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**Supporting Information**

# Graphene oxide decorated with Cu(I)Br nanoparticles: A reusable catalyst for the synthesis of potent bis(indolyl)methane based anti HIV drugs

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## 1. EDX spectrum of GO-CuBr nanocatalyst

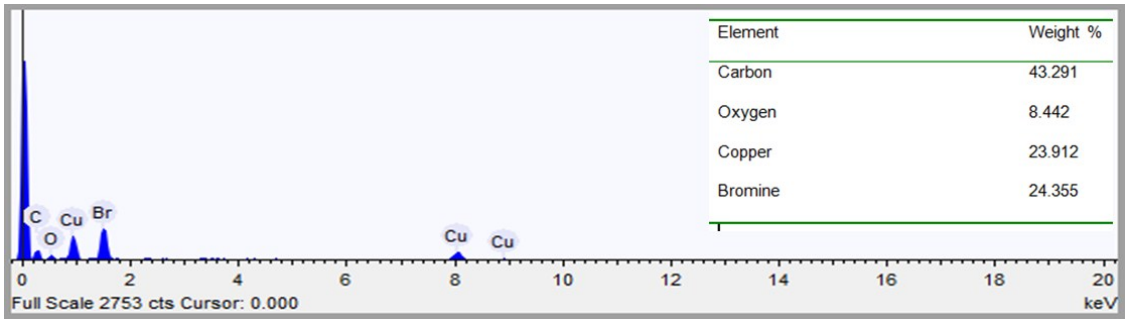



**Figure S1. EDX spectrum of GO-CuBr nanocatalyst**

## 2. Experimental procedures

### General Remarks

All reagents and solvents were of pure analytical grade. Thin layer chromatography (TLC) was performed on 60 $F_{254}$ silica gel, pre-coated on aluminium plates and revealed with either a UV lamp ($\lambda_{max}$ = 254 nm) or iodine vapours. The products were purified by column chromatography on silica gel 230-400 mesh. $^{1}H$ and $^{13}C$ NMR spectra were measured on a Bruker DPX-300 MHz spectrometer ($^{1}H$ 300 MHz, $^{13}C$ 75 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are given in δ (ppm) relative to TMS. The coupling constants (J) are given in Hz**.** The ESI - MS was performed on MICROTOF II mass instrument. Powder XRD was taken on powder X-ray diffractometer (Bruker). EDX was recorded on Oxford Instuments EDS Model Swift ED 3000 and RAMAN spectra on Labram HR 800 EvoRaman Spectrometer.

### Synthesis of Graphene Oxide (GO)

GO was synthesized by the modified Hummers' method. In a typical procedure, 500 mg of graphite powder and 2.0 g of sodium nitrate ($NaNO_3$) were put in cold (below 5 °C) concentrated $H_2SO_4$ (18 mL, 98%). The mixture was stirred continuously for 1 h and the temperature was kept below 5 °C by cooling in an ice bath. Thereafter, 3 g of potassium permanganate ($KMnO_4$) was added gradually and reaction was continued for another 2 h at a temperature below 5 °C. The mixture was heated to 35 °C for 30 min and 40 mL of deionised (DI) water was added to it slowly while increasing temperature. It was kept at 100 °C for 15 min, diluted with 70 mL of DI water and cooled to room temperature. The colour of the suspension changed to bright yellow after adding 10 mL of $H_2O_2$ (35%). The suspension was

filtered and washed with 400 mL of 5% HCl twice followed by further washing with 200 mL of DI water for 3 times. Finally, the precipitate was dried in the vacuum desiccator for at least 5 days before further use.

***In situ* synthesis of graphene oxide grafted with Cu(I)Br nanoparticles:**

In a typical synthesis, 100 mg of GO synthesized as above was dispersed in 20 mL of toluene by ultrasonication for about 30 min. Then 50 mg of $Cu_2O$ was also dispersed in 20 mL of toluene and was dropwise added to GO solution. Then to this mixture 0.5 mL of HBr in acetic acid was added dropwise. The mixture was stirred for 12 h at room temperature and then refluxed for next 12 h. The precipitate was separated by centrifugation and washed with diethylether for 3 times. The composite so obtained was then dried in oven at 50 °C for 24 h and was labelled as GO–CuBr.

**General procedure for synthesis of Bis(indolyl)methanes (3a-t)**

Indole (220 mg, 1.88 mmol), benzaldehyde (100 mg, 0.943 mmol) and GO–CuBr NPs (0.05 mol% CuBr) were taken in a round bottom flask. The contents were stirred for 2 hours at 50 $^{o}$C. Reaction was monitored through TLC. After completion of reaction, reaction mixture was extracted with dichloromethane, dried over anhydrous sodium sulphate and concentrated at reduced pressure. The product **3m** was purified through the column chromatography and obtained in 92% yield.

***In-vitro* anti-HIV-1 activity using TZM-bl cells**

TZM-bl cells [HeLa cell line expressing high levels of CD4, HIV-1 co-receptors CCR5 & CXCR4 with β-galactosidase and luciferase as reporter genes under HIV-1 LTR promoter] were maintained in Dulbecco's modified Eagle's medium (DMEM; Sigma-Aldrich Inc., St. Louis, MO, USA) supplemented with 10% fetal bovine serum (FBS; Biological Industries, Kibbutz beit Haemek, Israel) and an antibiotic-antimycotic cocktail [Penicillin (100 units/ml), Streptomycin (100 μg/ml) and Amphotericin B (250 ng/ml); Pen-Strep-Ampho sol, Biological Industries]. TZM-bl cells ($4.0 \times 10^4$/well) were seeded in 24-well plate and cultured overnight at 37 °C in a humidified atmosphere of 5% $CO_2$. In separate vials, HIV-$1_{NL4.3}$ (CXCR4 using virus) at a multiplicity of infection (MOI) of 0.05 was treated with various synthetic compounds or solvent for 1 h at 37ºC. Subsequently, pretreated viruses were added in duplicate to TZM-bl cells and cultured for 4 h. Nevirapine (Sigma-Aldrich

Inc.) was used as a positive reference control whereas negative control comprised of cells without HIV infection. After incubation, the cells were washed once with cold 50 mM PBS, pH-7.4 to remove the cell-free virus followed by addition of fresh culture medium with or without the synthetic compounds. Cells were further incubated for 48 h, washed twice with PBS and lysed with 1X lysis buffer (Promega Corporation, Madison, USA) by freeze-thaw. The supernatant was analyzed for luciferase activity by BrightGlo Luciferase Assay kit (Promega Corporation) in white opti-plate and luminescence was read using Fluorimeter (BMG Labtech GmbH, Offenberg, Germany) at a spectral range of 240-740 nm. The results were expressed as percentage inhibition, calculated by taking the luminescence in experimental group divided by the luminescence in infected cells in absence of test compound multiplied by hundred. Percent inhibition was calculated by subtracting the above value from hundred.

**Cytotoxicity assay using MTT**

The cytotoxicity of the synthetic compounds on TZM-bl cells lines was assessed by MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; Sigma-Aldrich Inc.] assay [1]. In brief, TZM-bl cells were seeded (6 x $10^3$/well) in 96-well cell culture plates (Greiner Bio-One, GmbH, Frickenhausen, Germany) and grown overnight at 37°C in humidified atmosphere of 5% $CO_2$. After 24 h, synthetic compounds were added in increasing concentrations followed by further incubation for 48 h. Negative control includes cells treated with solvent/medium. After incubation, cell viability was assessed by adding 20 µl MTT (5 mg/ml in PBS) per well and incubated at 37°C for 3 h followed by addition of MTT solvent (100 µl/well; absolute isopropanol, 0.04 N HCl). The absorbance (OD) was read at 570 nm with reference filter at 690 nm. Experiments were performed in triplicates and percent viability was calculated by dividing the OD obtained in treatment group by OD of untreated cell control multiplied by hundred.

**Statistical analysis**

Analyses of concentration-response data were performed by the use of nonlinear curve-fitting program Prism to determine $CC_{50}$ and $IC_{50}$ values.

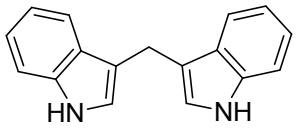
**Molecular modelling**

The crystal structure of the target reverse transcriptase enzyme (PDB ID: 3V81) was obtained from Protein Data Bank (RCSB) (http://www.rcsb.org/pdb) and used for docking after being shorn of the water molecules of crystallization, bounded nucleic acid, heteroatoms and other co-factors by using Discovery Studio 4.0 Visualizer (DSV).

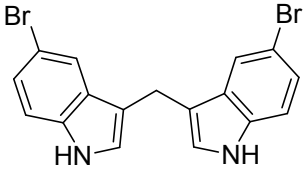
To carry out the docking studies, the 2D structures of the synthesized molecules (**3a–3t**) were drawn in Chem-BioOffice 2010 and converted to energy minimized 3D structures in pdb file format using MarvinSketch (ChemAxon). All the synthesized molecules were energy minimized using the Amber 10 software. Docking simulations for the compounds **3a–3t** and the control nevirapine were performed against the active site of reverse transcriptase enzyme. Then, finally docking results were visualized using Pymol visualizer. The 2D interaction plots of **3d** and nevirapine with reverse transcriptase were generated using ligplot+.

**3. Characterization data of the synthesized compounds.**

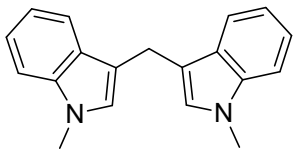
**Di(1H-indol-3-yl)methane (3a)**[1]: Yield 88%, 281 mg; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.85 (s, 2H), 7.61 (d, $J$ = 7.8 Hz, 2H), 7.34 (d, $J$ = 8.1 Hz, 2H), 7.18 (t, $J$ = 7.2 Hz, 2H), 7.08 (t, $J$ = 7.5 Hz, 2H), 6.92 (s, 2H), 4.24 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 136.49, 127.60, 122.22, 121.90, 119.24, 119.19, 115.72, 111.06, 21.21; ESI-MS for $C_{17}H_{14}N_2$ = 246.1043 $[M]^+$.



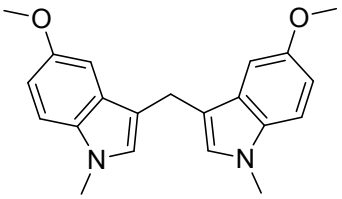

**Bis(5-bromo-1H-indol-3-yl)methane (3b):** Yield 87%, 454 mg; $^1$H NMR (300 MHz, d6 DMSO): $\delta$ 7.65 (s, 2H), 7.41 (d, $J$ = 8.7 Hz, 2H), 7.19 (s, 4H), 6.33 (t, $J$ = 7.2 Hz, 2H), 4.01 (s, 2H); $^{13}$C NMR (75 MHz, d6 DMSO): $\delta$ 134.58, 129.79, 127.55, 123.63, 121.09, 113.59, 112.33, 111.61, 68.56, 19.92; ESI-MS for $C_{17}H_{12}Br_2N_2$ = 401.8367 $[M]^+$.



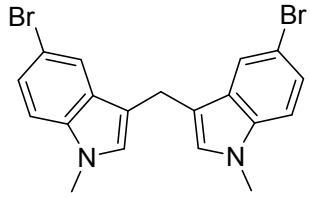

**Bis(1-methyl-1H-indol-3-yl)methane (3c):** Yield 85%, 302 mg, ; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.61 (d, $J$ = 7.8 Hz, 2H), 7.27 (d, $J$ = 8.1 Hz, 2H), 7.21 (t, J = 8.1 Hz, 2H), 7.07 (t, J = 7.5 Hz, 2H), 6.77 (s, 2H), 4.21 (s, 2H), 3.68 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 137.34, 128.12, 127.14, 1121.58, 119.47, 118.76, 114.48, 109.27, 32.66, 21.12; ESI-MS for $C_{19}H_{18}N_2$ = 274.1211 $[M]^+$.



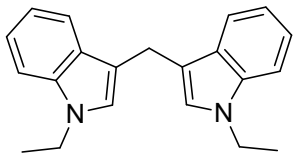

**Bis(5-methoxy-1-methyl-1H-indol-3-yl)methane (3d):** Yield 82%, 356 mg; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.14 (s, 1H), 7.08 (s, 1H), 6.99 (d, $J$ = 2.4 Hz, 2H), 6.82 (d, $J$ = 2.1 Hz, 1H), 6.79 (d, $J$ = 2.4 Hz, 1H), 6.66 (s, 2H), 4.06 (s, 2H), 3.74 (s, 6H), 3.58 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 153.63, 132.63, 128.17, 127.67, 113.71, 111.65, 109.93, 101.19, 56.04, 32.78, 21.04; ESI-MS for $C_{21}H_{22}N_2O_2$ = 334.0247 $[M]^+$.




**Bis(5-bromo-1-methyl-1H-indol-3-yl)methane (3e):** Yield 74%, 413 mg; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.60 (d, $J$ = 1.8 Hz, 2H), 7.20 (d, $J$ = 1.8 Hz, 1H), 7.17 (d, $J$ = 1.8, 1H), 6.67 (s, 2H), 3.99 (s, 2H), 3.57 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 135.88, 129.45, 128.15, 124.33, 121.72, 113.51, 112.16, 110.75, 32.81, 20.76; ESI-MS for $C_{19}H_{16}Br_2N_2$ = 429.9254 $[M]^+$.

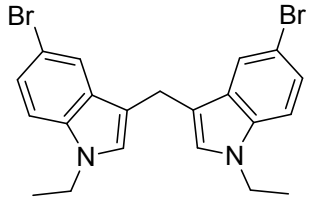



**Bis(1-ethyl-1H-indol-3-yl)methane (3f)**: Yield 77%, 302 mg; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.62 (d, $J$ = 7.8 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 7.21 (d, $J$ = 6.9 Hz, 2H), 7.07 (t, $J$ = 7.2 Hz, 2H), 6.85 (s, 2H), 4.22 (s, 2H), 4.08 (q, $J^1$ = 7.2 Hz, $J^2$ = 14.4 Hz, 4H), 1.39 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR

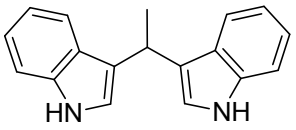


(75 MHz, $CDCl_3$): $\delta$ 136.17, 128.13, 125.32, 121.25, 119.47, 118.52, 114.35, 109.18, 40.76, 21.12, 15.58; ESI-MS for $C_{21}H_{22}N_2$ = 303.1246 $[M + H]^+$.

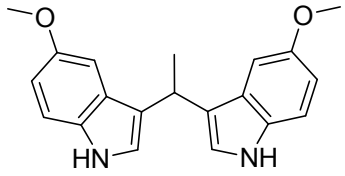
**Bis(5-bromo-1-ethyl-1H-indol-3-yl)methane (3g)**: Yield 85%, 506 mg; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.68 (s, 2H), 7.24 (m, 4H), 6.84 (s, 2H), 4.09 (m, 6H), 1.38 (t, $J$ = 7.2 Hz, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 134.91, 129.66, 126.44, 124.17, 121.91, 113.53, 112.01, 110.75, 40.99, 20.97, 15.49; ESI-MS for $C_{21}H_{20}Br_2N_2$ = 457.8963 $[M]^+$.



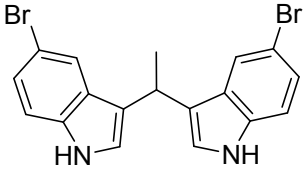

**3,3'-(ethane-1,1-diyl)bis(1H-indole) (3h)**[2]**:** Yield 72%, 149 mg; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.83 (s, 2H), 7.56 (d, $J$ = 8.1 Hz, 2H), 7.33 (d, $J$ = 8.1 Hz, 2H), 7.15 (t, $J$ = 7.8 Hz, 2H), 7.03 (t, $J$ = 7.8 Hz, 2H), 6.90 (d, $J$ = 2.1 Hz, 2H), 4.67 (q, $J$ = 6.9, 7.2 Hz, 1H), 1.80 (d, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 136.68, 126.94, 121.79, 121.73, 121.18, 119.74, 119.03, 111.05, 28.19, 21.73; ESI-MS for $C_{18}H_{16}N_2$ = 261.0132 $[M + H]^+$.



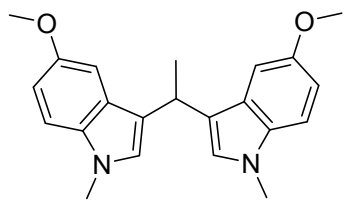

**3,3'-(ethane-1,1-diyl)bis(5-methoxy-1H-indole) (3i)**[2]: Yield 75%, 191 mg; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.70 (s, 2H), 6.98 (d, $J$ = 9 Hz, 2H), 6.90 (d, $J$ = 1.8 Hz, 2H), 6.71 (m, 4H), 4.43 (q, $J^1$ = 6.3 Hz, $J^2$ = 13.8 Hz, 1H), 3.62 (s, 6H), 1.64 (d, $J$ = 6.9 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 153.58, 132.02, 127.35, 122.34, 121.14, 111.92, 111.67, 101.96, 56.00, 28.23, 21.62; ESI-MS for $C_{20}H_{20}N_2O_2$ = 321.1265 $[M+H]^+$.



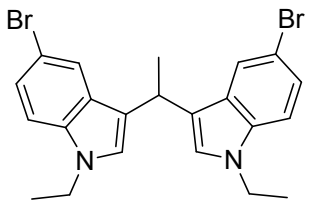

**3,3'-(ethane-1,1-diyl)bis(5-bromo-1H-indole) (3j)**[2]: Yield 71%, 235 mg; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.84 (s, 2H), 7.54 (s, 2H), 7.15 (m, 4H), 6.79 (s, 2H), 4.42 (q, $J^1$ = 8.1 Hz, $J^2$ = 13.8 Hz, 1H), 1.65 (d, $J$ = 6.9 Hz, 3H ); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 135.34, 128.51, 124.74, 122.47, 122.15, 120.80, 112.67, 112.41, 28.14, 21.54; ESI-MS for $C_{18}H_{14}Br_2N_2$ = 415.9011 $[M]^+$.




**3,3'-(ethane-1,1-diyl)bis(5-methoxy-1-methyl-1H-indole) (3k)**: Yield 76%, 210 mg; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.14 (s, 1H), 7.11 (s, 1H), 6.98 (d, $J$ = 2.1 Hz, 2H), 6.83 (s, 1H), 6.80 (s, 1H), 6.70 (s, 2H), 4.51 (q, $J^1$ = 6.9 Hz, $J^2$ = 14.1 Hz, 1H), 3.73(s, 6H), 3.62 (s, 6H), 1.72 (d, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 153.38, 132.82, 127.54, 126.72, 119.71, 111.34, 109.84, 102.00, 56.06, 32.81, 27.97, 21.98; ESI-MS for $C_{22}H_{24}N_2O_2$ = 348.1381 $[M]^+$.

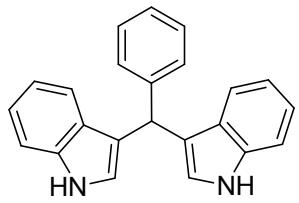


**3,3'-(ethane-1,1-diyl)bis(5-bromo-1-ethyl-1H-indole) (3l)**: Yield 71%, 266 mg; $^1$H NMR



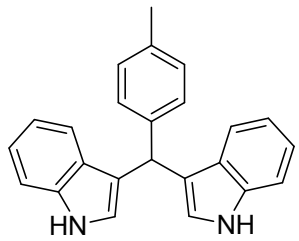

(300 MHz, $CDCl_3$): $\delta$ 7.61 (s, 2H), 7.21 (m, 4H), 6.78 (s, 2H), 4.07 (m, 5H), 1.38 (d, $J$ = 7.2, 3H), 1.32 (t, J = 7.2 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 134.88, 129.64, 126.42, 124.17, 121.91, 113.52, 112.00, 110.73, 40.99, 29.39, 22.72, 15.49; ESI-MS for $C_{22}H_{22}Br_2N_2$ = 472.0052 $[M]^+$.

**3,3'-(phenylmethylene)bis(1H-indole) (3m)[3]:** Yield 92%, 279 mg; $^1$H NMR (300 MHz,



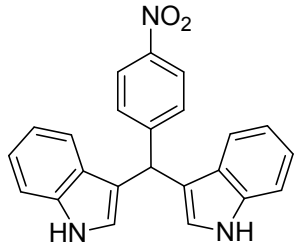

$CDCl_3$): $\delta$ 7.63 (s, 2H), 7.36 (d, $J$ = 8.1 Hz, 2H), 7.31 (d, $J$ = 7.2 Hz, 2H), 7.25 (d, $J$ = 8.4 Hz, 3H), 7.21 (m, 1H), 7.13 (t, $J$ = 7.2 Hz, 2H), 6.97 (t, $J$ = 7.2 Hz, 2H), 6.52 (s, 2H), 5.84 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 144.09, 136.69, 128.78, 128.29, 127.11, 126.20, 123.71, 121.95, 119.97, 119.65, 119.26, 111.14, 40.23; ESI-MS for $C_{23}H_{18}N_2$ = 323.0637 $[M+H]^+$.

**3, 3'-(p-tolylmethylene)bis(1H-indole) (3n)[3]:** Yield 91%, 255 mg; $^1$H NMR (300 MHz,



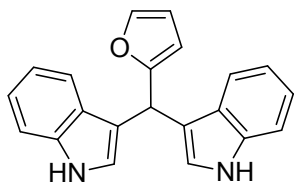

$CDCl_3$): $\delta$ 7.84 (s, 2H), 7.39 (d, $J$ = 7.8 Hz, 2H), 7.33 (d, $J$ = 8.1 Hz, 2H), 7.22 (d, $J$ = 8.7 Hz, 2H), 7.15 (t, $J$ = 7.5 Hz, 2H), 7.07 (d, $J$ = 7.5 Hz, 2H), 6.98 (t, $J$ = 7.5 Hz, 2H), 6.64 (s, 2H), 5.84 (s, 1H), 2.31 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 141.05, 136.70, 135.54, 128.98, 128.62, 127.13, 123.63, 121.90, 120.00, 119.86, 119.22, 111.09, 39.80, 21.14; ESI-MS for $C_{24}H_{20}N_2$ = 337.0743 $[M+H]^+$.

**3,3'-((4-nitrophenyl)methylene)bis(1H-indole) (3o)[4]:** Yield 88%, 214 mg; $^1$H NMR (300



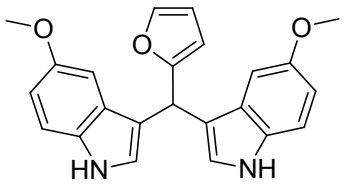

MHz, $d_6$ DMSO): $\delta$ 10.92 (s, 2H), 8.15 (d, $J$ = 7.8 Hz, 2H), 7.62 (d, $J$ = 7.8 Hz, 2H), 7.38 (d, $J$ = 7.8 Hz, 2H), 7.30 (d, $J$ = 7.8 Hz, 2H), 7.06 (t, $J$ = 7.2 Hz, 2H), 6.91 (s, 4H), 6.03 (s, 1H); $^{13}$C NMR (100 MHz, $d_6$ DMSO): $\delta$ 153.59, 146.25, 137.06, 129.91, 126.84, 124.32, 123.87, 121.57, 119.37, 118.89, 117.15, 112.05; ESI-MS for $C_{23}H_{17}N_3O_2$ = 368.0543 $[M+H]^+$.

