Electronic Supplementary Material (ESI) for ChemComm.

Enantioselective Synthesis of Fused Heterocycles with Contiguous Stereogenic Centers by Chiral Phosphoric Acid-Catalyzed Symmetry Breaking

Keiji Mori,[†‡] Ayaka Miyake,[†] and Takahiko Akiyama[†]*

[†]*Department of Chemistry, Faculty of Science,*
Gakushuin University,
1-5-1 Mejiro, Toshima-ku, Tokyo 171-8588, Japan
[‡] *Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Nakacho, Koganei, Tokyo 184-8588, Japan.*

takahiko.akiyama@gakushuin.ac.jp

Supporting Information

General experimental procedures

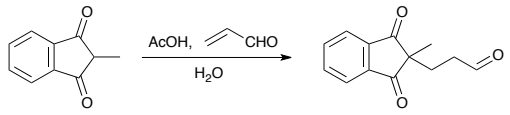
All reactions utilizing air- and moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry nitrogen. Ethereal solvents (THF, Et_2O) were distilled from benzophenone ketyl. Dichloromethane and 1,2-dichloroethane were distilled over CaH_2. Benzene and toluene were distilled over CaH_2, and stored over 4A molecular sieves. *N*,*N*-Dimethylformamide (DMF) was distilled over CaH_2, and stored over 4A molecular sieves.

For thin-layer chromatography (TLC) analysis, Merck pre-coated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) were used. Column chromatography and preparative TLC (PTLC) were performed on PSQ 60B, Fuji Silysia Chemical Ltd. and Wakogel B-5F, Wako Pure Chemical Industries, respectively.

Melting point (mp) determinations were performed by using a AS ONE ATM-01 instrument and are uncorrected. ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and ^{31}P NMR were measured on a varian-400 MR (Varian Ltd., 400 MHz) spectrometer. Chemical shifts are expressed in parts per million (ppm) downfield from internal standard (tetramethylsilane for ^{1}H, and C_6F_6 for ^{19}F, 0.00 ppm), and coupling constants are reported as hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; sep, septet; m, multiplet. Infrared (IR) spectra were recorded on a FTIR-8600PC instrument (Shimadzu Co.). Elemental analysis (EA) was carried out on Flash2000 instrument (Amco Inc.).

1. Preparation of starting materials.

Scheme S1. General synthetic route to aldehyde **5**. Preparation of **5a** is shown as a representative example according to the reported procedure.[1]



s1 **5a**

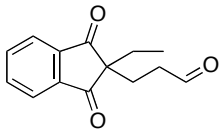
To a solution of **s1**[2] (2.01 g, 12.6 mmol) in AcOH (112 μL) and H_2O (12.0 mL) was added acrolein (1.30 mL, 19.5 mmol) at room temperature. After being stirred for 15 h, the reaction was stopped by addition of H_2O. The crude mixture was extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3/1) to afford aldehyde **5a** (2.64 g, 95%) as a yellow oil.

IR (neat) 3433, 3076, 2969, 2929, 2728, 1742, 1708, 1597, 1453, 1376, 1334, 1268, 1215, 1154, 1043, 988, 911 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 3H), 2.12 (t, 1H, J = 8.0 Hz), 2.42 (t, 1H, J = 8.0 Hz), 7.83–7.93 (m, 2H), 7.95–8.04 (m, 2H), 9.66 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 26.7, 38.9, 52.3, 123.6, 136.1, 140.8, 200.3, 203.6.

Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.51; H, 5.36.



3-(2-Ethyl-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)propanal (**5b**).

Yellow oil.

Yield: 65% (from 2-ethyl-1*H*-indene-1,3(2*H*)-dione[2]).

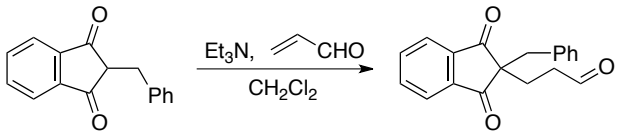
IR (neat) 3430, 2967, 2933, 1741, 1705, 1595, 1458, 1387, 1340, 1252, 1153, 1056, 972, 893, 793 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 0.72 (t, 3H, J = 7.6 Hz), 1.88 (q, 2H, J = 7.6 Hz), 2.07–2.15 (m, 2H), 2.32–2.40 (m, 2H), 7.84–7.92 (m, 2H), 7.96–8.03 (m, 2H), 9.64 (t, 1H, J = 1.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 9.2, 26.0, 27.8, 38.8, 57.2, 123.1, 136.0, 142.0, 200.3, 204.0.

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 72.89; H, 6.01.

Scheme S2. Synthesis of aldehydes **5c** and **5d**. .



s2 **5c**

To a solution of **s2**[2] (340 mg, 1.45 mmol) in CH_2Cl_2 (10.0 mL) were successively added Et_3N (0.10 mL, 0.71 mmol) and acrolein (0.16 mL, 2.4 mmol) at room temperature. After being stirred for 1.5 h, the reaction was stopped by addition of H_2O. The crude mixture was extracted with CH_2Cl_2 (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2/1) to afford aldehyde **5c** (450 mg, quant) as a pale yellow solid.

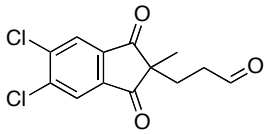
Mp. 115–117 °C.

IR (KBr) 3430, 3031, 2923, 2831, 2727, 1740, 1722, 1704, 1596, 1495, 1455, 1442, 1389, 1339, 1250, 1073, 1030, 935, 759 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 3.16 (s, 2H), 2.19–2.28 (m, 2H), 2.34–2.42 (m, 2H), 6.90–7.05 (m, 5H), 7.64–7.73 (m, 2H), 7.75–7.86 (m, 2H), 9.65 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 38.8, 40.9, 58.7, 122.8, 126.8, 128.1, 129.7, 134.9, 135.7, 142.2, 200.0, 203.3.

Anal. Calcd for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 78.31; H, 5.58.



3-(5,6-Dichloro-2-methyl-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)propanal (**5d**).

White solid.

Mp. 148–150 °C.

Yield: 51% (from commercially available 4,5-dichlorophthalic acid).

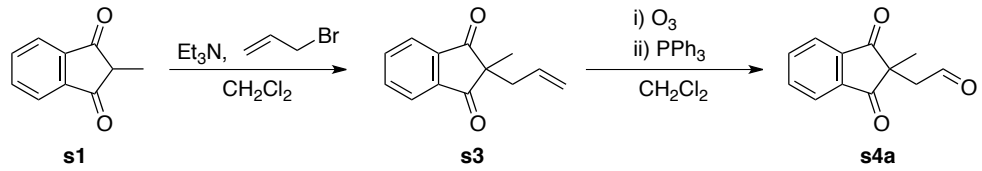
IR (KBr) 3062, 2932, 2719, 1747, 1714, 1580, 1451, 1378, 1297, 1264, 1222, 1195, 1100, 1041, 997, 898, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 3H), 2.10 (t, 1H, J = 7.6 Hz), 2.44 (t, 1H, J = 7.6 Hz), 8.06 (s, 2H), 9.66 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 26.6, 38.7, 52.7, 125.3, 139.4, 141.6, 199.9, 201.3.

Anal. Calcd for $C_{13}H_{10}Cl_2O_3$: C, 54.76; H, 3.54. Found: C, 54.51; H, 3.76.

Scheme S3. General synthetic route to aldehyde **s4**. Preparation of **s4a** is shown as a representative example.[1]



To a solution of **s1** (800 mg, 5.01 mmol) in CH_2Cl_2 (10.0 mL) were successively added Et_3N (1.10 mL, 7.83 mmol) and allyl bromide (0.65 mL, 7.5 mmol) at 0 °C. After being stirred for 38 h at room temperature, the reaction was stopped by addition of saturated aqueous NH_4Cl at 0 °C. The crude mixture was extracted with CH_2Cl_2 (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2/1) to afford **s3** (880 mg, 88%) as a pale yellow oil.

Ozone was bubbled through a solution of **s3** (600 mg, 3.00 mmol) in CH_2Cl_2 (42.0 mL) at –78 °C. Upon consumption of the **s3**, nitrogen was bubbled through the mixture followed by the addition of triphenylphosphine (790 mg, 3.00 mmol). The mixture was gradually warmed to room temperature and allowed to stir for 1 h. The solvent was removed in vacuo and the residue was purified by column chromatography (silica gel, hexane/EtOAc = 2/1) to afford aldehyde **s4a** (530 mg, 86%) as a white solid.

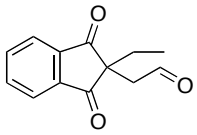
Mp. 162–164 °C.

IR (KBr) 3427, 2974, 2849, 2729, 1740, 1710, 1598, 1451, 1393, 1375, 1336, 1286, 1199, 1158, 1091, 1024, 1006, 961, 908, 761 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (s, 3H), 3.22 (s, 2H), 7.82–7.91 (m, 2H), 7.95–8.04 (m, 2H), 9.52 (brs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 48.9, 50.3, 123.5, 135.5, 140.5, 198.1, 202.4.

Anal. Calcd for $C_{13}H_{10}Cl_2O_3$: C, 54.76; H, 3.54. Found: C, 54.51; H, 3.76.



2-(2-Ethyl-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)acetaldehyde (**s4b**).

White solid.

Mp. 155–157 °C.

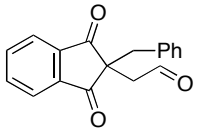
Yield: 85% (from 2-ethyl-1*H*-indene-1,3(2*H*)-dione[2]).

IR (KBr) 2916, 2835, 2729, 1743, 1713, 1597, 1439, 1394, 1382, 1360, 1330, 1258, 1188, 1159, 984, 946, 895, 790 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 0.77 (t, 3H, *J* = 7.2 Hz), 1.76 (q, 2H, *J* = 7.2 Hz), 3.23 (s, 2H), 7.82–7.89 (m, 2H), 7.95–8.02 (m, 2H), 9.53 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 8.9, 28.8, 47.9, 54.3, 123.1, 135.4, 141.6, 198.2, 202.6.

Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.03; H, 5.41.



2-(2-Benzyl-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)acetaldehyde (**s4c**).

Pale yellow solid.

Mp. 102–104 °C.

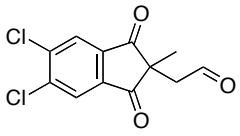
Yield: 94% (from **s2**).

IR (KBr) 3434, 3031, 2844, 2734, 1744, 1708, 1599, 1494, 1455, 1383, 1358, 1330, 1284, 1250, 1208, 1028, 964, 925, 764 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 3.02 (s, 2H), 3.31 (s, 2H), 6.86–6.93 (m, 2H), 6.97–7.08 (m, 2H), 9.52 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 41.7, 48.7, 55.6, 122.7, 127.1, 128.1, 129.7, 13.8, 135.1, 141.9, 197.8, 202.2.

Anal. Calcd for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.42; H, 5.21.



2-(5,6-Dichloro-2-methyl-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)acetaldehyde (**s4d**).

White solid.

Mp. 224–226 °C.

Yield: 92% (from commercially available 4,5-dichlorophthalic acid).

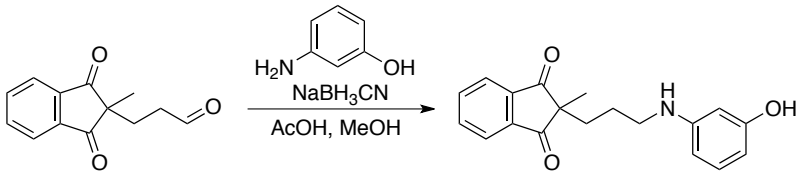
IR (neat) 2877, 2361, 1753, 1711, 1581, 1455, 1392, 1379, 1303, 1280, 1195, 1014, 969, 909, 871 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 3H), 3.27 (s, 2H), 8.06 (s, 2H), 9.49 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 49.3, 50.5, 125.4, 139.3, 140.8, 198.1, 200.2.

Anal. Calcd for $C_{18}H_{12}Cl_2O_3$: C, 62.27; H, 3.48. Found: C, 62.44; H, 3.67.

Scheme S4. General synthetic route to secondary amine **1**. Preparation of **1ac** is shown as a representative example.



5a **1ac**

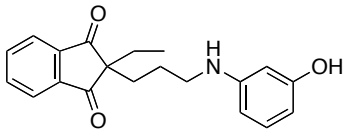
To a solution of **5a** (100 mg, 0.46 mmol) in MeOH (10.0 mL) and AcOH (1 drop) were successively added 3-aminophenol (54.7 mg, 0.501 mmol) and $NaBH_3CN$ (23.4 mg, 0.372 mmol) at 0 °C. After being stirred for 2 h at room temperature, the reaction was stopped by addition of H_2O. The crude mixture was extracted with CH_2Cl_2 (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by preparative TLC (hexane/EtOAc = 1/1) to afford **1ac** (58.7 mg, 42%) as a brown oil.

IR (neat) 3412, 3060, 2931, 2868, 1740, 1696, 1594, 1505, 1454, 1375, 1335, 1288, 1048, 983, 912, 829 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) d 1.28 (s, 3H), 1.31–1.42 (m, 2H), 1.86–1.95 (m, 2H), 2.91 (t, 2H, *J* = 6.8 Hz), 6.01 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.05 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.18 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.92 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.82–7.90 (m, 2H), 7.93–8.00 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 24.9, 32.6, 43.8, 53.7, 99.8, 104.6, 105.4, 123.4, 130.0, 136.0, 141.0, 149.4, 156.9, 204.8.

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.93; H, 5.96; N, 4.47.



2-Ethyl-2-(3-(3-hydroxyphenylamino)propyl)-1*H*-indene-1,3(2*H*)-dione (**1b**).

Brown oil.

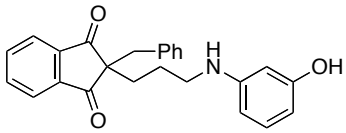
Yield: 49%.

IR (neat) 3402, 3020, 2965, 2934, 2876, 1739, 1702, 1594, 1497, 1459, 1341, 1260, 1184, 1159, 967, 894, 827 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 0.70 (t, 3H, *J* = 7.6 Hz), 1.28–1.40 (m, 2H), 1.82–1.97 (m, 4H), 2.96 (t, 2H, *J* = 6.8 Hz), 5.99 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.08 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.14 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.96 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.82–7.90 (m, 2H), 7.94–8.02 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 9.1, 24.8, 28.5, 31.9, 43.8, 58.6, 99.7, 104.5, 105.4, 123.0, 130.0, 135.9, 142.2, 149.5, 157.0, 205.1.

Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.10; H, 6.73; N, 4.19.



2-Benzyl-2-(3-(3-hydroxyphenylamino)propyl)-1*H*-indene-1,3(2*H*)-dione (**1c**).

Yellow amorphous.

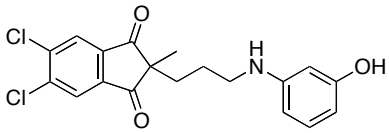
Yield: 48%.

IR (neat) 3403, 3030, 2921, 2852, 1739, 1703, 1595, 1496, 1454, 1339, 1249, 1183, 1159, 938, 829, 758 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.32–1.44 (m, 2H), 1.99–2.10 (m, 2H), 2.98 (t, 2H, *J* = 6.8 Hz), 3.13 (s, 2H), 6.06 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.13 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.19 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.90–7.05 (m, 6H), 7.63–7.91 (m, 2H), 7.75–7.82 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 32.7, 41.6, 43.9, 60.0, 99.5, 104.4, 105.7, 122.7, 126.7, 128.0, 129.7, 130.2, 135.2, 135.6, 142.5, 149.5, 156.8, 204.2.

Anal. Calcd for $C_{25}H_{23}NO_3$: C, 77.90; H, 6.01; N, 3.63. Found: C, 77.76; H, 6.25; N, 3.79.



5,6-Dichloro-2-(3-(3-hydroxyphenylamino)propyl)-2-methyl-1*H*-indene-1,3(2*H*)-dione (**1d**).

Brown oil.

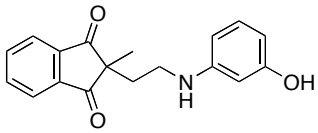
Yield: 33%.

IR (neat) 3393, 2924, 2852, 2355, 2336, 1744, 1712, 1579, 1496, 1456, 1376, 1299, 1159, 984, 757 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 3H), 1.33–1.43 (m, 2H), 1.87–1.97 (m, 2H), 2.96 (t, 2H, *J* = 6.8 Hz), 5.99 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.08 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.17 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.96 (dd, 1H, *J* = 8.0, 8.0 Hz), 8.04 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 25.0, 32.8, 43.8, 54.1, 99.6, 104.6, 105.8, 125.2, 130.1, 139.7, 141.4, 149.3, 156.7, 202.2.

Anal. Calcd for $C_{19}H_{17}Cl_2NO_3$: C, 60.33; H, 4.53; N, 3.70. Found: C, 60.14; H, 4.72; N, 3.86.



2-(2-(3-Hydroxyphenylamino)ethyl)-2-methyl-1*H*-indene-1,3(2*H*)-dione (**s5a**).

Yellow amorphous.

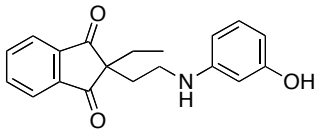
Yield: 54%.

IR (neat) 3393, 3019, 2968, 2929, 2868, 1739, 1701, 1597, 1497, 1335, 1189, 1040, 979, 758 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 3H), 2.21 (t, 2H, *J* = 6.8 Hz), 2.96 (t, 2H, *J* = 6.8 Hz), 5.84 (brs, 1H), 5.94 (d, 1H, *J* = 8.0 Hz), 6.10 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.87 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.73–7.80 (m, 2H), 7.87–7.95 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 34.9, 39.9, 53.1, 100.0, 105.0, 105.4, 123.1, 129.7, 135.4, 140.7, 148.3, 156.6, 204.2.

Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.12; H, 5.57; N, 4.98.



2-Ethyl-2-(2-(3-hydroxyphenylamino)ethyl)-1*H*-indene-1,3(2*H*)-dione (**s5b**).

Yellow oil.

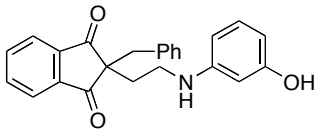
Yield: 52%.

IR (neat) 3393, 2965, 2924, 2359, 1739, 1700, 1595, 1397, 1458, 1339, 1252, 1184, 1159, 967, 830 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 0.71 (t, 3H, *J* = 7.6 Hz), 1.88 (q, 2H, *J* = 7.6 Hz), 2.20 (t, 2H, *J* = 6.8 Hz), 2.93 (t, 2H, *J* = 6.8 Hz), 5.81 (dd, 1H, *J* = 2.0, 2.0 Hz), 5.92 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.09 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.87 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.72–7.80 (m, 2H), 7.88–7.94 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 9.0, 28.8, 34.7, 39.8, 57.7, 99.5, 104.8, 105.5, 122.8, 129.9, 135.6, 142.2, 148.6, 156.6, 204.5.

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.66; H, 6.46; N, 4.31.



2-Benzyl-2-(2-(3-hydroxyphenylamino)ethyl)-1*H*-indene-1,3(2*H*)-dione (**s5c**).

Yellow oil.

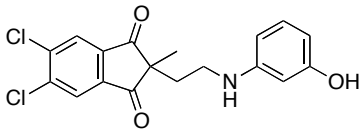
Yield: 89%.

IR (neat) 3394, 3030, 2921, 1737, 1701, 1595, 1496, 1455, 1438, 1358, 1250, 1202, 1160, 926, 830, 756 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 2.30 (t, 2H, *J* = 6.8 Hz), 2.92 (t, 2H, *J* = 6.8 Hz), 3.14 (s, 2H), 5.85 (brs, 1H), 5.88 (d, 1H, *J* = 8.0 Hz), 6.15 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.84 (dd, 1H, *J* = 8.0, 8.0 Hz), 6.88–7.04 (m, 5H), 7.49–7.58 (m, 2H), 7.66–7.72 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 35.3, 37.0, 41.8, 59.0, 99.5, 104.8, 105.5, 122.5, 126.8, 128.0, 129.8, 130.0, 134.9, 135.3, 142.3, 148.6, 156.6, 203.8.

Anal. Calcd for $C_{24}H_{21}NO_3$: C, 77.61; H, 5.70; N, 3.77. Found: C, 77.46; H, 5.88; N, 3.51.



5,6-Dichloro-2-(2-(3-hydroxyphenylamino)ethyl)-2-methyl-1*H*-indene-1,3(2*H*)-dione (**s5d**).

Pale orange amorphous.

Yield: 70%.

IR (neat) 3391, 2930, 2859, 1708, 1582, 1497, 1452, 1375, 1301, 1237, 1041, 991, 909, 833 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 3H), 2.21 (t, 2H, J = 6.8 Hz), 2.92 (t, 2H, J = 6.8 Hz), 5.88 (brs, 1H), 5.92 (d, 1H, J = 8.0 Hz), 6.16 (dd, 1H, J = 2.0, 8.0 Hz), 6.86 (dd, 1H, J = 8.0, 8.0 Hz), 7.87 (s, 2H).

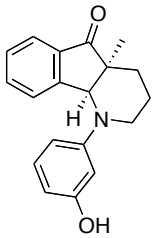
^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 35.9, 40.4, 54.5, 100.1, 10.5.7, 105.9, 125.0, 129.9, 139.7, 140.2, 147.8, 156.5, 206.2.

Anal. Calcd for $C_{18}H_{15}Cl_2NO_3$: C, 59.36; H, 4.15; N, 3.85. Found: C, 59.42; H, 4.30; N, 3.79.

2. Synthesis of tricyclic piperidine and pyrrolidine derivatives.

General procedure of the reductive amination.

To a mixture of amine **1** or **s5** (0.10 mmol), Hantzsch ester (0.15 mmol), activated MS3A (120 mg), and chiral phosphoric acid (0.01 mmol, 10 mol%) was added toluene (2.0 mL) at appropriate temperature. After completion of the reaction, the crude material was filtered through Celite® pad and the resulting filtrate was concentrated in vacuo. The residue was purified by preparative TLC to give cyclic amine derivatives **2** or **7**.



(4a*S*,9b*S*)-1-(3-Hydroxyphenyl)-4a-methyl-2,3,4,4a-tetrahydro-1*H*-indeno[1,2-*b*]pyridin-5(9b*H*)-one (**2ac**).

Yellow amorphous.

Yield: 87%, 94% ee.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 254 nm, retention time (min) = 28.9 (3.0%), 32.0 (97.0%)].

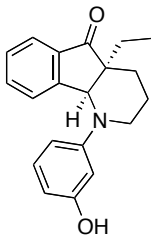
$[\alpha]_D^{20}$ +171 (c 0.610, $CHCl_3$).

IR (neat) 3364, 2934, 2855, 1698, 1603, 1497, 1463, 1322, 1203, 1011, 989, 909, 764 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.24–1.38 (m, 1H), 1.39 (s, 3H), 1.47–1.80 (m, 3H), 2.84–2.94 (m, 1H), 3.48–3.60 (m, 1H), 5.10 (s, 1H), 5.99 (brs, 1H), 6.35 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.55 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.59 (dd, 1H, *J* = 2.0, 8.0 Hz), 7.13 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.31 (d, 1H, *J* = 7.6 Hz), 7.39 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.49 (ddd, 1H, *J* = 0.8, 7.6, 7.6 Hz), 7.79 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 20.6, 31.7, 42.7, 50.1, 63.5, 101.1, 105.0, 106.5, 124.2, 125.4, 128.6, 130.4, 134.8, 135.7, 152.3, 152.5, 157.1, 208.4.

Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.68; H, 6.64; N, 4.51.



(4a*S*,9b*S*)-4a-Ethyl-1-(3-hydroxyphenyl)-2,3,4,4a-tetrahydro-1*H*-indeno[1,2-*b*]pyridin-5(9b*H*)-one (**2b**).

Yellow amorphous.

Yield: 52%, 83% ee.

HPLC [DAICEL CHIRALPAK® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 20/1, 1.0 mL/min, 254 nm, retention time (min) = 16.3 (91.4%), 30.6 (8.6%)].

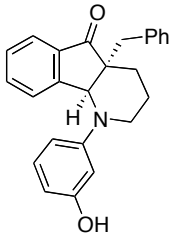
$[\alpha]_D^{20}$ +149 (c 0.340, $CHCl_3$).

IR (neat) 3355, 2959, 2937, 2877, 2855, 1692, 1603, 1498, 1462, 1391, 1322, 1268, 1197, 1150, 998, 970, 906, 820 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, 3H, *J* = 6.8 Hz), 1.18–1.28 (m, 1H), 1.60–1.95 (m, 6H), 2.90–3.01 (m, 1H), 3.45 (ddd, 1H, *J* = 6.8, 6.8, 14.0 Hz), 5.29 (brs, 1H), 5.36 (s, 1H), 6.32 (dd, 1H, *J* = 2.4, 8.0 Hz), 6.53 (dd, 1H, *J* = 2.4, 2.4 Hz), 6.62 (dd, 1H, *J* = 2.4, 8.0 Hz), 7.16 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.36 (dd, 1H, *J* = 0.8, 7.6 Hz), 7.41 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.51 (ddd, 1H, *J* = 0.8, 7.6, 7.6 Hz), 7.79 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 9.2, 19.8, 27.7, 30.6, 42.9, 54.6, 59.6, 100.7, 104.8, 106.2, 123.8, 125.5, 128.6, 130.4, 134.8, 136.6, 152.2, 153.7, 157.1, 208.9.

Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.39; H, 6.74; N, 4.32.



(4a*R*,9b*S*)-4a-Benzyl-1-(3-hydroxyphenyl)-2,3,4,4a-tetrahydro-1*H*-indeno[1,2-*b*]pyridin-5(9b*H*)-one (**2c**).

Yellow amorphous.

Yield: 16%, 79% ee.

HPLC [DAICEL CHIRALPAK® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 290 nm, retention time (min) = 11.2 (89.7%), 15.7 (10.3%)].

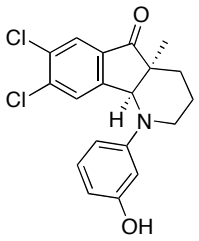
$[\alpha]_D^{20}$ +112 (c 0.220, $CHCl_3$).

IR (neat) 2283, 3028, 2938, 2855, 1697, 1603, 1496, 1455, 1392, 1324, 1262, 1197, 1053, 998, 962, 909, 821 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.36–1.50 (m, 1H), 1.62–1.90 (m, 3H), 2.83–2.95 (m, 1H), 2.94 (d, 1H, *J* = 13.6 Hz), 3.45 (d, 1H, *J* = 13.6 Hz), 3.53–3.62 (m, 1H), 5.18 (brs, 1H), 5.22 (s, 1H), 6.32 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.40 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.49 (dd, 1H, *J* = 2.0, 8.0 Hz), 7.07–7.22 (m, 7H), 7.33 (d, 1H, *J* = 7.6 Hz), 7.40 (ddd, 1H, *J* = 1.2, 7.6, 7.6 Hz), 7.76 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 31.8, 38.7, 42.7, 55.7, 58.4, 101.1, 105.1, 106.6, 124.1, 125.2, 126.5, 128.3, 128.4, 130.4, 130.6, 134.6, 135.5, 137.9, 152.2, 153.0, 157.0, 207.3.

Anal. Calcd for $C_{25}H_{23}NO_2$: C, 81.27; H, 6.27; N, 3.79. Found: C, 81.53; H, 6.13; N, 3.61.



(4a*S*,9b*S*)-7,8-Dichloro-1-(3-hydroxyphenyl)-4a-methyl-2,3,4,4a-tetrahydro-1*H*-indeno[1,2-*b*]pyridin-5(9b*H*)-one (**2e**).

Yellow amorphous.

Yield: 87%, 98% ee.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 0.5 mL/min, 330 nm, retention time (min) = 16.8 (99.0%), 18.1 (1.0%)].

$[\alpha]_D^{20}$ +292 (c 0.850, $CHCl_3$).

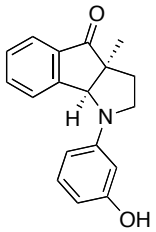
IR (neat) 3383, 2937, 2855, 1707, 1596, 1497, 1456, 1391, 1284, 1204, 1011, 956, 908, 826, 801 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.29–1.38 (m, 1H), 1.40 (s, 3H), 1.56–1.84 (m, 3H), 2.87–2.97 (m, 1H), 3.52–3.64 (m, 1H), 4.90 (brs, 1H), 5.09 (s, 1H), 6.33 (dd, 1H, *J* =

2.0, 8.0 Hz), 6.50 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.59 (dd, 1H, *J* = 2.0, 8.0 Hz), 7.16 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.43 (s, 1H), 7.87 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 20.5, 31.6, 42.8, 50.6, 63.1, 101.2, 105.5, 106.7, 125.7, 127.3, 130.6, 133.7, 135.3, 139.3, 151.3, 151.9, 157.0, 205.6.

Anal. Calcd for $C_{19}H_{17}Cl_2NO_2$: C, 63.00; H, 4.73; N, 3.87. Found: C, 62.86; H, 4.63; N, 3.64.



(3a*S*,8b*S*)-1-(3-Hydroxyphenyl)-3a-methyl-1,2,3,3a-tetrahydroindeno[1,2-*b*]pyrrol-4(8b*H*)-one (**7a**).

Yellow amorphous.

Yield: 81%, 81% ee.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 0.5 mL/min, 290 nm, retention time (min) = 14.7 (9.5%), 20.2 (90.5%)].

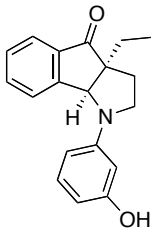
$[\alpha]_D^{20}$ +379 (c 0.840, $CHCl_3$).

IR (neat) 382, 2967, 2928, 2868, 1716, 1604, 1500, 1464, 1372, 1334, 1294, 1222, 1166, 1091, 1017, 969, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 3H), 1.90–2.01 (m, 1H), 2.18–2.21 (m, 1H), 3.36–3.57 (m, 2H), 4.99 (s, 1H), 6.31 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.39 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.50 (dd, 1H, *J* = 2.0, 8.0, 8.0 Hz), 7.16 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.44 (d, 1H, *J* = 7.6, 7.6 Hz), 7.55 (ddd, 1H, *J* = 1.2, 7.6, 7.6 Hz), 7.67 (d, 1H, *J* = 7.6 Hz), 7.77 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 35.3, 49.1, 56.4, 69.6, 100.2, 104.3, 106.0, 124.2, 126.7, 129.1, 130.3, 134.7, 135.5, 149.3, 152.9, 156.8, 206.8.

Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.16; H, 6.29; N, 5.15.



(3a*S*,8b*S*)-3a-Ethyl-1-(3-hydroxyphenyl)-1,2,3,3a-tetrahydroindeno[1,2-*b*]pyrrol-4(8b*H*)-one (**7b**).

Yellow amorphous.

Yield: 64%, 92% ee.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 254 nm, retention time (min) = 18.0 (3.9%), 39.0 (96.1%)].

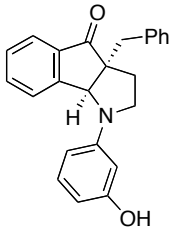
$[\alpha]_D^{20}$ +325 (c 0.640, $CHCl_3$).

IR (neat) 3360, 2965, 2929, 1697, 1604, 1500, 1462, 1363, 1336, 1296, 1219, 1167, 1011, 909, 822, 740 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, 3H, *J* = 7.6 Hz), 1.72–1.86 (m, 1H), 1.96–2.21 (m, 3H), 3.21–3.31 (m, 1H), 3.38–3.50 (m, 1H), 5.21 (s, 1H), 6.31 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.42 (brs, 1H), 6.51 (d, 1H, *J* = 8.0 Hz), 7.16 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.43 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.52 (ddd, 1H, *J* = 1.2, 7.6, 7.6 Hz), 7.66 (d, 1H, *J* = 7.6 Hz), 7.76 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9, 26.9, 34.5, 48.3, 61.1, 65.5, 100.4, 104.4, 106.1, 123.8, 126.7, 129.0, 130.2, 135.5, 135.7, 148.9, 153.2, 157.0, 207.9.

Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.63; H, 6.38; N, 4.86.



(3a*S*,8b*S*)-3a-Benzyl-1-(3-hydroxyphenyl)-1,2,3,3a-tetrahydroindeno[1,2-*b*]pyrrol-4(8b*H*)-one (**7c**).

Yellow amorphous.

Yield: 80%, 89% ee.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 254 nm, retention time (min) = 31.1 (5.4%), 39.5 (94.6%)].

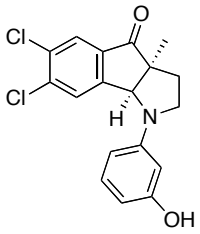
$[\alpha]_D^{20}$ +130 (c 0.240, $CHCl_3$).

IR (neat) 3382, 3028, 2930, 1698, 1604, 1499, 1455, 1366, 1294, 1224, 1099, 1015, 909, 822, 792 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 2.08–2.15 (m, 2H), 2.86 (d, 1H, *J* = 13.6 Hz), 3.27–3.39 (m, 2H), 3.51 (d, 1H, *J* = 13.6 Hz), 5.19 (s, 1H), 5.37 (brs, 1H), 6.28–6.35 (m, 2H), 6.41 (dd, 1H, *J* = 2.0, 8.4 Hz), 7.06–7.20 (m, 6H), 7.35 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.44 (ddd, 1H, *J* = 1.2, 7.6, 7.6 Hz), 7.56 (d, 1H, *J* = 7.6 Hz), 7.71 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 34.7, 38.8, 48.8, 61.9, 65.2, 99.9, 104.3, 105.7, 124.0, 126.5, 126.6, 128.4, 128.9, 130.0, 130.3, 134.9, 135.4, 137.4, 149.1, 153.4, 156.9, 206.1.

Anal. Calcd for $C_{24}H_{21}NO_2$: C, 81.10; H, 5.96; N, 3.94. Found: C, 81.37; H, 6.05; N, 3.88.



(3a*S*,8b*S*)-6,7-Dichloro-1-(3-hydroxyphenyl)-3a-methyl-1,2,3,3a-tetrahydroindeno[1,2-*b*]pyrrol-4(8b*H*)-one (**7d**).

Yellow amorphous.

Yield: 71%, 86% ee.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 254 nm, retention time (min) = 13.5 (7.2%), 18.0 (92.8%)].

$[\alpha]_D^{22}$ +377 (c 0.240, $CHCl_3$).

IR (neat) 3393, 2970, 2930, 2870, 1705, 1616, 1592, 1499, 1449, 1383, 1327, 1304, 1217, 1166, 1022, 956, 894, 823 cm^{-1}.

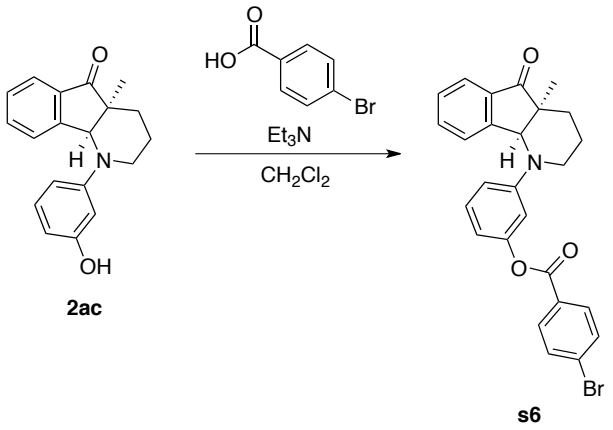
^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 3H), 1.91–2.02 (m, 1H), 2.04–2.18 (m, 1H), 3.37–3.55 (m, 2H), 4.92 (s, 1H), 5.44 (brs, 1H), 6.31–6.37 (m, 2H), 6.46 (dd, 1H, *J* = 2.0, 8.4 Hz), 7.18 (dd, 1H, *J* = 8.4, 8.4 Hz), 7.76 (s, 1H), 7.83 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 35.2, 49.2, 57.0, 69.0, 100.1, 104.9, 105.7, 125.6, 128.6, 130.5, 134.2, 134.2, 139.8, 148.9, 151.7, 157.0, 204.4.

Anal. Calcd for $C_{18}H_{15}Cl_2NO_2$: C, 62.08; H, 4.34; N, 4.02. Found: C, 61.79; H, 4.55; N, 3.92.

3. Determination of the absolute configuration.

Scheme S5. Transformation to *p*-bromobenzoate **s6**.



To a solution of **2ac** (13.9 mg, 0.048 mmol) in CH_2Cl_2 (1.0 mL) were successively added DMAP (11.9 mg, 0.0480 mmol), Et_3N (6.8 μL, 0.048 mmol), and 4-bromobenzoyl chloride (14.0 mg, 0.064 mmol) at 0 °C. After being stirred for 2 h at room temperature, the reaction was stopped by addition of saturated aqueous NH_4Cl at 0 °C. The crude mixture was extracted with CH_2Cl_2 (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by preparative TLC (hexane/EtOAc = 3/1) to afford **s6** (14.0 mg, 66%) as a white amorphous.

Colorless crystal (recrystallized from EtOH), which was subjected to X-ray crystal analysis.

Mp. 193–194 °C.

HPLC [DAICEL CHIRALCEL® OJ-H, ϕ 0.46 x 25 cm, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 254 nm, retention time (min) = 24.6 (6.3%), 39.1 (93.8%)].

$[\alpha]_D^{26}$ +216 (c 0.710, $CHCl_3$).

IR (neat) 3071, 2935, 2855, 1735, 1717, 1606, 1495, 1463, 1396, 1263, 1169, 1074, 1011, 987, 966, 936, 887 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.30–1.40 (m, 1H), 1.42 (s, 3H), 1.57–1.83 (m, 3H), 2.90–3.01 (m, 1H), 3.52–3.64 (m, 1H), 5.18 (s, 1H), 6.67 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.83 (dd, 1H, *J* = 2.0, 2.0 Hz), 6.94 (dd, 1H, *J* = 2.0, 8.0 Hz), 7.30–7.40 (m, 2H), 7.43 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.54 (ddd, 1H, *J* = 0.8, 7.6, 7.6 Hz), 7.62–7.69 (m, 2H), 7.81 (d, 1H, *J* = 7.6 Hz), 8.02–8.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 20.8, 31.6, 42.9, 50.1, 63.5, 107.1, 110.8, 111.4, 124.2, 125.3, 128.6, 128.7, 128.7, 130.2, 131.6, 131.9, 134.8, 135.9, 152.0, 152.1, 152.2, 164.5, 207.7.

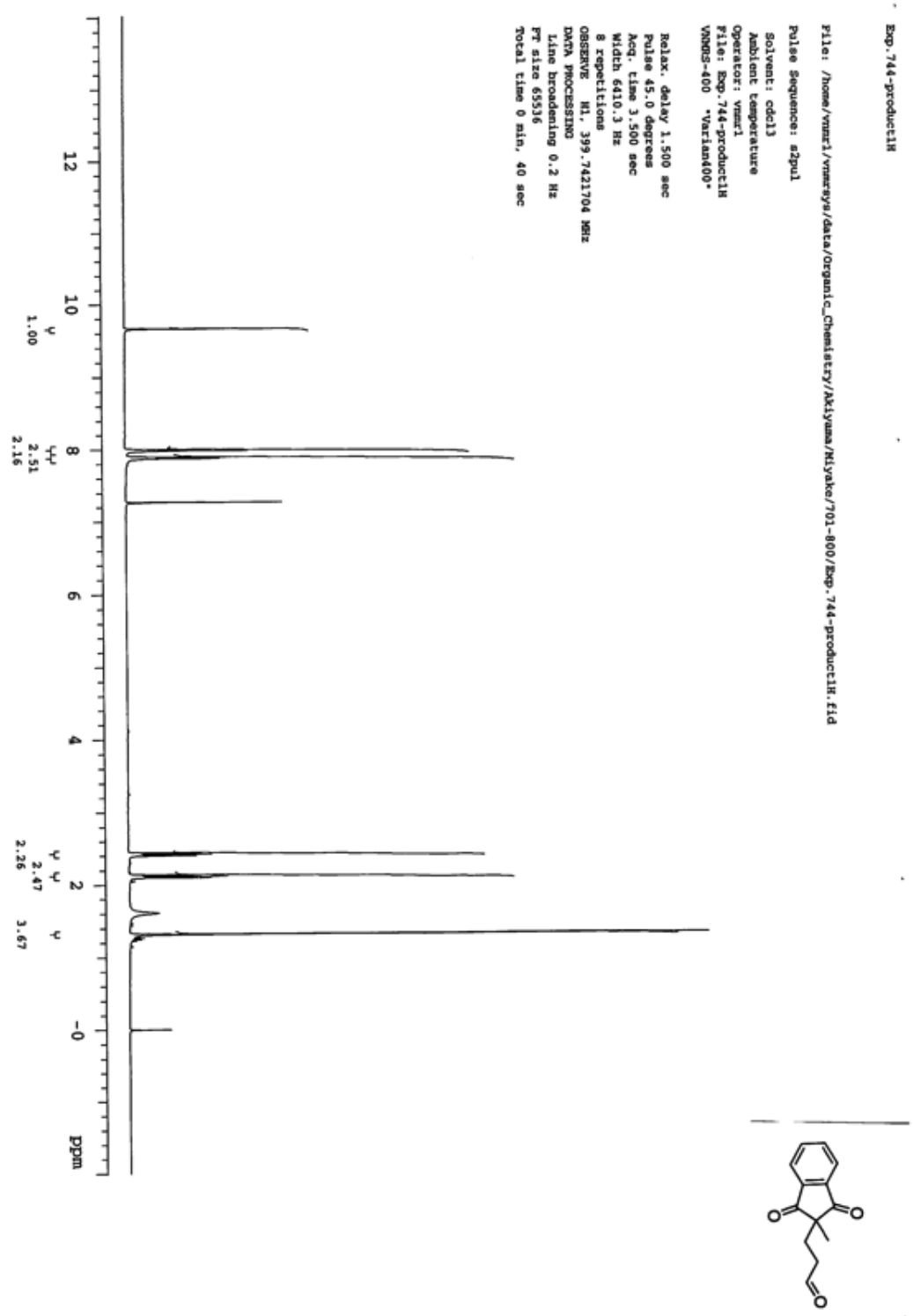
Anal. Calcd for $C_{26}H_{22}BrNO_3$: C, 65.55; H, 4.66; N, 2.94. Found: C, 65.71; H, 4.85; N, 3.05.

References

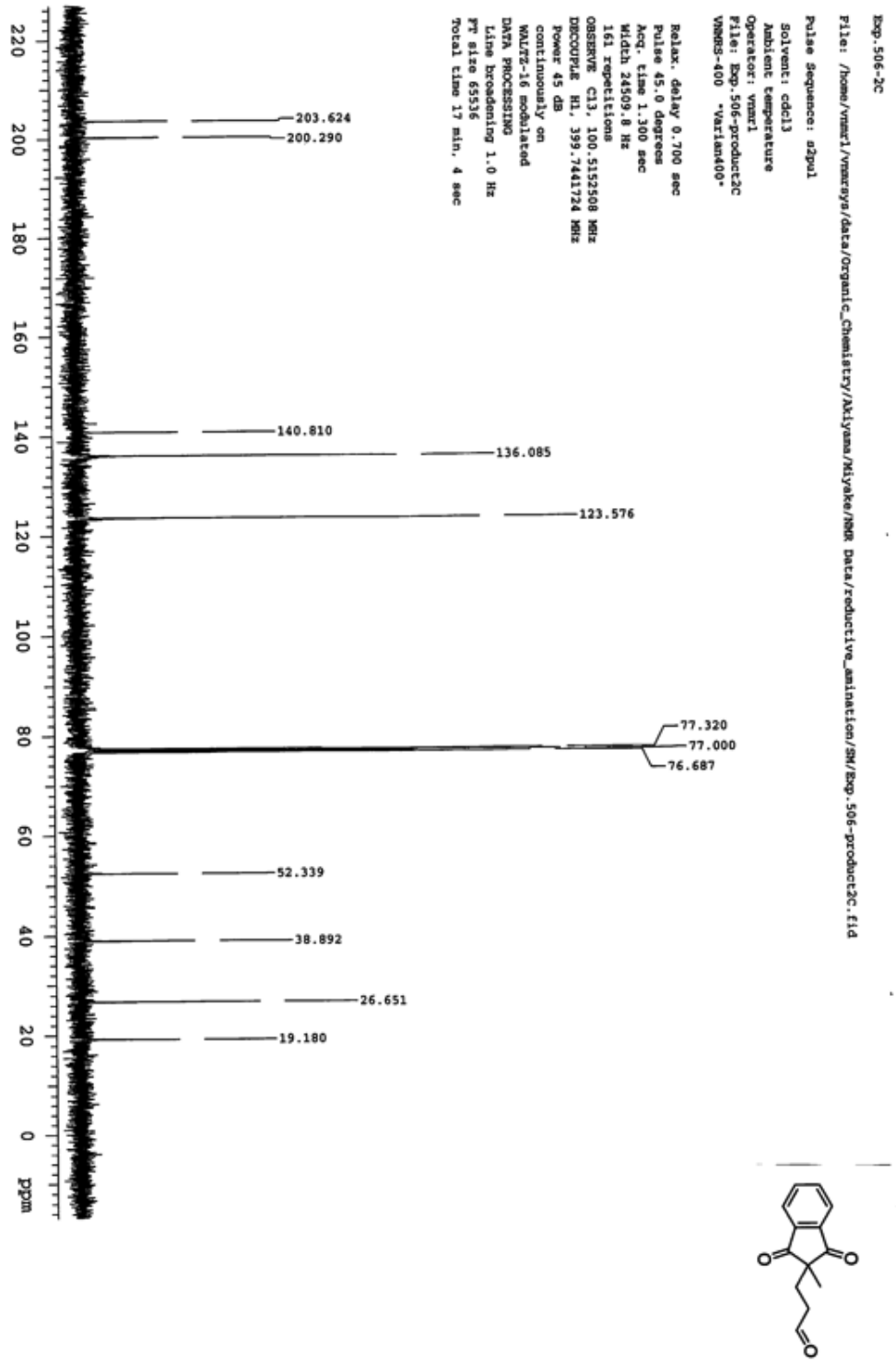
1) Agapiou, K.; Cauble, D. F.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 4528.

2) Mori, K.; Katoh, T.; Suzuki, T.; Noji, T.; Yamanaka, M.; Akiyama, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 9652.

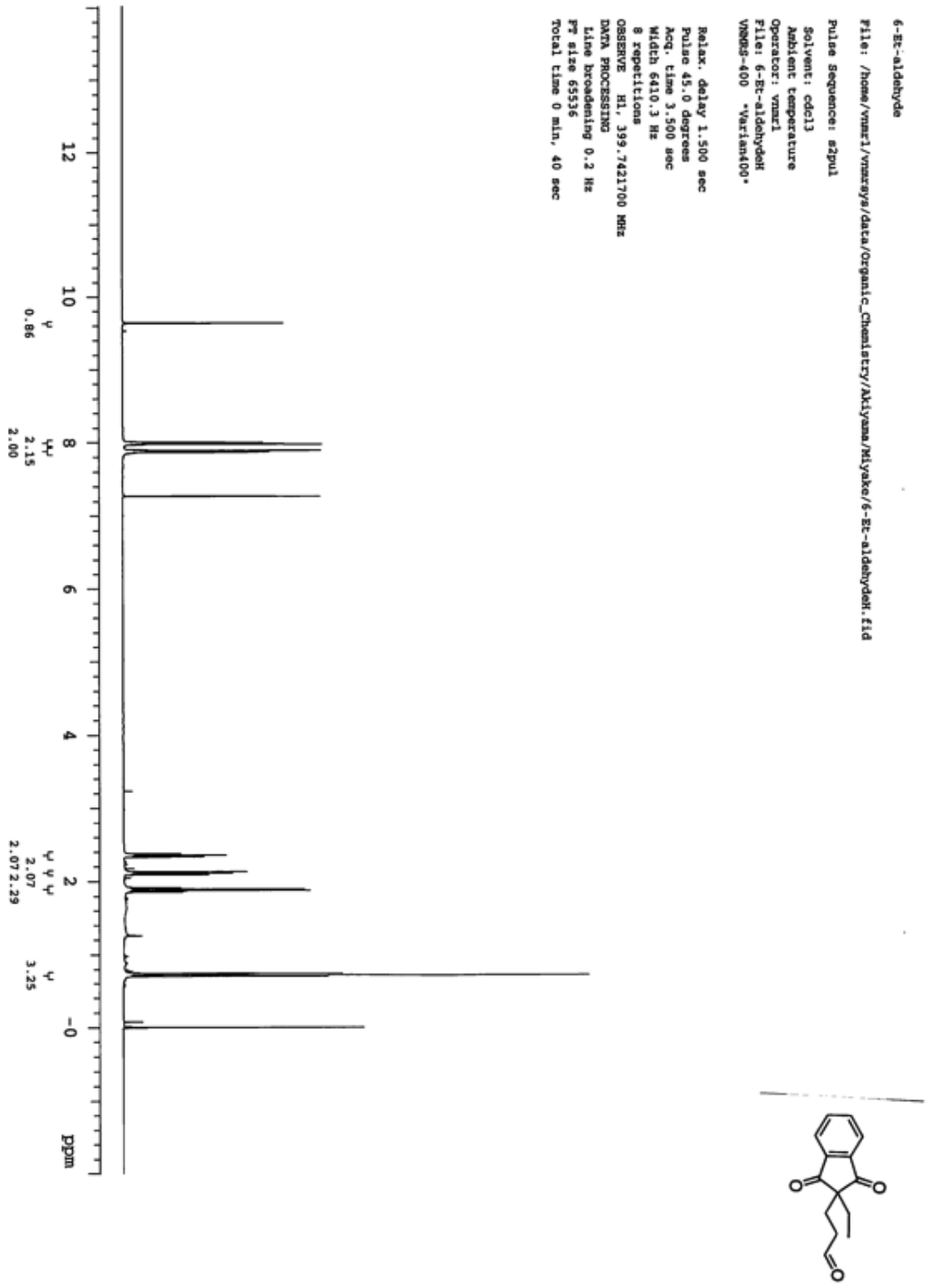
^{1}H NMR spectrum of **5a**.



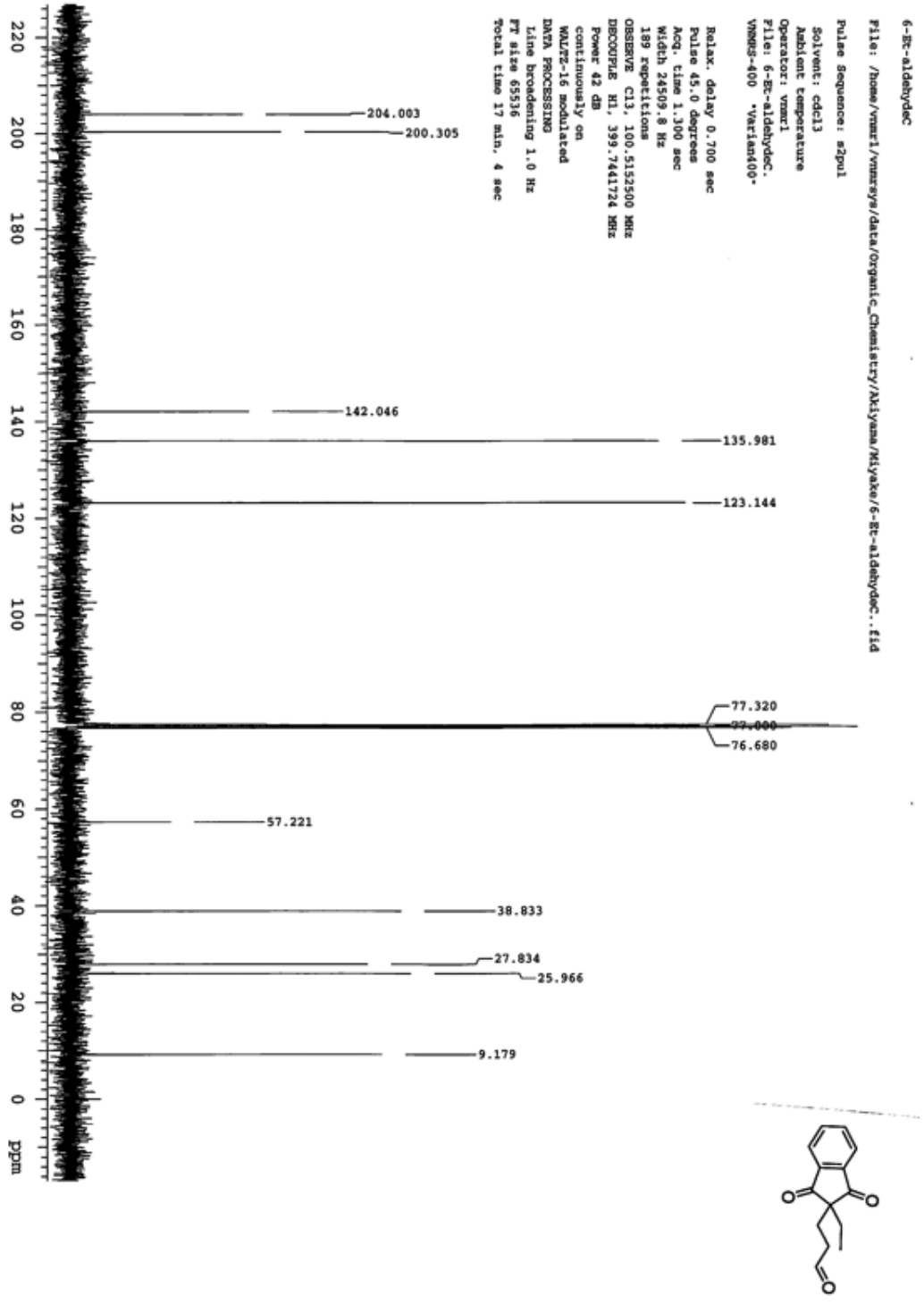
^{13}C NMR spectrum of **5a**.



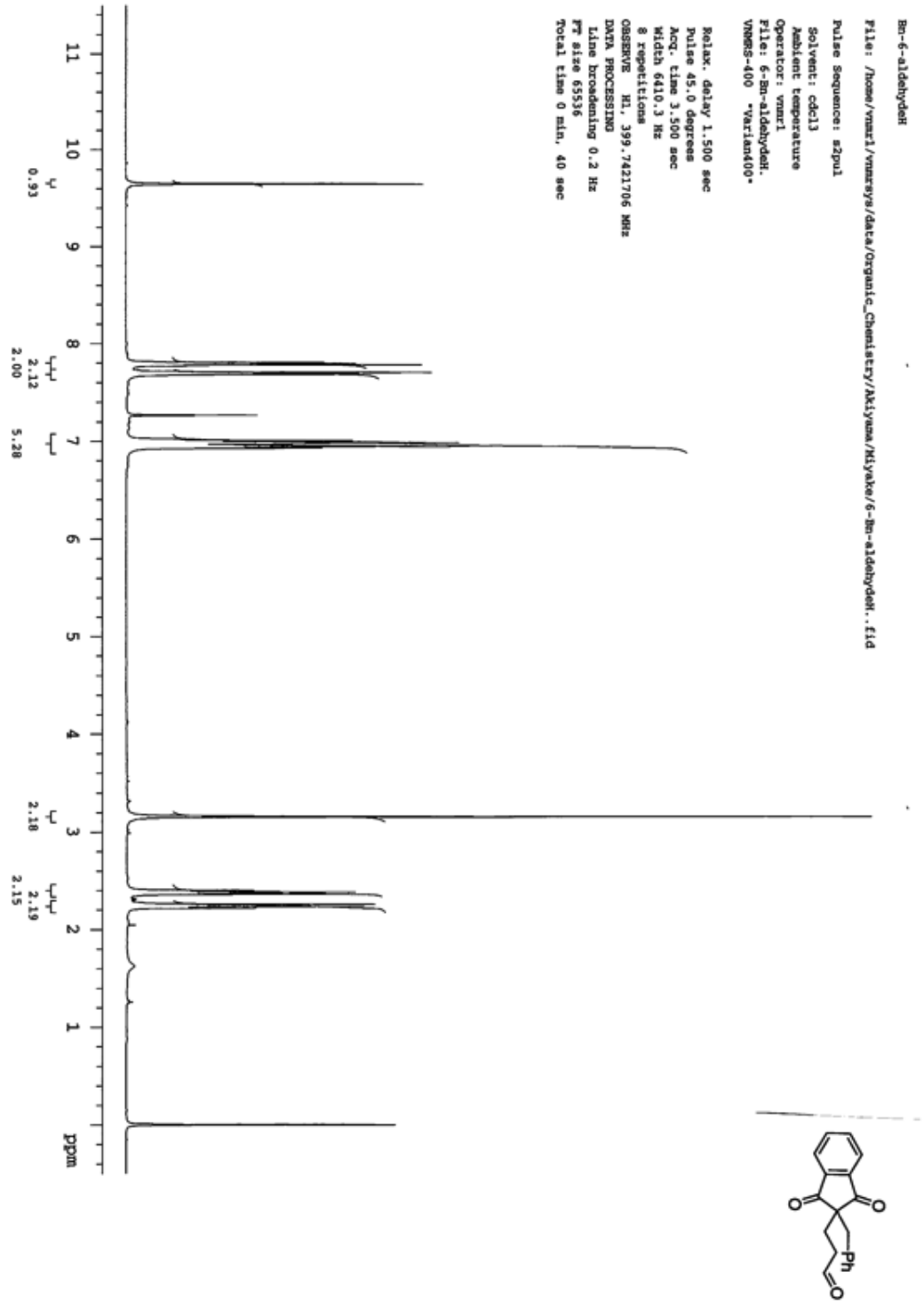
^{1}H NMR spectrum of **5b**.



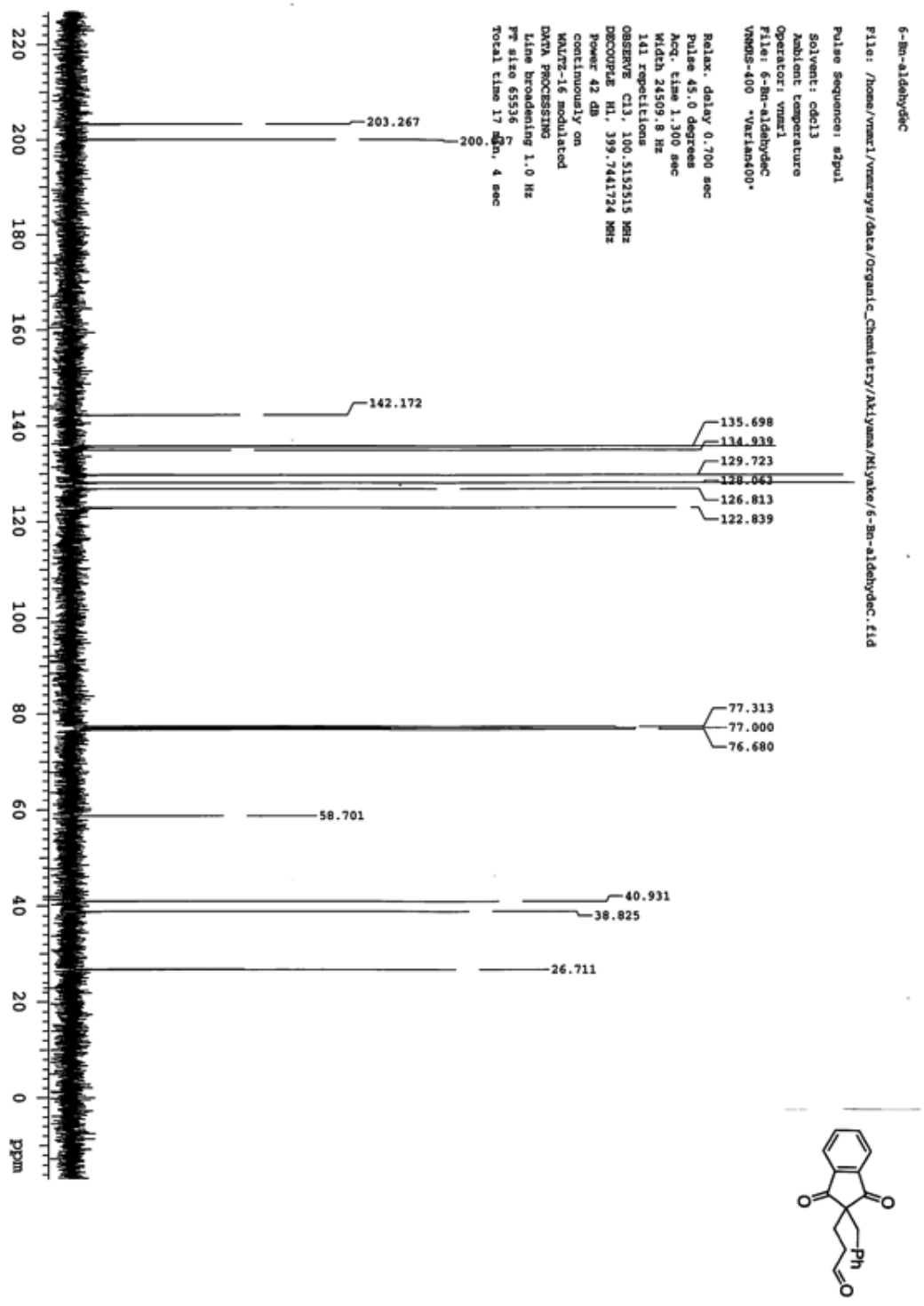
^{13}C NMR spectrum of **5b**.



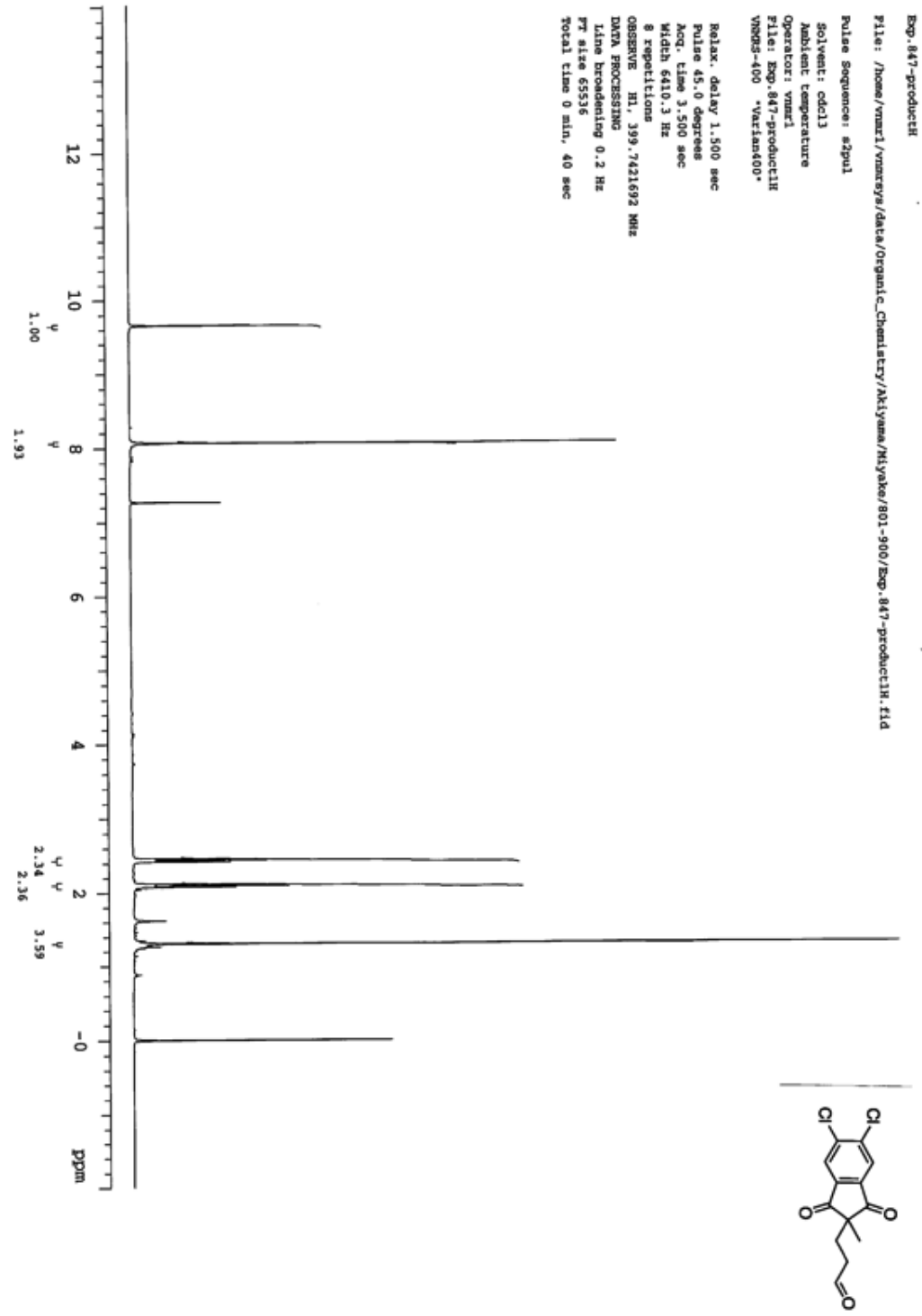
^{1}H NMR spectrum of **5c**.



