Supplementary Material (ESI) for Chemical Communications

A novel, facile route to beta-fluoroamines by hydrofluorination using superacid HF/SbF_5.

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Supporting Information

General Method

The authors draw the reader's attention to the dangerous features of superacidic chemistry. Handling of hydrogen fluoride and antimony pentafluoride must be done by experienced chemists with all the necessary safety arrangements in place.

Reactions performed in superacid were carried out in a sealed Teflon® flask with a magnetic stirrer. No further precautions have to be taken to prevent mixture from moisture (test reaction worked out in anhydrous conditions leads to the same results as expected).

Yields refer to isolated pure products.

^{1}H, ^{13}C and ^{19}F NMR were recorded on a 300 MHz Brüker spectrometer using $CDCl_3$ as solvent.

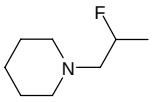
Melting points were determined in a capillary tube and are uncorrected.

High-resolution mass spectra were performed on a Micromass ZABSpec TOF by the Centre Regional de Mesures Physiques de l'Ouest, Université Rennes (France).

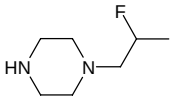
All separations were done under flash-chromatography conditions on silica gel (15-40 μm).

Optimized procedure in superacidic media

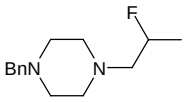
To a mixture of HF/SbF_5 (6 mL, 7/1 molar ratio) maintained at – 20 °C was added nitrogen derivative (1 mmol). The mixture was magnetically stirred at the same temperature for reaction time. The reaction mixture was then neutralized with water-ice-Na_2CO_3, extracted with dichloromethane (× 3). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Products were isolated by column chromatography over silica gel.



Compound 2a: 1-(2-fluoropropyl)piperidine Optimized procedure (60 min reaction time) was followed, starting from 250 mg of **1a** (2 mmol). Purification by flash column chromatography (97/2/1: dichloromethane/methanol/NH_3 aq.) afforded 209 mg of the title compound as a colourless oil (72%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.23 (3H, dd, J = 23.6 Hz, J = 6.4 Hz, $H_{3'}$), 1.36 (2H, m, H_4), 1.52 (4H, m, H_3 and H_5), 2.29 (1H, ddd, J = 31.2 Hz, J = 13.9 Hz, J = 3.0 Hz, $H_{1'a}$), 2.37 (4H, m, H_2 and H_6), 2.50 (1H, ddd, J = 21.6 Hz, J = 13.9 Hz, J = 7.7 Hz, $H_{1'b}$), 4.77 (1H, dm, J = 49.8 Hz, $H_{2'}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.9 (CH_3, d, J = 22 Hz, $C_{3'}$), 24.5 (CH_2, C_4), 26.3 (2 CH_2, C_3 and C_5), 55.4 (2 CH_2, C_2 and C_6), 65.0 (CH_2, d, J = 21 Hz, $C_{1'}$), 89.2 (CH, d, J = 167 Hz, $C_{2'}$). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, ppm): δ –173.7. MS (EI, 70 ev): *m/z* (relative intensity %) 146 $[M+H]^+$ (100). HRMS (ESI): Calc for $C_8H_{16}NF$: 145.12668, found 145.1269.

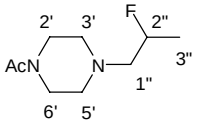


Compound 2b: 1-(2-fluoropropyl)piperazine Optimized procedure (60 min reaction time) was followed, starting from 0.14 mL of **1b** (1 mmol). Purification by flash column chromatography (92/5/3: dichloromethane/methanol/NH_3 aq.) afforded 83 mg of the title compound as a colourless oil (57%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.34 (3H, dd, J = 23.6 Hz, J = 6.4 Hz, $H_{3'}$), 1.82 (1H, broad s, NH), 2.44 (1H, ddd, J = 31.7 Hz, J = 13.9 Hz, J = 2.8 Hz, $H_{1'a}$), 2.52 (4H, m, H_3 and H_5), 2.61 (1H, ddd, J = 21.7 Hz, J = 13.9 Hz, J = 7.8 Hz, $H_{1'b}$) 2.91 (4H, broad t, J = 5.0 Hz, H_2 and H_6), 4.86 (1H, dm, J = 49.8 Hz, $H_{2'}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.9 (CH_3, d, J = 22 Hz, $C_{3'}$), 46.4 (2 CH_2, C_3 and C_5), 55.4 (2 CH_2, C_2 and C_6), 64.8 (CH_2, d, J = 21 Hz, $C_{1'}$), 89.2 (CH, d, J = 167 Hz, $C_{2'}$). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, ppm): δ –174.0. MS (EI, 70 ev): *m/z* (relative intensity %) 146 $[M]^+$ (8), 126 $[M-HF]^+$ (93), 99 $[M-CH_3CHF]^+$ (96), 85 $[M-CH_2CHFCH_3]^+$ (71). HRMS (ESI): Calc for $C_7H_{14}N_2$: 126.11570, found 126.1151.

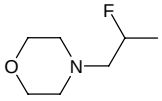


Compound 2c: 1-benzyl-4-(2-fluoropropyl)piperazine Optimized procedure (60 min reaction time) was followed, starting from 216 mg of **1c** (1 mmol). Purification by flash column chromatography (95/4/1: dichloromethane/methanol/NH_3 aq.) afforded 201 mg of the title compound as a colourless oil (85%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.30

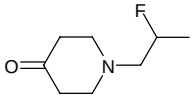
(3H, dd, J = 23.6 Hz, J = 6.2 Hz, $H_{3'}$), 2.55 (10H, m, $H_{1'}$,H_2, H_3, H_5 and H_6), 3.50 (2H, s, H_{benzyl}), 4.83 (1H, dm, J = 49.8 Hz, $H_{2'}$), 7.25 and 7.30 (5H, 2 m, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.5 (CH_3, d, J = 23 Hz, $C_{3'}$), 53.0 (2 CH_2, C_2 and C_6), 53.7 (2 CH_2, C_3 and C_5), 63.0 (CH_2, CH_2 benzyl), 63.8 (CH_2, d, J = 21 Hz, $C_{1'}$), 88.8 (CH, d, J = 167 Hz, $C_{2'}$), 127.0 (CH, C_{para}), 128.2 (2 CH, C_{meta}), 129.2 (2 CH, C_{ortho}), 138.1 (C $_{ipso}$). $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, ppm): δ –174.1. MS (EI, 70 ev) *m/z* (relative intensity %) 236 $[M]^+$ (32), 216 $[M-HF]^+$ (100). HRMS (ESI): Calc for $C_{14}H_{20}N_2$: 216.16265, found 216.1625.



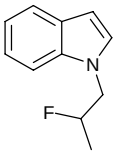
Compound 2d: 1-(4-(2-fluoropropyl)piperazin-1-yl)ethanone Optimized procedure (10 min reaction time) was followed, starting from 168 mg of **1d** (1 mmol). Purification by flash column chromatography (97/2/1: dichloromethane/methanol/NH_3 aq.) afforded 130 mg of the title compound as a colourless oil (69%). ^1H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.34 (3H, dd, J = 23.7 Hz, J = 6.4 Hz, $H_{3''}$), 2.09 (3H, s, H_2), 2.53 (6H, m, $H_{3'}$,$H_{5'}$ and $H_{1''}$), 3.48 (2H, t, J = 5.1 Hz, $H_{2'a}$ and $H_{6'a}$), 3.64 (2H, m, $H_{2'b}$ and $H_{6'b}$), 4.87 (1H, dm, J = 49.6 Hz, $H_{2''}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.3 (CH_3, d, J = 22 Hz, $C_{3''}$), 21.3 (CH_3, C_2), 41.4 (CH_2, $C_{2'}$ or $C_{6'}$), 46.2 (CH_2, $C_{2'}$ or $C_{6'}$), 53.3 (CH_2, $C_{3'}$ or $C_{5'}$), 53.7 (CH_2, $C_{3'}$ or $C_{5'}$), 63.5 (CH_2, d, J = 20 Hz, $C_{1''}$), 88.9 (CH, d, J = 167 Hz, $C_{2''}$), 168.9 (CO). $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, ppm): δ –174.3. MS (EI, 70 ev): *m/z* (relative intensity %) 189 $[M+H^+]^+$ (20). HRMS (ESI): Calc for $C_9H_{16}N_2O$: 168.12626, found 168.1263.



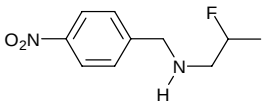
Compound 2e: 4-(2-fluoropropyl)morpholine Optimized procedure (60 min reaction time) was followed, starting from 127 mg of **1e** (1 mmol). Purification by flash column chromatography (96/3/1: dichloromethane/methanol/NH_3 aq.) afforded 90 mg of the title compound as a colourless oil (61%). ^1H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.26 (3H, dd, J = 23.6 Hz, J = 6.4 Hz, $H_{3'}$), 2.36 (1H, ddd, J = 31.1 Hz, J = 13.9 Hz, J = 2.8 Hz, $H_{1'a}$), 2.46 (4H, broad t, J = 4.7 Hz, H_3 and H_5), 2.55 (1H, ddd, J = 22.3 Hz, J = 13.9 Hz, J = 7.8 Hz, $H_{1'b}$), 3.66 (4H, m, H_2 and H_6), 4.80 (1H, dm, J = 49.7 Hz, $H_{2'}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.8 (CH_3, d, J = 22 Hz, $C_{3'}$), 54.6 (CH_2, C_3 and C_5), 64.6 (CH_2, d, J = 21 Hz, $C_{1'}$), 67.3 (CH_2, C_2 and C_6), 89.2 (CH, d, J = 167 Hz, $C_{2'}$). $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, ppm): δ –174.3. MS (EI, 70 ev): *m/z* (relative intensity %) 148 $[M+H^+]^+$ (100). HRMS (ESI): Calc for $C_7H_{13}NOF$: 146.09812, found 146.0992.



Compound 2f: 1-(2-fluoropropyl)piperidin-4-one Optimized procedure (60 min reaction time) was followed, starting from 139 mg of **1f** (1 mmol). Purification by flash column chromatography (95/4/1: dichloromethane/methanol/NH_3 aq.) afforded 112 mg of the title compound as a colourless oil (70%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.37 (3H, dd, J = 23.6 Hz, J = 6.2 Hz, $H_{3'}$), 2.47 (4H, t, J = 6.1 Hz, H_3 and H_5), 2.69 (2H, m, $H_{1'}$), 2.86 (4H, t, J = 6.2 Hz, H_2 and H_6), 4.88 (1H, dm, J = 49.6 Hz, $H_{2'}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.3 (CH_3, d, J = 22 Hz, $C_{3'}$), 41.2 (2 CH_2, C_3 and C_5), 53.7 (CH_2, C_2 and C_6), 62.4 (CH_2, d, J = 21 Hz, $C_{1'}$), 89.2 (CH, d, J = 167 Hz, $C_{2'}$), 208.7 (CO). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, ppm): δ −174.7. MS (EI, 70 ev): *m/z* (relative intensity %) 159 $[M]^+$ (10), 112 $[M\text{-}CH_3CHF]^+$ (100). HRMS (ESI): Calc for $C_8H_{14}NOF$: 159.10594, found 159.1058.



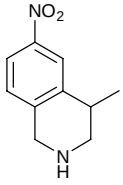
Compound 2g: 1-(2-fluoropropyl)-1*H*-indole Optimized procedure (10 min reaction time) was followed, starting from 157 mg of **1g** (1 mmol). Purification by flash column chromatography (98/2: petroleum ether/ethyl acetate) afforded 72 mg of the title compound as a colourless oil (41%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.26 (3H, dd, J = 23.5 Hz, J = 6.3 Hz, $H_{3'}$), 4.16 (2H, m, $H_{1'}$), 4.88 (1H, dm, J = 48.2 Hz, $H_{2'}$), 6.45 (1H, d, J=3.8 Hz, H_3), 7.04 (2H, m, H_6 and H_2), 7.12 (1H, t, J=4.7 Hz, H_5), 7.25 (1H, d, J=8.2 Hz, H_4), 7.56 (1H, d, J=7.9 Hz, H_7). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 18.8 (CH_3, d, J = 22 Hz, $C_{3'}$), 51.6 (CH_2, d, J = 24 Hz, $C_{1'}$), 89.6 (CH, d, J = 171 Hz, $C_{2'}$), 102.3 (CH, C_3), 109.6 (CH, C_4), 119.9 (CH, C_6), 121.4 (CH, C_7), 122.1 (CH, C_5), 128.9 (C_{3a}), 129.0 (CH, C_2), 136.8 (C_{7a}). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, ppm): δ −175.3. MS (EI, 70 ev): *m/z* (relative intensity %) 177 $[M]^+$ (30), 130 $[M\text{-}CH_3CHF]^+$ (100). HRMS (ESI): Calc for $C_{11}H_{12}N_F$: 177.09538, found 177.0962.



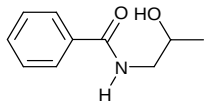
Compound 2i: N-(4-nitrobenzyl)-2-fluoropropan-1-amine Optimized procedure (10 min reaction time) was followed, starting from 324 mg of **1i** (1.68 mmol). Purification by flash column chromatography (99/1: dichloromethane/methanol) afforded 160 mg of the title compound as a colourless oil (45 %). The second compound 1,2,3,4-

tetrahydro-4-methyl-6-nitroisoquinoline **2i'** (80 mg, 24 %) was then eluted (95/4/1: dichloromethane/methanol/NH_3 aq.).

Compound 2i ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.27 (3H, dd, J = 23.9 Hz, J = 6.4 Hz, H_3), 1.66 (1H, NH), 2.70 (2H, m, H_1), 3.87 (2H, s, H_{benzyl}), 4.75 (1H, dm, J = 49.3 Hz, H_2), 7.45 (2H, d, J=8.8 Hz, H_{arom}), 8.11 (2H, d, J=8.8 Hz, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 17.7 (CH_3, d, J = 22 Hz, C_3), 51.8 (CH_2, C_{benzyl}), 53.5 (CH_2, d, J = 20 Hz, C_1), 89.3 (CH, d, J = 165 Hz, C_2), 122.6 (2 CH_2, C_{arom}), 127.5 (2 CH_2, C_{arom}), 146.0 (C_{arom}), 146.9 (C_{arom}).^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, ppm): δ –179.6. MS (GCT, CI^+): *m/z* (relative intensity %) 212 $[M]^+$ (100). HRMS (ESI): Calc for $C_{10}H_{13}N_2O_2F$: 212.09611, found 212.0967.

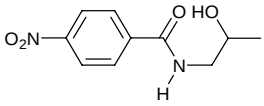


Compound 2i': 1,2,3,4-tetrahydro-4-methyl-6-nitroisoquinoline ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.27 (3H, d, J = 7.0 Hz, CH_3), 1.97 (1H, broad s, NH), 2.76 (1H, dd, J=12.6 Hz, J=6.3 Hz, H_{3a}), 2.89 (1H, m, H_4), 3.16 (1H, dd, J=12.6 Hz, J=5.0 Hz, H_{3b}), 4.01 (2H, s, H_1), 7.08 (1H, d, J=8.5 Hz, H_8), 7.88 (1H, dd, J=8.4 Hz, J=2.3 Hz, H_7), 8.02 (1H, d, J=2.3 Hz, H_5). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 19.2 (CH_3), 31.4 (CH, C_4), 48.4 (CH_2, C_1), 50.1 (CH_2, C_3), 120.3 (CH, C_7), 122.8 (CH, C_5), 126.6 (CH, C_8), 141.4 (C_{arom}), 142.8 (C_{arom}), 146.2 (C_6). MS (GCT, CI^+): *m/z* (relative intensity %) 192 $[M]^+$ (100). HRMS (ESI): Calc for $C_{10}H_{12}N_2O_2$: 192.08988, found 192.0907.



