

Supplementary Material

Preparation of symmetrical C2-C2-linked bis- and tris-6-bromoindoles by Sonogashira couplings and 5-*endo-dig* cyclization induced by nBu₄NF

**Raúl Balderrama-Martínez-Sotomayor, Mariana Flores-Jarillo,
and Alejandro Alvarez-Hernandez***

*Área Académica de Química. Universidad Autónoma del Estado de Hidalgo. Carr. Pachuca-Tulancingo Km 4.5. Pachuca, Hidalgo
42184 Mexico
Email: alvarez@uaeh.edu.mx*

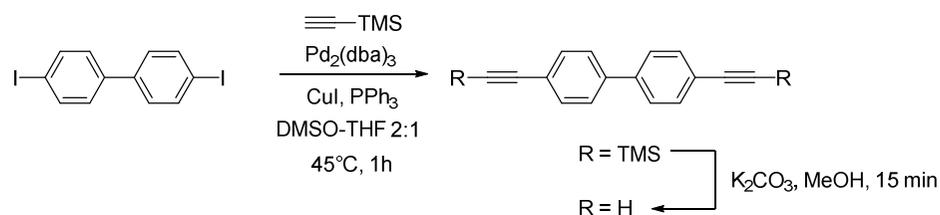
Table of contents

Experimental technique for preparation of compounds 3a-h	2S
1H and 13 C NMR spectra	
Compound 3a	8S
Compound 3b	10S
Compound 3c	12S
Compound 3d	14S
Compound 3e	16S
Compound 3f	18S
Compound 3g	20S
Compound 3h	22S
Compound 4a	24S
Compound 4b	26S
Compound 4c	28S
Compound 4d	30S
Compound 4e	32S
Compound 4f	34S
Compound 4g	36S
Compound 4h	38S
Compound 4i	40S
Compound 5d	42S
Compound 5e	44S
Compound 5f	46S
Compound 5g	48S
Compound 5i	50S

Preparation of dialkynes 3a-h

3,6-diethynyl-9-hexyl-9H-carbazole (3a) was prepared according to the reported procedure: Zhang, W.; Cho, H. M.; Moore, J. S. *Org. Synth.* **2007**, *84*, 177-191. 1-Iodohexane was used instead of the 1-bromotetradecane used in the original report for N-alkylation of carbazole.

4,4'-diethynyl-1,1'-biphenyl (3b) was prepared according to the following procedure:

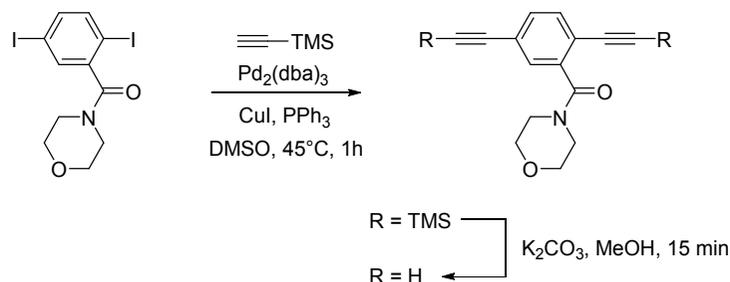


Sonogashira coupling. In a dry round bottom flask equipped with a stirring bar and septum under a N₂ atmosphere was added 405 mg (1 mmol, 1 equiv.) of 4,4'-diiodo-biphenyl, 23 mg (0.05 mmol, 0.05 equiv) of Pd₂(dba)₃, 6 mg (0.03 mmol, 0.03 equiv.) of CuI and 16 mg (0.06 mmol, 0.06 equiv.) of PPh₃ 10 mL of DMSO and 5 mL of THF. The flask was purged using vacuum, then a current of N₂. Then 240 μL (2.2 mmol, 2.2 equiv.) of trimethylsilylacetylene and 350 μL (2.5 mmol, 2.5 equiv.) of iPr₂NH were added to the flask. The mixture was left stirring at 45 °C during 1 h. Then the reaction mixture was diluted with 100 mL of ethyl acetate) and washed with water (2X100 mL) then with brine (1x100mL). The organic portion was dried over anh. Na₂SO₄, filtered and concentrated under vacuum. Column chromatography eluting with hexane gave 236 mg (76%) of a yellow solid, mp 158-160 °C; R_f = 0.60 (5% EtOAc/hexanes); IR (KBr) 3040, 2957, 2886, 2158, 1489 cm⁻¹; ¹H RMN (400 MHz, CDCl₃): δ 7.51 (s, 8H), 0.24 (d, J = 0.5 Hz, 18H); ¹³C RMN (100 MHz, CDCl₃): δ 140.2, 132.4, 126.7, 122.4, 104.8, 95.2, -0.1.

Deprotection. In a round bottom flask containing an stirring bar and under a N₂ atmosphere was added 186 mg (0.78 mmol, 1 equiv) the bis protected acetylene from the previous step, 1.078 g (7.8 mmol, 10 equiv) de K₂CO₃ and 5 mL of methanol. The mixture was

stirred for 15 min at room temperature and then concentrated under vacuum. The residue was chromatographed using 95:5 hexanes:EtOAc to obtain 99 mg (63%) of **3b** as a yellow solid, mp 160-162 °C; $R_f = 0.43$ (5% EtOAc/hexanes); IR (KBr) ν 3275, 3038, 2922, 2852, 2107, 1490 cm^{-1} ; ^1H RMN (400 MHz, CDCl_3): δ 7.56 (m, 8H), 3.15 (s, 2H); ^{13}C RMN (100 MHz, CDCl_3): δ 140.5, 132.6, 126.9, 121.4, 83.4, 78.1.

2,5-diethynyl-morpholinebenzamide (3c) was prepared according to the following procedure:



Sonogashira coupling. In a round bottom flask equipped with a stirring bar and under a N_2 atmosphere was added 221 mg (0.49 mmol, 1 equiv.) of 2,5-diiodo morpholine benzamide,* 13 mg (0.025 mmol, 0.05 equiv.) of $\text{Pd}_2(\text{dba})_3$, 3 mg (0.015 mmol, 0.03 equiv) of CuI , and 8 mg (0.03 mmol, 0.06 equiv) of PPh_3 . Then was added 5 mL de DMSO and the flask was purged with vacuum followed by a current of N_2 . Then, 150 μL (1.05 mmol, 2.1 equiv.) of trimethylsilylacetylene and 180 μL (1.25 mmol, 2.5 equiv.) of $i\text{Pr}_2\text{NH}$ were added and the mixture was stirred at 45 °C for 1 h. Then the crude was diluted with 100 mL of ethyl acetate and washed with water (3X60 mL) and brine 1x100 mL. The organic portion was dried over Na_2SO_4 , filtered and concentrated under vacuum. Column chromatography using hexane:ethyl acetate gradients (95:5, 90:10, 80:20) gave 166.4 mg (86%) the compound **3c** as a yellow solid. mp 155-157 °C; $R_f = 0.83$ (20% EtOAc/ 80% hexanes); IR (KBr) 3035, 2922, 2860, 2162, 1646, 1251 cm^{-1} ; ^1H RMN (400 MHz, CDCl_3): δ 7.41 (m, 3H), 3.75, (m, 8H), 0.24 (m, 18H); ^{13}C RMN (100 MHz, CDCl_3): δ 167.8, 139.0, 132.6, 132.2, 130.2, 124.1, 120.0,

103.7, 101.8, 100.6, 98.0, 67.1, 66.8, 47.4, 42.2, 0.1.

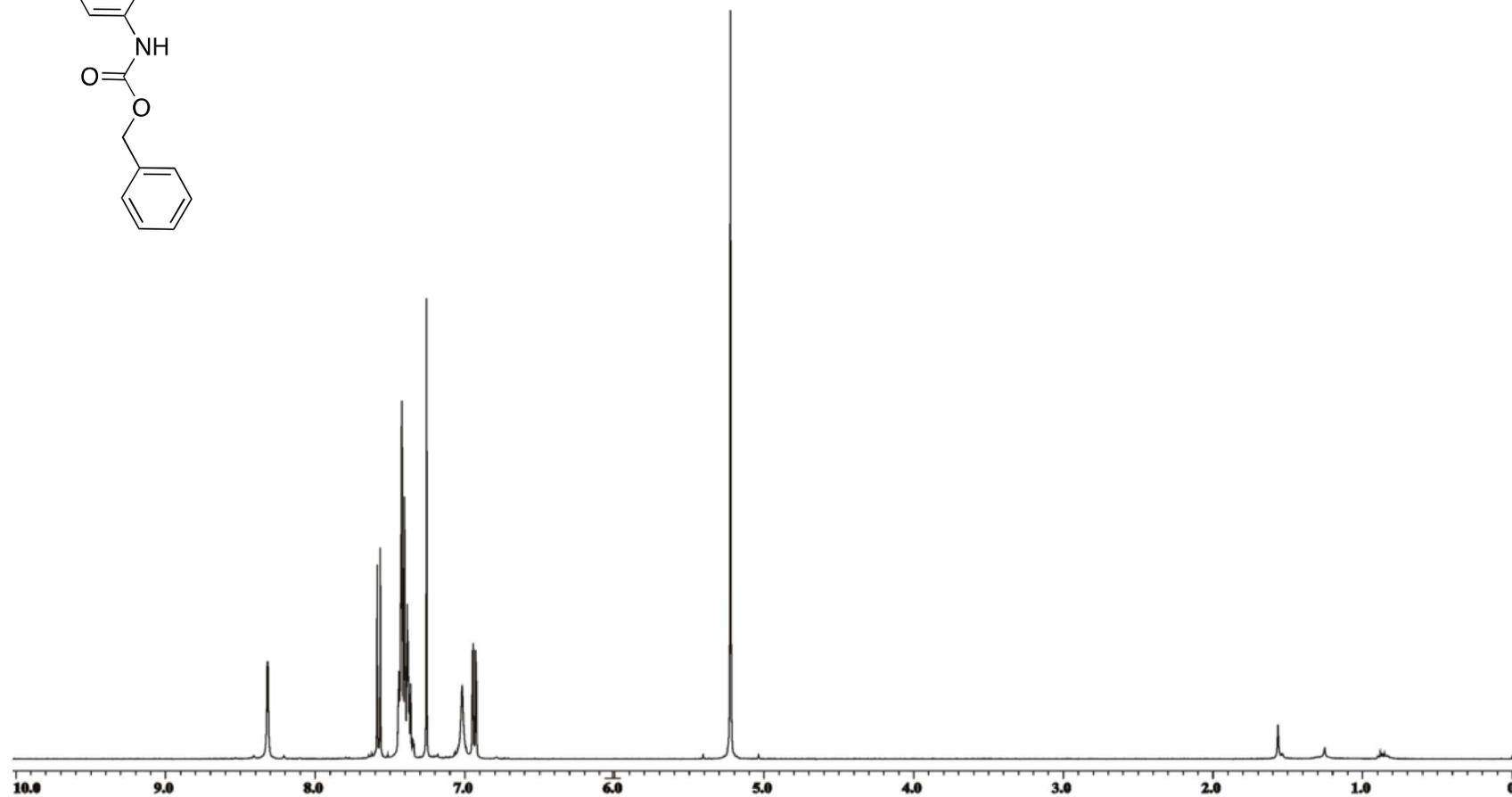
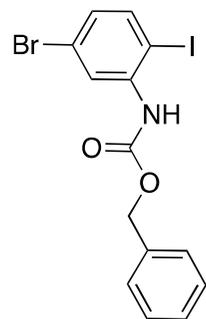
Deprotection. In a round bottom flask containing an stirring bar, under a N₂ atmosphere was added 133 mg (0.35 mmol, 1 equiv) of the coupling product from the previous step, 434 mg (3.5 mmol, 10 equiv) of K₂CO₃ and 5 mL of methanol and the mixture was stirred at room temperature for 15 min. Column chromatography using gradients of hexanes:ethyl acetate gave 70.4 mg (84%) of **3c** as a white solid. mp 129-131 °C; R_f = 0.33 (40% AcOEt/hexanes); IR (KBr) 3222, 3054, 2924, 2845, 2101, 1627, 1467 cm⁻¹; ¹H RMN (400 MHz, CDCl₃): δ 7.49-7.41 (m, 3H), 3.76 (s, 2H), 3.29-3.27 (m, 4H), 3.26-3.23 (m, 4); ¹³C RMN (100 MHz, CDCl₃): δ 167.44, 139.25, 132.9, 132.4, 129.94, 123.36, 119.28, 82.87, 80.29, 66.82, 66.64, 47.27, 42.11.

*For preparation of 2,5-diiodo-morpholinebenzamide see: Flores-Jarillo, M.; Ayala-Mata, F.; Zepeda-Vallejo, G.; Vázquez García, R. A.; Ramos-Ortiz, G.; Mendez-Rojas, M. A.; Suarez-Castillo, O. R.; Alvarez-Hernandez, A. *J. Mex. Chem. Soc.* **2015**, *59*, 151-160. *In press.*

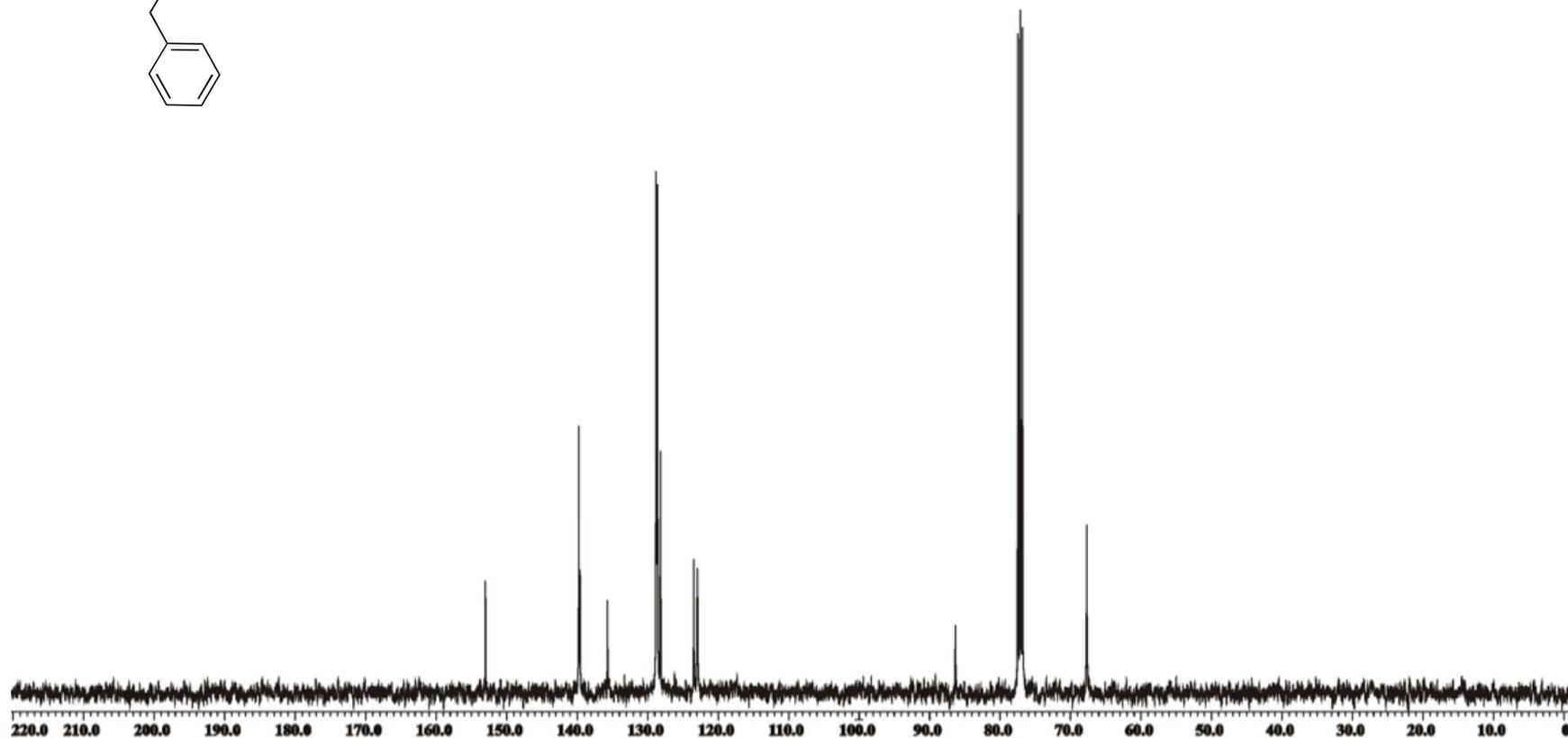
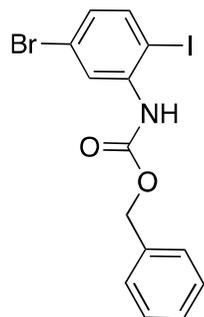
Alkynes **3d-i**.

These compounds were prepared according to the reported procedure: Wang, Y.; Ji, K.; Lan, S.; Zhang, L. *Angew. Chem. Int. Ed.* **2012**, *51*, 1915-1918. See the supporting material.

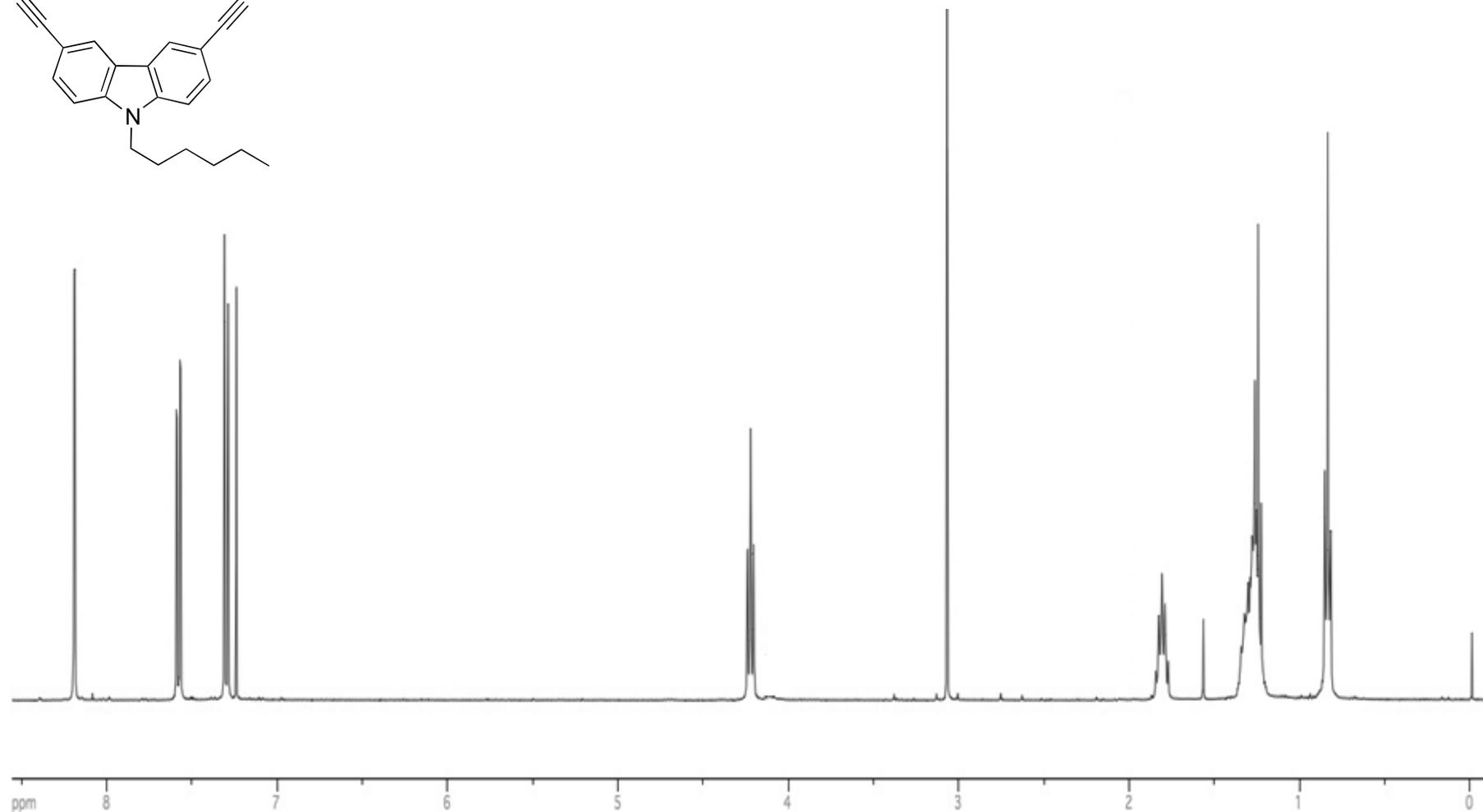
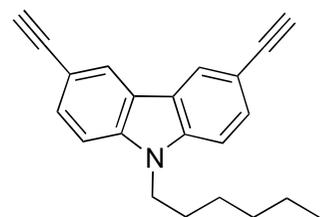
^1H and ^{13}C NMR Spectra



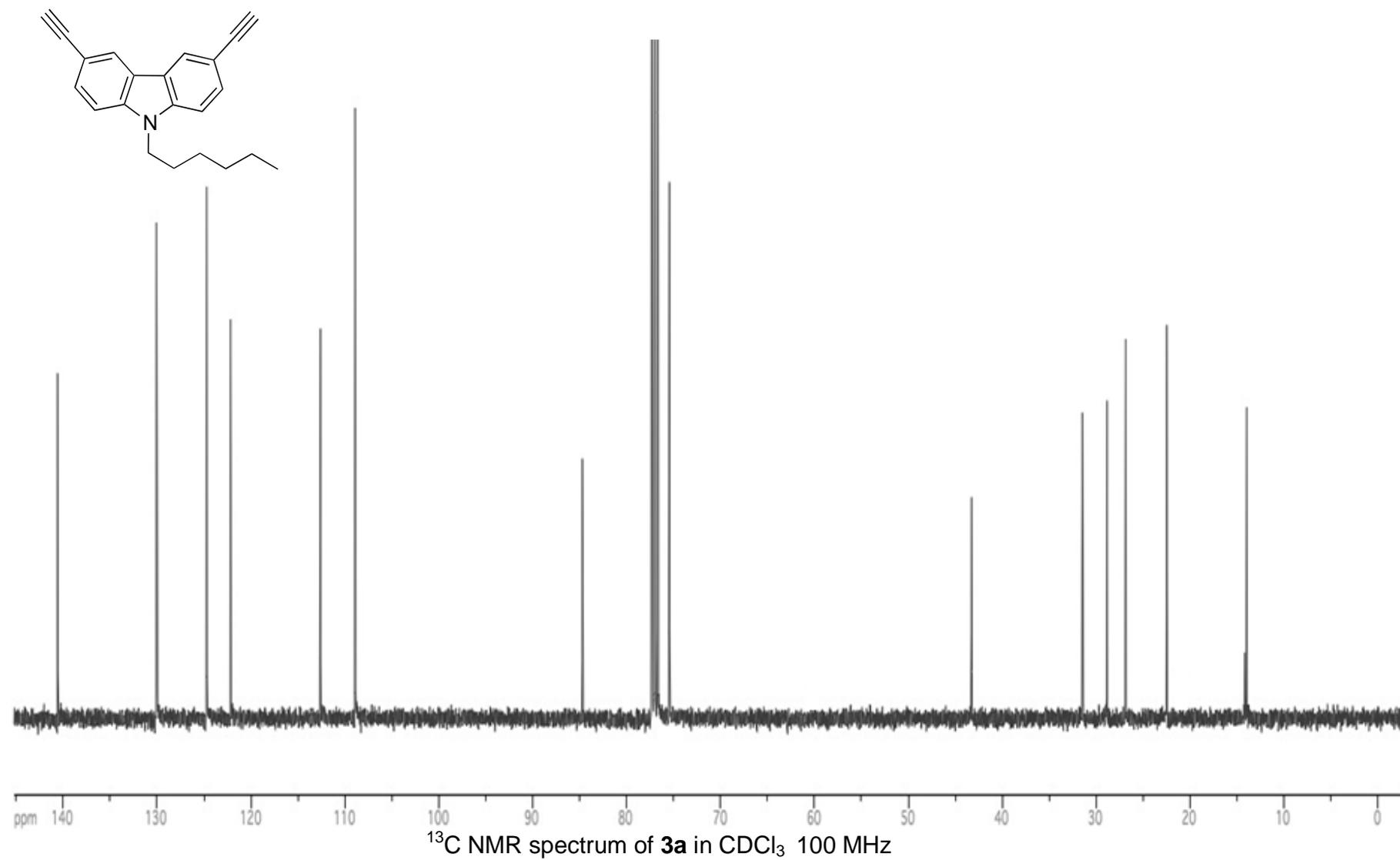
¹H NMR spectrum of **2** in acetone-*d*₆ 400 MHz.