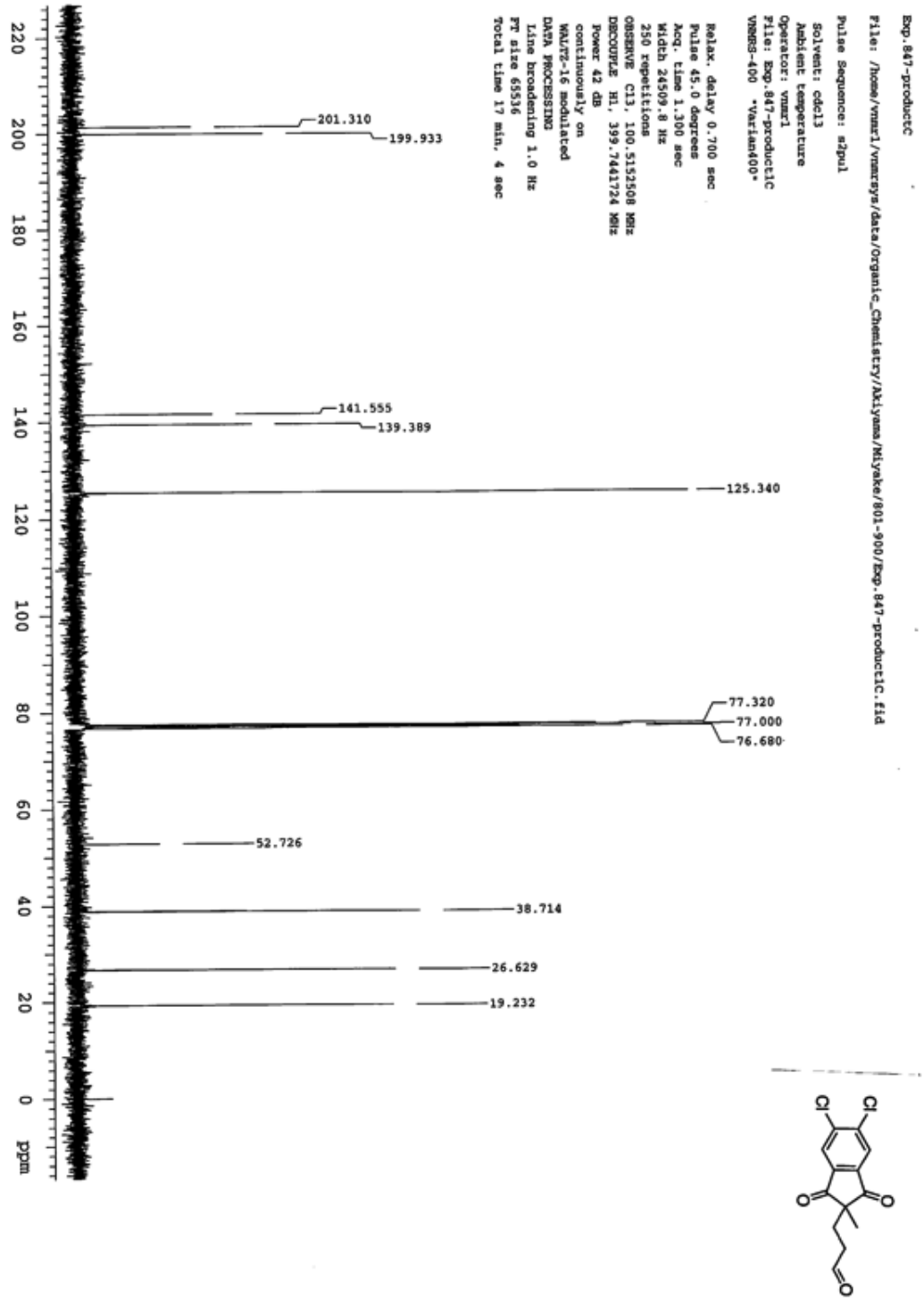
^{13}C NMR spectrum of **5c**.



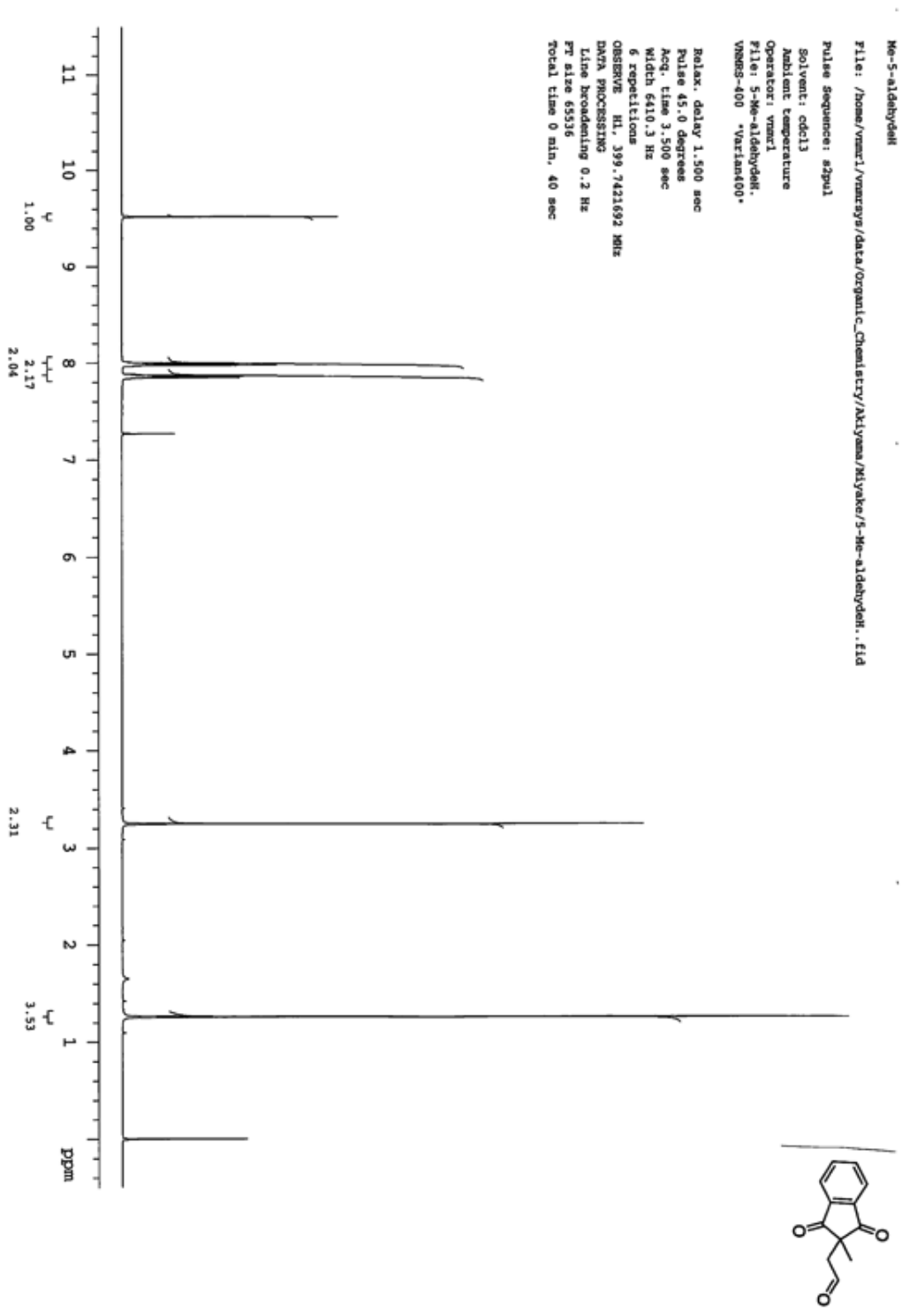
^{1}H NMR spectrum of **5d**.



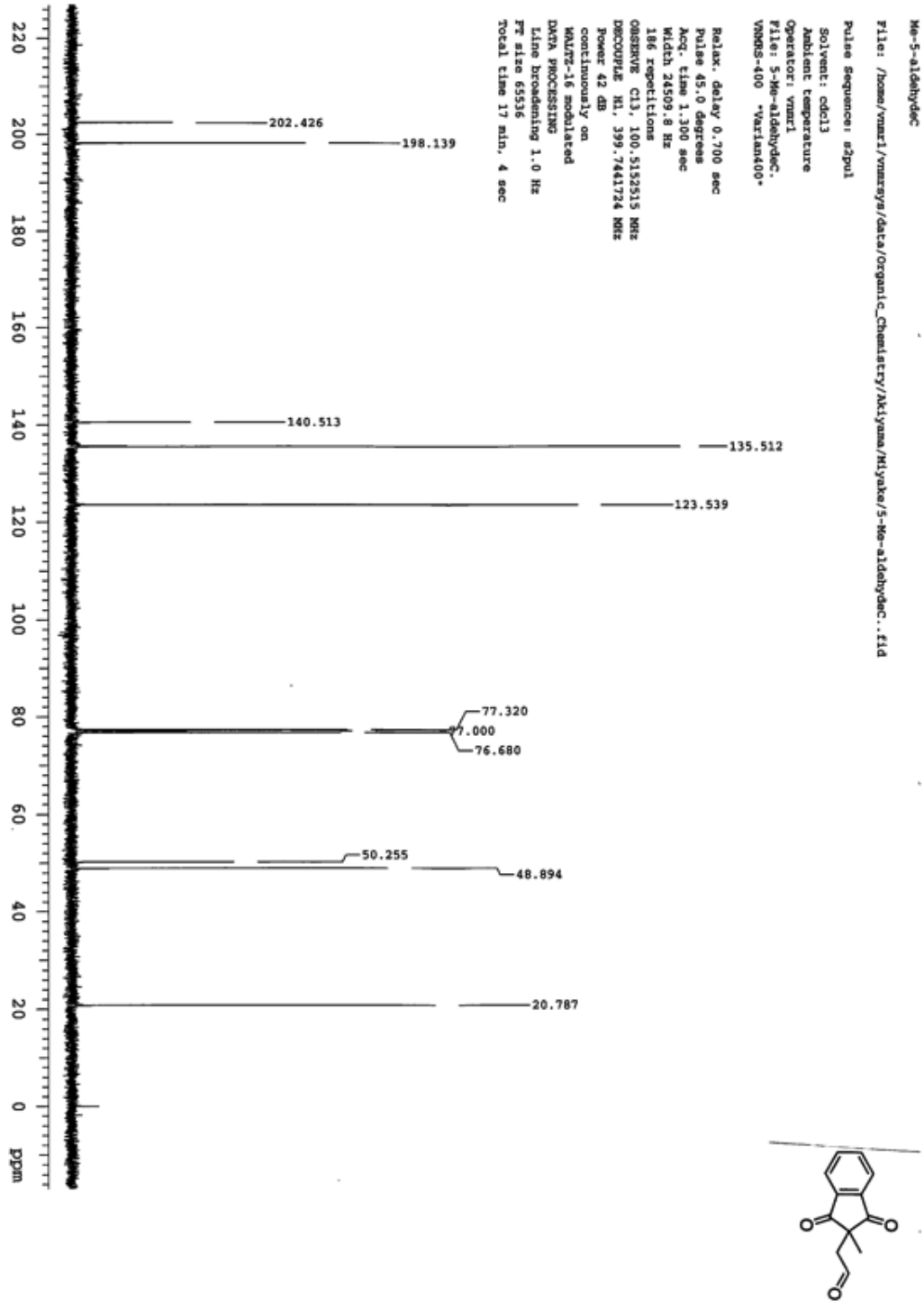
^{13}C NMR spectrum of **5d**.



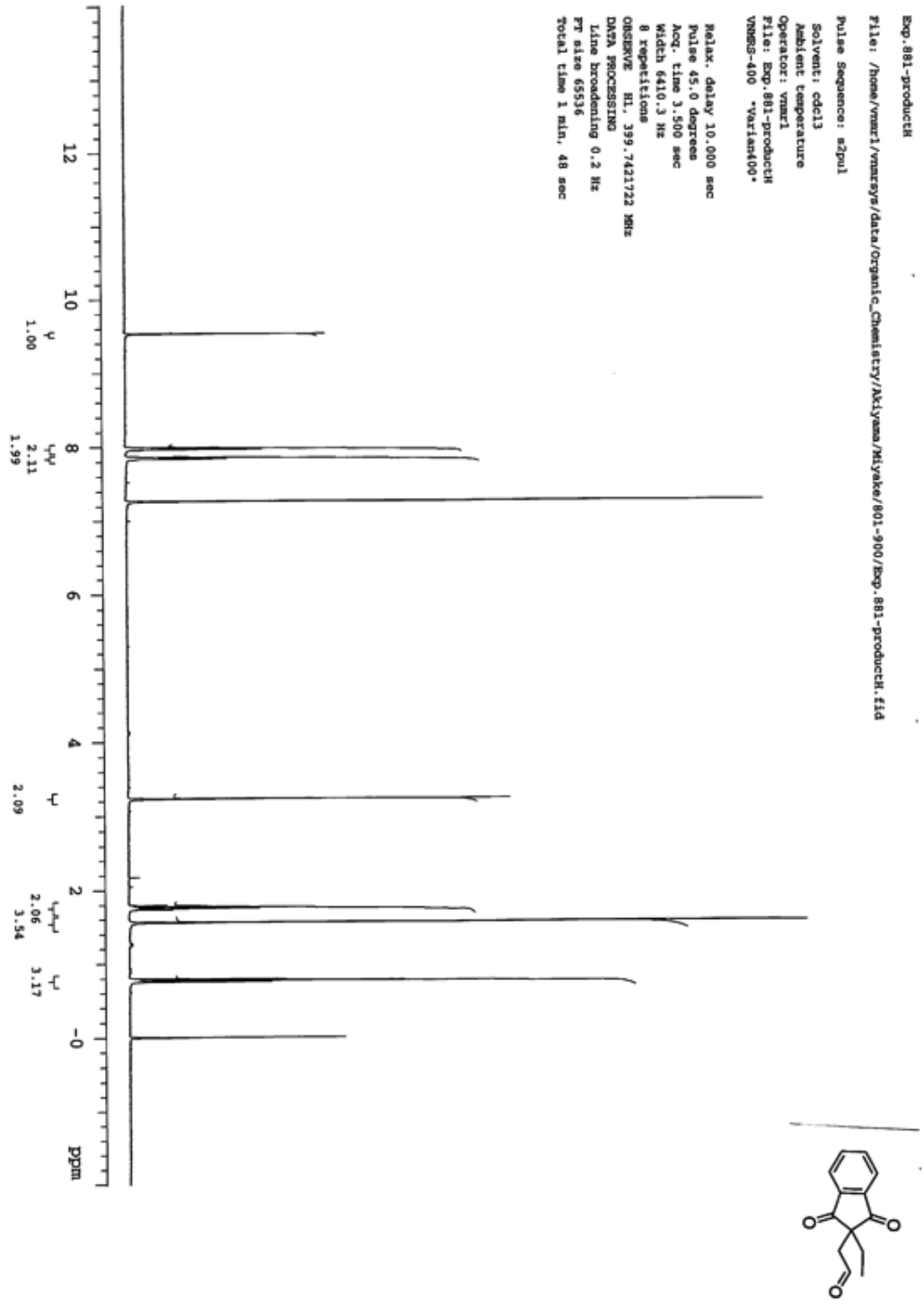
^{1}H NMR spectrum of **s4a**.



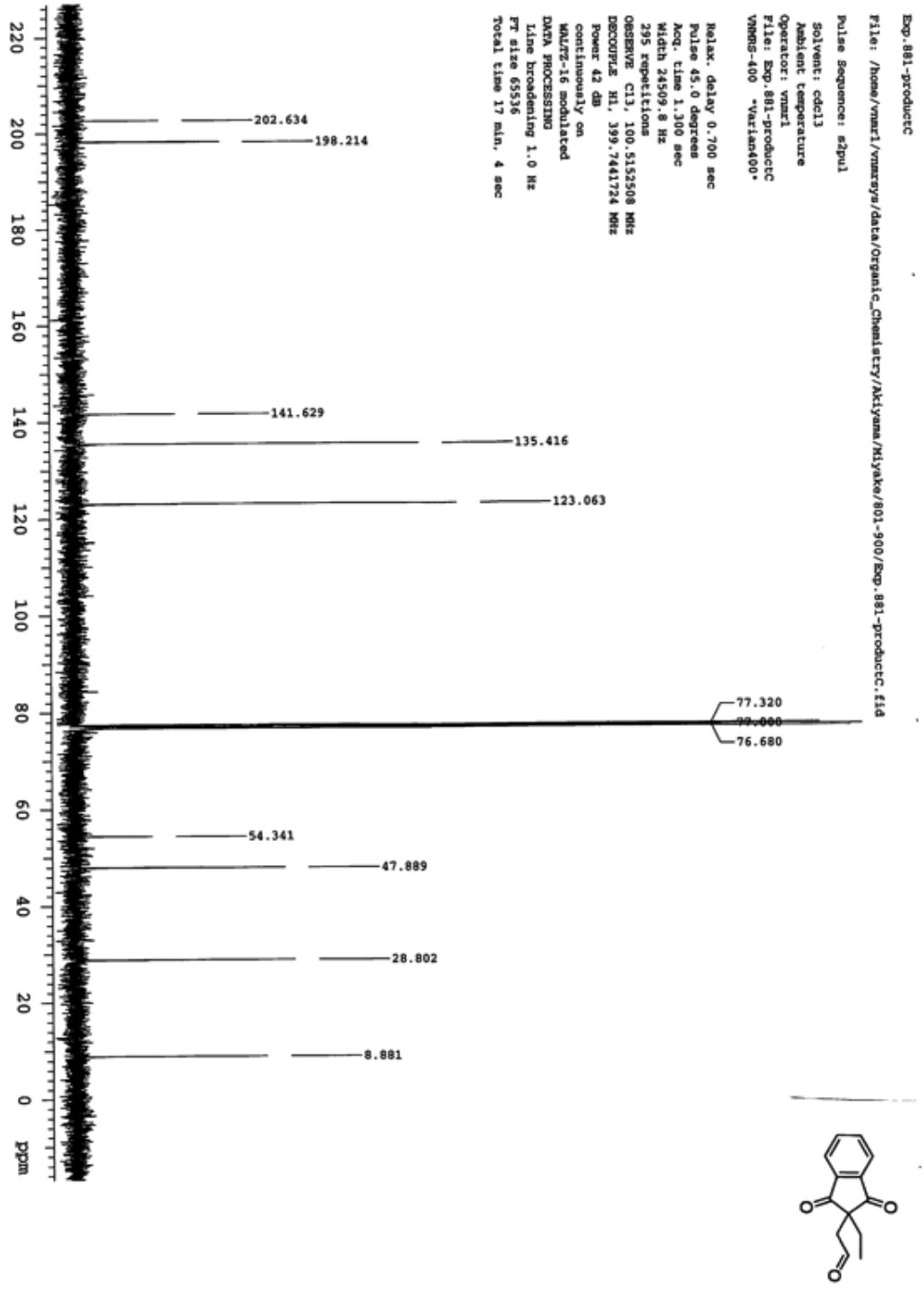
^{13}C NMR spectrum of **s4a**.



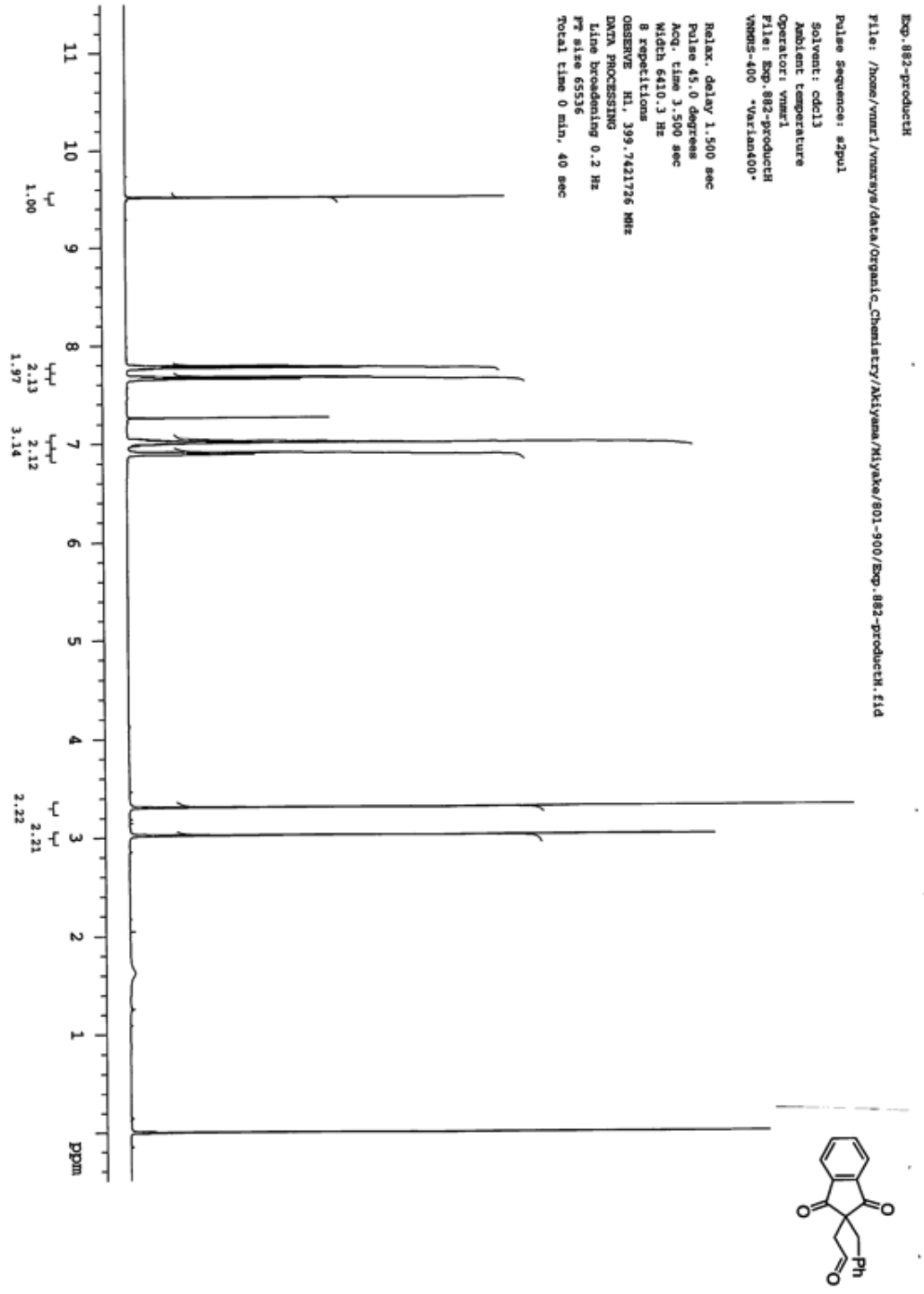
^{1}H NMR spectrum of **s4b**.



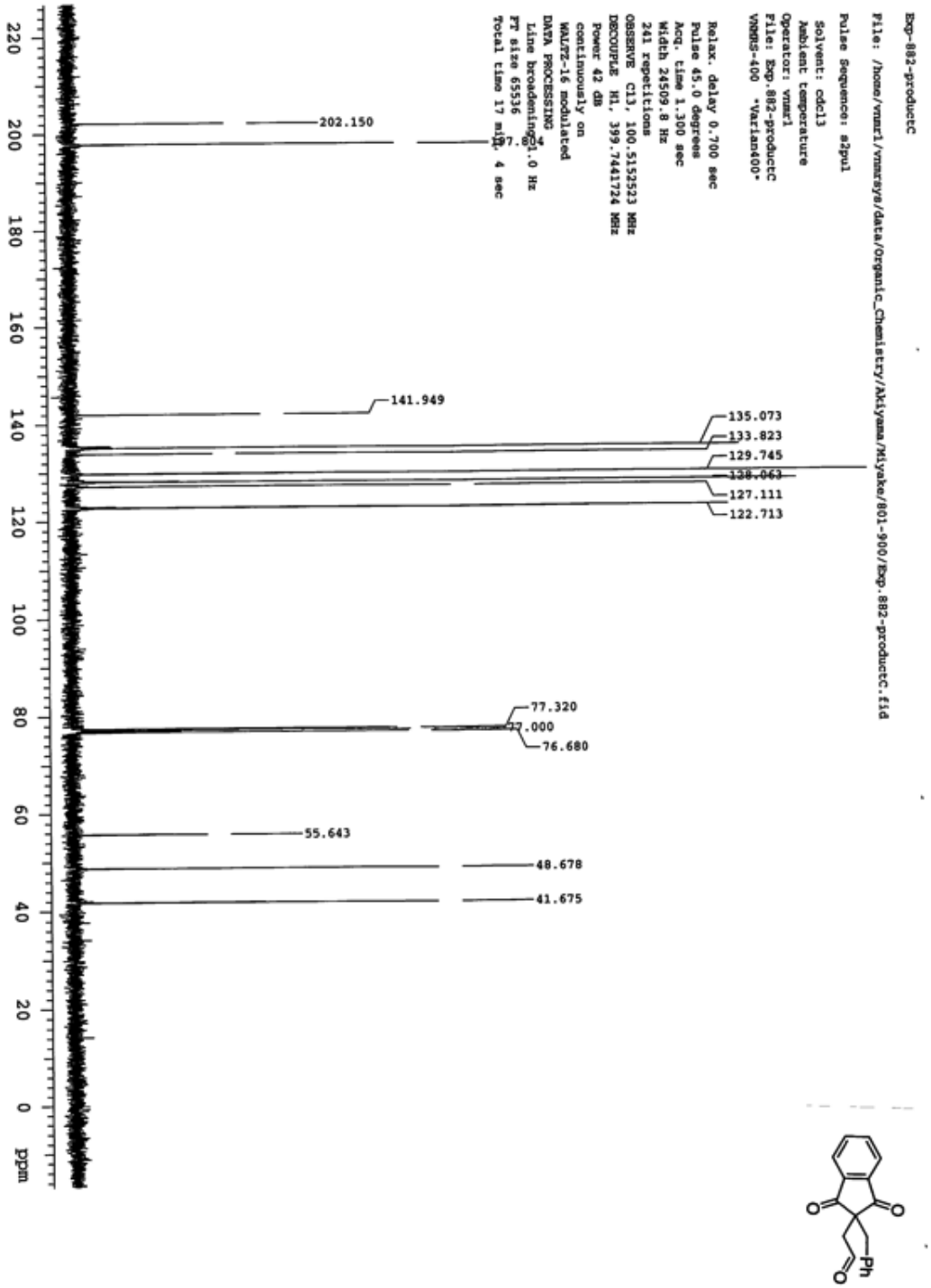
^{13}C NMR spectrum of **s4b**.



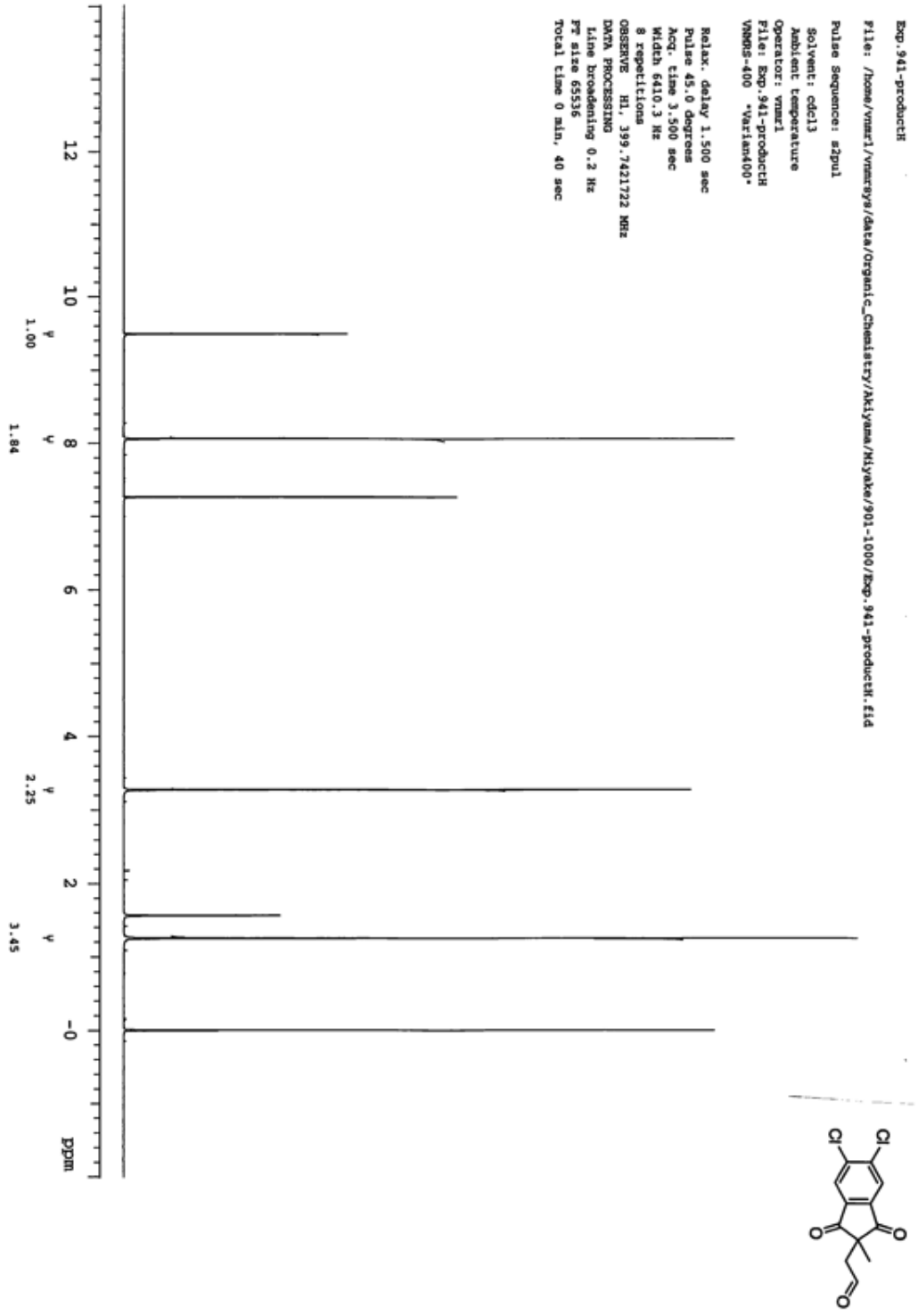
^{1}H NMR spectrum of **s4c**.



