Synthesis of substituted 1,2-dihydroisoquinolines *via* Ni(II) and Cu(I)/Ag(I) catalyzed double nucleophilic addition of arylamines to *ortho*-alkynyl donor-acceptor cyclopropanes (*o*-ADACs)

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Supporting Information

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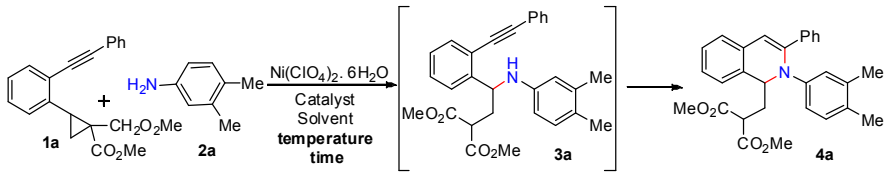
General Information:

All chemicals were purchased from Sigma-Aldrich, Alfa Aesar and S. D. Fine Chemicals, Pvt. Ltd. India and used without further purification. ACME silica gel (100ï 200 mesh) was used for column chromatography and thin-layer chromatography was performed on Merck-pre-coated silica gel 60-F254 plates. TLC plates are visualized by UV-light and developed by Iodine. All the solvents were obtained from commercial sources and purified using standard methods. All ^{1}H, ^{13}C NMR spectra were recorded on Avance-300, Avance-400 and Avance-500 MHz Spectrometer. Chemical shifts (ŭ) are reported in ppm, using TMS (ŭ = 0) as an internal standard in $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; dt, doublet of triplet. The coupling constants (J) are reported in Hertz (Hz). LC-MS samples were recorded on Agilent 1200 series (DAD-Diode Array Detector) using Zorbax (SB-C18, 3.0M x 50mm x 1.8 µm) column. Mass spectral data were compiled using MS (ESI), HRMS mass spectrometers.

Table 1: Optimization of the reaction conditions[a]



Entry	Catalyst (mol%)	Catalyst (mol%)	Solvent	Temperature (^{o}C)	Time (h)	Yield of 3a (%)[b]	Yield of 4a (%)[b]
1	$Ni(ClO_4)_2.6H_2O$ (10)	--	DCM	40	3	93	--
2	$Ni(ClO_4)_2.6H_2O$ (10)	--	DCM	40	24	89	
3	$Ni(ClO_4)_2.6H_2O$ (10)	--	DCE	80	24	80	--
4	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)	DCM	40	24	80	--
5	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)	DCE	80	48	65	10
6	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)	ACN	80	72	--	30
7	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)	DCM/ACN	40/80	3/72	--	45[c]
8	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)	THF	80	24	50	--
9	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)	toluene	100	24	--	--[d]
10	$Ni(ClO_4)_2.6H_2O$ (10)	AgOTf (10)/(N_2)	1,4-dioxnae	50	12	--	--[d]
11	$Ni(ClO_4)_2.6H_2O$ (10)	$AgNO_3$ (10)/N_2	MeOH	80	12	--	--
12	$Ni(ClO_4)_2.6H_2O$ (10)	$Pd(OAc)_2$ (10)	DCE	80	12	--	13
13	$Ni(ClO_4)_2.6H_2O$ (10)	$AuCl(PPh_3)$ (2) $AgSbF_6$ (5)	DCE	RT	4	--[d]	--
14	$Ni(ClO_4)_2.6H_2O$ (10)	CuI (10)	DCE	80	48	--	61
15	$Ni(ClO_4)_2.6H_2O$ (10)	CuI/ MS 4Å	DCE	80	48	--	36
16	$Ni(ClO_4)_2.6H_2O$ (10)[c]	CuI (10) (N_2)	DCE	80	72	--	42[e]
17	$Ni(ClO_4)_2.6H_2O$ (10)	CuI(100)	DCE	80	48	--	47
18	$Ni(ClO_4)_2.6H_2O$ (10)	Cu_2O(10)	DCE	80	48	--	26
19	$Ni(ClO_4)_2.6H_2O$ (10)	$Cu(OTf)_2$ (10)	DCE	80	24	--	--
20	$Ni(ClO_4)_2.6H_2O$ (10)	$CuPF_6(MeCN)_4$ (5)	DCE	80	6h	--	--
21	$Ni(ClO_4)_2.6H_2O$ (10)	$CuPF_6(MeCN)_4$ (5)	DCM	35	8h	--	--[e]
22	$Ni(ClO_4)_2.6H_2O$ (10)	Cu(I)OAc (10)	DCM	35	24	23	--
23	$Ni(ClO_4)_2.6H_2O$ (10)	Cp_2ZrCl_2 (10)	DCE	80	60	--	50
24	$Ni(ClO_4)_2.6H_2O$ (10)	Cp_2ZrCl_2(100)	DCE	80	48	--	48

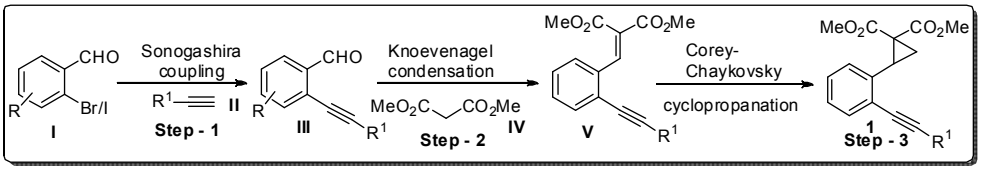
25	$Ni(ClO_4)_2.6H_2O$ (10)	$In(OTf)_3$ (10)	DCE	80	24	72	--
26	$Ni(ClO_4)_2.6H_2O$ (10)	$Zn(OTf)_2$ (10) (N_2)	DCE	80	24	60	
27	$Ni(ClO_4)_2.6H_2O$ (10)	$Sn(OTf)_3$	DCE	80	24	80	
28	$Ni(ClO_4)_2.6H_2O$	$Bi(OTf)_3$	toluene	80	24	75	--
29	$Ni(ClO_4)_2.6H_2O$ (10)	$CoCl_2$ (30 mol%)	DCE	80	24	52	--
30	$Ni(ClO_4)_2.6H_2O$ (10)	$FeCl_3$ (300)	DCE	80	24	20	--

Reaction conditions: [a] Compound **1a (**0.1 mmol), Compound **2a** (0.2 mmol), Solvent 3.0 mL. [b] Isolated yield; c = Sequential one-pot two step procedure [**Step 1:** 10 mol% $(NiClO_4)_2$. $6H_2O$ in DCM at 40 ^oC. Water work up. **Step 2:** AgOTf (10 mol%) in ACN (3.0 mL) at 80 ^oC]. d = Decompsed, e = N_2 atmosphere, NR = No Results

Based on previous literature reports, to deliver one-pot synthesis of the substituted 2-((1,2-dihydroisoquinolin-1-yl)methyl) malonates for our initial investigation dimethyl 2-(2-(phenylethynyl)phenyl) cyclopropane-1,1-dicarboxylate (**1a)** and 3,4-dimethyl aniline (**2a)** were selected as a model substrates. At the beginning, **1a (**0.1 mmol) with **2a** (0.2 mmol) in presence 10 mol% of $Ni(ClO_4)_2.6H_2O$ in DCM at 40 ^oC for 3 h which gave NRO adduct;[1d] dimethyl 2-(2-((3,4-dimethylphenyl)amino)-2-(2-(phenylethynyl)phenyl)ethyl) malonate (**3a**) in 93% of yield (Table 1, entry 1). Further it was confirmed by NMR, and IR analysis. A broad singlet at 4.50 ppm in ^1H NMR as well as broad peak 3200 cm^{-1} in IR indicated a free ñNHò group. Similarly, the peak at 95.0 and 87.4 ppm in ^{13}C NMR as well as peak at 2215 cm^{-1} represented the alkyne (Cſ C) functionality. However, continuing of the same reaction for 24 h also did not provide the desired product **4a,** only 3**a** was isolated in 89% of yield (Table 1, entry 2). Whereas, in DCE at 80 ^oC for 1 h-24 h also produced **3a** in 80% yield (Table 1, entry 3). Thereafter, 10 mol% of $Ni(ClO_4)_2.6H_2O$ is kept as standard catalyst for the ring-opening conditions and various catalysts and solvents were examined for one-pot regioselective intramolecular hydroamination process. In this regard, at first we focused on soft metal Lewis acid catalysts like Ag, Pd Au and Cu in different solvent systems (Table 1, entries 4-19). When the reaction was performed with 10 mol% AgOTf in DCM at 40 ^oC only **3a** was obtained in 80% yield after 24 h (entry 4). Then solvent was changed to DCE at 80 ^oC resulted the desired product dimethyl 2-((2-(3,4-dimethylphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (**4a**) in poorer yield (10%) along with 65% of **3a** after 48 h (entry 5). Same as, in ACN at 80 ^oC the yield of **4a** was raised upto 30% (entry 6). With these raising yields, we carried the sequential one-pot two step

procedure gave only in 45% overall yield (entry 7). However, other solvents like THF, toluene and 1,4-dioxane were screened but they failed to improve the yield of **4a** rather complex mixture was observed (entries 8-10). Similar results were observed with 10 mol% of $AgNO_3$ in EtOH (entry 11). In continuation, 10 mol % of $Pd(OAC)_2$ in DCE at 80 ^oC gave **4a** in low yield (entry 12) along with mixture of compounds were obtained. Combination of highly carbophilic and expensive gold(I) catalyst; $AuCl(PPh_3)$ (1 mol%) /$AgSbF_6$ (5 mol%) in DCE at room temperature was totally ineffective for this tandem process, only decomposed products were obtained in shorter reaction time (4 h) (entry 13). Later on, our attention was turned on inexpensive copper(I)/(II) catalysts (See the supporting information ESI); To our delight, 10 mol% of CuI in DCE at 80 ^oC exclusively formed **4a** in 61% of yield after 48 h (entry 14). Furthermore, by adding the 4 Å molecular sieves as well as under nitrogen atmosphere decreased yields were observed (entries 15-16). Likewise, stoichiometric amount of copper (I) iodide in DCE was failed to improve the yield of **4a**; also a dropped yield was obtained in comparison to catalytic system (entry 17). Whereas the use of Copper (I) oxide (10 mol%) gave 26% of tandem product **4a** (entry 18). However, other copper catalysts like $Cu(OTf)_2$, $CuPF_6(MeCN)_4$ (5) and Cu(I)OAc (10) were not a suitable catalyst for this transformation (entries 19-22). The examination of catalytic and non-catalytic amounts of $ZrCp_2Cl_2$ in DCE resulted in only 50% yield of 4**a** after a prolonged reaction time 60 h (entries 23-24). Further studies, the reaction screened with other Lewis acid catalysts like triflates and halides of In (III), Bi (III), Fe (III), Zn (II), tin (II) and Co (II); none of them were capable for this protocol, simply ring-opening product **3a** was obtained in low to high yield (entries 24-30). The above optimized conditions, conclude that 10 mol% of $Ni(ClO_4)_2.6H_2O$ and 10 mol% of Copper(I) iodide is the best optimum conditions for this tandem ring-opening/intramolecular hydroamino cyclization process.

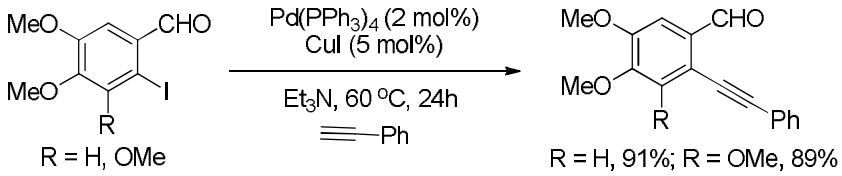
General procedure for synthesis of compound 1: The corresponding starting materials were synthesized in a three step procedure like palladium catalyzed Sonogashira reaction of 2-halo (Br/I) aryl aldehydes, Knoevenagal condensation followed by Corey-Chaykovsky cyclopropanation.



Step 1:

General experimental procedure for synthesis of compound III (a-d): Compounds (**IIIa-d)** were synthesized as per literature methods. (Compounds **IIIa**, **IIIb** and **IIIc**)[11] and **IIId.**[6]

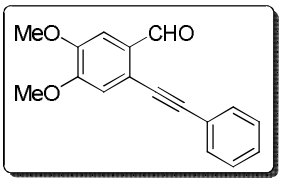
General experimental procedure for synthesis of compound III (e-f):



Compound (Ib/Ic, 10 mmol in 10 mL of THF) was added to a stirred solution of Pd $(PPh_3)_4$ (1 mol%) and CuI (5 mol%) in 40 mL of dry TEA under nitrogen atmosphere at room temperature. After 15 min. 1.2 equivalent of phenyl acetylene (**IIa**) was added over a period 10 min. Thereafter the reaction was subjected to heat for 60 ^oC for 24 h. After completion of the starting material (monitored by TLC) the reaction mixture was cooled to room temperature and filtered. The organic solvent was evaporated under reduced pressure. Finally the crude mixture was purified by column chromatography over a silica gel to obtain the corresponding compound **III**. The obtained data is matched to reported literature data.[11f]

Characterization data:

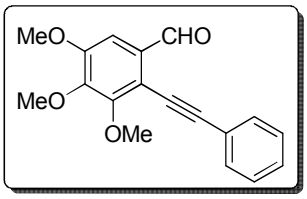
4,5-Dimethoxy-2-(phenylethynyl)benzaldehyde (IIIe): [Compound Ib (2.910 g, 10 mmol),



$Pd(PPh_3)_4$ (1 mol%; 115 mg, 0.1 mmol) CuI (5 mol%, 95 mg, 0.5 mmol), Phenyl acetylene (1.31 mL, 12.0 mmol,]; Yield 2.420 g, 91%; ^1H NMR (400 MHz, $CDCl_3$) ŭ 10.50 (s, 1H), 7.59 ï 7.51 (m, 2H), 7.42 (s, 1H),

7.41 ï 7.34 (m, 3H), 7.06 (s, 1H), 3.99 (s, 3H), 3.96 (s, 3H).

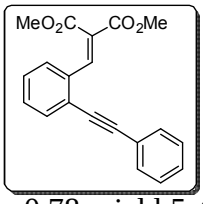
3,4,5-trimethoxy-2-(phenylethynyl)benzaldehyde (III f):



[Compound **Ib** (3.210 g, 10 mmol), $Pd(PPh_3)_4$ (1 mol%; 115 mg, 0.1 mmol) CuI (5 mol%, 95 mg, 0.5 mmol), Phenyl acetylene (1.31 mL, 12.0 mmol]; Yield 2.364 g, 89%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 10.54 (s, 1H), 7.59 ï 7.54 (m, 2H), 7.41 ï 7.34 (m, 3H), 7.29 (s, 1H), 4.04 (s, 3H), 3.99 (s, 3H), 3.94 (s, 3H).

General experimental procedure for synthesis of compounds V (a-f): To a stirred solution of dimethyl malonate (IV) (1.0 equiv.) in EtOH, AcOH (10 mol%) and piperidine (10 mol%) was added under nitrogen atmosphere. After 5 minutes 1.0 equivalents compound (III) was also added at the same temperature. Later on the reaction temperature was raised to 80 ^{o}C using oil bath and stirred for 24 h. After completion of the starting material (monitored by TLC) the reaction mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. Finally the crude mixture was purified by column chromatography over a silica gel to obtain the corresponding compound **V.**

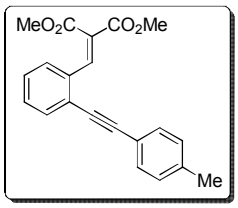
Dimethyl 2-(2-(p-tolylethynyl)benzylidene)malonate (Va):



[Compound **(IIIa)** (4.120 g, 20 mmol) was added to a stirred solution of dimethyl malonate **IV** (2.64 g, 20 mmol), AcOH (2.0 mmol, 114 μL) and piperidine (2.0 mmol, 196 μL) in 40 mL of EtOH]; Yellow semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 5.440 g, 85%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 8.31 (s, 1H), 7.51 ï 7.45 (m, 3H), 7.37 (d, J = 7.6 Hz, 1H), 7.31 ï 7.25 (m, 4H), 7.21 (td, J = 7.7, 1.2 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H). The H^1 NMR data was reported literature data.

Reference: J. K. Joo and S.W. Youn, *Adv. Synth. Catal*., 2013, **355**, 559.

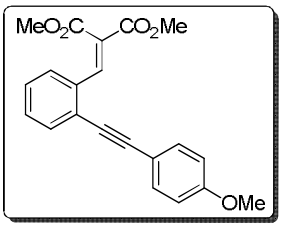
Dimethyl 2-(2-(p-tolylethynyl)benzylidene)malonate (Vb):



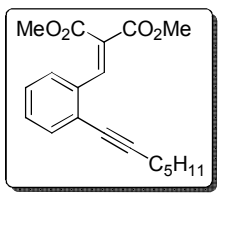
[Compound **(IIIb)** (1.650 g, 7.5 mmol) was added to a stirred solution of dimethyl malonate **IV** (0.990 g, 7.5 mmol), AcOH (1.0 mmol, 43 μL) and piperidine (1.0 mmol, 73 μL) in 15 mL of EtOH]; Yellow semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 2.029 g, 81%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 8.39 (s, 1H), 7.59 ï 7.54 (m, 1H), 7.45 (t, J = 8.0 Hz, 3H), 7.41 ï 7.33 (m, 1H), 7.32 ï 7.27 (m,

1H), 7.18 (d, *J* = 7.8 Hz, 2H), 3.88 (s, 3H), 3.80 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 167.1, 164.6, 142.0, 139.2, 134.7, 132.6, 131.8, 130.3, 129.4, 128.4, 127.7, 126.7, 125.2, 119.8, 96.9, 86.3, 52.9, 52.8, 21.8; **IR** (KBr, neat) 2996, 2952, 2213, 1909, 1727, 1630, 1513, 1441, 1370, 1249, 1213, 1066, 986, 820, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{21}H_{19}O_4$ $(M + H)^+$ 335.1278, found 335.1267.

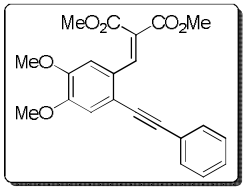
Dimethyl 2-(2-((4-methoxyphenyl)ethynyl)benzylidene)malonate (Vc): [Compound **(IIIc)** (1.770 g, 7.5 mmol) was added to a stirred solution of dimethyl malonate **IV** (0.990 g, 7.5 mmol), AcOH (1.0 mmol, 43 μL) and piperidine (1.0 mmol, 73 μL) in 15 mL of EtOH]; Pale yellow solid; mp 74-76 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 1.984 g, 81%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 8.39 (s, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.53 ï 7.47 (m, 2H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.91 ï 6.86 (m, 2H), 3.87 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 167.0, 164.5, 160.2, 141.9, 134.4, 133.3, 132.4, 130.3, 128.1, 127.5, 126.5, 125.3, 114.9, 114.2, 96.8, 85.7, 55.4, 52.8, 52.7; **IR** (KBr, neat) 3005, 2952, 2841, 2211, 1724, 1604, 1511, 1443, 1371, 1245, 1066, 1029, 986, 832, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{21}H_{19}O_5$ $(M + H)^+$ 351.1227, found 351.1229.



Dimethyl 2-(2-(hept-1-yn-1-yl)benzylidene)malonate (Vd): [Compound **(IIIe)** (3.00 g, 7.5 mmol) was added to a stirred solution of dimethyl malonate (1.980 g, 7.5 mmol) **IV,** AcOH (1.5 mmol, 86 μL) and piperidine (1.0 mmol, 147 μL) in 30 mL of EtOH]; Colour less liquid; R_f (hexane/EtOAc 9:1) 0.78; yield 3.921 g, 83%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 8.25 (s, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.41 ï 7.35 (m, 1H), 7.30 (t, *J* = 7.5, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 2.46 (t, *J* = 7.1 Hz, 2H), 1.69 ï 1.59 (m, 2H), 1.51 ï 1.41 (m, 2H), 1.40 ï 1.32 (m, 2H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 167.1, 164.6, 142.2, 134.7, 132.7, 130.2, 127.7, 127.5, 126.4, 125.8, 98.2, 78.2, 52.8, 52.7, 31.2, 28.5, 22.4, 19.8, 14.1; **IR** (KBr, neat) 2946, 2861, 2227, 1729, 1630, 1442, 1370, 1252, 1216, 1106, 1068, 986, 834, 766 cm^{-1}; **HRMS** (ESI) calcd. for $C_{29}H_{23}O_4$ $(M + H)^+$ 315.1591, found 315.1581.

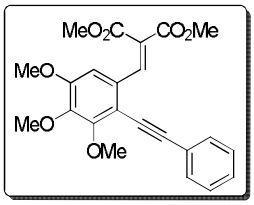


Dimethyl 2-(4,5-dimethoxy-2-(phenylethynyl)benzylidene)malonate (Ve): **[**Compound **(IIIe)** (1.862 g, 7.0 mmol) was added to a stirred solution of dimethyl malonate **IV** (0.924 g, 7.0 mmol), AcOH (0.7 mmol, 40 µL) and piperidine (0.7 mmol, 68



μL) in 14 mL of EtOH]; Yellow solid; mp 115-117 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 1.383 g, 52%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 8.38 (s, 1H), 7.60 ï 7.53 (m, 2H), 7.40 ï 7.33 (m, 3H), 7.05 (d, *J* = 2.0 Hz, 2H), 3.94 (s, 3H), 3.87 (s, 6H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 167.8, 164.8, 150.9, 149.4, 141.3, 131.7, 128.8, 128.6, 127.9, 124.5, 123.0, 119.1, 114.4, 110.0, 95.6, 86.9, 56.3, 56.08, 52.8; **IR** (KBr, neat) 3029, 2952, 2924, 2276, 1737, 1666, 1607, 1559, 1514, 1221, 1017, 820, 772 cm^{-1}; **HRMS** (ESI) calcd. for $C_{22}H_{21}O_6$ $(M + H)^+$ 381.1333, found 381.1356.

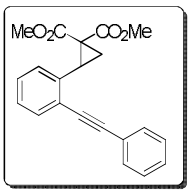
Dimethyl 2-(3,4,5-trimethoxy-2-(phenylethynyl)benzylidene)malonate (Vf): [Compound



(IIIe) (2.072 g, 7.0 mmol) was added to a stirred solution of dimethyl malonate **IV** (0.924 g, 7.0 mmol), AcOH (0.7 mmol, 40 μL) and piperidine (0.7 mmol, 68 μL) in in 14 mL of EtOH]; Yellow solid; mp ï 64-66 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 1.046 g, 49%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 8.33 (s, 1H), 7.61 ï 7.55 (m, 2H), 7.41 ï 7.31 (m, 3H), 6.89 (s, 1H), 4.02 (s, 3H), 3.93 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 167.3, 164.5, 154.8, 153.7, 144.2, 141.1, 131.6, 130.7, 128.7, 128.5, 125.9, 123.3, 113.5, 106.9, 99.6, 82.9, 61.5, 61.3, 56.2, 52.8; **IR** (KBr, neat) 3001, 2949, 2840, 1725, 2215, 1625, 1586, 1489, 1445, 1374, 1340, 1244, 1119, 1070, 1034, 987, 848, 760 cm^{-1}; **HRMS** (ESI) calcd. for $C_{23}H_{23}O_7$ $(M + H)^+$ 411.1438, found 411.1453.

General experimental procedure for synthesis of compound 1: Sodium hydride (1.1 equivalents) was added to a stirred solution of trimethyl sulfoxoniumiodide (TMSOI) 1.1 equiv. in dry DMF (4.0 mL/ mmol) under nitrogen atmosphere at room temperature. In the initial 10 min. H_2 gas evolution was observed. Thereafter, the stirring of the mixture is continued for another 1 h. After getting a clear solution 1.0 equivalents of condensation product **V** in dry DMF (1 mL/ mmol) was added at once via syringe. The reaction was monitored by TLC. After completion of starting material the reaction mixture was quenched with saturated ammonium chloride and poured in ice cold water. The organic layer was extracted with ethyl acetate and washed with brine. The combined organic layer was dried over Na_2SO_4. The solvent was evaporated under reduced pressure. Finally the crude mixture was purified by column chromatography over a silica gel to obtain the corresponding compound **1**.

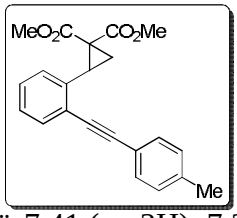
Dimethyl 2-(2-(phenylethynyl)phenyl)cyclopropane-1,1-dicarboxylate 1a: **[**Compound **(Iva)**



(4.800, 15 mmol in 15 mL of dry DMF) was added to a stirred solution of NaH (396 g, 16.5 mmol) and TMSOI (4.950 g, 16.5 mmol) in 60 mL of dry DMF after 1 h]; Yield 3.707 g, 74%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.56 ï 7.49 (m, 3H), 7.38 ï 7.31 (m, 3H), 7.26 ï 7.21 (m, 2H), 7.10 ï 7.05 (m, 1H), 3.69 (s, 3H), 3.62 (t, *J* = 9.0 Hz, 1H), 3.35 (s, 3H), 2.31 (dd, *J* = 8.4, 5.1 Hz, 1H, 1H), 1.81 (dd, *J* = 8.0, 3.0 Hz, 1H, 1H).

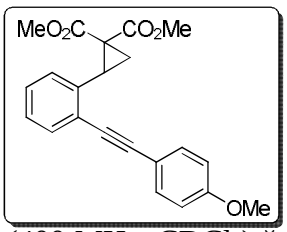
The data is matched to reported literature data.[6]

Dimethyl 2-(2-(p-tolylethynyl)phenyl)cyclopropane-1,1-dicarboxylate (1b): [Compound



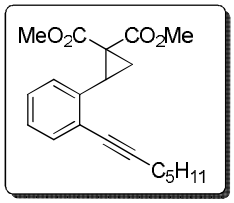
(IVb) (1.620, 5 mmol in 5 mL of dry DMF) was added to a stirred solution of NaH, (132 mg, 5.5 mmol) and TMSOI (1.210 g, 5.5 mmol) in 20 mL of dry DMF after 1h]; While solid; mp 72-74 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 1.287 g, 74%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.52 ï 7.48 (m, 1H), 7.46 ï 7.41 (m, 2H), 7.25 ï 7.21 (m, 2H), 7.18 ï 7.13 (m, 2H), 7.09 ï 7.04 (m, 1H), 3.70 (s, 3H), 3.62 (t, *J* = 8.5 Hz, 1H), 3.36 (s, 3H), 2.37 (d, *J* = 5.6 Hz, 3H), 2.31 (dd, *J* = 8.4, 5.1 Hz, 1H), 1.87 ï 1.78 (dd, *J* = 8.4, 5.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.4, 167.4, 138.6, 136.7, 131.8, 131.7, 129.2, 127.9, 127.5, 127.1, 125.7, 120.5, 95.0, 86.9, 52.9, 52.4, 37.0, 32.6, 21.7, 19.4; **IR** (KBr, neat) 3023, 2953, 2216, 1729, 1604, 1514, 1442, 1375, 1330, 1281, 1213, 1128, 982, 887, 820, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{22}H_{21}O_4$ $(M + H)^+$ 349.1434, found 349.1427.

Dimethyl 2-(2-((4-methoxyphenyl)ethynyl)phenyl)cyclopropane-1,1-dicarboxylate (1c):

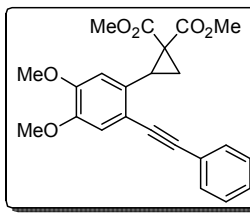


[Compound **(IVc)** (1.750 g, 5 mmol in 5 mL of dry DMF) was added to a stirred solution of NaH (132 mg, 5.5 mmol), TMSOI (1.210 g, 5.5 mmol) in 20 mL of dry DMF after 1h]; (5 mmol of reaction); Pale yellow solid; mp 90-92 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 1.365 g, 75%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.51 ï 7.45 (m, 3H), 7.25 ï 7.19 (m, 2H), 7.09 ï 7.04 (m, 1H), 6.90 ï 6.85 (m, 2H), 3.83 (s, 3H), 3.71 (s, 3H), 3.62 (t, *J* = 8.8 Hz, 1H), 3.35 (s, 3H), 2.31 (dd, *J* = 8.4, 5.2 Hz, 1H), 1.81 (dd, *J* = 9.2, 5.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.4, 167.3, 159.9, 136.6, 133.2, 131.7, 127.7, 127.4, 127.1, 125.8, 115.7, 114.1, 94.9, 86.3, 55.5, 52.8, 52.4, 37.0, 32.6, 19.4; **IR** (KBr, neat) 3008, 2952, 2843, 2215, 1728, 1605, 1512, 1443, 1283, 1128, 1030, 888, 834, 765 cm^{-1}; **HRMS** (ESI) calcd. for $C_{22}H_{21}O_5$ $(M + H)^+$ 365.1383, found 365.1380.

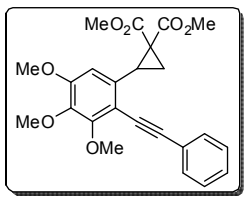
Dimethyl 2-(2-(hept-1-yn-1-yl)phenyl)cyclopropane-1,1-dicarboxylate (1d): **[IVa** (4.082, 13 mmol in 13 mL of dry DMF) was added to a stirred solution of (343 g, 14.5 mmol), TMSOI (3.146 g, 14.3 mmol) in 42 mL of dry DMF after 1h]; Colourless liquid; mp 81-83 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 3.027 g, 71%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.40 ï 7.33 (m, 1H), 7.19 ï 7.13 (m, 2H), 7.03 ï 6.97 (m, 1H), 3.78 (s, 3H), 3.52 (t, *J* = 9.2 Hz, 1H), 3.34 (s, 3H), 2.41 (t, *J* = 7.2 Hz, 2H), 2.26 (dd, *J* = 8.4, 5.1 Hz, 1H), 1.76 (dd, *J* = 9.2, 5.1 Hz, 1H), 1.65 ï 1.56 (m, 2H), 1.47 ï 1.31 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 167.3, 136.6, 131.8, 127.2, 127.2, 126.8, 126.2, 96.2, 78.6, 52.7, 52.2, 36.9, 32.4, 31.3, 28.5, 22.4, 19.7, 19.4, 14.1; **IR** (KBr, neat) 2948, 2862, 2229, 1731, 1441, 1375, 1330, 1280, 1209, 1127,982, 889, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{20}H_{25}O_4$ $(M + H)^+$ 329.1747, found 329.1739.



Dimethyl 2-(4,5-dimethoxy-2-(phenylethynyl)phenyl)cyclopropane-1,1-dicarboxylate (1e): [Compound (**IVe)** (1.140 g, 3.0 mmol in 3 mL of dry DMF) was added to a stirred solution of (80 mg, 3.3 mmol), TMSOI (726 mg, 3.3 mmol) in 12 mL of dry DMF after 1h]; White solid; mp 130-132 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 827 mg, 70%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.55 ï 7.49 (m, 2H), 7.38 ï 7.29 (m, 3H), 7.01 (s, 1H), 6.58 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.72 (s, 3H), 3.59 (t, *J* = 8.8 Hz, 1H), 3.42 (s, 3H), 2.29 (dd, *J* = 8.4, 5.1 Hz, 1H), 1.83 (dd, *J* = 9.3, 5.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 170.4, 167.5, 149.1, 148.1, 131.6, 130.2, 128.5, 128.3, 123.8, 117.4, 114.4, 110.6, 93.4, 87.8, 56.18, 52.85, 52.7, 37.0, 32.6, 20.0; **IR** (KBr, neat) 3006, 2949, 2850, 2275, 1729, 1602, 1517, 1448, 1385, 1282, 1260, 1214, 1129, 1028, 870, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{23}H_{23}O_6$ $(M + H)^+$ 395.1489, found 395.1508.



Dimethyl 2-(3,4,5-trimethoxy-2-(phenylethynyl)phenyl)cyclopropane-1,1-dicarboxylate (1f): [Compound (**IVf)** (1.230 g, 3.0 mmol in 3 mL of dry DMF) was added to a stirred solution of (80 mg, 3.3 mmol), TMSOI (726g, 16.5 mmol) in 12 mL of dry DMF after 1h]; (3 mmol of reaction); Yellow solid; mp 66-68 ^{o}C; R_f (hexane/EtOAc 9:1) 0.78; yield 852 mg, 67%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.55 ï 7.51 (m, 2H), 7.37 ï 7.29 (m, 3H), 6.40 (s, 1H), 4.01 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H), 3.69 (s, 3H), 3.57 (t, *J* = 8.8 Hz, 1H), 3.44 (s, 3H), 2.25 (dd, *J* = 8.4, 5.2 Hz, 1H), 1.80 (dd, *J* = 9.2, 5.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.3, 167.5, 154.8, 153.5, 141.6,

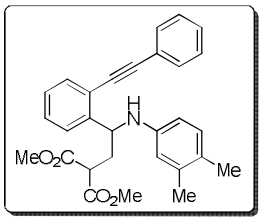


133.4, 131.6, 128.4, 128.2, 124.0, 112.8, 107.0, 97.7, 83.7, 61.6, 61.4, 56.3, 52.9, 52.6, 37.1, 32.7, 19.8; **IR** (KBr, neat) 2999, 2947, 2844, 2210, 1731, 1594, 1497, 1448, 1394, 1331, 1280, 1209, 1123, 1035, 909, 850, 766 cm^{-1}; **HRMS** (ESI) calcd. for $C_{23}H_{25}O_7$ $(M + H)^+$ 425.1595, found 425.1580.

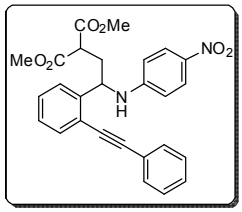
Experimental procedure for the synthesis of compound 4:

Method A: To a stirred solution of (0.2 mmol, l.0 equiv.) of *ortho*-alkyny donor-acceptor cyclopropane (*o*-ADAC) **1** and (0.4 mmol, 2.0 equiv.) of primary aryalmine **2** in DCE 5 mL was added 10 mol% of $Ni(ClO_4).6H_2O$, (0.02 mmol, 0.02 equiv.) and 10 mol% CuI (0.02 mmol, 0.02 equiv.) at room temperature. Thereafter the reaction temperature was increased to 80 ^oC and continued for 48 ï 96 h. (Note: The homo-Michel adducts **3** was formed with in short period of time (1.5 h to 5.0 h). After complete conversion of **3** into **4** (the reaction was monitored by -TLC), the reaction mixture was cooled; the solvent was removed under rotary evaporator, diluted with water and the organic layer was extracted with ethyl acetate. The organic layer was further washed with saturated ammonium chloride and brine solution for 2-3 times. The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. Finally, the crude was subjected to column chromatography over silica gel to obtain the desired product **4**.

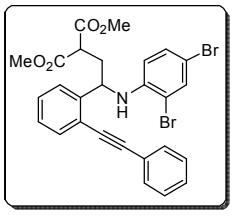
Method B: Step 1: To a stirred solution of (0.2 mmol, l.0 equiv.) of *ortho*-alkyny donor-acceptor cyclopropane (*o*-ADAC) **1** and (0.4 mmol, 2.0 equiv.) of primary aryalmine (**2m/2t)** in DCM (3.0 mL) was added 10 mol% of $Ni(ClO_4).6H_2O$, (0.02 mmol, 0.02 equiv.). After completion of starting material (**1a/2a**) the reaction mixture was cooled to room temperature and the solvent evaporated under reduce pressure. The organic layer was washed with water and extracted with ethyl acetate. **Step 2:** After evaporation of solvent, the obtained crude mixture (in 3.0 mL of ACN) was directly subjected to react with 10 mol% of AgOTf at room temperature. Thereafter, the reaction was stirred at 80 ^oC. After completion of intermediate (**3m/3t**) the reaction mixture was cooled to room temperature and the solvent was evaporated. The crude mixture was washed with sat.$NaHCO_3$ solution and the organic extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. Finally, the crude was subjected to column chromatography over silica gel to obtain the desired product **4m/4t**.

Dimethyl 2-(2-((3,4-dimethylphenyl)amino)-2-(2-(phenylethynyl)phenyl)ethyl)malonate (3a): Colour less liquid; R_f (hexane/EtOAc 9:1) 0.78; yield 84 mg, 93%; ^{1}H NMR (500 MHz, 

$CDCl_3$) ŭ 7.62 ï 7.57 (m, 2H), 7.54 ï 7.50 (m, 1H), 7.40 ï 7.33 (m, 4H), 7.26 (dd, *J* = 11.0, 4.5 Hz, 1H), 7.20 (td, *J* = 7.5, 1.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.43 (s, 1H), 6.31 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.98 (dd, *J* = 8.5, 5.5 Hz, 1H), 4.27 (brs, 1H), 3.66 (s, 3H), 3.62 (s, 3H), 3.59 (dd, *J* = 7.7, 6.0 Hz, 1H), 2.57 ï 2.44 (m, 2H), 2.10 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.4, 169.9, 145.0, 144.7, 137.4, 133.0, 131.8, 130.4, 129.2, 129.0, 128.7, 128.6, 127.3, 126.1, 125.9, 123.3, 121.8, 115.6, 111.0, 95.0, 87.4, 55.3, 52.9, 52.8, 50.0, 36.1, 20.2, 18.8; **IR** (KBr, neat) 3378, 3005, 2952, 2841, cm^{-1}; **HRMS** (ESI) calcd. for $C_{29}H_{30}NO_4$ $(M + H)^+$ 456.5523, found 456.5523.

Dimethyl 2-(2-((4-nitrophenyl)amino)-2-(2-(phenylethynyl)phenyl)ethyl)malonate (3m): 

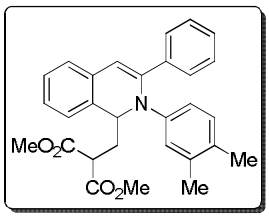
Pale Yellow semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 68 mg, 72%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 8.01 (d, *J* = 9.2 Hz, 2H), 7.62 ï 7.55 (m, 3H), 7.42 ï 7.37 (m, 3H), 7.34 ï 7.31 (m, 2H), 7.31 ï 7.26 (m, 1H), 6.51 (d, *J* = 9.2 Hz, 2H), 5.52 (brs, 1H), 5.10 (ddd, *J* = 8.6, 7.2, 5.5 Hz, 1H), 3.66 (s, 6H), 3.54 (dd, *J* = 7.9, 5.4 Hz, 1H), 2.67 ï 2.48 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.2, 169.7, 152.2, 142.5, 138.6, 133.4, 131.8, 129.5, 129.1, 128.8, 128.1, 126.5, 125.9, 122.8, 122.0, 112.1, 95.7, 86.6, 55.2, 53.2, 53.1, 49.7, 35.3; **IR** (KBr, neat) 3374, 3065, 3019, 2952, 2325, 1741, 1601, 1498, 1444, 1312, 1222, 1112, 841, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{23}N_2O_6$ $(M + H)^+$ 473.1707, found 473.1686.

Dimethyl 2-(2-((2,4-dibromophenyl)amino)-2-(2-(phenylethynyl)phenyl)ethyl)malonate (3n): Orange semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 92 mg, 79%; ^{1}H NMR (400 MHz, 

$CDCl_3$) ŭ 7.62 ï 7.58 (m, 2H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 2.4 Hz, 1H), 7.42 ï 7.35 (m, 3H), 7.31 ï 7.27 (m, 2H), 7.26 ï 7.22 (m, 1H), 7.10 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.39 (d, *J* = 8.8 Hz, 1H), 5.08 (t, *J* = 13.2, 6.4 Hz, 1H), 5.03 (brs, 1H), 3.68 (s, 3H), 3.64 (s, 3H), 3.57 (td, *J* = 7.8, 4.0 Hz, 1H), 2.66 (dt, *J* = 14.4, 8.4 Hz, 1H), 2.55 (dt, *J* = 14.4, 5.4 Hz, 1H).; ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.0, 169.6, 143.1, 143.0, 134.5, 133.1, 131.8, 131.4, 129.4, 128.9, 128.7, 127.8, 125.8, 123.0, 122.1, 113.8, 110.4, 108.9, 95.6, 86.8, 55.2, 53.1, 53.0, 49.8, 35.6; **IR** (KBr, neat) 3389, 3149, 3022,

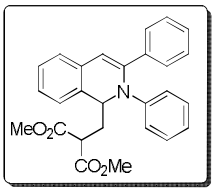
2952, 2851, 2330, 1741, 1589, 1500, 1445, 1273, 1231, 1159, 1083, 1159, 1082, 871, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{23}Br_2NO_4$ $(M + H)^+$ 584.0067, found 584.0049.

Dimethyl 2-((2-(3,4-dimethylphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4a): Dark brown red semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 55.5 mg, 61%;



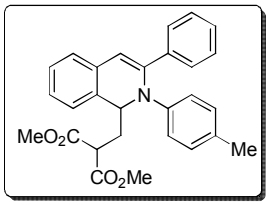
^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.62 ï 7.52 (m, 1H), 7.32 ï 7.18 (m, 3H), 7.18 ï 7.10 (m, 1H), 6.97 (t, *J* = 13.5 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 2.0 Hz, 1H), 6.63 (s, 1H), 6.54 (dd, *J* = 8.0, 2.5 Hz, 1H), 4.90 (t, *J* = 7.5 Hz, 1H), 3.81 (s, 1H), 3.77 (s, 1H), 3.75 (t, *J* = 5.5 Hz, 1H), 2.51 ï 2.38 (m, 1H), 2.33 ï 2.70 (m, 1H), 2.08 (s, 1H), 2.06 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.1, 145.2, 140.9, 137.9, 137.0, 131.9, 131.5, 130.7, 129.9, 128.6, 128.1, 127.7, 127.6, 126.6, 126.0, 124.8, 123.7, 120.2, 111.8, 63.2, 52.9, 48.4, 33.2, 20.2, 19.1; **IR** (KBr, neat) 3029, 2952, 2924, 2856, 1732, 1606, 1501, 1438, 1263, 1219, 1063, 817, 759 cm^{-1}; **HRMS** (ESI) calcd. for $C_{29}H_{30}NO_4$ $(M + H)^+$ 456.2169, found 456.2166. (1 mmol scale of this reacion 59% yield was obtained 269 mg).

Dimethyl 2-((2-(3,4-dimethylphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4b): Dark brown red semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 44.5 mg, 52%;



^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.55 (d, *J* = 8.0 Hz, 2H), 7.30 ï 7.18 (m, 5H), 7.14 (dd, *J* = 15.0, 8.0 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 2H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.90 ï 6.84 (m, 2H), 6.84 ï 6.78 (m, 1H), 6.67 (t, *J* = 3.5 Hz, 1H), 4.99 (dd, *J* = 7.5, 6.0 Hz, 1H), 3.77 (d, *J* = 2.5 Hz, 6H), 3.67 (td, *J* = 7.5, 1.5 Hz, 1H), 2.51 ï 2.41 (m, 1H), 2.37 ï 2.31 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 147.3, 140.5, 137.6, 131.7, 131.5, 128.9, 128.6, 128.2, 127.8, 127.5, 126.7, 126.0, 124.9, 122.2, 112.29, 62.8, 52.9, 48.3, 33.0; **IR** (KBr, neat) 3031, 3032, 2998, 2860, 1736, 1598, 1492, 1437, 1265, 1156, 1065, 767 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{26}NO_4$ $(M + H)^+$ 428.1846, found 428.1856.

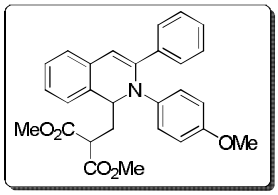
Dimethyl 2-((3-phenyl-2-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4c): Yellow



solid; mp 120-122 ^{o}C; R_f (hexane/EtOAc 17:3) 0.78; yield 47.6 mg, 54%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.60 ï 7.53 (m, 2H), 7.27 ï 7.19 (m 5H), 7.14 (t, *J* = 7.0 Hz, 1H), 6.95 (d, *J* = 7.0 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 7.4 Hz, 2H), 6.65 (s, 1H), 4.93 (t, *J* = 7.5 Hz, 1H), 3.78 (s,

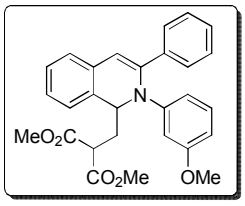
3H), 3.78 (s, 3H), 3.71 (t, *J* = 7.0 Hz, 1H), 2.49 ï 2.41 (m, 1H), 2.36 ï 2.25 (m, 1H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 145.0, 140.7, 137.7, 131.8, 131.3, 129.6, 129.5, 128.6, 128.2, 127.8, 127.6, 126.6, 126.0, 124.8, 122.4, 111.8, 63.1, 52.9, 48.4, 33.1, 20.8; **IR** (KBr, neat) 3062, 3003, 2949, 2900, 1741, 1657, 1608, 1561, 1506, 1445, 1391, 1262, 1226 1157,1067, 817, 766 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{28}NO_4$ $(M + H)^+$ 442.2013, found 442.1997.

Dimethyl 2-((2-(4-methoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate



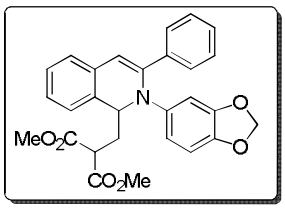
(4d): Brown red semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 55.0 mg, 60%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.56 (dt, *J* = 3.3, 1.9 Hz, 2H), 7.29 ï 7.23 (m, 4H), 7.21 (tdd, *J* = 8.5, 5.6, 3.6 Hz, 1H), 7.17 ï 7.12 (m, 1H), 6.93 (t, *J* = 6.2 Hz, 1H), 6.84 ï 6.79 (m, 2H), 6.61 (dt, *J* = 10.4, 3.1 Hz, 3H), 4.83 (t, *J* = 7.6 Hz, 1H), 3.81 ï 3.78 (m, 3H), 3.78 ï 3.75 (m, 3H), 3.75 ï 3.71 (m, 1H), 3.65 (s, 3H), 2.44 (dt, *J* = 14.0, 7.6 Hz, 1H), 2.29 (dt, *J* = 14.0, 7.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 155.3, 141.1, 141.0, 137.7, 131.9, 131.1, 128.5, 128.2, 127.7, 126.6, 126.0, 124.8, 124.1, 114.2, 111.3, 63.6, 55.5, 52.9, 48.4, 33.3; **IR** (KBr, neat) 3007, 2956, 2900, 2842, 1739, 1607, 1561, 1504, 1445, 1235, 1161, 1035, 838, 761 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{28}NO_5$ $(M + H)^+$ 458.1962, found 458.1947.

Dimethyl 2-((2-(3-methoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate



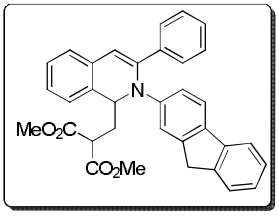
(4e): Brown red semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 45.7 mg, 50%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.55 (d, *J* = 6.9 Hz, 2H), 7.33 ï 7.21 (m, 5H), 7.16 (ddd, *J* = 7.3, 6.4, 2.4 Hz, 1H), 6.96 (t, *J* = 6.8 Hz, 2H), 6.65 (s, 1H), 6.47 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.44 (t, *J* = 2.2 Hz, 1H), 6.40 ï 6.31 (m, 1H), 5.01 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.67 (t, *J* = 7.2 Hz, 1H), 3.62 (s, 3H), 2.50 ï 2.40 (m, 1H), 2.37 ï 2.27 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.0, 169.9, 160.2, 148.6, 140.5, 137.8, 131.7, 131.6, 129.4, 128.7, 128.2, 127.9, 127.5, 126.7, 126.0, 125.0, 114.6, 112.4, 108.1, 108.0, 62.7, 55.3, 53.0, 48.4, 33.0; **IR** (KBr, neat) 3077, 2999, 2956, 2900, 1742, 1603, 1558, 1483, 1454, 1335, 1274, 1220, 890, 769 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{28}NO_5$ $(M + H)^+$ 458.1962, found 458.1961.

Dimethyl 2-((2-(benzo[*d*][1,3]dioxol-5-yl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4f): Orange red semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield



58 mg, 62%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.60 ï 7.54 (m, 2H), 7.31 ï 7.19 (m, 5H), 7.19 ï 7.12 (m, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.65 (s, 1H), 6.48 (d, *J* = 12.8 Hz, 1H), 6.48 (s, 1H), 6.33 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.80 (dd, *J* = 6.4, 1.2 Hz, 2H), 4.80 (t, *J* = 7.6 Hz, 1H), 3.81 ï 3.78 (m, 3H), 3.77 (d, *J* = 2.8 Hz, 3H), 3.72 (t, *J* = 7.6 Hz, 1H), 2.46 ï 2.35 (m, 1H), 2.34 ï 2.19 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.01, 170.0, 147.9, 143.4, 142.5, 141.0, 137.6, 131.8, 131.2, 128.6, 128.3, 127.9, 127.6, 126.8, 126.0, 124.9, 116.1, 111.8, 108.1, 104.9, 101.2, 63.8, 53.0, 48.4, 33.3; **IR** (KBr, neat) 3003, 2945, 2832, 1739, 1601, 1484, 1336,1211, 1117, 1038, 931, 849, 761 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{26}NO_6$ $(M + H)^+$ 472.1755, found 472.1753.

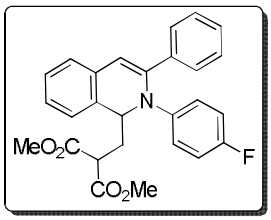
Dimethyl 2-((2-(9*H*-fluoren-2-yl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate



(4g): Brown red yellow semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield 67 mg, 65%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.61 ï 7.54 (m, 3H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.27 (dtd, *J* = 11.5, 7.6, 3.1 Hz, 5H), 7.22 ï 7.13 (m, 3H), 7.08 (s, 1H), 6.98 (d, *J* = 7.4 Hz, 1H), 6.88 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.68 (s, 1H), 5.04 (t, *J* = 7.6 Hz, 1H), 3.81 (s, 6H), 3.77 ï 3.61 (m, 3H), 2.55 ï 2.48 (m, 1H), 2.41 ï 2.32 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 146.5, 144.2, 143.1, 141.6, 140.7, 137.7, 136.3, 131.8, 131.3, 128.6, 128.2, 127.9, 127.6, 126.9, 126.7, 126.02, 125.0, 124.9, 121.5, 120.0, 119.4, 119.1, 112.0, 63.2, 53.0, 48.4, 37.0, 33.1; **IR** (KBr, neat) 3080, 3021, 2950, 1741, 1609, 1490, 1449, 1268, 1226, 1156, 1064, 1026, 819, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{34}H_{30}NO_4$ $(M + H)^+$ 516.2169, found 516.2162.

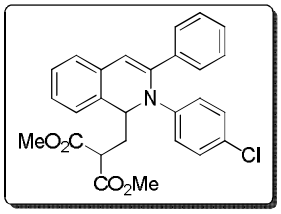
Dimethyl 2-((2-(4-fluorophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate

(4h): Dark brown solid; mp 122-124 ^{o}C; R_f (hexane/EtOAc 17:3) 0.78; yield 49 mg, 55%; ^{1}H



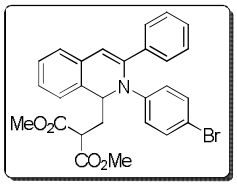
NMR (400 MHz, $CDCl_3$) ŭ 7.57 ï 7.51 (m, 2H), 7.30 ï 7.14 (m, 6H), 6.95 (d, *J* = 7.3 Hz, 1H), 6.87 ï 6.81 (m, 2H), 6.79 ï 6.72 (m, 2H), 6.67 (s, 1H), 4.88 (t, *J* = 7.6 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.67 (t, *J* = 7.6 Hz, 1H), 2.49 ï 2.41 (m, 1H), 2.35 ï 2.27 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.0, 169.9, 158.5 (d, *J* = 242.9 Hz), 143.6, 140.6, 137.3, 131.7, 131.1, 128.7, 128.4, 127.9, 127.6, 126.8, 125.9, 125.0, 123.8 (d, *J* = 8.0 Hz), 115.6 (d, *J* = 22.6 Hz), 112.1, 63.3, 53.0, 48.3, 33.1; ^{19}F NMR (377 MHz, $CDCl_3$) ŭ -121.1; **IR** (KBr, neat) 3046, 2954, 2899, 1740, 1607, 1559, 1503, 1443, 1391, 1266, 1222, 1159, 1065, 1024, 834, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{25}FNO_4$ $(M + H)^+$ 446.1762, found 446.1757.

Dimethyl 2-((2-(4-chlorophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate



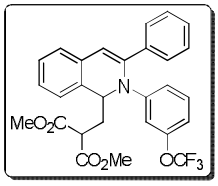
(4i): Dark brown solid; mp 165-167 ^{o}C; R_f (hexane/EtOAc 17:3) 0.78; yield 45 mg, 49%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.53 (d, *J* = 7.5 Hz, 2H), 7.30 ï 7.21 (m, 5H), 7.16 (t, *J* = 7.0, Hz, 1H), 7.03 (t, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 12.5 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.68 (s, 1H), 4.93 (t, *J* = 7.5 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.63 (t, *J* = 7.0 Hz, 1H), 2.49 ï 2.40 (m, 1H), 2.37 ï 2.27 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.0, 169.9, 145.9, 140.1, 137.2, 131.6, 131.3, 128.9, 128.8, 128.4, 128.0, 127.5, 127.4, 126.9, 125.9, 125.1, 123.3, 112.7, 62.8, 53.0, 48.3, 32.9; **IR** (KBr, neat) 3010, 2957, 2846, 1739, 1671, 1603, 1556, 1491, 1443, 1259, 1157, 1095, 1021, 819, 761 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{25}ClNO_4$ $(M + H)^+$ 462.1467, found 462.1462.

Dimethyl 2-((2-(4-bromophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate



(4j): Dark brown solid; mp 155-157 ^{o}C; R_f (hexane/EtOAc 17:3) 0.78; yield 49 mg, 49%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.68 ï 7.42 (m, 1H), 7.35 ï 7.21 (m, 2H), 7.19 ï 7.09 (m, 1H), 7.02 ï 6.82 (m, 1H), 6.68 (s, 1H), 4.94 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 1H), 3.77 (s, 1H), 3.68 ï 3.57 (t, *J* = 7.6 Hz, 1H), 2.48 ï 2.41 (m, 1H), 2.36 ï 2.25 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.0, 169.9, 146.4, 140.0, 137.2, 131.8, 131.6, 131.3, 128.8, 128.4, 128.0, 127.5, 126.9, 125.9, 125.1, 123.7, 114.9, 112.8, 62.7, 53.0, 48.27, 32.9; **IR** (KBr, neat) 3043, 2950, 1742, 1603, 1571 1491, 1446, 1267, 1232, 1160, 1071, 828, 767 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{25}BrNO_4$ $(M + H)^+$ 506.0961, found 506.0975.

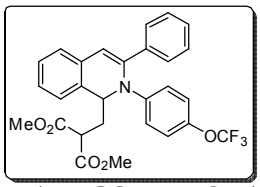
Dimethyl 2-((3-phenyl-2-(3-(trifluoromethoxy)phenyl)-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4k); Dark brown semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 35.7 mg, 35%; ^{1}H



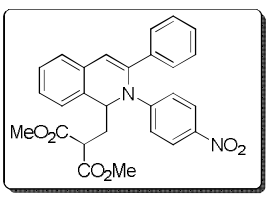
NMR (400 MHz, $CDCl_3$) ŭ 7.55 ï 7.49 (m, 2H), 7.32 ï 7.23 (m, 5H), 7.21 ï 7.15 (m, 1H), 7.07 (t, *J* = 8.1 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.81 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.69 (s, 1H), 6.67 ï 6.65 (m, 2H), 5.00 (t, *J* = 7.6 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.63 (t, *J* = 7.5 Hz, 1H), 2.49 ï 2.42 (m, 1H), 2.39 ï 2.30 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 169.9, 169.86, 149.7, 148.7, 139.8, 137.0, 131.6, 131.5, 129.8, 128.8, 128.49, 128.1, 127.4, 127.0, 125.9, 125.3, 120.5, (q, *J* = 258.2 Hz), 119.8, 114.6, 114.1, 113.3, 62.49, 53.0, 48.3, 32.8; ^{19}F NMR (377 MHz, $CDCl_3$) ŭ -57.9; **IR** (KBr, neat) 3023, 2955, 1743,

1605, 1491, 1446, 1397, 1259, 1166, 1019, 829, 769 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{25}F_3NO_5$ $(M + H)^+$ 512.1679, found 512.1687.

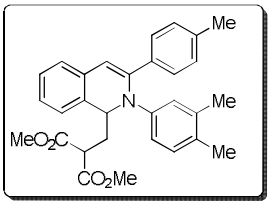
Dimethyl 2-((3-phenyl-2-(4-(trifluoromethoxy)phenyl)-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4l): Dark brown solid; mp 112-114 ^oC; R_f (hexane/EtOAc 17:3) 0.78; yield 30 mg, 29%; ^1H NMR (400 MHz, $CDCl_3$) ŭ 7.56 ï 7.50 (m, 2H), 7.32 ï 7.23 (m, 5H), 7.20 ï 7.14 (m, 1H), 6.98 ï 6.84 (m, 5H), 6.70 (s, 1H), 4.96 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.61 (t, *J* = 7.6 Hz, 1H), 2.49 ï 2.42 (m, 1H), 2.36 ï 2.28 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.0, 169.9, 146.0, 143.9, 140.1, 137.1, 131.5, 131.4, 128.8, 128.5, 128.1, 127.5, 127.0, 125.9, 125.2, 122.9, 121.7, 120.6 (q, *J* = 257.4 Hz), 112.9, 62.9, 53.0, 48.3, 32.9; ^{19}F NMR (377 MHz, $CDCl_3$) ŭ -58.2; **IR** (KBr, neat) 3050, 2955, 1745, 1607, 1560, 1506, 1446, 1259, 1166, 829, 769 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{25}F_3NO_5$ $(M + H)^+$ 512.1679, found 512.1686.



Dimethyl 2-((2-(4-nitrophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4m): Yellow solid; mp 132-134 ^oC; R_f (hexane/EtOAc 4:1) 0.78; yield 37.3 mg, 40%; ^1H NMR (NMR (400 MHz, $CDCl_3$) ŭ 7.91 ï 7.67 (m, 2H), 7.59 ï 7.31 (m, 2H), 7.26 ï 7.20 (m, 5H), 7.18 (s, 1H), 7.16 ï 7.12 (m, 1H), 6.91 (d, *J* = 7.4 Hz, 1H), 6.88 ï 6.82 (m, 1H), 6.68 (s, 1H), 5.11 (dd, *J* = 8.6, 6.6 Hz, 1H), 3.77 (s, 1H), 3.68 (s, 3H), 3.43 (dd, *J* = 8.7, 6.3 Hz, 1H), 2.46 ï 2.39 (m, 1H), 2.36 ï 2.27 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 169.8, 169.7, 152.2, 141.3, 138.7, 136.6, 131.8, 131.1, 129.1, 128.9, 128.5, 127.5, 127.1, 125.9, 125.8, 125.1, 120.1, 115.1, 61.4, 53.2, 53.1, 48.1, 32.2; **IR** (KBr, neat) 3019, 2954, 1740, 1595, 1504, 1445, 1391, 1270, 1112, 1067, 984, 850, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{25}N_2O_6$ $(M + H)^+$ 473.1707, found 473.1687.

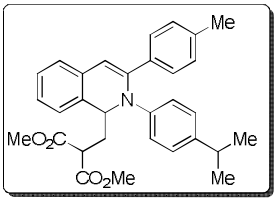


Dimethyl 2-((2-(4-nitrophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4p): Orange red semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 61 mg, 66%; ^1H NMR (500 MHz, $CDCl_3$) ŭ 7.46 (d, *J* = 8.0 Hz, 2H), 7.23 (dd, *J* = 13.5, 7.0 Hz, 2H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.71 (s, 1H), 6.60 (s, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 4.89 (t, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.76 (t, *J* = 8.0 Hz, 1H), 3.76 (s, 3H), 2.46 ï 2.39 (m, 1H), 2.32 ï 2.25 (m, 1H), 2.29 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.06, 145.5, 140.8, 138.0, 136.9, 135.0, 132.0, 131.5, 130.6, 129.9, 129.3,



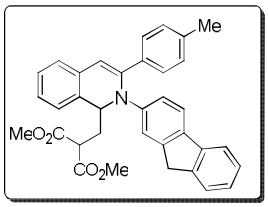
127.8, 127.5, 126.4, 126.0, 124.64, 123.64, 120.3, 111.2, 63.2, 52.9, 48.4, 33.2, 21.4, 20.2, 19.1; **IR** (KBr, neat) 3018, 2957, 1744, 1608, 1560, 1513, 1446, 1266, 1223, 1159, 1052, 823, 769 cm^{-1}; **HRMS** (ESI) calcd. for $C_{30}H_{32}NO_4$ $(M + H)^+$ 470.2326, found 470.2329.

Dimethyl 2-((2-(4-isopropylphenyl)-3-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl)methyl)malonate



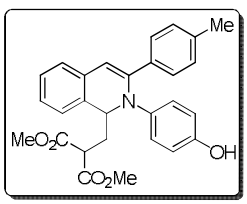
(**4q**): Orange red solid; mp 110-112 ^oC; R_f (hexane/EtOAc 17:3) 0.78; yield 60 mg, 61%; ^1H NMR (500 MHz, $CDCl_3$) ŭ 7.46 (d, *J* = 8.0 Hz, 2H), 7.25 ï 7.20 (m, 2H), 7.12 (td, *J* = 7.0, 2.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.93 (dd, *J* = 11.5, 8.0 Hz, 3H), 6.78 (d, *J* = 8.5 Hz, 2H), 6.62 (s, 1H), 4.93 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.72 (t, *J* = 7.4 Hz, 1H), 2.71 (septet, *J* = 7.0 Hz, 1H), 2.46 ï 2.37 (m, 1H), 2.33 ï 2.25 (m, 1H), 2.30 (s, 3H), 1.11 (dd, *J* = 7.0, 4.5 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.07, 145.4, 142.6, 140.7, 138.0, 135.0, 132.0, 131.6, 129.3, 127.7, 127.5, 126.8, 126.4, 126.0, 124.7, 122.2, 111.4, 63.0, 52.9, 48.4, 33.42, 33.06, 24.21, 24.04, 21.4; **IR** (KBr, neat) 3021, 2965, 1746, 1618, 1563, 1525, 1466, 1246, 1212, 1160, 1059, 835, 770 cm^{-1}; **HRMS** (ESI) calcd. for $C_{31}H_{34}NO_4$ $(M + H)^+$ 484.2482, found 484.2482.

Dimethyl 2-((2-(9*H*-fluoren-2-yl)-3-(p-tolyl)-1,2-dihydroisoquinolin-1-yl)methyl)malonate



(4r): Brown red semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield 71 mg, 67%; ^1H NMR (500 MHz, $CDCl_3$) ŭ 7.57 (d, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 10.0, 8.3 Hz, 3H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.29 ï 7.22 (m, 3H), 7.18 ï 7.13 (m, 2H), 7.07 (s, 1H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.88 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.65 (s, 1H), 5.02 (t, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.76 ï 3.67 (m, 3H), 2.53 ï 2.47 (m, 1H), 2.39 ï 2.32 (m, 1H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 146.7, 144.2, 143.1, 141.7, 140.7, 138.1, 136.3, 134.9, 132.0, 131.4, 129.4, 127.8, 127.5, 126.8, 126.5, 126.0, 125.0, 124.8, 121.5, 120.01, 119.40, 119.1, 111.3, 63.2, 53.0, 48.5, 37.0, 33.0, 21.4; **IR** (KBr, neat) 3018, 2951, 1742, 1609, 1564, 1449, 1268, 1229, 1157, 1061, 1026, 818, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{35}H_{32}NO_4$ $(M + H)^+$ 530.2326, found 530.2335.

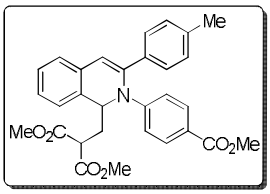
Dimethyl 2-((2-(4-hydroxyphenyl)-3-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl)methyl)malonate



(4s): Dark brown semisolid; R_f (hexane/EtOAc 4:1) 0.78; yield 59 mg, 65%; ^1H NMR (400 MHz, $CDCl_3$) ŭ 7.44 (d, *J* = 8.2 Hz, 2H), 7.26 ï 7.19 (m, 2H),

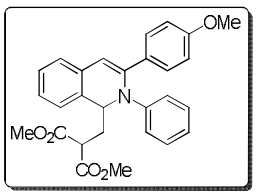
7.14 ï 7.08 (m, 1H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.92 (d, *J* = 7.3 Hz, 1H), 6.77 ï 6.71 (m, 2H), 6.57 (d, *J* = 6.3 Hz, 1H), 6.55 ï 6.49 (m, 2H), 5.07 (brs, 1H), 4.78 (t, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 4H), 3.73 (t, *J* = 7.6 Hz, 1H), 2.45 ï 2.38 (m, 1H), 2.31 ï 2.21 (m, 1H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.2, 170.1, 151.4, 141.1, 138.1, 134.8, 132.0, 131.0, 129.3, 127.7, 127.6, 126.4, 125.9, 124.6, 124.3, 115.7, 110.61, 63.6, 53.0, 48.4, 33.2, 21.4; **IR** (KBr, neat) 3452, 3021, 2951, 1735, 1606, 1557 1510, 1444, 1221, 1164, 1061, 1022, 821, 760 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{28}NO_5$ $(M + H)^+$ 458.1962, found 458.1965.