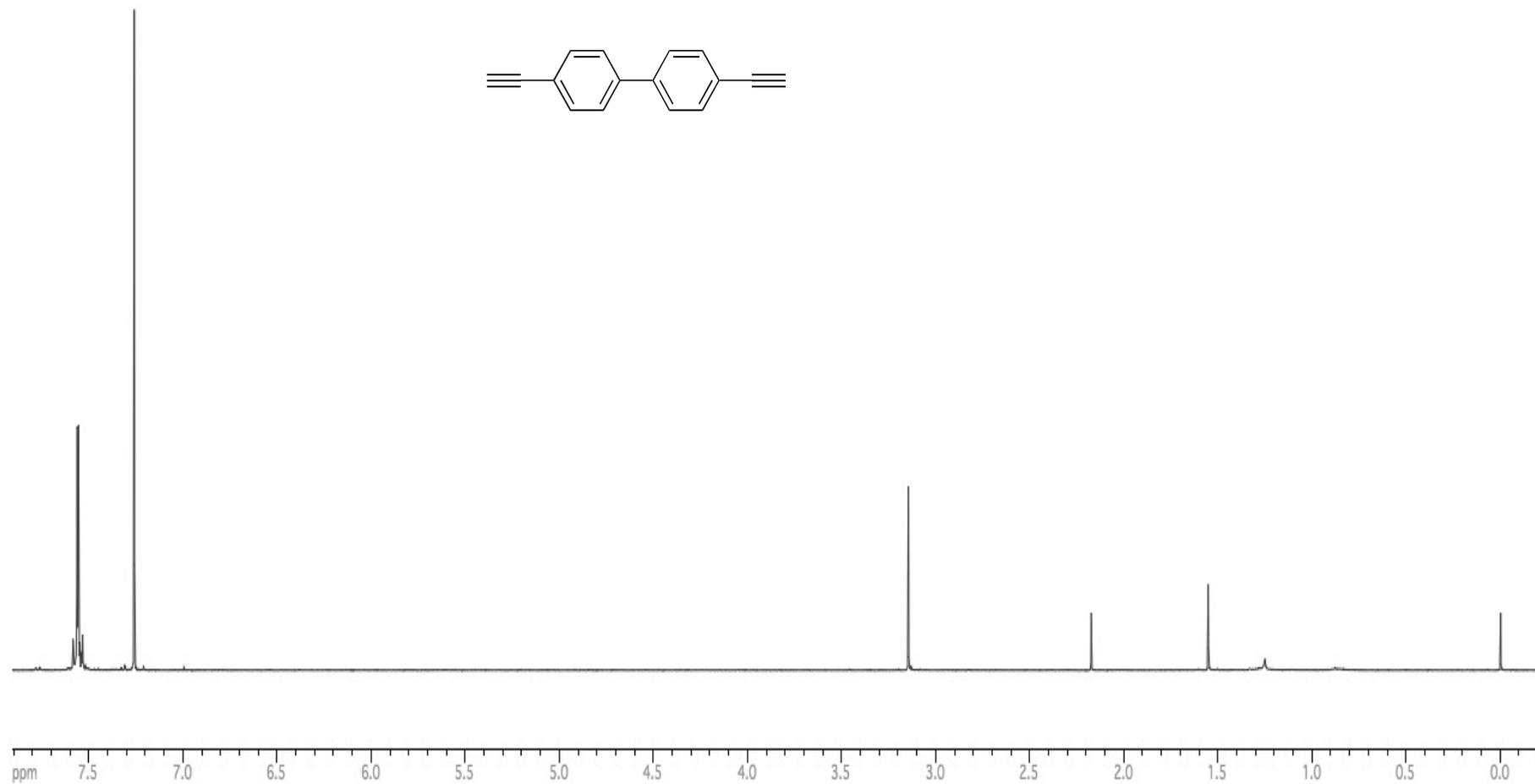


¹³C NMR spectrum of **2** in acetone-*d*₆ 100 MHz.

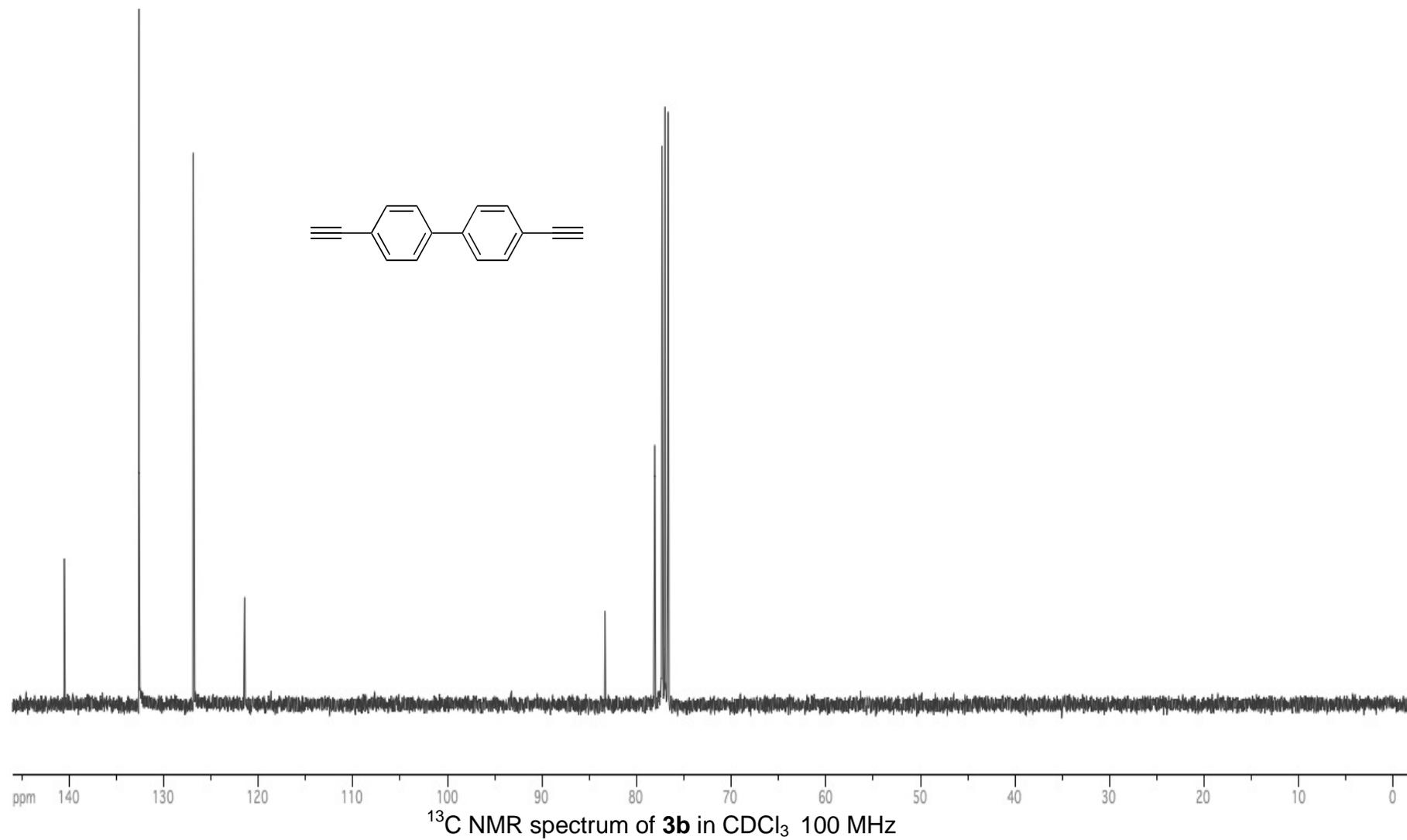


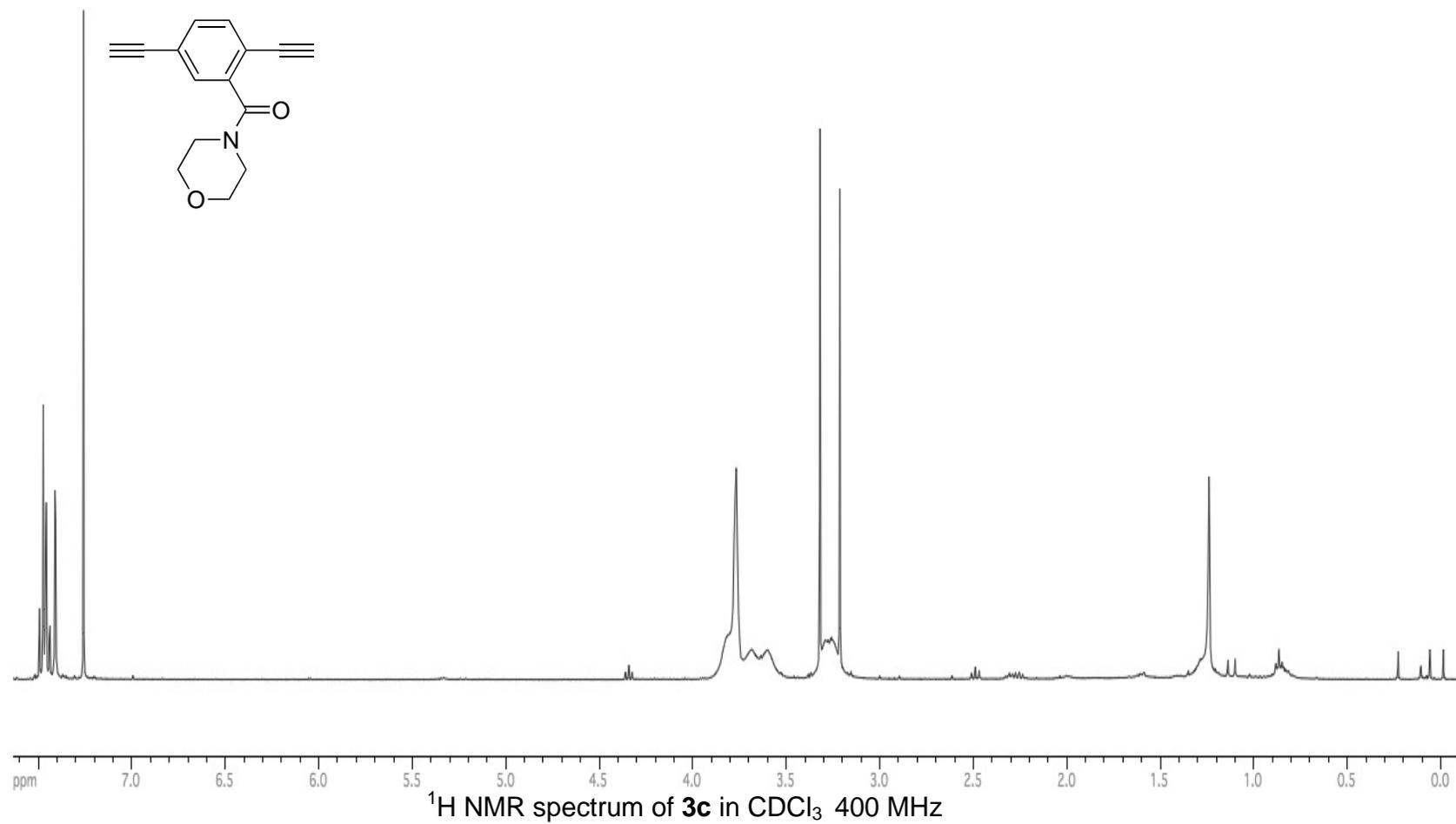
¹H NMR spectrum of **3a** in CDCl₃ 400 MHz

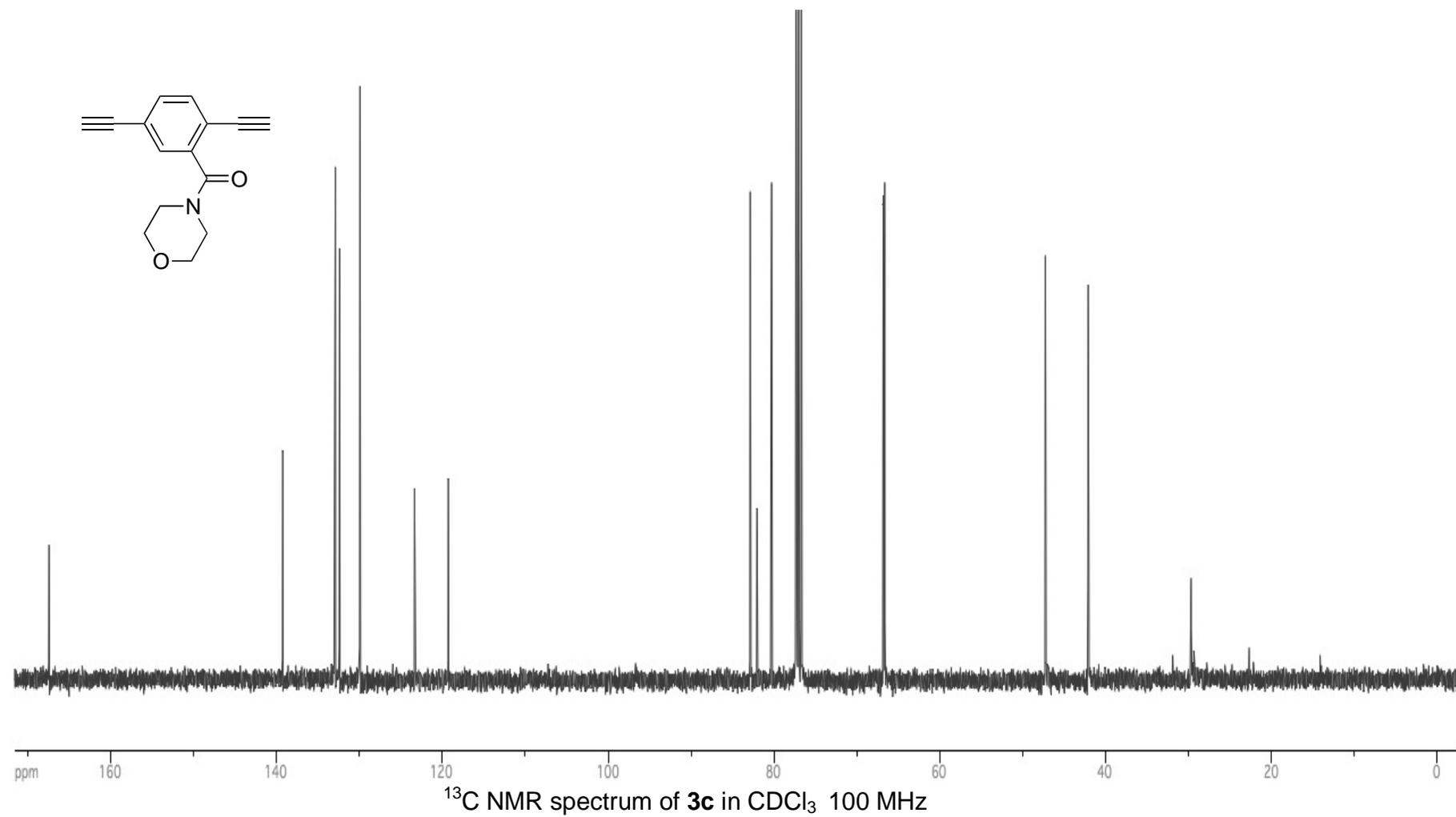


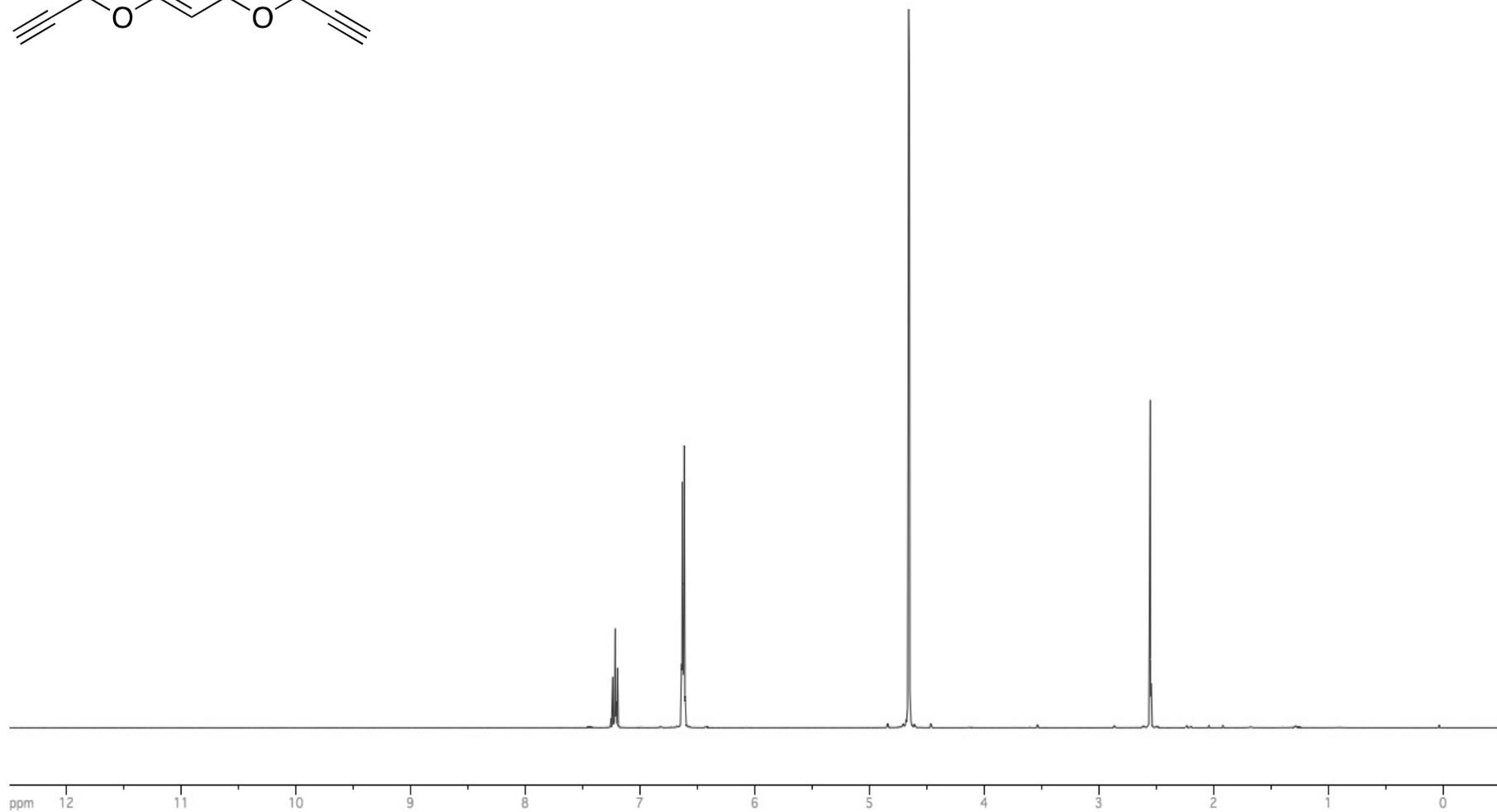
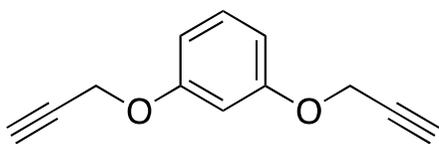


¹H NMR spectrum of **3b** in CDCl₃ 400 MHz

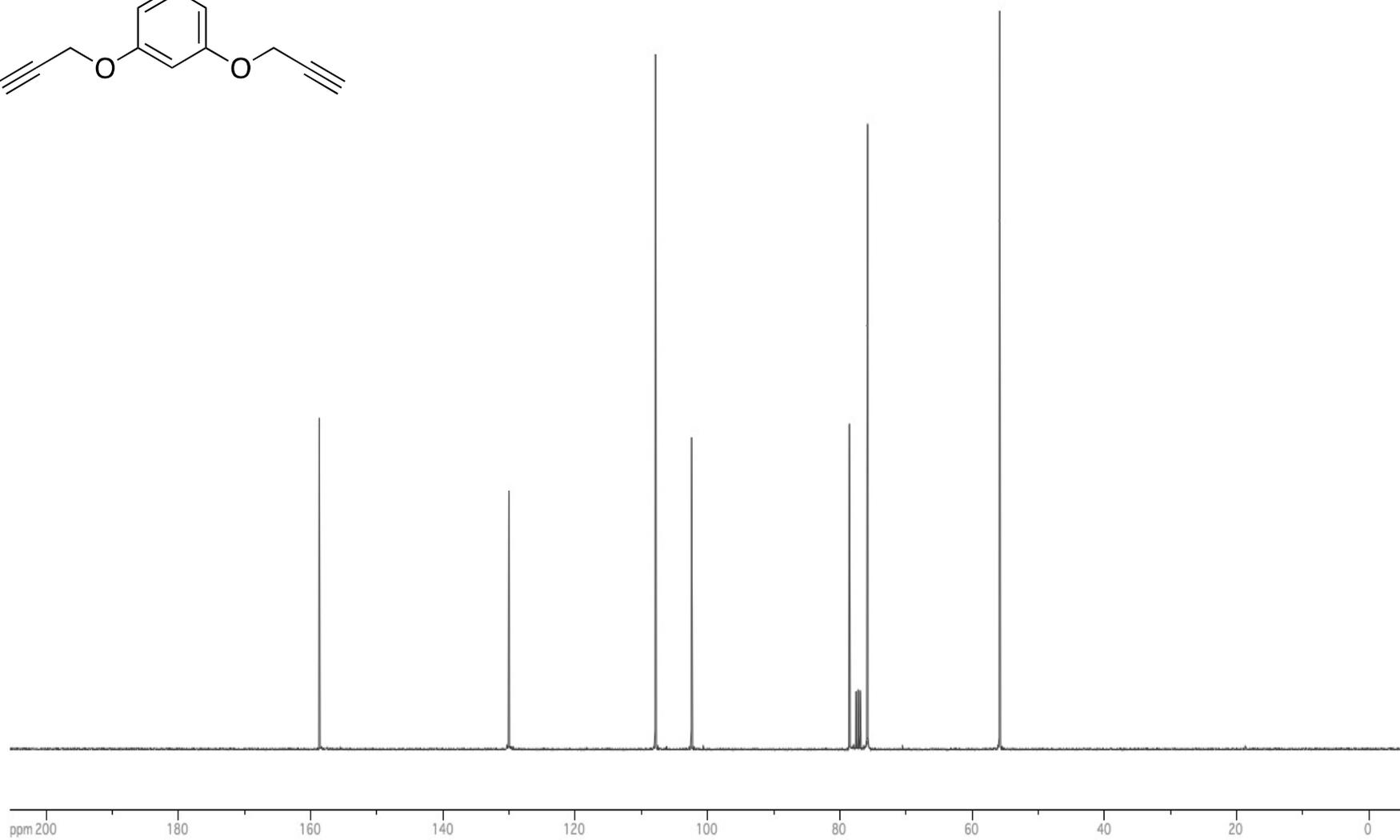
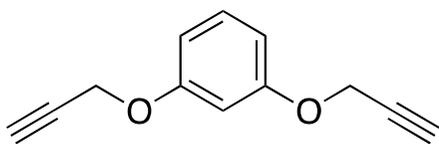




