Supporting Information

A deconstruction-reconstruction strategy to access 1-naphthol derivatives: application to synthesis of aristolactam scaffolds

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Table of Contents

1. General Information

All commercially available reagents were directly used without further purification. Anhydrous dichloromethane (DCM), dimethylformamide (DMF), and tetrahydrofuran (THF) were purchased and used as received. All reactions were monitored by thin layer chromatography (TLC) carried out Merk silica gel 60 F_{254} pre-coated plates (175-225 μm). TLC spots were visualized by ultraviolet (UV) lamp (254 nm). Flash column chromatography was conducted on Merck silica gel 60 (40–63 μm). Melting points were determined with a bibby scientific SMP30 apparatus and are uncorrected. Infrared spectra were recorded with a Nicole iS10 FTIR Spectrometer.

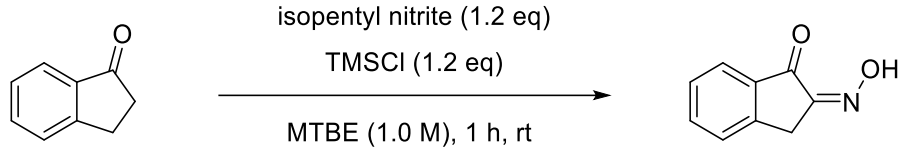
Chemical shifts of nuclear magnetic resonance (NMR) were reported in parts per million (ppm) relative to trimethylsilane (δ 0.0 ppm for ^{1}H and ^{13}C NMR), chloroform (δ 7.26 ppm for ^{1}H NMR and δ 77.16 ppm for ^{13}C NMR), dimethylsulfoxide (DMSO)-d_6 (δ 2.50 ppm for ^{1}H NMR and δ 39.52 ppm for ^{13}C NMR) or methanol-d_4 (δ 3.31 ppm for ^{1}H NMR and δ 49.00 ppm for ^{13}C NMR) as internal standard. The ^{19}F NMR spectra are unreferenced. NMR spectral data were presented as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dddd= doublet of doublet of doublet of doubles, dt = doublet of triplets, br = broad, m = multiplet. High-resolution mass spectra (HRMS) were reported for the molecular ion $[M+Na]^+$, $[M]^+$ or $[M+H]^+$.

At Yeongnam University, NMR and HRMS spectra were recorded using Bruker DPX 300, VNMR 600 MHz (either on 300 or 600 MHz for ^{1}H, 565 MHz for ^{19}F NMR, and 150 MHz for ^{13}C) and Vanquish UHPLC High Resolution Mass System with ion trap (orbitrap) mass analyzer [Ionization mode: ESI] at Core Research Support Center for Natural Products and Medical Materials at Yeungnam University and MStation (JEOL) JMS-700 [Ionization mode: EI, mass analyzer type: double-focusing type (magnetic sector-electrostatic sector)].

At Seoul National University of Science and Technology, measurement of NMR spectra were performed on Varian instrument (400 MHz for ^{1}H NMR, 100 for ^{13}C NMR and 282 MHz for ^{19}F NMR) and Agilent (600 MHz for ^{1}H NMR, 150 MHz for ^{13}C NMR and 565 MHz for ^{19}F NMR). HRMS spectra were measured on SYNAPT G2 (Waters, UK) [a time-of-flight (TOF) mass spectrometer fitted with an electrospray ESI] from the Korea Basic Science Institute (KBSI), and MStation (JEOL) JMS-700 [Ionization mode: EI, mass analyzer type: double-focusing type (magnetic sector-electrostatic sector)].

2. Experimental Procedures and Characterization Data

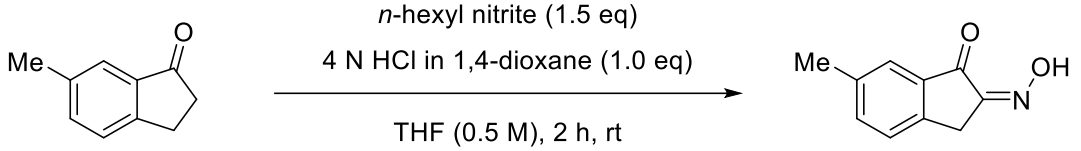
Preparation of α-oximinoketones 1



1a

To a stirred solution of 2,3-dihydro-1*H*-inden-1-one (500 mg, 3.78 mmol) in methyl *tert*-butyl ether (MTBE, 4 mL) was added trimethylsilyl chloride (0.57 mL, 4.54 mmol) and isopentyl nitrite (0.61 mL, 4.54 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h, then filtered and washed with MTBE. The crude was purified by trituration with ethyl acetate and hexane to afford **1a** (502 mg, 3.11 mmol, 82%) as a white solid.

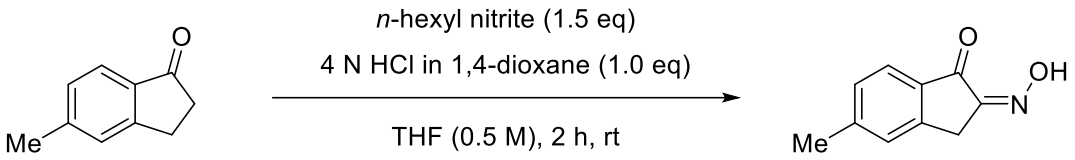
(*Z*)-2-(Hydroxyimino)-2,3-dihydro-1*H*-inden-1-one (1a); R_f = 0.3 (Hex:EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4 Hz, 1H), 7.79–7.75 (m, 2H), 7.56 (m, 1H), 4.24 (s, 2H); Data is consistent with that reported in literature.[1]



1b

To a stirred solution of 6-methyl-2,3-dihydro-1*H*-inden-1-one (500 mg, 3.42 mmol) in THF (7 mL) was added 4 N HCl in 1,4-dioxane (0.86 mL, 3.42 mmol) and *n*-hexyl nitrite (0.76 mL, 5.13 mmol) at 0 °C. After stirring at room temperature for 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic solution was dried over $MgSO_4$, filtered, and concentrated. The crude was washed with hexane, then further purified by trituration with ethyl acetate and hexane to afford **1b** (530 mg, 3.03 mmol, 89%) as a white solid.

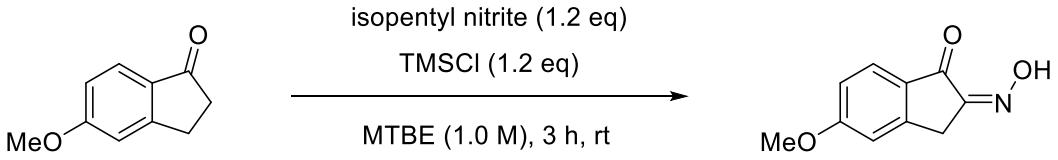
(*Z*)-2-(Hydroxyimino)-6-methyl-2,3-dihydro-1*H*-inden-1-one (1b); R_f = 0.2 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.59 (s, 1H), 7.56–7.49 (m, 3H), 3.71 (s, 2H), 2.38 (s, 3H); Data is consistent with that reported in literature.[1]



1c

To a stirred solution of 5-methyl-2,3-dihydro-1*H*-inden-1-one (500 mg, 3.42 mmol) in THF (7 mL) was added 4 N HCl in 1,4-dioxane (0.86 mL, 3.42 mmol) and *n*-hexyl nitrite (0.8 mL, 5.13 mmol) at 0 ºC. After stirring at room temperature for 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic solution was dried over $MgSO_4$, filtered, and concentrated. The crude was washed with hexane, then further purified by trituration with ethyl acetate and hexane to afford **1c** (476 mg, 2.72 mmol, 80%) as a white solid.

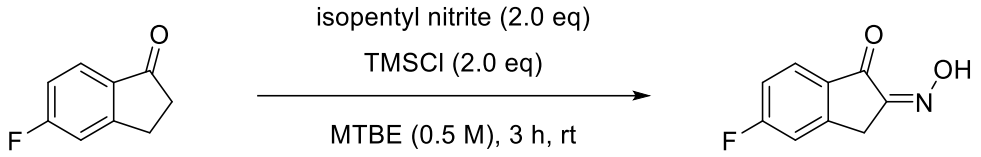
(*Z*)-2-(Hydroxyimino)-5-methyl-2,3-dihydro-1*H*-inden-1-one (1c); R_f = 0.2 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.43 (s, 1H), 7.31 (ddd, J = 0.7, 1.5, 7.9 Hz, 1H), 3.73 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.7, 154.5, 147.5, 146.9, 135.4, 128.9, 127.4, 123.5, 28.2, 21.8; HRMS[ESI] calcd for $C_{10}H_{10}NO_2^+$ $[M+H]^+$: 176.0706, found: 176.0706.



1d

To a stirred solution of 5-methoxy-2,3-dihydro-1*H*-inden-1-one (500 mg, 3.08 mmol) in methyl *tert*-butyl ether (MTBE, 3 mL) was added trimethylsilyl chloride (0.47 mL, 3.70 mmol) and isopentyl nitrite (0.50 mL, 3.70 mmol) at 0 ºC. The reaction mixture was stirred at room temperature for 3 h, then filtered and washed with MTBE. The crude was purified by trituration with ethyl acetate and hexane to afford **1d** (545 mg, 2.85 mmol, 93%) as a white solid.

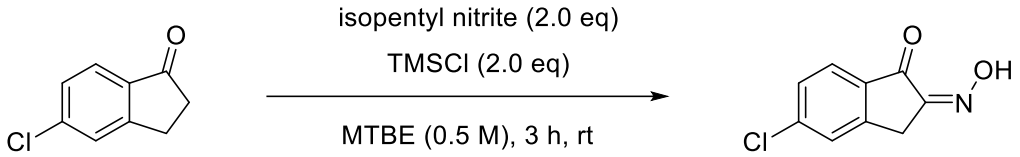
(*Z*)-2-(Hydroxyimino)-5-methoxy-2,3-dihydro-1*H*-inden-1-one (1d); R_f = 0.2 (Hex:EtOAc = 2:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 7.69 (d, J = 8.6 Hz, 1H), 7.14 (d, J = 1.8 Hz, 1H), 7.02 (dd, J = 2.4, 8.6 Hz, 1H), 3.88 (s, 3H), 3.72 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.4, 165.5, 154.5, 150.2, 131.0, 125.6, 115.7, 110.6, 55.9, 28.4; HRMS[ESI] calcd for $C_{10}H_9NO_3Na^+$ $[M+Na]^+$: 214.0475, found: 214.0475.



1e

To a stirred solution of 5-fluoro-2,3-dihydro-1*H*-inden-1-one (500 mg, 3.33 mmol) in methyl *tert*-butyl ether (MTBE, 7 mL) was added trimethylsilyl chloride (0.85 mL, 6.66 mmol) and isopentyl nitrite (0.89 mL, 6.66 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h, then filtered and washed with MTBE. The crude was purified by trituration with ethyl acetate and hexane to afford **1e** (476 mg, 2.66 mmol, 80%) as a white solid.

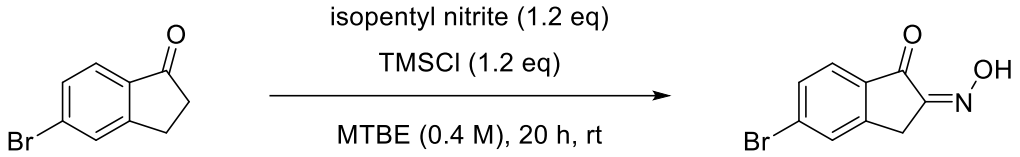
(*Z*)-5-Fluoro-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one (1e); R_f = 0.2 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.66 (s, 1H), 7.82 (dd, J = 5.5, 8.5 Hz, 1H), 7.47 (ddd, J = 1.3, 1.4, 9.0 Hz, 1H), 7.31 (m, 1H), 3.78 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.6, 166.5 (d, $J_{C,F}$ = 252.5 Hz), 154.0, 150.4 (d, $J_{C,F}$ = 11.0 Hz), 134.3, 126.4 (d, $J_{C,F}$ = 10.7 Hz), 115.9 (d, $J_{C,F}$ = 23.6 Hz), 114.0 (d, $J_{C,F}$ = 22.8 Hz), 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.52 (td, J = 5.6, 9.2 Hz, 1F); HRMS[ESI] calcd for $C_9H_6FNO_2Na^+$ $[M+Na]^+$: 202.0275, found: 202.0275.



1f

To a stirred solution of 5-chloro-2,3-dihydro-1*H*-inden-1-one (500 mg, 3.00 mmol) in methyl *tert*-butyl ether (MTBE, 6 mL) was added trimethylsilyl chloride (0.76 mL, 6.00 mmol) and isopentyl nitrite (0.81 mL, 6.00 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h, then filtered and washed with MTBE. The crude was purified by trituration with ethyl acetate and hexane to afford **1f** (509 mg, 2.60 mmol, 87%) as a yellow solid.

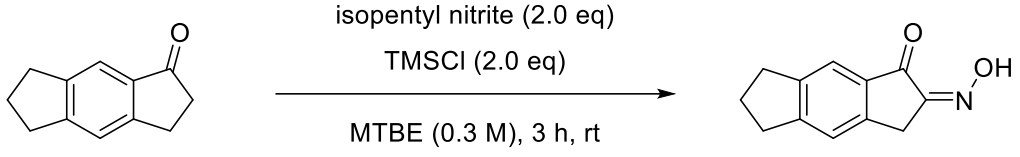
(*Z*)-5-Chloro-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one (1f); R_f = 0.3 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.74 (s, 1H), 7.75–7.72 (m, 2H), 7.52 (dd, J = 1.0, 1.0, 8.1 Hz, 1H), 3.77 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.1, 153.9, 149.1, 140.3, 136.3, 128.3, 127.3, 125.2, 28.3; HRMS[ESI] calcd for $C_9H_6ClNO_2Na^+$ $[M+Na]^+$: 217.9979, found: 217.9979.



1g

To a stirred solution of 5-bromo-2,3-dihydro-1*H*-inden-1-one (1.0 g, 4.73 mmol) in methyl *tert*-butyl ether (MTBE, 12 mL) was added trimethylsilyl chloride (0.72 mL, 5.68 mmol) and isopentyl nitrite (0.76 mL, 5.68 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 20 h, then filtered and washed with MTBE. The crude was purified by trituration with ethyl acetate and hexane to afford **1g** (952 mg, 3.97 mmol, 84%) as a white solid.

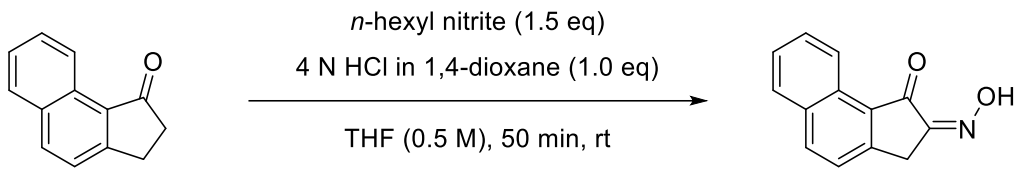
(*Z*)-5-Bromo-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one (1g); R_f = 0.6 (Hex:EtOAc = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.71 (s, 1H), 7.89 (dd, J = 1.1, 1.1 Hz, 1H), 7.67 (d, J = 1.1 Hz, 2H), 3.78 (d, J = 1.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.3, 153.9, 149.2, 136.6, 131.1, 130.3, 129.6, 125.3, 28.3; HRMS[ESI] calcd for $C_9H_7BrNO_2^+$ $[M+H]^+$: 239.9655, found: 239.9656.



1h

To a stirred solution of 3,5,6,7-tetrahydro-s-indacen-1(2*H*)-one (500 mg, 2.90 mmol) in methyl *tert*-butyl ether (MTBE, 10 mL) was added trimethylsilyl chloride (0.74 mL, 5.80 mmol) and isopentyl nitrite (0.78 mL, 5.80 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h, then filtered and washed with MTBE. The crude was purified by trituration with ethyl acetate and hexane to afford **1h** (476 mg, 2.37 mmol, 82%) as a white solid.

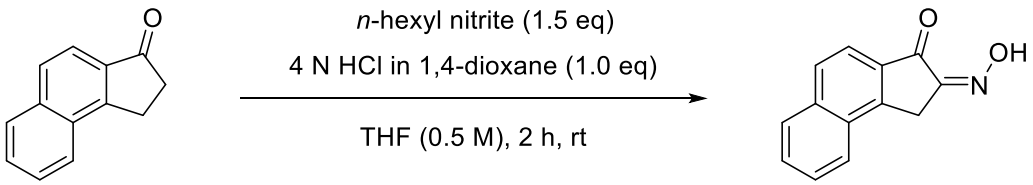
(*Z*)-2-(Hydroxyimino)-3,5,6,7-tetrahydro-s-indacen-1(2*H*)-one (1h); R_f = 0.2 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.51 (s, 1H), 7.55 (s, 1H), 7.44 (s, 1H), 3.69 (s, 2H), 2.95–2.89 (m, 4H), 2.06 (dddd, J = 7.4, 7.4, 7.4, 7.4 Hz, 1H); R_f = 0.2 (Hex:EtOAc = 3:1); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.7, 154.9, 153.7, 146.1, 144.2, 136.4, 122.7, 118.9, 32.8, 31.6, 28.1, 25.2; HRMS[ESI] calcd for $C_{12}H_{11}NO_2Na^+$ $[M+Na]^+$: 224.0682, found: 224.0681.



1i

To a stirred solution of 2,3-dihydro-1*H*-cyclopenta[a]naphthalen-1-one (750 mg, 4.12 mmol) and *n*-hexyl nitrite (0.92 mL, 6.18 mmol) in THF (8 mL) was added 4 N HCl in 1,4-dioxane (1.03 mL, 4.12 mmol). After 50 min, the reaction mixture was quenched with $NaHCO_3$ and extracted with ethyl acetate (3 X 30 mL). The combined organic solution was dried over $MgSO_4$, filtered, and concentrated. The crude was purified by trituration with hexane to afford **1i** (763 mg, 3.61 mmol, 88%) as a light yellow solid.

2,3-Dihydro-1*H*-cyclopenta[a]naphthalen-1-one (1i); R_f = 0.3 (Hex:EtOAc = 5:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.57 (s, 1H), 9.05 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.3 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.75 (m, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.64 (m, 1H), 3.87 (s, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 189.8, 154.3, 150.5, 136.9, 132.3, 131.5, 129.4, 128.8, 128.6, 127.0, 124.5, 123.1, 28.5; HRMS[EI+] calcd for $C_{13}H_9NO_2^+$ $[M]^+$: 211.0628, found: 211.0627.



1j

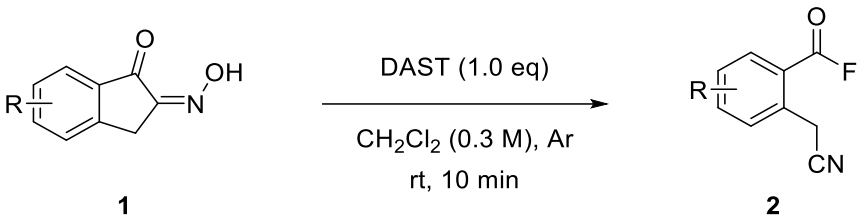
To a stirred solution of 1,2-dihydro-3*H*-cyclopenta[a]naphthalen-3-one (500 mg, 2.74 mmol) in THF (5 mL) was added 4 N HCl in 1,4-dioxane (0.68 mL, 2.74 mmol) and *n*-hexyl nitrite (0.61 mL, 4.11 mmol) at 0 °C. After stirring at room temperature for 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic solution was dried over $MgSO_4$, filtered, and concentrated. The crude was washed with hexane, then further purified by trituration with ethyl acetate and hexane to afford **1j** (443 mg, 2.10 mmol, 77%) as a brown solid.

(*Z*)-2-(Hydroxyimino)-1,2-dihydro-3*H*-cyclopenta[a]naphthalen-3-one (1j); R_f = 0.2 (Hex:EtOAc = 2:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.67 (s, 1H), 8.16 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.79–7.70 (m, 3H), 4.09 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.1, 154.2, 148.6, 136.4, 135.2, 129.9, 129.7, 129.0, 128.7, 127.6, 125.4, 118.9, 27.0; HRMS[ESI] calcd for

$C_{13}H_{10}NO_2^+$ $[M+H]^+$: 212.0706, found: 212.0711.

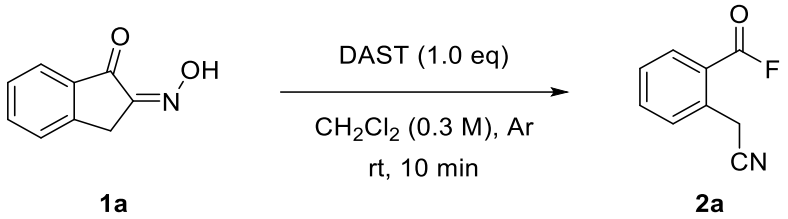
Synthesis of Acyl Fluorides 2 via DAST

General procedure



1 **2**

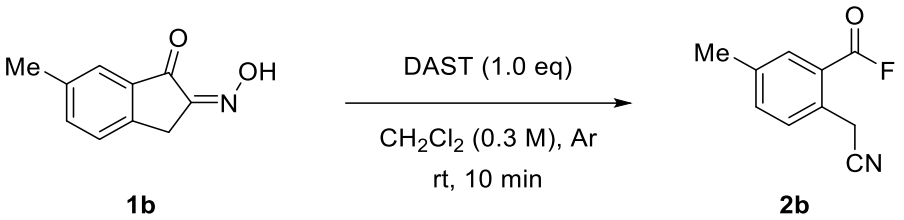
A 25 mL round bottom flask was charged with oxime **1** (1.0 equiv) and dry CH_2Cl_2 (0.3 M) under argon atmosphere. Then, (diethylamino)sulfur trifluoride (DAST, 1.0 equiv) was added to the solution at room temperature. After 10 min, the reaction mixture was diluted with CH_2Cl_2, washed with 1 N HCl solution and subsequently with saturated $NaHCO_3$ solution. The organic solution was dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography to afford the desired product **2**.



1a **2a**

According to general procedure with (*Z*)-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one **1a** (500 mg, 3.10 mmol), the product **2a** was obtained as a white solid in 84% yield (423 mg, 2.59 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

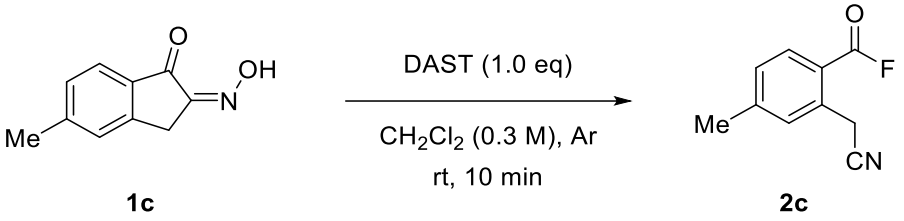
2-(Cyanomethyl)benzoyl fluoride (2a); R_f = 0.5 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 1.4, 7.7 Hz, 1H), 7.79–7.73 (m, 2H), 7.56 (m, 1H), 4.23 (s, 2H); Data is consistent with that reported in literature.[2]



1b **2b**

According to general procedure with (*Z*)-2-(hydroxyimino)-6-methyl-2,3-dihydro-1*H*-inden-1-one **1b** (438 mg, 2.50 mmol), the product **2b** was obtained as a yellow-white solid in 73% yield (323 mg, 1.82 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

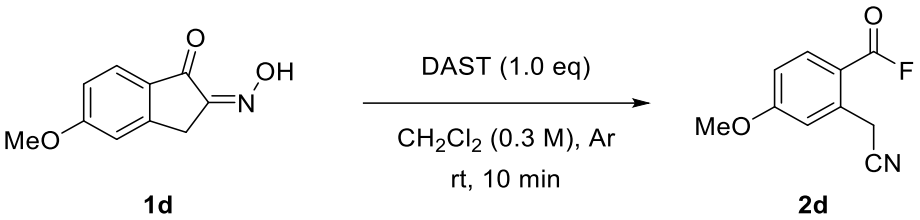
2-(Cyanomethyl)-5-methylbenzoyl fluoride (2b); R_f = 0.5 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 1.9 Hz, 1H), 7.61 (dd, *J* = 1.8, 7.9 Hz, 1H), 7.55 (dd, *J* = 1.9, 7.7 Hz, 1H), 4.18 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3 (d, $J_{C,F}$ = 343.7 Hz), 139.4, 136.6, 133.8, 131.8 (d, $J_{C,F}$ = 7.7 Hz), 130.6 (d, $J_{C,F}$ = 4.3 Hz), 122.6 (d, $J_{C,F}$ = 57.1 Hz), 117.2, 22.9, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ 27.51 (s, 1F); HRMS[EI+] calcd for $C_{10}H_8FNO^+$ $[M]^+$: 177.0584, found: 177.0581.



1c **2c**

According to general procedure with (*Z*)-2-(hydroxyimino)-5-methyl-2,3-dihydro-1*H*-inden-1-one **1c** (438 mg, 2.50 mmol), the product **2c** was obtained as a white solid in 59% yield (262 mg, 1.48 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

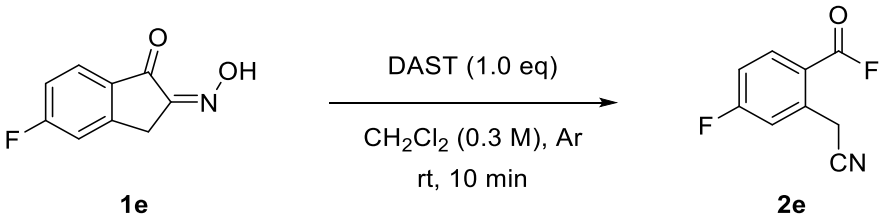
2-(Cyanomethyl)-4-methylbenzoyl fluoride (2c); R_f = 0.5 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 4.21 (s, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2 (d, $J_{C,F}$ = 341.9 Hz), 147.7, 134.8 (d, $J_{C,F}$ = 8.3 Hz), 133.4, 131.4 (d, $J_{C,F}$ = 4.1 Hz), 129.7, 119.9 (d, $J_{C,F}$ = 58.1 Hz), 117.1, 23.2, 22.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ 26.73 (s, 1F); HRMS[EI+] calcd for $C_{10}H_8FNO^+$ $[M]^+$: 177.0584, found: 177.0590.



1d **2d**

According to general procedure with (*Z*)-2-(hydroxyimino)-5-methoxy-2,3-dihydro-1*H*-inden-1-one **1d** (478 mg, 2.50 mmol), the product **2d** was obtained as a white solid in 75% yield (363 mg, 1.88 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

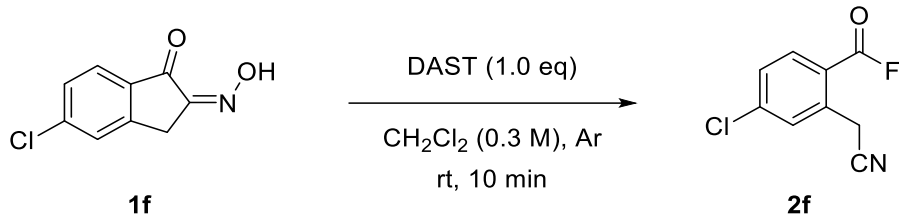
2-(Cyanomethyl)-4-methoxybenzoyl fluoride (2d); R_f = 0.3 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.9 Hz, 1H), 7.22 (s, 1H), 6.98 (dd, *J* = 2.6, 8.8 Hz, 1H), 4.21 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 156.0 (d, $J_{C,F}$ = 338.6 Hz), 137.4 (d, $J_{C,F}$ = 8.8 Hz), 135.8 (d, $J_{C,F}$ = 5.0 Hz), 117.0, 116.7 (dd, $J_{C,F}$ = 4.3, 4.3 Hz), 114.4 (d, $J_{C,F}$ = 58.7 Hz), 113.6, 56.0 (d, $J_{C,F}$ = 5.8 Hz), 23.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ 25.06 (s, 1F); HRMS[EI+] calcd for $C_{10}H_8FNO_2^+$ $[M]^+$: 193.0534, found: 193.0541.



1e **2e**

According to general procedure with (*Z*)-5-fluoro-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one **1e** (300 mg, 1.67 mmol), the product **2e** was obtained as a yellow-white solid in 68% yield (207 mg, 1.14 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

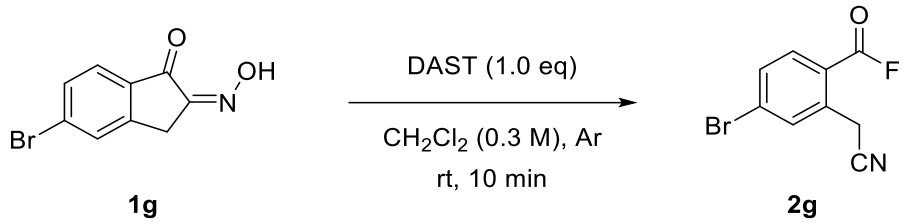
2-(Cyanomethyl)-4-fluorobenzoyl fluoride (2e); R_f = 0.6 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 5.6, 8.8 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.25 (m, 1H), 4.26 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8 (d, $J_{C,F}$ = 259.7 Hz), 155.3 (d, $J_{C,F}$ = 341.8 Hz), 138.5 (dd, $J_{C,F}$ = 8.9, 8.9 Hz), 136.3 (dd, $J_{C,F}$ =11.1, 11.1 Hz), 119.3 (d, $J_{C,F}$ = 3.4 Hz), 118.4 (m), 116.4 (dd, $J_{C,F}$ = 4.9, 5.5 Hz), 116.2 (d, $J_{C,F}$ = 9.9 Hz), 23.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ 27.90 (s, 1F), -98.23 (m, 1F); HRMS[EI+] calcd for $C_9H_5F_2NO^+$ $[M]^+$: 181.0334, found: 181.0353.



1f **2f**

According to general procedure with (*Z*)-5-chloro-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one **1f** (235 mg, 1.20 mmol), the product **2f** was obtained as a yellow-white solid in 59% yield (139 mg, 0.70 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

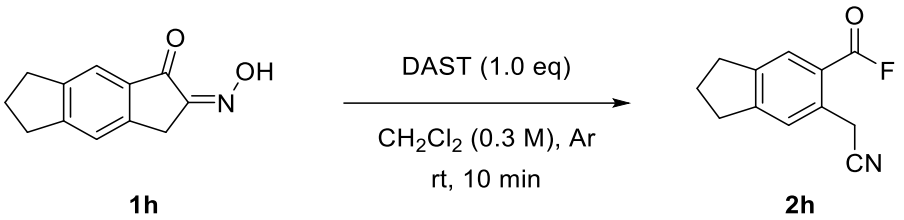
4-Chloro-2-(cyanomethyl)benzoyl fluoride (2f); R_f = 0.6 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.76 (s, 1H), 7.54 (dd, *J* = 2.1, 8.4 Hz, 1H), 4.23 (d, *J* = 0.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4 (d, $J_{C,F}$ = 342.9 Hz), 142.9, 136.6 (d, $J_{C,F}$ = 8.3 Hz), 134.5 (d, $J_{C,F}$ = 20.3 Hz), 131.0 (dd, $J_{C,F}$ = 4.2, 27.1 Hz), 129.4 (dd, $J_{C,F}$ = 27.8 Hz), 121.1 (d, $J_{C,F}$ = 59.7 Hz), 116.3, 23.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ 28.08 (s, 1F); HRMS[EI+] calcd for $C_9H_5ClFNO^+$ $[M]^+$: 197.0038, found: 197.0040.



1g **2g**

According to general procedure with (*Z*)-5-bromo-2-(hydroxyimino)-2,3-dihydro-1*H*-inden-1-one **1g** (144 mg, 0.60 mmol), the product **2g** was obtained as a white solid in 56% yield (81 mg, 0.34 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

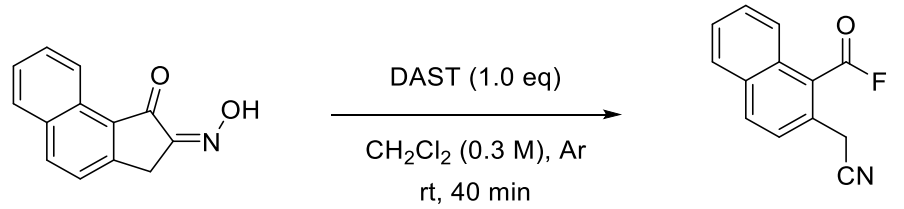
4-Bromo-2-(cyanomethyl)benzoyl fluoride (2g); R_f = 0.6 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.92 (s, 1H), 7.71 (dd, *J* = 2.0, 8.4 Hz, 1H), 4.23 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6 (d, $J_{C,F}$ = 342.9 Hz), 136.5 (d, $J_{C,F}$ = 8.1 Hz), 134.4, 133.9 (d, $J_{C,F}$ = 4.0 Hz), 132.6, 131.7, 121.7 (d, $J_{C,F}$ = 59.1 Hz), 116.3, 23.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ 28.11 (s, 1F); HRMS[EI+] calcd for $C_9H_5BrFNO^+$ $[M]^+$: 240.9533, found: 240.9537.



1h **2h**

According to general procedure with (*Z*)-2-(hydroxyimino)-3,5,6,7-tetrahydro-s-indacen-1(2*H*)-one **1h** (300 mg, 1.49 mmol), the product **2h** was obtained as a white solid in 66% yield (201 mg, 0.99 mmol) after flash column chromatography (Hex:EtOAc = 20:1 to 3:1).

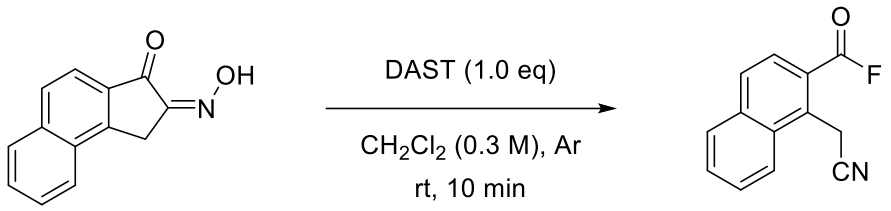
6-(Cyanomethyl)-2,3-dihydro-1*H*-indene-5-carbonyl fluoride (2h); R_f = 0.5 (Hex:EtOAc = 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.57 (s, 1H), 4.18 (s, 2H), 3.05–2.97 (m, 4H), 2.18 (dddd, *J* = 7.5, 7.5, 7.6, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6 (d, $J_{C,F}$ = 342.0 Hz), 154.0, 145.6, 133.1 (d, $J_{C,F}$ = 8.5 Hz), 129.0 (d, $J_{C,F}$ = 1.6 Hz), 126.7 (d, $J_{C,F}$ = 4.5 Hz), 120.5 (d, $J_{C,F}$ = 57.1 Hz), 117.5, 33.5, 32.4, 25.3, 23.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ 26.82 (s, 1F); HRMS[ESI] calcd for $C_{12}H_{11}FNO^+$ $[M+H]^+$: 204.0819, found: 204.0825.



1i **2i**

According to general procedure with 2,3-dihydro-1*H*-cyclopenta[a]naphthalen-1-one **1i** (317 mg, 1.50 mmol), product **2i** was obtained as light yellow solid in 97% yield (310 mg, 1.45 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 5:1).

2-(Cyanomethyl)-1-naphthoyl fluoride (2i); R_f = 0.7 (Hex:EtOAc = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 2.9, 8.6 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.71–7.69 (m, 2H), 7.63 (m, 1H), 4.15 (d, *J* = 1.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.3 (d, $J_{C,F}$ = 351.4 Hz), 134.7, 133.1, 130.9 (d, $J_{C,F}$ = 11.1 Hz), 129.4, 128.9, 127.7, 126.13, 126.12, 125.1 (d, $J_{C,F}$ = 5.8 Hz), 123.1 (d, $J_{C,F}$ = 55.5 Hz), 116.9, 23.4 (d, $J_{C,F}$ = 3.2 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ 59.20 (s, 1F); HRMS[EI+] calcd for $C_{13}H_8FNO^+$ $[M]^+$: 213.0584, found: 213.0583.



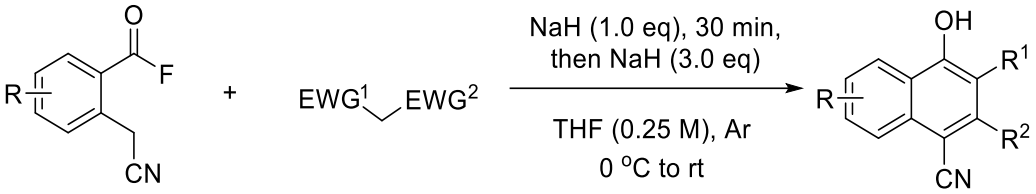
1j **2j**

According to general procedure with (*Z*)-2-(hydroxyimino)-1,2-dihydro-3*H*-cyclopenta[a]naphthalen-3-one **1j** (300 mg, 1.42 mmol), the product **2j** was obtained as a yellow-white solid in 43% yield (129 mg, 0.61 mmol) after flash column chromatography (Hex:EtOAc = 20:1 to 3:1).

1-(Cyanomethyl)-2-naphthoyl fluoride (2j); R_f = 0.5 (Hex:EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (m, 1H), 8.05–7.97 (m, 3H), 7.80–7.73 (m, 2H), 4.70 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8 (d, $J_{C,F}$ = 343.3 Hz), 136.5, 133.7 (d, $J_{C,F}$ = 8.8 Hz), 131.6 (d, $J_{C,F}$ = 4.4 Hz), 130.1, 130.0, 129.3, 128.9, 126.2 (d, $J_{C,F}$ = 2.7 Hz), 124.7, 121.7 (d, $J_{C,F}$ = 58.0 Hz), 116.8, 17.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ 33.77 (s, 1F); HRMS[EI+] calcd for $C_{13}H_8FNO^+$ $[M]^+$: 213.0584, found: 213.0598.

Synthesis of naphthalene derivatives 4

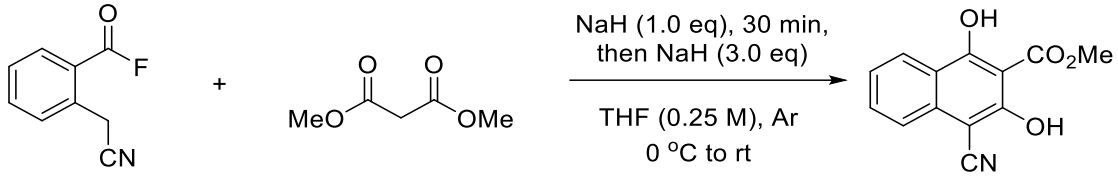
General procedure



2 **3** **4**

To a stirred solution of **3** (0.5 mmol, 1 equiv) in dry THF (0.5 mL) was added NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol, 1 equiv) at 0 °C under argon atmosphere. After stirring for 30 min at 0 °C, acyl fluoride **2** (0.5 mmol, 1 equiv) in dry THF (1.5 mL) was added dropwise to the reaction mixture. After an additional 30-min stirring at 0 °C, NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol, 1 equiv) was added at 0 °C. Subsequently, another portion of NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol, 1 equiv) was added at 0 °C. The mixture was stirred for 3 h at rt and NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol, 1 equiv) was added at 0 °C. After an additional 3 h of stirring at rt, the resulting mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The

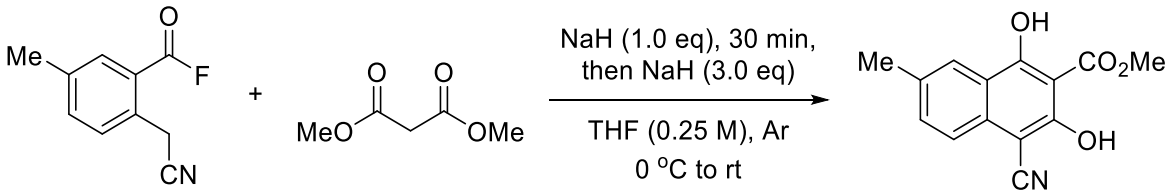
crude was purified over silica gel by flash chromatography to afford the desired product **4**.



2a **3a** **4a**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4a** was obtained as a white solid in 91% yield (110 mg, 0.45 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

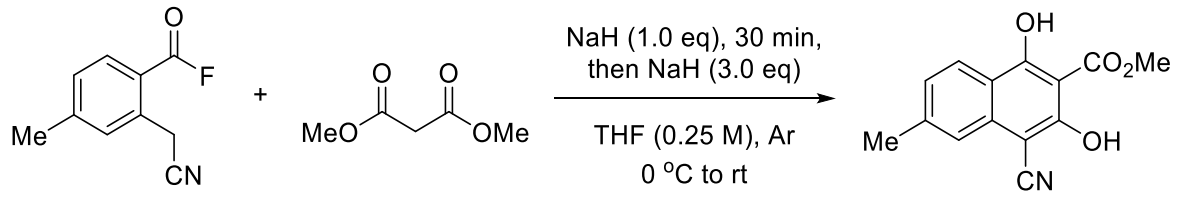
Methyl 4-cyano-1,3-dihydroxy-2-naphthoate (4a); MP 211-213 °C; R_f = 0.3 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.16 (br s, 1H), 8.27 (d, J = 8.3 Hz, 1H), 7.81–7.80 (m, 2H), 7.50 (m, 1H), 3.98 (s, 3H); IR (neat) ν_{max} 3398, 2219, 1658, 1631, 1240 cm^{-1}; Data is consistent with that reported in literature.[2]



2b **3a** **4b**

According to general procedure with 2-(cyanomethyl)-5-methylbenzoyl fluoride **2b** (89 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4b** was obtained as a yellow-white solid in 87% yield (112 mg, 0.44 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

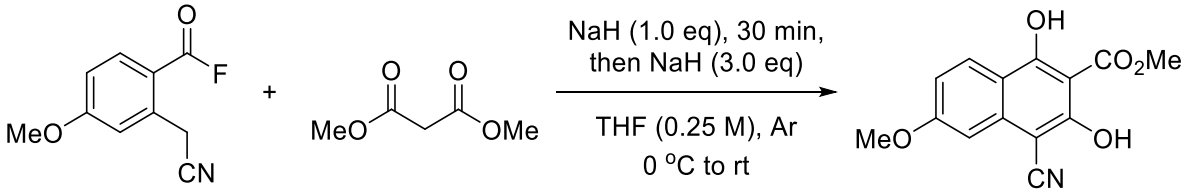
Methyl 4-cyano-1,3-dihydroxy-7-methyl-2-naphthoate (4b); MP 220-222 °C; R_f = 0.5 (Hex:EtOAc = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 10.89 (s, 1H), 8.03 (s, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.64 (dd, J = 1.8, 8.4 Hz, 1H), 4.00 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.9, 162.3, 160.2, 134.2, 134.1, 132.7, 123.4, 122.8, 120.0, 116.1, 100.8, 84.5, 53.3, 21.0; IR (neat) ν_{max} 3399, 2215, 1663, 1574, 1239 cm^{-1}; HRMS[ESI] calcd for $C_{14}H_{11}NO_4Na^+$ [M+Na]$^+$: 280.0580, found: 280.0582.



2c **3a** **4c**

According to general procedure with 2-(cyanomethyl)-4-methylbenzoyl fluoride **2c** (89 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4c** was obtained as a yellow-white solid in 97% yield (125 mg, 0.49 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

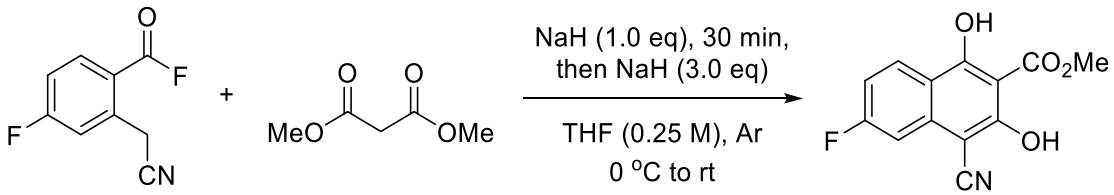
Methyl 4-cyano-1,3-dihydroxy-6-methyl-2-naphthoate (4c); MP 226-227 ºC; R_f = 0.2 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (br s, 2H), 8.15 (d, J = 8.6 Hz, 1H), 7.58 (s, 1H), 7.33 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.9, 162.6, 160.9, 143.0, 135.0, 126.7, 124.5, 122.0, 117.7, 115.9, 99.7, 84.5, 53.3, 21.6; IR (neat) ν_{max} 3395, 2214, 1662, 1635, 1251 cm^{-1}; HRMS[ESI] calcd for $C_{14}H_{11}NO_4Na^+$ [M+Na]$^+$: 280.0580, found: 280.0579.



2d **3a** **4d**

According to general procedure with 2-(cyanomethyl)-4-methoxybenzoyl fluoride **2d** (97 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4d** was obtained as a yellow solid in 80% yield (109 mg, 0.40 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

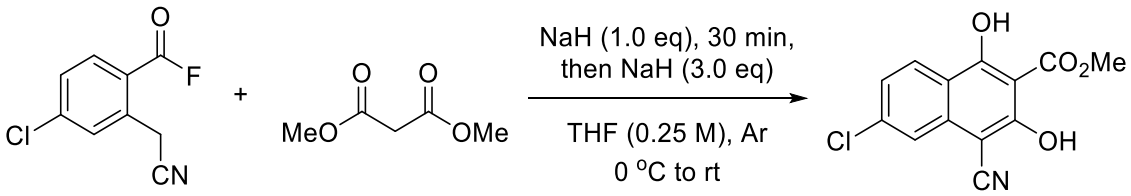
Methyl 4-cyano-1,3-dihydroxy-6-methoxy-2-naphthoate (4d); MP 203-204 ºC; R_f = 0.5 (Hex:EtOAc = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 11.01 (s, 1H), 8.14 (dd, J = 1.2, 9.2 Hz, 1H), 7.10 (m, 1H), 7.04 (m, 1H), 4.00 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.1, 162.7, 162.6, 161.6, 137.3, 126.7, 116.3, 115.9, 113.9, 102.2, 97.7, 84.5, 55.6, 53.3; IR (KBr) ν_{max} 3383, 2217, 1655, 1637, 1231 cm^{-1}; HRMS[ESI] calcd for $C_{14}H_{11}NO_5Na^+$ [M+Na]$^+$: 296.0529, found: 296.0529.



2e **3a** **4e**

According to general procedure with 2-(cyanomethyl)-4-fluorobenzoyl fluoride **2e** (91 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4e** was obtained as a yellow solid in 99% yield (129 mg, 0.49 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

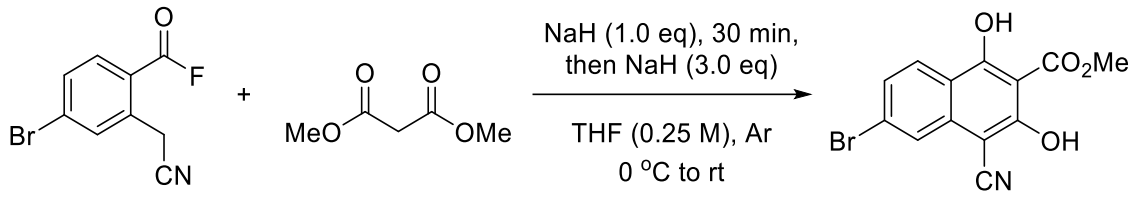
Methyl 4-cyano-6-fluoro-1,3-dihydroxy-2-naphthoate (4e); MP 156-158 °C; R_f = 0.3 (Hex:EtOAc = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.59 (br s, 1H), 8.32 (dd, J = 5.9, 9.2 Hz, 1H), 7.41–7.32 (m, 2H), 3.97 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.4, 165.1, 163.5, 162.0 (d, $J_{C,F}$ = 30.1 Hz), 136.7 (d, $J_{C,F}$ = 7.2 Hz), 128.4 (d, $J_{C,F}$ = 6.9 Hz), 116.8, 115.5, 114.4 (d, $J_{C,F}$ = 16.3 Hz), 107.0 (d, $J_{C,F}$ = 15.5 Hz), 100.8, 84.9 (d, $J_{C,F}$ = 2.9 Hz), 53.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.86 (m, 1F); IR (neat) ν_{max} 3385, 2922, 2217, 1633, 1583 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_8FNO_4Na^+$ $[M+Na]^+$: 284.0330, found: 284.0328.



2f **3a** **4f**

According to general procedure with 4-chloro-2-(cyanomethyl)benzoyl fluoride **2f** (99 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4f** was obtained as a yellow solid in 80% yield (111 mg, 0.40 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

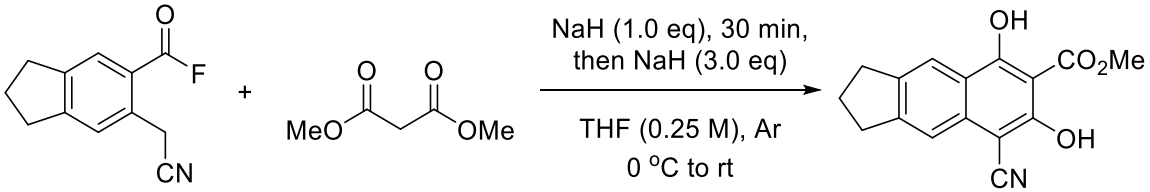
Methyl 6-chloro-4-cyano-1,3-dihydroxy-2-naphthoate (4f); MP 183-184 °C; R_f = 0.3 (Hex:EtOAc = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (br s, 1H), 8.21 (d, J = 8.9 Hz, 1H), 7.61 (d, J = 2.0 Hz, 1H), 7.38 (dd, J = 2.1, 8.8 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.4, 164.5, 163.6, 136.8, 135.9, 127.4, 124.1, 121.1, 120.3, 116.3, 100.7, 81.2, 52.8; IR (KBr) ν_{max} 3373, 2225, 1630, 1572, 1448 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_9ClNO_4^+$ $[M+H]^+$: 278.0215, found: 278.0220.



2g **3a** **4g**

According to general procedure with 4-bromo-2-(cyanomethyl)benzoyl fluoride **2g** (121 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4g** was obtained as a yellow solid in 66% yield (106 mg, 0.33 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

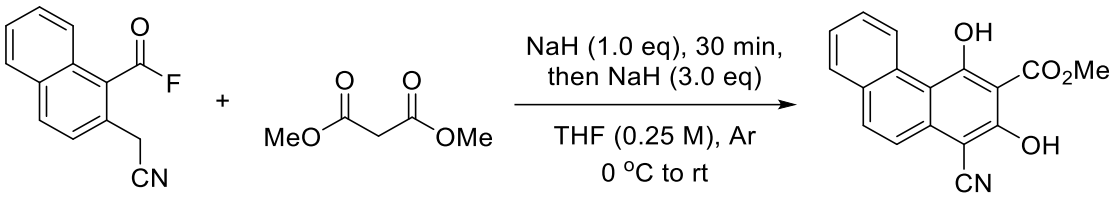
Methyl 6-bromo-4-cyano-1,3-dihydroxy-2-naphthoate (4g); MP 193-195 °C; R_f = 0.3 (Hex:EtOAc = 1:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.47 (br s, 1H), 8.15 (d, J = 5.9 Hz, 1H), 7.85 (d, J = 1.2 Hz, 1H), 7.60 (dd, J = 1.3, 5.9 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.4, 162.5, 161.9, 135.9, 127.5, 126.9, 126.3, 124.5, 119.1, 115.7, 101.8, 83.5, 53.2; IR (neat) ν_{max} 3441, 2217, 1604, 1571, 1498 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_9BrNO_4^+$ $[M+H]^+$: 321.9709, found: 321.9715.



2h **3a** **4h**

According to general procedure with 6-(cyanomethyl)-2,3-dihydro-1*H*-indene-5-carbonyl fluoride **2h** (102 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4h** was obtained as a yellow-white solid in 60% yield (85 mg, 0.30 mmol) after washing with ethyl acetate.

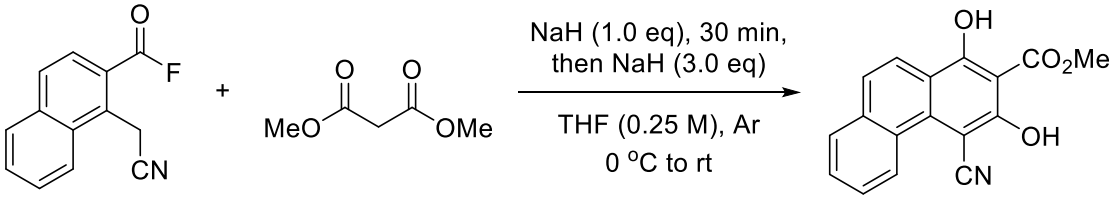
Methyl 8-cyano-5,7-dihydroxy-2,3-dihydro-1*H*-cyclopenta[b]naphthalene-6-carboxylate (4h); MP 228-229 °C; R_f = 0.2 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.88 (br s, 1H), 10.90 (br s, 1H), 8.08 (s, 1H), 7.64 (s, 1H), 3.99 (s, 3H), 3.06 (dd, J = 7.3, 7.3 Hz, 2H), 3.01 (dd, J = 7.3, 7.4 Hz, 2H), 2.09 (dddd, J = 7.3, 7.4, 7.4, 7.4 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.1, 162.5, 160.1, 150.8, 142.0, 134.2, 118.9, 118.8, 117.5, 116.2, 99.4, 84.8, 53.3, 32.6, 31.8, 25.4; IR (neat) ν_{max} 3395, 2213, 1658, 1638, 1336 cm^{-1}; HRMS[ESI] calcd for $C_{16}H_{14}NO_4^+$ $[M+H]^+$: 284.0917, found: 284.0922.



2i **3a** **4i**

According to general procedure with 2-(cyanomethyl)-1-naphthoyl fluoride **2i** (107 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4i** was obtained as a light yellow solid in 86% yield (126 mg, 0.43 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

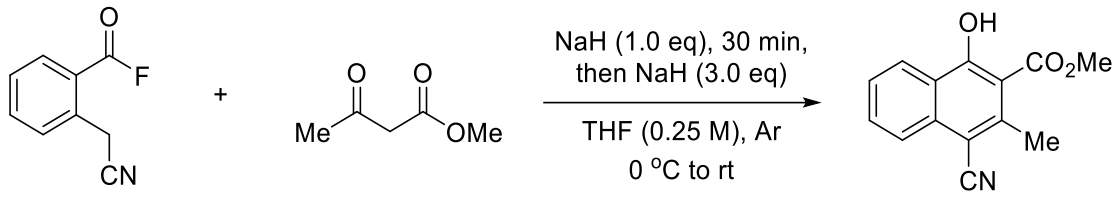
Methyl 1-cyano-2,4-dihydroxyphenanthrene-3-carboxylate (4i); MP 229-230 °C; R_f = 0.4 (Hex:EtOAc = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 13.25 (br s, 1H), 10.77 (br s, 1H), 9.52 (d, J = 8.6 Hz, 1H), 8.18 (d, J = 8.9 Hz, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.74 (m, 1H), 7.66 (m, 1H), 4.05 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.8, 165.6, 160.2, 137.3, 134.6, 131.1, 129.9, 129.3, 128.6, 127.0, 126.4, 121.7, 116.0, 113.3, 100.9, 88.3, 53.8; IR (neat) ν_{max} 3387, 2219, 1657, 1355, 1324 cm^{-1}; HRMS[EI+] calcd for $C_{17}H_{11}NO_4^+$ [M]$^+$: 293.0683, found: 293.0689.



2j **3a** **4j**

According to general procedure with 1-(Cyanomethyl)-2-naphthoyl fluoride **2j** (107 mg, 0.50 mmol) and dimethyl malonate **3a** (0.06 mL, 0.50 mmol), the product **4j** was obtained as a yellow-white solid in 81% yield (119 mg, 0.41 mmol) after flash column chromatography (Hex:EtOAc = 2:1 to 1:4).

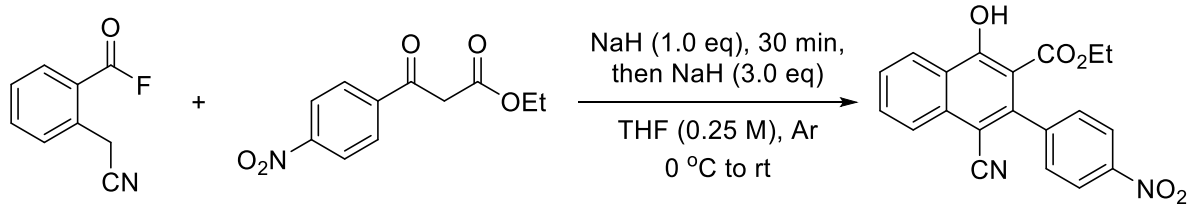
Methyl 4-cyano-1,3-dihydroxyphenanthrene-2-carboxylate (4j); MP 223-224 °C; R_f = 0.5 (Hex:EtOAc = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.48 (br s, 1 H), 9.61 (d, J = 8.9 Hz, 1H), 8.14 (d, J = 9.0 Hz, 1H), 8.04 (dd, J = 1.7, 7.6 Hz, 1H), 7.82–7.71 (m, 3H), 4.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 162.86, 161.3, 134.6, 133.0, 129.1, 129.1, 127.0, 126.7, 125.7, 124.9, 120.3, 118.5, 117.4, 100.8, 85.1, 53.5; IR (neat) ν_{max} 3386, 2213, 1681, 1448, 1422 cm^{-1}; HRMS[ESI] calcd for $C_{17}H_{12}NO_4^+$ [M+H]$^+$: 294.0761, found: 294.0765.



2a **3b** **4k**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and methyl 3-oxobutanoate **3b** (58 mg, 0.50 mmol), the product **4k** was obtained as a yellow-white solid in 75% yield (90 mg, 0.37 mmol) after flash column chromatography (Hex:EtOAc = 30:1 to 3:1).

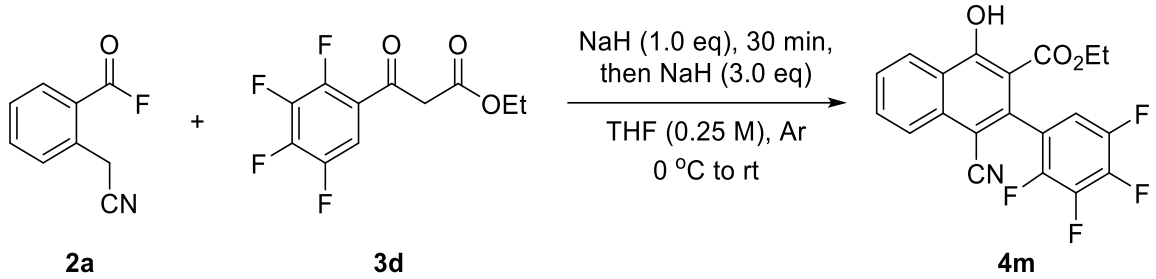
Methyl 4-cyano-1-hydroxy-3-methyl-2-naphthoate (4k); MP 158-160 °C; R_f = 0.5 (Hex:EtOAc = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.29 (s, 1H), 8.42 (ddd, *J* = 0.7, 1.3, 8.4 Hz, 1H), 8.10 (ddd, *J* = 0.9, 0.9, 8.3 Hz, 1H), 7.77 (ddd, *J* = 1.3, 7.0, 8.3 Hz, 1H), 7.58 (ddd, *J* = 1.2, 7.0, 8.4 Hz, 1H), 4.06 (s, 3H), 2.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 165.6, 144.1, 134.9, 132.1, 126.8, 124.9, 124.8, 123.6, 117.5, 106.7, 103.0, 53.0, 22.9; IR (neat) ν_{max} 2923, 2213, 1649, 1621, 1342 cm^{-1}; HRMS[ESI] calcd for $C_{14}H_{12}NO_3^+$ $[M+H]^+$: 242.0812, found: 242.0811.



