Supplementary Material (ESI) for Chemical Communications

Supporting Information

Facile Synthesis of 3-(Aminomethyl)isoquinolines and 3-(2-Pyridinyl)isoquinolines by Copper-Catalysed Domino Four-Component Coupling and Cyclisation Reactions

Yusuke Ohta, Shinya Oishi, Nobutaka Fujii,* and Hiroaki Ohno*

Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

E-mail: hohno@pharm.kyoto-u.ac.jp; nfujii@pharm.kyoto-u.ac.jp

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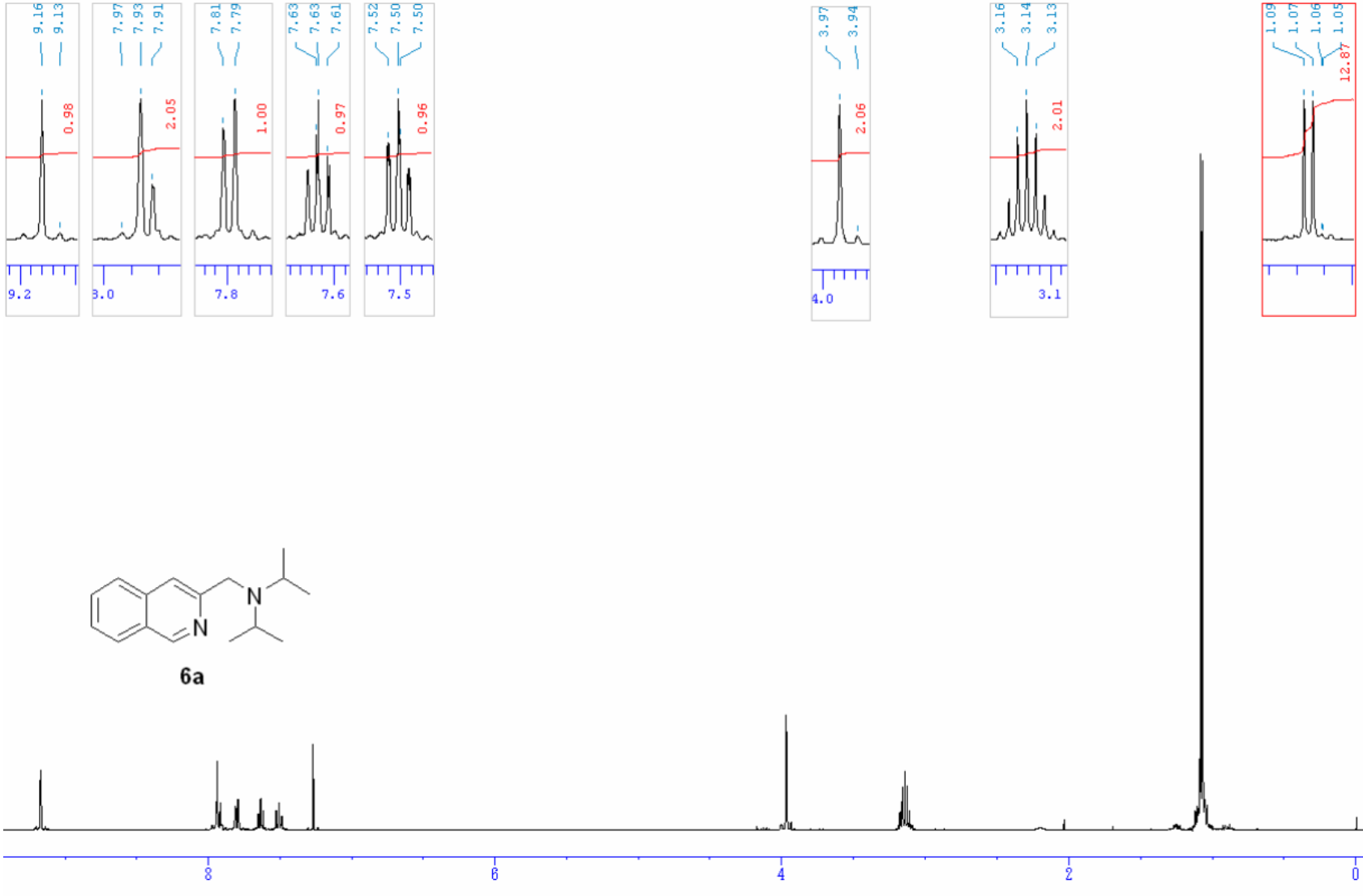
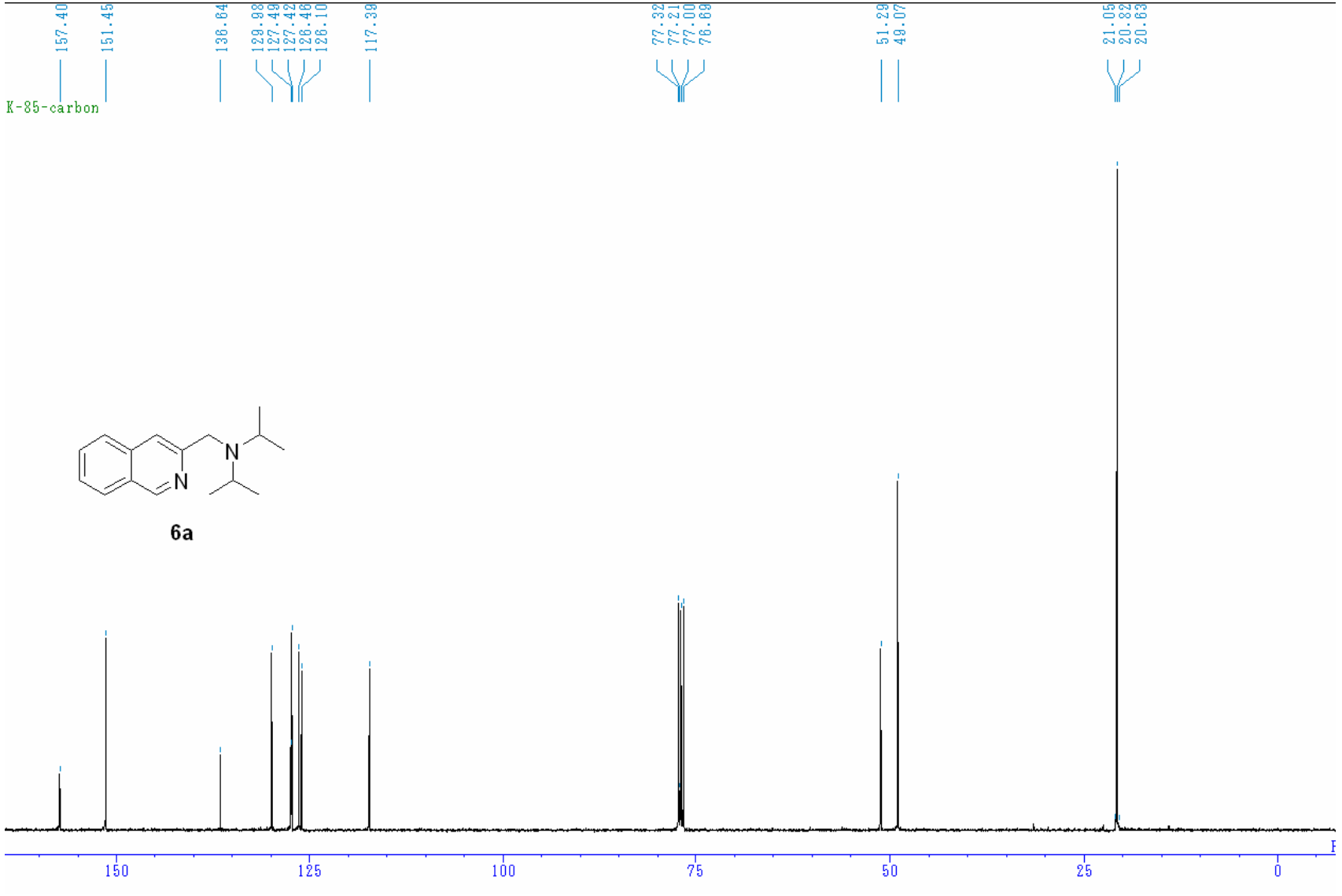
General Methods. IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. Exact mass (HRMS) spectra were recorded on JMS-HX/HX 110A mass spectrometer. ^{1}H NMR spectra were recorded using a JEOL AL-400 spectrometer at 400 MHz frequency. Chemical shifts are reported in δ (ppm) relative to Me_4Si (in $CDCl_3$) as internal standard. ^{13}C NMR spectra were recorded using a JEOL AL-400 and referenced to the residual $CHCl_3$ signal. Melting points (uncorrected) were measured by a hot stage melting point apparatus. For column chromatography, Wakosil C-300 was employed.