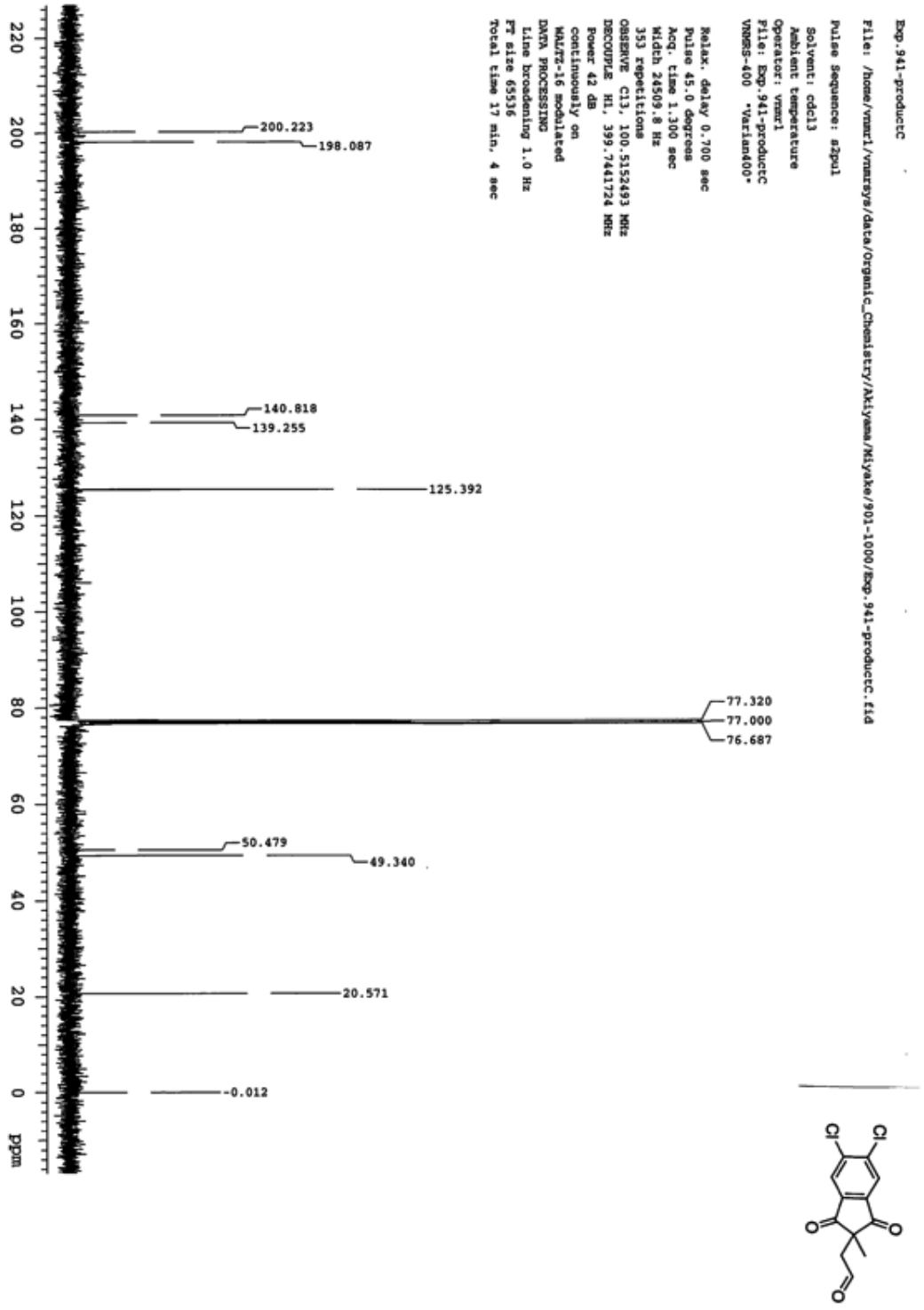
^{13}C NMR spectrum of **s4c**.



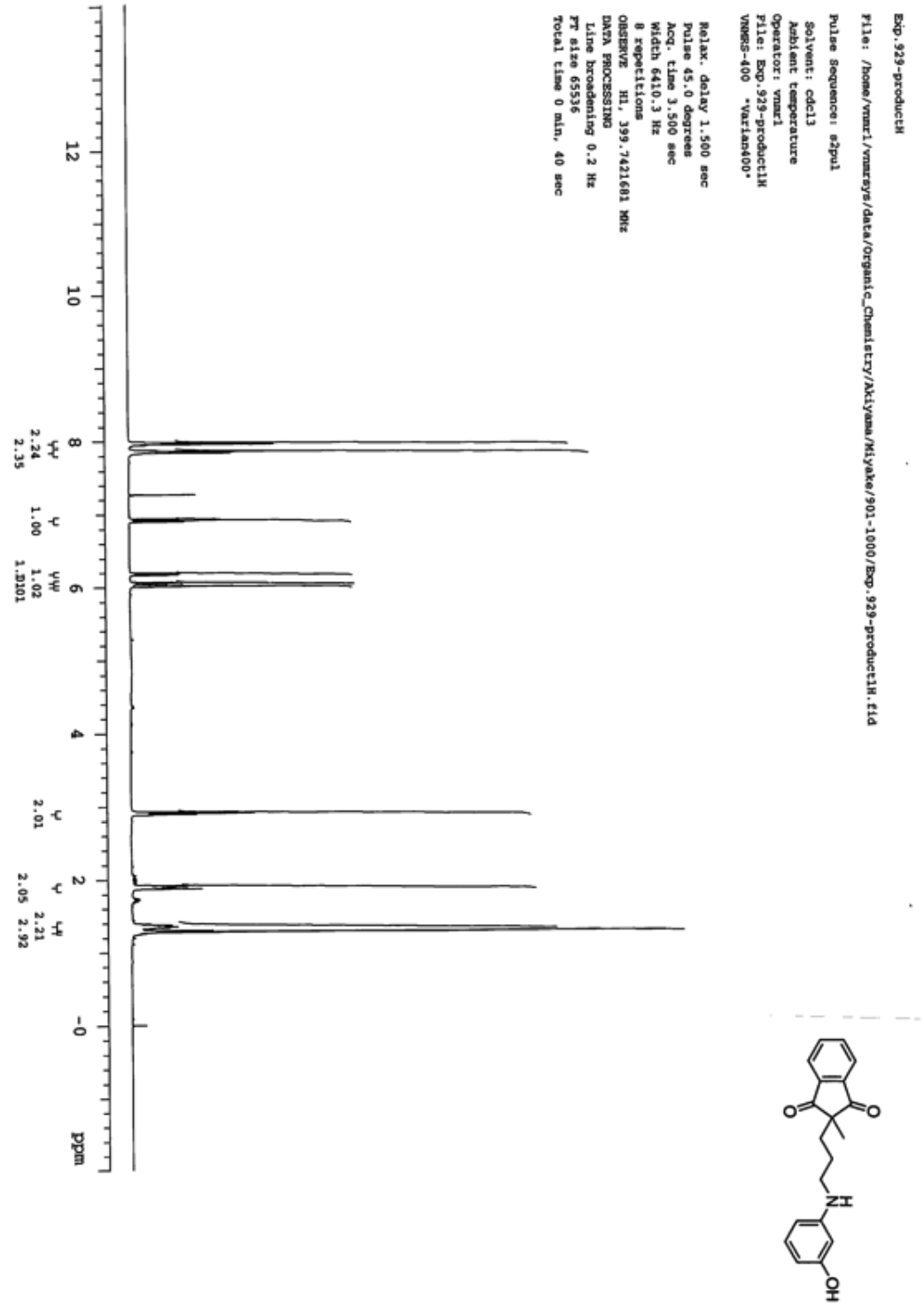
^{1}H NMR spectrum of **s4d**.



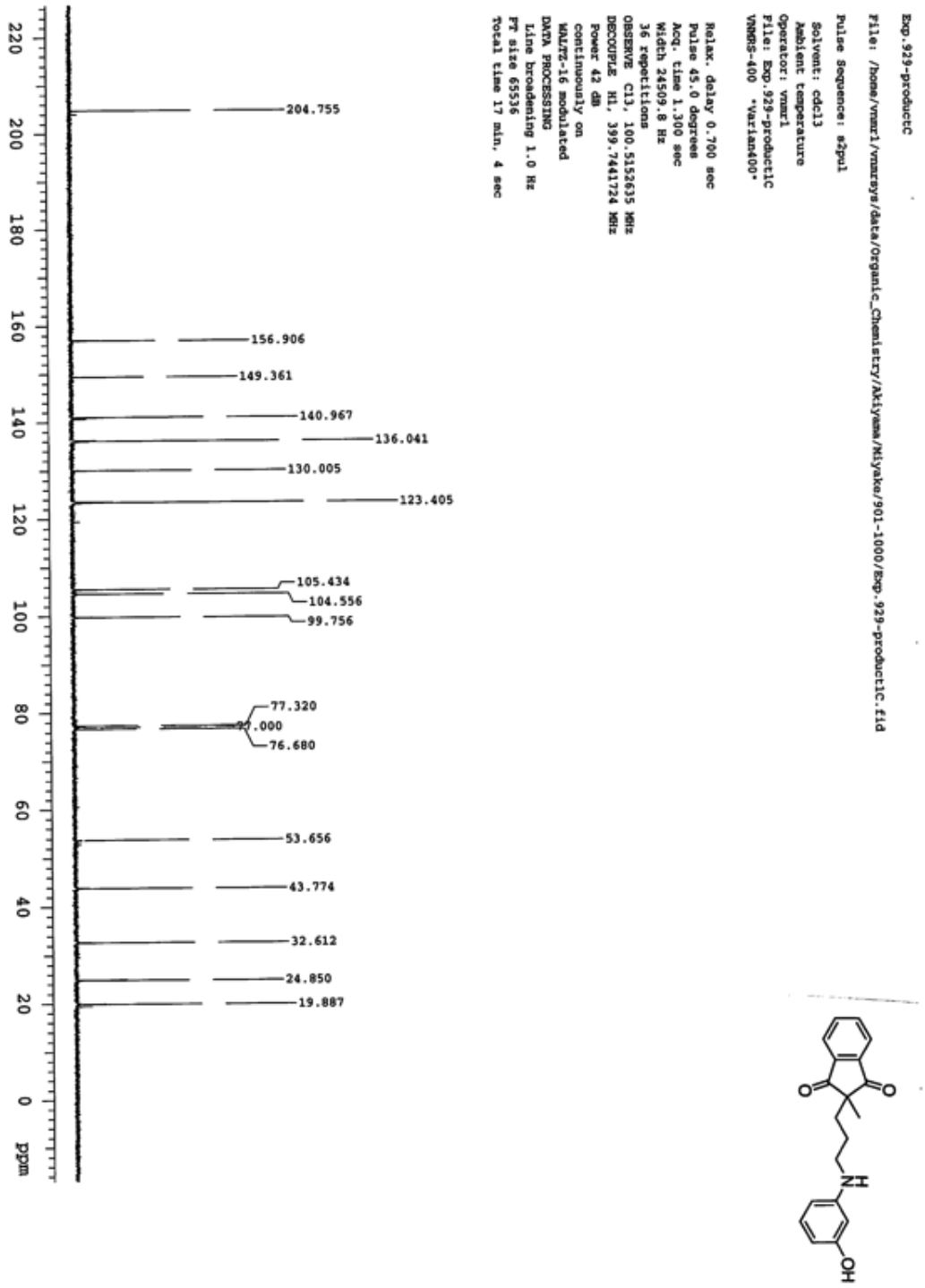
^{13}C NMR spectrum of **s4d**.



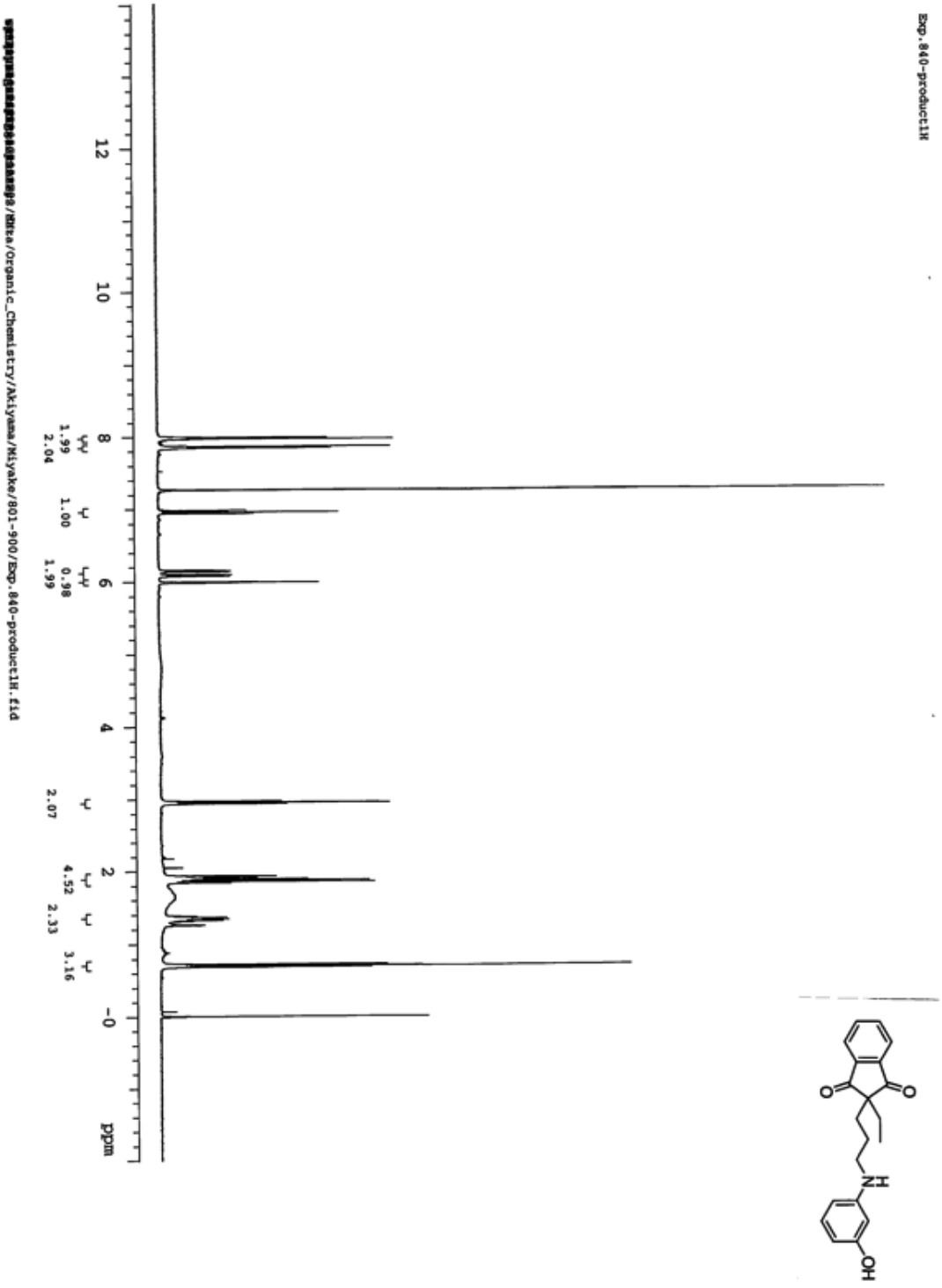
^{1}H NMR spectrum of **1ac**.



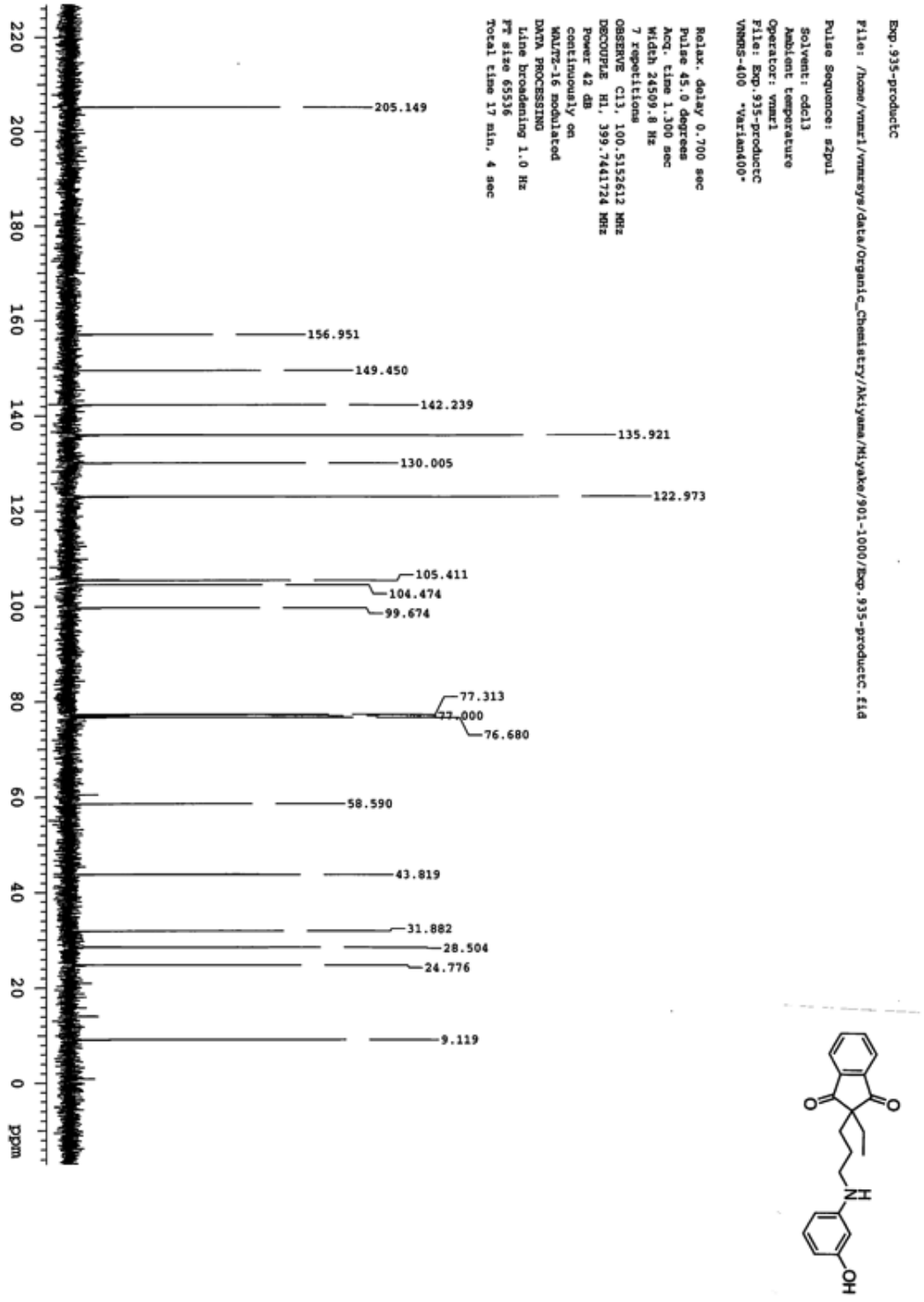
^{13}C NMR spectrum of **1ac**.



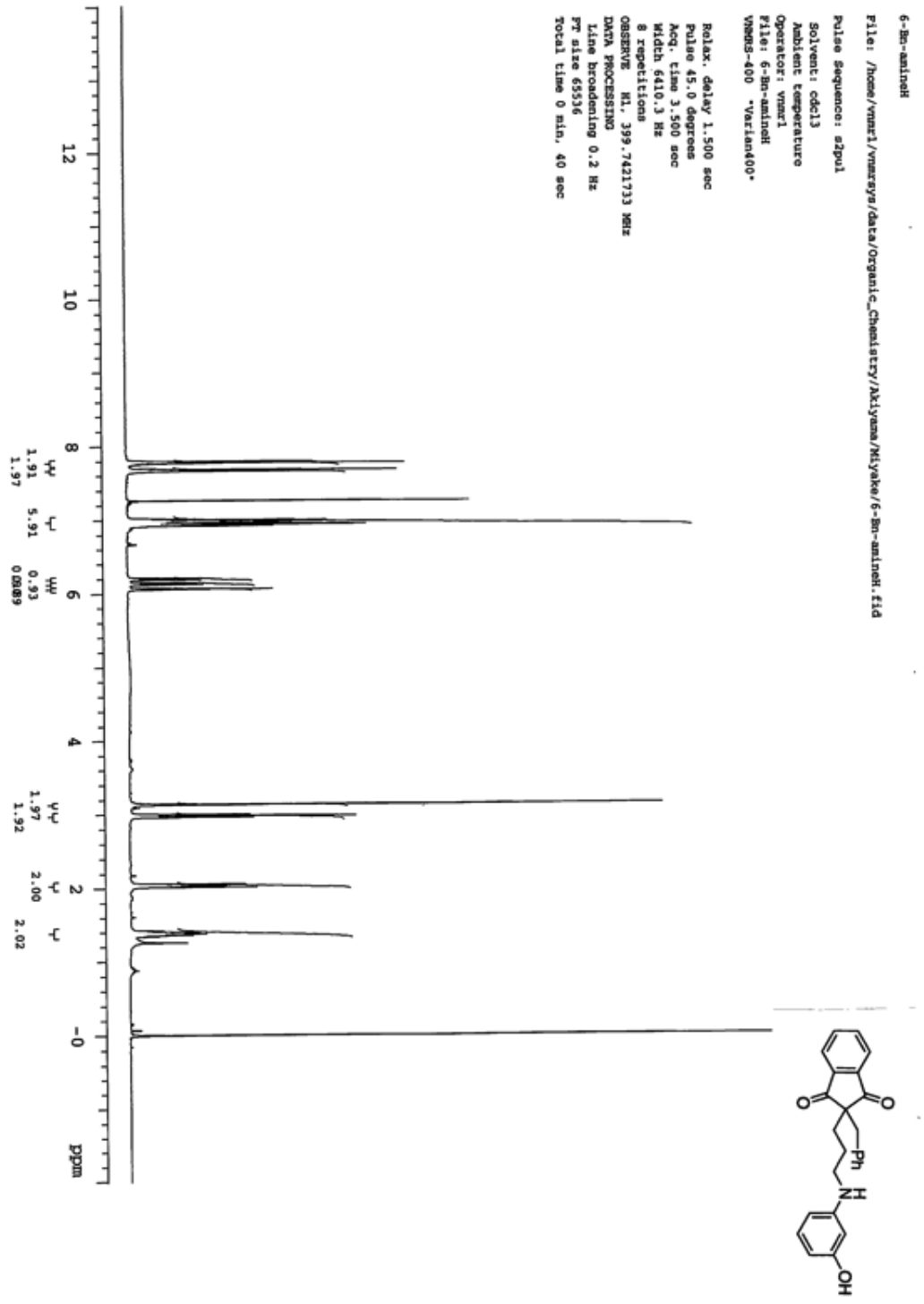
^{1}H NMR spectrum of **1b**.



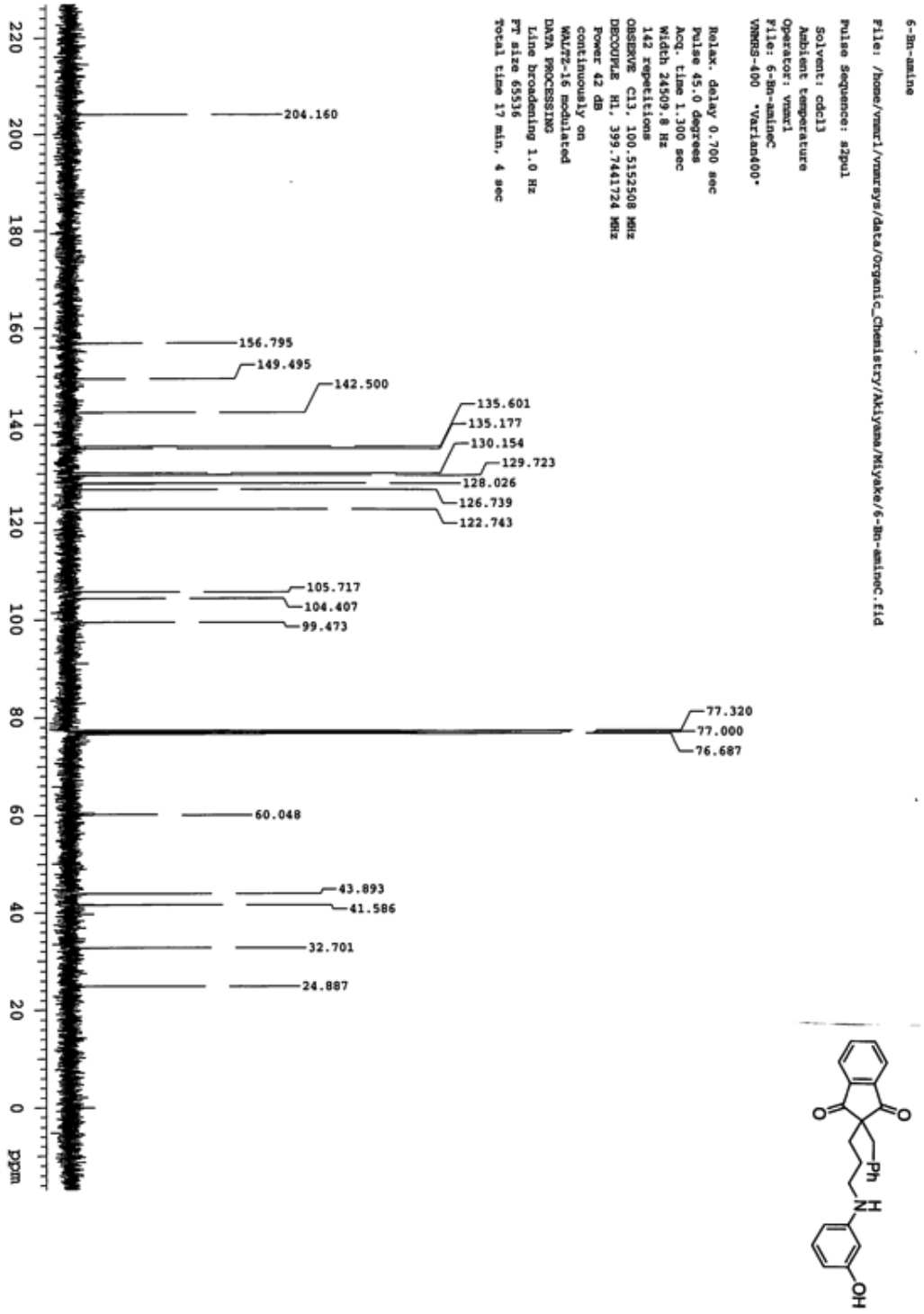
^{13}C NMR spectrum of **1b**.



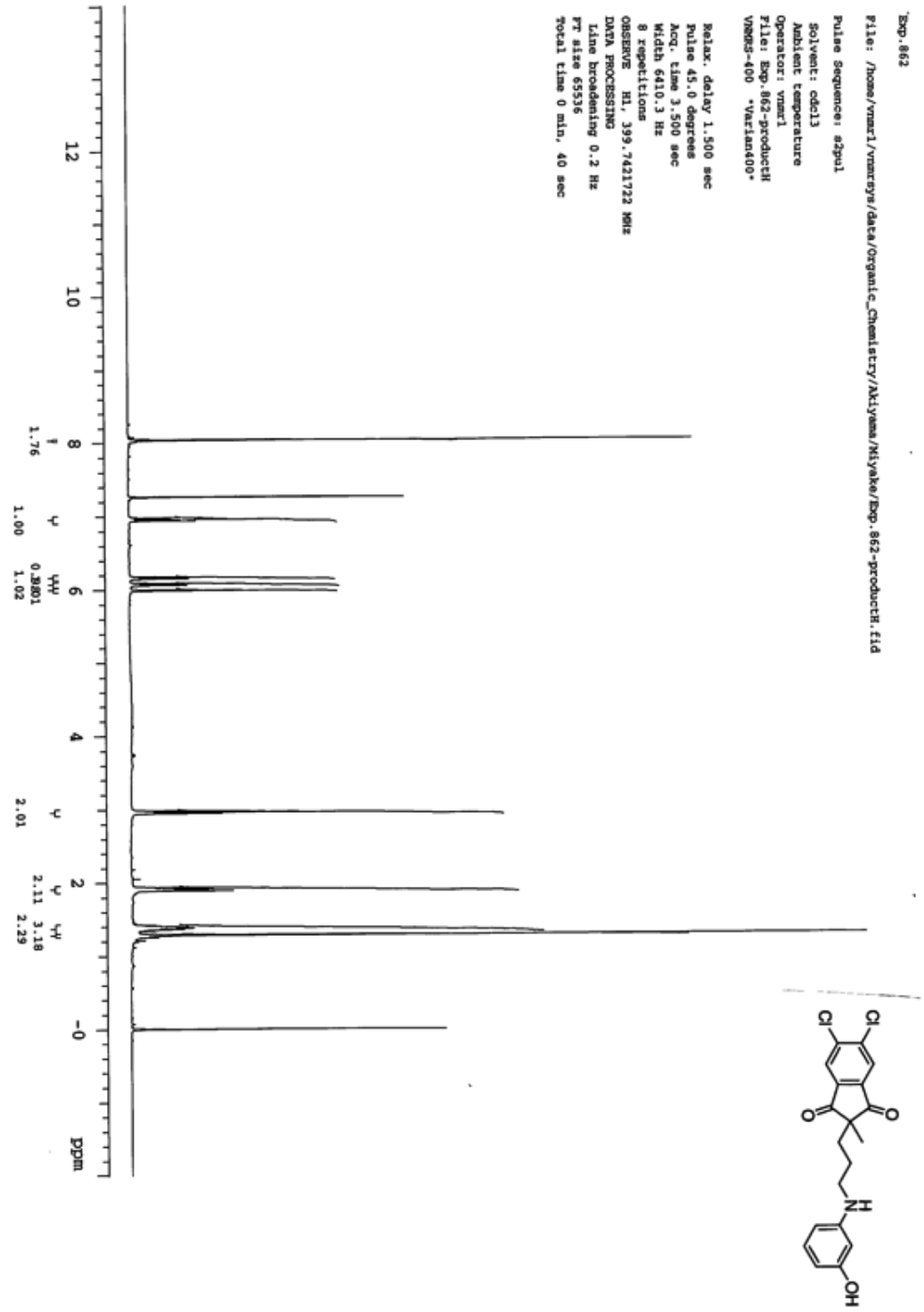
^{1}H NMR spectrum of **1c**.



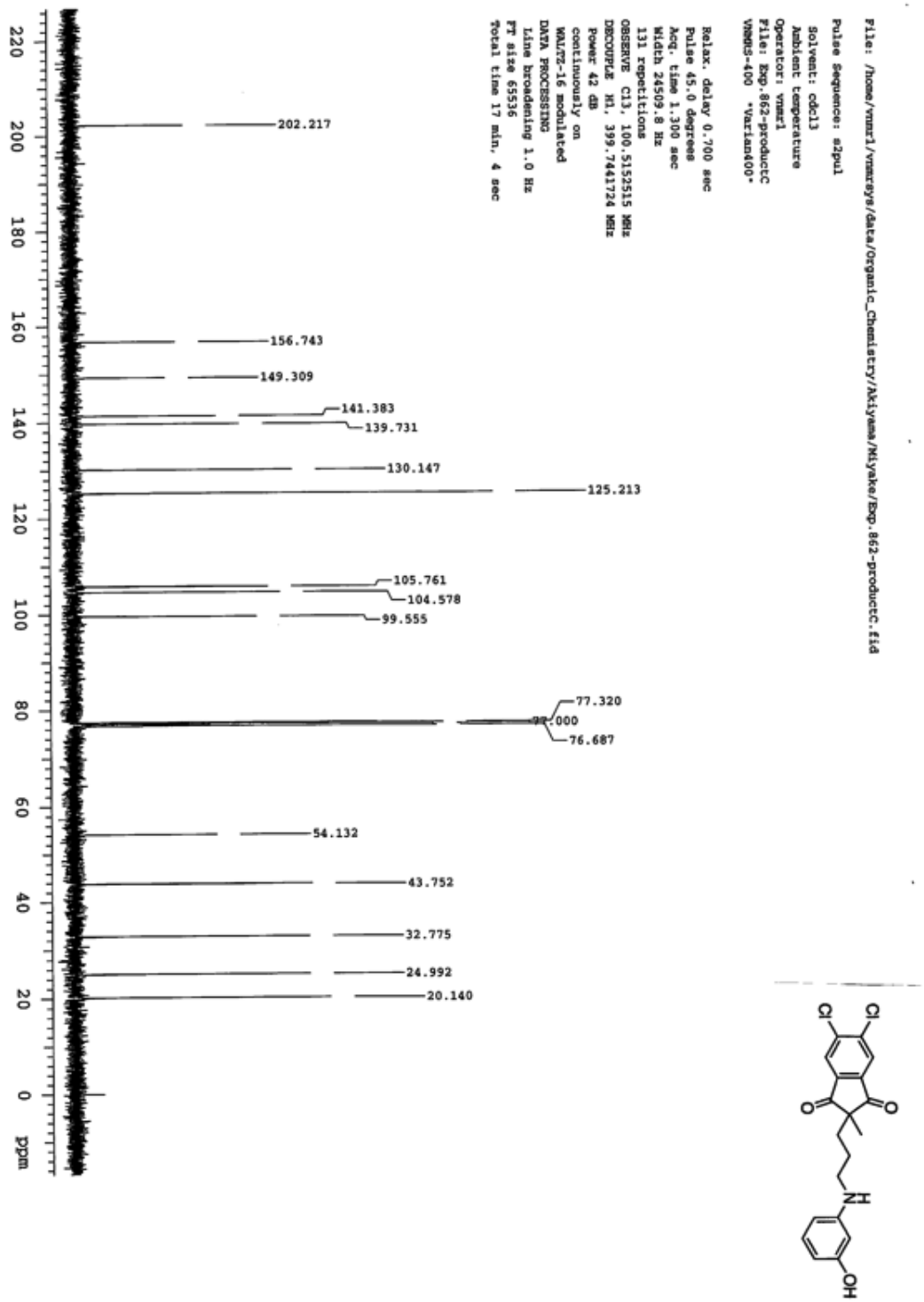
^{13}C NMR spectrum of **1c**.