2a **3c** **4l**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and ethyl 3-(4-nitrophenyl)-3-oxopropanoate **3c** (119 mg, 0.50 mmol), the product **4l** was obtained as a brown solid in 57% yield (103 mg, 0.28 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

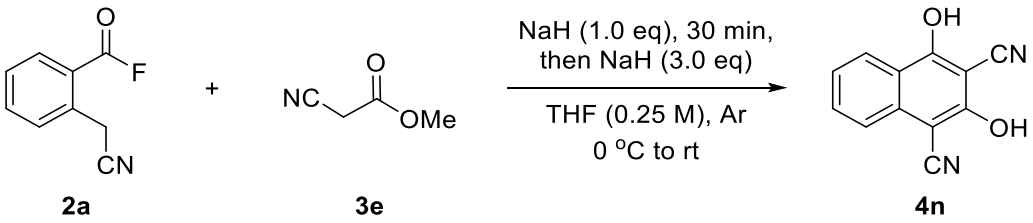
Ethyl 4-cyano-1-hydroxy-3-(4-nitrophenyl)-2-naphthoate (4l); MP 153-154 °C; R_f = 0.4 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.26 (s, 1H), 8.54 (ddd, *J* = 0.7, 1.4, 8.4 Hz, 1H), 8.36 (d, *J* = 8.8 Hz, 2H), 8.19 (ddd, *J* = 0.7, 4.0, 9.9 Hz, 1H), 7.87 (ddd, *J* = 1.3, 7.0, 8.3 Hz, 1H), 7.72 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1H), 7.53 (d, *J* = 8.8 Hz, 2H), 4.05 (q, *J* = 7.2 Hz, 2H), 0.77 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 165.4, 147.8, 146.8, 144.7, 134.2, 132.7, 129.7, 128.1, 125.5, 124.9, 124.5, 123.4, 116.3, 105.5, 103.1, 62.3, 13.1; IR (neat) ν_{max} 3348, 2219, 1654, 1519, 1243 cm^{-1};HRMS[ESI] calcd for $C_{20}H_{14}N_2O_5Na^+$ $[M+Na]^+$: 385.0795, found: 385.0794.



2a **3d** **4m**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and ethyl 3-oxo-3-(2,3,4,5-tetrafluorophenyl)propanoate **3d** (132 mg, 0.50 mmol), the product **4m** was obtained as a yellow solid in 75% yield (146 mg, 0.38 mmol) after flash column chromatography (Hex:EtOAc = 10:1 to 3:1).

Ethyl 4-cyano-1-hydroxy-3-(2,3,4,5-tetrafluorophenyl)-2-naphthoate (4m); MP 138-140 °C; R_f = 0.6 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.41 (s, 1H), 8.56 (ddd, *J* = 0.7, 1.3, 8.4 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.88 (ddd, *J* = 1.3, 7.0, 8.4 Hz, 1H), 7.74 (ddd, *J* = 1.2, 7.1, 8.4 Hz, 1H), 6.99 (m, 1H), 4.27–4.12 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.9, 165.6, 147.7 (d, $J_{C,F}$ = 11.9 Hz), 145.9 (dd, $J_{C,F}$ = 9.7, 46.0 Hz), 144.1 (d, $J_{C,F}$ = 11.2 Hz), 141.6 (dd, $J_{C,F}$ = 14.3, 14.7 Hz), 139.9 (dd, $J_{C,F}$ = 14.3, 15.4 Hz), 137.1, 134.2, 132.7, 128.3, 125.5, 124.9, 124.8, 115.9, 111.9 (d, $J_{C,F}$ = 20.0 Hz), 105.5, 104.2, 62.4, 13.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -139.1 (m, 1F), -139.6 (m, 1F), -154.8 (m, 1F), -155.6 (dd, *J* = 20.4, 20.6 Hz, 1F); IR (neat) ν_{max} 3445, 2924, 2223, 1657, 1525 cm^{-1}; HRMS[ESI] calcd for $C_{20}H_{12}F_4NO_3^+$ $[M+H]^+$: 390.0748, found: 390.0748.

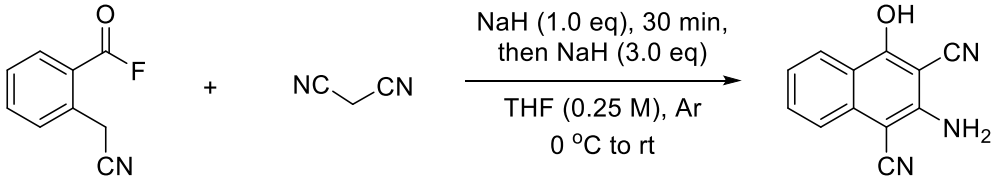


2a **3e** **4n**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and methyl 2-cyanoacetate **3e** (50 mg, 0.50 mmol), the product **4n** was obtained as a white solid in 77% yield (81 mg, 0.39 mmol) after flash column chromatography (CH_2Cl_2:MeOH = 20:1 to 5:1).

2,4-Dihydroxynaphthalene-1,3-dicarbonitrile (4n); decomposed at 291 °C; R_f = 0.2 (CH_2Cl_2:MeOH = 5:1); ^{1}H NMR (600 MHz, CD_3OD) δ 8.20 (dd, *J* = 0.6, 8.2 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.49 (ddd, *J* = 1.3, 7.0, 8.2 Hz, 1H), 7.17 (ddd, *J* = 1.0, 7.1, 8.1 Hz, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 176.6, 166.7, 137.3, 131.5, 126.1, 126.0, 123.8, 123.3, 119.6, 119.1, 88.1, 78.5; IR (KBr) ν_{max} 3588, 2219,

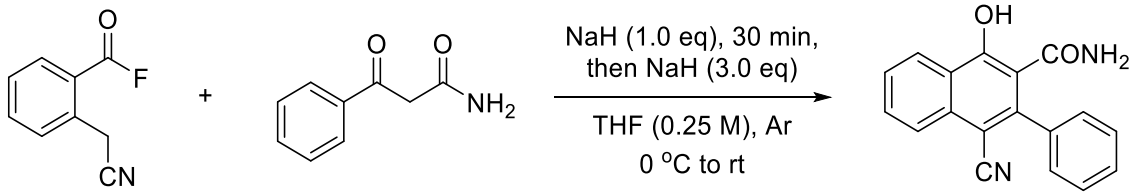
1619, 1595, 1554 cm^{-1}; HRMS[ESI] calcd for $C_{12}H_6N_2O_2Na^+$ $[M+Na]^+$: 233.0321, found: 233.0321.



2a **3f** **4o**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and malononitrile **3f** (33 mg, 0.50 mmol), the product **4o** was obtained as a yellow solid in 100% yield (105 mg, 0.50 mmol) after flash column chromatography (CH_2Cl_2:MeOH = 30:1 to 5:1).

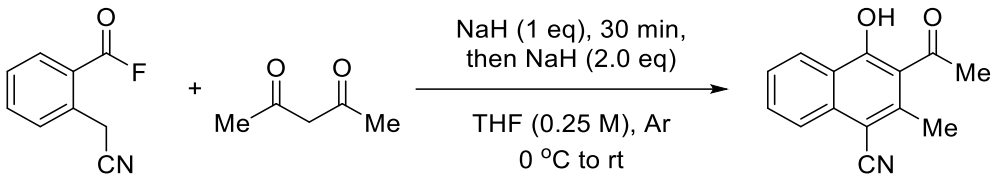
2-Amino-4-hydroxynaphthalene-1,3-dicarbonitrile (4o); decomposed at 288 °C; R_f = 0.6 (CH_2Cl_2:MeOH = 5:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (d, J = 8.2 Hz, 1H), 7.53 (d, J = 3.4 Hz, 2H), 7.16 (ddd, J = 3.2, 4.9, 8.2 Hz, 1H), 6.12 (s, 2H); ^{13}C NMR (100 MHz, , DMSO-d_6) δ 170.3, 153.8, 136.2, 130.9, 124.7, 121.9, 121.9, 121.4, 118.5, 117.4, 83.1, 72.7; IR (KBr) ν_{max} 3452, 3336, 2218, 1644, 1577 cm^{-1}; HRMS[ESI] calcd for $C_{12}H_8N_3O^+$ $[M+H]^+$: 210.0662, found: 210.0661.



2a **3g** **4p**

According to general procedure with 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) and 3-oxo-3-phenylpropanamide **3g** (82 mg, 0.50 mmol), the product **4p** was obtained as a white solid in 79% yield (114 mg, 0.40 mmol) after flash column chromatography (Hex:EtOAc = 3:1 to 1:1).

4-Cyano-1-hydroxy-3-phenyl-2-naphthamide (4p); MP 230-231 °C; R_f = 0.3 (Hex:EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.30 (s, 1H), 8.54 (d, J = 8.3 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H), 7.82 (ddd, J = 1.3, 7.0, 8.3 Hz, 1H), 7.66 (ddd, J = 1.2, 7.1, 8.4 Hz, 1H), 7.62–7.60 (m, 3H), 7.52–7.49 (m, 2H), 5.62 (br s, 1H), 5.33 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 166.5, 145.1, 137.8, 134.1, 132.2, 130.3, 129.9, 129.2, 127.5, 125.2, 125.0, 125.0, 117.0, 106.3, 102.4; IR (KBr) ν_{max} 3475, 3326, 2214, 1652, 1574 cm^{-1}; HRMS[ESI] calcd for $C_{18}H_{13}N_2O_2^+$ $[M+H]^+$: 289.0972, found: 289.0971.

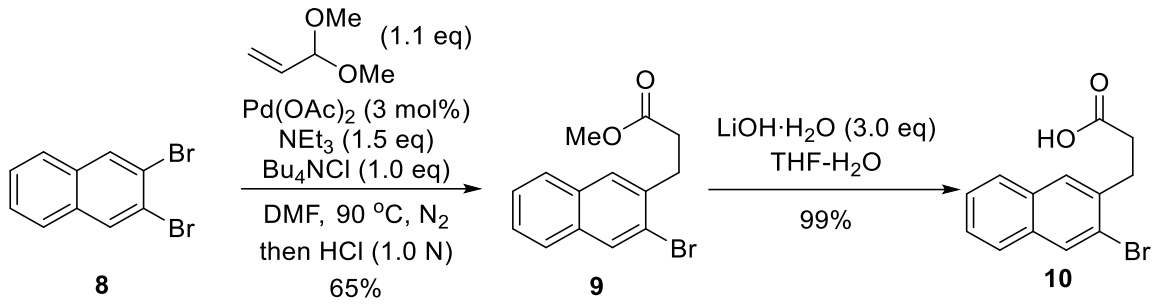


2a **3h** **4q**

To a stirred solution of pentane-2,4-dione **3h** (0.05 mL, 0.50 mmol) in dry THF (0.5 mL) was added NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol, 1 equiv) at 0 °C under argon atmosphere. After stirring for 30 min at 0 °C, 2-(cyanomethyl)benzoyl fluoride **2a** (82 mg, 0.50 mmol) in dry THF (1.5 mL) was added dropwise to the reaction mixture. After an additional 30-min stirring at 0 °C, NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol) was added at 0 °C. Subsequently, another portion of NaH (60% dispersion in mineral oil, 20 mg, 0.5 mmol) was added at 0 °C. The mixture was stirred for 3 h at rt, the resulting mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified over silica gel by flash chromatography (Hex:EtOAc = 5:1 to 3:1) to afford the desired product **4q** as a white solid in 41% yield (46 mg, 0.20 mmol).

3-acetyl-4-hydroxy-2-methyl-1-naphthonitrile (4q); MP 142 °C; R_f = 0.6 (Hex:EtOAc = 3:1); ^{1}H NMR (600 MHz, MeOD) δ 8.34 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.77 (ddd, , *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.60 (ddd, , *J* = 8.2, 7.0, 1.0 Hz, 1H), 2.75 (s, 3H), 2.69 (s, 3H); ^{13}C NMR (150 MHz, MeOD) δ 206.7, 160.7, 143.3, 135.6, 132.1, 127.7, 125.6, 125.1, 124.8, 122.5, 118.1, 103.0, 32.9, 21.0; IR (neat) ν_{max} 2216, 1619, 1571, 1498, 1412 cm^{-1}; HRMS[ESI] calcd for $C_{14}H_{12}O_2N^+$ $[M+H]^+$: 226.0868, found: 226.0862.

Procedures for Synthesis of Aristolactam Scaffold

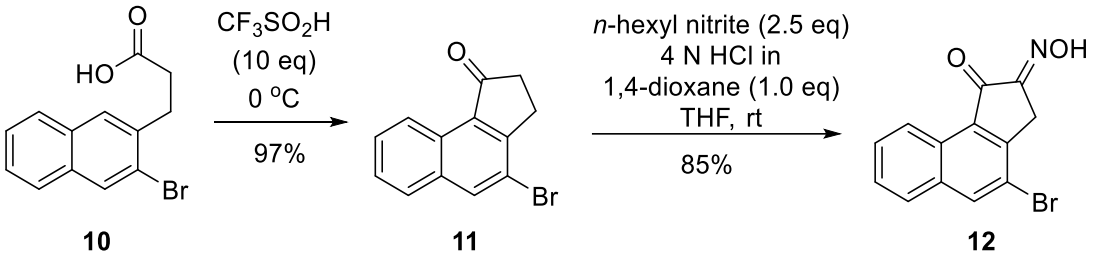


Step 1: A mixture of 2,3-dibromonaphthalene (1.0 g, 3.5 mmol), acrolein dimethyl acetal (0.45 mL, 3.85 mmol), $Pd(OAc)_2$ (24 mg, 105 μmol), tetrabutylammonium chloride (1.04 g, 3.5 mmol), triethylamine (0.72 mL, 5.25 mmol), and degassed DMF (10 mL) in sealed tube was stirred at 90 °C under nitrogen atmosphere for 6 hours. The reaction mixture was quenched with 1 N HCl (8 mL) and additionally stirred for 30 min. Then, it was further diluted with water (50 mL) and extracted with diethyl ether (3 X 50 mL). The combined organic solution was washed with water (3 X 50 mL), dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography (Hex:EtOAc = 7:1) to afford **9** (0.67 g, 2.29 mmol, 65%) as a colorless oil.

Methyl 3-(3-bromonaphthalen-2-yl)propanoate (9); R_f = 0.5 (Hex:EtOAc = 10:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.75 (m, 1H), 7.71–7.70 (m, 2H), 7.48–7.44 (m, 2H), 3.70 (s, 3H), 3.23 (t, J = 7.9 Hz, 2H), 2.76 (t, J = 7.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.2, 137.0, 133.3, 132.6, 131.5, 128.8, 127.5, 126.7, 126.51, 126.49, 122.6, 51.8, 34.3, 31.6; IR (neat) ν_{max} 2949, 1738, 1589, 1435, 1172 cm^{-1}; HRMS[ESI] calcd for $C_{14}H_{13}O_2BrNa^+$ $[M+Na]^+$: 314.9991, found: 314.9989.

Step 2: To a stirred solution of **9** (2.00 g, 6.82 mmol) in THF/H_2O (10 mL/3 mL) was added $LiOH·H_2O$ (0.86 g, 20.46 mmol) at room temperature. After stirring for 5 h, THF was removed under reduced pressure and the residue was acidified with 1 N HCl (25 mL). The mixture was then extracted with ethyl acetate (3 X 30 mL). The organic solution was dried over $MgSO_4$, filtered, and concentrated to afford **10** (1.89 g, 6.77 mmol, 99%) as a white solid.

3-(3-Bromonaphthalen-2-yl)propanoic acid (10); R_f = 0.26 (Hex:EtOAc = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.76 (m, 1H), 7.73–7.72 (m, 2H), 7.49–7.45 (m, 2H), 3.24 (t, J = 7.7 Hz, 2H), 2.81 (t, J = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.2, 136.8, 133.4, 132.6, 131.7, 128.9, 127.6, 126.7, 126.6 (2C), 122.6, 34.1, 31.3; IR (neat) ν_{max} 2950, 1713, 1589, 1434, 1309 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_{11}O_2BrNa^+$ $[M+Na]^+$: 300.9835, found: 300.9834.

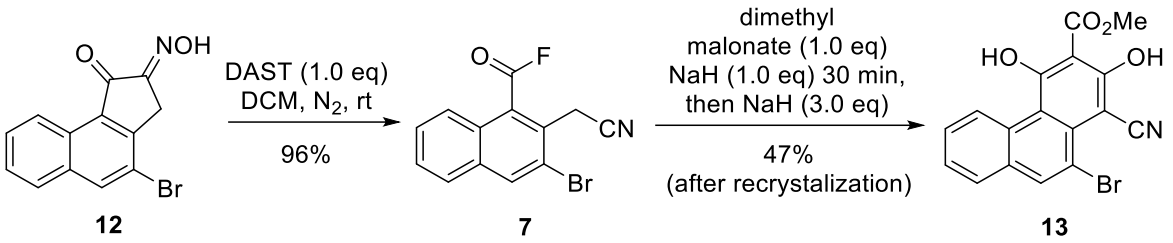


Step 3: Triflic acid (5.98 mL, 67.7 mmol) was slowly added to **10** (1.89 g, 6.77 mmol) in 100 mL round bottom flask at 0 °C. The reaction mixture was stirred at this temperature for 6 h. Then, the reaction mixture was poured into ice water and extracted with ethyl acetate (100 mL). The organic solution was washed with sat. $NaHCO_3$ solution, dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography (Hex:EtOAc = 10:1 to 3:1) to afford **11** (1.72 g, 6.59 mmol, 97%) as a yellow solid.

4-Bromo-2,3-dihydro-1*H*-cyclopenta[a]naphthalen-1-one (11); R_f = 0.8 (Hex:EtOAc = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.13 (d, *J* = 8.6 Hz, 1H), 8.24 (s, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.67 (m, 1H), 7.57 (m, 1H), 3.18–3.16 (m, 2H), 2.84–2.83 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.0, 157.5, 137.4, 134.2, 133.1, 129.3, 128.4, 127.6, 127.3, 124.2, 119.4, 37.0, 27.5; IR (neat) ν_{max} 2922, 1695, 1585, 1437, 1156 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_{10}OBr^+$ $[M+H]^+$: 260.9910, found: 260.9910.

Step 4: To a stirred solution of **11** (1.72 g, 6.58 mmol) and *n*-hexyl nitrite (2.45 mL, 16.45 mmol) in THF (15 mL) was added 4 N HCl in 1,4-dioxane (1.65 mL, 6.58 mmol). After 30 min, the reaction mixture was quenched with sat. $NaHCO_3$ solution and extracted with ethyl acetate (3 X 30 mL). The combined organic solution was dried over $MgSO_4$, filtered, concentrated. The crude product was purified by trituration with hexane to afford **12** (1.63 g, 5.62 mmol, 85%) as a yellow solid.

(*Z*)-4-Bromo-2-(hydroxyimino)-2,3-dihydro-1*H*-cyclopenta[a]naphthalen-1-one (12); R_f = 0.3 (Hex:EtOAc = 3:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.76 (s, 1H), 9.04 (d, *J* = 8.3 Hz, 1H), 8.67 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.80 (td, *J* = 6.9, 1.3 Hz, 1H), 7.69 (m, 1H), 3.78 (s, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 189.5, 153.6, 149.7, 138.3, 133.8, 133.5, 129.9, 128.1, 127.9, 127.5, 123.1, 118.6, 29.8; IR (KBr) ν_{max} 3228, 1716, 1505, 1276, 1153 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_9O_2NBr^+$ $[M+H]^+$: 289.9811, found: 289.9808.



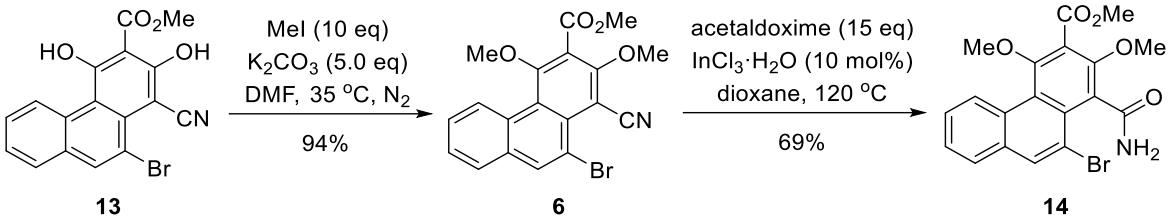
Step 5: A 100 mL round bottom flask was charged with **12** (489 mg, 1.69 mmol) and dry CH_2Cl_2 (6 mL) under nitrogen atmosphere. Then, (diethylamino)sulfur trifluoride (DAST, 0.22 mL, 1.69 mmol) was added to the solution at room temperature. After 10 min, the reaction mixture was diluted with diethyl ether (30 mL), and it was washed with 1 N HCl solution (10 mL) and subsequently with sat. $NaHCO_3$ solution. The organic solution was dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography (Hex:EtOAc = 1:1) to afford **7** (472 mg, 1.62 mmol, 96%) as a yellow solid.

3-Bromo-2-(cyanomethyl)-1-naphthoyl fluoride (7); R_f = 0.6 (Hex:EtOAc = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) 8.32 (s, 1H), 7.99 (dd, J = 8.5, 2.3 Hz, 1H), 7.79 (m, 1H), 7.64 (m, 1H), 7.60 (m, 1H), 4.10 (d, J = 1.1 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.7 (d, $J_{C,F}$ = 353.7 Hz), 137.1, 133.9, 129.6, 129.3, 128.9, 128.8, 127.8, 127.0 (d, $J_{C,F}$ = 56.8 Hz), 125.1 (d, $J_{C,F}$ = 3.8 Hz), 121.4 (d, $J_{C,F}$ = 2.6 Hz), 115.5, 23.7; ^{19}F NMR (565 MHz, $CDCl_3$) δ 59.21 (s, 1F); IR (neat) ν_{max} 2916, 2256, 1815, 1582, 1418 cm^{-1}; HRMS[ESI] calcd for $C_{13}H_7ONBrFNa^+$ $[M+Na]^+$: 313.9587, found: 313.9586.

Step 6: To a stirred solution of dimethylmalonate (0.28 mL, 2.19 mmol) in dry THF (4 mL) was added NaH (60% dispersion in mineral oil, 88 mg, 2.19 mmol) at 0 °C under nitrogen atmosphere. After stirring for 30 min, **7** (639 mg, 2.19 mmol) in THF (7 mL) was added dropwise to the reaction mixture and additionally stirred for 30 min at 0 °C. Subsequently, NaH (60% dispersion in mineral oil, 88 mg, 2.19 mmol) was added and stirred for 30 min at 0 °C. Then, NaH (60% dispersion in mineral oil, 88 mg, 2.19 mmol) was added at 0 °C and stirred for 3 h at room temperature. Finally, NaH (60% dispersion in mineral oil, 88 mg, 2.19 mmol) was added at 0 °C and stirred for 3 h at room temperature. The reaction mixture was acidified with 1N HCl, and the precipitated solid was filtered and washed with water three times. The collected yellow solid was dried in vacuum drying oven for 3 hours. The resulting powder was washed with hexane, and recrystallized with MeOH to afford **13** (381 mg, 1.02 mmol, 47%) as a yellow solid.

Methyl 10-bromo-1-cyano-2,4-dihydroxyphenanthrene-3-carboxylate (13); MP 223-225 °C; R_f = 0.8 (DCM/MeOH = 3%); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.10 (br s, 1H), 9.49 (d, J = 8.8 Hz, 1H), 8.59 (s, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.73 (m, 1H), 7.65 (m, 1H), 4.04 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.2, 164.3, 162.3, 139.6, 134.3, 131.1, 129.2, 128.8, 128.2, 127.3, 126.9, 116.0, 115.5,

114.6, 102.5, 88.4, 53.8; IR (KBr) ν_{max} 3372, 2921, 2214, 1674, 1220 cm^{-1}; HRMS[ESI] calcd for $C_{17}H_{10}O_4NBrNa^+$ $[M+Na]^+$: 393.9685, found: 393.9682.

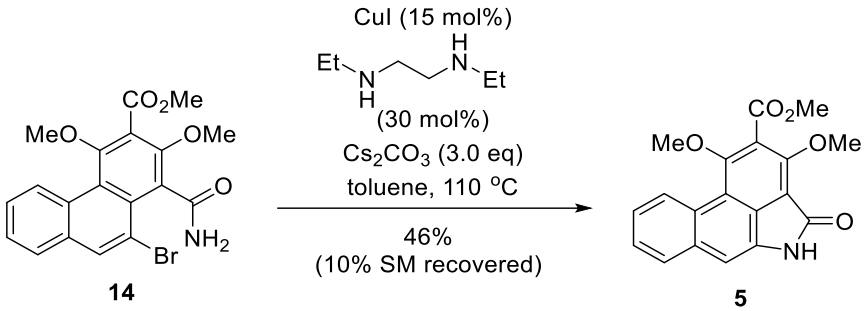


Step 7: Methyl iodide (0.54 mL, 8.7 mmol) was added to a stirred mixture of **13** (325 mg, 0.87 mmol) and K_2CO_3 (604 mg, 4.35 mmol) in dry DMF (3.0 mL). The reaction mixture was stirred at 35 °C under nitrogen atmosphere for 20 h. Then, it was neutralized with 1 N HCl (20 mL) and extracted with ethyl acetate (3 X 15 mL). The combined organic solution was washed with water (3 X 20 mL), dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography (Hex:EtOAc = 5:1 to 1:1) to afford **6** (328 mg, 0.82 mmol, 94%) as a yellow solid.

Methyl 10-bromo-1-cyano-2,4-dimethoxyphenanthrene-3-carboxylate (6); MP 138-140 °C; R_f= 0.9 (Hex:EtOAc = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.31 (m, 1H), 8.29 (s, 1H), 7.82 (m, 1H), 7.73–7.63 (m, 2H), 4.18 (s, 3H), 4.06 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 162.7, 160.2, 138.1, 133.6, 132.1, 128.8, 128.4, 128.3, 127.9, 127.0, 124.0, 123.1, 116.2, 115.0, 100.8, 63.6, 62.5, 53.3; IR (neat) ν_{max} 2949, 2217, 1767, 1365, 1325 cm^{-1}; HRMS[ESI] calcd for $C_{19}H_{15}O_4NBr^+$ $[M+H]^+$: 400.0179, found: 400.0179.

Step 8: A mixture of **6** (250 mg, 0.63 mmol), acetaldoxime (0.58 mL, 9.45 mmol) and $InCl_3{\cdot}4H_2O$ (18 mg, 0.063 mmol) in 1,4-dioxane (2.5 mL) was stirred at 120 °C for 13 h. The reaction mixture was diluted with water (25 mL) and extracted with ethyl acetate (3 X 25 mL). The organic solution was dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography (Hex:EtOAc = 5:1 to 1:1) to afford **14** (180 mg, 0.43 mmol, 69%) as an off white solid.

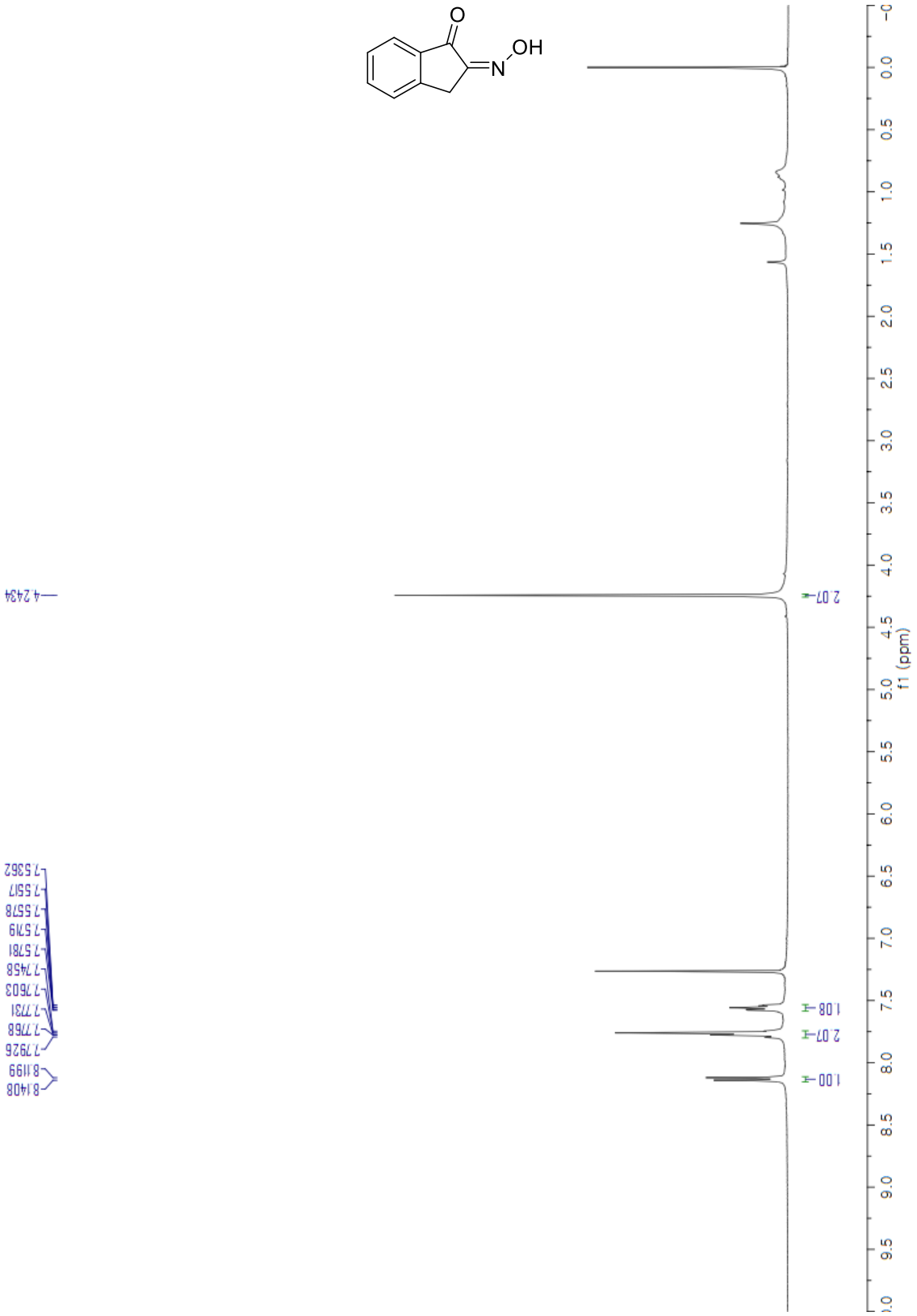
Methyl 10-bromo-1-carbamoyl-2,4-dimethoxyphenanthrene-3-carboxylate (14); MP 212-213 °C; R_f= 0.3 (Hex:EtOAc = 1:1); ^{1}H NMR (600MHz, $CDCl_3$) δ 9.34 (d, J = 8.6 Hz, 1H), 8.21 (s, 1H), 7.77 (dd, J = 1.4 , 7.7 Hz, 1H), 7.66 (m, 1H), 7.62 (m, 1H), 6.10 (d, J = 55.6 Hz, 2H), 4.05 (s, 3H), 3.98 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.3, 166.2, 157.3, 153.6, 136.6, 132.1, 130.8, 128.5, 128.3, 127.9, 127.6, 127.2, 125.8, 124.2, 123.5, 116.6, 64.5, 62.3, 53.1; IR (neat) ν_{max} 3452, 2949, 1734, 1666, 1354 cm^{-1}; HRMS[ESI] calcd for $C_{19}H_{16}O_5NBrNa^+$ $[M+Na]^+$: 440.0104, found: 440.0103.



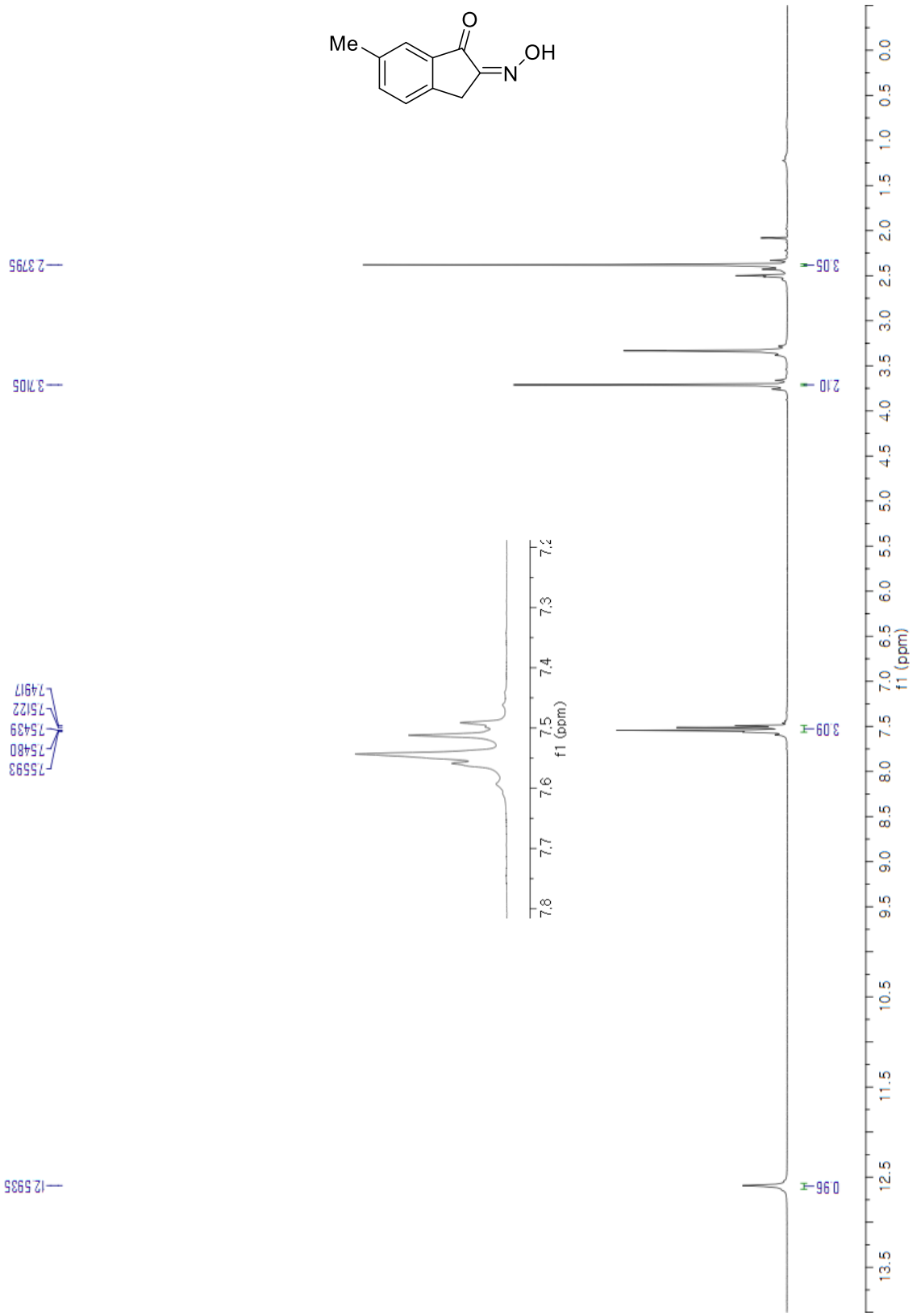
Step 9: A mixture of **14** (20 mg, 0.048 mmol), CuI (1.4 mg, 7.2 μmol), Cs_2CO_3 (46 mg, 0.14 mmol), *N*,*N*–diethylethylenediamine (2.0 μL, 14.4 μmol) and degassed toluene (1.0 mL) in sealed tube was stirred at 110 °C under nitrogen atmosphere for 5 h. The reaction mixture was quenched with saturated NH_4Cl and extracted with ethyl acetate (3 X 5 mL). The organic solution was dried over $MgSO_4$, filtered, concentrated, and subjected to silica gel column chromatography (Hex:EtOAc = 5:1 to 1:1) to afford **5** (7.4 mg, 0.022 mmol, 46%) a yellow solid.

Methyl 1,3-dimethoxy-4-oxo-4,5-dihydrodibenzo[cd,f]indole-2-carboxylate (5); MP 252-254 °C; R_f = 0.7 (Hex:EtOAc = 1:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.18 (br s, 1H), 8.90 (m, 1H), 8.04 (m, 1H), 7.62–7.60 (m, 2H), 7.39 (s, 1H), 4.37 (s, 3H), 3.98 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.72, 165.70, 159.8, 154.8, 134.6, 133.3, 131.3, 129.1, 127.0, 126.1, 125.8, 125.0, 123.3, 115.0, 109.5, 107.1, 63.0, 62.2, 52.8; IR (neat) ν_{max} 3452, 3040, 1735, 1684, 1588 cm^{-1}; HRMS[ESI]: calcd for $C_{19}H_{15}O_5NNa^+$ $[M+Na]^+$: 360.0842, found: 360.0842.

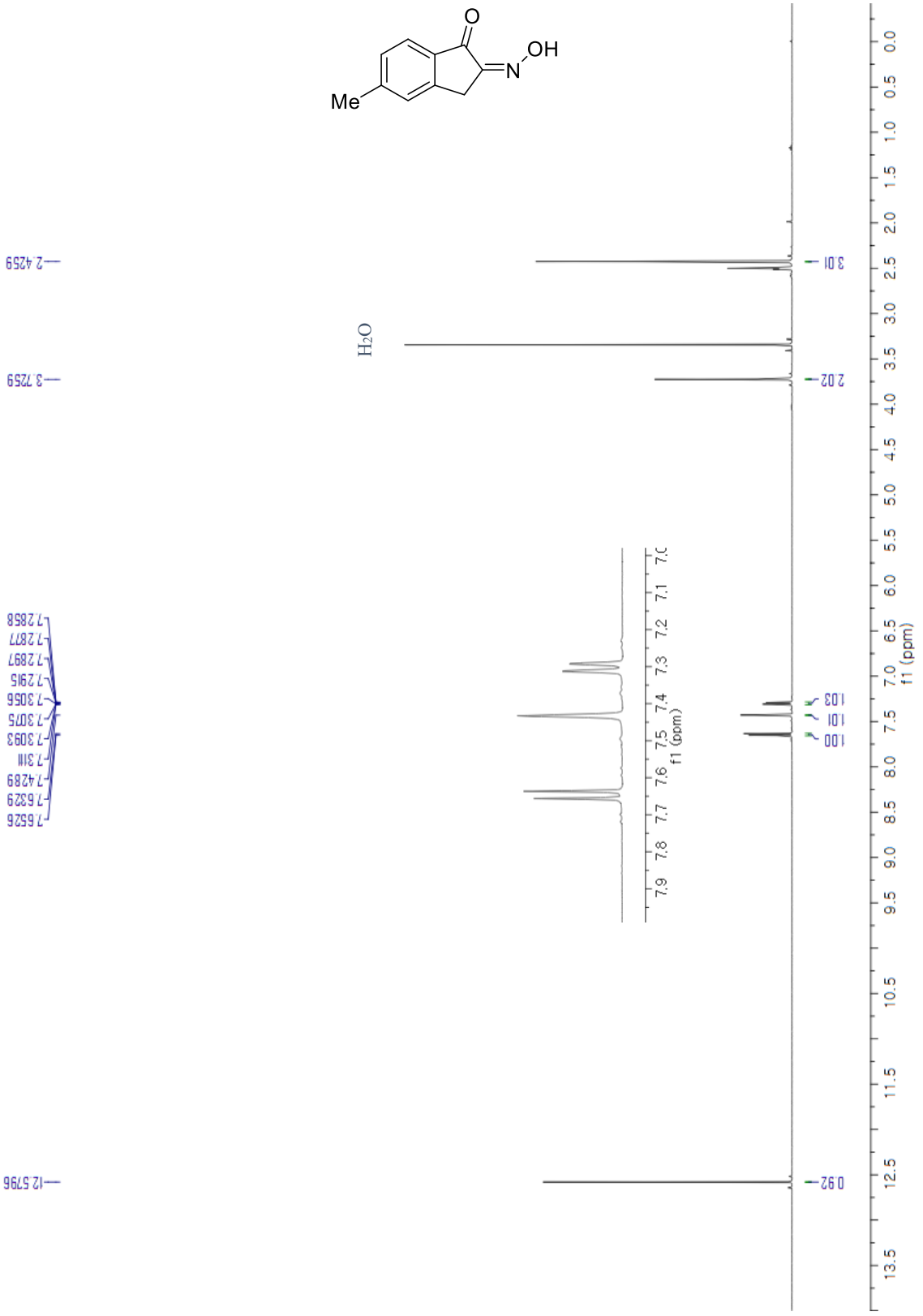
3. ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR



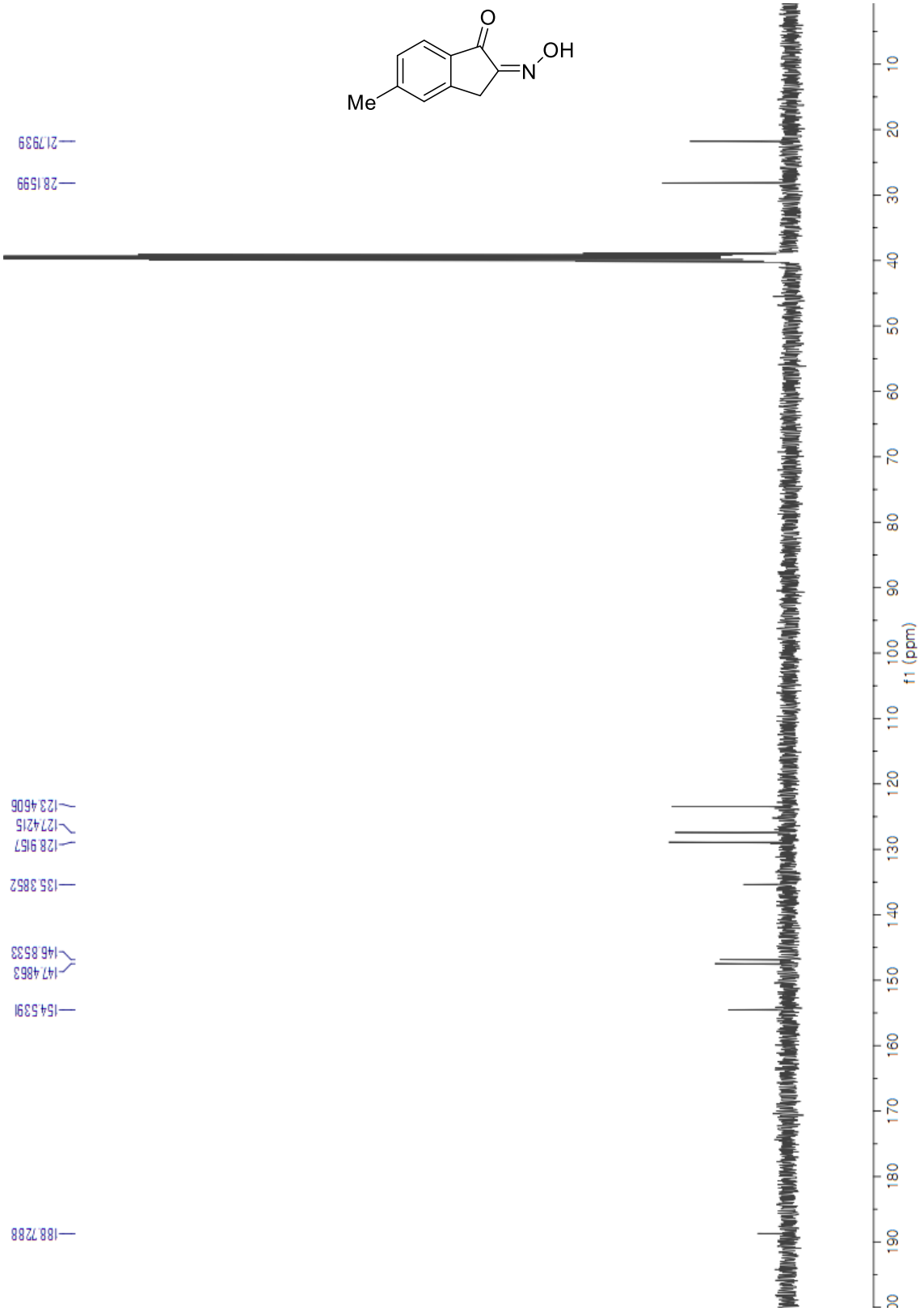
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1a**



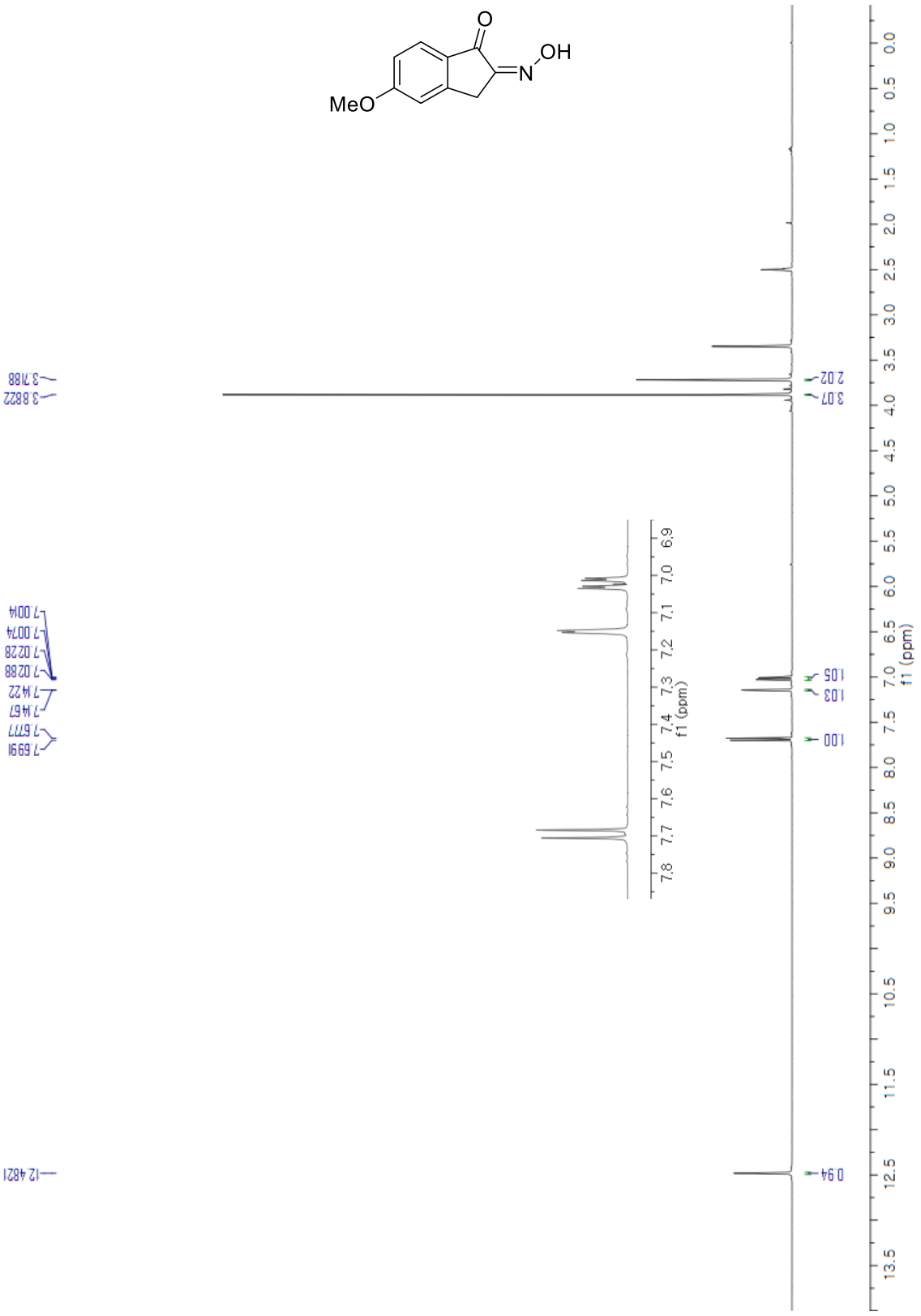
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1b**



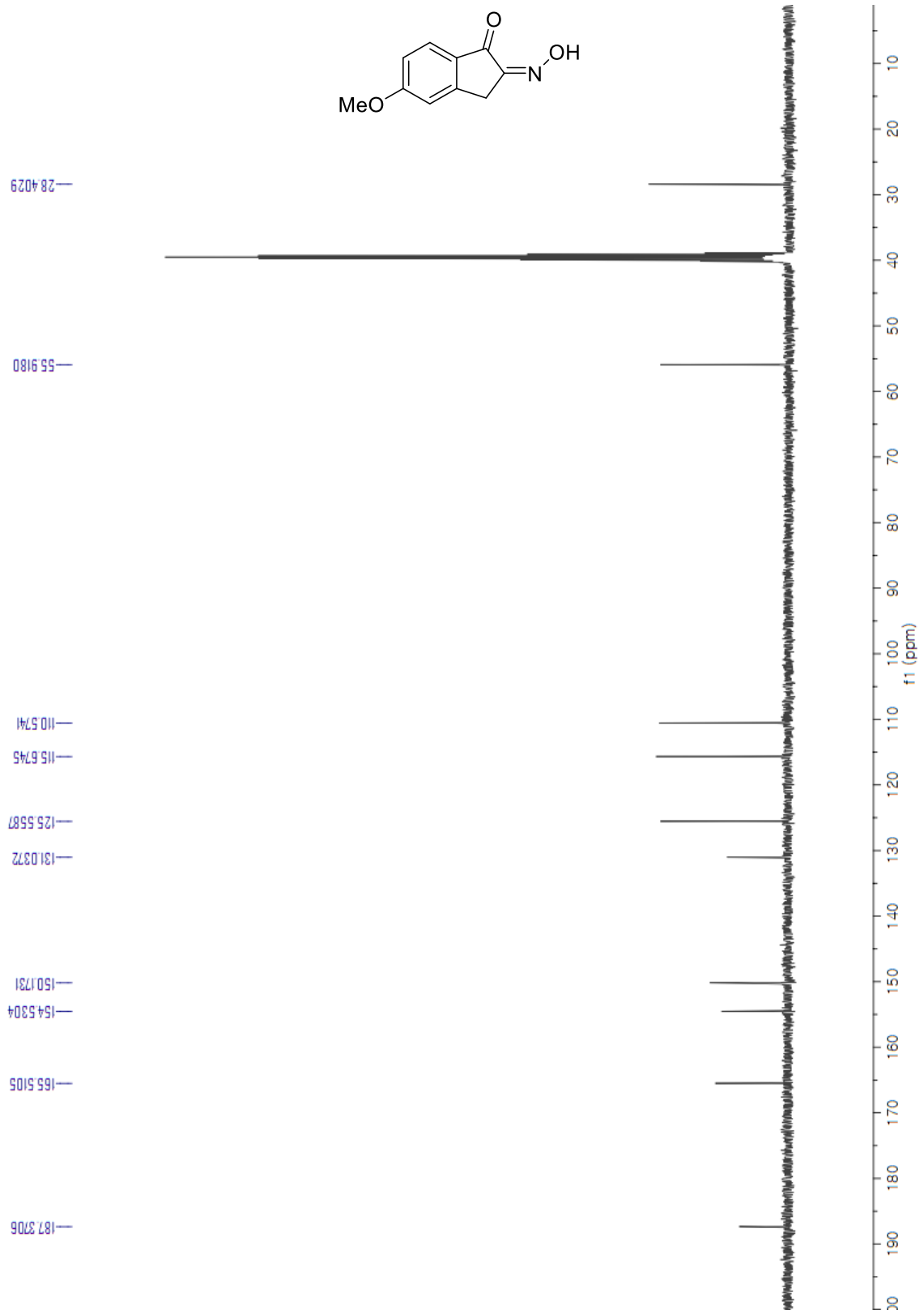
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1c**



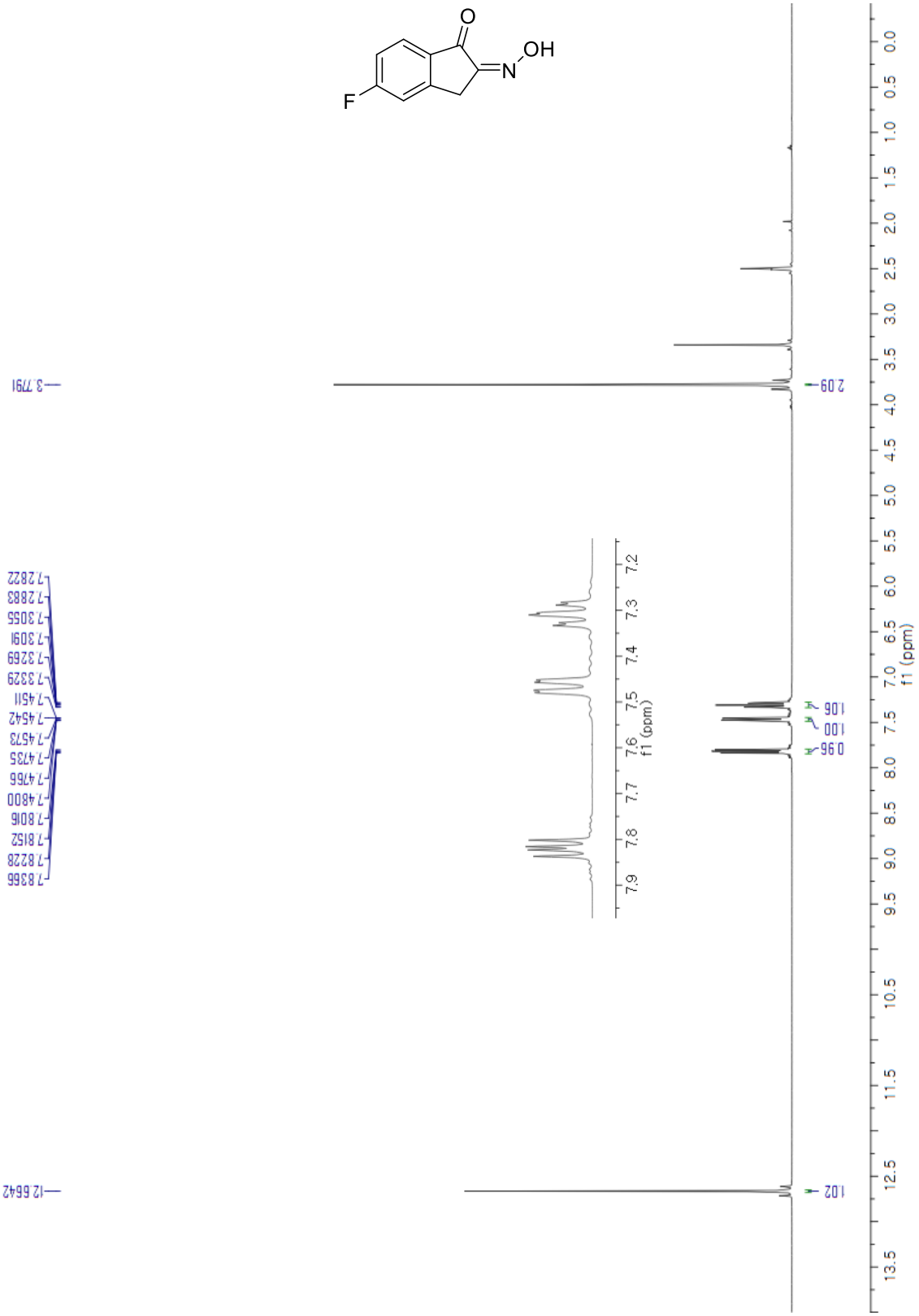
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1c**



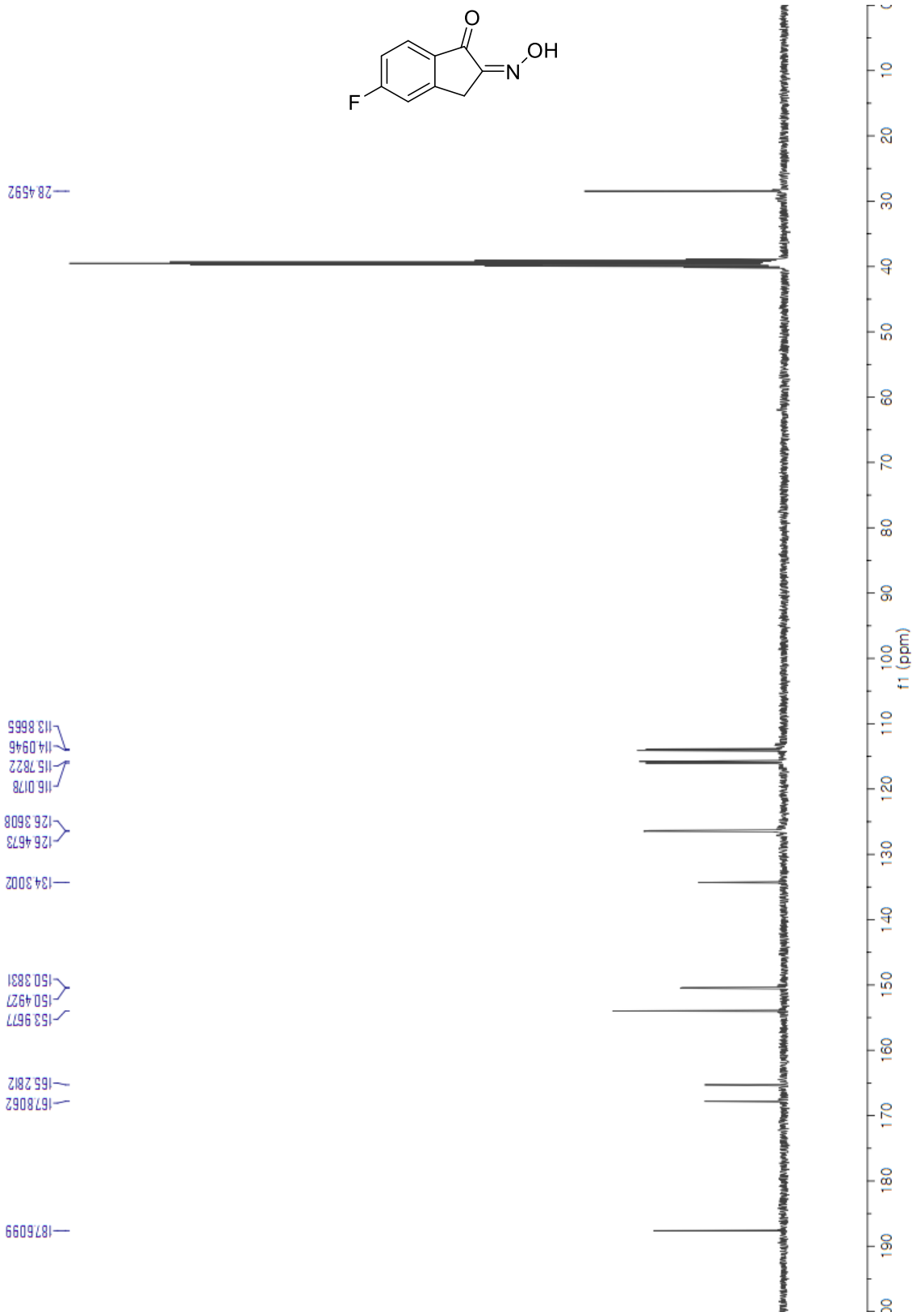
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1d**



