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SUPPORTING INFORMATION

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Supporting Information for:

One-pot, Three-Component Synthesis of Novel Pyrroloacridinones via Intramolecular *Ipso*-Dearomatization / Intramolecular Aza-Michael Addition Sequence

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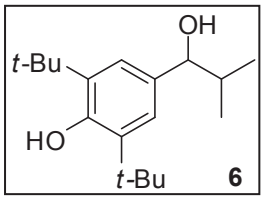
1. General Information.

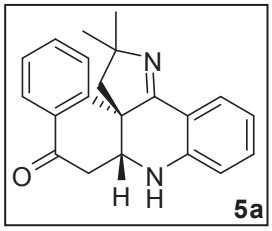
All commercial reagents were used directly as obtained. Thin-layer chromatography was performed using commercially prepared Sorbfil UV-254 silica gel plates. Compounds on TLC were visualized under UV light (254 nm) and with a 0.5% *p*-chloranil solution in toluene. Column chromatography was performed using silica gel (0.06-0.20 mm, 70-230 mesh, Lancaster). Melting points (mp) were determined on a PTP apparatus and are uncorrected. Infra-red spectra (IR) were recorded on a Bruker IFS 66 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury Plus 300 spectrometer (^{1}H: 300.06 MHz, ^{13}C: 75.46 MHz) and a Bruker AVANCE-500 spectrometer (^{1}H: 500.13 MHz, ^{13}C: 125.76 MHz). The ^{1}H chemical shifts were measured from internal $SiMe_4$, ^{13}C — from the solvent signal ($CDCl_3$, δ_C 77.0 ppm). All the signals in the ^{1}H and ^{13}C NMR spectra of the compounds **4g**, **5h**, **5h'**, **5i**, **5i'**, **5j'**, and **7** were assigned on the basis of 2D ^{1}H–^{1}H COSY and NOESY, ^{1}H–^{13}C HSQC and HMBC experiments. The stereochemistry of **5a** was determined by 2D ^{1}H-^{1}H NOESY experiment. Mass spectra (MS) were obtained on an Agilent 6890N/5975B GC-MS system (column: HP-5ms, 30 m × 0.25 mm, 0.25 μm; helium as a carrier gas, electron impact ionization mode (200°C, 70 eV)). Elemental analyses were carried out on a Leco CHNS-932 analyzer. X-ray data were collected at 295(2) K with an XCALIBUR-3 diffractometer, CCD detector (ω-scanning technique, MoKα radiation, graphite monochromator). Structures were solved by direct method and refined with SHELX-97 program package[1]. All non-hydrogen atoms were refined anisotropically. Crystallographic data and data collection parameters are summarized in Table 1.

2. Experimental procedures and Characterization Data

2,6-Di-*tert*-butyl-4-(1-hydroxy-2-methylpropyl)phenol (6). To a stirred suspension of sodium borohydride (1.75 g, 46 mmol) in 15 ml of ethanol was added a solution of 1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-methylpropan-1-one[2] (11.56 g, 42 mmol) in 15 ml of ethanol dropwise at such a rate that the temperature of the reaction mixture was maintained at 20-30 °C. The reaction mixture was stirred at room temperature for 4 hours. Then ethanol was removed on a rotary evaporator and 10 ml of a 10% NaOH solution was added. The aqueous phase was extracted with Et_2O (3×50 ml). The combined organic phases were washed with water, dried under Na_2SO_4, and evaporated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate 20:1) to give pure compound **6** (8.01 g, 69%) as a colorless solid: R_f 0.44 (hexane/ethyl acetate, 10:1); mp: 92.5-94.5 °C; **IR** (film) ν: 3398, 2957, 2872, 1435, 1365 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 0.76 (d, 3H, *J* = 6.7, Me), 1.01 (d, 3H, *J* = 6.7, Me), 1.44 (s, 18H, $C^2C(\underline{Me})_3$, $C^6C(\underline{Me})_3$), 1.87 (d, 1H, *J* = 2.9, OH-$C^{1'}$), 1.91 (m, 1H, H-2'), 4.23 (dd, 1H, *J* = 7.5, 2.9, H-1'), 5.15 (s, 1H, OH-C^1), 7.09 (s, 2H, H-3 and H-5); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 18.59 (Me), 19.09 (Me), 30.27 ($2C(\underline{Me})_3$), 34.23 ($2\underline{C}(Me)_3$), 35.05 (C-2'), 80.53 (C-1'), 123.13 (C-3, C-5), 134.20 (C-4), 135.38 (C-2, C-6), 152.93 (C-1); **MS** (EI) m/z (%): 278 $[M]^+$ (3), 260 $[M-H_2O]^+$ (7), 245 (9), 235 $[M-CH(Me)_2]^+$ (100); Anal. Calcd for $C_{18}H_{30}O_2$: C 77.65, H 10.85; found: C 77.65, H 10.86.

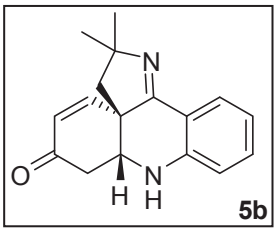


(6a*R,14a*S**)-13,13-Dimethyl-6a,7,13,14-tetrahydrobenzo[a]pyrrolo[2,3-m]acridin-5(6H)-one (5a).** A mixture of 1-methoxynaphthalene **1a** (316 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol), and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) was added dropwise to stirred concentrated sulfuric acid (92%, 1 ml, 17 mmol) at 5-7 °C. The reaction mixture was stirred at room temperature for 25 min and poured into a mixture of ice (25 g) and NH_3 (aq) (7 mL). The product was extracted with CH_2Cl_2 (3×15 ml), and the combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and filtered. After the solvent was removed, the crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 4:1 to 2:1) to give pure **5a** (516 mg, 82%). **Data for 5a**: Pale yellow solid; R_f 0.63 (hexane/ethyl acetate, 2:1); mp: 267-269 °C; **IR** (film) ν: 3364, 3066, 3026, 2964, 2867, 1674, 1610 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.42 (s, 3H, Me-C^{13}), 1.47 (s, 3H, Me-C^{13}), 2.05 (d, 1H, *J* = 13.1, H-14^B), 2.10 (d, 1H, *J* = 13.1, H-14^A), 2.79 (dd, 1H, *J* = 18.0, 3.0, H-6^B), 3.02 (dd, 1H, *J* = 18.0, 3.0, H-6^A),



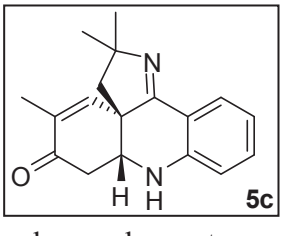
3.96 (t, 1H, *J* = 3.0, H-6a), 4.32 (br s, 1H, NH), 6.41 (br d, 1H, *J* = 8.3, H-8), 6.72 (ddd, 1H, *J* = 7.9, 7.1, 1.2, H-10), 7.06-7.10 (m, 2H, H-1 and H-9), 7.29 (td, 1H, *J* = 7.6, 1.0, H-3), 7.41 (td, 1H, *J* = 7.6, 1.4, H-2), 7.92 (dd, 1H, *J* = 7.9, 1.5, H-11), 8.03 (dd, 1H, *J* = 7.8, 1.4, H-4); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 29.29 (Me-C^{13}), 32.46 (Me-C^{13}), 40.53, 48.41 (C-6, C-14), 56.30 (C-14a), 58.45 (C-6a), 72.87 (C-13), 114.75 (C-8), 115.62 (C-11a), 118.32 (C-10), 126.85, 127.00, 127.31 and 127.90 (C-1, C-4, C-9, and C-11), 131.08 (C-4a), 131.81 and 134.17 (C-2, C-3), 143.59 and 147.00 (C-7a and C-14b), 166.59 (C-11b), 195.23 (C-5); **MS** (EI) m/z (%): 316 $[M]^+$ (78), 316 $[M\text{-}Me]^+$ (100); **Anal. Calcd for** $C_{21}H_{20}N_2O$: C 79.72, H 6.37, N 8.85; found: C 79.42, H 6.43, N 8.64.

(3a*S,7a*R**)-2,2-Dimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5b).** The



title compound was prepared from anisole **1b** (216 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol), and 2-aminobenzonitrile **3** in a similar manner as described for the preparation of **5a**. The crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 2:1) to give starting 2-aminobenzonitrile **3** (71 mg, 30%), and **5b** (213 mg, 40%). **Data for 5b**: Yellow solid; R_f 0.30 (hexane/ethyl acetate, 1:1); mp: 230.5-232 °C; **IR** (film) ν: 3265, 3030, 2968, 2924, 1670, 1605 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.40 (s, 3H, Me-C^2), 1.48 (s, 3H, Me-C^2), 2.04 (d, 1H, *J* = 12.9, H-3^B), 2.19 (d, 1H, *J* = 12.9, H-3^A), 2.56 (ddd, 1H, *J* = 17.1, 3.0, 0.9, H-7^B), 2.75 (dd, 1H, *J* = 17.1, 2.7, H-7^A), 3.85 (q, 1H, *J* = 2.6, H-7a), 4.39 (s, 1H, NH), 5.96 (dd, 1H, *J* = 10.0, 0.9, H-5), 6.57 (dd, 1H, *J* = 8.3, 1.0, H-9), 6.63 (dd, 1H, *J* = 10.0, 2.3, H-4), 6.72 (ddd, 1H, *J* = 7.9, 7.1, 1.0, H-11), 7.18 (ddd, 1H, *J* = 8.3, 7.1, 1.5, H-10), 7.85 (dd, 1H, *J* = 7.9, 1.5, H-12); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 30.02 and 31.27 (2Me-C^2), 40.85 (C-7), 49.24 (C-3), 53.71 (C-3a), 58.26 (C-7a), 72.13 (C-2), 114.69 (C-9), 114.97 (C-12a), 118.20 (C-11), 126.98 and 128.27 (C-12 and C-5), 132.51 (C-10), 146.40 (C-8a), 148.40 (C-4), 166.08 (C-12b), 195.80 (C-6); **MS** (EI) m/z (%): 266 $[M]^+$ (100); **Anal. Calcd for** $C_{17}H_{18}N_2O$: C 76.66, H 6.81, N 10.52; found: C 76.83, H 6.58, N 10.48.

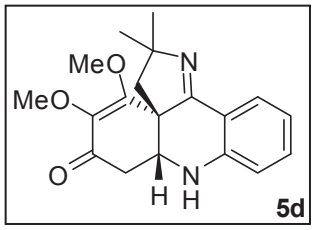
(3a*S,7a*R**)-2,2,5-Trimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5c).**



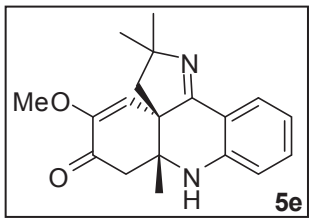
The title compound was prepared from 2-methylanisole **1c** (244 mg, 2.0 mmol), isobutyraldehyde **2** (216 mg, 3.0 mmol), and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) in a similar manner as described for the preparation of **5a**. The crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 2:1) to give pure **5c** (406 mg, 73%).

Data for 5c: Yellow solid; R_f 0.33 (hexane/ethyl acetate, 2:1); mp: 202-203.5 °C; **IR** (film) ν: 3332, 2956, 1668, 1606 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.41 (s, 3H, Me-C^2), 1.47 (s, 3H, Me-C^2), 1.74 (d, 3H, *J* = 1.5, Me-C^5), 2.02 (d, 1H, *J* = 12.8, H-3^B), 2.17 (d, 1H, *J* = 12.8, H-3^A), 2.57 (dd, 1H, *J* = 17.1, 3.2, H-7^B), 2.76 (dd, 1H, *J* = 17.1, 2.7, H-7^A), 3.81 (q, 1H, *J* = 2.7, H-7a), 4.37 (s, 1H, NH), 6.38 (qd, 1H, *J* = 1.7, 1.5, H-4), 6.56 (dd, 1H, *J* = 8.2, 1.0, H-9), 6.71 (ddd, 1H, *J* = 7.9, 7.0, 1.0, H-11), 7.18 (ddd, 1H, *J* = 8.2, 7.0, 1.5, H-10), 7.85 (dd, 1H, *J* = 7.9, 1.5, H-12); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 15.93 (Me-C^5), 30.00 and 31.28 (2Me-C^2), 40.84 (C-7), 49.25 (C-3), 53.96 (C-3a), 58.60 (C-7a), 71.91 (C-2), 114.66 (C-9), 114.94 (C-2a), 117.92 (C-11), 126.95 (C-12), 132.30 (C-10), 134.51 (C-5), 143.35 (C-4), 146.57 (C-8a), 166.59 (C-12b), 196.29 (C-6); **MS** (EI) m/z (%): 280 $[M]^+$ (100); **Anal. Calcd for** $C_{18}H_{20}N_2O$: C 77.11, H 7.19, N 9.99; found: C 76.92, H 7.06, N 9.93.

(3a*S,7a*R**)-4,5-Dimethoxy-2,2-dimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5d).** A solution of 1,2,3-trimethoxybenzene **1d** (336 mg, 2.0 mmol) and isobutyric aldehyde **2** (216 mg, 3.0 mmol) in CH_2Cl_2 (0.5 ml) was added dropwise to stirred solution of 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) in concentrated sulfuric acid (92%, 1 ml, 17 mmol) at 5-7 °C. The reaction mixture was stirred at room temperature for 1.5 h and poured into a mixture of ice (25 g) and NH_3 (aq) (7 mL). The product was extracted with CH_2Cl_2 (3×15 ml), and the combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and filtered. After the solvent was removed, the crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 3:1 to 1:1) to give starting 2-aminobenzonitrile **3** (89 mg, 38%) and **5d** (290 mg, 44%). **Data for 5d**: Pale yellow solid; R_f 0.25 (hexane/ethyl acetate, 1:1); mp: 197-199 °C; **IR** (film) ν: 3348, 3245, 3004, 2962, 1665, 1632, 1612 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.41 (s, 3H, Me-C^2), 1.44 (s, 3H, Me-C^2), 2.02 (d, 1H, *J* = 13.4, H-3^B), 2.13 (d, 1H, *J* = 13.4, H-3^A), 2.53 (dd, 1H, *J* = 17.2, 3.0, H-7^B), 2.74 (dd, 1H, *J* = 17.2, 3.0, H-7^A), 3.59 (s, 3H, OMe), 3.74 (t, 1H, *J* = 3.0, H-7a), 3.93 (s, 3H, OMe), 4.40 (s, 1H, NH), 6.55 (dd, 1H, *J* = 8.2, 0.9, H-9), 6.69 (ddd, 1H, *J* = 7.8, 7.1, 0.9, H-11), 7.15 (ddd, 1H, *J* = 8.2, 7.1, 1.5, H-10), 7.75 (dd, 1H, *J* = 7.8, 1.5, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 28.65 and 31.86 (2Me-C^2), 40.21 (C-7), 48.02 (C-3), 57.05 (OMe), 57.98 (C-7a), 60.89 (C-3a), 60.92 (OMe), 72.96 (C-2), 114.18 (C-9), 115.75 (C-12a), 117.77 (C-11), 126.79 (C-12), 131.85 (C-10), 135.72 (C-5), 145.96 (C-8a), 162.85 (C-4), 163.87 (C-12b), 192.41 (C-6); **MS** (EI) m/z (%): 326 $[M]^+$ (98), 311 $[M\text{-}Me]^+$ (59), 208 (16), 193 (40), 183 (17), 159 (100); **Anal. Calcd for** $C_{19}H_{22}N_2O_3$: C 69.92, H 6.79, N 8.58; found: C 70.03, H 6.68, N 8.51.



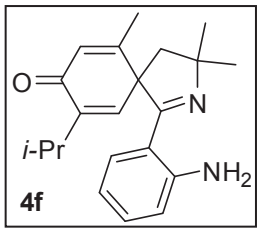
(3a*S,7a*R**)-5-Methoxy-2,2,7a-trimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5e).** The title compound was prepared from 1,2-dimethoxy-4-methylbenzene **1e** (304 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol) and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) in a similar manner as described for the preparation of **5a**. The crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 2:1) to give starting 2-aminobenzonitrile **3** (77 mg, 33%) and **5e** (340 mg, 55%).



Data for 5e: Pale yellow solid; R_f 0.18 (hexane/ethyl acetate, 2:1); mp: 245-247 °C; IR (film) ν: 3322, 2967, 1687, 1617 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.23 (s, 3H, Me-C^{7a}), 1.45 (s, 3H, Me-C^2), 1.47 (s, 3H, Me-C^2), 1.97 (d, 1H, *J* = 13.4, H-3^B), 2.26 (d, 1H, *J* = 13.4, H-3^A), 2.62 (d, 1H, *J* = 16.9, H-7^B), 2.71 (d, 1H, *J* = 16.9, H-7^A), 3.50 (s, 3H, OMe), 4.14 (s, 1H, NH), 5.45 (s, 1H, H-4), 6.53 (d, 1H, *J* = 8.3, H-9), 6.71 (ddd, 1H, *J* = 7.9, 7.1, 0.9, H-11), 7.18 (ddd, 1H, *J* = 8.3, 7.1, 1.5, H-10), 7.91 (dd, 1H, *J* = 7.9, 1.5, H-12); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 23.15 (Me-C^{7a}), 30.59 and 31.54 (2Me-C^2), 45.81 (C-3), 48.35 (C-7), 54.91 (OMe), 57.81, 57.84 (C-3a, C-7a), 71.90 (C-2), 114.19 (C-12a), 115.14 (C-9), 117.04 and 117.67 (C-4, C-11), 126.96 (C-12), 132.24 (C-10), 145.16 (C-8a), 149.60 (C-5), 165.69 (C-12b), 192.18 (C-6); **MS** (EI) m/z (%): 310 $[M]^+$ (95), 295 $[M\text{-}Me]^+$ (100); **Anal. Calcd for** $C_{19}H_{22}N_2O_2$: C 73.52, H 7.14, N 9.03; found: C 73.60, H 7.05, N 8.94.

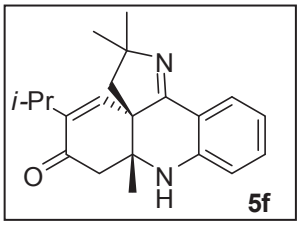
1-(2-aminophenyl)-9-isopropyl-3,3,6-trimethyl-2-azaspiro[4.5]deca-1,6,9-trien-8-one (4f) and (3a*S,7a*R**)-5-isopropyl-2,2,7a-trimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5f).** The title compounds were prepared from 1-isopropyl-2-methoxy-4-methylbenzene **1f** (328 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol) and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) in a similar manner as described for the preparation of **5a**. The crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 4:1 to 1:1) to give **4f** (59 mg, 9%) and **5f** (340 mg, 53%).

Data for 4f: Colorless solid; R_f 0.75 (hexane/ethyl acetate, 2:1); mp: 136-138 °C; **IR** (film) ν: 3426, 3254, 2964, 2874, 1656, 1616 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.04 (d, 3H, *J* = 6.9, Me-$C^{9'}$), 1.09 (d, 3H, *J* = 6.9, Me-$C^{9'}$), 1.47 (s, 3H, Me-C^3), 1.53 (s, 3H, Me-C^3), 1.83 (d, 3H, *J* = 1.3, Me-C^6), 1.98 (d, 1H, *J* = 13.8, H-4^B), 2.15 (d, 1H, *J* = 13.8, H-4^A), 3.07 (spd, 2H, *J* = 6.9, 1.1, H-9'), 6.24 (q, 1H, *J* = 1.3, H-7), 6.40 (ddd, 1H, *J* = 8.1, 7.0, 1.2, H-5'), 6.55 (br s, 2H, NH_2), 6.66 (dd, 1H, *J* = 8.3, 1.2, H-3'), 6.77 (d, 1H, *J* = 1.1, H-10), 7.02 (dd, 1H, *J* = 8.1, 1.5, H-6'), 7.08 (ddd, 1H, *J* = 8.3, 7.0, 1.5, H-4'); **^{13}C NMR**



(75 MHz, $CDCl_3$), δ, ppm: 19.94 (Me-C^6), 21.36 and 21.59 (2Me-$C^{9'}$), 25.84 (C-9'), 31.16 and 31.61 (2Me-C^3), 49.47 (C-4), 65.29 (C-5), 72.06 (C-3), 114.11 (C-1'), 115.66 and 116.16 (C-3', C-5'), 127.69 and 128.65 (C-4', C-6'), 131.25 (C-7), 142.32 (C-9), 145.31 (C-10), 149.22 (C-2'), 160.28 (C-6), 167.36 (C-1), 185.41 (C-8); **MS** (EI) m/z (%): 322 $[M]^+$ (14), 204 $[M-H_2NC_6H_4CN]^+$ (79), 189 $[M-H_2NC_6H_4CN-Me]^+$ (100); **Anal. Calcd for** $C_{21}H_{26}N_2O$: C 78.22, H 8.13, N 8.69; found: C 78.22, H 8.02, N 8.64.

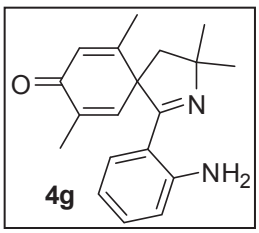
Data for 5f: Pale yellow solid; R_f 0.38 (hexane/ethyl acetate, 2:1); mp: 166.5-167 °C; **IR** (film) ν: 3359, 3316, 2963, 2876, 1669, 1618 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 0.87 (d, 3H, *J* = 6.9, Me-$C^{5'}$); 0.96 (d, 3H, *J* = 6.9, Me-$C^{5'}$); 1.22 (s, 3H, Me-C^{7a}), 1.43 (s, 3H, Me-C^2), 1.46 (s, 3H, Me-C^2), 1.88 (d, 1H, *J* = 13.4, H-3^B), 2.22 (d, 1H, *J* = 13.4, H-3^A), 2.52 (d, 1H, *J* = 16.7, H-7^B), 2.60 (d, 1H, *J* = 16.7, H-7^A), 2.80 (spd, 1H, *J* = 6.9, 1.1, H-5'), 3.86 (s, 1H, NH), 6.25 (d, 1H, *J* = 1.1, H-4), 6.49 (dd, 1H, *J* = 8.3, 0.9, H-9), 6.70 (ddd, 1H, *J* = 7.9, 7.1, 0.9, H-11), 7.16 (ddd, 1H, *J* = 8.3, 7.1, 1.5, H-10), 7.87 (dd, 1H, *J* = 7.9, 1.5, H-12); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 21.35 and 21.63 (2Me-$C^{5'}$), 23.30 and 26.00 (C5' and Me-C^{7a}), 30.58 and 31.56 (2Me-C^2), 45.40 (C-3), 45.51 (C-7), 57.68 and 58.51 (C-3a and C-7a), 71.88 (C-2), 114.12 (C-12a), 114.80 (C-9), 117.37 (C-11), 126.84 (C-12), 132.23 (C-10), 142.49, 142.83 and 145.19 (C-4, C-5, C-8a), 165.72 (C-12b), 196.92 (C-6); **MS** (EI) m/z (%): 322 $[M]^+$ (74), 307 $[M-Me]^+$ (100); **Anal. Calcd for** $C_{21}H_{26}N_2O$: C 78.22, H 8.13, N 8.69; found: C 78.20, H 8.12, N 8.66.



5f

1-(2-Aminophenyl)-3,3,6,9-tetramethyl-2-azaspiro[4.5]deca-1,6,9-trien-8-one (4g) and (3a*S,7a*R**)-2,2,5,7a-tetramethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5g).** The title compounds were prepared from 2-methoxy-1,4-dimethylbenzene **1f** (272 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol), and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) in a similar manner as described for the preparation of **5a**. The crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 3:1 to 1:1) to give **4g** (67 mg, 11%) and **5g** (372 mg, 63%).