General Procedure for Four-Component Isoquinoline Formation: Synthesis of 3-[(Diisopropylamino)methyl]isoquinoline (6a). To a stirred suspension of 2-ethynylbenzaldehyde **1a** (25 mg, 0.19 mmol), $(HCHO)_n$ **2** (12 mg, 0.38 mmol), and CuI (3.7 mg, 0.019 mmol) in DMF (1.5 mL) was added *i*-Pr_2NH **3a** (54 μL, 0.38 mmol) at room temperature under Ar. After the reaction mixture was stirred for 1 h at this temperature, *t*-$BuNH_2$ **4j** (121 μL, 1.2 mmol) was added and the mixture was stirred for 6 h at room temperature before stirring for 45 min at 140 °C. The reaction mixture was concentrated *in vacuo* and purified by column chromatography over alumina with hexane/EtOAc (50:1) as the eluent to give **6a** (38.6 mg, 83% yield) as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (d, J = 6.6 Hz, 12H, 4 × CH_3), 3.09-3.19 (m, 2H, 2 × NCH), 3.97 (s, 2H, NCH_2), 7.48-7.52 (m, 1H, Ar), 7.61-7.65 (m, 1H, Ar), 7.80 (d, J = 7.6 Hz, 1H, Ar), 7.91-7.93 (m, 1H, Ar, 4-H), 9.16 (s, 1H, 1-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8 (4C), 49.1 (2C), 51.3, 117.4, 126.1, 126.5, 127.4, 127.5, 130.0, 136.6, 151.5, 157.4; MS (FAB) *m/z* (%): 243 (MH^+, 100); HRMS (FAB) calcd for $C_{16}H_{23}N_2$ (MH^+): 243.1861; found: 243.1857.

In all cases, after the three-component reaction of **1**, **2** (2 