Supplementary Material

Ultrasound-promoted rapid and efficient iodination of aromatic and heteroaromatic compounds in the presence of iodine and hydrogen peroxide in water

Irlon M. Ferreira,[1] Gleison A. Casagrande,[1] Lucas Pizzuti,[1] and Cristiano Raminelli[2]

[1]Universidade Federal da Grande Dourados, Faculdade de Ciências Exatas e Tecnologia, Rodovia Dourados-Itahum, Km 12, Dourados, MS 79.804-970, Brazil. Address correspondence to Lucas Pizzuti - e-mail: lucas.pizzuti@gmail.com

[2]Universidade Federal de São Paulo, Departamento de Ciências Exatas e da Terra, Rua Prof. Artur Riedel, 275, Diadema, SP 09972-270, Brazil. Address correspondence to Cristiano Raminelli - e-mail: raminelli@unifesp.br

Contents

1. Equipments and methods

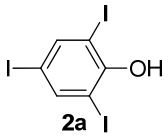
Reactions were carried out with a Microtip Probe connected to a Sonics Vibra-cell Ultrasonic Processor (500 W) operating at 20 KHz (100 W). ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA 300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) and on a Bruker DRX 500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometers in $CDCl_3$, DMSO-d_6 or CD_3OD solutions using TMS as internal standard. Mass spectra were produced at 70 eV using a Shimadzu MS-QP5050A mass spectrometer connected to a Shimadzu GC-17A gas chromatograph or a Varian MS-210 mass spectrometer connected to a Varian GC-431 gas chromatograph. Infrared spectra were recorded on a Bomem MB-100 FT-IR spectrometer using KBr pellets in the 4000-400 cm^{-1} region. Uncorrected melting point values were recorded on an Instrutherm DF-3600 apparatus.

2. Procedure for ultrasound-promoted iodination of aromatic and heteroaromatic compounds

To a suspension of the appropriate aromatic or heteroaromatic compound (**1a-q**) (2 mmol) and molecular iodine (2-4 mmol) in distilled water (10 mL) was added hydrogen peroxide 30% (m/v) (4-8 mmol). The mixture was sonicated and the progress of reaction was monitored by TLC. Afterwards, a saturated sodium thiosulfate aqueous solution (10 mL) was added to the mixture, which was extracted with ethyl acetate (3 × 20 mL). The organic phase was dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using an appropriate eluent, affording the desired product (**2a-q**).

3. Characterization data for compounds 2a-q

*3.1. 2,4,6-Triiodophenol (**2a**) (CAS number: 609-23-4)*

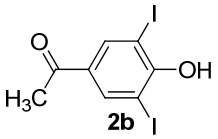


2a

Yield: 0.6980 g (74%); yellowish solid; mp 153-154°C (hexane as eluent) (lit.[1] 152-153°C); IR (KBr, cm^{-1}): 3439, 3053, 1434, 1369, 1136, 533; ^{1}H NMR 500 MHz ($CDCl_3$, ppm): 7.93 (s, 2H), 5.77 (s, 1H); ^{13}C NMR 125 MHz ($CDCl_3$, ppm): 153.7, 146.4, 83.3, 83.2; EI-MS (*m/z*, %): 472 (100.0), 218 (8.3), 127 (7.3).

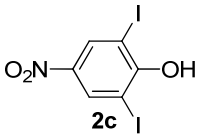
[1] Moorthy, J. N.; Senapati, K.; Kumar, S. *J. Org. Chem.* **2009**, *74*, 6287.

*3.2. 4-Hydroxy-3,5-diiodoacetophenone (**2b**) (CAS number: 7191-55-1)*



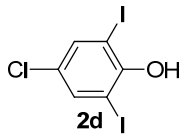
Yield: 0.7527 g (97%); off-white solid; mp 175-177°C (hexane as eluent) (lit.[2] 173°C); IR (KBr, cm^{-1}): 3141, 1666, 1525, 1355, 1233, 1121, 1070; ^{1}H NMR 400 MHz ($CDCl_3$, ppm): 8.28 (s, 2H), 6.15 (s, 1H), 2.53 (s, 3H); ^{13}C NMR 125 MHz (DMSO-d_6, ppm): 194.3, 159.4, 139.4, 132.5, 86.0, 26.3; EI-MS (*m/z*, %): 388 (72.8), 373 (100.0), 345 (9.3), 207 (6.3).

*3.3. 2,6-Diiodo-4-nitrophenol (**2c**) (CAS number: 305-85-1)*



Yield: 0.6860 g (88%); yellowish solid; mp 157-158°C (CH_2Cl_2 as eluent) (lit.[3] 155-156 °C); IR (KBr, cm^{-1}): 3375, 3077, 1504, 1399, 1317, 1230, 1116; ^{1}H NMR 300 MHz (CD_3OD, ppm): 8.57 (s, 2H); ^{13}C NMR 75 MHz (CD_3OD, ppm): 163.1, 143.0, 136.2, 83.1; EI-MS (*m/z*, %): 391 (100.0), 361 (32.0), 345 (8.1), 218 (16.9), 127 (18.6).

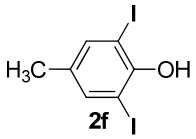
*3.4. 4-Chloro-2,6-diiodophenol (**2d**) (CAS number: 15459-50-4)*



Yield: 0.6840 g (90%); brownish solid; mp 104-106°C (hexane/CH_2Cl_2 (1:1) as eluent) (lit.[4] 107-108°C); IR (KBr, cm^{-1}): 3455, 3068, 1440, 1306, 1145, 857, 700; ^{1}H NMR 300 MHz ($CDCl_3$, ppm): 7.66 (s, 2H), 5.72 (s, 1H); ^{13}C NMR 75 MHz ($CDCl_3$, ppm): 152.8, 138.3, 126.8, 81.7; EI-MS (*m/z*, %): 380 (100.0), 382 (34.4), 253 (2.8), 255 (0.9), 126 (20.9), 127 (12.8), 128 (7.7).

[2] Baker, W.; Sansbury, H.; Simmonds, W. H. C. *J. Soc. Chem. Ind.* **1943**, *62*, 193.
[3] Sapountzis, I.; Dube, H.; Lewis, R.; Gommermann, N.; Knochel, P. *J. Org. Chem.* **2005**, *70*, 2445.
[4] Hunter, W. H.; Joyce, F. E. *J. Am. Chem. Soc.* **1917**, *39*, 2640.

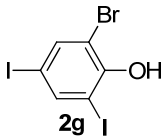
*3.5. 2,6-Diiodo-4-methylphenol (**2f**) (CAS number: 2432-18-0)*



2f

Yield: 0.2870 g (40%); off-white solid; mp 53-54°C (hexane as eluent) (lit.[5] 55-56°C); IR (KBr, cm^{-1}): 3448, 1542, 1456, 1148, 852; ^{1}H NMR 300 MHz ($CDCl_3$, ppm): 7.49 (d, J = 0.6 Hz, 2H), 5.57 (s, 1H), 2.22 (s, 3H); ^{13}C NMR 75 MHz ($CDCl_3$, ppm): 151.4, 139.6, 133.9, 81.9, 19.4; EI-MS (*m/z*, %): 360 (100.0), 233 (10.3), 105 (6.7).

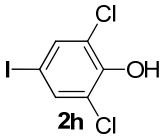
*3.6. 2-Bromo-4,6-diiodophenol (**2g**) (CAS number: 89466-01-3)*



2g

Yield: 0.8160 g (96%); off-white solid; mp 125-127°C (hexane/CH_2Cl_2 (1:1) as eluent) (lit.[6] 128 °C); IR (KBr, cm^{-1}): 3446, 3060, 1441, 1372, 1231, 1143, 857; ^{1}H NMR 300 MHz (DMSO-d_6, ppm): 10.07 (s, 1H), 7.98 (d, J = 2.0 Hz, 1H), 7.83 (d, J = 2.0 Hz, 1H), 5.74 (s, 1H); ^{13}C NMR 75 MHz (DMSO-d_6, ppm): 153.2, 145.1, 140.1, 111.5, 90.0, 83.8; EI-MS (*m/z*, %): 426 (100.0), 424 (98.0), 268 (6.5), 297 (12.8), 170 (19.1), 127 (9.9).

*3.7. 2,6-Dichloro-4-iodophenol (**2h**) (CAS number: 34074-22-1)*

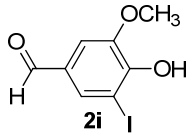


2h

Yield: 0.5600 g (97%); off-white solid; mp 90-91°C (hexane/AcOEt (1:1) as eluent) (lit.[7] 91-92°C); IR (KBr, cm^{-1}): 3378, 3065, 1468, 1457, 1384, 1236, 855; ^{1}H NMR 300 MHz (DMSO-d_6, ppm): 10.42 (s, 1H), 7.67 (s, 2H); ^{13}C NMR 75 MHz (DMSO-d_6, ppm): 149.8, 136.7, 124.0, 81.4; EI-MS (*m/z*, %): 288 (100.0), 290 (63.1), 292 (10.7), 161 (17.9), 163 (11.6), 165 (2.1).

[5] Venkateshwarlu, G. *Helv. Chim. Acta* **2010**, *93*, 345.
[6] Brenans, P.; Yeu, K. *Compt. Rend.* **1930**, *190*, 1560.
[7] Brazier, S. A.; McCombie, H. *J. Chem. Soc. Perkin Trans.* **1912**, *101*, 968.

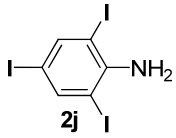
*3.8. 4-Hydroxy-3-iodo-5-methoxybenzaldehyde (**2i**) (CAS number: 438-36-8)*



2i

Yield: 0.5560 g (>99%); yellowish solid; mp 179-180°C (CH_2Cl_2 as eluent) (lit.[8] 179-181°C); IR (KBr, cm^{-1}): 3065, 1468, 1457, 1384, 1236, 855; ^{1}H NMR 300 MHz (DMSO-d_6, ppm): 9.74 (s, 1H), 7.87 (d, J = 1.8 Hz, 1H), 7.40 (d, J = 1.5 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR 75 MHz (DMSO-d_6, ppm): 189.9, 152.4, 147.2, 134.6, 129.7, 110.0, 84.1, 56.1; EI-MS (*m/z*, %): 278 (100.0), 235 (6.6), 135 (9.2).

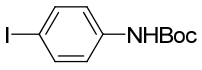
*3.9. 2,4,6-Triiodoaniline (**2j**) (CAS number: 24154-37-8)*



2j

A 10% $NaHCO_3$ solution (20 mL) was added to the mixture before extraction; yield: 0.8578 g (91%); brownish solid; mp 175-176°C (hexane as eluent) (lit.[1] 177-179°C); IR (KBr, cm^{-1}): 3395, 3294, 1605, 1436, 860, 536; ^{1}H NMR 500 MHz (DMSO-d_6, ppm): 7.86 (s, 2H), 5.23 (s, 2H); ^{13}C NMR 125 MHz (DMSO-d_6, ppm): 146.9, 145.3, 82.8, 78.6; EI-MS (*m/z*, %): 471 (100.0), 344 (12.5), 217 (7.3).

*3.10. tert-Butyl 4-iodophenylcarbamate (**2l**) (CAS number: 159217-89-7)*

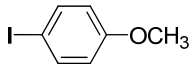


2l

Yield: 0.5805 g (91%); off-white solid; mp 134-136°C (hexane/AcOEt (10:1) as eluent) (lit.[9] 144-147°C); IR (KBr, cm^{-1}): 3385, 1704, 1586, 1513, 820, 600; ^{1}H NMR 300 MHz ($CDCl_3$, ppm): 7.56 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 9.3 Hz, 2H), 6.48 (s, 1H), 1.51 (s, 9H); ^{13}C NMR 75 MHz ($CDCl_3$, ppm): 152.4, 138.2, 137.8, 120.4, 85.7, 80.9, 28.3; EI-MS (*m/z*, %): 319 (5.9), 219 (100.0), 127 (14.4), 263 (70.0).

[8] Raiford, L. C.; Wells, E. H. *J. Am. Chem. Soc.* **1935**, *57*, 2500.
[9] Yokoyama, A.; Maruyama, T.; Tagami, K.; Masu, H.; Katagiri, K.; Azumaya, I.; Yokozawa, T. *Org. Lett*. **2008**, *10*, 3207.

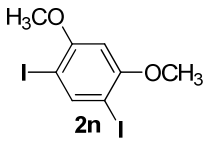
*3.11. 1-Iodo-4-methoxybenzene (**2m**) (CAS number: 696-62-8)*



2m

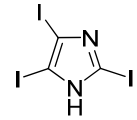
Yield: 0.4680 g (>99%); off-white solid; mp 41-42°C (CH_2Cl_2 as eleuent) (lit.[10] 43-45°C); IR (KBr, cm^{-1}): 1585, 1406, 1287, 1175, 806, 584; ^1H NMR 400 MHz ($CDCl_3$, ppm): 7.56 (d, J = 9.0 Hz, 2H), 6.68 (d, J = 9.0 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR 75 MHz ($CDCl_3$, ppm): 159.5, 138.2, 116.4, 82.6, 55.3; EI-MS (*m/z*, %): 235 (100.0), 63 (11.7).

*3.12. 1,5-Diiodo-2,4-dimethoxybenzene (**2n**) (CAS number: 51560-17-9)*



Yield: 0.7800 g (>99%); brownish solid; mp 198-199°C (hexane as eluent) (lit.[11] 200-201°C); IR (KBr, cm^{-1}): 1568, 1460, 1359, 1036, 1015, 654; ^1H NMR 300 MHz ($CDCl_3$, ppm): 8.04 (s, 1H), 6.37 (s, 1H), 3.89 (s, 6H); ^{13}C NMR 75 MHz ($CDCl_3$, ppm): 159.6, 146.8, 95.8, 75.5, 56.5; EI-MS (*m/z*, %): 390 (100.0).

*3.13. 2,4,5-Triiodo-1H-imidazole (**2o**) (CAS number: 1746-25-4)*

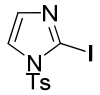


2o

Yield: 0.8470 g (95%); off-white solid; mp 180-183°C (CH_2Cl_2 as eluent) (lit.[12] 180-183°C); IR (KBr, cm^{-1}): 3421, 1804, 1508, 974, 656; ^1H NMR 300 MHz (DMSO-d_6, ppm): 13.33 (s, 1H); ^{13}C NMR 75 MHz (DMSO-d_6, ppm): 89.5; EI-MS (*m/z*, %): 446 (100.0), 319 (37.9), 127 (20.8), 129 (7.9).

[10] Pavlinac, J.; Zupan, M.; Stavber, S. *J. Org. Chem.* **2006**, *71*, 1027.
[11] Kajigaeshi, S.; Kakinami, T.; Moriwaki, M.; Watanabe, M.; Fujisaki, S.; Okamoto, T. *Chem. Lett.* **1988**, 795.
[12] Iddon, B.; Lim, B. L. J. *J. Chem Soc. Perkin Trans. I* **1983**, *1*, 735.

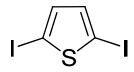
*3.14. 2-Iodo-1-tosyl-imidazole (**2p**) (CAS number: 956704-70-4)*



2p

Yield: 0.4870 g (70%); off-white solid; mp 140-142°C (hexane/AcOEt (50:1) as eluent) (lit.[13] 140-141°C); IR (KBr, cm^{-1}): 3439, 1383, 1078, 901, 810, 690, 581; ^{1}H NMR 500 MHz ($CDCl_3$, ppm): 7.91 (d, *J* = 6.5 Hz, 2H), 7.67 (d, *J* = 2.0 Hz, 1H), 7.38 (d, *J* = 6.5 Hz, 2H), 7.06 (d, *J* = 2.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR 125 MHz ($CDCl_3$, ppm): 146.6, 133.8, 132.9, 130.2, 128.4, 123.3, 84.3, 21.8; EI-MS (*m/z*, %): 91 (100.0), 349 (88.6), 155 (98.1), 65 (32.0).

*3.15. 2,5-Diiodothiophene (**2q**) (CAS number: 625-88-7)*



2q

To a mixture of thiophene (**1q**) (2 mmol) in distilled water (10 mL) under sonication were added hydrogen peroxide 30% (m/v) (8 mmol) and, afterwards, iodine (4 mmol) in several portions; yield: 0.5712 g (85%); brownish solid; mp 31-32°C (hexane as eluent) (lit.[14] 38°C); IR (KBr, cm^{-1}): 3077, 1520, 948, 784, 728, 454; ^{1}H NMR 300 MHz (DMSO-d_6, ppm): 7.06 (s, 2H); ^{13}C NMR 75 MHz (DMSO-d_6, ppm): 138.9, 79.4; EI-MS (*m/z*, %): 336 (100.0), 127 (11.5), 82 (28.6).