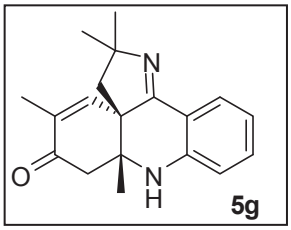
Data for 4g: Colorless solid; R_f 0.75 (hexane/ethyl acetate, 2:1); mp: 193-197 °C; **IR** (film) ν: 3348, 3245, 3004, 2942, 2962, 1665, 1632, 1612 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.46 (s, 3H, Me-C^3), 1.53 (s, 3H, Me-C^3), 1.84 (d, 3H, *J* = 1.3, Me-C^6), 1.94 (d, 3H, *J* = 1.5, Me-C^9), 2.03 (d, 1H, *J* = 13.9, H-4^B), 2.14 (d, 1H, *J* = 13.9, H-4^A), 6.25 (q, 1H, *J* = 1.3, H-7), 6.42 (ddd, 1H, *J* = 8.1, 7.0, 1.2, H-5'), 6.56 (br s, 2H, NH_2), 6.66 (dd, 1H, *J* = 8.2, 1.2, H-3'), 6.88 (q, 1H, *J* = 1.5, H-10), 7.04 (dd, 1H, *J* = 8.1, 1.4, H-6'), 7.09 (ddd,



4g

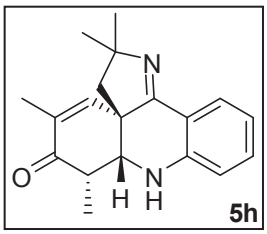
1H, J = 8.2, 7.0, 1.4, H-4'); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 15.70 (Me-C^9), 20.11 (Me-C^6), 31.23 and 31.64 (2Me-C^3), 49.29 (C-4), 65.60 (C-5), 72.18 (C-3), 114.16 (C-1'), 115.88 (C-5'), 116.21 (C-3'), 127.22 (C-7), 128.69 (C-6'), 131.33 (C-4'), 132.92 (C-9), 148.33 (C-10), 149.29 (C-2'), 161.31 (C-6), 167.17 (C-1), 186.47 (C-8); **MS** (EI) m/z (%): 294 $[M]^+$ (10), 176 $[M\text{-}H_2NC_6H_4CN]^+$ (60), 161 $[M\text{-}H_2NC_6H_4CN\text{-}Me]^+$ (62), 118 $[H_2NC_6H_4CN]^+$ (100); **Anal. Calcd for** $C_{19}H_{22}N_2O$: C 77.52, H 7.53, N 9.52; found: C 77.70, H 7.42, N 9.50.

Data for 5g: Yellow solid; R_f 0.38 (hexane/ethyl acetate, 2:1); mp: 228-229 °C; **IR** (film) ν: 3325, 2967, 1661, 1612 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, J/Hz: 1.23 (s, 3H, Me-C^{7a}), 1.43 (s, 3H, Me-C^2), 1.46 (s, 3H, Me-C^2), 1.72 (d, 3H, J = 1.5, Me-C^5), 1.93 (d, 1H, J = 13.5, H-3^B), 2.22 (d, 1H, J = 13.5, H-3^A), 2.54 (d, 1H, J = 16.8, H-7^B), 2.60 (d, 1H, J = 16.8, H-7^A), 4.18 (s, 1H, NH), 6.36 (q, 1H, J = 1.5, H-4), 6.52 (dd, 1H, J = 8.3, 1.0, H-9), 6.70 (ddd, 1H, J = 7.9, 7.0, 1.0, H-11), 7.17 (ddd, 1H, J = 8.3, 7.0, 1.5, H-10), 7.88 (dd, 1H, J = 7.9, 1.5, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 15.51 (Me-C^5), 23.38 (Me-C^{7a}), 30.56 and 31.54 (2Me-C^2), 45.08 (C-3), 48.06 (C-7), 58.19 and 58.79 (C-3a and C-7a), 71.97 (C-2), 114.24 (C-12a), 114.97 (C-9), 117.50 (C-11), 126.88 and 132.25 (C10 and C12), 133.04 (C-5), 145.39 (C-8a), 145.52 (C-4), 165.44 (C-12b), 197.73 (C-6); MS (EI) m/z (%): 294 $[M]^+$ (79), 279 $[M\text{-}Me]^+$ (100); **Anal. Calcd for** $C_{19}H_{22}N_2O$: C 77.52, H 7.53, N 9.52; found: C 77.26, H 7.52, N 9.48.



5g

(3a*S,7*S**,7a*R**)-2,2,5,7-Tetramethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5h) and (3a*S**,7*R**,7a*R**)-2,2,5,7-tetramethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5h').** 2,6-Dimethylphenol **1h** (244 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol), and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) were combined in CH_2Cl_2 (0.5 ml) and the mixture was added dropwise to stirred concentrated sulfuric acid (92%, 1 ml, 17 mmol) at 5-7 °C. The reaction mixture was stirred at room temperature for 25 min and poured into mixture of ice (25 g) and NH_3 (aq) (7 mL). The product was extracted with CH_2Cl_2 (3×15 ml), and the combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and filtered. After the solvent was removed, the crude mixture was purified by column chromatography on silica gel (hexane/acetone, 7:1) to give a mixture of diastereomers **5h** and **5h'** (390 mg, 66%; **5h:5h'** = 84:16). Pure **5h** was obtained after recrystallization of the mixture of diastereomers from ethyl acetate.

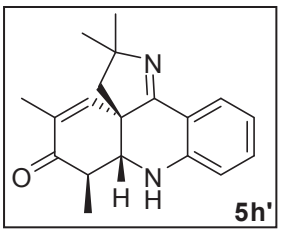


5h

Data for 5h: Pale yellow solid; R_f 0.25 (hexane/acetone, 7:1); mp: 248-250°C; **IR** (film) ν: 3372, 2956, 2861, 1669, 1611 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, J/Hz: 1.29 (d, 3H, J = 7.2, Me-C^7), 1.41 (s, 3H,

Me-C^2), 1.48 (s, 3H, Me-C^2), 1.73 (d, 3H, *J* = 1.5, Me-C^5), 2.06 (d, 1H, *J* = 12.7, H-3^B), 2.19 (d, 1H, *J* = 12.7, H-3^A), 2.82 (qd, 1H, *J* = 7.2, 2.2, H-7), 3.65 (t, 1H, *J* = 2.3, H-7a), 4.12 (s, 1H, NH), 6.31 (dq, 1H, *J* = 2.5, 1.5, H-4), 6.55 (dd, 1H, *J* = 8.3, 1.0, H-9), 6.72 (ddd, 1H, *J* = 7.9, 7.0, 1.0, H-11), 7.18 (ddd, 1H, *J* = 8.3, 7.0, 1.5, H-10), 7.86 (dd, 1H, *J* = 7.9, 1.5, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 11.43 (Me-C^5), 16.01 (Me-C^7), 30.00 and 31.37 (2Me-C^2), 42.16 (C-7), 49.07 (C-3), 54.87 (C-3a), 64.20 (C-7a), 71.90 (C-2), 114.85 (C-9), 115.43 (C-12a), 118.01 (C-11), 126.90 (C-12), 132.21 (C-10), 134.30 (C-5), 142.09 (C-4), 146.32 (C-8a), 166.60 (C-12b), 198.80 (C-6); **MS** (EI) m/z (%): 294 $[M]^+$ (100); **Anal. Calcd for** $C_{19}H_{22}N_2O$: C 77.52, H 7.53, N 9.52; found: C 77.44, H 7.31, N 9.46.

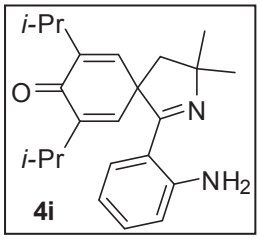
Data for 5h': R_f 0.13 (hexane/acetone, 7:1). 1.26 (d, 3H, *J* = 7.6, Me-C^7), 1.40 (s, 3H, Me-C^2), 1.47 (s, 3H, Me-C^2), 1.75 (d, 3H, *J* = 1.5, Me-C^5), 2.07 (d, 1H, *J* = 12.8, H-3^B), 2.24 (d, 1H, *J* = 12.8, H-3^A), 2.54 (qd, 1H, *J* = 7.6, 2.6, H-7), 3.66 (t, 1H, *J* = 2.5, H-7a), 4.00 (s, 1H, NH), 6.33 (m, 1H, H-4), 6.51 (dd, 1H, *J* = 8.3, 1.0, H-9), 6.69 (ddd, 1H, *J* = 7.9, 7.3, 1.0, H-11), 7.17 (ddd, 1H, *J* = 8.3, 7.3, 1.5, H-10), 7.86 (dd, 1H, *J* = 7.9, 1.5, H-12); **MS** (EI) m/z (%): 294 $[M]^+$ (100).



5h'

1-(2-Aminophenyl)-7,9-diisopropyl-3,3-dimethyl-2-azaspiro[4.5]deca-1,6,9-trien-8-one (4i), (3a*S,7*S**,7a*R**)-5,7-diisopropyl-2,2-dimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5i) and (3a*S**,7*R**,7a*R**)-5,7-diisopropyl-2,2-dimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5i').** The title compounds were prepared from 2,6-diisopropylphenol **1i** (356 mg, 2.0 mmol), isobutyric aldehyde **2** (216 mg, 3.0 mmol), and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) in a similar manner as described for the preparation of **5h/5h'**. The crude mixture was purified by column chromatography on silica gel (hexanes/ethyl acetate, 5:1) to give **4i** (155 mg, 22%), starting 2-aminobenzonitrile **3** (60 mg, 25%), and mixture of diastereomers **5i** and **5i'** (305 mg, 44%; **5i:5i'**=25:75). The mixture **5i+5i'** (305 mg) was separated by using silica gel column chromatography (hexane/isopropanol, 30:1) to give **5i** (60 mg), **5i+5i'** (27 mg), and **5i'** (204 mg).

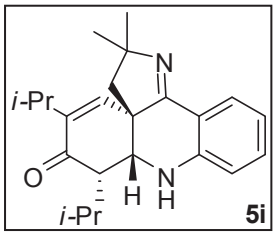
Data for 4i: Colorless solid; R_f 0.70 (hexane/ethyl acetate, 5:1); mp: 118-122 °C; **IR** (film) ν: 3439, 3252, 2964, 2873, 1623, 1611, 1550 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.03 and 1.08 (both d, 3H, *J* = 6.9, Me-$C^{7'}$and Me-$C^{9'}$), 1.49 (s, 6H, 2Me-C^3), 2.07 (s, 2H, H-4), 3.10 (sp, 2H, *J* = 6.9, H-7', H-9'), 6.37 (ddd, 1H, *J* = 8.2, 7.0, 1.2, H-5'), 6.55 (br s, 2H, NH_2), 6.65 (dd, 1H, *J* = 8.2, 1.2, H-3'), 6.72 (s, 2H, H-6, H-10), 7.06 (ddd, 1H, *J* = 8.2, 7.0, 1.5, H-4'), 7.09 (dd, 1H, *J* = 8.2, 1.5, H-6'); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm:



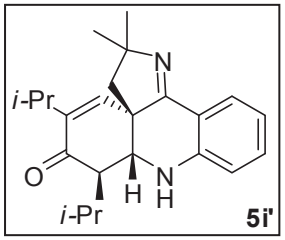
4i

21.48 and 21.68 (2Me-$C^{7'}$, 2Me-$C^{9'}$), 26.31 (C-7', C-9'), 31.24 (2Me-C^{3}), 49.68 (C-4), 61.36 (C-5), 71.82 (C-3), 114.51 (C-1'), 115.30, 116.09 (C-3', C-5'), 129.49, 131.13 (C-4', C-6'), 143.56 (C-7, C-9), 144.32 (C-6, C-10), 149.19 (C-2'), 167.82 (C-1), 184.29 (C-8); **MS** (EI) m/z (%): 350 $[M]^+$ (11), 232 $[M\text{-}H_2NC_6H_4CN]^+$ (100); **Anal. Calcd for** $C_{23}H_{30}N_2O$: C 78.82, H 8.63, N 7.99; found: C 78.62, H 8.50, N 7.92.

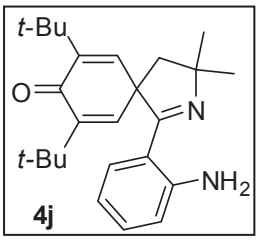
Data for 5i: Pale yellow solid; R_f 0.25 (hexane/isopropanol, 30:1); mp: 169-171°C; **IR** (film) ν: 3391, 3326, 2961, 2871, 1677, 1618 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 0.89 (d, 3H, *J* = 6.9, Me-$C^{5'}$), 0.95 (d, 3H, *J* = 6.9, Me-$C^{5'}$), 1.01 (d, 3H, *J* = 6.5, Me-$C^{7'}$), 1.16 (d, 3H, *J* = 6.5, Me-$C^{7'}$), 1.42 (s, 3H, Me-C^{2}), 1.49 (s, 3H, Me-C^{2}), 2.00 (d, 1H, *J* = 12.8, H-3^{B}), 2.15 (d, 1H, *J* = 12.8, H-3^{A}), 2.31 (dsp, 1H, *J* = 8.2, 6.5, H-7'), 2.34 (dd, 1H, *J* = 8.2, 1.7, H-7), 2.82 (spd, 1H, *J* = 6.9, 1.1, H-5'), 3.84 (dd, 1H, *J* = 2.1, 1.7, H-7a), 4.06 (s, 1H, NH), 6.13 (dd, 1H, *J* = 2.1, 1.1, H-4), 6.49 (dd, 1H, *J* = 8.4, 1.0, H-9), 6.69 (ddd, 1H, *J* = 7.8, 7.0, 1.0, H-11), 7.14 (ddd, 1H, *J* = 8.4, 7.0, 1.5, H-10), 7.85 (dd, 1H, *J* = 7.8, 1.5, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 19.73 (Me-$C^{7'}$), 21.65 and 21.68 (2Me-$C^{5'}$), 23.32 (Me-$C^{7'}$), 24.05 (C-7'), 26.49 (C-5'), 30.00 and 31.45 (2Me-C^{2}), 49.29 (C-3), 53.80 (C-7), 54.66 (C-3a), 60.65 (C-7a), 71.65 (C-2), 114.58 (C-9), 115.27 (C-12a), 117.76 (C-11), 126.88 (C-12), 132.11 (C-10), 137.27 (C-4), 144.78 (C-5), 146.30 (C-8a), 166.89 (C-12b), 197.98 (C-6); **MS** (EI) m/z (%): 350 $[M]^+$ (100); **Anal. Calcd for** $C_{23}H_{30}N_2O$: C 78.82, H 8.63, N 7.99; found: C 78.61, H 8.69, N 7.85.



Data for 5i': Pale yellow solid; R_f 0.20 (hexane/isopropanol, 30:1); mp: 187-189 °C; **IR** (film) ν: 3255, 2964, 2871, 1667, 1612 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 0.90 (d, 3H, *J* = 6.4, Me-$C^{7'}$), 0.91 (d, 3H, *J* = 6.9, Me-$C^{5'}$), 0.96 (d, 3H, *J* = 6.9, Me-$C^{5'}$), 1.08 (d, 3H, *J* = 6.4, Me-$C^{7'}$), 1.43 (s, 3H, Me-C^{2}), 1.48 (s, 3H, Me-C^{2}), 1.99 (dsp, 1H, *J* = 11.2, 6.4, H-7'), 2.07 (dd, 1H, *J* = 11.2, 2.9, H-7), 2.16 (d, 1H, *J* = 12.9, H-3^{B}), 2.28 (d, 1H, *J* = 12.9, H-3^{A}), 2.82 (spd, 1H, *J* = 6.9, 1.1, H-5'), 3.98 (t, 1H, *J* = 2.5, H-7a), 4.25 (s, 1H, NH), 6.12 (dd, 1H, *J* = 2.3, 1.1, H-4), 6.49 (dd, 1H, *J* = 8.3, 1.0, H-9), 6.63 (ddd, 1H, *J* = 7.9, 7.0, 1.0, H-11), 7.10 (ddd, 1H, *J* = 8.3, 7.0, 1.5, H-10), 7.84 (dd, 1H, *J* = 7.9, 1.5, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 20.98 (Me-$C^{5'}$), 21.57 (Me-$C^{7'}$), 21.91 and 21.94 (Me-$C^{5'}$, Me-$C^{7'}$), 26.26 (C-7'), 26.46 (C5'), 29.79 and 31.78 (2Me-C^{2}), 51.10 (C-3), 53.28 (C-3a), 59.36 (C-7a), 61.05 (C-7), 71.65 (C-2), 114.13 (C-9), 114.20 (C-12a), 117.19 (C-11), 126.60 (C-12), 132.05 (C-10), 138.04 (C-4), 142.76 (C-5), 146.17 (C-8a), 166.50 (C-12b), 199.21 (C-6); **MS** (EI) m/z (%): 350 $[M]^+$ (100); **Anal. Calcd for** $C_{23}H_{30}N_2O$: C 78.82, H 8.63, N 7.99; found: C 78.68, H 8.64, N 7.95.



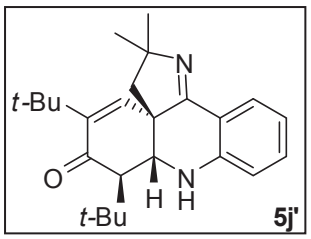
1-(2-aminophenyl)-7,9-di-*tert*-butyl-3,3-dimethyl-2-azaspiro[4.5]deca-1,6,9-trien-8-one (4j), (3a*S,7*R**,7a*R**)-5,7-Di-*tert*-butyl-2,2-dimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (5j'), and (3a*S**,7*R**,7a*R**)--5,7,11-tri-tert-butyl-2,2-dimethyl-2,3,7a,8-tetrahydropyrrolo[3,2-l]acridin-6(7H)-one (7). Method A.** The title compounds were prepared from 2,6-di-*tert*-butylphenol (416 mg, 2.0 mmol), isobutyric aldehyde (216 mg, 3.0 mmol), and 2-aminobenzonitrile (236 mg, 2.0 mmol) in a similar manner as described for the preparation of **5h/5h'**. The crude mixture was purified by column chromatography on silica gel (hexanes/ethyl acetate, 7:1) to give starting 2-aminobenzonitrile **3** (52 mg, 22 %), spirodienone **4j'** (56 mg, 7 %) and **5j** (36 mg, 5 %). **Method B.** 2,6-Di-tert-butyl-4-(1-hydroxy-2-methylpropyl)phenol **6** (556 mg, 2.0 mmol) and 2-aminobenzonitrile **3** (236 mg, 2.0 mmol) were combined in CH_2Cl_2 (1 ml) and the mixture was added dropwise to stirred concentrated sulfuric acid (92%, 1 ml, 17 mmol) at 5-7 °C. The reaction mixture was stirred at room temperature for 25 min and poured into a mixture of ice (25 g) and NH_3 (aq) (7 mL). The product was extracted with CH_2Cl_2 (3×15 mL), and the combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and filtered. The crude mixture was purified by column chromatography on silica gel (hexane/acetone, 7:1) to give **4j** (100 mg, 13%), a mixture of **5j'** and **7** (120 mg) and pure **5j'** (310 mg, 41%). The mixture of **5j'** and **7** (120 mg) was separated by column chromatography on silica gel (hexane/acetone, 15:1) to give pure compound **7** (60 mg, 7%).



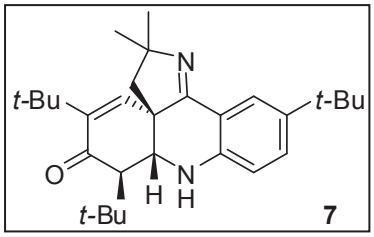
4j

Data for 4j: Colorless solid; R_f 0.63 (hexane/acetone, 7:1); mp: 156-158 °C; **IR** (film) ν: 3451, 3253, 2968, 2947, 2867, 1652, 1616, 1586, 1549 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.23 (s, 18H, *t*-Bu-C^7, *t*-Bu-C^9), 1.48 (s, 6H, 2Me-C^3), 2.06 (s, 2H, H-4), 6.39 (ddd, 1H, *J* = 8.1, 7.0, 1.2, H-5'), 6.54 (br s, 2H, NH_2), 6.65 (dd, 1H, *J* = 8.3, 1.20, H-3'), 6.73 (s, 2H, H-6, H-10), 7.06 (ddd, 1H, *J* = 8.3, 7.0, 1.5, H-4'), 7.11 (dd, 1H, *J* = 8.1, 1.5, H-6'); **^{13}C NMR** (75 MHz, $CDCl_3$), δ, ppm: 29.20 (6C, *t*-Bu-C^7, *t*-Bu-C^9), 31.22 (2Me-C^3), 34.83 (C-7', C-9'), 50.02 (C-4), 61.18 (C-5), 71.80 (C-3), 114.53 (C-1'), 115.34 and 116.22 (C-3', C-5'), 129.50 and 131.13 (C-4', C-6'), 143.95 (C-6, C-10), 145.55 (C-2'), 149.16 (C-7, C-9), 168.38 (C-1), 185.78 (C-8); **MS** (EI) m/z (%): 378 $[M]^+$ (11), 260 $[M-H_2NC_6H_4CN]^+$ (100); **Anal. Calcd for** $C_{25}H_{34}N_2O$: C 79.32, H 9.05, N 7.40; found: C 79.38, H 8.99, N 7.34.

Data for 5j': Pale yellow solid; R_f 0.37 (hexane/acetone, 7:1); mp: 217-218 °C. **IR** (film) ν: 3383, 3260, 2960, 2871, 1658, 1614, 1520 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.11 (s, 18H, *t*-Bu-C^5, *t*-Bu-C^7), 1.38 (s, 3H, Me-C^2), 1.46 (s, 3H, Me-C^2), 2.10 (d, 1H, *J* = 2.0, H-7), 2.07 (d, 1H, *J* = 12.6, H-3^B), 2.19 (d, 1H, *J* = 12.6, H-3^A), 3.76 (s, 1H, NH), 3.91 (t,



1H, *J* = 2.0, H-7a), 6.16 (d, 1H, *J* = 2.1, H-4), 6.48 (d, 1H, *J* = 8.3, H-9), 6.66 (ddd, 1H, *J* = 7.9, 7.0, 1.0, H-11), 7.14 (ddd, 1H, *J* = 8.3, 7.0, 1.4, H-10), 7.86 (dd, 1H, *J* = 7.9, 1.4, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), δ, ppm: 29.31 and 29.36 (*t*-Bu-C^5, *t*-Bu-C^7); 29.75 and 31.67 (2Me-C^2), 32.77 (C-7'), 34.89 (C-5'), 52.74 (C-3a), 52.97 (C-3), 58.65 (C-7a), 65.12 (C-7), 71.08 (C-2), 113.89 (C-12a), 113.96 (C-9), 117.42 (C-11), 126.78 (C-12), 132.23 (C-10), 138.41 (C-4), 146.02 (C-8a), 146.94 (C-5), 166.59 (C-12b), 199.71 (C-6); **MS** (EI) m/z (%): 378 $[M]^+$ (100). **Anal. Calcd for** $C_{25}H_{34}N_2O$: C 79.32, H 9.05, N 7.40; found: C 79.09, H 9.27, N 7.44.



