

Supporting Information for:

A Convenient One-pot Synthesis of 2-Substituted Benzofurans from Salicylaldehydes

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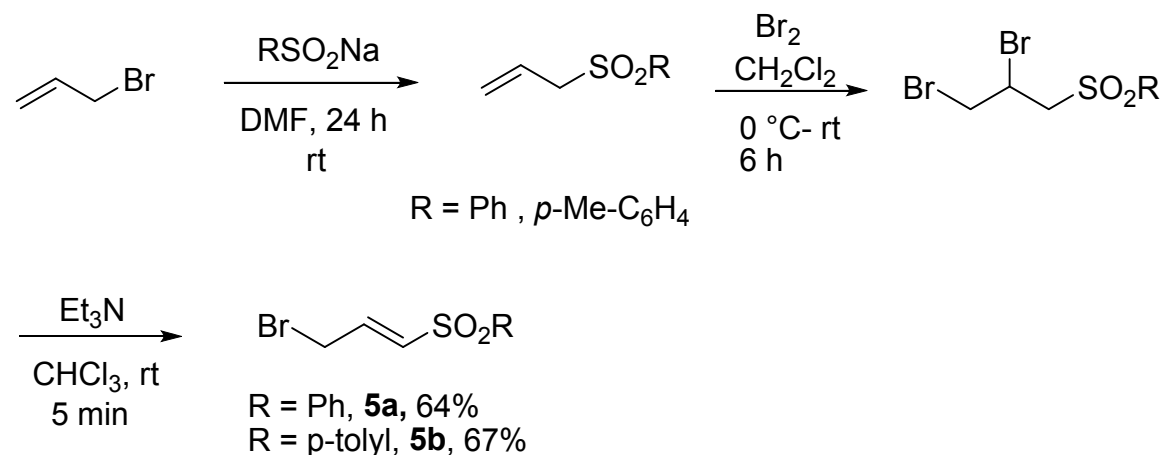
General Information

All ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ solvent on Varian Bruker 300 MHz, a Varian Unity 400 MHz and Avance 500 MHz spectrometer at ambient temperature, chemical shift δ are given in ppm on a scale downfield from TMS, and the coupling constant J are in Hz. The signal patterns are indicated as follows: s, Singlet; d, doublet; t, triplet; dd, doublet of doublet; m, multiplet. FTIR spectra were recorded as neat. Mass spectra were obtained on a Finnegan Mat1020B, a micromass VG 70-70H or an Agilent technologies LC/MSD treapSL spectrometer operating at 70eV using the direct inlet system and high resolution mass spectra (HRMS) were recorded on a QSTAR XL Hybrid MS/MS mass spectrometer. Melting points were recorded on an electrothermal apparatus and are uncorrected. All the reagents and solvents were used without further purification unless specified otherwise. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. Dichloromethane and water used as solvent.

Column chromatography was carried out using silica gel (60-120 mesh and 100-200 mesh) packed in glass columns. All reactions were performed in oven-dried glassware with magnetic stirring. Salicylaldehydes (**4a-d**), methyl-4-bromocrotonates (**8a**, 85% technical grade) and ethyl-4-bromocrotonates (**8b**, 75% technical grade) used in the study were obtained from Aldrich and were used as received. 4-(2-Formylphenoxy)-but-2-enoate **3** was prepared by potassium carbonate-mediated alkylation of salicylaldehyde **4a** with **8a**.¹

Preparation of the (*E*)-3-bromo-1-(arylsulfonyl)propenes **5a-b**

Both **5a** and **5b** were prepared by following the method described by Gallagher and Grayson (Scheme 1).²



Scheme 1: Synthesis of **5a-b**

General procedure for the synthesis of 2-(β-sulfonylvinyl)benzofurans **6aa-cb**

Cesium carbonate (326 mg, 1 mmol) was added to a solution of salicylaldehyde **4a-d** (0.5 mmol) and 3-bromo-1-(arylsulfonyl)propene **5a-b** (0.5 mmol) in anhydrous acetonitrile (5mL). The resulting solution was stirred at ambient temperature for 12h. The reaction mixture was then partitioned between dichloromethane and ice cold water, and aqueous phase was extracted with

¹ E. Ciganek, *Synthesis* **1995**, 1311.

² E. T. Gallagher, D. H. Grayson, *Org. Biomol. Chem.* **2003**, *1*, 1374

ethyl acetate. The combined organic phases were dried with anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure samples of 2-(β -sulfonylvinyl)benzofurans **6aa-6cb**.

General procedure for the synthesis of 2-(β -alkoxycarbonylvinyl)benzofurans **7aa-db**

DBU (152 mg, 1 mmol) was added to a solution of salicylaldehyde **4a-d** (0.5 mmol) and the 4-bromocrotonate ester **8** (0.5 mmol; 0.07 mL for **8a** and 0.09 mL for **8b**) in anhydrous acetonitrile (5mL). The resulting solution was stirred at ambient temperature for 12h. The reaction mixture was then partitioned between dichloromethane and ice cold water, and aqueous phase was extracted with ethyl acetate. The combined organic phases were dried with anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure samples of 2-substituted benzofurans **7aa-7db**.

Conversion of **7aa** into the pyrrole derivative **9**³

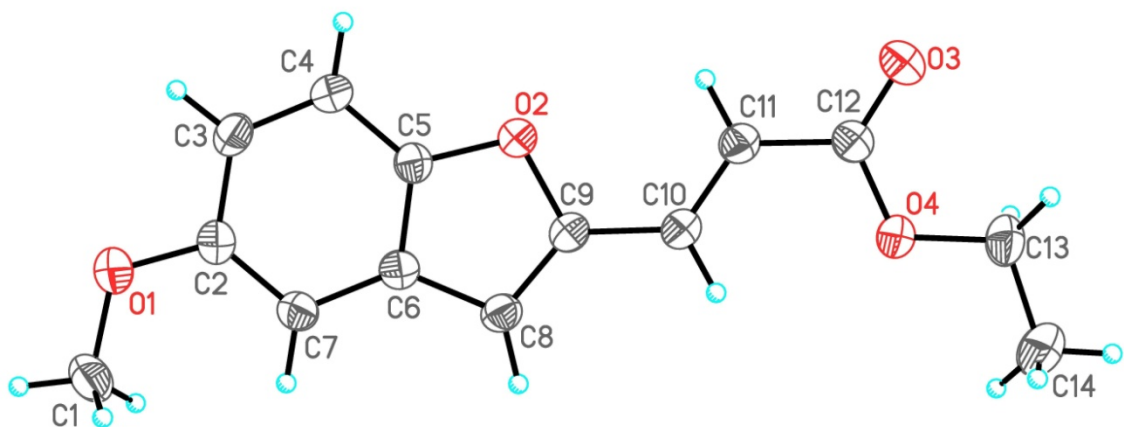
A solution of **7aa** (101 mg, 0.5 mmol) and tosylmethyl isocyanide (108 mg, 0.55 mmol) in anhydrous THF-DMSO (1 mL and 2 mL respectively) was added dropwise into a suspension of sodium hydride (60 % dispersion in mineral oil, 42 mg, 1.1 mmol) in THF (2mL). The mixture was stirred at room temperature for 6h. The reaction mixture was then treated with water and extracted with ethyl acetate. The combined extracts were dried over anhydrous sodium sulfate, solvent was removed on a rotavapor and the residue obtained was chromatographed on silica gel using petroleum ether-ethyl acetate as eluent to afford the pyrrole derivative **9** (63 mg) and unreacted **7aa** (40 mg).

Single crystal X-ray diffraction analysis of **7cb**

C₁₄H₁₄O₄, $M = 246.25$, $0.43 \times 0.27 \times 0.15 \text{ mm}^3$, triclinic, space group *P***Error!** (No. 2), $a = 8.0907(15)$, $b = 8.1765(15)$, $c = 10.6283(19)$ Å, $\alpha = 91.440(3)^\circ$, $\beta = 101.366(3)^\circ$, $\gamma = 114.809(3)^\circ$, $V = 621.1(2) \text{ \AA}^3$, $Z = 2$, $D_c = 1.317 \text{ g/cm}^3$, $F_{000} = 260$, CCD area detector, MoK α radiation, $\lambda = 0.71073 \text{ \AA}$, $T = 293(2)\text{K}$, $2\theta_{\text{max}} = 50.0^\circ$, 6041 reflections collected, 2189 unique ($R_{\text{int}} = 0.0228$), Final $\text{Goof} = 1.109$, $RI = 0.0470$, $wR2 = 0.1141$, R indices based on 1932 reflections with $I > 2\sigma(I)$ (refinement on F^2), 165 parameters, $\mu = 0.097 \text{ mm}^{-1}$. Crystallographic data for the structure in this paper has been deposited with the Cambridge Crystallographic Data Centre and

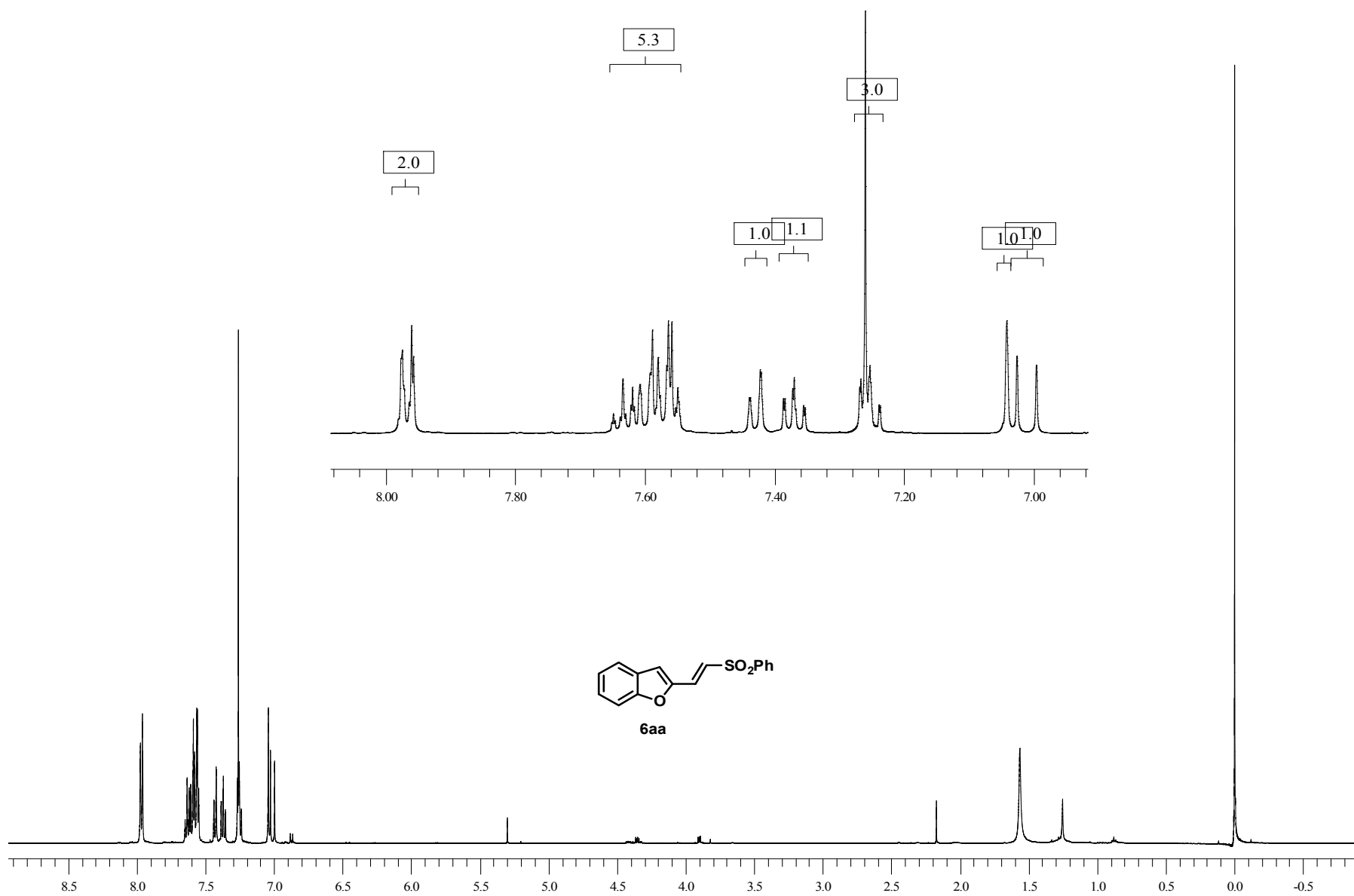
³ H. Siderius, B. E. Hugenboom, D. van Leusen, A. M. van Leusen. *Tetrahedron Lett.* 1972, 5337.

obtained a unique depository number, CCDC 1020845, which can be obtained free of charge from <http://www.ccdc.cam.ac.uk/Community/Requestastructure/Pages/DataRequest.aspx> or by writing to the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk

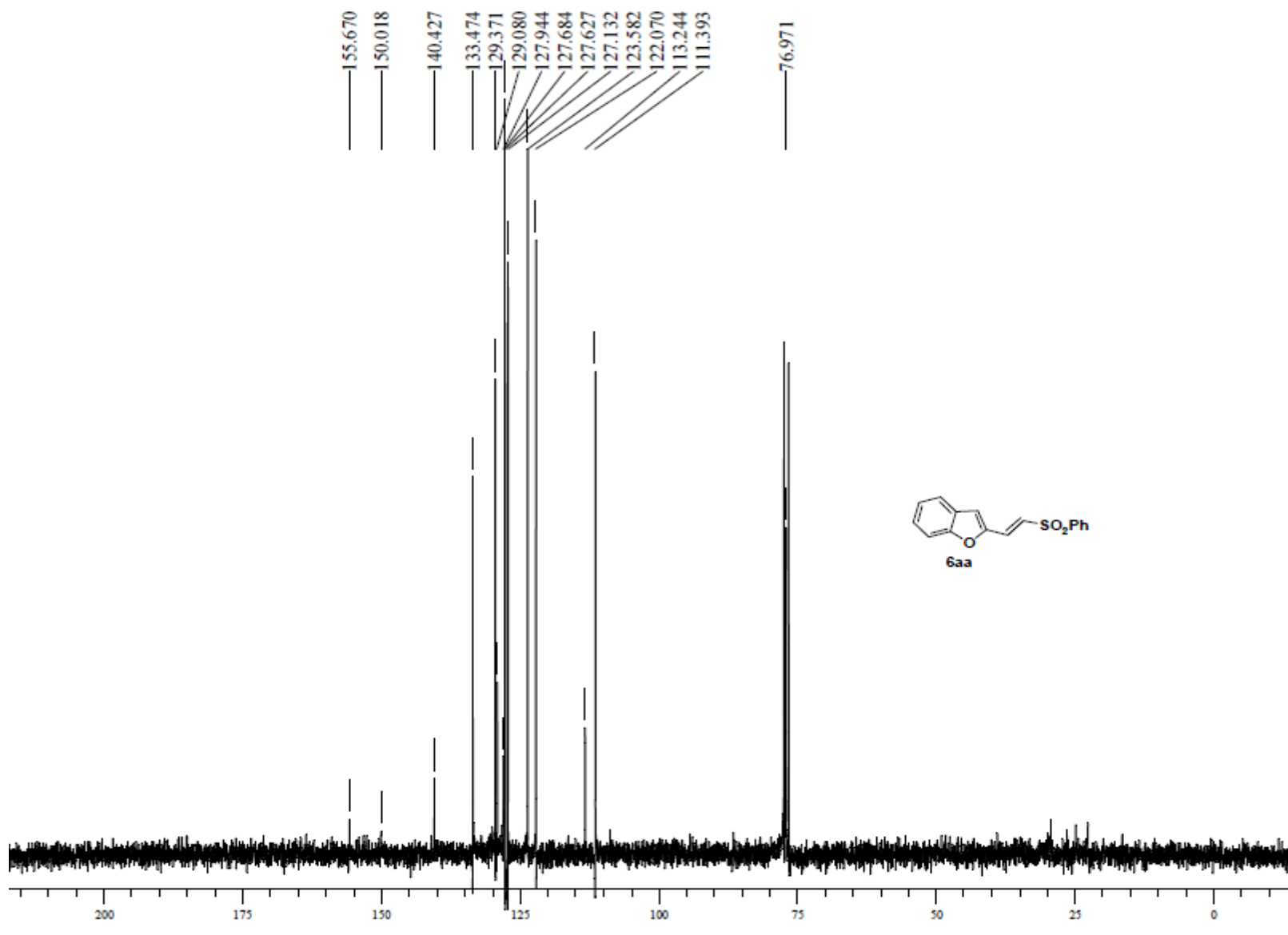


ORTEP diagram of **7cb** with the atom-numbering scheme; displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius.