[13] Murata, T.; Morita, Y.; Yakiyama, Y.; Nishimura, Y.; Ise, T.; Shiomi, D.; Sato, K.; Takui, T.; Nakasuji, K. *Chem. Commun.* **2007**, 4009.
[14] Vaitiekunas, A.; Nord, F. F. *J. Am. Chem. Soc.* **1953**, *75*, 1764.

4. Copies of ^{1}H and ^{13}C NMR spectra of compounds 2a-q

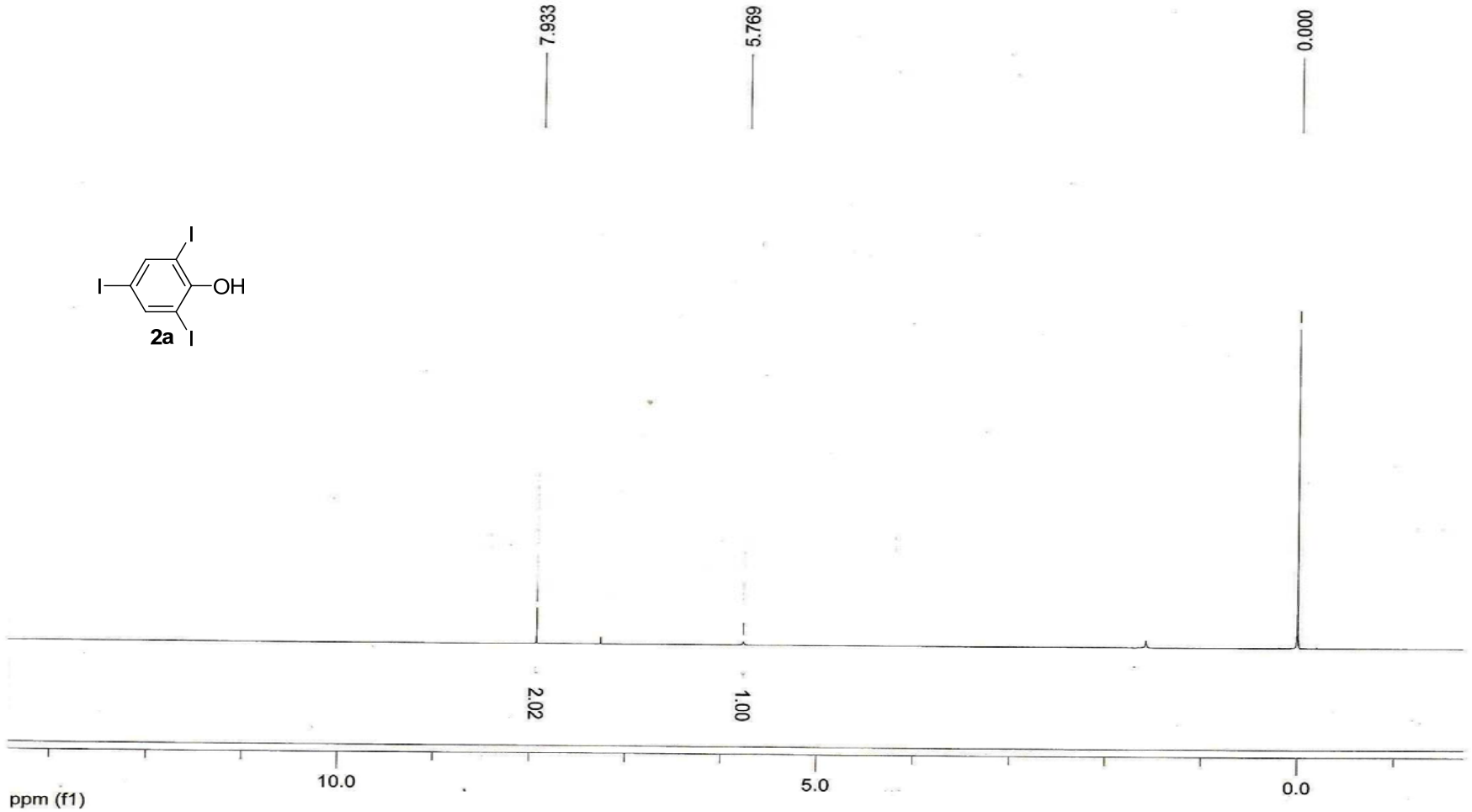


Figure 1: ^{1}H NMR spectrum in $CDCl_3$ of compound **2a**.

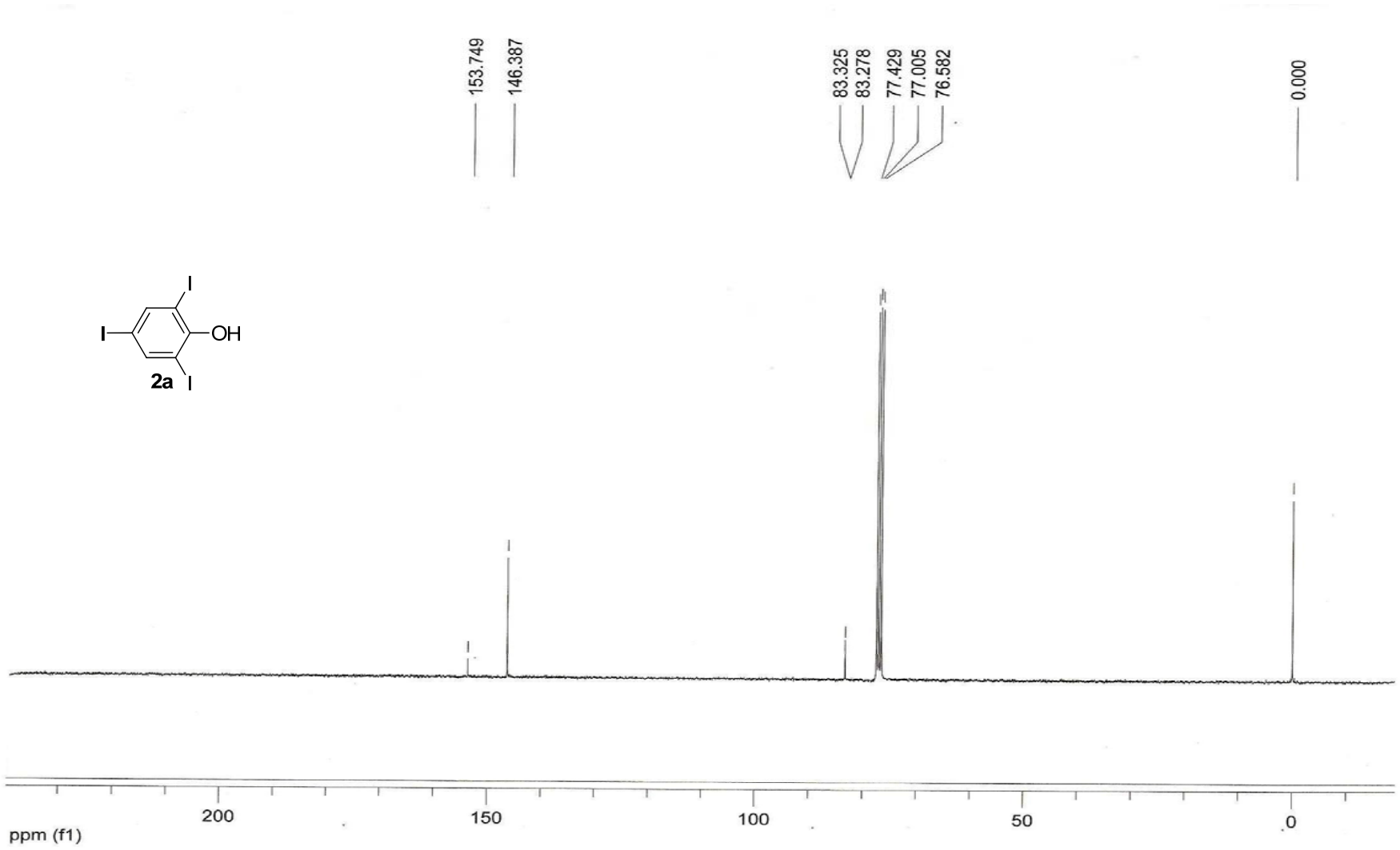


Figure 2: ^{13}C NMR spectrum in $CDCl_3$ of compound **2a**.

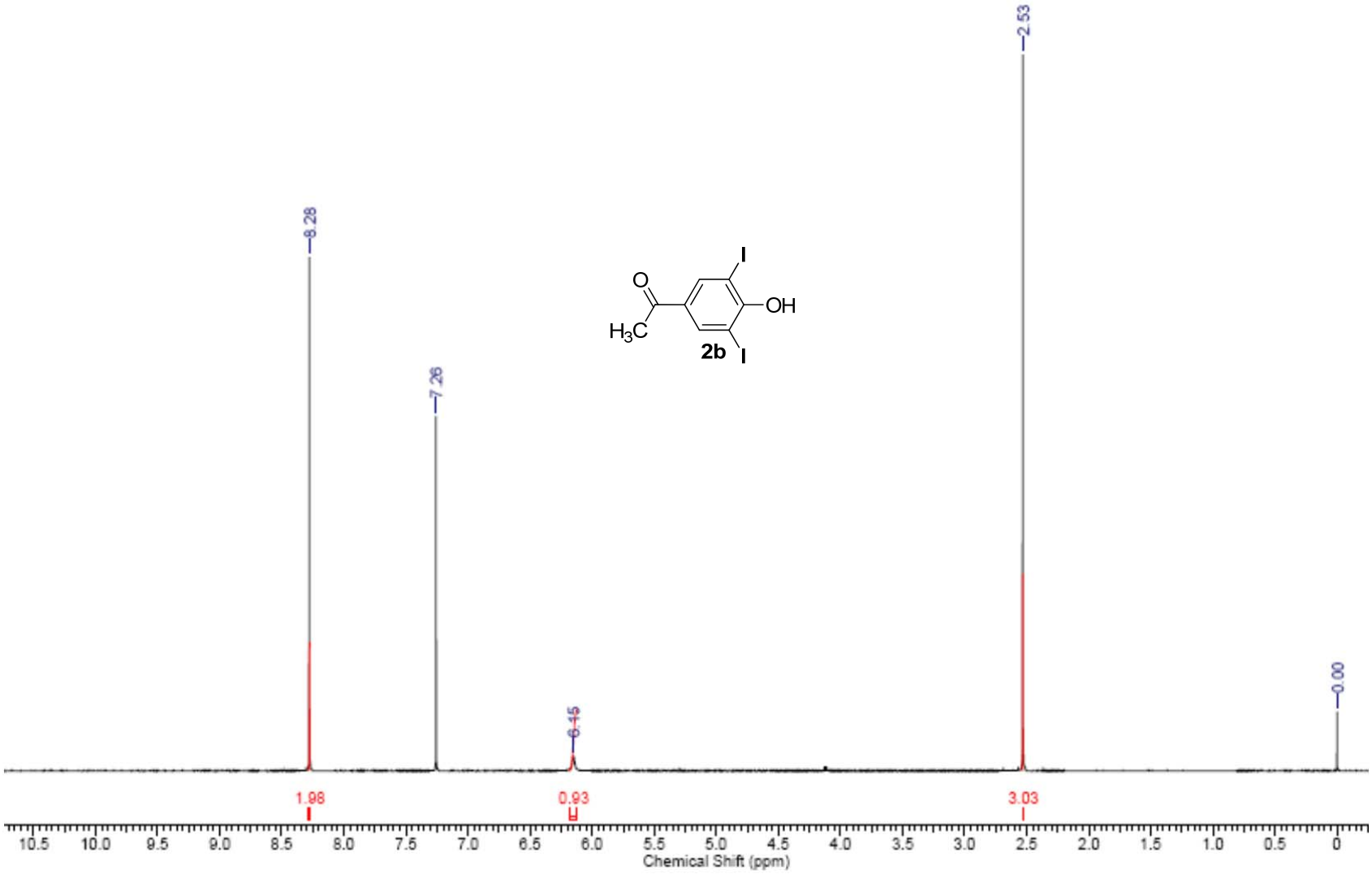


Figure 3: ^{1}H NMR spectrum in $CDCl_3$ of compound **2b**.

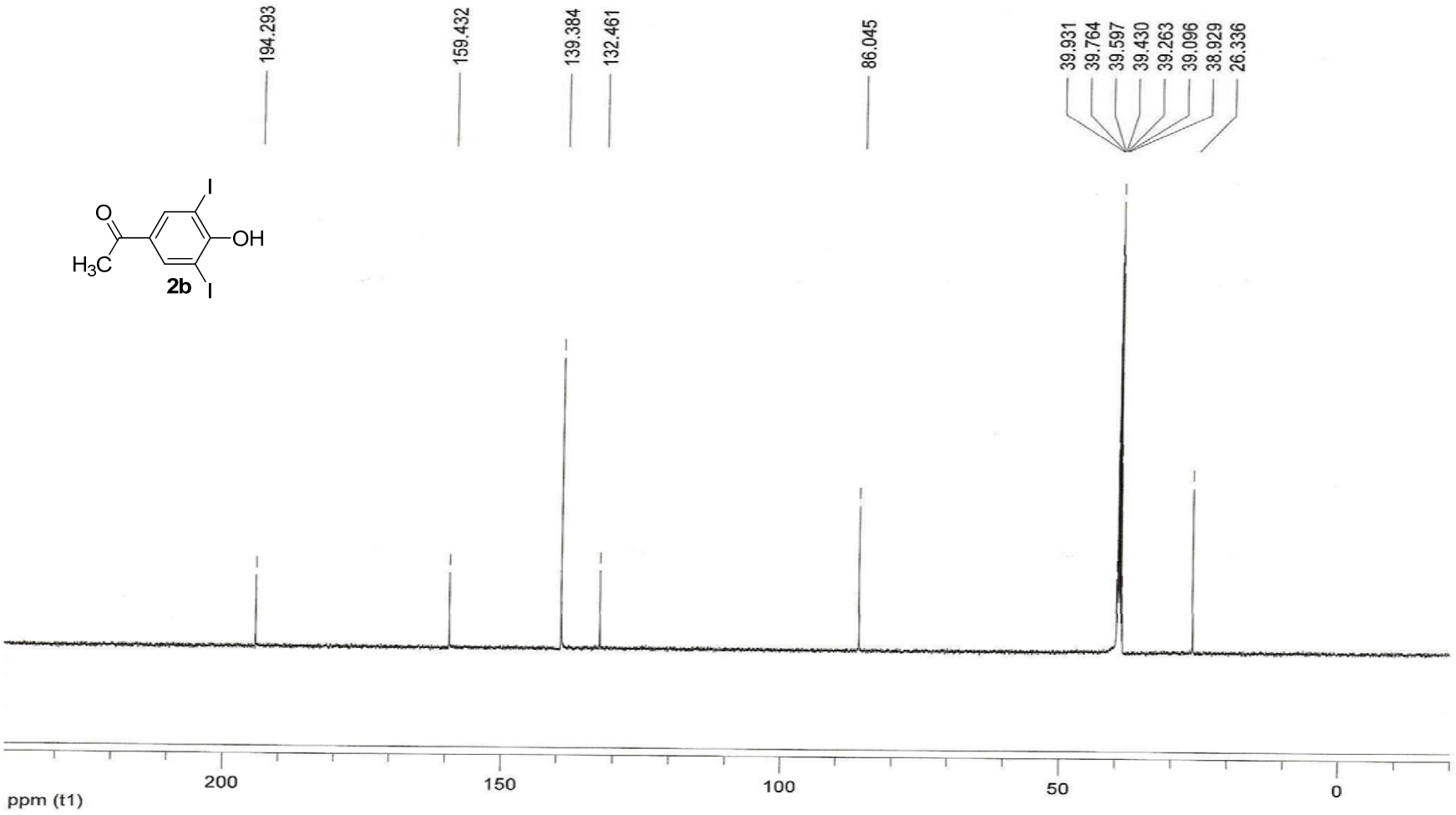


Figure 4: ^{13}C NMR spectrum in DMSO-d_6 of compound **2b**.