Data for 7: pale yellow solid; R_f 0.46 (hexane/acetone, 7:1); mp: 215-217 °C; **IR** (film) ν: 3378, 3269, 2958, 2871, 1664, 1617, 1506 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ, ppm, *J*/Hz: 1.11 (s, 9H, t-Bu), 1.12 (s, 9H, t-Bu), 1.29 (s, 9H, t-Bu-C^{11}), 1.37 (s, 3H, Me-C^2), 1.46 (s, 3H, Me-C^2), 2.02 (d, 1H, *J* = 12.4, H-3^B), 2.07 (d, 1H, *J* = 2.0, H-7), 2.13 (d, 1H, *J* = 12.4, H-3^A), 3.64 (s, 1H, NH), 3.85 (t, 1H, *J* = 2.0, H-7a), 6.17 (d, 1H, *J* = 2.0, H-4), 6.45 (d, 1H, *J* = 8.6, H-9), 7.22 (dd, 1H, *J* = 8.6, 2.3, H-10), 7.83 (d, 1H, *J* = 2.3, H-12); **^{13}C NMR** (126 MHz, $CDCl_3$), *δ*, ppm: 29.29 and 29.34 (*t*-Bu-C^5, *t*-Bu-C^7), 29.72 (Me-C^2), 31.41 (*t*-Bu-C^{11}), 31.66 (Me-C^2), 32.71 (C-7'), 34.08 (C-11'), 34.90 (C-5'), 52.99 (C-3a), 53.35 (C-3), 58.64 (C-7a), 65.28 (C-7), 70.98 (C-2), 113.50 (C-12a), 114.03 (C-9), 122.72 (C-12), 129.99 (C-10), 138.52 (C-4), 140.36 (C-11), 144.05 (C-8a), 147.15 (C-5), 166.96 (C-12b), 200.11 (C-6); **MS** (EI) m/z (%): 434 $[M]^+$ (60), 419 $[M-Me]^+$ (100); **Anal. Calcd for** $C_{25}H_{34}N_2O$: C 80.13, H 9.74, N 6.44; found: C 80.12, N 9.57, H 6.69.

3. ORTEP Drawing and Crystallographic Data

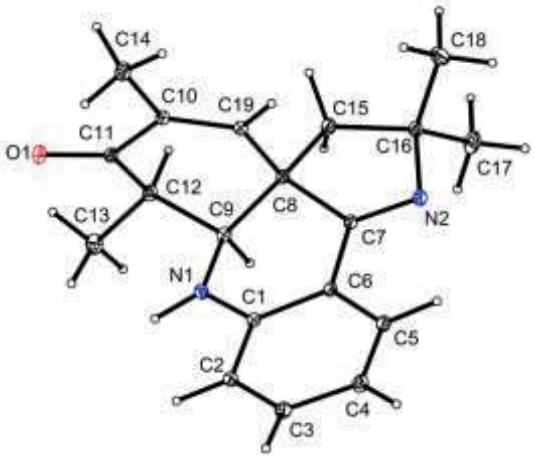


Figure 1.

ORTEP drawing of (±)-**5h** (CDCC No 988502)

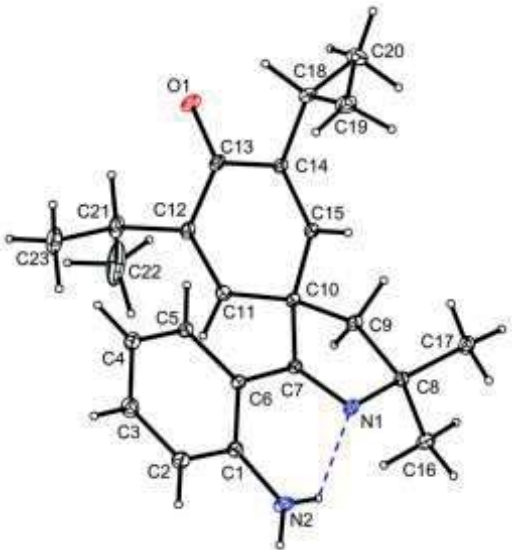


Figure 2.

ORTEP drawing of **4i** (CDCC No 988501)

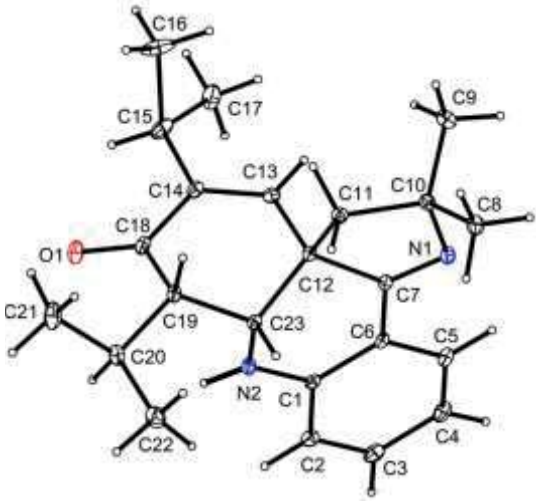


Figure 3.

ORTEP drawing of (±)-**5i** (CDCC No 988503)

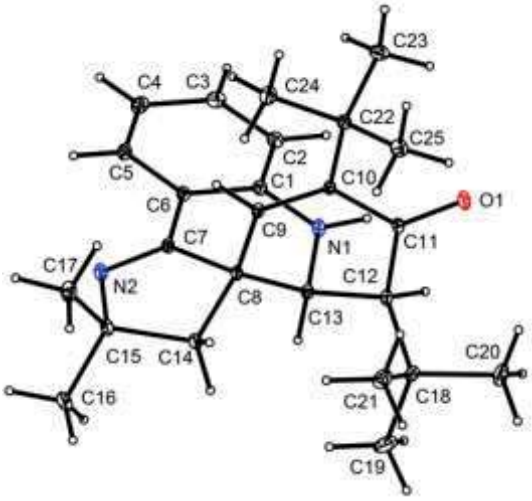


Figure 4.

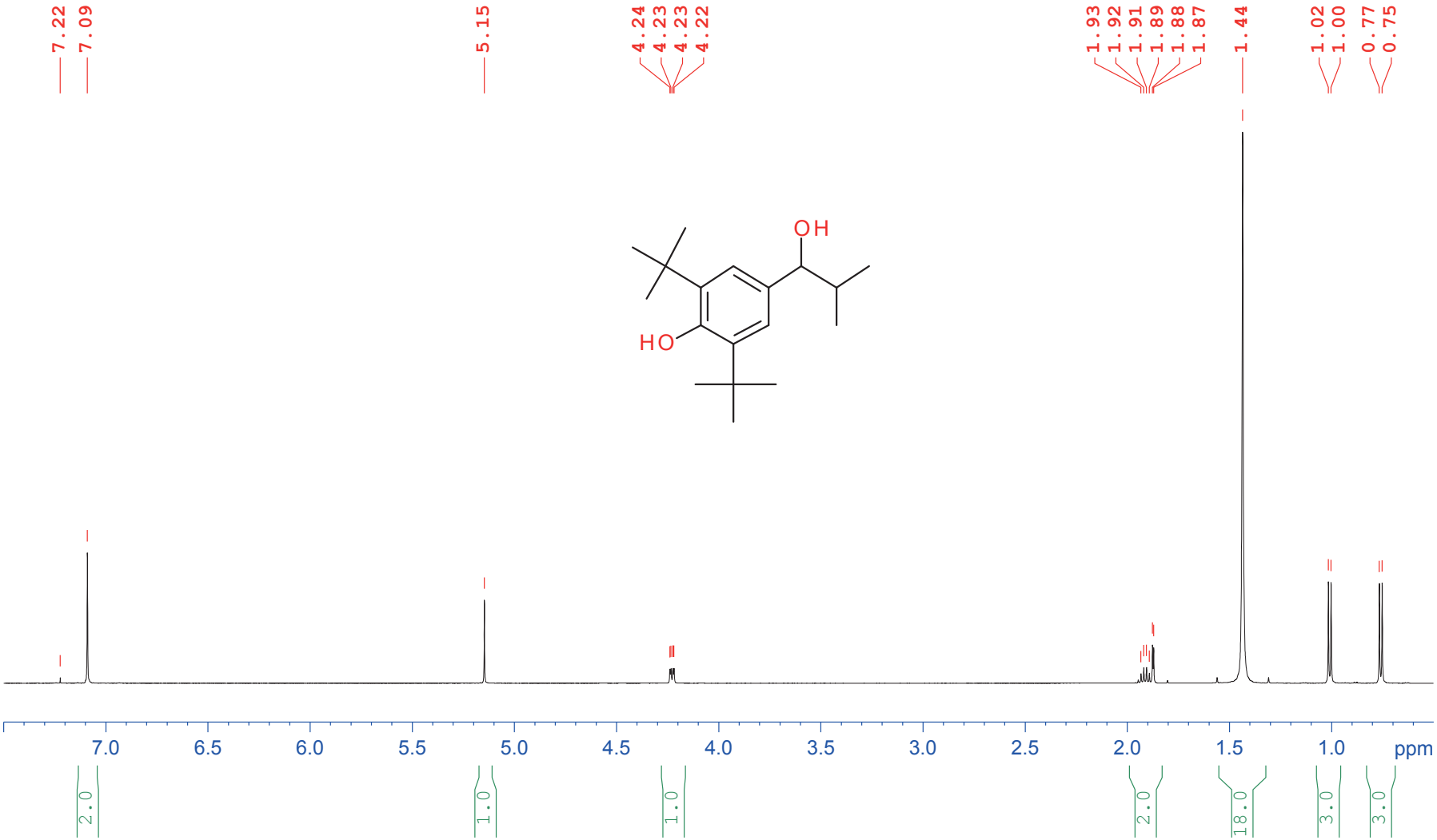
ORTEP drawing of (±)-**5j'** (CDCC No 988504)

Table 1

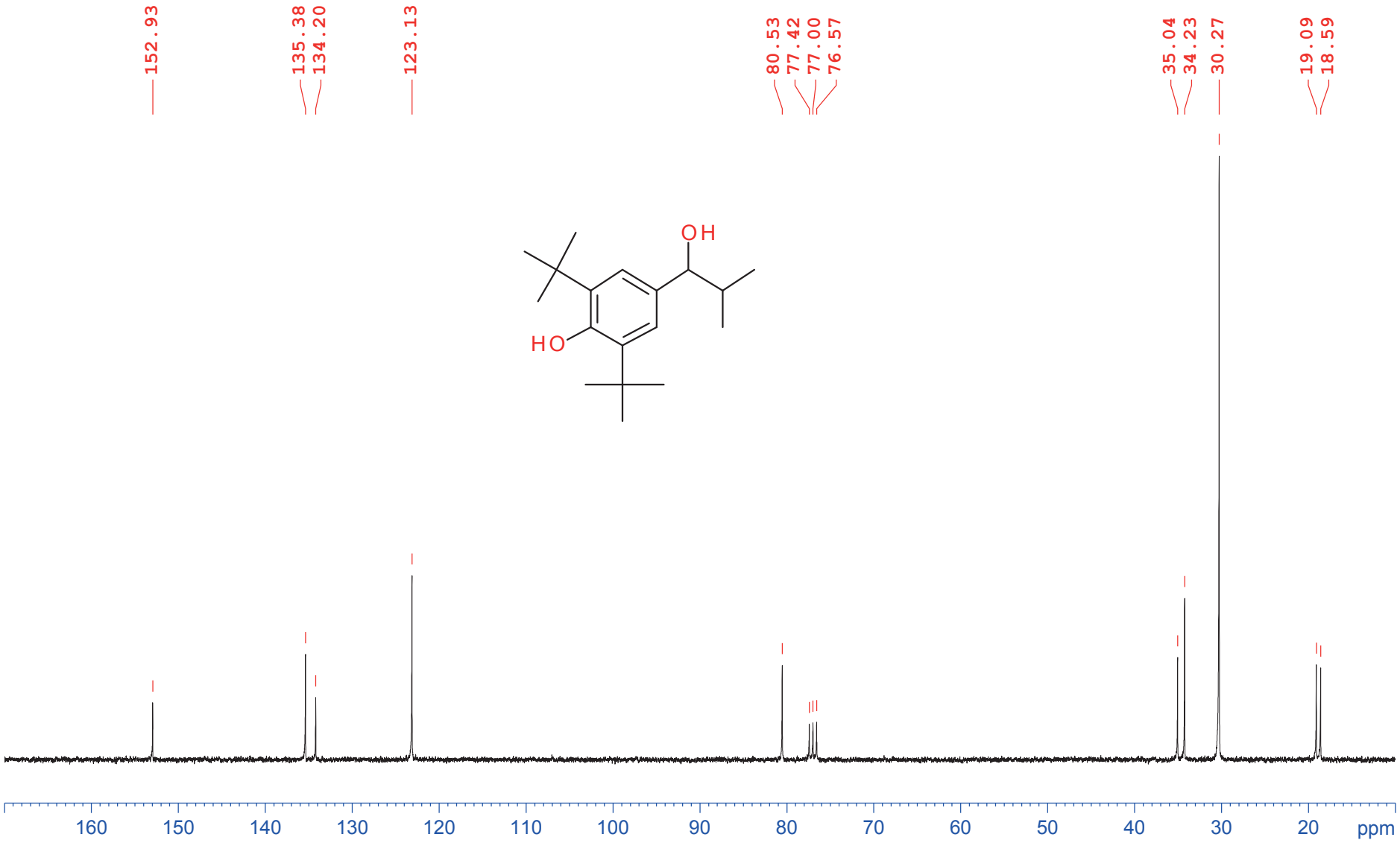
Crystallographic Data and Structure Refinement for **5h**, **4i**, **5i** and **5j'**

Identification code	**5h**	**4i**	**5i**	**5j'**
CDCC No	988502	988501	988503	988504
Empirical formula	$C_{19}H_{22}N_2O$	$C_{23}H_{30}N_2O$	$C_{23}H_{30}N_2O$	$C_{25}H_{34}N_2O$
Formula weight	294.39	350.49	350.49	378.54
Crystal description	prism	prism	prism	prism
Crystal colour	colorless	colorless	yellow	colorless
Crystal size, mm	0.25×0.19×0.16	0.21×0.16×0.09	0.21×0.15×0.09	0.25×0.20×0.15
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	P 2_1/n	P 2_1/c	C 2/c	P 2_1/c
a, Å	12.2990(9)	9.5020(15)	19.2894(4)	9.7929(7)
b, Å	10.4923(8)	21.727(3)	9.7066(9)	9.9455(10)
c, Å	12.5948(12)	10.9938(11)	22.2610(18)	22.885(2)
α, º	90.00	90.00	90.00	90.00
β, º	97.493(7)	113.802(12)	98.072(13)	93.459(7)
γ, º	90.00	90.00	90.00	90.00
V, Å^3	1611.4(2)	2076.7(5)	4126.7(5)	2224.8(4)
Z	4	4	8	4
ρ_{calcld}, g/cm^{-3},	1.213	1.121	1.128	1.130
μ, mm^{-1}	0.075	0.068	0.069	0.068
F(000)	632	760	1520	824
Theta range for data collection	2.92- 28.28	3.00- 26.38	2.90-26.40	2.66-26.41
Reflections collected	8823	15767	9782	13376
Independent reflections (R_{int})	3899 (0.0311)	4193 (0.0704)	4156 (0.0418)	4511 (0.0457)
Data / restraints / parameter	3899/0/231	4193/0/243	4156/0/257	4511/0/265
Goodness-of-Fit on $F2$	1.005	1.000	1.000	1.006
Final R indices [I>2sigma(I)]	R_1=0.0400 wR_2=0.0774	R_1=0.1344 wR_2=0.1562	R_1=0.1045 wR_2=0.0888	R_1=0.0989 wR_2=0.0885
R indices (all data)	R_1=0.0998 wR_2=0.0825	R_1=0.0600 wR_2=0.1426	R_1=0.0414 wR_2=0.0835	R_1= 0.0440 wR_2=0.0817
Completeness to theta (deg)	97.5 (28.28)	98.8 (26.38)	98.2 (26.40)	98.5 (26.41)
Largest diff. peak and hole, e·Å^{-3}	0.134 and -0.140	0. 344 and -0.206	0.182 and -0.176	0.192 and -0.187

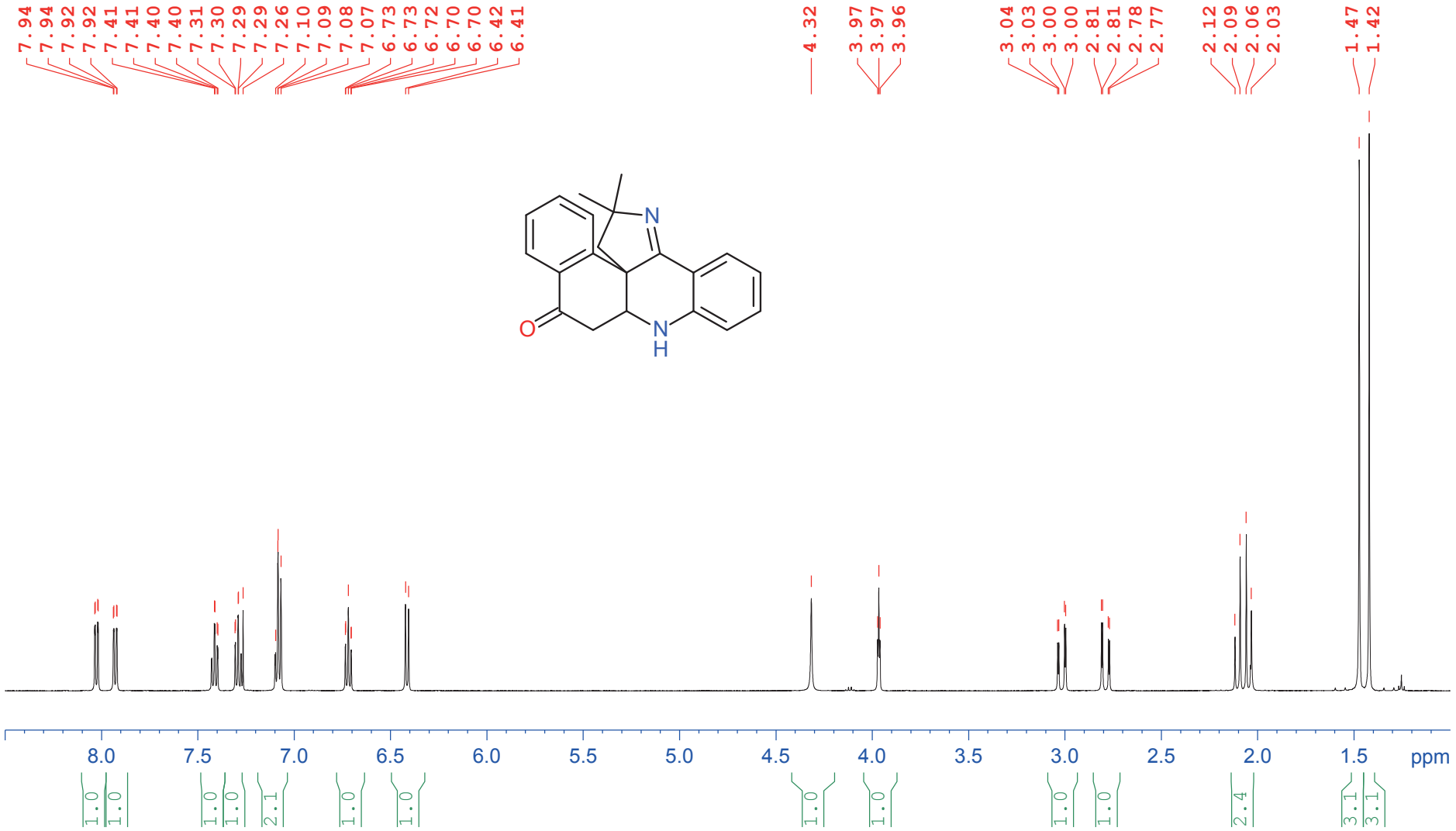
4. ^{1}H and ^{13}C NMR Spectra



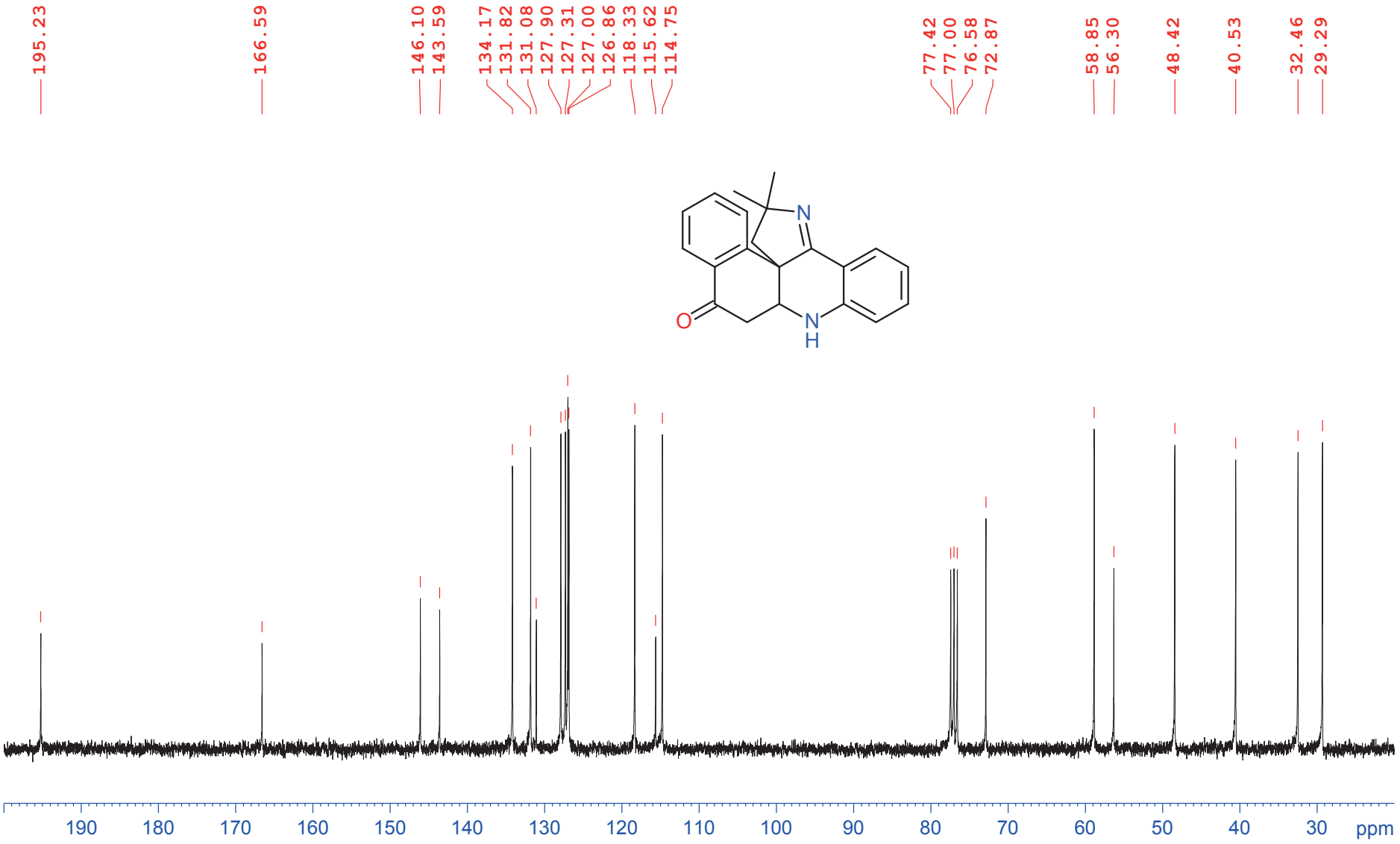
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **6**.