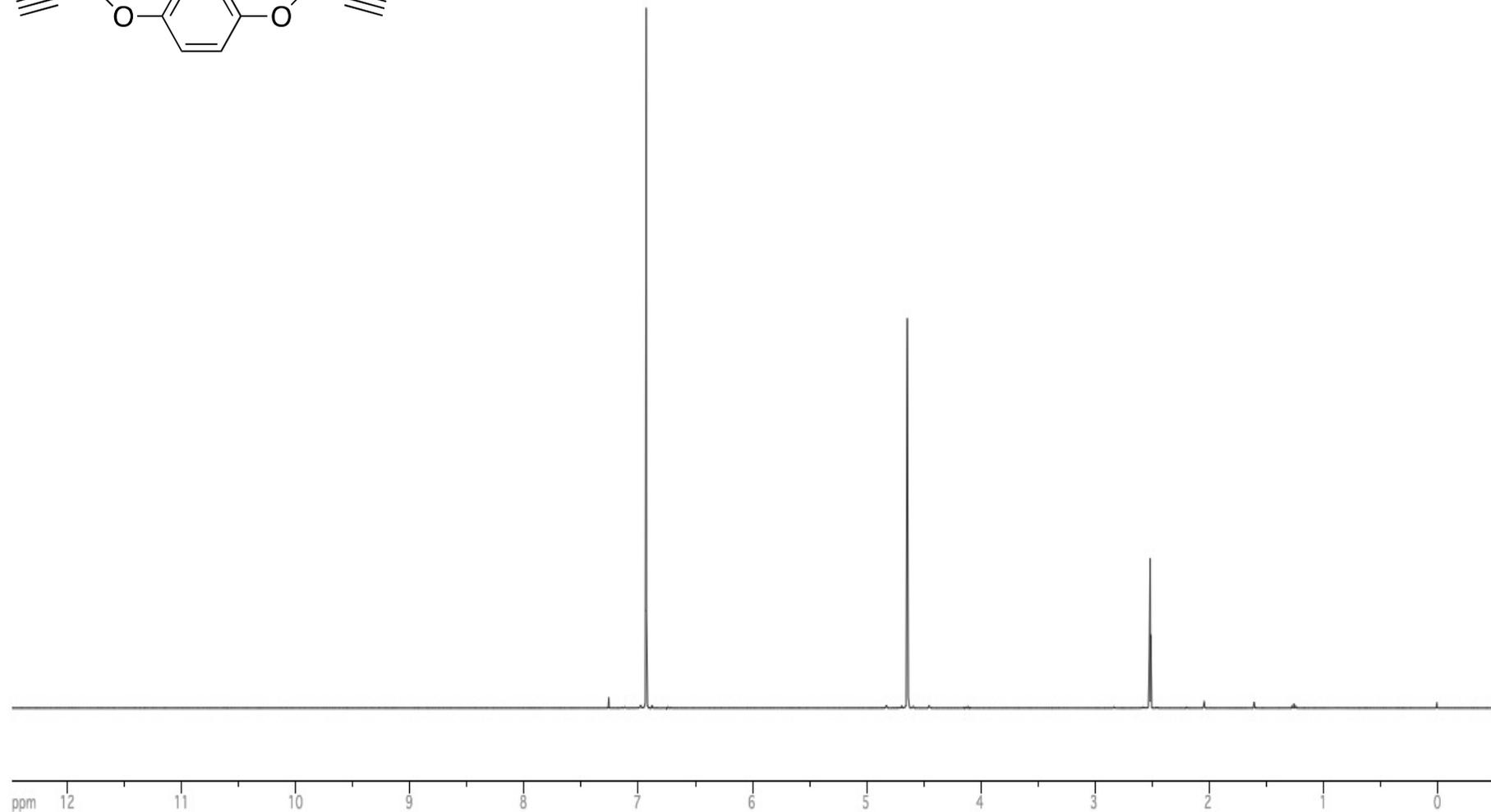
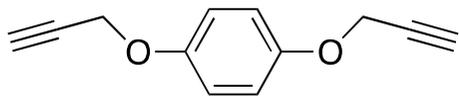




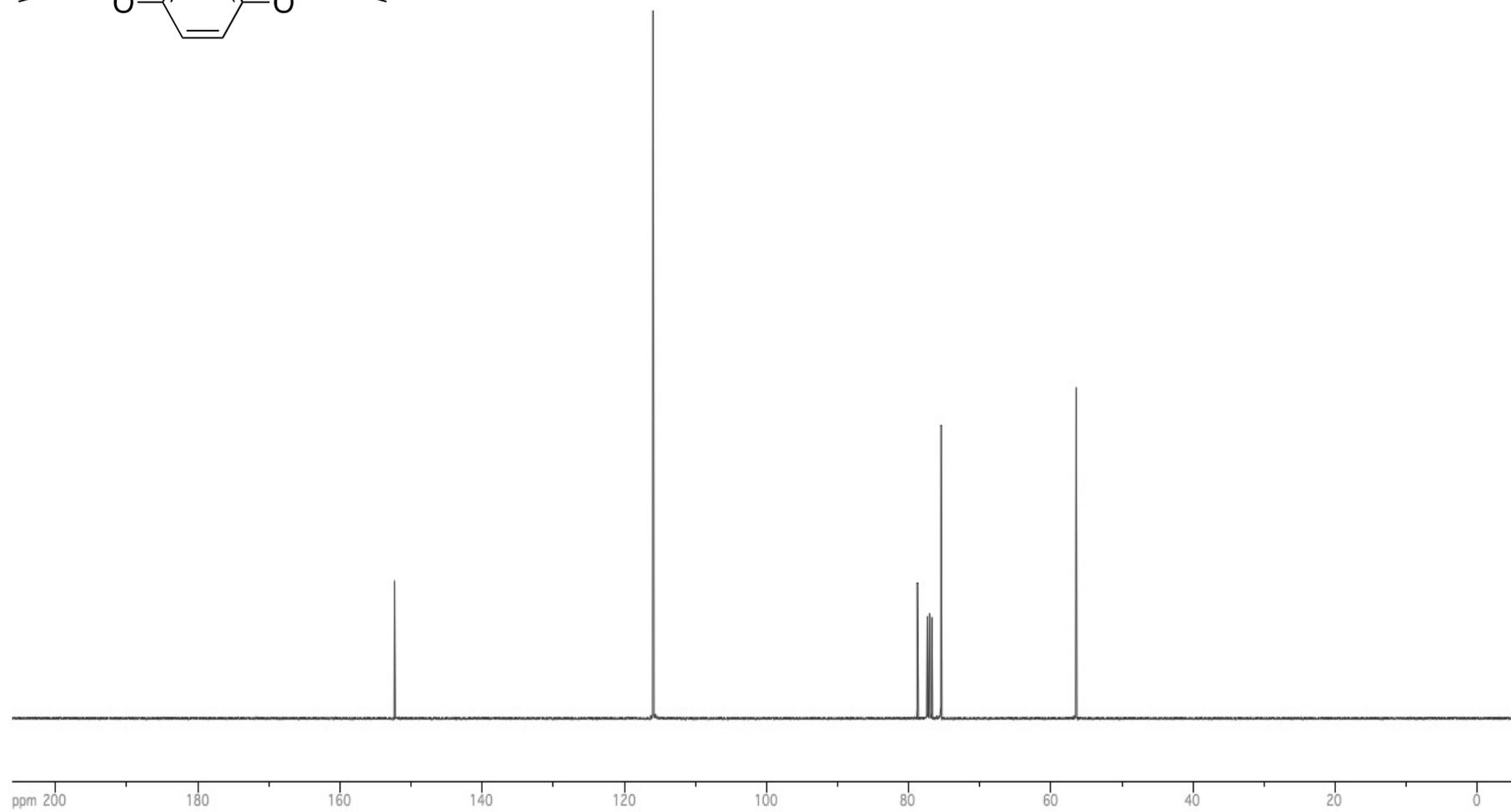
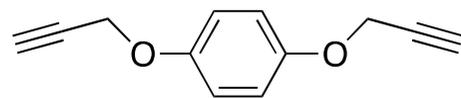
¹H NMR spectrum of compound **3d** in CDCl₃ 400 MHz



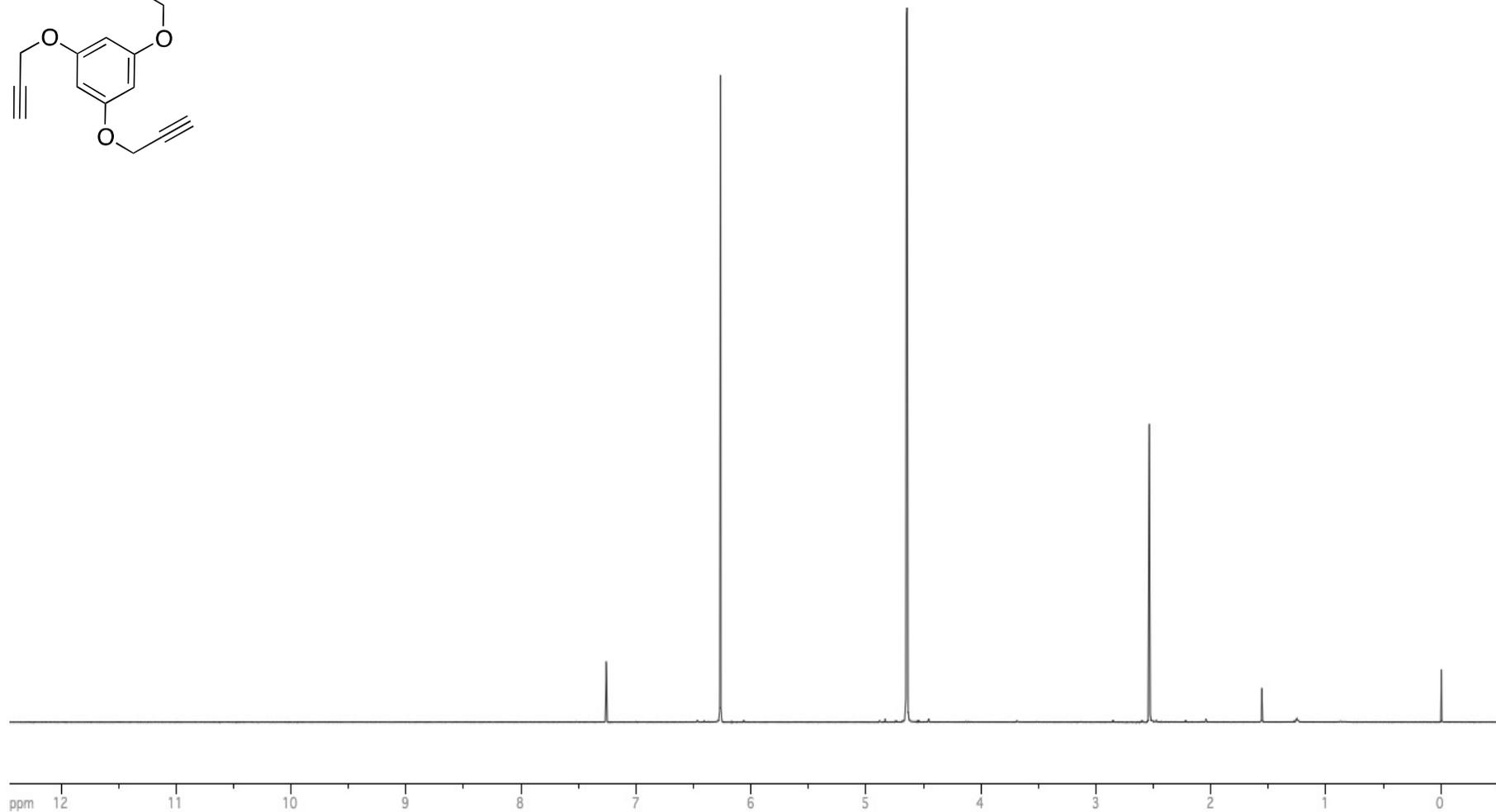
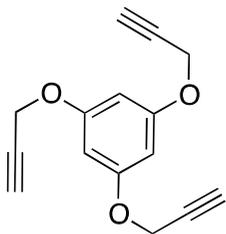
¹³C NMR spectrum of compound **3d** in CDCl₃ 100 MHz



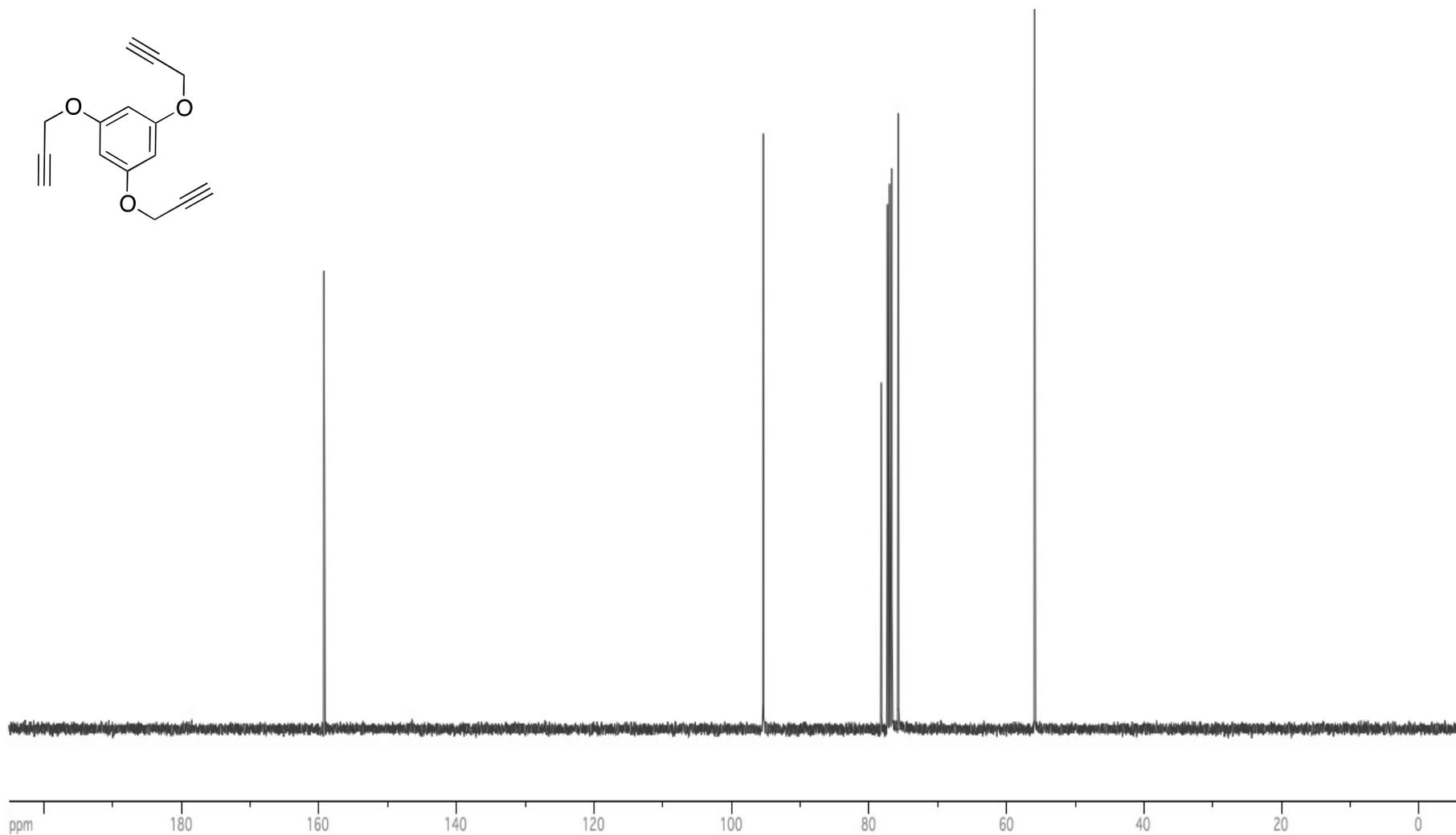
¹H NMR spectrum of compound **3e** in CDCl₃ 400 MHz



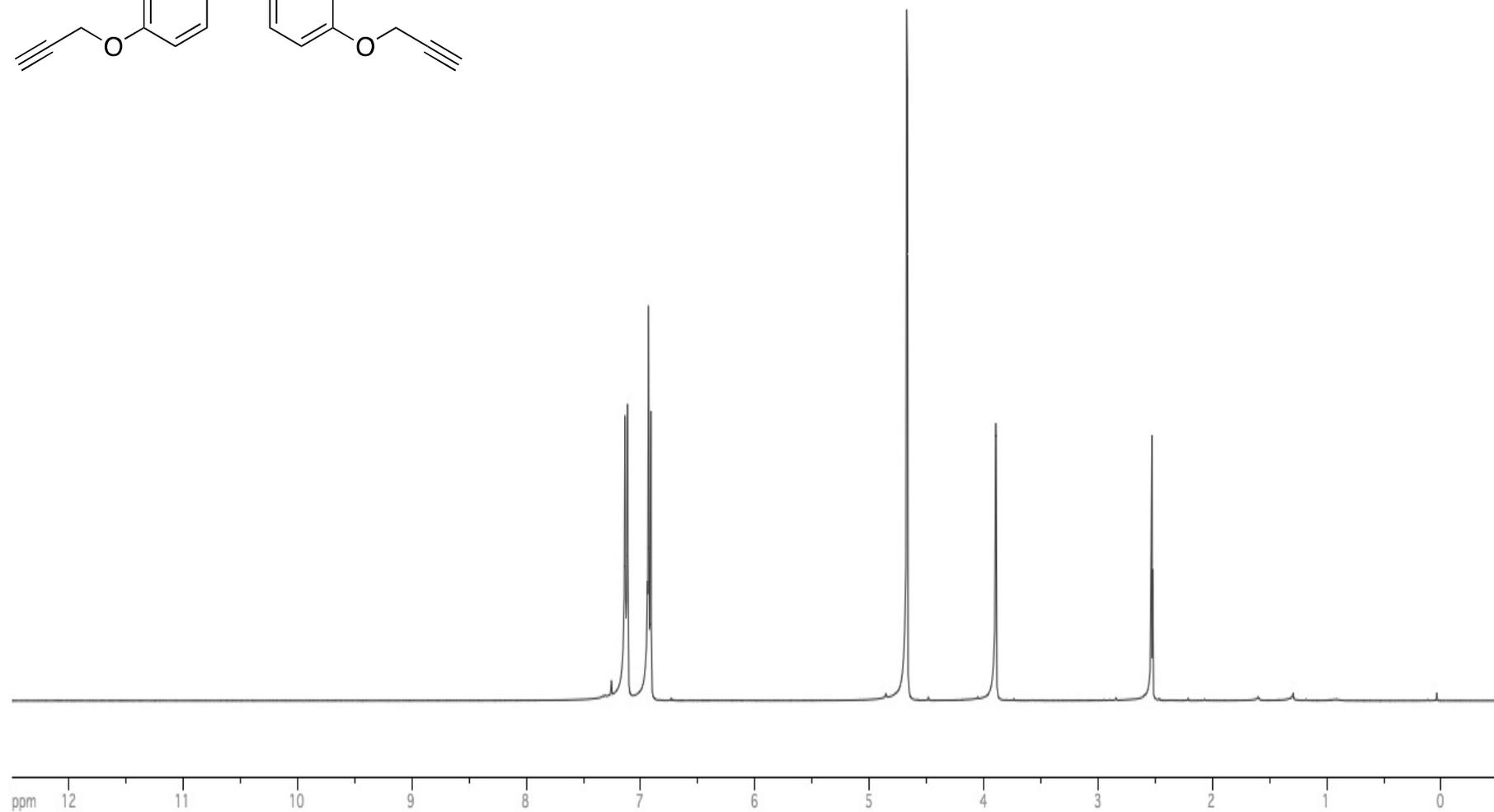
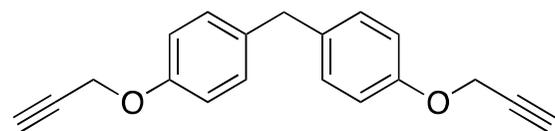
^{13}C NMR spectrum of compound **3e** in CDCl_3 100 MHz



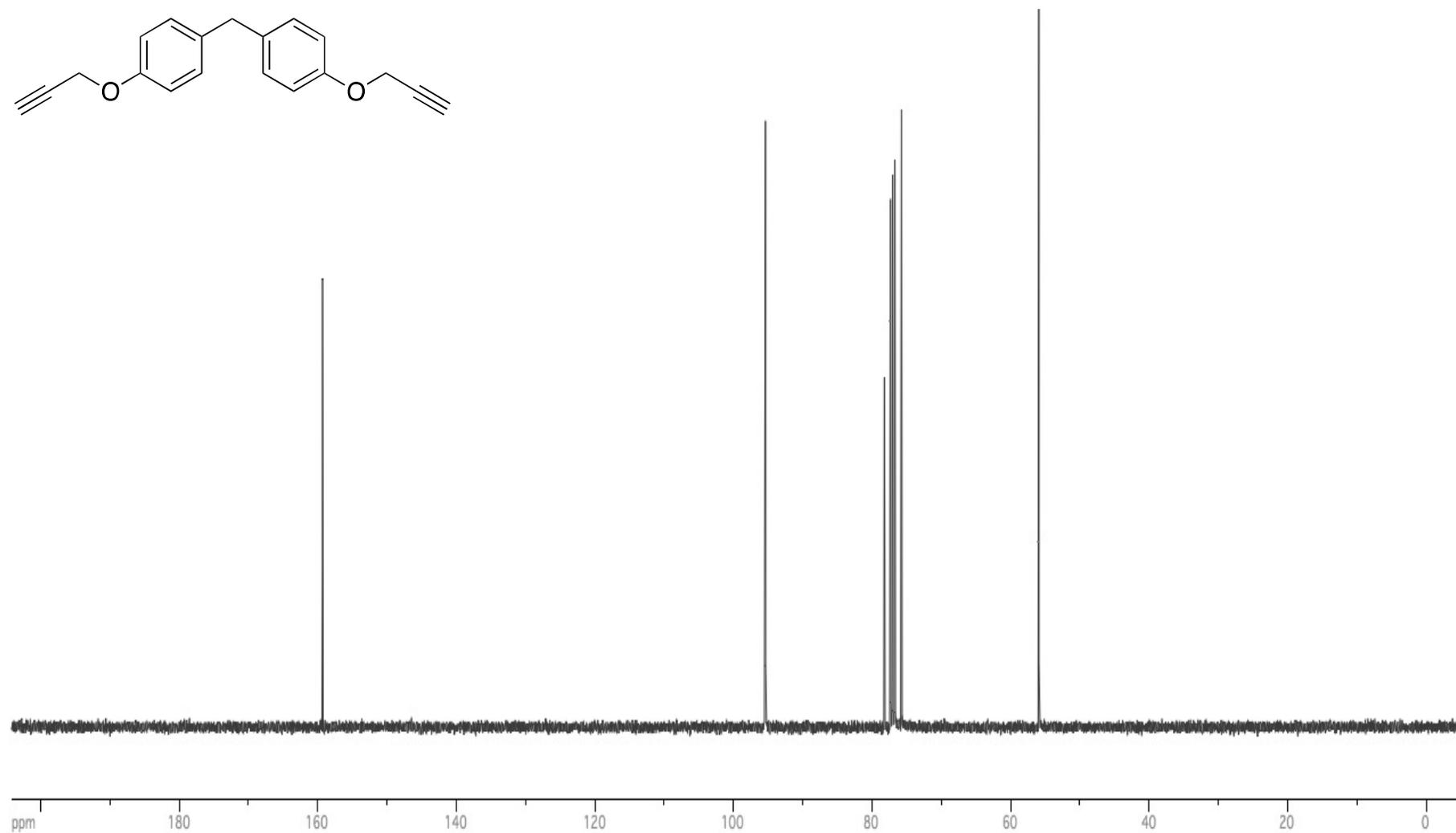
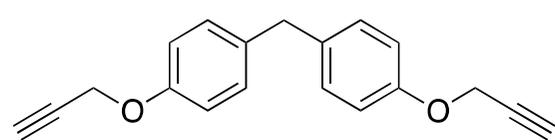
¹H NMR spectrum of compound **3f** in CDCl₃ 400 MHz