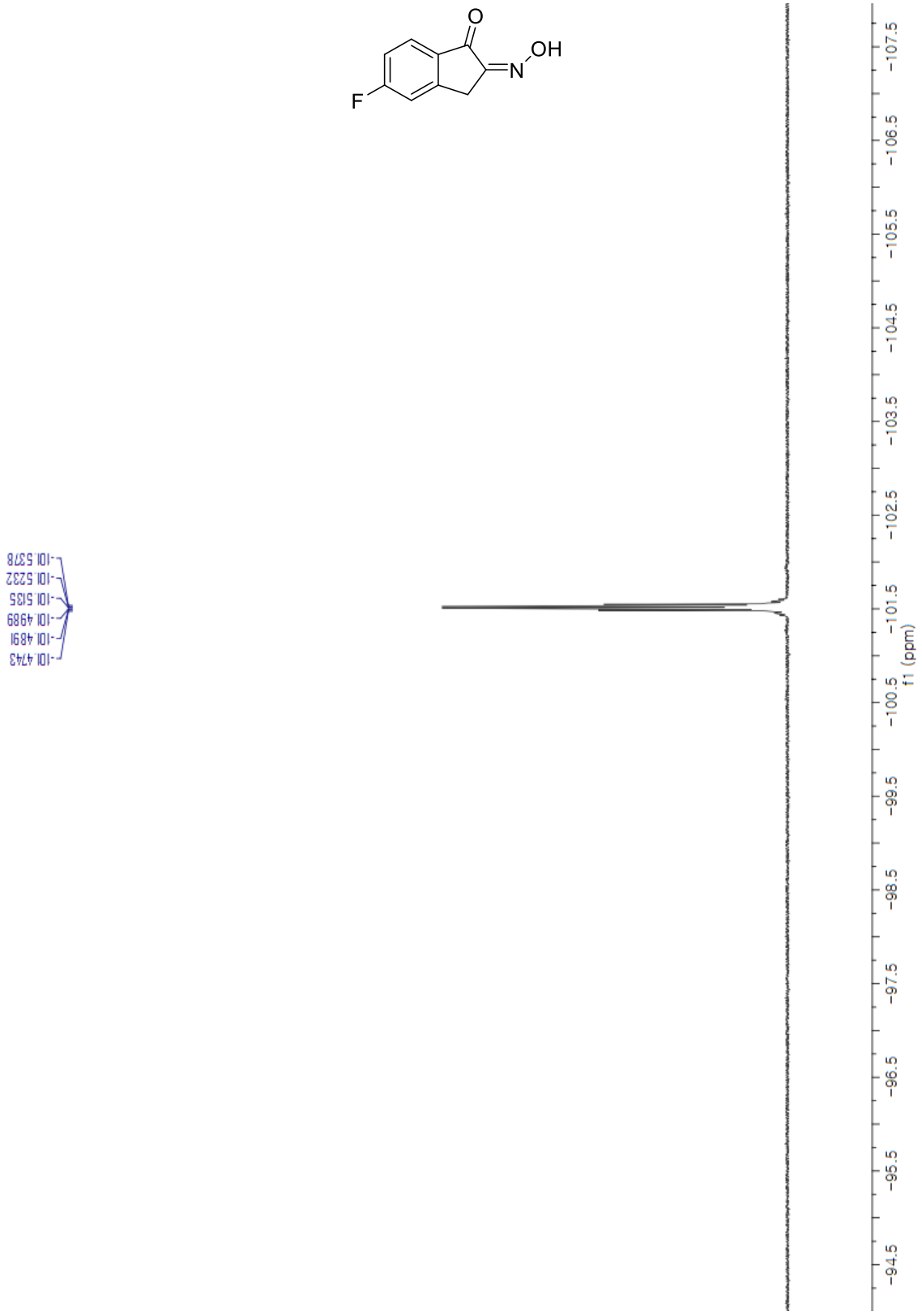
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1d**



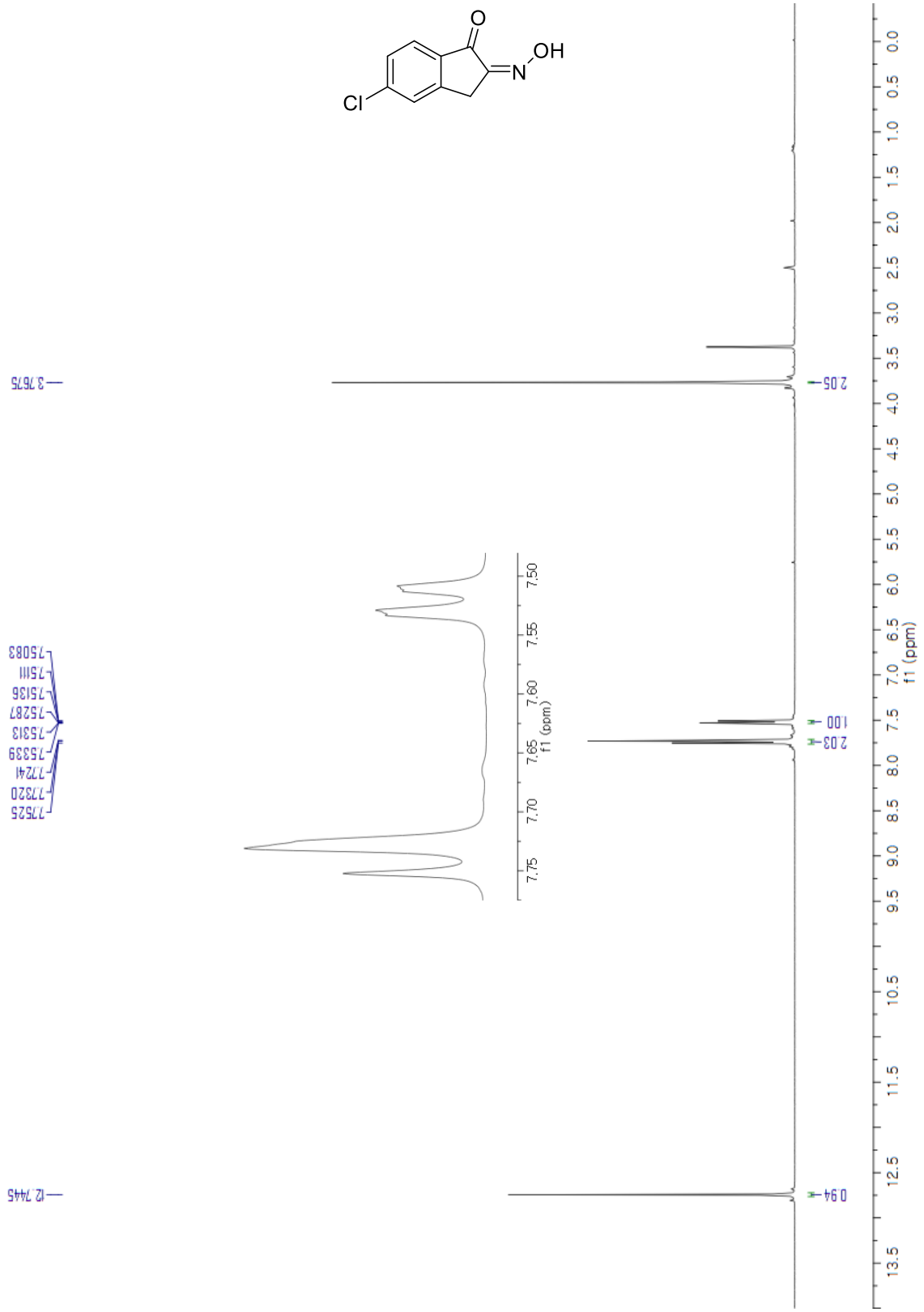
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1e**



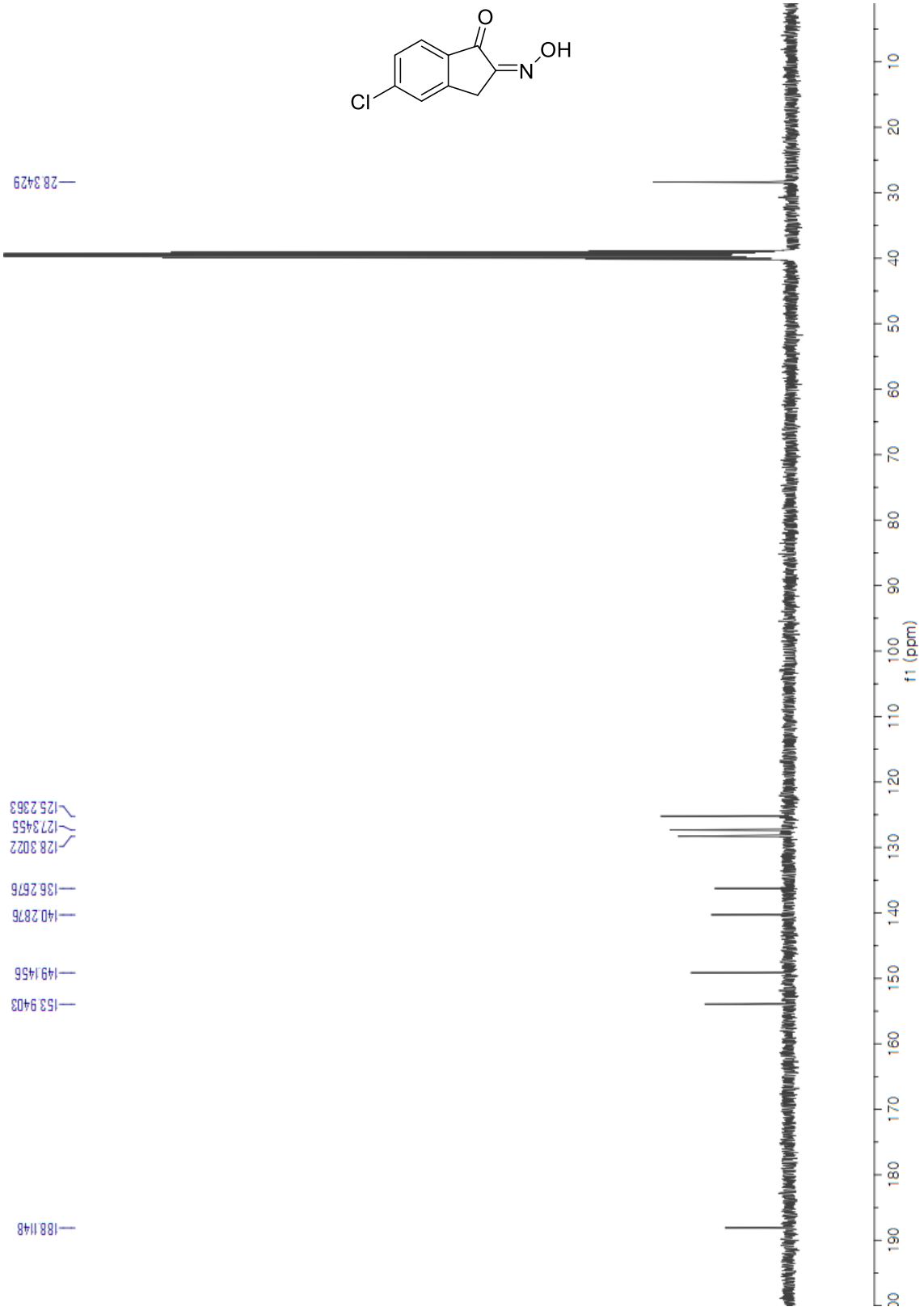
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1e**



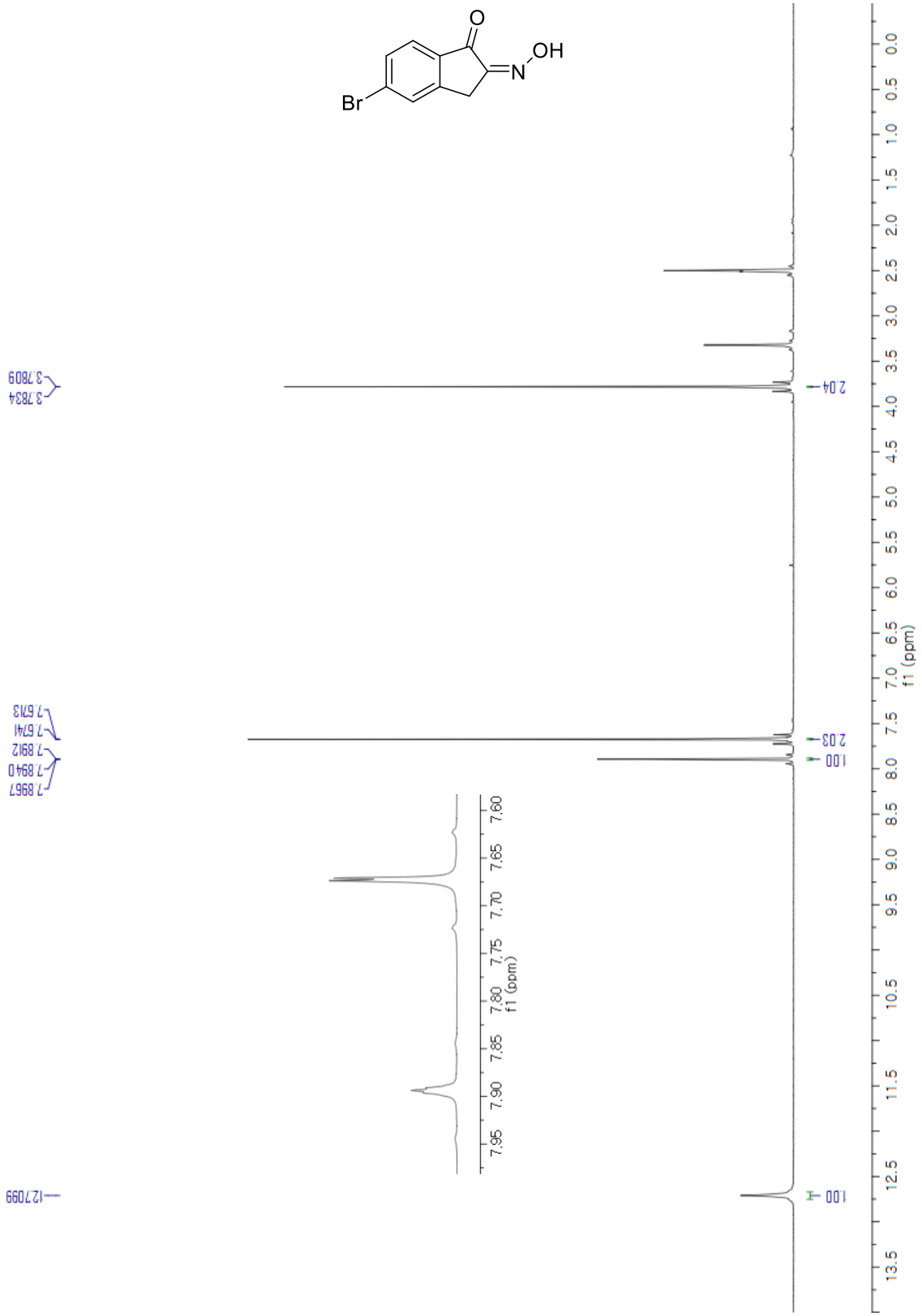
^{19}F NMR (DMSO-d_6, 376 MHz) of compound **1e**



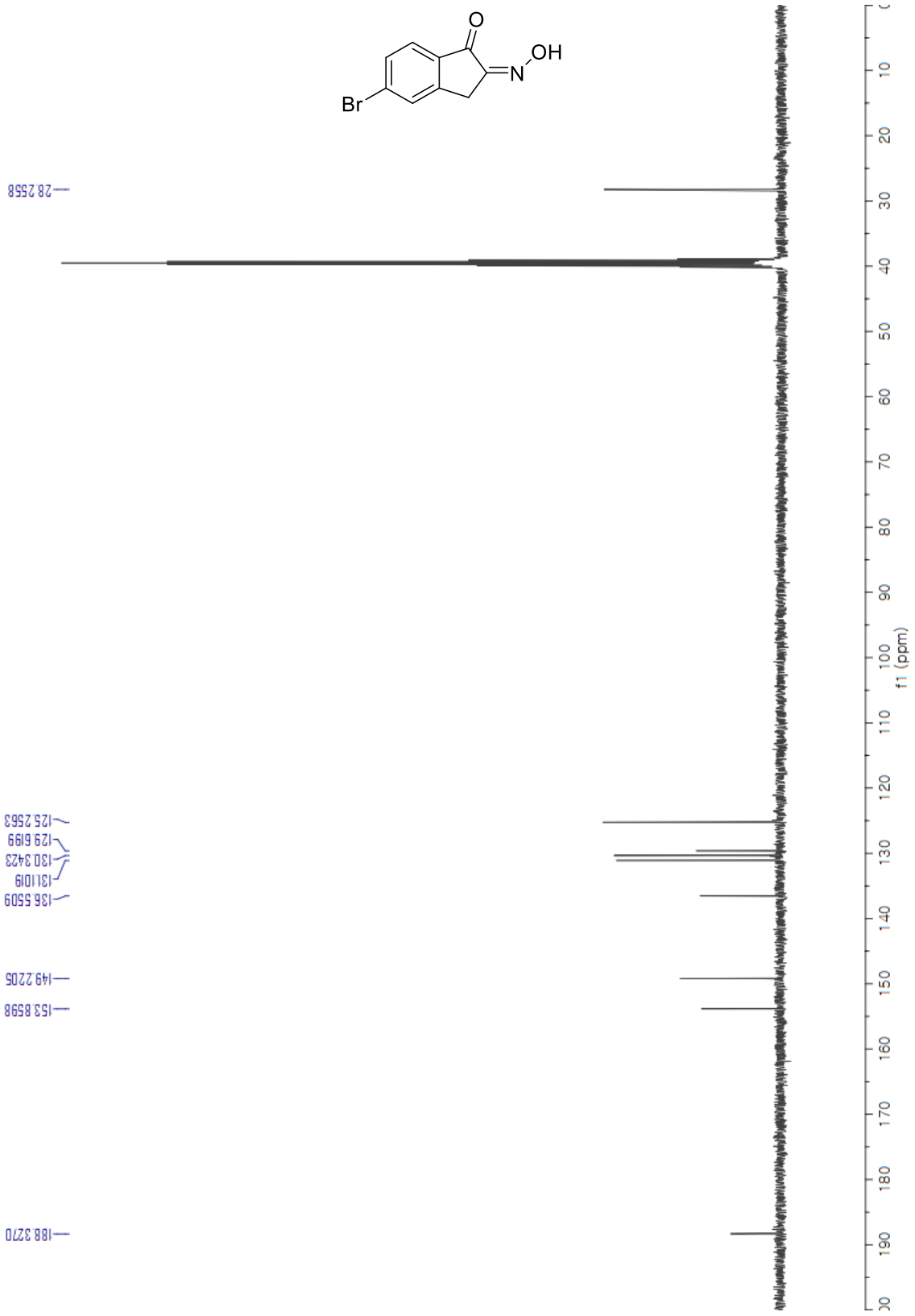
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1f**



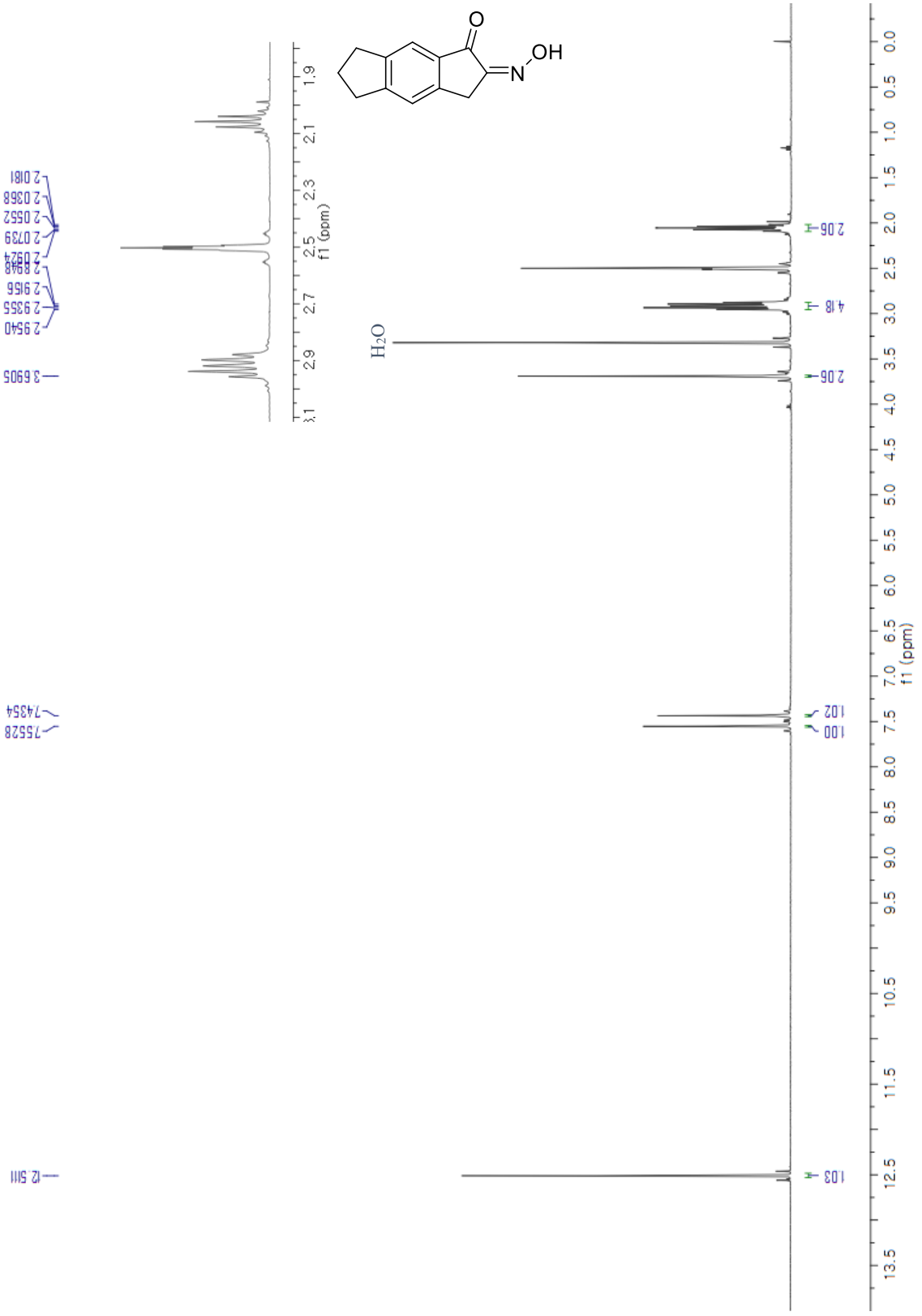
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1f**



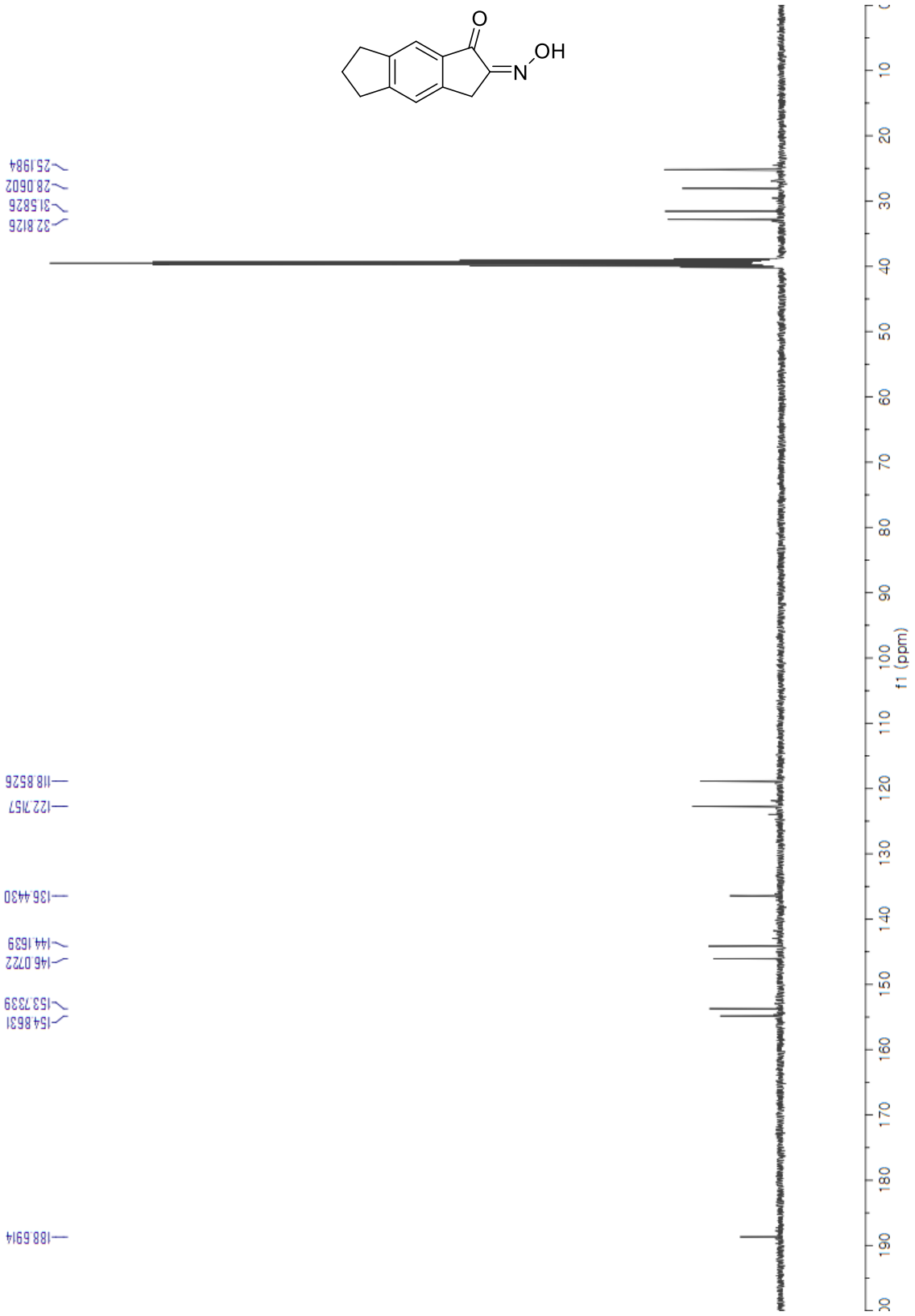
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1g**



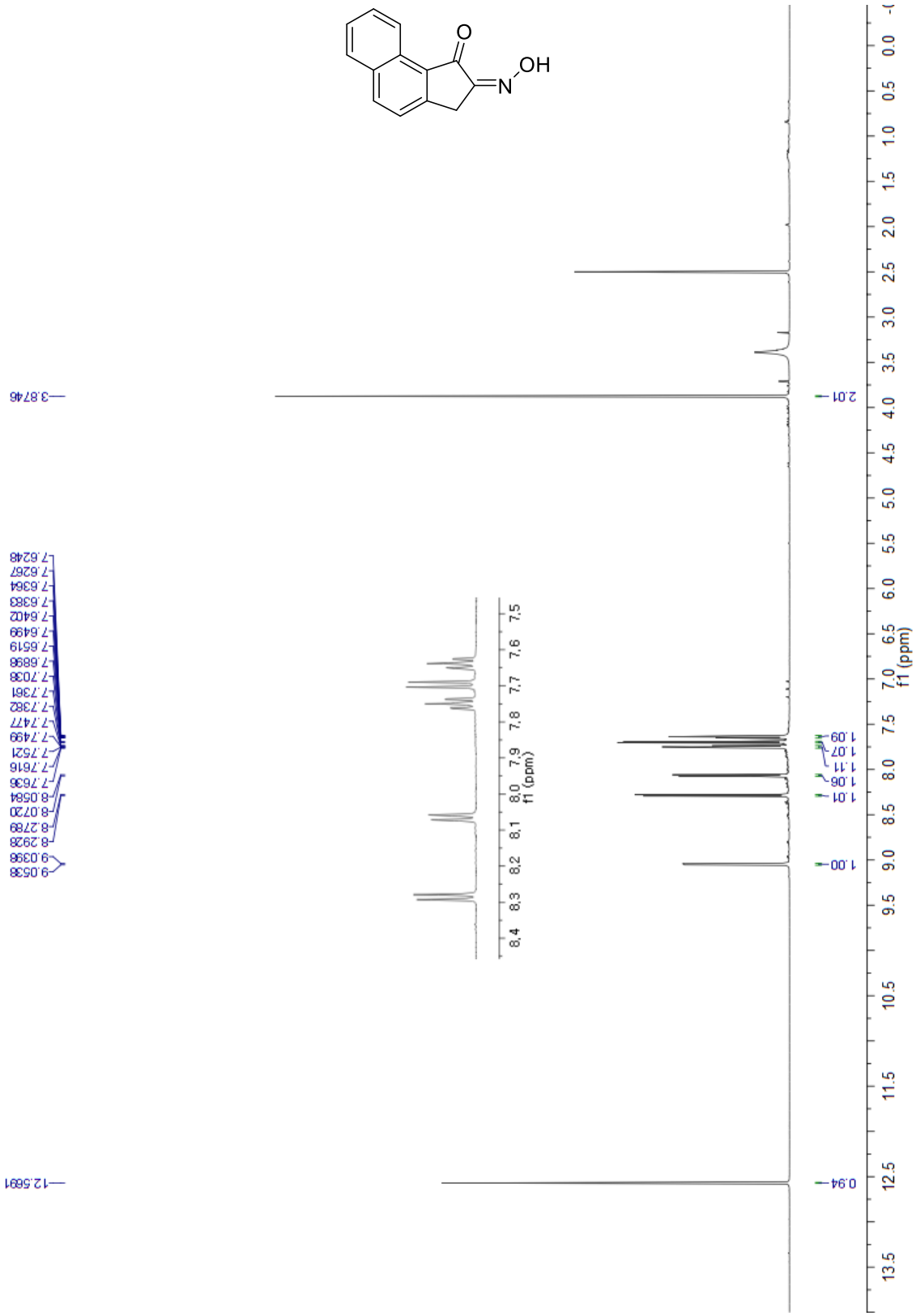
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1g**



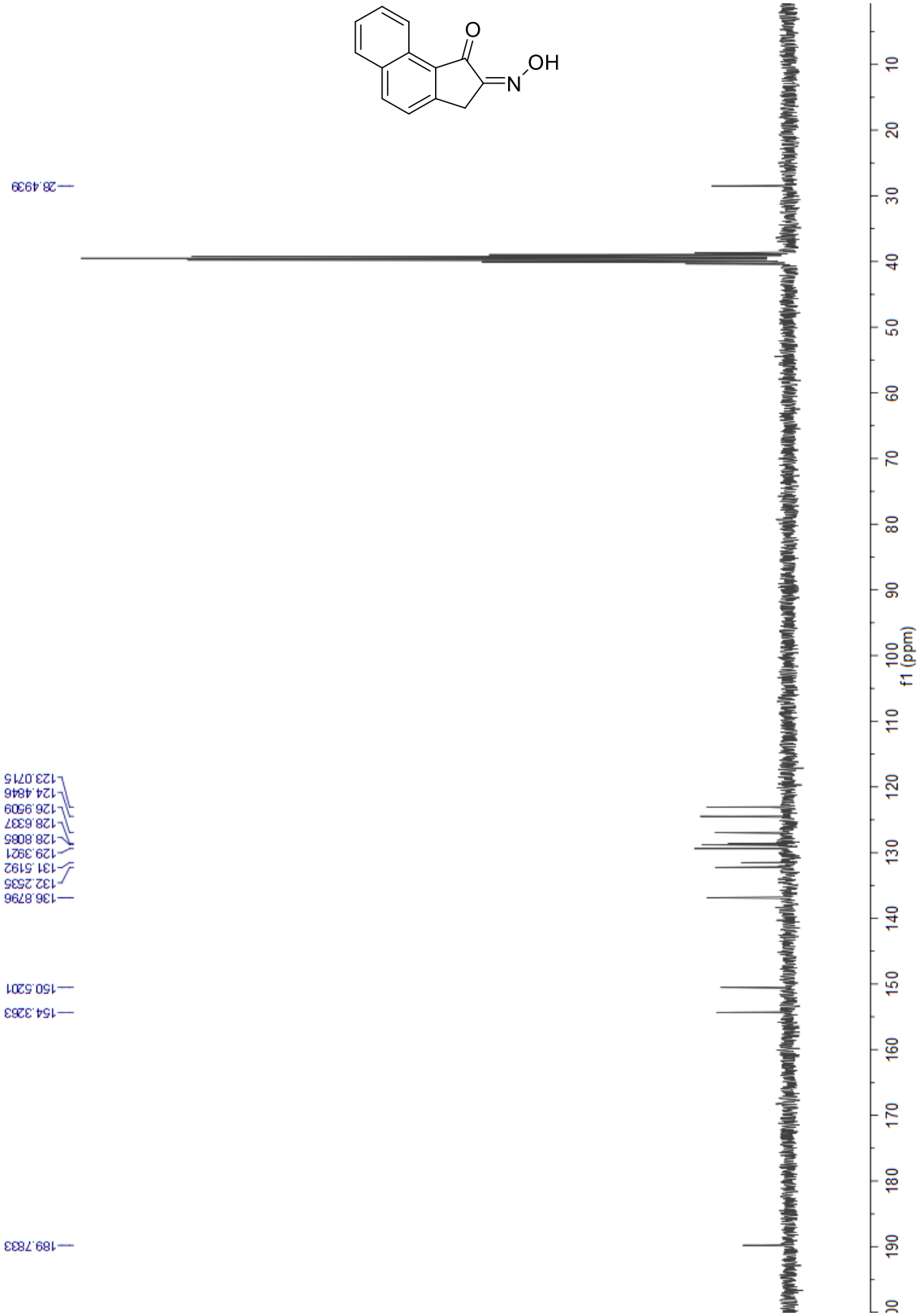
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1h**



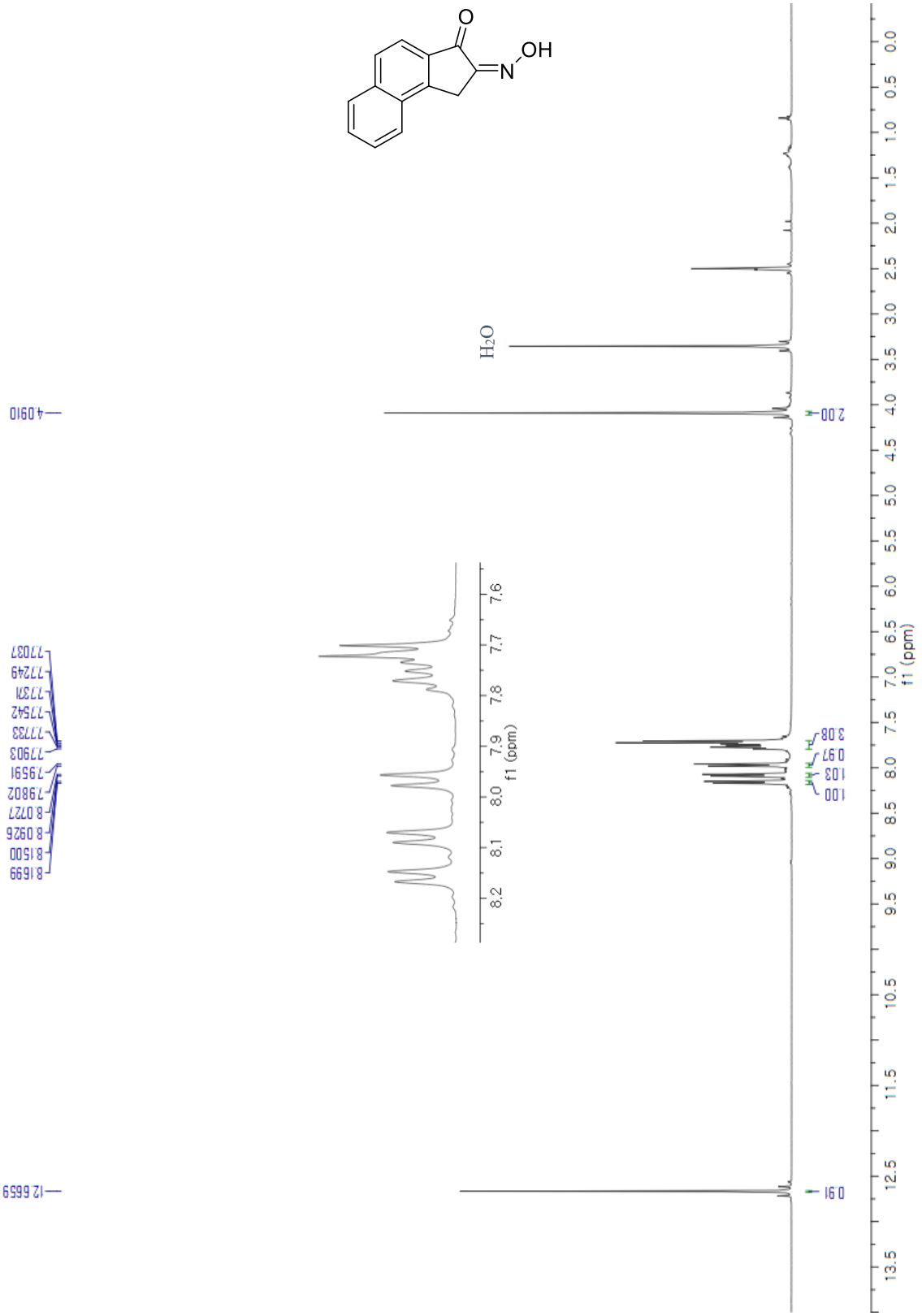
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1h**



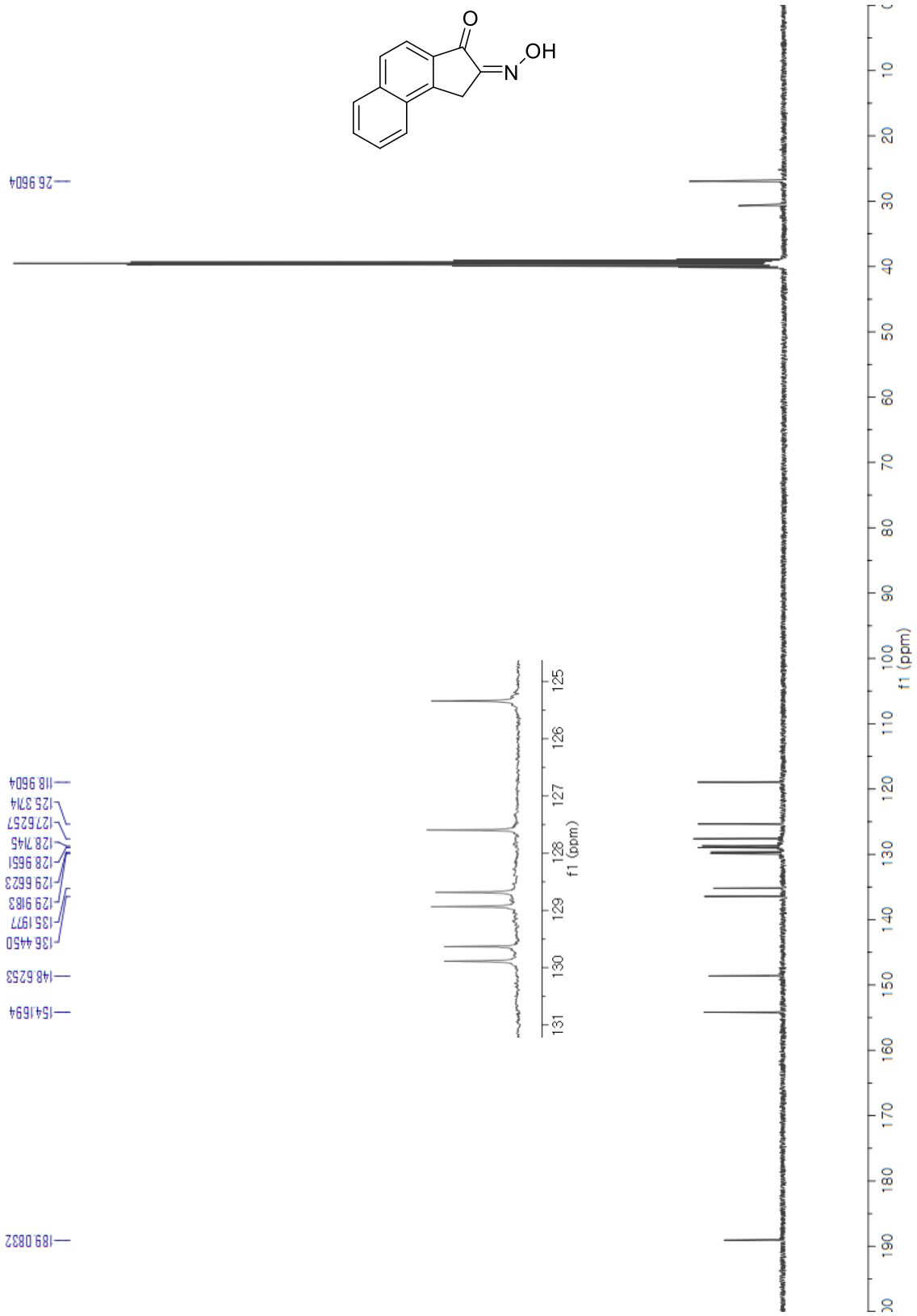
^{1}H NMR (DMSO-d_6, 600 MHz) of compound **1i**



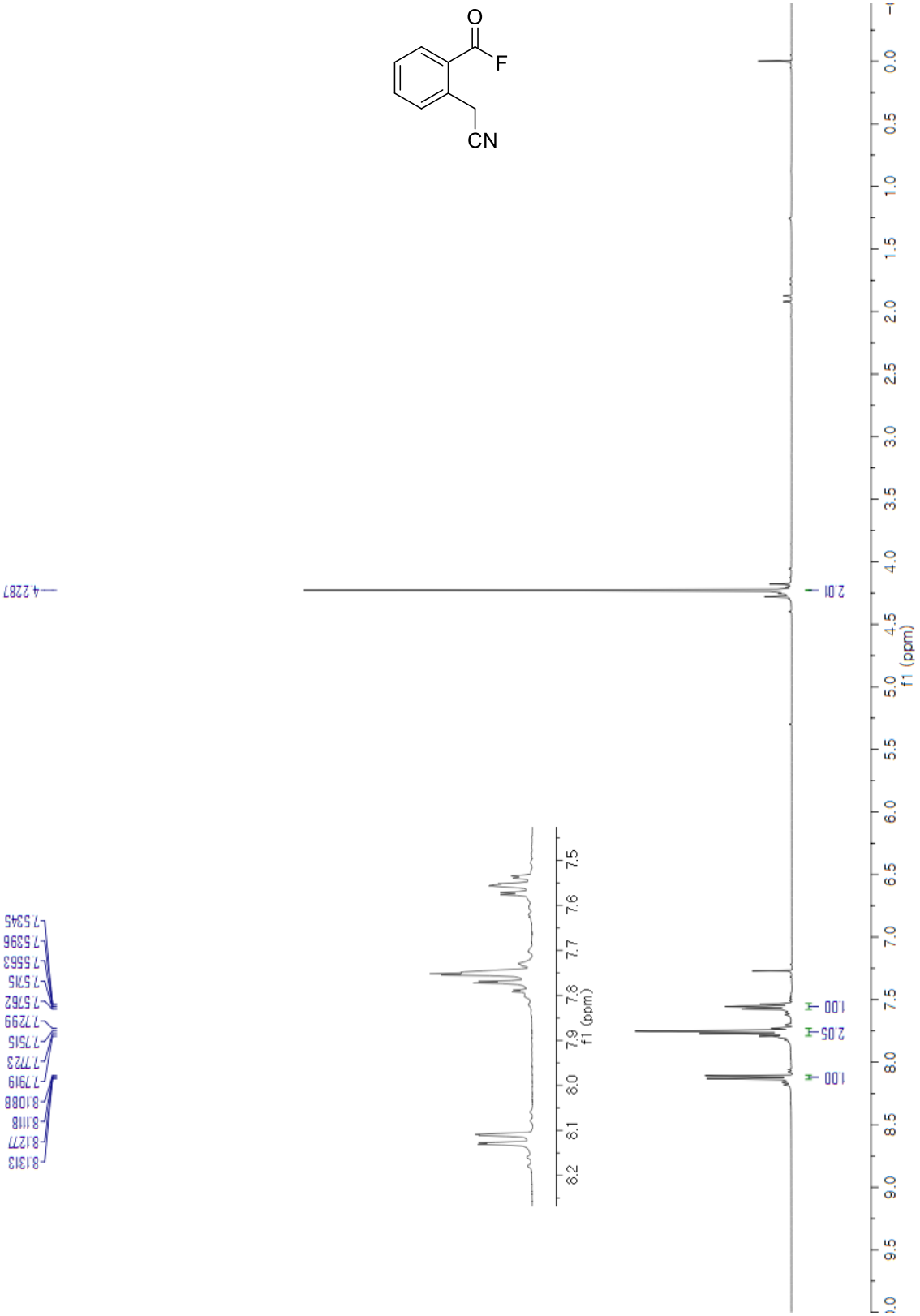
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **1i**



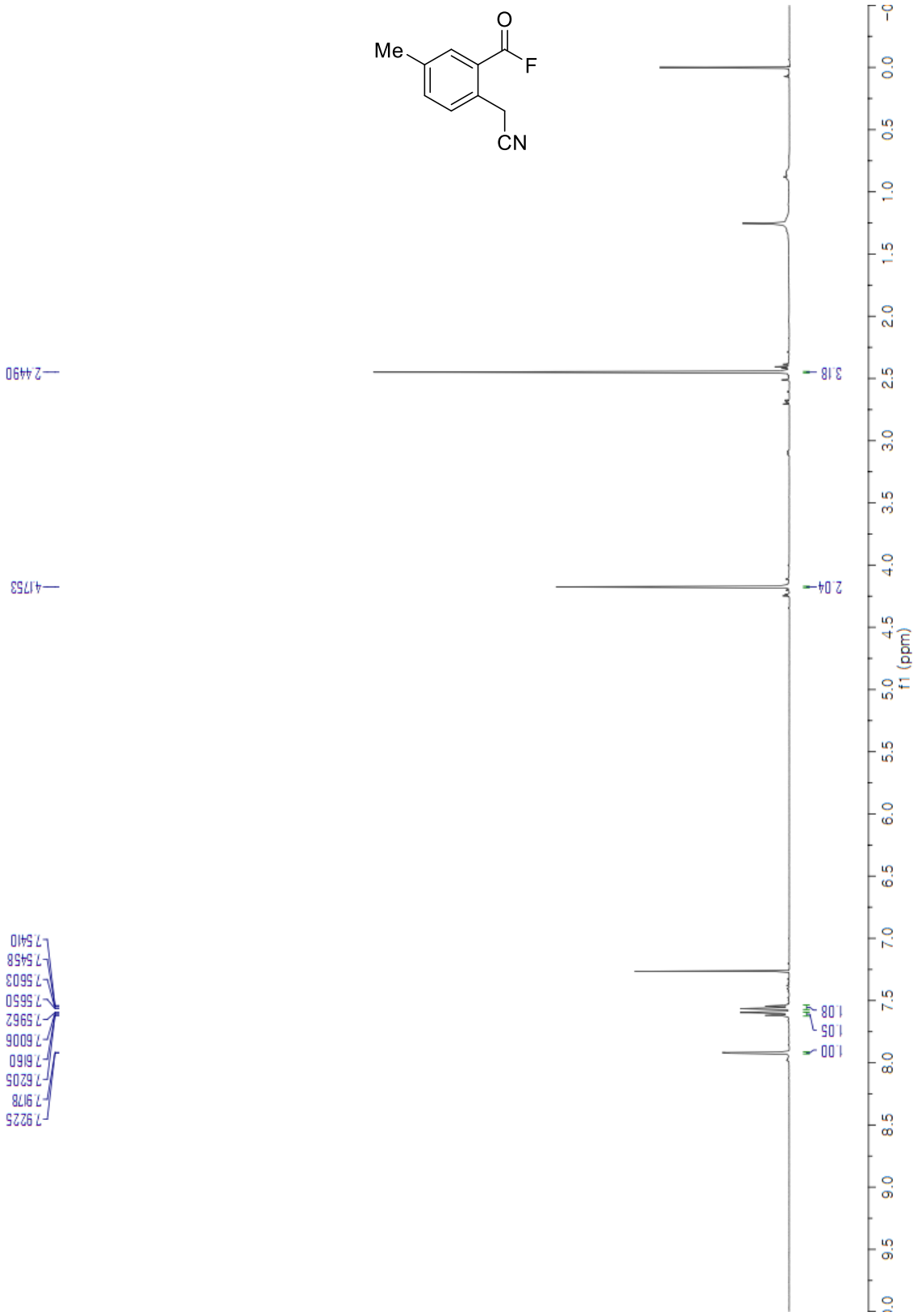
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1j**



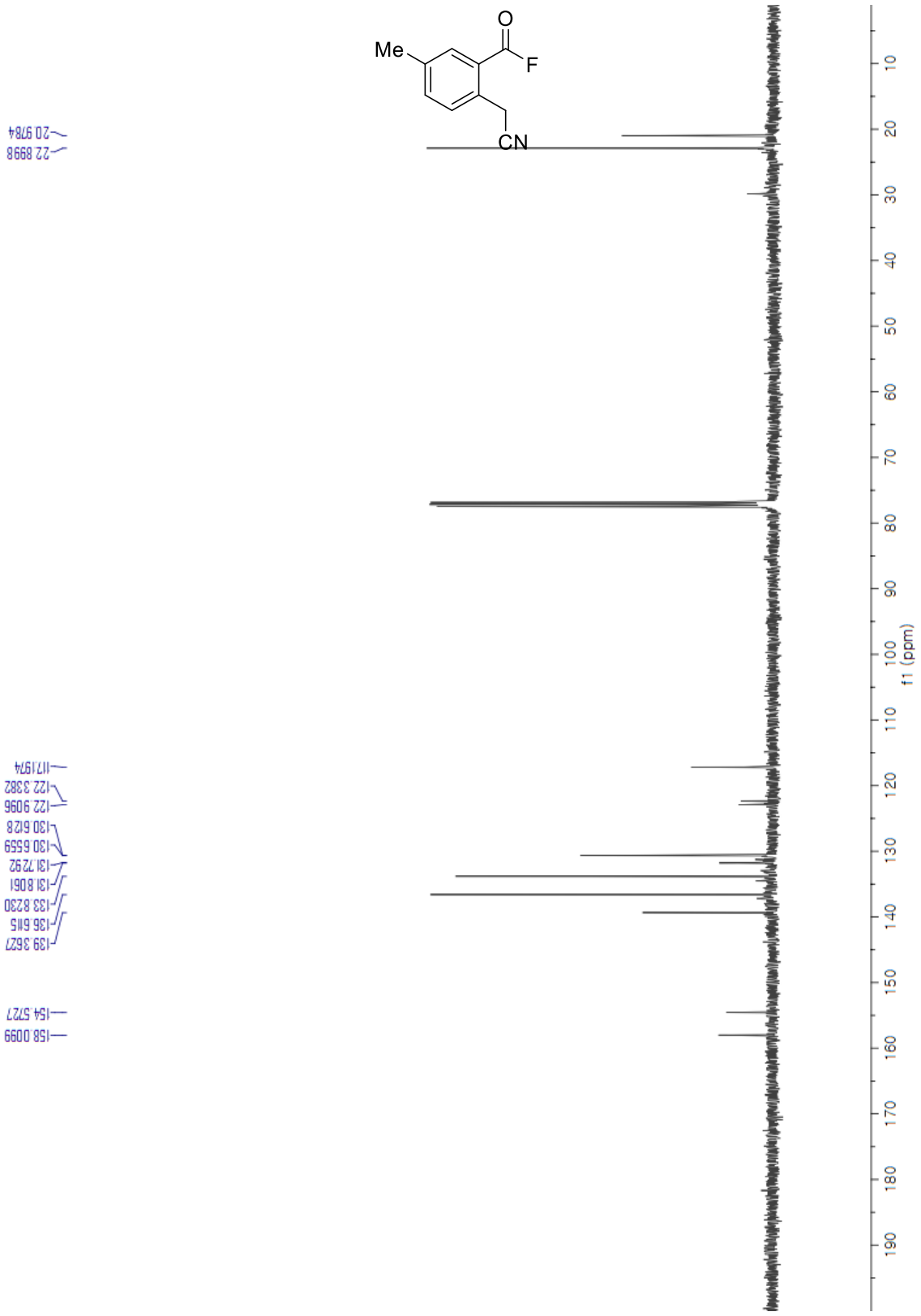
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1j**



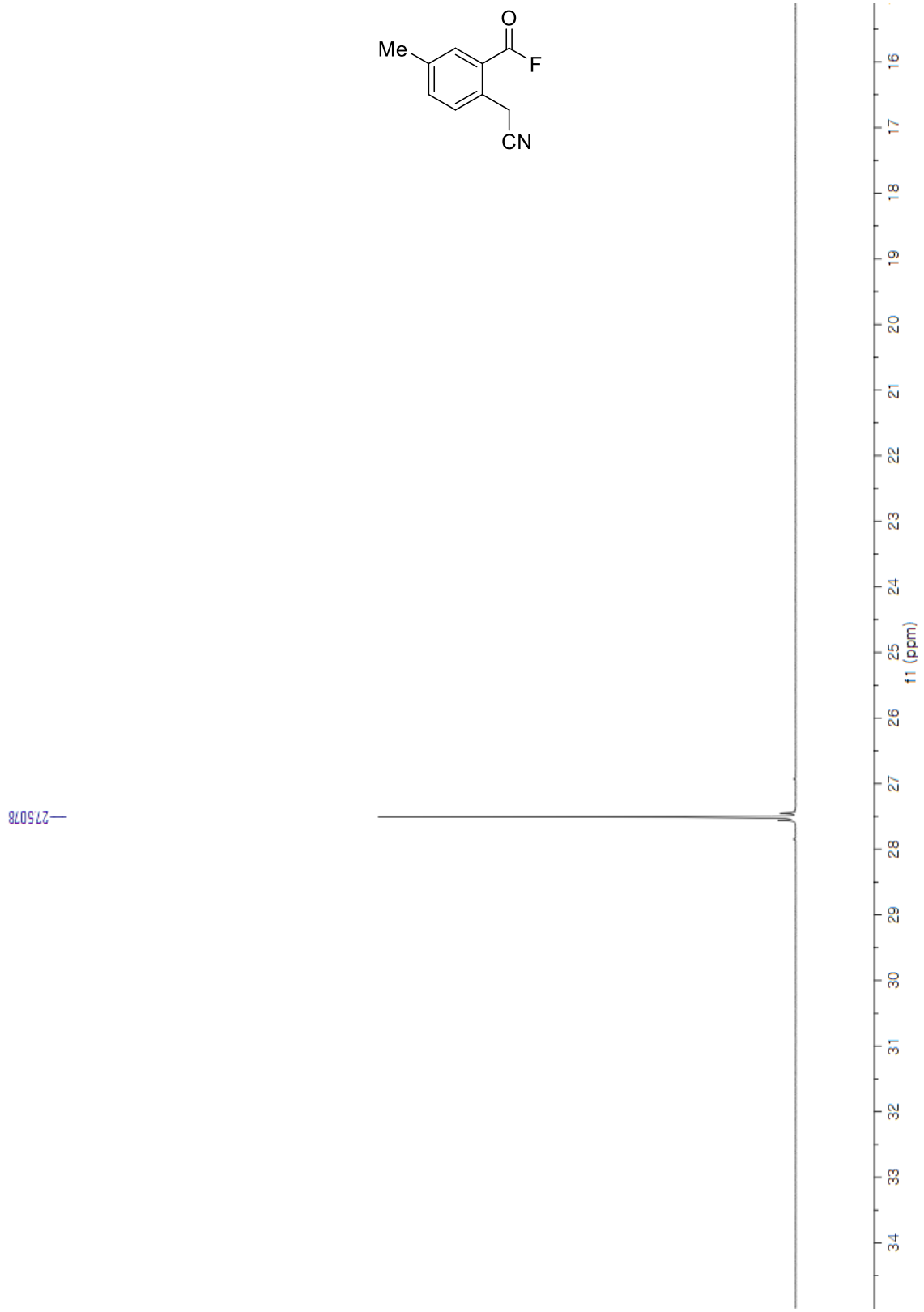
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2a**



