Construction of Seven- and Eight-Membered Carbocycles by Lewis Acid Catalyzed C(sp^3)–H Bond Functionalization

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Supporting Information

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General experimental procedures

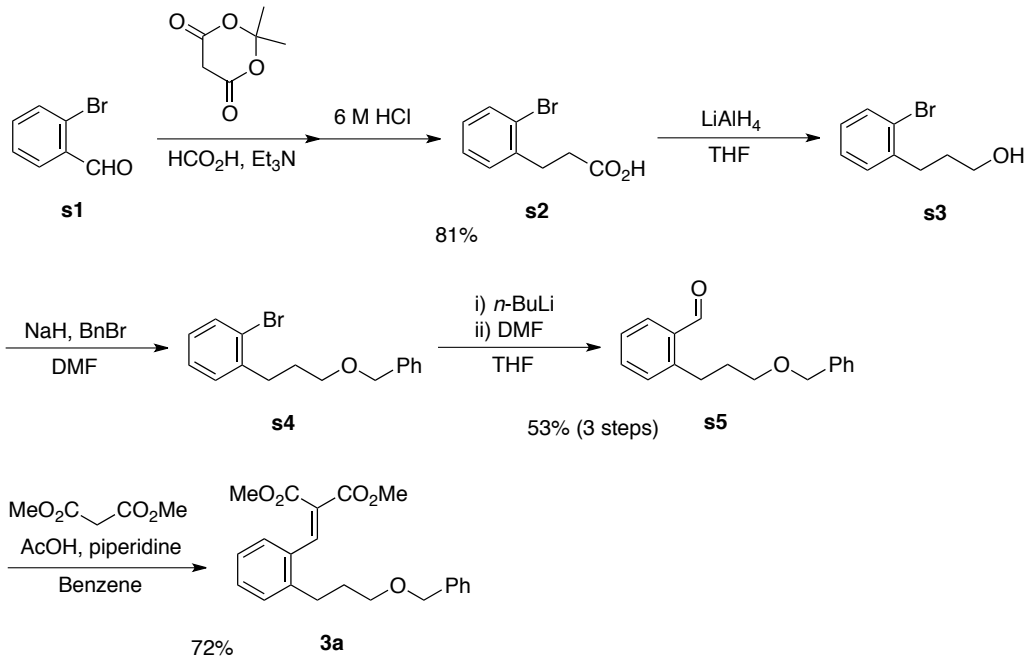
All reactions utilizing air- and moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry nitrogen. Anhydrous ethereal solvents (THF, Et_2O) were purchased from Kanto Chemical Co., INC., and used directly. Dichloromethane and 1,2-dichloroethane were distilled over CaH_2. 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.

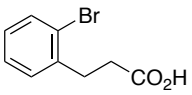
For thin-layer chromatography (TLC) analysis, Merck pre-coated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) were used. Column chromatography and preparative TLC (PTLC) were performed on Silica Gel 60N (spherical, neutral), Kanto Chemical Ltd. and Wakogel B-5F, Wako Pure Chemical Industries, respectively.

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 were measured on a AL-300 MR (JEOL Ltd., 300 MHz), ECX-400 (JEOL Ltd., 400 MHz), and ECA-500 (JEOL Ltd., 500 MHz) spectrometers. 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; 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.

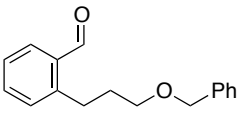
Scheme S1. Preparation of starting materials **1**. Preparation of **3a** was shown as a representative example.





Synthesis of 3-(2-bromophenyl)propanoic acid (s2):[1]

To HCO_2H (85%, 4.40 mL) were successively added Et_3N (6.40 mL, 46.2 mmol), **s1** (2.0 mL, 17.1 mmol), and Meldrum's acid (2.48 g, 17.2 mmol) at 0 °C. The reaction mixture was heated to 95 °C for 4 h. After the reaction mixture was cooled to 0 °C, ice-cooled water (22.0 mL) was added. After being stirred for 14 h, the white precipitates were collected with filtration (washed with H_2O) to afford **s2** (3.18 g, 81%) as white solid. This material had enough purity, so directly used next reaction without further purification.



Synthesis of 2-(3-(benzyloxy)propyl)benzaldehyde (s5):

To a solution of **s2** (1.62 g, 7.07 mmol) in Et_2O (35.5 mL) was added $LiAlH_4$ (410 mg, 10.8 mmol) at 0 °C (portion wise). After being stirred for 2 h at refluxing temperature,

the reaction was stopped by adding Na_2SO_4•$10H_2O$. After being stirred for another 0.5 h at room temperature, the crude material was filtered through Celite® pad and the resulting filtrate was concentrated in vacuo to give crude alcohol **s3** (1.56 g). The crude material was used for the next reaction without further purification.

To a solution of **s3** in DMF (23.6 mL) were successively added NaH (60 % oil, 478 mg, 12.0 mmol), and BnBr (1.30 mL, 10.9 mmol). After being stirred for 16 h at room temperature, the reaction was quenched by addition of Et_2NH (0.36 ml, 7.09 mmol) at 0 °C. 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 = 30/1) to give **s4** (1.54 g) as colorless oil. At this moment, **s4** could not be isolated as pure compound, so this material was used for next reaction without further purification.

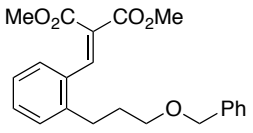
To a solution of **s4** in THF (25.2 mL) was added *n*-BuLi (1.57 M in hexane, 4.18 mL, 6.56 mmol) at –78 °C. The reaction mixture was stirred for 10 min at –78 °C, to which DMF (0.78 mL, 10.1 mmol) was added. After being stirred for 2 h, the reaction was quenched by addition of saturated aqueous NH_4Cl at –78 °C. 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 = 15/1) to afford aldehyde **s5** (953 mg, 53% from **s2**) as colorless oil.

IR (neat) 3087, 3064, 3030, 2940, 2859, 2793, 2736, 1695, 1600, 1574, 1495, 1488, 1453, 1405, 1364, 1290, 1207, 1193, 1160, 1102, 1028, 954, 907 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.94 (tt, 2H, *J* = 6.0, 7.6 Hz), 3.16 (t, 2H, *J* = 7.6 Hz), 3.51 (t, 2H, *J* = 6.0 Hz), 4.52 (s, 2H), 7.24–7.32 (m, 2H), 7.33–7.42 (m, 5H), 7.49 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.83 (dd, 1H, *J* = 8.0 Hz), 10.29 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 29.0, 31.8, 69.2, 72.9, 126.5, 127.6, 127.7, 128.4, 131.1, 131.8, 133.8, 138.4, 144.8, 192.5.

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.43; H, 6.89.



Synthesis of 2-(2-(3-(benzyloxy)propyl)benzylidene)malonate (3a):

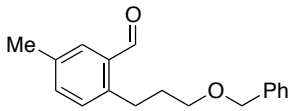
To a solution of **s5** (430 mg, 1.69 mmol) in benzene (8.4 mL) were successively added dimethyl malonate (193 μL, 1.69 mmol), piperidine (179 μL, 1.69 mmol), and AcOH (193 μL, 3.38 mmol) at room temperature. The reaction mixture was heated to reflux for 17 h. The crude mixture was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, hexane/EtOAc = 9/1) to give **3a** (449 mg, 72%) as colorless oil.

IR (neat) 3063, 3029, 3005, 2951, 2858, 1735, 1627, 1600, 1495, 1483, 1454, 1436, 1365, 1263, 1215, 1184, 1105, 1071, 1028, 986 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.89 (tt, 2H, *J* = 6.0, 7.6 Hz), 2.81 (t, 2H, *J* = 7.6 Hz), 3.46 (t, 2H, *J* = 6.0 Hz), 3.69 (s, 3H), 3.81 (s, 3H), 4.50 (s, 2H), 7.17 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.22 (d, 1H, *J* = 8.0 Hz), 7.26–7.38 (m, 7H), 8.08 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 30.0, 30.8, 52.4, 52.6, 69.0, 72.8, 126.2, 127.3, 127.5, 127.6, 127.9, 128.3, 129.7, 130.1, 132.2, 138.4, 141.6, 142.6, 164.3, 166.7.

Anal. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 71.87; H, 6.38.



2-(3-(Benzyloxy)propyl)-5-methylbenzaldehyde (**s6**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 20/1).

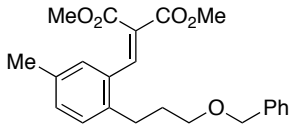
Yield: 743 mg (48%, synthesized from commercially available, 2-bromo-4-methylbenzaldehyde).

IR (neat) 3063, 3030, 2922, 2857, 2793, 2731, 1689, 1610, 1568, 1497, 1454, 1402, 1364, 1280, 1240, 1203, 1157, 1103, 1072, 1028, 941 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.92 (tt, 2H, *J* = 6.0, 7.6 Hz), 2.38 (s, 3H), 3.10 (t, 2H, *J* = 7.6 Hz), 3.50 (t, 2H, *J* = 6.0 Hz), 4.50 (s, 2H), 7.16 (d, 1H, *J* = 7.6 Hz), 7.24–7.41 (m, 6H), 7.64 (s, 1H), 10.26 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 28.5, 31.9, 69.2, 72.9, 127.5, 127.7, 128.4, 131.1, 132.0, 133.6, 134.6, 136.2, 138.4, 141.9, 192.6.

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.59; H, 7.75.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-5-methylbenzylidene)malonate (**3b**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

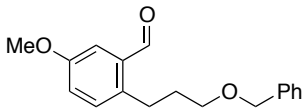
Yield: 482 mg (84%, synthesized from **s6**).

IR (neat) 3029, 2951, 2858, 1734, 1627, 1609, 1495, 1454, 1436, 1365, 1267, 1228, 1183, 1102, 1071, 1028, 987, 957, 926 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.87 (tt, 2H, J = 6.0, 7.6 Hz), 2.29 (s, 3H), 2.77 (t, 2H, J = 7.6 Hz), 3.45 (t, 2H, J = 6.0 Hz), 3.71 (s, 3H), 3.81 (s, 3H), 4.49 (s, 2H), 7.08–7.13 (m, 3H), 7.25–7.32 (m, 1H), 7.32–7.39 (m, 4H), 8.06 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 29.5, 30.9, 52.3, 52.5, 69.0, 72.7, 126.9, 127.4, 127.6, 128.3, 128.3, 129.7, 131.0, 132.0, 135.7, 138.5, 138.6, 142.6, 164.3, 166.8.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.04; H, 6.58.



2-(3-(Benzyloxy)propyl)-5-methoxybenzaldehyde (**s7**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

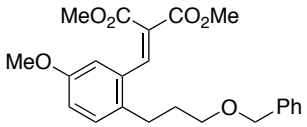
Yield: 520 mg (58%, synthesized from commercially available, 2-bromo-4-methoxylbenzaldehyde).

IR (neat) 3063, 3030, 3004, 2940, 2857, 2793, 2760, 1686, 1608, 1571, 1497, 1464, 1454, 1423, 1401, 1364, 1328, 1276, 1261, 1249, 1189, 1163, 1102, 1038, 937 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.91 (tt, 2H, J = 6.0, 7.6 Hz), 3.07 (t, 2H, J = 7.6 Hz), 3.48 (t, 2H, J = 6.0 Hz), 3.84 (s, 3H), 4.50 (s, 2H), 7.05 (d, 1H, J = 2.8, 8.4 Hz), 7.18 (d, 1H, J = 8.4 Hz), 7.26–7.32 (m, 1H), 7.33–7.38 (m, 5H), 10.29 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 27.7, 32.3, 55.4, 68.9, 72.9, 113.4, 121.0, 127.6, 127.7, 128.4, 132.3, 134.4, 137.3, 138.4, 158.1, 191.7.

Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.84; H, 7.26.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-5-methoxybenzylidene)malonate (**3c**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

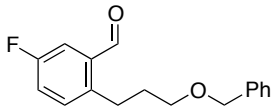
Yield: 395 mg (78%, synthesized from **s7**).

IR (neat) 3062, 3029, 3003, 2951, 2858, 2794, 1733, 1625, 1607, 1572, 1495, 1454, 1436, 1365, 1290, 1268, 1237, 1203, 1166, 1102, 1071, 1039, 989 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.85 (tt, 2H, J = 6.0, 7.6 Hz), 2.74 (t, 2H, J = 7.6 Hz), 3.45 (t, 2H, J = 6.0 Hz), 3.73 (s, 3H), 3.75 (s, 3H), 3.81 (s, 3H), 4.49 (s, 2H), 6.83–6.89 (m, 2H), 7.11 (d, 1H, J = 8.0 Hz), 7.25–7.32 (m, 1H), 7.32–7.37 (m, 4H), 8.03 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 29.1, 31.1, 52.5, 52.6, 55.2, 68.9, 72.8, 112.5, 116.4, 127.3, 127.5, 127.6, 128.3, 130.8, 132.9, 133.8, 138.5, 142.3, 157.7, 164.2, 166.7.

Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.26; H, 6.72.



2-(3-(Benzyloxy)propyl)-5-fluorobenzaldehyde (**s8**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

Yield: 487 mg (36%, synthesized from commercially available, 2-bromo-4-fluorobenzaldehyde).

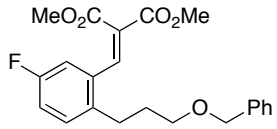
IR (neat) 3087, 3064, 3032, 2940, 2859, 2793, 1690, 1609, 1583, 1494, 1454, 1420, 1364, 1310, 1266, 1240, 1206, 1177, 1148, 1103, 1028, 968 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.92 (tt, 2H, J = 6.0, 7.6 Hz), 3.11 (t, 2H, J = 7.6 Hz), 3.48 (t, 2H, J = 6.0 Hz), 4.50 (s, 2H), 7.15–7.25 (m, 2H), 7.26–7.40 (m, 5H), 7.86 (dd, 1H, J = 2.8, 9.2 Hz), 10.26 (d, 1H, J = 1.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 32.1, 68.8, 73.0, 116.5 (d, J_{C-F} = 22.0 Hz), 120.9 (d, J_{C-F} = 21.0 Hz), 127.6, 127.7, 128.4, 132.9 (d, J_{C-F} = 6.7 Hz), 135.1 (d, J_{C-F} = 5.7 Hz), 138.3, 140.6 (d, J_{C-F} = 3.8 Hz), 161.3 (d, J_{C-F} = 246.0 Hz), 190.8.

^{19}F NMR (283 MHz, $CDCl_3$) δ 46.3 (dd, 1F, J = 6.8, 13.9 Hz).

Anal. Calcd for $C_{17}H_{17}FO_2$: C, 74.98; H, 6.29. Found: C, 75.24; H, 6.14.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-5-methylbenzylidene)malonate (**3d**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

Yield: 366 mg (83%, synthesized from **s8**).

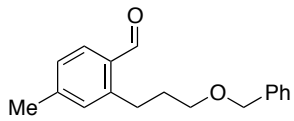
IR (neat) 2952, 2856, 1733, 1630, 1609, 1583, 1489, 1454, 1437, 1365, 1268, 1229, 1179, 1160, 1101, 1070, 1028, 994, 972 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86 (tt, 2H, J = 6.0, 7.6 Hz), 2.77 (t, 2H, J = 7.6 Hz), 3.45 (t, 2H, J = 6.0 Hz), 3.74 (s, 3H), 3.82 (s, 3H), 4.49 (s, 2H), 6.96–7.04 (m, 2H), 7.17 (dd, 1H, J = 5.6, 8.0 Hz), 7.25–7.32 (m, 1H), 7.33–7.39 (m, 4H), 7.98 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 29.2, 30.8, 52.6, 114.5 (d, J_{C-F} = 22.9 Hz), 116.9 (d, J_{C-F} = 20.9 Hz), 127.5, 127.6, 128.3, 131.2 (d, J_{C-F} = 7.6 Hz), 133.7 (d, J_{C-F} = 8.5 Hz), 137.3 (d, J_{C-F} = 3.8 Hz), 138.4, 141.0, 160.9 (d, J_{C-F} = 244.1 Hz), 164.0, 166.2.

^{19}F NMR (283 MHz, $CDCl_3$) δ 45.5 (dd, 1F, J = 9.3, 13.6 Hz).

Anal. Calcd for $C_{22}H_{23}FO_5$: C, 68.38; H, 6.00. Found: C, 68.26; H, 5.79.



2-(3-(Benzyloxy)propyl)-4-methylbenzaldehyde (**s9**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 15/1).

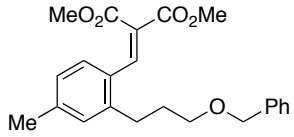
Yield: 745 mg (65%, synthesized from commercially available, 2-bromo-5-methylbenzaldehyde).

IR (neat) 3063, 3030, 2922, 2857, 2793, 2732, 1736, 1694, 1607, 1569, 1496, 1478, 1454, 1399, 1364, 1307, 1292, 1276, 1234, 1211, 1200, 1154, 1103, 1073, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (tt, 2H, J = 6.0, 7.6 Hz), 2.38 (s, 3H), 3.10 (t, 2H, J = 7.6 Hz), 3.51 (t, 2H, J = 6.0 Hz), 4.51 (s, 2H), 7.08 (s, 1H), 7.17 (d, 1H, J = 8.0 Hz), 7.24–7.33 (m, 1H), 7.33–7.40 (m, 4H), 7.72 (d, 1H, J = 8.0 Hz), 10.21 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 29.0, 31.8, 69.3, 72.9, 127.3, 127.6, 127.7, 128.4, 131.5, 131.8, 132.2, 138.5, 144.7, 144.8, 192.1.

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.46; H, 7.27.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-4-methylbenzylidene)malonate (**3e**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

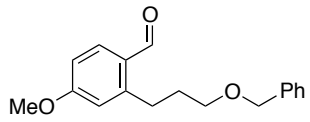
Yield: 534 mg (88%, synthesized from **s9**).

IR (neat) 3030, 3002, 2951, 2857, 1735, 1626, 1610, 1496, 1454, 1436, 1365, 1264, 1245, 1216, 1182, 1113, 1102, 1069, 1028, 987 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.88 (tt, 2H, *J* = 6.0, 7.6 Hz), 2.31 (s, 3H), 2.78 (t, 2H, *J* = 7.6 Hz), 3.47 (t, 2H, *J* = 6.0 Hz), 3.72 (s, 3H), 3.81 (s, 3H), 4.50 (s, 2H), 6.98 (d, 1H, *J* = 8.0 Hz), 7.03 (s, 1H), 7.20 (d, 1H, *J* = 8.0 Hz), 7.25–7.32 (m, 1H), 7.32–7.39 (m, 4H), 8.05 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 29.9, 31.0, 52.4, 52.5, 69.0, 72.8, 126.2, 127.1, 127.5, 127.6, 127.9, 128.3, 129.3, 130.6, 138.5, 140.6, 141.8, 142.3, 164.5, 167.1.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.45; H, 6.94.



2-(3-(Benzyloxy)propyl)-4-methoxybenzaldehyde (**s10**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc =9/1).

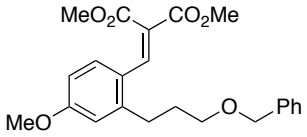
Yield: 439 mg (40%, synthesized from commercially available, 2-bromo-5-methoxylbenzaldehyde).

IR (neat) 3087, 3063, 3029, 2940, 2856, 2793, 2733, 1687, 1599, 1566, 1496, 1454, 1430, 1364, 1327, 1289, 1251, 1207, 1167, 1105, 1076, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.94 (tt, 2H, *J* = 6.0, 7.6 Hz), 3.12 (t, 2H, *J* = 7.6 Hz), 3.53 (t, 2H, *J* = 6.0 Hz), 3.85(s, 3H), 4.52 (s, 2H), 6.77 (d, 1H, *J* = 2.0 Hz), 6.86 (dd, 1H, *J* = 2.0, 8.4 Hz), 7.24–7.33 (m, 1H), 7.33–7.40 (m, 4H), 7.79 (d, 1H, *J* = 8.4 Hz), 10.12 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 29.3, 31.6, 55.4, 69.4, 72.9, 111.8, 116.2, 127.4, 127.6, 127.7, 128.4, 134.7, 138.5, 147.5, 163.7, 190.8.

Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.25; H, 6.79.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-4-methoxybenzylidene)malonate (**3f**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

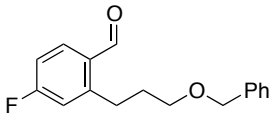
Yield: 296 mg (82%, synthesized from **s10**).

IR (neat) 33030, 3003, 2951, 2856, 1734, 1602, 1568, 1496, 1454, 1436, 1366, 1310, 1253, 1218, 1181, 1109, 1069, 1029, 987 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.89 (tt, 2H, J = 6.0, 7.6 Hz), 2.81 (t, 2H, J = 7.6 Hz), 3.48 (t, 2H, J = 6.0 Hz), 3.75 (s, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 4.50 (s, 2H), 6.71 (dd, 1H, J = 2.4, 8.0 Hz), 6.77 (d, 1H, J = 2.4 Hz), 7.25–7.39 (m, 6H), 8.02 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 30.2, 30.9, 52.5, 52.5, 55.2, 69.0, 72.8, 111.8, 115.2, 124.5, 124.9, 127.5, 127.6, 128.3, 129.6, 138.4, 141.6, 144.2, 161.2, 164.6, 167.4.

Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.51; H, 6.34.



2-(3-(Benzyloxy)propyl)-4-fluorobenzaldehyde (**s11**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

Yield: 697 mg (52%, synthesized from commercially available, 2-bromo-5-fluorobenzaldehyde).

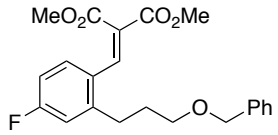
IR (neat) 3087, 3064, 3031, 2924, 2860, 2795, 2761, 1692, 1605, 1582, 1494, 1454, 1432, 1399, 1364, 1271, 1242, 1199, 1157, 1104, 1028, 961 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.94 (tt, 2H, J = 6.0, 7.6 Hz), 3.14 (t, 2H, J = 7.6 Hz), 3.51 (t, 2H, J = 6.0 Hz), 4.51 (s, 2H), 6.97 (dd, 1H, J = 2.4, 9.6 Hz), 7.04 (ddd, 1H, J = 2.4, 8.4, 8.4 Hz), 7.27–7.40 (m, 5H), 7.86 (dd, 1H, J = 6.0, 8.4 Hz), 10.21 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 28.7, 31.4, 68.9, 73.0, 113.8 (d, J_{C-F} = 21.0 Hz), 117.8 (d, J_{C-F} = 20.9 Hz), 127.6, 127.7, 128.4, 130.4 (d, J_{C-F} = 2.8 Hz), 134.5 (d, J_{C-F} = 9.5 Hz), 138.3, 148.3 (d, J_{C-F} = 8.6 Hz), 165.7 (d, J_{C-F} = 255.5 Hz), 190.7.

^{19}F NMR (283 MHz, $CDCl_3$) δ 58.0 (dd, 1F, J = 7.9, 14.9 Hz).

Anal. Calcd for $C_{17}H_{17}FO_2$: C, 74.98; H, 6.29. Found: C, 74.74; H, 6.45.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-4-fluorobenzylidene)malonate (**3g**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

Yield: 320 mg (68%, synthesized from **s11**).

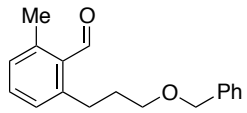
IR (neat) 3087, 3064, 3031, 3004, 2952, 2858, 1735, 1629, 1605, 1583, 1492, 1454, 1437, 1365, 1247, 1221, 1182, 1101, 1070, 1028, 986 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.89 (tt, 2H, J = 6.0, 7.6 Hz), 2.80 (t, 2H, J = 7.6 Hz), 3.46 (t, 2H, J = 6.0 Hz), 3.71 (s, 3H), 3.82 (s, 3H), 4.50 (s, 2H), 6.87 (ddd, 1H, J = 2.0, 8.4, 8.4 Hz), 7.17 (dd, 1H, J = 2.8, 9.6 Hz), 7.25–7.32 (m, 2H), 7.33–7.39 (m, 4H), 7.99 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 30.0, 30.5, 52.5, 52.6, 68.7, 72.8, 113.4 (d, J_{C-F} = 21.0 Hz), 116.6 (d, J_{C-F} = 21.0 Hz), 127.3, 127.6, 127.6, 128.4, 129.9 (d, J_{C-F} = 8.5 Hz), 138.3, 141.3, 144.6 (d, J_{C-F} = 7.7 Hz), 163.6 (d, J_{C-F} = 248.9 Hz), 164.2, 166.6.

^{19}F NMR (283 MHz, $CDCl_3$) δ 51.5 (dd, 1F, J = 7.6, 14.7 Hz).

Anal. Calcd for $C_{22}H_{23}FO_5$: C, 68.38; H, 6.00. Found: C, 68.49; H, 5.93.



2-(3-(Benzyloxy)propyl)-6-methylbenzaldehyde (**s12**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 30/1).

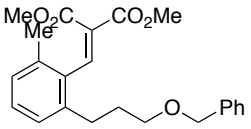
Yield: 364 mg (26%, synthesized from 2-iodo-3-methylbenzaldehyde[2]).

IR (neat) 3063, 3030, 2024, 2858, 2791, 1690, 1592, 1577, 1496, 1466, 1454, 1411, 1380, 1364, 1283, 1255, 1236, 1191, 1169, 1104, 1028, 824 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.92 (tt, 2H, J = 6.0, 7.6 Hz), 2.60 (s, 3H), 3.05 (t, 2H, J = 7.6 Hz), 3.51 (t, 2H, J = 6.0 Hz), 4.51 (s, 2H), 7.10 (d, 2H, J = 8.0 Hz), 7.24–7.41 (m, 6H), 10.60 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 29.8, 32.1, 69.3, 72.9, 127.6, 127.7, 128.4, 129.1, 129.9, 132.2, 132.9, 138.4, 141.1, 145.3, 193.5.

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.77; H, 7.45.



Dimethyl 2-(2-(3-(benzyloxy)propyl)-6-methylbenzylidene)malonate (**3h**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 12/1).

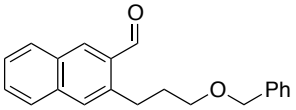
Yield: 276 mg (89%, synthesized from **s12**).

IR (neat) 3063, 3030, 2924, 2858, 2791, 1690, 1592, 1577, 1496, 1466, 1454, 1411, 1380, 1364, 1283, 1255, 1236, 1191, 1169, 1104, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.86 (tt, 2H, *J* = 6.4, 7.6 Hz), 2.20 (s, 3H), 2.63 (t, 2H, *J* = 7.6 Hz), 3.46 (t, 2H, *J* = 6.4 Hz), 3.53 (s, 3H), 3.85 (s, 3H), 4.49 (s, 2H), 7.01–7.07 (m, 2H), 7.14 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.25–7.32 (m, 1H), 7.32–7.38 (m, 4H), 7.97 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 30.0, 52.1, 52.6, 69.5, 72.7, 126.3, 127.5, 127.6, 128.2, 128.3, 130.4, 132.8, 135.1, 138.5, 139.0, 145.8, 163.9, 165.3.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.09; H, 6.73.



3-(3-(Benzyloxy)propyl)-2-naphthaldehyde (**s13**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 15/1).

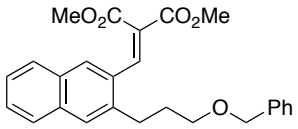
Yield: 462 mg (34%, synthesized from 3-iodo-2-naphthaldehyde[3]).

IR (neat) 3058, 3030, 2921, 2855, 2795, 2750, 2721, 1699, 1695, 1652, 1627, 1593, 1575, 1496, 1463, 1454, 1408, 1362, 1330, 1308, 1276, 1256, 1231, 1205, 1175, 1157, 1148, 1101, 1028, 1018, 957 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 2.00 (tt, 2H, *J* = 6.0, 7.6 Hz), 3.28 (t, 2H, *J* = 7.6 Hz), 3.56 (t, 2H, *J* = 6.0 Hz), 4.53 (s, 2H), 7.26–7.42 (m, 5H), 7.52 (d, 1H, *J* = 8.0, 8.0 Hz), 7.61 (d, 1H, *J* = 8.0, 8.0 Hz), 7.67 (s, 1H), 7.79 (d, 1H, *J* = 8.0 Hz), 7.95 (d, 1H, *J* = 8.0 Hz), 8.33 (s, 1H), 10.32 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 29.7, 31.4, 69.5, 72.9, 126.3, 127.3, 127.5, 127.7, 128.4, 129.1, 129.2, 129.5, 131.2, 132.5, 135.7, 136.8, 138.5, 139.1, 192.9.

Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.97; H, 6.47.



Dimethyl 2-((3-(3-(benzyloxy)propyl)naphthalen-2-yl)methylene)malonate (**3i**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

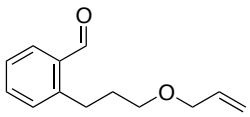
Yield: 325 mg (84%, synthesized from **s13**).

IR (neat) 3058, 3030, 3005, 2950, 2858, 1734, 1621, 1596, 1495, 1454, 1436, 1365, 1267, 1221, 1181, 1150, 1103, 1071, 1028, 984, 951 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.98 (tt, 2H, *J* = 6.4, 7.6 Hz), 2.95 (t, 2H, *J* = 7.6 Hz), 3.51 (t, 2H, *J* = 6.4 Hz), 3.66 (s, 3H), 3.85 (s, 3H), 4.51 (s, 2H), 7.25–7.38 (m, 5H), 7.43 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.49 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.64 (s, 1H), 7.74 (d, 1H, *J* = 8.0 Hz), 7.78 (d, 1H, *J* = 8.0 Hz), 7.82 (s, 1H), 8.17 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 30.2, 30.6, 52.5, 52.7, 69.1, 72.8, 125.9, 127.1, 127.2, 127.5, 127.6, 127.8, 127.8, 127.9, 128.1, 128.4, 131.3, 131.6, 134.0, 138.1, 138.5, 142.7, 164.2, 166.7.

Anal. Calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.83; H, 6.06.



2-(3-(Allyloxy)propyl)benzaldehyde (**s14**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 15/1).

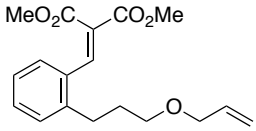
Yield: 892 mg (46%, synthesized from **s1**).

IR (neat) 2921, 2858, 2733, 1696, 1600, 1574, 1486, 1453, 1431, 1420, 1403, 1345, 1289, 1207, 1193, 1104, 1070, 1017, 996 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.91 (tt, 2H, *J* = 6.0, 7.6 Hz), 3.13 (t, 2H, *J* = 7.6 Hz), 3.46 (t, 2H, *J* = 6.0 Hz), 3.97 (t, 1H, *J* = 7.0 Hz), 5.18 (dd, 1H, *J* = 2.0, 10.0 Hz), 5.29 (dd, 1H, *J* = 2.0, 17.0 Hz), 5.88–5.98 (m, 1H), 7.30 (d, 1H, *J* = 8.0 Hz), 7.38 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.51 (ddd, 1H, *J* = 1.0, 8.0, 8.0 Hz), 7.84 (dd, 1H, *J* = 2.0, 8.0 Hz), 10.29 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 28.9, 31.8, 69.1, 71.8, 116.8, 126.5, 131.1, 131.7, 133.7, 134.8, 144.8, 192.4.

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.26; H, 8.15.



Dimethyl 2-(2-(3-(allyloxy)propyl)benzylidene)malonate (**3j**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

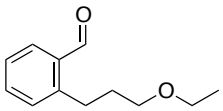
Yield: 733 mg (82%, synthesized from **s14**).

IR (neat) 3069, 3017, 2952, 2856, 1734, 1627, 1601, 1483, 1436, 1367, 1262, 1215, 1184, 1164, 1143, 1107, 1071, 1018, 989, 927 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.87 (tt, 2H, *J* = 6.0, 7.6 Hz), 2.79 (t, 2H, *J* = 7.6 Hz), 3.42 (t, 2H, *J* = 6.0 Hz), 3.70 (s, 3H), 3.86 (s, 3H), 3.97 (dd, 2H, *J* = 1.6, 6.0 Hz), 5.17 (dd, 1H, *J* = 1.6, 10.0 Hz), 5.28 (dd, 1H, *J* = 1.6, 17.2 Hz), 5.88–5.99 (m, 1H), 7.18 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.22–7.36 (m, 3H), 8.08 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9, 30.8, 52.4, 52.6, 68.9, 71.7, 116.7, 126.2, 127.3, 127.9, 129.7, 130.1, 132.3, 134.9, 141.6, 142.6, 164.3, 166.7.

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 68.14; H, 6.76.



2-(3-Ethoxypropyl)benzaldehyde (**s15**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

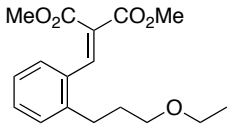
Yield: 543 mg (44%, synthesized from **s1**).

IR (neat) 2974, 2932, 2864, 1696, 1600, 1575, 1488, 1453, 1404, 1377, 1350, 1290, 1238, 1208, 1186, 1159, 1113, 1030, 956 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, 3H, *J* = 6.8 Hz), 1.91 (tt, 2H, *J* = 6.0, 7.6 Hz), 3.13 (t, 2H, *J* = 7.6 Hz), 3.43(t, 2H, *J* = 6.0 Hz), 3.47 (q, 2H, *J* = 6.8 Hz), 7.31 (d, 1H, *J* = 8.0 Hz), 7.37 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.51 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.84 (d, 1H, *J* = 8.0 Hz), 10.30 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 28.8, 31.8, 66.1, 66.3, 126.5, 131.1, 131.5, 133.7, 144.9, 192.4.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.78; H, 8.57.



Dimethyl 2-(2-(3-(benzyloxy)propyl)benzylidene)malonate (**3k**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

Yield: 377 mg (92%, synthesized from **s15**).

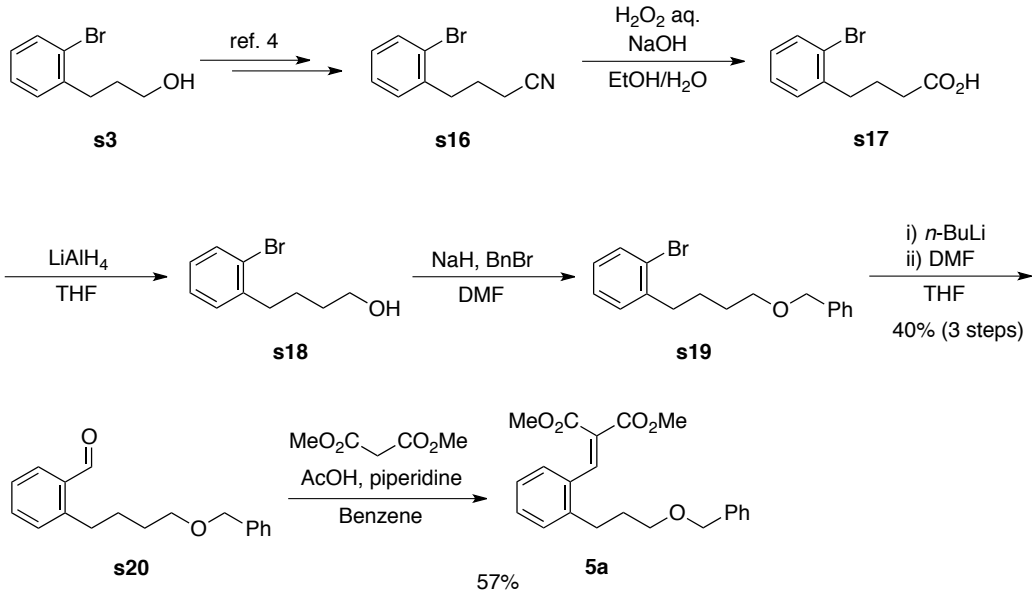
IR (neat) 2974, 2952, 2866, 1733, 1627, 1601, 1571, 1484, 1436, 1375, 1262, 1214, 1184, 1164, 1113, 1070, 987, 944 cm^{-1}.

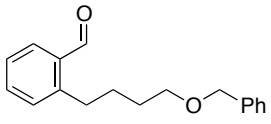
^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, 3H, *J* = 6.8 Hz), 1.86 (tt, 2H, *J* = 6.0, 7.6 Hz), 2.78 (t, 2H, *J* = 7.6 Hz), 3.39 (t, 2H, *J* = 6.0 Hz), 3.46 (q, 2H, *J* = 6.8 Hz), 3.70 (s, 3H), 3.88 (s, 3H), 7.17 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.22–7.34 (m, 3H), 8.08 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 29.8, 30.8, 52.4, 52.6, 66.0, 69.1, 126.2, 127.3, 127.8, 129.7, 130.1, 132.3, 141.6, 142.7, 164.3, 166.7.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.48; H, 7.02.

Scheme S2. Preparation of starting materials **5**. Preparation of **5a** was shown as a representative example.





Synthesis of 2-(4-(benzyloxy)butyl)benzaldehyde (s20):

To a solution of **s16** (343 mg, 1.53 mmol) in EtOH (2.0 mL) and H_2O (1.0 mL) were successively added NaOH (444 mg, 11.1 mmol) and aqueous H_2O_2 (5 μL, 0.153 mmol). After the mixture was heated to reflux for 19 h, the reaction was quenched by addition of conc. HCl. The crude mixture was extracted with EtOAc (x4) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give crude **s17** (350 g) as orange solid. This crude material was used for the next reaction without further purification.

To a solution of **s17** in Et_2O (7.2 mL) was added $LiAlH_4$ (82.7 mg, 2.18 mmol) at 0 °C (portion wise). After being stirred for 3 h at refluxing temperature, the reaction was stopped by adding Na_2SO_4•$10H_2O$. After being stirred for another 0.5 h at room temperature, the crude material was filtered through Celite® pad and the resulting filtrate was concentrated in vacuo to give crude alcohol **s18** (321 mg) as yellow liquid. The crude material was used for the next reaction without further purification.

To a solution of **s18** in DMF (3.5 mL) were successively added NaH (60 % oil, 116 mg, 2.90 mmol), and BnBr (0.30 mL, 2.52 mmol). After being stirred for 16 h at room temperature, the reaction was quenched by addition of Et_2NH (217 μl, 2.10 mmol) at 0 °C. 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 = 30/1) to give **s19** (408 g) as colorless oil. At this moment, **s19** could not be isolated as pure compound, so this material was used for next reaction without further purification.

To a solution of **s19** in THF (6.4 mL) was added *n*-BuLi (1.57 M in hexane, 1.10 mL, 1.73 mmol) at –78 °C. The reaction mixture was stirred for 10 min at –78 °C, to which DMF (0.20 mL, 2.58 mmol) was added. After being stirred for 1 h, the reaction was quenched by addition of saturated aqueous NH_4Cl at –78 °C. 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 = 15/1) to afford aldehyde **s20** (164 mg, 40% from **s16**) as colorless oil.

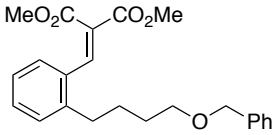
IR (neat) 3029, 2916, 2852, 1697, 1600, 1573, 1453, 1363, 1288, 1207, 1102, 753 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.68–1.77 (m, 4H), 3.05 (t, 2H, *J* = 7.2 Hz), 3.51 (t, 2H,

J = 6.0 Hz), 4.50 (s, 2H), 7.24–7.40 (m, 7H), 7.49 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.83 (dd, 1H, *J* = 1.2, 8.0 Hz), 10.27 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 29.5, 32.2, 70.0, 72.9, 126.5, 127.5, 127.6, 128.3, 131.0, 131.7, 133.6, 133.7, 138.5, 145.3, 192.3.

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.81; H, 7.32.



Synthesis of dimethyl 2-(2-(4-(benzyloxy)butyl)benzylidene)malonate (5a):

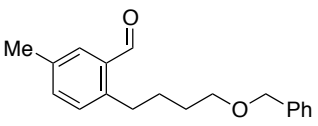
To a solution of **s20** (164 mg, 0.611 mmol) in benzene (3.1 mL) were successively added dimethyl malonate (70 μL, 0.611 mmol), piperidine (65 μL, 0.611 mmol), and AcOH (35 μL, 0.611 mmol) at room temperature. The reaction mixture was heated to reflux for 20 h. The crude mixture was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, hexane/EtOAc = 9/1) to give **5a** (134 mg, 57%) as colorless oil.

IR (neat) 3029, 2950, 2859, 1733, 1626, 1600, 1483, 1436, 1365, 1263, 1215, 1102, 1072, 986 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61–1.73 (m, 4H), 2.71 (t, 2H, *J* = 7.2 Hz), 3.48 (t, 2H, *J* = 6.0 Hz), 3.69 (s, 3H), 3.84 (s, 3H), 4.49 (s, 2H), 7.17 (dd, 1H, *J* = 7.6. 7.6 Hz), 7.21 (d, 1H, *J* = 7.6 Hz), 7.25–7.35 (m, 7H), 8.06 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 27.6, 29.3, 33.3, 52.4, 52.6, 70.0, 72.9, 126.2, 127.2, 127.5, 127.6, 127.9, 128.3, 129.7, 130.1, 132.1, 138.5, 142.0, 142.7, 164.3, 166.8.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.44; H, 6.59.



2-(4-(Benzyloxy)butyl)-5-methylbenzaldehyde (**s21**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 10/1).

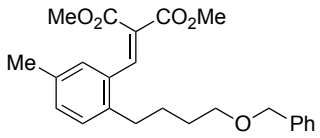
Yield: 317 mg (25%, synthesized from commercially available, 2-bromo-4-methylbenzaldehyde).

IR (neat) 3029, 2918, 2855, 1687, 1609, 1567, 1497, 1454, 1409, 1364, 1281, 1239, 1202, 1157, 1103, 1028, 942 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.64–1.72 (m, 4H), 2.38 (s, 3H), 3.00 (t, 2H, *J* = 7.6 Hz), 3.49 (t, 2H, *J* = 6.0 Hz), 4.49 (s, 2H), 7.15 (d, 1H, *J* = 8.0 Hz), 7.22–7.38 (m, 6H), 6.63 (s, 1H), 10.23 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 28.9, 29.5, 31.8, 70.0, 72.9, 127.5, 127.6, 128.3, 131.0, 131.9, 133.4, 134.6, 136.1, 138.5, 142.4, 192.5.

Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.59; H, 7.94.



Dimethyl 2-(2-(4-(benzyloxy)butyl)-5-methylbenzylidene)malonate (**5b**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

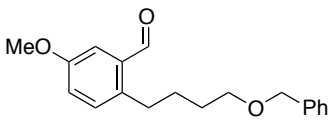
Yield: 266 mg (76%, synthesized from **s21**).

IR (neat) 3029, 2949, 2859, 1735, 1627, 1566, 1495, 1454, 1436, 1365, 1270, 1227, 1163, 1103, 1071, 1028, 988 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.61–1.70 (m, 4H), 2.28 (s, 3H), 2.67 (t, 2H, *J* = 6.8 Hz), 3.47 (t, 2H, *J* = 5.6 Hz), 3.71 (s, 3H), 3.84 (s, 3H), 4.49 (s, 2H), 7.07–7.13 (m, 3H), 7.24–7.30 (m, 1H), 7.31–7.36 (m, 4H), 8.03 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 27.7, 29.3, 32.8, 52.3, 52.6, 70.1, 72.8, 126.8, 127.4, 127.6, 128.3, 128.3, 129.6, 131.0, 131.9, 135.6, 138.5, 139.1, 142.7, 164.4, 166.8.

Anal. Calcd for $C_{24}H_{28}O_5$: C, 72.70; H, 7.12. Found: C, 72.61; H, 6.98.



2-(4-(Benzyloxy)butyl)-5-methoxybenzaldehyde (**s22**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

Yield: 276 mg (36%, synthesized from commercially available, 2-bromo-4-methoxylbenzaldehyde).

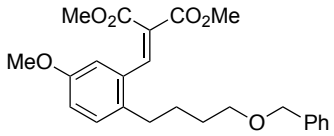
IR (neat) 3030, 2937, 2858, 1686, 1607, 1571, 1497, 1454, 1400, 1364, 1327, 1264,

1190, 1163, 1103, 1038, 938 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.61–1.76 (m, 4H), 2.97 (t, 2H, *J* = 7.6 Hz), 3.49 (t, 2H, *J* = 6.0 Hz), 3.84 (s, 3H), 4.49 (s, 2H), 7.06 (d, 1H, *J* = 2.8, 8.4 Hz), 7.17 (d, 1H, *J* = 8.4 Hz), 7.26–7.31 (m, 1H), 7.31–7.39 (m, 4H), 10.27 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 29.4, 31.1, 55.5, 70.0, 72.9, 113.4, 121.1, 127.5, 127.6, 128.4, 132.2, 134.2, 137.9, 138.5, 158.1, 191.6.

Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.37; H, 7.67.



Dimethyl 2-(2-(4-(benzyloxy)butyl)-5-methoxybenzylidene)malonate (**5c**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 4/1).

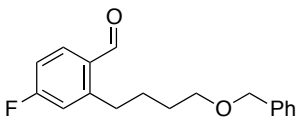
Yield: 258 mg (87%, synthesized from **s1**).

IR (neat) 3029, 3003, 2949, 2860, 1732, 1625, 1606, 1572, 1495, 1454, 1436, 1366, 1271, 1237, 1203, 1167, 1103, 1071, 1039, 989 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.57–1.70 (m, 4H), 2.64 (t, 2H, *J* = 7.2 Hz), 3.47 (t, 2H, *J* = 5.6 Hz), 3.73 (s, 3H), 3.74 (s, 3H), 3.83 (s, 3H), 4.48 (s, 2H), 6.83–6.89 (m, 2H), 7.11 (d, 1H, *J* = 8.4 Hz), 7.24–7.31 (m, 1H), 7.31–7.37 (m, 4H), 8.01 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 29.2, 32.4, 52.5, 52.6, 55.2, 70.0, 72.8, 112.5, 116.3, 127.2, 127.4, 127.5, 128.3, 130.7, 132.7, 134.3, 138.5, 142.3, 157.6, 164.2, 166.7.

Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84. Found: C, 70.04; H, 6.73.



2-(4-(Bbenzyloxy)butyl)-5-methoxybenzaldehyde (**s23**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

Yield: 354 mg (23%, synthesized from commercially available, 2-bromo-5-fluorobenzaldehyde).

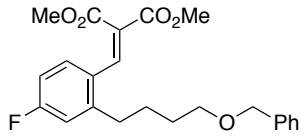
IR (neat) 3063, 3031, 2937, 2860, 1693, 1605, 1582, 1493, 1454, 1431, 1399, 1363, 1240, 1194, 1155, 1103, 1028, 965 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65–1.80 (m, 4H), 3.04 (t, 2H, J = 7.2 Hz), 3.50 (t, 2H, J = 5.6 Hz), 4.49 (s, 2H), 6.95 (dd, 1H, J = 2.4, 9.6 Hz), 7.02 (ddd, 1H, J = 2.4, 8.0, 8.0 Hz), 7.26–7.30 (m, 1H), 7.31–7.38 (m, 4H), 7.83 (dd, 1H, J = 6.0, 8.0 Hz), 10.18 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 29.4, 32.0, 69.8, 72.9, 113.7 (d, J_{C-F} = 21.9 Hz), 117.6 (d, J_{C-F} = 21.0 Hz), 127.5, 127.6, 128.3, 130.2 (d, J_{C-F} = 2.9 Hz), 134.5 (d, J_{C-F} = 9.4 Hz), 138.2, 148.7 (d, J_{C-F} = 9.6 Hz), 165.7 (d, J_{C-F} = 254.6 Hz), 190.5.

^{19}F NMR (283 MHz, $CDCl_3$) δ 57.9 (dd, 1F, J = 9.1, 15.8 Hz).

Anal. Calcd for $C_{18}H_{19}FO_2$: C, 75.50; H, 6.69. Found: C, 75.72; H, 6.82.



Dimethyl 2-(2-(4-(benzyloxy)butyl)-4-fluorobenzylidene)malonate (**5d**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

Yield: 168 mg (80%, synthesized from **s23**).

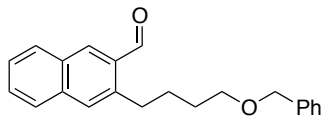
IR (neat) 3031, 2951, 2852, 1735, 1605, 1583, 1492, 1436, 1365, 1245, 1220, 1155, 1102, 1071, 986 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61–1.73 (m, 4H), 2.69 (t, 2H, J = 7.2 Hz), 3.49 (t, 2H, J = 6.0 Hz), 3.71 (s, 3H), 3.84 (s, 3H), 4.49 (s, 2H), 6.87 (ddd, 1H, J = 2.8, 8.4, 8.4 Hz), 6.93 (dd, 1H, J = 2.8, 9.6 Hz), 7.25–7.36 (m, 4H), 7.97 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 29.2, 33.2, 52.5 (m), 52.7 (m), 69.9, 72.9, 113.3 (d, J_{C-F} = 21.9 Hz), 116.5 (d, J_{C-F} = 24.7 Hz), 127.2, 127.5, 127.6, 128.2 (d, J_{C-F} = 3.9 Hz), 128.3, 129,8 (d, J_{C-F} = 8.6 Hz), 138.4, 141.3, 145.0 (d, J_{C-F} = 7.7 Hz), 163.6 (d, J_{C-F} = 249.8 Hz), 155.6, 164.2,

^{19}F NMR (283 MHz, $CDCl_3$) δ 51.5 (dd, 1F, J = 9.1, 13.6 Hz).

Anal. Calcd for $C_{23}H_{25}FO_5$: C, 68.99; H, 6.29. Found: C, 69.23; H, 6.17.



3-(4-(Benzyloxy)butyl)-2-naphthaldehyde (**s24**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

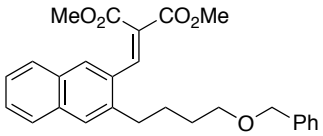
Yield: 240 mg (25%, synthesized from 3-iodo-2-naphthaldehyde[3]).

IR (neat) 3058, 2936, 2858, 1696, 1629, 1594, 1496, 1454, 1361, 1255, 1173, 1102, 889 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.69–1.82 (m, 4H), 3.19 (t, 2H, *J* = 7.2 Hz), 3.52 (t, 2H, *J* = 6.0 Hz), 4.50 (s, 2H), 7.26–7.30 (m, 1H), 7.31–7.37 (m, 4H), 7.50 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.60 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.66 (s, 1H), 7.80 (d, 1H, *J* = 8.0 Hz), 7.94 (d, 1H, *J* = 8.0 Hz), 8.31 (s, 1H), 11.32 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 29.6, 32.9, 20.2, 72.9, 126.3, 127.3, 127.5, 127.6, 128.3, 129.1, 129.2, 129.4, 131.2, 12.5, 135.7, 136.6, 138.5, 139.6, 192.9.

Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.96. Found: C, 83.24; H, 7.14.



Dimethyl 2-((3-(4-(benzyloxy)butyl)naphthalen-2-yl)methylene)malonate (**5e**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

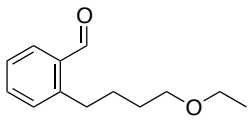
Yield: 173 mg (92%, synthesized from **s24**).

IR (neat) 3058, 3030, 2949, 2861, 1732, 1621, 1596, 1496, 1454, 1436, 1363, 1266, 1220, 1181, 1150, 1103, 1071, 1028, 984, 951 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.64–1.82 (m, 4H), 32.85 (t, 2H, *J* = 7.2 Hz), 3.51 (t, 2H, *J* = 6.0 Hz), 3.66 (s, 3H), 3.87 (s, 3H), 4.50 (s, 2H), 7.26–7.37 (m, 4H), 7.43 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.49 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.64 (s, 1H), 7.76 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.81 (s, 1H), 8.15 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 29.3, 33.4, 52.4, 52.6, 70.0, 72.8, 125.8, 127.1, 127.1, 127.4, 127.5, 127.6, 127.6, 127.8, 128.1, 128.3, 131.1, 131.5, 134.0, 138.4, 138.5, 142.7, 164.2, 166.9.

Anal. Calcd for $C_{27}H_{28}O_5$: C, 74.89; H, 6.53. Found: C, 74.72; H, 6.78.



2-(4-Ethoxybutyl)benzaldehyde (**s25**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 9/1).

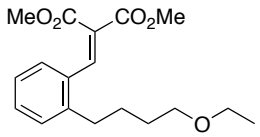
Yield: 319 mg (42%, synthesized from **s1**).

IR (neat) 2974, 2934, 2861, 1697, 1600, 1574, 1487, 1452, 1377, 1354, 1289, 1208, 1191, 1160, 1112 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, 3H, *J* = 6.8 Hz), 1.62–1.75 (m, 4H), 3.06 (t, 2H, *J* = 7.2 Hz), 3.41–3.50 (m, 2H), 3.47 (q, 2H, *J* = 6.8 Hz), 3.70 (s, 3H), 3.86 (s, 3H), 7.28 (dd, 1H, *J* = 1.2, 7.6 Hz), 7.36 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.50 (ddd, 1H, *J* = 1.2, 7.6, 7.6 Hz), 7.83 (dd, 1H, *J* = 1.2, 7.6 Hz), 10.28 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 28.9, 29.5, 32.3, 66.1, 70.3, 126.5, 131.0, 131.6, 133.6, 133.8, 145.4, 192.4.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.46; H, 8.94.



Dimethyl 2-(2-(4-ethoxybutyl)benzylidene)malonate (**5f**).

Colorless oil (purified by silica gel column chromatography, Hexane/EtOAc = 6/1).

Yield: 283 mg (85%, synthesized from **s25**).

IR (neat) 2950, 2863, 2800, 1731, 1627, 1601, 1565, 1484, 1436, 1375, 1263, 1215, 1184, 1113, 1071, 987 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, 3H, *J* = 6.8 Hz), 1.56–1.70 (m, 4H), 2.71 (t, 2H, *J* = 6.8 Hz), 3.37–3.48 (m, 2H), 3.46 (q, 2H, *J* = 6.8 Hz), 3.70 (s, 3H), 3.86 (s, 3H), 7.17 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.23 (d, 1H, *J* = 7.6 Hz), 7.25–7.34 (m, 2H), 8.06 (s, 1H).

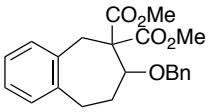
^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 27.5, 29.3, 33.3, 52.4, 52.6, 66.0, 70.3, 126.1, 127.1, 127.8, 129.6, 131.0, 132.1, 142.0, 142.6, 164.3, 166.7.

Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.19; H, 7.71.

2. Synthesis of spiro isochroman derivatives.

General Procedure of the formation of 7- or 8-membred ring adducts.

To a solution of benzylidene malonate **3** or **5** (0.10 mmol) in $ClCH_2CH_2Cl$ (1.0 mL) was added $Sc(OTf)_3$ (5 or 10 mol%), and the mixture was heated at reflux. After completion of the reaction, the reaction was stopped by adding saturated aqueous $NaHCO_3$. The crude products were 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 preparative TLC to give 7- or 8-membred ring adducts **4** or **6**.



Dimethyl 7-(benzyloxy)-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4a**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 6/1).

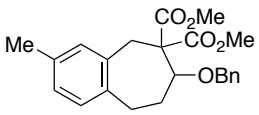
Yield: 27.6 mg (75%).

IR (neat) 3063, 3027, 2951, 2857, 1739, 1496, 1455, 1435, 1348, 1329, 1306, 1273, 1246, 1222, 1208, 1185, 1172, 1159, 1101, 1065, 1029, 959 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 2.01–2.12 (m, 1H), 2.27–2.45 (m, 2H), 3.17–3.26 (m, 1H), 3.27 (d, 1H, *J* = 14.4 Hz), 3.48 (s, 3H), 3.64 (s, 3H), 3.73 (d, 1H, *J* = 14.4 Hz), 4.41 (d, 1H, *J* = 12.0 Hz), 4.39–4.46 (m, 1H), 4.72 (d, 1H, *J* = 12.0 Hz), 7.01–7.12 (m, 4H), 7.24–7.39 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.6, 27.6, 34.2, 51.9, 52.6, 70.6, 78.2, 125.9, 127.1, 127.4, 127.5, 128.2, 128.3, 130.6, 135.6, 138.2, 143.6, 169.1, 170.5.

Anal. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 71.54; H, 6.67.



Dimethyl 7-(benzyloxy)-3-methyl-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicar boxylate (**4b**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

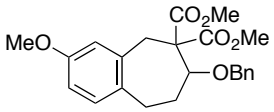
Yield: 27.7 mg (69%).

IR (neat) 3029, 3006, 2950, 2858, 1348, 1327, 1303, 1272, 1243, 1210, 1153, 1112, 1093, 1065, 1029, 968 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.97–2.10 (m, 1H), 2.25 (s, 3H), 2.22–2.43 (m, 2H), 3.12–3.27 (m, 2H), 3.49 (s, 3H), 3.63 (s, 3H), 3.61–3.75 (m, 1H), 4.40 (d, 1H, *J* = 12.0 Hz), 4.36–4.47 (m, 1H), 4.72 (d, 1H, *J* = 12.0 Hz), 6.87–6.99 (m, 3H), 7.23–7.40 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 26.8, 27.1, 34.2, 51.8, 52.6, 60.4, 70.6, 78.3, 127.4, 127.5, 127.6, 128.1, 128.3, 131.4, 135.2, 135.4, 138.2, 140.5, 169.1, 170.6.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.46; H, 6.59.



Dimethyl 7-(benzyloxy)-3-methoxy-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4c**).

Colorless crystal (purified by preparative TLC, Hexane/EtOAc = 9/1), which was subjected to the X-ray crystallographic analysis.

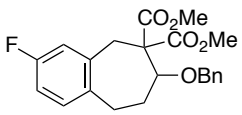
Yield: 31.0 mg (72%).

IR (neat) 3027, 3001, 2951, 2857, 2837, 1739, 1610, 1582, 1506, 1455, 1434, 1348, 1327, 1276, 1262, 1245, 1211, 1159, 1111, 1094, 1066, 1029, 965 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 2.01–2.12 (m, 1H), 2.26–2.38 (m, 2H), 3.15–3.28 (m, 2H), 3.50 (s, 3H), 3.63 (s, 3H), 3.61–3.78 (m, 1H), 3.75 (s, 3H), 4.41 (d, 1H, *J* = 12.0 Hz), 4.38–4.47 (m, 1H), 4.72 (d, 1H, *J* = 12.0 Hz), 6.59 (dd, 1H, *J* = 2.8, 8.4 Hz), 6.63 (d, 1H, *J* = 2.8 Hz), 6.98 (d, 1H, *J* = 8.4 Hz), 7.25–7.40 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 27.8, 33.3, 51.9, 52.6, 55.1, 60.5, 70.7, 78.2, 110.7, 114.0, 127.4, 127.5, 127.6, 128.3, 131.6, 138.2, 144.9, 158.5, 169.2, 170.6.

Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.56; H, 6.45.



Dimethyl 7-(benzyloxy)-3-fluoro-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4d**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

Yield: 23.4 mg (65%).

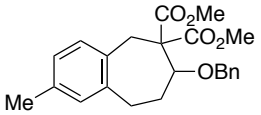
IR (neat) 3064, 3031, 3005, 2952, 2859, 1739, 1612, 1593, 1499, 1455, 1435, 1348, 1327, 1307, 1271, 1256, 1244, 1212, 1065, 1029, 978 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.97–2.06 (m, 1H), 2.25–2.35 (m, 1H), 2.39 (dd, 1H, *J* = 6.5, 14.0 Hz), 3.17 (d, 1H, *J* = 14.0 Hz), 3.23 (d, 1H, *J* = 14.0 Hz), 3.53 (s, 3H), 3.64 (s, 3H), 3.71 (d, 1H, *J* = 14.0 Hz), 4.40 (d, 1H, *J* = 11.0 Hz), 4.39–4.46 (m, 1H), 4.71 (d, 1H, *J* = 11.0 Hz), 6.75–6.83 (m, 2H), 7.00 (dd, 1H, *J* = 6.0, 8.0 Hz), 7.25–7.38 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 26.6, 26.8, 34.1, 52.0, 52.7, 60.2, 70.7, 78.1, 113.4 (d, J_{C-F} = 20.4 Hz), 117.3 (d, J_{C-F} = 21.4 Hz), 127.4, 127.6, 128.3, 129.5 (d, J_{C-F} = 6.6 Hz), 137.8 (d, J_{C-F} = 5.7 Hz), 138.1, 139.3, 161.0 (d, J_{C-F} = 242.0 Hz), 168.8, 170.2.

^{19}F NMR (283 MHz, $CDCl_3$) δ 43.4 (dd, 1F, *J* = 9.1, 13.6 Hz).

Anal. Calcd for $C_{22}H_{23}FO_5$: C, 68.38; H, 6.00. Found: C, 68.12; H, 6.25.



Dimethyl 7-(benzyloxy)-2-methyl-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4e**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

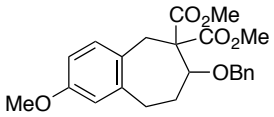
Yield: 25.7 mg (68%).

IR (neat) 3029, 3006, 2951, 2858, 1739, 1506, 1497, 1455, 1435, 1347, 1329, 1305, 1273, 1253, 1240, 1220, 1207, 1176, 1156, 1112, 1093, 1065, 1029, 968 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.99–2.10 (m, 1H), 2.25 (s, 3H), 2.25–2.39 (m, 2H), 3.15–3.28 (m, 2H), 3.49 (s, 3H), 3.63 (s, 3H), 3.61–3.72 (m, 1H), 4.40 (d, 1H, *J* = 12.0 Hz), 4.38–4.46 (m, 1H), 4.72 (d, 1H, *J* = 12.0 Hz), 6.84–6.89 (m, 2H), 6.96 (d, 1H, *J* = 7.6 Hz), 7.25–7.38 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 26.7, 27.5, 33.8, 51.9, 52.6, 60.4, 70.6, 78.3, 126.5, 127.4, 127.5, 128.3, 129.1, 130.5, 132.4, 136.6, 138.2, 143.4, 169.2, 170.6.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.27; H, 6.72.



Dimethyl 7-(benzyloxy)-2-methoxy-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4f**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

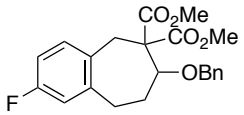
Yield: 21.1 mg (53%).

IR (neat) 3001, 2951, 1738, 1609, 1580, 1506, 1454, 1436, 1331, 1310, 1280, 1263, 1243, 1219, 1207, 1185, 1173, 1156, 1114, 1093, 1064, 1044, 1029, 1013, 948 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.96–2.08 (m, 1H), 2.24–2.41 (m, 2H), 3.13 (d, 1H, *J* = 12.4 Hz), 3.21 (d, 1H, *J* = 14.0 Hz), 3.52 (s, 3H), 3.63 (s, 3H), 3.60–3.78 (m, 1H), 3.74 (s, 3H), 4.41 (d, 1H, *J* = 11.2 Hz), 4.36–4.48 (m, 1H), 4.72 (d, 1H, *J* = 11.2 Hz), 6.63 (dd, 1H, *J* = 2.4, 8.0 Hz), 6.67 (d, 1H, *J* = 2.4 Hz), 6.97 (d, 1H, *J* = 8.0 Hz), 7.25–7.38 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.6, 26.9, 34.4, 51.9, 52.6, 55.2, 60.4, 70.6, 78.2, 111.6, 116.7, 127.4, 127.5, 128.3, 129.0, 135.8, 136.9, 138.2, 157.7, 169.0, 170.5.

Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.15; H, 6.75.



Dimethyl 7-(benzyloxy)-2-fluoro-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4g**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 6/1).

Yield: 24.3 mg (64%).

IR (neat) 3064, 3031, 3005, 2952, 2861, 1739, 1610, 1594, 1501, 1455, 1436, 1348, 1330, 1308, 1273, 1242, 1216, 1206, 1164, 1147, 1094, 1063, 1029, 972 cm^{-1}.

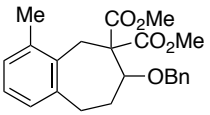
^1H NMR (500 MHz, $CDCl_3$) δ 2.01–2.12 (m, 1H), 2.28–2.40 (m, 2H), 3.17–3.30 (m, 1H), 3.26 (d, 1H, *J* = 14.0 Hz), 3.49 (s, 3H), 3.64 (s, 3H), 3.71 (d, 1H, *J* = 14.0 Hz), 3.66 (d, 1H, *J* = 14.0 Hz), 4.39–4.48 (m, 1H), 4.40 (d, 1H, *J* = 12.0 Hz), 4.71 (d, 1H, *J* = 12.0 Hz), 6.72–6.83 (m, 2H), 7.03 (dd, 1H, *J* = 6.0, 8.0 Hz), 7.25–7.38 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 27.6, 33.4, 52.0, 52.7, 60.2, 70.7, 78.1, 112.3 (d, J_{C-F} = 21.0 Hz), 115.1 (d, J_{C-F} = 21.0 Hz), 127.4, 127.6, 128.3, 131.3 (d, J_{C-F} = 2.9 Hz),

132.0 (d, J_{C-F} = 7.7 Hz), 138.1, 145.8 (d, J_{C-F} = 7.7 Hz), 161.7 (d, J_{C-F} = 243.1 Hz), 169.0, 170.3.

^{19}F NMR (283 MHz, $CDCl_3$) δ 45.2 (dd, 1F, J = 9.1, 13.6 Hz).

Anal. Calcd for $C_{22}H_{23}FO_5$: C, 68.38; H, 6.00. Found: C, 68.12; H, 6.25.



Dimethyl 7-(benzyloxy)-4-methyl-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4h**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

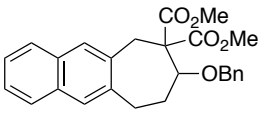
Yield: 23.3 mg (60%).

IR (neat) 3065, 3028, 2951, 2858, 1738, 1575, 1497, 1466, 1455, 1434, 1348, 1328, 1302, 1271, 1239, 1211, 1185, 1171, 1092, 1069, 1028, 972, 957 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08–2.22 (m, 1H), 2.26–2.46 (m, 2H), 2.39 (s, 3H), 3.15–3.29 (m, 1H), 3.45–3.53 (m, 1H), 3.46 (s, 3H), 3.62–3.73 (m, 1H), 3.64 (s, 3H), 4.37–4.45 (m, 1H), 4.41 (d, 1H, J = 12.0 Hz), 4.72 (d, 1H, J = 12.0 Hz), 6.88–7.03 (m, 3H), 7.23–7.40 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 26.5, 28.2, 51.6, 52.6, 60.0, 70.5, 78.3, 126.5, 126.6, 127.4, 127.5, 128.3, 128.5, 134.1, 137.0, 138.3, 143.9, 169.3, 170.7.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.51; H, 6.58.