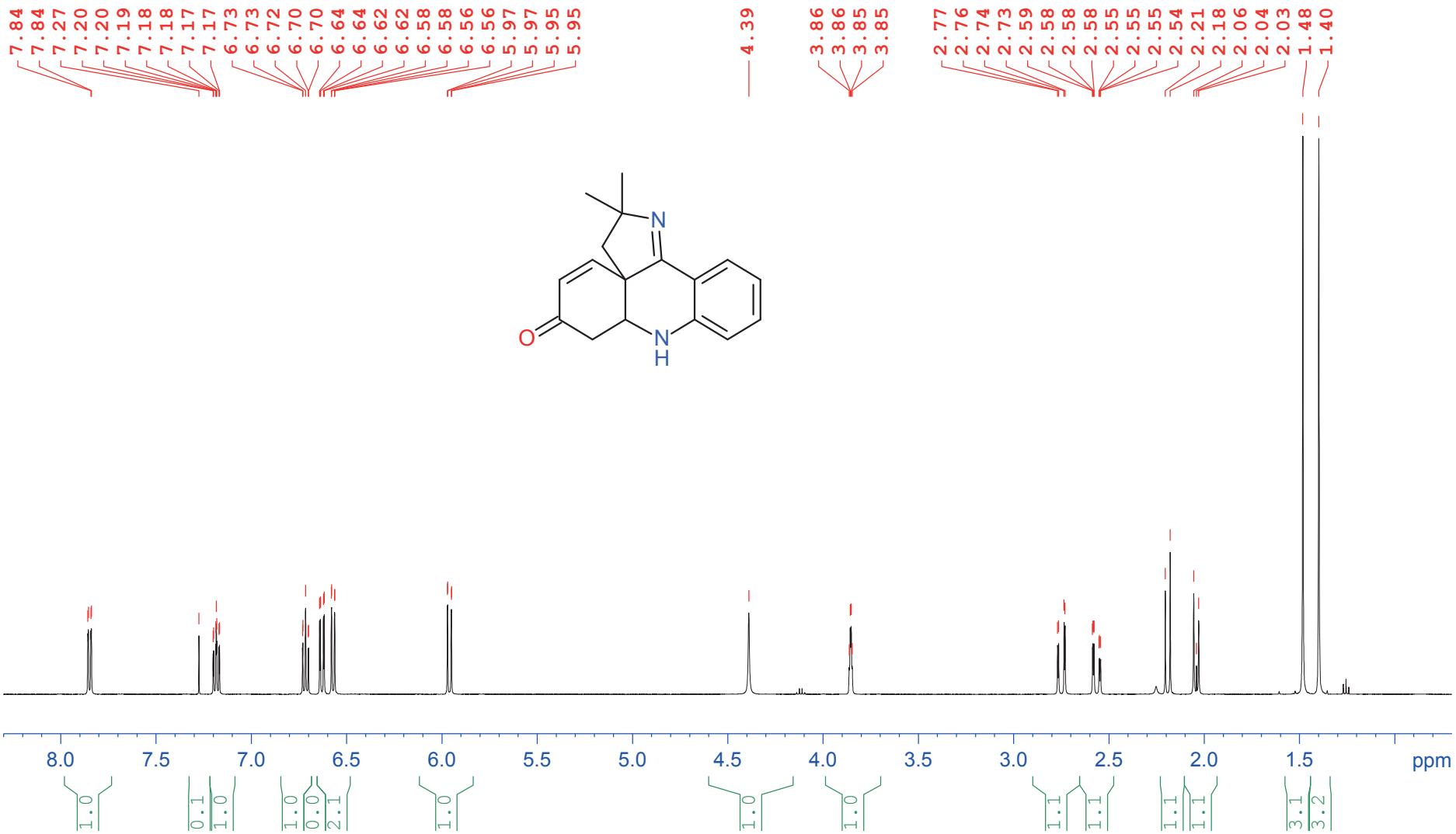
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **6**.



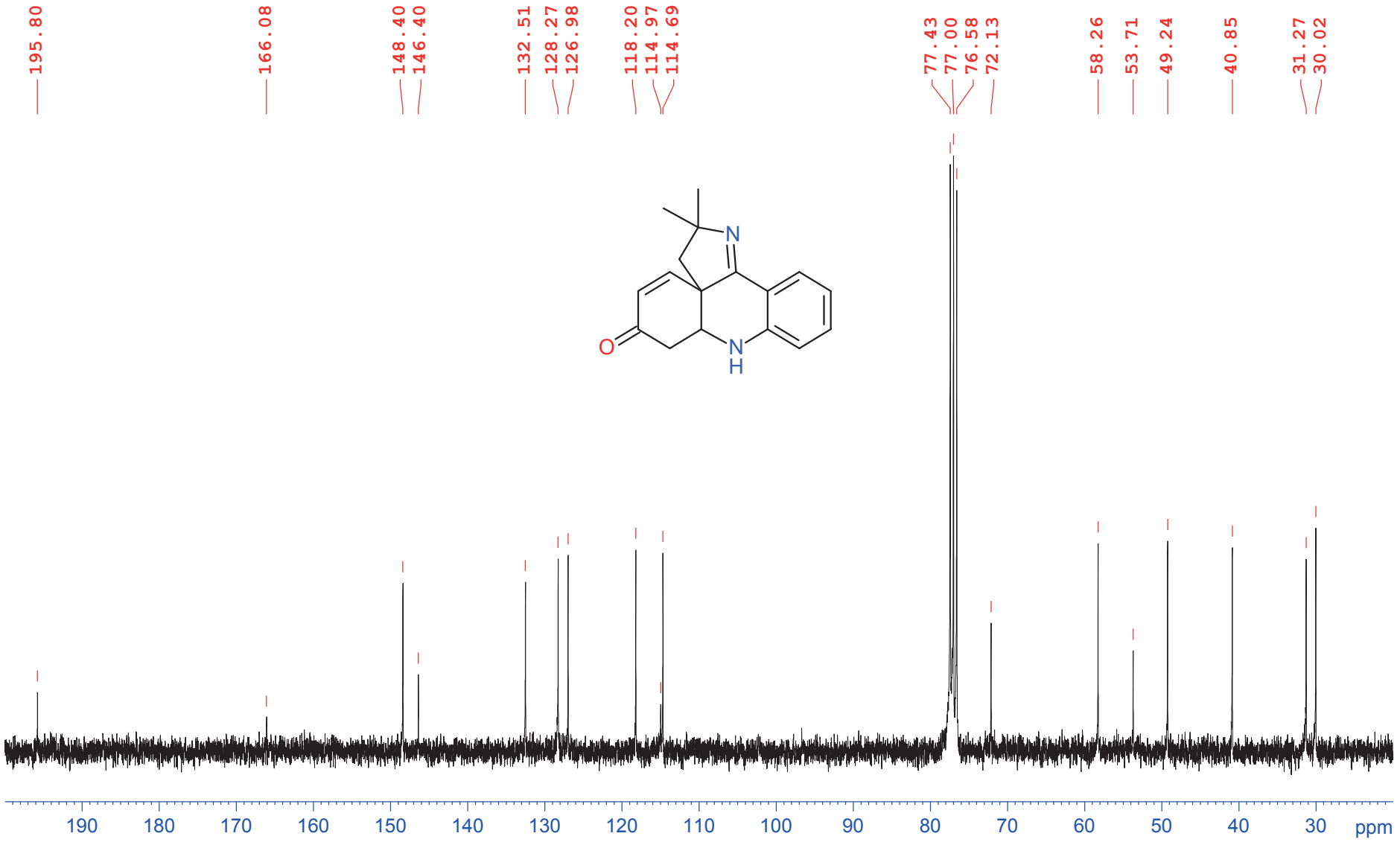
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5a**.



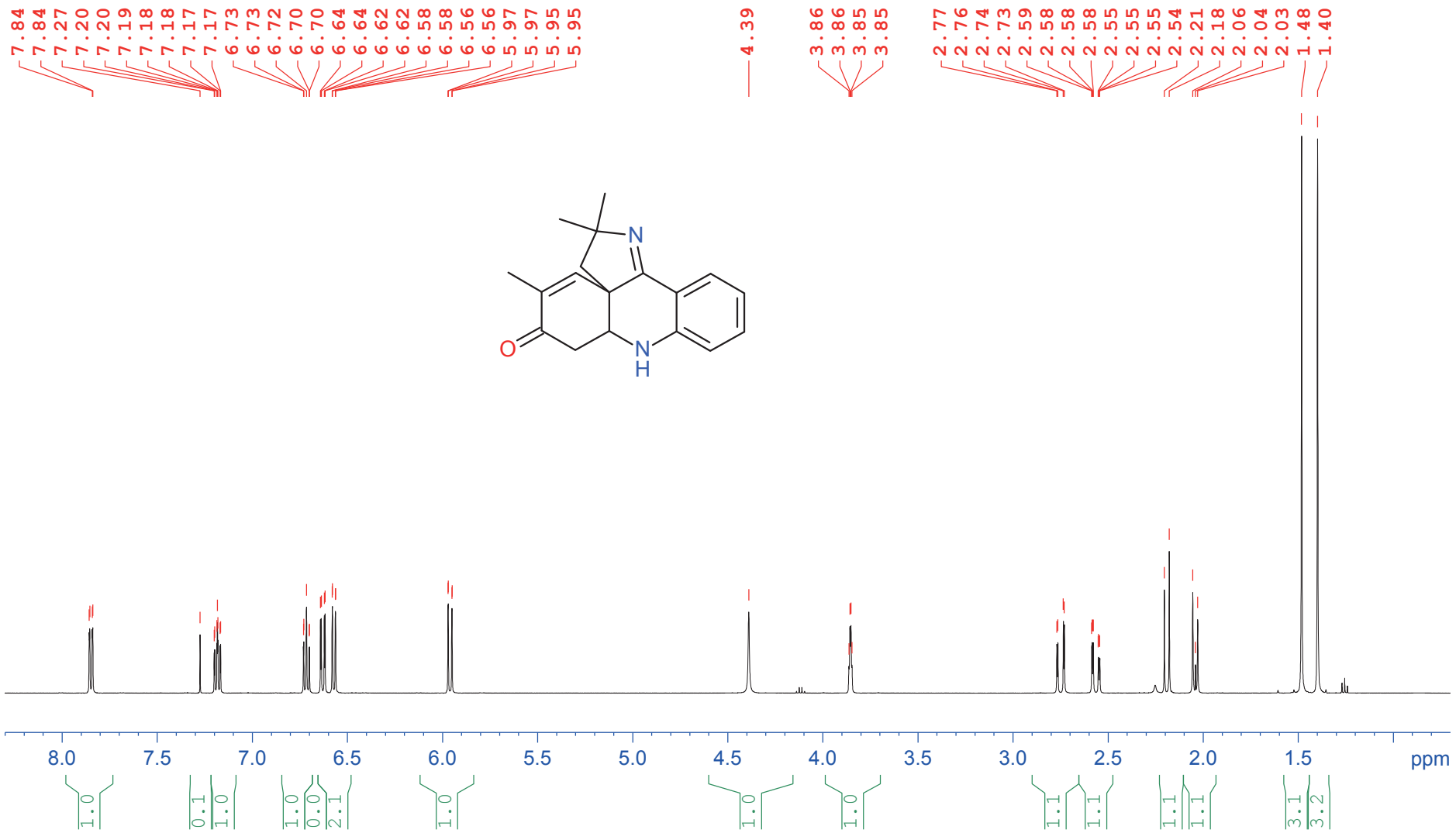
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **5a**.



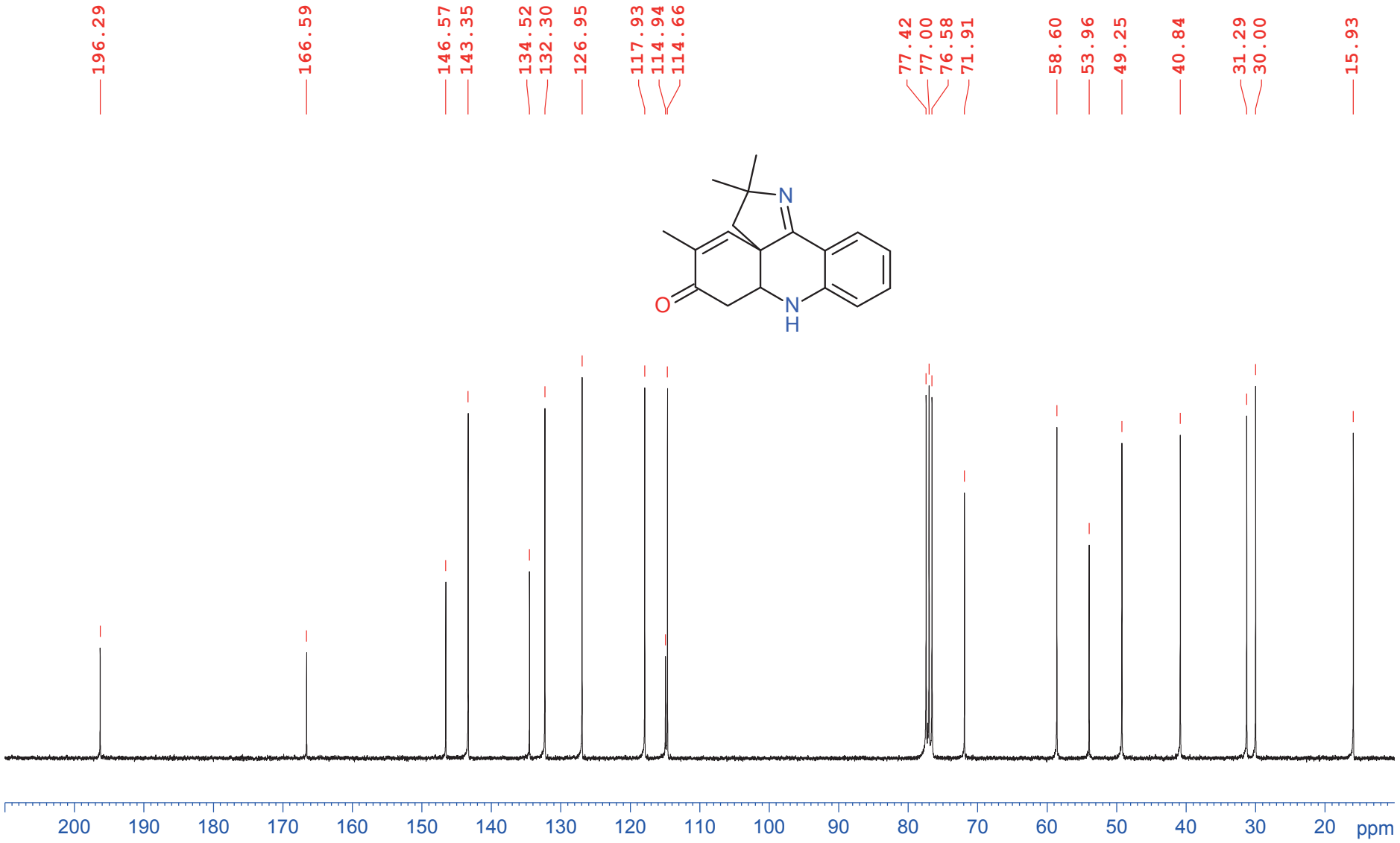
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5b**.



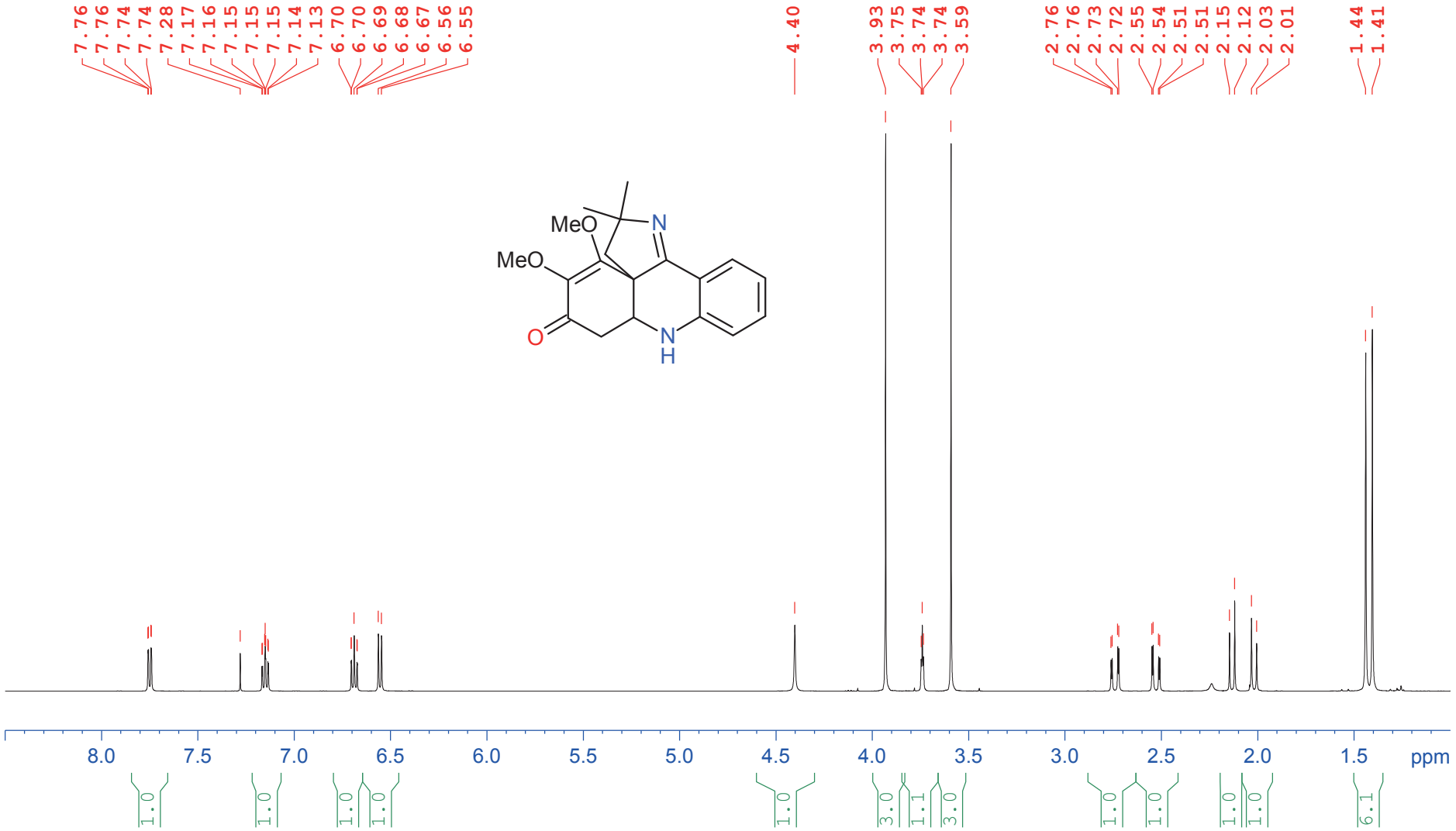
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **5b**.



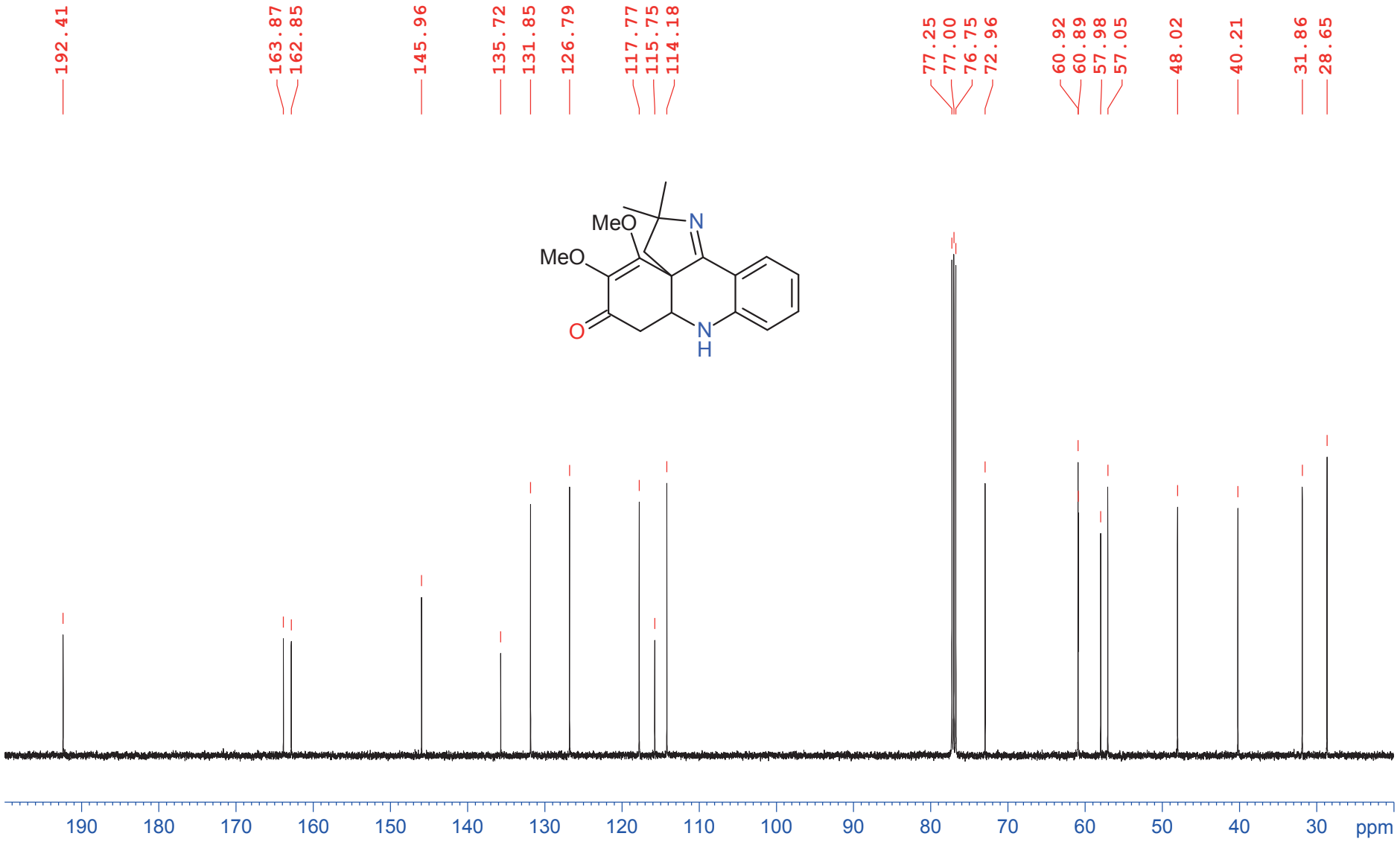
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5c**.



