Supplementary Material

Synthesis of [1,2-*a*]-fused tricyclic dihydroquinolines by palladium-catalyzed intramolecular C–N cross-coupling of polarized heterocyclic enamines

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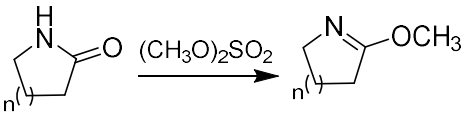
Experimental procedures

All the solvents and reagents were used commercial without further purification. All the palladium sources, ligands and bases used in the cross-couplings were used commercial (Aldrich, Acros, Strem) and stored under argon in a desiccator. Dry solvents were used commercial (Aldrich, Acros) and stored under argon using Sure/Seal™ or AcroSeal™ technology. TLC Analyses were performed on silica gel coated aluminium plates 60 F254 under UV visualization (254 or 365 nm). Column chromatography was performed using silica gel 60 (230–400 mesh) (Sigma Aldrich) containing ~ 0.1% Ca. Melting points were measured using Kofler hot plate microscope Boetius PHMK 80/2644. NMR Spectra were measured using either Bruker AVANCE III spectrometer operating at 400.13 (^{1}H) and 100.12 MHz (^{13}C) or Bruker Ascend™ spectrometer operating at 500.13 (^{1}H) and 125.15 MHz (^{13}C). Multiplicity of the signals is depicted as s (singlet), d (doublet), t (triplet), quint (quintet), m (multiplet), dd (doublet of doublets), td (triplet of doublets), br (broad signal). Proton NMR spectra in $CDCl_3$ were calibrated using internal TMS (δ = 0.00) and in DMSO-d6 on the middle signal of the solvent multiplet (δ = 2.50). Carbon NMR spectra were referenced against the middle signal of the solvent multiplet (δ = 77.23 for $CDCl_3$ and 39.51 for DMSO-d6). Measurement of ^{13}C NMR was done in an ordinary way using broadband proton decoupling or by means of APT pulse sequence. Elemental analyses were performed on a Flash EA 2000 CHNS automatic analyser (Thermo Fisher Scientific). HRMS were measured using dried droplet method on a MALDI LTQ Orbitrap XL (Thermo Fisher Scientific) with 2,5-dihydroxybenzoic acid (DHB) or 9-aminoacridine (9-AA) as the matrices for positive or negative mode respectively.

Experimental procedures

Synthesis of lactimethers ***6a–c***



1a n = 1
1b n = 2
1c n = 3

2a–c
77 % n = 1
86 % n = 2
79 % n = 3

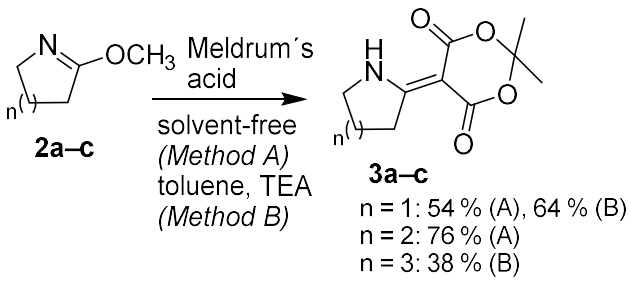
The procedure published in[1] was adopted and modified. A screw-cup thick wall tube (*Ace Pressure Tube*®) equipped with a magnetic stirring bar was charged with dimethyl sulphate (25.2 g, 0.2 mol) and lactam **1a–c** (0.2 mol) under cooling. The tube was sealed and heated to 75 °C for 24 h. The mixture was then ice-cooled and saturated aqueous potassium carbonate (60 mL) was subsequently added. The mixture was stirred for 30 min, then extracted with diethyl ether (4 × 50 mL). Combined organic layers were washed with brine (2 × 50 mL) and dried over anhydrous sodium sulphate. After evaporation (20 °C at 8–10 kPa) a light yellow liquid residue was obtained.

*5-Methoxy-3,4-dihydro-2H-pyrrole (**2a**).* Prepared from **1a**, further purification by vacuum distillation, b.p. 50–58 °C/10.5–11 kPa (ref.[2] gives 59–60 °C/10.7 kPa). Yield 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H); 3.66 (tt, *J* = 7.0, 1.3 Hz, 2H); 2.48–2.43 (m, 2H); 2.07–2.00 (m, 2H).

*6-Methoxy-2,3,4,5-tetrahydropyridine (**2b**).* Prepared from **1b**. The product is, according to NMR and GC-MS analyses, suitable for the next reaction step. Yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 3H); 3.51–3.45 (m, 2H); 2.16 (tt, *J* = 6.7, 1.2 Hz, 2H); 1.78–1.69 (m, 2H); 1.61–1.53 (m, 2H). NMR data are in accordance with these published in ref.[3]

*7-Methoxy-3,4,5,6-tetrahydro-2H-azepine (**2c**).* Prepared from **1c**, further purification by vacuum distillation, b.p. 79–85 °C/7.5–8.0 kPa. Yield 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 3H); 3.43–3.41 (m, 2H); 2.42–2.39 (m, 2H); 1.80–1.73 (m, 2H); 1.61–1.49 (m, 4H). Both NMR data and boiling point are in accordance with those published in ref.[4]

Synthesis of substituted Meldrum´s acids ***3a–c***



The procedure published in ref.[5] was adopted and slightly modified.

Solvent-free alternative (method A): a 25 mL flask equipped with a magnetic stirring bar and a reflux condenser was charged with lactimether **2a, b** (60 mmol, 1.2 eq.) followed with Meldrum´s acid (50 mmol). Upon dissolving the acid the mixture spontaneously warm-up and a solid product precipitated from the mixture during one hour.

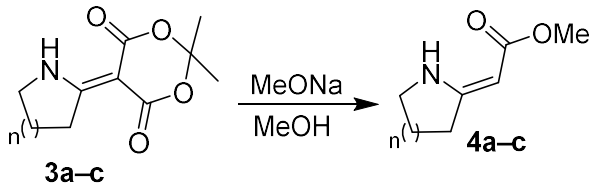
Solvent alternative (method B): a 100 mL flask equipped with a magnetic stirring bar and a reflux condenser was charged with Meldrum´s acid (50 mmol) and toluene (50 mL). After partial dissolution of the acid, TEA (1 mL, 15 mol. %) was added followed with lactimether **2a, c** (60 mmol, 1.2 eq.) The mixture was heated to 85 °C for 3 days, then cooled to laboratory temperature. The product precipitated was isolated by suction. Another portion of the product can be obtained by concentrating the filtrate.

*2,2-Dimethyl-5-(pyrrolidin-2-ylidene)-1,3-dioxane-4,6-dione (**3a**).* Prepared from **2a**. Recrystallization from toluene, m.p. 171–174 °C, ref.[5] reports 171 °C. Yield 54% (method A) or 64% (method B) of white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (br s, 1H), 3.76 (td, *J* = 7.5, 0.8 Hz, 2H); 3.40 (t, *J* = 8.0 Hz, 2H); 2.18 (quint, *J* = 7.7 Hz, 2H); 1.69 (s, 6H).

*2,2-Dimethyl-5-(piperidin-2-ylidene)-1,3-dioxane-4,6-dione (**3b**).* Prepared from **2b**, purification by washing with ether (2 × 20 mL), can be recrystallized from *n*-heptane, if needed, m.p. 118–123 °C, ref.[5] reports 116 °C. Yield 76% (method A) of ochre solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.63 (br s, 1H); 3.54–3.49 (m, 2H); 3.21 (t, *J* = 6.2 Hz, 2H); 1.90–1.78 (m, 4H); 1.68 (s, 6H).

*5-(Azepan-2-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3c**)*. Prepared from **2c**, recrystallization from aqueous ethanol (1:1 v/v), m.p. 146–151 °C, ref.[5] reports 147 °C. Yield 38% (method B) of yellowish solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (br s, 1H); 3.61–3.56 (m, 2H); 3.35–3.31 (m, 2H); 1.89–1.82 (m, 2H); 1.77–1.66 (m, 10H).

*Synthesis of exocyclic enaminoesters **4a–c***



99 % n = 1
97 % n = 2
92 % n = 3

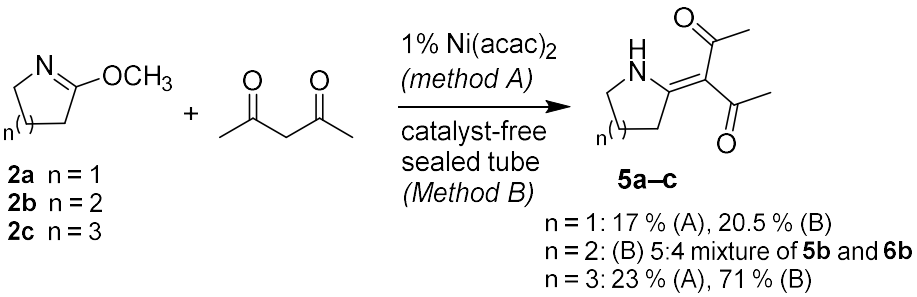
The protocol was adopted from ref.[5] and slightly modified. Sodium methoxide solution was freshly prepared (from 15 mmol of sodium and 30 mL of methanol) in dry 50 mL flask equipped with a magnetic stirring bar and a reflux condenser equipped with a calcium chloride drying tube. To this solution **3a–c** (15 mmol) was added and the mixture was refluxed for 3 h. The volatile components were evaporated in vacuo and the residue was suspended in water (30 mL) and pH was adjusted to 6–7 by HCl (ca 6M). The mixture was extracted with EtOAc (3 × 20 mL), the combined organic layers were washed with brine (20 mL), dried over anhydrous sodium sulphate and evaporated to dryness.

*Methyl pyrrolidine-2-ylideneacetate (**4a**).* Prepared from **3a**, m.p. 100–102 °C, ref.[6] reports 100–101 °C. Yield 99% of white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (br s, 1H); 4.54 (s, 1H); 3.64 (s, 3H); 3.52 (t, *J* = 6.9 Hz, 2H); 2.59 (t, *J* = 7.8 Hz, 2H); 1.98 (quint, *J* = 7.3 Hz, 2H).

*Methyl piperidine-2-ylideneacetate (**4b**)*. Prepared from **3b**, m.p. 29.6–34.7 °C. Yield 97% of yellowish crystalline compounds. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (br s, 1H); 4.36 (s, 1H); 3.61 (s, 3H); 3.29 (td, *J* = 6.1, 2.3 Hz, 2H); 2.35 (t, *J* = 6.4 Hz, 2H); 1.82–1.74 (m, 2H); 1.72–1.65 (m, 2H). Proton NMR data are in accordance with these in ref.[7]

*Methyl azepane-2-ylideneacetate (**4c**)*. Prepared from **3c**, m.p. 61.1–62.5 °C. Yield 92% of white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (br s, 1H); 4.45 (s, 1H); 3.62 (s, 3H); 3.33–3.29 (m, 2H); 2.33–2.29 (m, 2H); 1.72–1.63 (m, 4H); 1.63–1.56 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 168.7, 80.4, 50.0, 44.3, 35.1, 30.5, 30.2, 26.5. HRMS-MALDI (*m/z*): Calcd for $C_9H_{16}NO_2$ 170.11756 $[M+H]^+$, found 170.11761. Elemental analysis: Calcd for $C_9H_{15}NO_2$ C, 63.88; H, 8.93; N, 8.28; found C, 63.95; H, 9.00; N, 8.25.

Synthesis of ylidenepentanediones ***5a–c***



Method A: A slightly modified procedure taken from ref.[8] was used. A 25 mL flask equipped with a magnetic stirring bar and reflux condenser was charged with lactimether **2** (50 mmol) together with freshly distilled acetylacetone (4 g, 40 mmol). Catalytic amount of nickel(II) acetylacetonate (103 mg, 0.4 mmol, 1 mol. %) was subsequently added and the flask was heated to 100 °C for 20 h. The colour of the mixture changed from green to red-brown. The mixture was cooled, diluted with EtOAc (30 mL) and washed with water (3×15 mL). Combined organic layers were washed with brine (15 mL), dried over anhydrous sodium sulphate and evaporated in vacuo to give crude **5**.

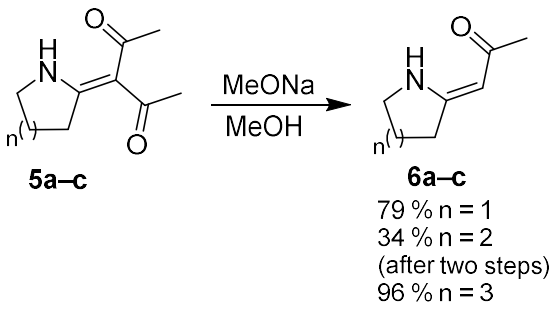
Method B (catalyst free): a thick wall pressure tube equipped with magnetic stirring bar was charged with lactimether **2** (50 mmol) and acetylacetone (60 mmol). The tube was sealed and heated to 75 °C for two days. Volatile components from the resulting mixture were evaporated in vacuo to give crude **5**.

*3-(Pyrrolidin-2-ylidene)pentane-2,4-dione (**5a**).* Prepared from **2a** using method A, chromatography (EtOAc, R_f = 0.28) followed with recrystallization from *n*-hexane, m.p. 86–89 °C, ref.[8] reports 87–88 °C. Yield 17% of white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.51 (br s, 1H); 3.64 (t, *J* = 7.3 Hz, 2H); 3.07 (t, *J* = 7.8 Hz, 2H); 2.38 (s, 3H); 2.36 (s, 3H); 2.04 (quint, *J* = 7.6 Hz, 2H).

*3-(Piperidin-2-ylidene)pentane-2,4-dione (**5b**)*. Prepared from **2b**, using method B, chromatography (EtOAc, R_f = 0.35). According to NMR, only 5:4 mixture of **5b** and **6b** was obtained, which was used in the following reaction step. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.71 (br s, 1H); 3.41 (td, *J* = 6.1, 2.6 Hz, 2H); 2.60 (t, *J* = 6.4 Hz, 2H); 2.28 (s, 6H); 1.83–1.77 (m, 2H); 1.75–1.68 (m, 2H). Data are in accordance with these published in ref.[9]

*3-(Azepan-2-ylidene)pentane-2,4-dione (**5c**).* Prepared from **2c** using both the method A and B. Recrystallization from petroleum ether, m.p. 66–69 °C, ref.[10] reports 66.5–67.8 °C. Yield 23% (method A) or 71% (method B) of ochre solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.26 (br s, 1H); 3.44–3.40 (m, 2H); 2.48–2.45 (m, 2H); 2.27 (br s, 6H); 1.82–1.74 (m, 6H).

Synthesis of enaminoketones ***6a–c***



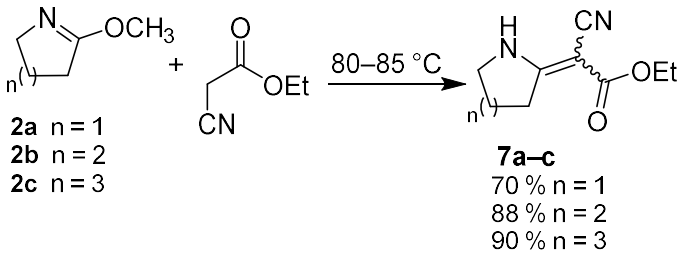
The compounds were prepared from **5** using the same procedure as for enaminoesters **4**, only the time of reflux was prolonged to 5 h. No purification of the crude products was necessary.

*1-(Pyrrolidin-2-ylidene)propan-2-one (**6a**)*. Prepared from **5a**, m.p. 50–55 °C, ref.[8] reports 49–53 °C. Yield 79% of yellowish solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (br s, 1H); 5.11 (s, 1H); 3.57 (t, *J* = 7.0 Hz, 2H); 2.60 (t, *J* = 7.8 Hz, 2H); 2.03 (s, 3H); 1.98 (quint, *J* = 7.5 Hz, 2H).

*1-(Piperidin-2-ylidene)propan-2-one (**6b**).* Prepared from **5b**, yield 34% (after two steps from **2b**, see comments for the synthesis of **5b**) of yellowish solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (br s, 1H); 4.87 (s, 1H); 3.33 (td, *J* = 6.1, 2.4 Hz, 2H); 2.35 (t, *J* = 6.4 Hz, 2H); 1.99 (s, 3H); 1.83–1.76 (m, 2H); 1.74–1.67 (m, 2H). NMR data are in accordance with ref.[8]

*1-(Azepan-2-ylidene)propan-2-one (**6c**).* Prepared from **5c**, yield 96% of yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.94 (br s, 1H); 4.96 (s, 1H); 3.35–3.31 (m, 2H); 2.30–2.27 (m, 2H); 2.01 (s, 3H); 1.75–1.70 (m, 2H); 1.67–1.58 (m, 4H). NMR data are in accordance with ref.[8]

Synthesis of α-cyanoenaminoesters ***7a–c***



2a n = 1
2b n = 2
2c n = 3

7a–c
70 % n = 1
88 % n = 2
90 % n = 3

Method A: A 25 mL flask equipped with a magnetic stirring bar and a reflux condenser was charged with lactimether **2** (25.3 mmol, 1.1 eq.) and ethyl cyanoacetate (5.09 g, 23 mmol). The flask was heated at 85 °C for 1 h. The mixture meanwhile solidified.

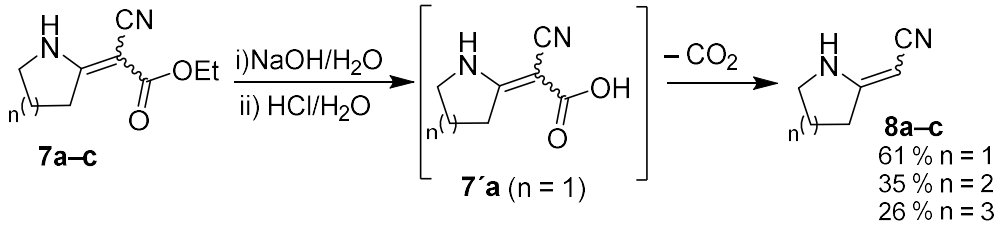
Method B: the same way as Method A but in thick-walled pressure tube with slightly higher amount of lactimether **2**. Reaction time 20 h at 80 °C. Crude products were obtained upon cooling the reaction mixture in an ice bath.

*Ethyl 2-cyano-2-(pyrrolidin-2-ylidene)acetate (**7a**).* Prepared from **2a** using method A. Crude product was recrystallized from ethanol, m.p. 152–157 °C (ref.[11] reports 153–154 °C). Yield 70% of white needles. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H); 4.21 (q, *J* = 7.1 Hz, 2H); 3.76–3.70 (m, 2H); 2.95 (t, *J* = 7.9 Hz, 2H); 2.14 (quint, *J* = 7.6 Hz, 2H); 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$,) δ 174.1, 168.2, 119.0, 67.6, 60.4, 49.2, 33.4, 21.1, 14.5.

*Ethyl 2-cyano-2-(piperidin-2-ylidene)acetate (**7b**)*. Prepared from **2b** using method B. Crude reaction mixture recrystallized from cyclohexane, m.p. 94.5–97 °C (ref.[12] reports 99–100 °C). Yield 88% of white crystalline solid. The product contains, according to ^{1}H NMR, about 10% of its methylester. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.15 (s, 1H); 4.19 (q, *J* = 7.1 Hz, 2H); 3.44–3.40 (m, 2H); 2.72 (t, *J* = 6.2 Hz, 2H); 1.87–1.78 (m, 4H); 1.30 (t, *J* = 7.1 Hz, 3H). HRMS-MALDI (*m/z*): Calcd for $C_{10}H_{15}N_2O_2$ 195.11280 $[M+H]^+$, found 195.11293. Calcd for $C_{10}H_{14}N_2NaO_2$ 217.09475 $[M+Na]^+$, found: 217.09492.

*Ethyl azepan-2-ylidene(cyano)acetate (**7c**).* Prepared from **2c** using method B. Column chromatography (*n*-hexane-EtOAc 3:2, R_f = 0.45), m.p. 57–70 °C (ref.[13] reports 63 °C). Yield 90% of white crystalline solid. The product contains about 33% of its methylester. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (br s, 1H); 4.20 (q, *J* = 7.1 Hz, 2H); 3.50–3.43 (m, 2H); 2.82–2.77 (m, 2H); 1.84–1.76 (m, 2H); 1.76–1.68 (m, 2H); 1.68–1.61 (m, 2H); 1.31 (t, *J* = 7.1 Hz, 3H). HRMS-MALDI (*m/z*): Calcd for $C_{11}H_{17}N_2O_2$ 209.12845 $[M+H]^+$, found 209.12863. Calcd for $C_{11}H_{16}N_2NaO_2$ 231.11040 $[M+Na]^+$, found 231.11055.

*Synthesis of enaminonitriles **8a–c***



The procedure published in ref.[14] was used and slightly modified. A flask equipped with a magnetic stirring bar and a reflux condenser was charged with **7** (10 mmol) and 1M aqueous NaOH (30 mL, 3 eq.). The mixture was refluxed until dissolution of all the solid (about 1 h). The solution was then cooled in an ice bath and concentrated aqueous HCl (10 mL, ca 11 eq.) was subsequently added (intermediate cyanoacid **7´a** precipitated at pH = 7 upon slow addition of HCl). An excessive foaming was observed and the mixture was stirred for half an hour. Solid potassium bicarbonate was then added to adjust pH of the mixture to 7. The mixture was then extracted with DCM (3 × 50 mL), combined organic layers were dried over anhydrous sodium sulphate and evaporated to dryness to give crude **8**.

*Pyrrolidin-2-ylideneethanenitrile (**8a**)*. Prepared from **7a**, crude product was pure enough for next reaction step, m.p. 65–71 °C (ref.[14] reports 73 °C). Yield 61% of beige crystals. Product is 2:3 mixture of *E/Z* isomers. ^{1}H NMR (500 MHz, $CDCl_3$) major form δ 5.48 (s, 1H); 3.71 (s, 1H); 3.49 (t, *J* = 6.8 Hz, 2H); 2.57 (td, *J* = 7.8, 1.0 Hz, 2H); 2.08–2.01 (m, 2H). Minor form: δ 5.33 (s, 1H); 3.99 (s, 1H); 3.45 (t, *J* = 6.8 Hz, 2H); 2.77 (td, *J* = 7.8, 1.4 Hz, 2H); 2.08–2.01 (m, 2H). HRMS-MALDI (*m/z*): Calcd for $C_{12}H_{17}N_4$ 217.14477 $[2M+H]^+$, found 217.14481. Calcd for $C_{12}H_{16}N_4Na$ 239.12672 $[2M+Na]^+$, found 239.12687. Calcd for $C_{18}H_{25}N_6$ 325.21352 $[3M+H]^+$, found 325.21386.

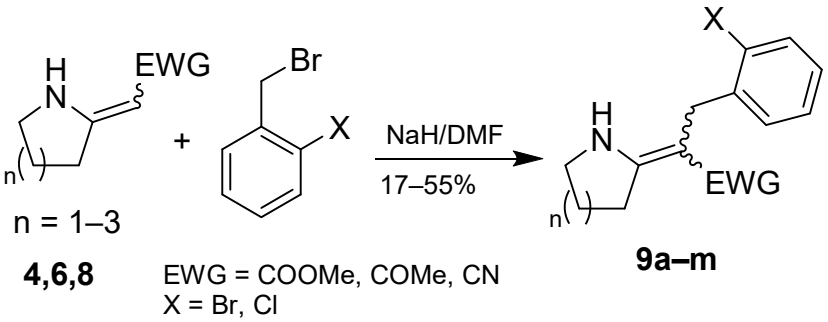
*Piperidin-2-ylideneethanenitrile (**8b**)*. Prepared from **7b**, recrystallization from *n*-hexane m.p. 47–62 °C (ref.[12] reports 61–63 °C). Yield 35% of white solid. Product is 3:1 mixture of *E/Z* isomers. ^{1}H NMR (400 MHz, $CDCl_3$) major form δ 5.32 (s, 1H); 3.61 (s, 1H); 3.27 (td, *J* = 6.0, 2.2 Hz, 2H); 2.34 (t, *J* = 6.3 Hz, 2H); 1.82–1.64 (m, 4H). Minor form: δ 5.02 (s, 1H); 3.90 (s, 1H); 3.20 (td, *J* = 6.0, 2.1 Hz, 2H); 2.61 (t, *J* = 6.2 Hz, 2H); 1.82–1.64 (m, 4H). HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{21}N_4$ 245.17607 $[2M+H]^+$, found 245.17605. Calcd for $C_{14}H_{23}N_4O$ 263.18664 $[2M+H+H_2O]^+$, found 263.18688. Calcd for $C_7H_{13}N_2O$ 141.10224 $[M+H+H_2O]^+$, found 141.10228. Elemental analysis: Calcd for $C_7H_{10}N_2$ C, 68.82; H, 8.25; N, 22.93; found C, 68.75; H, 8.33; N, 22.89.

*Azepan-2-ylideneethanenitrile (**8c**)*. Prepared from **7c**, crude product was pure enough for next reaction step, m.p. 66–75 °C. Yield 26% of yellowish crystals. Product is 4:1 mixture of *E/Z* isomers. NMR data are in accordance with these reported in ref.[15] ^{1}H NMR (500 MHz, $CDCl_3$) major form δ 5.60 (s, 1H); 3.66 (s, 1H); 3.30–3.25 (m, 2H); 2.34–2.26 (m, 2H); 1.71–1.55 (m, 6H). Minor form δ 5.29 (s, 1H); 3.84 (s, 1H); 3.23–3.19 (m, 2H); 2.67–2.59 (m, 2H); 1.71–1.55 (m, 6H). HRMS-MALDI

(*m/z*): Calcd for $C_{16}H_{27}N_4O$ 291.21794 $[2M+H+H_2O]^+$, found 291.21823. Calcd for $C_{16}H_{26}N_4NaO$ 313.19988 $[2M+Na+H_2O]^+$, found: 313.20028. Calcd for $C_8H_{15}N_2O$ 155.11789 $[M+H+H_2O]^+$, found 155.11789. Elemental analysis: Calcd for $C_8H_{12}N_2$ C, 70.55; H, 8.88; N, 20.57; found C, 70.70; H, 8.91; N, 20.52.

*2-Cyano-2-(pyrrolidin-2-ylidene)acetic acid (**7′a**).* Prepared from **2a** using method A, precipitated from the reaction mixture at pH = 7 upon slow addition of HCl. Product was isolated by suction, washed with water and dried in vacuo to give 22% of white crystalline solid with m.p. 132–133 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (br s, 1H); 3.57 (t, J = 7.2 Hz, 2H); 2.81 (t, J = 7.9 Hz, 2H); 1.96 (quint, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.1, 168.3, 119.8, 65.3, 49.6, 33.8, 20.4. HRMS-MALDI (*m/z*): Calcd for $C_7H_7N_2O_2$ 151.05130 $[M–H]^–$, found 151.05130. Elemental analysis: Calcd for $C_7H_8N_2O_2$ C, 55.26; H, 5.30; N, 18.41; found C, 55.24; H, 5.31; N, 18.39.

*Synthesis of C-benzylated enamines **9a–m***



A modified procedure from ref.[16] was used. A dried Schlenk flask equipped with a magnetic stirring bar was charged with the starting substrate **4**, **6** or **8** (10 mmol). The flask was 3 × evacuated and backfilled with argon. Dry DMF (20 mL) was added via syringe. The apparatus was then cooled to –40 °C (acetone-dry ice bath) and sodium hydride (12 mmol, 1.2 eq.) was added in one portion. The mixture was stirred at –40 °C until foaming ceased (ca 1.5 h). 2-Bromobenzylbromide (12 mmol, 1.2 eq.) was then added in one portion under cooling. The flask was removed from cooling bath and heated under inert to 80 °C for 24 h. After cooling in an ice bath, the reaction was quenched with saturated aq. NH_4Cl (50 mL). Organic layer was diluted with ethyl acetate (125 mL), washed with water (3 × 50 mL) and brine (2 × 50 mL) and dried over anhydrous sodium sulphate. Evaporation to dryness gave crude **9**. For purification see details at individual compounds.

*Methyl 3-(2-bromophenyl)-2-(pyrrolidin-2-ylidene)propanoate (**9a**):* Prepared from **4a**, crude product was suspended in ether (110 mL). The suspension was inserted into an ultrasound bath for half an hour. Solid impurities were filtered off and the filtrate was evaporated to dryness, the residue was recrystallized from *n*-hexane to give 41% of white solid with m.p. 106–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (br s, 1H); 7.52 (dd, *J* = 7.9, 1.2 Hz, 1H); 7.19 (td, *J* = 7.7, 1.2 Hz, 1H); 7.10–7.09 (m, 1H); 7.04–7.00 (m, 1H); 3.61 (s, 3H); 3.59 (s, 2H); 3.56 (t, *J* = 7.0 Hz, 2H); 2.49 (t, *J* = 7.8 Hz, 2H); 1.95 (quint, *J* = 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 166.6, 141.6, 132.5, 128.8, 127.4, 127.3, 124.9, 85.5, 50.7, 47.6, 34.0, 31.2, 22.2. HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{17}{}^{79}BrNO_2$ 310.04372 $[M+H]^+$, found 310.04403. Calcd for $C_{14}H_{16}{}^{79}BrNNaO_2$ $[M+Na]^+$ 332.02566, found 332.02600. Elemental analysis: Calcd for $C_{14}H_{16}BrNO_2$ C, 54.21; H, 5.20; N, 4.52; found C, 54.40; H, 5.15; N, 4.51.

*Methyl 3-(2-bromophenyl)-2-(piperidin-2-ylidene)propanoate (**9b**):* Prepared from **4b**, the residue was recrystallized from ethanol to give 43% of light beige solid with m.p. 132–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (br s, 1H); 7.51 (dd, *J* = 7.9, 1.2 Hz, 1H); 7.20 (td, *J* = 7.7, 1.2 Hz, 1H); 7.10–7.07 (m, 1H); 7.04–7.00 (m, 1H); 3.60 (br s, 2H); 3.59 (s, 3H); 3.35 (td, *J* = 6.0, 2.5 Hz, 2H); 2.24 (t, *J* = 6.5 Hz, 2H); 1.74–1.68 (m, 2H); 1.66–1.59 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 162.4, 141.6, 132.4, 128.6, 127.5, 127.2, 125.0, 86.6, 50.6, 41.7, 32.5, 26.1, 22.4, 20.1. HRMS-MALDI

(*m/z*): Calcd for $C_{15}H_{19}{}^{79}BrNO_2$ 324.05937 $[M+H]^+$, found 324.05955. Calcd for $C_{15}H_{18}{}^{79}BrNNaO_2$ $[M+Na]^+$ 346.04131, found 346.04163. Elemental analysis: Calcd for $C_{15}H_{18}BrNO_2$ C, 55.57; H, 5.60; N, 4.32; found C, 55.65; H, 5.58; N, 4.31.

*Methyl 2-(azepan-2-ylidene)-3-(2-bromophenyl)propanoate (**9c**):* Prepared from **4c**, the residue was subjected to column chromatography (DCM:AcOEt 10:1, R_f = 0.74) followed by recrystallization from *n*-hexane. Yield 26% of white crystalline solid, m.p. 80–81.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (br s, 1H); 7.51 (dd, *J* = 7.9, 1.2 Hz, 1H); 7.19 (td, *J* = 7.6, 1.2 Hz, 1H); 7.11–7.08 (m, 1H); 7.04–6.99 (m, 1H); 3.70 (s, 2H); 3.60 (s, 3H); 3.38–3.34 (m, 2H); 2.32–2.27 (m, 2H); 1.70–1.56 (m, 4H); 1.50–1.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 168.7, 142.2, 132.4, 129.3, 127.3, 127.2, 124.7, 87.1, 50.7, 44.3, 33.4, 30.5, 30.2, 29.3, 25.4. HRMS-MALDI (*m/z*): Calcd for $C_{16}H_{21}{}^{79}BrNO_2$ 338.07502 $[M+H]^+$, found 338.07528. Calcd for $C_{16}H_{23}{}^{79}BrNO_3$ $[M+H_2O+H]^+$ 356.08558, found 356.08598. Calcd for $C_{16}H_{22}{}^{79}BrNNaO_3$ $[M+H_2O+Na]^+$ 378.06753, found 378.06795. Elemental analysis: Calcd for $C_{16}H_{20}BrNO_2$ C, 56.82; H, 5.96; N, 4.14; found C, 56.91; H, 5.95; N, 4.15.

*4-(2-Bromophenyl)-3-(pyrrolidin-2-ylidene)butane-2-one (**9d**):* Prepared from **6a**, the residue was subjected to column chromatography (DCM:AcOEt 10:1, R_f = 0.44). Yield 42% of sandy solid, m.p. 109–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (br s, 1H); 7.48 (dd, *J* = 7.8, 1.2 Hz, 1H); 7.17–7.12 (m, 1H); 7.03–6.97 (m, 2H); 3.60–3.54 (m, 4H); 2.45 (t, *J* = 7.8 Hz, 2H); 1.93–1.87 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 168.2, 140.7, 132.7, 128.6, 127.73, 127.72, 125.1, 97.5, 48.2, 35.9, 31.7, 27.0, 21.4. HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{17}{}^{79}BrNO$ 294.04880 $[M+H]^+$, found 294.04904. Calcd for $C_{14}H_{16}{}^{79}BrNNaO$ $[M+Na]^+$ 316.03075, found 316.03103. Elemental analysis: Calcd for $C_{14}H_{16}BrNO$ C, 57.16; H, 5.48; N, 4.76; found C, 57.29; H, 5.32; N, 4.61.

*4-(2-Bromophenyl)-3-(piperidin-2-ylidene)butane-2-one (**9e**):* Prepared from **6b**, the residue was subjected to column chromatography (DCM:AcOEt 10:1, R_f = 0.44). Yield 51% of yellowish solid, m.p. 64–68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.63 (s, 1H); 7.55 (dd, *J* = 7.9, 1.2 Hz, 1H); 7.23 (td, *J* = 7.7, 1.2 Hz, 1H); 7.14–7.11 (m, 1H); 7.09–7.04 (m, 1H); 3.59 (s, 2H); 3.39 (td, *J* = 5.9, 2.5 Hz, 2H); 2.24 (t, *J* = 6.4 Hz, 2H); 1.99 (s, 3H); 1.77–1.70 (m, 2H); 1.69–1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 164.5, 140.6, 132.7, 128.4, 127.74, 127.70, 125.1, 98.8, 41.5, 34.5, 27.5, 26.0, 21.8, 19.8. HRMS-MALDI (*m/z*) Calcd for $C_{15}H_{19}{}^{79}BrNO$ $[M+H]^+$ 308.06445, found 308.06433. Calcd for $C_{15}H_{18}{}^{79}BrNNaO$ 330.04640 $[M+Na]^+$, found 330.04648. Calcd for $C_{15}H_{18}NO$ 228.13829 $[M–Br]^+$, found 228.13831. Elemental analysis: Calcd for $C_{15}H_{18}BrNO$ C, 58.45; H, 5.89; N, 4.54; found C, 58.52; H, 5.96; N, 4.50.

*2-Bromobenzyl-1,5-bis(2-bromophenyl)-4-(piperidine-2-ylidene)pentane-3-one (**10a**):* Obtained from **6b** as a by-product from the above-mentioned chromatography (R_f = 0.78), m.p. 127–129 °C. Yield 10.5% of yellow crystals. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.14 (br s, 1H); 7.47 (d, *J* = 7.7 Hz, 1H); 7.36 (d, *J* = 7.7 Hz, 2H); 7.14–7.11 (m, 4H); 7.03–6.97 (m, 2H); 6.94 (t, *J* = 7.5 Hz, 1H); 6.80 (t, *J* =

7.4 Hz, 1H); 6.28 (d, *J* = 7.4 Hz, 1H); 3.42–3.39 (m, 2H); 3.36–3.29 (m, 1H); 3.25 (s, 2H); 3.03 (dd, *J* = 13.1, 8.5 Hz, 2H); 2.79 (dd, *J* = 12.9, 6.2 Hz, 2H); 2.07 (t, *J* = 6.5 Hz, 2H); 1.73–1.68 (m, 2H); 1.61–1.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 165.7, 140.6, 139.8, 132.9, 132.3, 132.2, 128.2, 127.8, 127.7, 127.2, 127.0, 125.4, 124.9, 99.4, 44.9, 41.5, 39.1, 32.9, 26.2, 21.8, 19.7 ppm. HRMS-MALDI (*m/z*): Calcd for $C_{29}H_{29}{}^{79}Br_3NO$ $[M+H]^+$ 643.97938, found 643.98068. Calcd for $C_{29}H_{28}{}^{79}Br_2NO$ $[M–Br]^+$ 564.05322, found 564.05412. Elemental analysis: Calcd for $C_{29}H_{28}Br_3NO$ C, 53.90; H, 4.37; N, 2.17; Br, 37.09; found C, 53.93; H, 4.38; N, 2.17; Br, 37.01.

*3-(Azepan-2-ylidene)-4-(2-bromophenyl)butane-2-one (**9f**):* Prepared from **6c**, the residue was subjected to column chromatography (DCM:AcOEt 6:1, R_f = 0.55). Yield 36% of yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.39 (br s, 1H); 7.54 (dd, *J* = 7.9, 1.2 Hz, 1H); 7.23 (t, *J* = 7.5 Hz, 1H); 7.13 (d, *J* = 7.8 Hz, 1H); 7.06 (t, *J* = 7.7 Hz, 1H); 3.68 (s, 2H); 3.42–3.38 (m, 2H); 2.29–2.27 (m, 2H); 2.03 (s, 3H); 1.73–1.67 (m, 2H); 1.65–1.60 (m, 2H); 1.51–1.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 170.5, 141.0, 132.5, 129.2, 127.6, 127.5, 124.7, 98.8, 44.1, 35.5, 30.5, 29.4, 29.3, 28.1, 24.8. HRMS-MALDI (*m/z*): Calcd for $C_{16}H_{21}{}^{79}BrNO$ 322.08010 $[M+H]^+$, found 322.07990. Calcd for $C_{16}H_{20}{}^{79}BrNNaO$ 344.06205 $[M+Na]^+$, found 344.06218. Elemental analysis: Calcd for $C_{16}H_{20}BrNO$ C, 59.64; H, 6.26; N, 4.35; found C, 59.60; H, 6.35; N, 4.32.

*3-(2-Bromophenyl)-2-(pyrrolidin-2-ylidene)propanenitrile (**9g**):* Prepared from **8a**, the crude oil was suspended in ether and immersed in an ultrasound bath for ca 10 min. Precipitated white solid was isolated by suction. Another portion of the product was obtained on concentrating the ether solution. Product can be recrystallized from cyclohexane to obtain white solid, m.p. 113–117 °C and 133–136 °C. Total yield 39%. Product is 3:1 mixture of E/Z isomers. ^{1}H NMR (500 MHz, $CDCl_3$) major form δ 7.54–7.52 (m, 1H); 7.35 (dd, *J* = 7.7, 1.6 Hz, 1H); 7.29–7.25 (m, 1H); 7.11–7.06 (m, 1H); 4.94 (br s, 1H); 3.49–3.42 (m, 4H); 2.81 (t, *J* = 7.8 Hz, 2H); 2.07–2.00 (m, 2H). Minor form δ 7.54–7.52 (m, 1H); 7.33–7.31 (m, 1H); 7.29–7.25 (m, 1H); 7.11–7.06 (m, 1H); 5.15 (br s, 1H); 3.49–3.42 (m, 4H); 2.59 (t, *J* = 7.7 Hz, 2H); 2.07–2.00 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) major form δ 163.3, 138.0, 132.8, 130.0, 128.5, 128.0, 124.3, 124.1, 67.9, 47.9, 34.2, 31.8, 23.0. Minor form δ 165.3, 139.1, 132.9, 129.9, 128.2, 127.8, 124.4, 122.5, 65.9, 46.8, 34.8, 29.7, 23.2. HRMS-MALDI (*m/z*): Calcd for $C_{13}H_{16}{}^{79}BrN_2$ 279.04914 $[M+2H+H]^+$, found 279.04887. Calcd for $C_{13}H_{14}{}^{79}BrN_2$ 277.03349 $[M+H]^+$, found 277.03367. Calcd for $C_{13}H_{13}{}^{79}BrN_2Na$ 299.01543 $[M+Na]^+$, found 299.01564. Elemental analysis: Calcd for $C_{13}H_{13}BrN_2$ C, 56.34; H, 4.73; N, 10.11; Br, 28.83; found C, 56.42; H, 4.69; N, 10.09; Br, 28.99.

*3-(2-Bromophenyl)-2-(piperidin-2-ylidene)propanenitrile (**9h**):* Prepared from **8b**, the crude oil was suspended in *n*-heptane and immersed in an ultrasound bath for ca 20 min. Precipitated compound was isolated by suction to give 43% of yellowish solid. The product is ca 10:3 mixture of E/Z isomers. On recrystallization from cyclohexane, 17% of white crystals were obtained as 15:1 *E/Z* mixture with m.p.

112–117 °C. ^{1}H NMR (500 MHz, $CDCl_3$) major form δ 7.54–7.52 (m, 1H); 7.33–7.26 (m, 2H); 7.10 (td, *J* = 7.9, 1.9 Hz, 1H); 4.74 (br s, 1H); 3.45 (s, 2H); 3.20–3.17 (m, 2H); 2.70–2.68 (m, 2H); 1.77–1.70 (m, 4H). Minor form δ 7.54–7.52 (m, 1H); 7.32–7.26 (m, 3H); 5.31 (br s, 1H); 3.47 (s, 2H); 3.27 (td, *J* = 6.0, 2.2 Hz, 2H); 2.35 (t, *J* = 6.5 Hz, 2H); 1.77–1.70 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) major form δ 158.0, 137.5, 132.9, 129.7, 128.5, 128.0, 124.5, 123.7, 72.1, 42.7, 33.0, 28.0, 23.0, 20.5. Minor form δ 160.0, 139.0, 128.2, 127.8, 123.4, 69.9, 42.8, 33.2, 25.4 (only some signals on the minor form were detected). HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{16}{}^{79}BrN_2$ 291.04914 $[M+H]^+$, found 291.04943. Elemental analysis: Calcd for $C_{14}H_{15}BrN_2$ C, 57.75; H, 5.19; N, 9.62; found C, 57.96; H, 5.14; N, 9.60.

*2-(Azepan-2-ylidene)-3-(2-bromophenyl)propanenitrile (**9i**):* Prepared from **8c**. The crude yellow oil was subjected to repeated column chromatography (DCM:AcOEt 20:1, R_f = 0.67 and AcOEt:*n*-hexane 6:1, R_f = 0.92) and subsequently purified by recrystallization from *n*-heptane to give 25% of white crystals with m.p. 76–97 °C. Product is then ca 7:1 mixture of *E/Z* isomers and still contains ca 20 mol.% of *N*-benzyl isomer. This almost inseparable by-product was finally removed by another column chromatography (silica gel, DCM, R_f = 0.28) and the product was isolated in 7% yield. ^{1}H NMR (400 MHz, $CDCl_3$) major form δ 7.47–7.45 (m, 1H); 7.26–7.24 (m, 1H); 7.22–7.18 (m, 1H); 7.05–7.00 (m, 1H); 4.88 (br s, 1H); 3.36 (s, 2H); 3.16–3.12 (m, 2H); 2.66–2.64 (m, 2H); 1.64–1.57 (m, 4H); 1.46–1.41 (m, 2H). Minor form δ 7.47–7.44 (m, 1H); 7.22–7.18 (m, 3H); 5.48 (br t, 1H); 3.46 (s, 2H); 3.24–3.20 (m, 2H); 2.31–2.28 (m, 2H); 1.64–1.57 (m, 4H); 1.46–1.41 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) major form δ 163.8, 137.2, 132.9, 129.5, 128.5, 128.0, 124.6, 124.2, 71.9, 45.0, 33.6, 32.1, 30.7, 30.2, 26.8. Minor form δ 165.9, 139.5, 129.9, 128.2, 44.8, 34.2, 30.6, 30.3, 28.1, 26.0. HRMS-MALDI (*m/z*) Calcd for $C_{15}H_{18}{}^{79}BrN_2$ 305.06479 $[M+H]^+$, found 305.06536. Elemental analysis: Calcd for $C_{15}H_{17}BrN_2$ C, 59.03; H, 5.61; N, 9.18; found C, 59.20; H, 5.60; N, 9.14.

Methyl 3-(2-chlorophenyl)-2-(piperidin-2-ylidene)propanoate (**9j**): Prepared from **4b**, the residue was subjected to a column chromatography (DCM:AcOEt 4:1, R_f = 0.76) to give 33% of white solid with m.p. 120–123 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (br s, 1H); 7.33–7.31 (m, 1H); 7.17–7.14 (m, 1H); 7.11–7.08 (m, 2H); 3.63 (s, 2H); 3.59 (s, 3H); 3.35 (td, *J* = 6.0, 2.5 Hz, 2H); 2.25 (t, *J* = 6.5 Hz, 2H); 1.74–1.69 (m, 2H); 1.66–1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 162.4, 140.0, 134.1, 129.1, 128.4, 126.9, 126.8, 86.2, 50.6, 41.7, 29.5, 26.1, 22.4, 20.2. HRMS-MALDI (*m/z*): Calcd for $C_{15}H_{19}{}^{35}ClNO_2$ 280.10988 $[M+H]^+$, found 280.10992. Calcd for $C_{15}H_{18}{}^{35}ClNNaO_2$ $[M+Na]^+$ 302.09183, found 302.09195. Elemental analysis: Calcd for $C_{15}H_{18}ClNO_2$ C, 64.40; H, 6.49; N, 5.01; found: C, 64.49; H, 6.55; N, 4.99.

*4-(2-Chlorophenyl)-3-(pyrrolidin-2-ylidene)butane-2-one (**9k**):* Prepared from **6a**, the residue was subjected to column chromatography (DCM:AcOEt 1:1, R_f = 0.54). The product can be recrystallized from *n*-hexane. Yield 55% of yellowish solid, m.p. 102–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.58

(br s, 1H); 7.36 (dd, *J* = 7.3, 1.7 Hz, 1H); 7.19–7.10 (m, 3H); 3.67 (s, 3H); 3.64 (t, *J* = 7.3 Hz, 2H); 2.52 (t, *J* = 7.8 Hz, 2H); 2.00–1.92 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 168.0, 139.1, 134.2, 129.4, 128.4, 127.3, 127.0, 97.1, 48.1, 32.8, 31.6, 27.0, 21.4. HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{17}{}^{35}ClNO$ 250.09932 $[M+H]^+$, found 250.09931. Calcd for $C_{14}H_{16}{}^{35}ClNNaO$ $[M+Na]^+$ 272.08126, found 272.08127. Elemental analysis: Calcd for $C_{14}H_{16}ClNO$ C, 67.33; H, 6.46; N, 5.61; found C, 67.29; H, 6.42; N, 5.59.

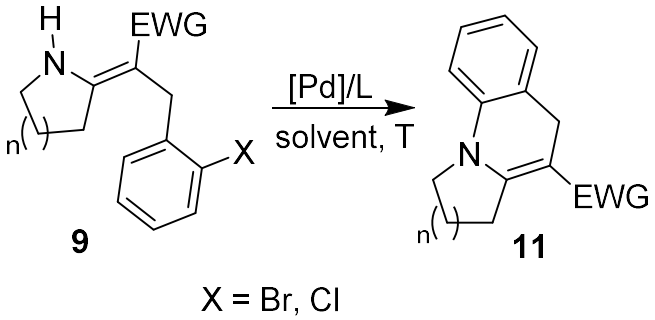
*3-(Azepan-2-ylidene)-4-(2-chlorophenyl)butane-2-one (**9l**):* Prepared from **6c**, the residue was subjected to a column chromatography (DCM:AcOEt 10:1, R_f = 0.44). Yield 31% of yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.39 (br s, 1H); 7.36–7.34 (m, 1H); 7.20–7.11 (m, 3H); 3.71 (s, 2H); 3.42–3.38 (m, 2H); 2.30–2.27 (m, 2H); 2.03 (s, 3H); 1.71–1.67 (m, 2H); 1.65–1.60 (m, 2H); 1.50–1.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 170.5, 139.5, 133.9, 129.2, 129.0, 127.3, 126.9, 98.4, 44.1, 32.5, 30.6, 29.4, 29.2, 28.1, 24.8. HRMS-MALDI (*m/z*): Calcd for $C_{16}H_{21}{}^{35}ClNO$ 278.13062 $[M+H]^+$, found 278.13074. Calcd for $C_{16}H_{20}{}^{35}ClNNaO$ 300.11256 $[M+Na]^+$, found 300.11272. Elemental analysis: Calcd for $C_{16}H_{20}BrNO$ C, 69.18; H, 7.26; N, 5.04; found C, 69.17; H, 7.29; N, 5.01.

2-(Azepan-2-ylidene)-4-(2-chlorobenzyl)-1,5-bis(2-chlorphenyl)-pentan-3-one (10b): Obtained from **6c** as a by-product from the above-mentioned chromatography (R_f = 0.78), m.p. 124–126 °C. Yield 11% of yellowish crystals. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.83 (br s, 1H); 7.27 (d, *J* = 9.1 Hz, 1H); 7.18–7.16 (m, 2H); 7.13–7.07 (m, 6H); 7.01 (t, *J* = 7.5 Hz, 1H); 6.76 (t, *J* = 7.5 Hz, 1H); 6.25 (d, *J* = 7.6 Hz, 1H); 3.41–3.39 (m, 2H); 3.37–3.34 (m, 1H); 3.32 (s, 2H); 3.02 (dd, *J* = 13.1, 8.6 Hz, 2H); 2.81 (dd, *J* = 13.1, 6.1 Hz, 2H); 2.12–2.10 (m, 2H); 1.66–1.62 (m, 4H); 1.36–1.32 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.2, 171.6, 139.4, 138.0, 134.6, 133.7, 131.9, 129.6, 128.9, 128.8, 127.5, 126.9, 126.8, 126.4, 99.2, 45.2, 44.2, 36.9, 30.7, 30.6, 29.45, 29.40, 24.6 ppm. HRMS-MALDI (*m/z*): Calcd. for $C_{30}H_{31}{}^{35}Cl_3NO$ $[M+H]^+$ 526.14657, found 526.14551. Calcd. for $C_{30}H_{30}{}^{35}Cl_3NNaO$ $[M+Na]^+$ 548.12852, found 548.12729. *Anal.* Calcd. for $C_{30}H_{30}Cl_3NO$ (526.92) C, 68.38; H, 5.74; N, 2.66%. Found C, 68.41; H, 5.75; N, 2.66%.

*3-(2-Chlorophenyl)-2-(pyrrolidin-2-ylidene)propanenitrile (**9m**):* Prepared from **8a**, the crude product was subjected to a column chromatography (DCM:EtOAc 4:1, R_f = 0.72). The product was then recrystallized from *n*-heptane and subsequently from cyclohexane to give white solid, m.p. 91–107 °C. Total yield 34%. Product is 1.8:1 mixture of *E/Z* isomers. ^{1}H NMR (400 MHz, $CDCl_3$) major form δ 7.37–7.31 (m, 2H); 7.26–7.15 (m, 2H); 4.89 (br s, 1H); 3.49–3.41 (m, 4H); 2.81 (t, *J* = 7.8 Hz, 2H); 2.08–1.99 (m, 2H). Minor form δ 7.37–7.31 (m, 2H); 7.26–7.15 (m, 2H); 5.10 (br s, 1H); 3.49–3.42 (m, 4H); 2.59 (t, *J* = 7.7 Hz, 2H); 2.08–1.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) major form δ 163.1, 136.5, 133.6, 130.0, 129.6, 128.2, 127.4, 124.0, 68.1, 47.8, 31.8, 31.4, 23.1. Minor form δ 165.1, 137.5, 133.8, 129.9, 129.6, 127.9, 127.1, 122.4, 66.1, 46.8, 32.1, 29.6, 23.2. HRMS-MALDI

(*m/z*): Calcd for $C_{13}H_{16}{}^{35}ClN_2$ 235.09965 $[M+2H+H]^+$, found 235.09971. Calcd for $C_{13}H_{14}{}^{35}ClN_2$ 233.08400 $[M+H]^+$, found 233.08429. Calcd for $C_{13}H_{13}{}^{35}ClN_2Na$ 255.06595 $[M+Na]^+$, found 255.06618. Elemental analysis: Calcd for $C_{13}H_{13}ClN_2$ C, 67.10; H, 5.63; N, 12.04; found C, 67.17; H, 5.59; N, 12.00.