Dimethyl 8-(benzyloxy)-9,10-dihydro-6*H*-cyclohepta[*b*]naphthalene-7,7(8*H*)-dicarboxylate (**4i**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

Yield: 26.4 mg (65%).

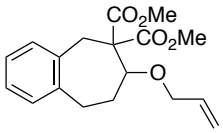
IR (neat) 3005, 2950, 2851, 1738, 1574, 1454, 1432, 1345, 1324, 1280, 1264, 1240, 1210, 1146, 1092, 1065, 1045, 1028, 1013, 953 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08–2.18 (m, 1H), 2.38–2.49 (m, 1H), 2.55–2.66 (m, 1H), 3.32–3.52 (m, 2H), 3.45 (s, 3H), 3.66 (s, 3H), 3.83 (d, 1H, J = 13.6 Hz), 4.41–4.49

(m, 1H), 4.44 (d, 1H, J = 12.0 Hz), 4.75 (d, 1H, J = 12.0 Hz), 7.21–7.45 (m, 7H), 7.52 (s, 1H), 7.56 (s, 1H), 7.71 (d, 2H, J = 8.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 27.4, 27.8, 34.5, 52.0, 52.7, 61.2, 70.7, 78.0, 125.2, 125.6, 126.1, 127.0, 127.1, 127.4, 127.6, 128.3, 129.3, 132.2, 132.8, 134.4, 138.2, 141.6, 169.0, 170.5.

Anal. Calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.39; H, 6.03.



Dimethyl 7-(allyloxy)-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4j**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

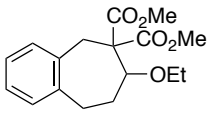
Yield: 20.5 mg (62%).

IR (neat) 3065, 3020, 2952, 2856, 1739, 1574, 1495, 1456, 1434, 1410, 1328, 1306, 1273, 1246, 1223, 1208, 1185, 1172, 1130, 1103, 1086, 1065, 1015, 996, 961 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.95–2.06 (m, 1H), 2.18–2.28 (m, 1H), 2.34–2.43 (m, 1H), 3.18 (d, 1H, J = 14.4 Hz), 3.25 (d, 1H, J = 14.4 Hz), 3.49 (s, 3H), 3.67 (d, 1H, J = 14.4 Hz), 3.74 (s, 3H), 3.87 (tdd, 1H, J = 1.2, 5.6, 12.8 Hz), 3.87 (tdd, 1H, J = 1.2, 5.6, 12.8 Hz), 4.32 (brs, 1H), 5.15 (tdd, 1H, J = 1.2, 1.2, 10.8 Hz), 5.28 (tdd, 1H, J = 1.2, 1.2, 17.2 Hz), 5.79–5.93 (m, 1H), 7.02–7.14 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 27.6, 34.2, 51.9, 52.6, 60.3, 69.8, 78.1, 116.5, 125.9, 127.1, 128.2, 130.6, 134.6, 135.6, 143.6, 169.1, 170.5.

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 68.15; H, 7.25.



Dimethyl 7-ethoxy-8,9-dihydro-5*H*-benzo[7]annulene-6,6(7*H*)-dicarboxylate (**4k**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

Yield: 21.9 mg (70%).

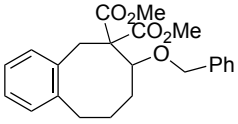
IR (neat) 3021, 2975, 2952, 1741, 1495, 1455, 1436, 1346, 1328, 1305, 1272, 1247, 1222, 1208, 1185, 1115, 1091, 1067, 1047, 1025, 958 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, 3H, J = 6.8 Hz), 1.92–2.05 (m, 1H), 2.17–2.28

(m, 1H), 2.32–2.42 (m, 1H), 3.12–3.27 (m, 2H), 3.29–3.38 (m, 1H), 3.49 (s, 3H), 3.60–3.80 (m, 2H), 3.75 (s, 3H), 4.26 (brs, 1H), 7.02–7.13 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 26.9, 27.6, 34.2, 51.9, 52.6, 60.4, 62.4, 78.1, 125.9, 127.0, 128.2, 130.6, 135.7, 143.8, 169.2, 170.7.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.84; H, 7.52.



Dimethyl 7-(benzyloxy)-7,8,9,10-tetrahydrobenzo[8]annulene-6,6(5*H*)-dicarboxylate (**6a**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

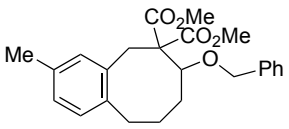
Yield: 21.9 mg (56%).

IR (neat) 3062, 3027, 2950, 2850, 1739, 1566, 1495, 1452, 1235, 1204, 1164, 1116, 1076, 1060, 1028, 978, 921 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40–1.65 (m, 2H), 1.90–2.15 (m, 2H), 2.61–2.72 (m, 1H), 2.91–3.03 (m, 1H), 3.27 (d, 1H, *J* = 14.0 Hz), 3.65 (s, 3H), 3.60–3.73 (m, 1H), 3.73 (s, 3H), 4.18 (d, 1H, *J* = 8.4 Hz), 4.37 (d, 1H, *J* = 12.0 Hz), 4.63 (d, 1H, *J* = 12.0 Hz), 7.01–7.13 (m, 3H), 7.17 (ddd, 1H, *J* = 1.2, 8.0, 8.0 Hz), 7.23–7.38 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 27.4, 32.3, 33.8 52.1, 52.4, 64.3, 72.1, 78.9, 126.0, 127.3, 127.4, 127.5, 128.2, 129.2, 130.0, 135.4, 138.3, 141.5, 170.4, 170.5.

Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.01; H, 7.11.



Dimethyl 7-(benzyloxy)-3-methyl-7,8,9,10-tetrahydrobenzo[8]annulene-6,6(5*H*)-dicarboxylate (**6b**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

Yield: 25.8 mg (66%).

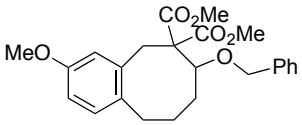
IR (neat) 3029, 3005, 2950, 2863, 1731, 1605, 1498, 1470, 1454, 1435, 1335, 1304, 1265, 1235, 1197, 1164, 1120, 1089, 1062, 1029, 983 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40–1.65 (m, 2H), 1.87–2.21 (m, 2H), 2.26 (s, 3H),

2.59–2.69 (m, 1H), 2.86–2.98 (m, 1H), 3.22 (d, 1H, *J* = 14.0 Hz), 3.52–3.64 (m, 1H), 3.65 (s, 3H), 3.74 (s, 3H), 4.08–4.21 (m, 1H), 4.37 (d, 1H, *J* = 12.0 Hz), 4.62 (d, 1H, *J* = 12.0 Hz), 6.85 (brs, 1H), 6.94–7.03 (m, 2H), 7.23–7.36 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 25.7, 27.6, 31.9, 33.9, 51.9, 52.4, 64.3, 72.0, 79.1, 127.3, 127.3, 127.3, 128.2, 128.2, 129.1, 130.7, 135.1, 135.3, 138.3, 169.3, 170.5.

Anal. Calcd for $C_{24}H_{28}O_5$: C, 72.70; H, 7.12. Found: C, 72.45; H, 7.18.



Dimethyl 7-(benzyloxy)-3-methoxy-7,8,9,10-tetrahydrobenzo[8]annulene-6,6(5*H*)-dicarboxylate (**6c**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

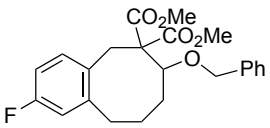
Yield: 28.9 mg (72%).

IR (neat) 3028, 3001, 2950, 2934, 2849, 1738, 1608, 1579, 1500, 1434, 1327, 1257, 1235, 1196, 1108, 1062, 914 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37–1.70 (m, 2H), 1.87–2.22 (m, 2H), 2.58–2.66 (m, 1H), 2.80–2.95 (m, 1H), 3.22 (d, 1H, *J* = 14.0 Hz), 3.52–3.62 (m, 1H), 3.64 (s, 3H), 3.73 (s, 3H), 3.75 (s, 3H), 4.16 (brd, 1H, *J* = 6.4 Hz), 4.37 (d, 1H, *J* = 12.0 Hz), 4.62 (d, 1H, *J* = 12.0 Hz), 6.62 (s, 1H), 6.72 (dd, 1H, *J* = 2.4, 8.0 Hz), 6.98 (d, 1H, *J* = 8.0 Hz), 7.23–7.36 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 27.6, 31.5, 34.0, 52.1, 52.4, 55.0, 64.2, 72.1, 79.0, 112.7, 115.6, 127.3, 127.3, 128.2, 130.0, 133.6, 136.5, 138.3, 157.7, 170.3, 170.5.

Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84. Found: C, 70.05; H, 6.59.



Dimethyl 7-(benzyloxy)-2-fluoro-7,8,9,10-tetrahydrobenzo[8]annulene-6,6(5*H*)-dicarboxylate (**6d**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

Yield: 32.5 mg (82%).

IR (neat) 3063, 3030, 951, 2851, 1738, 1610, 1591, 1498, 1472, 1452, 1435, 1335, 1319,

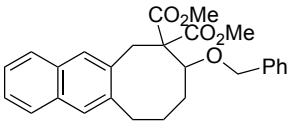
1265, 1235, 1200, 1175, 1113, 1078, 1060, 1007, 984 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.42–1.64 (m, 2H), 1.91–2.18 (m, 2H), 2.58–2.69 (m, 1H), 2.89–3.02 (m, 1H), 3.25 (d, 1H, *J* = 14.4 Hz), 3.55 (d, 1H, *J* = 14.4 Hz), 3.64 (s, 3H), 3.72 (s, 3H), 4.22 (brd, 1H, *J* = 8.4 Hz), 4.37 (d, 1H, *J* = 11.6 Hz), 4.63 (d, 1H, *J* = 11.6 Hz), 6.75–6.83 (m, 2H), 7.01 (dd, 1H, *J* = 6.4, 7.2 Hz), 7.24–7.38 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 27.0, 32.3, 32.9, 52.1, 52.4, 64.2, 72.2, 78.7, 112.7 (d, J_{C-F} = 20.0 Hz), 115.6 (d, J_{C-F} = 21.0 Hz), 127.3, 127.4, 128.2, 131.1, 131.4, 138.1, 143.8 (d, J_{C-F} = 6.7 Hz), 162.1 (d, J_{C-F} = 244.1 Hz), 170.2, 170.3.

^{19}F NMR (283 MHz, $CDCl_3$) δ 45.7 (d, 1F, *J* = 4.5 Hz).

Anal. Calcd for $C_{23}H_{25}FO_5$: C, 68.99; H, 6.29. Found: C, 69.26; H, 6.46.



Dimethyl 8-(benzyloxy)-8,9,10,11-tetrahydrocycloocta[*b*]naphthalene-7,7(6*H*)-dicarboxylate (**6e**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

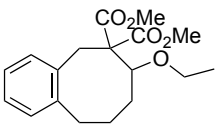
Yield: 19.4 mg (45%).

IR (neat) 3057, 3028, 2950, 2851, 1738, 1598, 1498, 1454, 1434, 1335, 1288, 1232, 1200, 1147, 1113, 1082, 1063, 1029, 890 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 1.45–1.68 (m, 2H), 1.95–2.22 (m, 2H), 2.82–2.92 (m, 1H), 3.02–3.18 (m, 1H), 3.47 (d, 1H, *J* = 14.0 Hz), 3.65–3.77 (m, 1H), 3.67 (s, 3H), 3.75 (s, 3H), 4.22 (brd, 1H, *J* = 8.0 Hz), 4.37 (d, 1H, *J* = 11.2 Hz), 4.64 (d, 1H, *J* = 11.2 Hz,

^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 27.8, 32.3, 33.8, 52.1, 52.5, 64.6, 72.2, 78.8, 125.2, 125.6, 126.9, 127.2, 127.3, 127.3, 127.4, 128.2, 129.0, 132.2, 133.1, 134.3, 138.3, 139.9, 170.3, 170.5.

Anal. Calcd for $C_{27}H_{28}O_5$: C, 74.98; H, 6.53. Found: C, 75.14; H, 6.79.



Dimethyl 7-ethoxy-7,8,9,10-tetrahydrobenzo[8]annulene-6,6(5*H*)-dicarboxylate (**6f**).

Colorless oil (purified by preparative TLC, Hexane/EtOAc = 9/1).

Yield: 15.5 mg (46%).

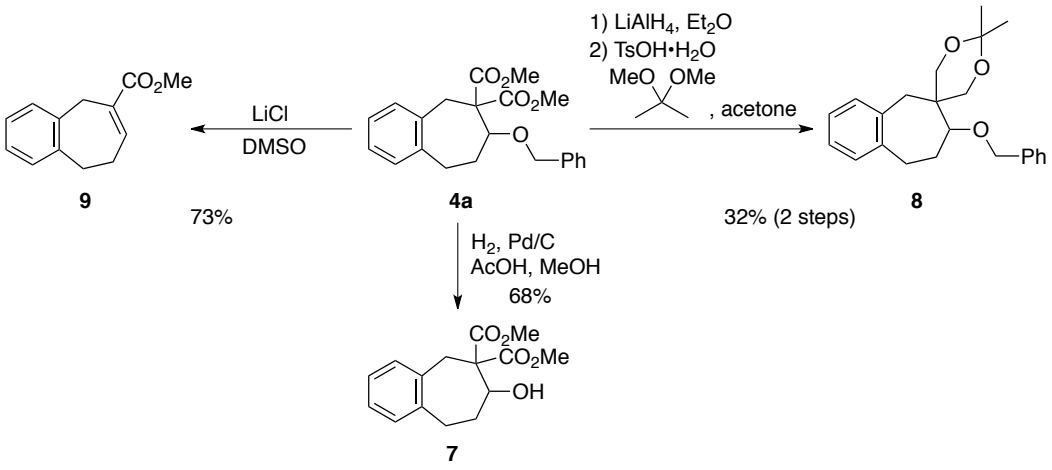
IR (neat) 3021, 2972, 2951, 2927, 2877, 2852, 1739, 1435, 1264, 1235, 1200, 1172, 1113, 1086, 1065, 1027, 987 cm^{-1}.

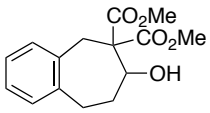
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, 3H, *J* = 6.0 Hz), 1.41–1.56 (m, 2H), 1.87–2.03 (m, 2H), 2.64–2.72 (m, 1H), 2.89–3.00 (m, 1H), 3.25 (d, 1H, *J* = 14.0 Hz), 3.28–3.37 (m, 1H), 3.55 (brd, 1H, *J* = 14.0 Hz), 3.59–3.66 (m, 1H), 3.74 (s, 3H), 3.76 (s, 3H), 4.04 (brd, 1H, *J* = 7.0 Hz), 7.01–7.12 (m, 3H), 7.17 (ddd, 1H, *J* = 1.5, 7.5, 7.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 25.2, 27.2, 32.0, 33.8, 52.0, 52.4, 64.3, 65.6, 78.9, 125.9, 127.4, 129.1, 130.0, 135.5, 141.5, 170.4, 170.6.

Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.19; H, 7.44.

3. Transformation from the adduct.





Synthesis of dimethyl 7-hydroxy-8,9-dihydro-5H-benzo[7]annulene-6,6(7H)-dicarboxylate (7):

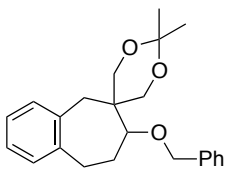
To a solution of **4a** (31.9 mg, 0.0866 mmol) in MeOH (0.60 mL) were succesively added AcOH (5 μL, 0.87 mmol) and 10% Pd/C (18.1 mg) at room temperature. After being stirred under H_2 (1 atm) at 40 °C for 18 h, the reaction mixture was filtered through Celite® pad and concentrated in vacuo. The residue was purified by preparative TLC (hexane/EtOAc = 3/1) to give **7** (16.5 mg, 68%) as colorless oil.

IR (neat) 3518, 3022, 2952, 2849, 1738, 1575, 1495, 1455, 1435, 1410, 1309, 1273, 1246, 1223, 1048, 1033, 1102, 1079, 1048, 1033, 977 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.78–1.98 (m, 1H), 2.21–2.32 (m, 1H), 2.55–4.40 (m, 12H), 7.04–7.20 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 30.2, 32.8, 36.1, 51.9, 52.4, 61.4, 126.1, 127.3, 128.5, 131.3, 135.4, 142.2, 170.9.

Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.49; H, 6.35.



Synthesis of 7-(denzyloxy)-2',2'-dimethyl-5,7,8,9-tetrahydrospiro[benzo[7]annulene-6,5'-[1,3]dioxane] (8):

To a solution of **4a** (35.4 mg, 0.0496 mmol) in THF (1.0 mL) was added $LiAlH_4$ (6.8 mg, 0.179 mmol) at 0 °C. After being stirred for 3.0 h at 0 °C, the reaction was stopped by adding Na_2SO_4•$10H_2O$. After being stirred for another 1 h at room temperature, the crude material was filtered through Celite® pad, and the resulting filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2/1) to give diol (12.4 mg, 41%) as colorless oil.

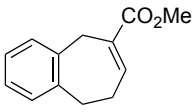
To a solution of diol (12.4 mg, 0.0397 mmol) in acetone (1.0 mL) were successively added 2,2-dimethoxypropane (9.7 μL, 0.0794 mmol) and TsOH•H_2O (2.4 mg, 0.012 mmol) at 0 °C. After being stirred for 1.5 h at 0 °C, the reaction was stopped by adding saturated aqueous $NaHCO_3$ at 0 °C. The crude products were 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 preparative TLC (hexane/EtOAc = 2/1) to give **8** (10.9 mg, 78%) as colorless oil.

IR (neat) 3063, 3027, 2989, 2925, 2855, 1495, 1454, 1370, 1350, 1296, 1263, 1227, 1197, 1158, 1121, 1091, 1068, 1030, 938 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 1.15–1.73 (m, 2H), 1.39 (s, 3H), 1.44 (s, 3H), 2.00–2.65 (m, 2H), 2.96–3.90 (m, 6H), 3.94 (d, 1H, *J* = 11.5 Hz), 4.47 (d, 1H, *J* = 11.5 Hz), 4.72 (d, 1H, *J* = 11.5 Hz), 6.98–7.49 (m, 10H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 25.9, 28.7, 29.7, 34.9, 38.6, 65.1, 68.0, 70.9, 97.9, 126.2, 126.5, 127.5, 128.3, 128.3, 130.5, 137.6, 138.7, 142.3.

Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.38; H, 8.01. Found: C, 78.15; H, 7.79.



Synthesis of methyl 8,9-dihydro-5H-benzo[7]annulene-6-carboxylate (9):

To a solution of **4a** (15.8 mg, 0.0429 mmol) in DMSO (1.39 mL) was added LiCl (20.5 mg, 0.484 mmol) at room temperature, and the mixture were heated at 120 °C for 16 h. After cooling to room temperature, the reaction was stopped by adding H_2O. The

crude products were 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 preparative TLC (hexane/EtOAc = 6/1) to give **9** (6.3 mg, 73%) as colorless oil.

IR (neat) 3064, 3021, 2949, 2887, 1708, 1645, 1494, 1456, 1435, 1284, 1257, 1222, 1196, 1177, 1165, 1107, 1086, 1055, 1043, 1011, 967 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 2.48–2.63 (m, 2H), 3.27 (dd, 1H, J = 6.0, 6.0 Hz), 3.75 (s, 3H), 3.84 (s, 2H), 6.89 (brs, 1H), 7.08–7.26 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 29.8, 30.9, 31.3, 52.0, 126.3, 126.8, 128.0, 128.4, 129.0, 140.7, 141.1, 141.1, 168.4.

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.34; H, 7.13.

References

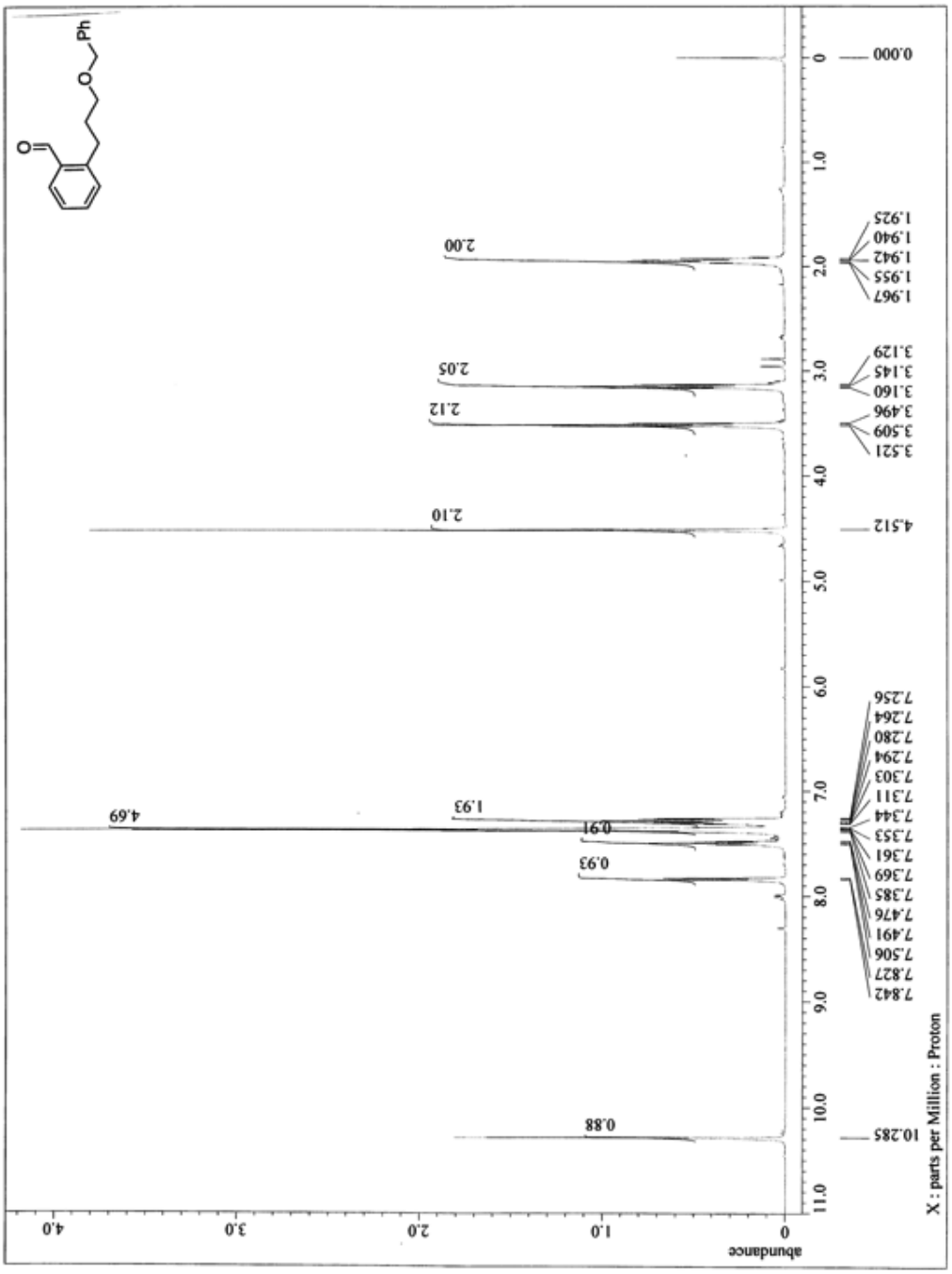
1) Doušová, H.; Horák, R.; Ružicková, Z.; Šimunek, P. *Beilstein J. Org. Chem.* **2015**, *11*, 884.

2) Fan, Y. C.; Kwon, O. *Org. Lett.* **2015**, *9*, 2058.

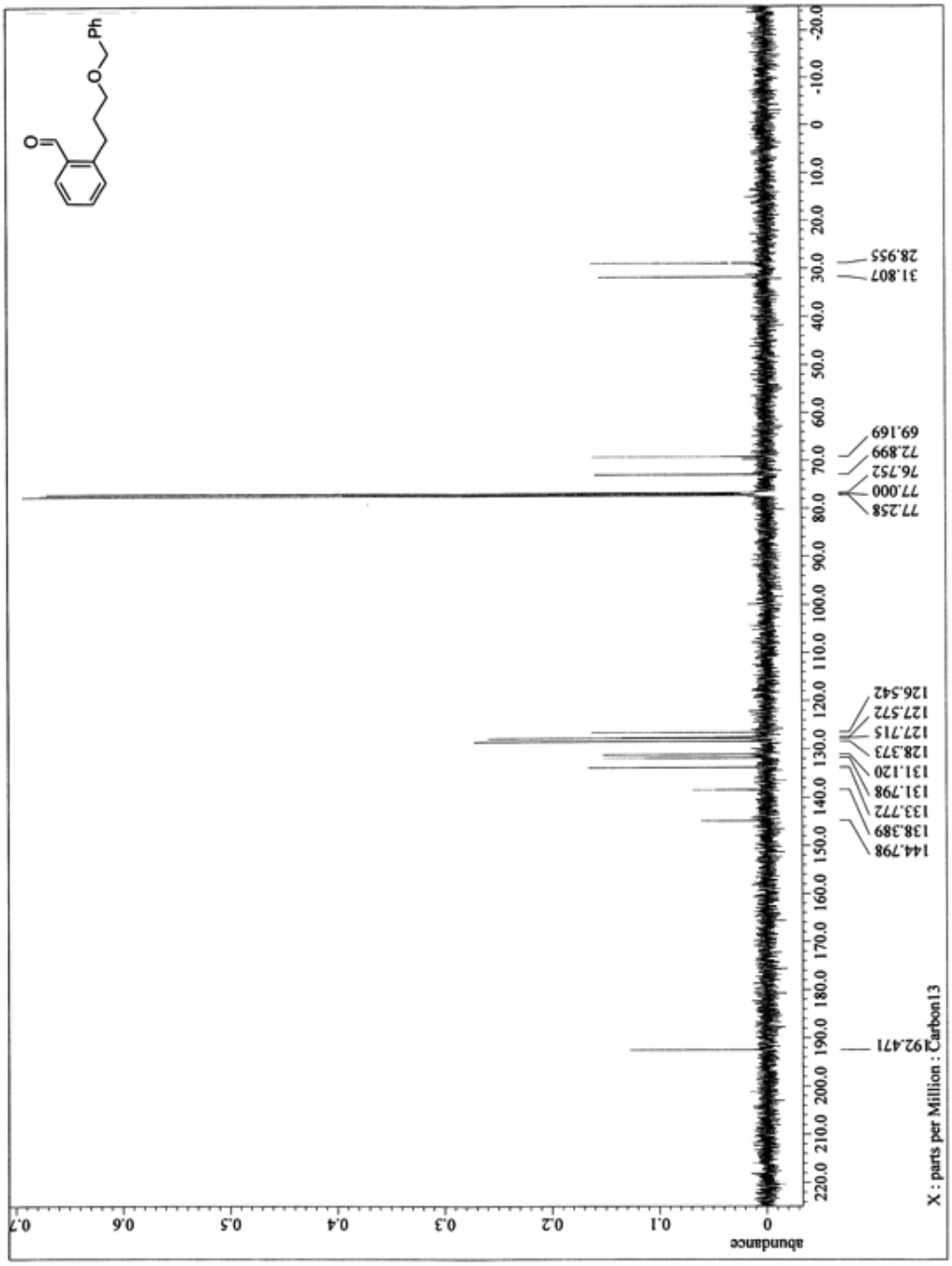
3) K. Grudzien´, K.; Z˙ukowska, K.; Malin´ska, M.; Woz´niak, K.; Barbasiewicz, M. *Chem. Eur. J.* **2014**, *20*, 2819.

4) Romanov-Michailidis, F.; Pupier, M.; Guénée, L.; Alexakis, A. *Chem. Commun.* **2014**, *50*, 13461

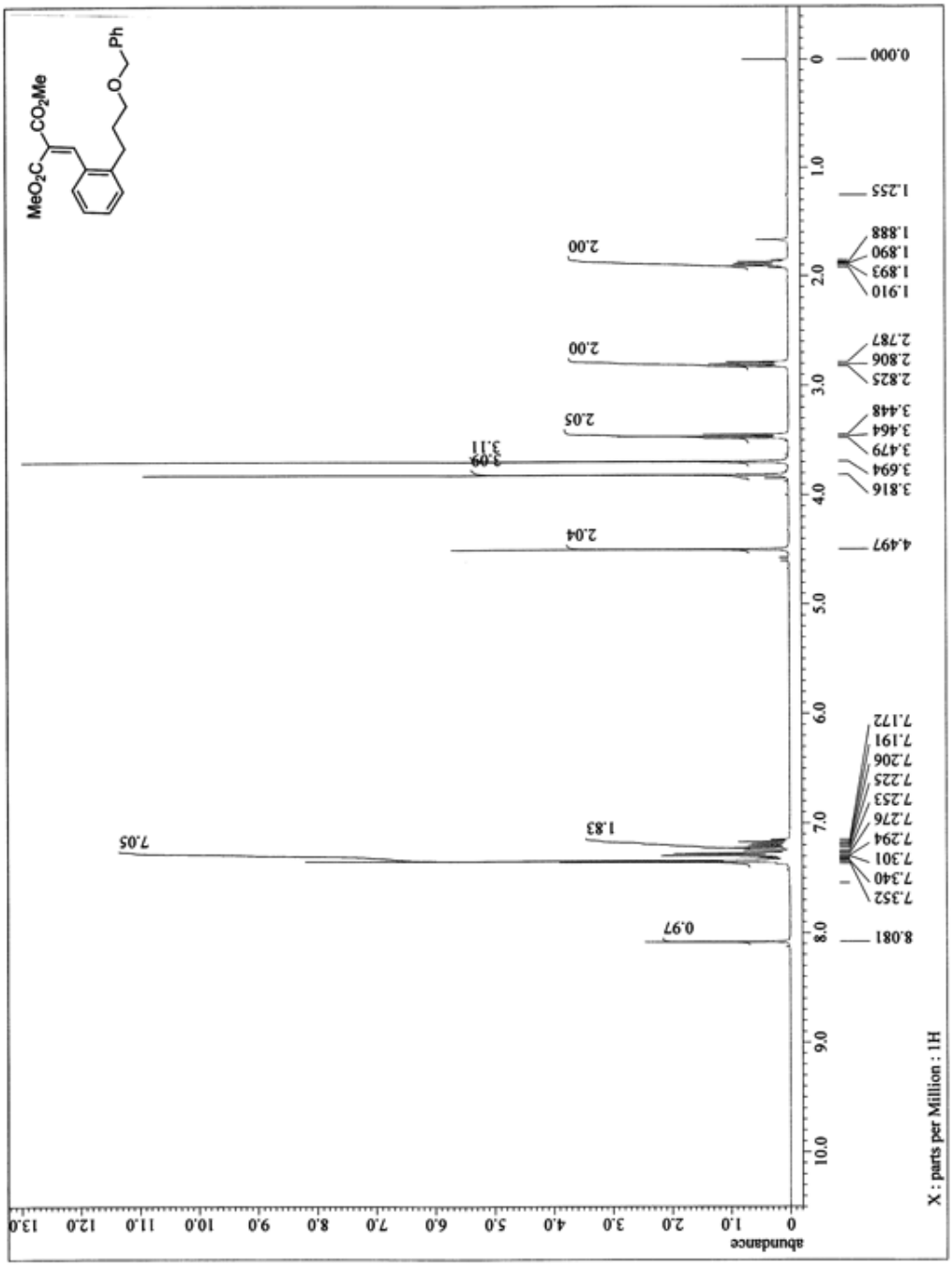
^{1}H NMR spectrum of **s5**.



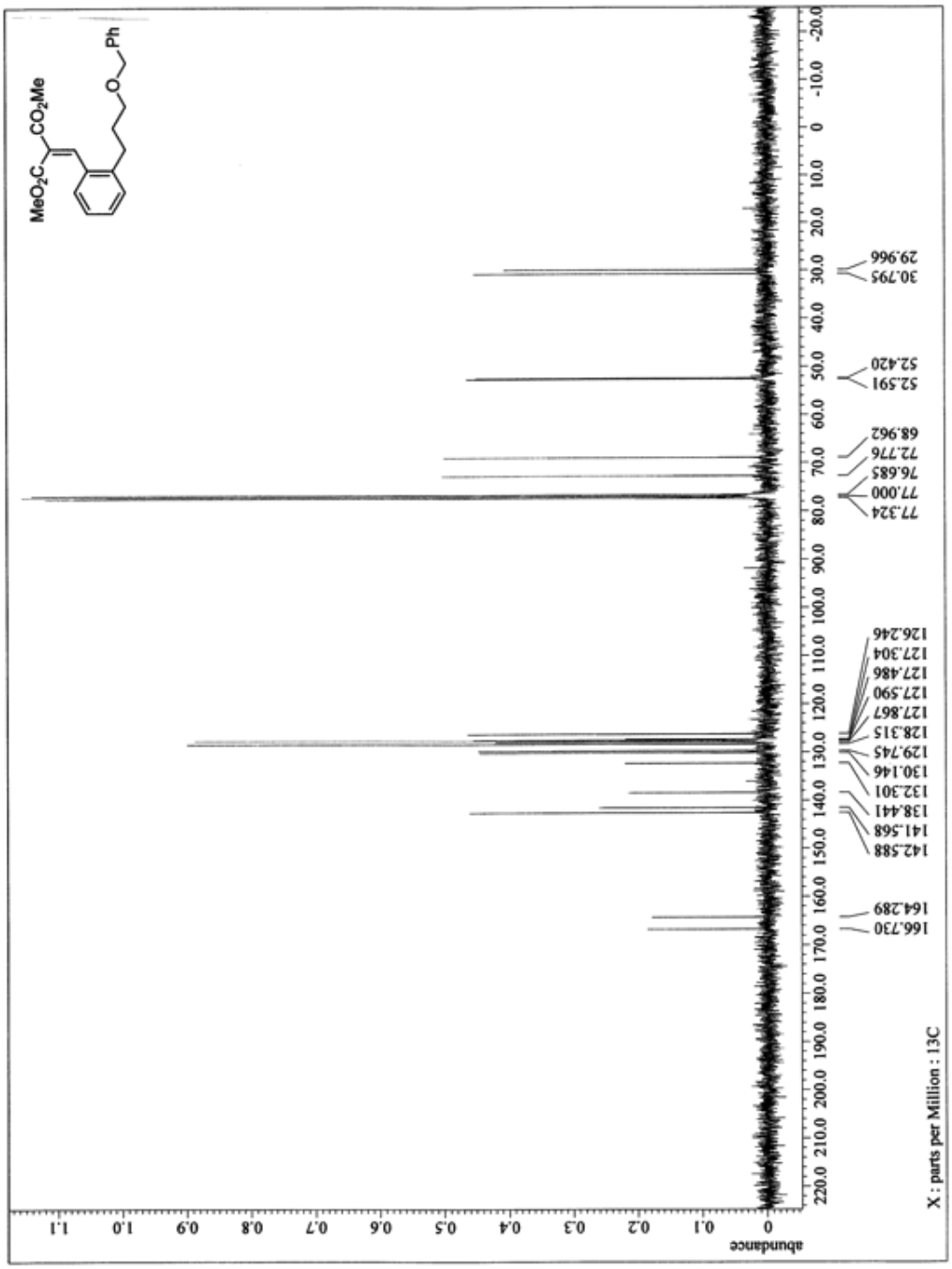
^{13}C NMR spectrum of **s5**.



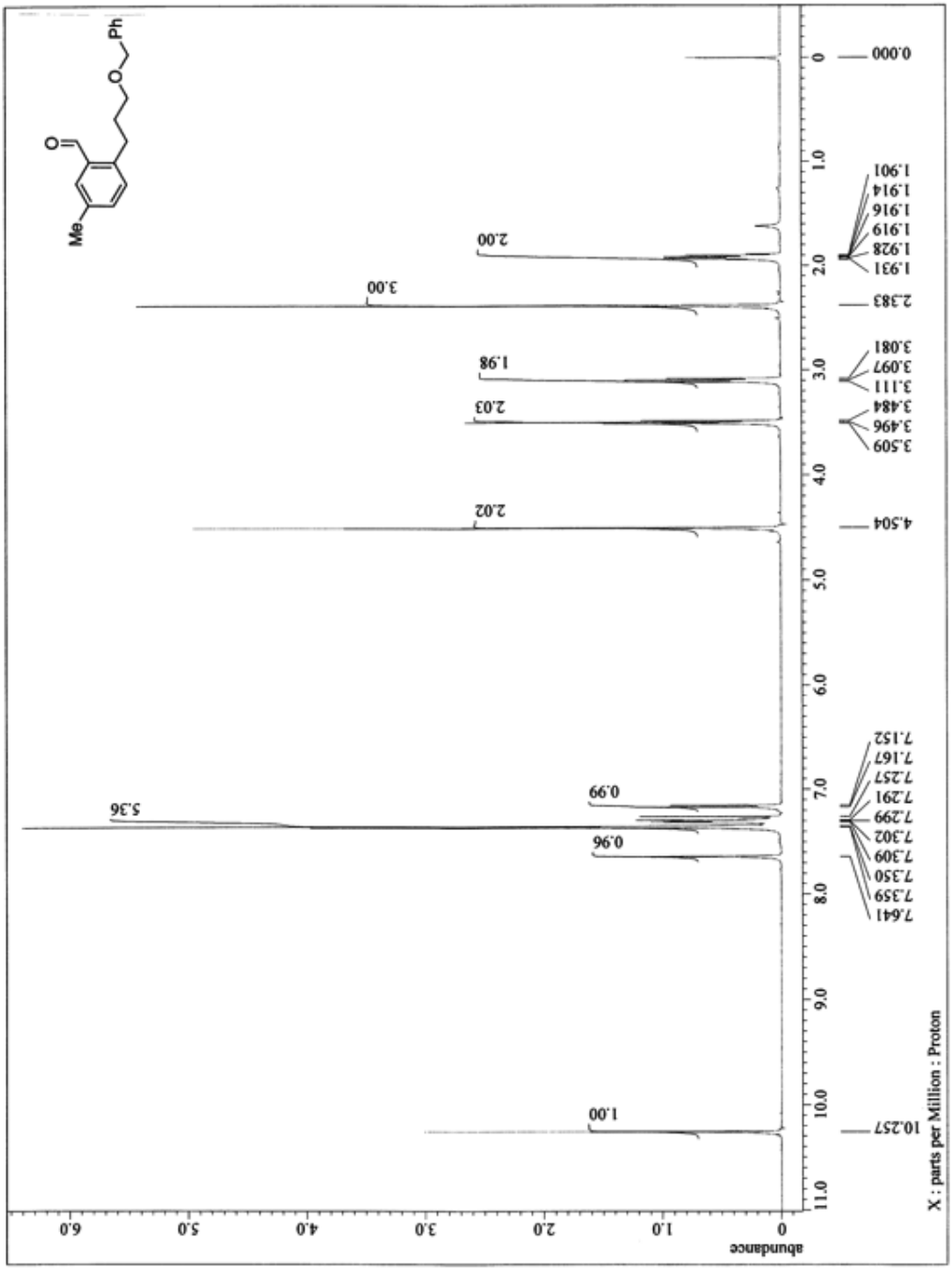
^{1}H NMR spectrum of **3a**.



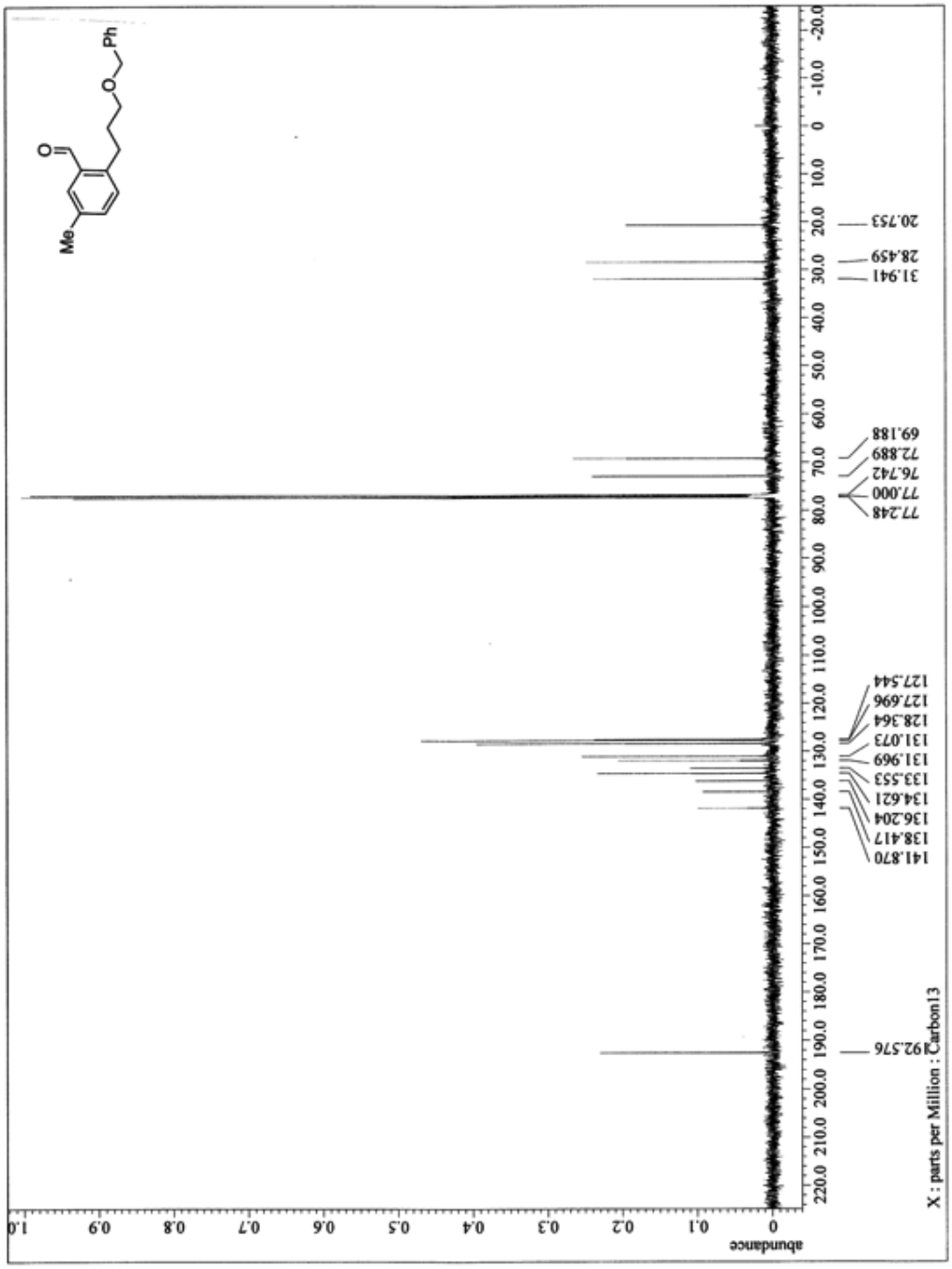
^{13}C NMR spectrum of **3a**.



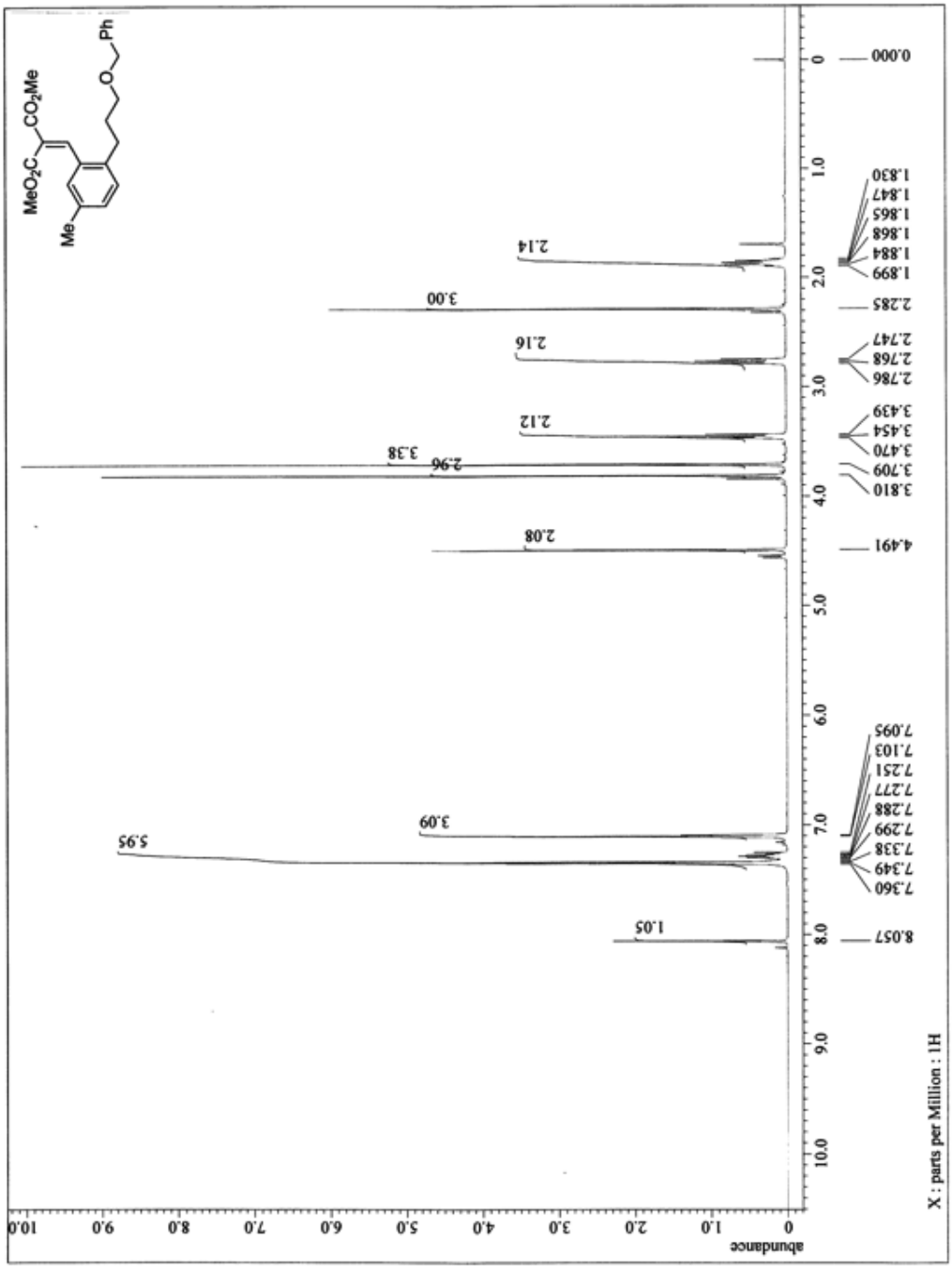
^{1}H NMR spectrum of **s6**.



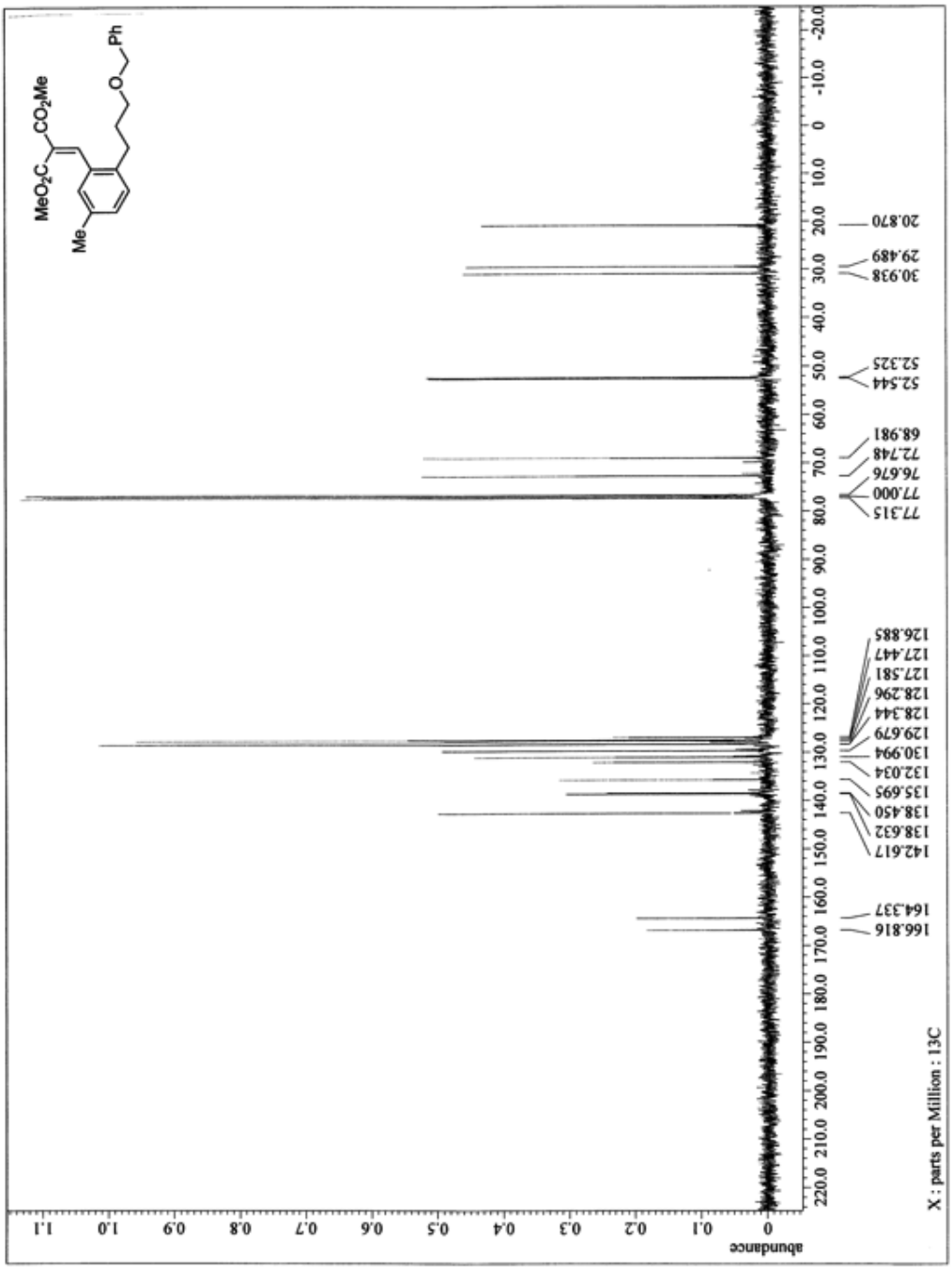
^{13}C NMR spectrum of **s6**.



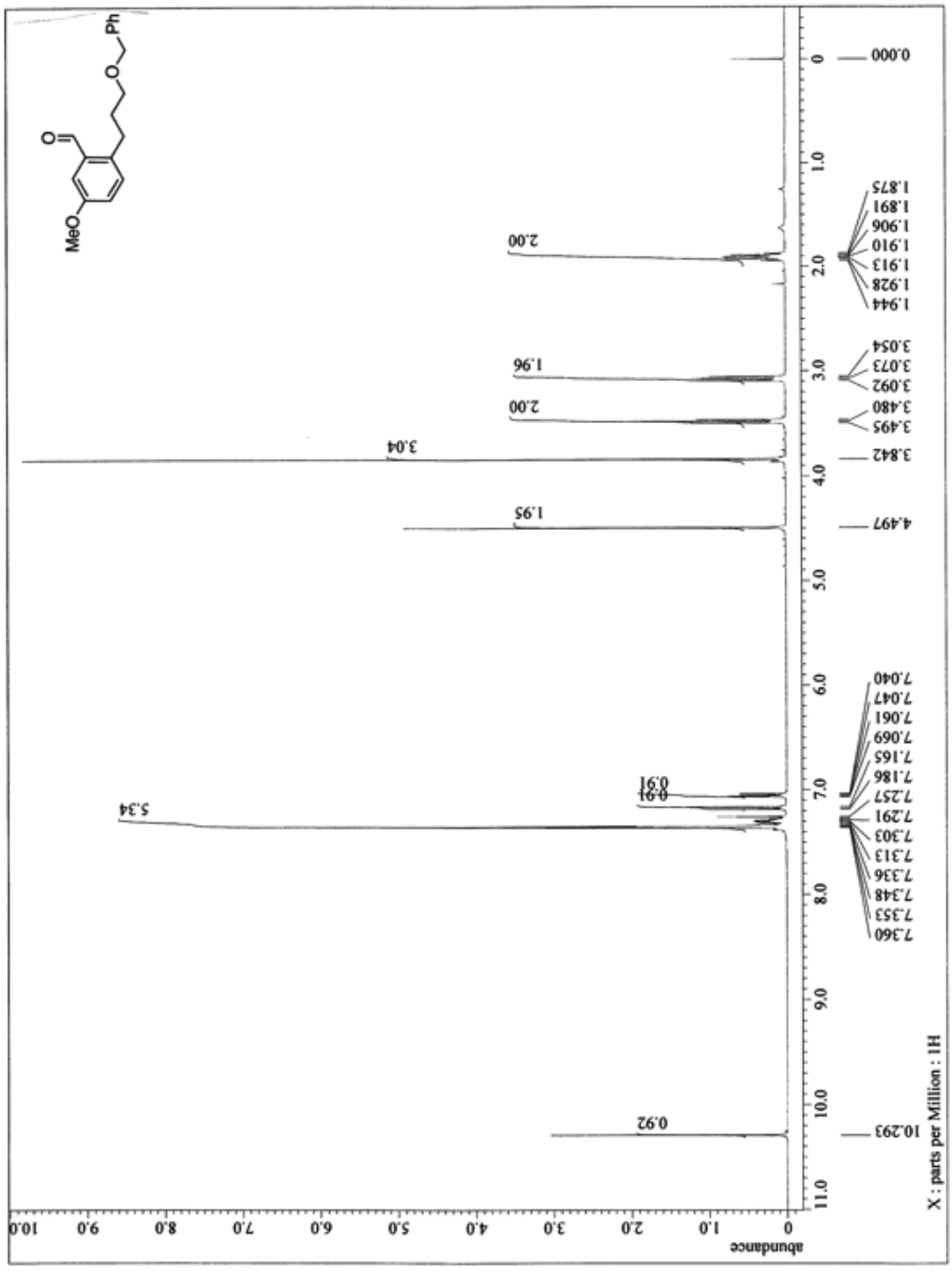
^{1}H NMR spectrum of **3b**.



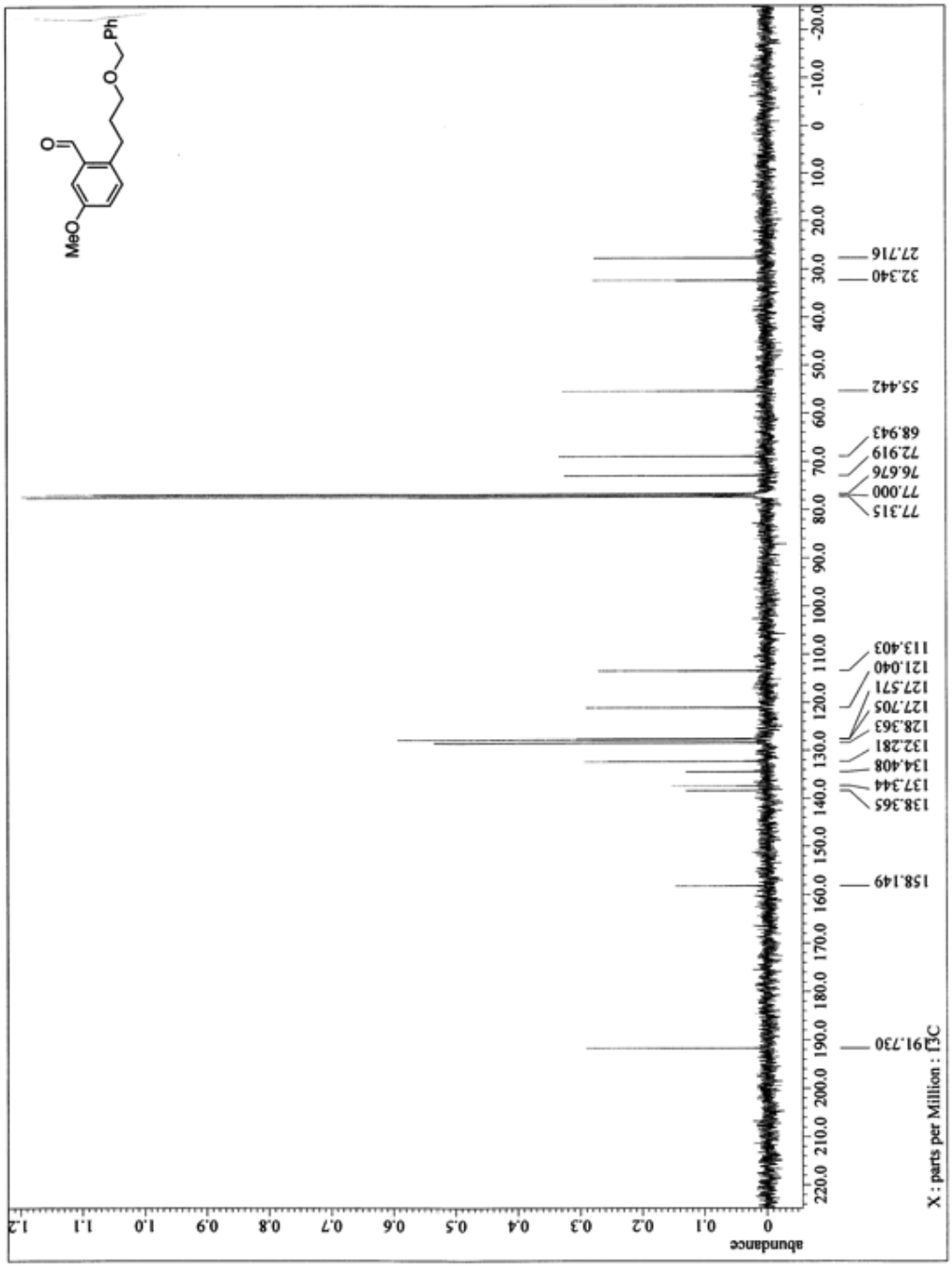
^{13}C NMR spectrum of **3b**.



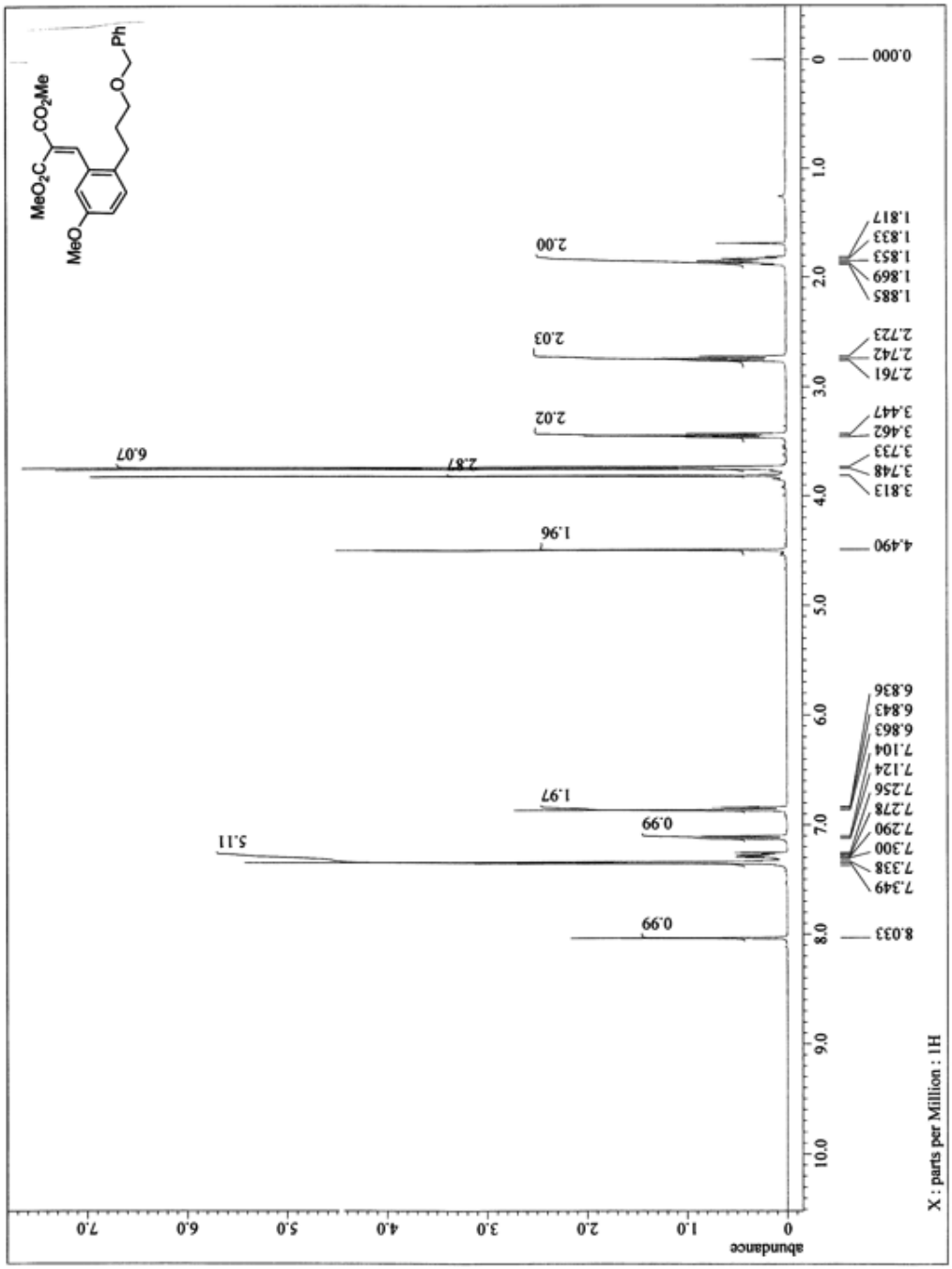
^{1}H NMR spectrum of **s7**.



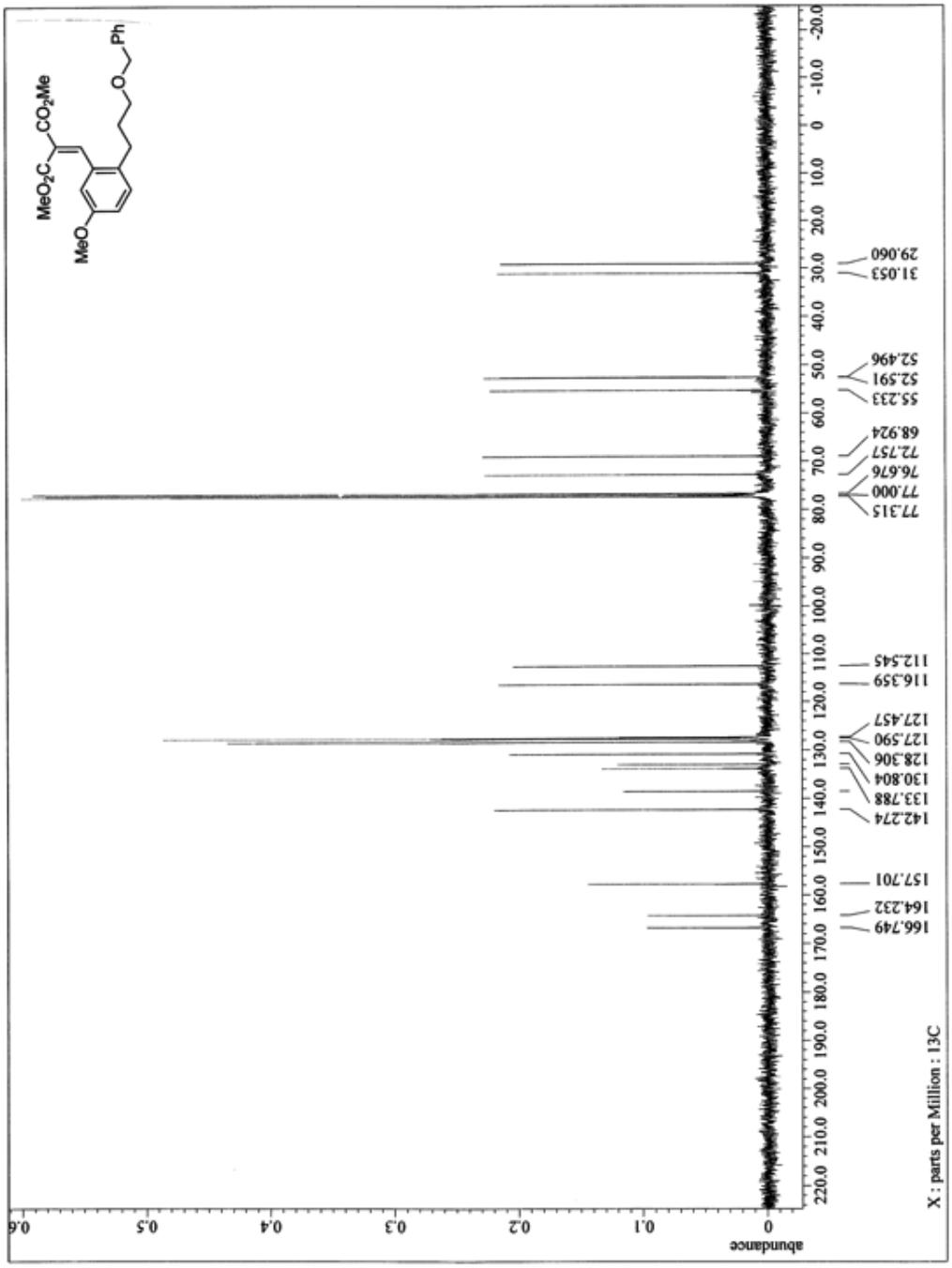
^{13}C NMR spectrum of **s7**.