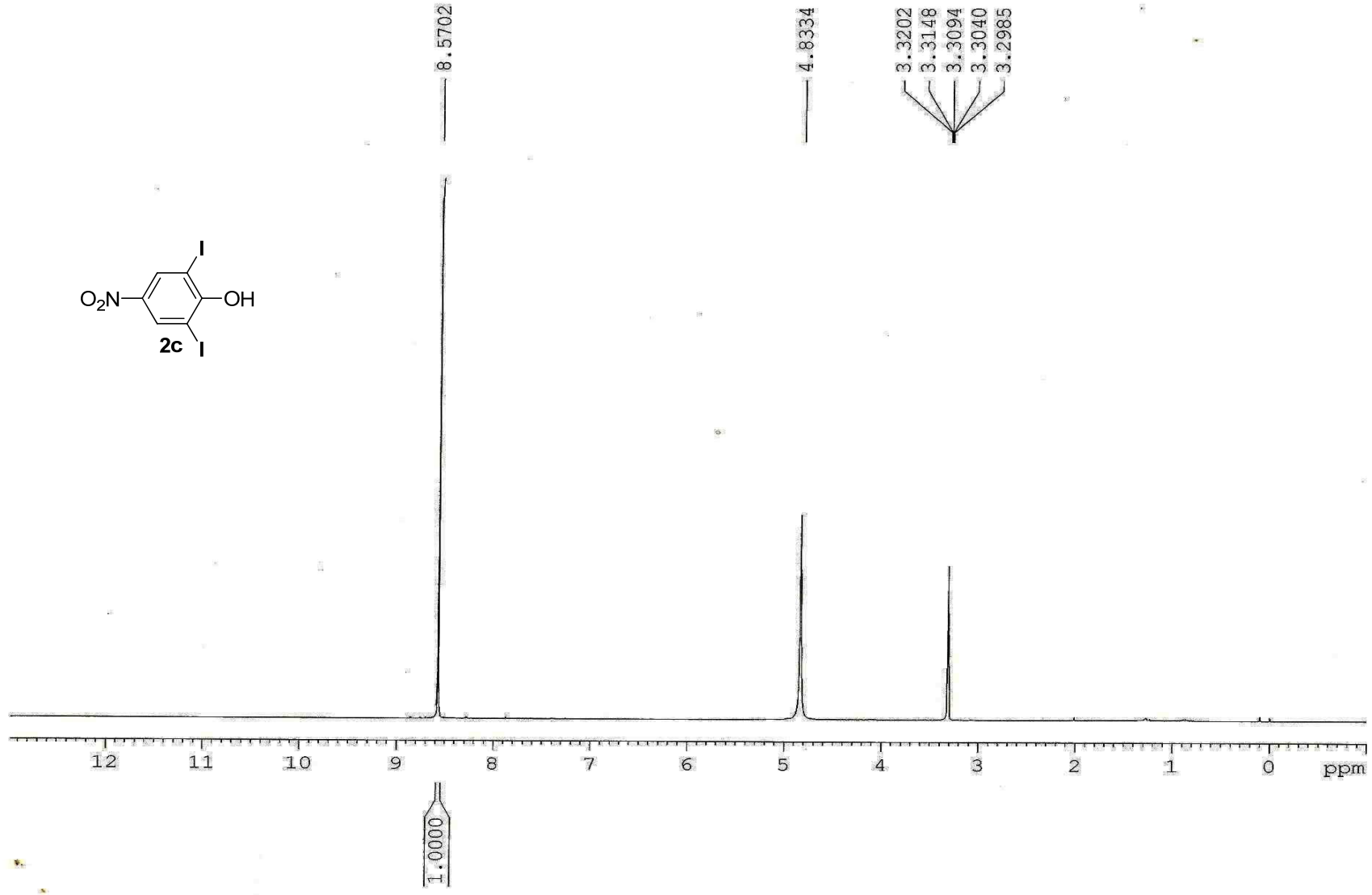


Figure 5: ^{1}H NMR spectrum in CD_3OD of compound **2c**.

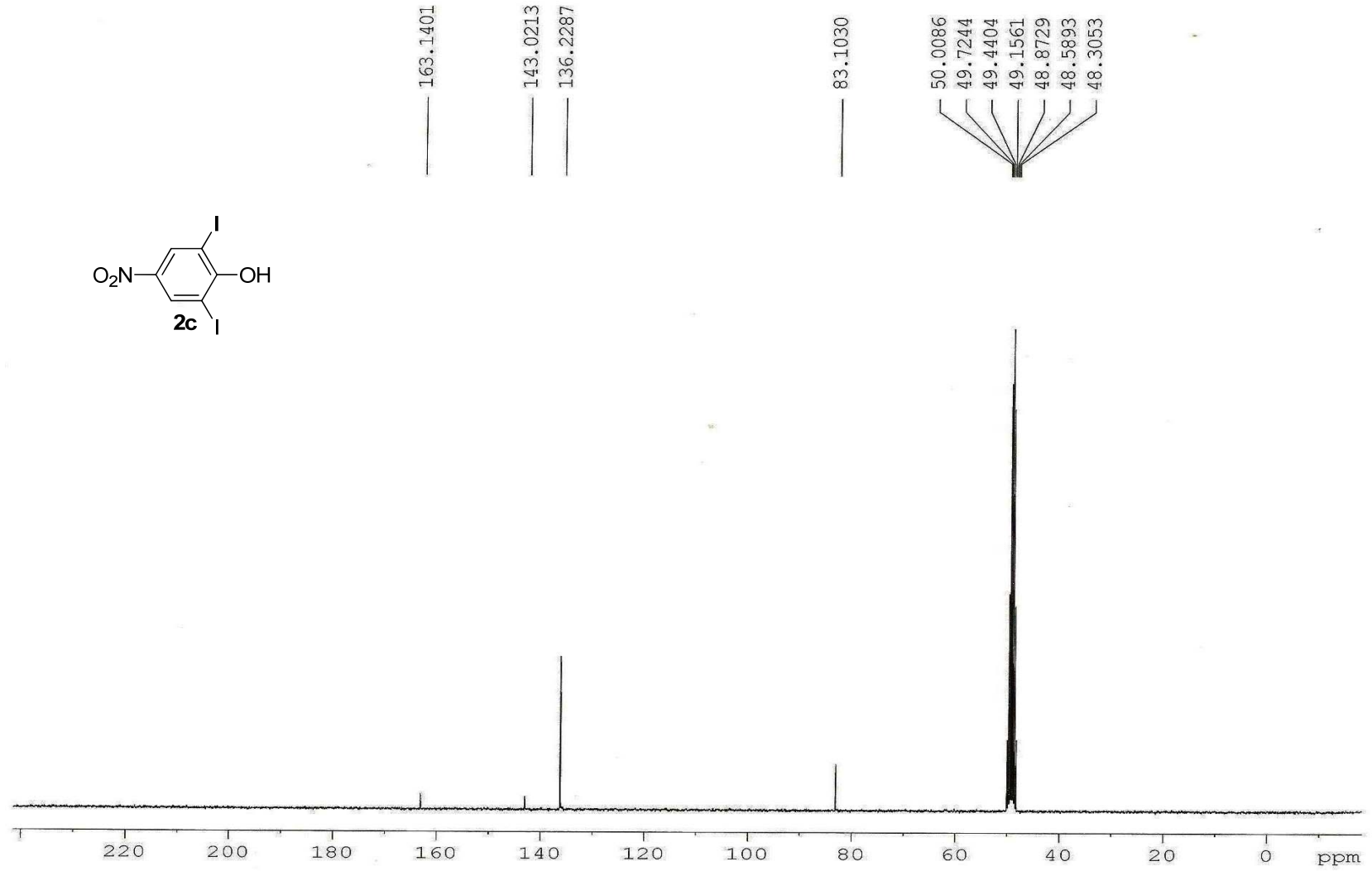


Figure 6: ^{13}C NMR spectrum in CD_3OD of compound **2c**.

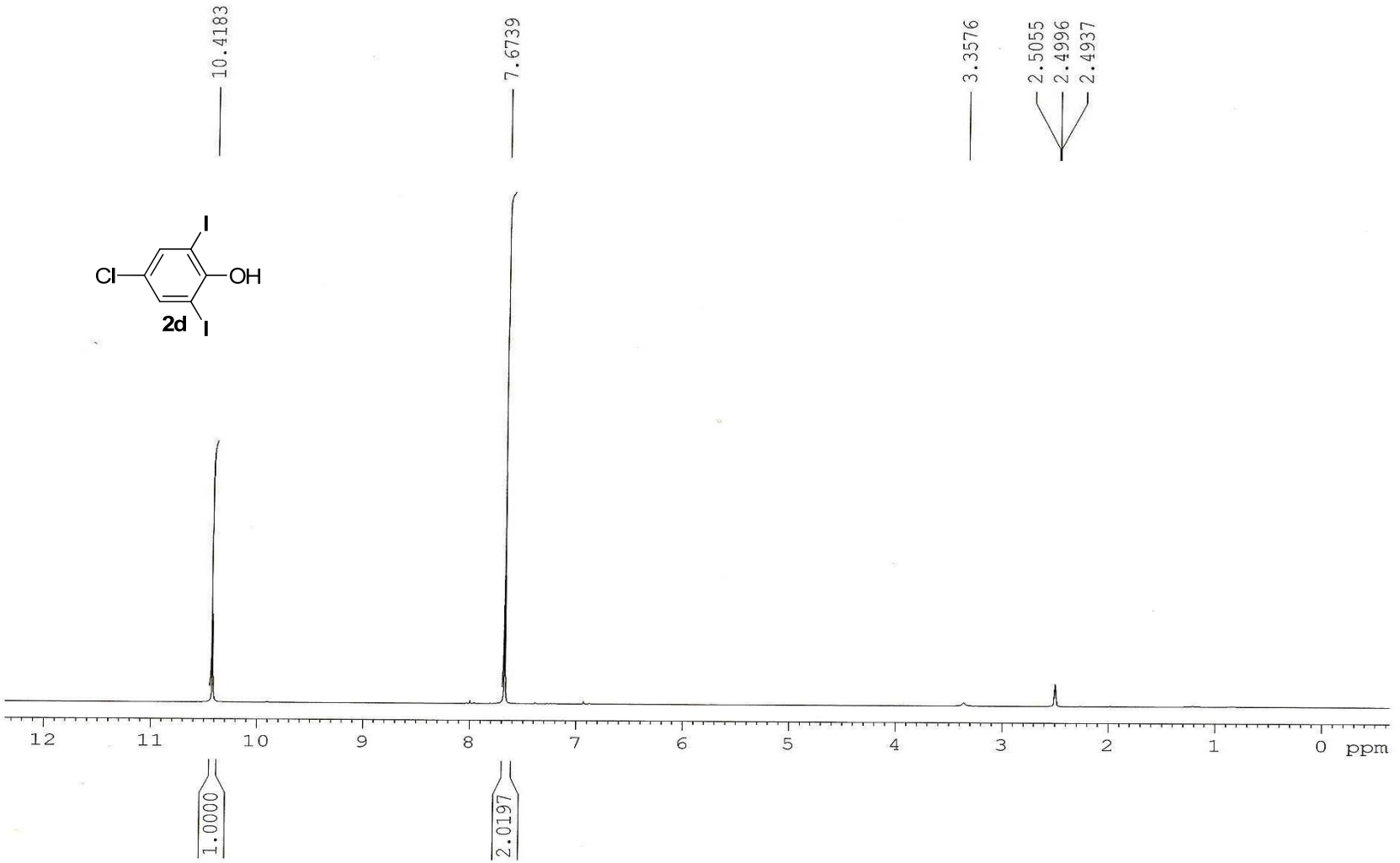


Figure 7: ^{1}H NMR spectrum in DMSO-d_6 of compound **2d**.

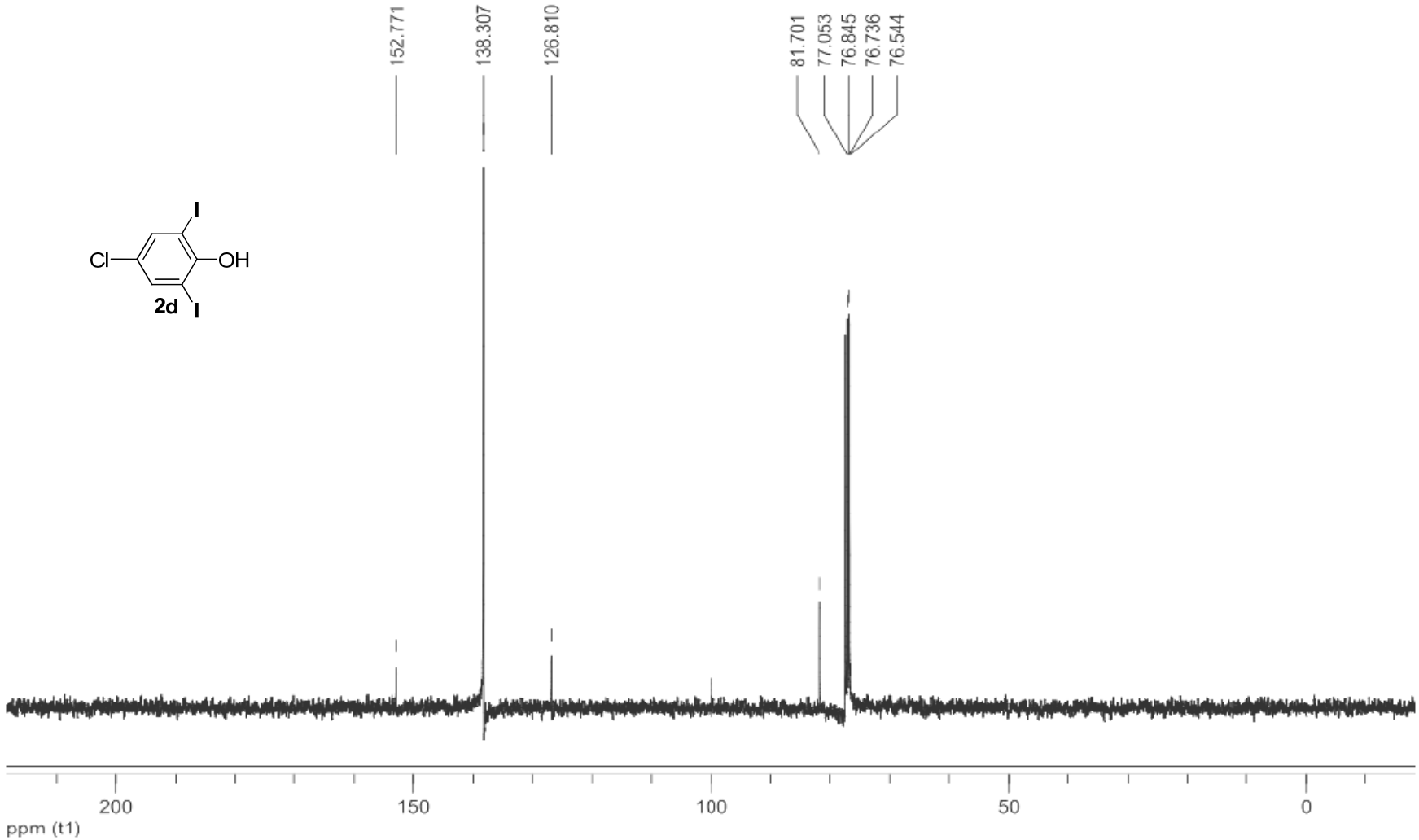


Figure 8: ^{13}C NMR spectrum in $CDCl_3$ of compound **2d**.