**3,3'-(furan-2-ylmethylene)bis(1H-indole) (3p)**[3]: Yield 87%, 283 mg; $^1$H NMR (300 MHz,



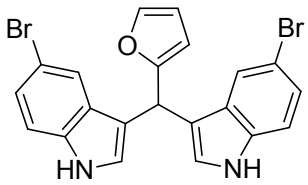

$CDCl_3$): $\delta$ 7.90 (s, 2H), 7.47 (d, $J$ = 8.1 Hz, 2H), 7.33 (d, $J$ = 8.1 Hz, 2H), 7.16 (t, $J$ = 7.2 Hz, 2H), 7.03 (t, $J$ = 7.2 Hz, 2H), 6.83(s, 2H), 6.29 (s, 1H), 6.05 (s, 1H), 5.93 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 156.65, 140.77, 136.00, 126.25, 122.69, 121.46, 119.18, 118.87, 116.56, 110.75, 109.74, 106.17, 33.61; ESI-MS for $C_{21}H_{16}N_2O^+$ 313.0793 $[M+H]^+$.

**3,3'-(furan-2-ylmethylene)bis(5-methoxy-1H-indole) (3q):** Yield 89%, 345 mg; $^1$H NMR



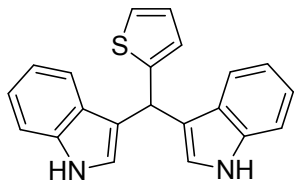

(300 MHz, $CDCl_3$): $\delta$ 7.85 (s, 2H), 7.35 (s, 1H), 7.24 (d, $J$ = 4.8 Hz, 1H), 7.20 (s, 1H), 6.89 (s, 2H), 6.84 (s, 3H), 6.81 (s, 1H), 6.30 (s, 1H), 6.07 (s, 1H), 5.83 (s, 1H), 3.72 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 157.23, 153.75, 141.28, 131.83, 127.19, 124.14, 116.58, 112.04, 111.94, 110.28, 106.74, 101.72, 55.91, 34.26; ESI-MS for $C_{23}H_{20}N_2O_3$ = 373.0794 $[M+H]^+$.

**3, 3'-(furan-2-ylmethylene)bis(5-bromo-1H-indole) (3r):** Yield 82%, 399 mg; $^1$H NMR



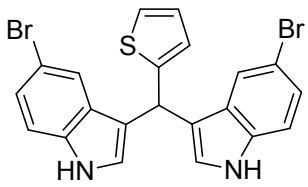

(300 MHz, $d_6$ DMSO): $\delta$ 11.09 (s, 2H), 7.52 (s, 3H), 7.33 (d, $J$ = 8.4 Hz, 2H), 7.14 (d, $J$ = 8.4 Hz, 2H), 7.09 (s, 2H), 6.37 (s, 1H), 6.09 (s, 1H), 5.92 (s, 1H); $^{13}$C NMR (75 MHz, $d_6$ DMSO): $\delta$ 157.29, 141.96, 135.58, 128.54, 125.41, 123.87, 121.65, 115.63, 113.97, 111.49, 110.67, 106.49, 33.58; ESI-MS for $C_{21}H_{14}Br_2N_2O$ = 467.5743 $[M]^+$.

**3,3'-(thiophen-2-ylmethylene)bis(1H-indole) (3s)**[5]: Yield 86%, 252 mg; $^1$H NMR (300



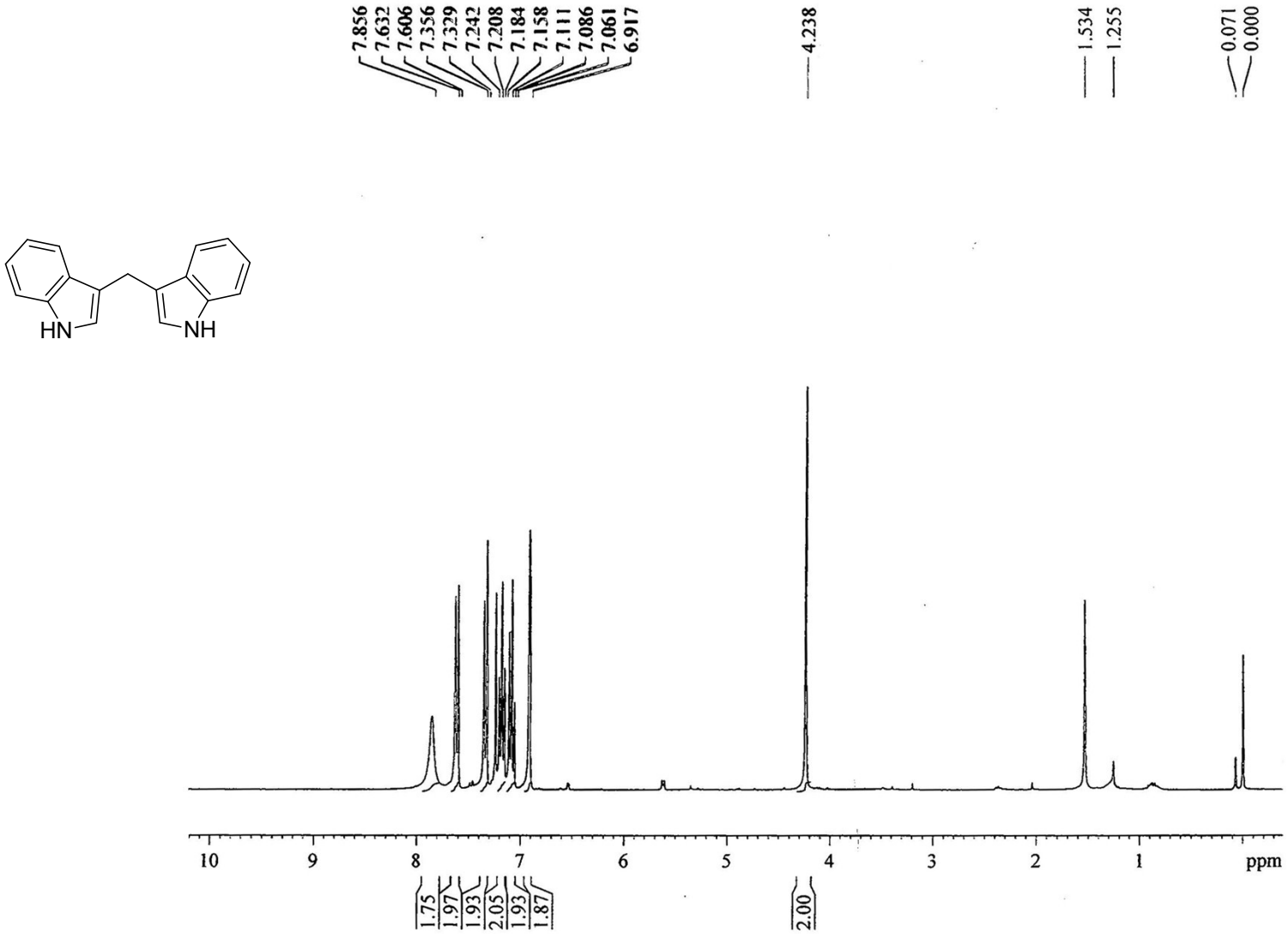

MHz, $CDCl_3$): $\delta$ 7.70 (s, 2H), 7.62 (d, $J$ = 7.8 Hz, 2H), 7.43 (s, 1H), 7.28 (s, 4H), 7.20 (m, 2H), 6.73 (s, 1H), 6.41 (s, 1H), 6.17 (s, 1H), 6.05 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 157.34, 141.34, 136.61, 126.85, 123.42, 122.02, 119.75, 119.46, 116.96, 111.48, 110.40, 106.78, 34.25; ESI-MS for $C_{21}H_{16}N_2S$ = 329.0794 $[M+H]^+$.

**3,3'-(thiophen-2-ylmethylene)bis(5-bromo-1H-indole) (3t)**: Yield 81%, 349 mg; $^1$H NMR

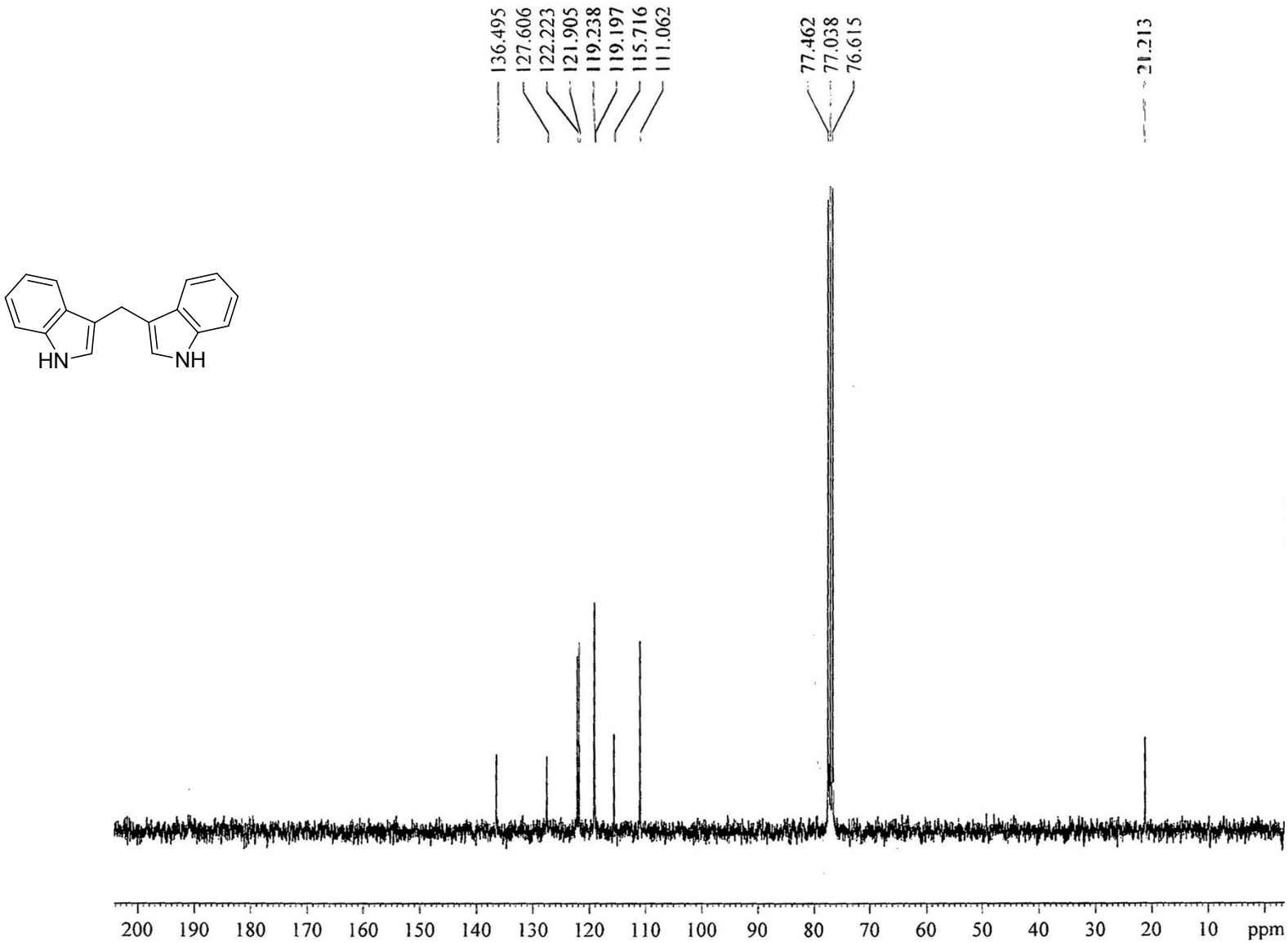



(300 MHz, $CDCl_3$): $\delta$ 11.09 (s, 2H), 7.52 (s, 3H), 7.33 (d, $J$ = 8.7 Hz, 2H), 7.15 (d, $J$ = 9.9 Hz, 2H), 7.08 (s, 2H), 6.37 (s, 1H), 6.09 (s, 1H), 5.92 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 156.78, 141.44, 135.08, 128.04, 124.90, 123.37, 121.15, 115.13, 113.46, 111.00, 110.16, 105.99, 33.09; ESI-MS for $C_{21}H_{14}Br_2N_2S$ = 484.3746 $[M+H]^+$.

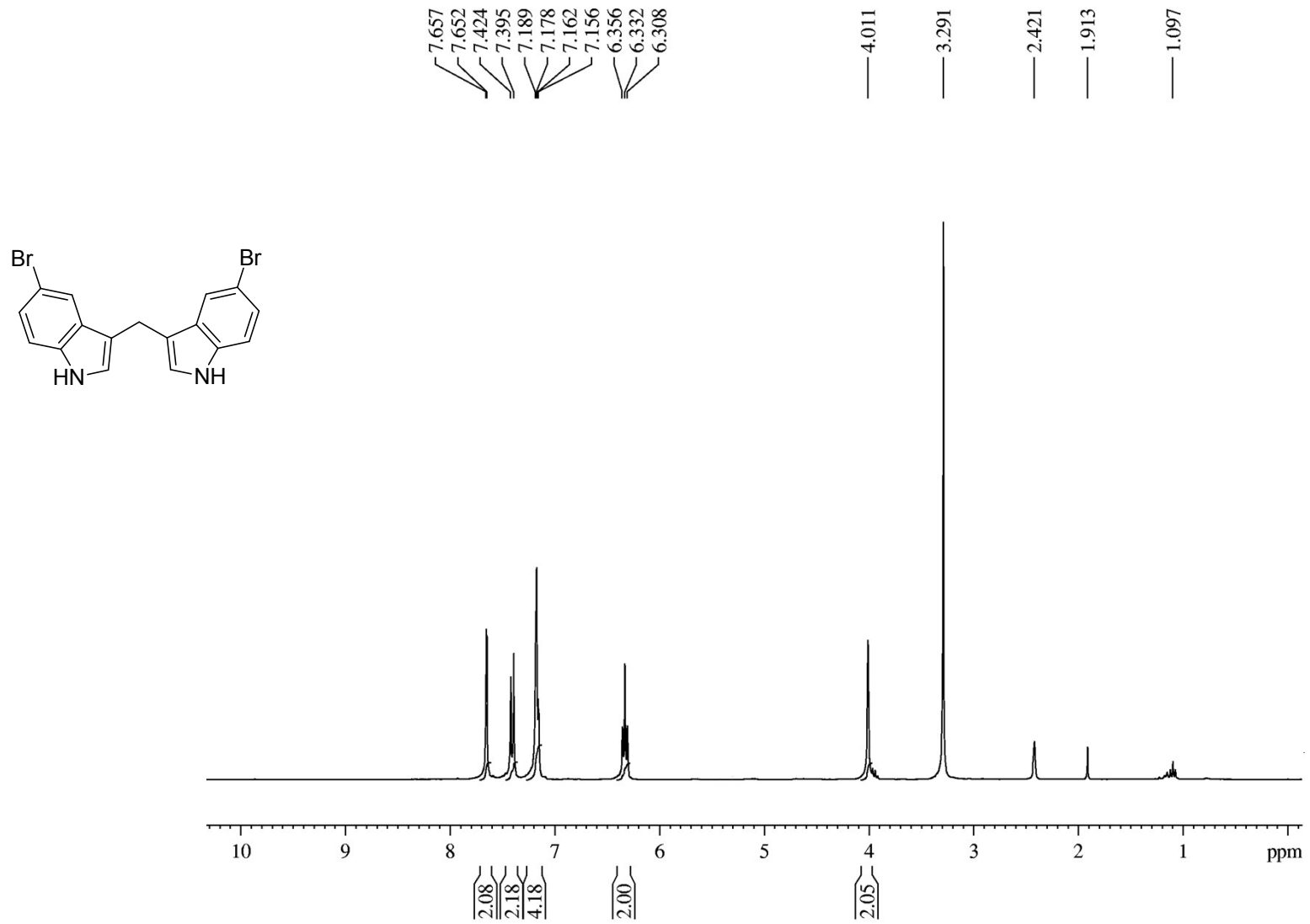
## 4. Copies of $^{1}H$ NMR and $^{13}C$ NMR (Spectrum 1-40)