*Synthesis of [1,2-a]-fused tricyclic dihydroquinolines **11a–i***



Method A: A dried screw-cup vial, equipped with a magnetic stirring bar and septum was charged with substrate **9** (0.5 mmol), $Pd_2(dba)_3$ (3.5–5 mol. %), DPPP (7–10 mol. %) and *t*BuONa (0.6 mmol, 1.2 eq.). The vial was sealed and three-times evacuated and backfilled with argon. Dry toluene (2 mL) was then added via syringe and the mixture was heated to 100 °C for 24–36 h (for exact conditions see Table 3). The mixture was then cooled, diluted with AcOEt and filtered through a plug of Celite®. The filtrate was evaporated to dryness, the residue was suspended in ether (25 mL) and subjected to an ultrasound irradiation. Precipitated impurities were removed by a filtration through Celite®. The pure product **11** was obtained upon evaporation of the filtrate.

Method B: A dried screw-cup vial, equipped with a magnetic stirring bar and septum was charged with substrate **9** (0.5 mmol), precatalyst **L1** (1.5–2 mol. %) and K_3PO_4 (1 mmol, 2 eq.). The vial was sealed and three-times evacuated and backfilled with argon. Dry *t*BuOH (2 mL) was added via syringe and the mixture was heated to 80 °C for 16–24 h (for exact conditions see Table 3). The mixture was then cooled, diluted with AcOEt and filtered through a plug of Celite®. The pure product **11** was obtained upon evaporation of the filtrate.

Method C: A dried screw-cup vial (A) equipped with a magnetic stirring bar and septum was charged with substrate **9** (0.5 mmol) and Cs_2CO_3 (0.7 mmol, 1.4 eq.). Another vial (B) equipped with a magnetic stirring bar and septum was charged with $Pd_2(dba)_3$ (22.9 mg, 5 mol.%) and RuPhos (23.3 mg, 10 mol.%). Both the vials were sealed and three-times evacuated and backfilled with argon. Toluene (3 mL) was added via syringe into the vial B. The mixture was then heated to 100 °C for 30 minutes and subsequently transferred into the vial A via syringe. The mixture was then heated to 100 °C for 60 h. The mixture was then cooled, diluted with AcOEt and filtered through a plug of Celite®. The filtrate was evaporated to dryness to give product **11**.

*Methyl 1,2,3,5-tetrahydropyrrolo[1,2-a]quinoline-4-carboxylate (**11a**):* Prepared by method A, reaction time 24 h, 5% $Pd_2(dba)_3$, 10% DPPP, yield 65% of red-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12–7.07 (m, 2H); 6.94 (td, *J* = 7.4, 1.1 Hz, 1H); 6.65 (d, *J* = 7.5 Hz, 1H); 3.79 (s, 2H); 3.72 (s, 3H); 3.60 (t, *J* = 7.1 Hz, 2H); 3.14 (t, *J* = 7.8 Hz, 2H); 2.12 (quint, *J* = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 156.1, 138.7, 129.2, 127.2, 124.1, 123.2, 112.8, 90.5, 51.0, 48.5, 32.3, 28.0,

21.9. HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{14}NO_2$ 228.10191 $[M–H]^+$, found 228.10216. Calcd for $C_{12}H_{12}N$ 170.09643 $[M–COOCH_3]^+$, found 170.09664.

*Methyl 1,2,3,4,6-pentahydropyrido[1,2-a]quinoline-5-carboxylate (**11b**):* Prepared by method B, reaction time 16 h, 1.5% **L1**, yield 95% of yellow oil and method C, reaction time 66 h, yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.12 (m, 1H); 7.08 (dd, *J* = 7.4, 1.2 Hz, 1H); 6.98 (td, *J* = 7.4, 1.0 Hz, 1H); 6.87 (d, *J* = 8.2 Hz, 1H); 3.71 (s, 3H); 3.65 (s, 2H); 3.63–3.60 (m, 2H); 3.21 (tt, *J* = 7.0, 0.9 Hz, 2H); 1.95–1.88 (m, 2H); 1.74 (quint, *J* = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 154.1, 141.5, 128.3, 126.8, 125.1, 123.1, 112.6, 94.3, 51.0, 45.2, 28.1, 26.8, 22.8, 19.4. HRMS-MALDI (*m/z*): Calcd for $C_{15}H_{16}NO_2$ 242.11756 $[M–H]^+$, found 242.11782. Elemental analysis: Calcd for $C_{15}H_{17}NO_2$ C, 74.05; H, 7.04; N, 5.76; found C, 74.02; H, 7.00; N, 5.70.

*Methyl 5,7,8,9,10,11-hexahydroazepino[1,2-a]quinoline-6-carboxylate (**11c**):* Prepared by method B, reaction time 16 h, 1.5% **L1**, yield 97% of red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.12 (m, 1H); 7.08 (dd, *J* = 7.4, 1.1 Hz, 1H); 6.96 (td, 1H, *J* = 7.4, 1.0 Hz); 6.88 (d, 1H, *J* = 8.2 Hz); 3.90–3.86 (m, 2H); 3.72 (s, 3H); 3.57 (s, 2H); 3.29 (br m, 2H); 1.85–1.77 (m, 2H); 1.73–1.66 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 158.2, 141.9, 128.1, 126.8, 125.5, 122.7, 112.8, 95.7, 51.2, 47.4, 29.1, 28.7, 28.6, 27.9, 26.6. HRMS-MALDI (*m/z*): Calcd for $C_{16}H_{18}NO_2$ 256.13321 $[M–H]^+$, found 256.13364. Elemental analysis: Calcd for $C_{16}H_{19}NO_2$ C, 74.68; H, 7.44; N, 5.44; found C, 74.71; H, 7.46; N, 5.43.

*4-Acetyl-1,2,3,5-tetrahydropyrrolo[1,2-a]quinoline (**11d**):* Prepared by method A, reaction time 36 h, 3.5% $Pd_2(dba)_3$, 7% DPPP, yield 87% of yellow-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14–7.10 (m, 1H); 6.96 (t, *J* = 7.4 Hz, 1H); 6.68 (d, *J* = 7.9 Hz, 1H); 3.86 (s, 2H); 3.62 (t, *J* = 7.1 Hz, 2H); 3.16 (t, *J* =7.7 Hz, 2H); 2.23 (s, 3H); 2.14 (quint, *J* = 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 156.0, 138.2, 129.0, 127.3, 124.5, 123.4, 112.9, 101.4, 48.2, 33.1, 29.4, 29.1, 21.9. HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{14}NO$ 212.10699 $[M–H]^+$, found 212.10725. Calcd for $C_{12}H_{12}N$ 170.09643 $[M–CH_3CO]^+$, found 170.09660.

*5-Acetyl-1,2,3,4,6-pentahydropyrido[1,2-a]quinoline (**11e**):* Prepared by method B, reaction time 24 h, 2% **L1**, yield 98% of yellow-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.7 Hz, 1H); 7.10 (d, *J* = 7.4 Hz, 1H); 7.00 (td, *J* = 7.4, 1.0 Hz, 1H); 6.89 (d, *J* = 8.0 Hz, 1H); 3.67 (s, 2H); 3.64 (t, *J* = 6.0 Hz, 2H); 3.19 (t, *J* = 7.0 Hz, 2H); 2.26 (s, 3H); 1.95–1.88 (m, 2H); 1.73 (quint, *J* = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 154.1, 141.3, 128.2, 126.9, 125.3, 123.4, 112.9, 104.1, 45.4, 30.6, 29.8, 27.6, 22.6, 19.3. HRMS-MALDI (*m/z*): Calcd for $C_{15}H_{16}NO$ 226.12264 $[M–H]^+$, found 226.12213. Calcd for $C_{15}H_{18}NO$ 228.13829 $[M+H]^+$, found 228.13772. Elemental analysis: Calcd for $C_{15}H_{17}NO$ C, 79.26; H, 7.54; N, 6.16; found C, 79.26; H, 7.55; N, 6.16.

*6-Acetyl-5,7,8,9,10,11-hexahydroazepino[1,2-a]quinoline (**11f**):* Prepared by method B, reaction time 24 h, 2% **L1**, yield 96% of yellow oil and method C, reaction time 60 h, yield 91%. ^{1}H NMR (400

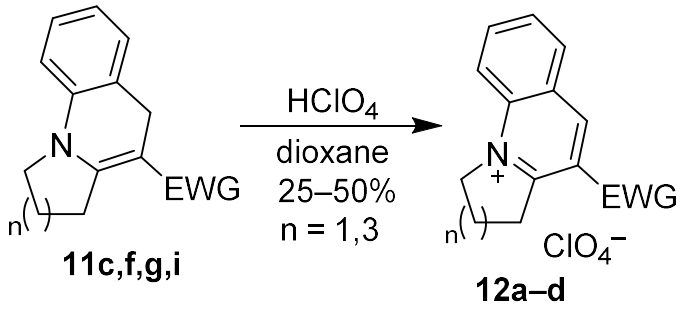
MHz, $CDCl_3$) δ 7.19–7.14 (m, 1H); 7.10 (d, *J* = 7.3 Hz, 1H); 6.99 (td, *J* = 7.4, 0.9 Hz, 1H); 6.91 (d, *J* = 8.2 Hz, 1H); 3.92–3.88 (m, 2H); 3.54 (s, 2H); 3.18–3.14 (br m, 2H); 2.30 (s, 3H); 1.85–1.79 (m, 2H); 1.73–1.66 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 157.3, 141.6, 128.0, 126.8, 125.6, 122.9, 112.9, 106.3, 47.3, 30.5, 29.7, 29.1, 28.9, 27.7, 26.6. HRMS-MALDI (*m/z*): Calcd for $C_{16}H_{18}NO$ $[M–H]^+$ 240.13829, found 240.13849. Elemental analysis: Calcd for $C_{16}H_{19}NO$ C, 79.63; H, 7.94; N, 5.80; found C, 79.55; H, 7.97; N, 5.77.

*1,2,3,5-Tetrahydropyrrolo[1,2-a]quinoline-4-carbonitrile (**11g**):* Prepared by method A, reaction time 36 h, 5% $Pd_2(dba)_3$, 10% DPPP, yield 67% of red-brown oil and method C, reaction time 60 h, yield 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.11 (m, 1H); 7.02–6.99 (m, 1H); 6.94 (td, *J* = 7.4, 1.1 Hz, 1H); 6.63 (dd, *J* = 8.0, 0.9 Hz, 1H); 3.72 (s, 2H); 3.63 (t, *J* = 6.9 Hz, 2H); 2.83 (t, *J* = 7.8 Hz, 2H); 2.15 (quint, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 137.7, 128.9, 127.7, 123.4, 121.8, 120.9, 113.1, 69.3, 49.0, 30.6, 28.0, 21.4. HRMS-MALDI (*m/z*): Calcd for $C_{13}H_{11}N_2$ 195.09167 $[M–H]^+$, found 195.09248. Calcd for $C_{26}H_{23}N_4$ 391.19172 $[2M–H]^+$, found 391.19065. Elemental analysis: Calcd for $C_{13}H_{12}N_2$ C, 79.56; H, 6.16; N, 14.27; found C, 79.49; H, 6.21; N, 14.17.

*1,2,3,4,6-Pentahydropyrido[1,2-a]quinoline-5-carbonitrile (**11h**):* Prepared by method B, reaction time 24 h, 2% **L1**, yield 97% of yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19–7.16 (m, 1H); 7.01–6.97 (m, 2H); 6.90 (d, *J* = 8.3 Hz, 1H); 3.63 (s, 2H); 3.53 (t, *J* = 6.1 Hz, 2H); 2.78 (t, *J* = 6.8 Hz, 2H); 1.95 (quint, *J* = 6.3 Hz, 2H); 1.76–1.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$); δ 152.4, 140.1, 128.9, 127.5, 123.7, 121.9, 121.7, 113.0, 74.3, 45.1, 28.4, 28.1, 23.4, 19.3. HRMS-MALDI (*m/z*): Calcd for $C_{14}H_{13}N_2$ 209.10732 $[M–H]^+$, found 209.10774. Calcd for $C_{14}H_{15}N_2O$ 227.11789 $[M–H+H_2O]^+$, found 227.11841. Elemental analysis: Calcd for $C_{14}H_{14}N_2$ C, 79.97; H, 6.71; N, 13.32; found C, 79.92; H, 6.84; N, 13.31.

*5,7,8,9,10,11-Hexahydroazepino[1,2-a]quinoline-6-carbonitrile (**11i**):* Prepared by method B, reaction time 24 h, 2% **L1**, yield 98% of yellow-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.16 (m, 1 H); 7.05–7.03 (m, 1H); 7.01–6.97 (m, 1H); 6.88 (d, *J* = 8.3 Hz, 1H); 3.82–3.79 (m, 2H); 3.52 (s, 2H); 2.85–2.83 (m, 2H); 1.77–1.70 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 140.8, 128.6, 127.5, 123.2, 122.3, 122.0, 113.1, 76.0, 47.8, 32.9, 29.3, 28.9, 27.8, 27.0. HRMS-MALDI (*m/z*): Calcd for $C_{15}H_{15}N_2$ 223.12298 $[M–H]^+$, found 223.12315. Elemental analysis: Calcd for $C_{15}H_{16}N_2$ C, 80.32; H, 7.19; N, 12.49; found C, 80.06; H, 7.39; N, 12.33.

*Synthesis of fused quinolinium perchlorates **12a–d***



To the solution of **11** in dry dioxane (ca 1.5 mL per 0.1 mmol of **11**) was added ca 11.6M perchloric acid (ca 2–5 eq.). The mixture was left to stand at laboratory temperature until the product precipitated (1–24 h). The product was isolated by suction, washed with ether (6 × 2 mL) and left to dry under vacuum in a desiccator.

*4-Cyano-2,3-dihydro-1H-pyrrolo[1,2-a]quinolinium perchlorate (**12a**):* Prepared from from **11g**, reaction time 2 h, recrystallization from ethanol, m.p. 273–278 °C (dec.). Yield 31% of greyish solid. ^{1}H NMR (500 MHz, DMSO) δ 9.71 (s, 1H); 8.38 (d, *J* = 8.1 Hz, 1H); 8.32 (s, 2H); 8.07–7.98 (m, 1H); 5.09 (t, *J* = 7.4 Hz, 2H); 3.77 (t, *J* = 7.4 Hz, 2H); 2.39 (br s, 2H). ^{13}C NMR (125 MHz, DMSO) δ 164.9, 151.4, 138.3, 137.1, 131.1, 130.7, 127.0, 119.7, 114.2, 105.0, 57.9, 34.6, 19.7. HRMS-MALDI (*m/z*): Calcd for $C_{13}H_{11}N_2$ 195.09167 $[M]^+$, found 195.09170. Calcd for ClO_4 98.94906 $[ClO_4]^-$, found 98.94906. Elemental analysis: Calcd for $C_{13}H_{11}ClN_2O_4$ C, 52.98; H, 3.76; N, 9.51; found C, 53.04; H, 3.77; N, 9.49.

*6-Acetyl-8,9,10,11-tetrahydro-7H-azepino[1,2-a]quinolinium perchlorate (**12b**):* Prepared from **11f**, reaction time 1 h, m.p. 225–229 °C, yield 25.5% of off-white solid. ^{1}H NMR (400MHz, DMSO) δ 9.60 (s, 1H); 8.72 (d, *J* = 9.0 Hz, 1H); 8.47 (d, *J* = 8.2 Hz, 1H); 8.33 (t, *J* = 7.9 Hz, 1H); 8.08 (t, *J* = 7.5 Hz, 1H); 5.24–5.26 (m, 2H); 3.63 (br, 2H); 2.81 (s, 3H); 1.98 (br, 2H); 1.84 (br, 4H). ^{13}C NMR (125 MHz, DMSO) δ 199.5, 163.7, 145.5, 139.3, 137.0, 134.2, 131.4, 130.0, 127.4, 119.1, 52.2, 30.7, 30.5, 26.6, 23.8, 22.7. HRMS-MALDI (*m/z*): Calcd for $C_{16}H_{18}NO$ 240.13829 $[M]^+$, found 240.13799. Calcd for ClO_4 98.94906 $[ClO_4]^-$, found 98.94904.

*6-Cyano-8,9,10,11-tetrahydro-7H-azepino[1,2-a]quinolinium perchlorate (**12c**):* Prepared from **11i**, reaction time 1 h, m.p. 254–258 °C (dec.). Yield 36% of off-white solid. ^{1}H NMR (400 MHz, DMSO) δ 9.88 (s, 1H); 8.79 (d, *J* = 8.9 Hz, 1H); 8.49 (d, *J* = 8.3 Hz, 1H); 8.43 (t, *J* = 8.3 Hz, 1H); 8.14 (t, *J* = 7.6 Hz, 1H); 5.26–5.24 (m, 2H); 3.80 (br, 2H); 1.97–1.92 (br, 6H). ^{13}C NMR (100 MHz, DMSO) δ 165.9, 152.0, 139.9, 138.8, 131.5, 130.5, 127.4, 119.2, 114.9, 108.9, 53.3, 33.7, 26.8, 23.5, 22.1. HRMS-MALDI (*m/z*): Calcd for $C_{15}H_{15}N_2$ 223.12298 $[M]^+$, found 223.12262. Calcd for ClO_4 98.94906 $[ClO_4]^-$, found 98.94905.

*6-Methoxycarbonyl-8,9,10,11-tetrahydro-7H-azepino[1,2-a]quinolinium perchlorate (**12d**):* Prepared from **4c**, reaction time 1 h, m.p. 213–216 °C. Yield 50% of off-white solid. ^{1}H NMR (400 MHz, DMSO) δ 9.61 (s, 1H); 8.74 (d, *J* = 9.0 Hz, 1H); 8.57 (dd, *J* = 8.1, 1.4 Hz, 1H); 8.35 (ddd, *J* = 8.8, 7.0, 1.5 Hz, 1H); 8.08 (t, *J* = 7.5 Hz, 1H); 5.28–5.25 (m, 2H); 4.02 (s, 3H); 3.82 (br, 2H); 1.99 (br, 2H); 1.86 (br, 4H). ^{13}C NMR (100 MHz, DMSO) δ 164.7, 164.4, 147.6, 139.8, 137.5, 131.7, 129.9, 127.4, 126.4, 119.0, 53.8, 52.4, 30.7, 26.6, 23.7, 22.6. HRMS-MALDI (m/z): Calcd for $C_{16}H_{18}NO_2$ 256.13321 $[M]^+$, found 256.13277. Calcd for ClO_4 98.94906 $[ClO_4]^-$, found 98.94904. Elemental analysis: Calcd for $C_{16}H_{18}ClNO_6$ C, 54.02; H, 5.10; N, 3.94; found C, 53.79; H, 5.09; N, 3.85.

X-Ray data

General information

The X-ray data for colorless crystals of **9d**, **10a**, **12d** were obtained at 150 K using Oxford Cryostream low-temperature device on a Nonius Kappa CCD diffractometer with Mo K_α radiation (λ = 0.71073 Å), a graphite monochromator, and the ϕ and χ scan mode. Data reductions were performed with DENZO-SMN.[17] The absorption was corrected by integration methods.[18] Structures were solved by direct methods (Sir92)[19] and refined by full matrix least-square based on F^2 (SHELXL97).[20] Hydrogen atoms were mostly localized on a difference Fourier map, however to ensure uniformity of treatment of crystal, all hydrogen were recalculated into idealized positions (riding model) and assigned temperature factors $H_{iso}(H) = 1.2\ U_{eq}$ (pivot atom) or of $1.5U_{eq}$ (methyl). H atoms in methyl, methylene, and hydrogen atoms in aromatic rings were placed with C–H distances of 0.96, 0.97 and 0.93Å and 0.86 Å for N–H bonds.

$R_{int} = \sum | F_o^2 - F_{o,mean}^2 | / \sum F_o^2$, GOF = $[\sum(w(F_o^2 - F_c^2)^2)/(N_{diffrs} - N_{params})]^{½}$ for all data, $R(F) = \sum | \ | F_o | - | F_c | \ | / \sum | F_o |$ for observed data, $wR(F^2) = [\sum(w(F_o^2 - F_c^2)^2)/(\sum w(F_o^2)^2)]^{½}$ for all data.

Crystallographic data for structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 1442790, 1442792, and 1442791 for **9d, 12d**, and **10a**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EY, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Crystal structures

The structure of three compounds predicted on the basis of physico-chemical and spectral measurements was unambiguously proven by X-ray diffraction techniques on single-crystalline material. In both **9d** and **10a** (see Figs. S1 and S2), the structures are influenced by rather strong in-plane intramolecular H-bonds of NH to the carbonyl group, which has in **9d** also a centrosymmetric counterpart making thus a dimer in the solid state. This particular dimeric arrangement is most probably prevented in the structure of **10a** by the presence of bulky and highly flexible benzyl substituents. The presence of C=C bond is seen from interatomic distances of C8–C11 in **9d** and C8–C10 in **10a** (see Fig. S2 captions), where the later one is slightly longer due to its connection to more strained six-membered ring in combination with more steric hindrance at C8 atom. The only reported structures of related pyrrolidin-2-ylidenes and piperidin-2-ylidenes[21–24] have very similar arrangements and parameters of interest.

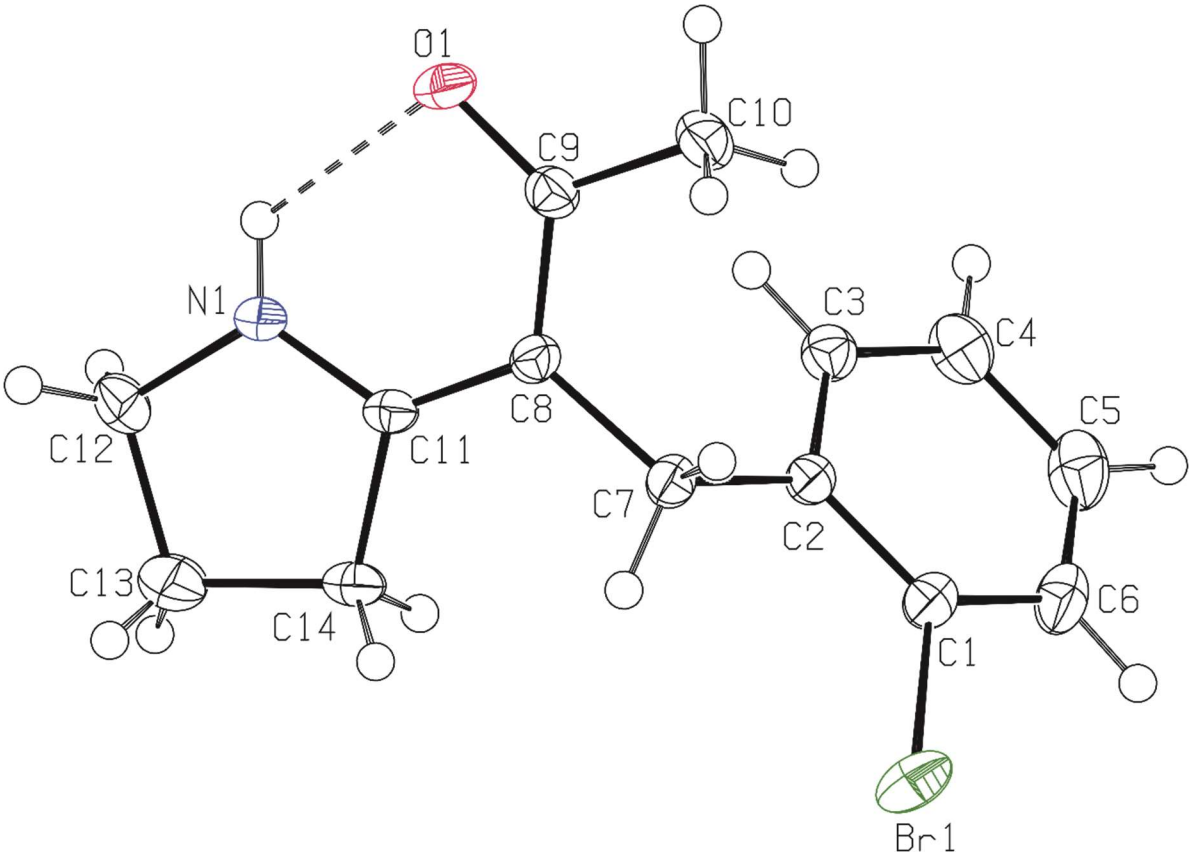


FIGURE S1. The molecular structure (ORTEP view, 50% probability level) of **9d**, the second independent molecule is omitted for clarity, appropriate parameters are given in parentheses. Selected interatomic distances [Å] and angles [°]: N1–C11 1.333(3) (1.327(3)), N1–C12 1.454(3) (1.455(3)), C8–C11 1.386(4) (1.385(4)), C8–C9 1.432(4) (1.429(4)), C7–C8 1.514(4) (1.509(4)), O1–C9 1.251(3) (1.254(3)); C11–N1–C12 115.6(2) (116.1(2)); interplanar angle: ring (N1–C11–C14–C13–C120) vs. ring (C1–C2–C3–C4–C5–C6) 67.82(1) (80.85(2)). The crystal was obtained upon slow evaporation of the solution of **9d** in acetonitrile.

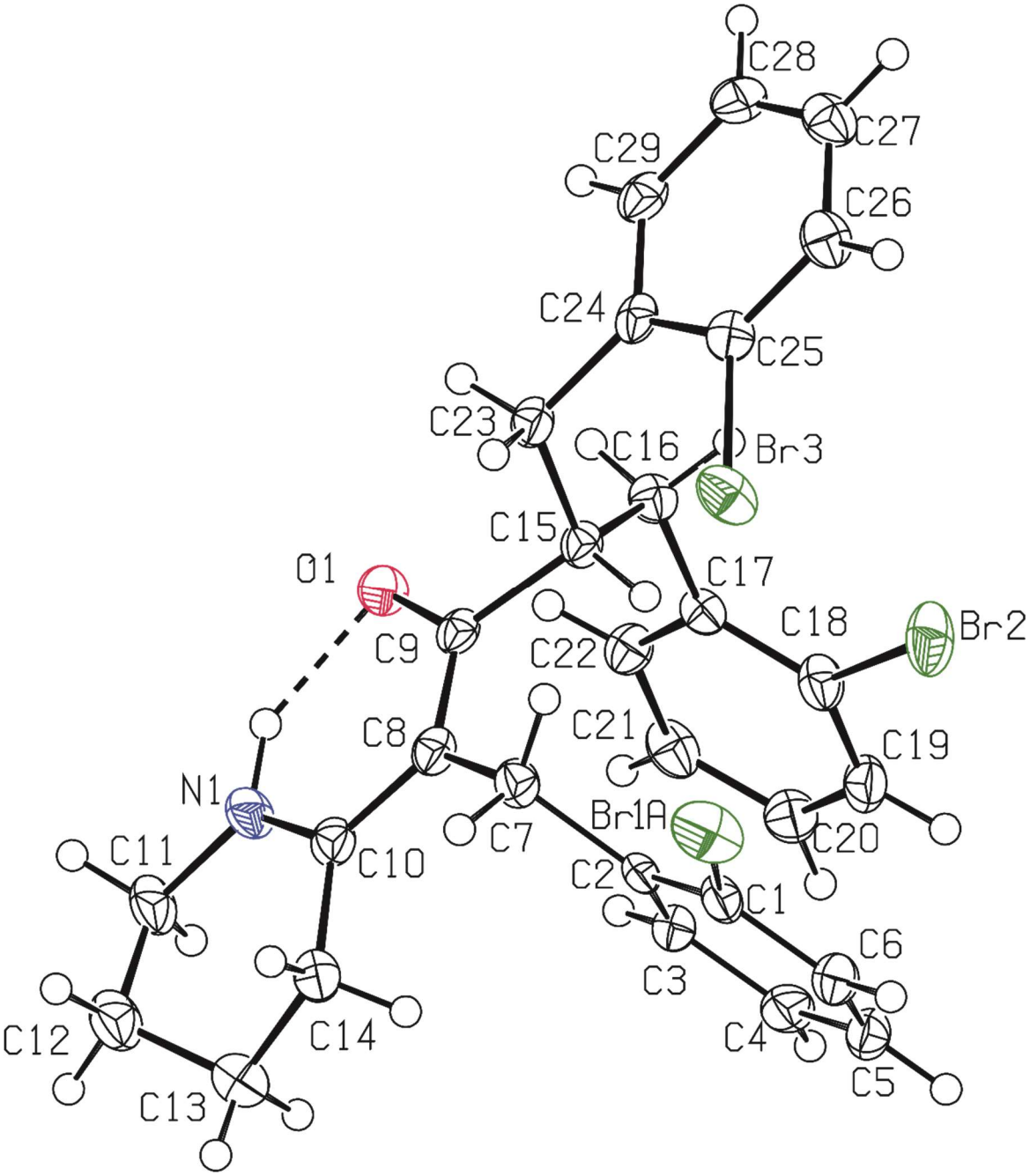


FIGURE S2. The molecular structure (ORTEP view, 50% probability level) of **10a**, disordered part of phenyl ring is omitted for clarity. Selected interatomic distances [Å] and angles [°]: N1–C11 1.465(5), N1–C10 1.322(5), C8–C10 1.405(6), C9–C8 1.422(6), C15–C9 1.543(6), O1–C9 1.252(5); C10–N1–C11 126.7(4). The crystal was obtained upon slow cooling and subsequent gradual evaporation of the hot ethanolic solution of **10a**.

In **12d** (Fig. S3), the expected parameters of interatomic separations as well as the bonding angles were found.[25] On the other hand there is no mention about similar structure of such kind in the literature, and only modestly related structures of azepines were determined.[26–28] The seven membered ring in **12d** is flapped below the plane of the aromatic system interacting weakly via C-H···O connections with perchlorate anion.

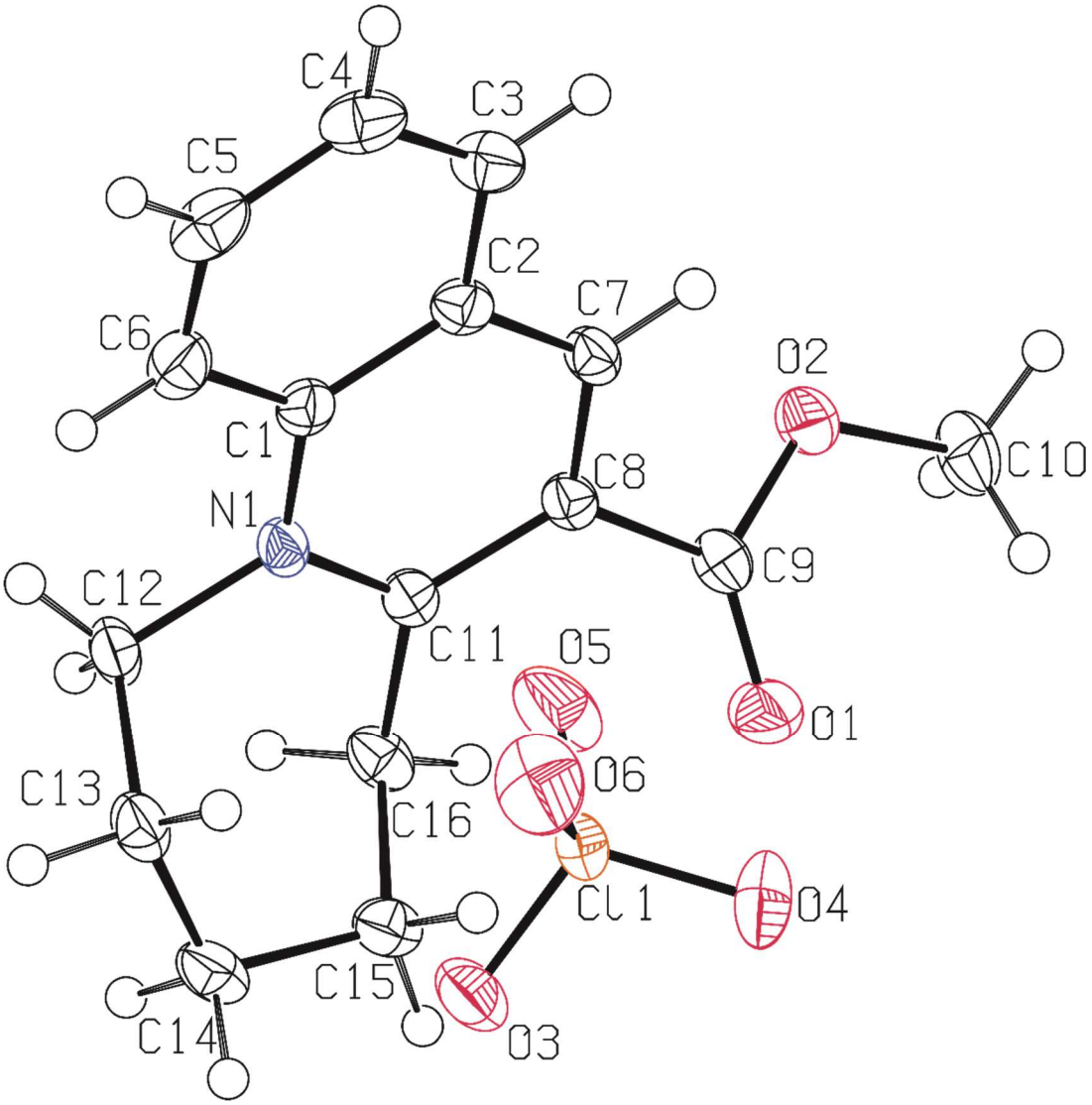


FIGURE S3. The molecular structure (ORTEP view, 50% probability level) of **12d**. Selected interatomic distances [Å] and angles [°]: N1–C11 1.342(2), N1–C12 1.498(2), N1–C1 1.393(2), C1–C2 1.414(2), C7–C2 1.404(2), C8–C7 1.367(2), C8–C11 1.413(2), C8–C9 1.500(2), O1–C9 1.198(2); C11–N1–C1 122.38(13); interplanar angle: aromatic system vs. ester group 39.54(2). The crystal was obtained upon gradual cooling and subsequent slow evaporation of the solution of **12d** in aqueous methanol (4:1).

Table S1 Crystallographic data for compounds **9d, 12d**, and **10a**.

Compound	9d	12d	10a
Empirical formula	$C_{14}H_{16}BrNO$	$C_{16}H_{18}NO_2^+ \cdot ClO_4^-$	$C_{29}H_{28}Br_3NO$
Crystal system	monoclinic	triclinic	monoclinic
Space group	$P2_1/c$	P-1	$C\,2/c$
a (Å)	12.6060(8)	8.5601(3)	20.1762(5)
b (Å)	7.1370(5)	8.8390(4)	8.7970(2)
c (Å)	28.5641(13)	11.0820(4)	29.6163(5)
α (°)	90	89.727(4)	90
β (°)	100.389(4)	68.473(3)	104.291(3)
γ (°)	90	84.906(4)	90
Z	8	2	8
V (Å^3)	2527.8(3)	776.57(6)	5093.9(2)
D_c (g cm^{-3})	1.546	1.521	1.685
Crystal size (mm)	0.48 × 0.30 × 0.15	0.59 × 0.24 × 0.09	0.34 × 0.21 × 0.19
μ (mm^{-1})	3.235	0.280	4.775
F(000)	1200	372	2576
h; k; l range	–16, 16; –9, 9; –36, 36	–11, 11; –11, 11; –14, 14	–25, 26; –11, 10; –38, 37
θ range (°)	1.99–27.50	1.98–27.49	2.08–27.50
Reflections measured	35057	15399	26040
- independent (R_{int}) [a]	34966 (0.0662)	15321 (0.0245)	25965 (0.0797)
- observed [I>2σ(I)]	4770	2967	4044
Parameters refined	307	217	305
Max/min τ (eÅ^{-3})	0.309 / –0.585	0.283 / –0.474	0.982 / –0.708
GOF [b]	1.203	1.129	1.135
R [c] / wR [d]	0.0397 / 0.0754	0.0367 / 0.0865	0.0491 / 0.0913

[a] $R_{int} = \sum \left| F_o^2 - F_{o,mean}^2 \right| / \sum F_o^2$, [b] GOF = $[\sum(w(F_o^2 - F_c^2)^2)/(N_{diffrs} - N_{params})]^{½}$ for all data, [c] $R(F) = \sum \left| \left| F_o \right| - \left| F_c \right| \right| / \sum \left| F_o \right|$ for observed data, [d] $wR(F^2) = [\sum(w(F_o^2 - F_c^2)^2)/(\sum w(F_o^2)^2)]^{½}$ for all data.

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NMR Data

NMR Spectra were measured using either Bruker AVANCE III spectrometer operating at 400 MHz (^{1}H) and 100 MHz (^{13}C) or Bruker Ascend™ operating at 500 MHz (^{1}H) and 125 MHz (^{13}C). Proton NMR spectra in $CDCl_3$ were calibrated using internal TMS ($\delta = 0.00$) and in DMSO-d6 on the middle signal of the solvent multiplet ($\delta = 2.50$). Carbon NMR spectra were referenced against the middle signal of the solvent multiplet ($\delta = 77.26$ for $CDCl_3$ and 39.51 for DMSO-d6). Measurement of ^{13}C NMR was done using composite pulse proton decoupling in an ordinary way or APT pulse sequence.

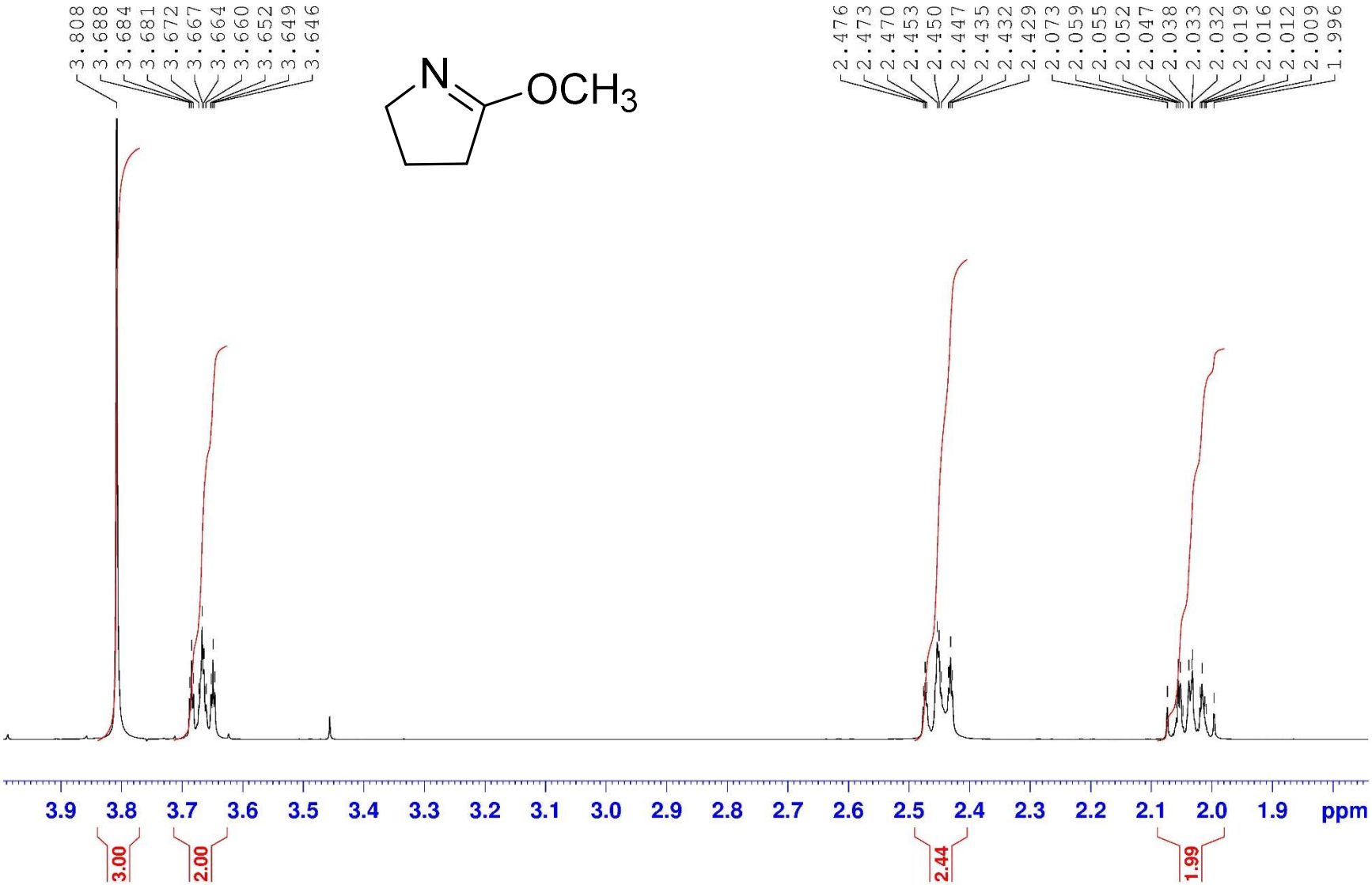

FIGURE S4: 400 MHz ^{1}H NMR spectrum of **2a** in $CDCl_3$.

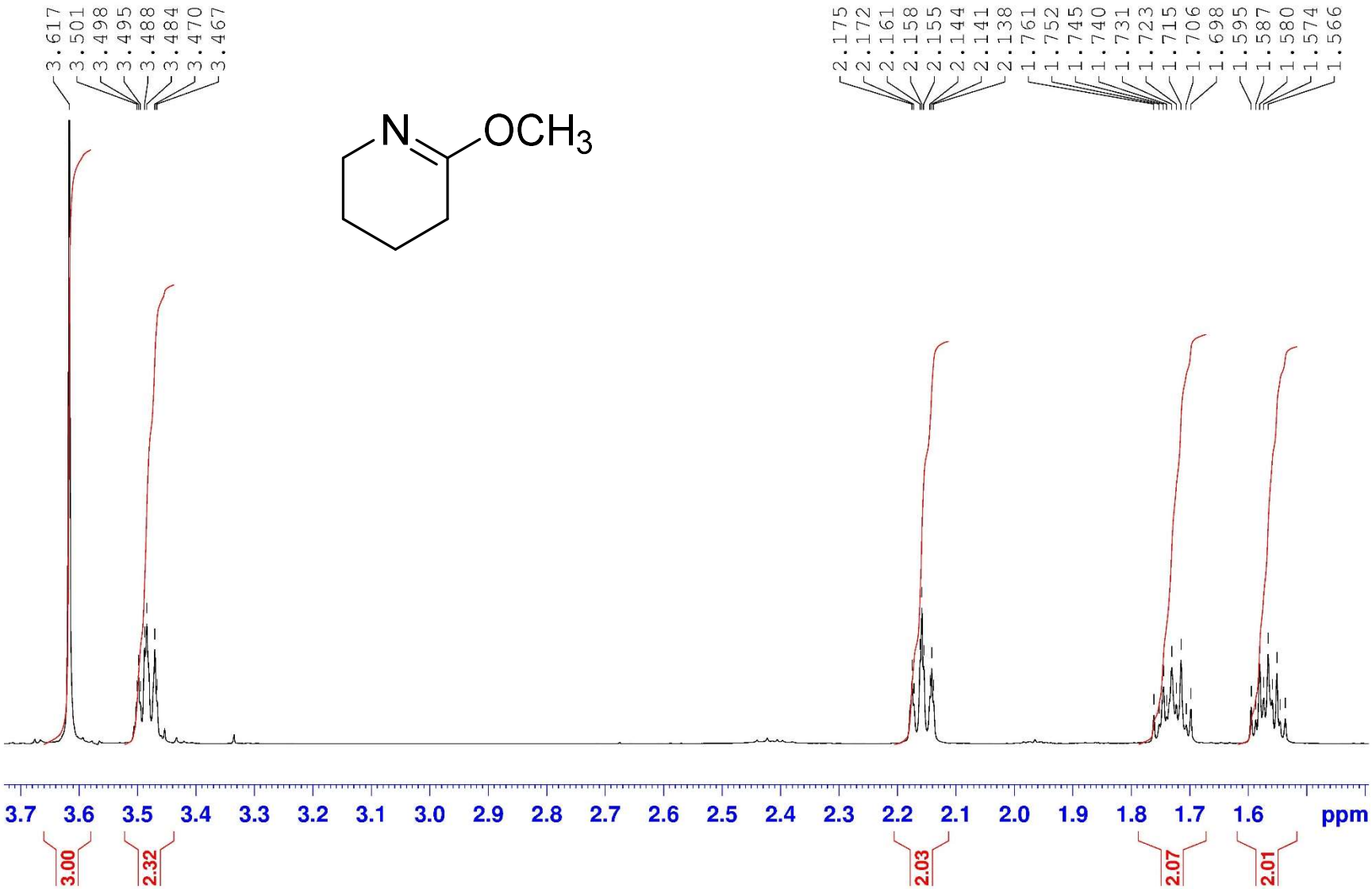

FIGURE S5: 400 MHz ^{1}H NMR spectrum of **2b** in $CDCl_3$.

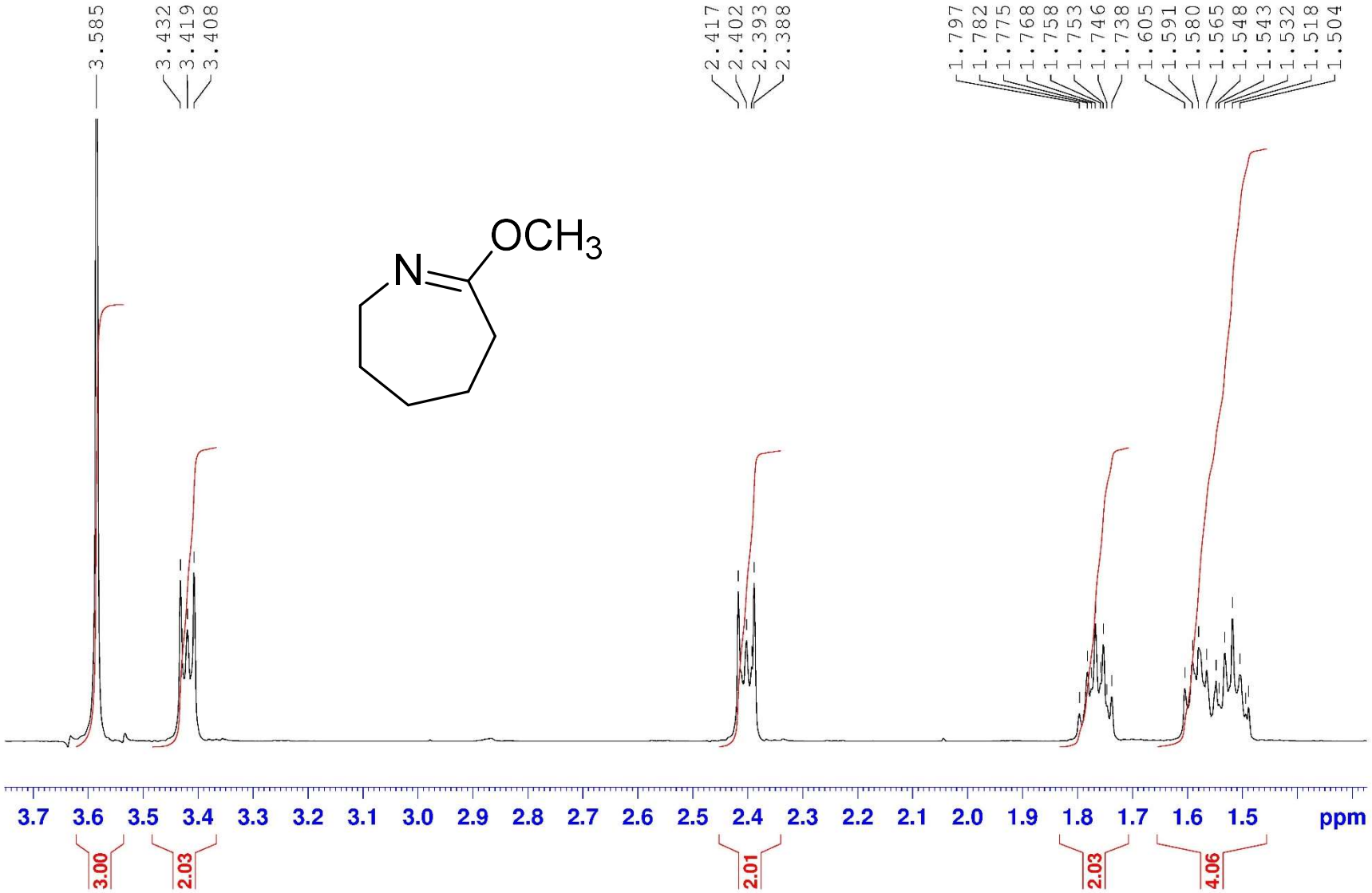

FIGURE S6: 400 MHz ^{1}H NMR spectrum of **2c** in $CDCl_3$.

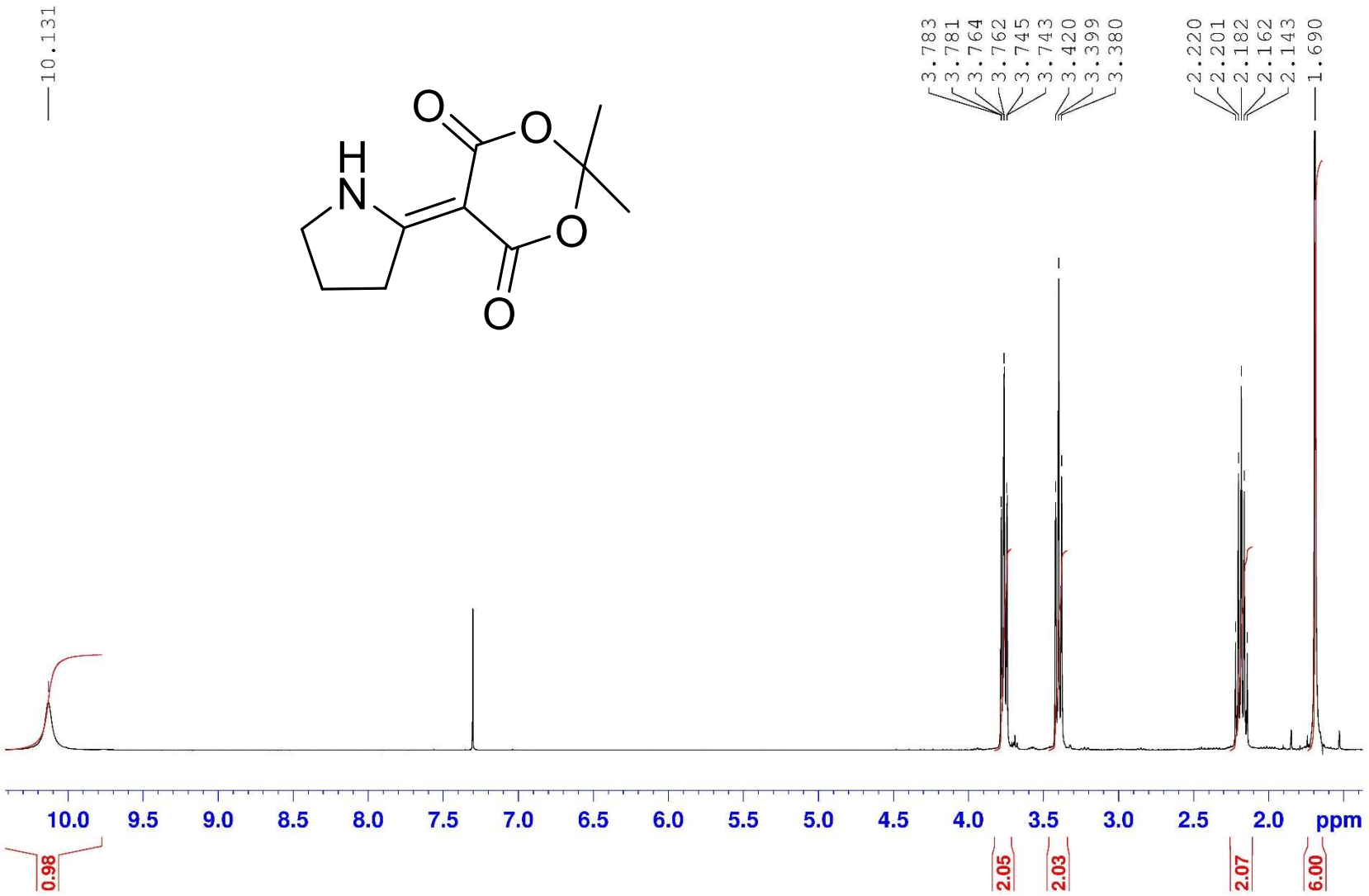

FIGURE S7: 400 MHz ^{1}H NMR spectrum of **3a** in $CDCl_3$.