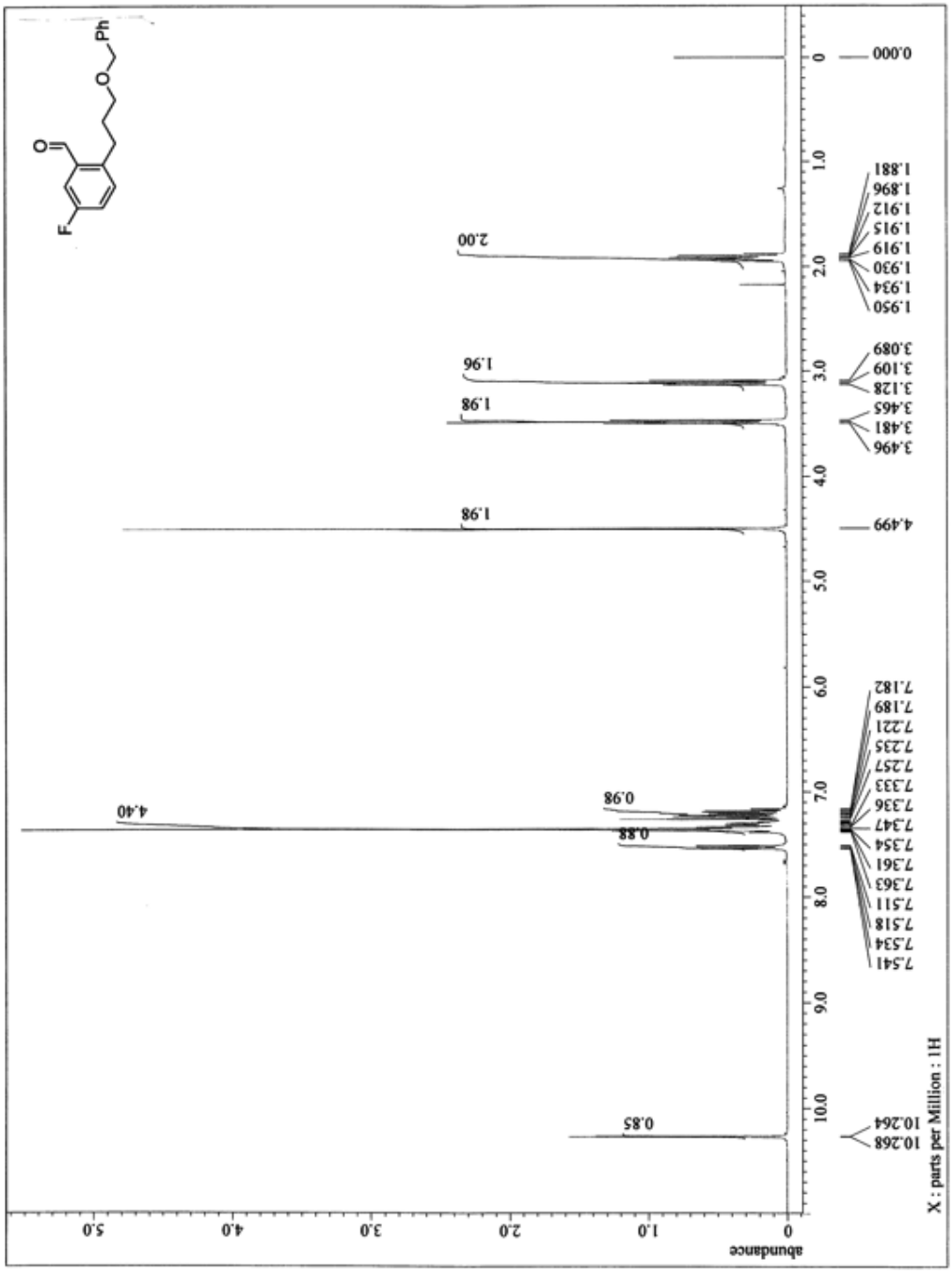
^{1}H NMR spectrum of **3c**.



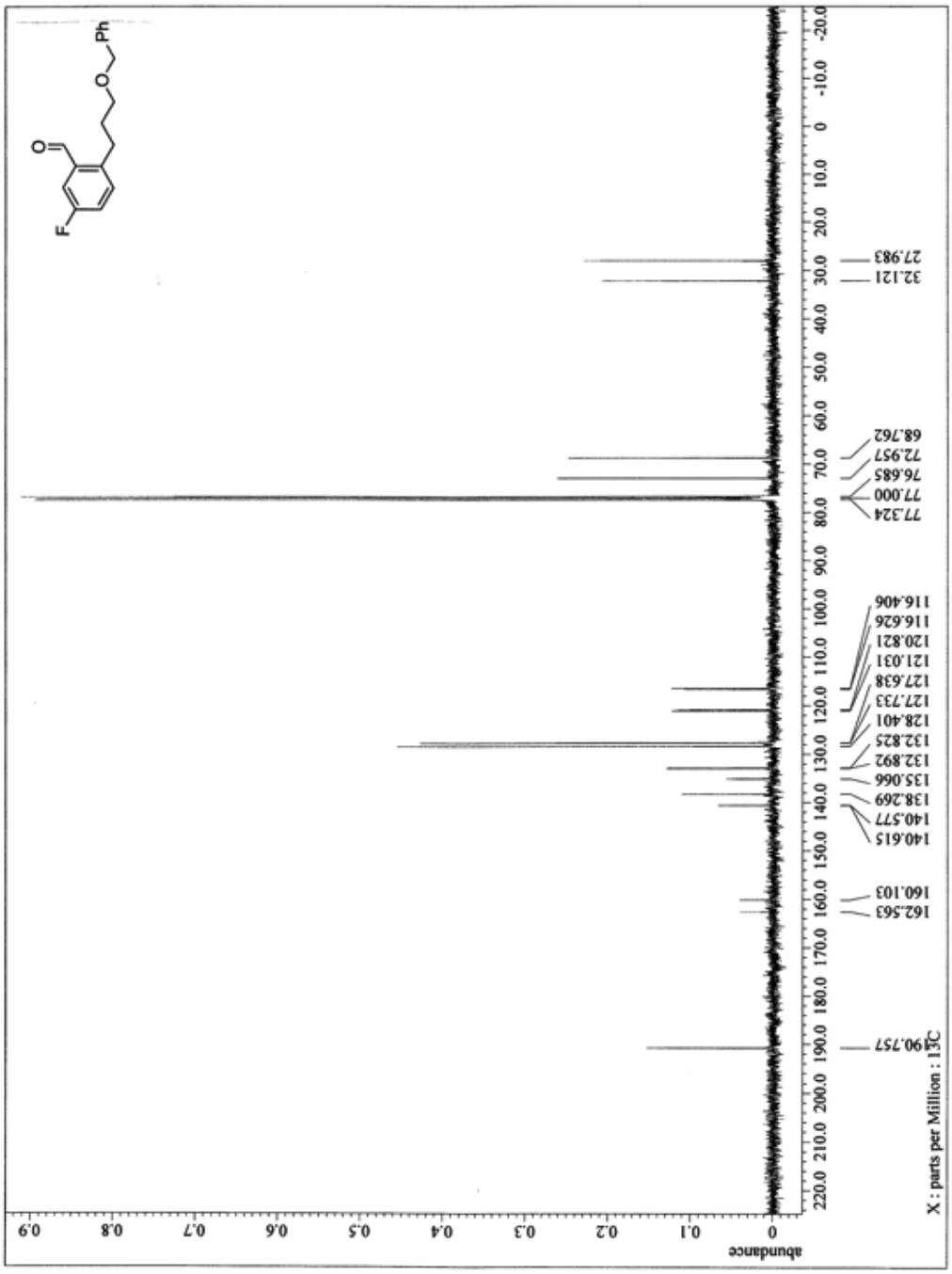
^{13}C NMR spectrum of **3c**.



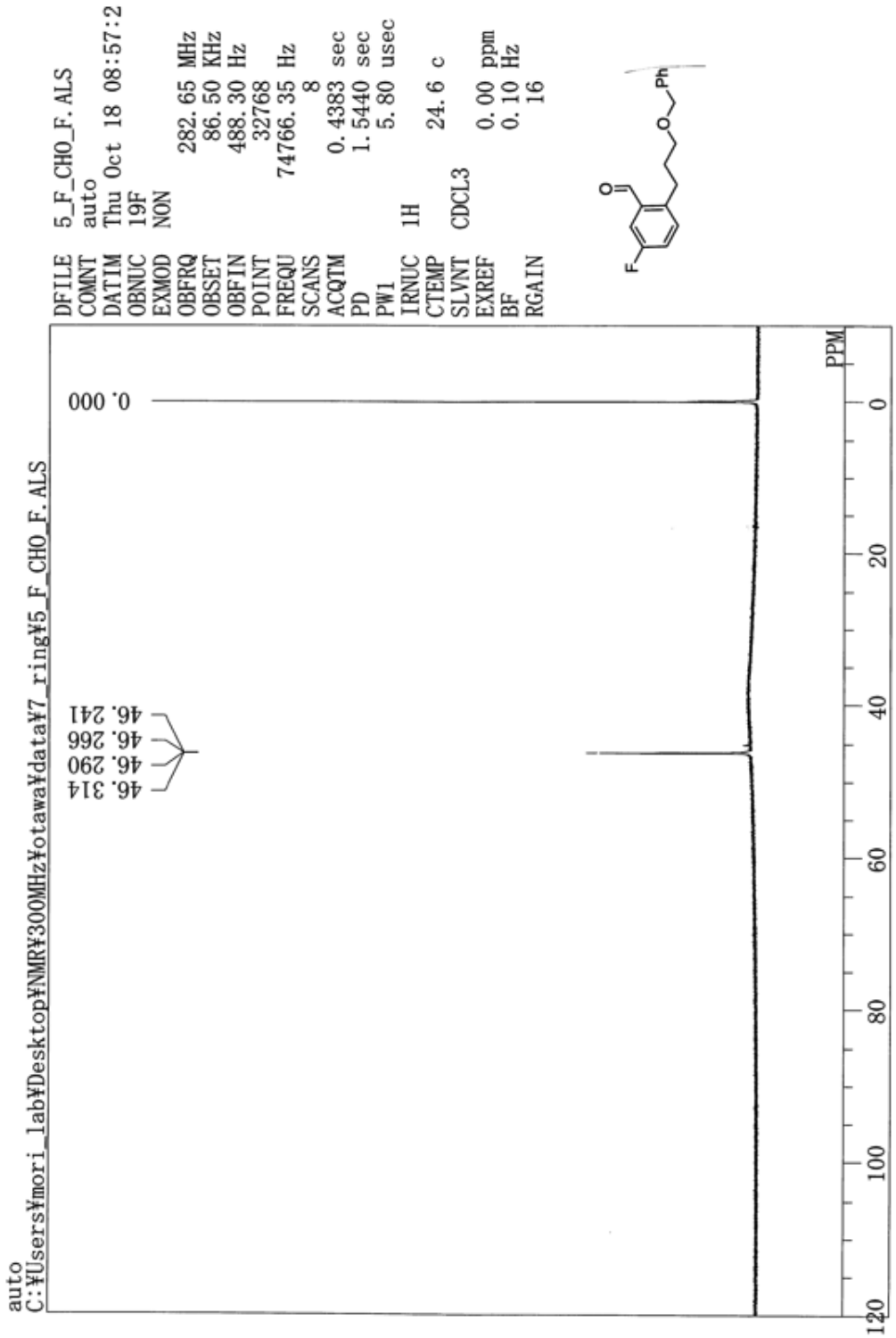
^{1}H NMR spectrum of **s8**.



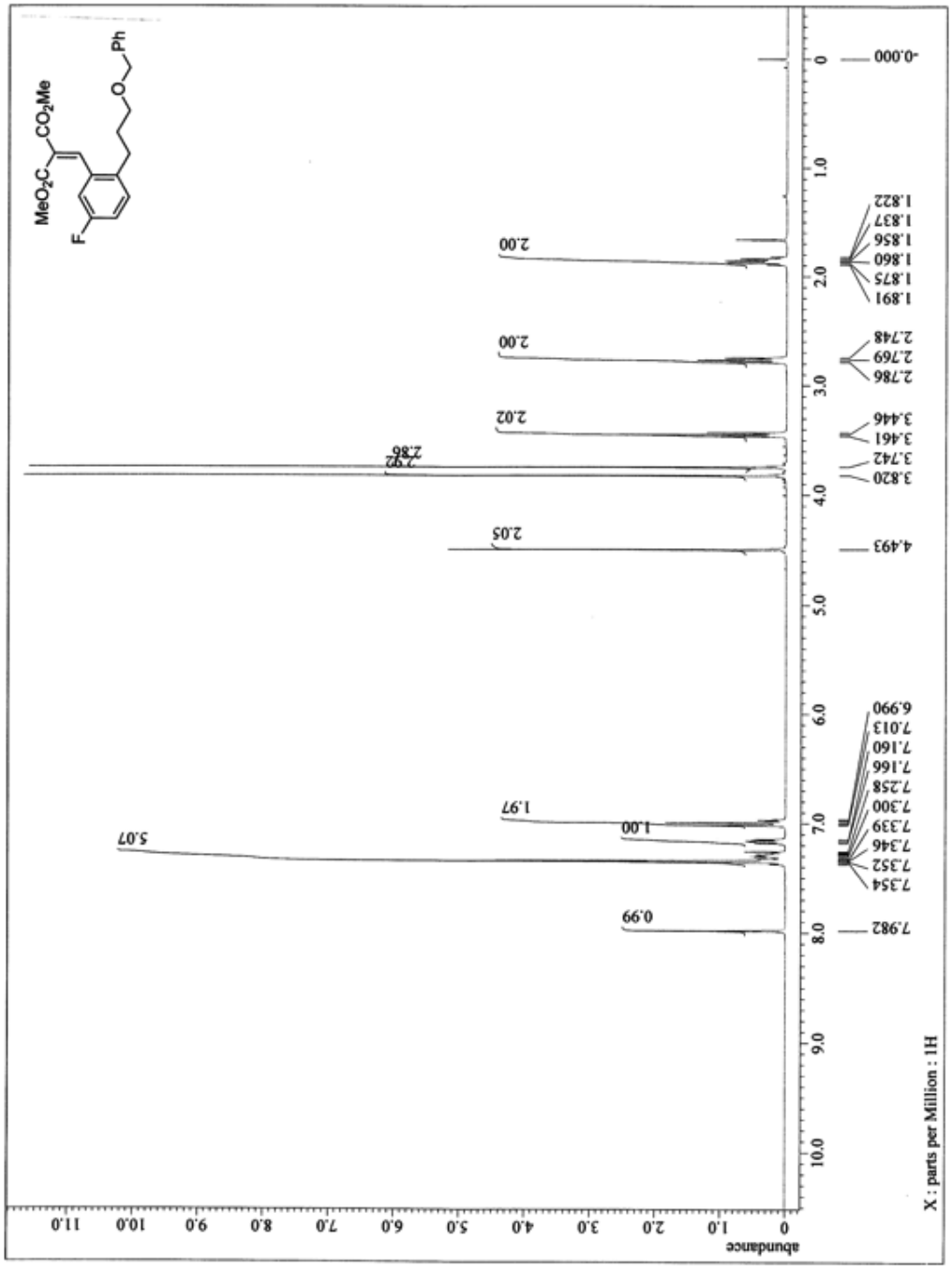
^{13}C NMR spectrum of **s8**.



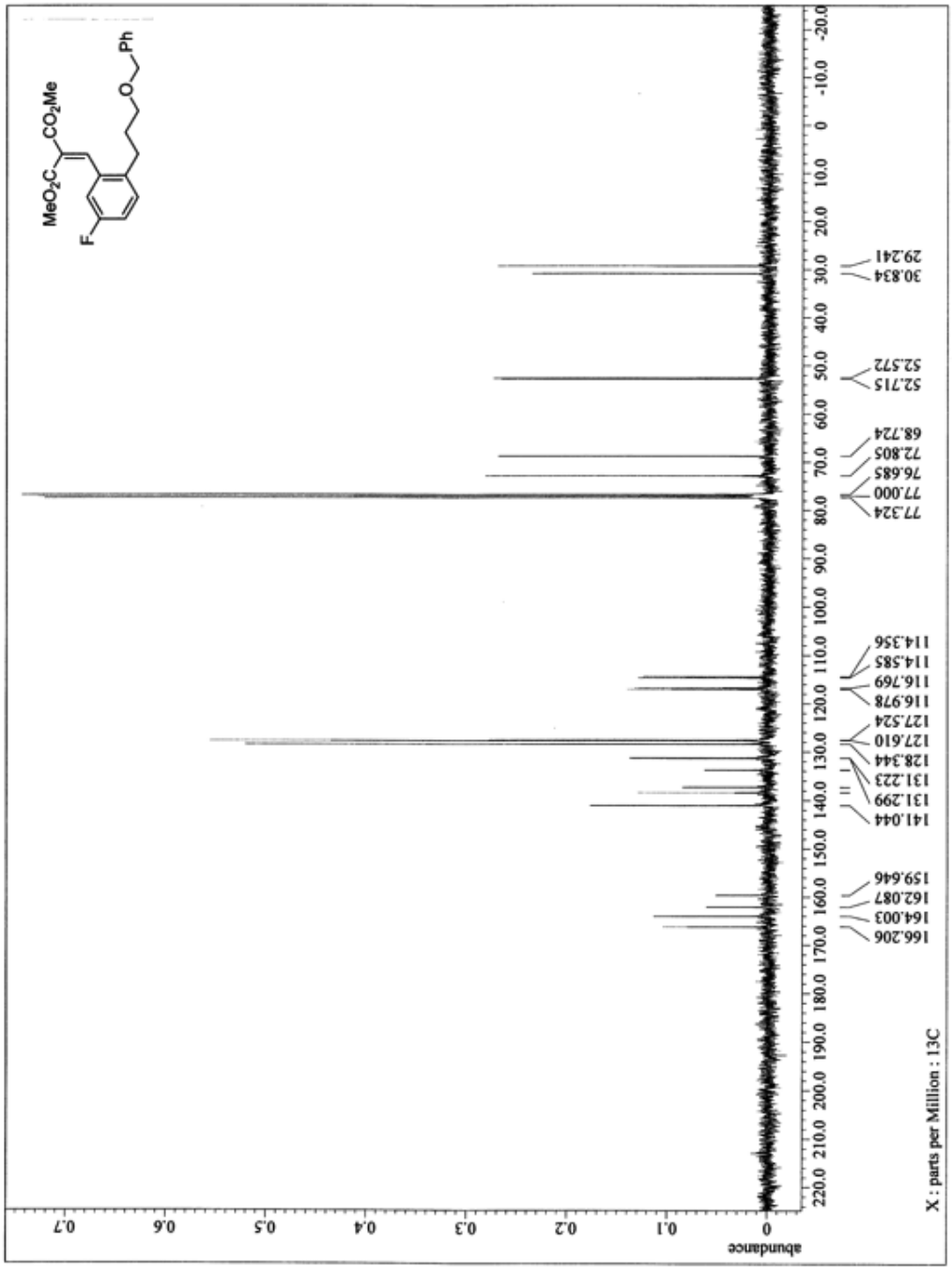
^{19}F NMR spectrum of **s8**.



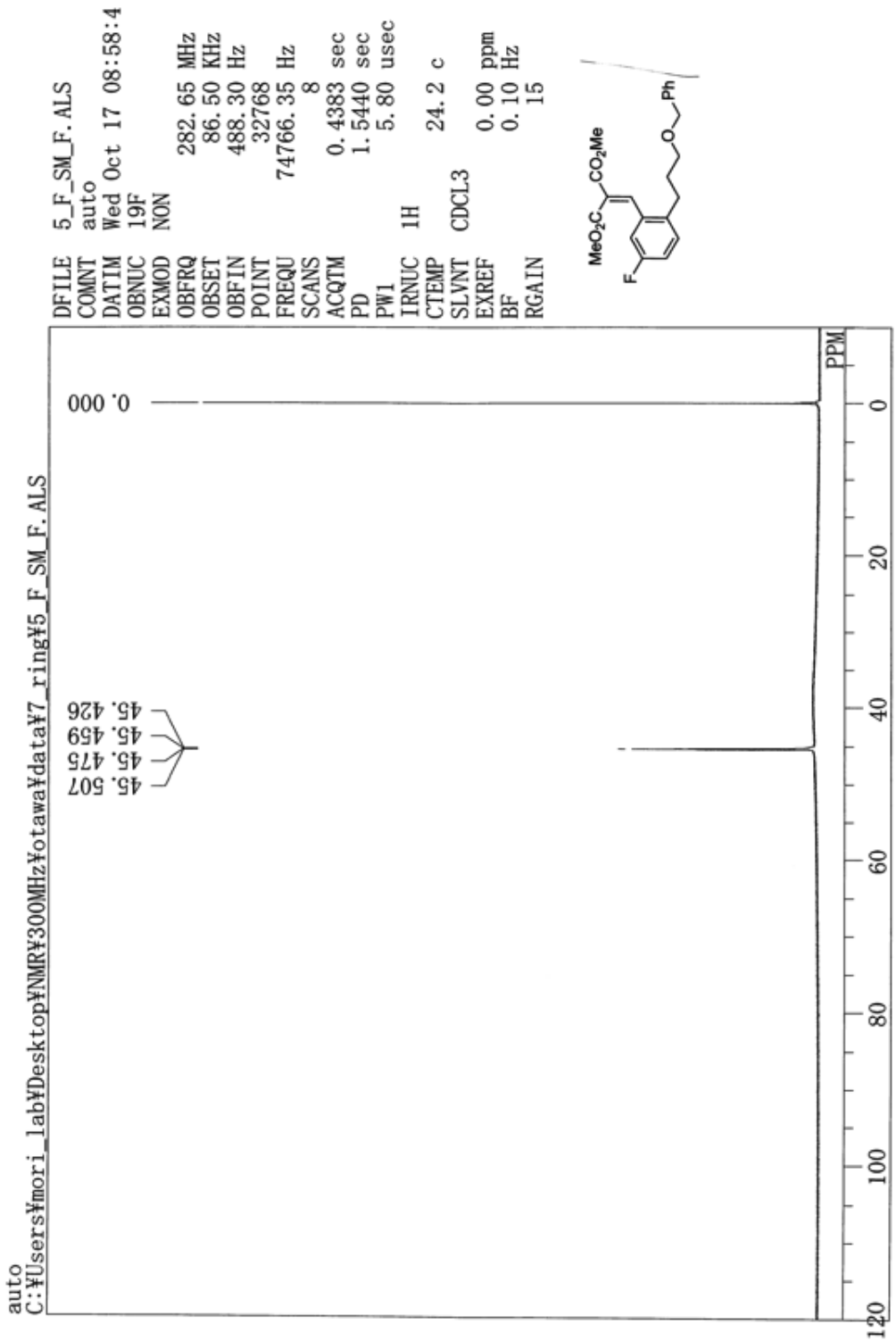
^{1}H NMR spectrum of **3d**.



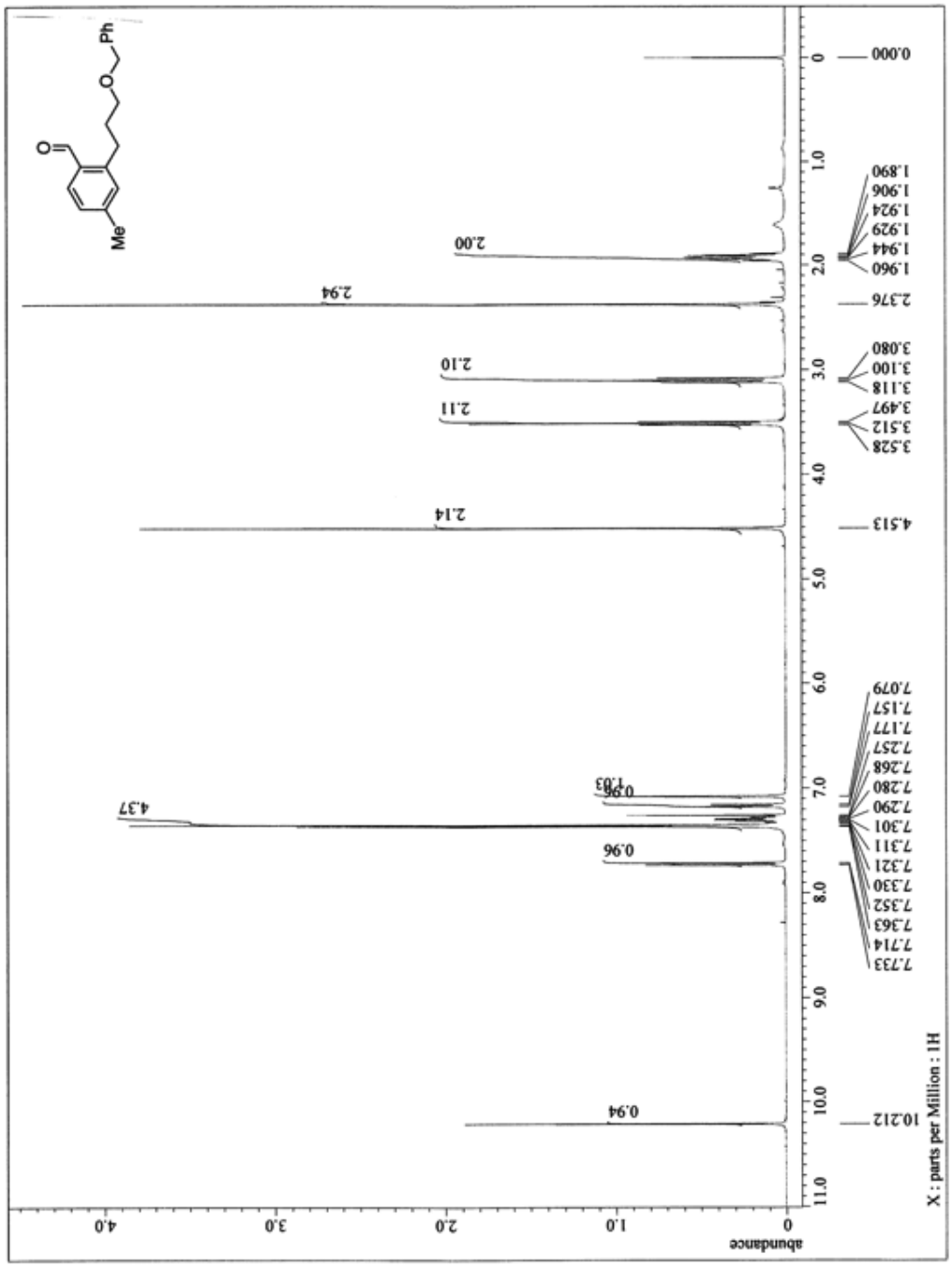
^{13}C NMR spectrum of **3d**.



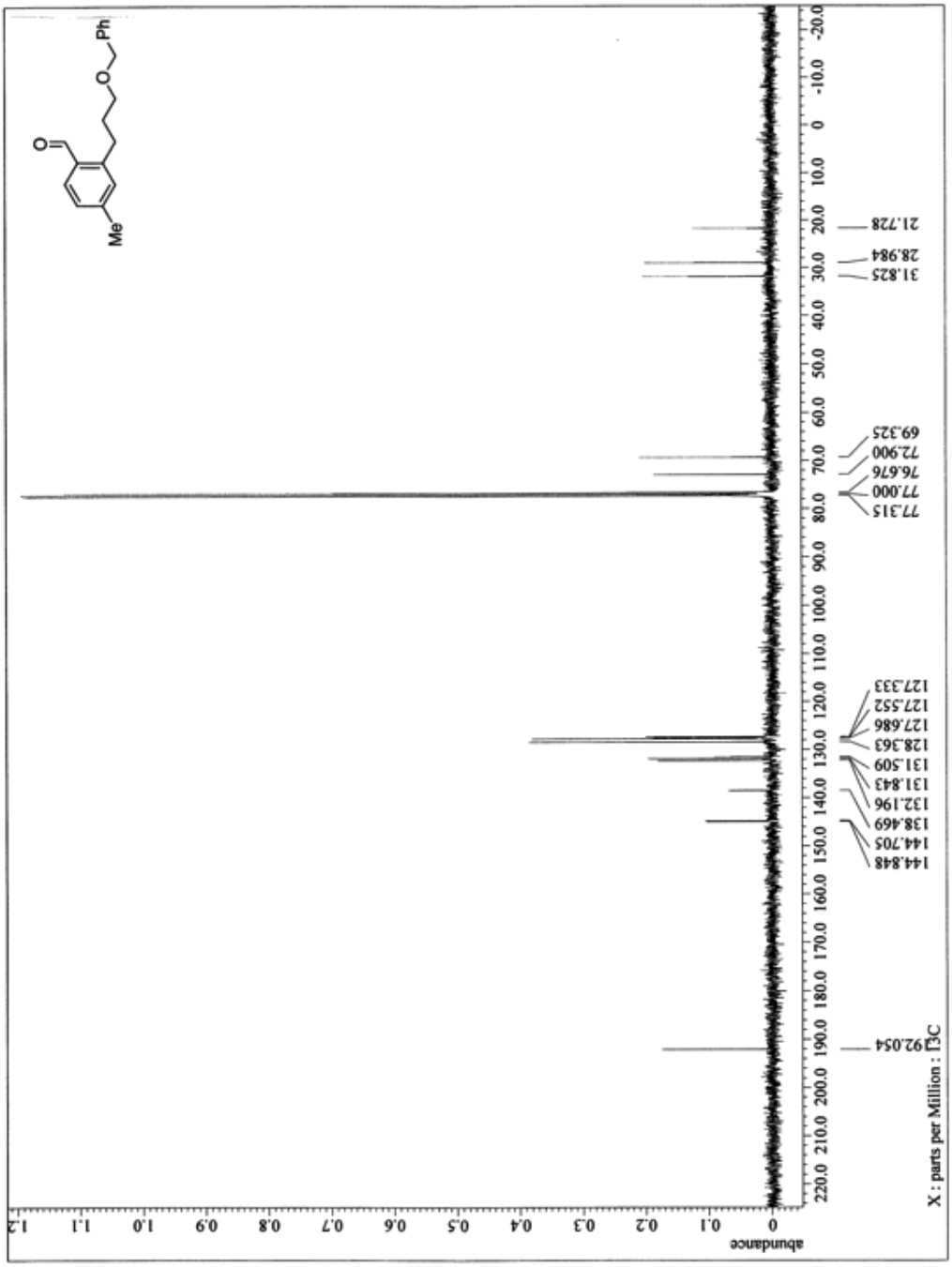
^{19}F NMR spectrum of **3d**.



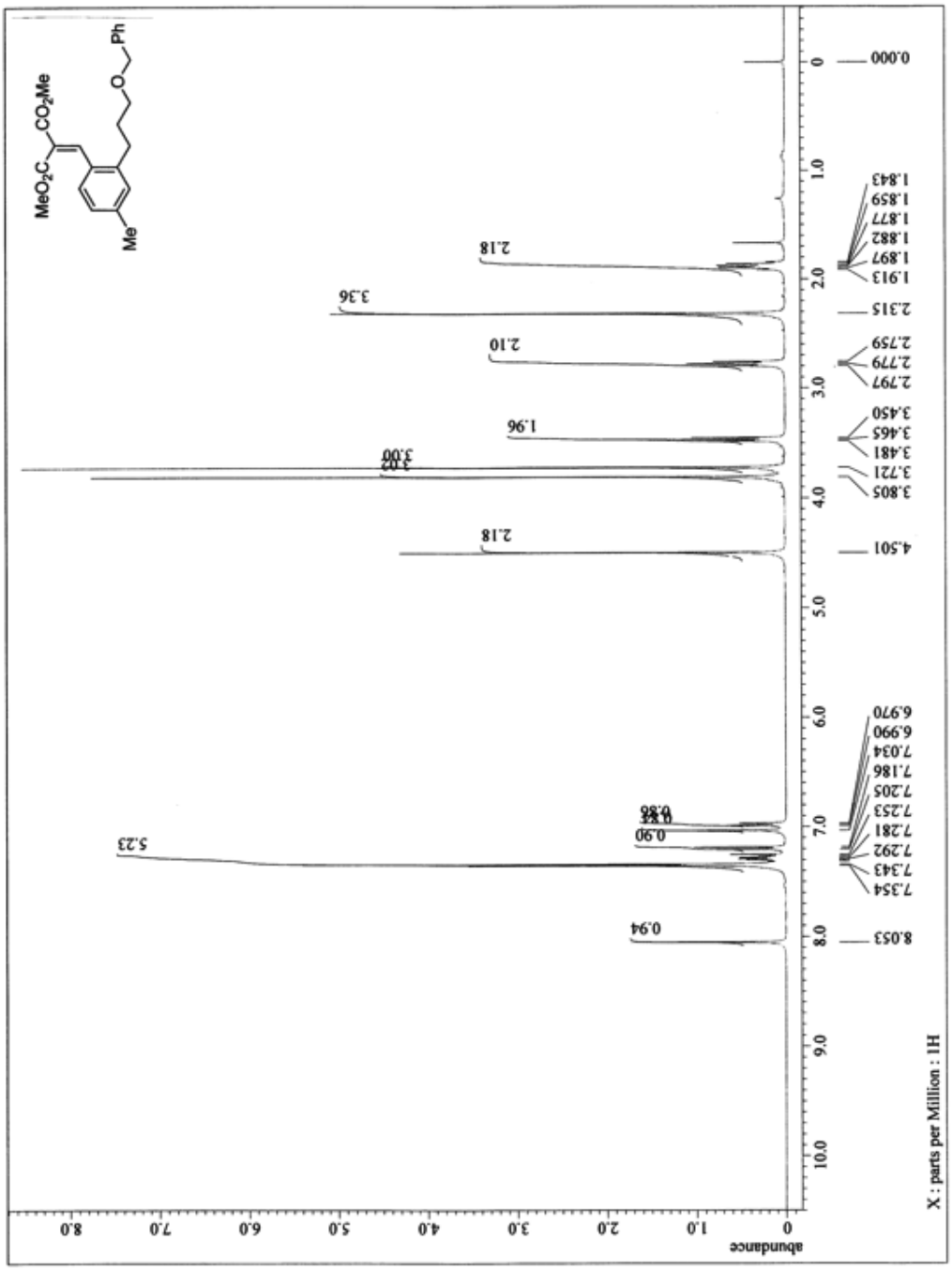
^{1}H NMR spectrum of **s9**.



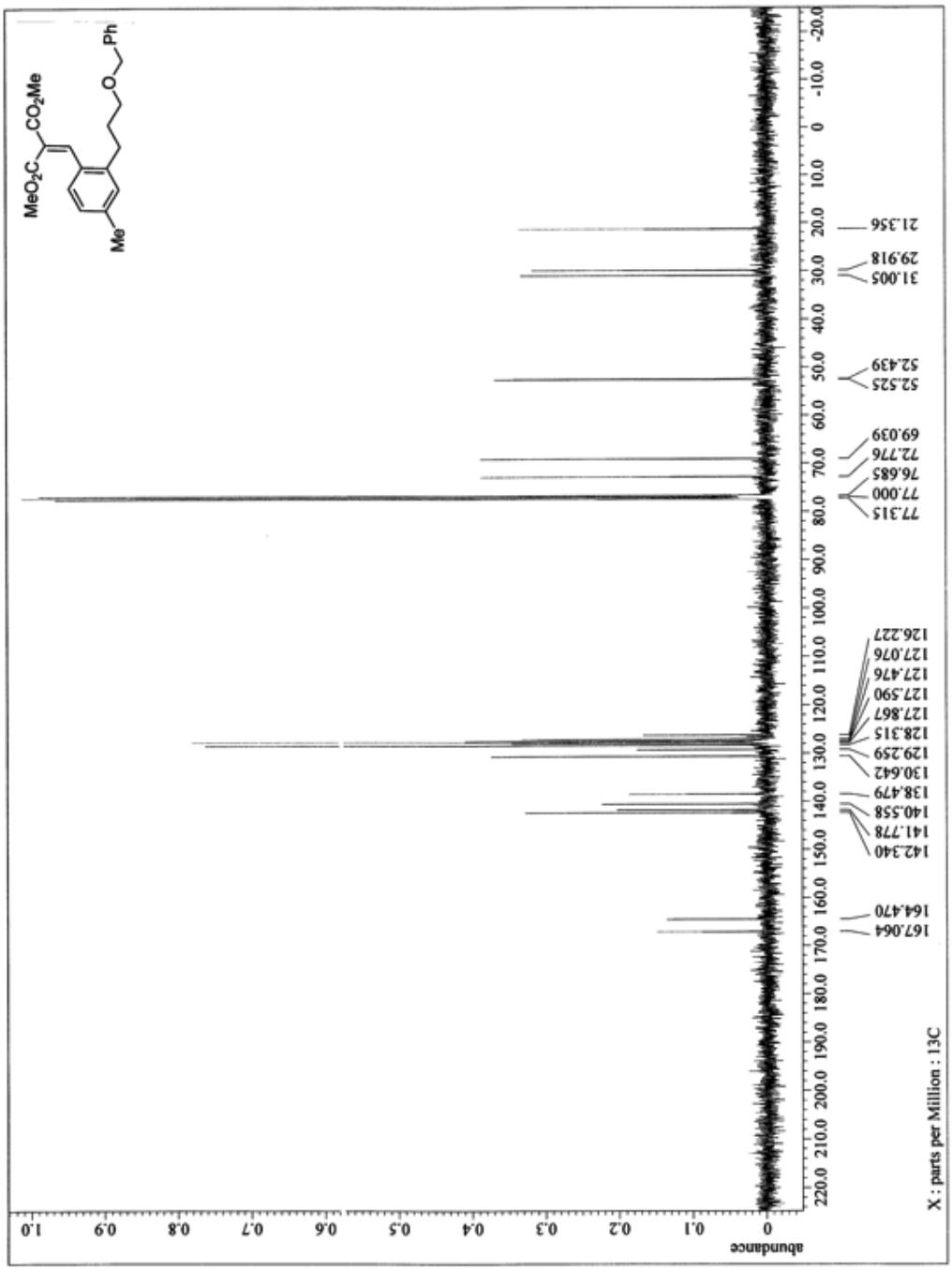
^{13}C NMR spectrum of **s9**.



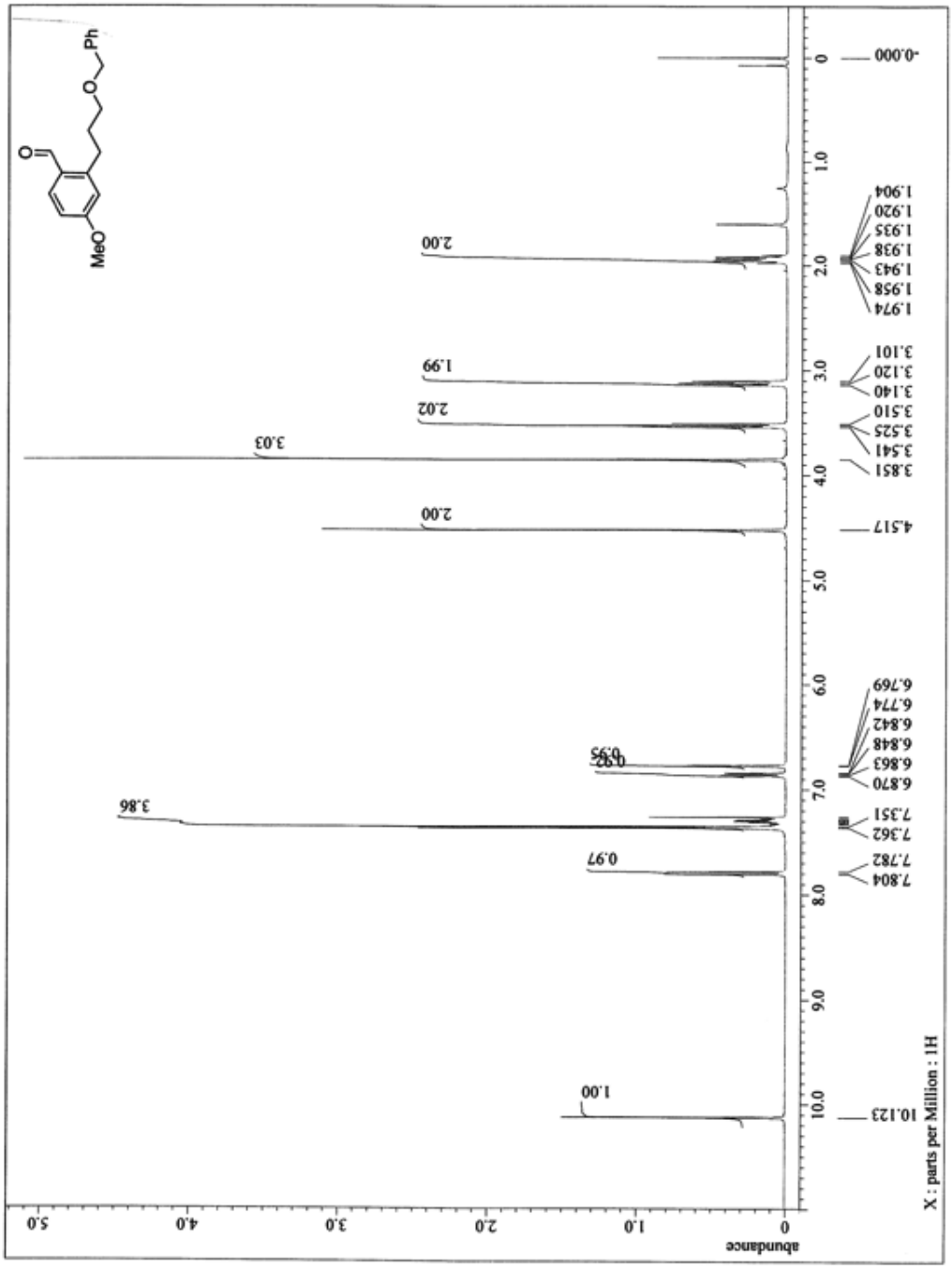
^{1}H NMR spectrum of **3e**.



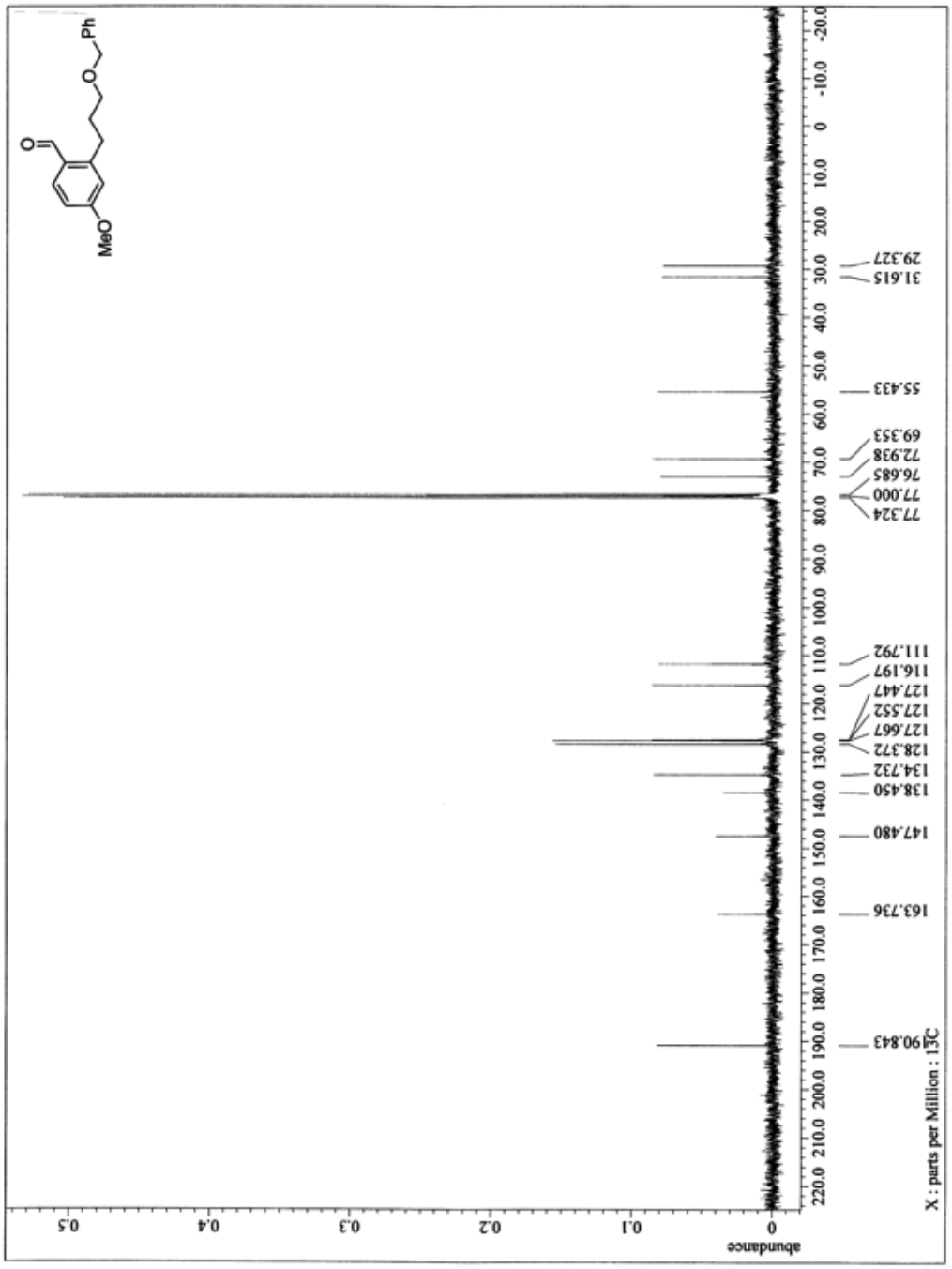
^{13}C NMR spectrum of **3e**.



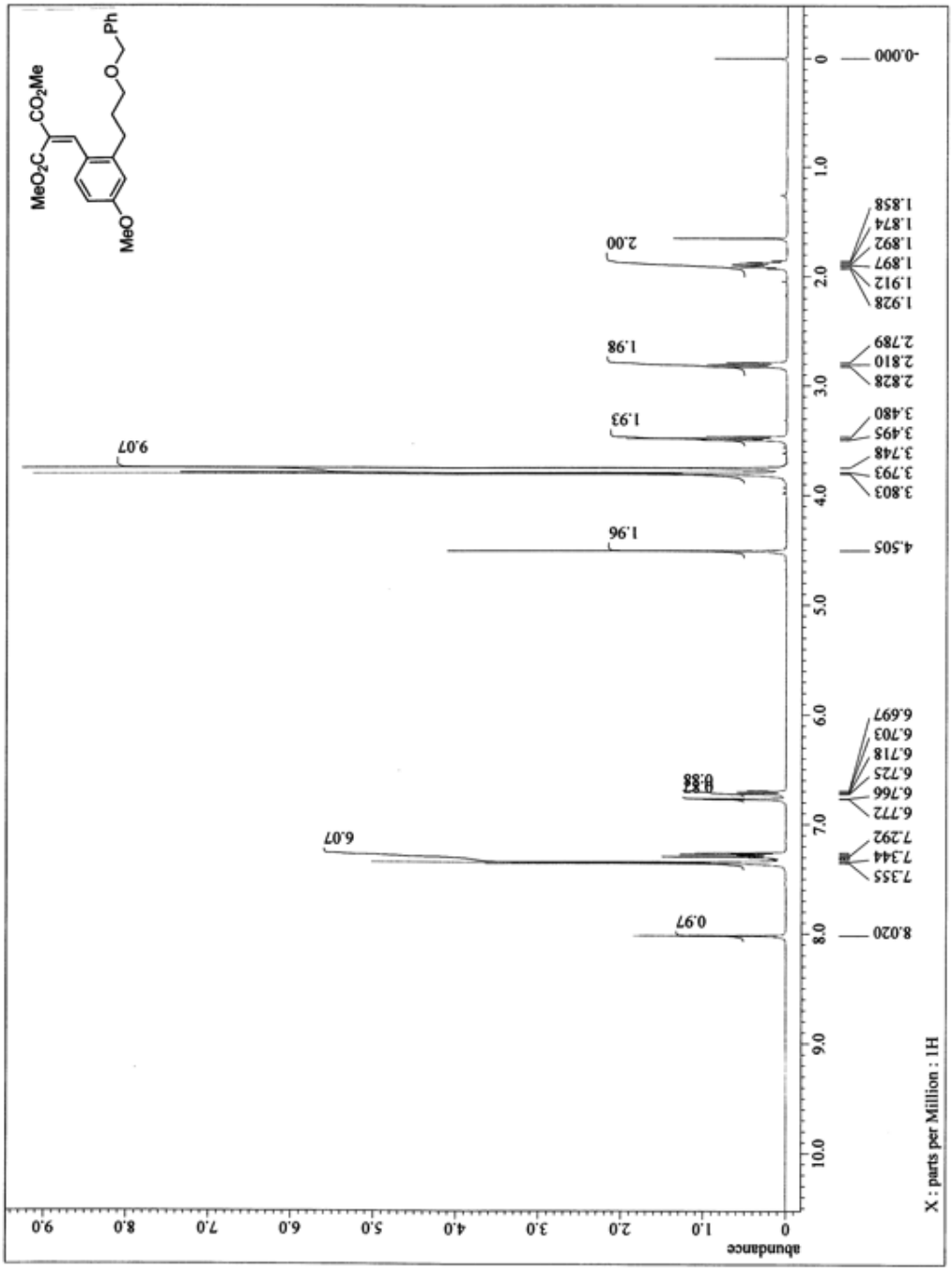
^{1}H NMR spectrum of **s10**.



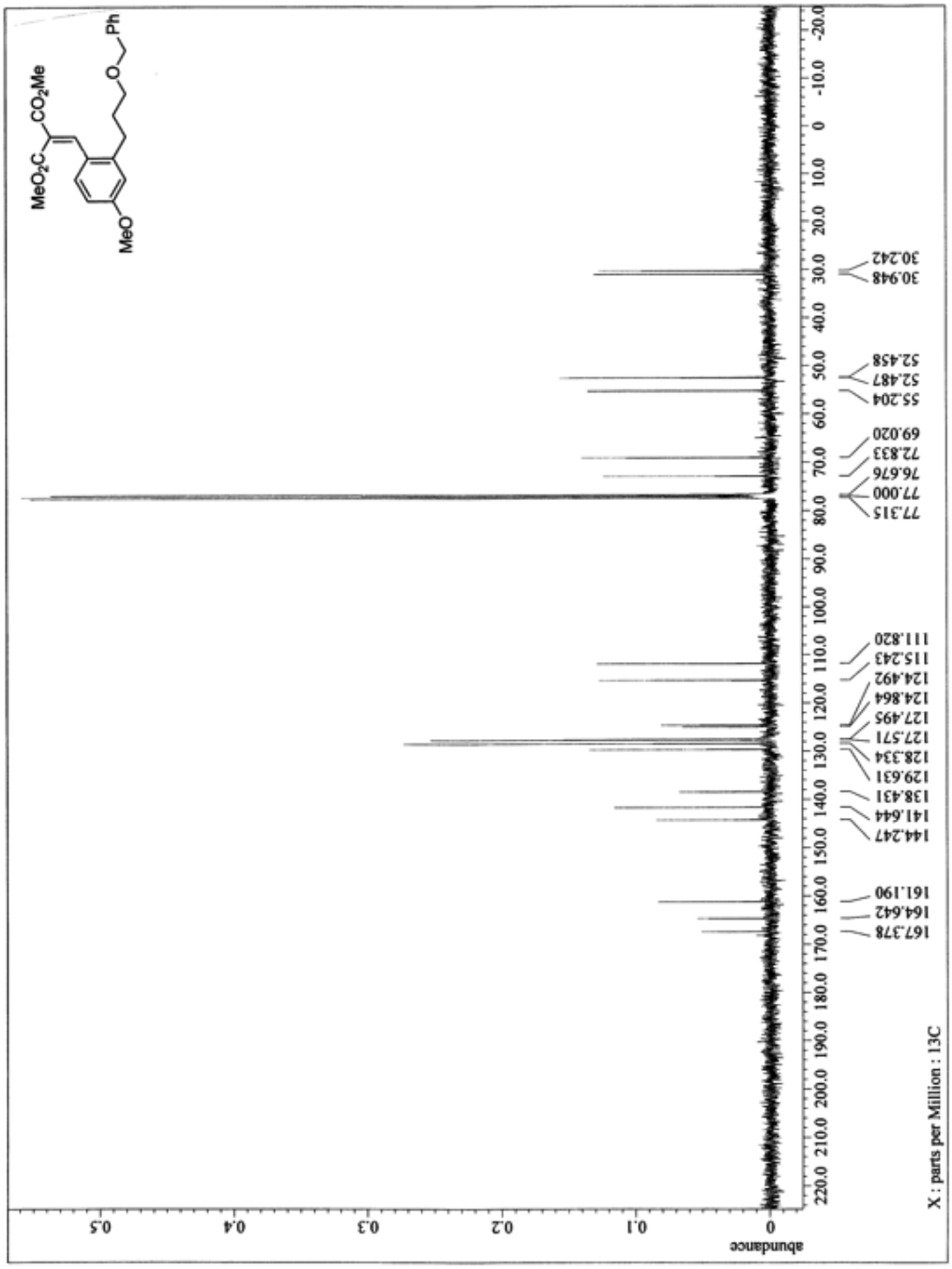
^{13}C NMR spectrum of **s10**.



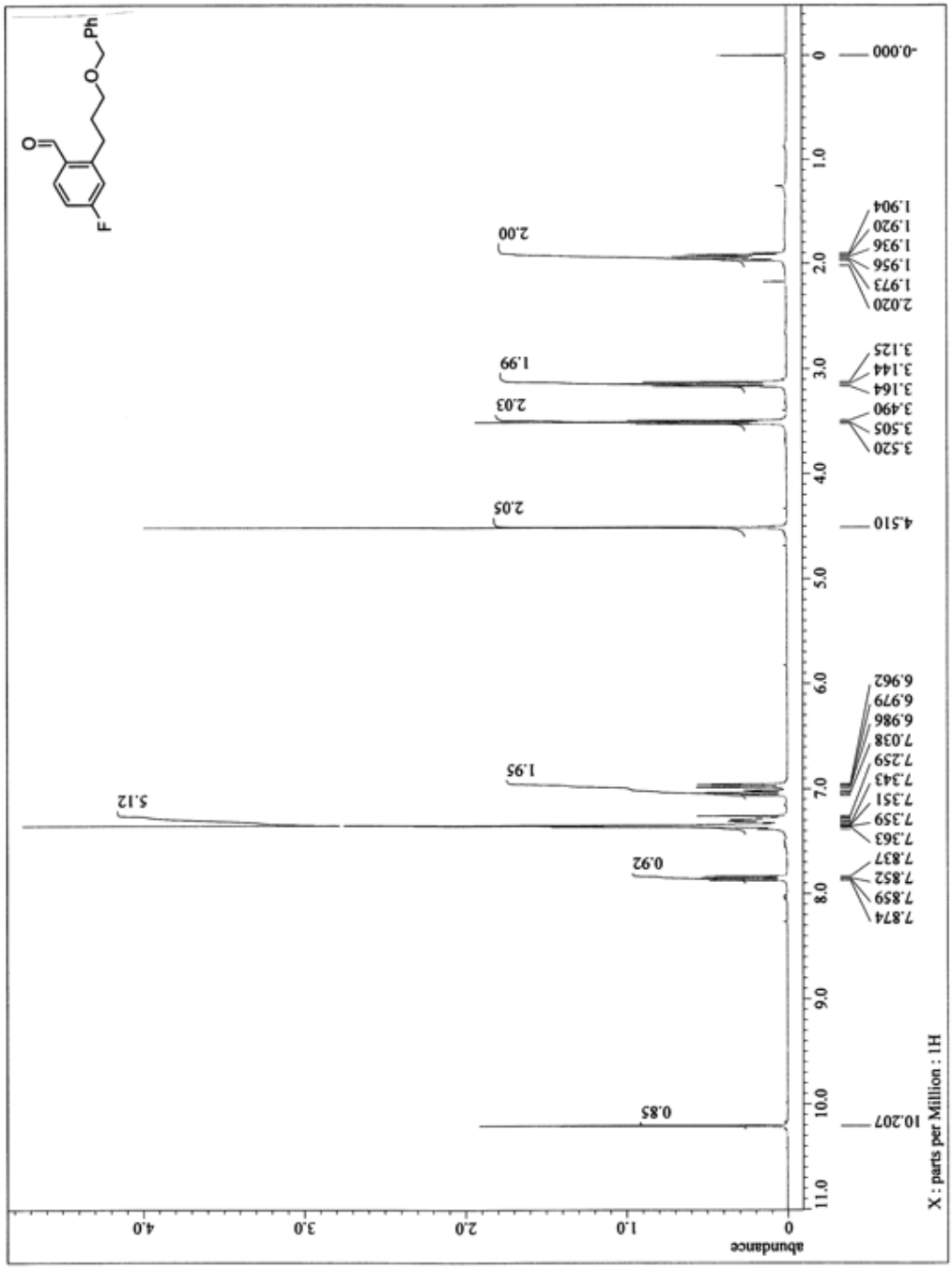
^{1}H NMR spectrum of **3f**.



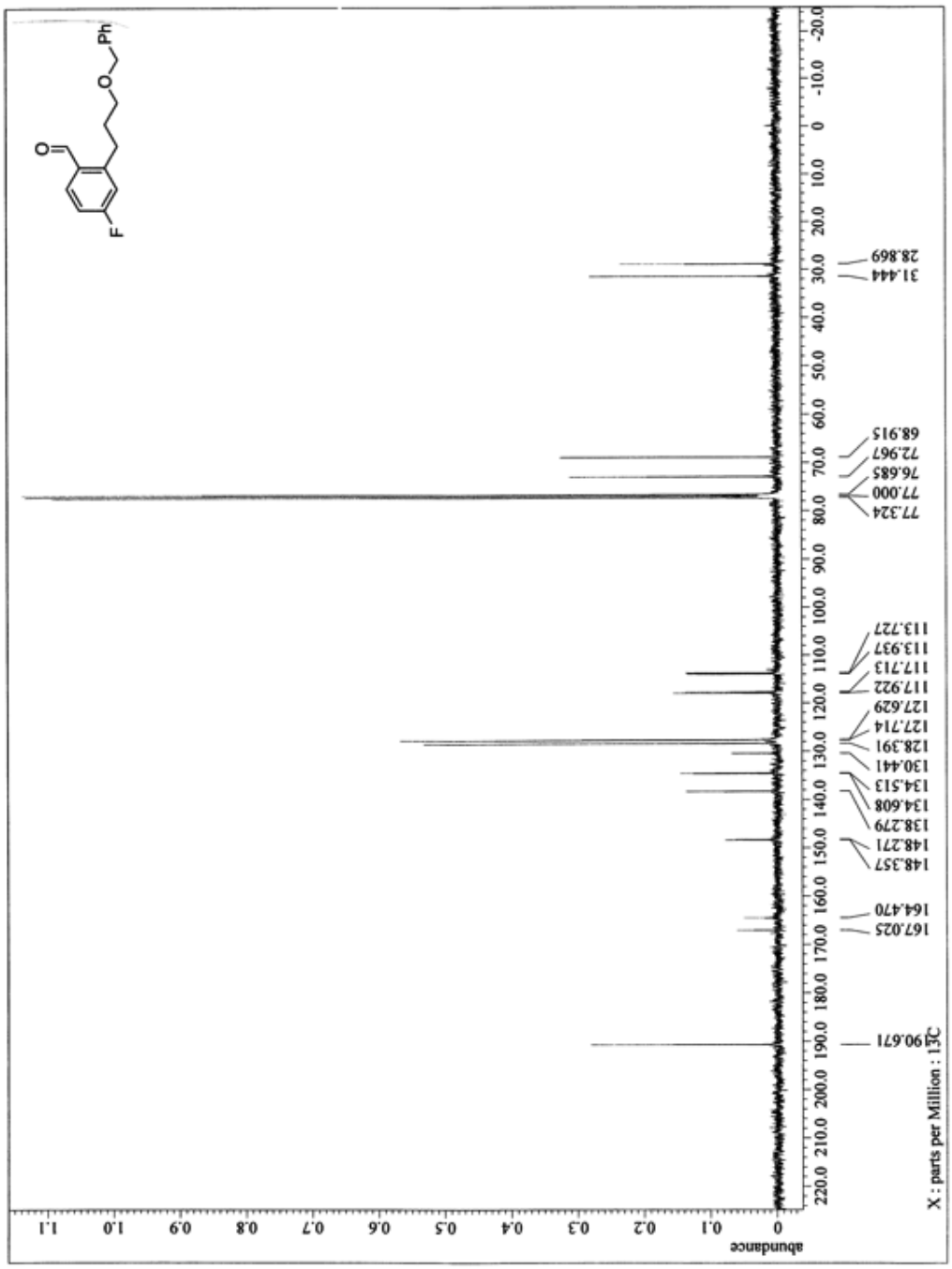
^{13}C NMR spectrum of **3f**.



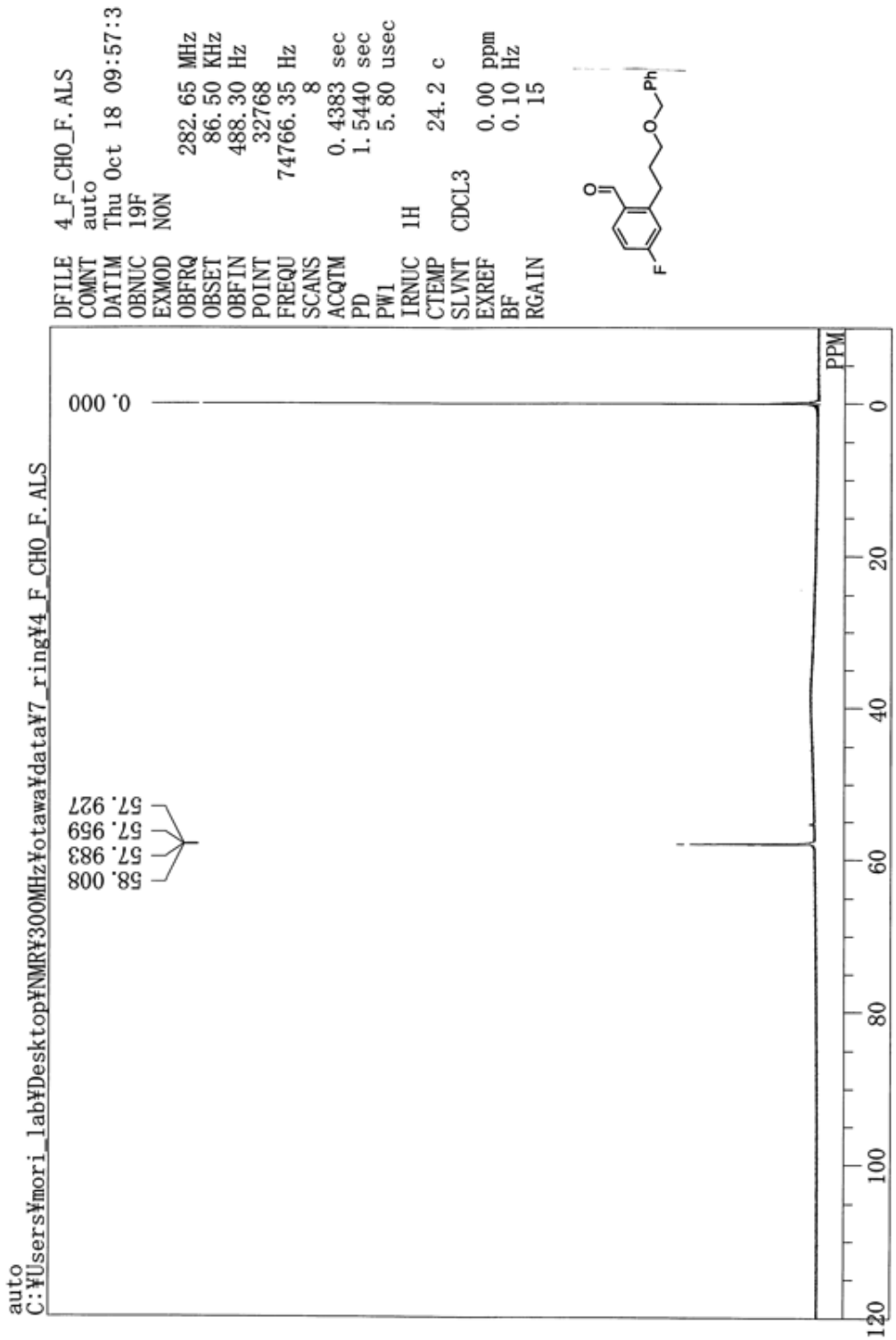
^{1}H NMR spectrum of **s11**.