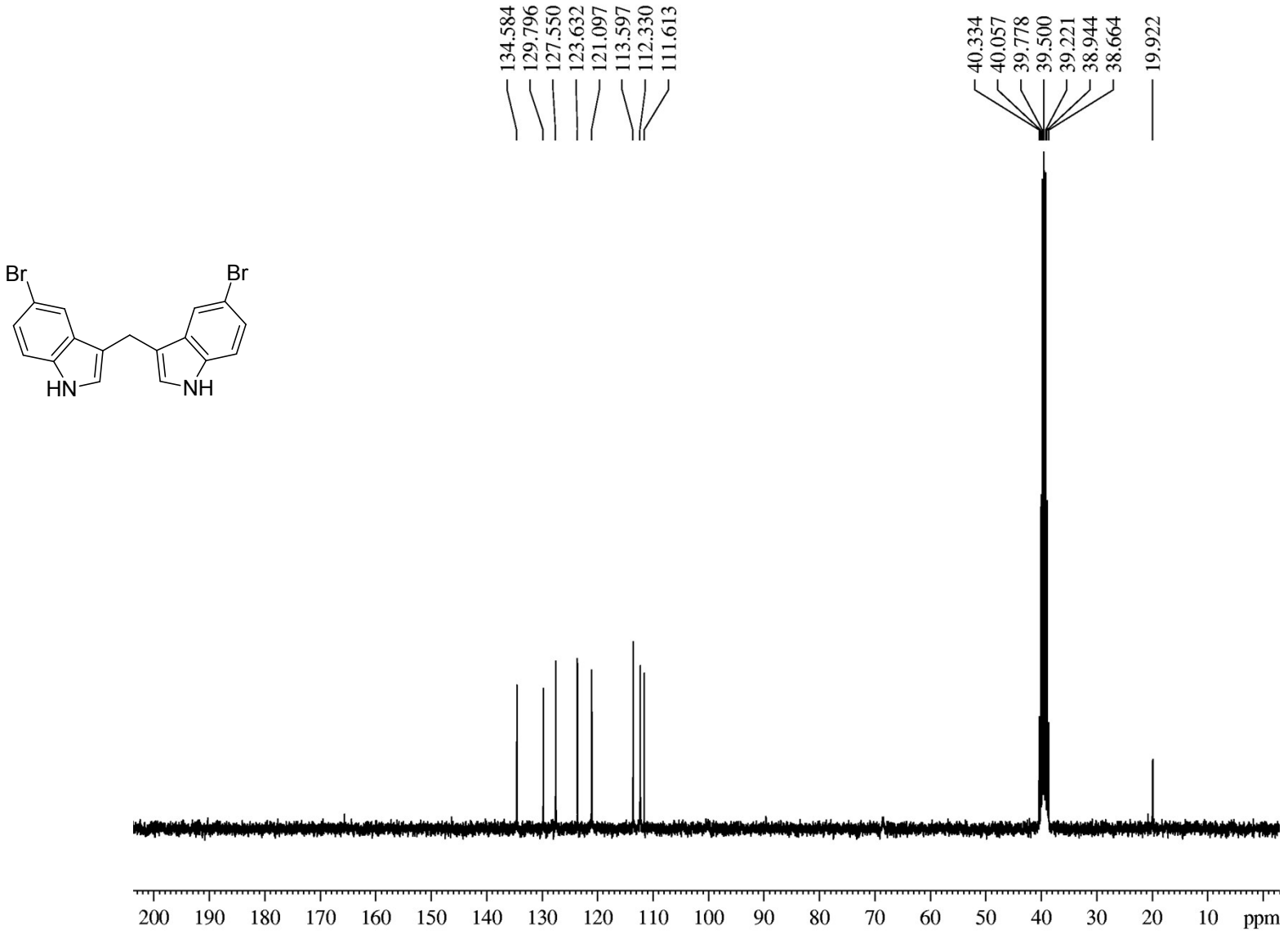

**Spectrum 1.** $^{1}H$ NMR of compound **3a**



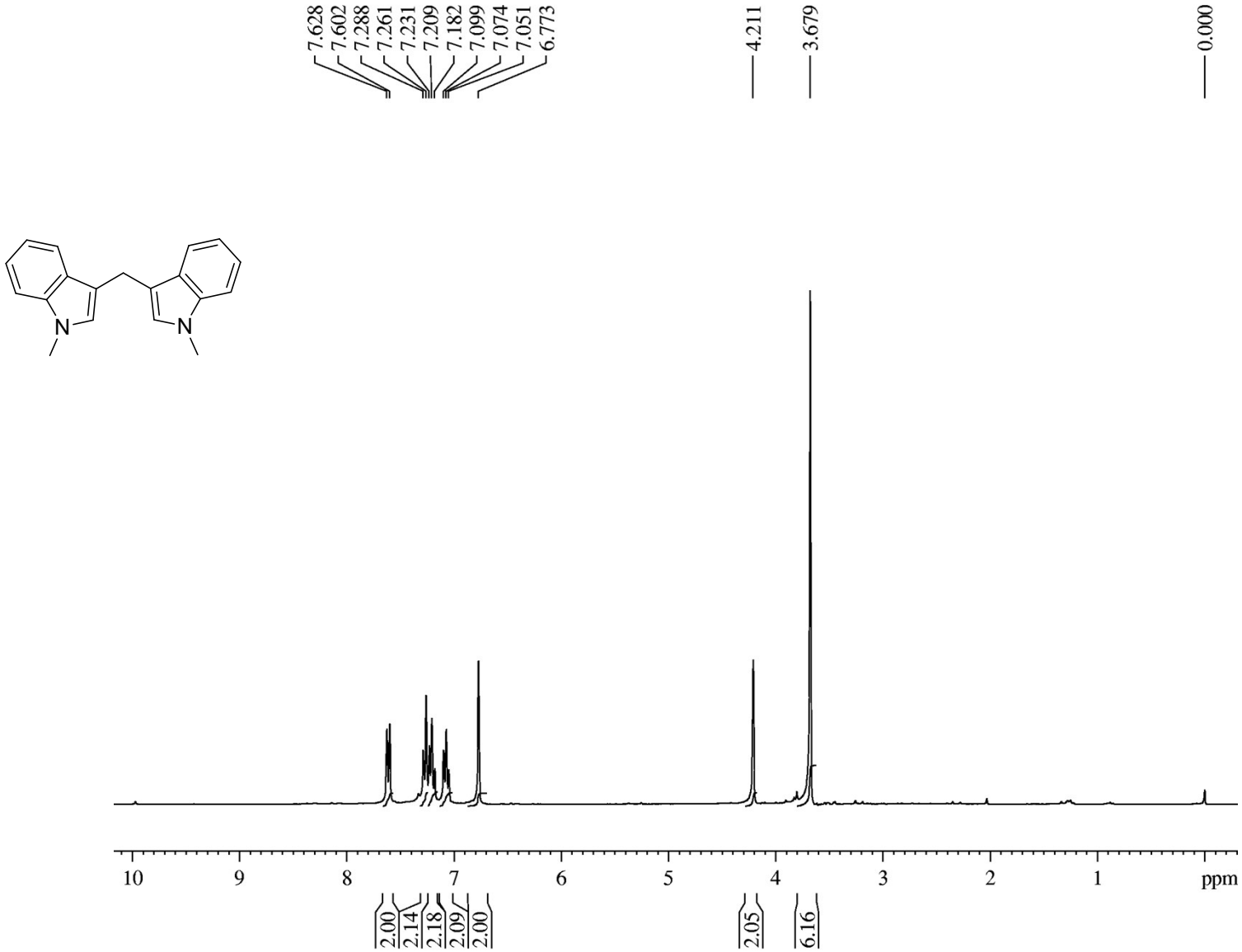

**Spectrum 2.** $^{13}$C NMR of compound **3a**



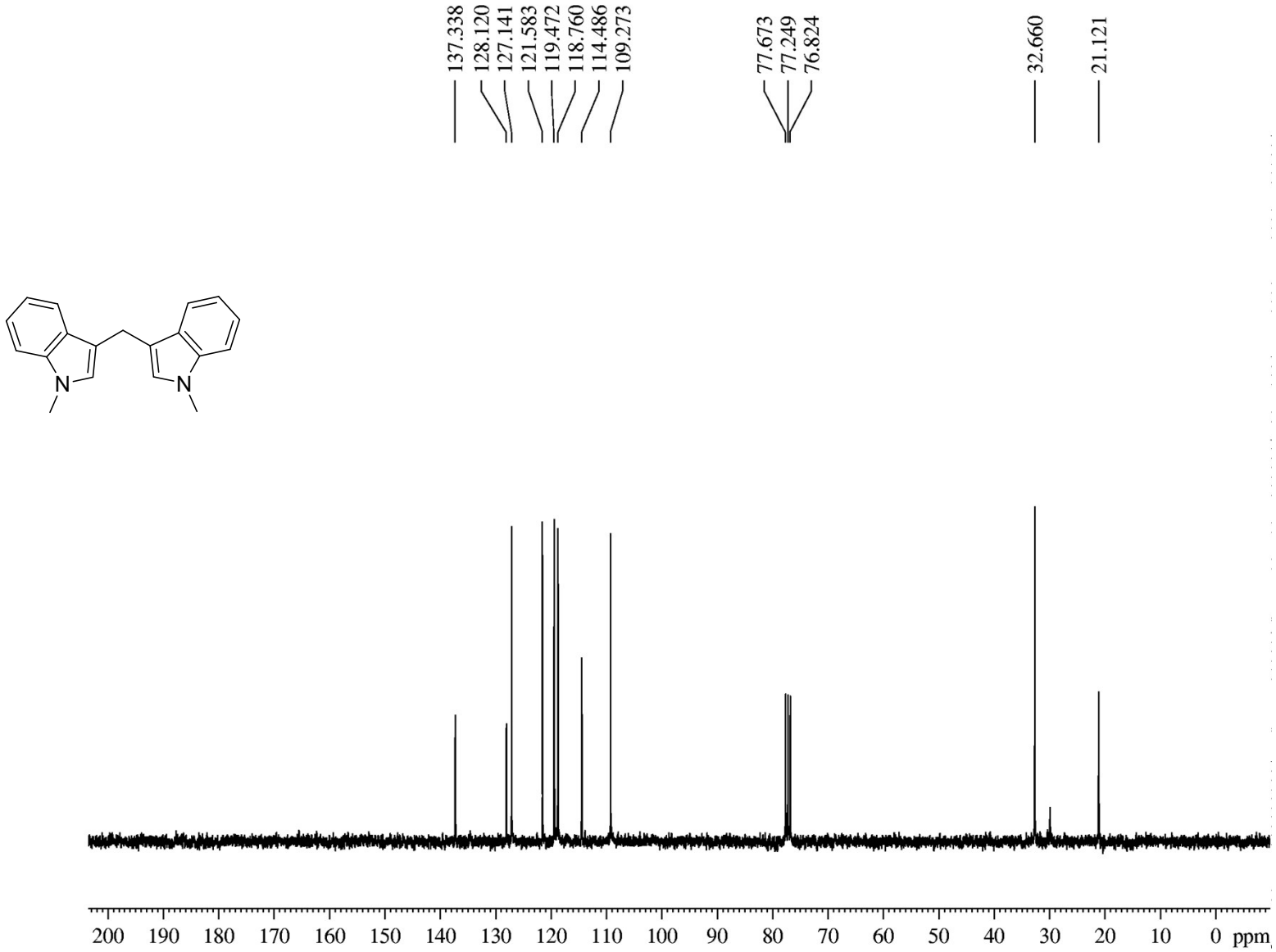

**Spectrum 3.** [1]H NMR of compound **3b**



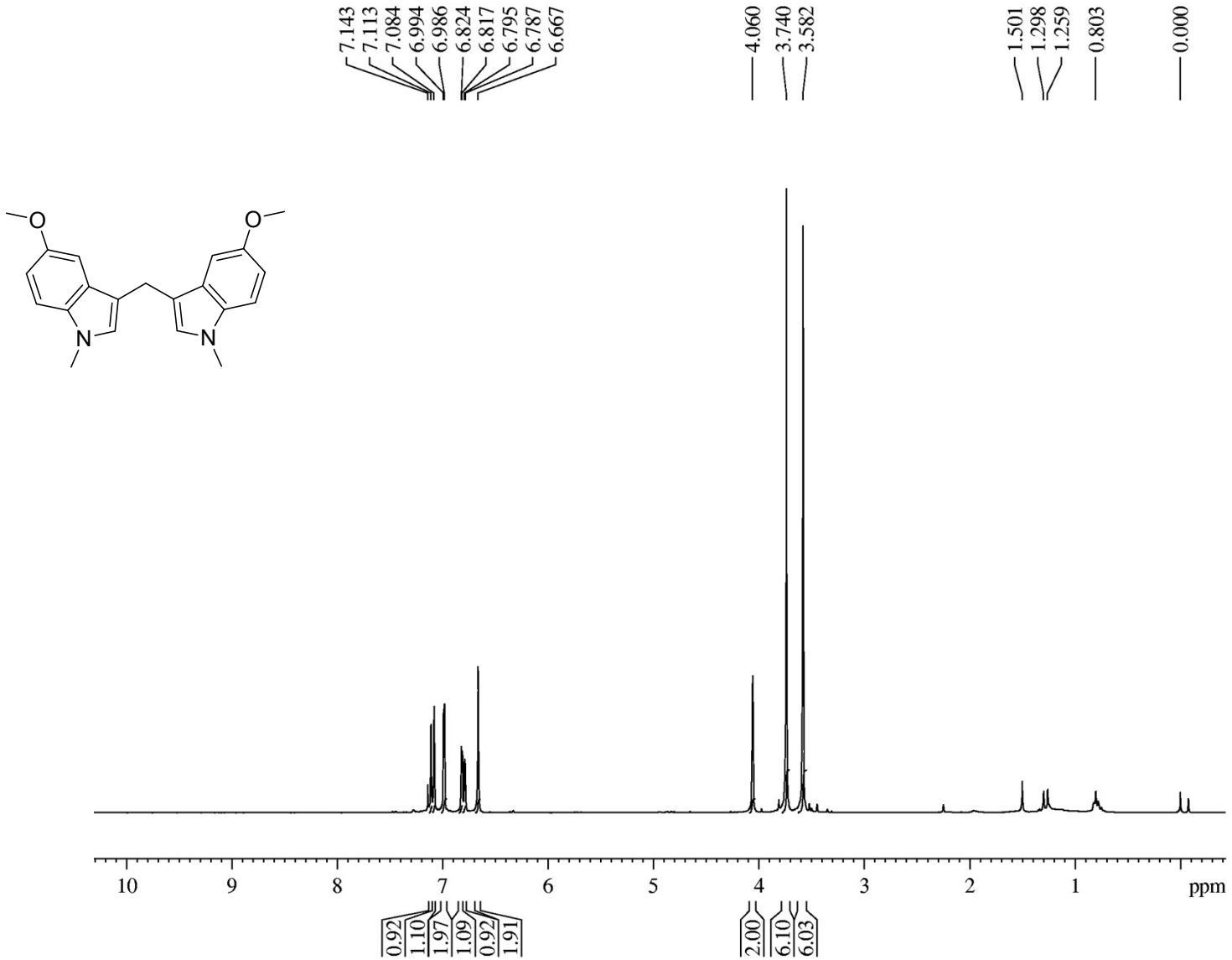

**Spectrum 4.** $^{13}$C NMR of compound **3b**



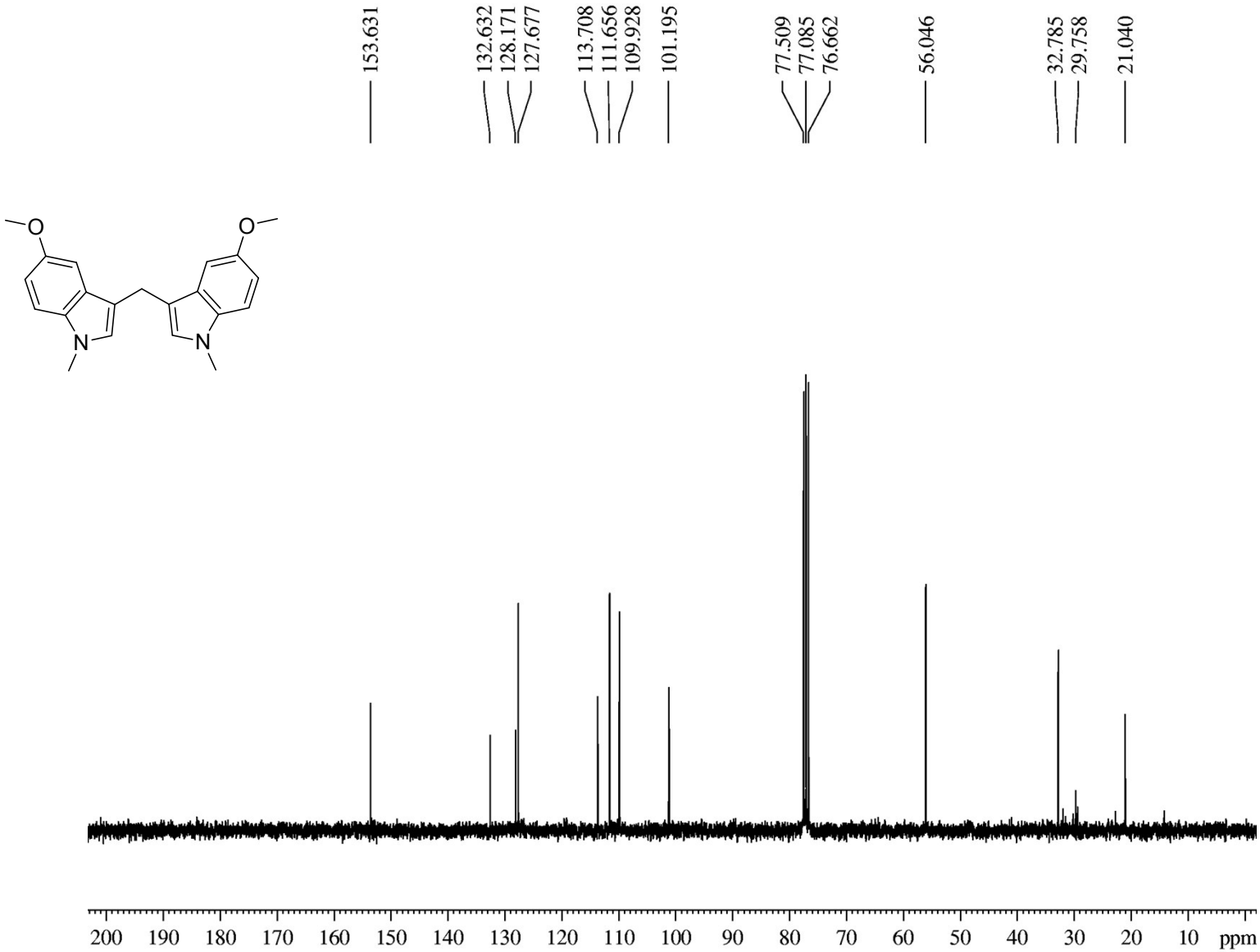

**Spectrum 5.** $^{1}$H NMR of compound **3c**



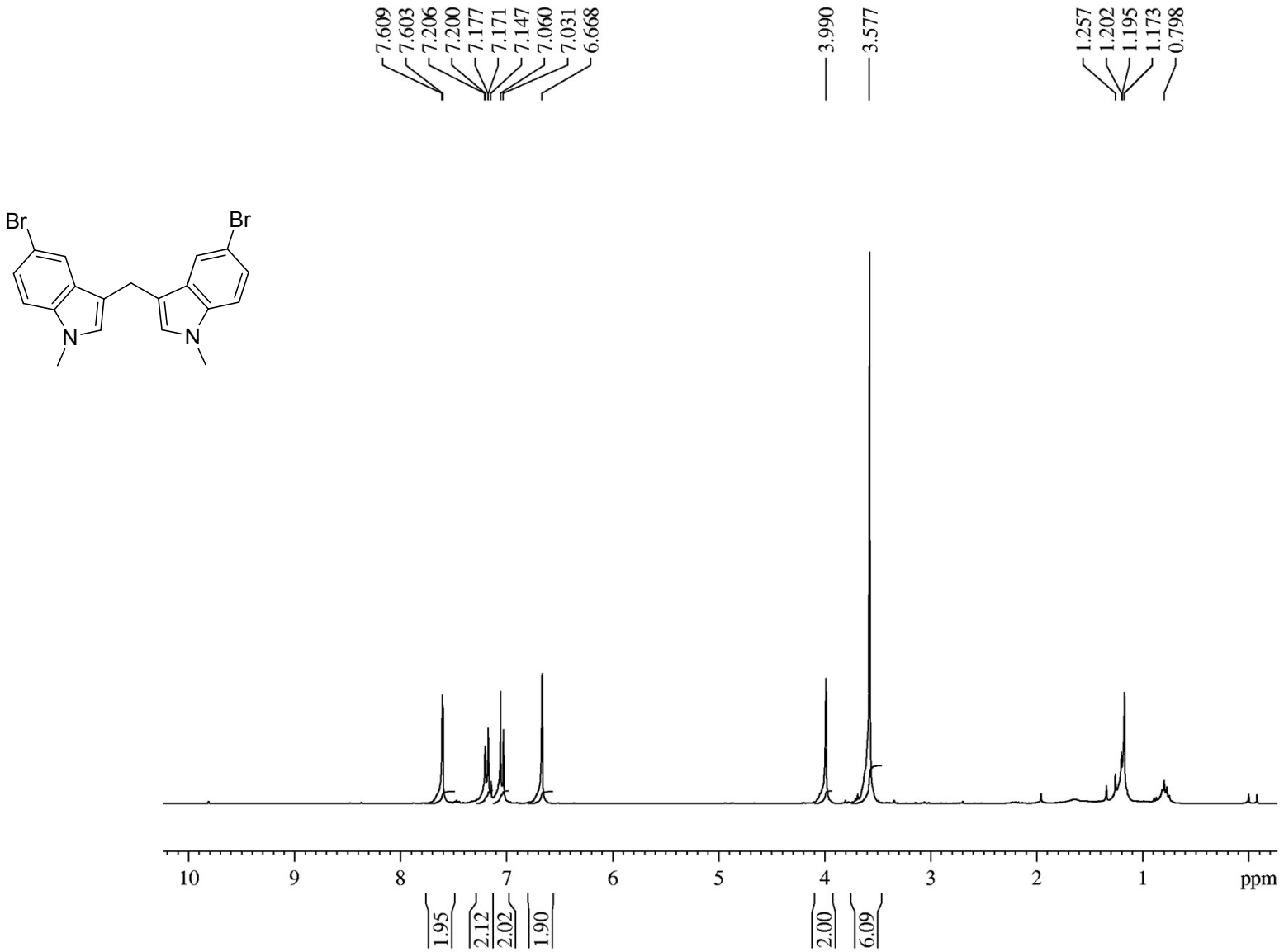

**Spectrum 6.** $^{13}$C NMR of compound **3c**



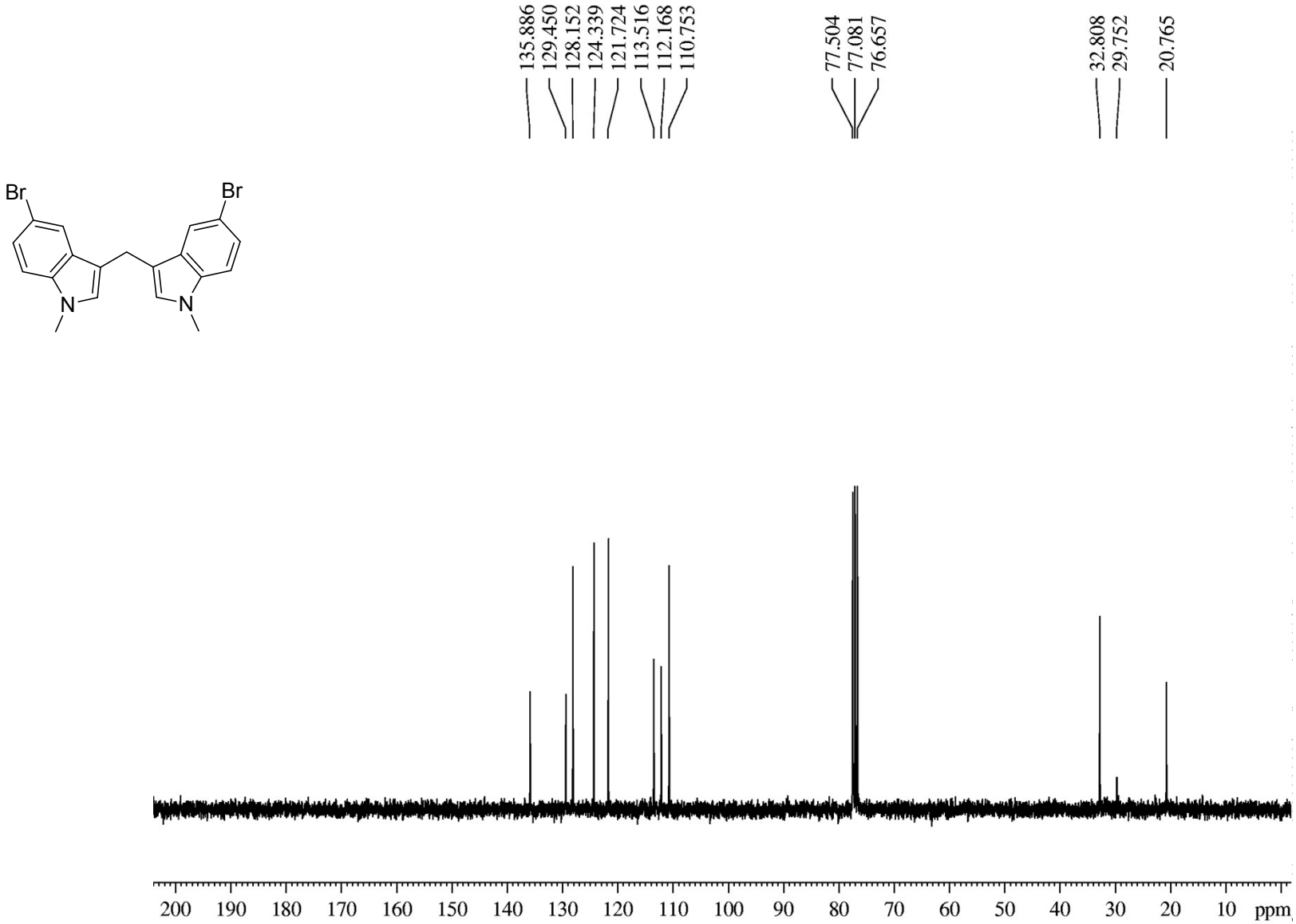

**Spectrum 7.** [1]H NMR of compound **3d**



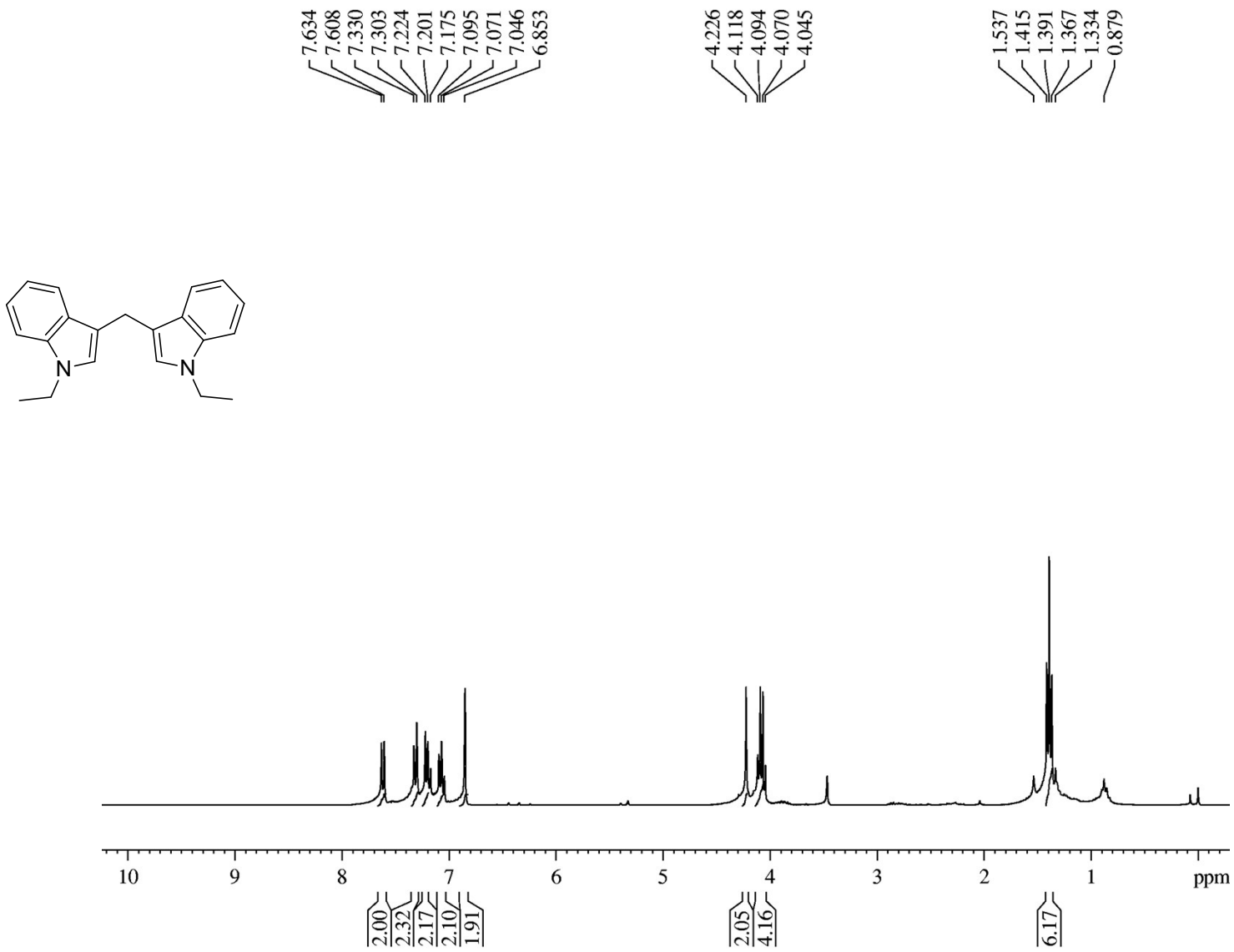