equiv), and **3** (2 equiv) in the presence of CuI (10 mol%) in DMF was completed on TLC (conditions are listed in Table 2), *t*-$BuNH_2$ (**4j**, 6 equiv) was added. For the reaction using **3d**–**f**, a mixture of **2**, **3** and CuI in DMF was stirred for 30 min at room temperature before **1** was added.

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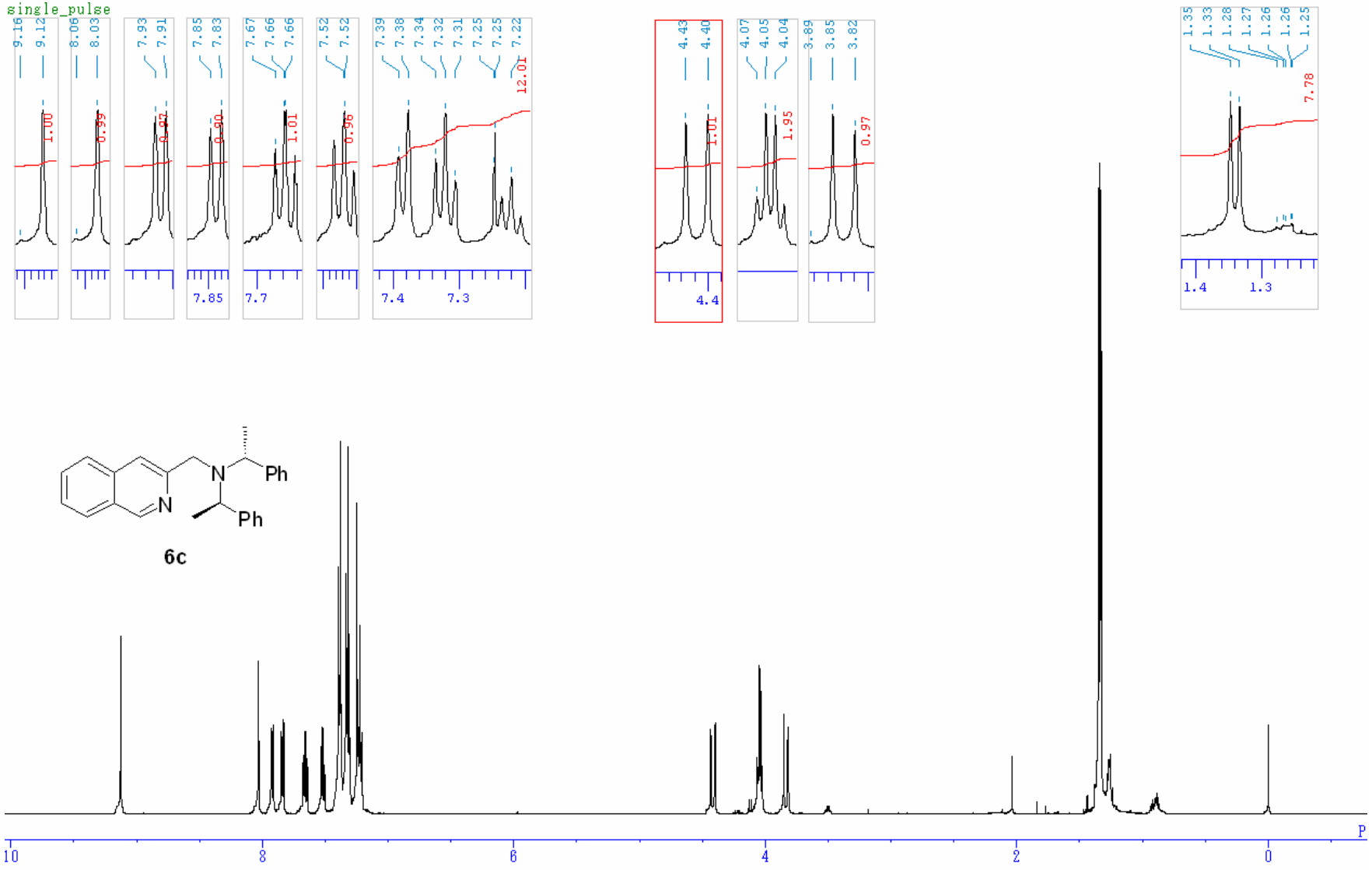