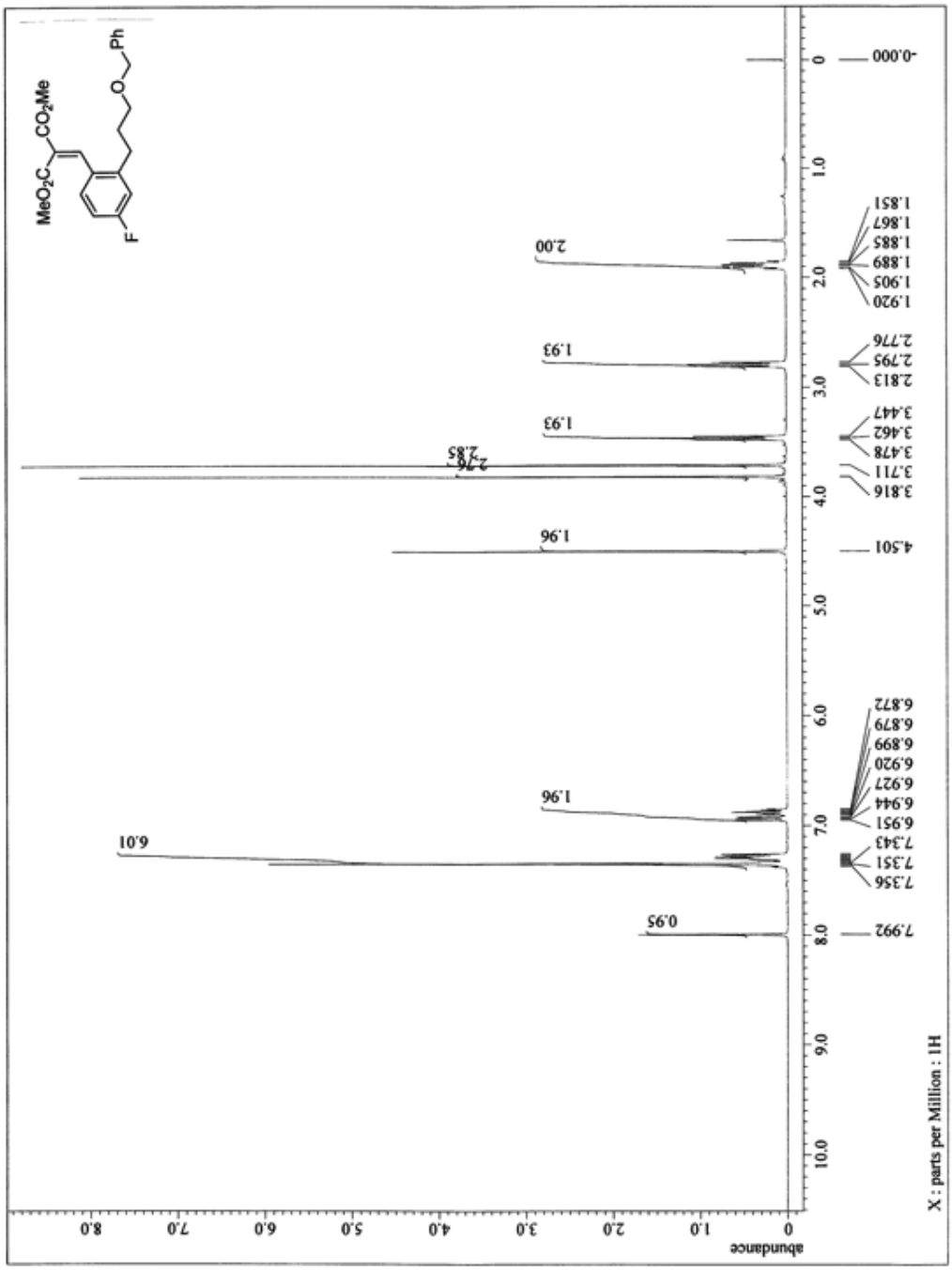
^{13}C NMR spectrum of **s11**.



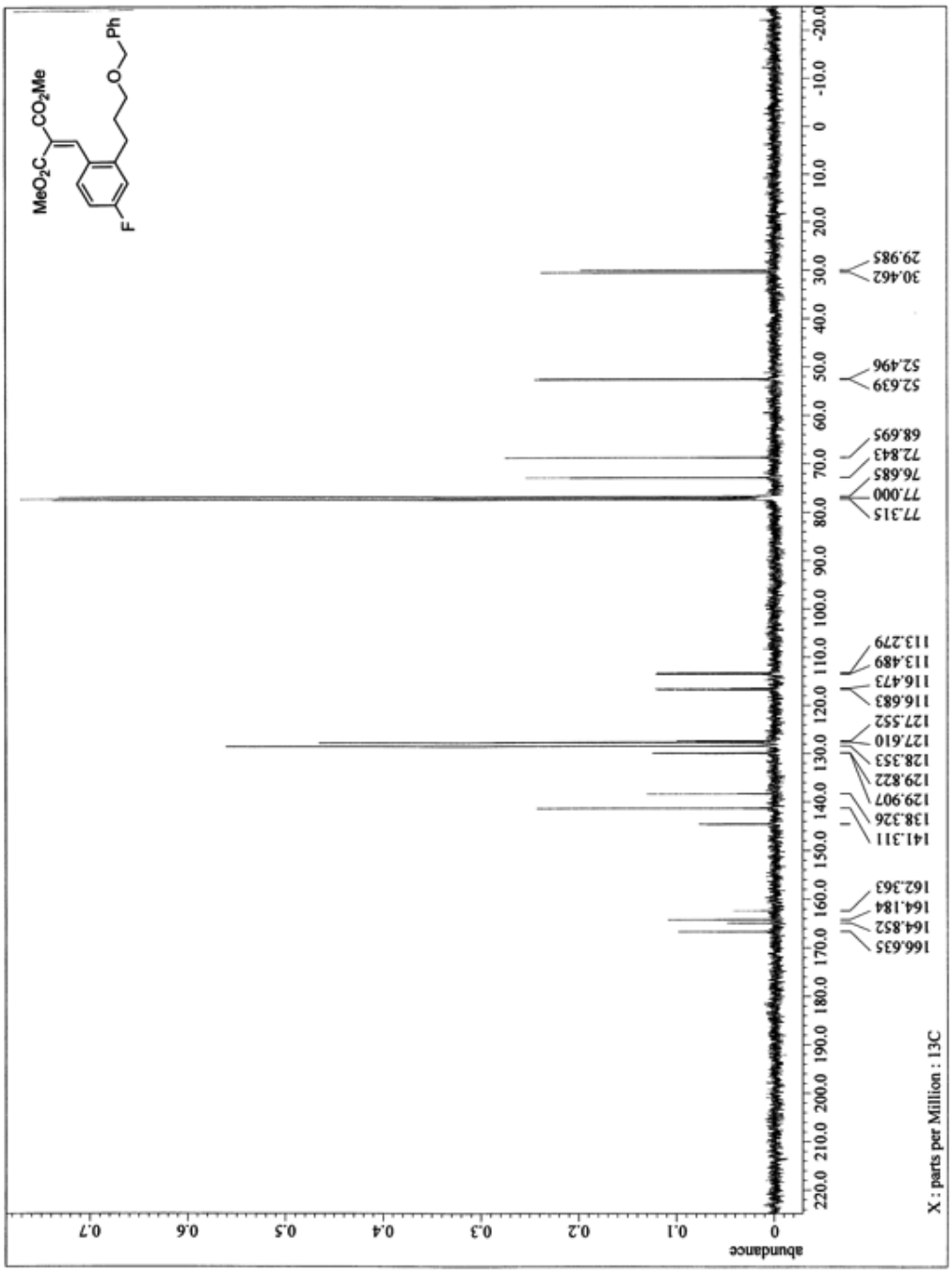
^{19}F NMR spectrum of **s11**.



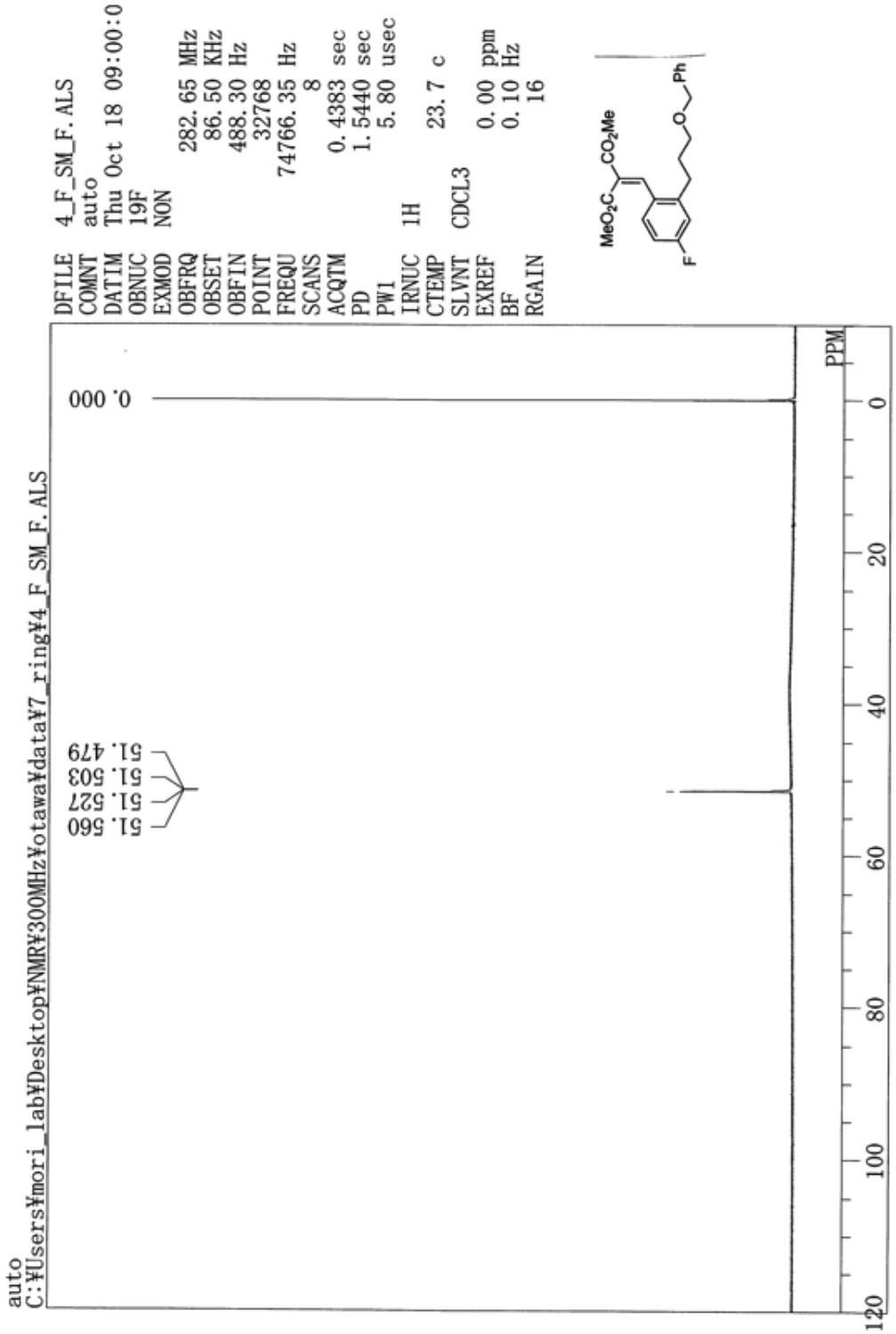
^{1}H NMR spectrum of **3g**.



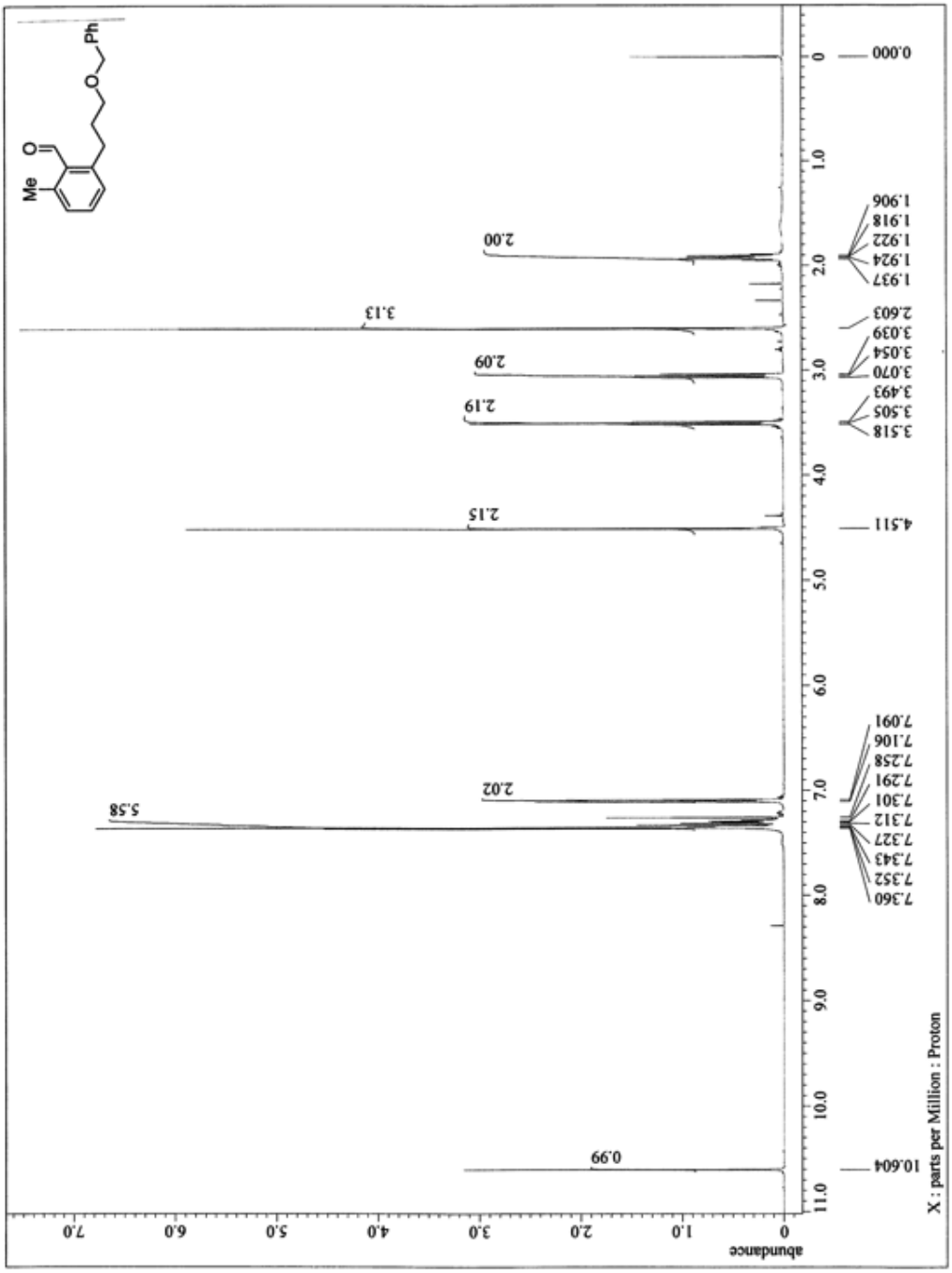
^{13}C NMR spectrum of **3g**.



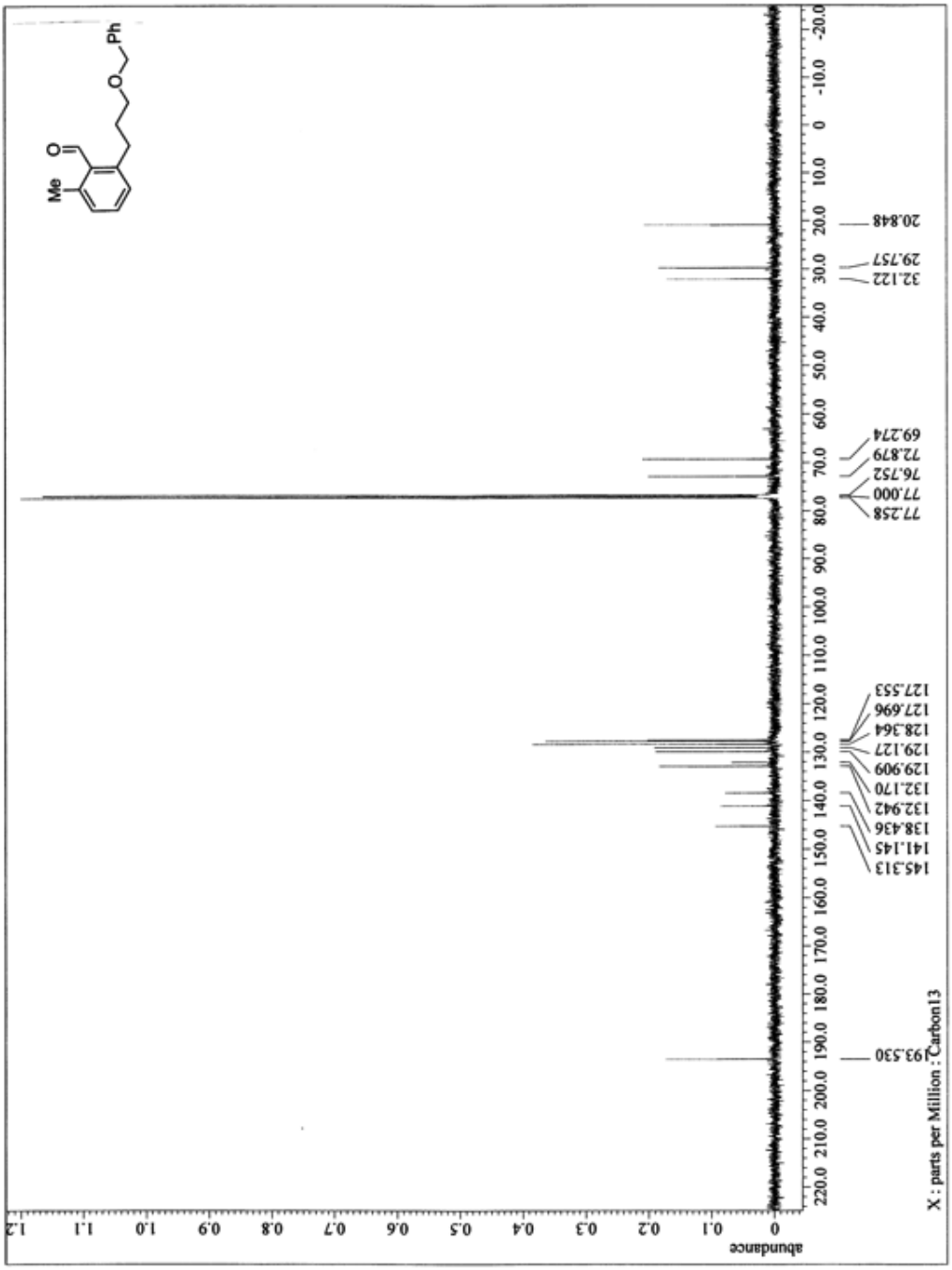
^{19}F NMR spectrum of **3g**.



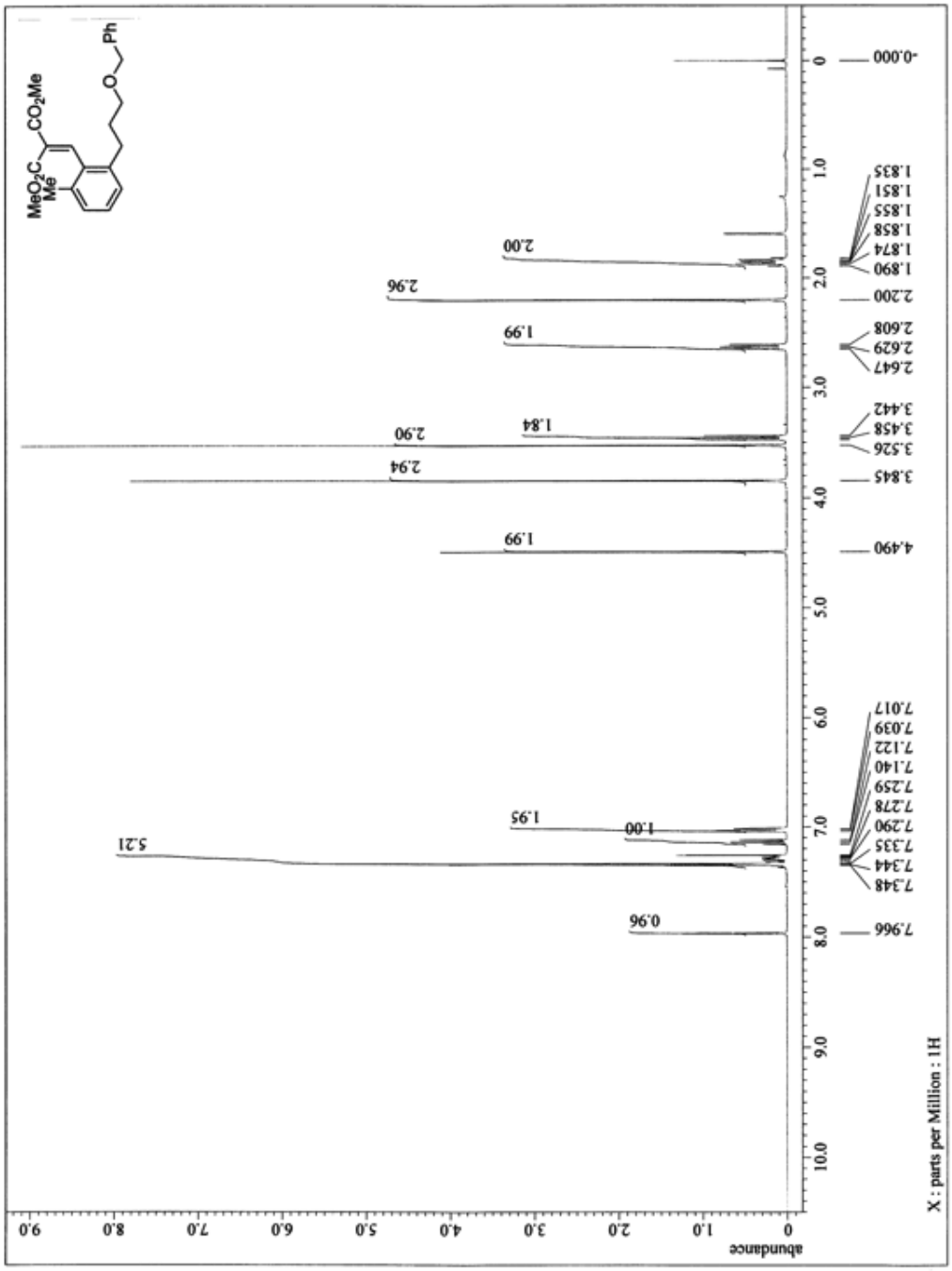
^{1}H NMR spectrum of **s12**.



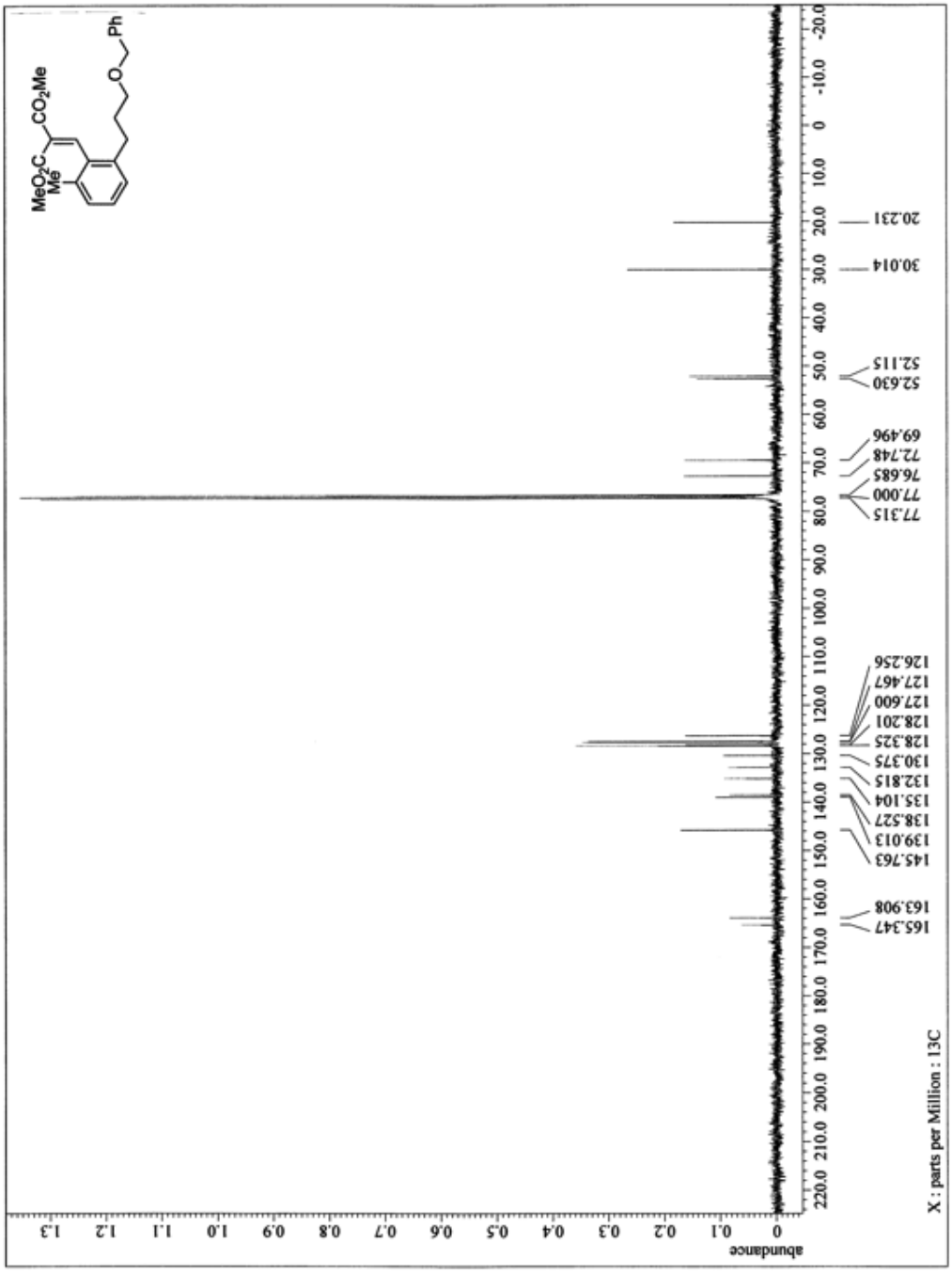
^{13}C NMR spectrum of **s12**.



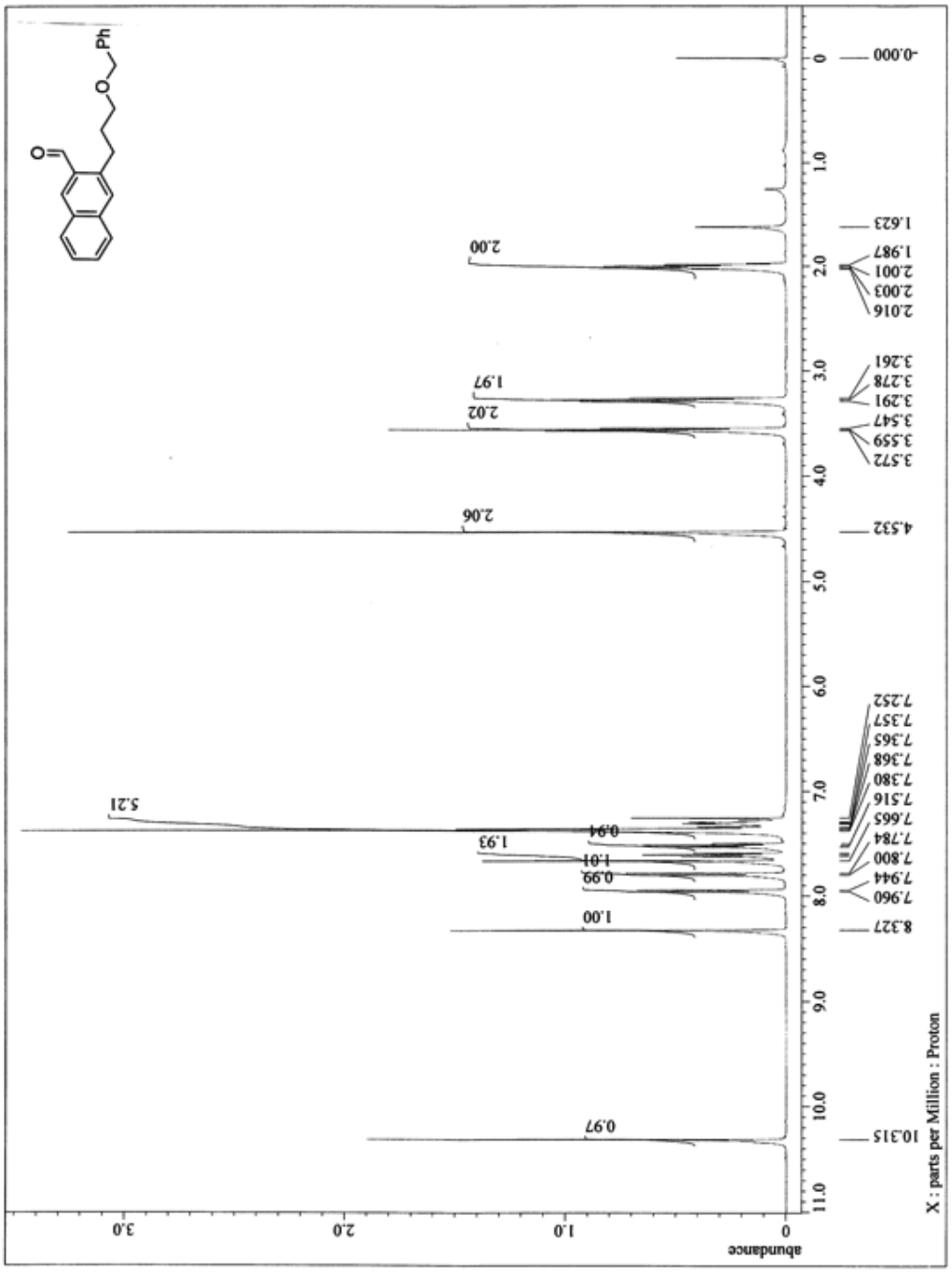
^{1}H NMR spectrum of **3h**.



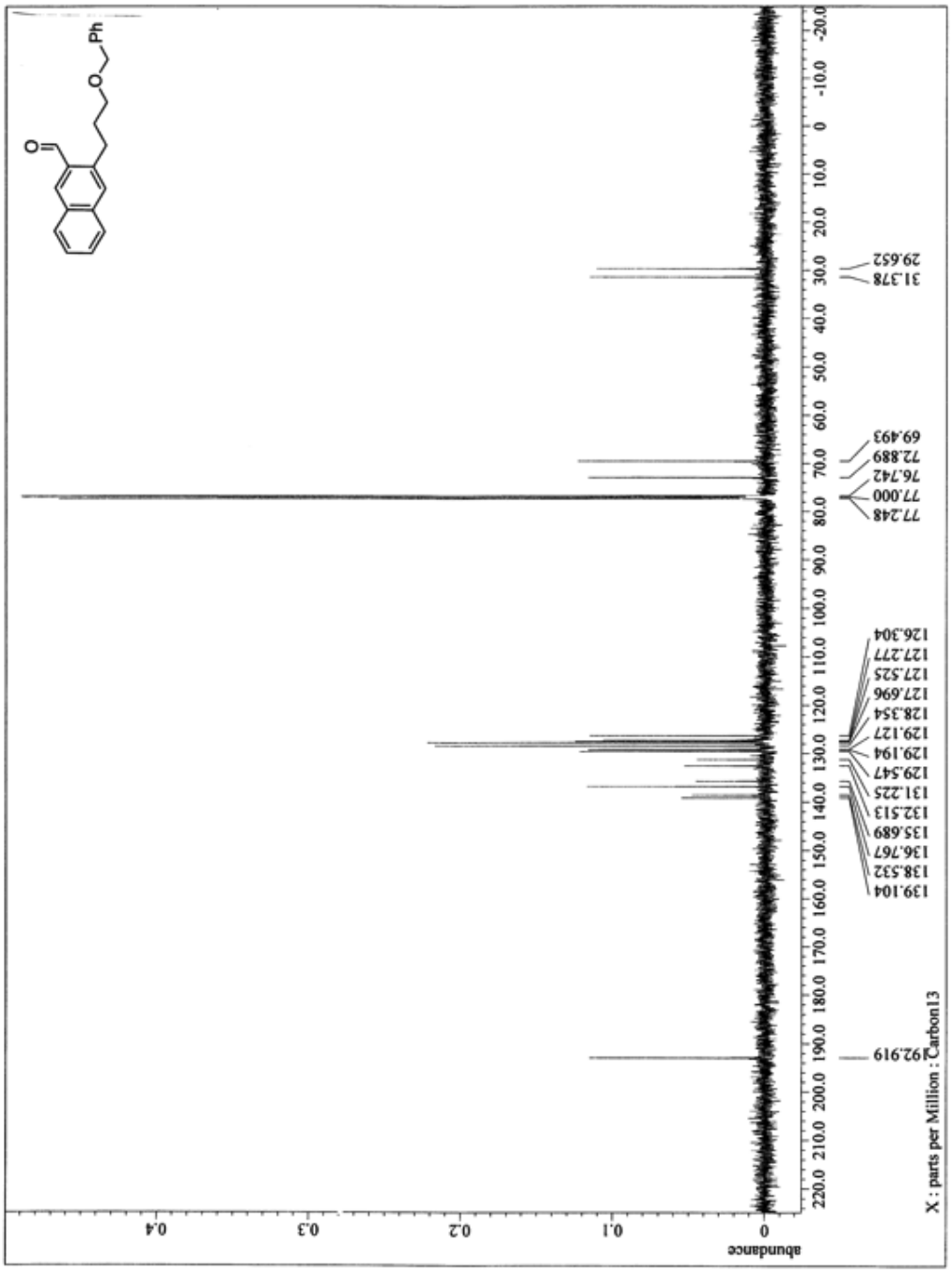
^{13}C NMR spectrum of **3h**.



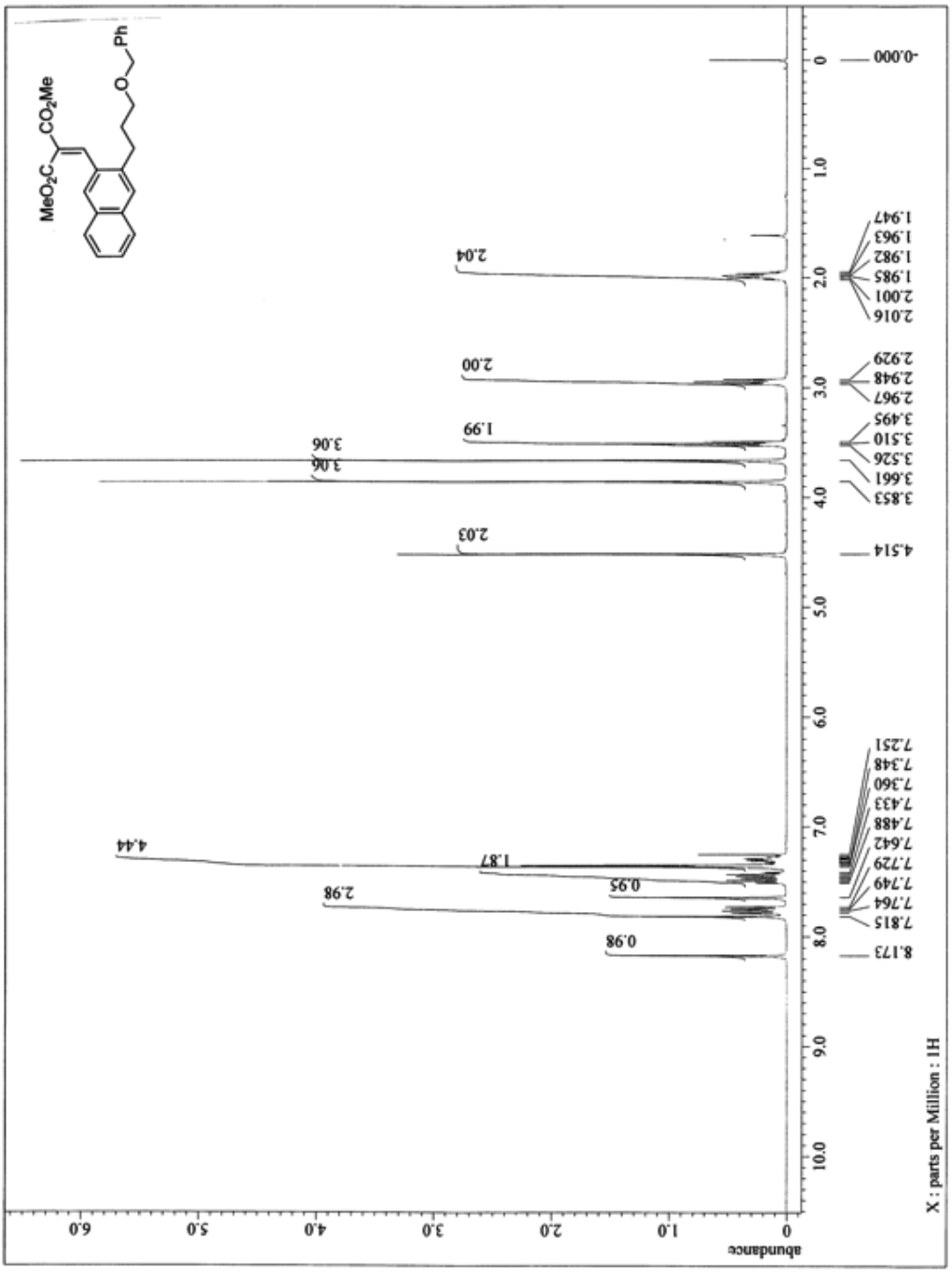
^{1}H NMR spectrum of **s13**.



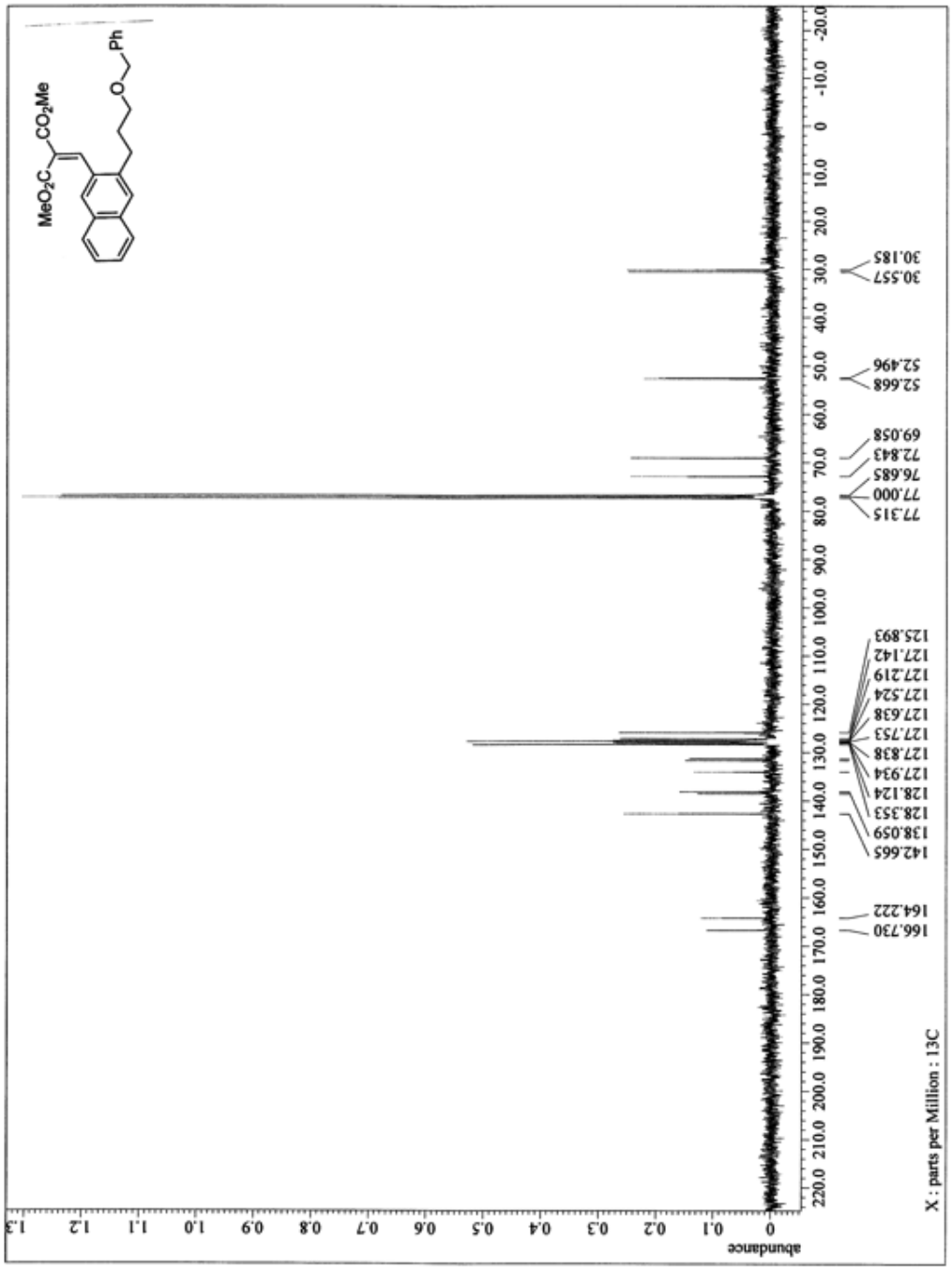
^{13}C NMR spectrum of **s13**.



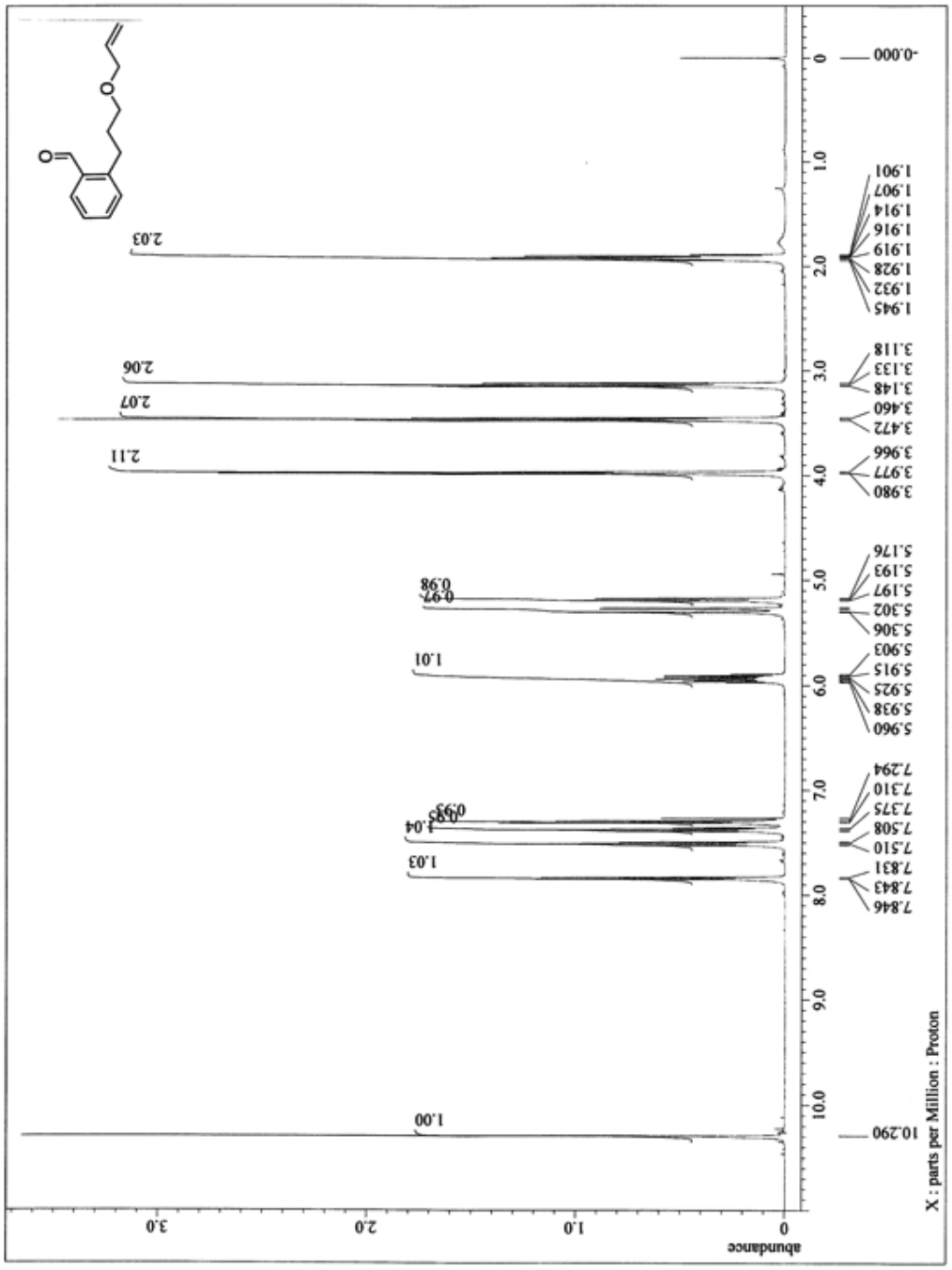
^{1}H NMR spectrum of **3i**.



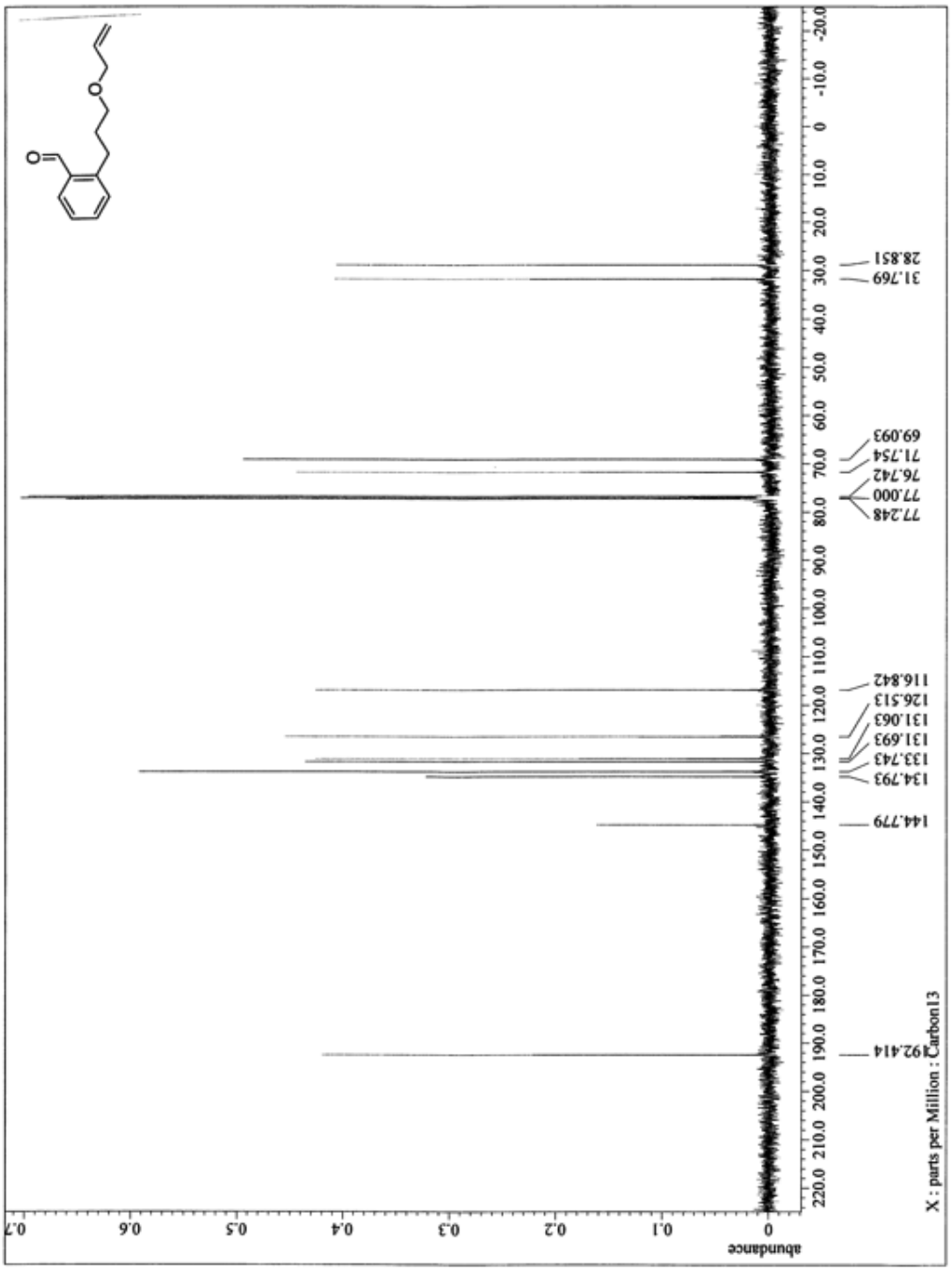
^{13}C NMR spectrum of **3i**.



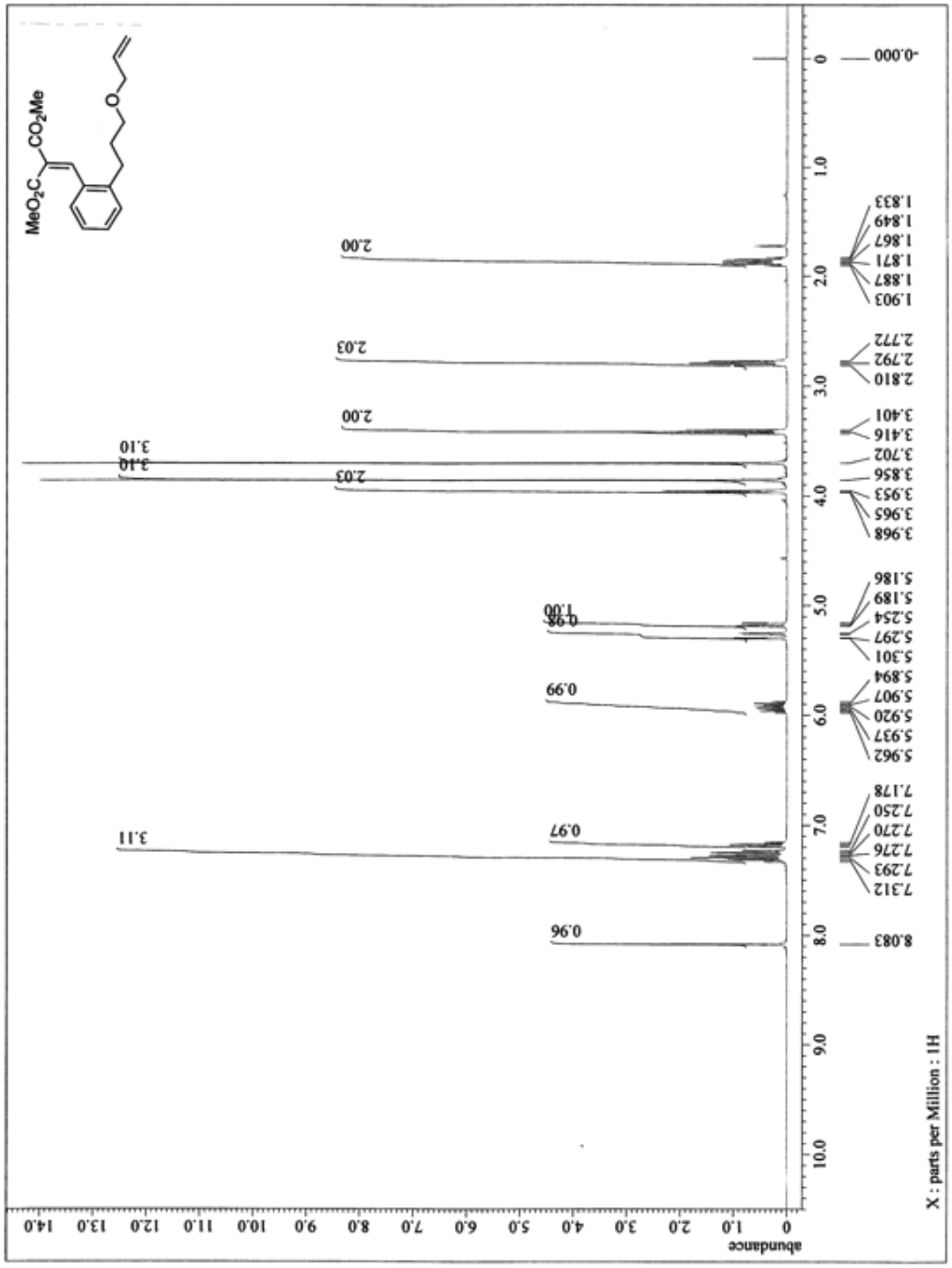
^{1}H NMR spectrum of **s14**.



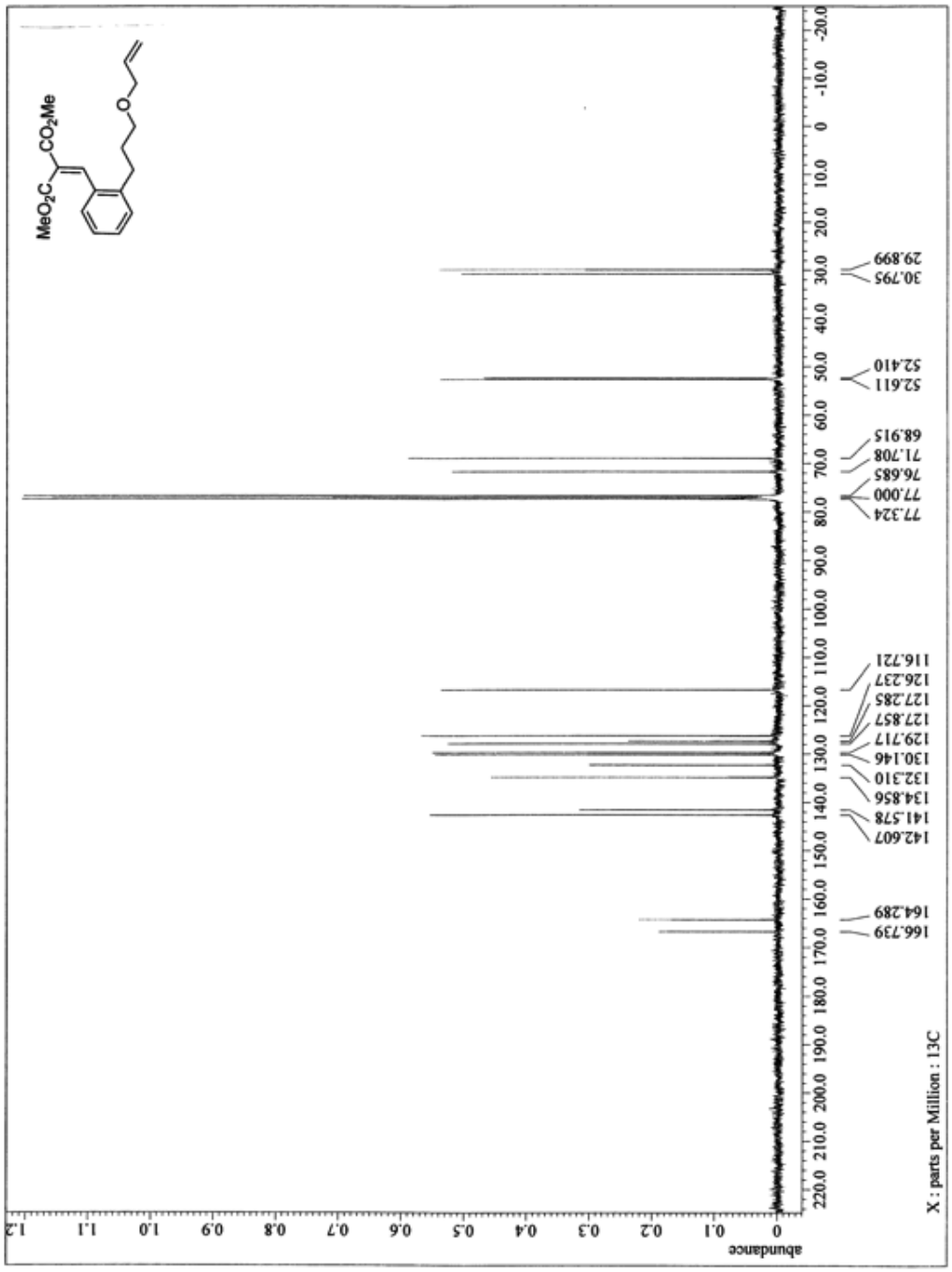
^{13}C NMR spectrum of **s1**.



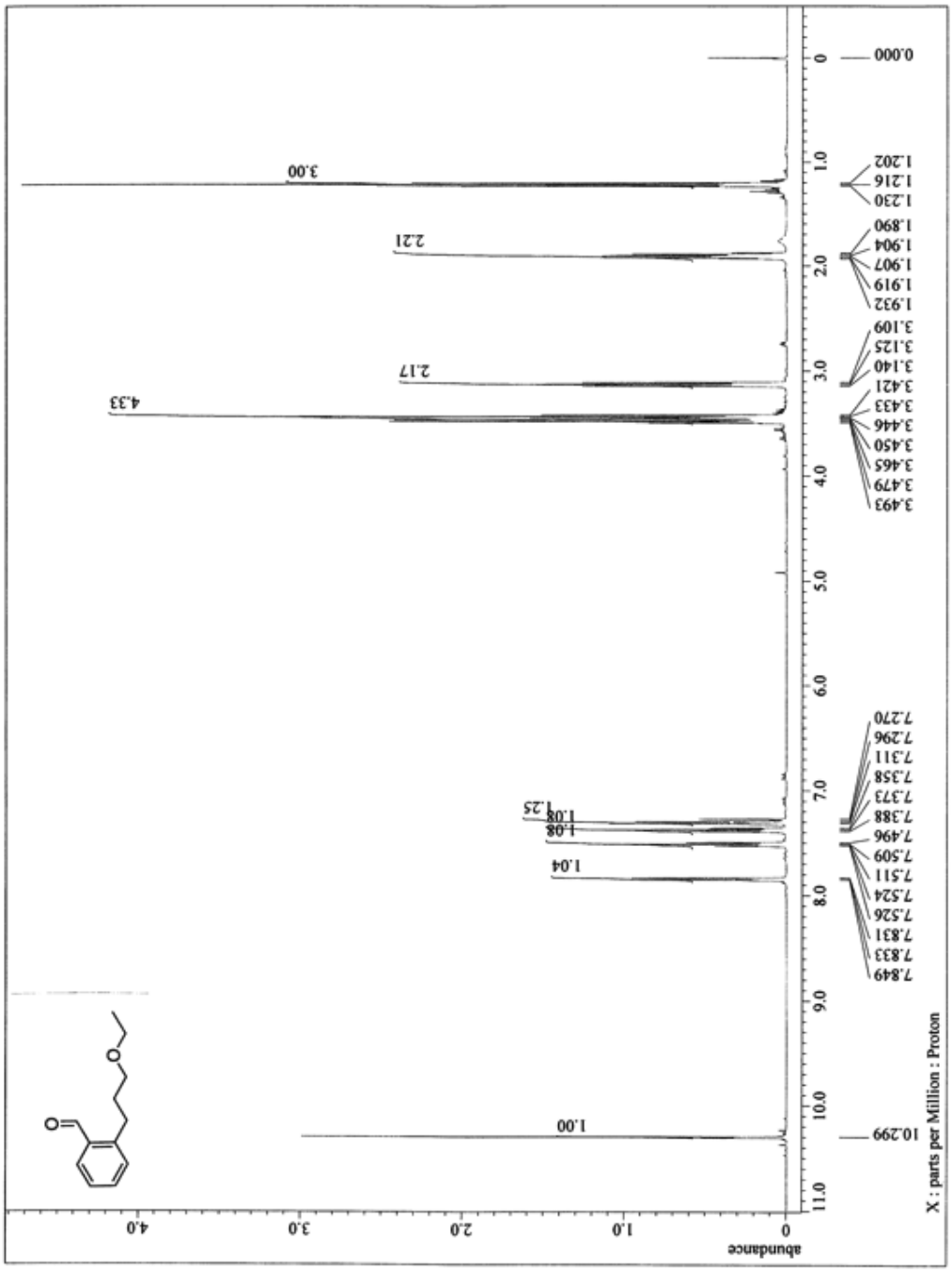
^{1}H NMR spectrum of **3j**.



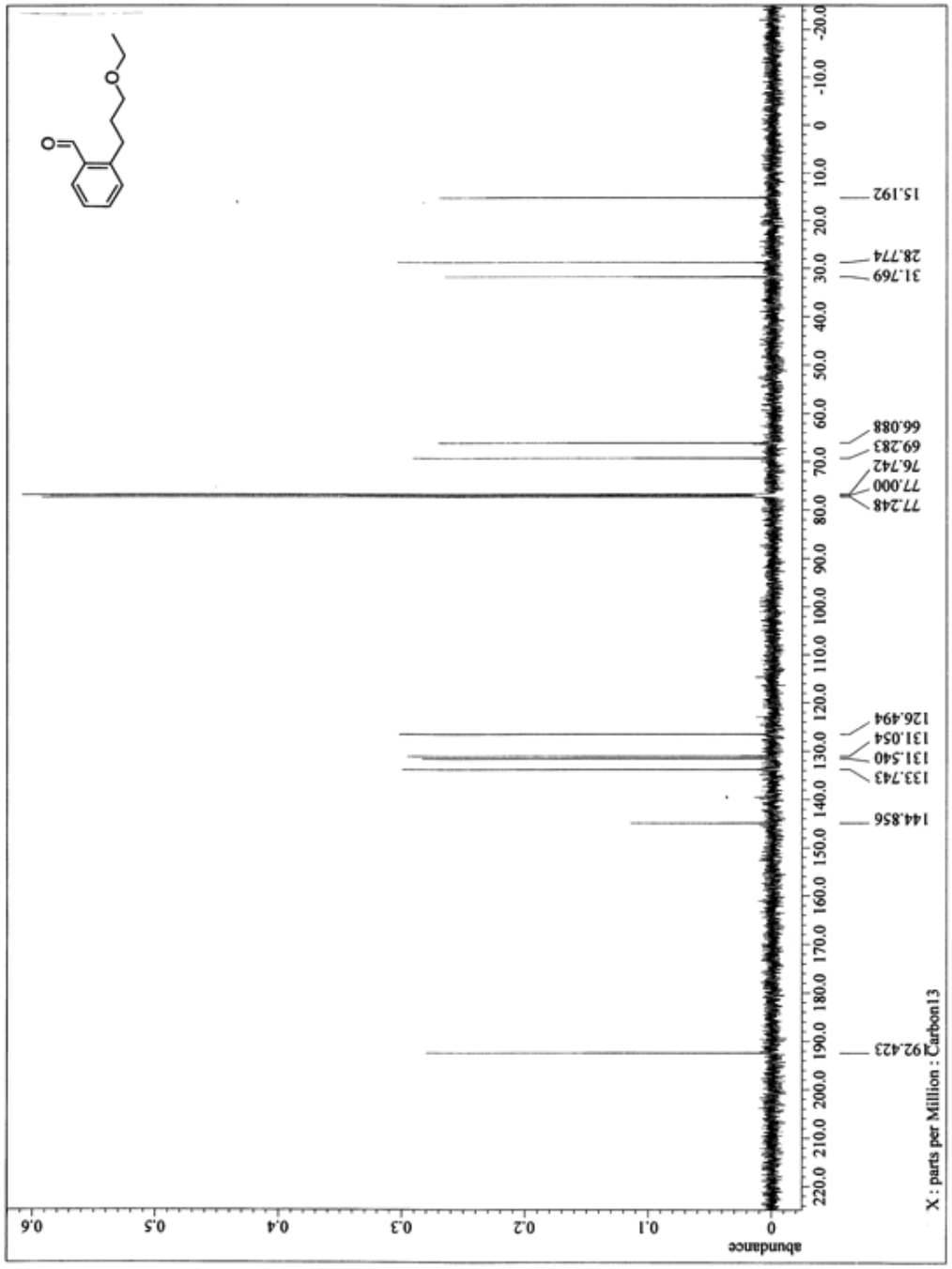
^{13}C NMR spectrum of **3j**.



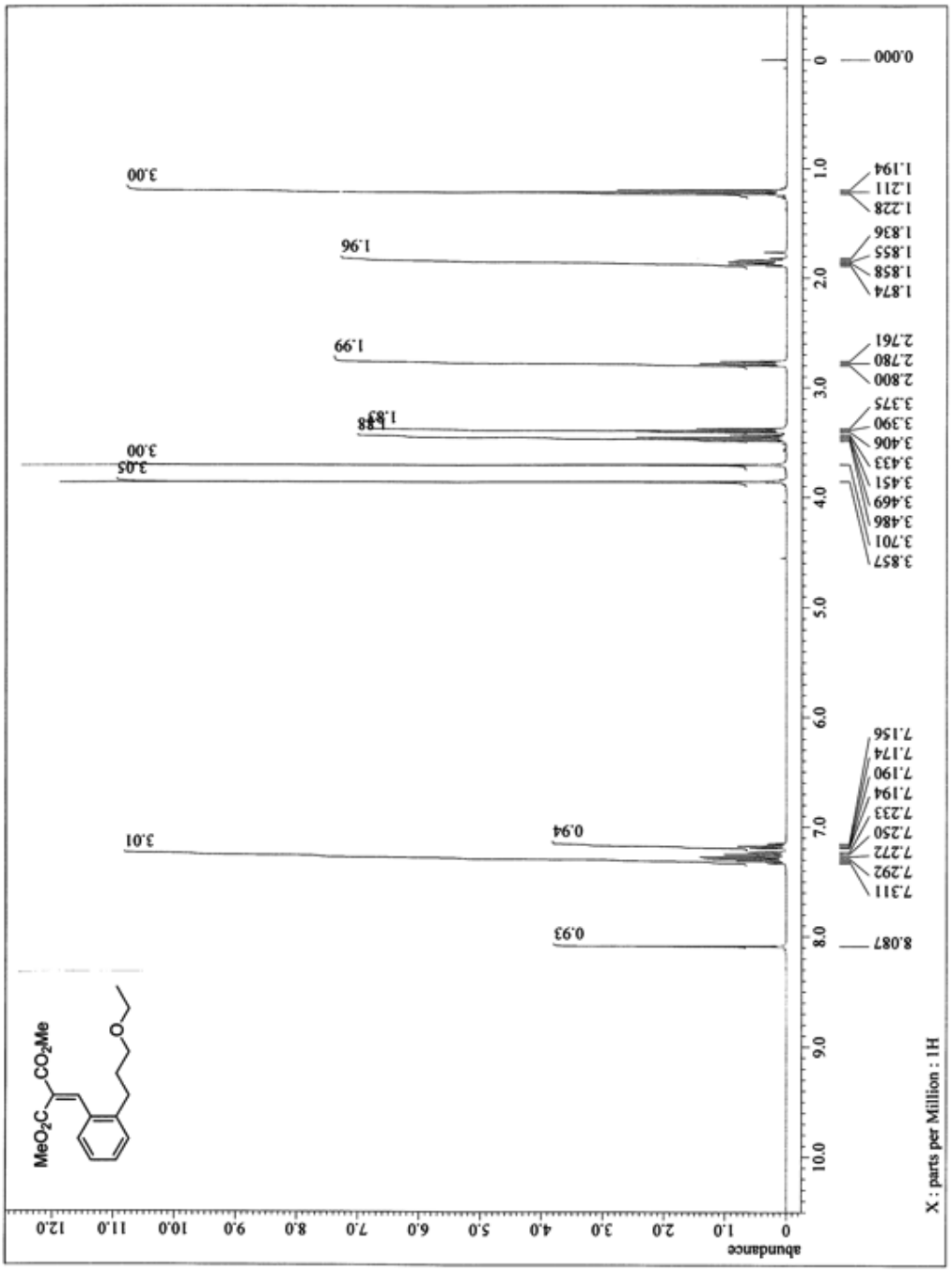
^{1}H NMR spectrum of **s15**.