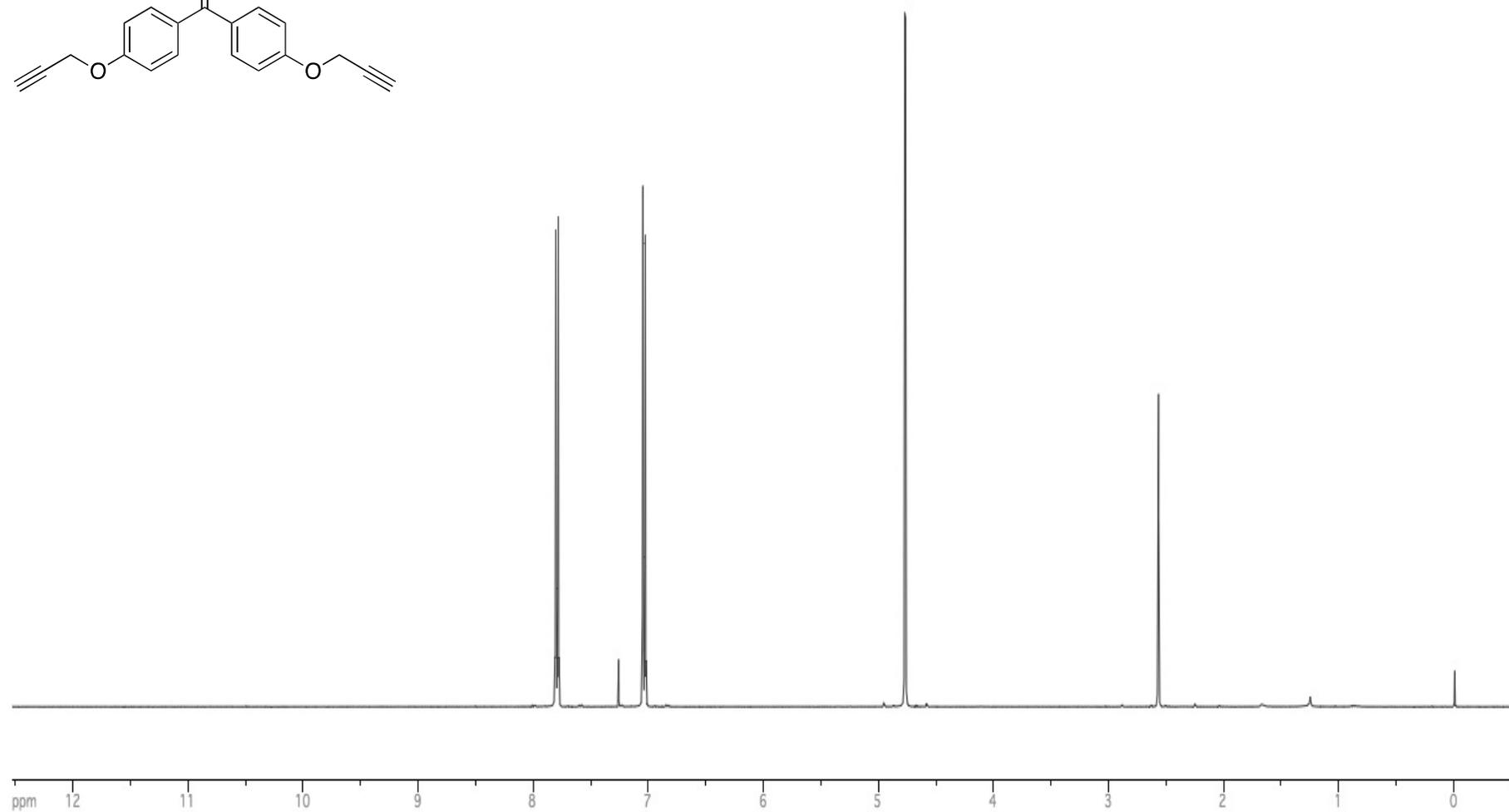
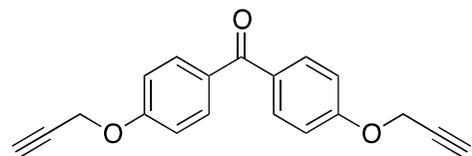
¹³C NMR spectrum of compound **3f** in CDCl₃ 100 MHz



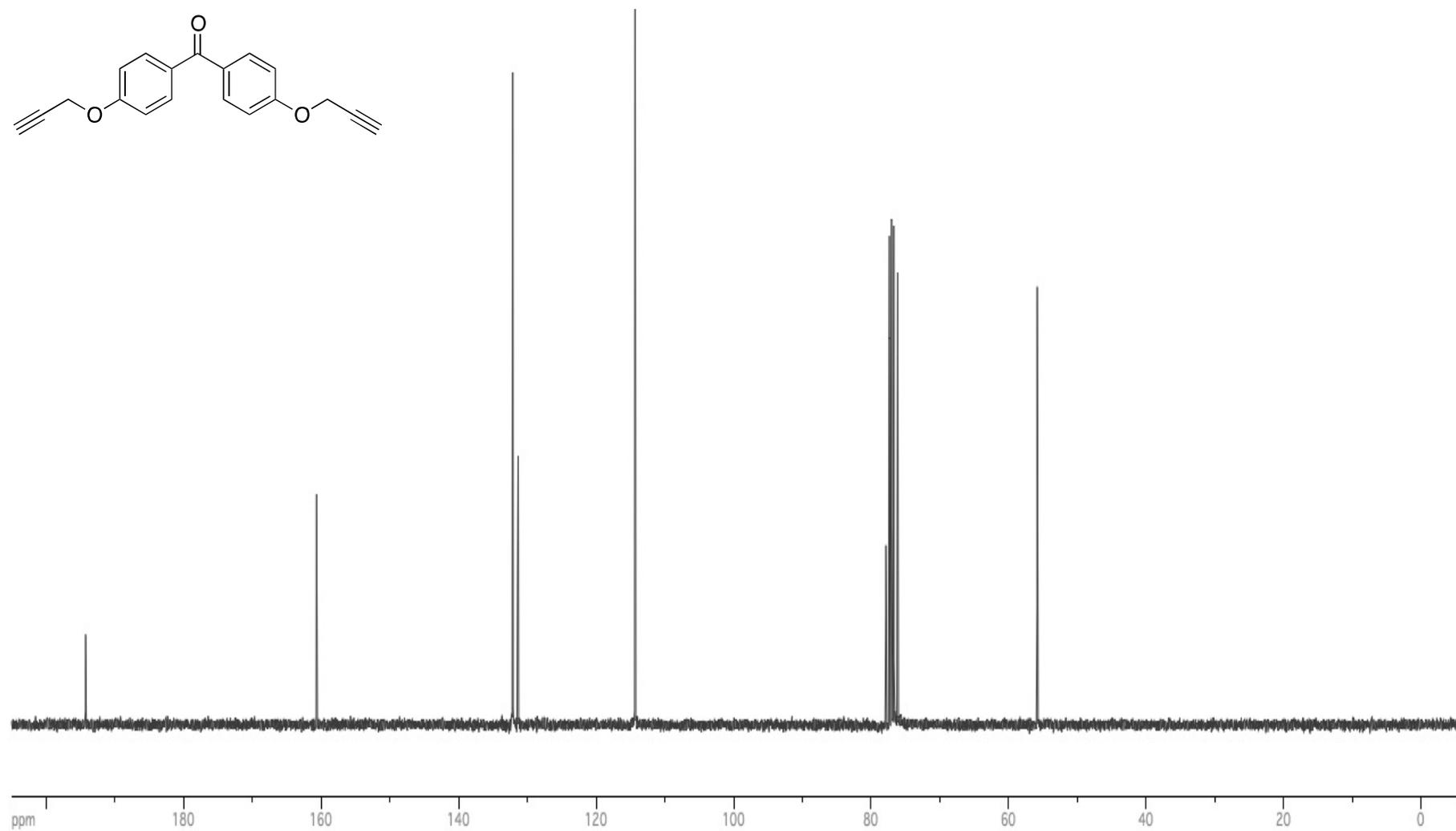
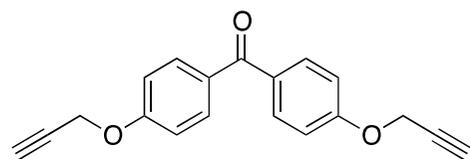
¹H NMR spectrum of compound **3g** in CDCl₃ 400 MHz



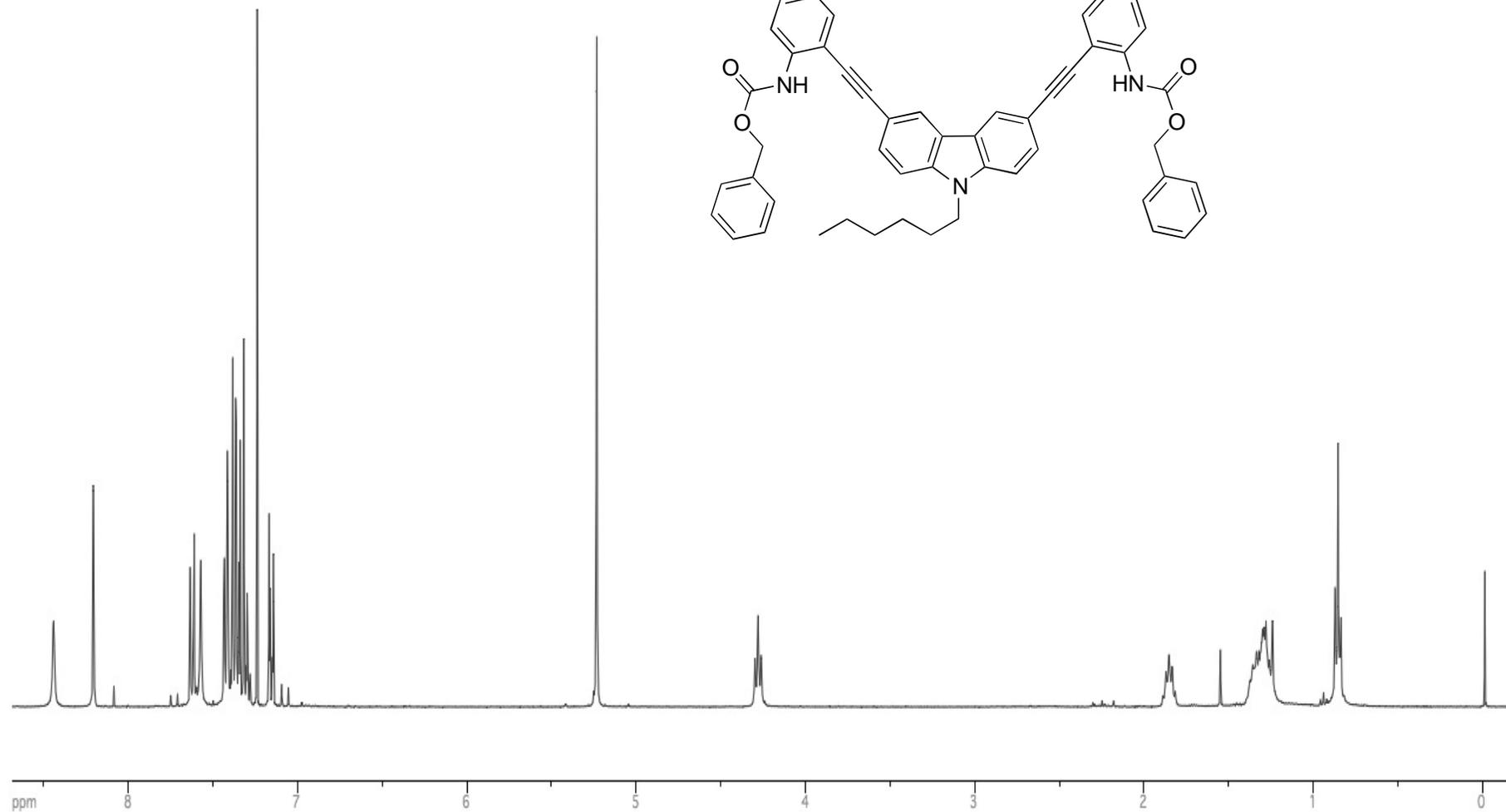
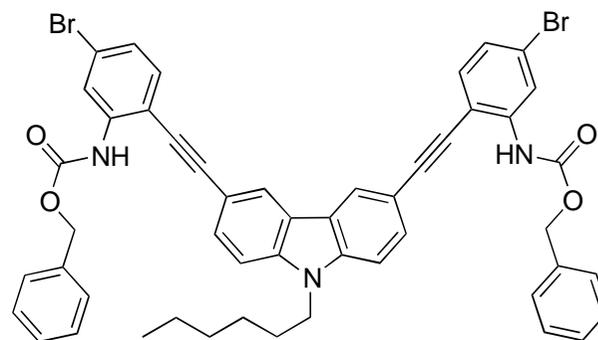
¹³C H NMR spectrum of compound **3g** in CDCl₃ 100 MHz



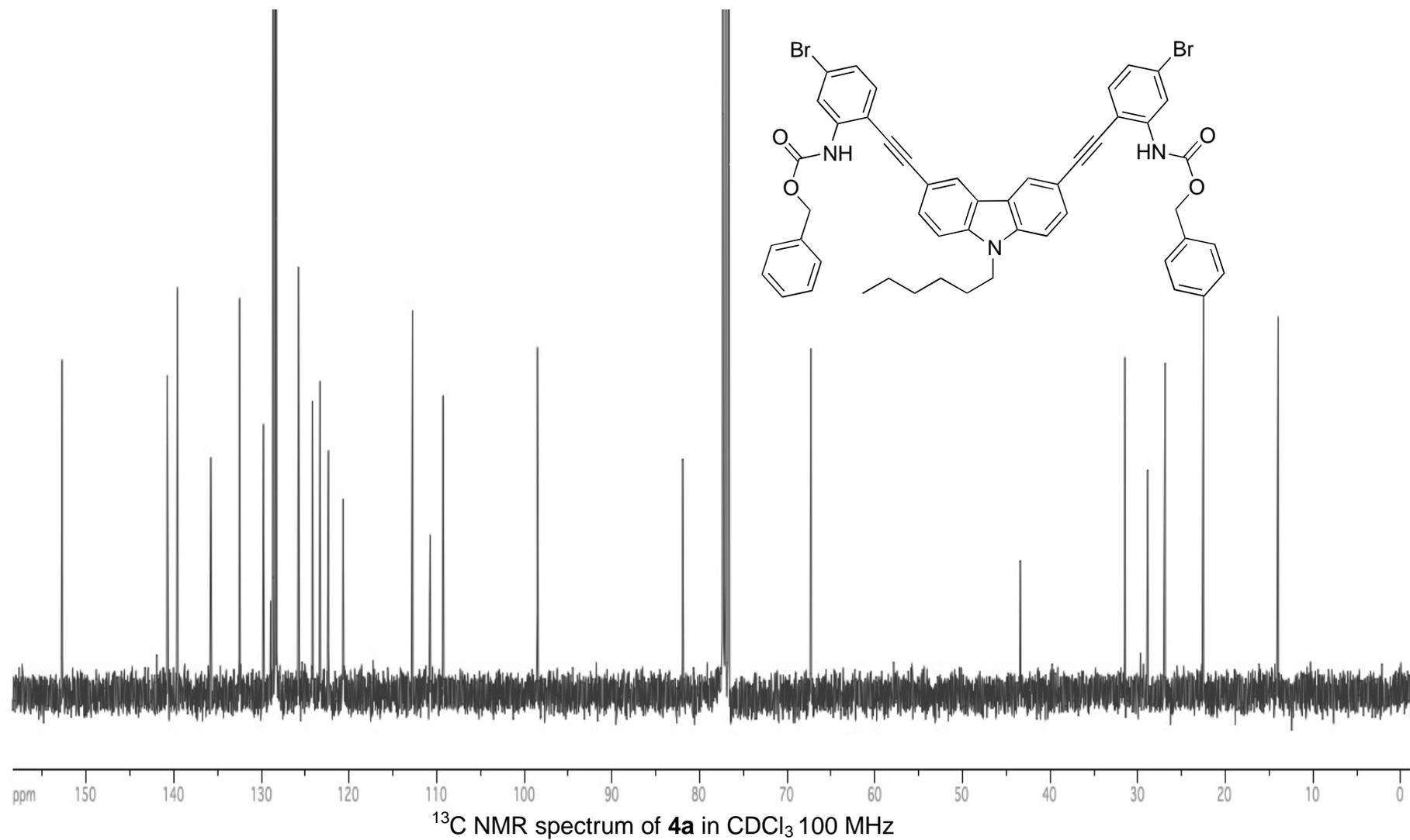
¹H NMR spectrum of compound **3h** in CDCl₃ 400 MHz