**Spectrum 8.** $^{13}$C NMR of compound **3d**



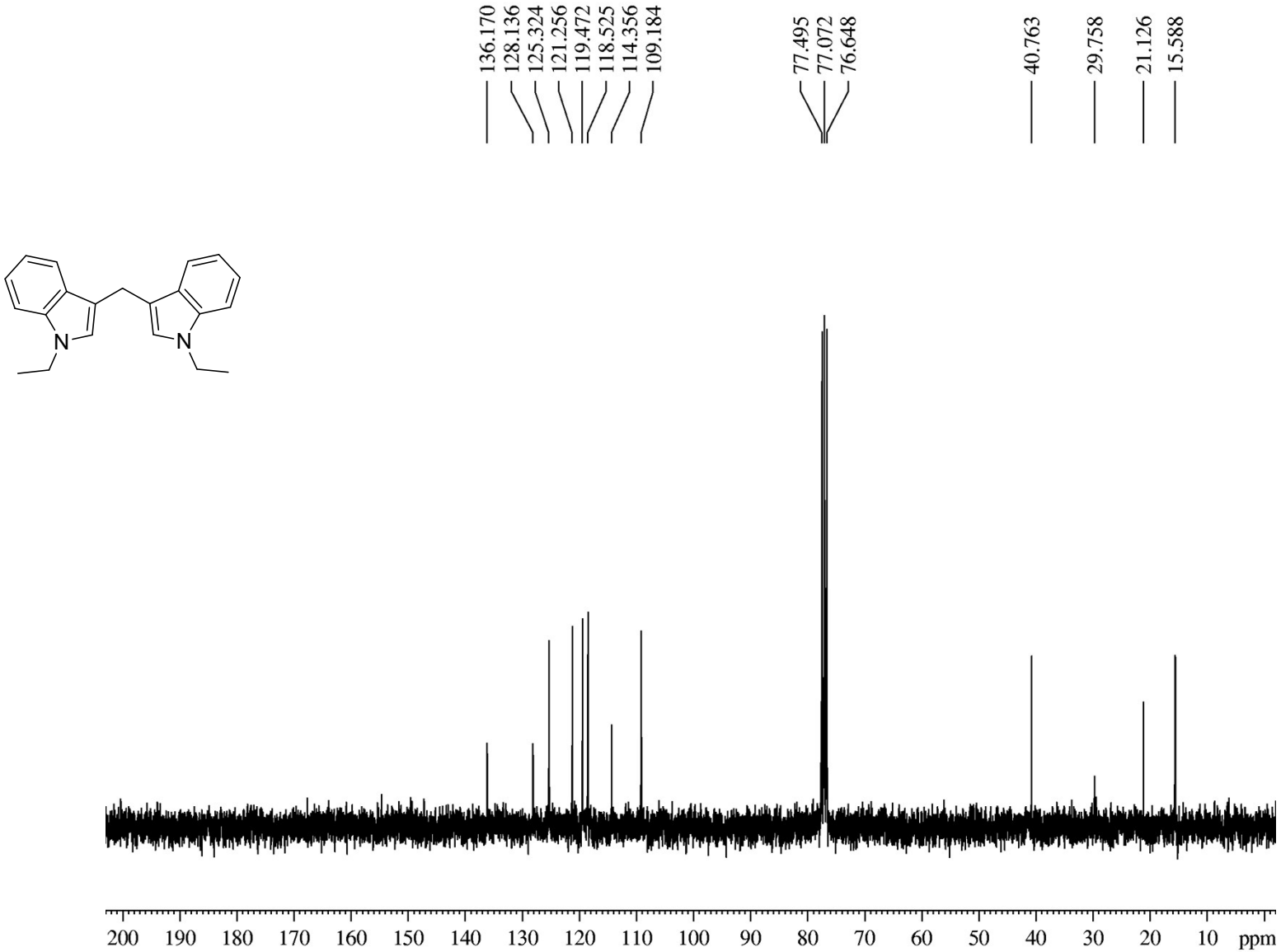

**Spectrum 9.** [1]H NMR of compound **3e**



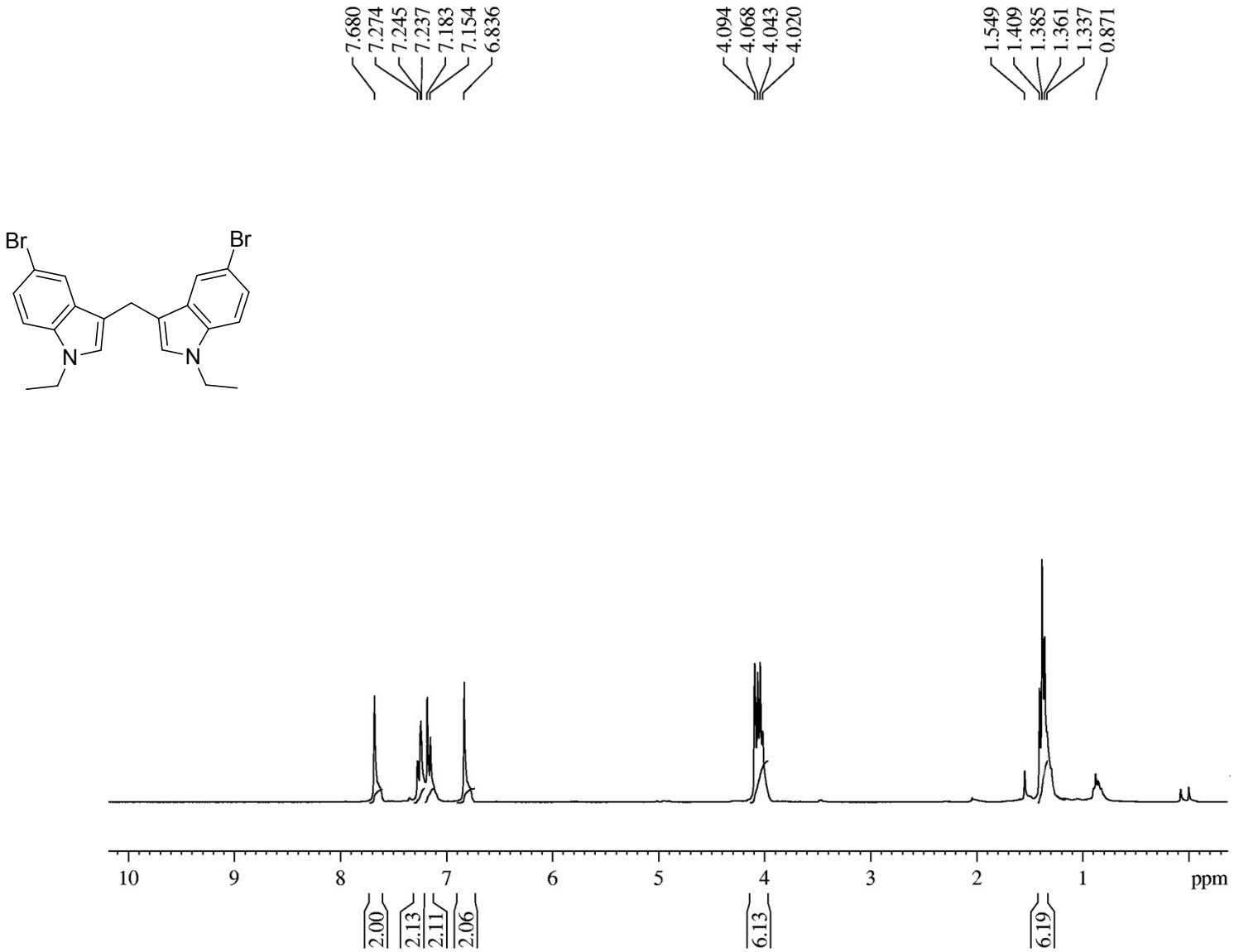

**Spectrum 10.** $^{13}$C NMR of compound **3e**



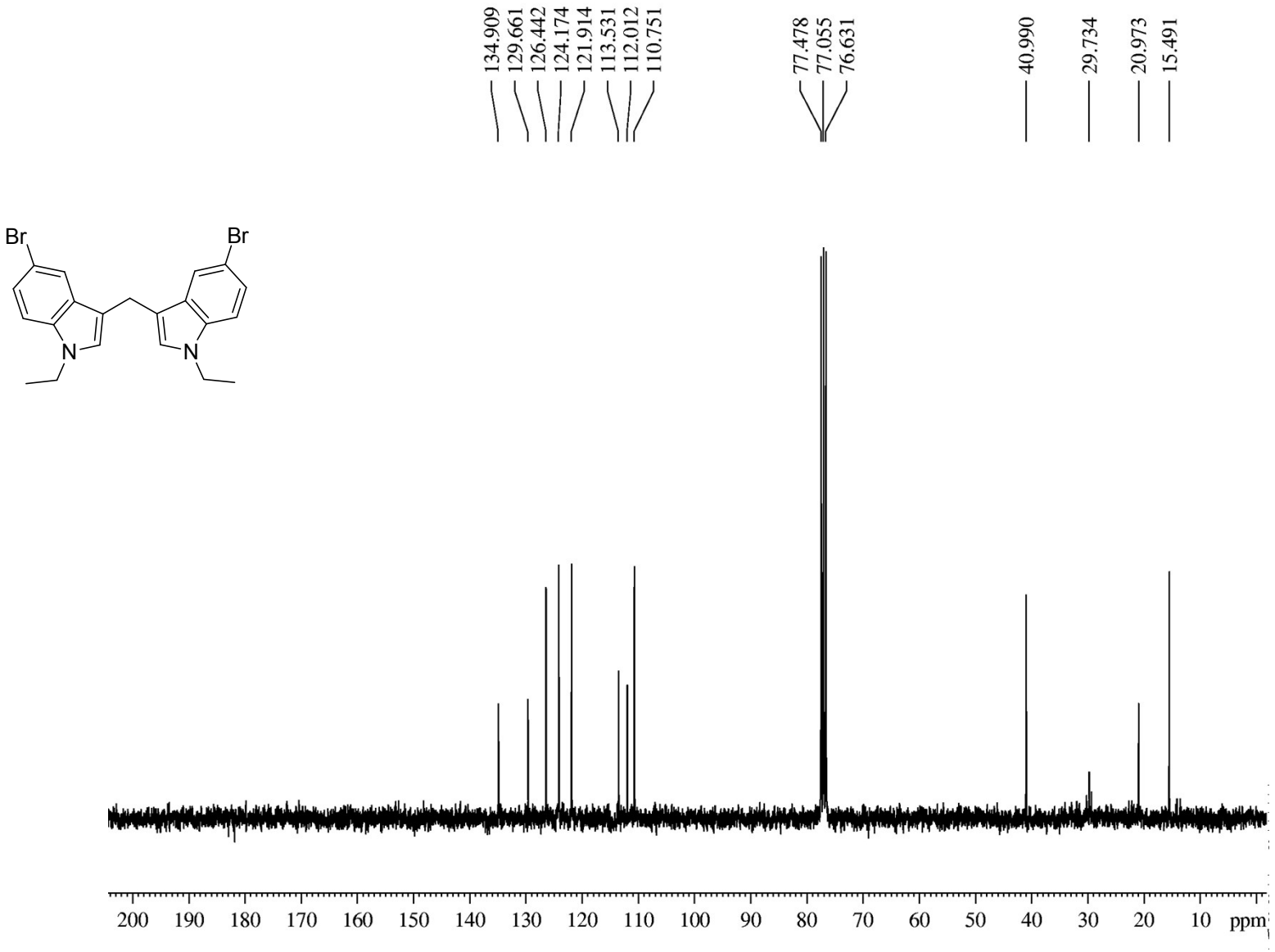

**Spectrum 11.** [1]H NMR of compound **3f**



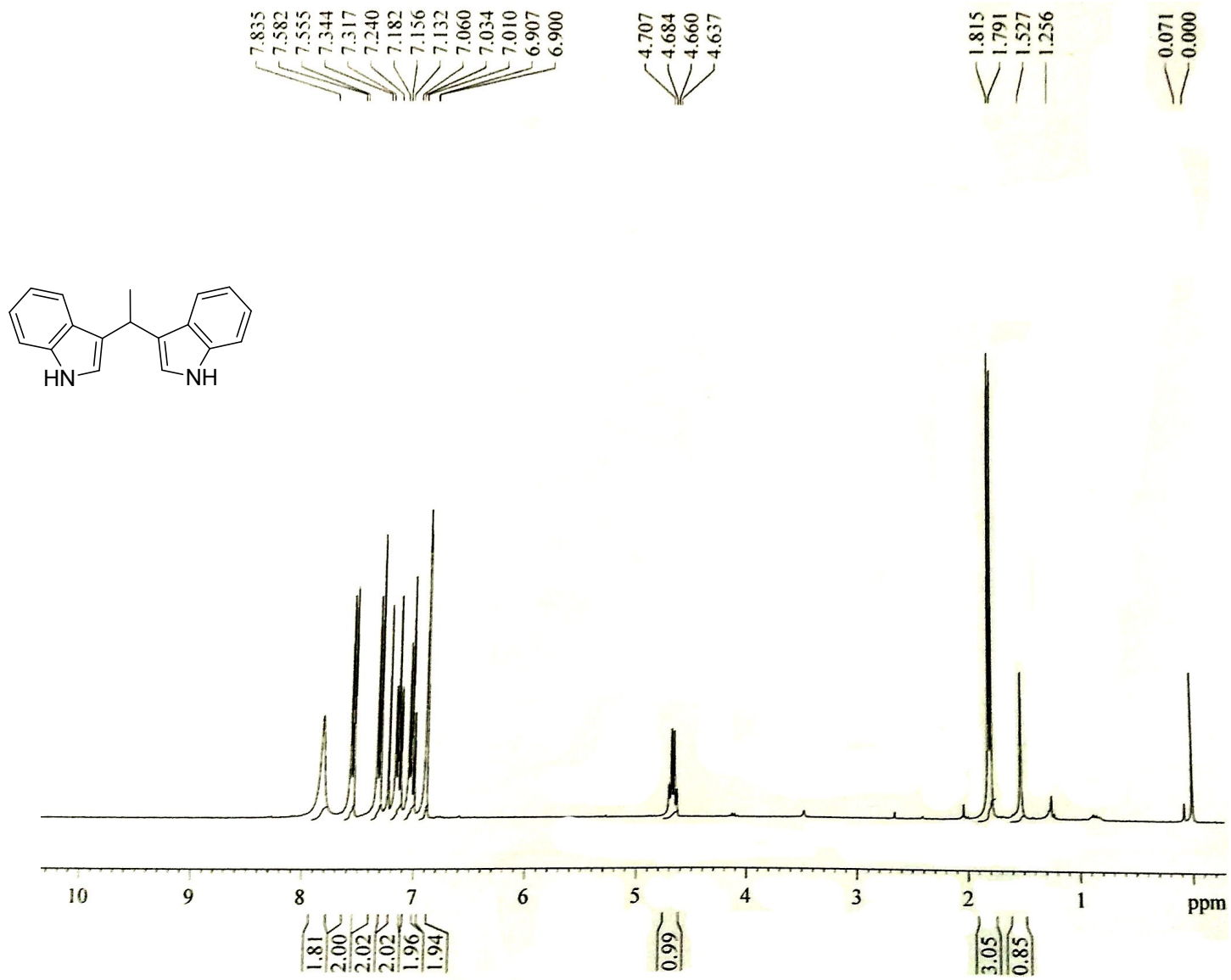

**Spectrum 12.** $^{13}$C NMR of compound **3f**



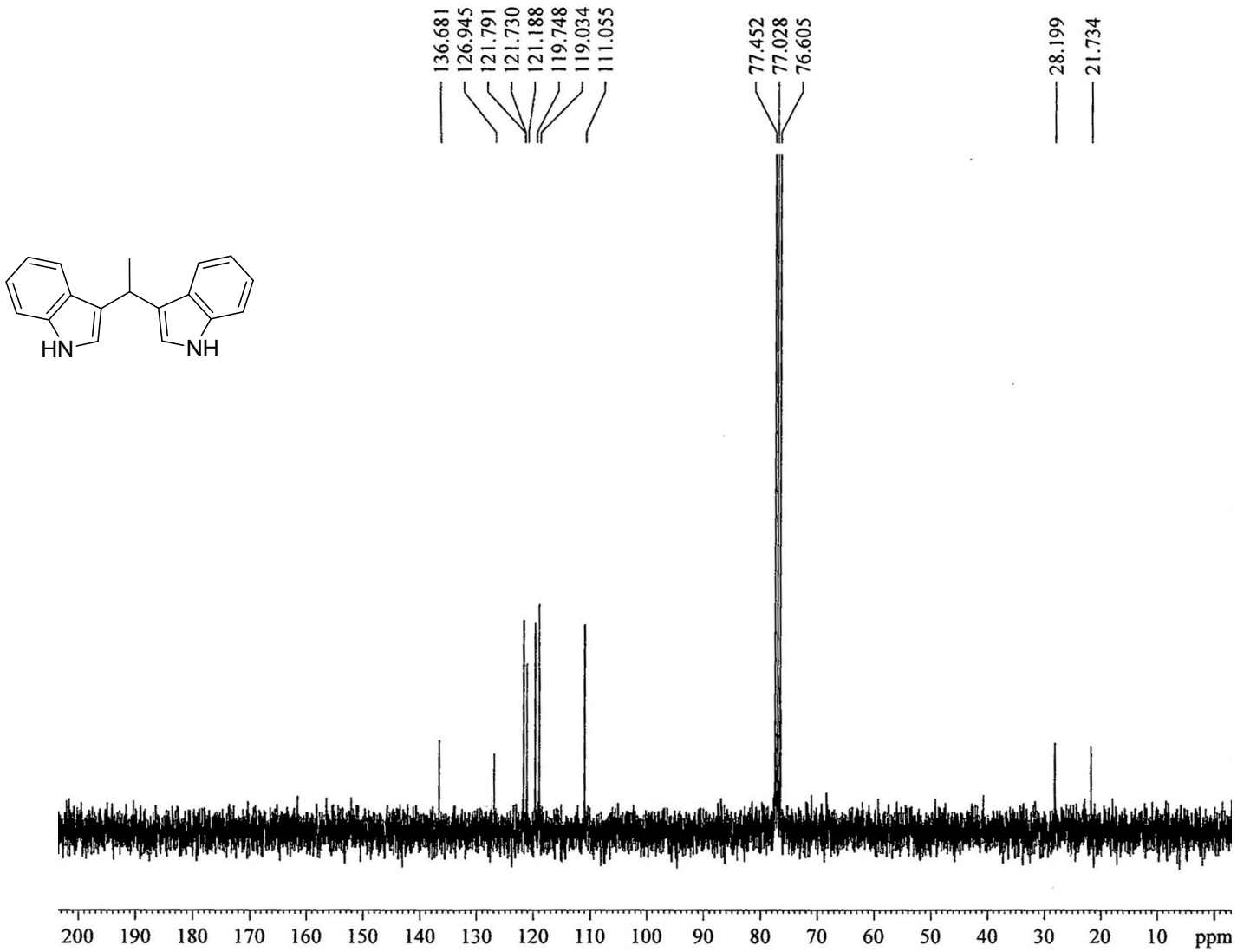

**Spectrum 13.** $^{1}$H NMR of compound **3g**



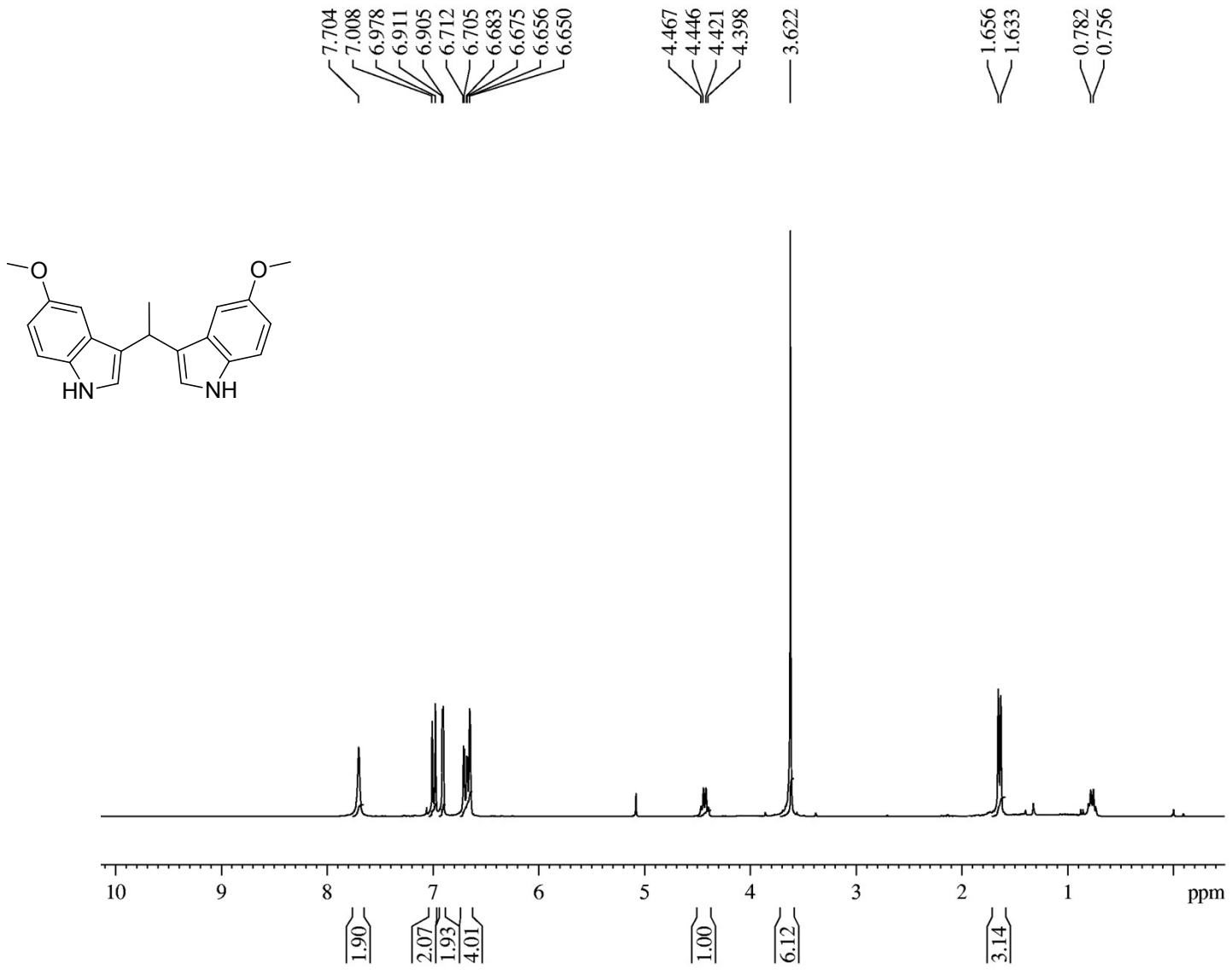

**Spectrum 14.** $^{13}$C NMR of compound **3g**



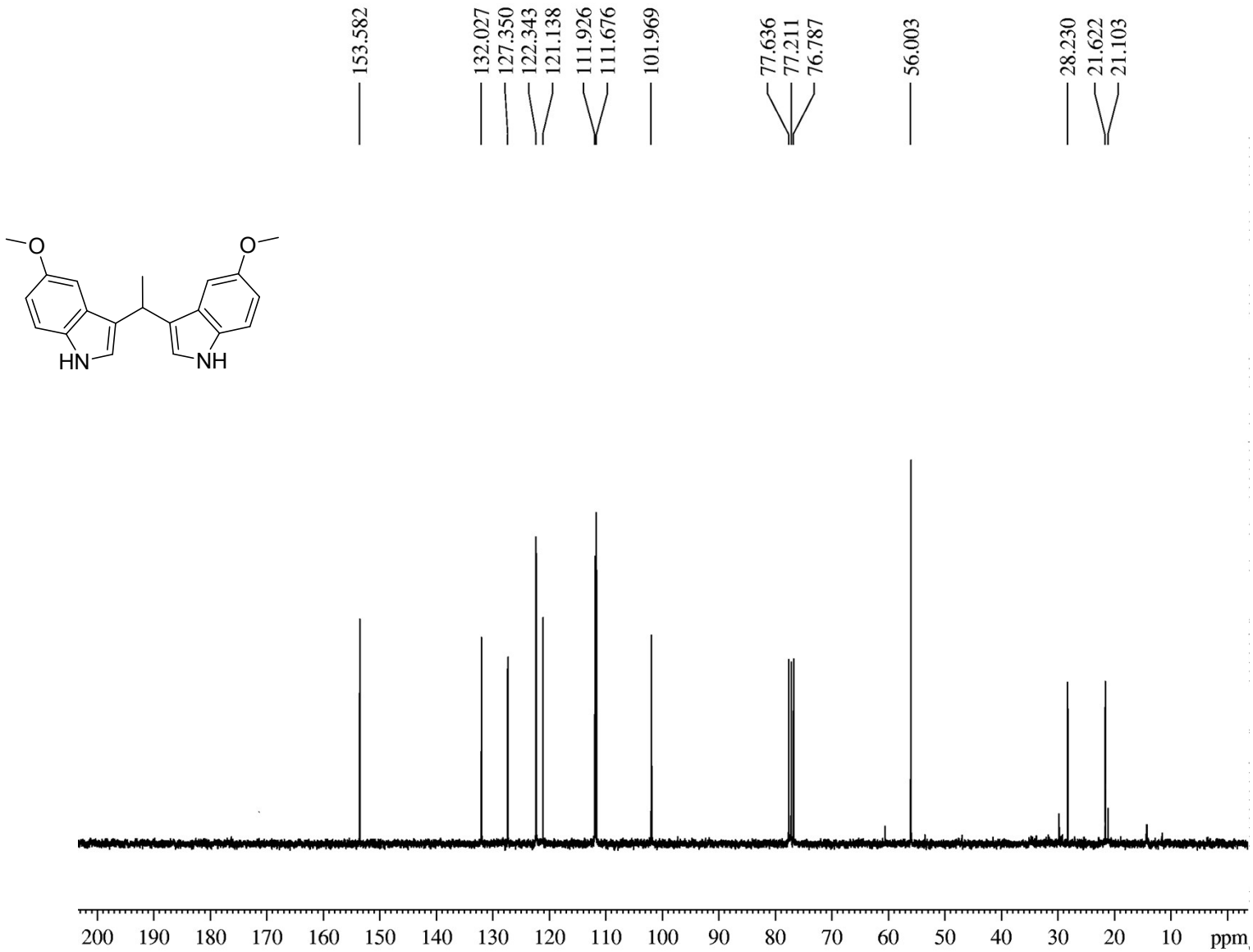

**Spectrum 15.** $^{1}$H NMR of compound **3h**



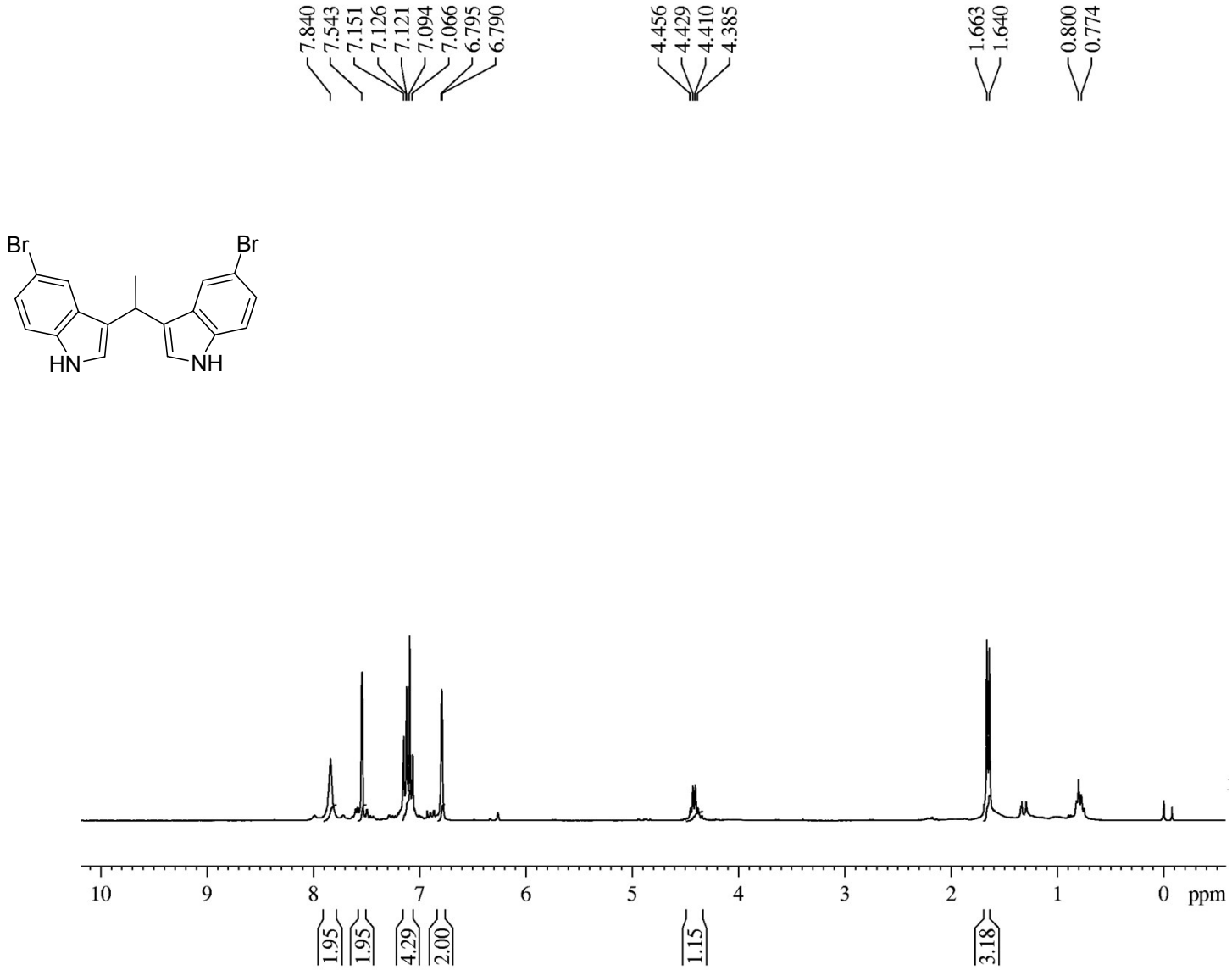