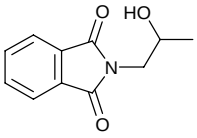
Compound 4b: N-(2-hydroxypropyl)benzamide[19] Optimized procedure (10 min reaction time) was followed, starting from 161 mg of **3b** (1 mmol). Purification by flash column chromatography (dichloromethane) afforded 154 mg of the title compound as a colourless oil (86 %)

Compound 4b ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.42 (3H, d, J = 6.2 Hz, $H_{3'}$), 3.61 (1H, dd, J=14.4 Hz, J=7.4 Hz, $H_{1'a}$), 4.14 (1H, dd, J=14.4 Hz, J=9.4 Hz, $H_{1'b}$), 4.85 (1H, m, $H_{2'}$), 7.42 (3H, m, H_{meta} and H_{para}), 7.94 (2H, d, J=6.7 Hz, H_{ortho}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 21.5 (CH_3, $C_{3'}$), 62.0 (CH_2, $C_{1'}$), 76.6 (CH, $C_{2'}$), 128.4 (CH, C_{arom}), 128.5 (CH, C_{arom}), 128.7 (CH, C_{arom}), 131.6 (C_{arom}), 164.2 (CO).



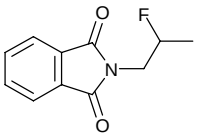
Compound 4c : N-(2-hydroxypropyl)-4-nitrobenzamide Optimized procedure (10 min reaction time) was followed, starting from 412 mg of **3c** (2 mmol). Purification by flash column chromatography (99/1,dichloromethane/methanol) afforded 310 mg of the title compound as a white solid (69 %)

Compound 4c ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.46 (3H, d, J = 6.3 Hz, $H_{3'}$), 3.67 (1H, dd, J=14.9 Hz, J=7.5 Hz, $H_{1'a}$), 4.21 (1H, dd, J=14.9 Hz, J=9.5 Hz, $H_{1'b}$), 4.94 (1H, m, $H_{2'}$), 8.10 (2H, d, J=9.0 Hz, H_2 and H_6), 8.27 (2H, d, J=9.0 Hz, H_3 and H_5). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 21.5 (CH_3, $C_{3'}$), 62.2 (CH_2, $C_{1'}$), 77.4 (CH, $C_{2'}$), 123.8 (2CH, C_3 and C_5), 129.5 (2CH, C_2 and C_6), 134.2 (C_1), 149.8 (C_4), 162.5 (CO). MS (GCT, CI^+): *m/z* (relative intensity %) 206 $[M]^+$ (100). HRMS (ESI): Calc for $C_{10}H_{10}N_2O_3$: 206.06914, found 206.0692. Mp: 136°C (CH_2Cl_2/hexane (20/80, v/v)).



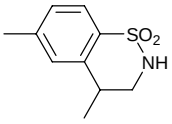
Compound 4d: 2-(2-hydroxypropyl)isoindoline-1,3-dione[20] Optimized procedure (60 min reaction time) was followed, starting from 95 mg of **3d** (0.5 mmol). Purification by flash column chromatography (98/2,dichloromethane/methanol) afforded 100 mg of the title compound as a white solid (97 %)

Compound 4d ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.26 (3H, d, J = 6.4 Hz, $H_{3'}$), 2.80 (1H, broad s, OH), 3.73 (2H, m, $H_{1'}$), 4.12 (1H, m, $H_{2'}$), 7.72 (2H, m, H_{arom}), 7.83 (2H, m, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 21.0 (CH_3, $C_{3'}$), 45.5 (CH_2, $C_{1'}$), 66.5 (CH, $C_{2'}$), 123.4 (2CH, C_{arom}), 131.9 (C_{arom}), 134.1 (2CH, C_{arom}), 168.9 (CO).



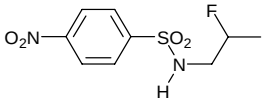
Compound 4d': 2-(2-fluoropropyl)isoindoline-1,3-dione Optimized procedure (10 min reaction time) was followed, starting from 374 mg of **3d** (2 mmol). After reaction time 3 mL of HF/pyridine (70/30 w/w) were added to reaction mixture , stirred for 24 hours at reaction temperature, and worked up as described procedure. Purification by flash column chromatography (dichloromethane) afforded 131 mg of the title compound as a white solid (31 %). The second compound **4d** (140 mg, 34 %) was then eluted (98/2: dichloromethane/methanol).

Compound 4d': ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.42 (3H, dd, J = 23.6 Hz, J = 6.3 Hz, $H_{3'}$), 3.74 (1H, ddd, J=27.7 Hz, J=14.4 Hz, J=3.5 Hz, $H_{1'a}$), 3.98 (1H, ddd, J=22.6 Hz, J=14.4 Hz, J=8.2 Hz, $H_{1'b}$), 4.95 (1H, dm, J = 49.3 Hz, $H_{2'}$), 7.74 (2H, dd, J=5.3 Hz, J=3.0 Hz, H_{arom}), 7.87 (2H, dd, J=5.3 Hz, J=3.0 Hz, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 18.6 (CH_3, d, J = 21 Hz, $C_{3'}$), 42.9 (CH_2, d, J = 24 Hz, $C_{1'}$), 87.6 (CH, d, J = 171 Hz, $C_{2'}$), 123.4 (2CH, C_{arom}), 132.0 (C_{arom}), 134.1 (2CH, C_{arom}), 168.1 (CO). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, ppm): δ −180.5. MS (EI, 70 ev): *m/z* (relative intensity %) 208 $[M+H^+]^+$ (70), 207 $[M]^+$ (100) 187 $[M-HF]^+$ (100) 160 $[M-CH_3CHF]^+$ (100). HRMS (ESI): Calc for $C_9H_6NO_2$: 160.03985, found 160.0394. Mp: 99°C (CH_2Cl_2/hexane (20/80, v/v)).



Compound 4e: 4,6-dimethyl-3,4-dihydro-2*H*,benzo[e][1,2]thiazine 1,1-dioxide Optimized procedure (10 min reaction time) was followed, starting from 422 mg of **3e** (2 mmol). Purification by flash column chromatography (98/2,dichloromethane/methanol) afforded 270 mg of the title compound as a colourless oil (64 %).

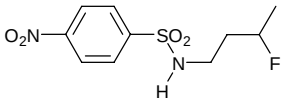
Compound 4e ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.34 (3H, d, J = 7.2 Hz, CH_3), 2.37 (3H, s, CH_3), 2.98 (1H, m, H_4), 3.41 (1H, m, H_{3a}), 3.82 (1H, m, H_{3b}), 4.89 (1H, t, J=7.7 Hz, NH), 7.09 (1H, s, H_5), 7.14 (1H, d, J=8.1 Hz, H_7), 7.62 (1H, d, J=8.1 Hz, H_8). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 19.5 (CH_3), 21.6 (CH_3), 31.5 (CH, C_4), 48.2 (CH_2, C_3), 124.0 (CH, C_7), 128.2 (CH, C_8), 129.0 (C_5), 134.2 (C_{8a}), 140.2 (C_6), 142.7 (C_{4a}). MS (EI, 70 ev): *m/z* (relative intensity %) 211 $[M]^+$ (40). HRMS (ESI): Calc for $C_{10}H_{13}NO_2S$: 211.06670, found 211.0664.



Compound 4f : N-(2-fluoropropyl)-4-nitrobenzenesulfonamide Optimized procedure (10 min reaction time) was followed, starting from 242 mg of **3f** (1 mmol). Purification by flash column chromatography (90/10: petroleum ether/ethylacetate) afforded 195 mg of the title compound as a white solid (74 %).

Compound 2f ^{1}H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.32 (3H, dd, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 3.10 (1H, m, $H_{1'a}$), 3.26 (1H, dm, J=28.1 Hz, $H_{1'b}$), 4.73 (1H, dm, J = 48.9 Hz, $H_{2'}$), 5.38 (1H, m, NH), 8.07 (2H, d, J=9.1 Hz, H_2 and H_6), 8.38 (2H, d, J=9.1 Hz, H_3 and H_5). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 18.0 (CH_3, d, J = 22 Hz, $C_{3'}$), 48.2 (CH_2, d, J = 21 Hz, $C_{1'}$), 89.1 (CH, d, J = 168 Hz, $C_{2'}$), 124.5 (2 CH, C_3 and C_5), 128.3 (2 CH, C_2 and C_6), 145.8 (C_1), 150.1

(C_4).$^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, ppm): δ –180.2. MS (GCT, CI^+): *m/z* (relative intensity %) 215 $[M\text{-}CH_3CHF]^+$ (20). HRMS (ESI): Calc for $C_7H_7N_2O_4S$: 215.01265, found 215.0122. Mp: 109°C (CH_2Cl_2/hexane (20/80, v/v)).

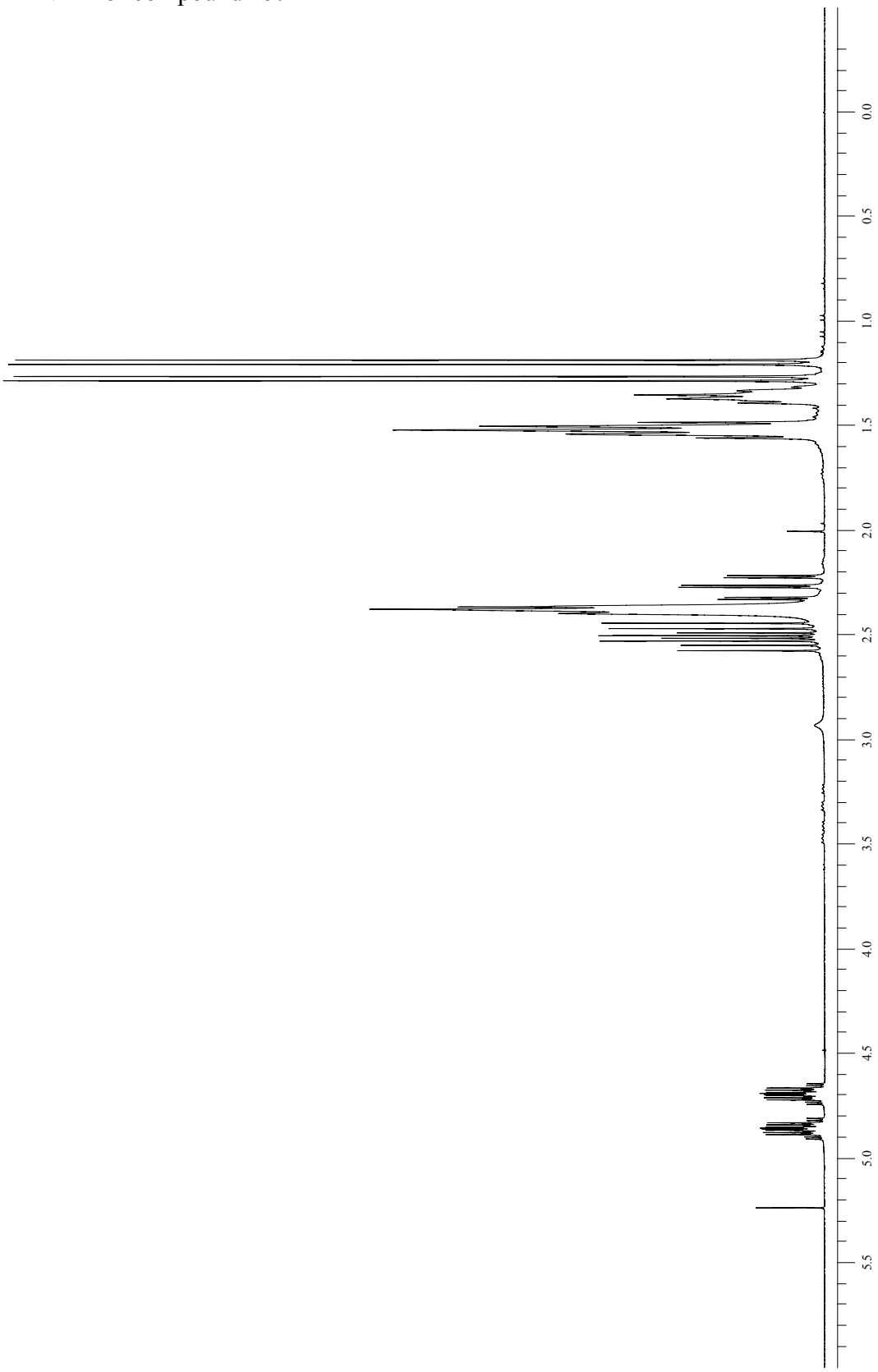


Compound 4g: N-(3-fluorobutyl)-4-nitrobenzenesulfonamide

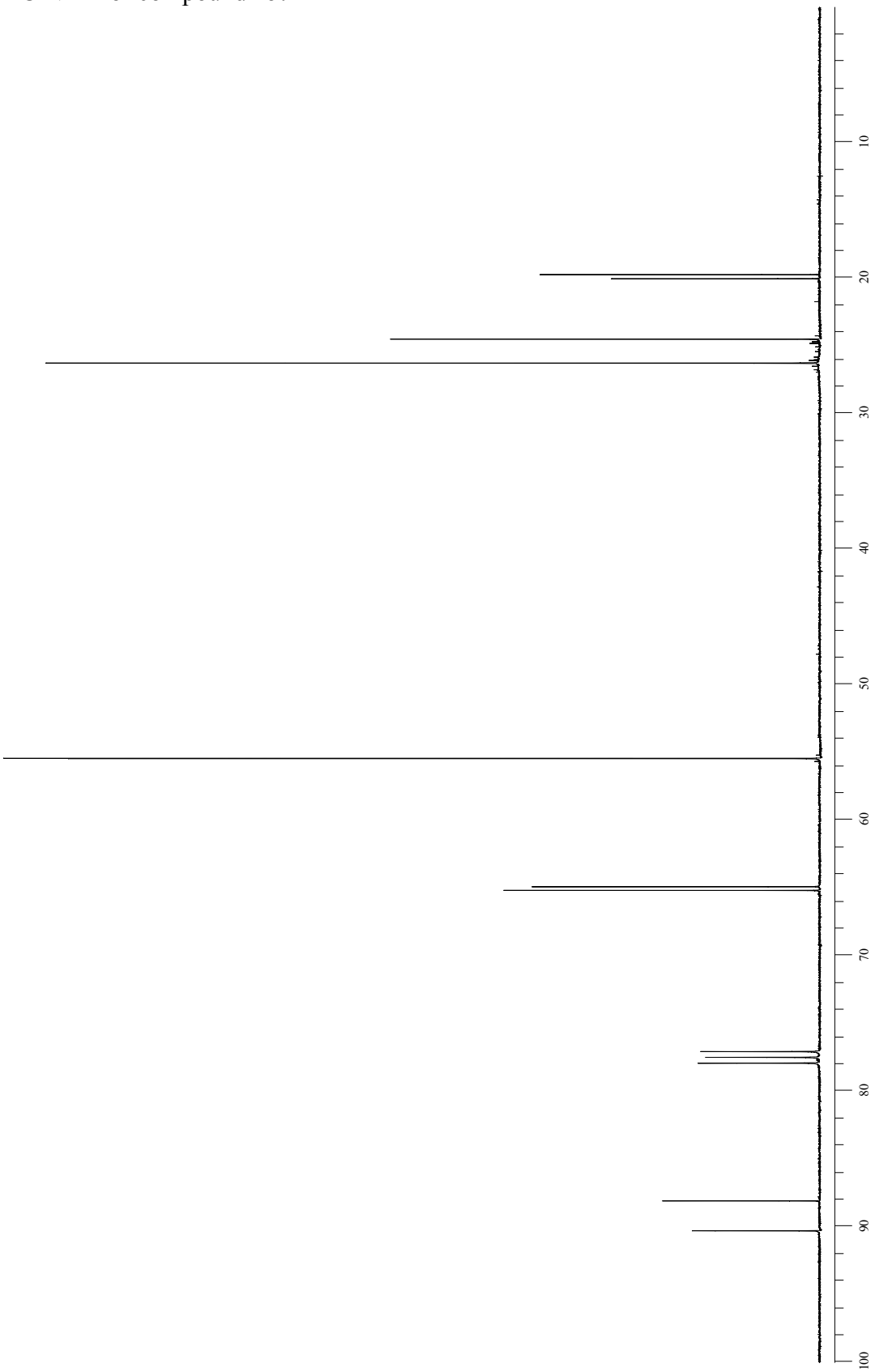
Optimized procedure (10 min reaction time) was followed, starting from 150 mg of **3g** (0.58 mmol). Purification by flash column chromatography (80/20: petroleum ether/ethylacetate) afforded 50 mg of the title compound as a pale yellow oil (30 %).