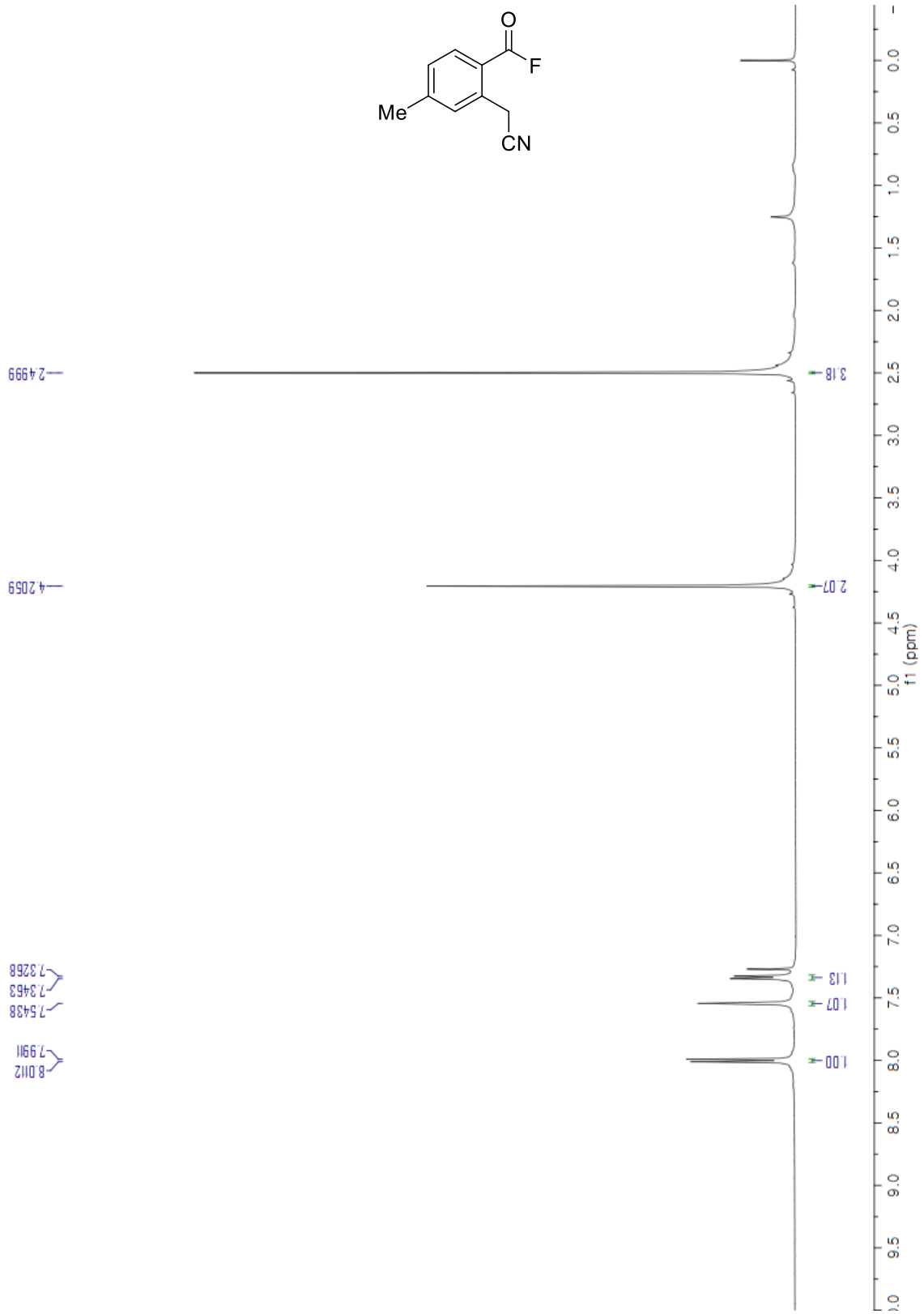
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2b**



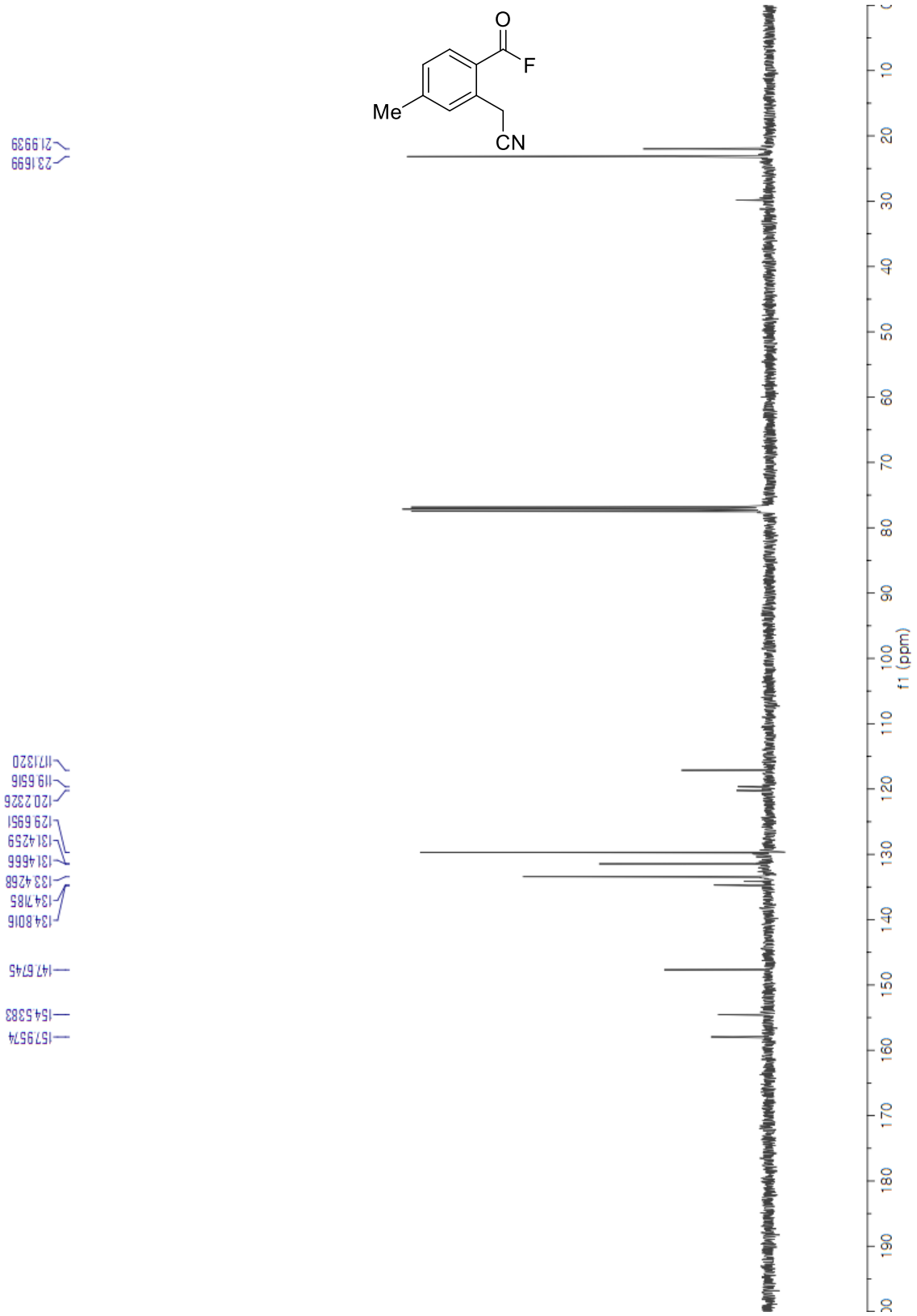
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2b**



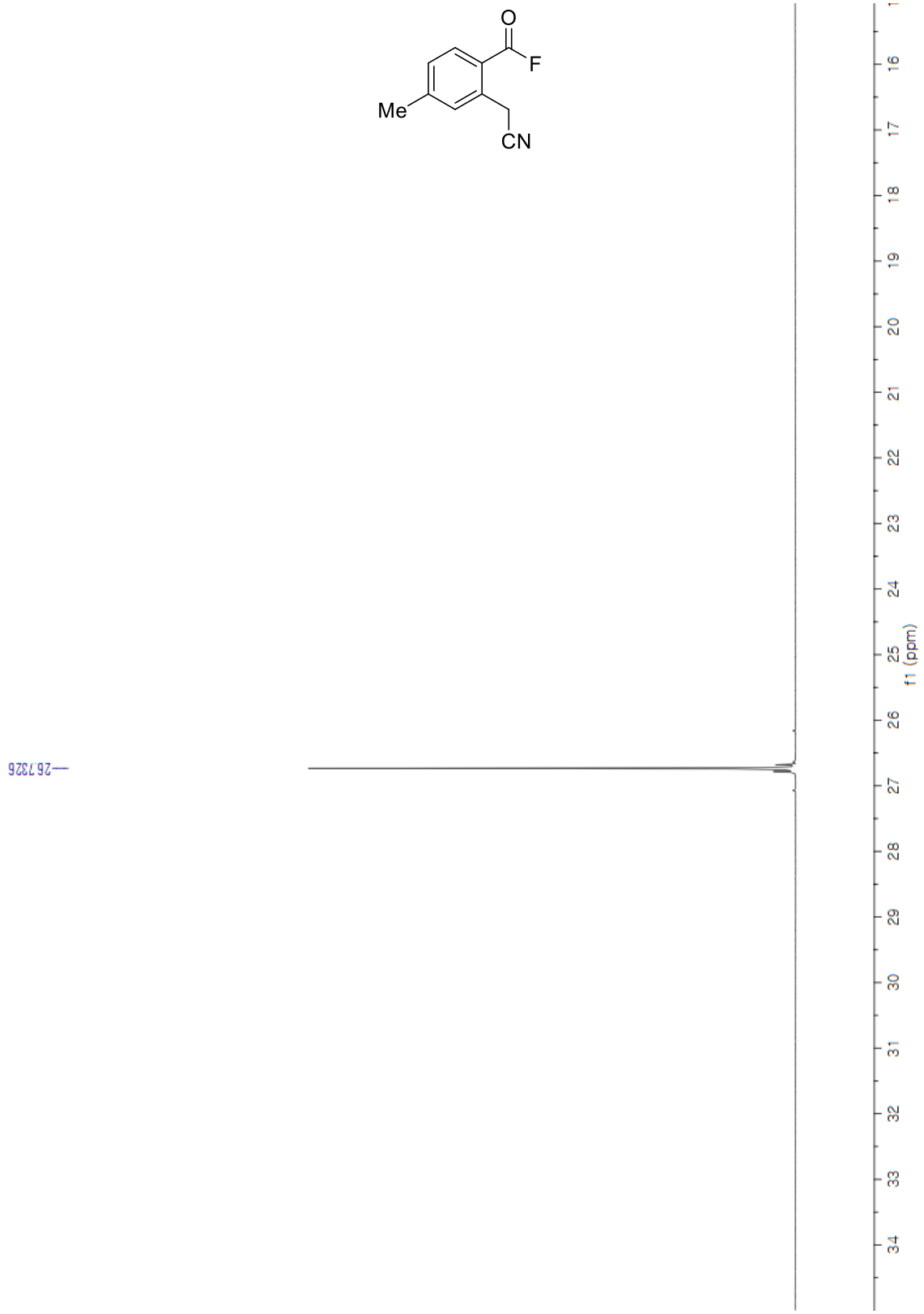
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2b**



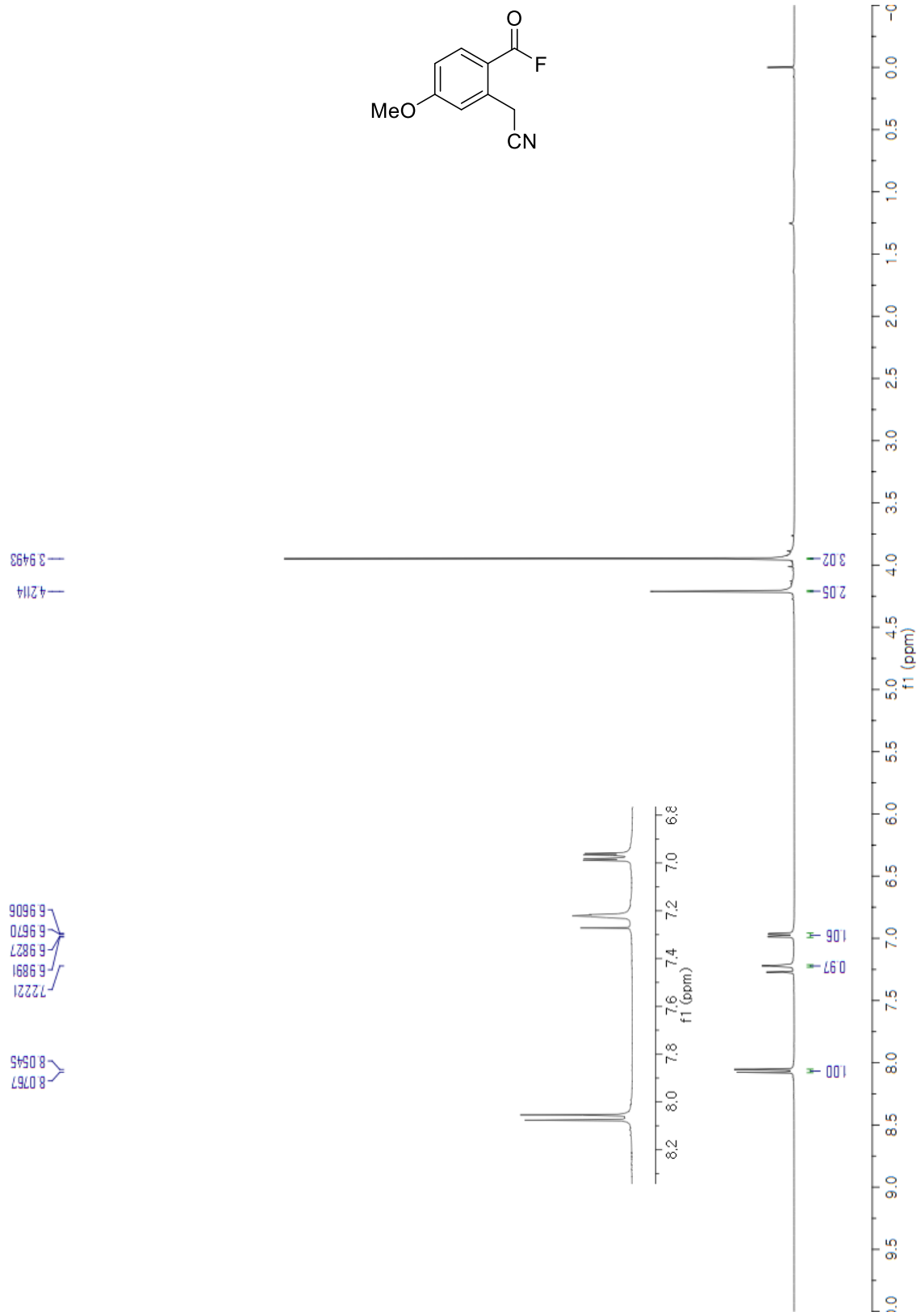
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2c**



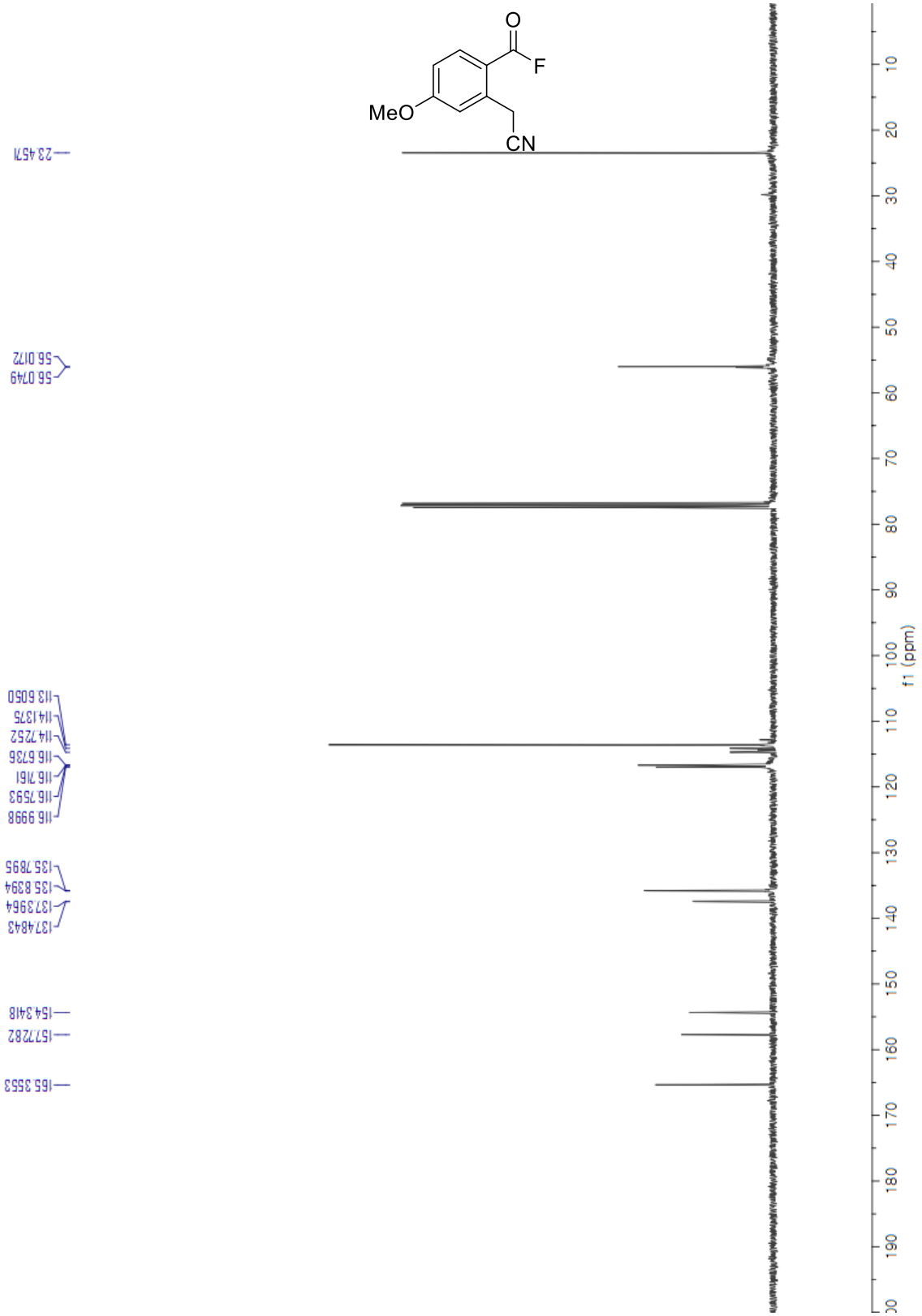
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2c**



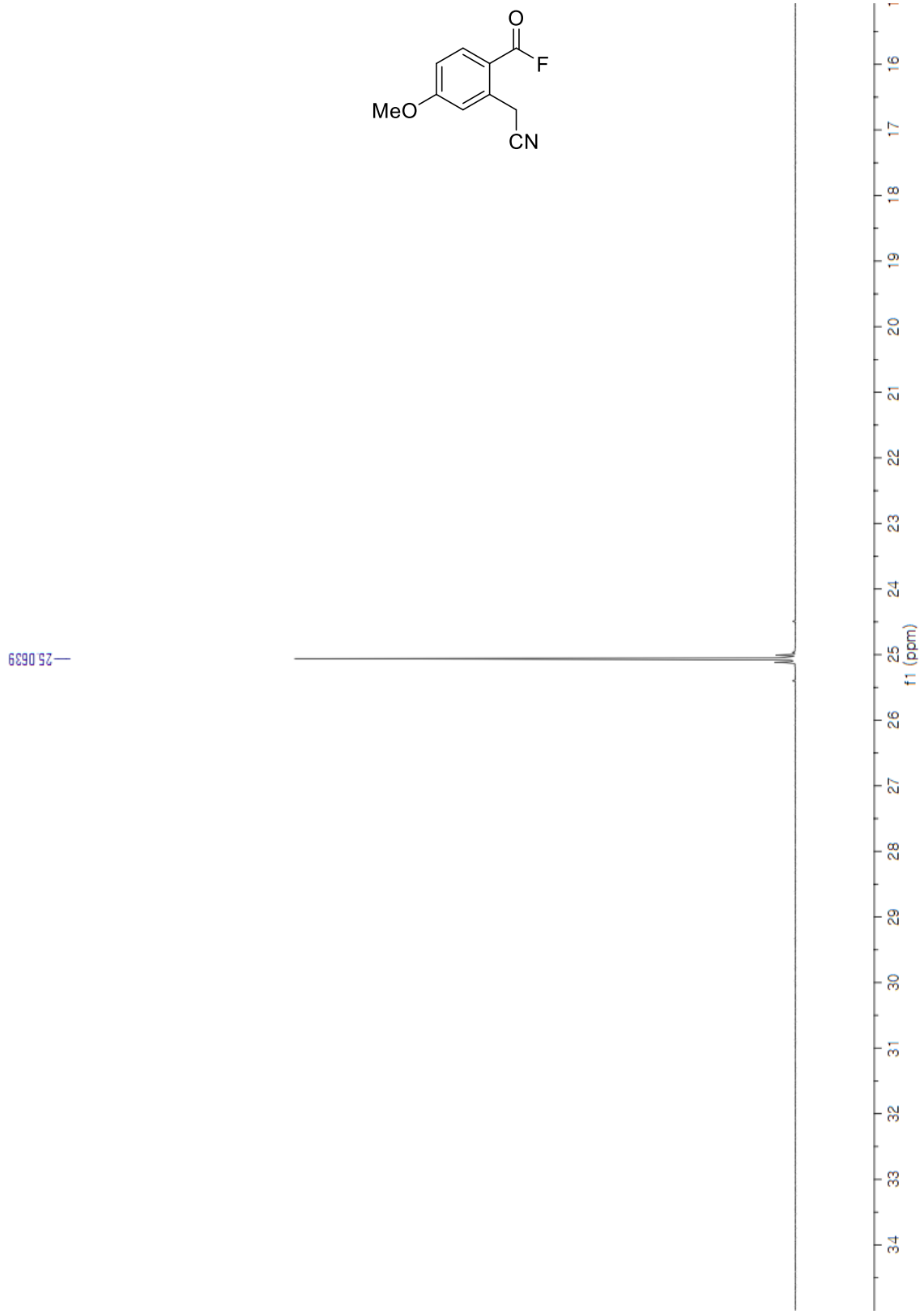
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2c**



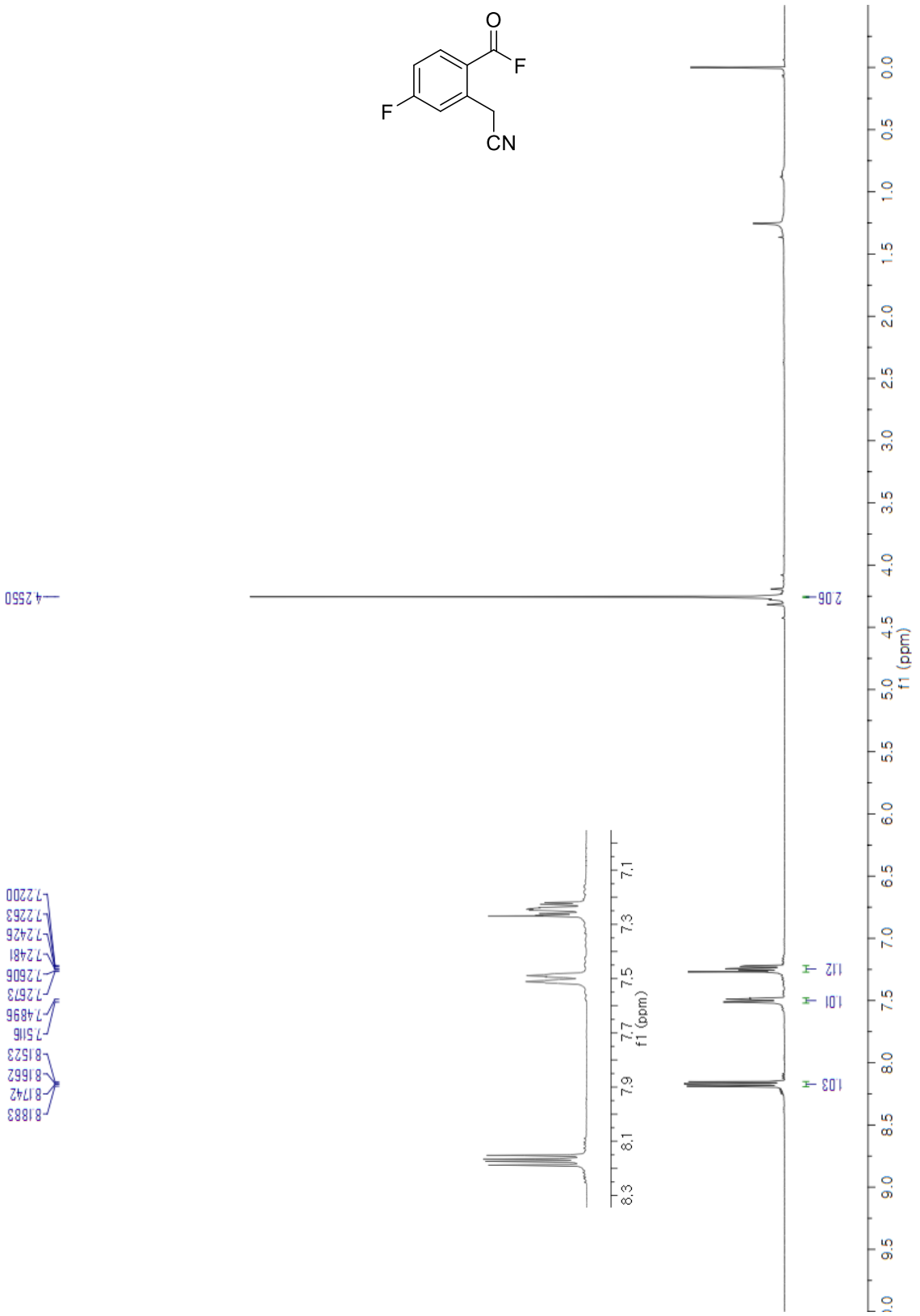
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2d**



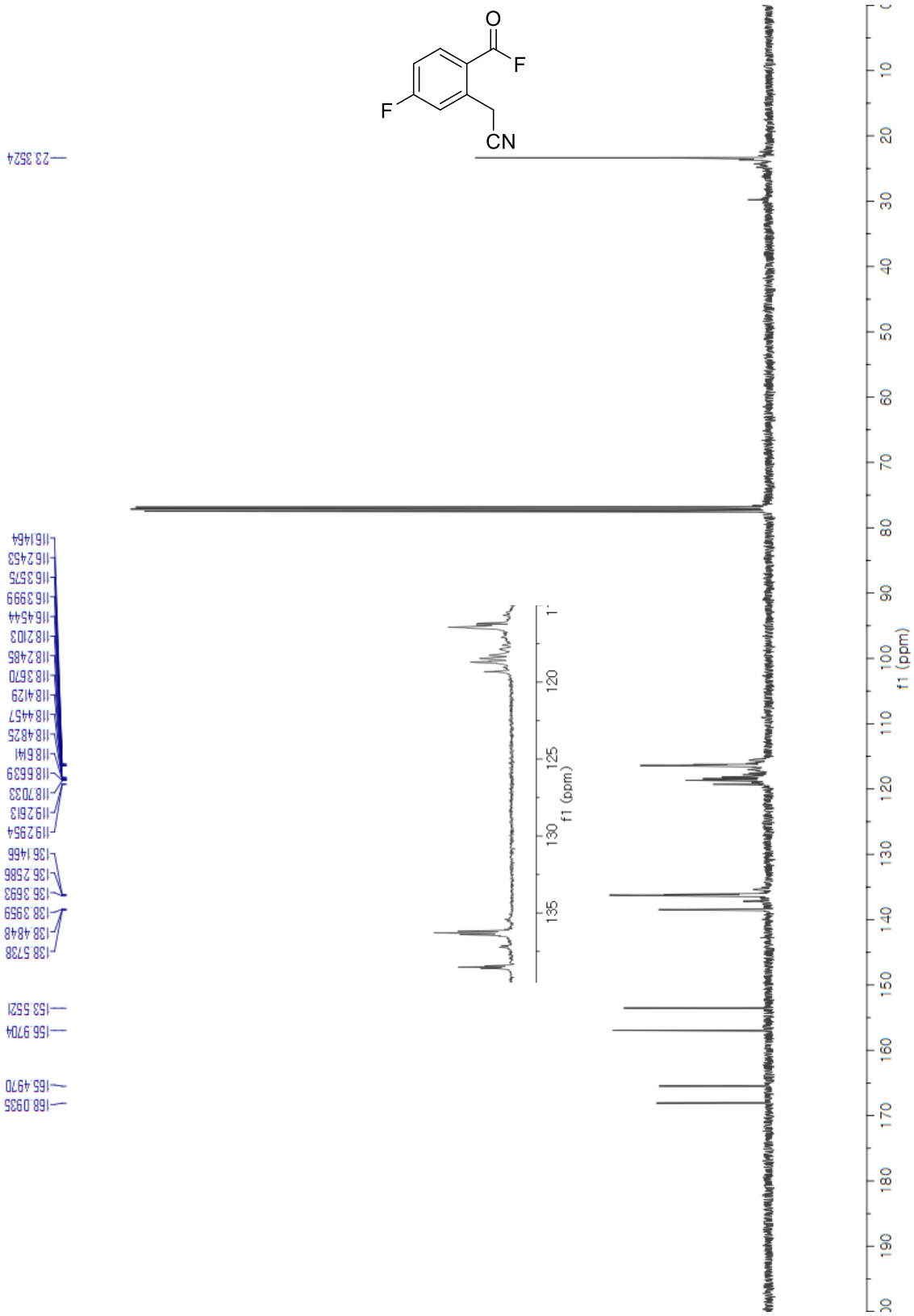
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2d**



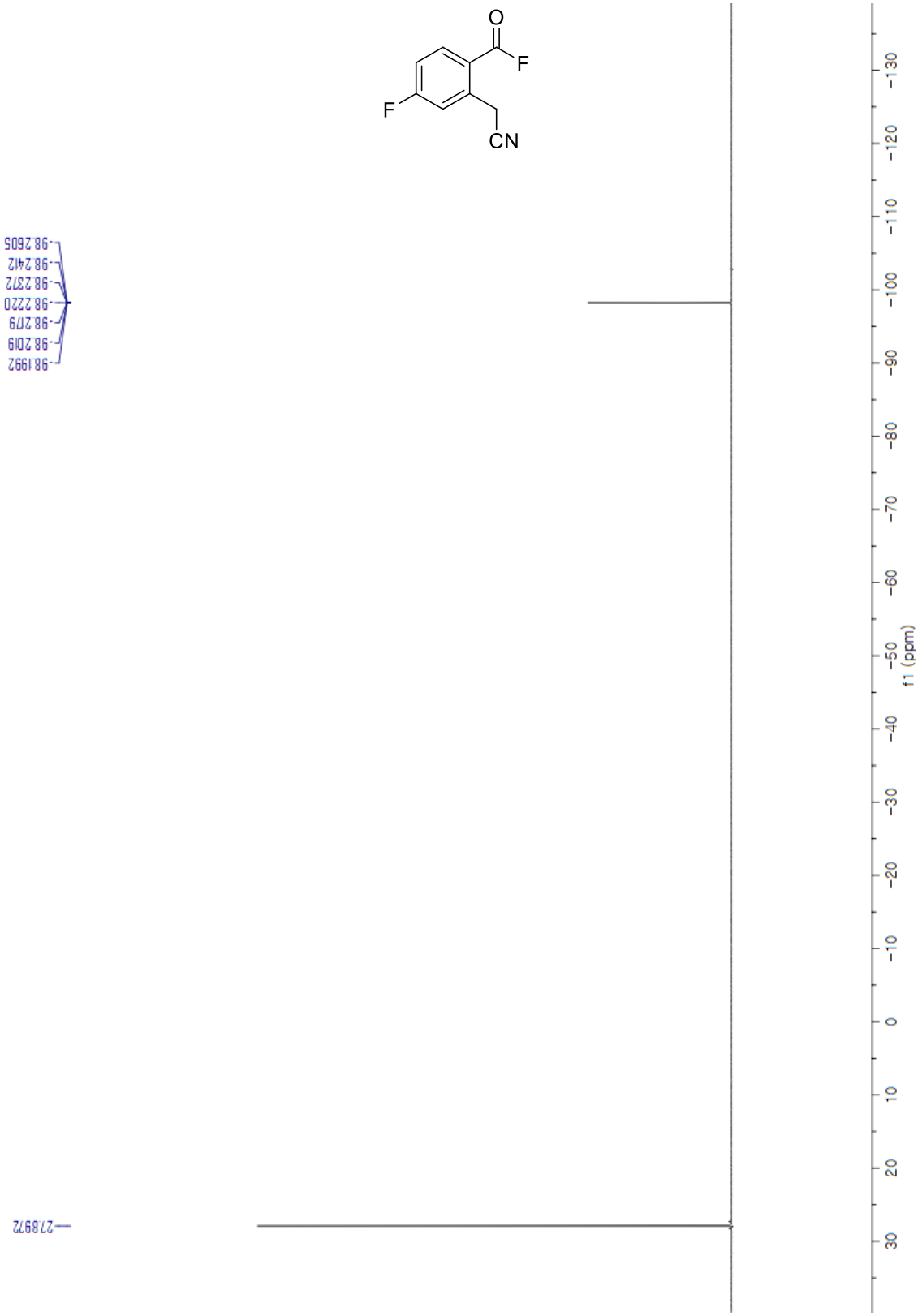
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2d**



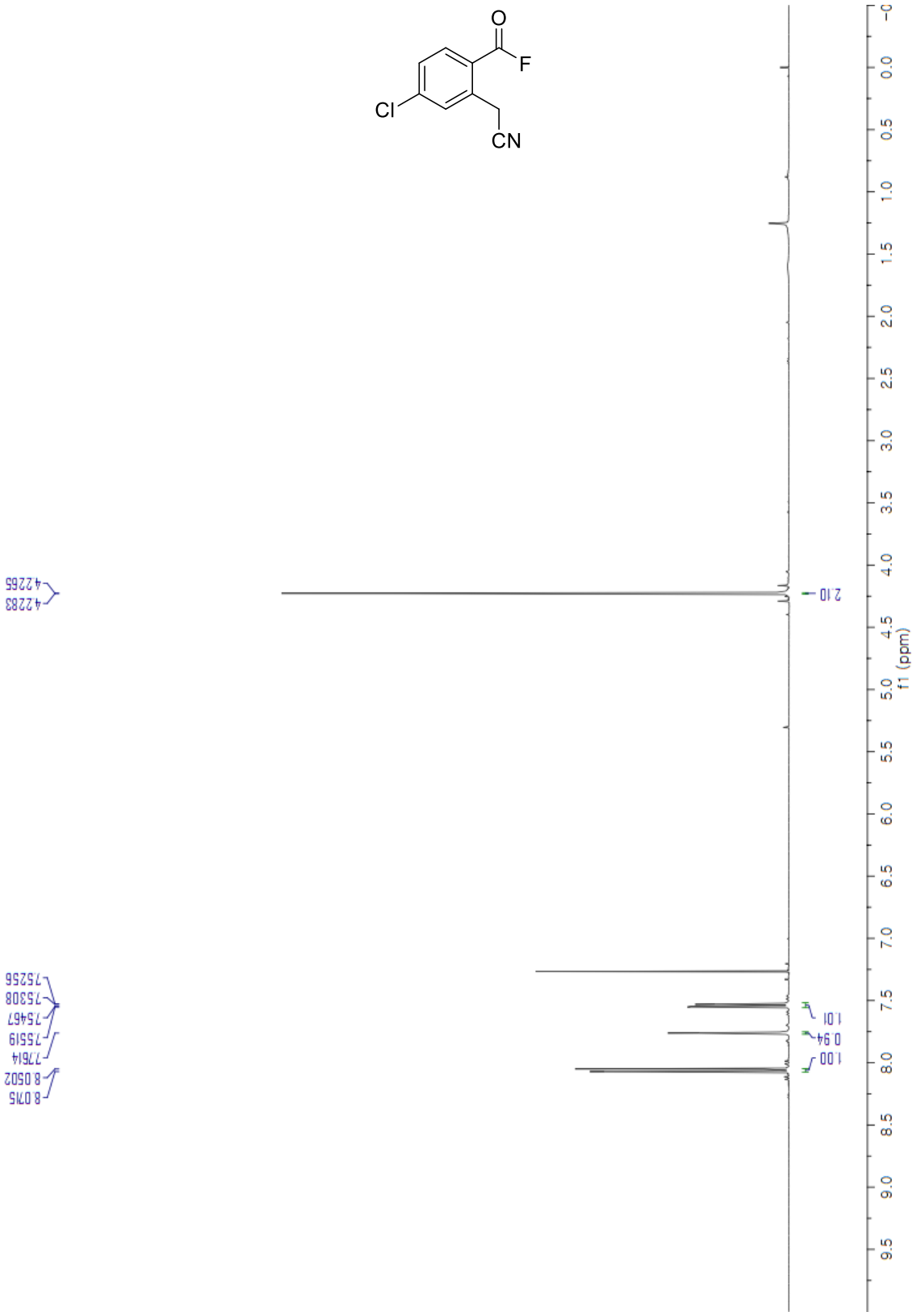
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2e**



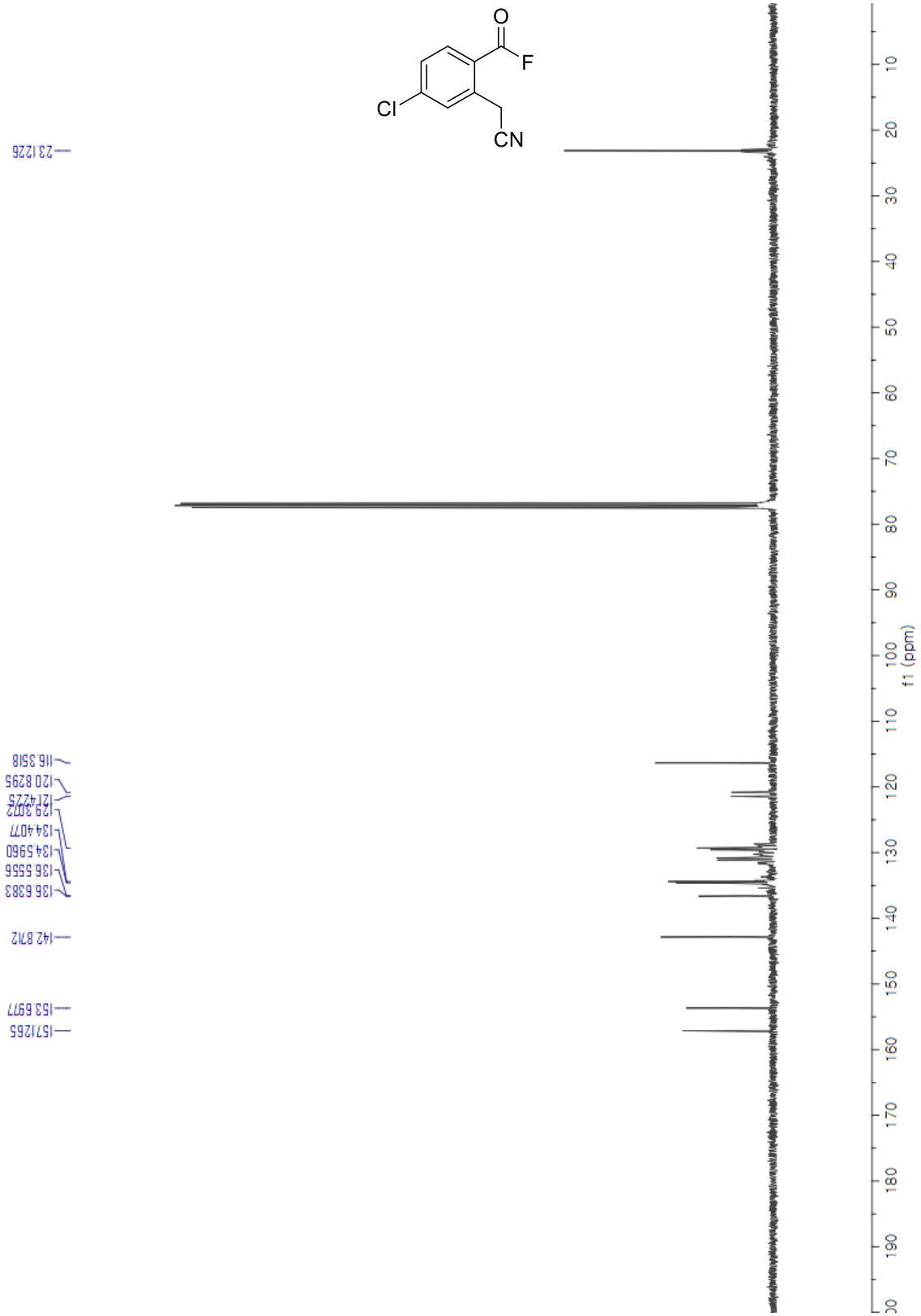
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2e**



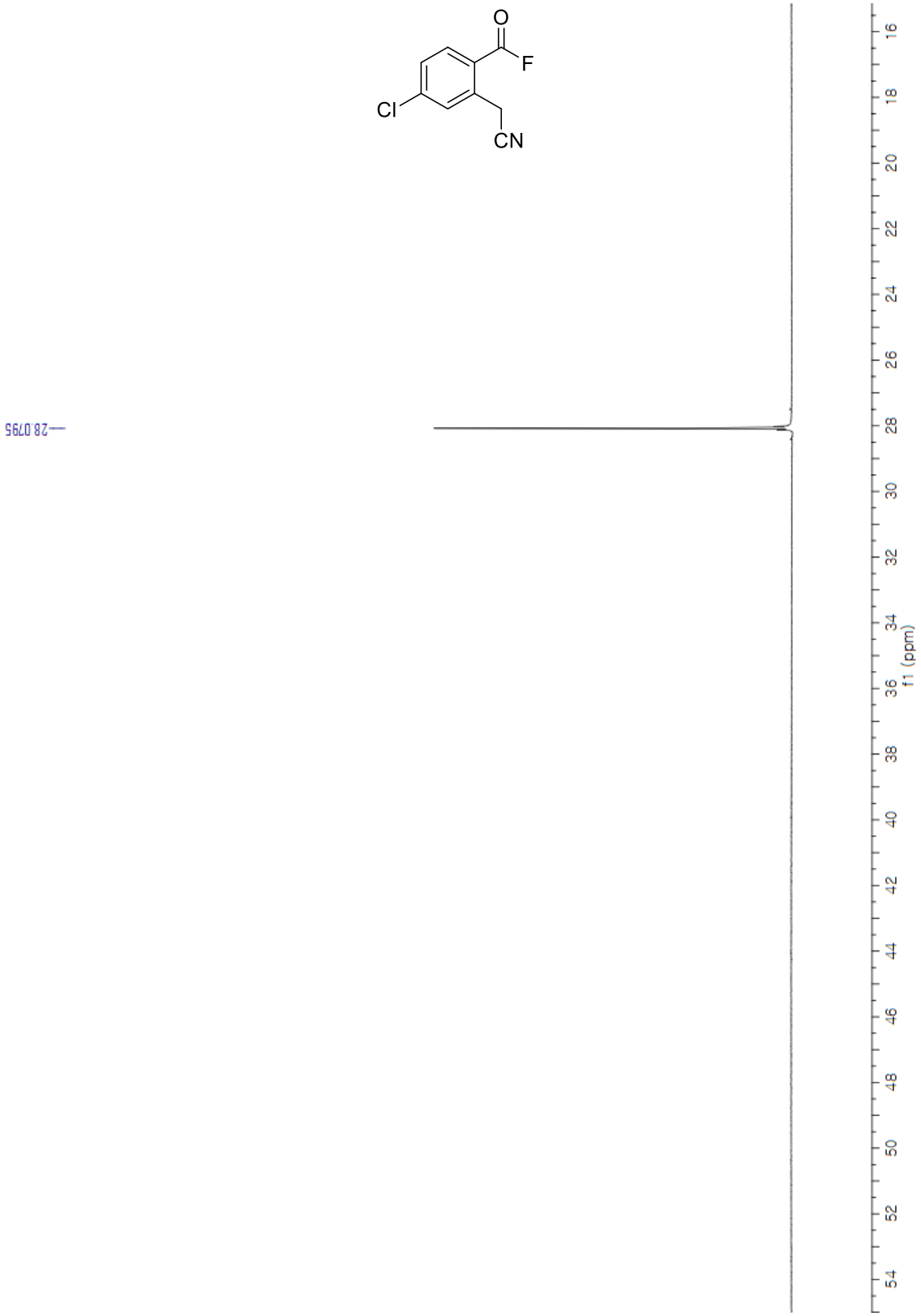
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2e**



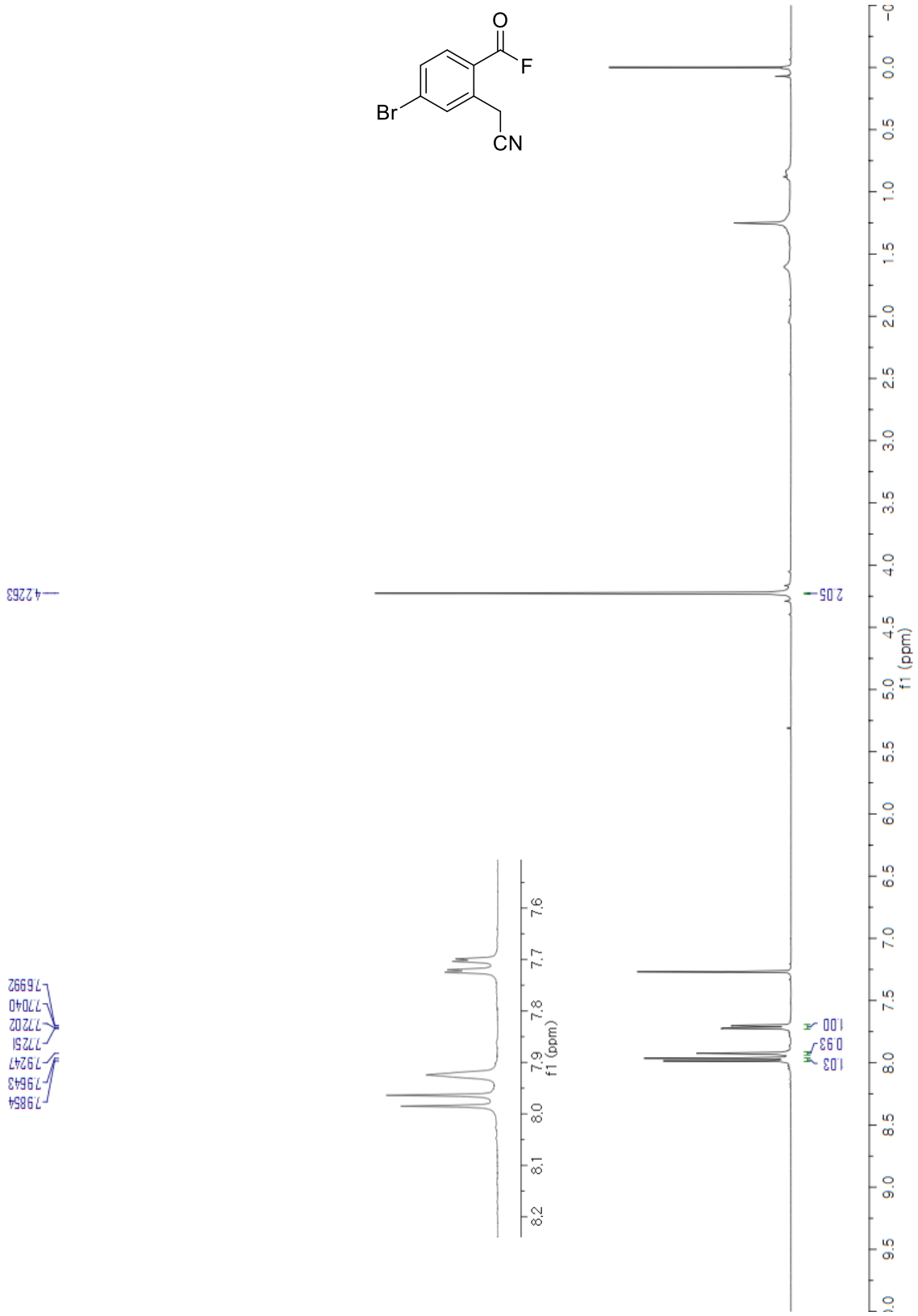
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2f**



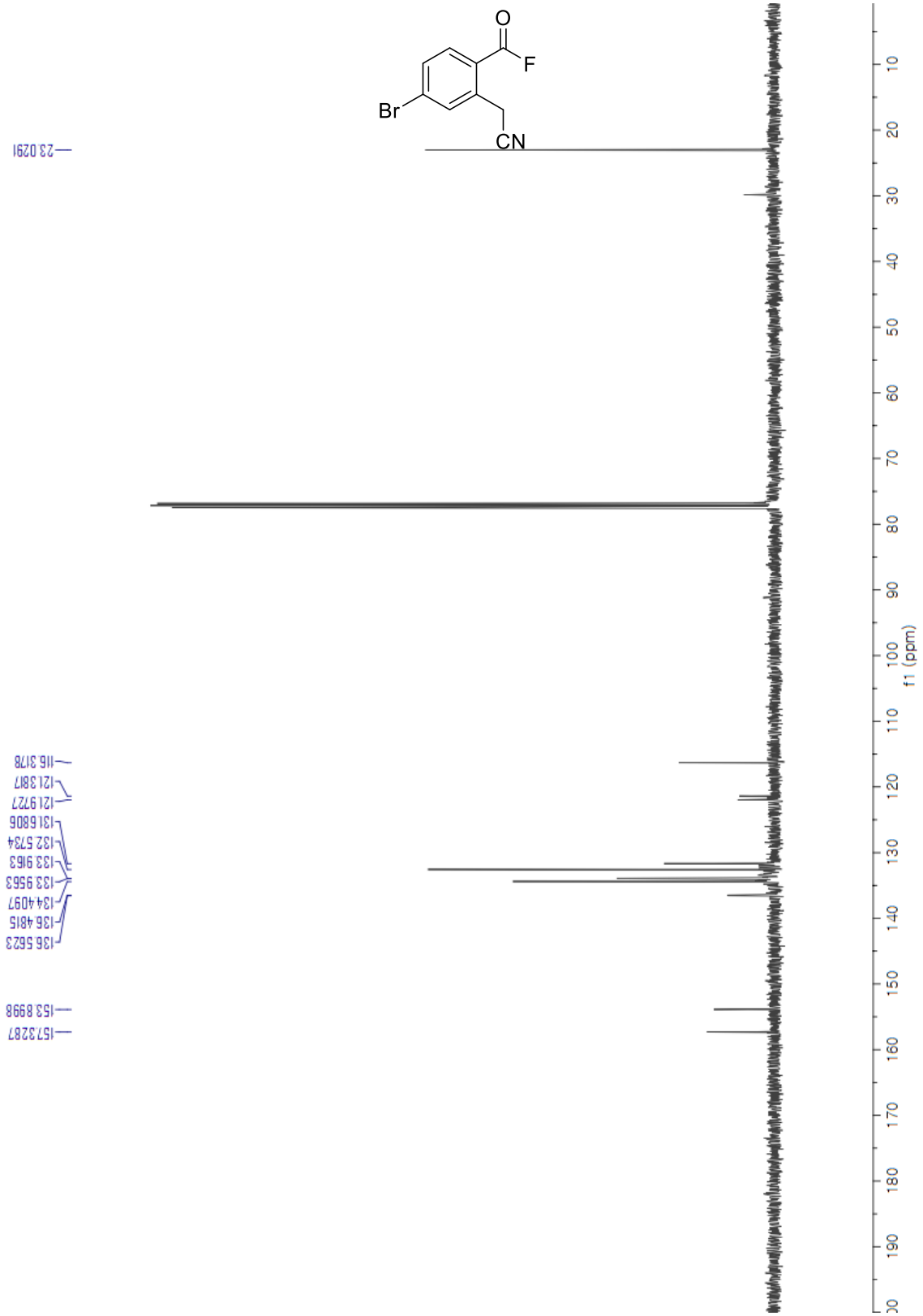
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2f**



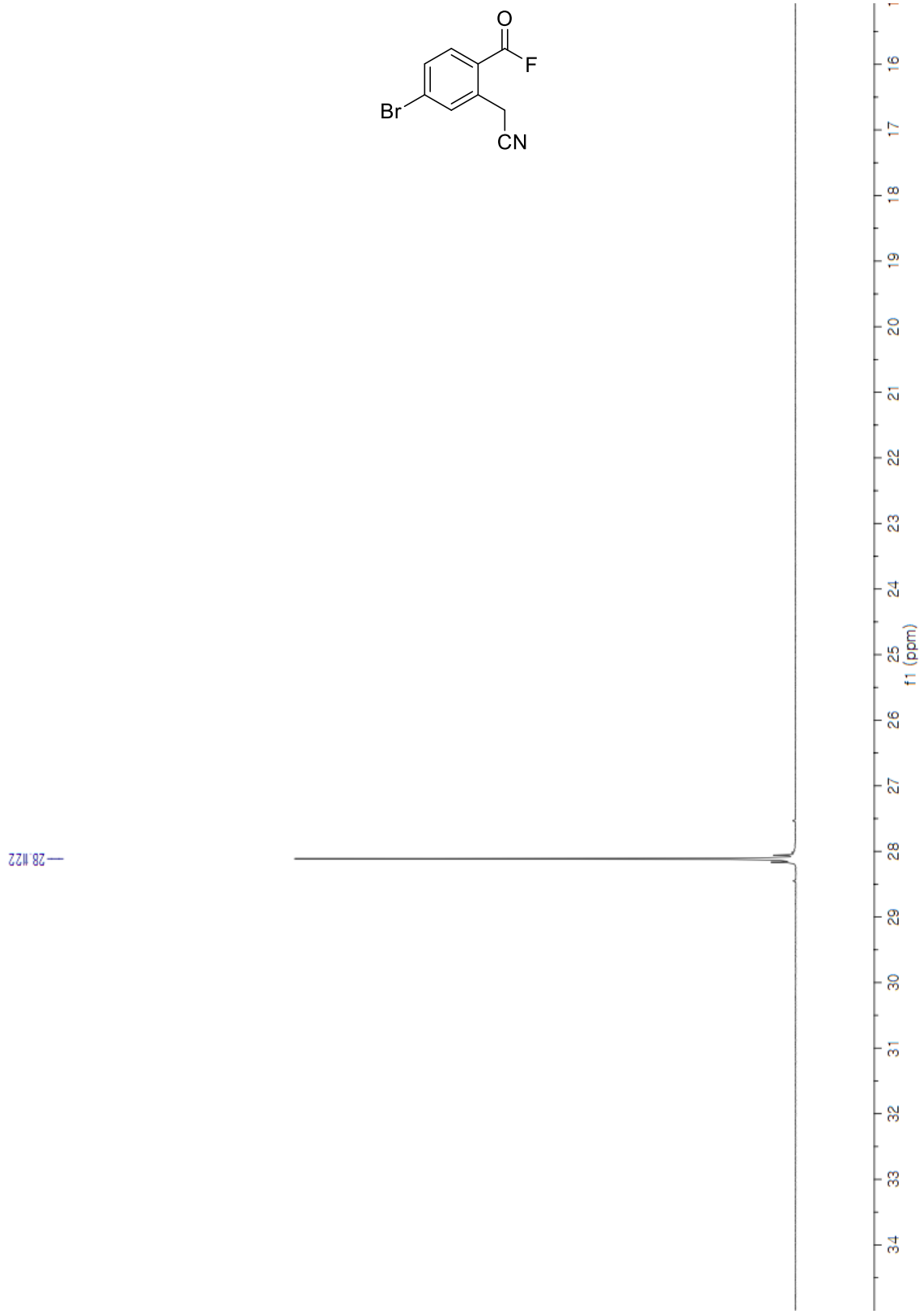
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2f**



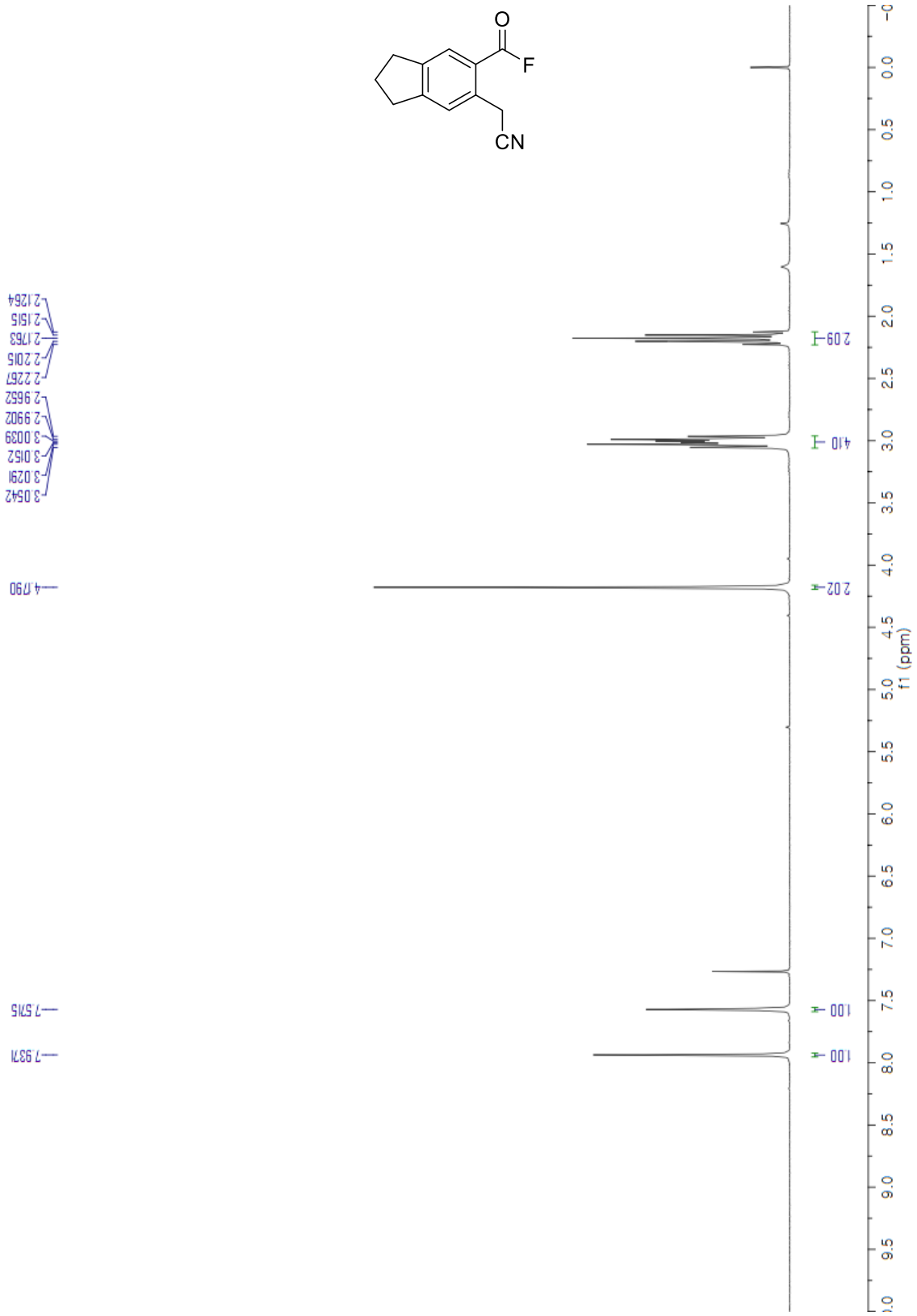
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2g**