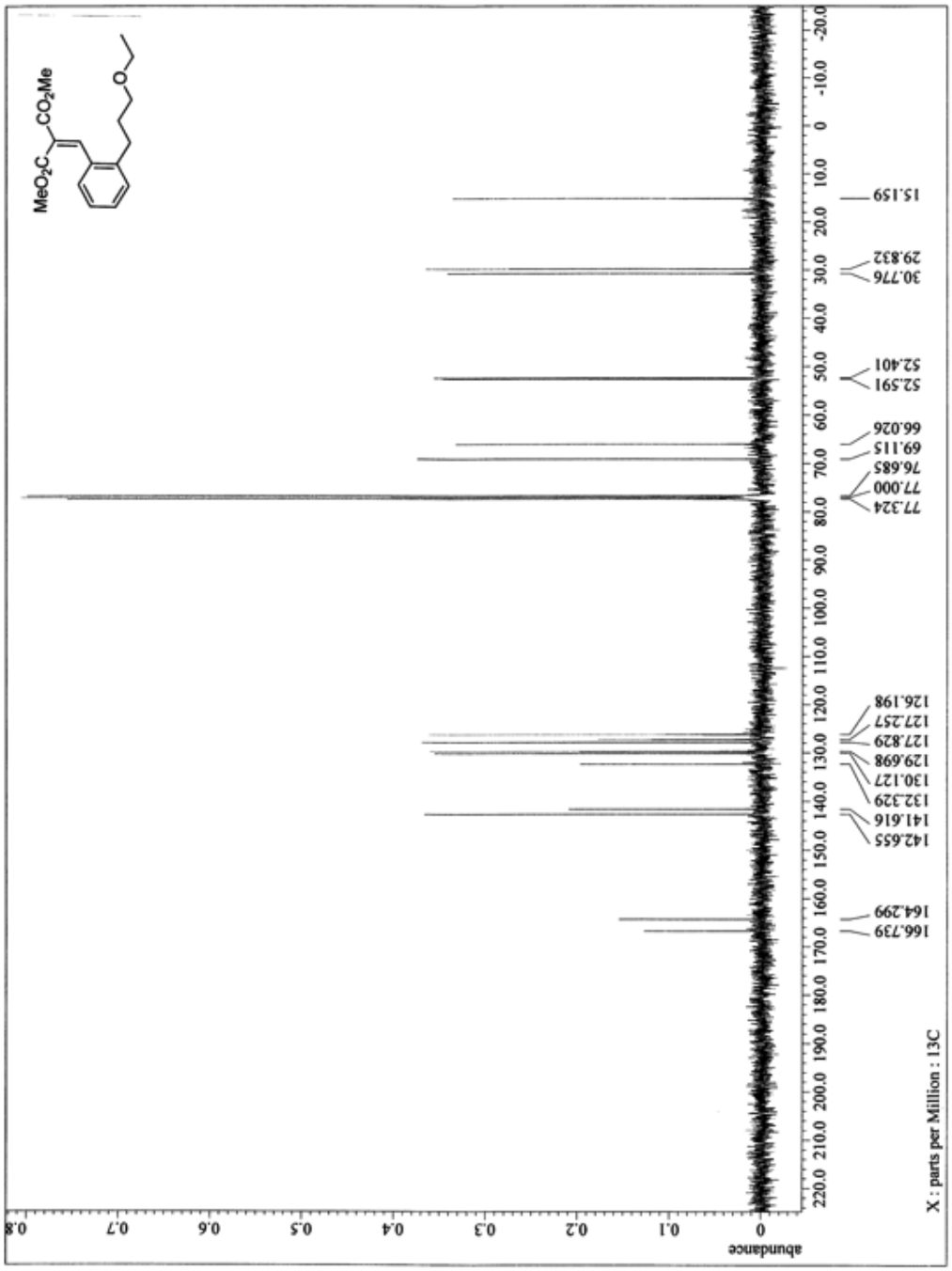
^{13}C NMR spectrum of **s15**.



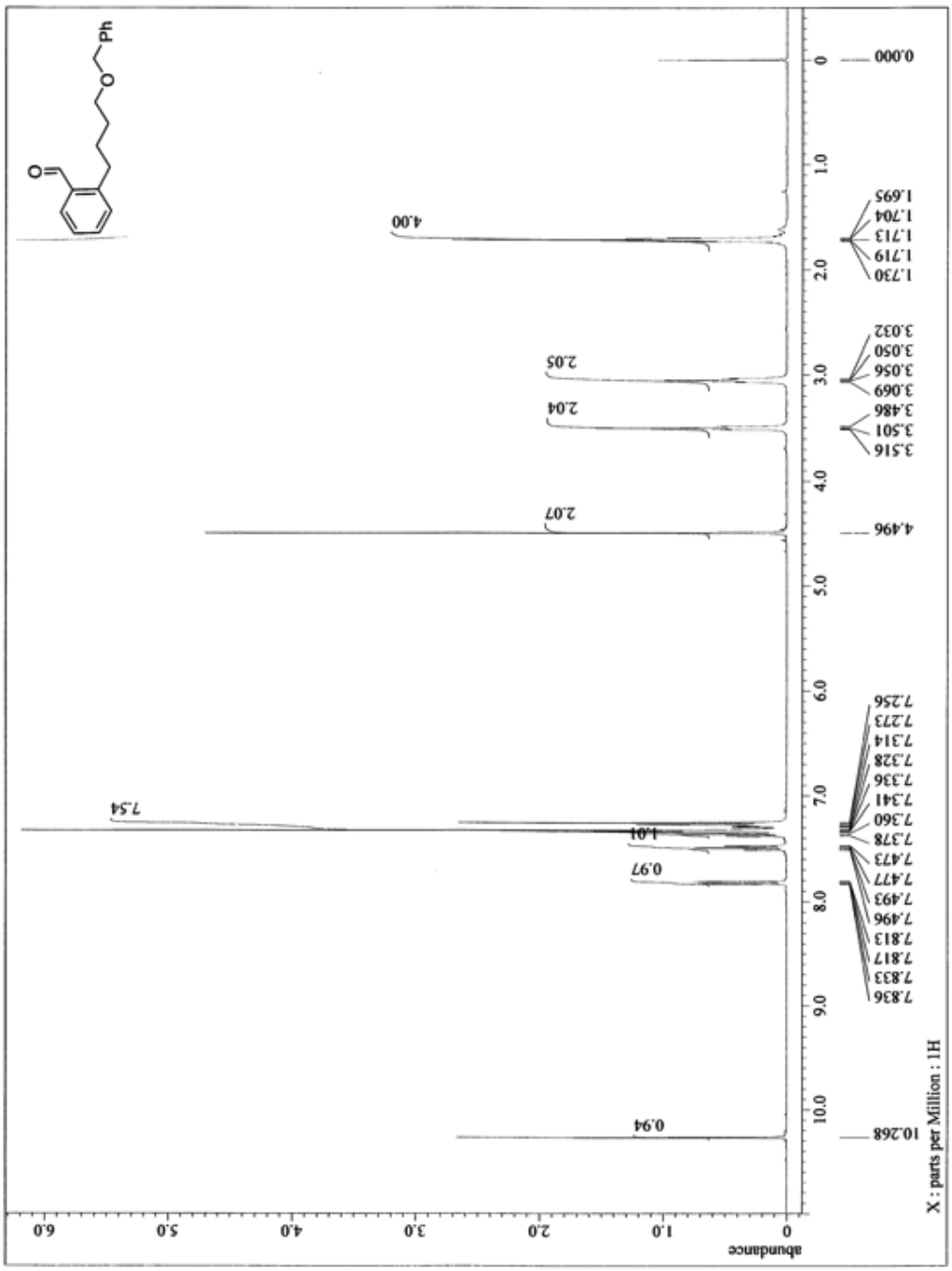
^{1}H NMR spectrum of **3k**.



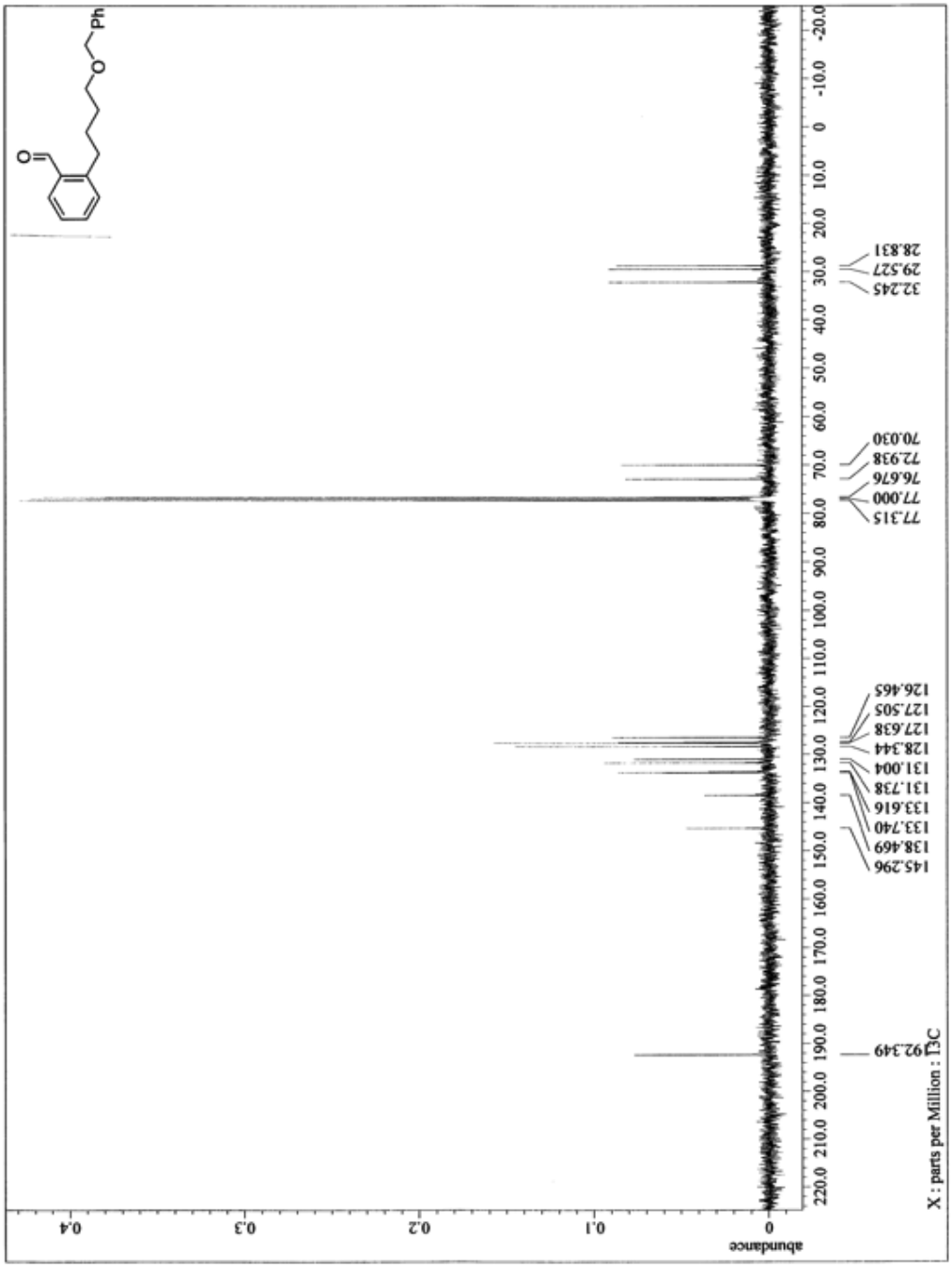
^{13}C NMR spectrum of **3k**.



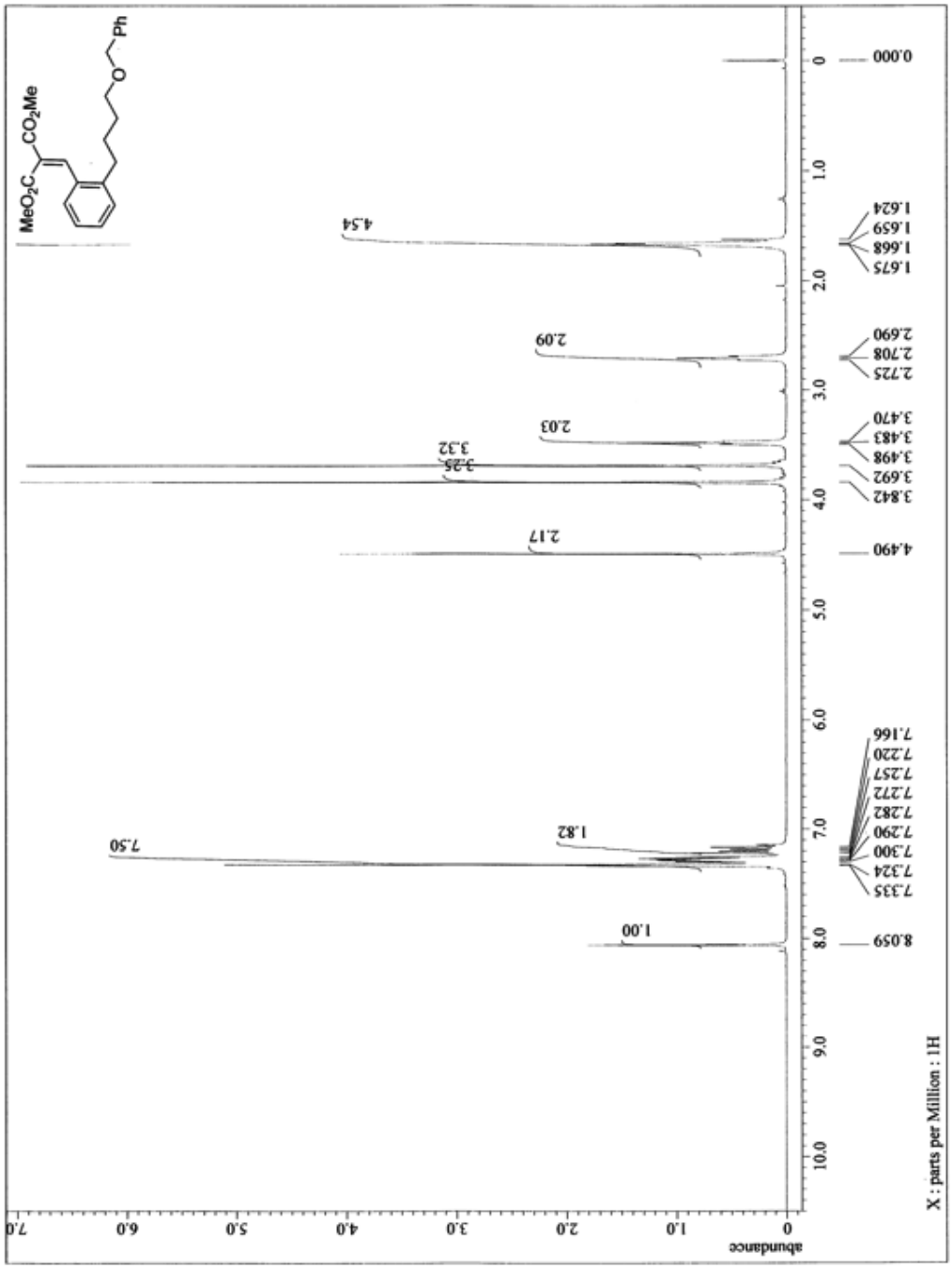
^{1}H NMR spectrum of **s20**.



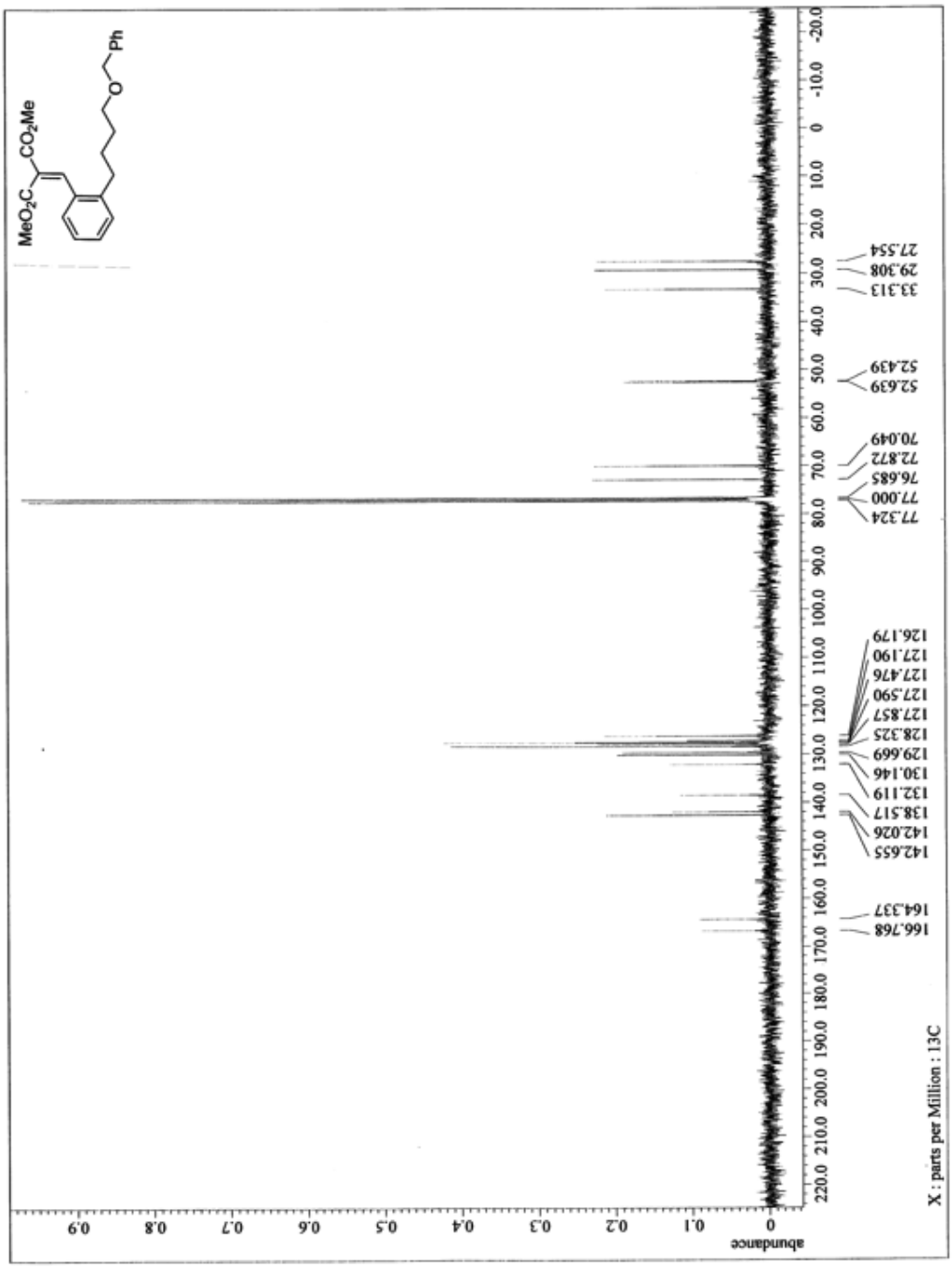
^{13}C NMR spectrum of **s20**.



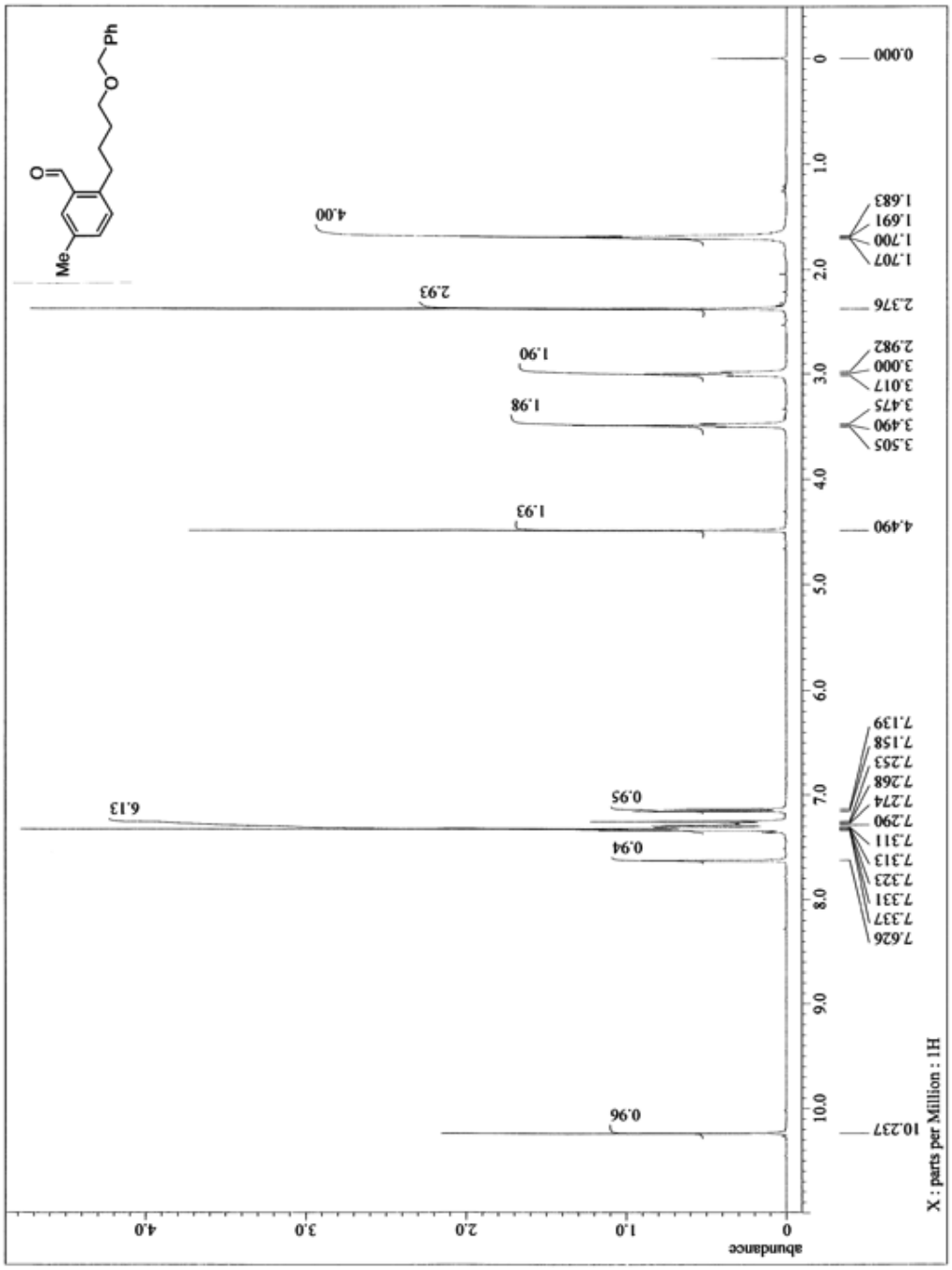
^{1}H NMR spectrum of **5a**.



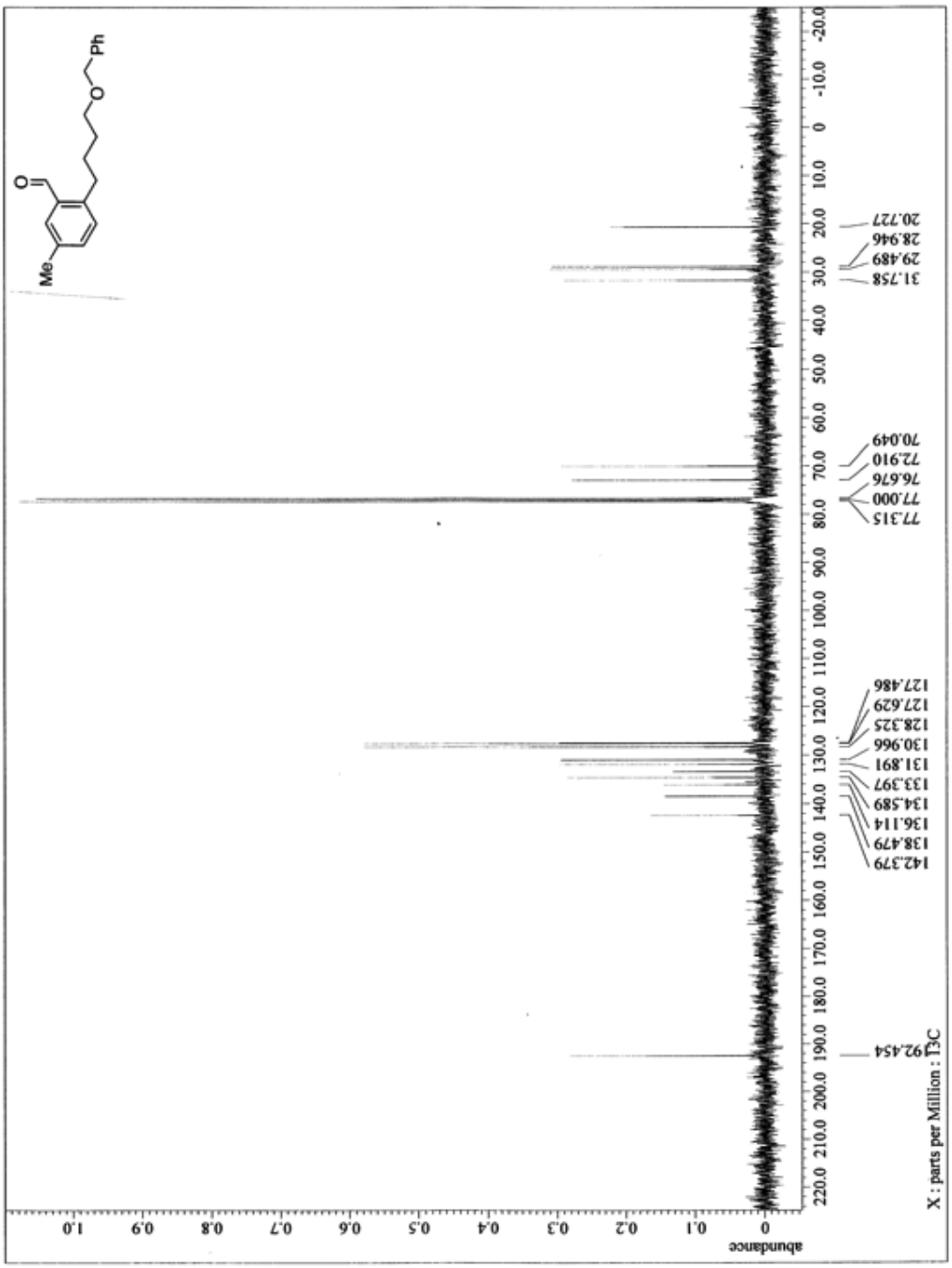
^{13}C NMR spectrum of **5a**.



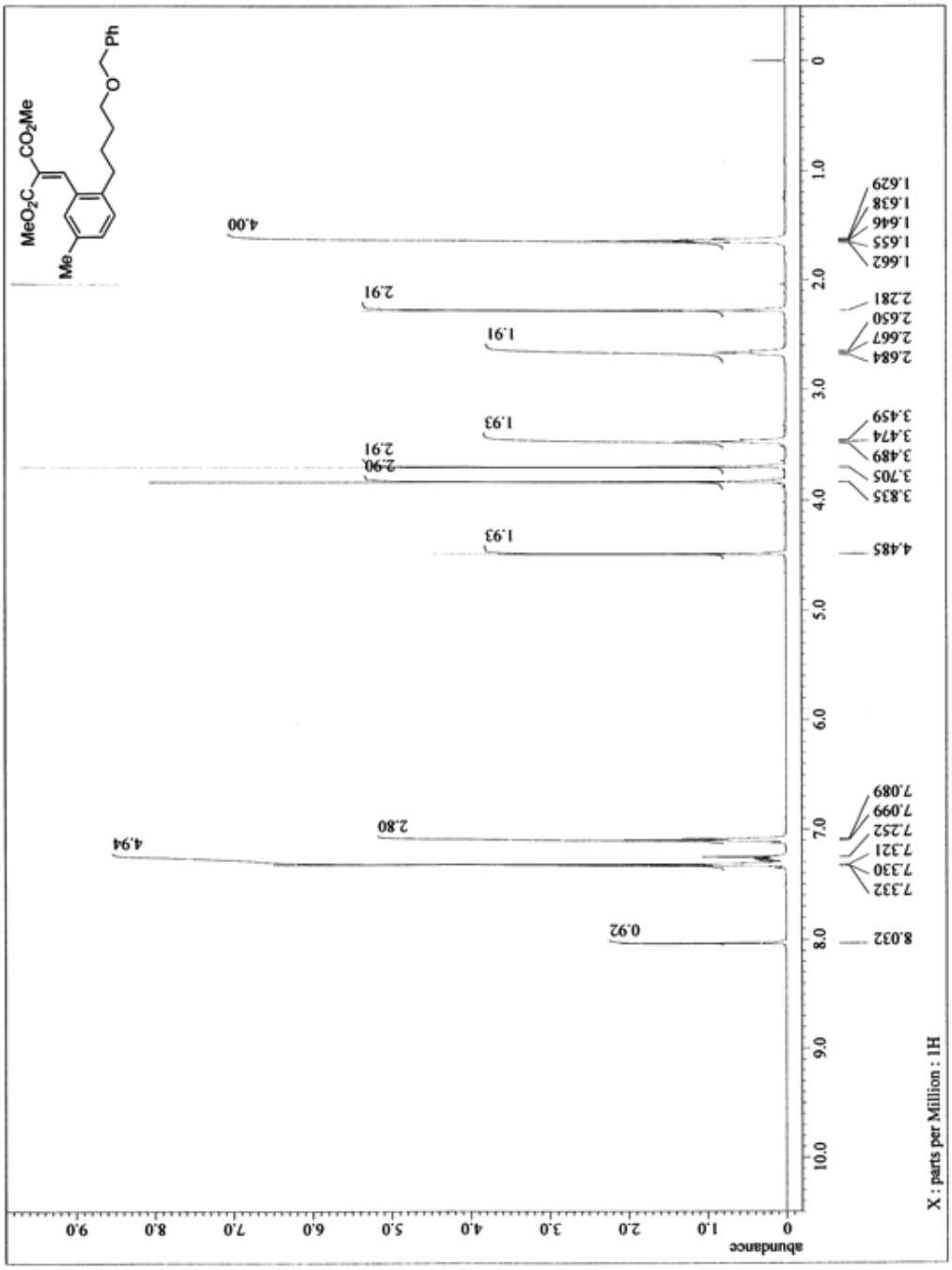
^{1}H NMR spectrum of **s21**.



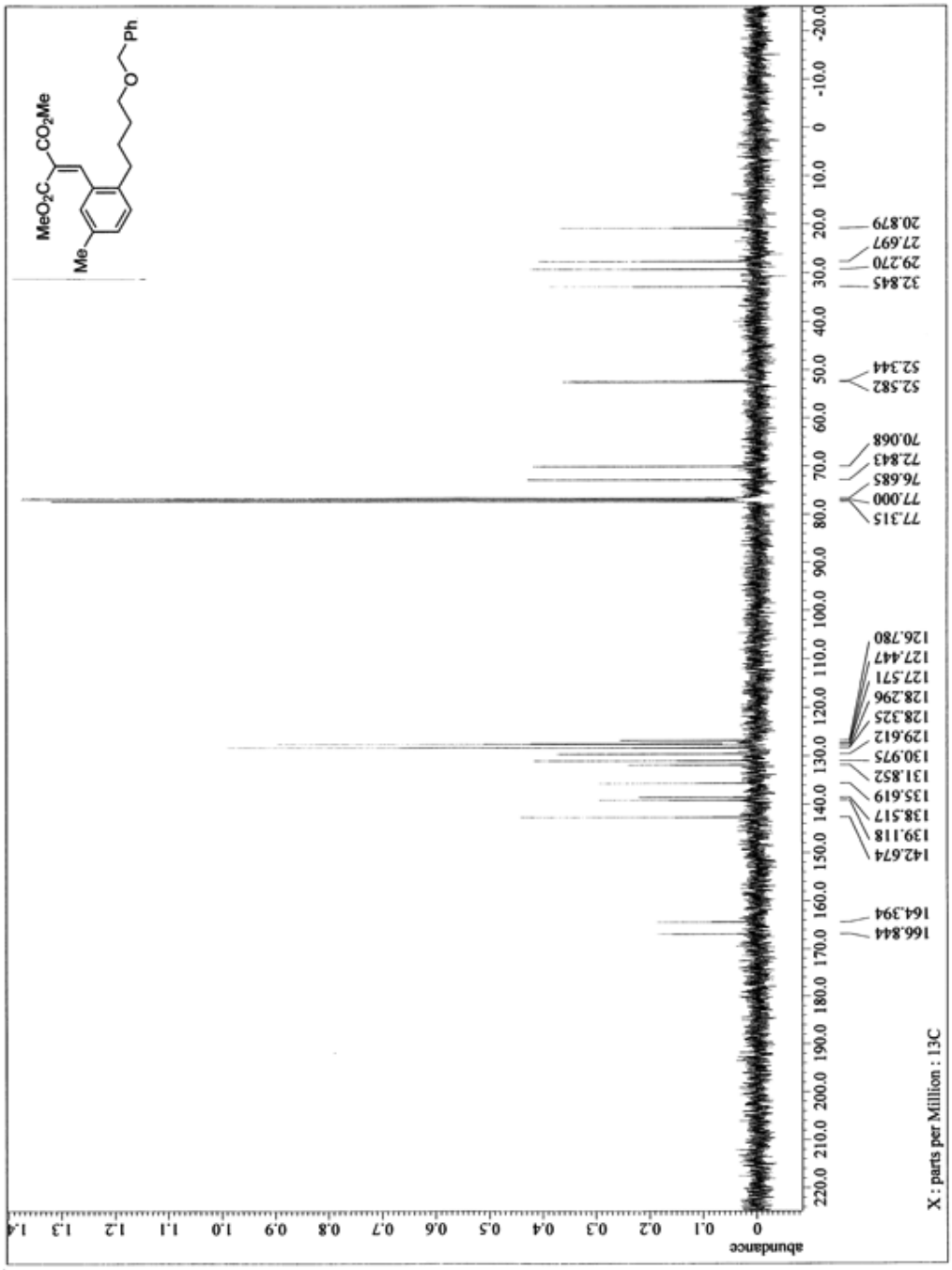
^{13}C NMR spectrum of **s21**.



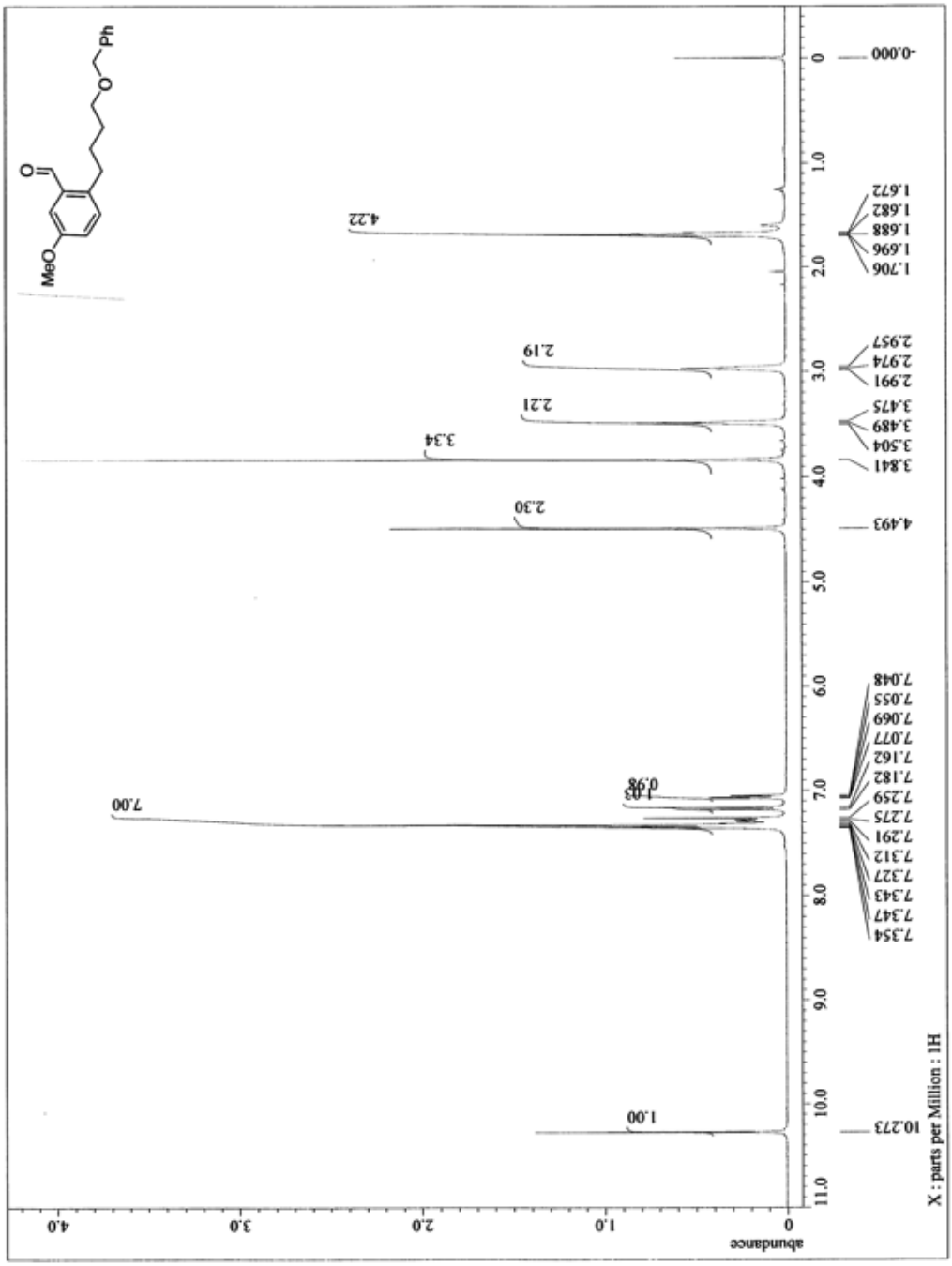
^{1}H NMR spectrum of **5b**.



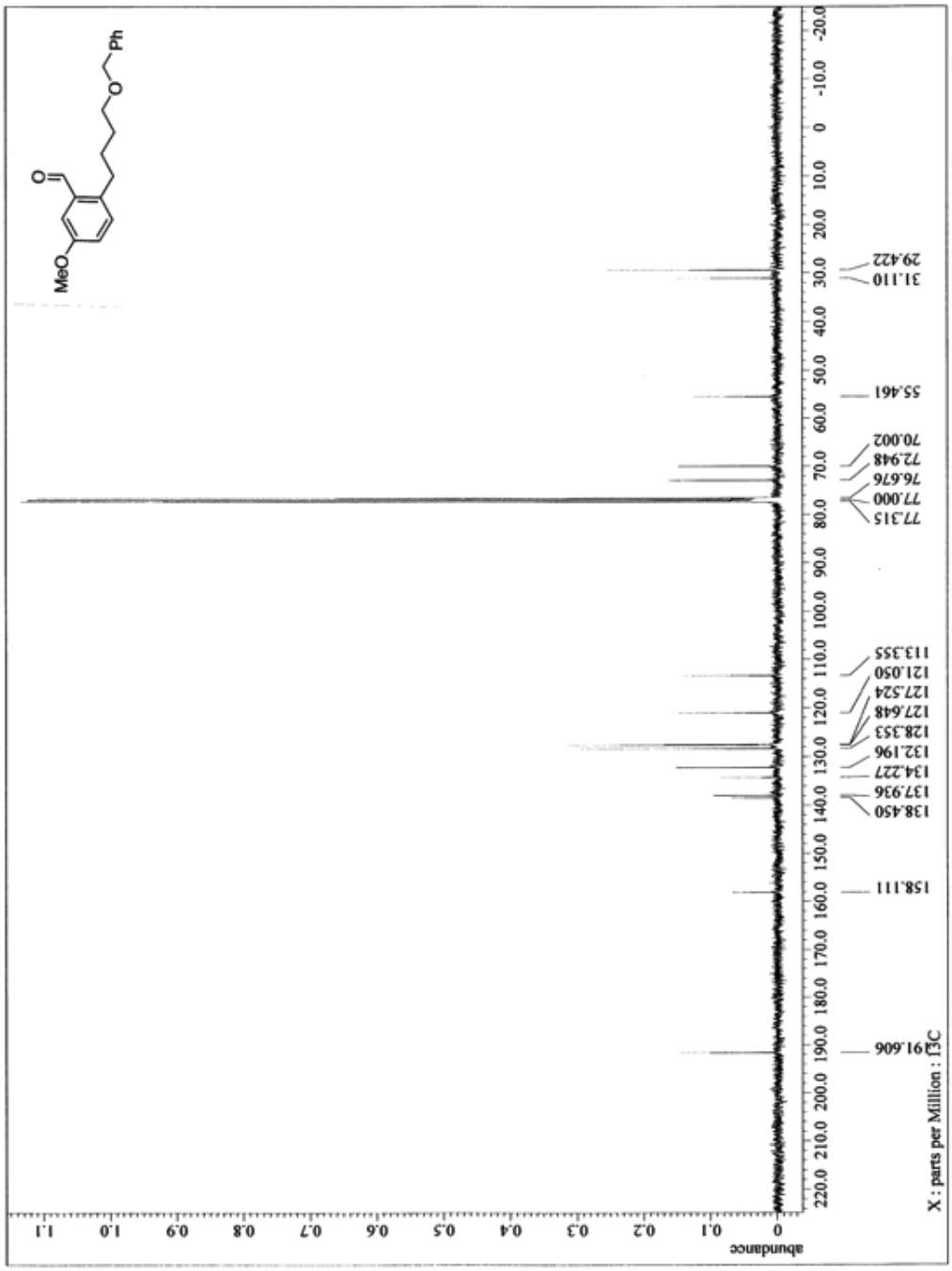
^{13}C NMR spectrum of **5b**.



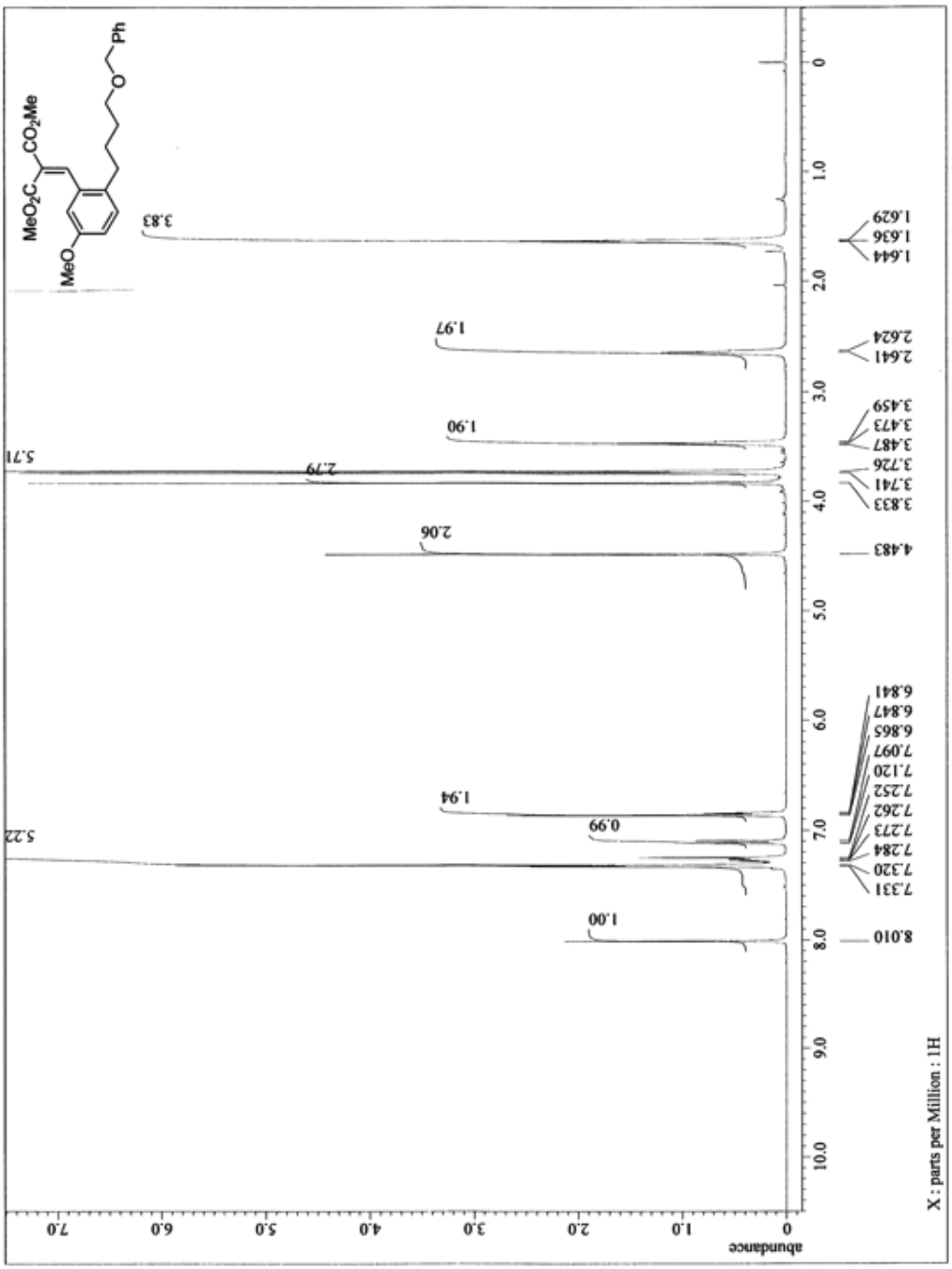
^{1}H NMR spectrum of **s22**.



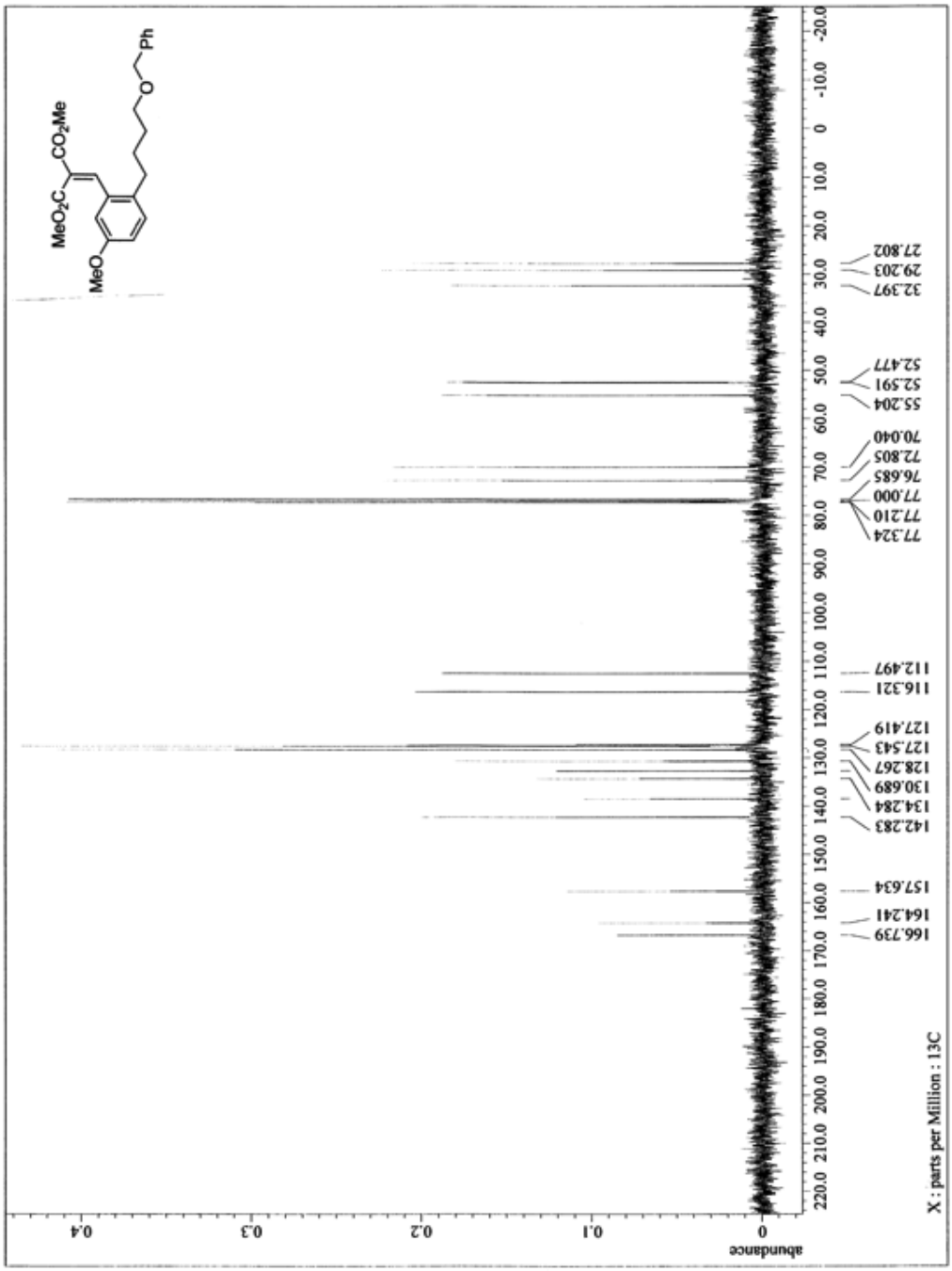
^{13}C NMR spectrum of **s22**.



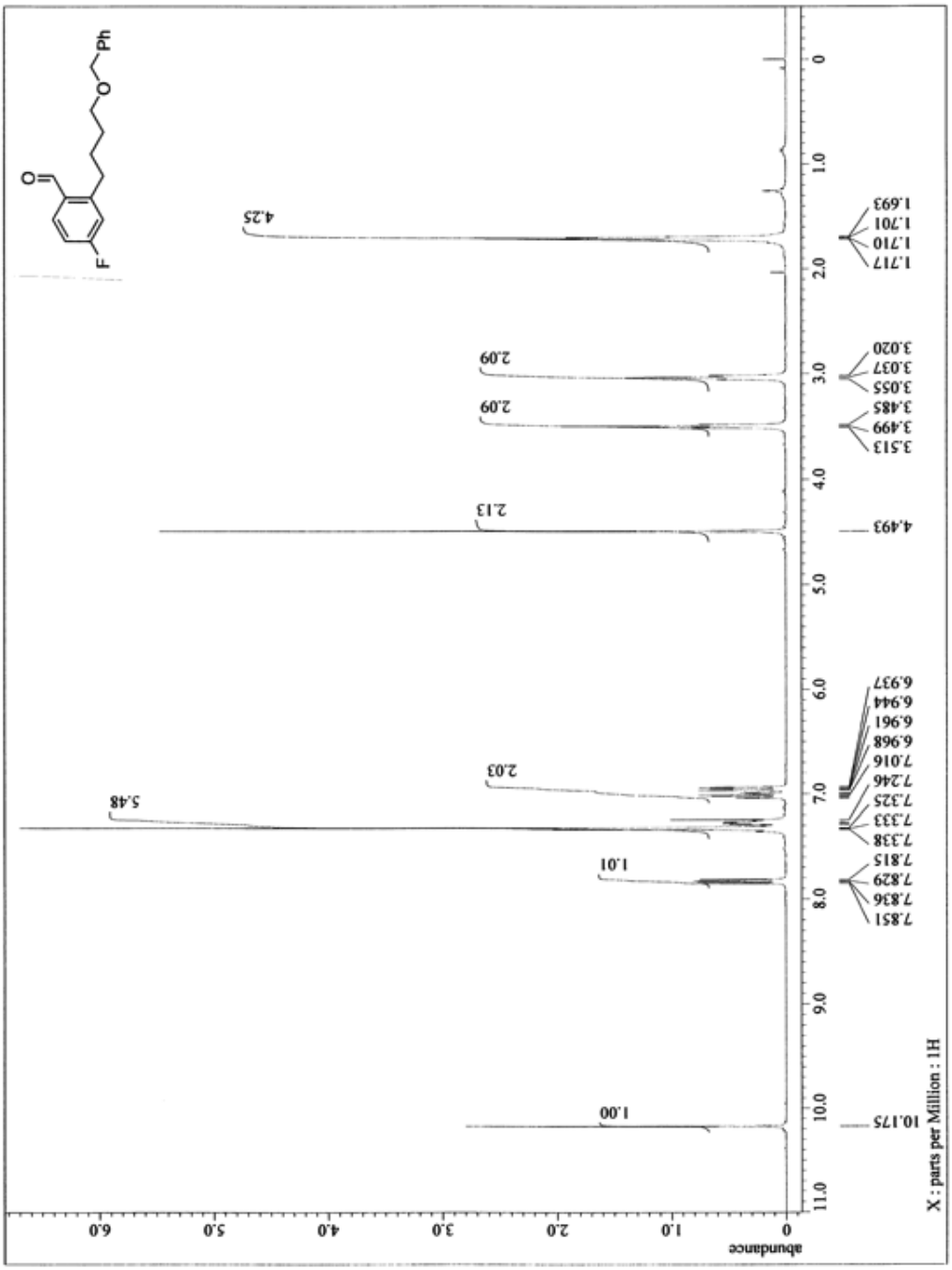
^{1}H NMR spectrum of **5c**.



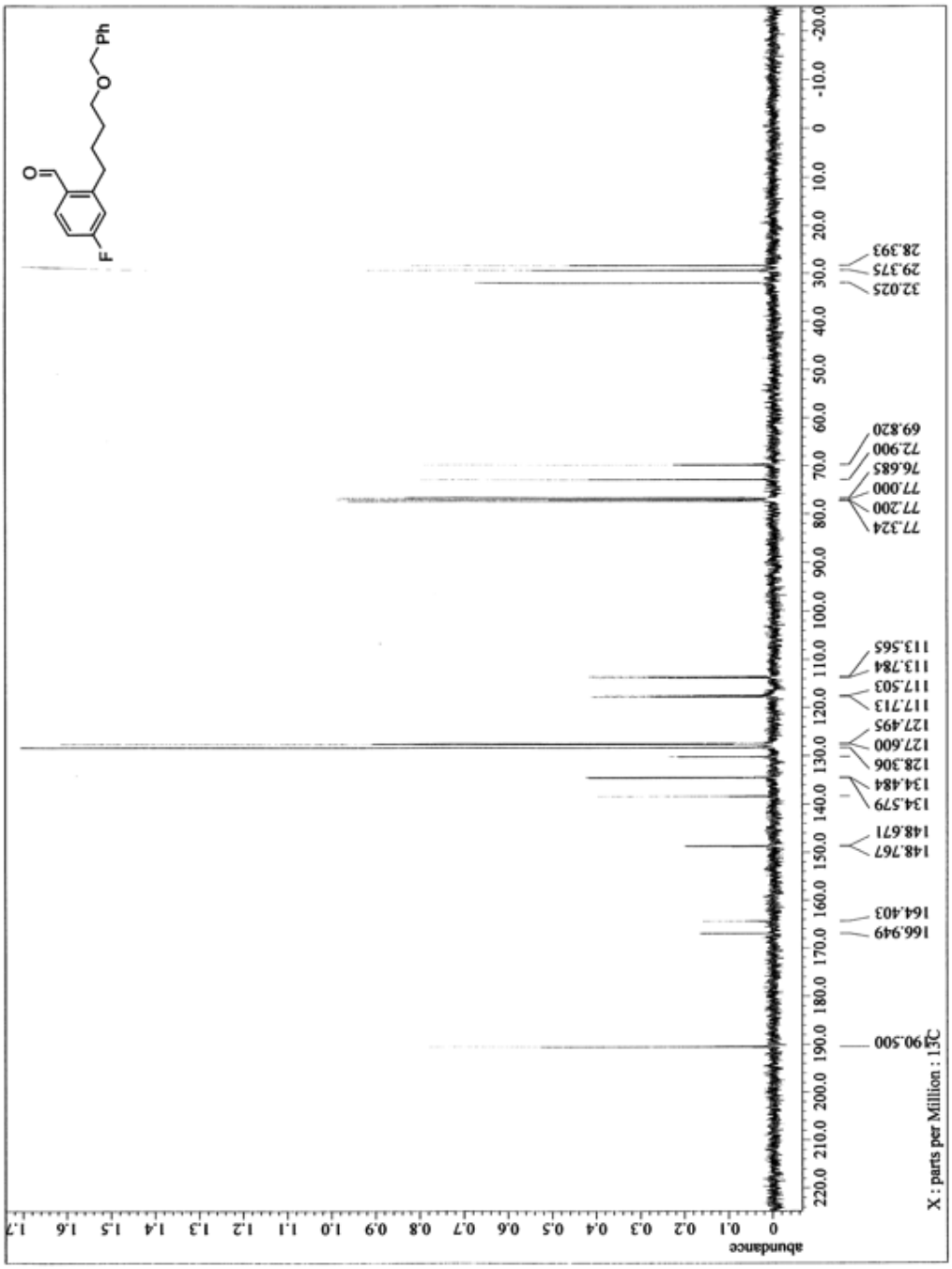
^{13}C NMR spectrum of **5c**.



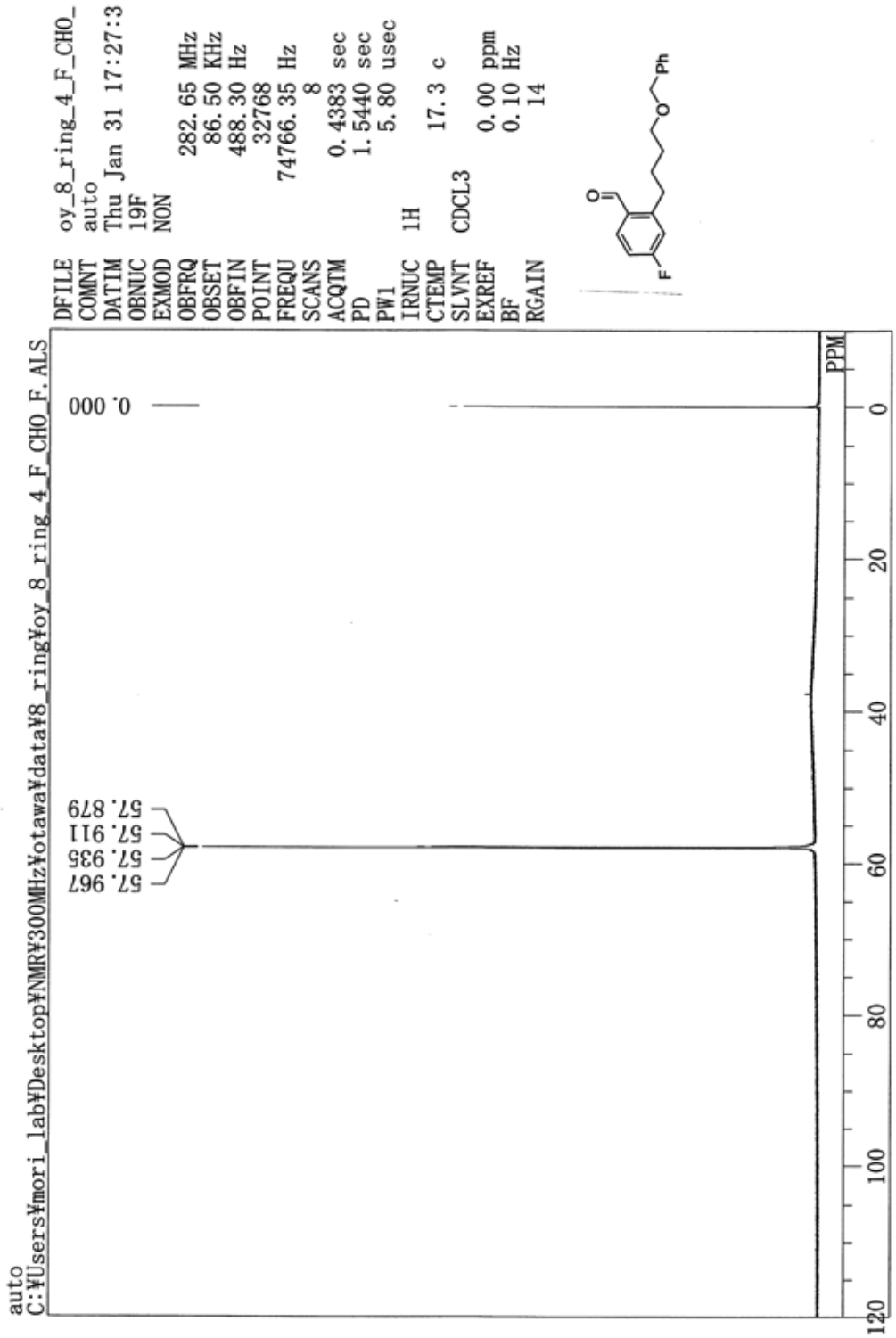
^{1}H NMR spectrum of **s23**.



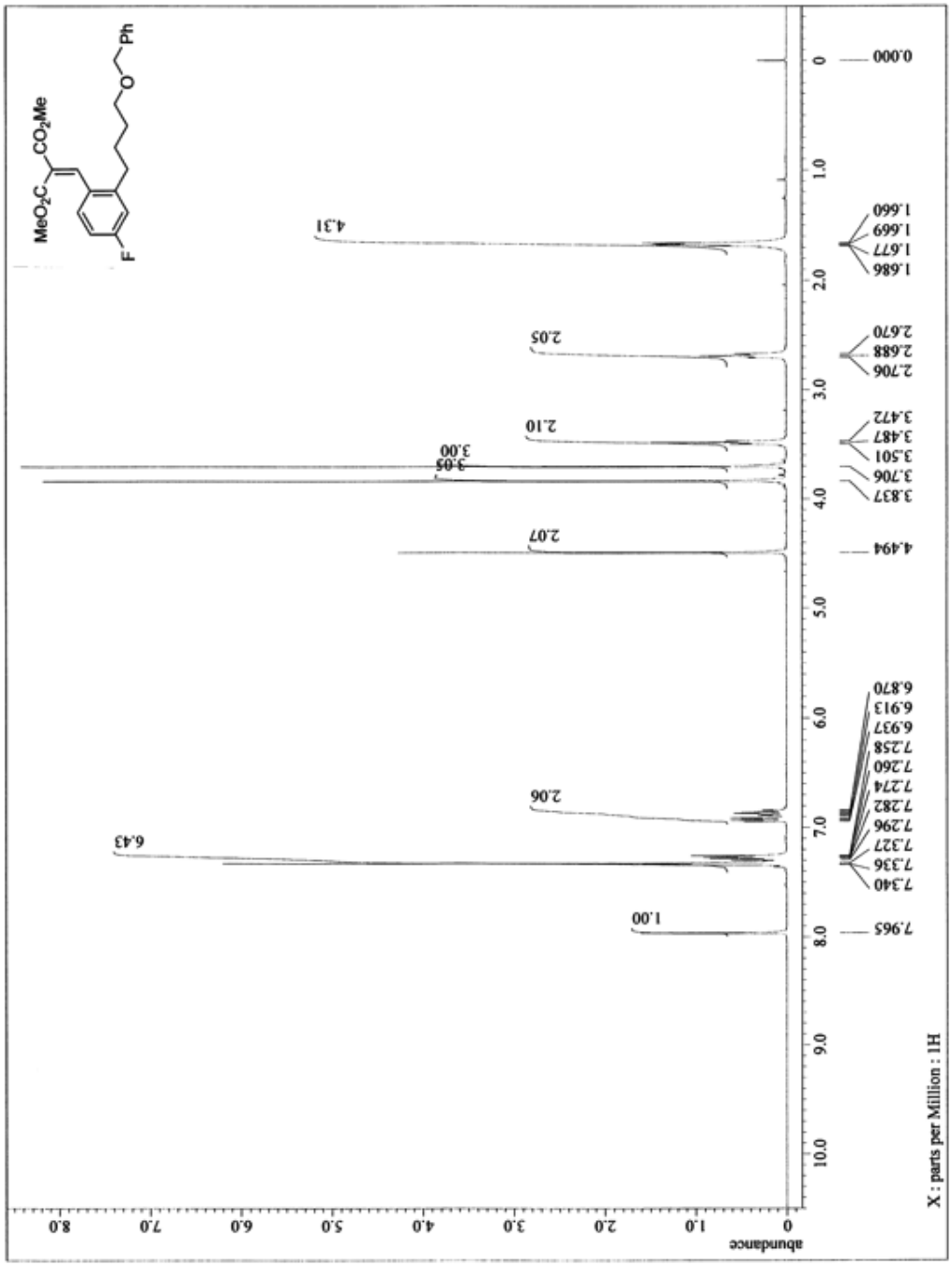
^{13}C NMR spectrum of **s23**.