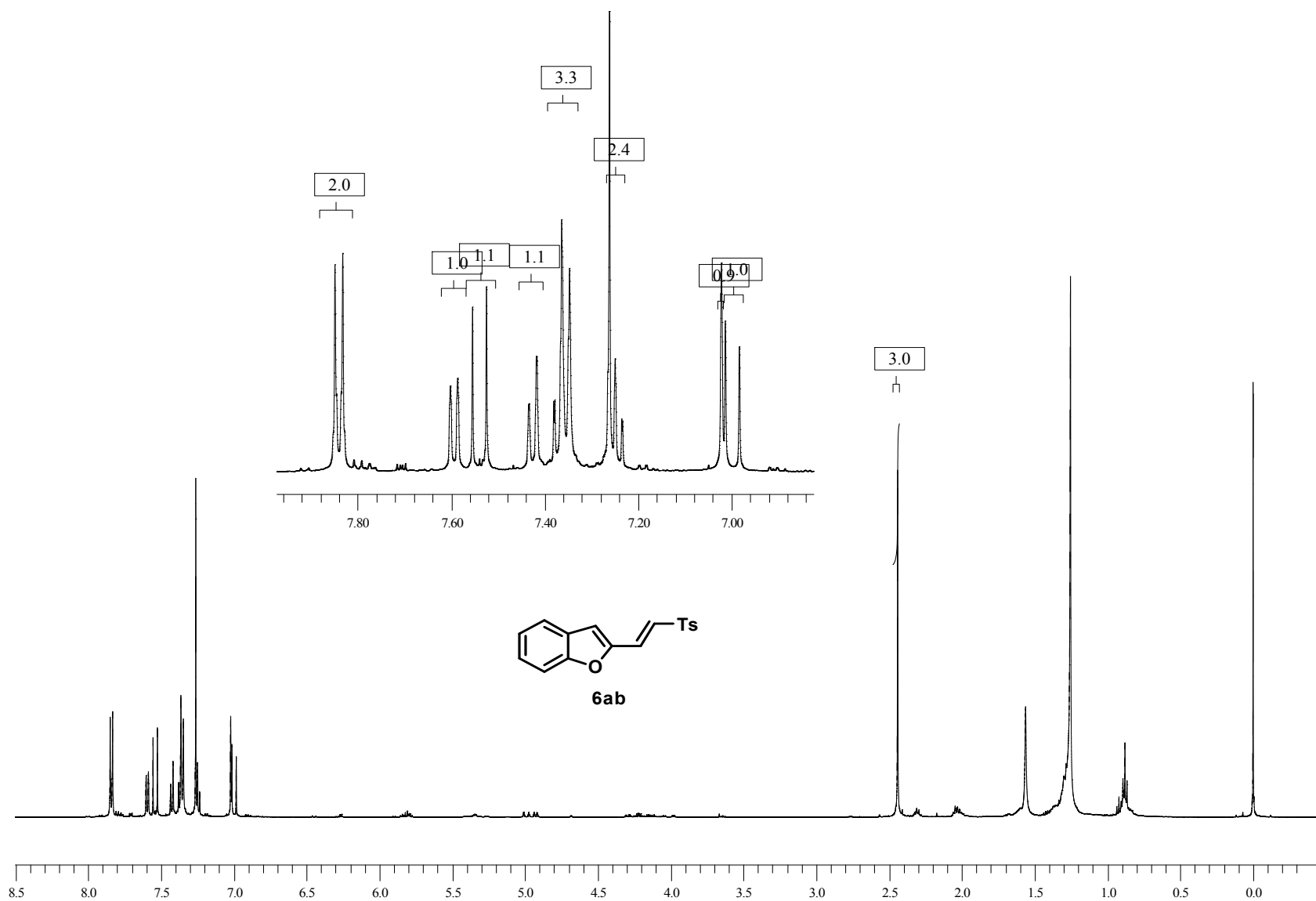
¹H spectrum of **6aa**, 500 MHz, CDCl₃



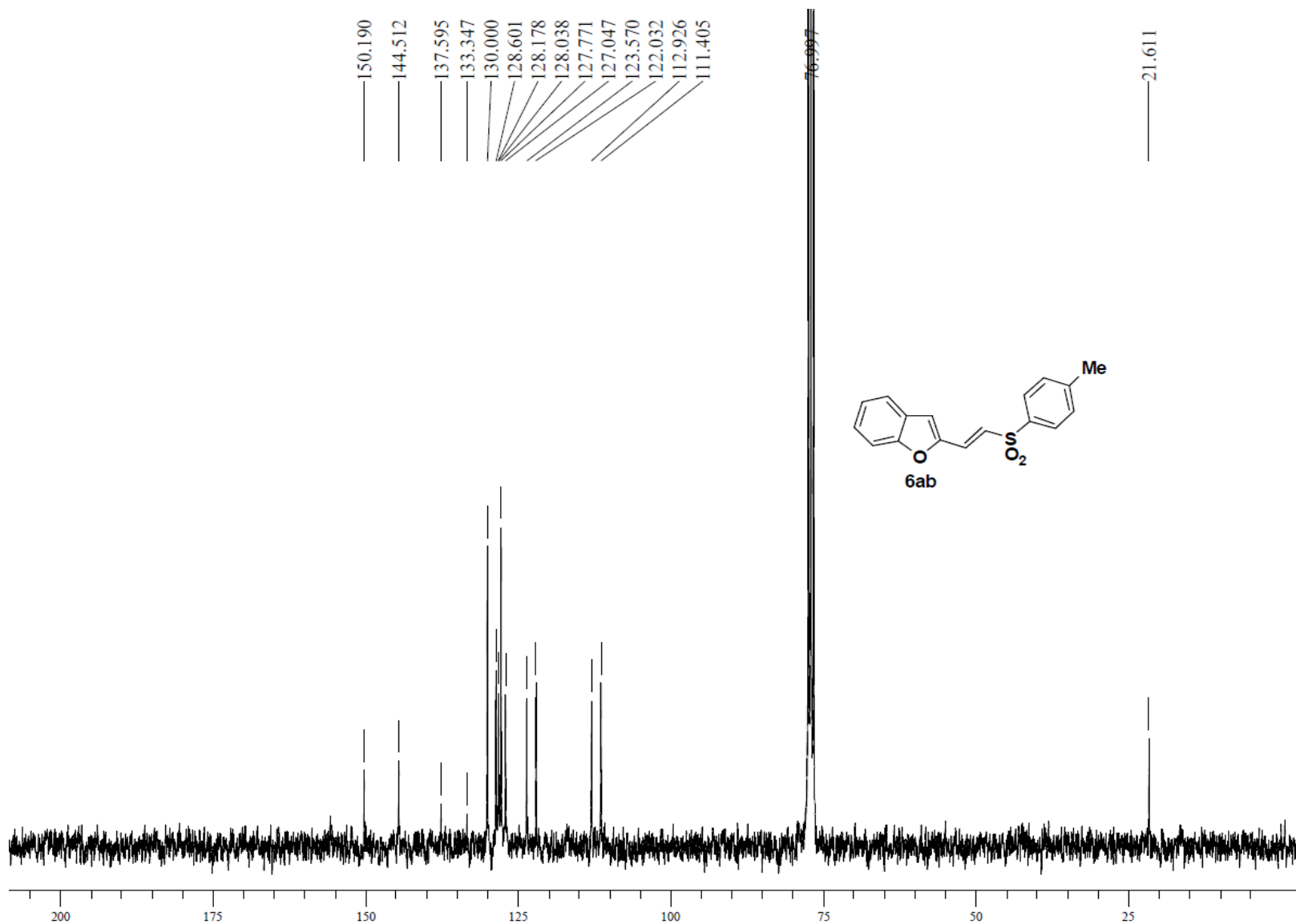
^{13}C spectrum of **6aa**, 75 MHz, CDCl_3



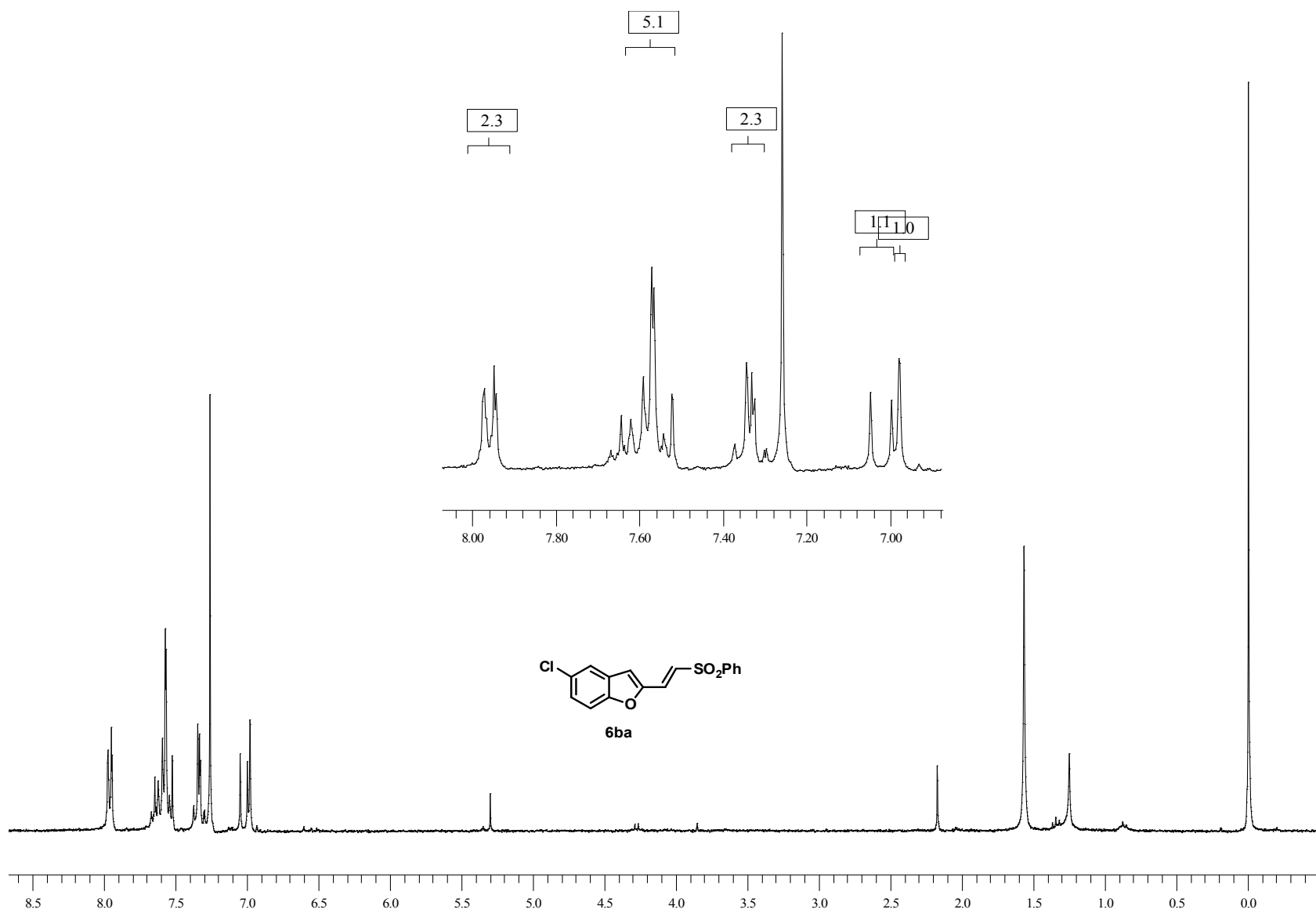
^{13}C NMR spectrum of **6ab**, 500 MHz, CDCl_3



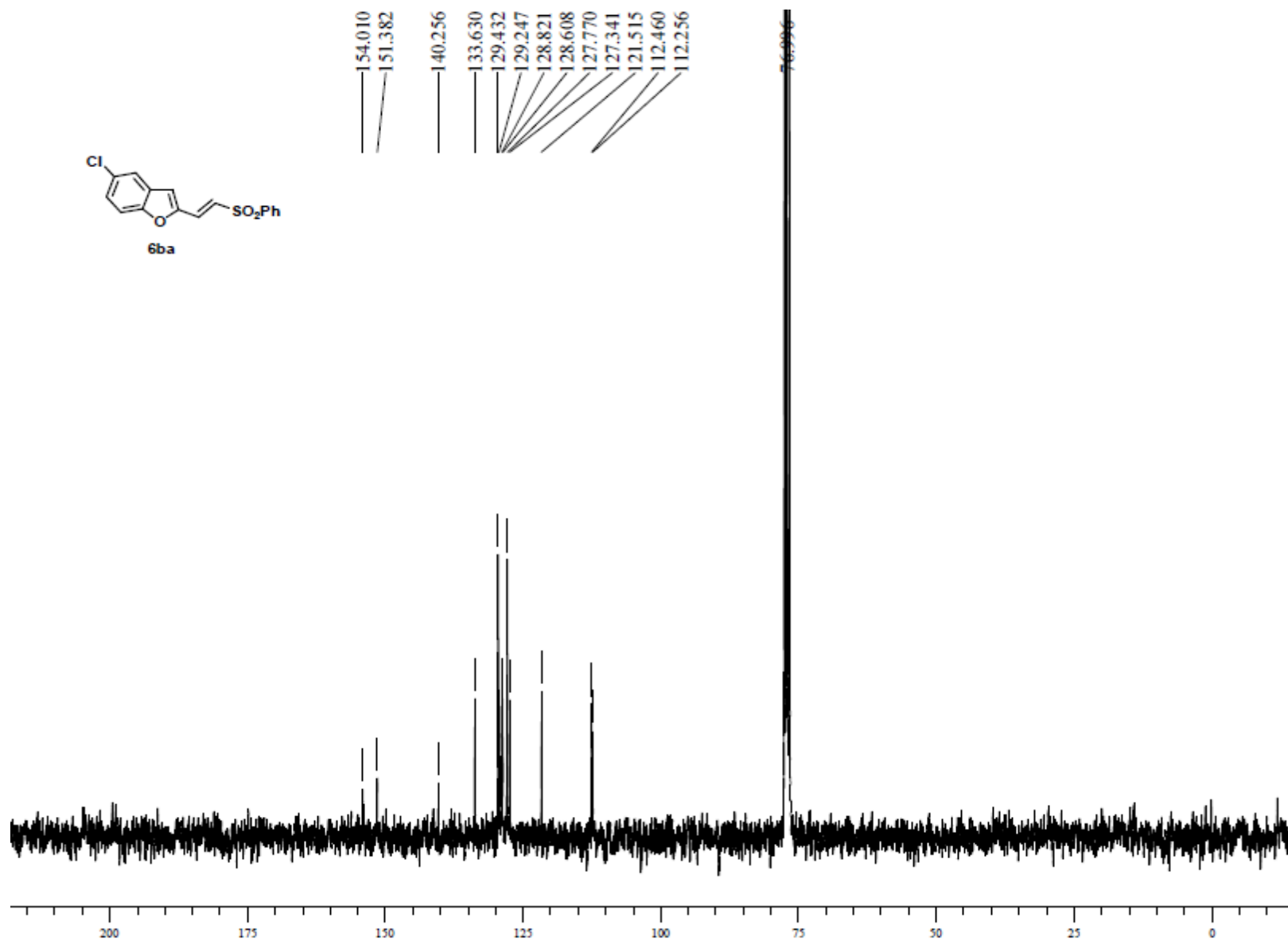
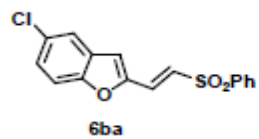
^{13}C spectrum of **6ab**, 75 MHz, CDCl_3