Dimethyl 2-((2-(4-(methoxycarbonyl)phenyl)-3-(p-tolyl)-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4t): Orange semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield 42 mg, 42%;



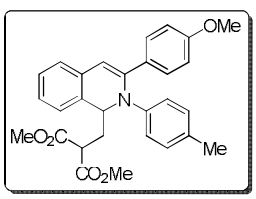
^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.79 ï 7.71 (m, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.29 ï 7.22 (m, 2H), 7.19 ï 7.13 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 7.4 Hz, 1H), 6.90 ï 6.83 (m, 2H), 6.68 (s, 1H), 5.11 (t, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.58 (t, *J* = 8.0 Hz, 1H), 2.51 ï 2.44 (m, 1H), 2.40 ï 2.33 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 169.9, 169.8, 167.0, 151.1, 139.5, 138.5, 134.2, 131.8, 131.5, 130.6, 129.5, 128.1, 127.2, 126.9, 125.9, 125.2, 122.8, 120.6, 113.1, 61.7, 53.0, 52.9, 51.9, 48.2, 32.4, 21.3; **IR** (KBr, neat) 3021, 2954, 1920, 1722, 1604, 1561, 1510, 1439, 1396, 1271, 1182, 1112, 1058, 1021, 978, 816, 761 cm^{-1}; **HRMS** (ESI) calcd. for $C_{30}H_{30}NO_6$ $(M + H)^+$ 500.2068, found 500.2076.

Dimethyl 2-((3-(4-methoxyphenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate



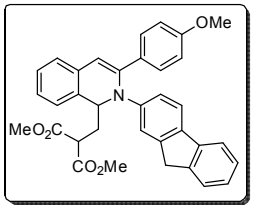
(4u): Pale yellow semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield 53 mg, 58%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.48 (d, *J* = 8.7 Hz, 2H), 7.27 ï 7.19 (m, 2H), 7.15 ï 7.09 (m, 1H), 7.07 (t, *J* = 7.9 Hz, 2H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.9 Hz, 2H), 6.84 ï 6.76 (m, 3H), 6.59 (s, 1H), 4.97 (t, *J* = 7.6 Hz, 1H), 3.78 (s, 6H), 3.75 (s, 3H), 3.68 (t, *J* = 7.2 Hz, 1H), 2.50 ï 2.40 (m, 1H), 2.37 ï 2.27 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 159.7, 147.48, 140.2, 132.0, 131.4, 130.0, 128.8, 128.8, 127.8, 126.3, 125.9, 124.7, 122.3, 122.1, 114.0, 110.9, 62.9, 55.39, 52.9, 48.4, 32.9; **IR** (KBr, neat) 3004, 2948, 1744, 1606, 1557, 1507, 1446, 1258, 1033, 768 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{28}NO_5$ $(M + H)^+$ 458.1962, found 458.1965.

Dimethyl 2-((3-(4-methoxyphenyl)-2-(p-tolyl)-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4v): Dark red semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield 57 mg, 62%; ^{1}H NMR (500 MHz,

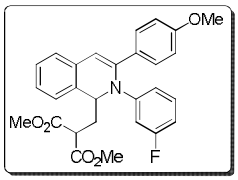


$CDCl_3$) ŭ 7.49 (d, *J* = 8.5 Hz, 2H), 7.25 ï 7.18 (m, 2H), 7.11 (ddt, *J* = 12.5, 8.2, 4.2 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.81 ï 6.73 (m, 4H), 6.56 (s, 1H), 4.89 (t, *J* = 7.6 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.74 (s, 3H), 3.71 (t, *J* = 7.4 Hz, 1H), 2.47 ï 2.39 (m, 1H), 2.34 ï 2.26 (m, 1H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 159.6, 145.2, 140.5, 132.1, 131.8, 131.2, 130.2, 129.5, 128.8, 127.7, 126.2, 125.9, 124.6, 122.5, 114.0, 110.5, 63.17, 55.4, 52.9, 48.4, 33.1, 20.8; **IR** (KBr, neat) 3009, 2953, 2845, 1739, 1606, 1564, 1509, 1441, 1389, 1246, 1164, 1032, 821, 757 cm^{-1}; **HRMS** (ESI) calcd. for $C_{29}H_{30}NO_5$ $(M + H)^+$ 472.2119, found 472.2120.

Dimethyl 2-((2-(9*H*-fluoren-2-yl)-3-(4-methoxyphenyl)-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4w): Pale yellow semisolid; R_f (hexane/EtOAc 4:1) 0.78; yield 74 mg, 68%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.58 (d, *J* = 7.5 Hz, 1H), 7.54 ï 7.48 (m, 2H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.29 ï 7.22 (m, 3H), 7.20 ï 7.10 (m, 2H), 7.06 (s, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.88 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.81 ï 6.75 (m, 2H), 6.60 (s, 1H), 5.01 (t, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.81 (s, 3H), 3.74 (s, 3H), 3.73ï 3.69 (m, 3H), 2.53ï 2.46 (m, 1H), 2.40 ï 2.32 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 159.7, 146.7, 144.2, 143.1, 141.7, 140.4, 136.3, 132.1, 131.3, 130.2, 128.9, 127.8, 126.9, 126.3, 126.0, 125.0, 124.7, 121.6, 120.0, 119.4, 119.2, 114.0, 110.6, 63.2, 55.4, 53.0, 48.5, 37.1, 33.0; **IR** (KBr, neat) 3009, 2950, 2846, 1741, 1670, 1608, 1566, 1503, 1449, 1398, 1255, 1166, 1032, 825, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{35}H_{32}NO_5$ $(M + H)^+$ 546.2275, found 546.2256.

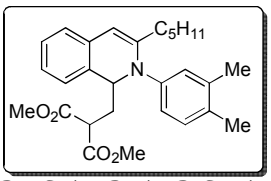


Dimethyl 2-((2-(3-fluorophenyl)-3-(4-methoxyphenyl)-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4x): Brown red semisolid; R_f (hexane/EtOAc 95:1) 0.78; yield 53 mg, 56%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.50 ï 7.44 (m, 2H), 7.24 (t, *J* = 5.6 Hz, 2H), 7.18 ï 7.12 (m, 1H), 6.99 (dt, *J* = 11.8, 7.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.62 (s, 1H), 6.58 (dd, *J* = 11.2, 2.1 Hz, 1H), 6.51 (d, *J* = 8.2, 1.5 Hz, 1H), 4.96 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.65 (t, *J* = 7.5 Hz, 1H), 2.47 ï 2.40 (m, 1H), 2.35 ï 2.26 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 169.9, 163.2 (d, *J* = 244.5 Hz), 159.9, 149.3, 149.2, 139.6, 131.7, 131.6, 129.8 (d, *J* = 9.6 Hz), 129.6, 128.6, 128.0, 126.7, 125.9, 125.0, 117.6, 114.2, 111.8, 109.2 (d, *J* = 24.1 Hz), 108.8 (d, *J* = 21.4 Hz), 62.7, 55.4, 53.0, 48.3, 32.8; ^{19}F NMR (377 MHz, $CDCl_3$) ŭ -112.5; **IR**



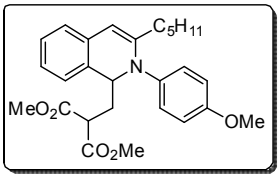
(KBr, neat) 3012, 2955, 2841, 1740, 1603, 1500, 1447, 1390, 1258, 1165, 1.32, 823, 765 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{27}FNO_5$ $(M + H)^+$ 476.1868, found 476.1873.

Dimethyl 2-((2-(3,4-dimethylphenyl)-3-pentyl-1,2-dihydroisoquinolin-1-yl)methyl) malonate (4y): Brown red semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 40 mg, 45%; ^{1}H NMR



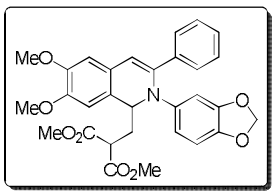
(500 MHz, $CDCl_3$) ŭ 7.16 (d, *J* = 8.0, 1H), 7.09 ï 7.02 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.3 Hz, 1H), 6.75 (t, *J* = 6.8 Hz, 1H), 6.71 (dd, *J* = 8.0, 2.3 Hz, 1H), 6.08 (s, 1H), 4.58 (t, *J* = 7.5 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.65 (t, *J* = 7.0 Hz, 1H), 2.39 ï 2.29 (m, 2H), 2.34 ï 2.101 (m, 2H), 2.19 (s, 3H), 2.18 (s, 3H), 1.52 ï 1.42 (m, 2H), 1.30 ï 1.22 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 170.2, 170.0, 144.9, 143.2, 137.2, 131.9, 131.7, 130.1, 129.9, 127.5, 125.8, 125.6, 124.9, 123.6, 121.0, 109.4, 63.4, 52.8, 48.3, 33.4, 33.2, 31.7, 28.5, 22.7, 20.1, 19.3, 14.2, **IR** (KBr, neat) 3001, 2949, 2861, 1743, 1614, 1502, 1446, 1256,1163, 1025, 818, 767 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{36}NO_4$ $(M + H)^+$ 450.2639, found 450.2641. (Gram Scale 43%, 0.965 g)

dimethyl 2-((2-(4-methoxyphenyl)-3-pentyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4z): Pale yellow semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 41 mg, 46%; ^{1}H NMR (500



MHz, $CDCl_3$) ŭ 7.16 (t, *J* = 8.8, 1H), 7.07 ï 7.03 (m, 2H), 6.93 (d, *J* = 9.2 Hz, 2H), 6.85 (d, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.03 (s, 1H), 4.50 (t, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.74 (s, 1H), 3.65 (t, *J* = 7.6 Hz, 1H), 2.36 - 2.26 (m, 2H), 2.24 ï 2.15 (m, 1H), 2.12 ï 2.04 (m, 1H), 1.52 - 1.39 (s, 2H), 1.30 ï 1.18 (m, 4H), 0.84 (t, *J* = 7.2 Hz, 3H); ŭ ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.2, 170.0, 156.3, 143.5, 140.4, 132.0, 129.4, 127.5, 125.8, 125.5, 125.4, 123.6, 114.3, 108.6, 63.7, 55.6, 52.8, 48.3, 33.3, 33.3, 31.6, 28.3, 22.6, 14.2; **IR** (KBr, neat) 3080, 2999, 1744, 1652, 1552, 1512, 1453, 1259, 1222, 1084, 1038, 770 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{36}NO_4$ $(M + H)^+$ 452.2431, found 452.2405.

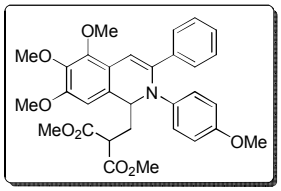
Dimethyl 2-((2-(benzo[d][1,3]dioxol-5-yl)-6,7-dimethoxy-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4aa): Dark red semisolid; R_f (hexane/EtOAc 7:3) 0.78; yield 37 mg,



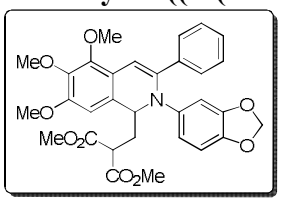
35%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.59 ï 7.52 (m, 2H), 7.30 ï 7.24 (m, 2H), 7.23 ï 7.19 (m, 1H), 6.81 (s, 1H), 6.62 (s, 1H), 6.51 (s, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 6.46 (d, *J* = 2.2 Hz, 1H), 6.32 (dd, *J* = 8.3, 2.3 Hz, 1H),

5.80 (dd, *J* = 6.1, 1.4 Hz, 2H), 4.73 (t, *J* = 7.6 Hz, 1H), 3.92 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.76 (t, *J* = 12.8 Hz, 1H), 3.76 (s, 3H), 2.40 ï 2.33 (m, 1H), 2.29 ï 2.20 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 170.1, 148.7, 148.3, 148.0, 143.4, 142.7, 139.2, 137.7, 128.6, 128.0, 127.3, 124.8, 123.9, 115.8, 111.8, 109.4, 108.2, 108.1, 104.7, 101.2, 63.6, 56.2, 53.0, 52.9, 48.5, 33.5; **IR** (KBr, neat) 3003, 2955, 2896, 1742, 1610, 1500, 1450, 1347, 1239, 1122, 1041, 933, 765 cm^{-1}; **HRMS** (ESI) calcd. for $C_{30}H_{30}NO_8$ $(M + H)^+$ 532.1967, found 532.1959.

Dimethyl 2-((5,6,7-trimethoxy-2-(4-methoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4ab): Dark brown red semisolid; R_f (hexane/EtOAc 7:3) 0.78; yield 36 mg, 33%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.59 (d, *J* = 8.8 Hz, 2H), 7.29 ï 7.23 (m, 2H), 7.19 (ddd, *J* = 7.3, 3.6, 1.2 Hz, 1H), 6.87 (s, 1H), 6.82 ï 6.77 (m, 2H), 6.65 ï 6.59 (m, 2H), 6.31 (s, 1H), 4.74 (dd, *J* = 8.3, 6.9 Hz, 1H), 4.00 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H), 3.81 (s, 3H), 3.82 ï 3.79 (m, 1H), 3.75 (s, 3H), 3.66 (s, 3H), 2.41 ï 2.34 (m, 1H), 2.31 ï 2.21 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 170.1, 155.3, 152.6, 148.8, 141.4, 141.1, 138.9, 137.8, 128.5, 127.9, 127.4, 123.7, 118.9, 114.3, 106.6, 105.4, 63.5, 61.6, 61.2, 56.2, 55.5, 53.0, 52.9, 48.5, 33.3; **IR** (KBr, neat) 3007, 2999, 2949, 2895, 1744, 1667, 1602, 1559, 1504, 1454, 1337, 1244, 1188, 1120, 1.39, 837, 768 cm^{-1}; **HRMS** (ESI) calcd. for $C_{31}H_{34}NO_8$ $(M + H)^+$ 548.2279, found 548.2293.



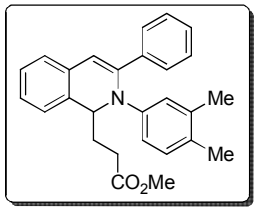
Dimethyl 2-((2-(benzo[*d*][1,3]dioxol-5-yl)-5,6,7-trimethoxy-3-phenyl-1,2-dihydroisoquinolin-1-yl)methyl)malonate (4ac): Brown red semisolid; R_f (hexane/EtOAc 7:3) 0.78; yield 39 mg, 35%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.61 ï 7.57 (m, 2H), 7.31 ï 7.26 (m, 2H), 7.23 ï 7.18 (m, 1H), 6.88 (s, 1H), 6.53 ï 6.48 (m, 1H), 6.45 (d, *J* = 2.3 Hz, 1H), 6.34 ï 6.31 (m, 1H), 6.32 (s, 1H) 5.82 ï 5.78 (dd, *J* = 5.5, 1.5 Hz, 2H), 4.71 (t, *J* = 8.5 Hz, 1H), 4.00 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H), 3.82 (s, 3H), 3.78 (t, *J* = 8.5 Hz, 1H), 3.75 (s, 3H), 2.38 ï 2.32 (m, 1H), 2.28 ï 2.20 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 170.1, 170.0, 152.7, 148.9, 148.0, 143.3, 142.7, 141.4, 138.7, 137.71, 128.6, 128.0, 127.6, 127.3, 118.7, 115.6, 108.1, 107.0, 105.3, 104.5, 101.2, 63.7, 61.7, 61.2, 56.2, 53.0, 52.9, 48.5, 33.2; **IR** (KBr, neat) 3002, 2948, 2844, 1743, 1605, 1557, 1491, 1340, 1216, 1160, 1121, 1042, 852, 766 cm^{-1}; **HRMS** (ESI) calcd. for $C_{31}H_{32}NO_9$ $(M + H)^+$ 562.2072, found 562.2070.



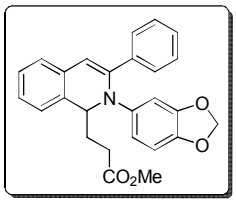
Experimental procedure for the synthesis of compound 5: To a stirred solution of compound **4** in DMF and H_2O was added 2.0 equivalents of lithium chloride (LiCl) under nitrogen atmosphere at room temperature. Thereafter, the reaction mixture was heated at reflux temperatures using oil bath. The reaction was monitored by TLC. After completion staring material (8h), the reaction was cooled to room temperature; diluted with cold water and then extracted with DCM. The solvent was evaporated under reduced pressure. The crude was subjected to column chromatography over silica gel to obtain the desired product **5**.

Methyl 3-(2-(3,4-dimethylphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoate (5a):

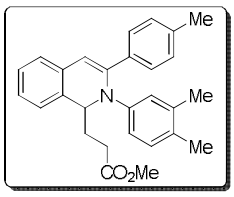
(0.55 mmol, 252 mg, of reaction in DMF (7 mL), H_2O (24 μL), LiCl (47mg, 1.1 mmol)); Dark brown red semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 175 mg, 75%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.59 ï 7.52 (m, 2H), 7.29 ï 7.16 (m, 5H), 7.12 (ddd, *J* = 8.7, 7.0, 2.0 Hz, 1H), 6.96 (d, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.71 (s, 1H), 6.60 (s, 1H), 6.57 (dd, *J* = 8.1, 2.3 Hz, 1H), 4.91 ï (t, *J* = 7.4 Hz, 1H), 3.73 (s, 3H), 2.68 ï 2.48 (m, 2H), 2.18 (tt, *J* = 15.7, 7.9 Hz, 1H), 2.07 (s, 3H), 2.05 (s, 3H), 2.05 ï 1.95 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 174.2, 145.7, 140.9, 138.1, 136.9, 132.3, 131.9, 130.4, 129.8, 128.5, 128.0, 127.6, 127.5, 126.4, 126.0, 124.6, 123.7, 120.2, 111.6, 64.6, 51.9, 30.6, 29.7, 20.2, 19.1; **IR** (KBr, neat) 3020, 2926, 2859, 1736, 1607, 1561, 1499, 1448, 1263, 1218, 1170,1031, 817, 765 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{28}NO_2$ $(M + H)^+$ 398.2111, found 398.2115.



Methyl 3-(2-(benzo[*d*][1,3]dioxol-5-yl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoate (5b): (47 mg, 0.1 mmol, of reaction in DMF (3 mL), H_2O (5 μL), LiCl (8.5 mg, 0.2 mmol)); Brown red semisolid; R_f (hexane/EtOAc 5:1) 0.78; yield 28.7 mg, 70%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.60 ï 7.53 (m, 2H), 7.30 ï 7.18 (m, 5H), 7.17 ï 7.10 (m, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.62 (s, 1H), 6.49 (dd, *J* = 5.3, 3.0 Hz, 2H), 6.37 ï 6.30 (m, 1H), 5.78 (dd, *J* = 6.5, 1.3 Hz, 2H), 4.81 (t, *J* = 8.0, Hz, 1H), 3.72 (s, 3H), 2.65 ï 2.48 (m, 2H), 2.21 - 2.12 (m, 1H), 2.04 ï 1.92 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 174.2, 148.0, 143.3, 143.0, 141.1, 137.9, 132.15, 131.9, 128.7, 128.3, 127.7, 126.7, 126.1, 124.8, 116.1, 111.7, 108.1, 104.9, 101.3, 65.3, 52.0, 30.6, 29.8; **IR** (KBr, neat) 3017, 2952, 1735 1608, 1559, 1489, 1446, 1402, 1338, 1208, 1039, 935, 811, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{24}H_{26}NO_4$ $(M + H)^+$ 414.1700, found 414.1680.

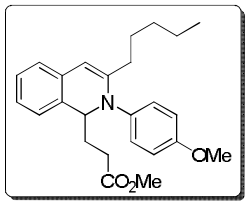


Methyl 3-(2-(3,4-dimethylphenyl)-3-(p-tolyl)-1,2-dihydroisoquinolin-1-yl)propanoate (5c):



(47 mg, 0.1 mmol, of reaction in DMF (3 mL), H_2O (5 μL), LiCl (8.5 mg, 0.2 mmol)); Orange red semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 35 mg, 74%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.48 ï 7.42 (m, 2H), 7.24 ï 7.17 (m, 2H), 7.11 (ddd, *J* = 7.4, 6.4, 2.4 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.72 (d, *J* = 2.3 Hz, 1H), 6.58 (s, 1H), 6.56 ï 6.53 (m, 1H), 4.89 (dd, *J* = 8.3, 6.6 Hz, 1H), 3.73 (s, 3H), 2.68 ï 2.49 (m, 2H), 2.28 (s, 3H), 2.24 ï 2.11 (m, 1H), 2.09 (s, 3H), 2.06 (s, 3H), 2.03 ï 1.93 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 174.2, 145.9, 140.9, 137.9, 136.9, 135.2, 132.3, 132.1, 130.3, 129.8, 129.3, 127.5, 126.3, 126.0, 124.5, 123.7, 120.25, 111.0, 64.6, 51.9, 30.6, 29.6, 21.4, 20.2, 19.1; **IR** (KBr, neat) 3015, 2926, 1715, 1607, 1562, 1502, 1445, 1265, 1219, 1137, 928, 814, 759 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{30}NO_2$ $(M + H)^+$ 412.2271, found 412.2251.

Methyl 3-(2-(4-methoxyphenyl)-3-pentyl-1,2-dihydroisoquinolin-1-yl)propanoate (5d):

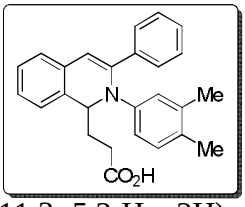


(1.0 mmol, 451 mg, of reaction in DMF (10 mL), H_2O (43 μL) LiCl (85 mg, 2.0 mmol)); Brown red semisolid; R_f (hexane/EtOAc 9:1) 0.78; yield 260 mg, 66%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.18 ï 7.13 (m, 1H), 7.04 (dtd, *J* = 7.3, 3.7, 1.3 Hz, 2H), 6.98 ï 6.92 (m, 2H), 6.86 ï 6.82 (m, 1H), 6.80 ï 6.75 (m, 2H), 5.97 (s, 1H), 4.50 (t, *J* = 7.4 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 2.44 (t, *J* = 7.4 Hz, 2H), 2.36 ï 2.26 (m, 1H), 2.12 ï 2.01(m, 2H), 2.00 - 1.89 (m, 1H), 1.50 ï 1.37 (m, 2H), 1.32 ï 1.14 (m, 4H), 0.84 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 174.2, 156.2, 143.6, 140.6, 132.2, 130.0, 127.3, 125.8, 125.5, 125.2, 123.4, 114.3, 107.9, 65.1, 55.7, 51.8, 33.3, 31.6, 30.2, 29.1, 28.0, 22.7, 14.2; **IR** (KBr, neat) 3002, 2946, 2859, 1736, 1617, 1563, 1506, 1448, 1364, 1238, 1175, 1035, 834, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{25}H_{32}NO_3$ $(M + H)^+$ 394.2377, found 394.2357.

Experimental procedure for the synthesis of compound 6a: To a stirred solution of compound **5a** (100 mg**,** 0.251 mmol) in THF (5 mL) was added a solution of $LiOH.H_2O$ (1.22 mmol) in MeOH-H_2O (4:1, 5 mL) and the resulting mixture was allowed to stir at room temperature for overnight. After complete consumption of starting material, the reaction mixture was quenched with 10% HCl (pH 1-2, maintained), and then organic layer was extracted with DCM. Thereafter, the organic layer was diluted with water and washed brine solution 2-3 times. The

combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel using hexane/EA (3:2) to obtain the corresponding product **6a**.

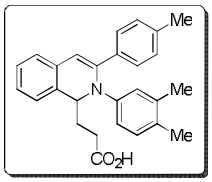
3-(2-(3,4-Dimethylphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propanoic acid (6a):



Brown red semisolid; R_f (hexane/EtOAc 13:7) 0.78; yield 91 mg, 95%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.56 (dt, *J* = 3.3, 1.9 Hz, 2H), 7.28 ï 7.16 (m, 5H), 7.13 (td, *J* = 7.1, 2.0 Hz, 1H), 6.98 (d, *J* = 7.3 Hz, 1H), 6.77 (dd, *J* = 11.3, 5.2 Hz, 2H), 6.61 (s, 1H), 6.57 (dd, *J* = 8.1, 2.4 Hz, 1H), 4.96 ï 4.89 (m, 1H), 2.73 ï 2.56 (m, 2H), 2.26 ï 2.15 (m, 1H), 2.06 (s, 3H), 2.04 (s, 3H), 2.04 ï 1.97 (m, 1H);^{13}C NMR (126 MHz, $CDCl_3$) ŭ 179.4, 145.7, 141.0, 138.1, 137.0, 132.2, 131.9, 130.5, 129.8, 128.5, 128.3, 128.0, 127.6, 127.5, 126.4, 126.1, 124.6, 123.7, 120.3, 111.6, 64.5, 30.7, 29.5, 20.1, 19.1; **IR** (KBr, neat) 3015, 2928, 1718, 1607, 1563, 1499, 1446, 1393, 1266, 1220, 1030, 820, 761 cm^{-1}; **HRMS** (ESI) calcd. for $C_{26}H_{25}NO_2$ $(M - H)^+$ 384.1802, found. 382.1800.

Experimental procedure for the synthesis of compound (6b): A stirred mixture of compound **5c** (60 mg, 0.15 mmol) and PPA (200 mg) was subjected to heat at 140 ^oC for 2h. The reaction was monitored by TLC. After completion of starting material, the reaction mixture was brought to 60 ^oC and then poured in water and maintained (pH = 9) by adding 25% ammonia solution. The organic layer was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel using hexane/EA (3:2) to obtain the product **6b.**

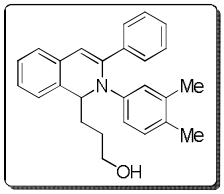
3-(2-(3,4-Dimethylphenyl)-3-(p-tolyl)-1,2-dihydroisoquinolin-1-yl)propanoic acid (6b): Pale



Orange red semisolid; R_f (hexane/EtOAc 13:7) 0.78; yield 21 mg, 37%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.45 (d, *J* = 8.0 Hz, 2H), 7.25 ï 7.17 (m, 2H), 7.14 ï 7.08 (m, 1H), 7.05 (t, *J* = 7.3 Hz, 2H), 6.96 (d, *J* = 7.4 Hz, 1H), 6.80 ï 6.72 (m, 2H), 6.60 ï 6.53 (m, 2H), 4.91 (t, *J* = 7.4 Hz, 1H), 2.72 ï 2.54 (m, 2H), 2.28 (s, 3H), 2.20 (dd, *J* = 14.5, 7.1 Hz, 1H), 2.07 (s, 3H), 2.04 (s, 3H), 1.98 (dt, *J* = 13.3, 6.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 179.3, 145.8, 140.9, 137.9, 136.9, 135.2, 132.2, 132.0, 130.4, 129.8, 129.3, 127.4, 126.3, 126.0, 124.4, 123.7, 120.3, 111.0, 64.5, 30.7, 29.4, 21.4, 20.2, 19.2; **IR** (KBr, neat) 3015, 2928, 1718, 1607, 1563, 1499, 1446, 1393, 1266, 1220, 1030, 820, 761 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{28}NO_2$ $(M + H)^+$ 398.2115, found 398.2099.

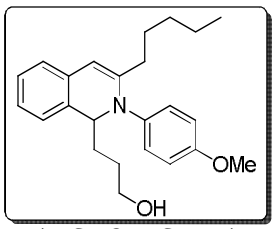
Experimental procedure for the synthesis of compound (7): 4.0 Equivalents of LAH was added to a stirred solution of compound **5** in 4.0 mL THF at 0 ^{o}C under nitrogen atmosphere. Thereafter, the reaction mixture was slowly brought to room temperature and continued stirring for 4h. After completion of reaction, diluted with ethyl acetate and washed with saturated ammonium chloride solution. The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel using hexane/EA (7:3) to give the corresponding product **7**.

3-(2-(3,4-Dimethylphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)propan-1-ol (7a): (0.15 mmol, 60 mg, of reaction in THF (3.0 mL), $LiAlH_4$ (23 mg, 0.6 mmol)); Dark brown red semisolid; R_f (hexane/EtOAc 7:3) 0.78; yield 44 mg, 82%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 7.59 ï 7.53 (m, 2H), 7.28 ï 7.16 (m, 5H), 7.11 (td, *J* = 7.2, 2.0 Hz, 1H), 6.96 (d, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.72 (s, 1H), 6.62 ï 6.56 (m, 1H), 6.57 (s, 1H), 4.83 (dd, *J* = 7.9, 6.4 Hz, 1H), 3.74 ï 3.61 (m, 2H), 2.08 (s, 3H), 2.06 (s, 3H), 2.02 ï 1.91 (m, 2H), 1.87 ï 1.78 (m, 1H), 1.77 ï 1.69 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) ŭ 145.8, 141.1, 138.3, 136.9, 133.0, 131.9, 130.3, 129.8, 128.5, 127.9, 127.6, 127.3, 126.3, 125.9, 124.5, 123.8, 120.2, 111.6, 65.7, 63.3, 31.2, 29.9, 20.2, 19.1; **IR** (KBr, neat) 3353, 3251, 3019, 2940, 1607, 1559, 1499, 1451, 1389, 1270, 1219, 1065, 814, 763 cm^{-1}; **HRMS** (ESI) calcd. for $C_{26}H_{28}NO$ $(M + H)^+$ 370.2009, found 370.2012.



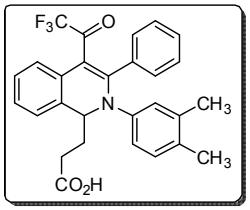
3-(2-(4-Methoxyphenyl)-3-pentyl-1,2-dihydroisoquinolin-1-yl)propan-1-ol (7b):

(0.2 mmol, 80 mg, of reaction in THF (4.0 mL), $LiAlH_4$ (30 mg, 0.8 mmol)); Dark brown red semisolid; R_f (hexane/EtOAc 7:3) 0.78; yield 61 mg, 82%; ^{1}H NMR (500 MHz, $CDCl_3$) ŭ 7.14 (t, *J* = 8.5 Hz, 1H), 7.02 (dd, *J* = 11.3, 4.2 Hz, 2H), 6.94 (t, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 7.4 Hz, 1H), 6.79 ï 6.75 (m, 2H), 5.95 (s, 1H), 4.4 (t, *J* = 7.0 Hz, 1H), 3.75 (s, 3H), 3.66 ï 3.58 (m, 2H), 2.35 ï 2.28 (m, 1H), 2.11 ï 2.05 (m, 1H), 1.84 ï 1.74 (m, 2H), 1.69 ï 1.59 (m, 2H), 1.46 ï 1.38 (m, 2H), 1.28 ï 1.18 (m, 4H), 0.83 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 155.9, 143.4, 140.6, 132.0, 130.6, 126.9, 125.6, 125.4, 124.9, 123.0, 114.1, 107.5, 63.0, 63.0, 55.5, 33.2, 31.4, 31.0, 29.5, 28.1, 22.5, 14.0; **IR** (KBr, neat) 3348, 2945, 2868, 1607, 1560, 1510, 1456, 1386, 1297, 1248, 1178, 1036, 831, 764 cm^{-1}; **HRMS** (ESI) calcd. for $C_{24}H_{32}NO_2$ $(M + H)^+$ 366.2428, found 364.2271.

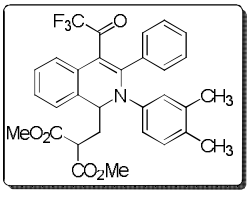


Experimental procedure for the synthesis of compound 8 and 9: 10.0 Equivalents of TFAA was added to stirred solution of compound **6a/4a** in benzene 6.0 mL under nitrogen atmosphere at 0 ^{o}C. Thereafter the reaction was heated at reflux temperature for 10 h. The reaction was monitored by TLC. After completion of starting martial; the reaction mixture was cooled; the solvent evaporated under reduced pressure. The crude mixture was diluted 5% sodium carbonate solution and the organic layer was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel to give the corresponding product **8/9**.

3-(2-(3,4-dimethylphenyl)-3-phenyl-4-(2,2,2-trifluoroacetyl)-1,2-dihydroisoquinolin-1-yl)propanoic acid (8): (0.2 mmol, 77 mg, of reaction in benzene (5.0 mL), TFAA (277 μL, 2.0 mmol)); Yellow semisolid; R_f (hexane/EtOAc 3:2) 0.78; yield 44 mg, 46%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 8.30 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.40 ï 7.35 (m, 1H), 7.33 ï 7.19 (m, 4H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.83 (s, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 1H), 5.00 (dd, *J* = 9.3, 5.2 Hz, 1H), 2.59 ï 2.30 (m, 4H), 2.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 185.0 (q, *J* = 33.7 Hz) 179.4, 154.0, 143.5, 137.6, 136.2, 134.1, 132.1, 130.9, 130.1, 129.3, 128.6, 128.4, 127.9, 126.2, 126.2, 126.0, 122.8, 122.6, 116.1 (q, *J* = 294.2 Hz), 112.7, 65.7, 30.3, 27.7, 19.9, 19.3.^{19}F NMR (377 MHz, $CDCl_3$) ŭ -71.5; **IR** (KBr, neat) 3027, 2925, 2862, 1708, 1670, 1586, 1490, 1437, 1245, 1192, 1143, 1080, 1027, 875, 759 cm^{-1}; **HRMS** (ESI) calcd. for $C_{28}H_{25}F_3NO_3$ $(M + H)^+$ 480.1781, found 480.1760.

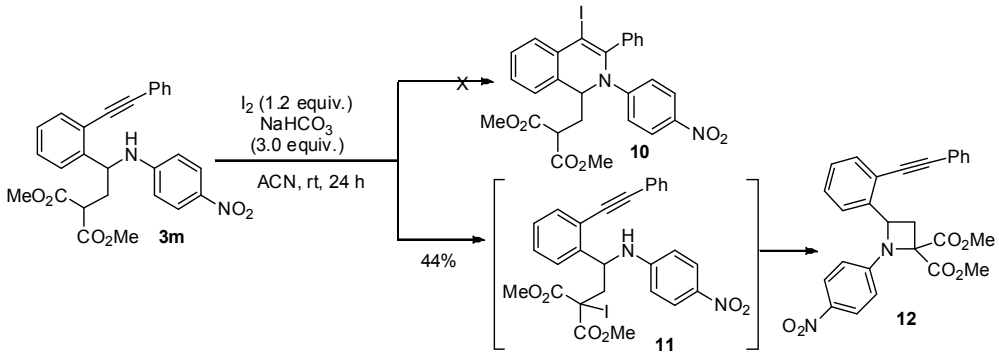


Dimethyl 2-((2-(3,4-dimethylphenyl)-3-phenyl-4-(2,2,2-trifluoroacetyl)-1,2-dihydroisoquinolin-1-yl)methyl)malonate (9): (0.1 mmol, 45 mg, of reaction in benzene (4.0 mL), TFAA (138 μL, 1.0 mmol)); Yellow semisolid; R_f (hexane/EtOAc 17:3) 0.78; yield 27 mg, 50%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 8.25 (d, *J* = 7.7 Hz, 1H), 7.44 ï 7.41 (m, 2H), 7.38 (td, *J* = 8.0, 1.3 Hz, 1H), 7.34 ï 7.29 (m, 1H), 7.28 ï 7.20 (m, 3H), 6.98 ï 6.92 (m, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 2.1 Hz, 1H), 6.62 (dd, *J* = 8.1, 2.3 Hz, 1H), 4.97 (dd, *J* = 9.5, 5.9 Hz, 1H), 3.83 (s, 3H), 3.71 (s, 3H), 3.48 (dd, *J* = 8.0, 3.6 Hz, 1H), 2.73 ï 2.66 (m, 1H), 2.63 ï 2.56 (m, 1H), 2.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 185.3 (q, 33.9 Hz), 169.7, 169.3, 153.5, 143.4, 137.6, 136.1, 134.1, 132.0, 130.9, 130.1, 129.3, 128.7, 128.6, 127.5, 126.4, 126.1, 125.9, 125.7, 122.7,



122.6, 116.1 (q, 294.3 Hz), 113.0, 64.5, 53.1, 53.1, 48.4, 31.90, 19.9, 19.3; ^{19}F NMR (377 MHz, $CDCl_3$) ŭ -71.8; **IR** (KBr, neat) 3161, 2998, 2426, 1745, 1669, 1514, 1443, 1282, 1222, 1153, 1082, 879, 770 cm^{-1}; **HRMS** (ESI) calcd. for $C_{31}H_{29}F_3NO_5$ $(M + H)^+$ 552.1992, found 552.1983.

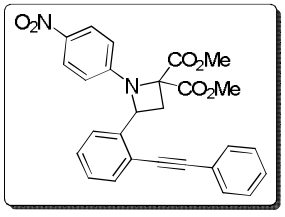
The attempts of cyclization of **3m** with $I_2/NaHCO_3$ in ACN resulted the formation of substituted azetidine **12** instead electrophilic iodo cyclized product **10**. This result explains that, the iodination is preferentially taking place at active C-H function to form intermediate **11** followed by intramolecular *N*-alkylation to give **12** (Scheme 6).



Scheme 6: Synthesis of substituted azitedine

Experimental procedure for the synthesis of compound 12: 1.2 Equivalents of iodine and 3.0 equivalent of sodium bicarbonate were added to a stirred solution of compound **3m** (47 mg, 0.1 mmol) in ACN (3.0 mL) at room temperature. The reaction was monitored by TLC. After completion of starting martial (24 h); the reaction mixture was washed with saturated sodium thiosulpahte solution and the organic layer was extracted with ethyl acetate. The combined organic layers were dried over /Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel using hexane/EA (7/3) as eluents to give the corresponding product **12**.

Dimethyl 1-(4-nitrophenyl)-4-(2-(phenylethynyl)phenyl)azetidine-2,2-dicarboxylate (12):

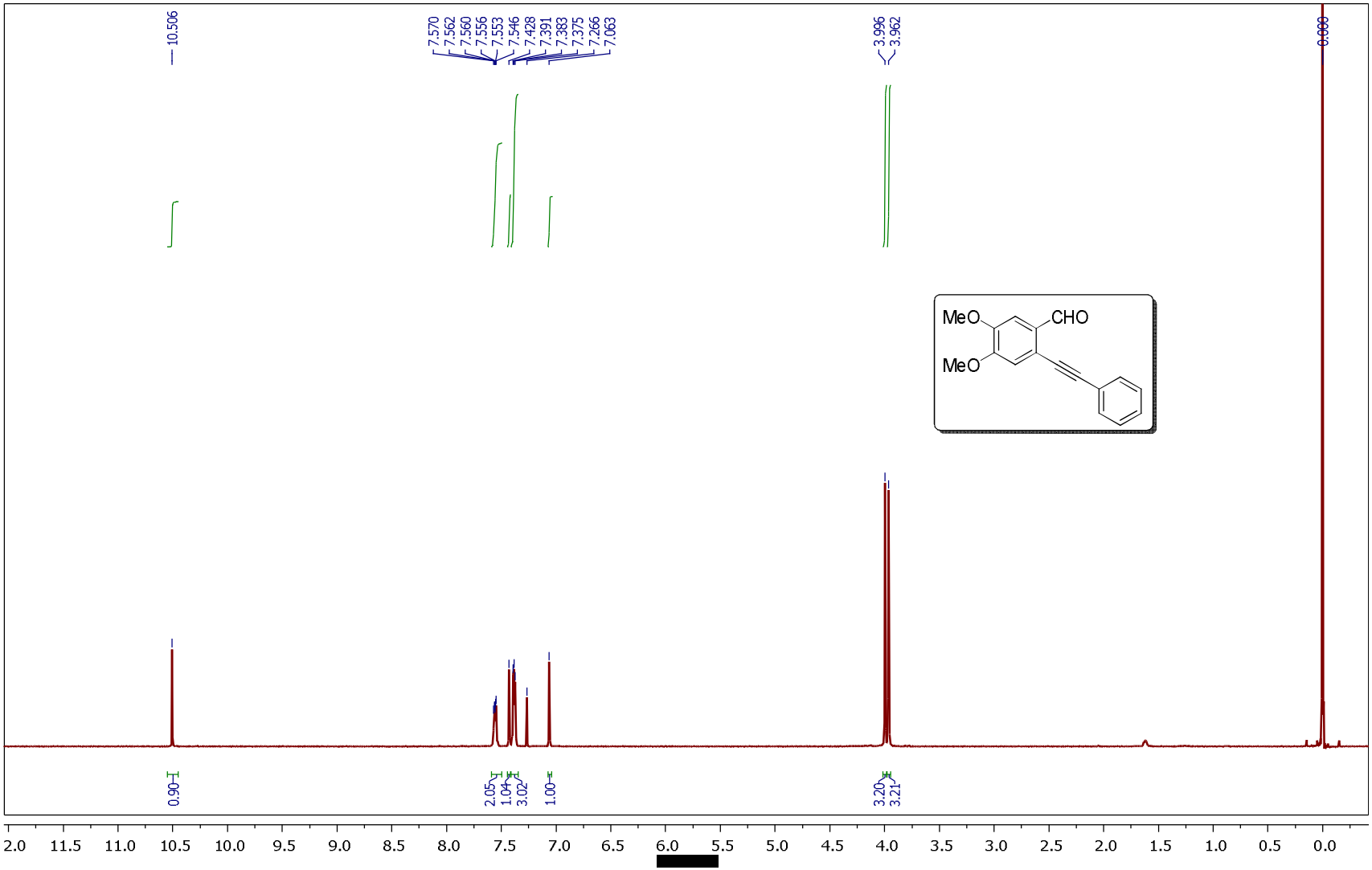


Orange red semi solid; 0.4 R_f (hexane/EtOAc 7:3) 0.78; yield 20 mg, 44%; ^{1}H NMR (400 MHz, $CDCl_3$) ŭ 8.07 (d, *J* = 9.4 Hz, 2H), 7.62 ï 7.57 (m, 1H), 7.56 ï 7.53 (m, 2H), 7.49 ï 7.42 (m, 1H), 7.41 ï 7.37 (m, 3H), 7.37 ï

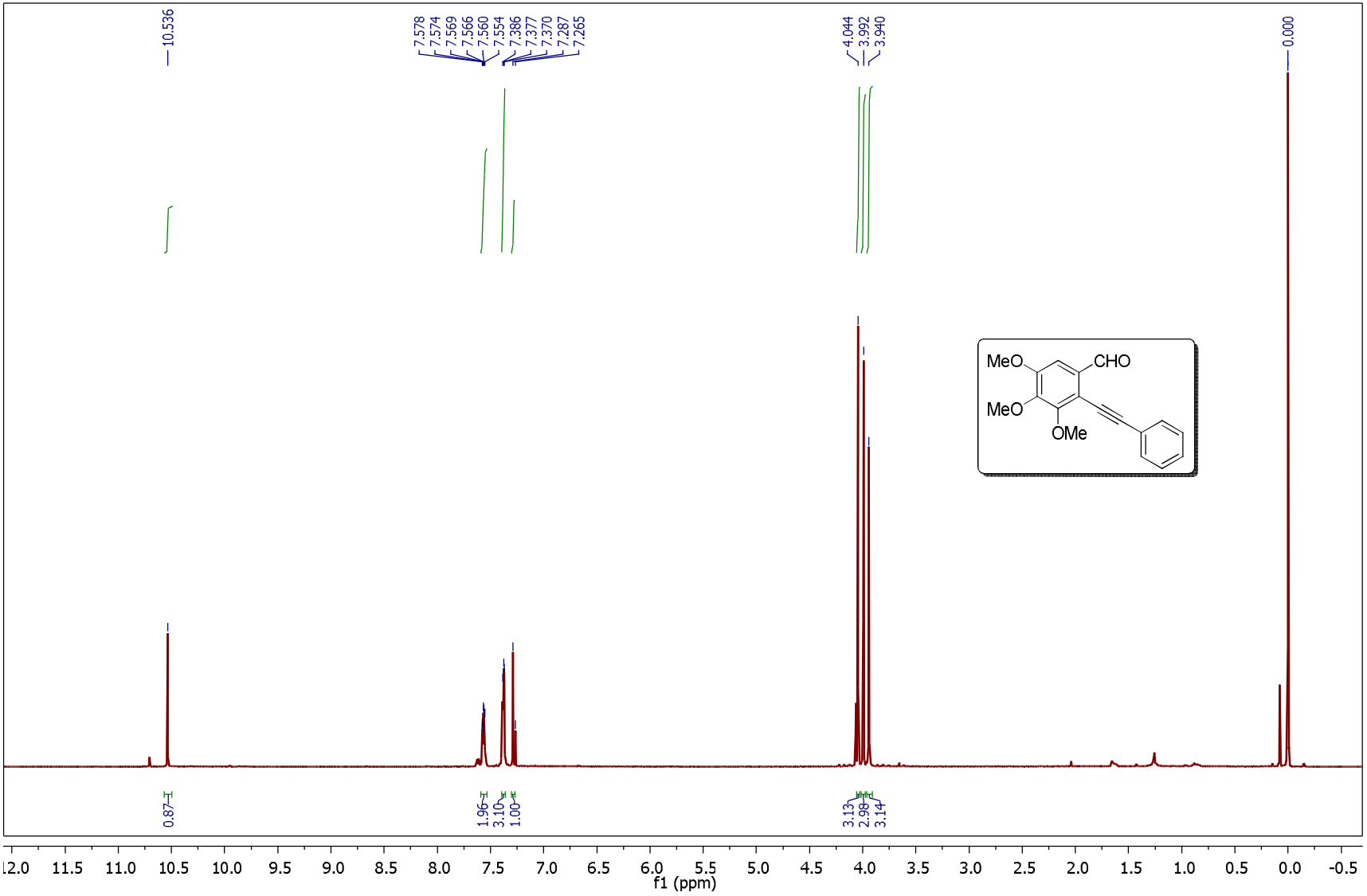
7.32 (m, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 5.83 (dd, *J* = 8.4, 6.8 Hz, 1H), 3.92 (s, 3H), 3.79 (s, 3H), 3.39 (dd, *J* = 15.8, 7.9 Hz, 1H), 2.75 (dd, *J* = 11.7, 6.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) ŭ 169.7, 168.8, 152.2, 141.8, 140.5, 132.7, 131.7, 129.5, 129.0, 128.8, 128.3, 125.7, 125.5, 122.9, 120.6, 112.8, 95.7, 86.3, 61.7, 53.6, 53.5, 36.0; **IR** (KBr, neat) 3021, 2957, 2892, 2425, 2216, 1746, 1597, 1504, 1443, 1325,1192, 1144, 1119, 1049, 975, 846, 765 cm^{-1}; **HRMS** (ESI) calcd. for $C_{27}H_{23}N_2O_6$ $(M + H)^+$ 471.1551, found 471.1548.

Spectral Data:

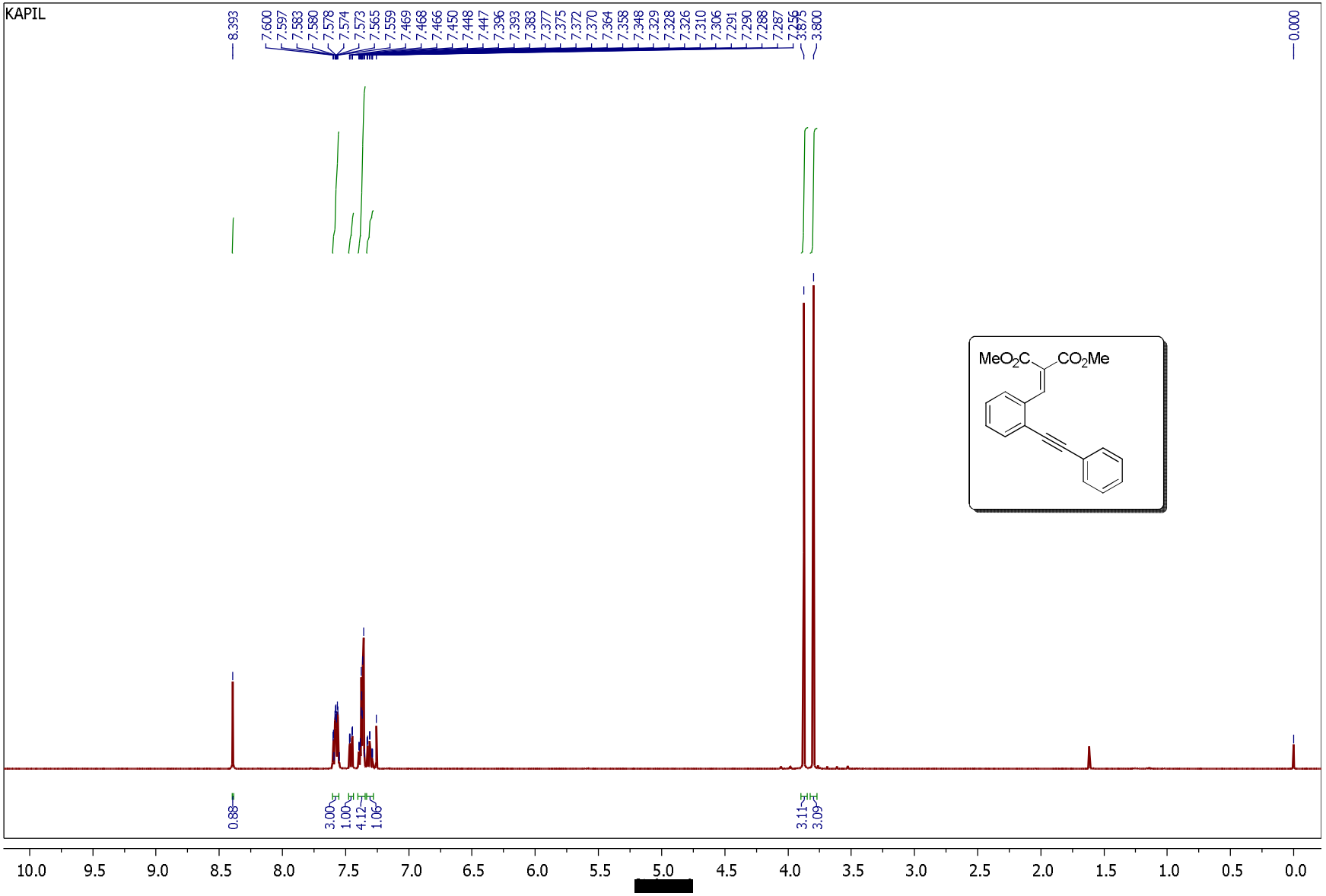
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound IIIe



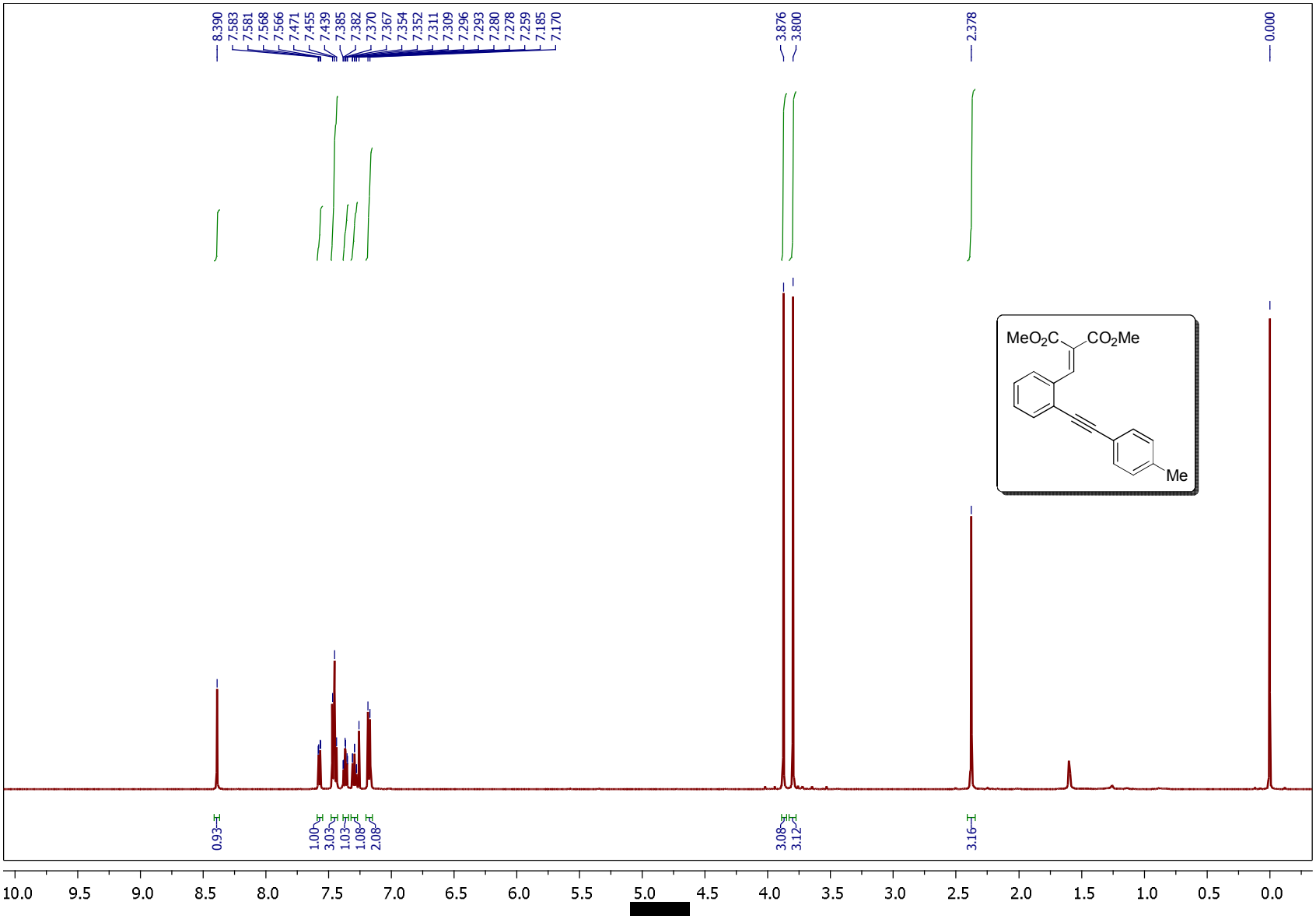
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound IIIf



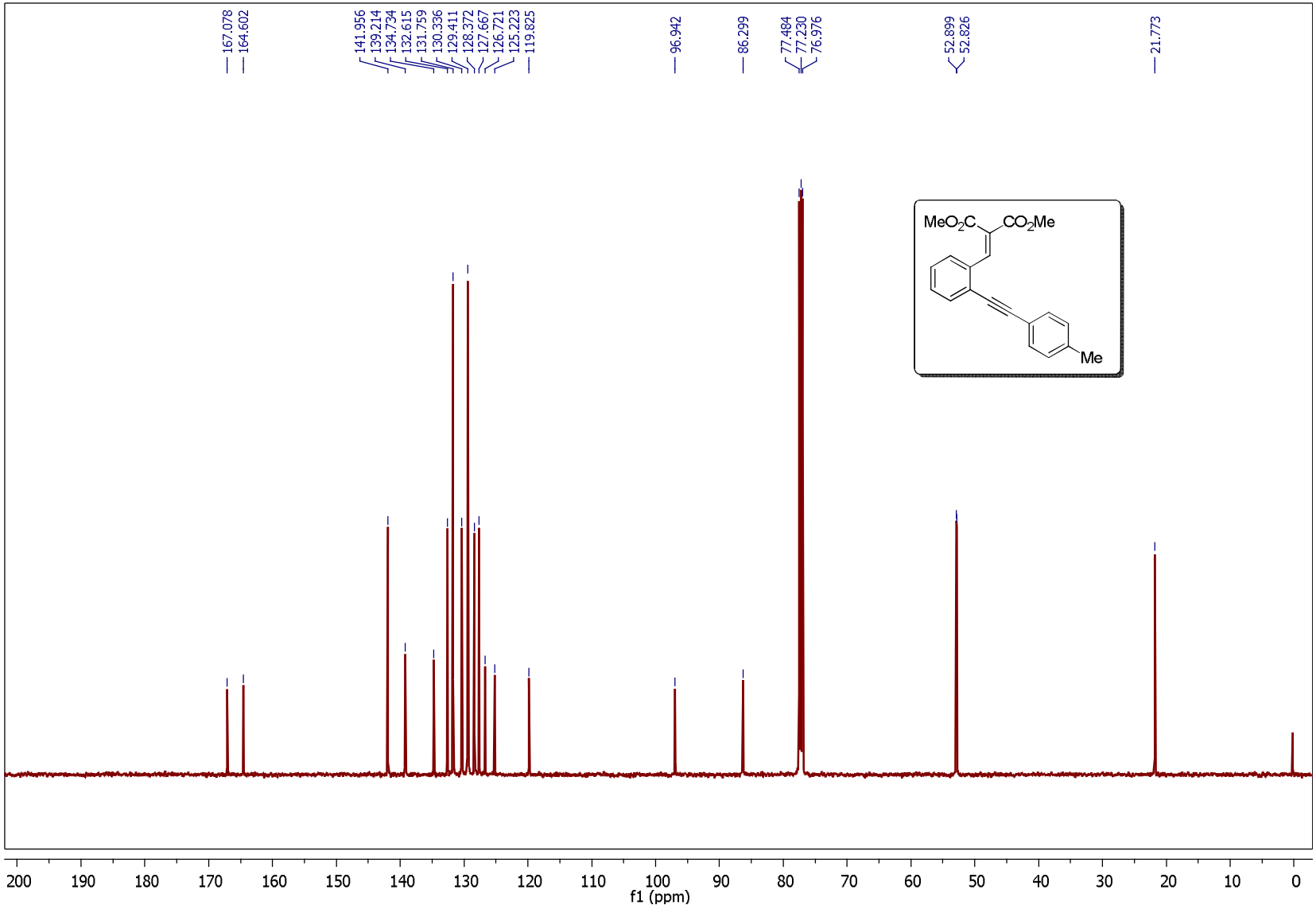
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound Va



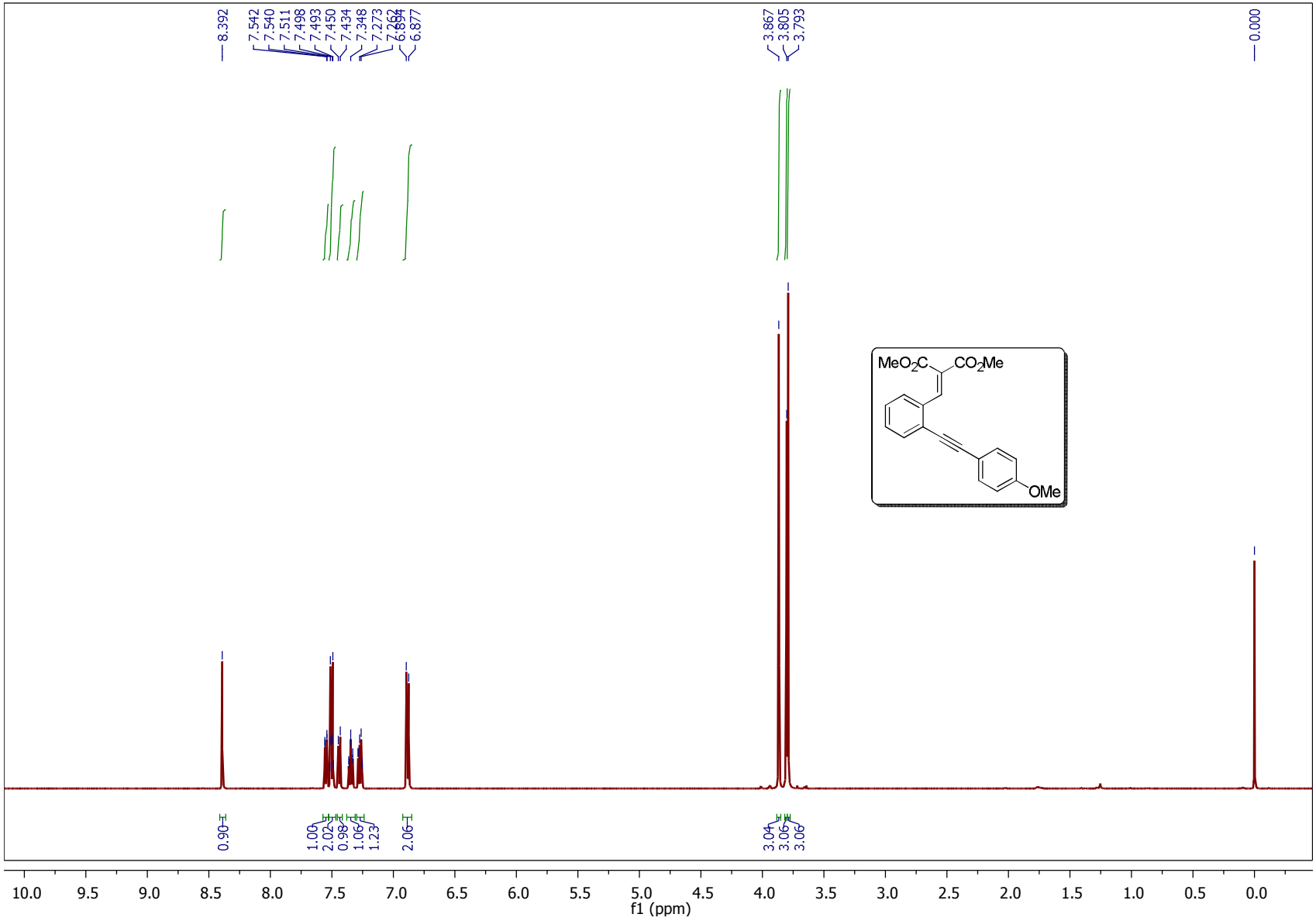
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound Vb



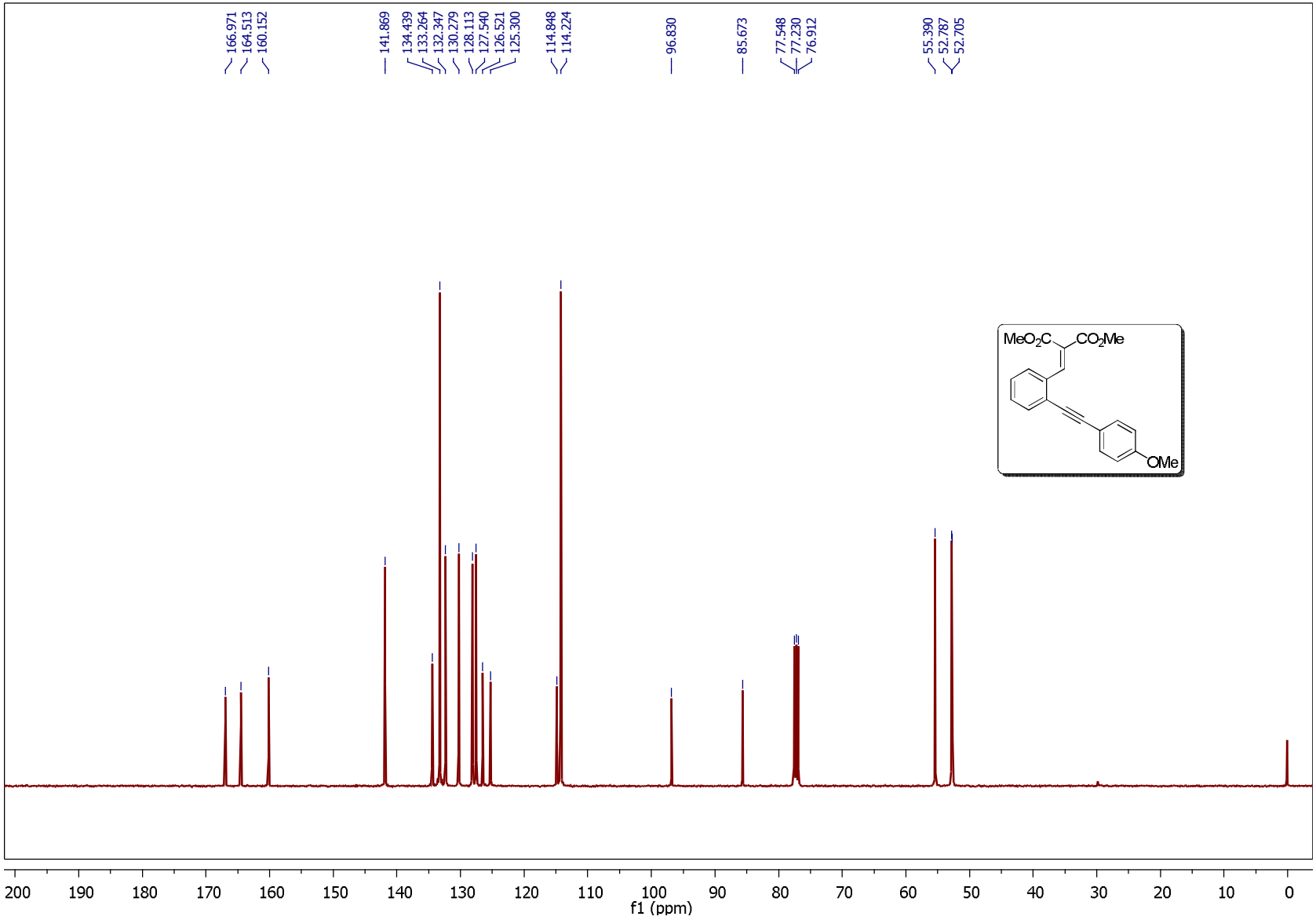
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound Vb