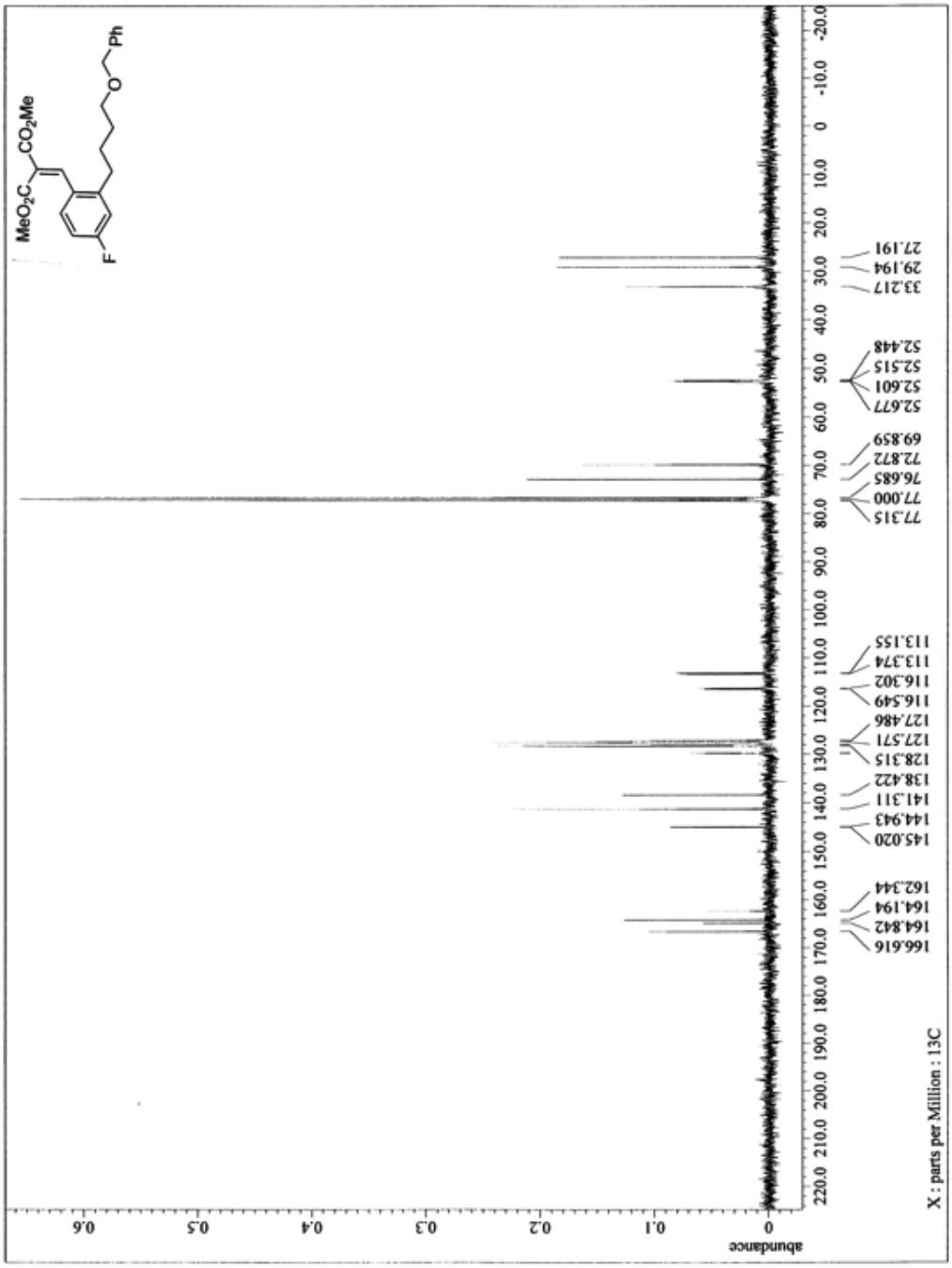
^{19}F NMR spectrum of **s23**.



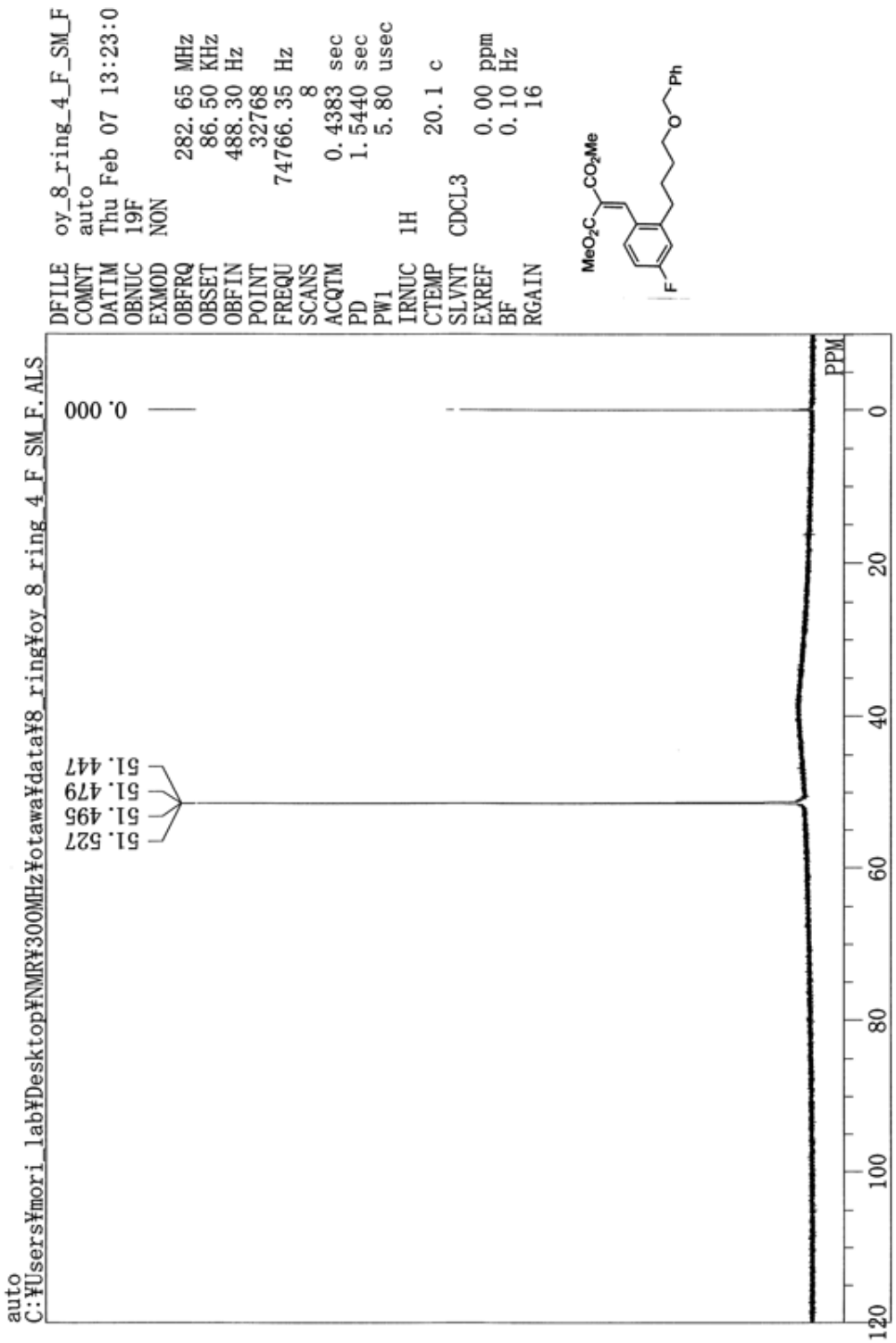
^{1}H NMR spectrum of **5d**.



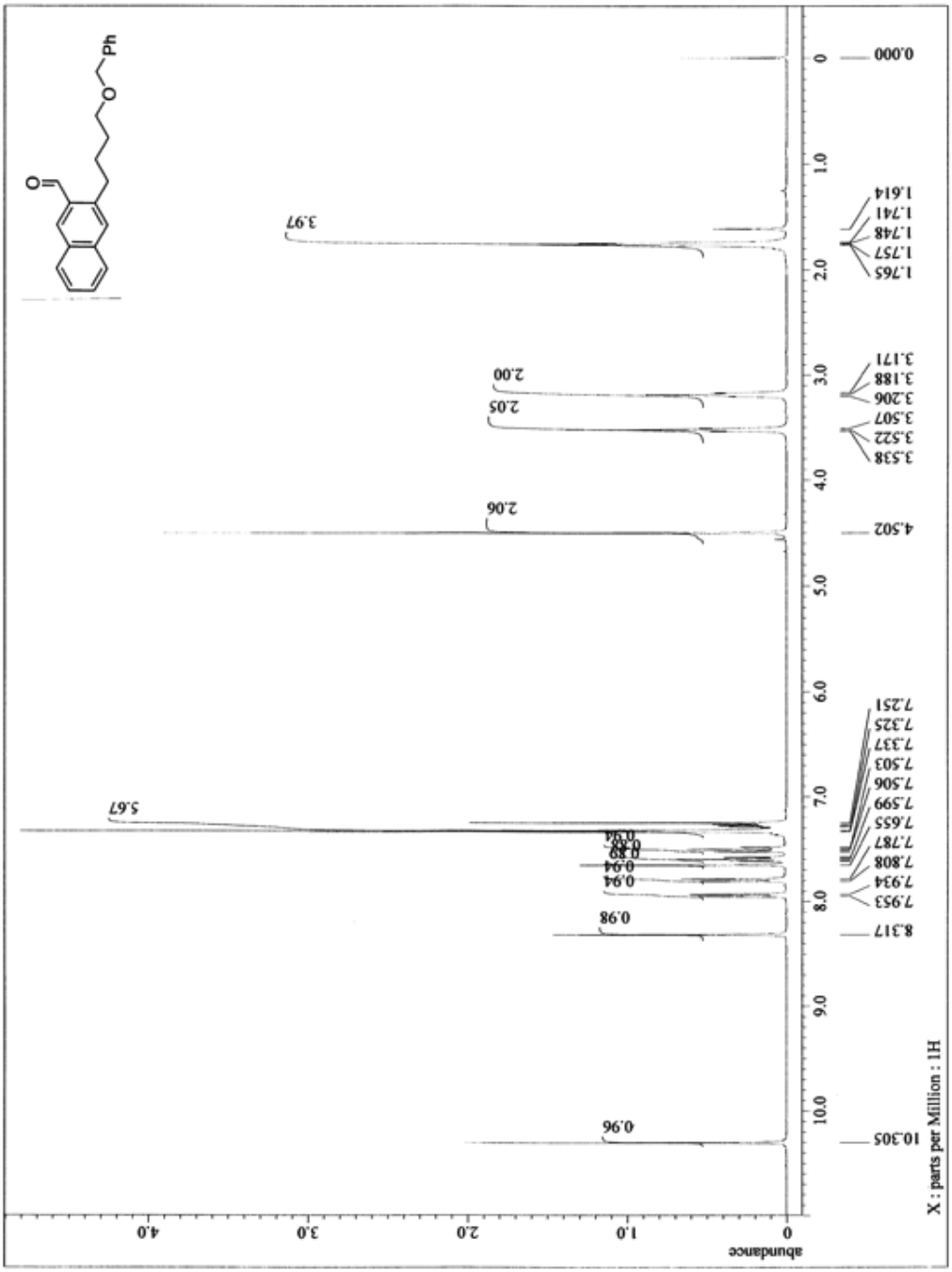
^{13}C NMR spectrum of **5d**.



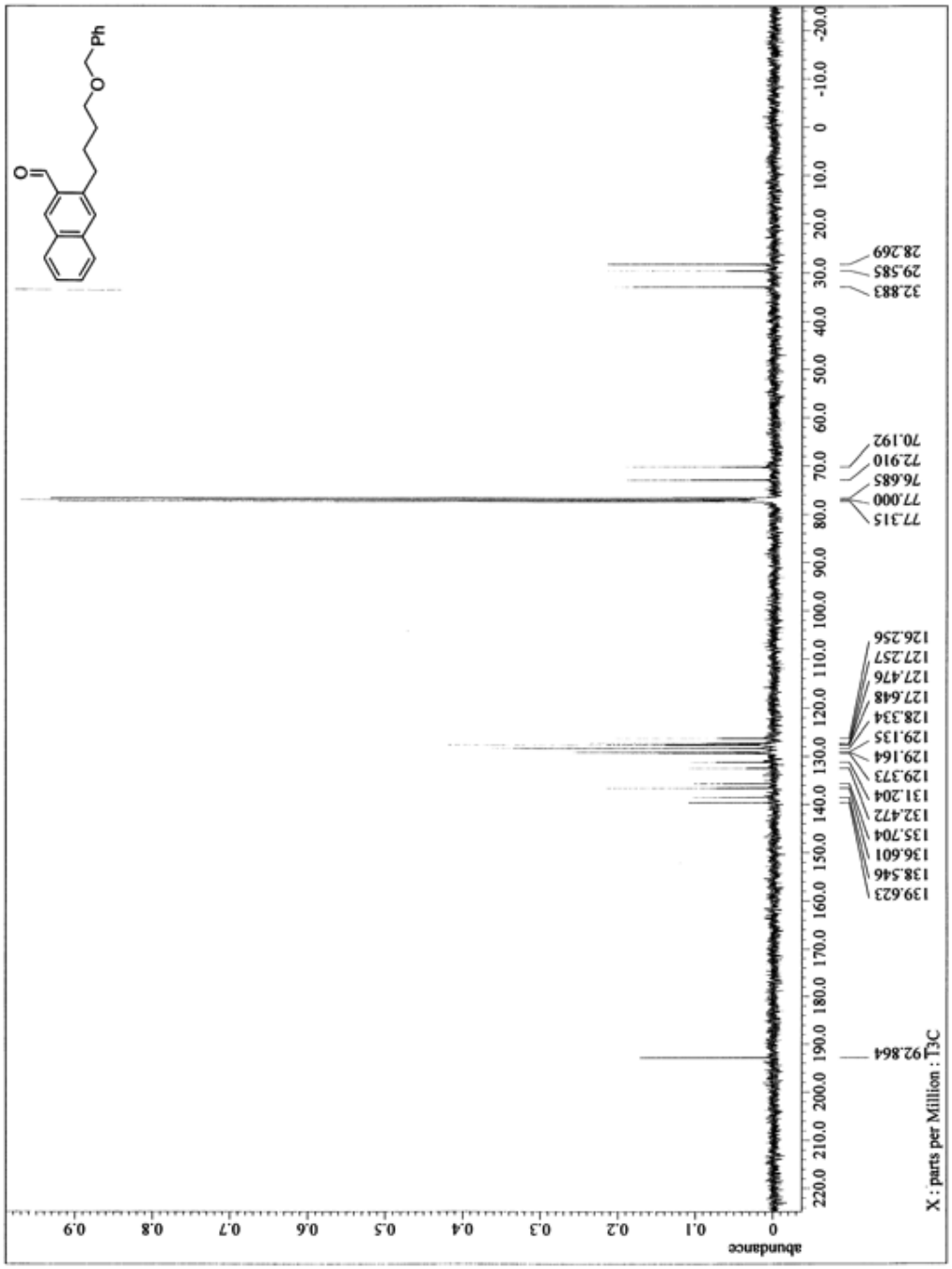
^{19}F NMR spectrum of **5d**.



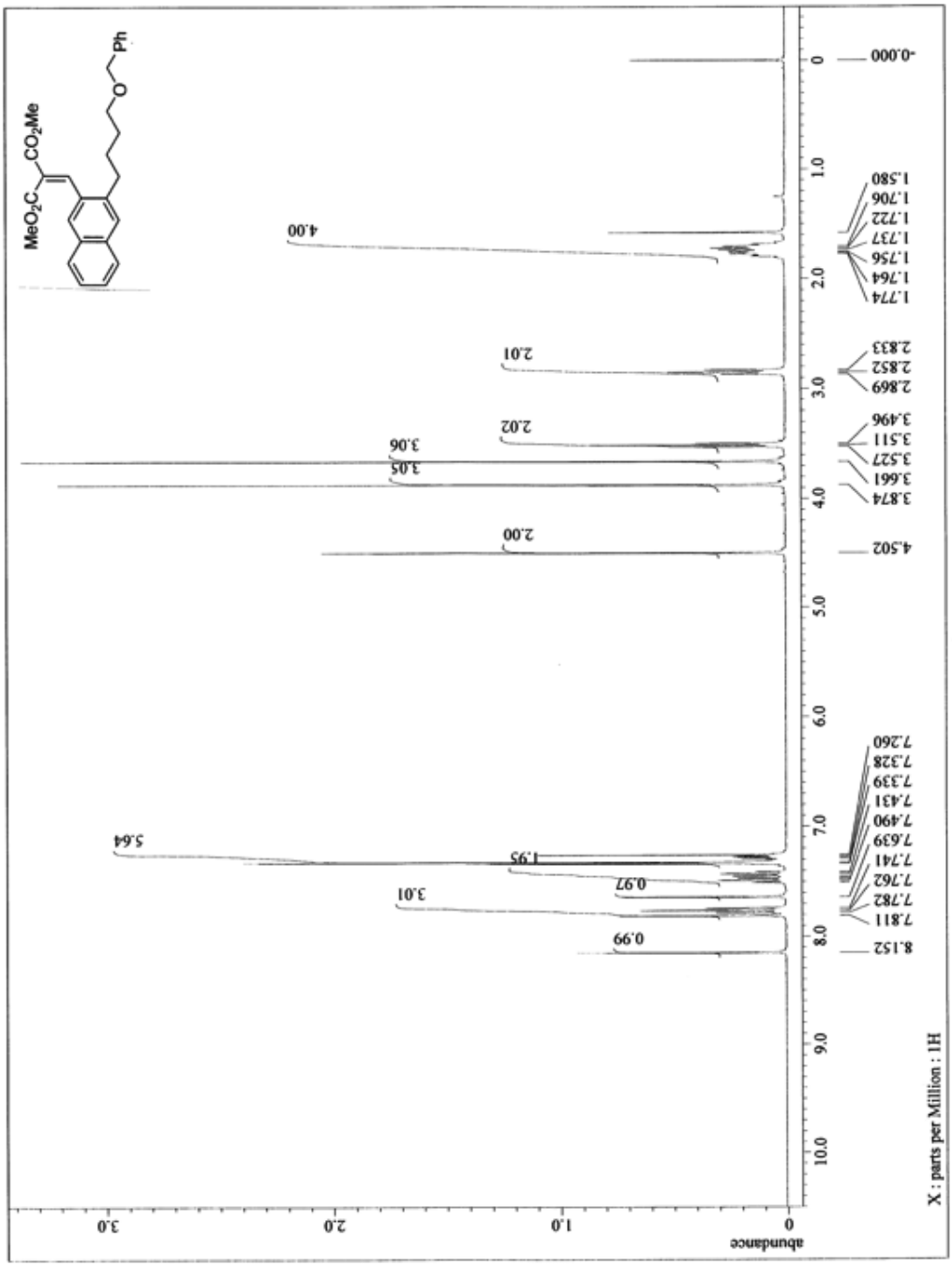
^{1}H NMR spectrum of **s24**.



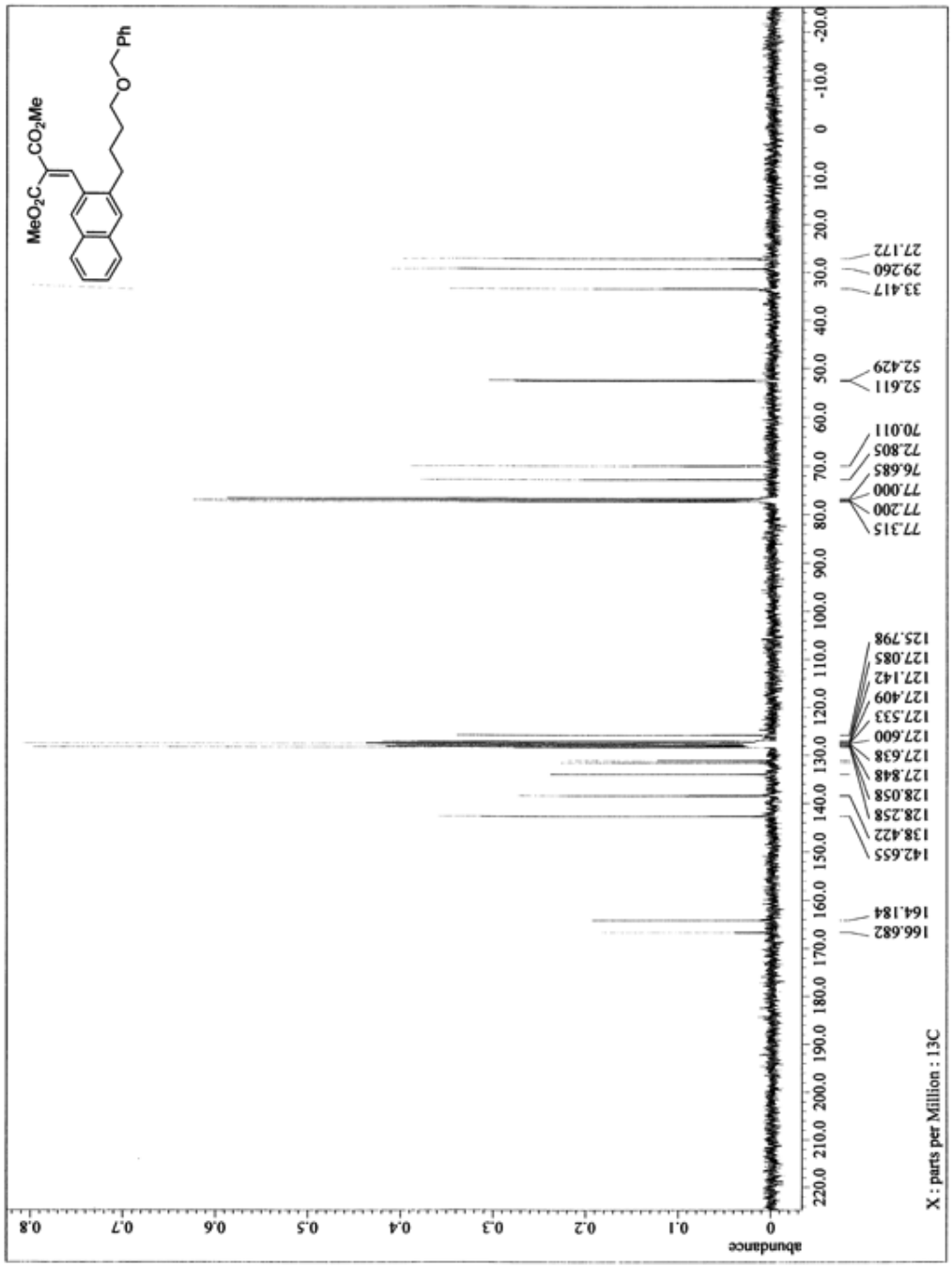
^{13}C NMR spectrum of **s24**.



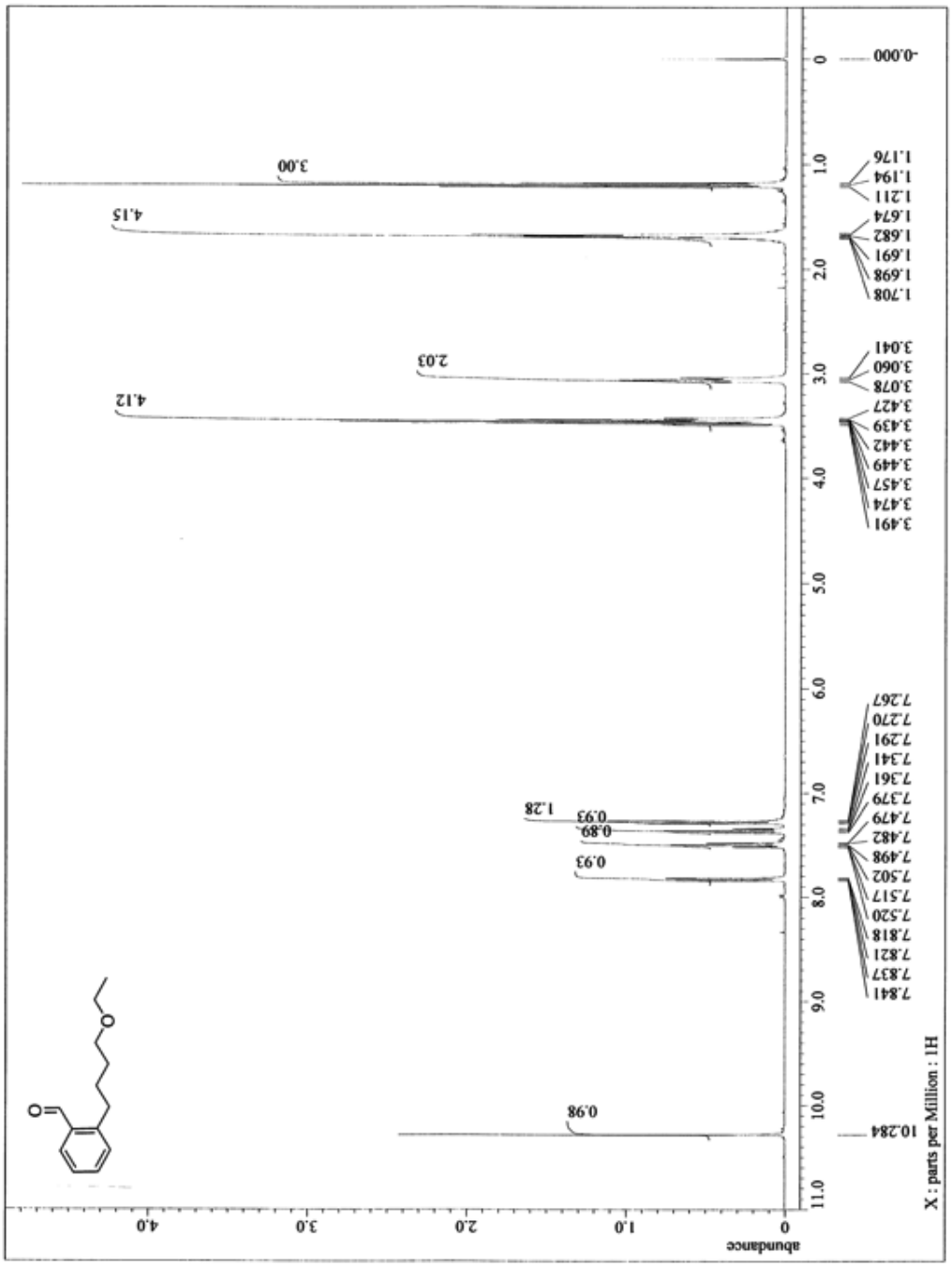
^{1}H NMR spectrum of **5e**.



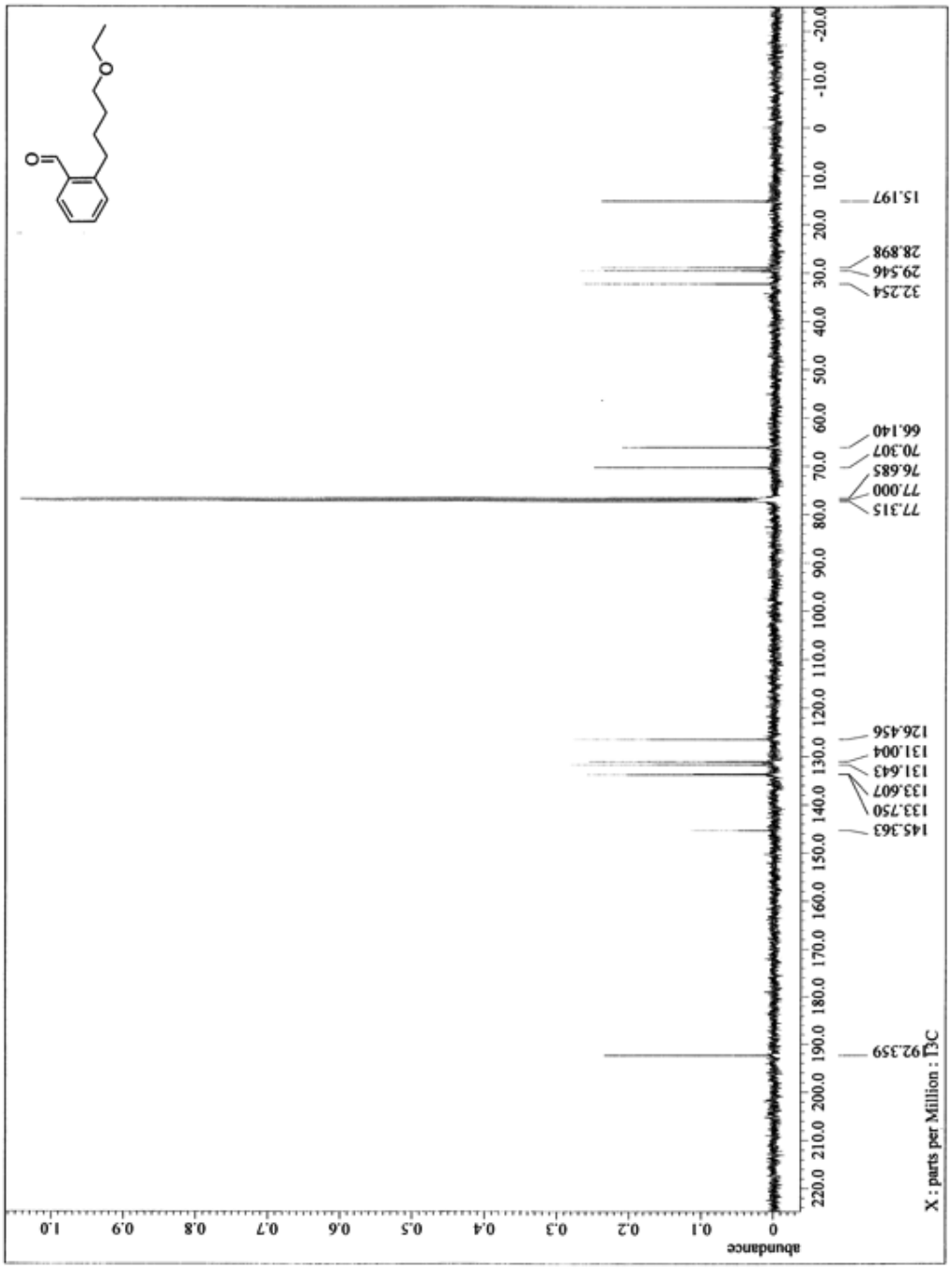
^{13}C NMR spectrum of **5e**.



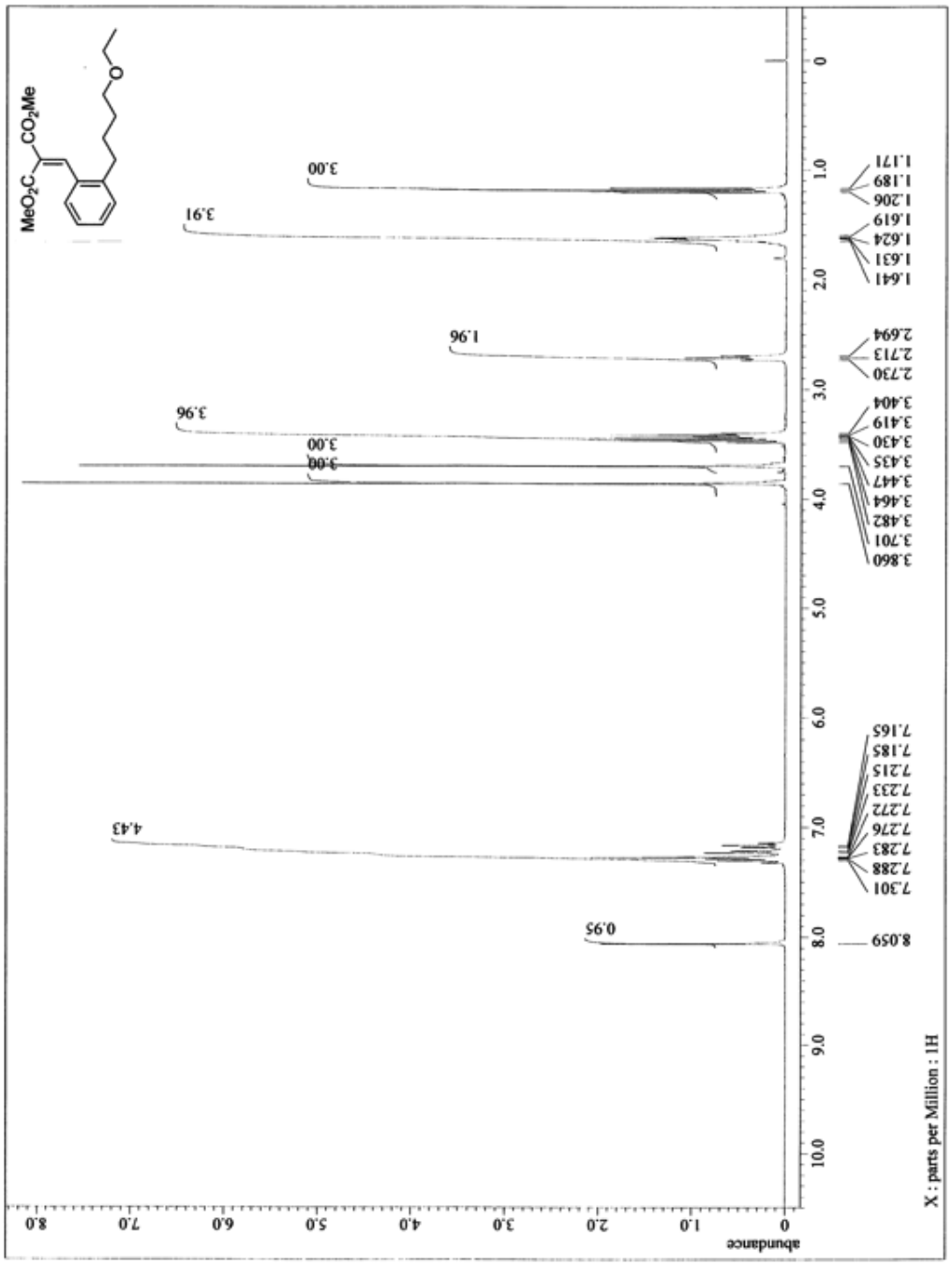
^{1}H NMR spectrum of **s25**.



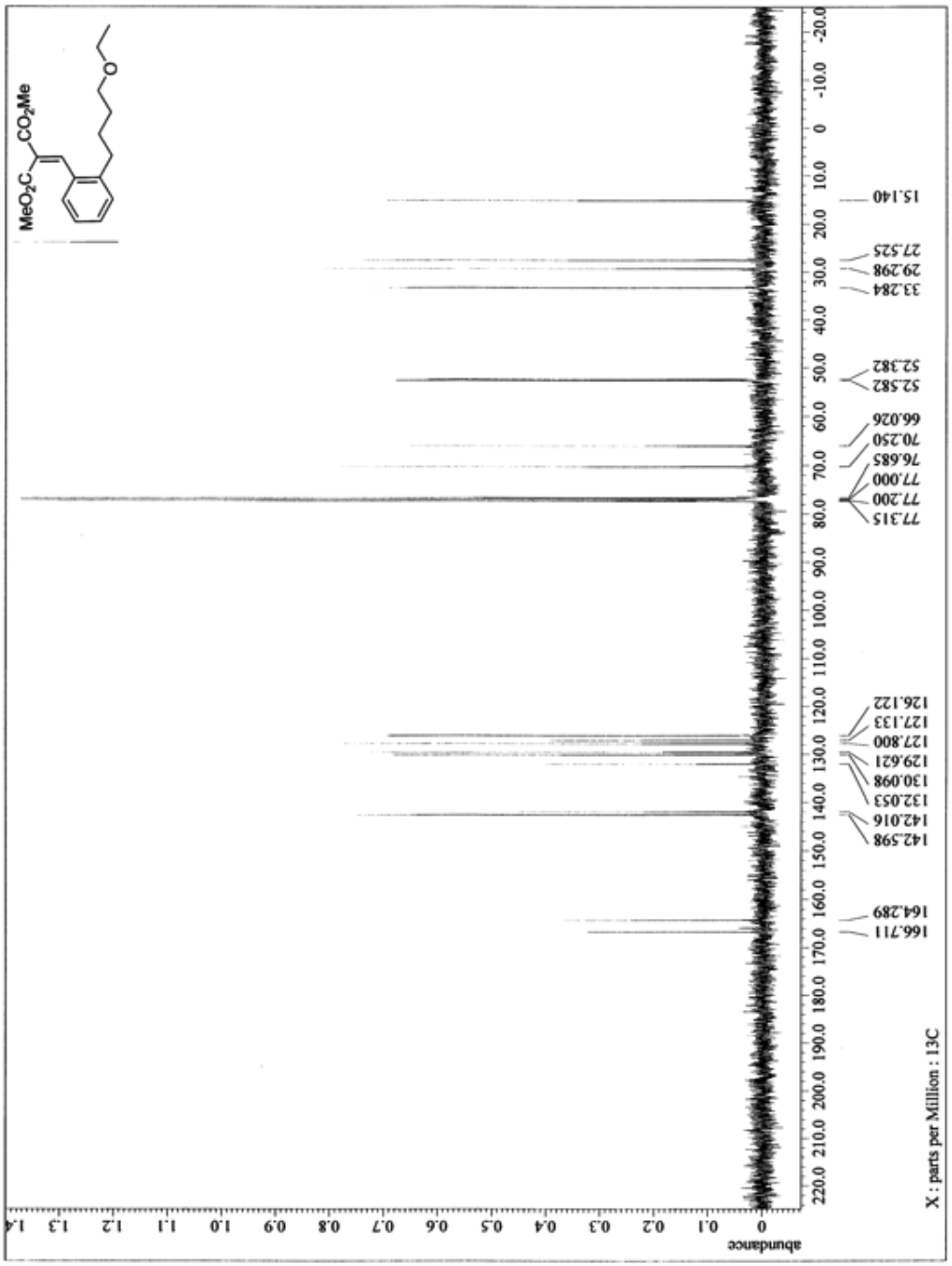
^{13}C NMR spectrum of **s25**.



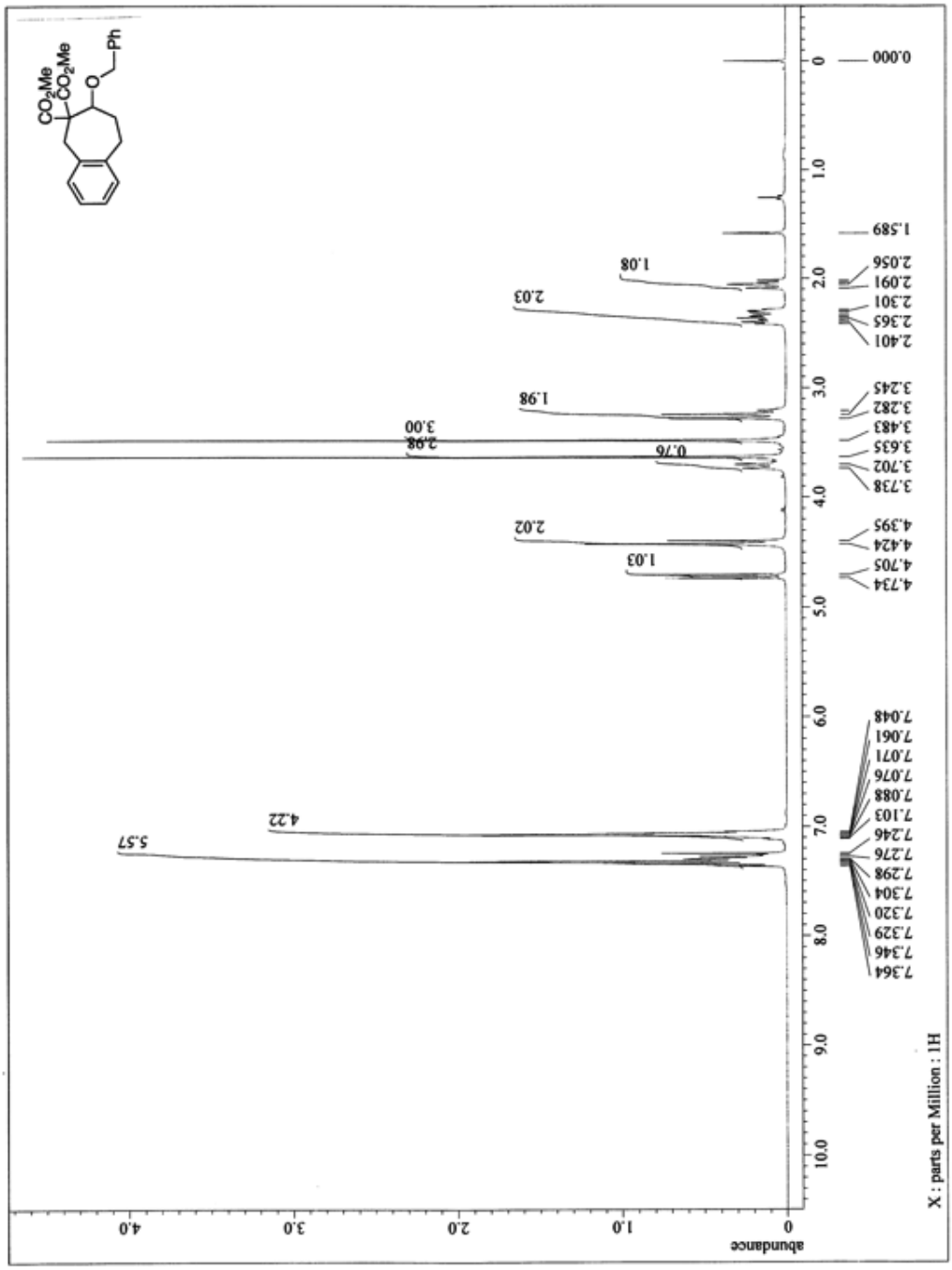
^{1}H NMR spectrum of **5f**.



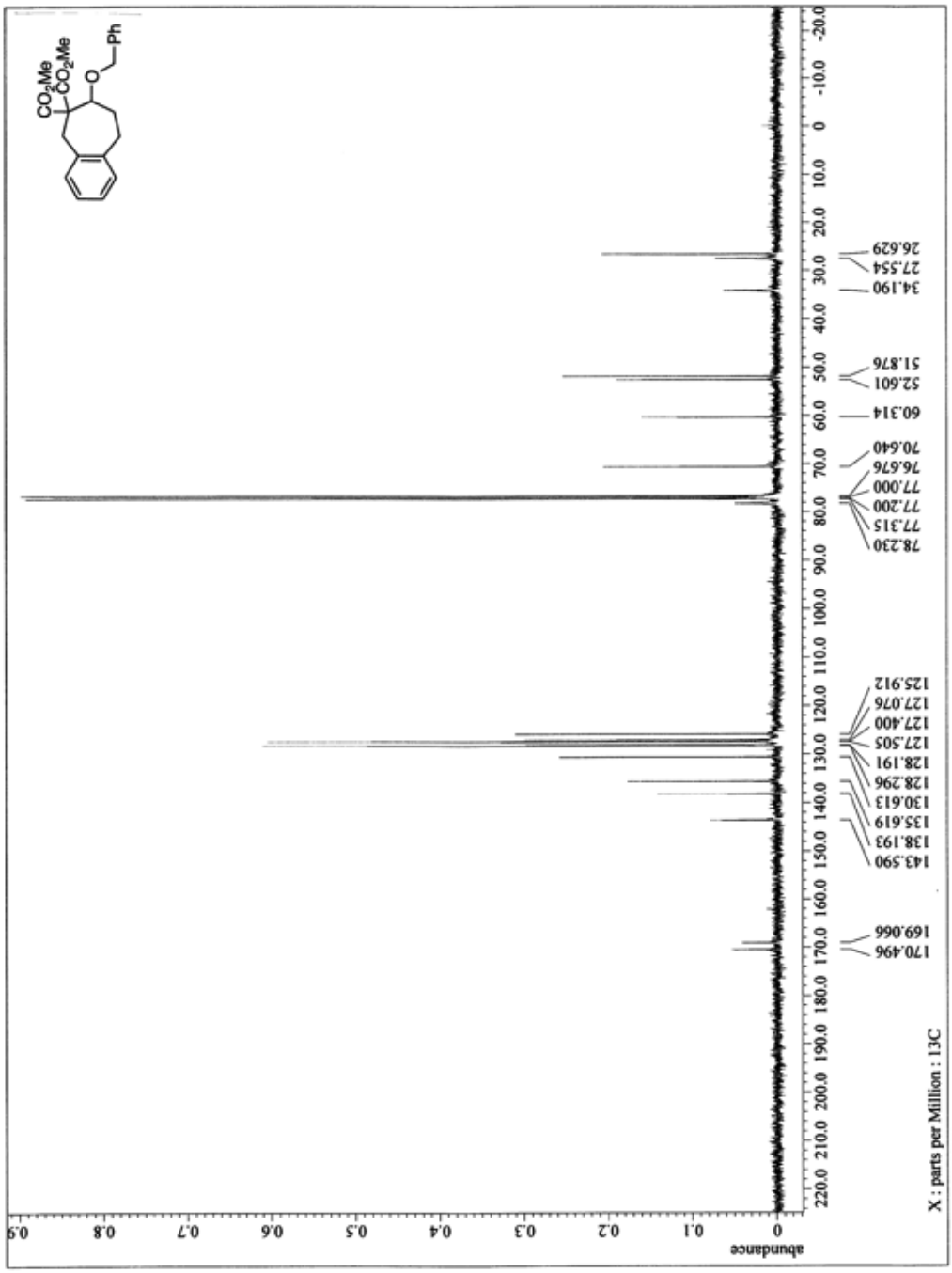
^{13}C NMR spectrum of **5f**.



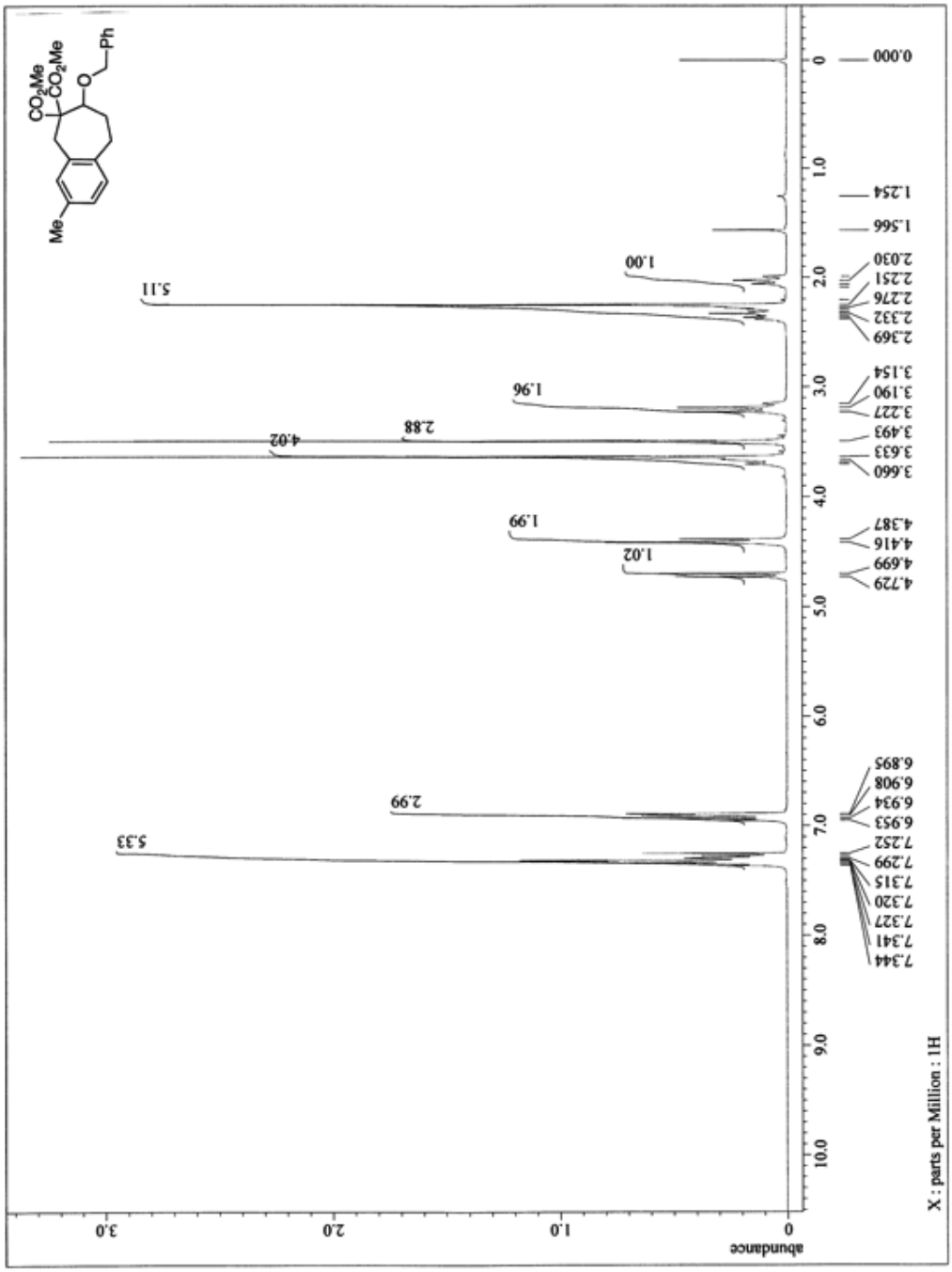
^{1}H NMR spectrum of **4a**.



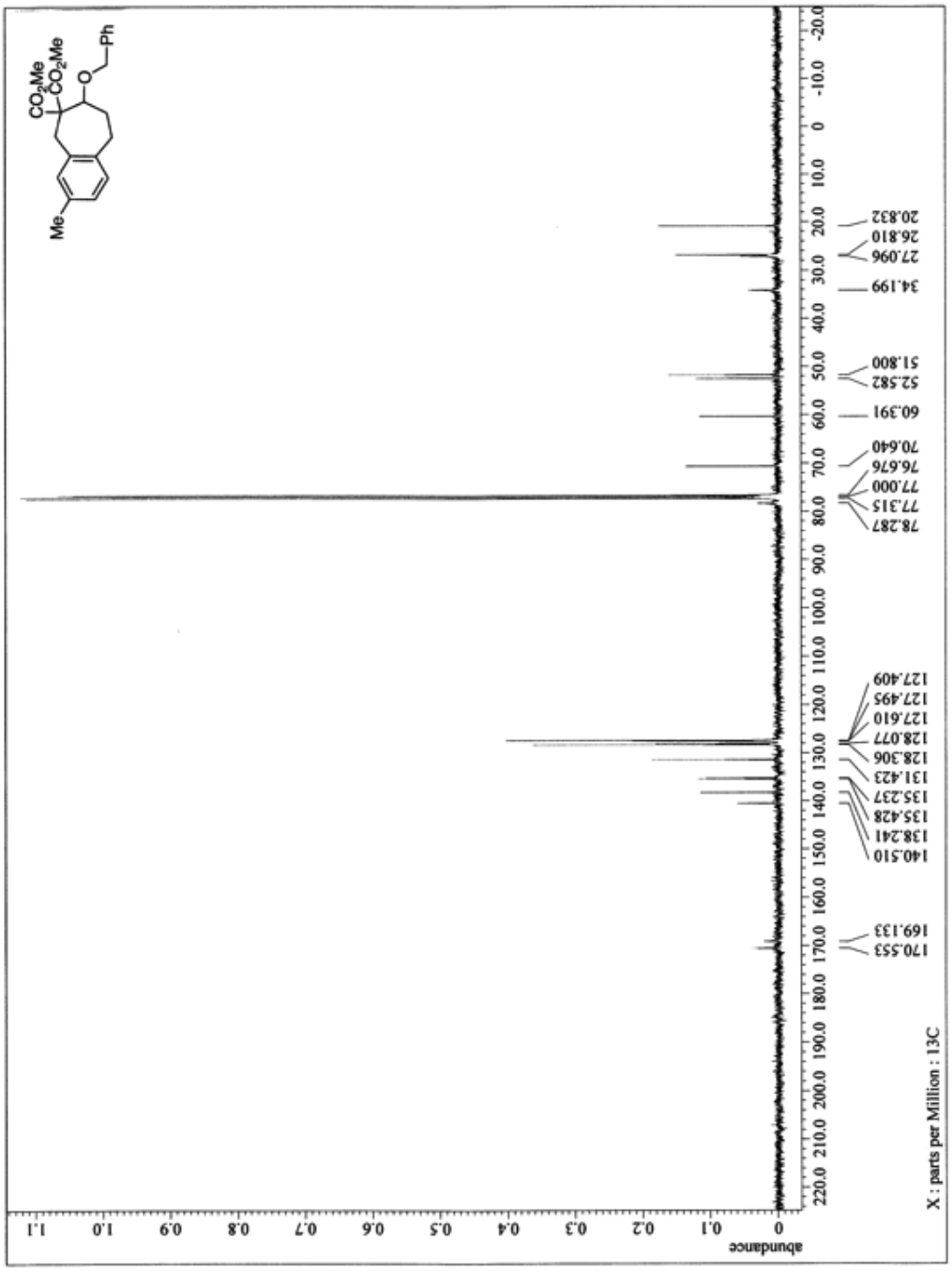
^{13}C NMR spectrum of **4a**.



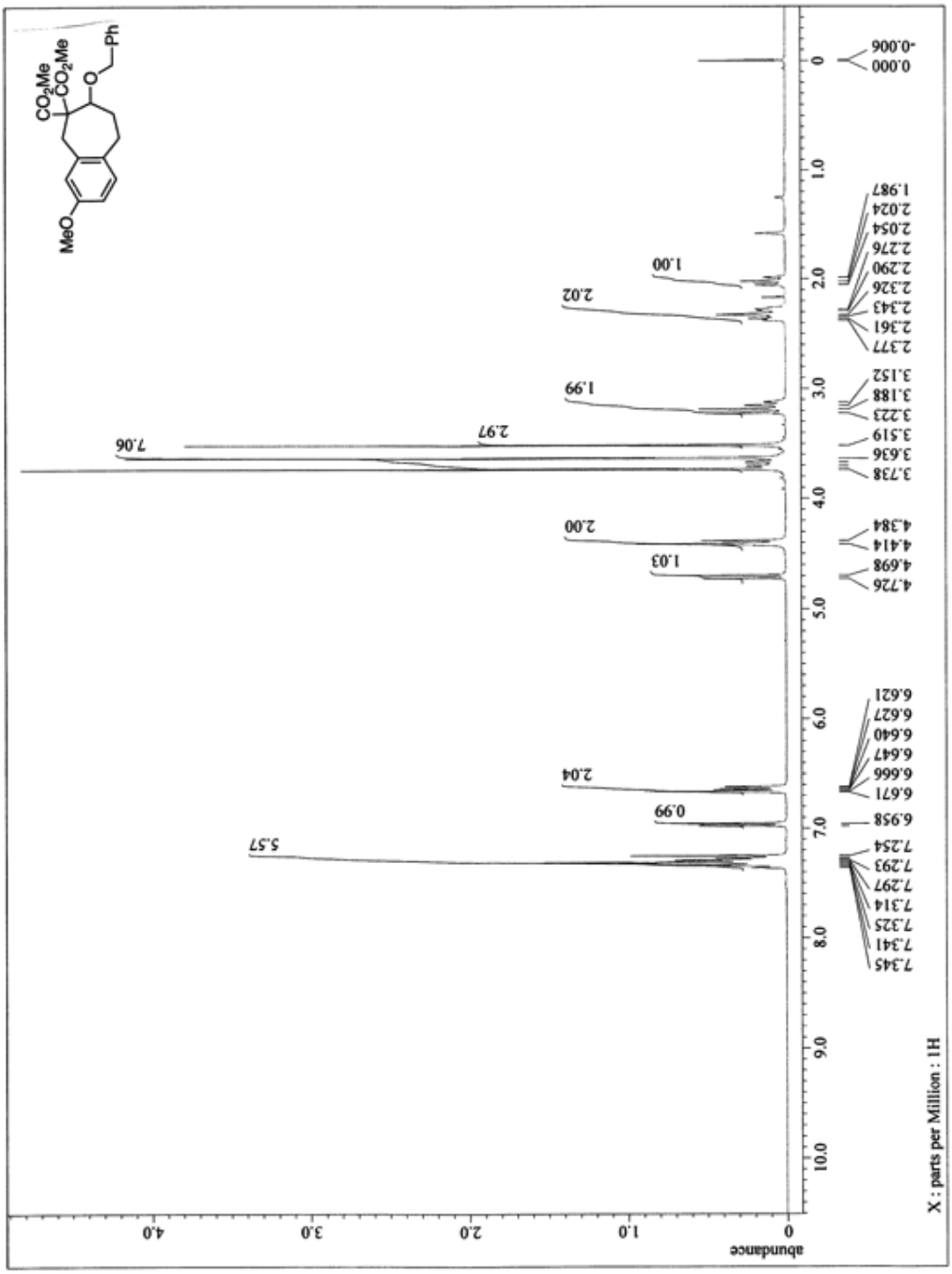
^{1}H NMR spectrum of **4b**.



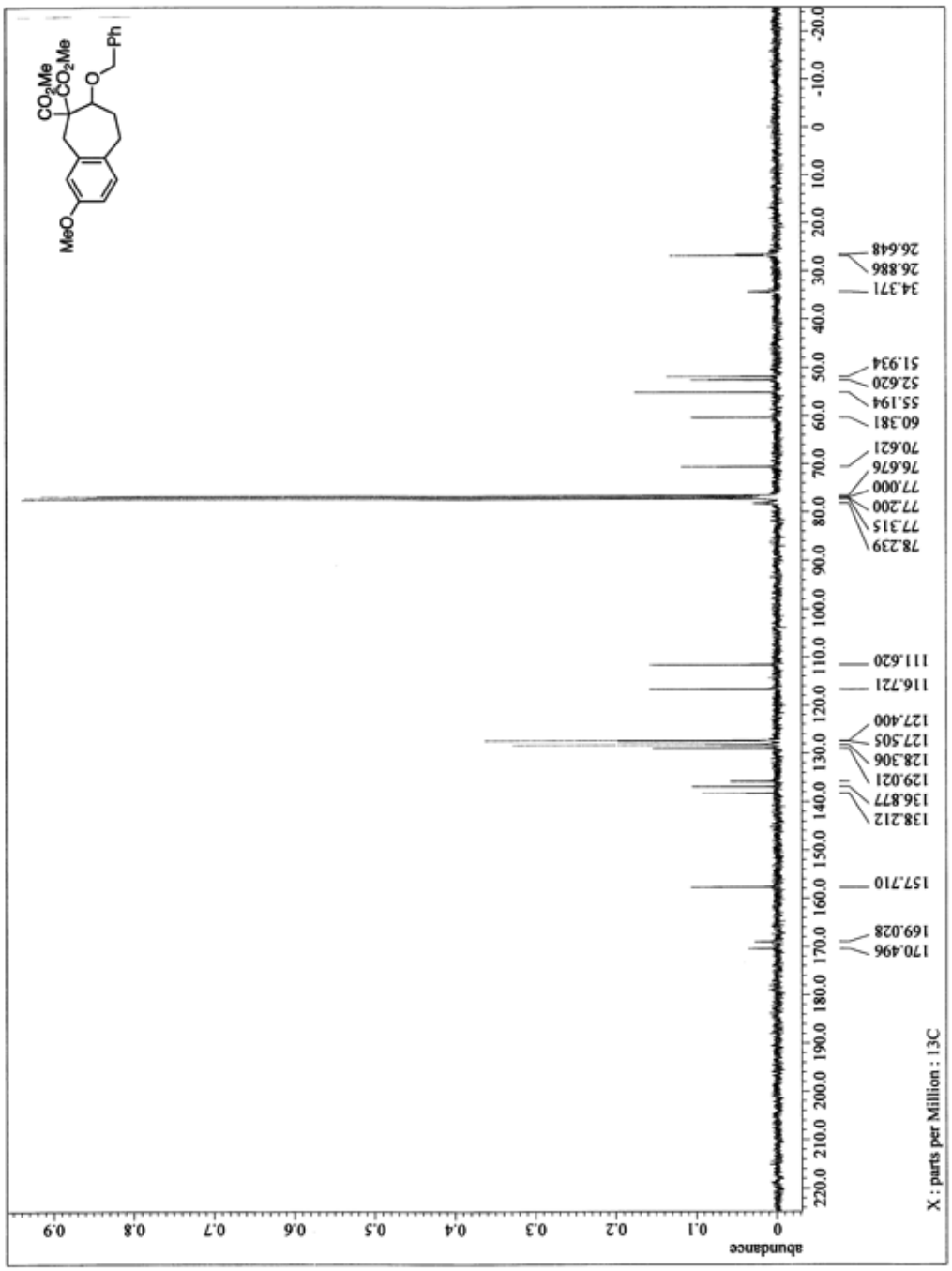
^{13}C NMR spectrum of **4b**.



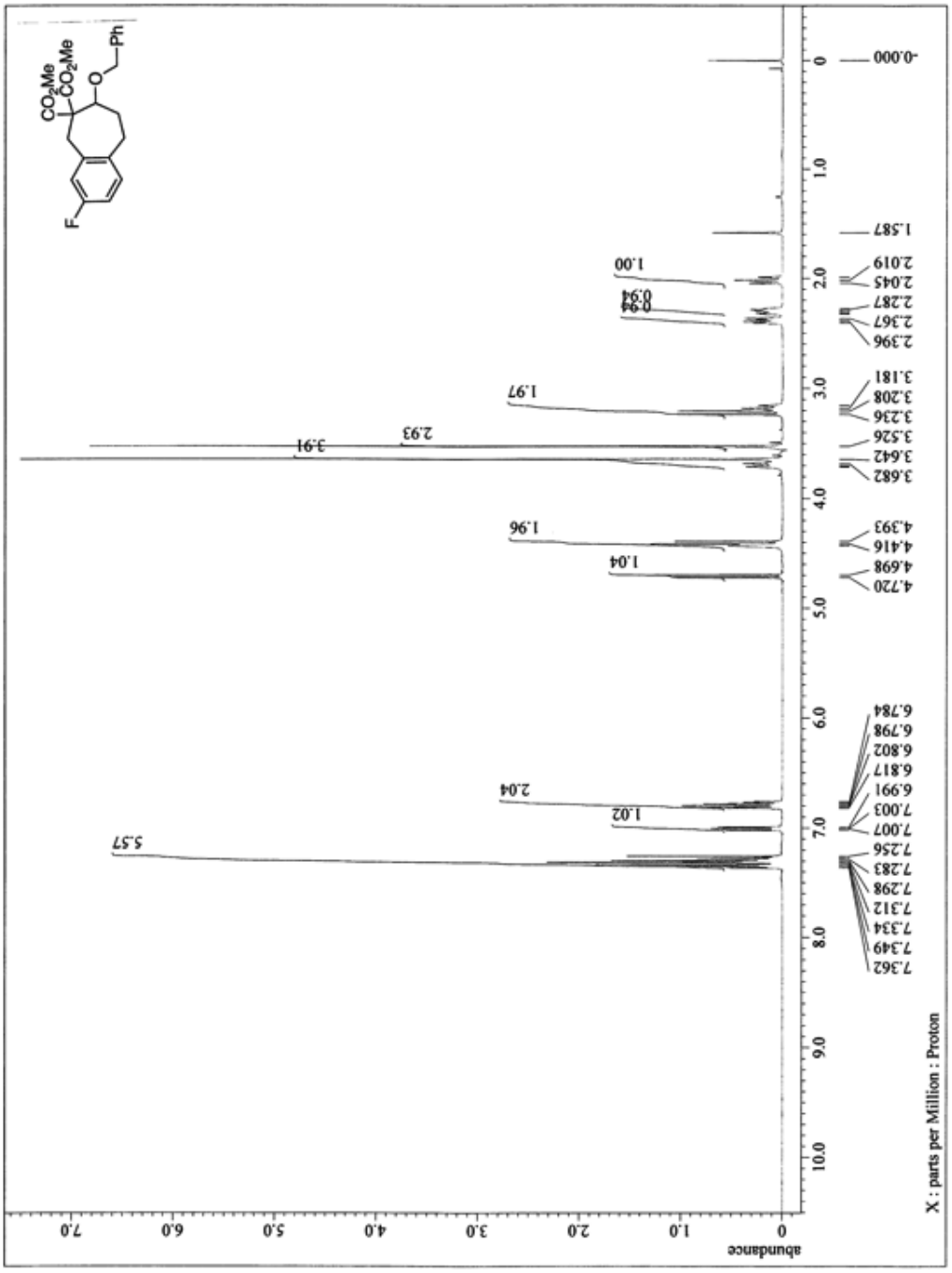
^{1}H NMR spectrum of **4c**.