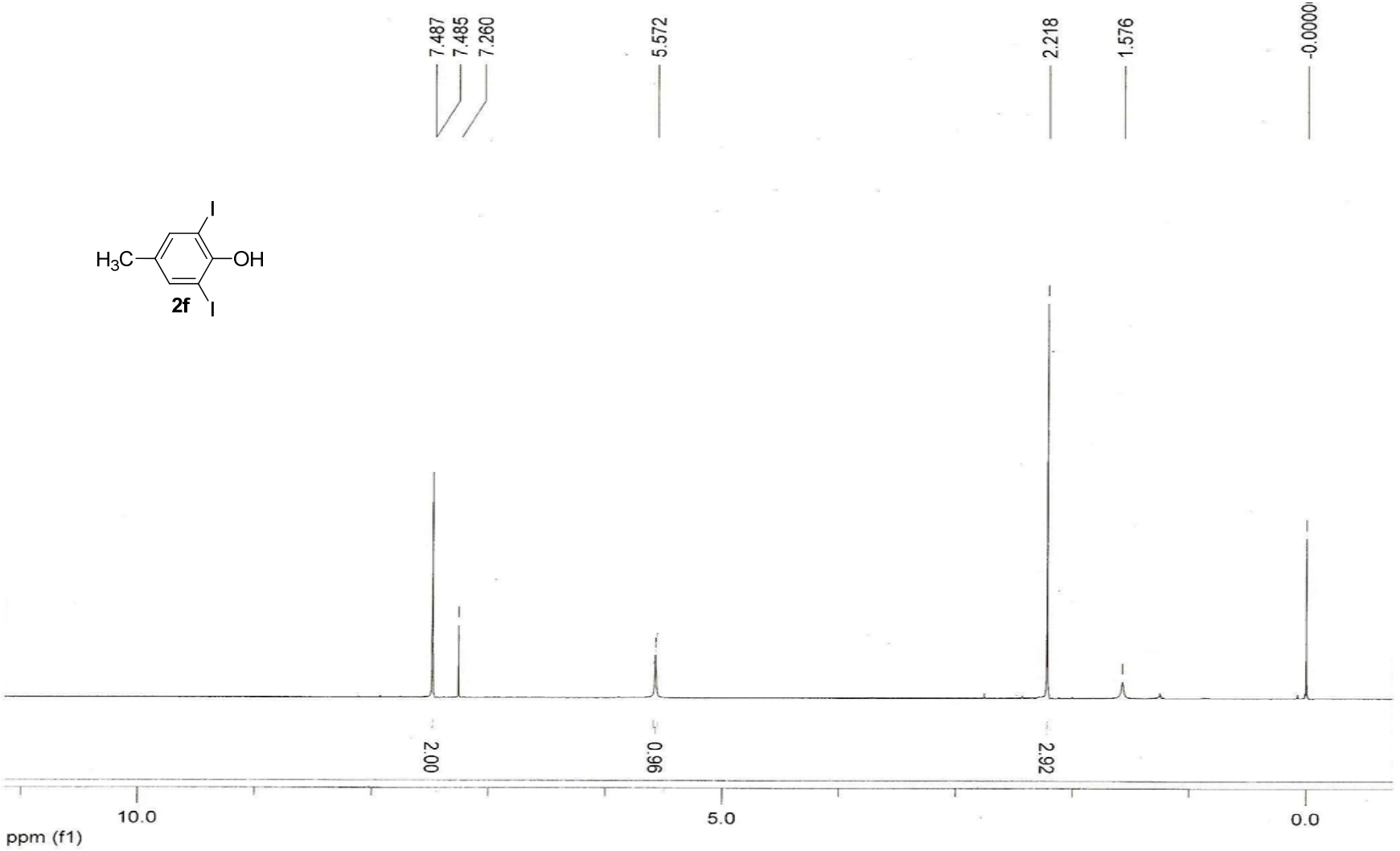


Figure 9: ^{1}H NMR spectrum in $CDCl_3$ of compound **2f**.

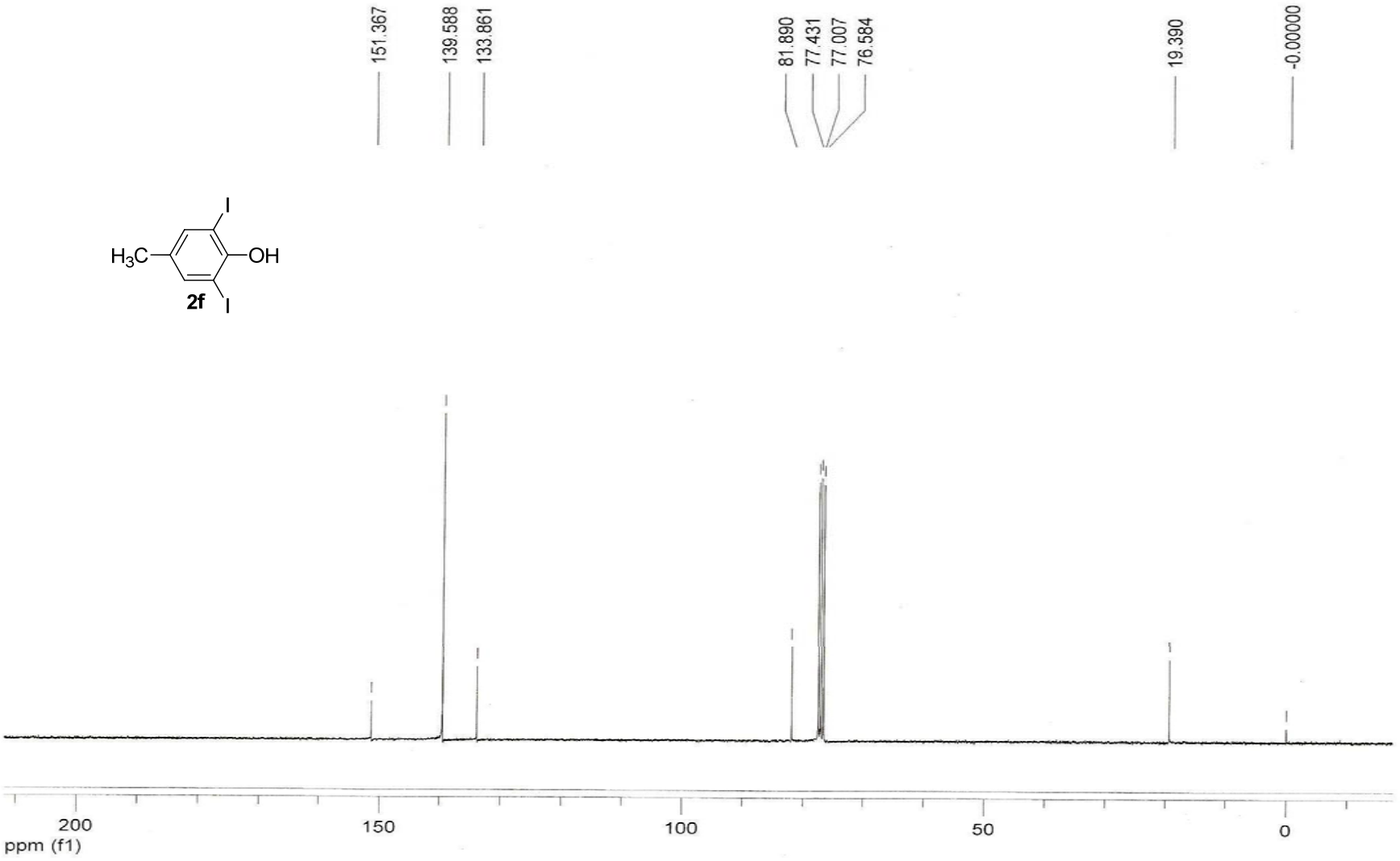


Figure 10: ^{13}C NMR spectrum in $CDCl_3$ of compound **2f**.

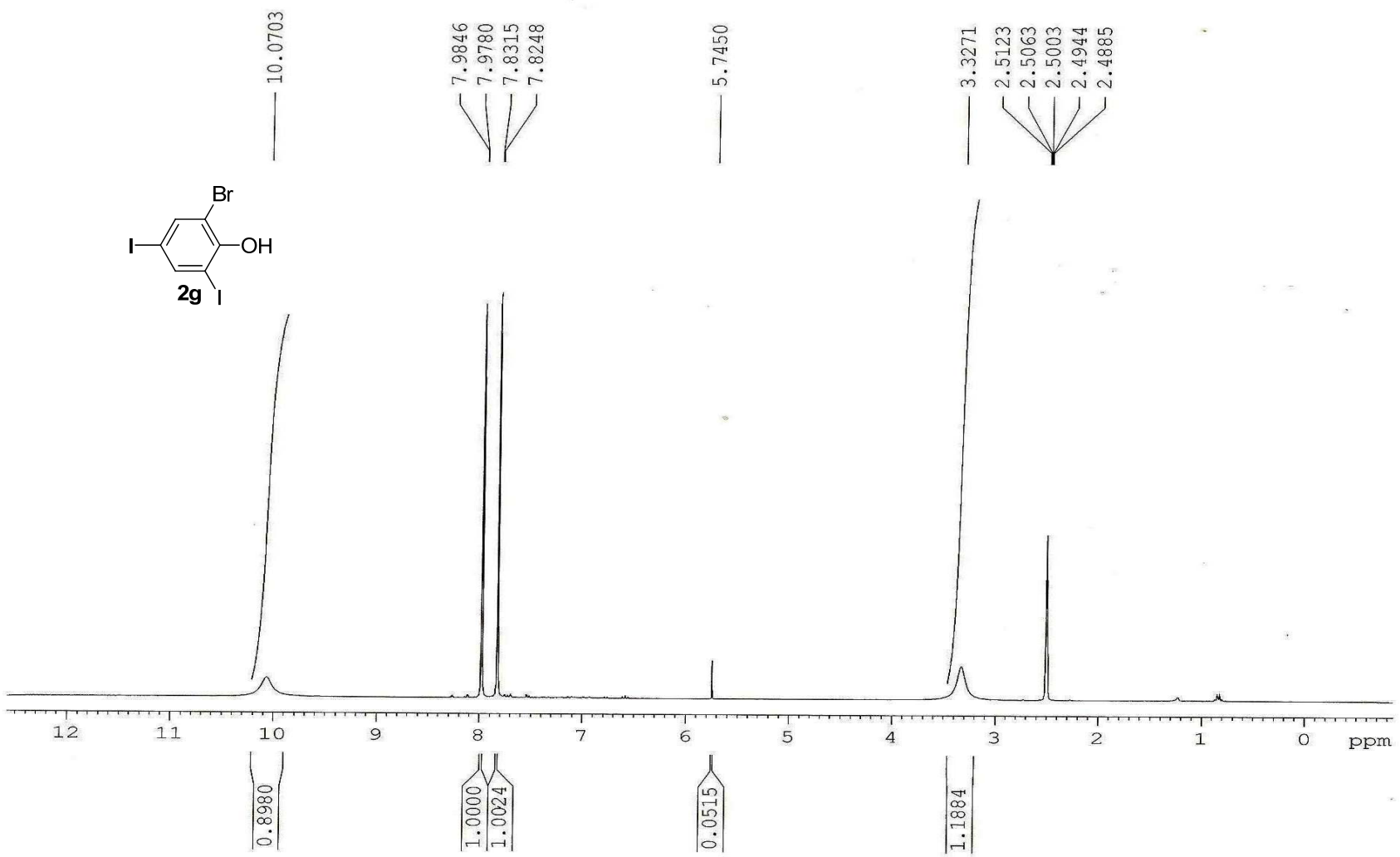


Figure 11: ^{1}H NMR spectrum in DMSO-d_6 of compound **2g**.

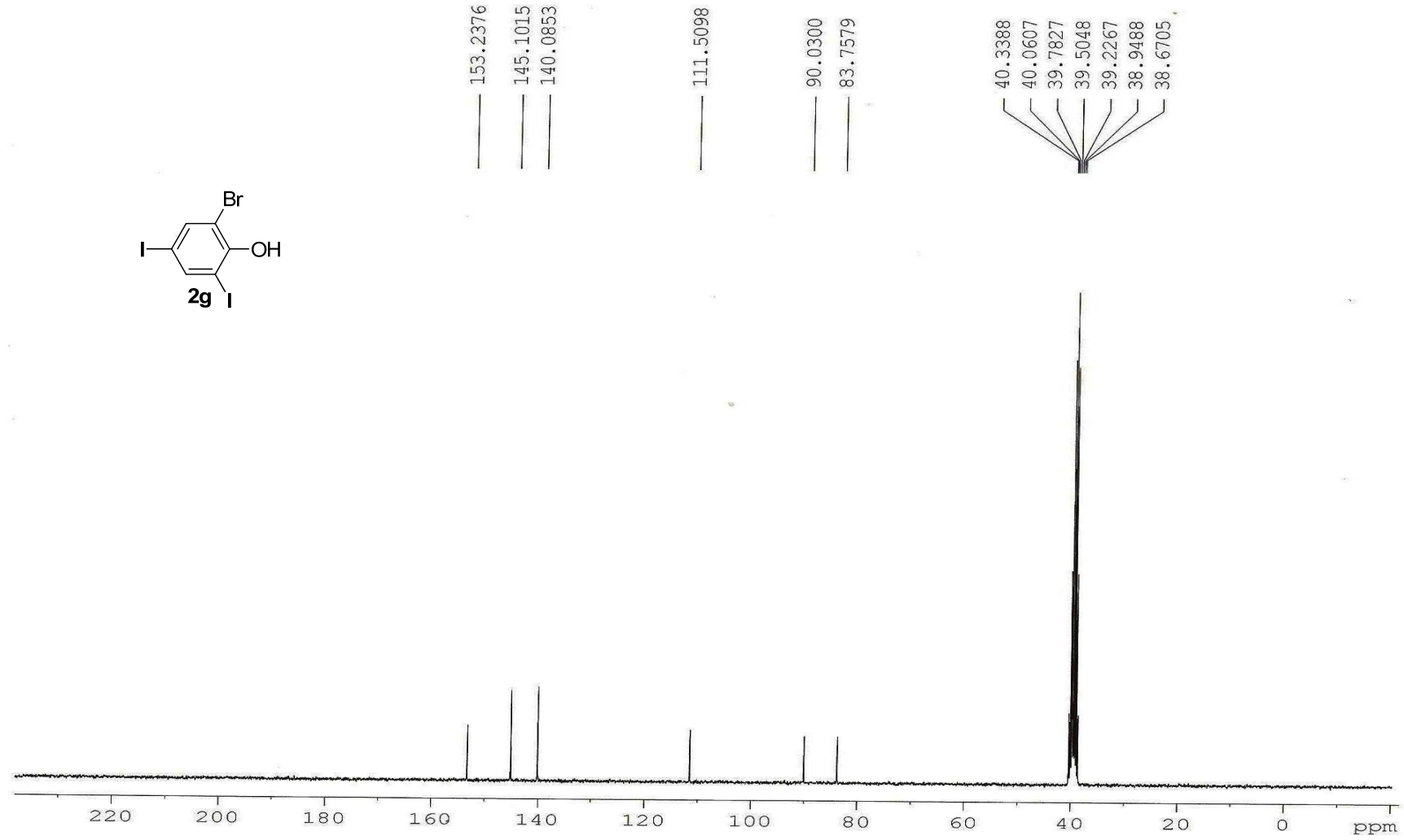


Figure 12: ^{13}C NMR spectrum in DMSO-d_6 of compound **2g**.

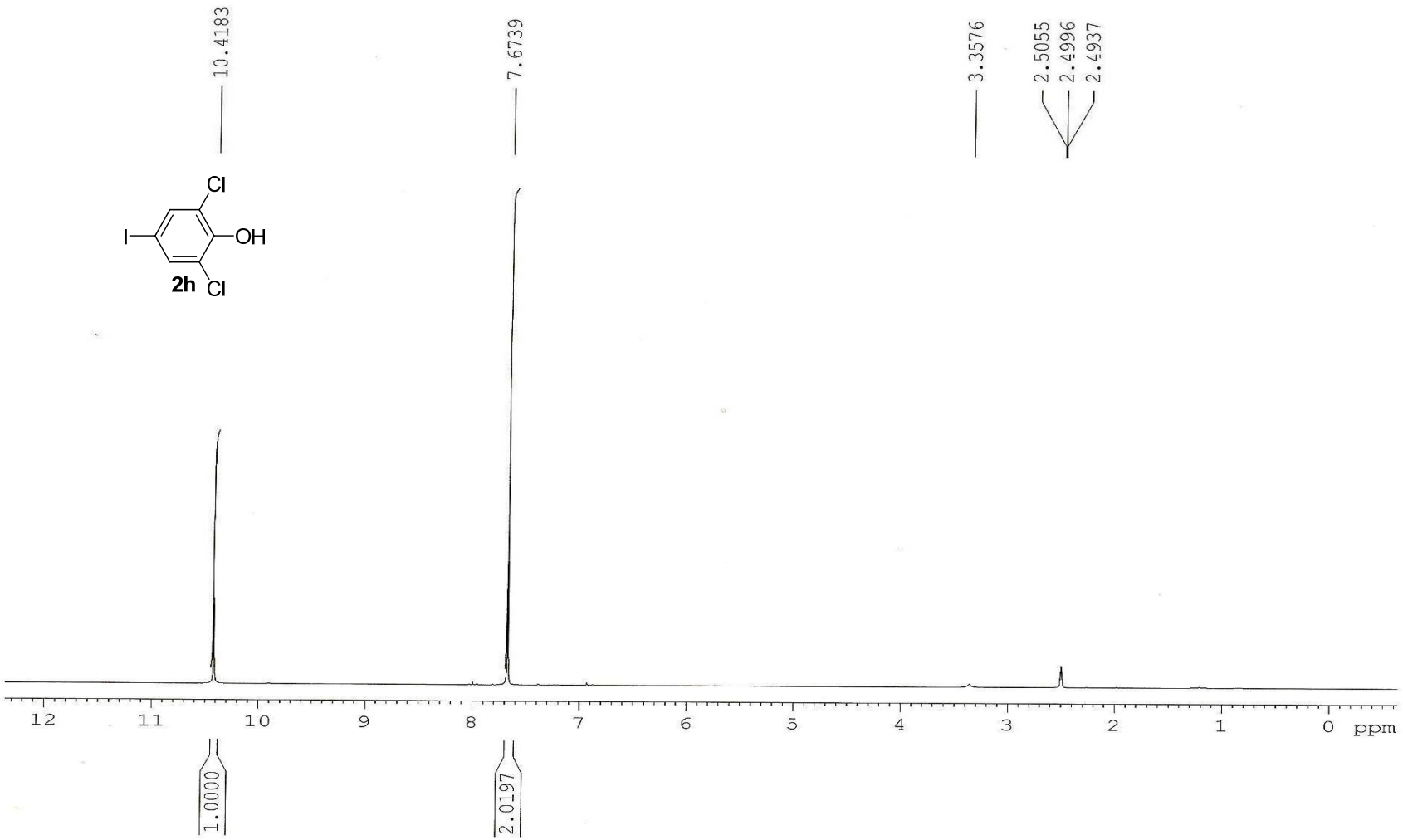


Figure 13: ^{1}H NMR spectrum in DMSO-d_6 of compound **2h**.