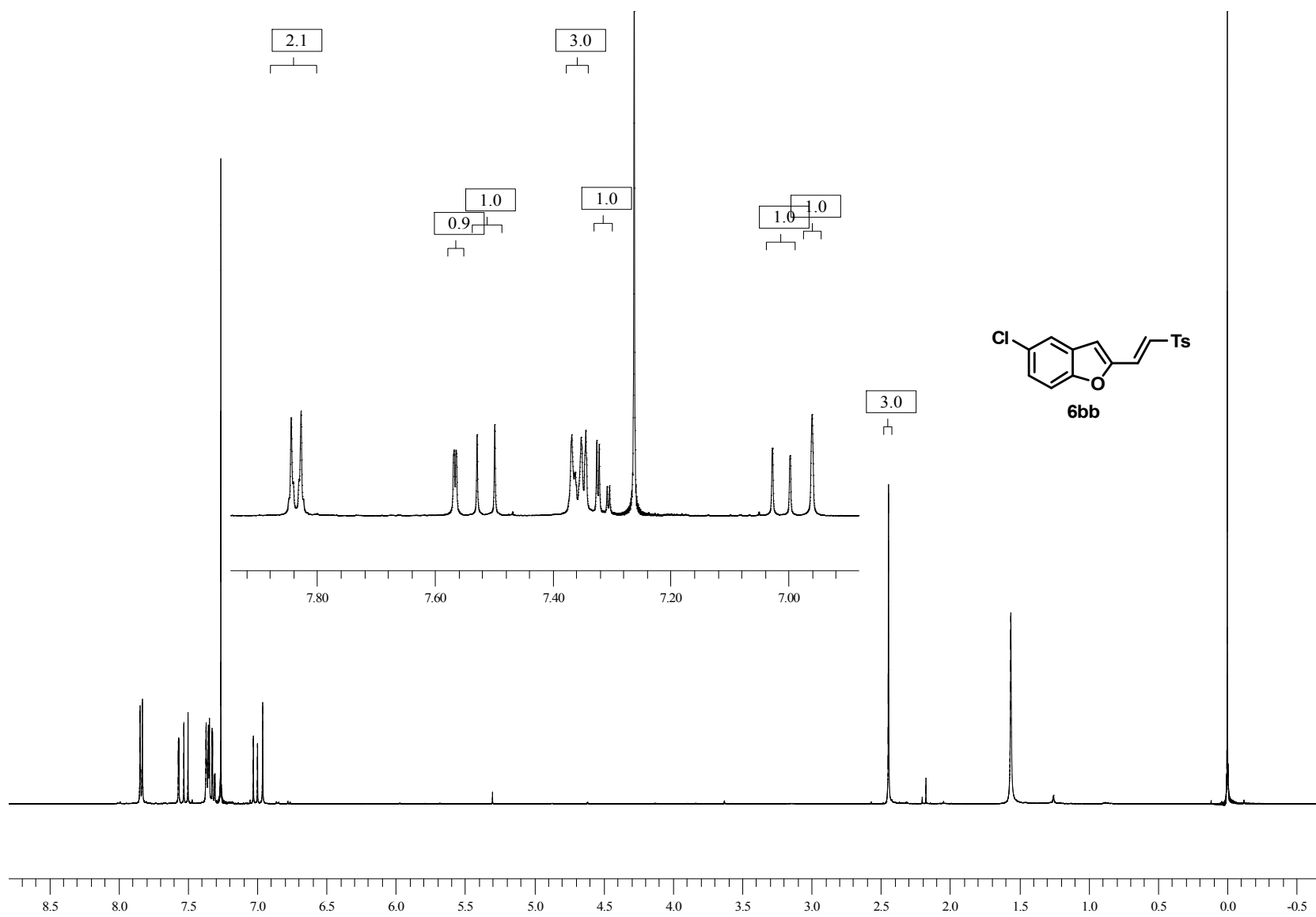
^{13}C spectrum of **6ba**, 300 MHz, CDCl_3



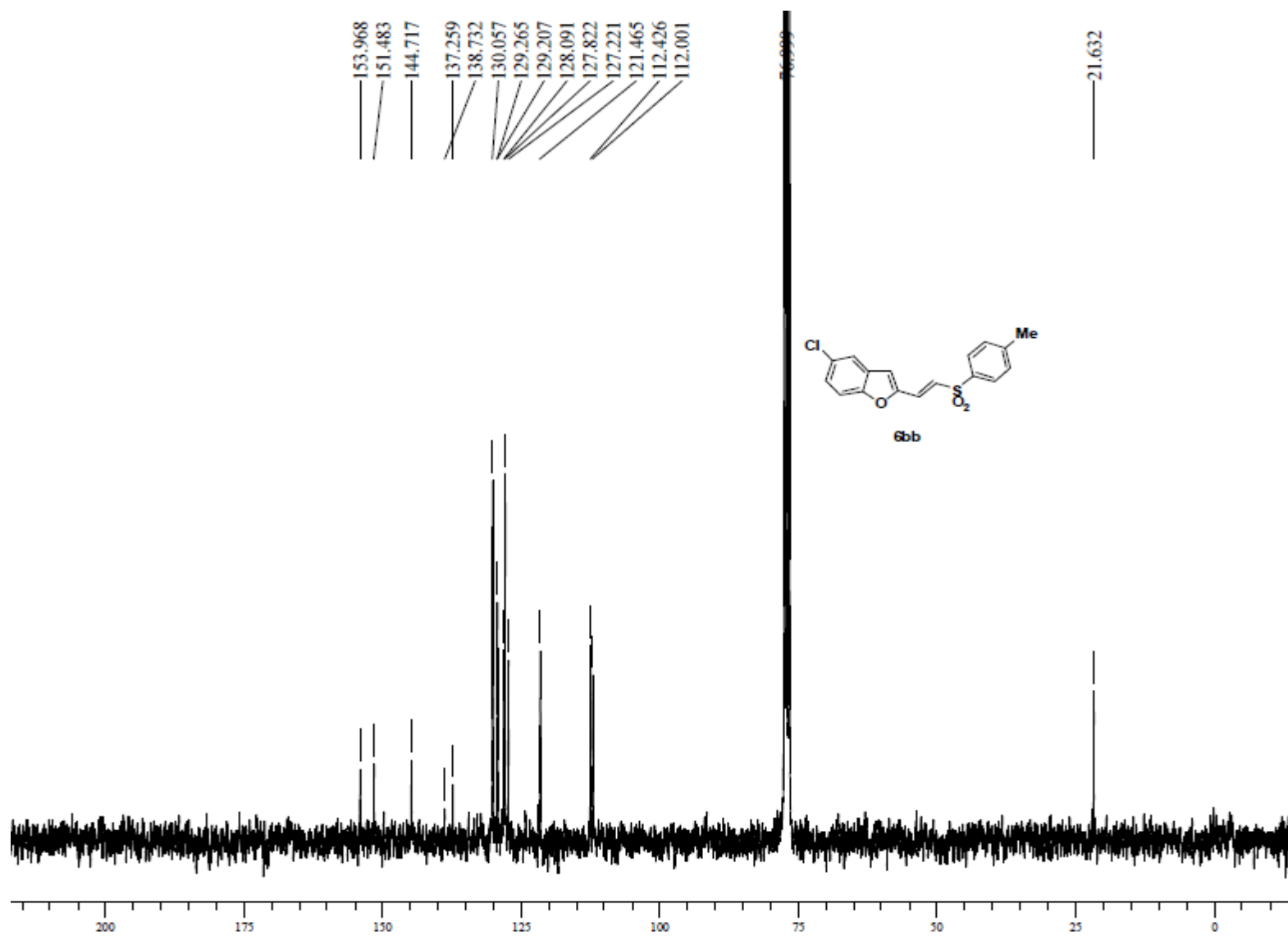
^{13}C spectrum of **6ba**, 75 MHz, CDCl_3



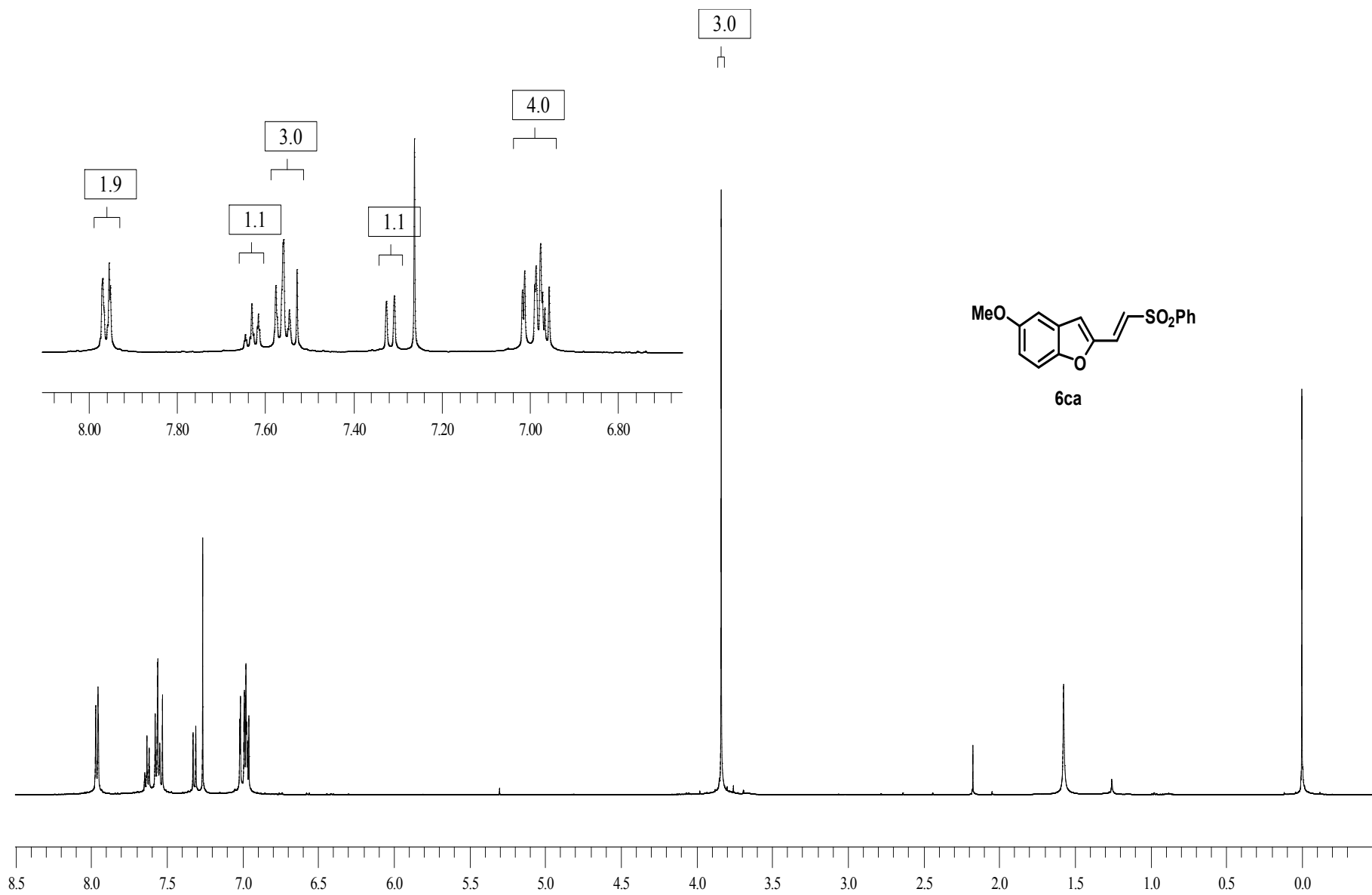
^{13}C spectrum of **6ba**, 500 MHz, CDCl_3



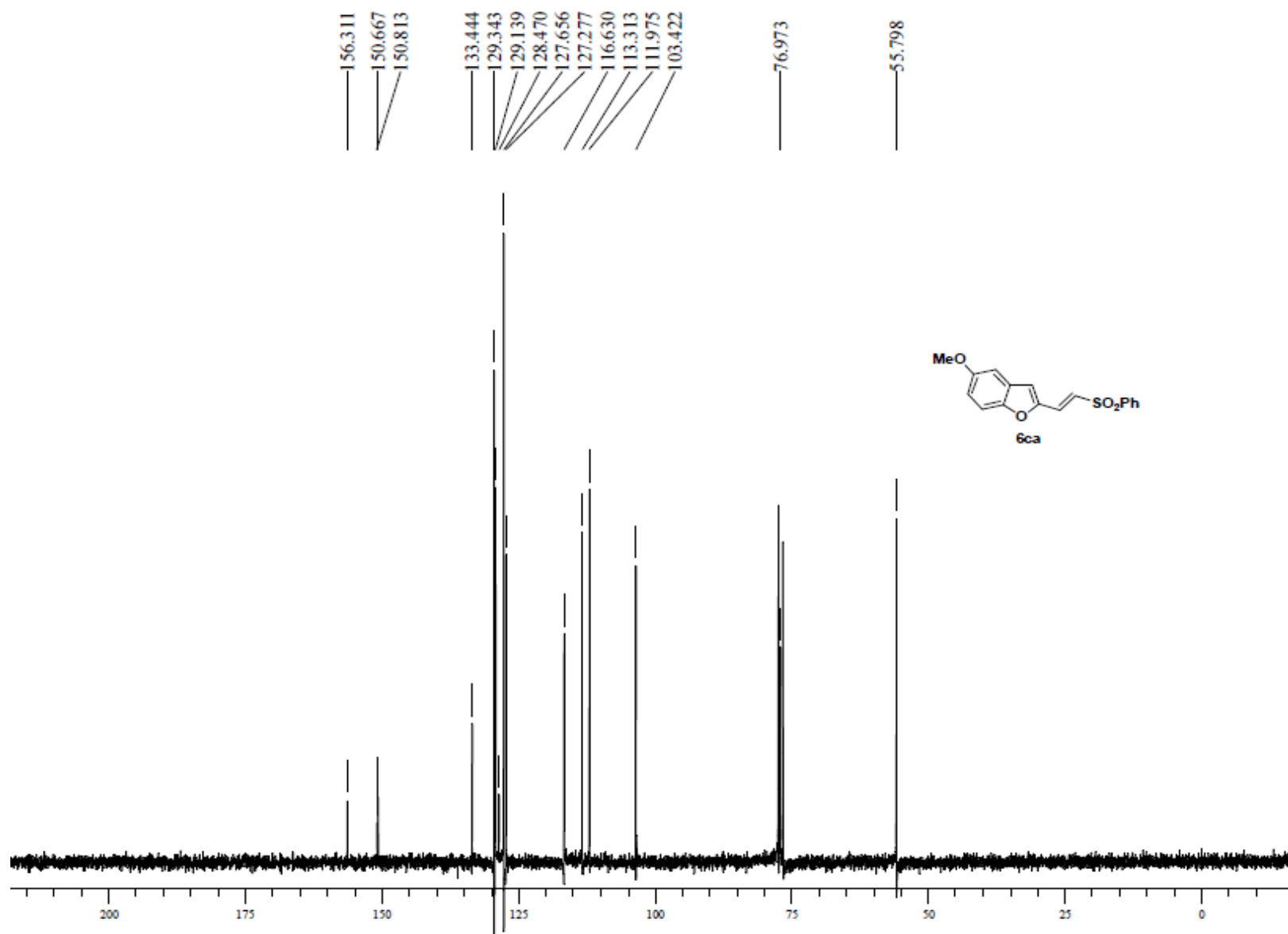
^{13}C spectrum of **6bb**, 75 MHz, CDCl_3