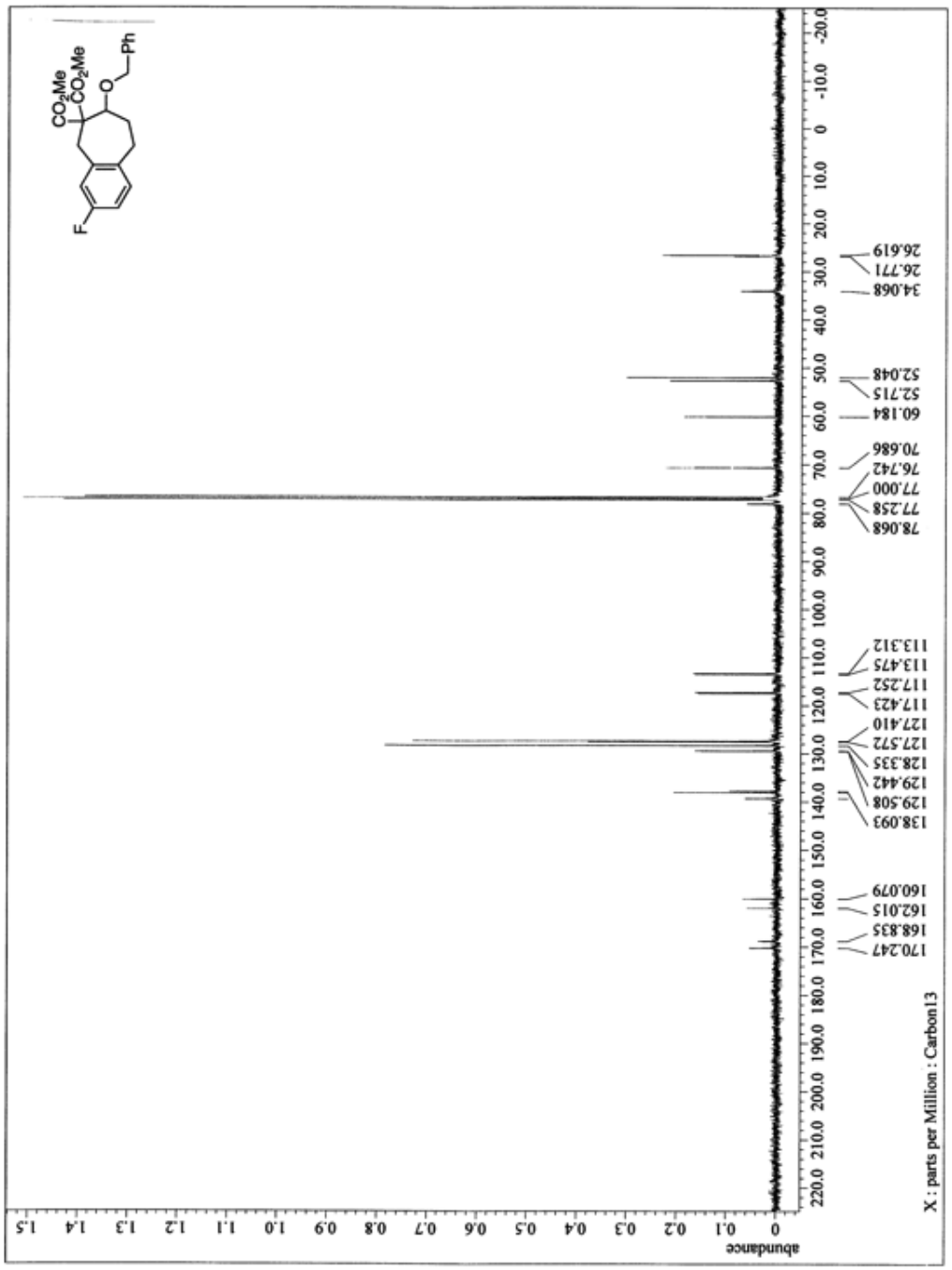
^{13}C NMR spectrum of **4c**.



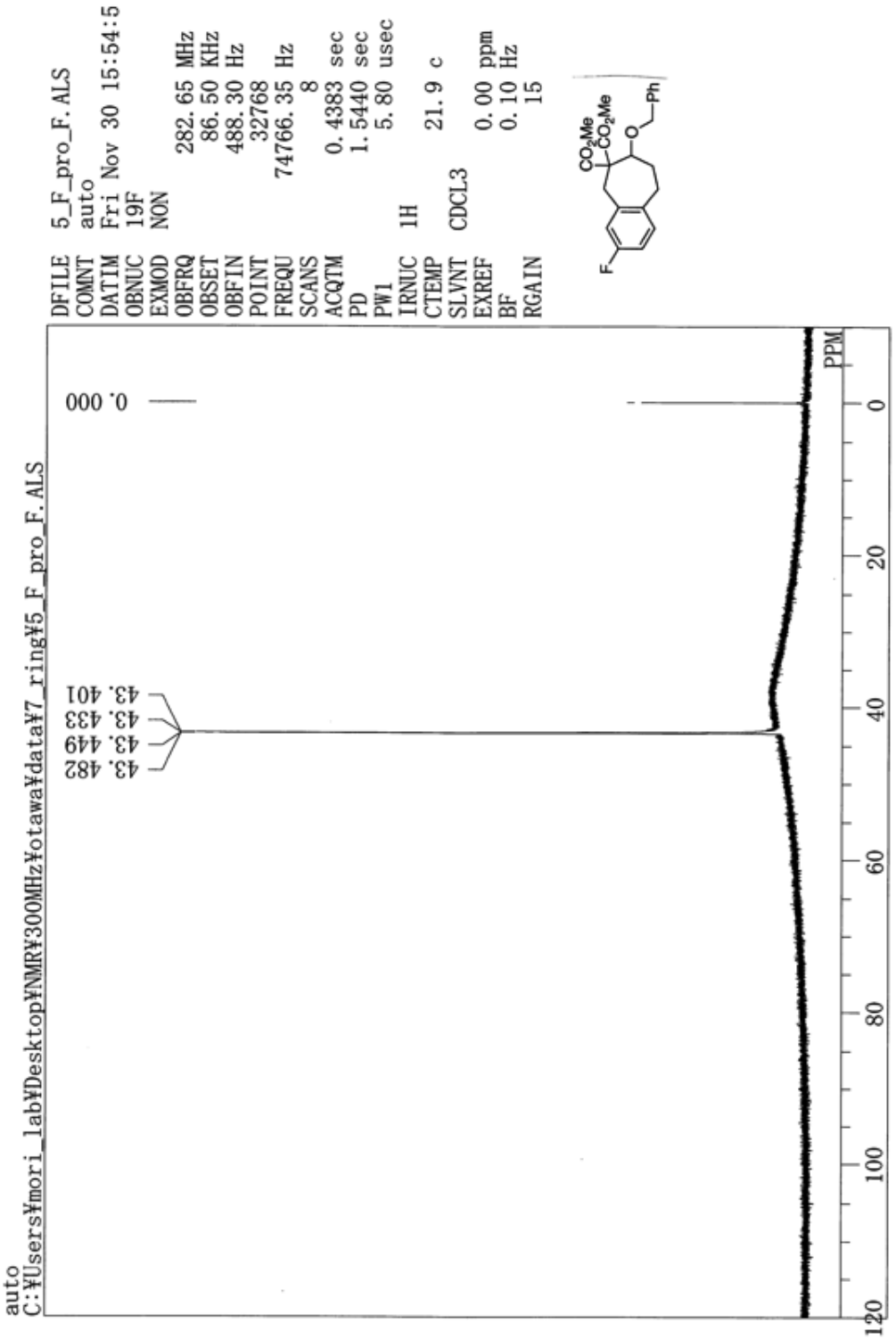
^{1}H NMR spectrum of **4d**.



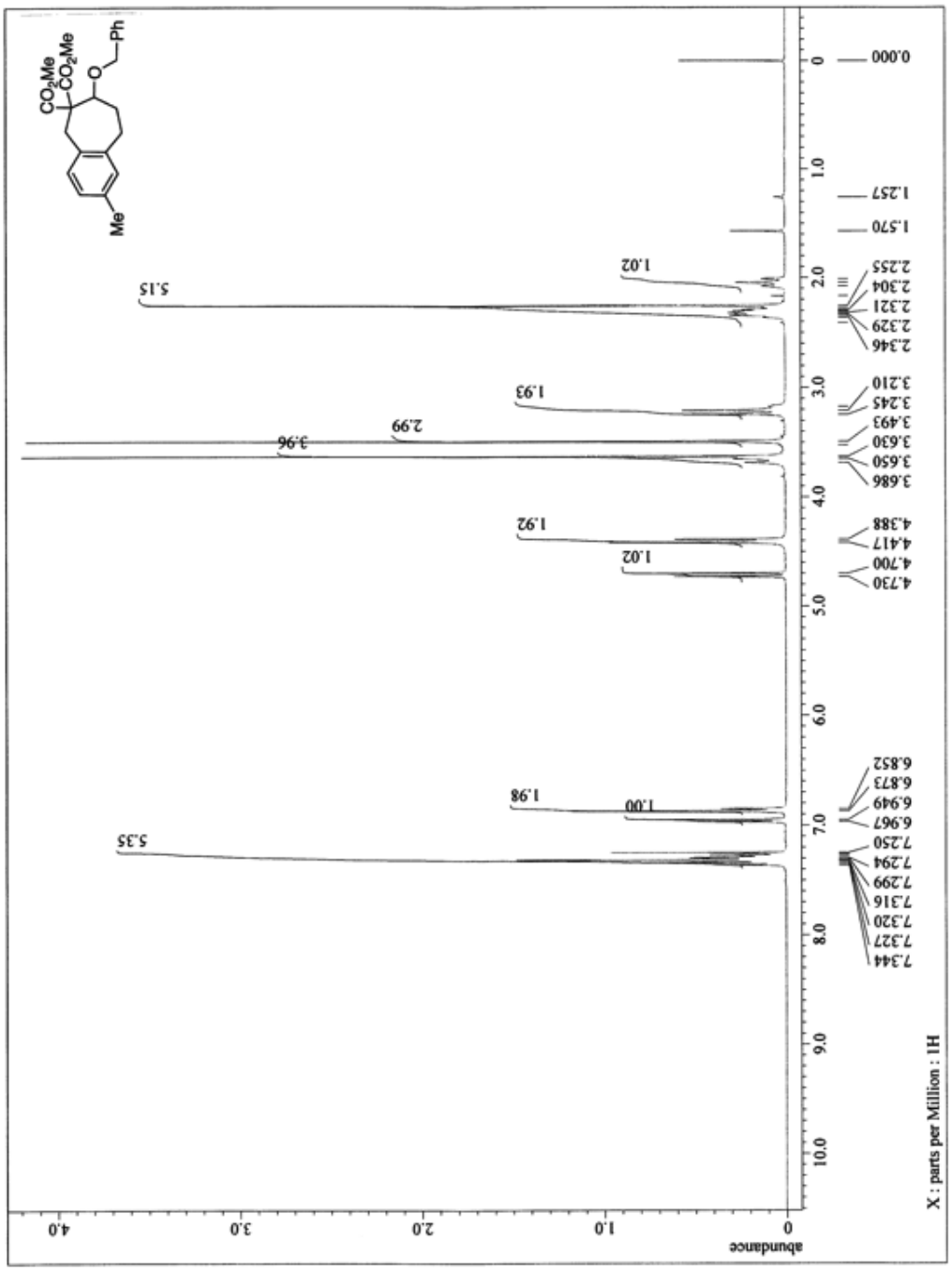
^{13}C NMR spectrum of **4d**.



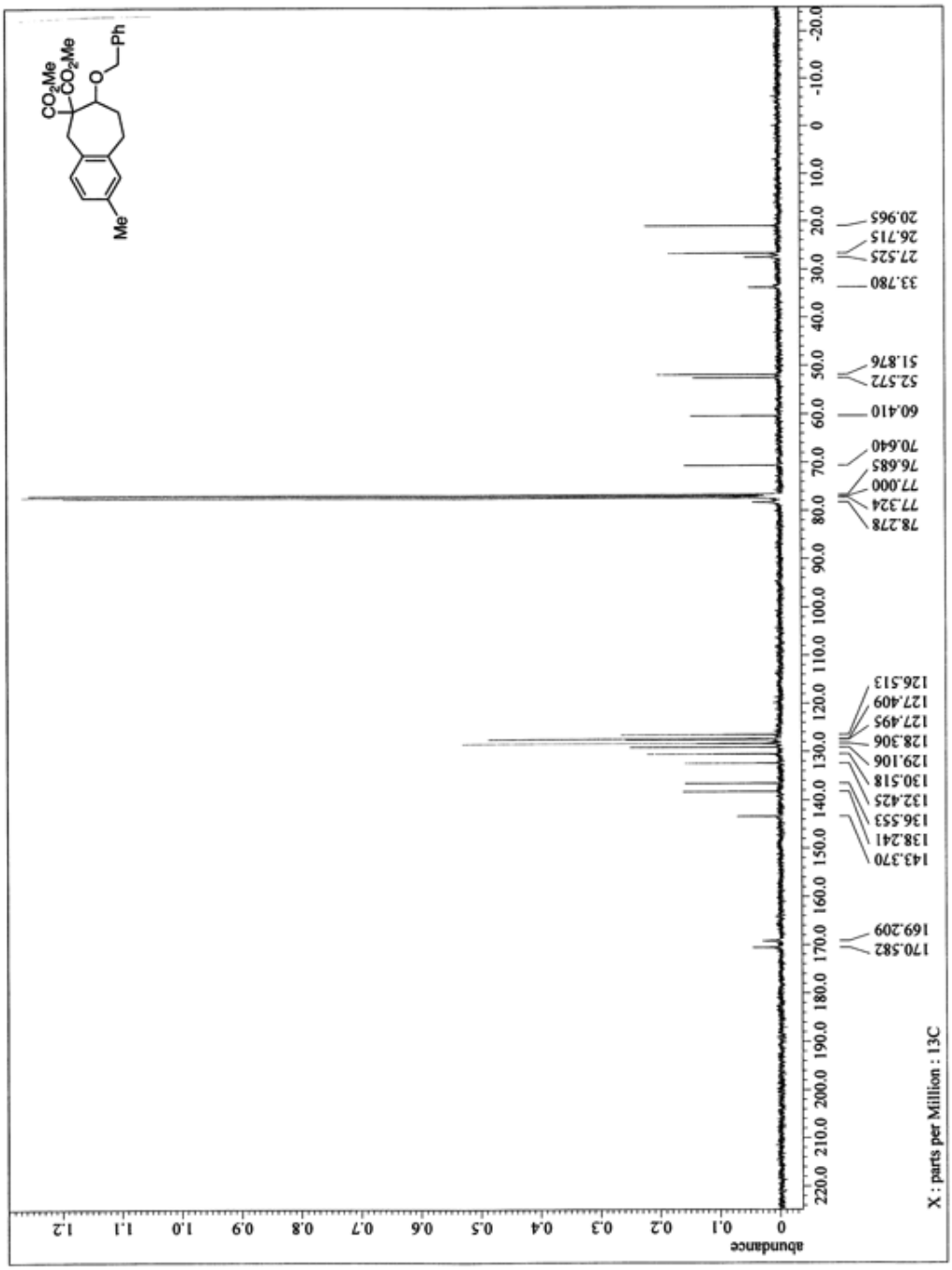
^{19}F NMR spectrum of **4d**.



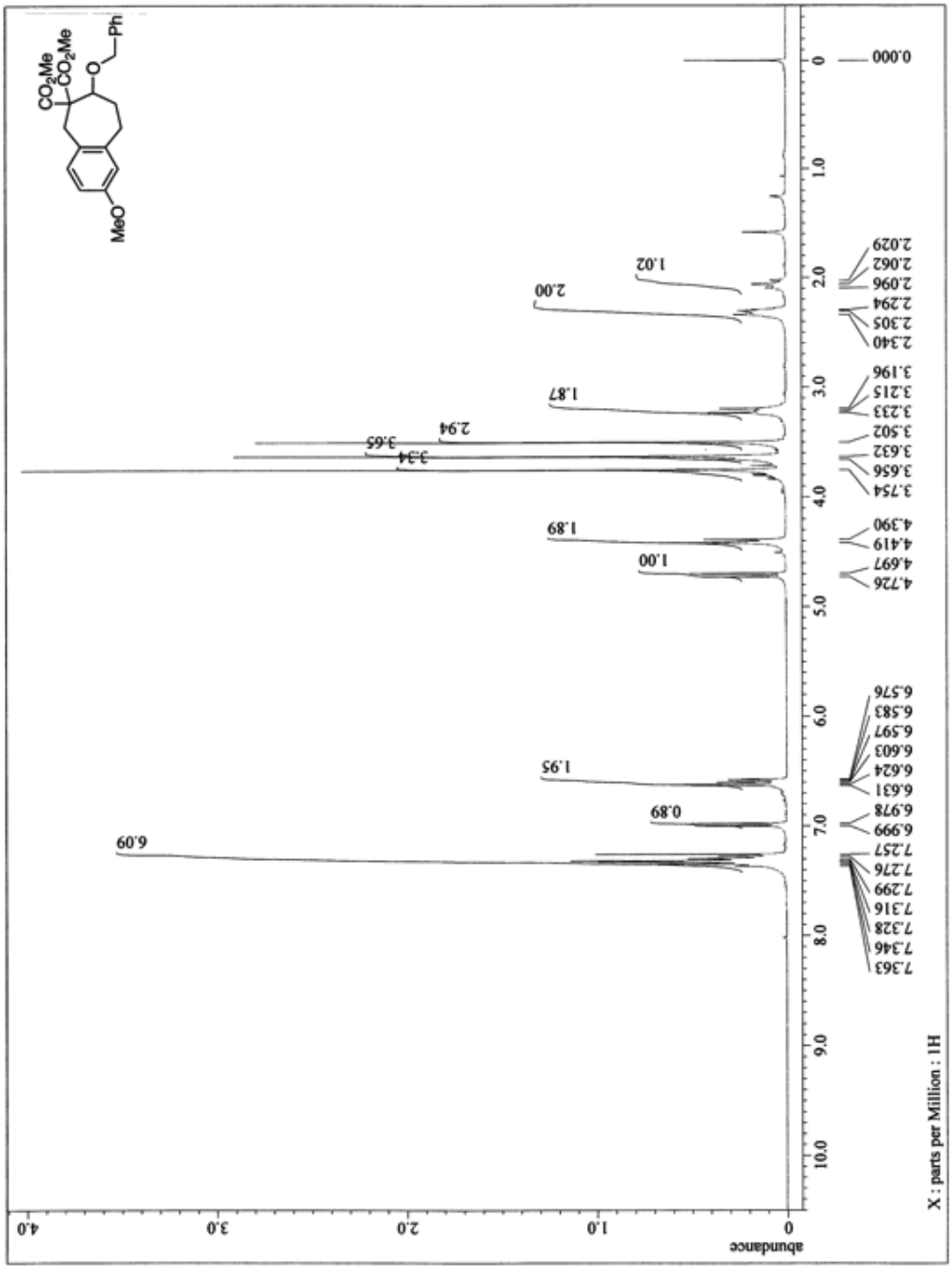
^{1}H NMR spectrum of **4e**.



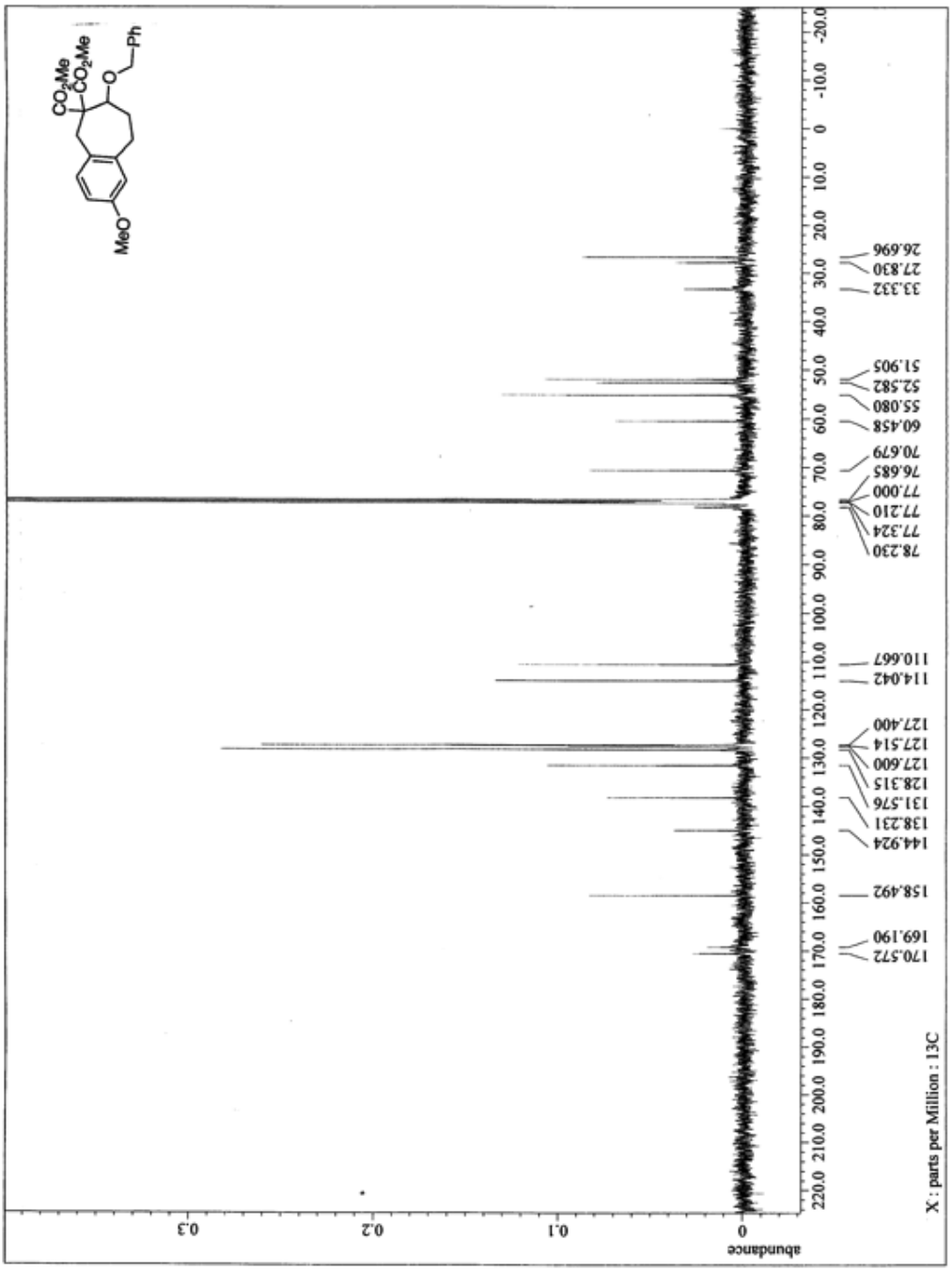
^{13}C NMR spectrum of **4e**.



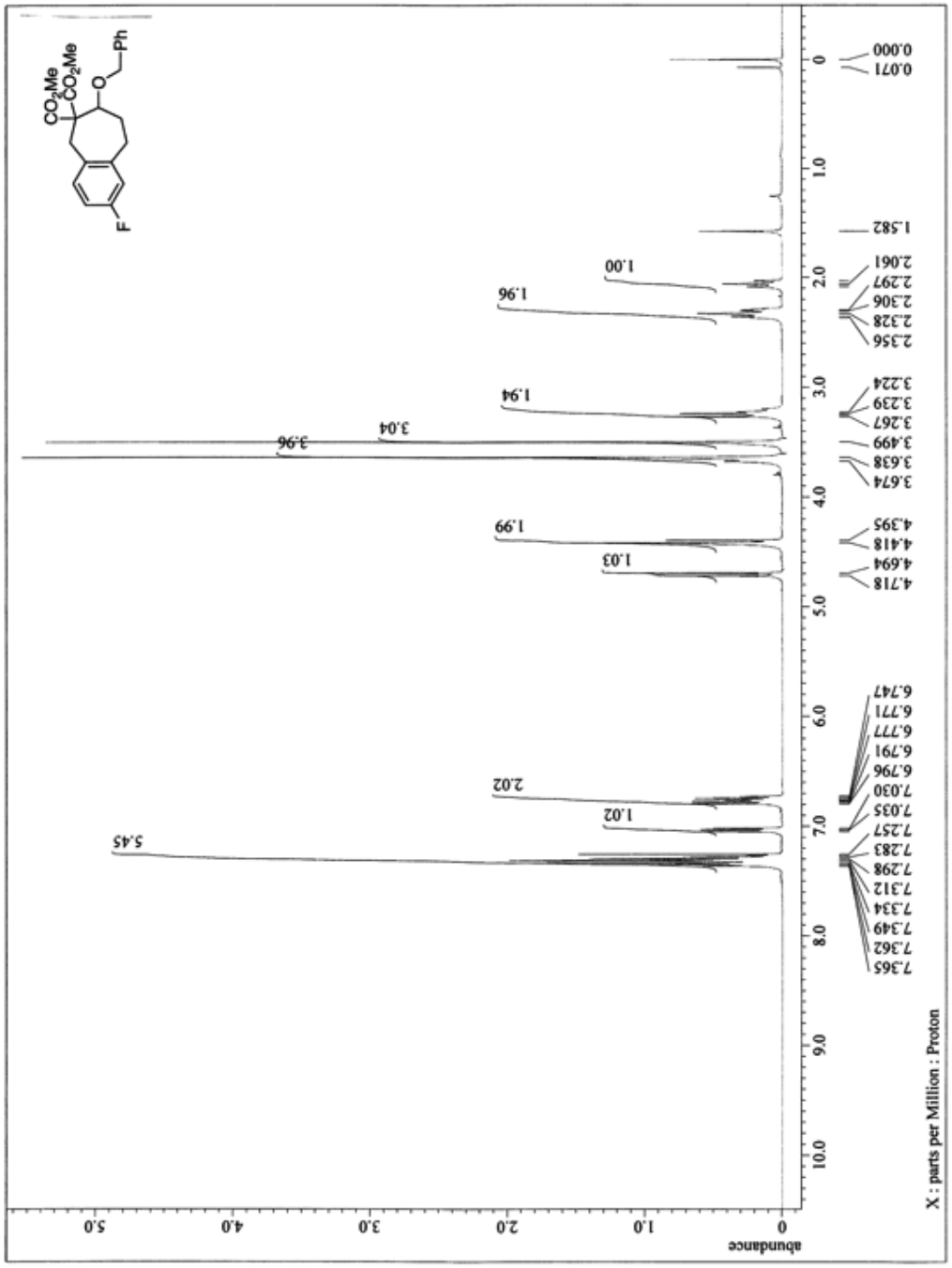
^{1}H NMR spectrum of **4f**.



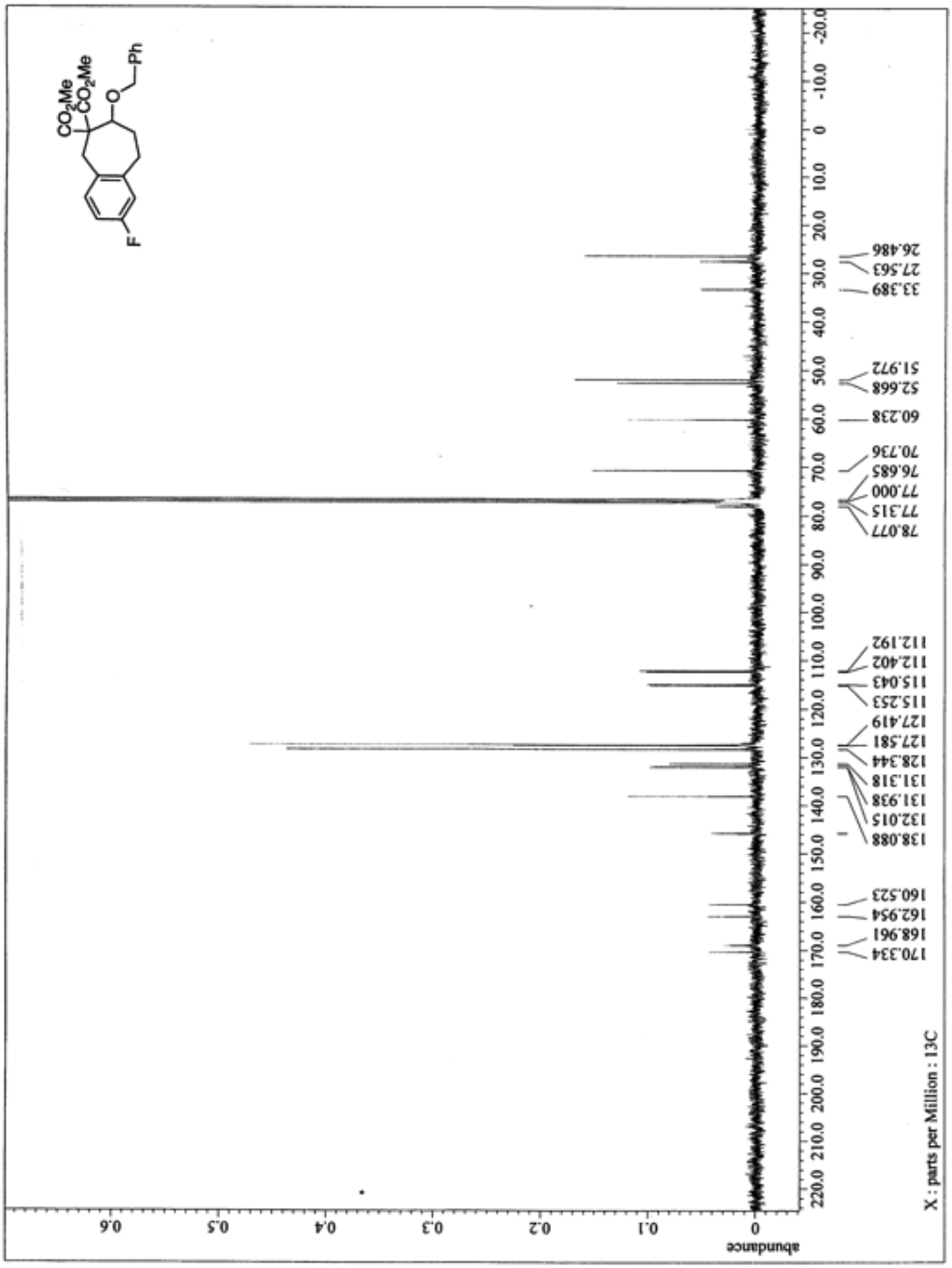
^{13}C NMR spectrum of **4f**.



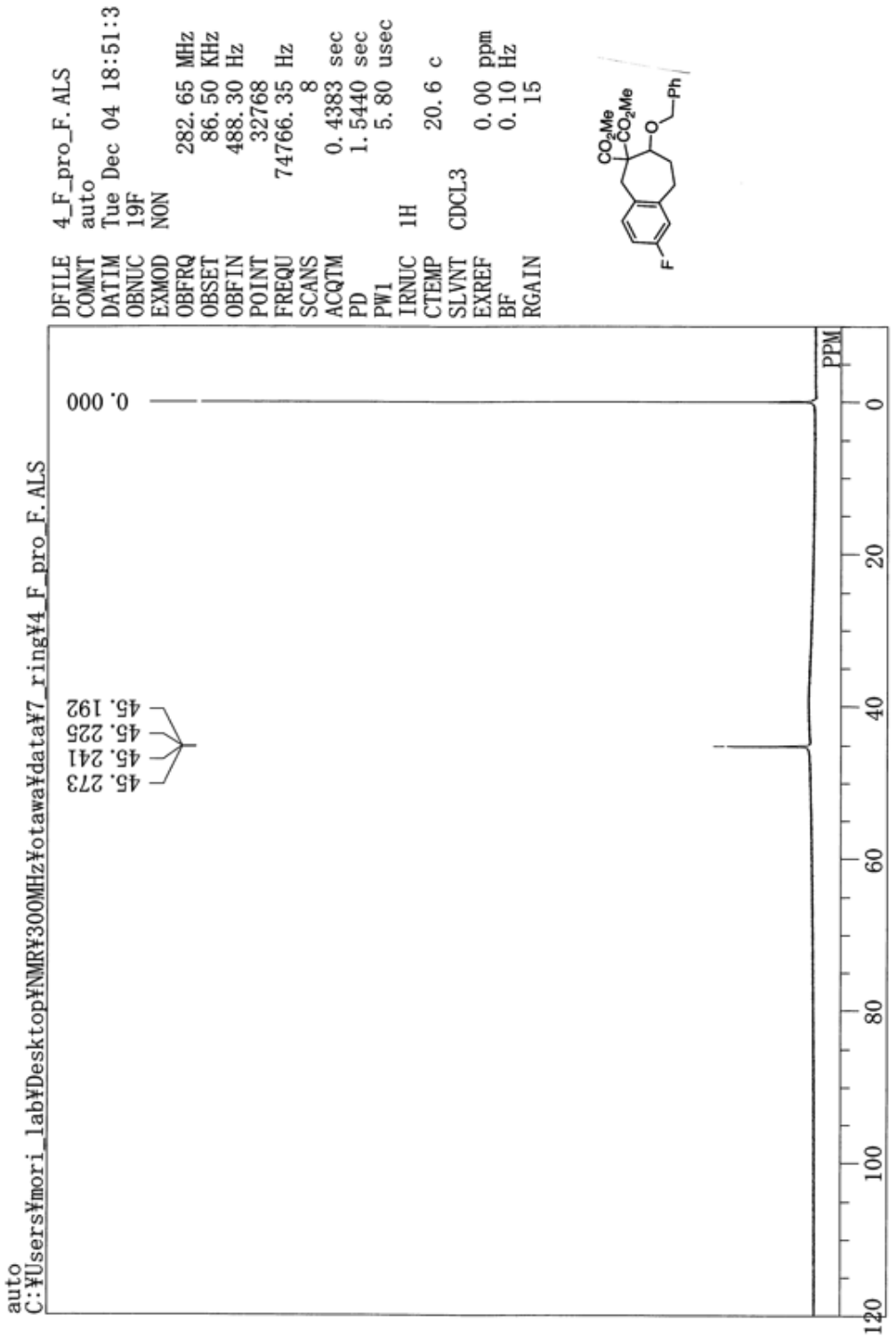
^{1}H NMR spectrum of **4g**.



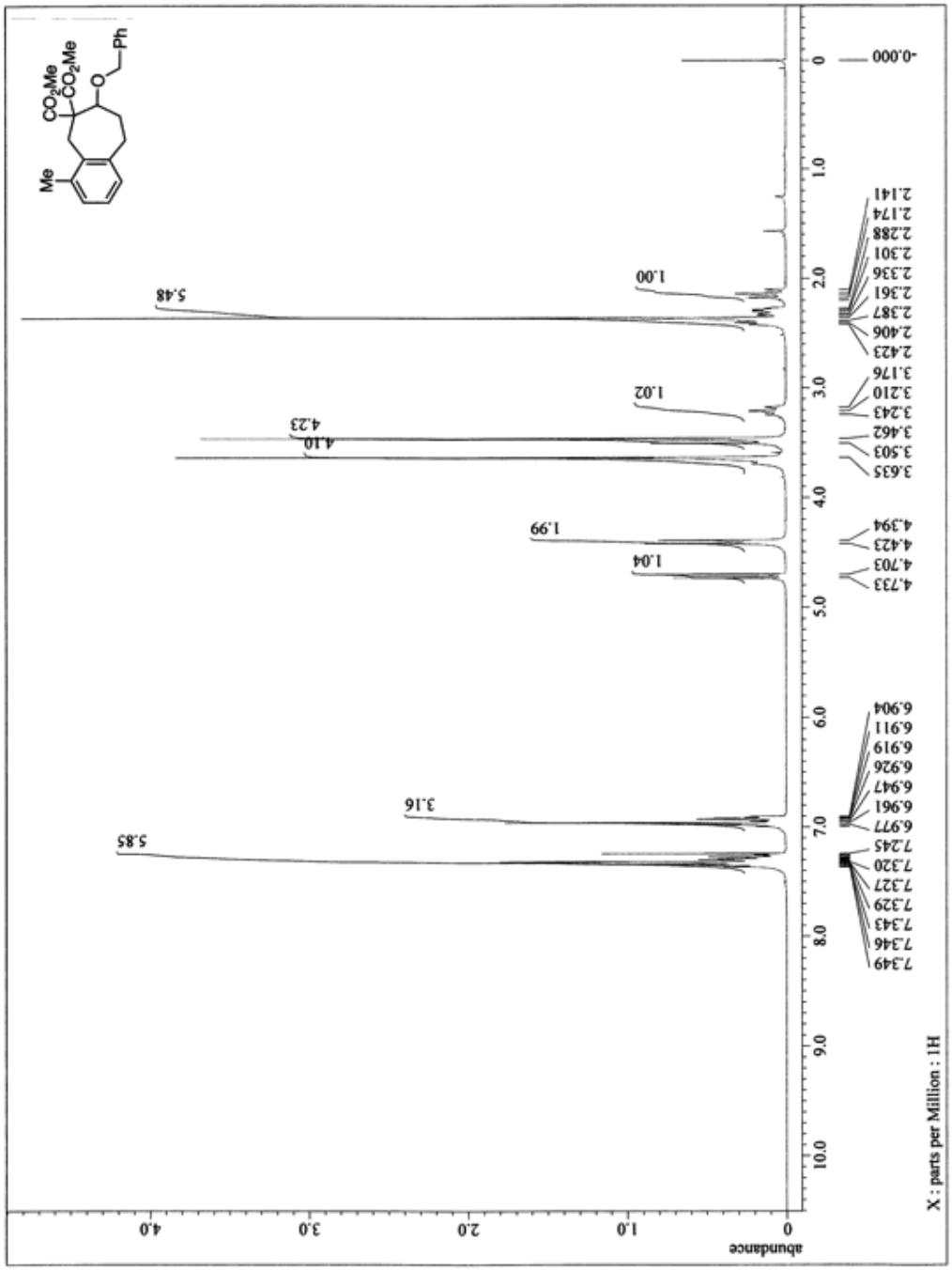
^{13}C NMR spectrum of **4g**.



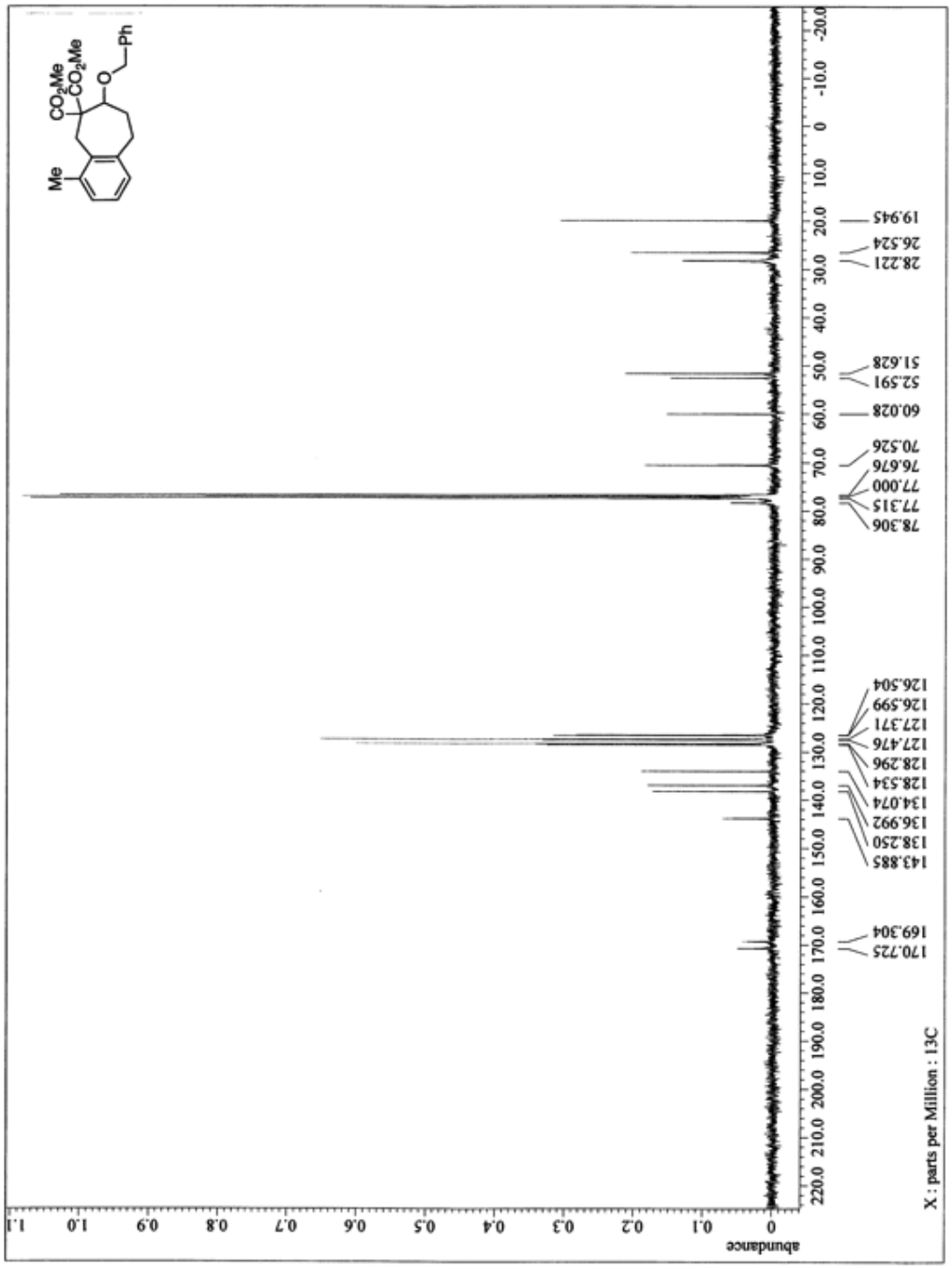
^{19}F NMR spectrum of **4g**.



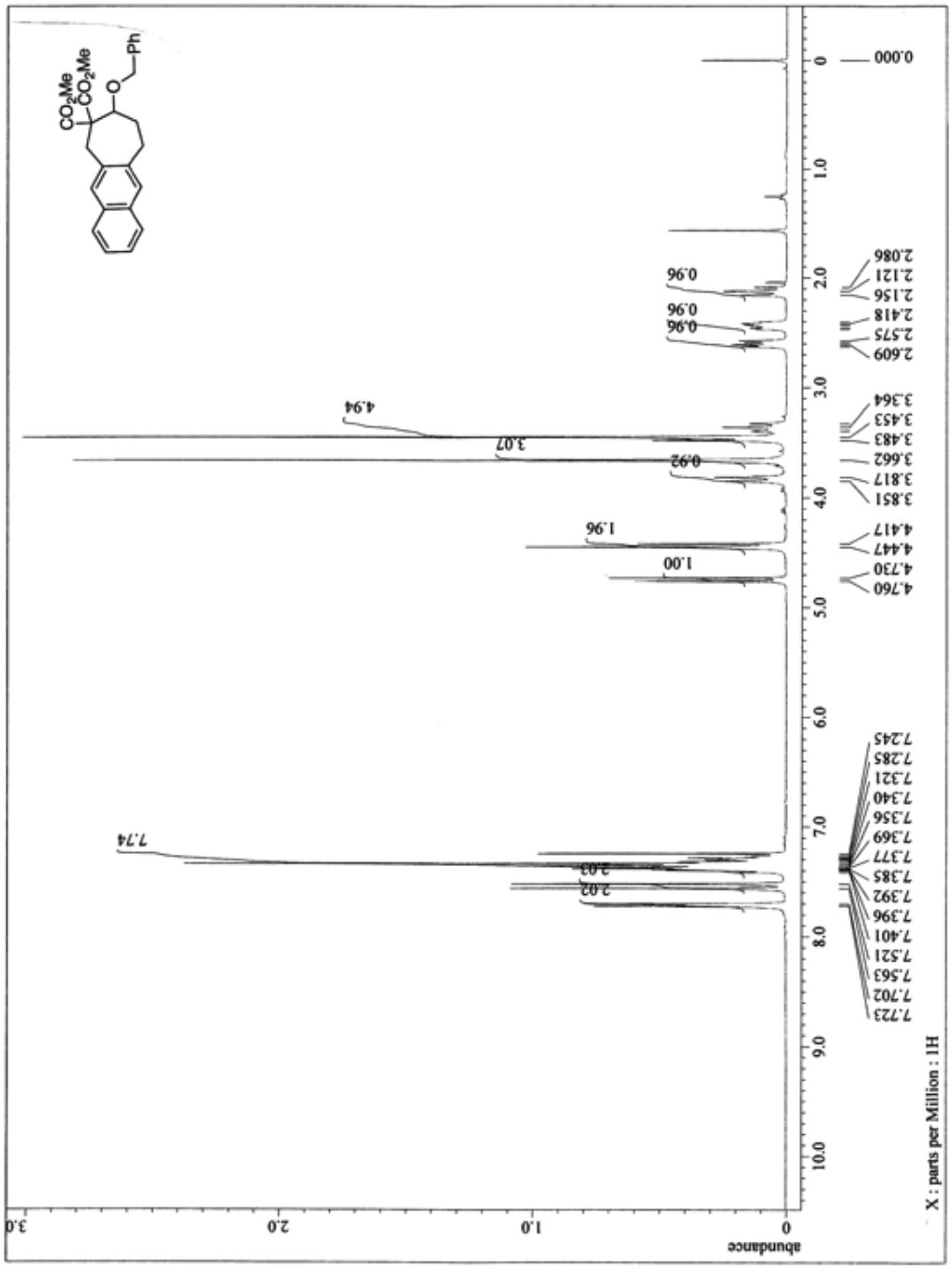
^{1}H NMR spectrum of **4h**.



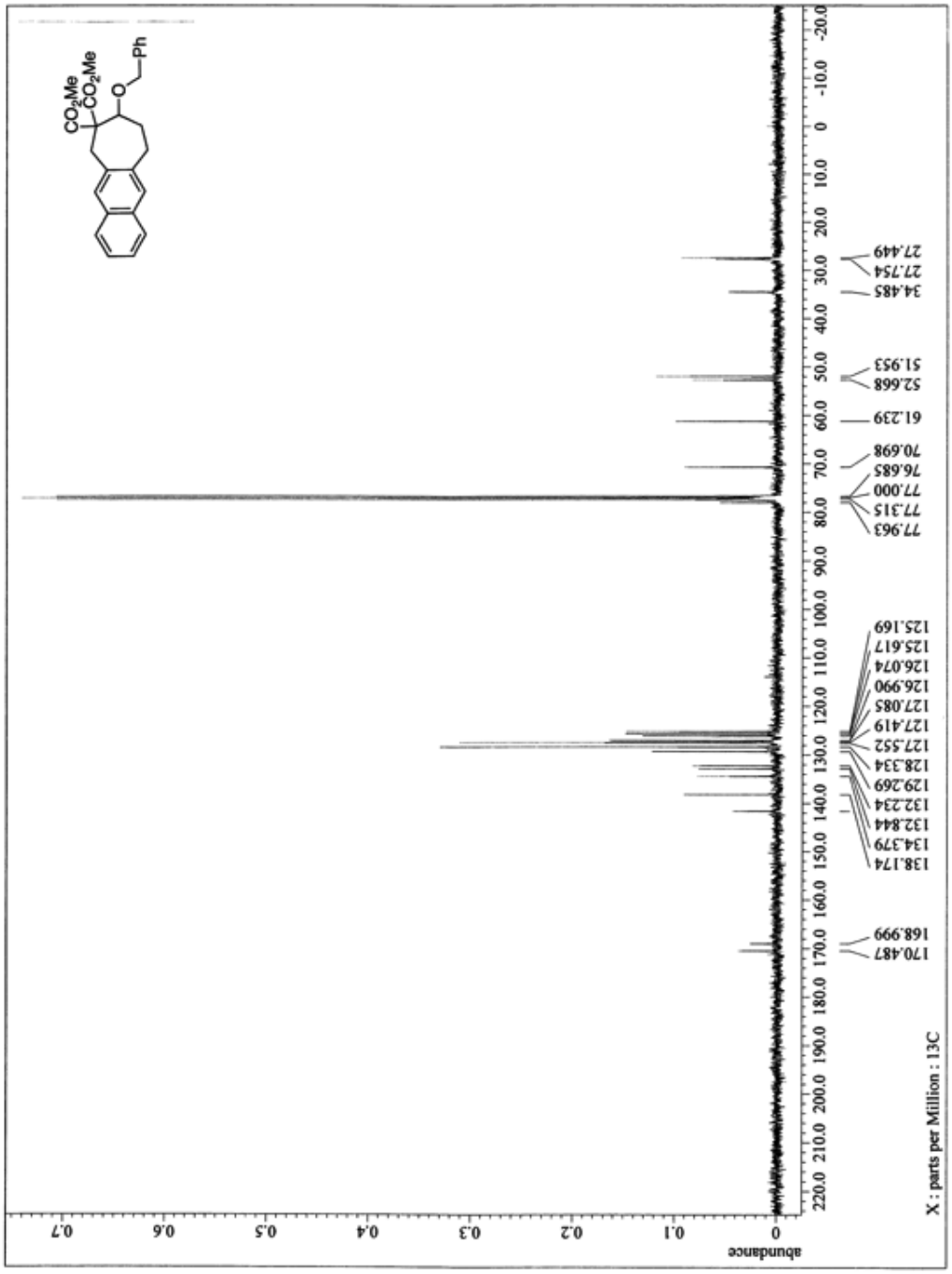
^{13}C NMR spectrum of **4h**.



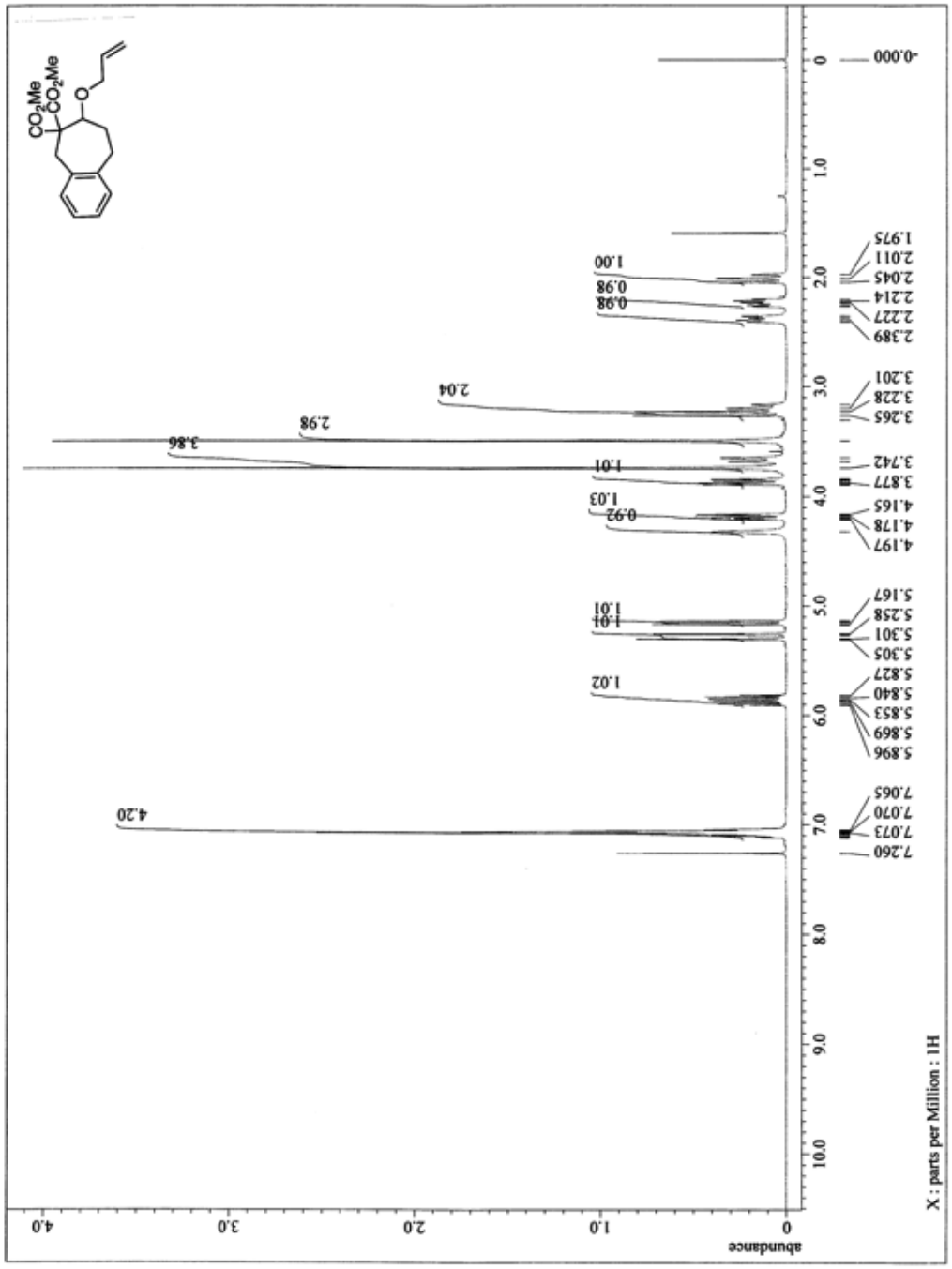
^{1}H NMR spectrum of **4i**.



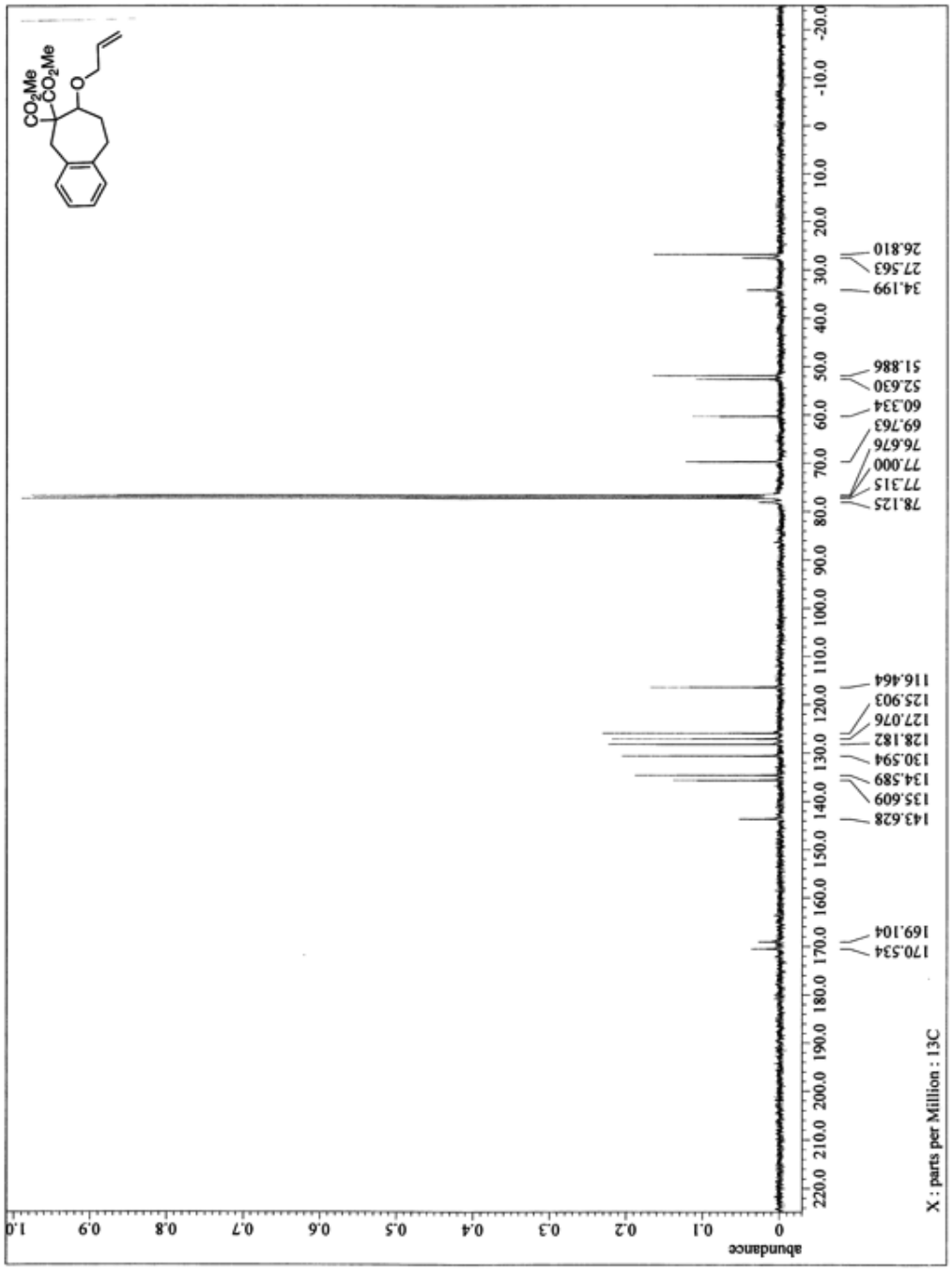
^{13}C NMR spectrum of **4i**.



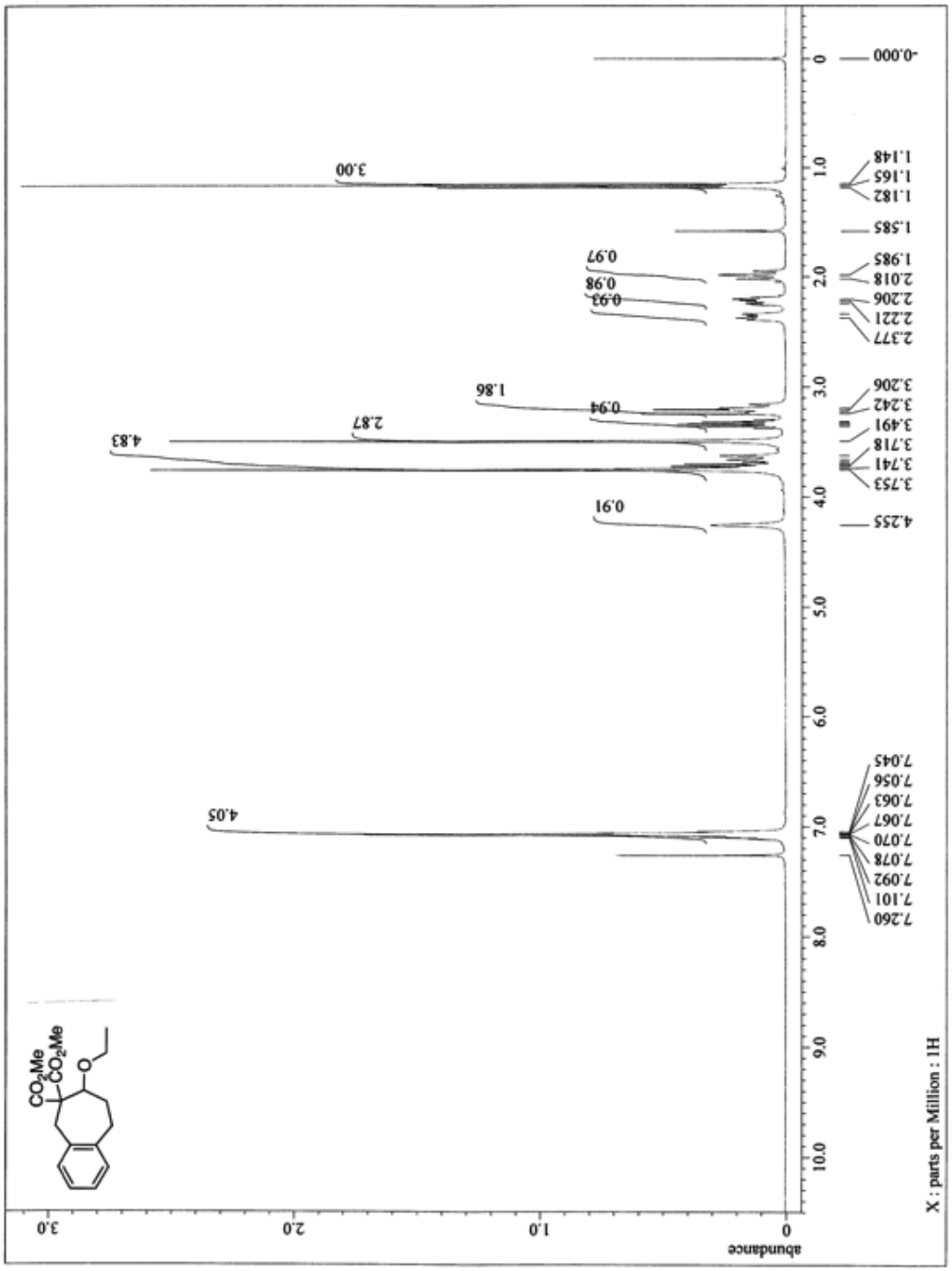
^{1}H NMR spectrum of **4j**.



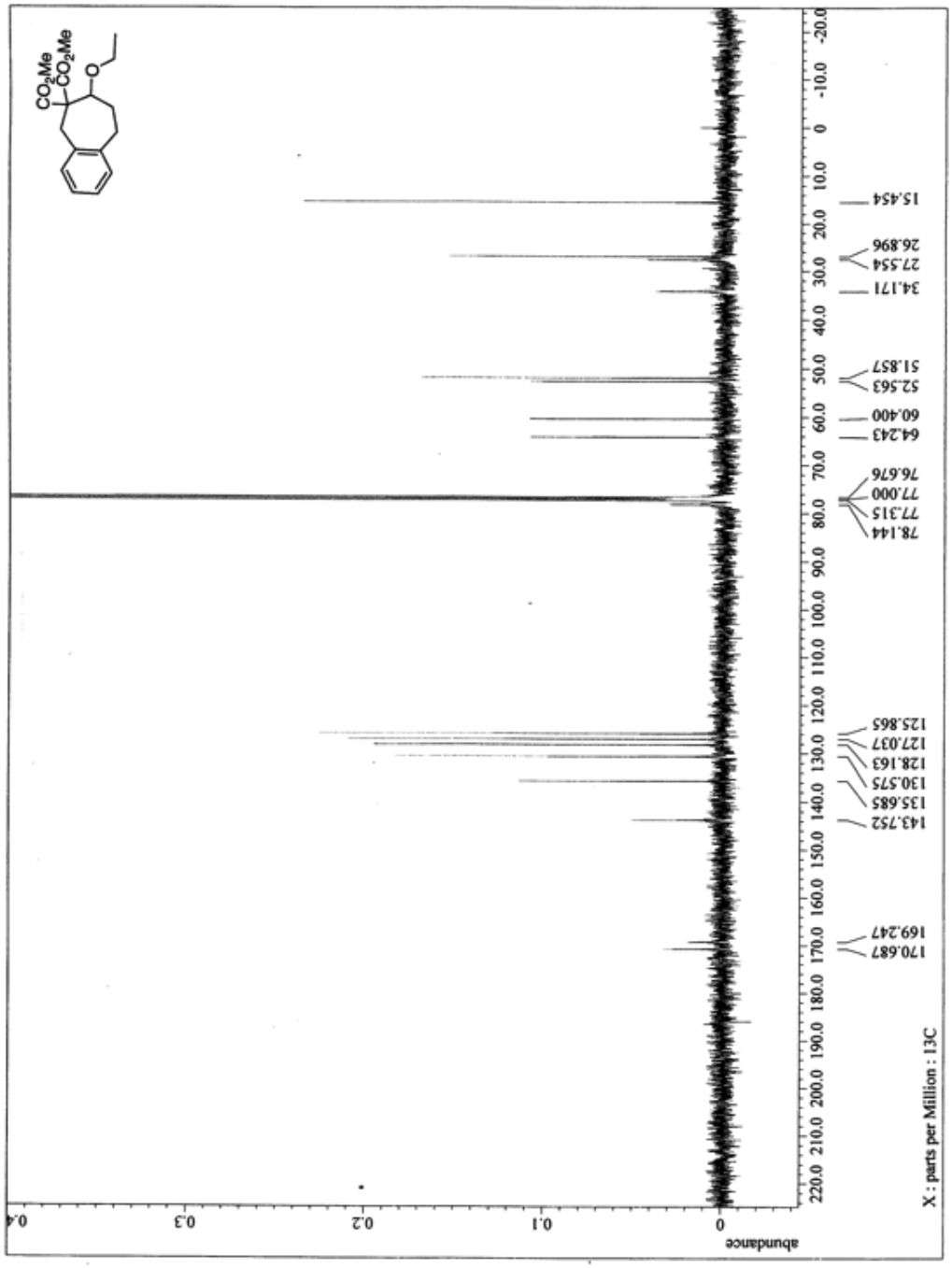
^{13}C NMR spectrum of **4j**.



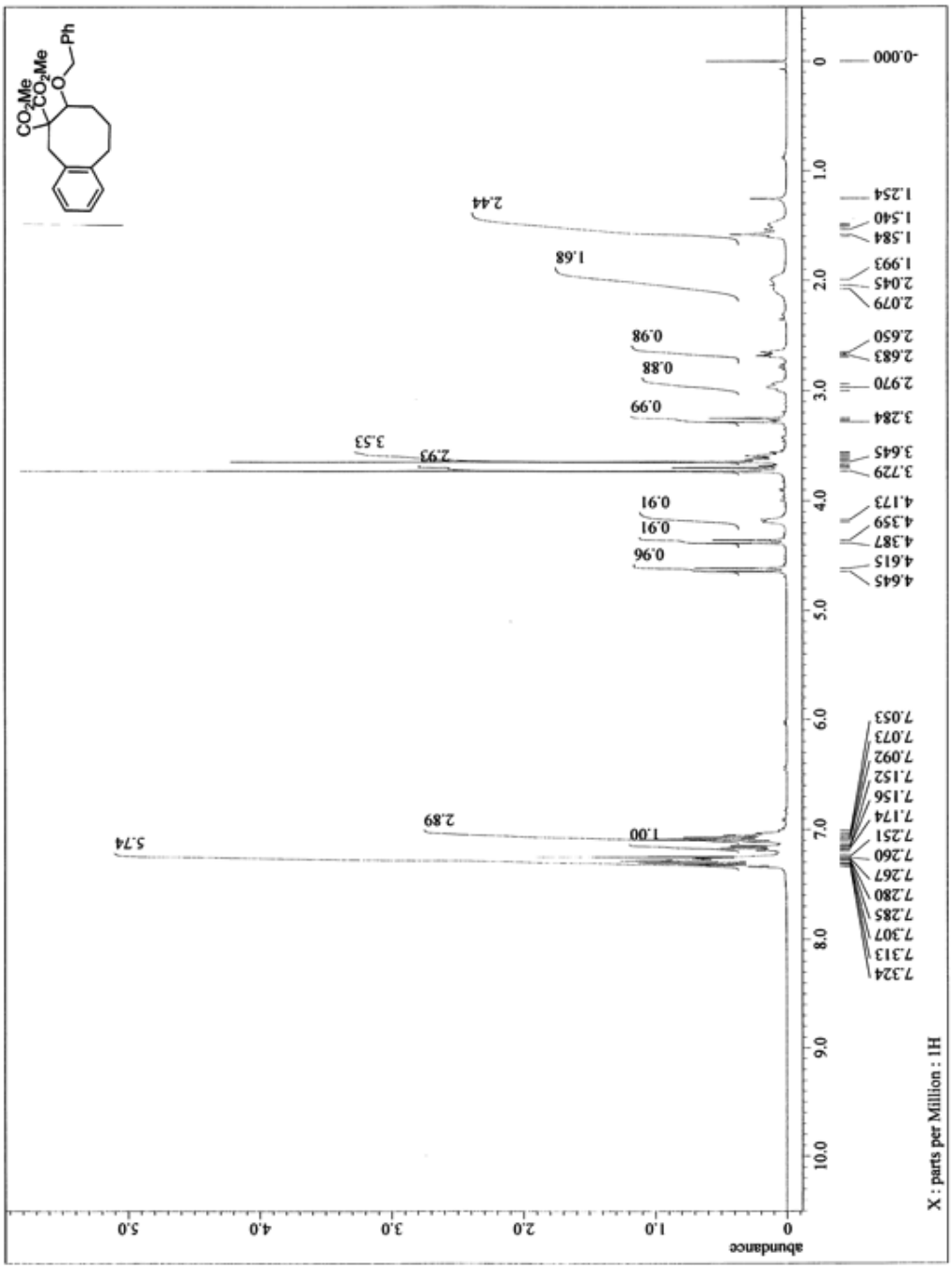
^{1}H NMR spectrum of **4k**.