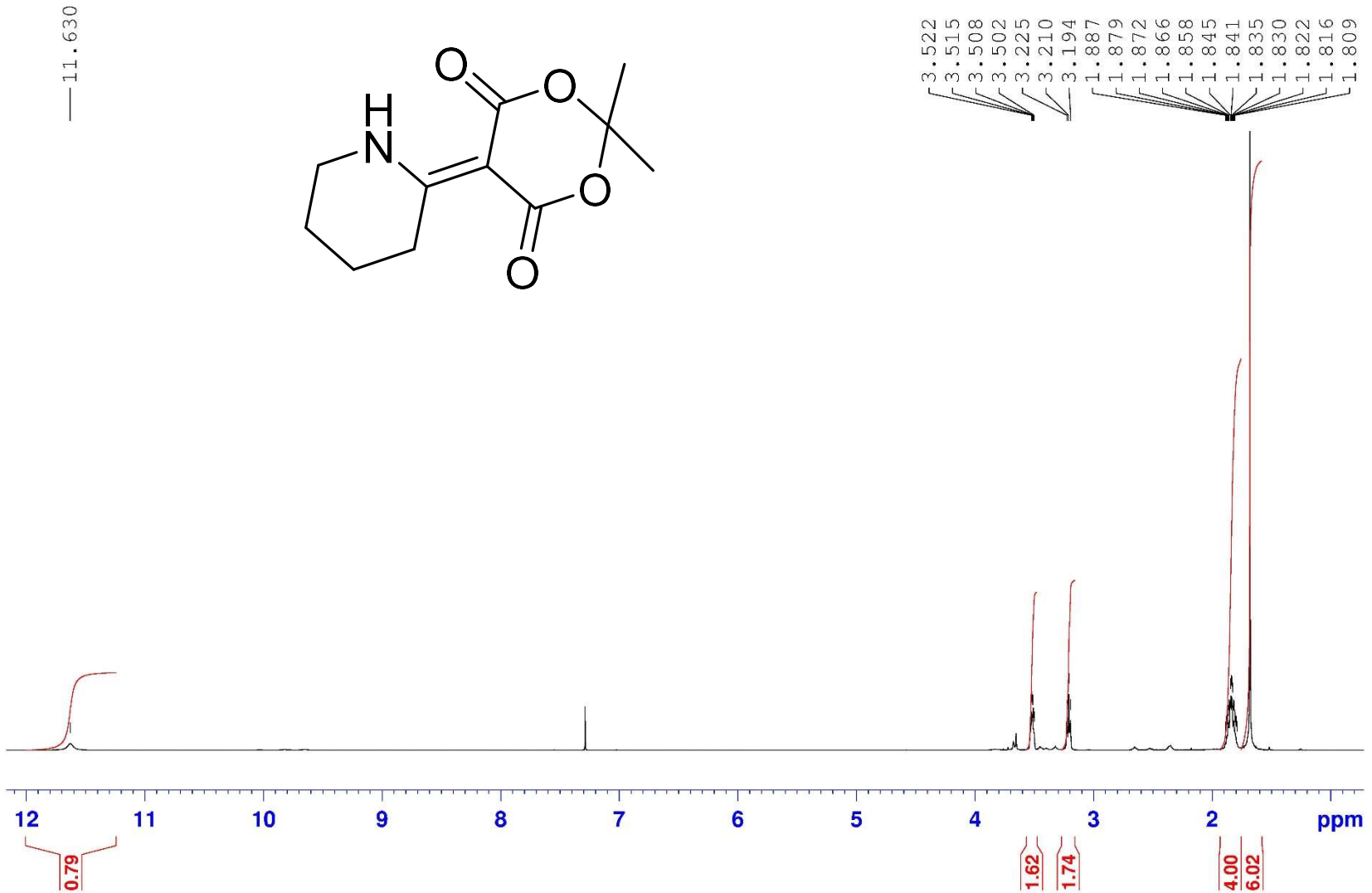

FIGURE S8: 400 MHz ^{1}H NMR spectrum of **3b** in $CDCl_3$.

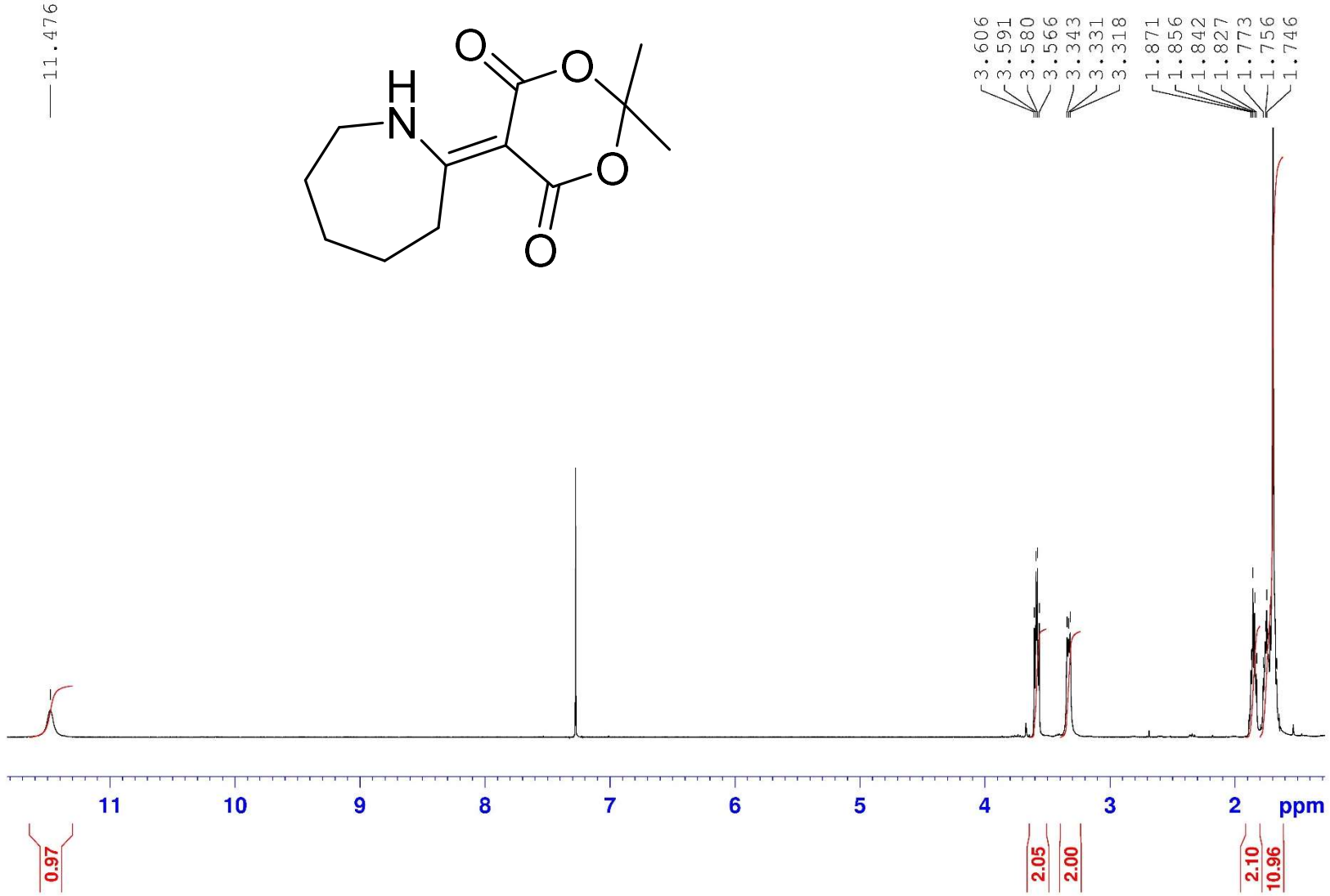

FIGURE S9: 400 MHz ^{1}H NMR spectrum of **3c** in $CDCl_3$.

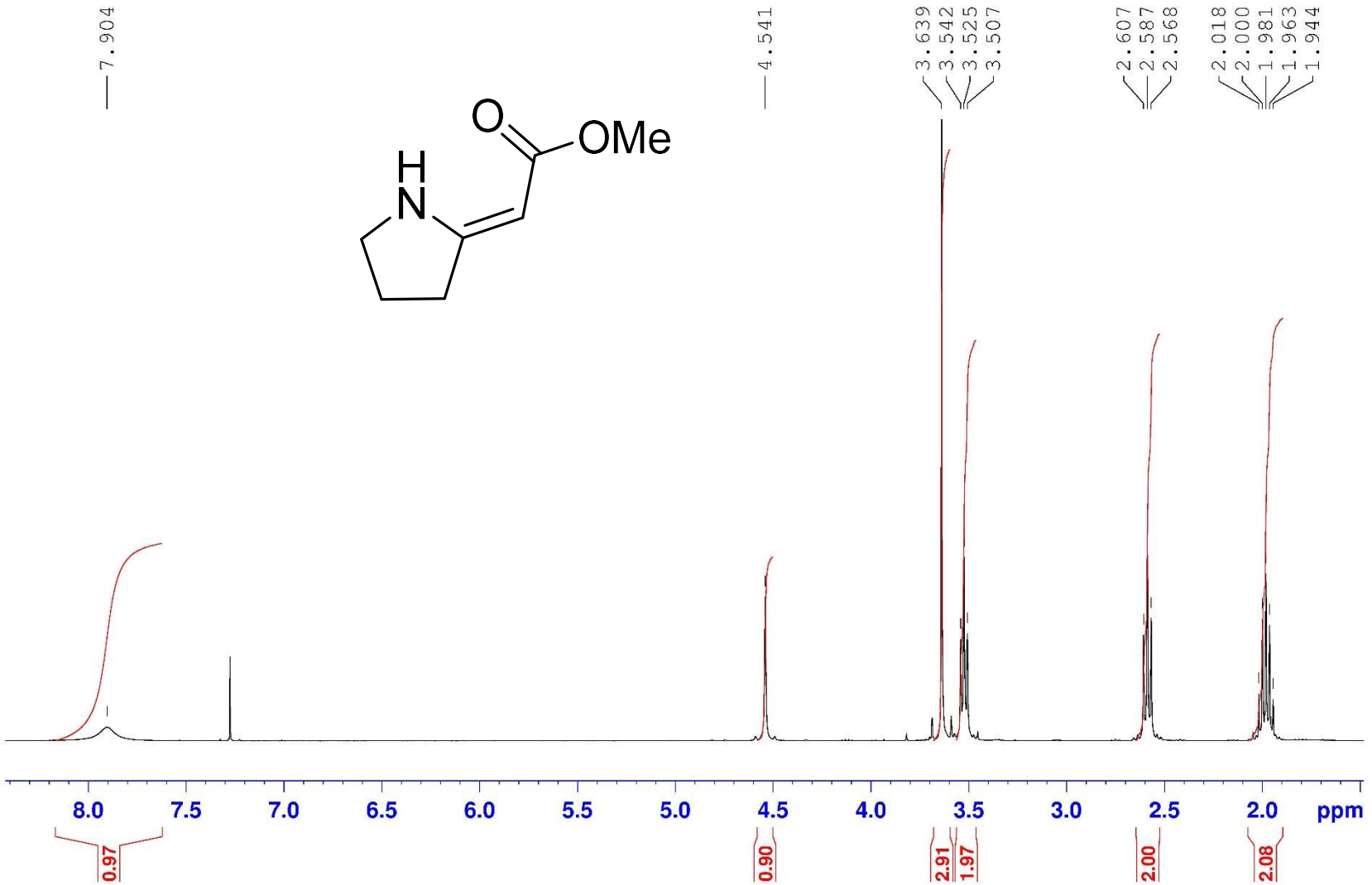

FIGURE S10: 400 MHz ^{1}H NMR spectrum of **4a** in $CDCl_3$.

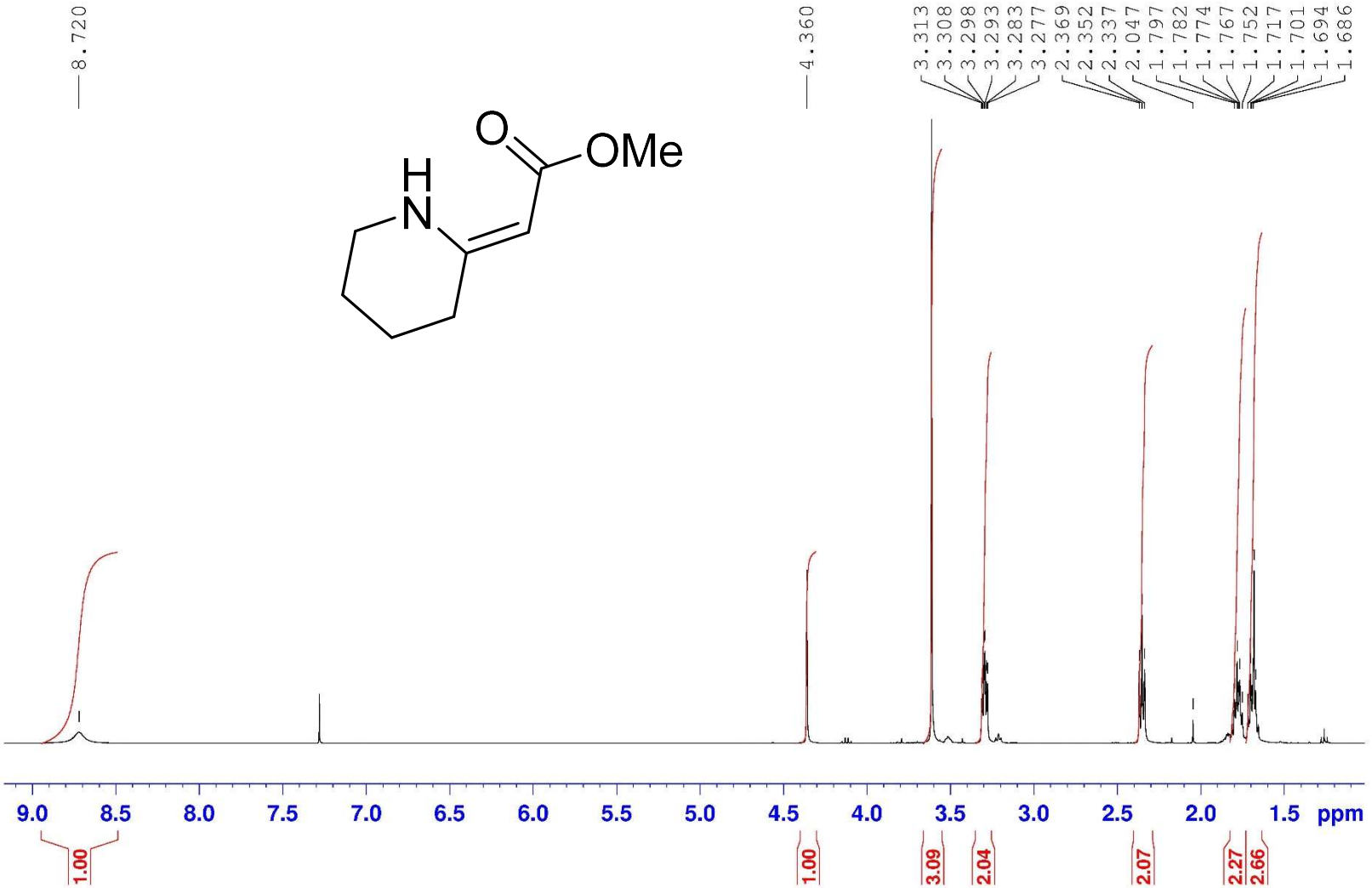

FIGURE S11: 400 MHz ^{1}H NMR spectrum of **4b** in $CDCl_3$.

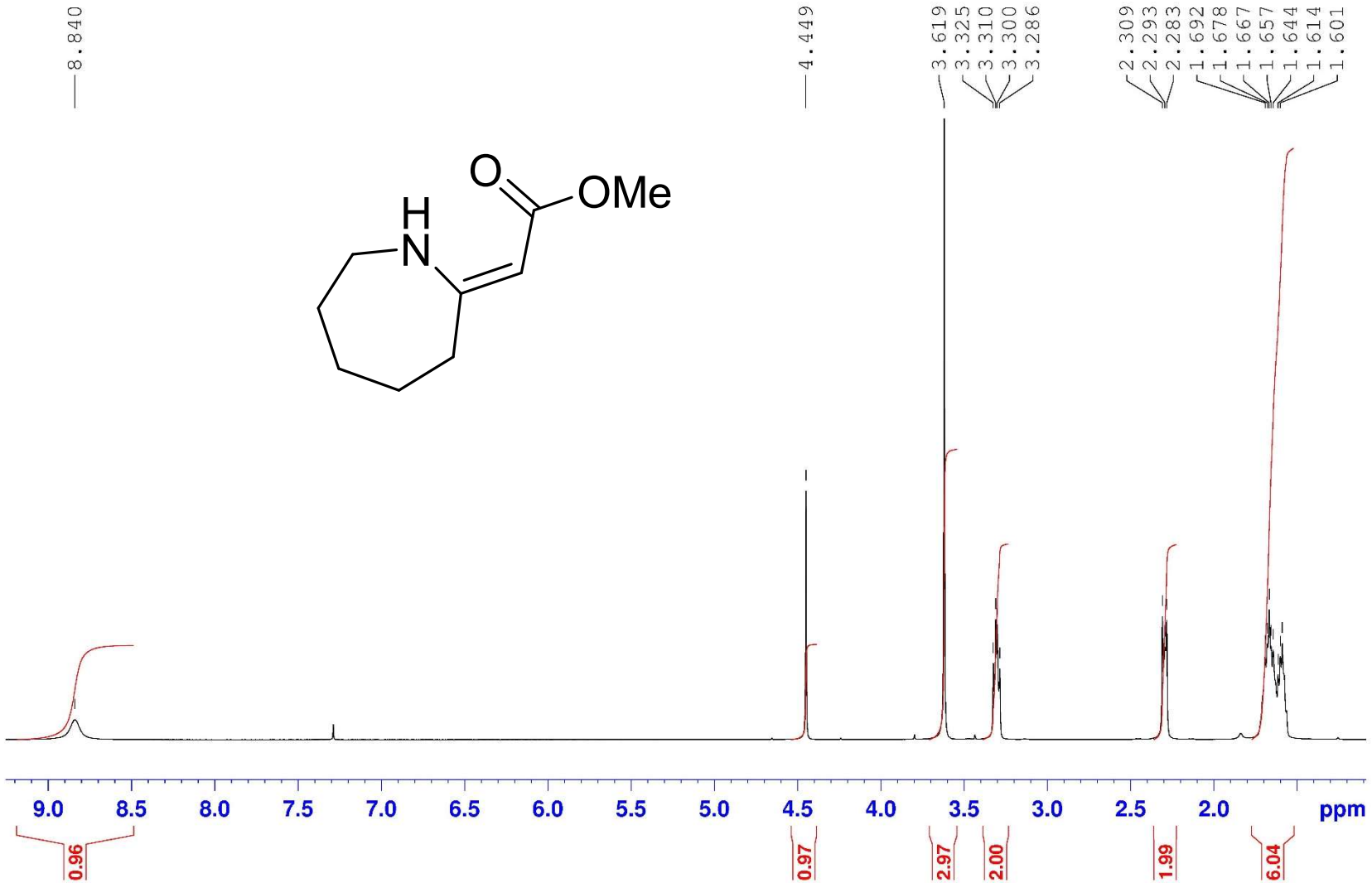

FIGURE S12: 400 MHz ^{1}H NMR spectrum of **4c** in $CDCl_3$.

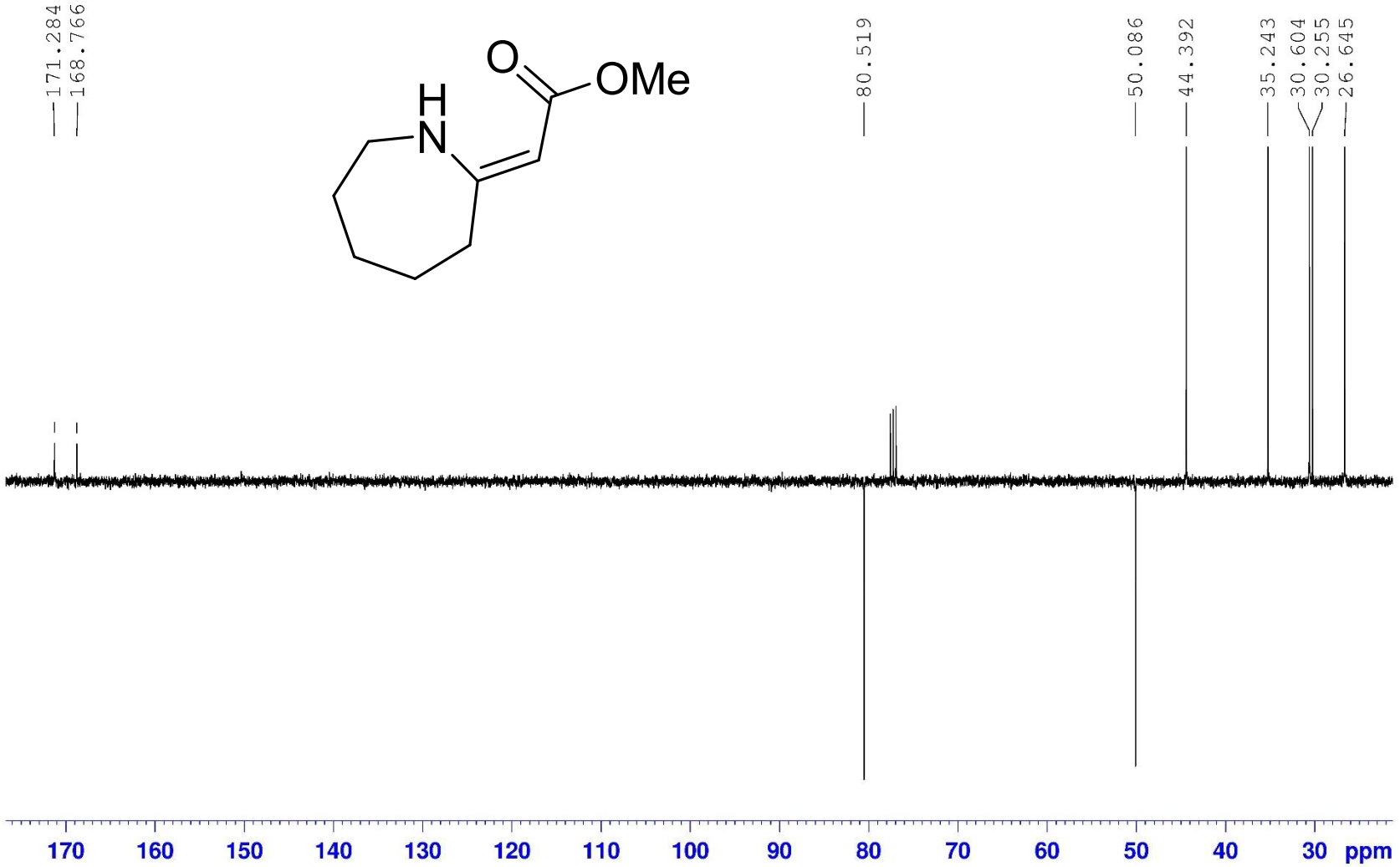

FIGURE S13: 100 MHz ^{13}C APT spectrum of **4c** in $CDCl_3$.

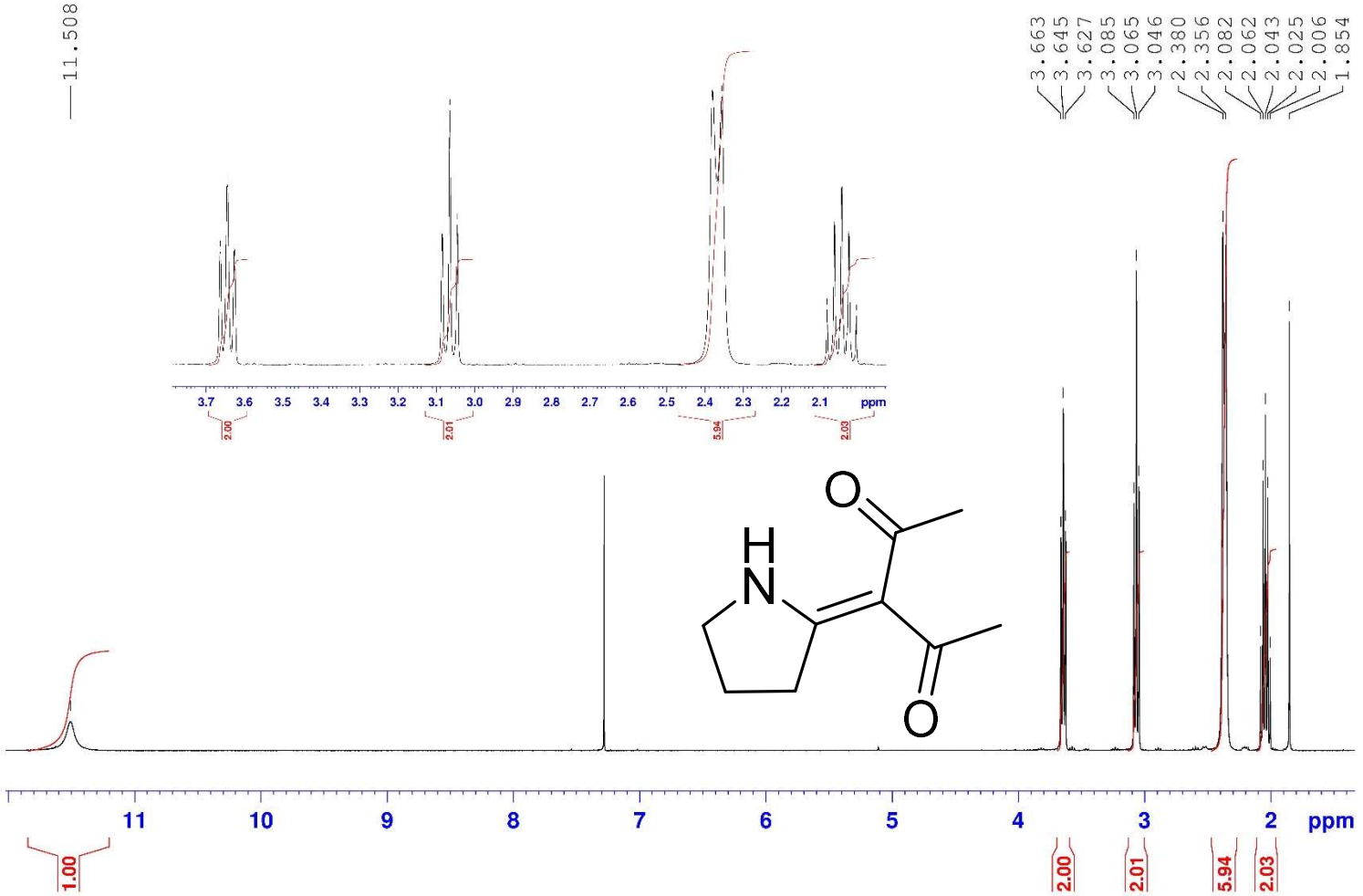

FIGURE S14: 400 MHz ^{1}H NMR spectrum of **5a** in $CDCl_3$.

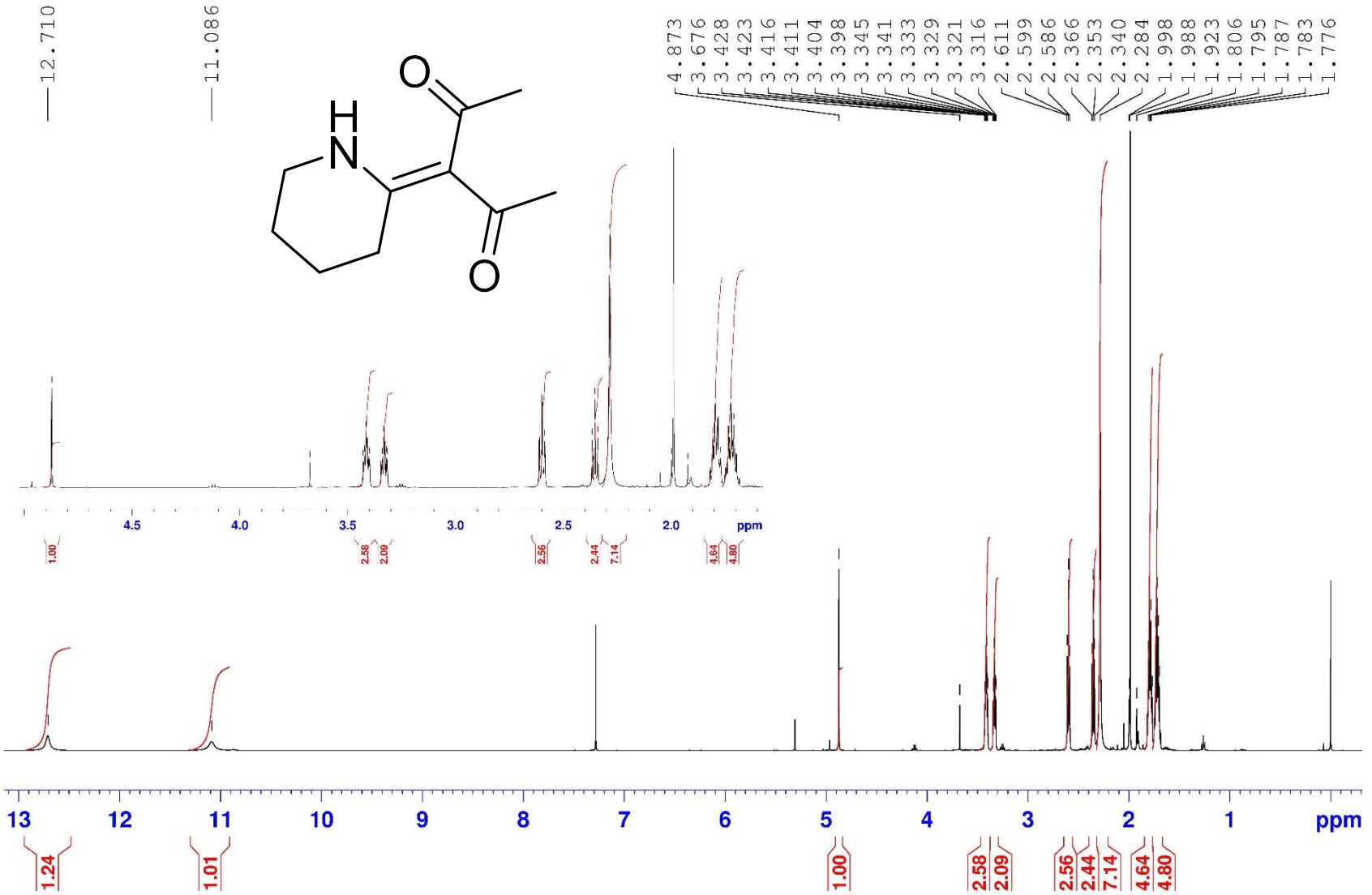

FIGURE S15: 500 MHz ^{1}H NMR spectrum of **5b** in $CDCl_3$.

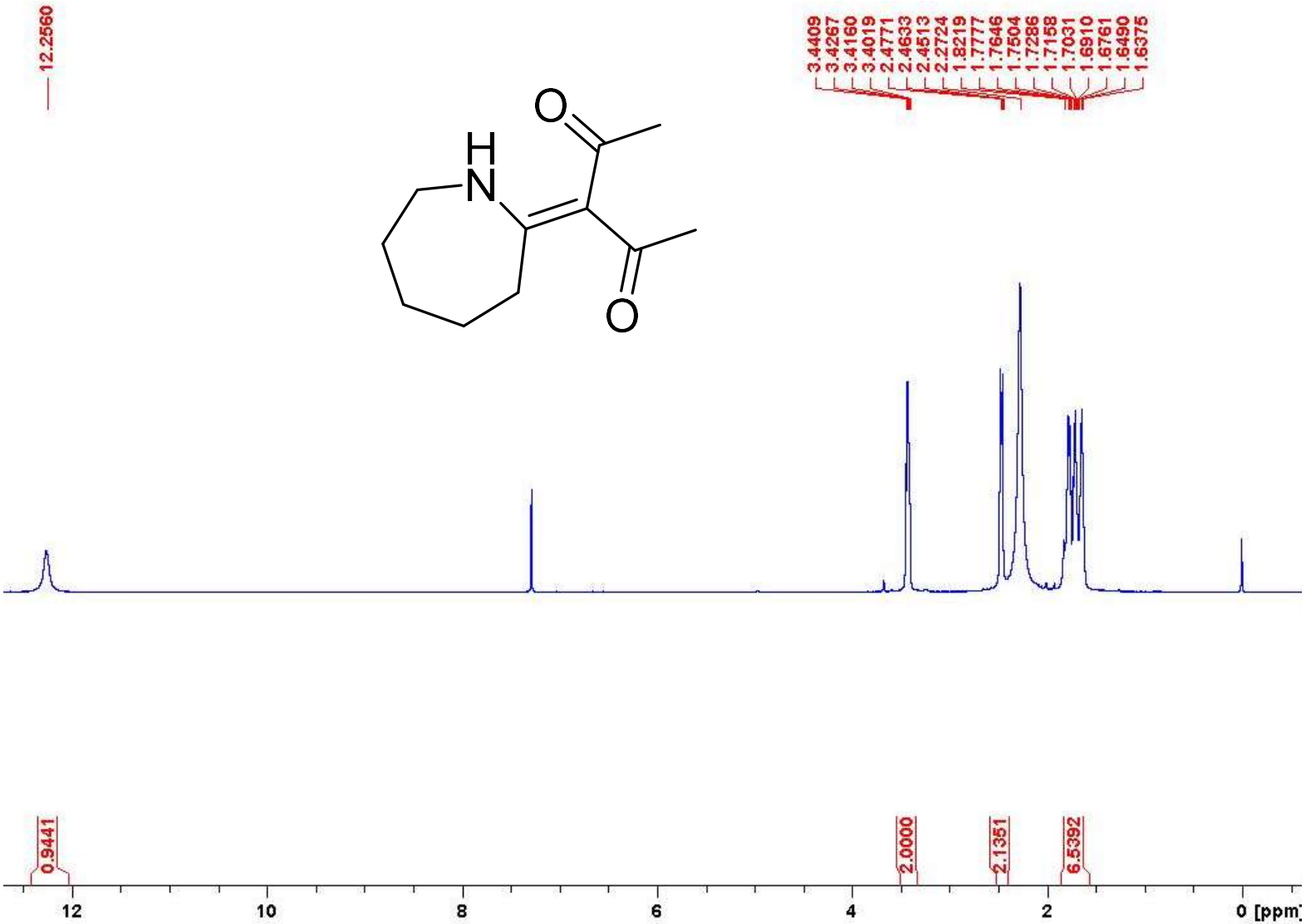

FIGURE S16: 400 MHz ^{1}H NMR spectrum of **5c** in $CDCl_3$.

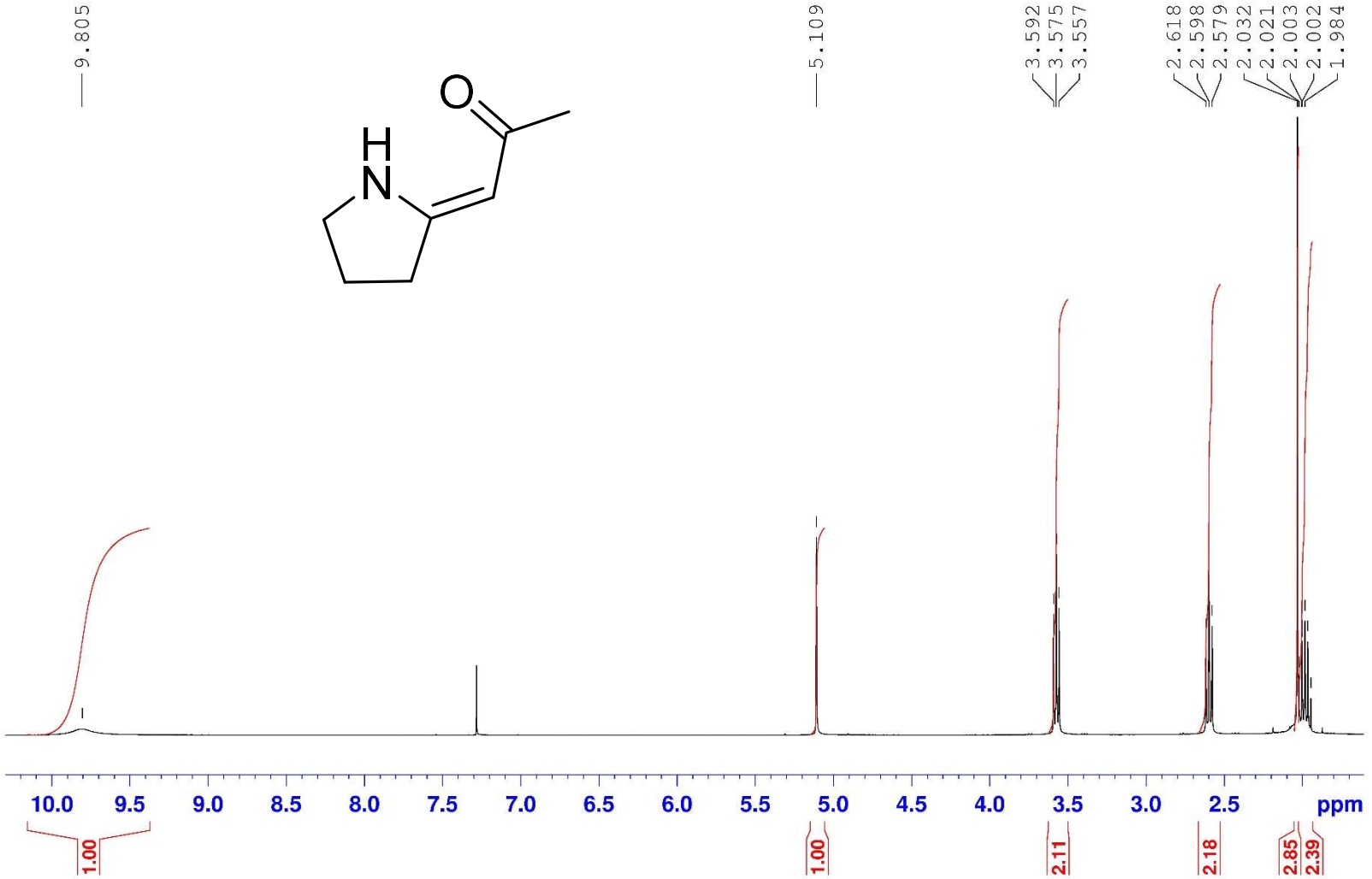

FIGURE S17: 400 MHz ^{1}H NMR spectrum of **6a** in $CDCl_3$.

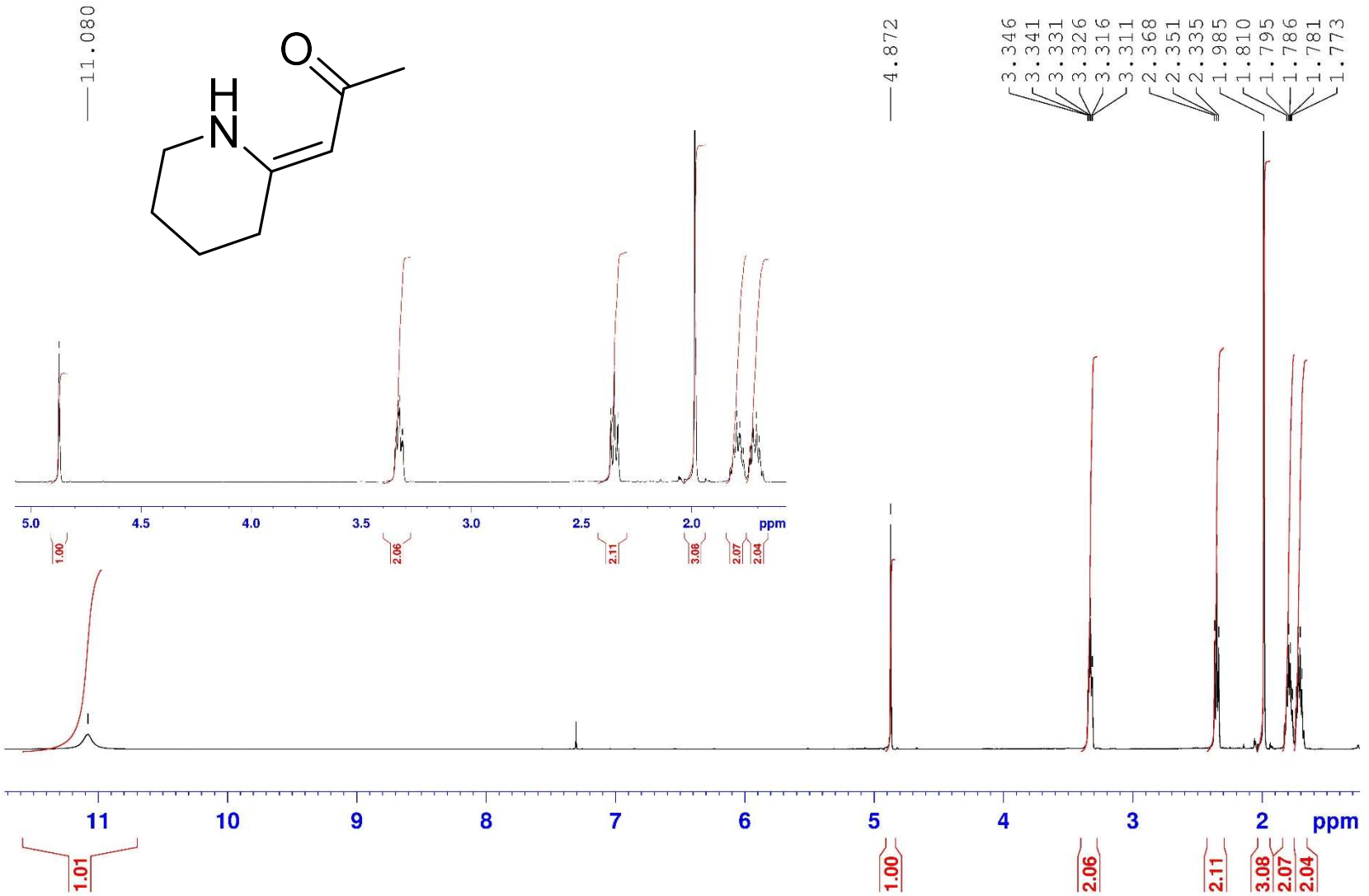

FIGURE S18: 400 MHz ^{1}H NMR spectrum of **6b** in $CDCl_3$.

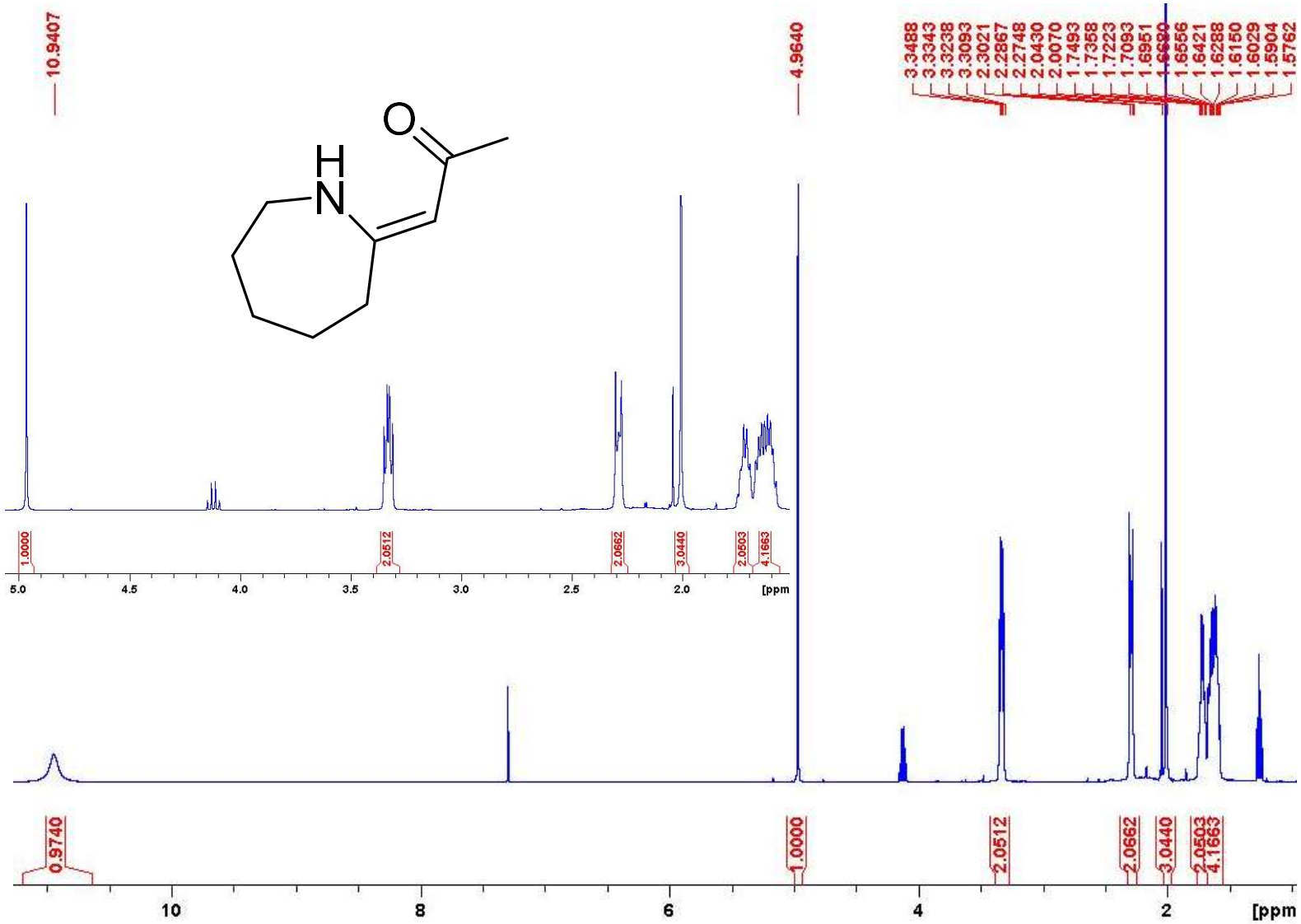

FIGURE S19: 400 MHZ ^{1}H NMR spectrum of **6c** in $CDCl_3$.

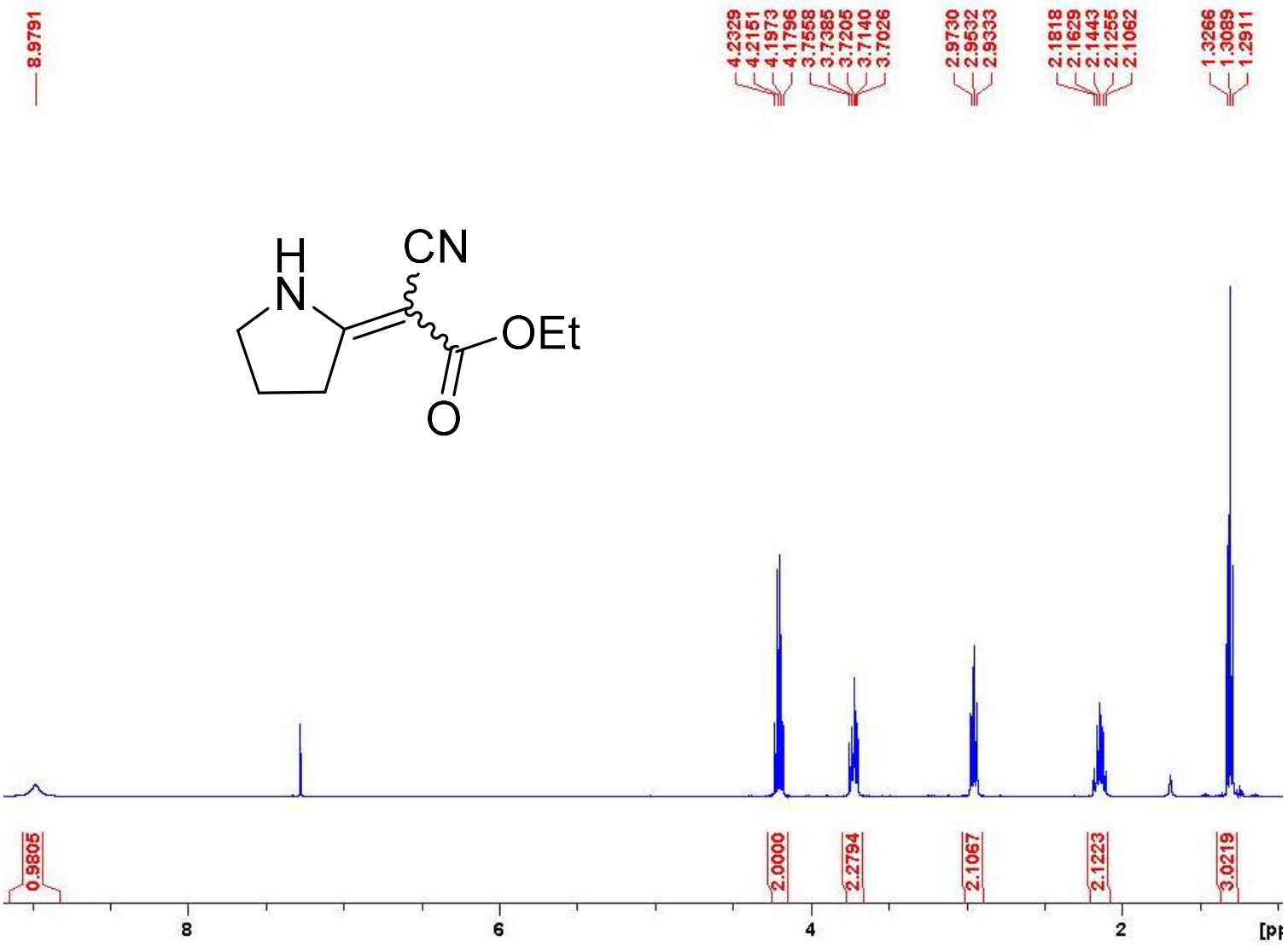

FIGURE S20: 400 MHz ^{1}H NMR spectrum of **7a** in $CDCl_3$.

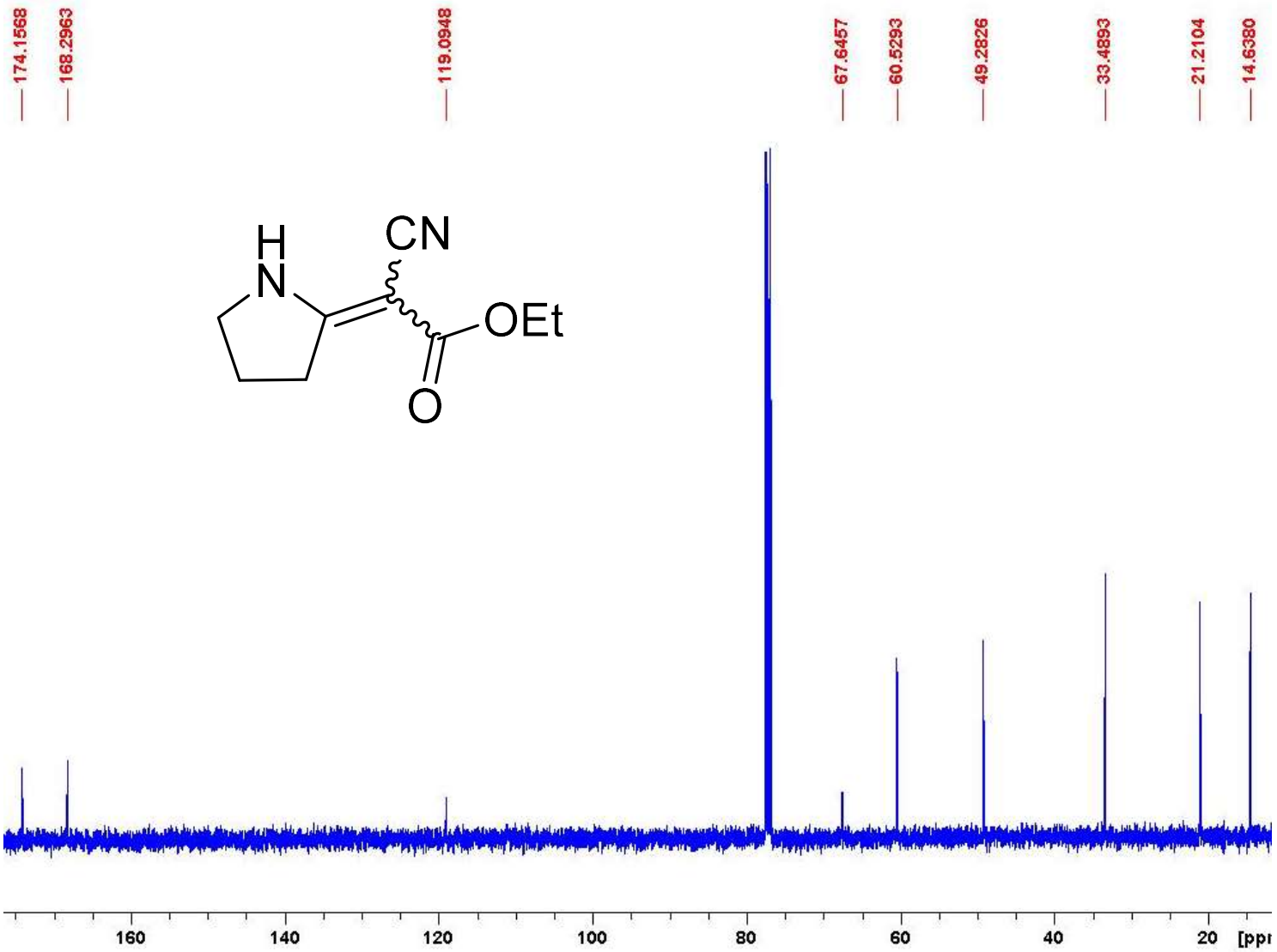

FIGURE S21: 100 MHz ^{13}C NMR spectrum of **7a** in $CDCl_3$.