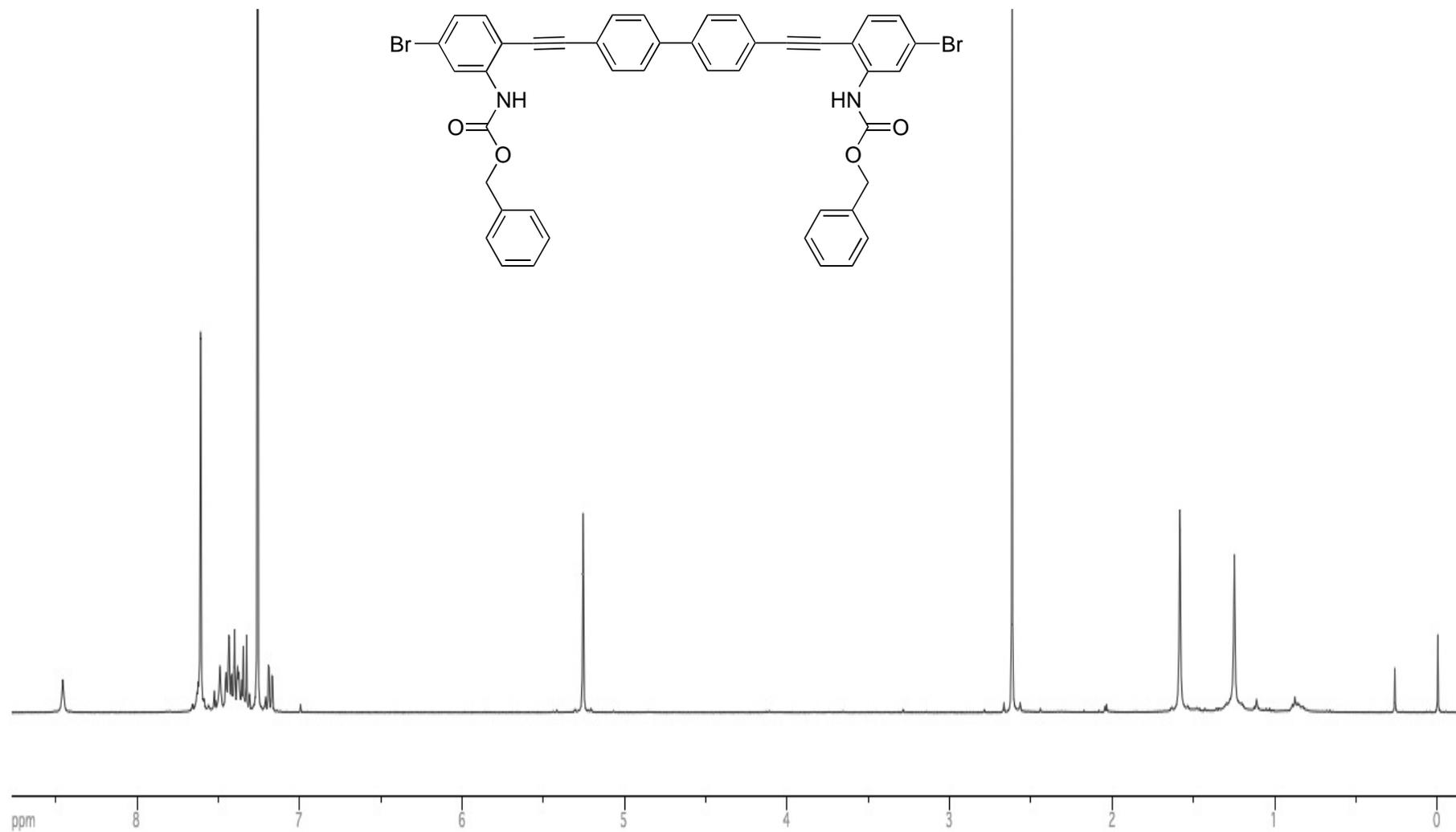


¹³C NMR spectrum of compound **3h** in CDCl₃ 100 MHz

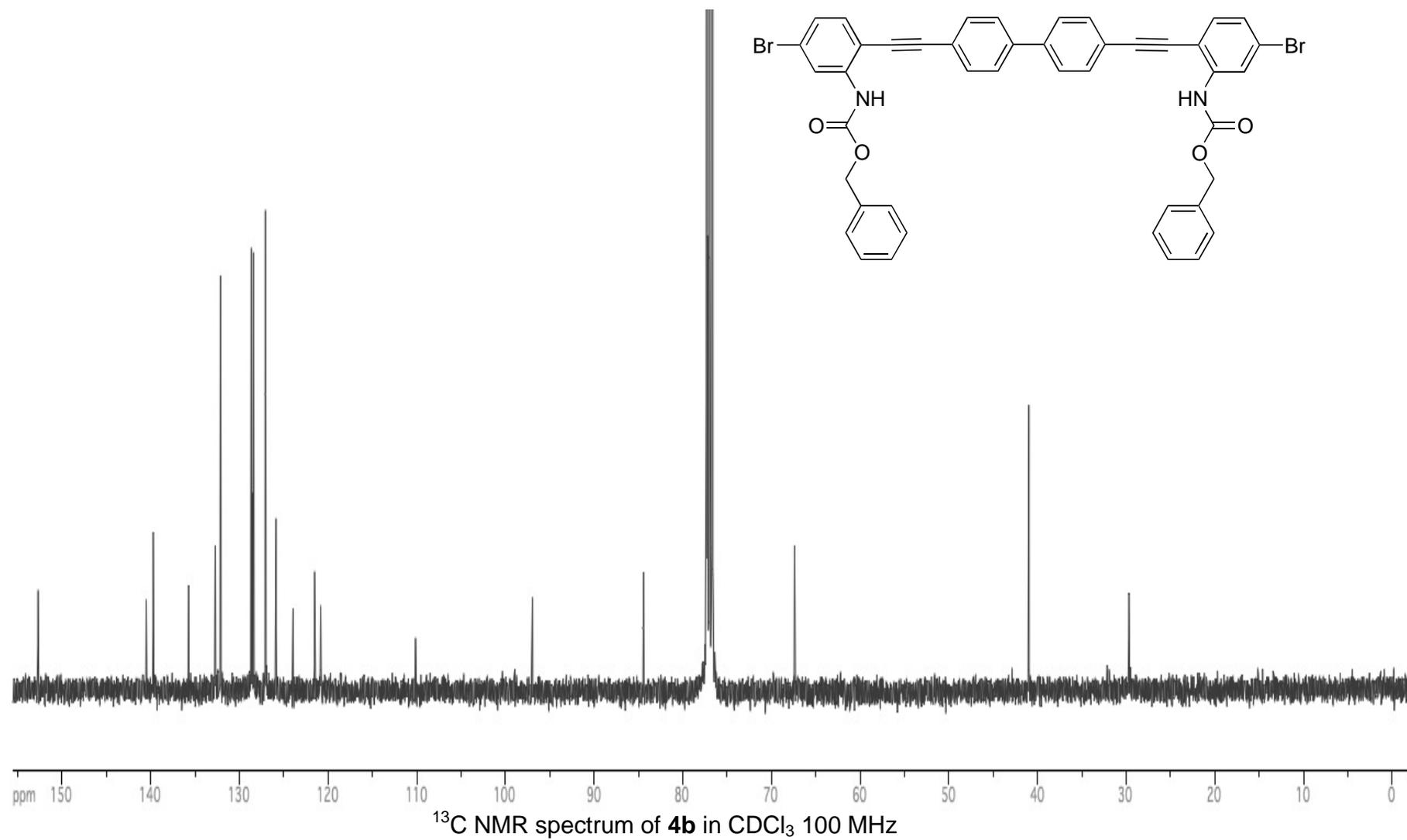


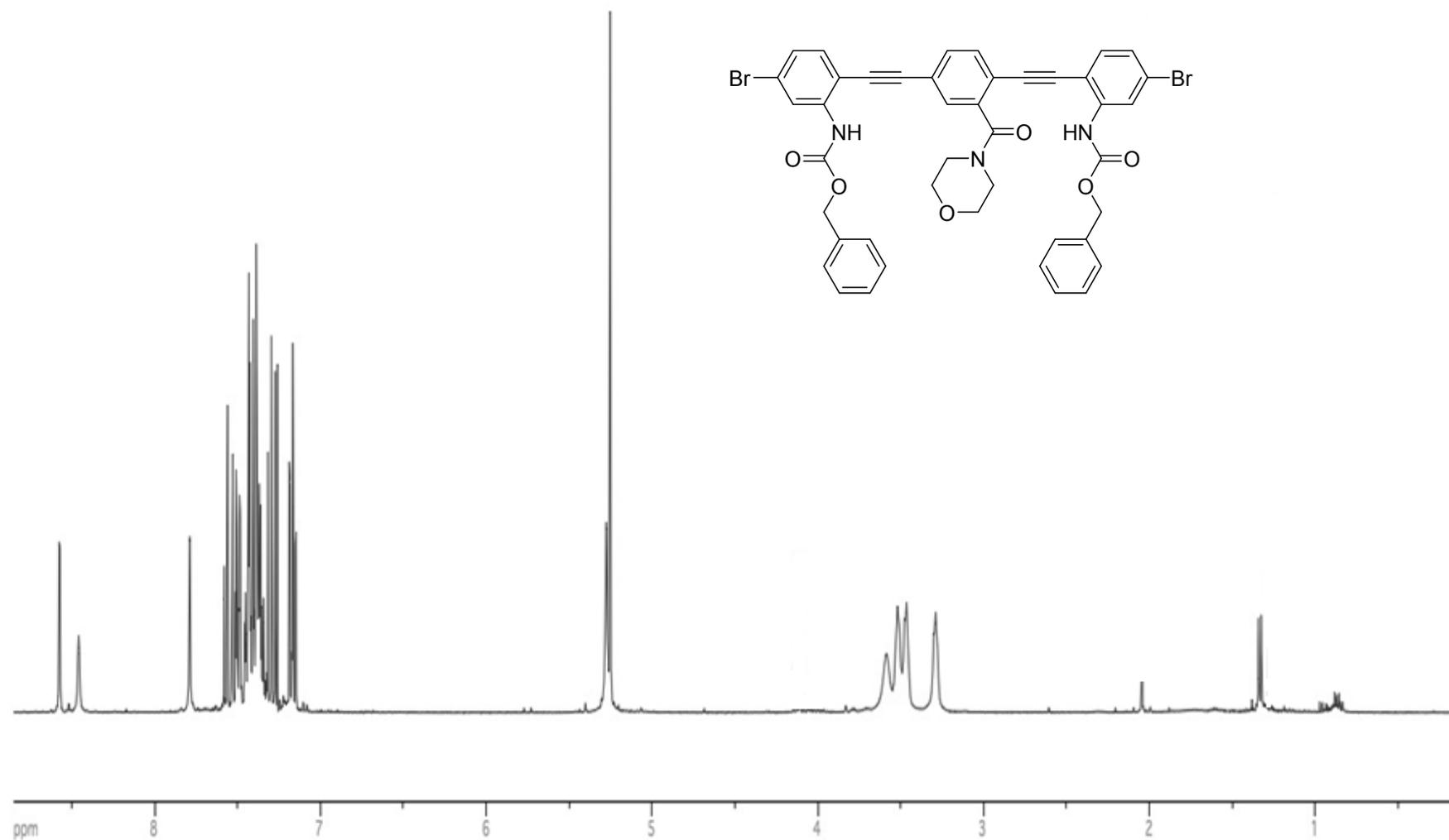
¹H NMR spectrum of **4a** in CDCl₃ 400 MHz



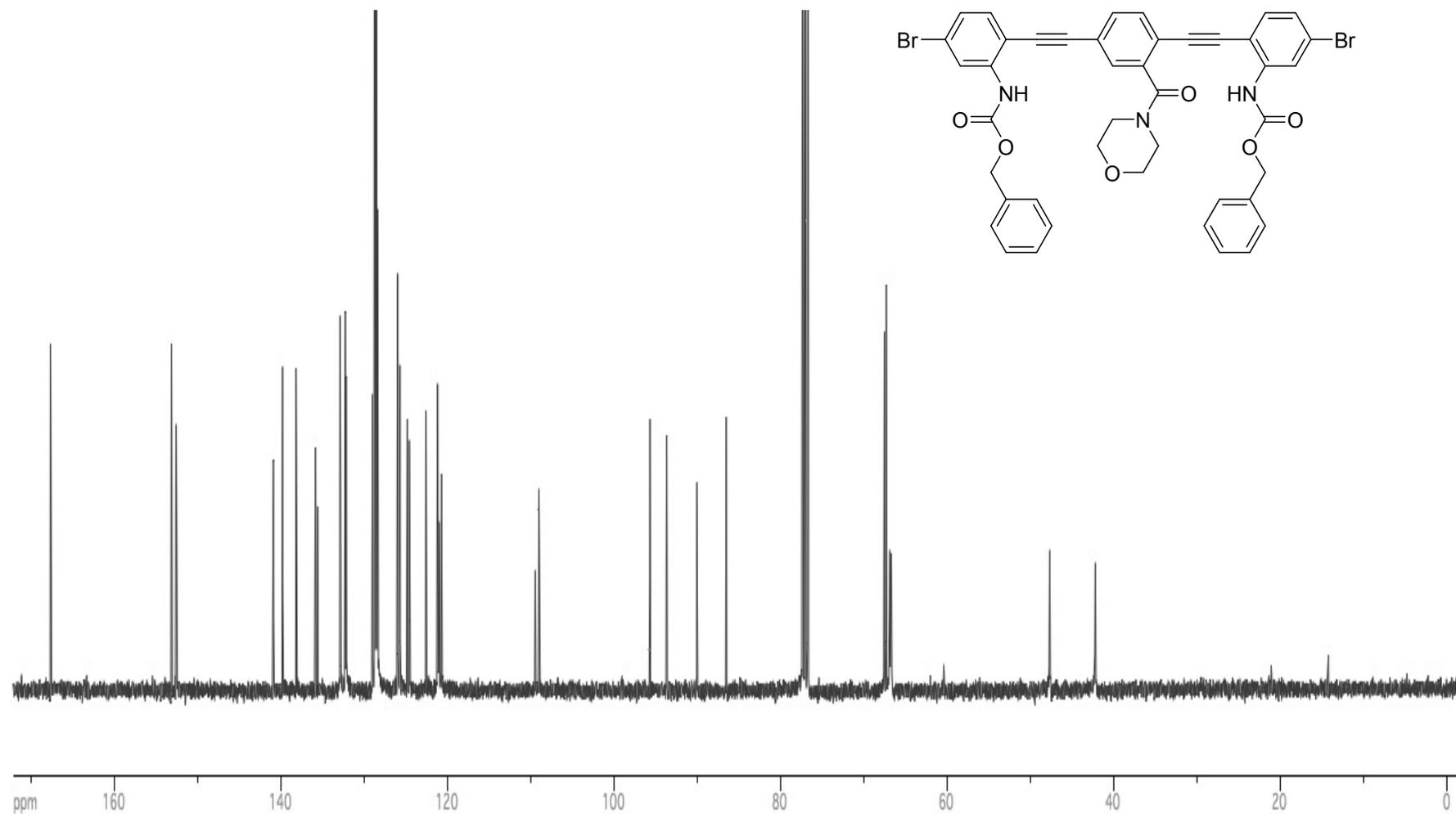


¹H NMR spectrum of **4b** in CDCl₃ 400 MHz

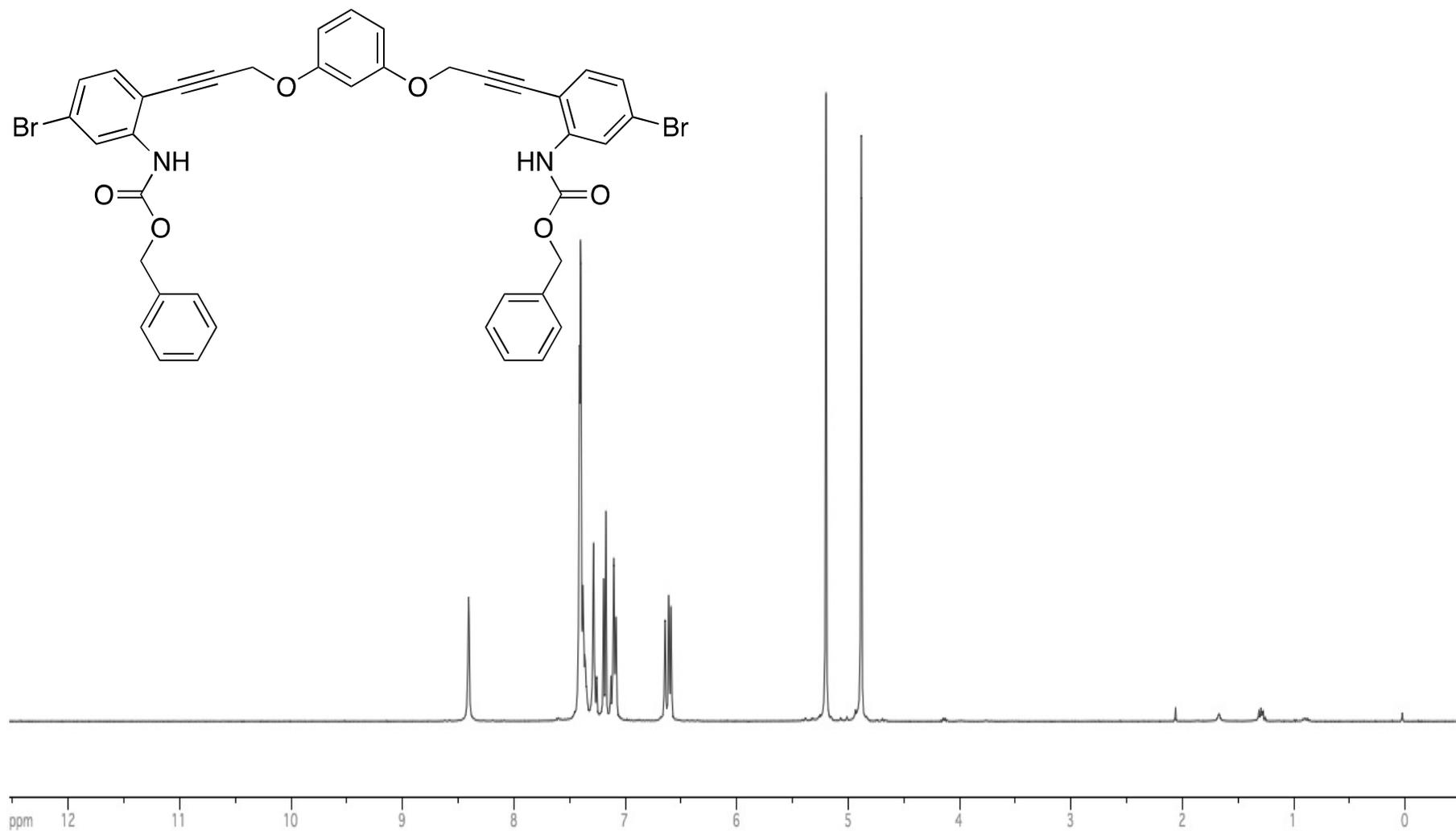




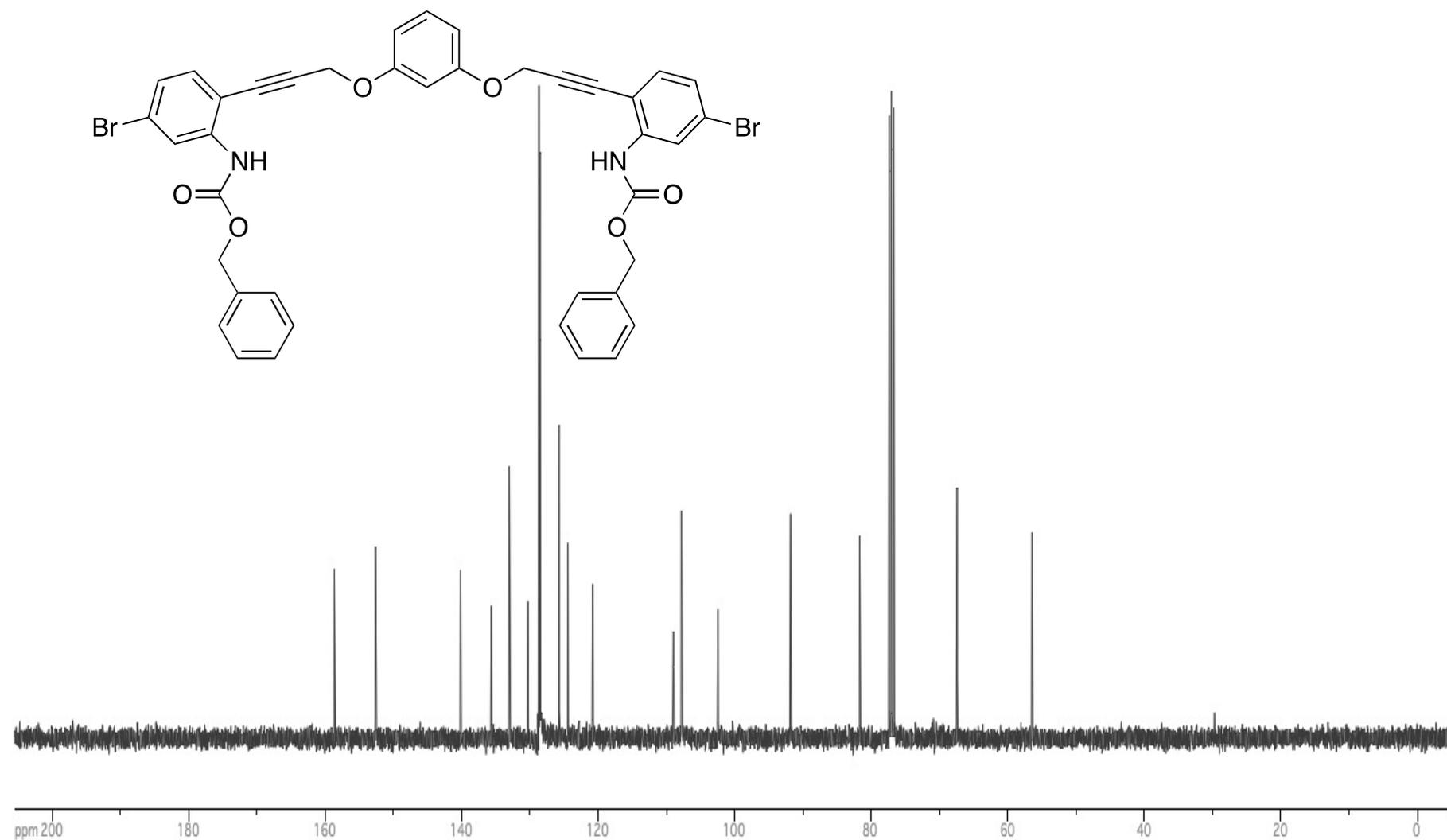
¹H NMR spectrum of compound **4c** in CDCl₃ 400 MHz



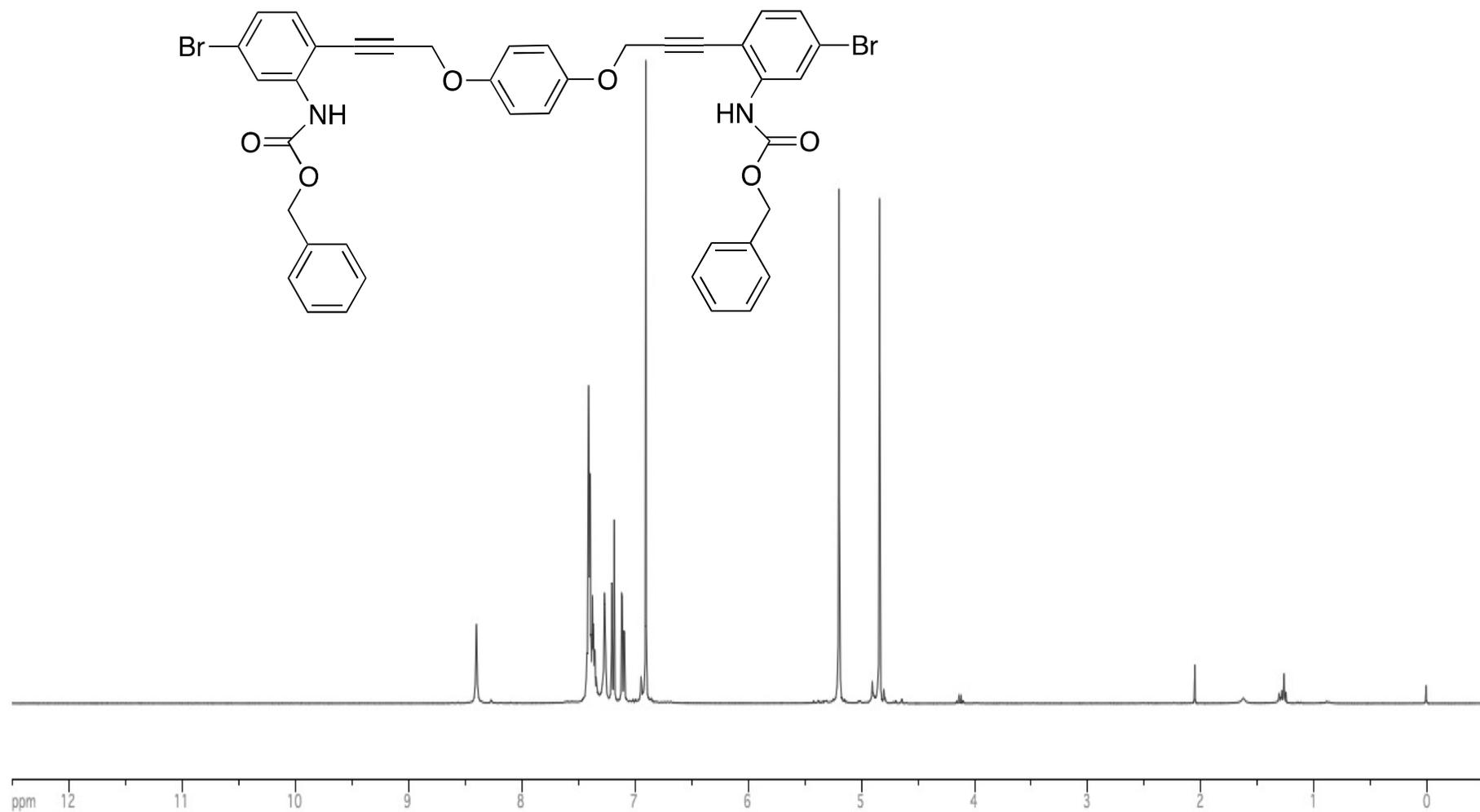
^{13}C NMR spectrum of compound **4c** in CDCl_3 100 MHz



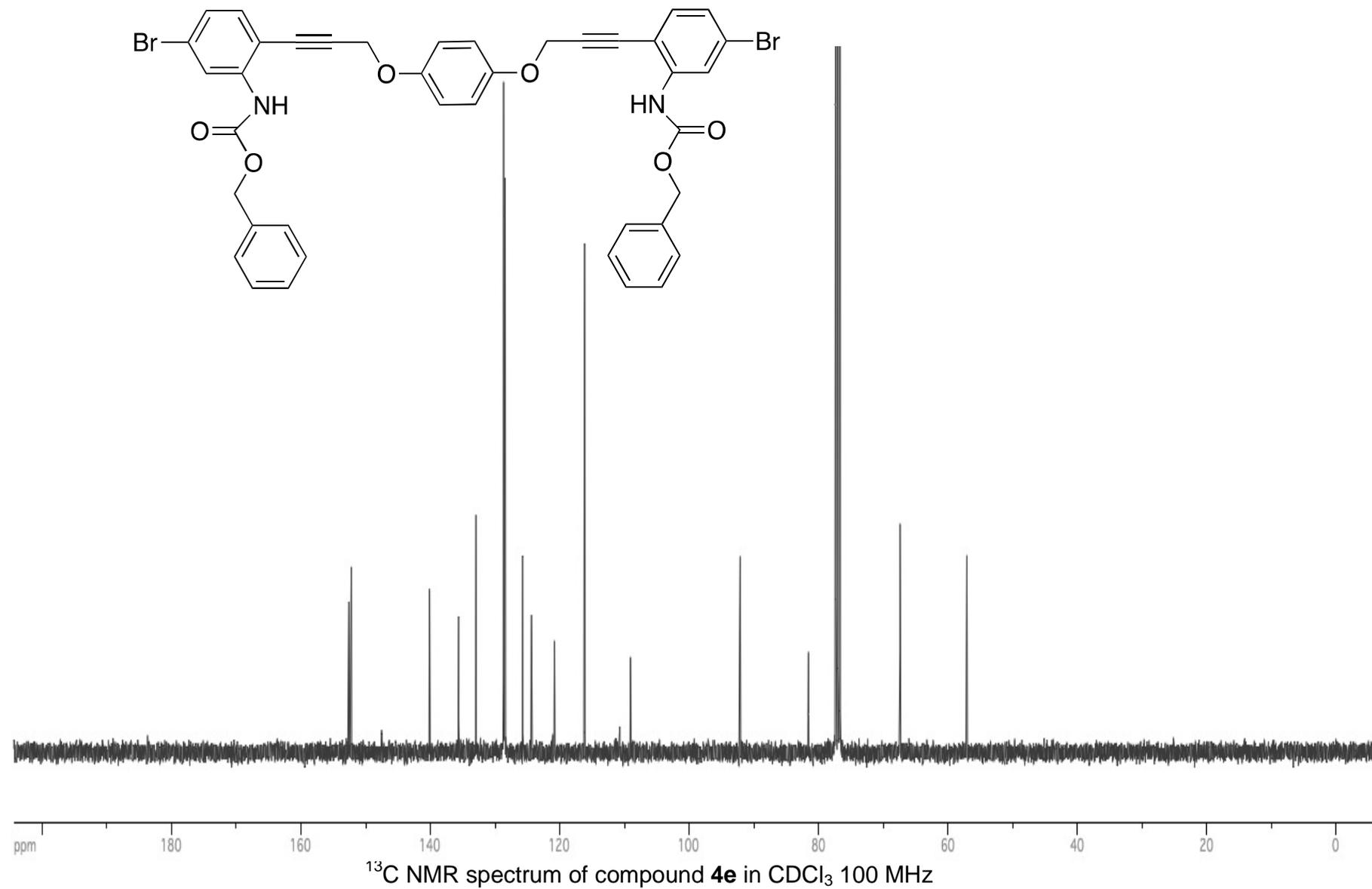
¹H NMR spectrum of compound **4d** in CDCl₃ 400 MHz