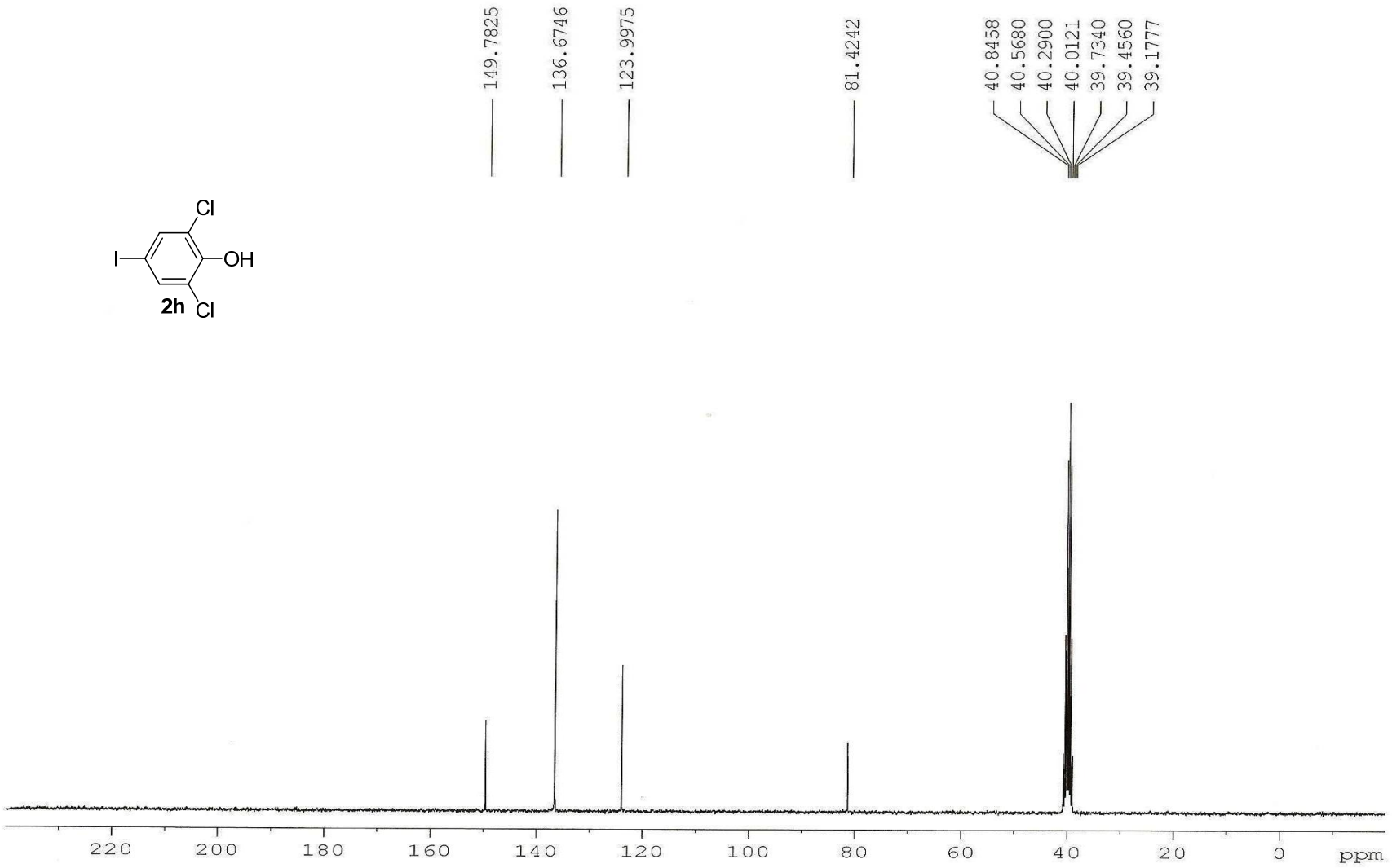


Figure 14: ^{13}C NMR spectrum in DMSO-d_6 of compound **2h**.

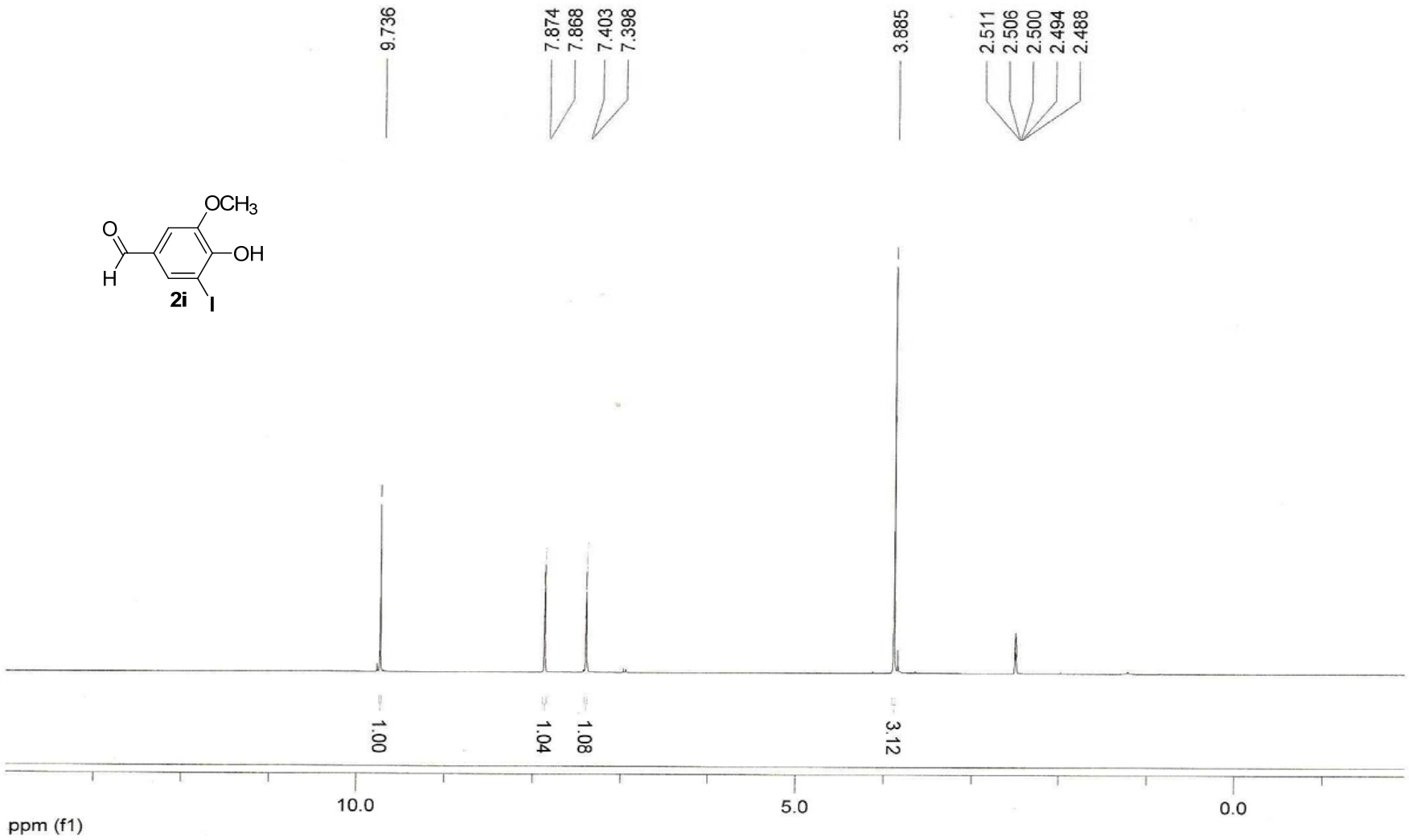


Figure 15: ^{1}H NMR spectrum in DMSO-d_6 of compound **2i**.

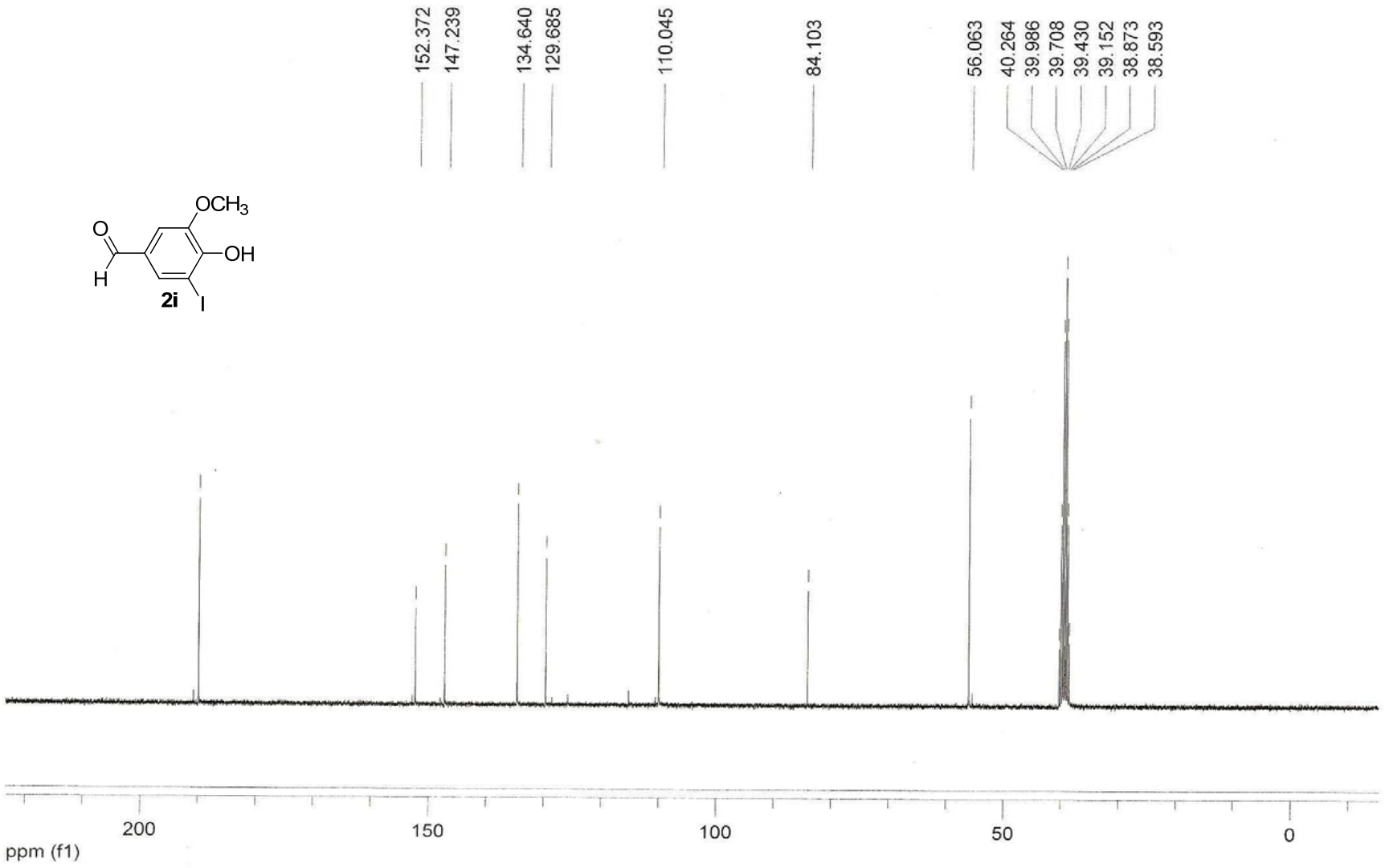


Figure 16: ^{13}C NMR spectrum in DMSO-d_6 of compound **2i**.

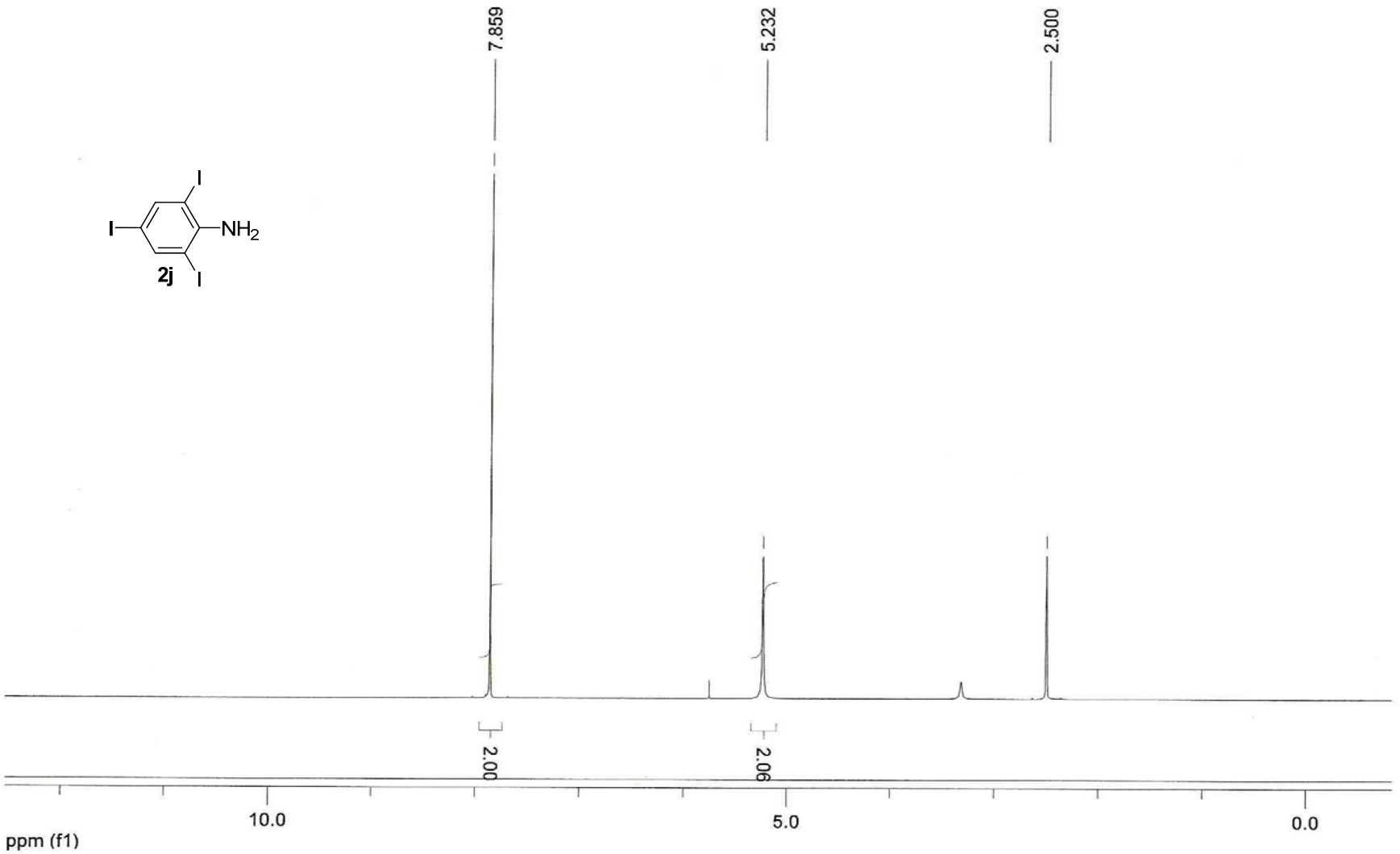


Figure 17: ^{1}H NMR spectrum in DMSO-d_6 of compound **2j**.