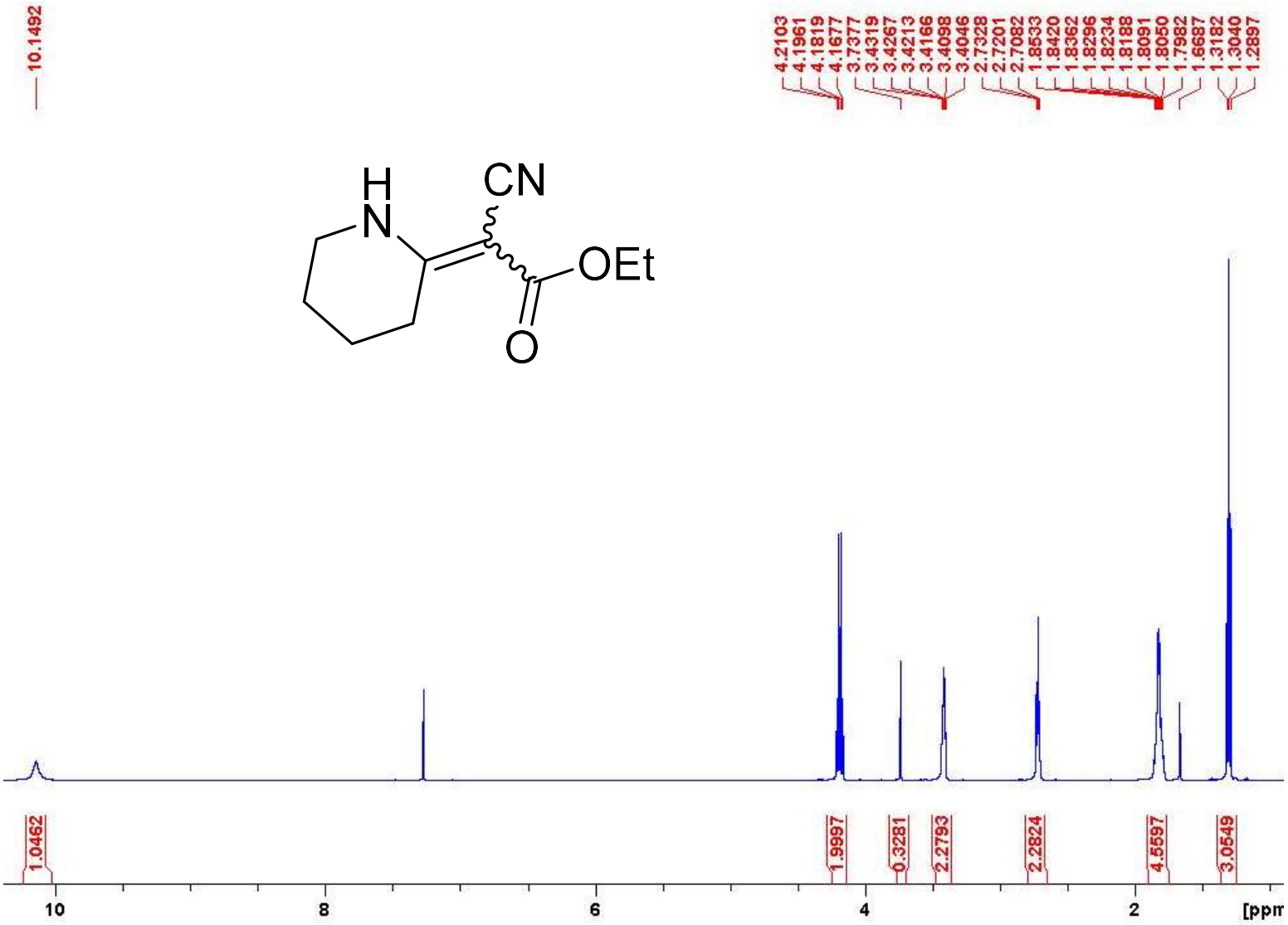

FIGURE S22: 500 MHz ^{1}H NMR spectrum of **7b** in $CDCl_3$.

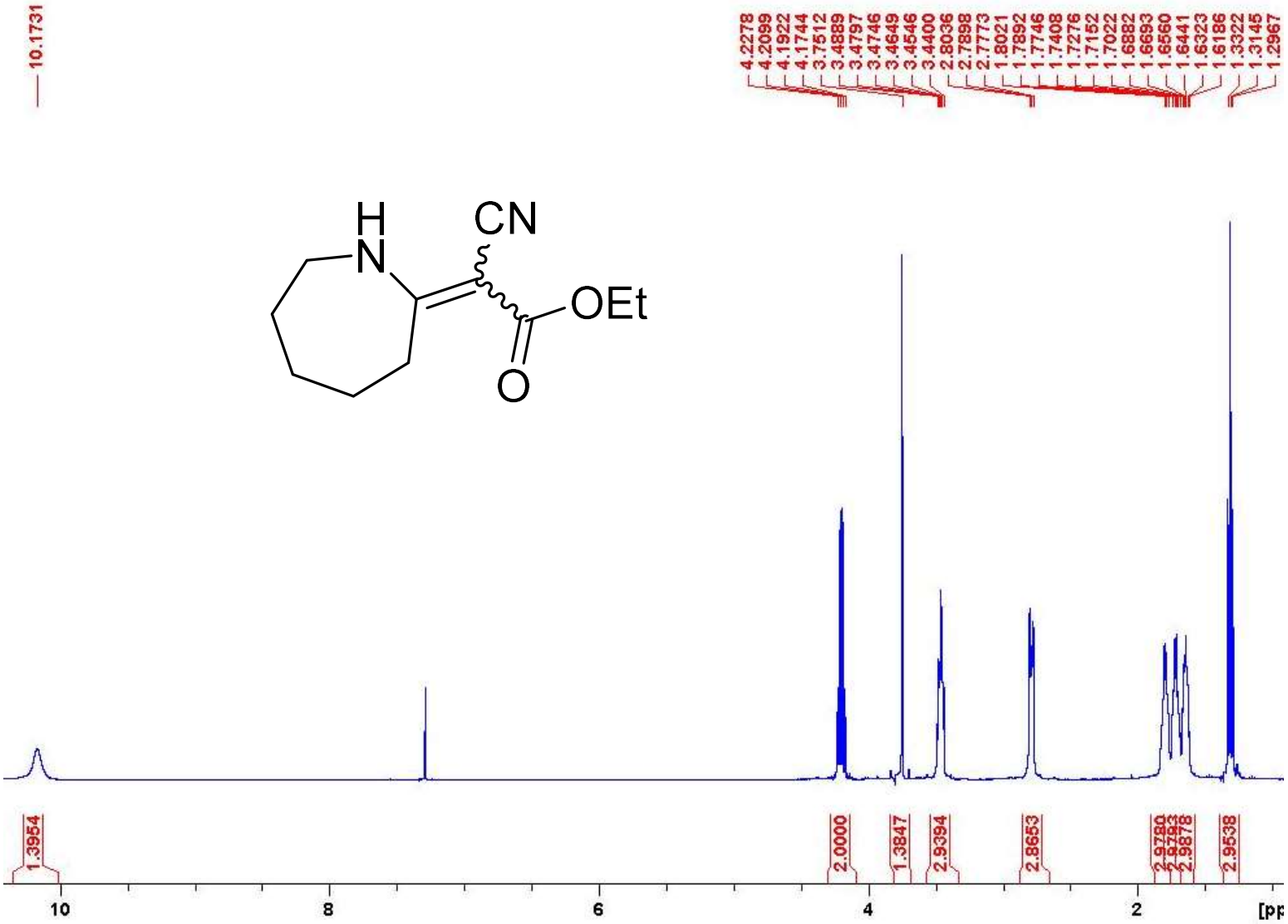

FIGURE S23: 400 MHz ^{1}H NMR spectrum of **7c** in $CDCl_3$.

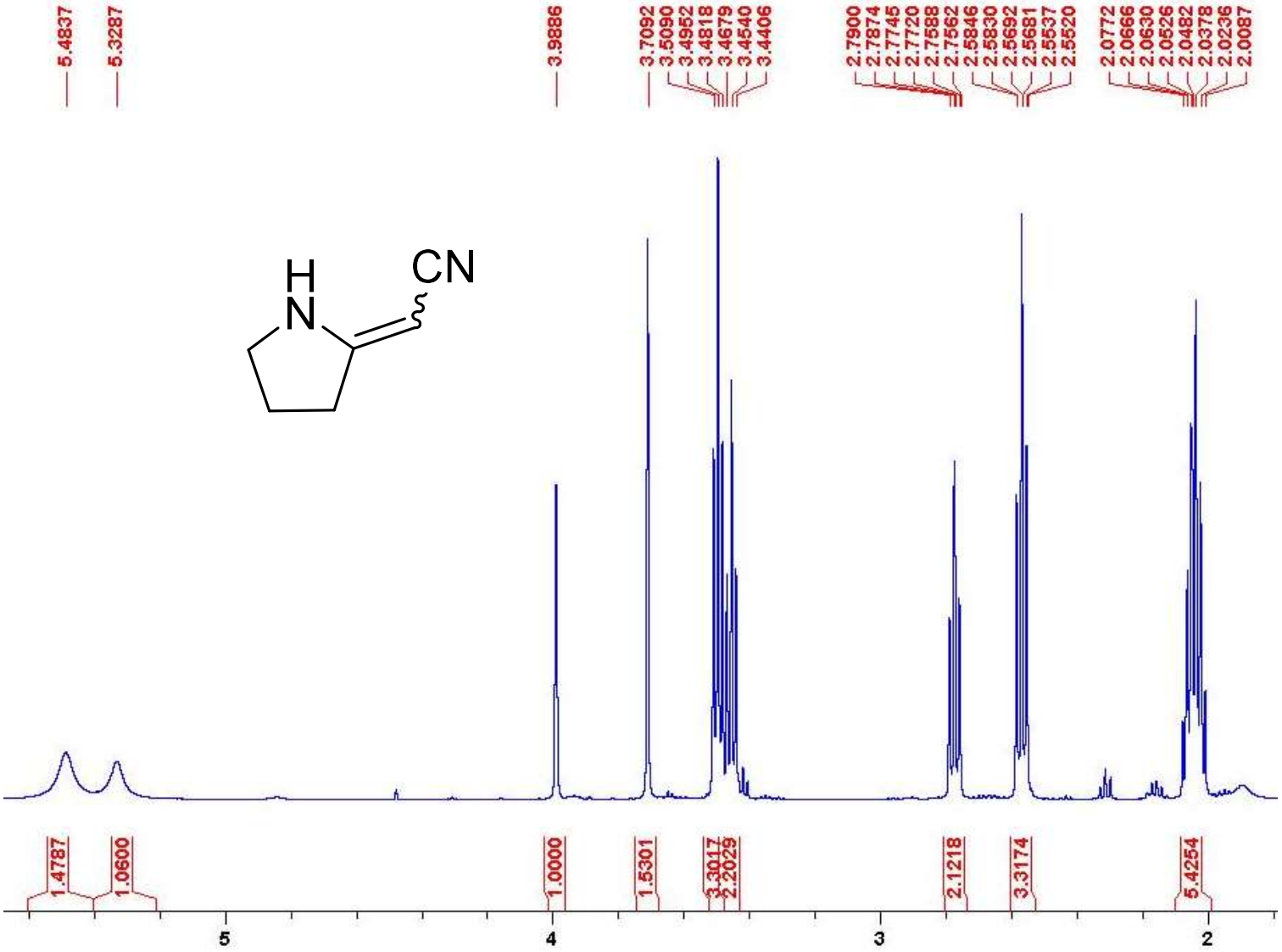

FIGURE S24: 500 MHz ^{1}H NMR spectrum of **8a** in $CDCl_3$.

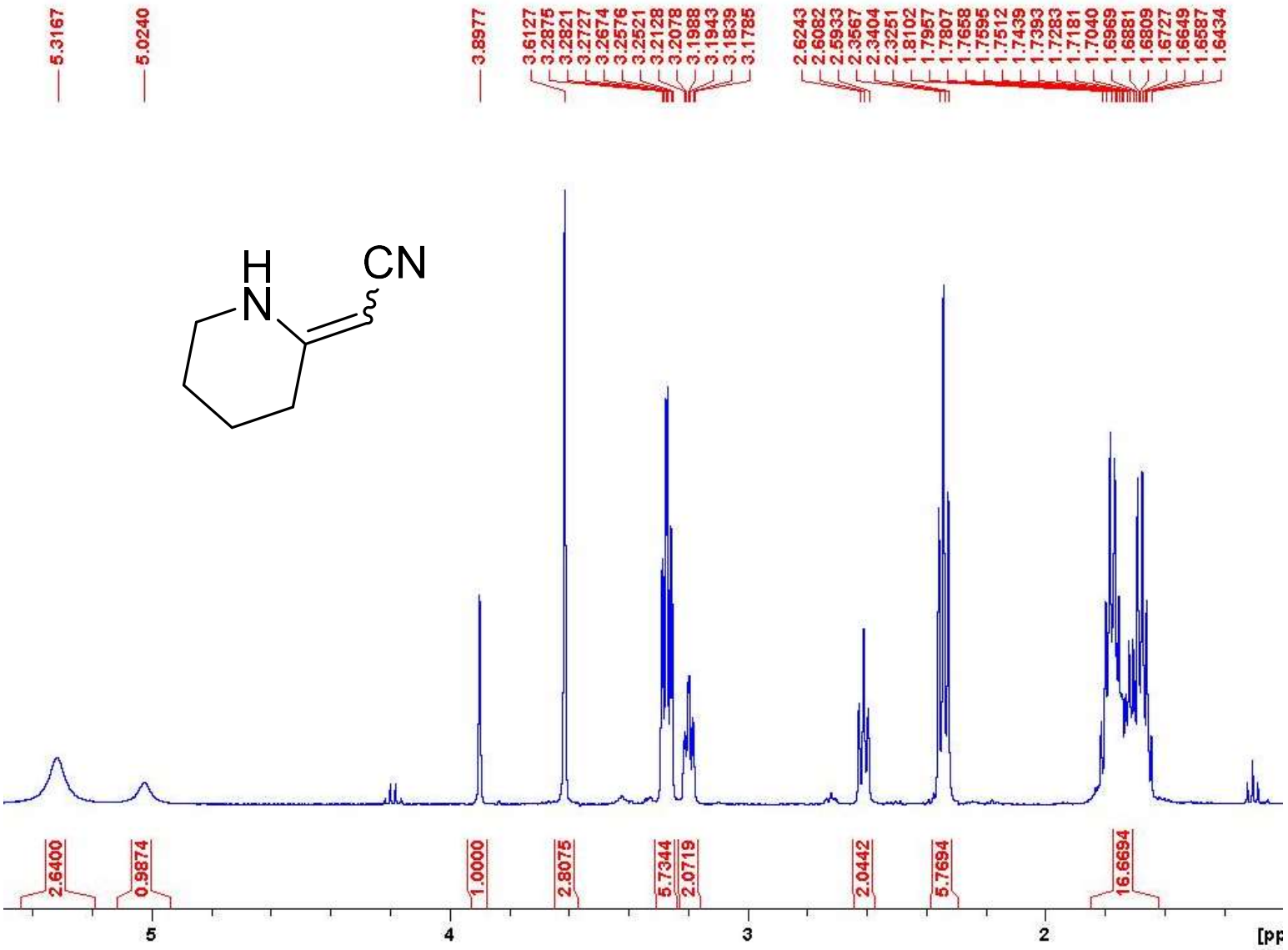

FIGURE S25: 400 MHz ^{1}H NMR spectrum of **8b** in $CDCl_3$.

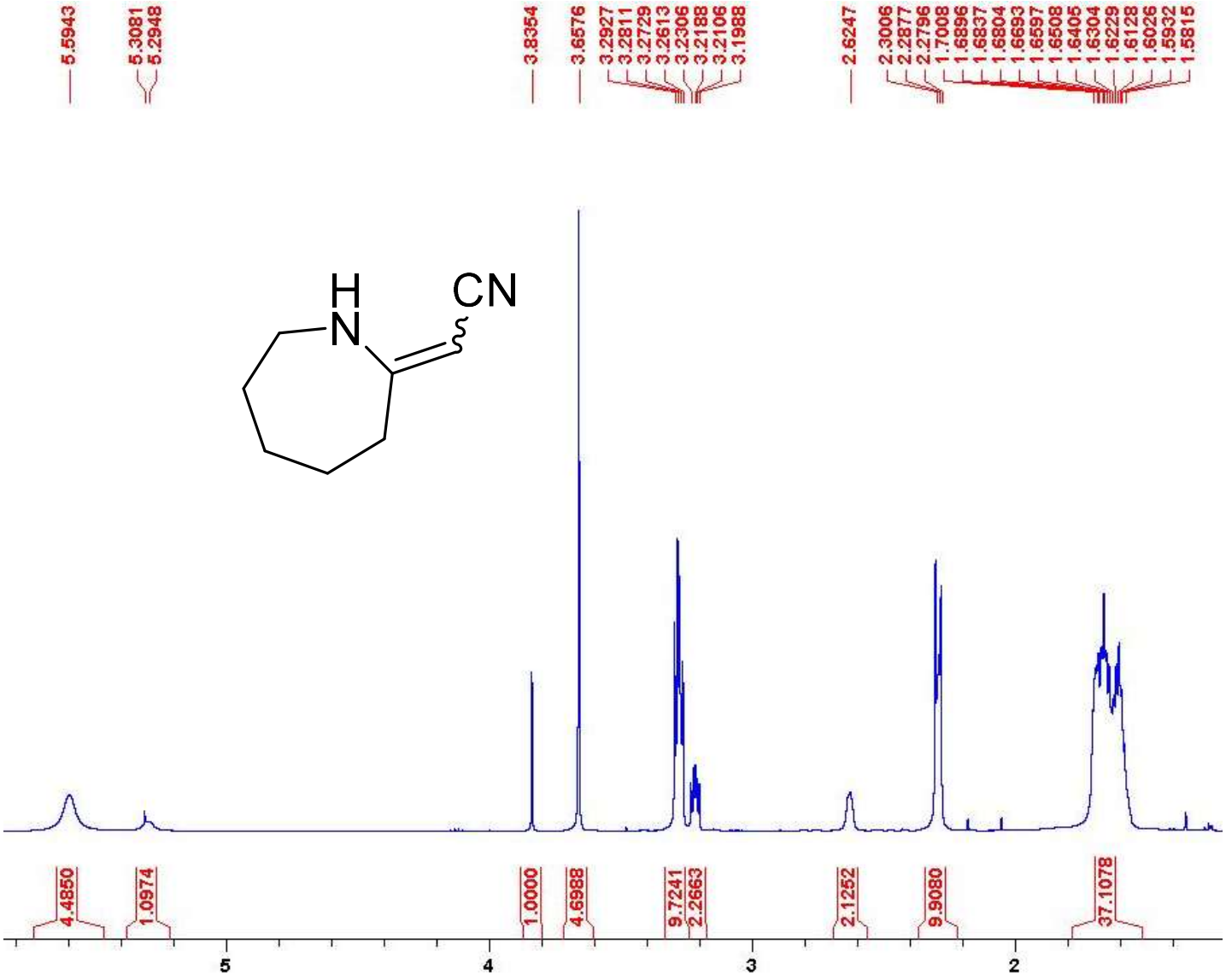

FIGURE S26: 500 MHz ^{1}H NMR spectrum of **8c** in $CDCl_3$.

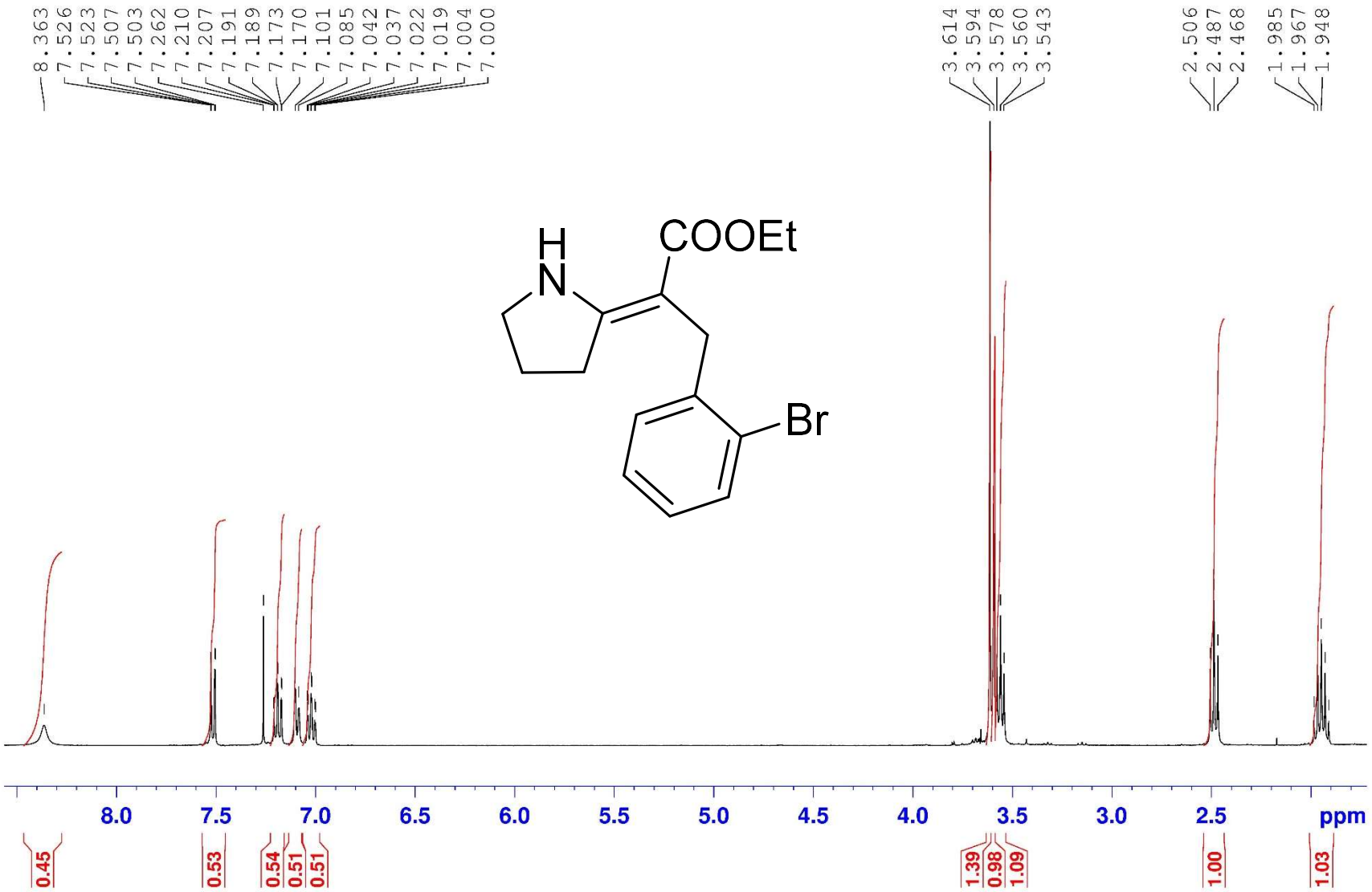

FIGURE S27: 400 MHz ^{1}H NMR spectrum of **9a** in $CDCl_3$.

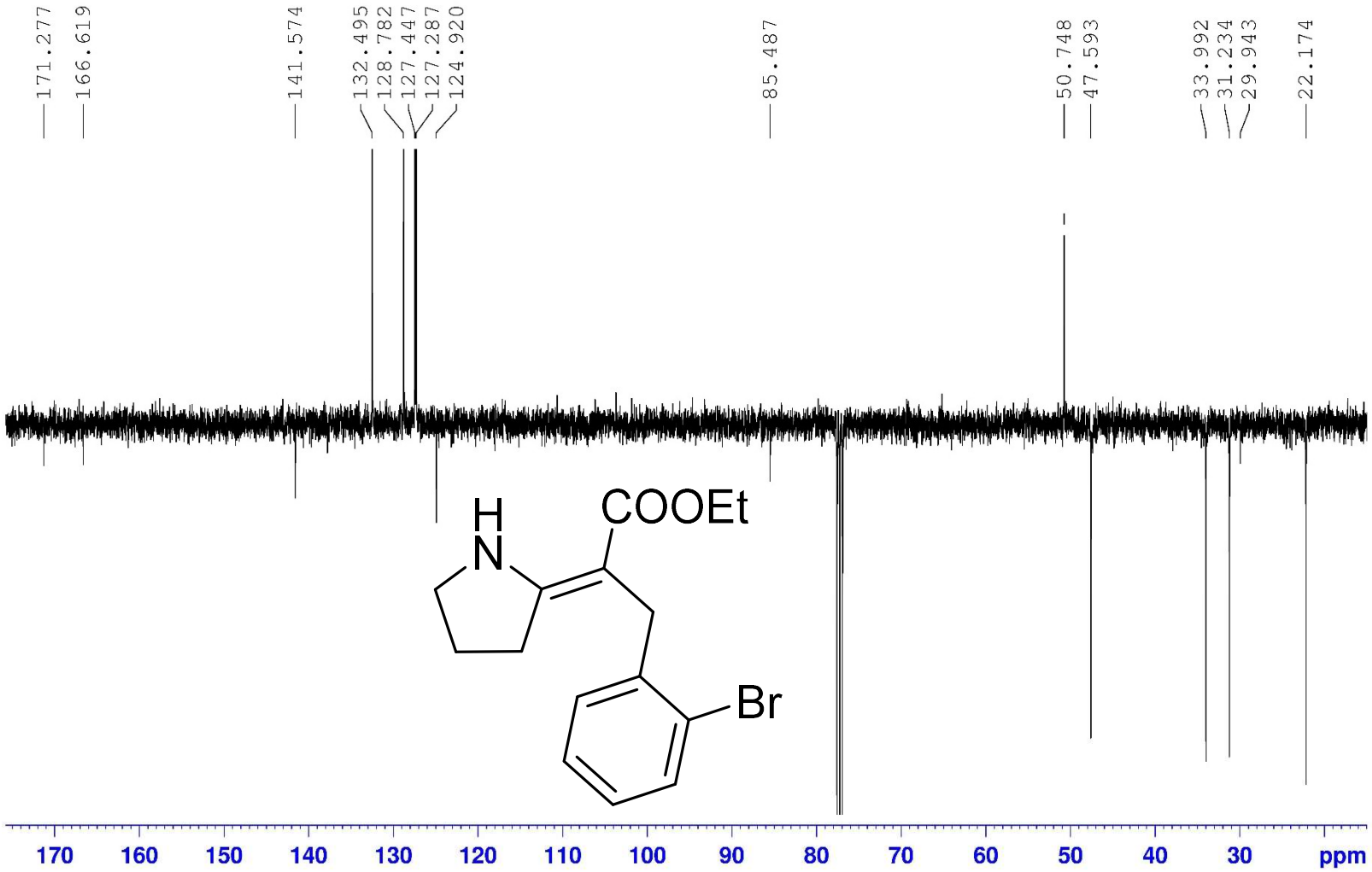

FIGURE S28: 100 MHz ^{13}C NMR (APT) spectrum of **9a** in $CDCl_3$.

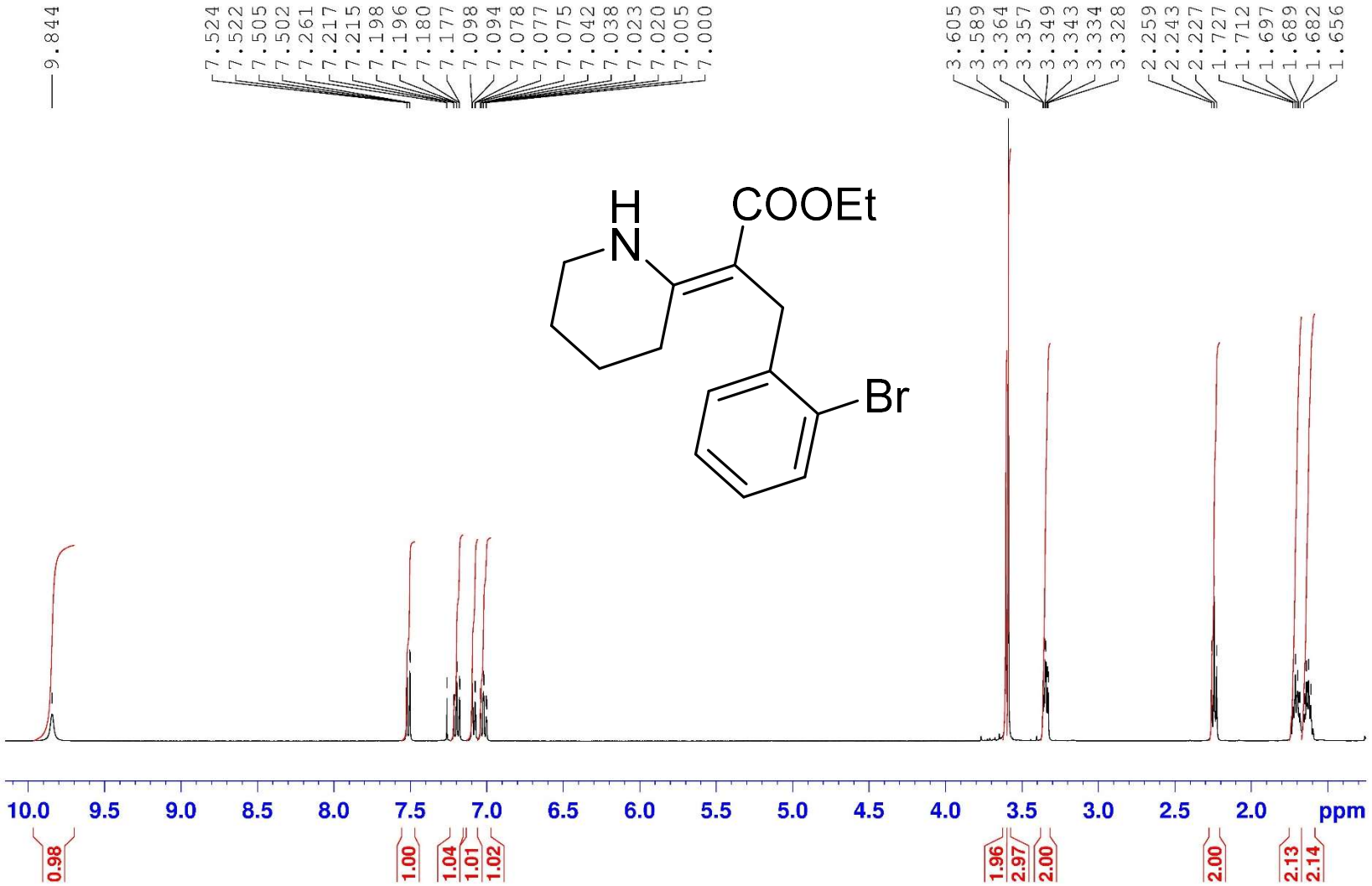

FIGURE S29: 400 MHz ^{1}H NMR spectrum of **9b** in $CDCl_3$.

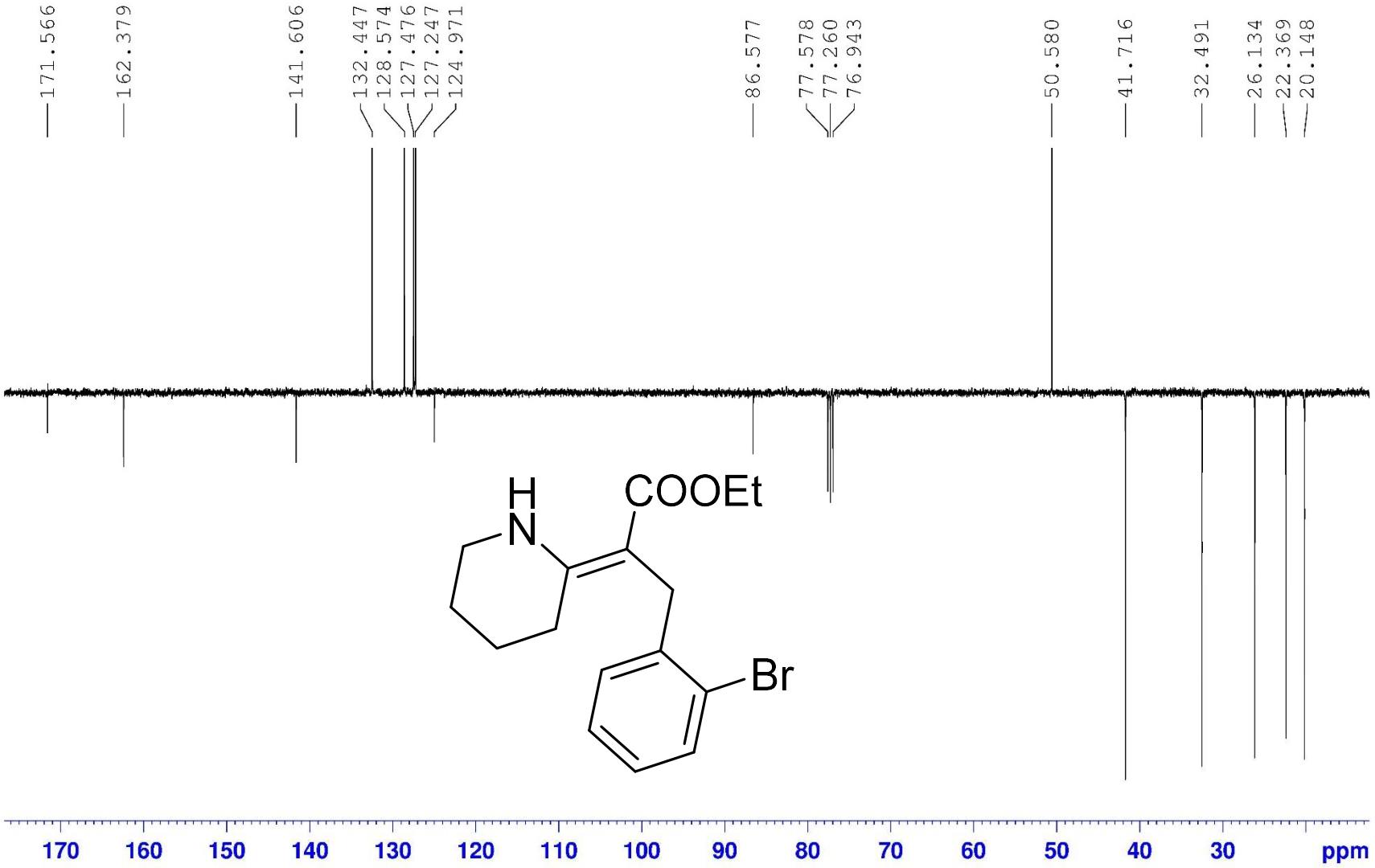

FIGURE S30: 100 MHz ^{13}C NMR (APT) spectrum of **9b** in $CDCl_3$.

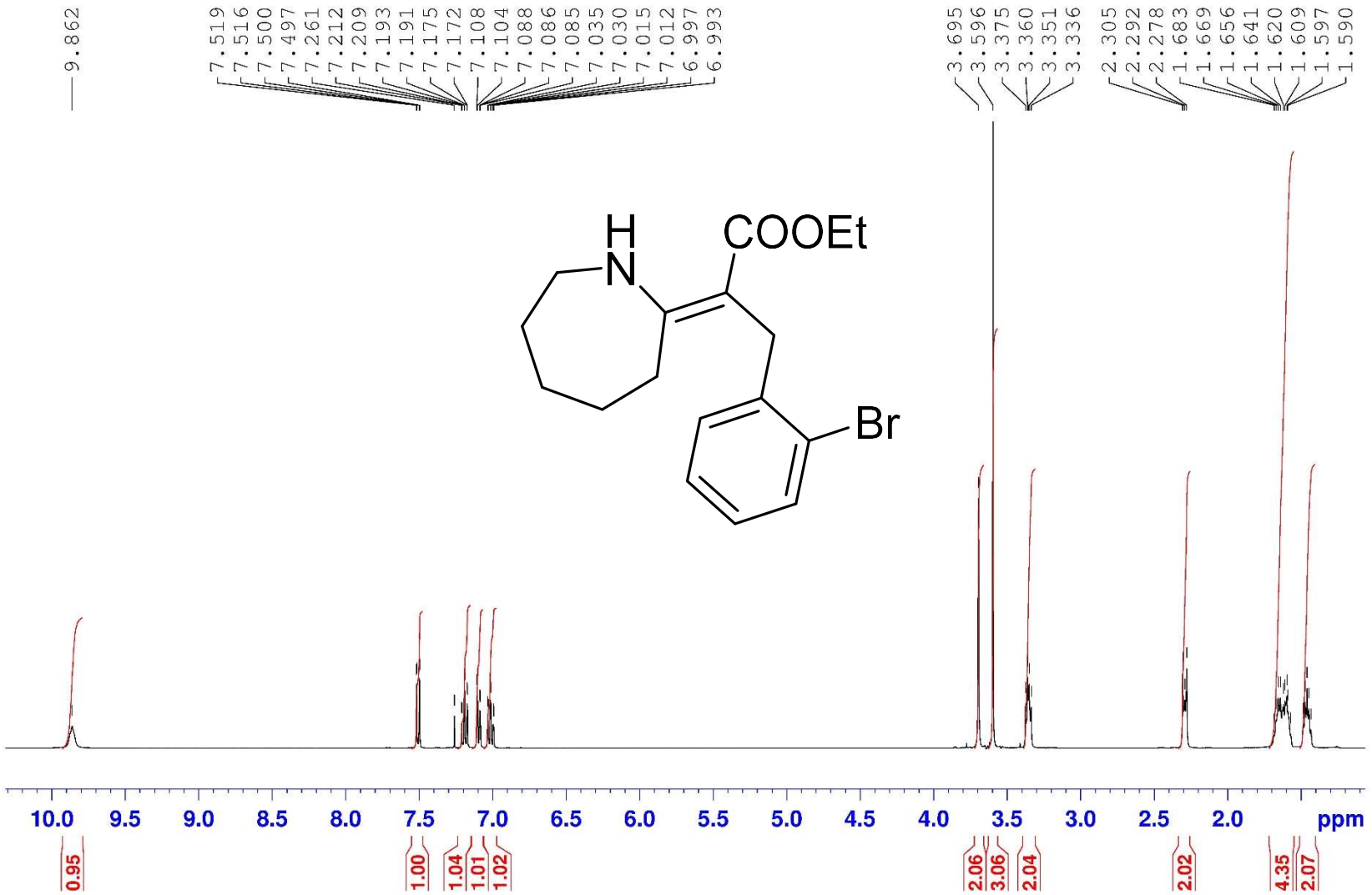

FIGURE S31: 400 MHz ^{1}H NMR spectrum of **9c** in $CDCl_3$.

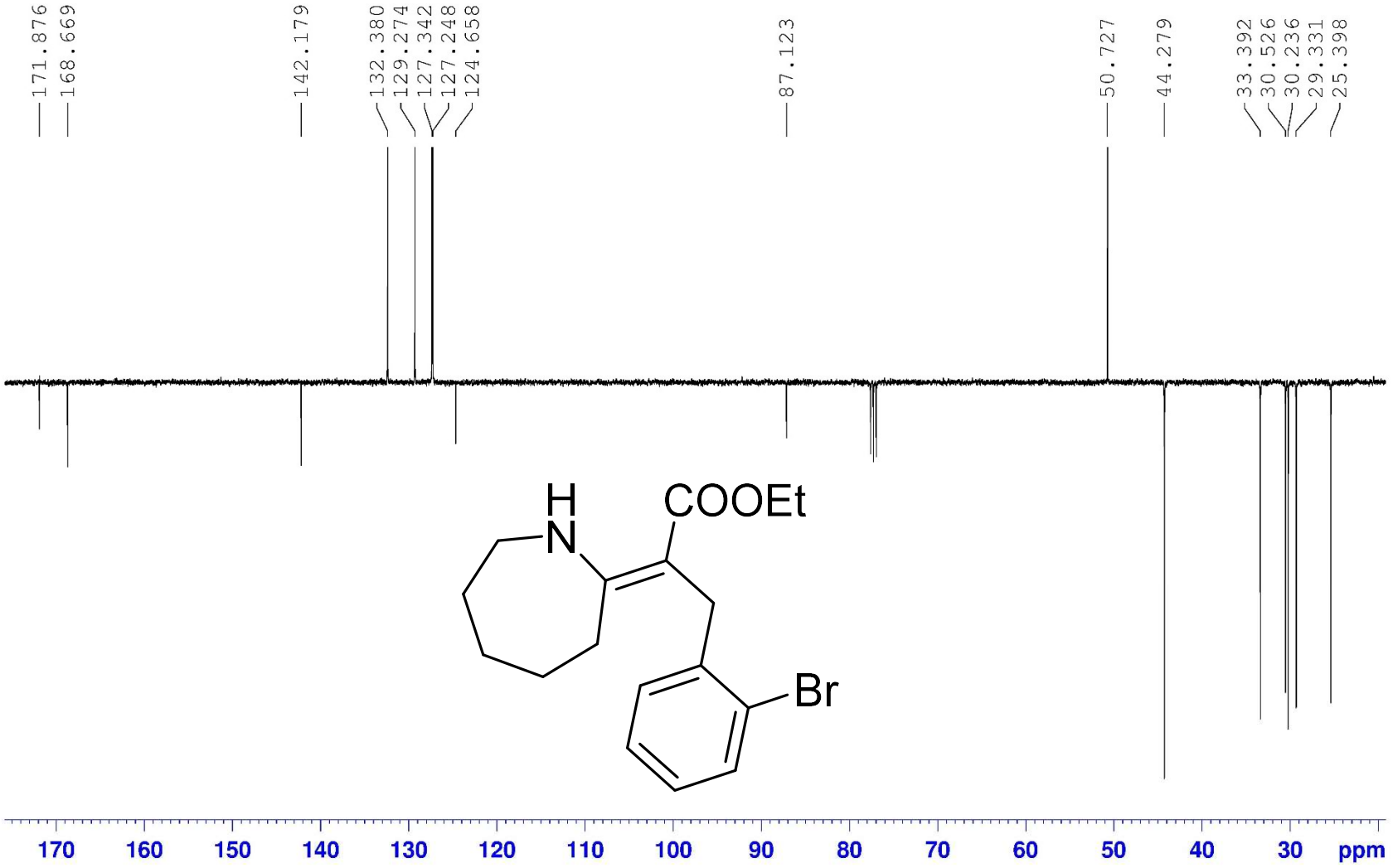

FIGURE S32: 100 MHz ^{13}C NMR (APT) spectrum of **9c** in $CDCl_3$.

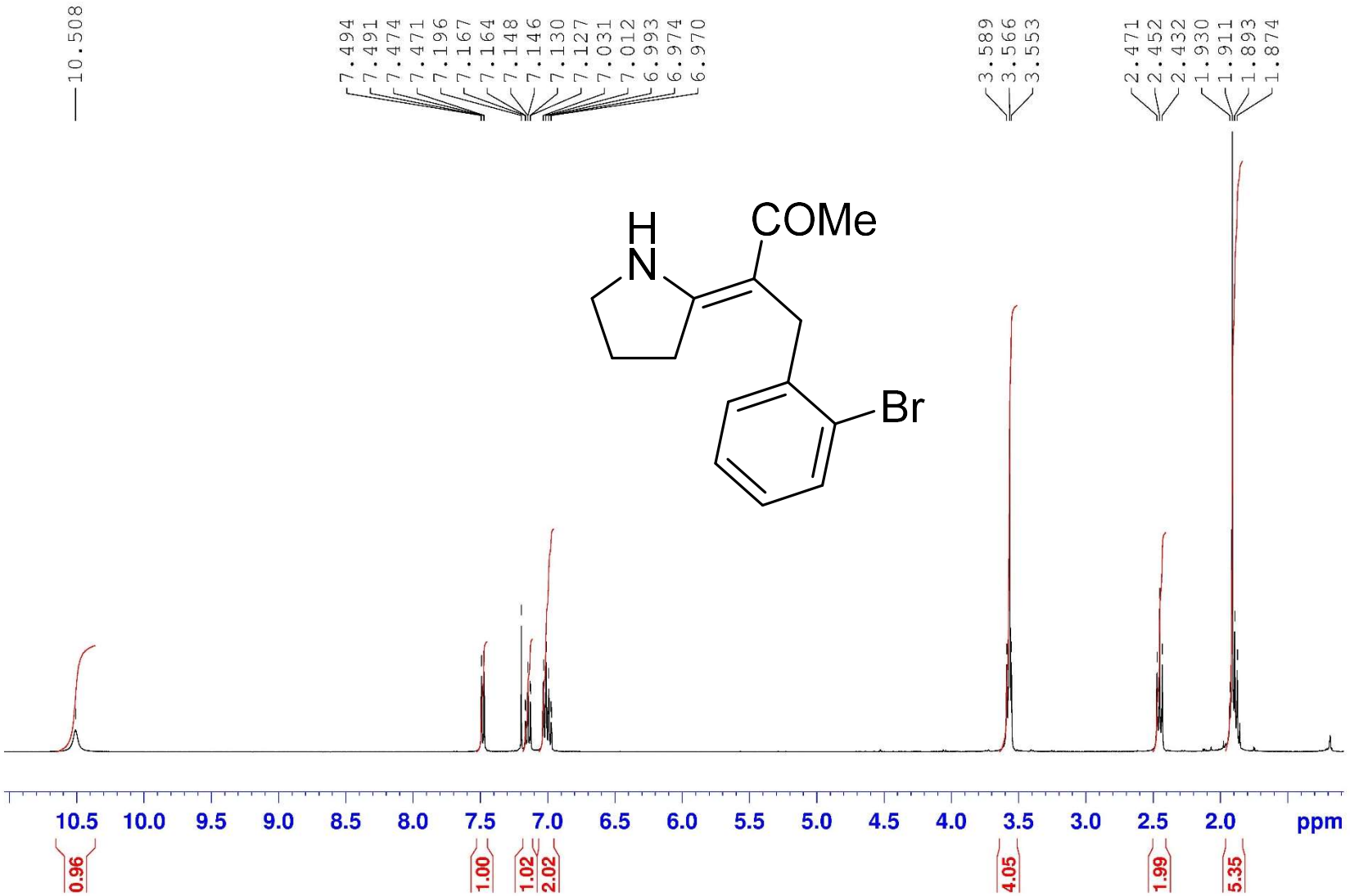

FIGURE S33: 400 MHz ^{1}H NMR spectrum of **9d** in $CDCl_3$.

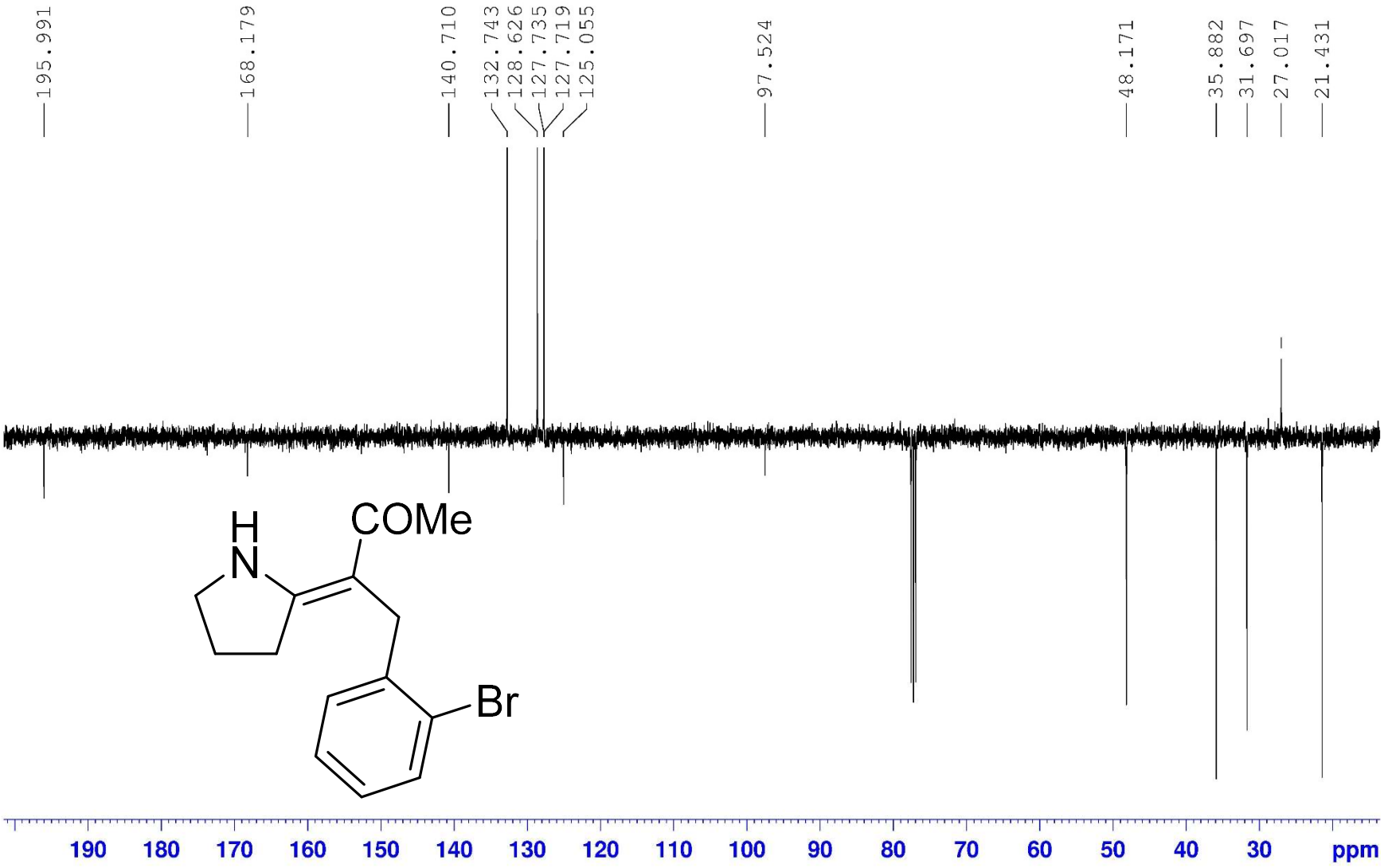

FIGURE S34: 100 MHz ^{13}C NMR (APT) spectrum of **9d** in $CDCl_3$.