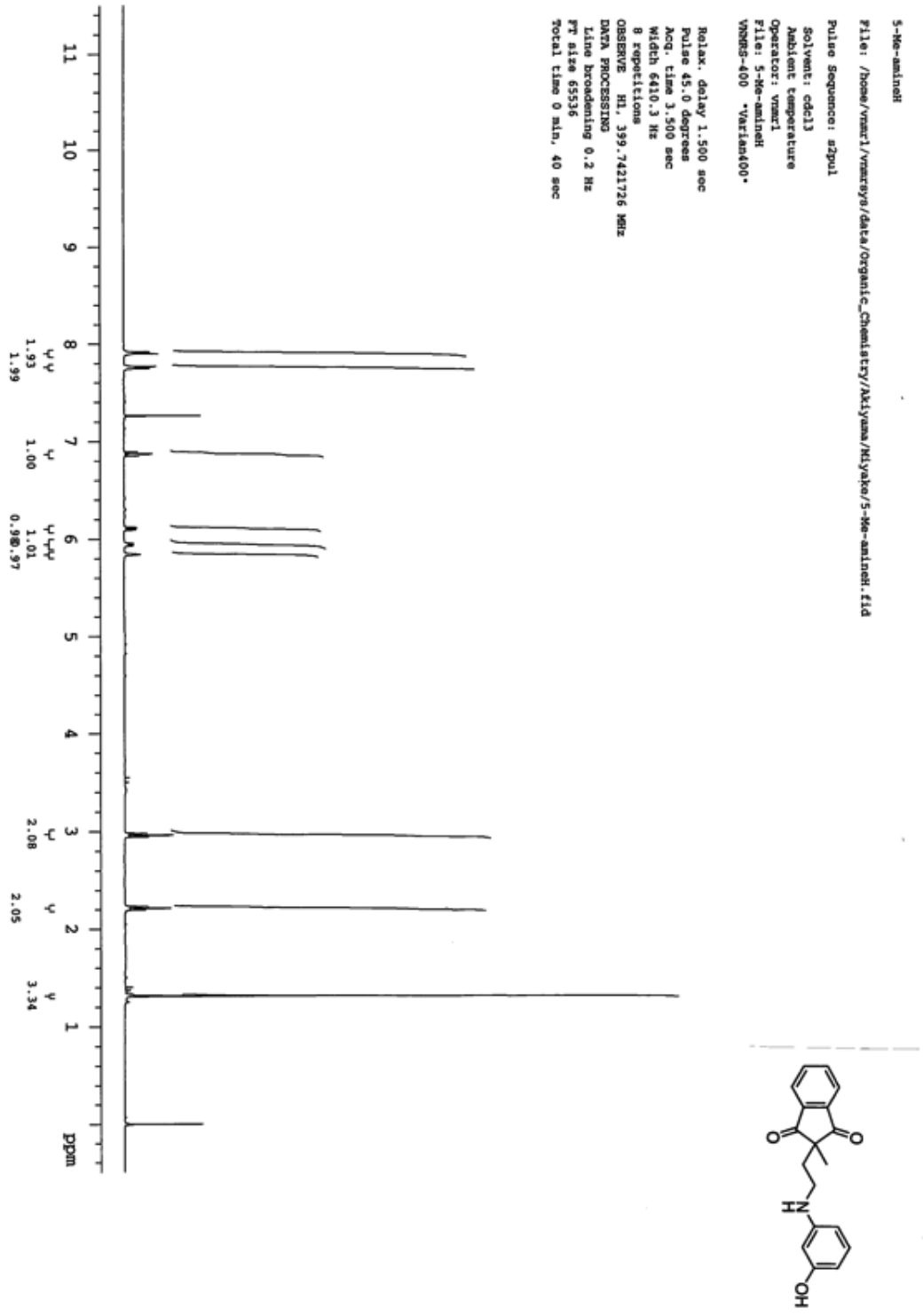
^{1}H NMR spectrum of **1d**.



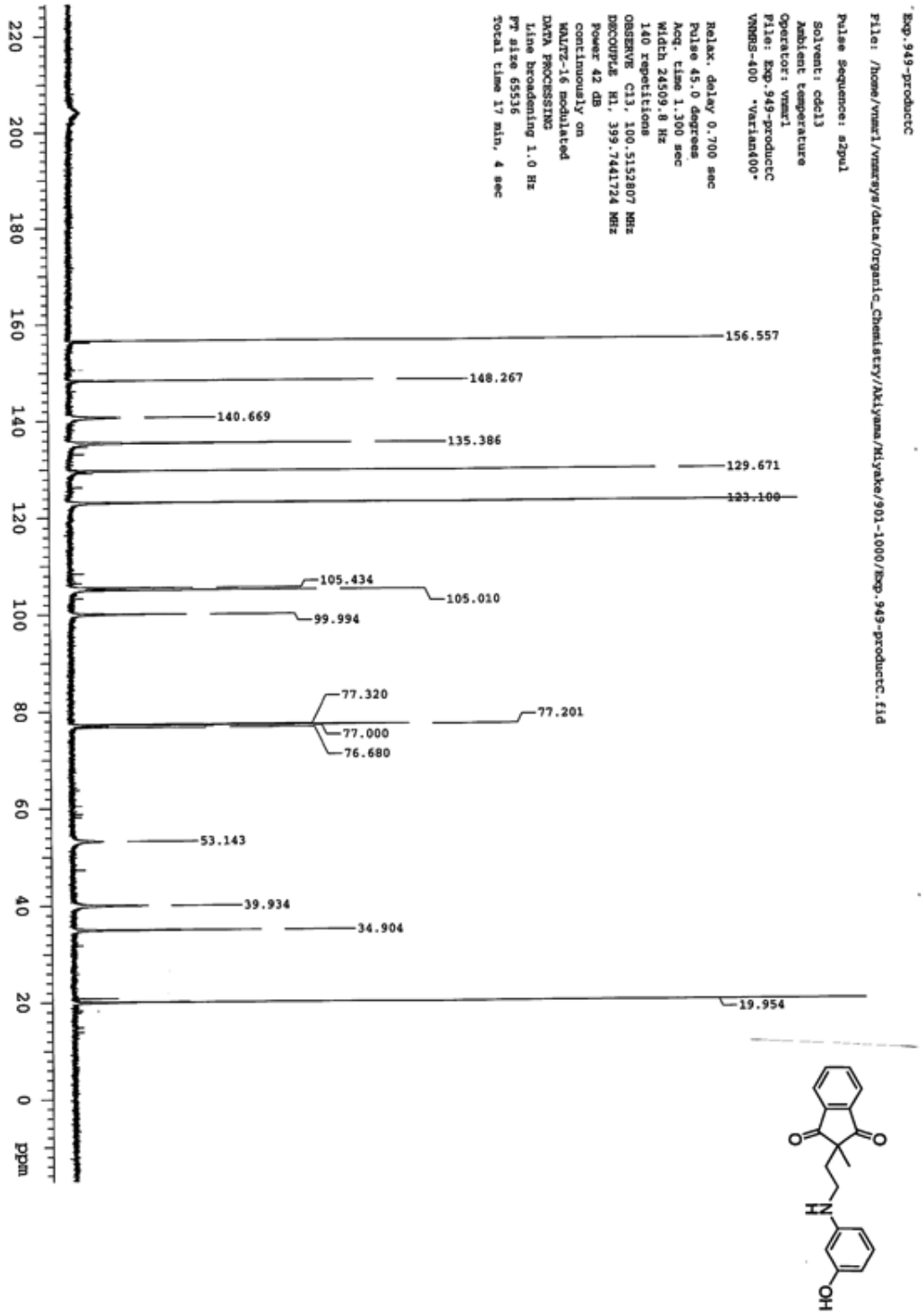
^{13}C NMR spectrum of **1d**.



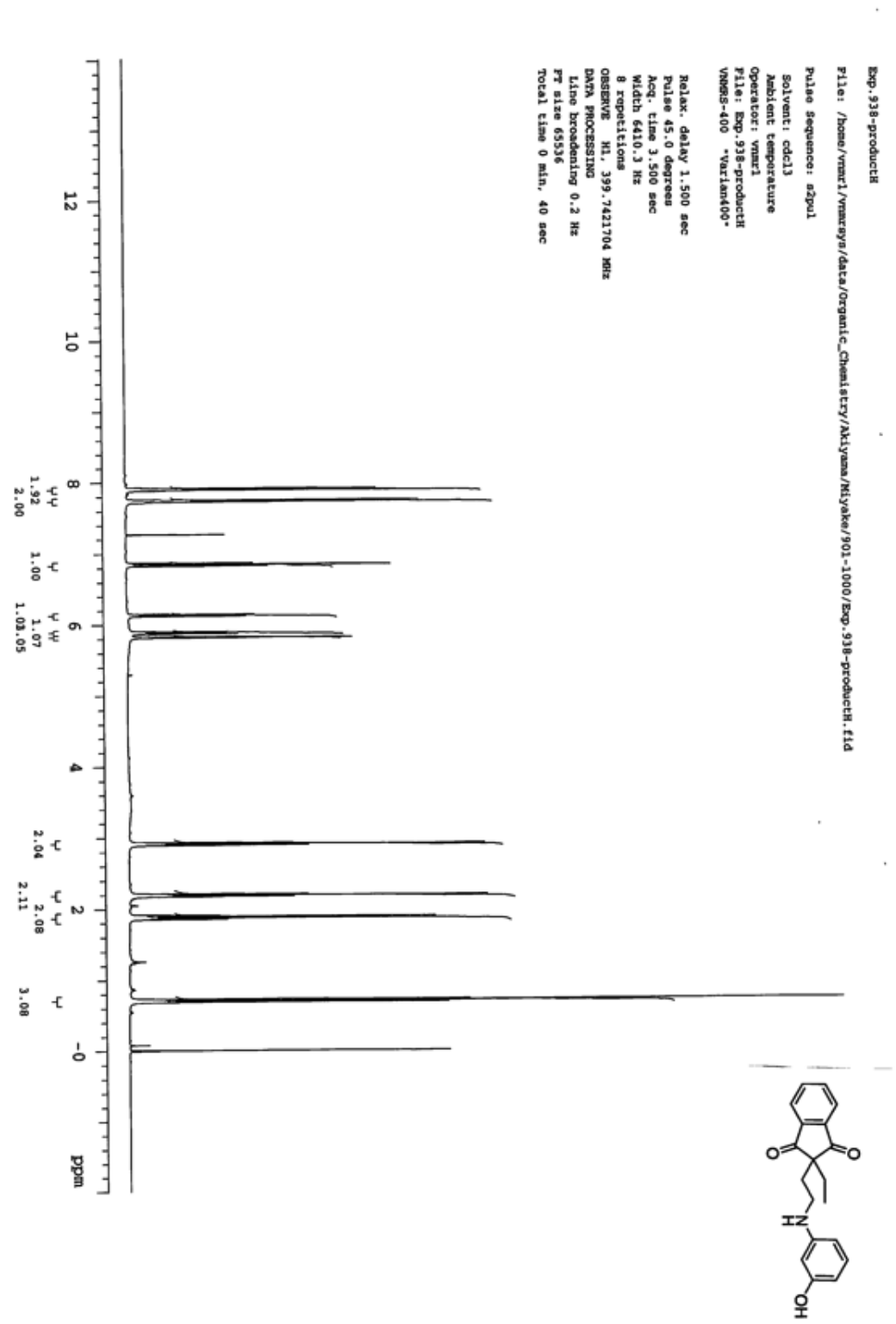
^{1}H NMR spectrum of **s5a**.



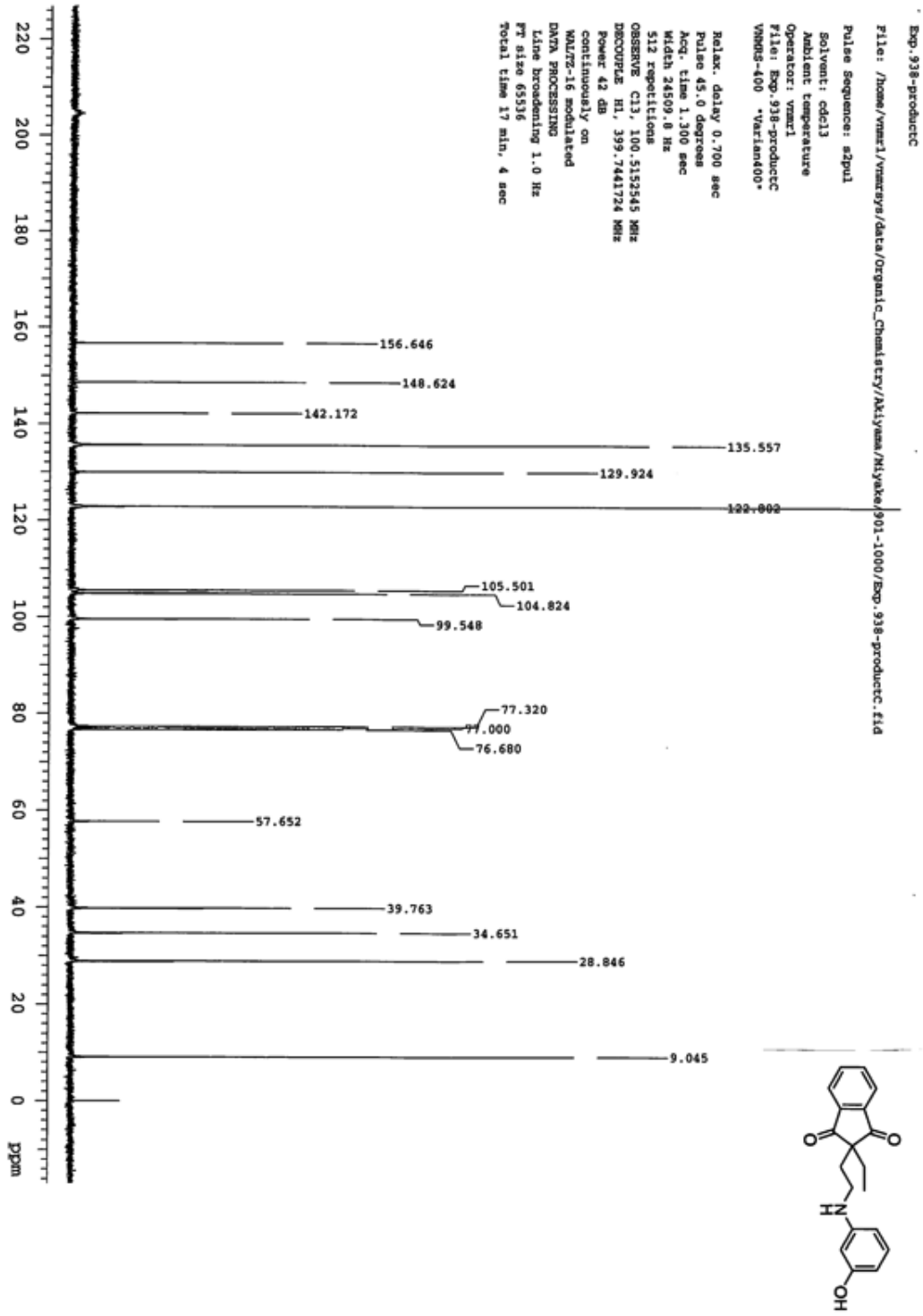
^{13}C NMR spectrum of **s5a**.



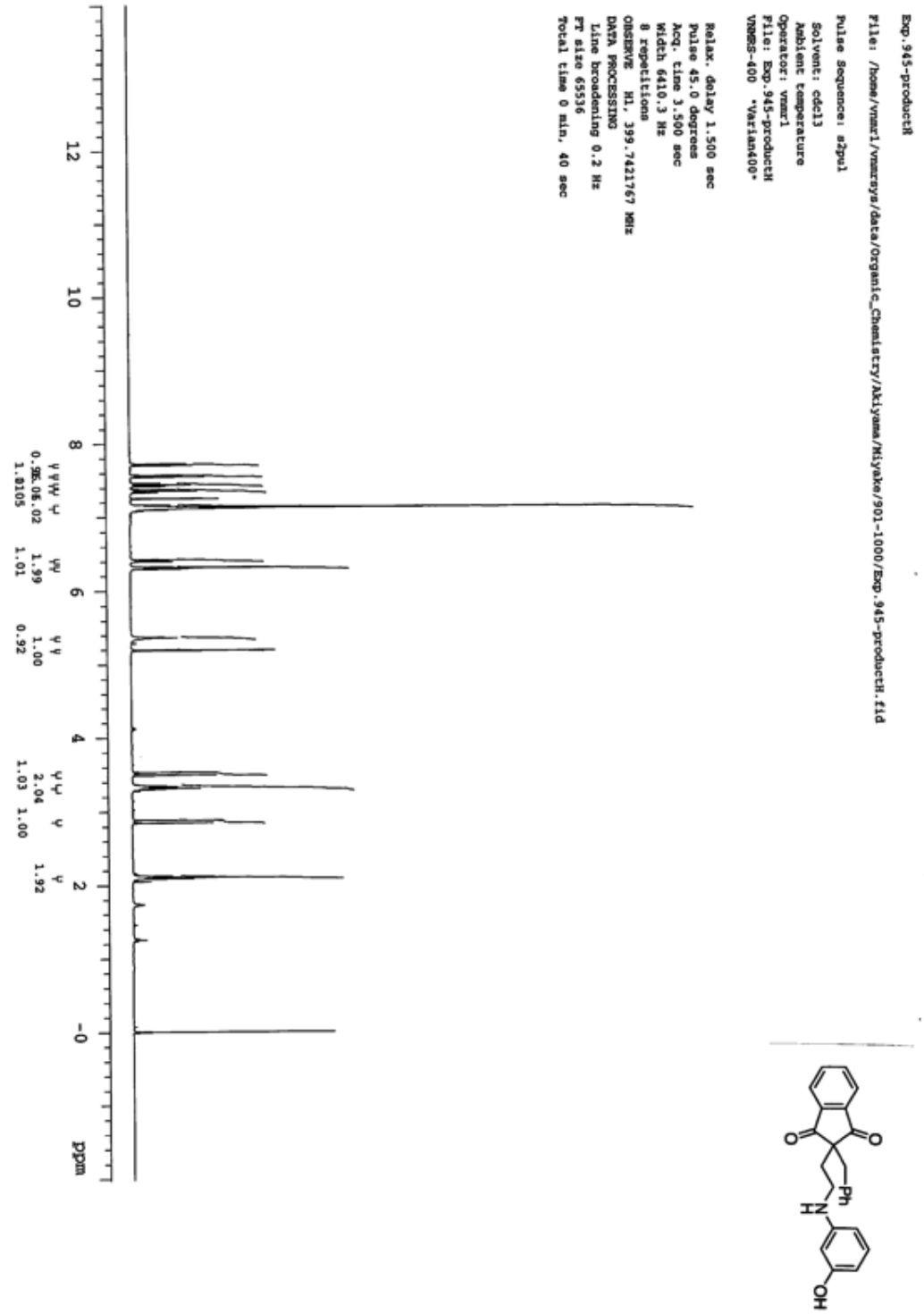
^{1}H NMR spectrum of **s5b**.



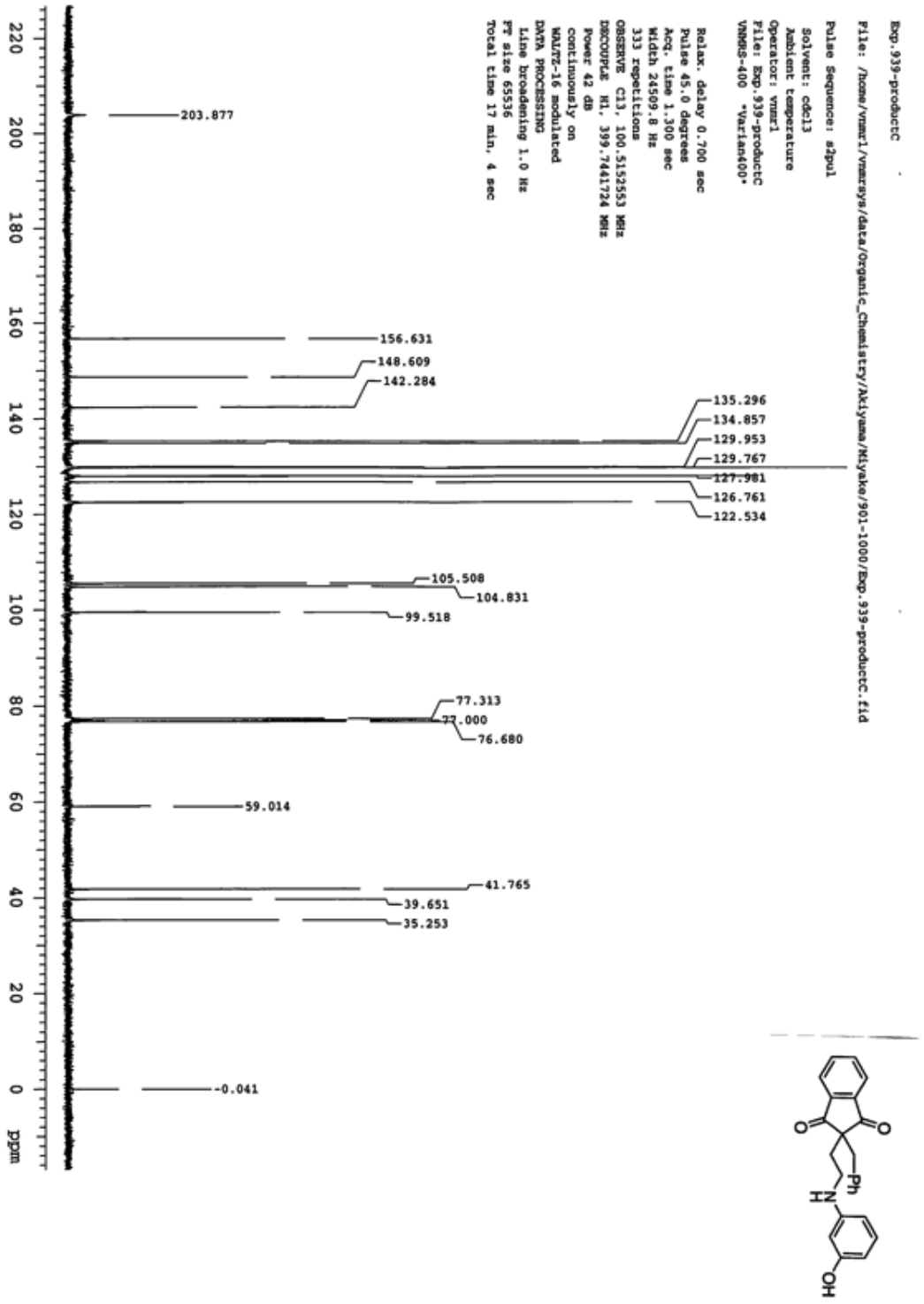
^{13}C NMR spectrum of **s5b**.



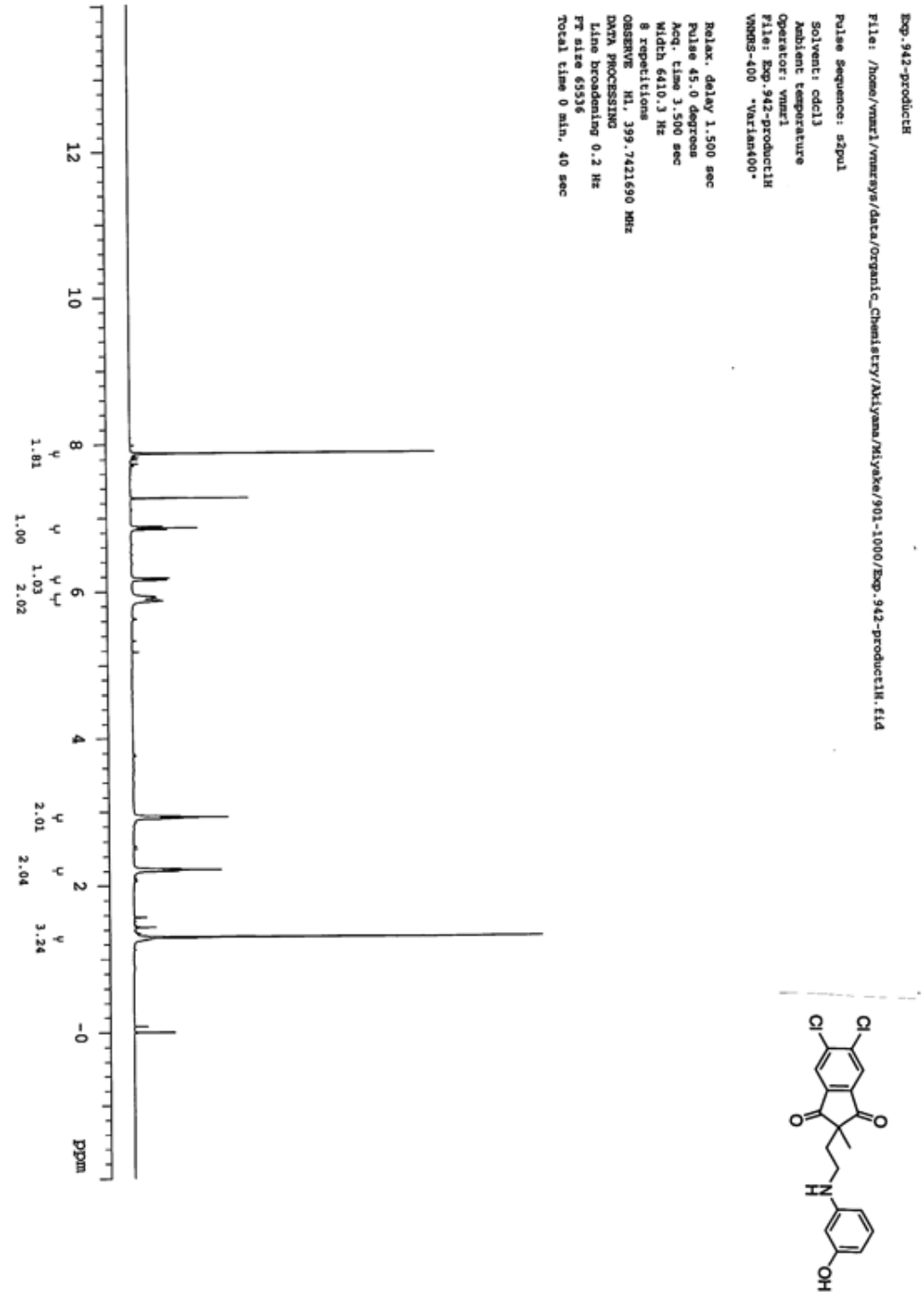
^{1}H NMR spectrum of **s5c**.



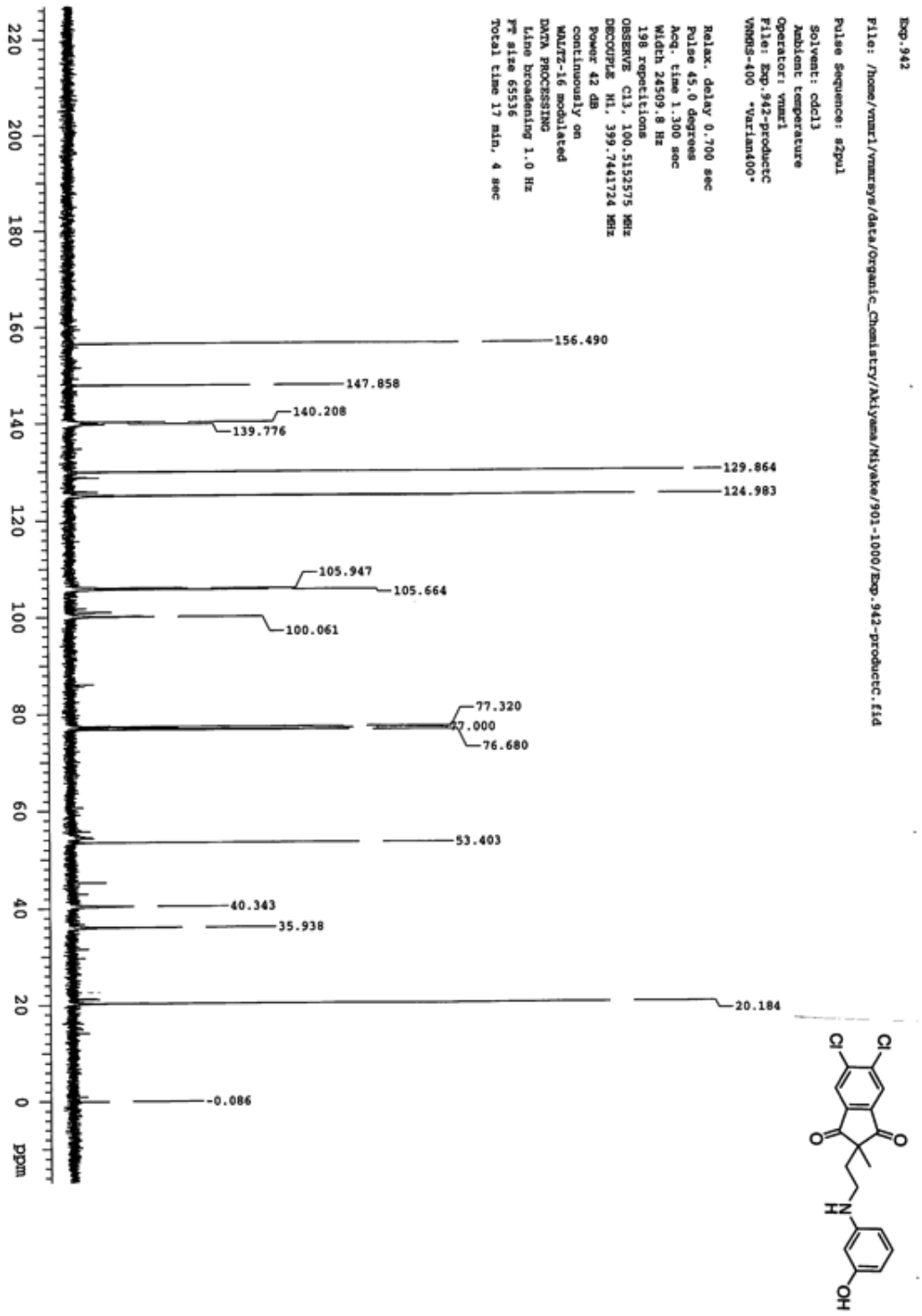
^{13}C NMR spectrum of **s5c**.