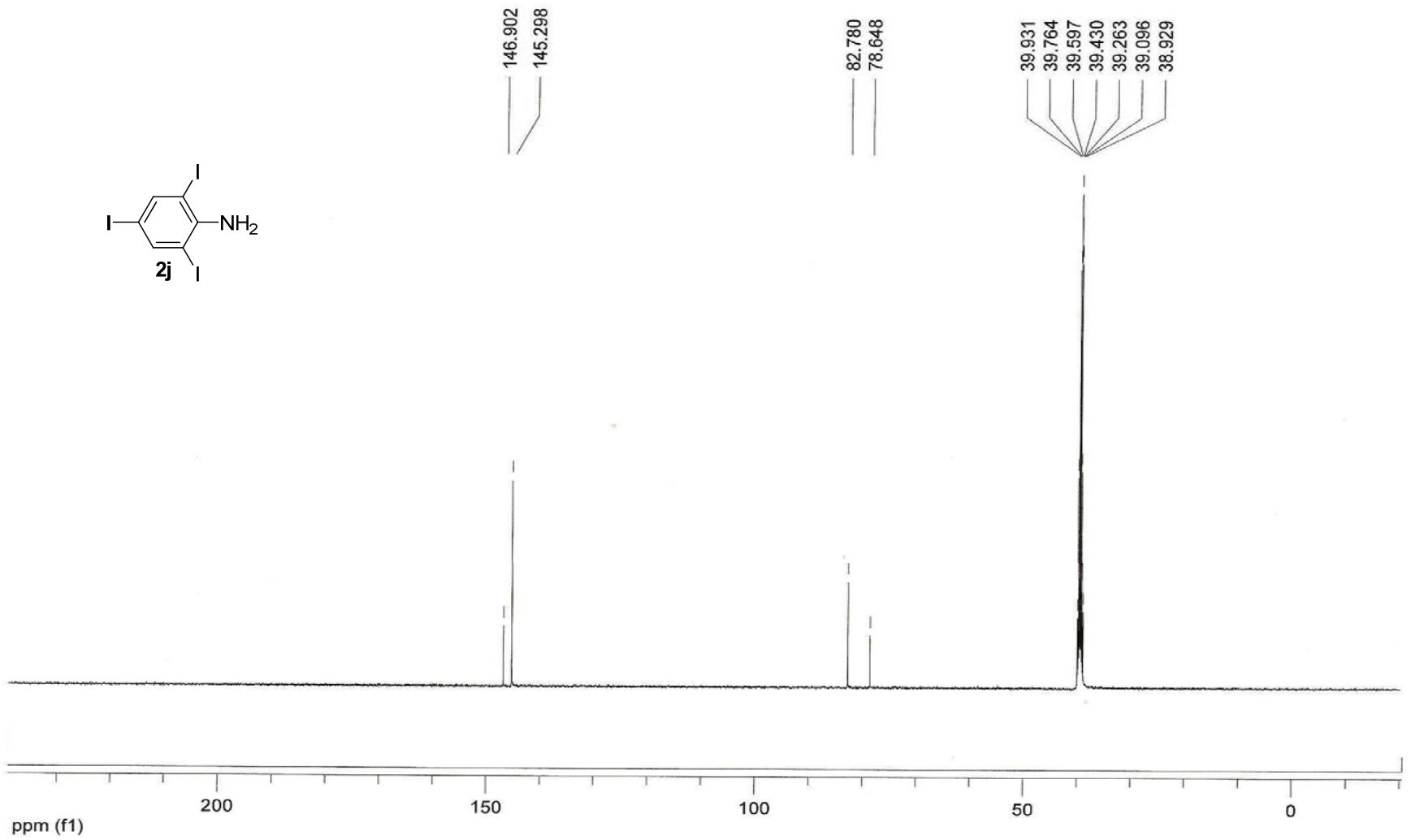


Figure 18: ^{13}C NMR spectrum in DMSO-d_6 of compound **2j**.

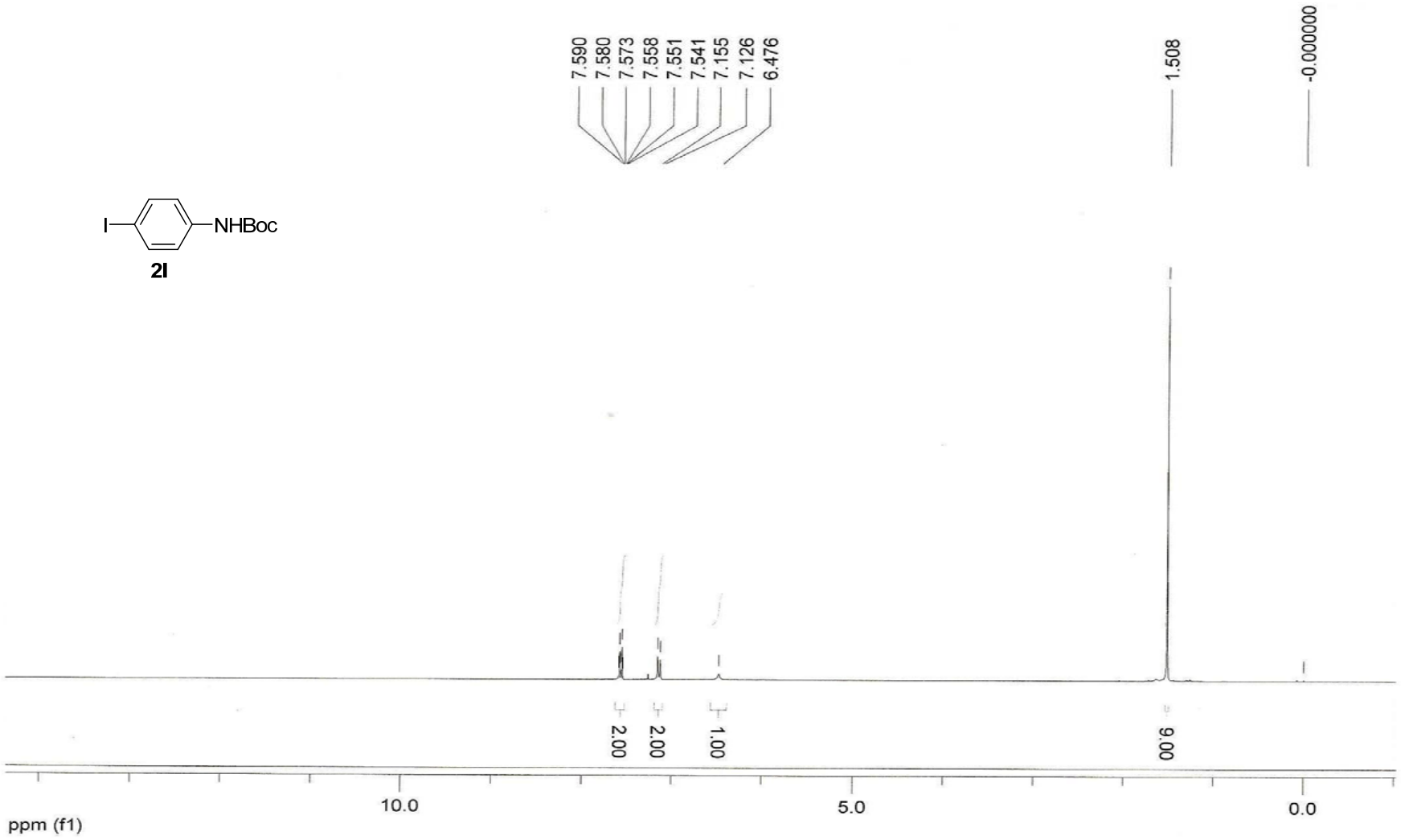


Figure 19: ^{1}H NMR spectrum in $CDCl_3$ of compound **2l**.

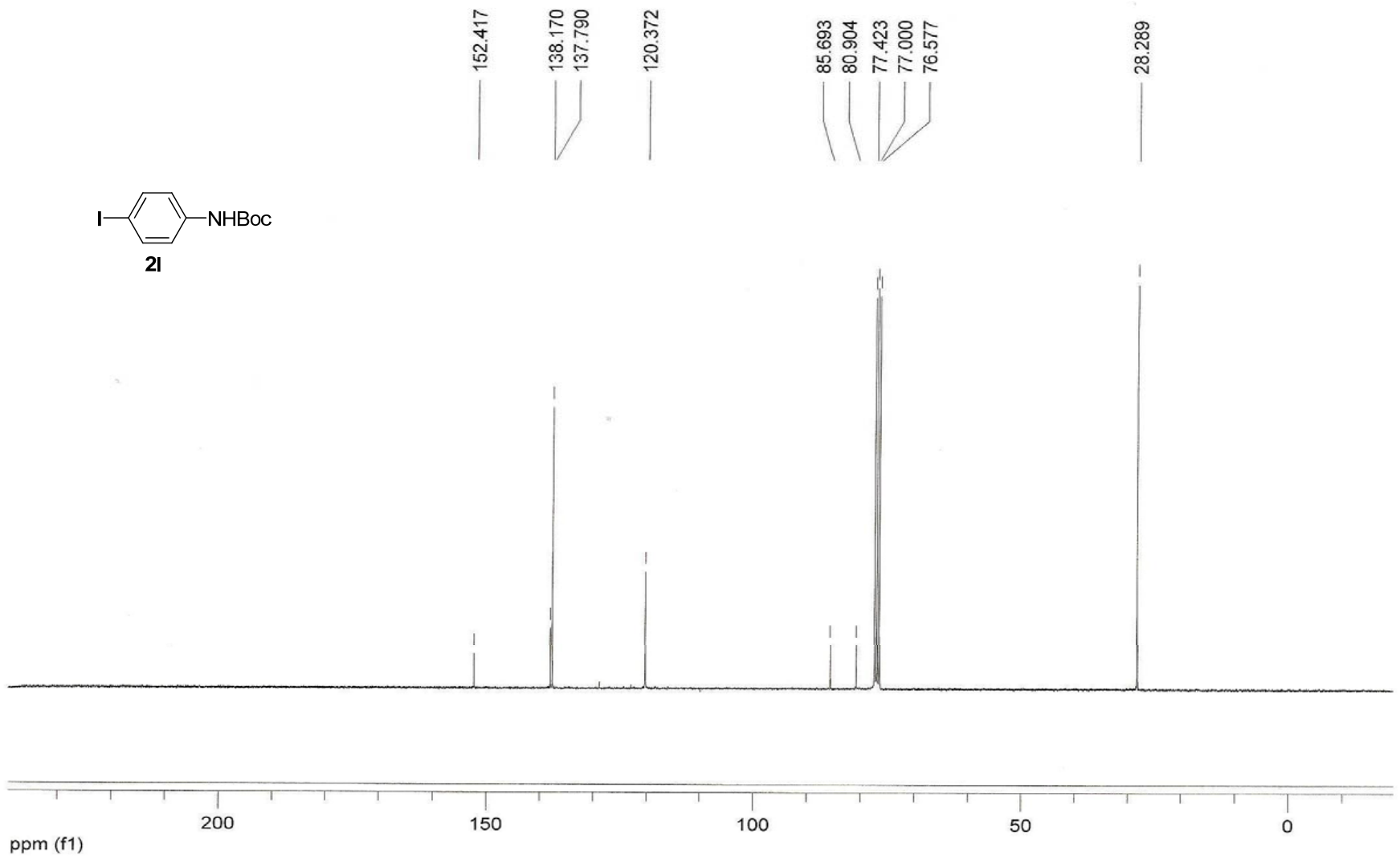


Figure 20: ^{13}C NMR spectrum in $CDCl_3$ of compound **2l**.

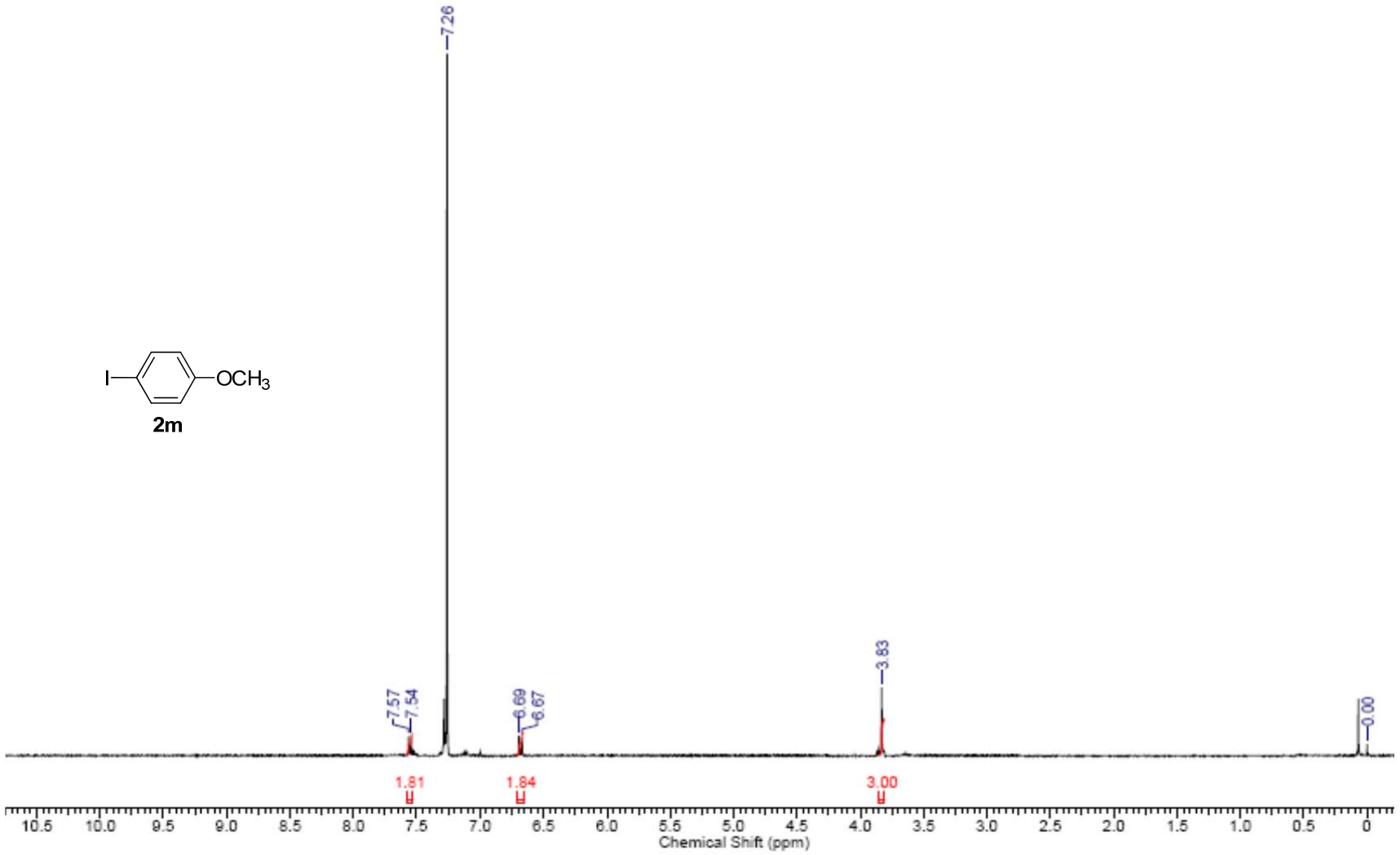


Figure 21: ^{1}H NMR spectrum in $CDCl_3$ of compound **2m**.