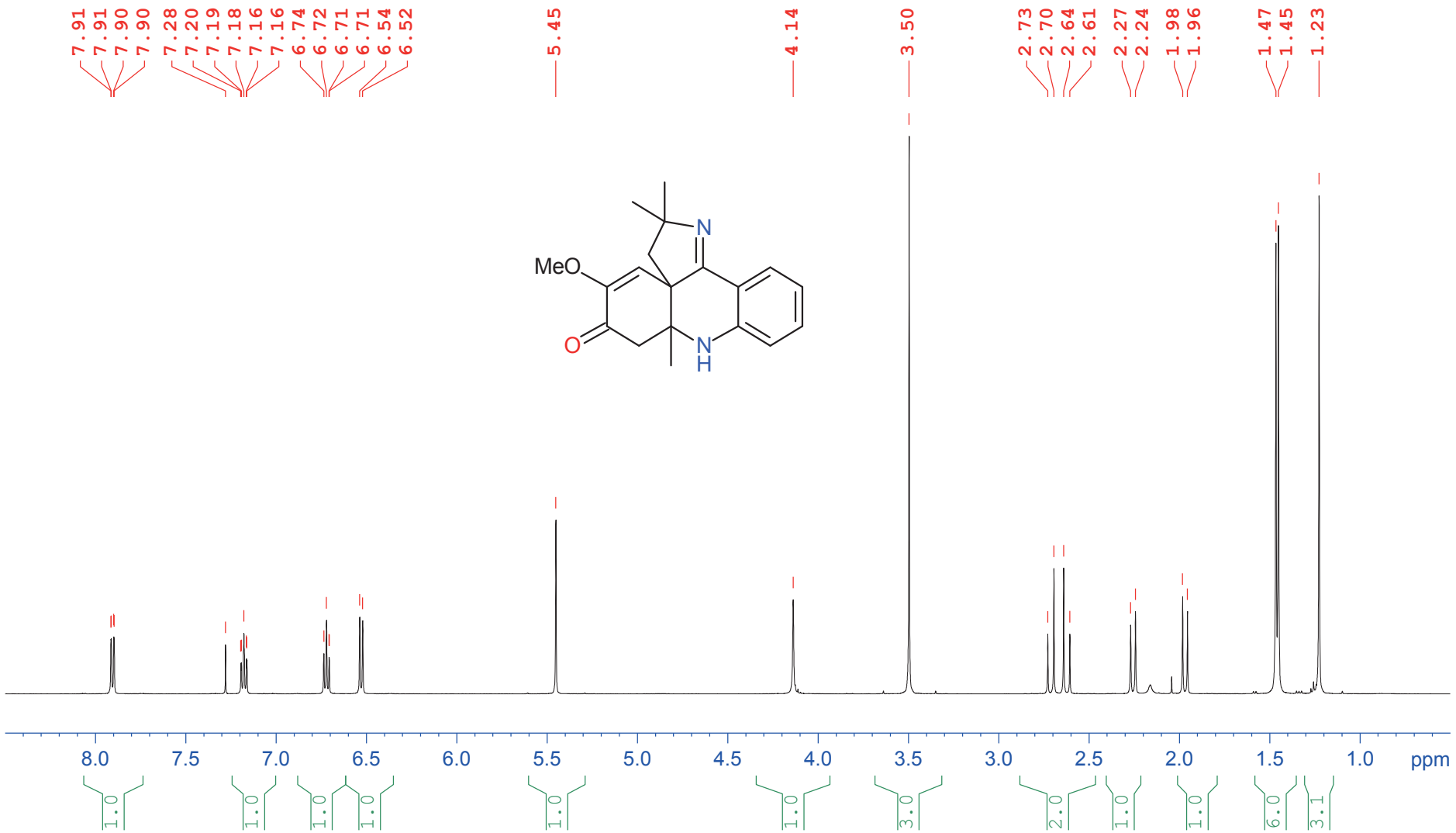
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **5c**.



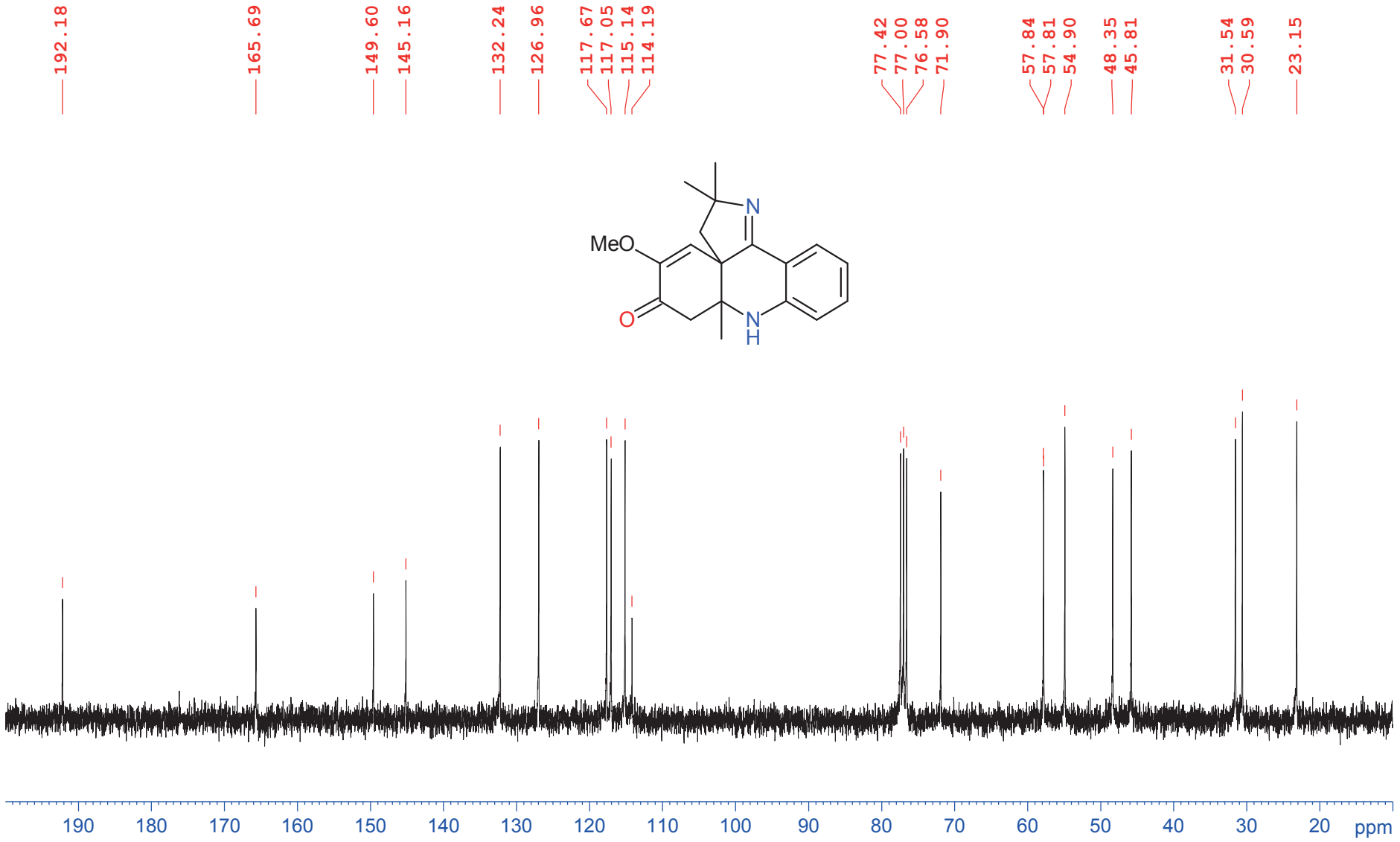
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5d**.



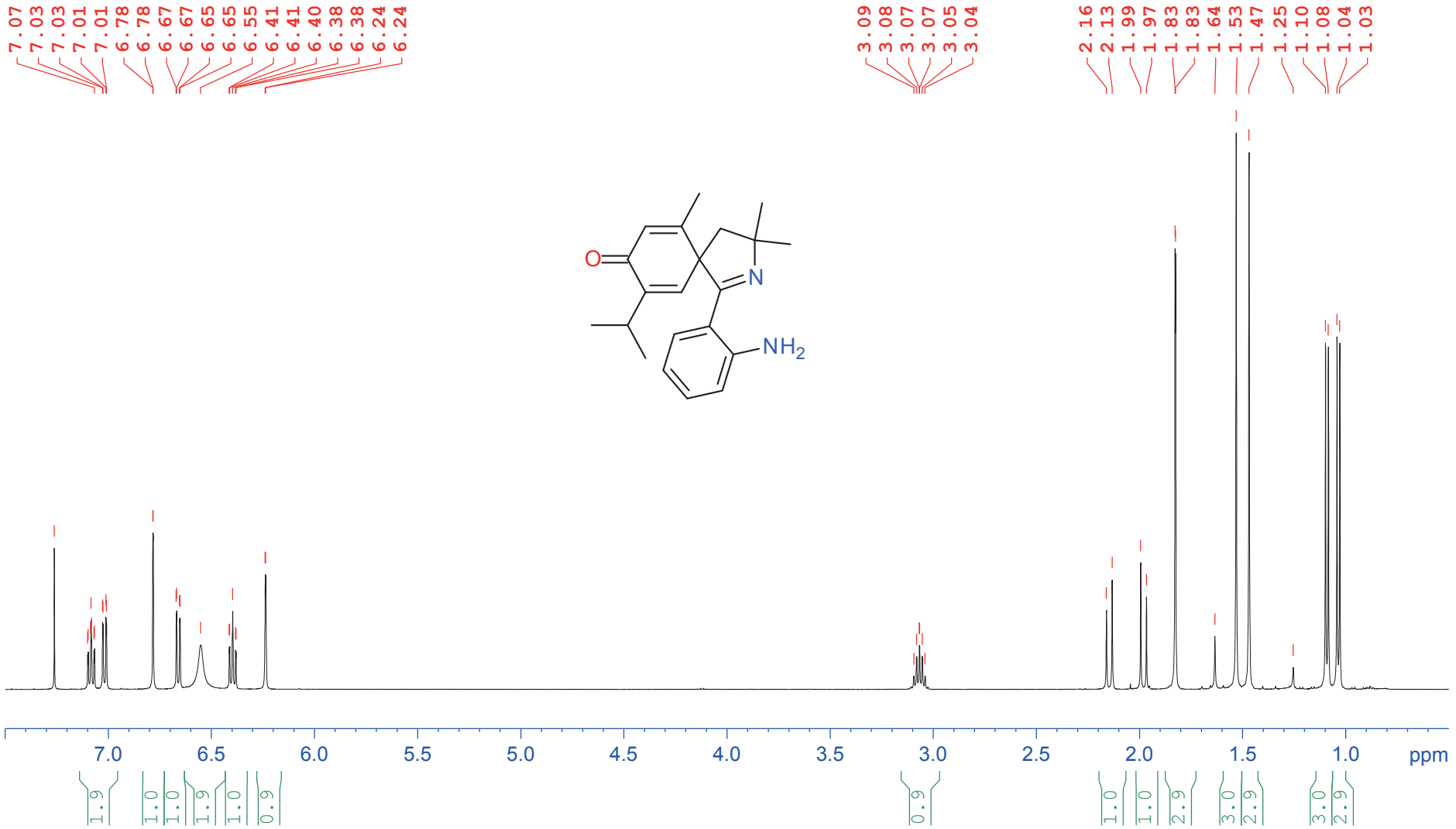
^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5d**.



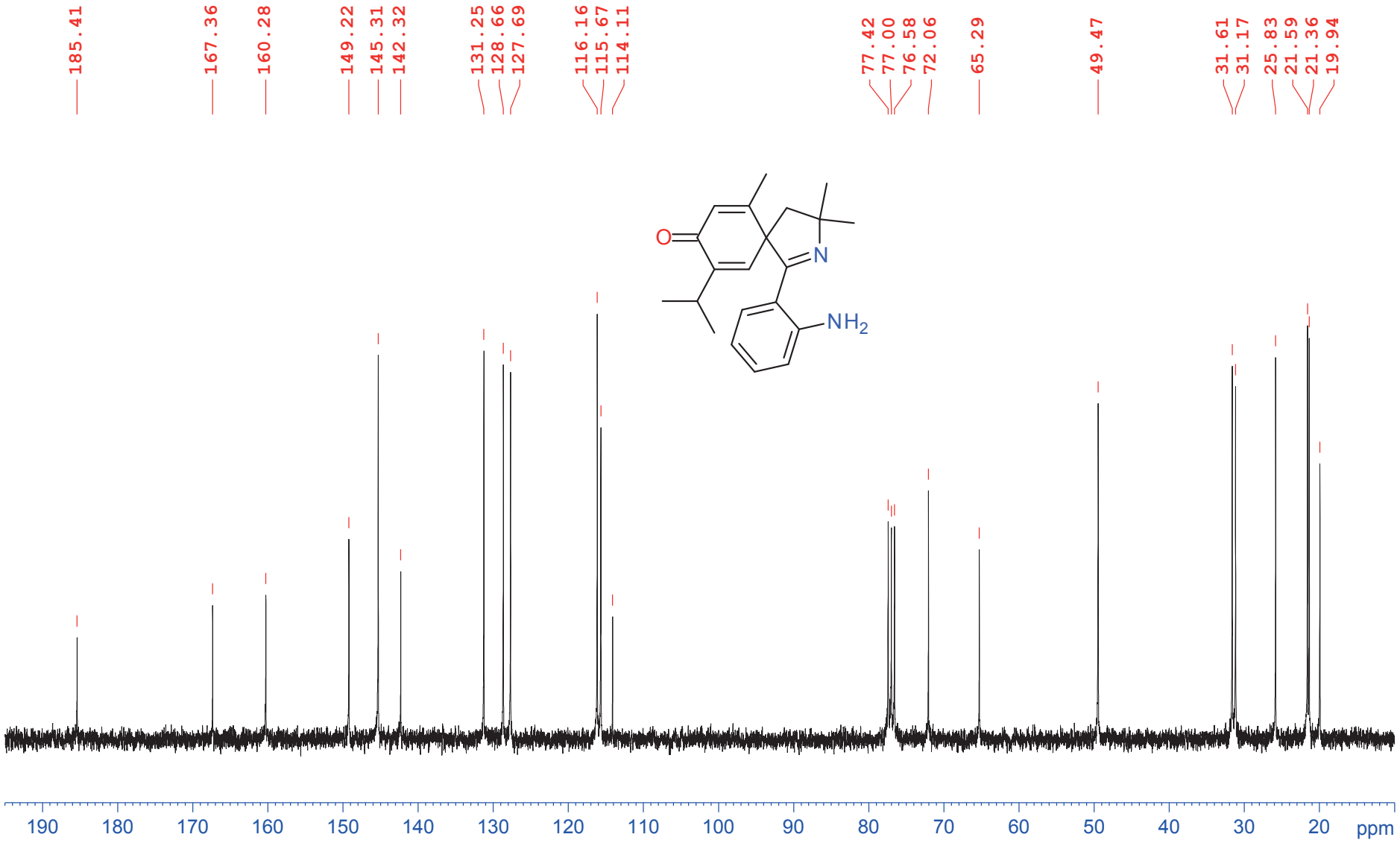
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5e**.



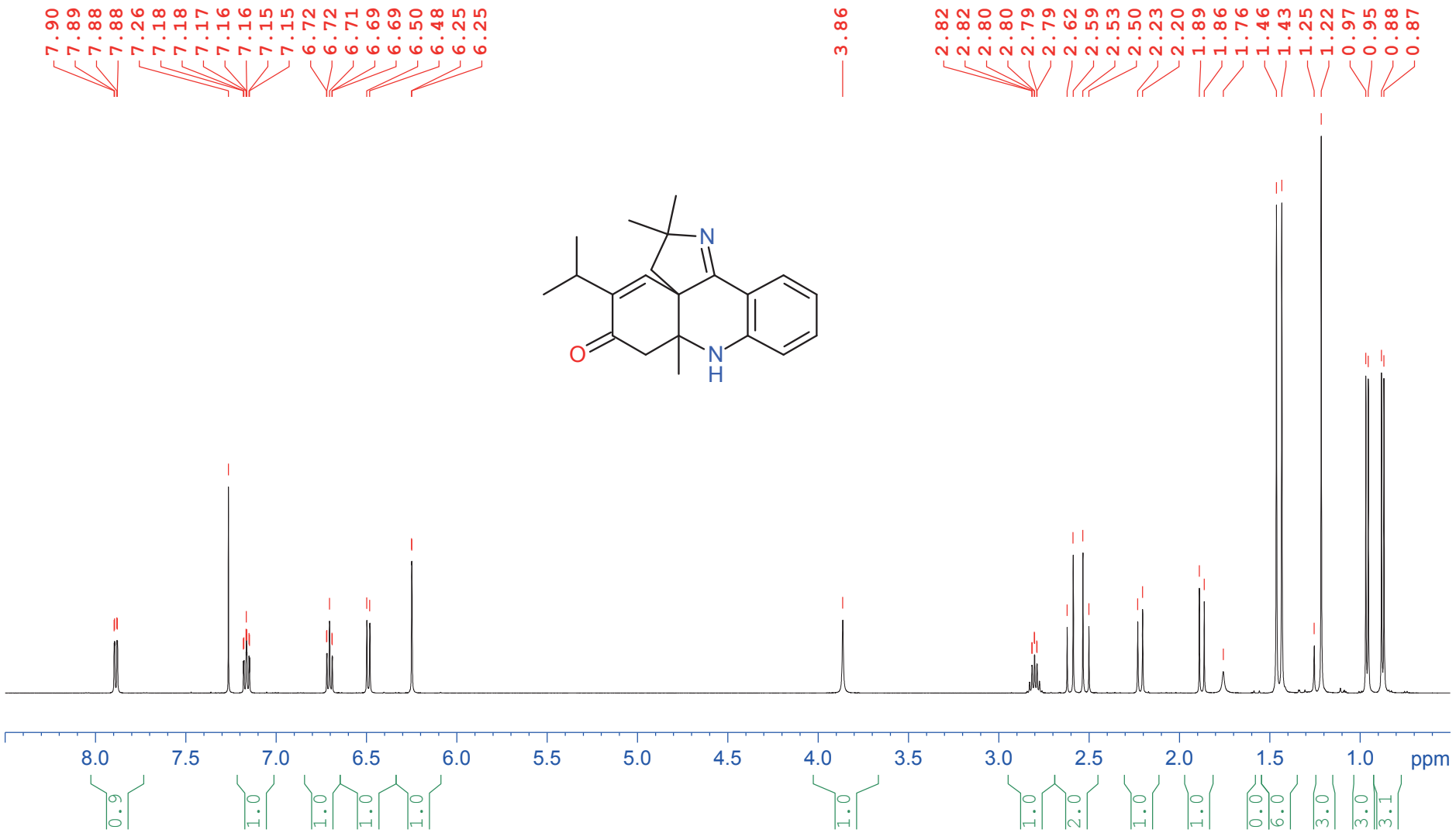
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **5e**.



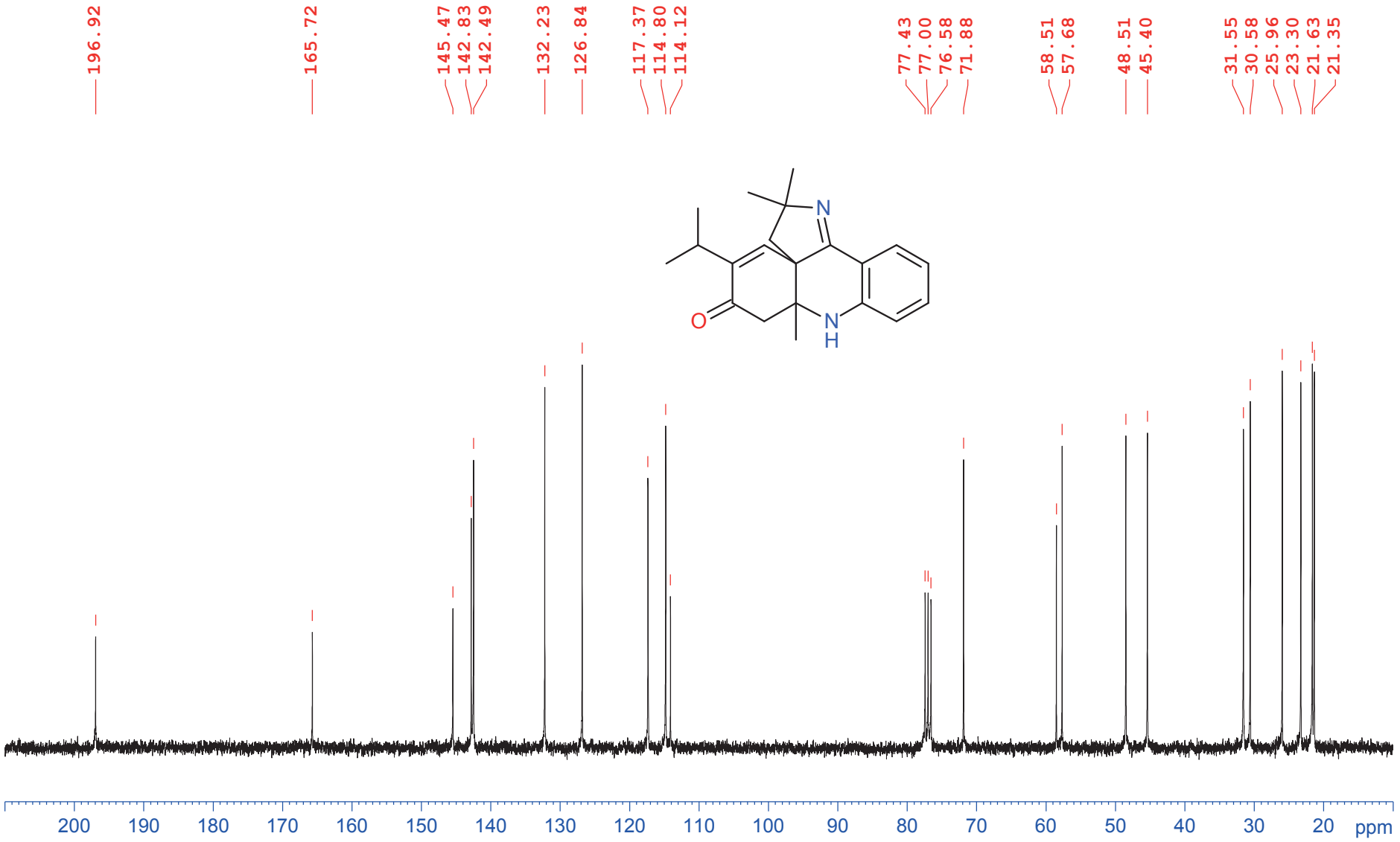
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **4f**.