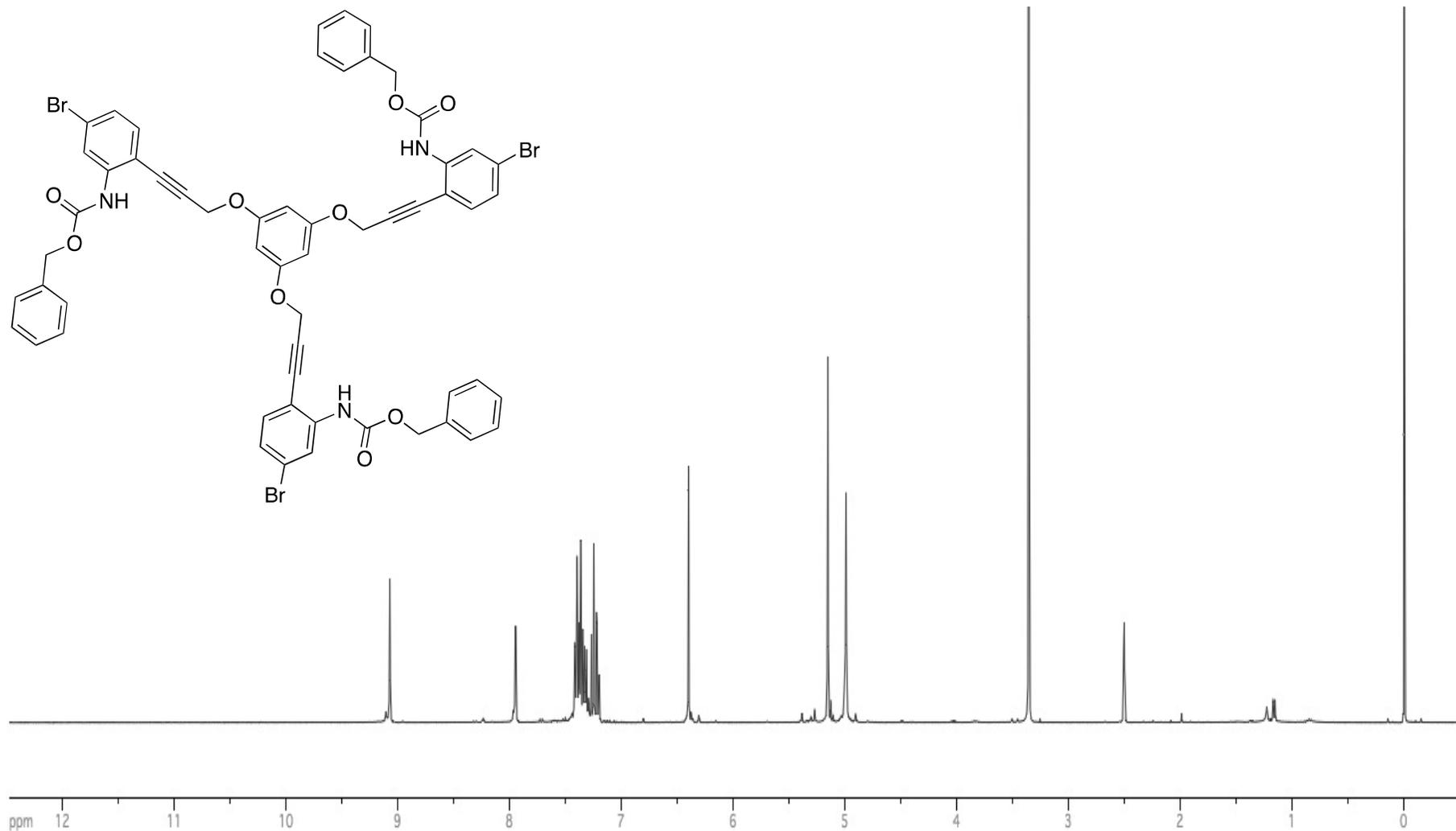


¹³C NMR spectrum of compound **4d** in CDCl₃ 100 MHz

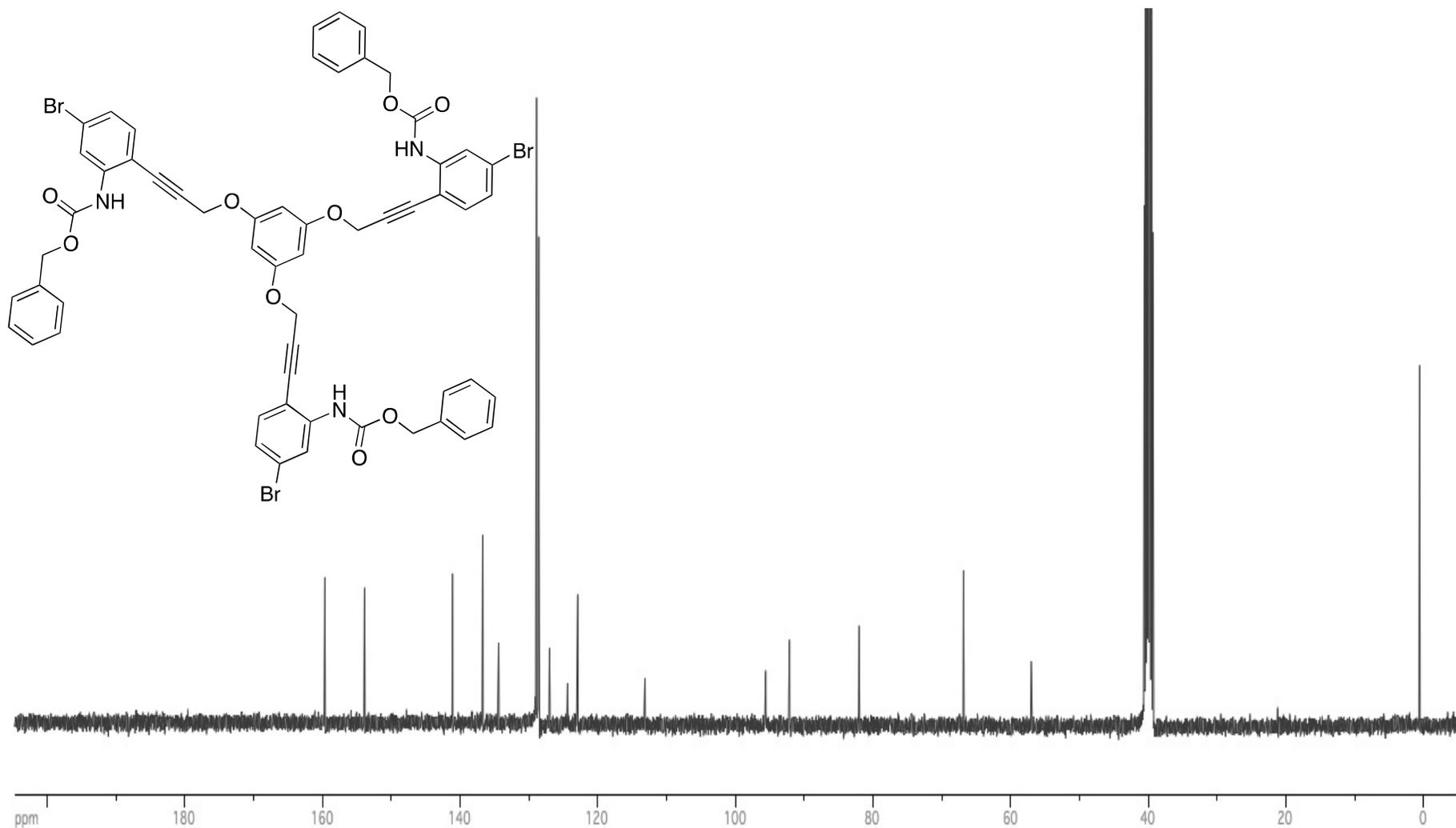


¹H NMR spectrum of compound **4e** in CDCl₃ 400 MHz

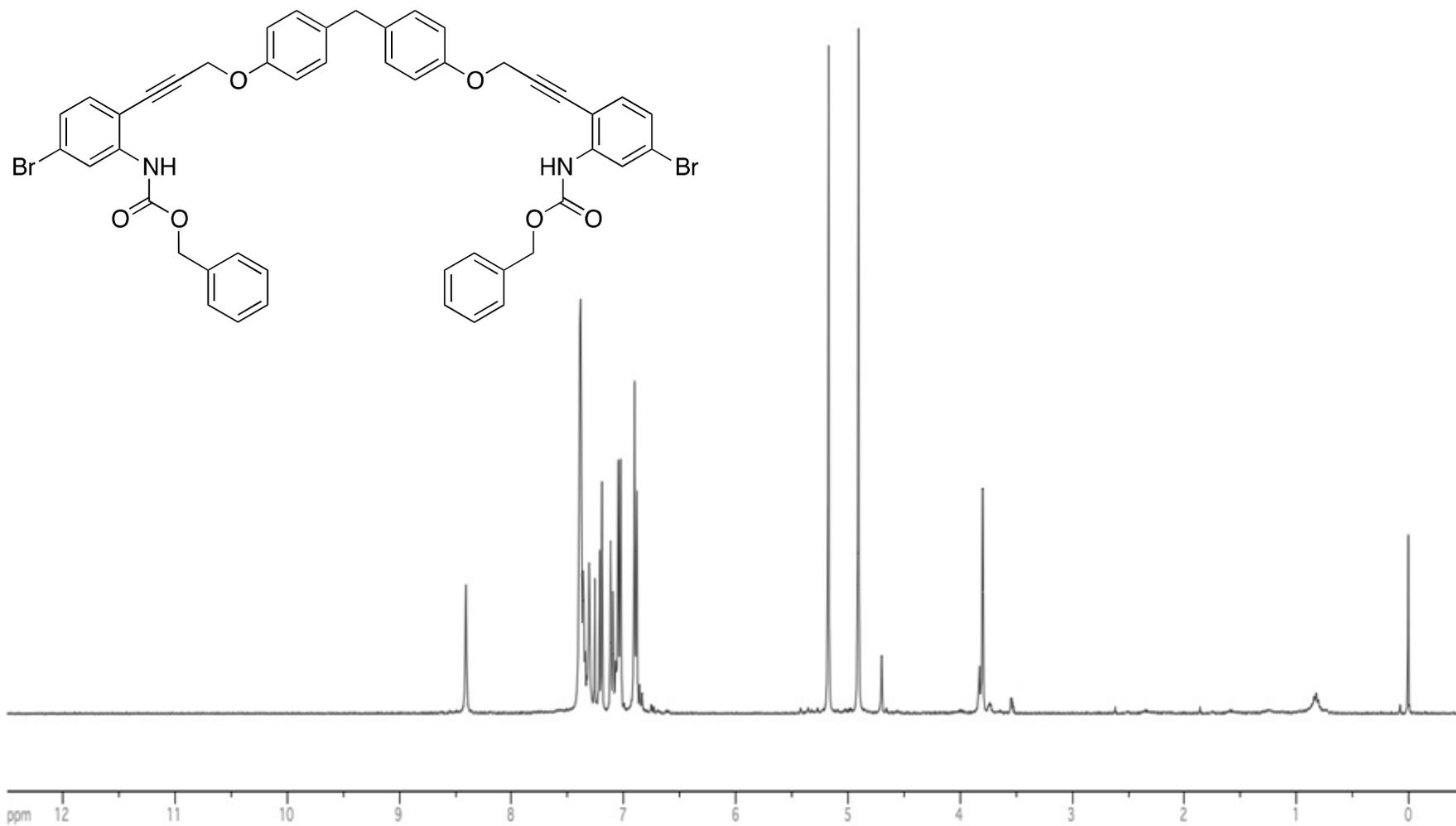




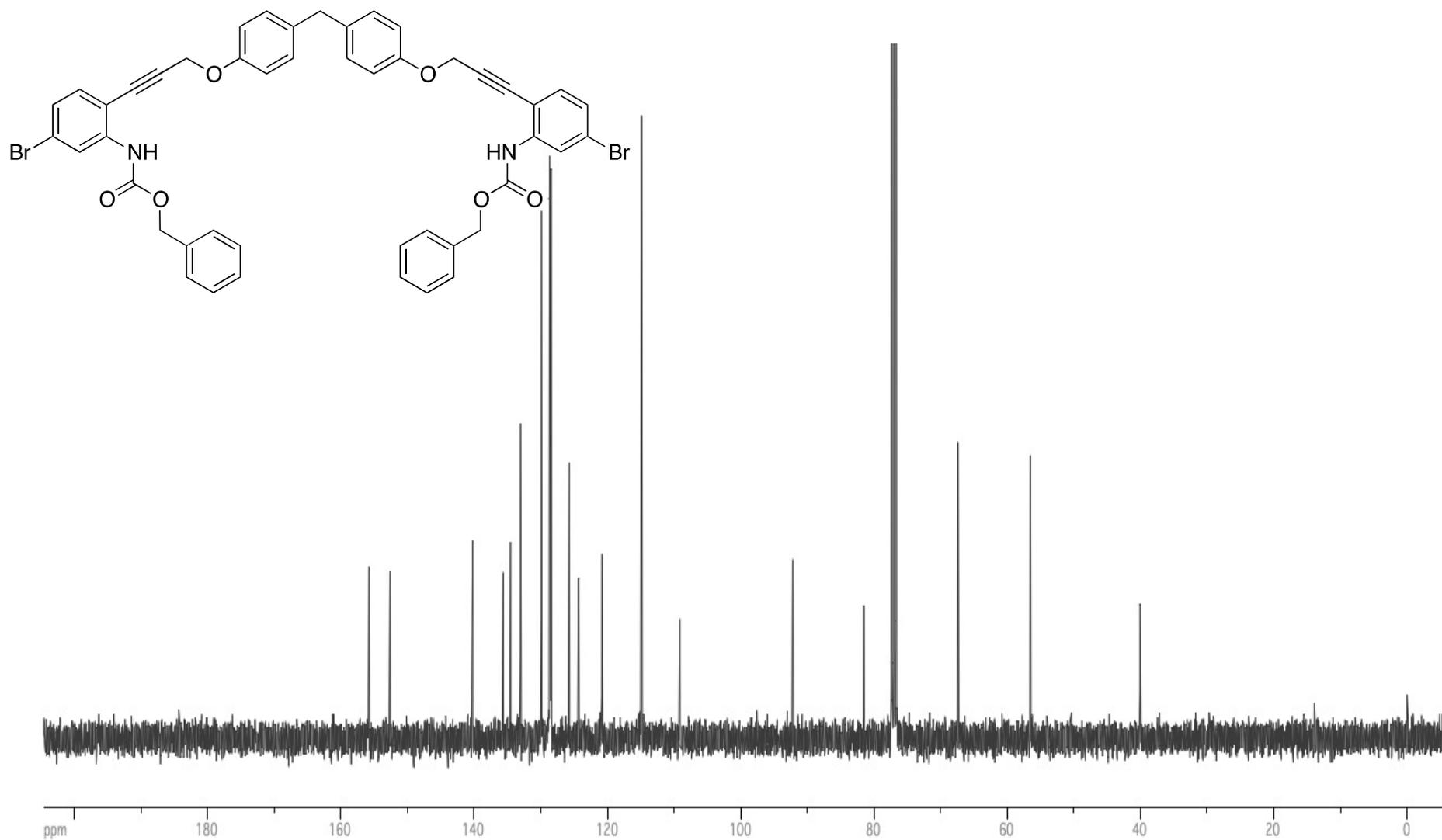
¹H NMR spectrum of compound **4f** in CDCl₃ 400 MHz



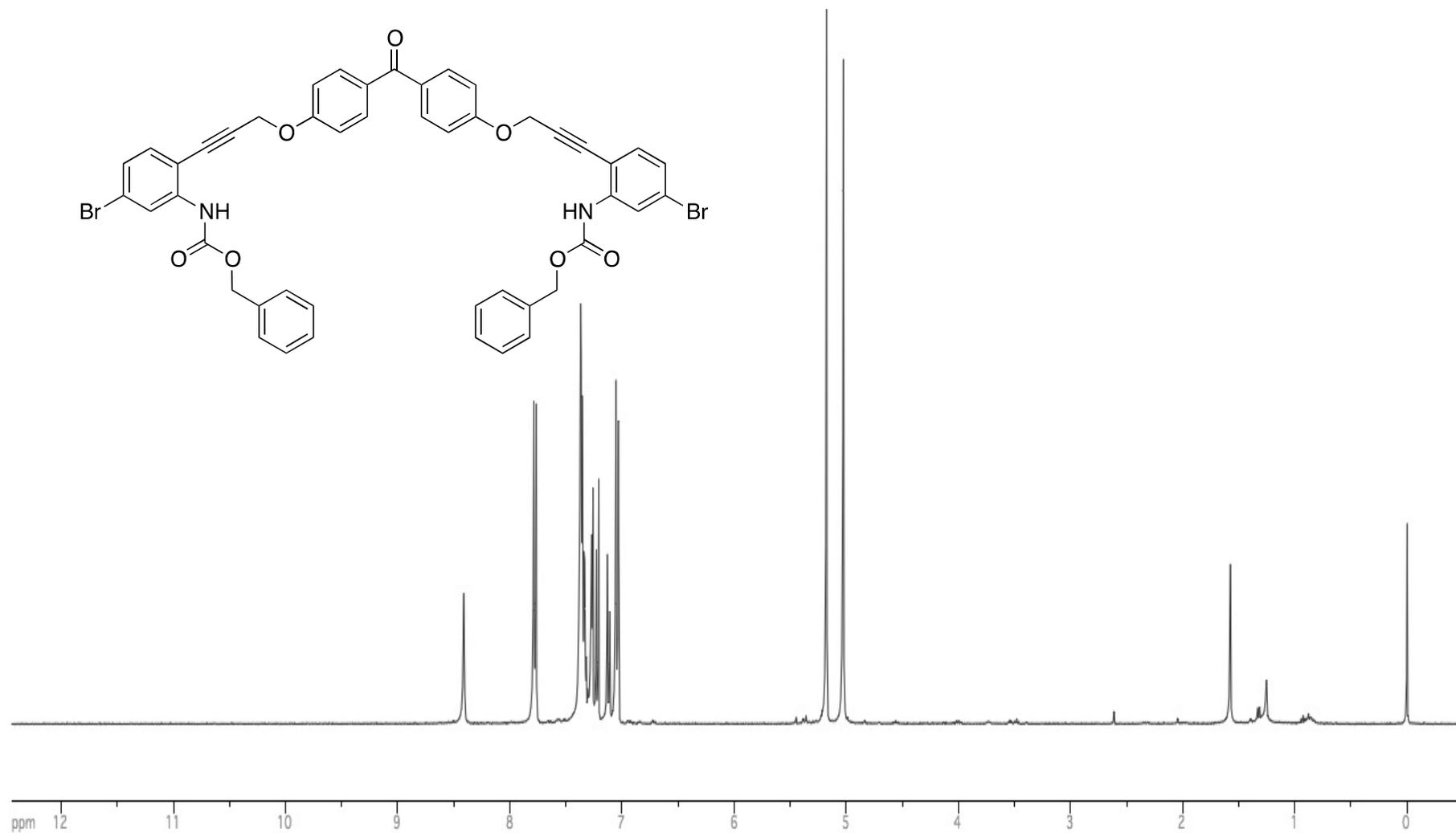
^{13}C NMR spectrum of compound **4f** in CDCl₃ 100 MHz



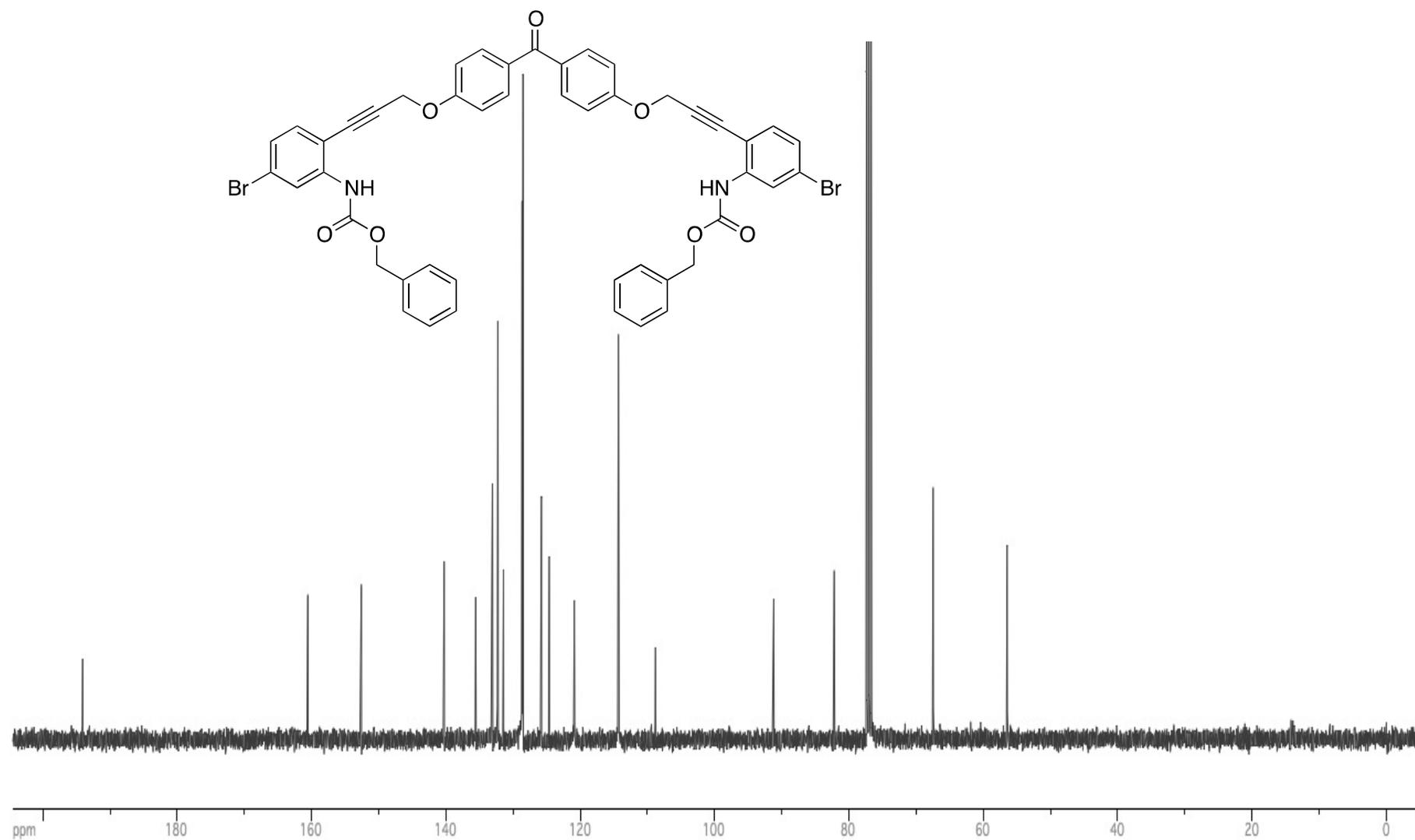
¹H NMR spectrum of compound **4g** in CDCl₃ 400 MHz

