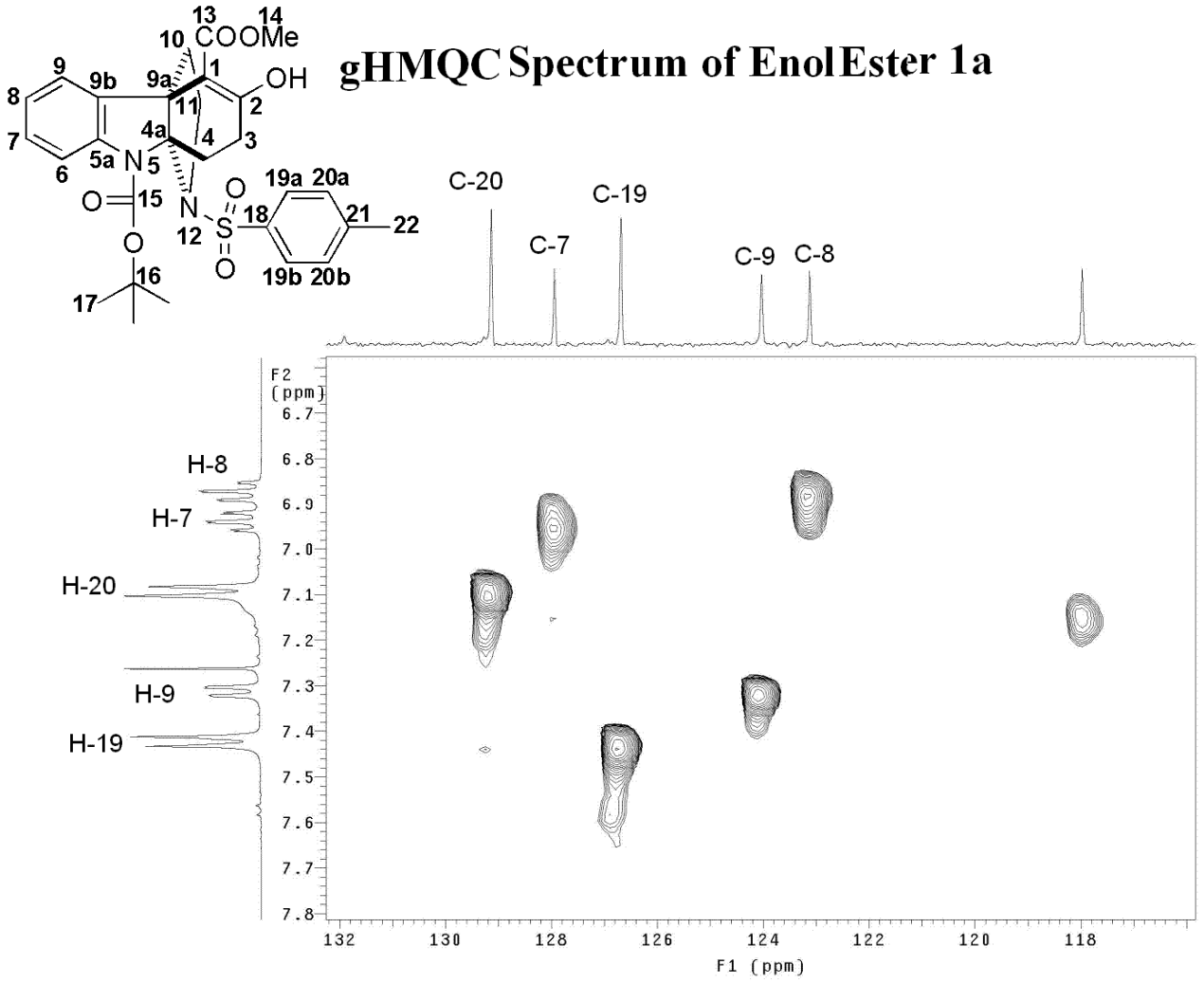
gHMBC Spectrum of Enol Ester 1a



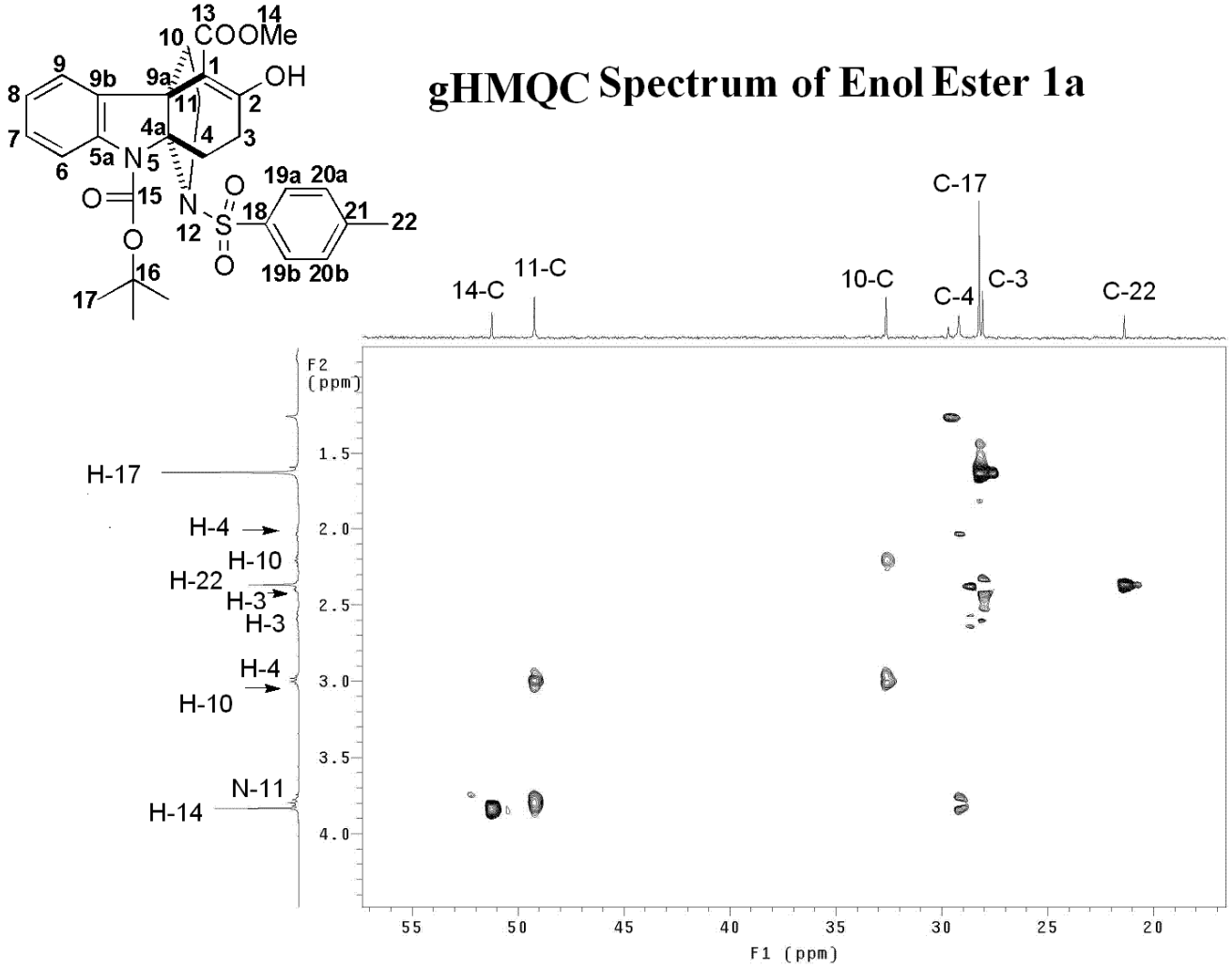
gHMBC Spectrum of Enol Ester 1a

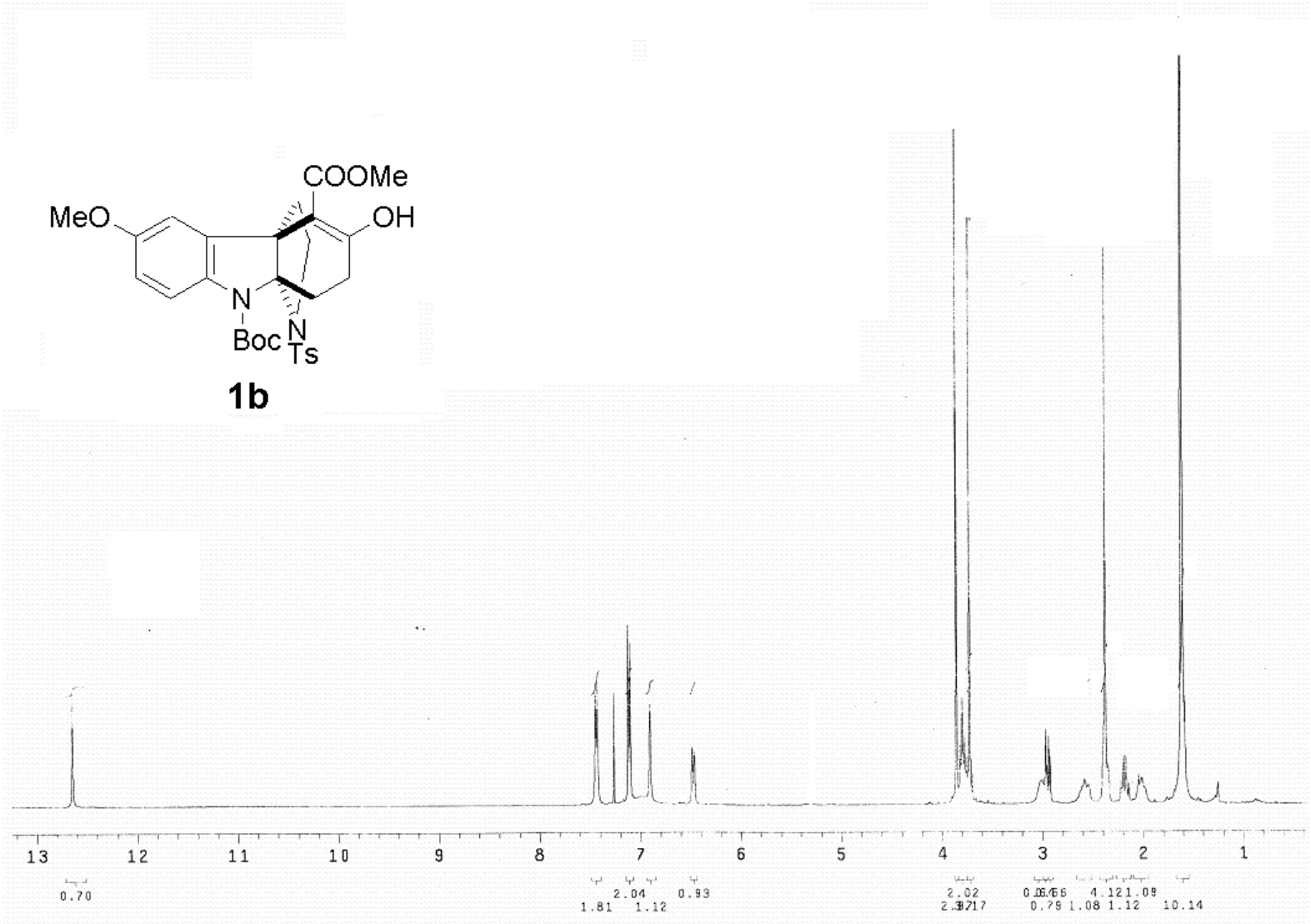


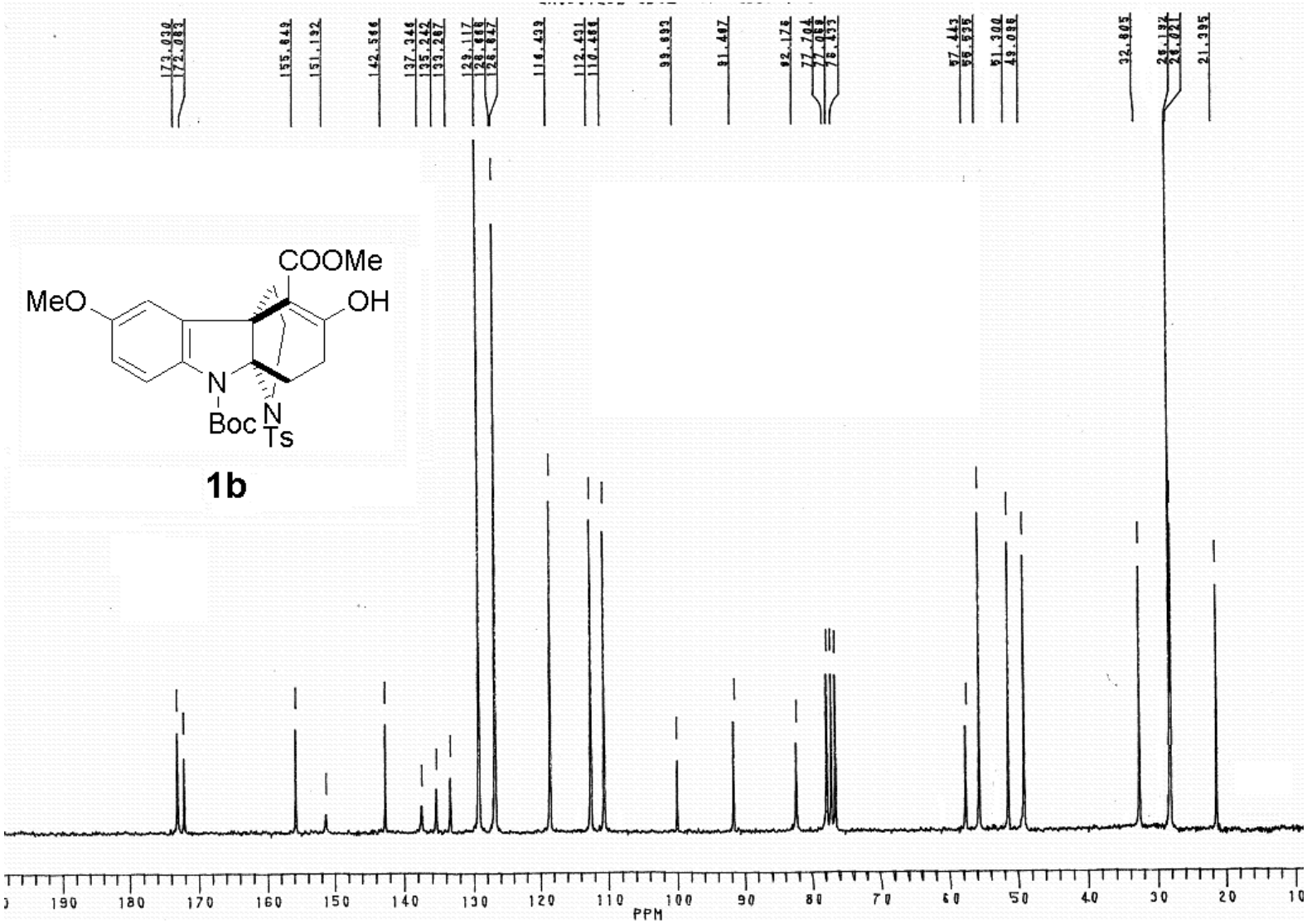

gHMQC Spectrum of Enol Ester 1a
13
14
10
COOMe
9
9b
9a
1
OH
8
11
2
4a
7
4
3
5a
N
5
6
19a
20a
O
15
N
18
21
22
12
S
O
19b
20b
O
16
17
C-17
C-7
C-19
C-3
C-20
C-8
C-4
C-6
C-14
C-11
C-13
C-15
C-5a
C-22
C-2
C-21
C-1
C-16
C-9a
F2
(ppm)
C-18
C-9b
C-9
C-4a
C-10
H-17
H-10
H-4
H-22
H-3
H-3
H-10
H-4
H-14
H-11
H-8
H-6
H-7
H-20
H-9
H-19
200
180
160
140
120
100
80
60
40
20
0
F1 (ppm)

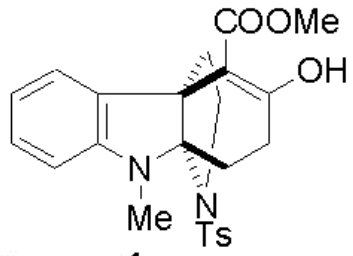

gHMQC Spectrum of EnolEster 1a
13
14
10
COOMe
9
9b
9a
1
OH
8
11
2
7
4a
4
3
6
5a
N
5
19a
20a
15
O
N
18
21
22
12
S
19b
20b
16
17
C-20
C-19
C-7
C-9
C-8
H-8
H-7
H-20
H-9
H-19
F2 (ppm)
6.7
6.8
6.9
7.0
7.1
7.2
7.3
7.4
7.5
7.6
7.7
7.8
132
130
128
126
124
122
120
118
F1 (ppm)

gHMQC Spectrum of Enol Ester 1a



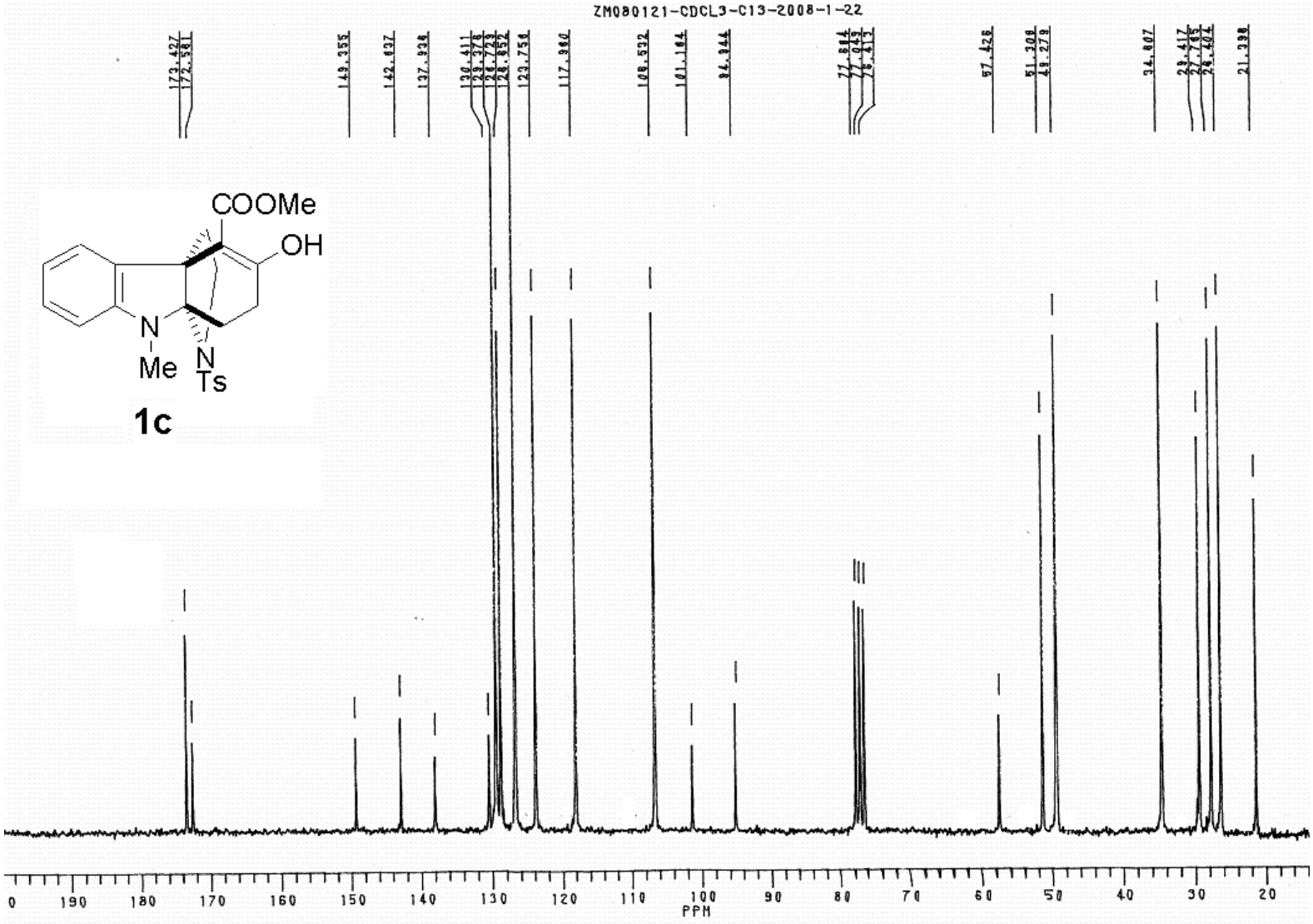

COOMe
MeO
OH
N
Boc
N
Ts
1b
13
12
11
10
9
8
7
6
5
4
3
2
1
0.70
1.81
2.04
1.12
0.93
2.02
0.79
1.08
4.12
1.12
1.09
10.14

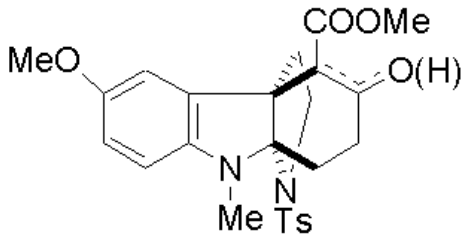

COOMe
MeO
OH
N
Boc
N
Ts
1b
PPM


COOMe
OH
N
Me
N
Ts

1c

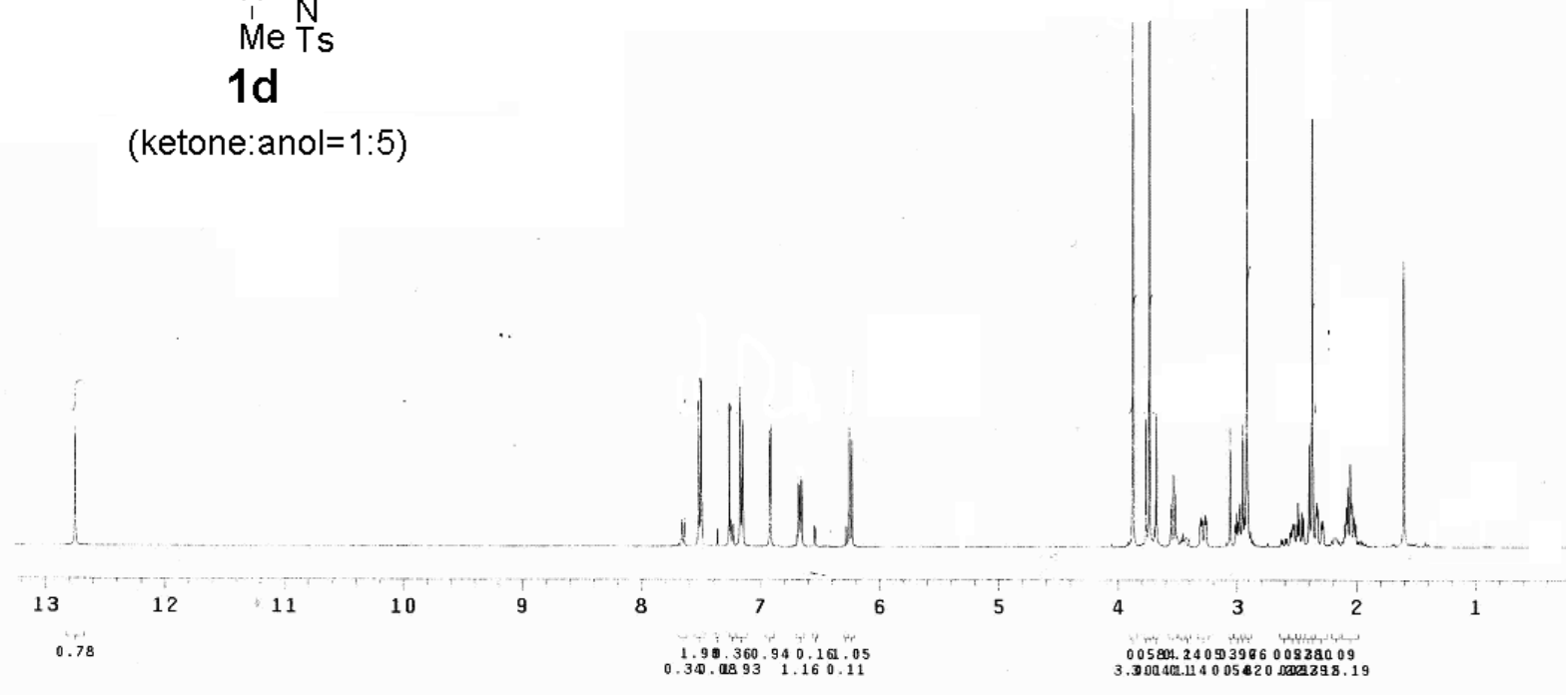
13
12
11
10
9
8
7
6
5
4
3
2
1
0.70
1.88
2.03
1.02
0.96
0.06
0.03
0.20
0.03
7.06
6.06
1.62
1.51
3.00
0.05
3.17
8
3.04
1.24