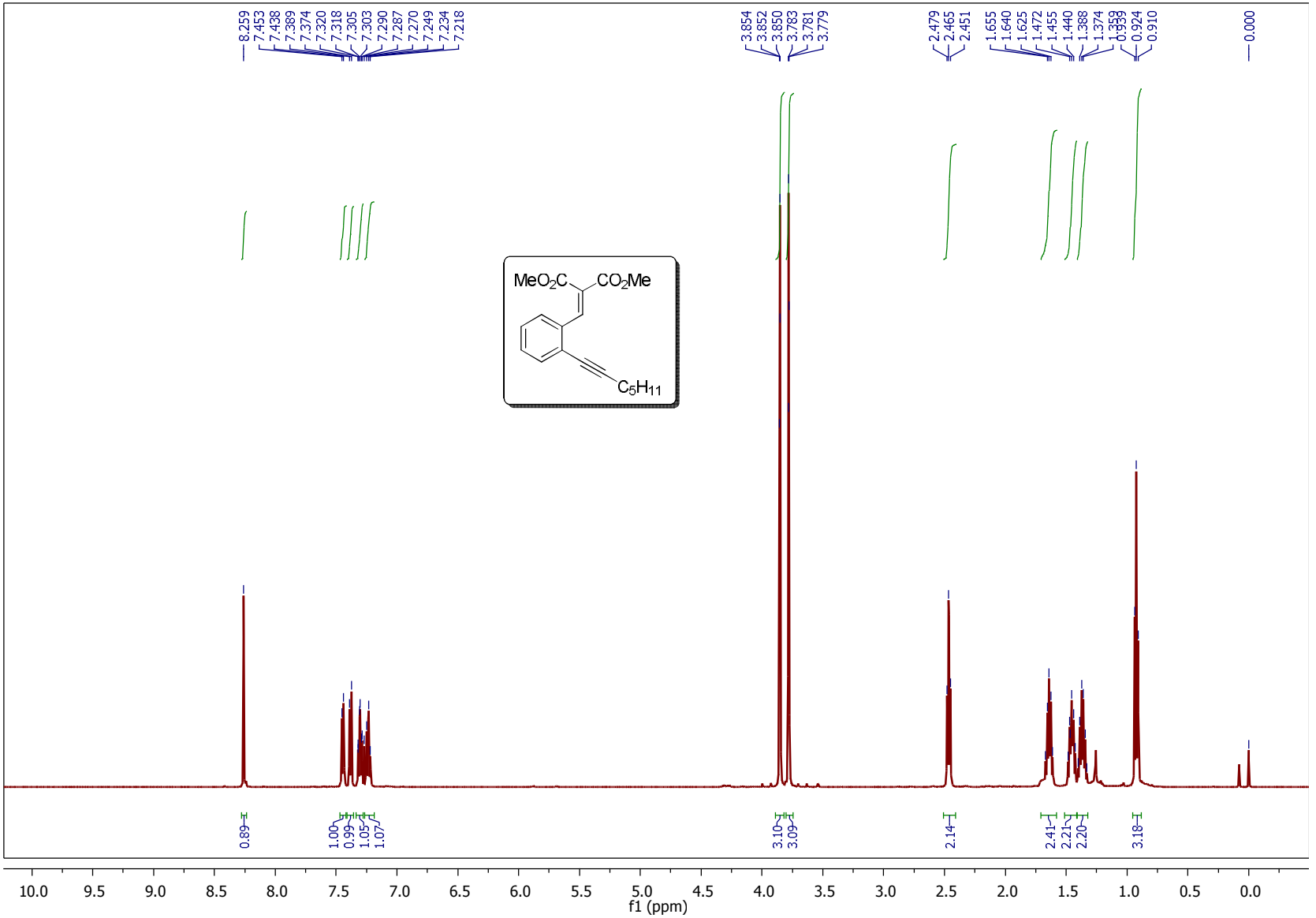
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound Vc



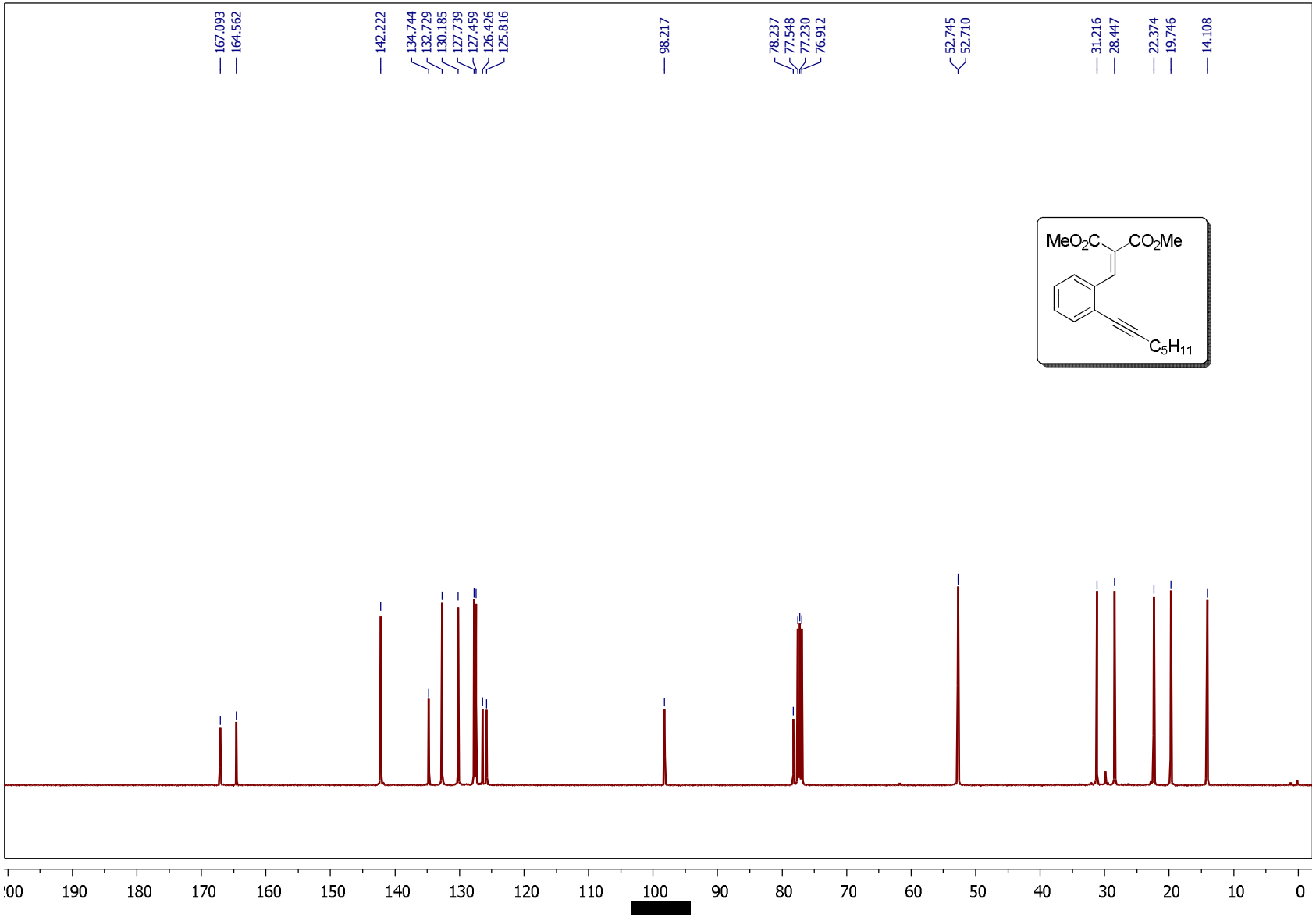
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound Vc



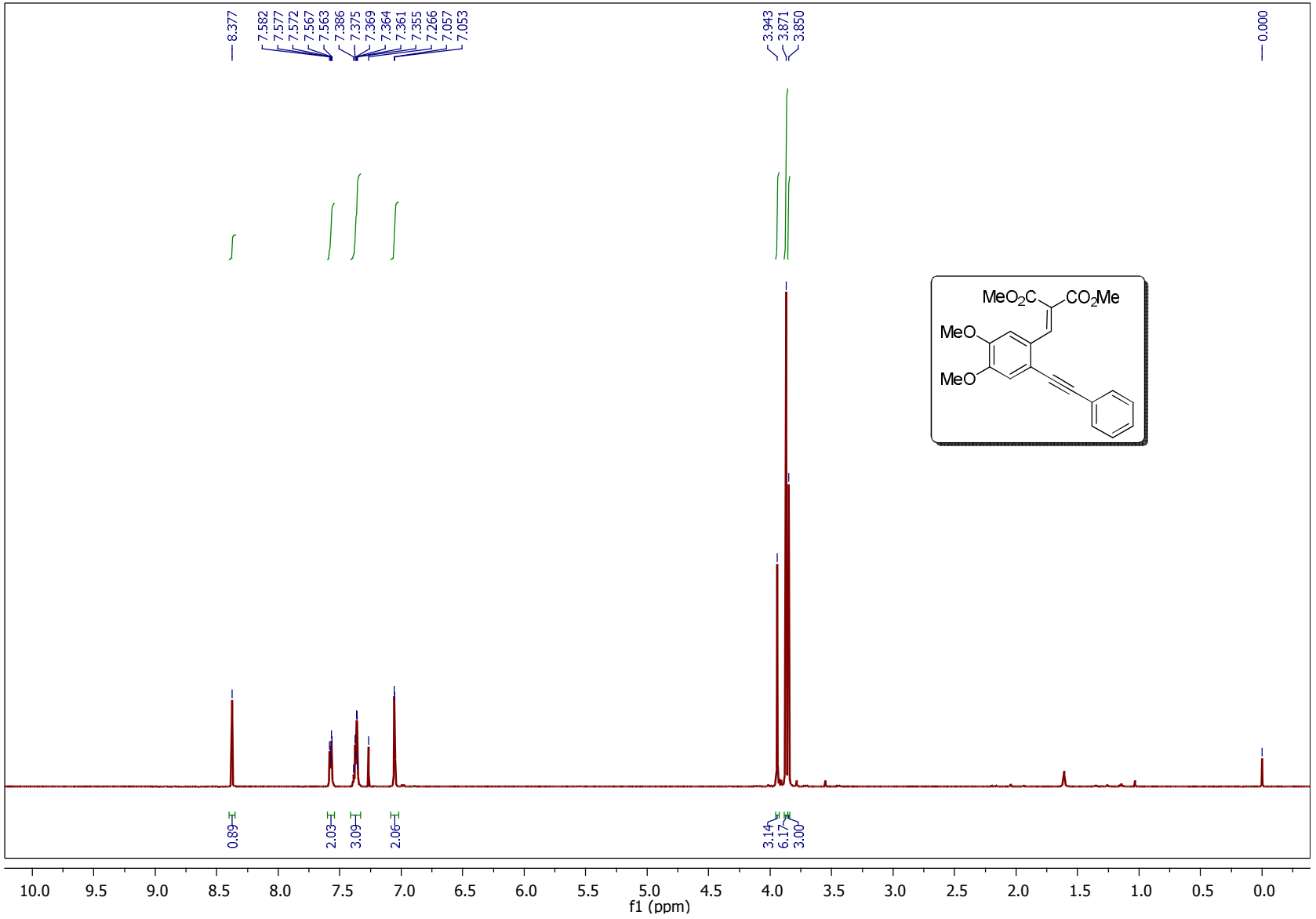
^{1}H NMR ^{13}C NMR (500 MHz, $CDCl_3$) Spectrum of compound Vd



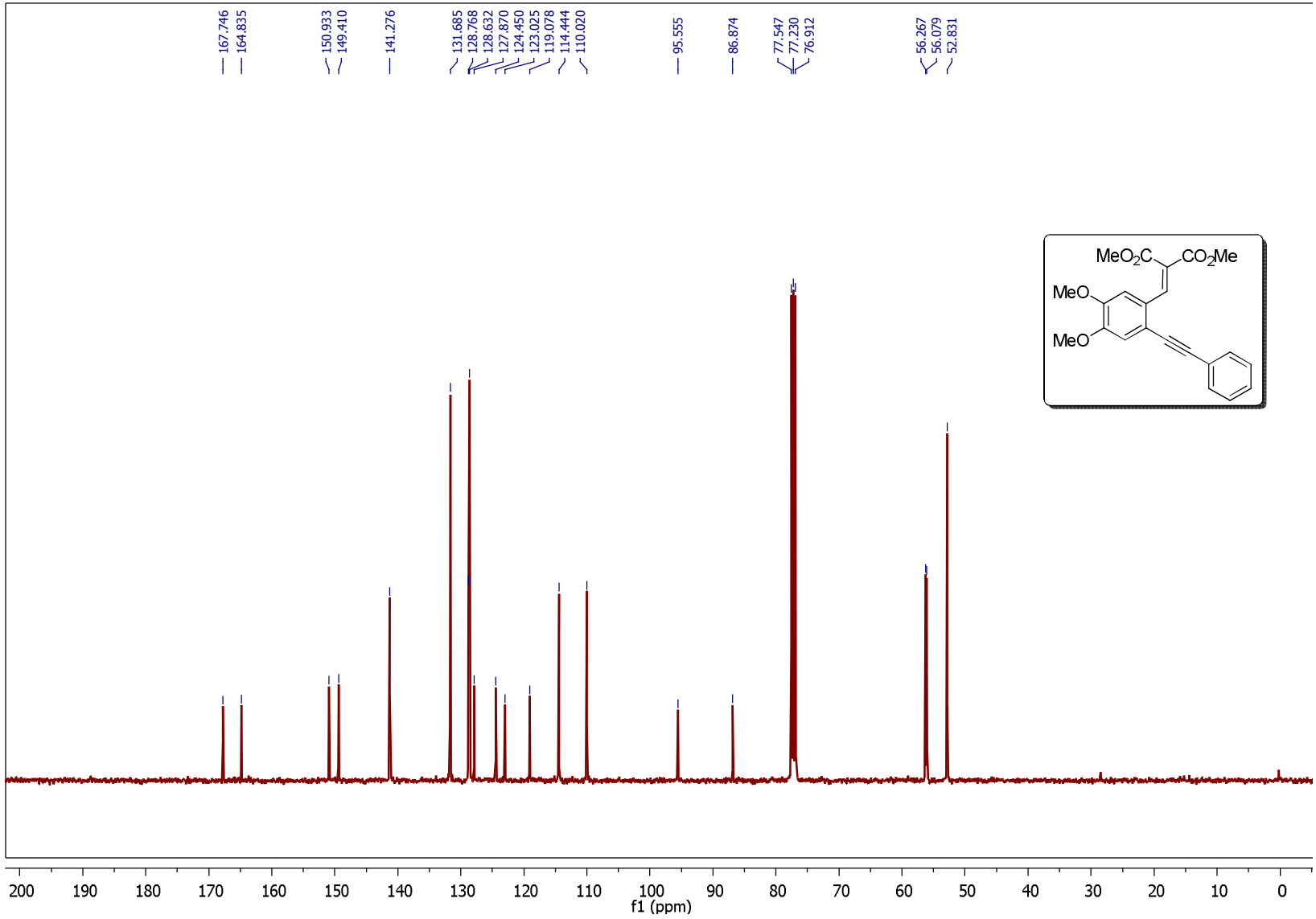
^{1}H NMR ^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound Vd



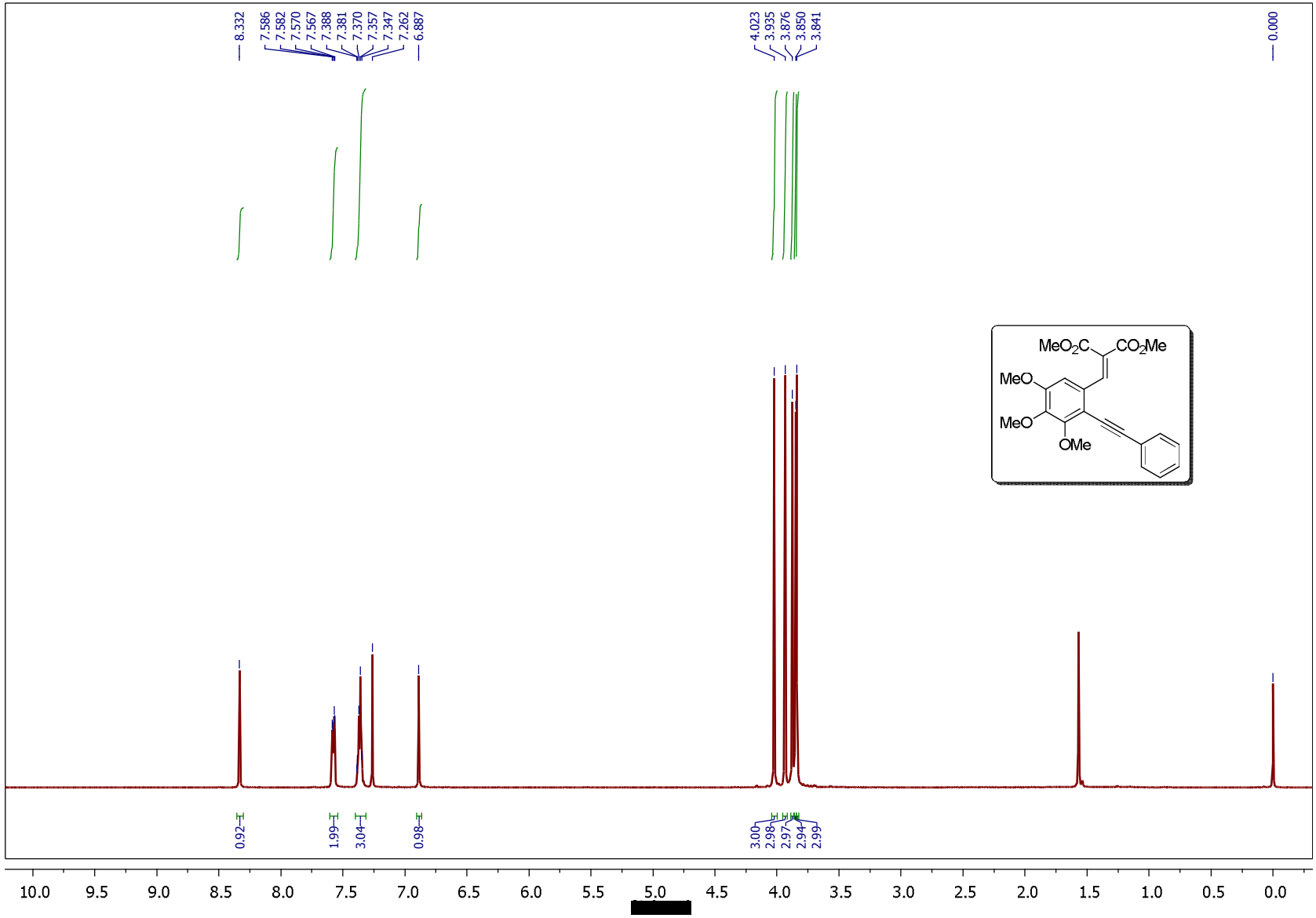
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound Ve



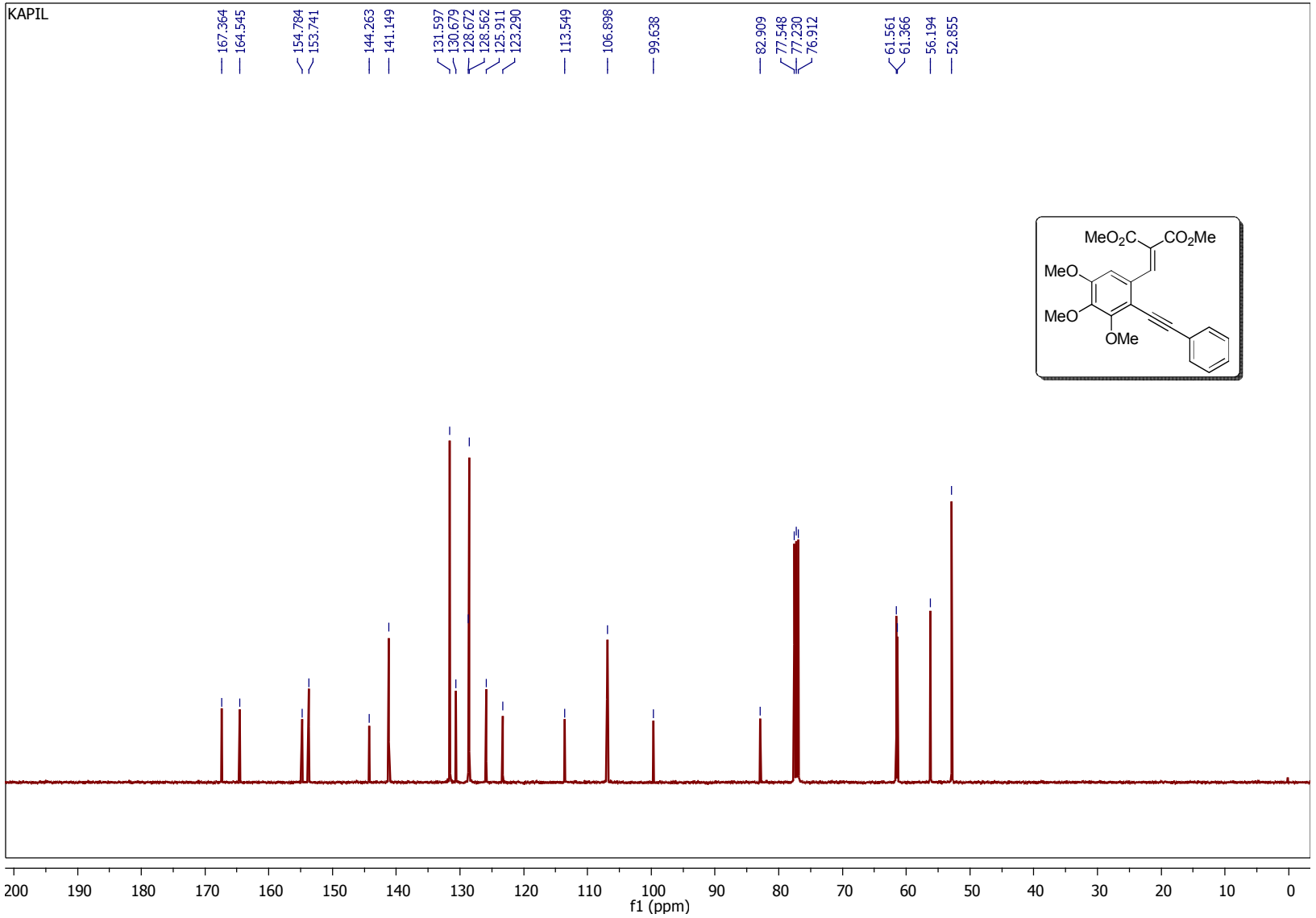
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound Ve



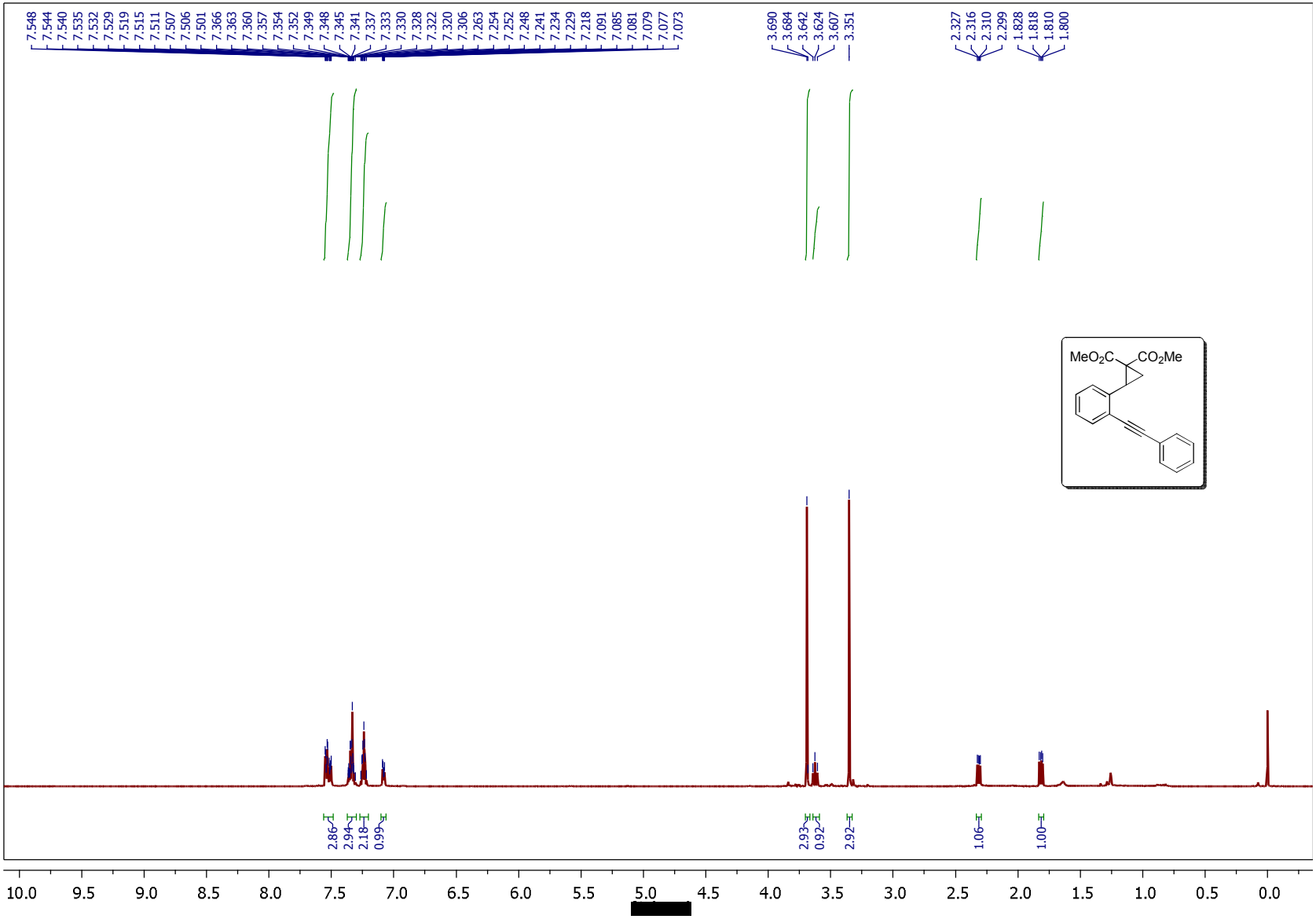
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound Vf



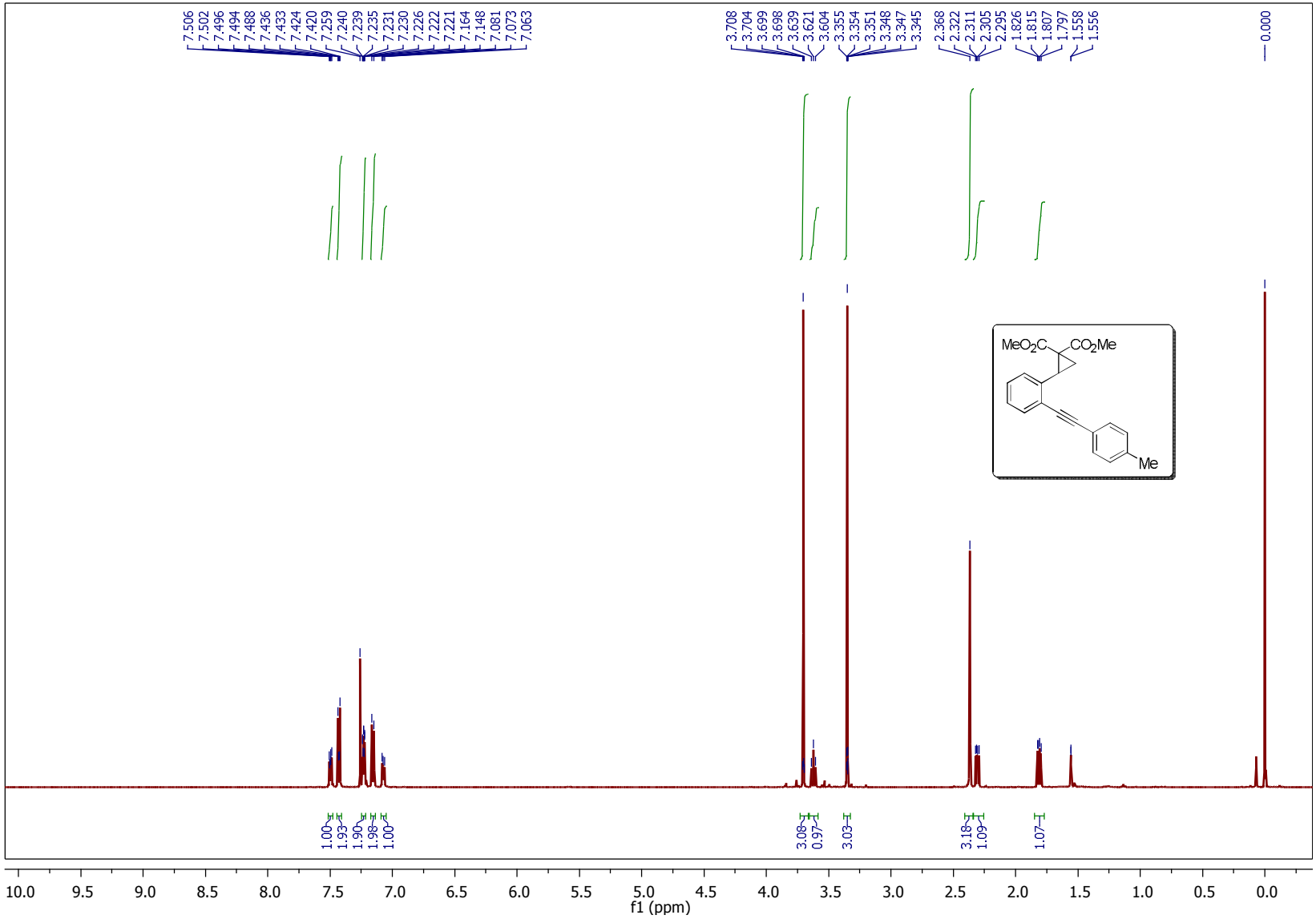
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound Vf



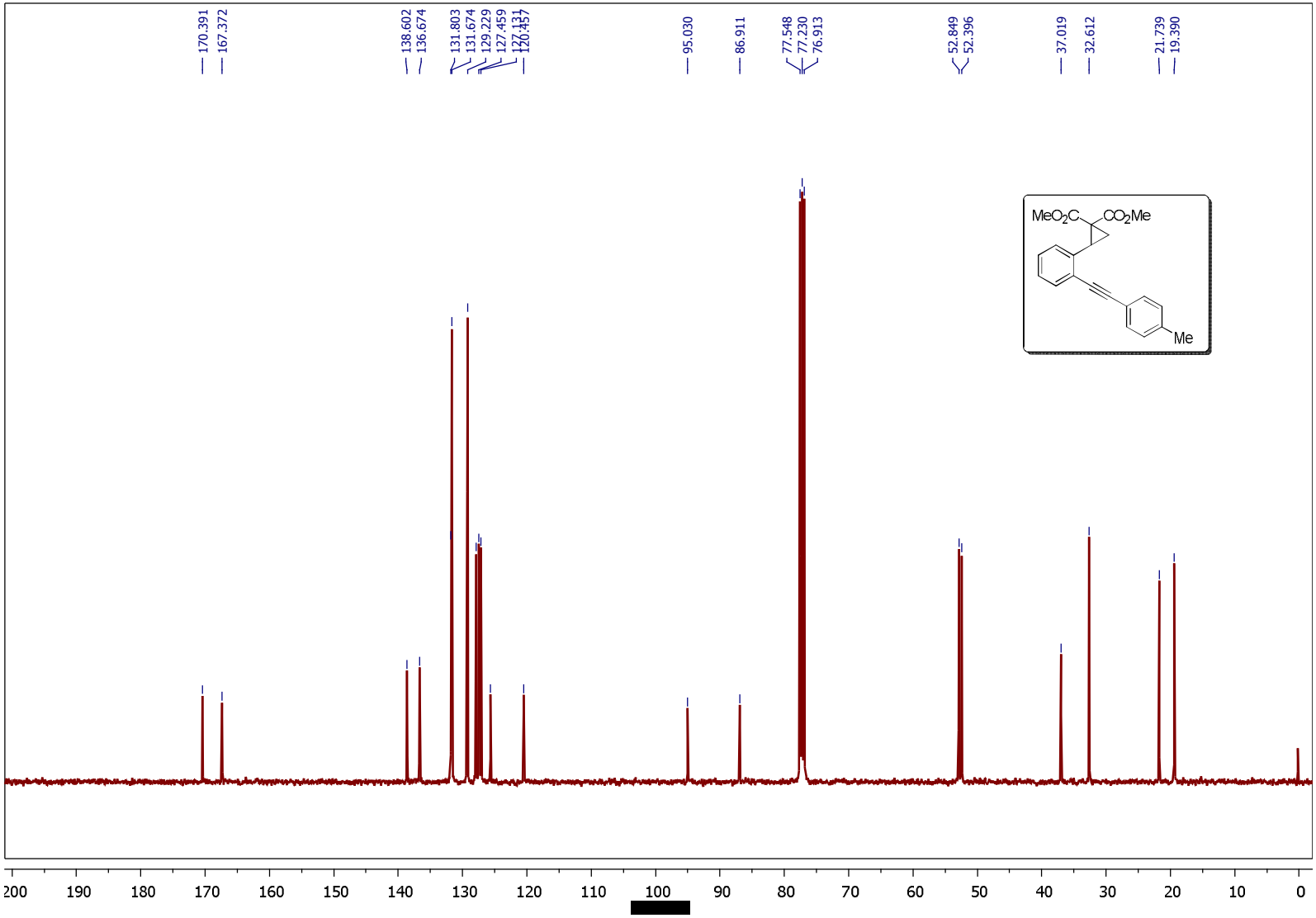
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 1a



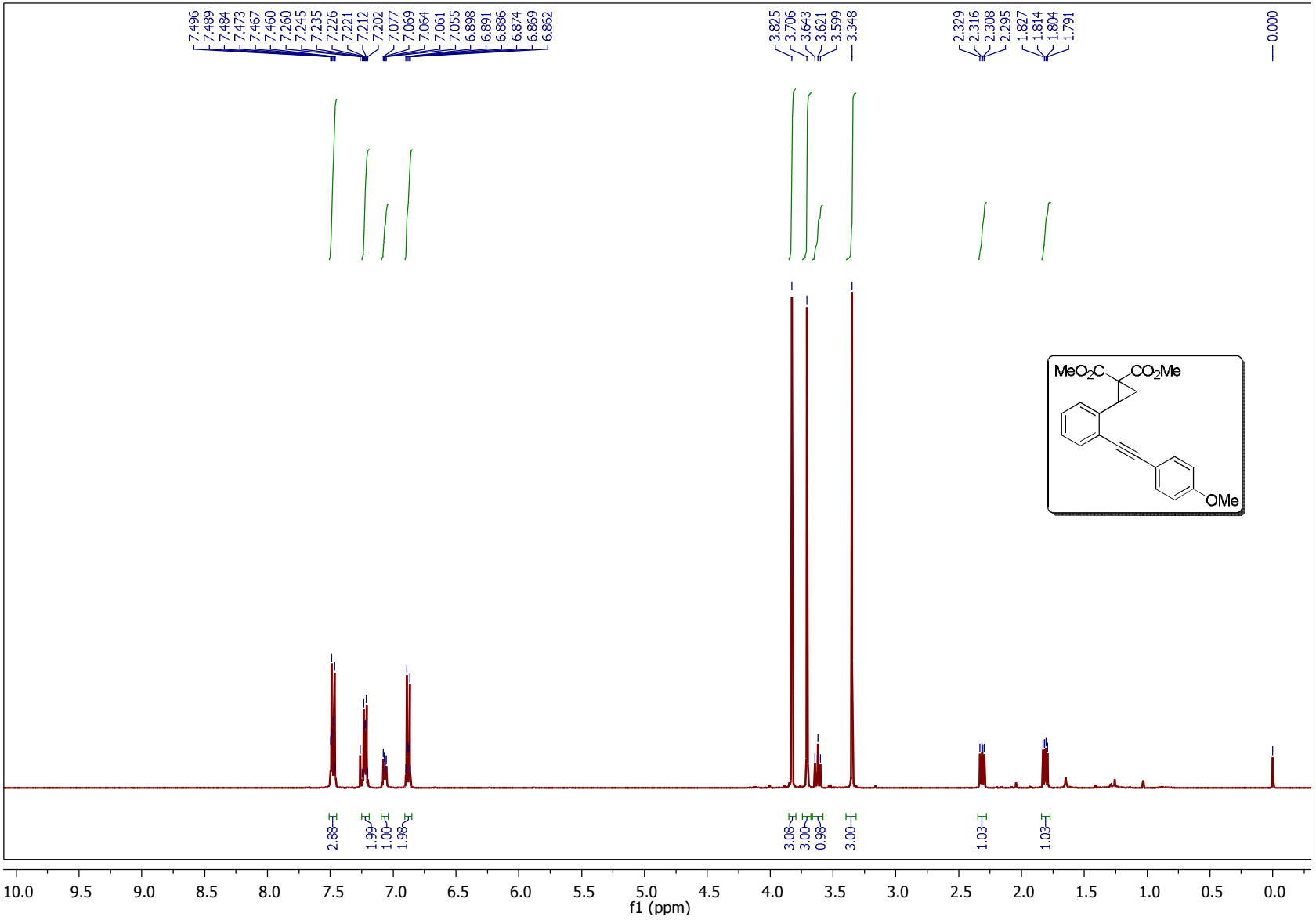
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 1b



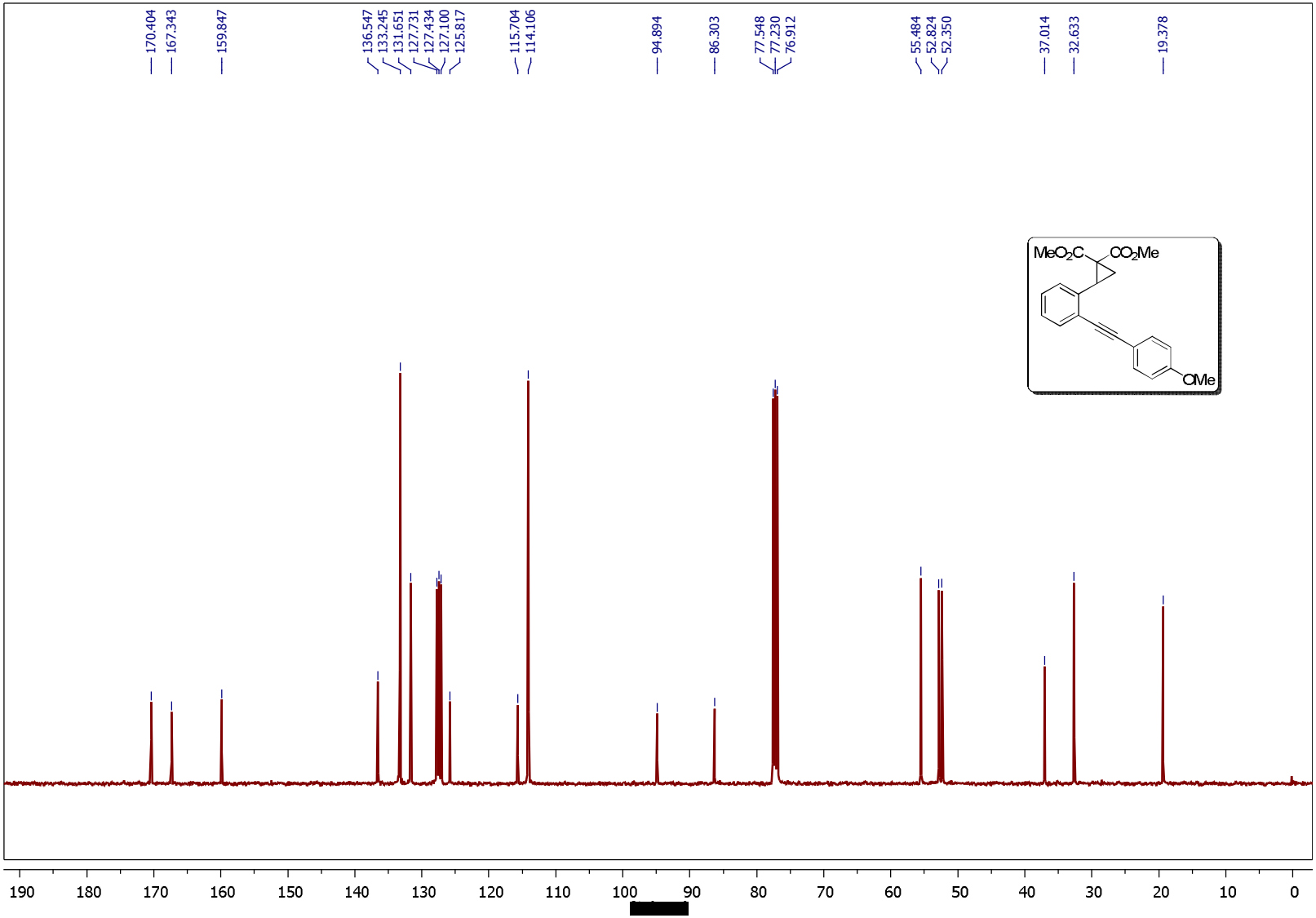
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 1b



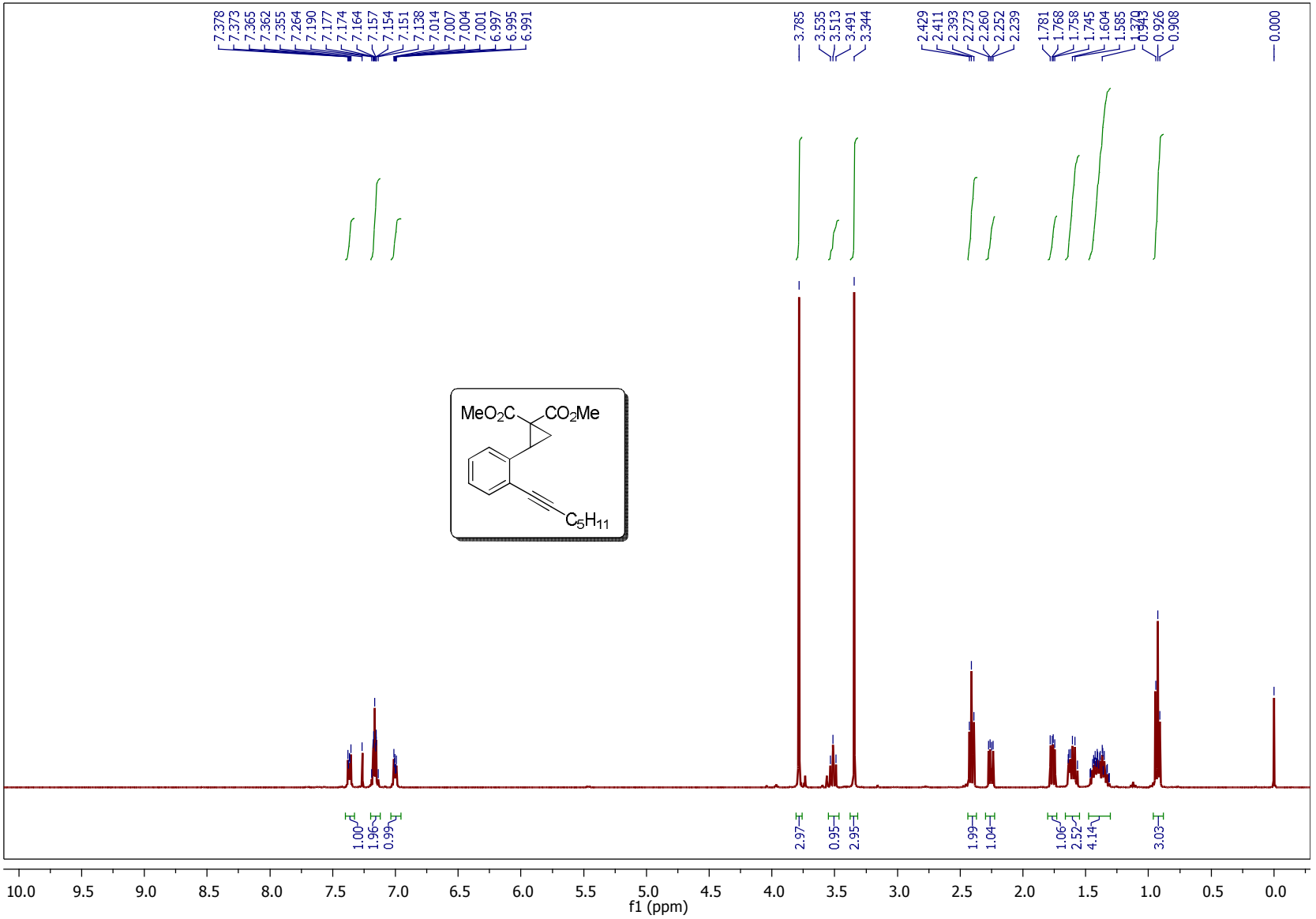
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 1c



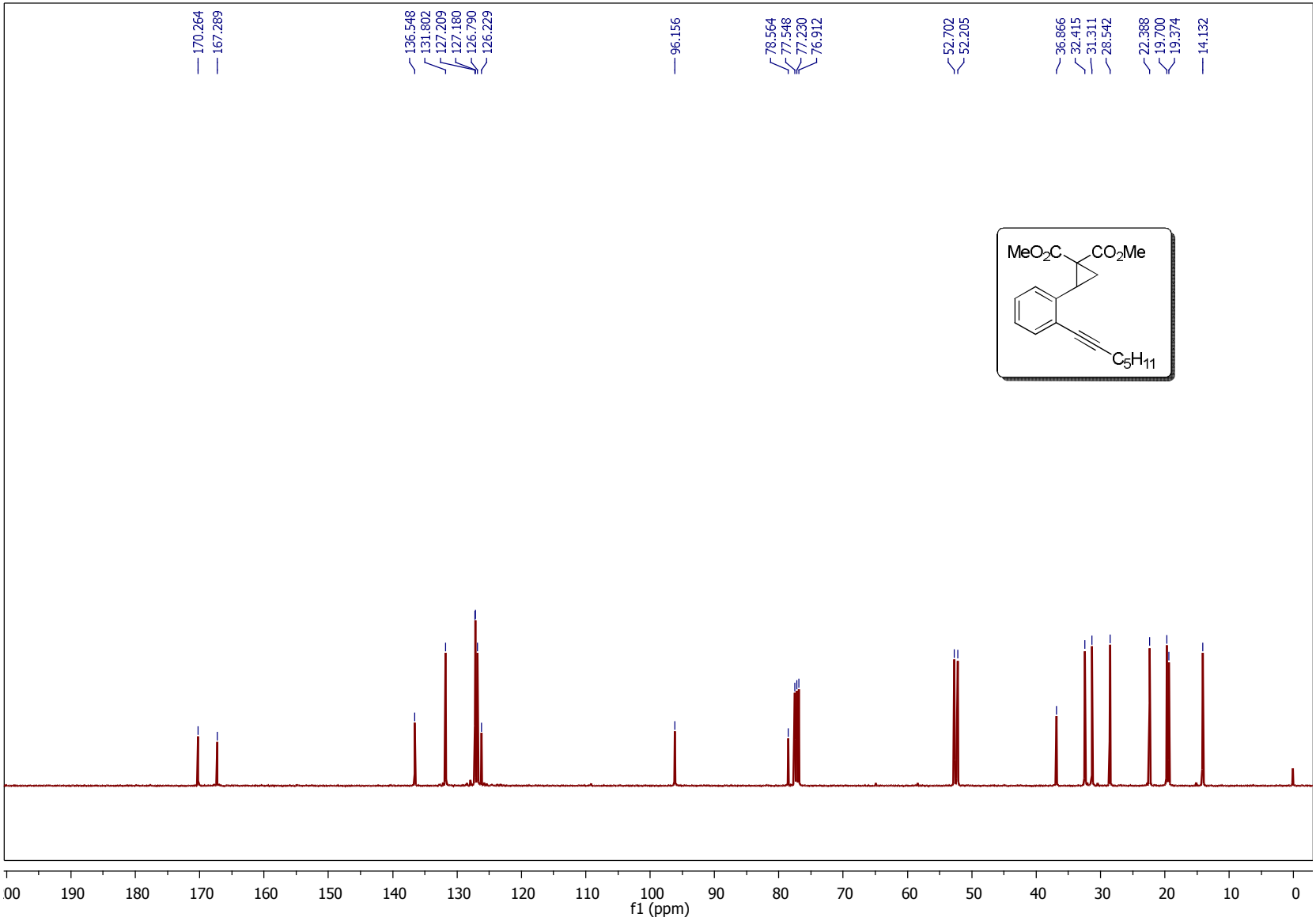
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 1c



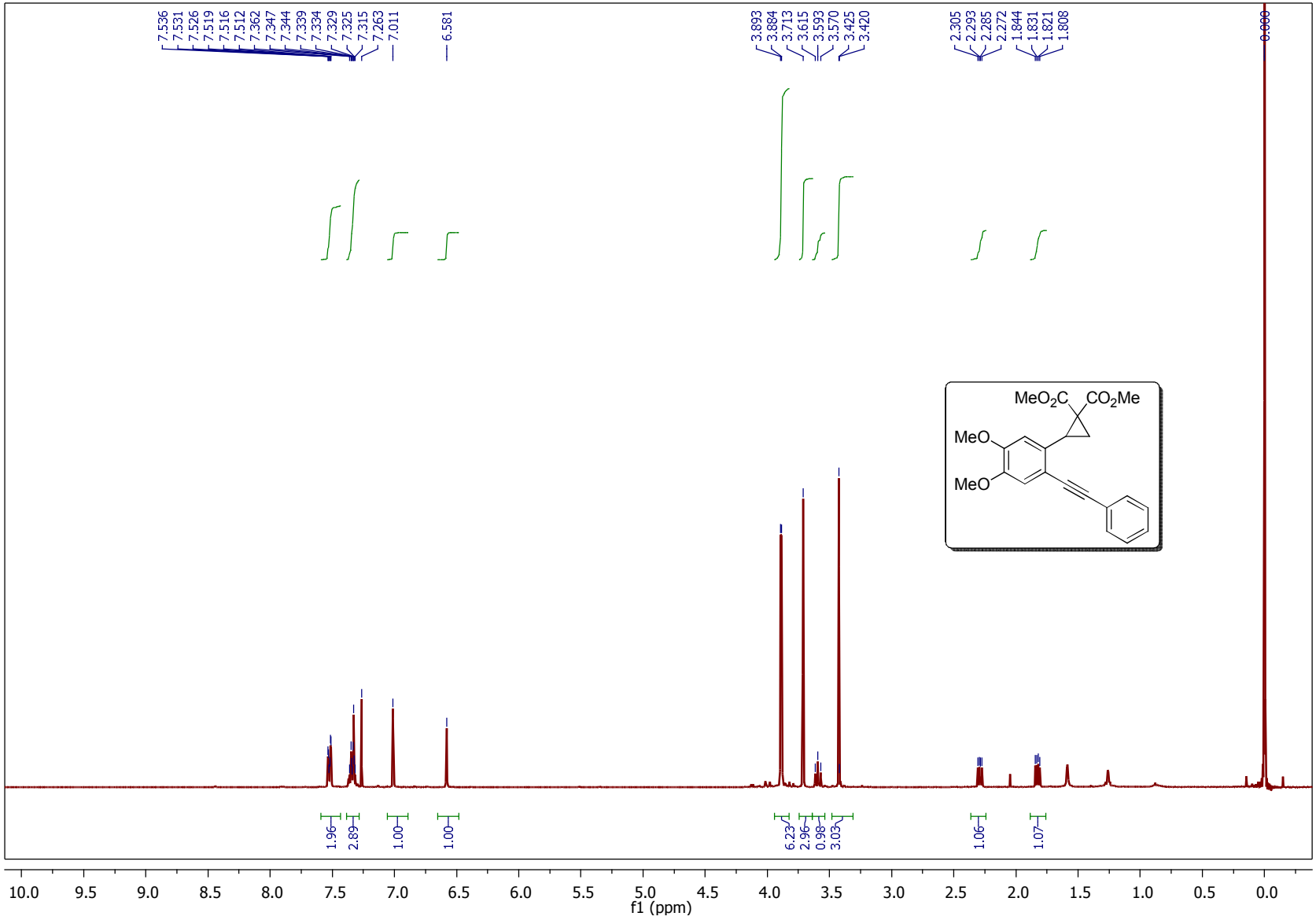
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 1d



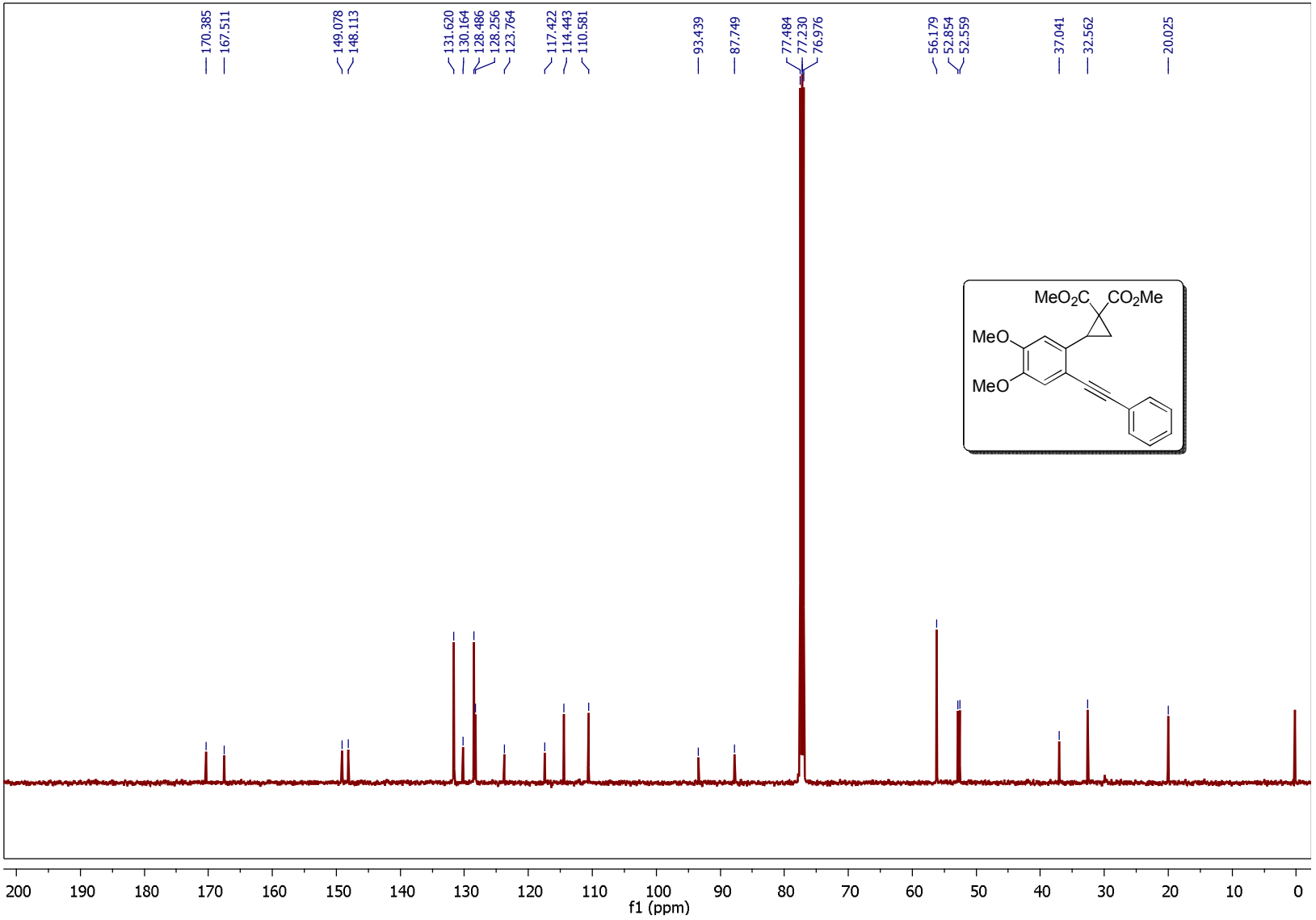
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 1d



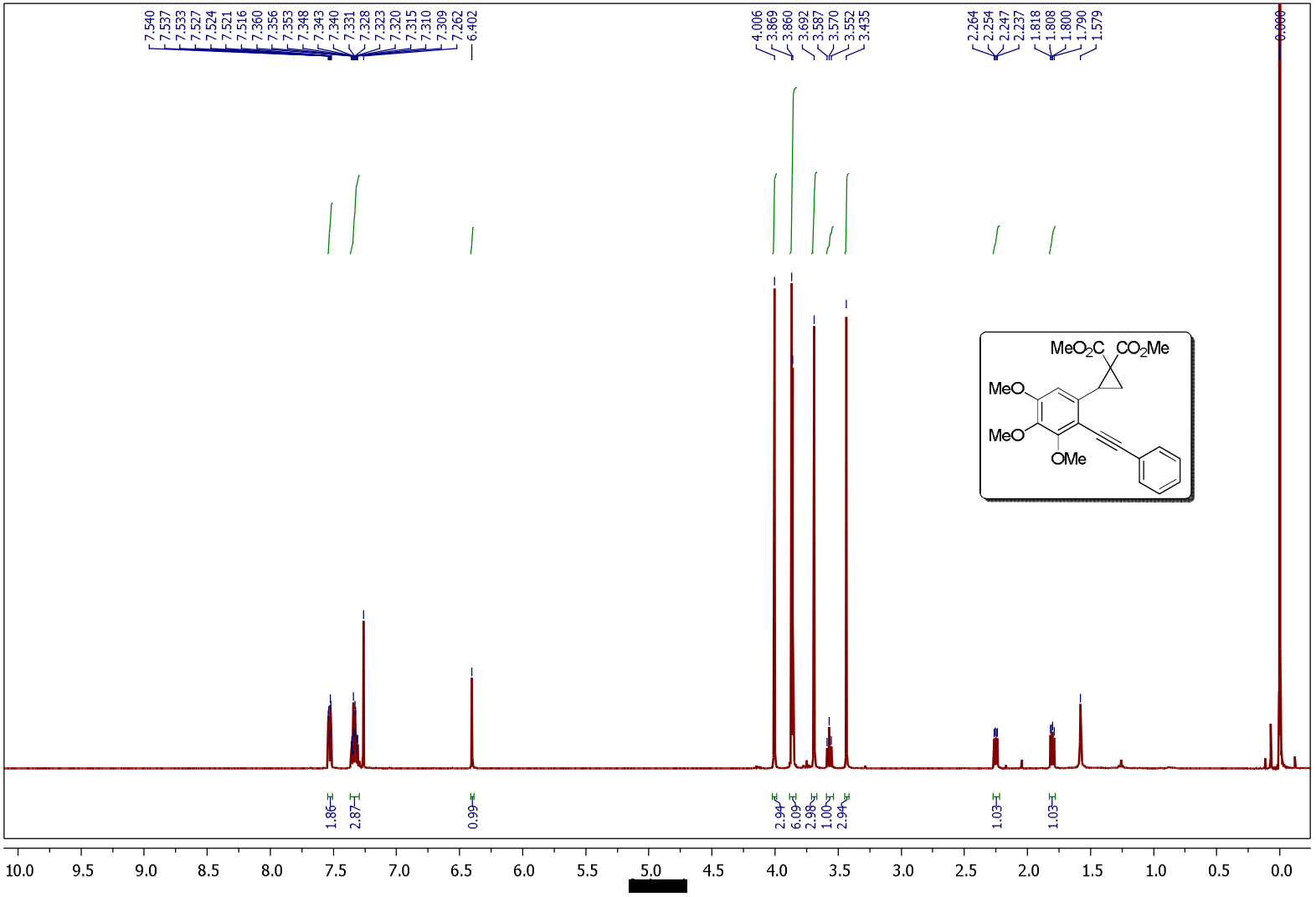
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 1e



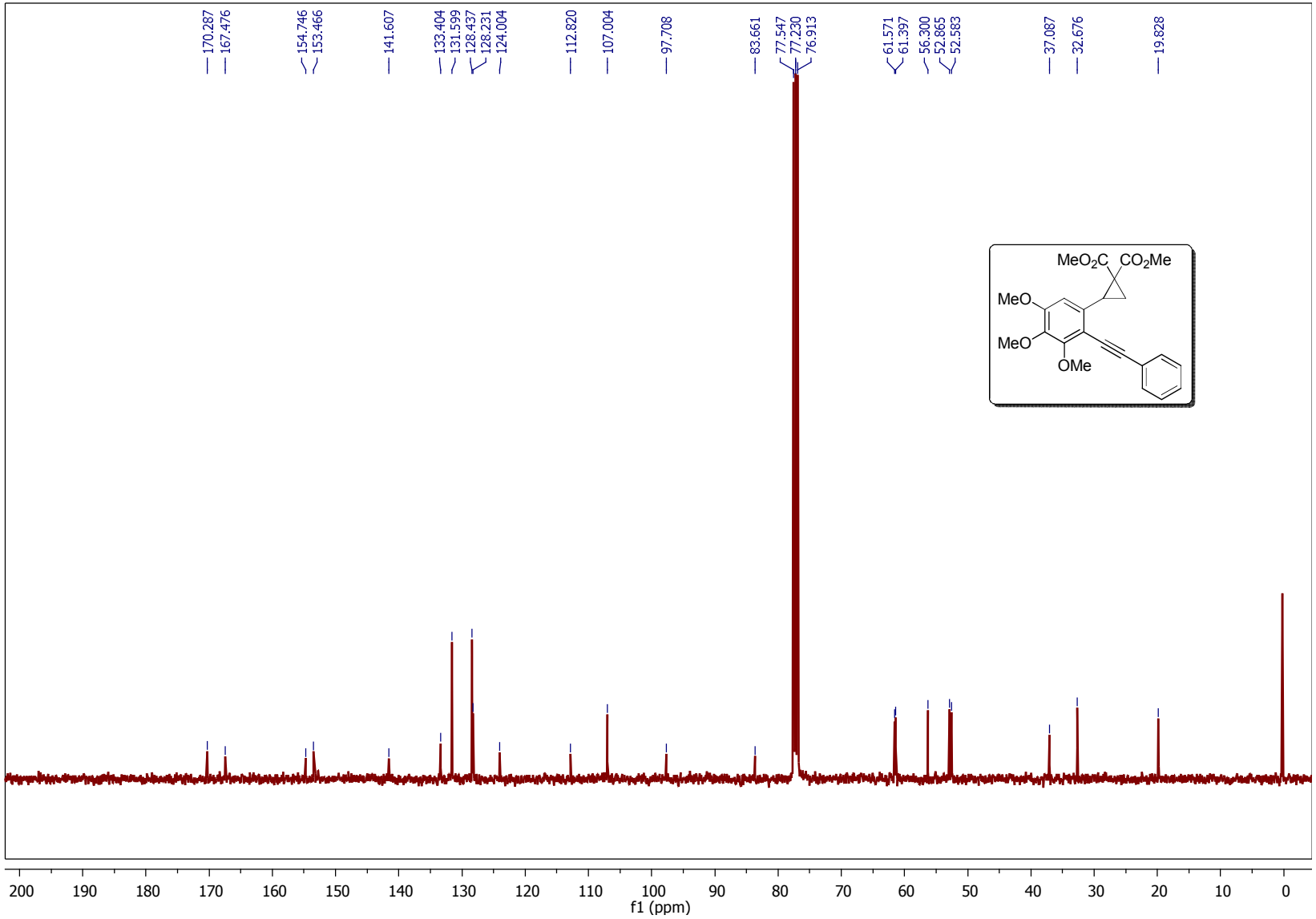
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 1e