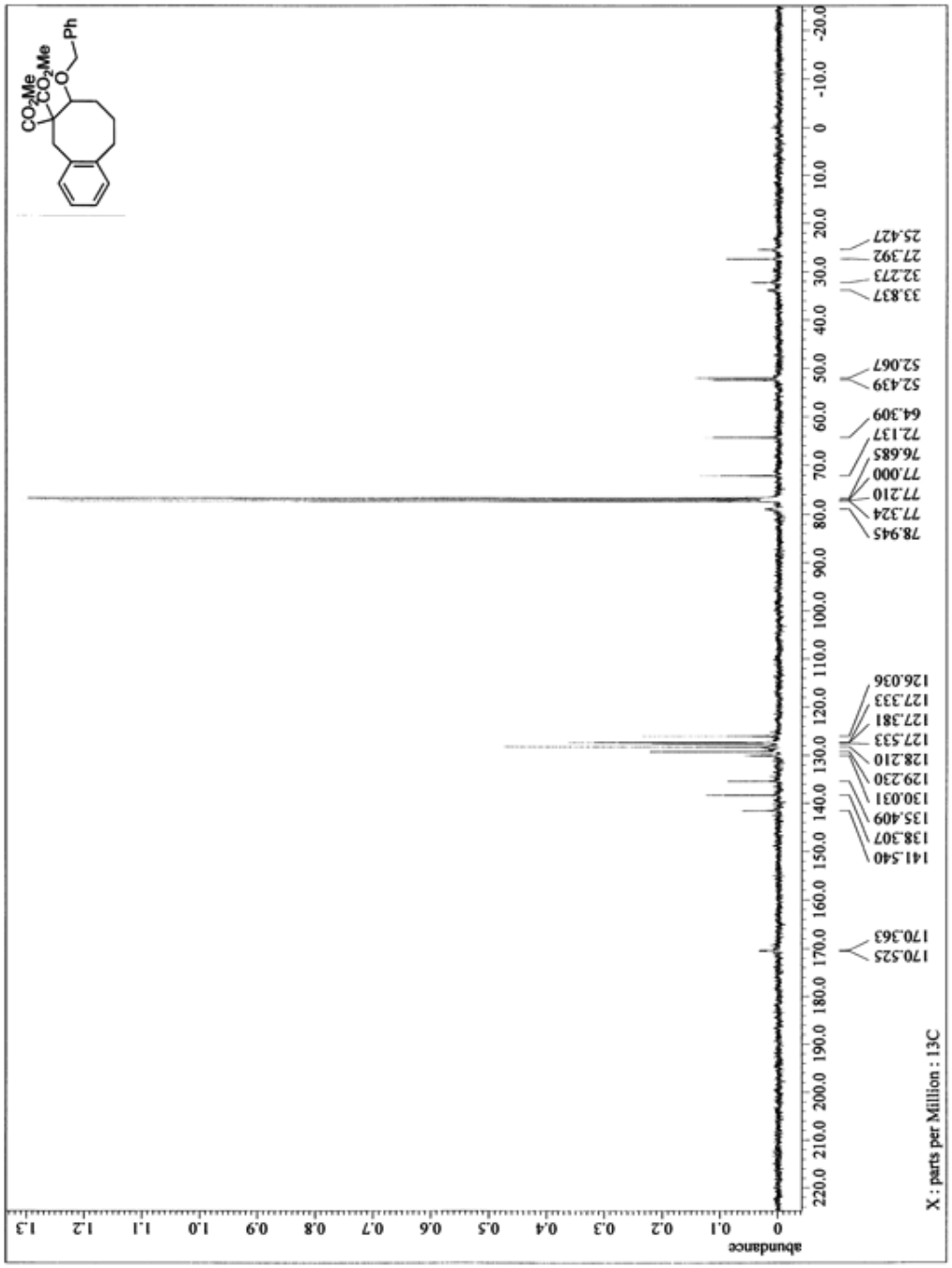
^{13}C NMR spectrum of **4k**.



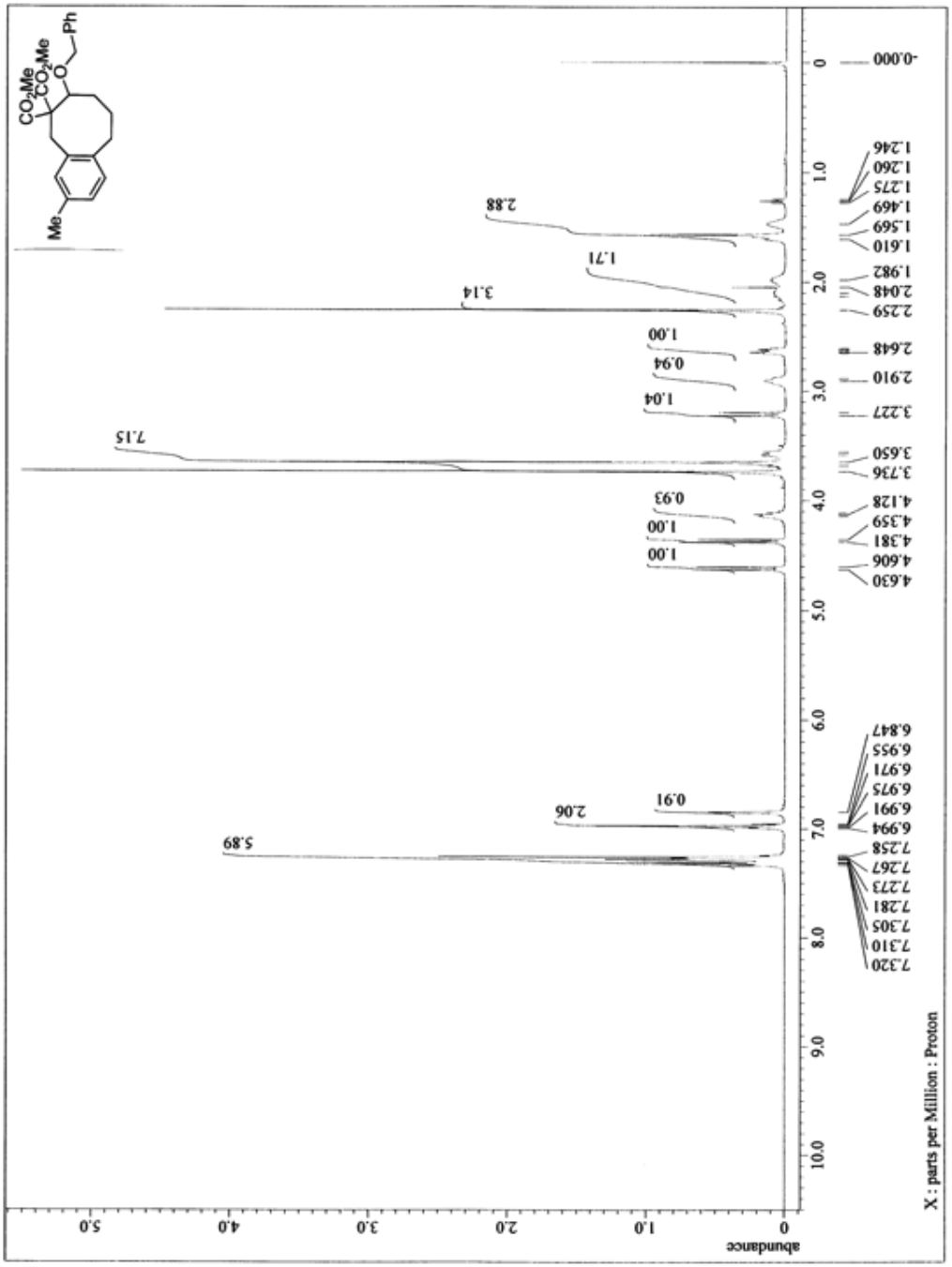
^{1}H NMR spectrum of **6a**.



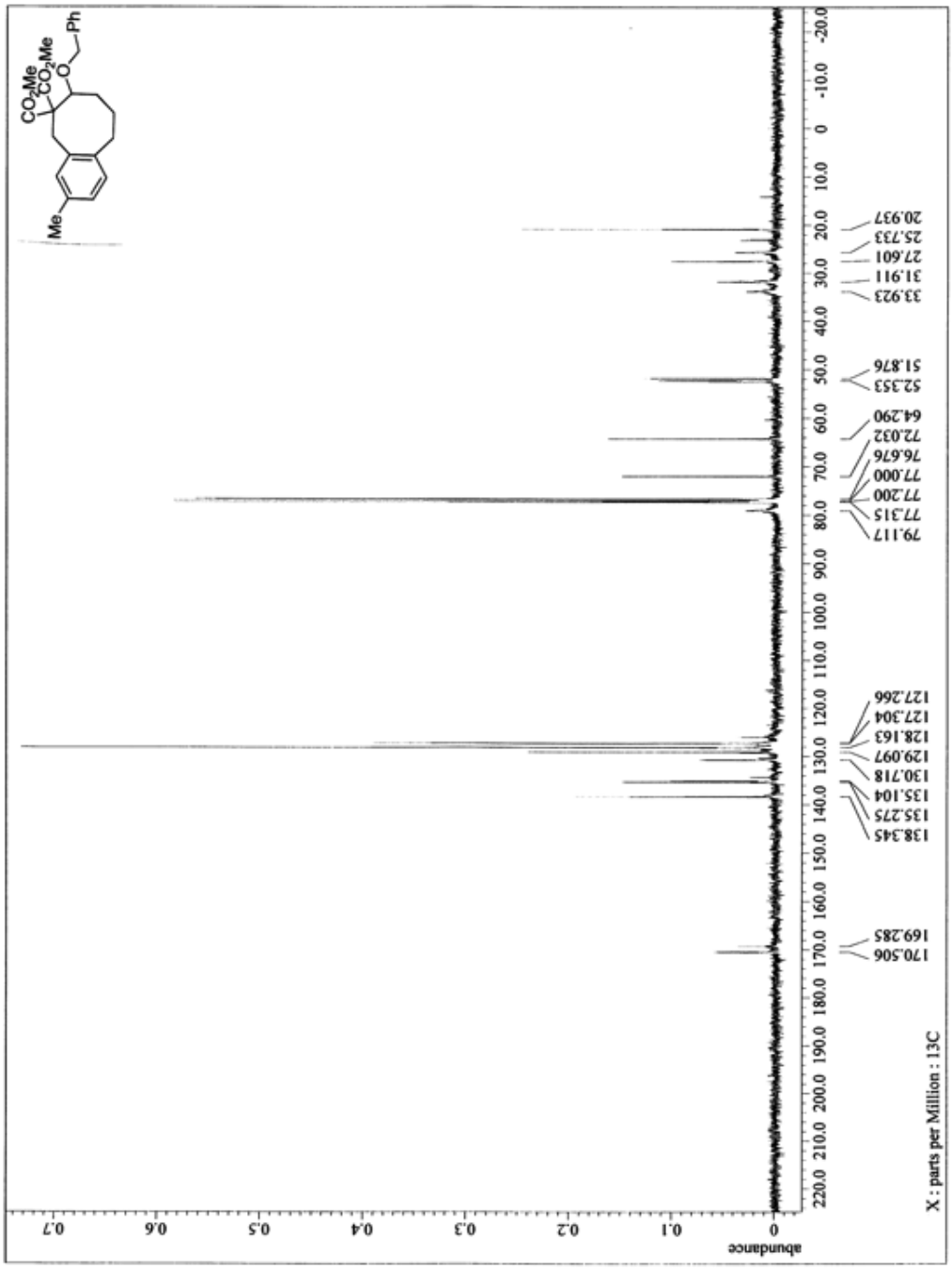
^{13}C NMR spectrum of **6a**.



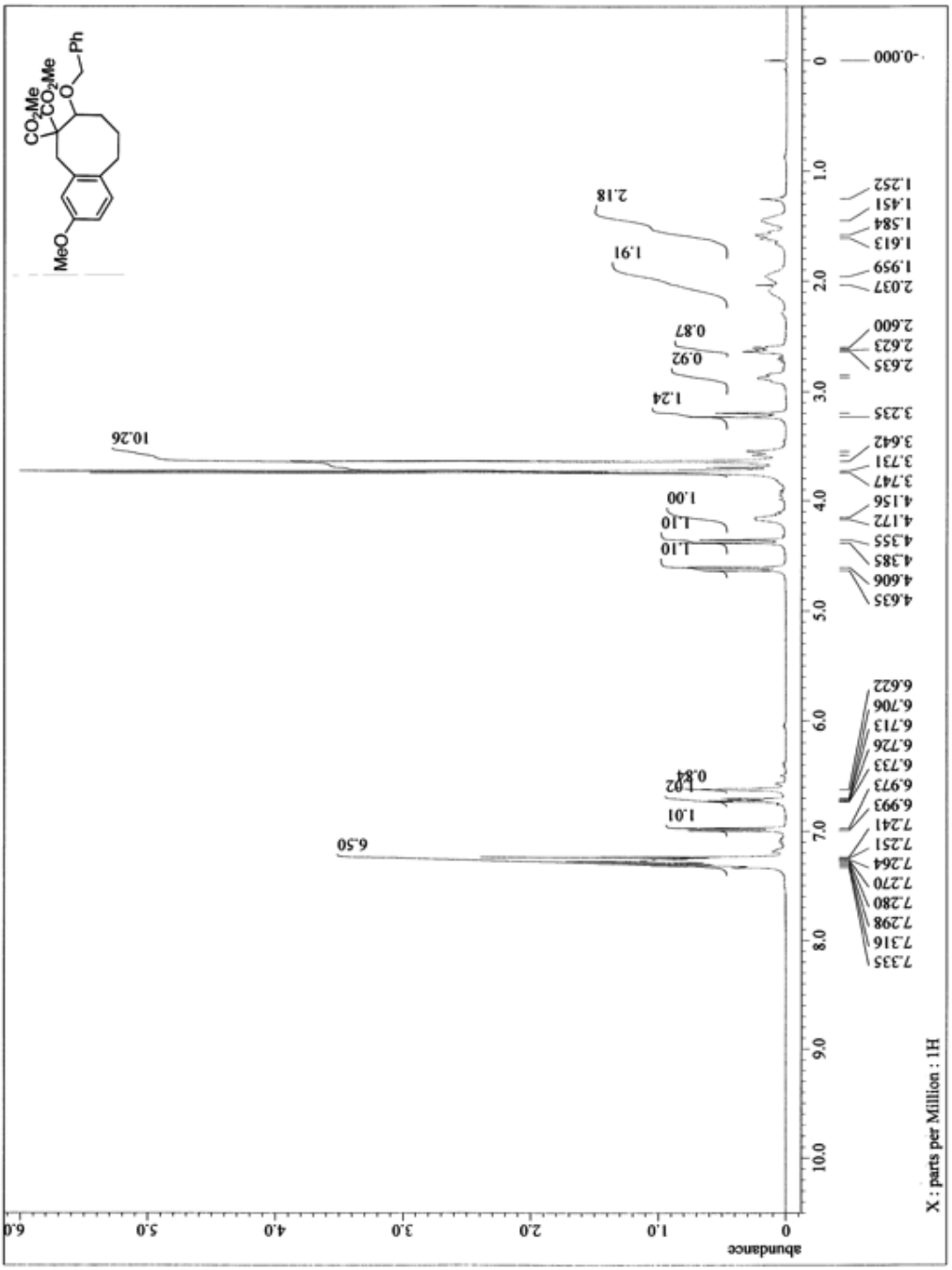
^{1}H NMR spectrum of **6b**.



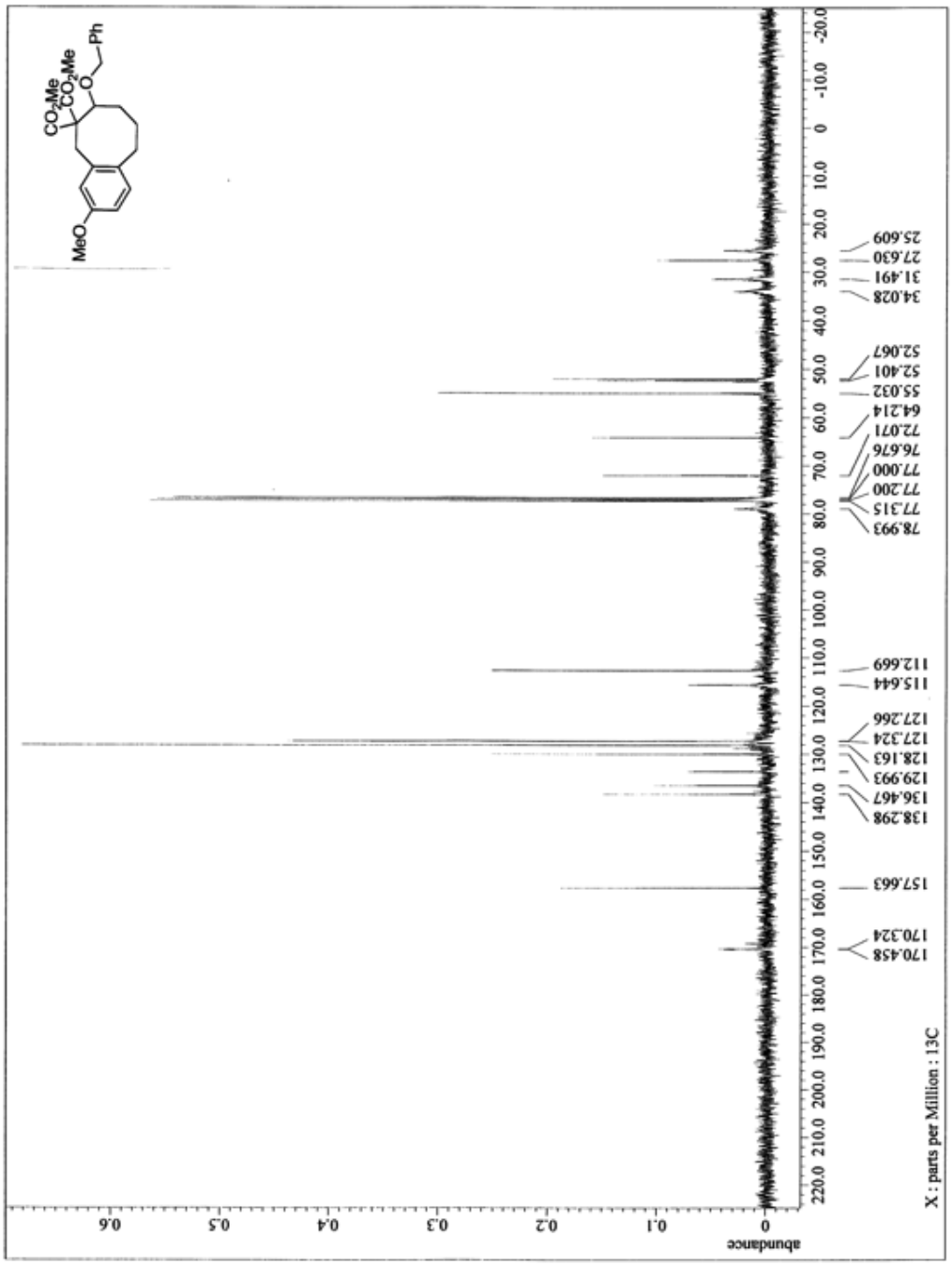
^{13}C NMR spectrum of **6b**.



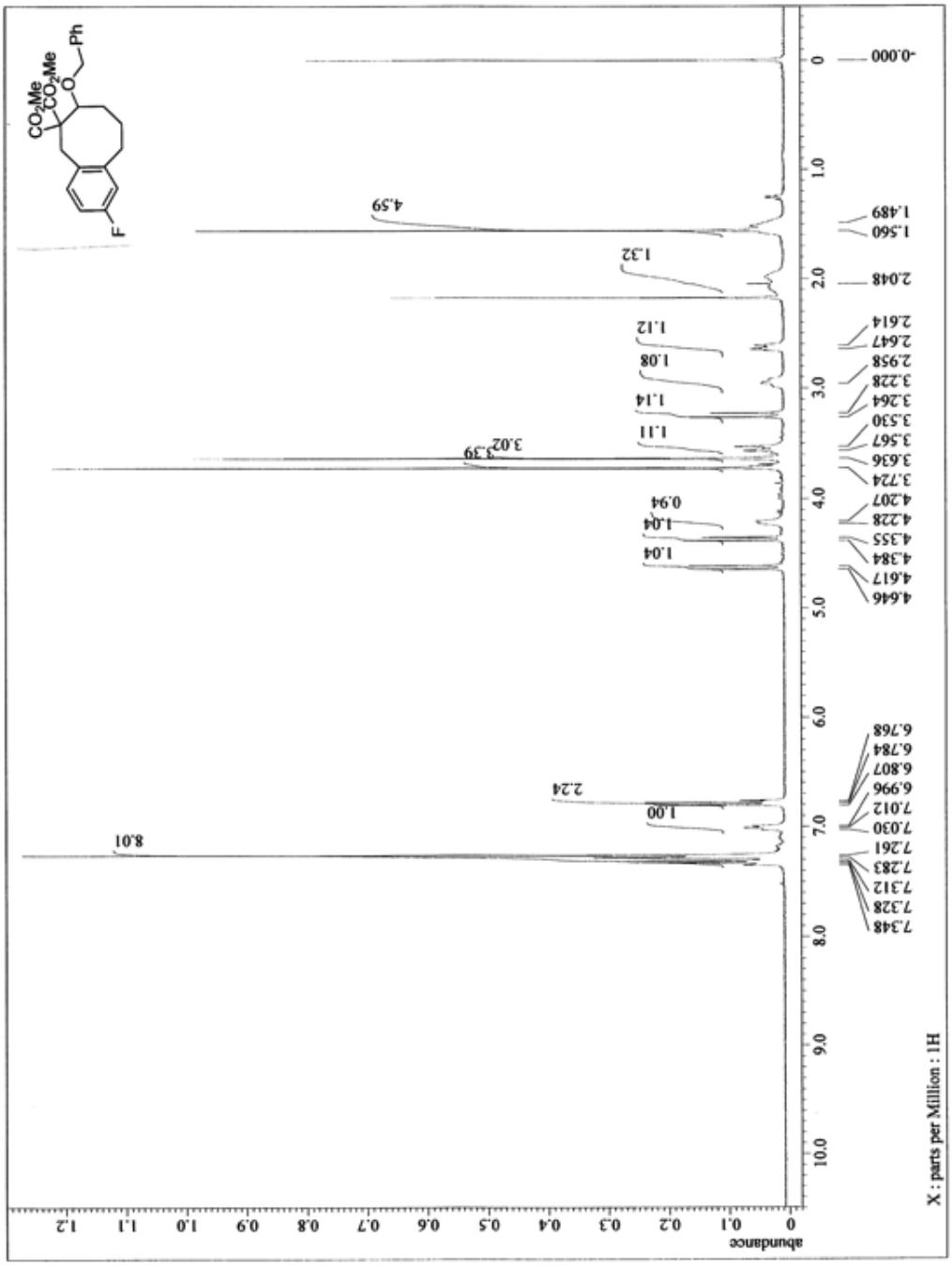
^{1}H NMR spectrum of **6c**.



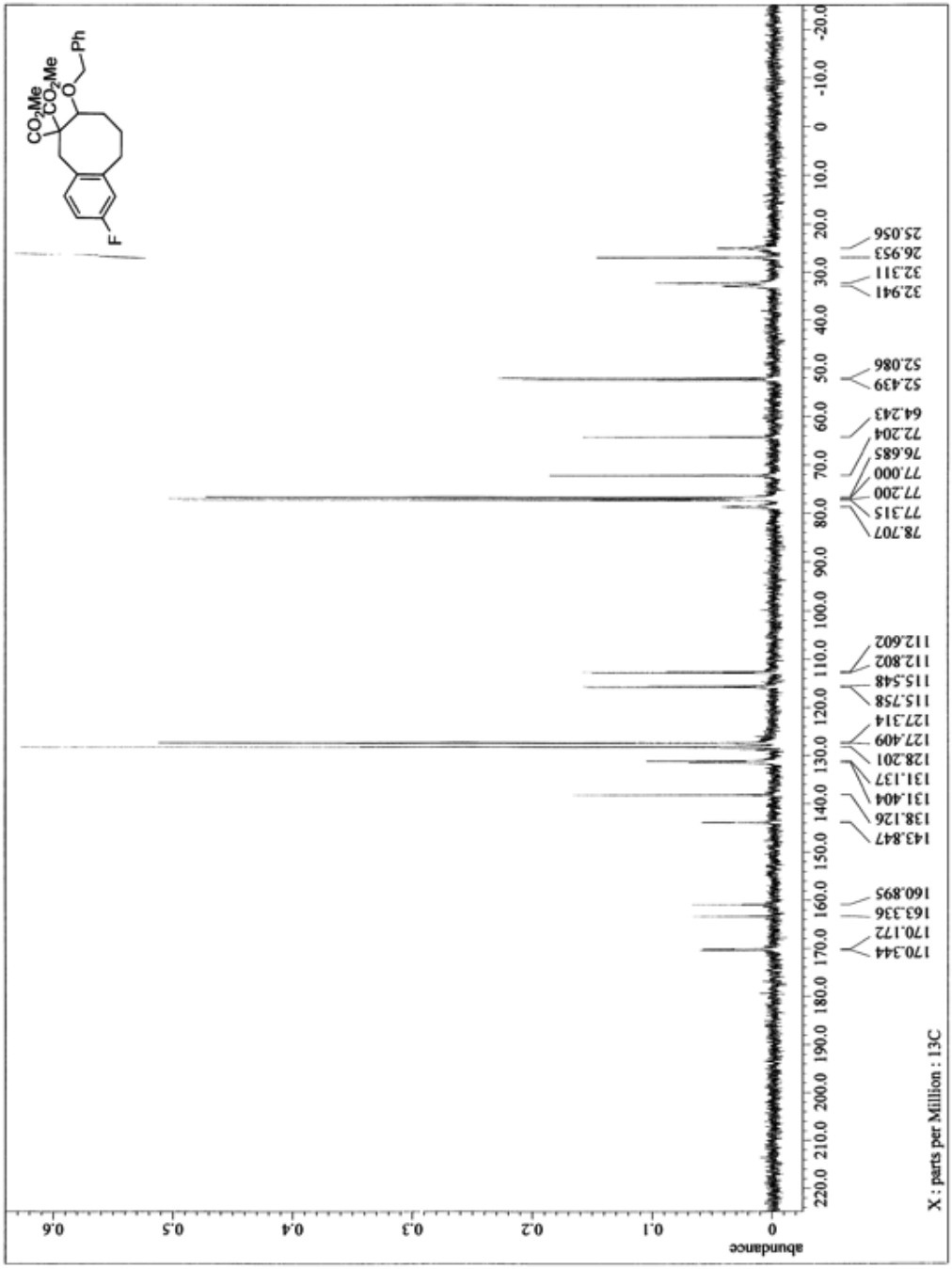
^{13}C NMR spectrum of **6c**.



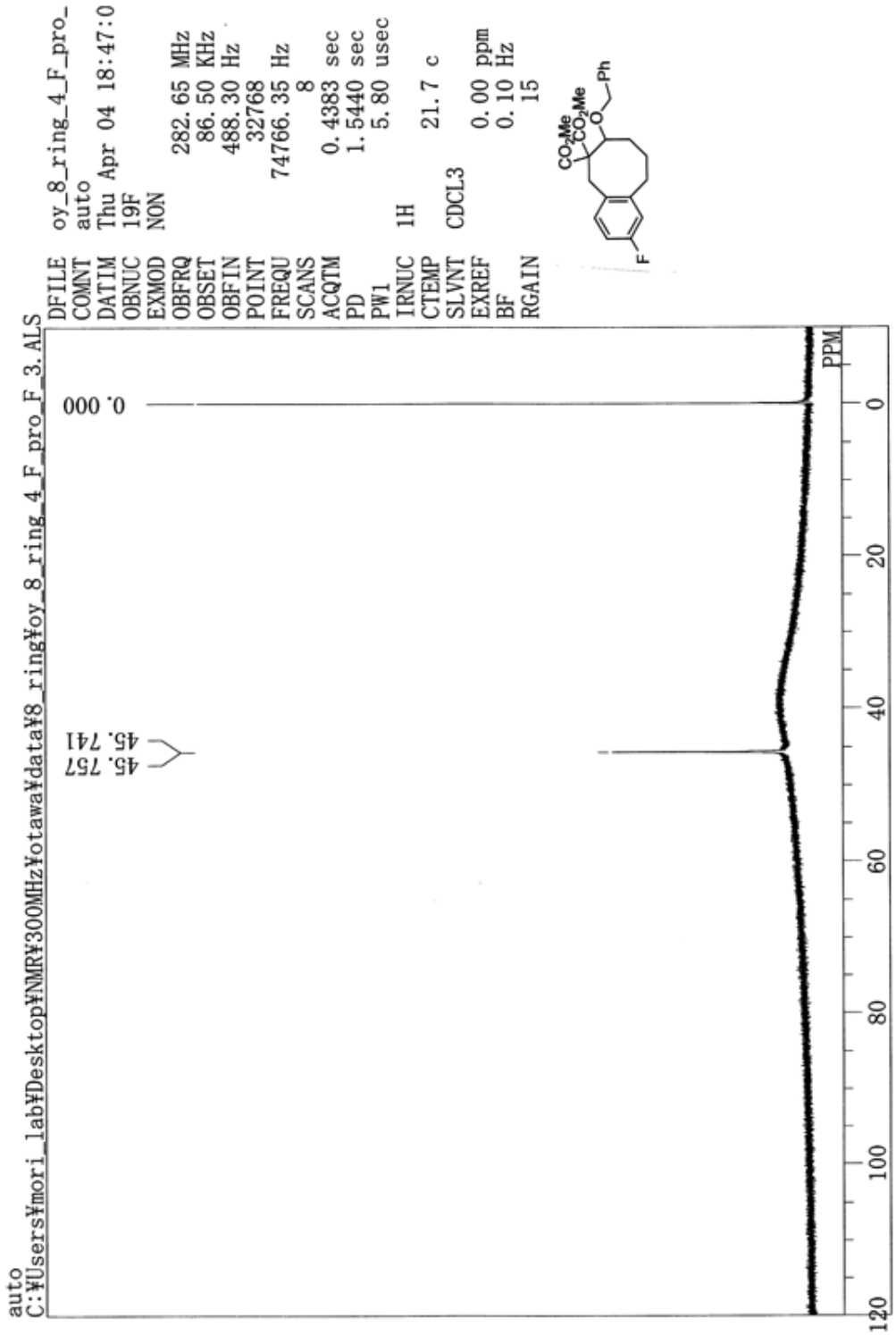
^{1}H NMR spectrum of **6d**.



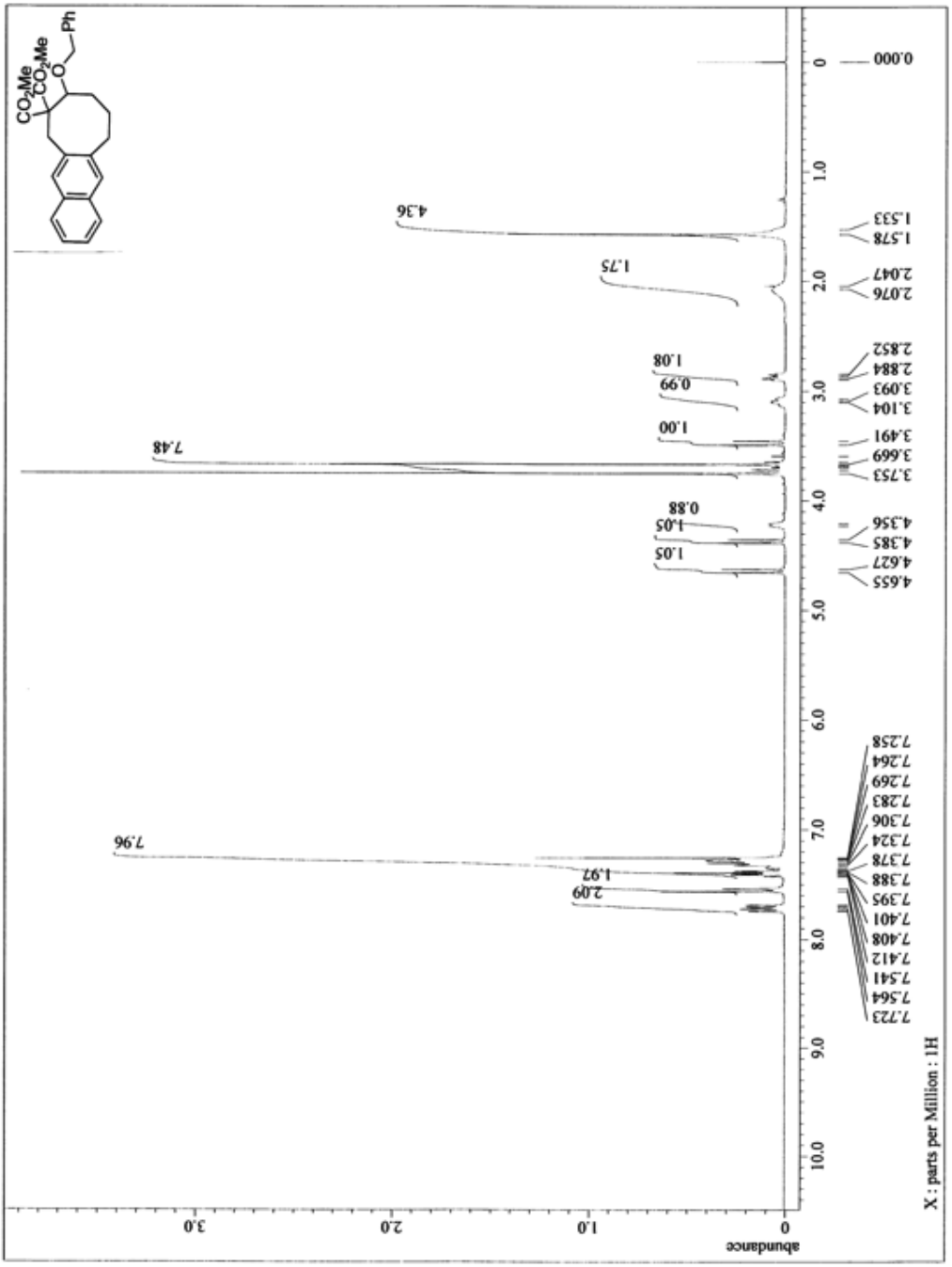
^{13}C NMR spectrum of **6d**.



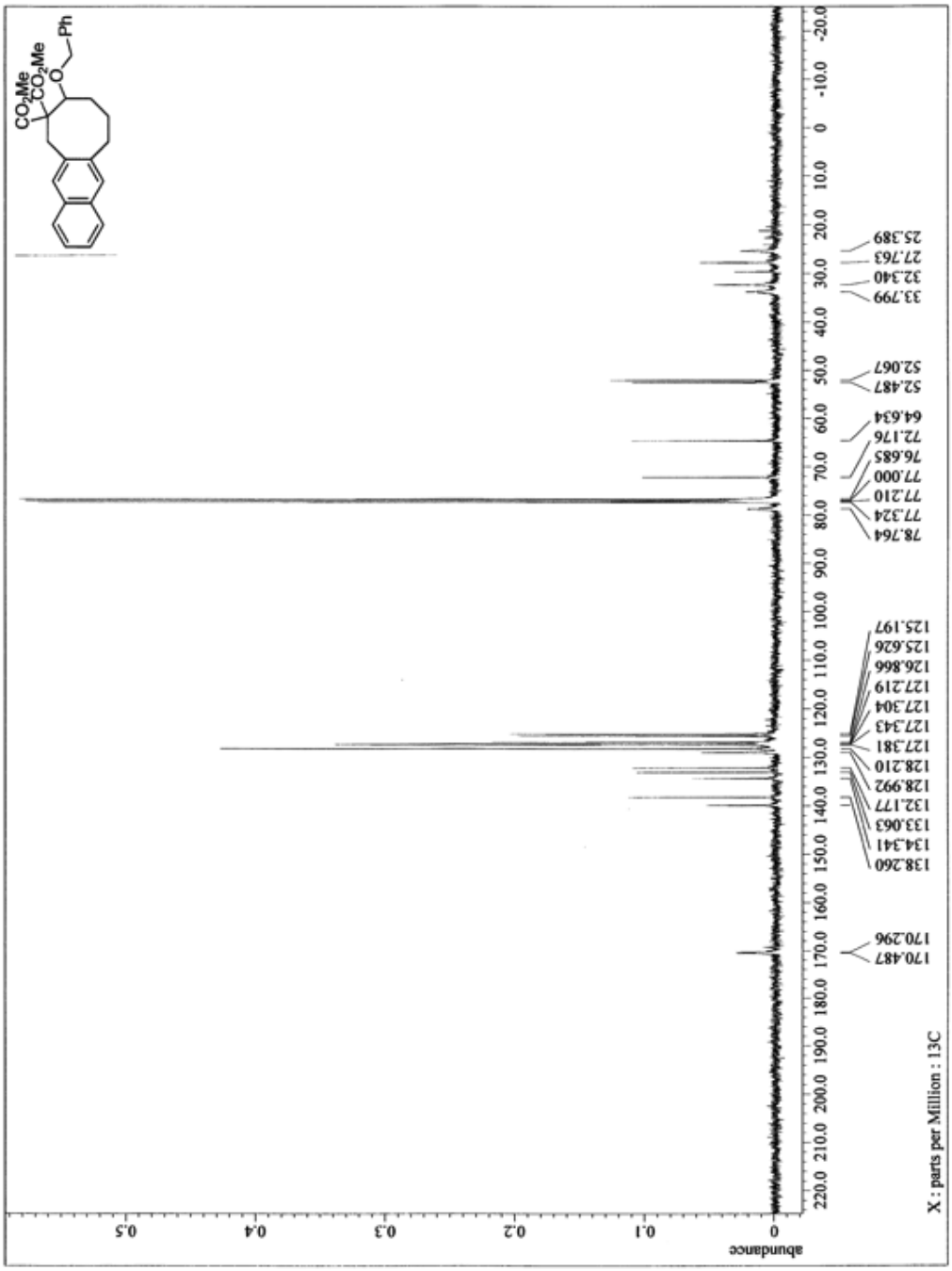
^{19}F NMR spectrum of **6d**.



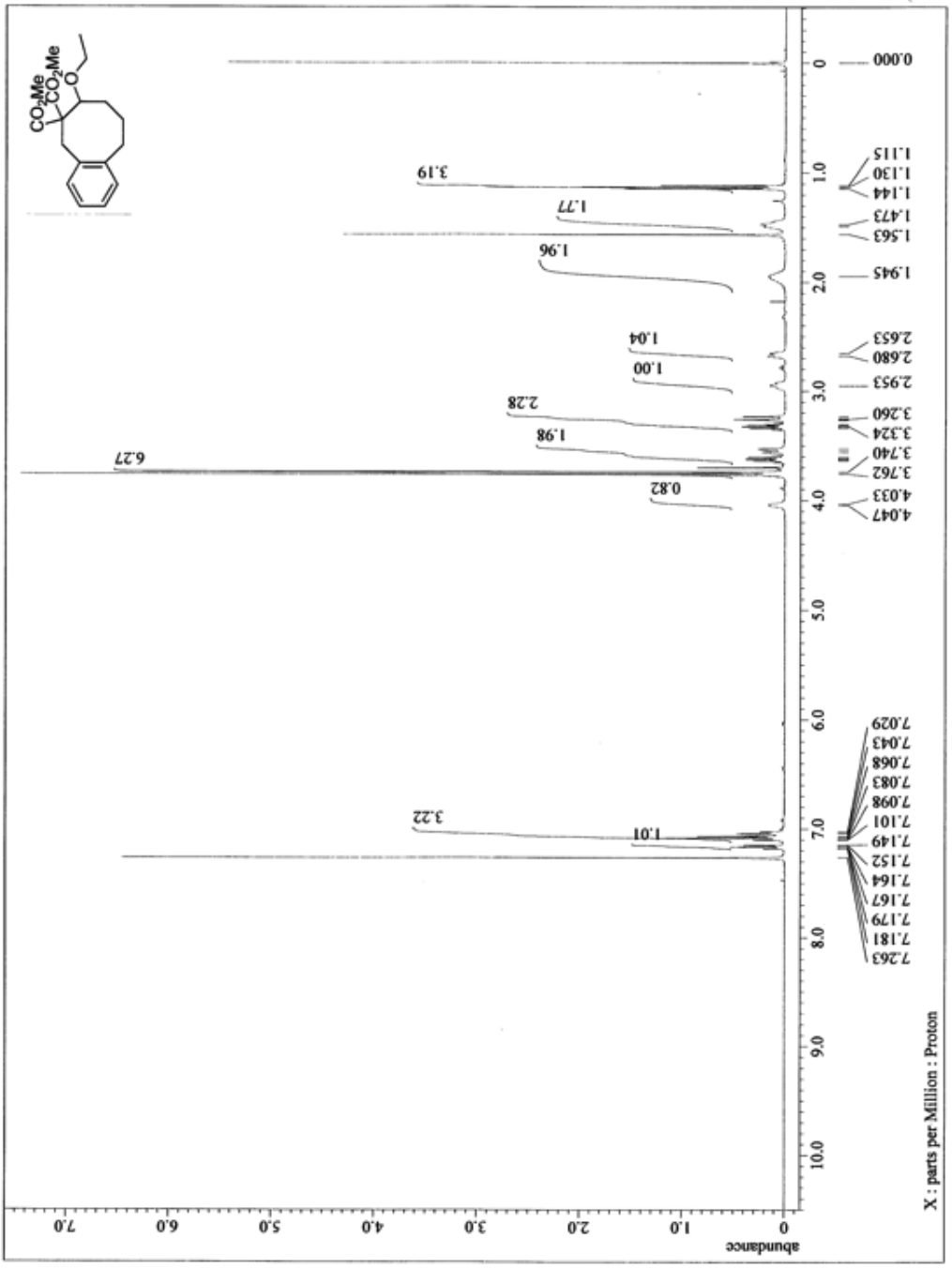
^{1}H NMR spectrum of **6e**.



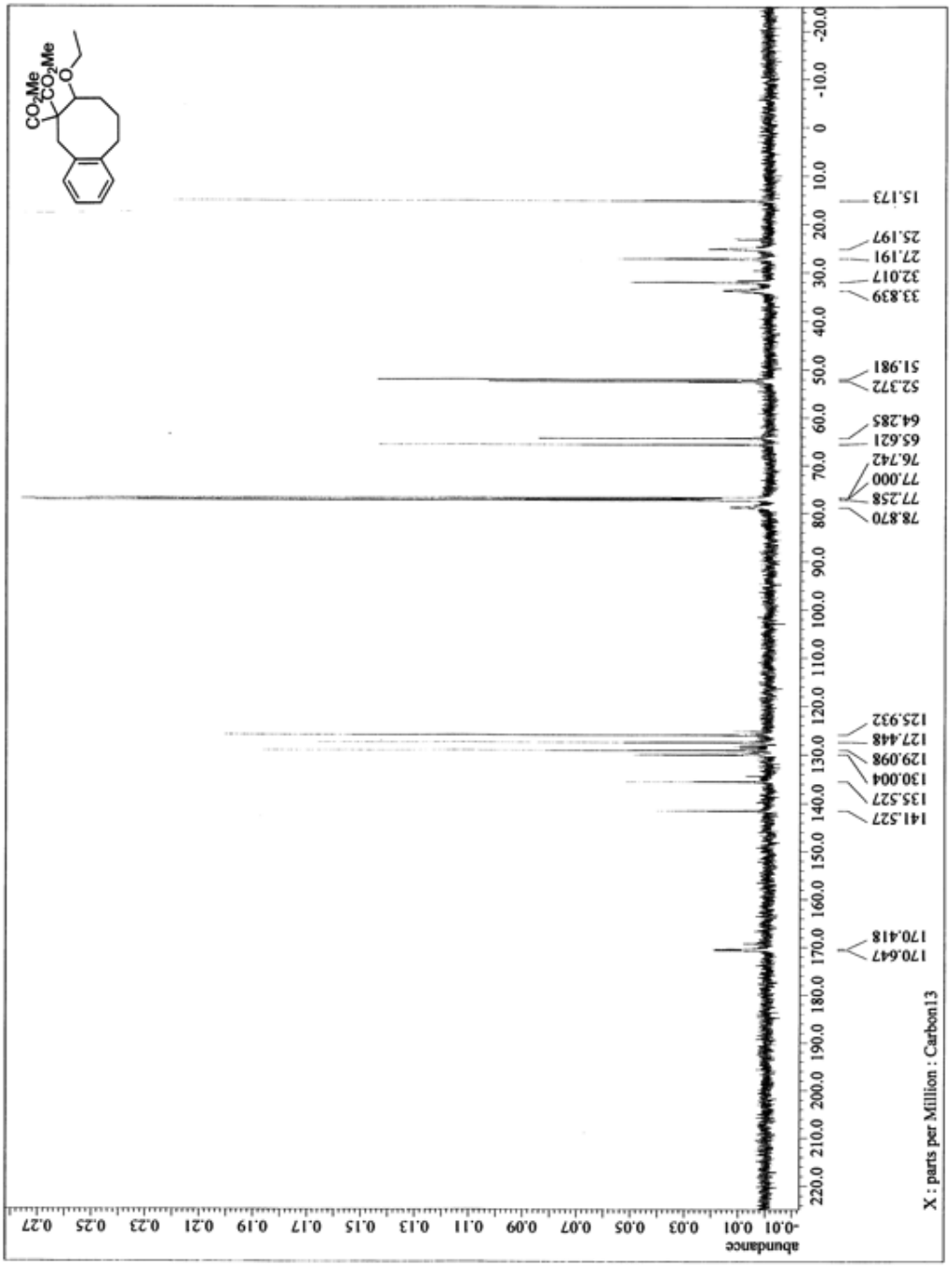
^{13}C NMR spectrum of **6e**.



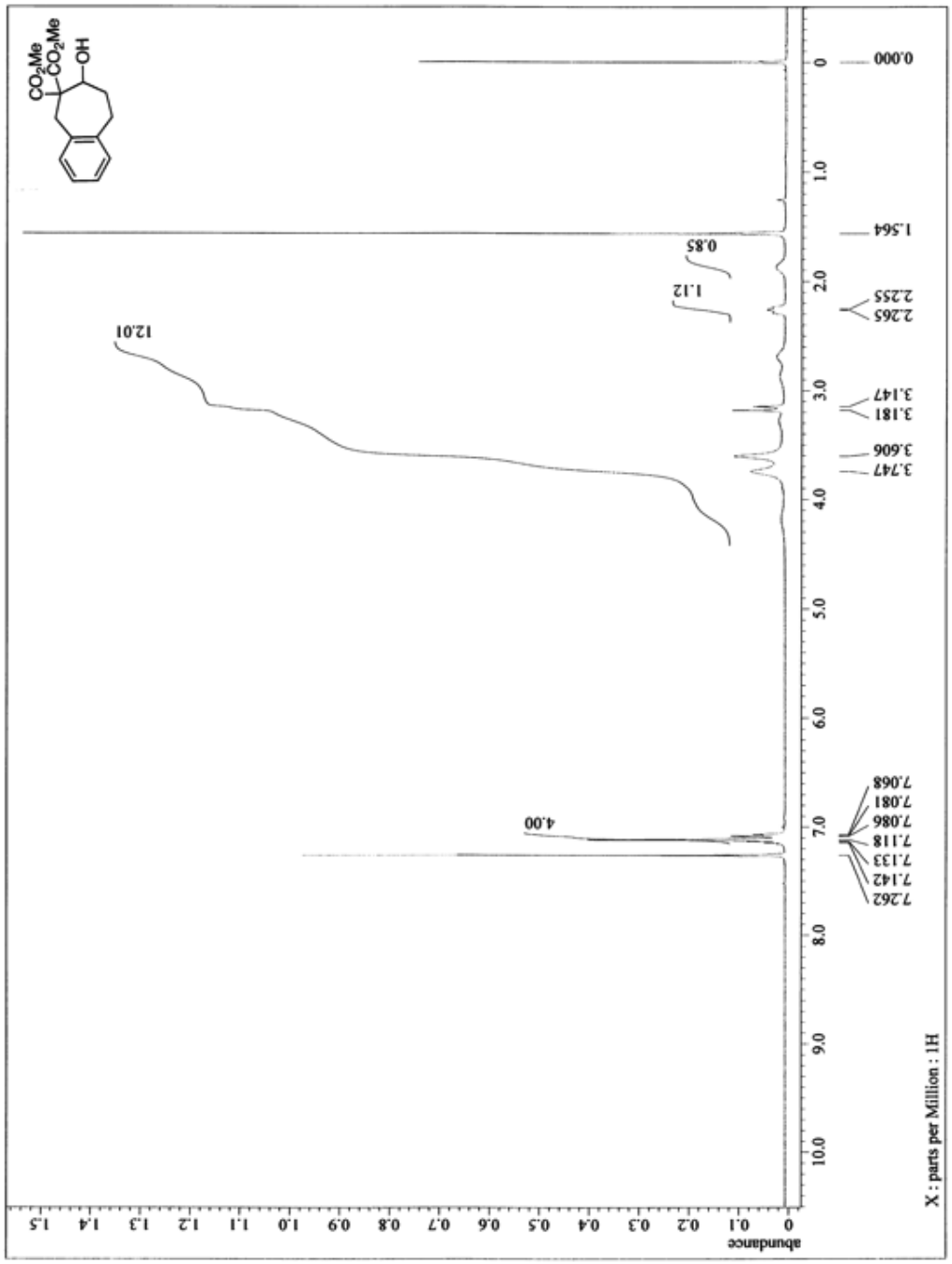
^{1}H NMR spectrum of **6f**.



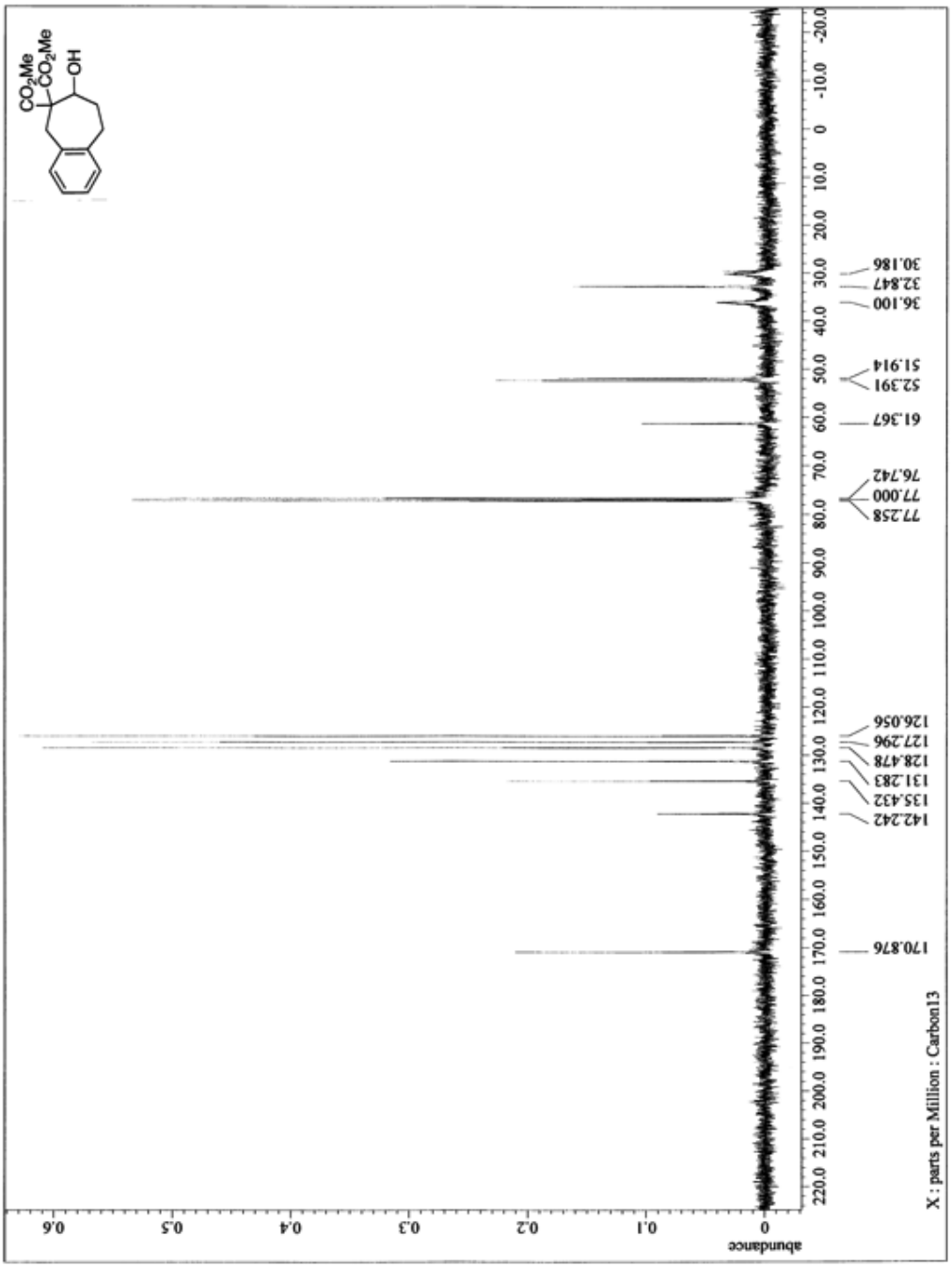
^{13}C NMR spectrum of **6f**.



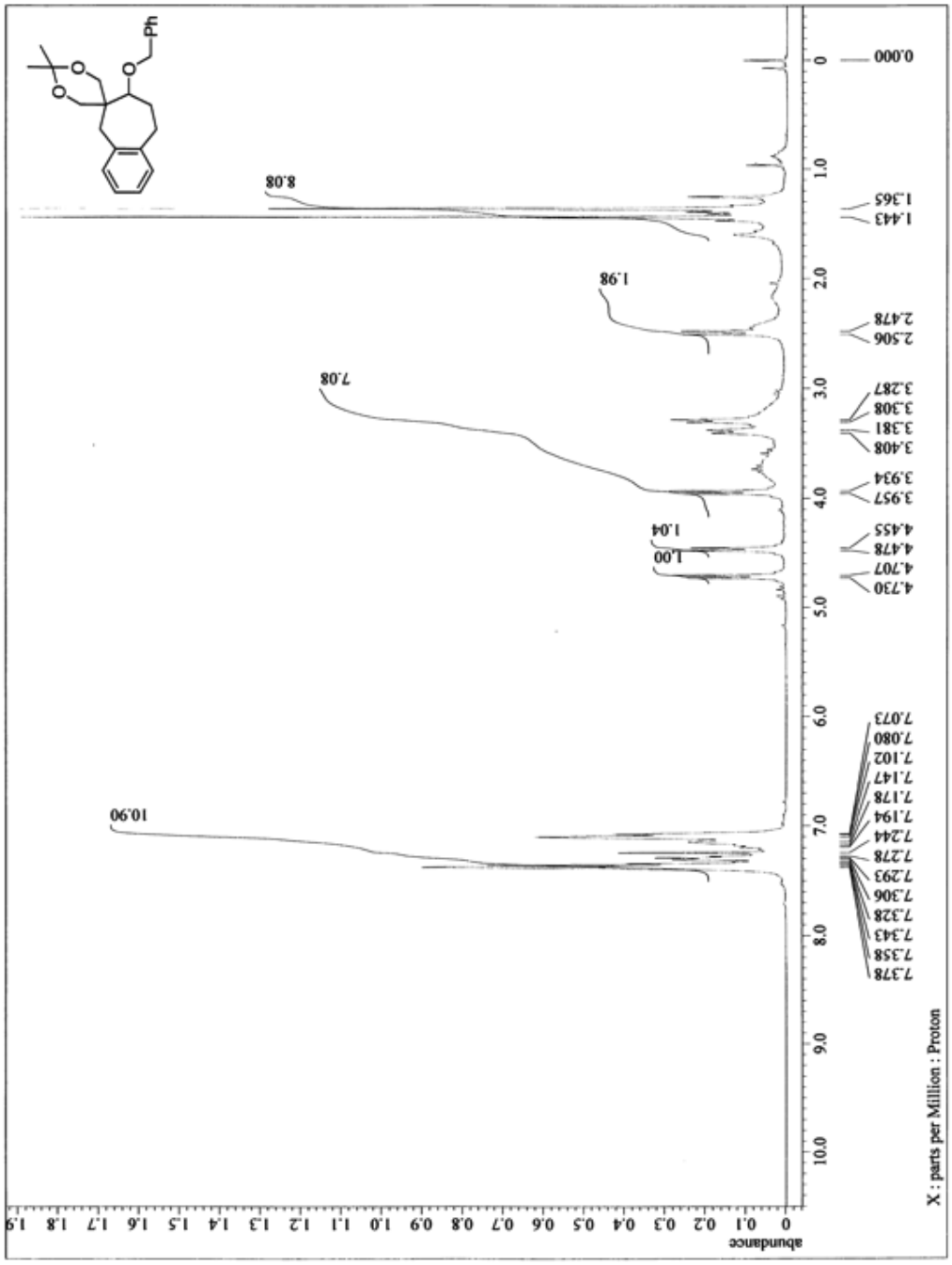
^{1}H NMR spectrum of **7**.



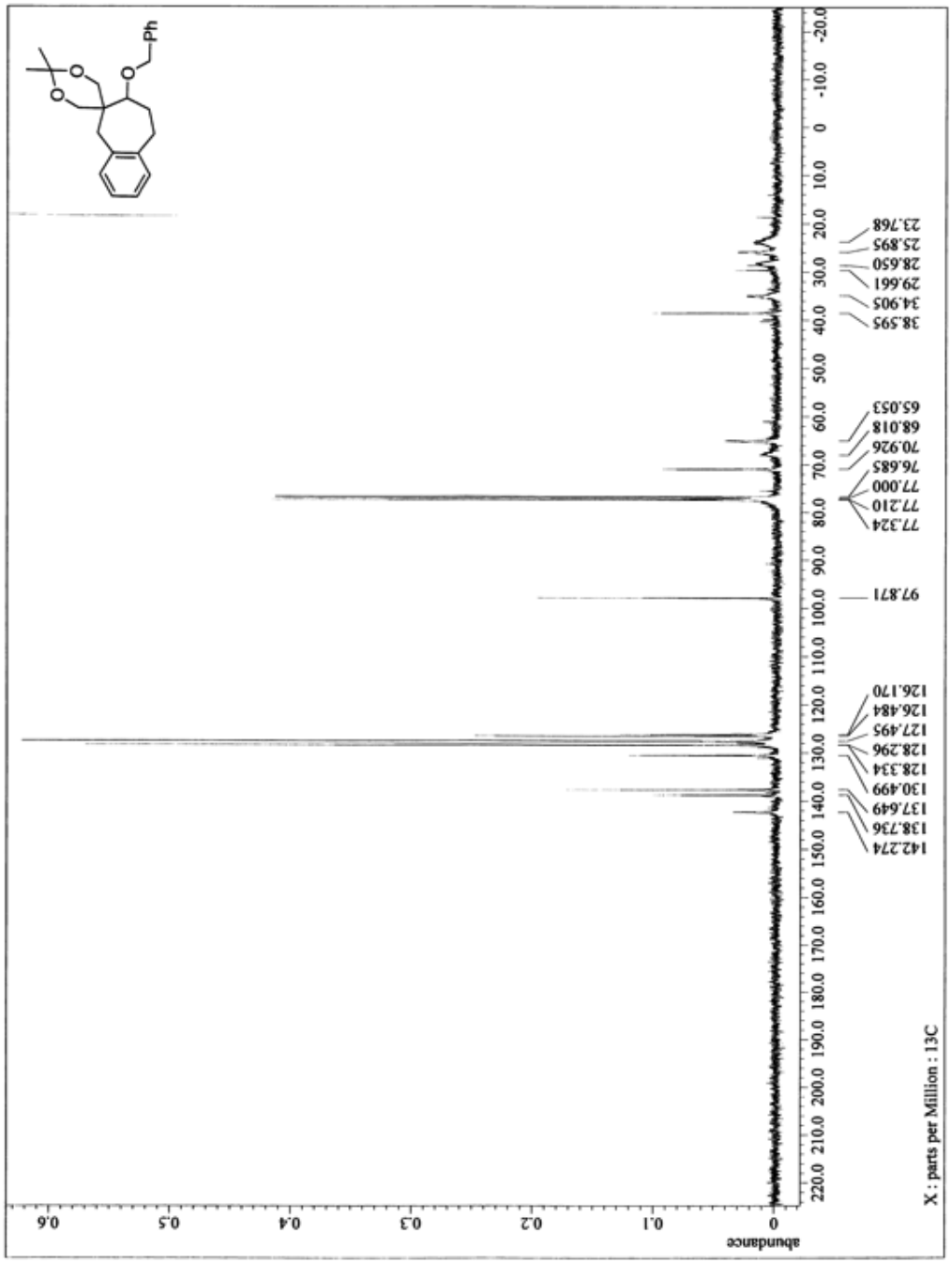
^{13}C NMR spectrum of **7**.



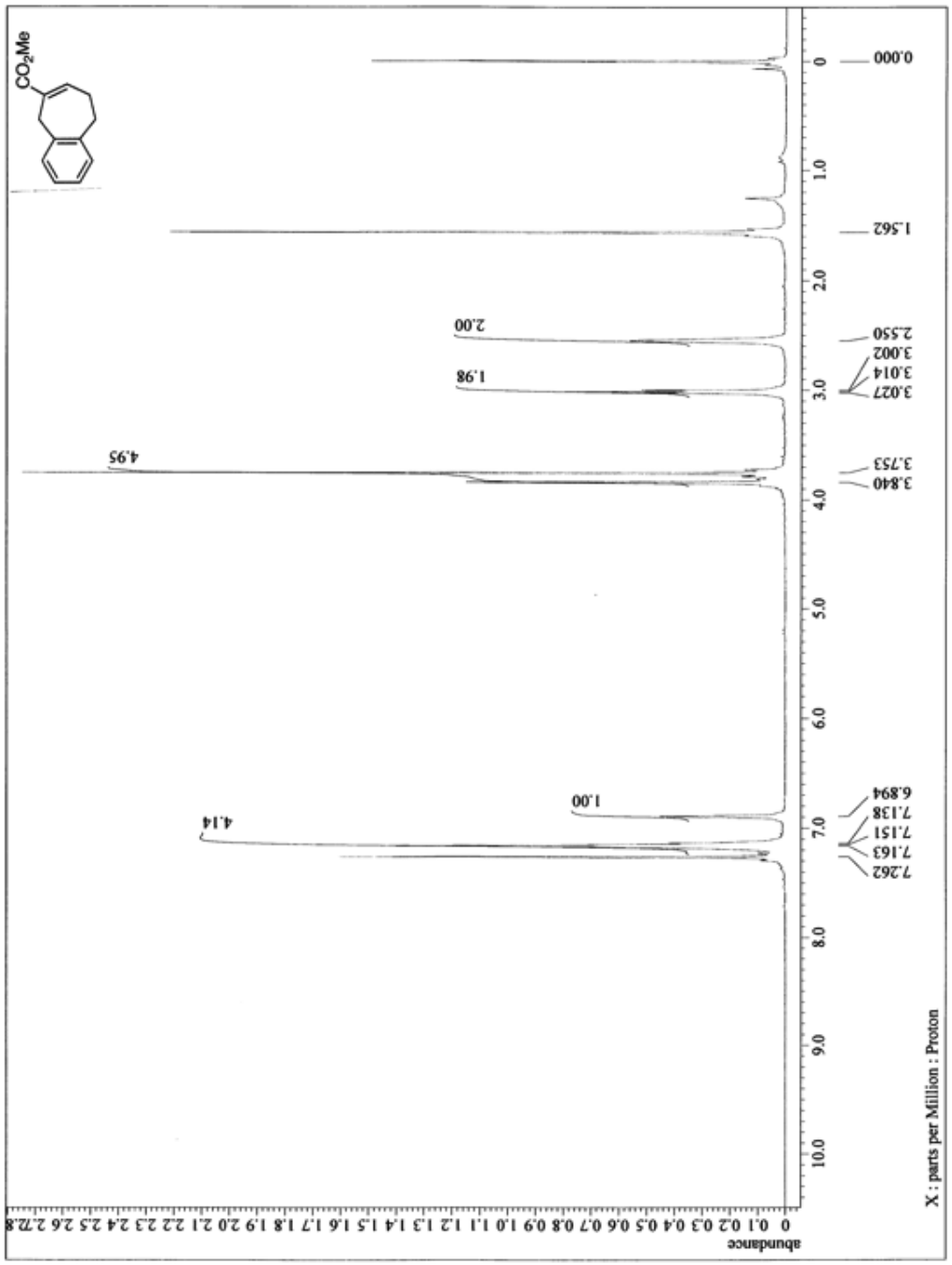
^{1}H NMR spectrum of **8**.



^{13}C NMR spectrum of **8**.



^{1}H NMR spectrum of **9**.



^{13}C NMR spectrum of **9**.