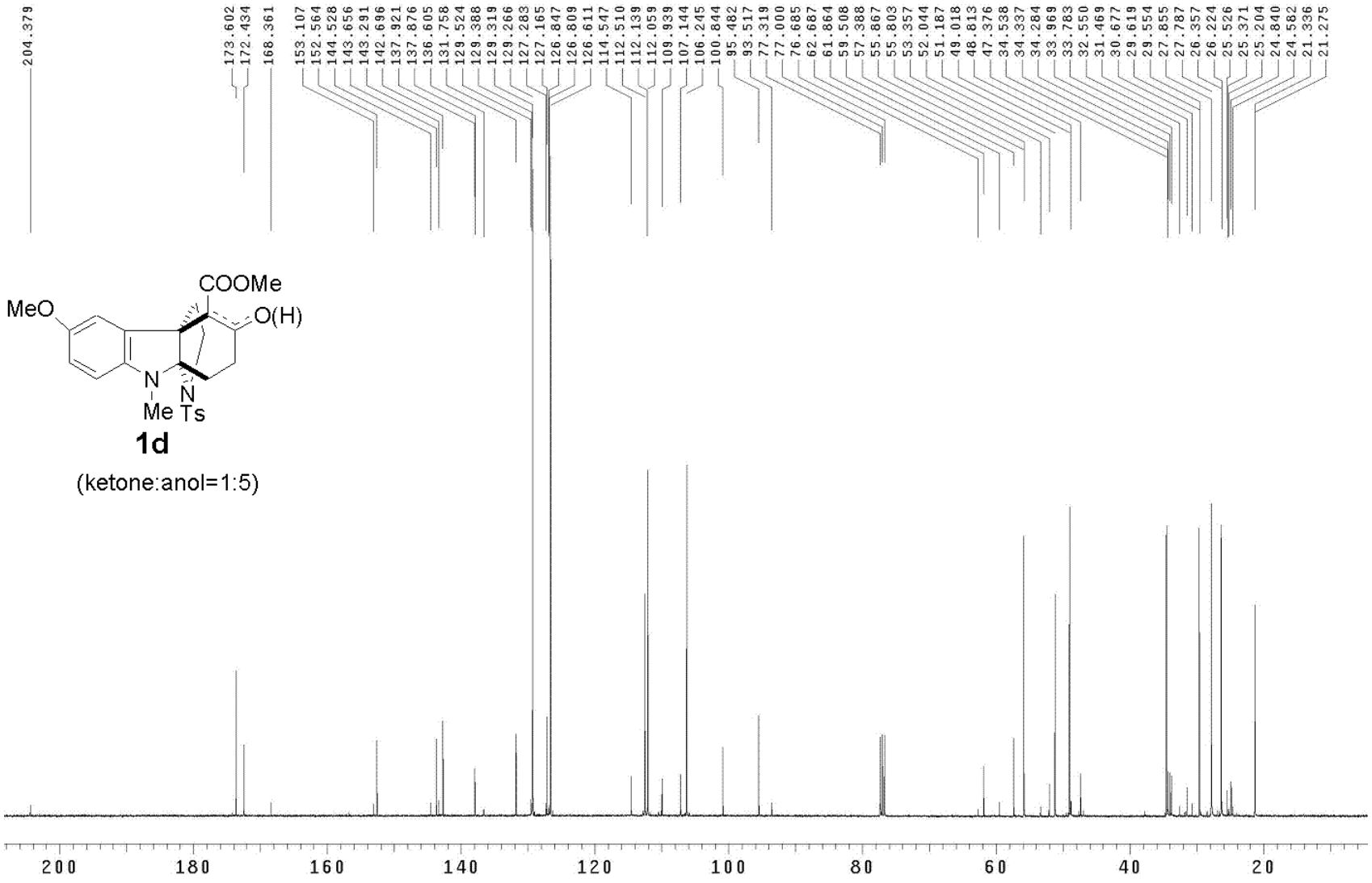

ZM080121-CDCL3-C13-2008-1-22
COOMe
OH
N
Me
N
Ts
1c
PPM

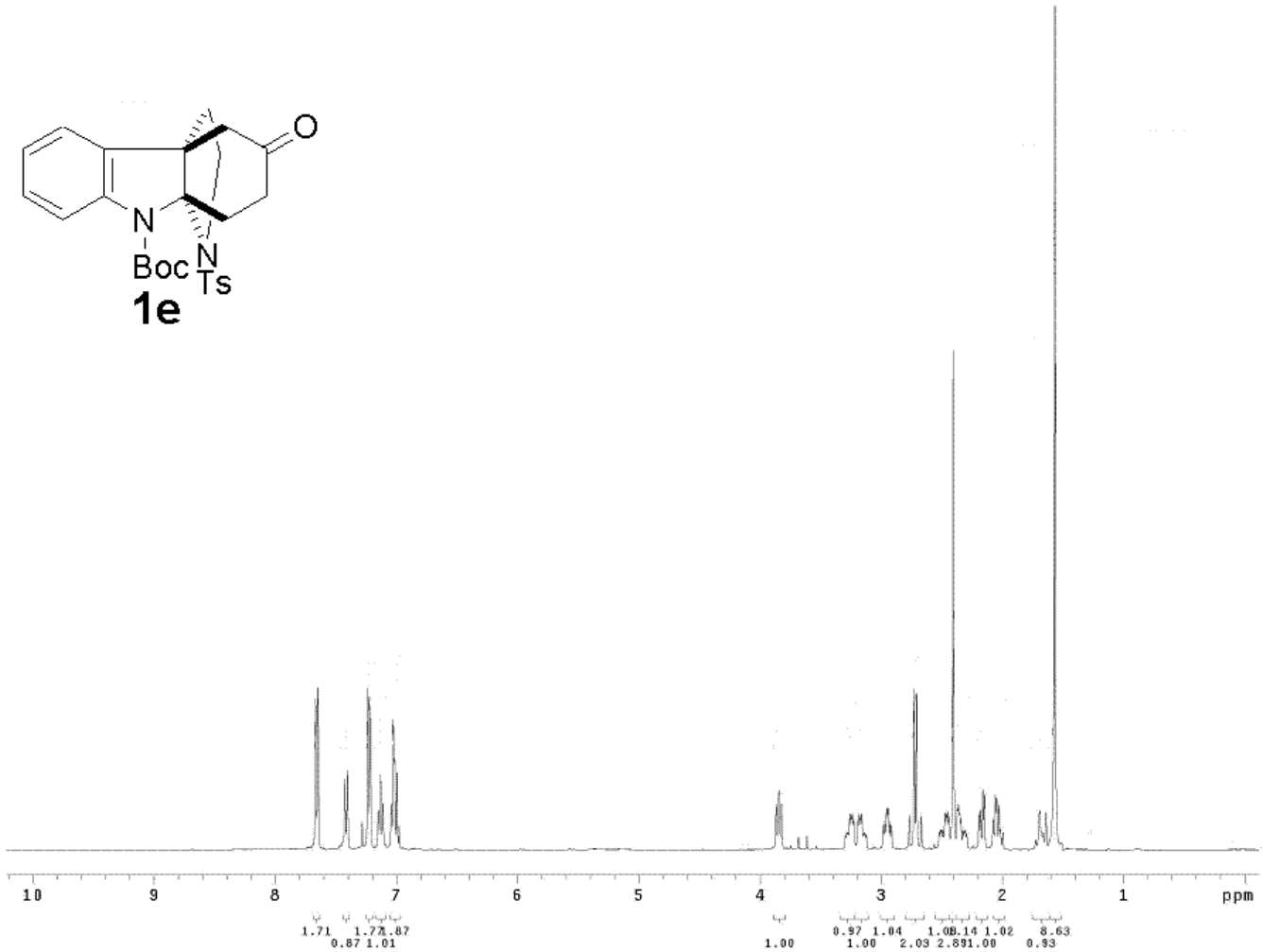


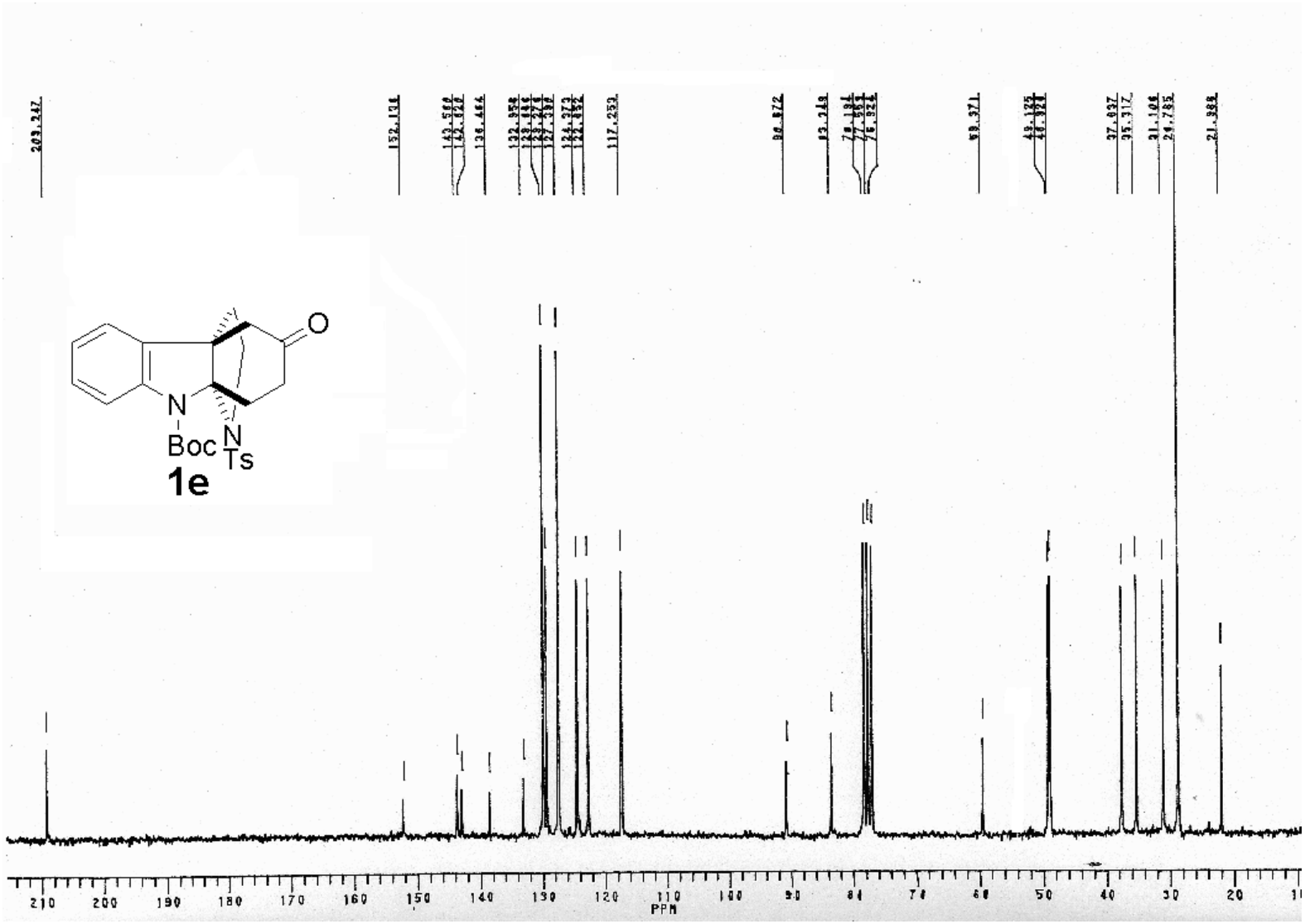
1d

(ketone:anol=1:5)

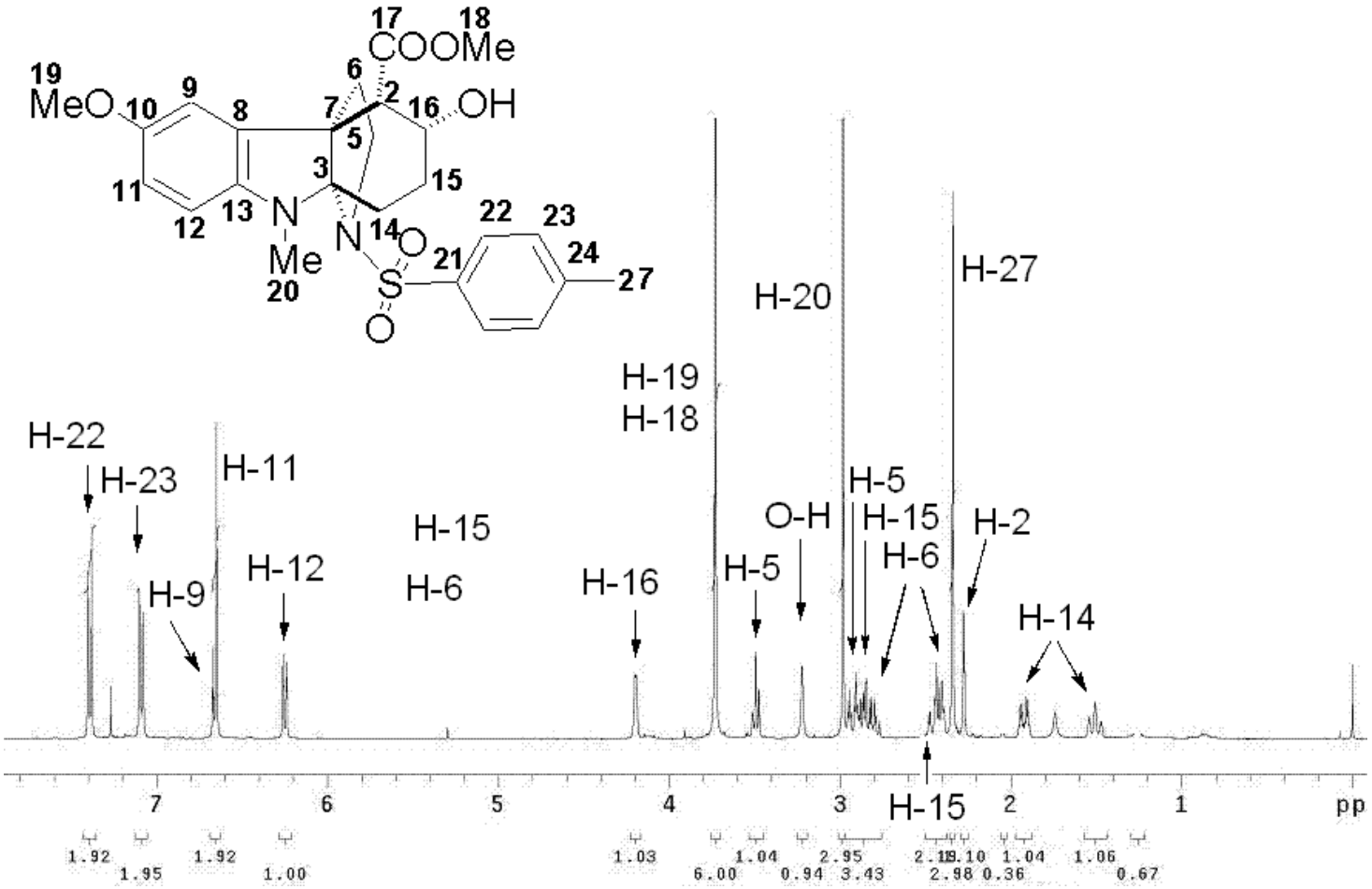



204.379
173.602
172.434
168.361
153.107
152.564
144.528
143.656
143.291
142.696
137.921
137.876
136.605
131.758
129.524
129.388
129.319
129.266
127.283
127.165
126.847
126.809
126.611
114.547
112.510
112.139
112.059
109.939
107.144
106.245
100.844
95.482
93.517
77.319
77.000
76.685
62.687
61.864
59.508
57.388
55.867
55.803
53.357
52.044
51.187
49.018
48.813
47.376
34.538
34.337
34.284
33.969
33.783
32.550
31.469
30.677
29.619
29.554
27.855
27.787
26.357
26.224
25.526
25.371
25.204
24.840
24.582
21.336
21.275
COOMe
MeO
O(H)
N
N
Me
Ts
1d
(ketone:anol=1:5)
200
180
160
140
120
100
80
60
40
20

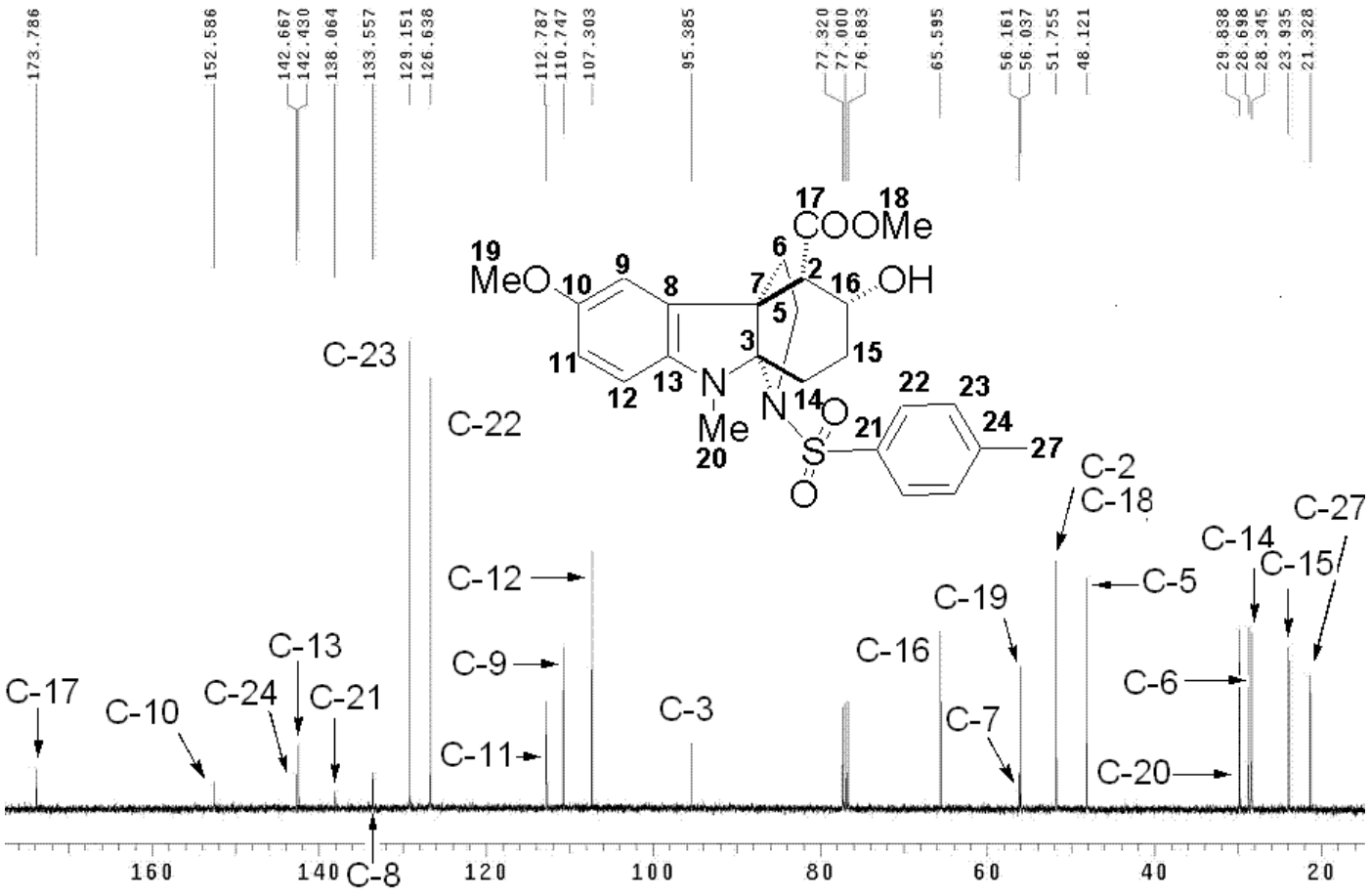

O
N
Boc
N
Ts
1e
10
9
8
7
6
5
4
3
2
1
ppm
1.71
1.77
1.87
0.87
1.01
1.00
0.97
1.04
1.08
1.14
1.02
8.63
1.00
2.03
2.89
1.00
0.93


O
N
Boc
N
Ts
1e
PPM

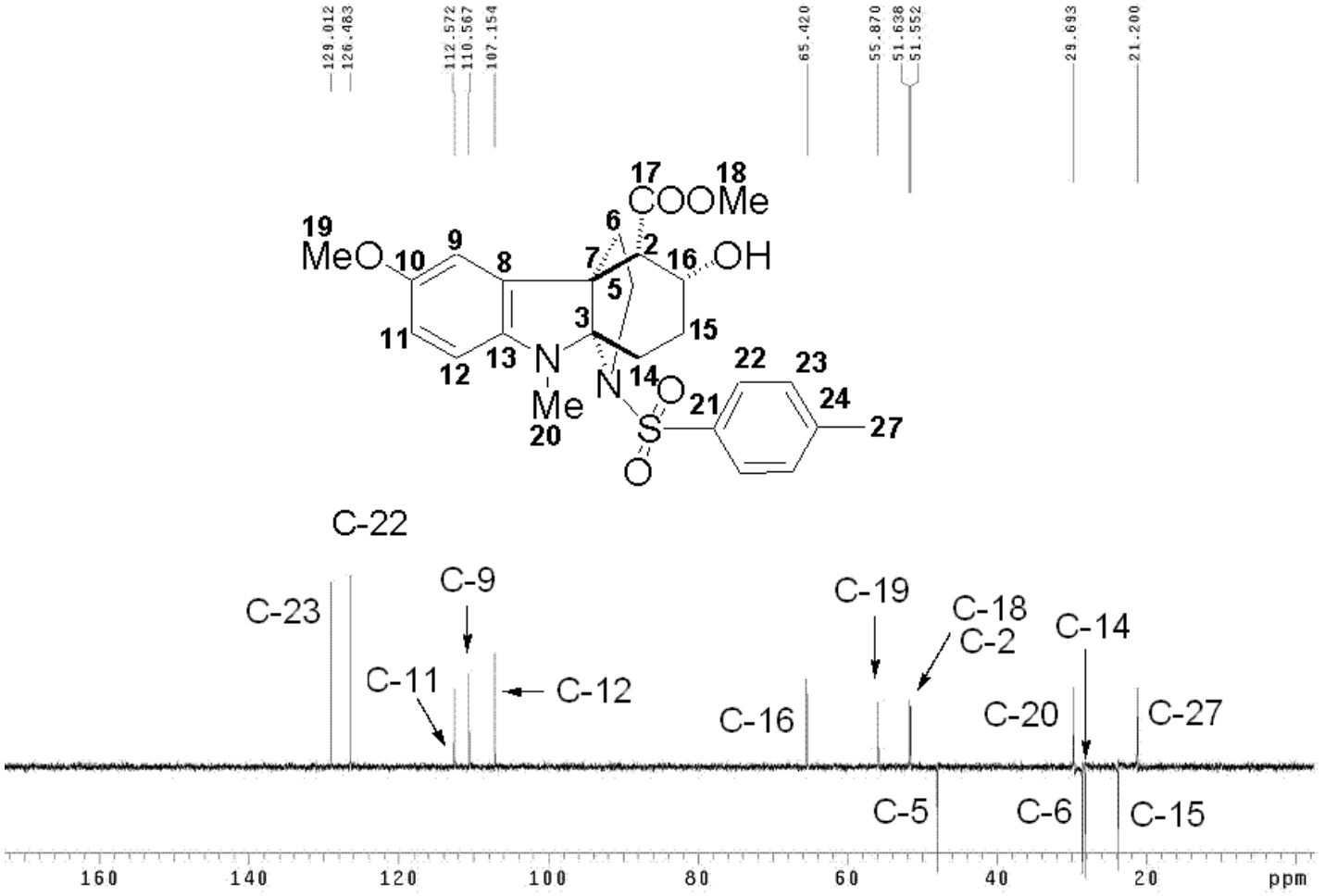
^{1}H NMR Spectrum of β-Hydroxyester 9a



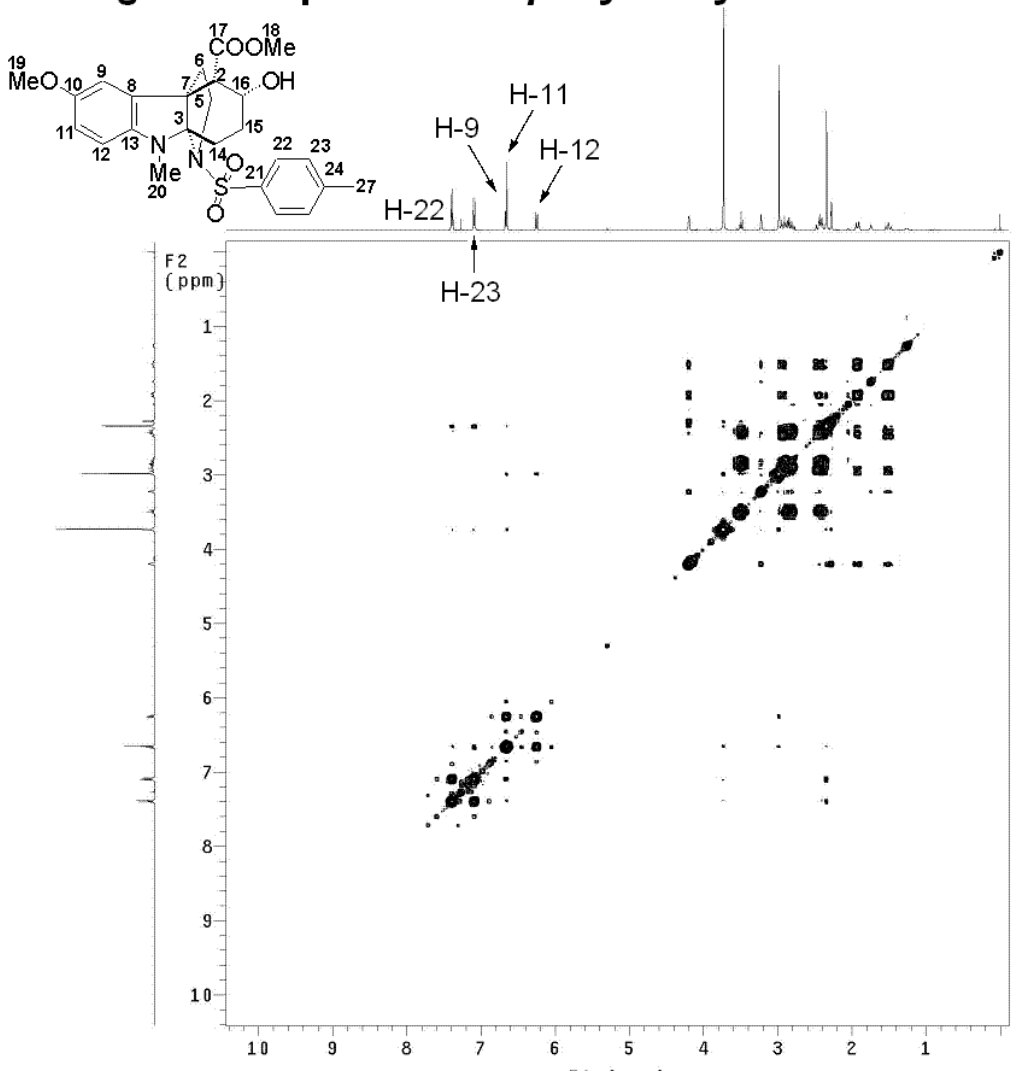
^{13}C NMR Spectrum of β-Hydroxyester 9a