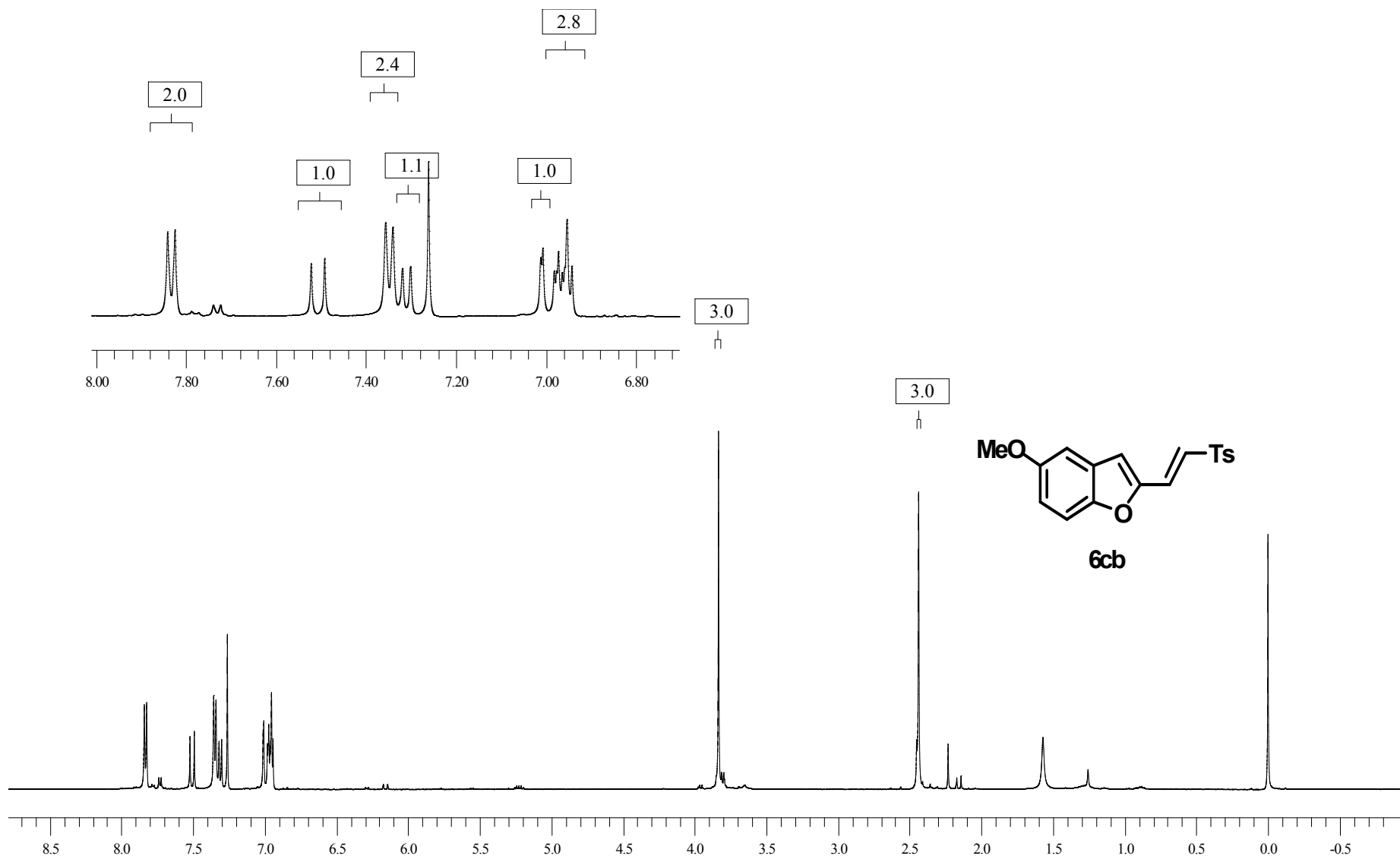
¹H spectrum of **6ca**, 500 MHz, CDCl₃



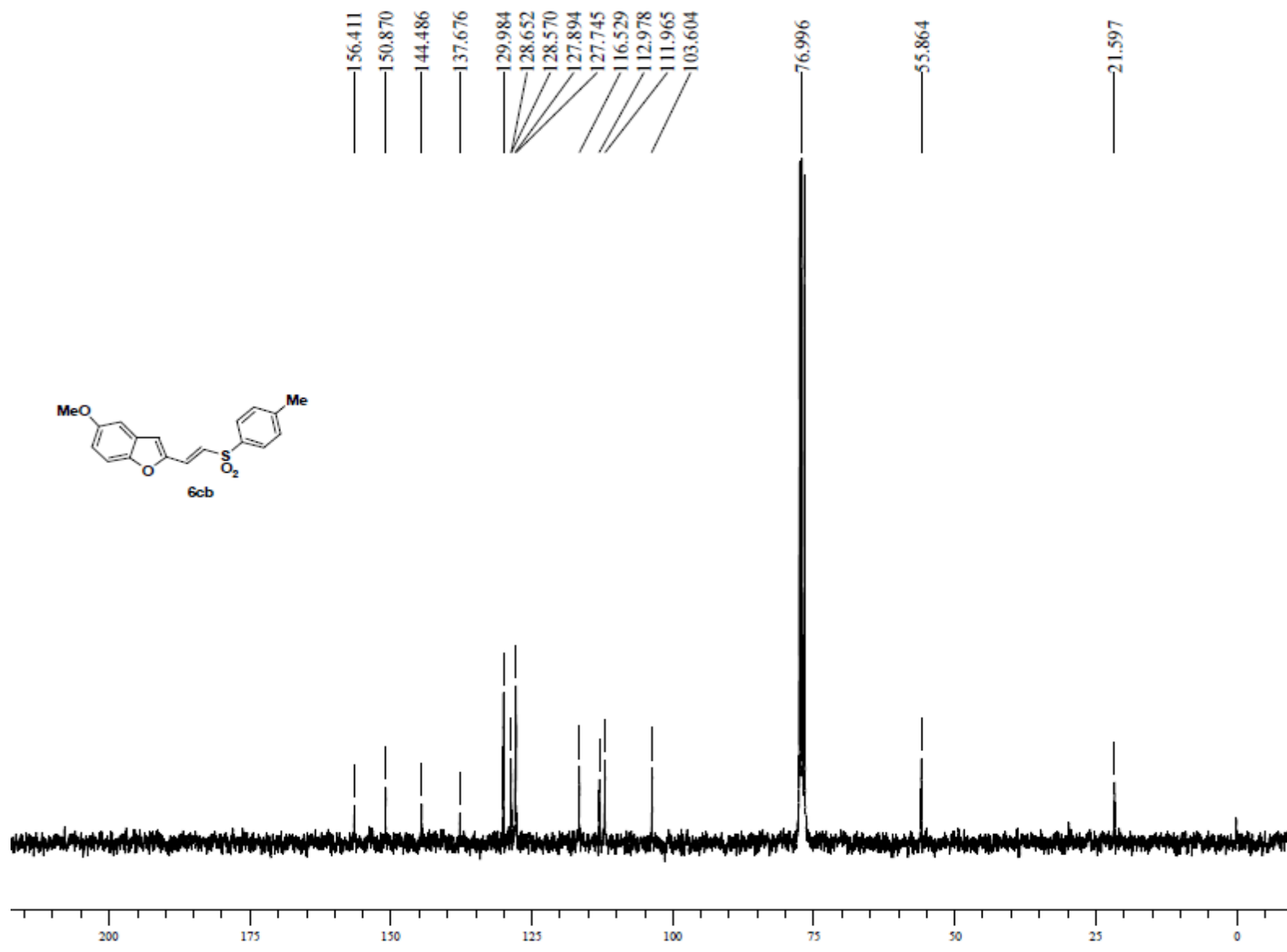
^{13}C spectrum of **6ca**, 75 MHz, CDCl_3



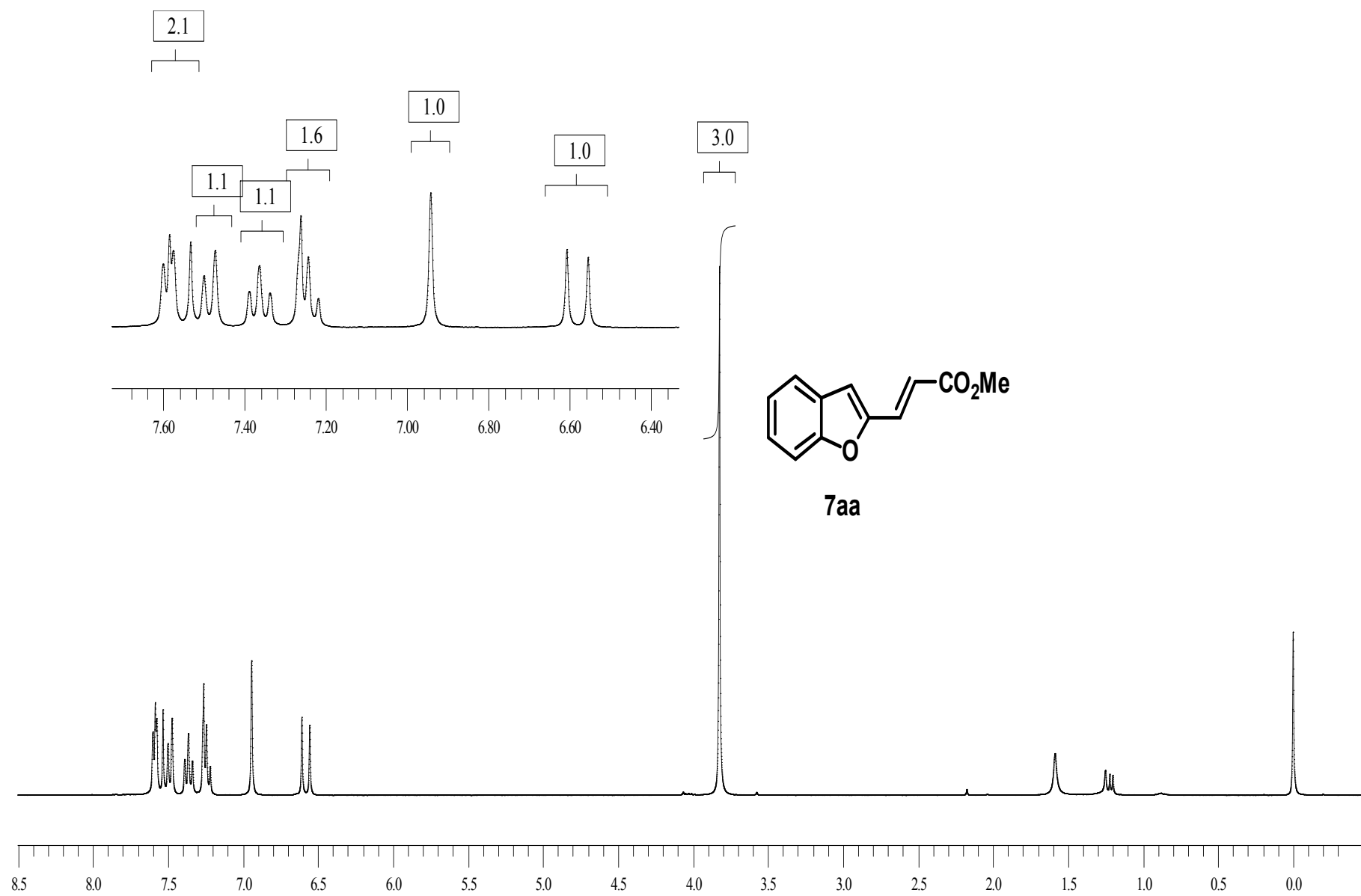
¹H spectrum of **6cb**, 500 MHz, CDCl₃



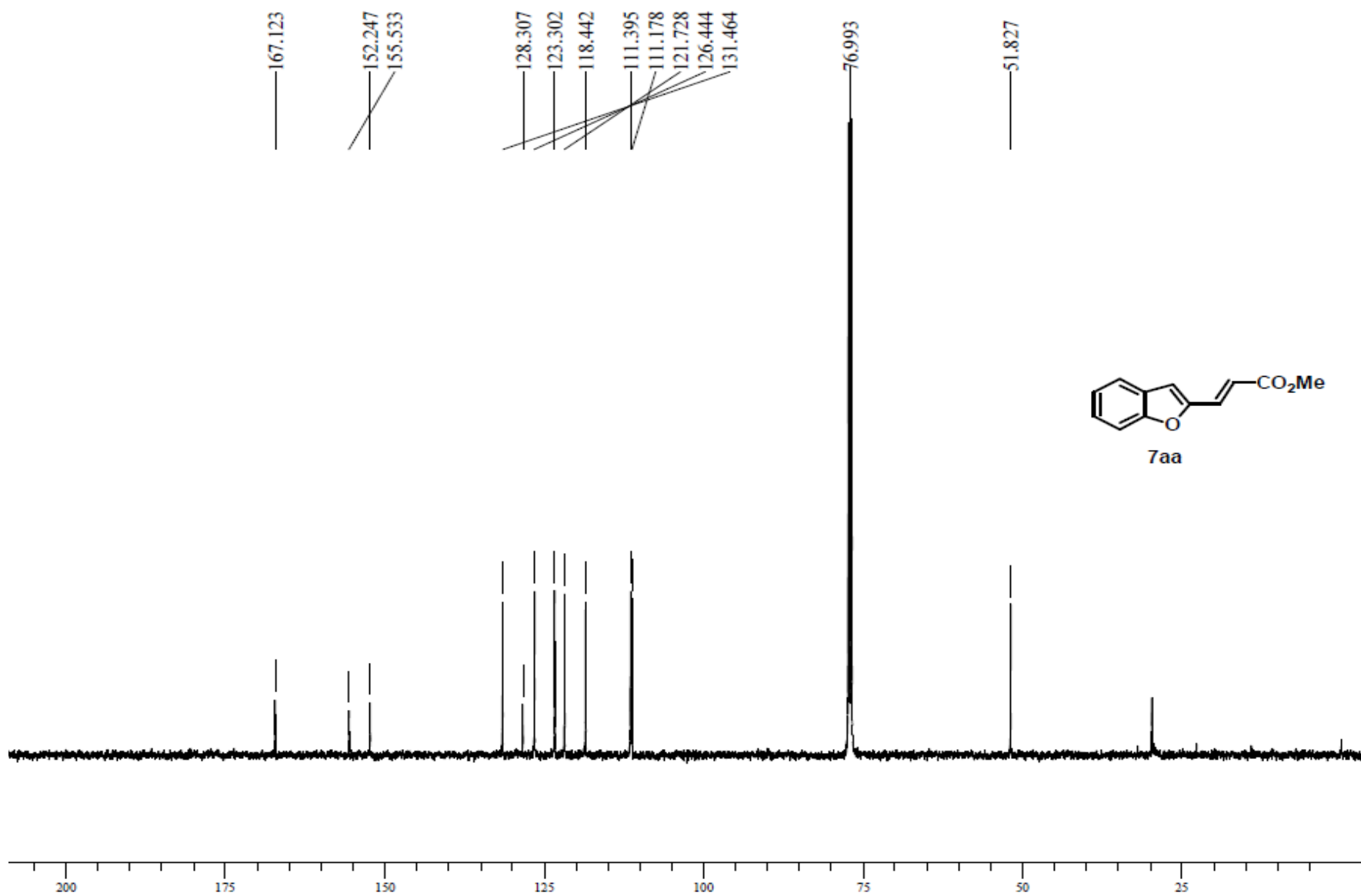
^{13}C spectrum of **6b**, 75 MHz, CDCl_3