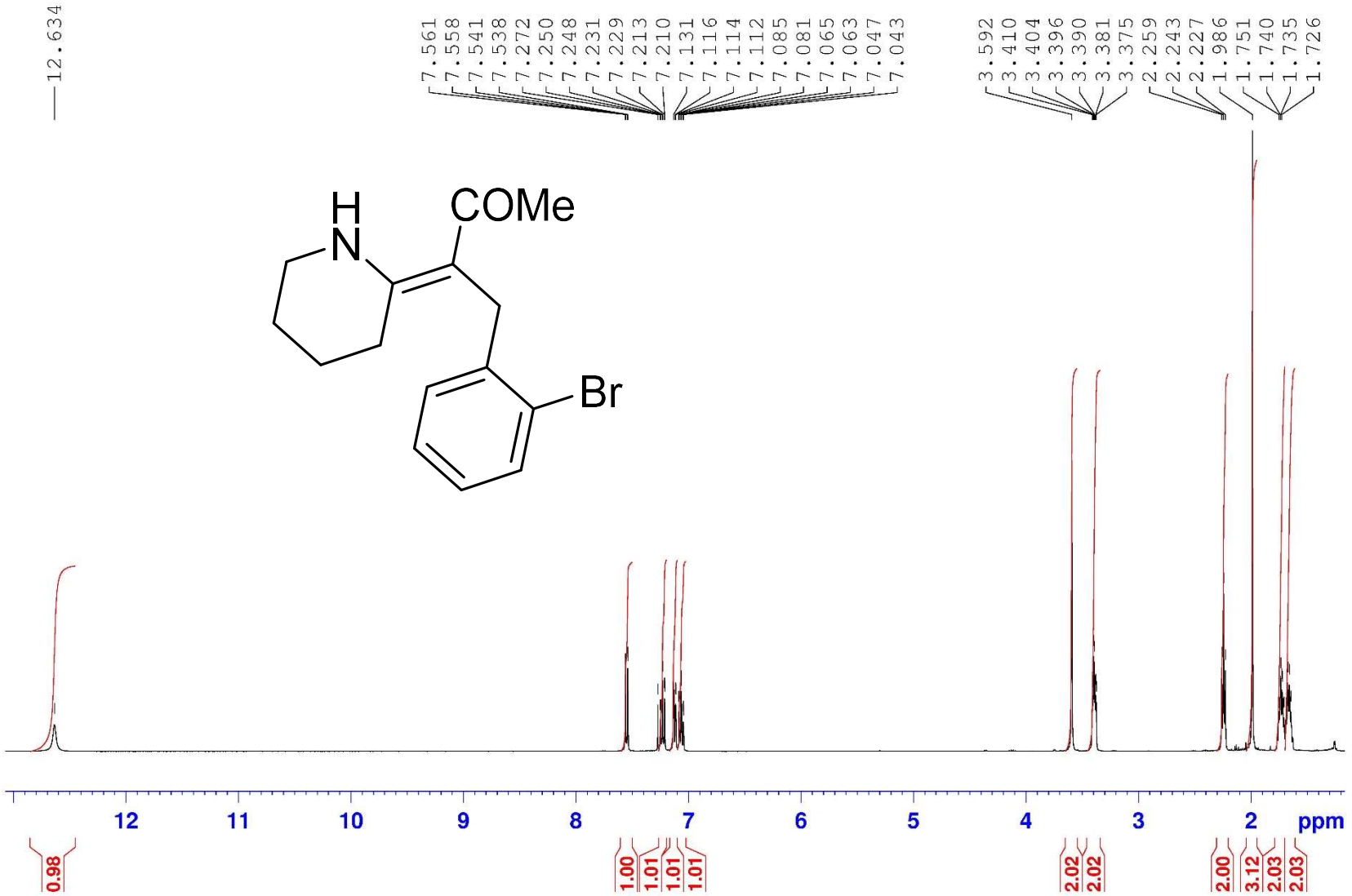

FIGURE S35: 400 MHz ^{1}H NMR spectrum of **9e** in $CDCl_3$.

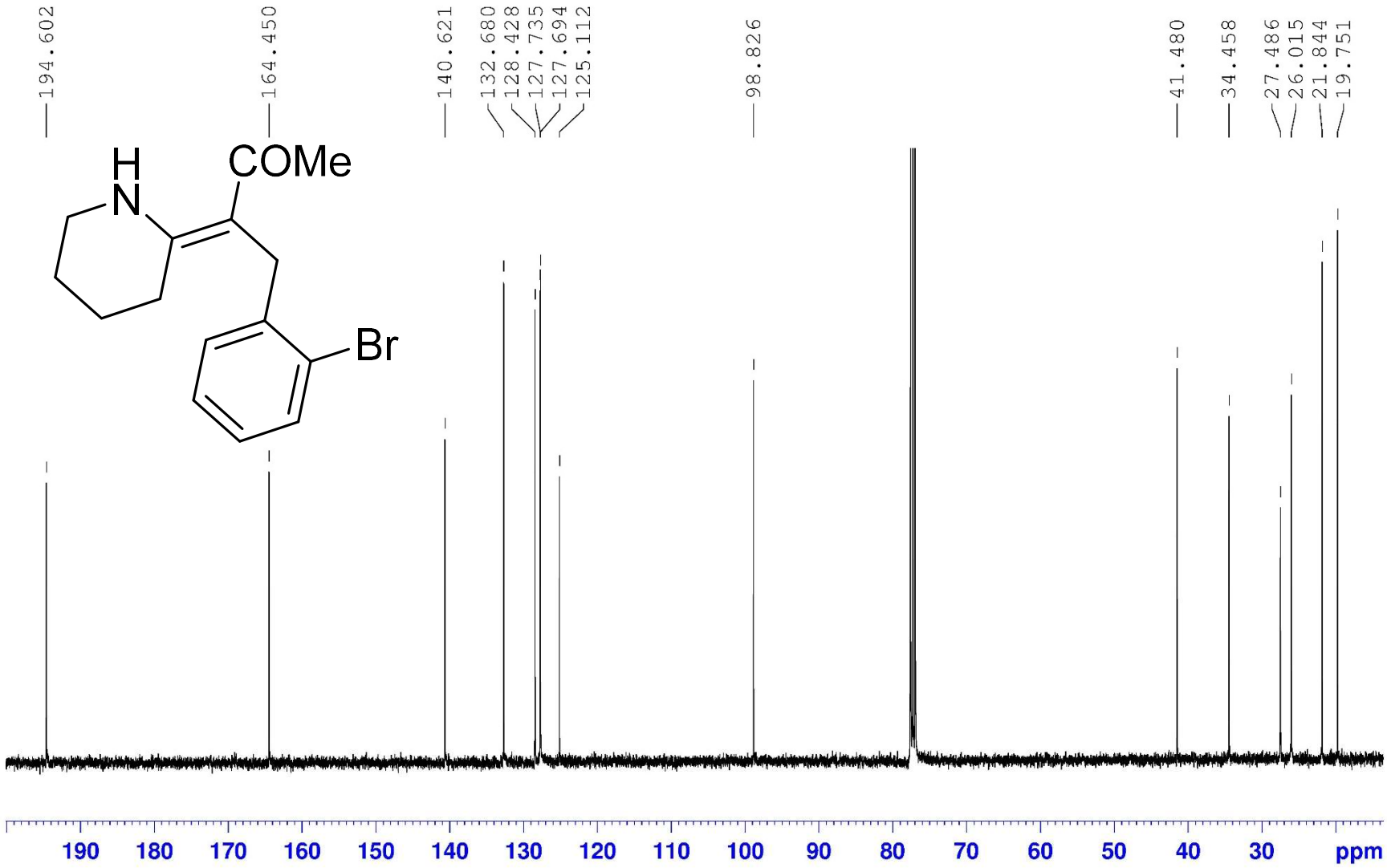

FIGURE S36: 100 MHz ^{13}C NMR spectrum of **9e** in $CDCl_3$.

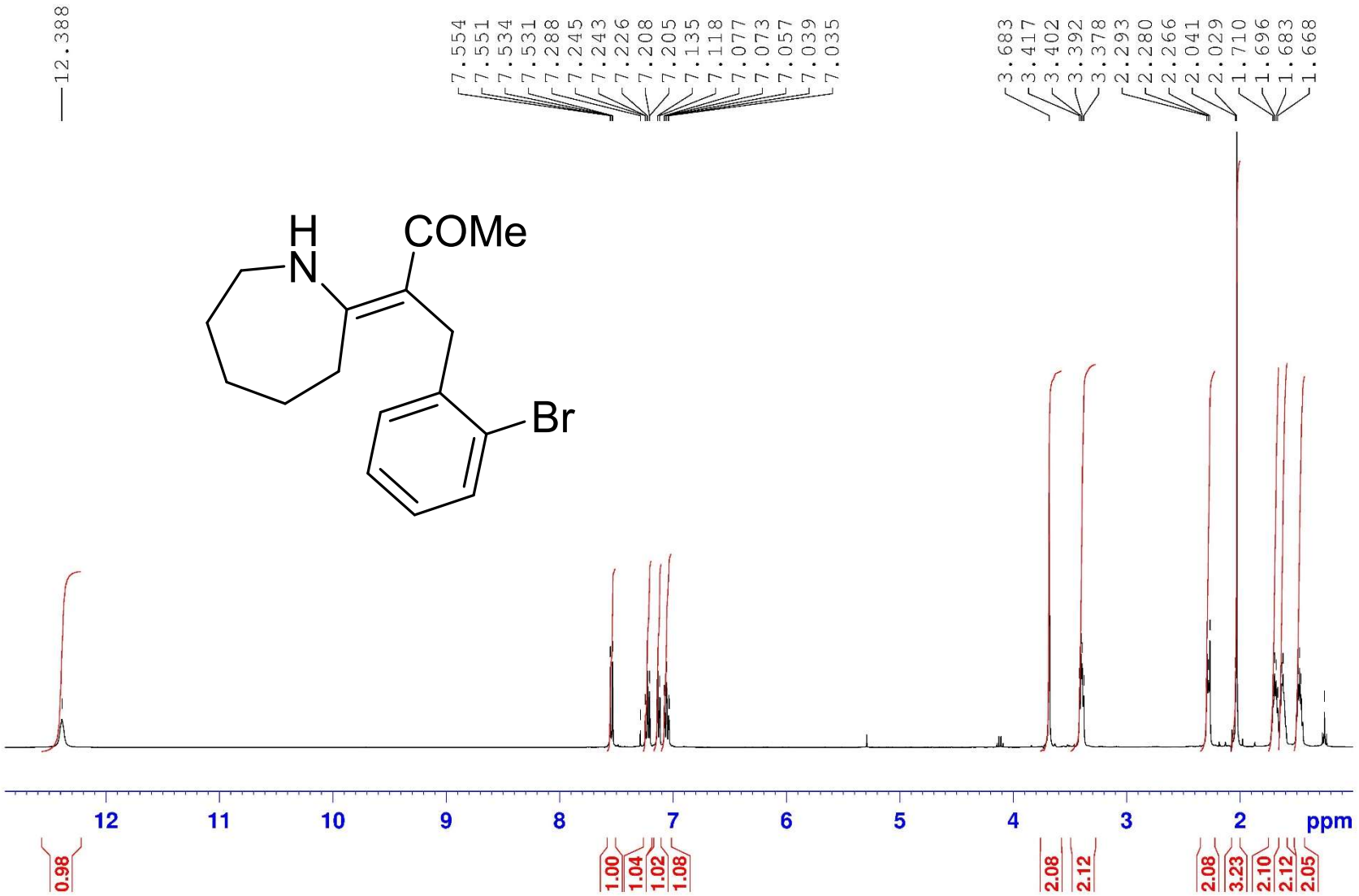

FIGURE S37: 400 MHz ^{1}H NMR spectrum of **9f** in $CDCl_3$.

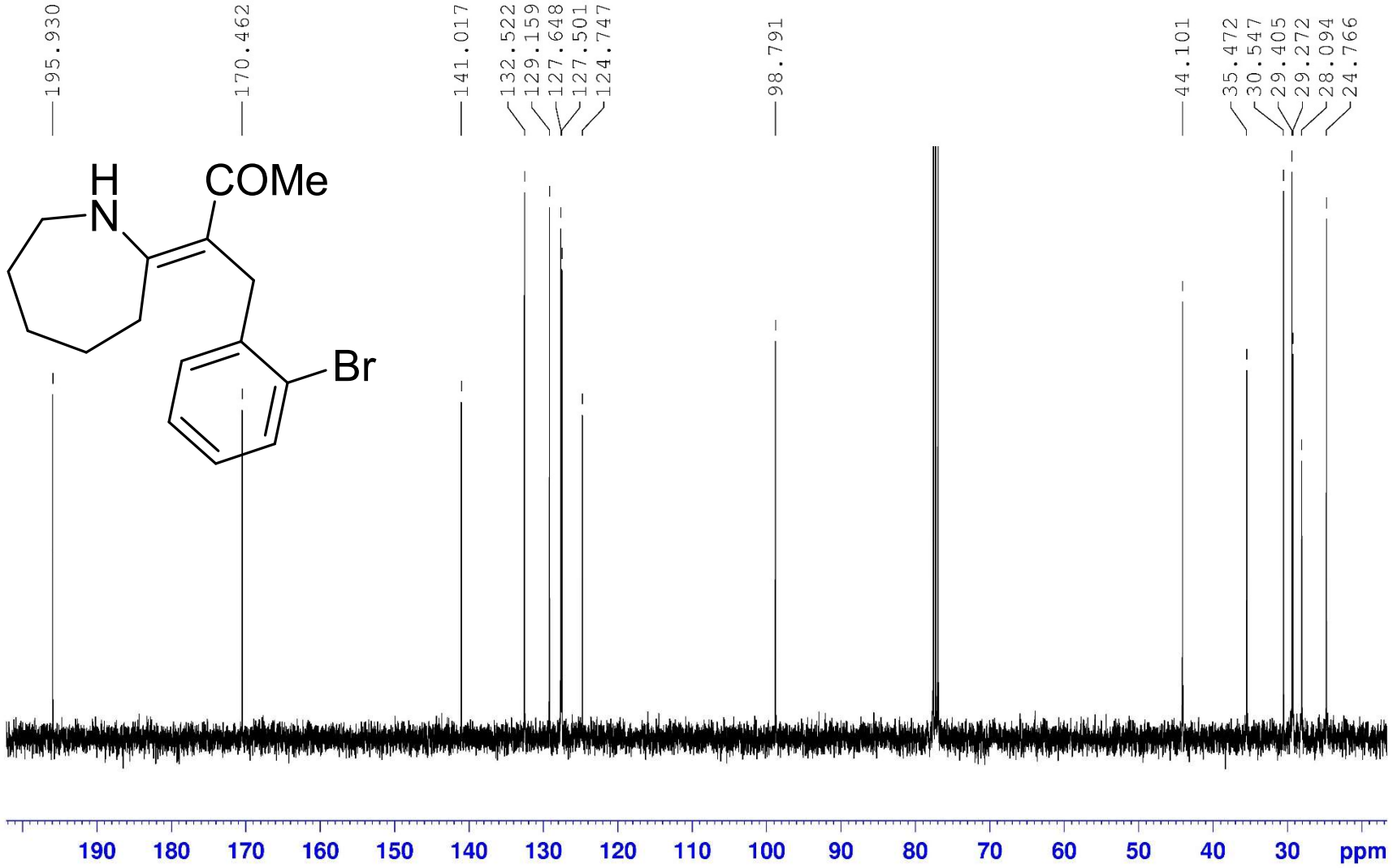

FIGURE S38: 100 MHz ^{13}C NMR spectrum of **9f** in $CDCl_3$.

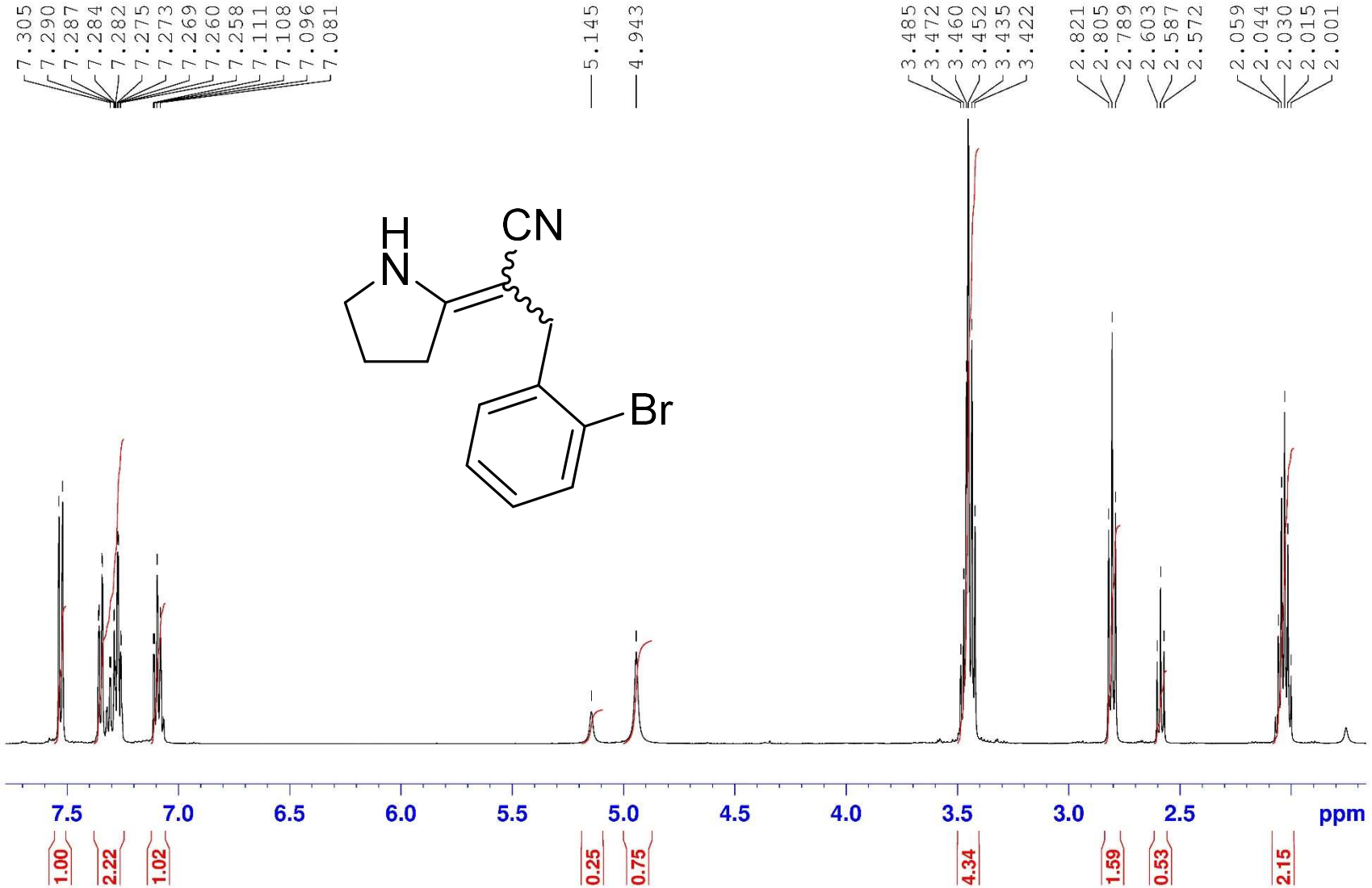

FIGURE S39: 500 MHz ^{1}H NMR spectrum of **9g** in $CDCl_3$.

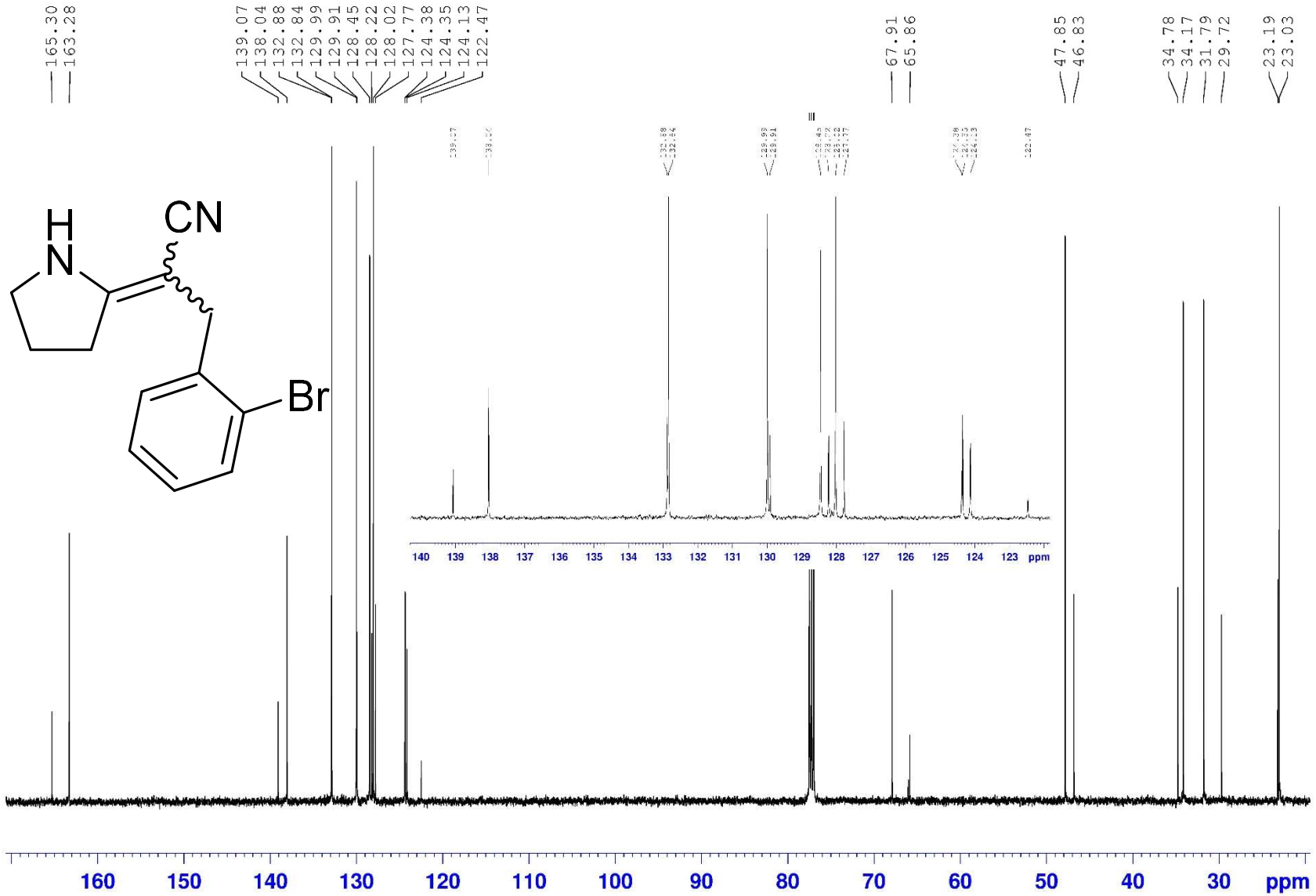

FIGURE S40: 125 MHz ^{13}C NMR spectrum of **9g** in $CDCl_3$.

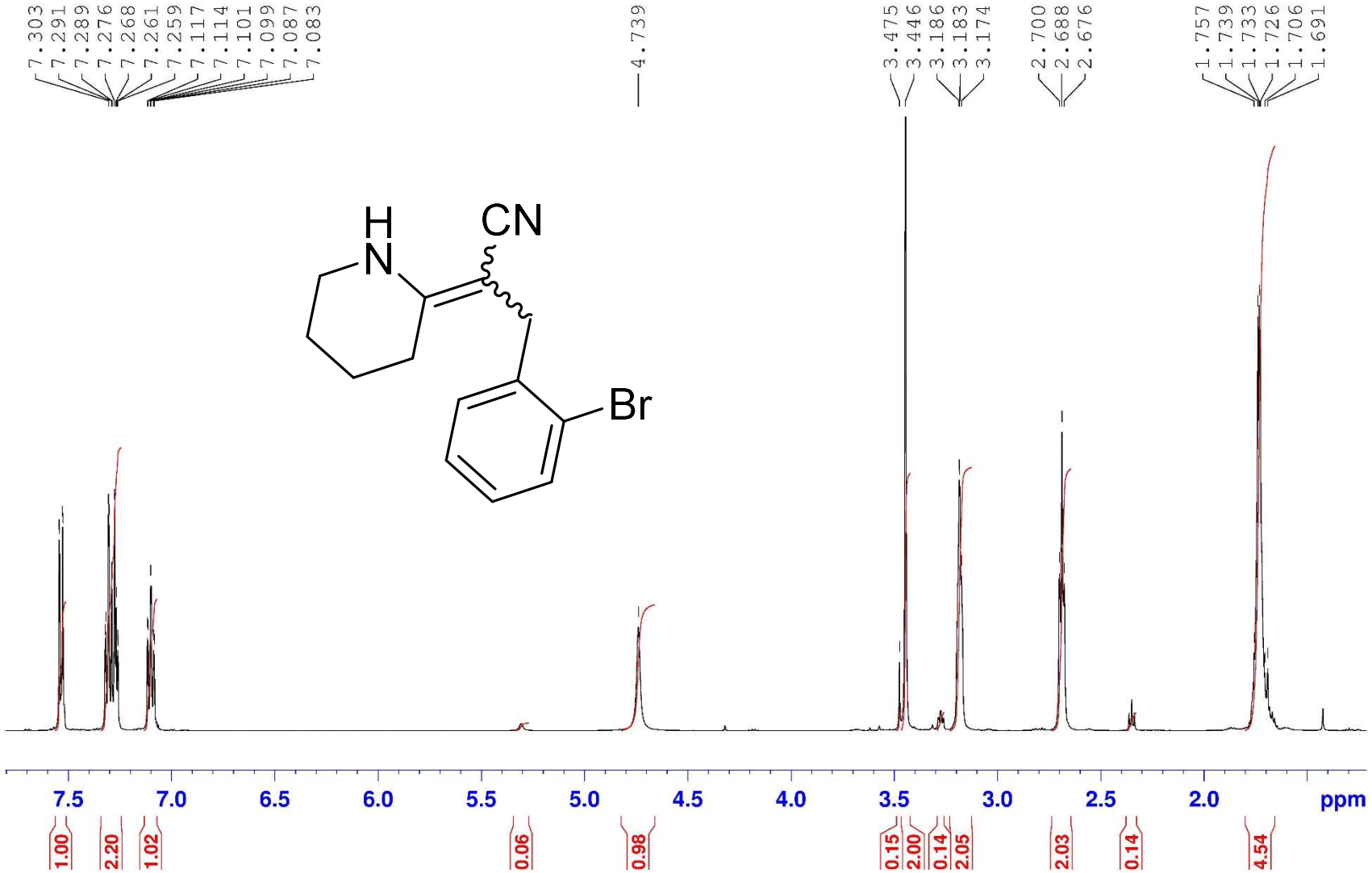

FIGURE S41: 500 MHz ^{1}H NMR spectrum of **9h** in $CDCl_3$. The sample is after recrystallization from cyclohexane.

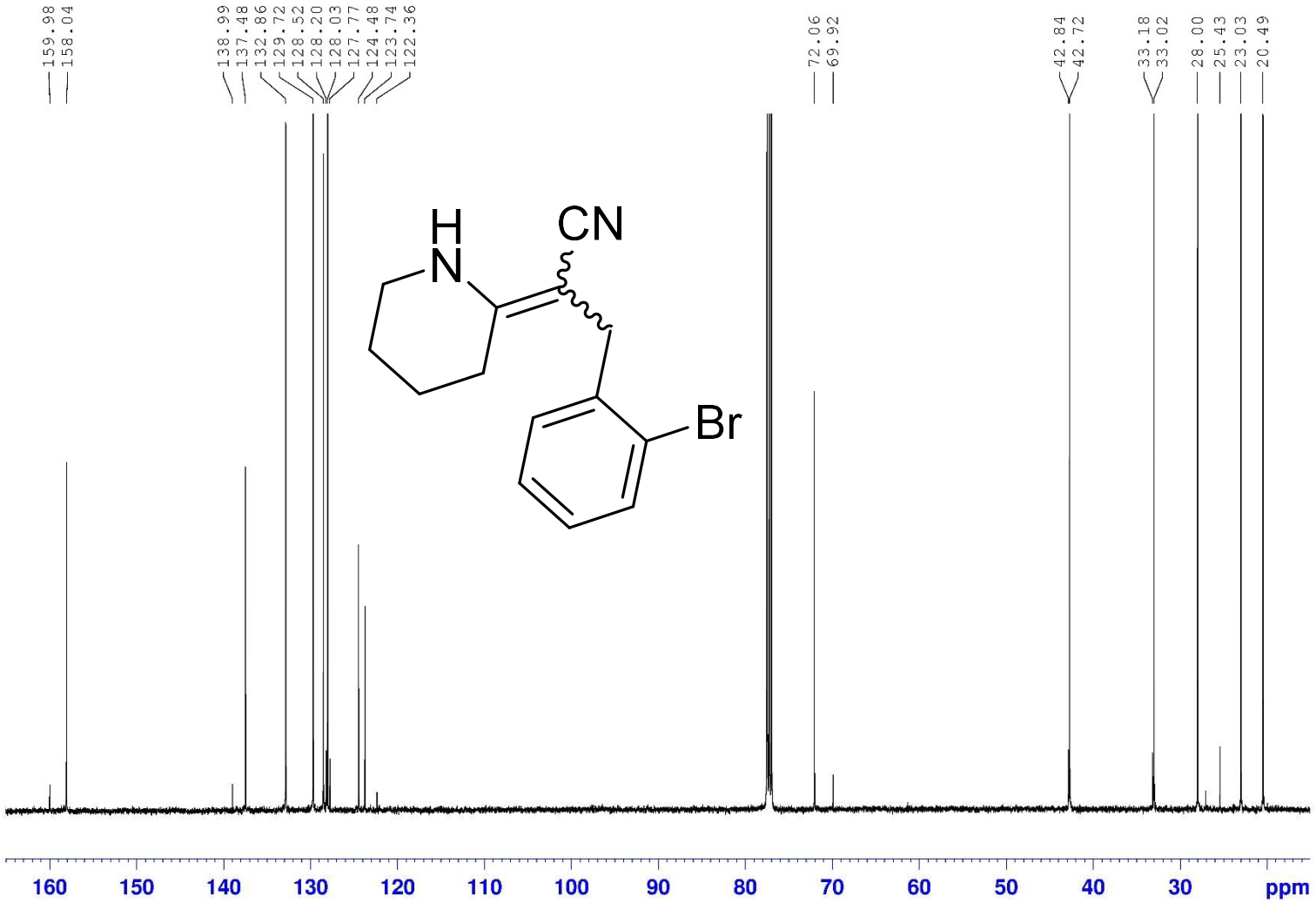

FIGURE S42: 125 MHz ^{13}C NMR spectrum of **9h** in $CDCl_3$. The sample is after recrystallization from cyclohexane.

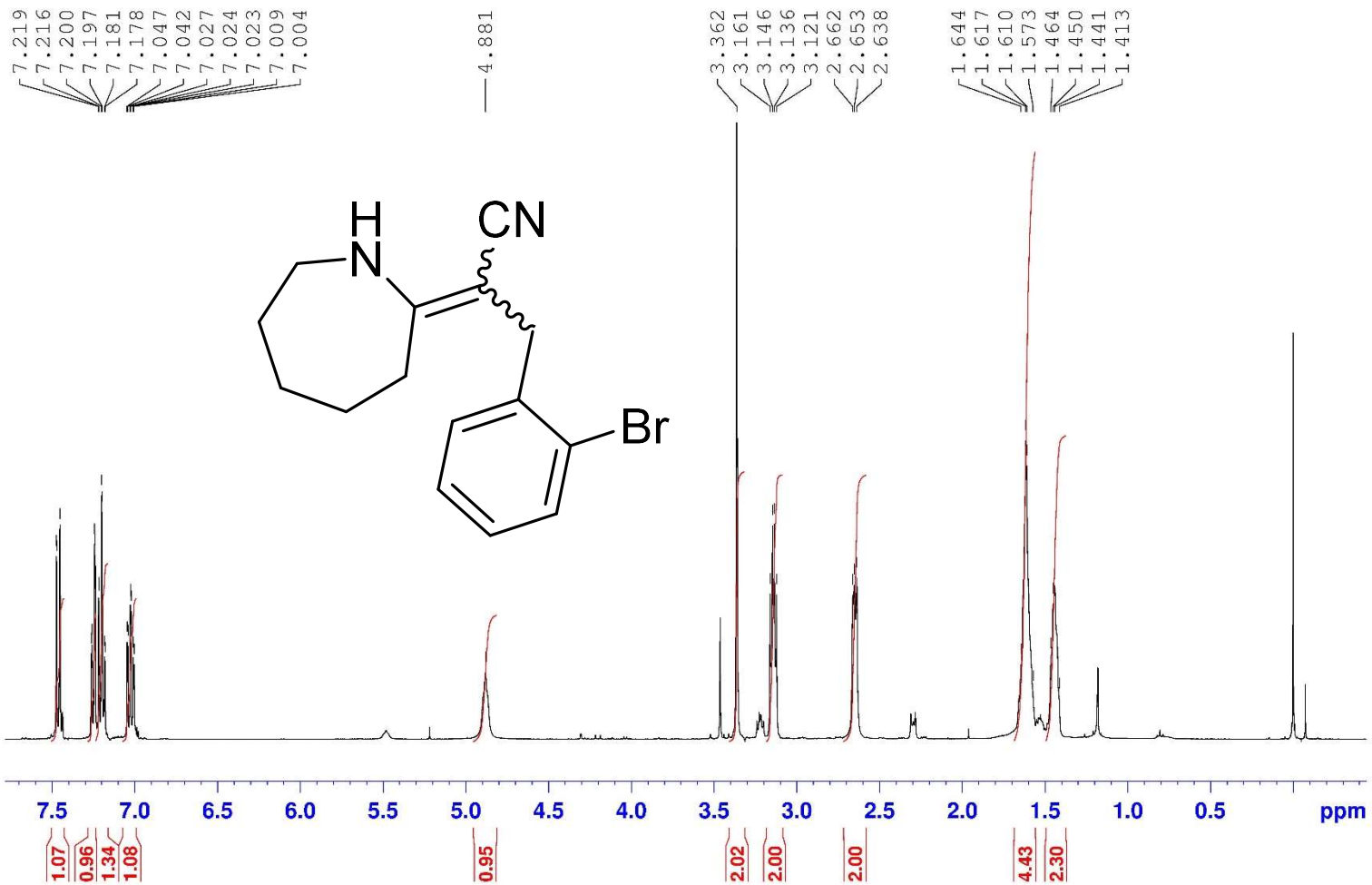

FIGURE S43: 400 MHz ^{1}H NMR spectrum of **9i** after third chromatography in $CDCl_3$.

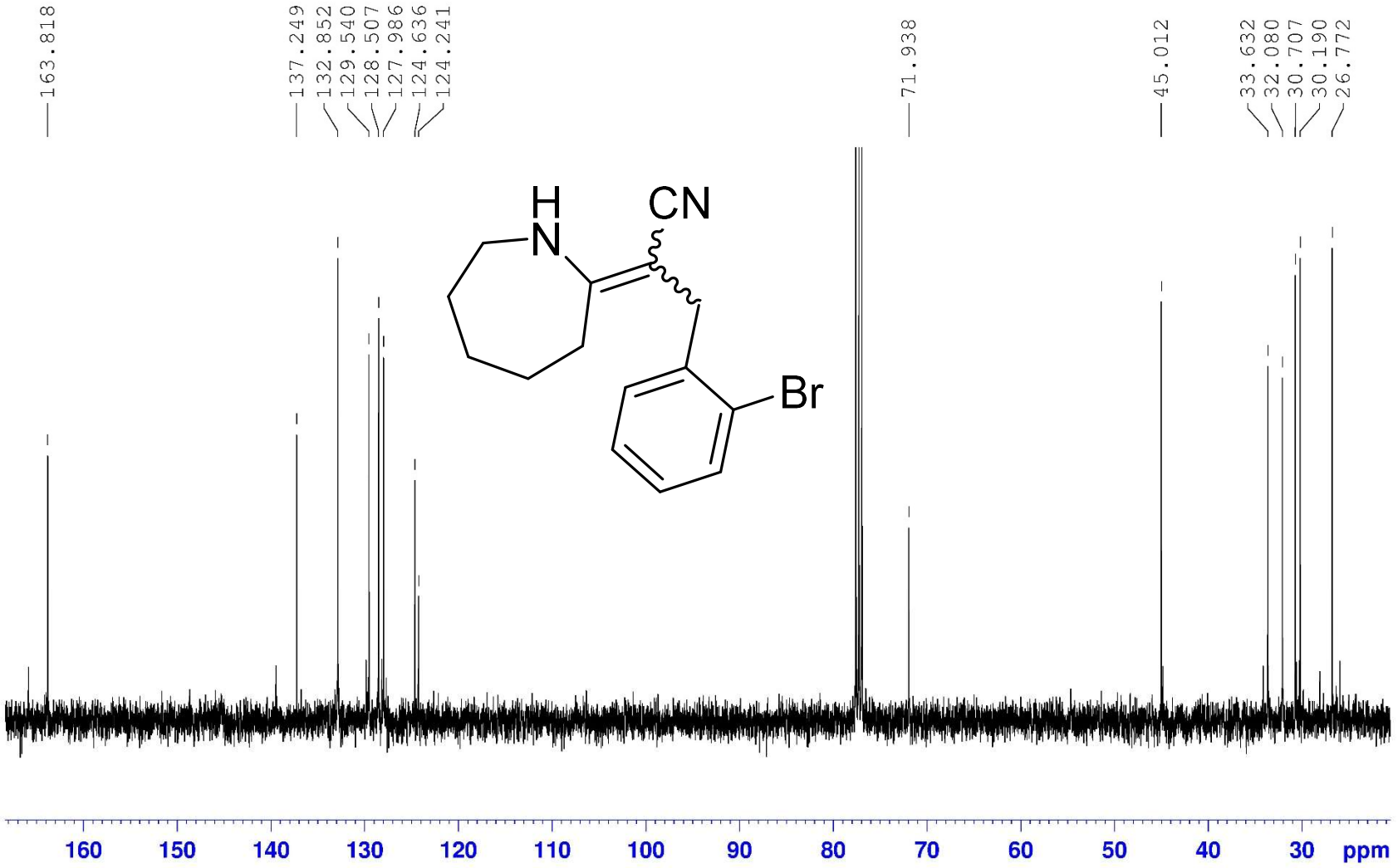

FIGURE S44: 100 MHz ^{13}C NMR spectrum of **9i** after third chromatography in $CDCl_3$.

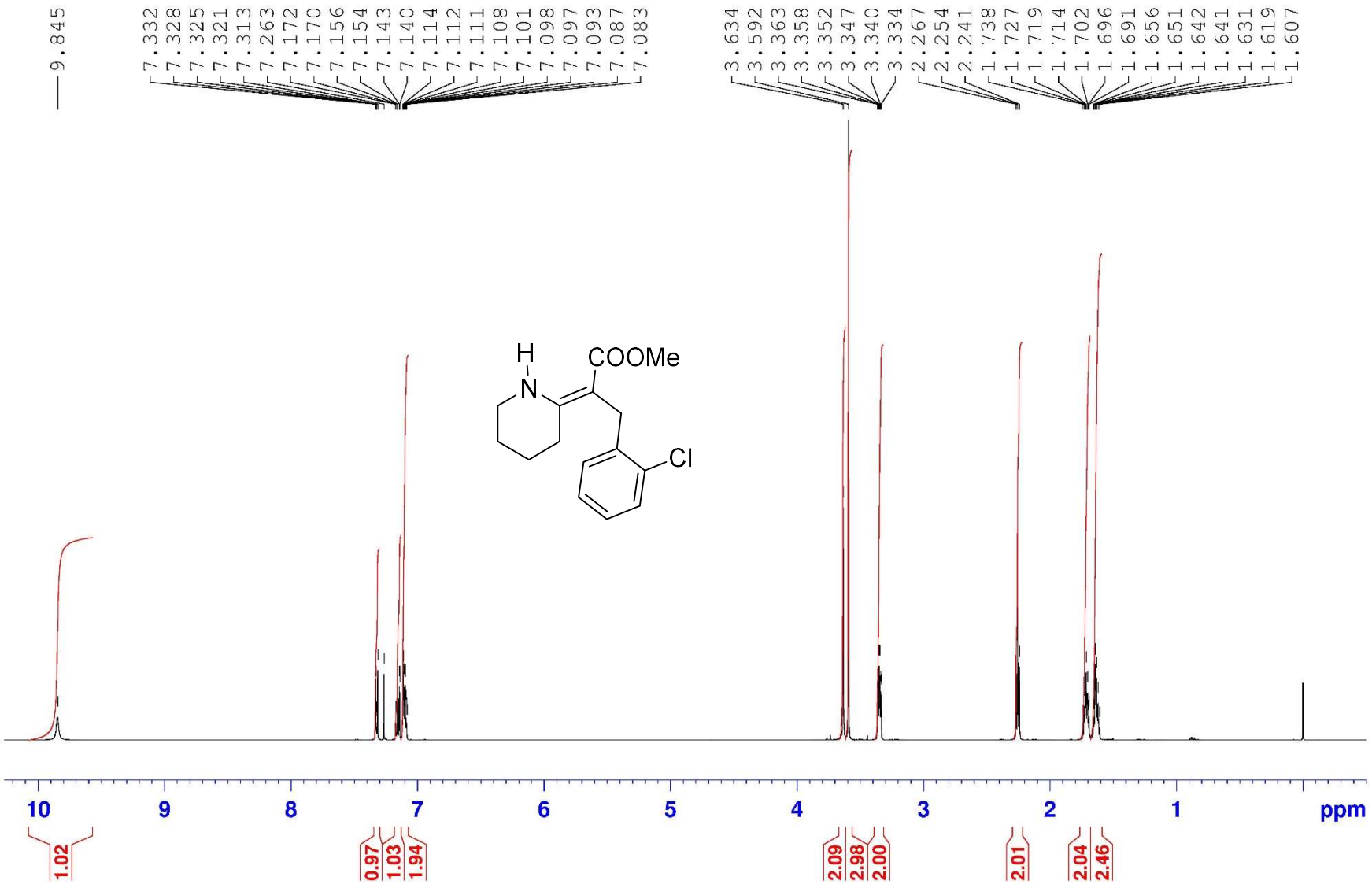

FIGURE S45: 500 MHz ^{1}H NMR spectrum of **9j** in $CDCl_3$.

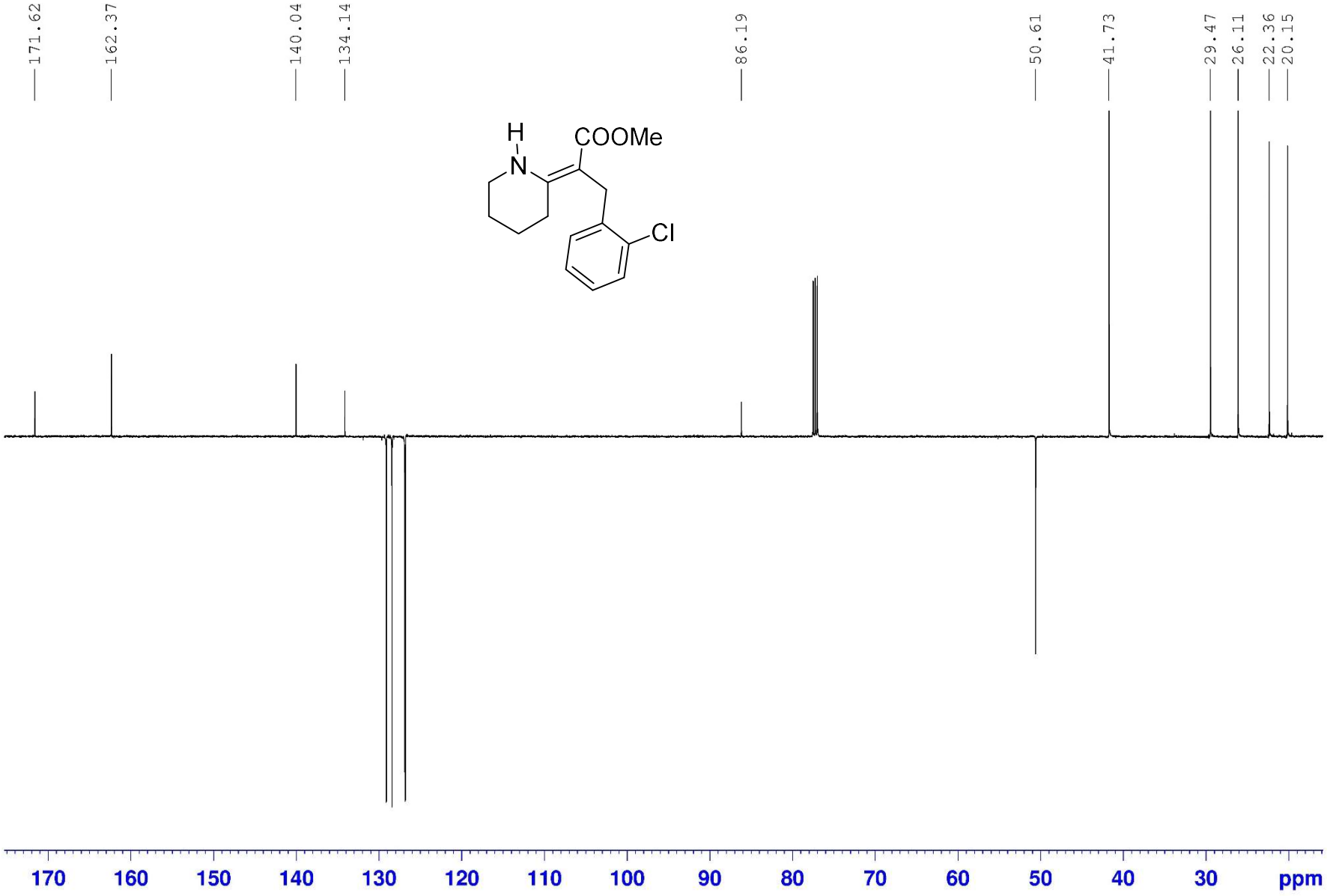

FIGURE S46: 125 MHz ^{13}C APT NMR spectrum of **9j** in $CDCl_3$.

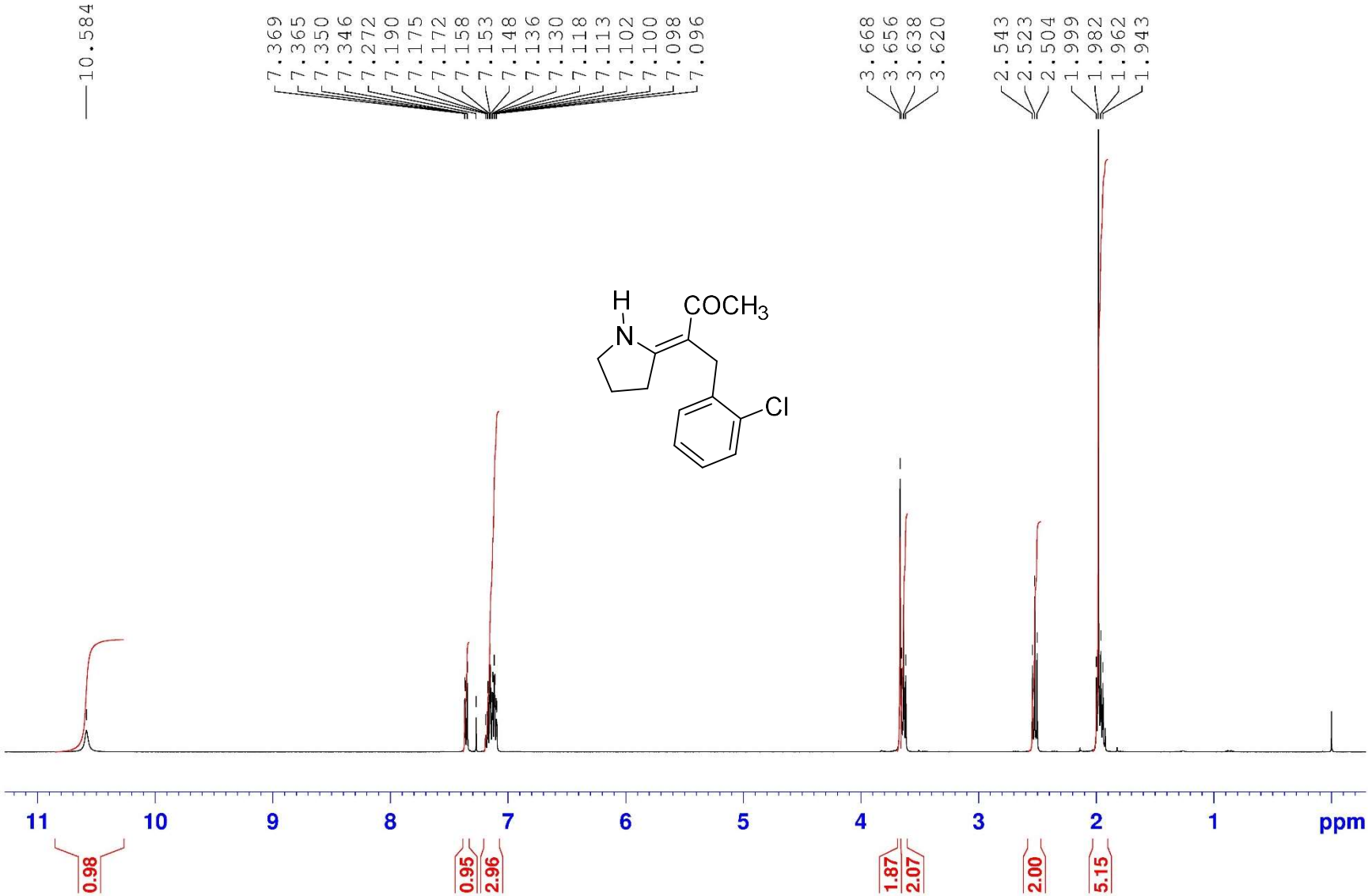

FIGURE S47: 400 MHz ^{1}H NMR spectrum of **9k** in $CDCl_3$.

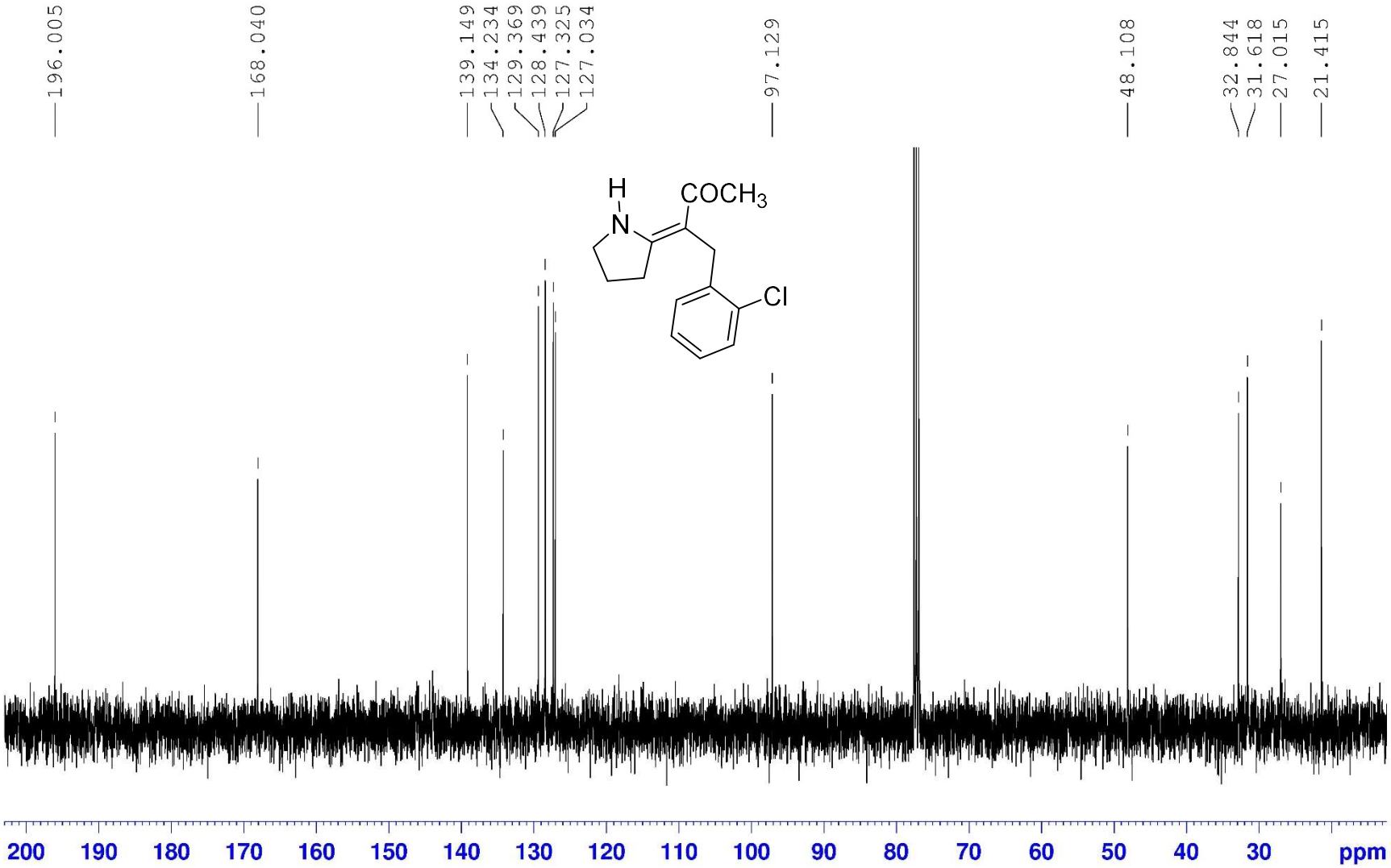

FIGURE S48: 100 MHz ^{13}C NMR spectrum of **9k** in $CDCl_3$.