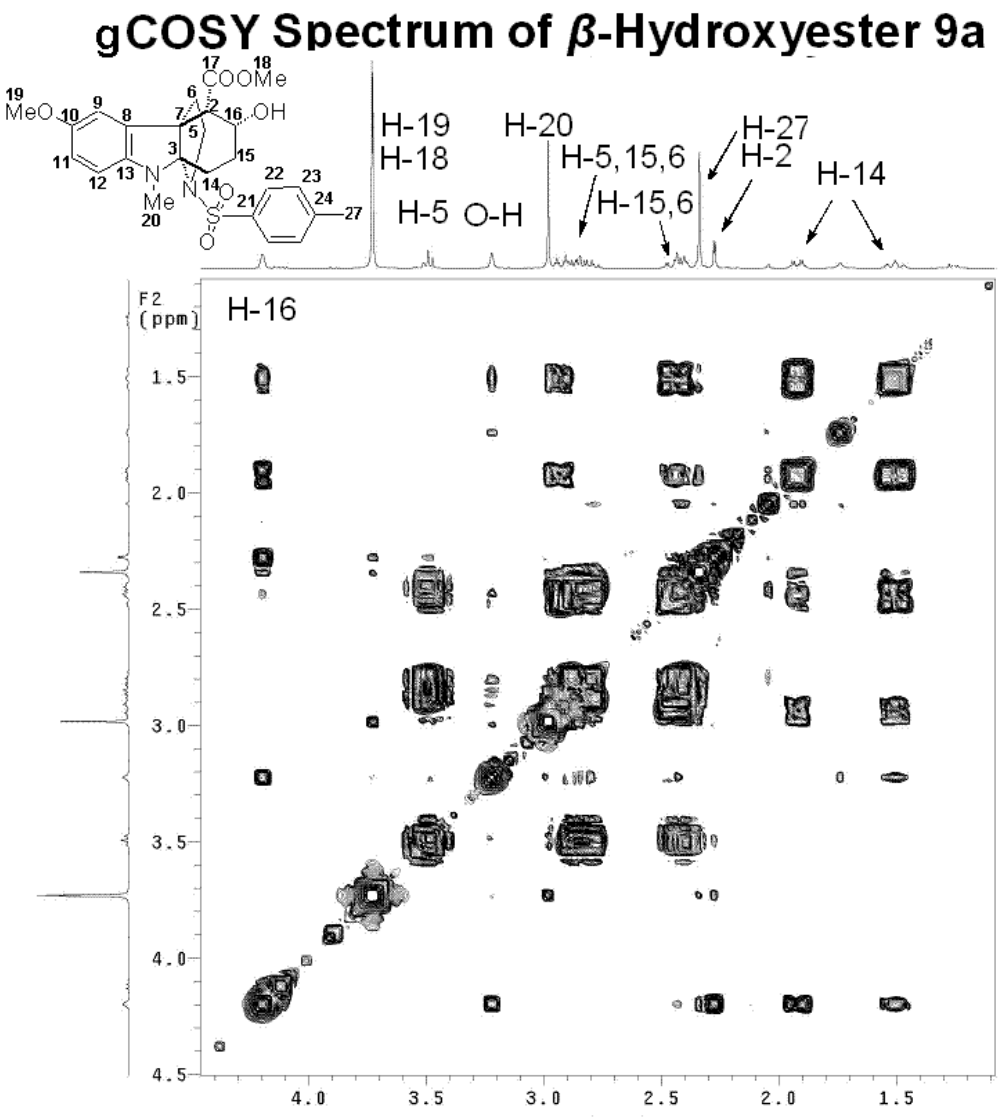


DEPT Spectrum of β-Hydroxyester 9a

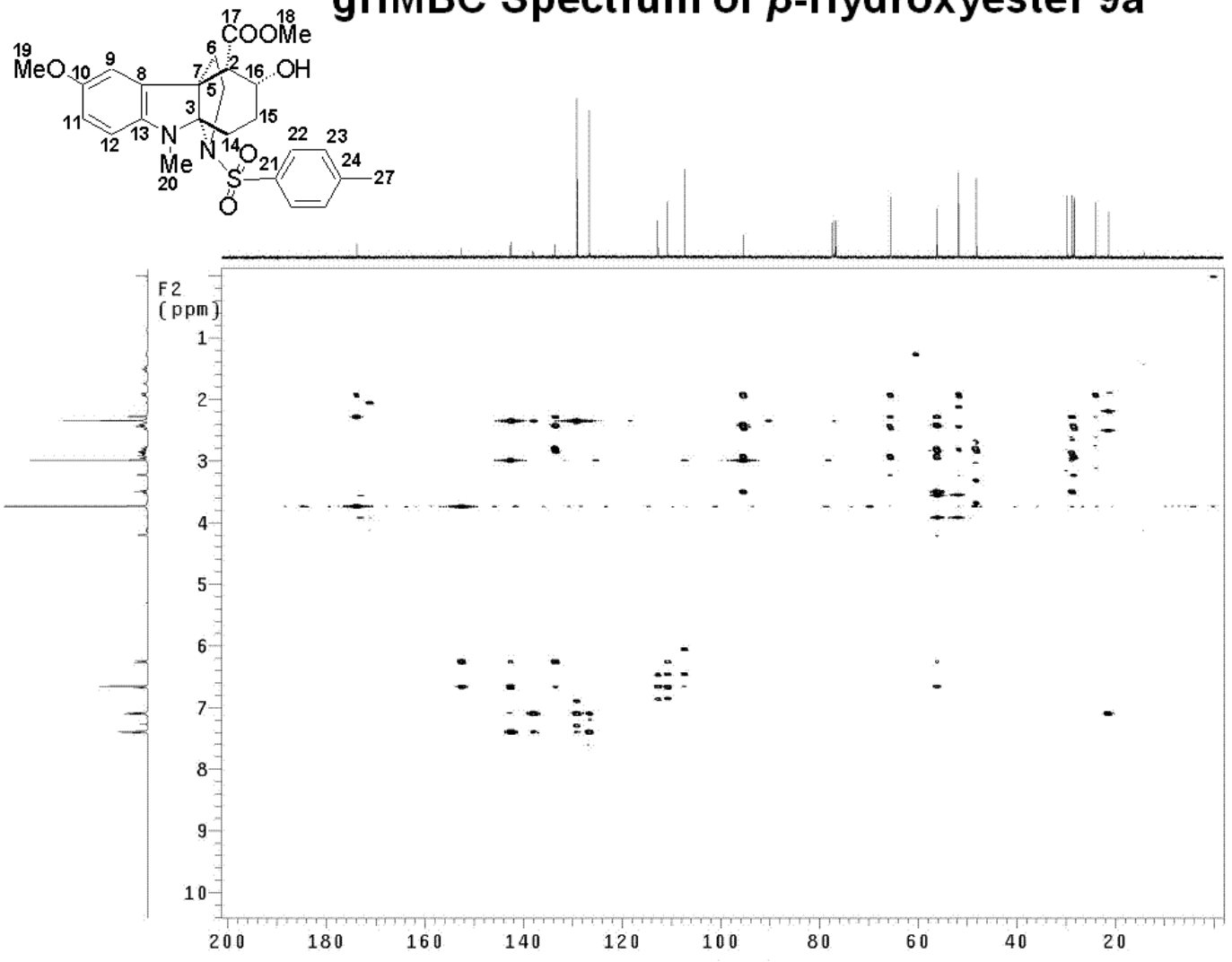


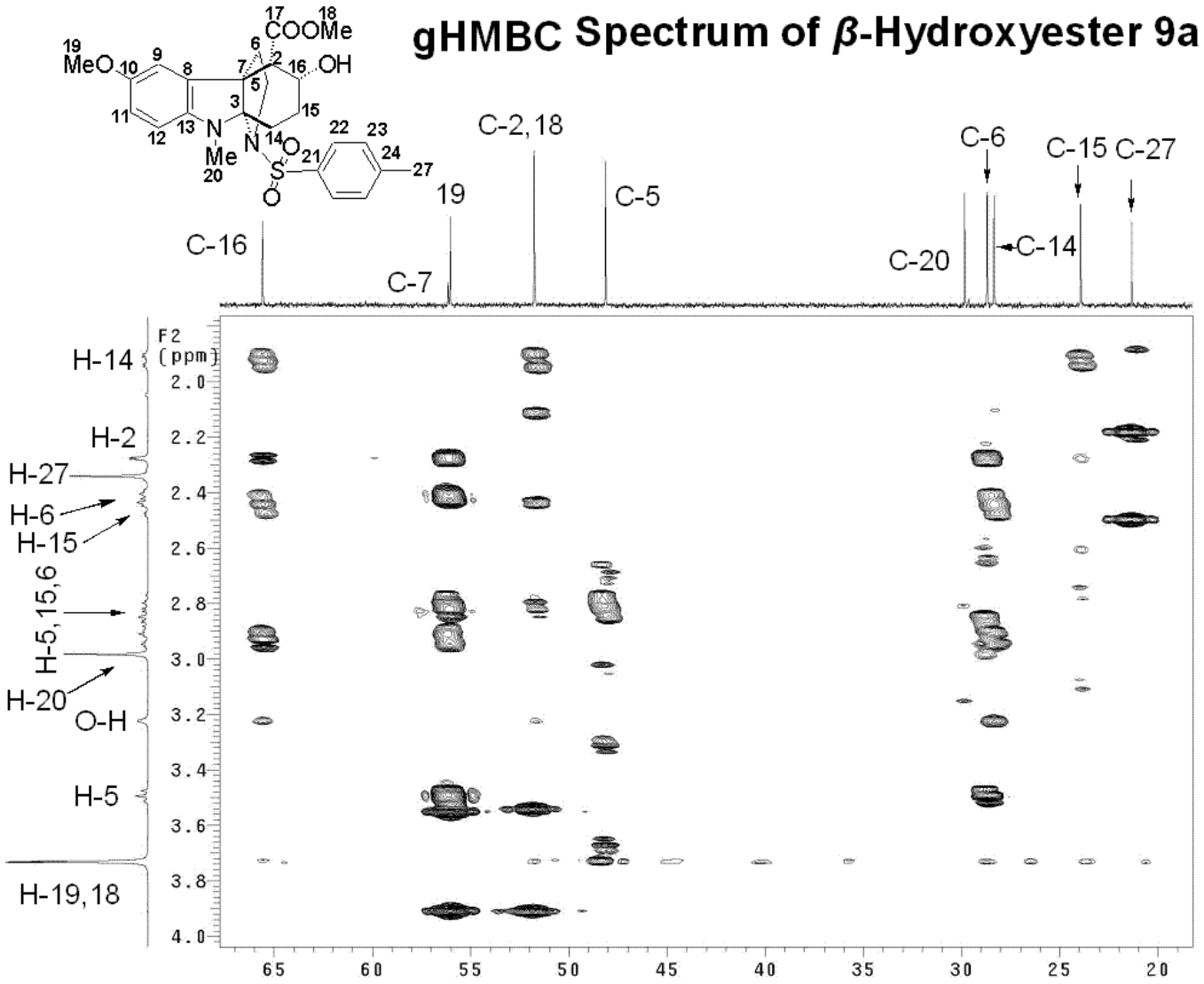
gCOSY Spectrum of β-Hydroxyester 9a

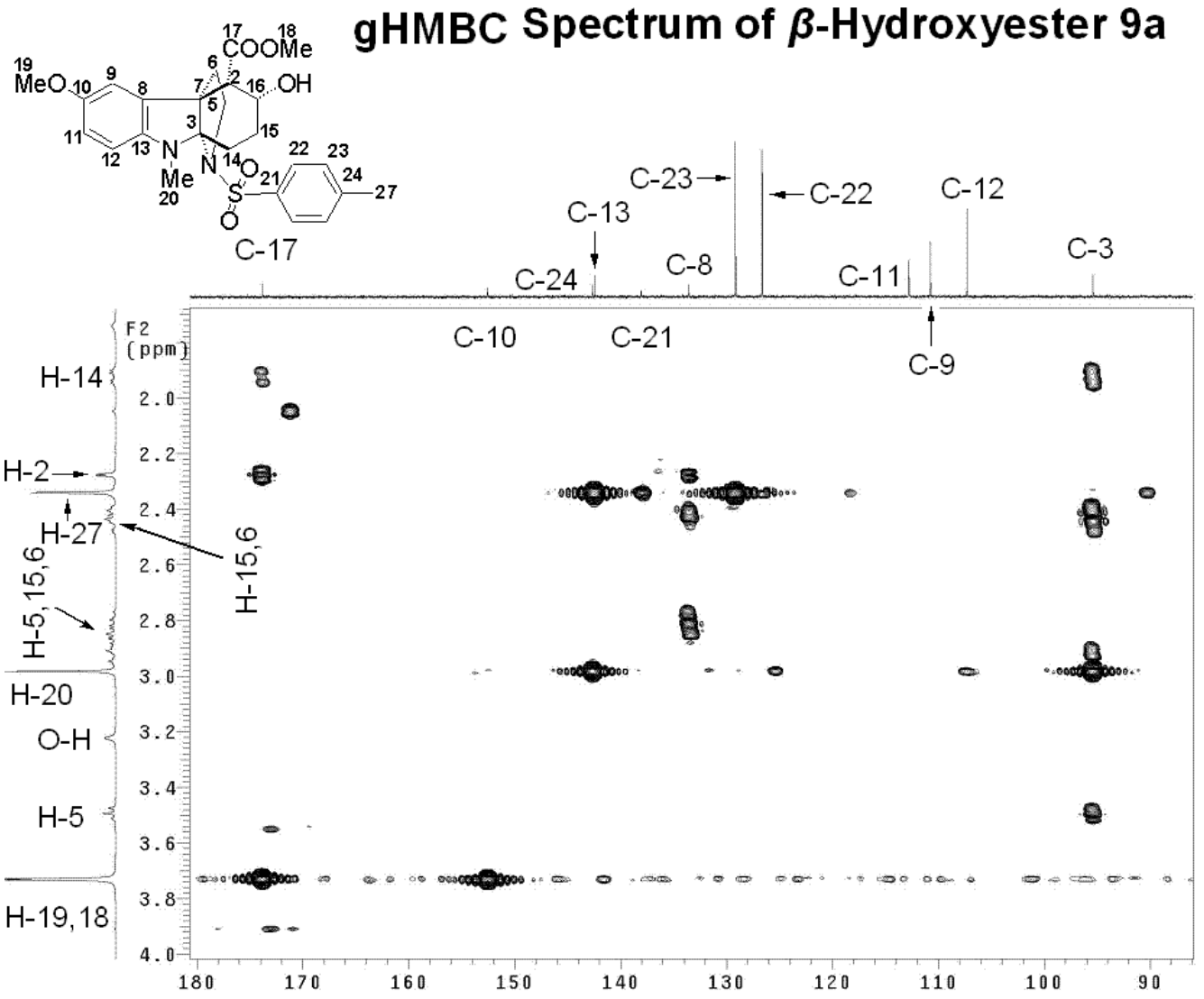


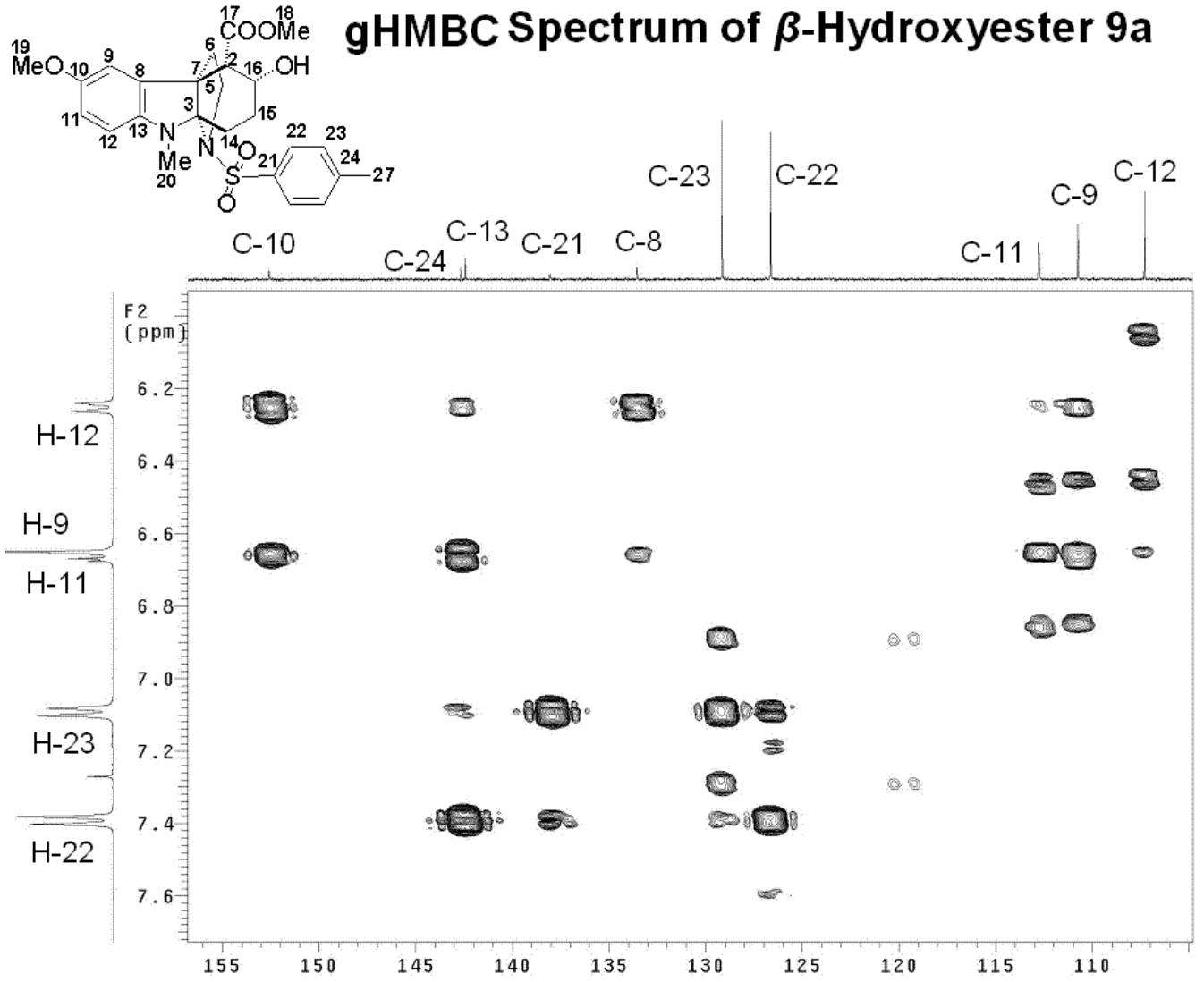

gCOSY Spectrum of β-Hydroxyester 9a
H-19
H-18
H-20
H-5, 15,6
H-27
H-2
H-14
H-5
O-H
H-15,6
H-16
F2 (ppm)
1.5
2.0
2.5
3.0
3.5
4.0
4.5

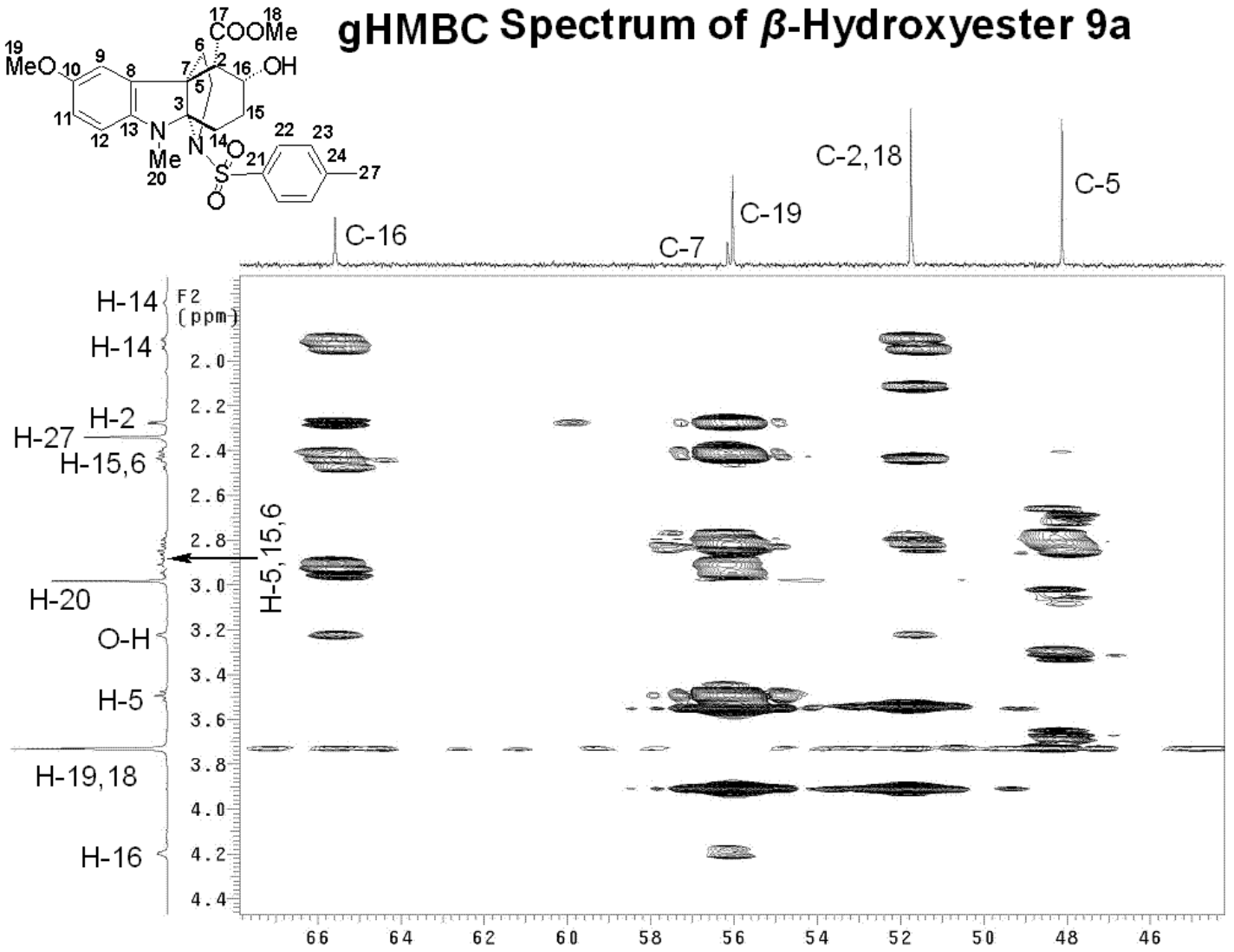
gHMBC Spectrum of β-Hydroxyester 9a

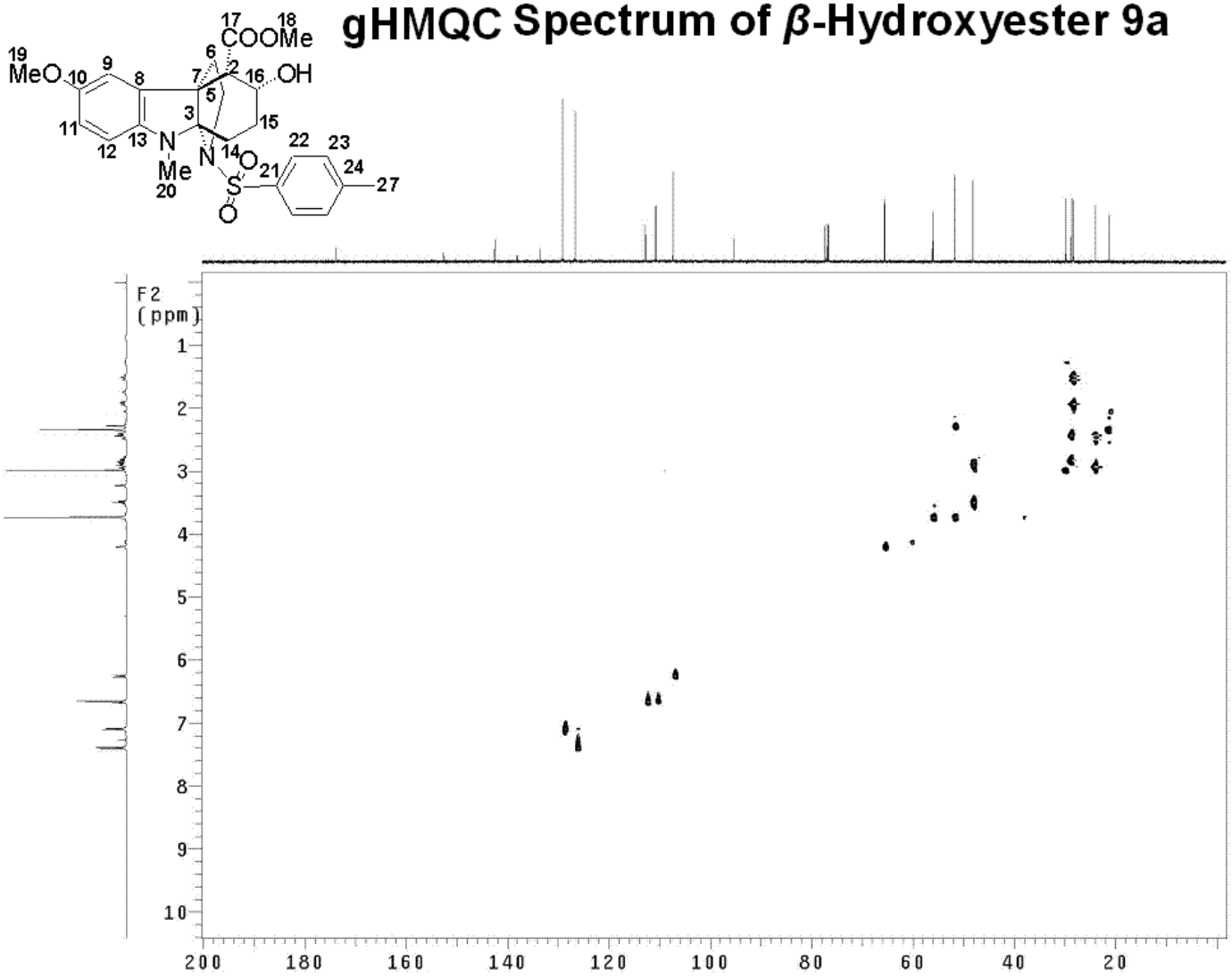


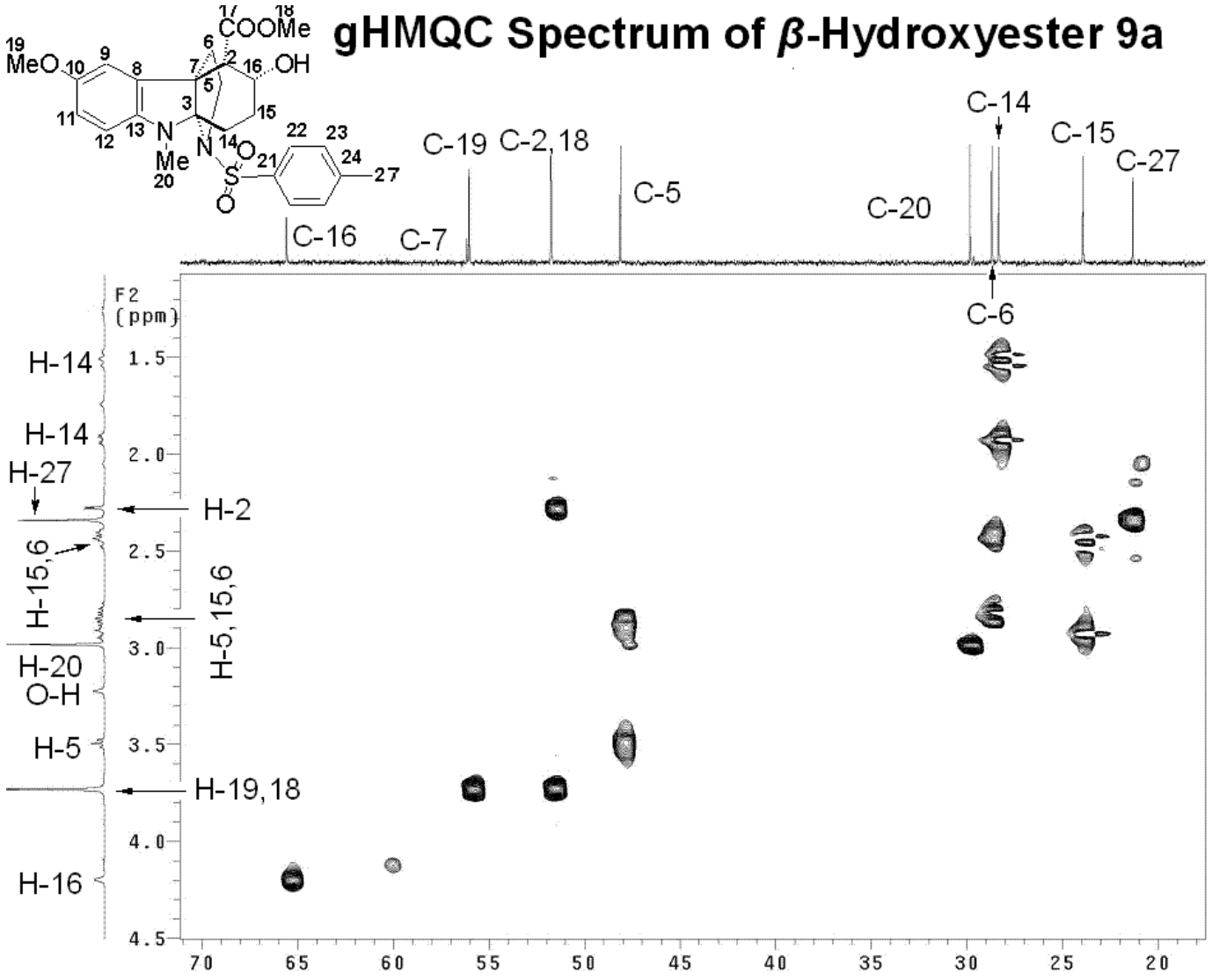

gHMBC Spectrum of β-Hydroxyester 9a
MeO
COOMe
OH
Me
O
S
C-16
C-7
19
C-2,18
C-5
C-20
C-6
C-14
C-15
C-27
H-14
H-2
H-27
H-6
H-15
H-5,15,6
H-20
O-H
H-5
H-19,18
F2 (ppm)
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
65
60
55
50
45
40
35
30
25
20

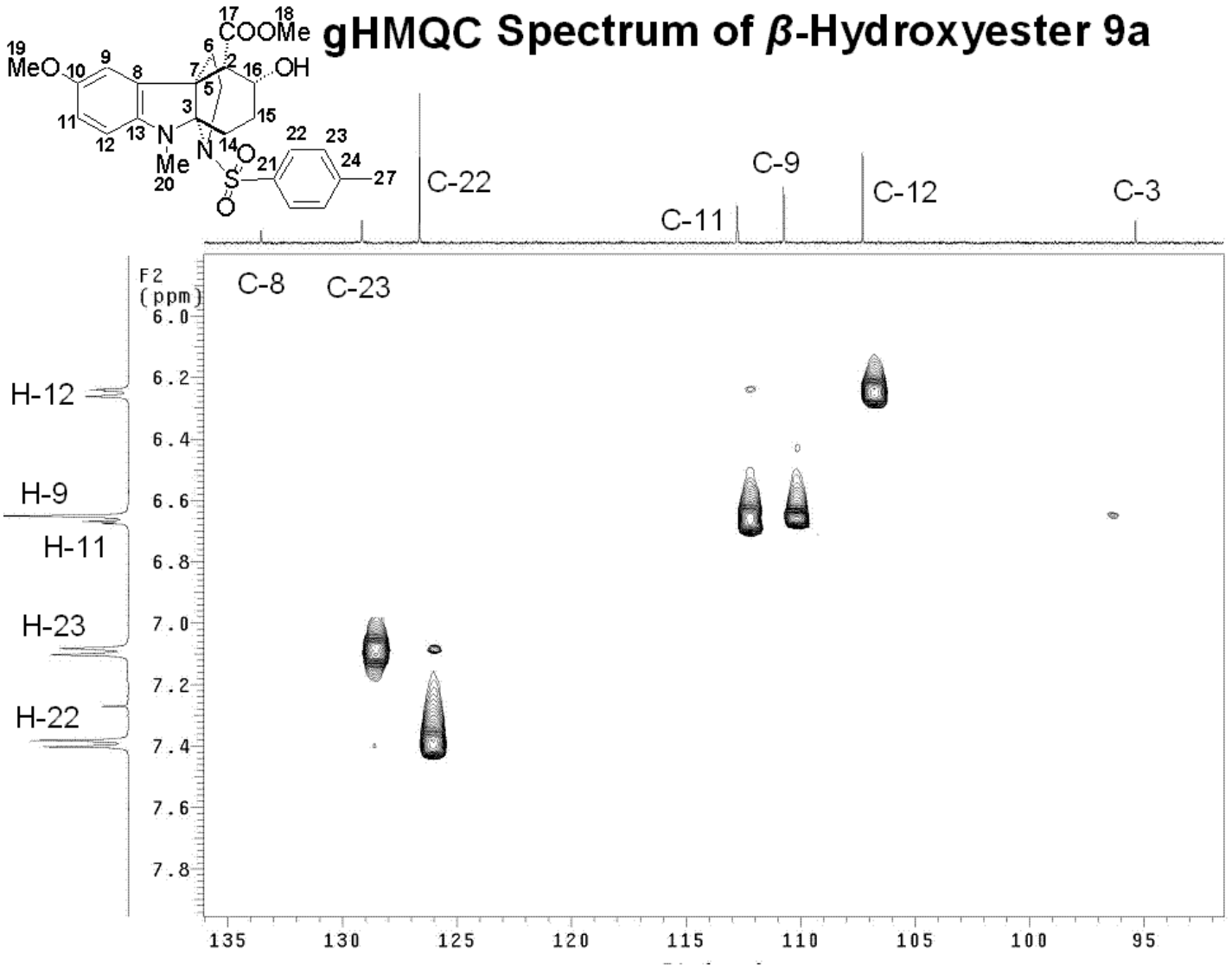

gHMBC Spectrum of β-Hydroxyester 9a
COOMe
MeO
OH
Me
C-17
C-24
C-13
C-8
C-23
C-22
C-11
C-12
C-3
C-10
C-21
C-9
F2 (ppm)
H-14
H-2
H-27
H-5,15,6
H-15,6
H-20
O-H
H-5
H-19,18
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
180
170
160
150
140
130
120
110
100
90