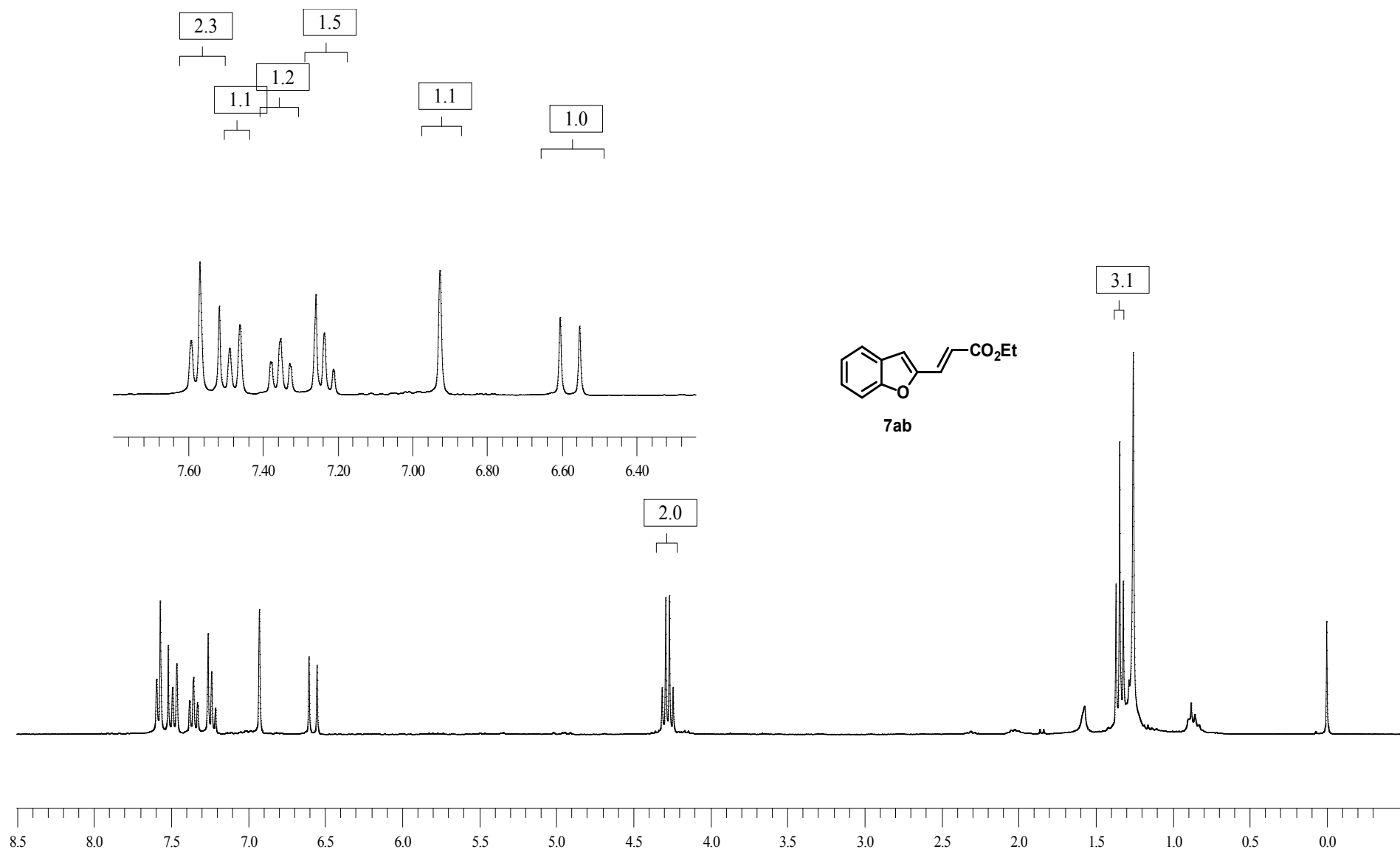
¹³C NMR spectrum of **7aa**, 300 MHz, CDCl₃



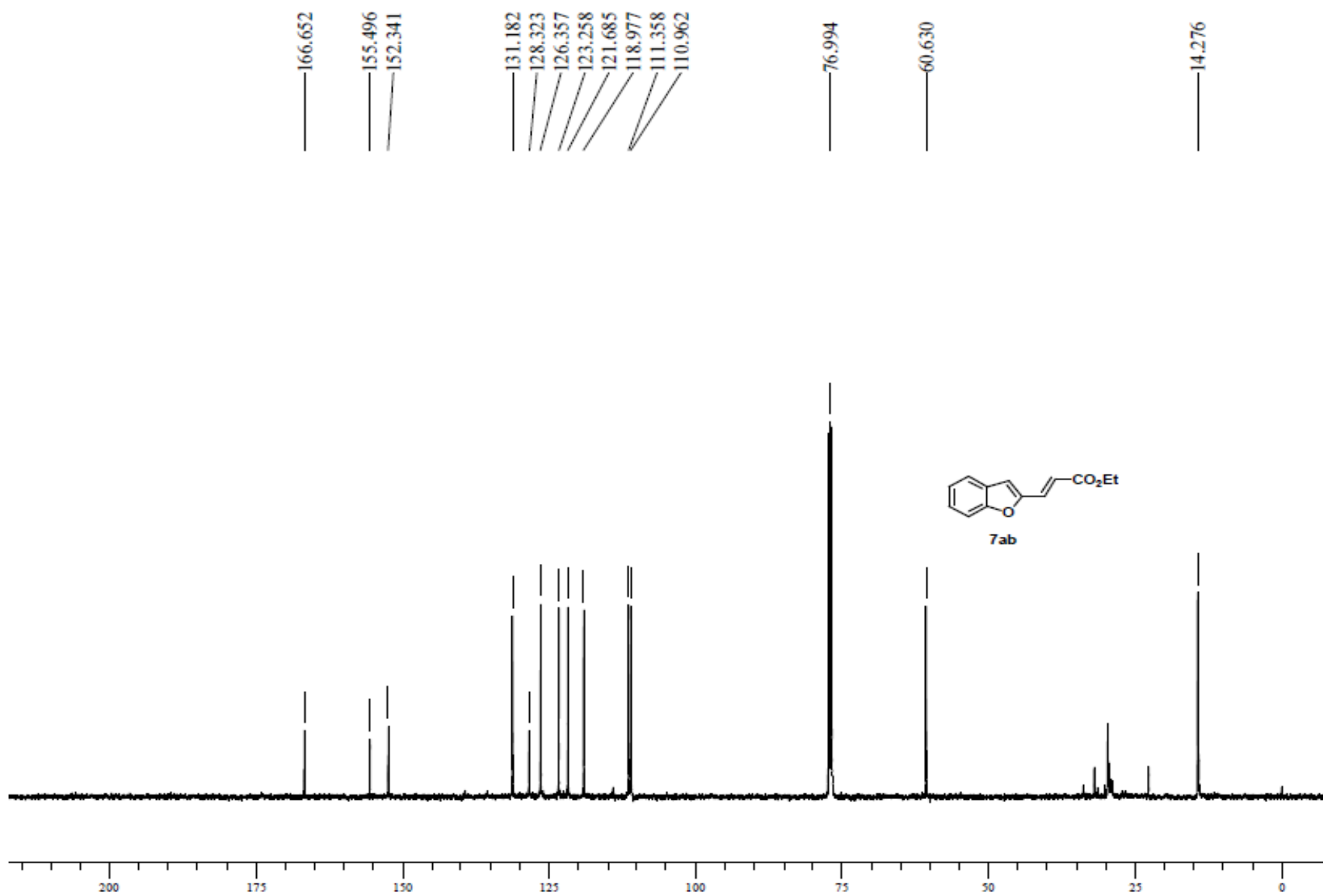
^{13}C spectrum of **7aa**, 125 MHz, CDCl_3



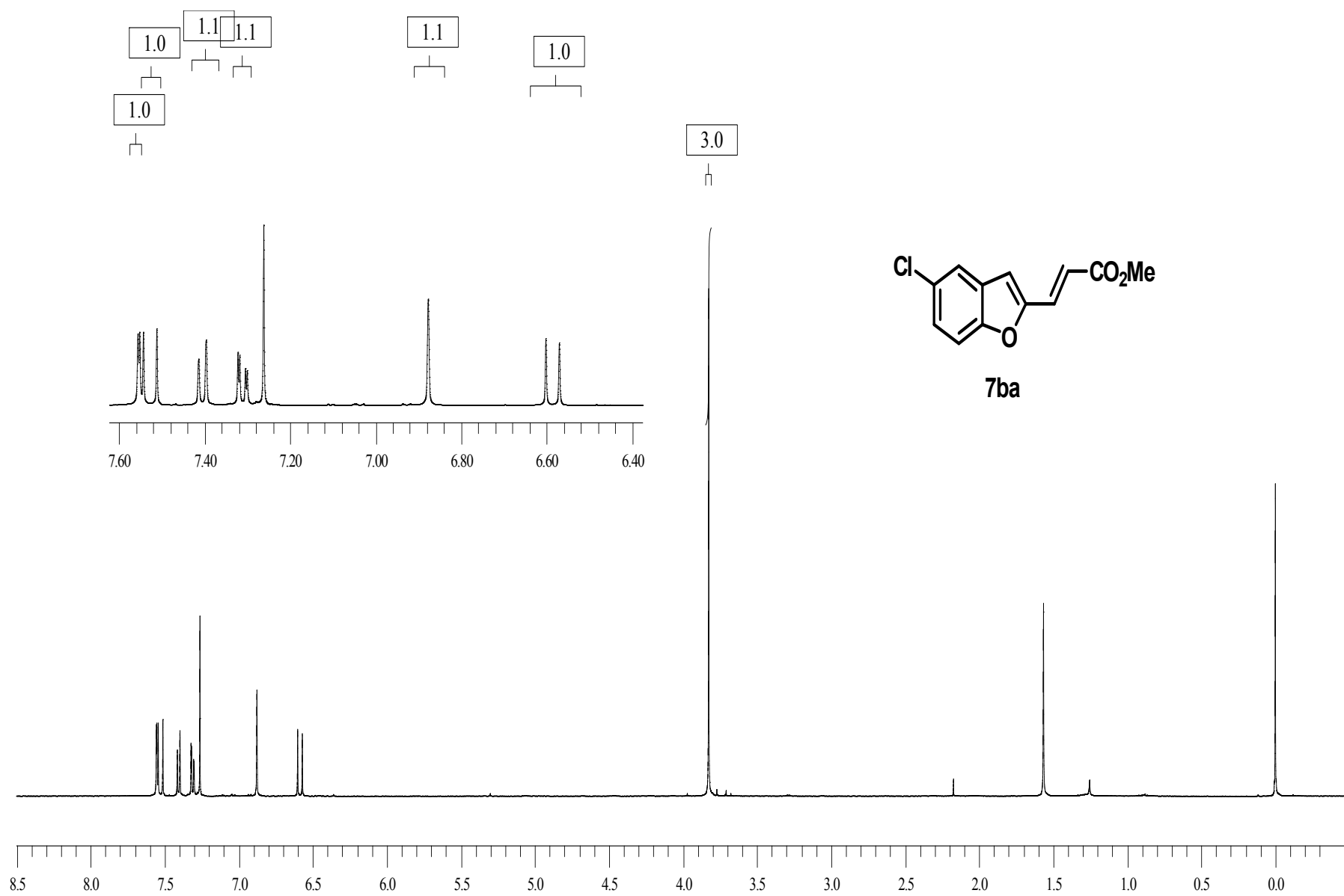
¹³C NMR spectrum of **7ab**, 300 MHz, CDCl₃