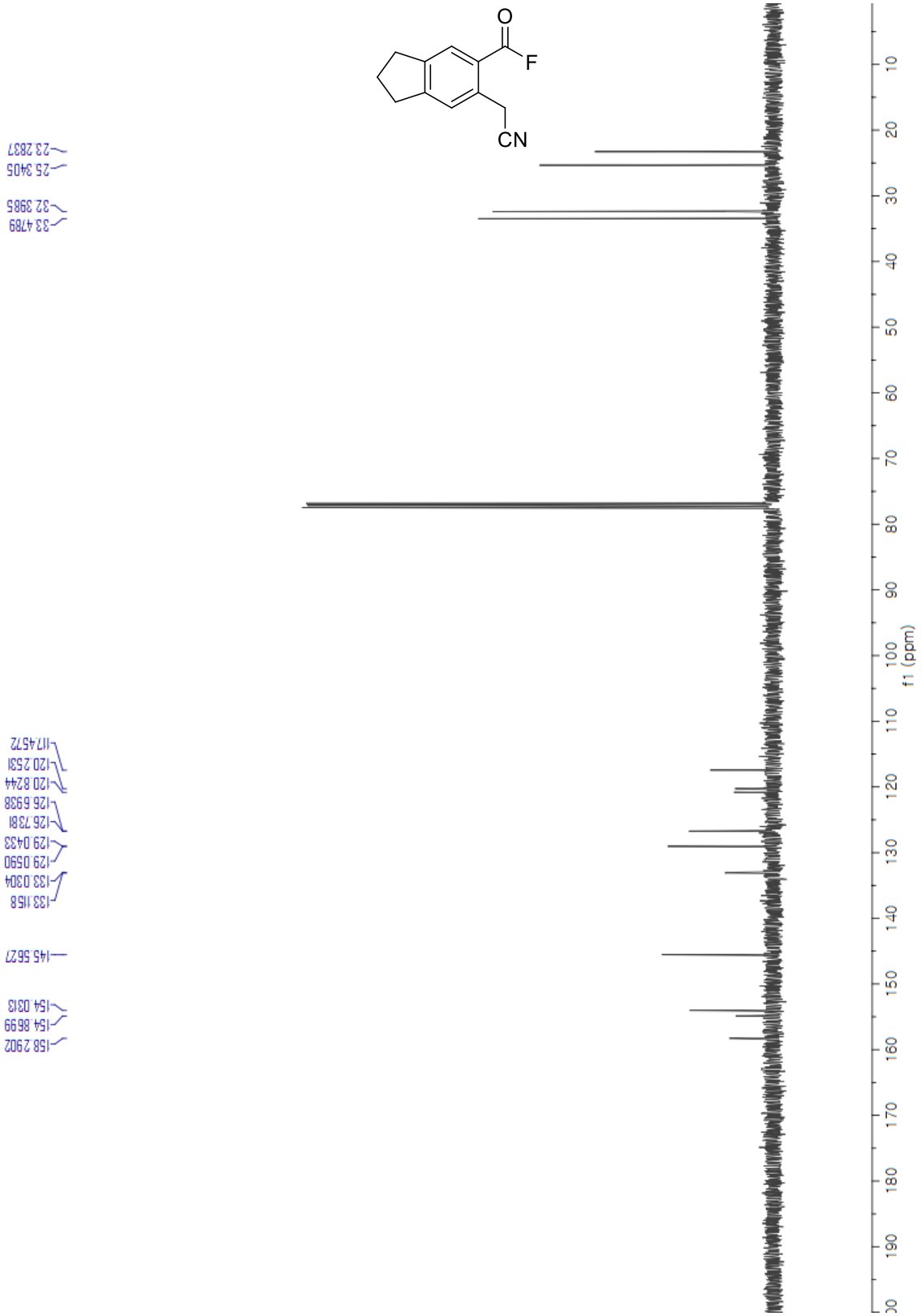
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2g**



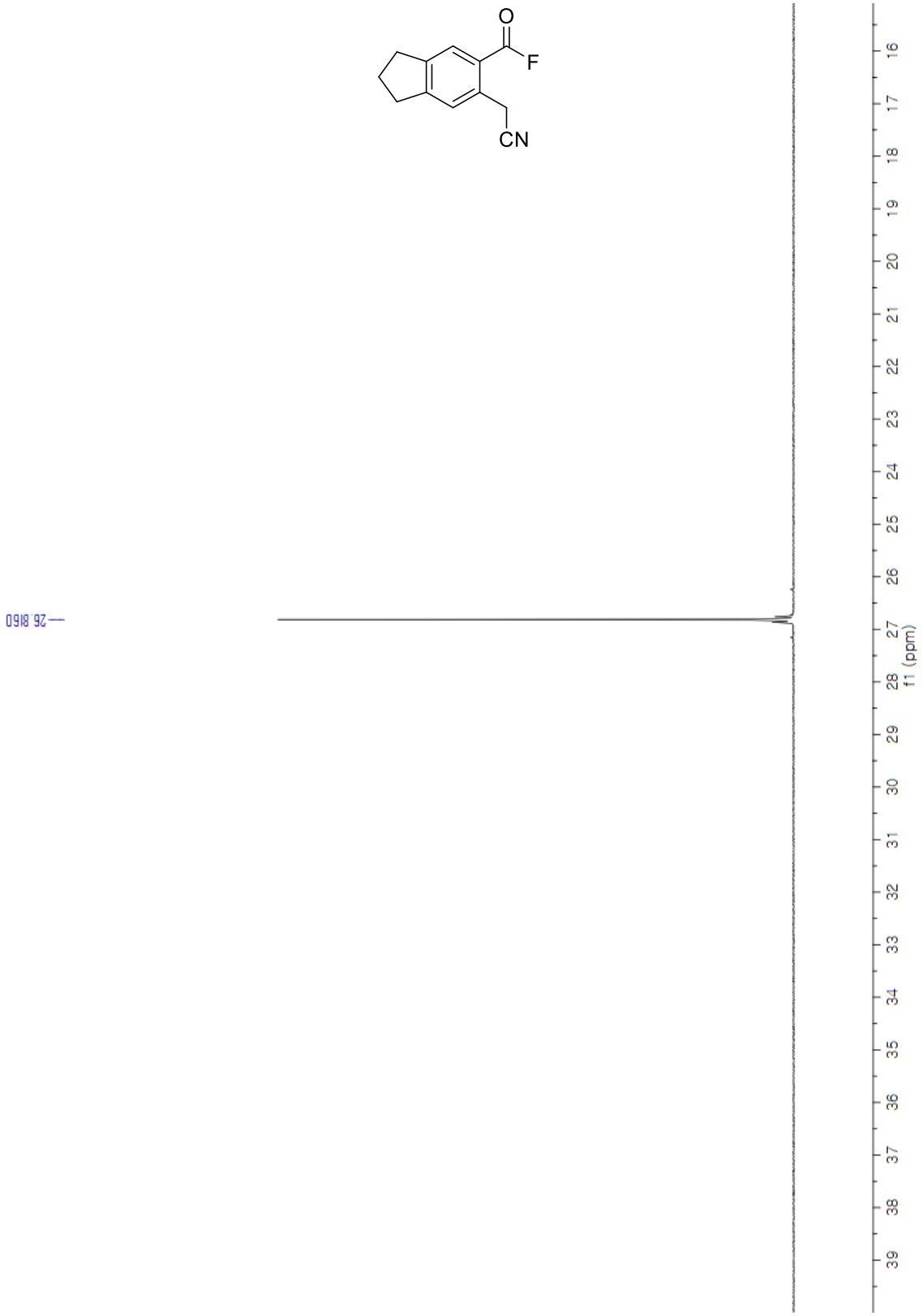
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2g**



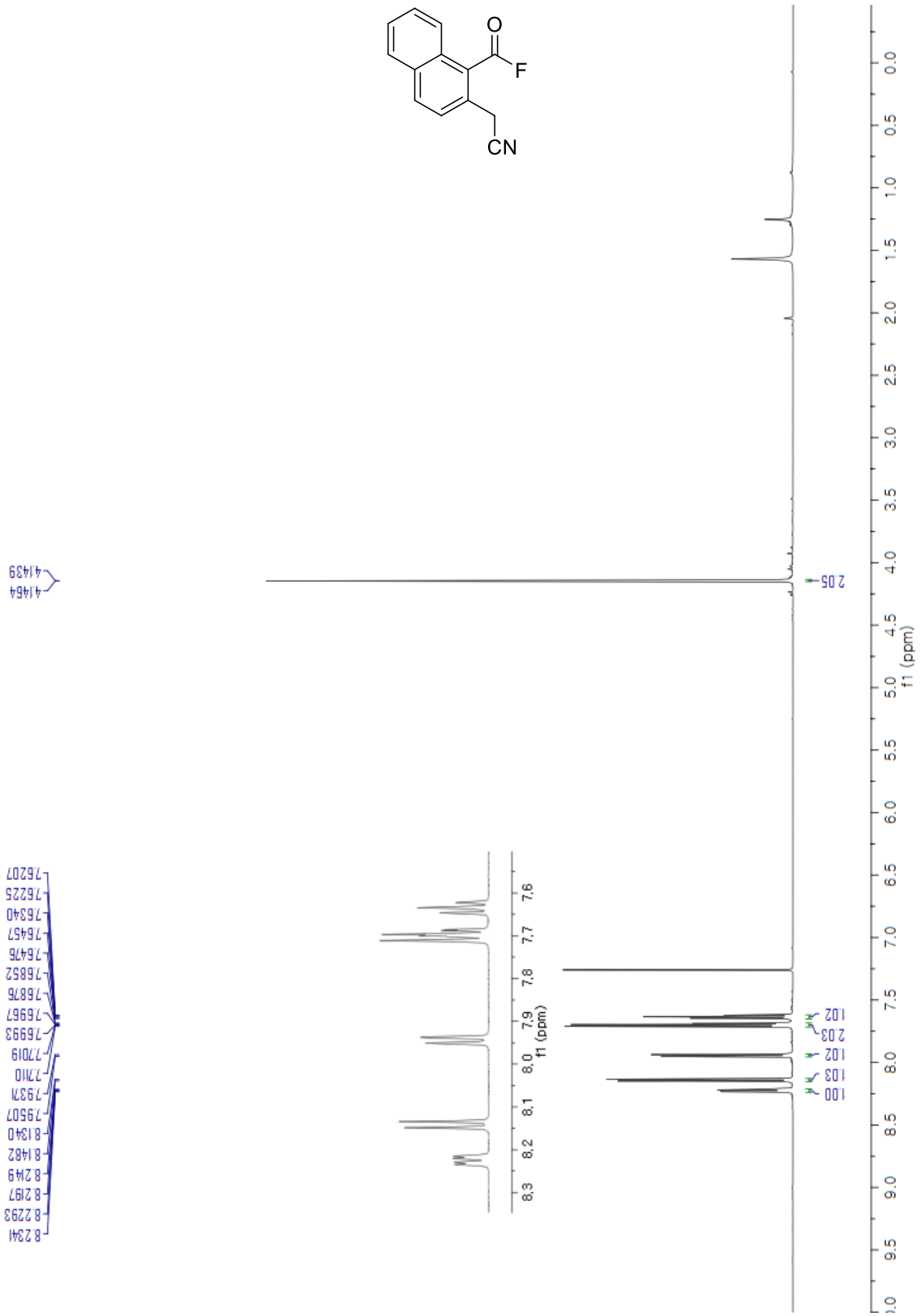
^{1}H NMR ($CDCl_3$, 300 MHz) of compound **2h**



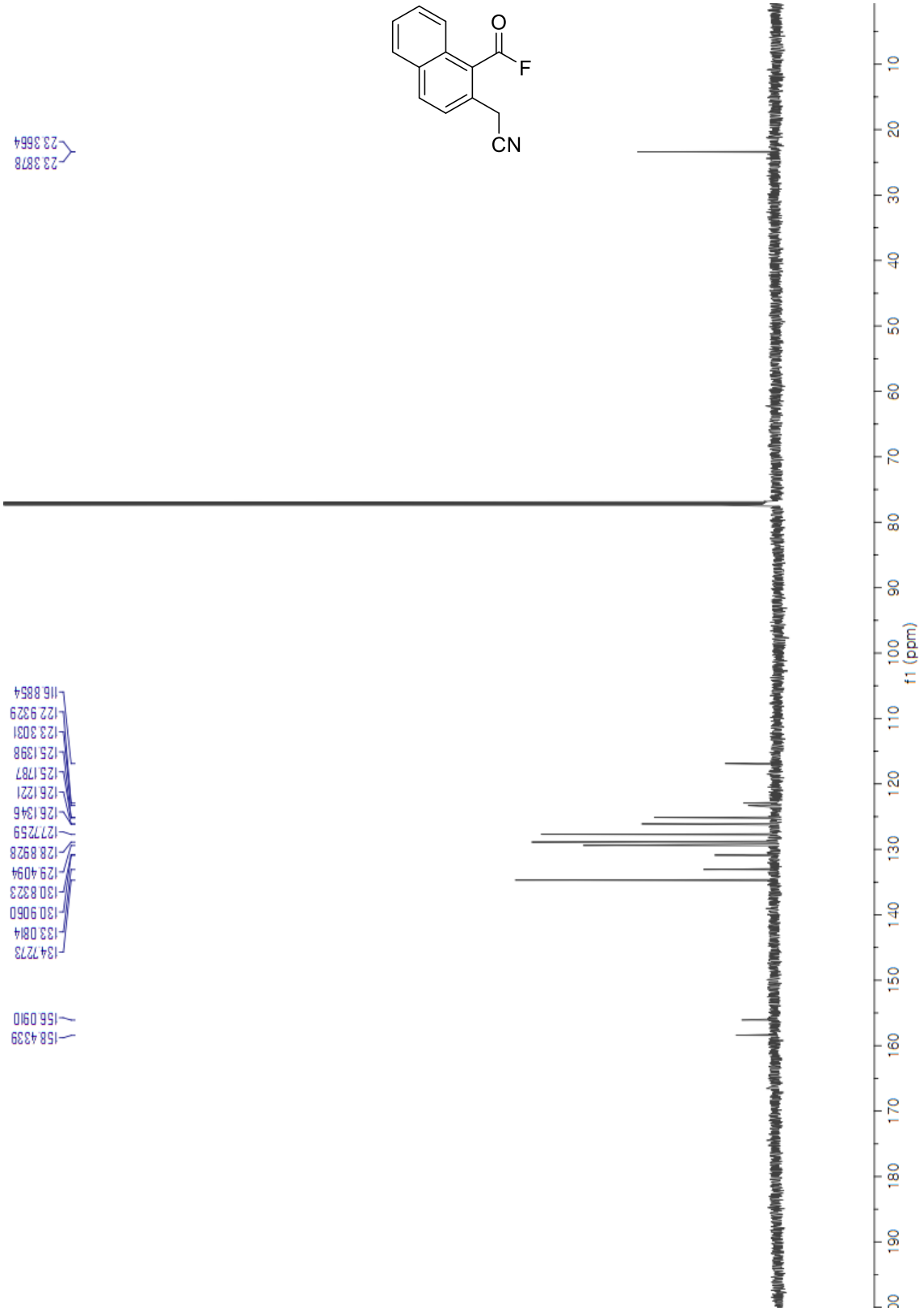
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2h**



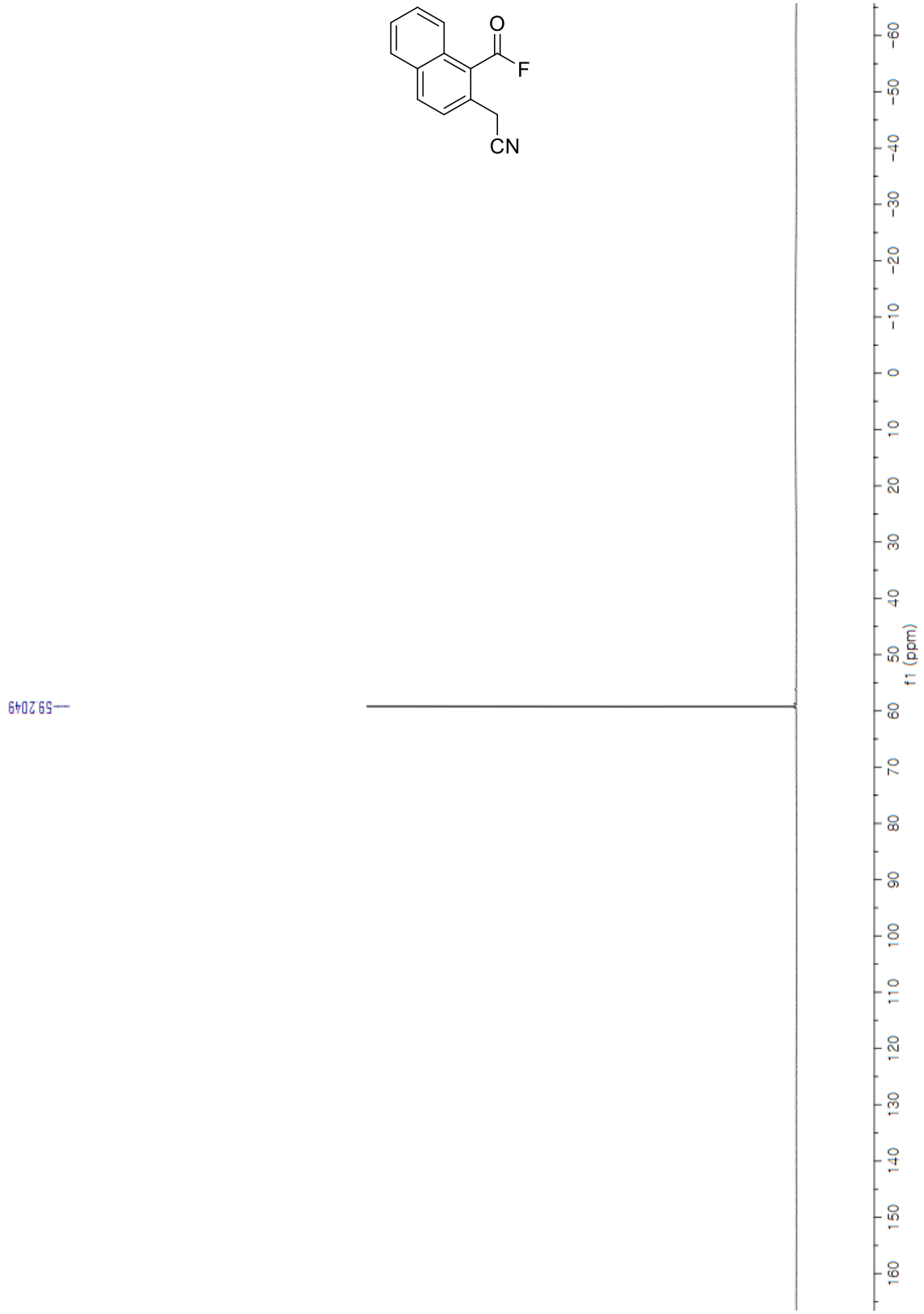
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2h**



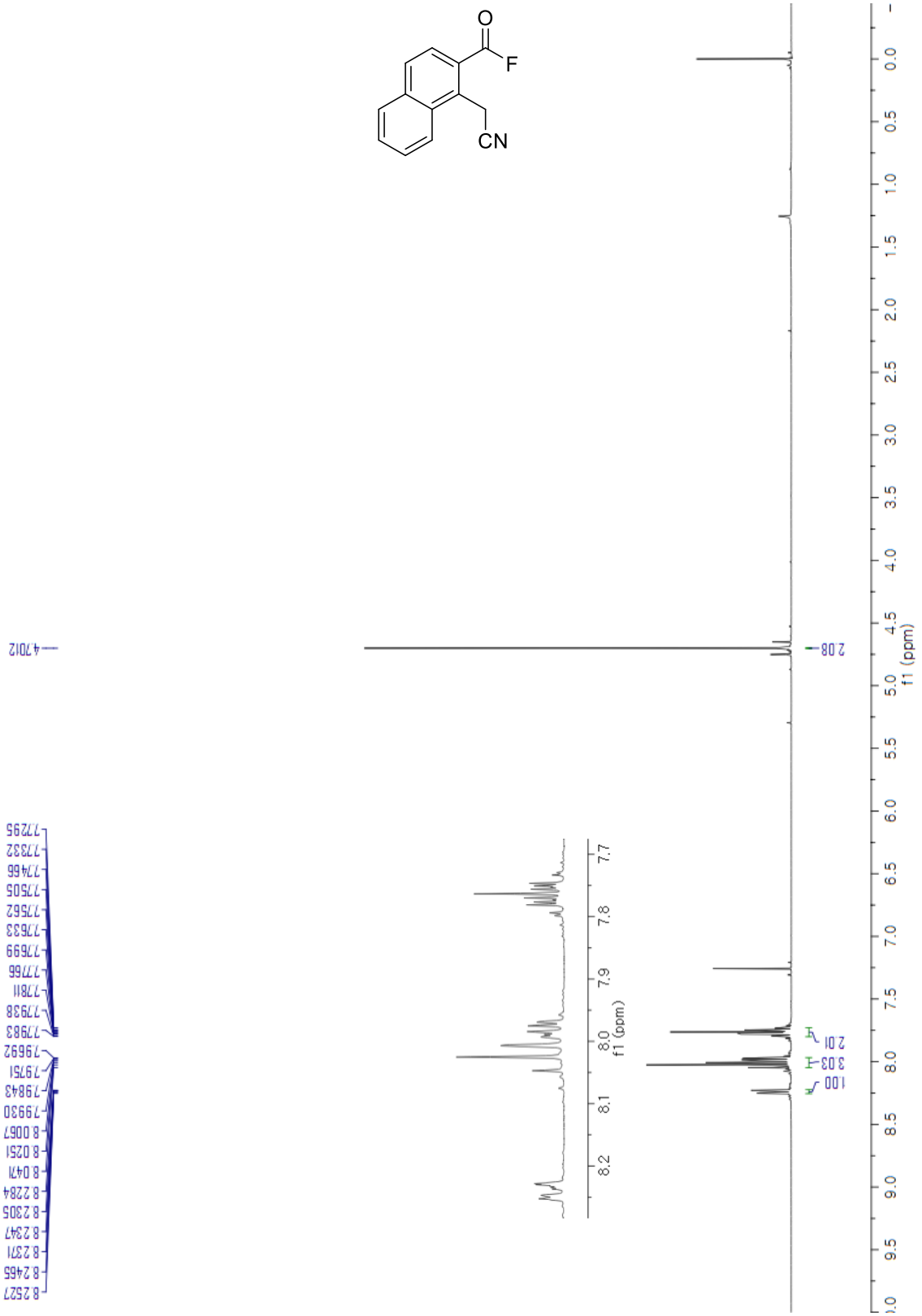
^{1}H NMR ($CDCl_3$, 600 MHz) of compound **2i**



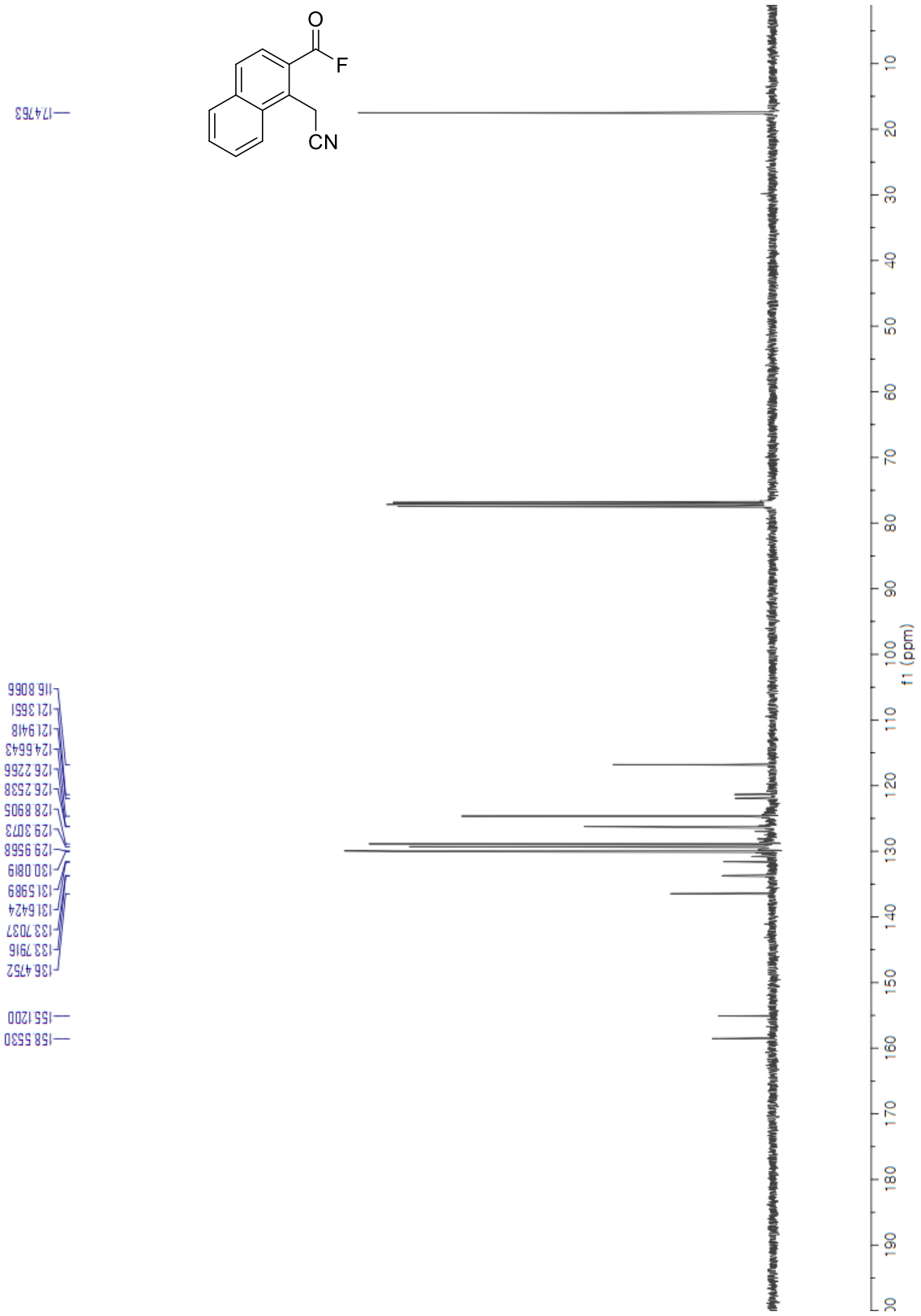
^{13}C NMR ($CDCl_3$, 150 MHz) of compound **2i**



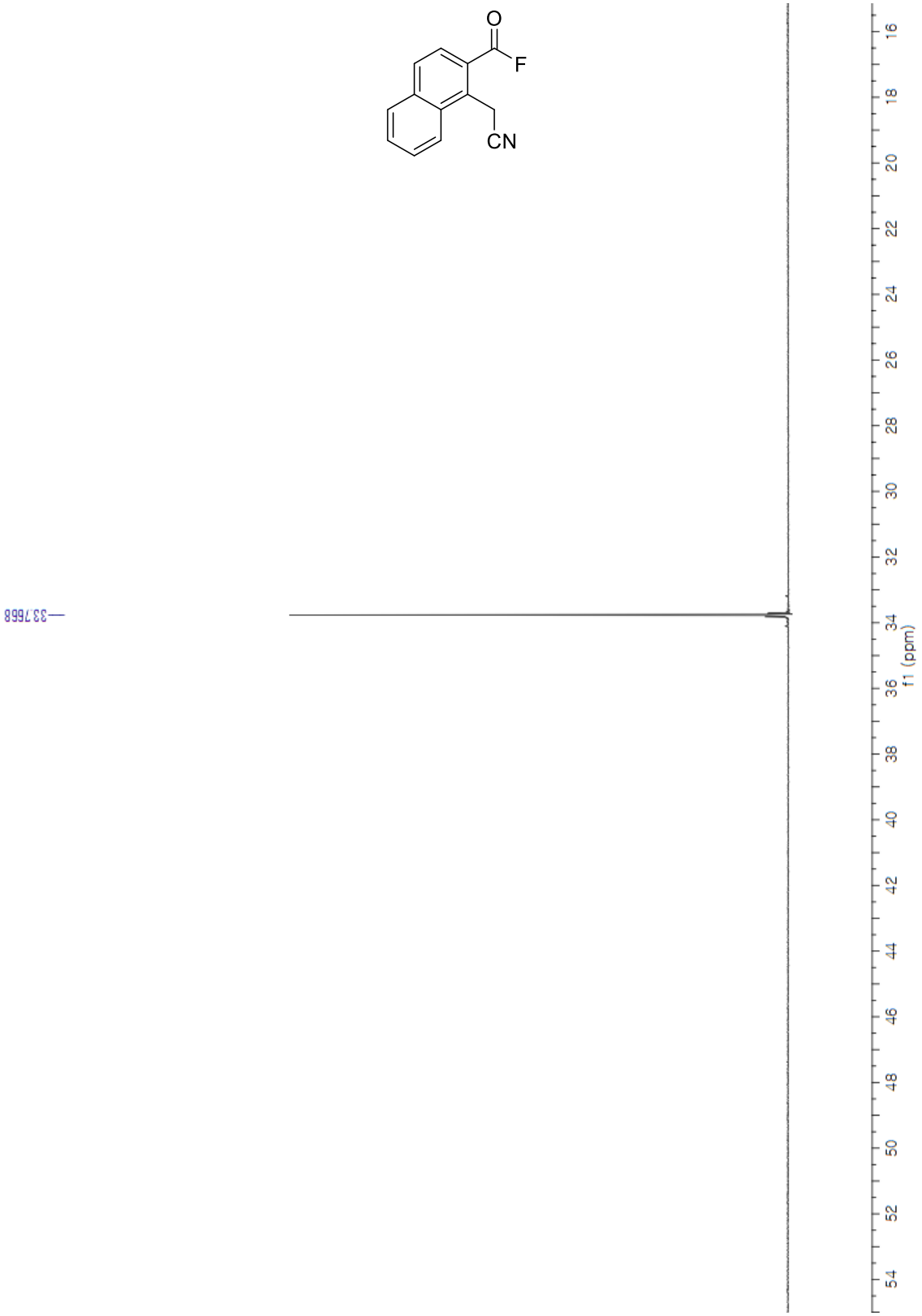
^{19}F NMR ($CDCl_3$, 565 MHz) of compound **2i**



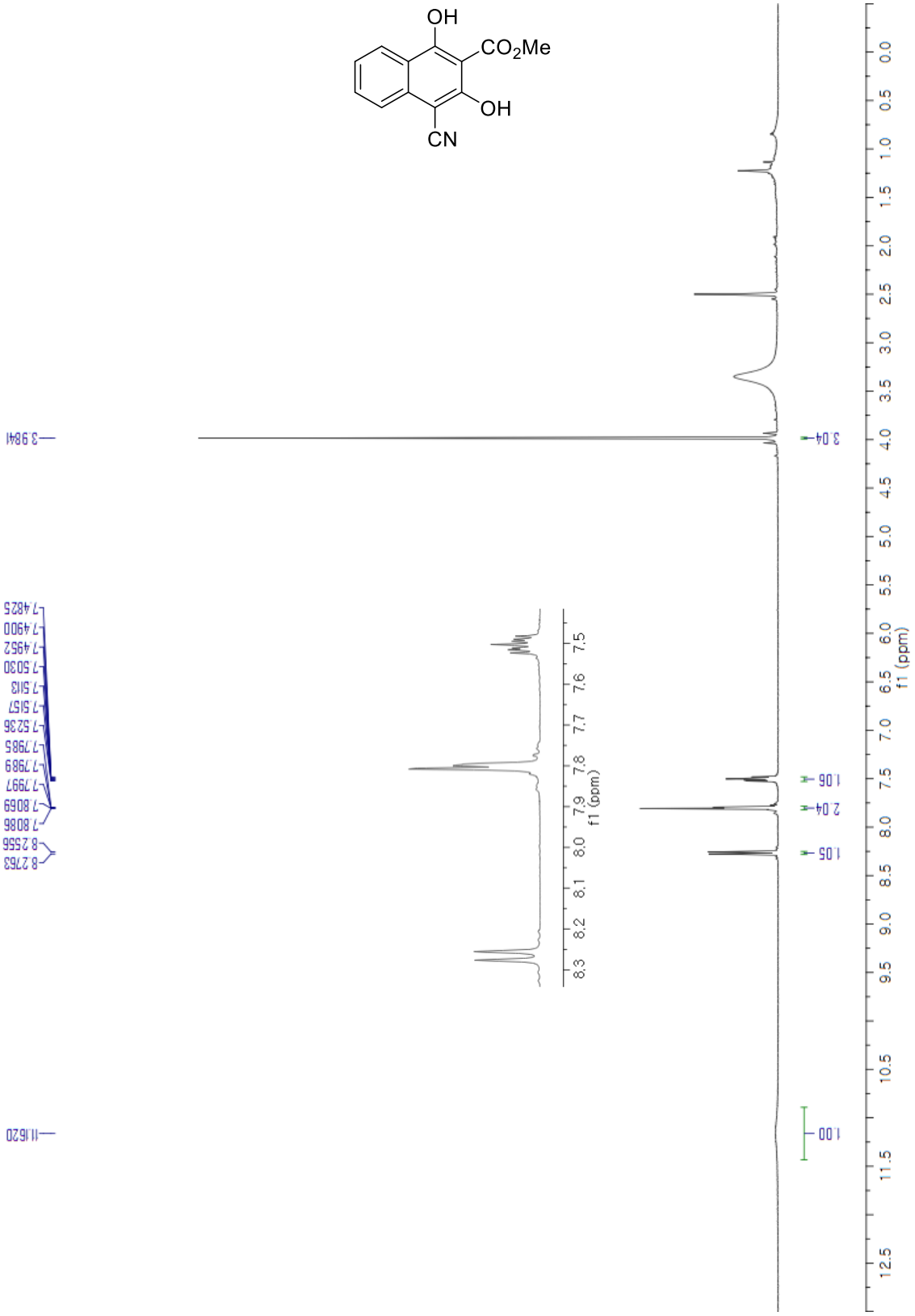
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **2j**



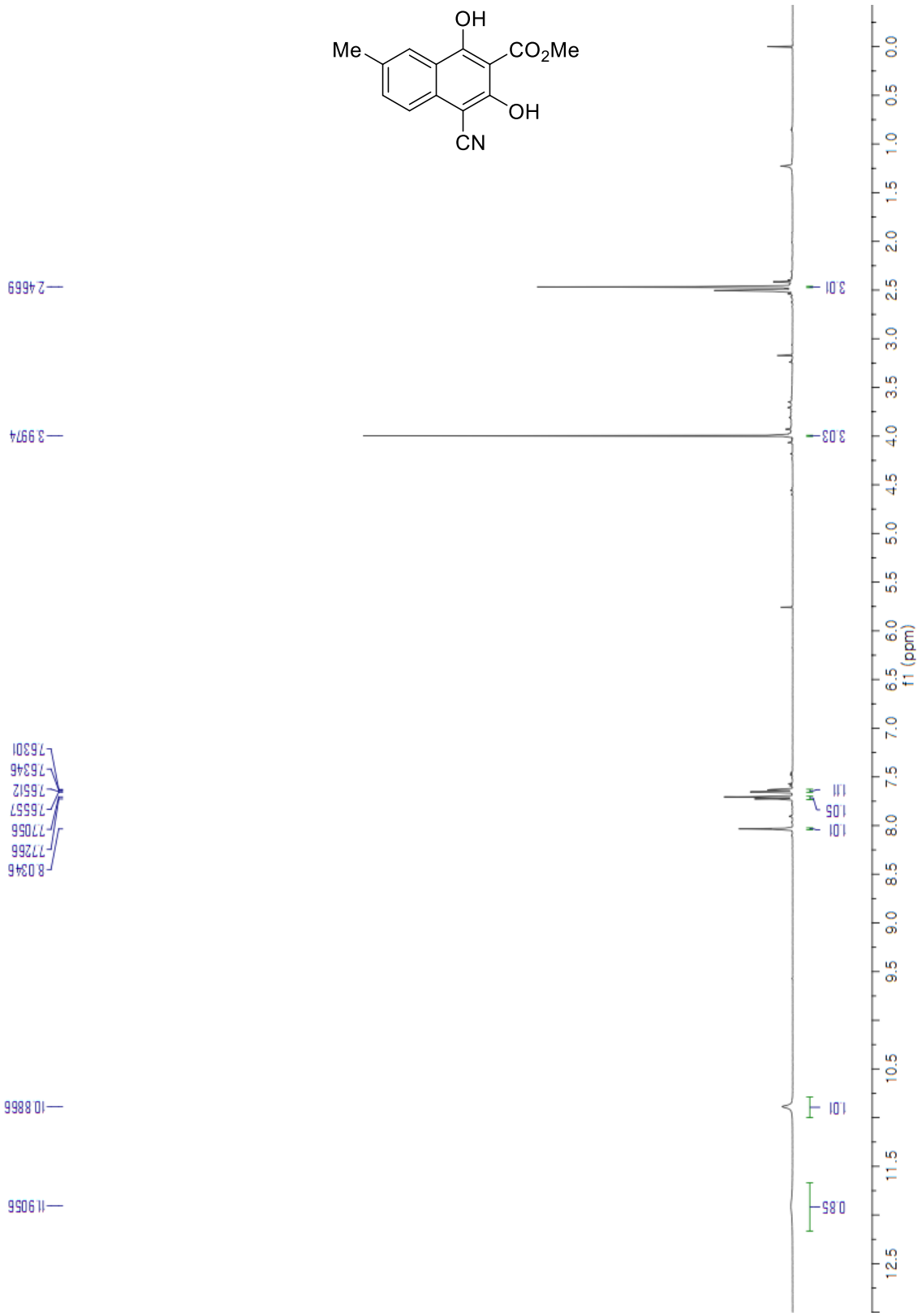
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2j**



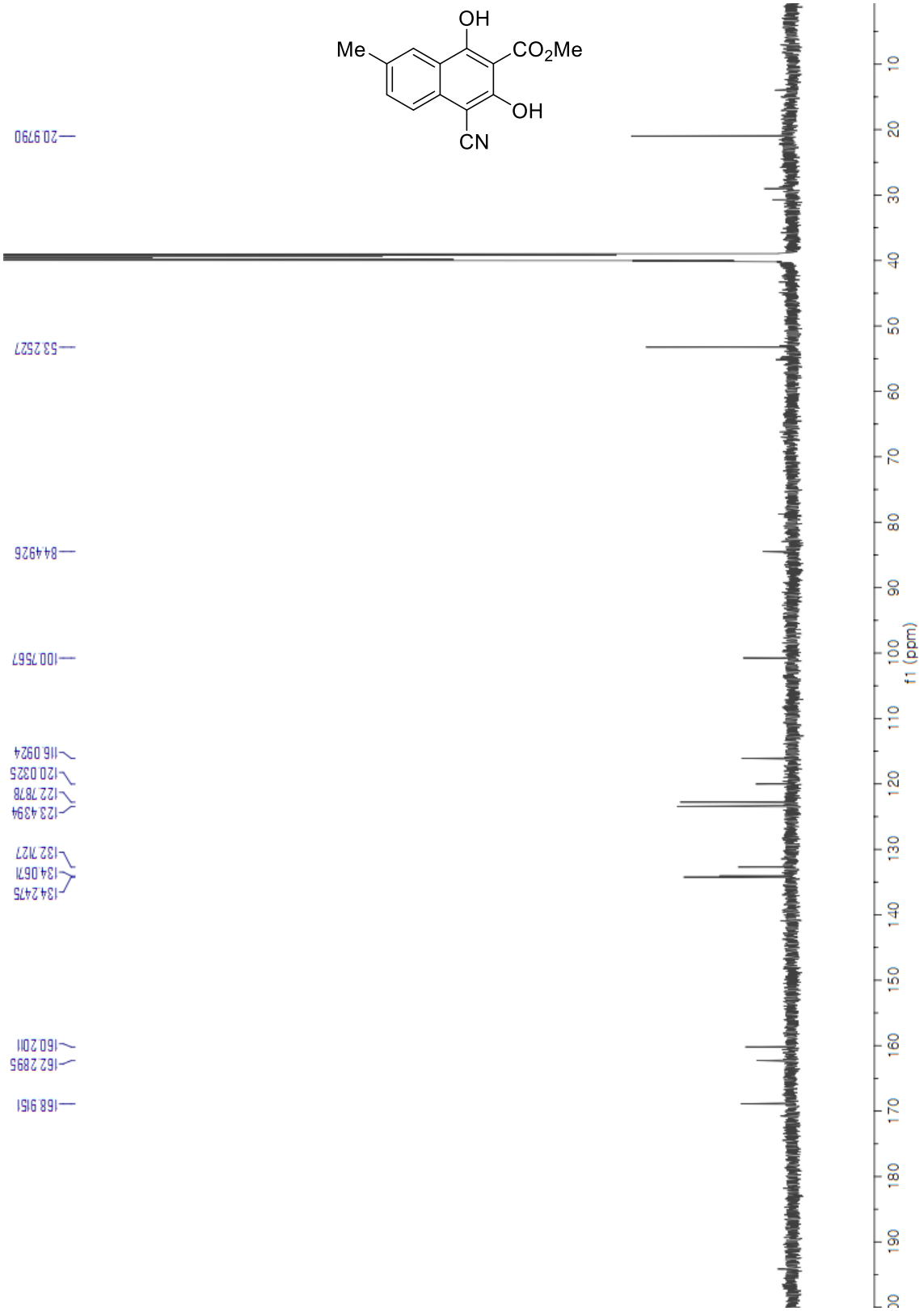
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **2j**



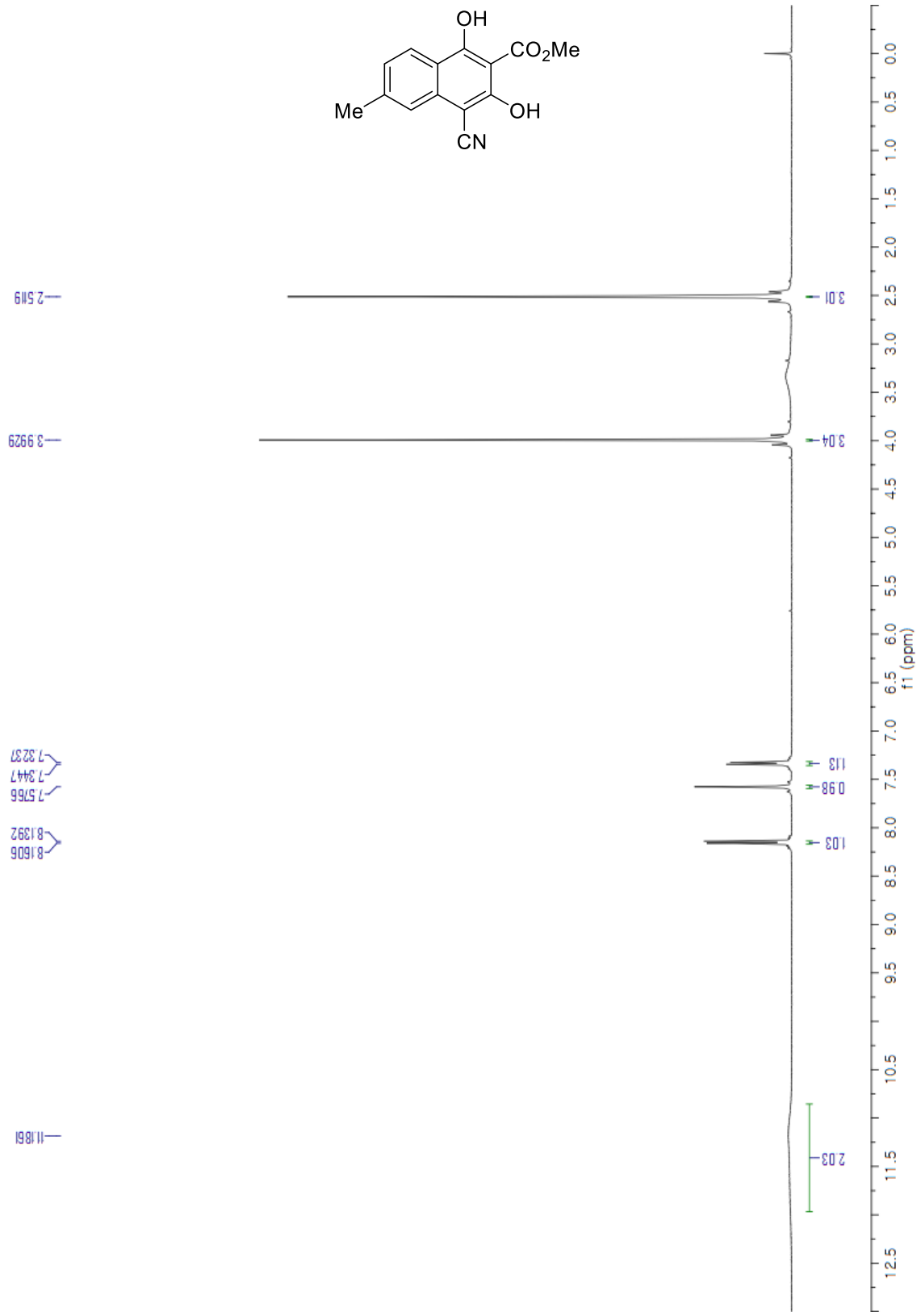
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4a**



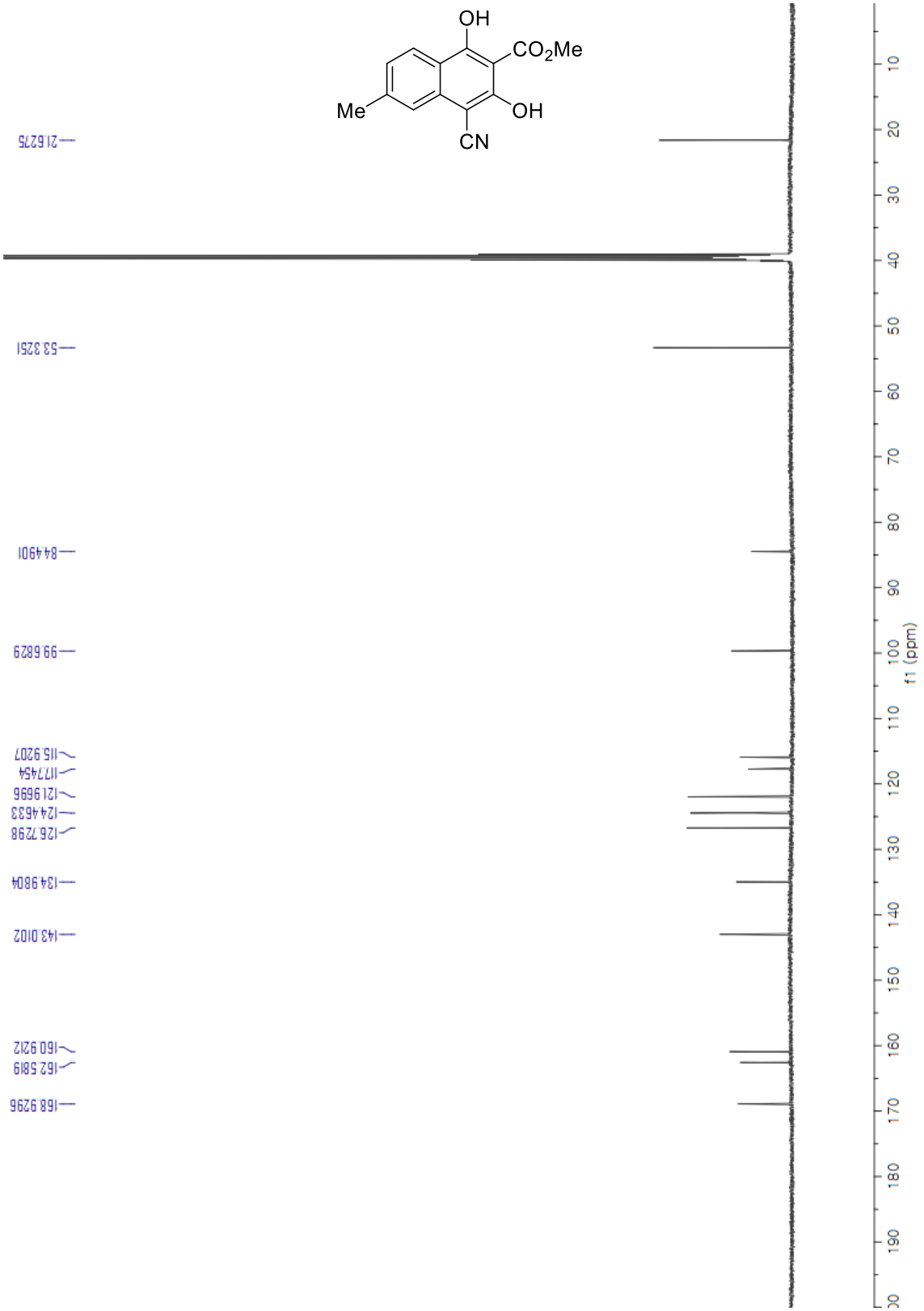
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4b**



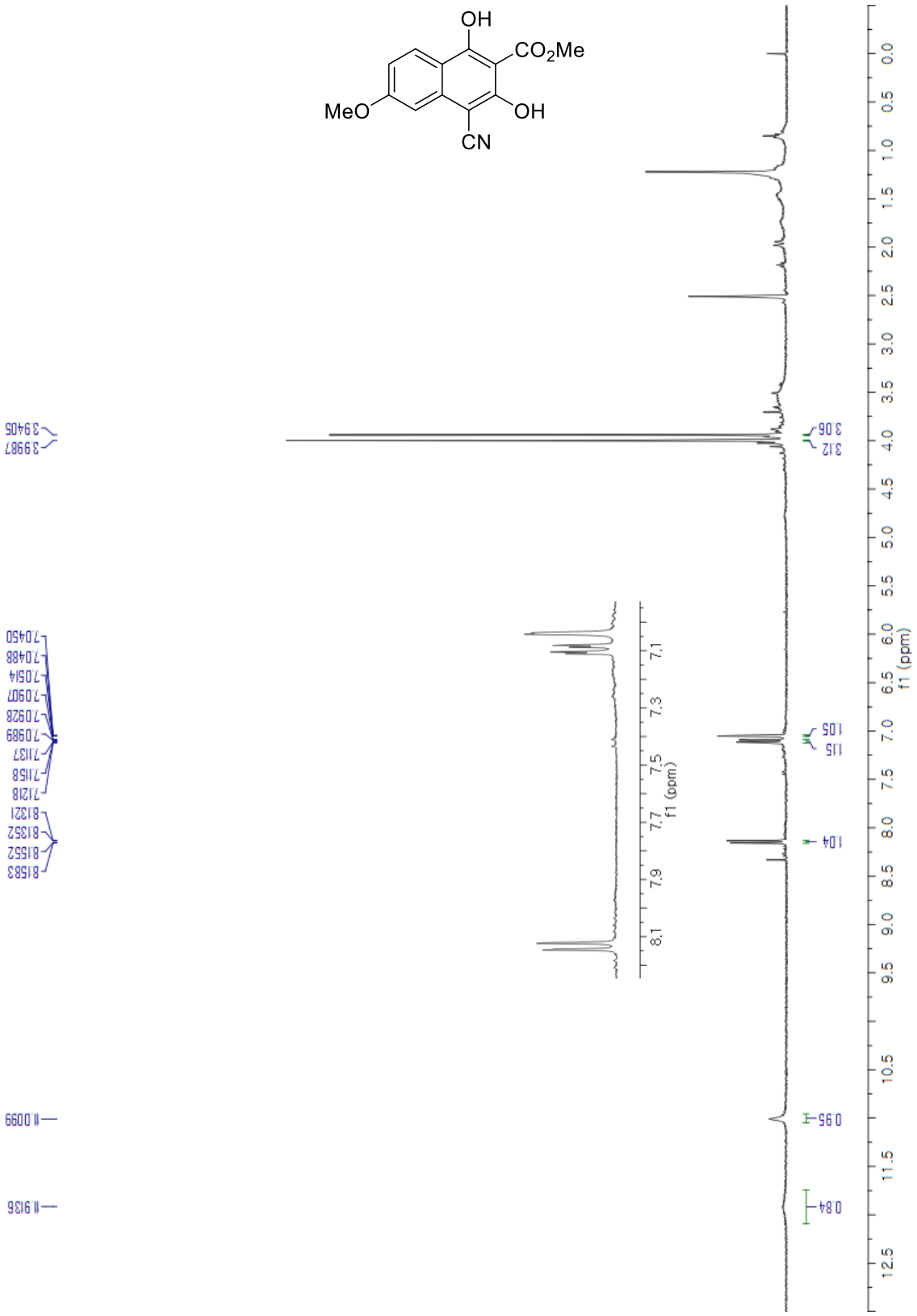
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4b**



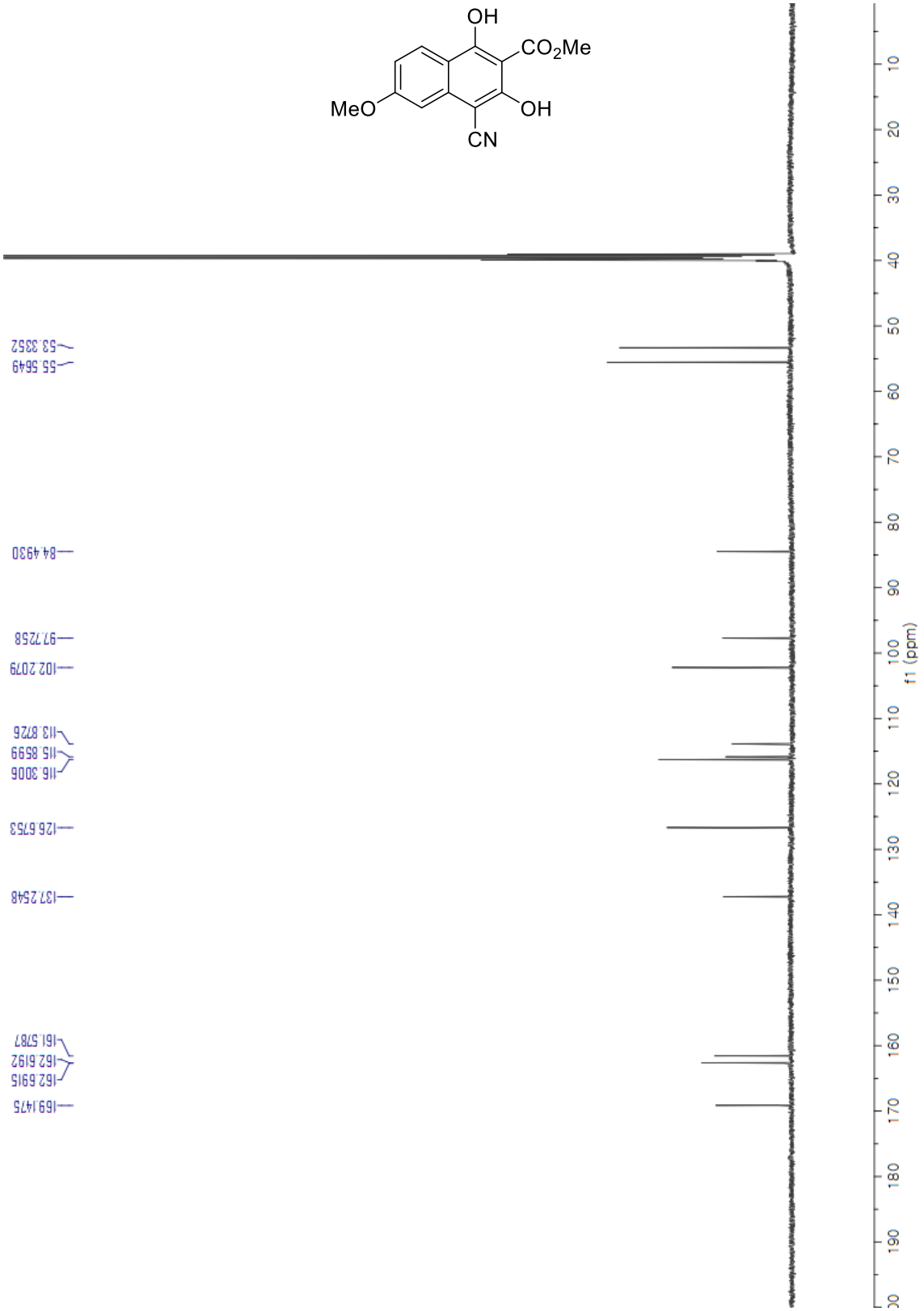
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4c**



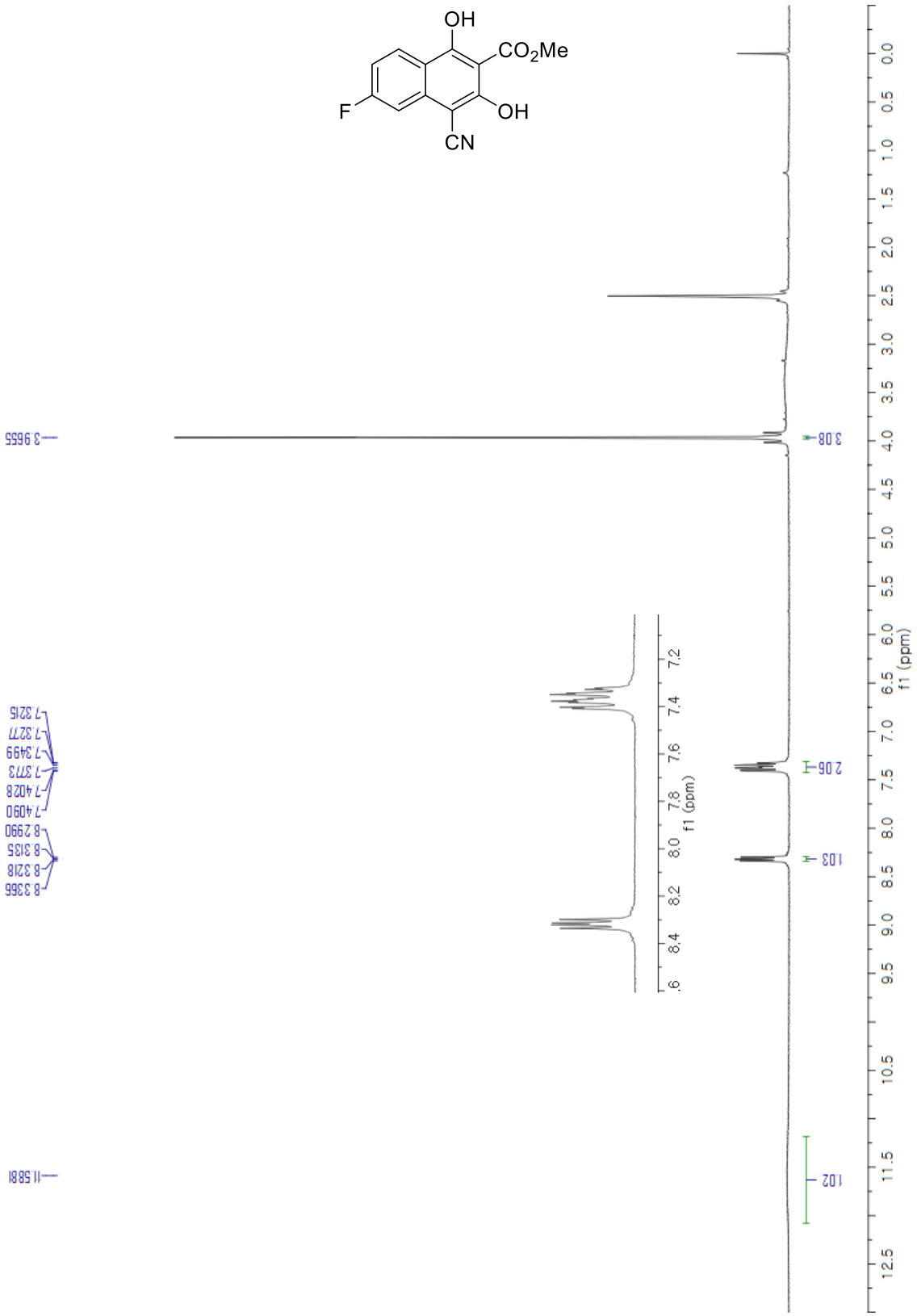
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4c**