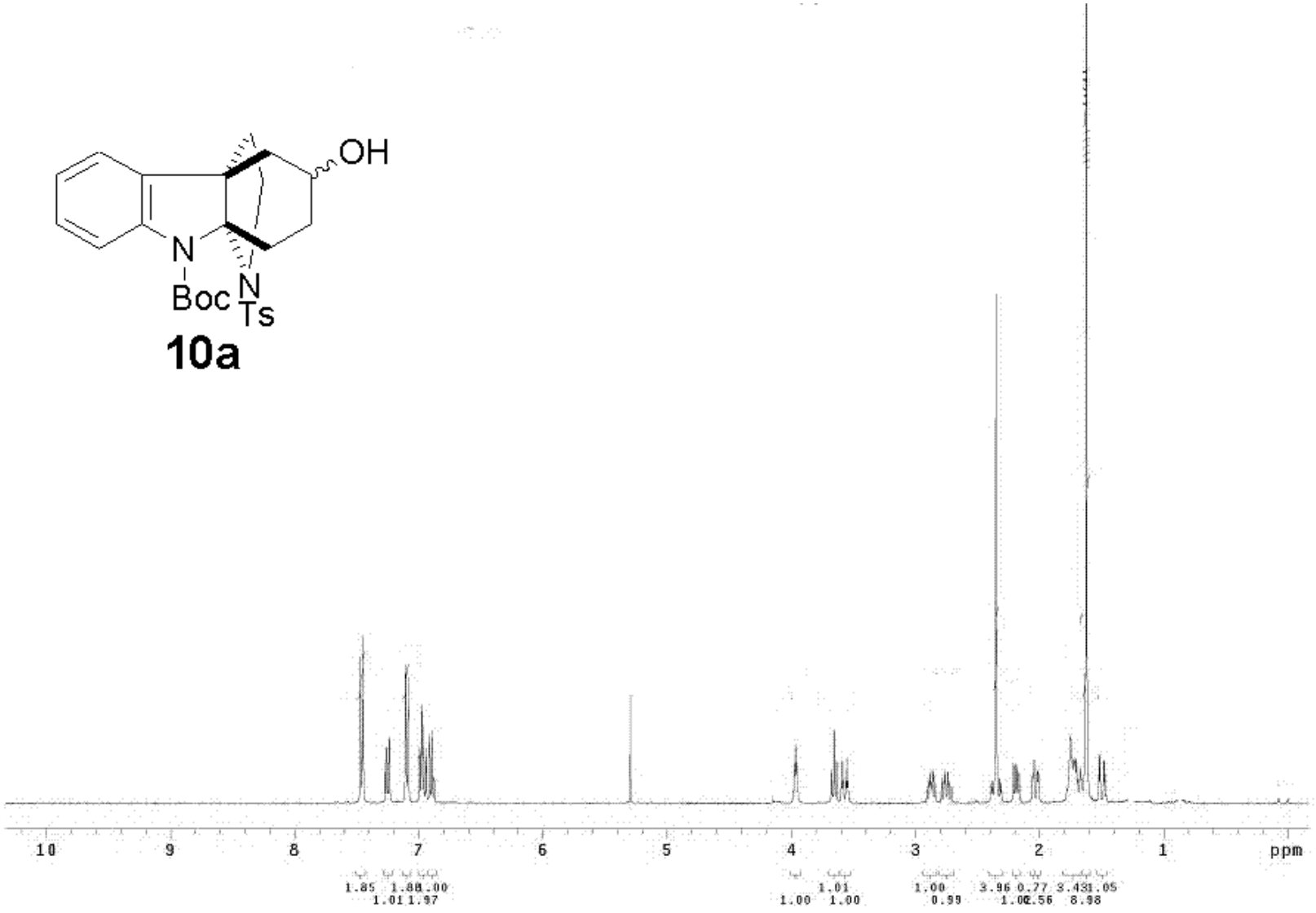

gHMBC Spectrum of β-Hydroxyester 9a
MeO
COOMe
OH
N
Me
S
O
C-10
C-24
C-13
C-21
C-8
C-23
C-22
C-11
C-9
C-12
H-12
H-9
H-11
H-23
H-22
F2 (ppm)
6.2
6.4
6.6
6.8
7.0
7.2
7.4
7.6
155
150
145
140
135
130
125
120
115
110

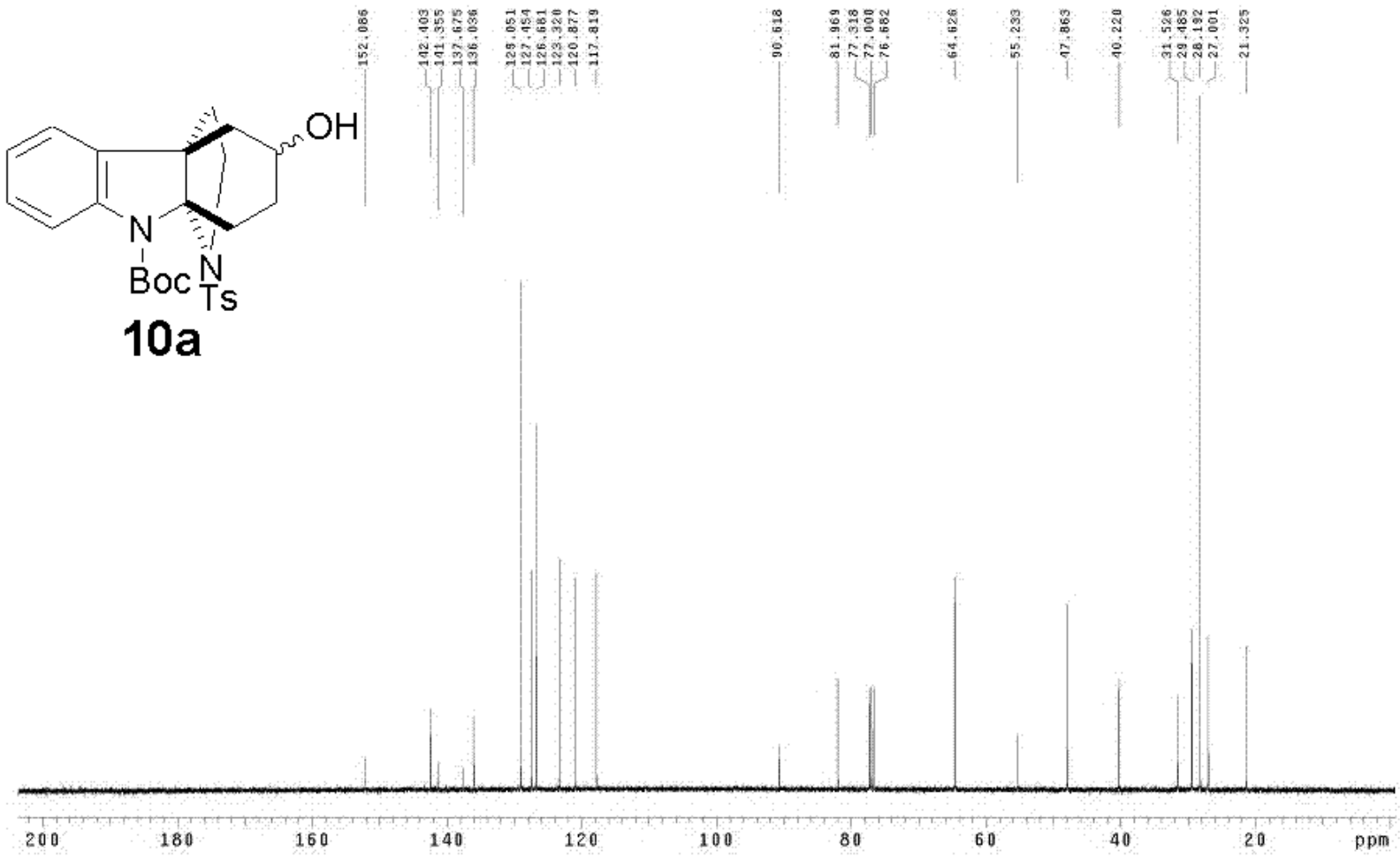

gHMBC Spectrum of β-Hydroxyester 9a
19
MeO
10
9
8
7
6
17
COOMe
18
2
16
OH
5
3
15
11
12
13
N
Me
20
N
14
O
21
22
23
24
27
S
O
C-16
C-7
C-19
C-2,18
C-5
F2
(ppm)
H-14
H-14
H-2
H-27
H-15,6
H-5,15,6
H-20
O-H
H-5
H-19,18
H-16
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
4.2
4.4
66
64
62
60
58
56
54
52
50
48
46

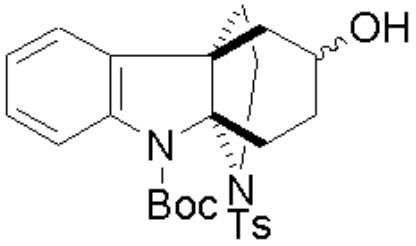

gHMQC Spectrum of β-Hydroxyester 9a
19
MeO
10
9
8
11
12
13
N
Me
20
7
6
5
3
2
17
COOMe
18
16
OH
15
N
14
O
21
S
O
22
23
24
27
F2
(ppm)
1
2
3
4
5
6
7
8
9
10
200
180
160
140
120
100
80
60
40
20


gHMQC Spectrum of β-Hydroxyester 9a
COOMe
MeO
OH
Me
C-14
C-15
C-27
C-19
C-2,18
C-5
C-20
C-16
C-7
C-6
F2 (ppm)
H-14
H-14
H-27
H-2
H-15,6
H-5,15,6
H-20
O-H
H-5
H-19,18
H-16
1.5
2.0
2.5
3.0
3.5
4.0
4.5
70
65
60
55
50
45
40
35
30
25
20


gHMQC Spectrum of β-Hydroxyester 9a
MeO
COOMe
OH
Me
C-22
C-11
C-9
C-12
C-3
C-8
C-23
H-12
H-9
H-11
H-23
H-22
F2 (ppm)
6.0
6.2
6.4
6.6
6.8
7.0
7.2
7.4
7.6
7.8
135
130
125
120
115
110
105
100
95

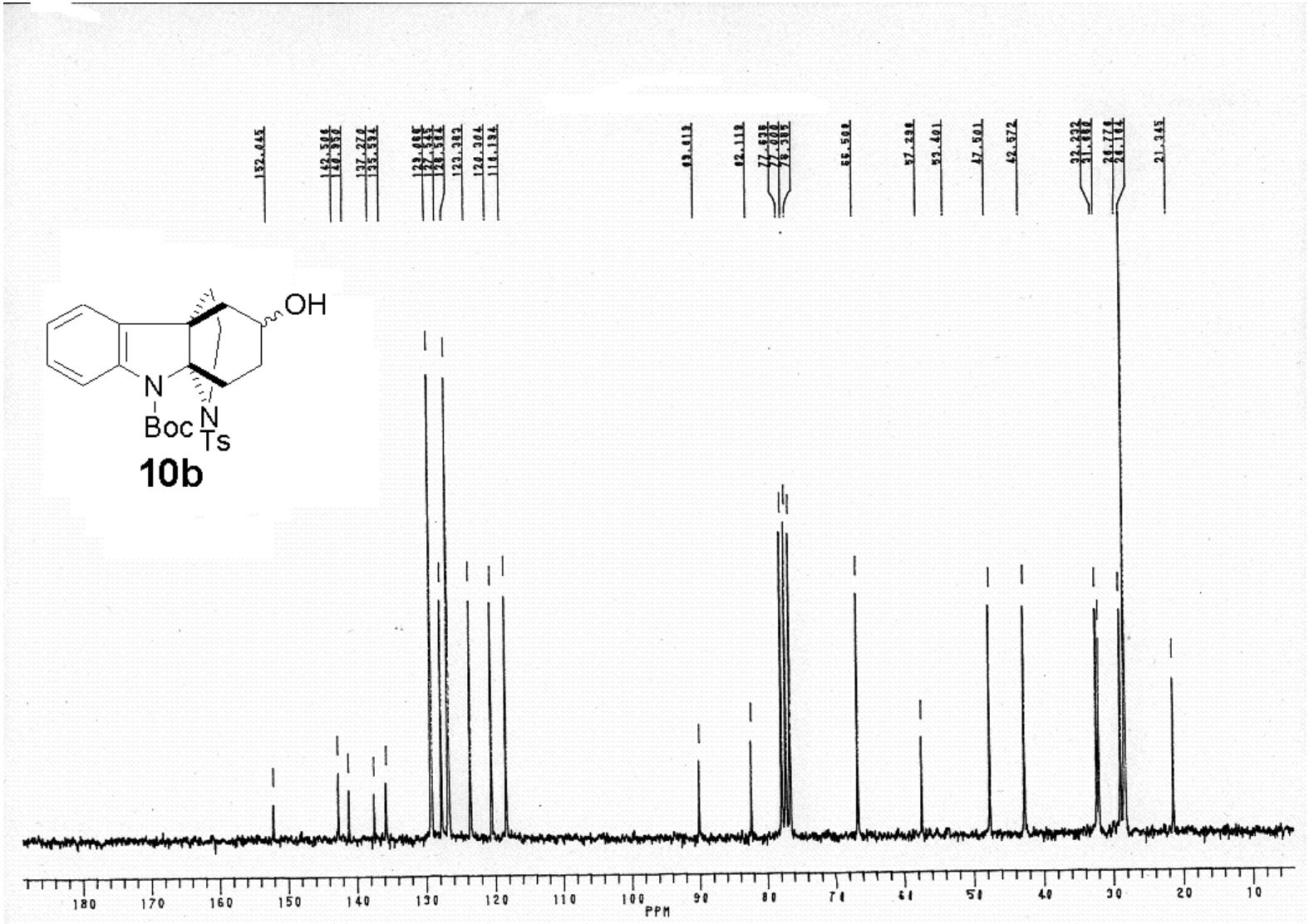

OH
N
Boc
N
Ts
10a
10
9
8
7
6
5
4
3
2
1
ppm

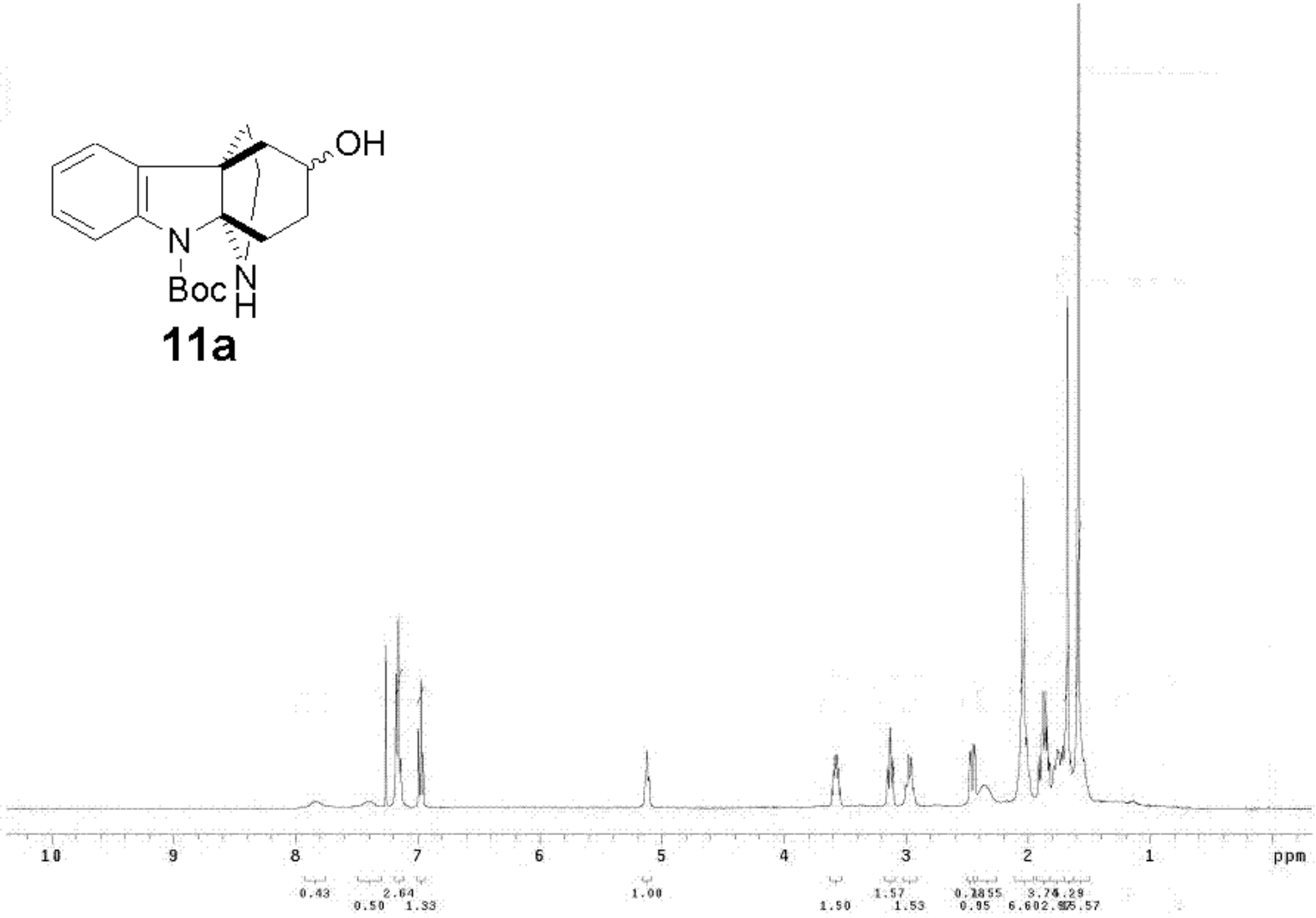

OH
N
Boc
N
Ts
10a
152.086
142.403
141.355
137.675
136.036
129.051
127.454
126.681
123.320
120.877
117.819
90.618
81.969
77.318
77.000
76.682
64.626
55.233
47.863
40.220
31.526
29.485
28.192
27.001
21.325
200
180
160
140
120
100
80
60
40
20
ppm

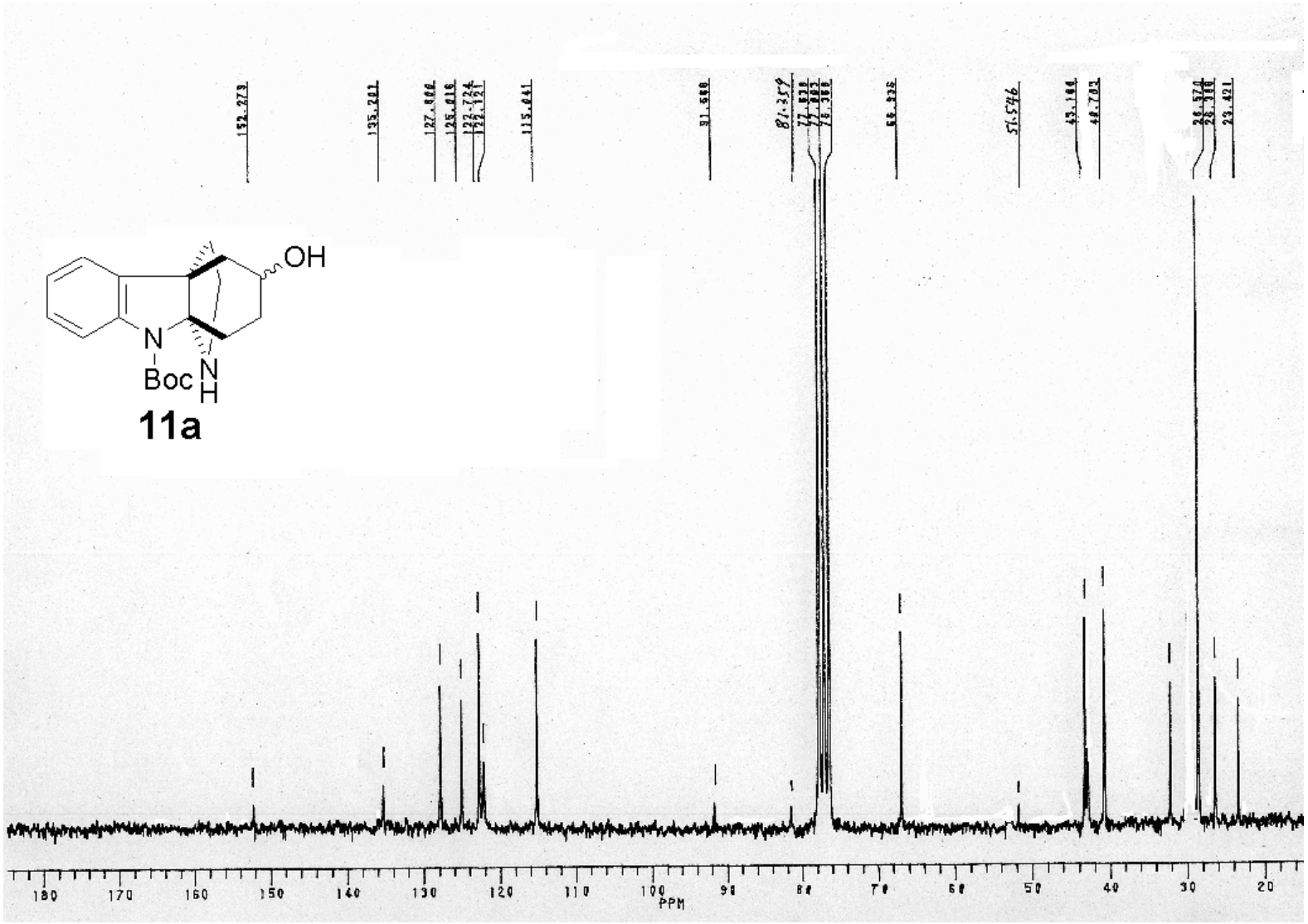

OH
N
Boc
N
Ts

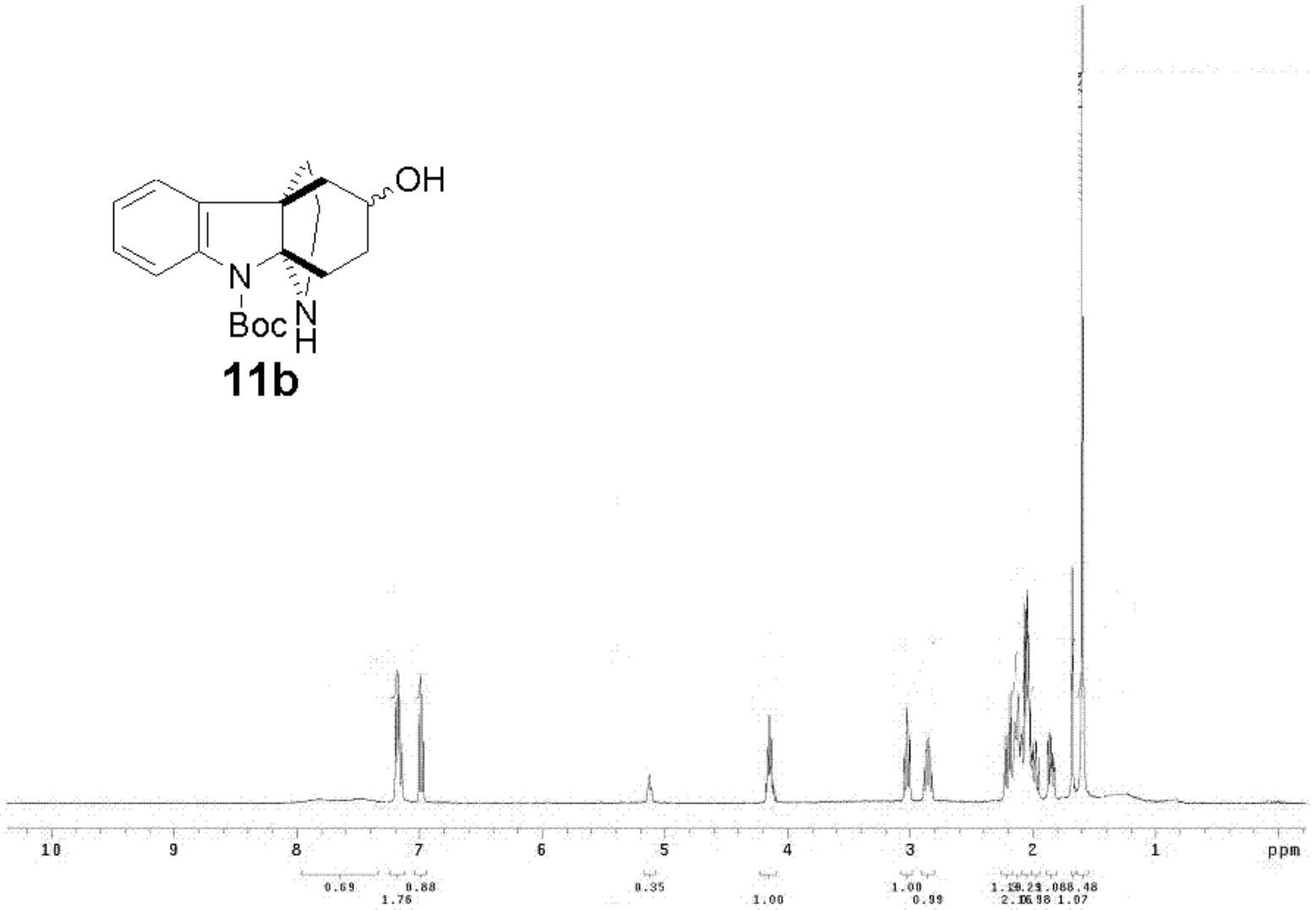
10b

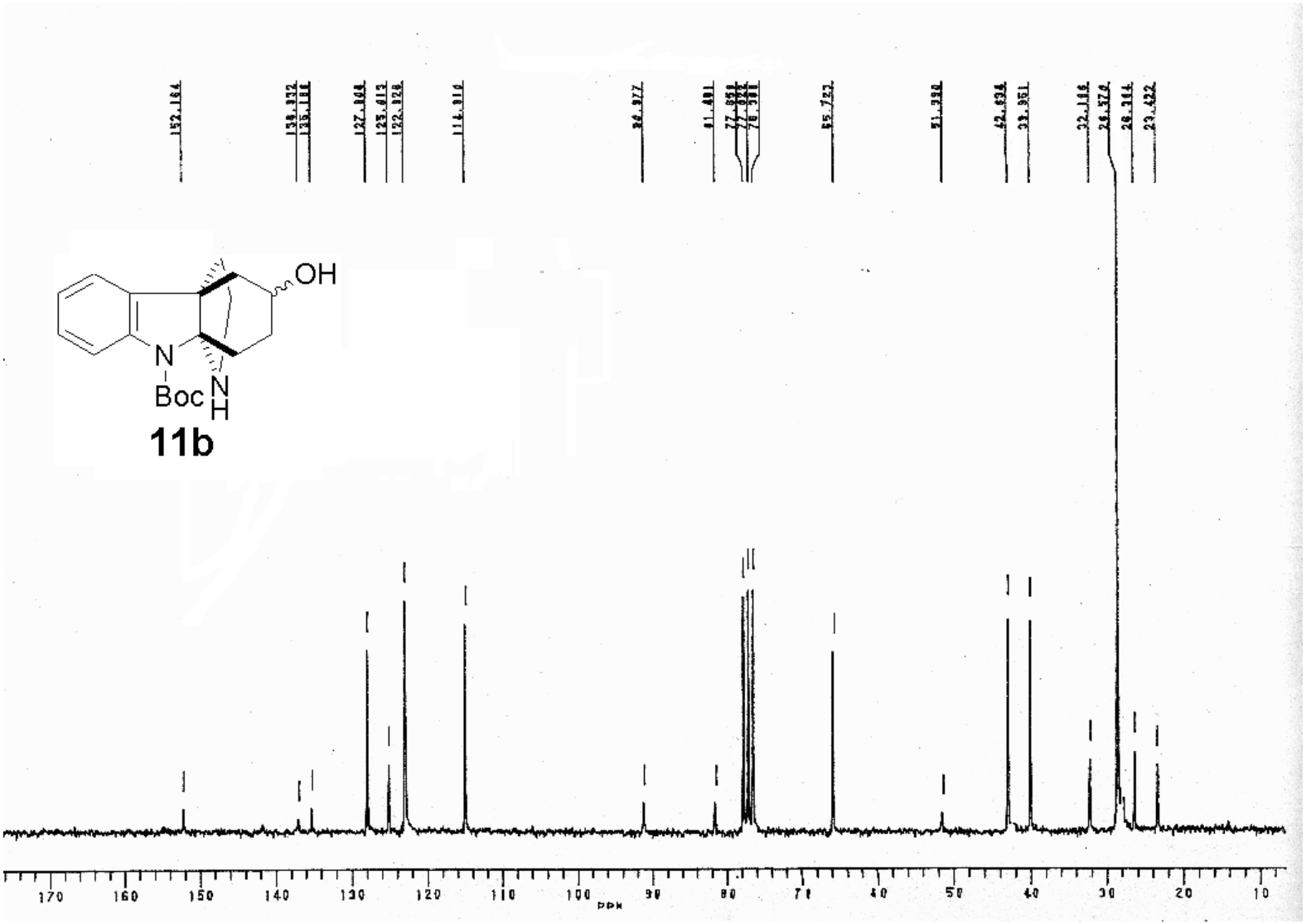
10
9
8
7
6
5
4
3
2
1
ppm
0.90 0.90 0.55
0.46 0.97
1.00
0.51
0.49
0.36 0.48 0.51 0.57
1.68 1.08 0.60 1.88 0.69