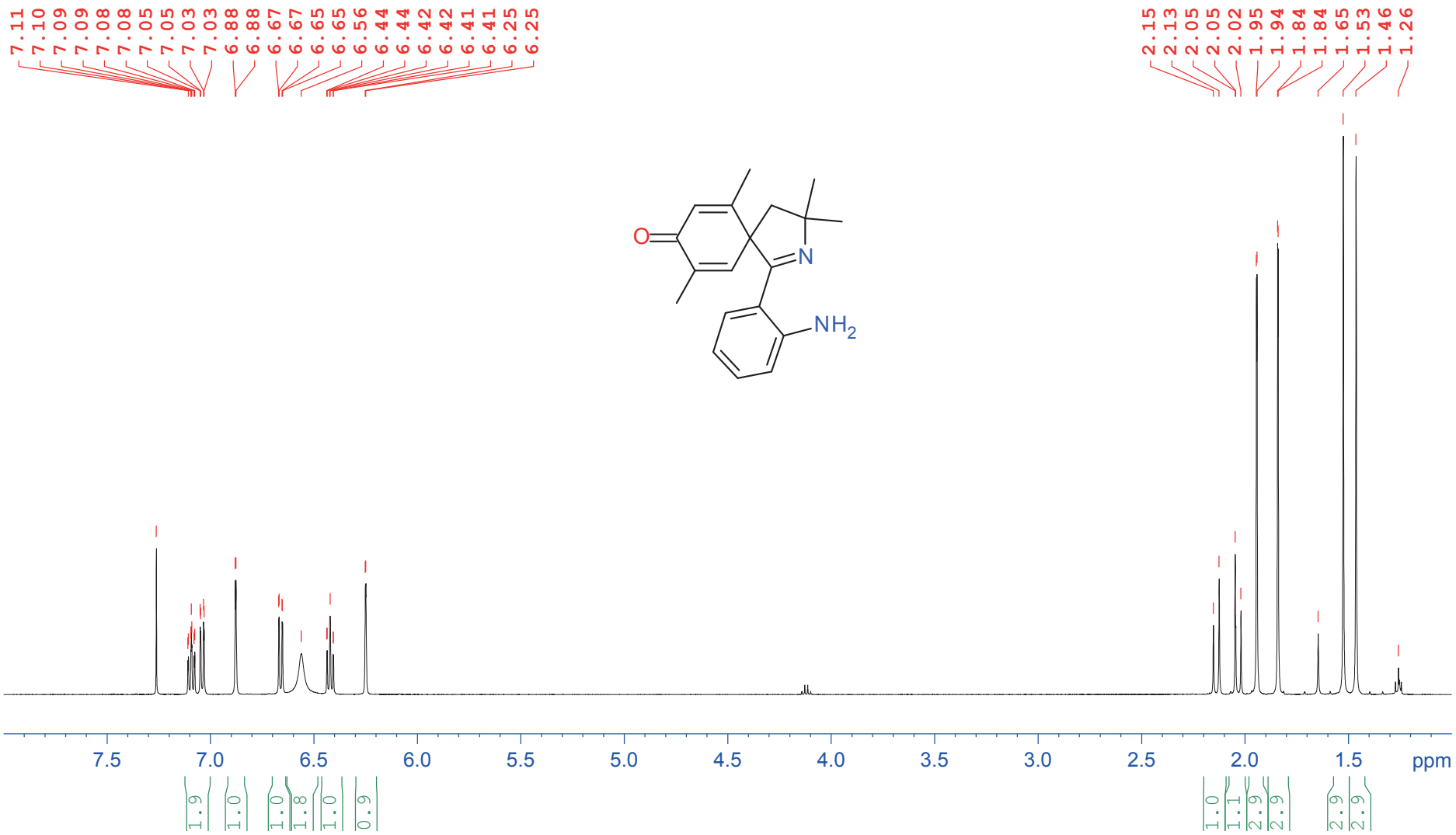
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **4f**.



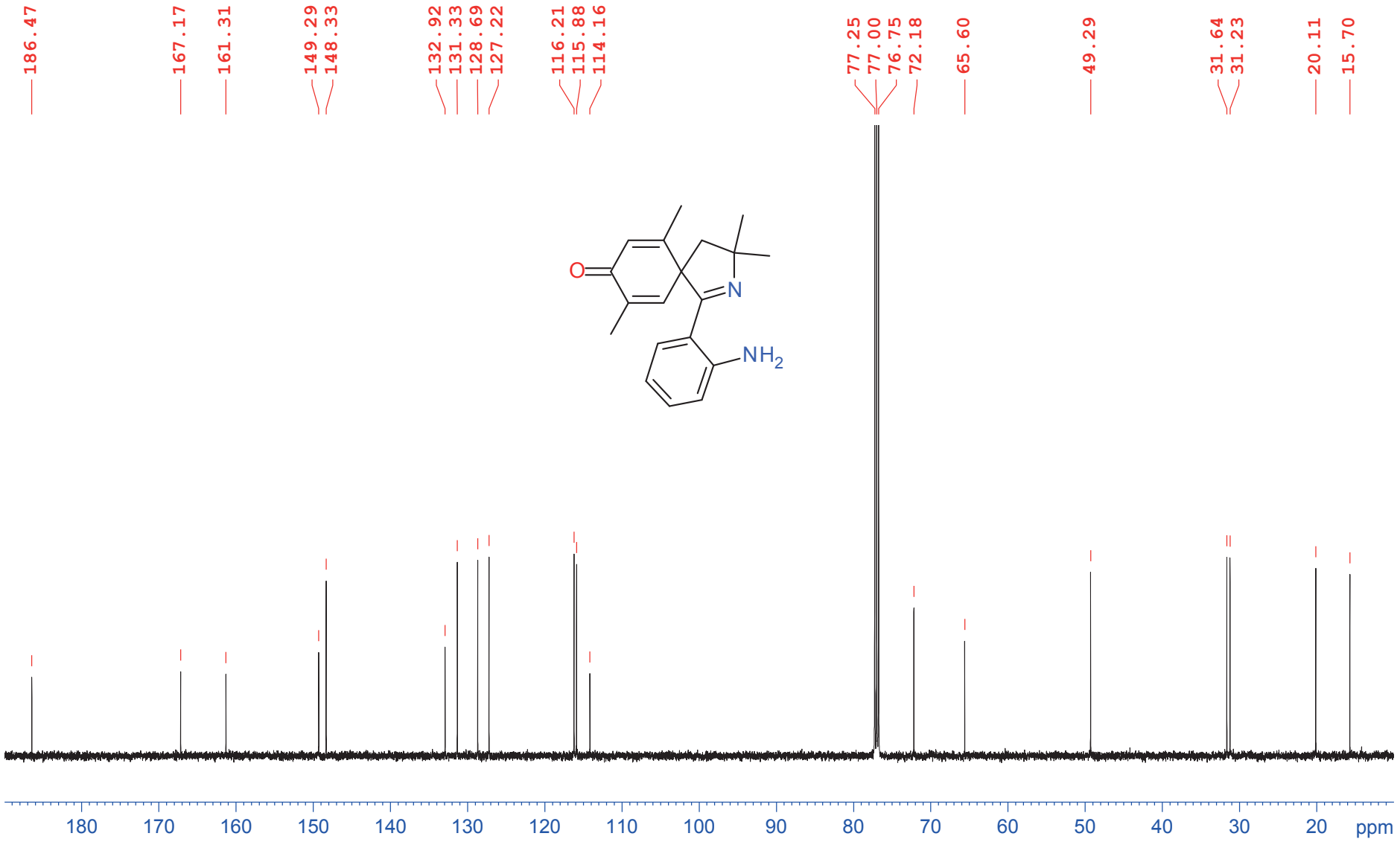
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5f**.



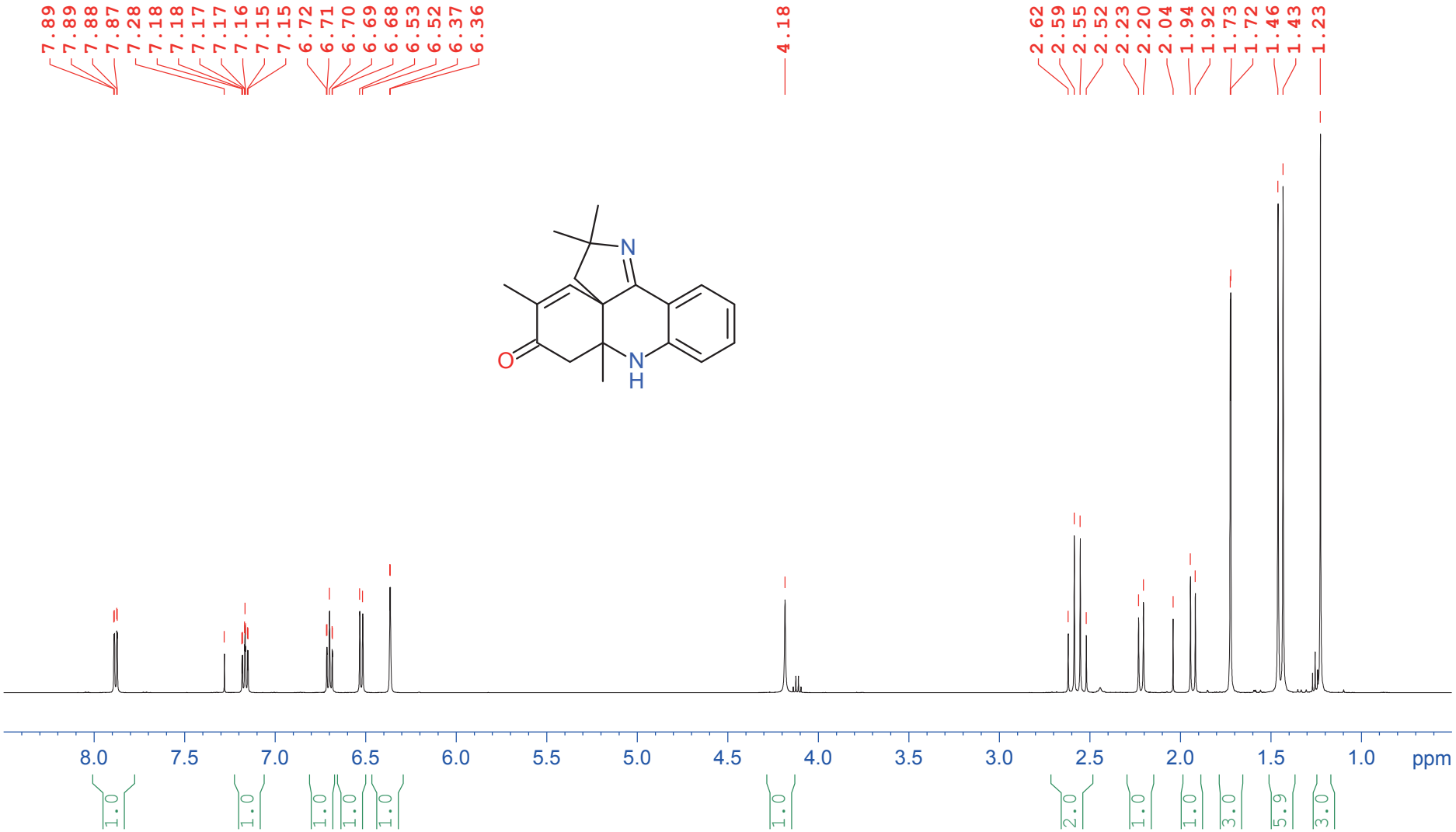
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **5f**.



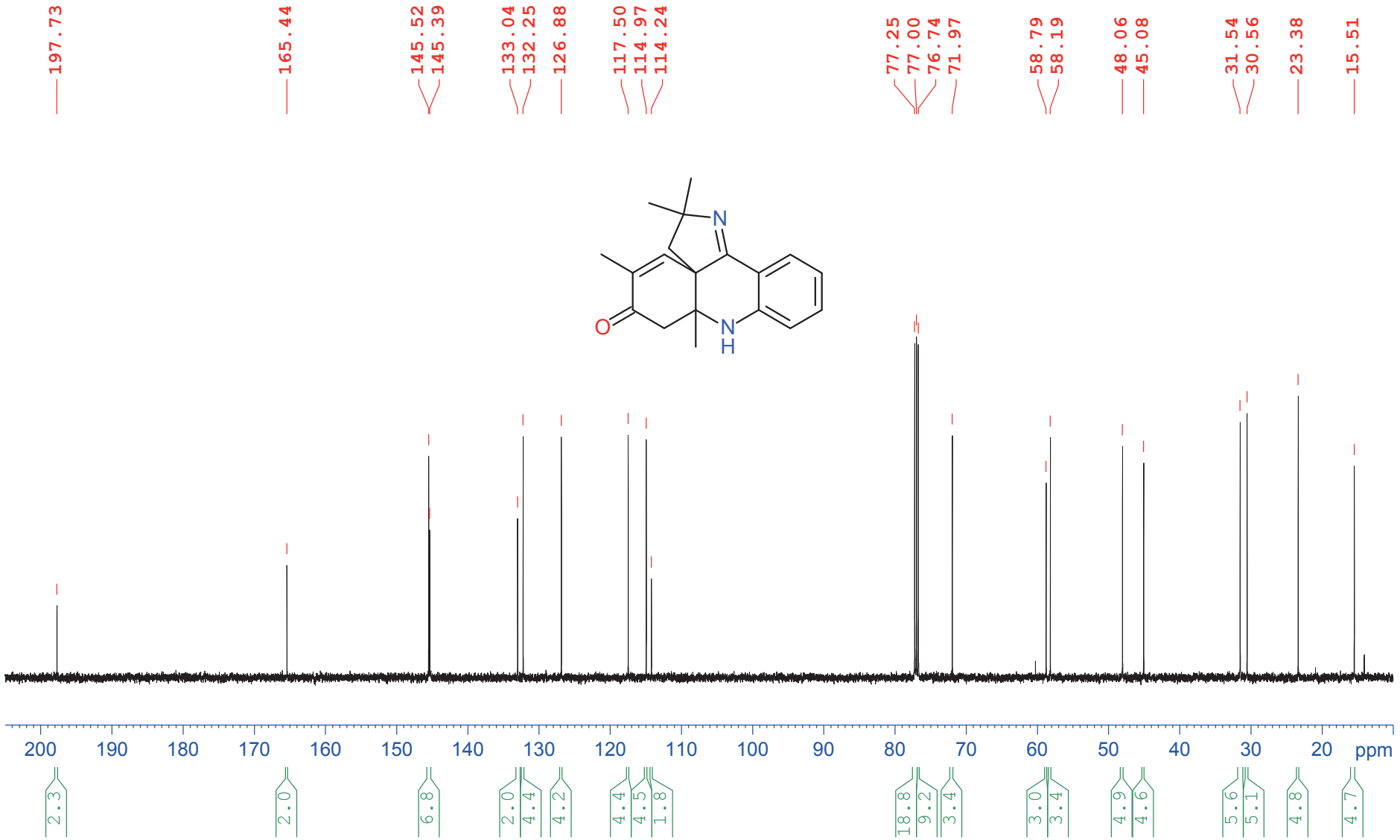
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **4g**.



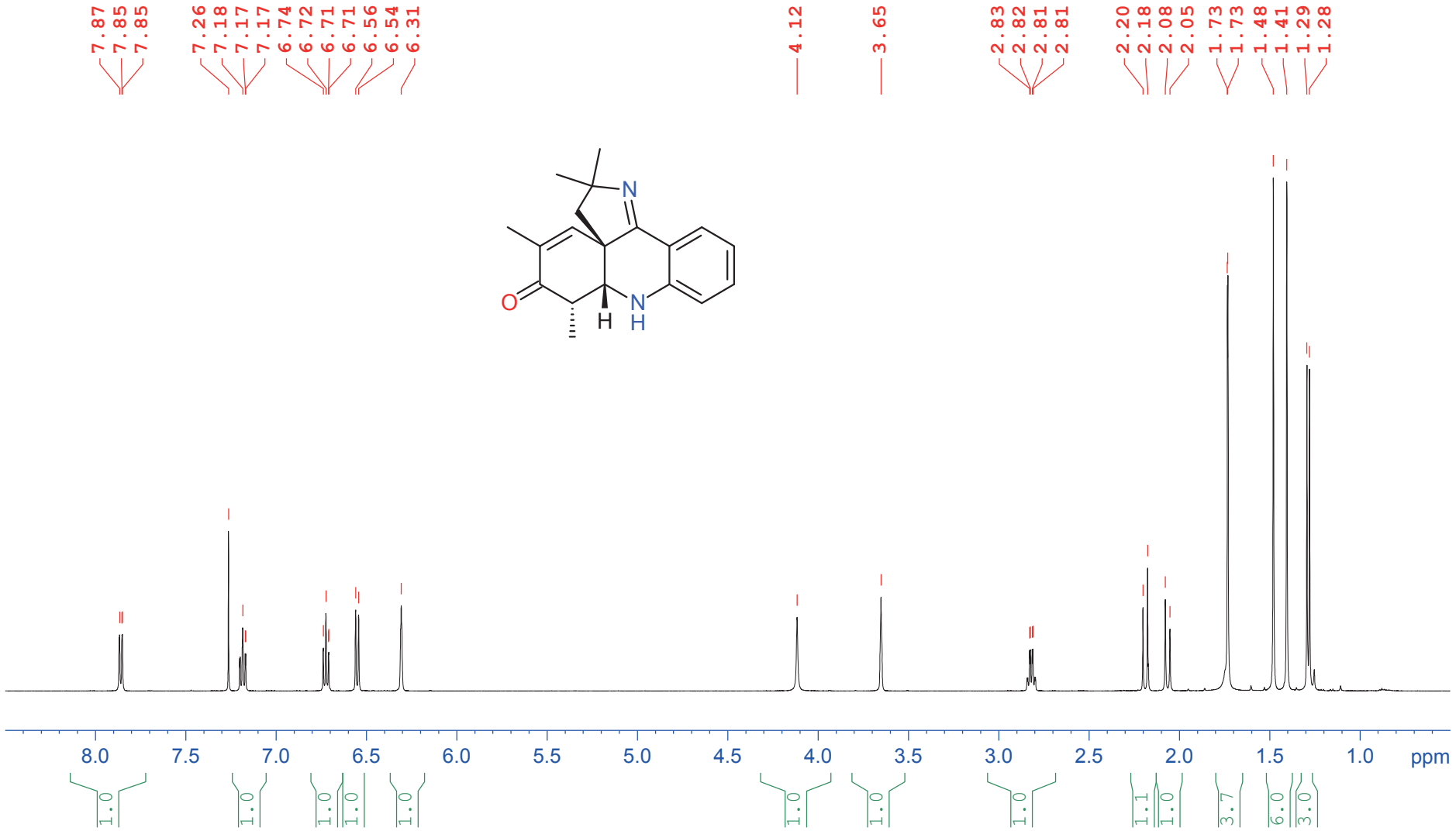
^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **4g**.



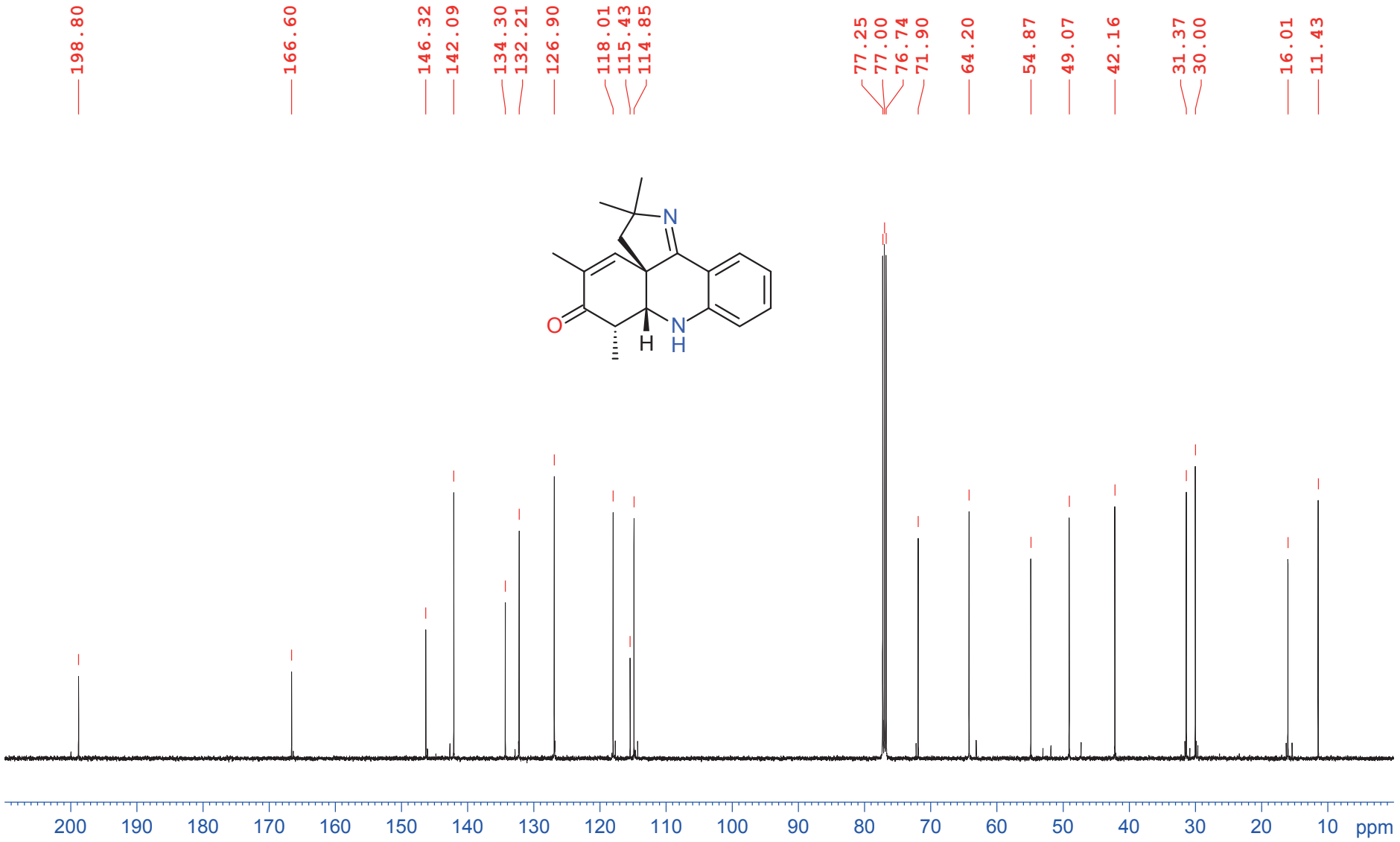
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5g**.



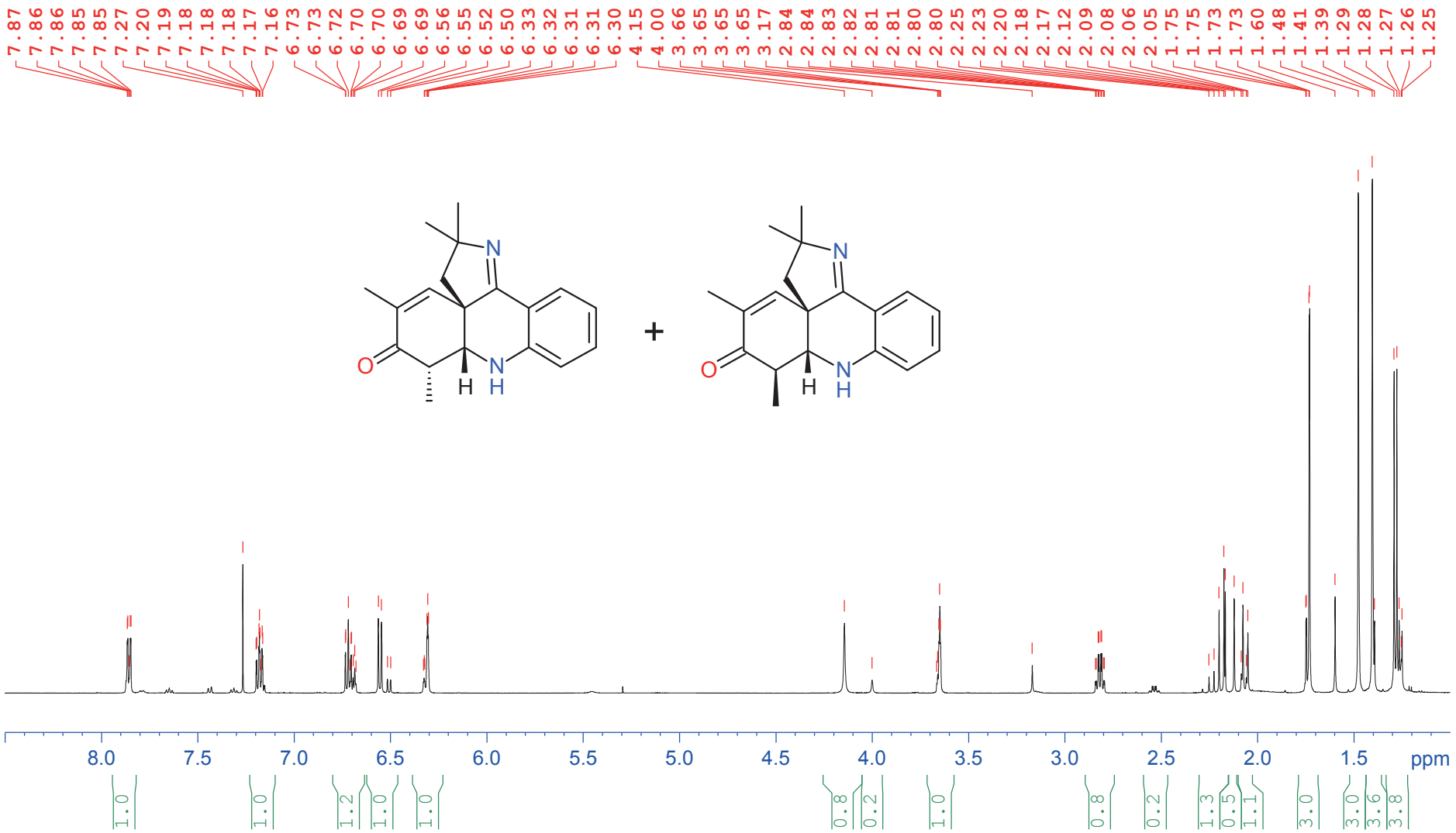
^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5g**.