**Spectrum 16.** $^{13}C$ NMR of compound **3h**



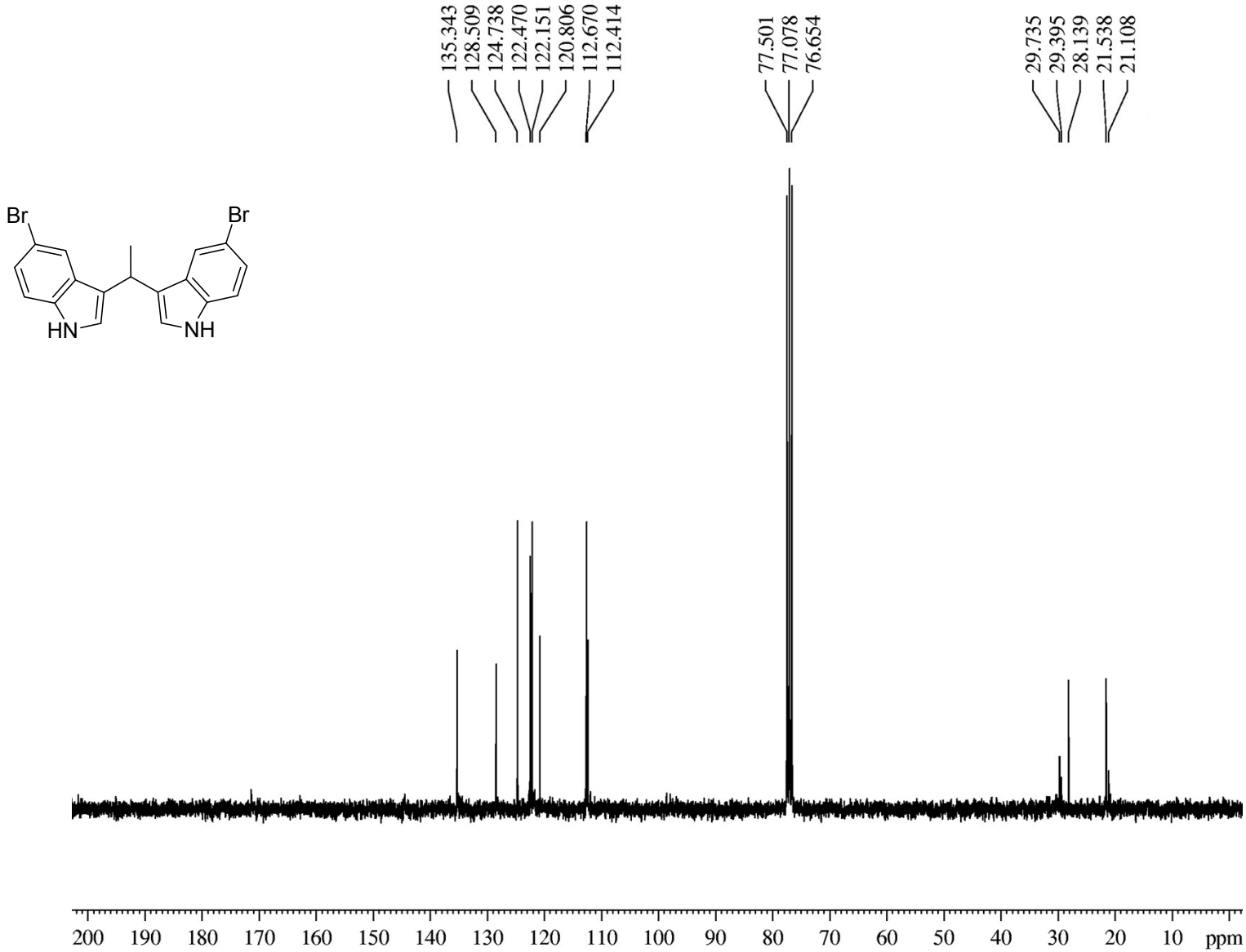

**Spectrum 17.** $^{1}$H NMR of compound **3i**



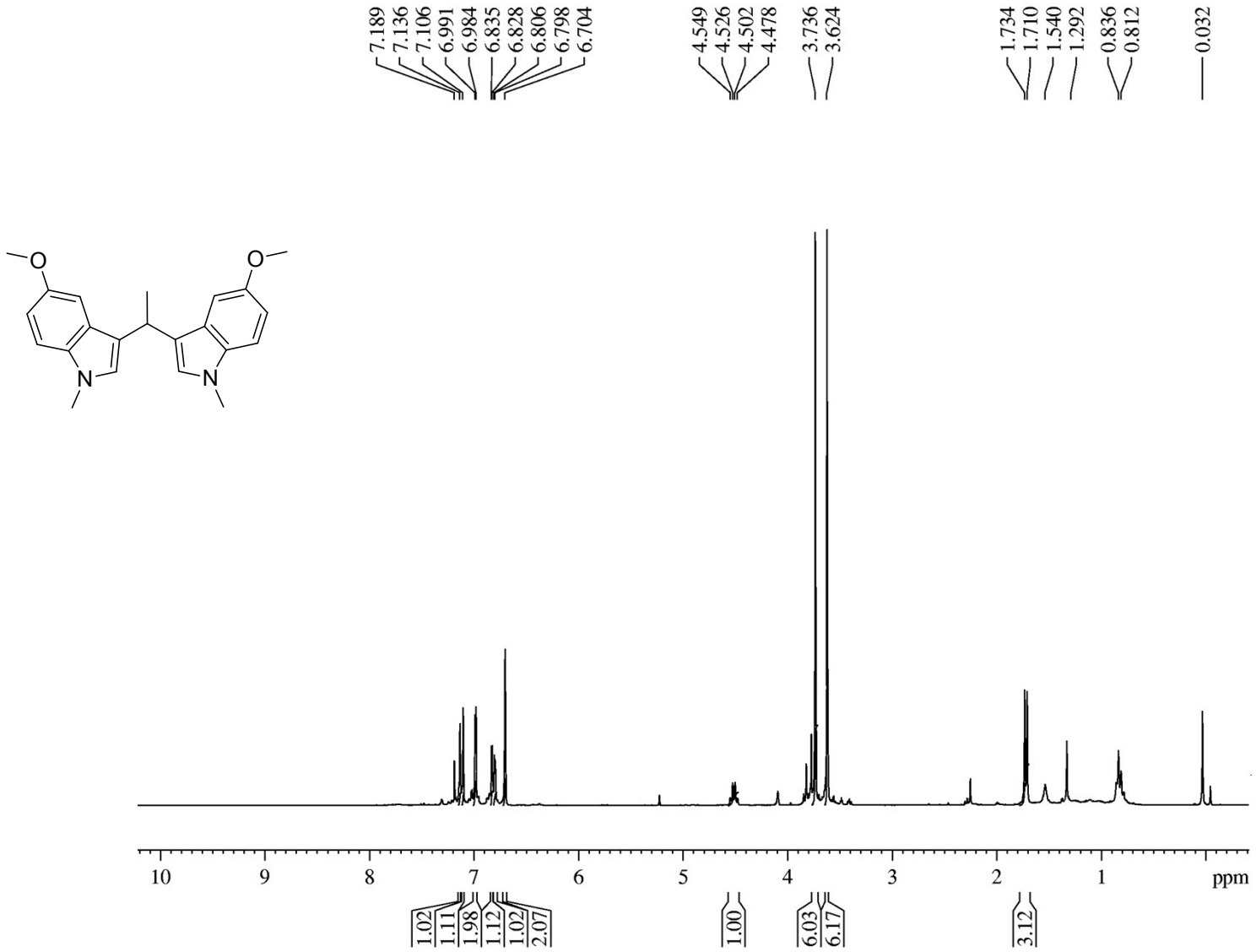

**Spectrum 18.** $^{13}$C NMR of compound **3i**



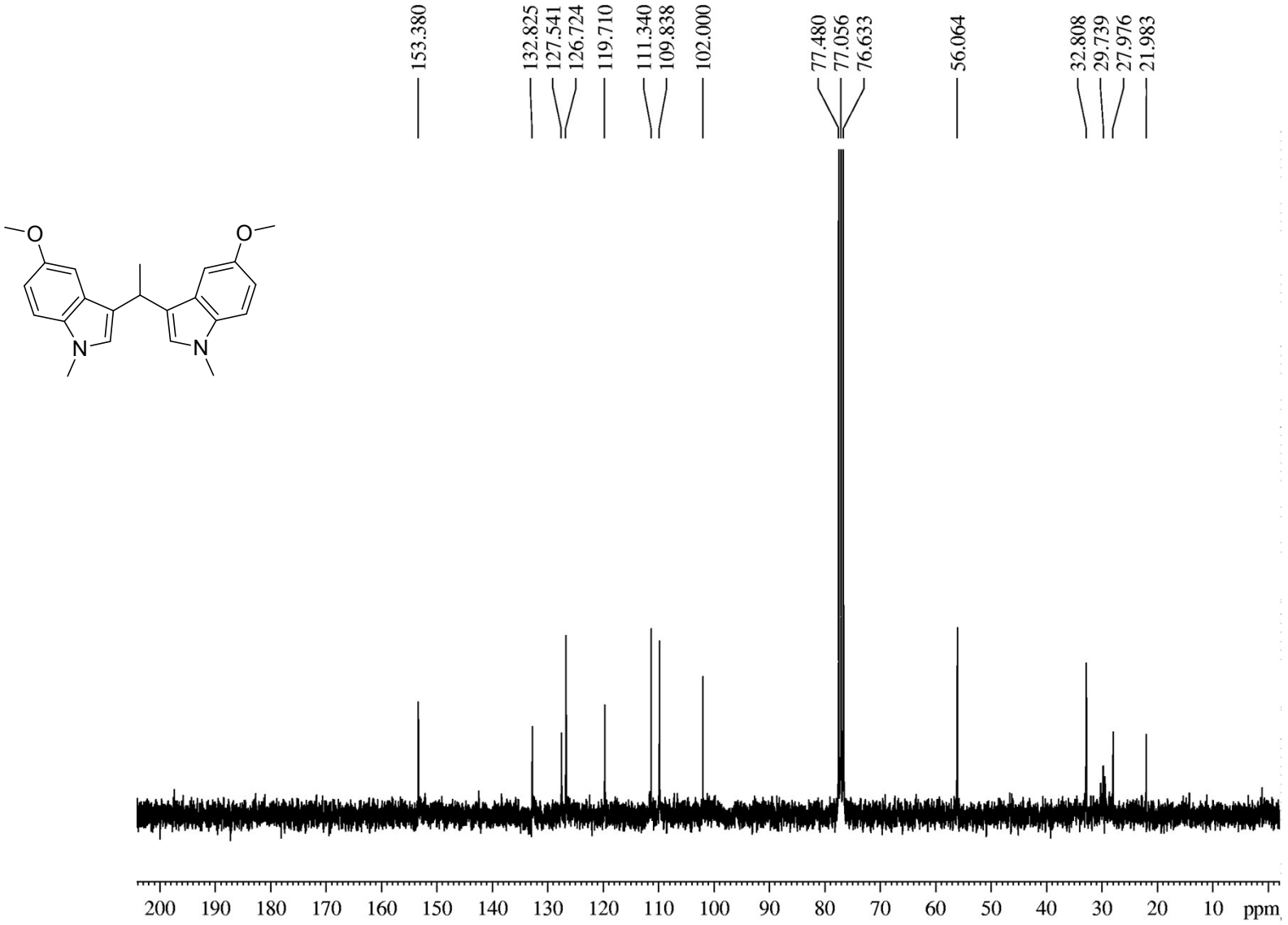

**Spectrum 19.** $^{1}$H NMR of compound **3j**



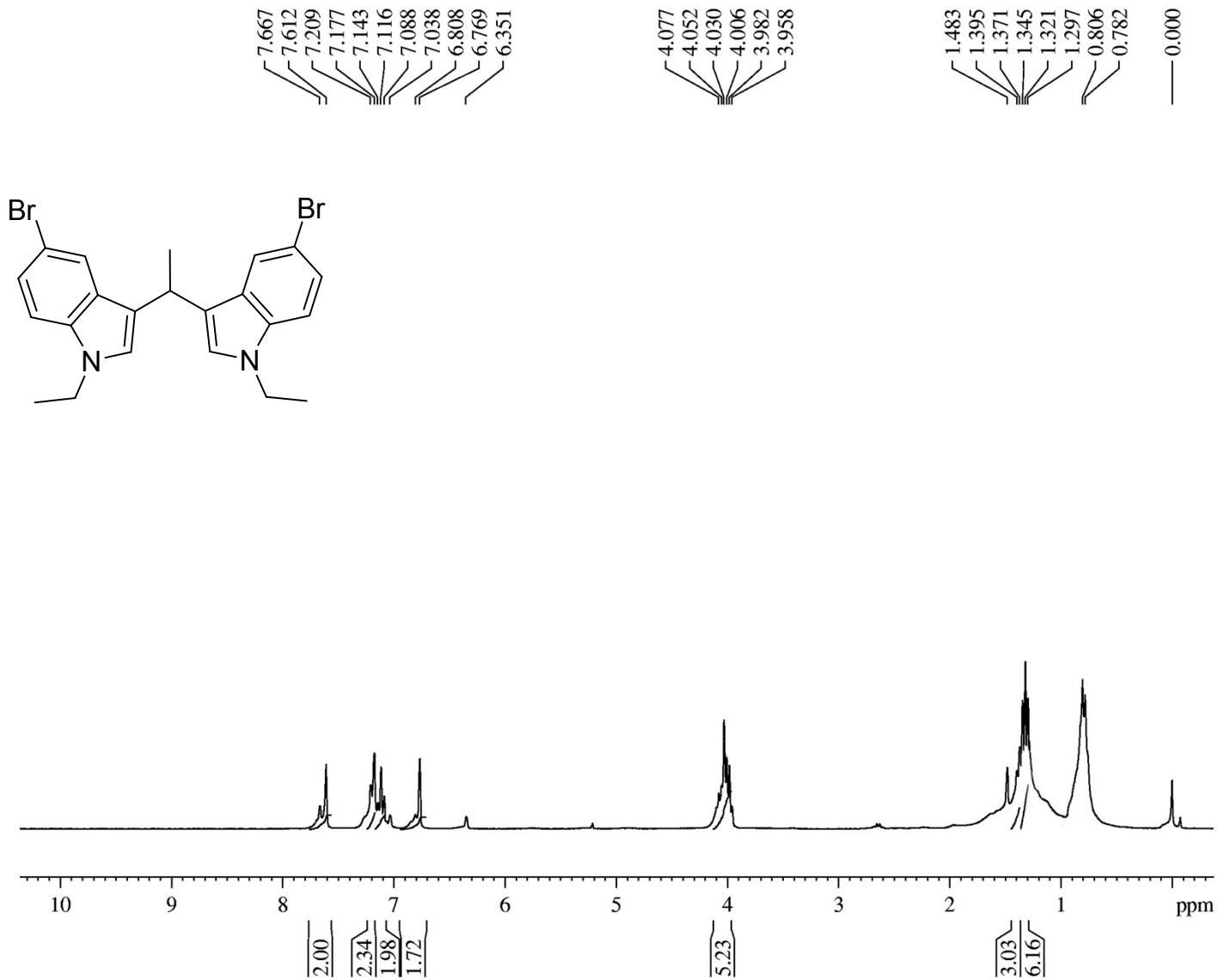

**Spectrum 20.** $^{13}$C NMR of compound **3j**



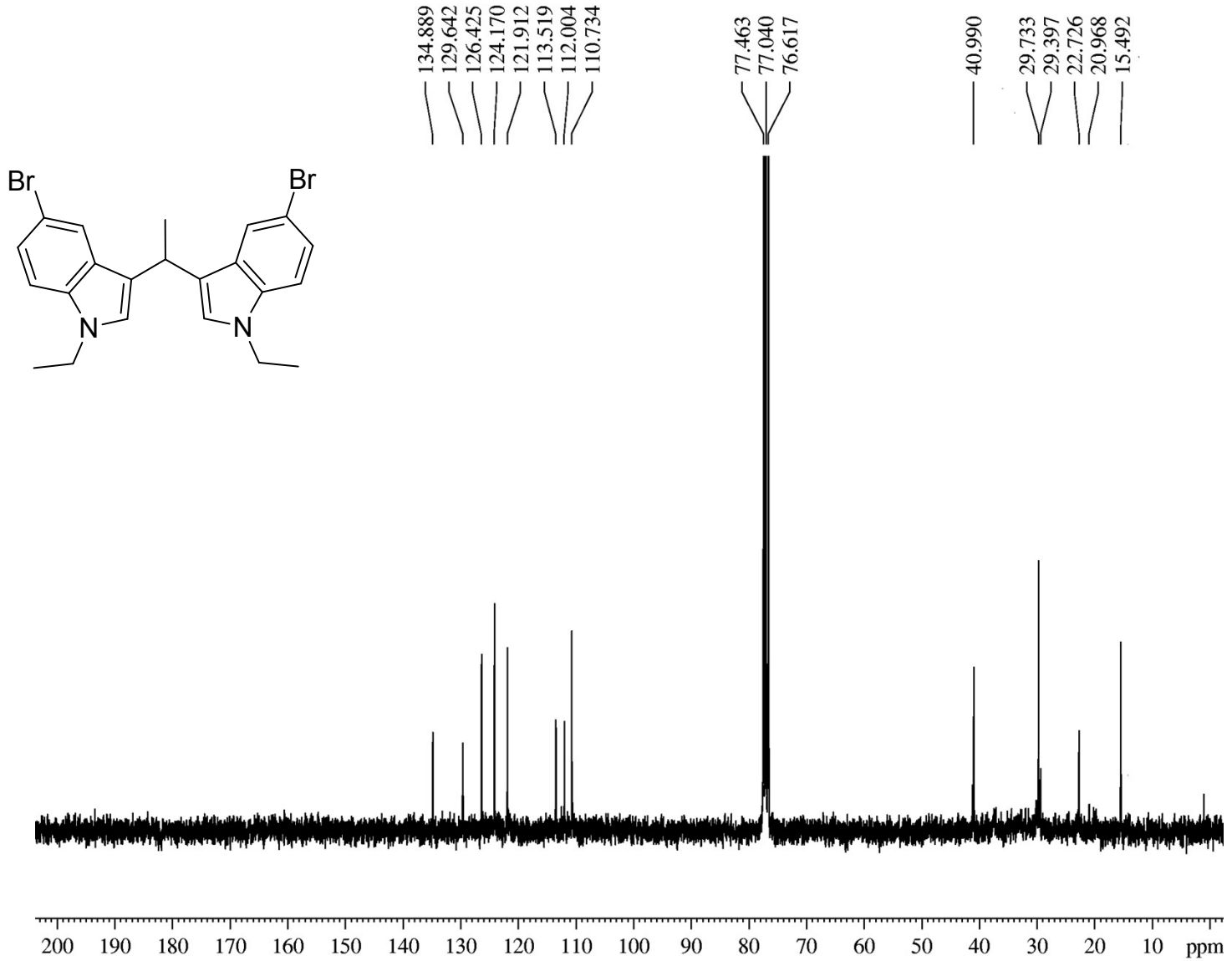

**Spectrum 21.** $^{1}$H NMR of compound **3k**



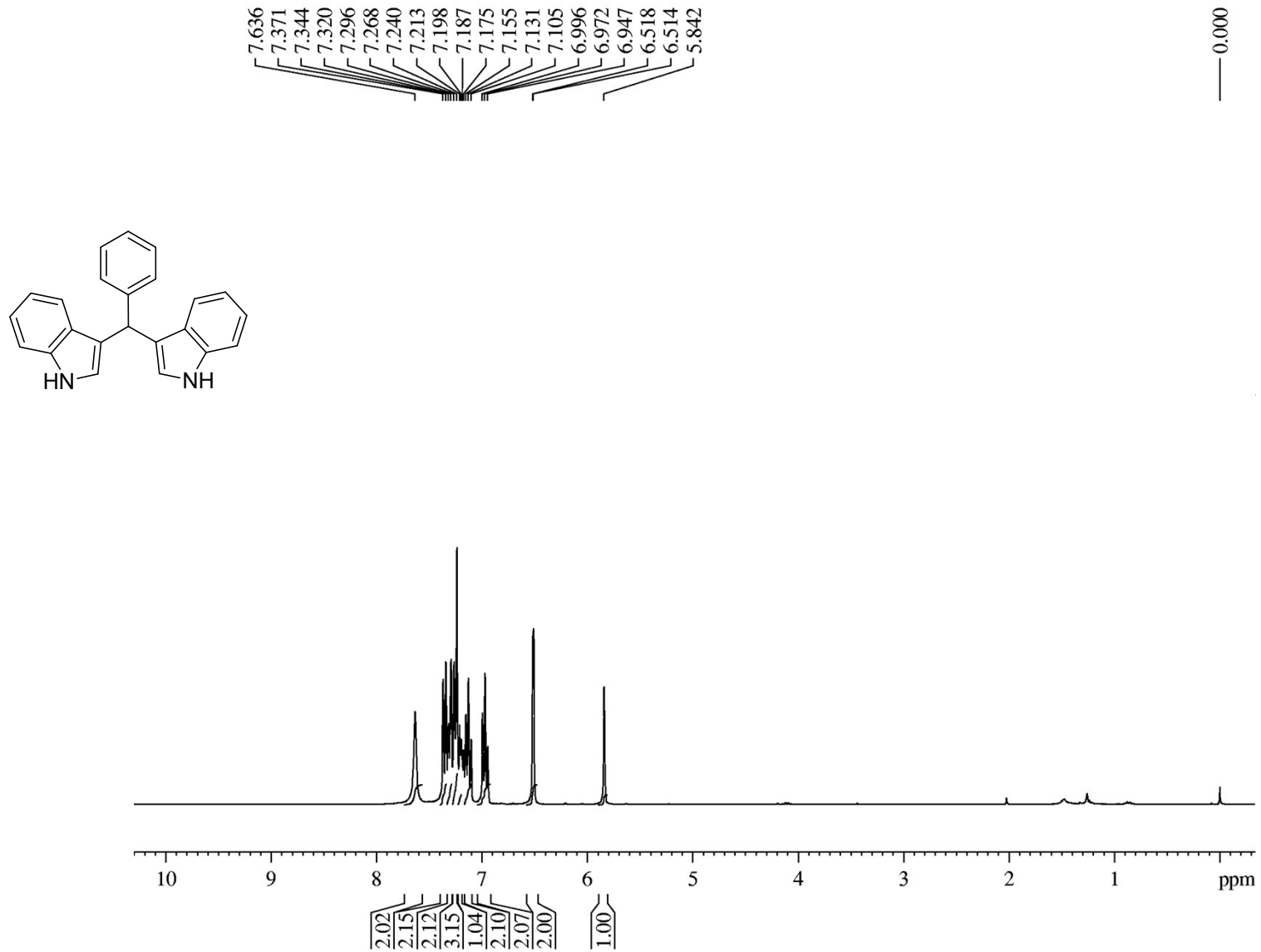

**Spectrum 22.** $^{13}$C NMR of compound **3k**



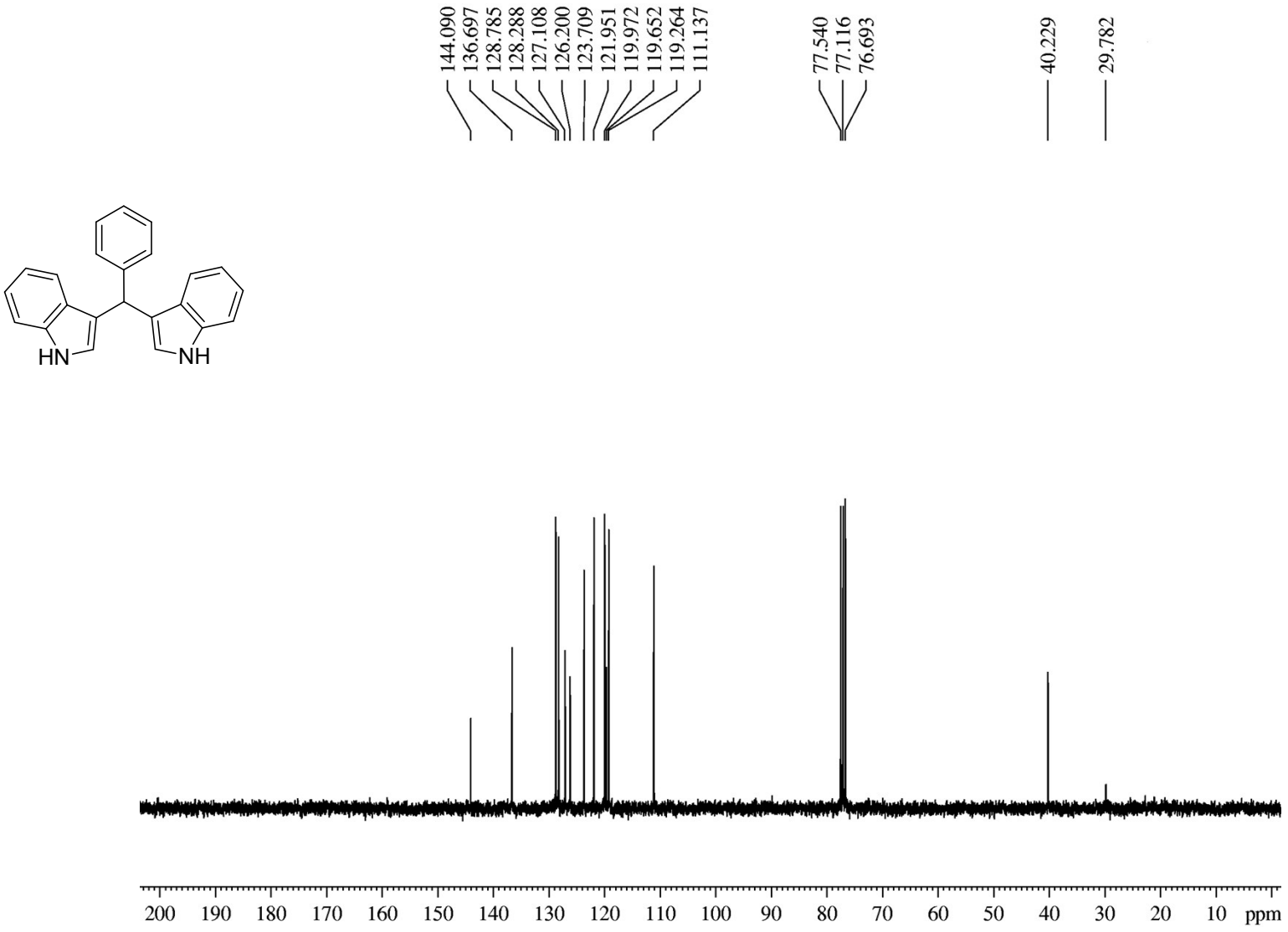