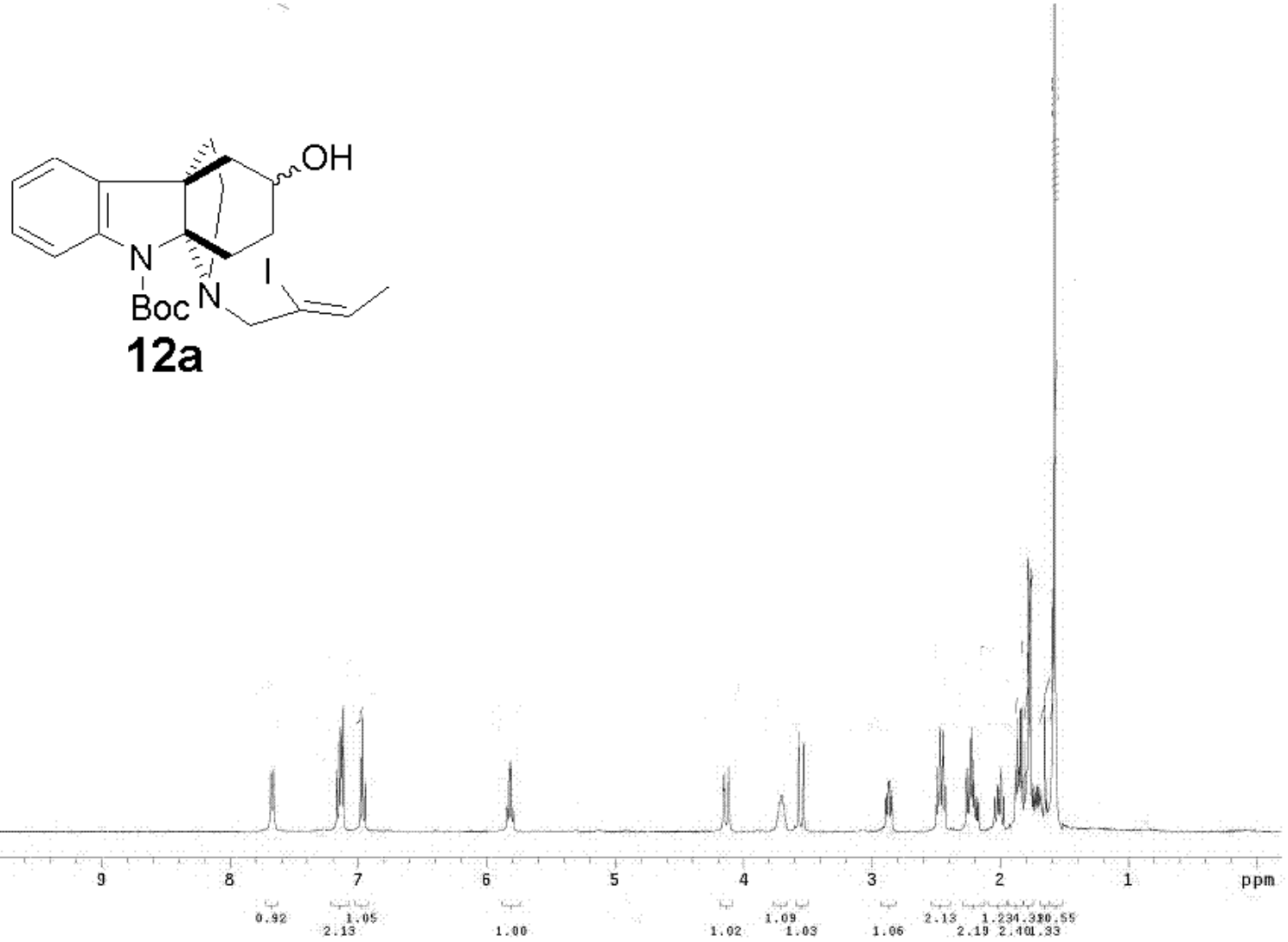

OH
N
Boc
N
Ts
10b
PPM

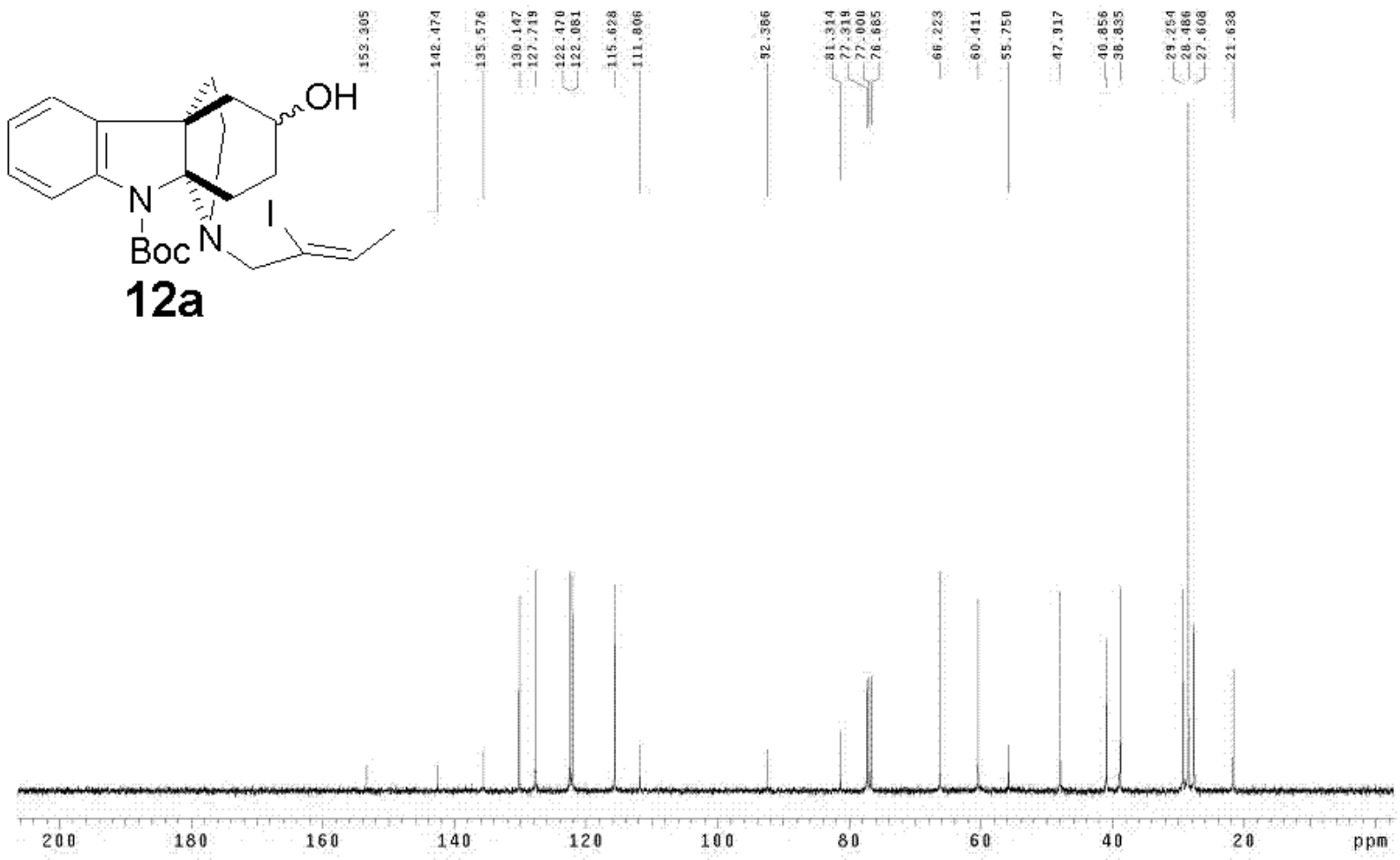

OH
N
Boc
N
H
11a
10
9
8
7
6
5
4
3
2
1
ppm
0.43
2.64
0.50
1.33
1.00
1.50
1.57
1.53
0.95
6.60

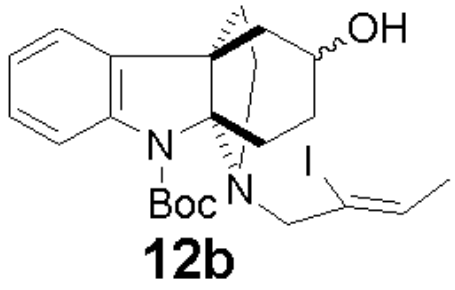

OH
N
Boc
N
H
11a
PPM


OH
N
Boc
N
H
11b
10
9
8
7
6
5
4
3
2
1
ppm
0.69
0.88
1.76
0.35
1.00
1.00
0.99

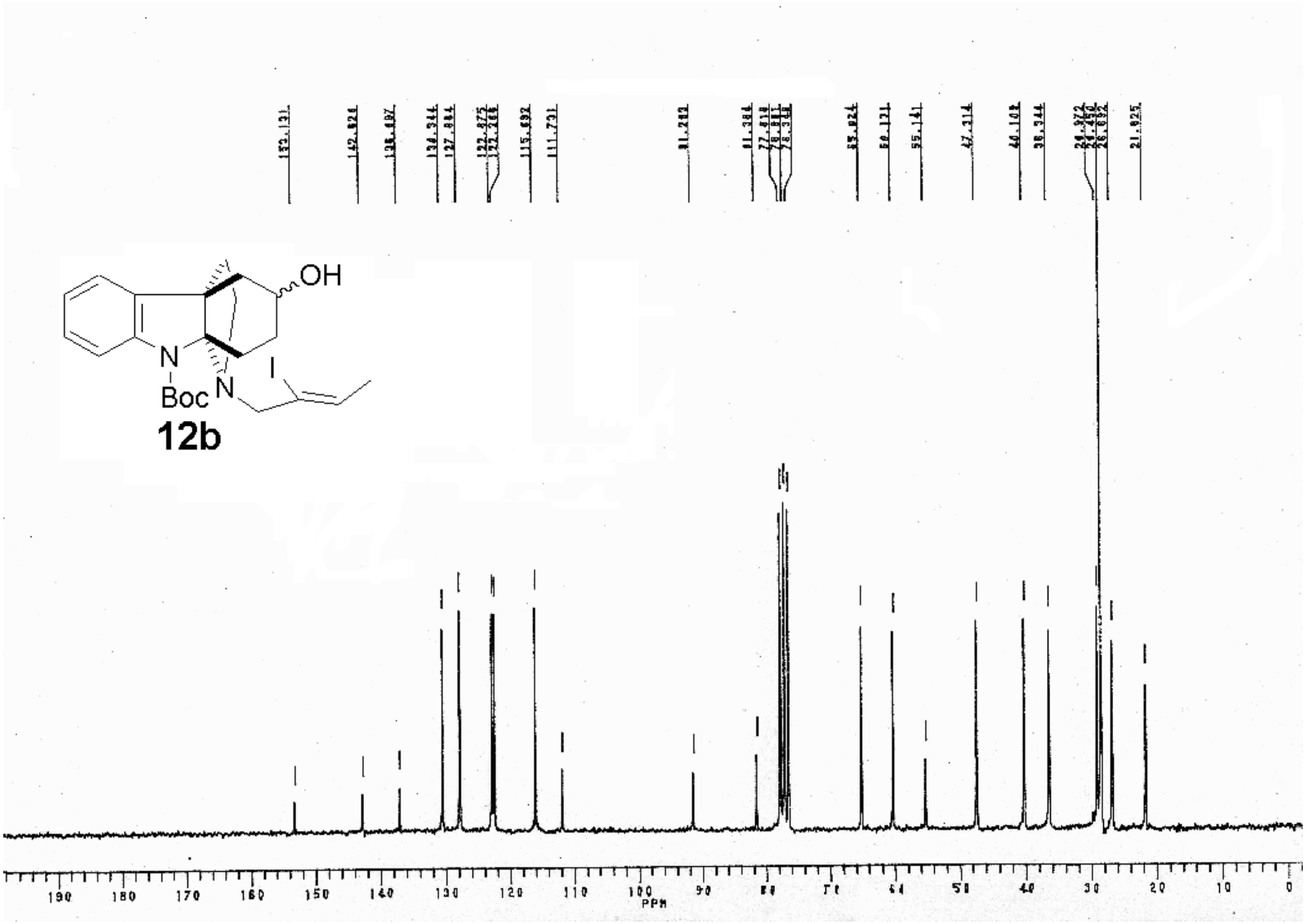

OH
N
Boc
N
H
11b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

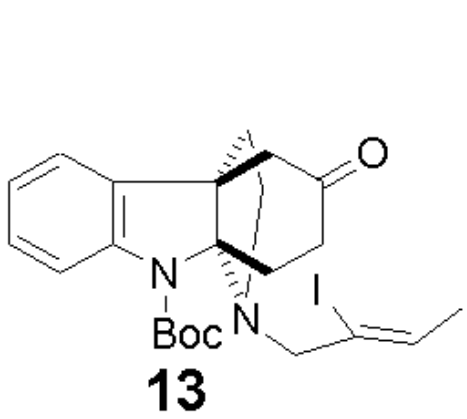

OH
N
Boc
N
I
12a
10
9
8
7
6
5
4
3
2
1
ppm
0.92
1.05
2.13
1.00
1.02
1.09
1.03
1.06
2.13
1.23
4.38
0.55
2.19
2.40
1.33


OH
N
Boc
N
I
12a
153.305
142.474
135.576
130.147
127.719
122.470
122.081
115.628
111.806
92.386
81.314
77.319
77.000
76.685
66.223
60.411
55.750
47.917
40.856
38.835
29.254
28.486
27.608
21.638
200
180
160
140
120
100
80
60
40
20
ppm



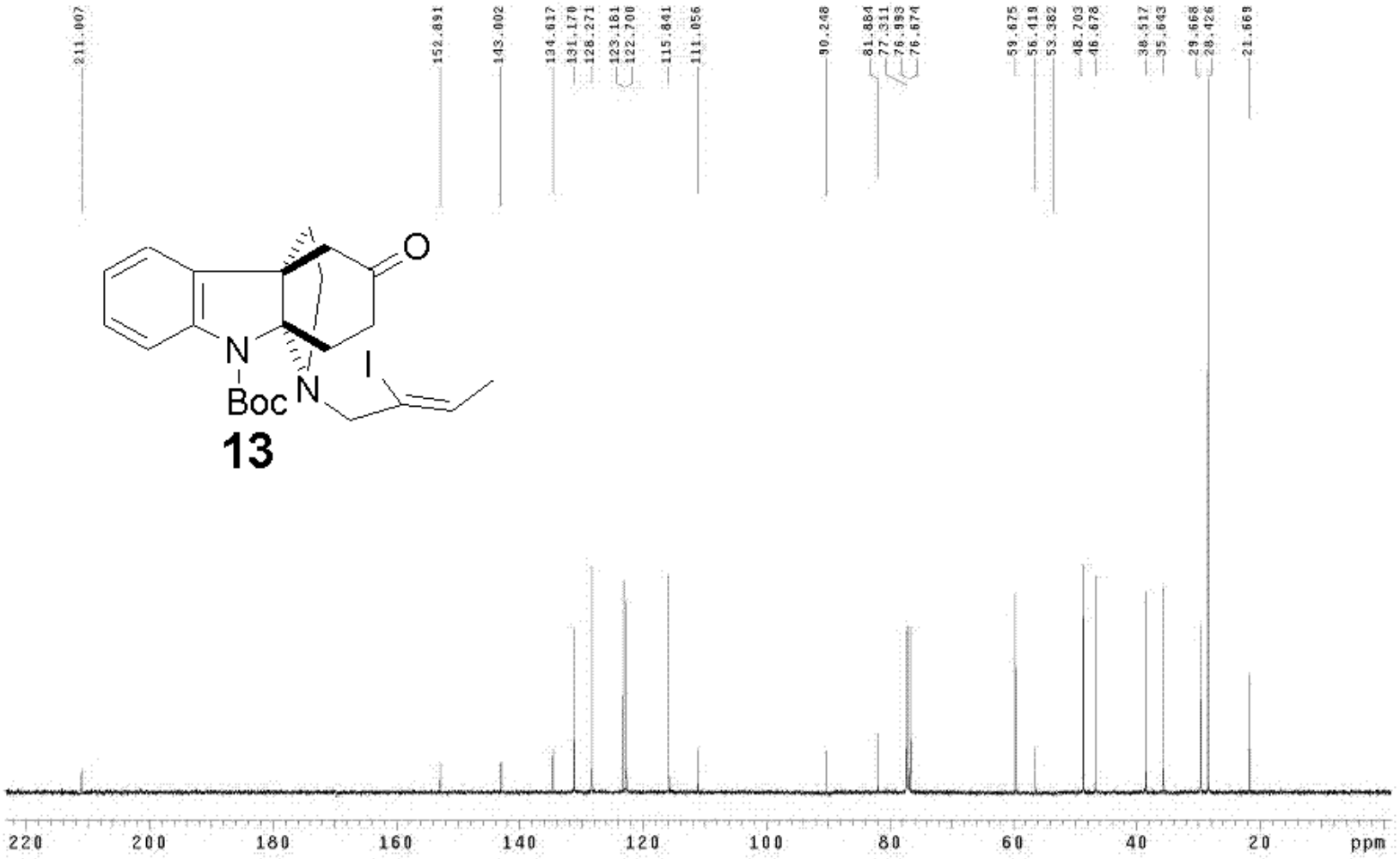
12b

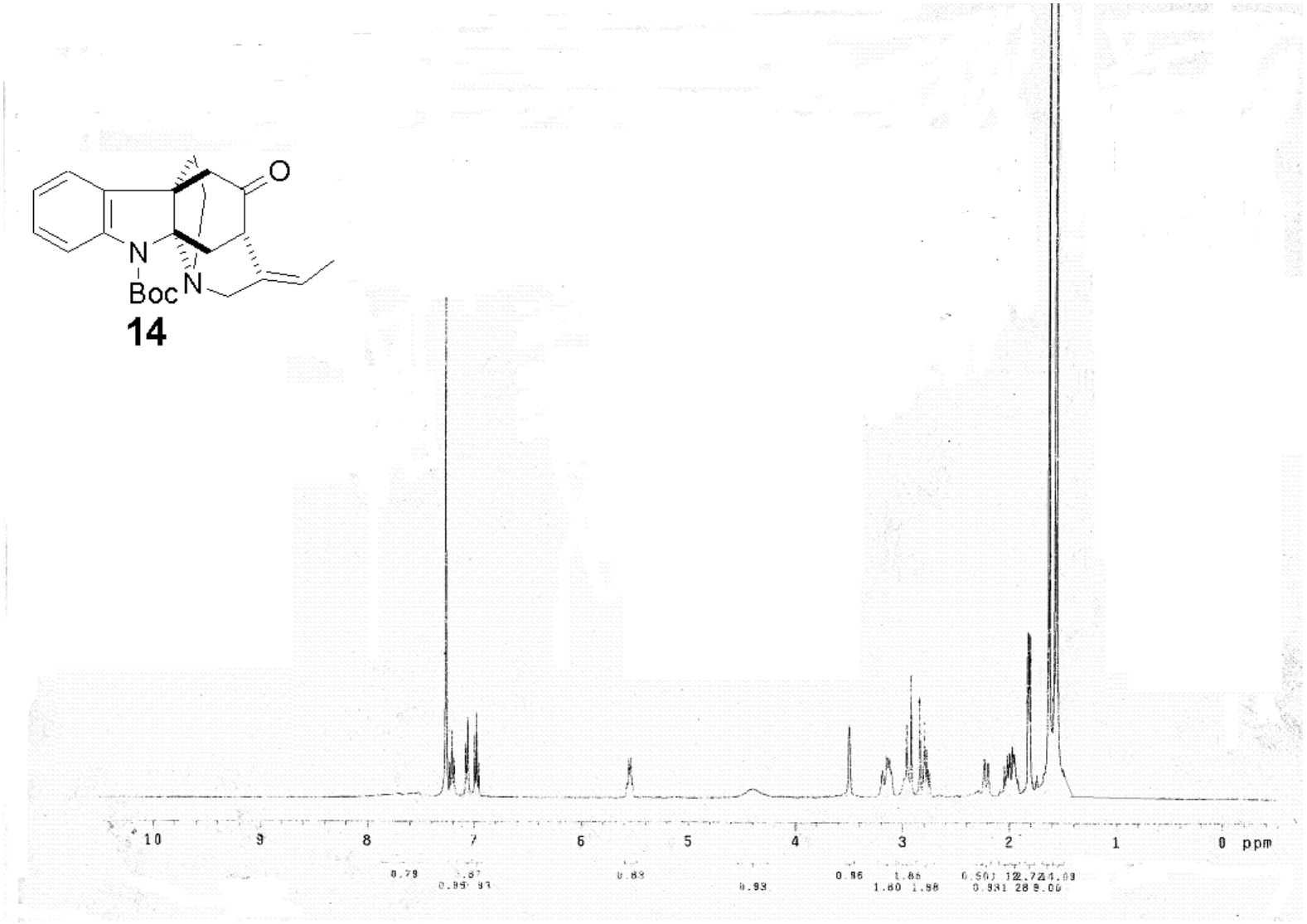

OH
N
Boc
N
I
12b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM

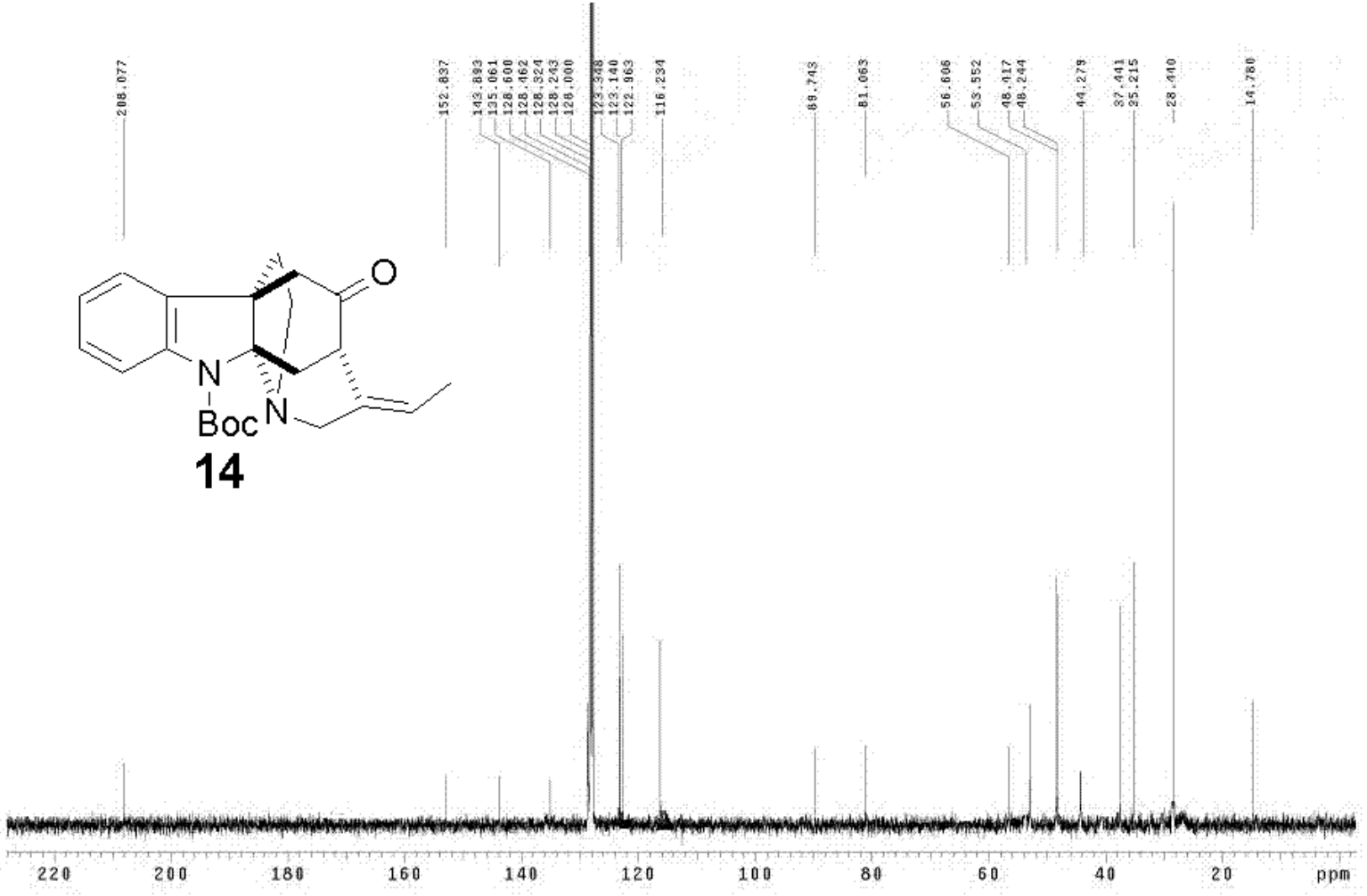

O
N
Boc
N
I

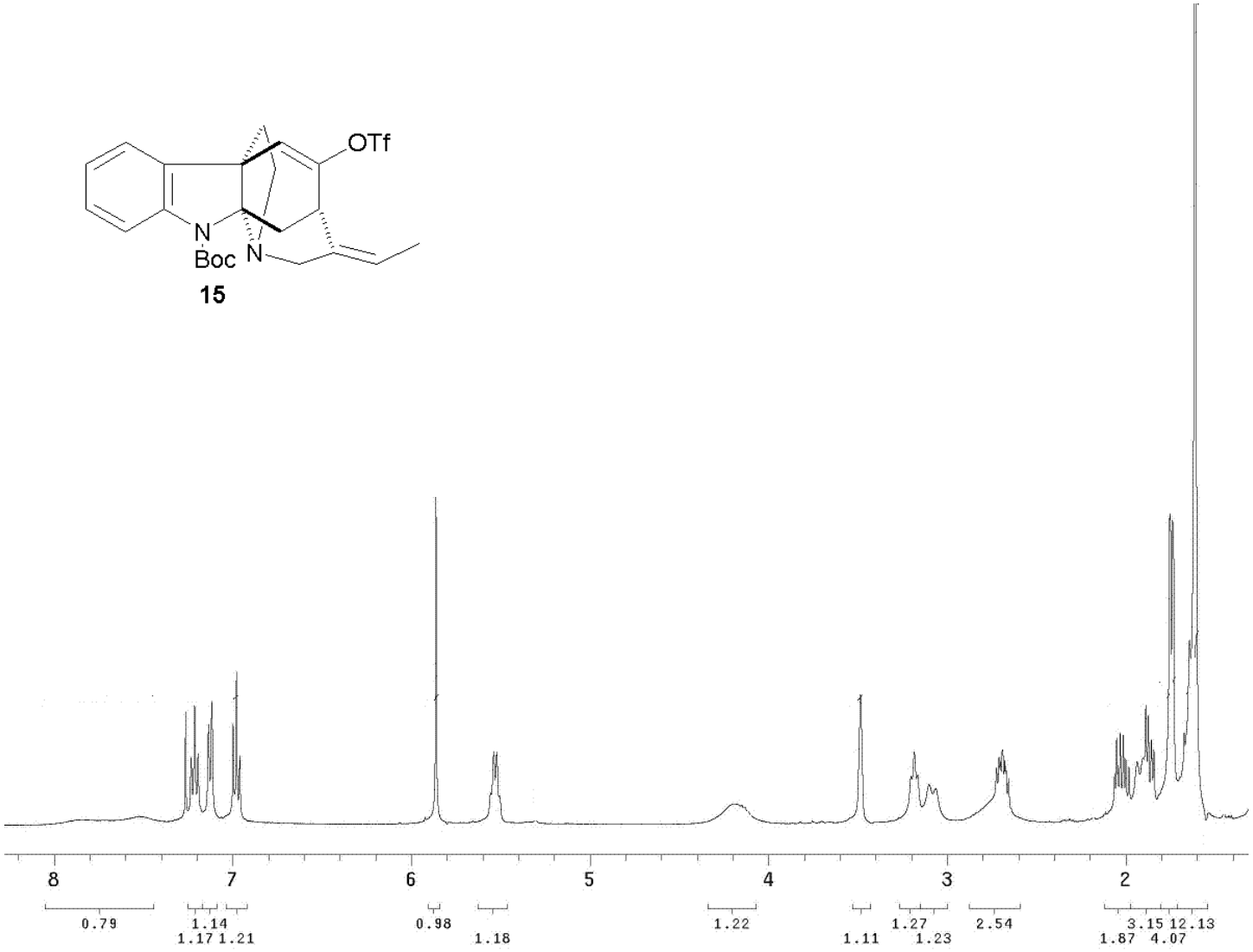
13

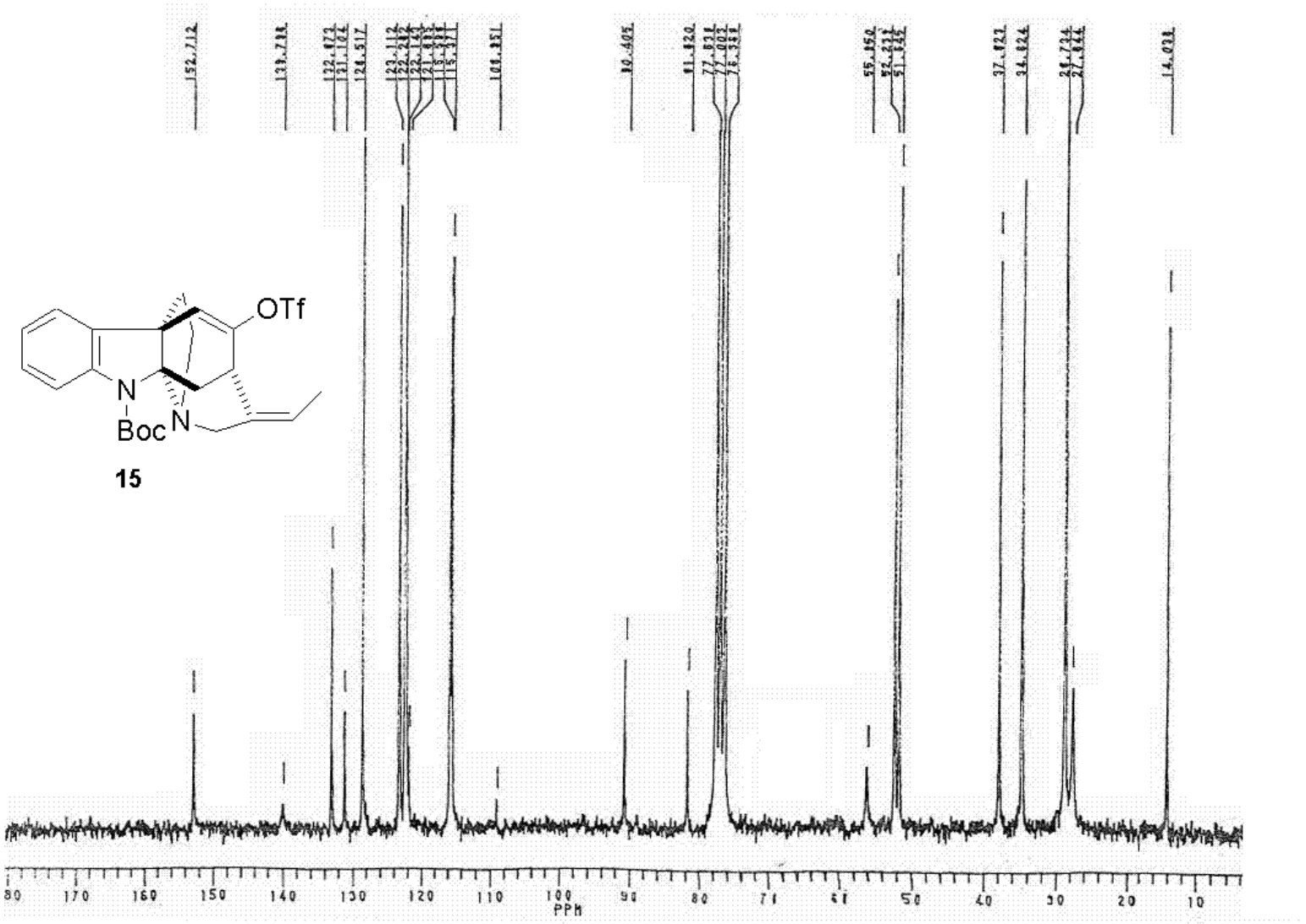
10
9
8
7
6
5
4
3
2
1
ppm
1.44
3.63
1.79
1.71
1.75
1.74
1.70
0.86
1.06
3.00