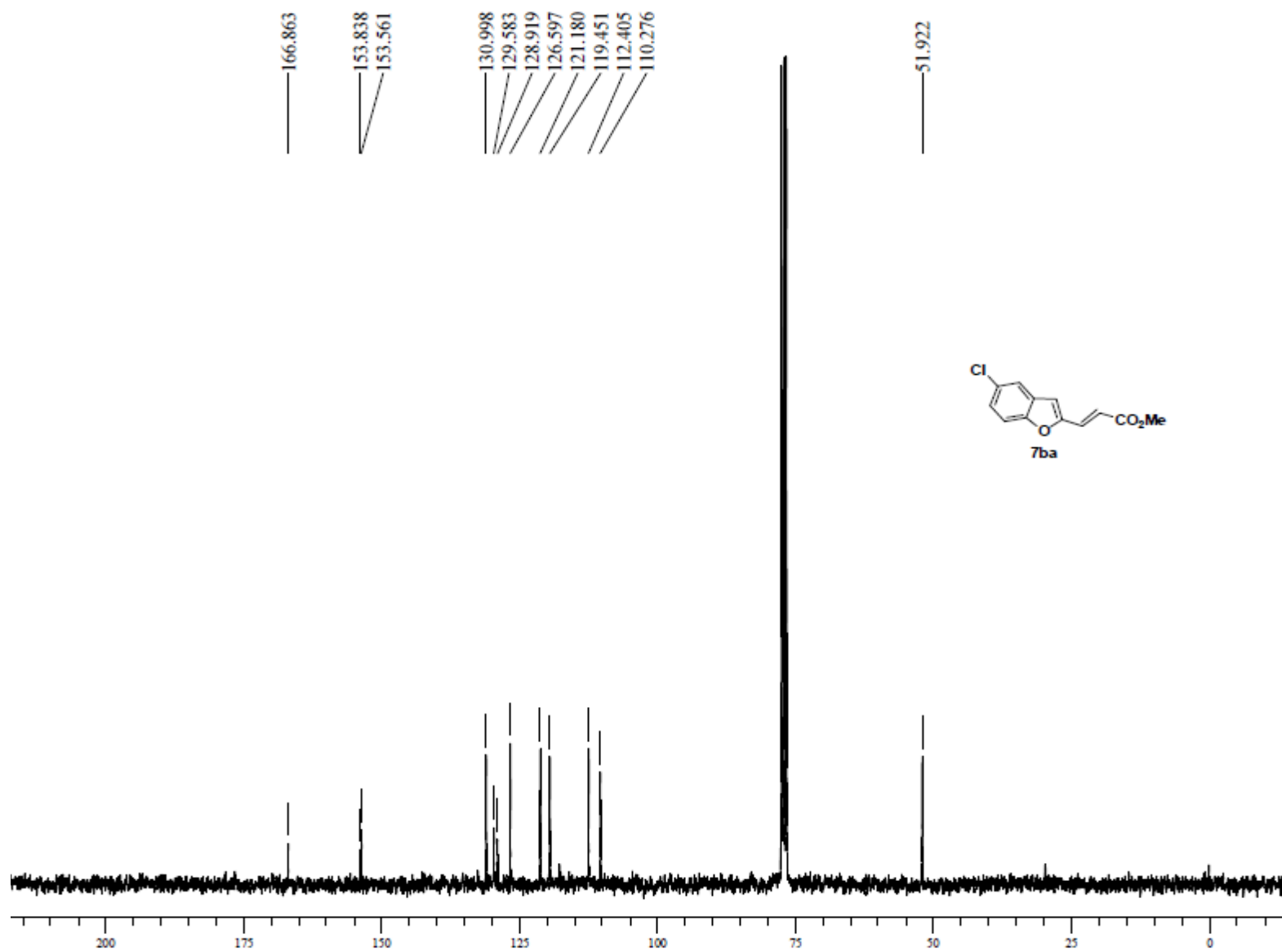
^{13}C spectrum of **7ab**, 125 MHz, CDCl_3



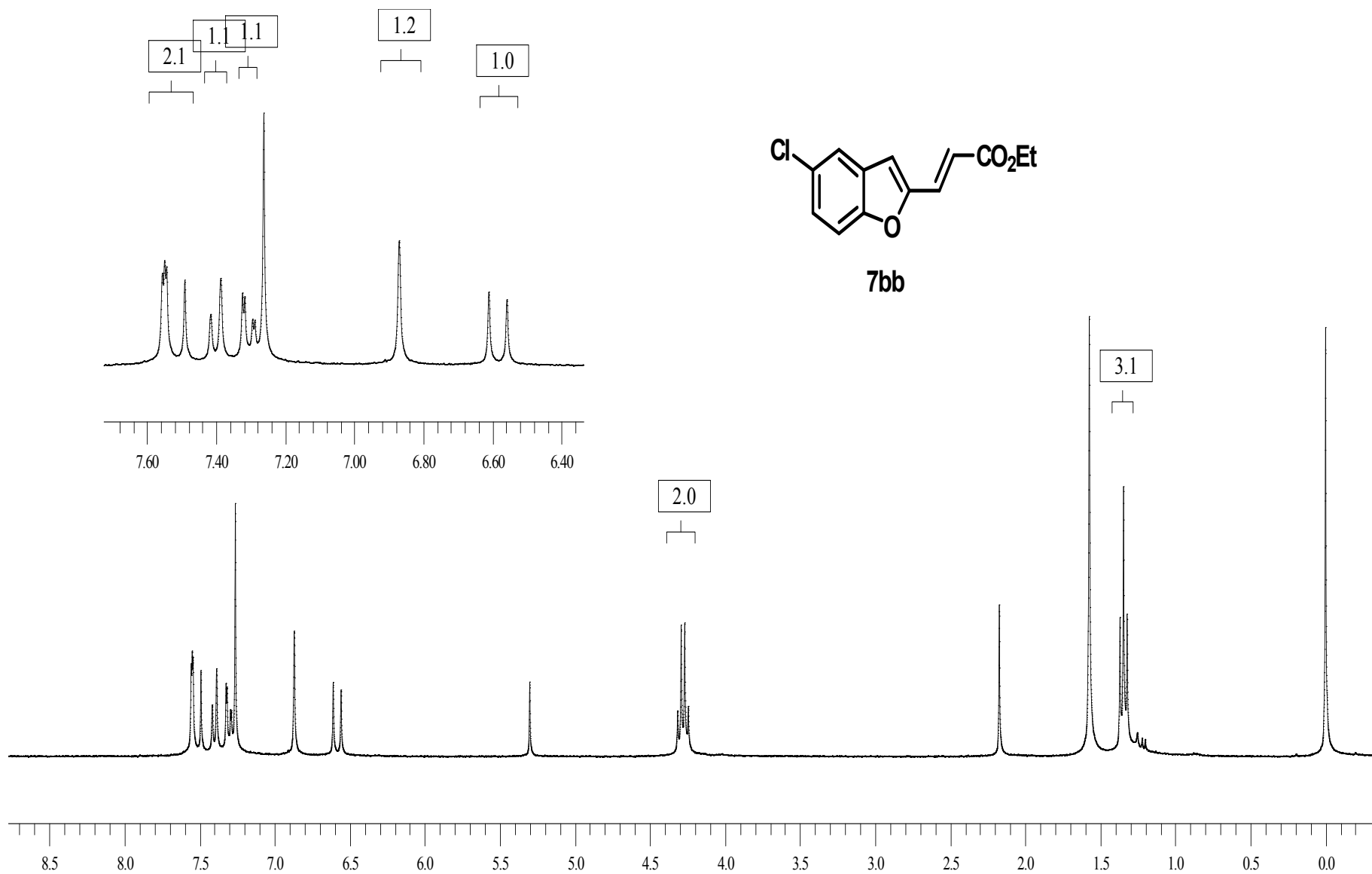
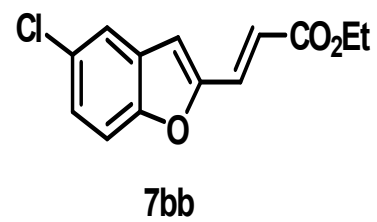
¹³C NMR spectrum of **7ba**, 500 MHz, CDCl₃



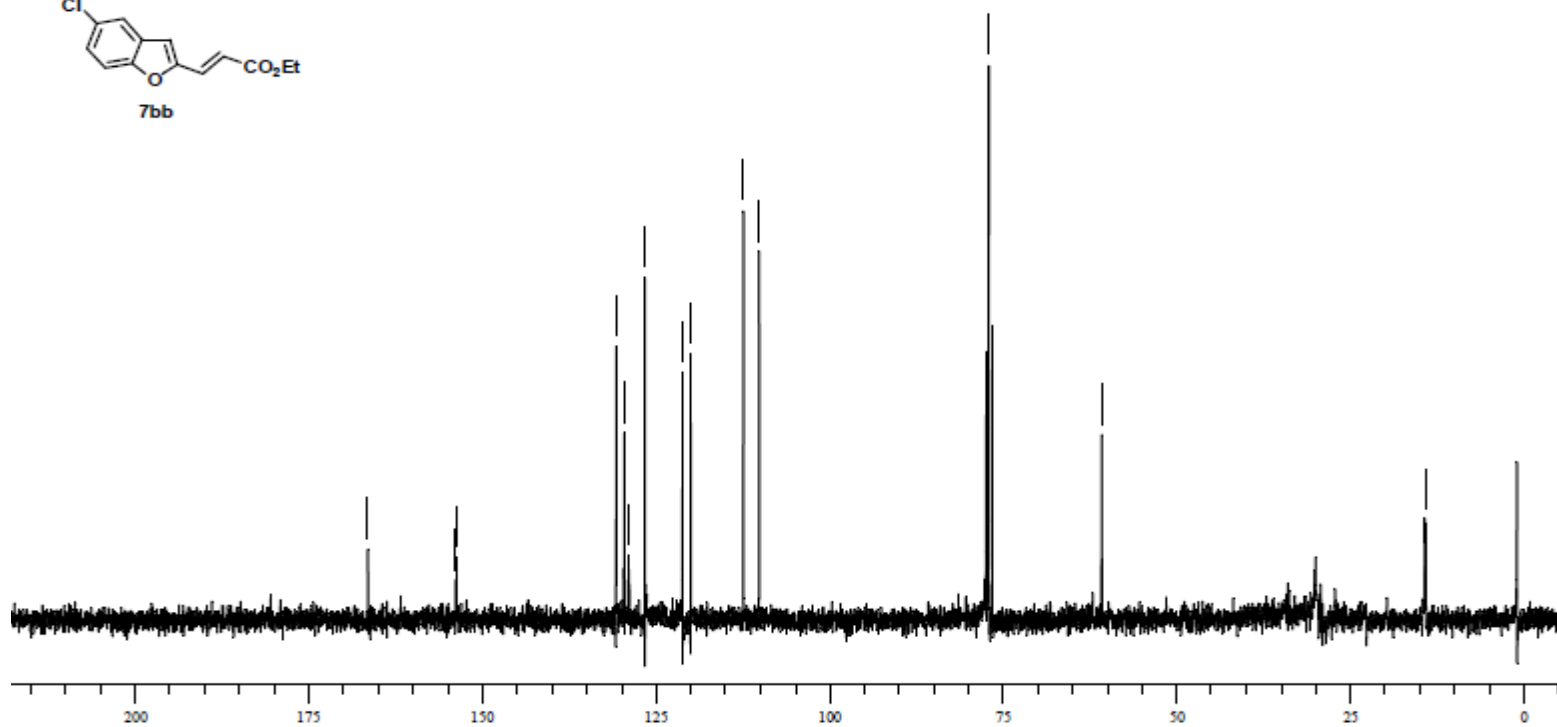
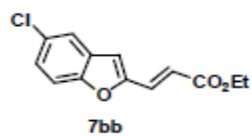
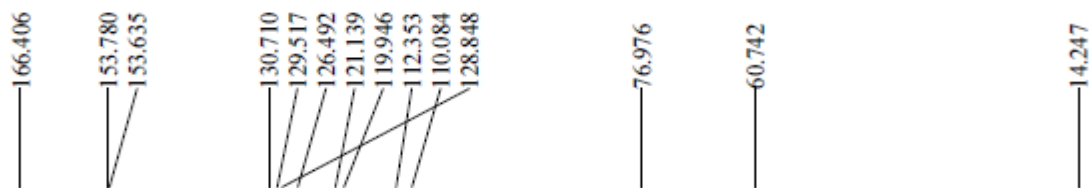
^{13}C spectrum of **7ba**, 75 MHz, CDCl_3



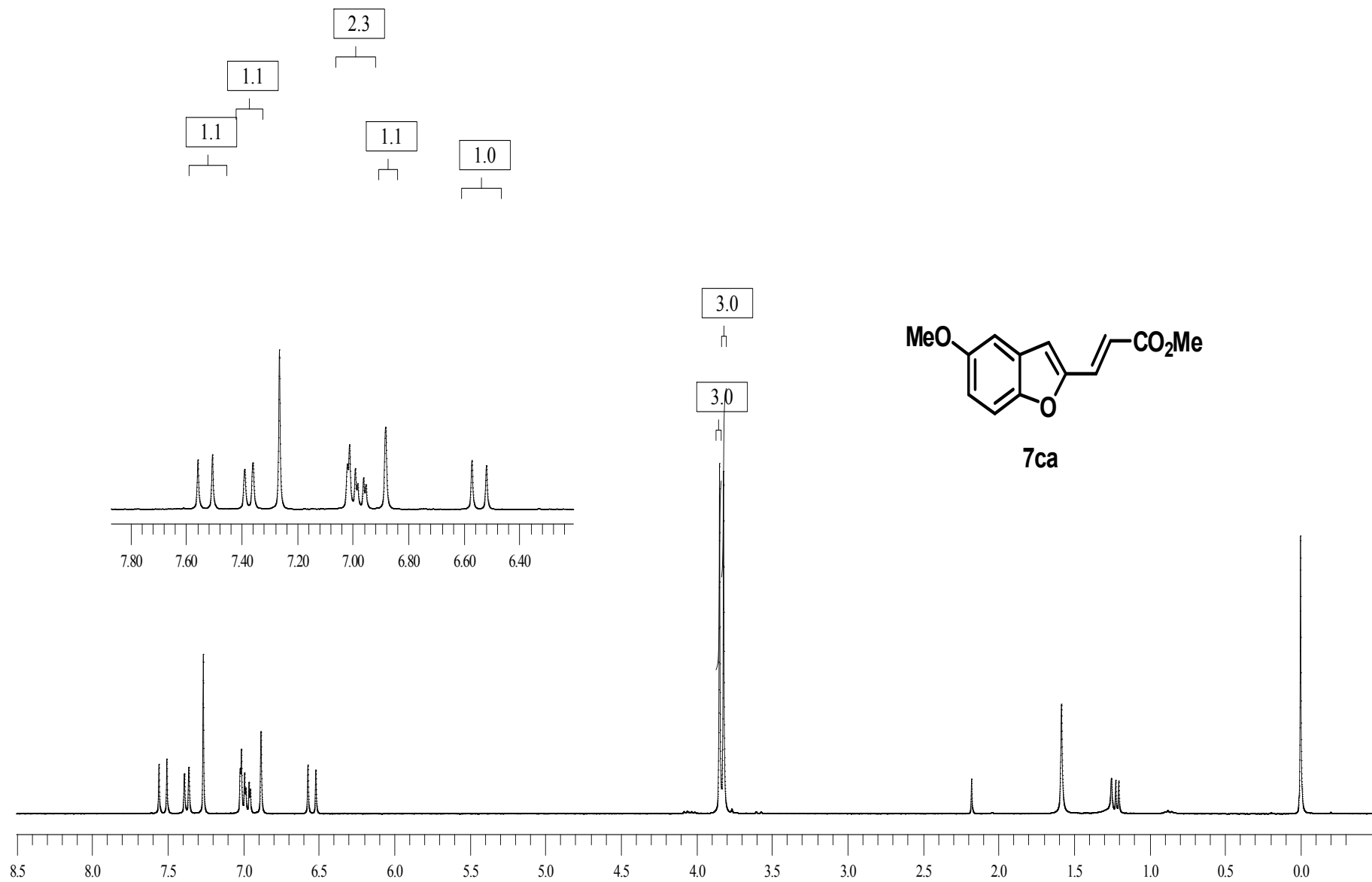
^{13}C spectrum of **7ba**, 300 MHz, CDCl_3