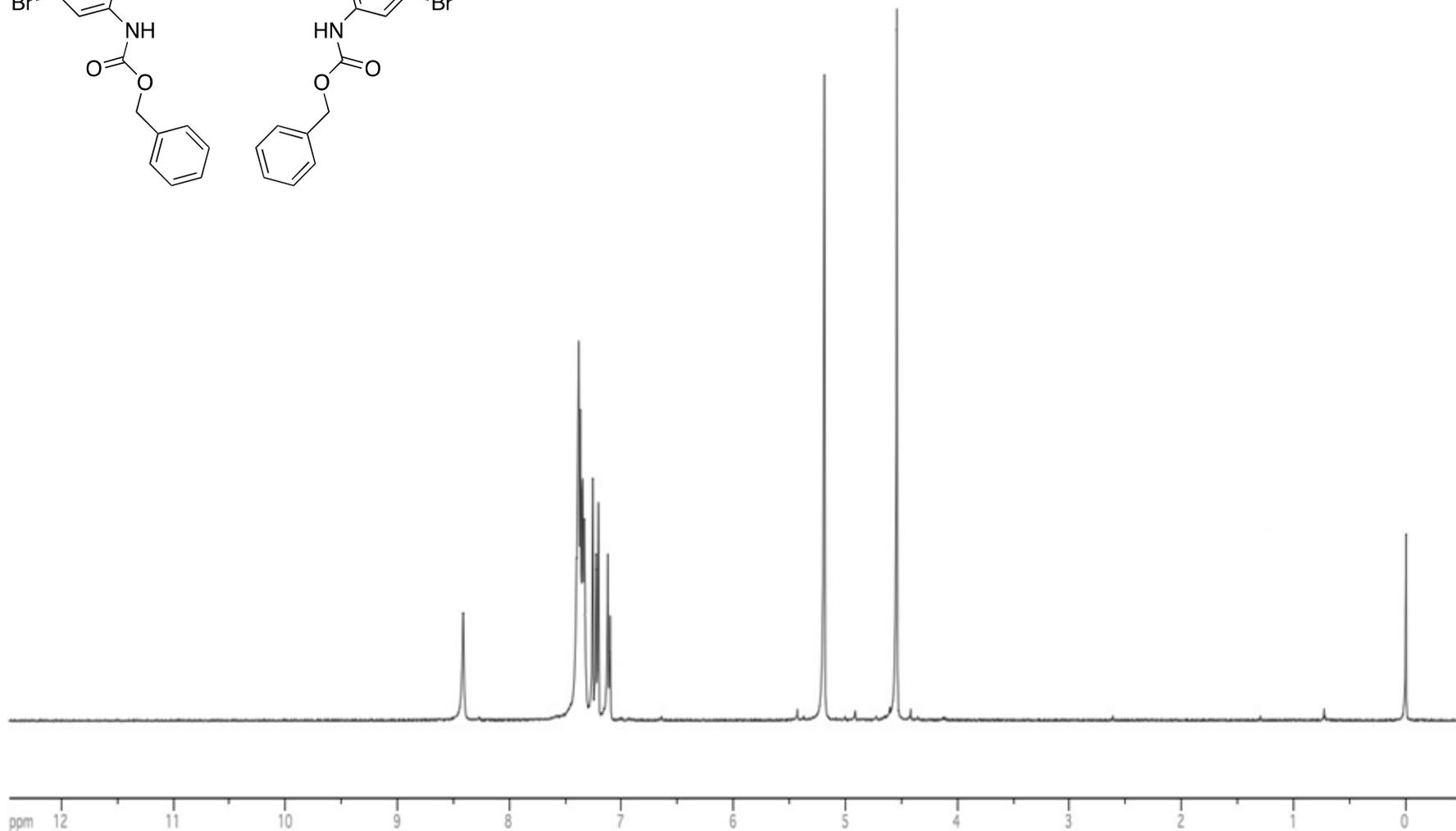
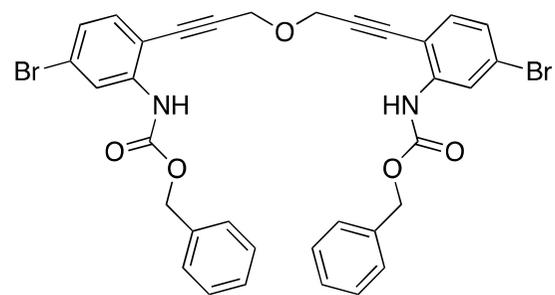


^{13}C NMR spectrum of compound **4g** in CDCl_3 100 MHz

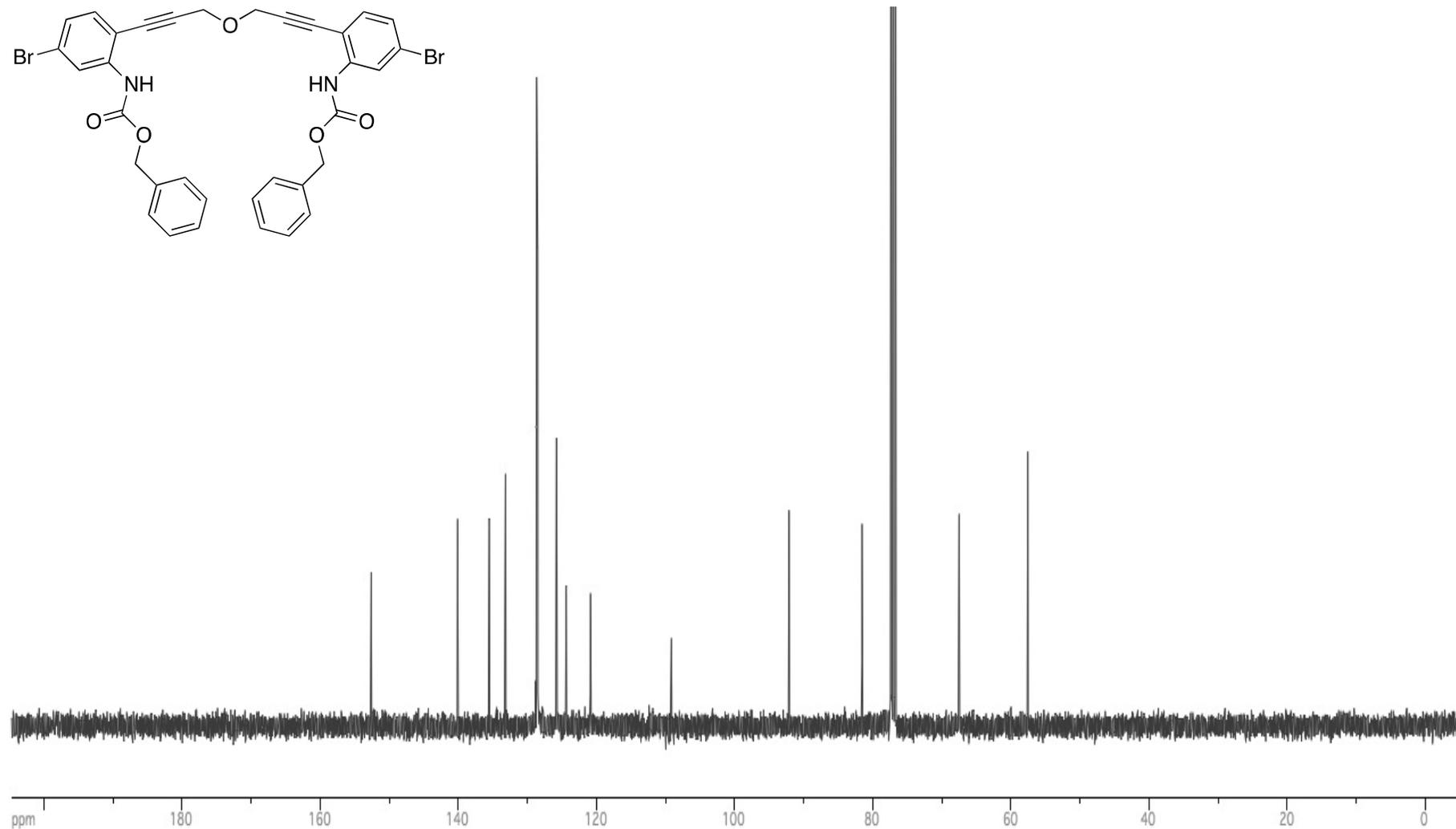
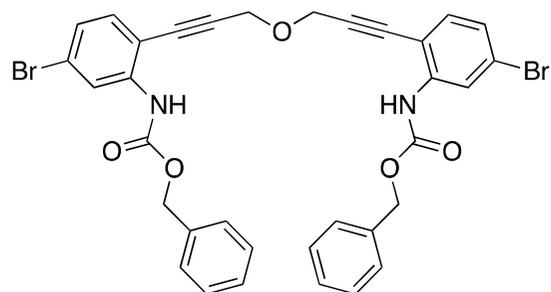


¹H NMR spectrum of compound **4h** in CDCl₃ 400 MHz

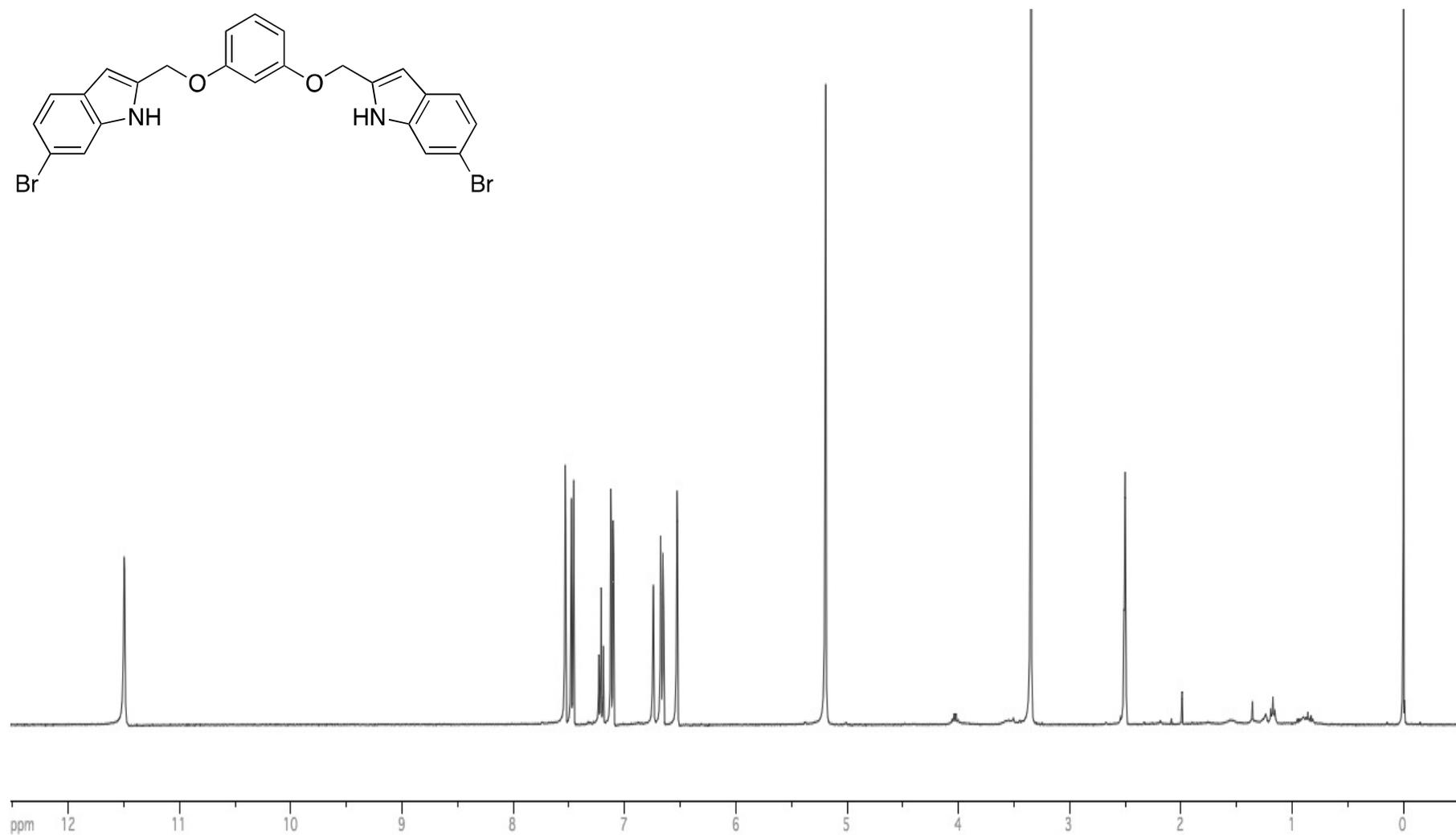
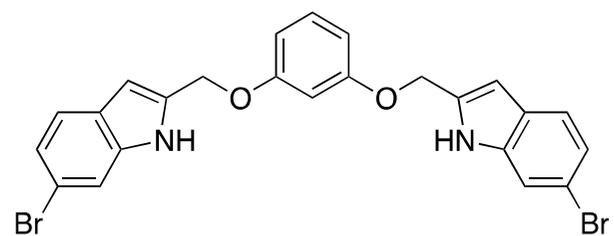




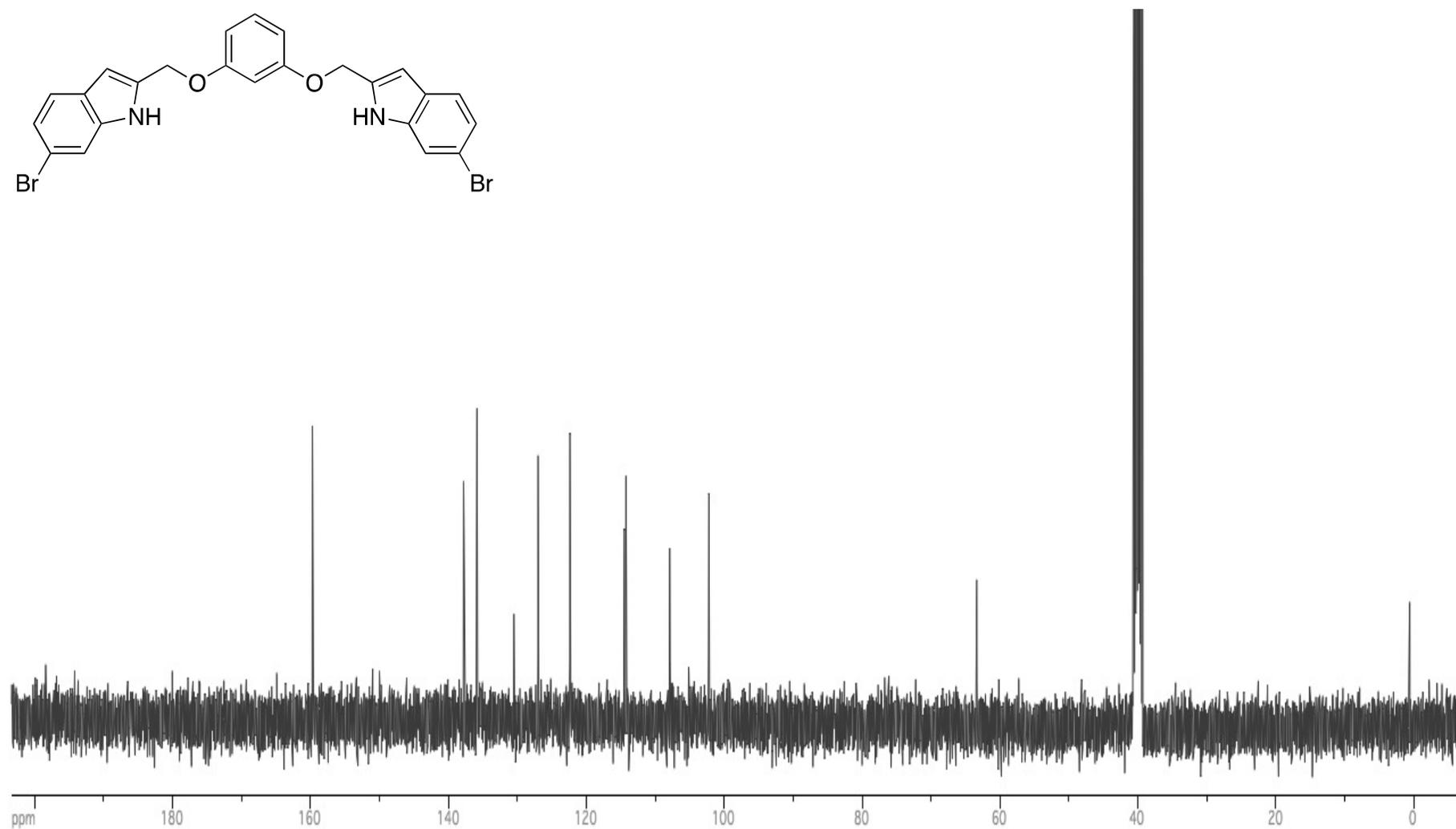
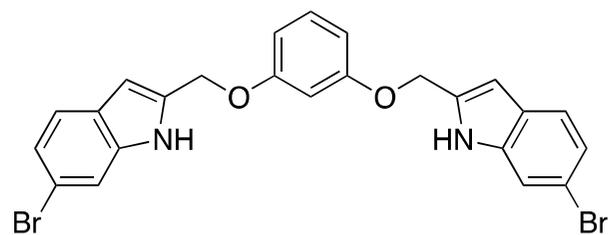
¹H NMR spectrum of compound **4i** in CDCl₃ 400 MHz



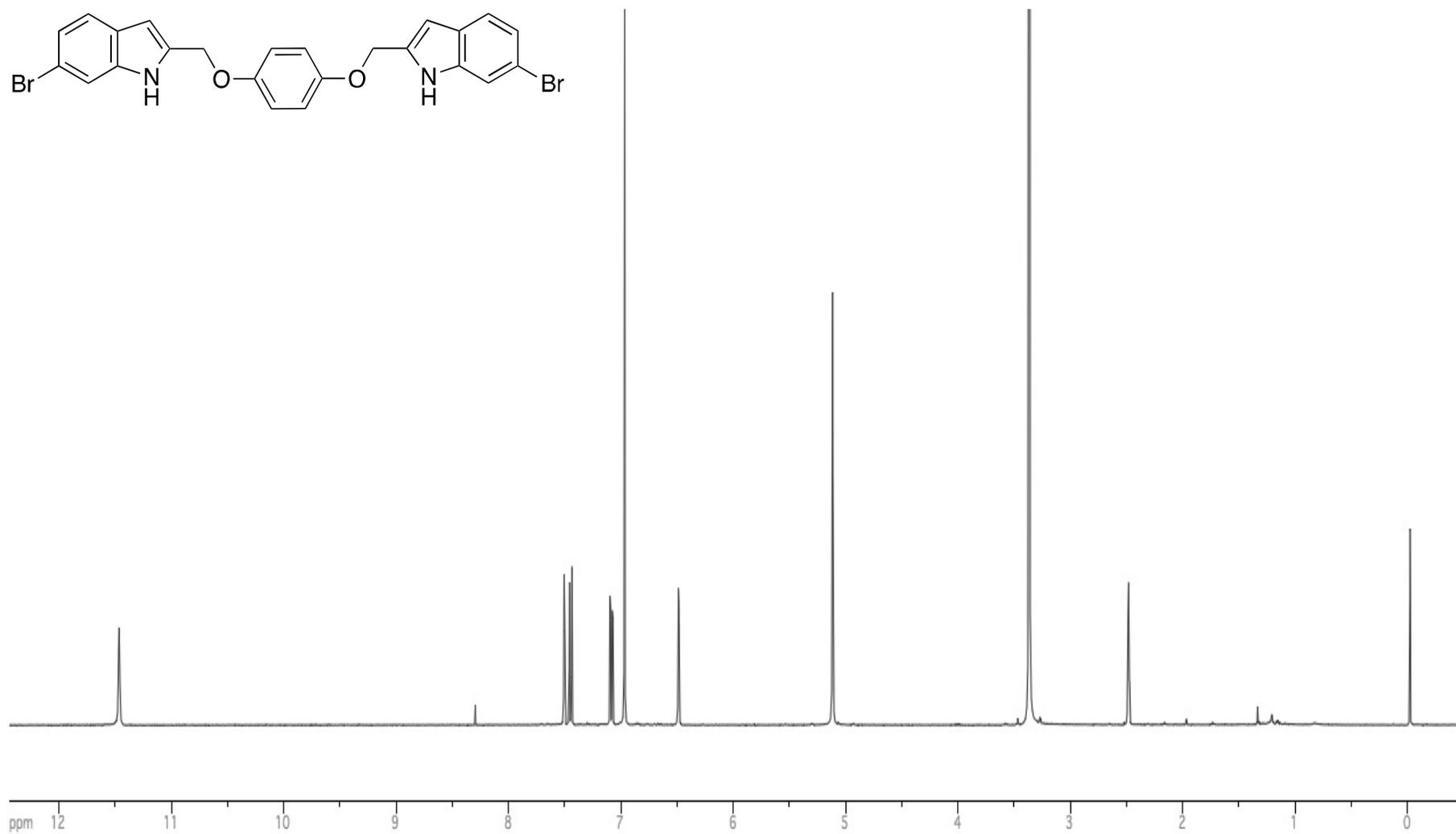
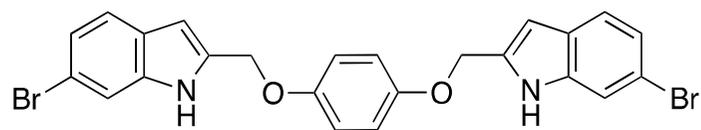
¹³C NMR spectrum of compound **4i** in CDCl₃ 100 MHz