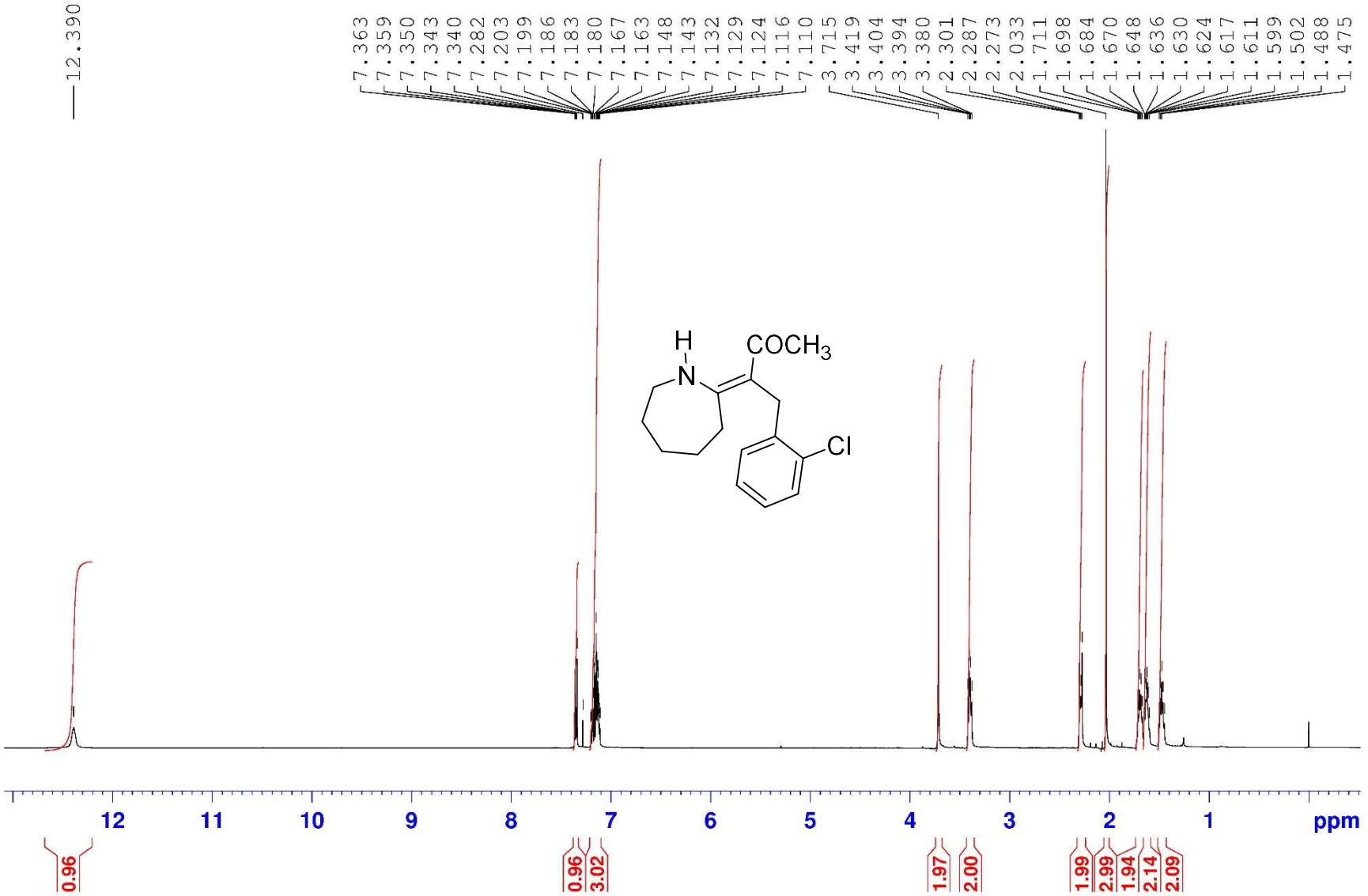

FIGURE S49: 400 MHz ^{1}H NMR spectrum of **9l** in $CDCl_3$.

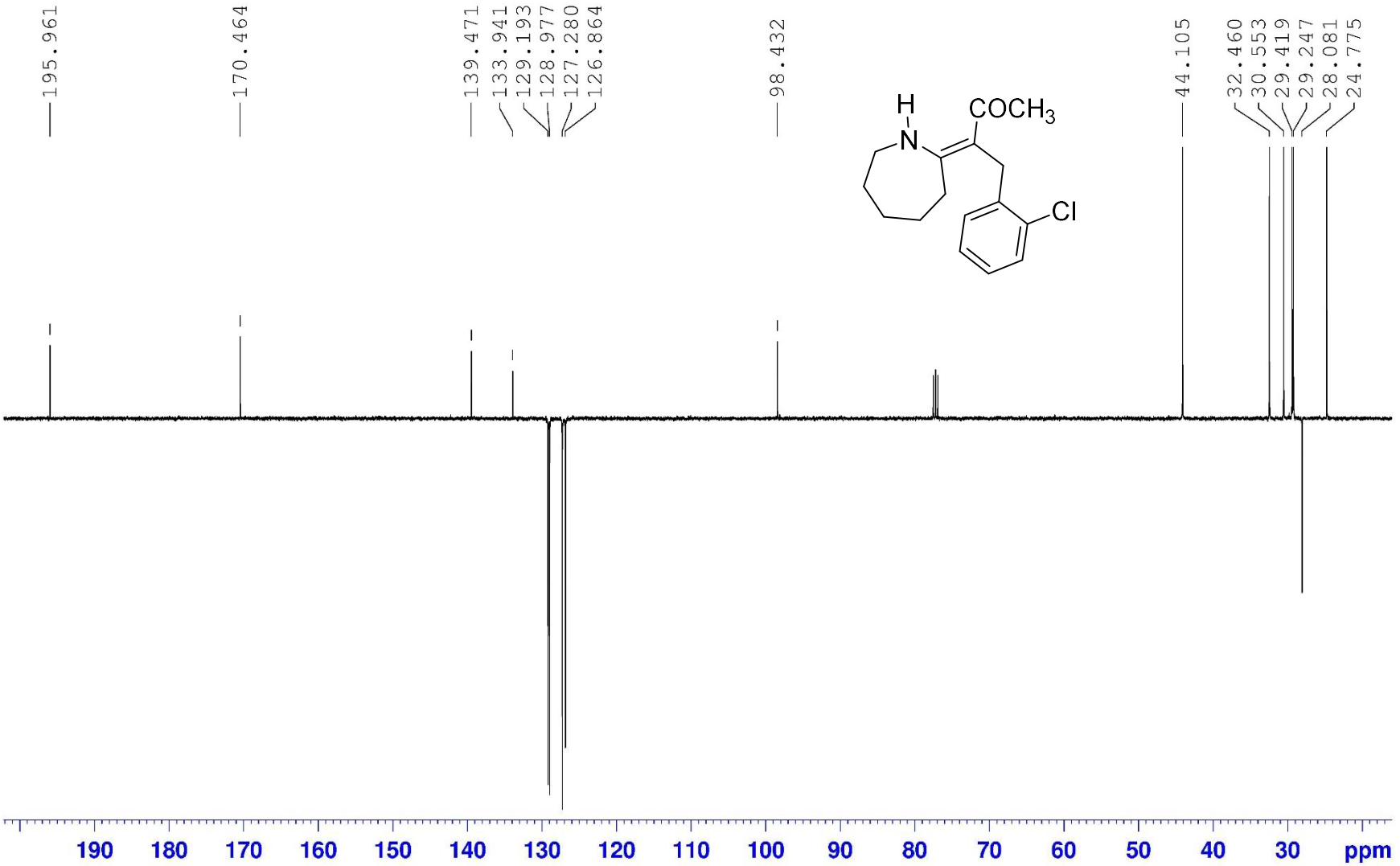

FIGURE S50: 100 MHz ^{13}C APT NMR spectrum of **9l** in $CDCl_3$.

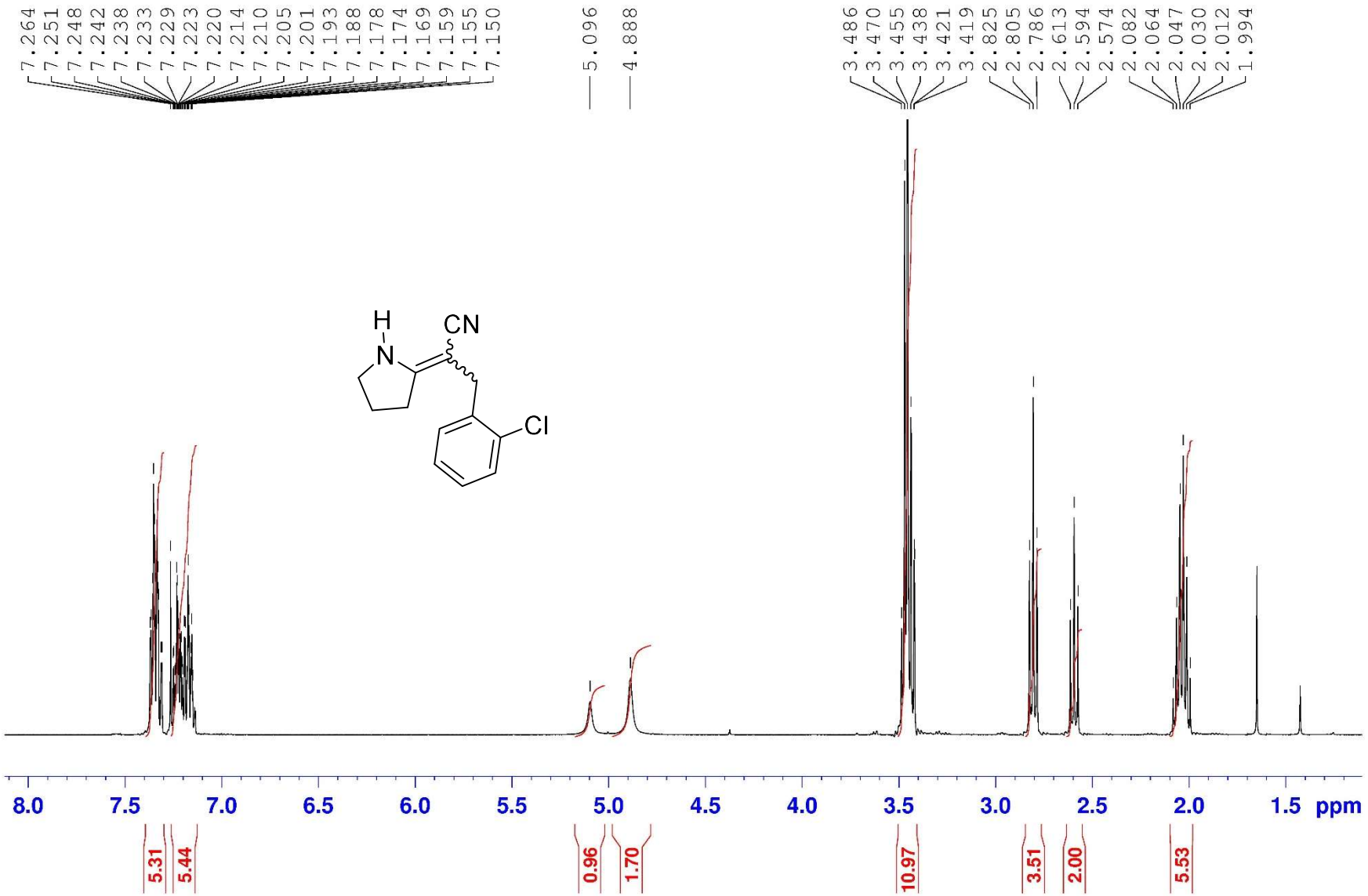

FIGURE S51: 400 MHz ^{1}H NMR spectrum of **9m** in $CDCl_3$.

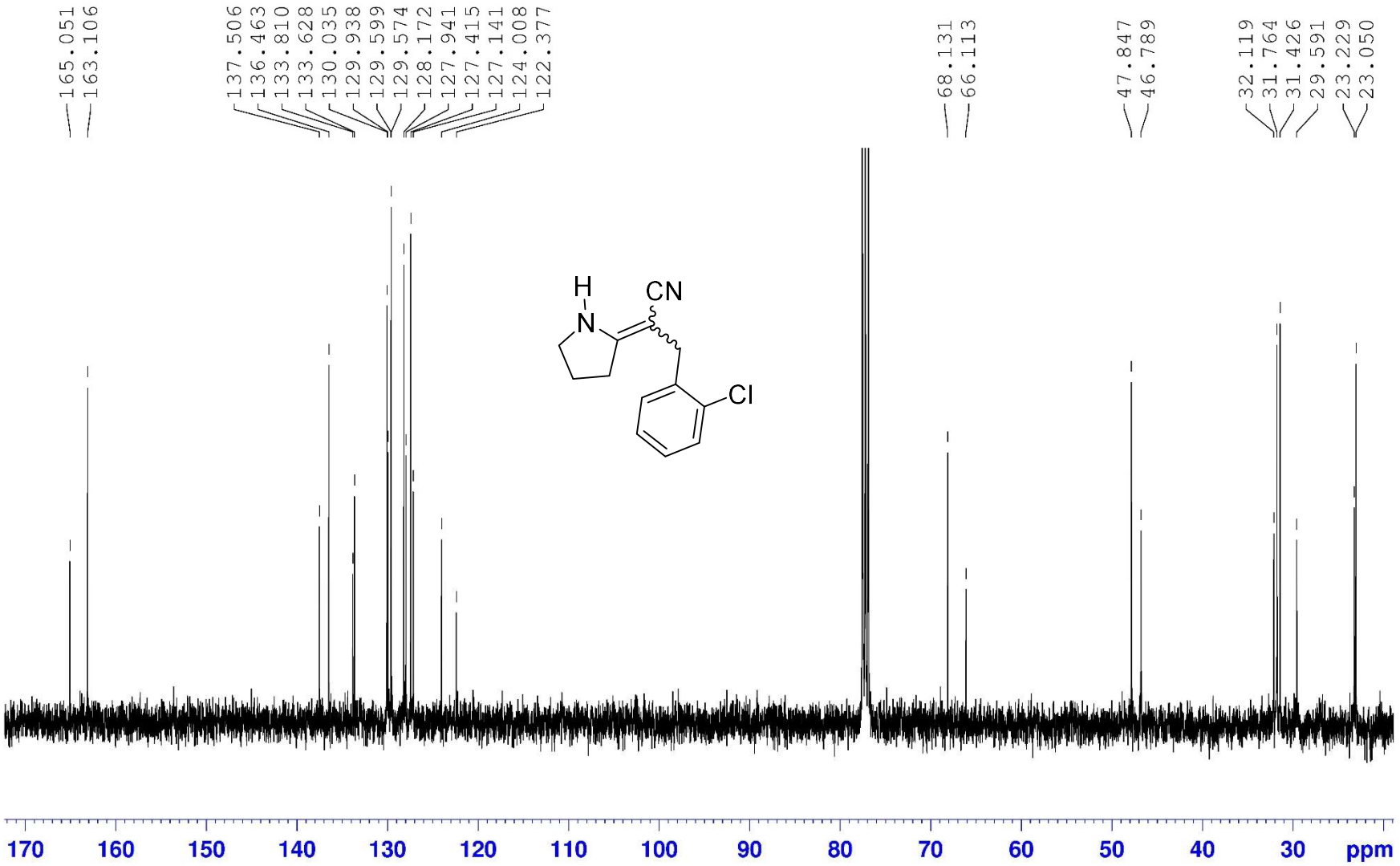

FIGURE S52: 100 MHz ^{13}C NMR spectrum of **9m** in $CDCl_3$.

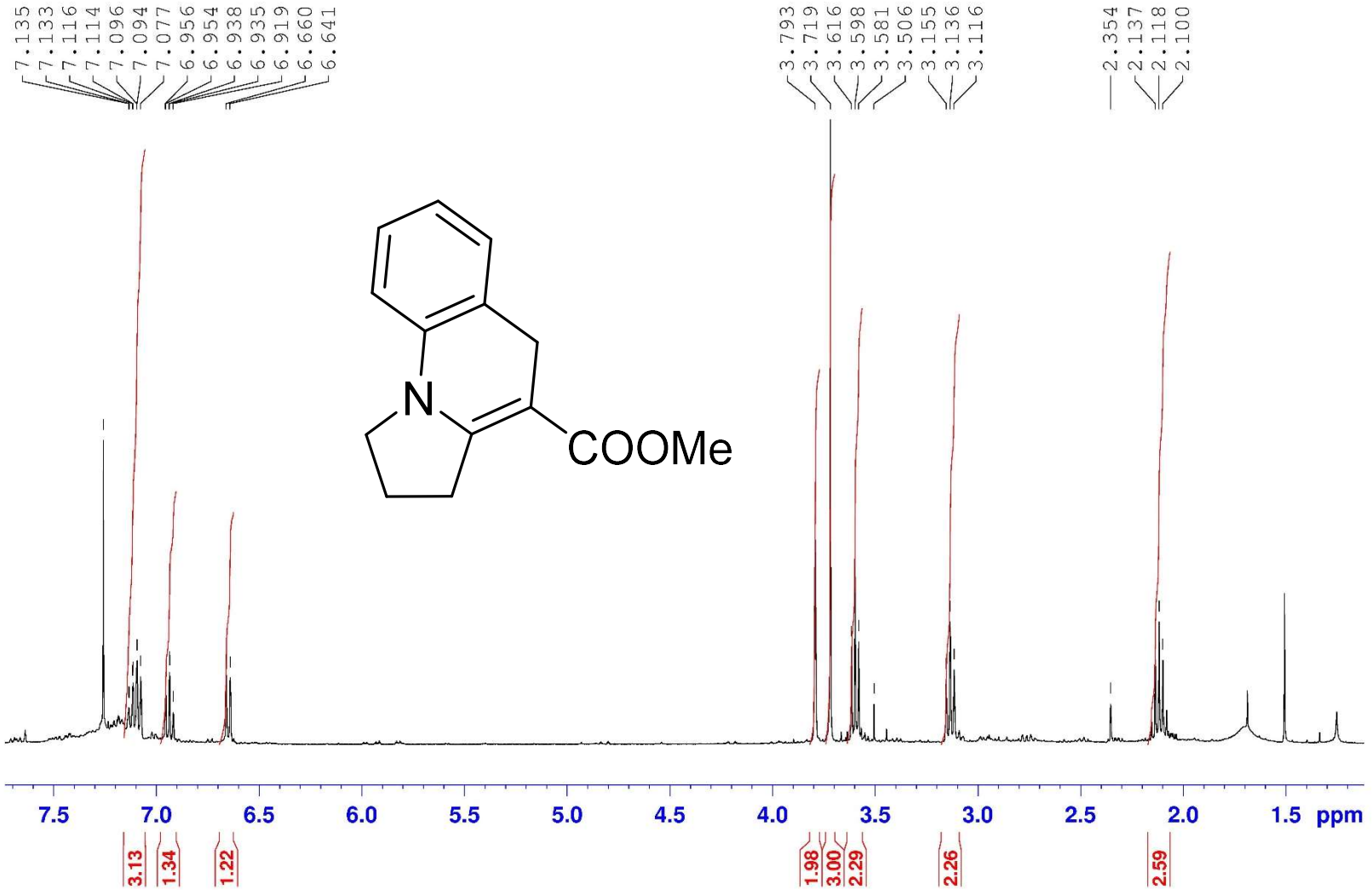

FIGURE S53: 400 MHz ^{1}H NMR spectrum of **11a** in $CDCl_3$.

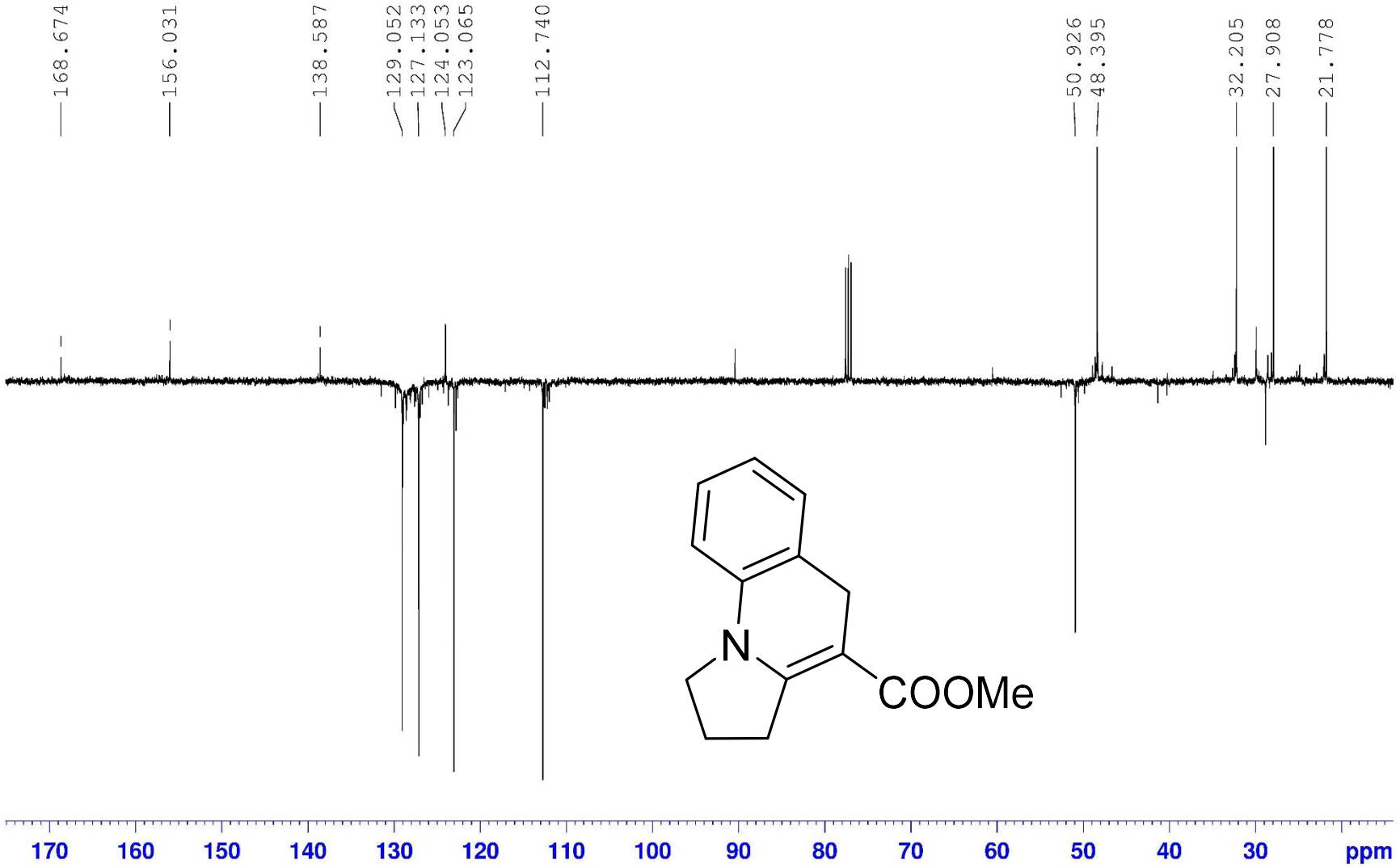

FIGURE S54: 100 MHz ^{13}C NMR (APT) spectrum of **11a** in $CDCl_3$.

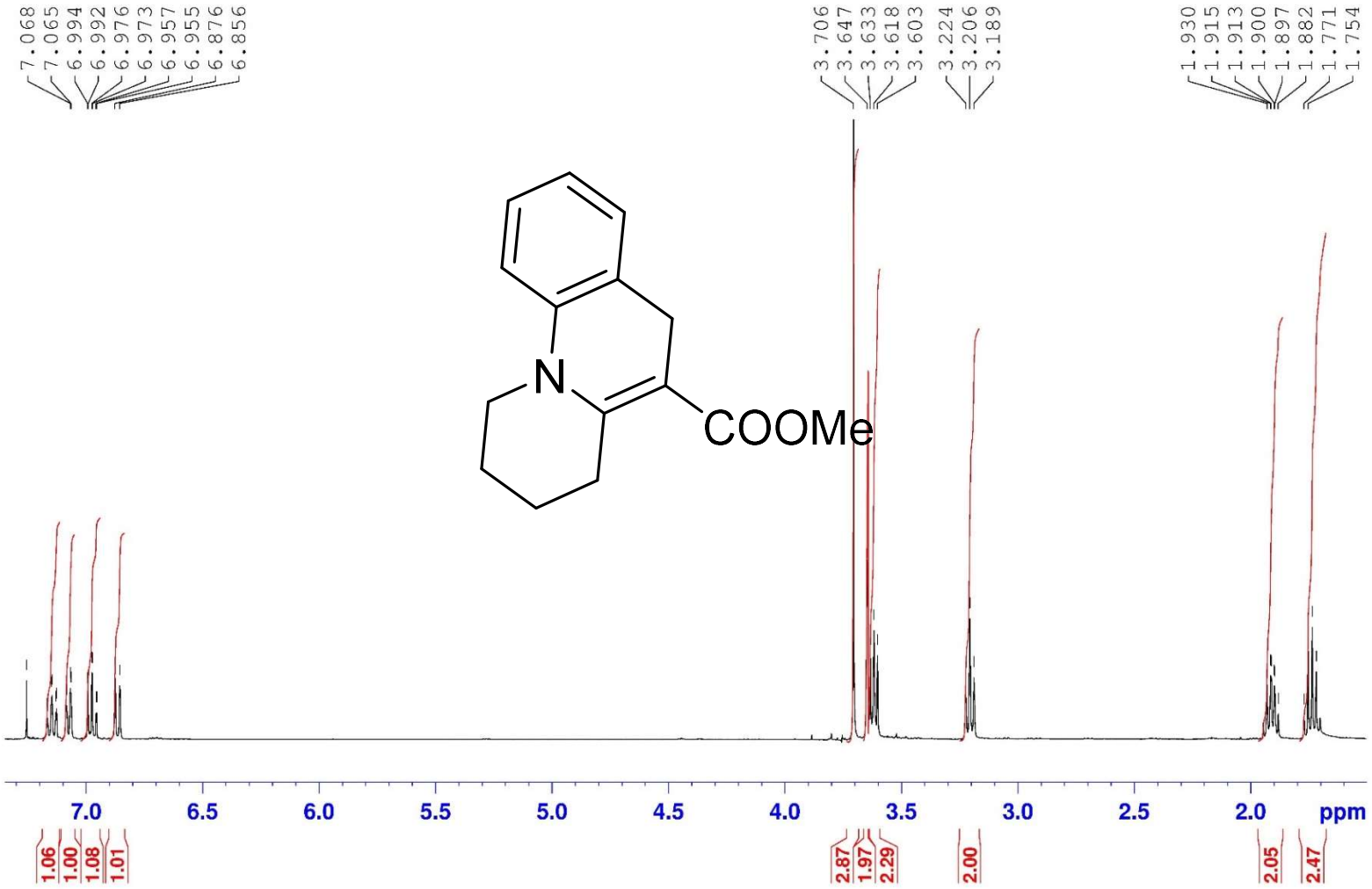

FIGURE S55: 400 MHz ^{1}H NMR spectrum of **11b** in $CDCl_3$.

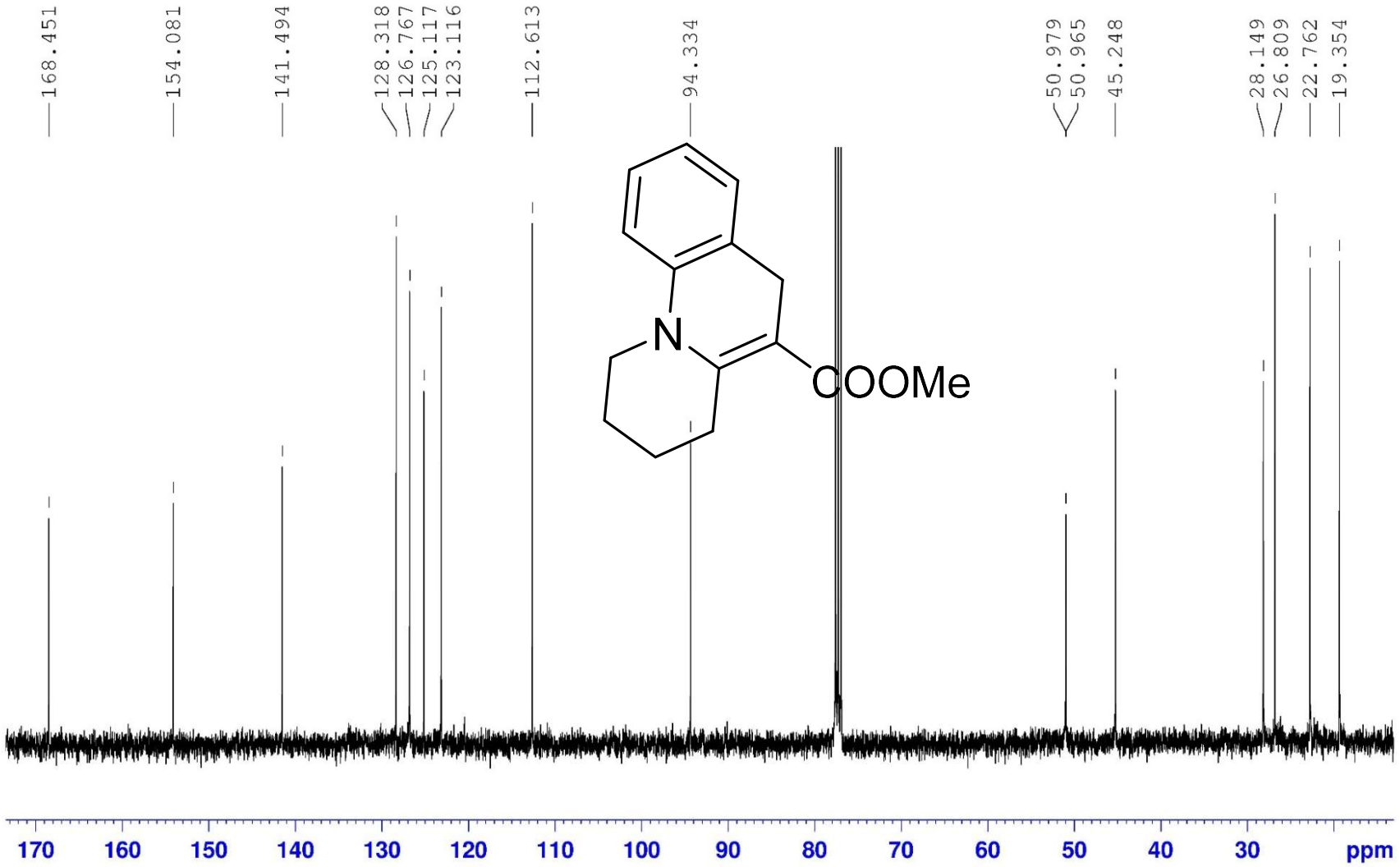

FIGURE S56: 100 MHz ^{13}C NMR spectrum of **11b** in $CDCl_3$.

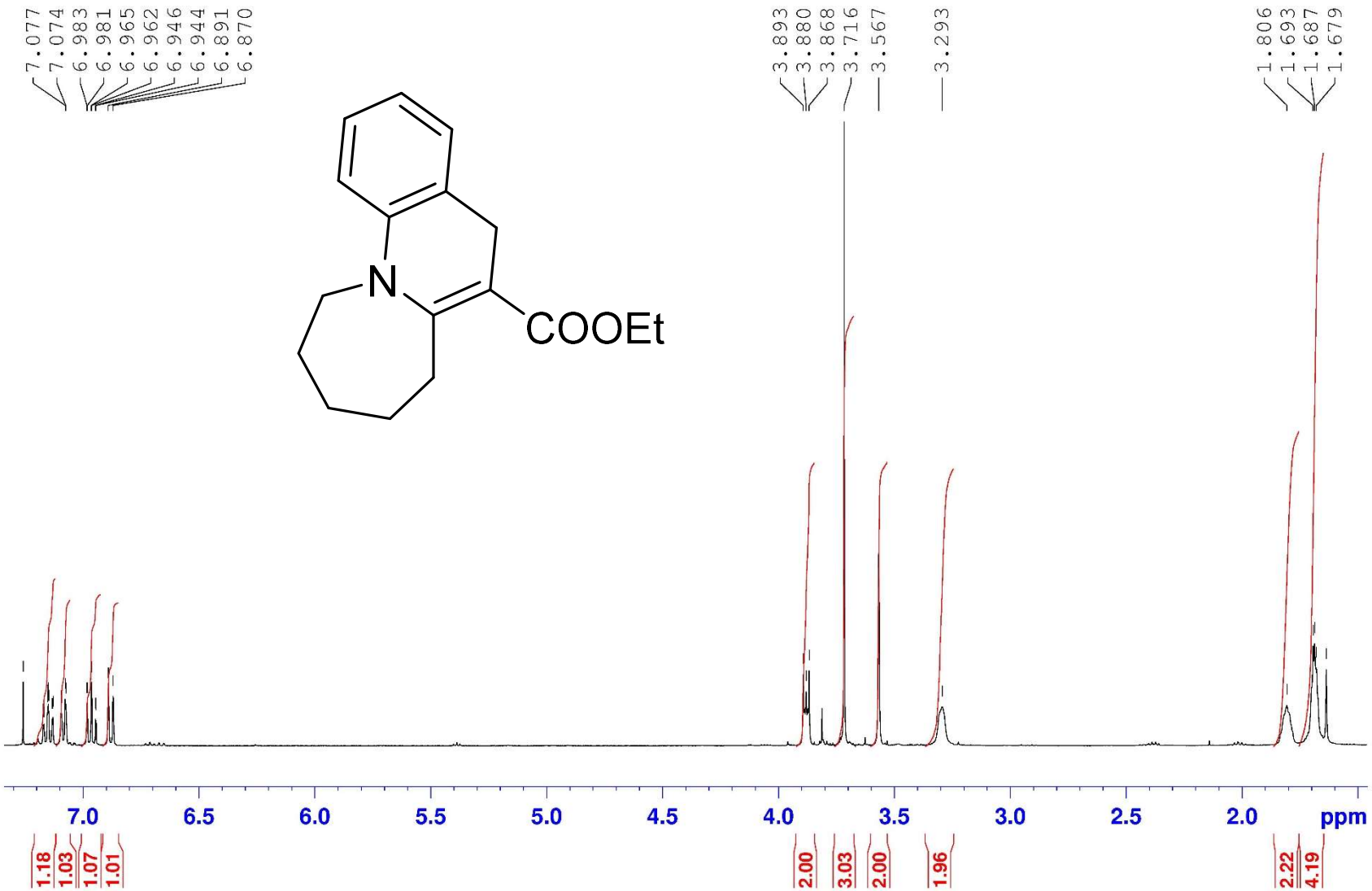

FIGURE S57: 400 MHz ^{1}H NMR spectrum of **11c** in $CDCl_3$.

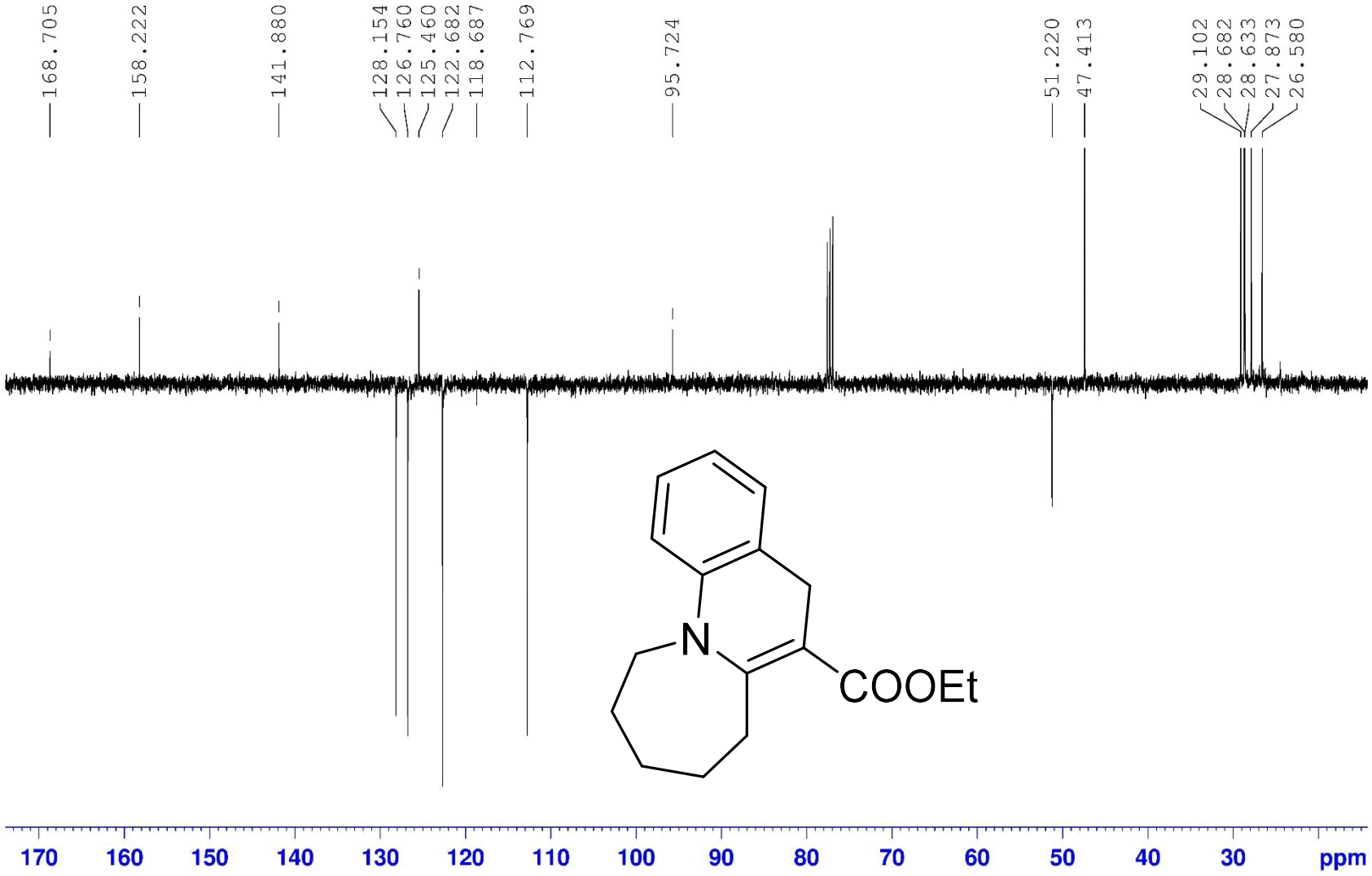

FIGURE S58: 100 MHz ^{13}C NMR (APT) spectrum of **11c** in $CDCl_3$.

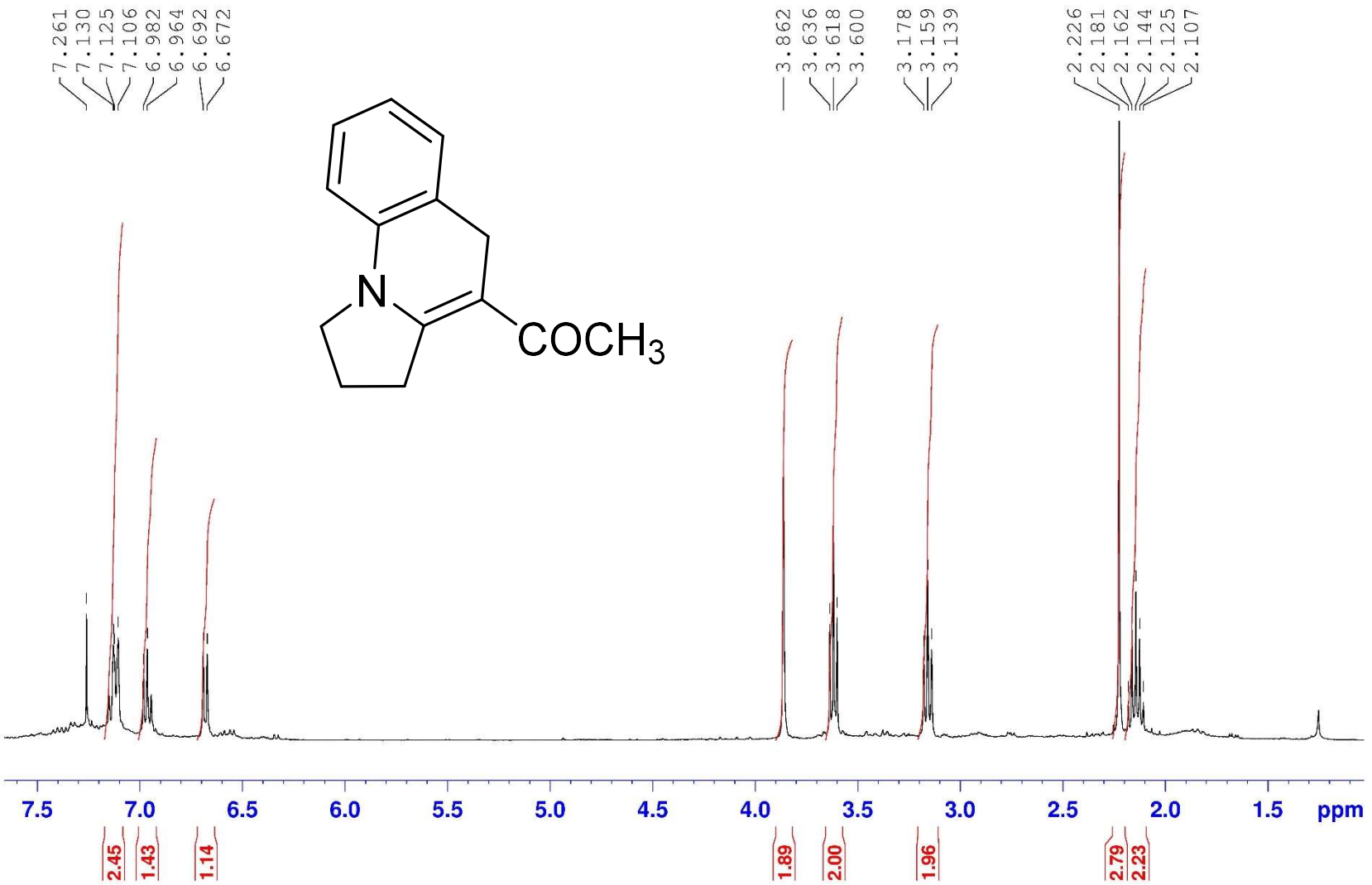

FIGURE S59: 400 MHz ^{1}H NMR spectrum of **11d** in $CDCl_3$.

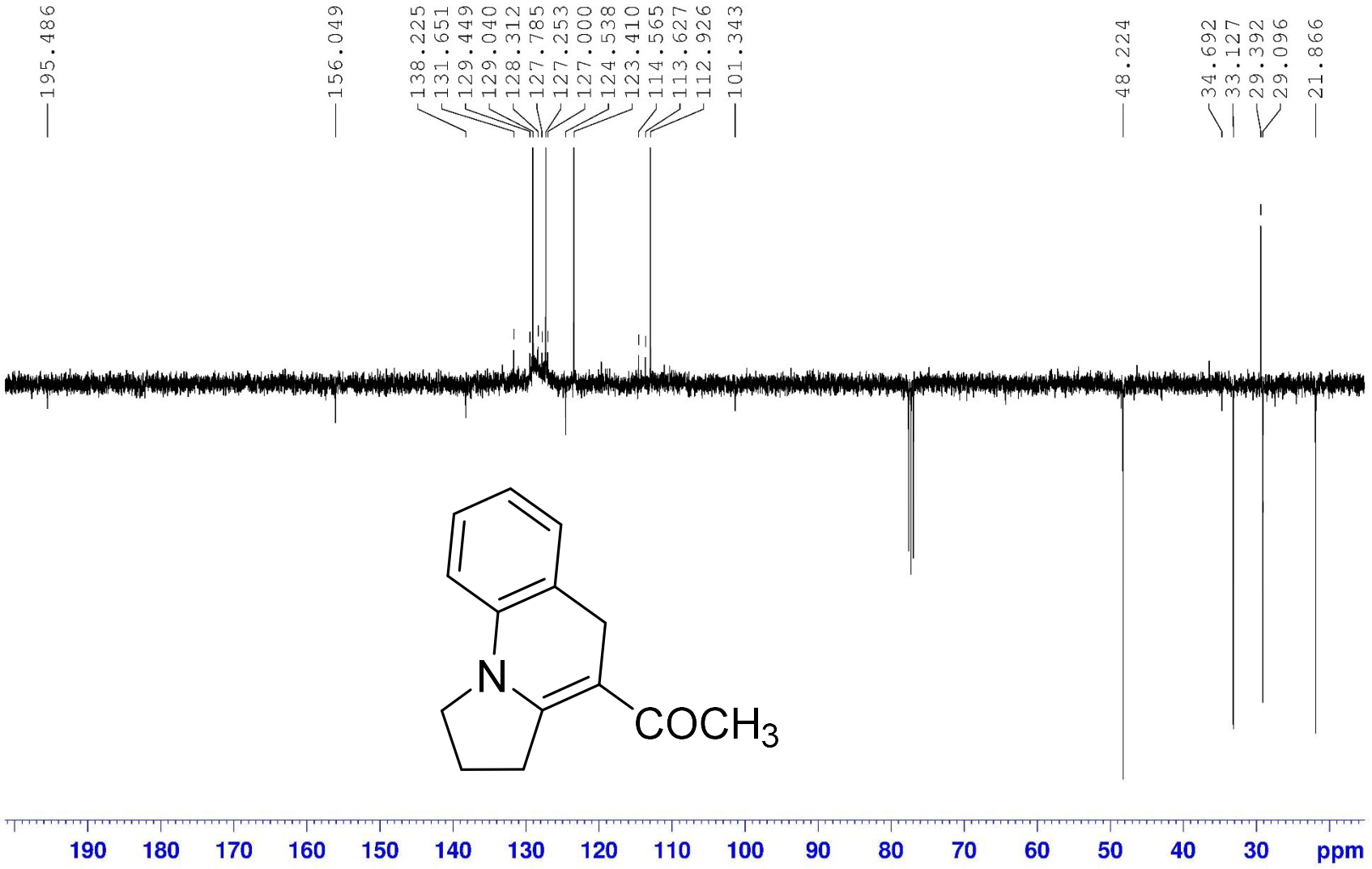

Figure S60: 100 MHz ^{13}C NMR (APT) spectrum of **11d** in $CDCl_3$.

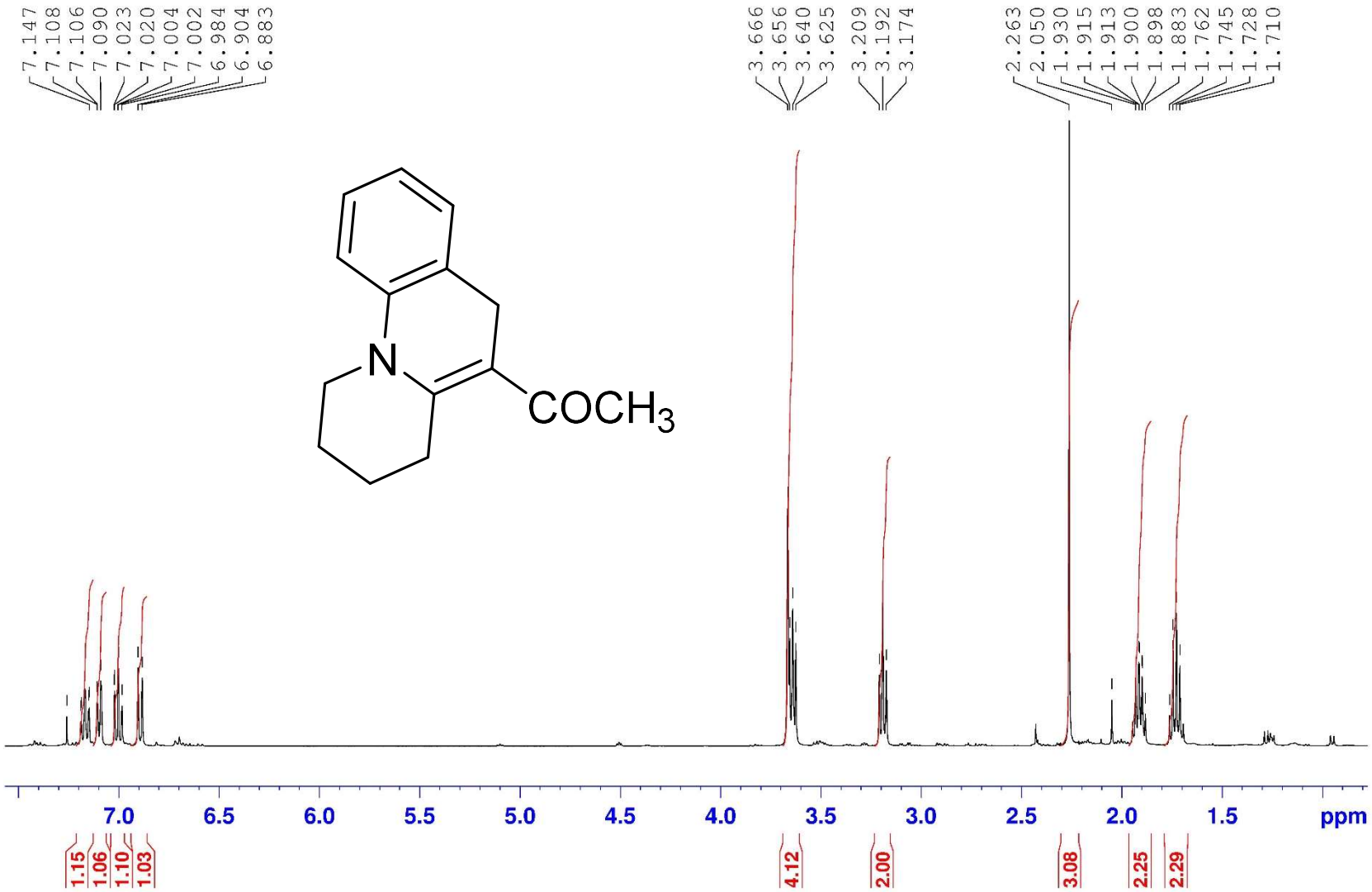

FIGURE S61: 400 MHz ^{1}H NMR spectrum of **11e** in $CDCl_3$.