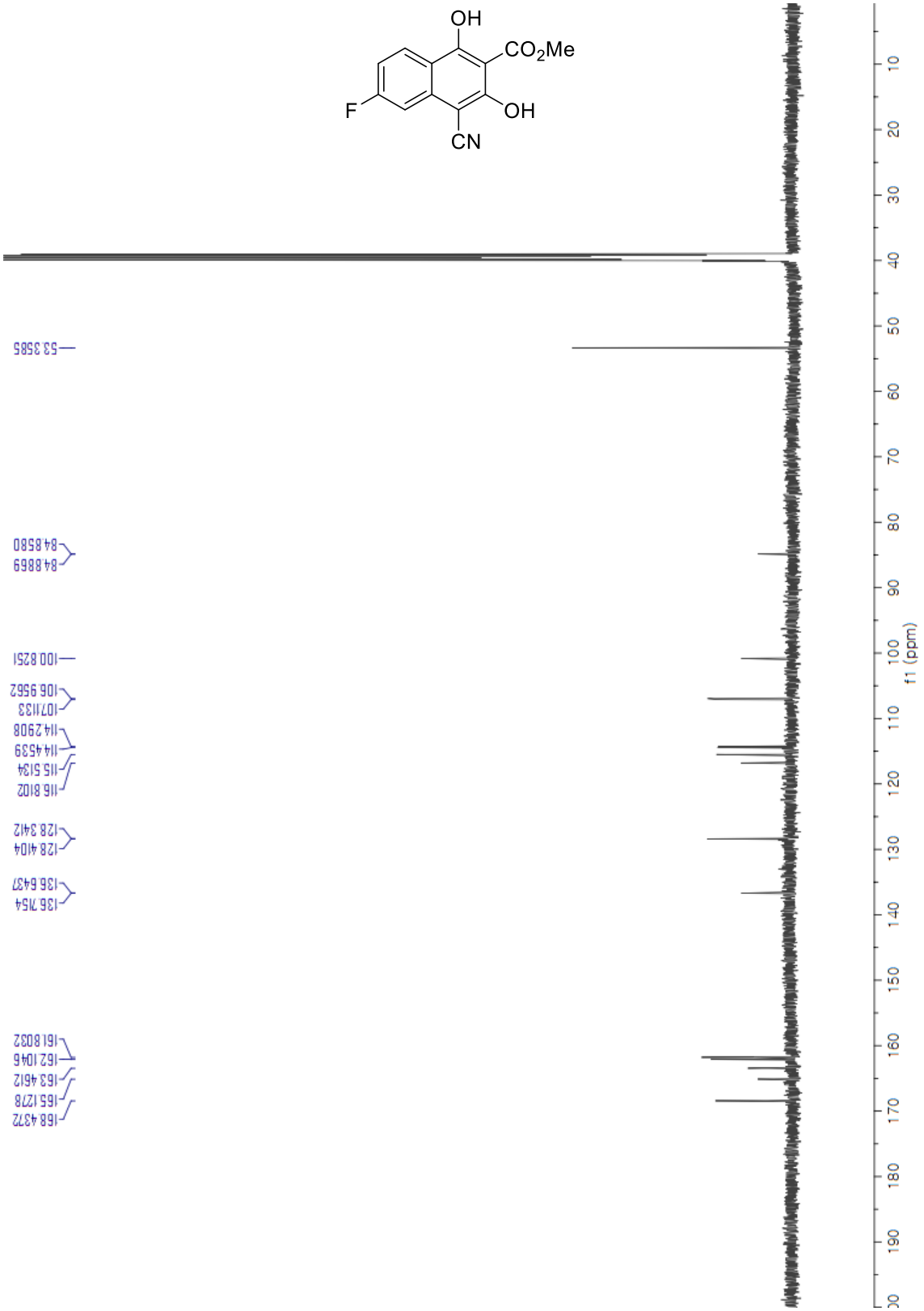
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4d**



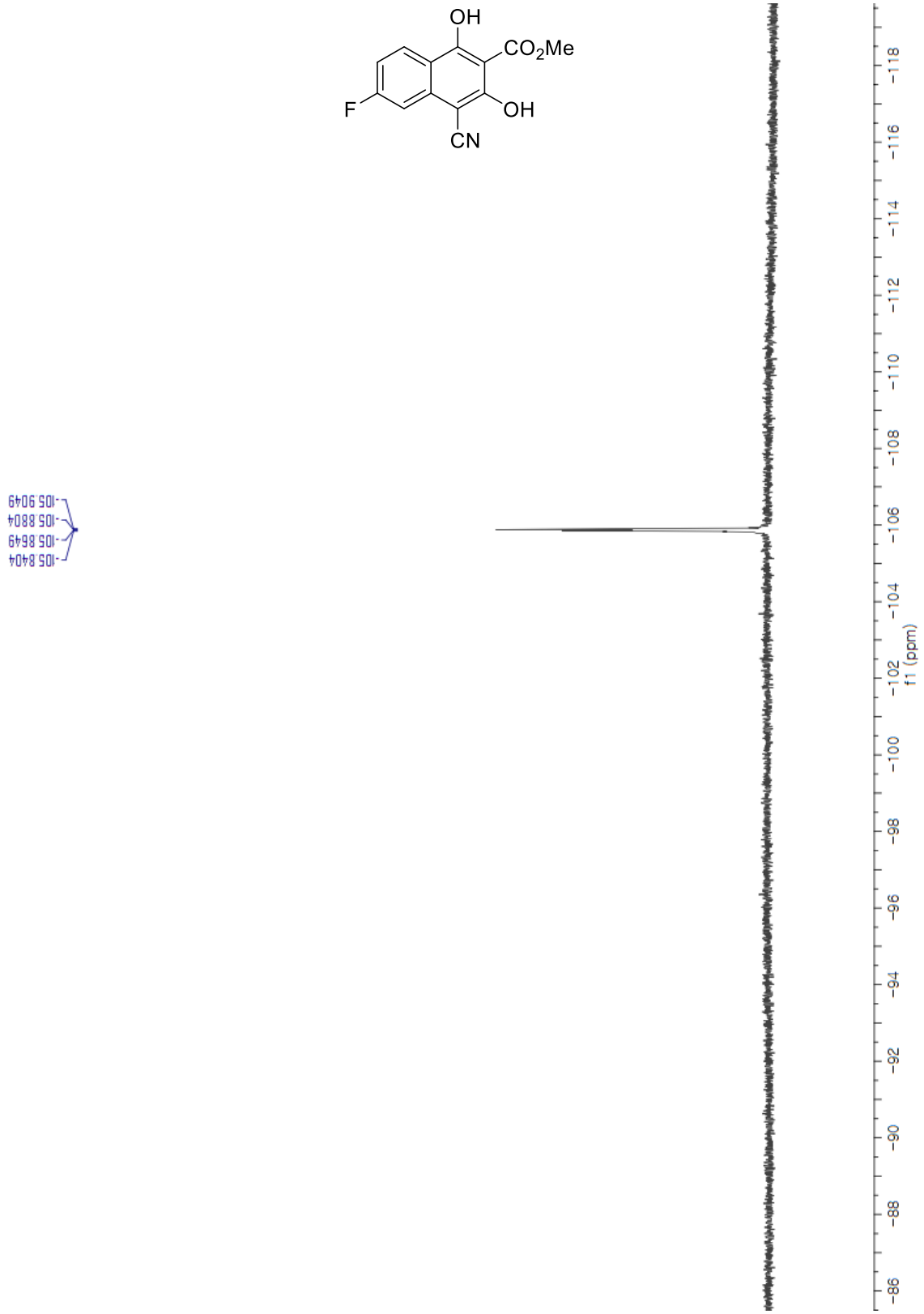
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4d**



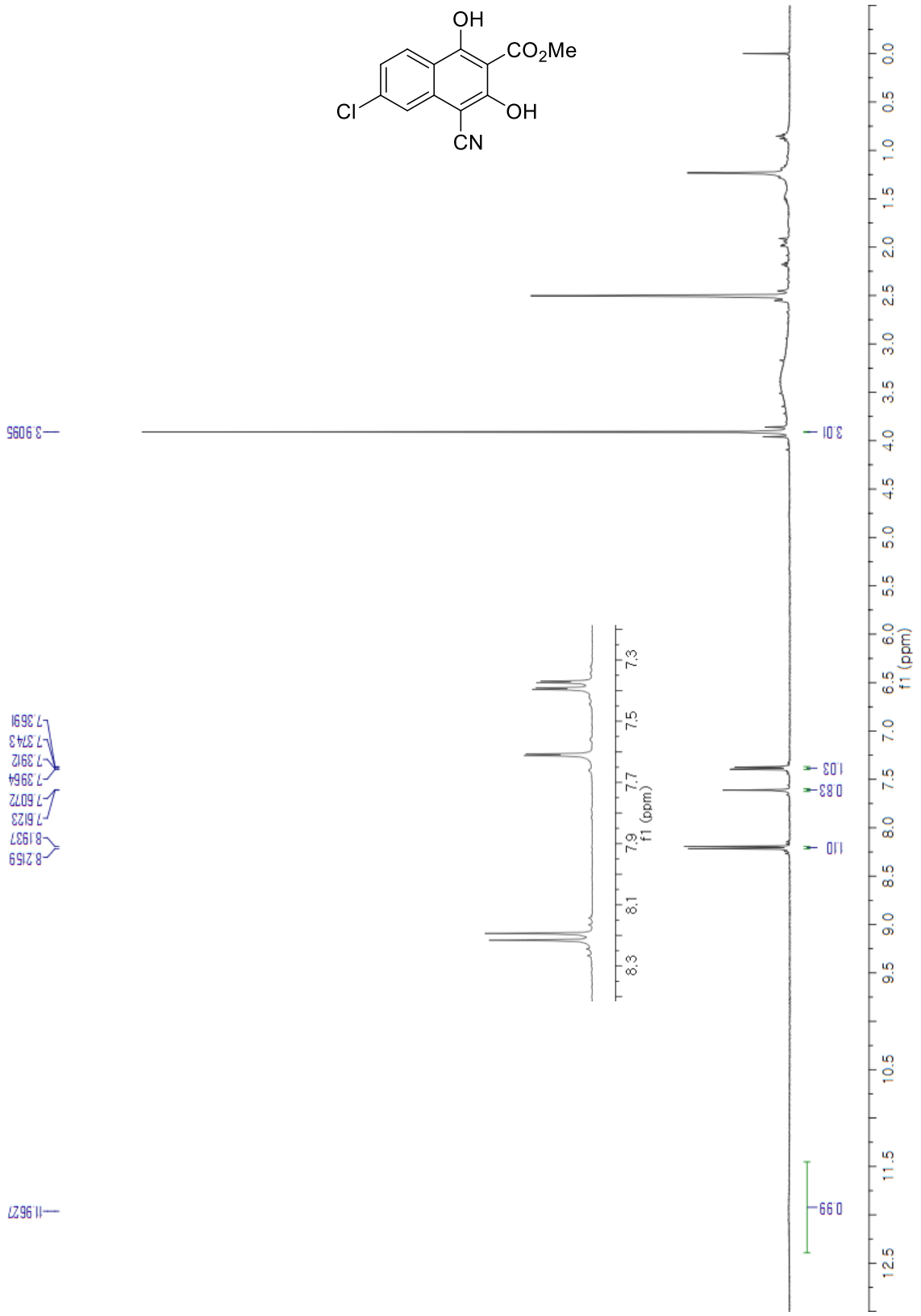
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4e**



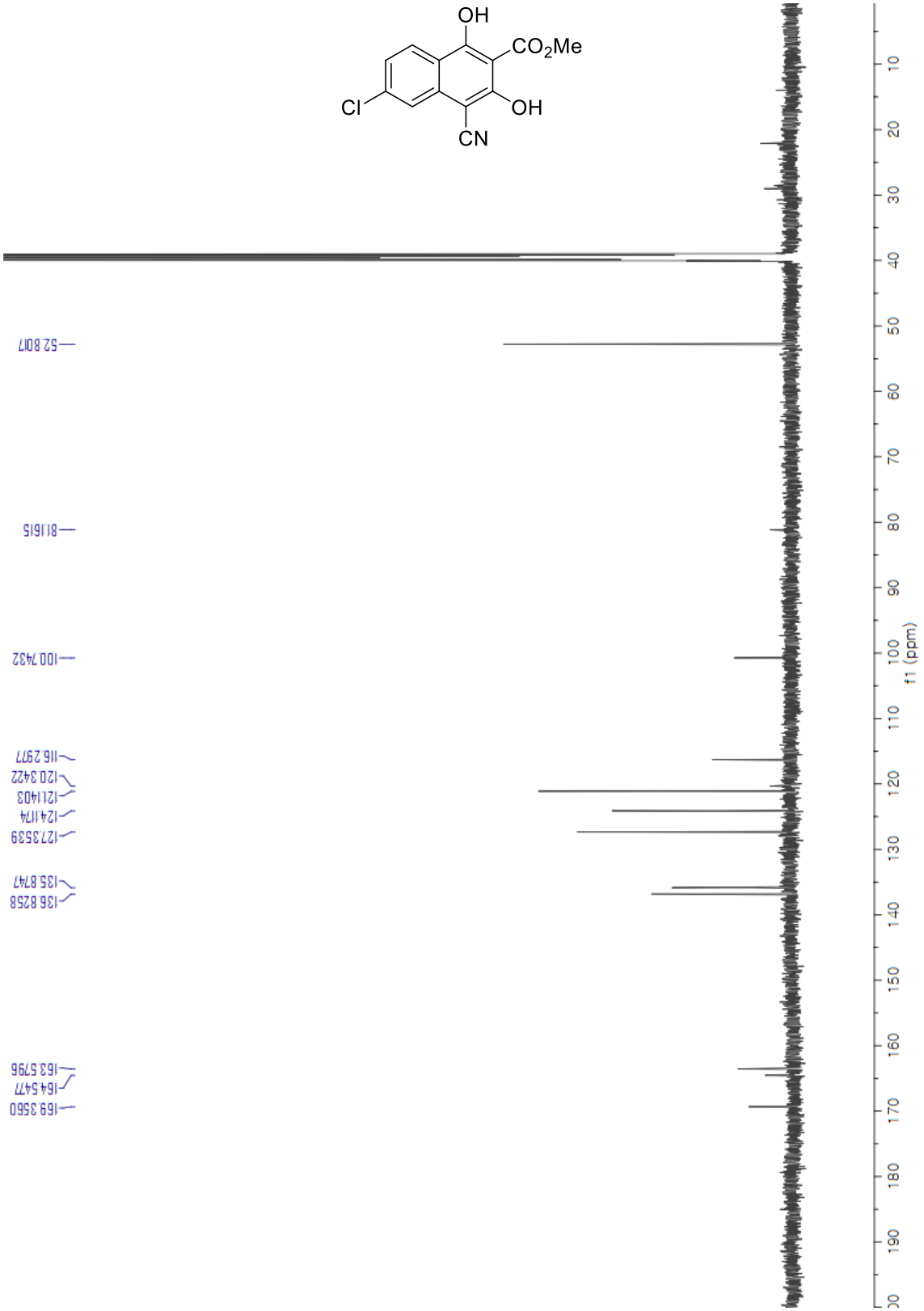
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4e**



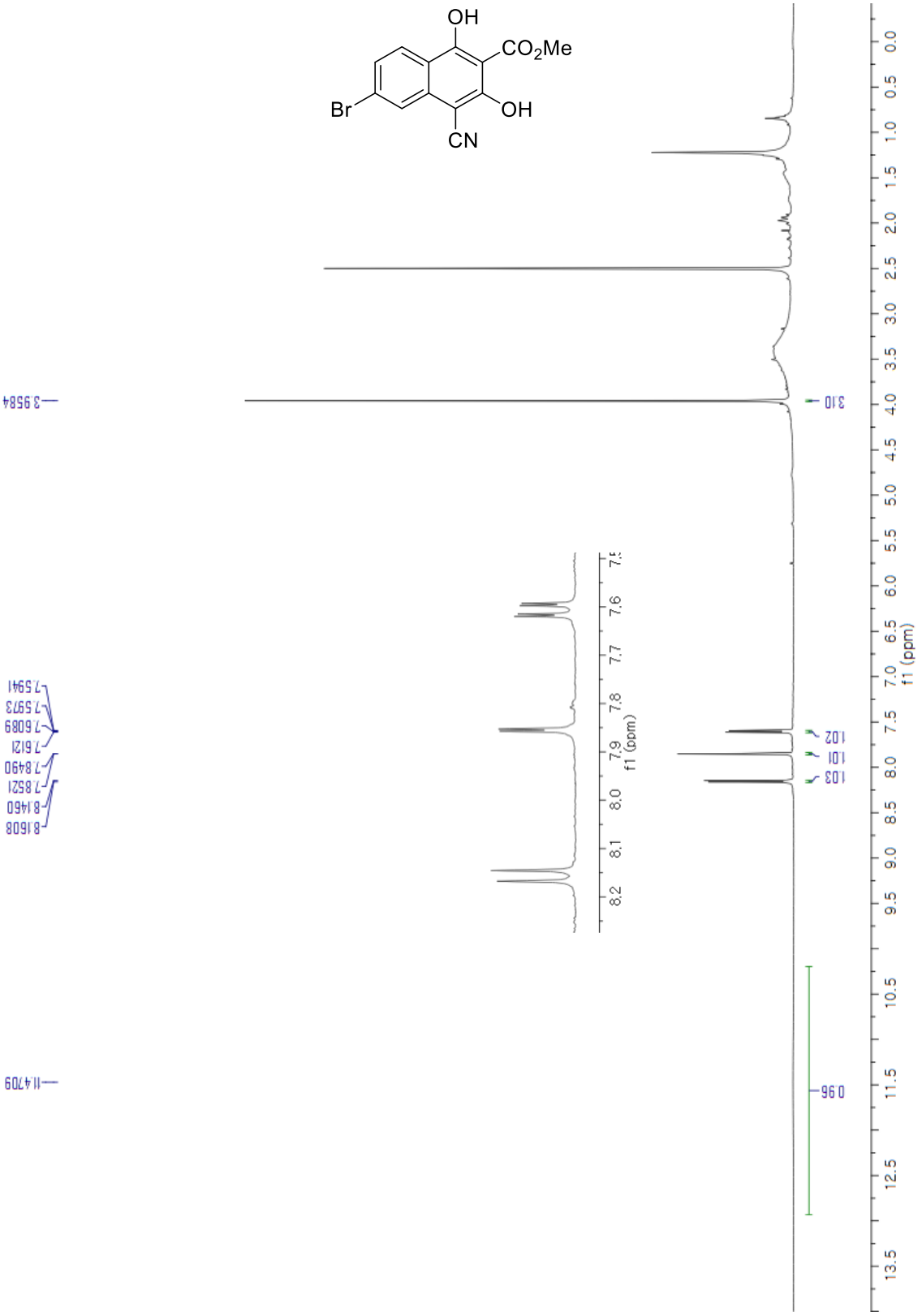
^{19}F NMR (DMSO-d_6, 376 MHz) of compound **4e**



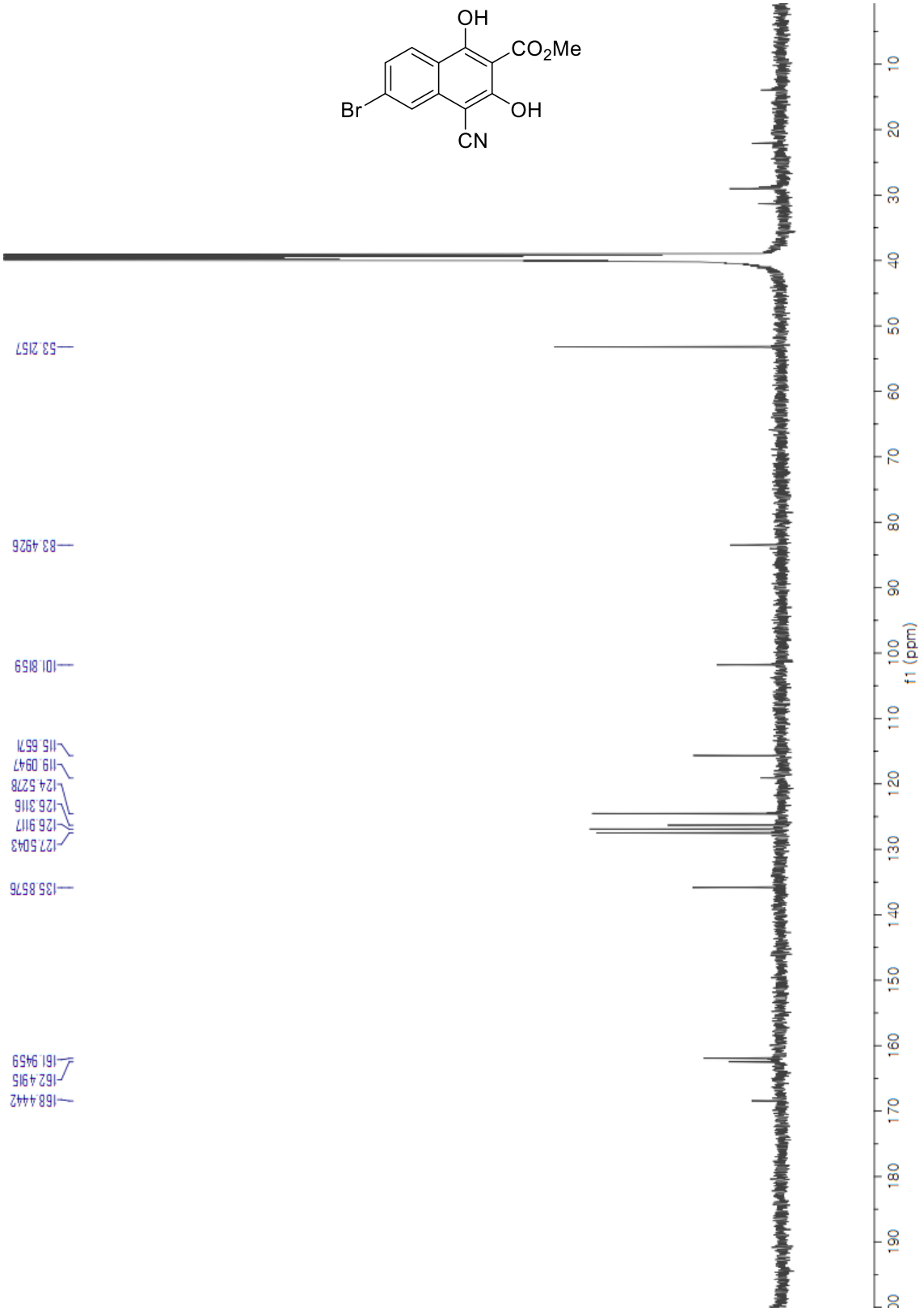
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4f**



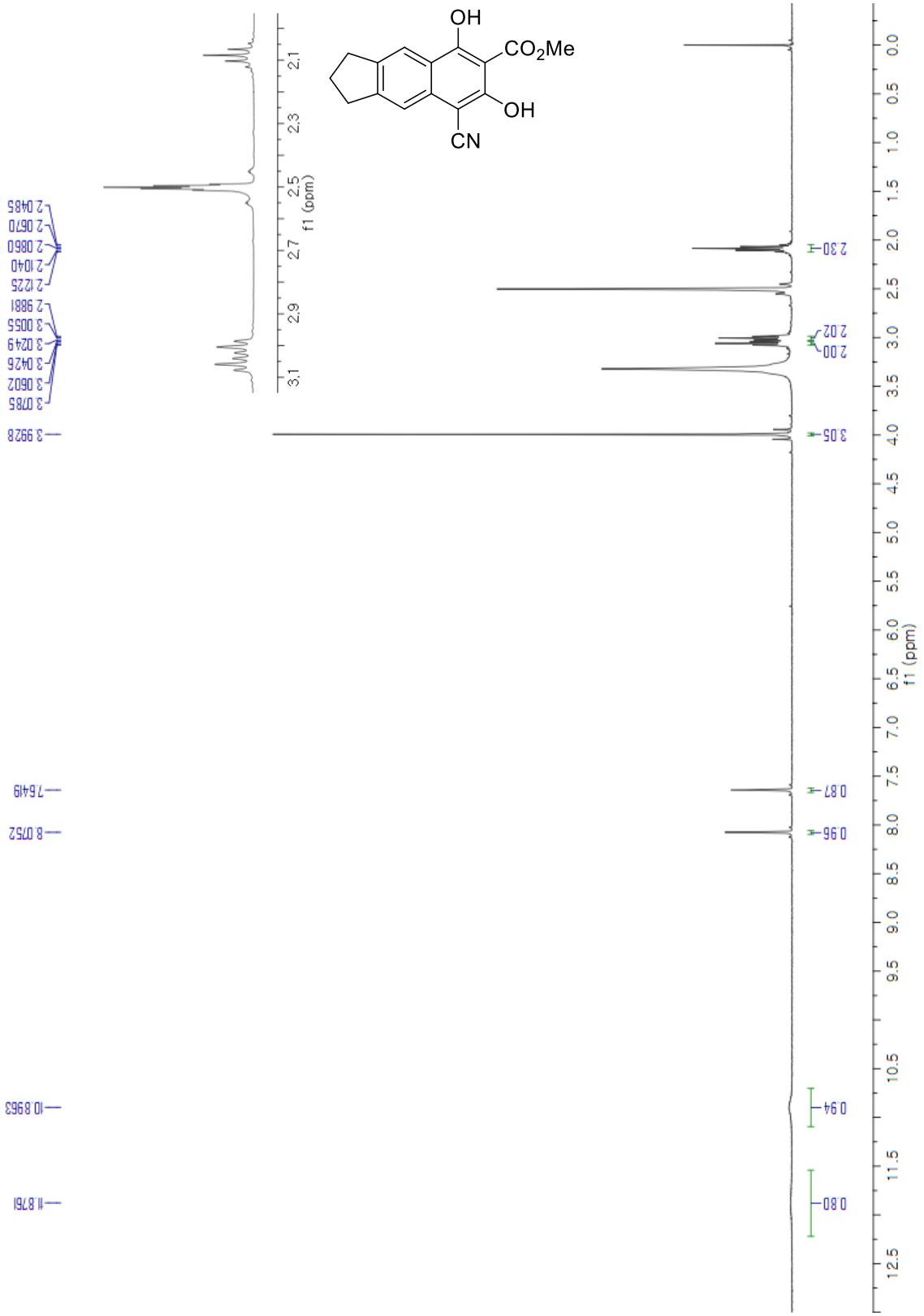
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4f**



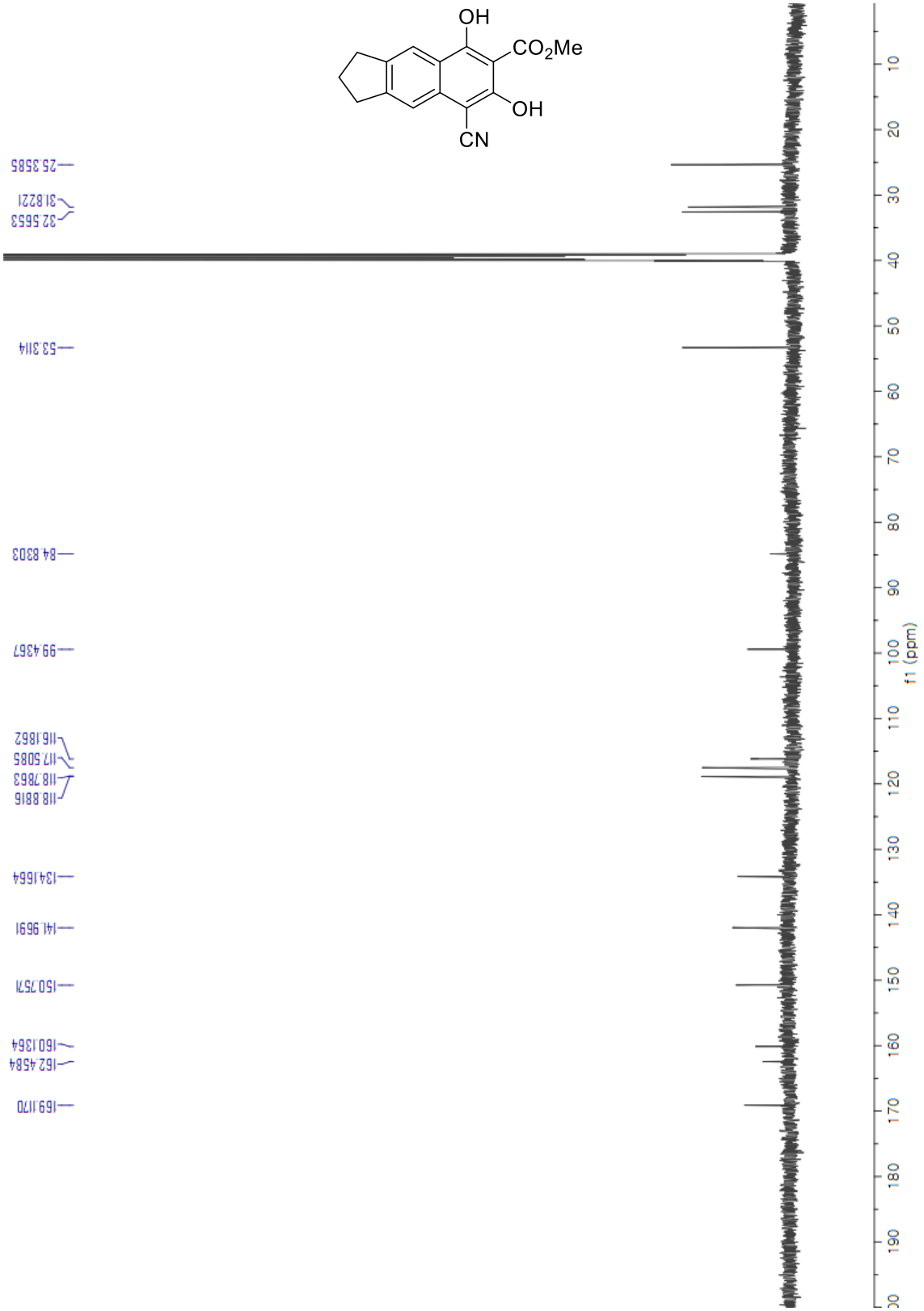
^{1}H NMR (DMSO-d_6, 600 MHz) of compound **4g**



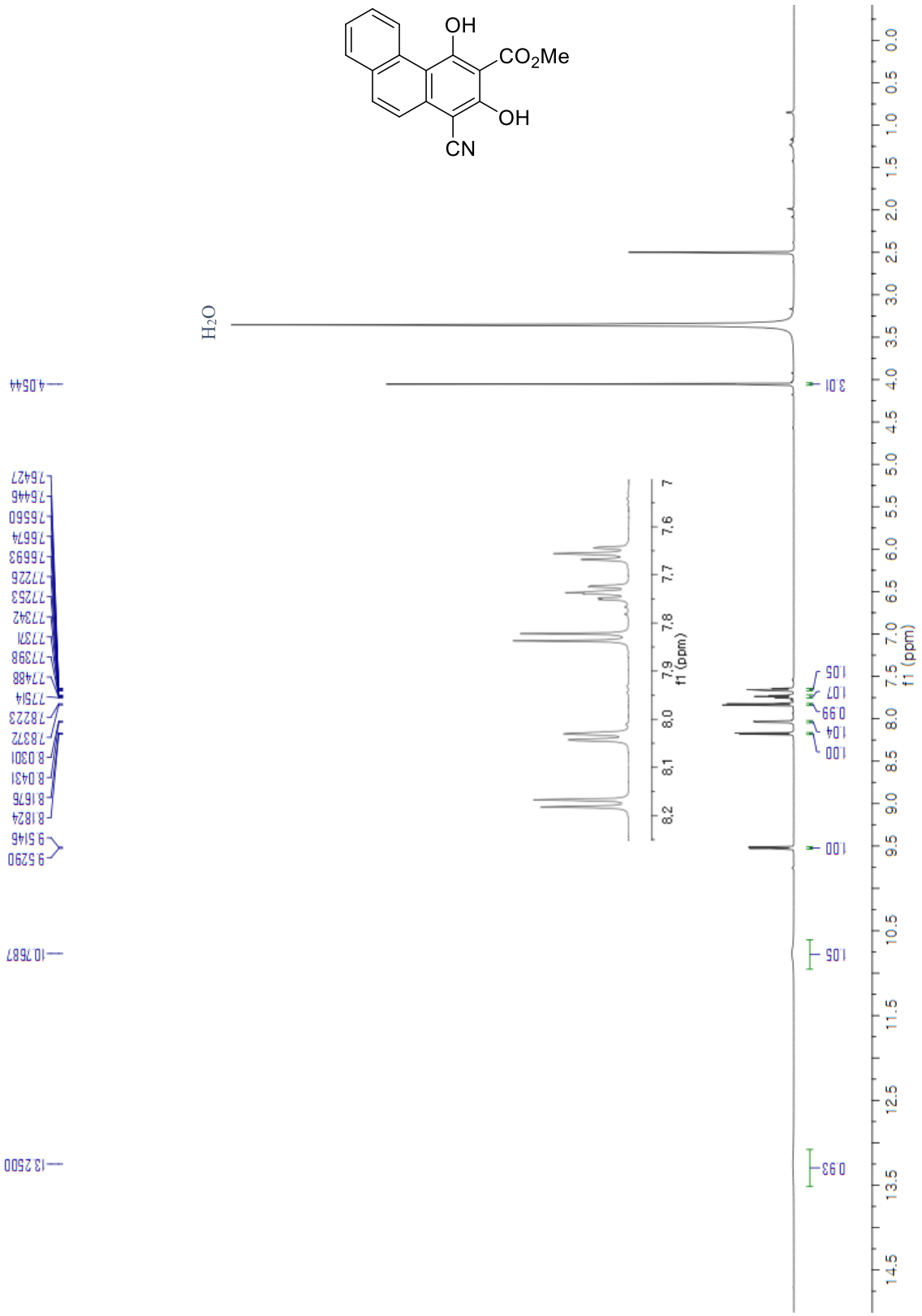
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4g**



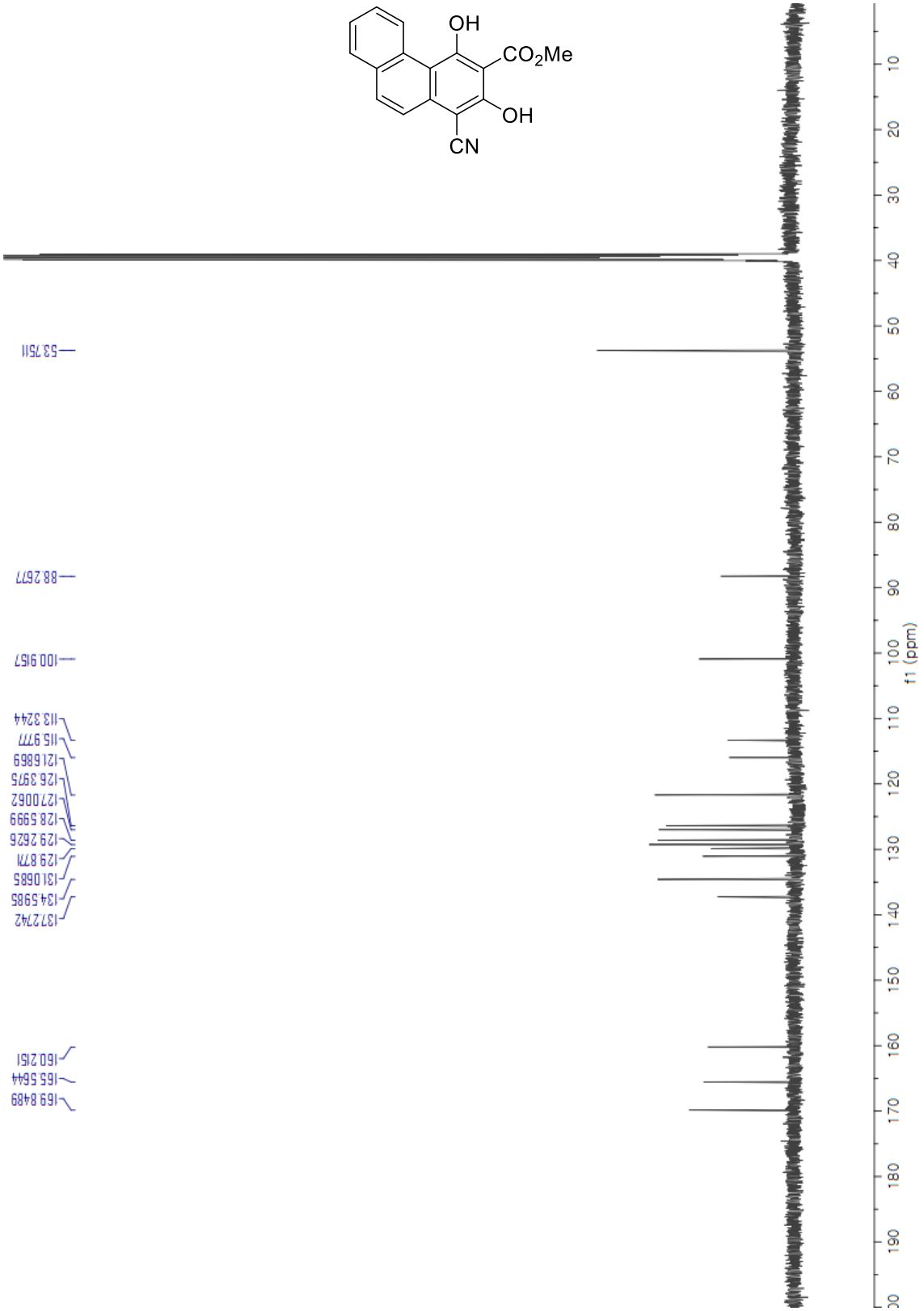
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4h**



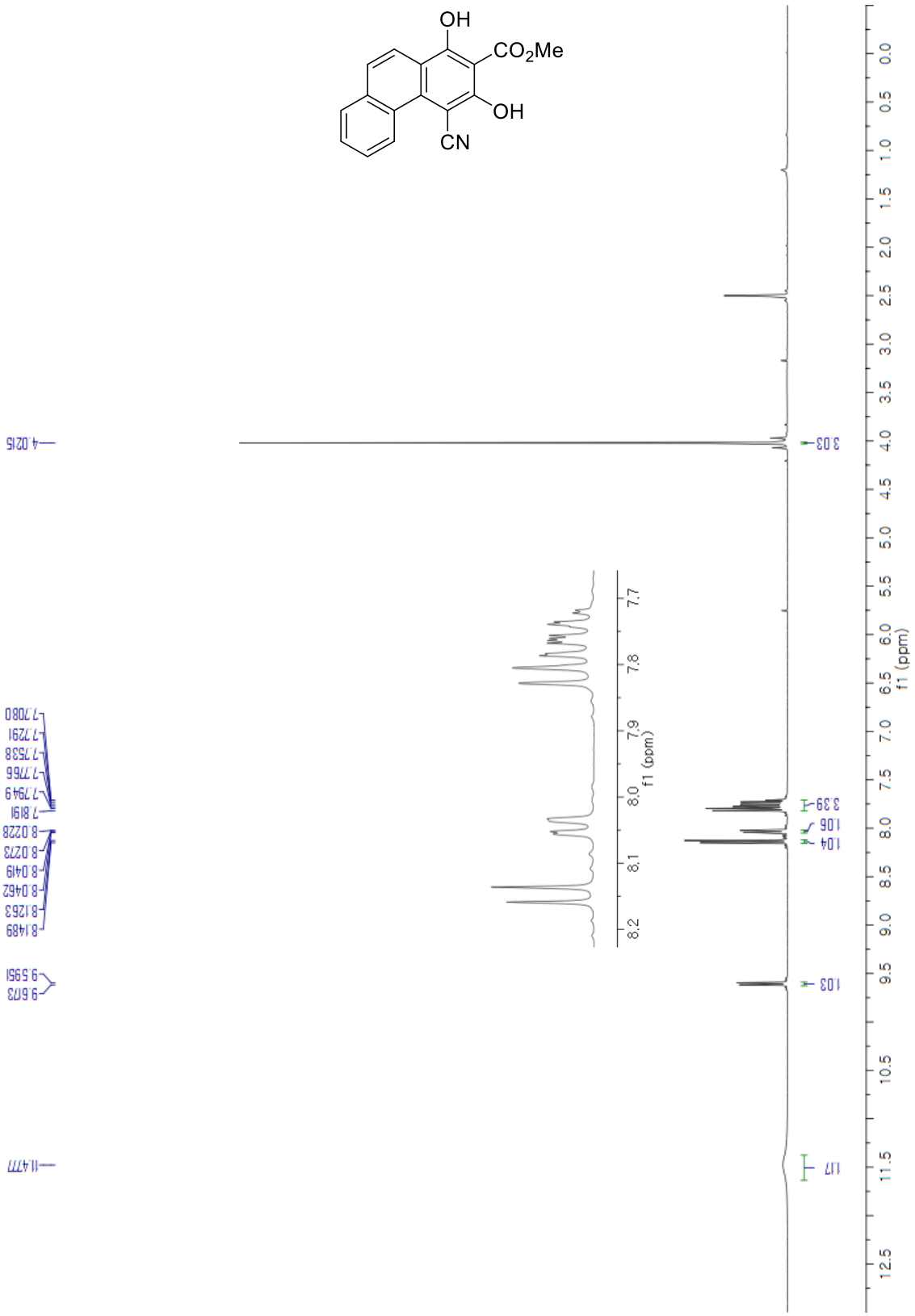
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4h**



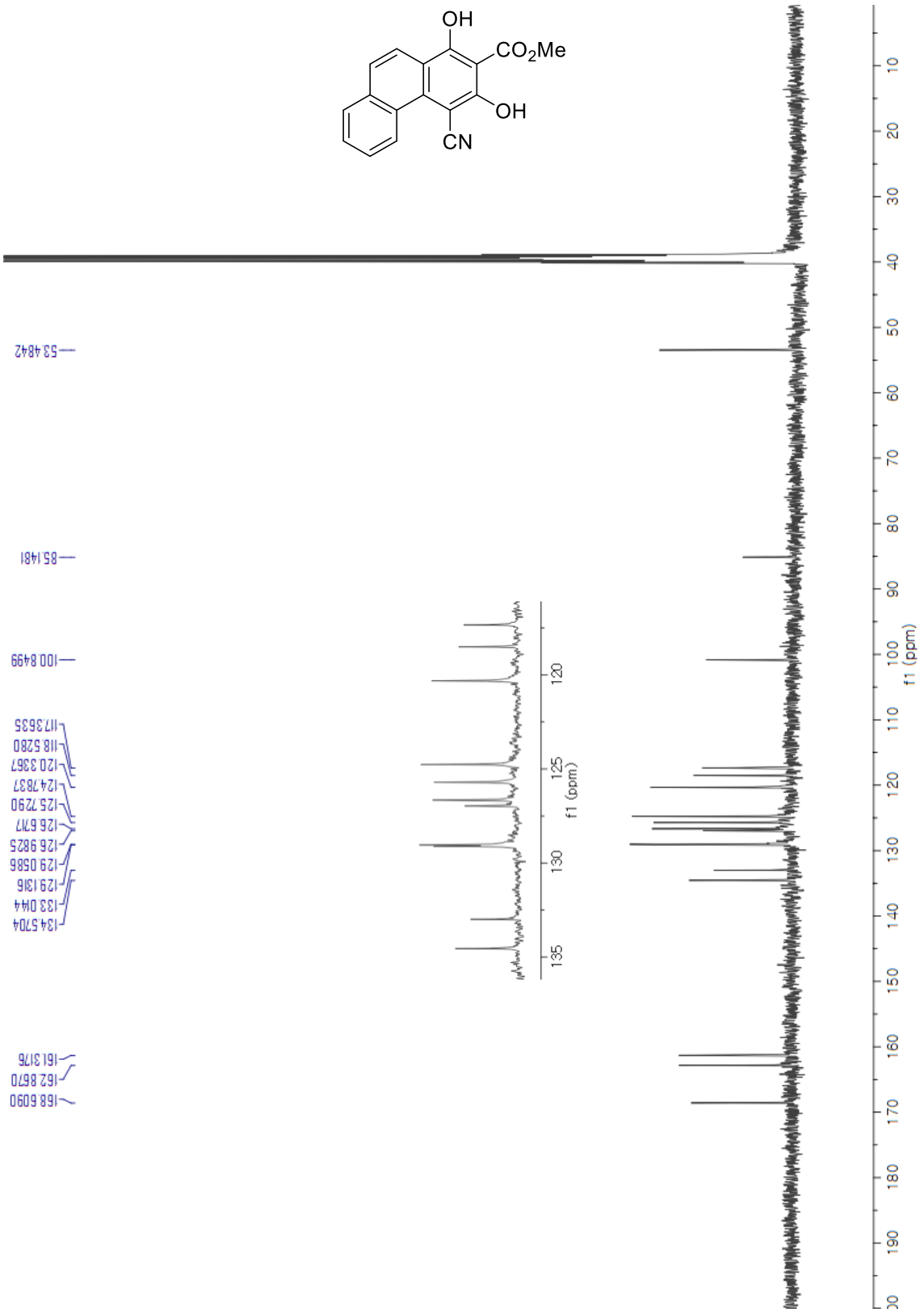
^{1}H NMR (DMSO-d_6, 600 MHz) of compound **4i**



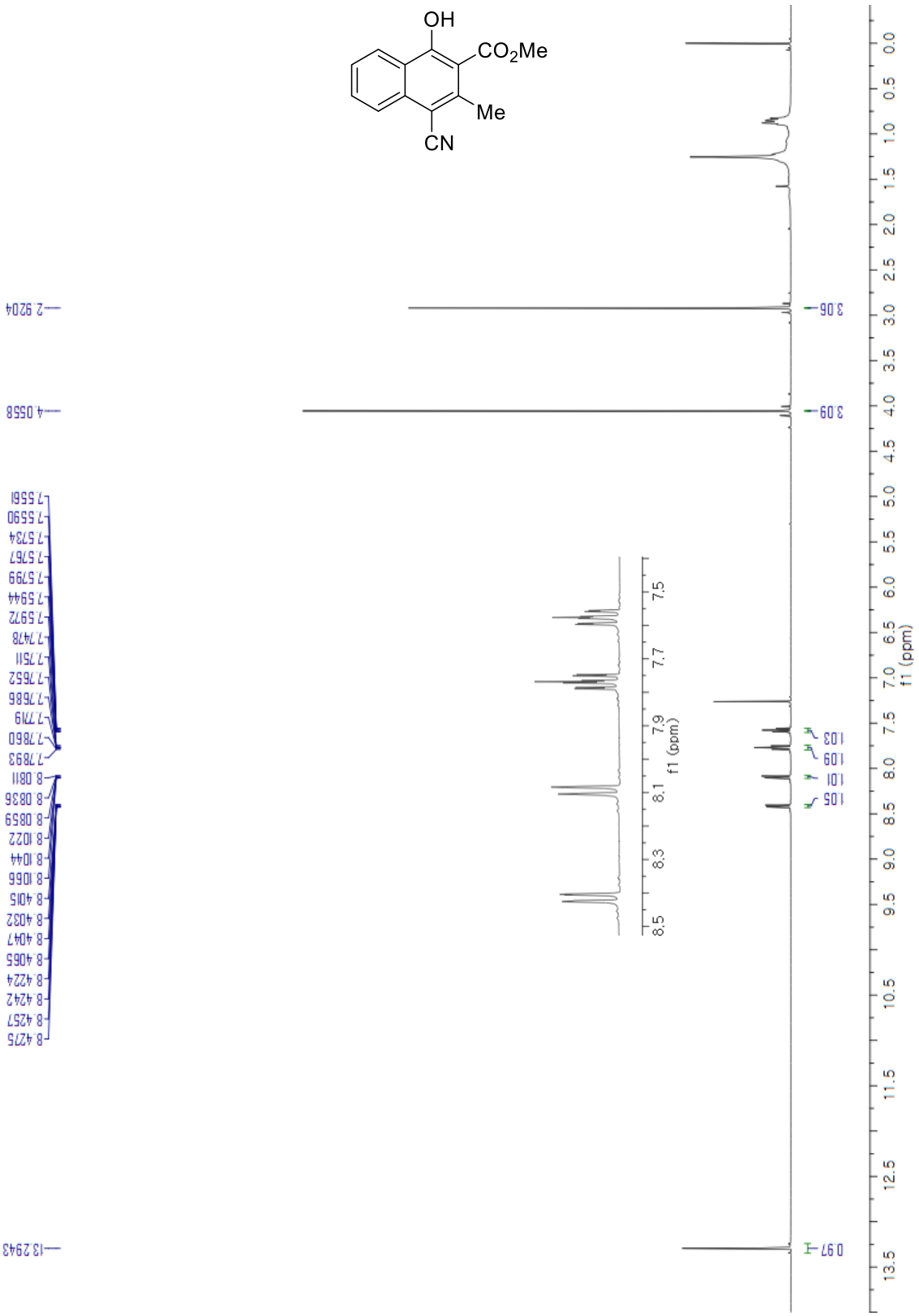
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **4i**



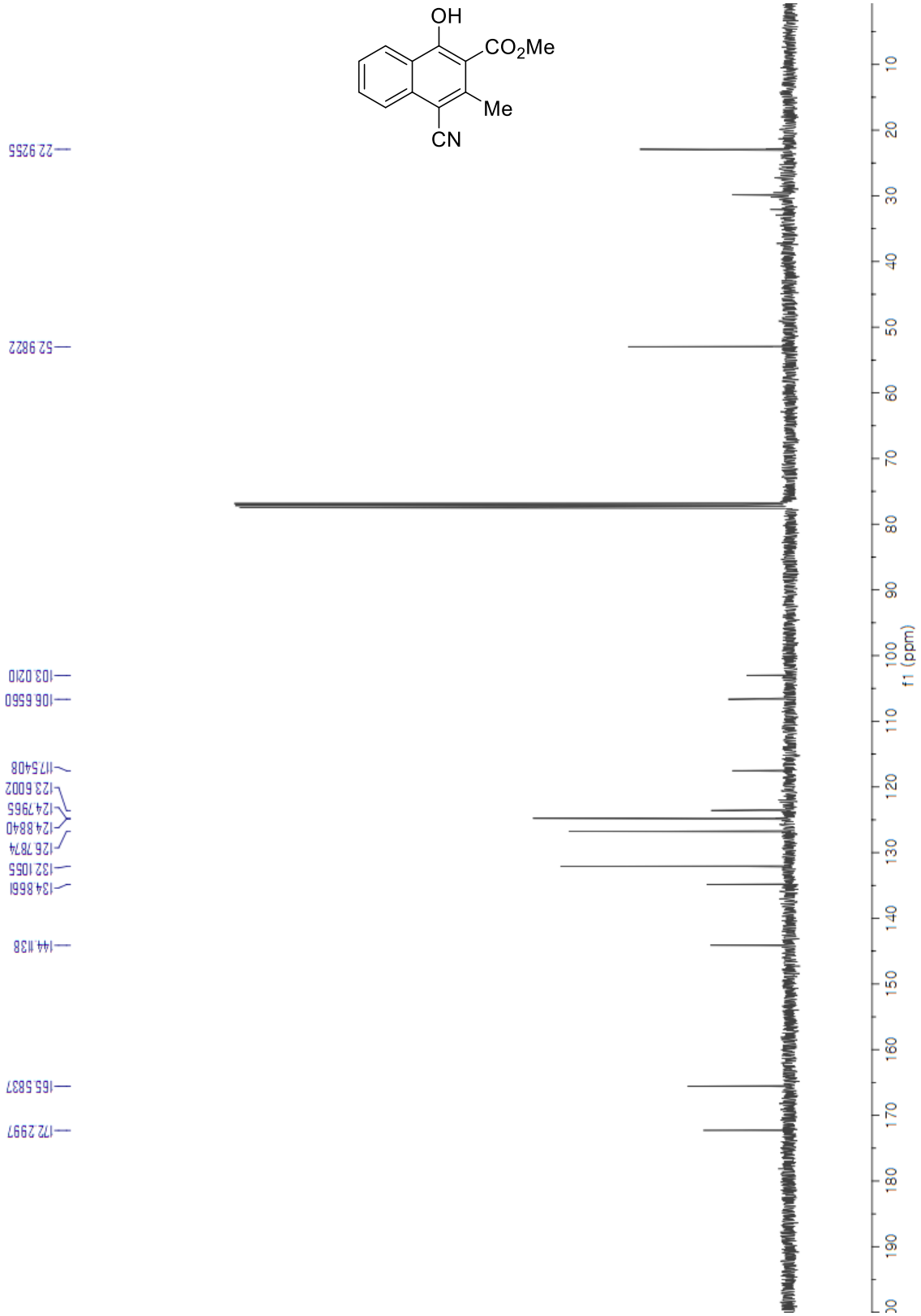
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4j**



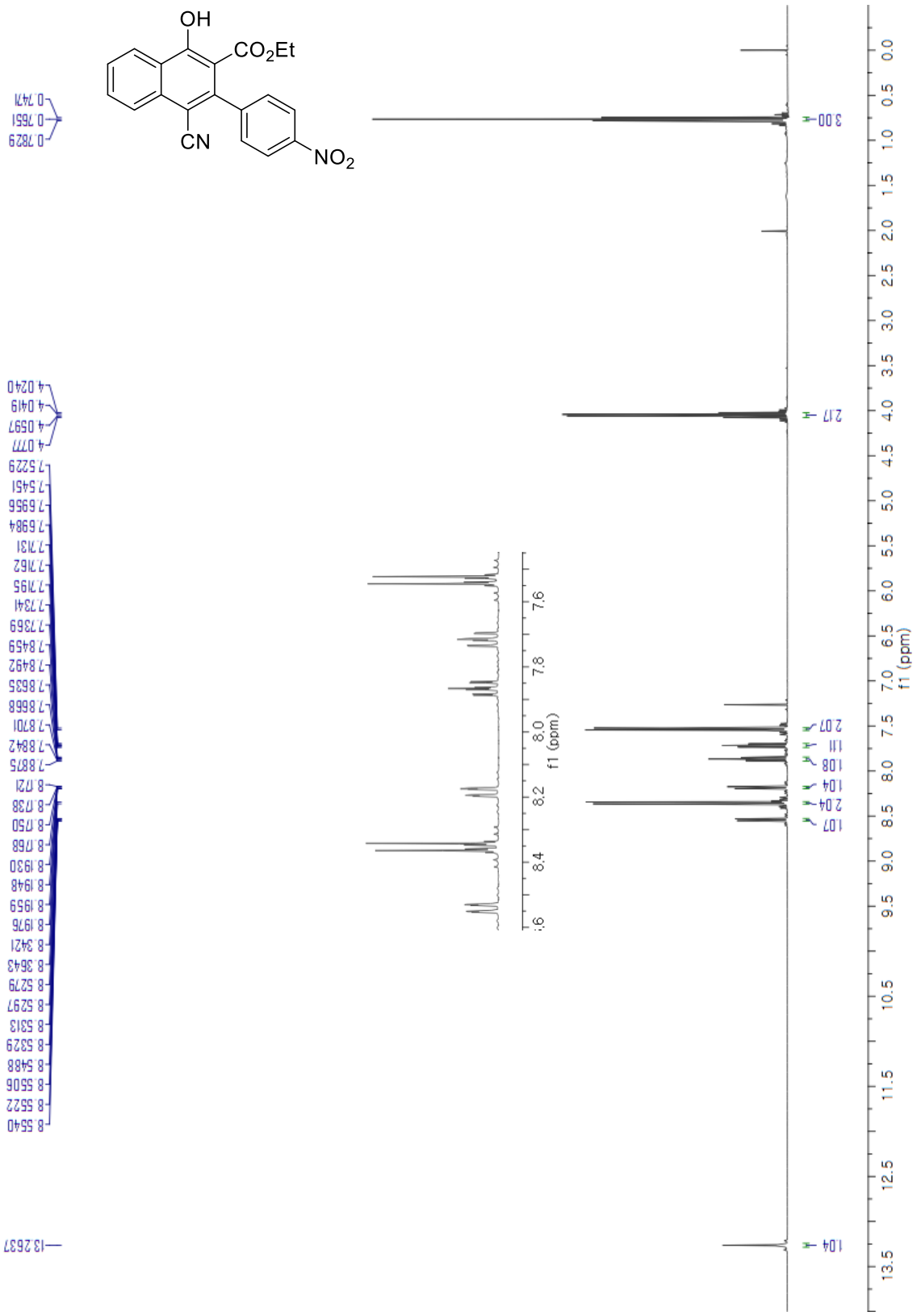
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **4j**