**Spectrum 23.** [1]H NMR of compound **3l**



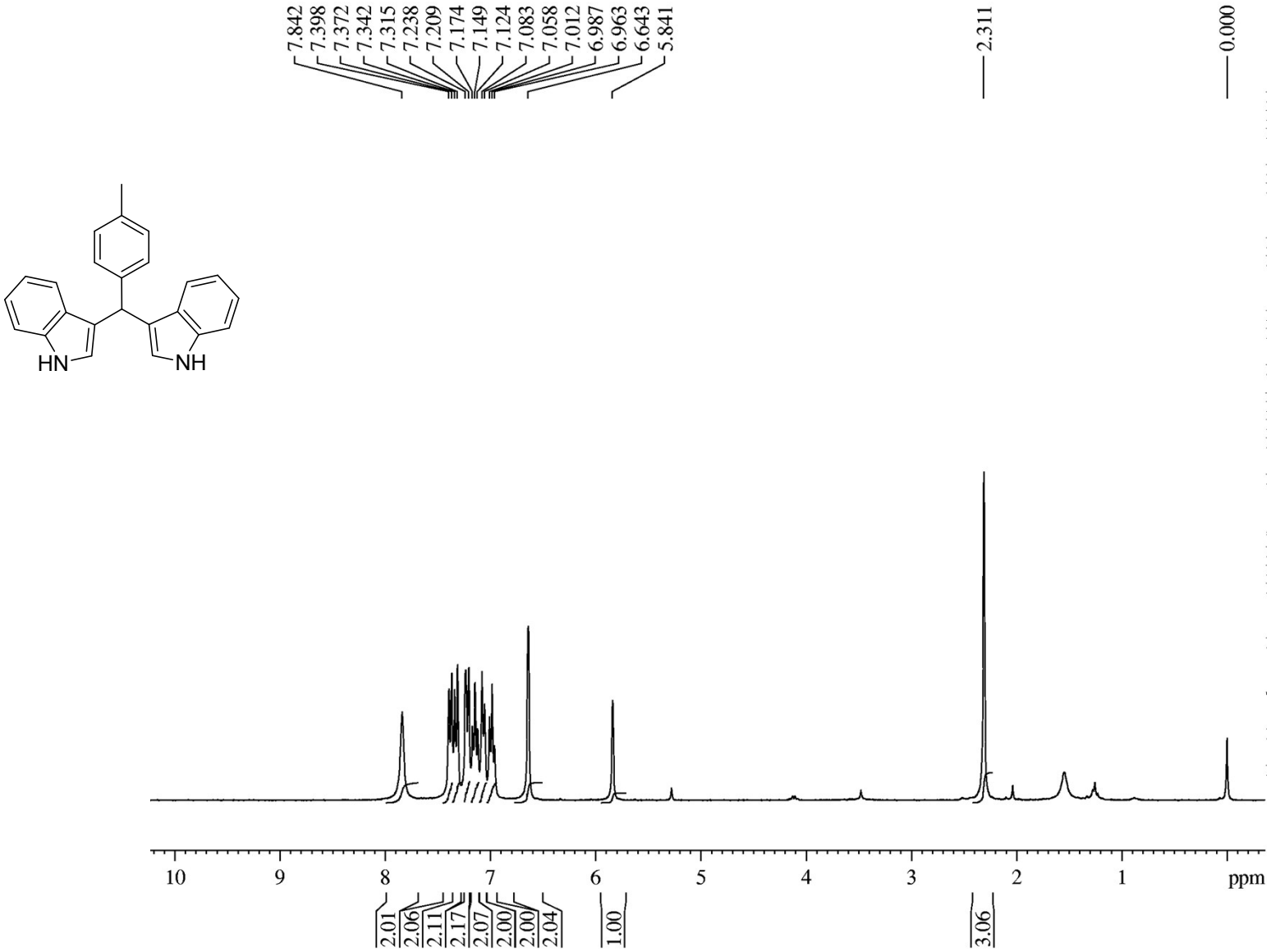

**Spectrum 24.** $^{13}$C NMR of compound **3l**



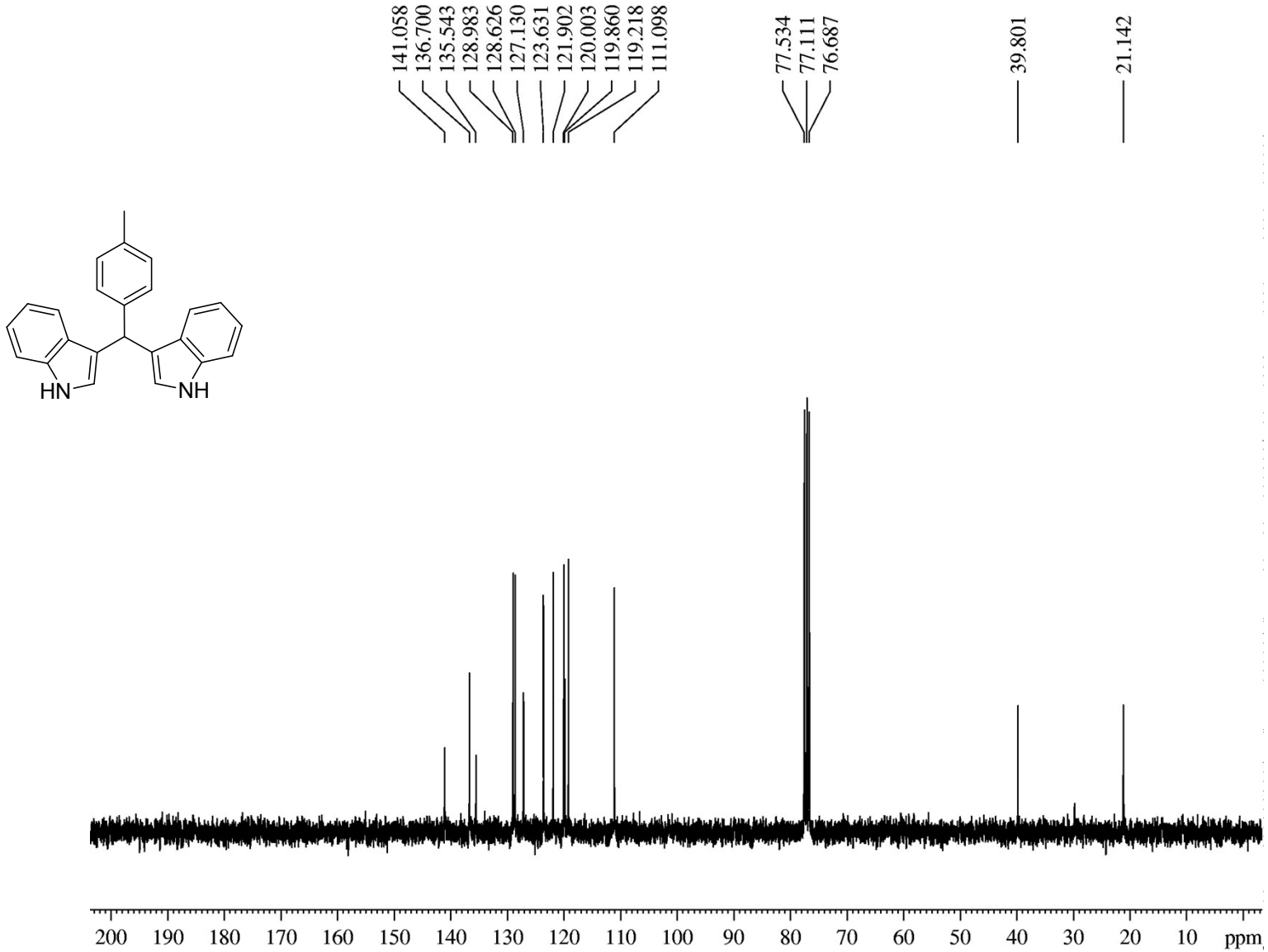

**Spectrum 25.** $^{1}$H NMR of compound **3m**



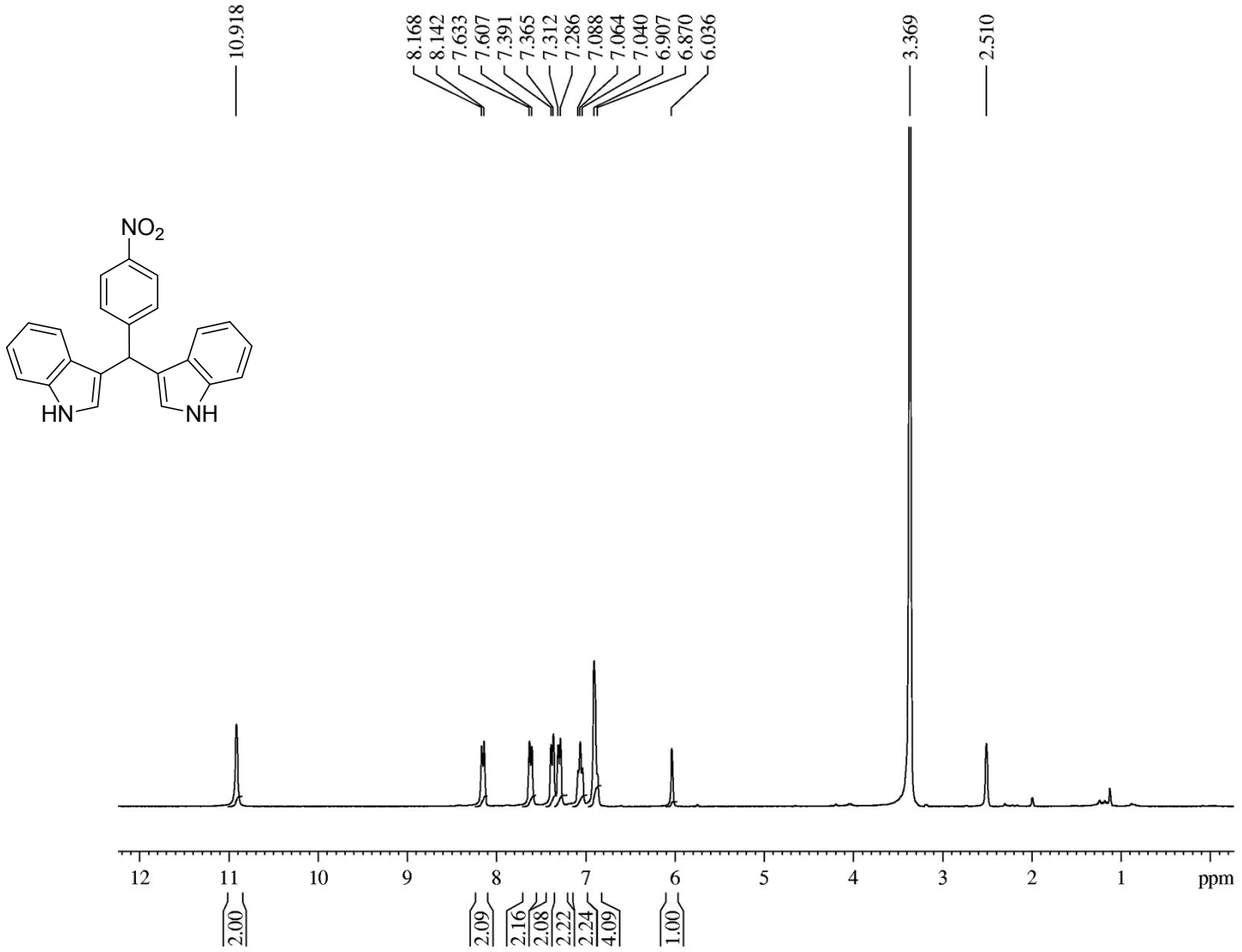

**Spectrum 26.** $^{13}$C NMR of compound **3m**



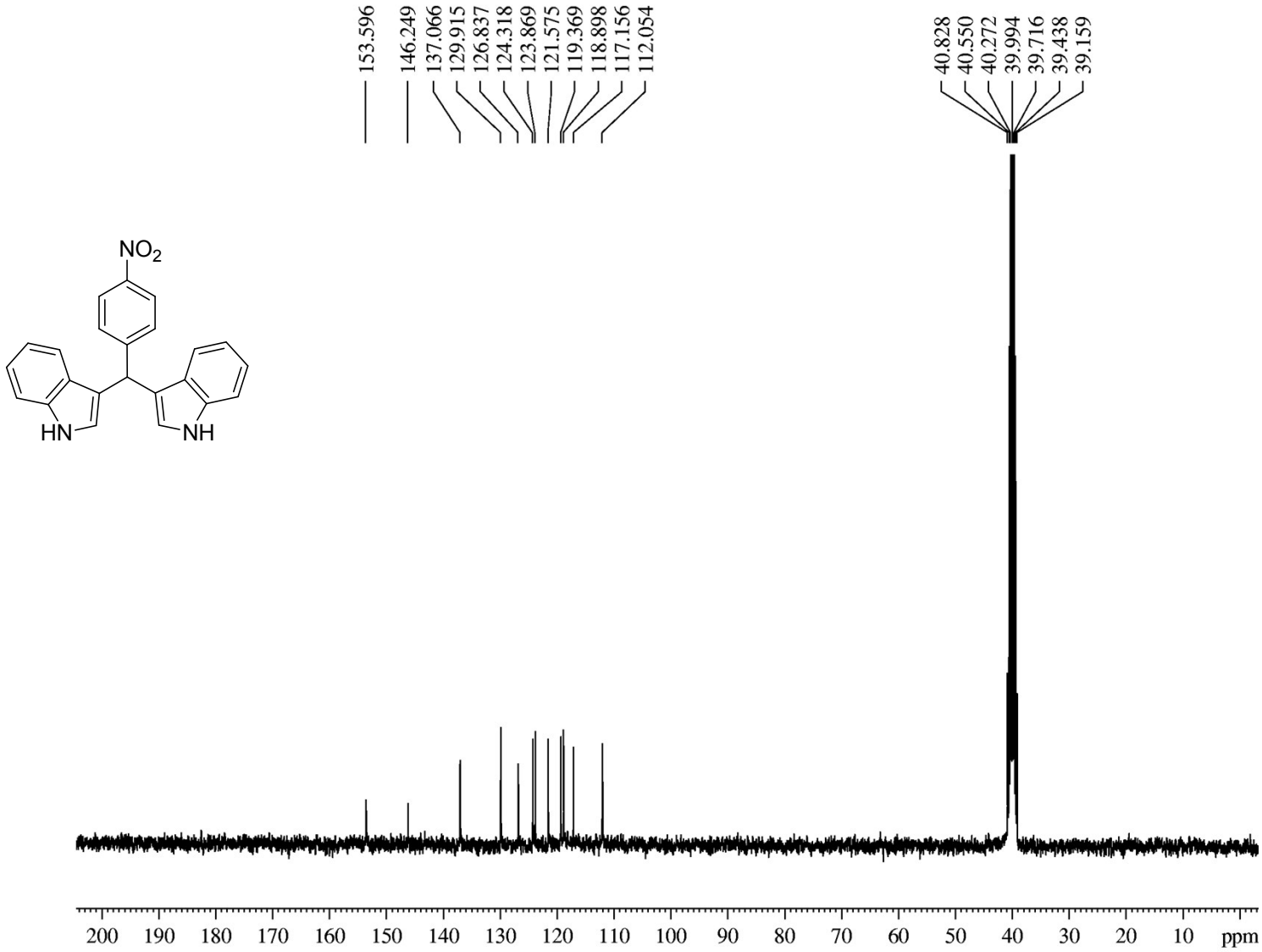

**Spectrum 27.** $^{1}$H NMR of compound **3n**



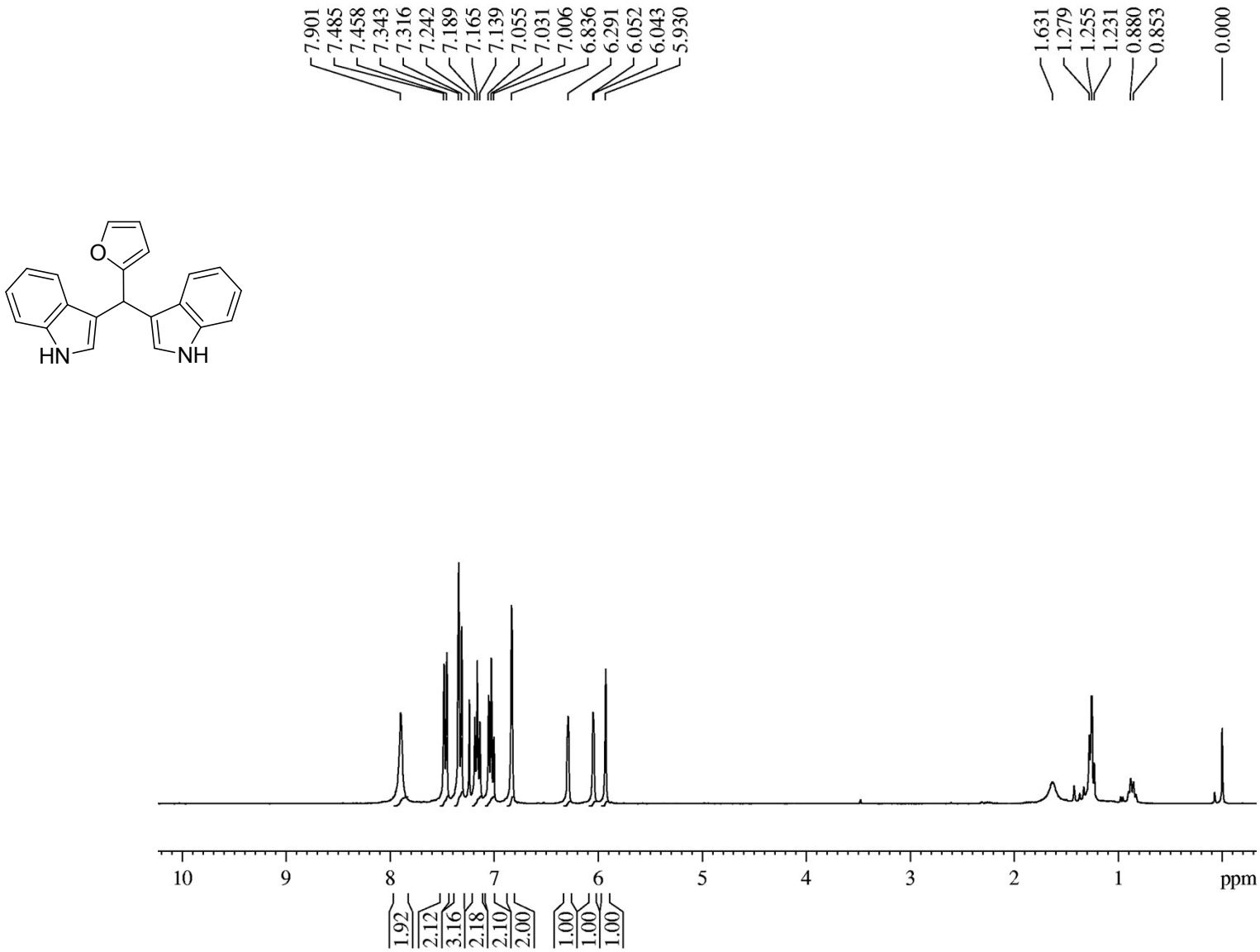

**Spectrum 28.** $^{13}C$ NMR of compound **3n**



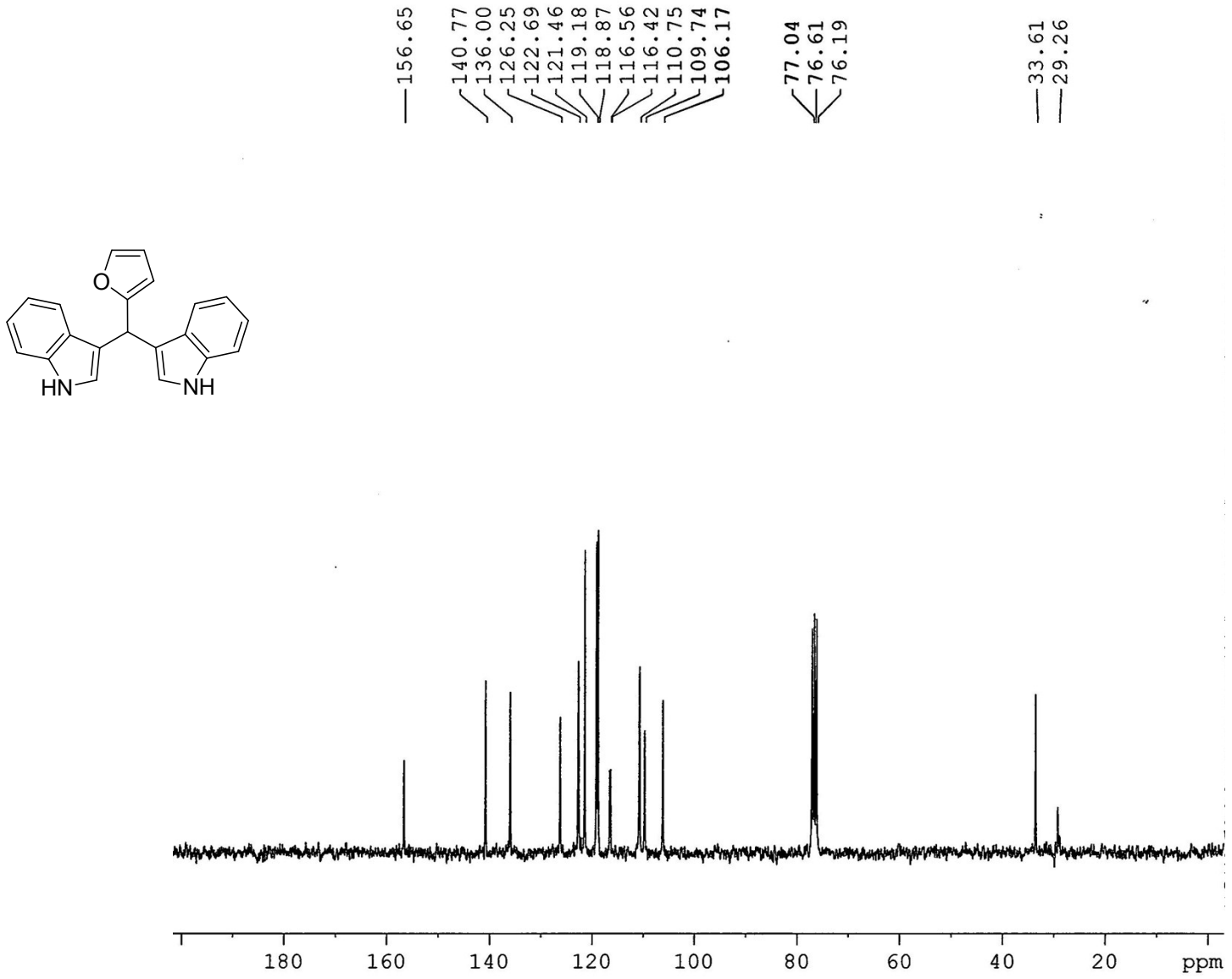

**Spectrum 29.** $^{1}$H NMR of compound **3o**



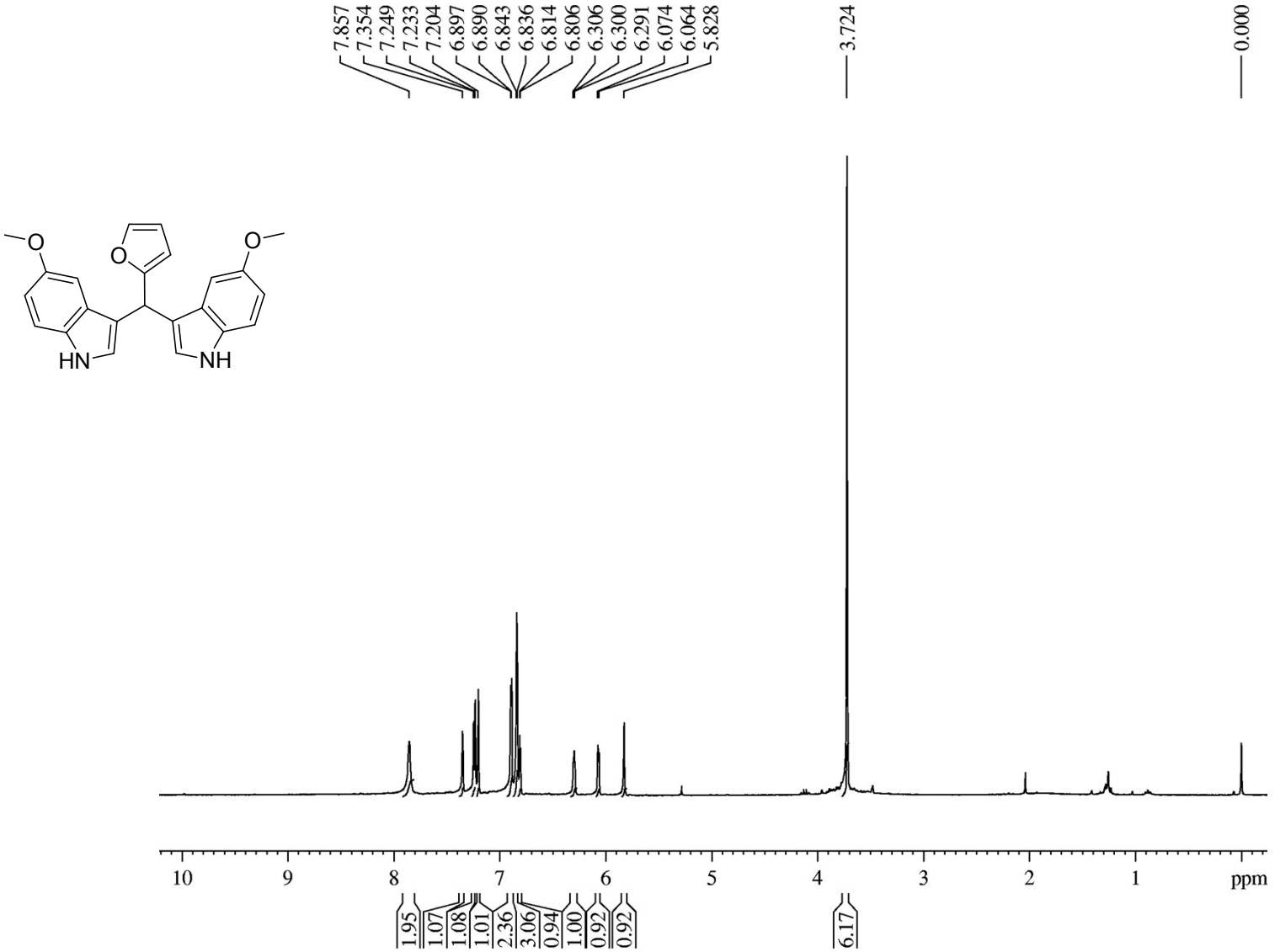

**Spectrum 30.** $^{13}$C NMR of compound **3o**



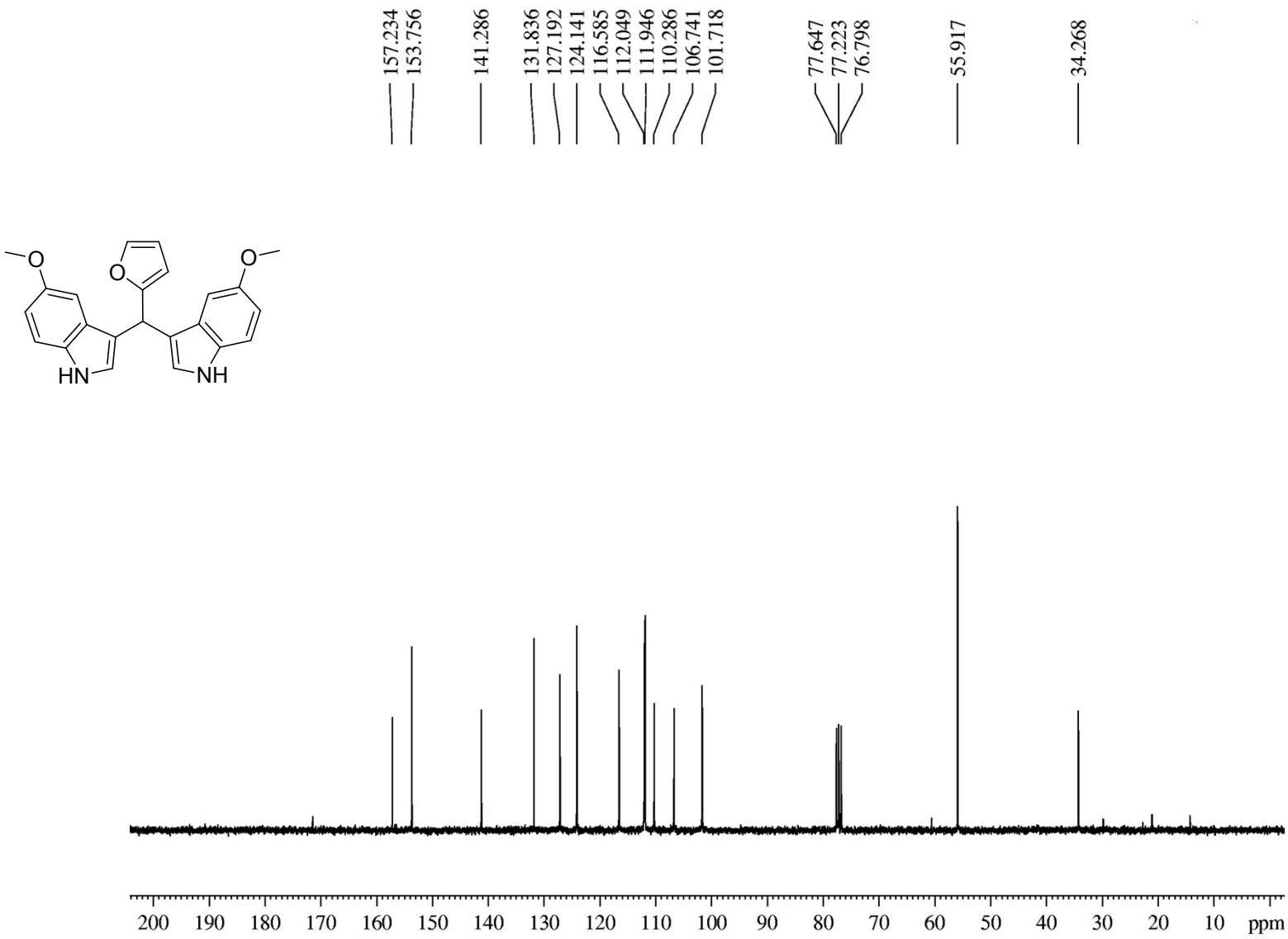