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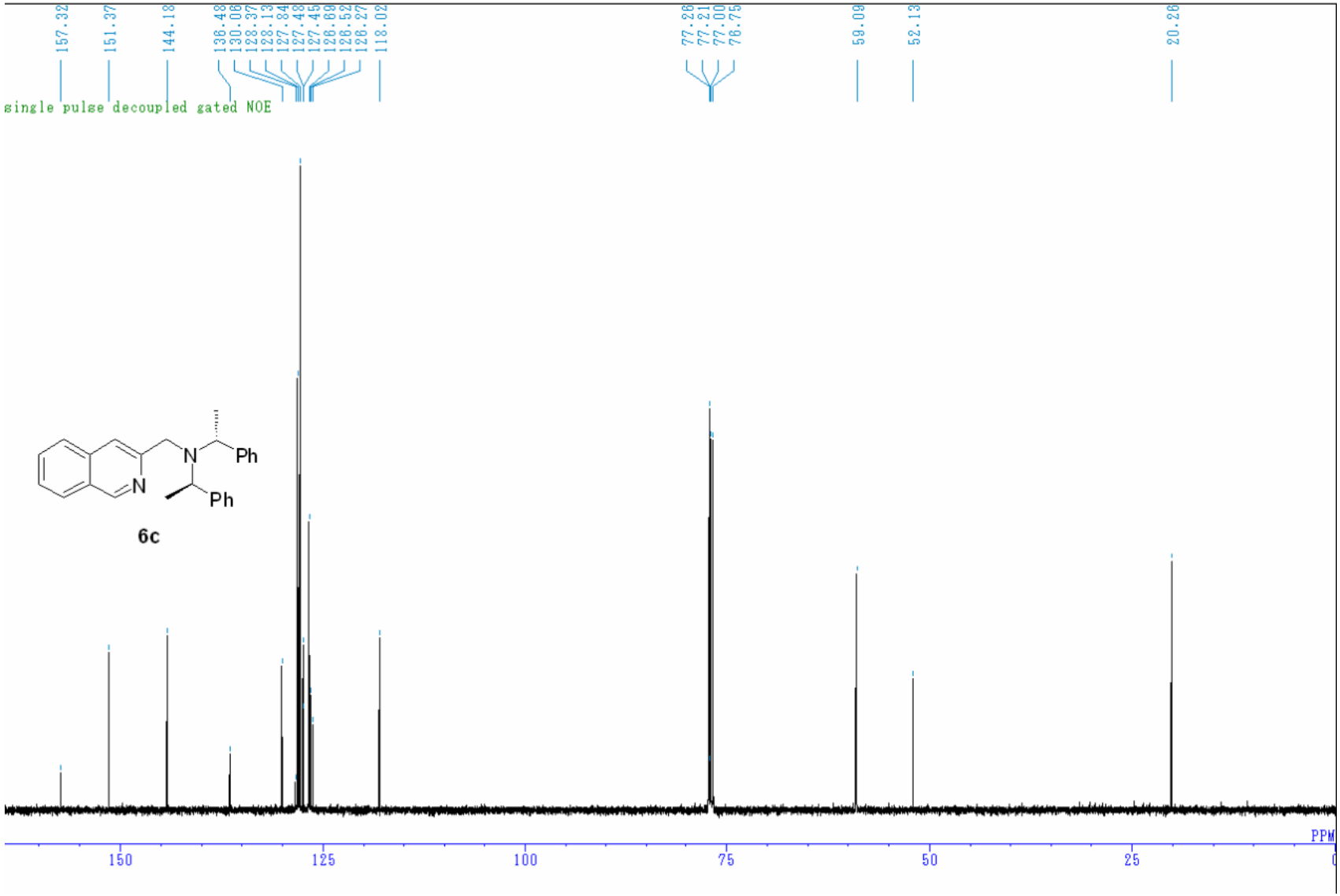
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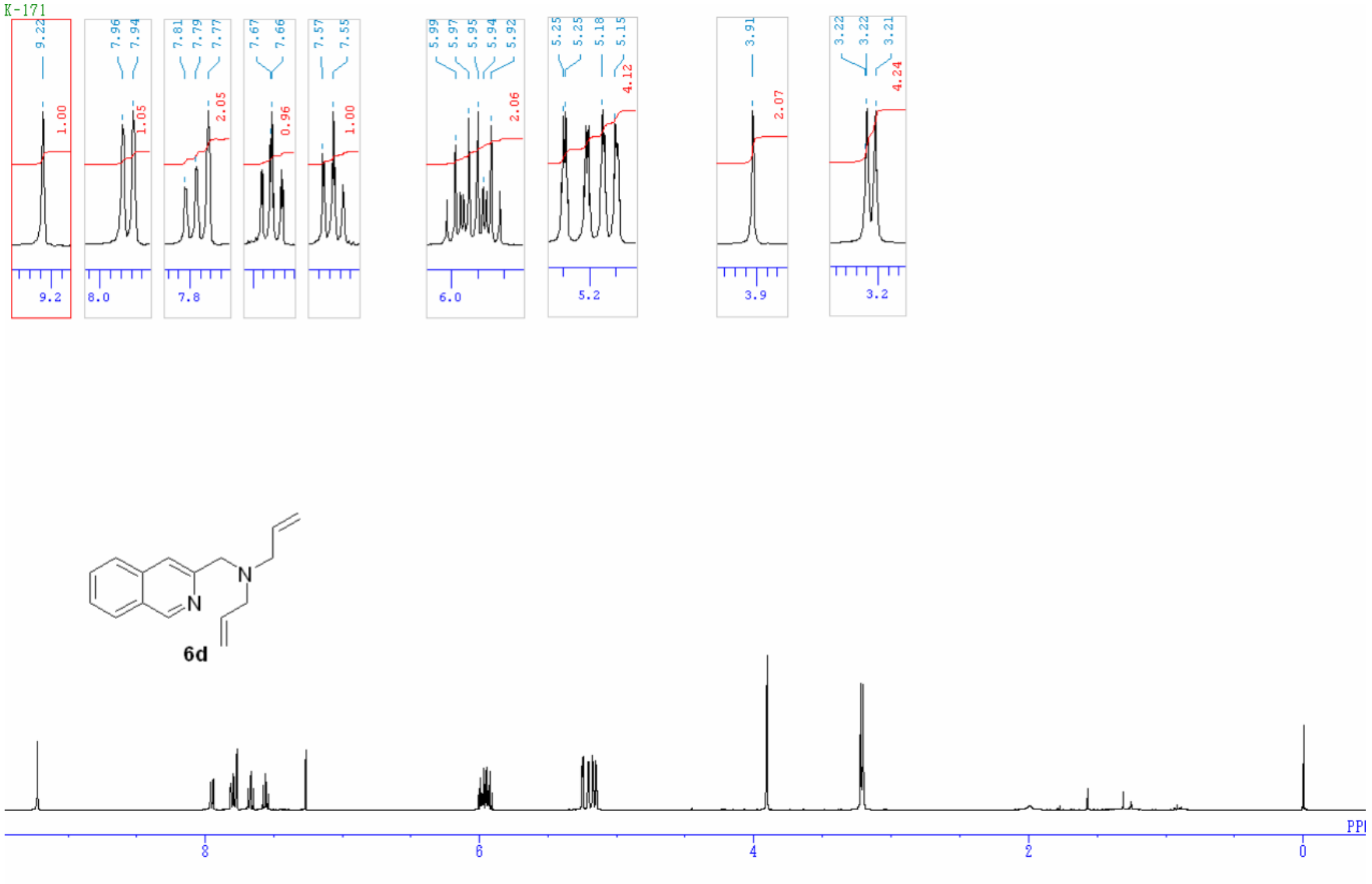
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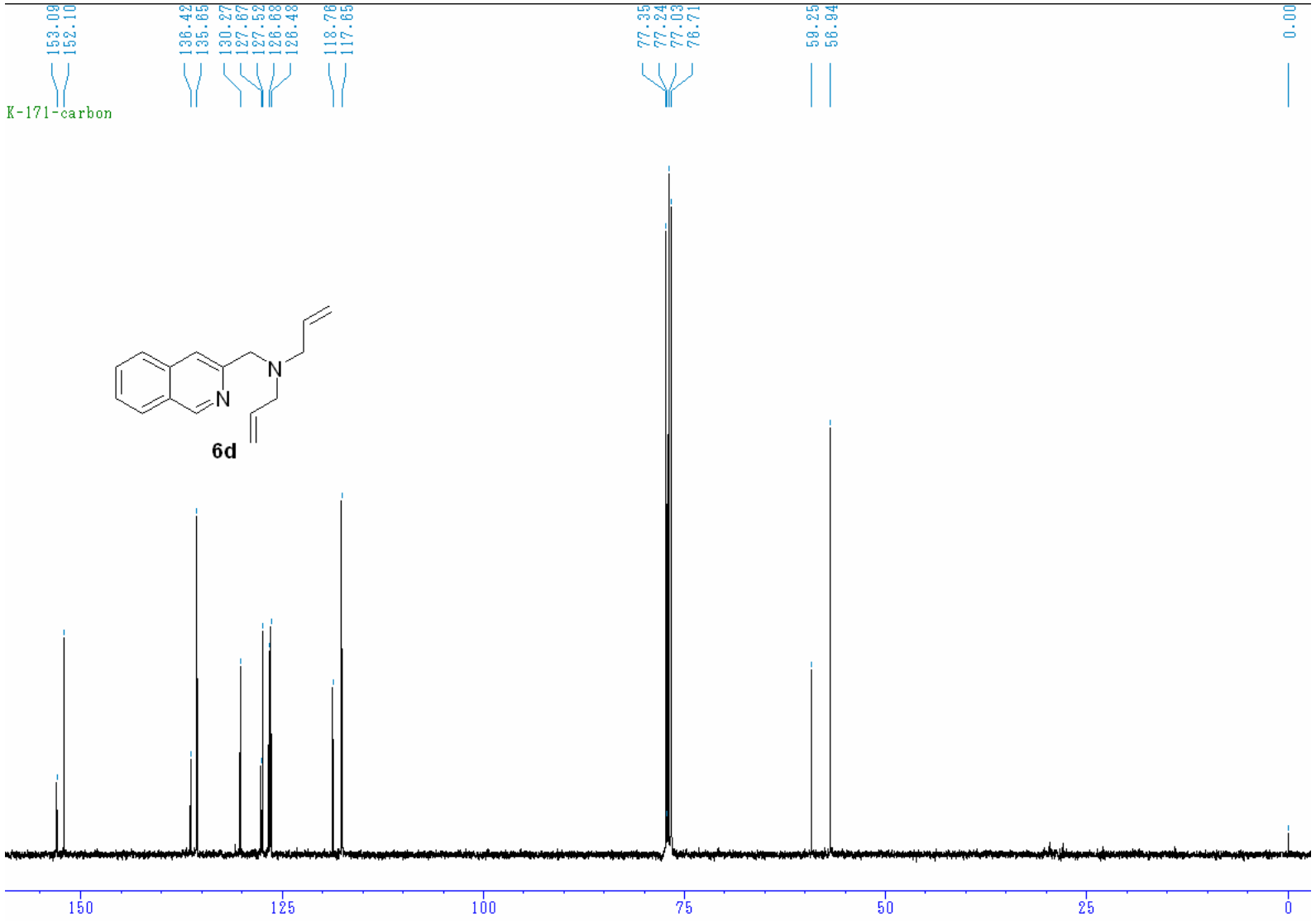
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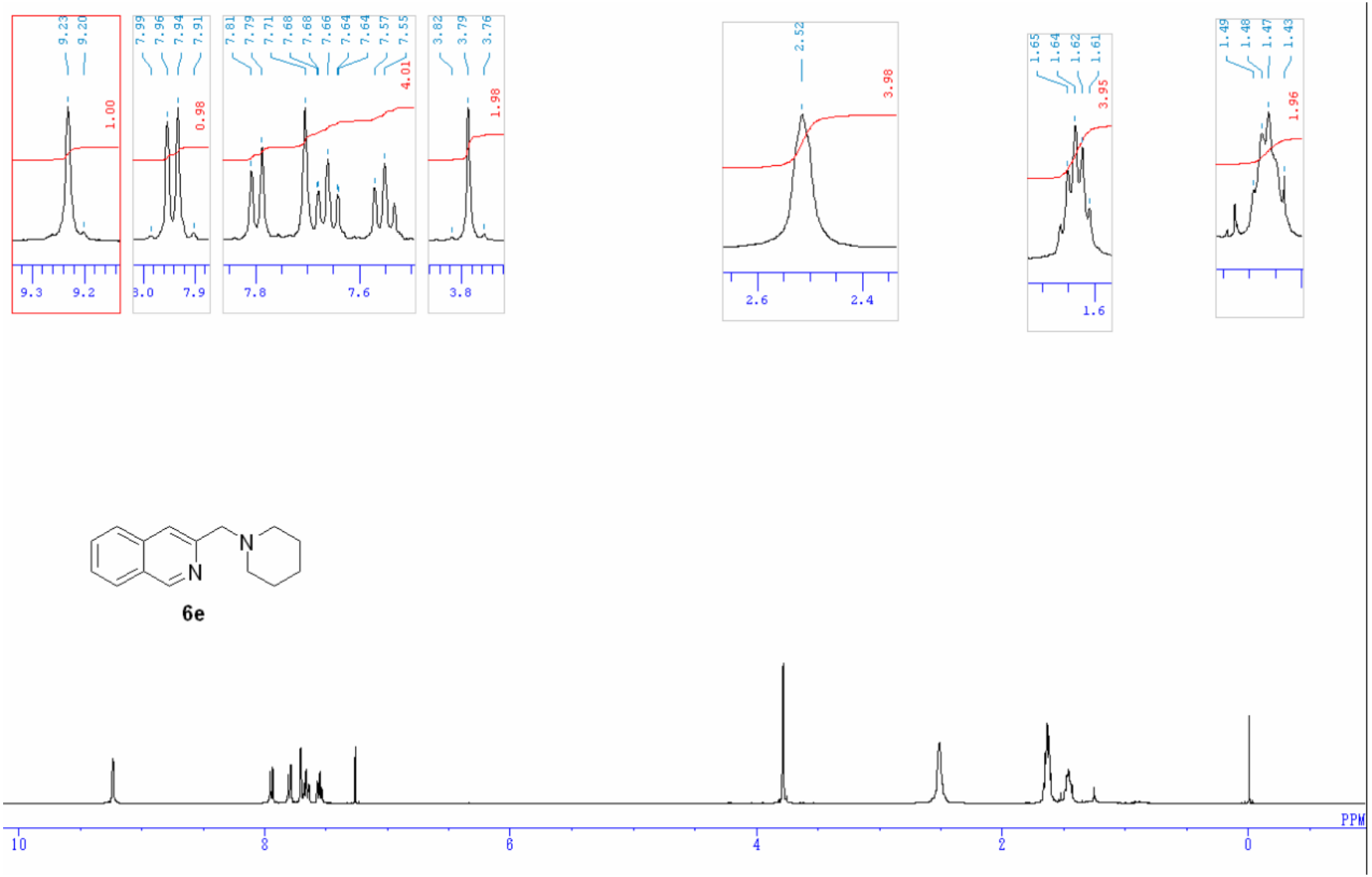
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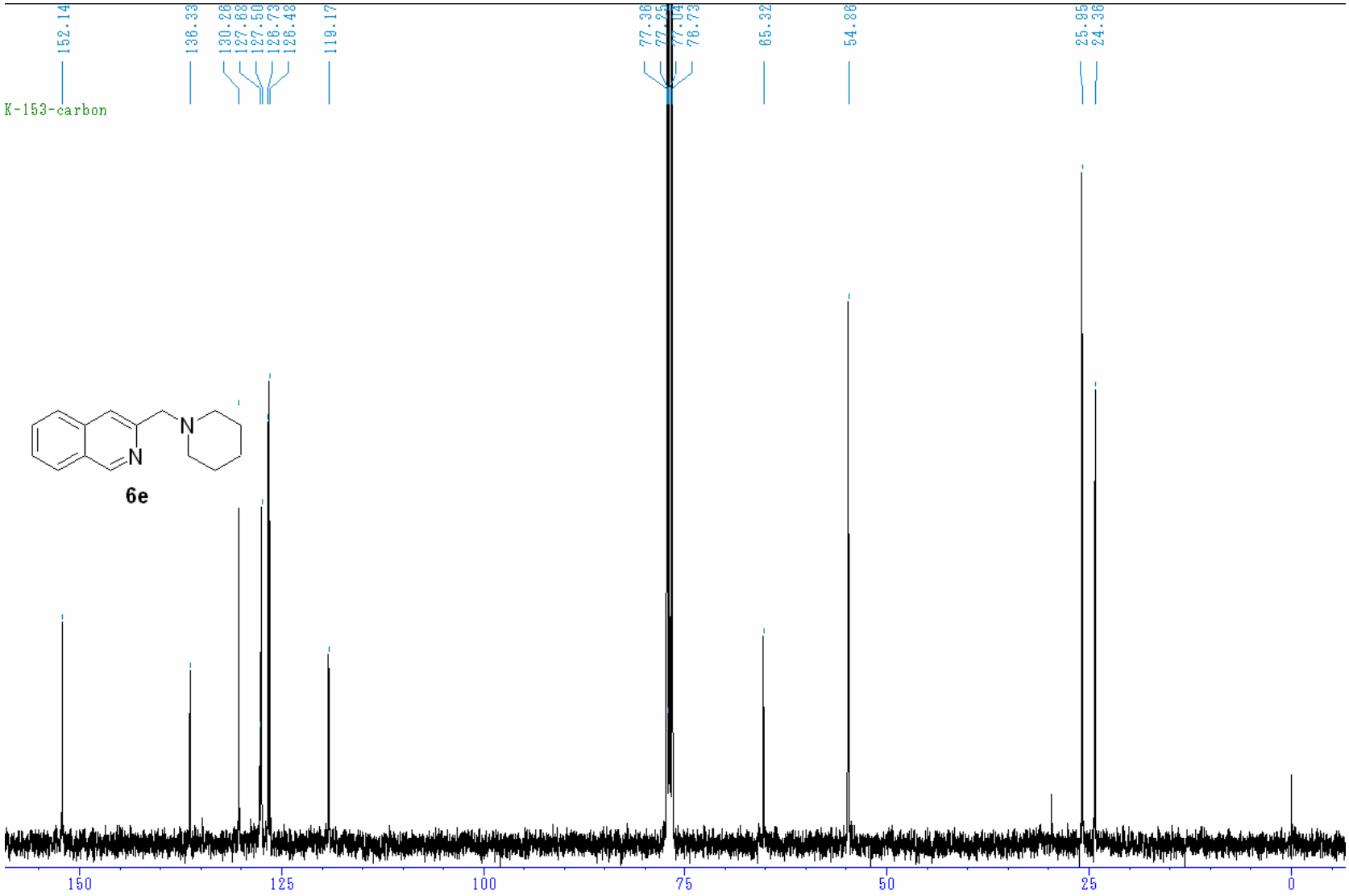