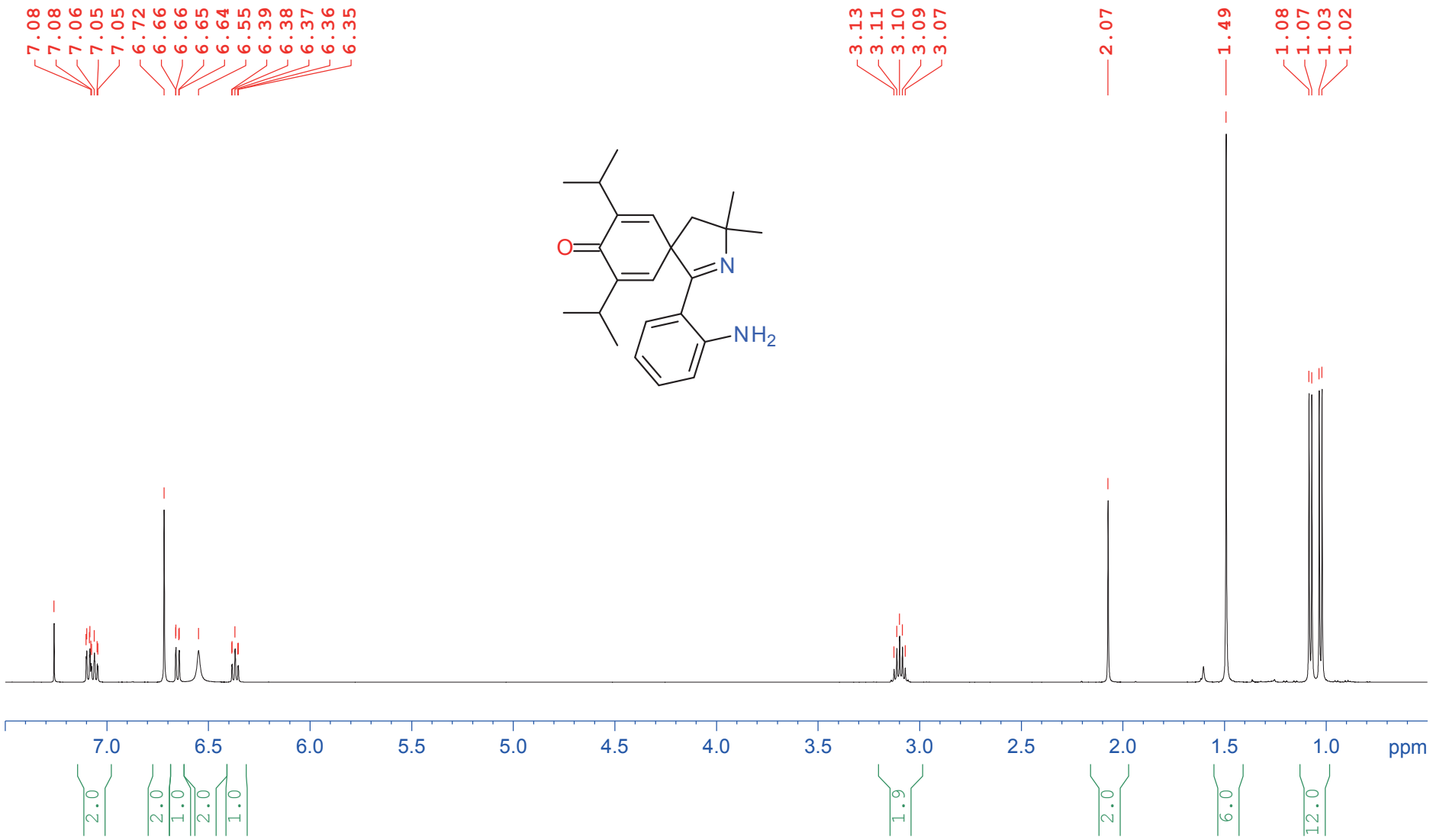
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5h**.



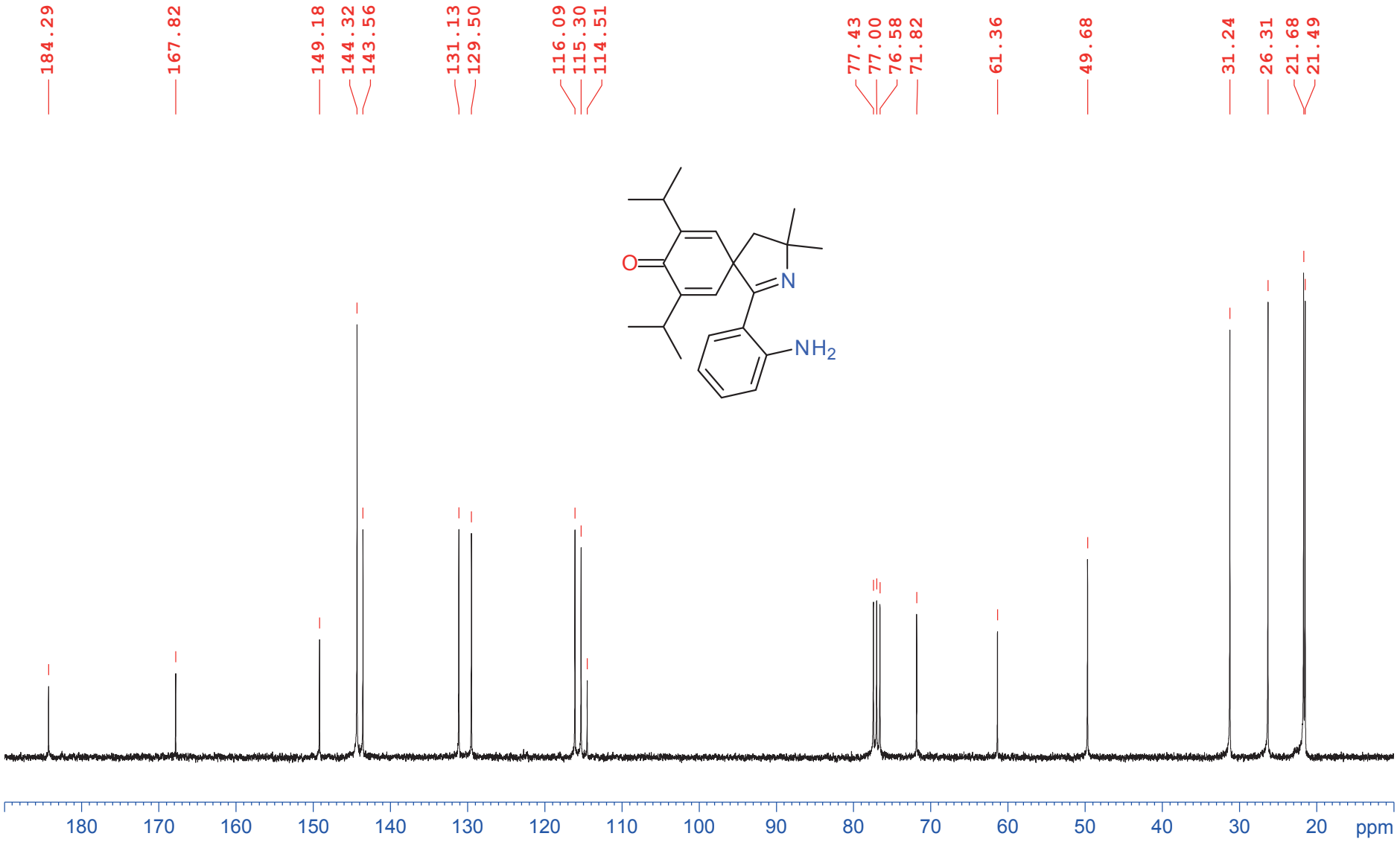
^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5h**.



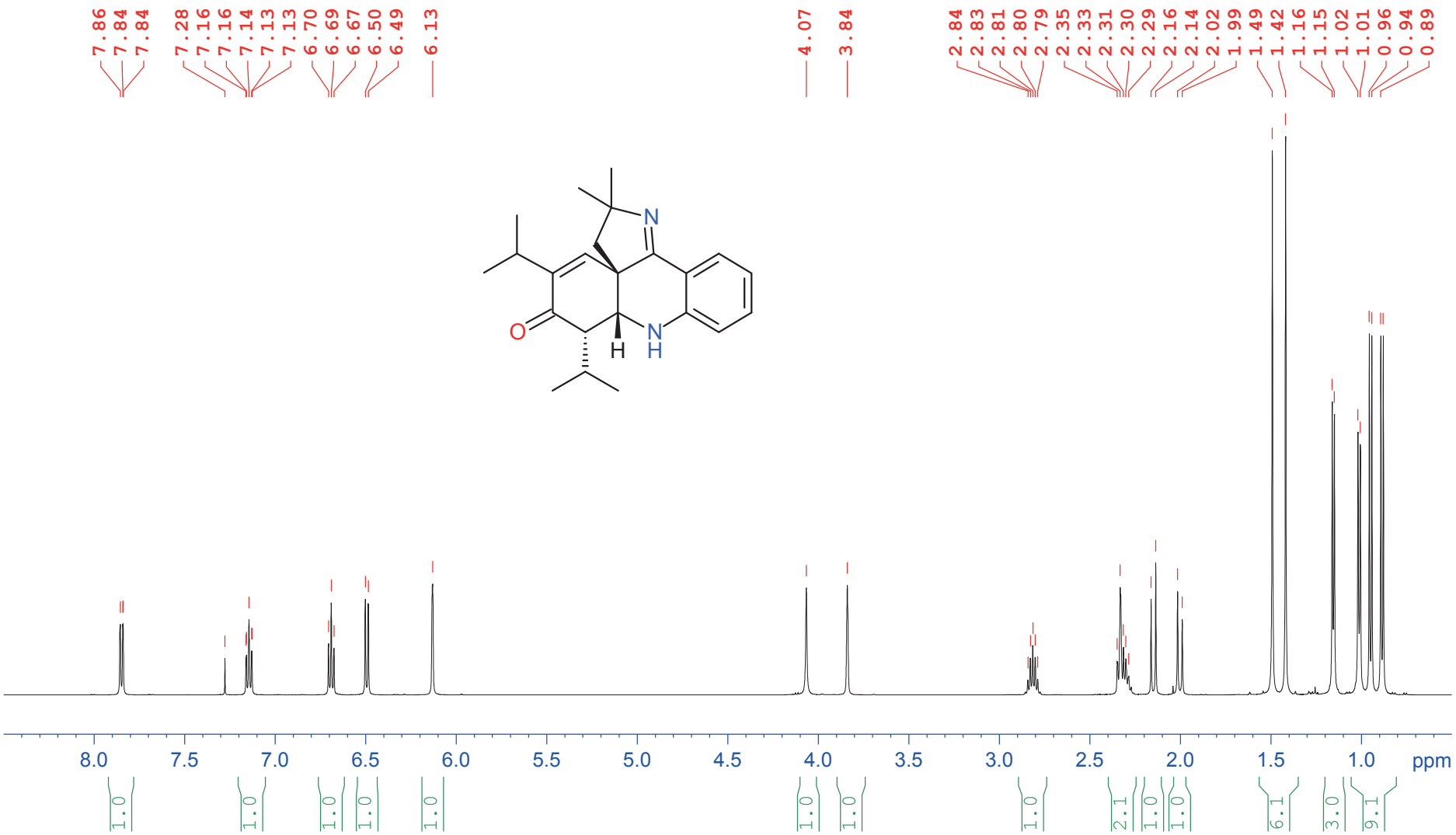
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of mixture of diastereomers **5h** and **5h'**.



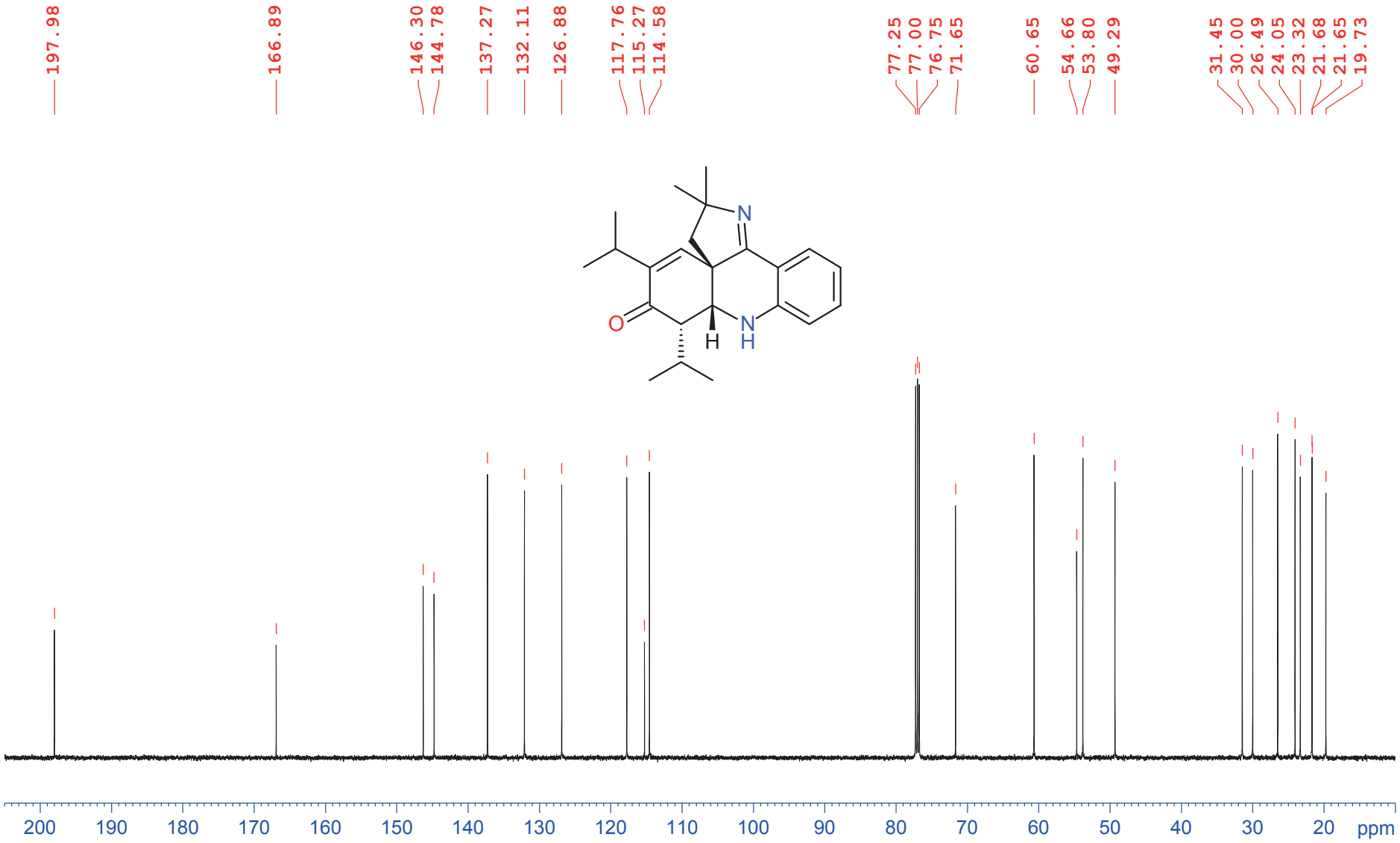
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **4i**.



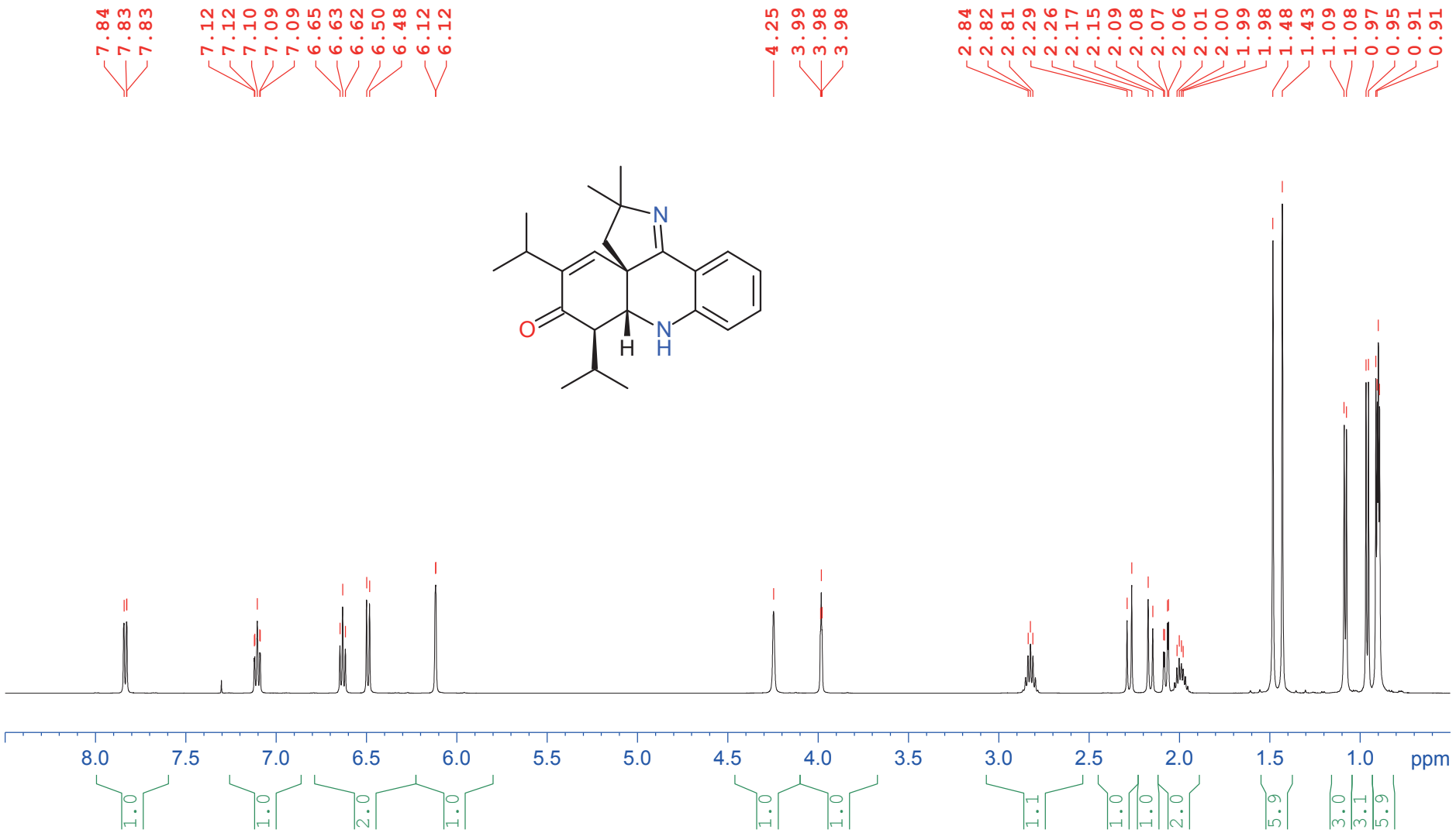
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **4i**.



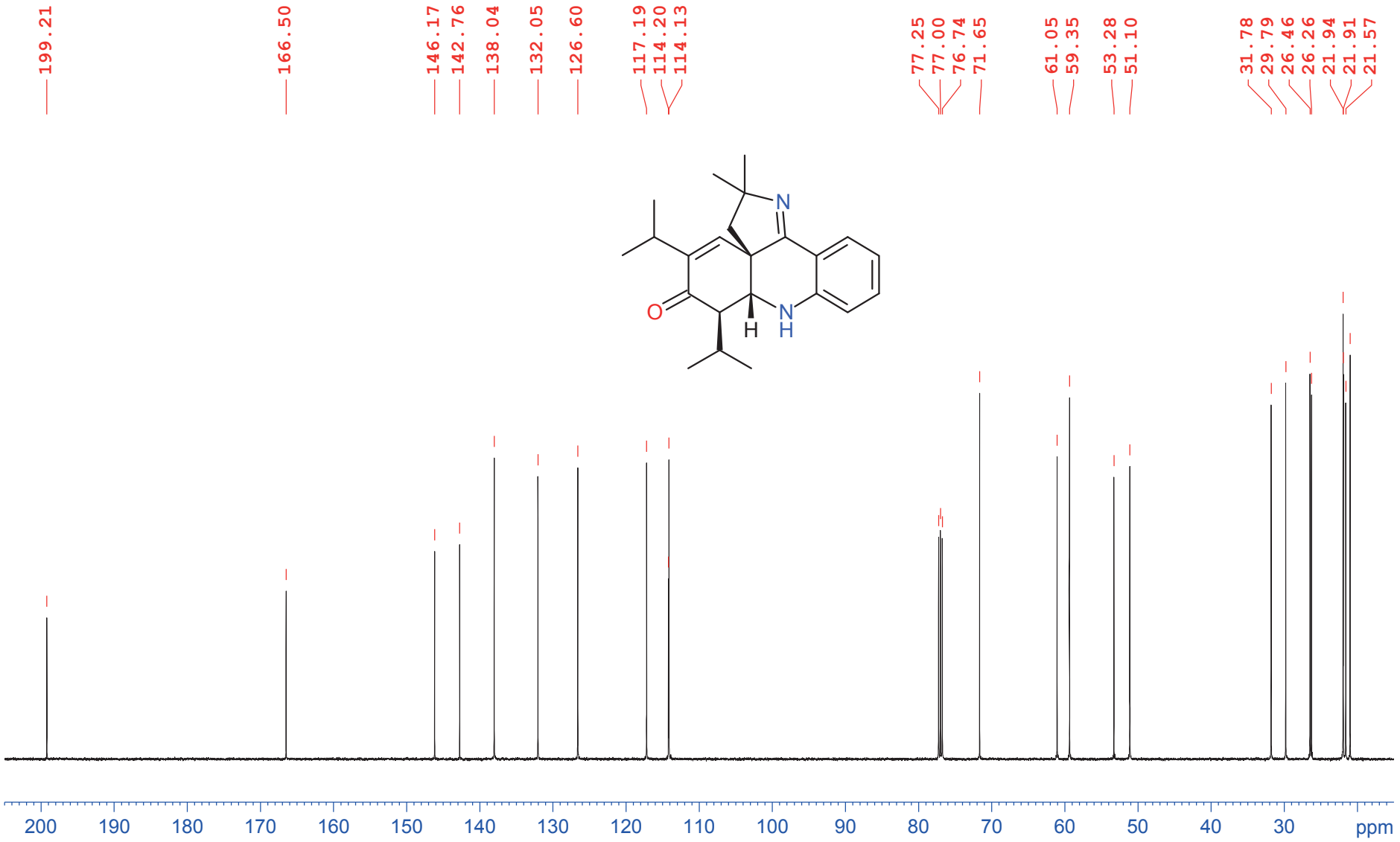
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5i**.