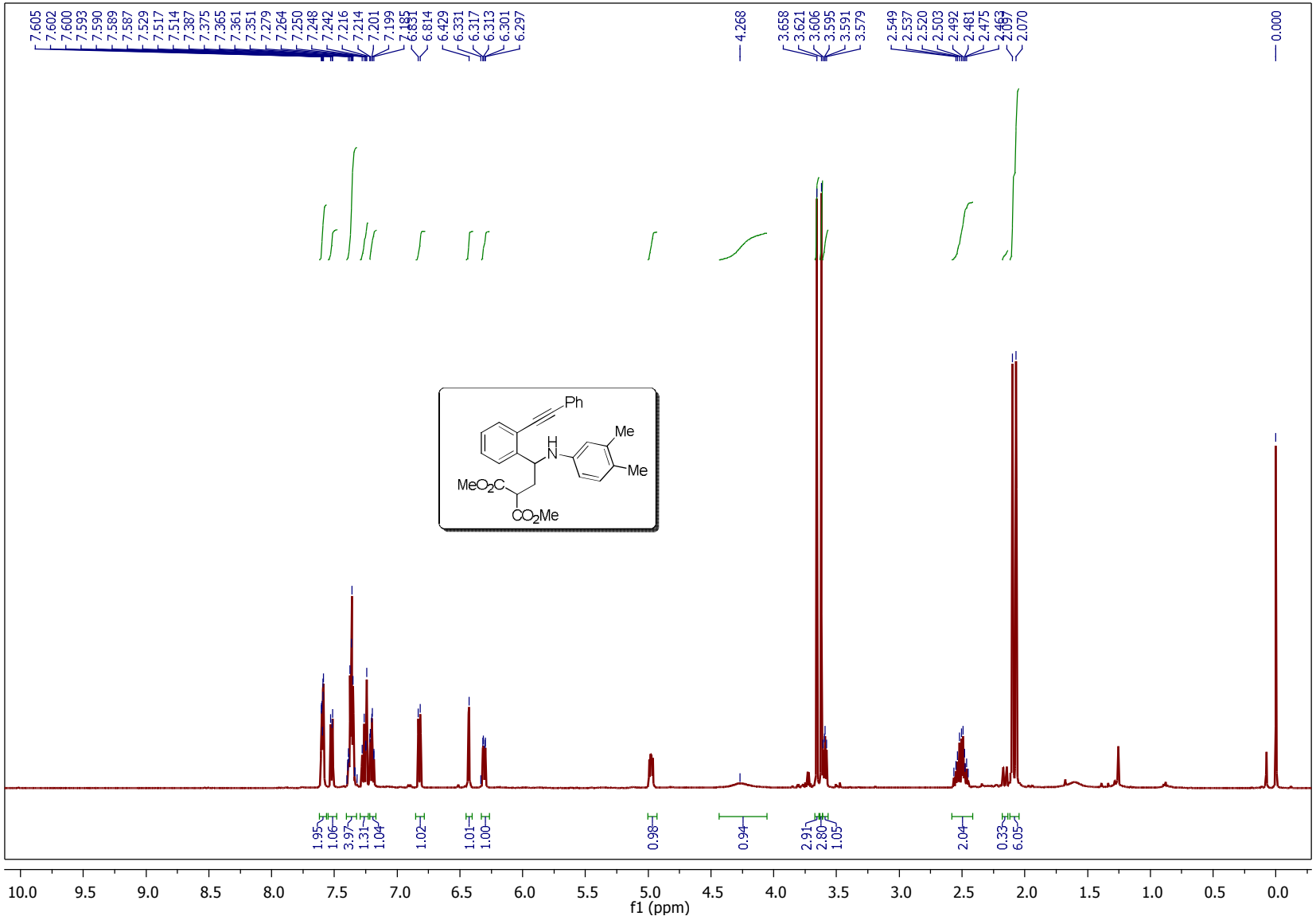
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 1f



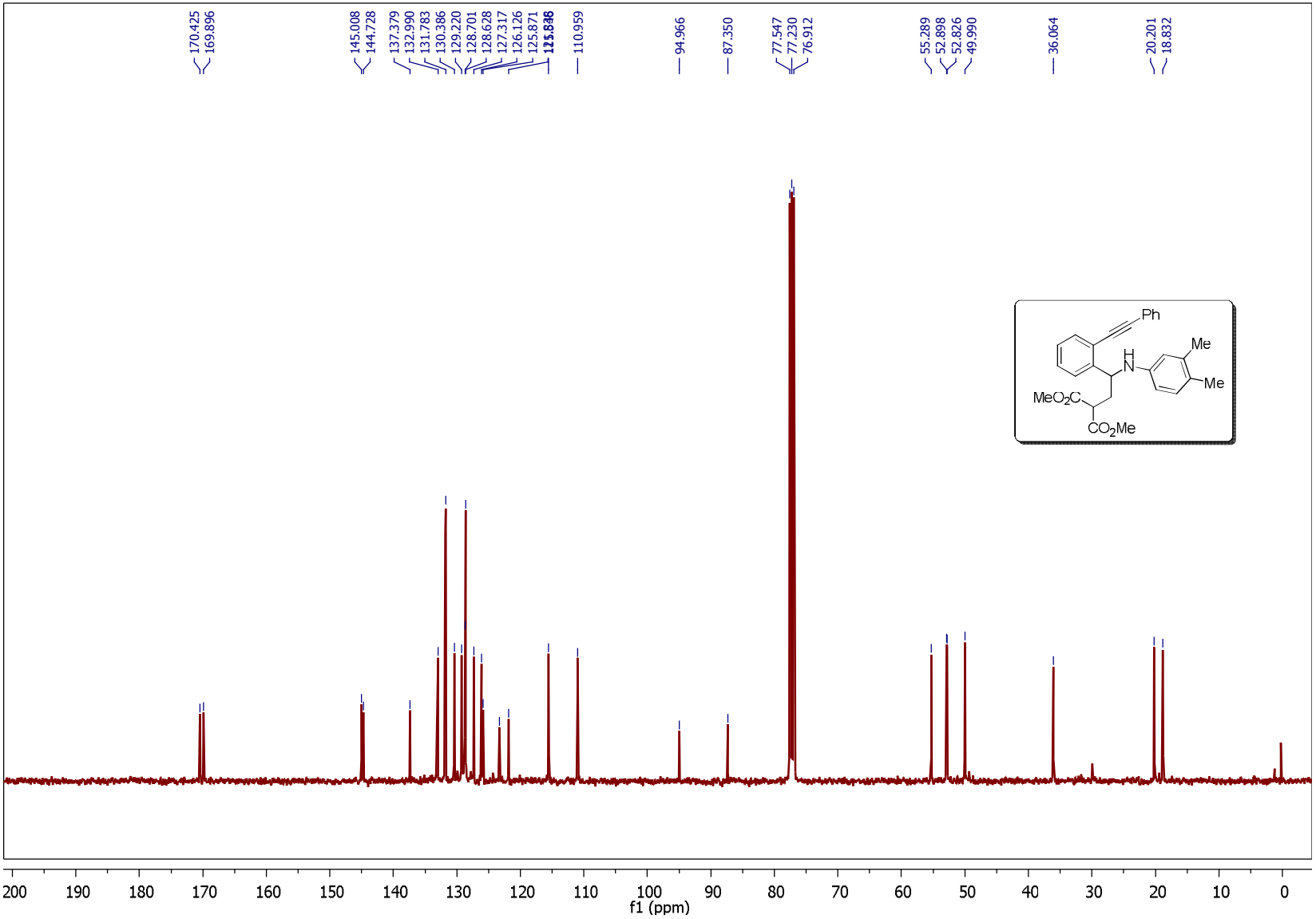
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 1f



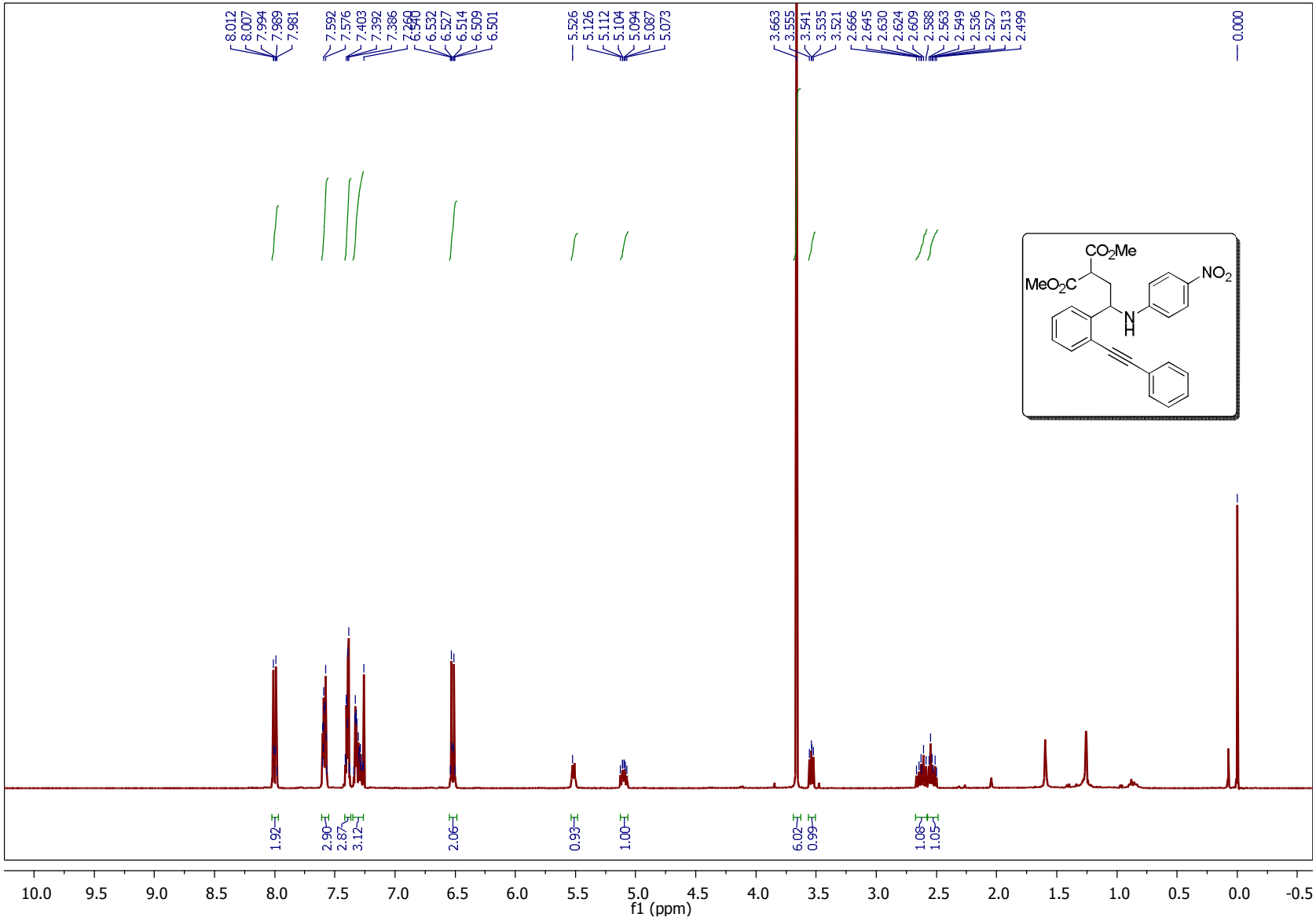
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound of 3a



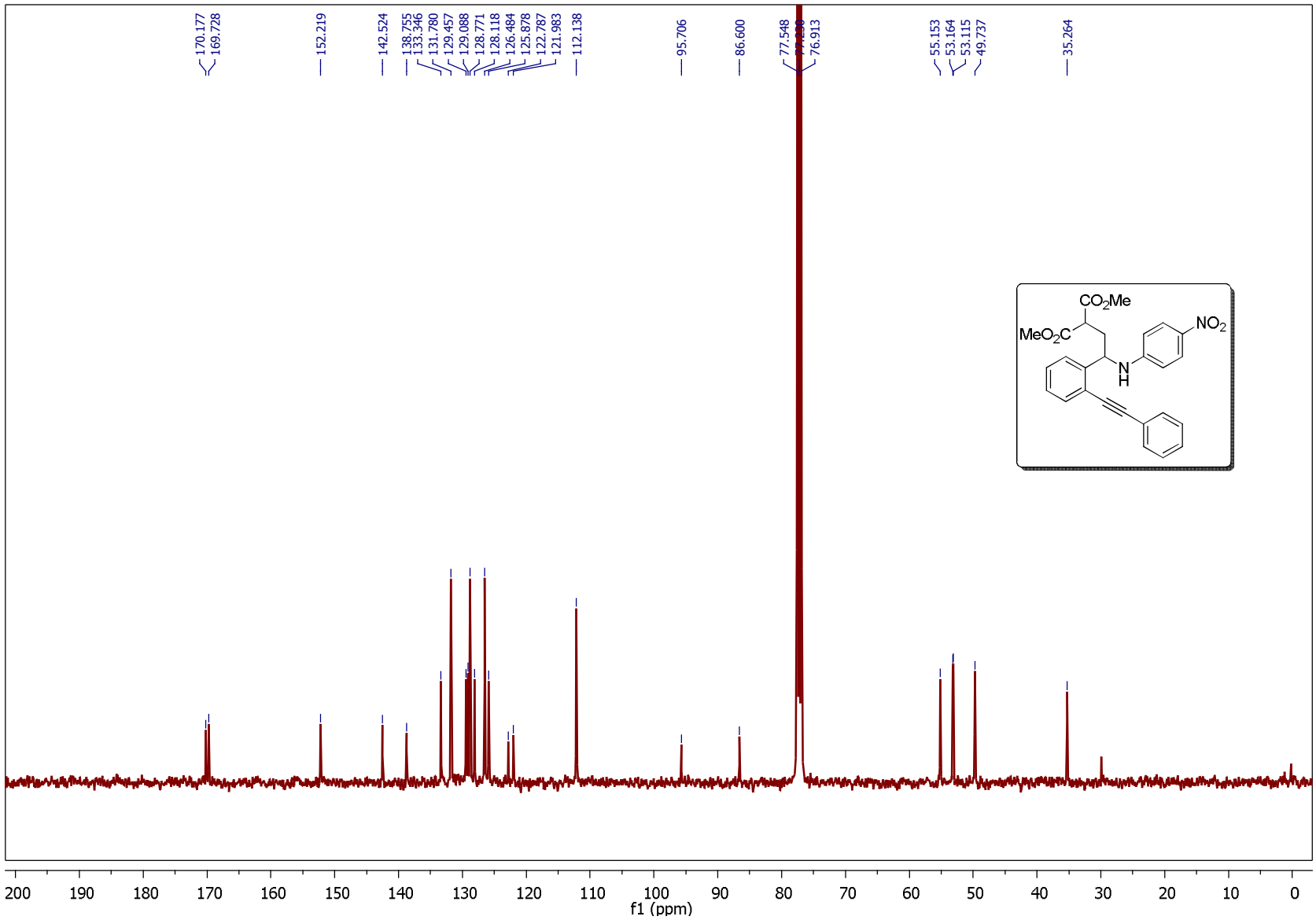
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound of 3a



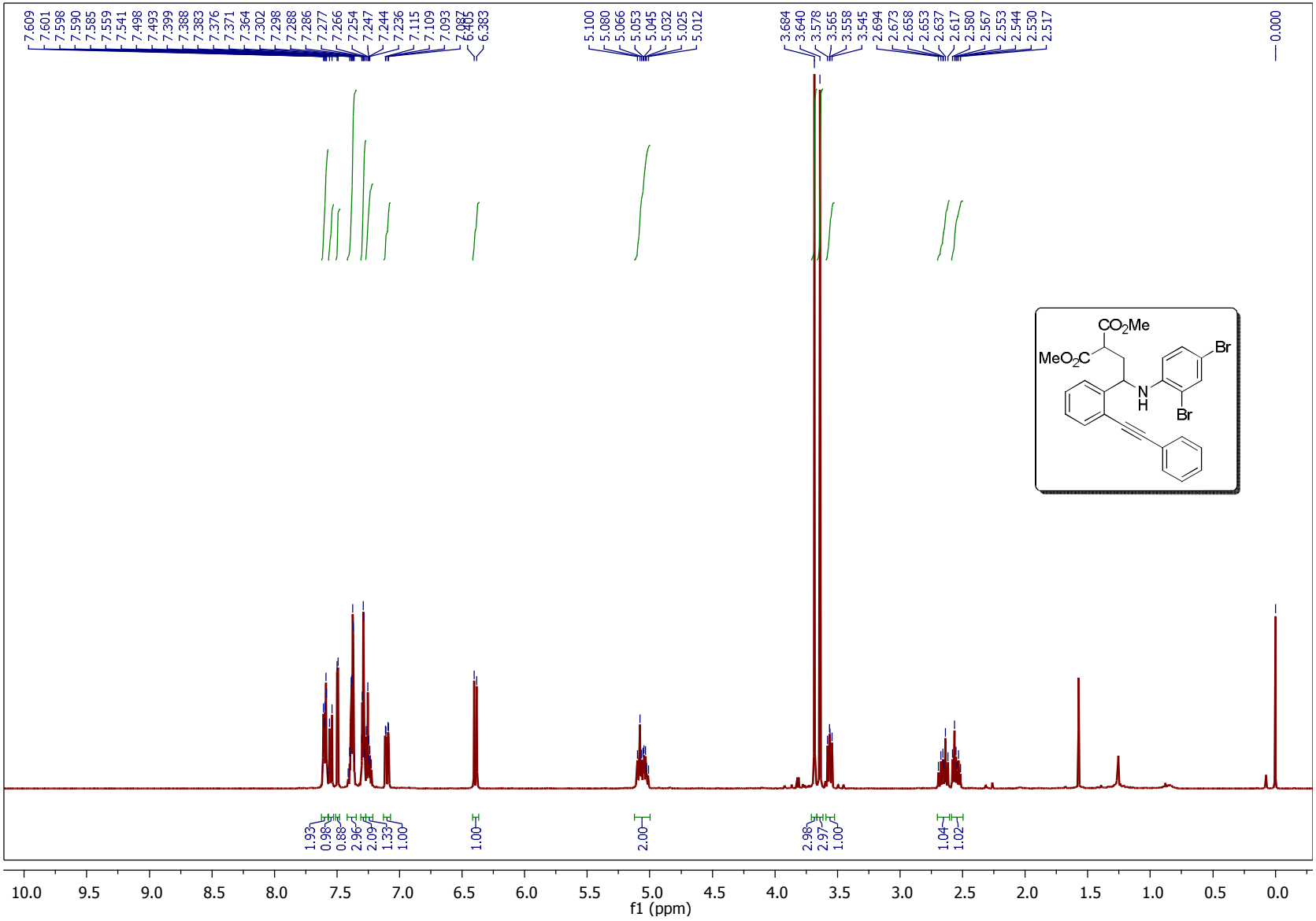
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 3m



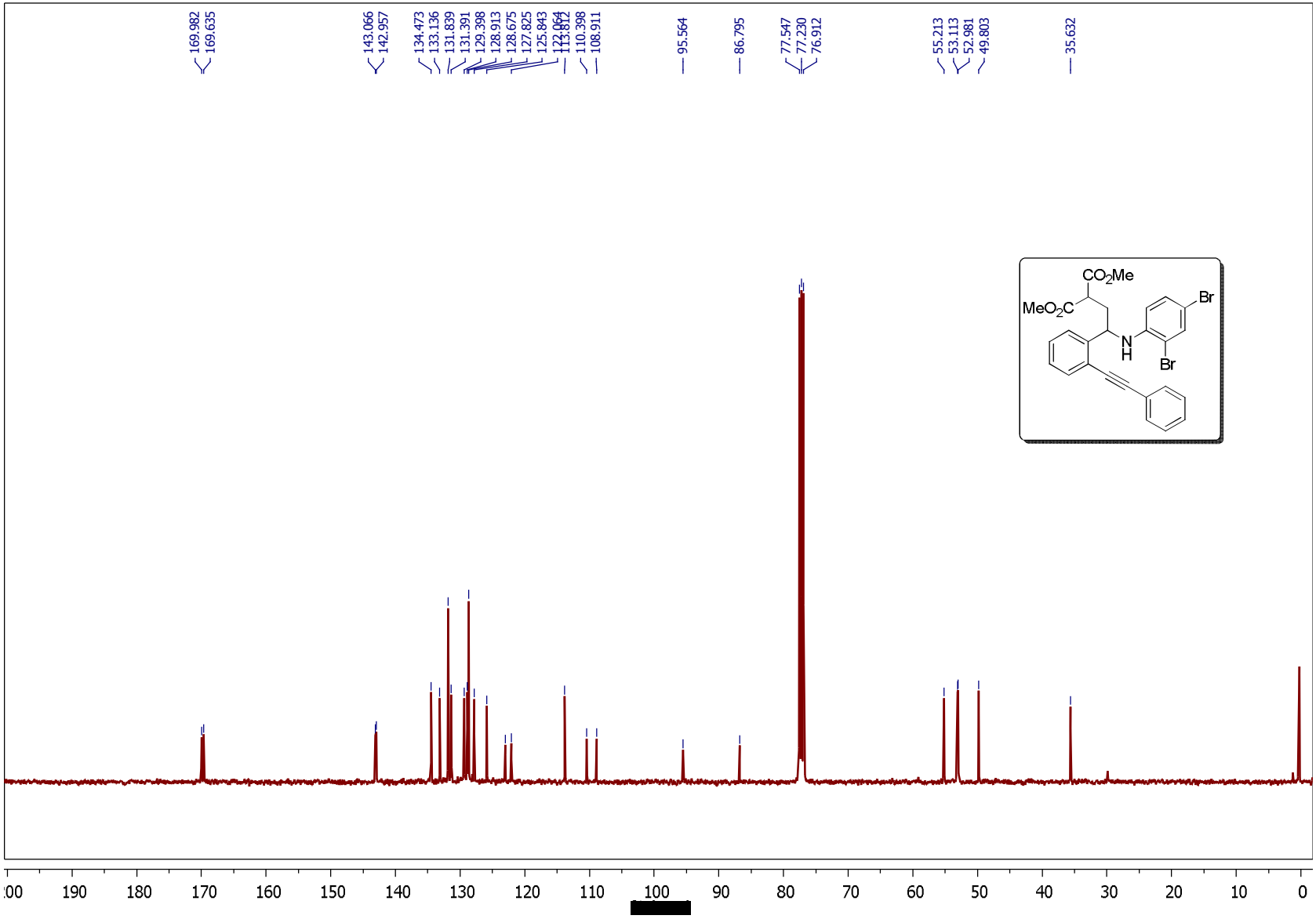
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 3m



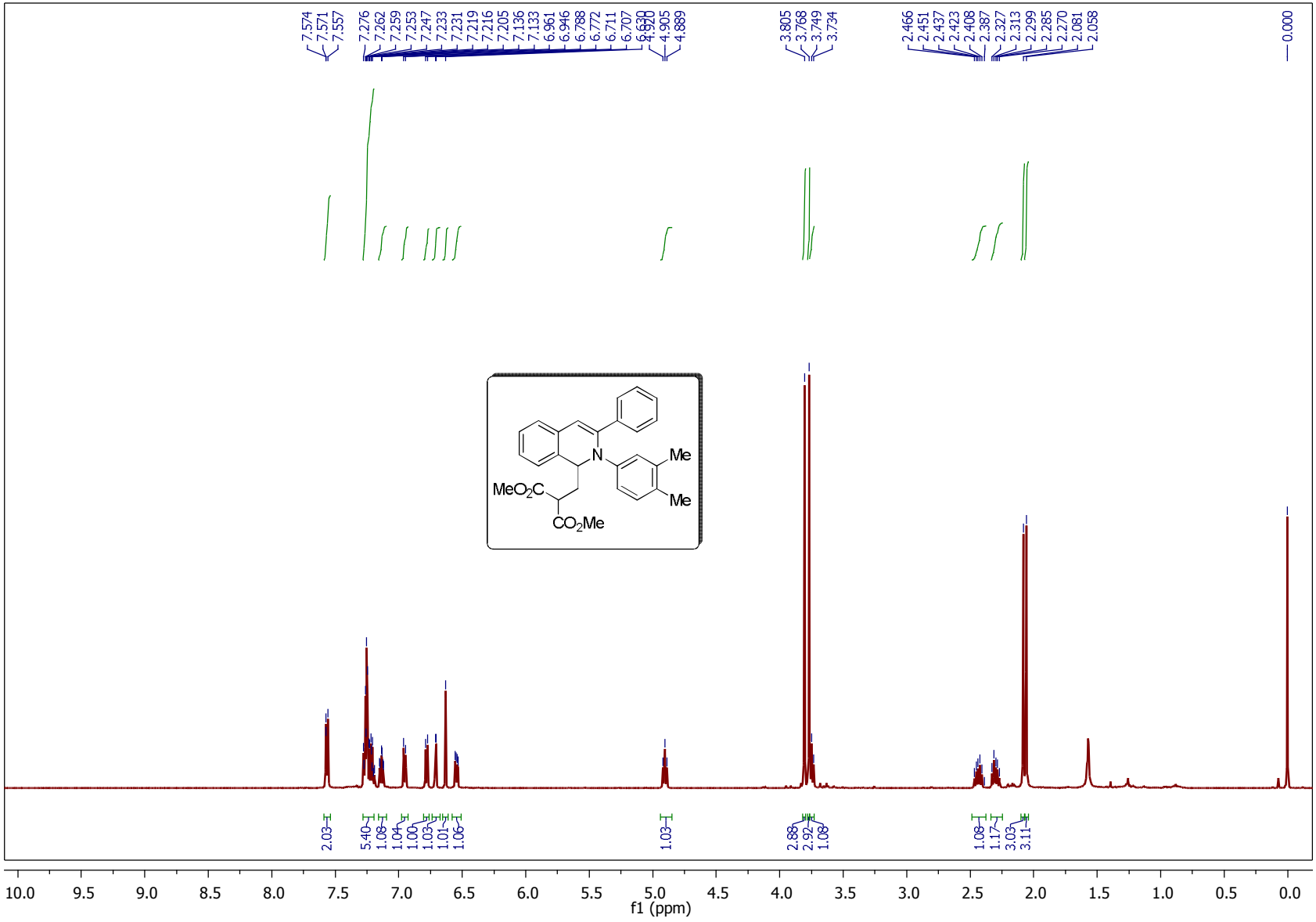
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 3n



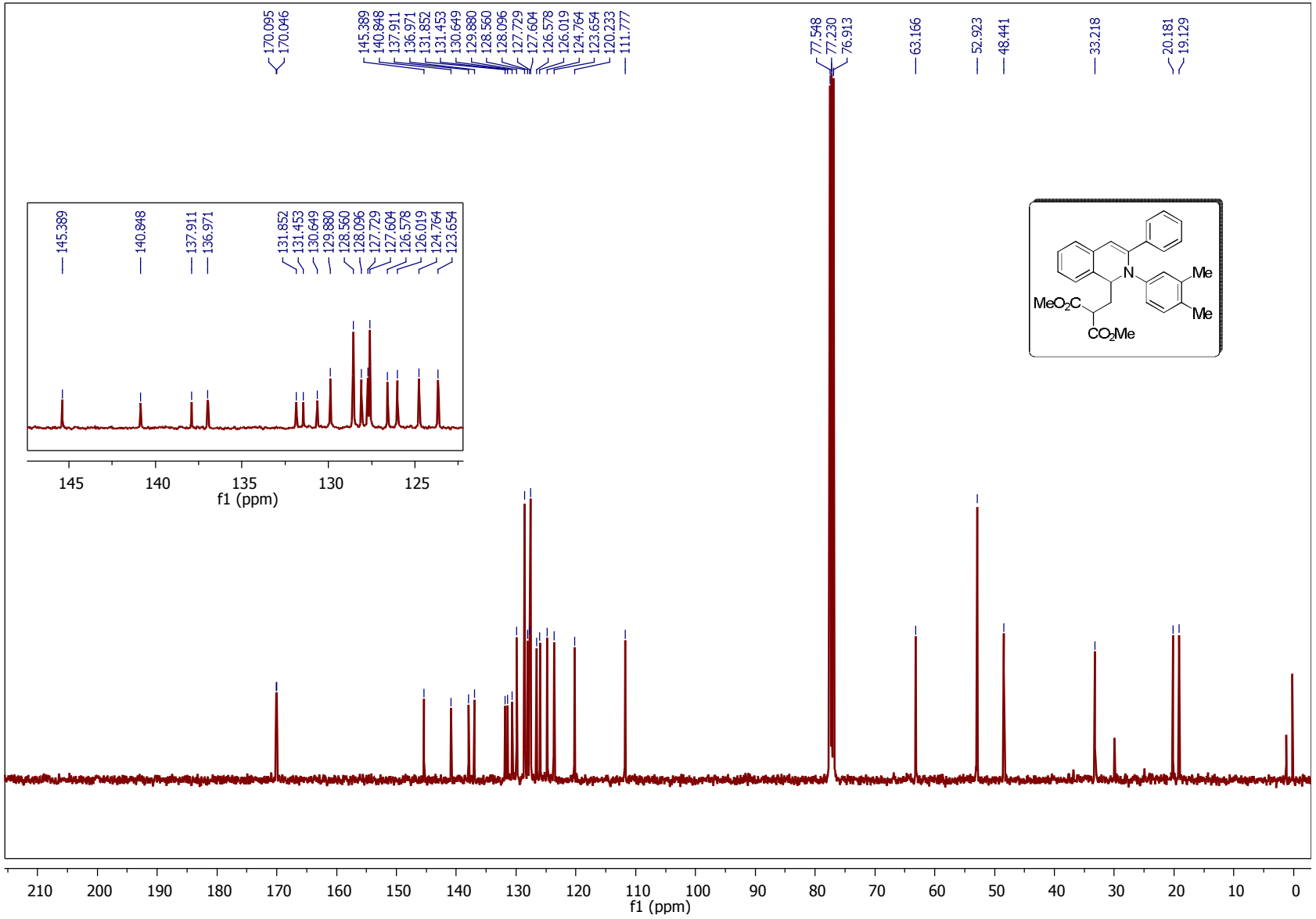
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 3n



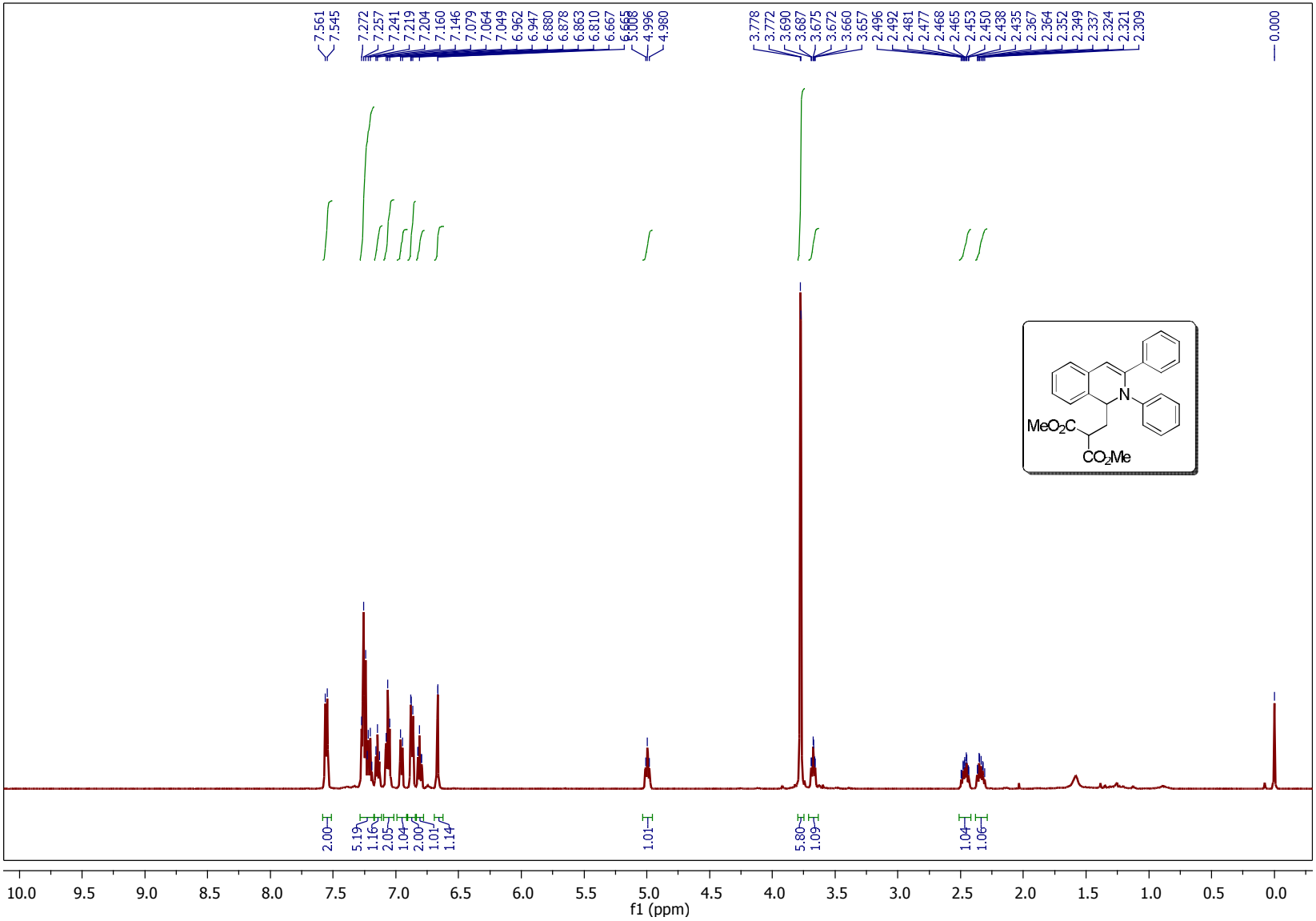
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4a



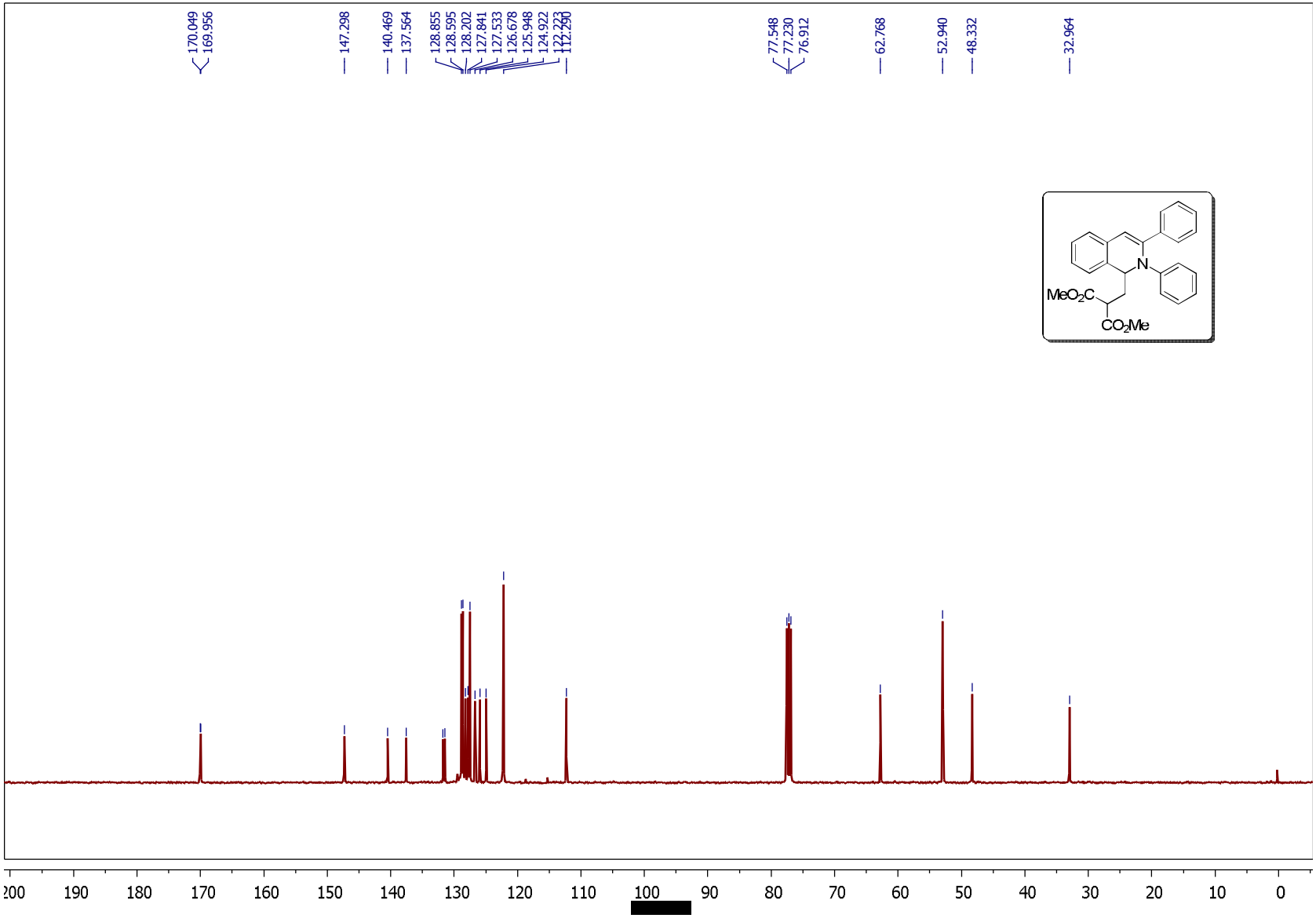
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4a



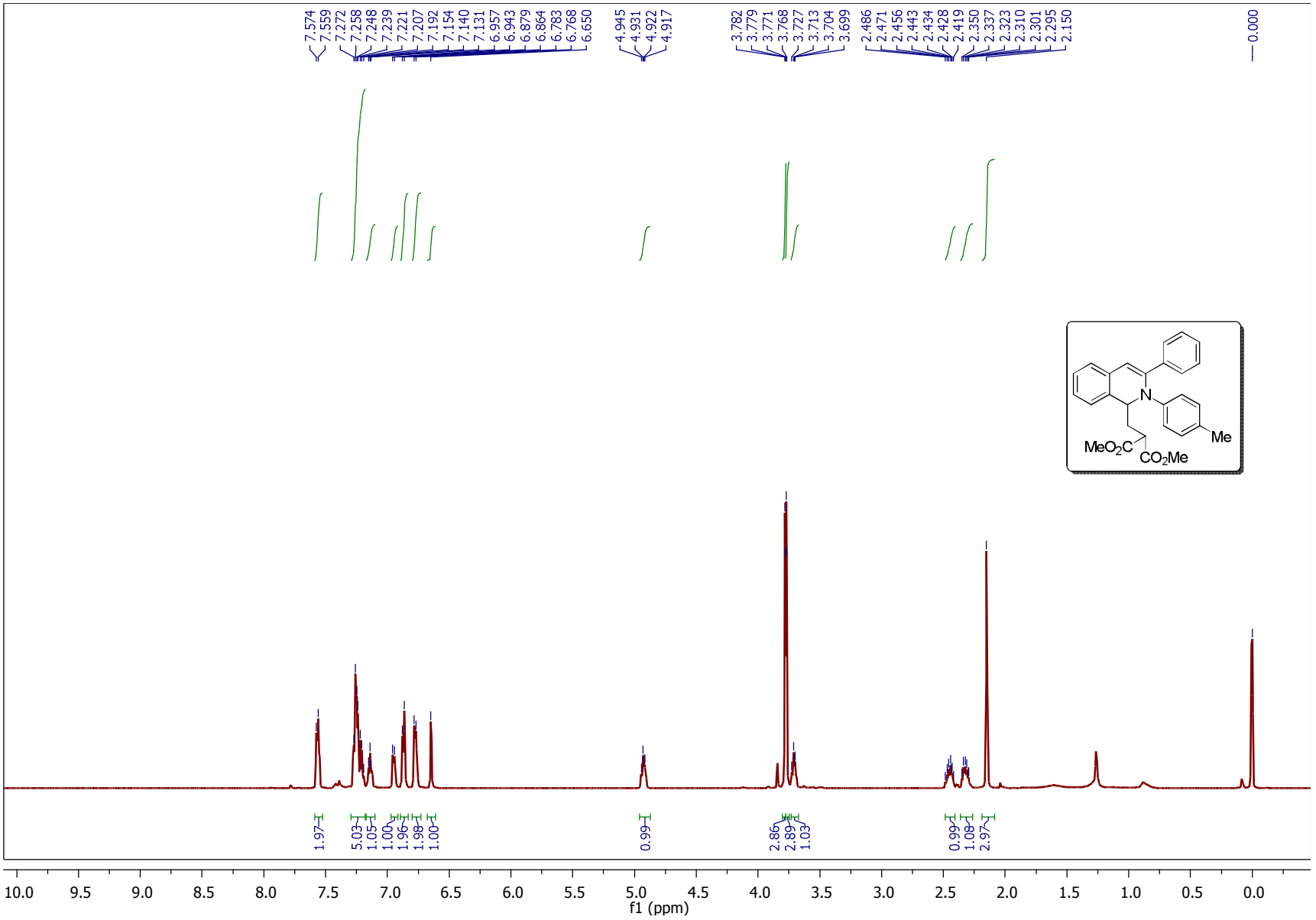
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4b



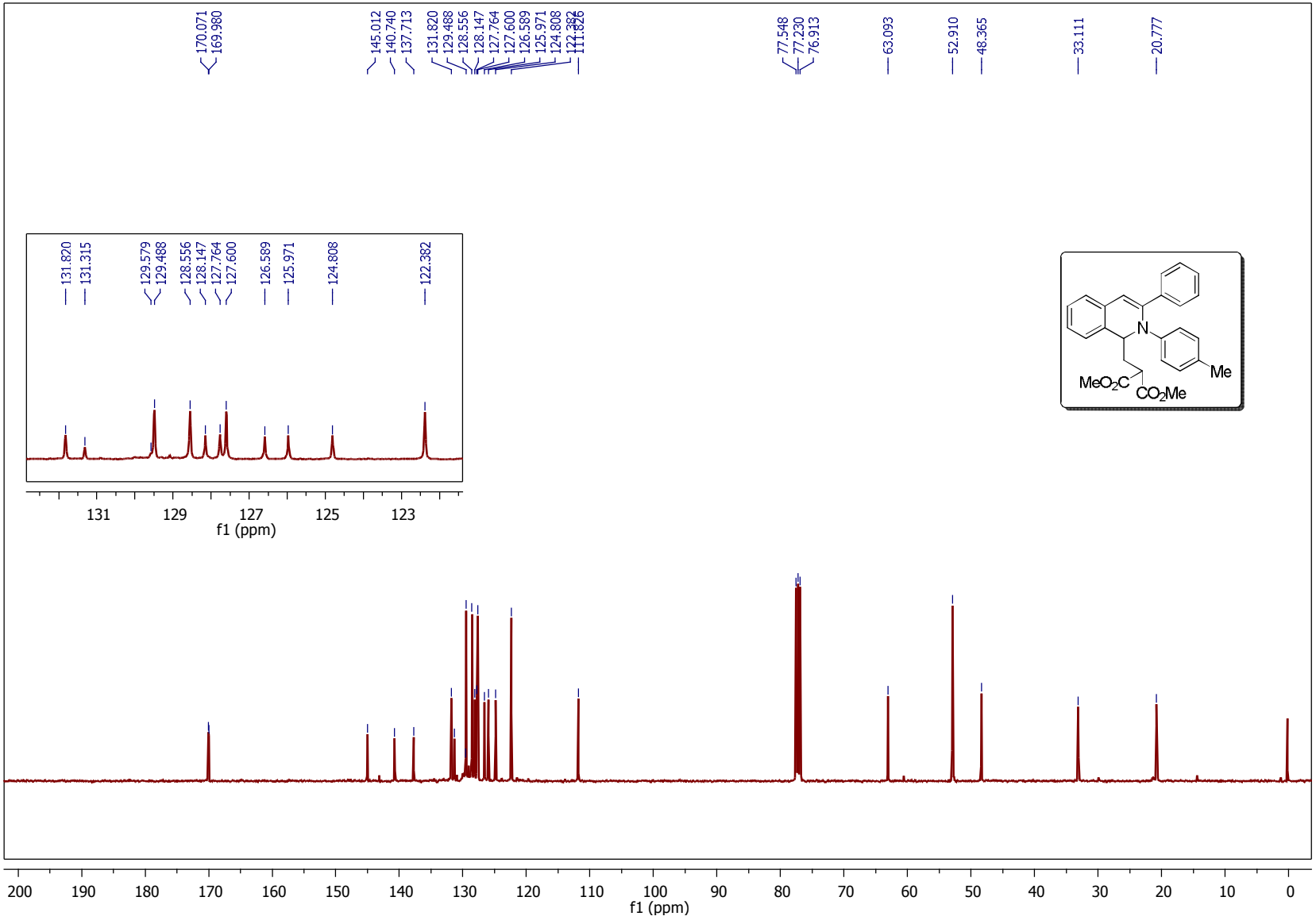
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4b



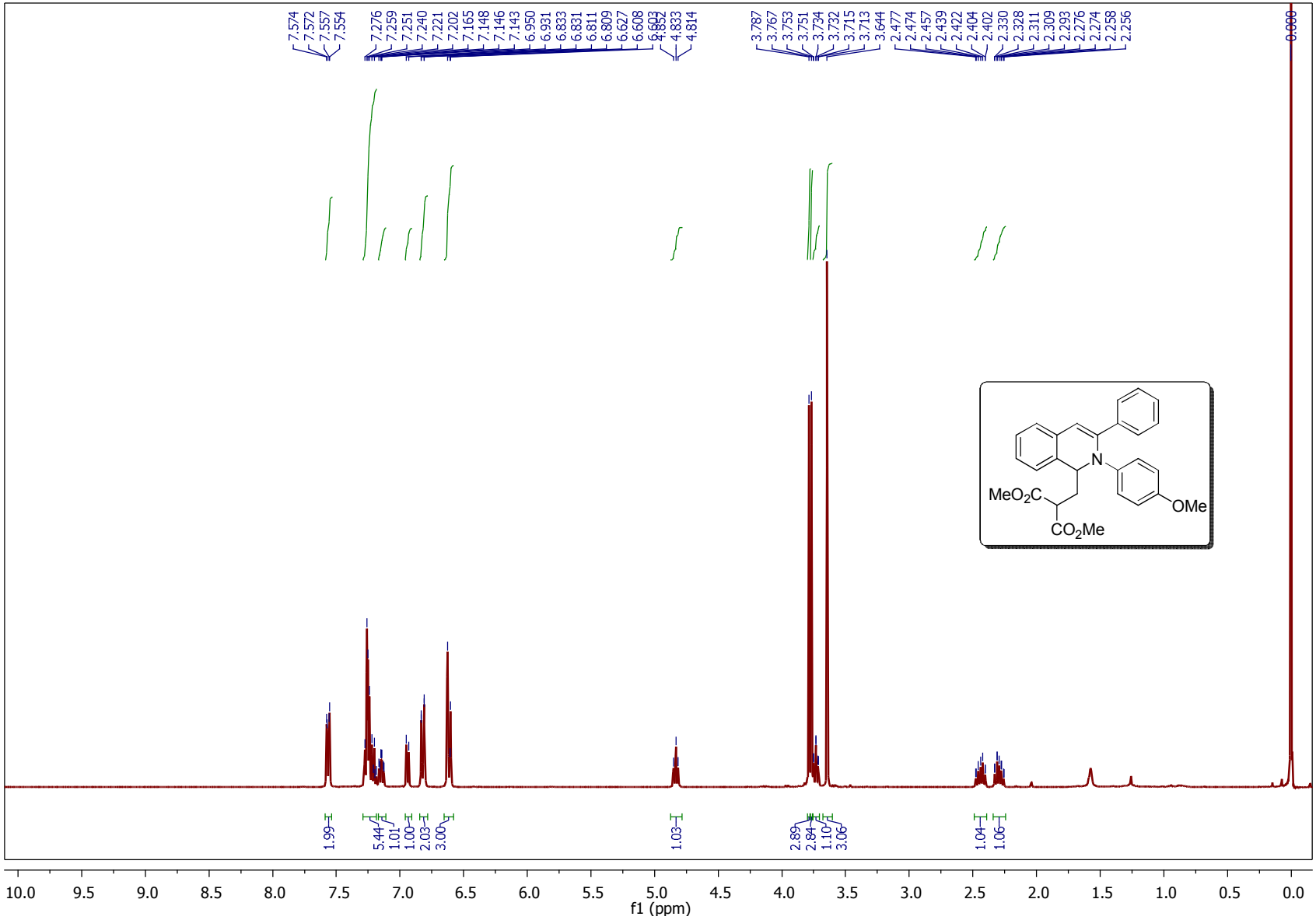
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4c



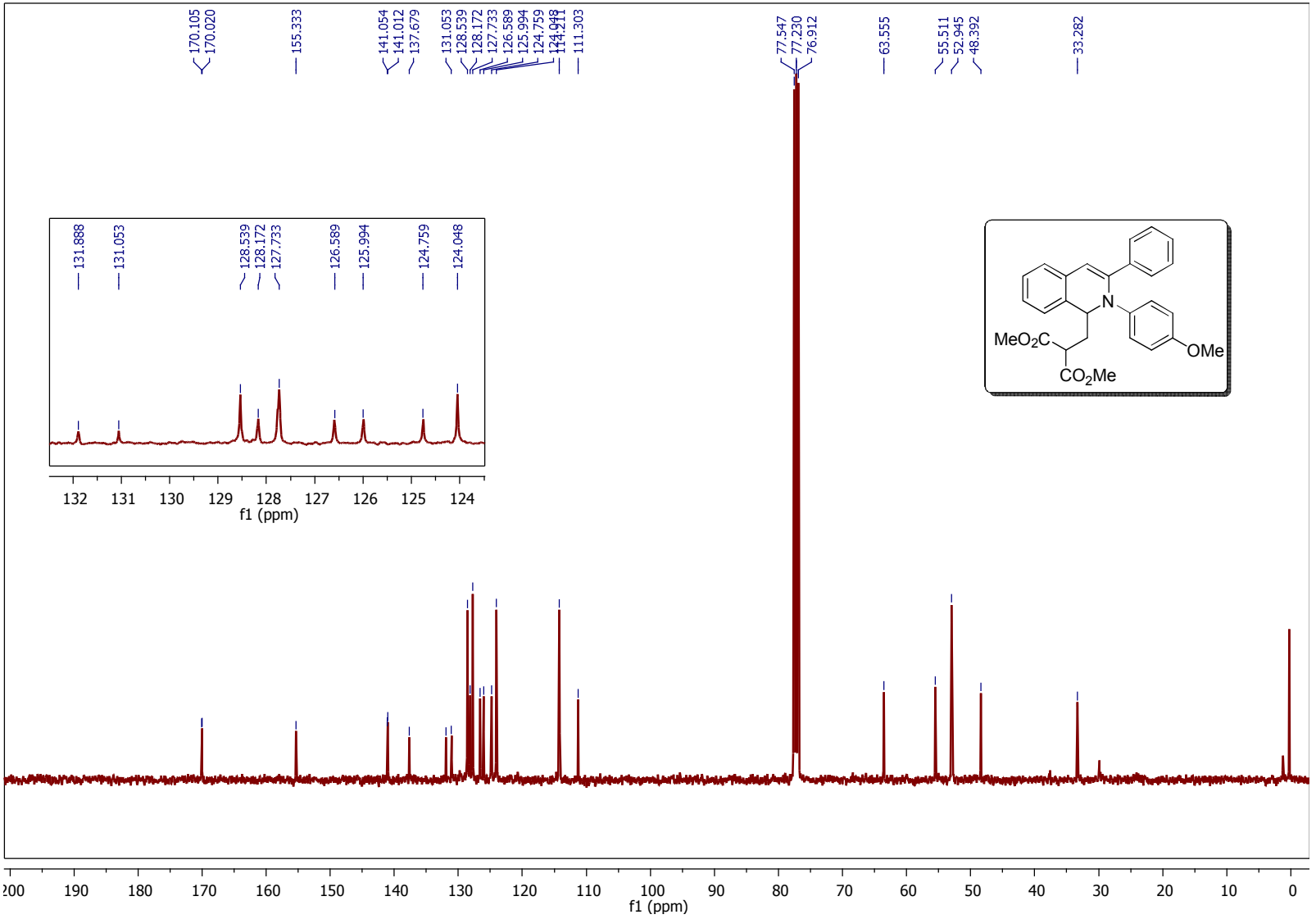
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4c



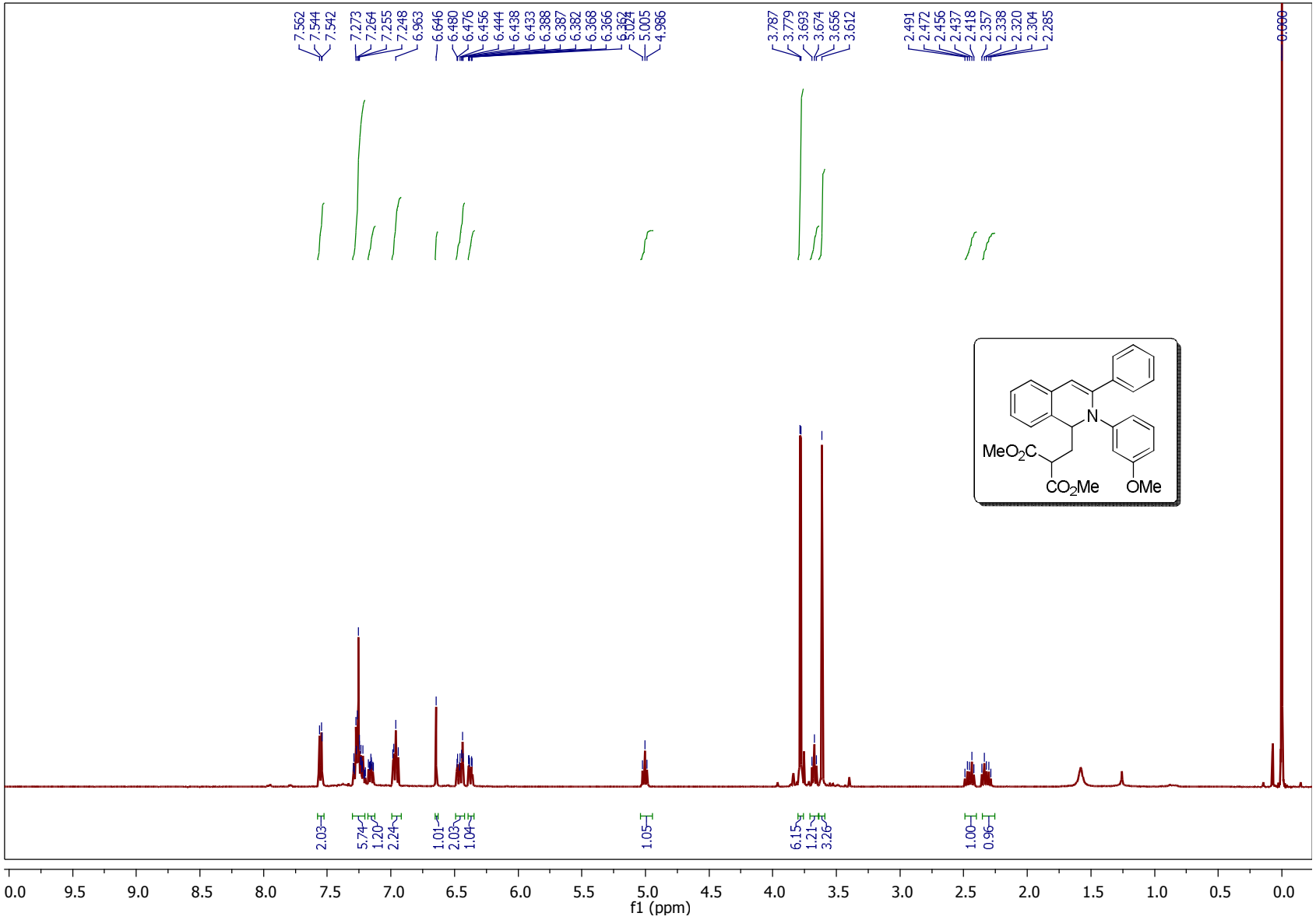
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4d



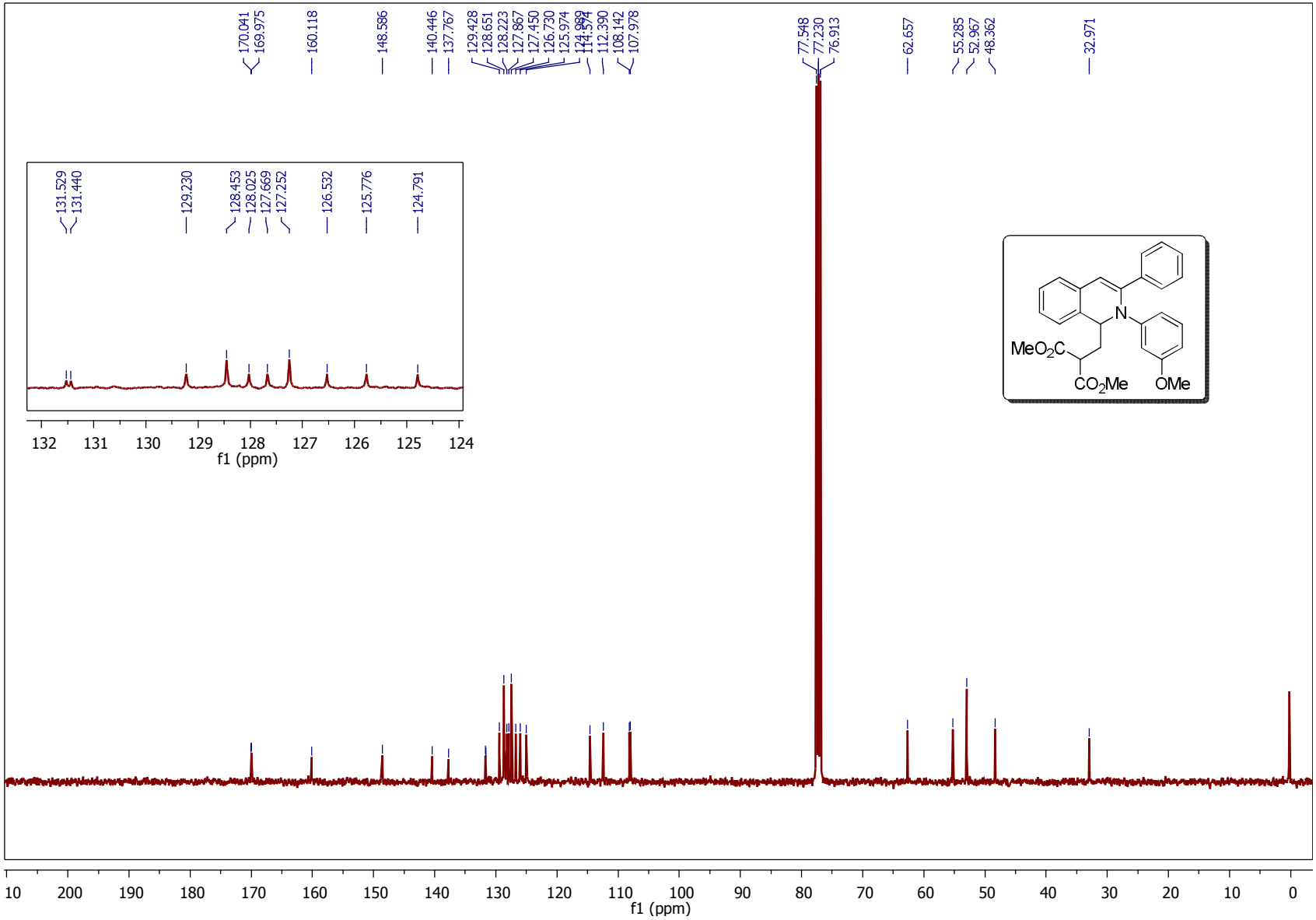
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4d



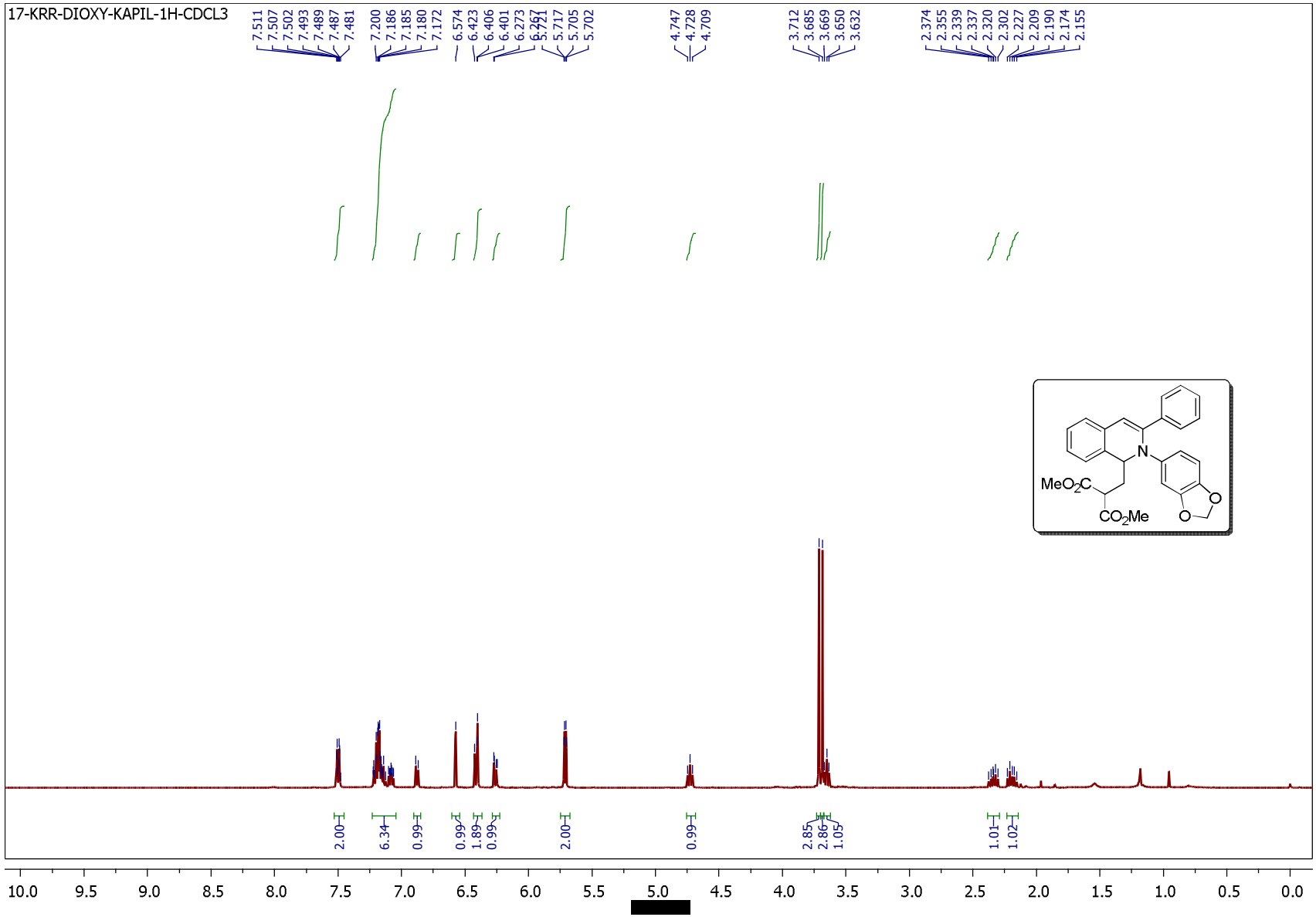
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4e



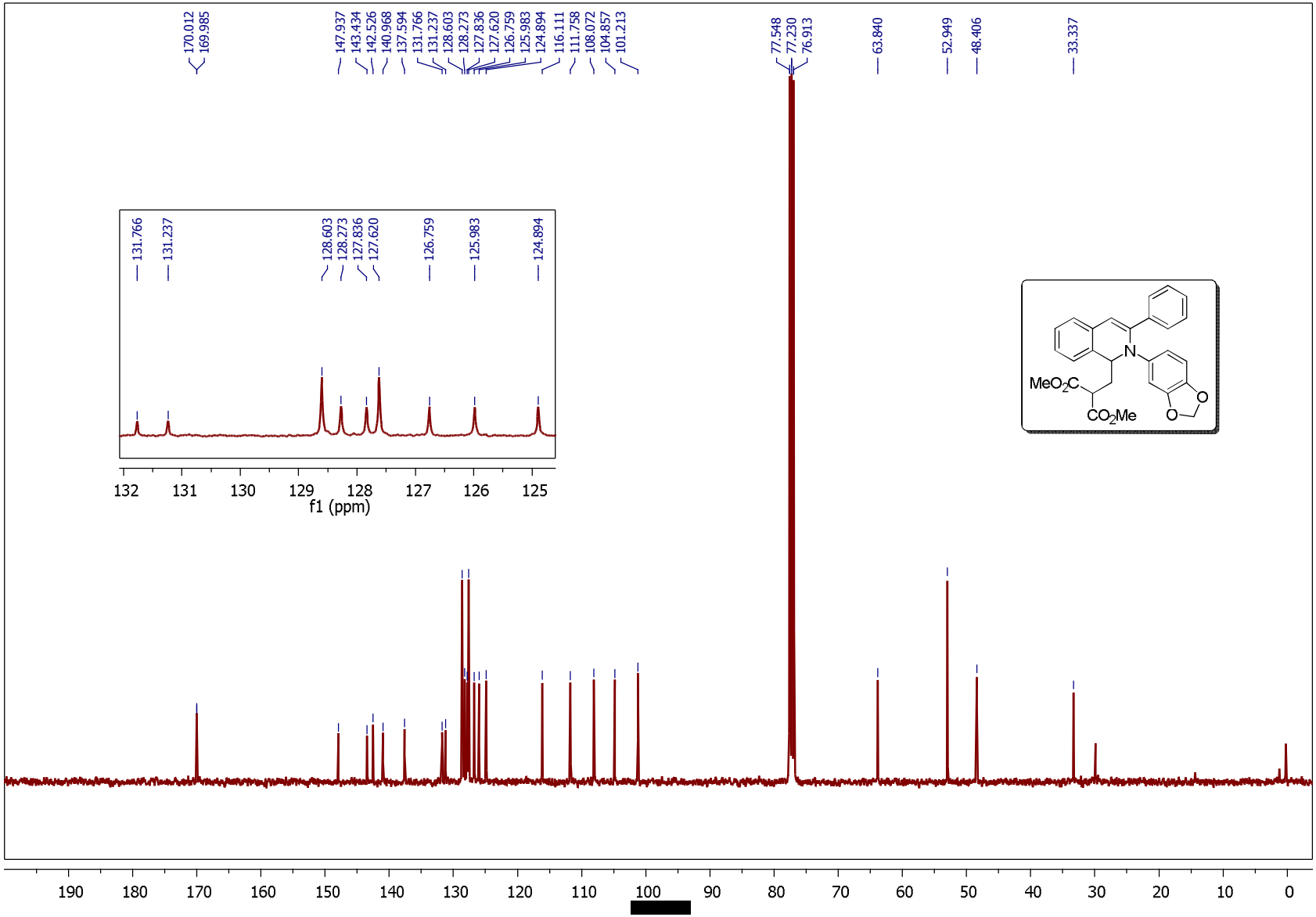
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4e