**Spectrum 31.** $^{1}$H NMR of compound **3p**



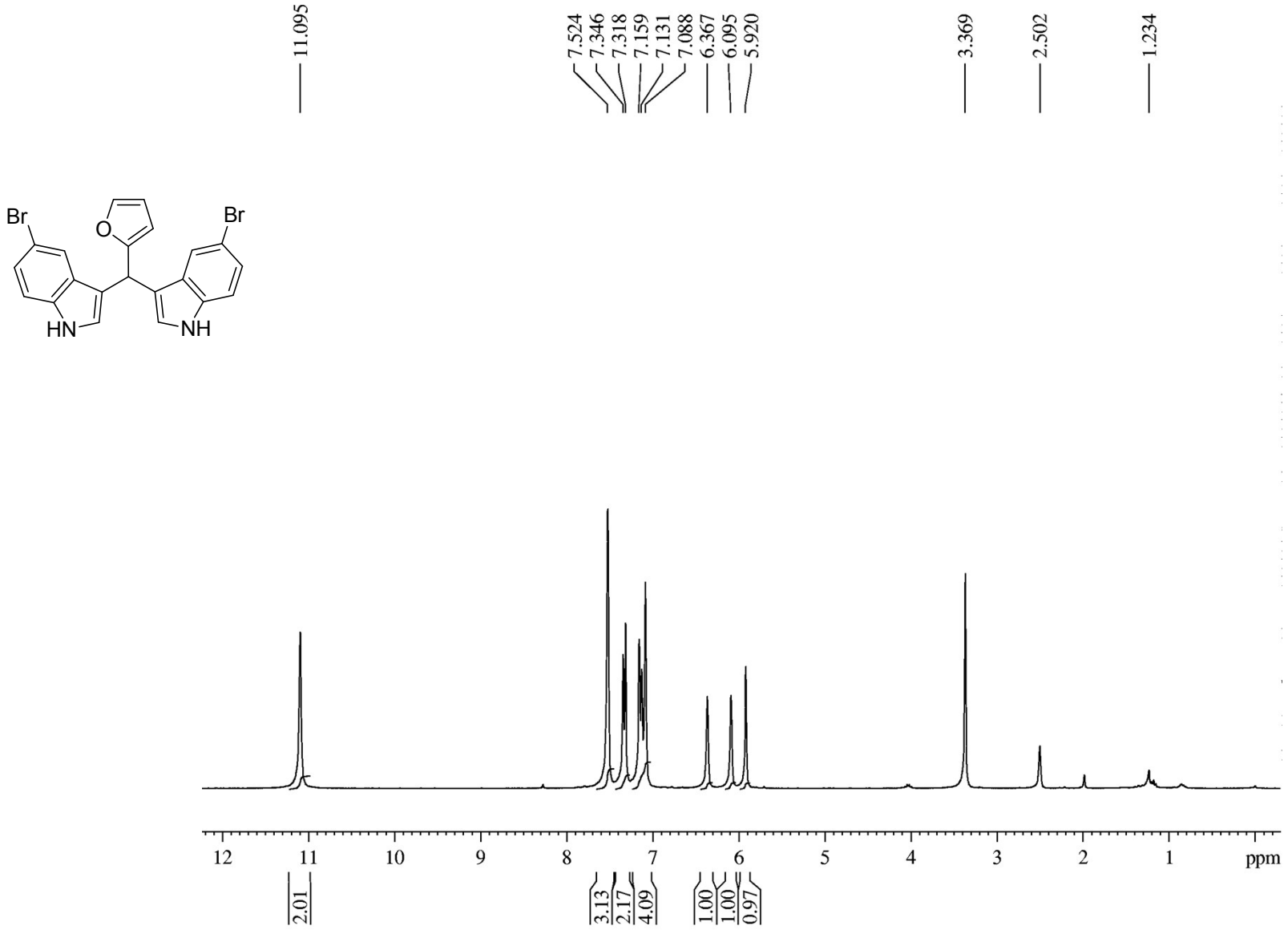

**Spectrum 32.** $^{13}$C NMR of compound **3p**



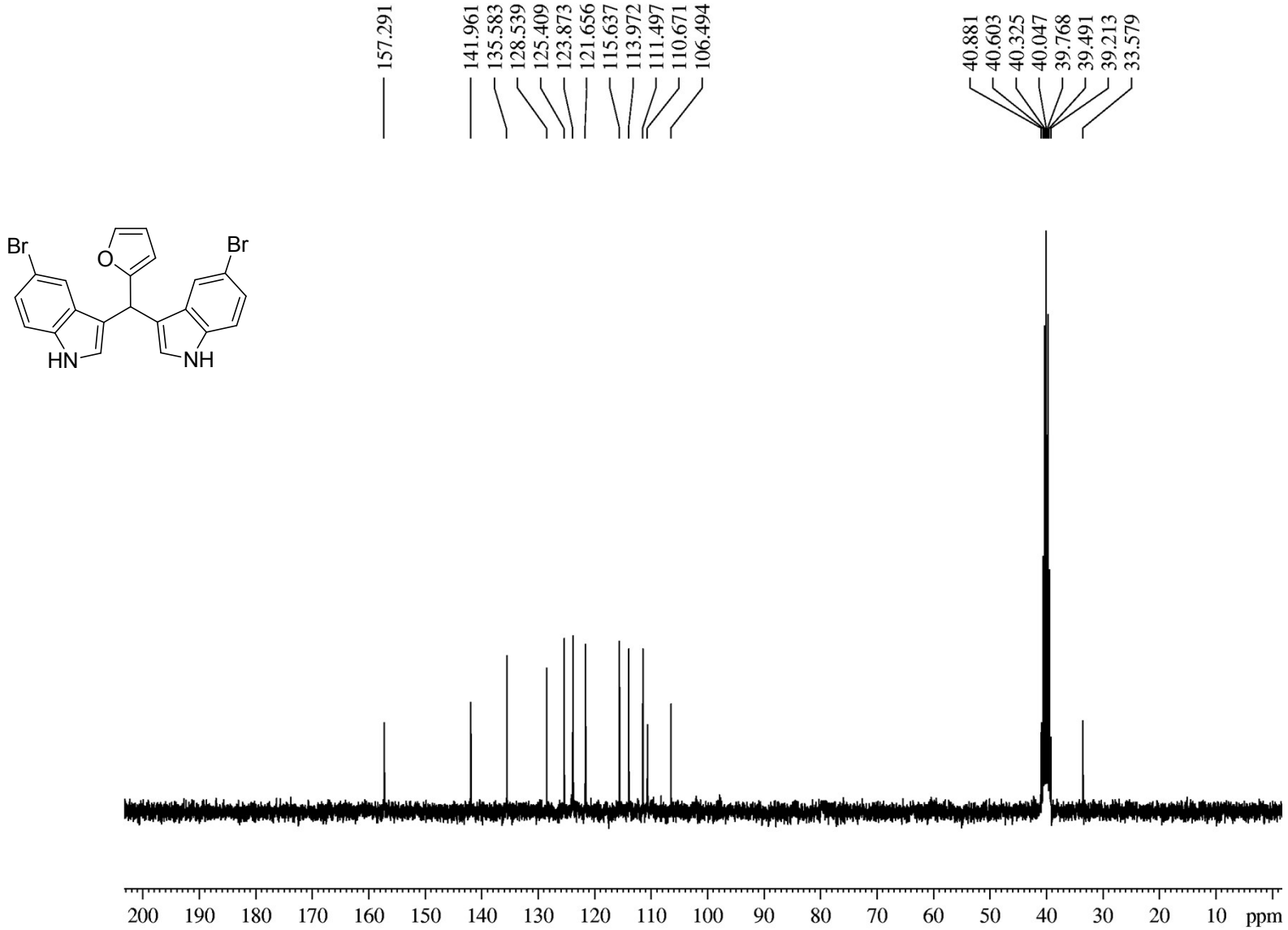

**Spectrum 33.** $^{1}$H NMR of compound **3q**



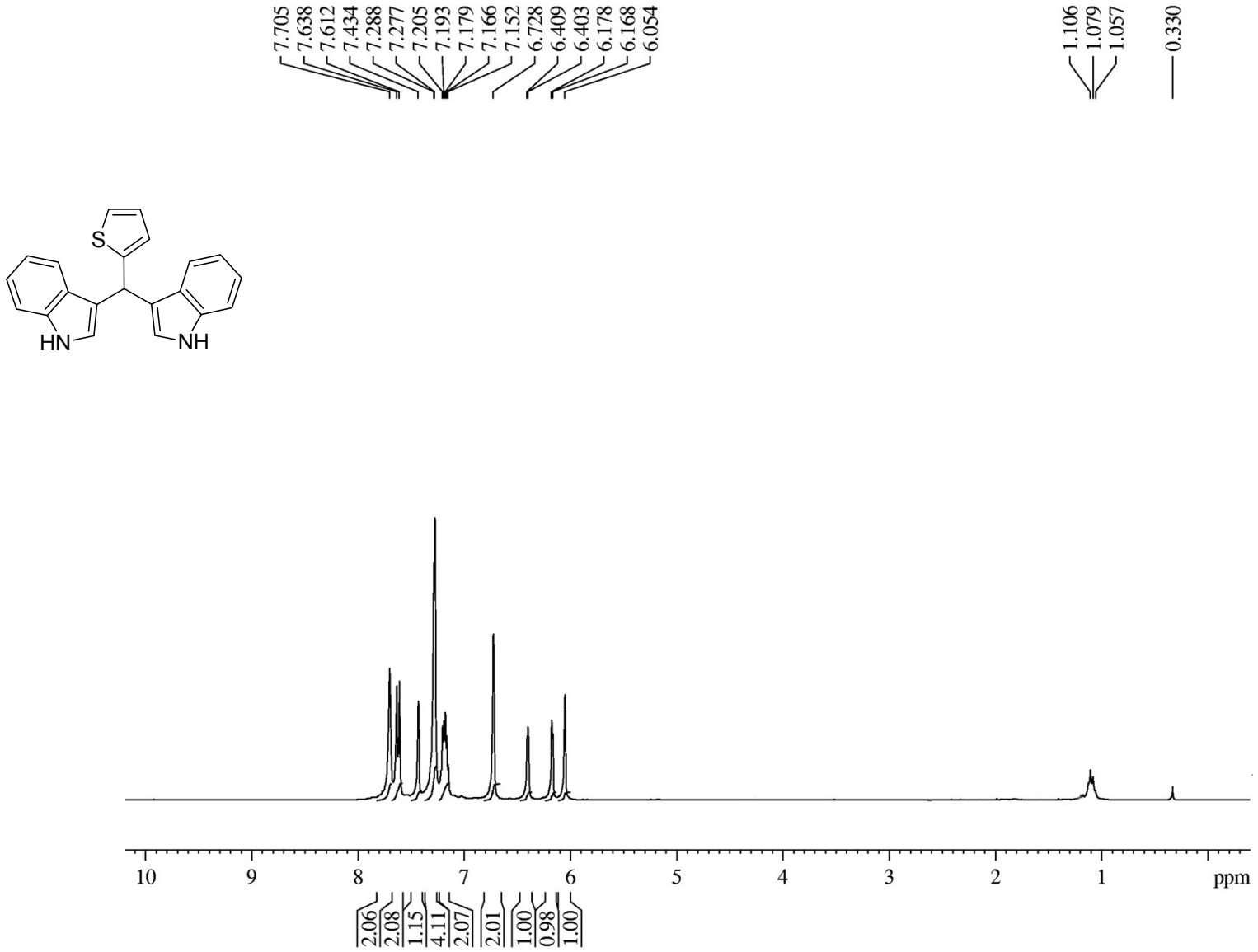

**Spectrum 34.** $^{13}$C NMR of compound **3q**



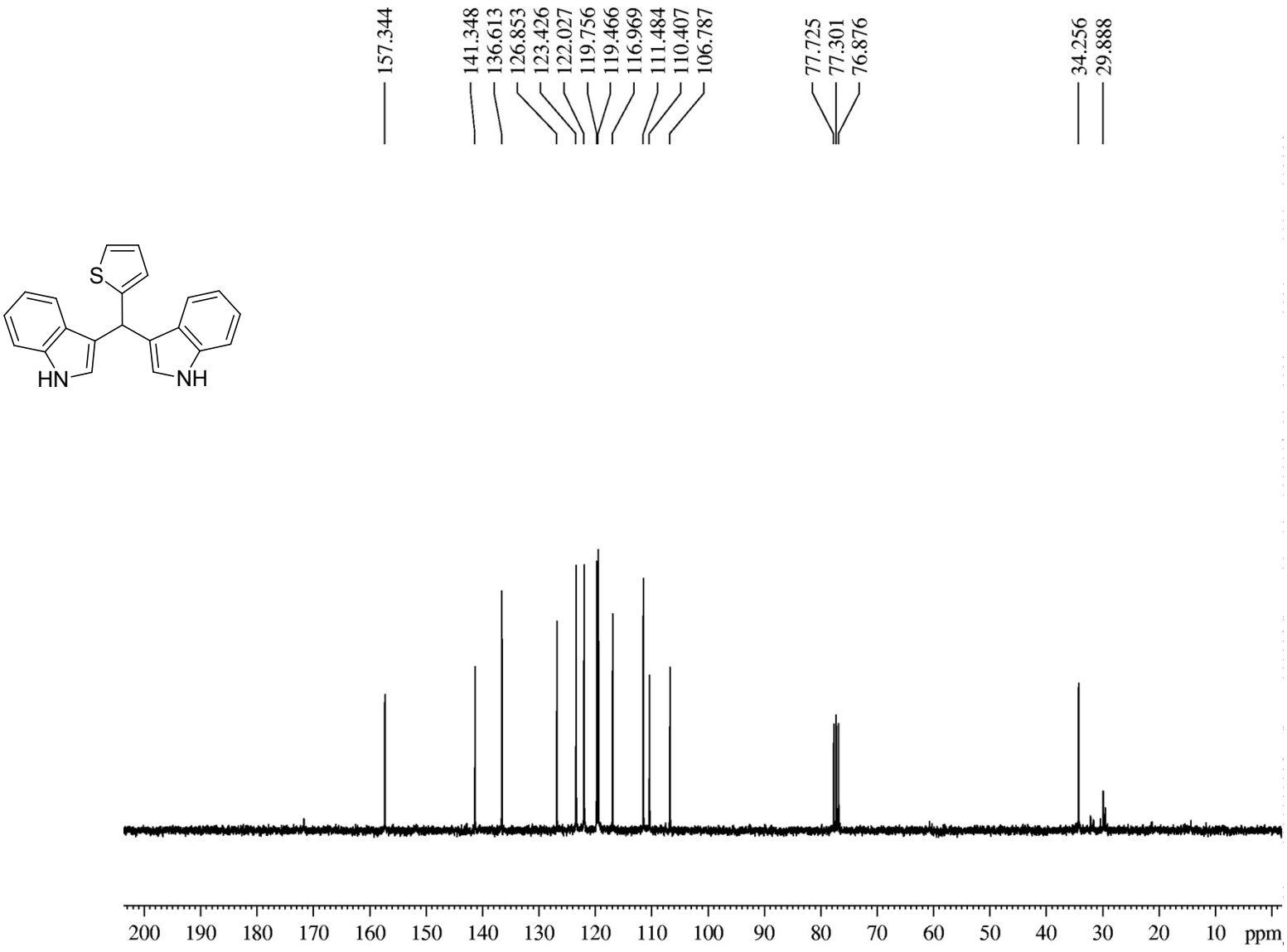

**Spectrum 35.** $^{1}$H NMR of compound **3r**



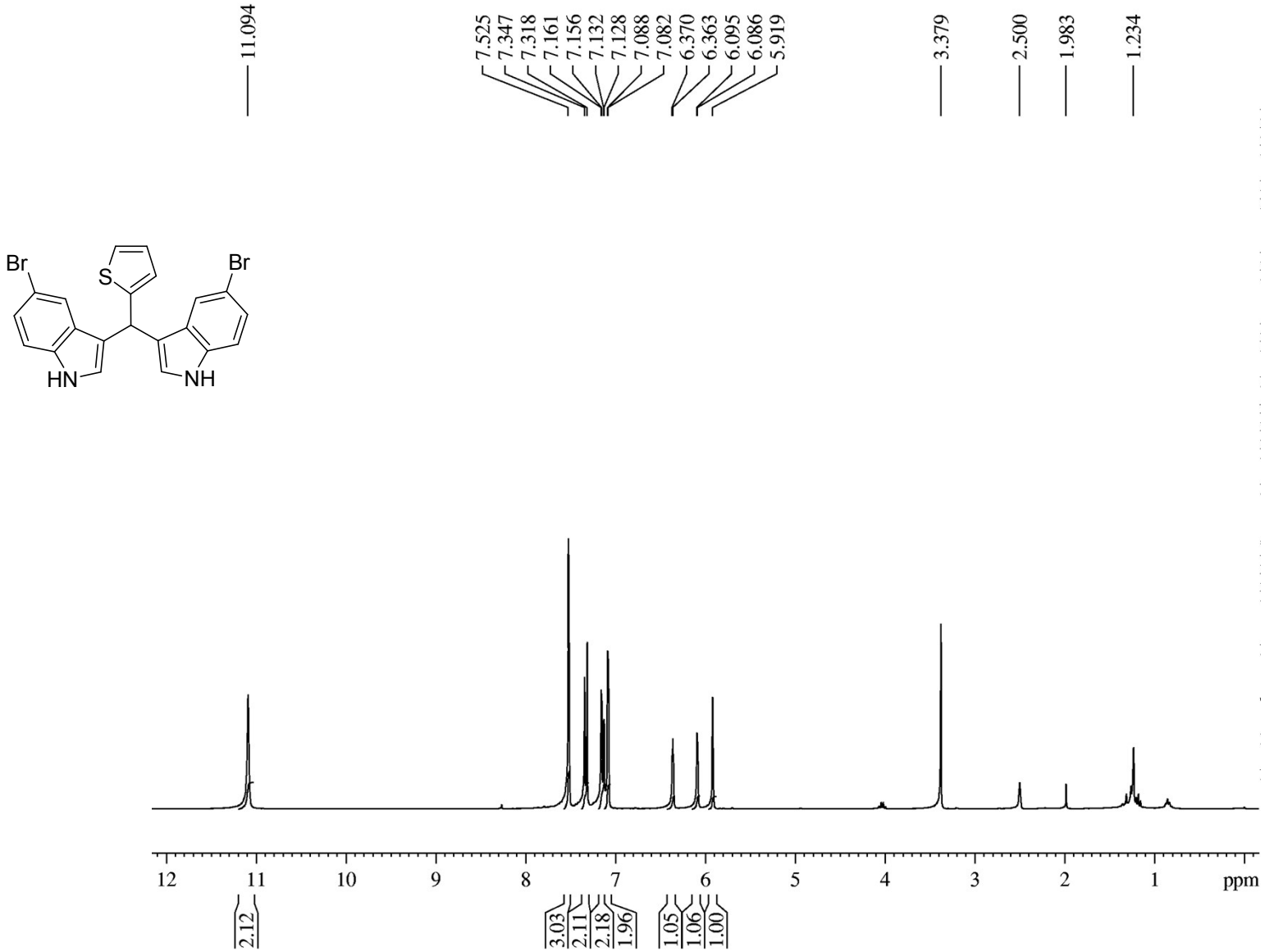

**Spectrum 36.** $^{13}$C NMR of compound **3r**



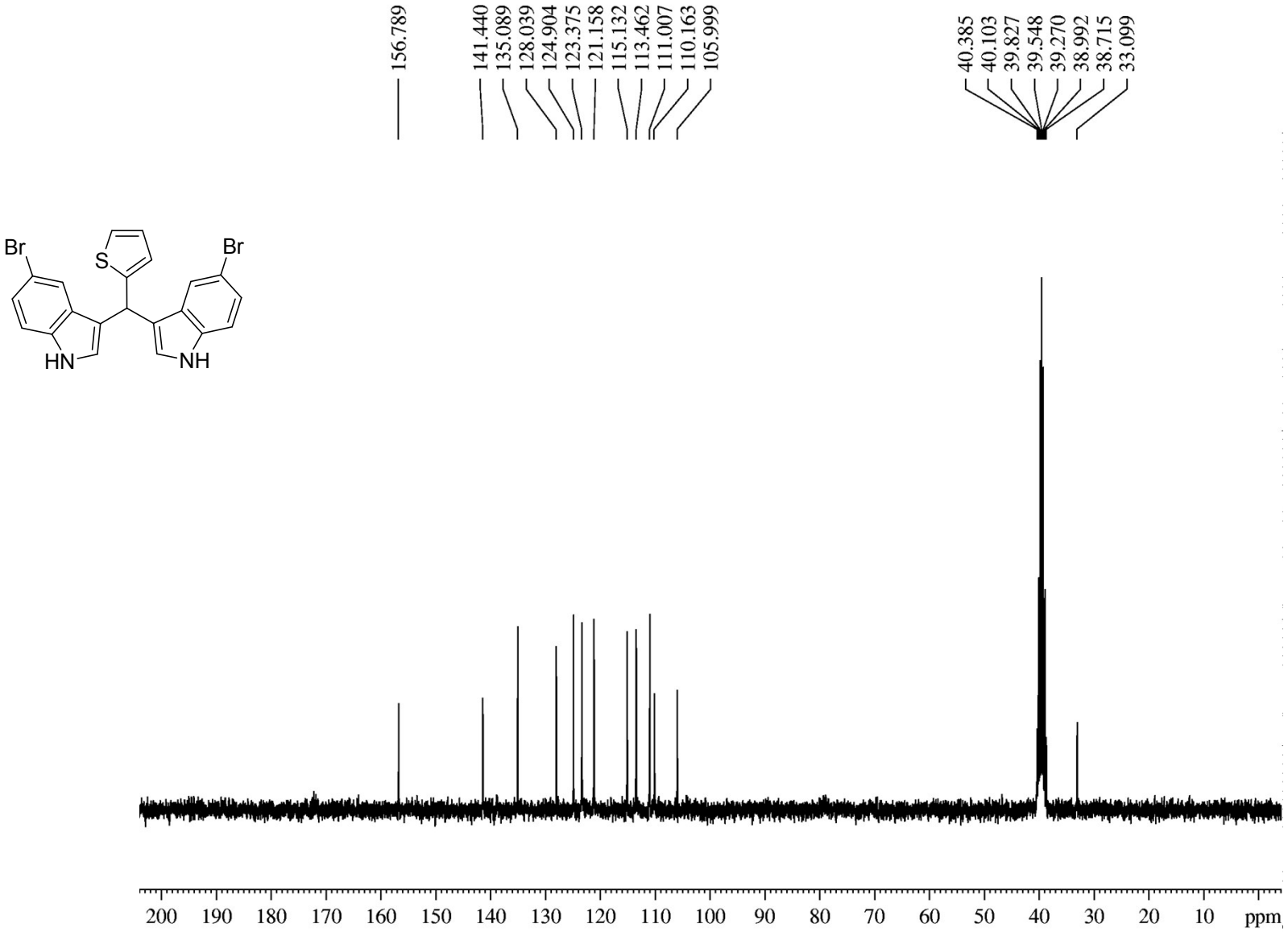

**Spectrum 37.** $^{1}$H NMR of compound **3s**




**Spectrum 38.** $^{13}$C NMR of compound **3s**




**Spectrum 39.** [1]H NMR of compound **3t**




**Spectrum 40.** $^{13}C$ NMR of compound **3t**

**References:**


1. D. Maciejewska, I. Szpakowska, I. Wolska, M. Niemyjska, M. Mascini and M. M. –Zurawska, *Bioelectrochemistry,* 2006, **69**, 1 – 9.
2. K. Ramachandiran, D. Muralidharan and P. T. Perumal, *Tet. Lett.*, 2011, **52**, 3579–3583.
3. D. M. Pore, U. V. Desai, T. S. Thopate, and P. P. Wadgaonkar, *ARKIVOC*, 2006 (xii), 75-80.
4. X. -F. Xu, Y. Xiong, X. -G. Ling, X. -M. Xie, J. Yuan, S. -T. Zhang and Z. -R. Song, *Chinese Chemical Letters,* 2014, **25**, 406–410.
5. K. R. M. Naidu, S. I. Khalivulla, P. C. R. Kumar and O. Lasekan, *Org. Commun*., 2012, **5:3**, 150-159.