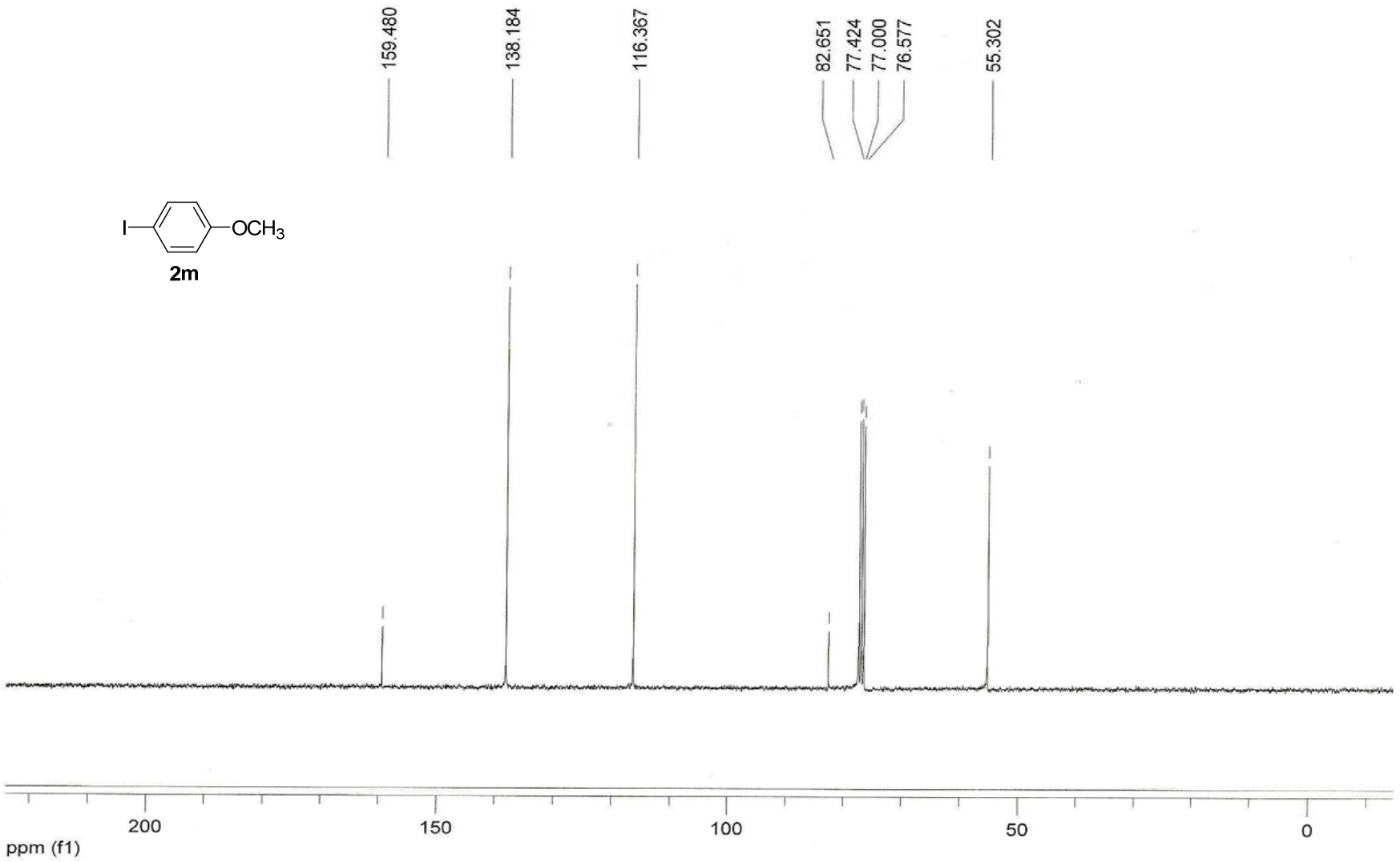


Figure 22: ^{13}C NMR spectrum in $CDCl_3$ of compound **2m**.

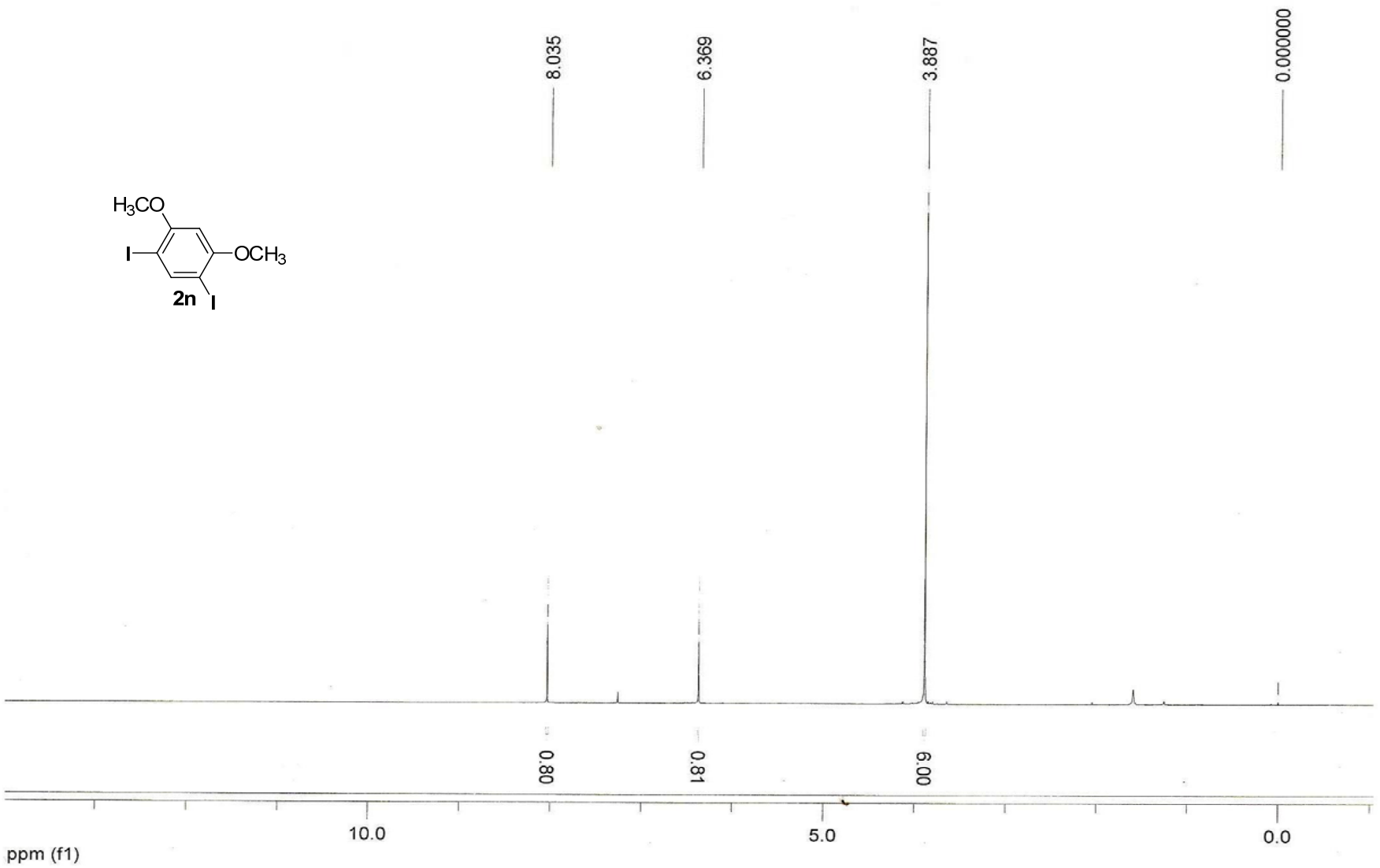


Figure 23: ^{1}H NMR spectrum in $CDCl_3$ of compound **2n**.

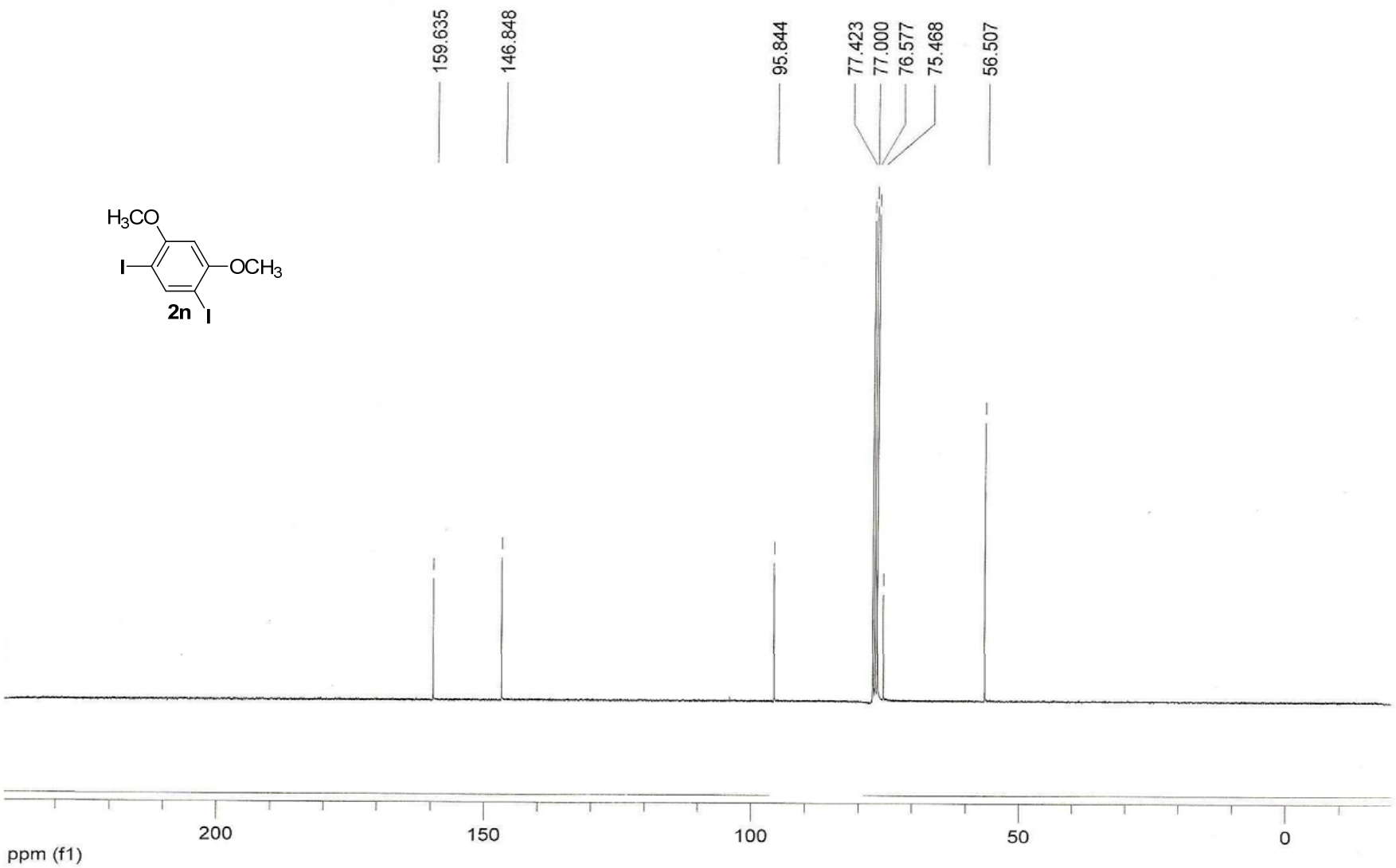


Figure 24: ^{13}C NMR spectrum in $CDCl_3$ of compound **2n**.

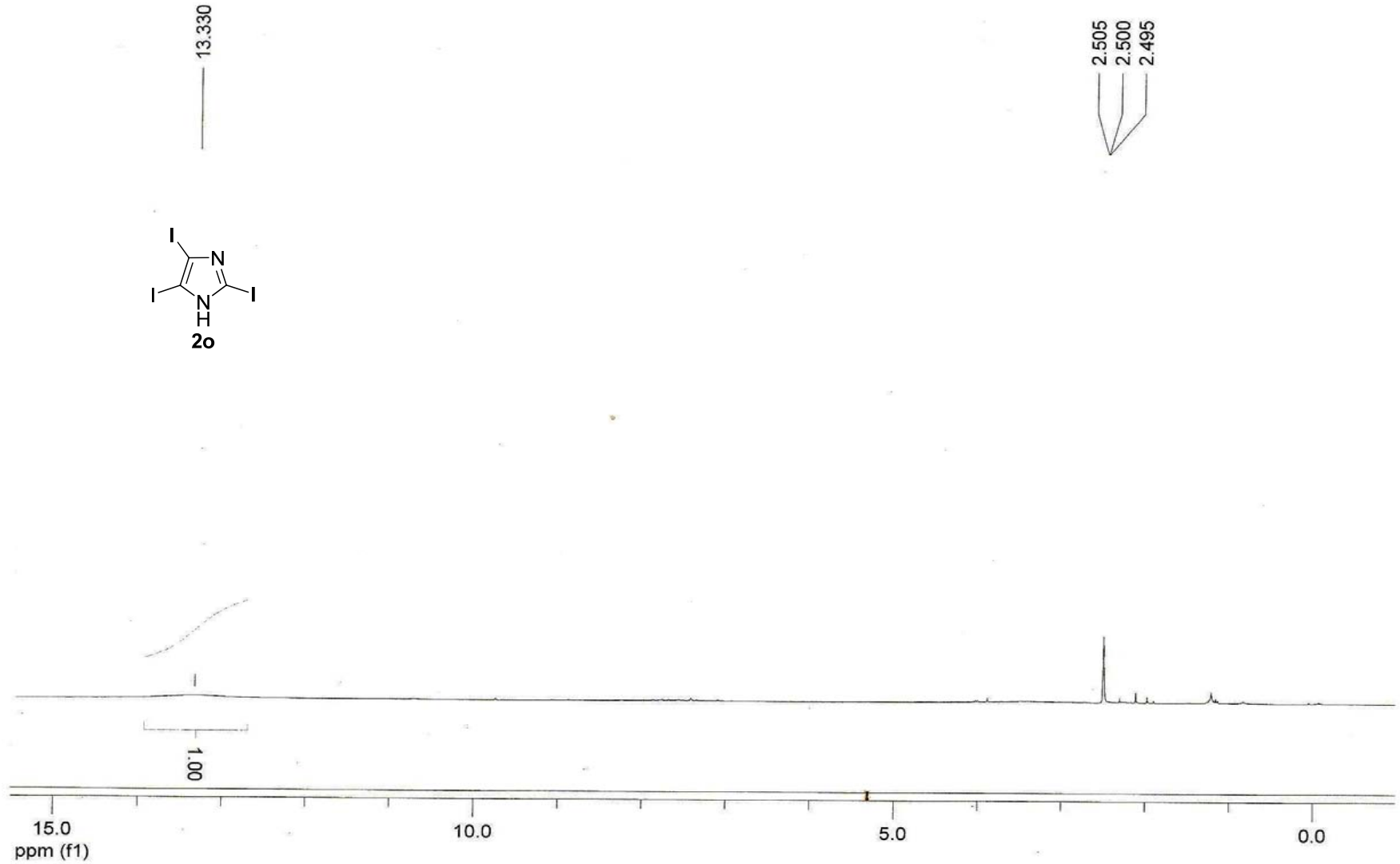


Figure 25: ^{1}H NMR spectrum in DMSO-d_6 of compound **2o**.

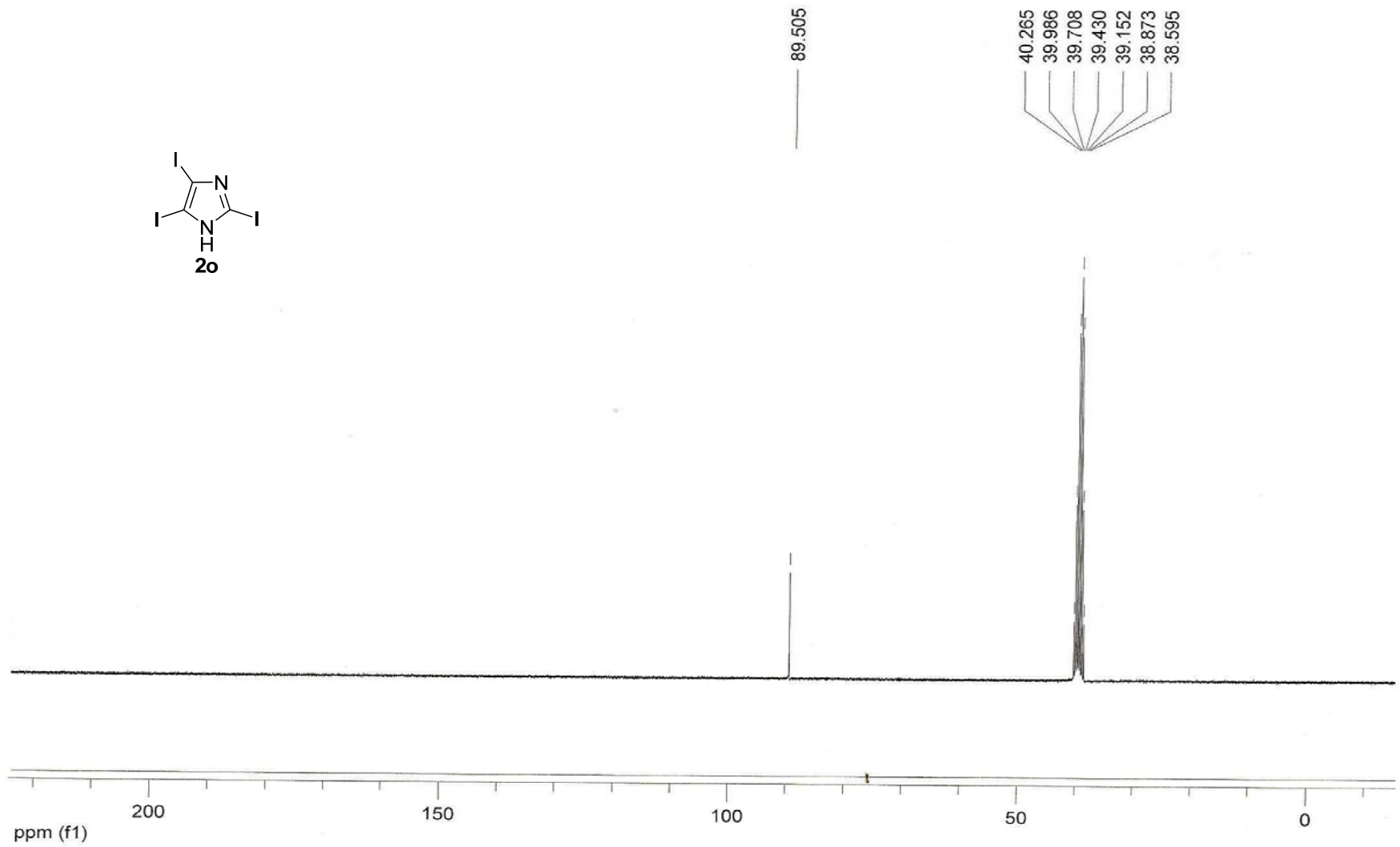


Figure 26: ^{13}C NMR spectrum in DMSO-d_6 of compound **2o**.