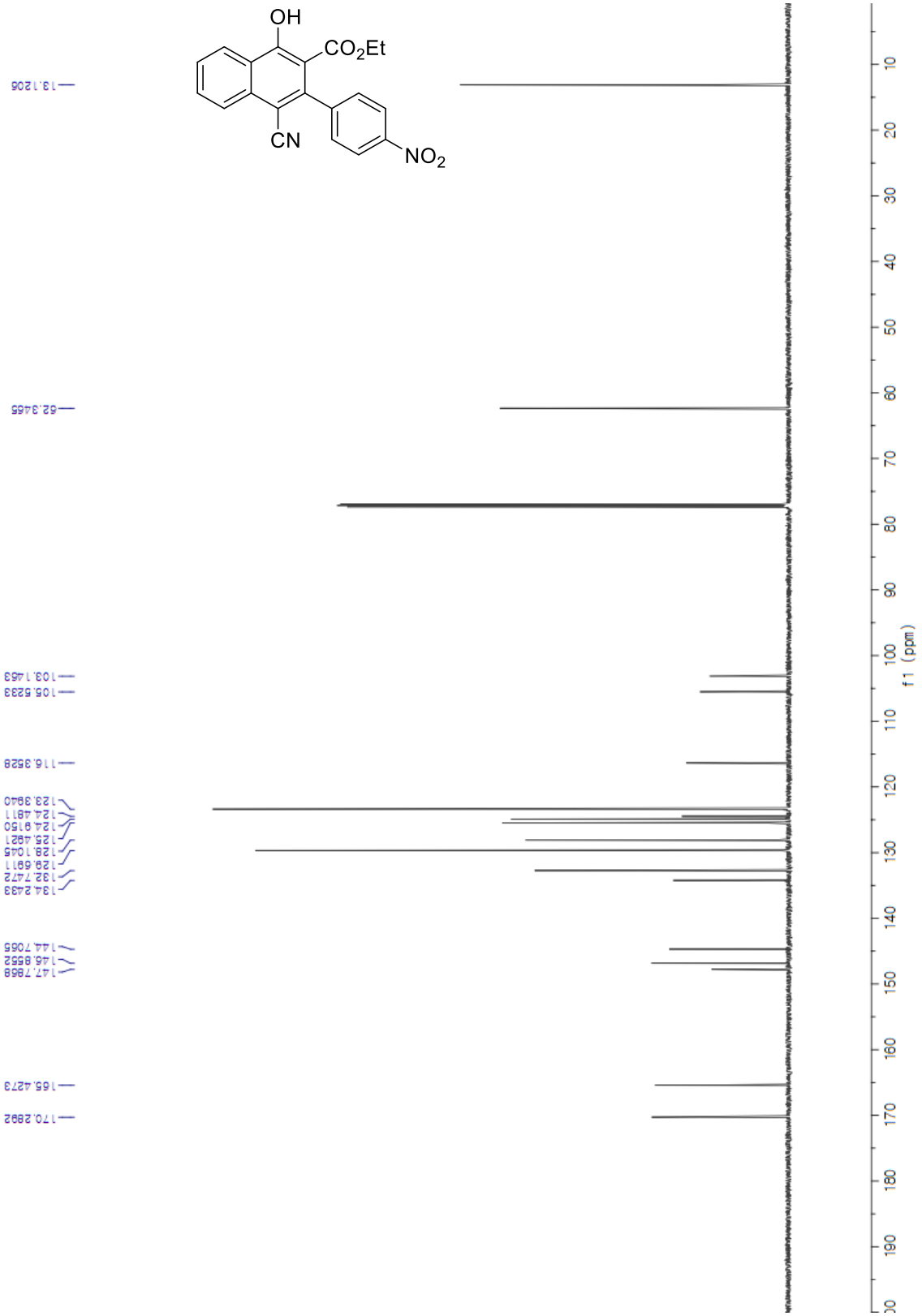
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **4k**



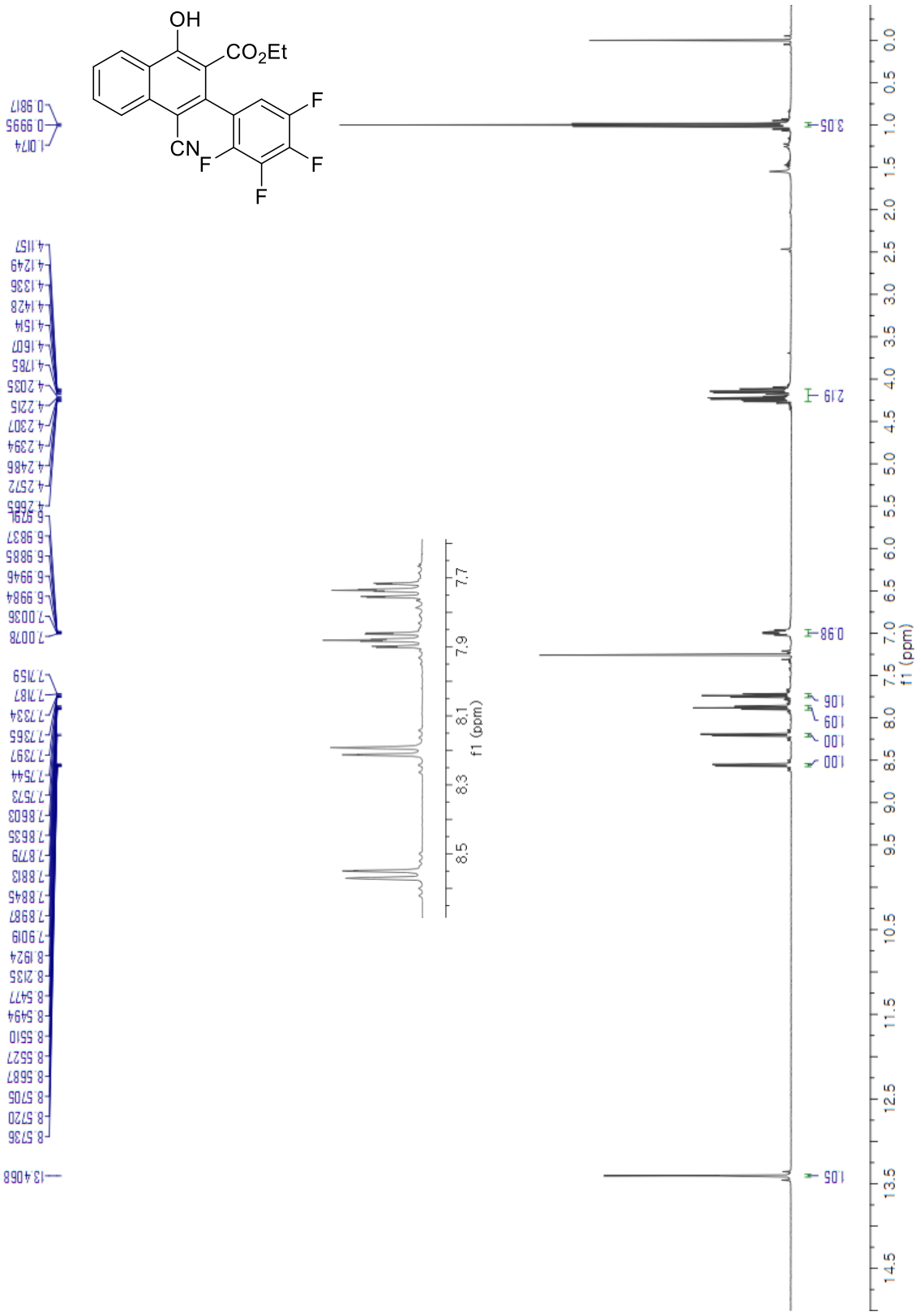
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **4k**



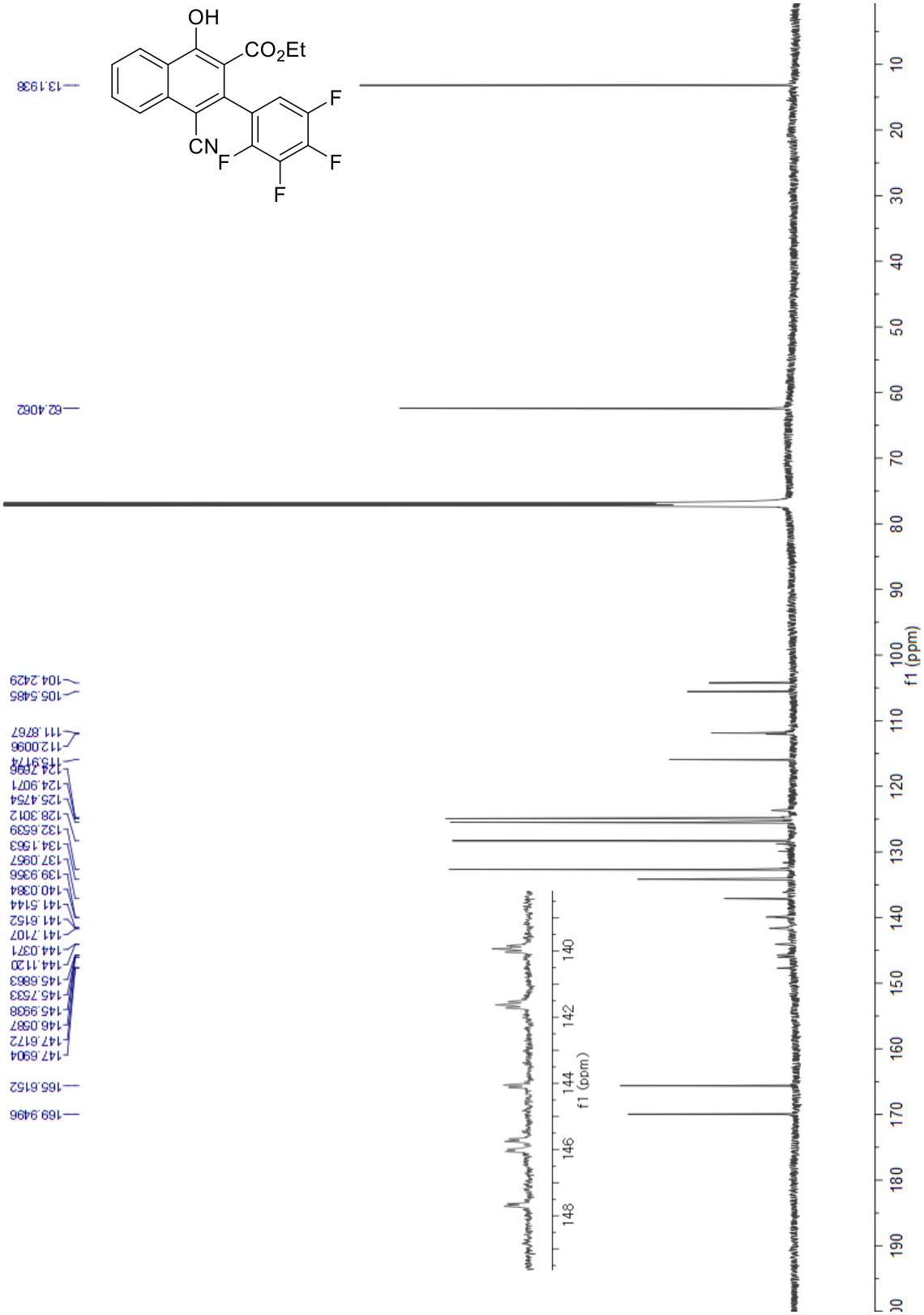
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **4l**



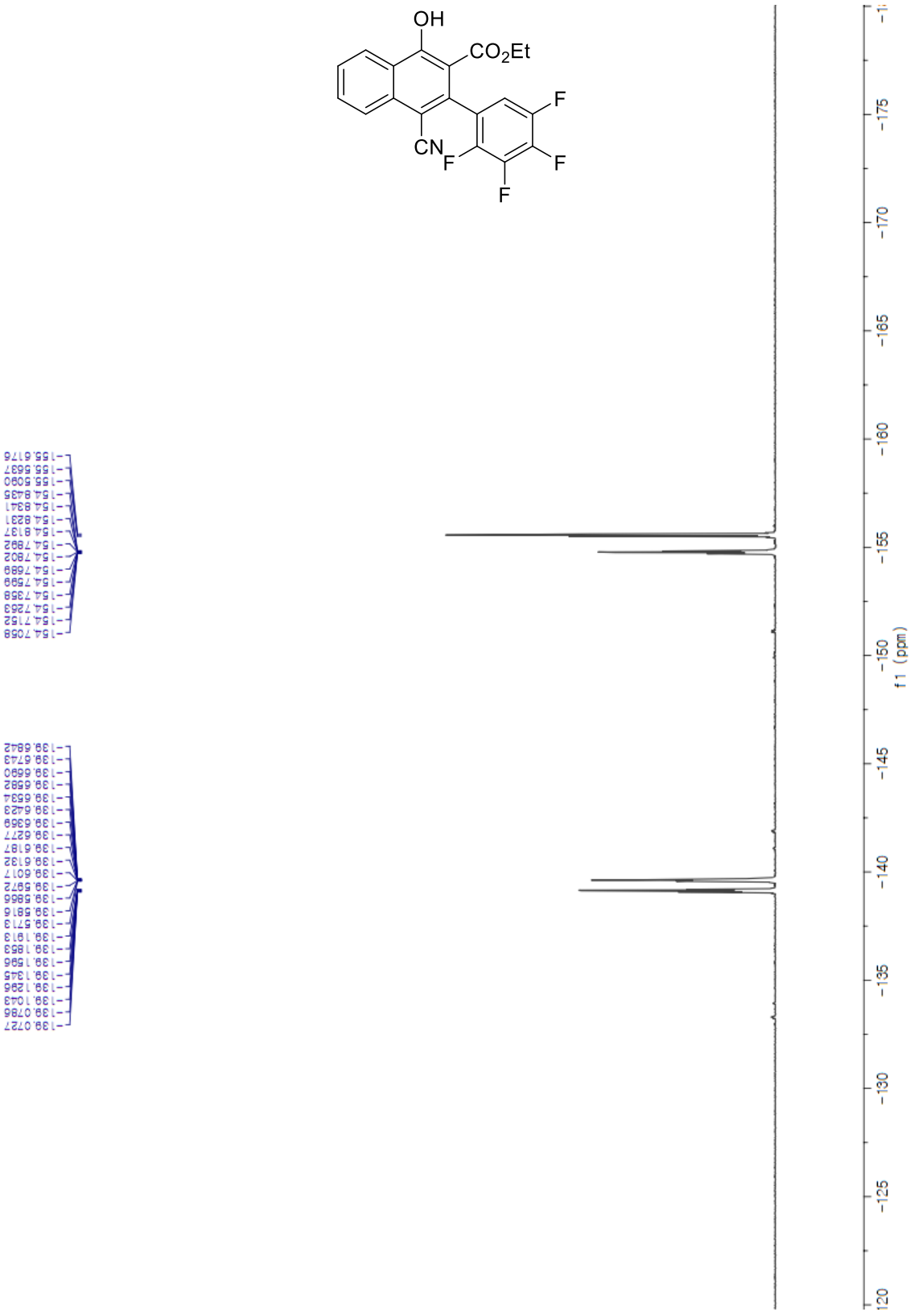
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **4l**



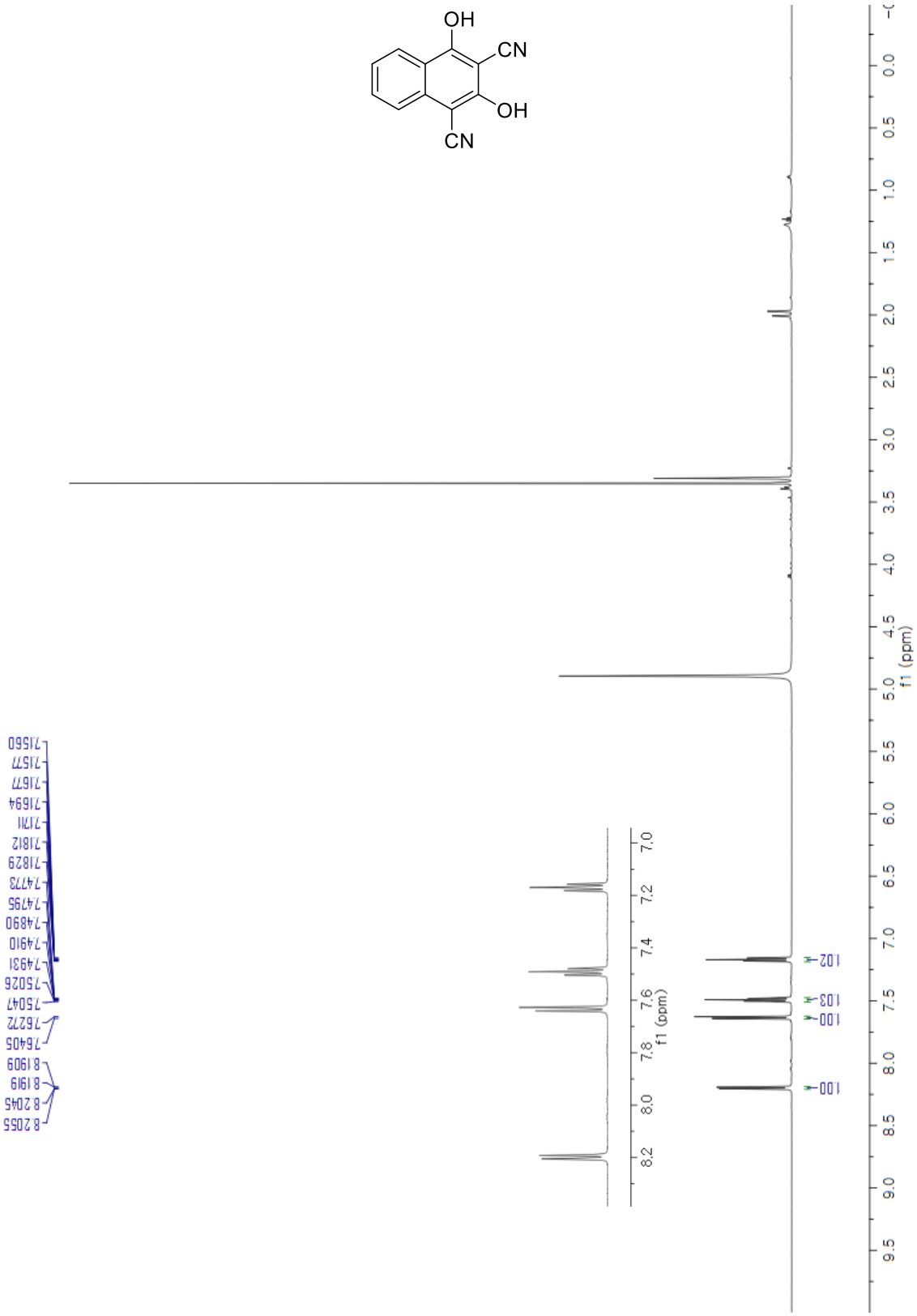
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **4m**



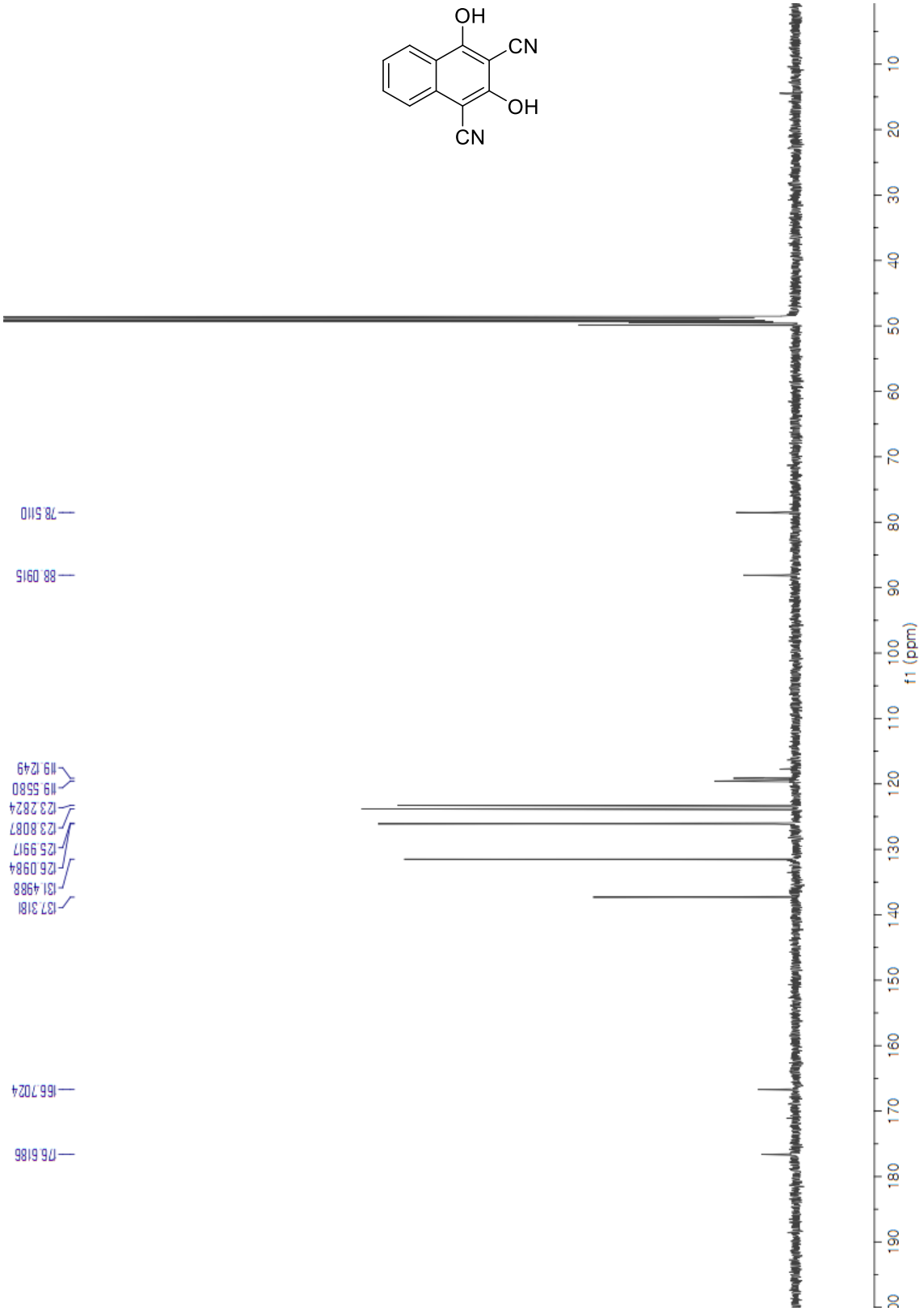
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **4m**



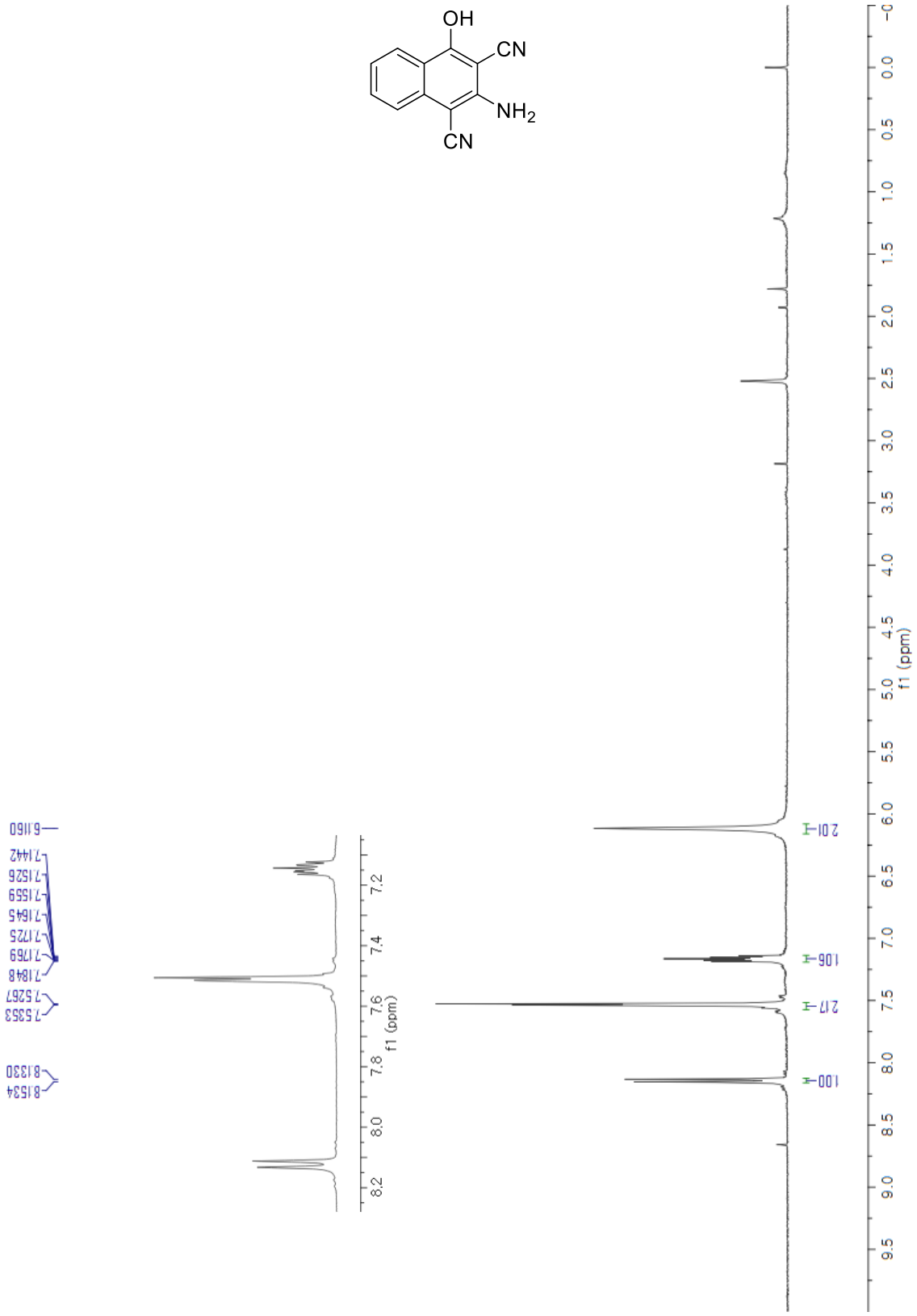
^{19}F NMR ($CDCl_3$, 376 MHz) of compound **4m**



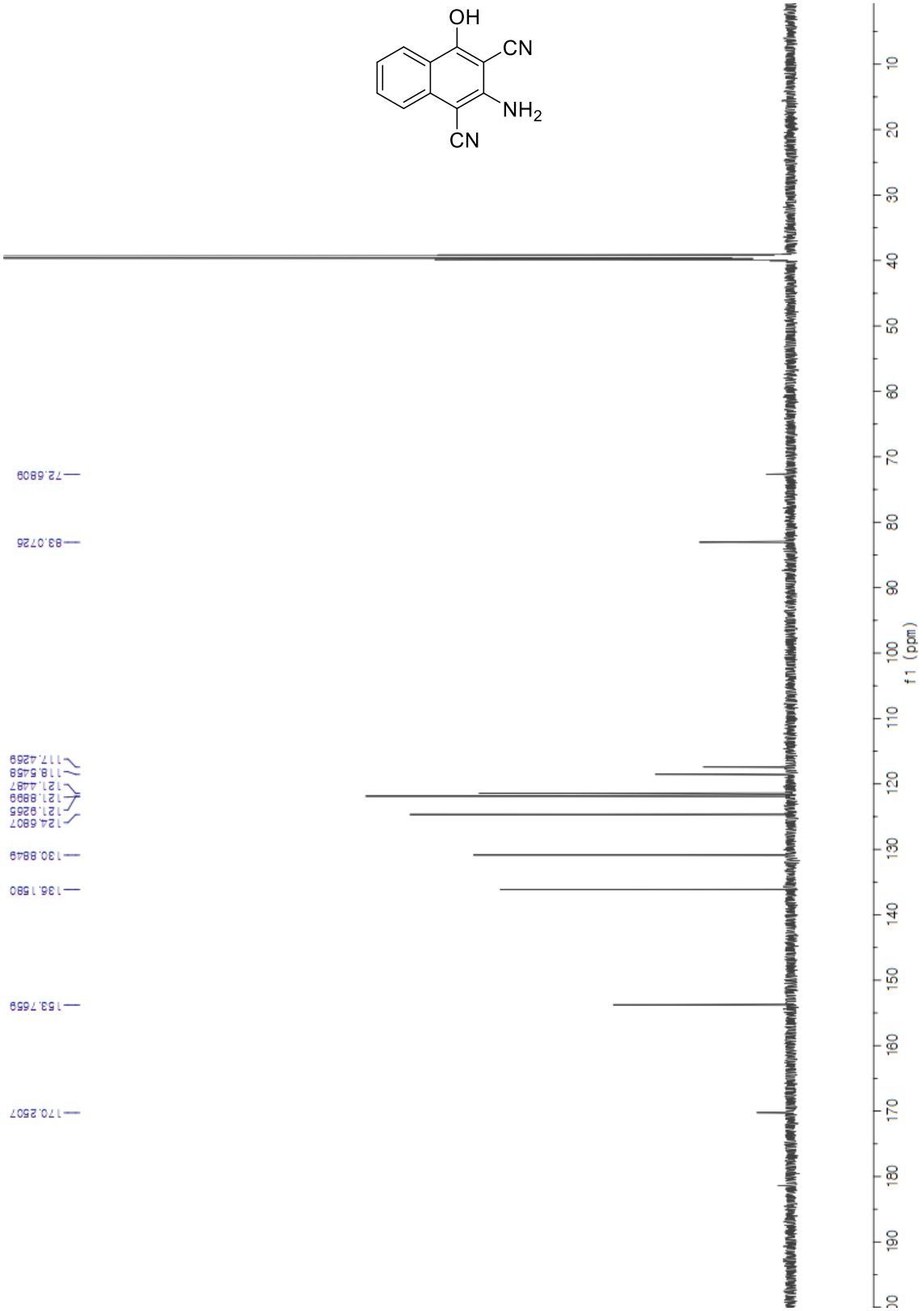
^{1}H NMR (CD_3OD, 600 MHz) of compound **4n**



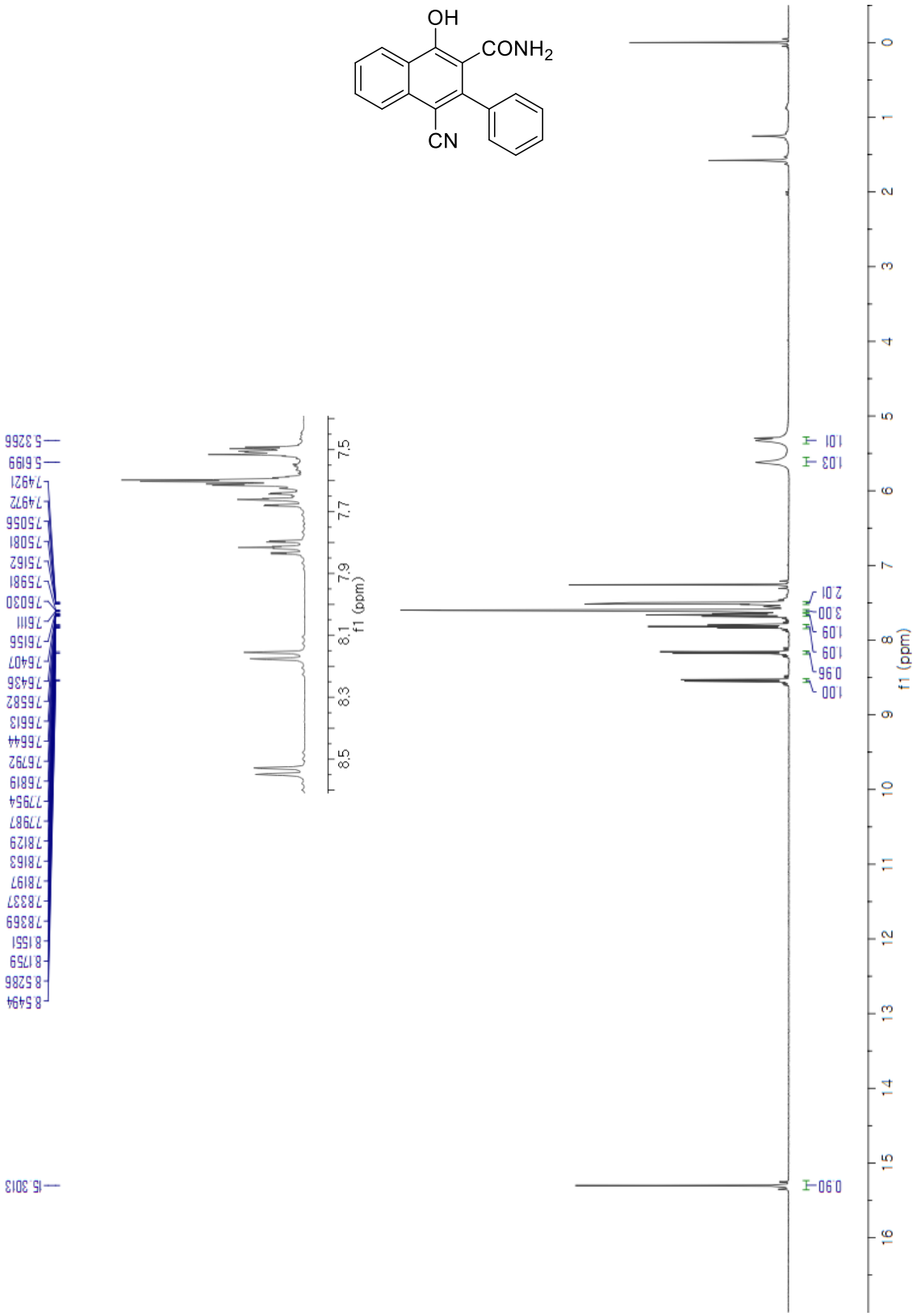
^{13}C NMR (CD_3OD, 150 MHz) of compound **4n**



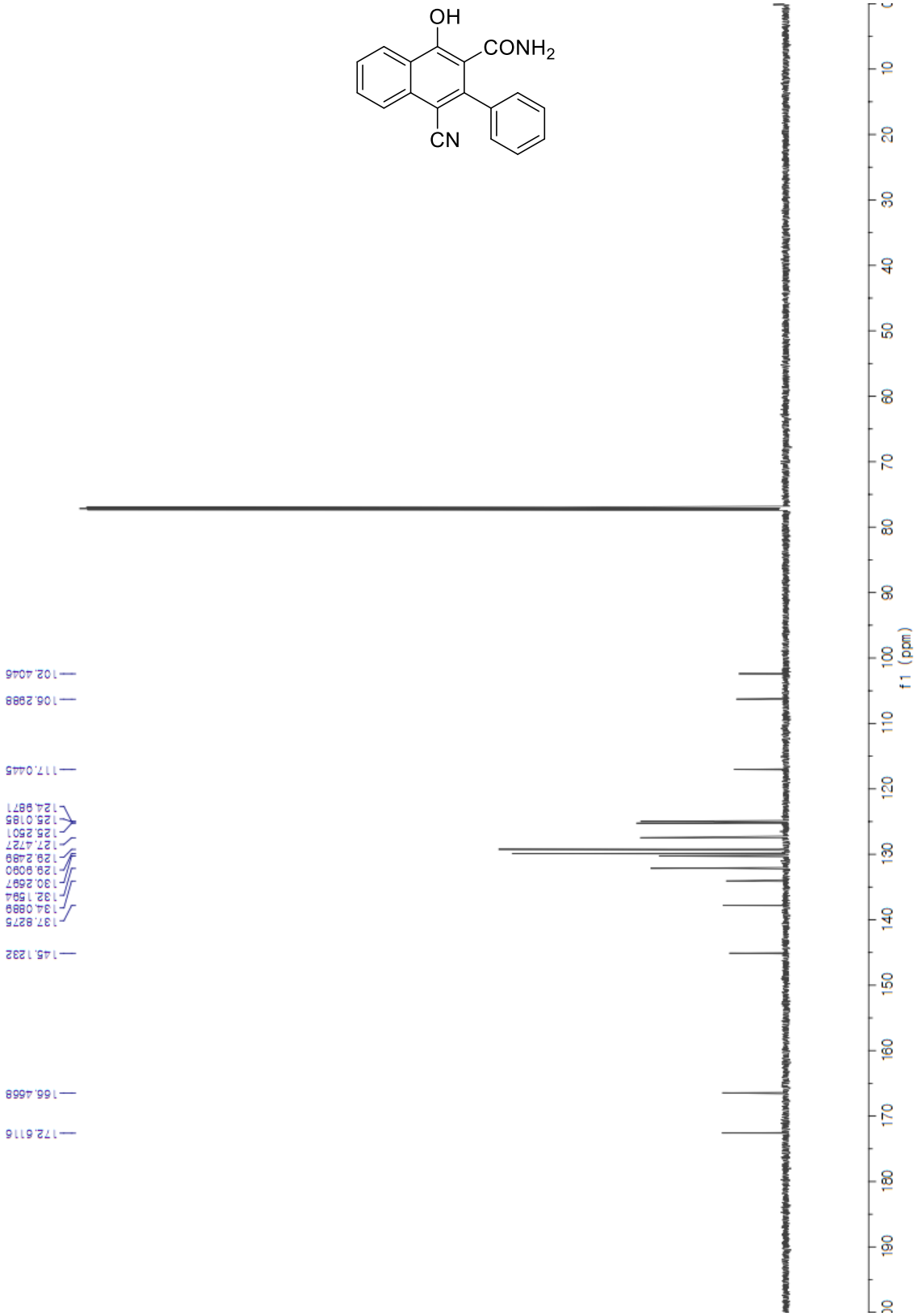
^{1}H NMR (DMSO-d_6, 400 MHz) of compound **4o**



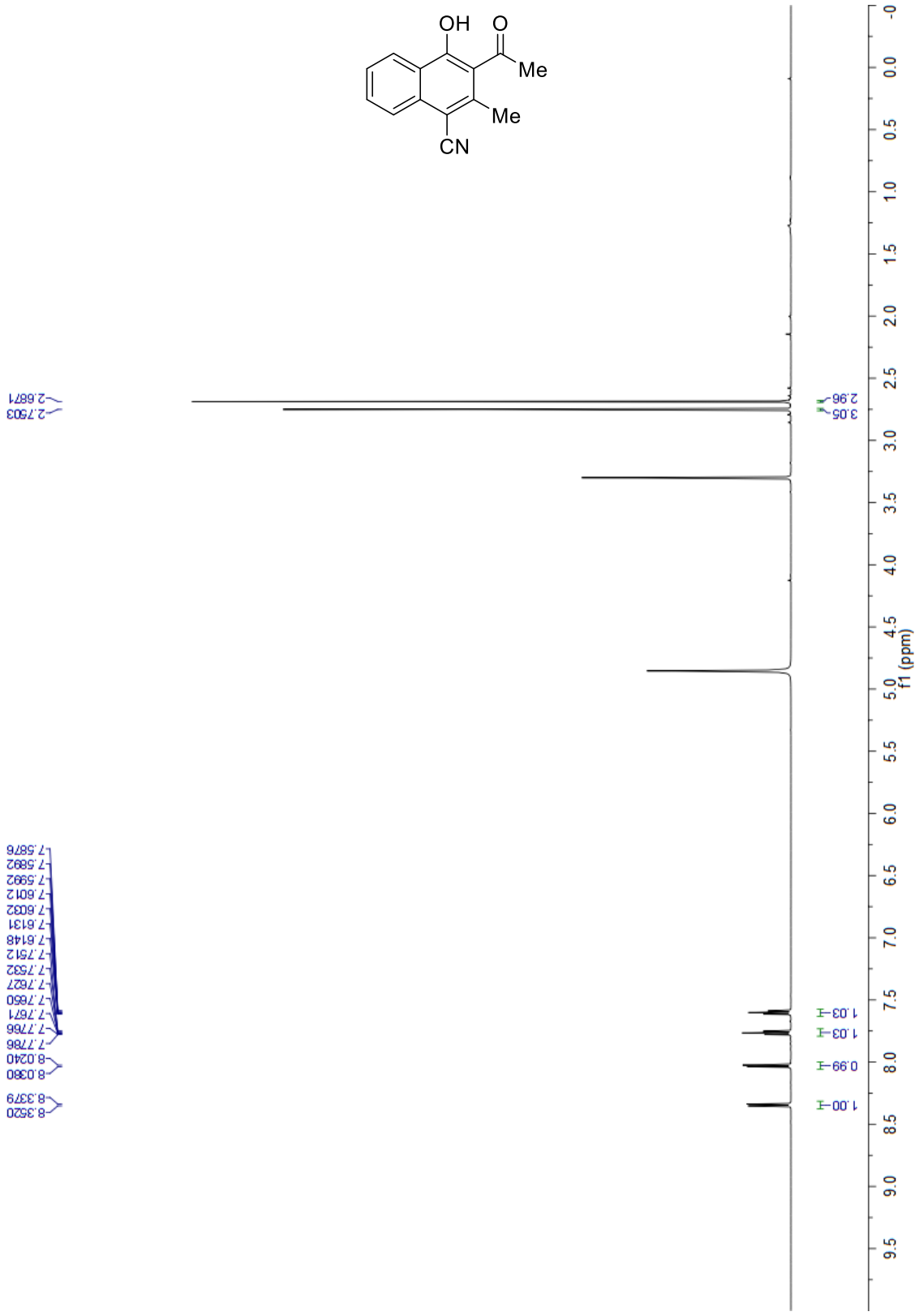
^{13}C NMR (DMSO-d_6, 100 MHz) of compound **4o**



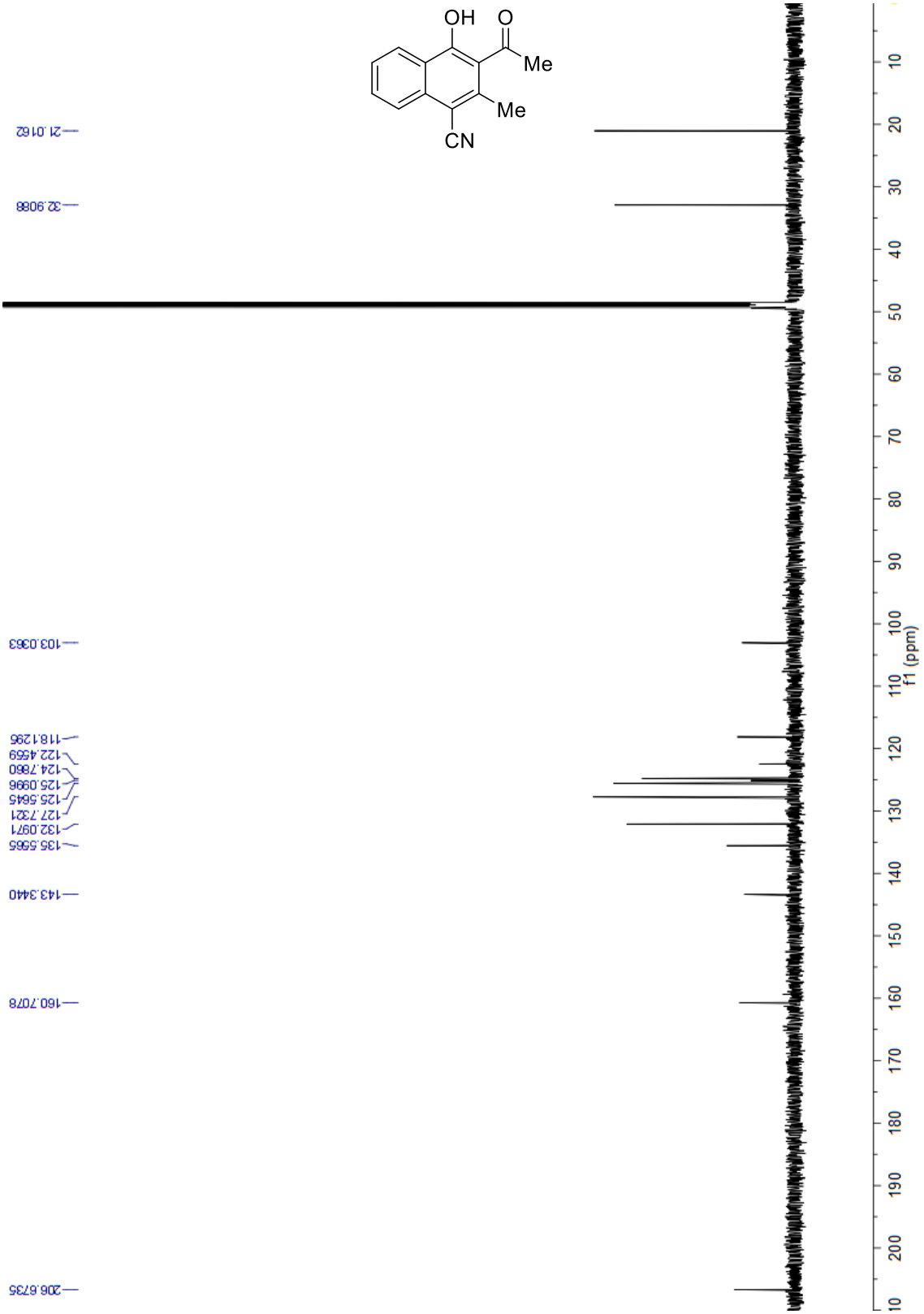
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **4p**



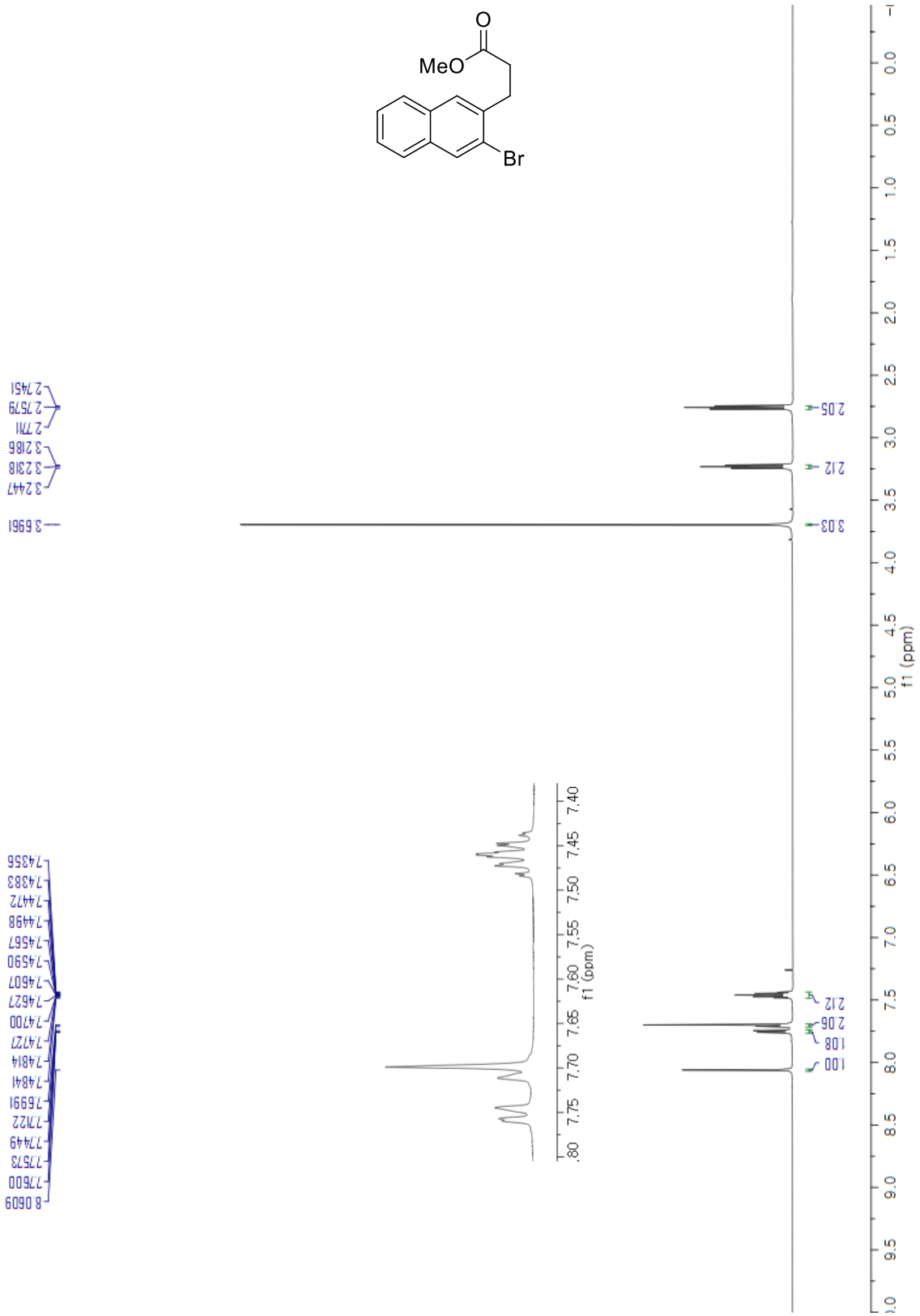
^{13}C NMR ($CDCl_3$, 100 MHz) of compound **4p**



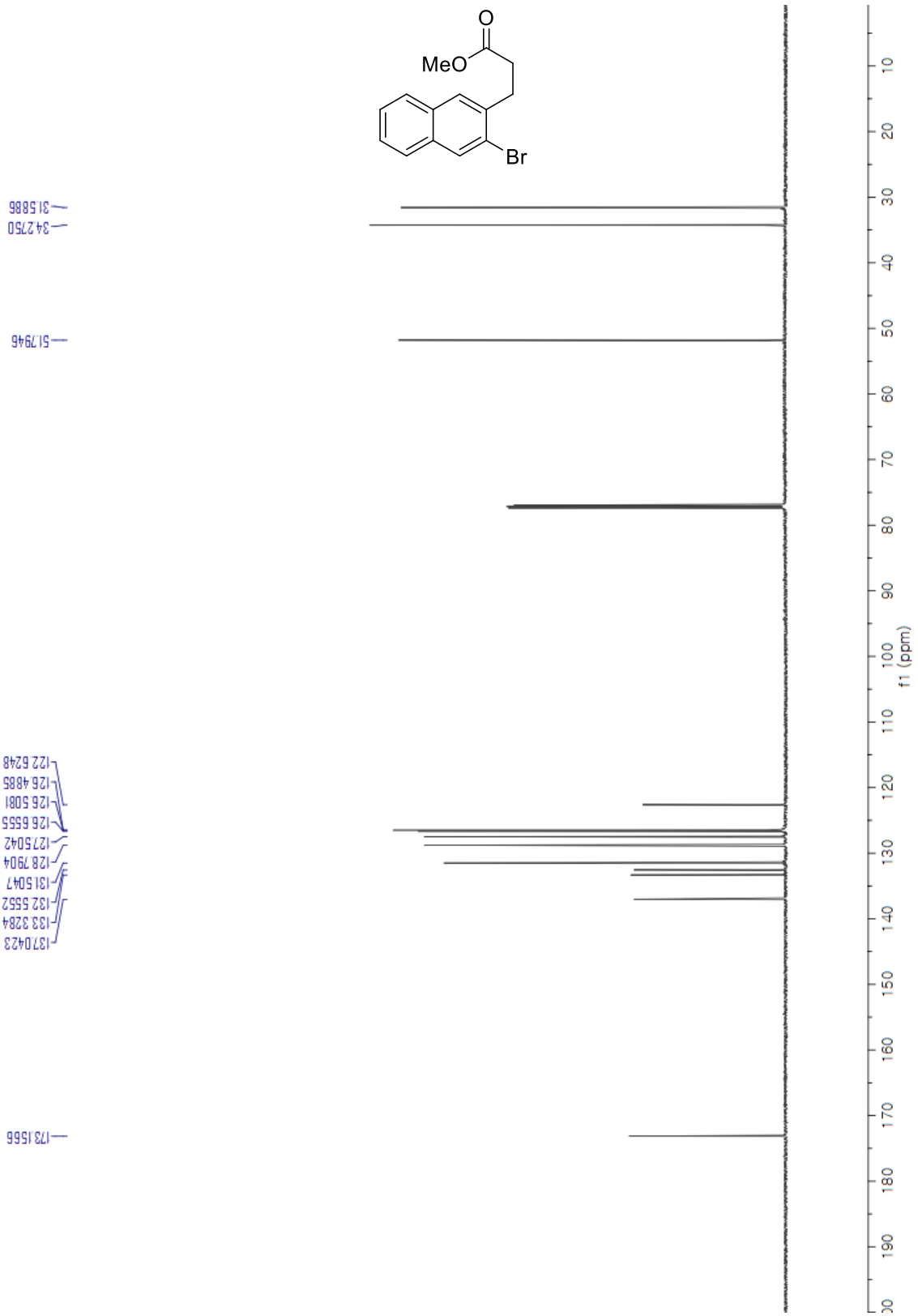
^{1}H NMR (MeOD, 600 MHz) of compound **4q**



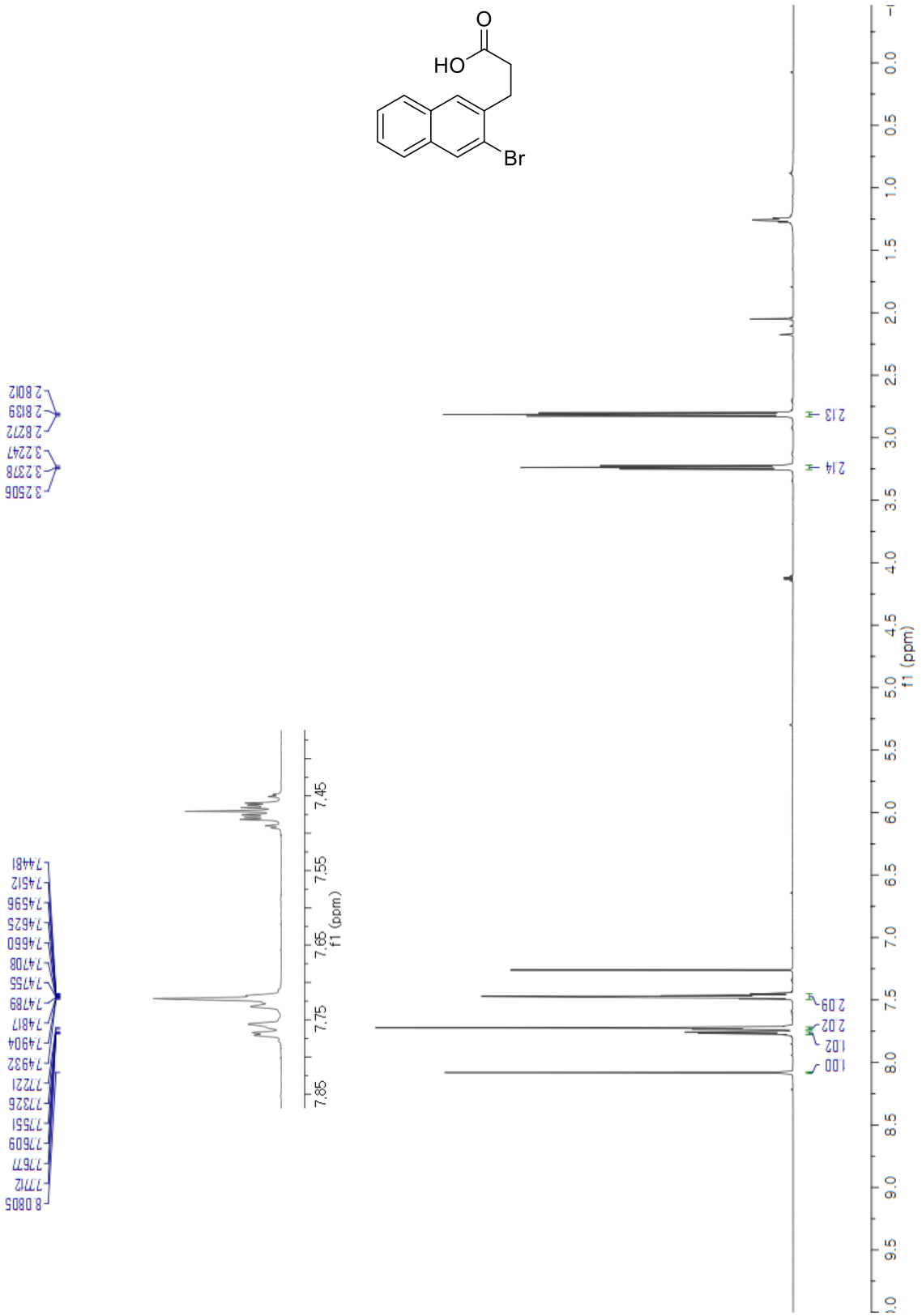
^{13}C NMR (MeOD, 150 MHz) of compound **4q**



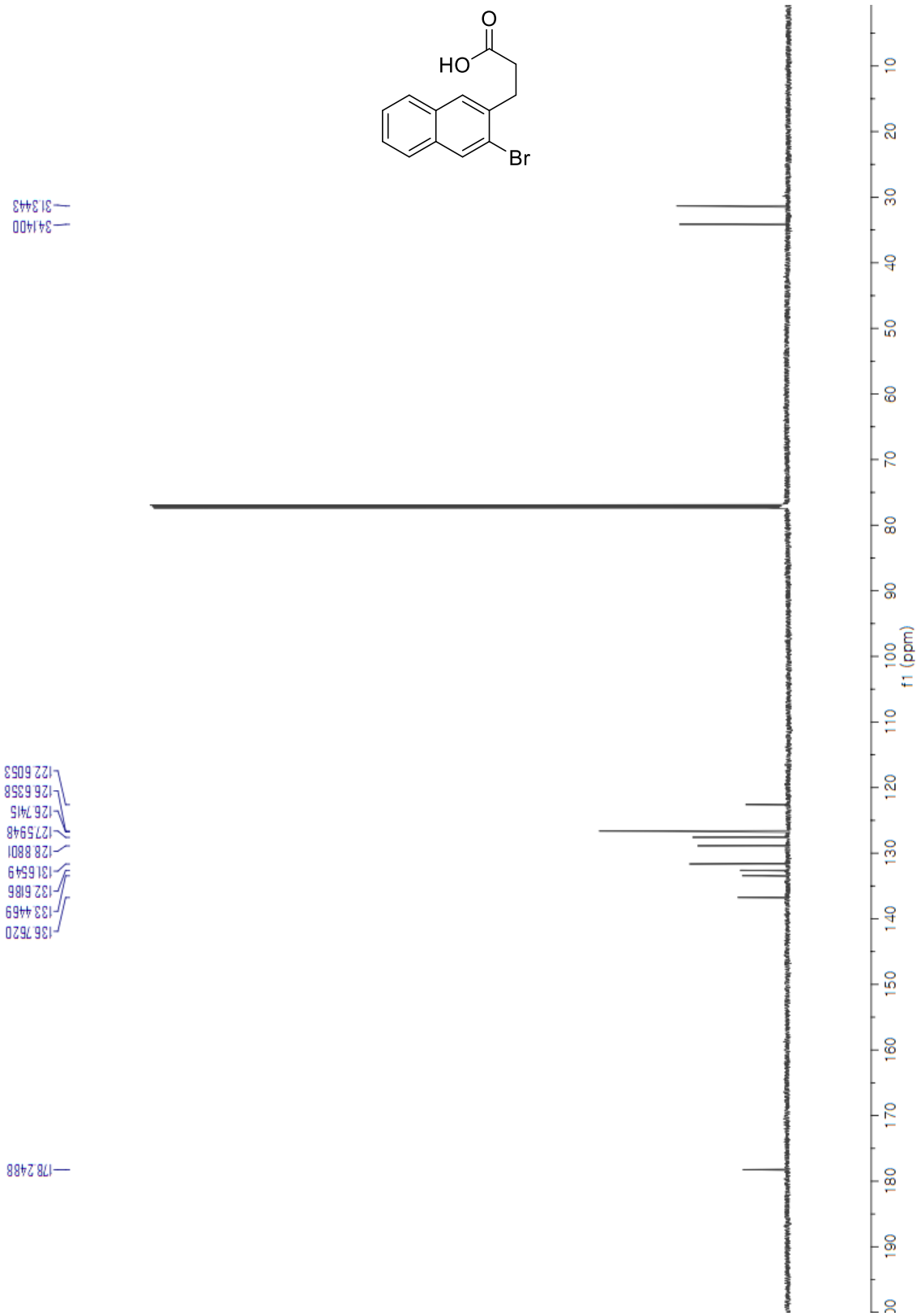
^{1}H NMR ($CDCl_3$, 600 MHz) of compound **9**