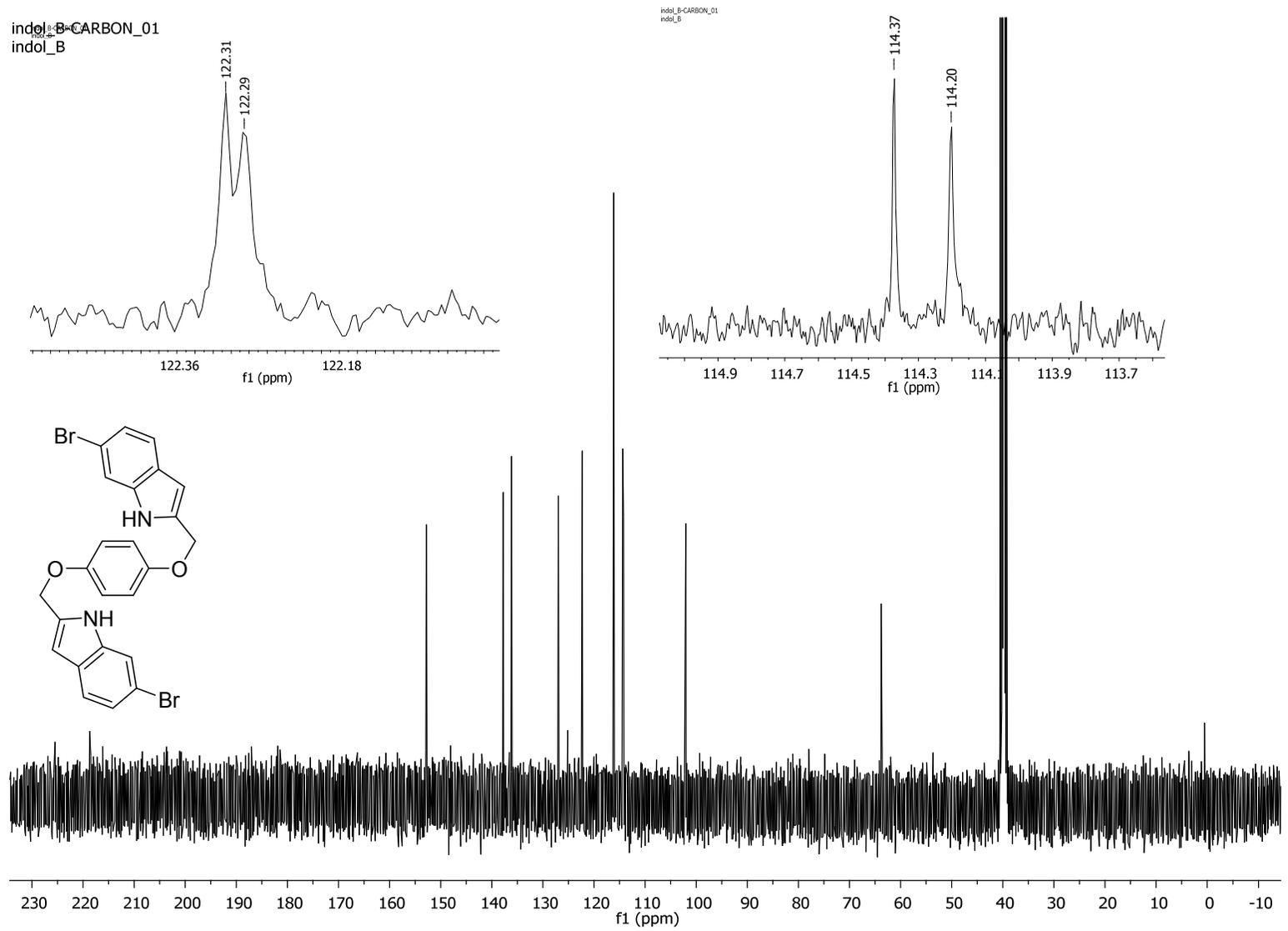
¹H NMR spectrum of compound **5d** in DMSO-*d*₆ 400 MHz



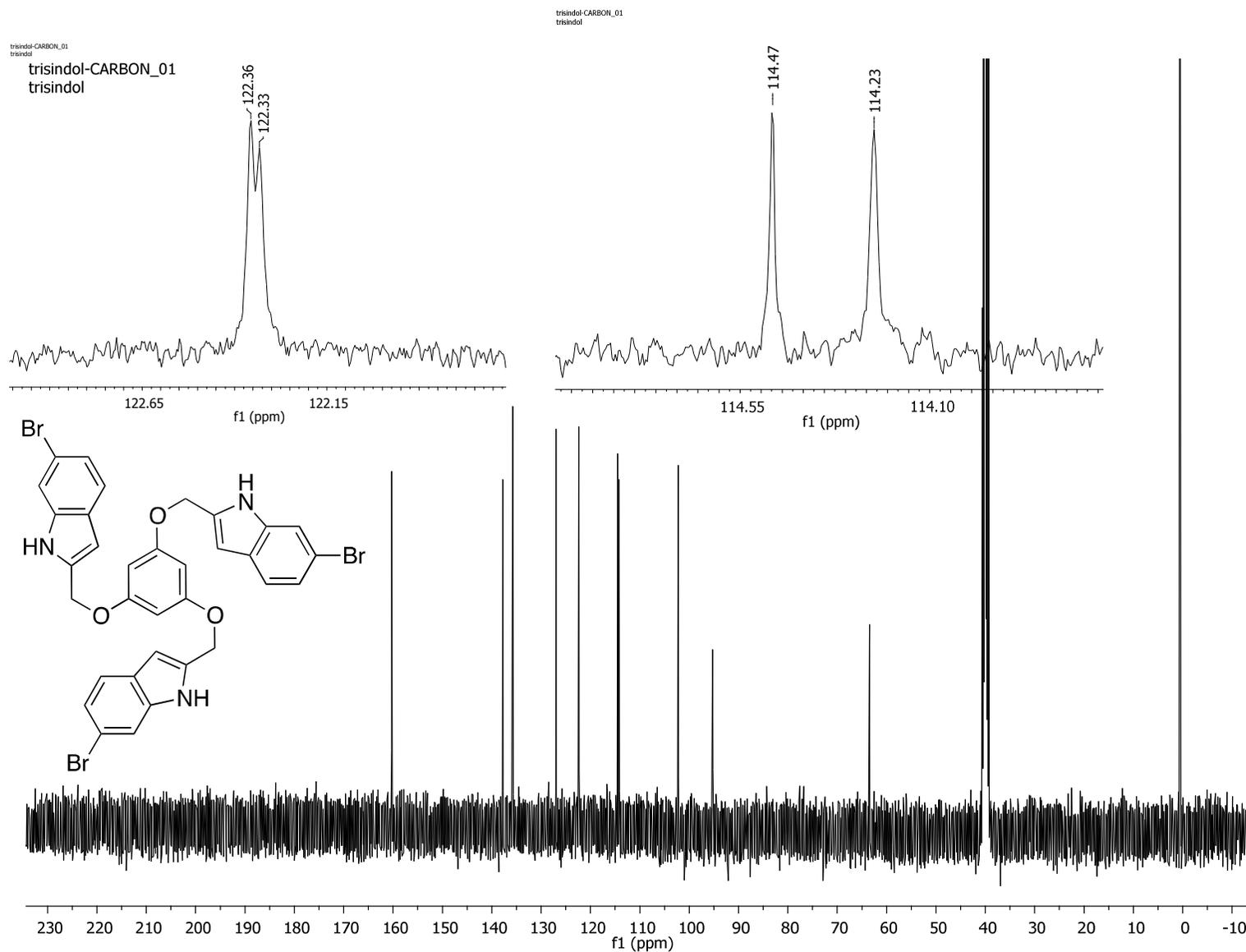
¹³C NMR spectrum of compound **5d** in DMSO-*d*₆ 100 MHz



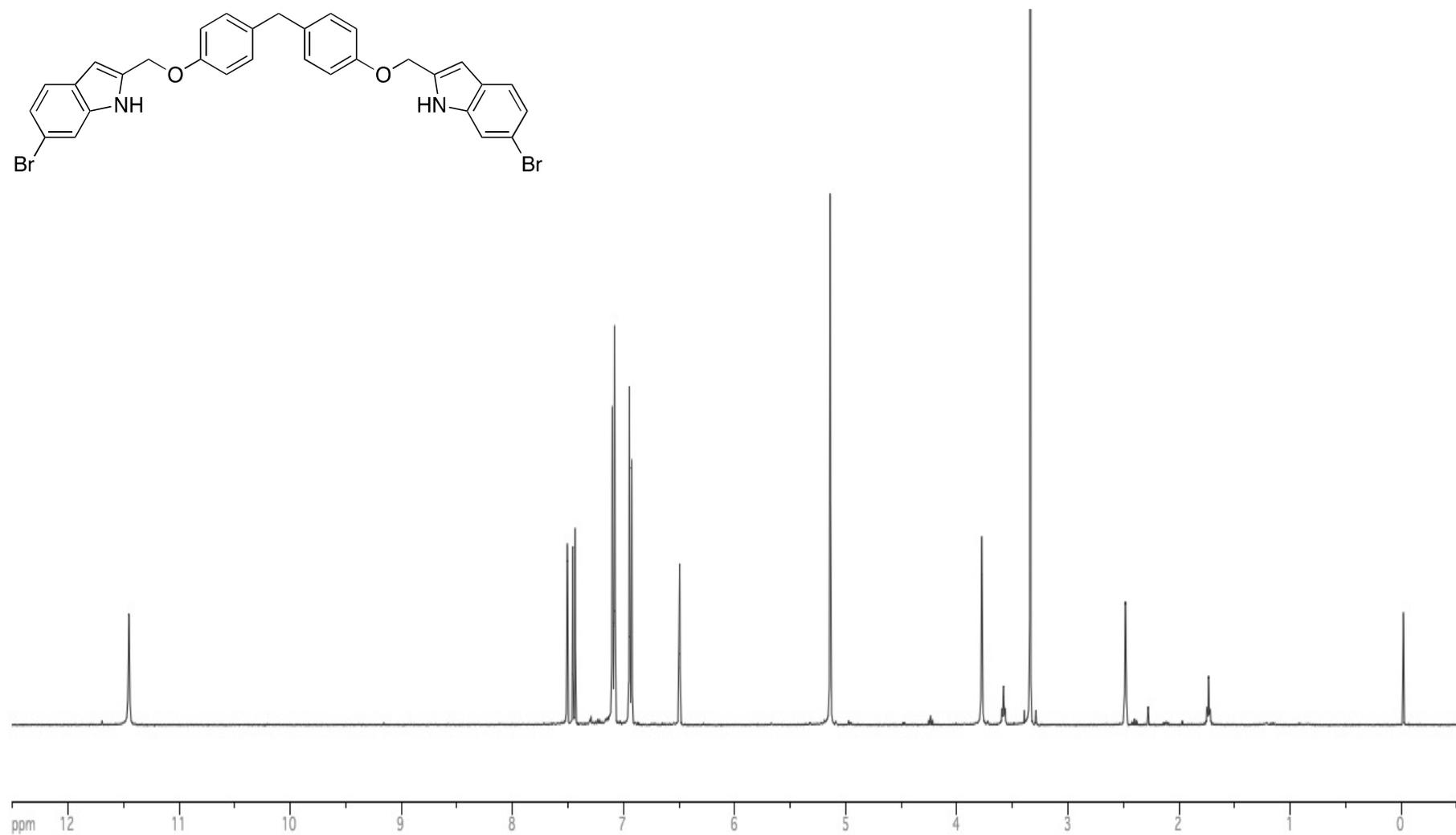
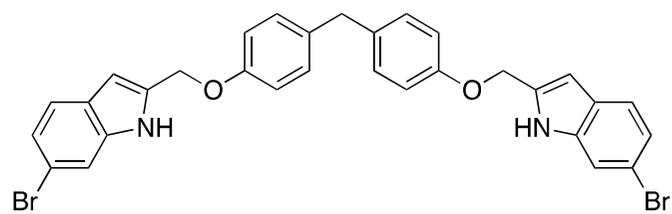
¹H NMR spectrum of compound **5e** in DMSO-*d*₆ 400 MHz



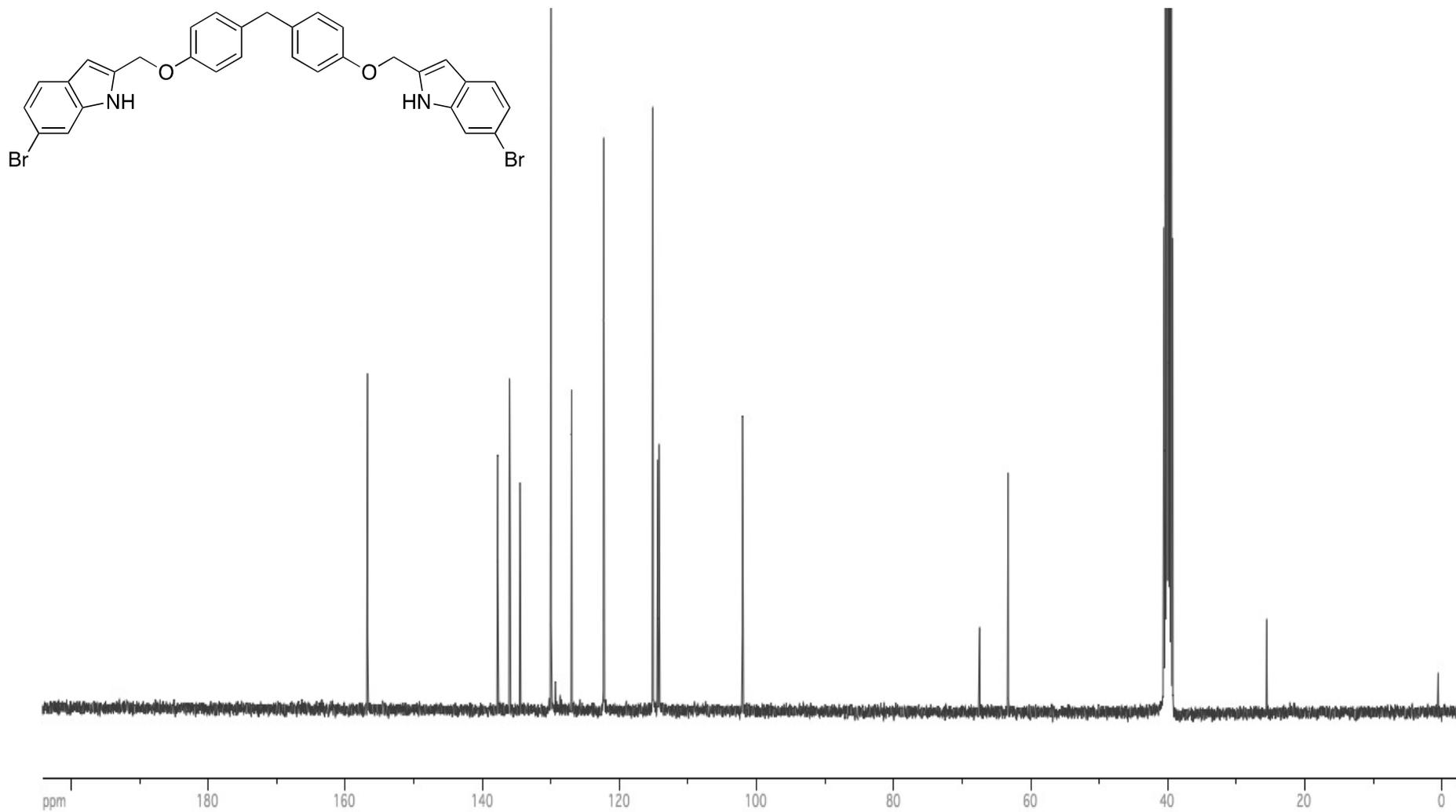
¹³C NMR spectrum of compound **5e** in DMSO-*d*₆ 100 MHz



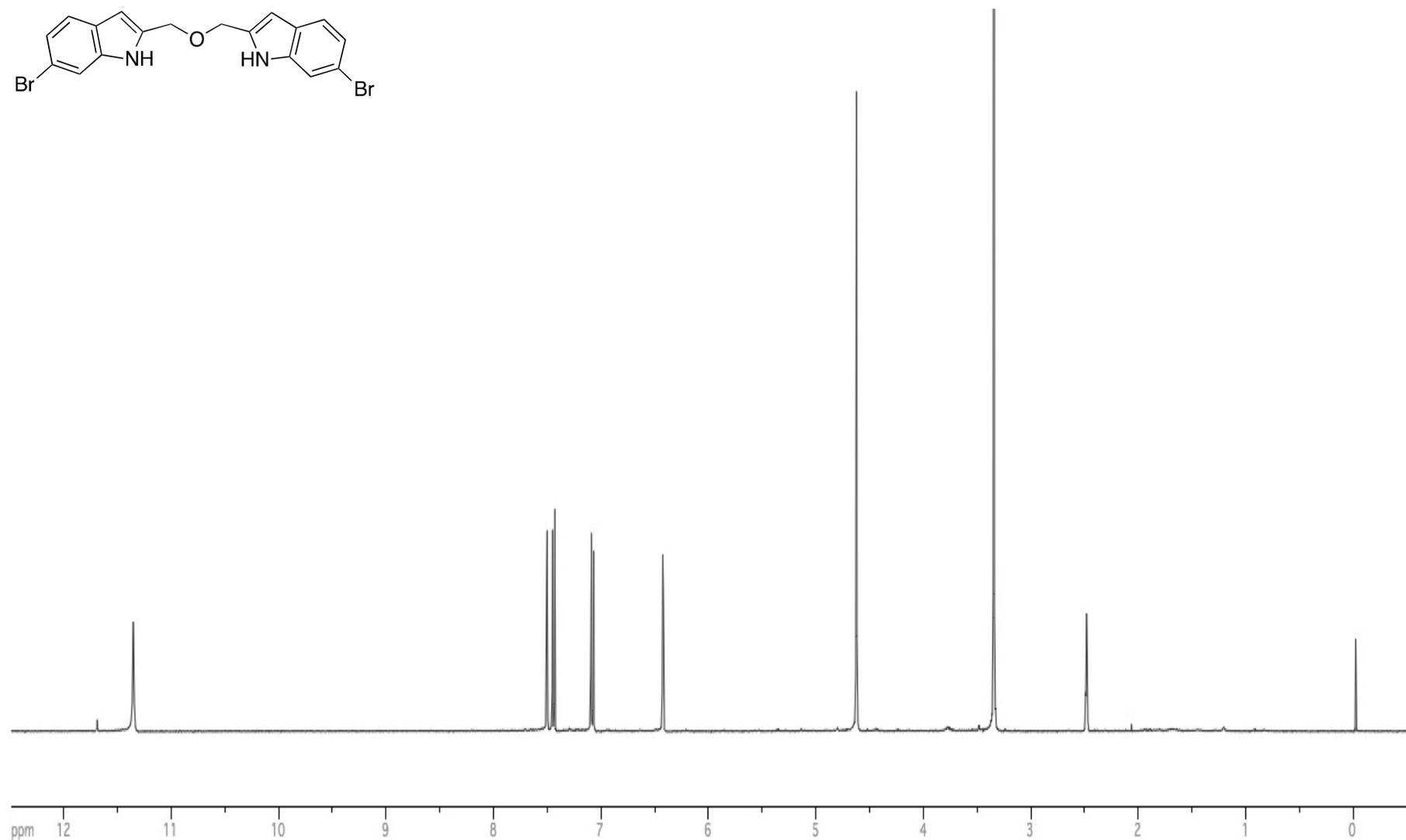
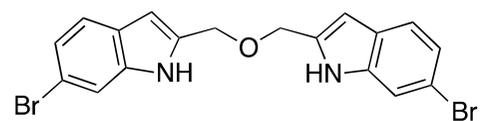
¹³C NMR spectrum of compound **5f** in DMSO-*d*₆ 100 MHz



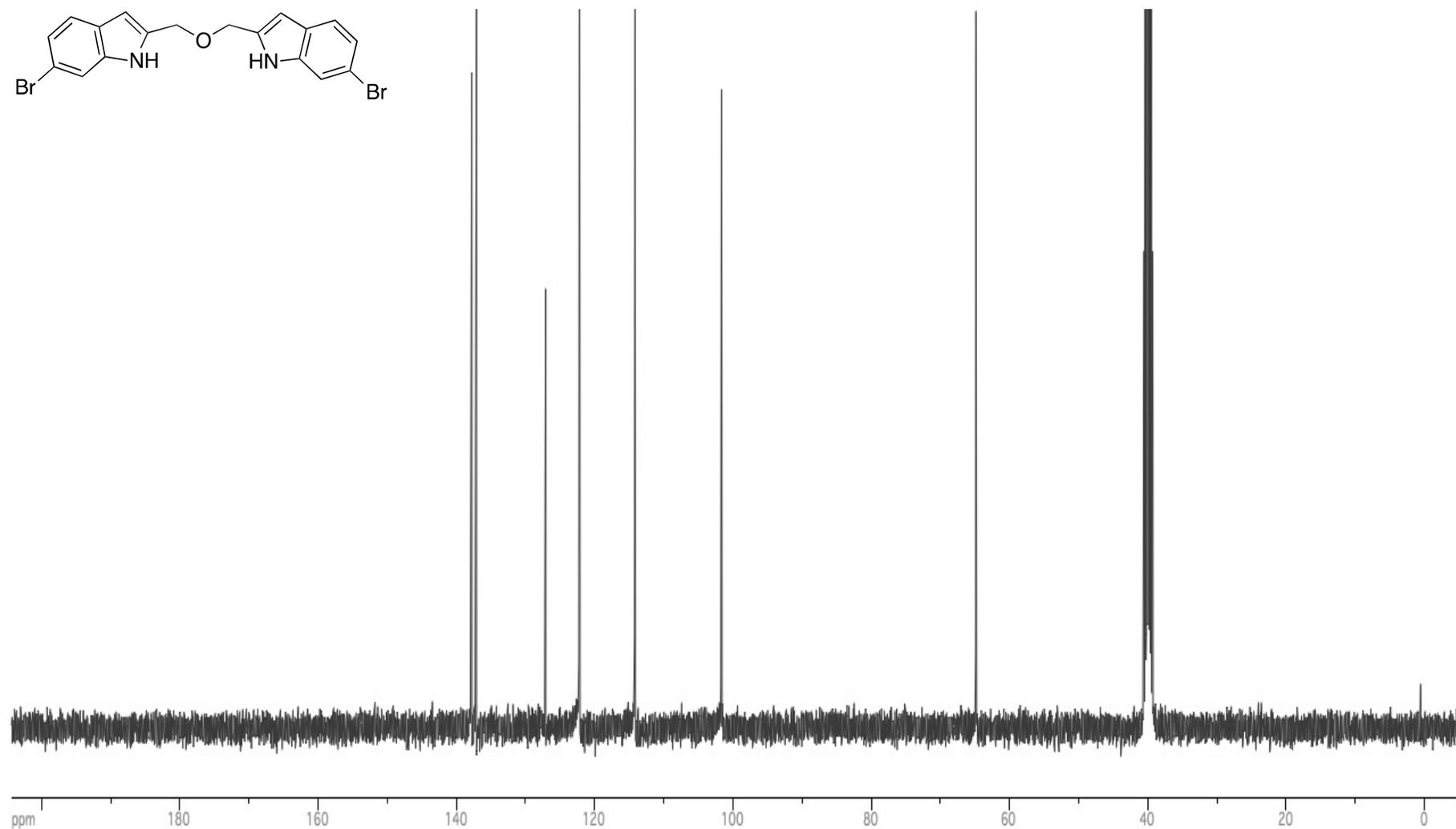
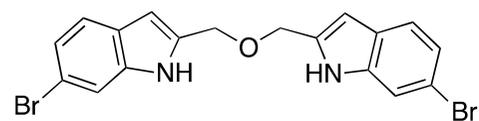
¹H NMR spectrum of compound **5g** in DMSO-*d*₆ 400 MHz



¹³C NMR spectrum of compound **5g** in DMSO-*d*₆ 100 MHz



¹H NMR spectrum of compound 5i in DMSO-*d*₆ 400 MHz



¹³C NMR spectrum of compound **5i** in DMSO-*d*₆ 100 MHz