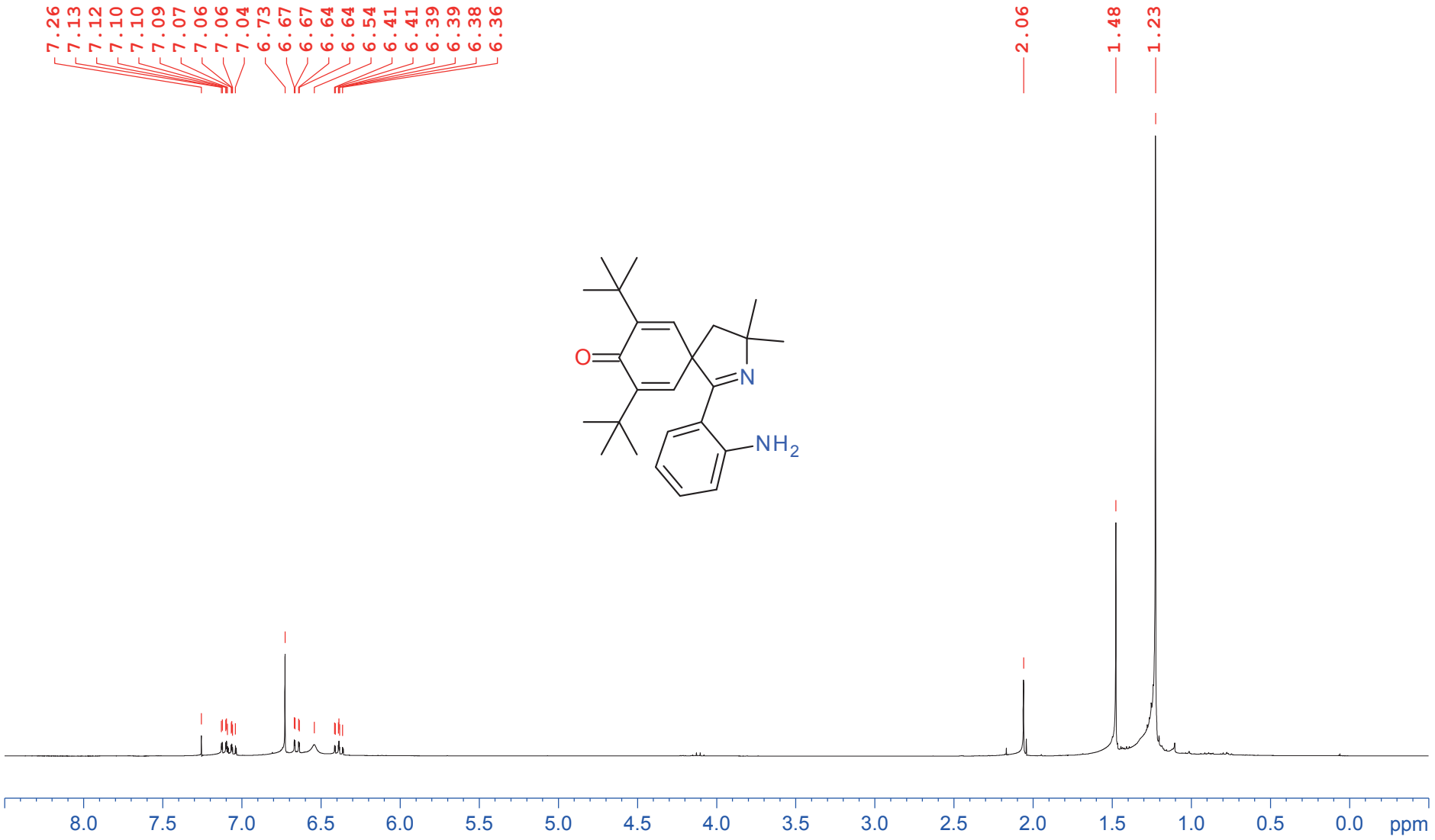
^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5i**.



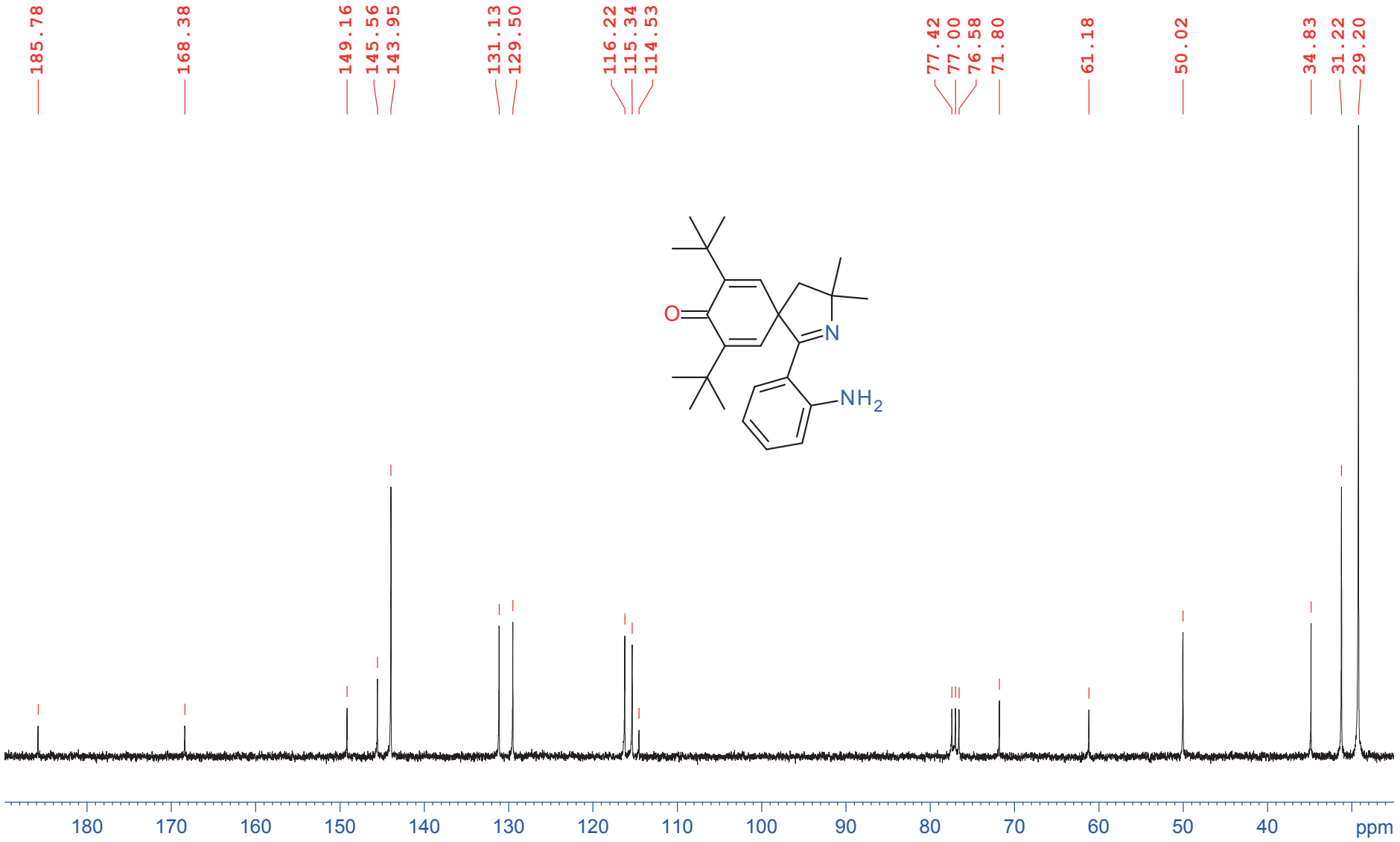
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5i'**.



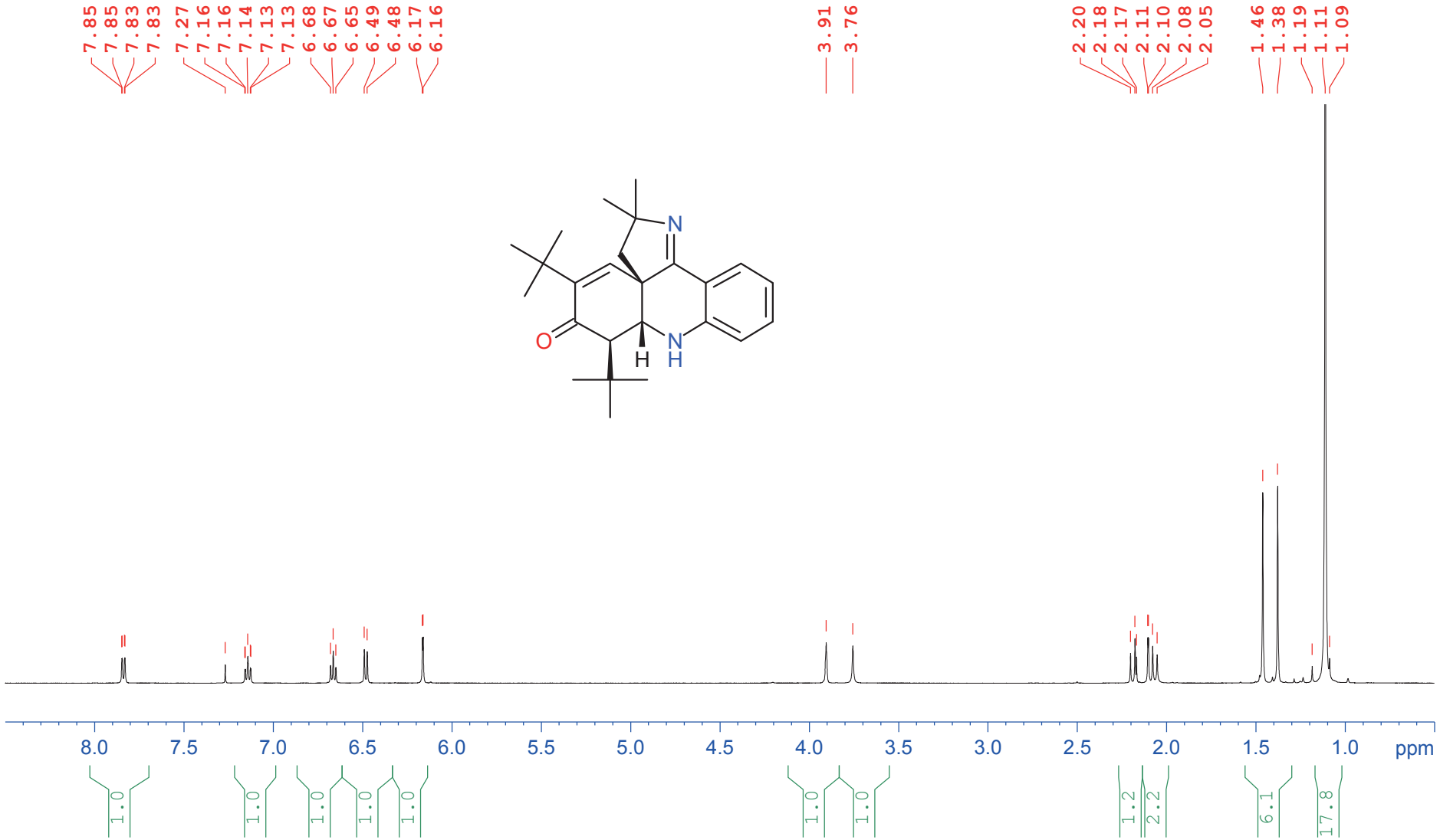
^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5i'**.



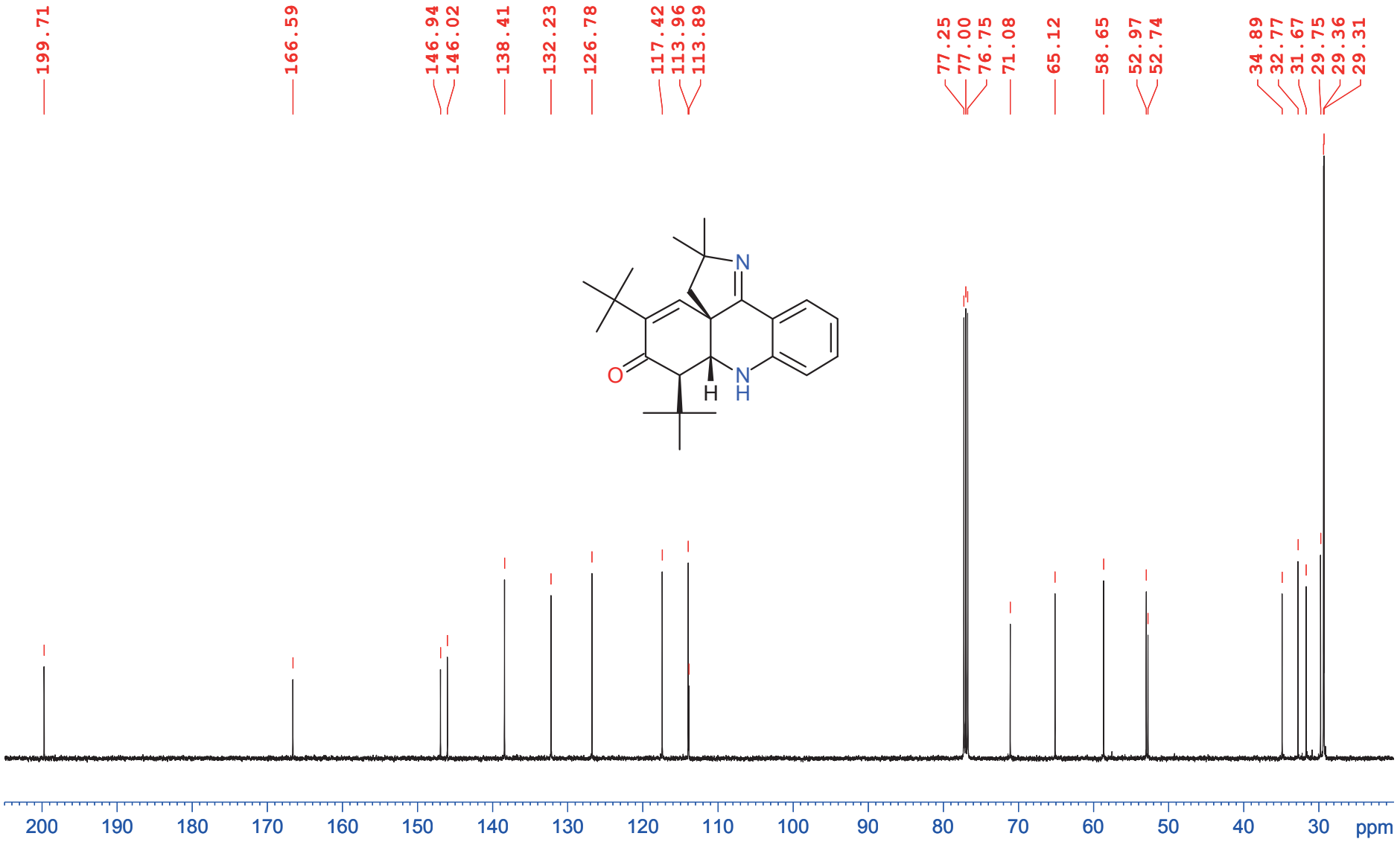
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **4j**.



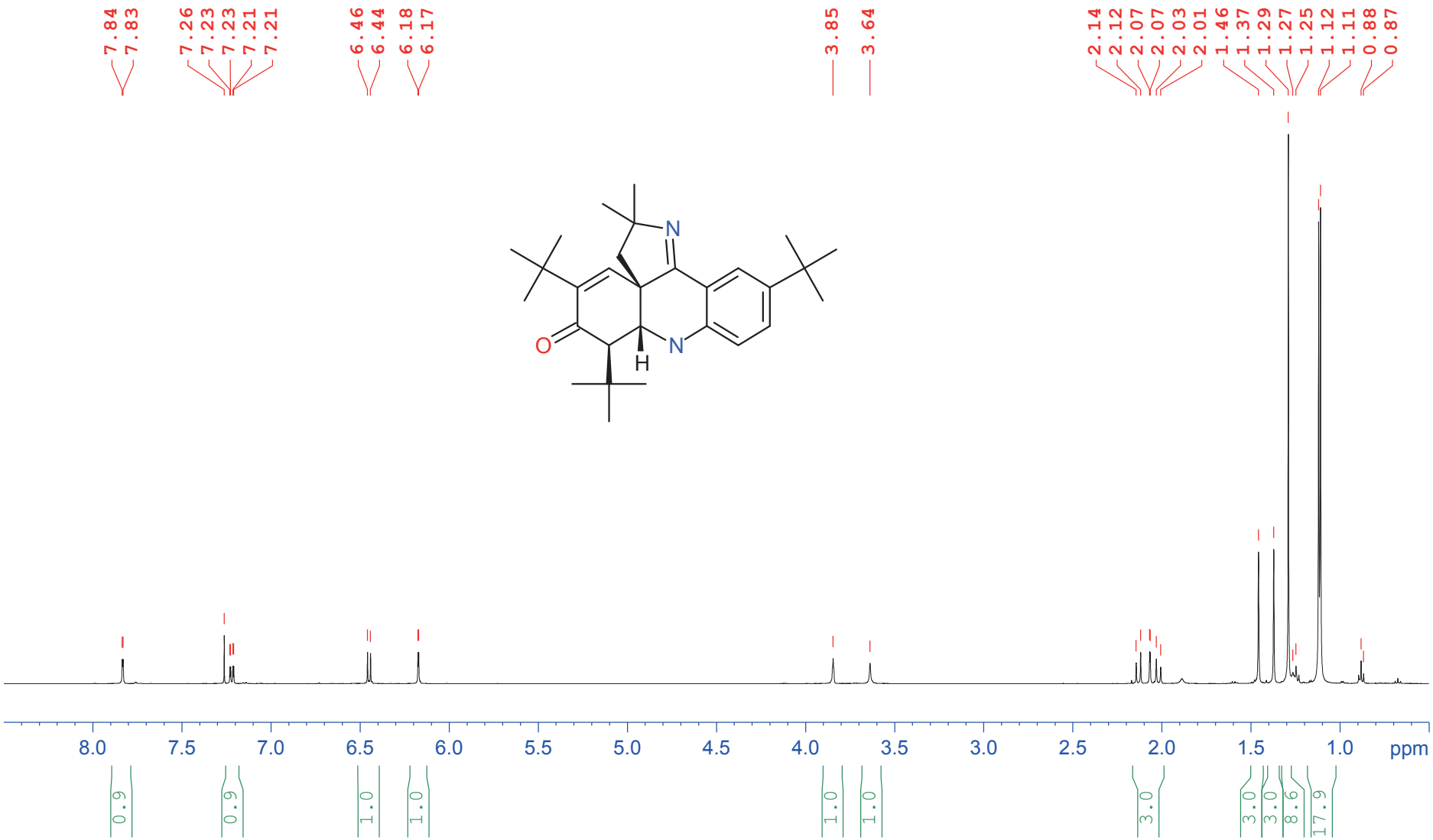
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **4j**.



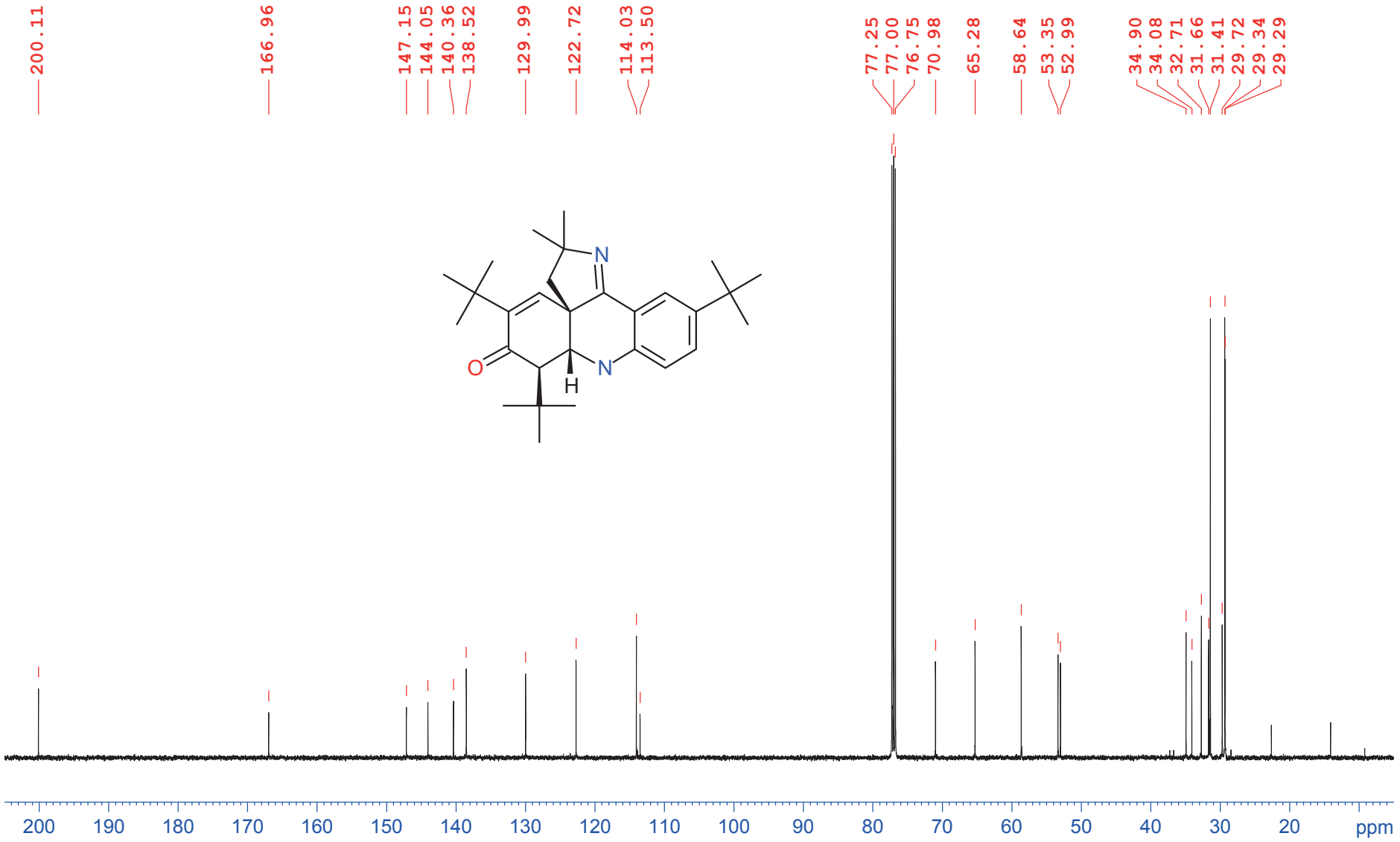
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5j'**.



^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5j'**.



^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **7**.



^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **7**.

5. References and notes

1. Sheldrick, G. M. *Acta Crystallogr., Sect. A*. **2008**, *64*, 112.

2. The 1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-methylpropan-1-one was synthesized as previously reported. Nishinaga A.; Shimizu T.; Toyoda Y.; Matsuura T. *J. Org. Chem*. **1982**, *47*, 2283.