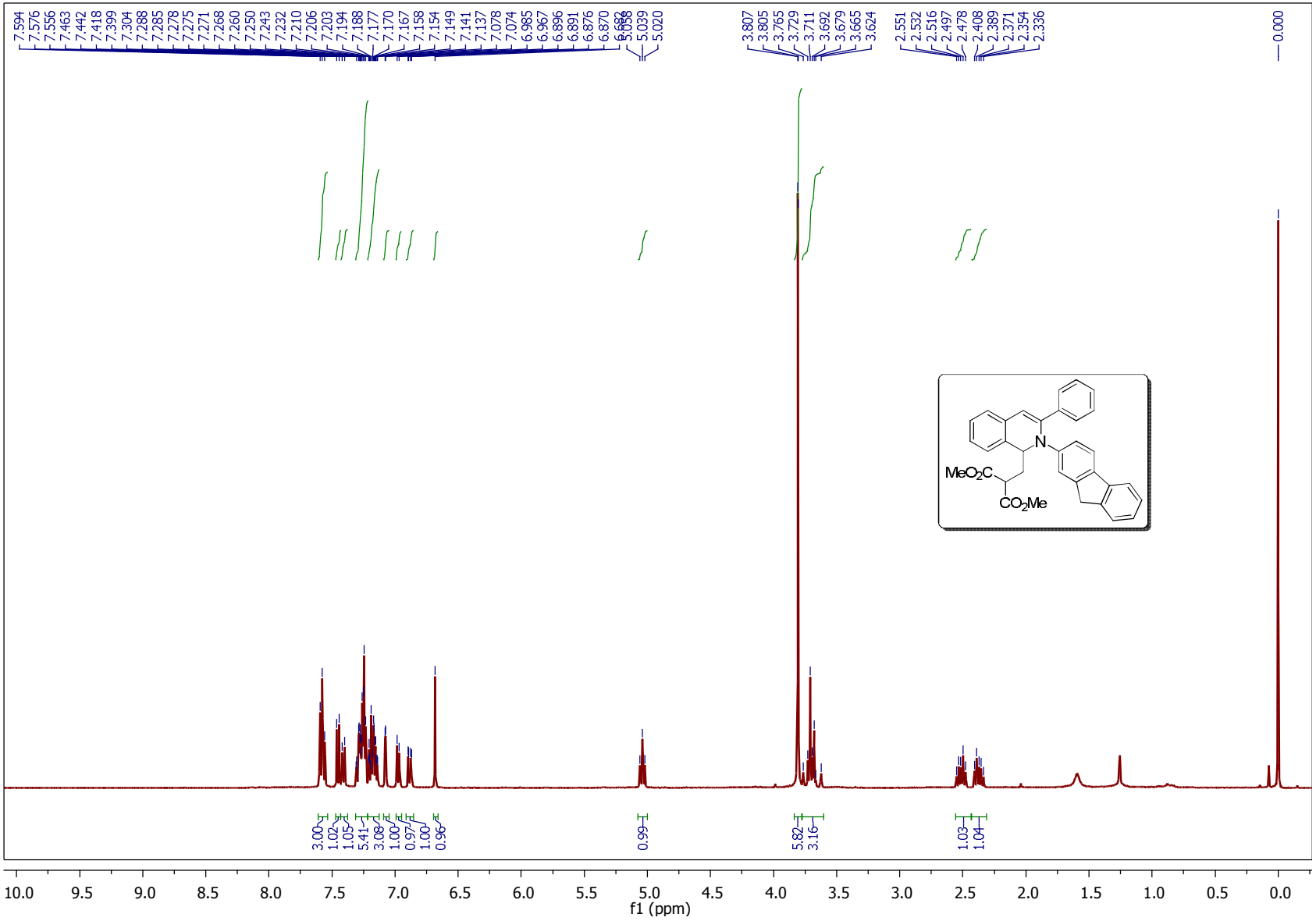
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4f



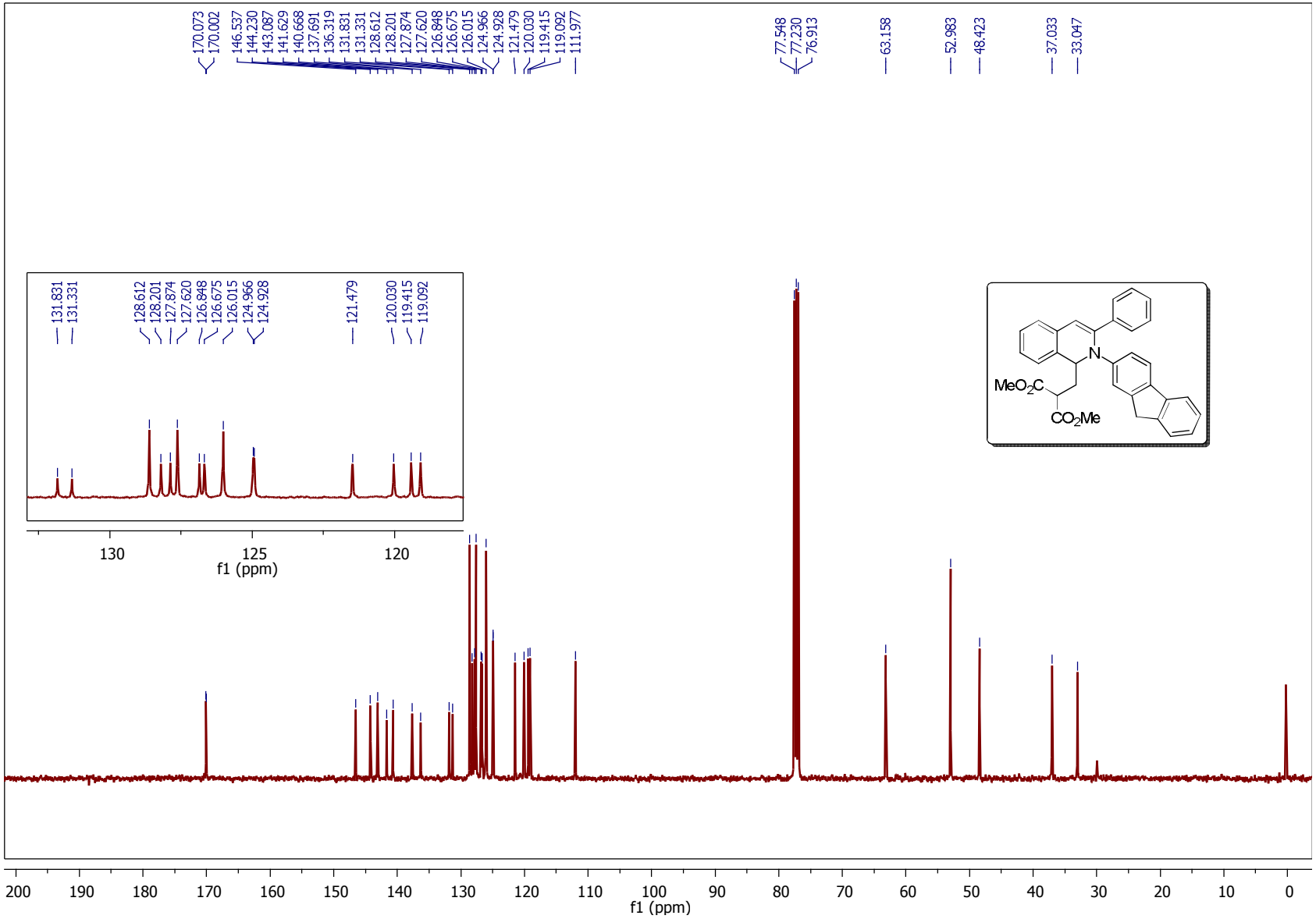
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4f



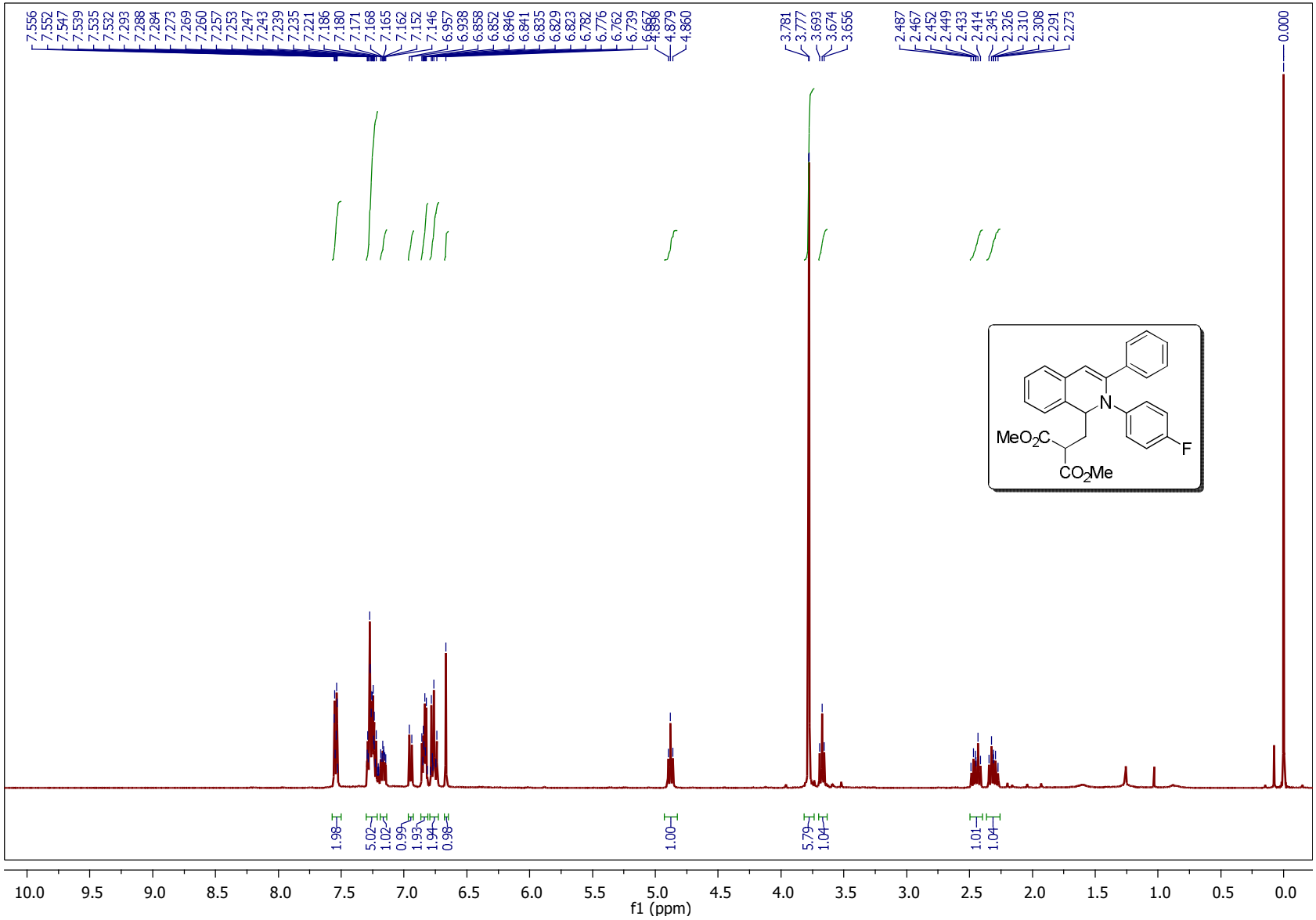
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4g



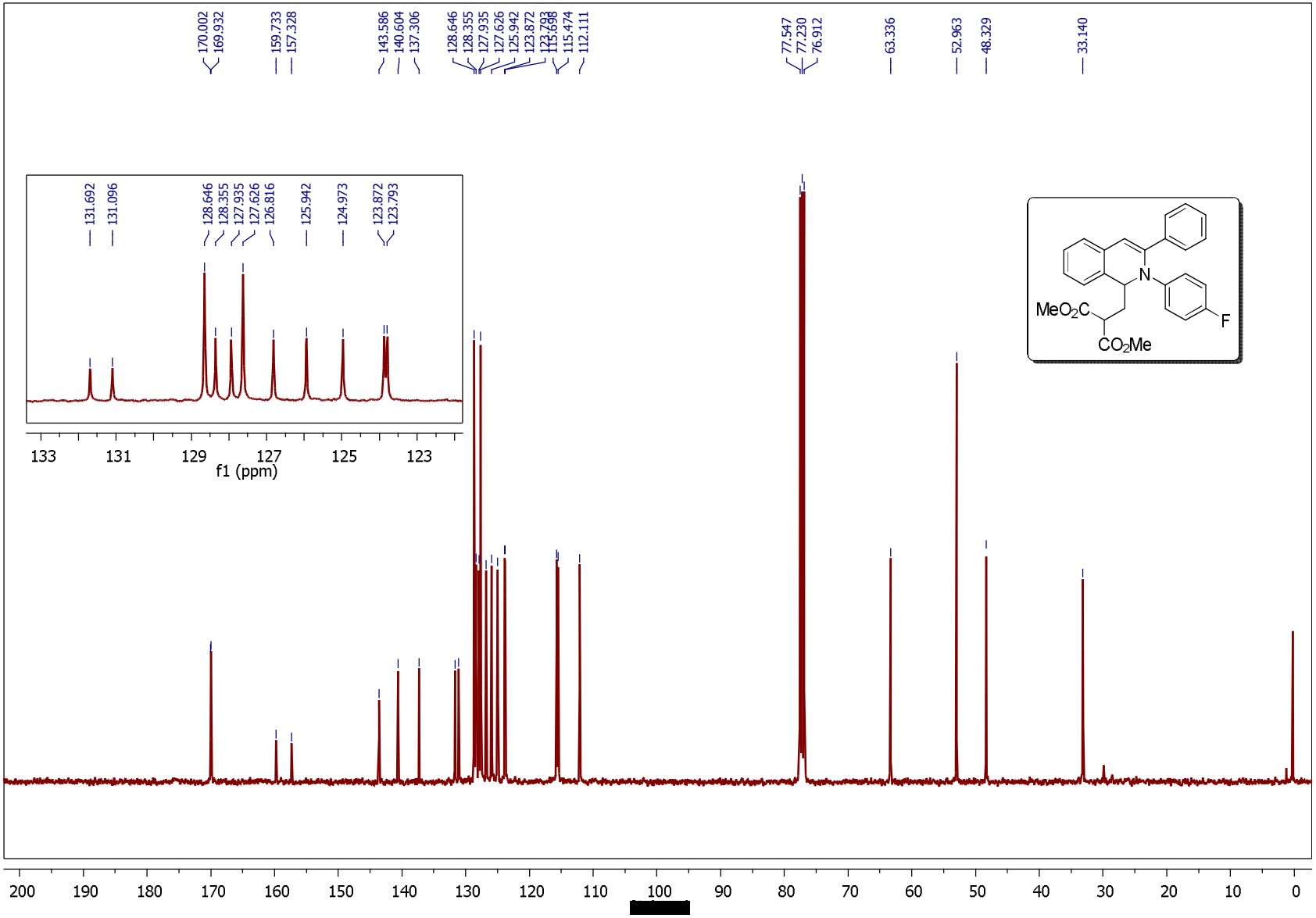
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4g



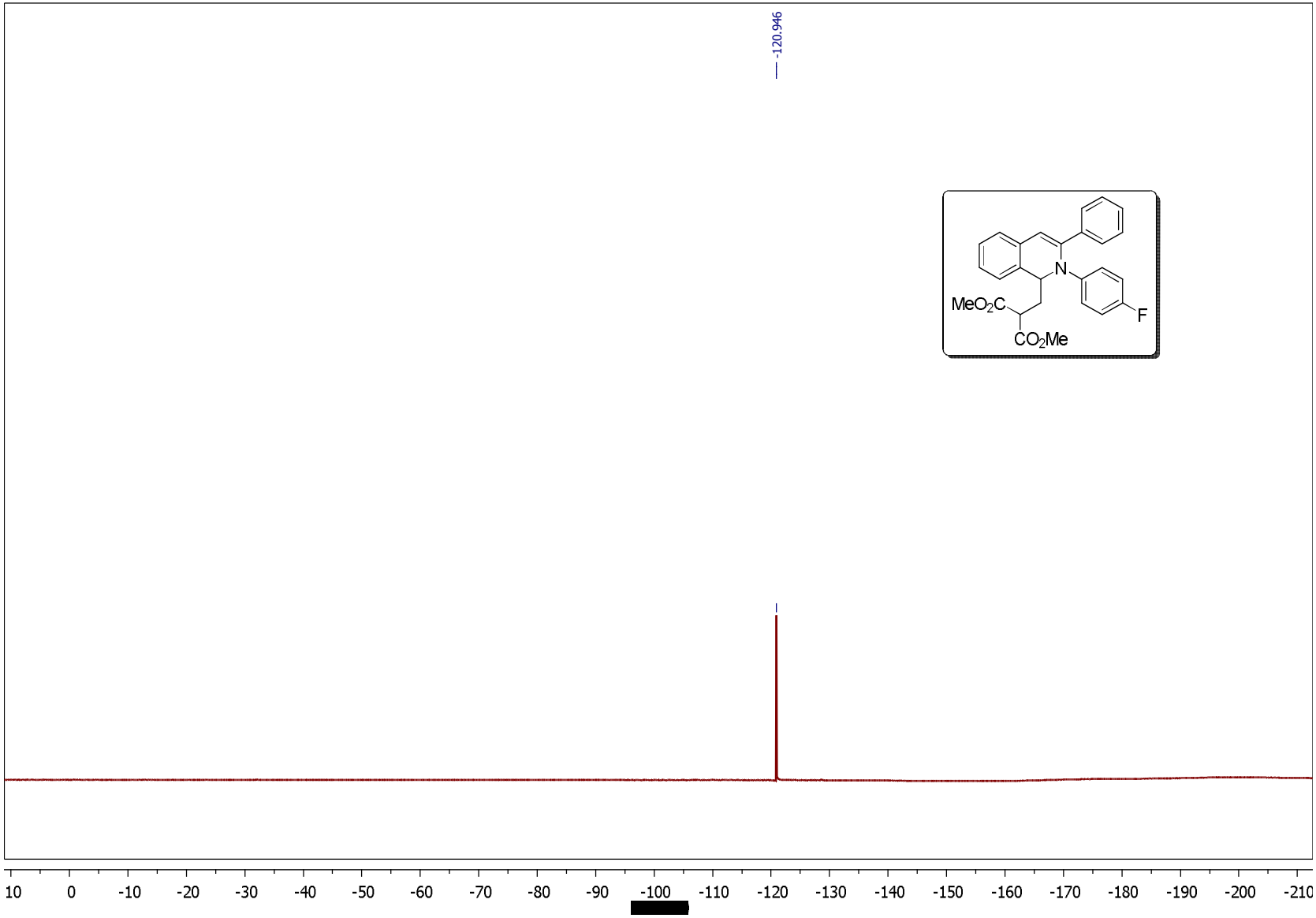
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4h



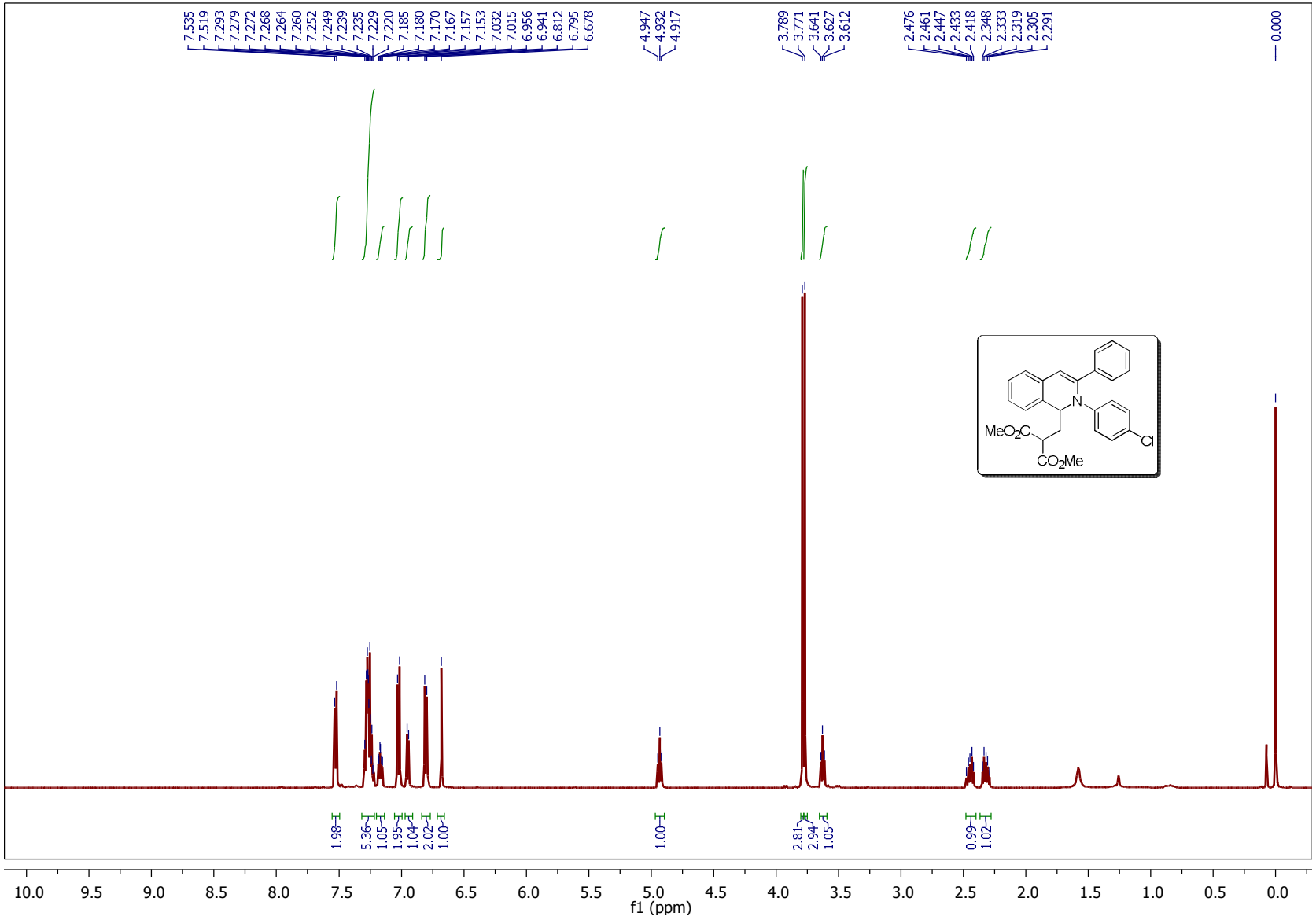
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4h



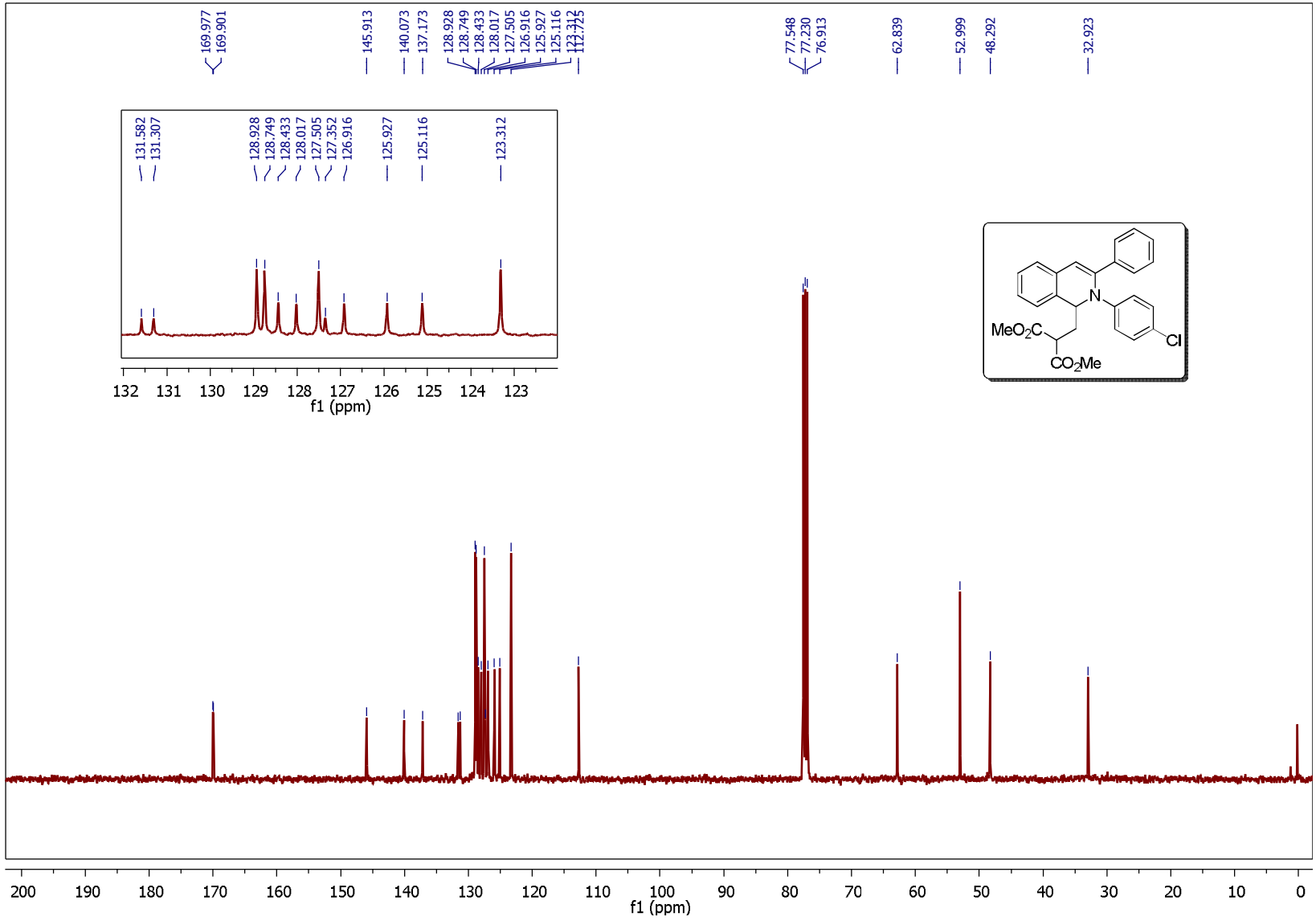
^{19}F NMR (377 MHz, $CDCl_3$) Spectrum of compound 4h



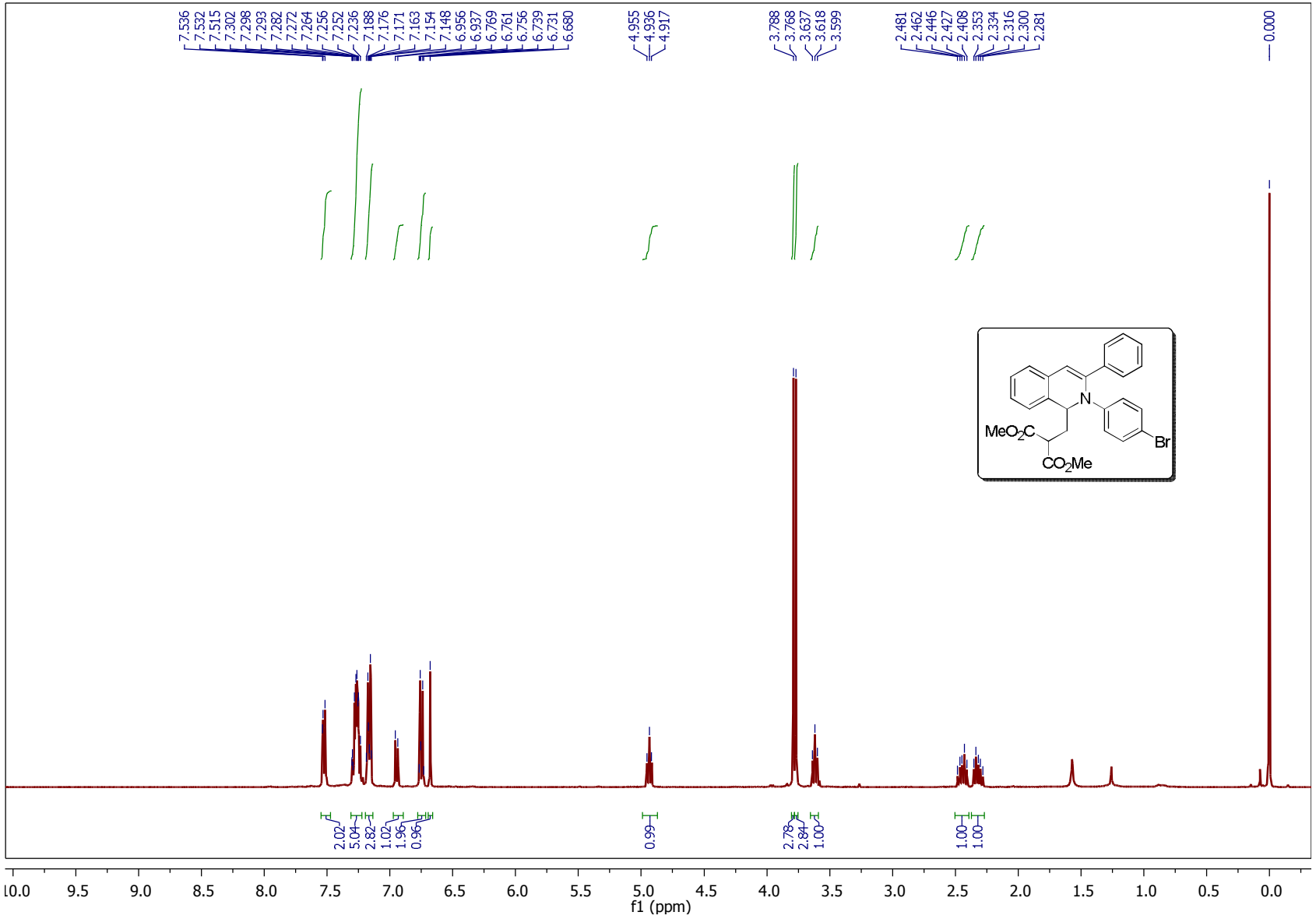
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4i



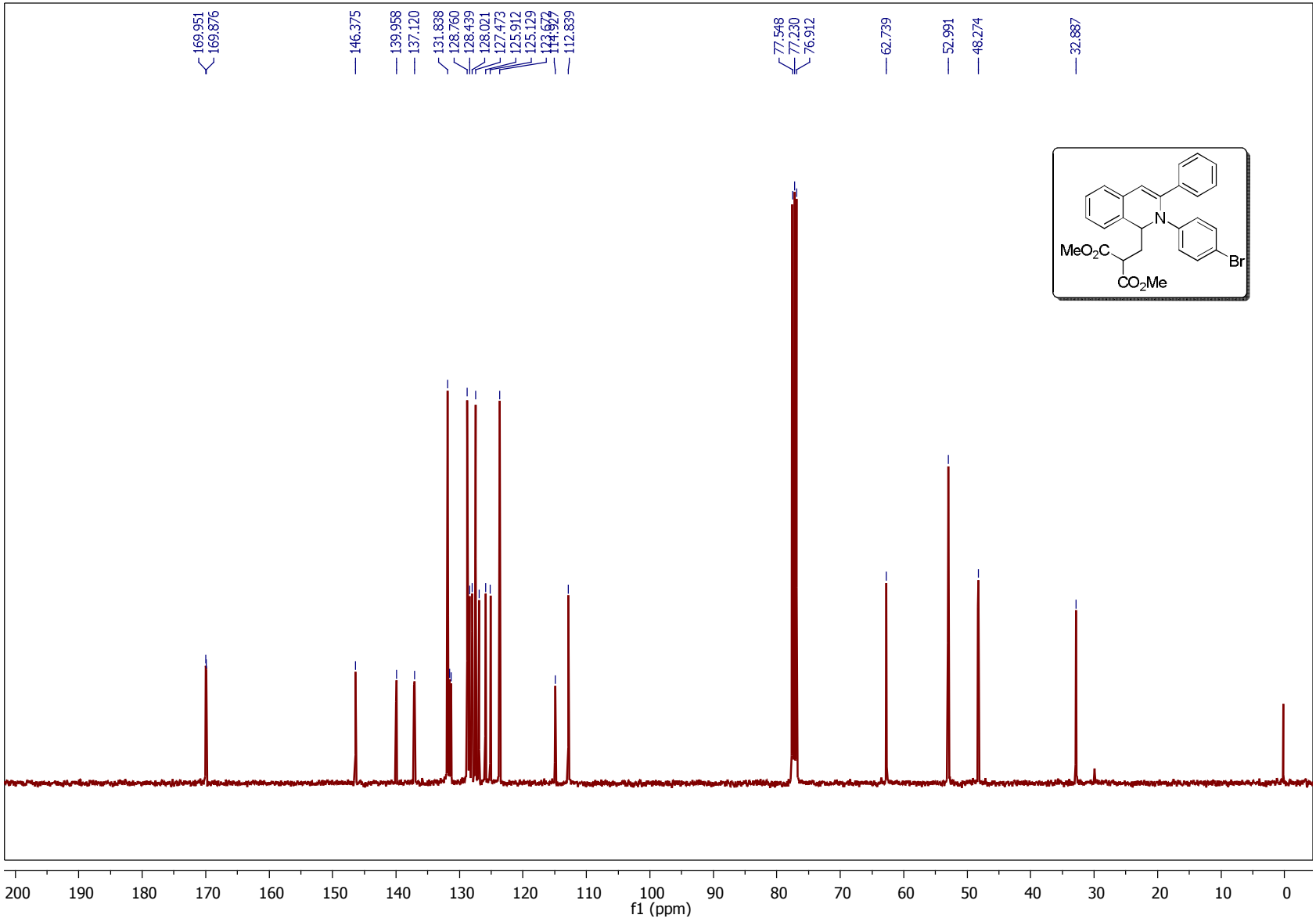
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4i



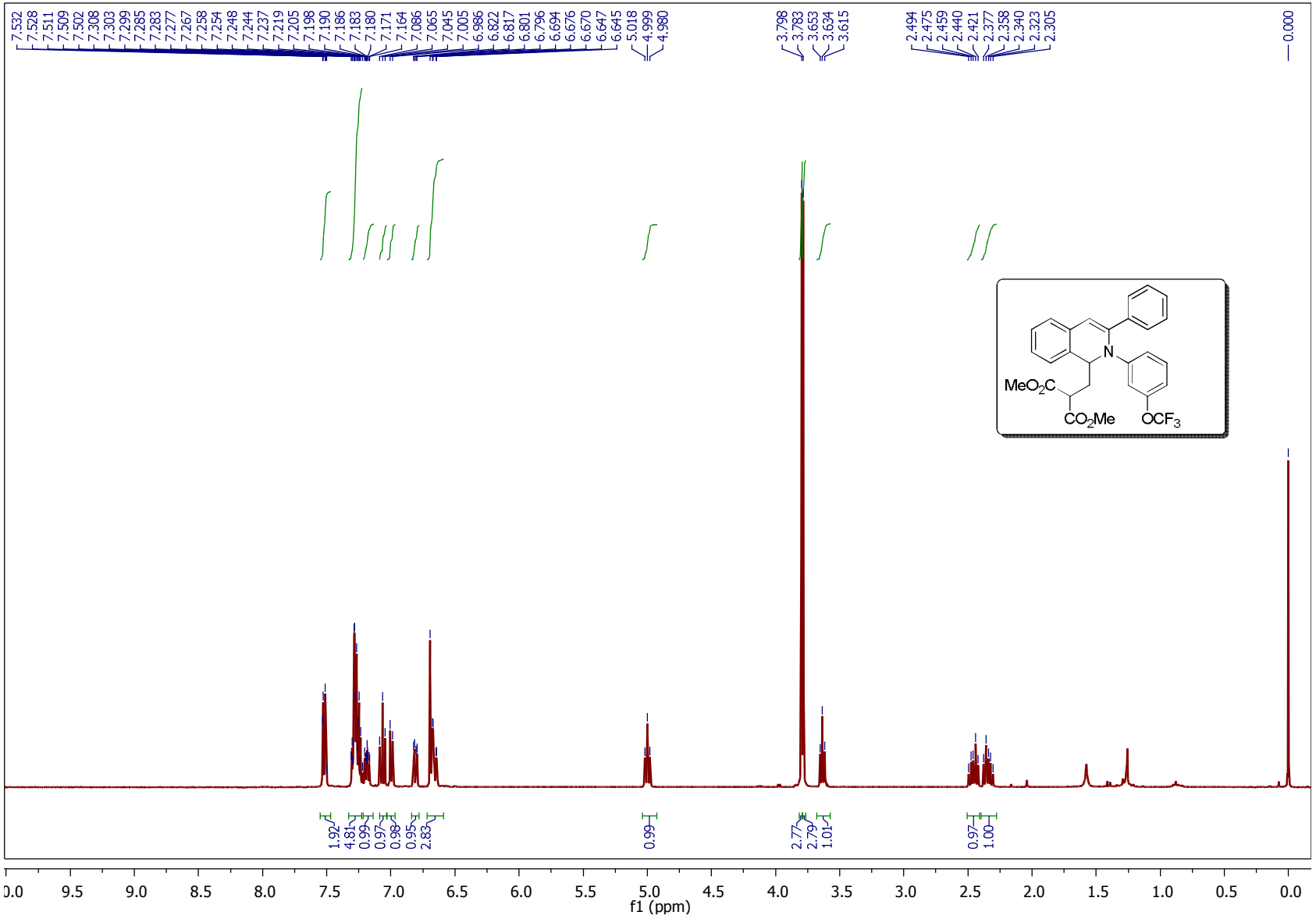
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4j



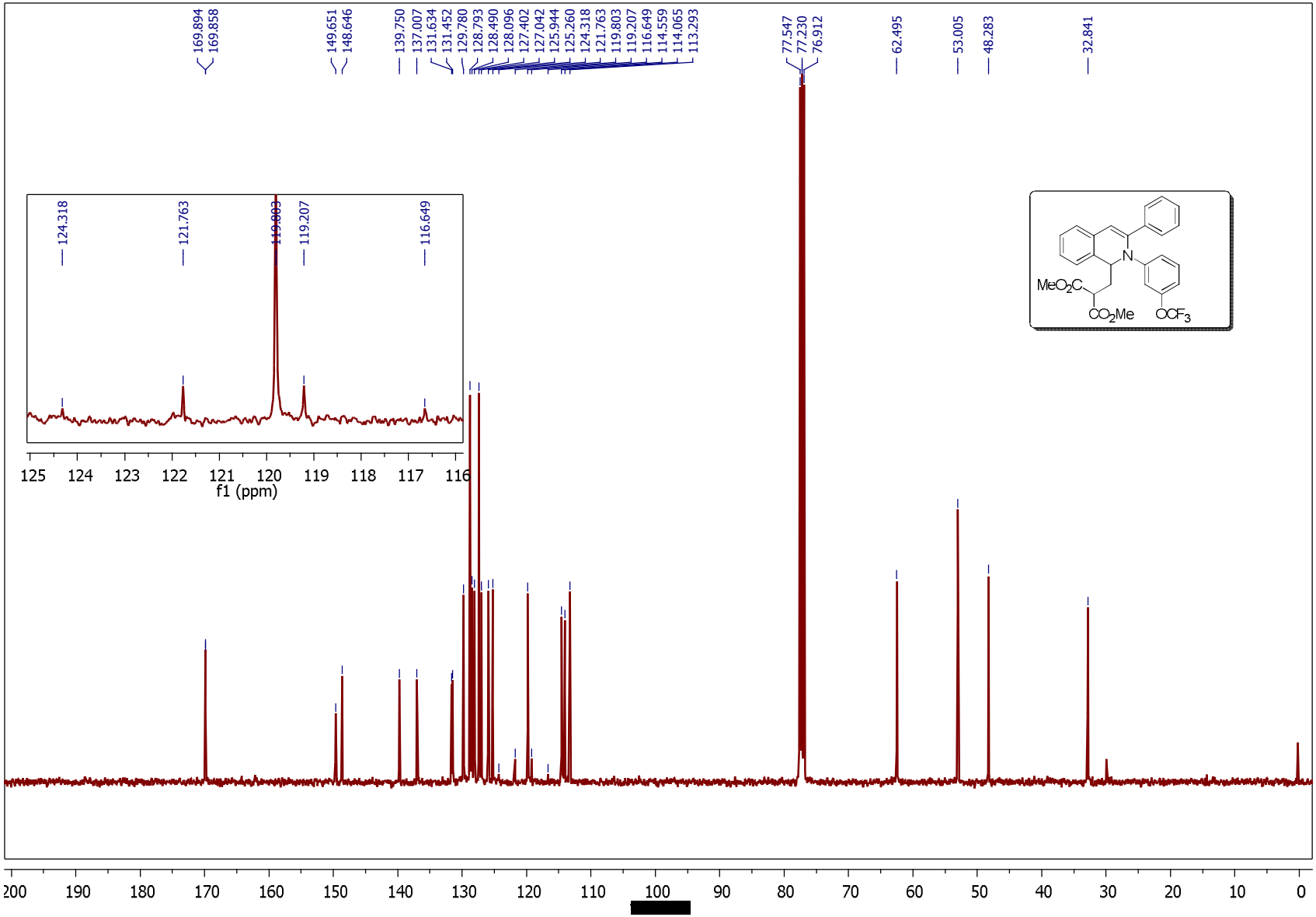
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4j



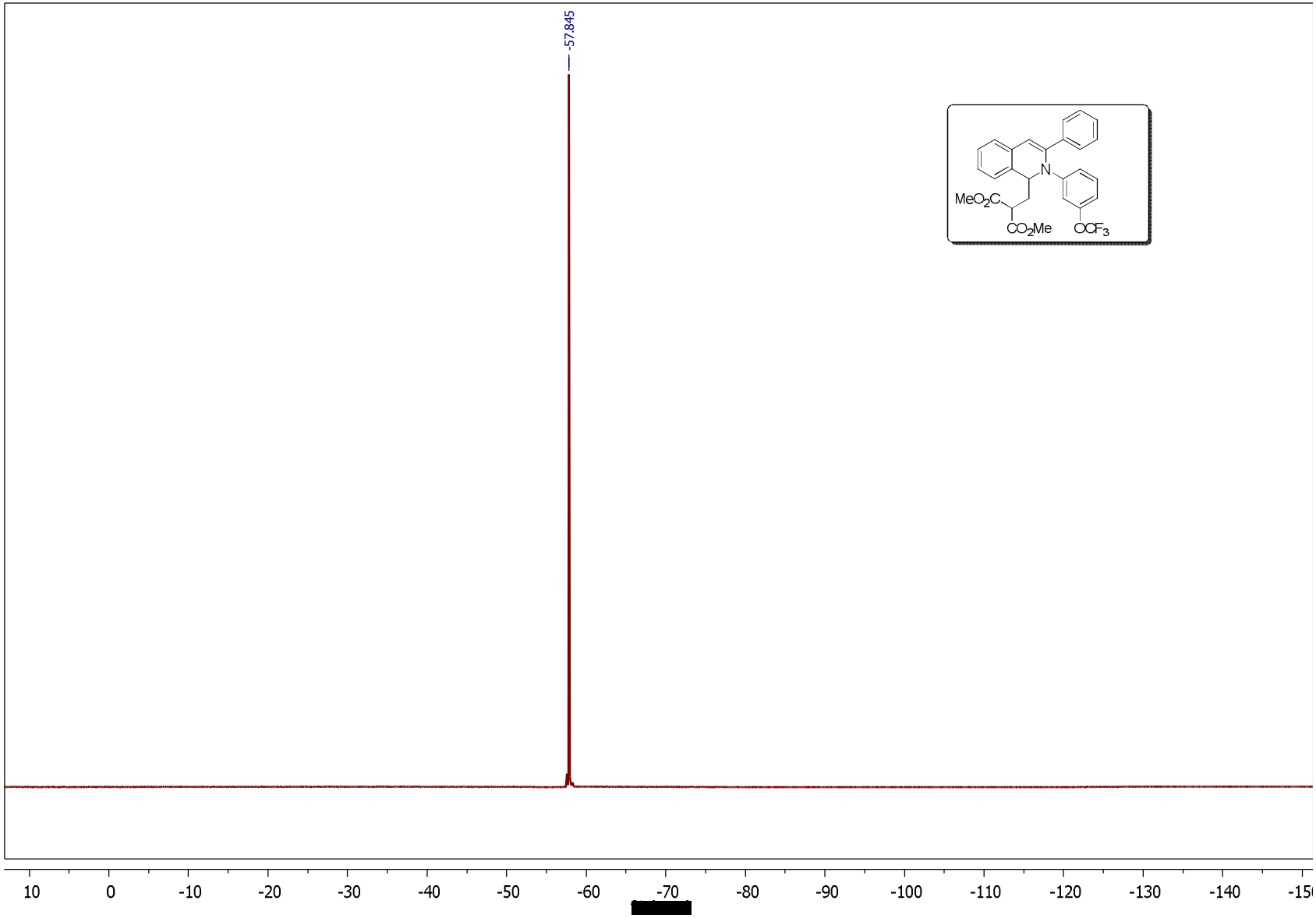
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4k



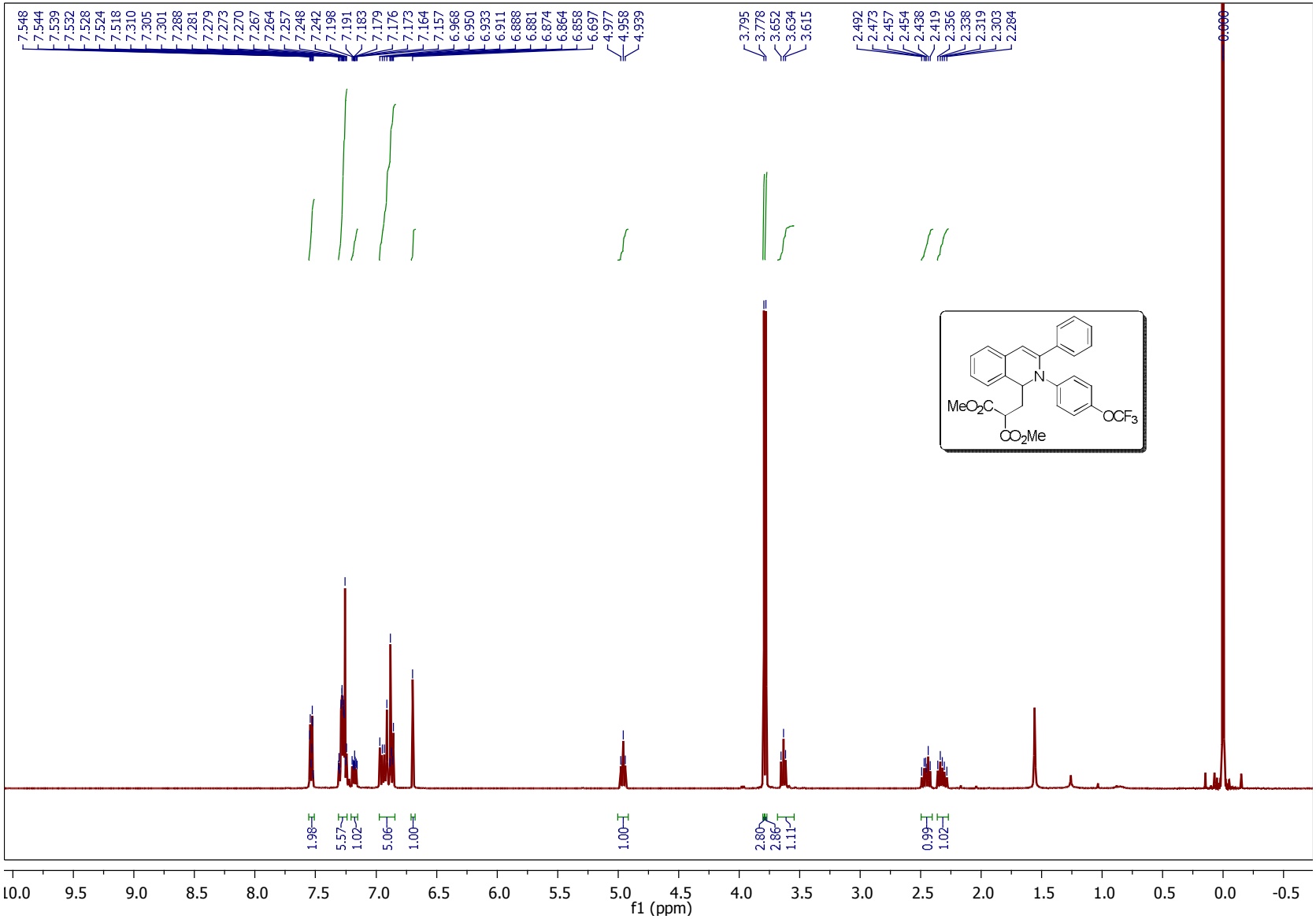
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4k



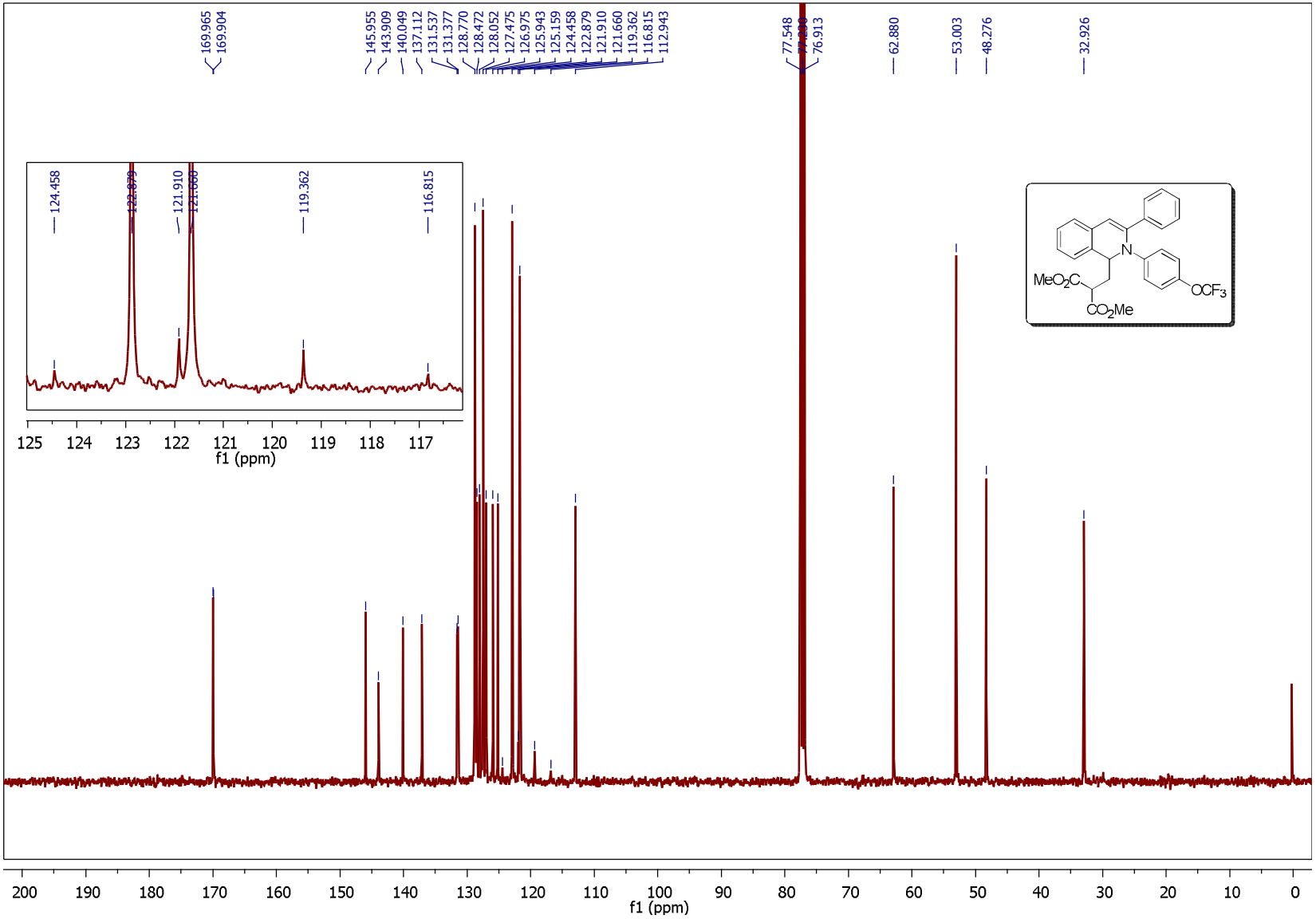
^{13}F NMR (377 MHz, $CDCl_3$) Spectrum of compound 4k



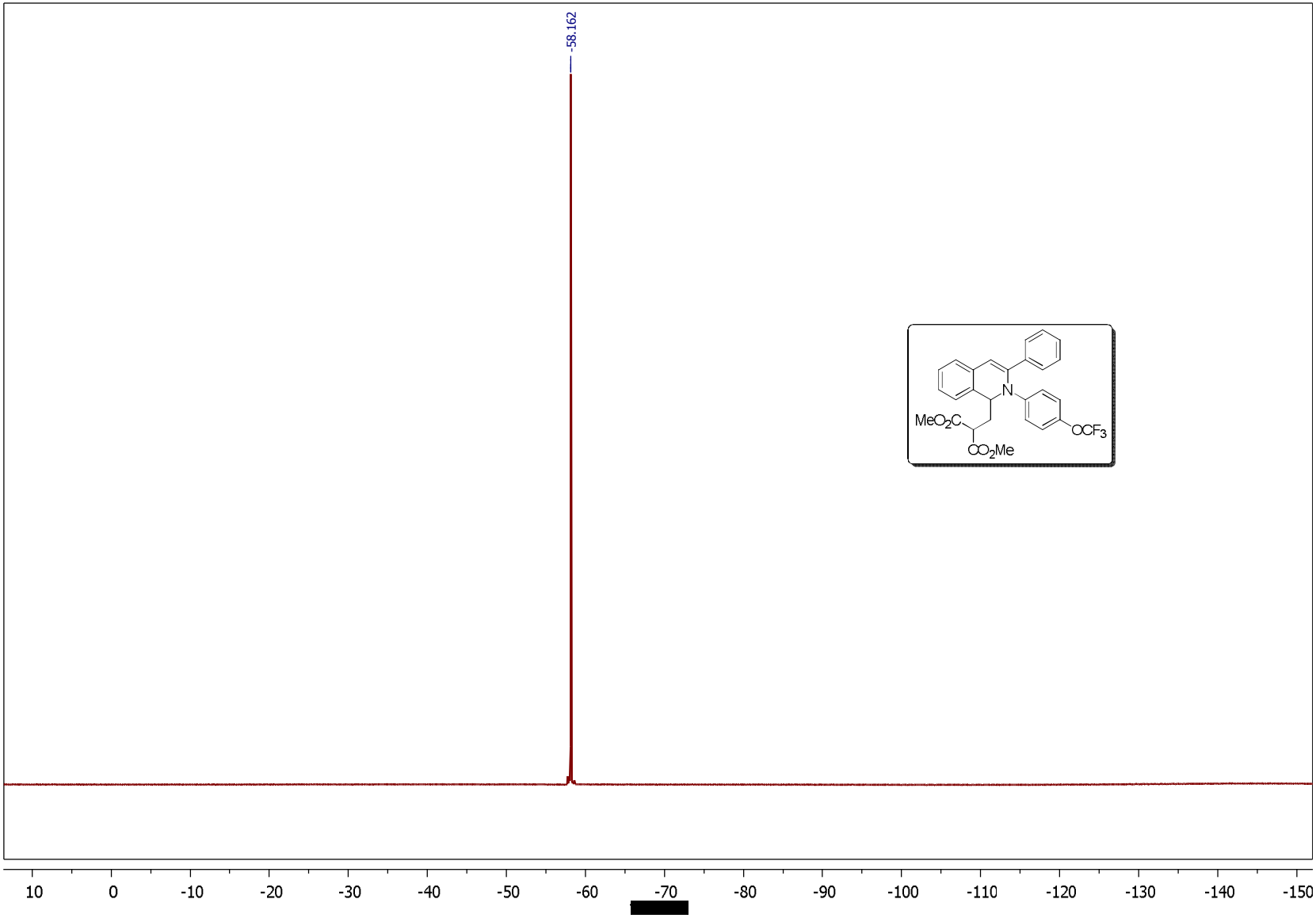
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4l



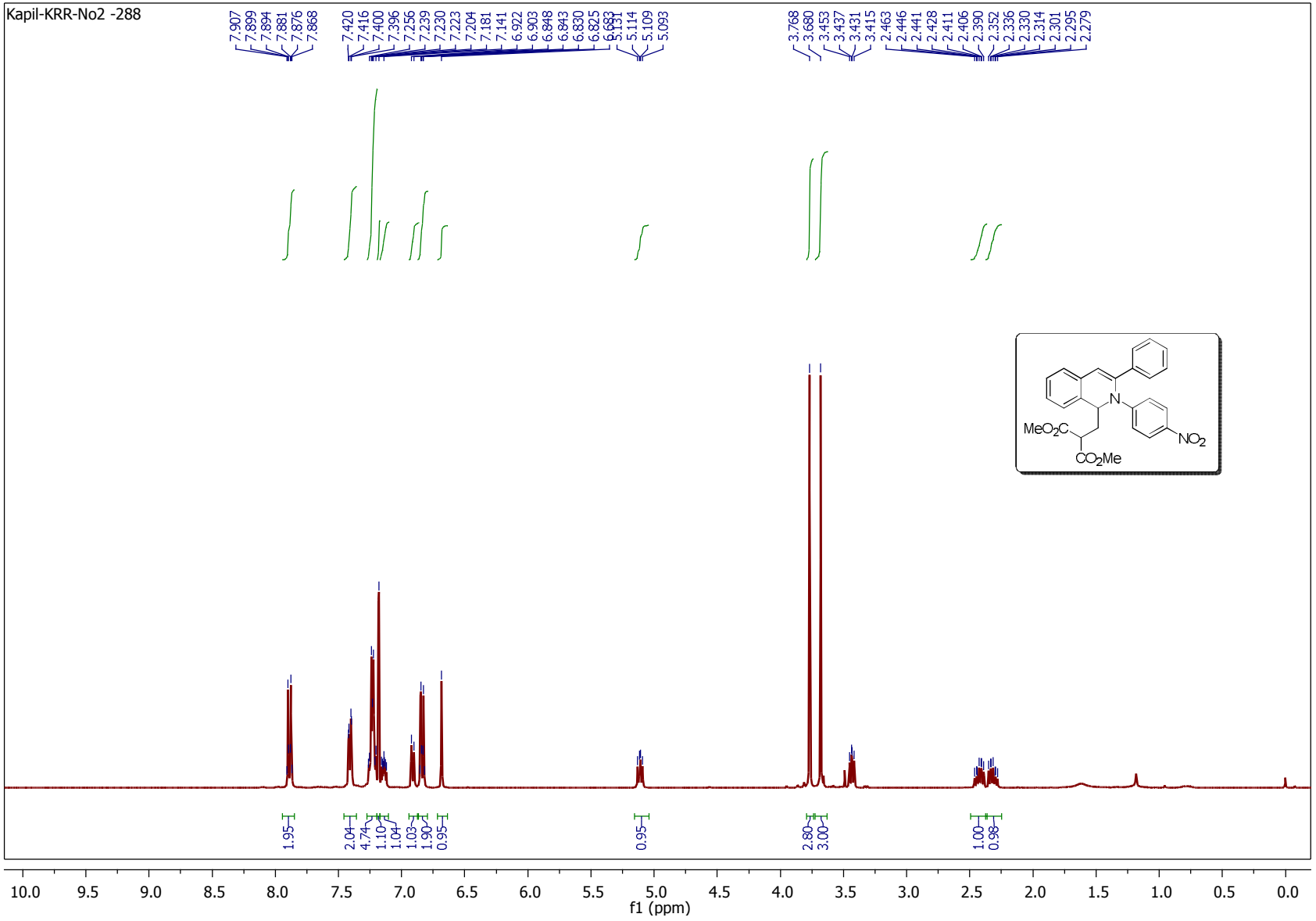
^{13}C NMR & (101 MHz, $CDCl_3$) NMR Spectrum of compound 4l



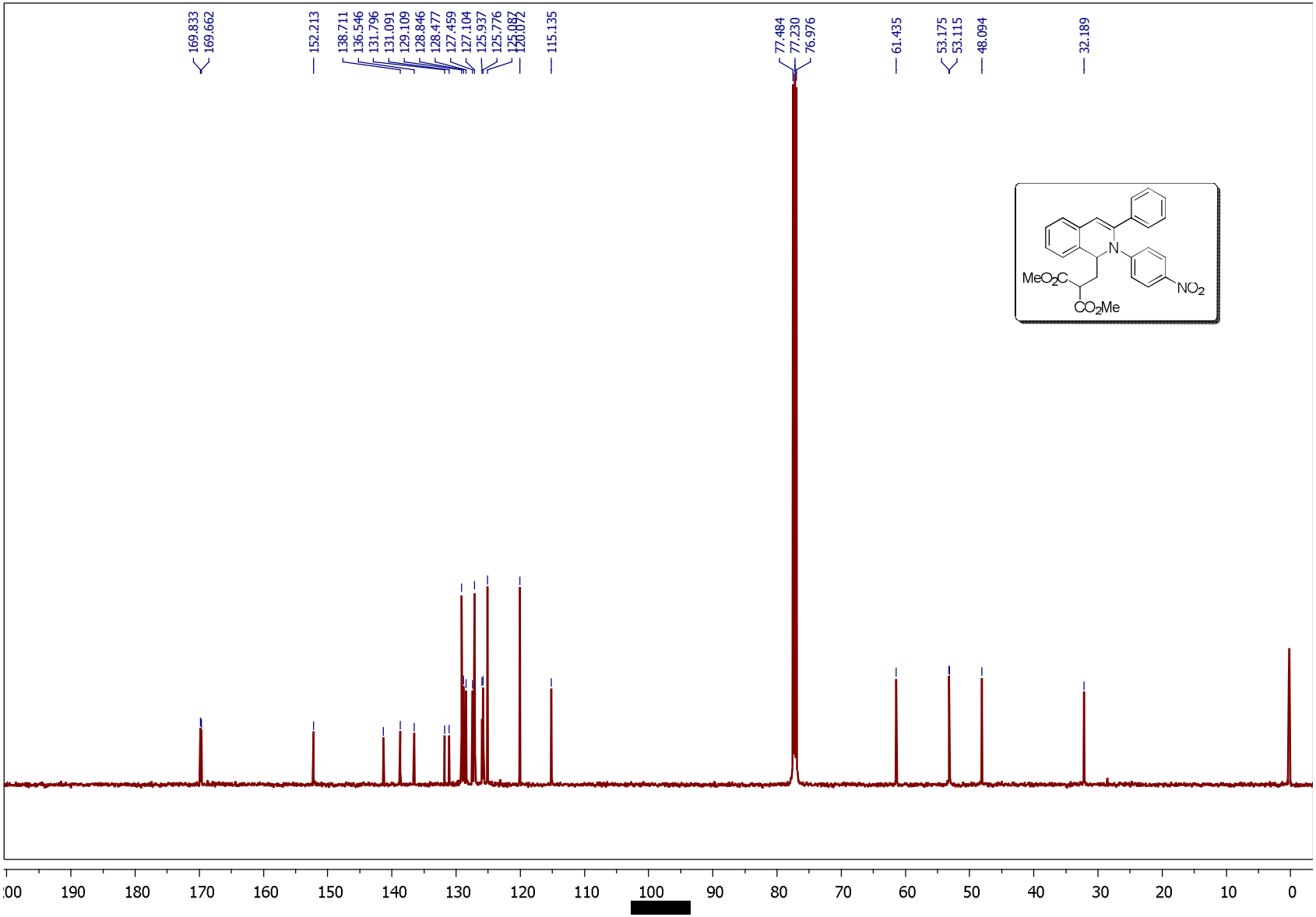
^{19}F NMR (377 MHz, $CDCl_3$) Spectrum of compound 4l