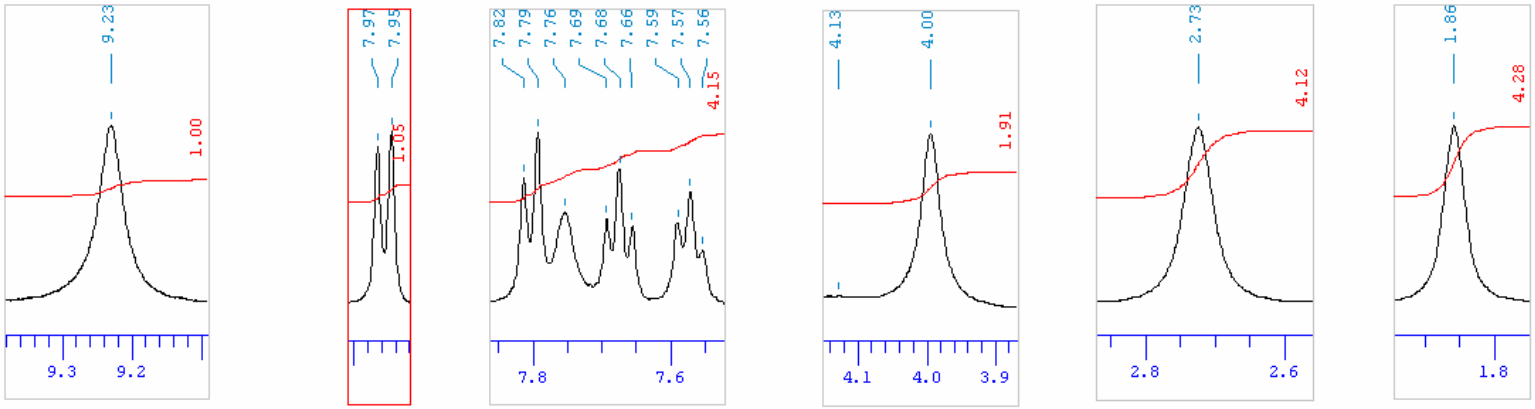
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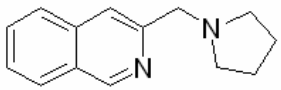
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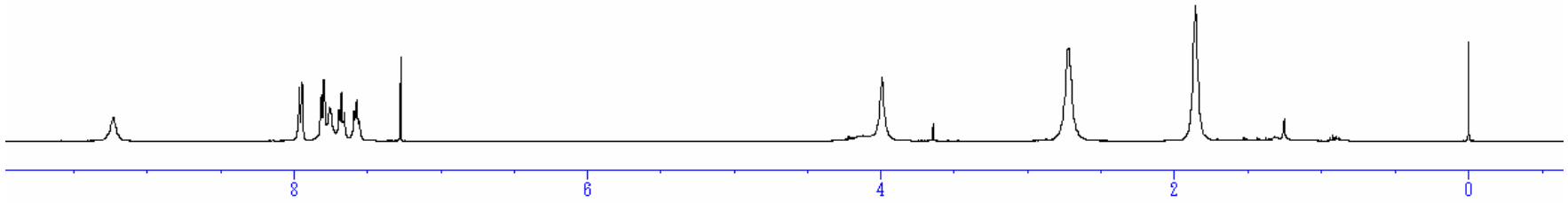
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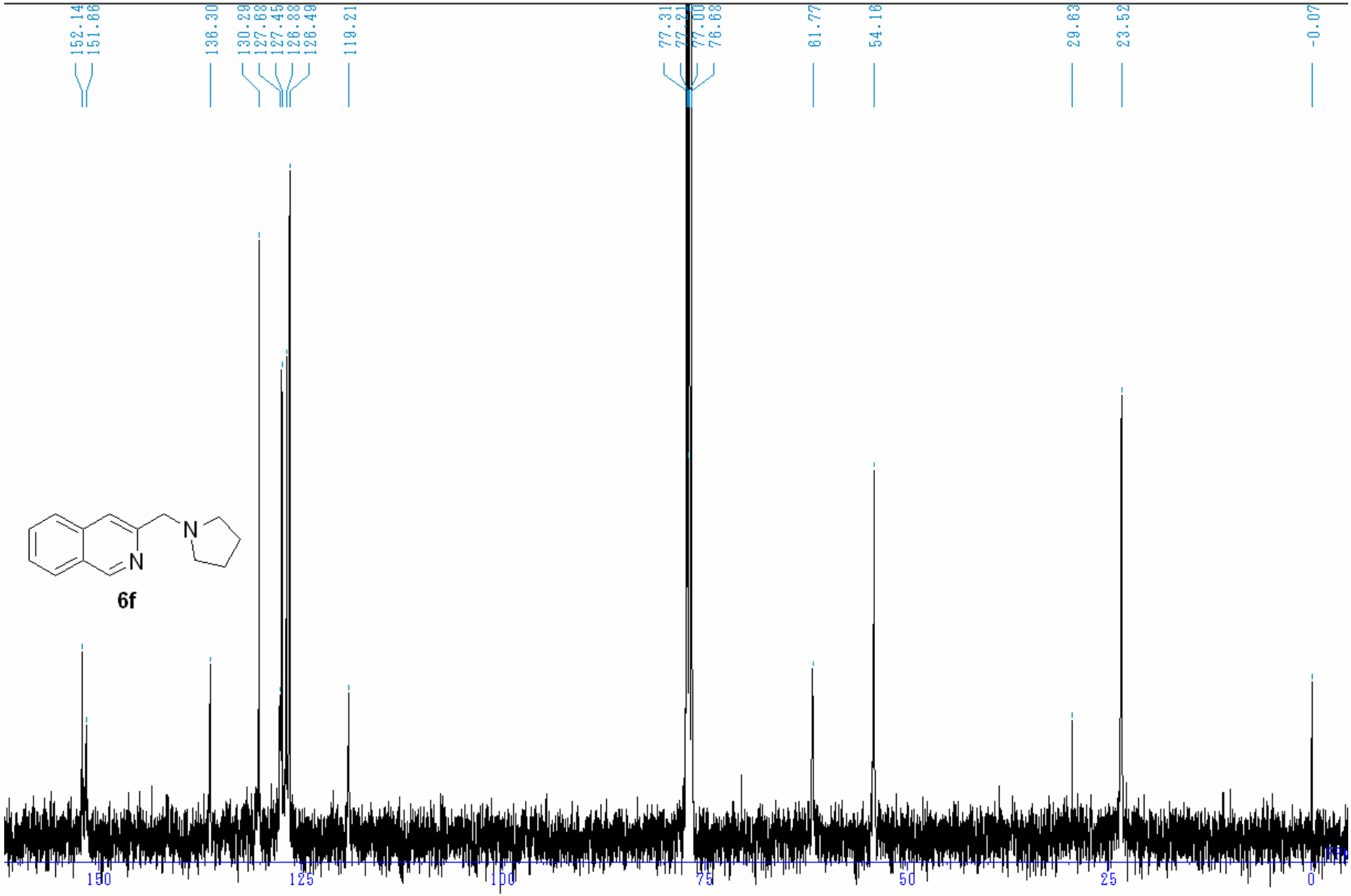

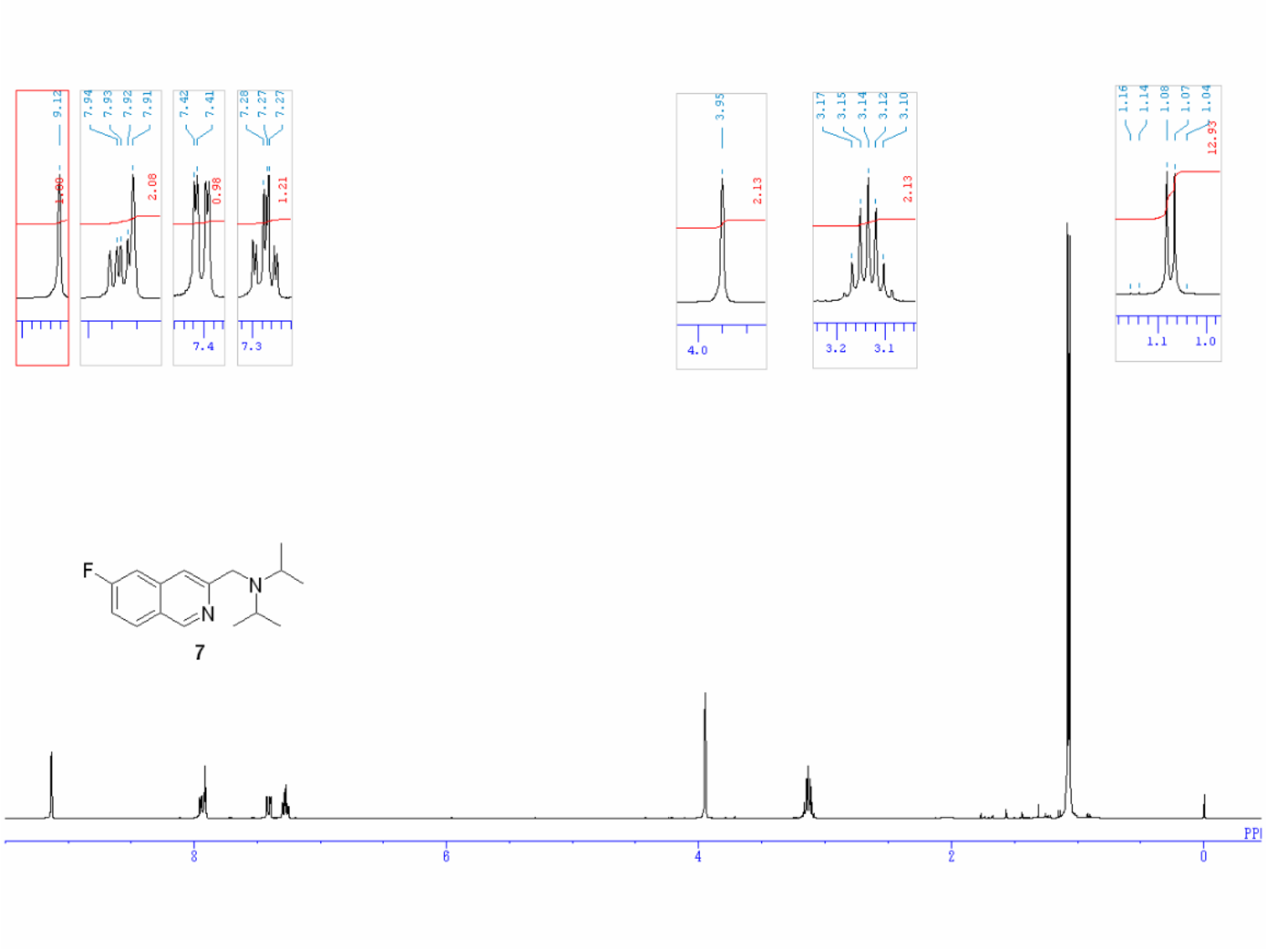

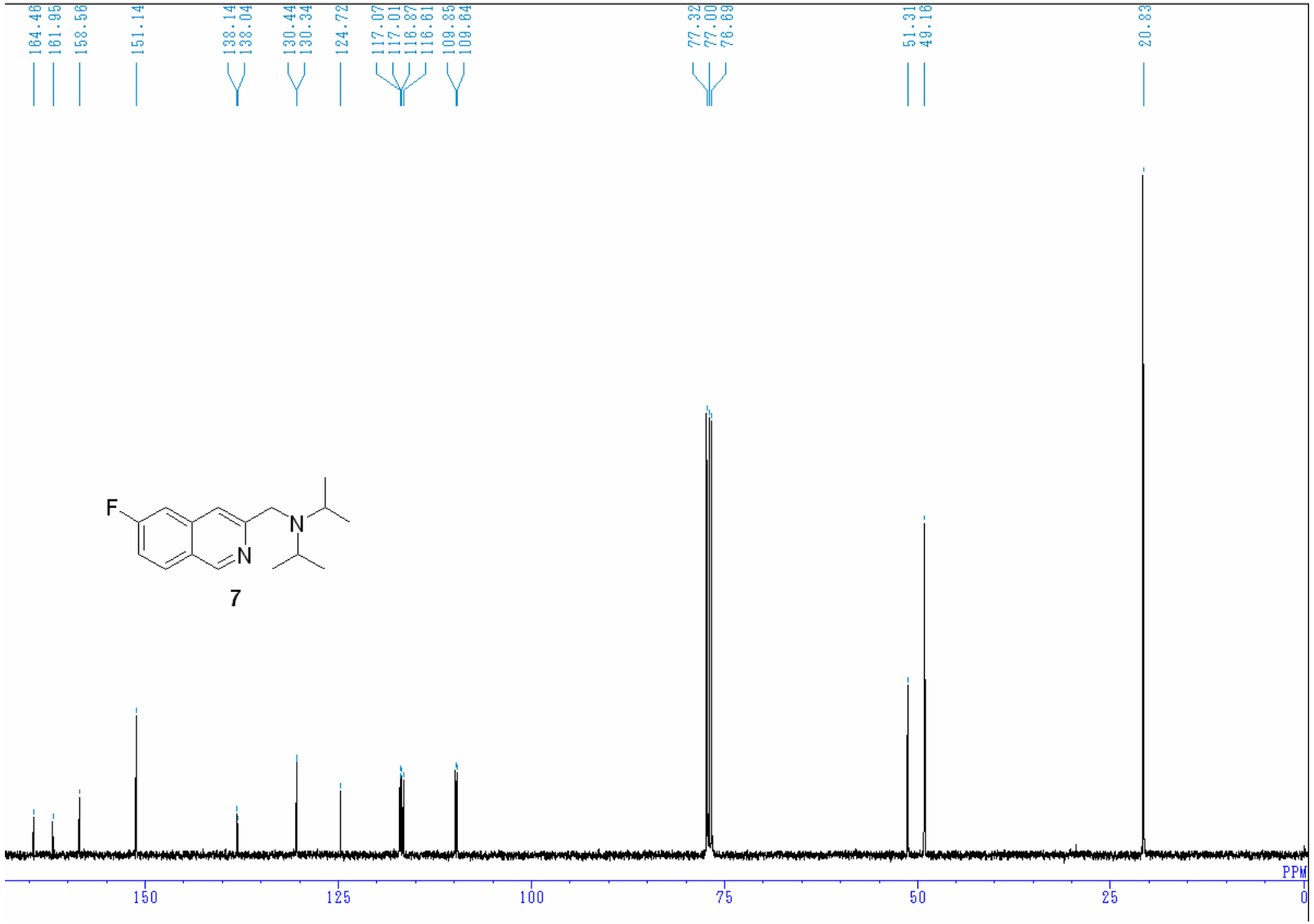