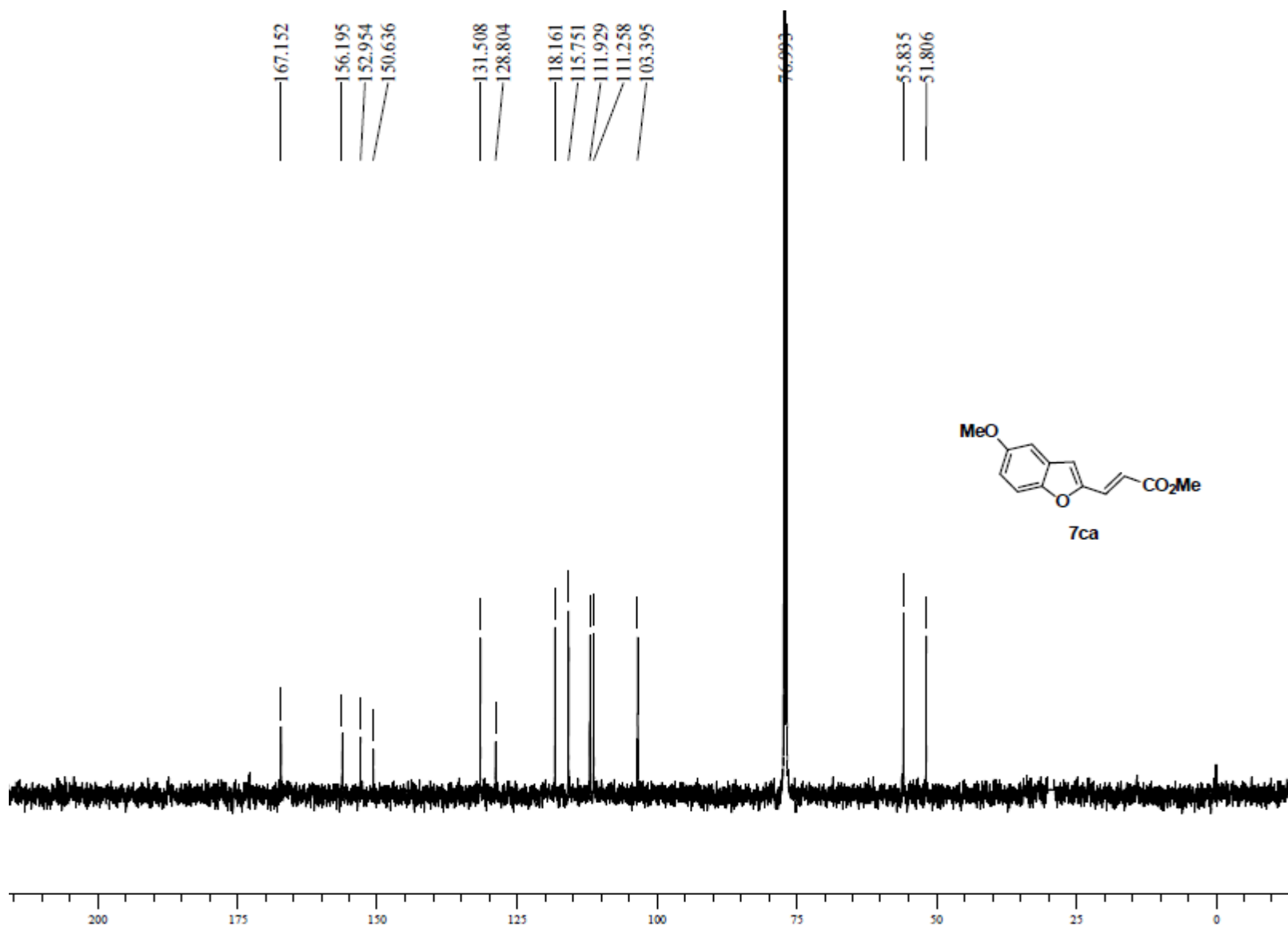
^{13}C spectrum of **7bb**, 75 MHz, CDCl_3



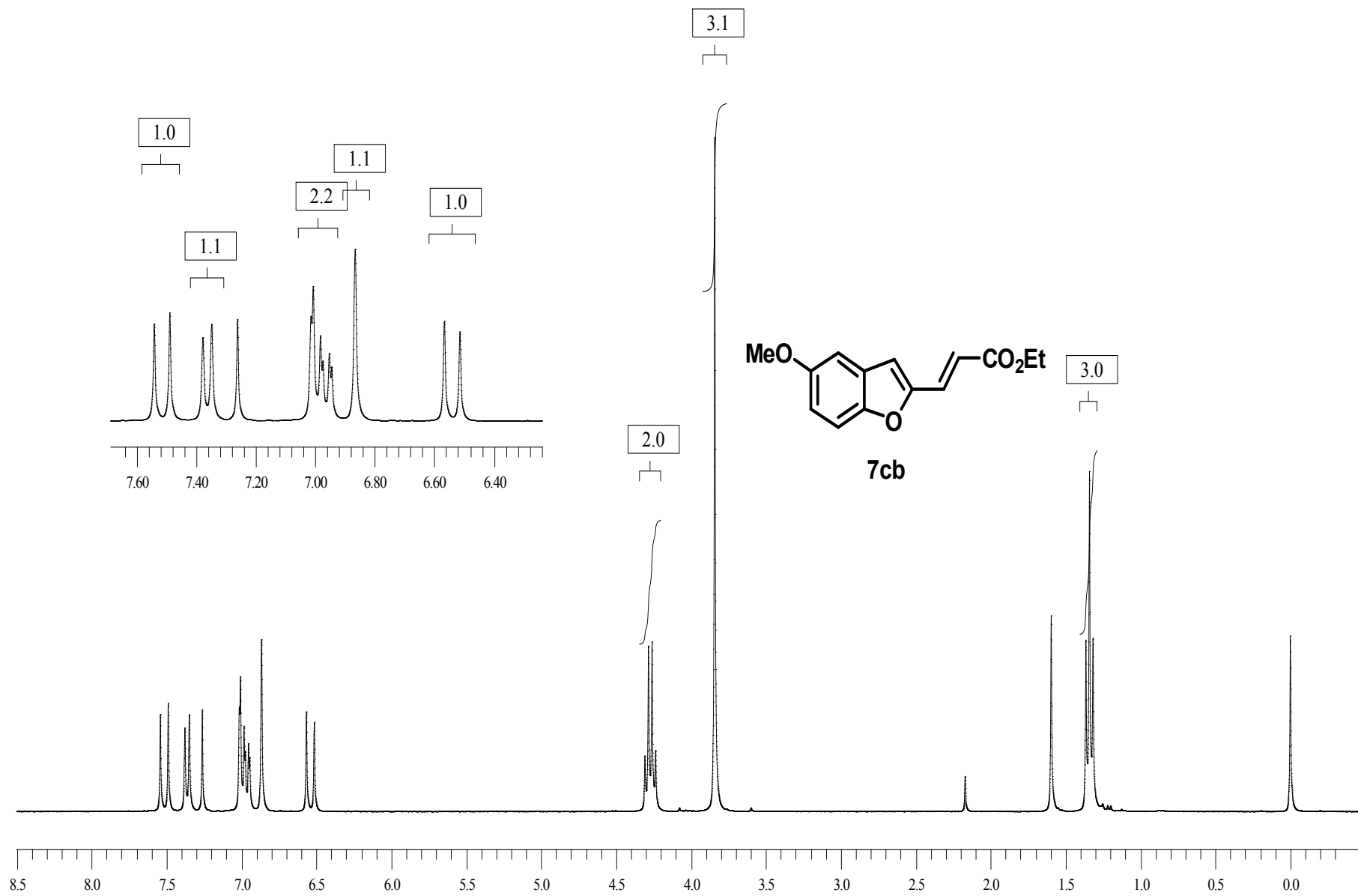
¹H spectrum of 7ca, 300 MHz, CDCl₃



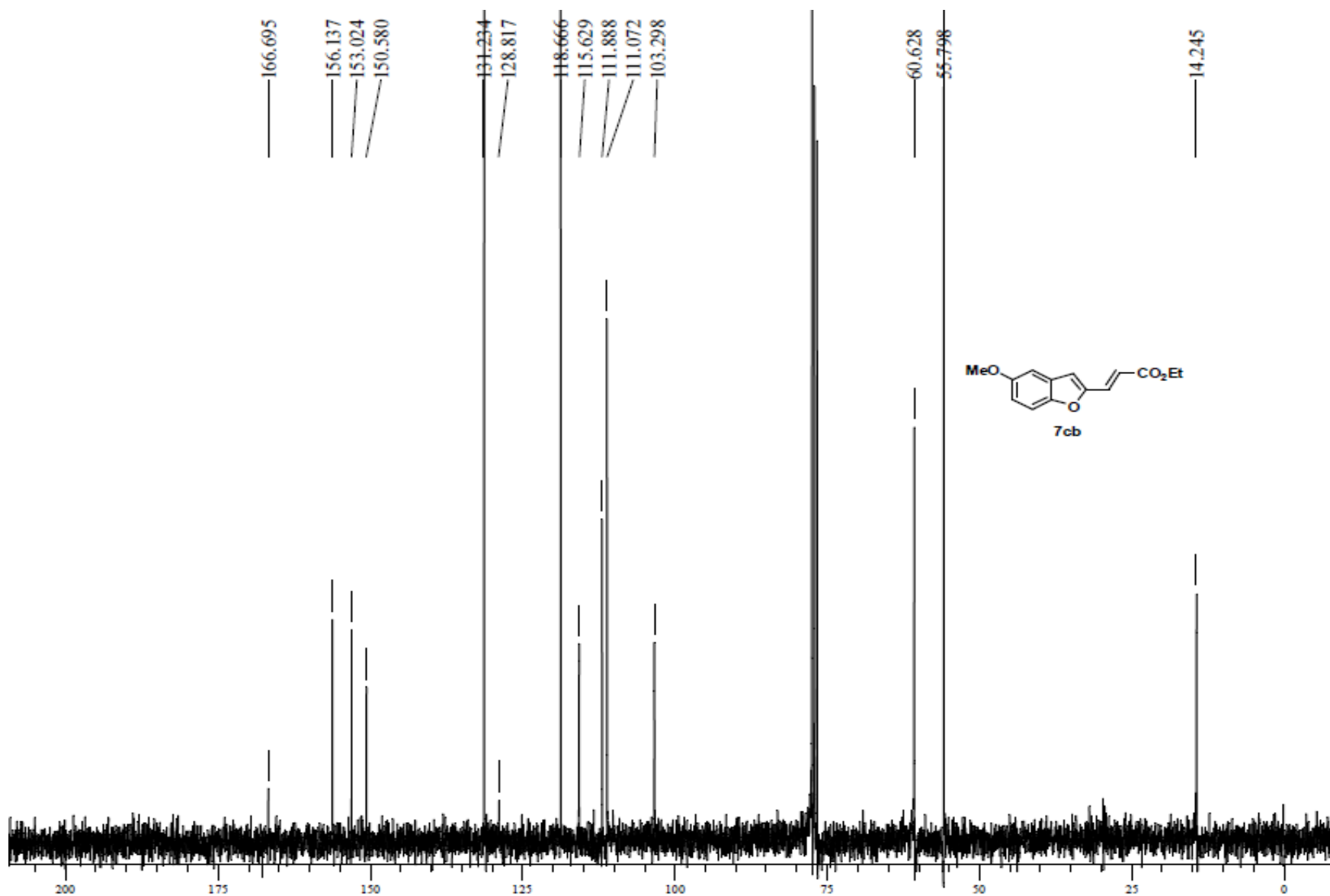
^{13}C spectrum of **7ca**, 75 MHz, CDCl_3