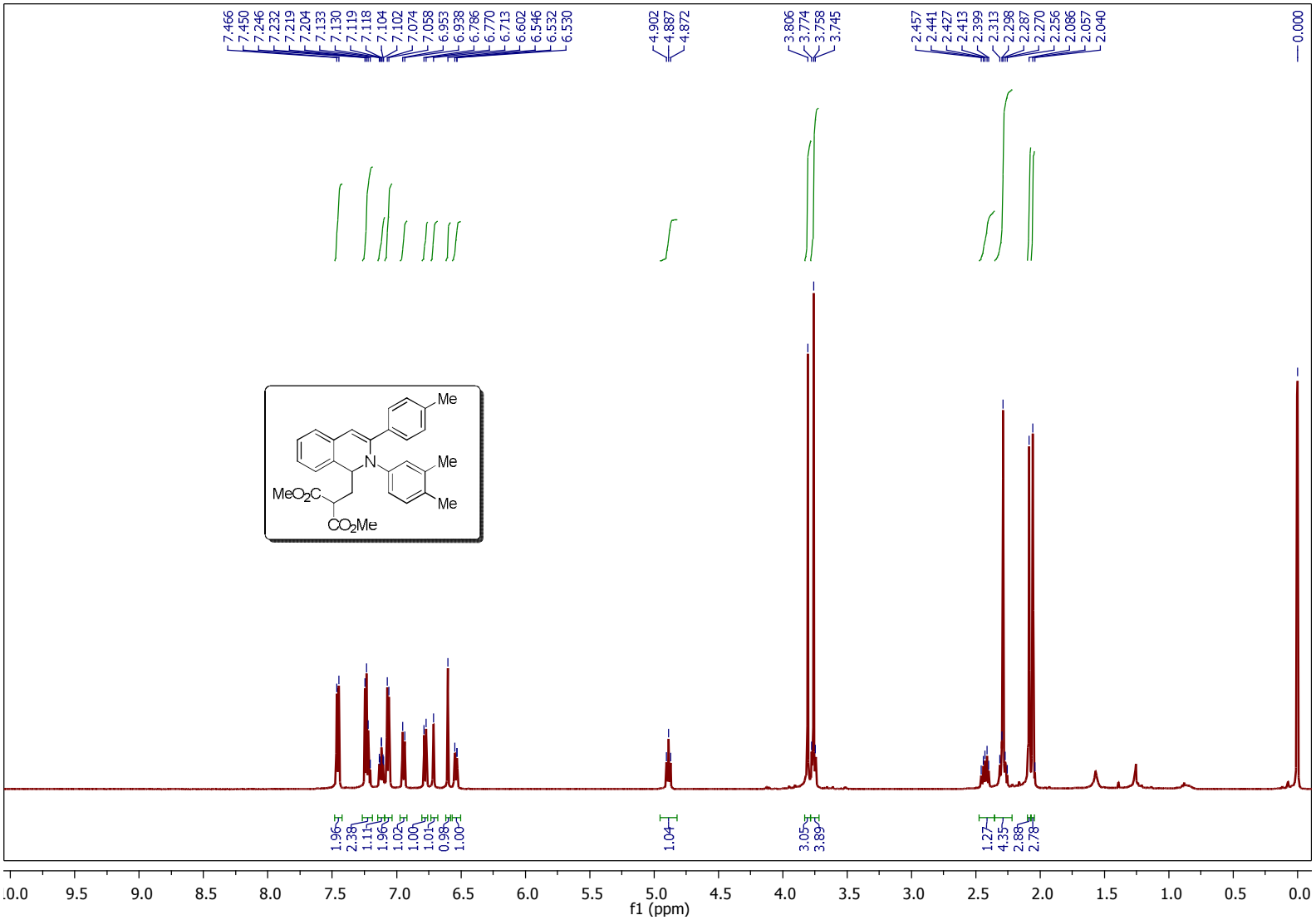
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4m



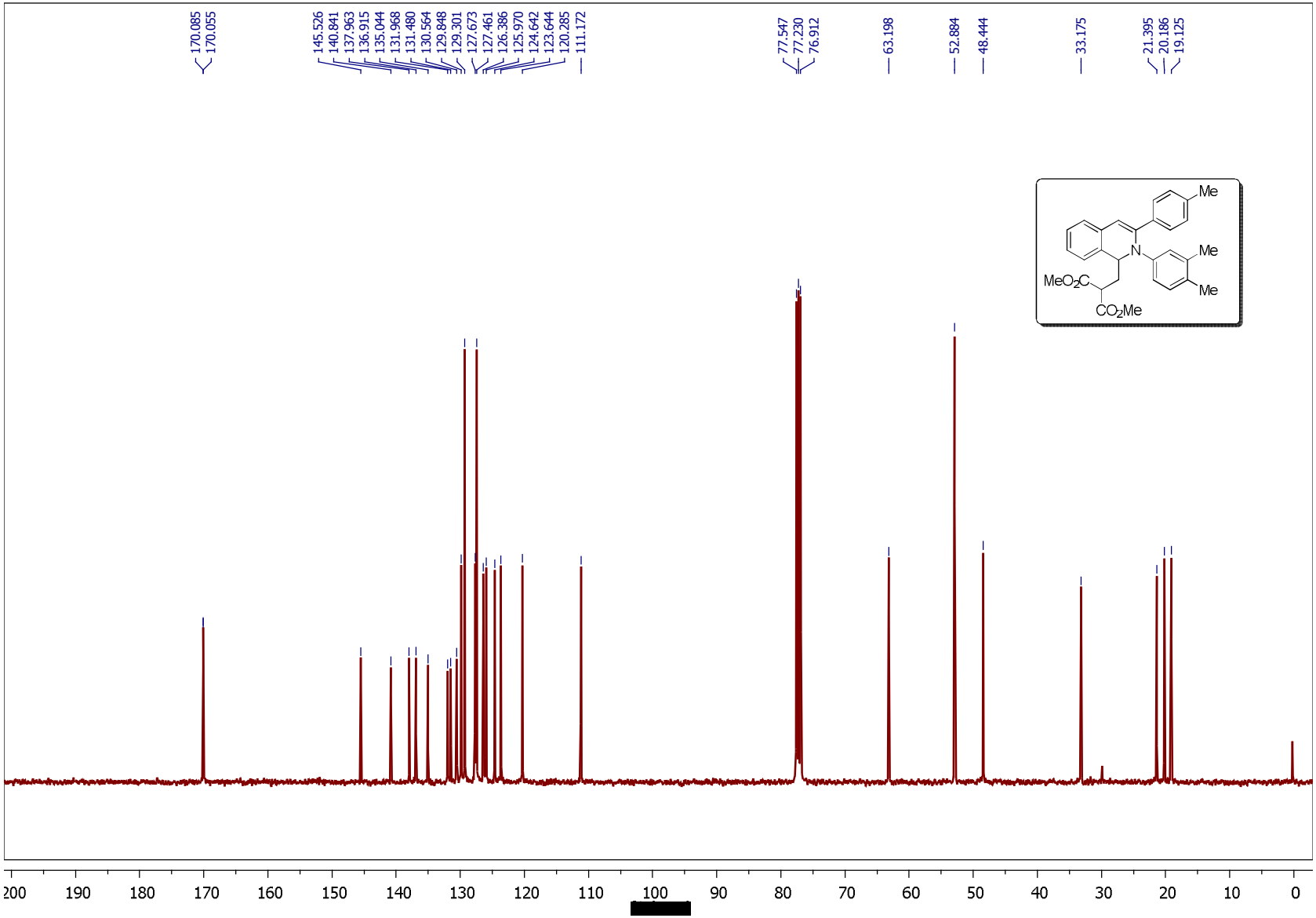
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 4m



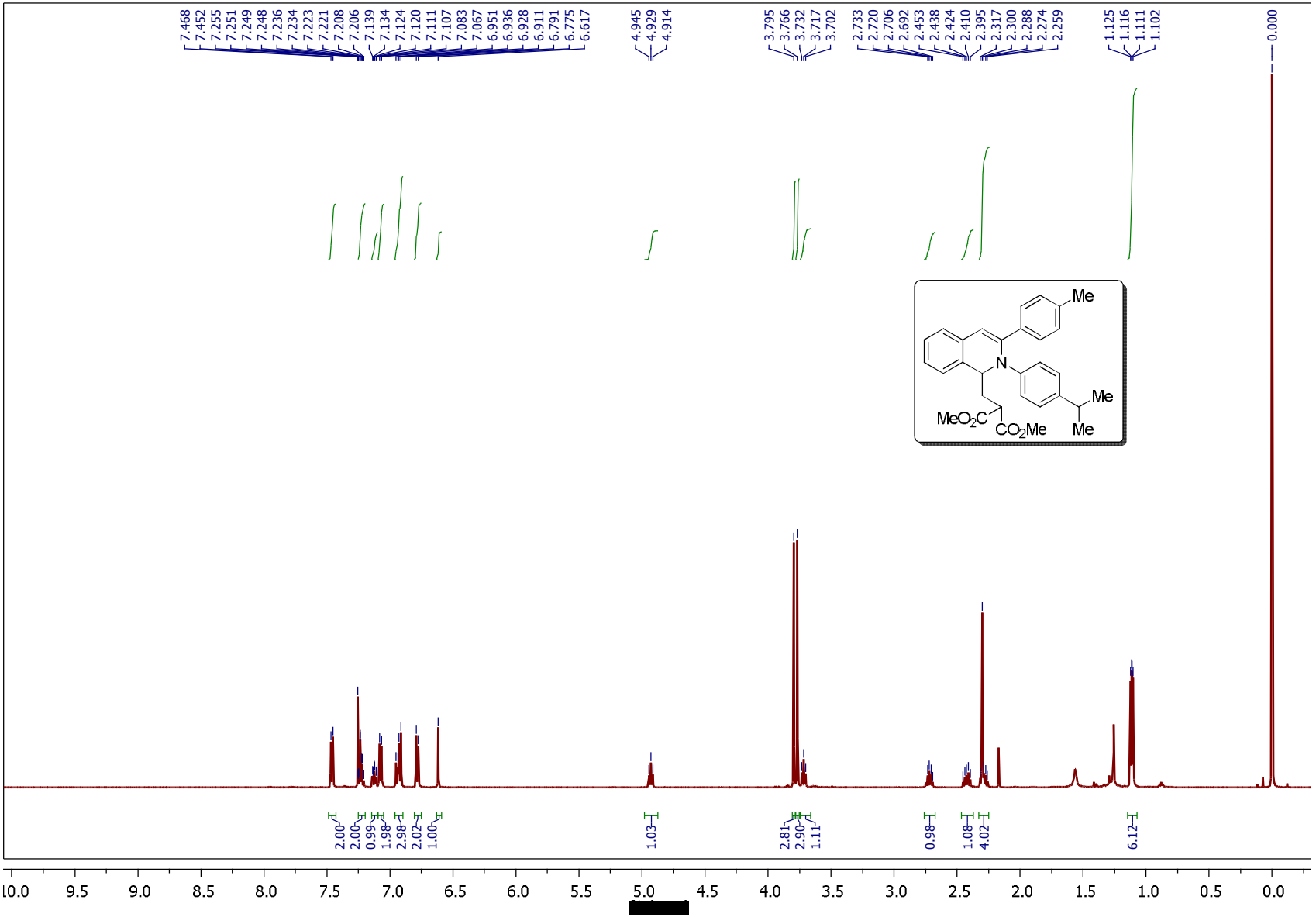
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4p



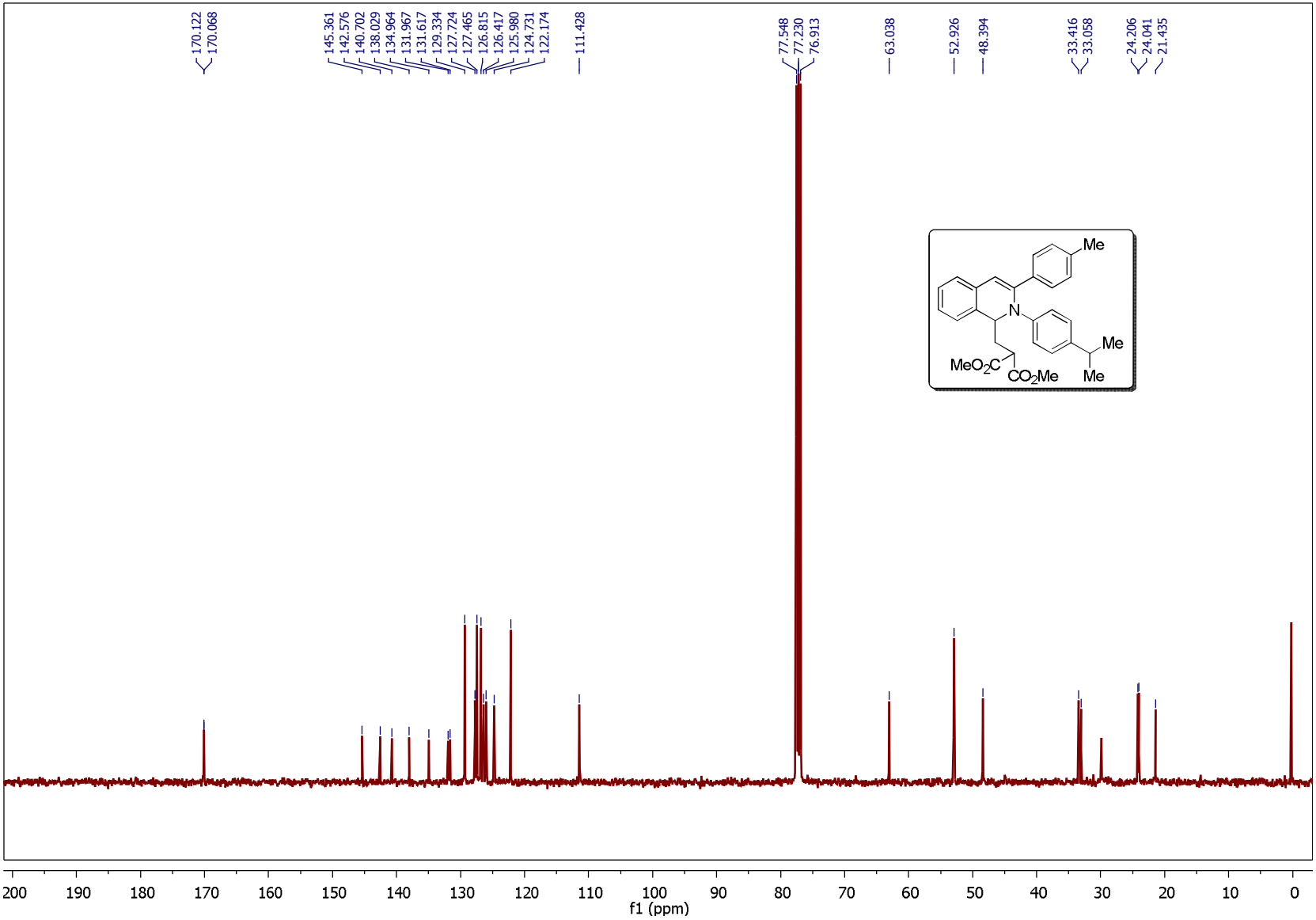
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4p



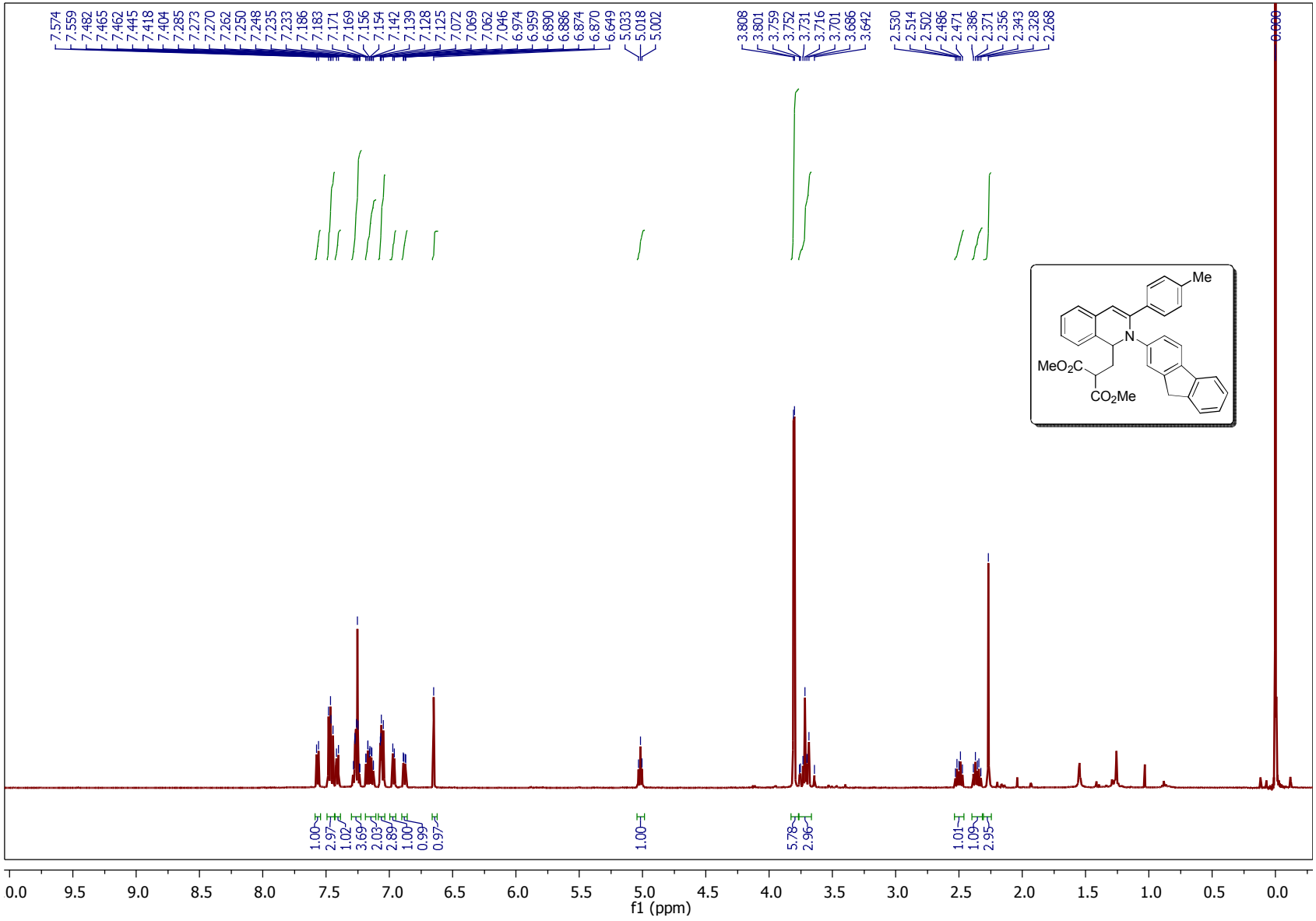
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4q



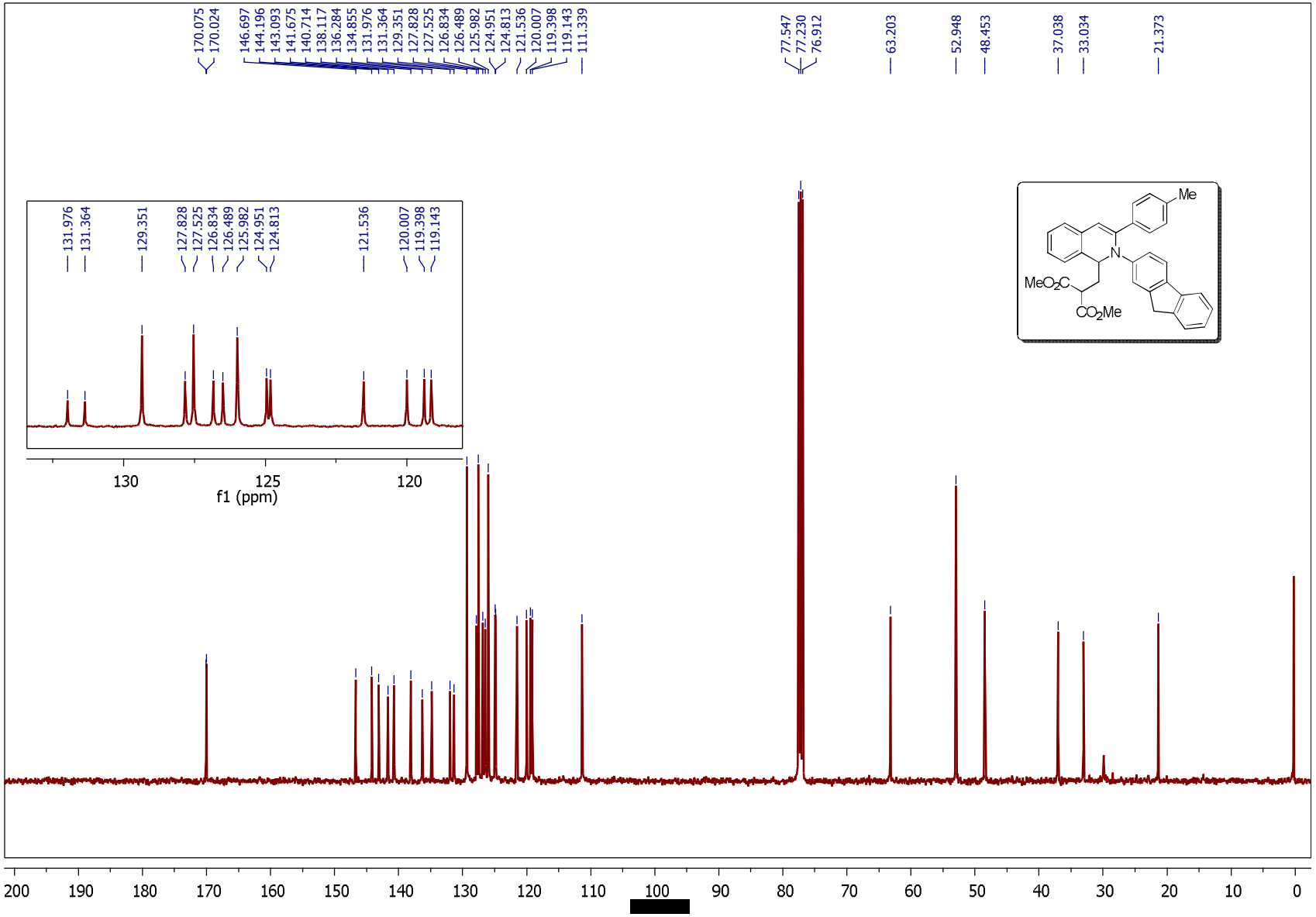
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4q



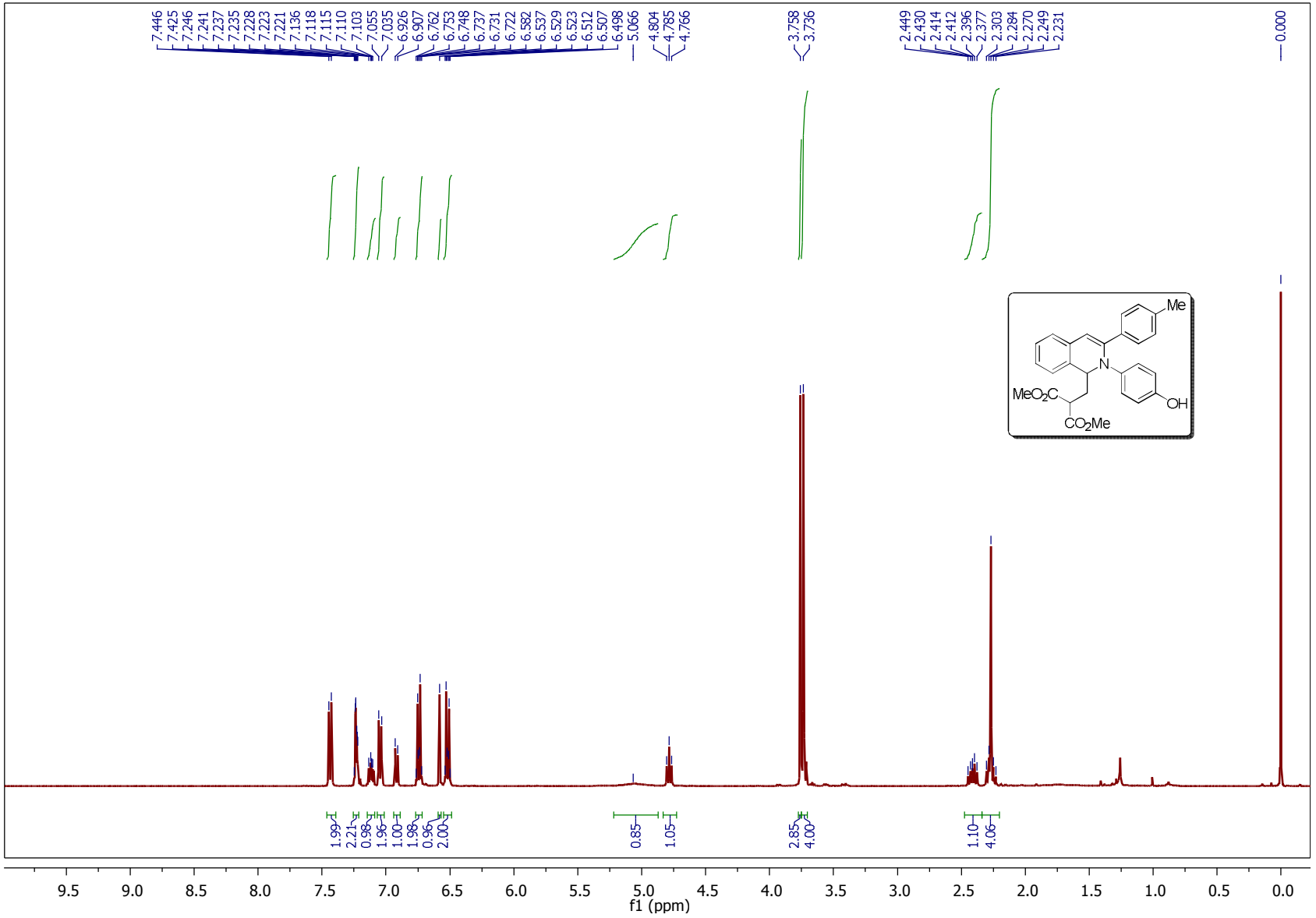
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4r



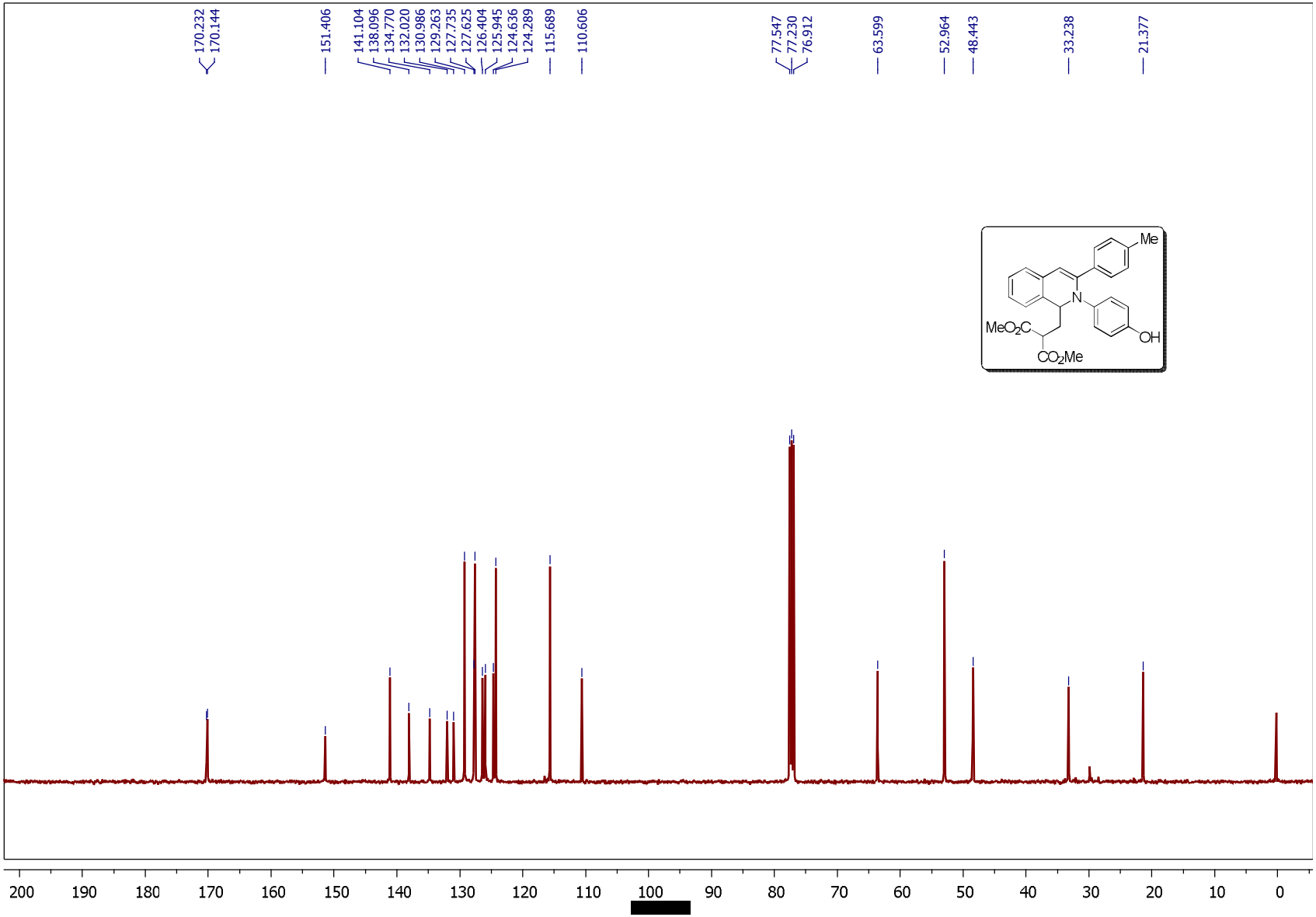
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4r



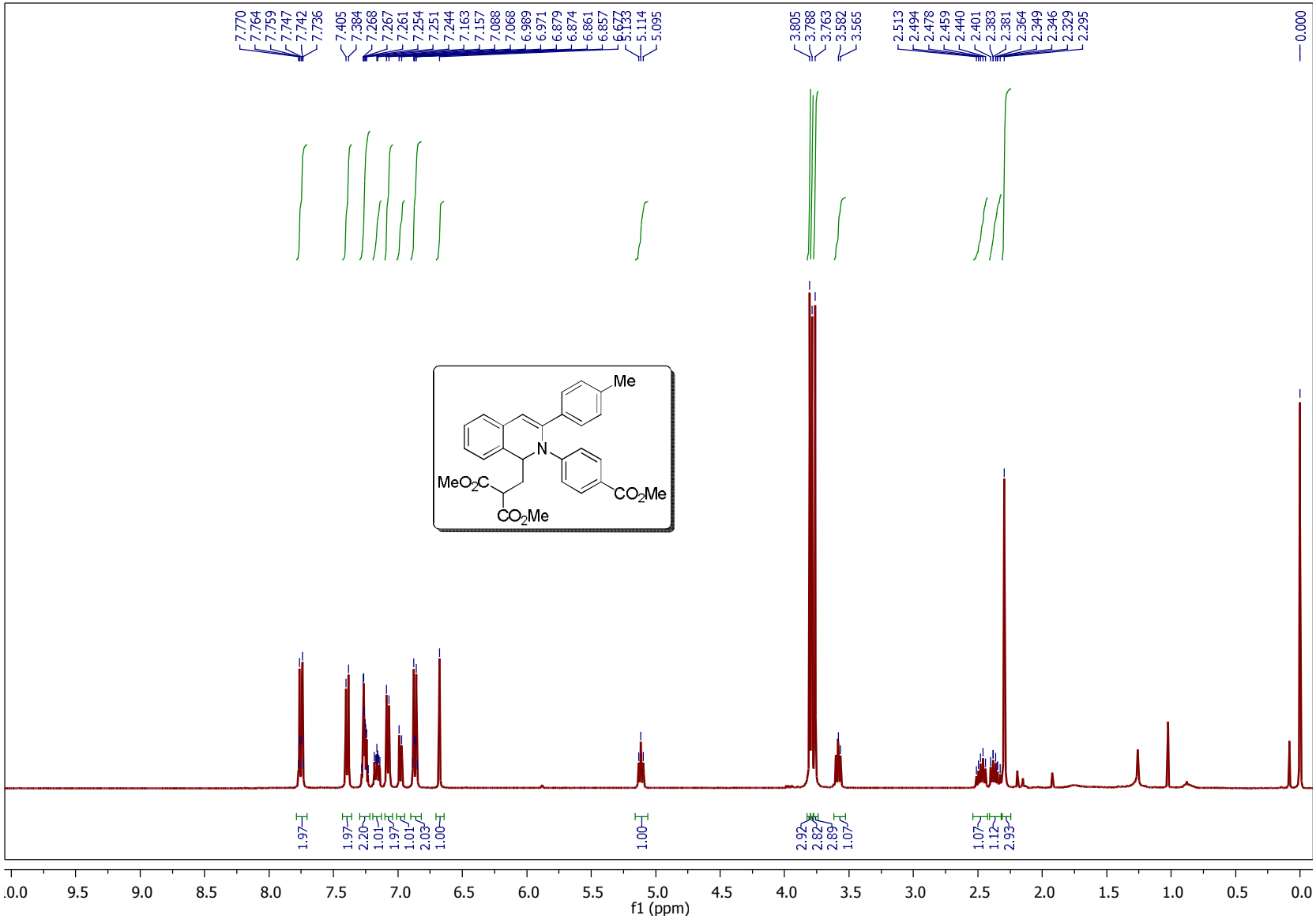
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4s



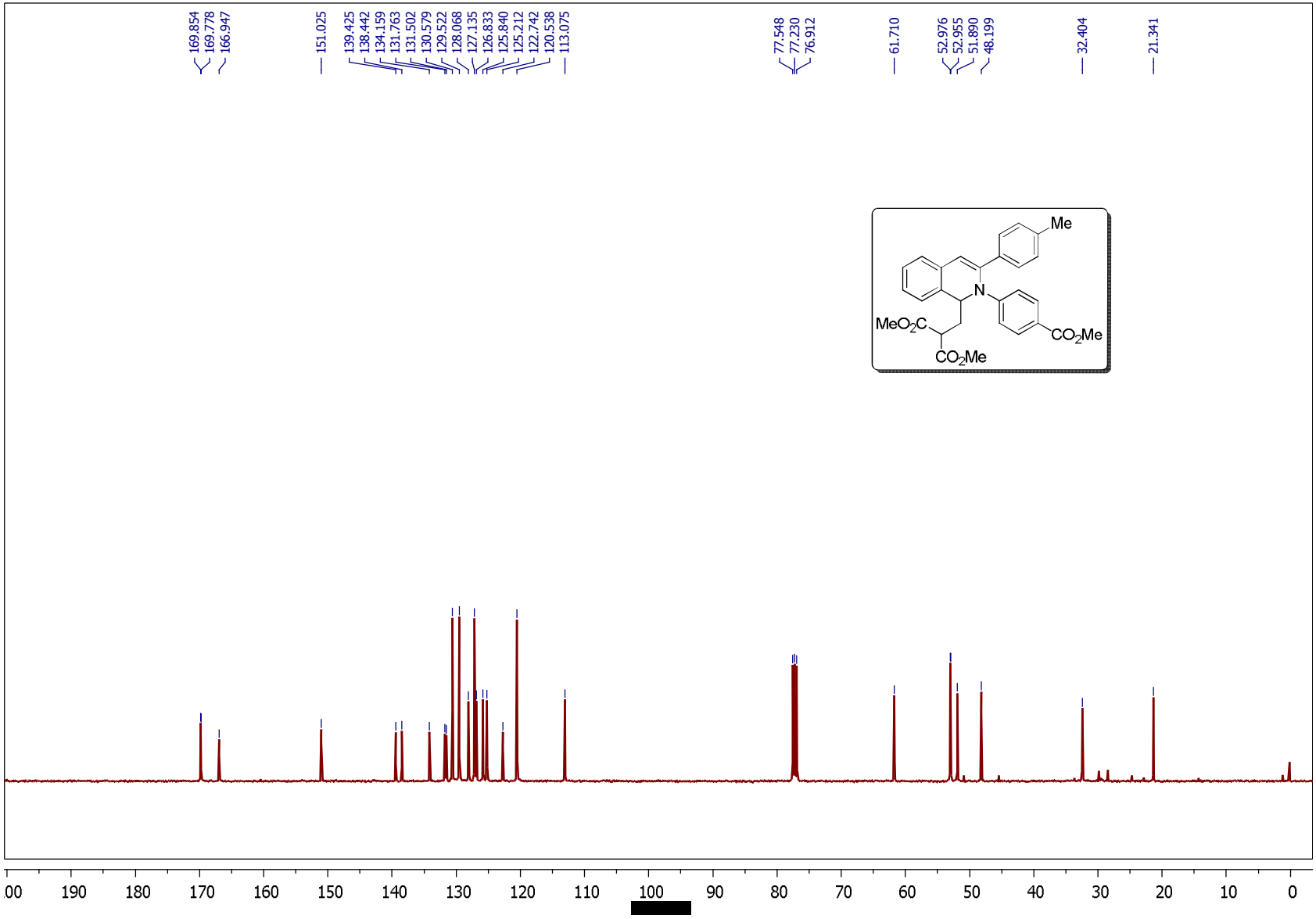
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4s



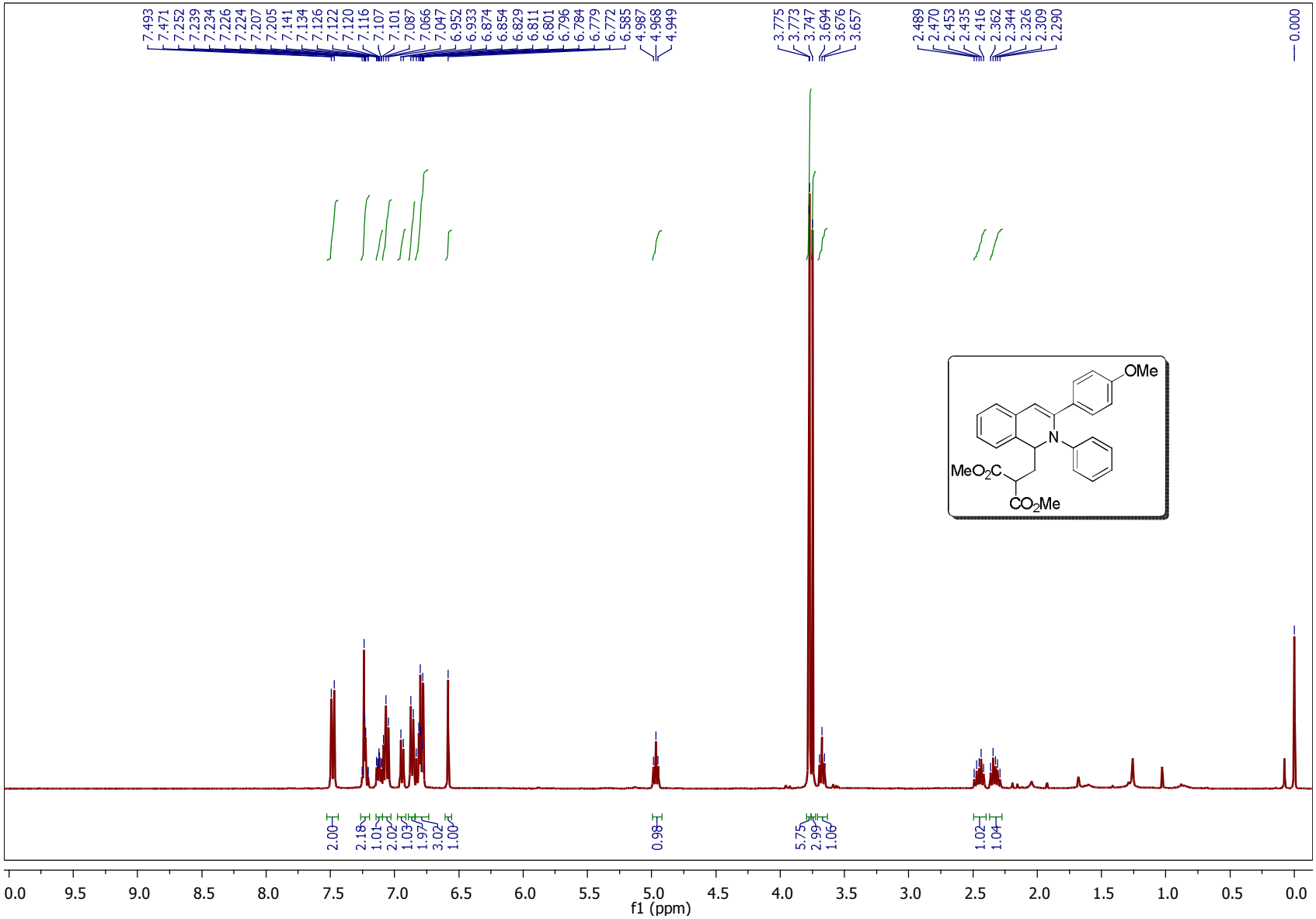
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4t



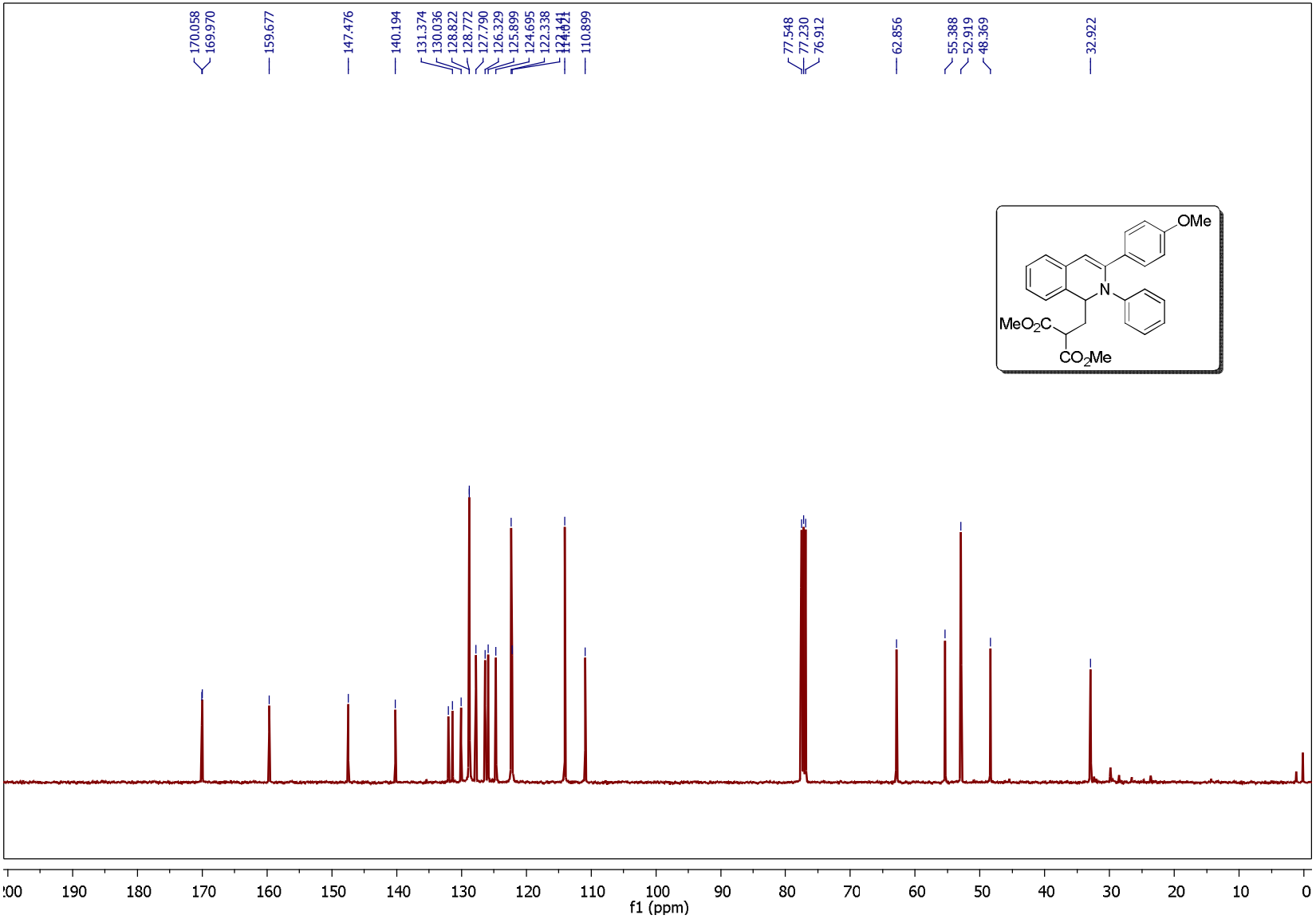
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4t



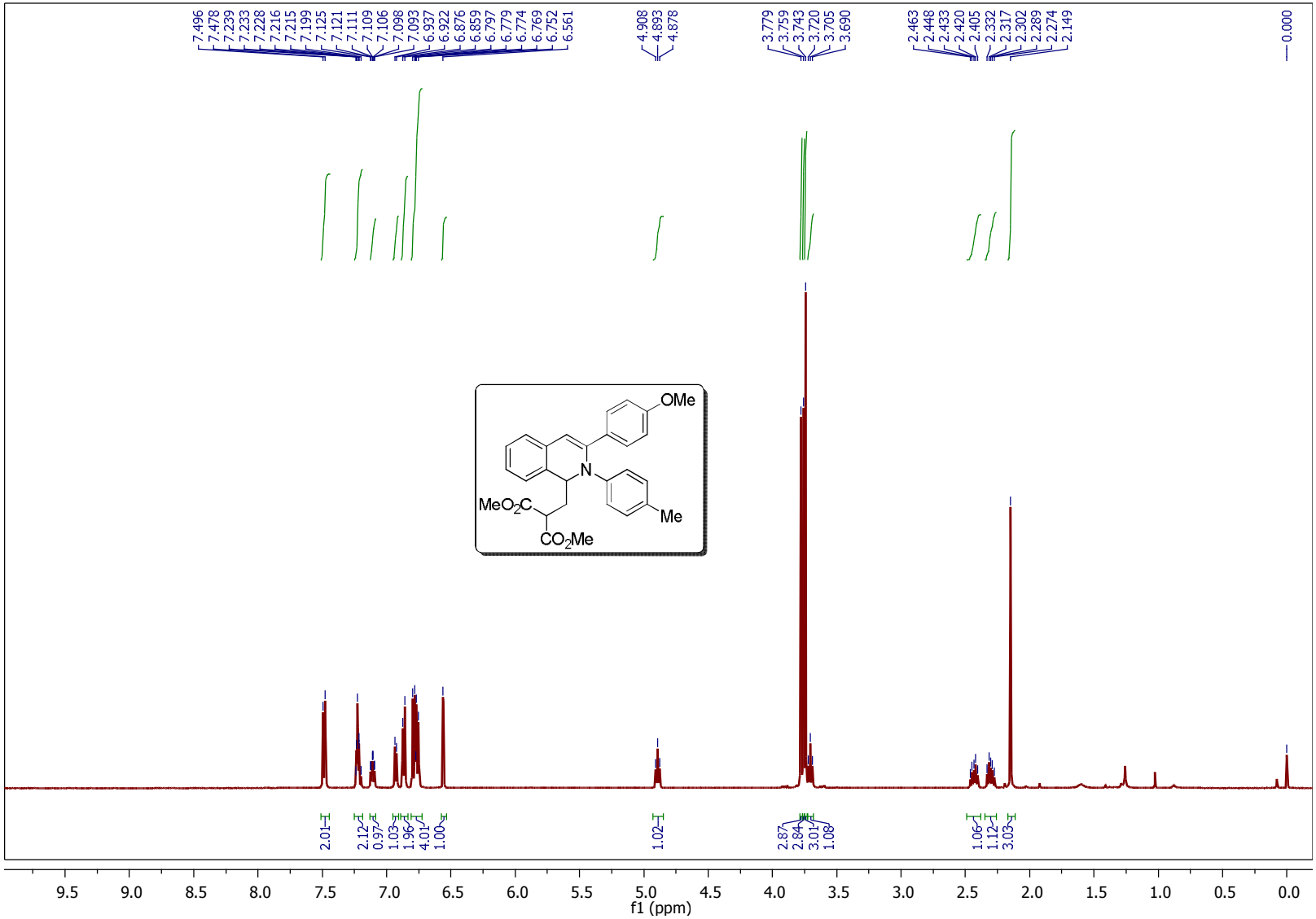
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4u



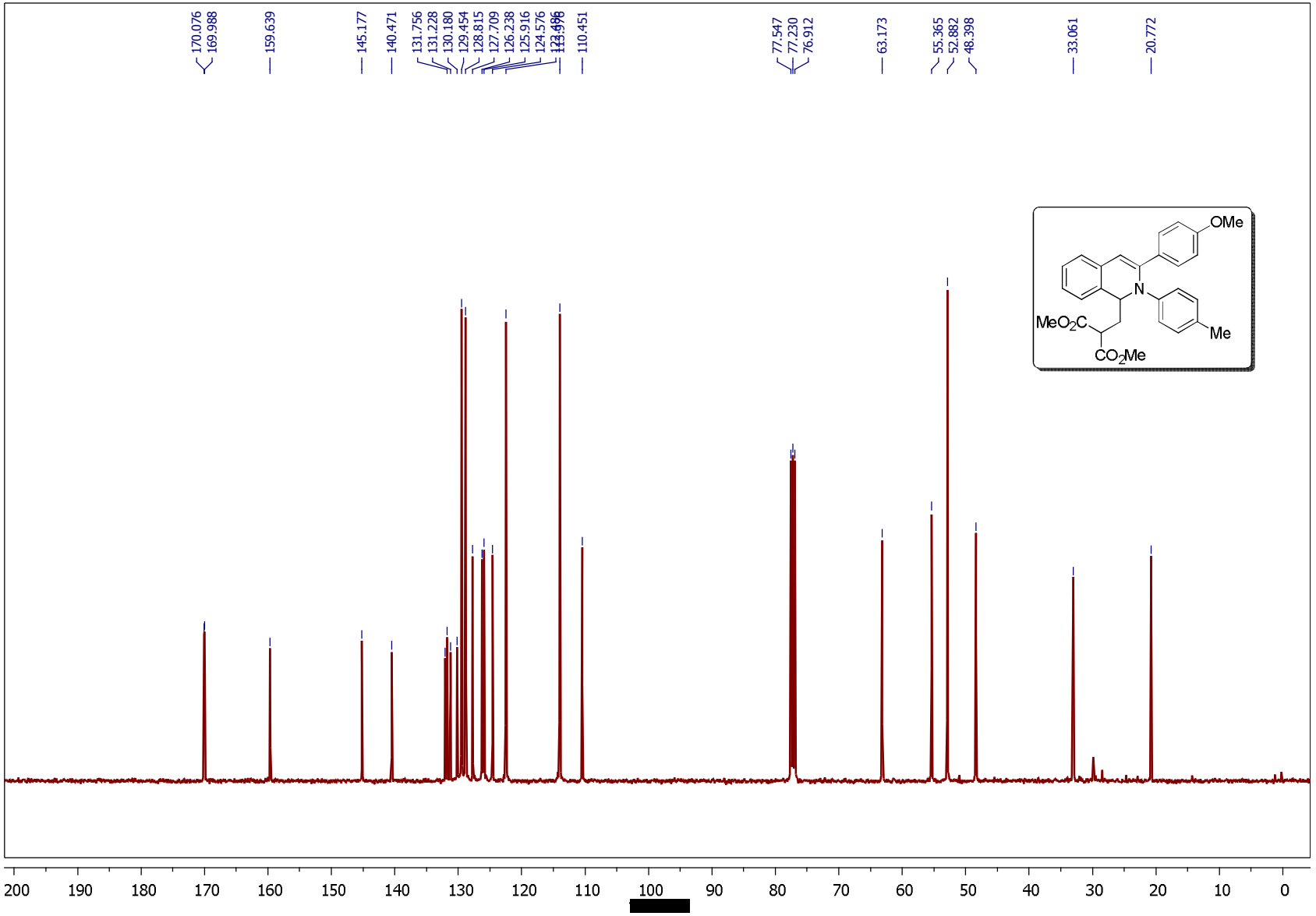
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4u



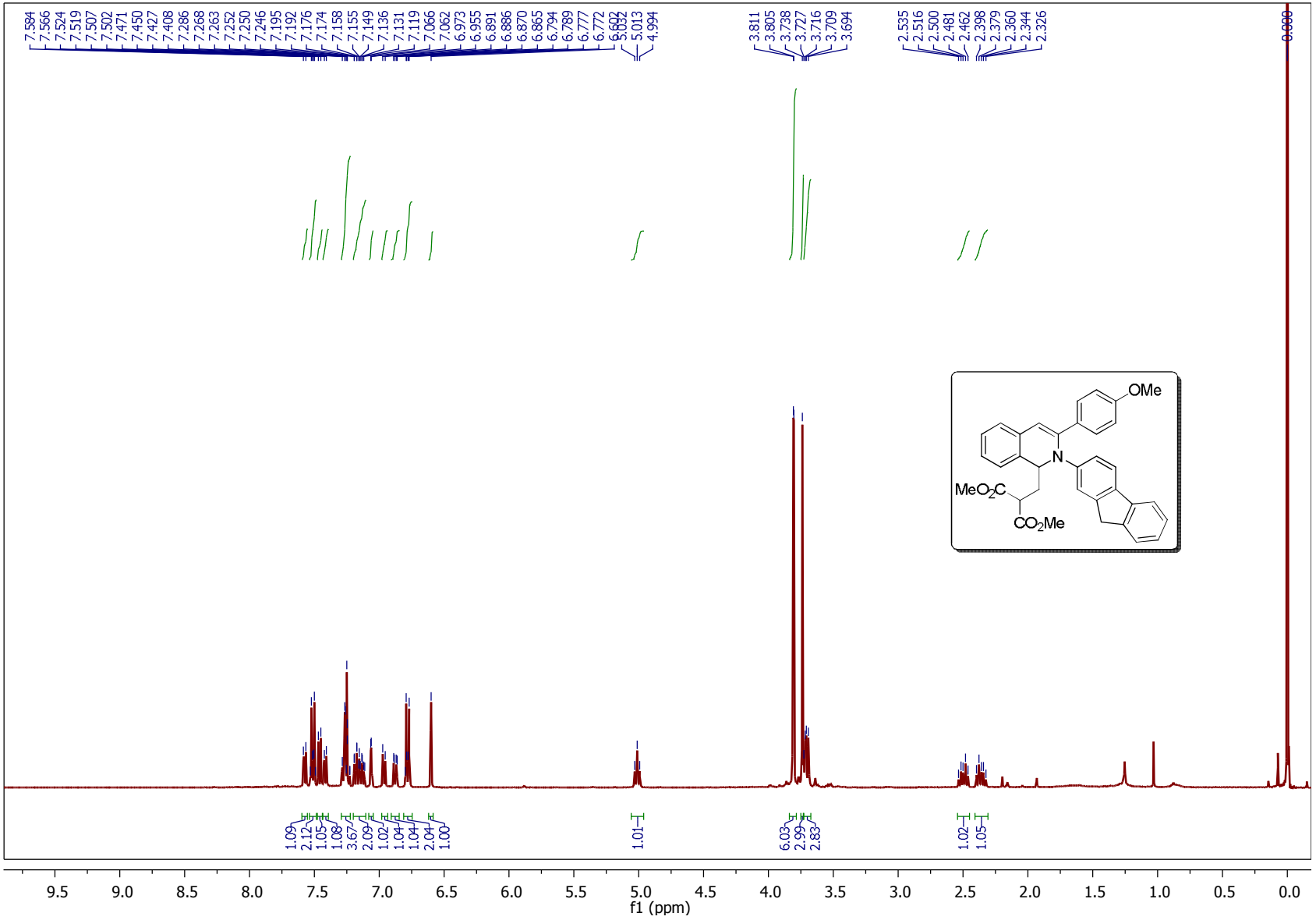
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4v



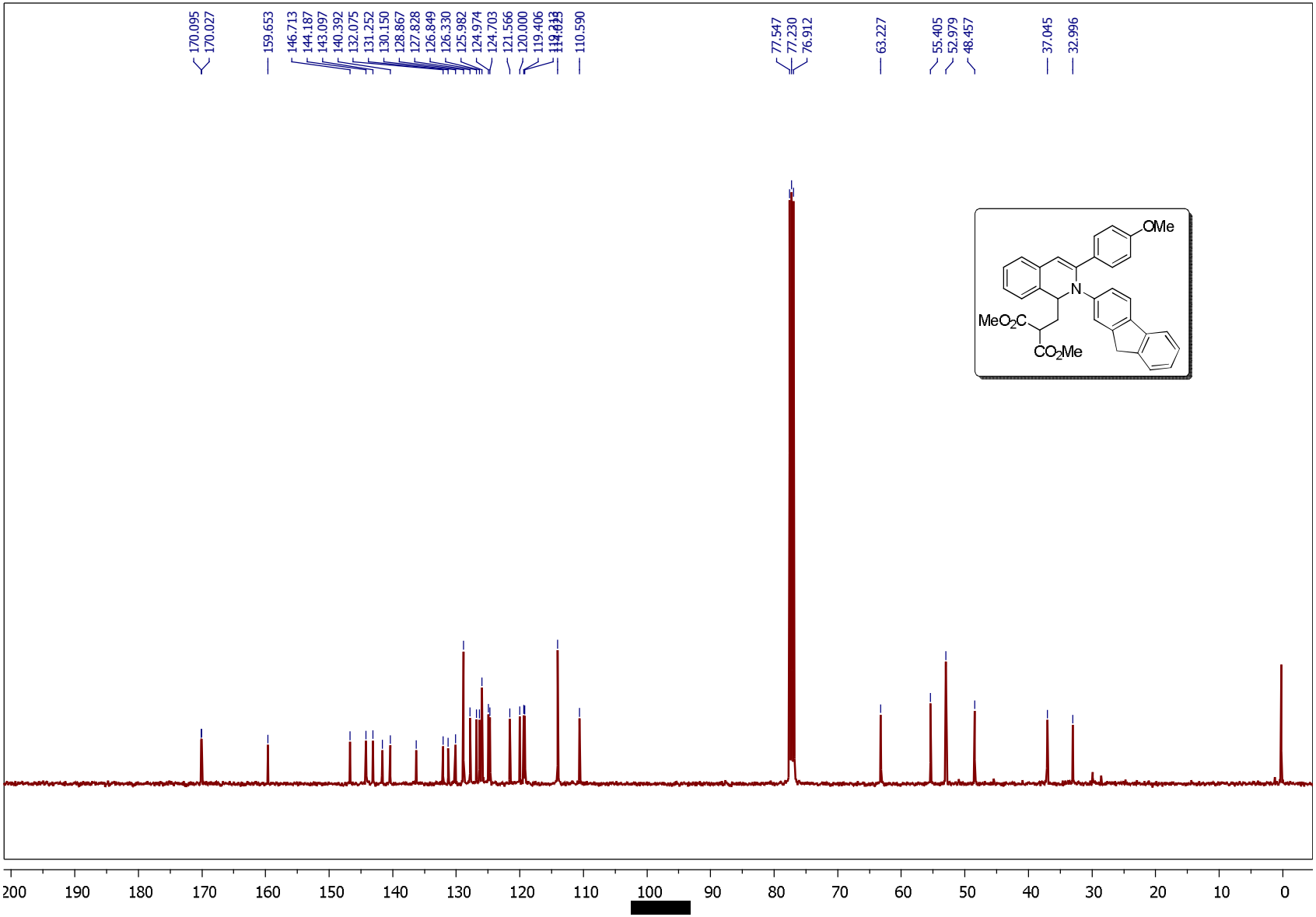
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4v



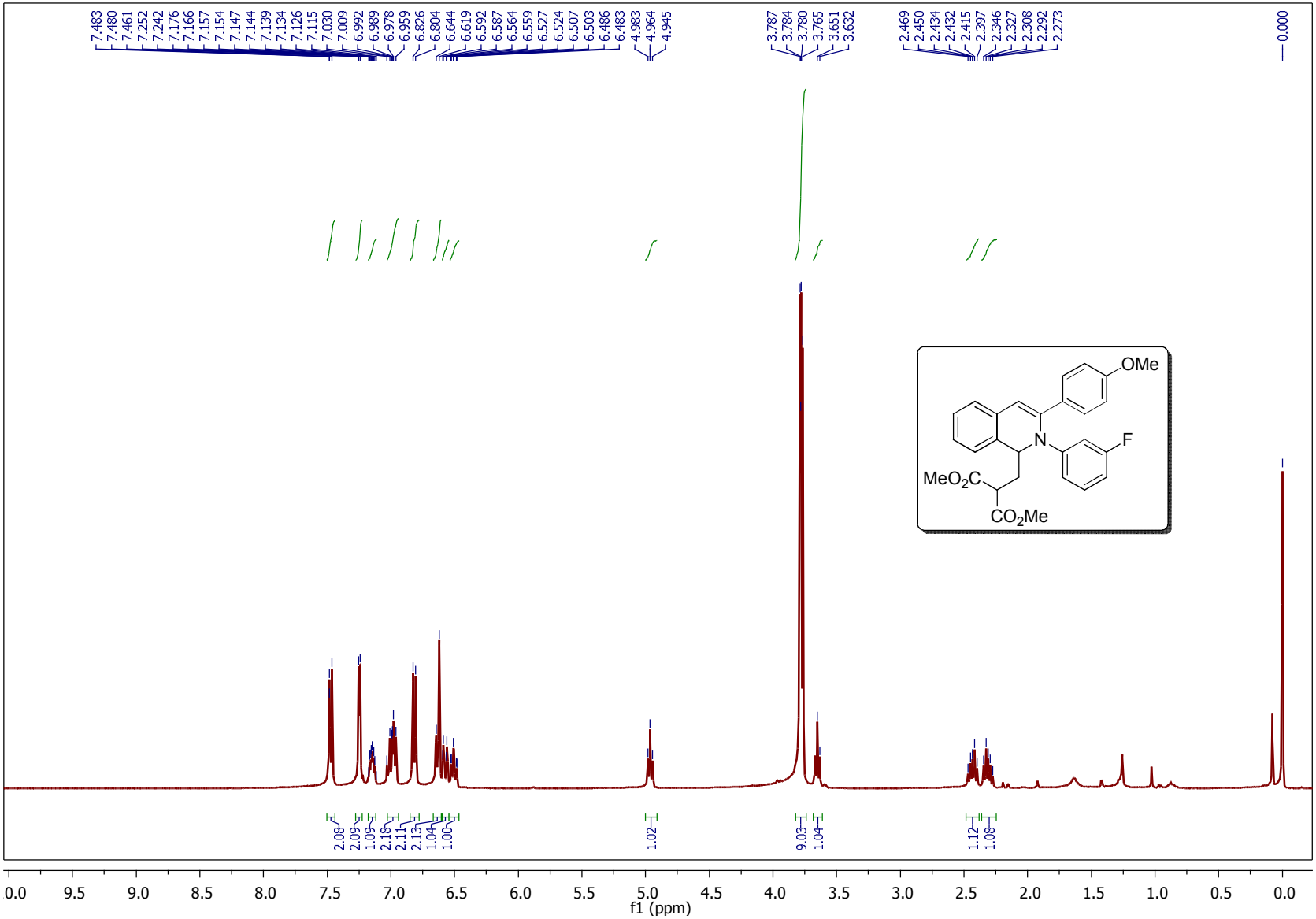
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4w