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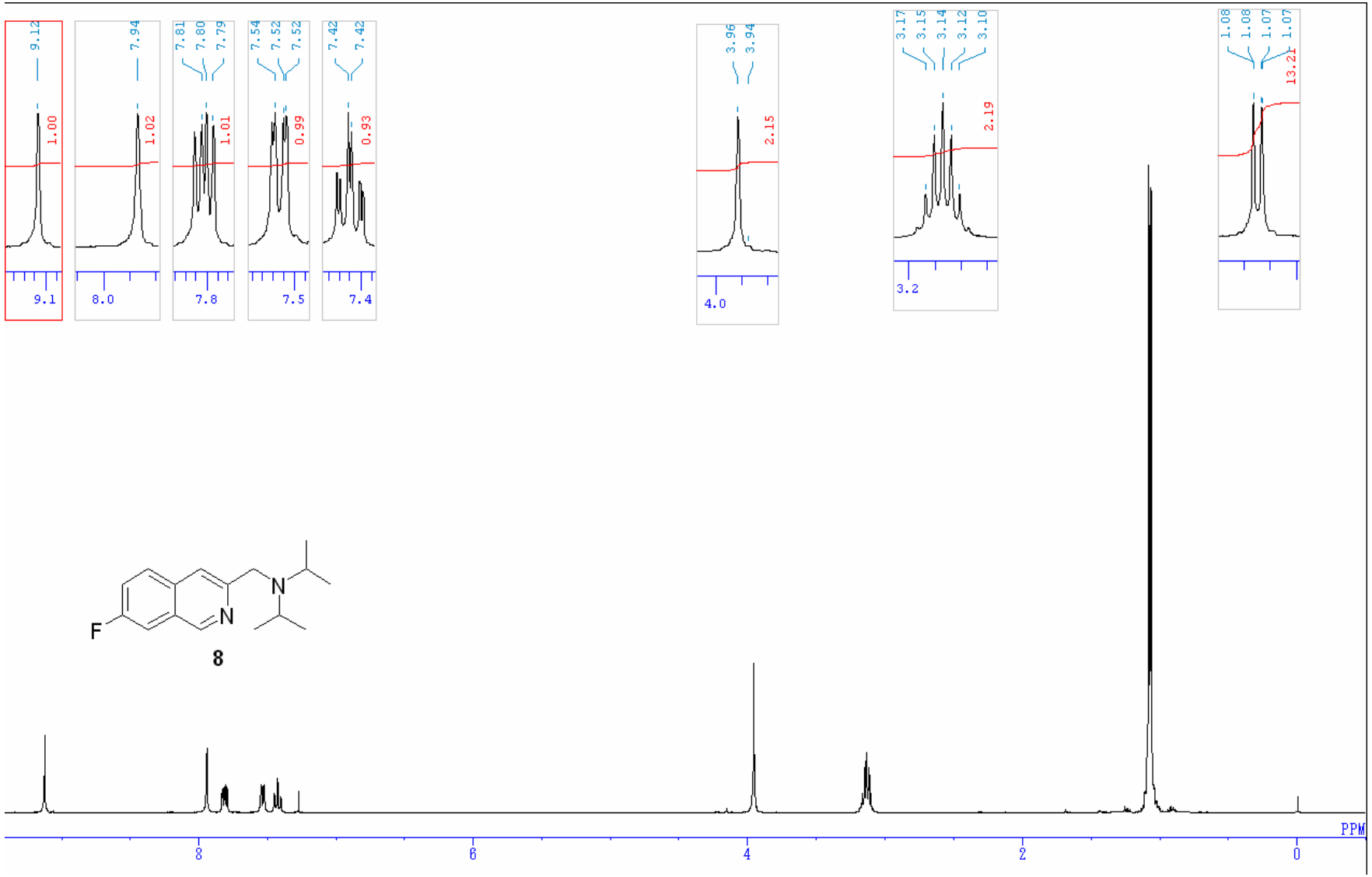

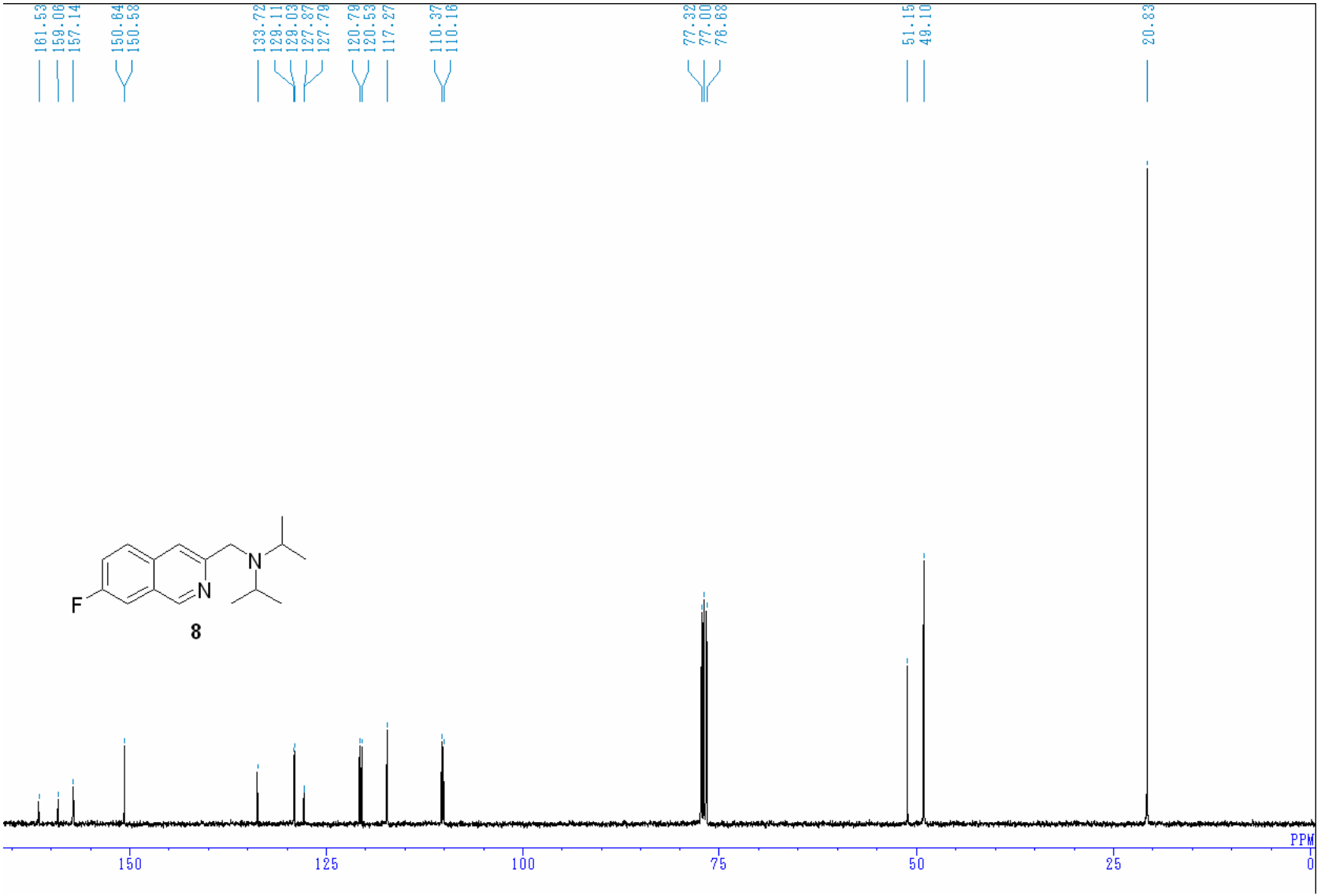
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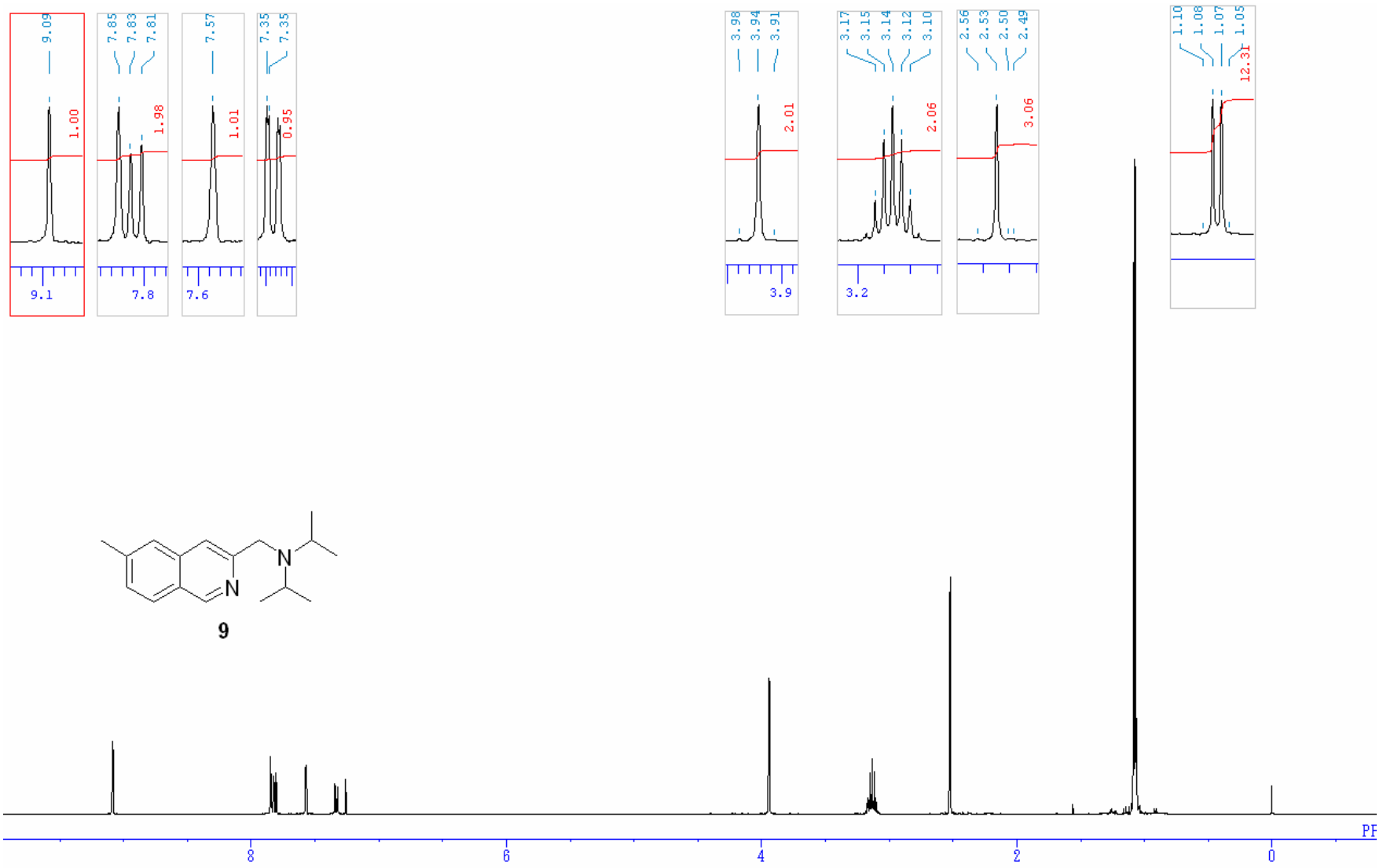
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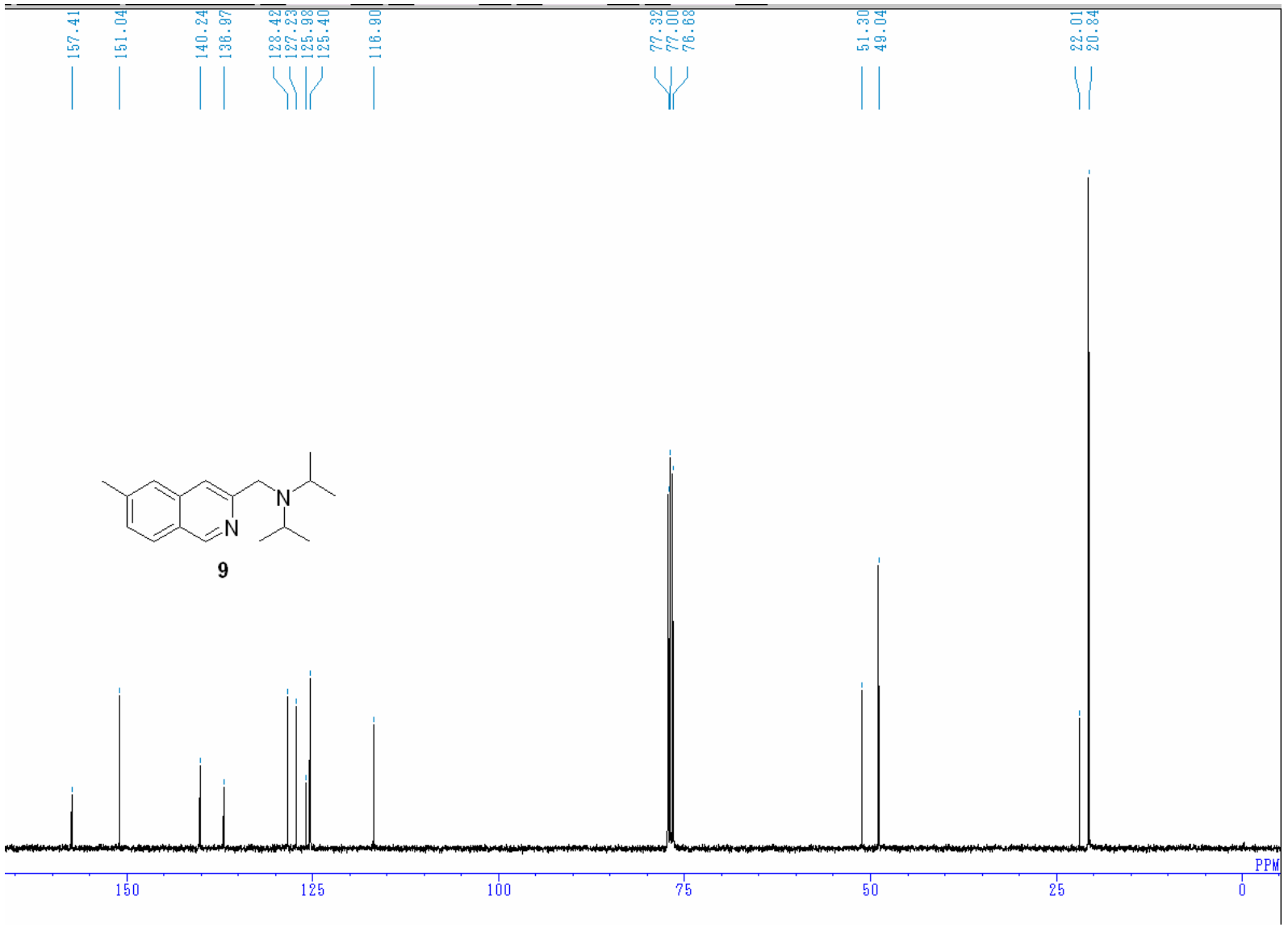
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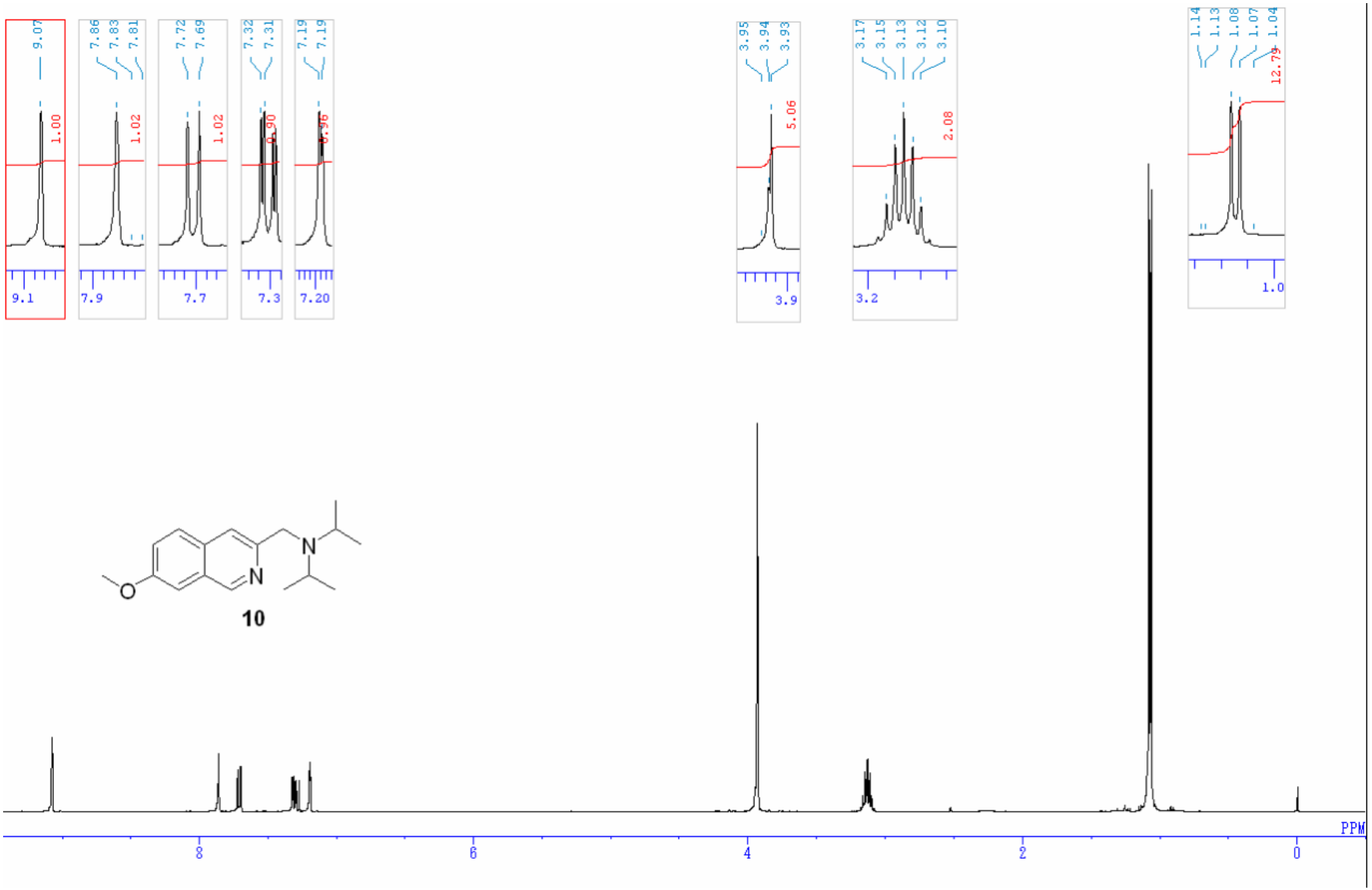
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