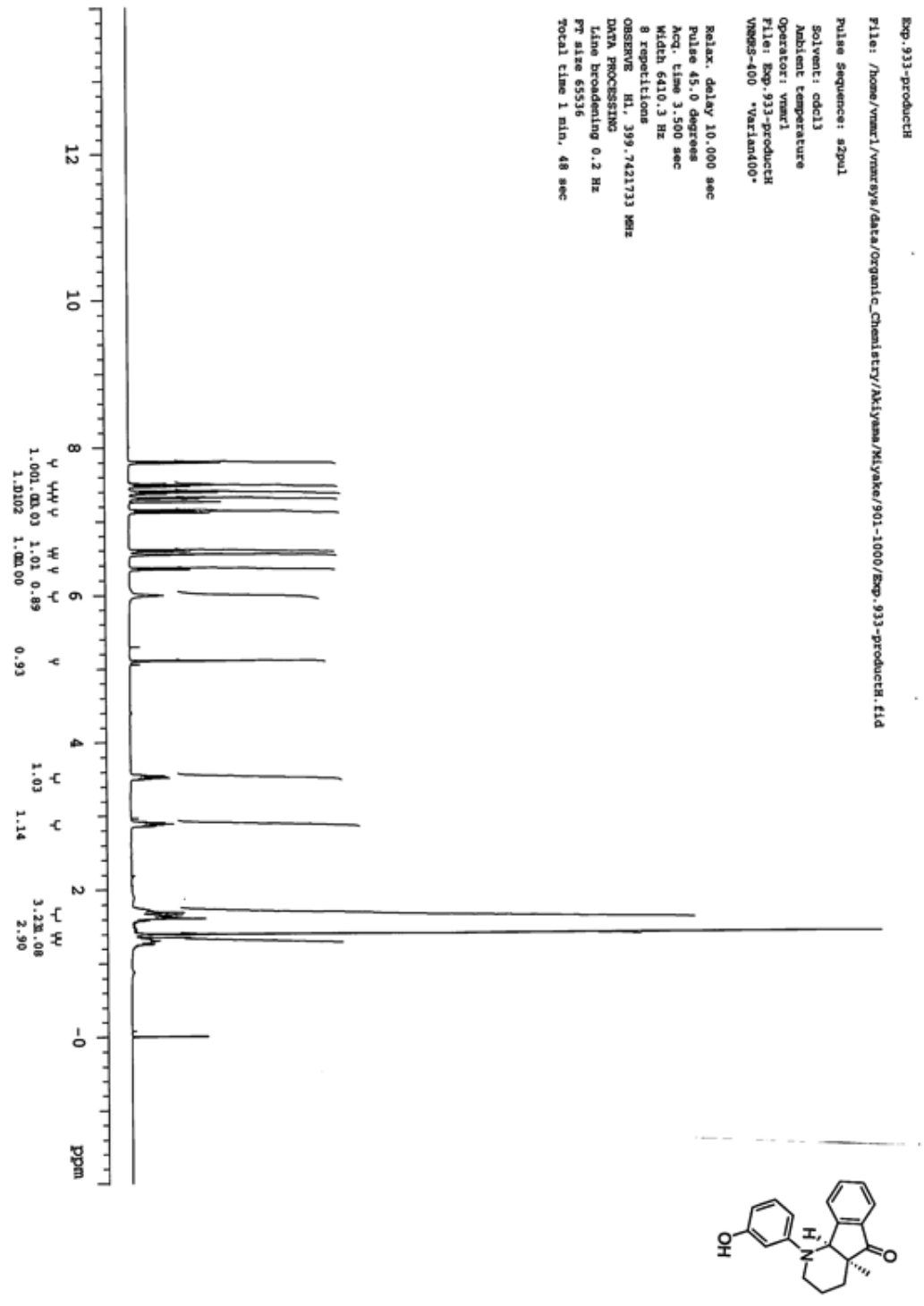
^{1}H NMR spectrum of **s5d**.



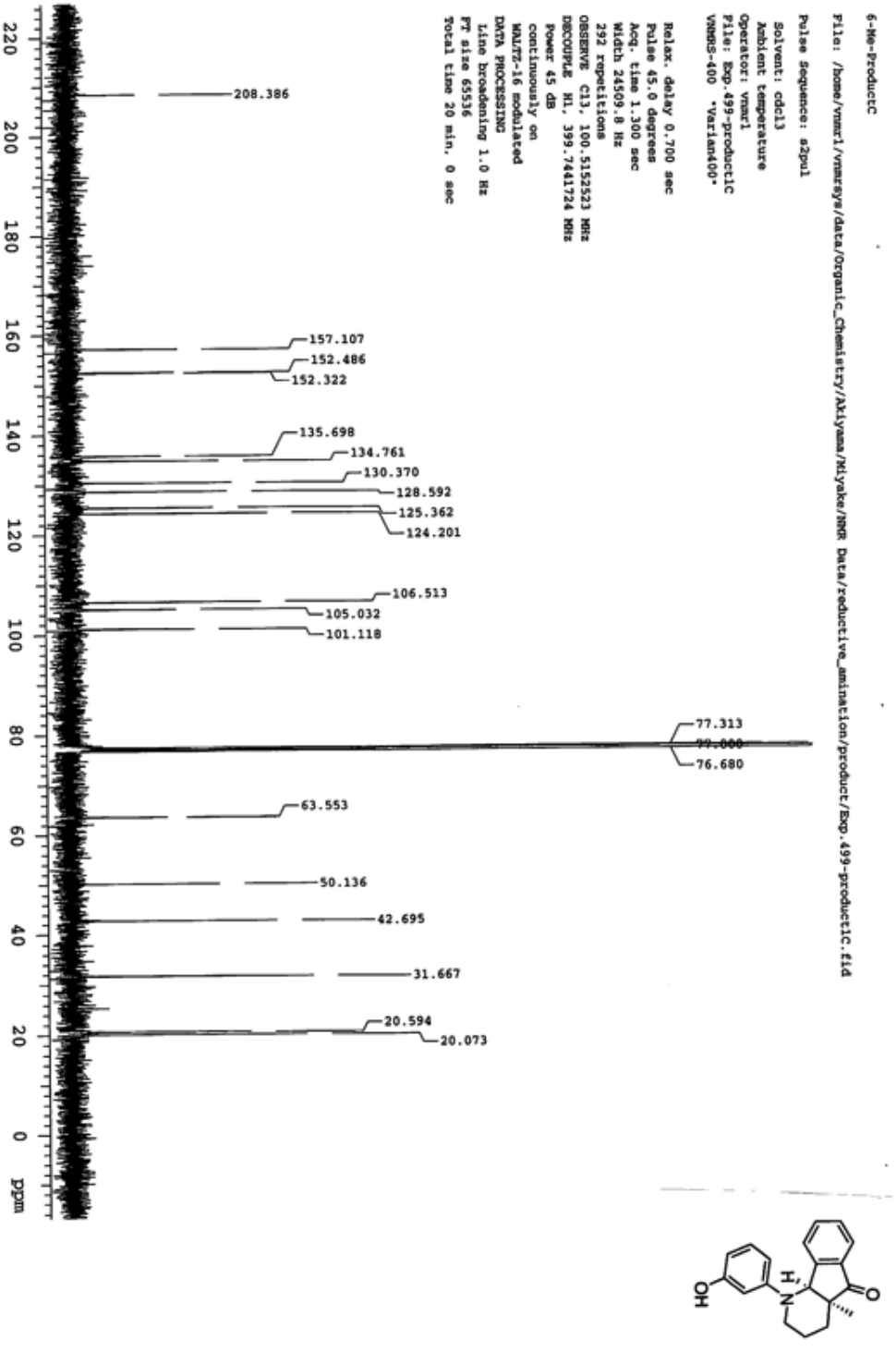
^{13}C NMR spectrum of **s5d**.



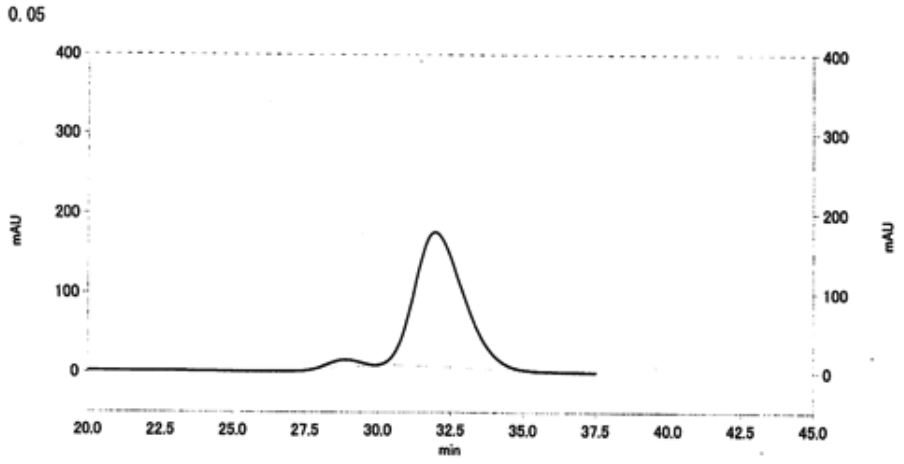
^{1}H NMR spectrum of **2ac**.



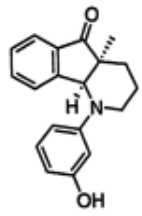
^{13}C NMR spectrum of **2ac**.



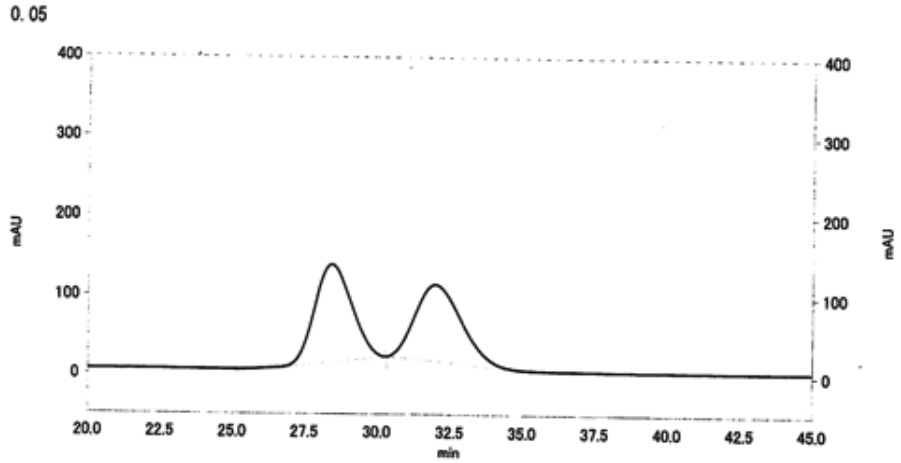
HPLC chart of **2ac**.



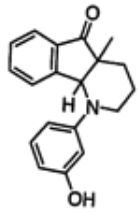
Peak #	Retention time	Type	Area	Area %
1	28.93	BB	2468403	3.013
2	31.96	BB	79459642	96.987



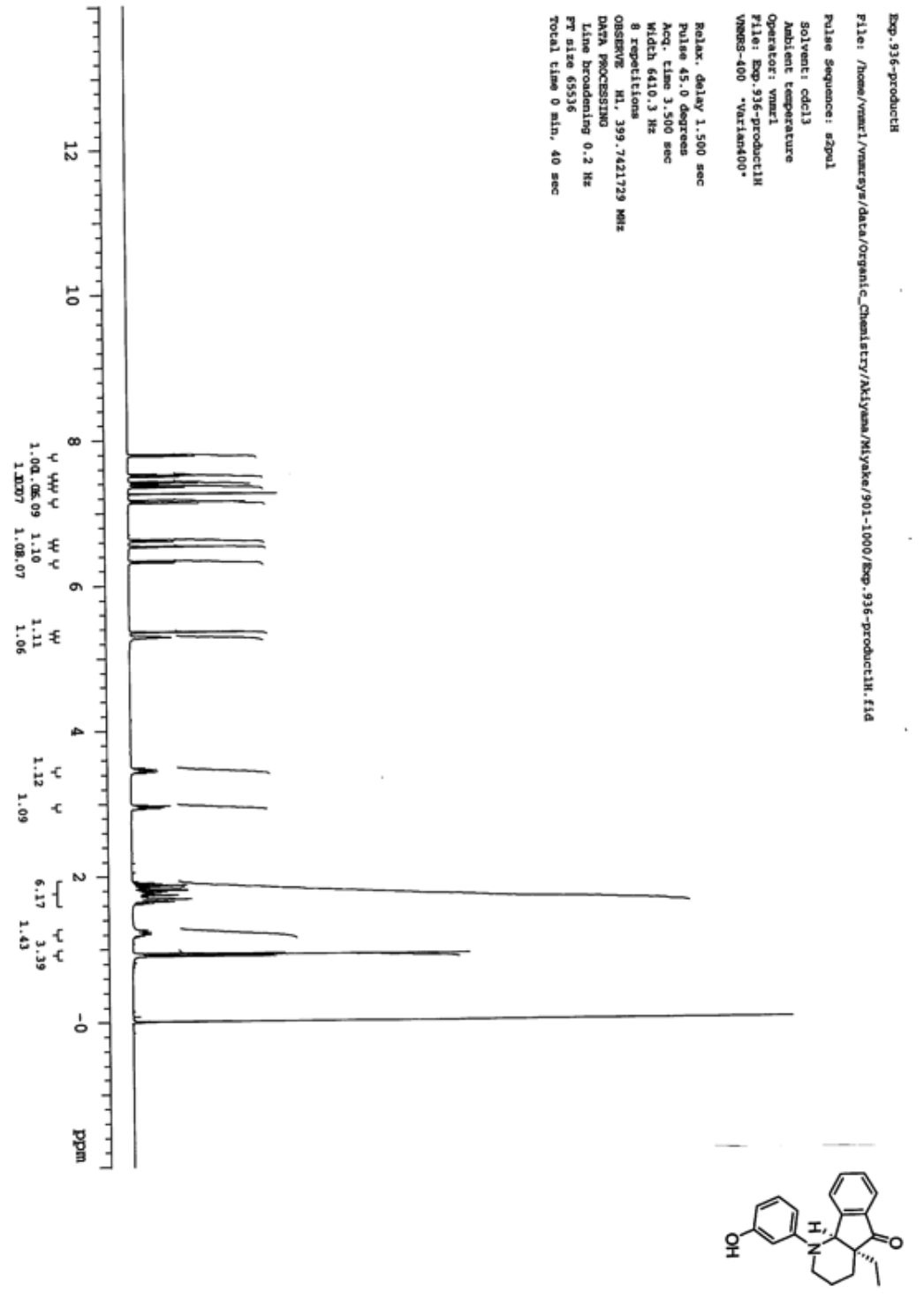
HPLC chart of **2ac** (racemic).



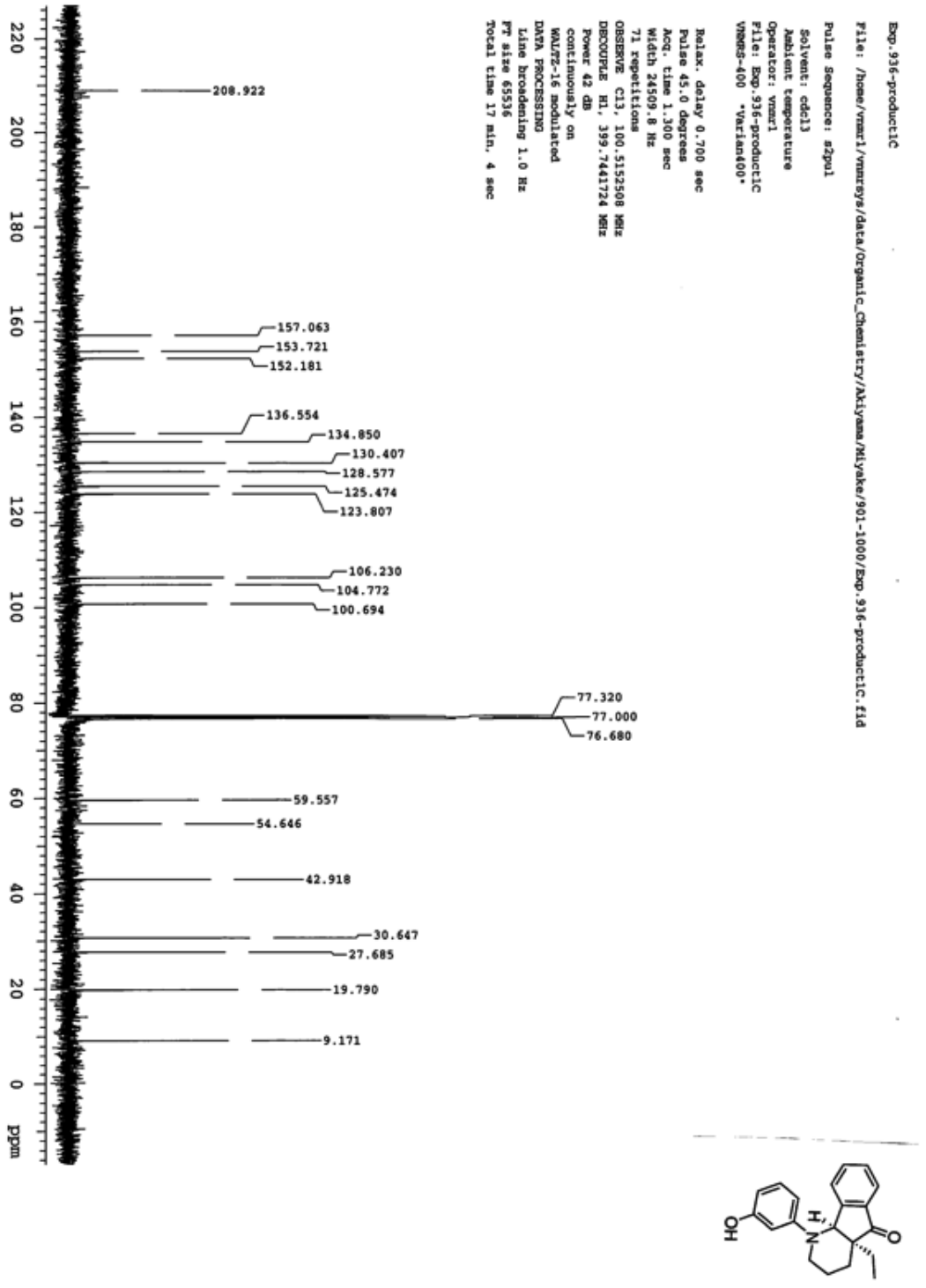
Peak #	Retention time	Type	Area	Area %
1	28.39	BB	44050824	50.491
2	31.96	IB	43194477	49.509



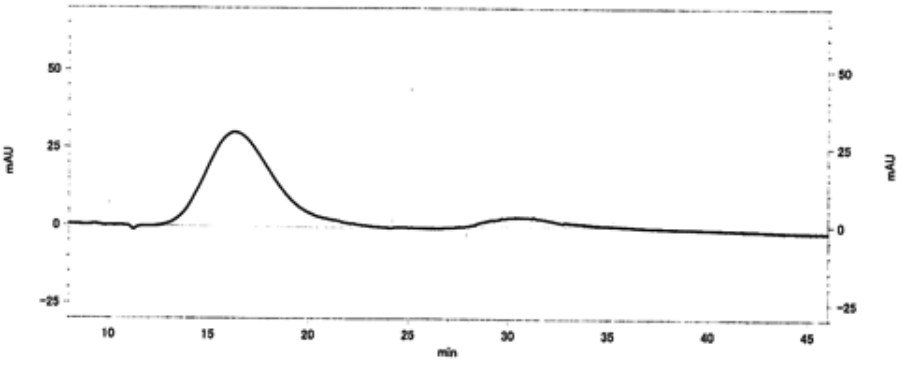
^{1}H NMR spectrum of **2b**.



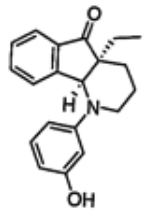
^{13}C NMR spectrum of **2b**.



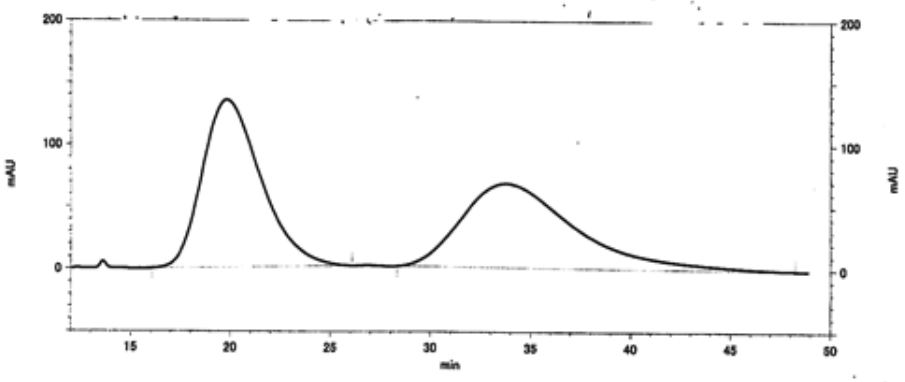
HPLC chart of **2b**.



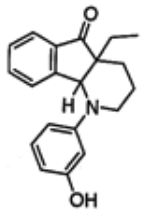
Peak #	Retention time	Type	Area	Area %
1	16.307	BB	29181447	91.448
2	30.553	BB	2728958	8.552



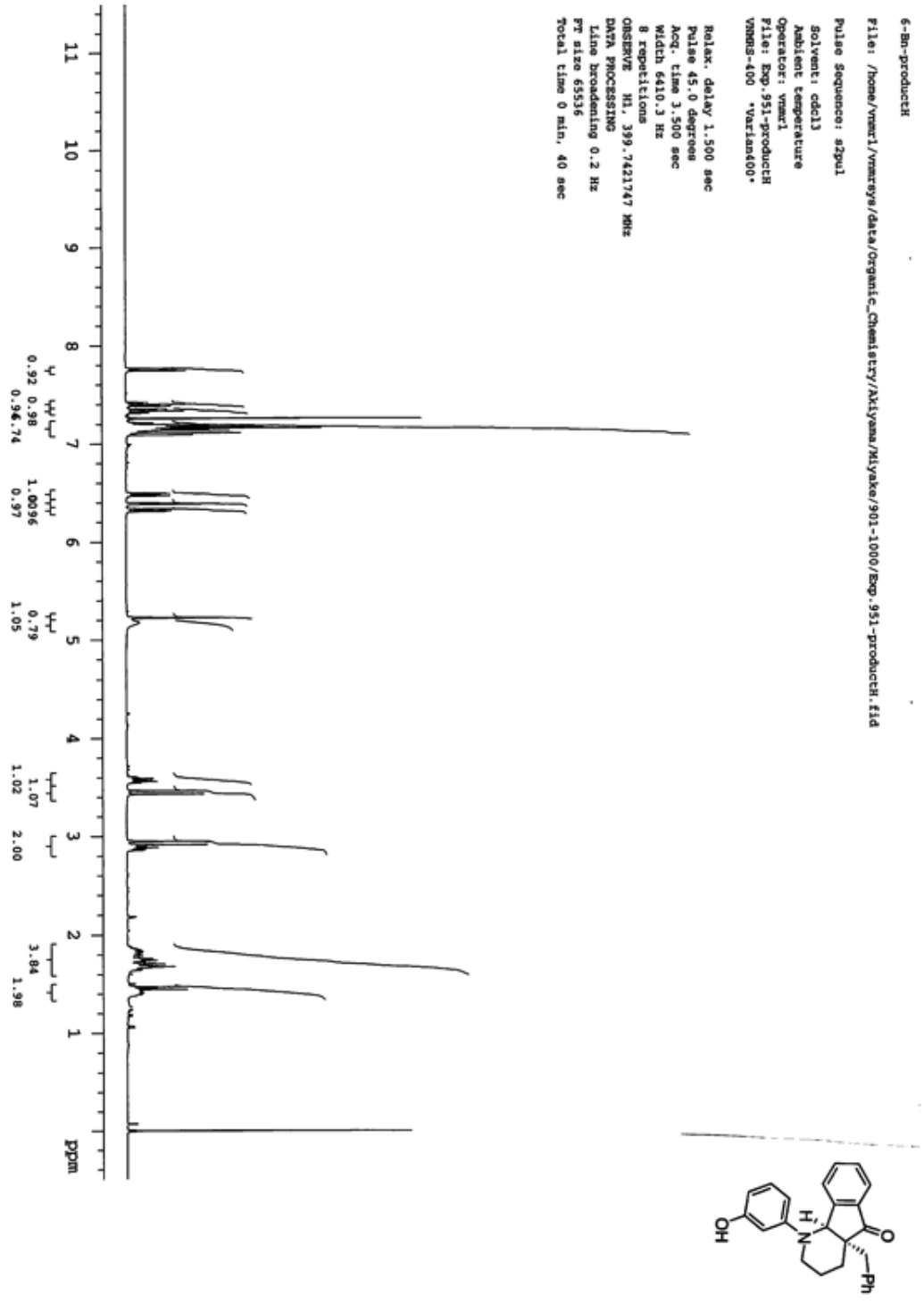
HPLC chart of **2b** (racemic).



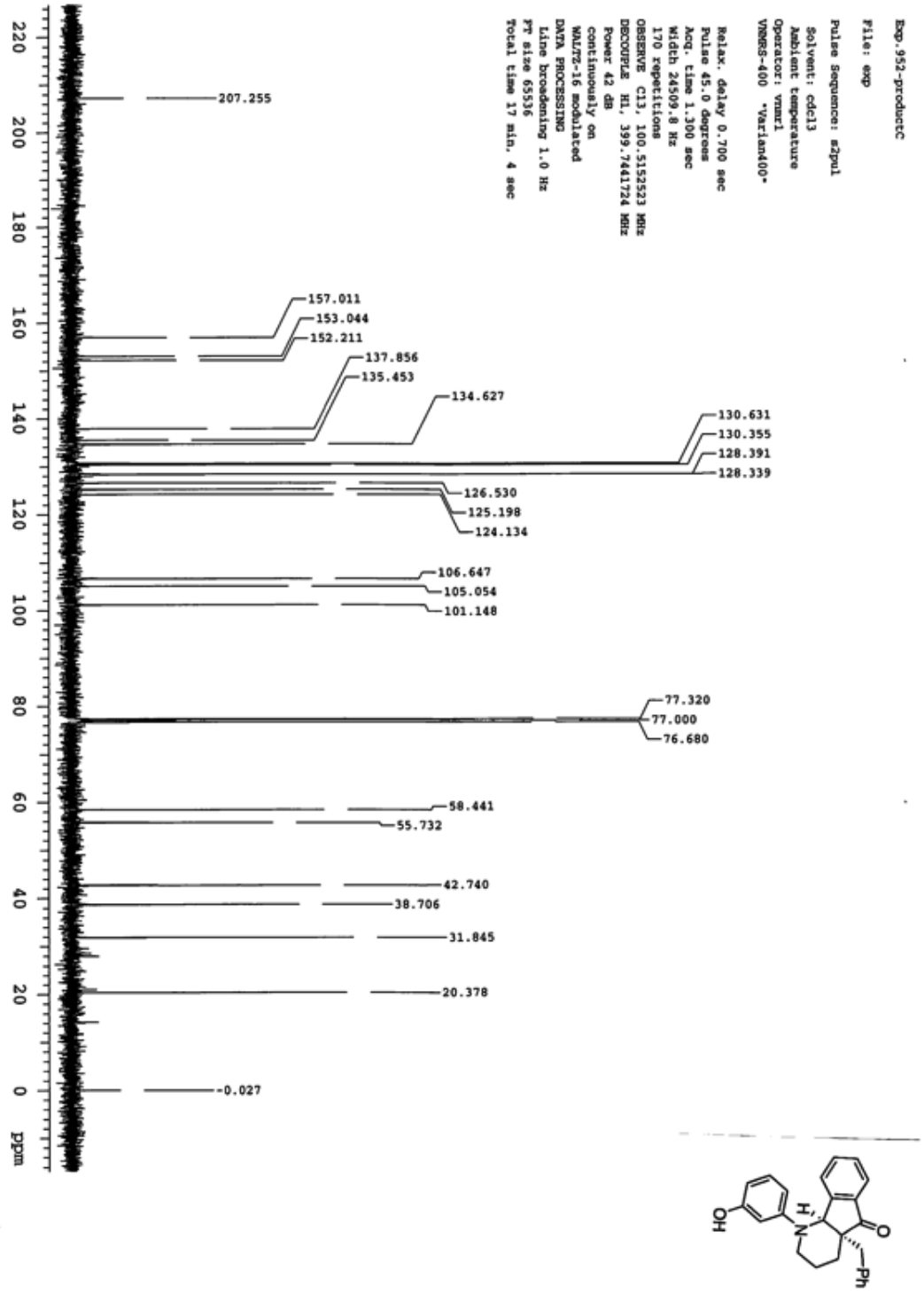
Peak #	Retention time	Type	Area	Area %
1	19.813	BB	109631014	50.665
2	33.767	BI	106751258	49.335



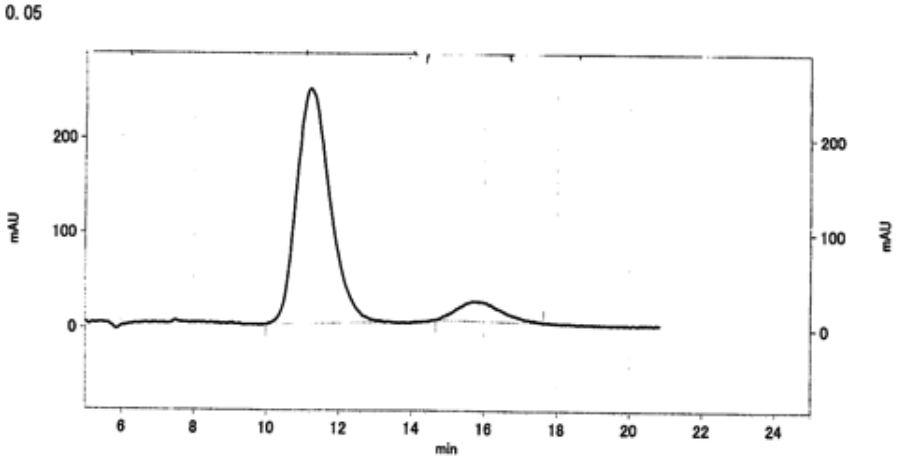
^{1}H NMR spectrum of **2c**.



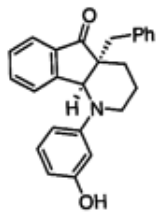
^{13}C NMR spectrum of **2c**.



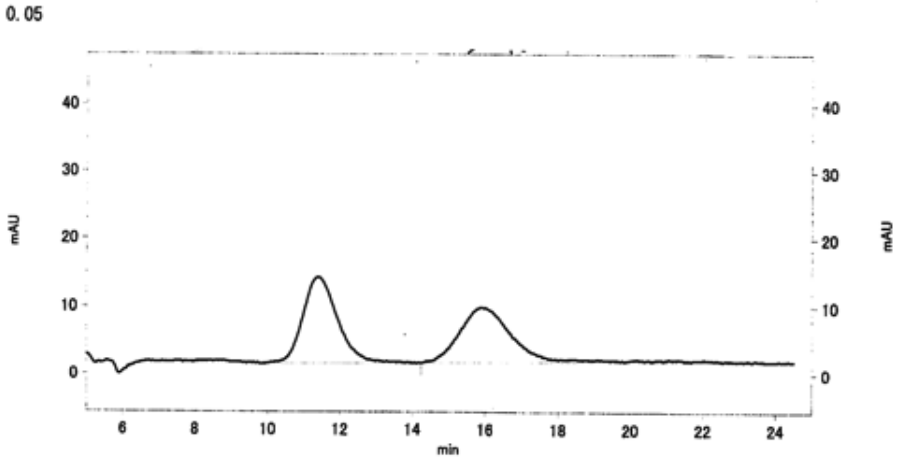
HPLC chart of **2c**.