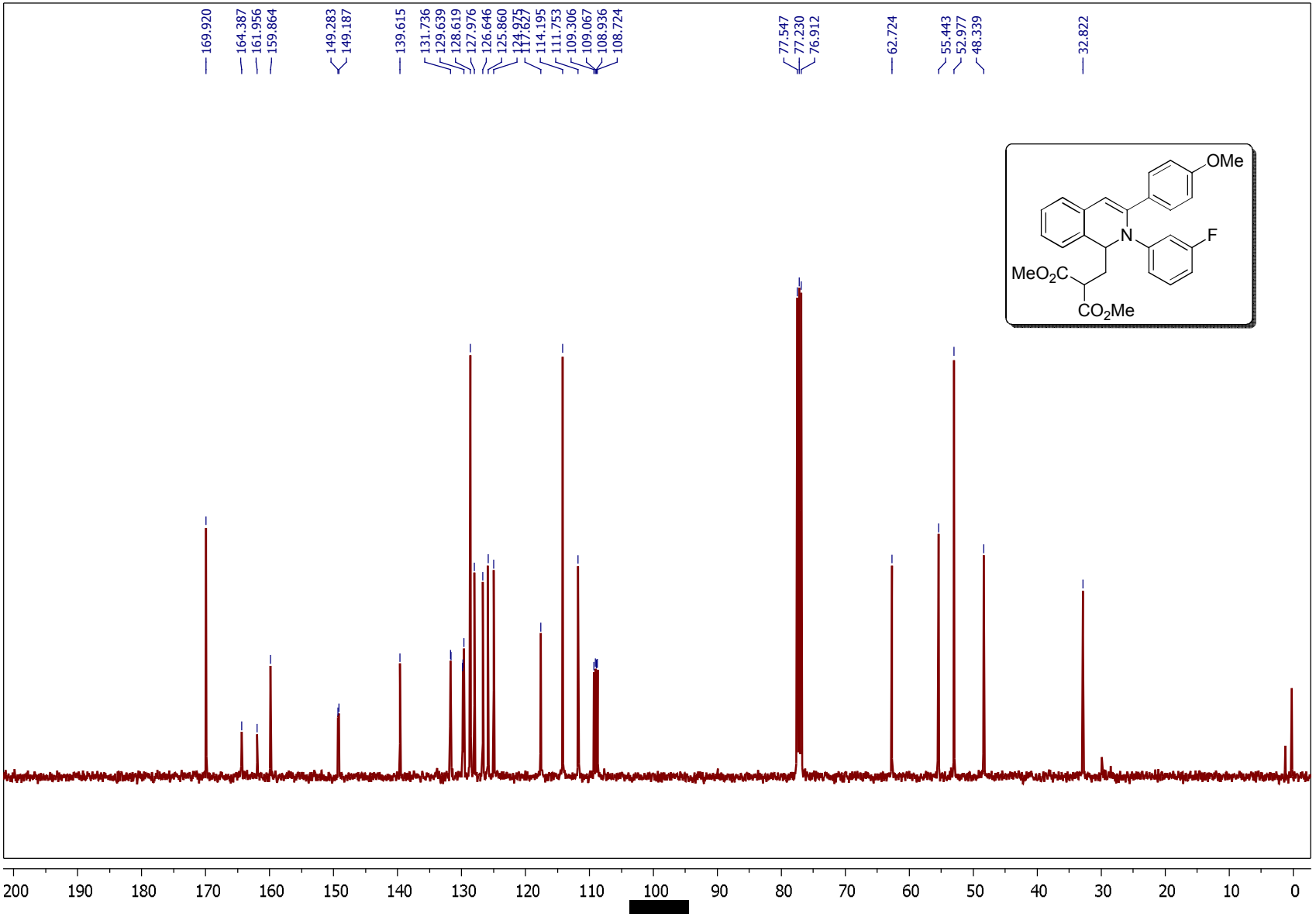
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4w



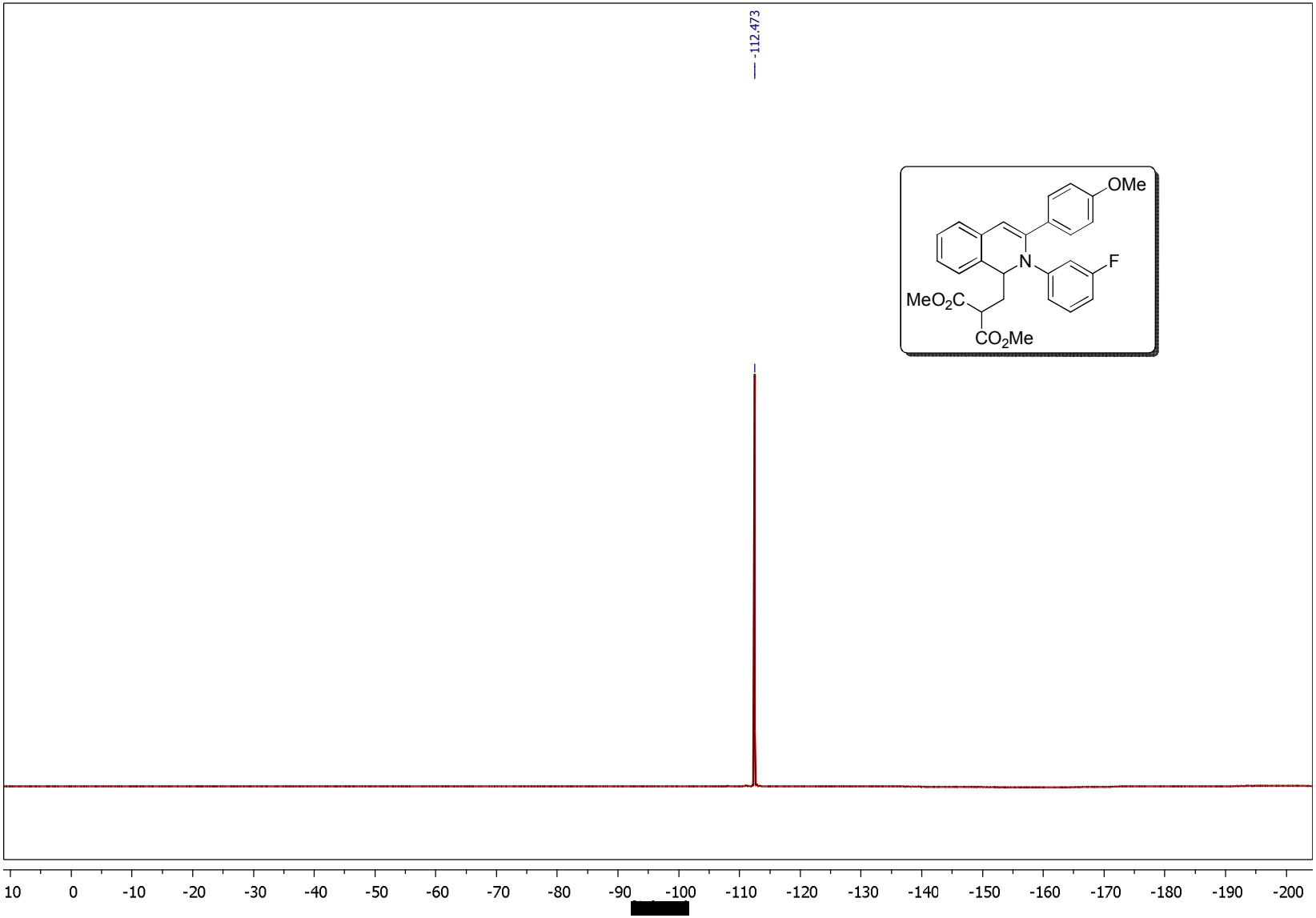
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4x



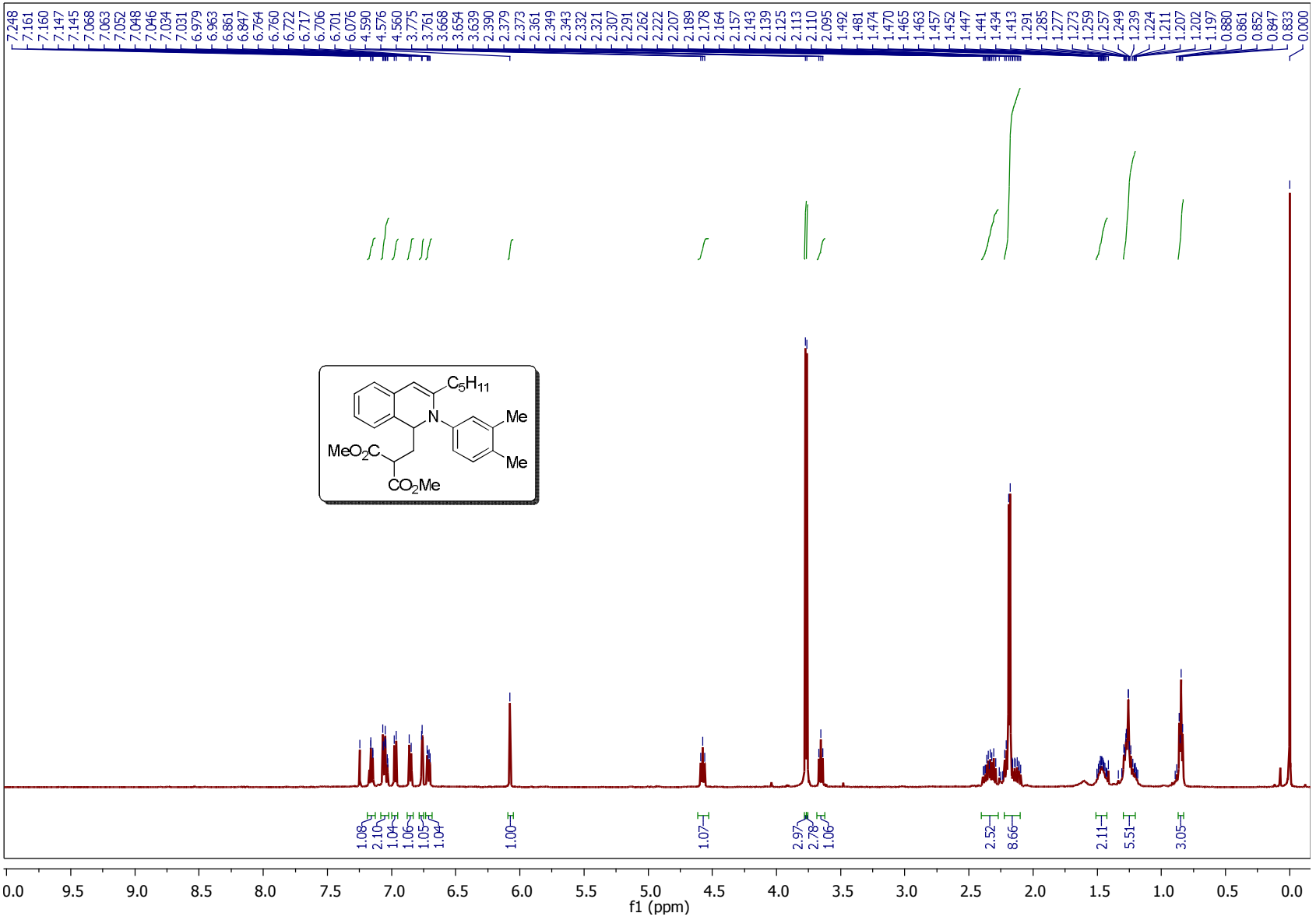
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4x



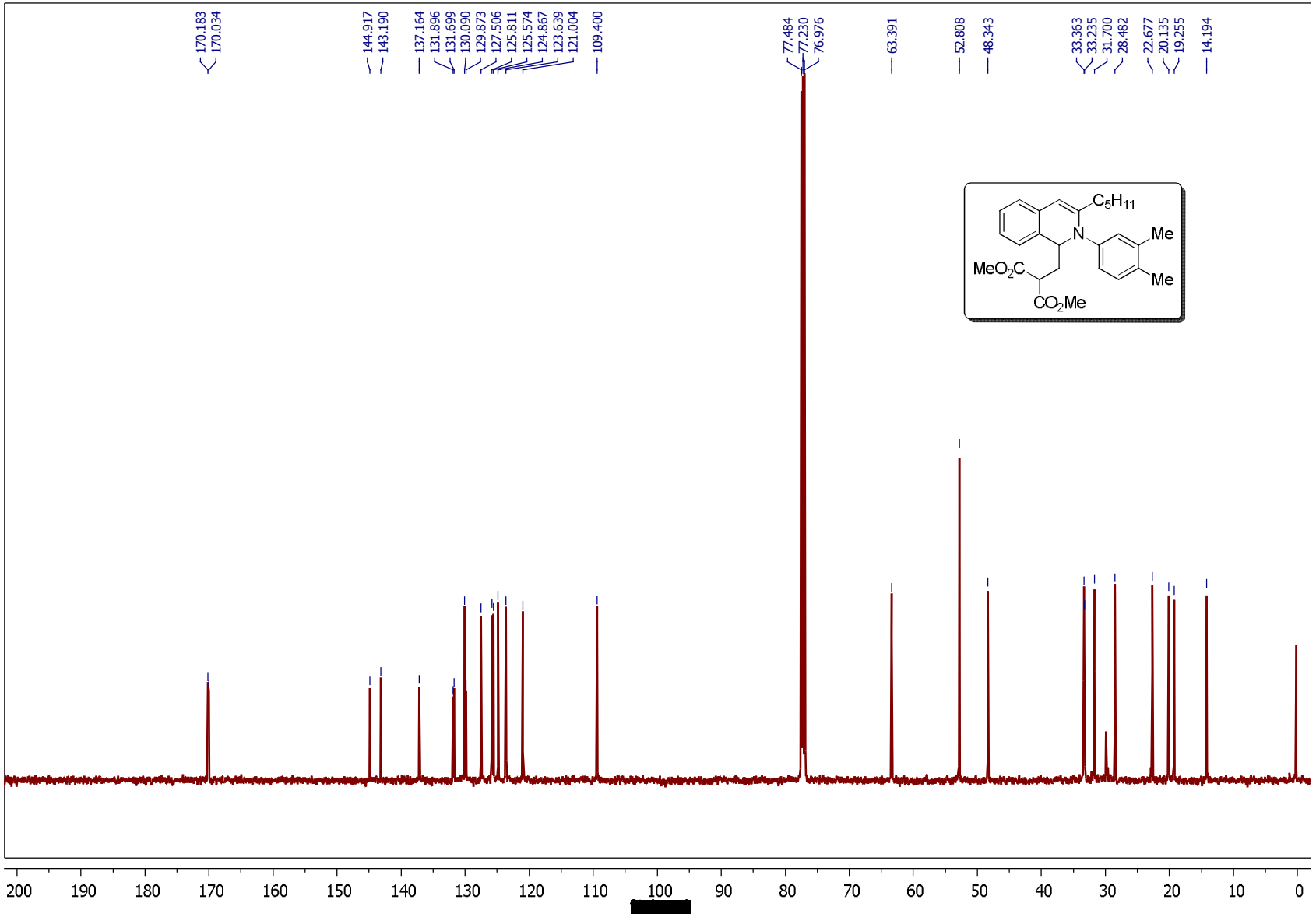
^{19}F NMR (377 MHz, $CDCl_3$) Spectrum of compound 4x



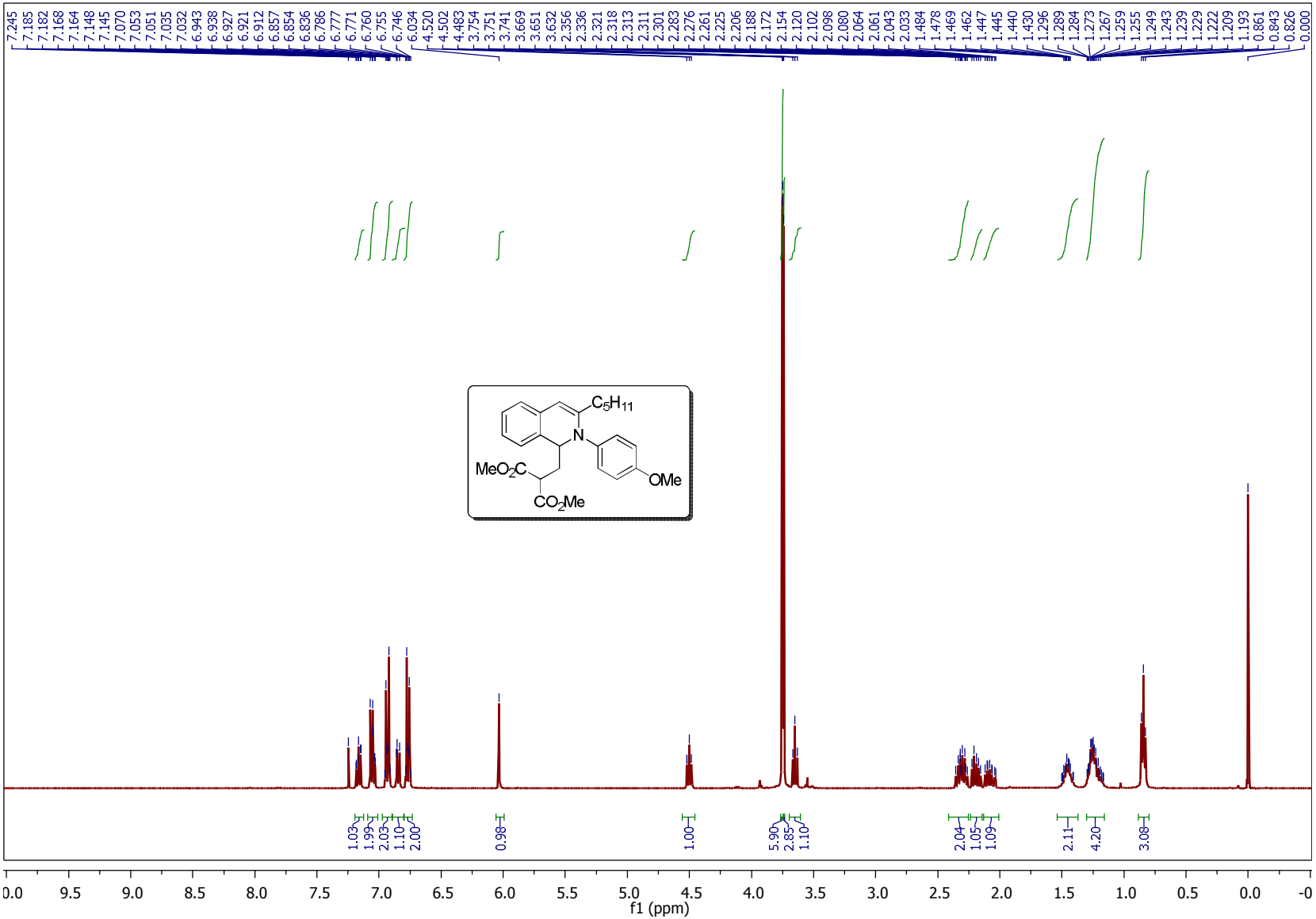
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4y



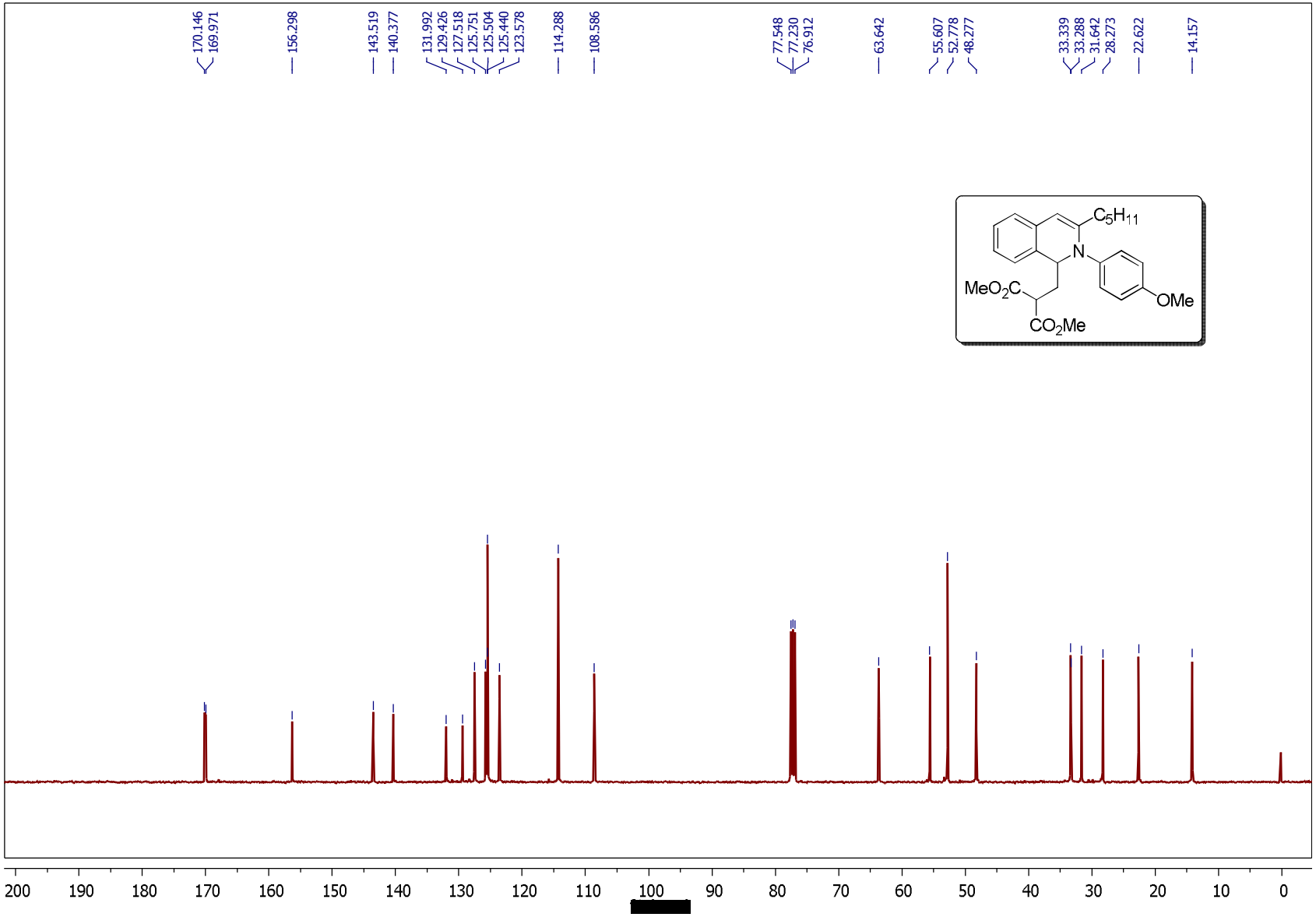
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 4y



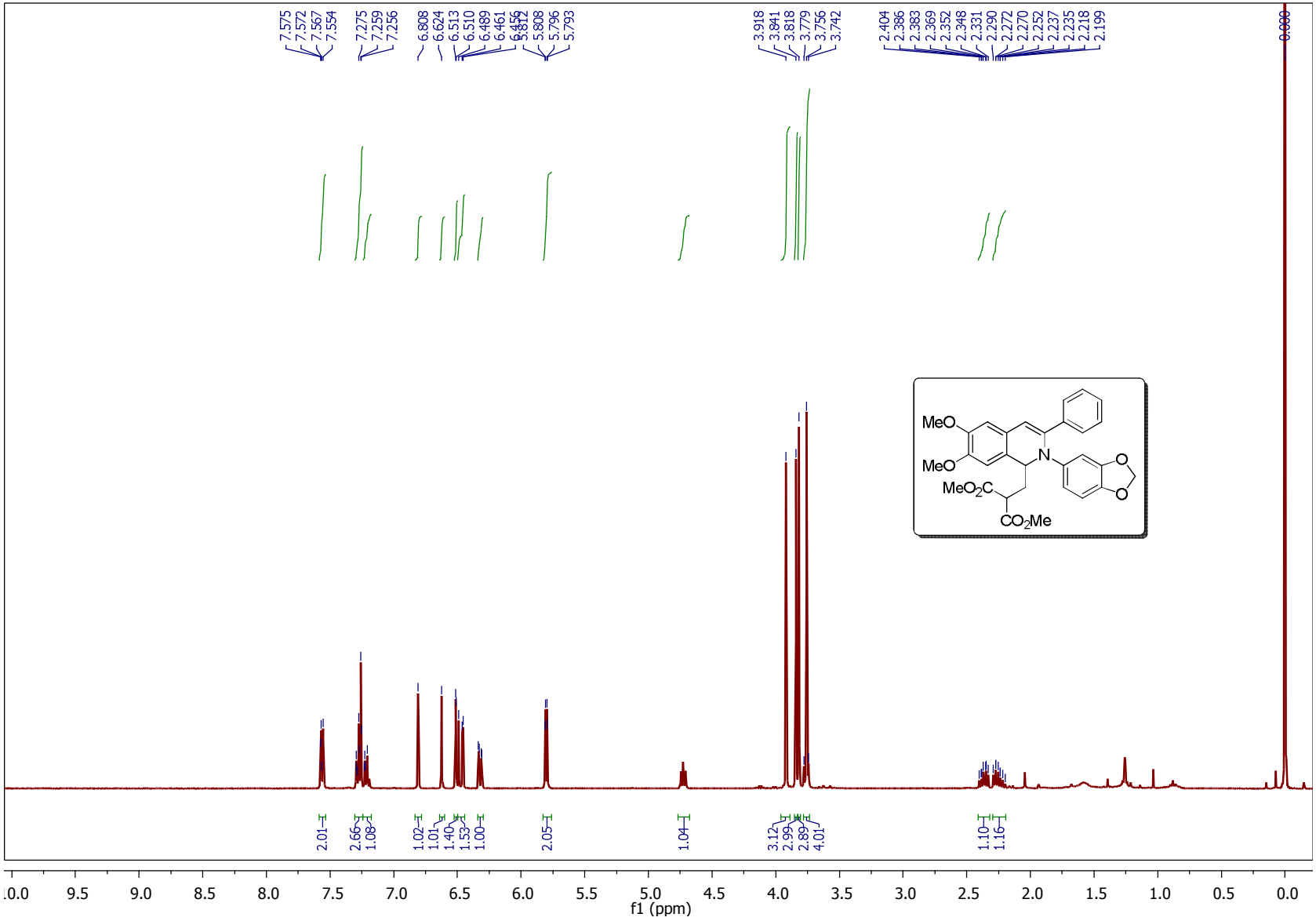
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4z



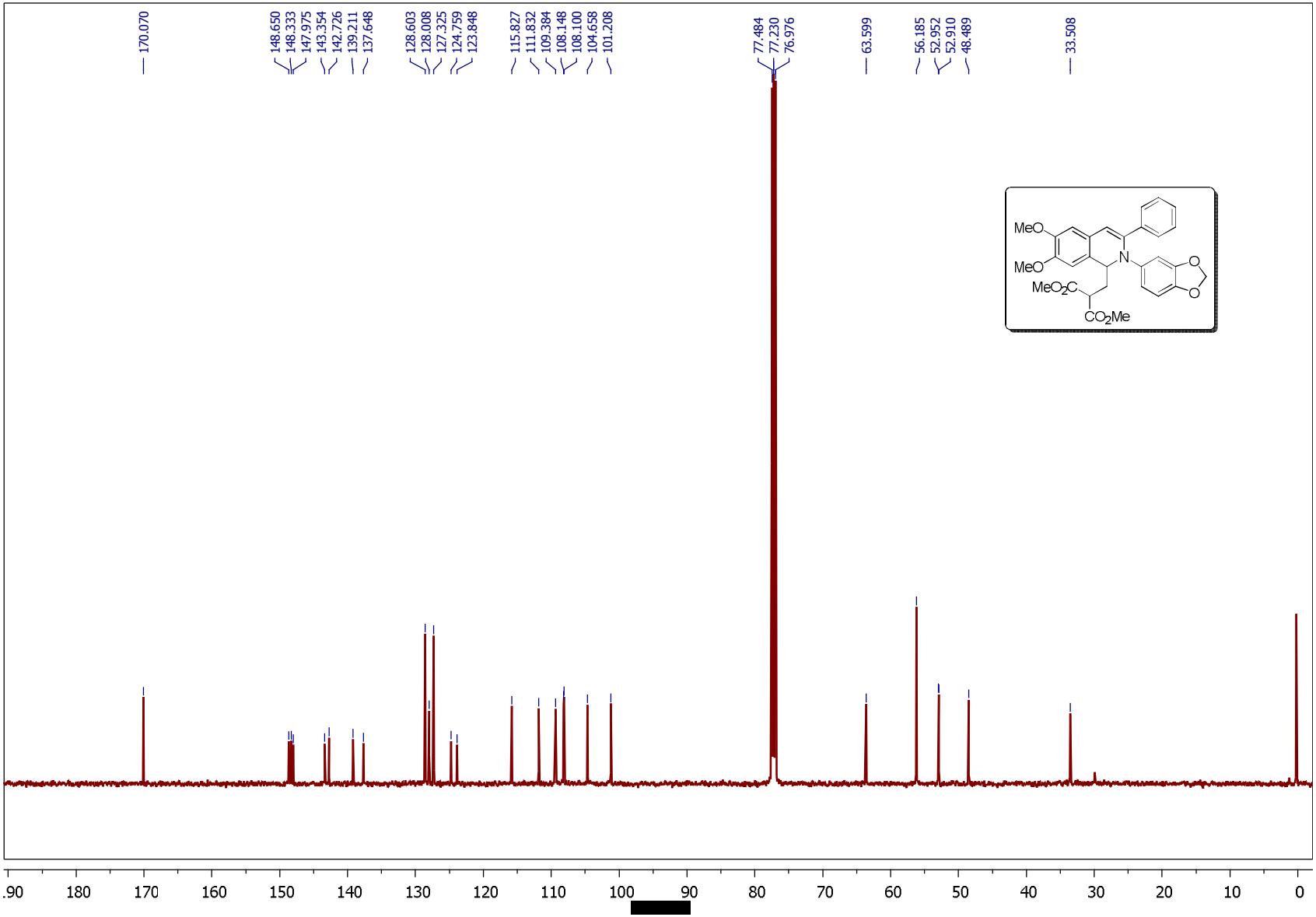
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4z



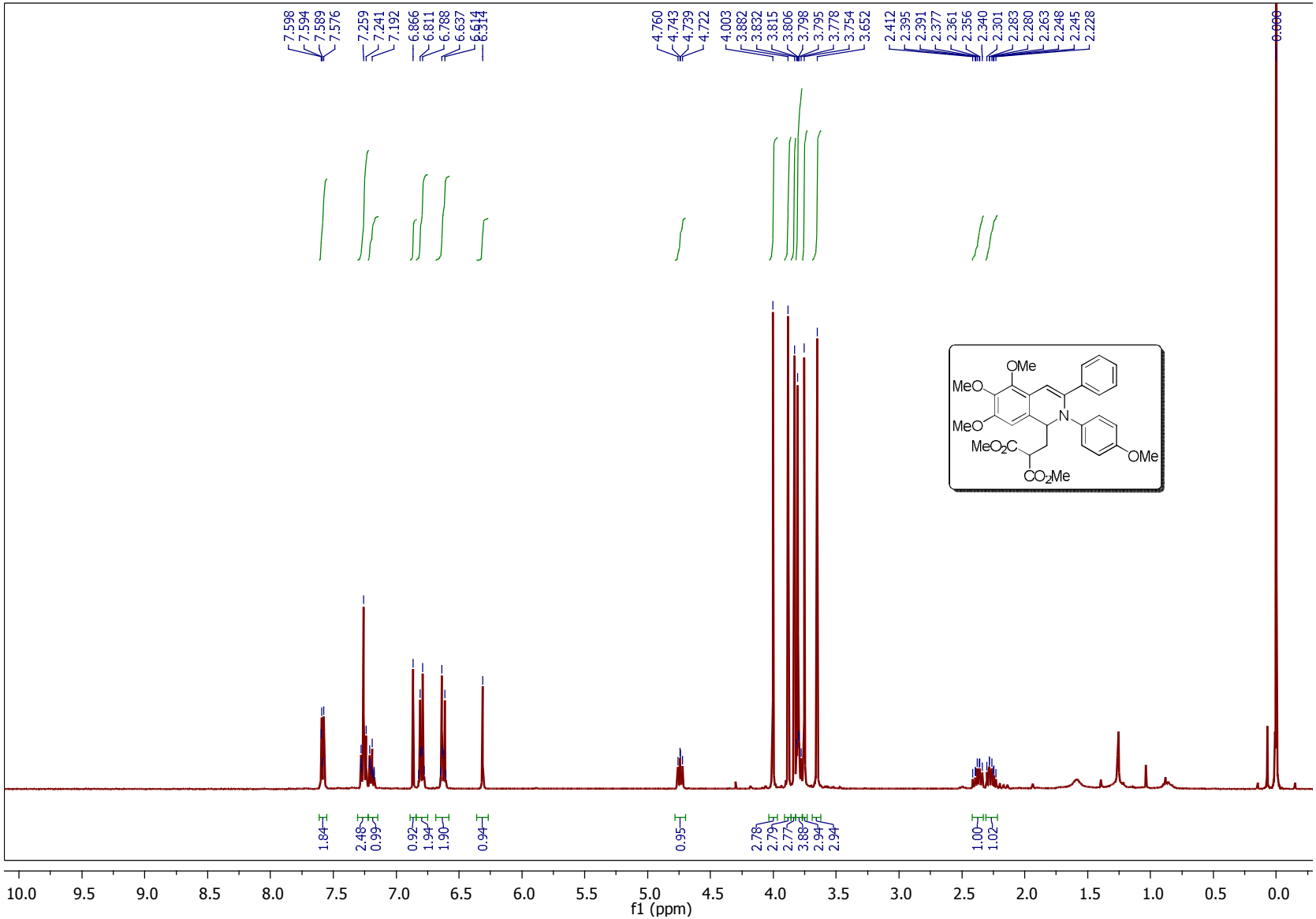
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4aa



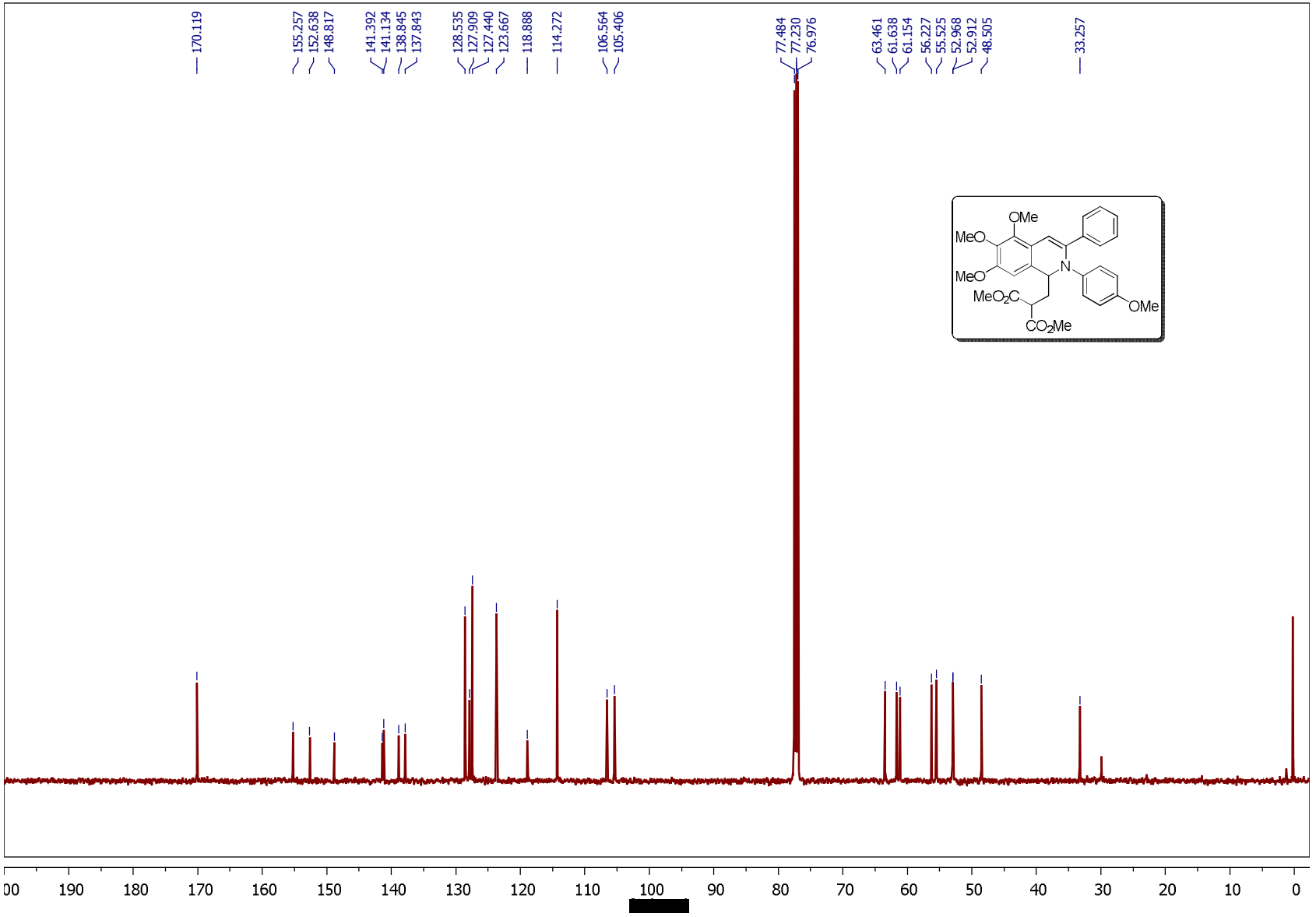
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 4aa



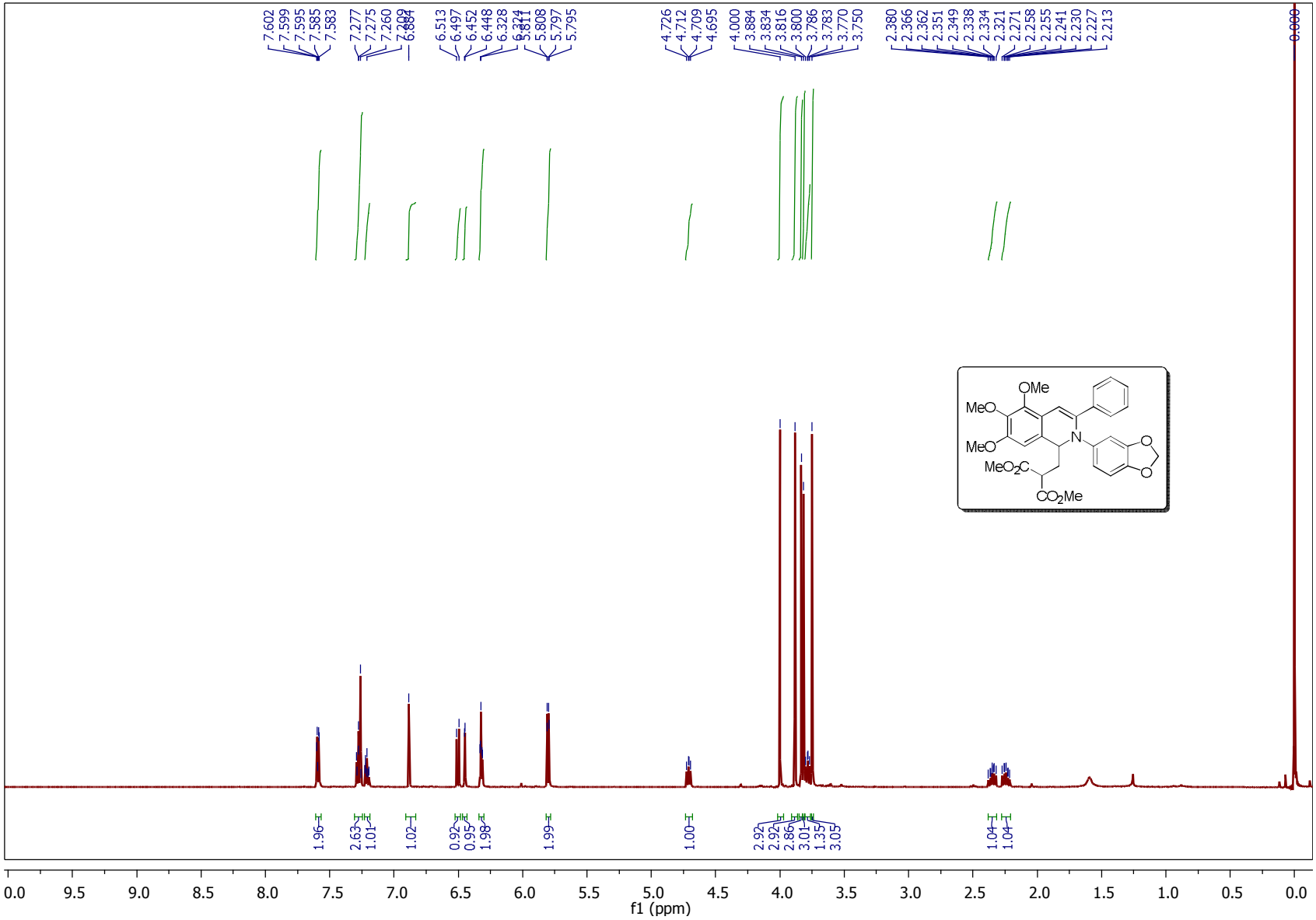
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 4ab



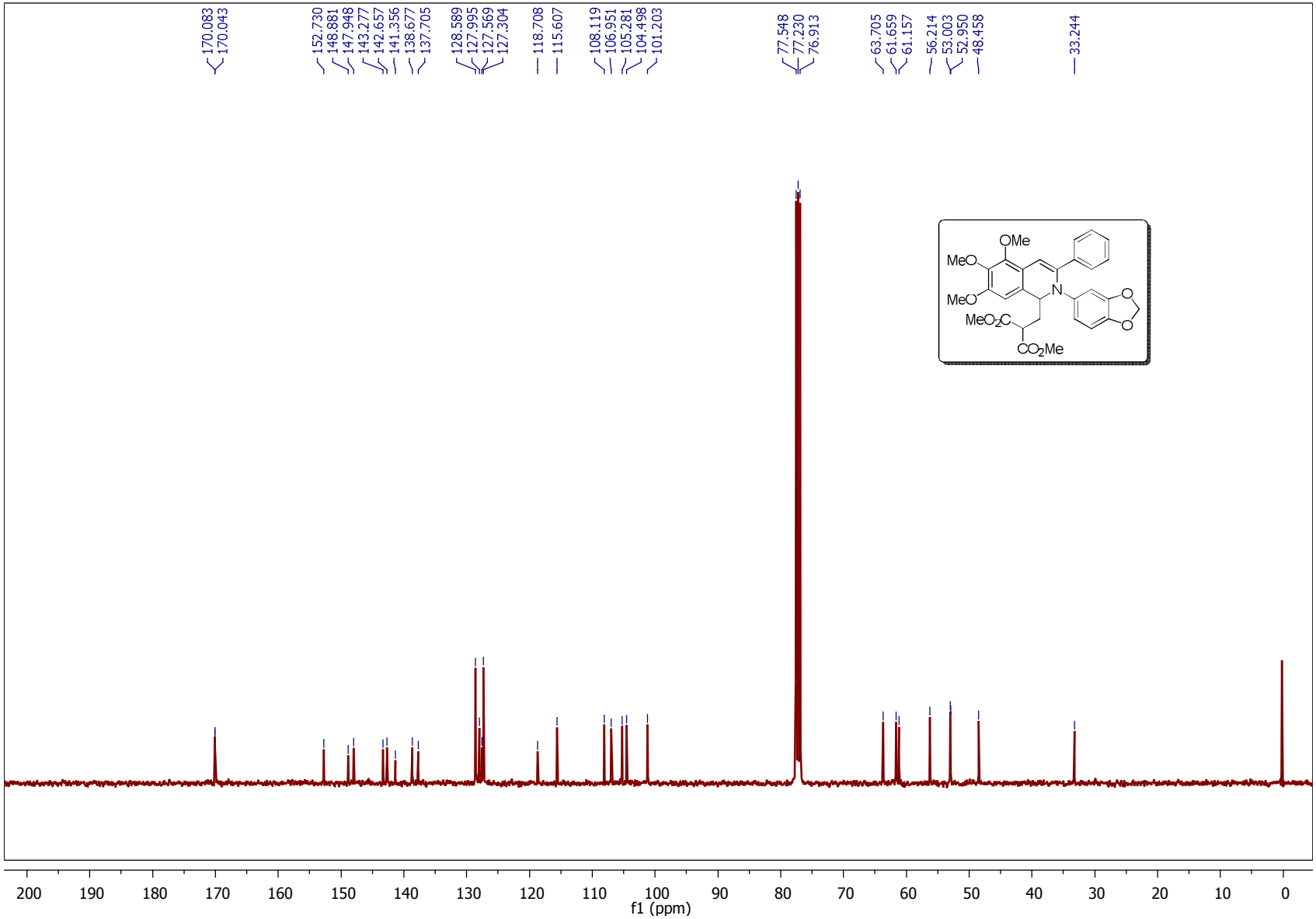
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 4ab



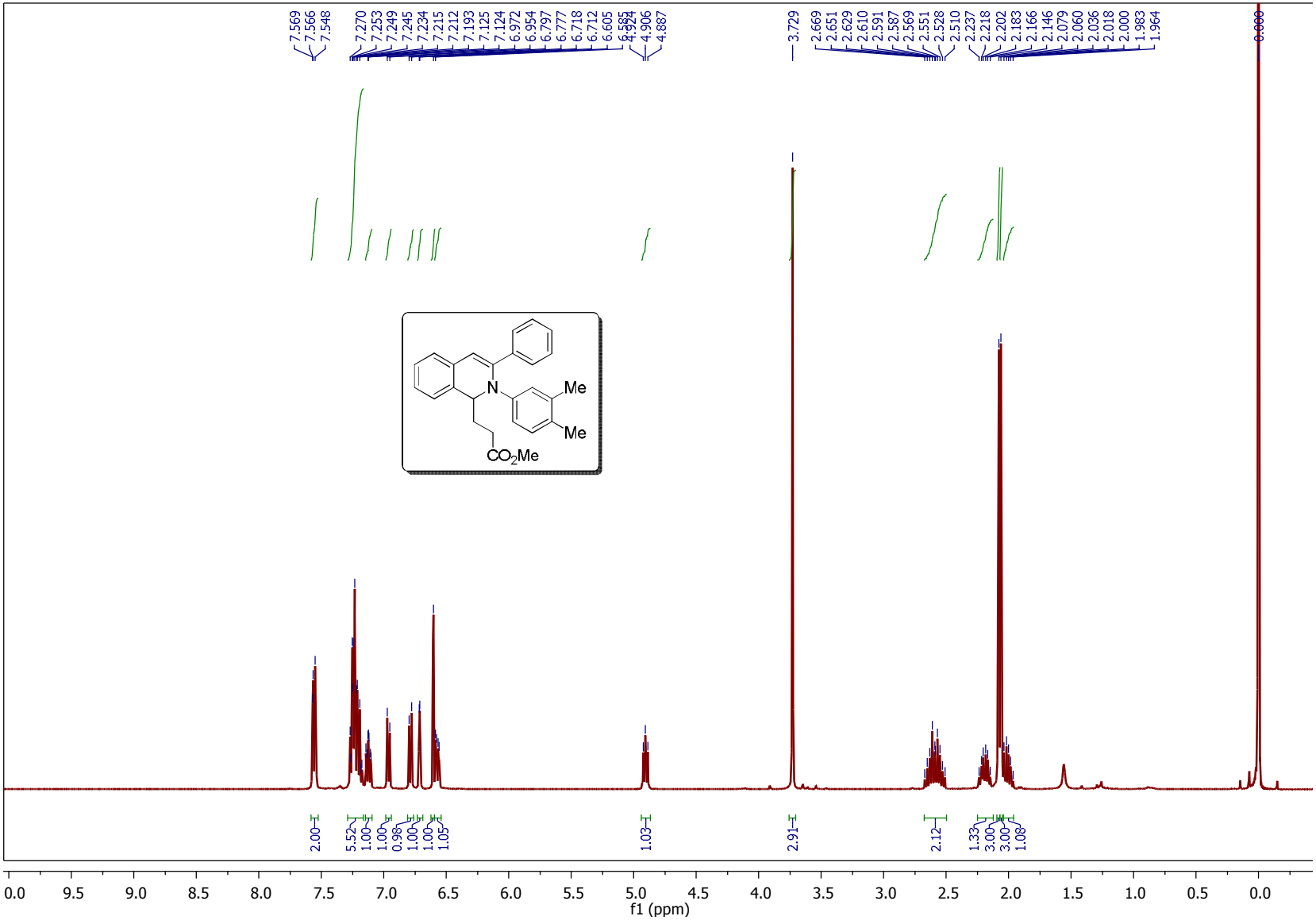
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 4ac



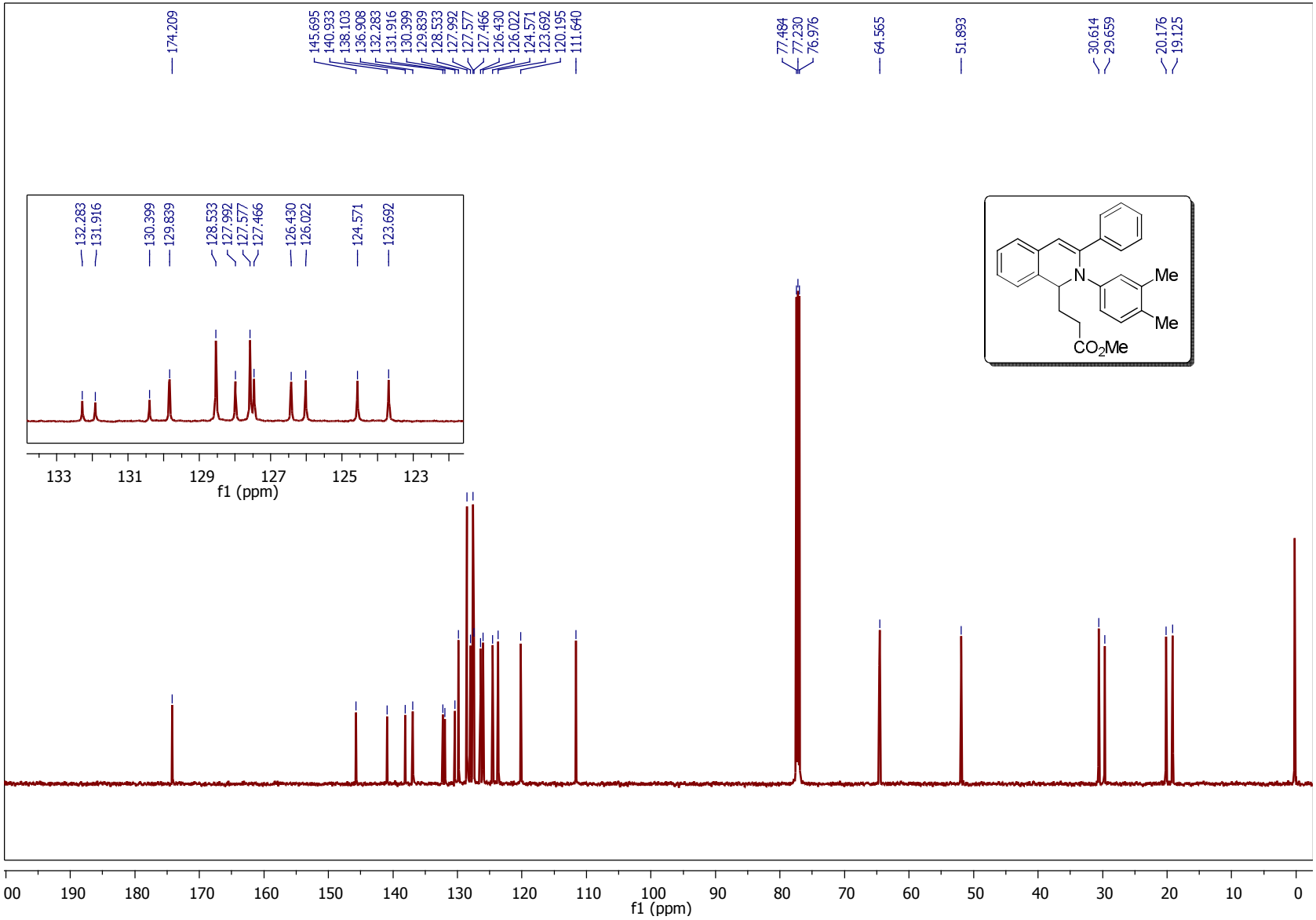
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 4ac



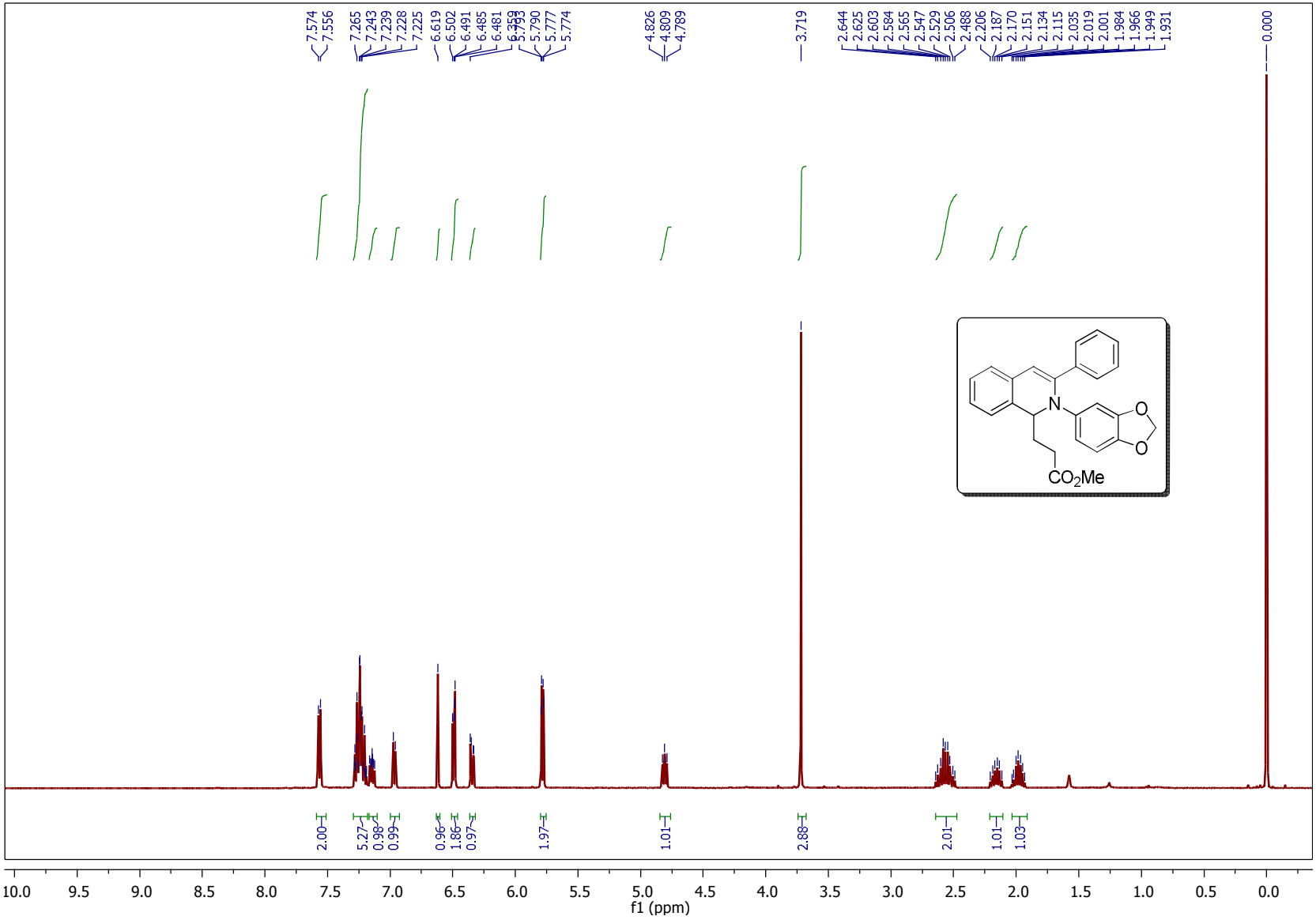
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 5a



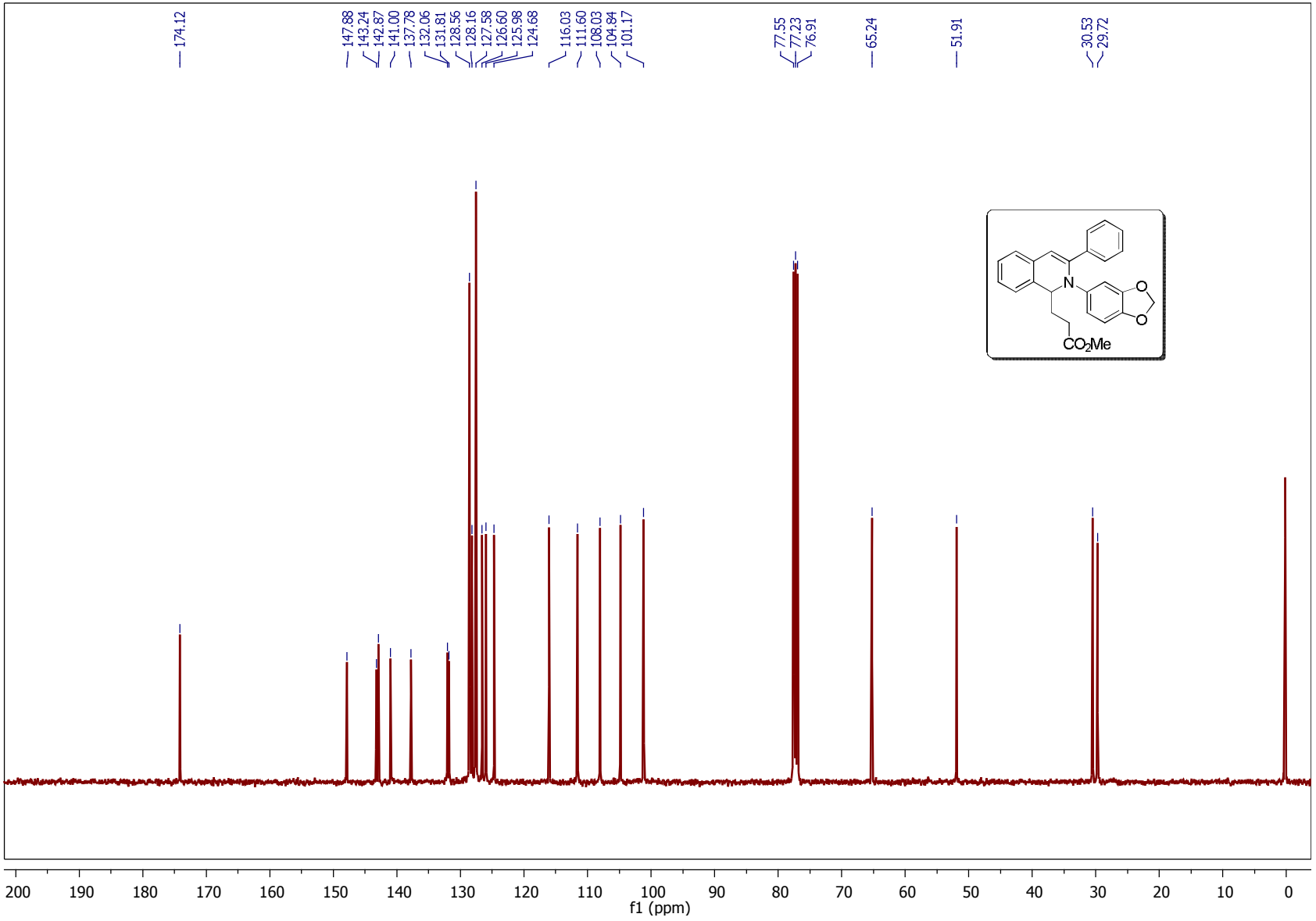
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 5a



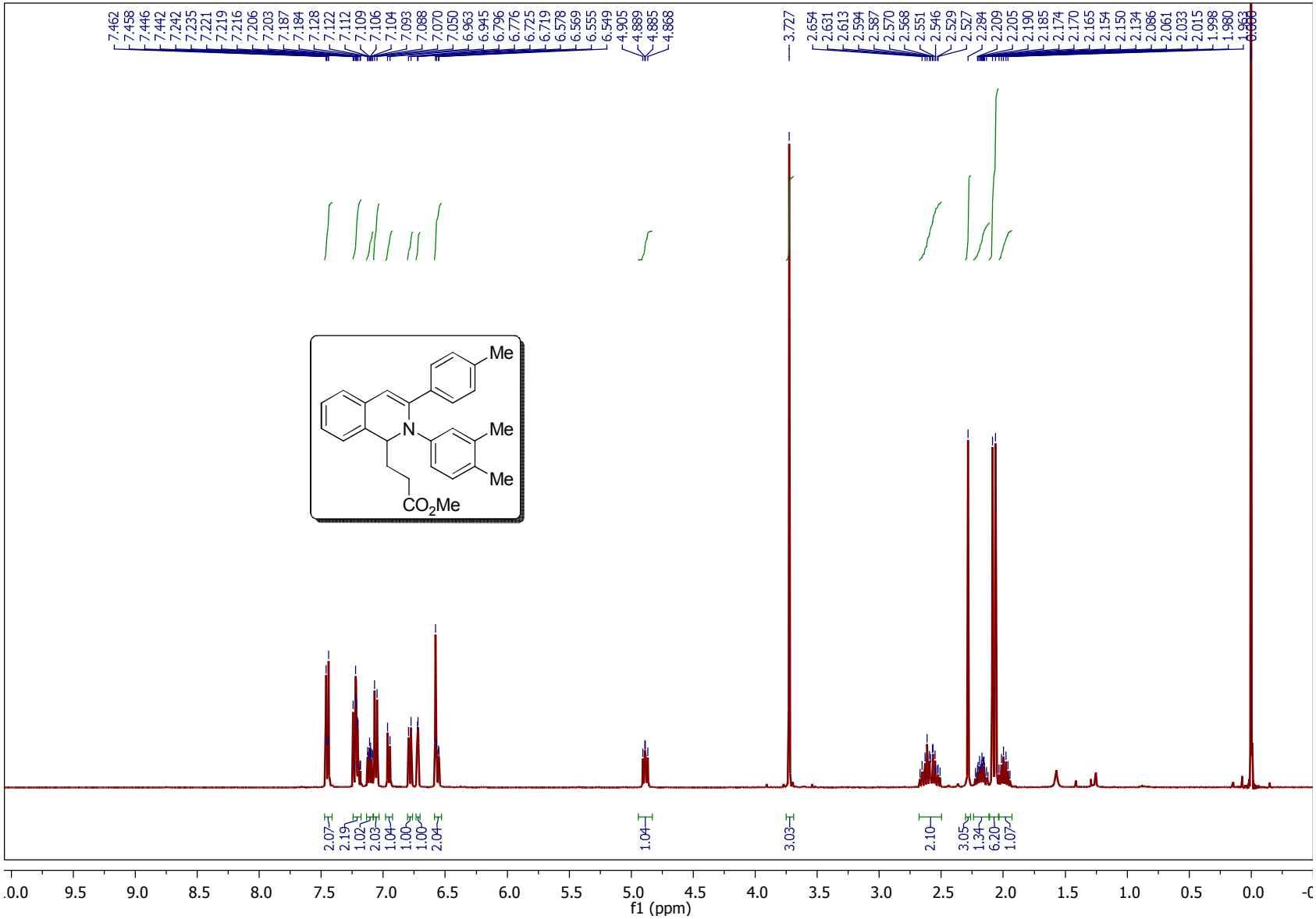
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 5b



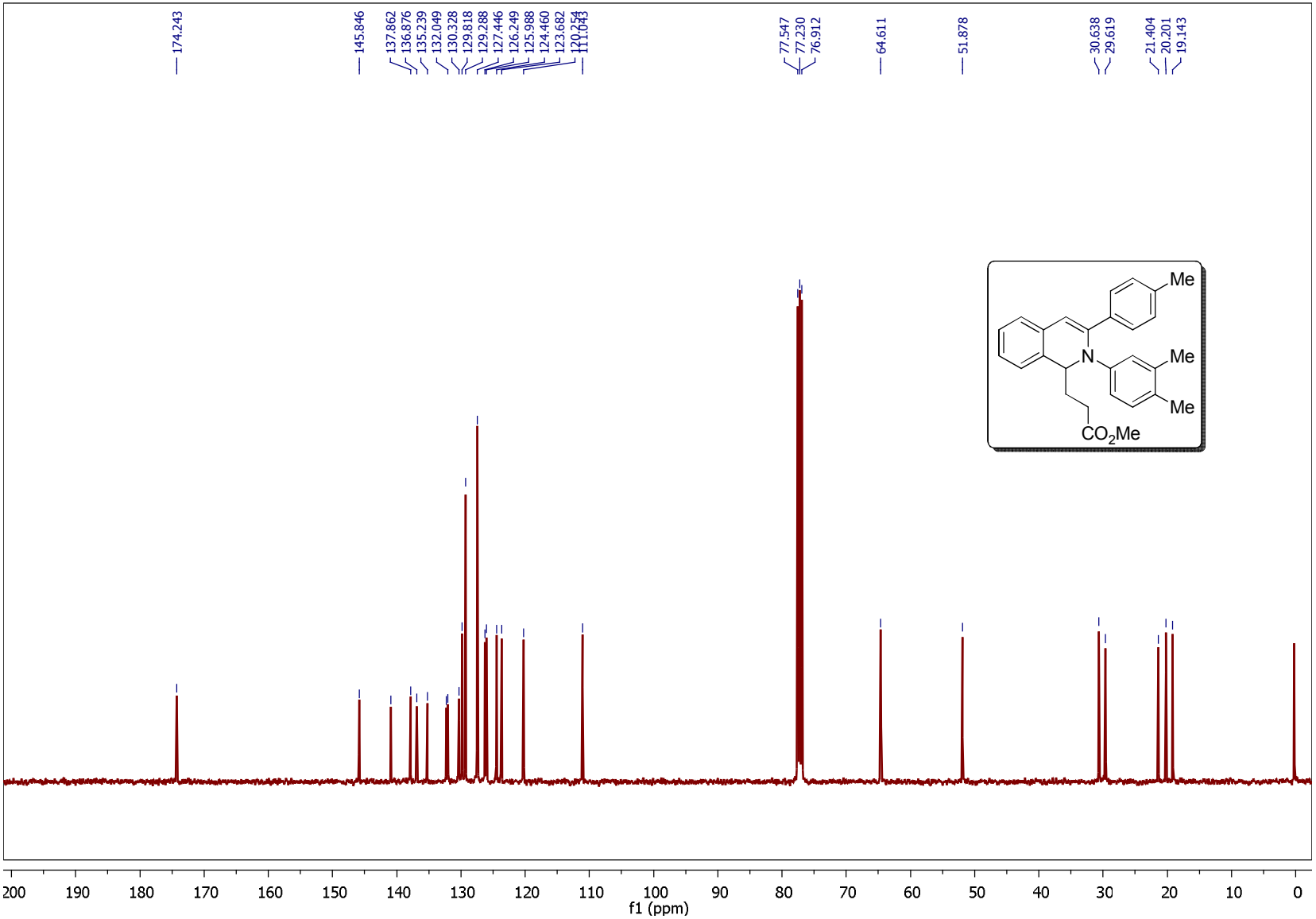
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 5b