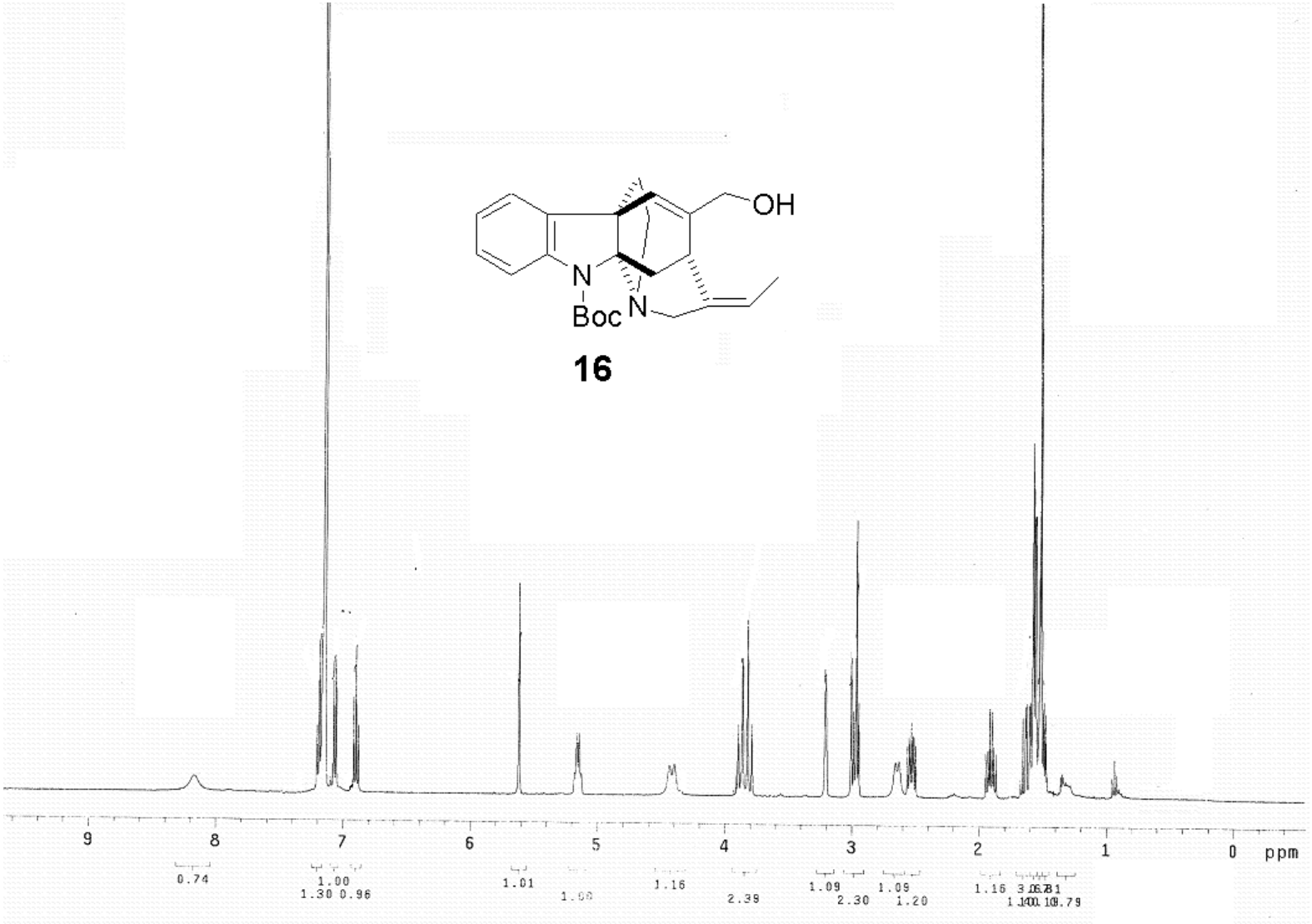

211.007
152.891
143.002
134.617
131.170
128.271
123.161
122.700
115.841
111.056
90.248
81.884
77.311
76.993
76.674
59.675
56.419
53.382
48.703
46.678
38.517
35.643
29.668
29.426
21.669
O
N
Boc
N
I
13
220
200
180
160
140
120
100
80
60
40
20
ppm

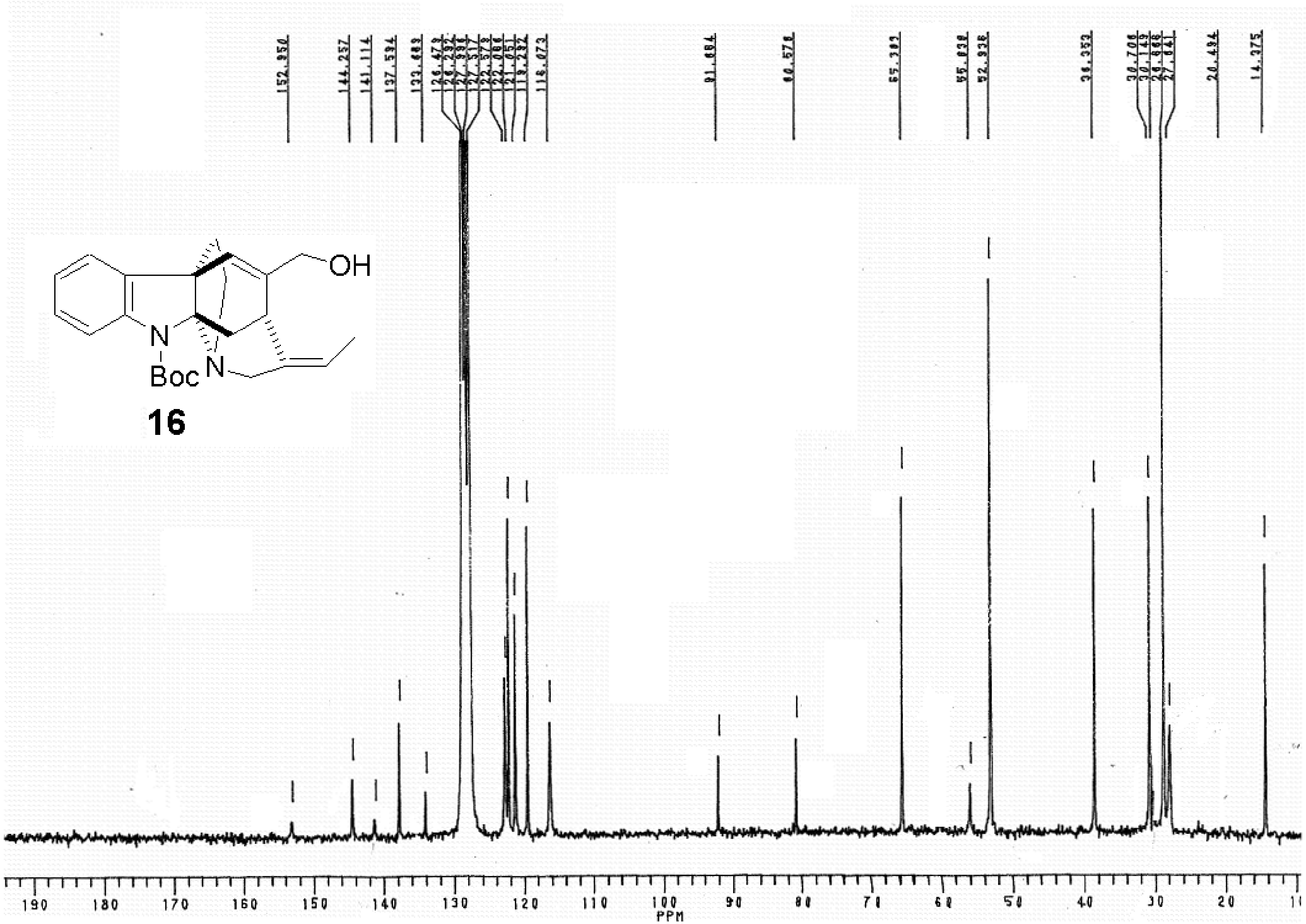

O
N
Boc
N
14
10
9
8
7
6
5
4
3
2
1
0 ppm


208.077
152.837
143.893
135.061
128.600
128.462
128.324
128.243
128.000
123.348
123.140
122.963
116.234
69.743
81.063
56.606
53.552
48.017
48.244
44.279
37.441
25.215
28.400
14.780
O
N
Boc
N
14
220
200
180
160
140
120
100
80
60
40
20
ppm

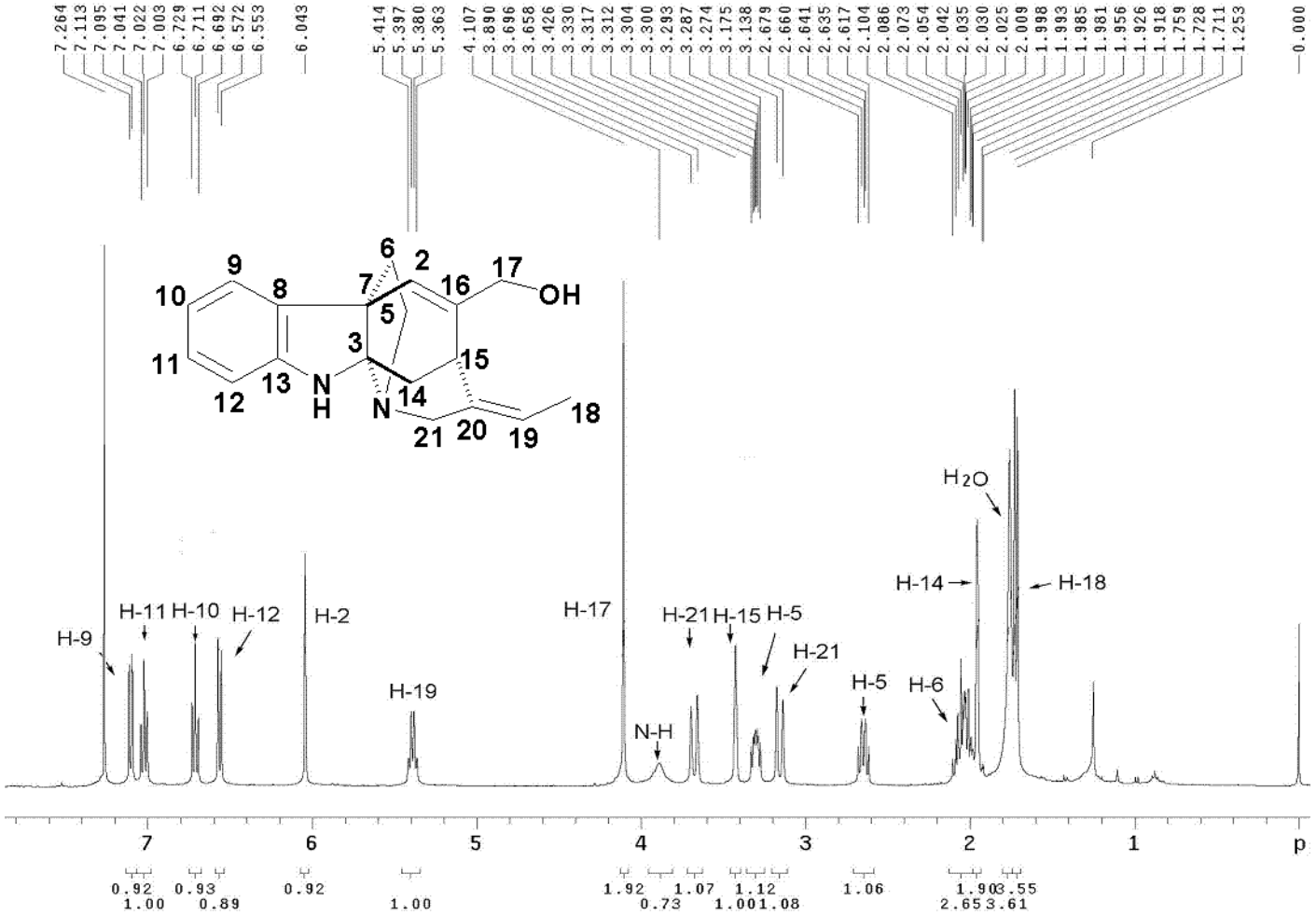

OTf
N
Boc
N
15
8
7
6
5
4
3
2
0.79
1.14
1.17
1.21
0.98
1.18
1.22
1.11
1.27
1.23
2.54
3.15
12.13
1.87
4.07


OTf
N
Boc
N
15
PPM

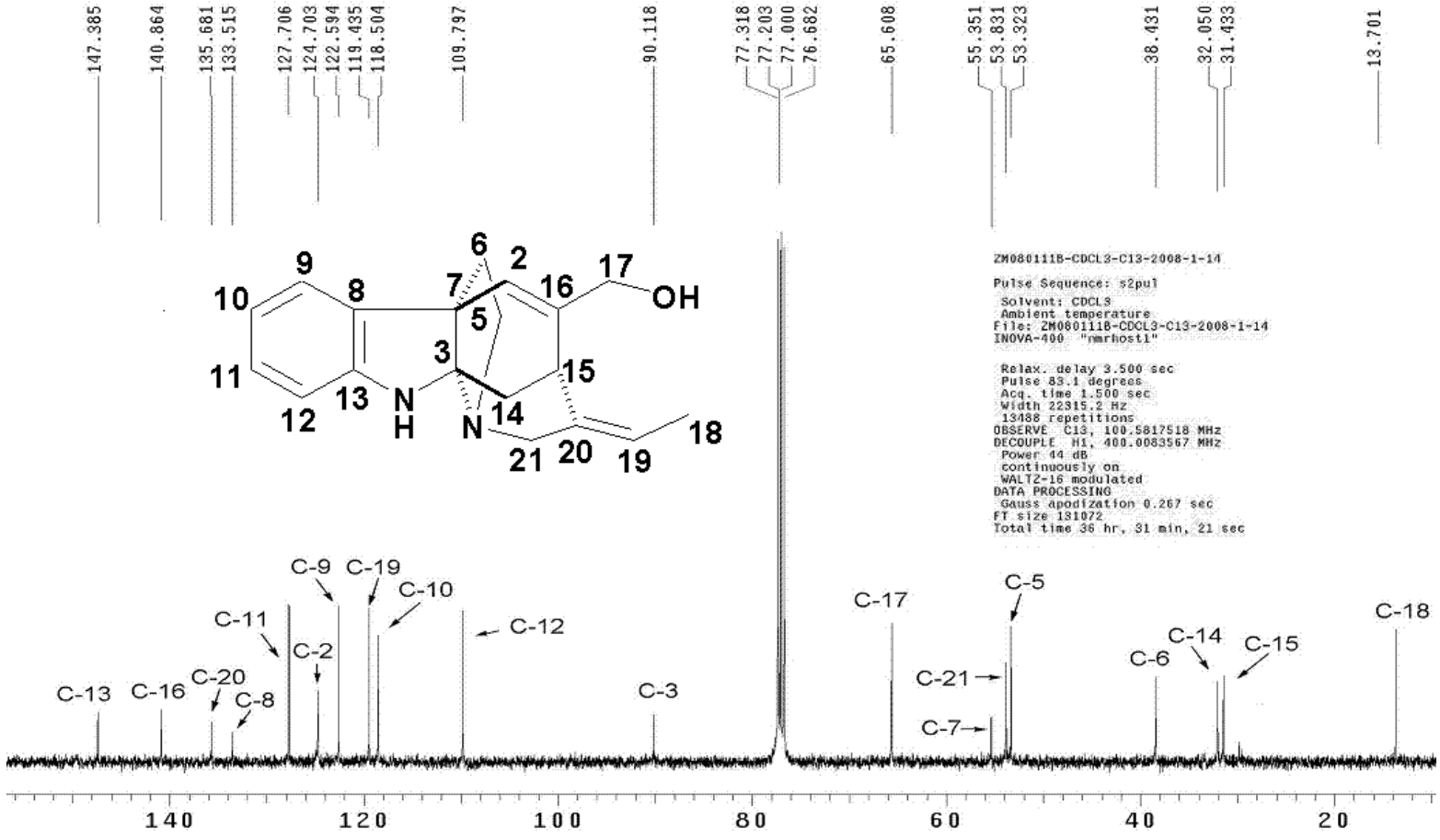

OH
N
Boc
N
16
9
8
7
6
5
4
3
2
1
0
ppm
0.74
1.00
1.30
0.96
1.01
1.16
2.39
1.09
2.30
1.09
1.20
1.16



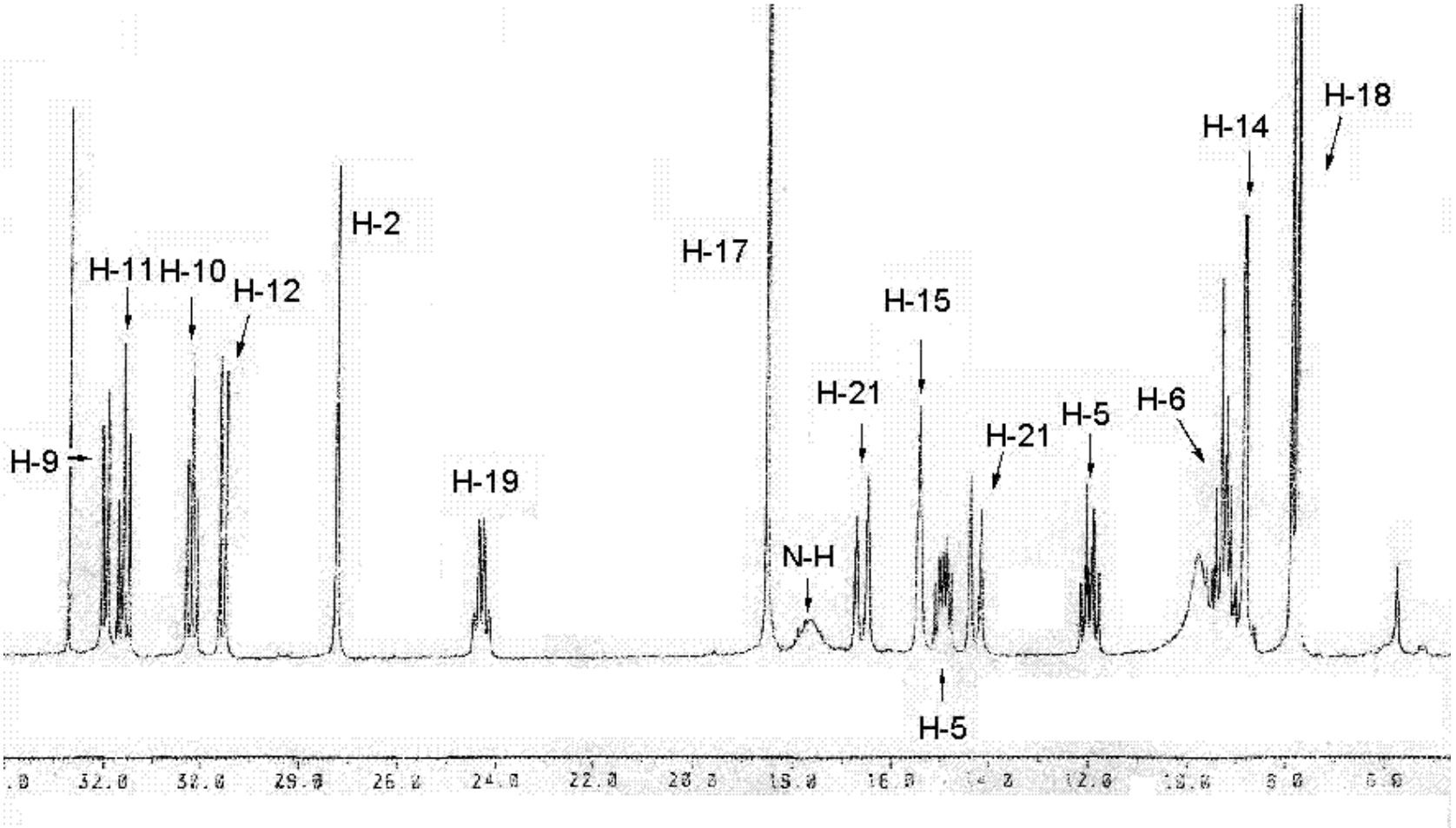
^{1}H NMR Spectrum of Synthetic (±)-Minfiensine



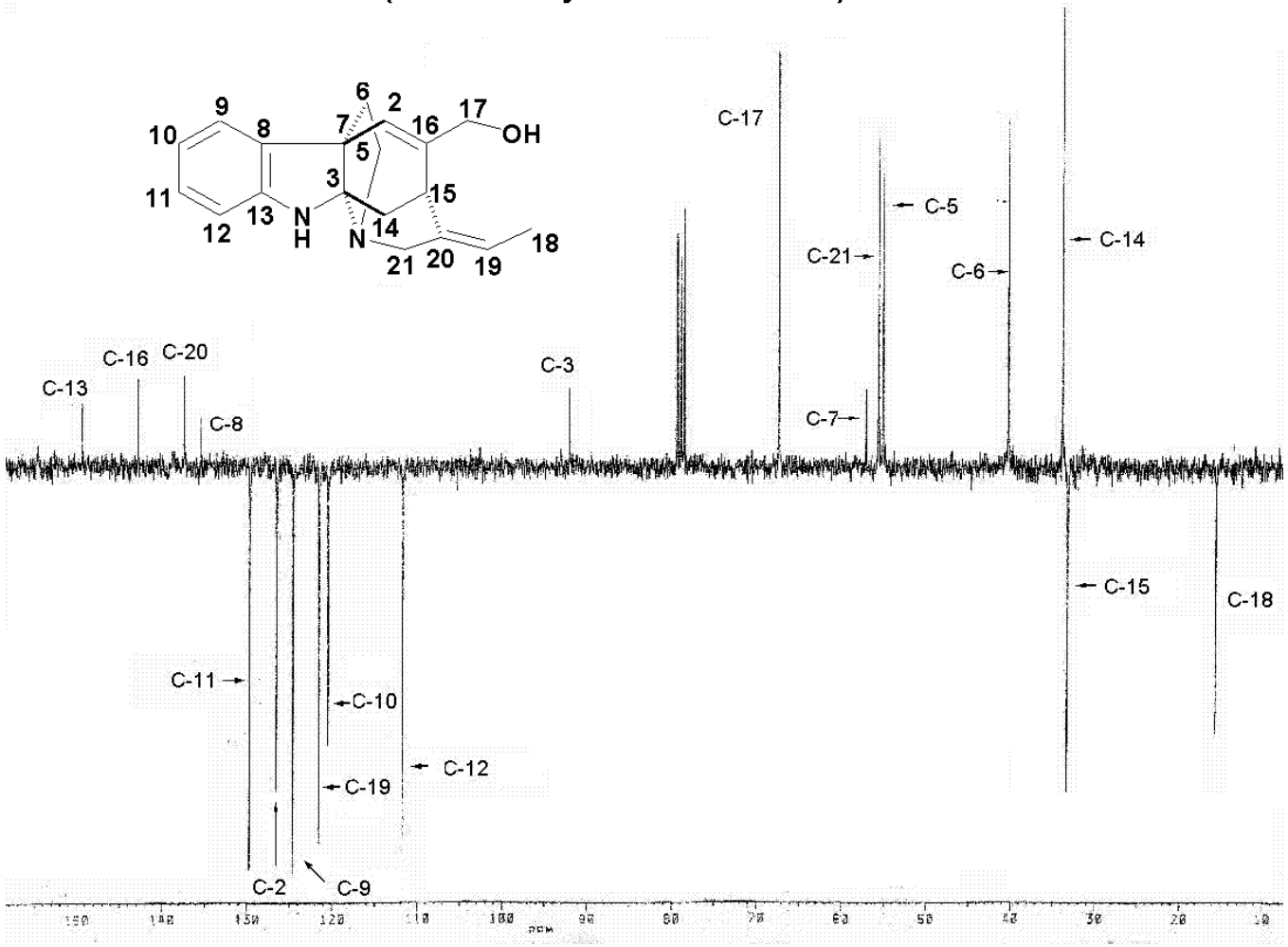
^{13}C NMR Spectrum of Synthetic (±)-Minfiensine



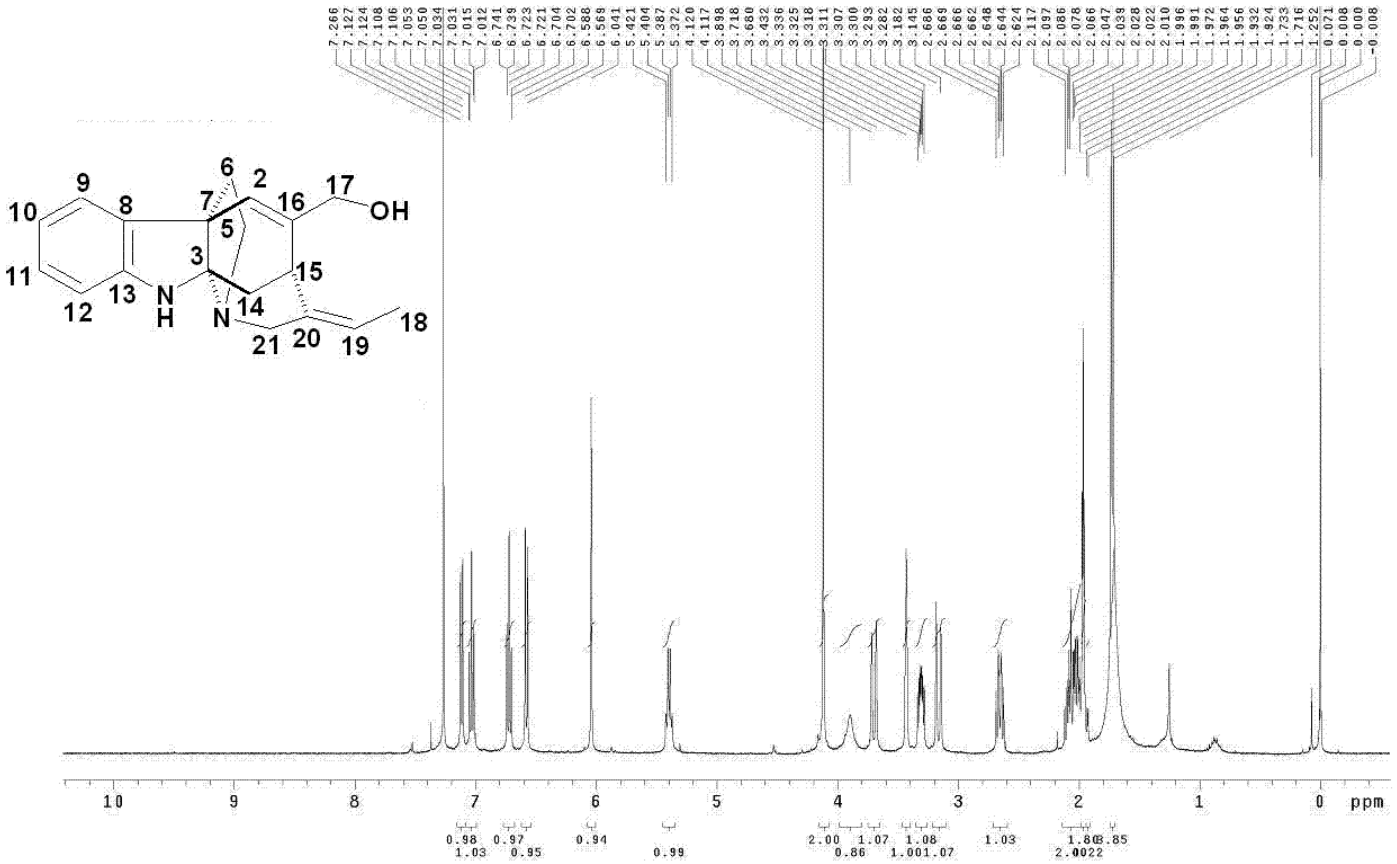
^{1}H NMR Spectrum of Natural (+)-Minfiensine
(Provided by Prof. G. Massiot)