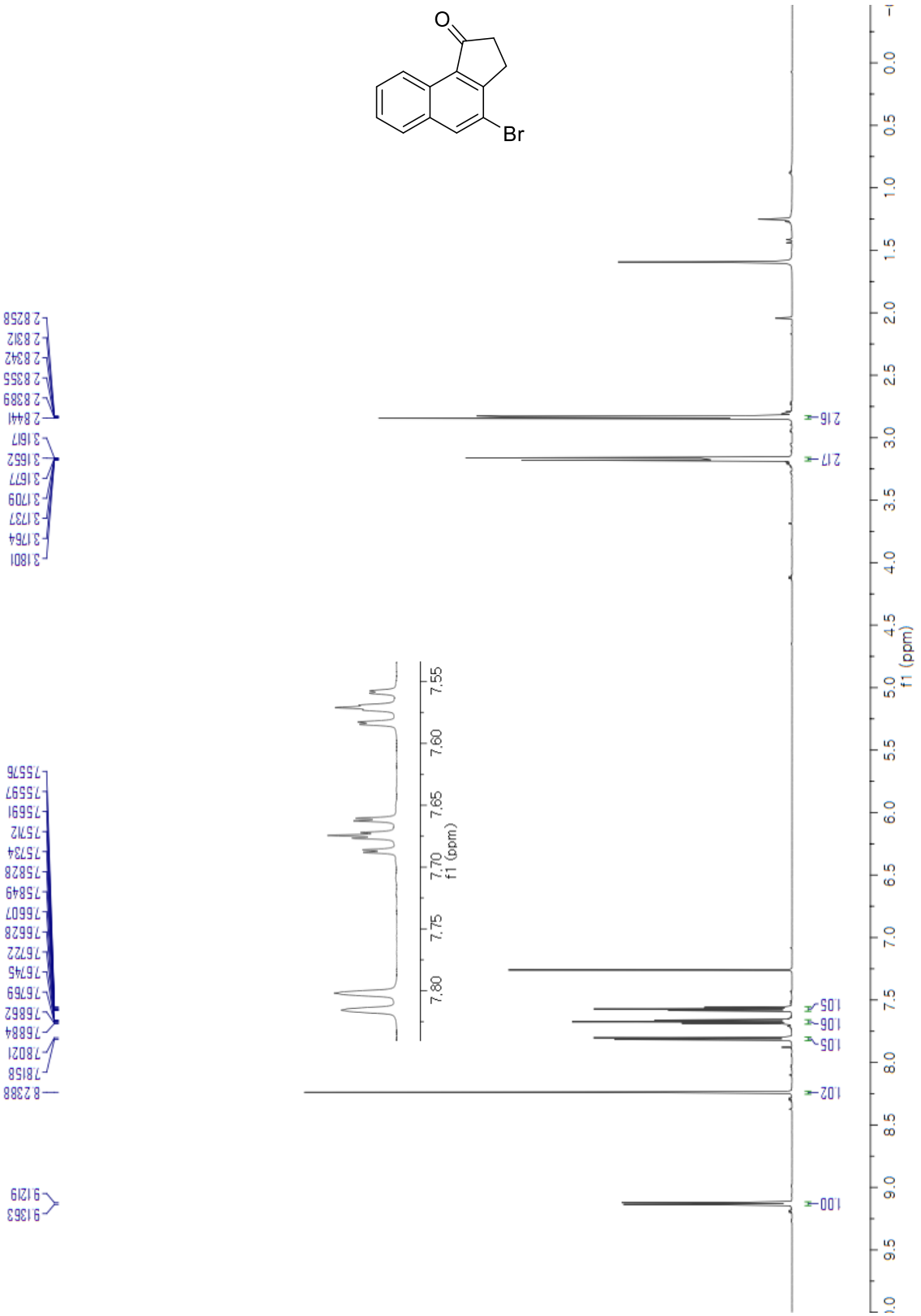
^{13}C NMR ($CDCl_3$, 150 MHz) of compound **9**



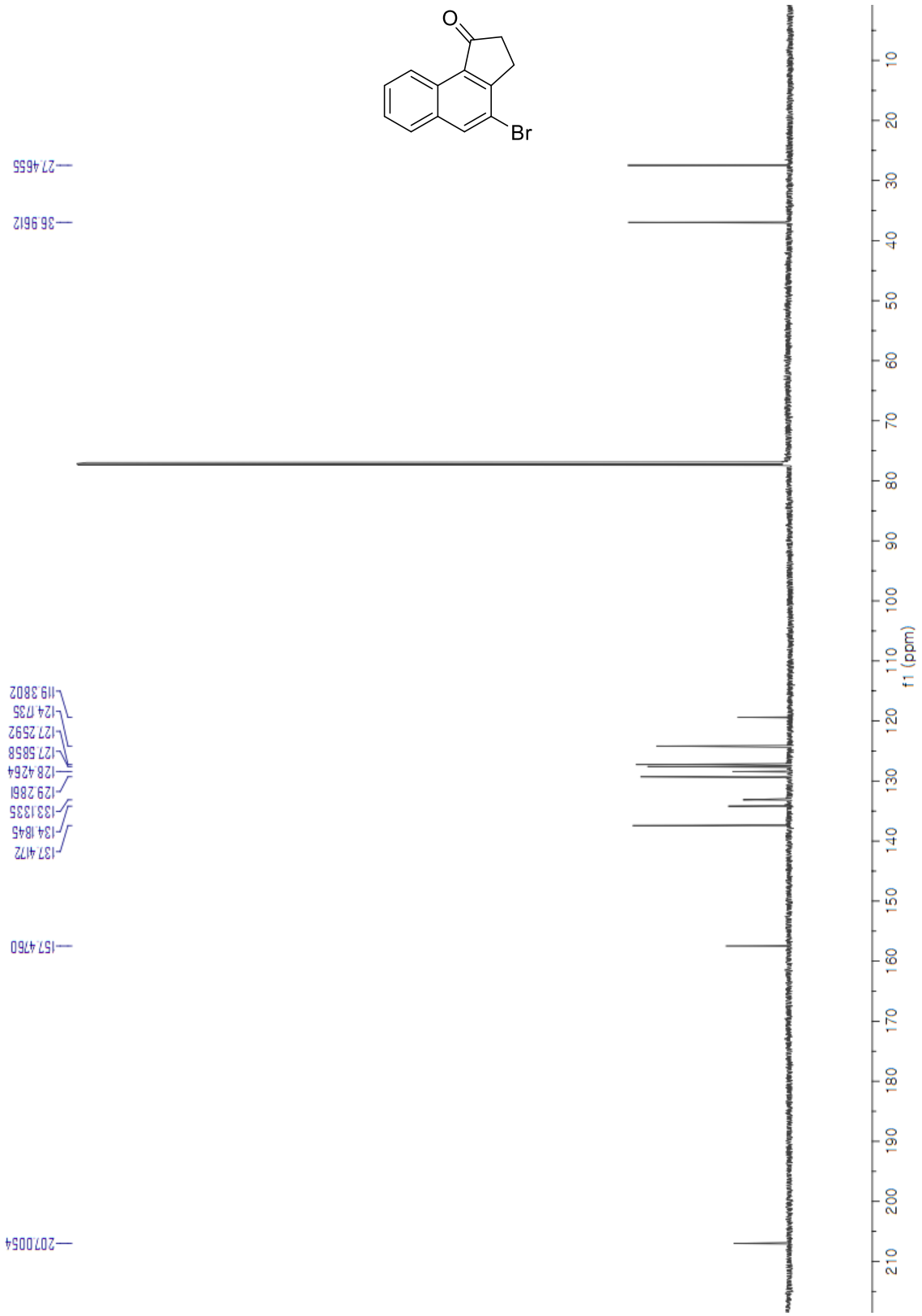
^{1}H NMR ($CDCl_3$, 600 MHz) of compound **10**



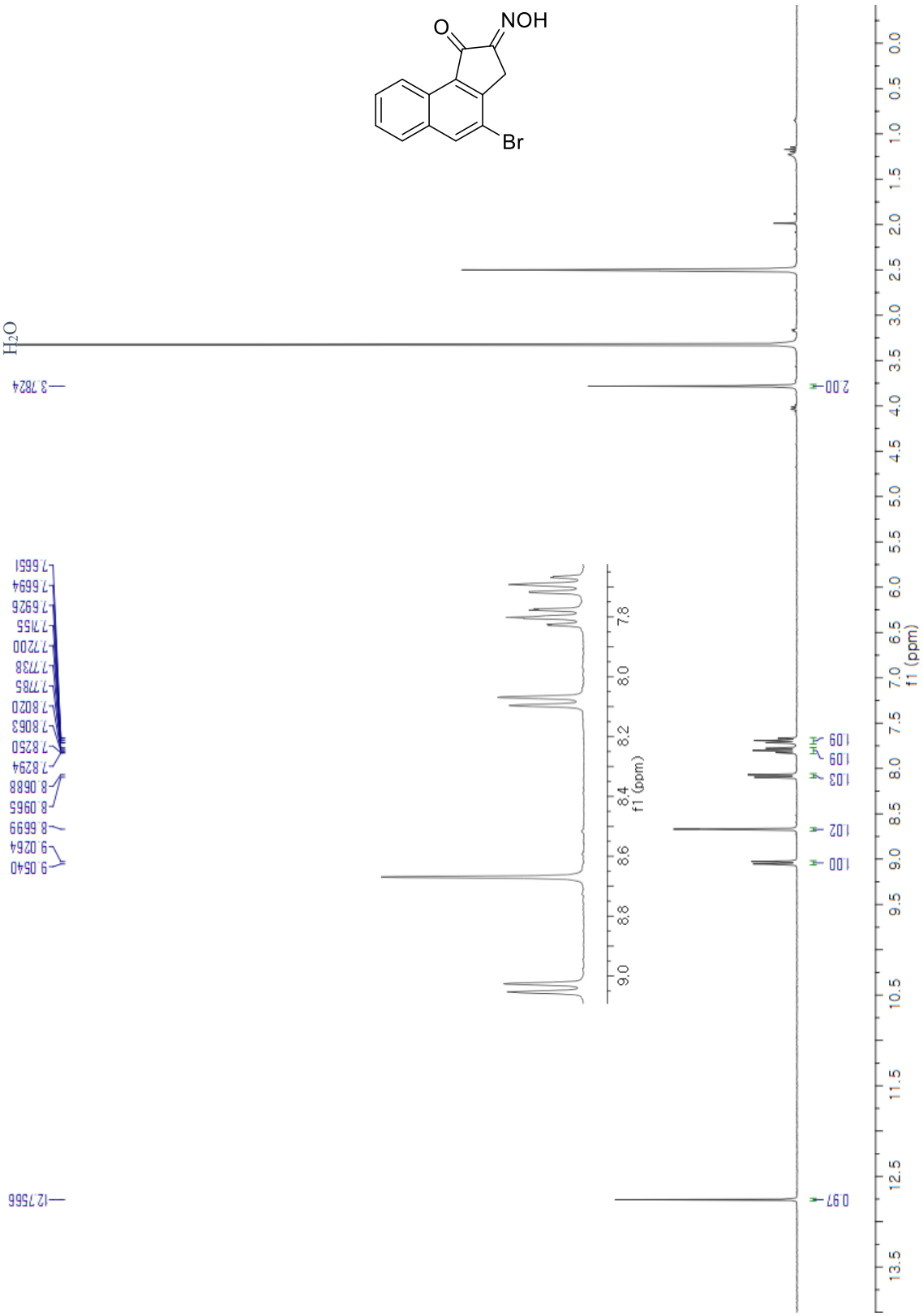
^{13}C NMR ($CDCl_3$, 150 MHz) of compound **10**



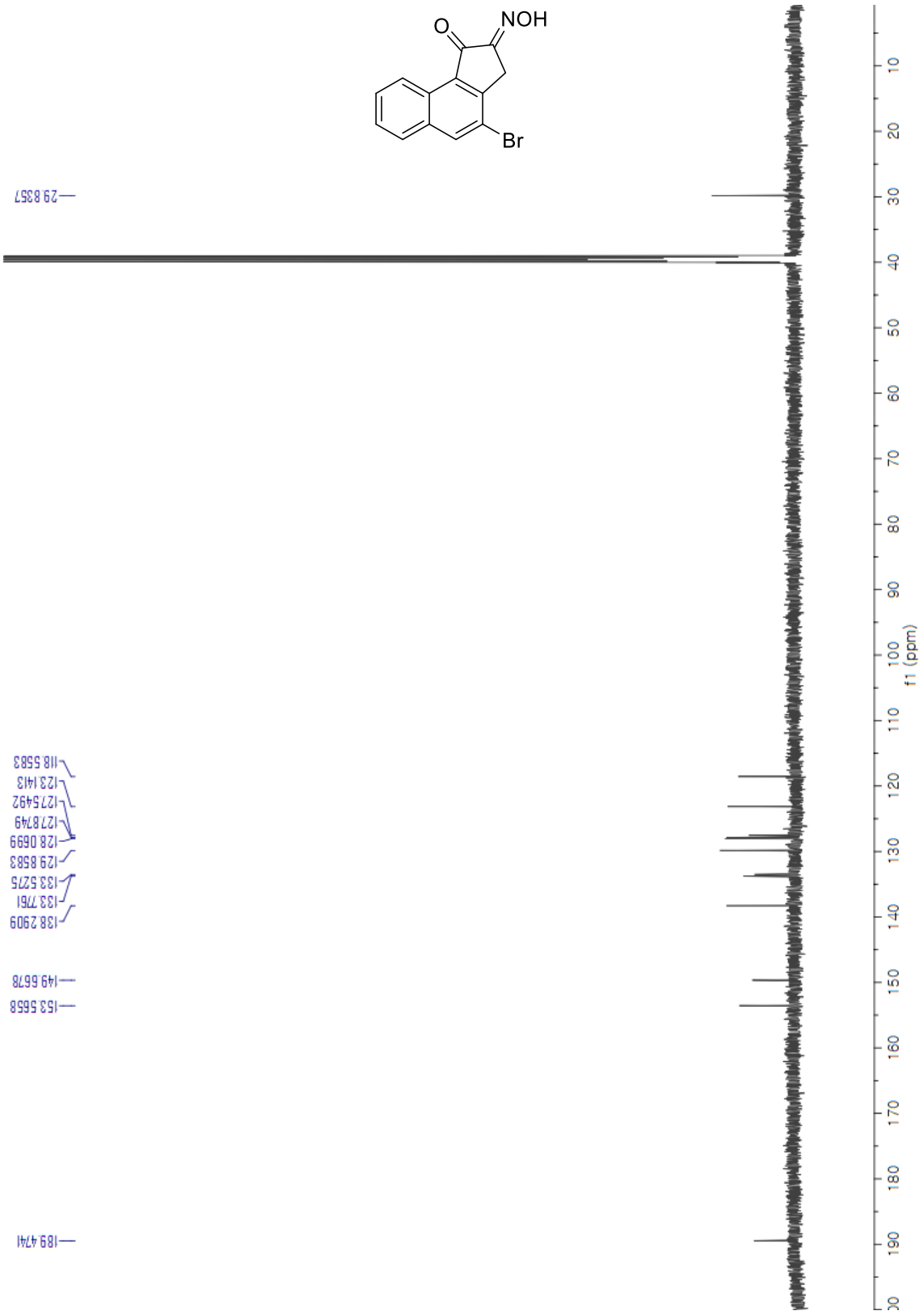
^{1}H NMR ($CDCl_3$, 600 MHz) of compound **11**



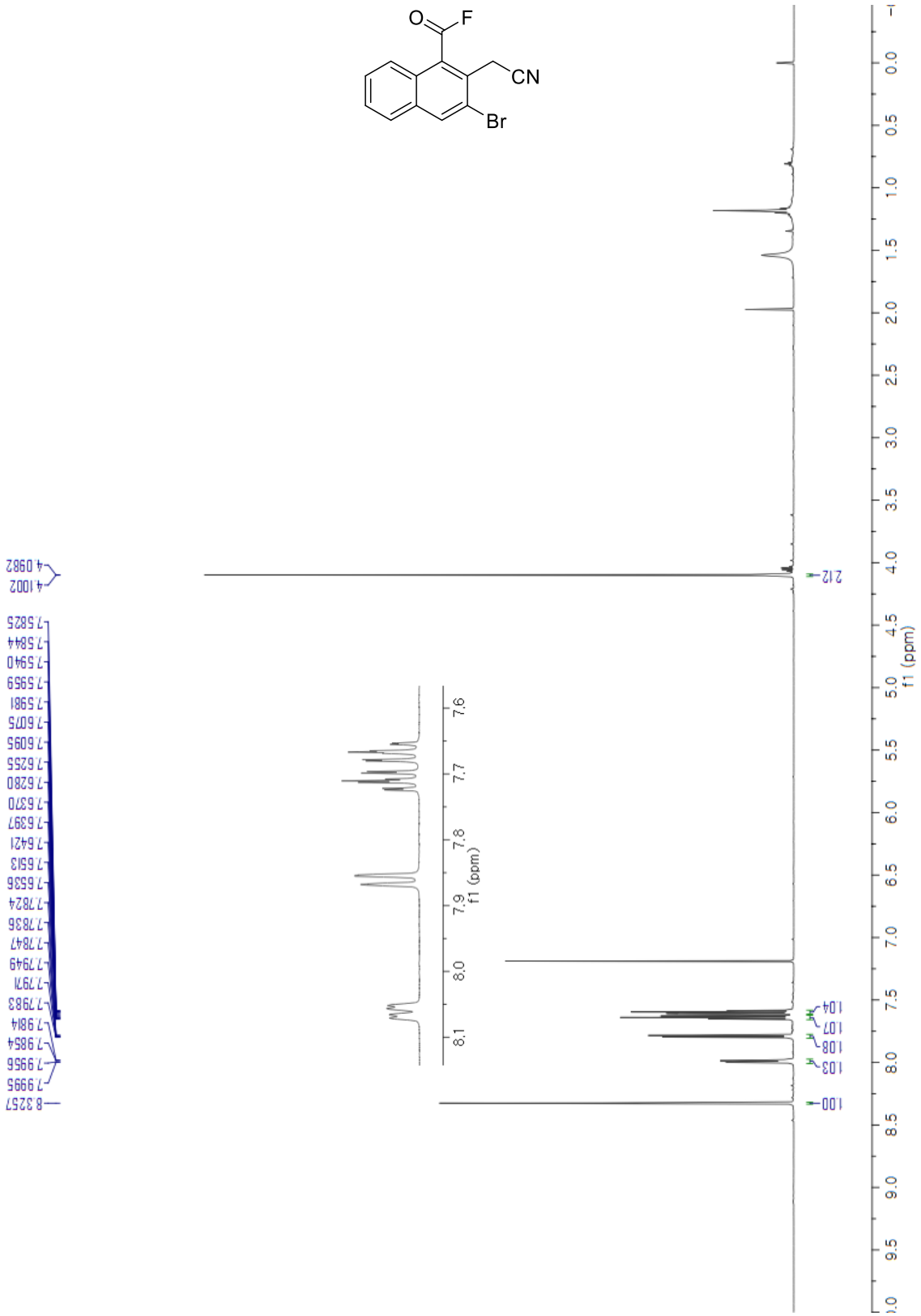
^{13}C NMR ($CDCl_3$, 150 MHz) of compound **11**



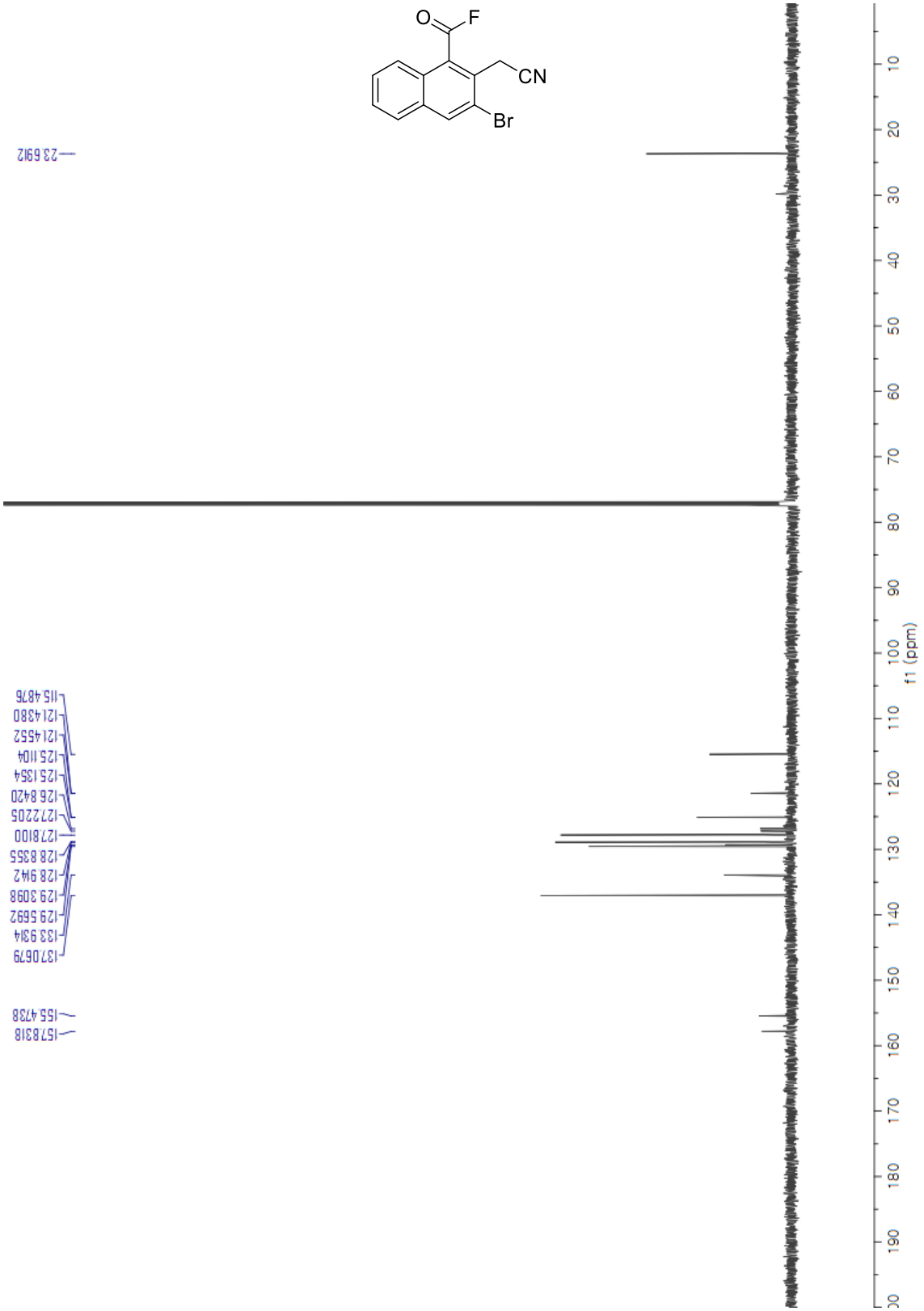
^{1}H NMR (DMSO-d_6, 300 MHz) of compound **12**



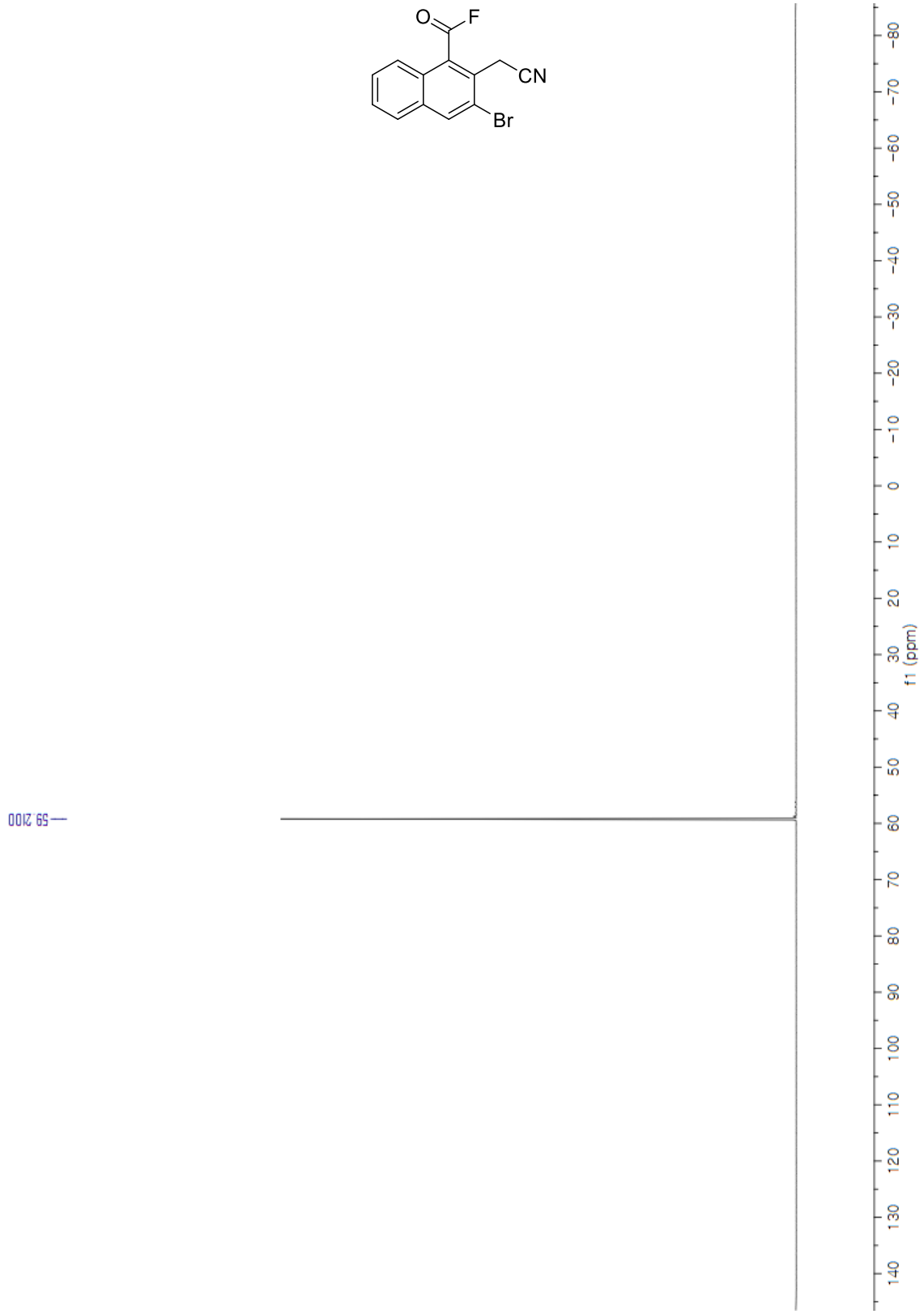
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **12**



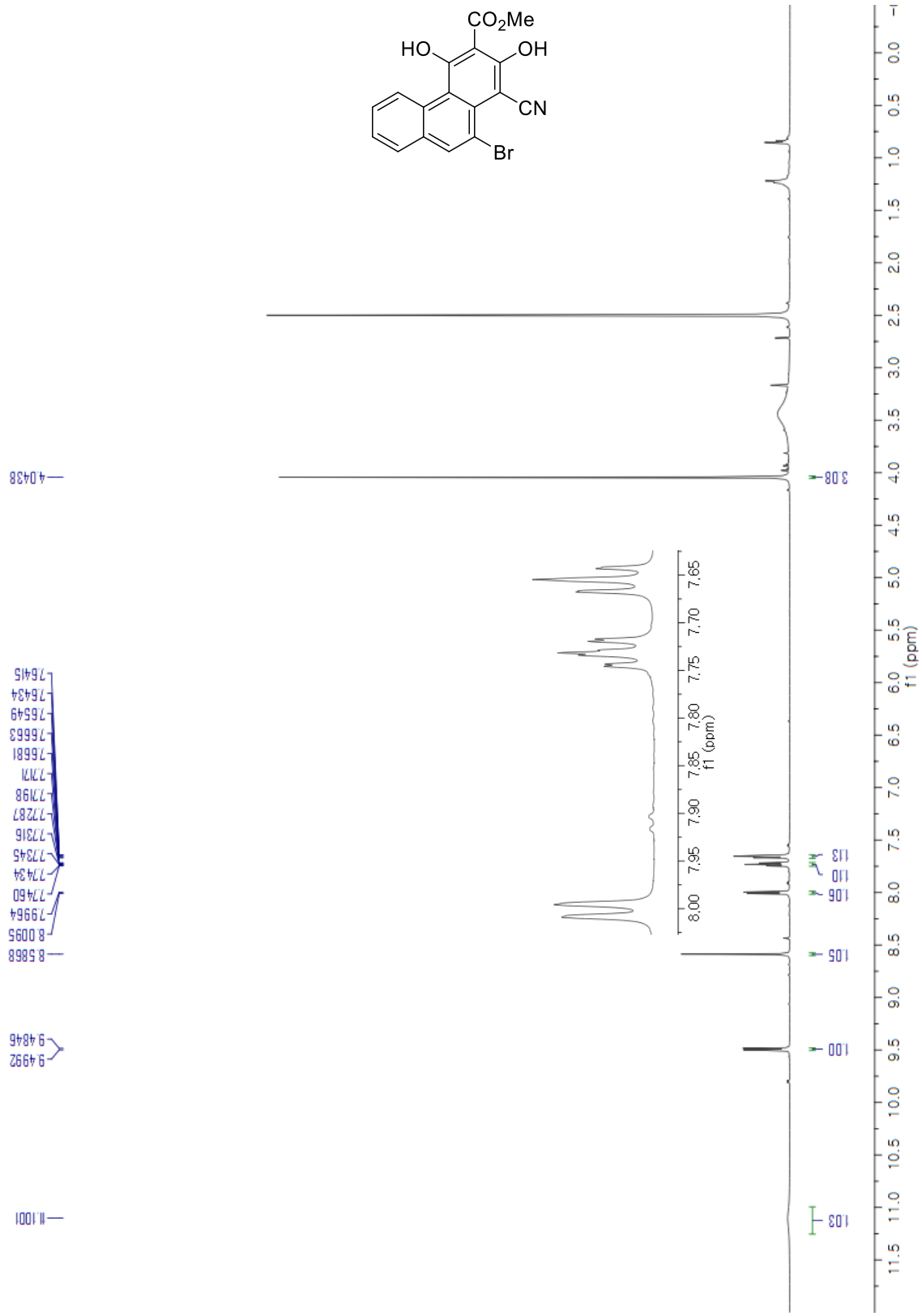
^{1}H NMR ($CDCl_3$, 600 MHz) of compound **7**



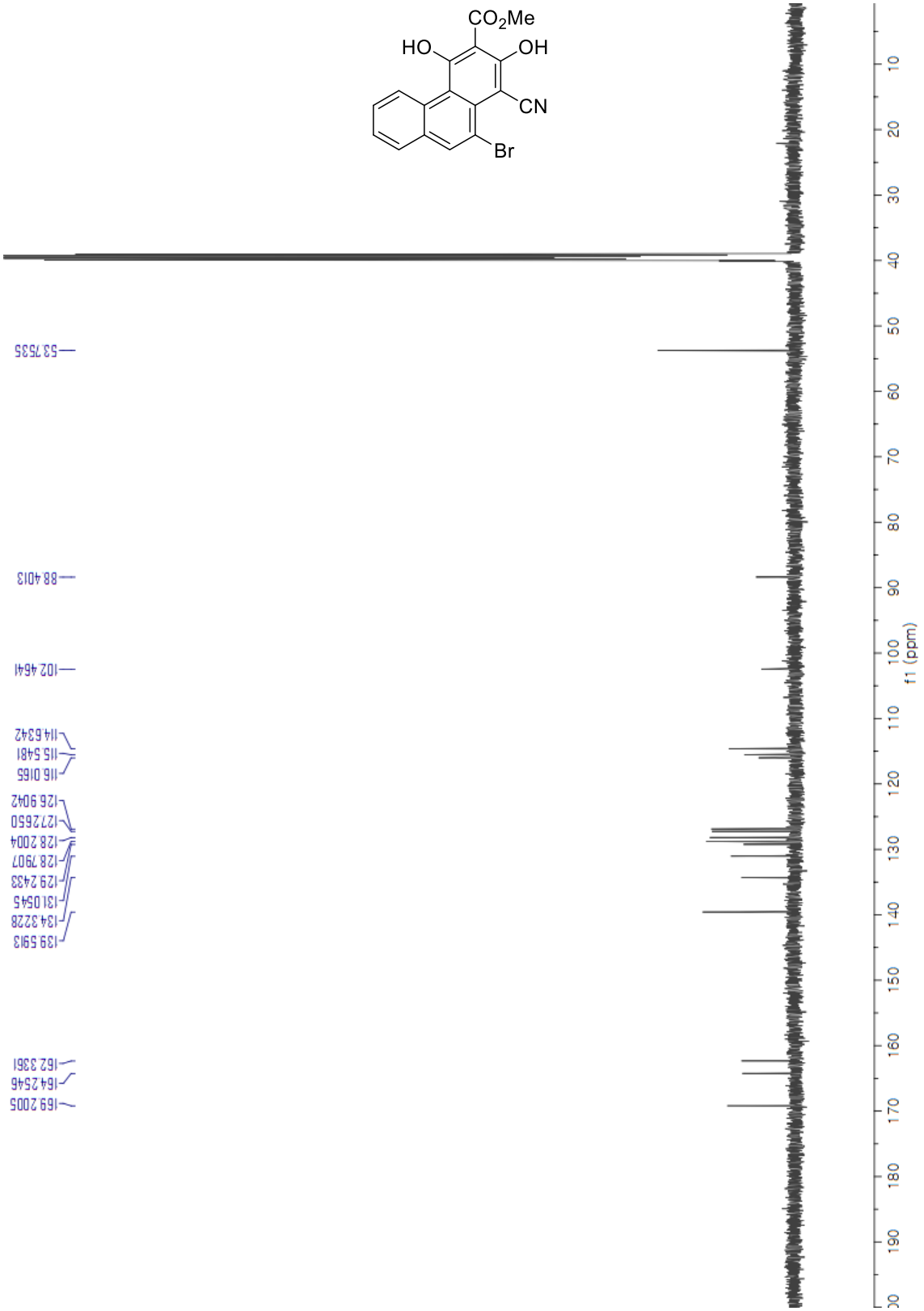
^{13}C NMR ($CDCl_3$, 150 MHz) of compound **7**



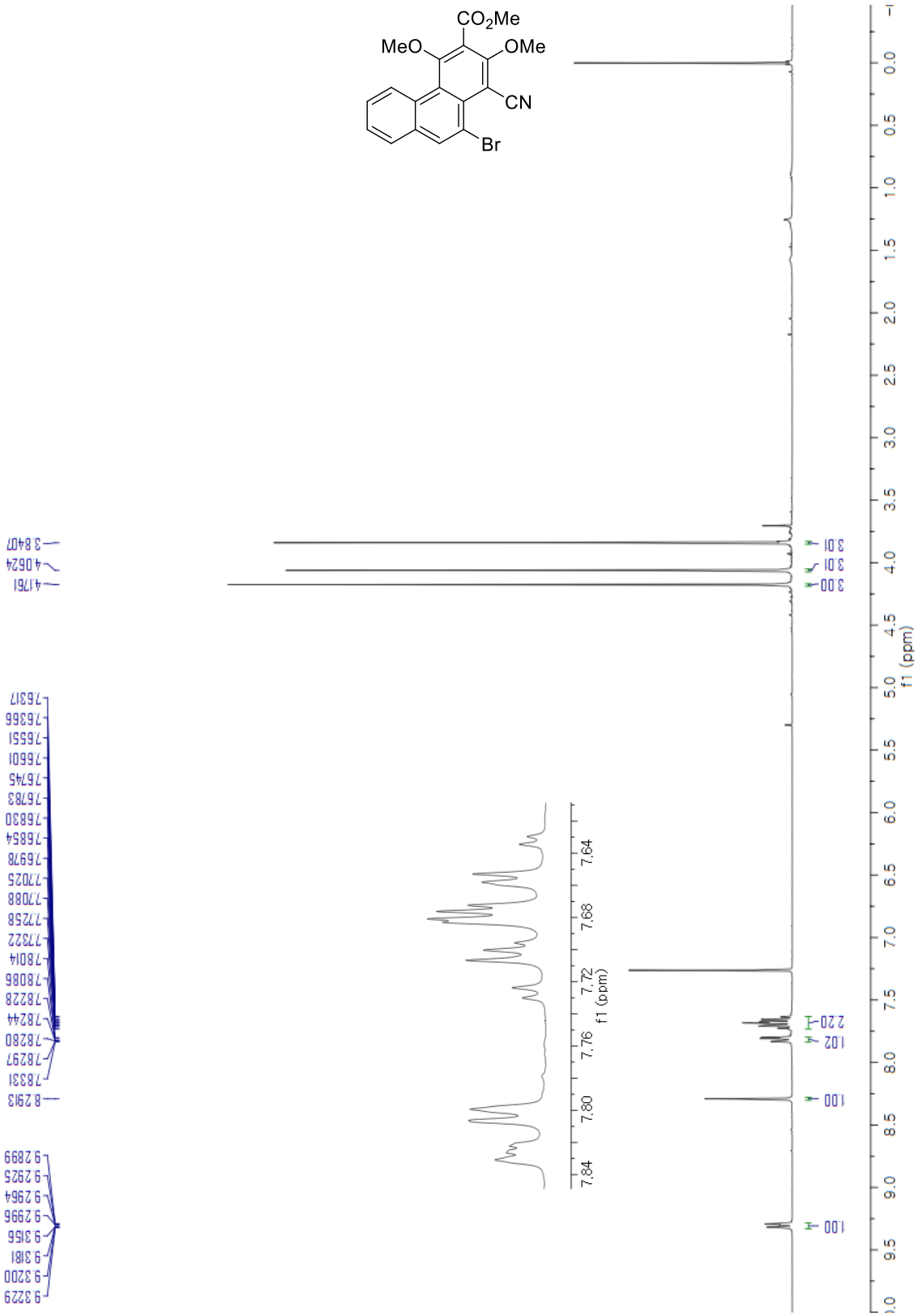
^{19}F NMR ($CDCl_3$, 565 MHz) of compound **7**



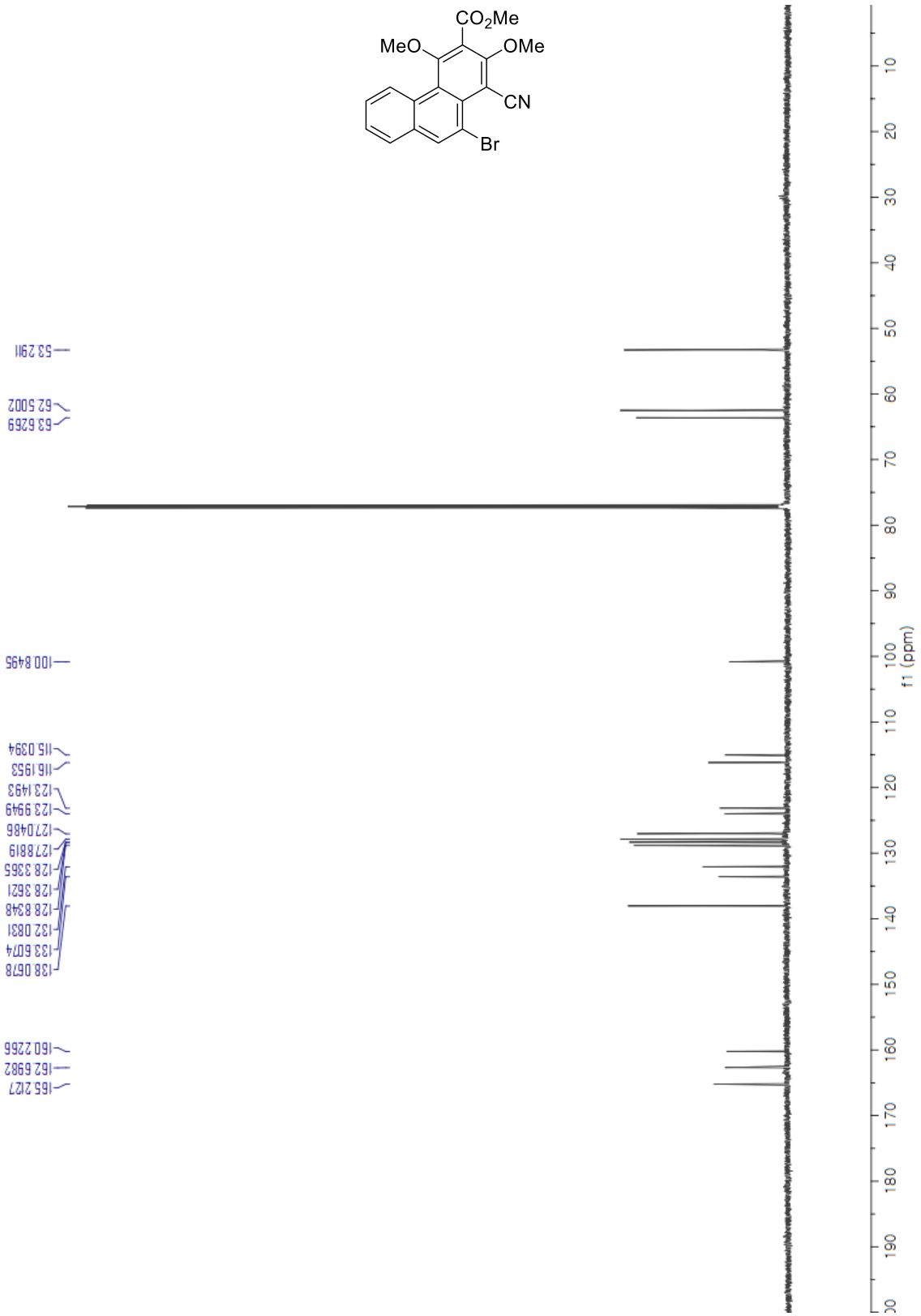
^{1}H NMR (DMSO-d_6, 600 MHz) of compound **13**



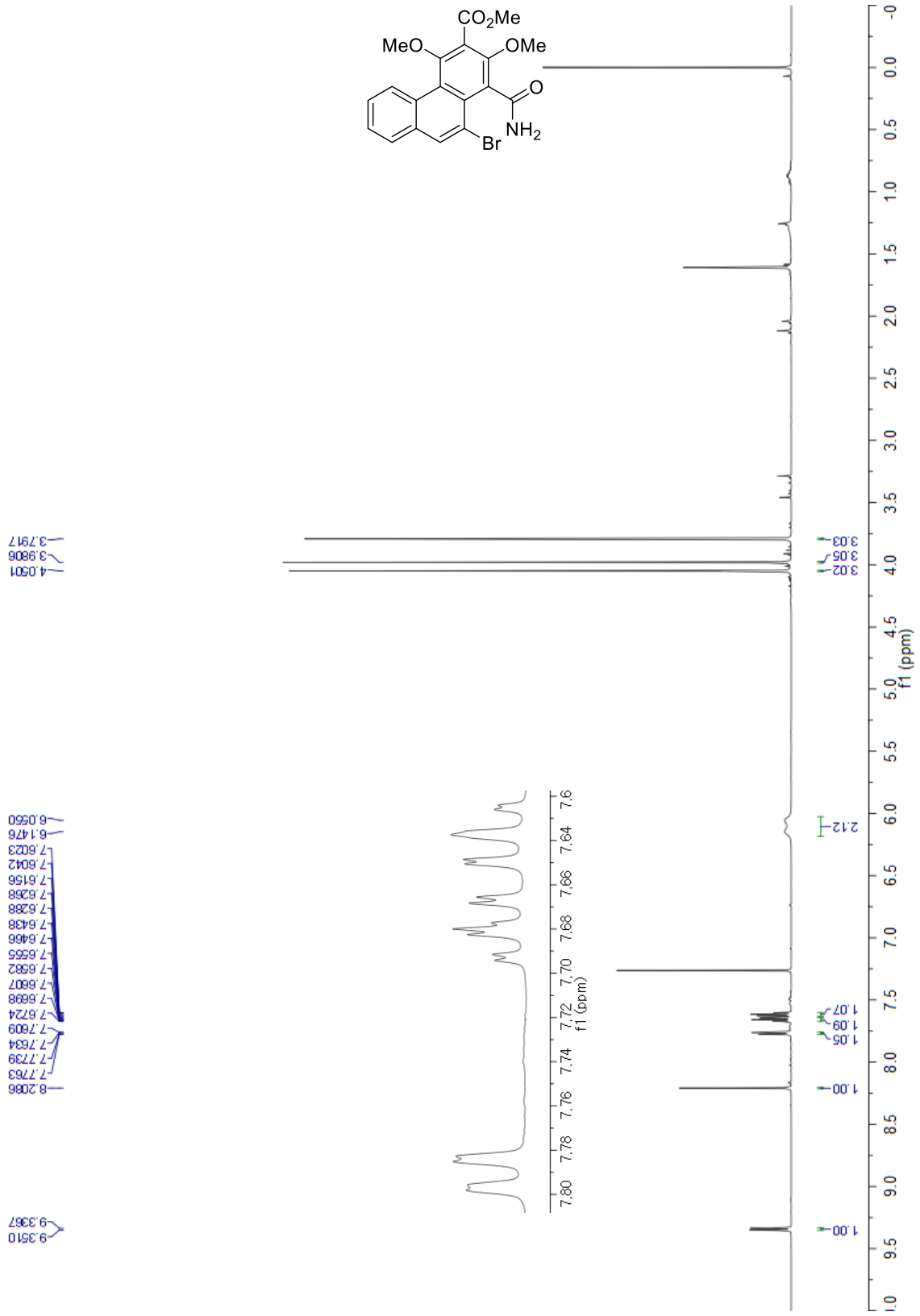
^{13}C NMR (DMSO-d_6, 150 MHz) of compound **13**



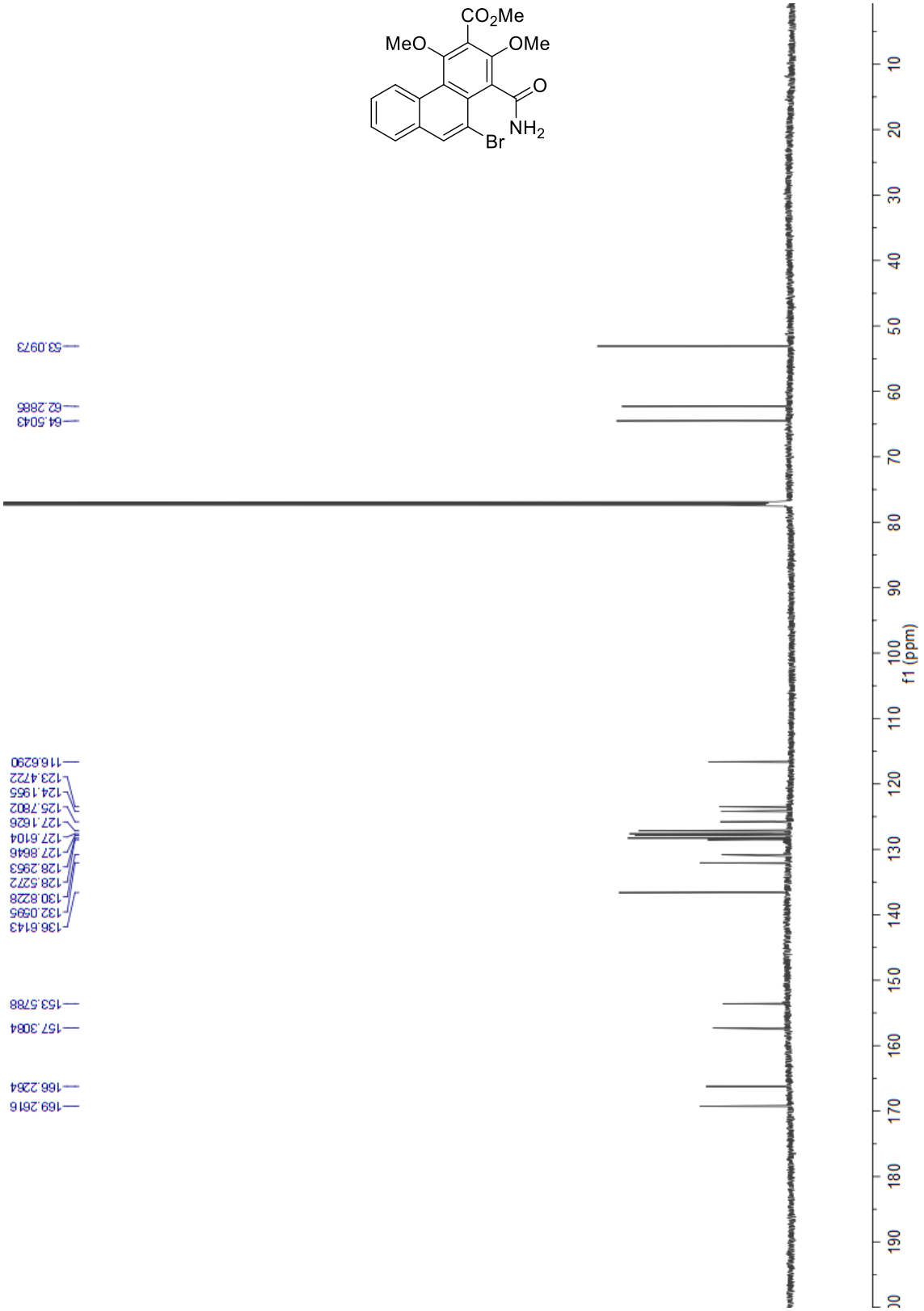
^{1}H NMR ($CDCl_3$, 600 MHz) of compound **6**



^{13}C NMR ($CDCl_3$, 150 MHz) of compound **6**

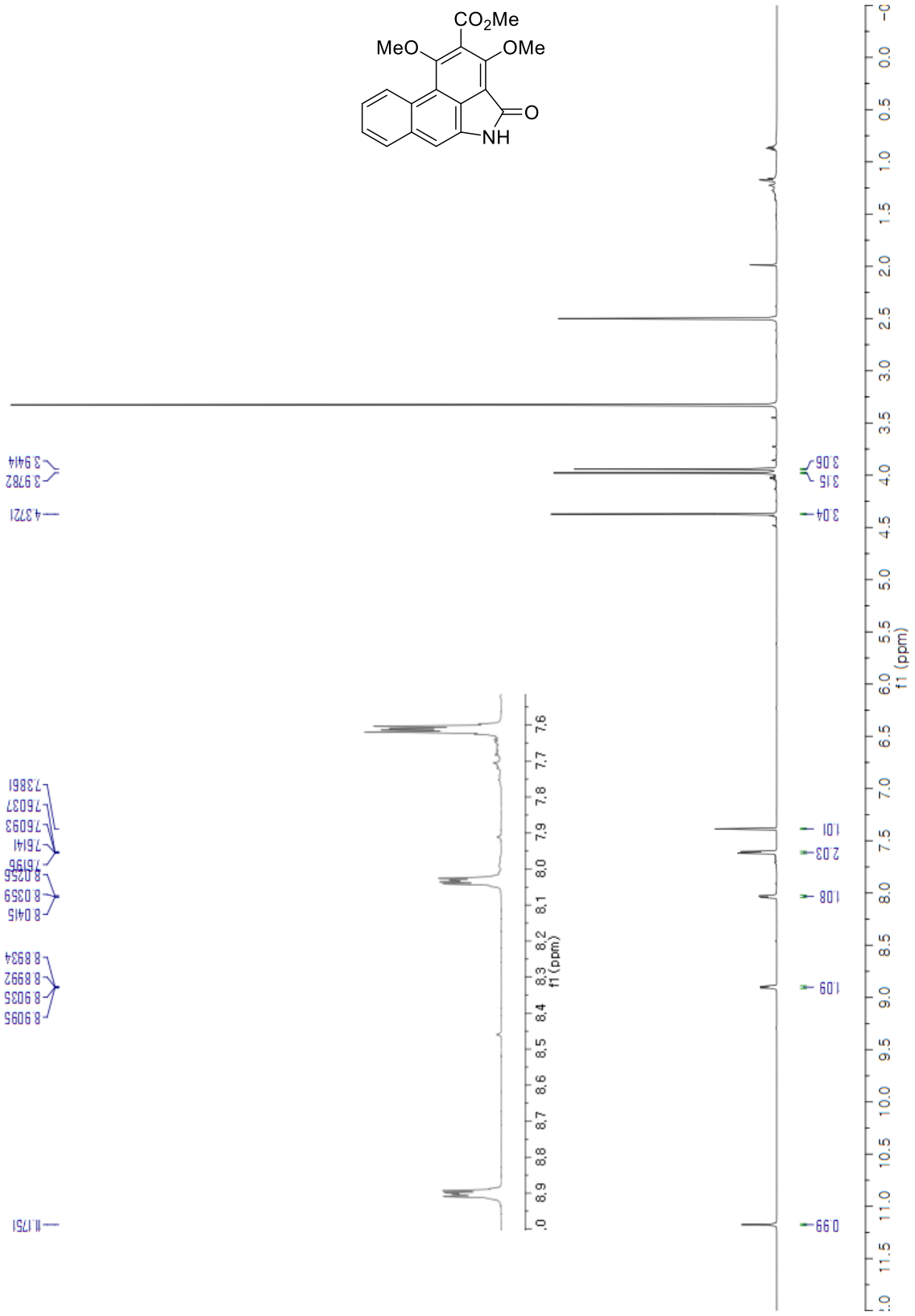


^{1}H NMR ($CDCl_3$, 600 MHz) of compound **14**

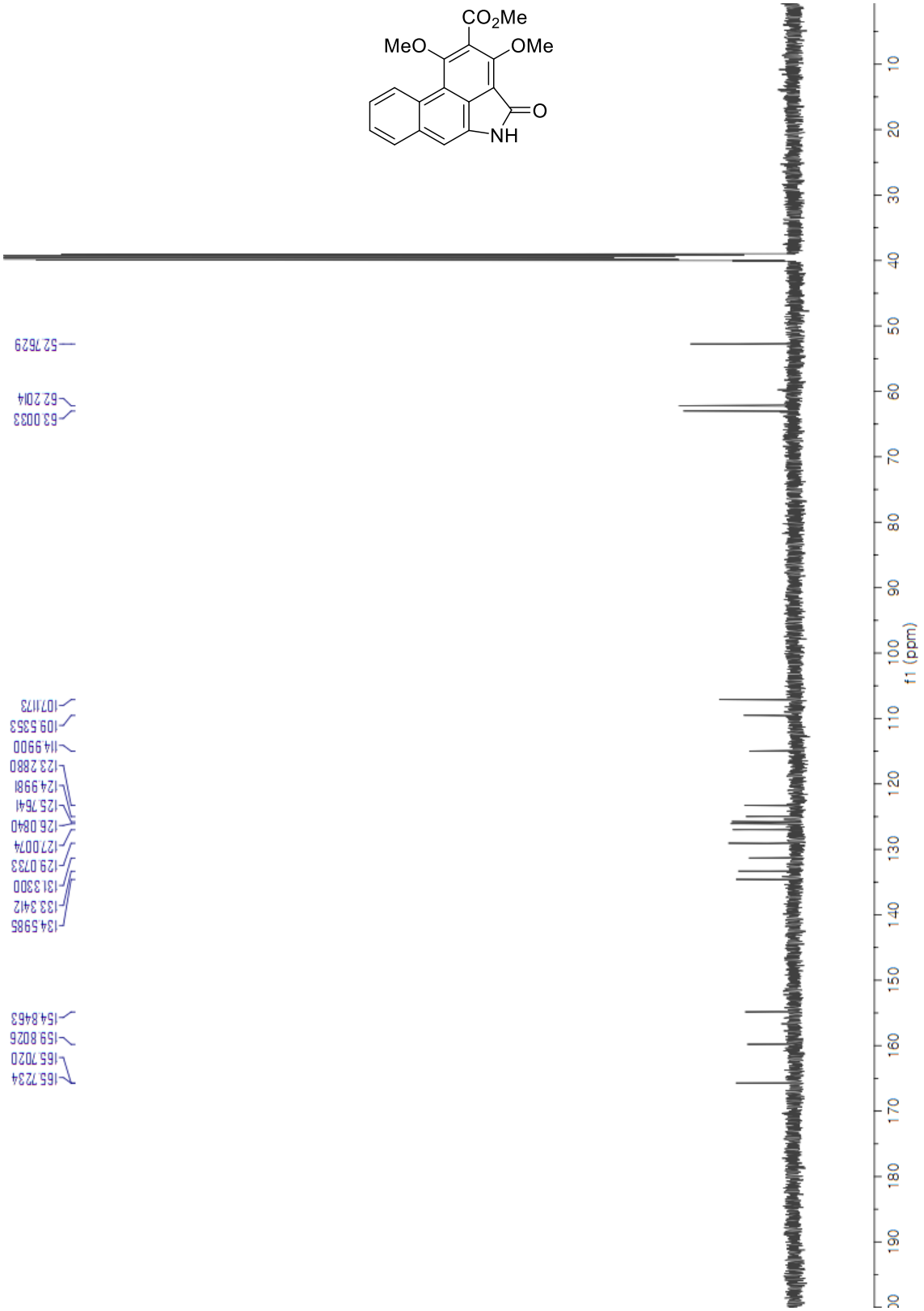


^{13}C NMR ($CDCl_3$, 150 MHz) of compound **14**

H_2O



^{1}H NMR (DMSO-d_6, 600 MHz) of compound **5**



^{13}C NMR (DMSO-d_6, 150 MHz) of compound **5**

4. References:

1) M. Schlegel and C. Schneider, *Org. Lett.,* 2018, **20**, 3119–3123.

2) D. Kim and H. N. Lim, *Org. Lett.,* 2020, **22**, 7465−7469