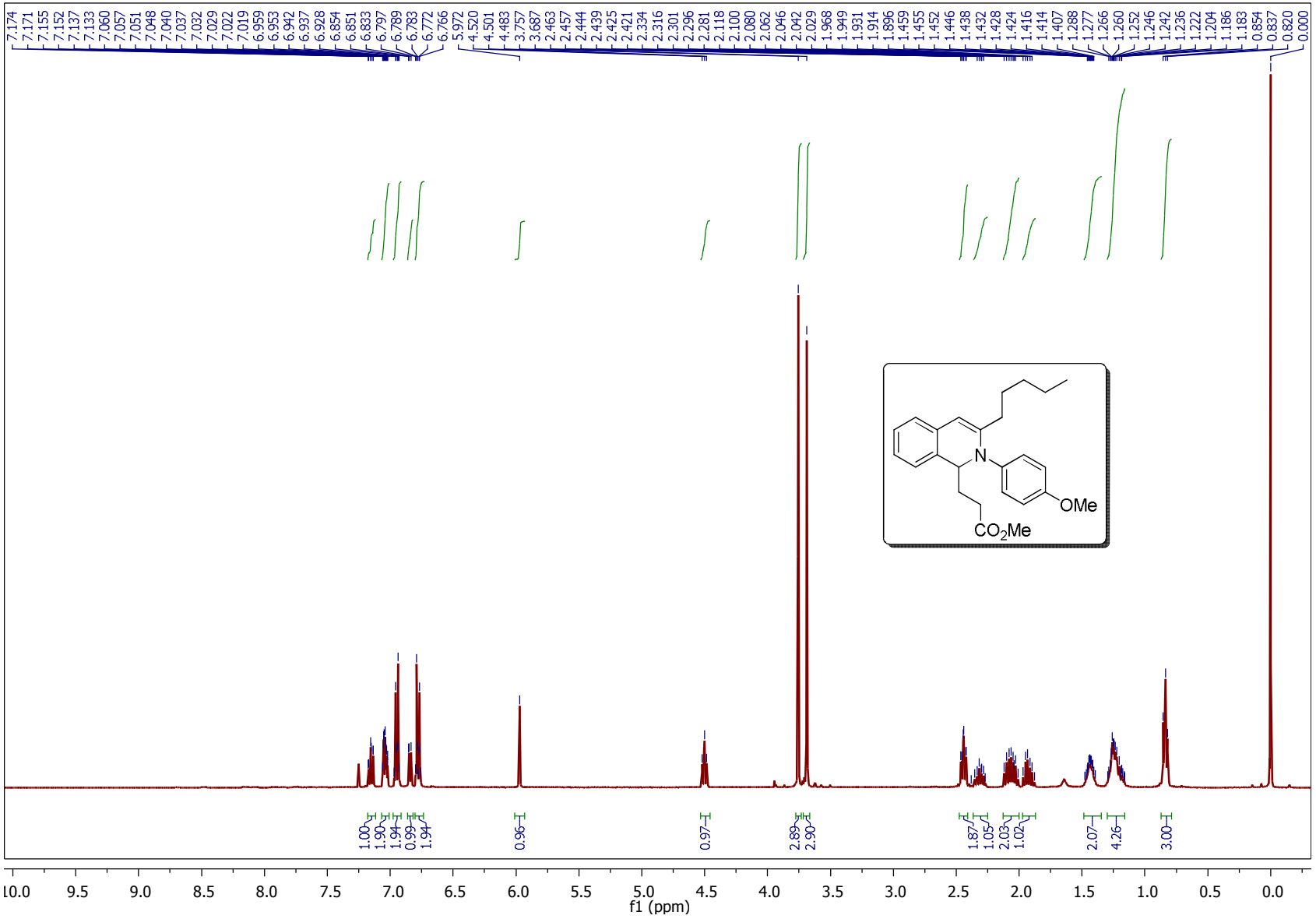
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 5c



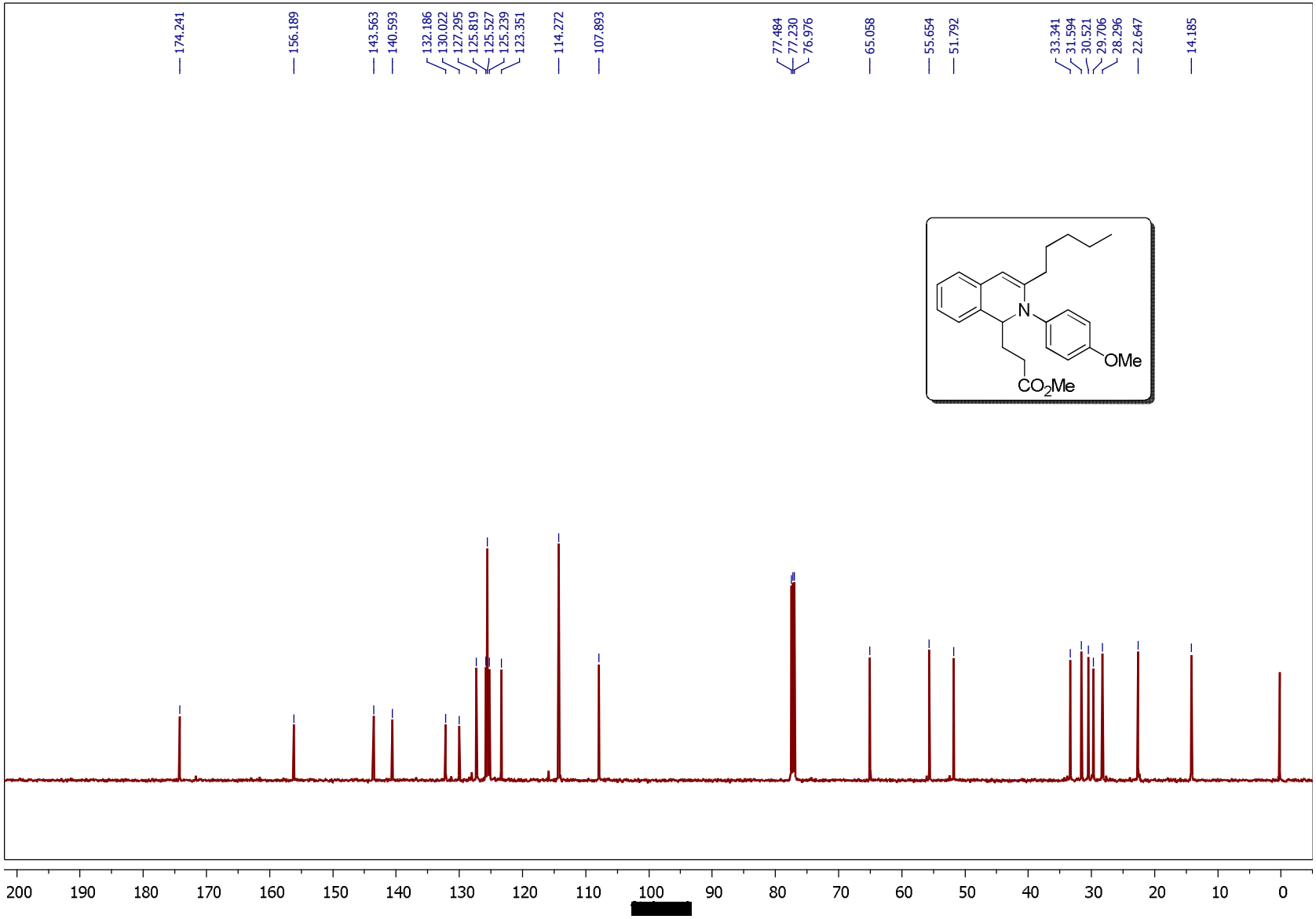
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 5c



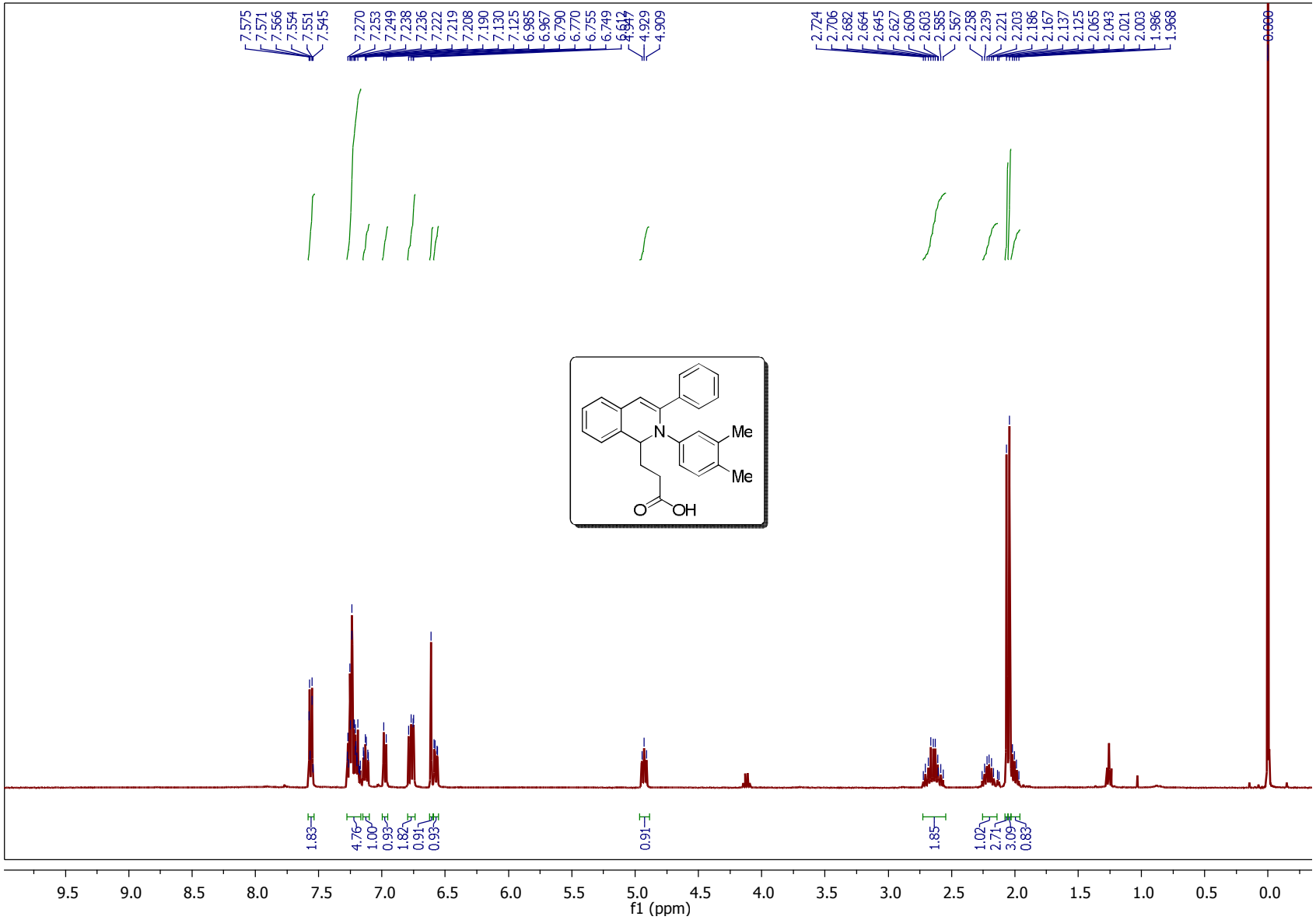
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 5d



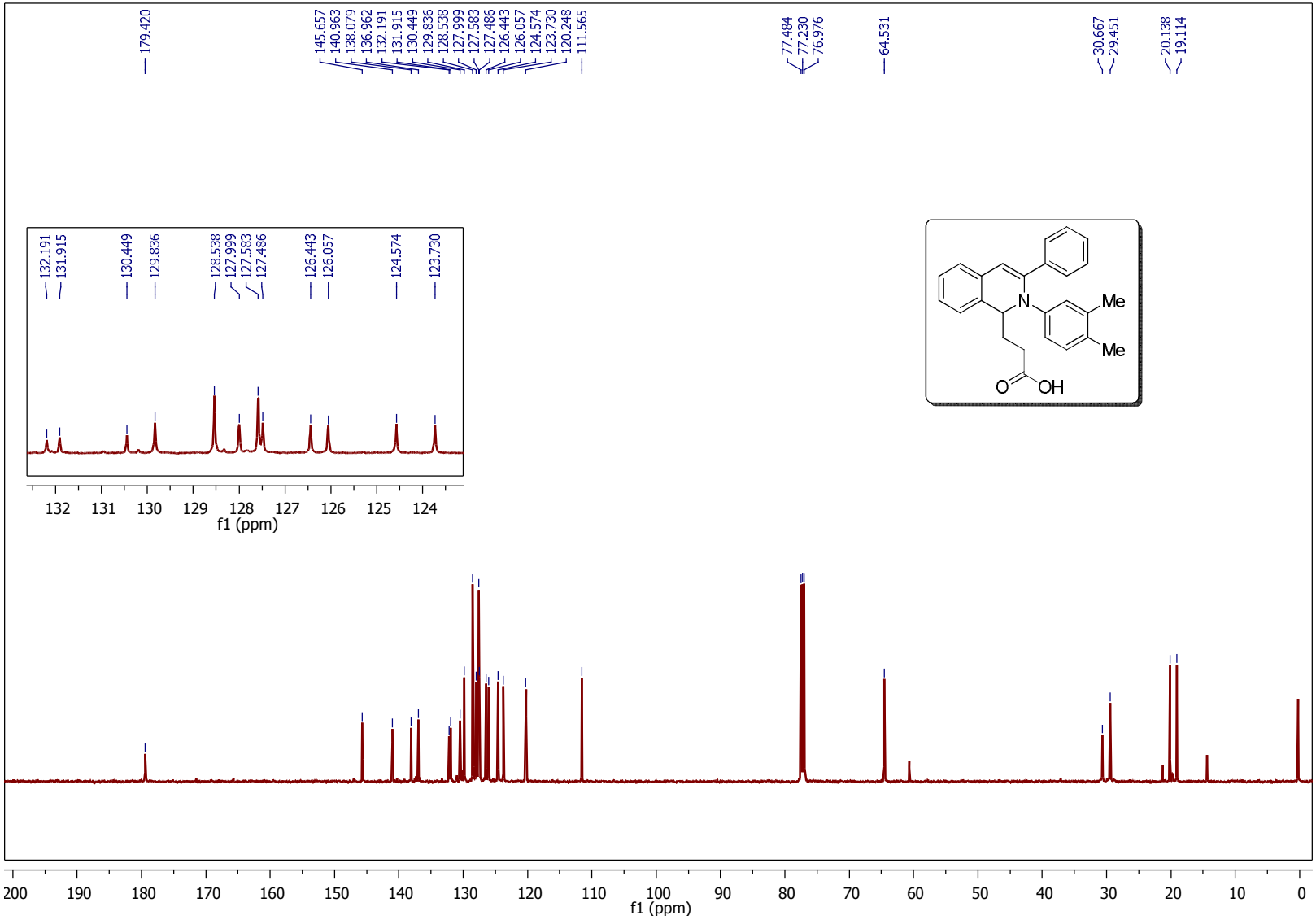
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 5d



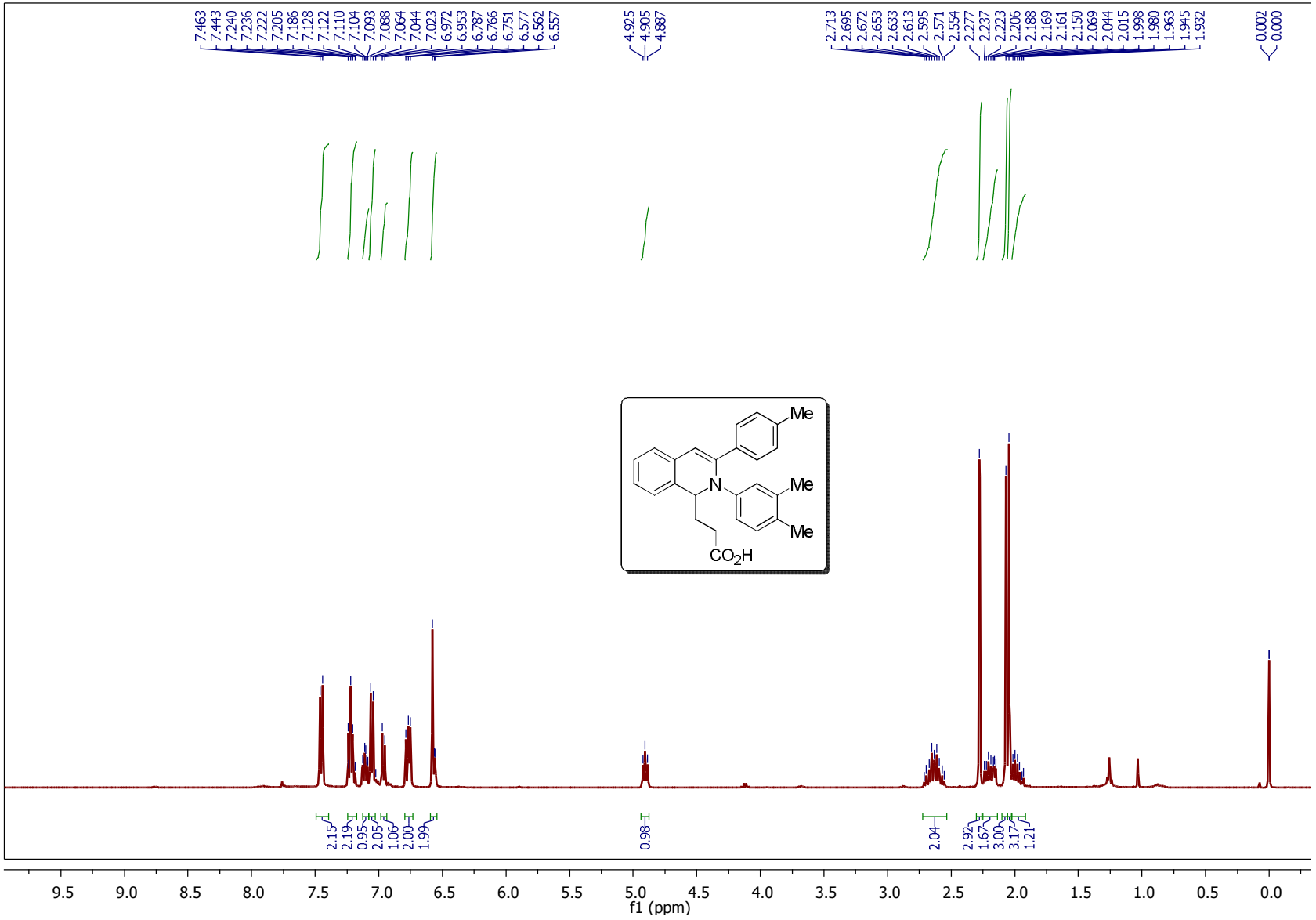
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 6a



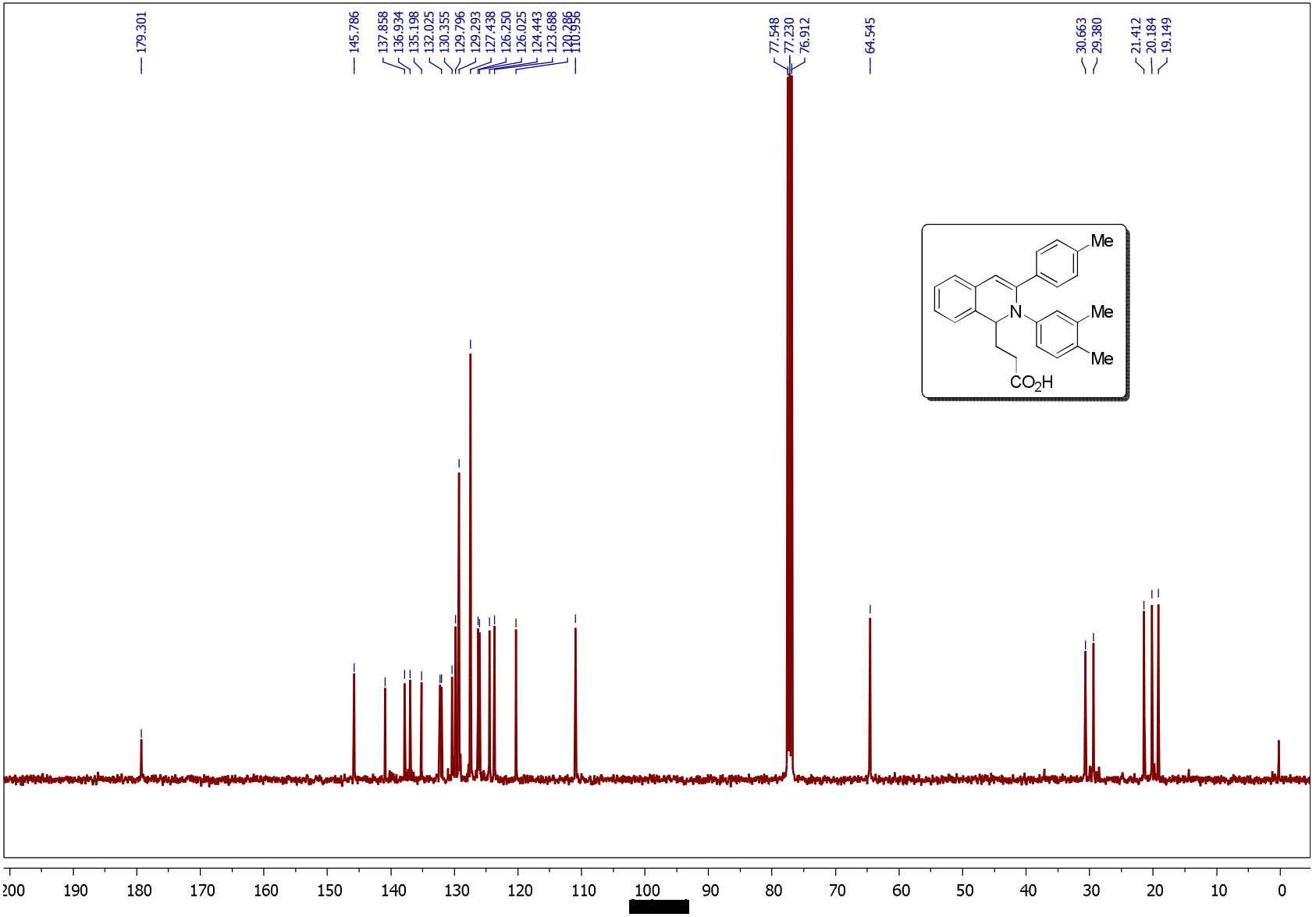
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 6a



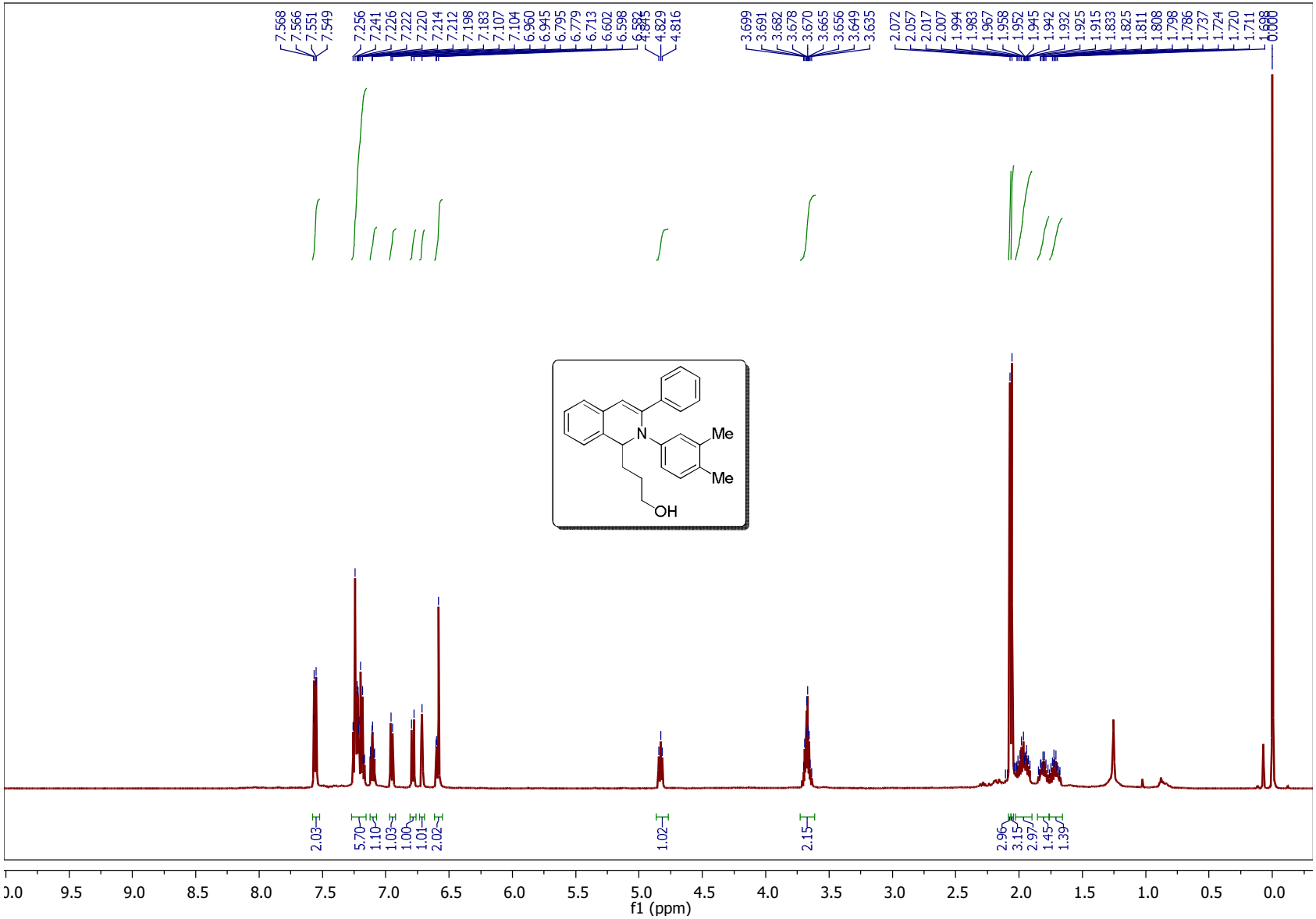
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 6b



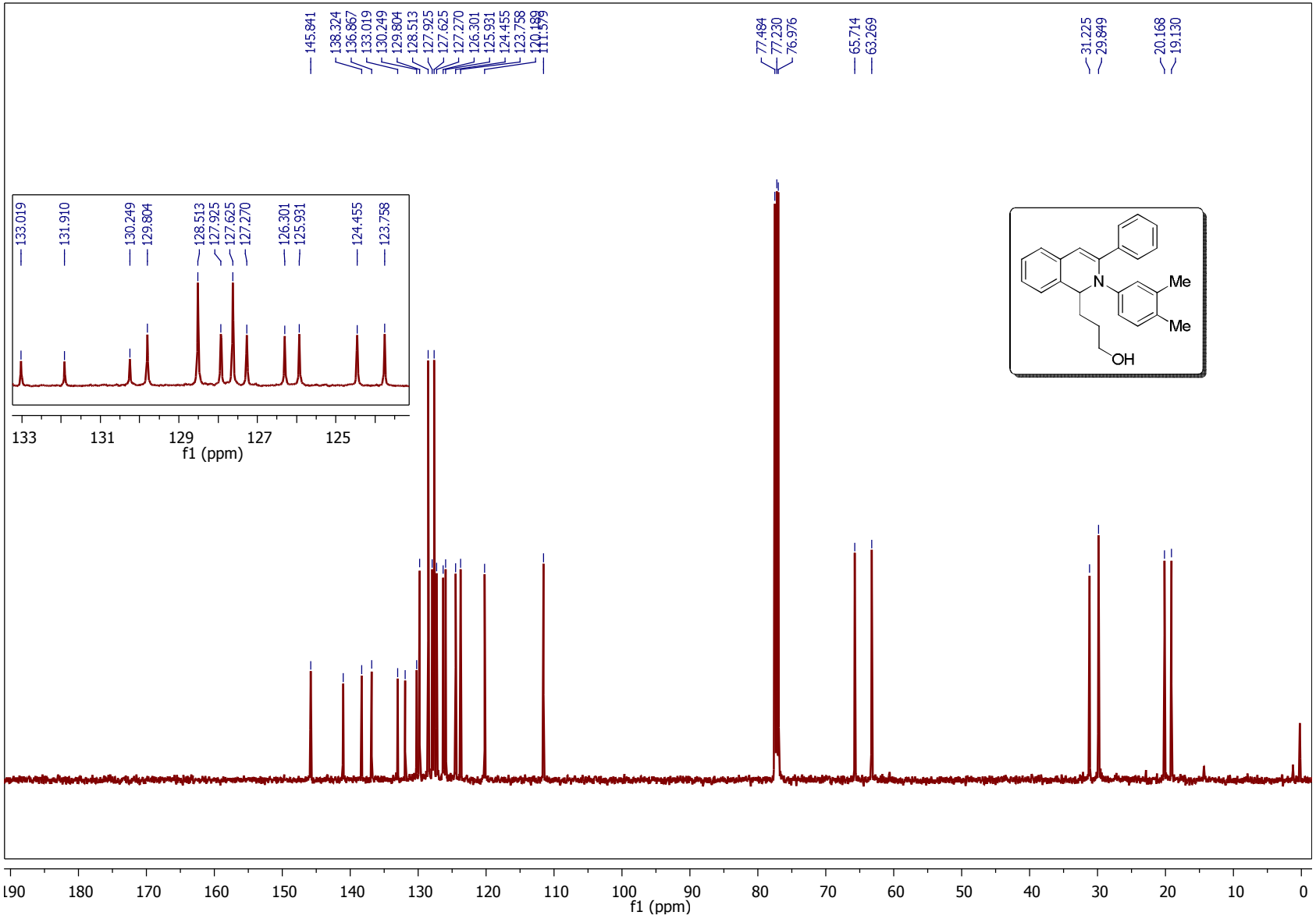
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 6b



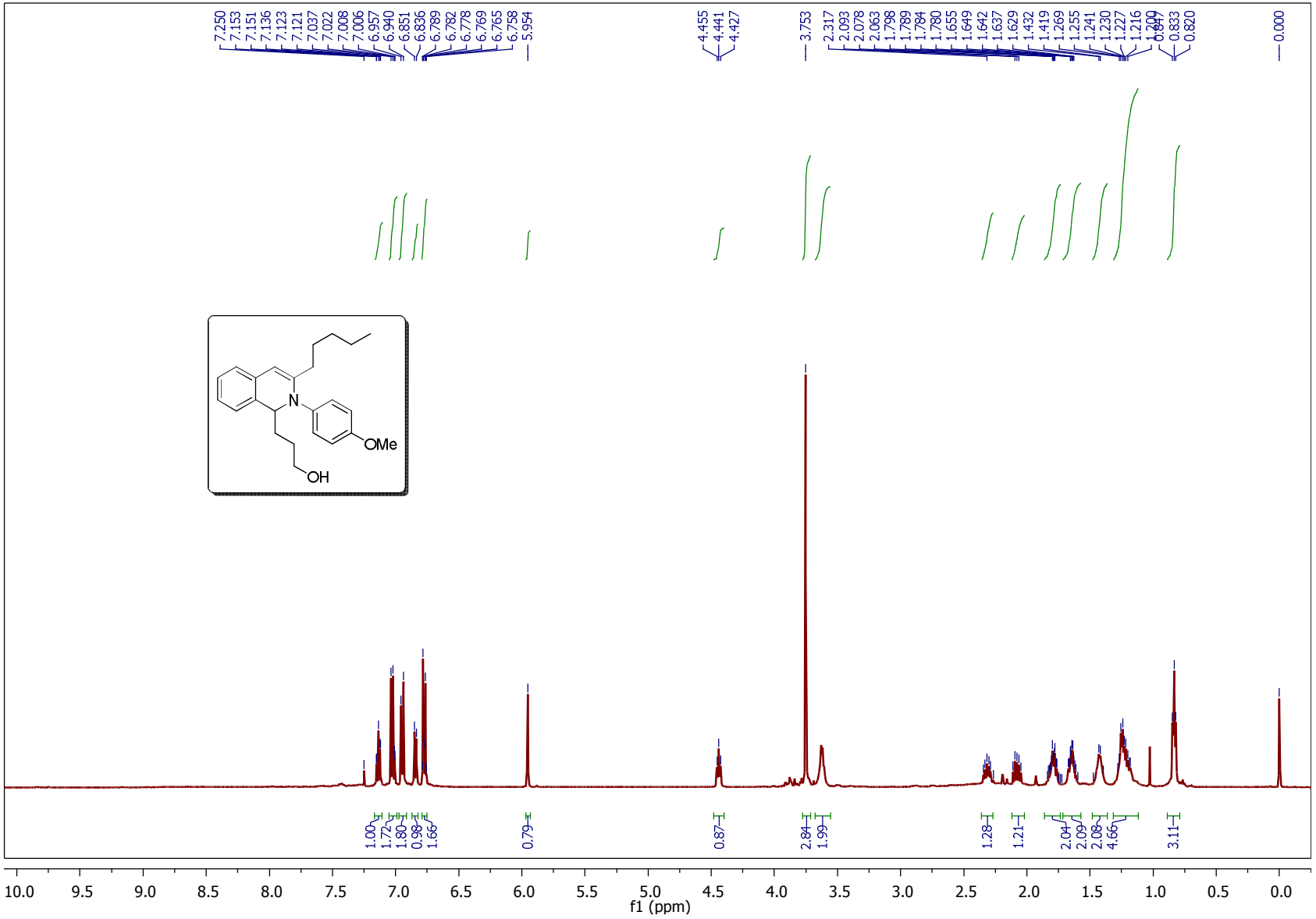
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 7a



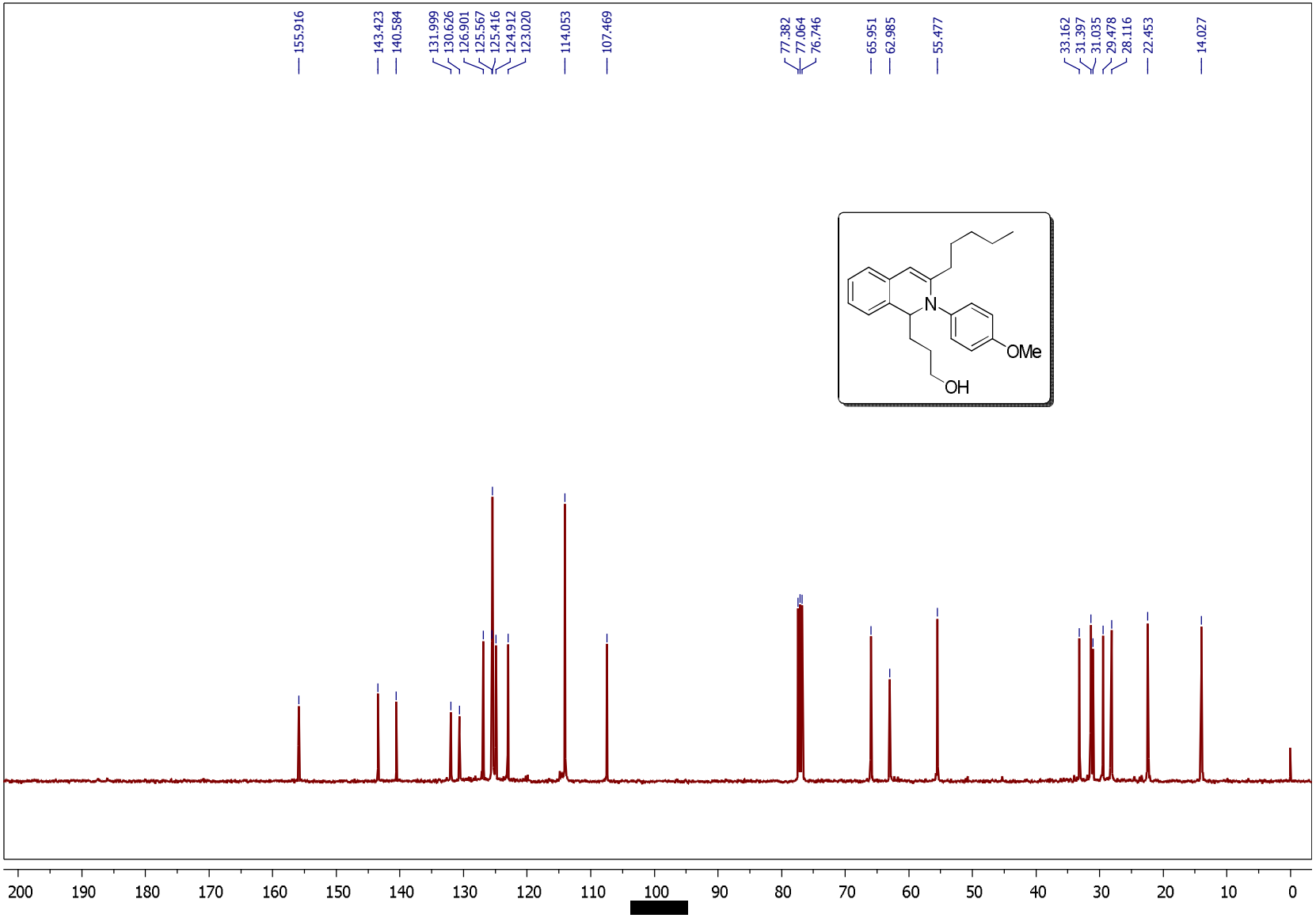
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of compound 7a



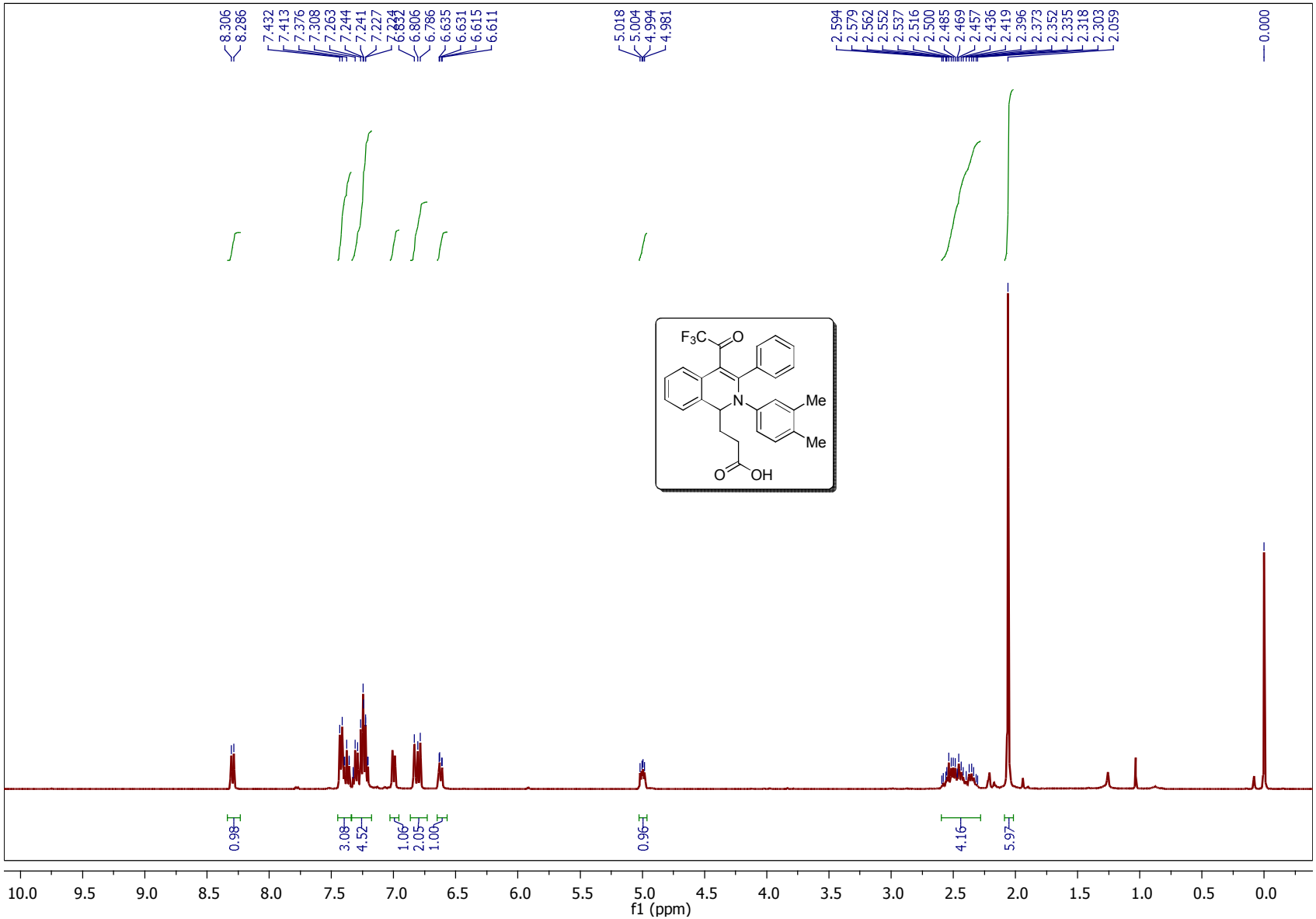
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of compound 7b



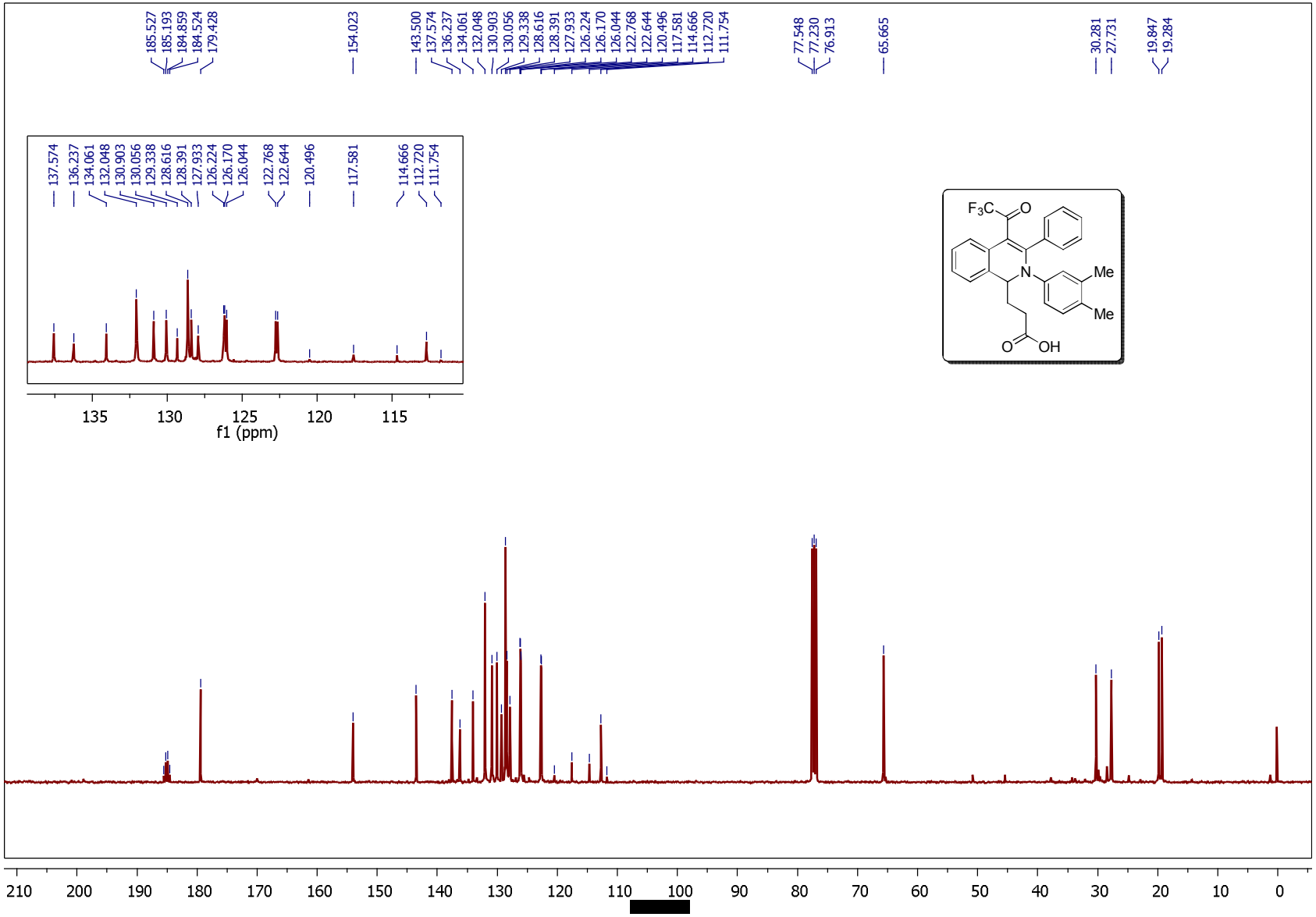
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 7b



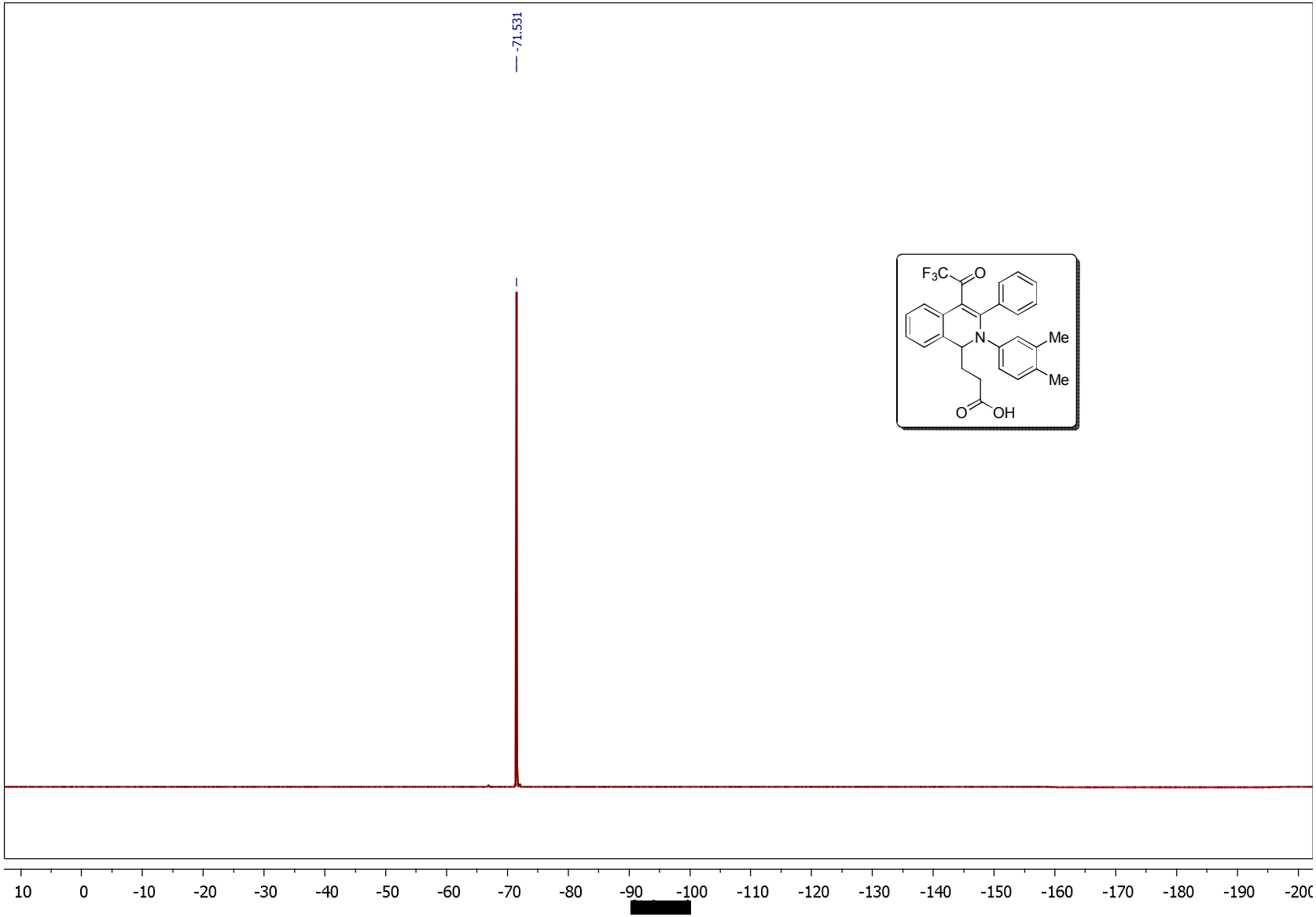
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 8



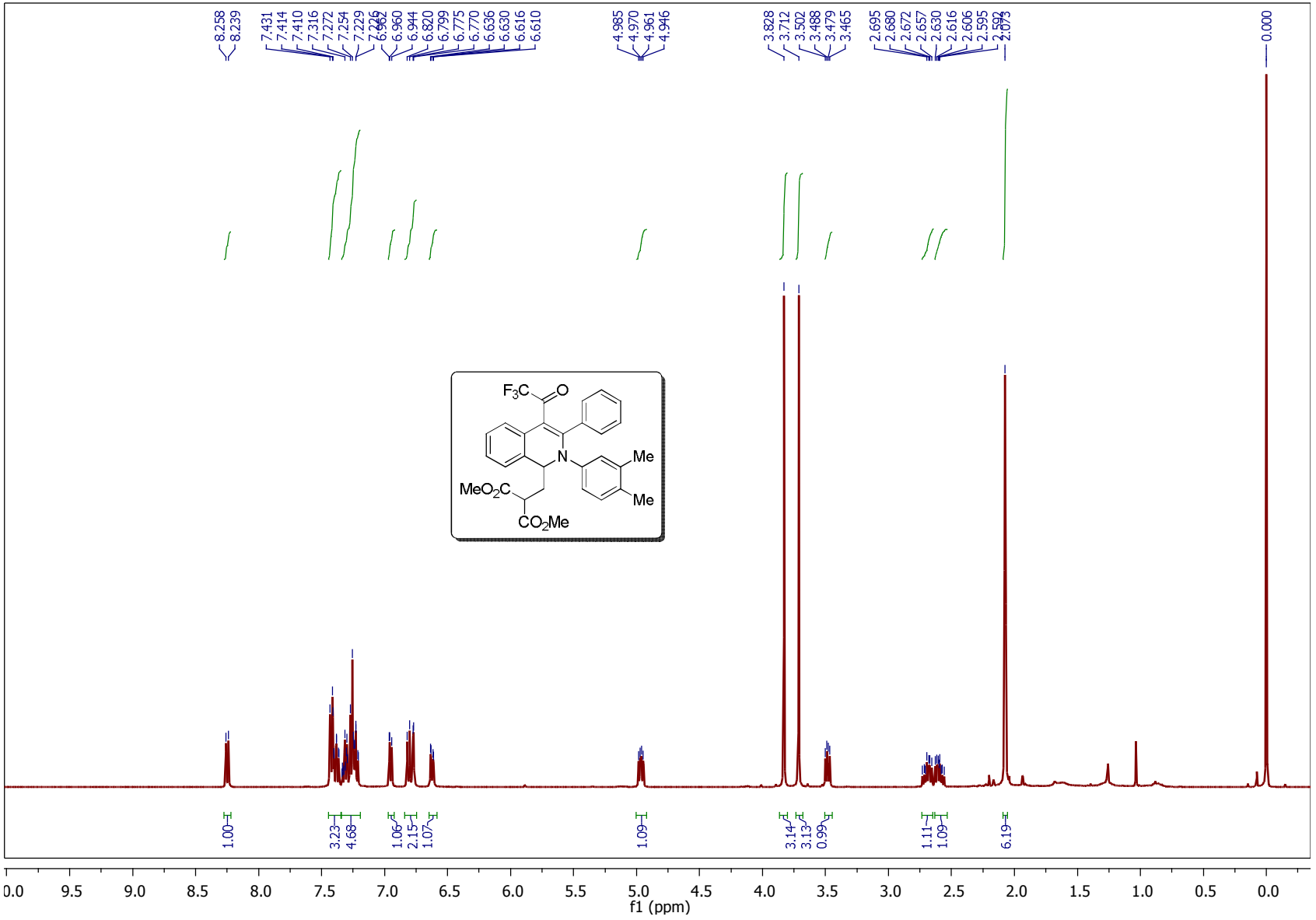
^{13}C NMR 101 MHz, $CDCl_3$) Spectrum of compound 8



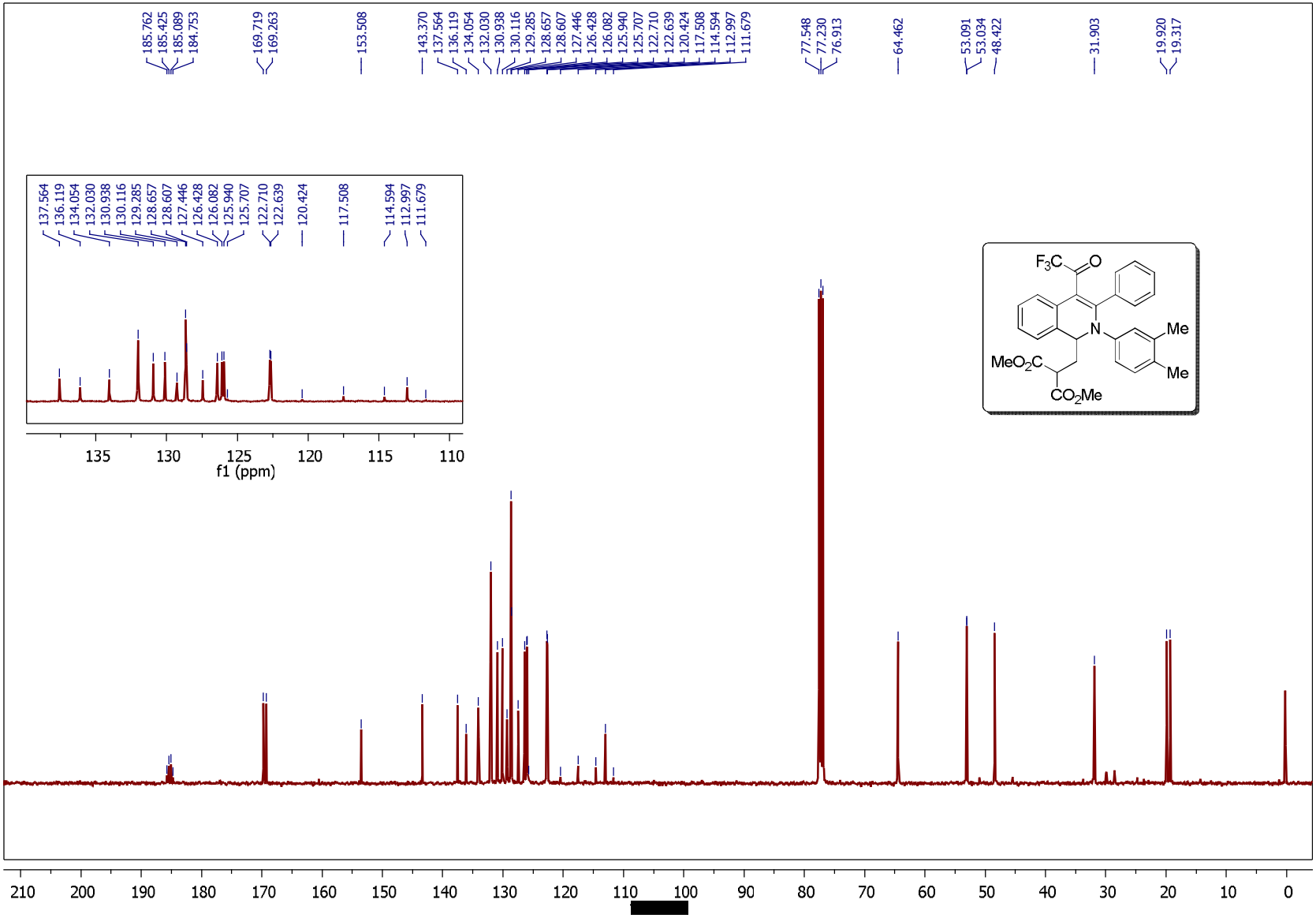
^{19}F NMR (377 MHz, $CDCl_3$) Spectrum of compound 8



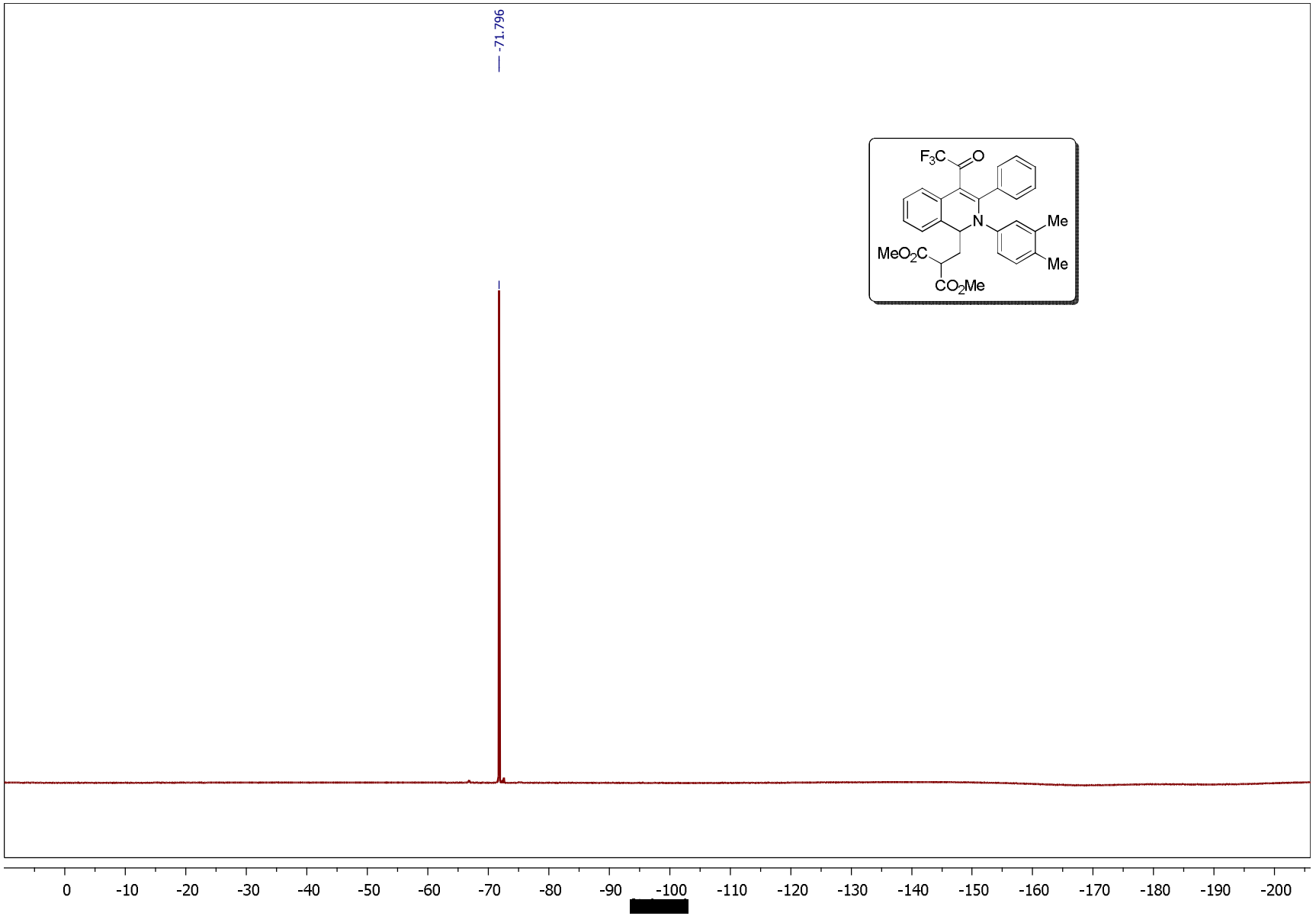
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of compound 9



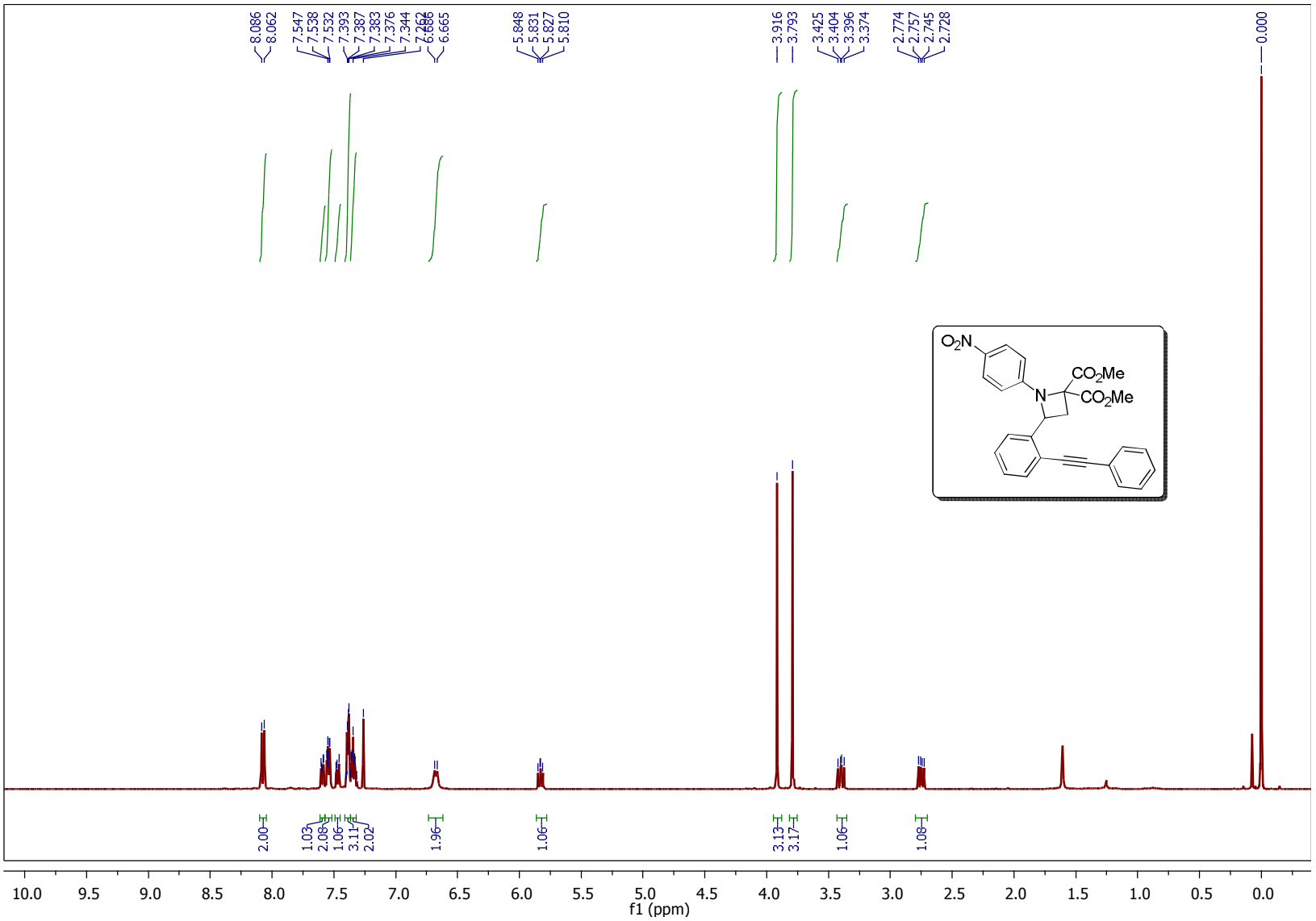
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 9



^{19}F NMR (377 MHz, $CDCl_3$) Spectrum of compound 9



^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 12



^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of compound 12