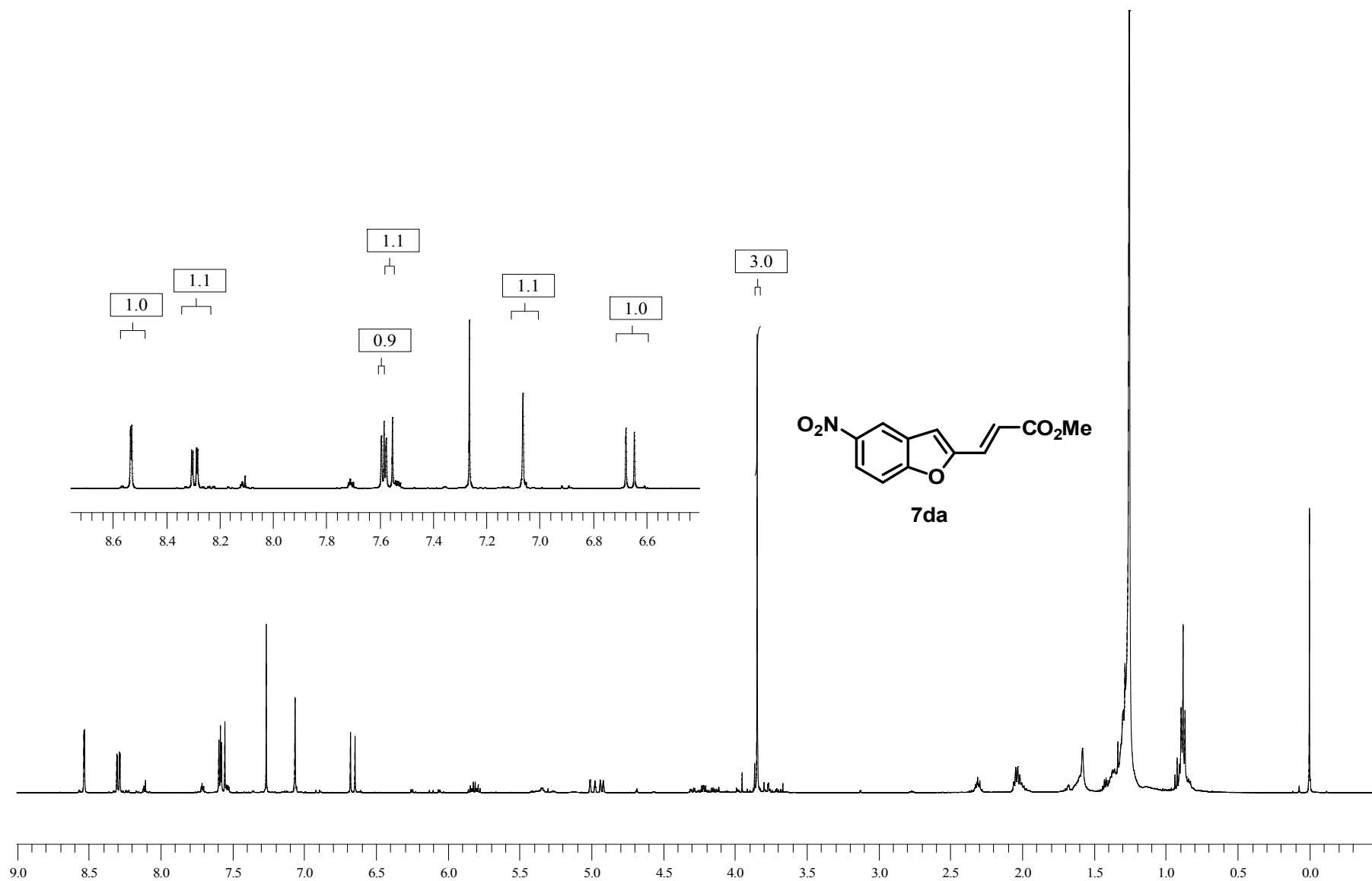
¹H spectrum of **7cb**, 300 MHz, CDCl₃



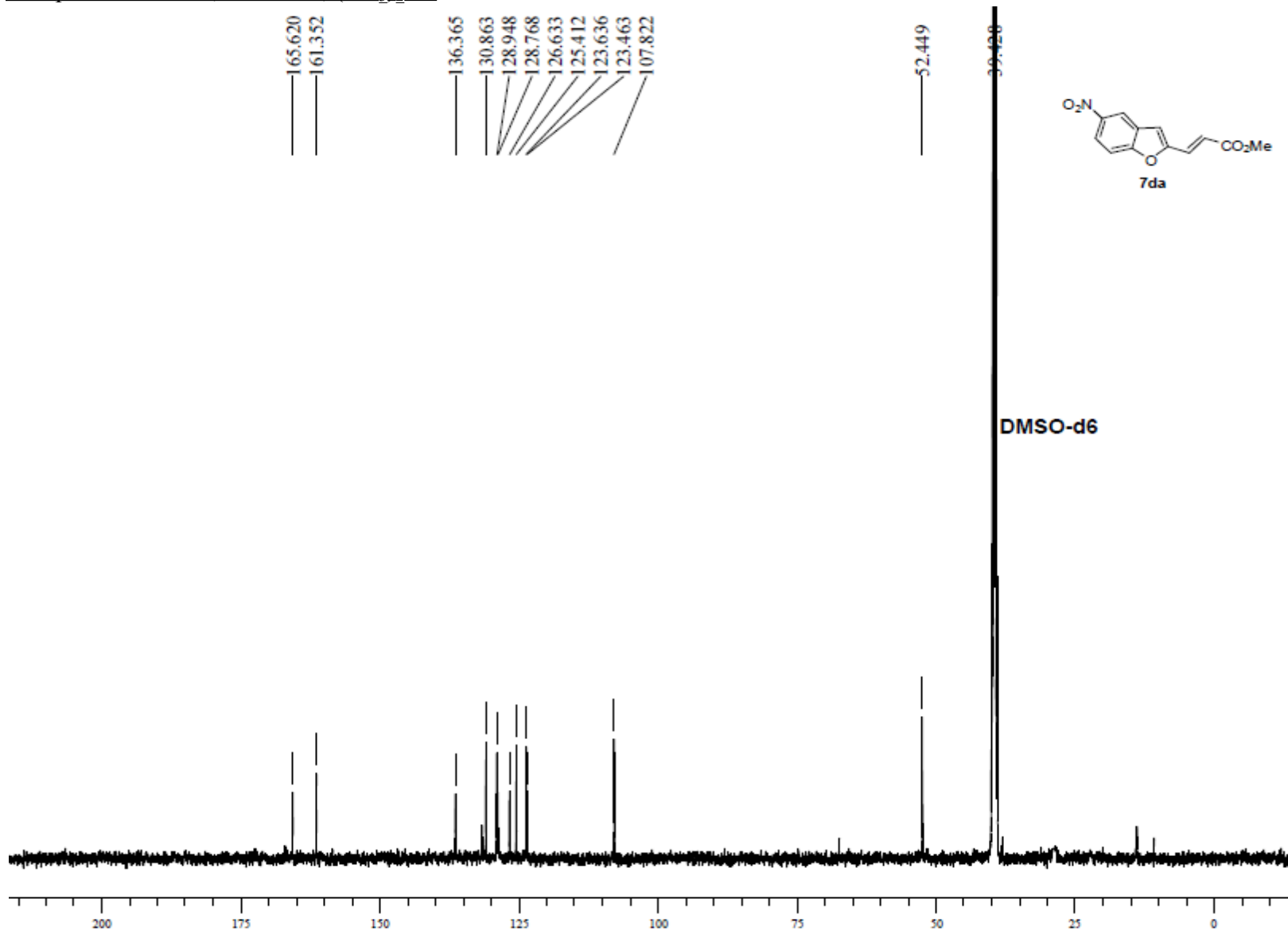
^{13}C spectrum of **7cb**, 75 MHz, CDCl_3



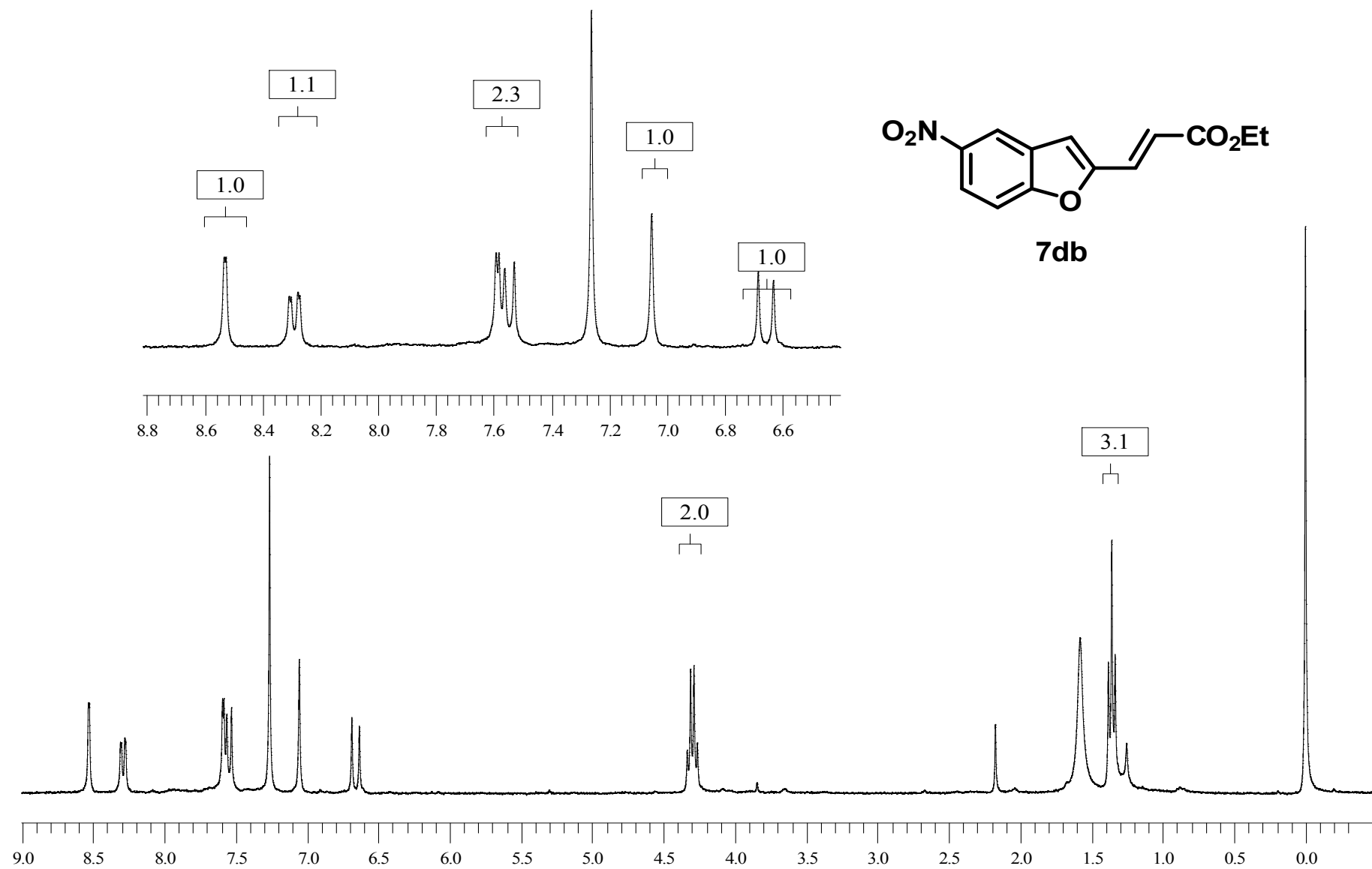
¹H spectrum of 7da, 500 MHz, CDCl₃



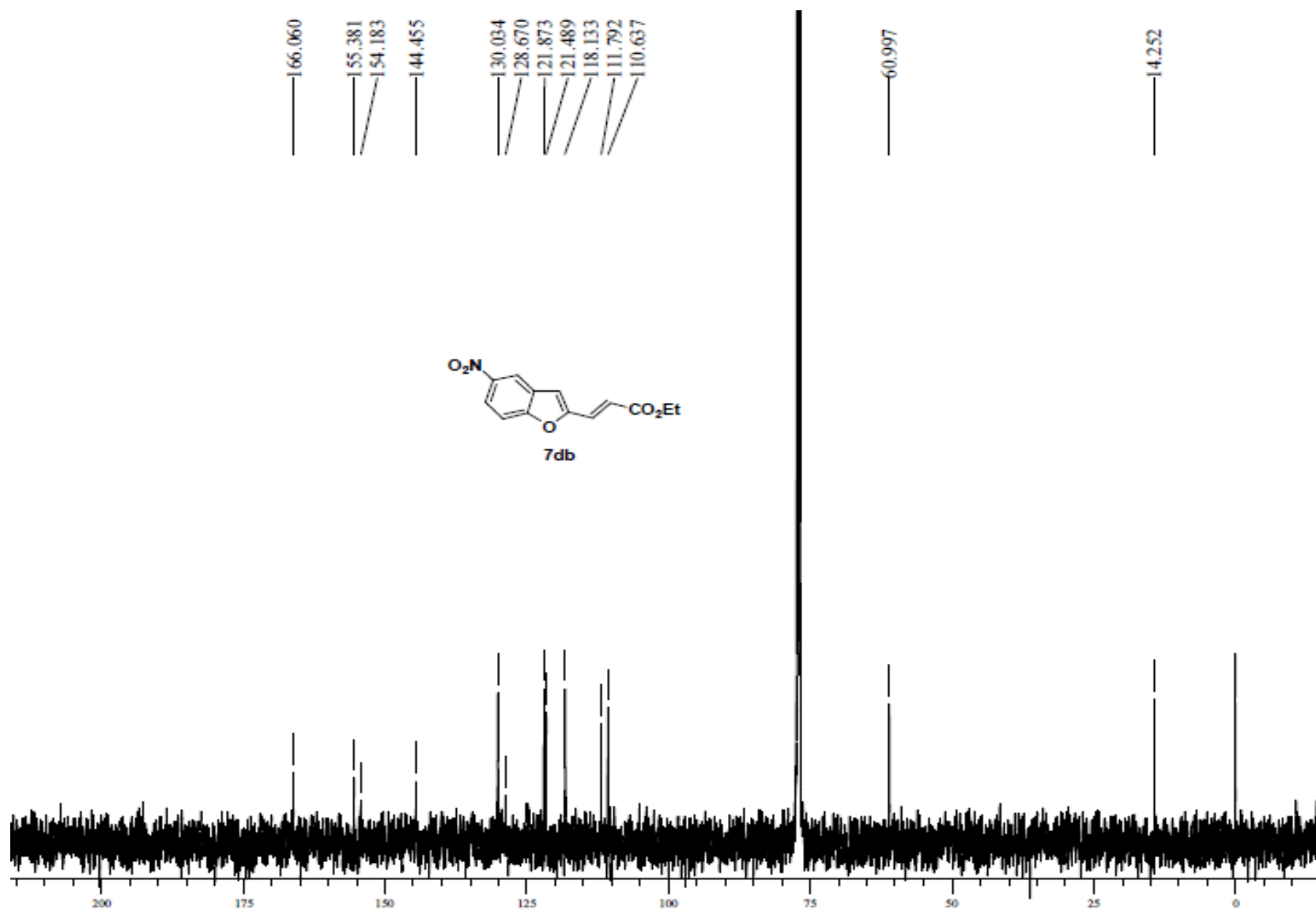
^{13}C spectrum of **7da**, 125 MHz, $(\text{CD}_3)_2\text{SO}$



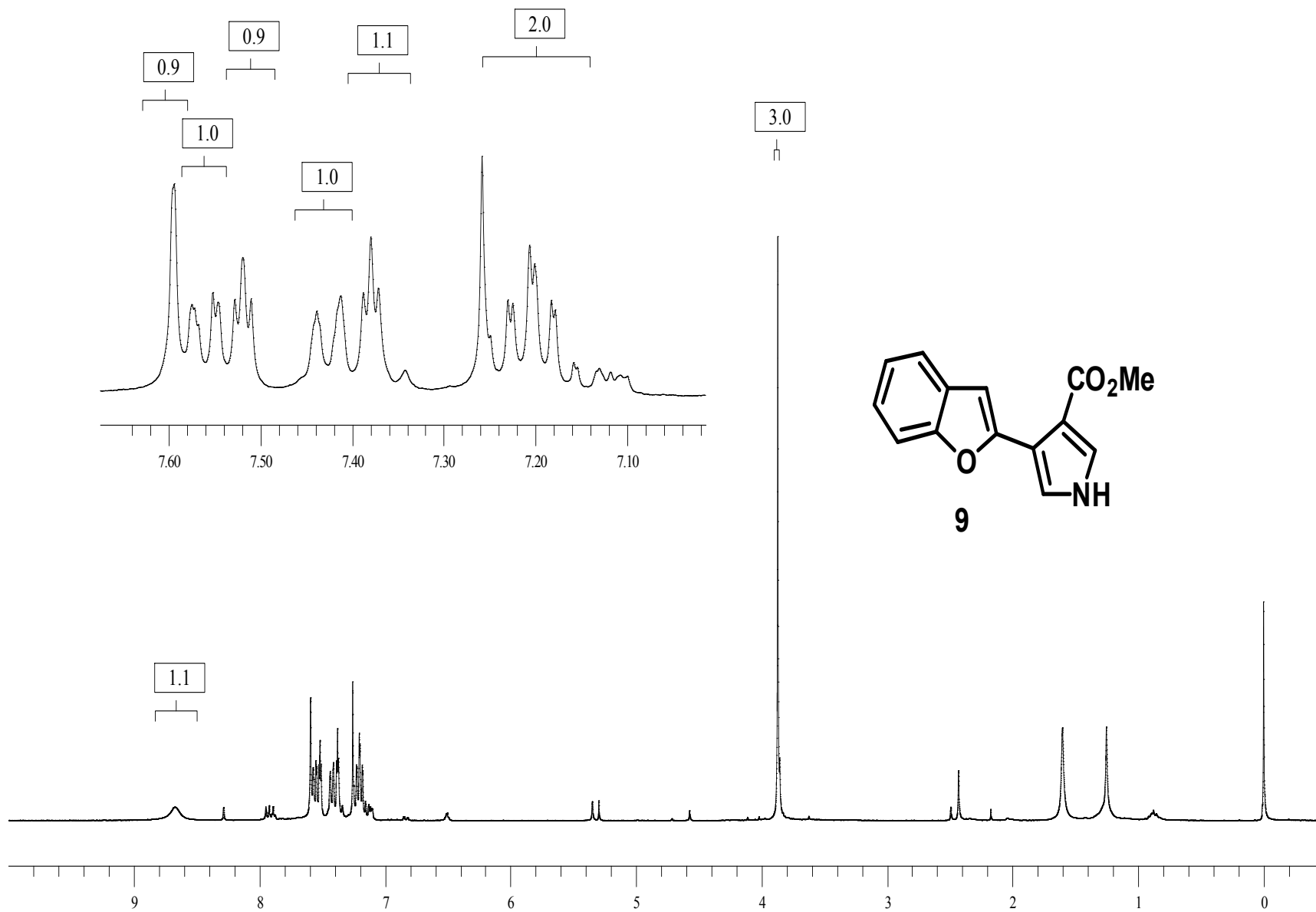
¹H spectrum of **7db**, 300 MHz, CDCl₃



^{13}C spectrum of **7db**, 125 MHz, CDCl_3



¹H spectrum of **9**, 300 MHz, CDCl₃



^{13}C spectrum of **9**, 75 MHz, CDCl_3 and $(\text{CD}_3)_2\text{SO}$