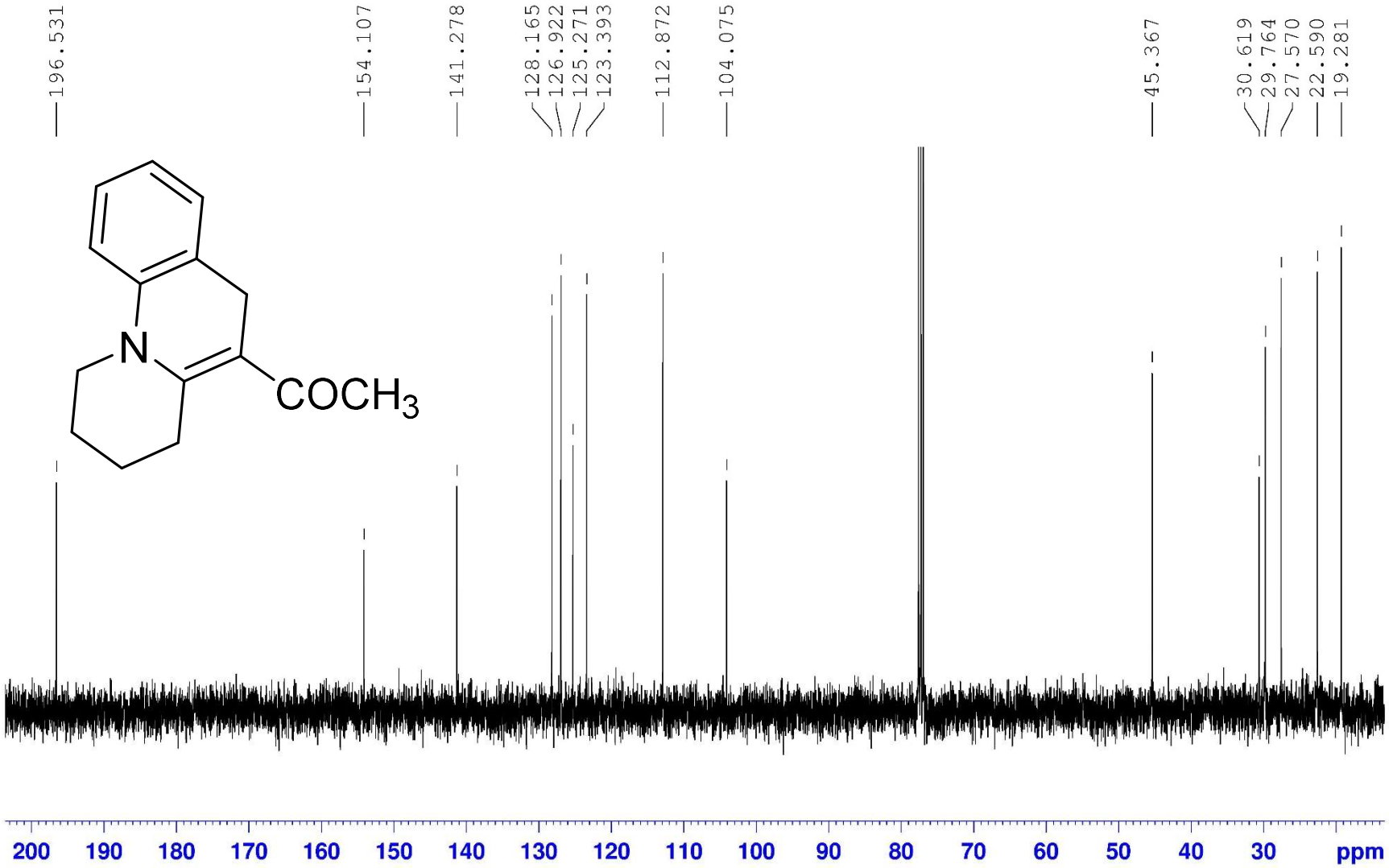

FIGURE S62: 100 MHz ^{13}C NMR spectrum of **11e** in $CDCl_3$.

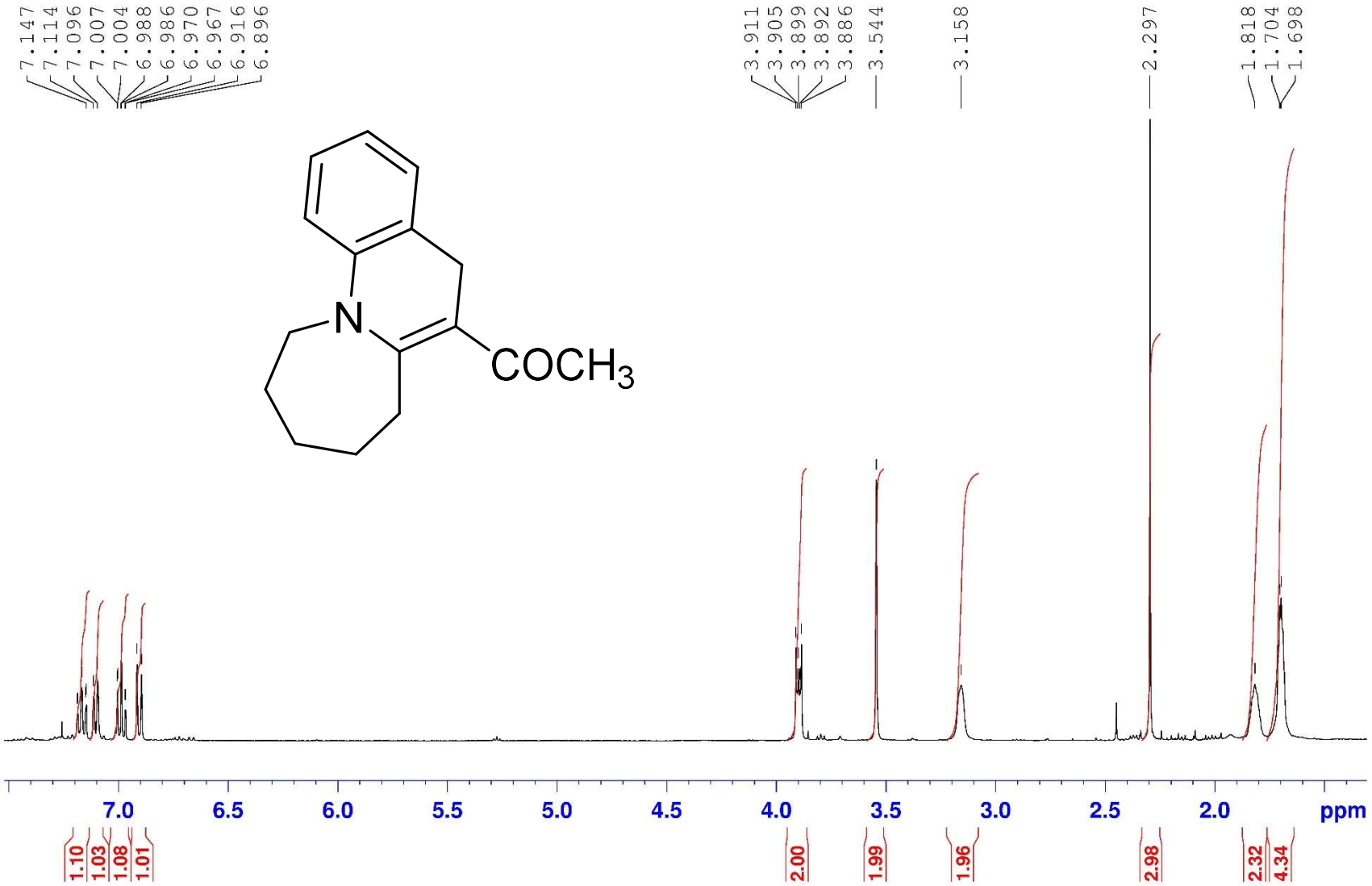

FIGURE S63: 400 MHz ^{1}H NMR spectrum of **11f** in $CDCl_3$.

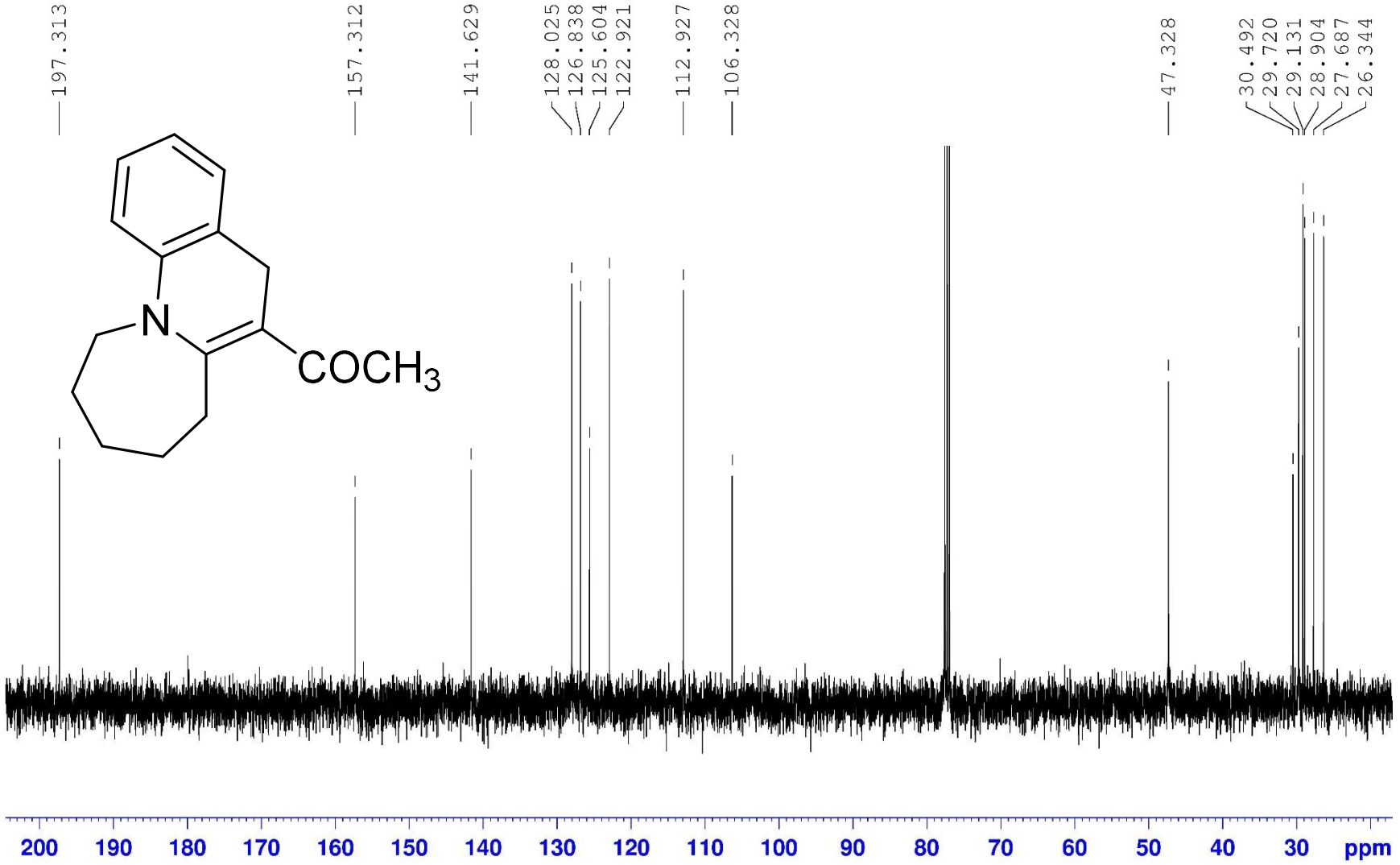

FIGURE S64: 100 MHz ^{13}C NMR spectrum of **11f** in $CDCl_3$.

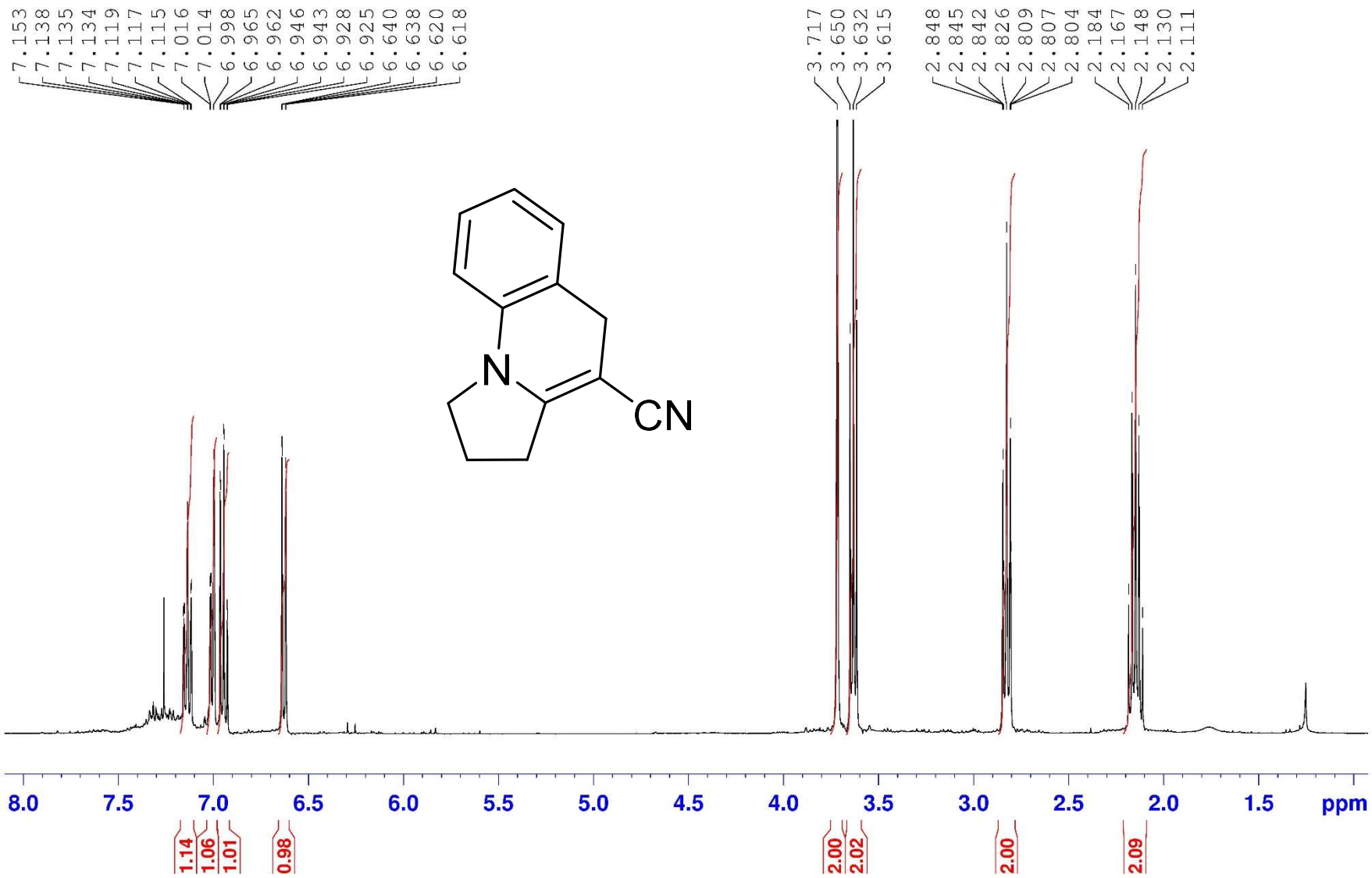

FIGURE S65: 400 MHz ^{1}H NMR spectrum of **11g** in $CDCl_3$.

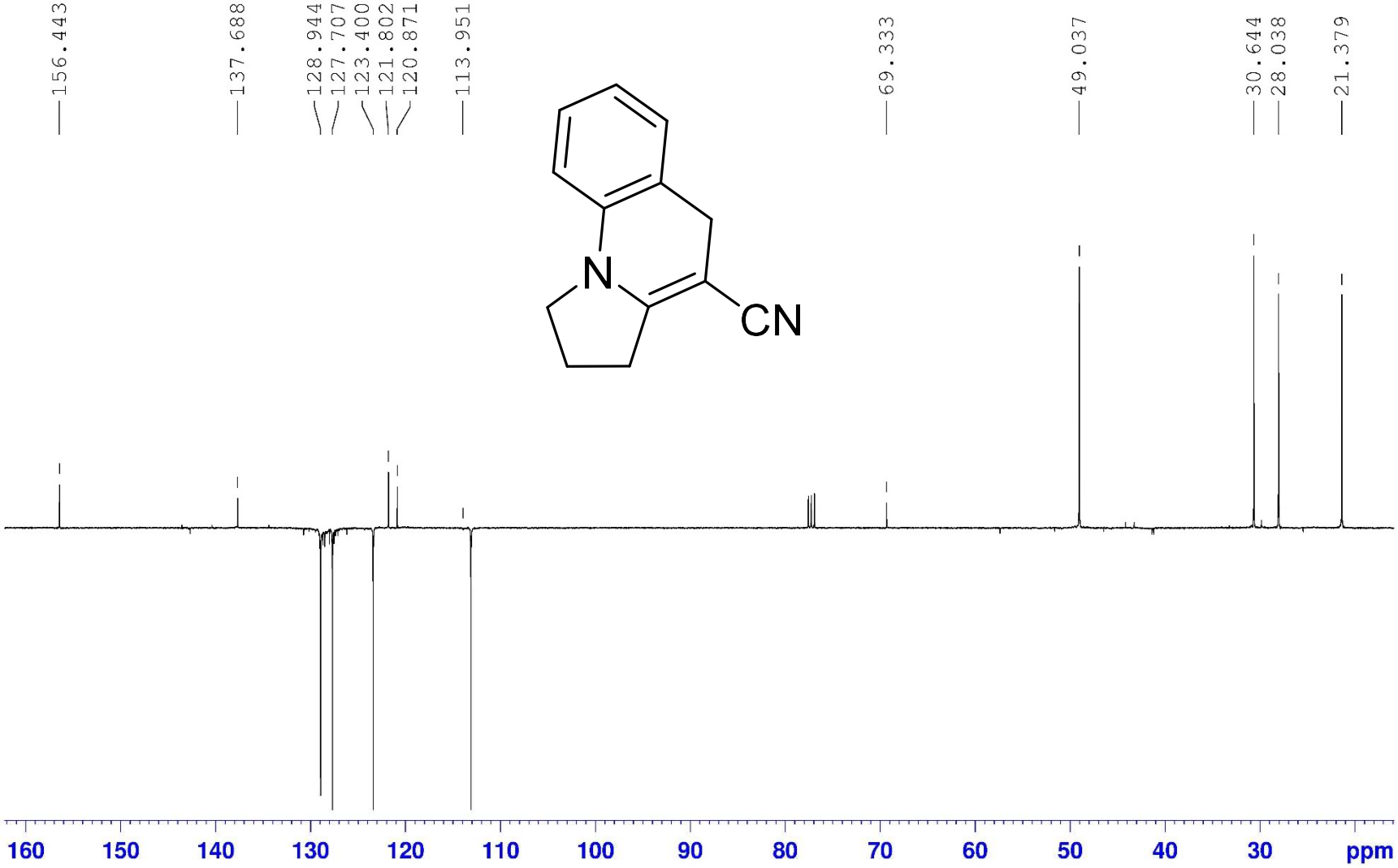

FIGURE S66: 100 MHz ^{13}C NMR (APT) spectrum of **11g** in $CDCl_3$.

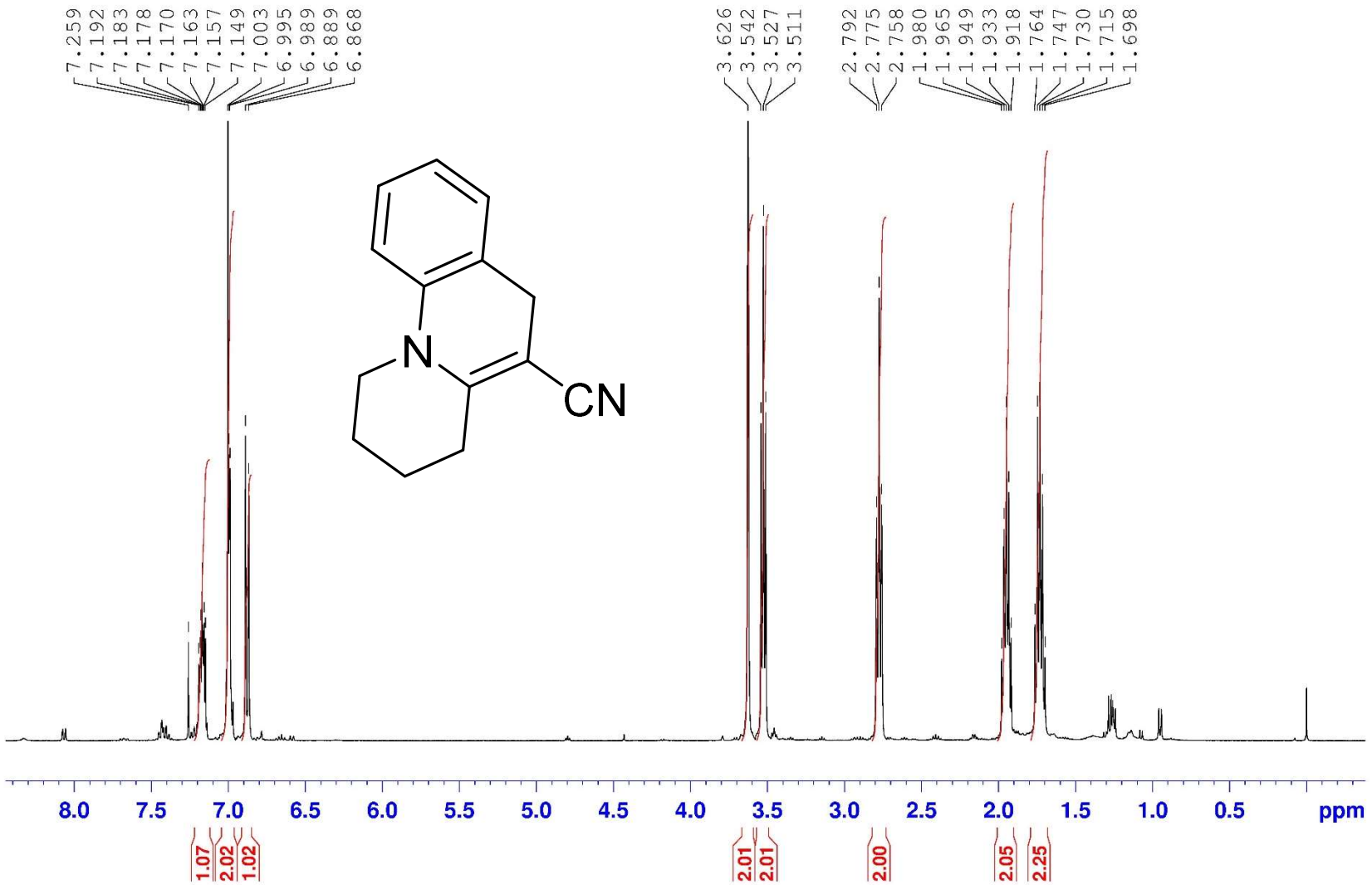

FIGURE S67: 400 MHz ^{1}H NMR spectrum of **11h** in $CDCl_3$.

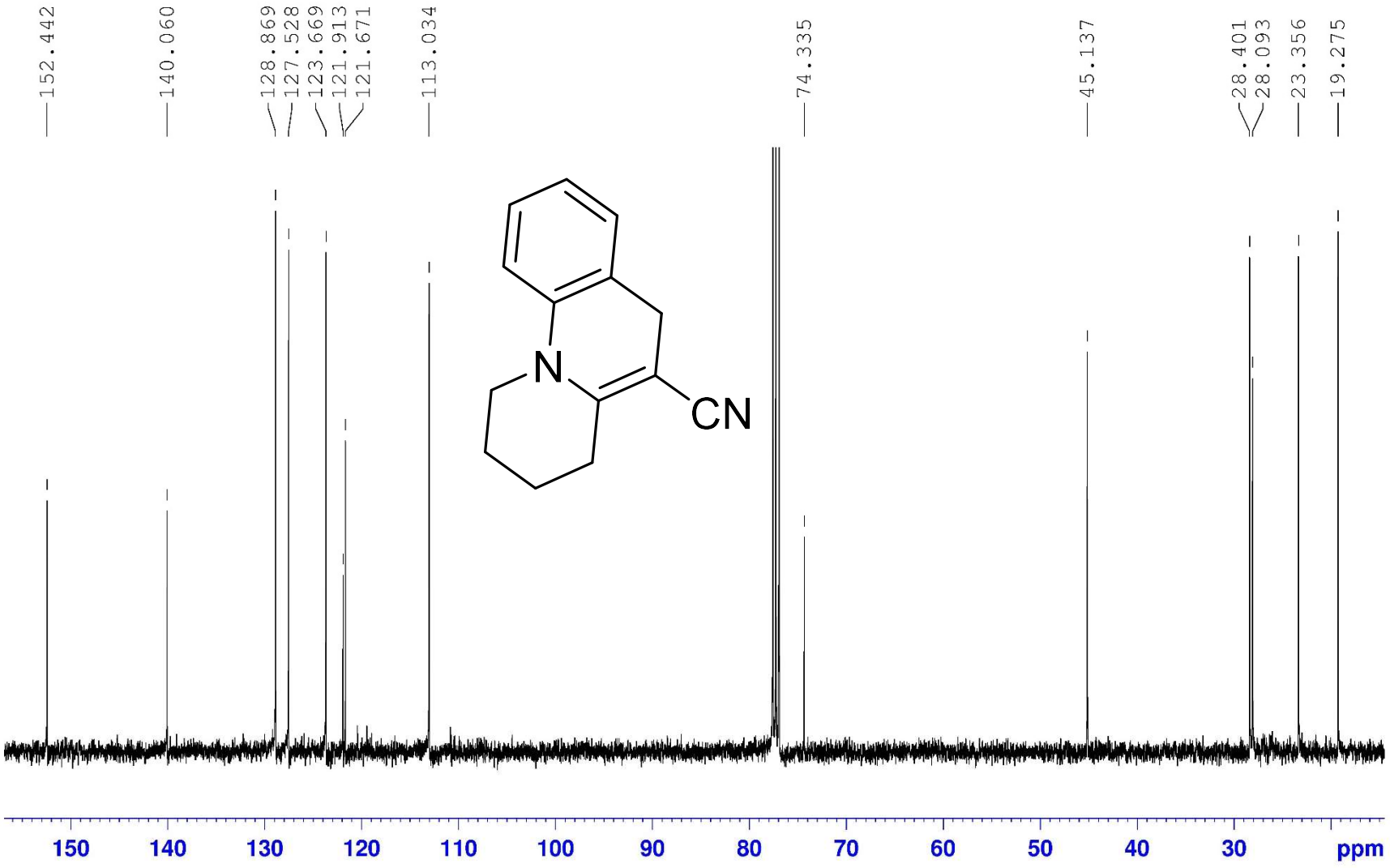

FIGURE S68: 100 MHz ^{13}C NMR spectrum of **11h** in $CDCl_3$.

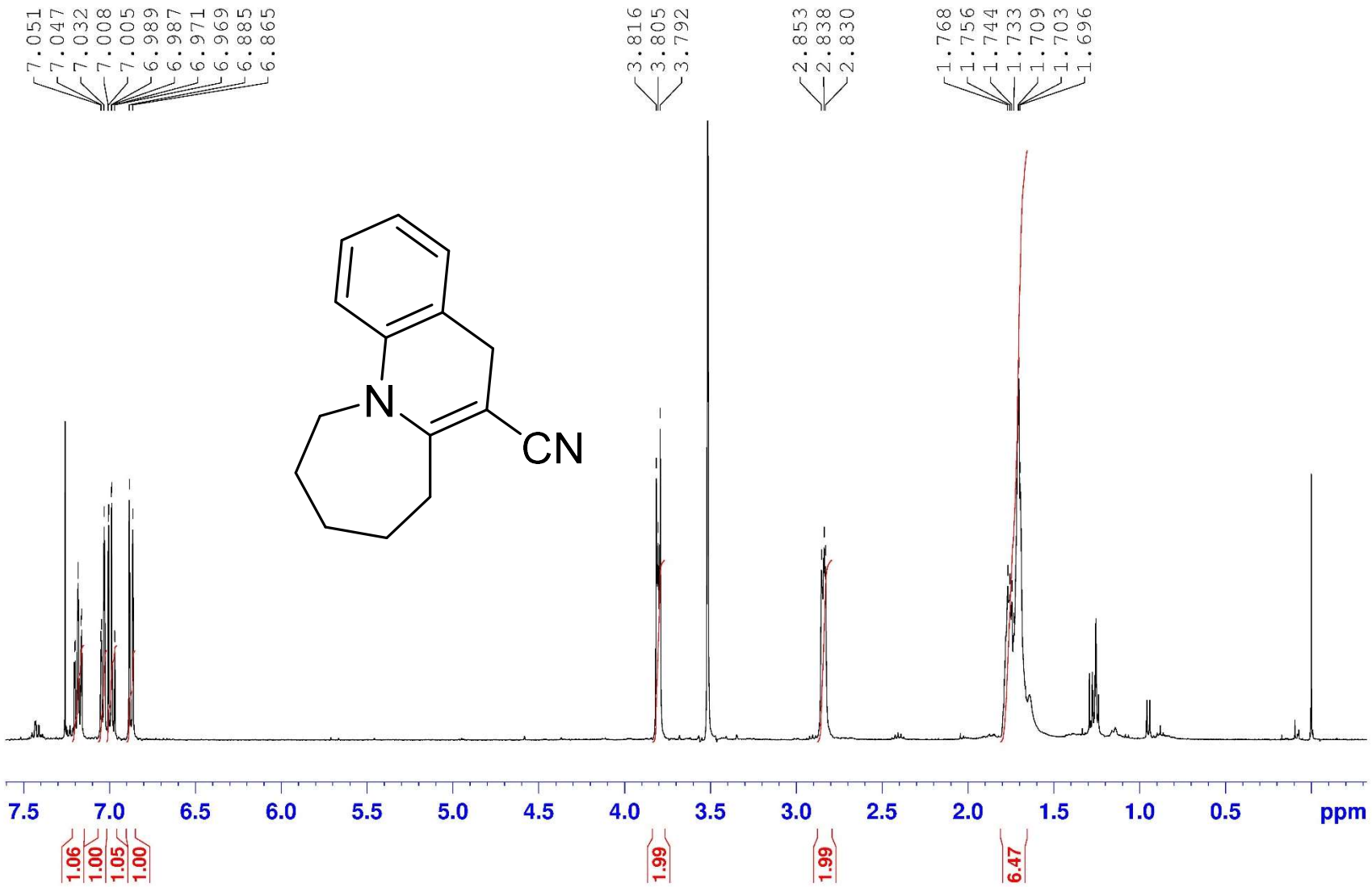

FIGURE S69: 400 MHz ^{1}H NMR spectrum of **11i** in $CDCl_3$.

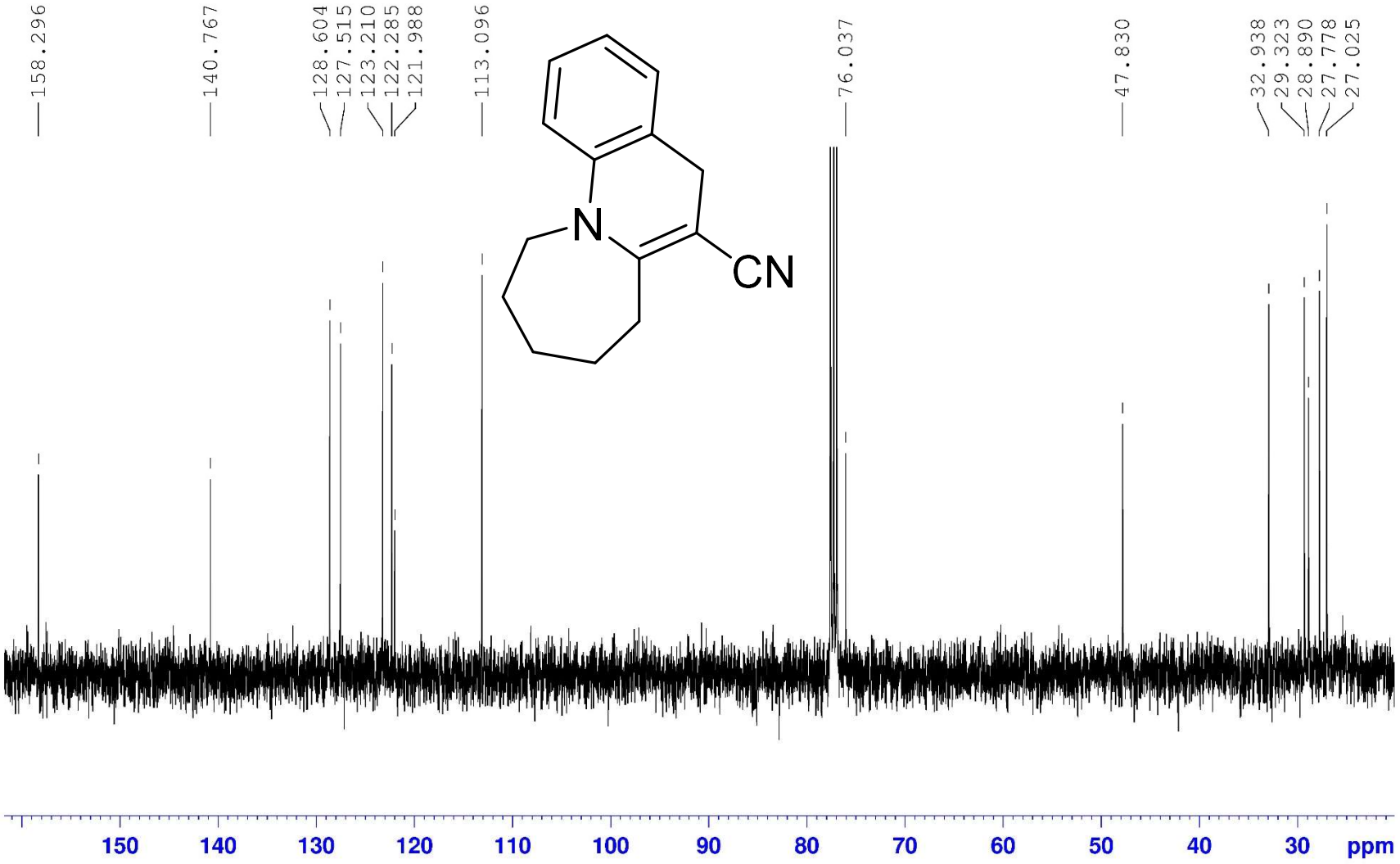

FIGURE S70: 100 MHz ^{13}C NMR spectrum of **11i** in $CDCl_3$

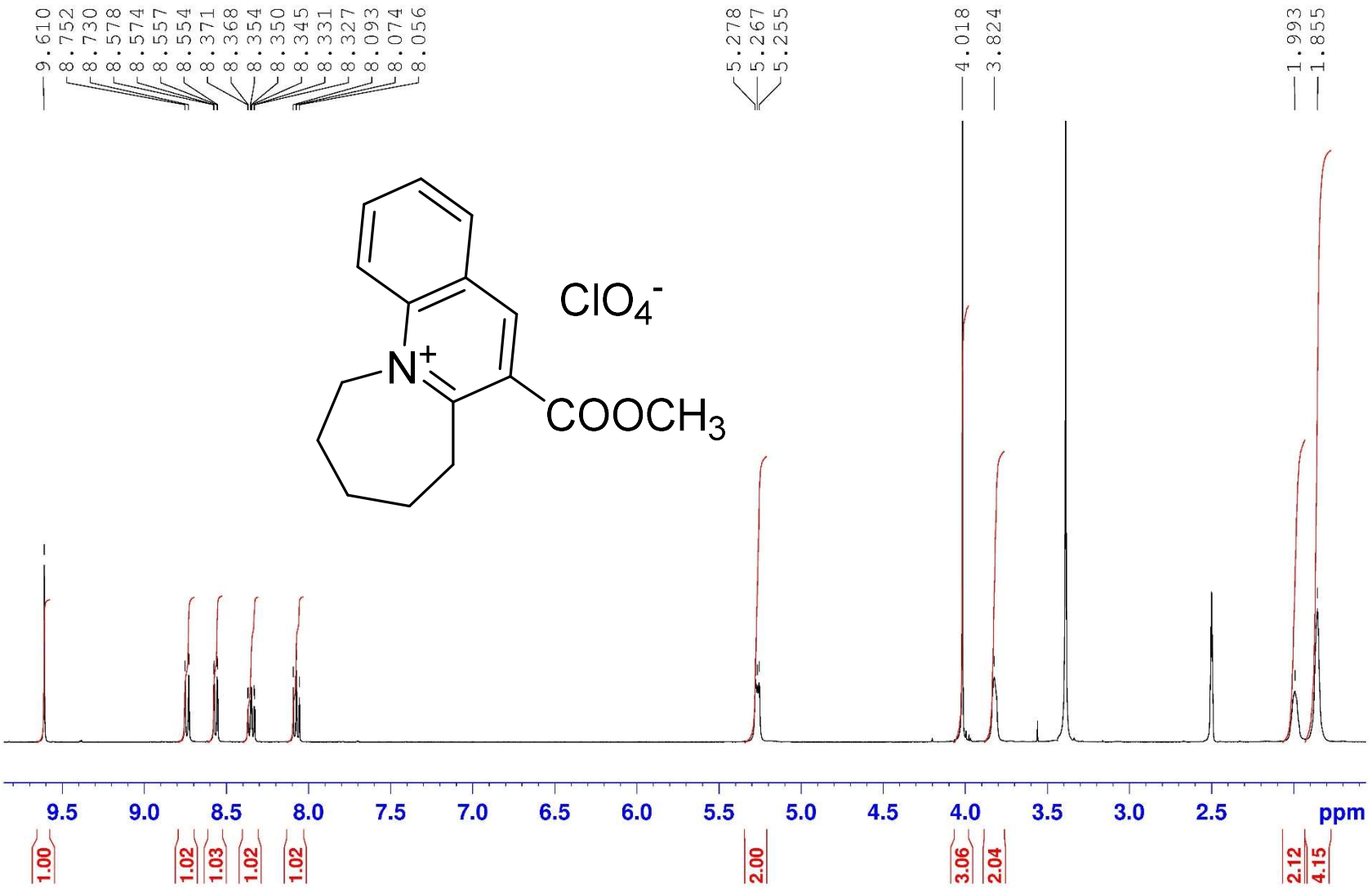

FIGURE S71: 400 MHz ^{1}H NMR spectrum of **12d** in DMSO.

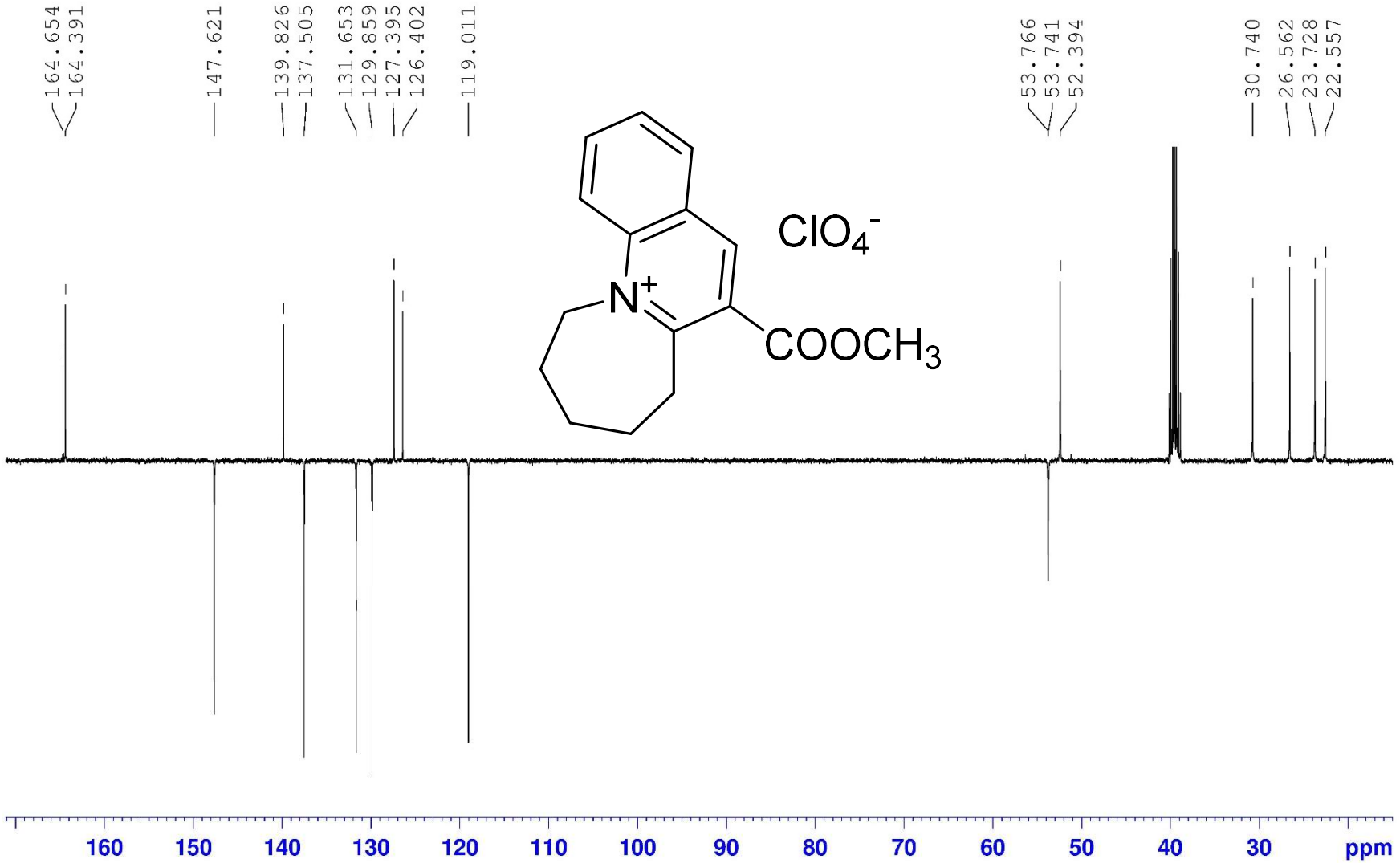

FIGURE S72: 100 MHz ^{13}C (APT) NMR spectrum of **12d** in DMSO.

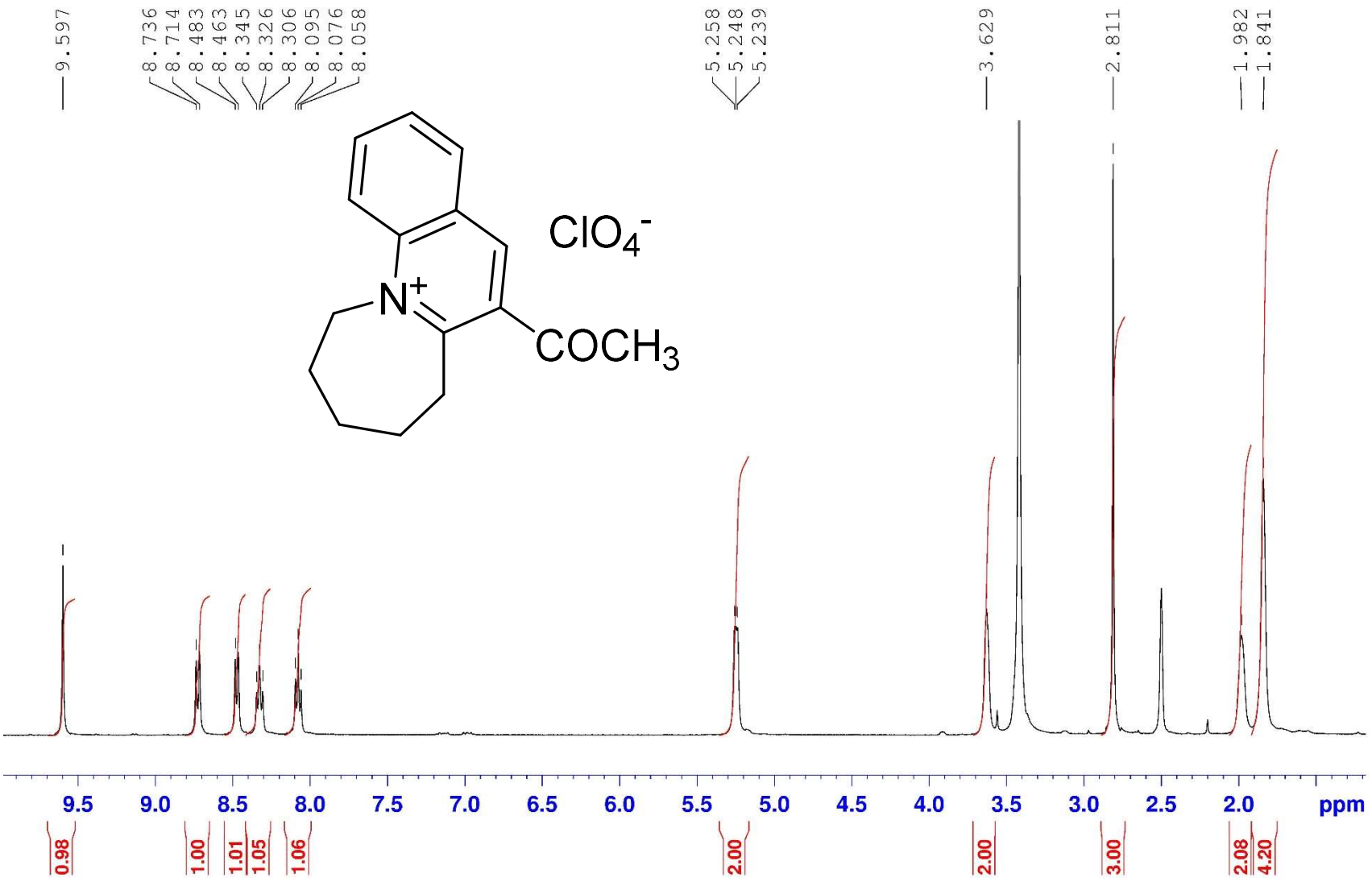

FIGURE S73: 400 MHz ^{1}H NMR spectrum of **12b** in DMSO.

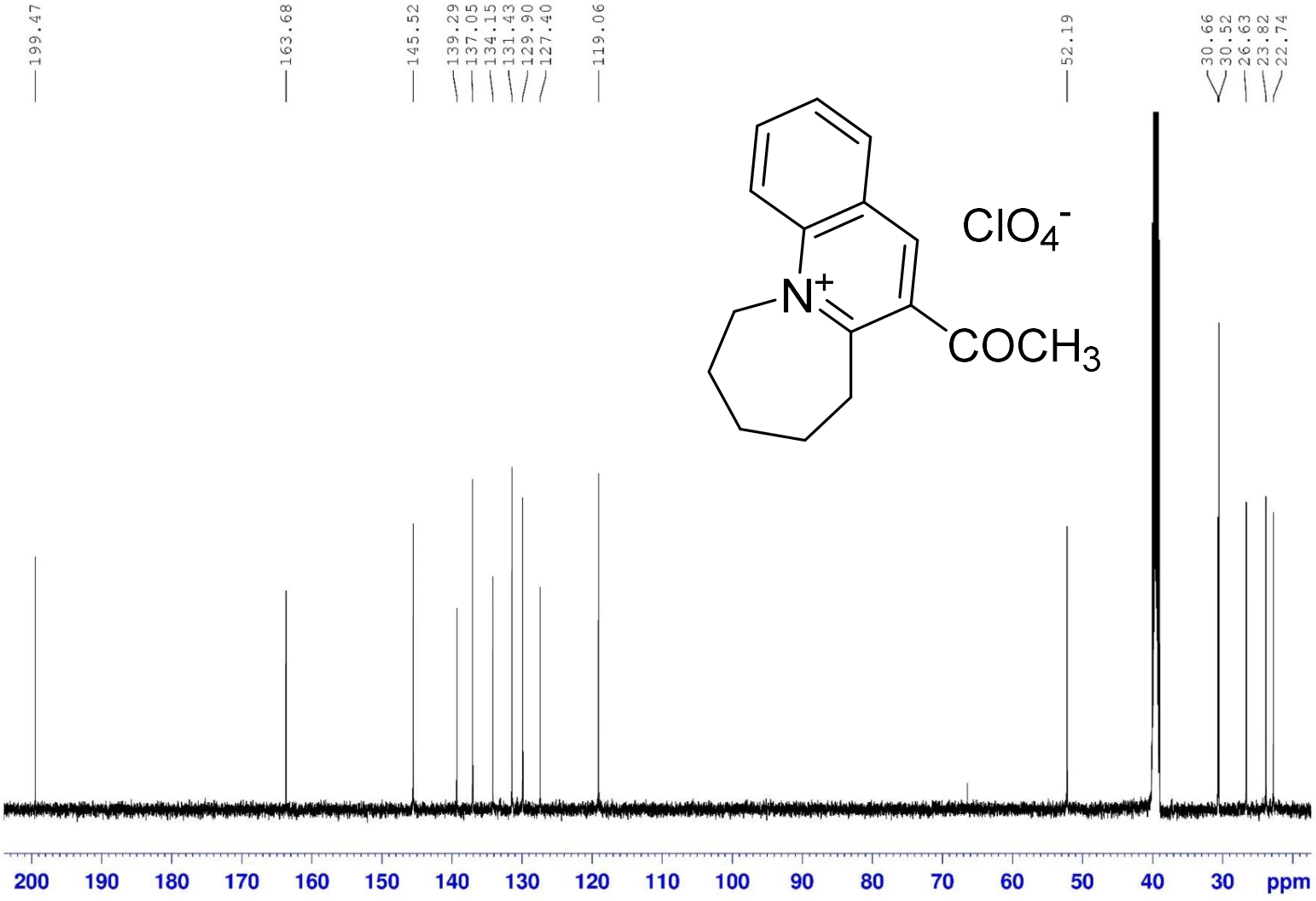

FIGURE S74: 125 MHz ^{13}C NMR spectrum of **12b** in DMSO.

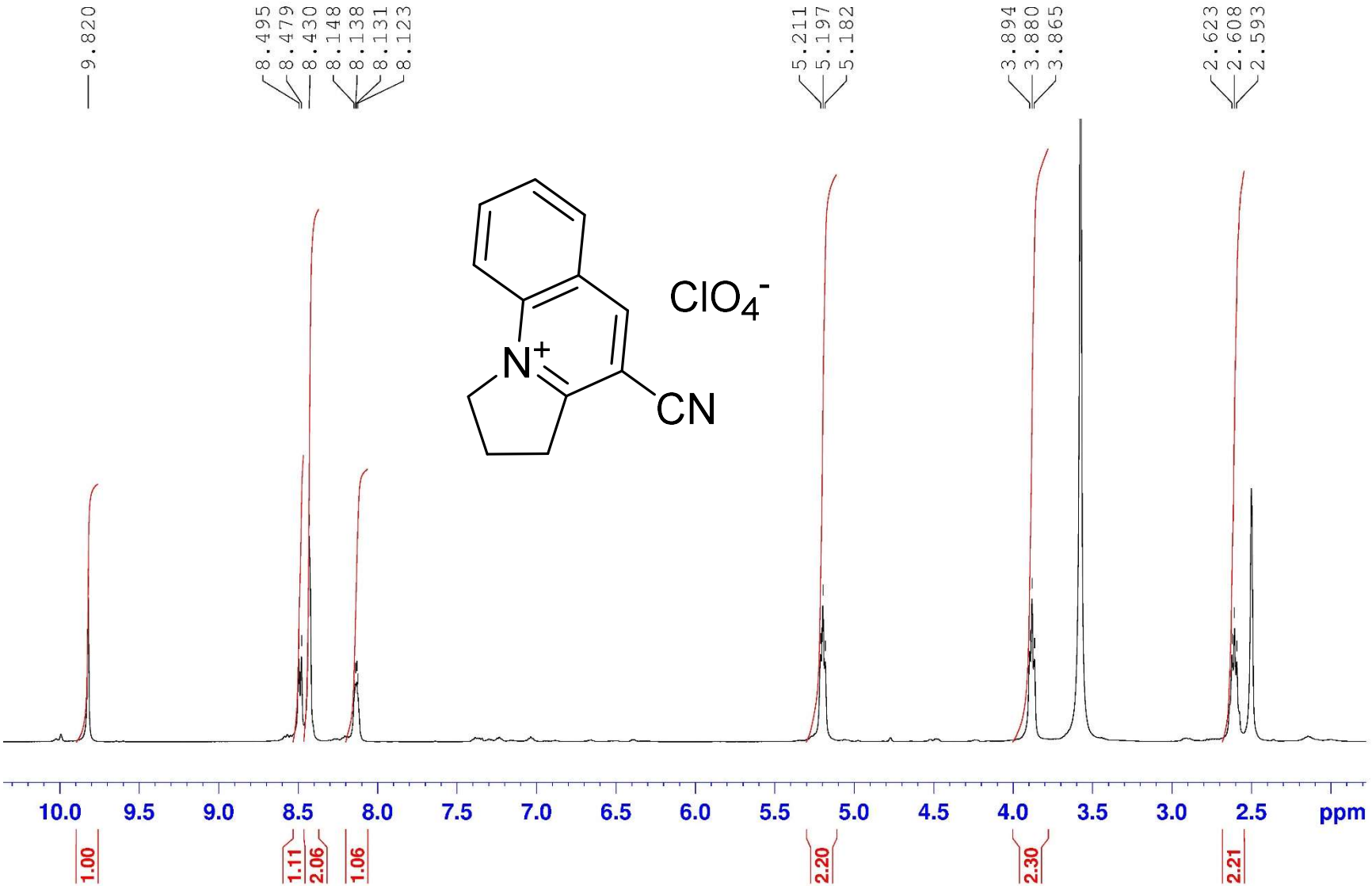

FIGURE S75: 500 MHz ^{1}H NMR spectrum of **12a** in DMSO.