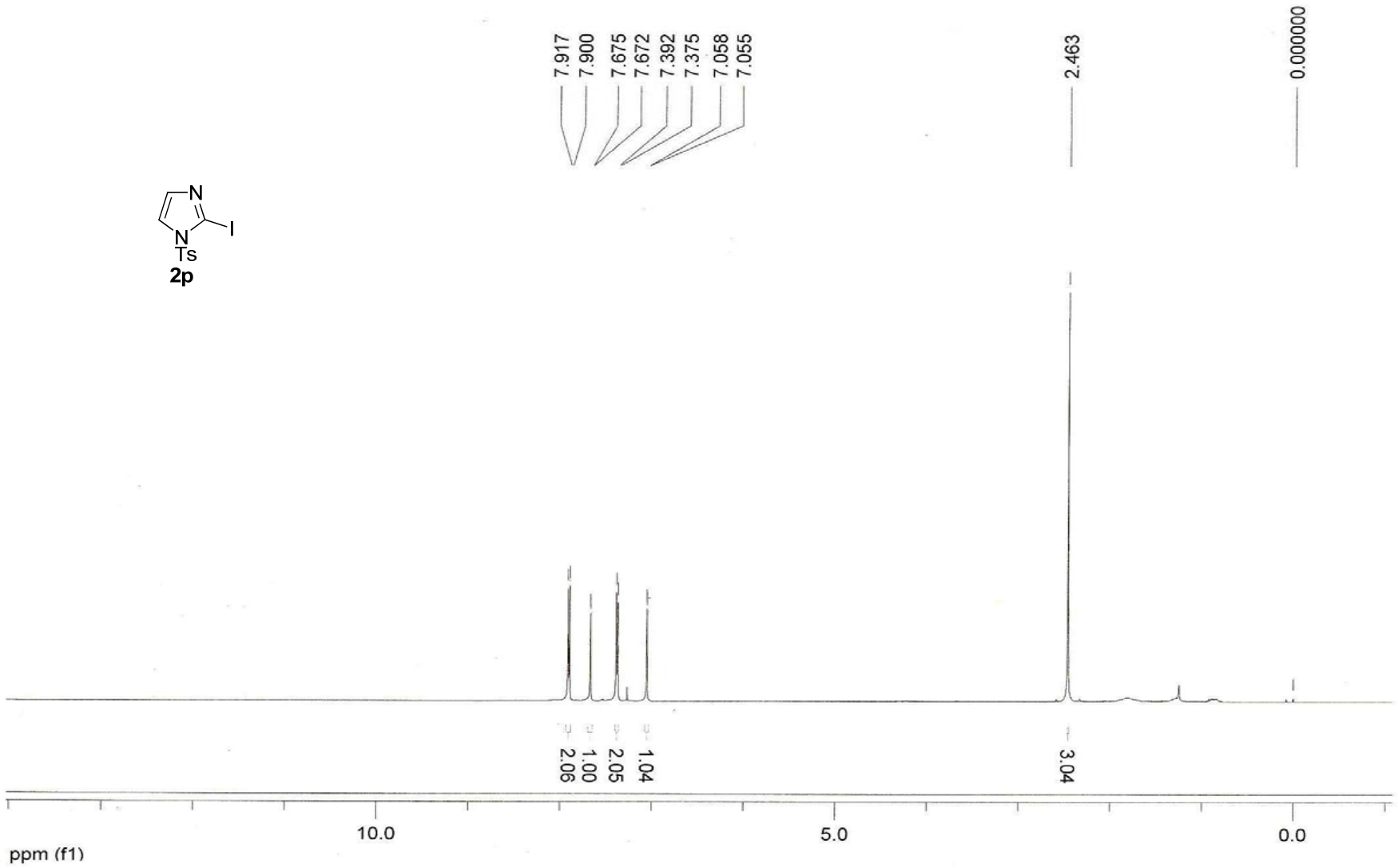


Figure 27: ^{1}H NMR spectrum in $CDCl_3$ of compound **2p**.

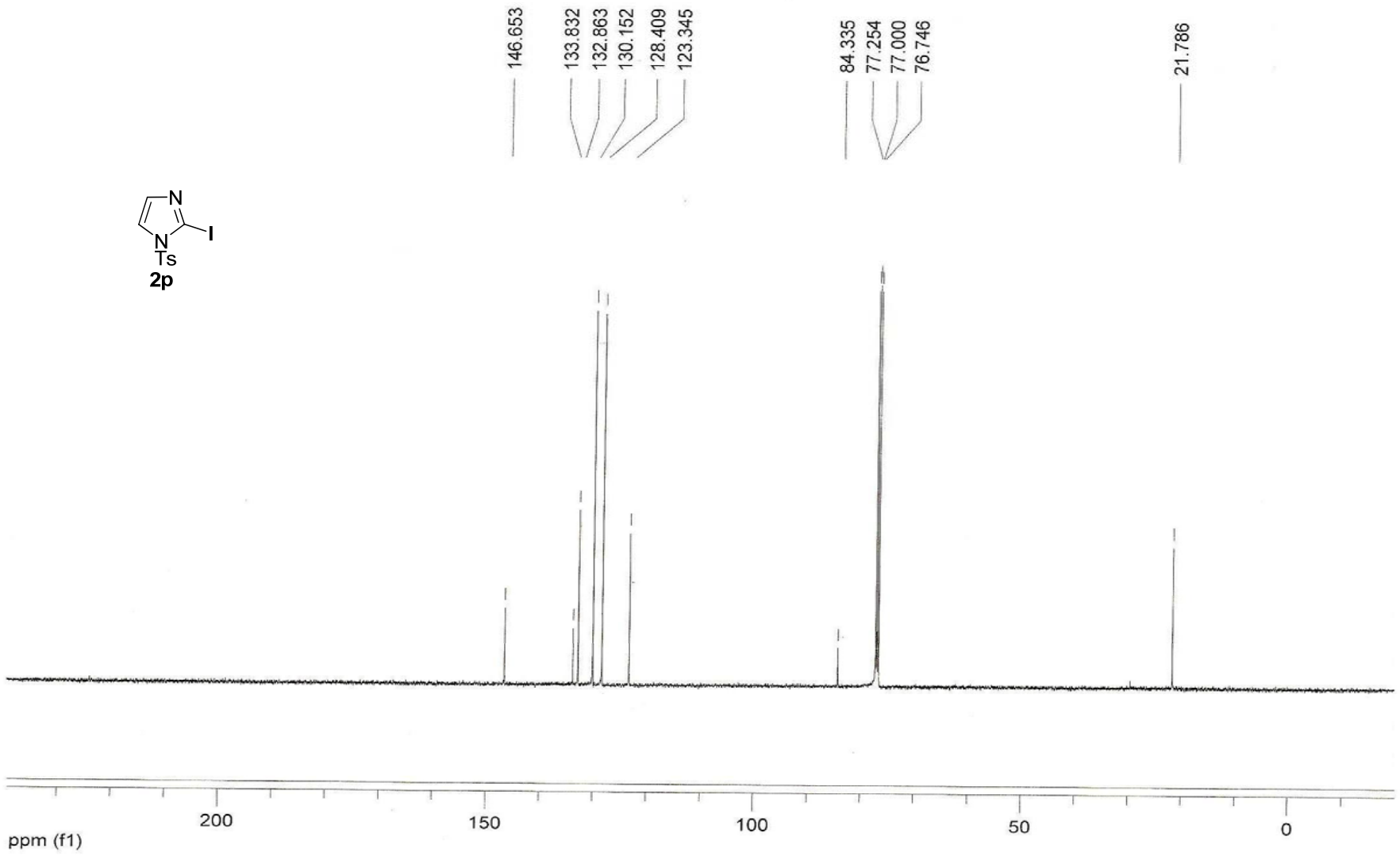


Figure 28: ^{13}C NMR spectrum in $CDCl_3$ of compound **2p**.

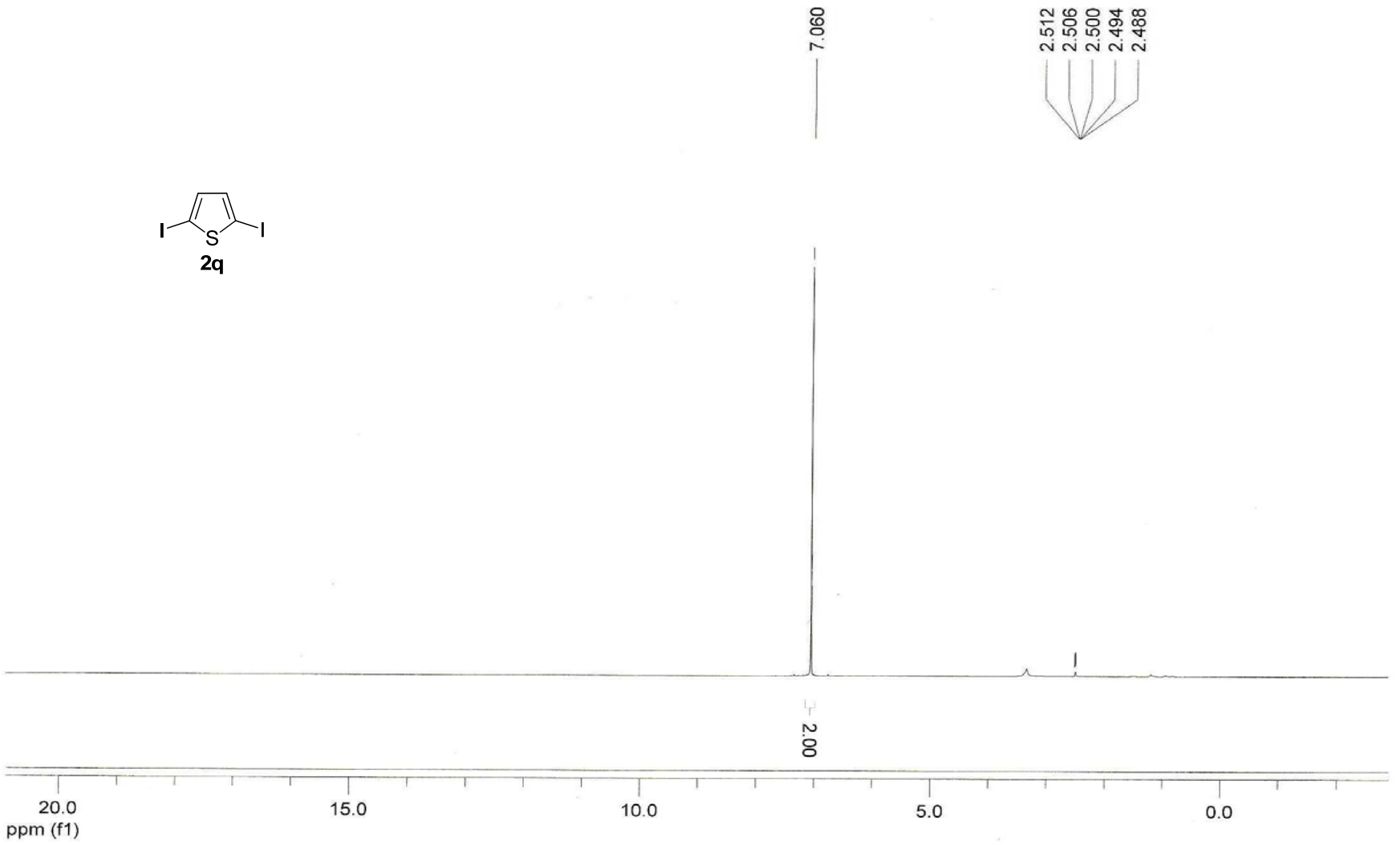


Figure 29: ^{1}H NMR spectrum in DMSO-d_6 of compound **2q**.

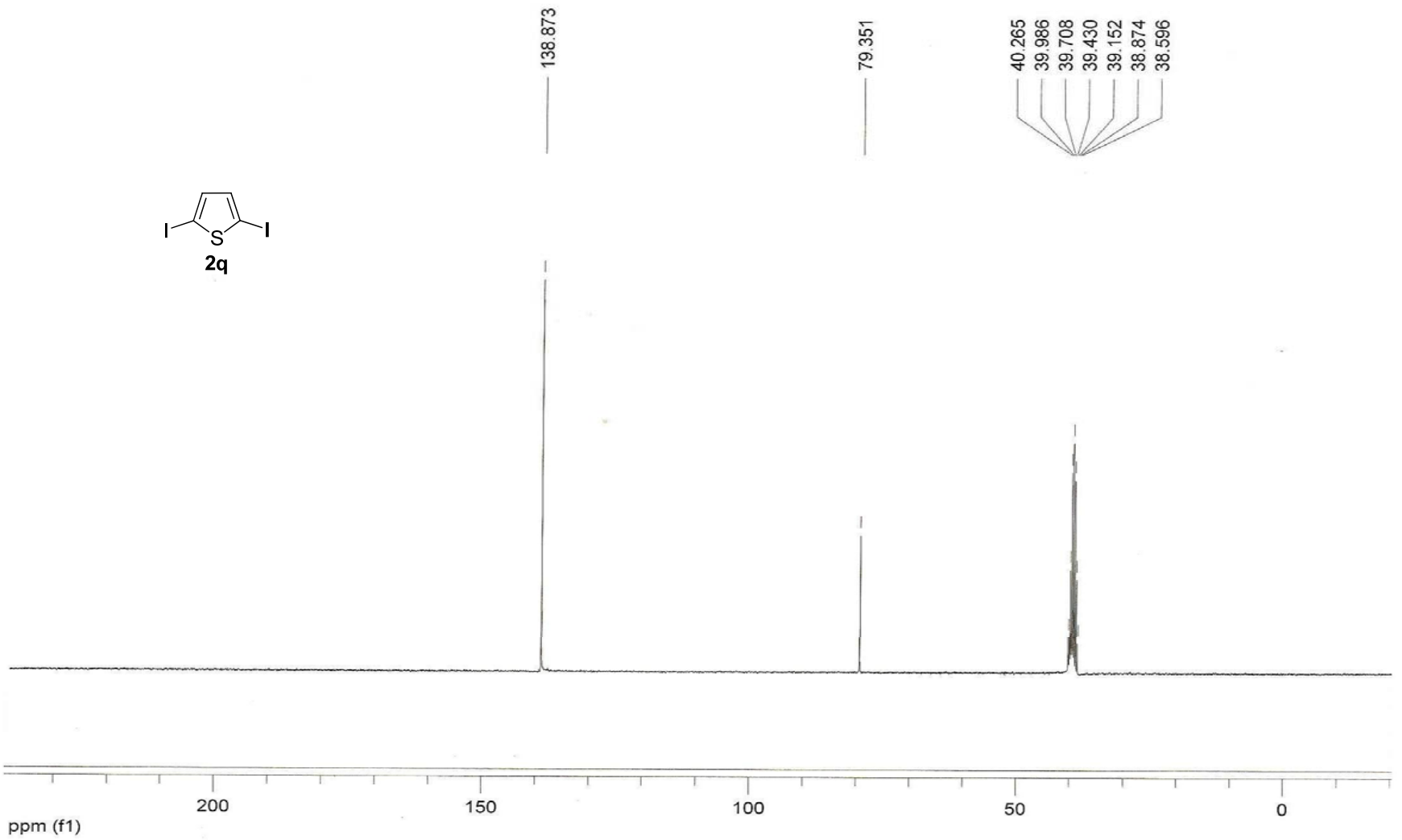


Figure 30: ^{13}C NMR spectrum in DMSO-d_6 of compound **2q**.