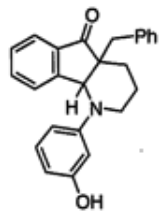
Peak #	Retention time	Type	Area	Area %
1	11.21	BB	63161354	89.746
2	15.69	BB	7216925	10.254



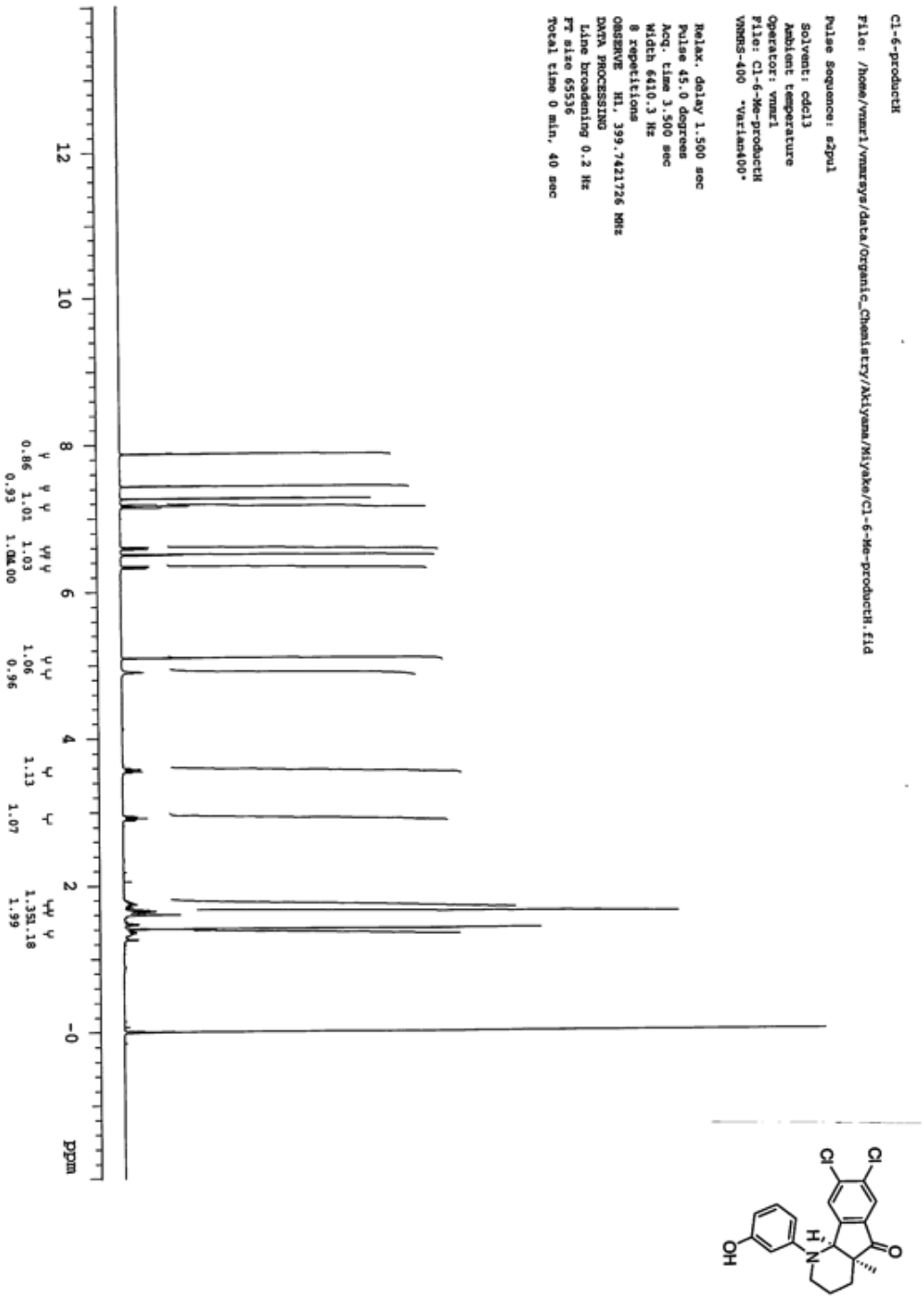
HPLC chart of **2c** (racemic).



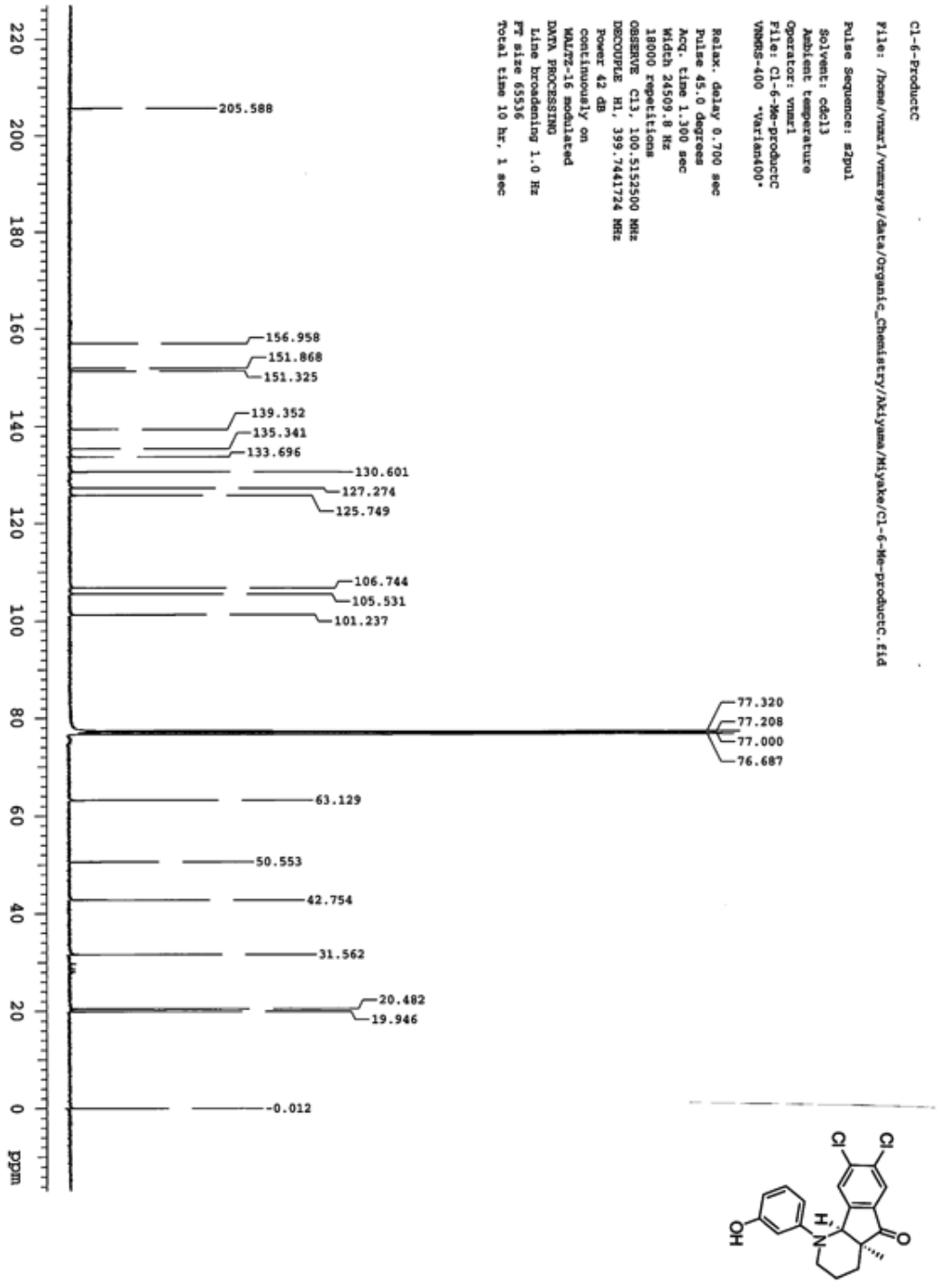
Peak #	Retention time	Type	Area	Area %
1	11.37	BI	3388434	50.777
2	15.87	BB	3284747	49.223



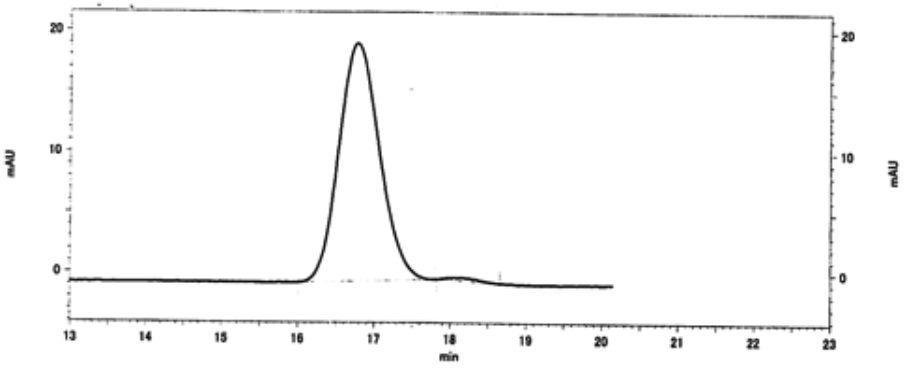
^{1}H NMR spectrum of **2e**.



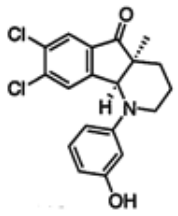
^{13}C NMR spectrum of **2e**.



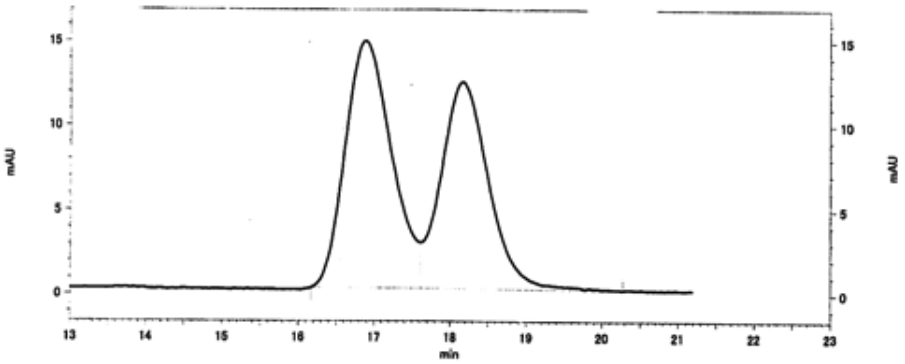
HPLC chart of **2e**.



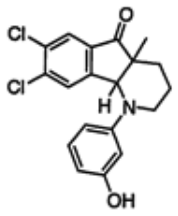
Peak #	Retention time	Type	Area	Area %
1	16.773	BB	2930333	98.974
2	18.060	BB	30364	1.026



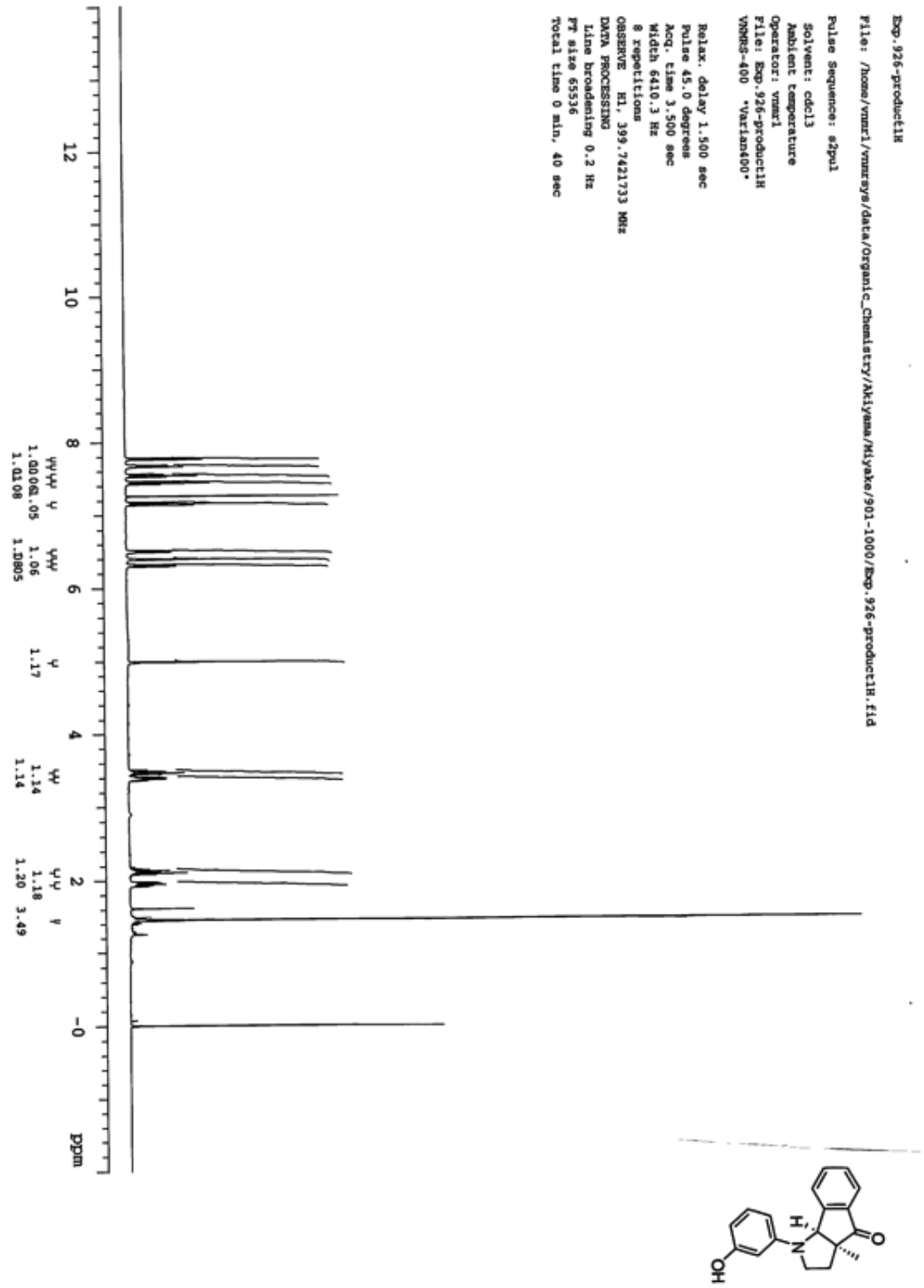
HPLC chart of **2e** (racemic).



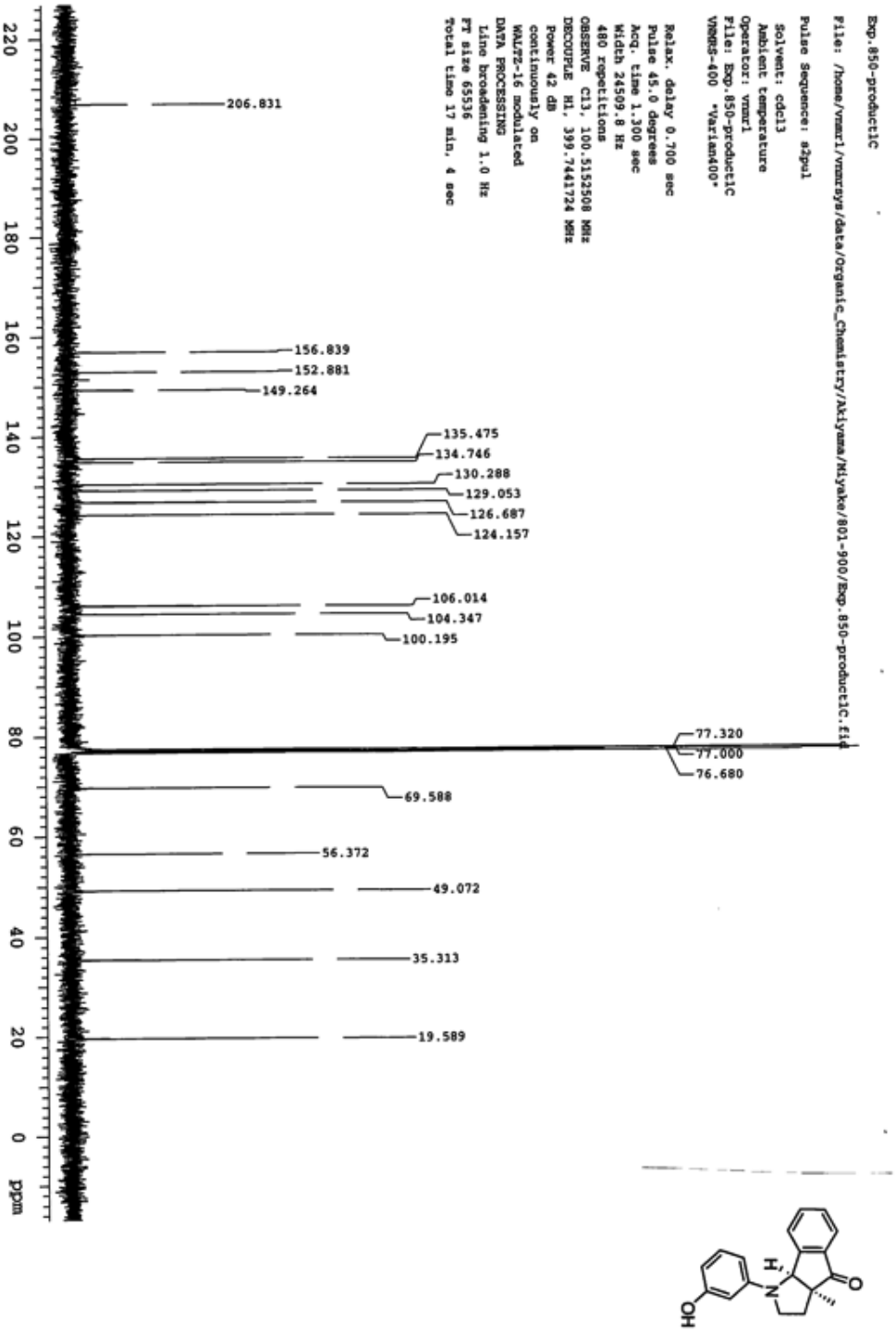
Peak #	Retention time	Type	Area	Area %
1	16.887	BV	2491695	53.709
2	18.160	VB	2147572	46.291



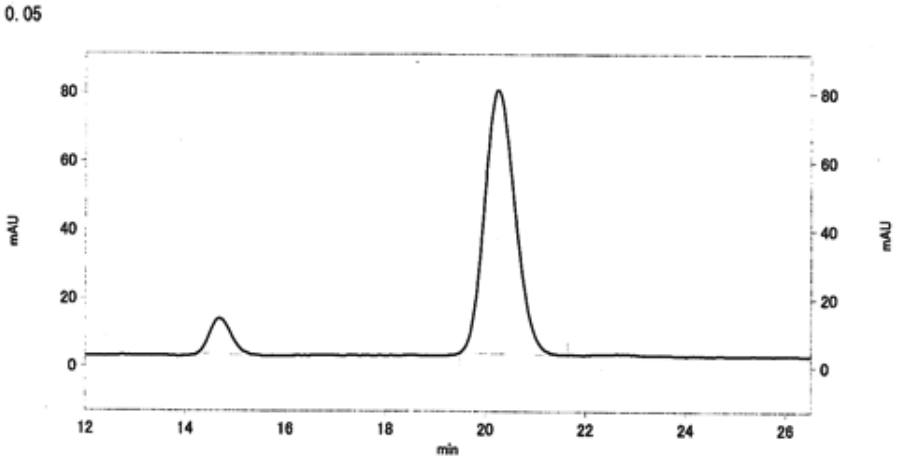
^{1}H NMR spectrum of **7a**.



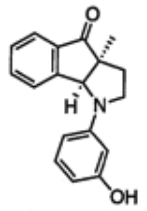
^{13}C NMR spectrum of **7a**.



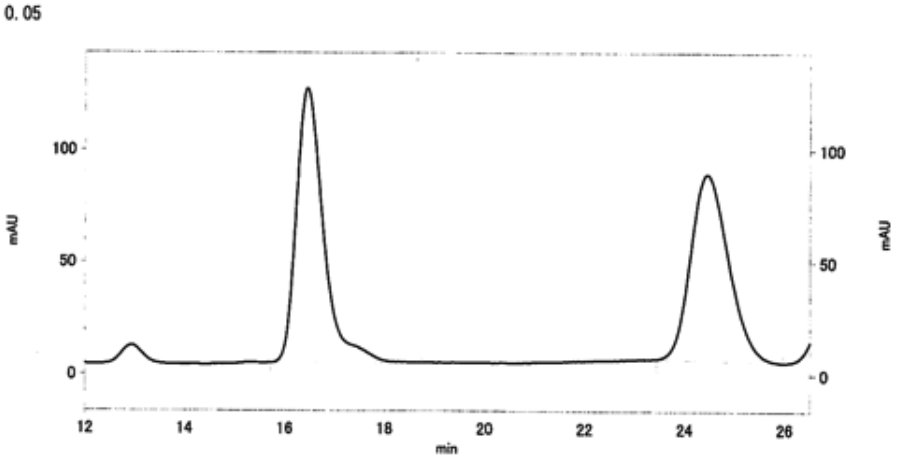
HPLC chart of **7a**.



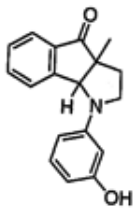
Peak #	Retention time	Type	Area	Area %
1	14.67	BB	1257284	8.783
2	20.24	BB	13057487	91.217



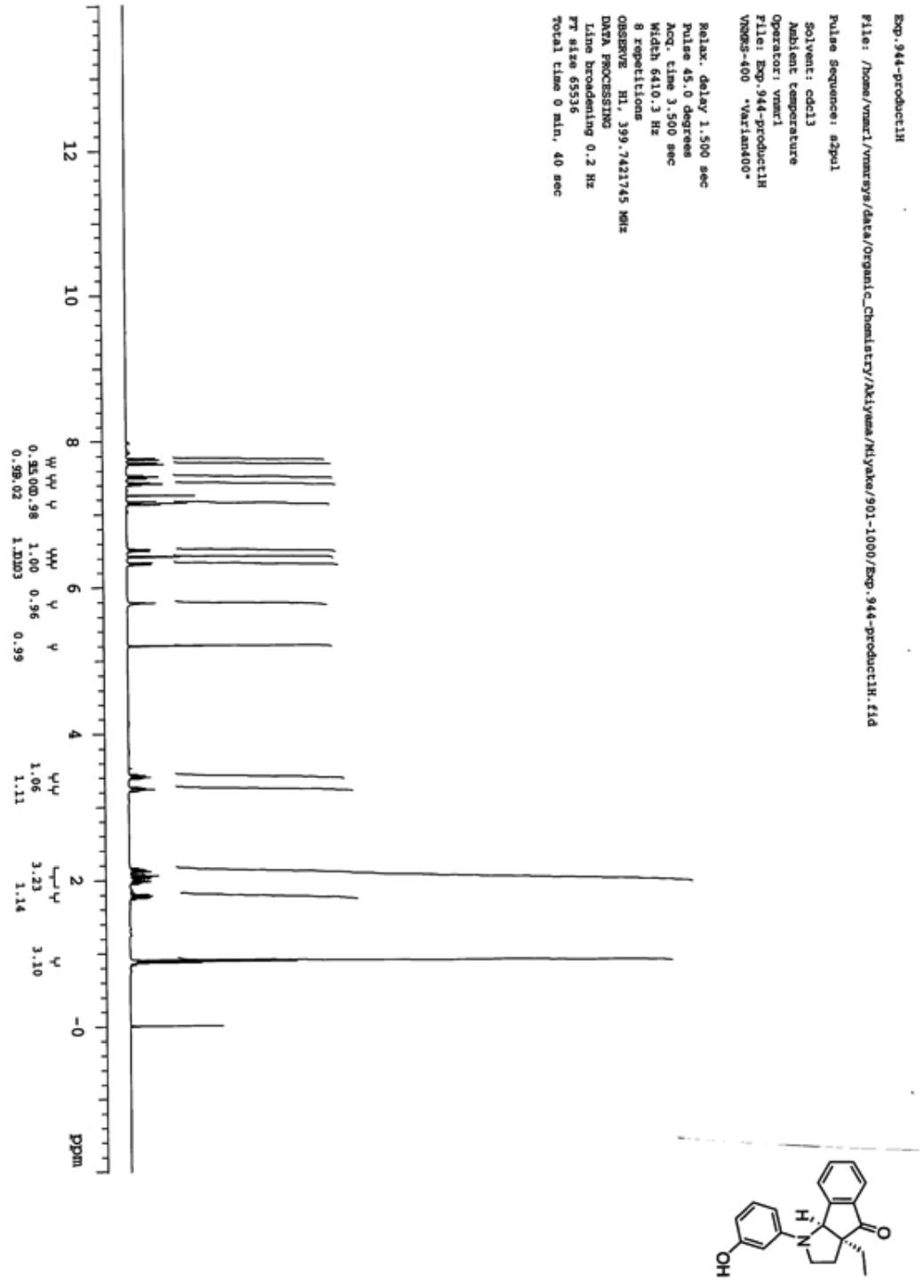
HPLC chart of **7a** (racemic).



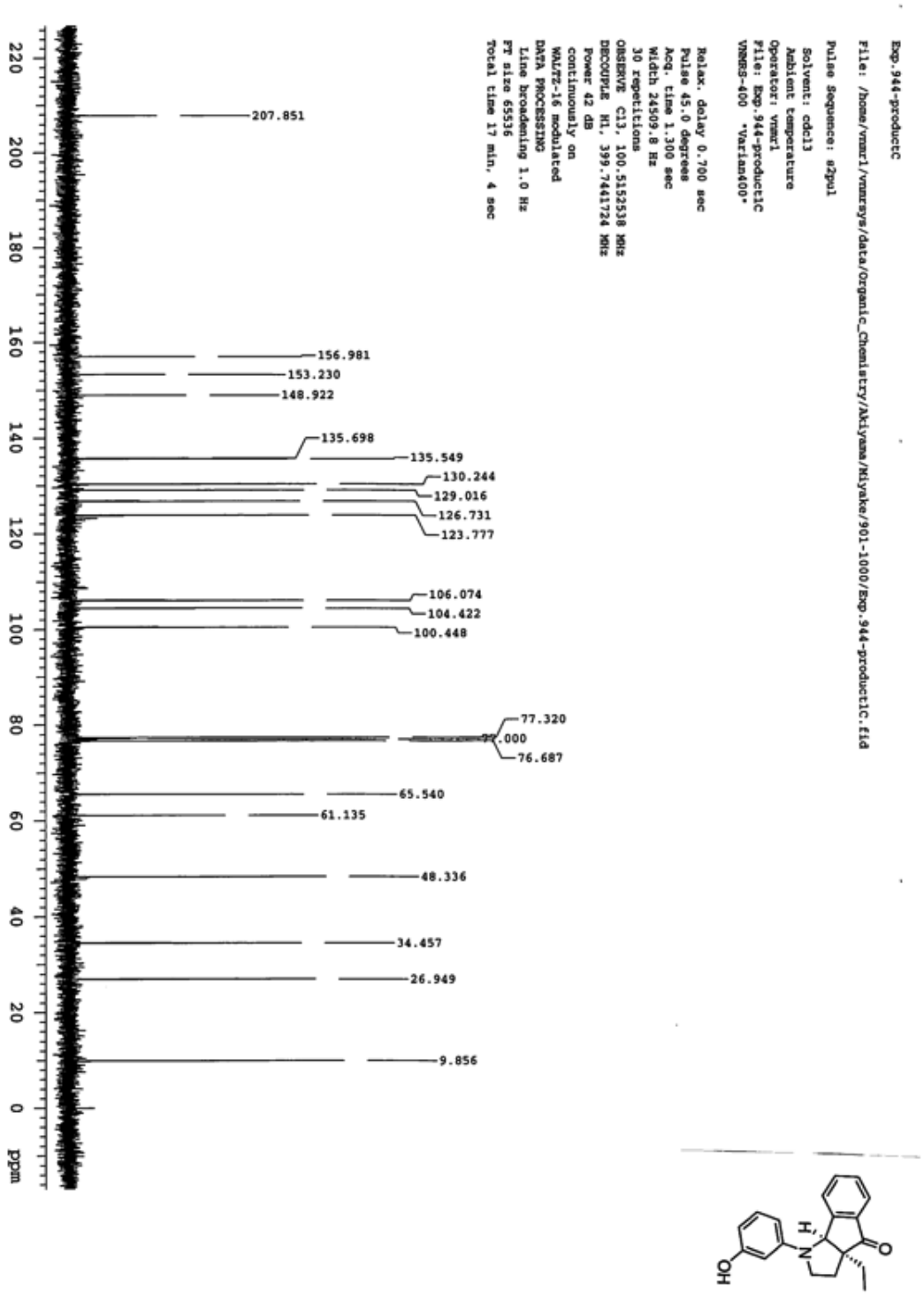
Peak #	Retention time	Type	Area	Area %
1	16.45	BB	18419633	51.462
2	24.45	BB	17372793	48.538



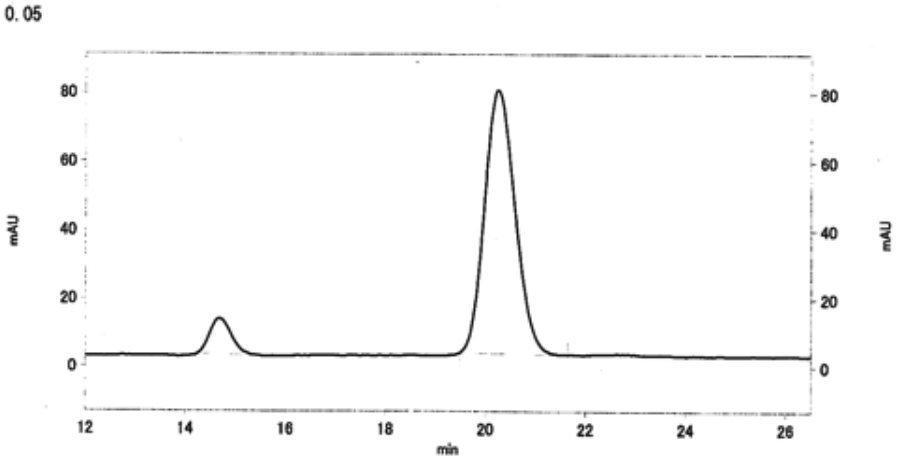
^{1}H NMR spectrum of **7b**.



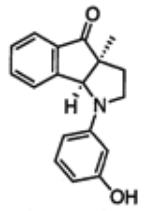
^{13}C NMR spectrum of **7b**.



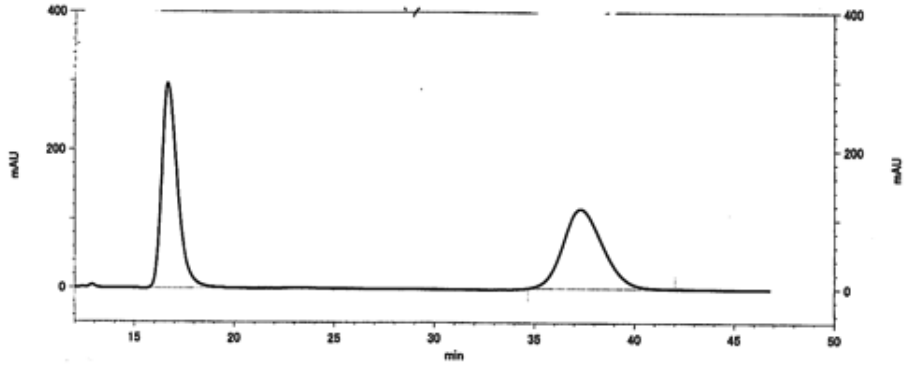
HPLC chart of **7b**.