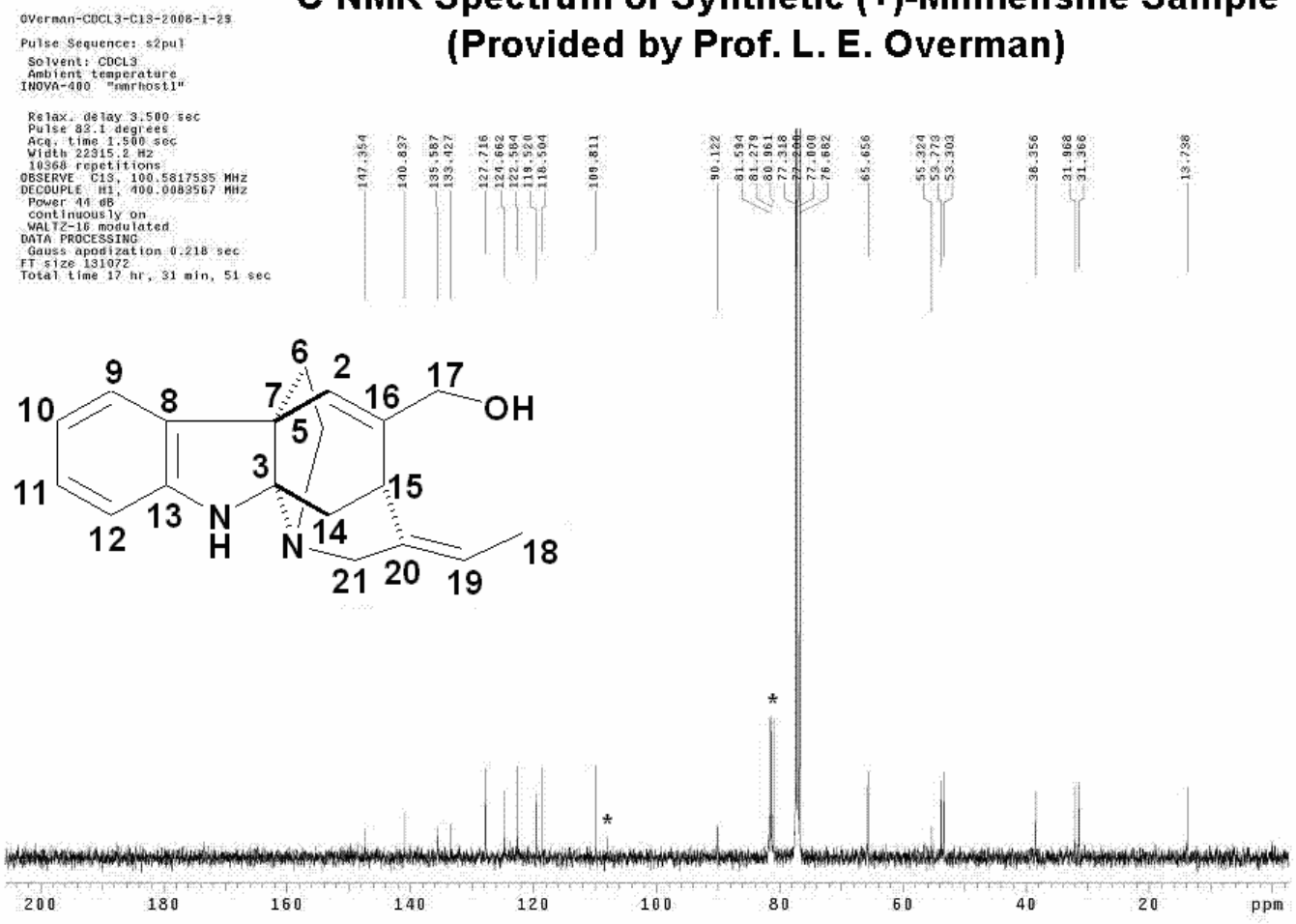
^{13}C NMR Spectrum of Natural (+)-Minfiensine
(Provided by Prof. G. Massiot)



^{1}H NMR Spectrum of Synthetic (+)-Minfiensine Sample
(Provided by Prof. L. E. Overman)

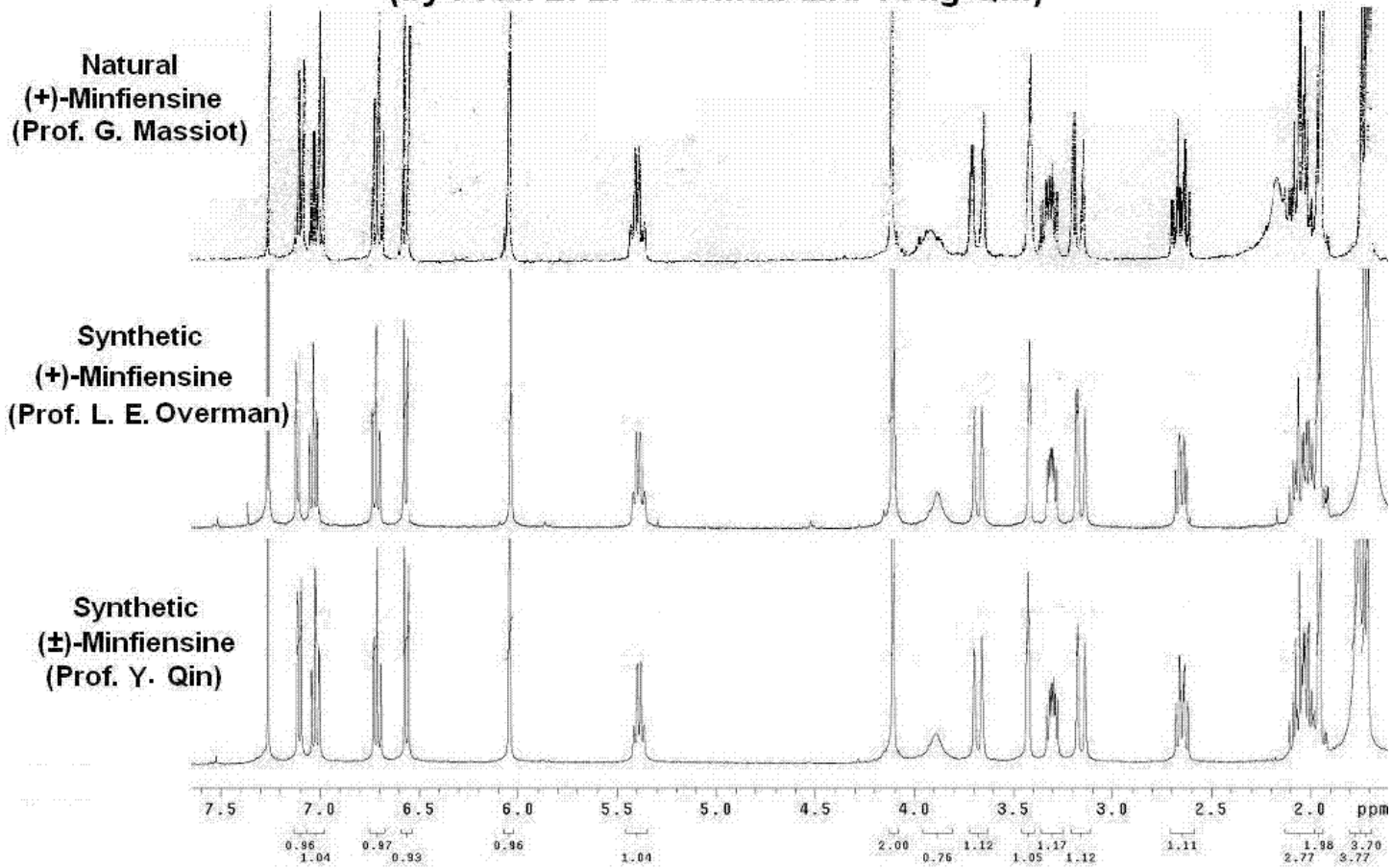


^{13}C NMR Spectrum of Synthetic (+)-Minfiensine Sample (Provided by Prof. L. E. Overman)

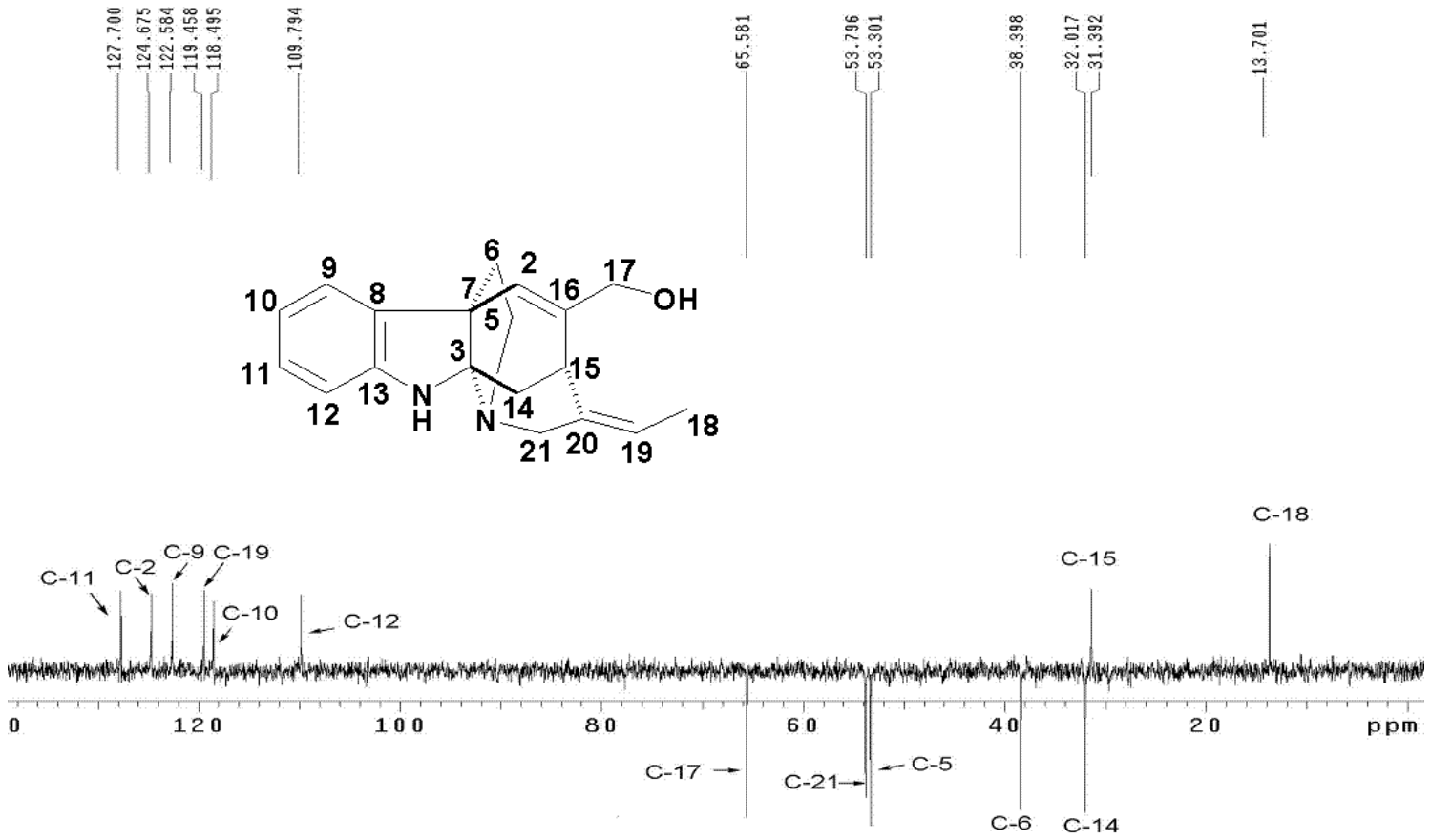


*: Impurity due to long time storage

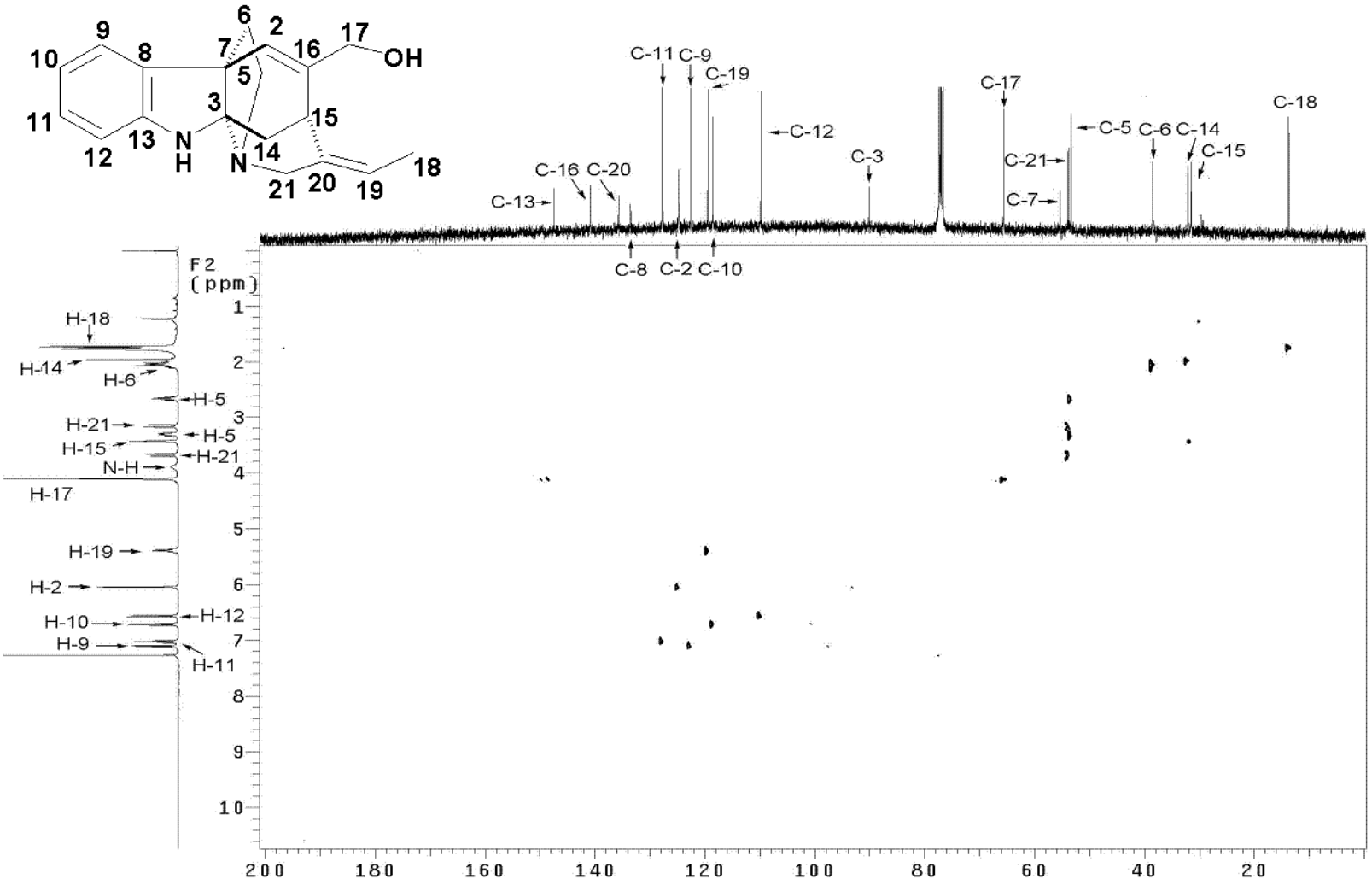
Comparison of ^{1}H NMR Spectrum between the Natural (+)-Minfiensien (Provided by Prof. G. Massiot) and the Synthetic Minfiensien (by Prof. L. E. Overman and Yong Qin)



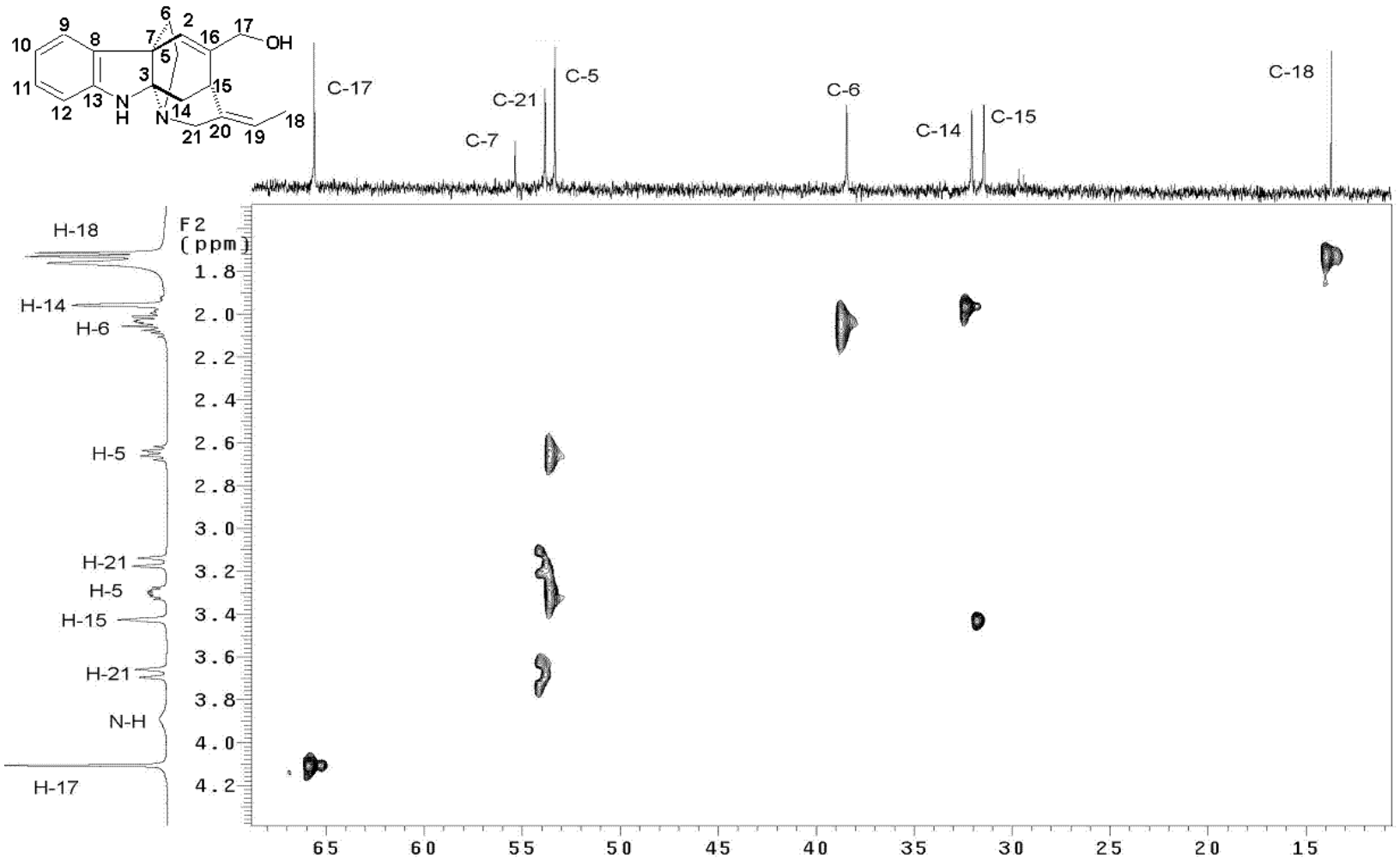
DEPT Spectrum of Synthetic (±)-Minfiensine



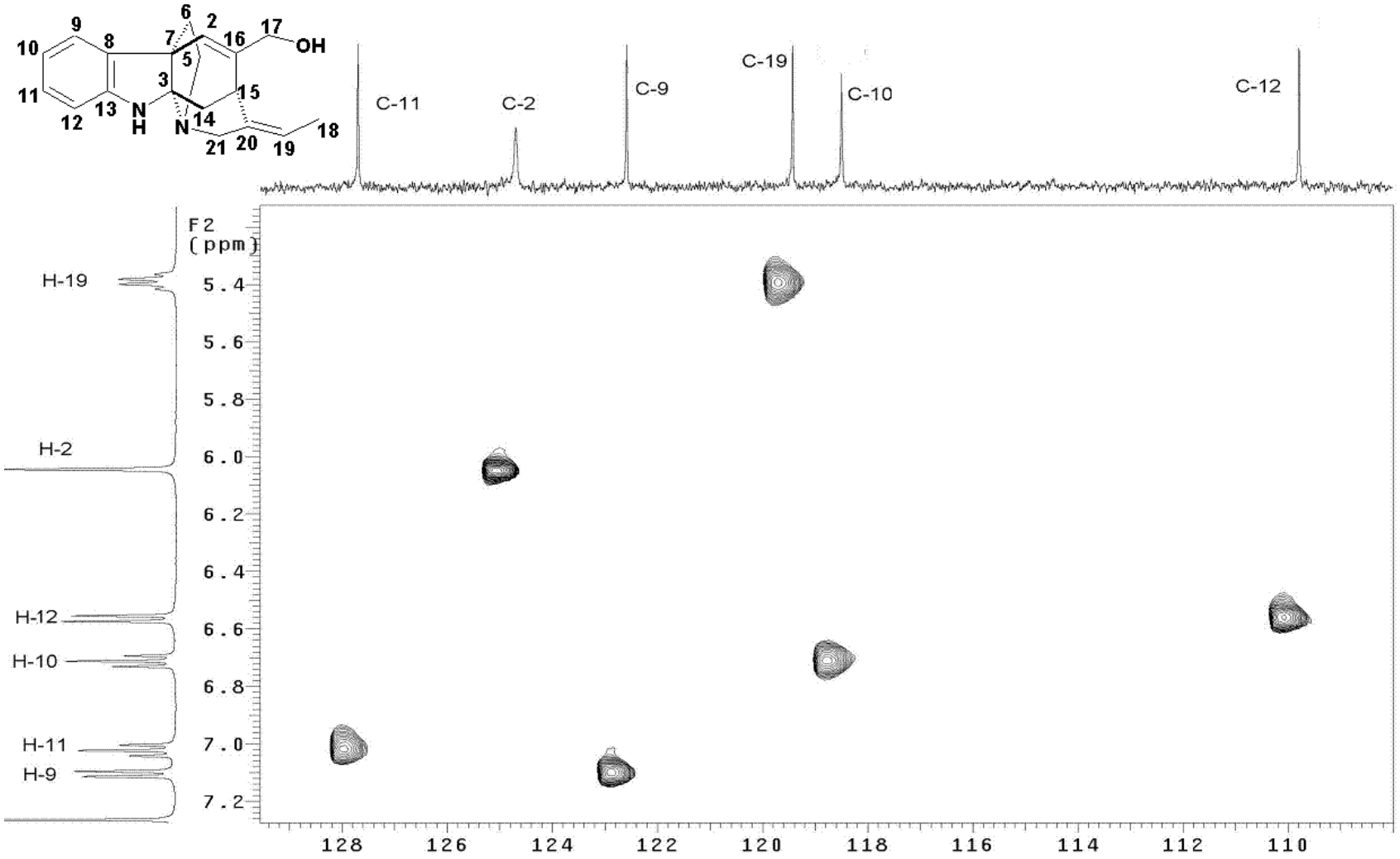
gHMQC Spectrum of Synthetic (±)-Minfiensine



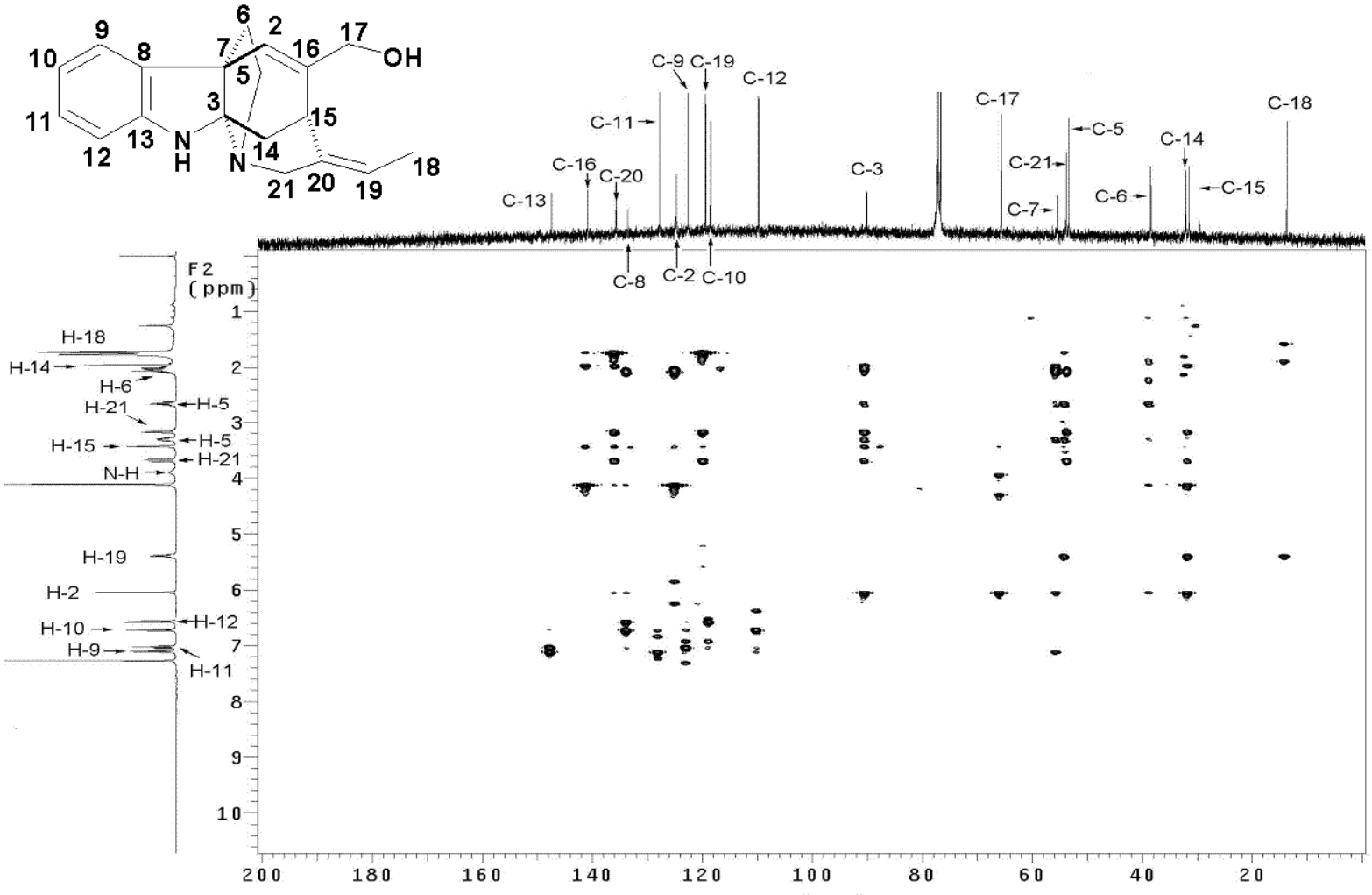
gHMQC Spectrum of Synthetic (±)-Minfiensine