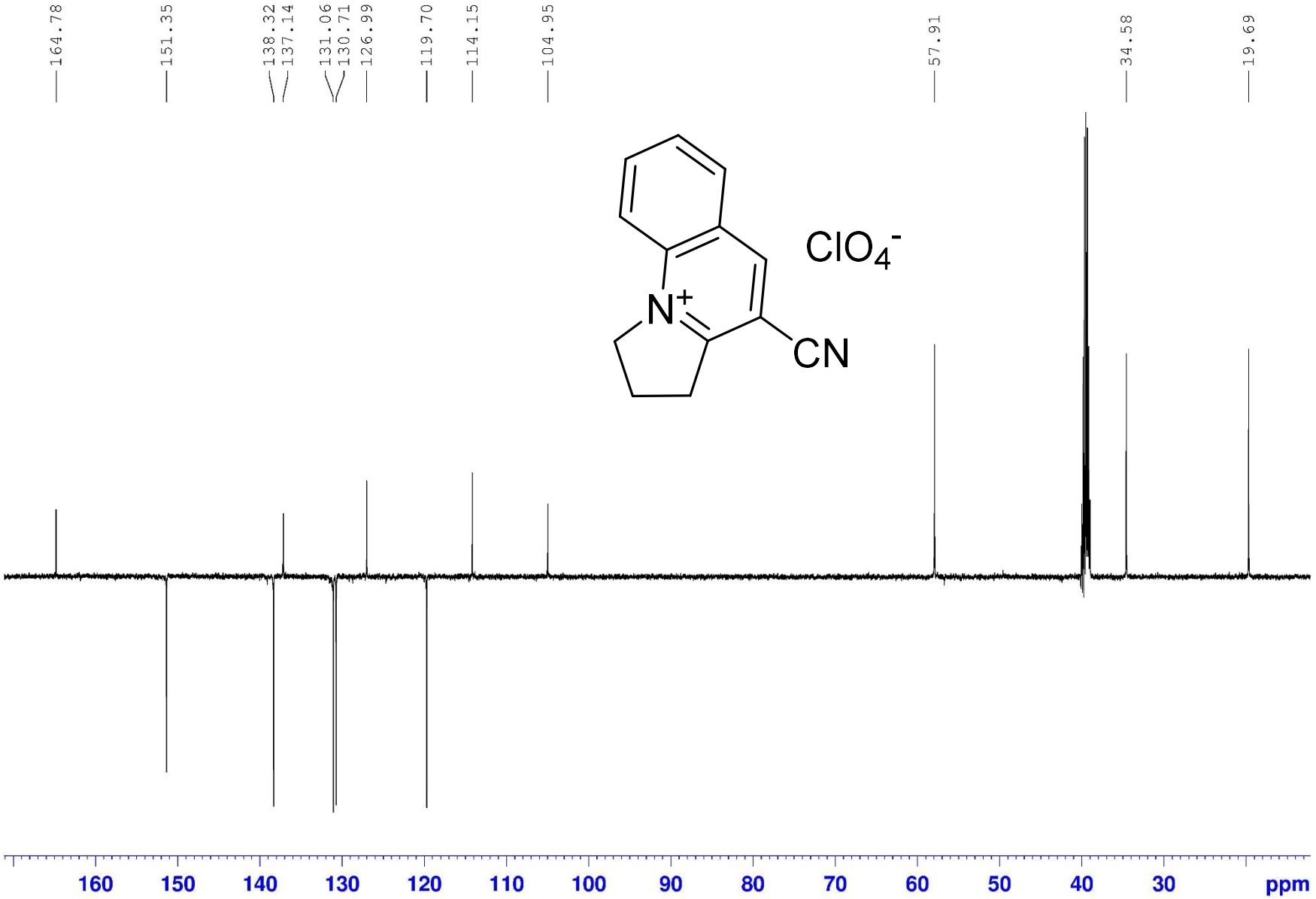

FIGURE S76: 125 MHz APT spectrum of **12a** in DMSO.

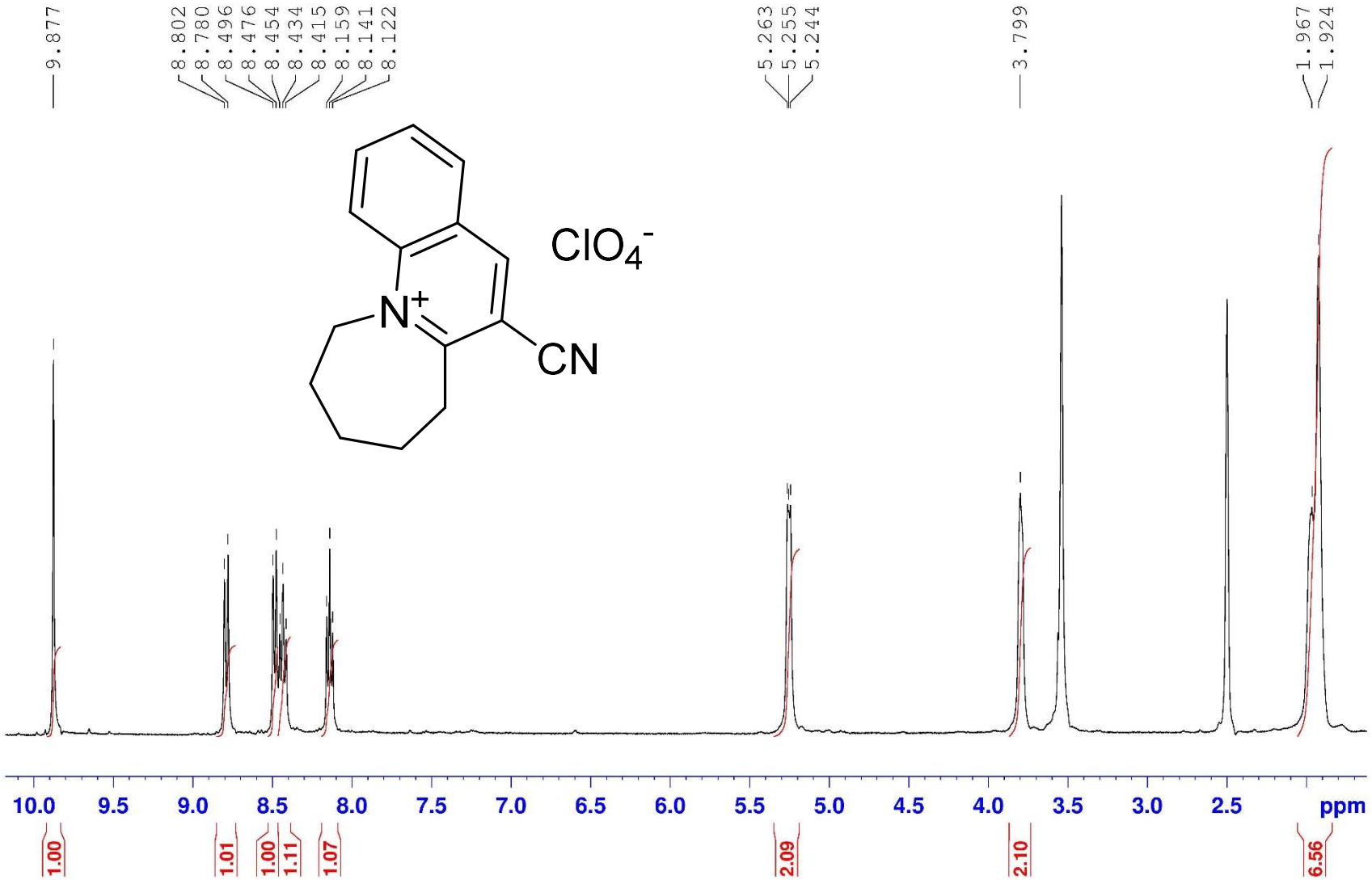

FIGURE S77: 400 MHz ^{1}H NMR spectrum of **12c** in DMSO.

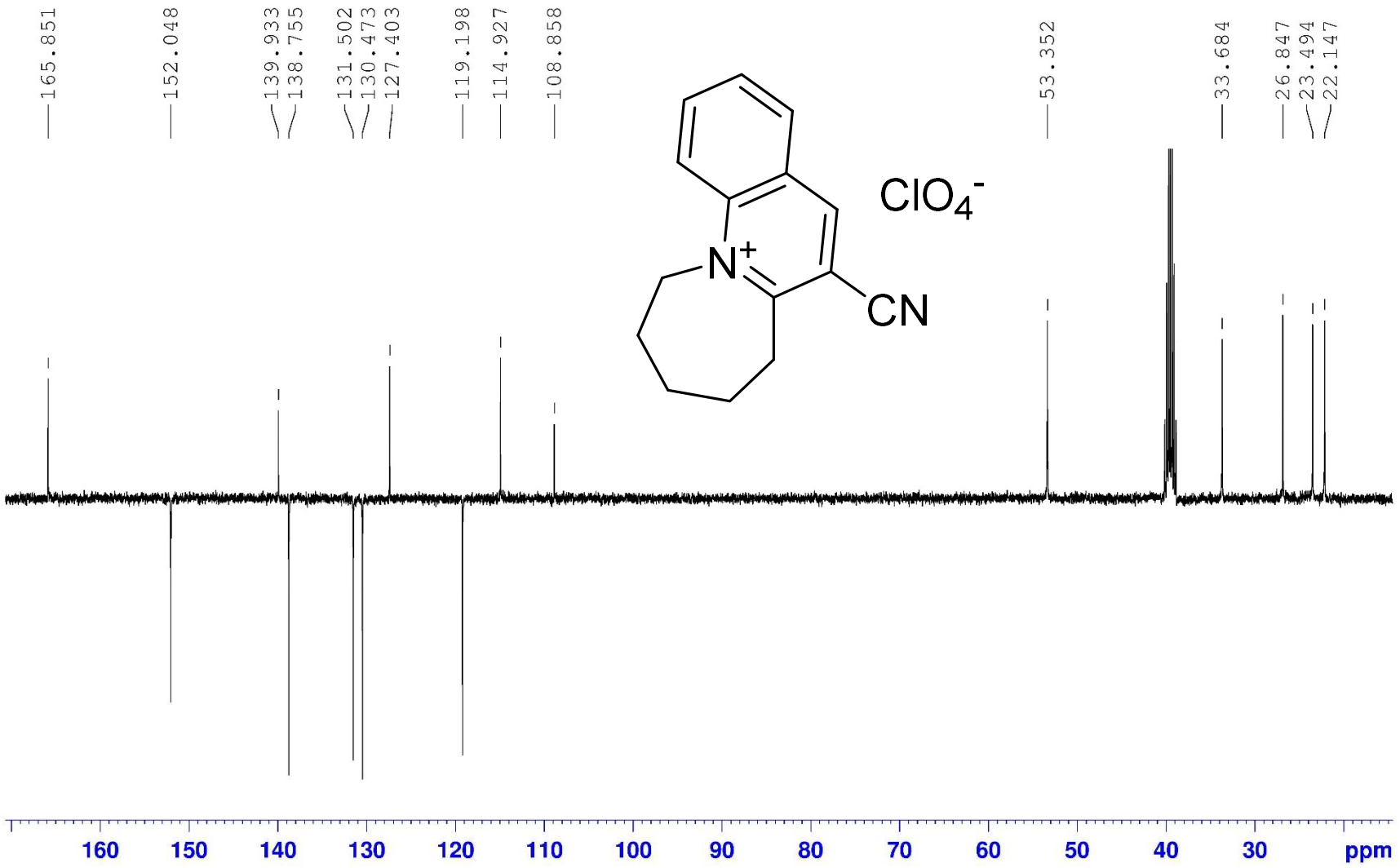

FIGURE S78: 100 MHz ^{13}C (APT) spectrum of **12c** in DMSO.

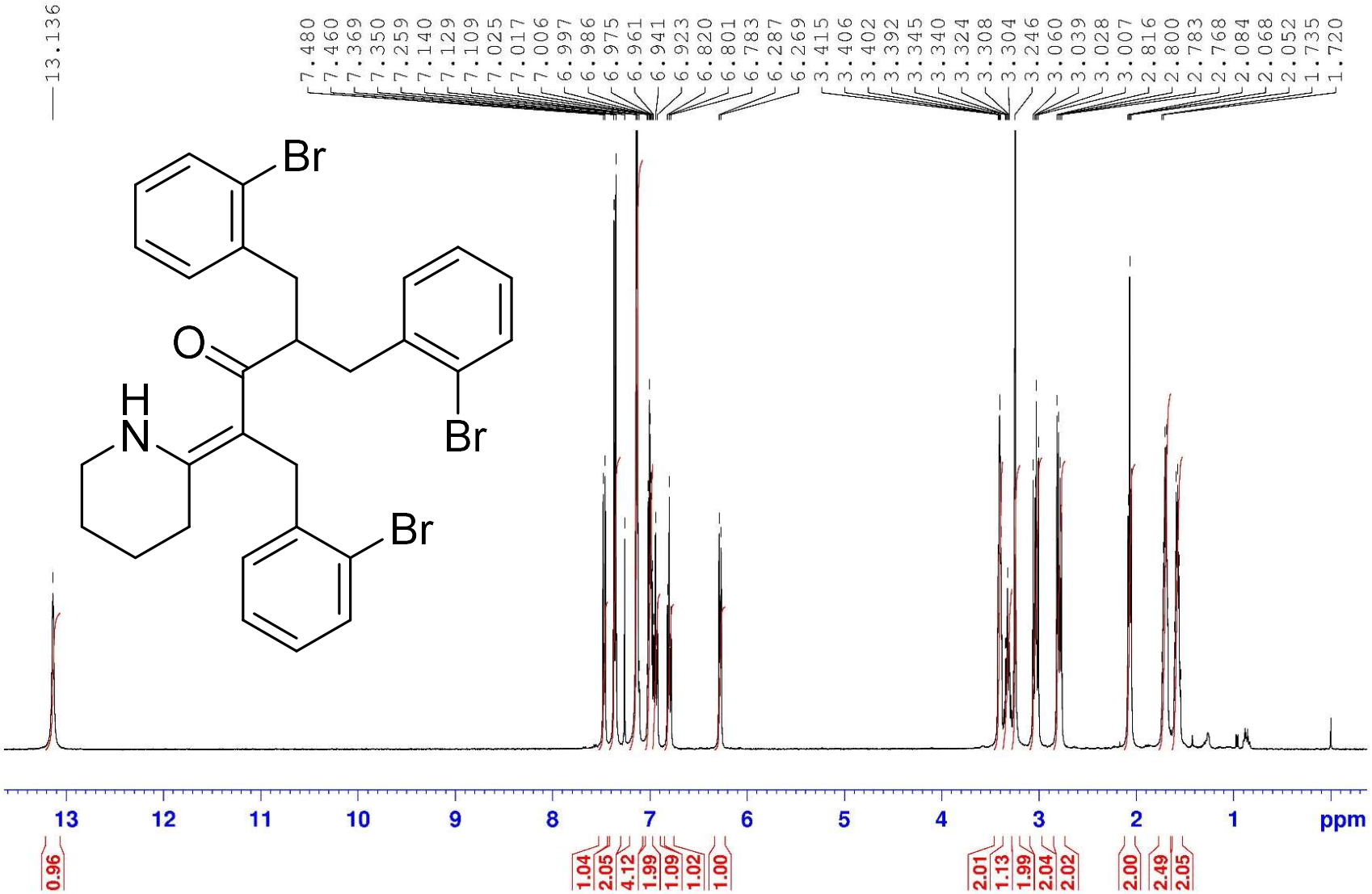

FIGURE S79: 400 MHz ^{1}H NMR spectrum of **10a** in $CDCl_3$.

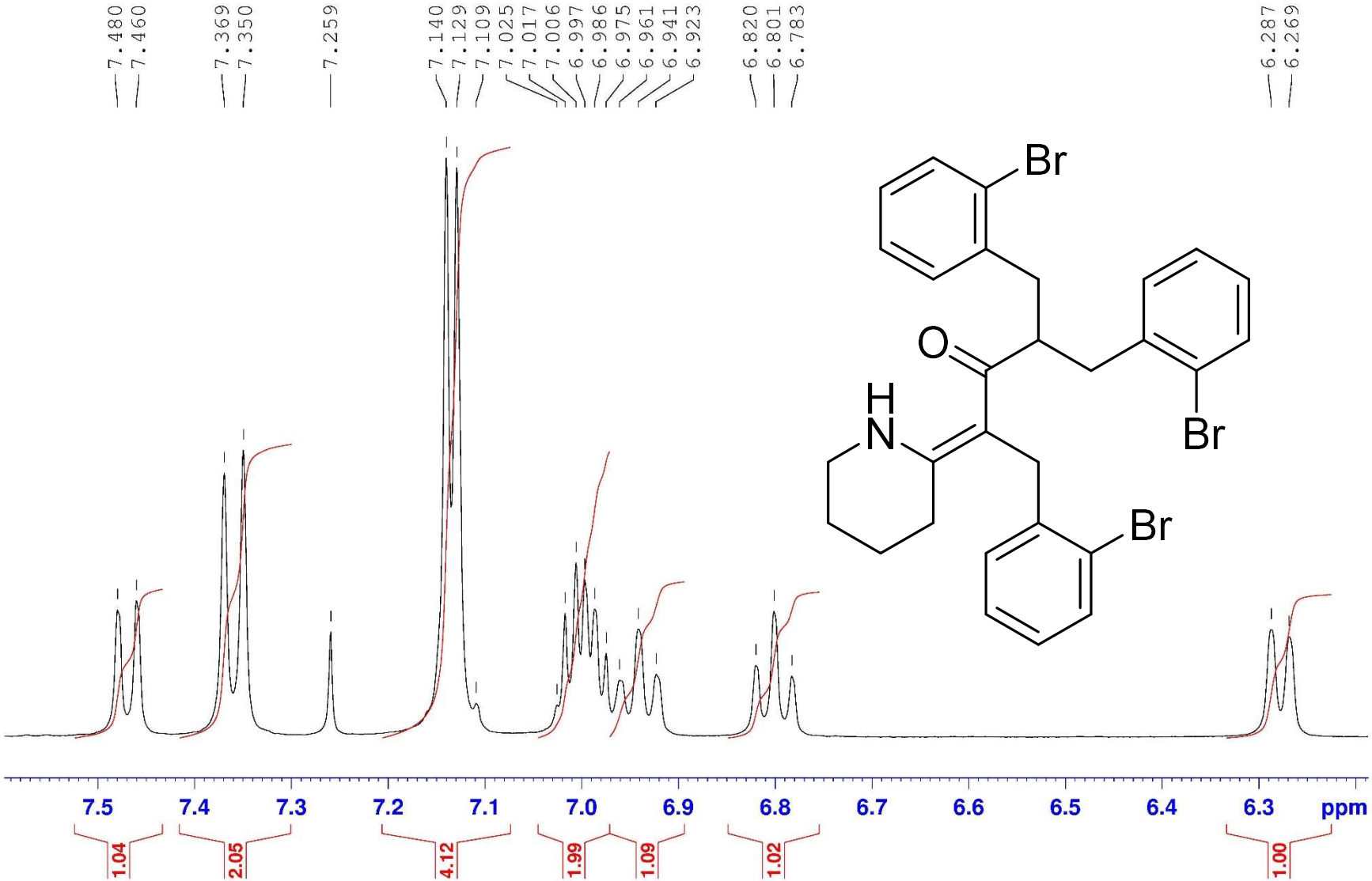

FIGURE S79A: 400 MHz ^{1}H NMR spectrum of **10a** in $CDCl_3$. Detail of the aromatic region.

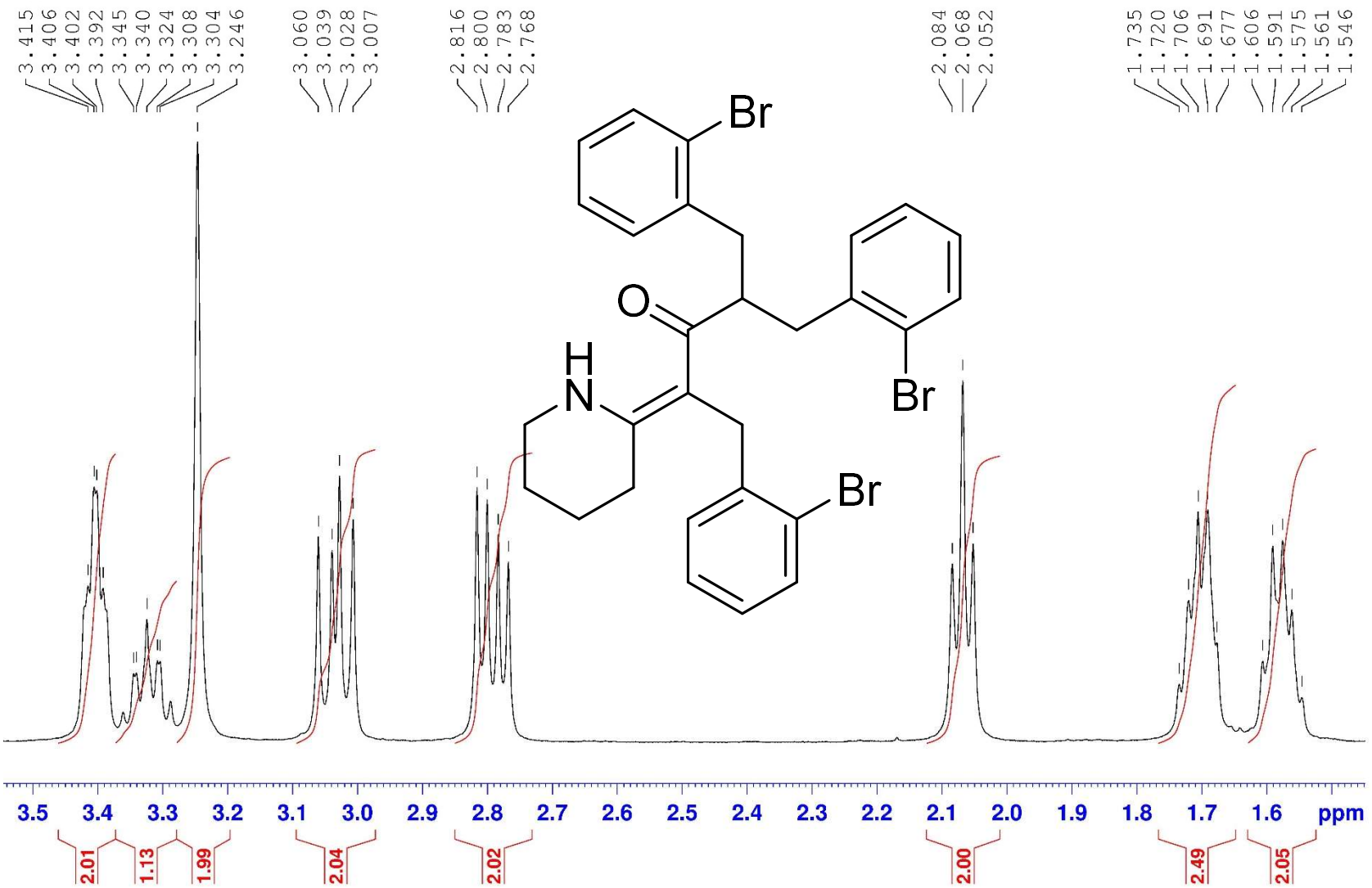

FIGURE S79B: 400 MHz ^{1}H NMR spectrum of **10a** in $CDCl_3$. Detail of the upfield region.

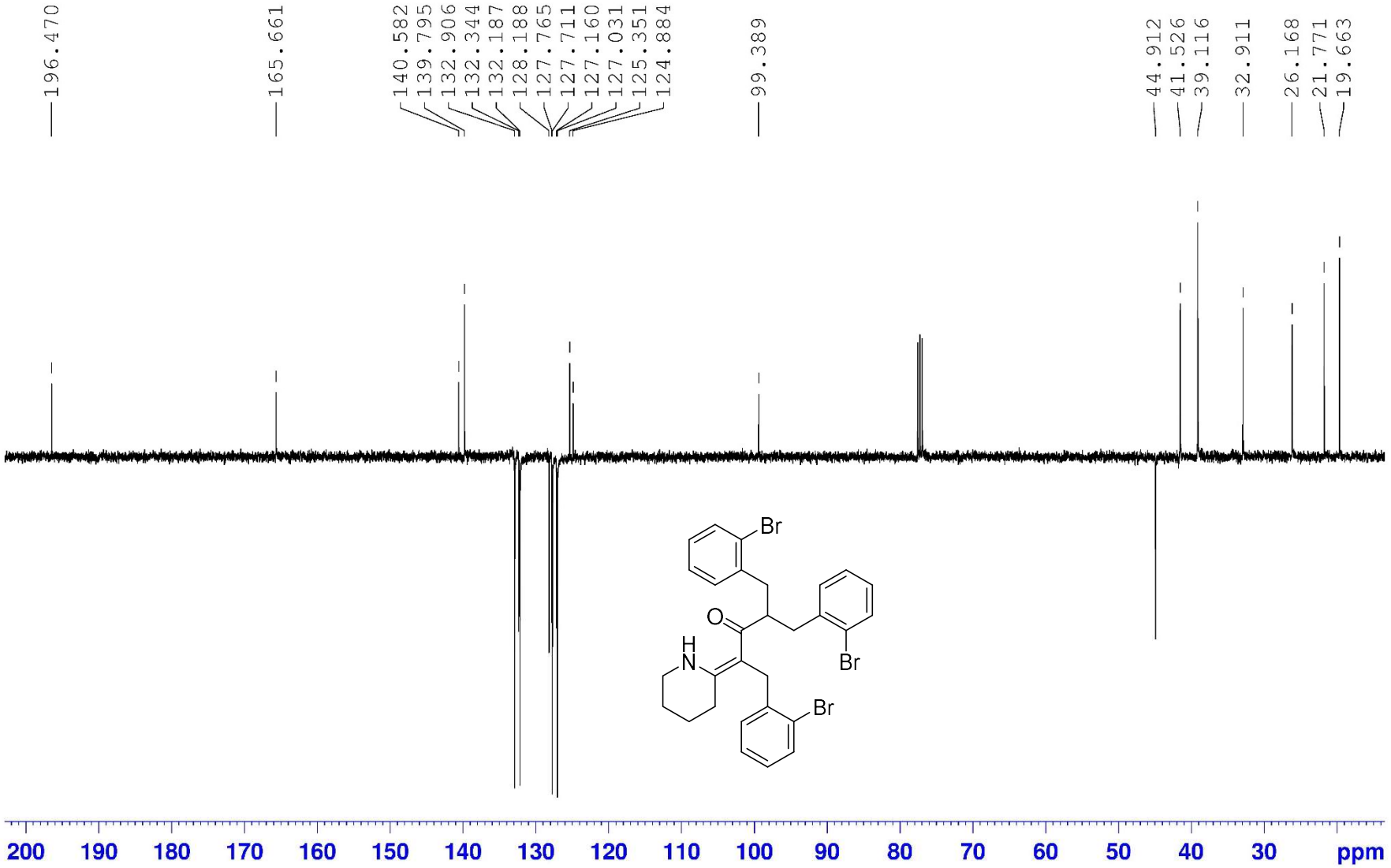

FIGURE S80: 100 MHz ^{13}C (APT) NMR spectrum of **10a** in $CDCl_3$.

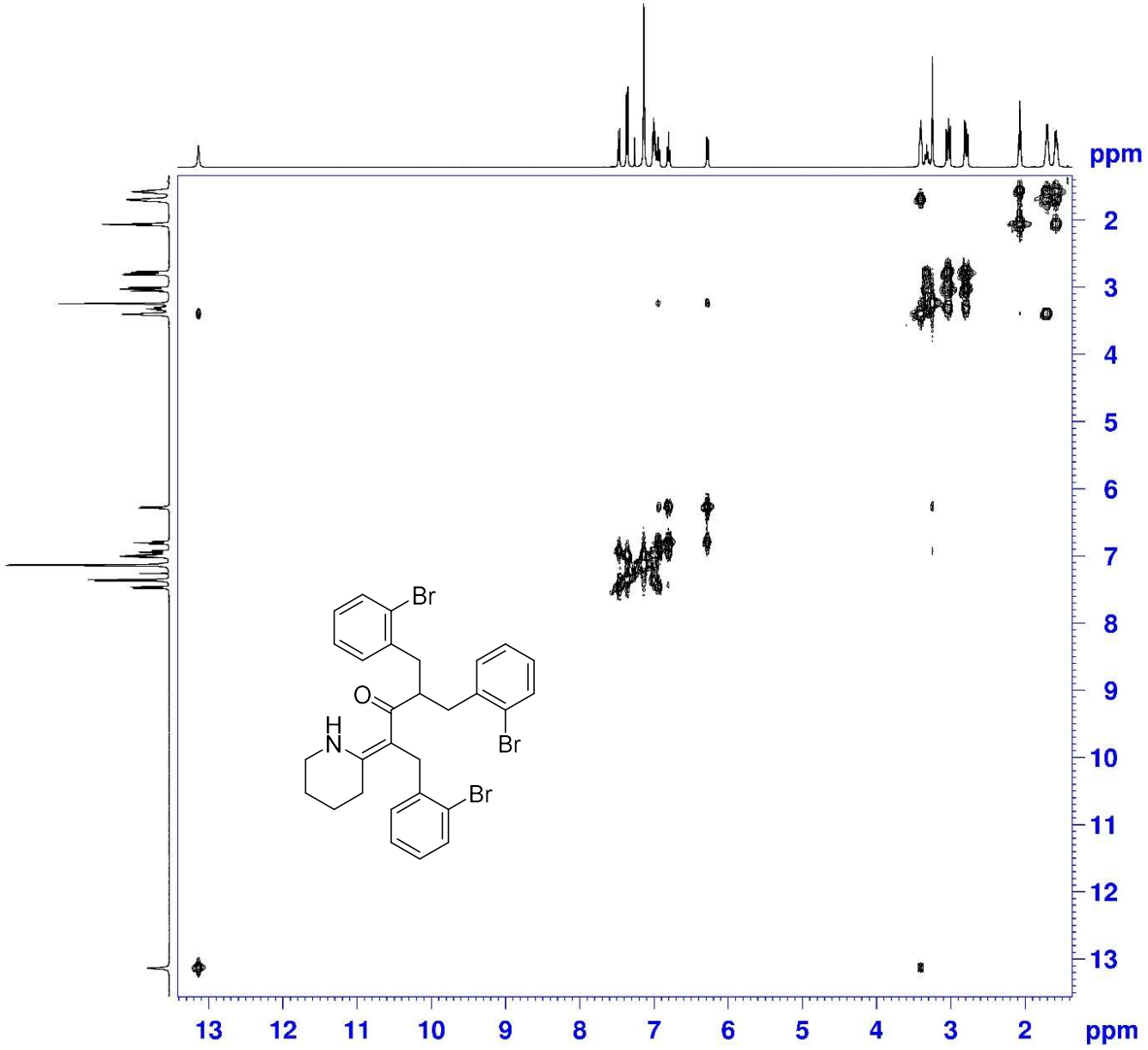

FIGURE S81: 400 MHz ^{1}H–^{1}H COSY spectrum of **10a** in $CDCl_3$.

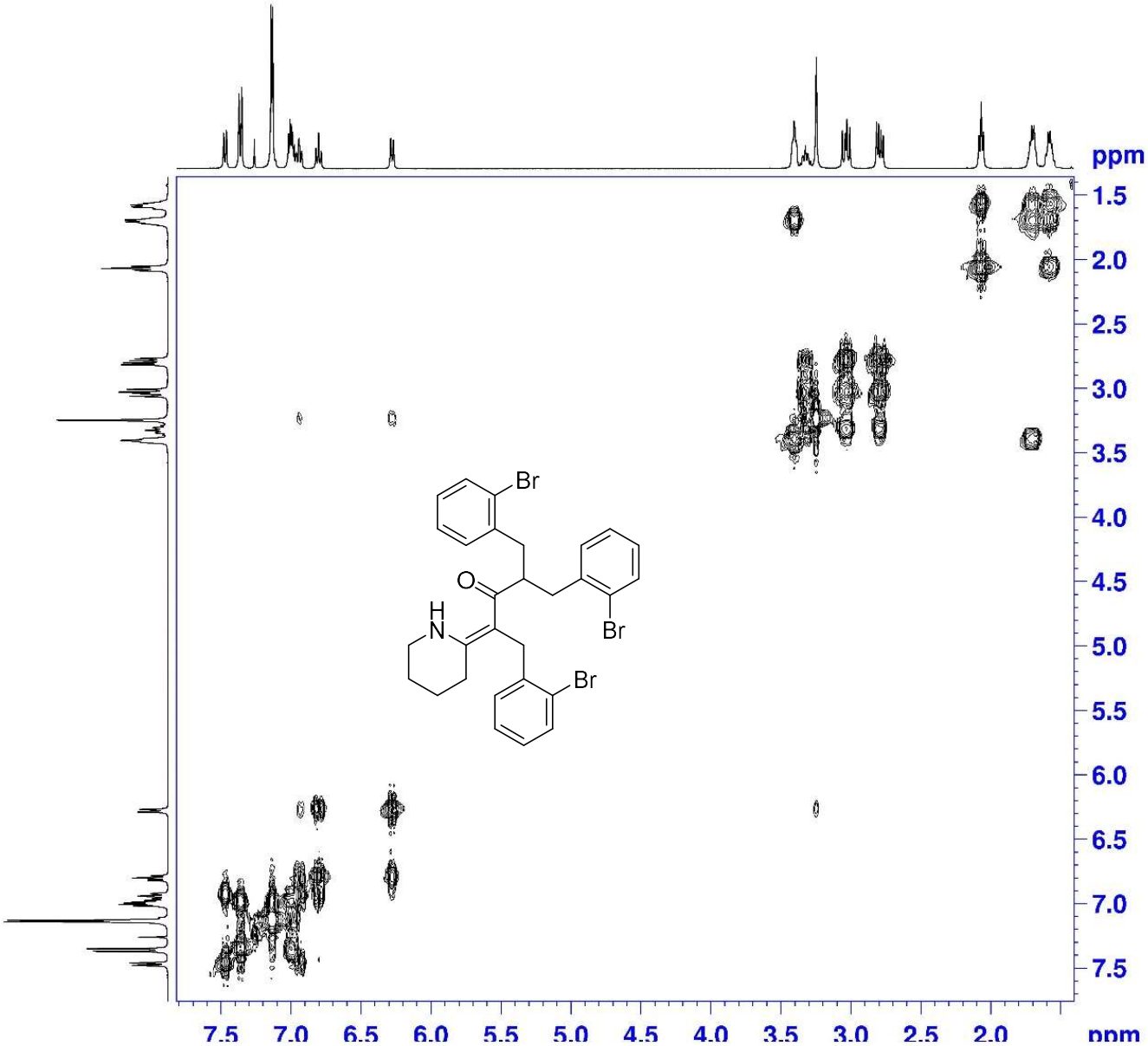

FIGURE S81A: Detail of 400 MHz ^{1}H–^{1}H COSY spectrum of **10a** in $CDCl_3$.

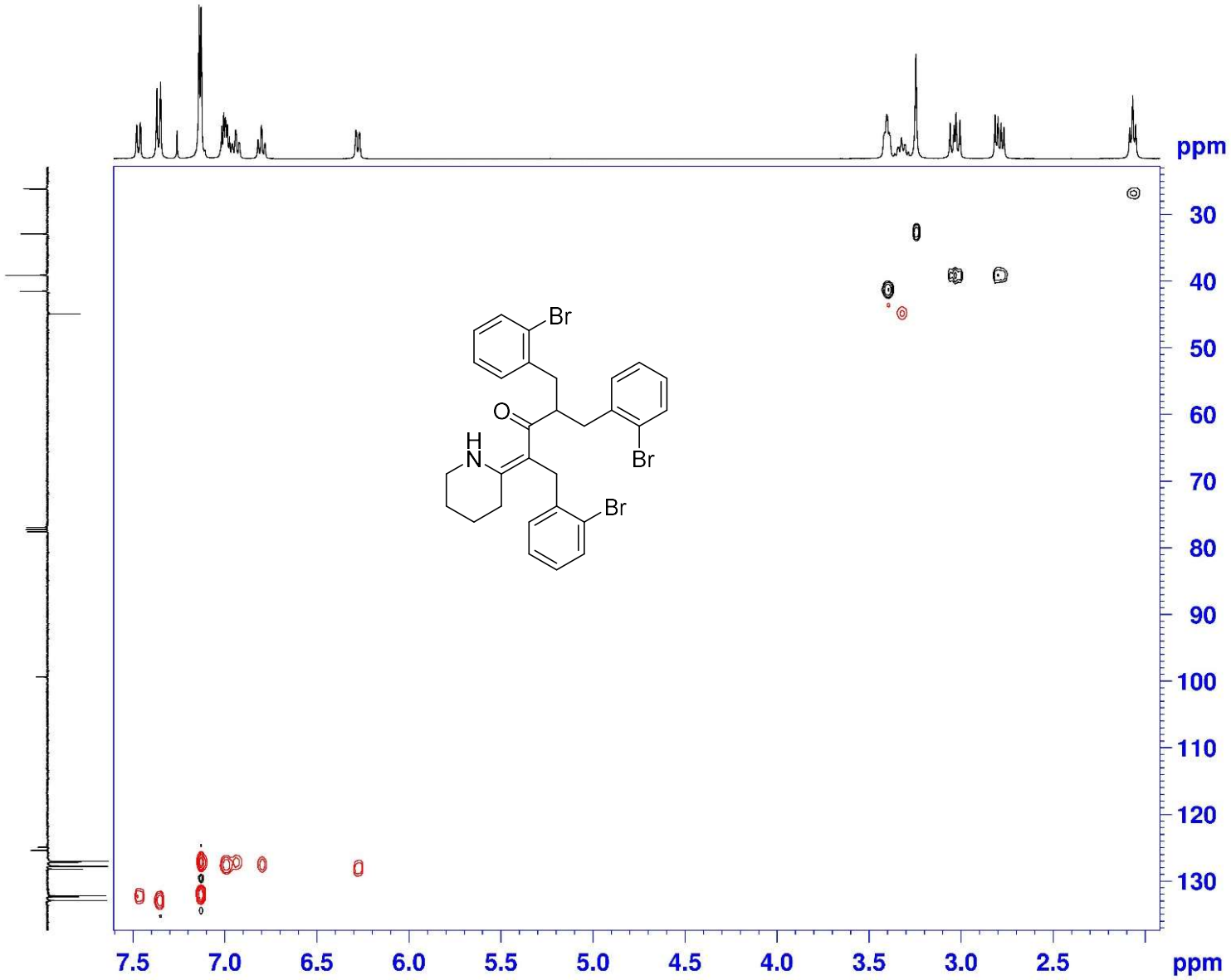

FIGURE S82: 400 MHz edited ^{1}H–^{13}C HSQC spectrum of **10a** in $CDCl_3$. CH_2 carbons black, CH carbons red.

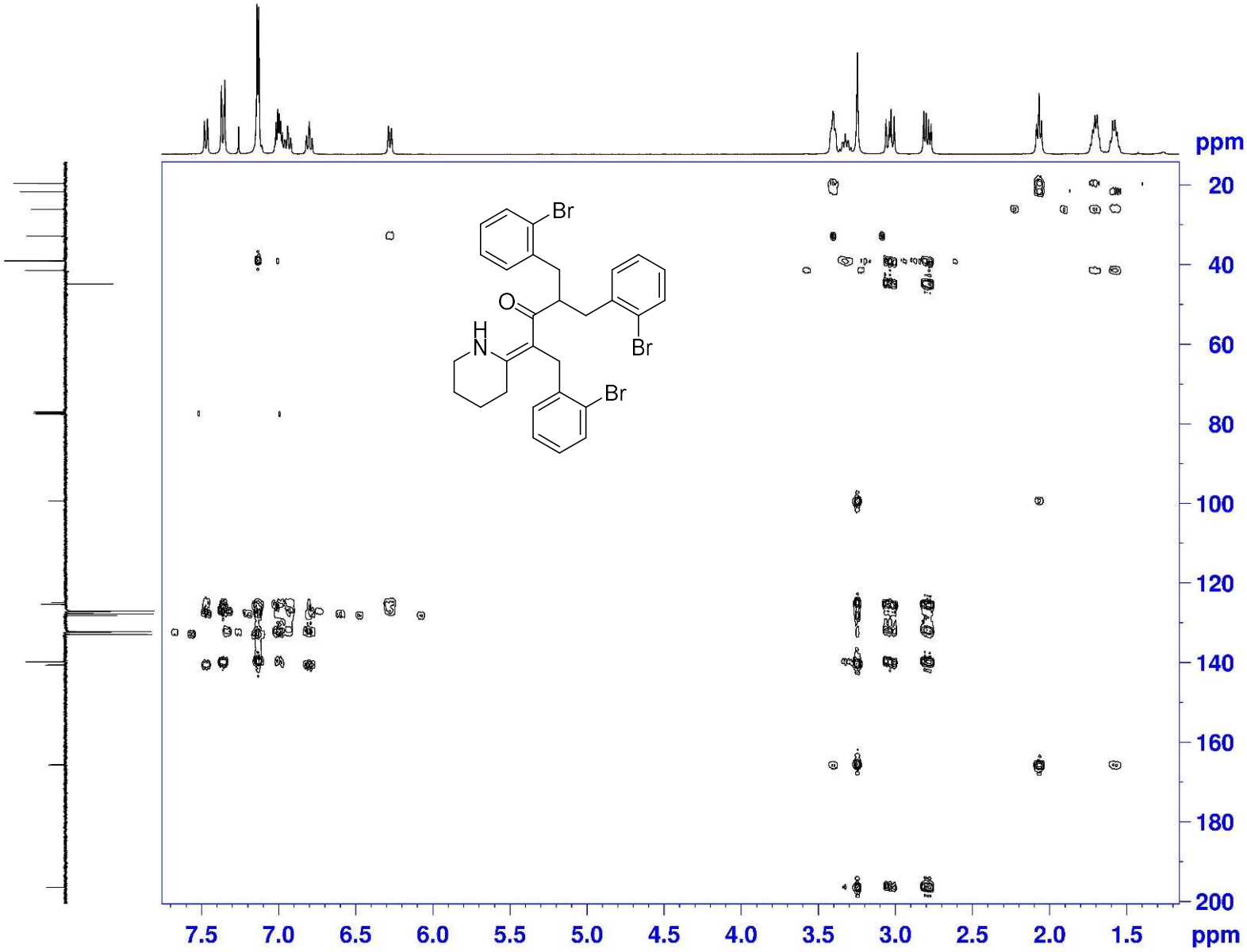

FIGURE S83: 400 MHz ^{1}H–^{13}C HMBC spectrum of **10a** in $CDCl_3$.

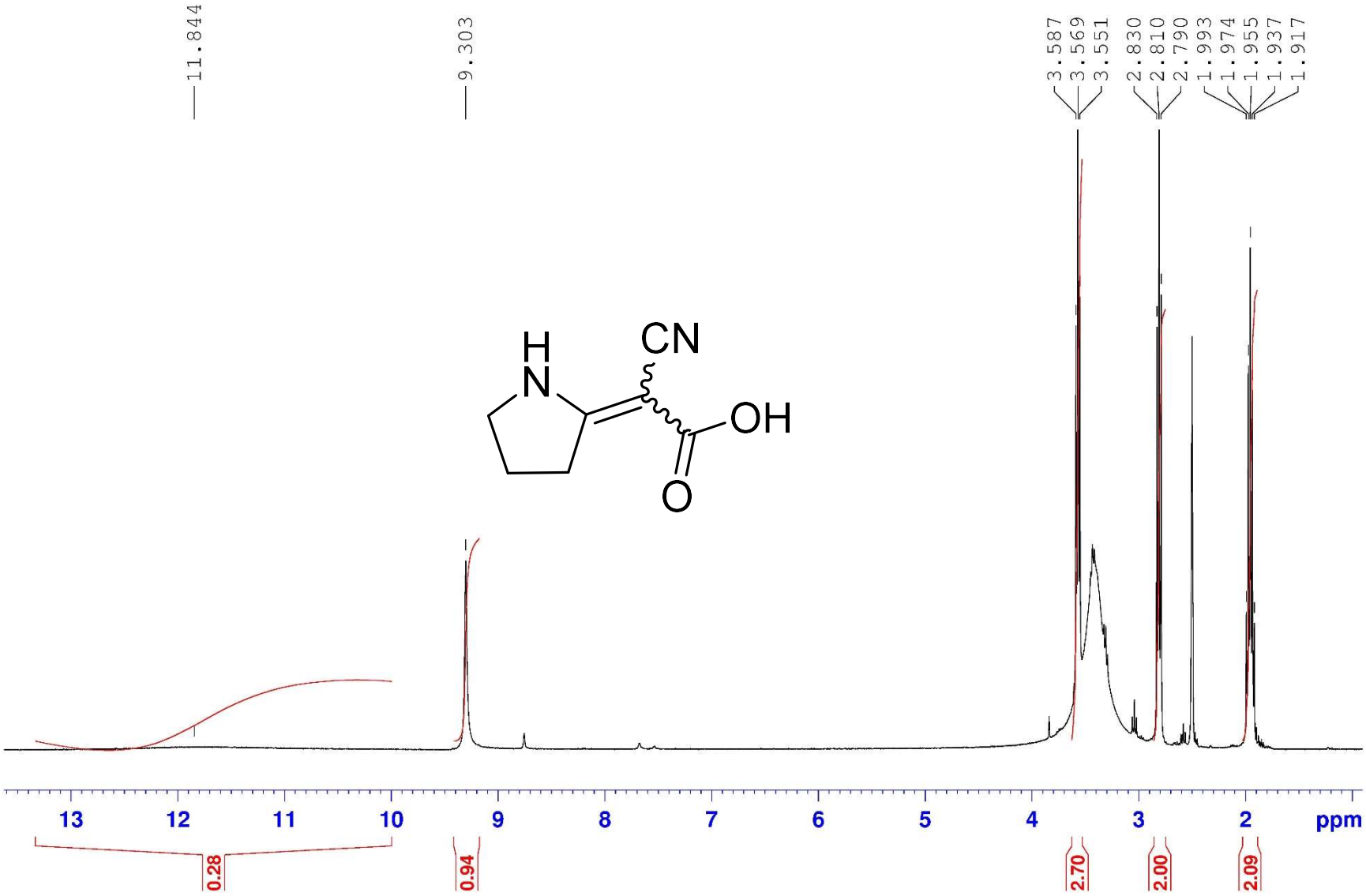

FIGURE S84: 400 MHz ^{1}H NMR spectrum of **7´a** in DMSO-d6.

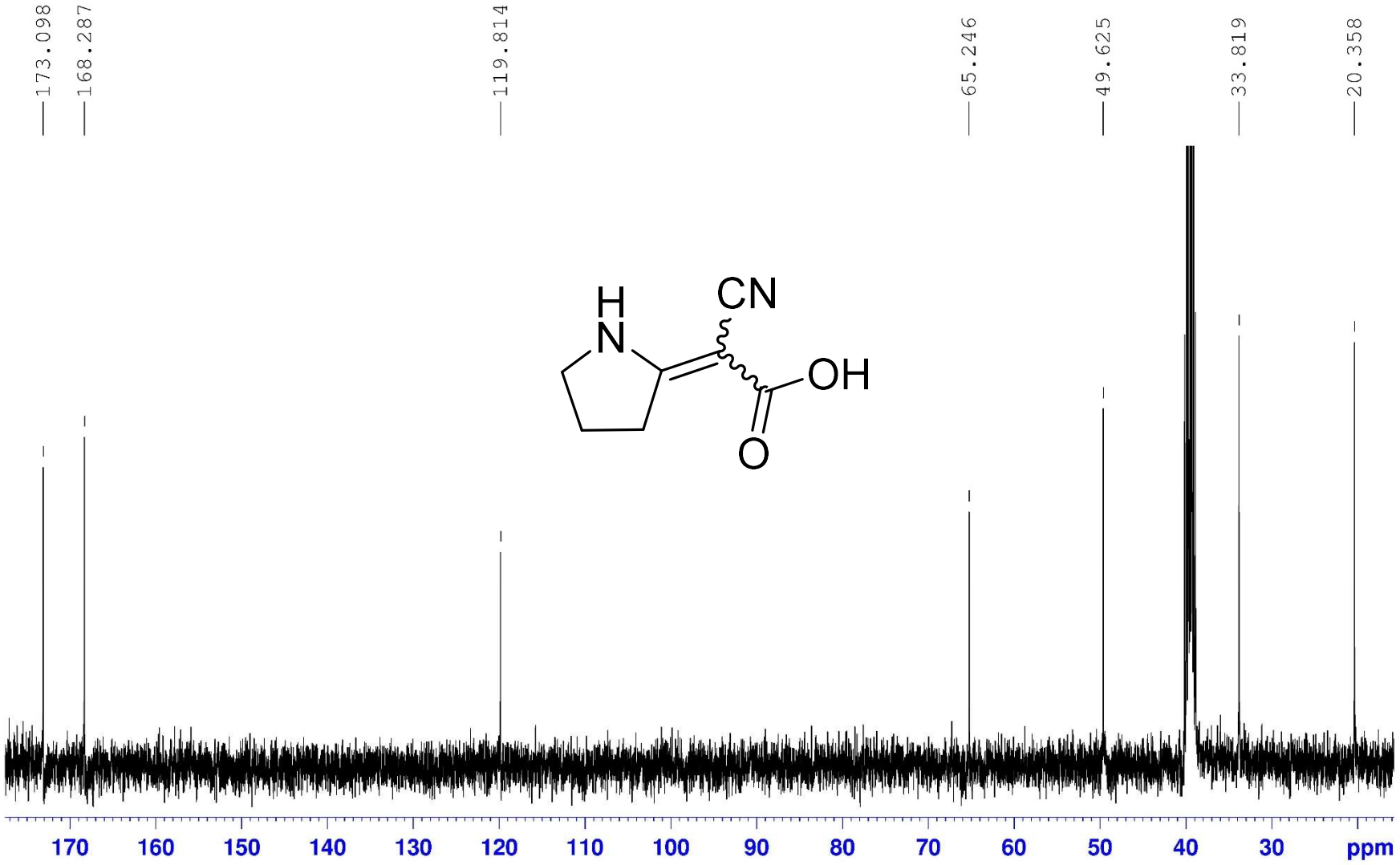

FIGURE S85: 100 MHz ^{13}C NMR spectrum of **7′a** in DMSO-d6.

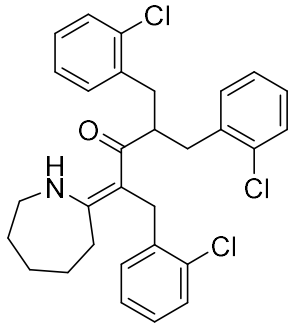

FIGURE S86: 500 MHz ^{1}H NMR spectrum of **10b** in $CDCl_3$.

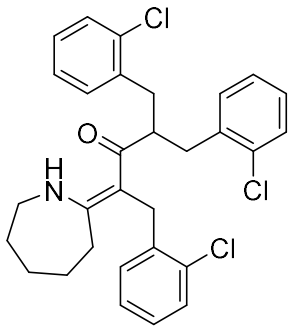

FIGURE S87: Detail of 500 MHz ^{1}H NMR spectrum of **10b** in $CDCl_3$.

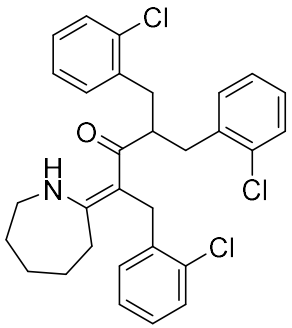

FIGURE S88: 125 MHz ^{13}C (APT) NMR spectrum of **10b** in $CDCl_3$.