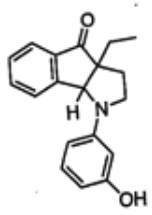
Peak #	Retention time	Type	Area	Area %
1	14.67	BB	1257284	8.783
2	20.24	BB	13057487	91.217



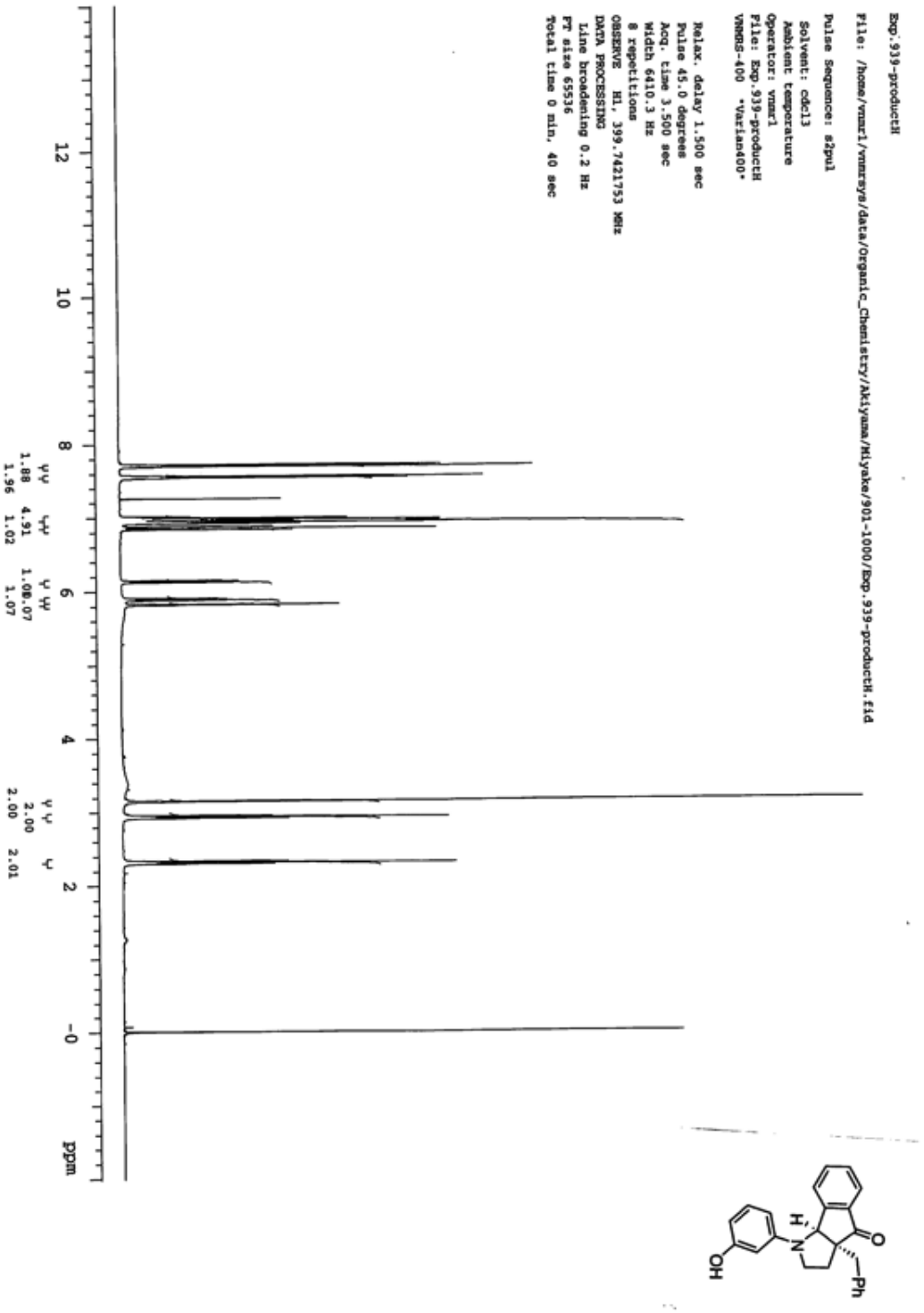
HPLC chart of **7b** (racemic).



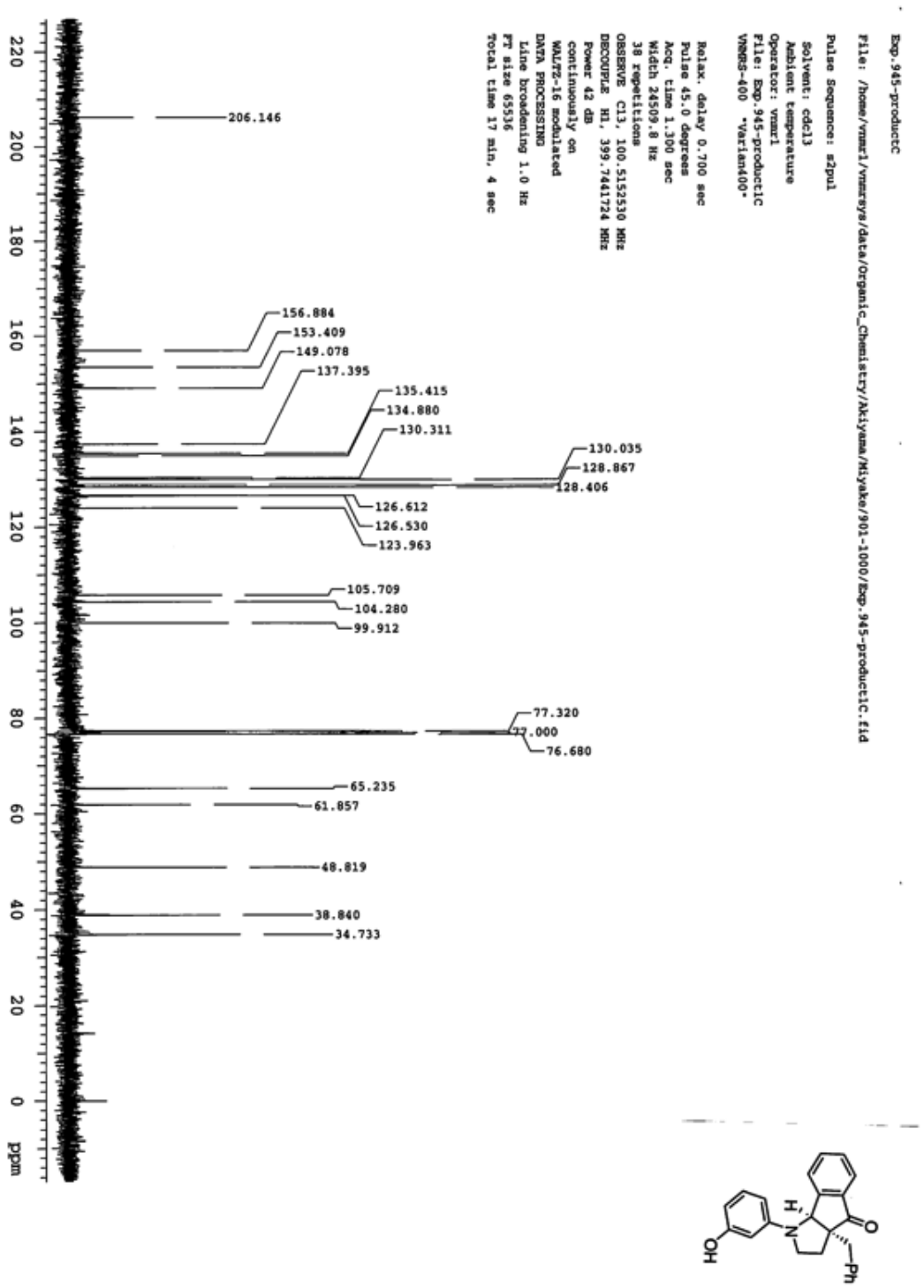
Peak #	Retention time	Type	Area	Area %
1	16.660	BB	65675160	50.586
2	37.300	BB	64152553	49.414



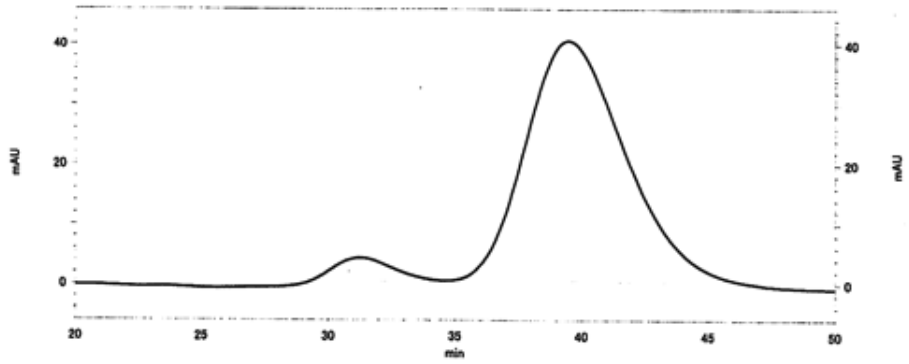
^{1}H NMR spectrum of **7c**.



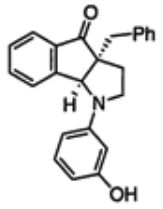
^{13}C NMR spectrum of **7c**.



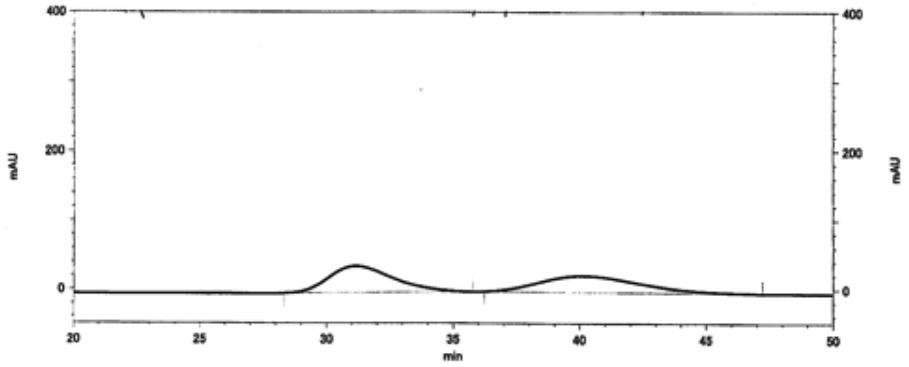
HPLC chart of **7c**.



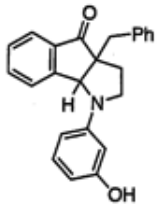
Peak #	Retention time	Type	Area	Area %
1	31.153	BB	2467697	5.360
2	39.460	BB	43569015	94.640



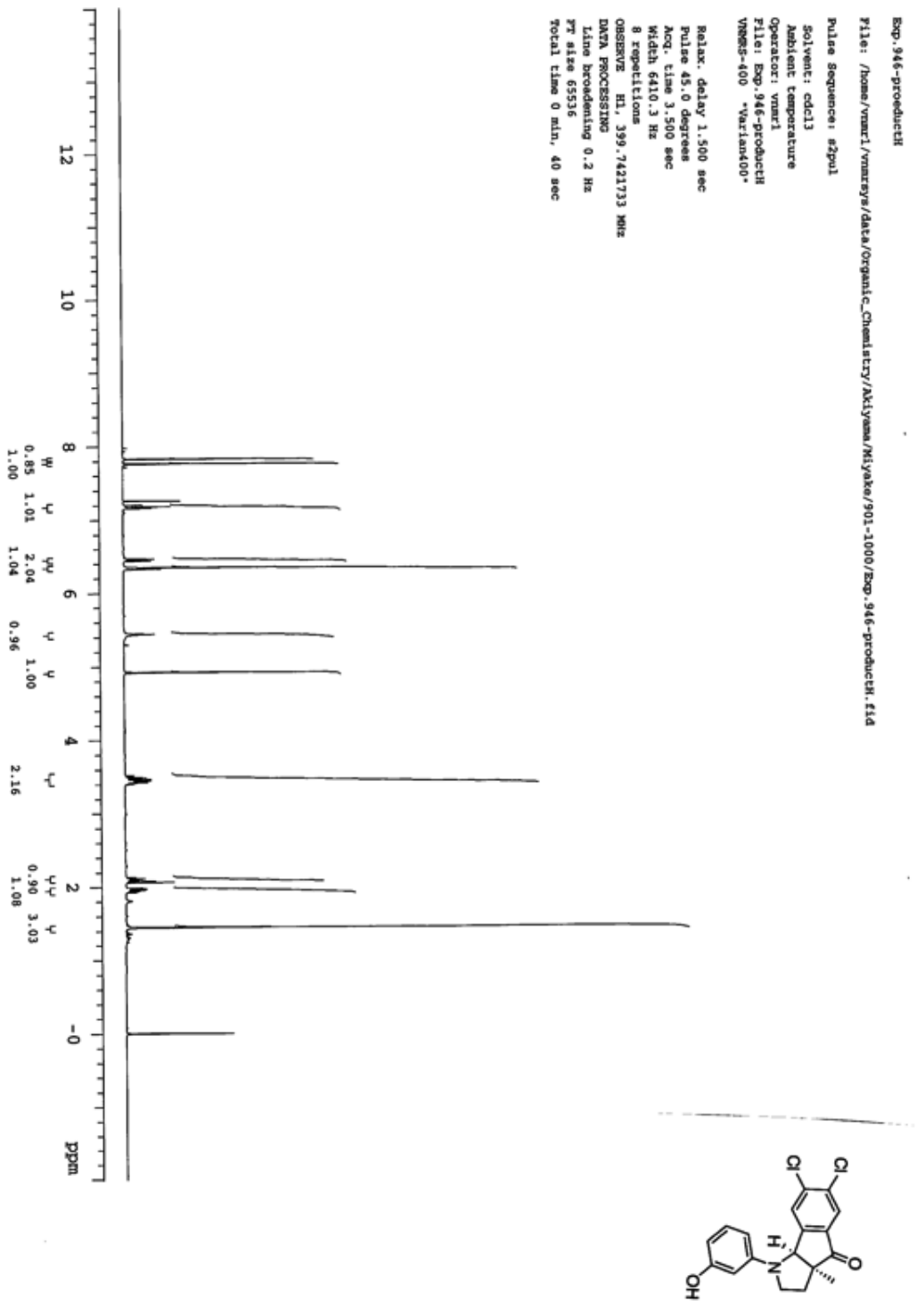
HPLC chart of **7c** (racemic).



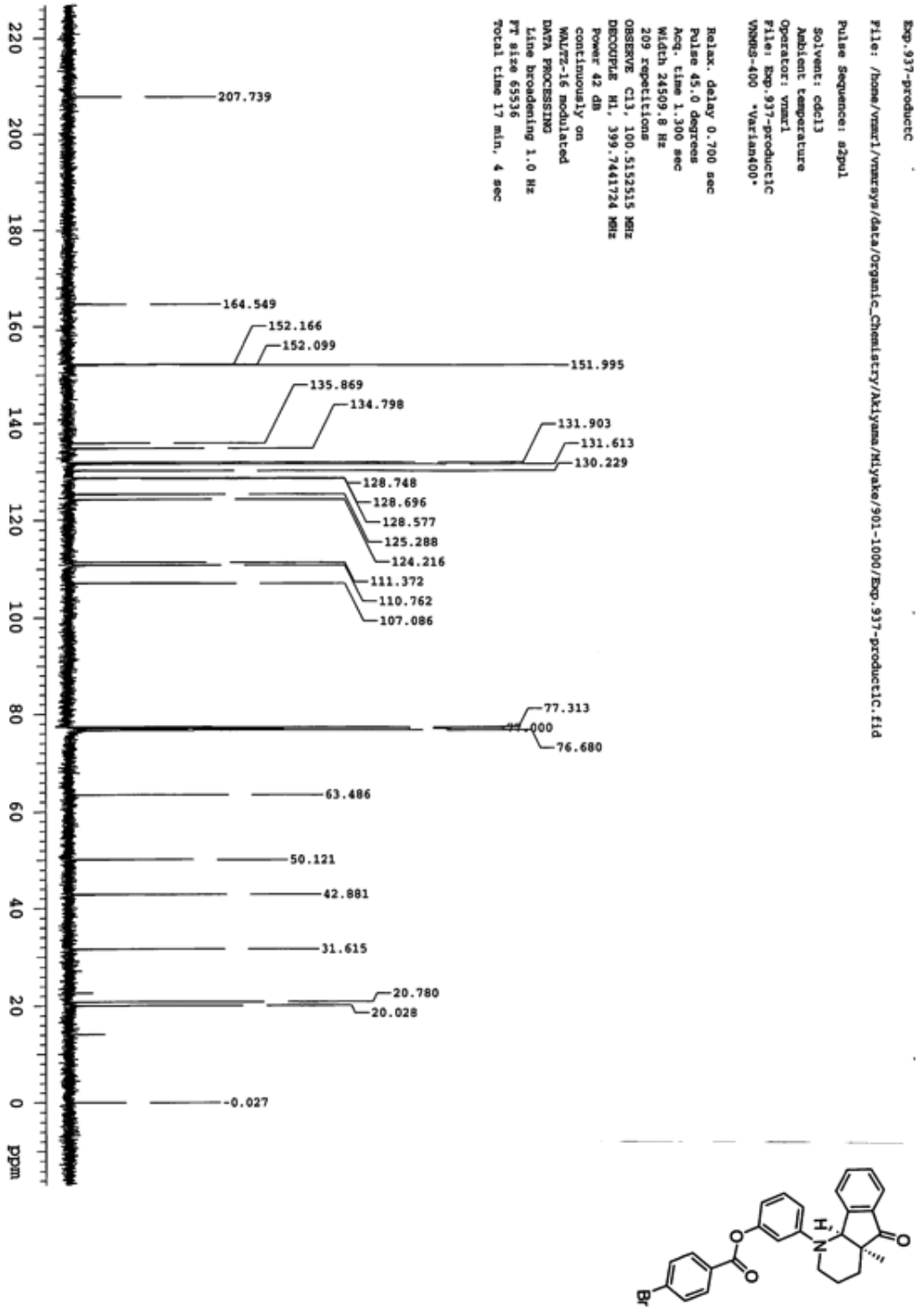
Peak #	Retention time	Type	Area	Area %
1	31.173	BB	27298433	50.511
2	40.087	BB	26746296	49.489



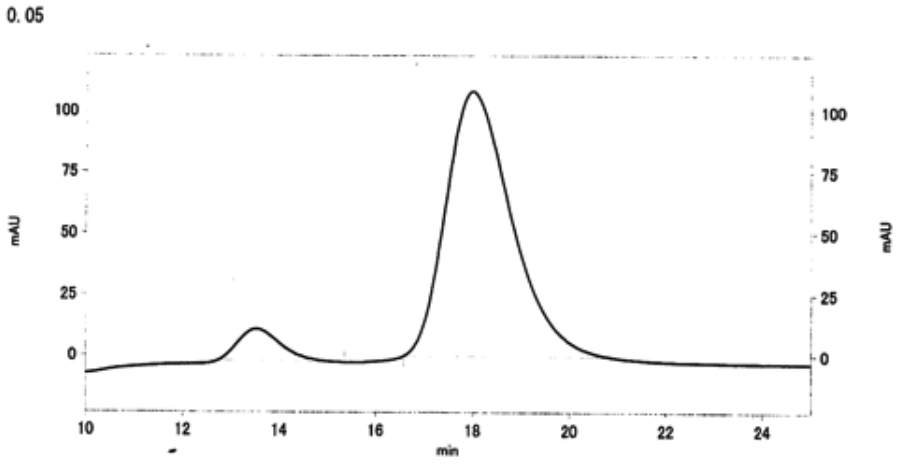
^{1}H NMR spectrum of **7d**.



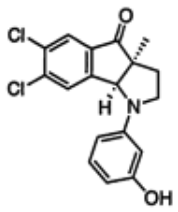
^{13}C NMR spectrum of **7d**.



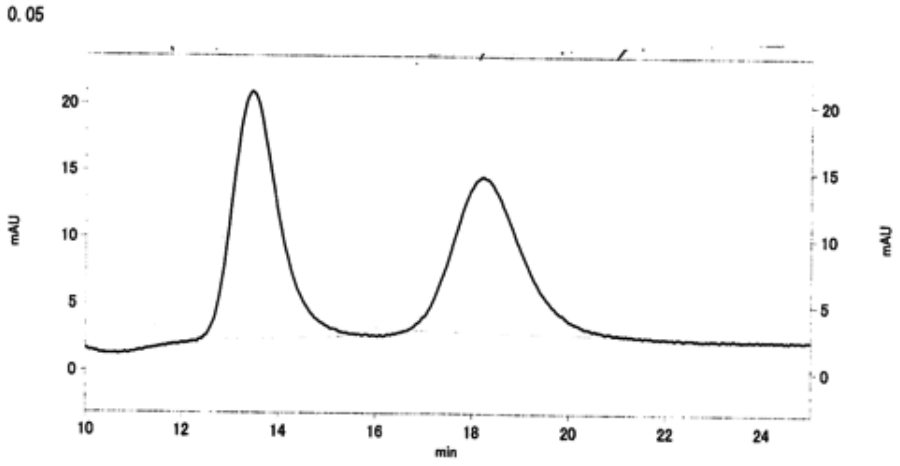
HPLC chart of **7d**.



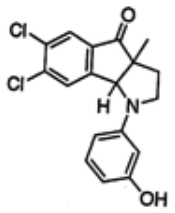
Peak #	Retention time	Type	Area	Area %
1	13.54	BB	3194504	7.232
2	18.00	BB	40974949	92.768



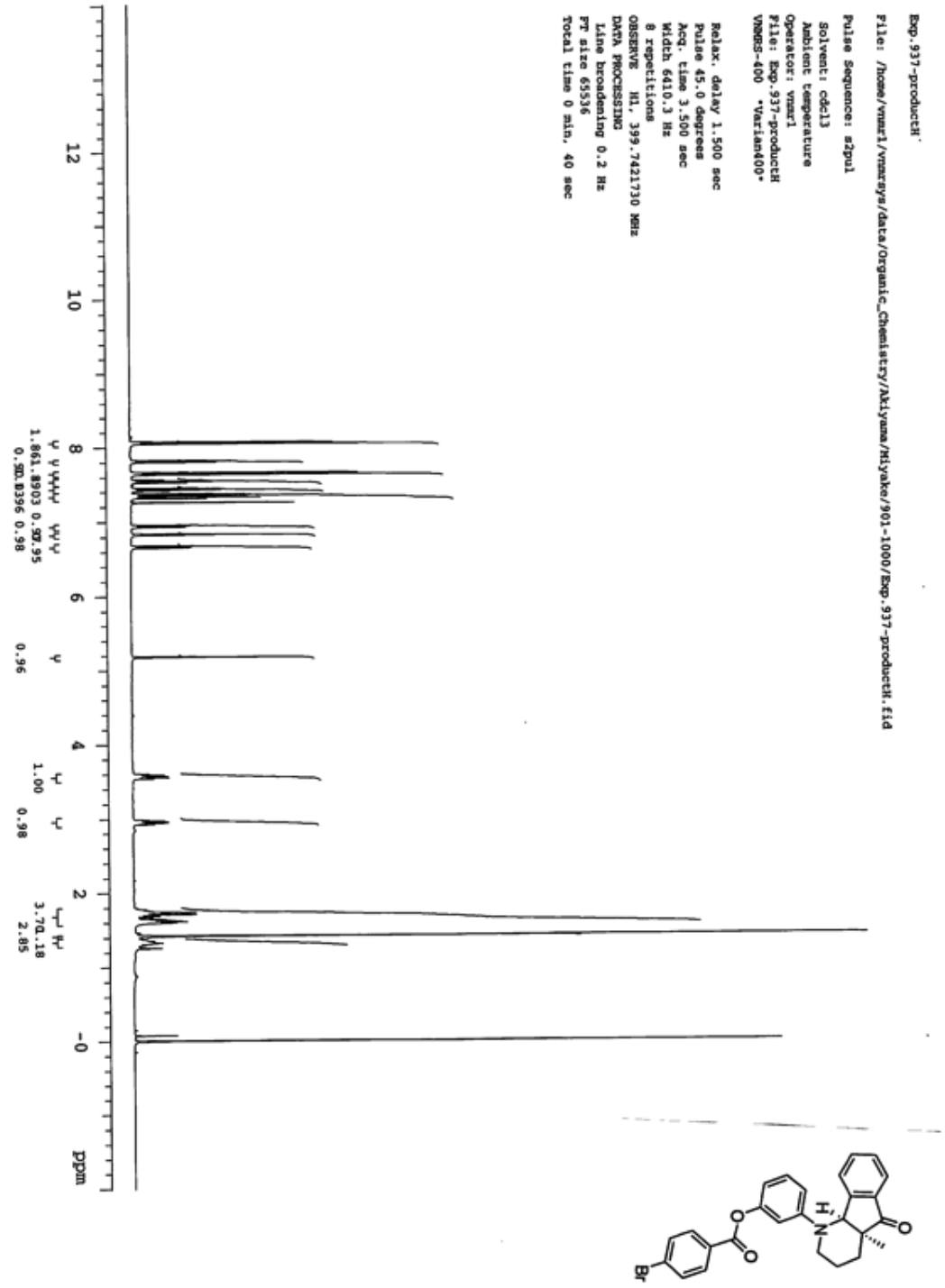
HPLC chart of **7d** (racemic).



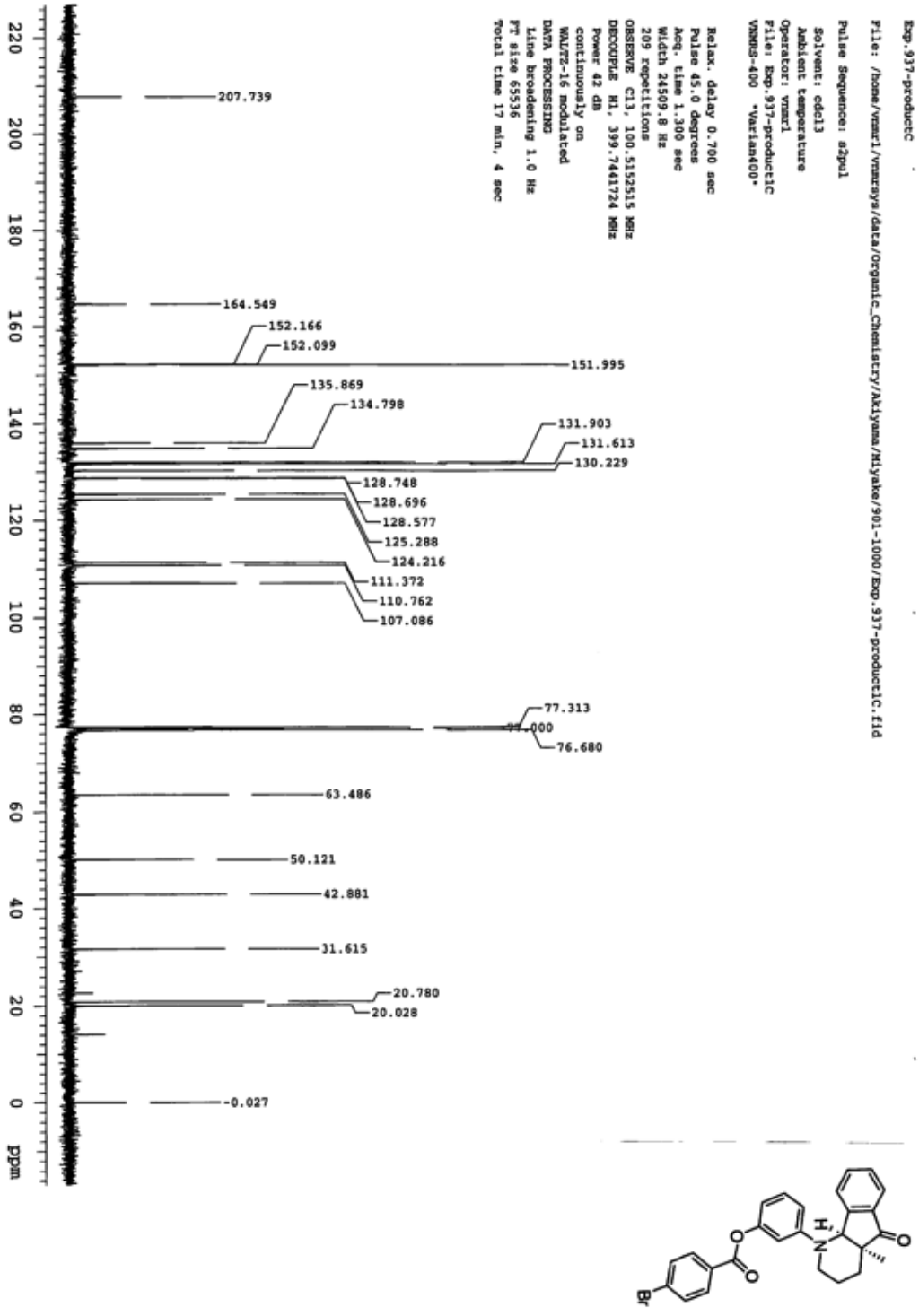
Peak #	Retention time	Type	Area	Area %
1	13.43	BI	4898030	51.676
2	18.21	BB	4580338	48.324



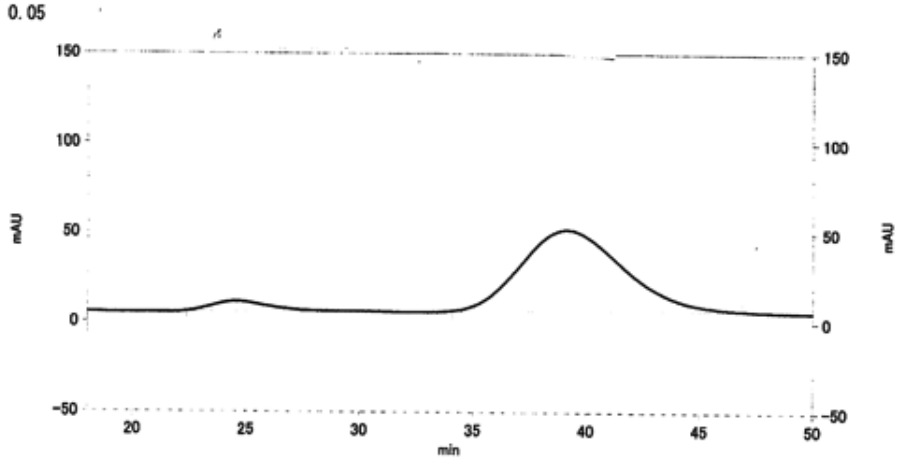
^{1}H NMR spectrum of **s6**.



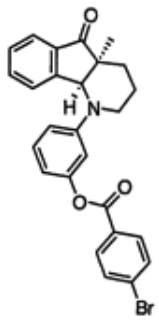
^{13}C NMR spectrum of **a6**.



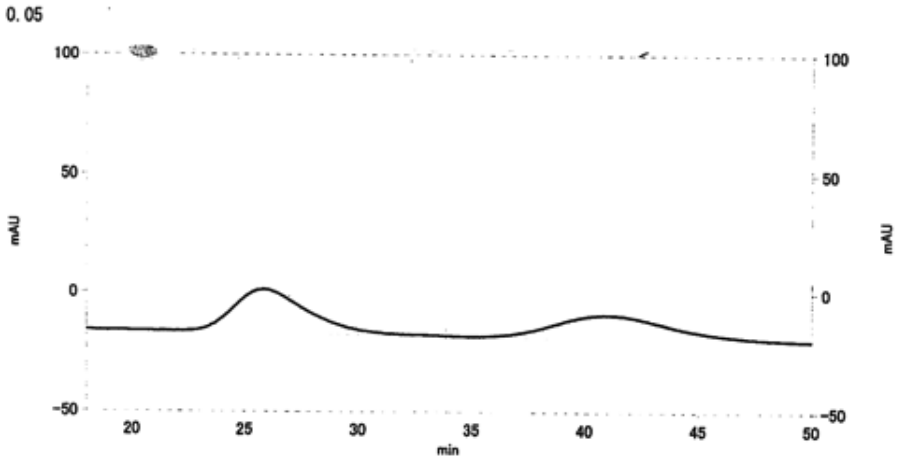
HPLC chart of **s6**.



Peak #	Retention time	Type	Area	Area %
1	24.55	BB	3799111	6.250
2	39.07	BB	56982298	93.750



HPLC chart of **s6** (racemic).



Peak #	Retention time	Type	Area	Area %
1	25.81	BB	16916575	52.943
2	40.79	BI	15035559	47.057