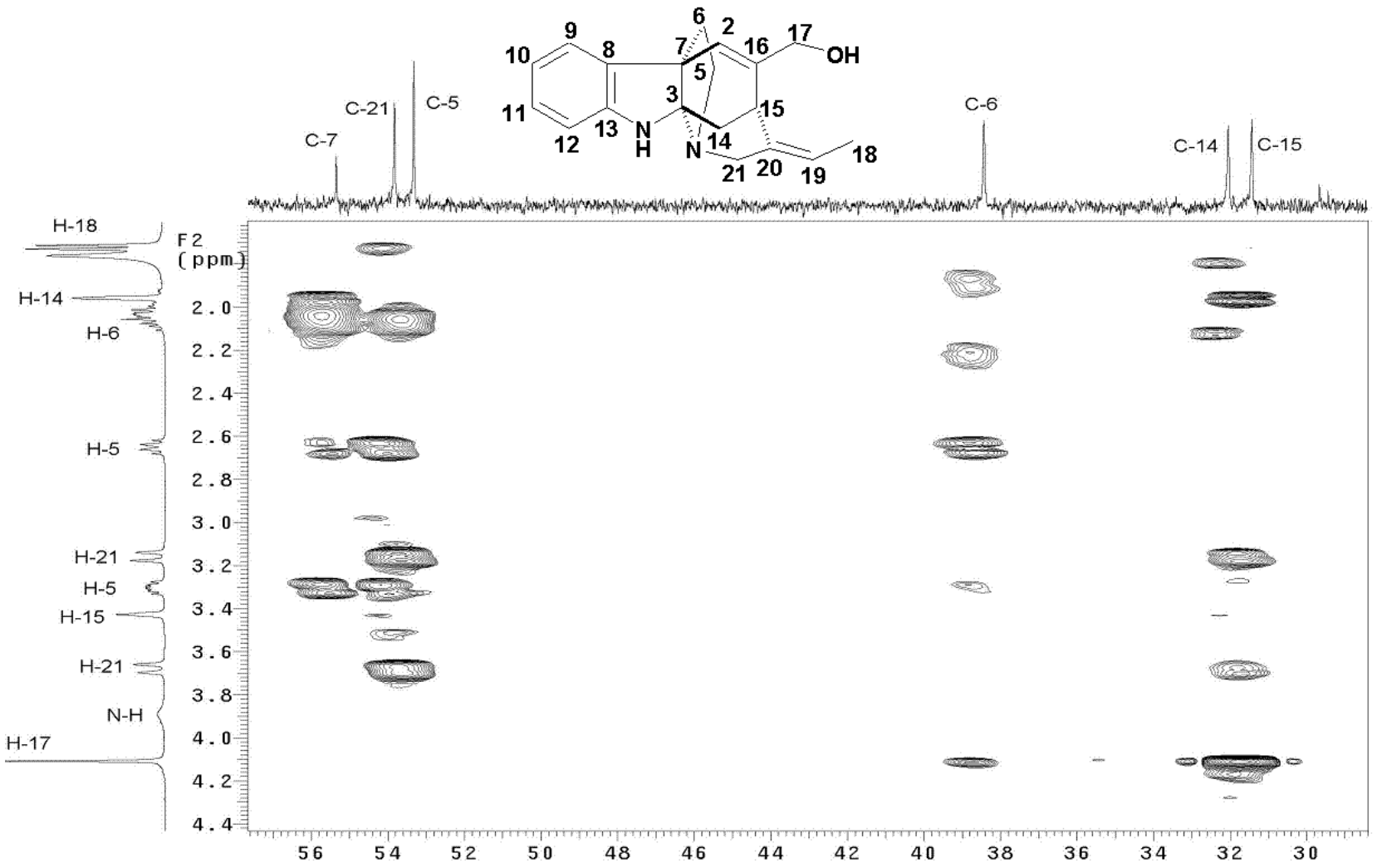
gHMQC Spectrum of Synthetic (±)-Minfiensine



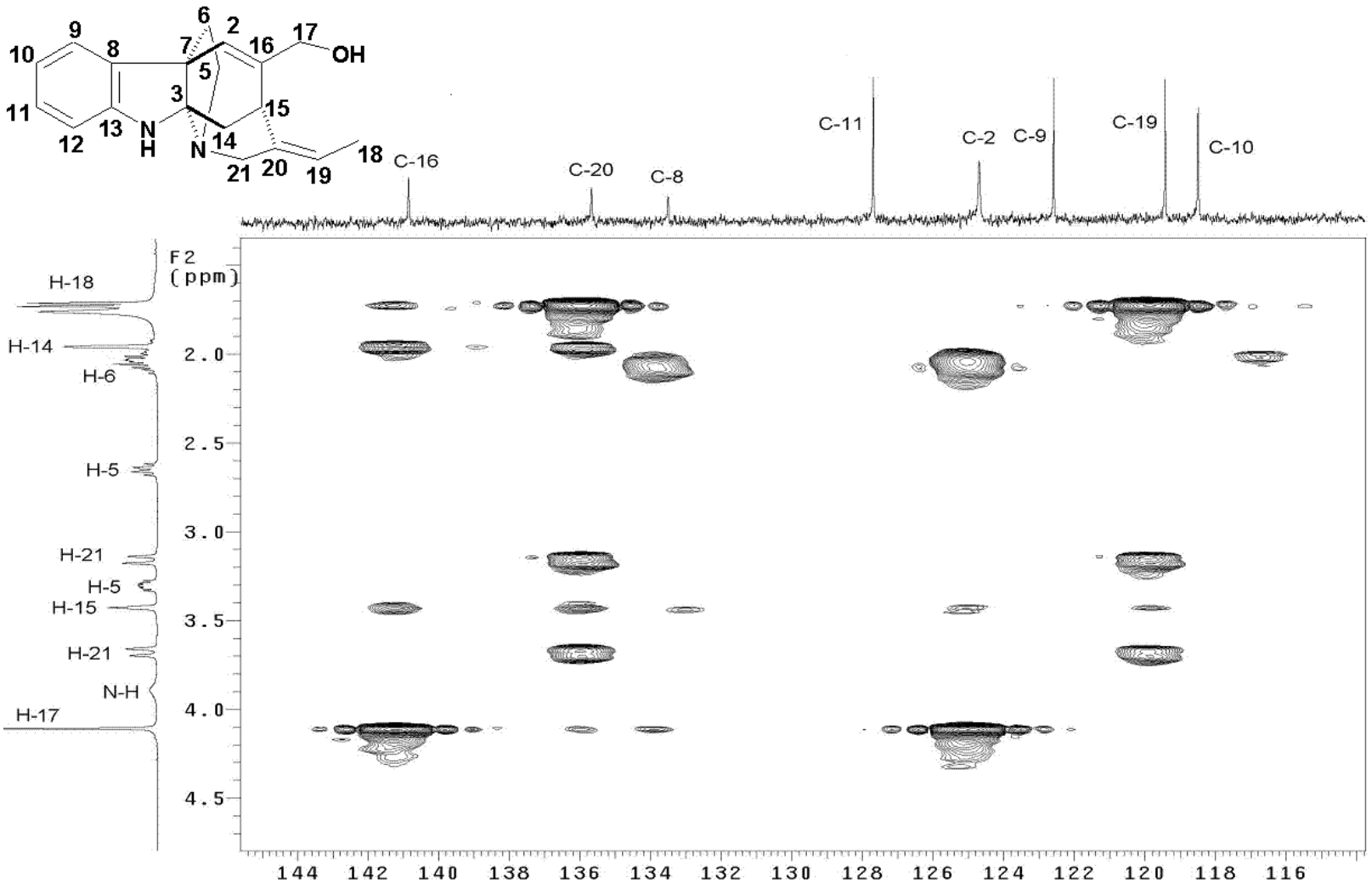
gHMBC Spectrum of Synthetic (±)-Minfiensine



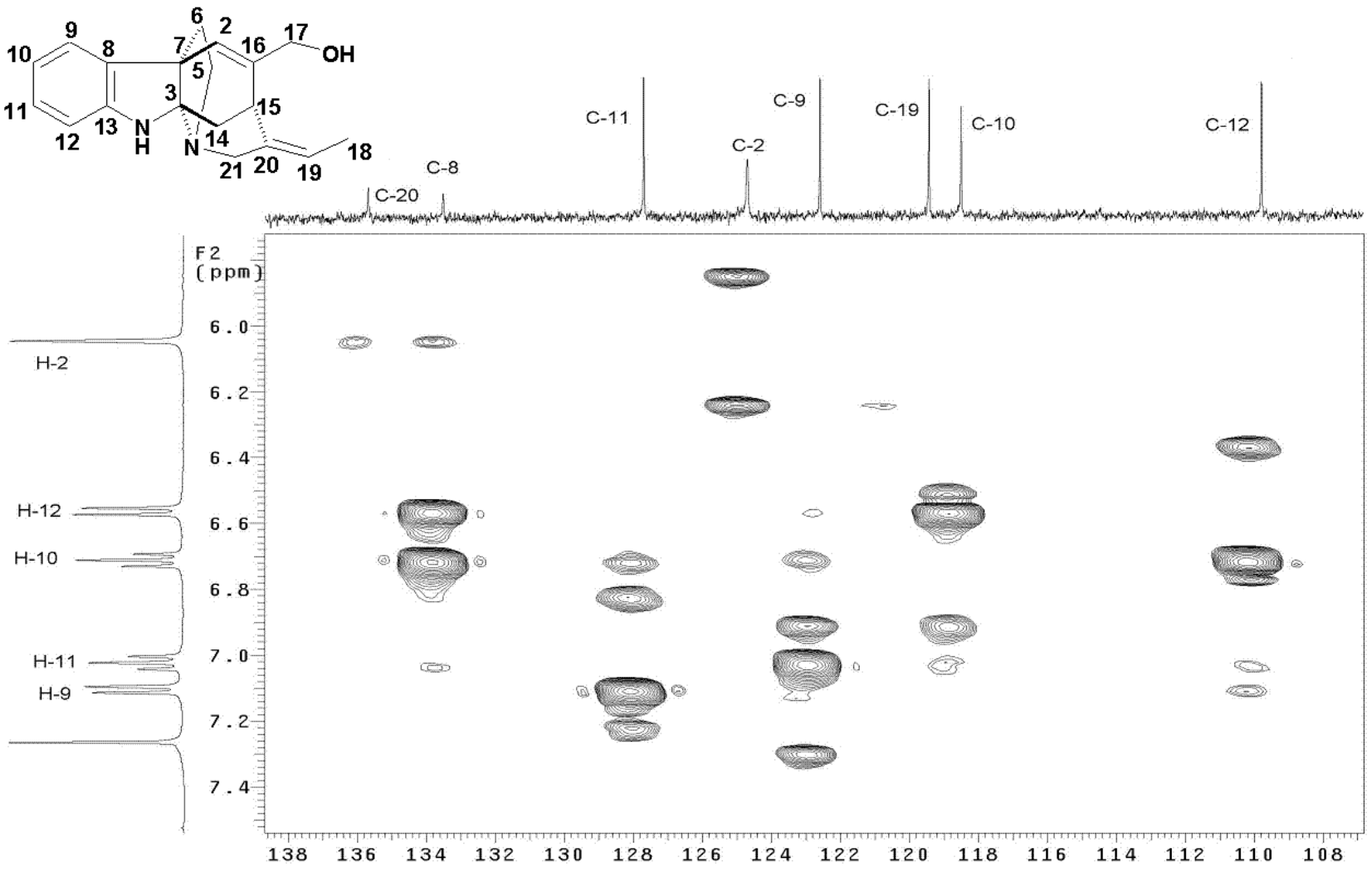
gHMBC Spectrum of Synthetic (±)-Minfiensine



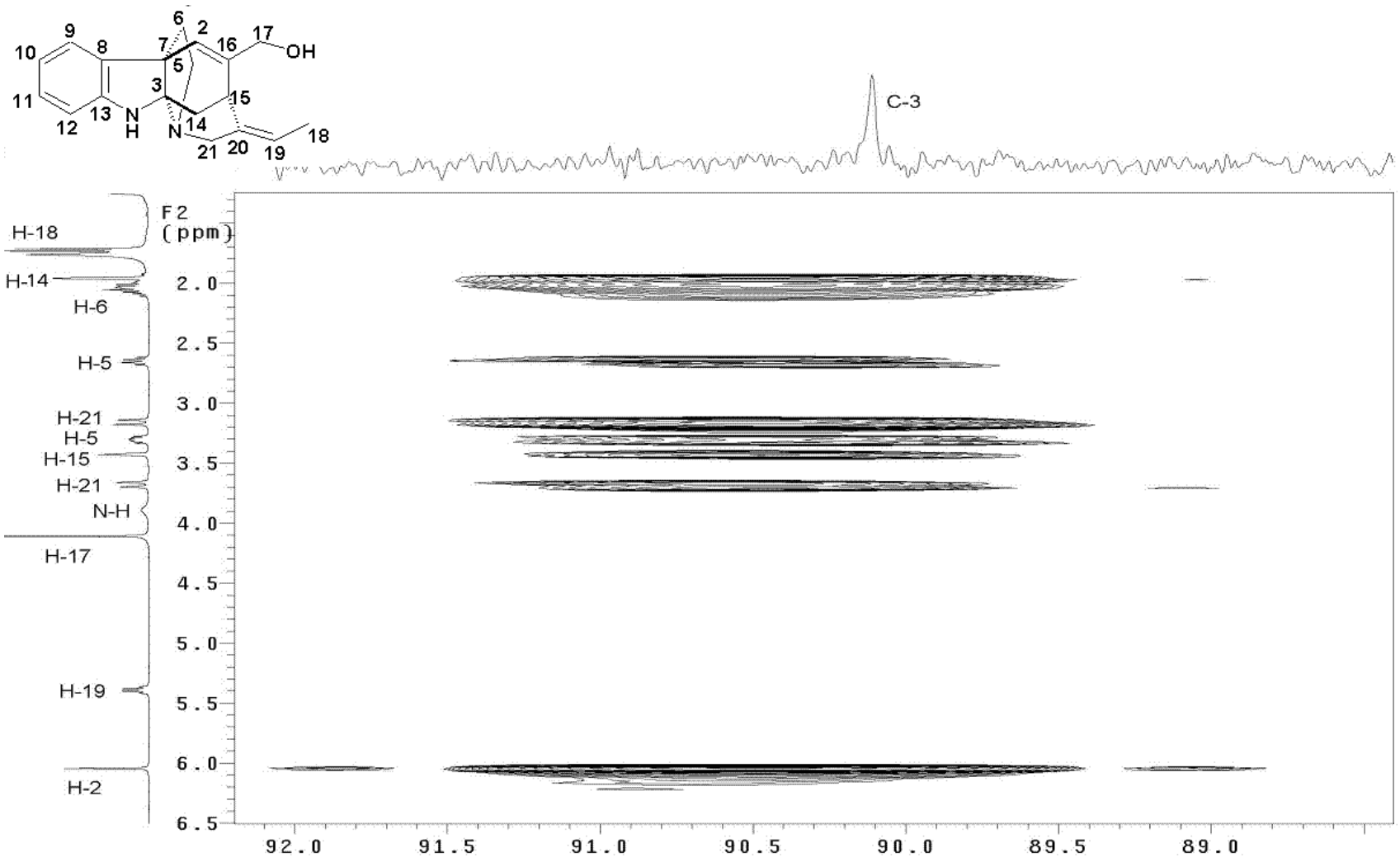
gHMBC Spectrum of Synthetic (±)-Minfiensine



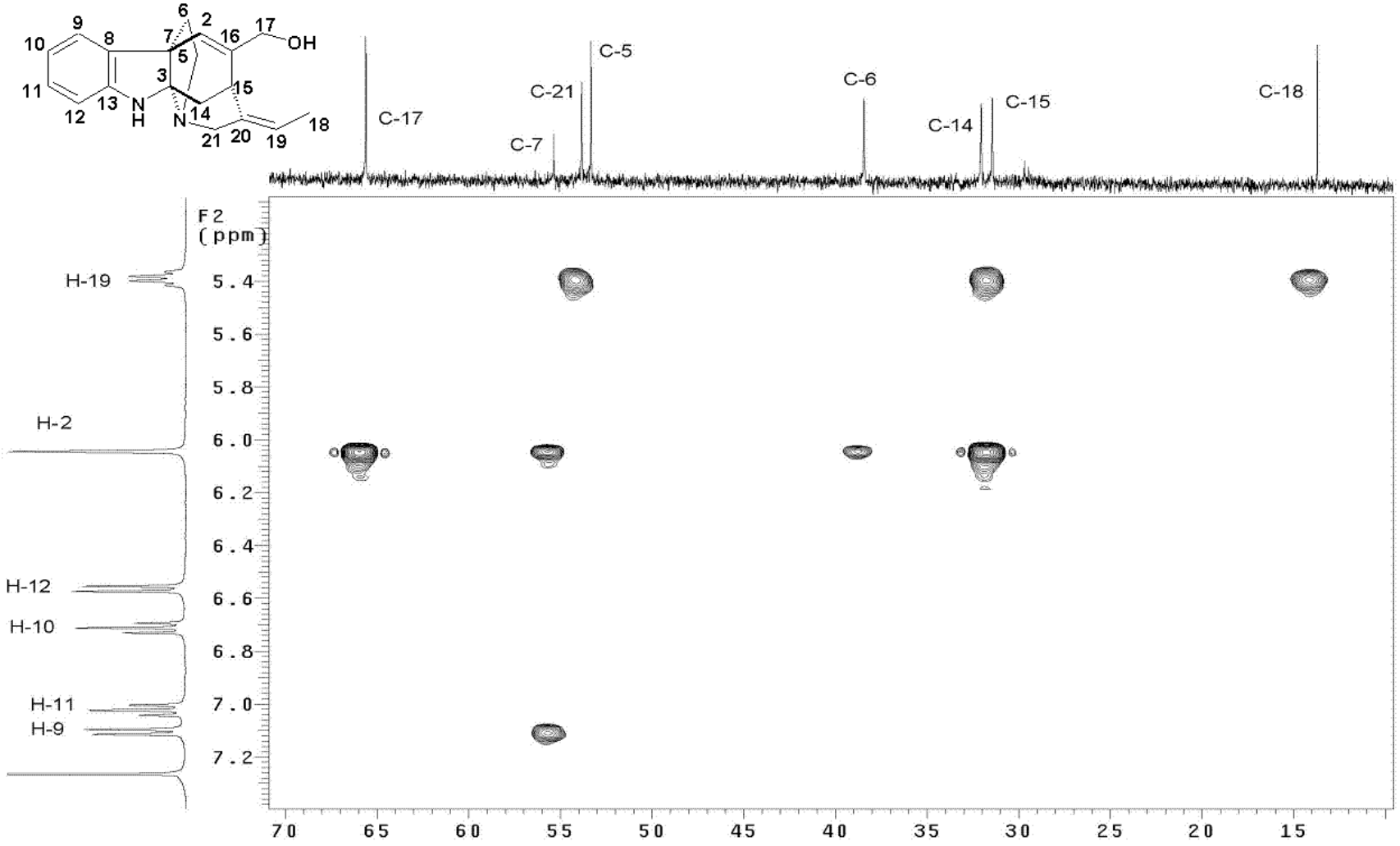
gHMBC Spectrum of Synthetic (±)-Minfiensine



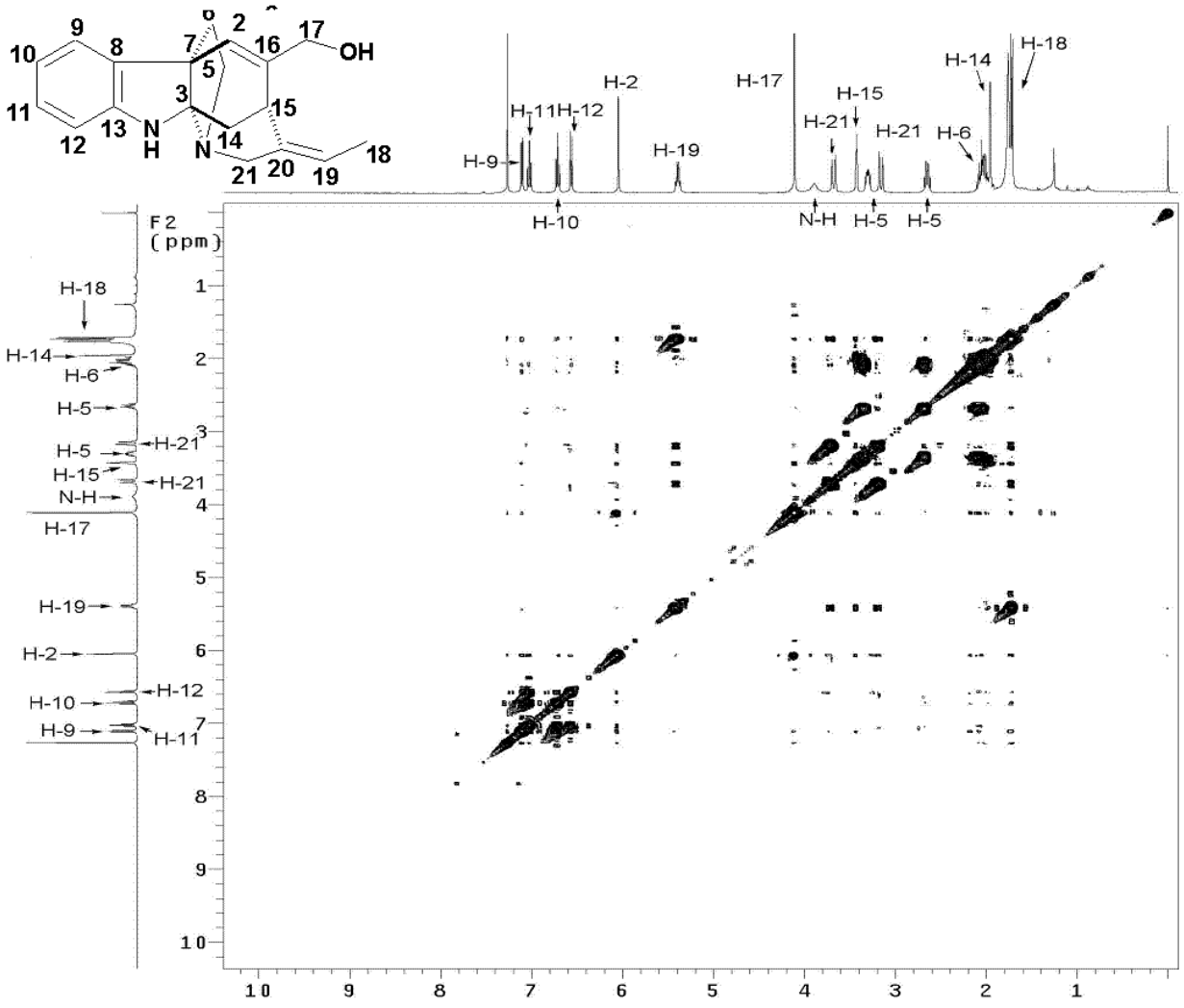
gHMBC Spectrum of Synthetic (±)-Minfiensine



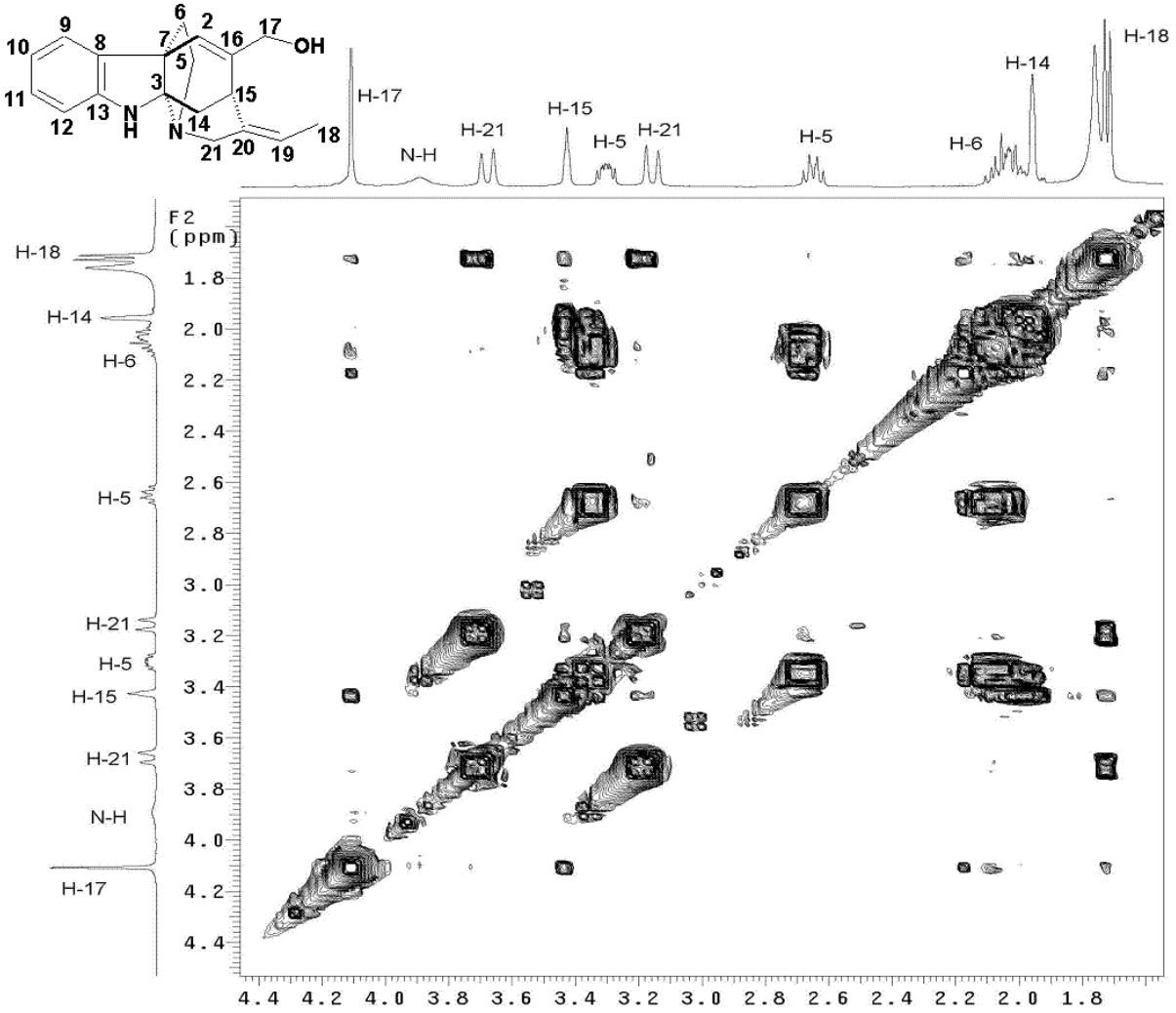
gHMBC Spectrum of Synthetic (±)-Minfiensine



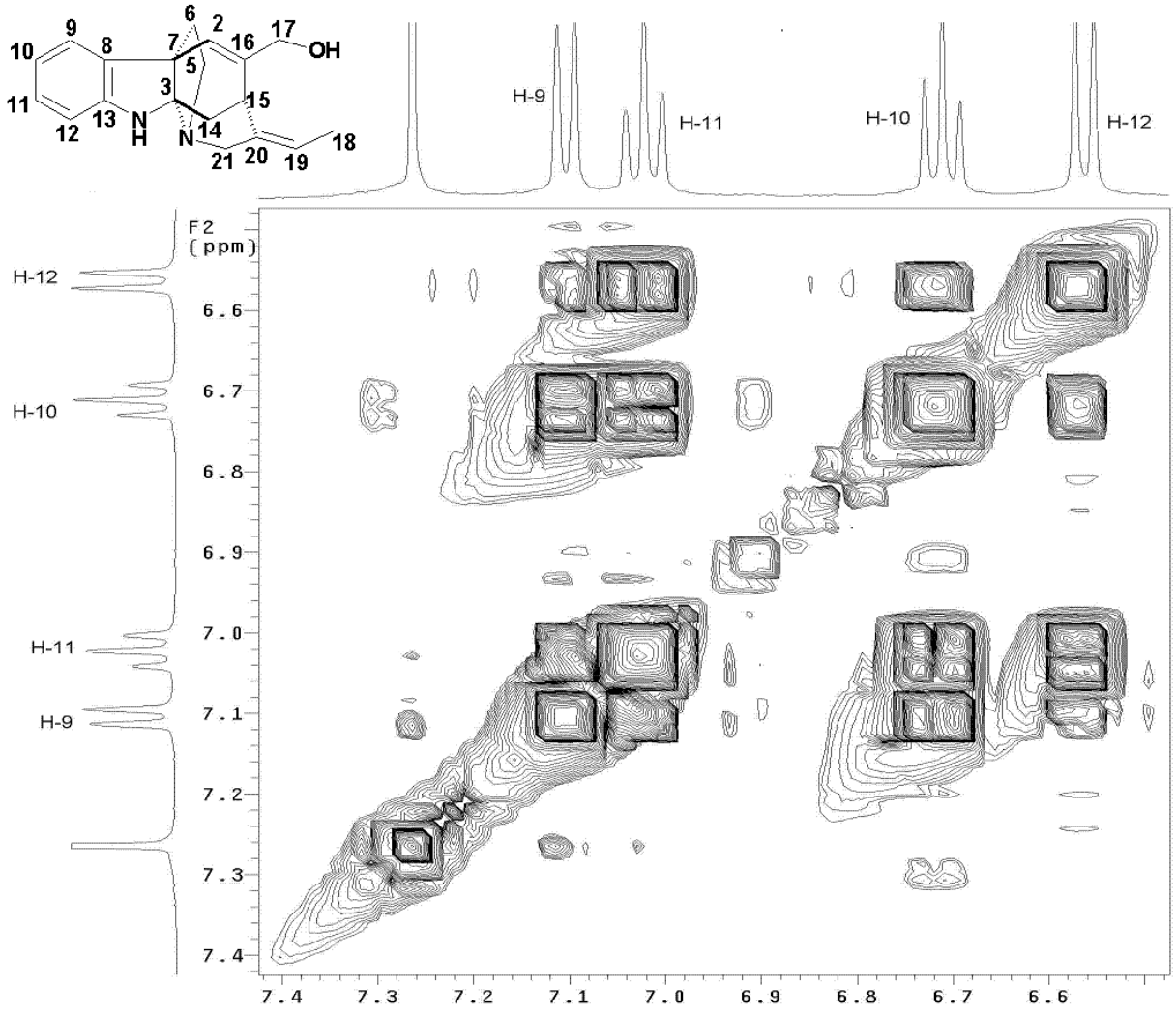
gCOSY Spectrum of Synthetic (±)-Minfiensine



gCOSY Spectrum of Synthetic (±)-Minfiensine



gCOSY Spectrum of Synthetic (±)-Minfiensine



NOEDS Spectrum of Synthetic (±)-Minfiensine