Compound 2f ^1H NMR (300 MHz, $CDCl_3$, ppm) : δ 1.26 (3H, dd, J = 24.2 Hz, J = 6.3 Hz, $H_{4'}$), 1.74 (2H, m, H_2'), 3.10 (2H, m, $H_{1'}$), 4.66 (1H, dm, J = 49.1 Hz, $H_{3'}$), 4.91 (1H, m, NH), 8.00 (2H, d, J=9.1 Hz, H_2 and H_6), 8.37 (2H, d, J=9.1 Hz, H_3 and H_5). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) : δ 21.3 (CH_3, d, J = 22 Hz, $C_{4'}$), 36.9 (CH_2, d, J=20.0 Hz, $C_{2'}$), 40.6 (CH_2, d, J = 3 Hz, $C_{1'}$), 90.0 (CH, d, J = 164 Hz, $C_{3'}$), 124.8 (2 CH, C_3 and C_5), 128.7 (2 CH, C_2 and C_6), 146.2 (C_1), 150.5 (C_4).$^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, ppm): δ –175.4. MS (GCT, CI^+): *m/z* (relative intensity %) 276 $[M]^+$ (60), 215 $[M\text{-}CH_2CHFCH_3]^+$ (100). HRMS (ESI): Calc for $C_{10}H_{13}N_2O_4FS$: 276.05801, found 276.0576.

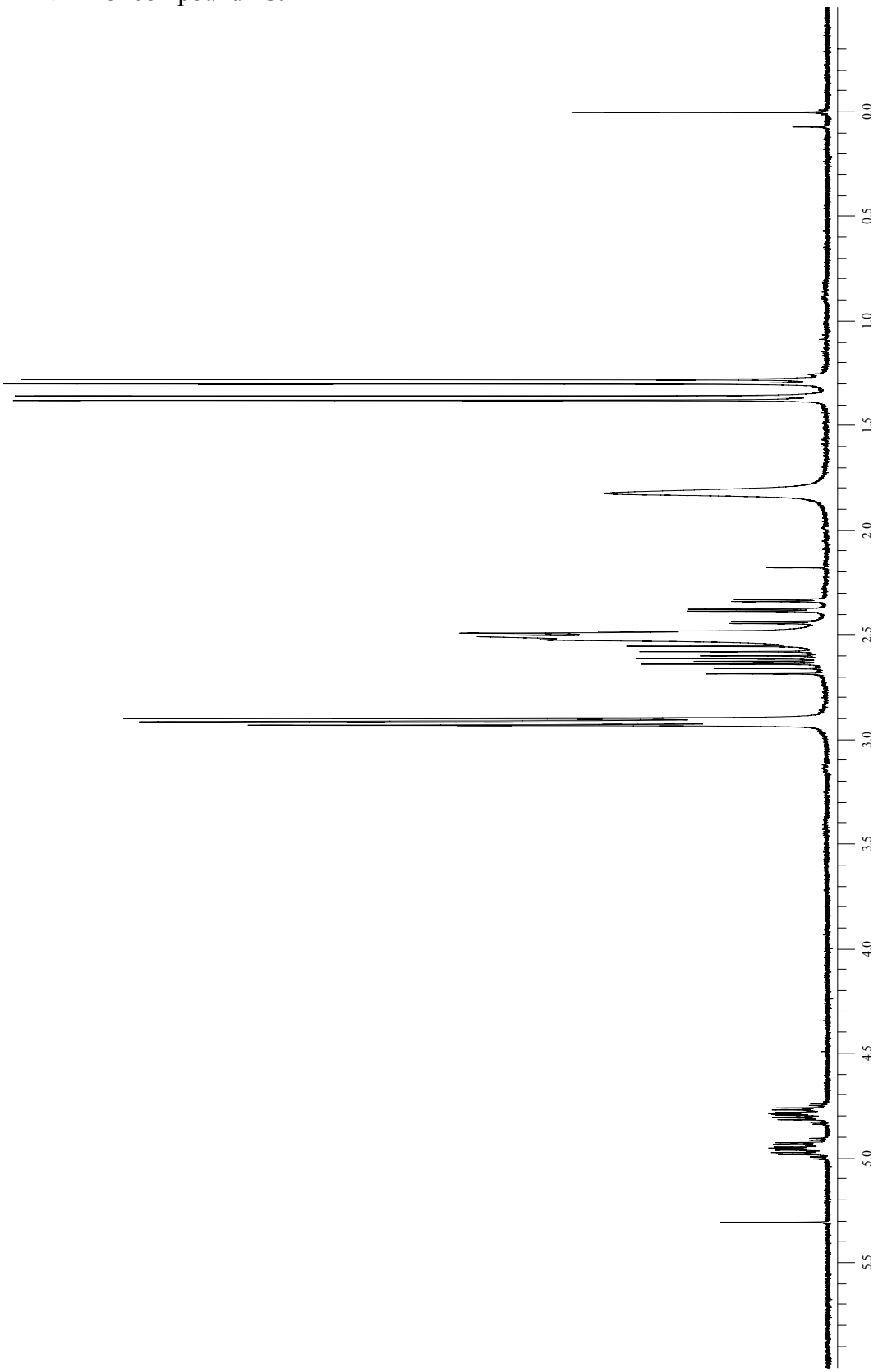
^{1}H NMR of compound **2a**:



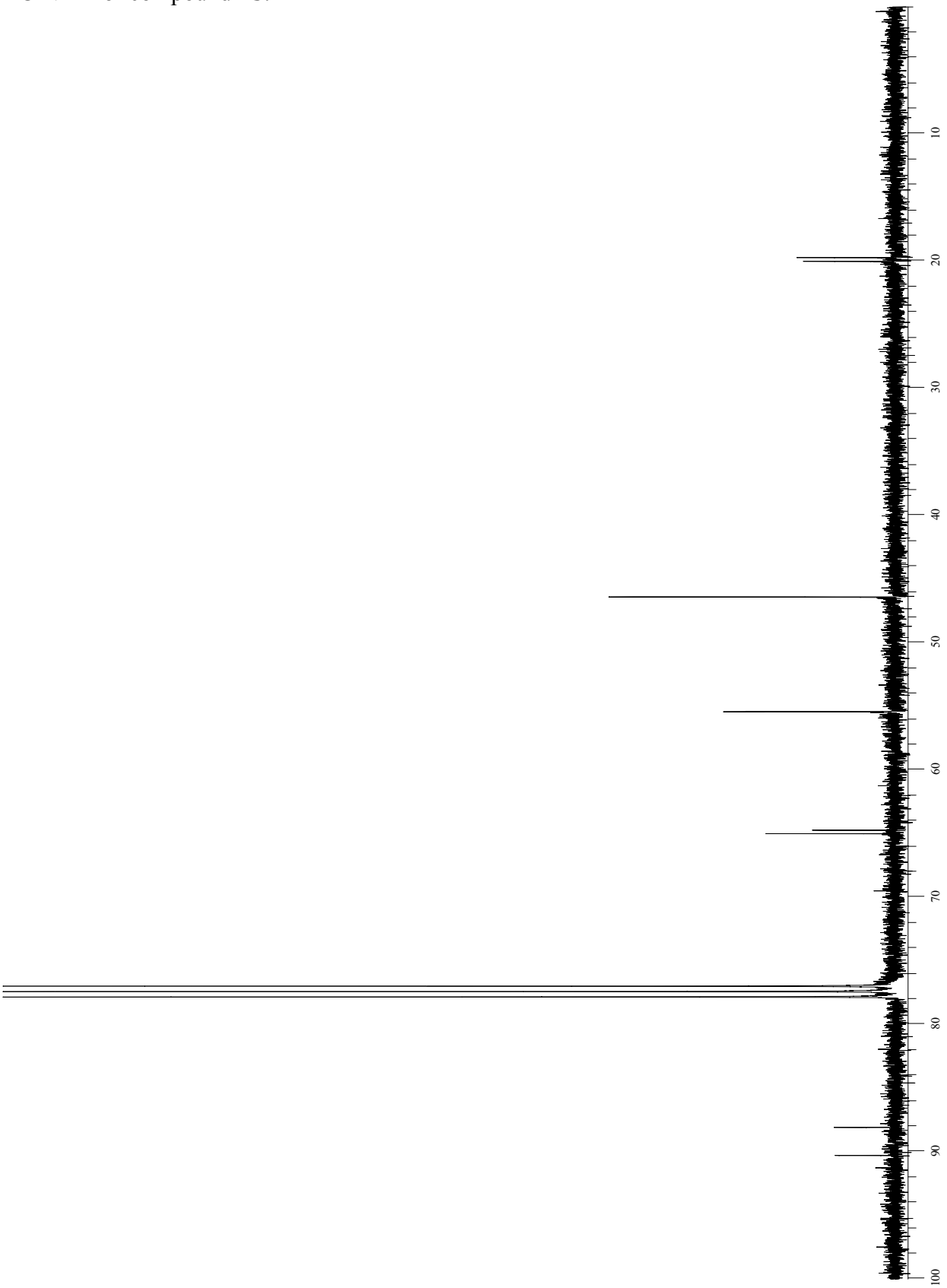
^{13}C NMR of compound **2a**:



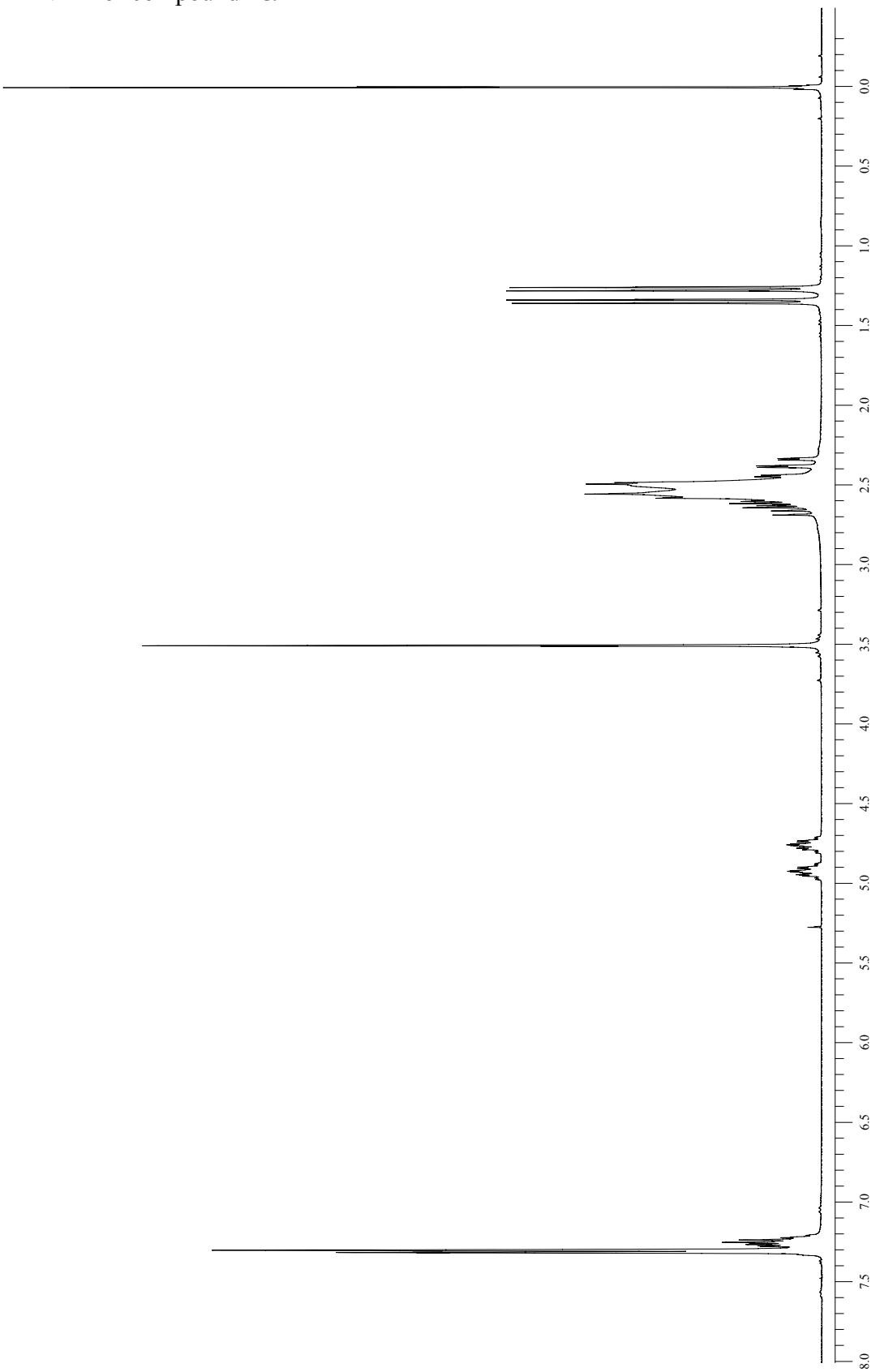
^{1}H NMR of compound **2b**:



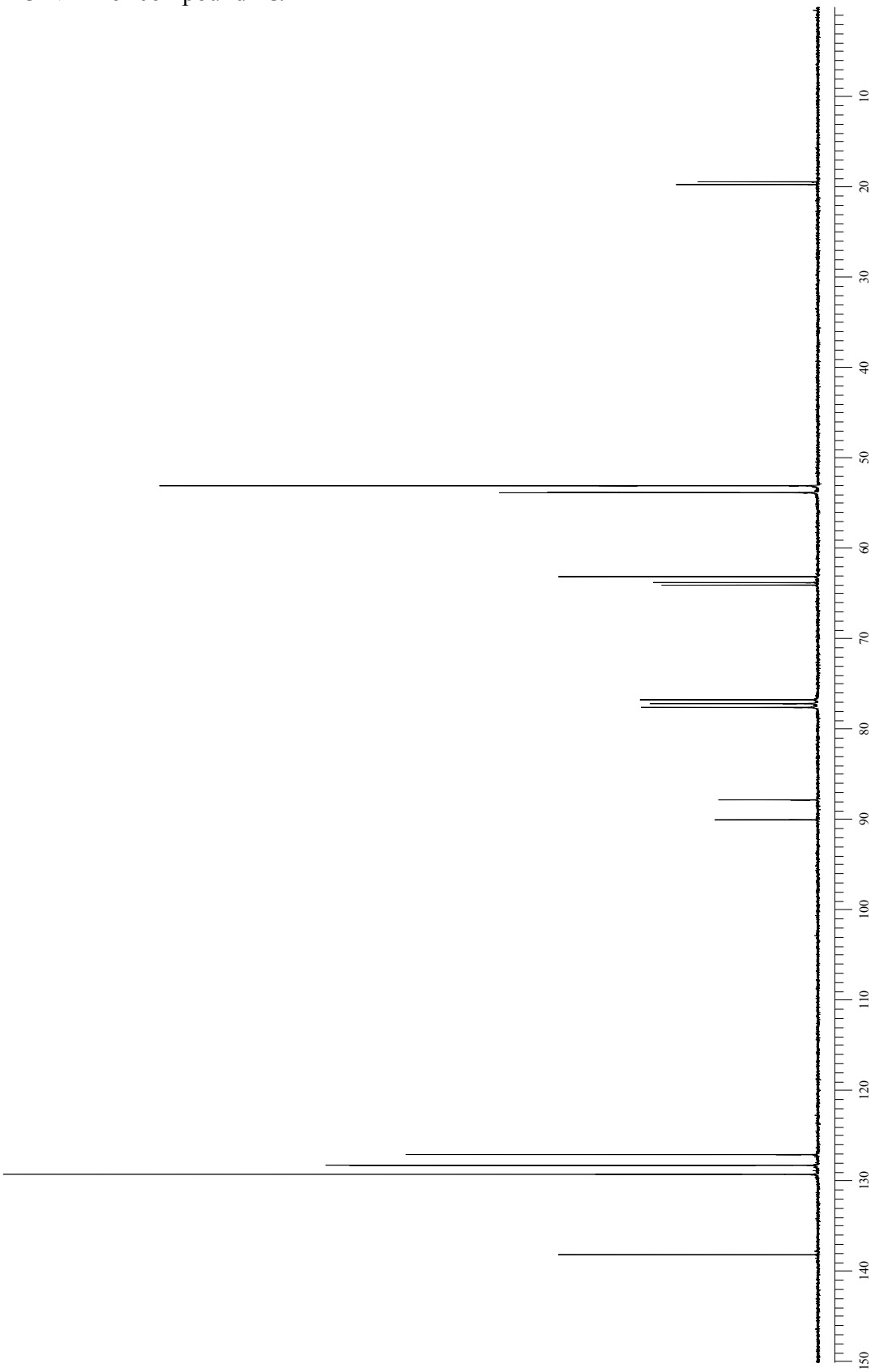
^{13}C NMR of compound **2b**:



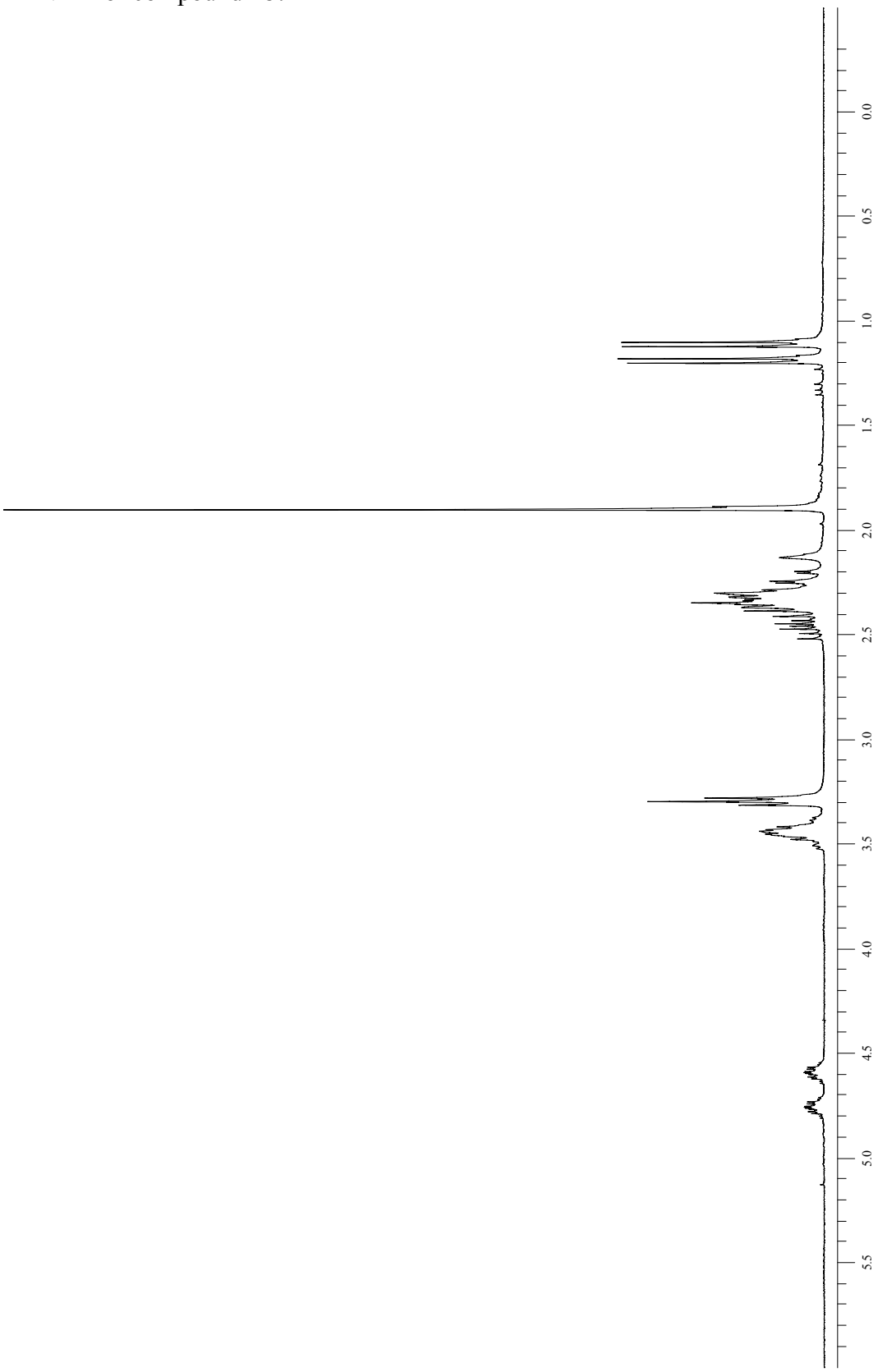
^{1}H NMR of compound **2c**:



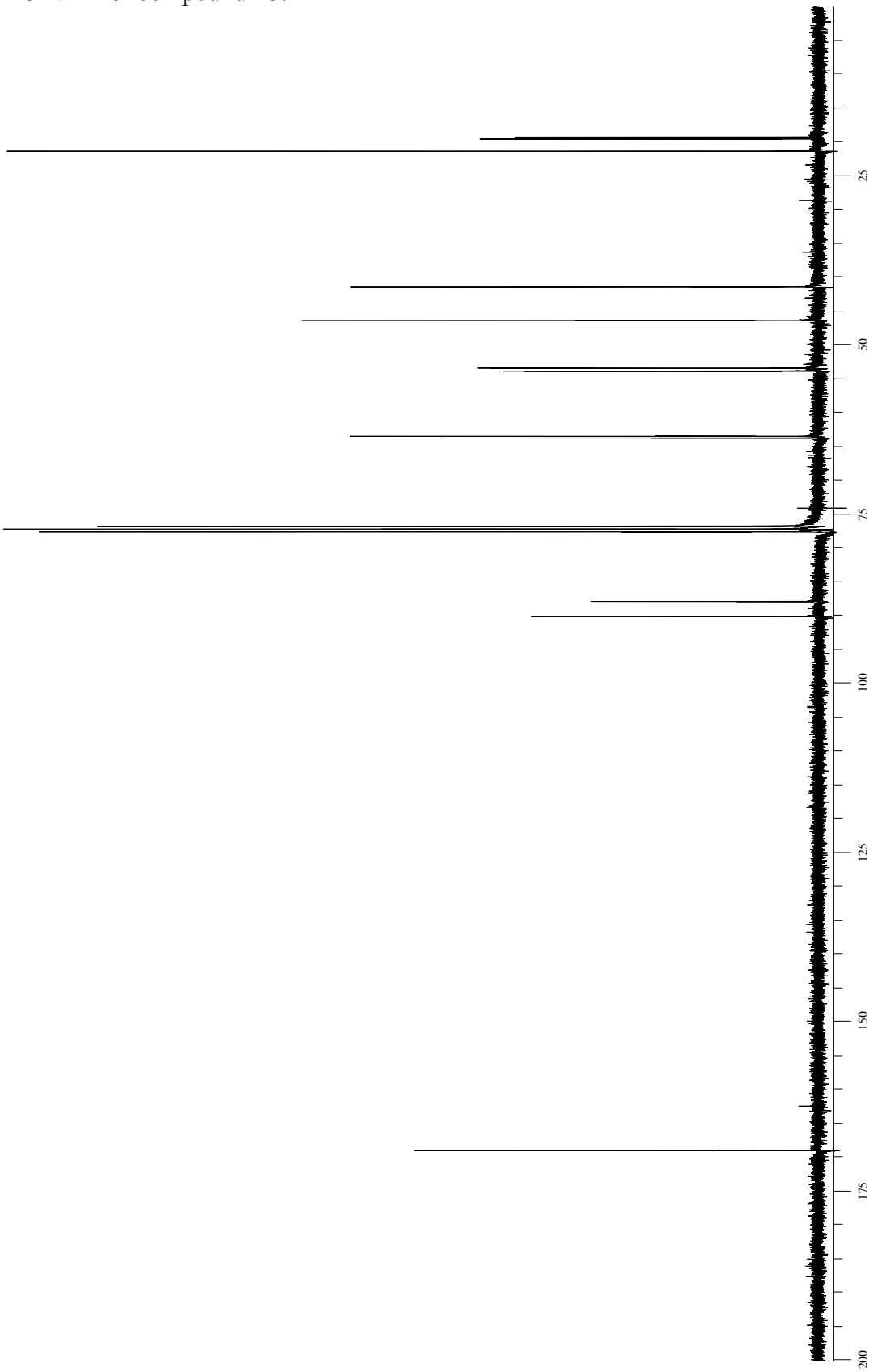
^{13}C NMR of compound **2c**:



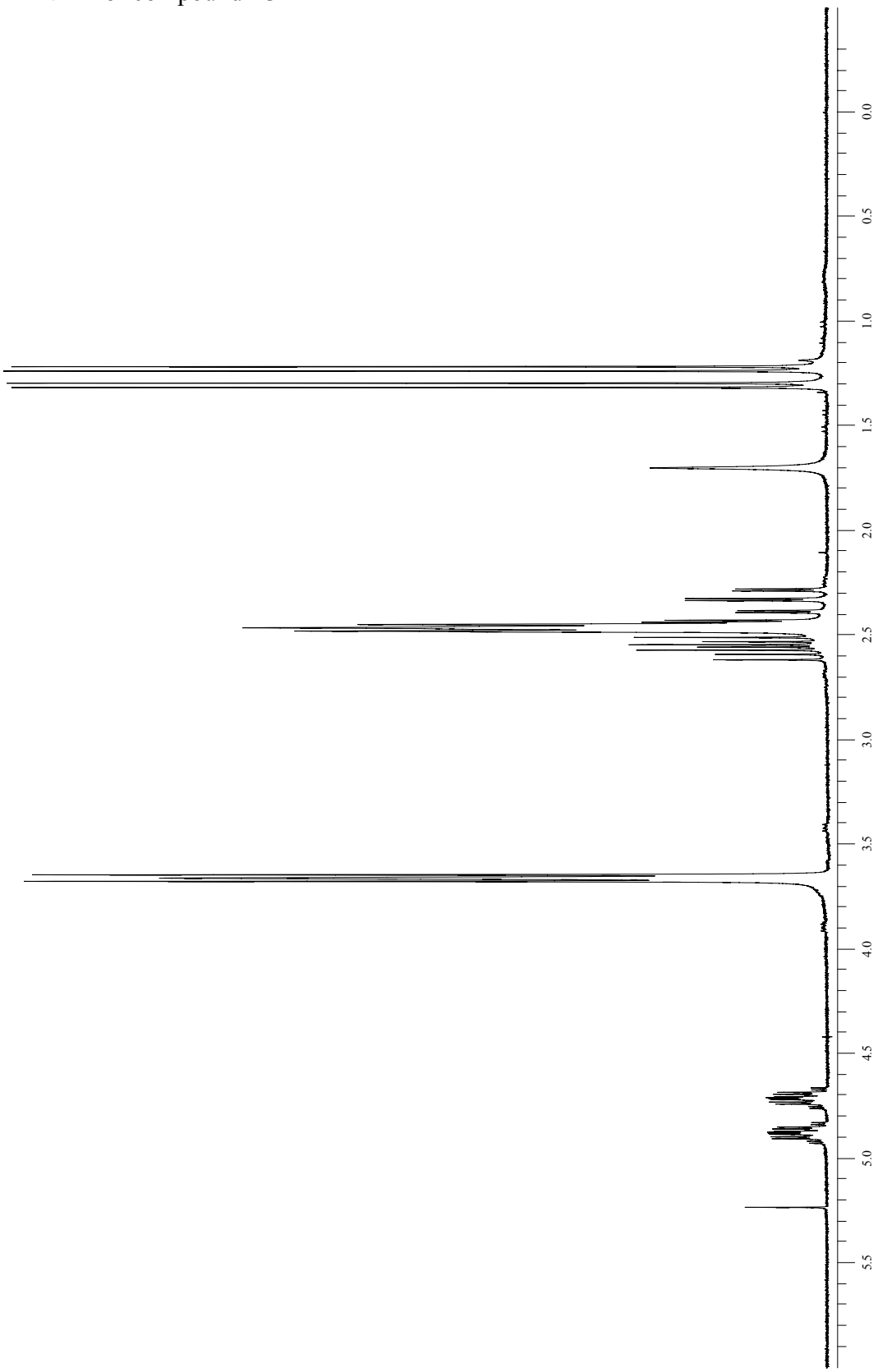
^{1}H NMR of compound **2d**:



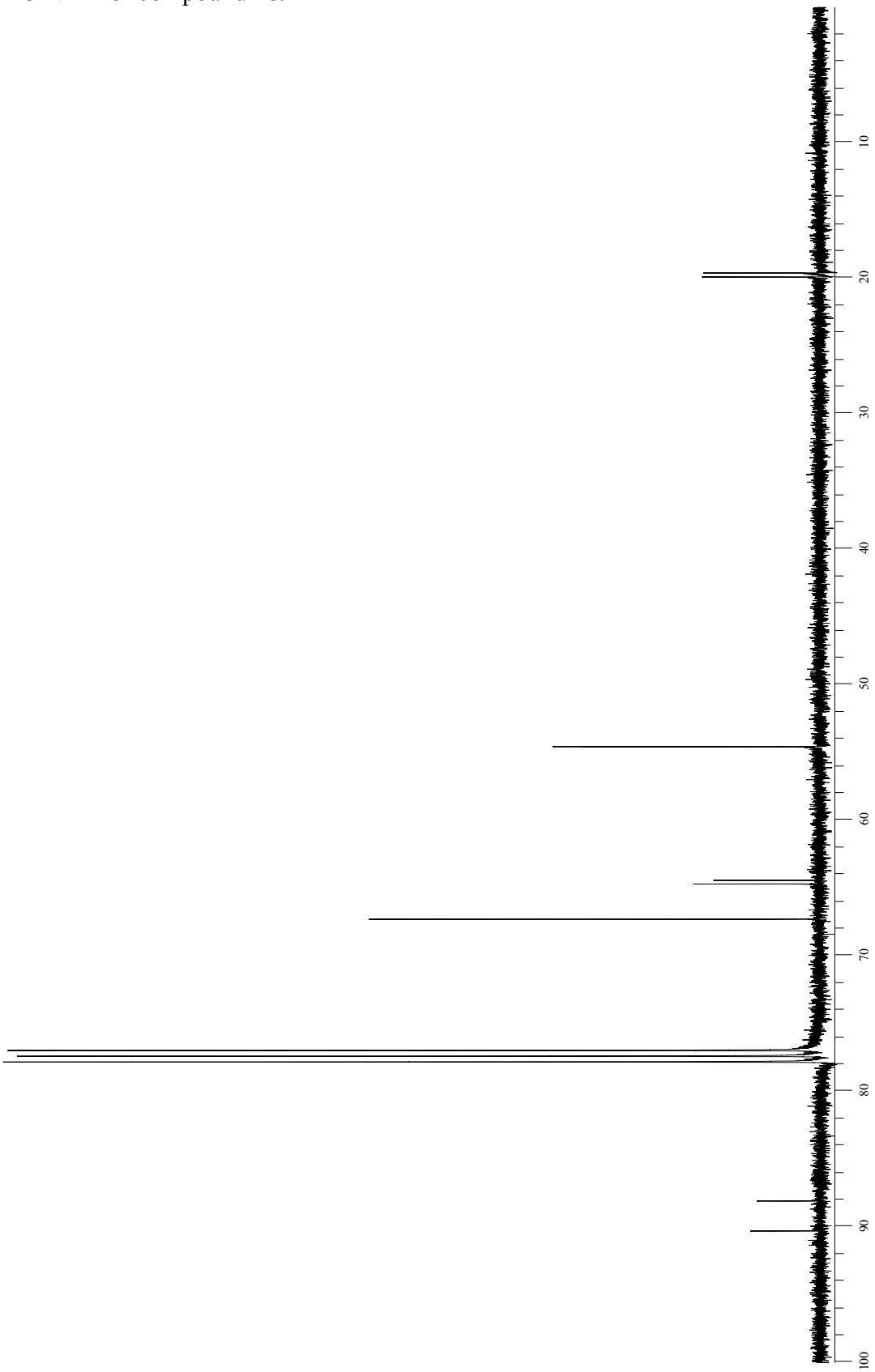
^{13}C NMR of compound **2d**:



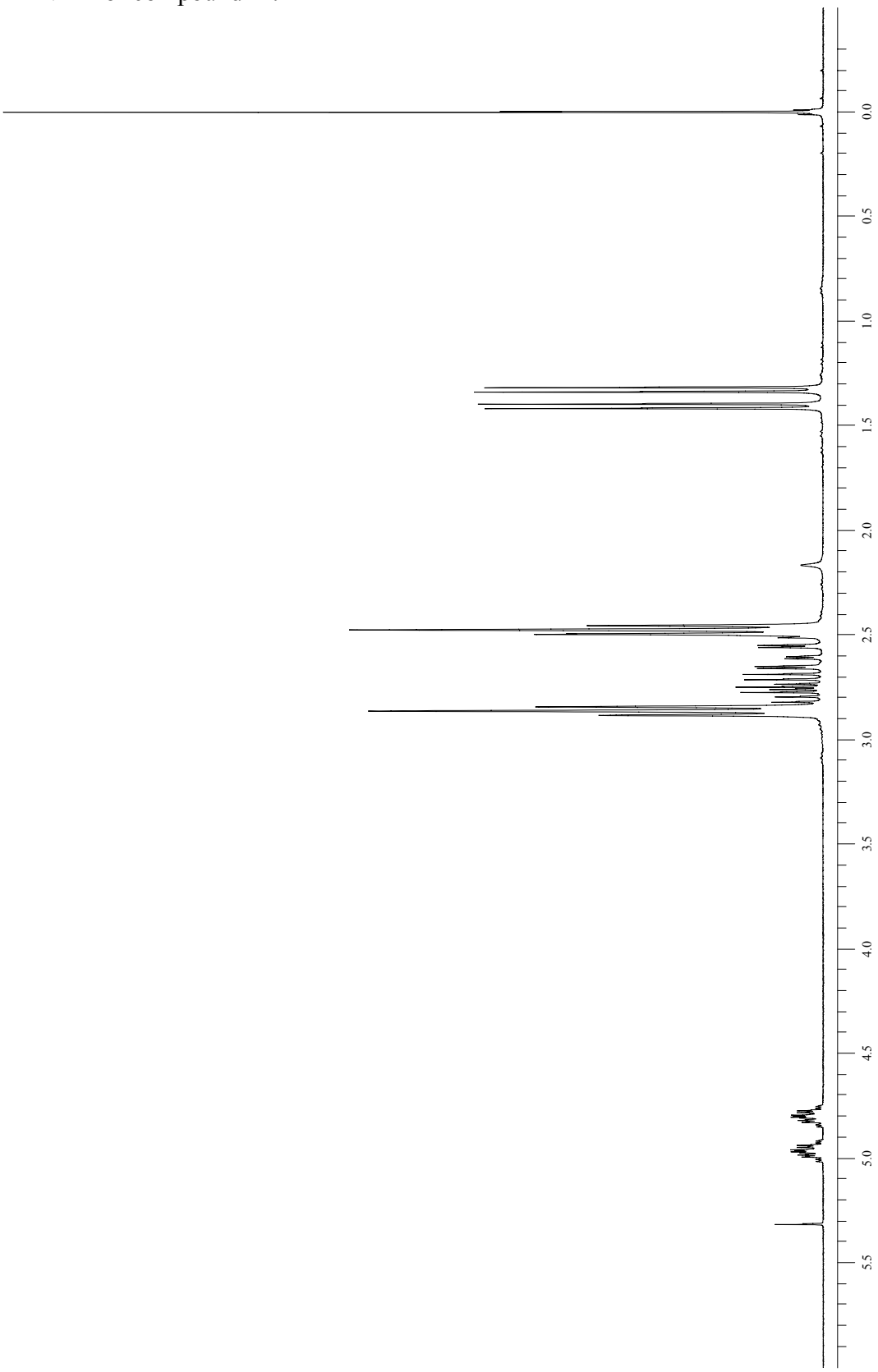
^{1}H NMR of compound **2e**



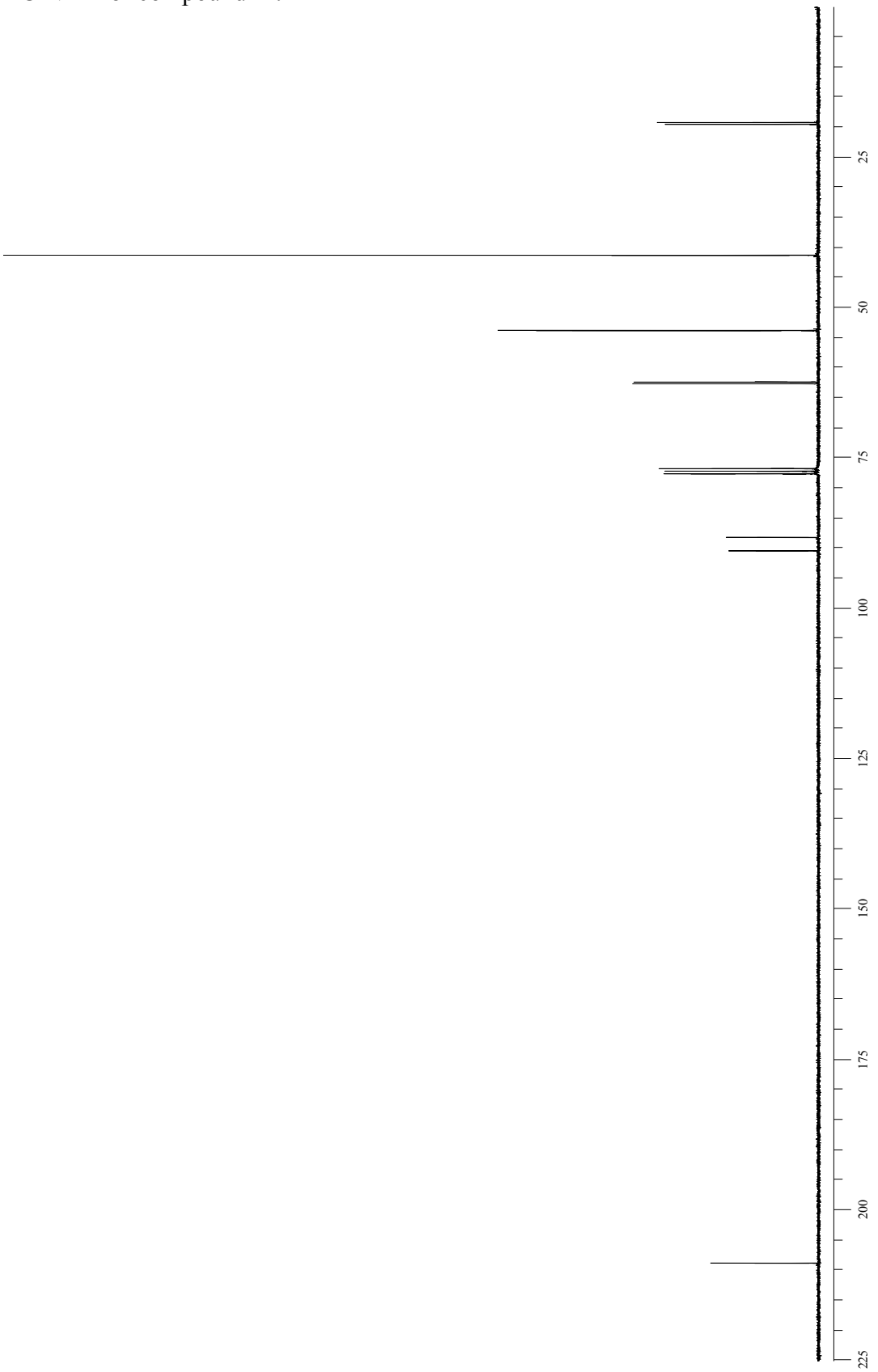
^{13}C NMR of compound **2e**:



^{1}H NMR of compound **2f**:

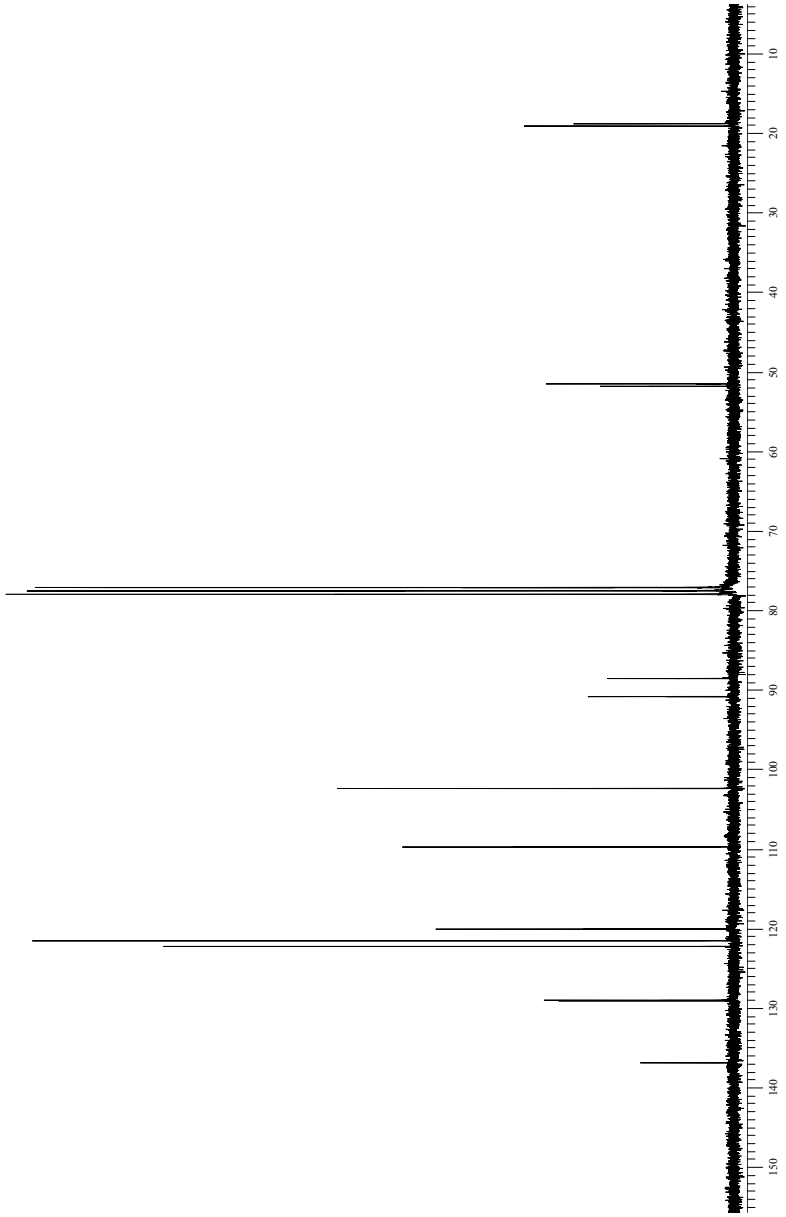


^{13}C NMR of compound **2f**:

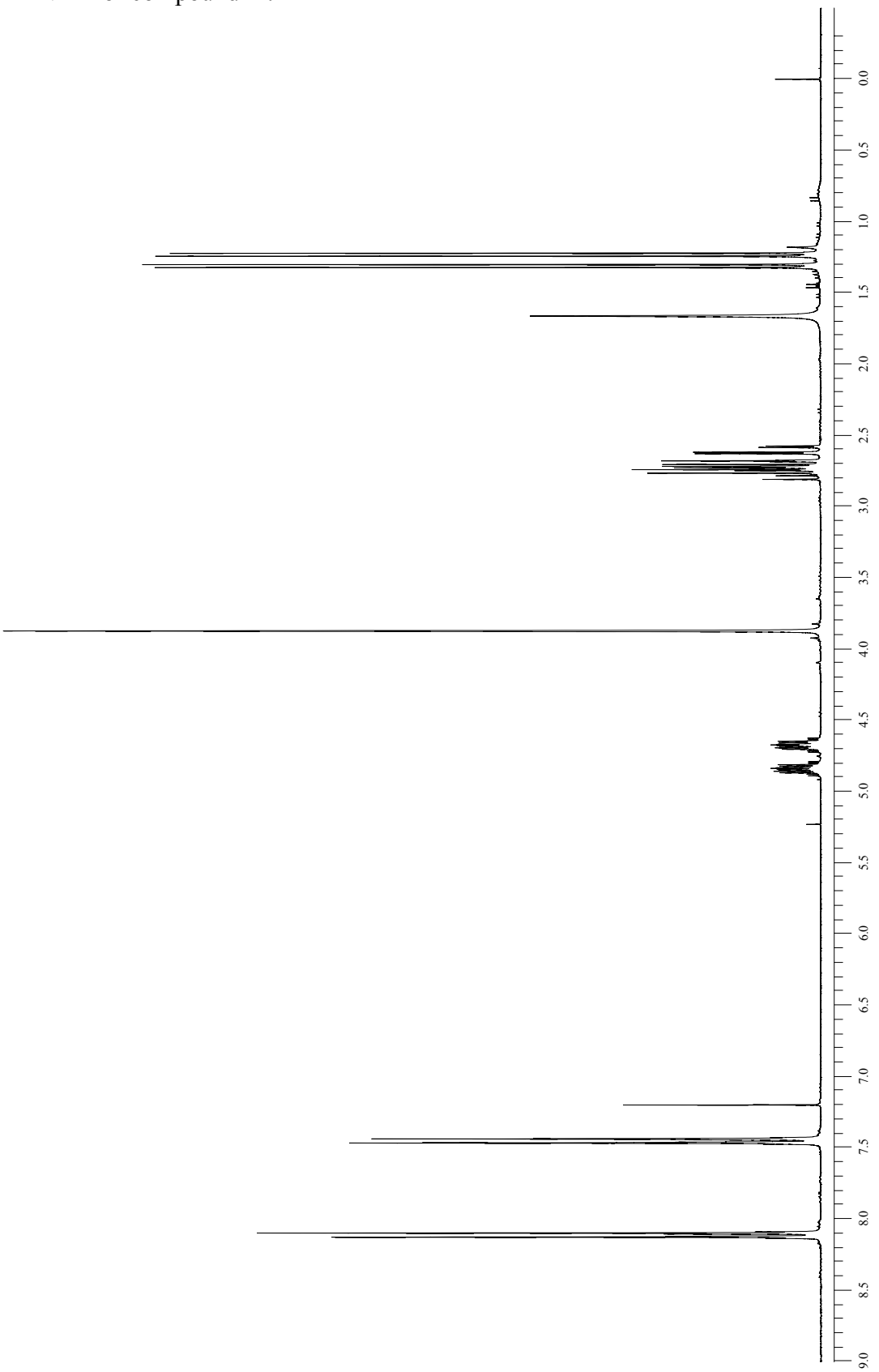


^{1}H NMR of compound **2g**:

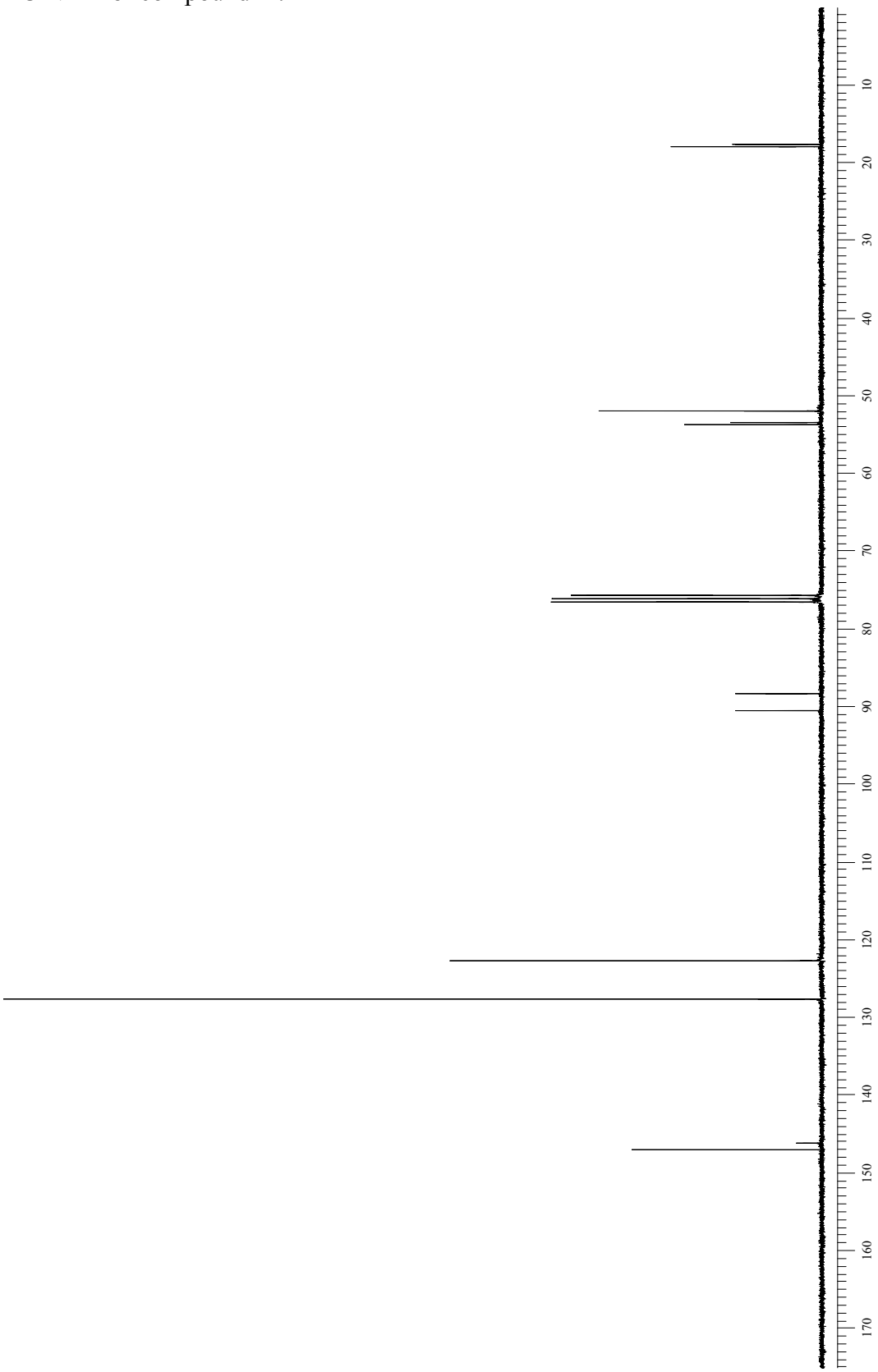
^{13}C NMR of compound **2g**:



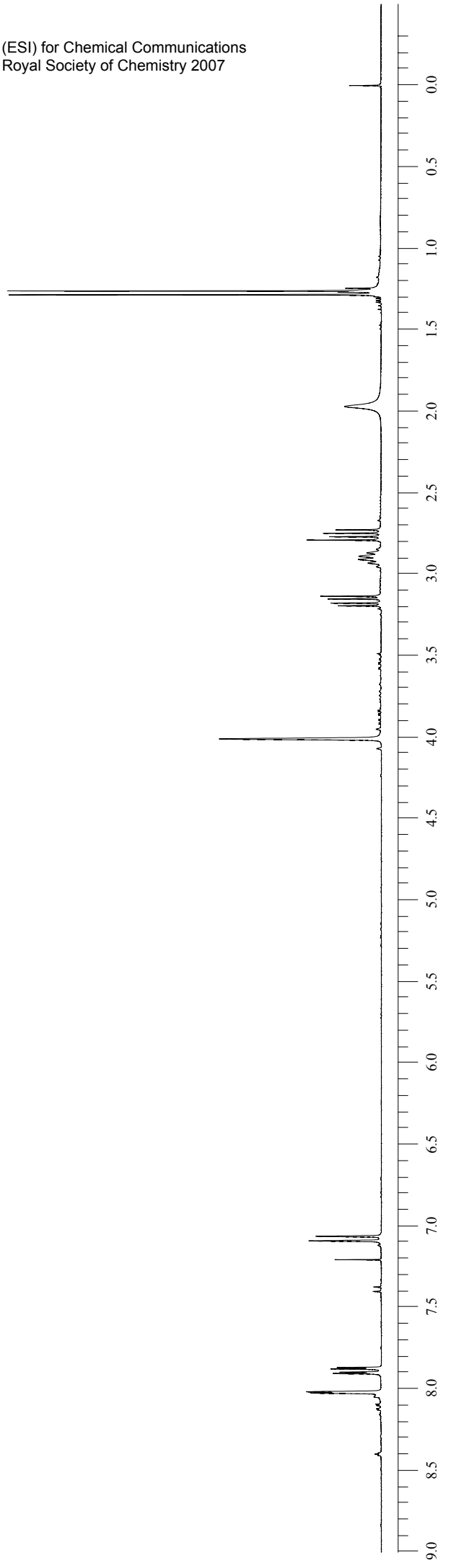
^{1}H NMR of compound **2i**:



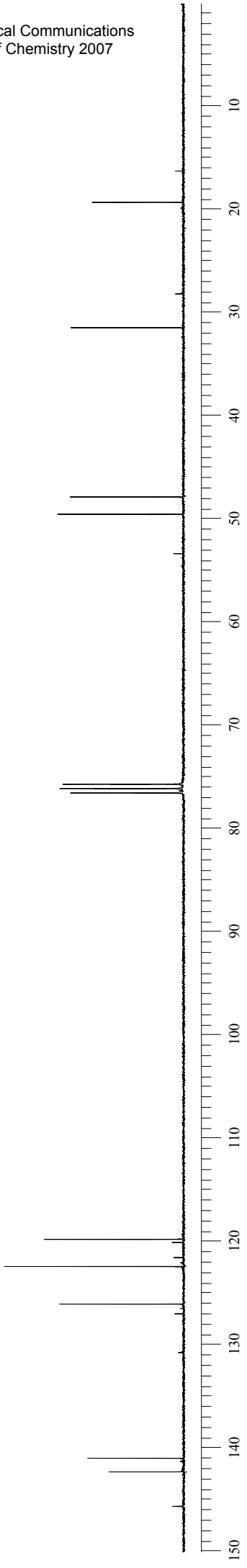
^{13}C NMR of compound **2i**:



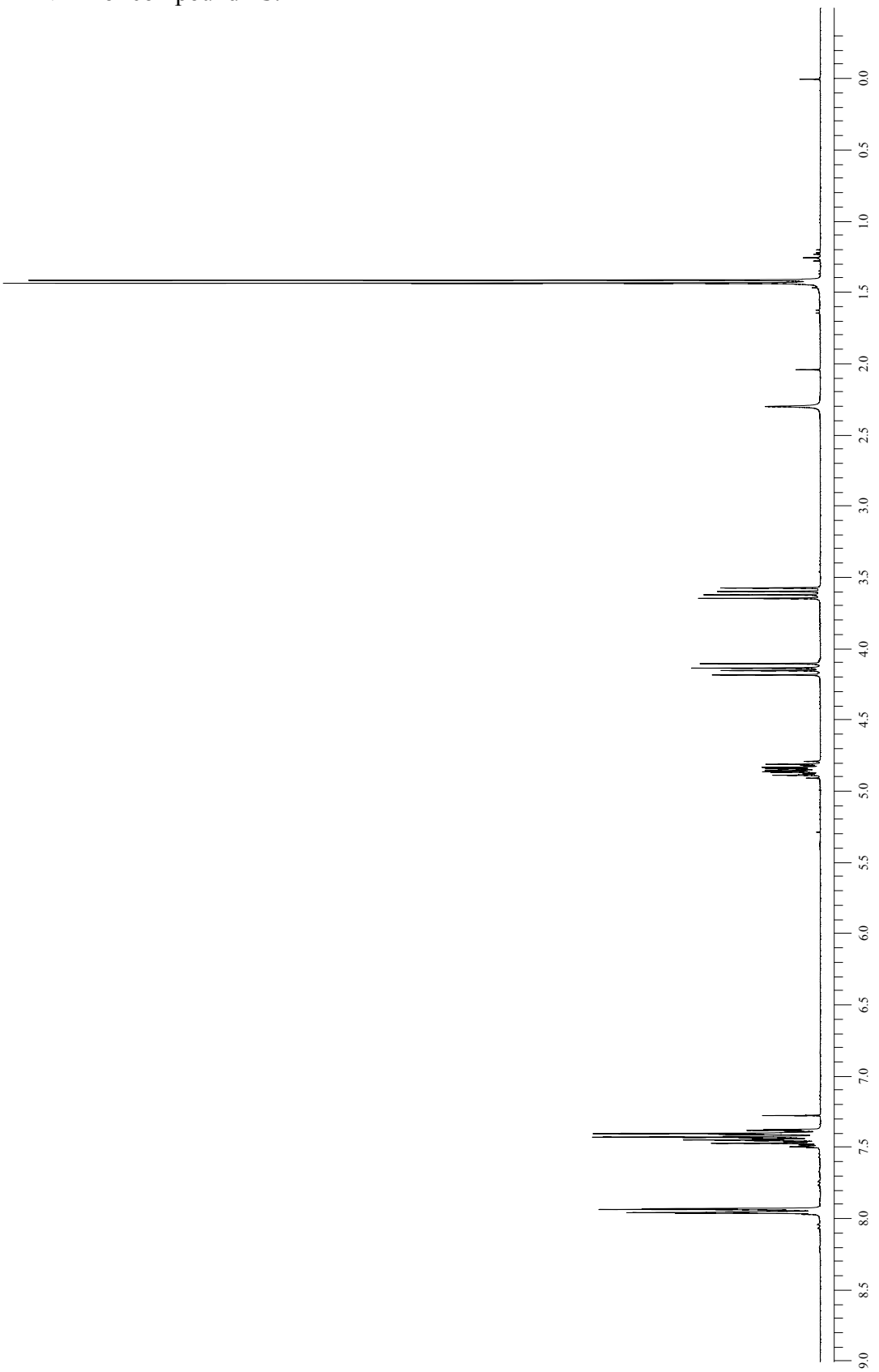
^{1}H NMR of compound **2i'**:



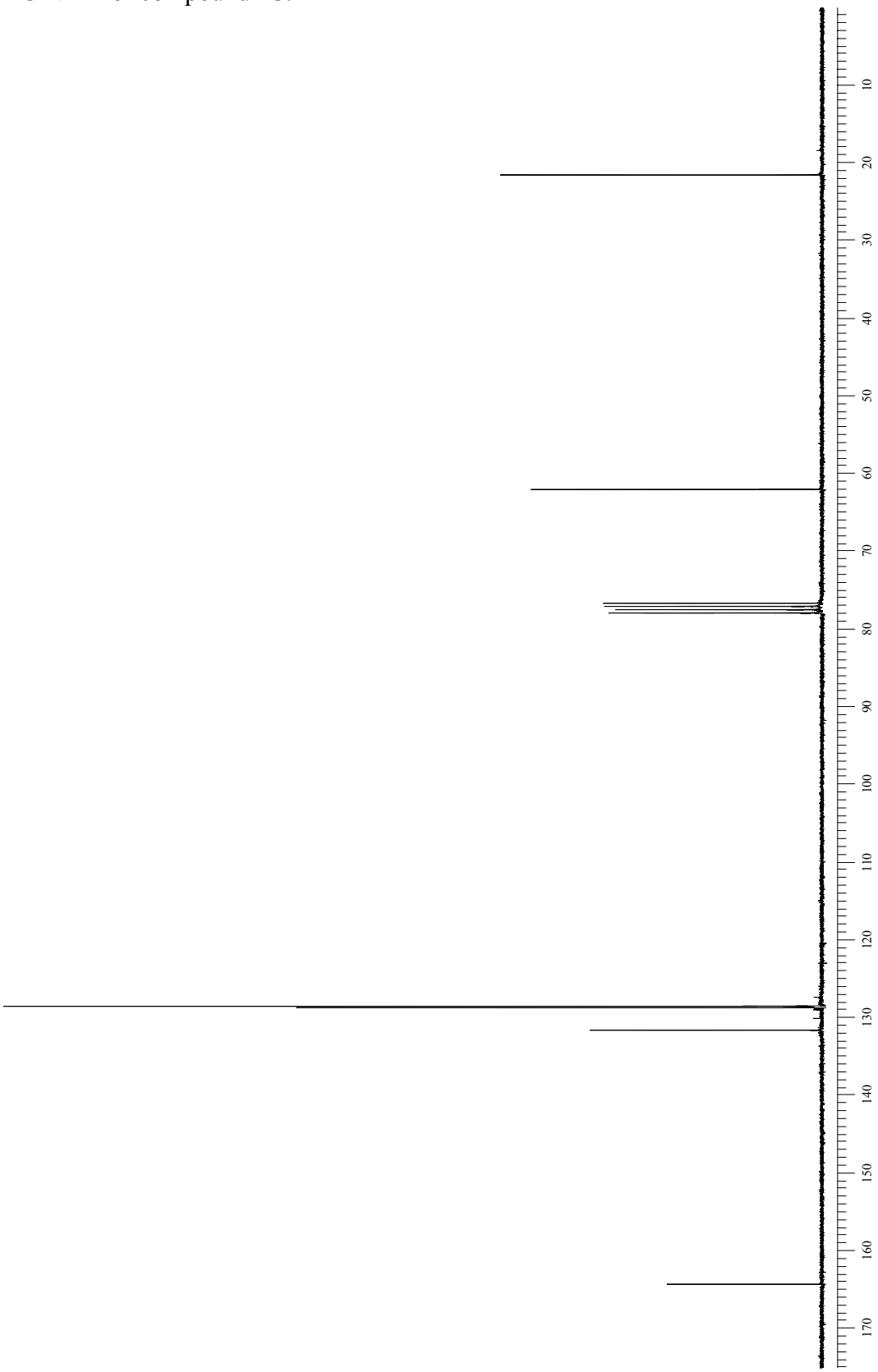
^{13}C NMR of compound **2i'**:



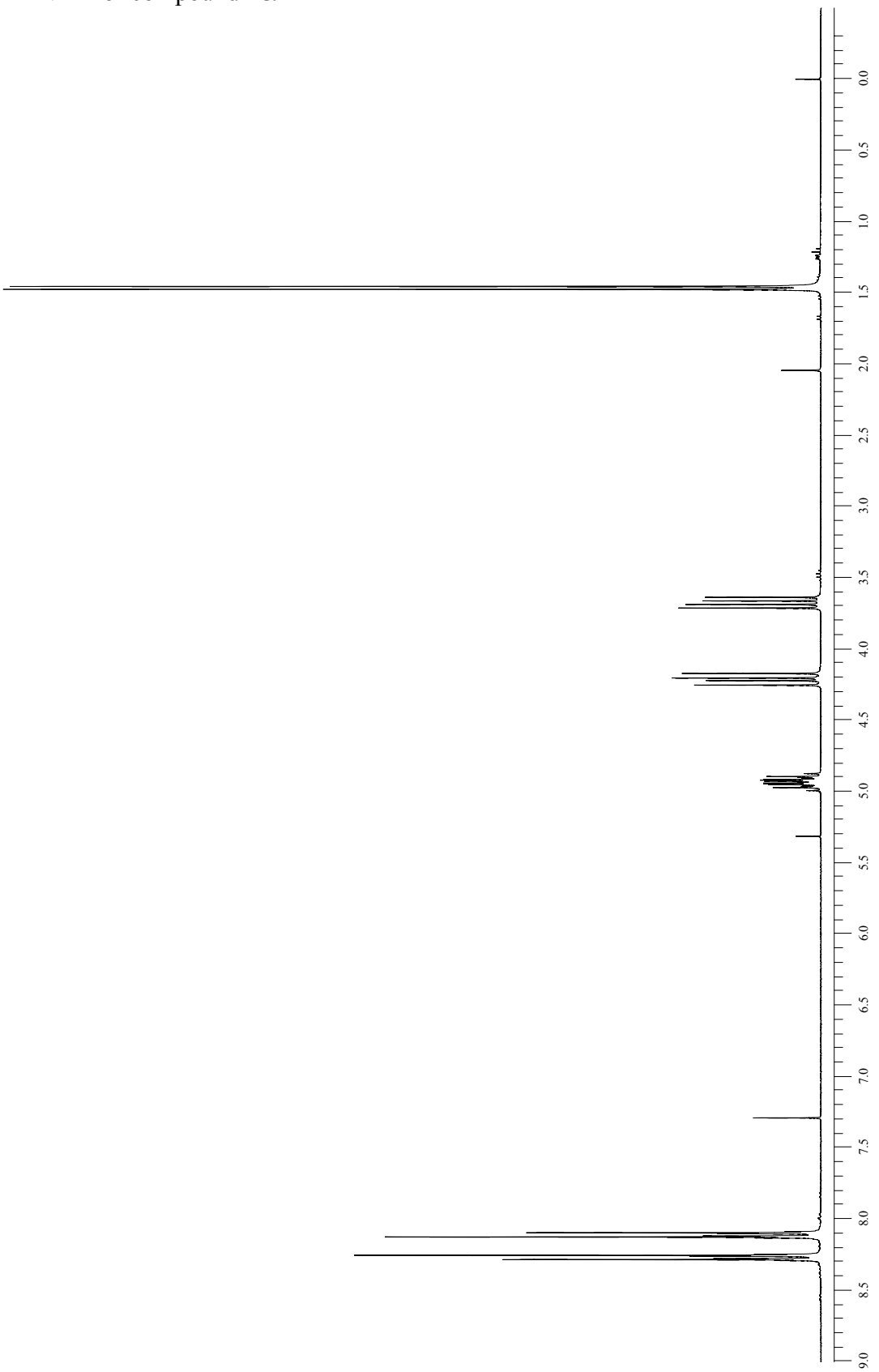
^{1}H NMR of compound **4b**:



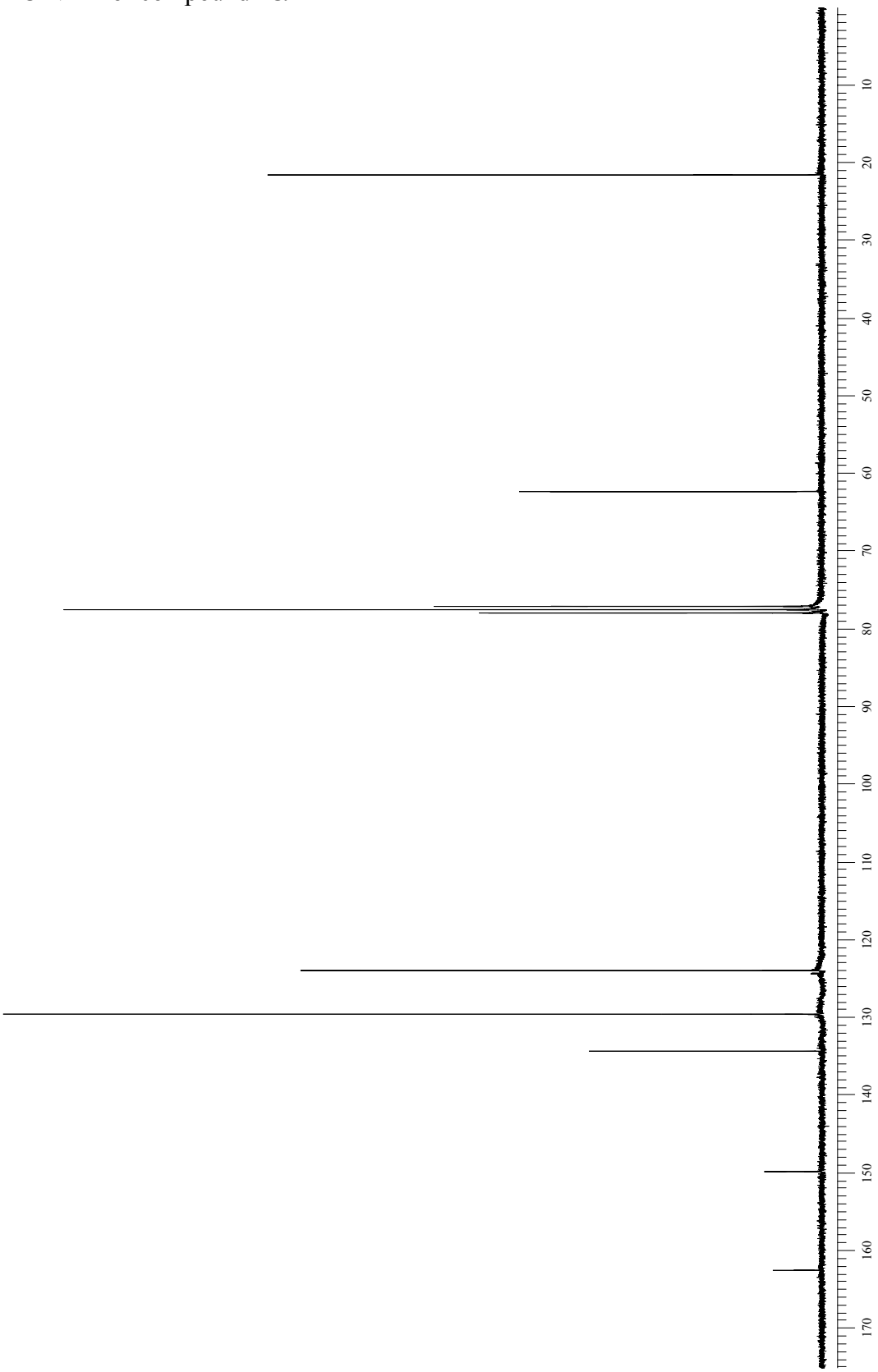
^{13}C NMR of compound **4b**:



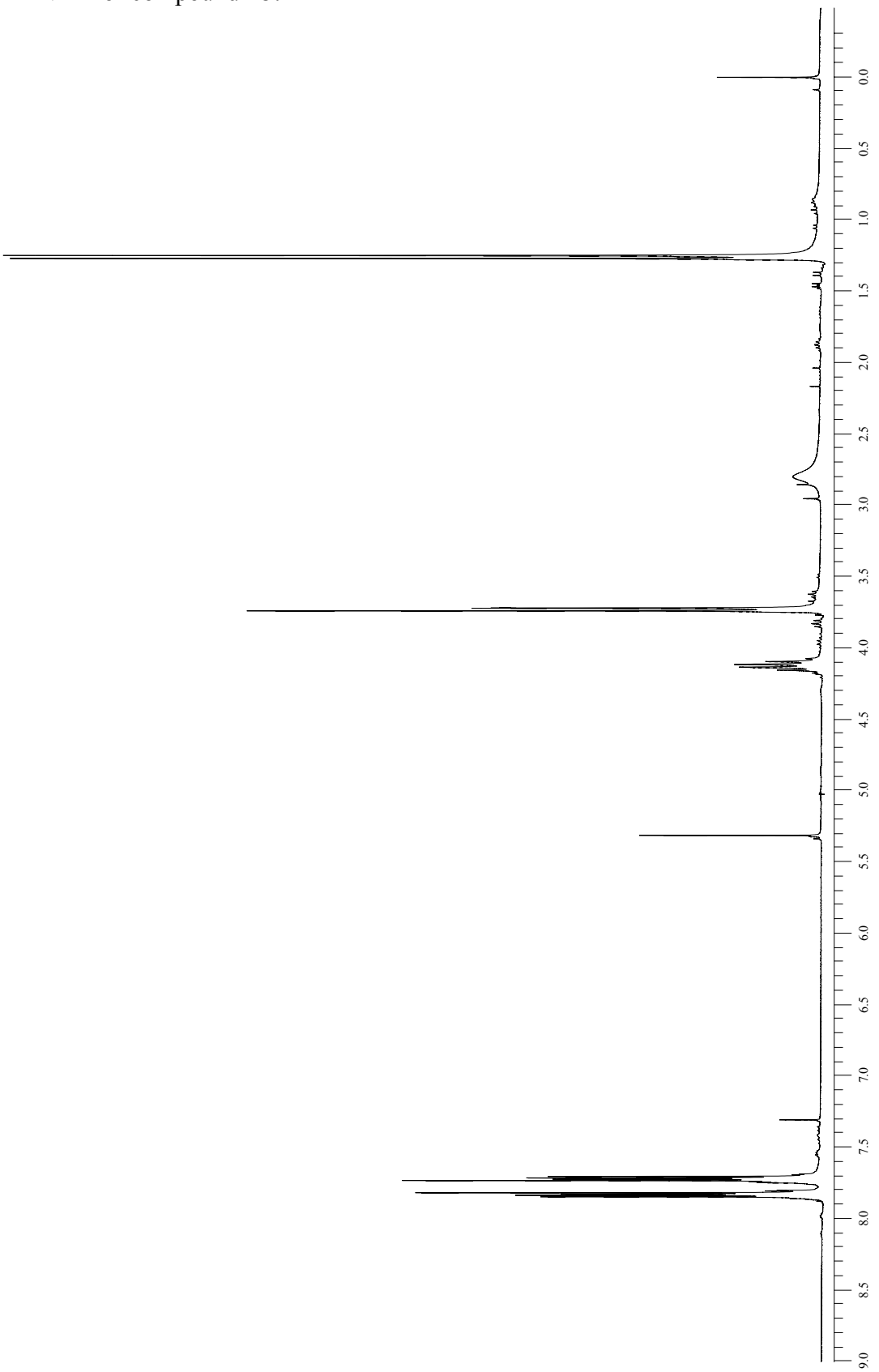
^{1}H NMR of compound **4c**:



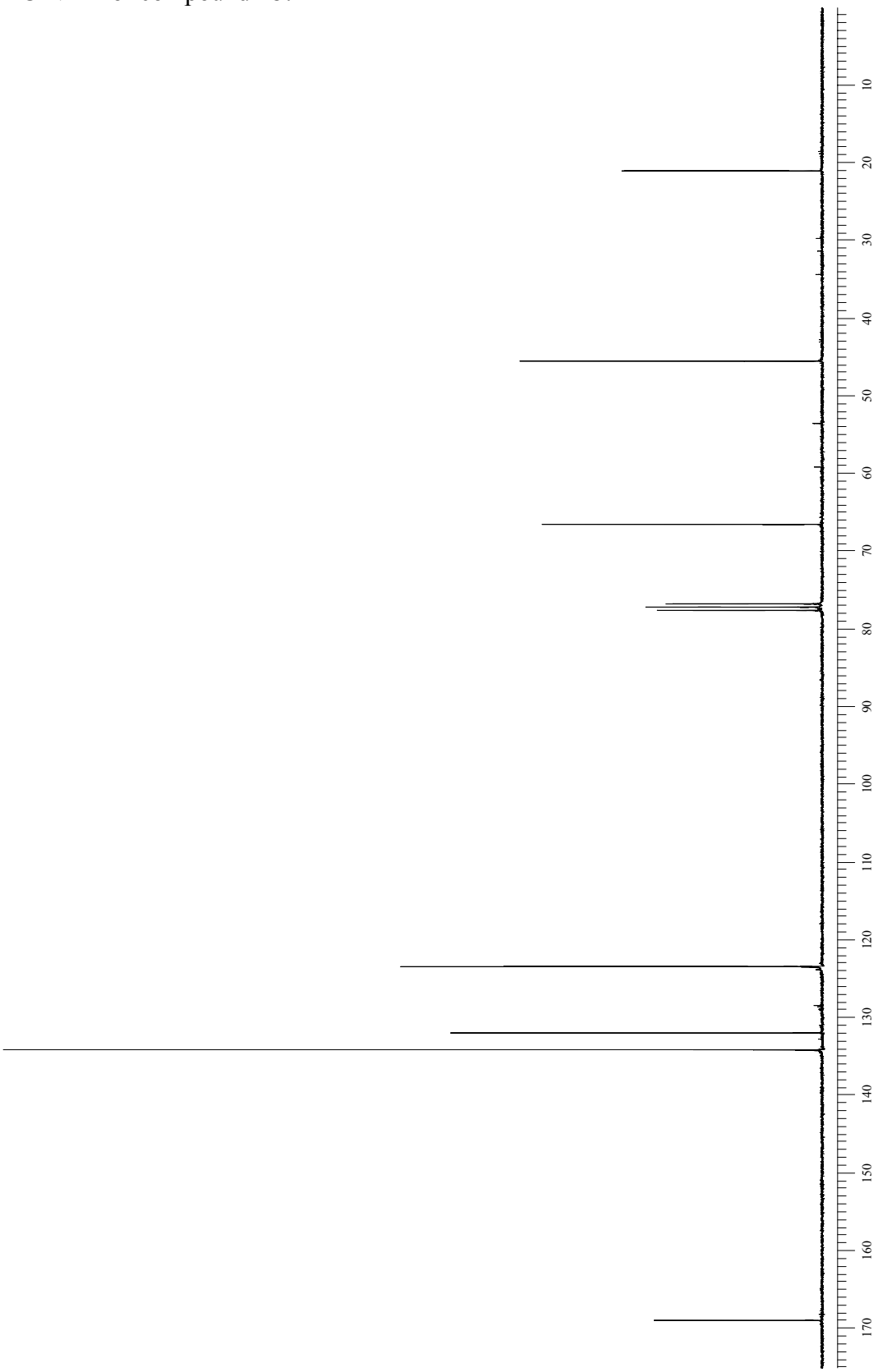
^{13}C NMR of compound **4c**:



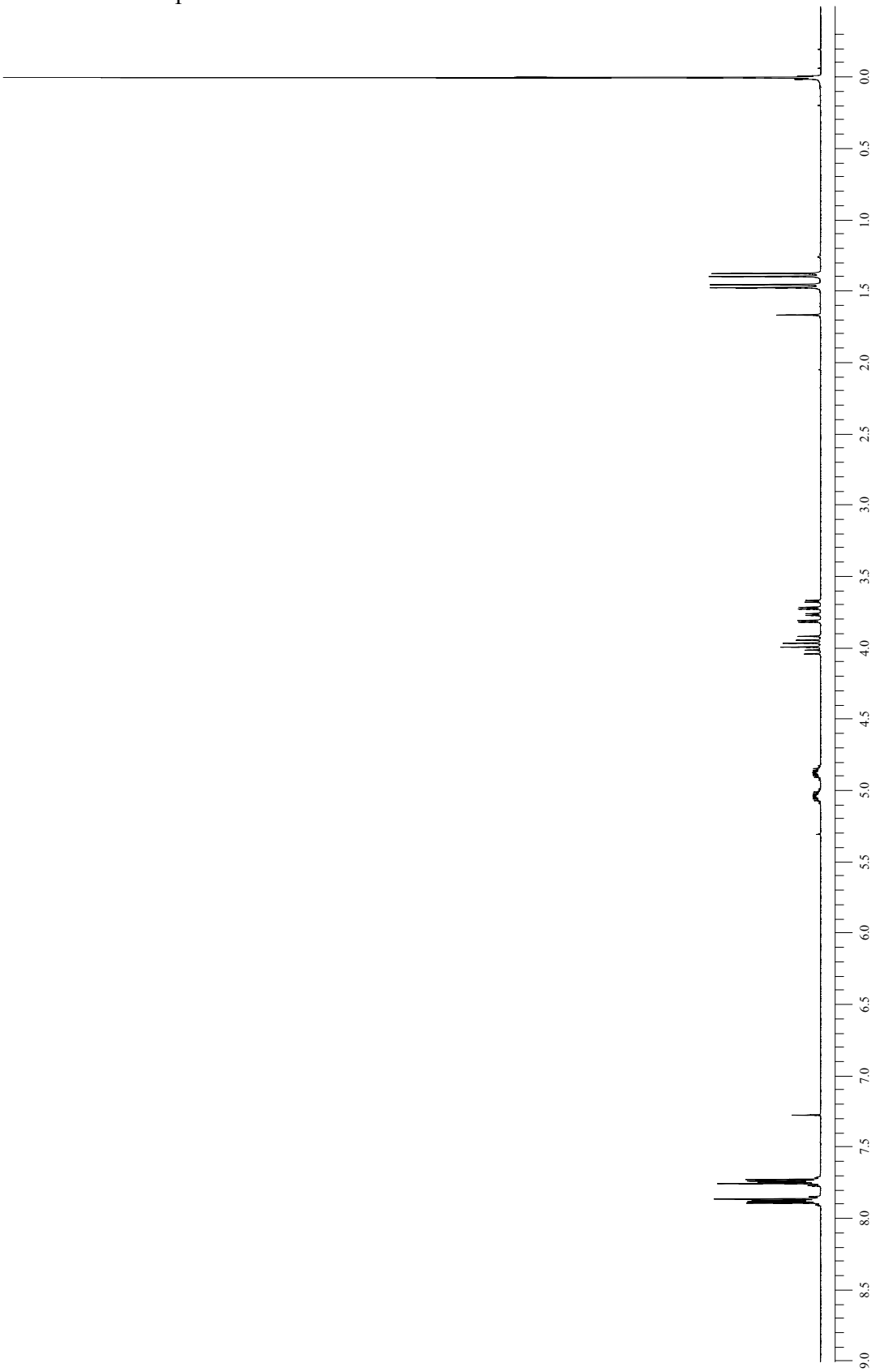
^{1}H NMR of compound **4d**:



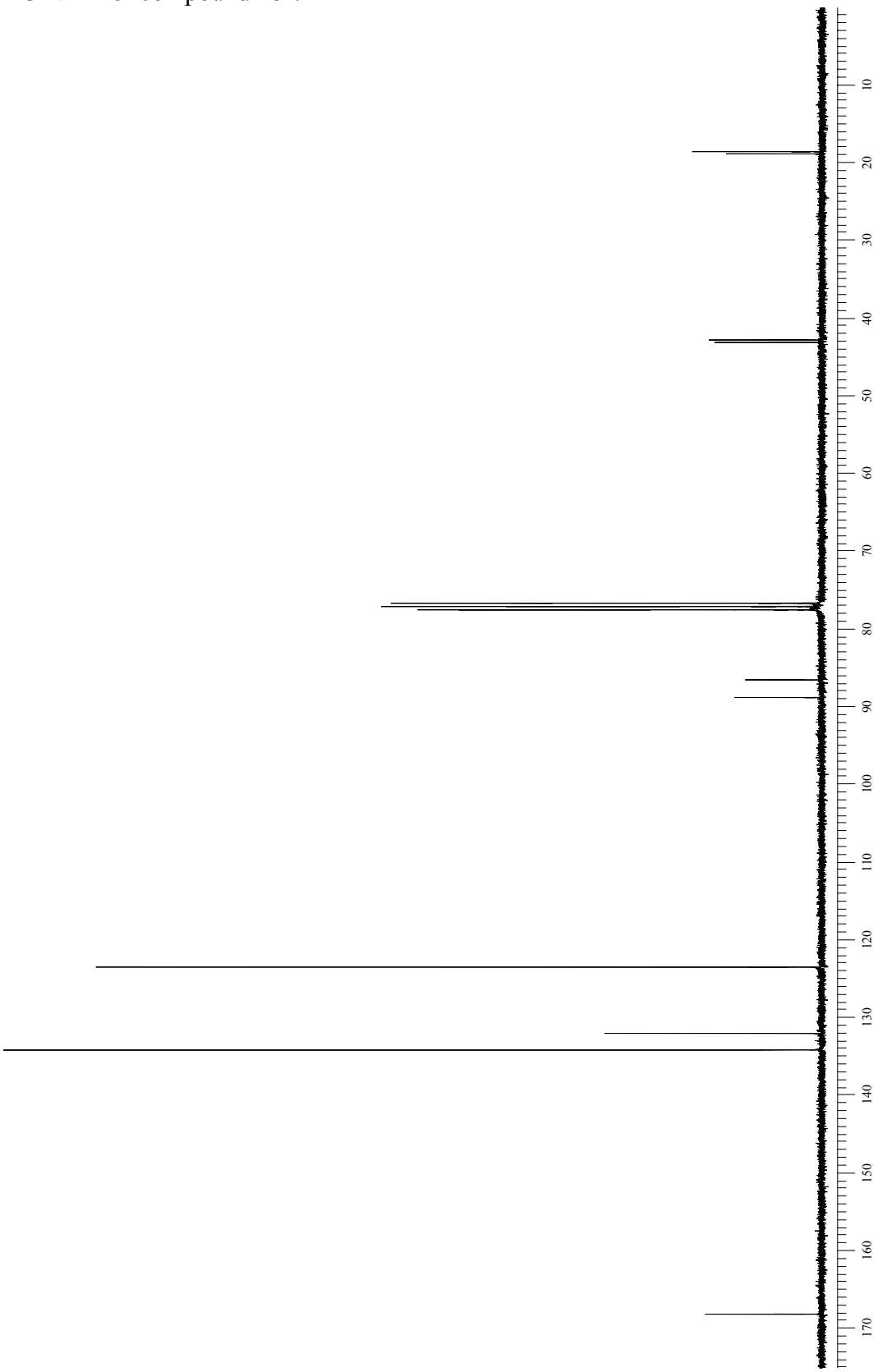
^{13}C NMR of compound **4d**:



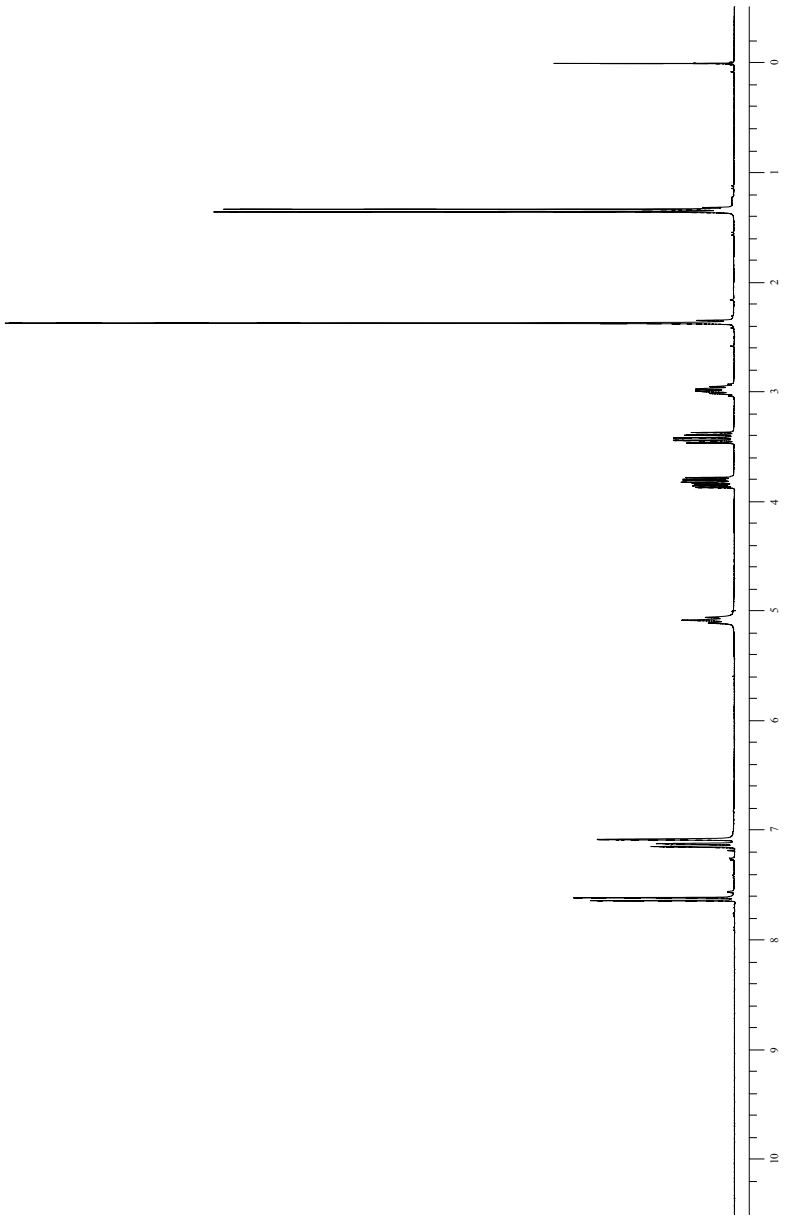
^{1}H NMR of compound **4d'**:



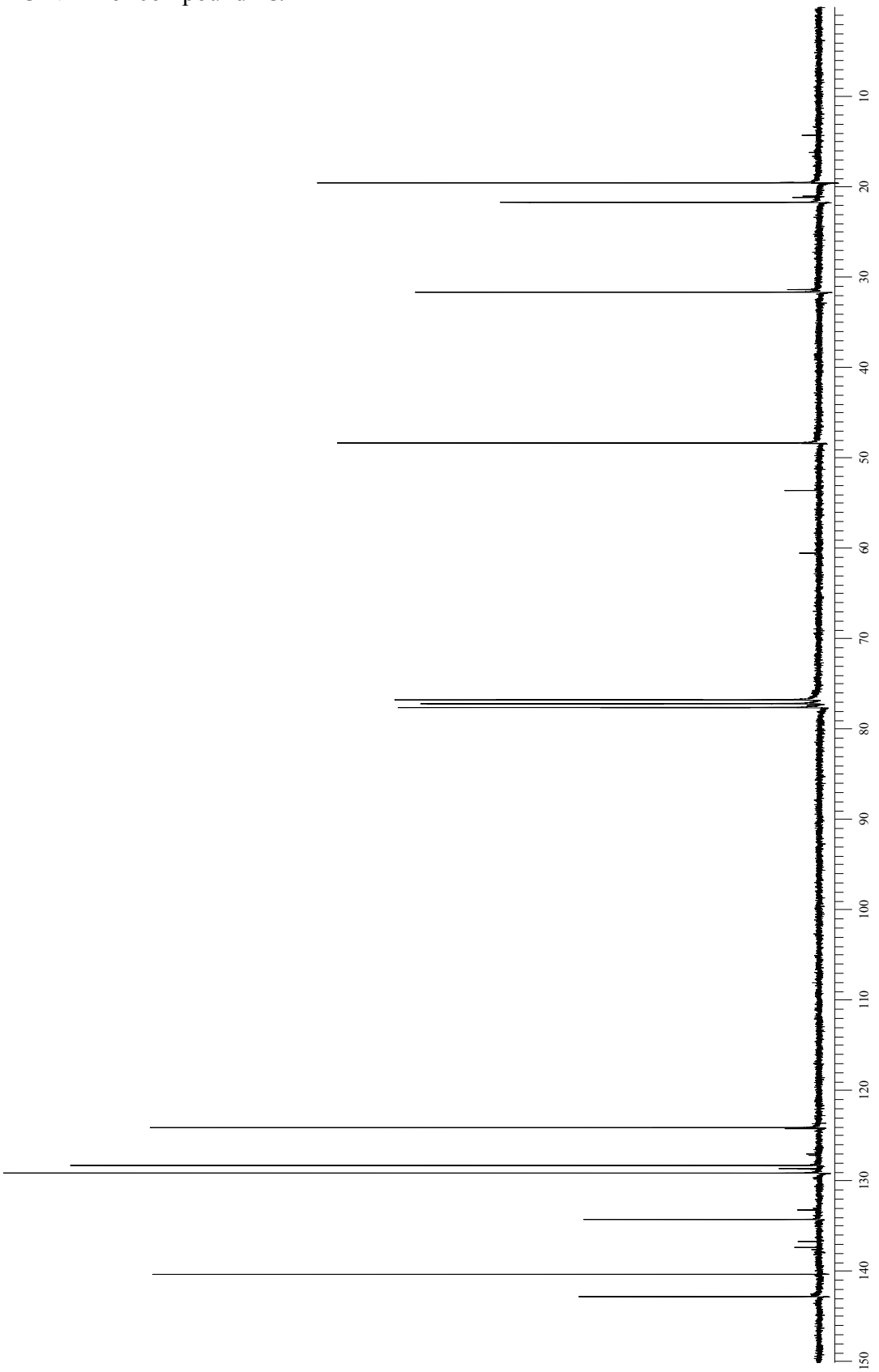
^{13}C NMR of compound **4d'**:



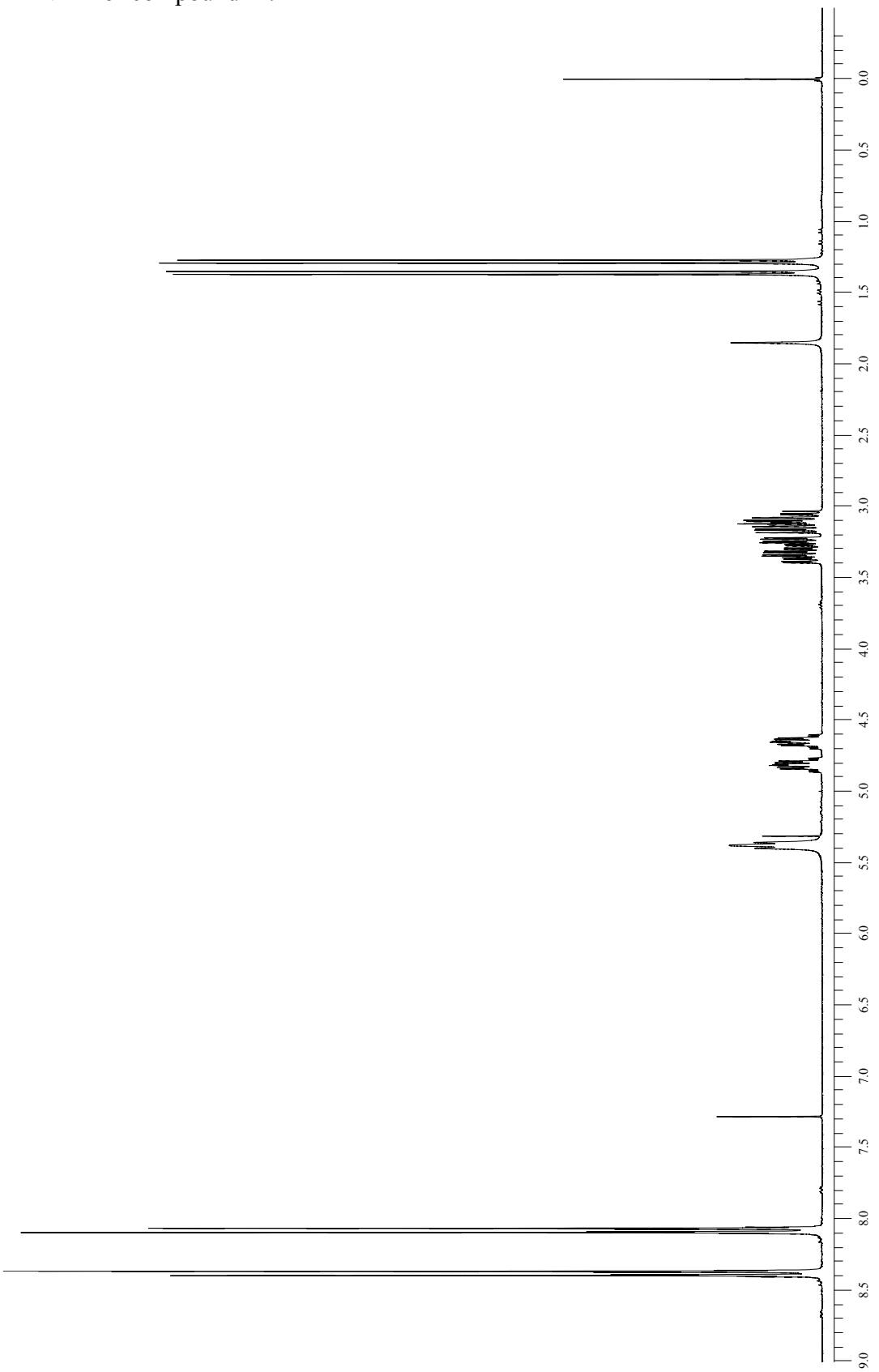
^{1}H NMR of compound **4e**:



^{13}C NMR of compound **4e**:



^{1}H NMR of compound **4f**:



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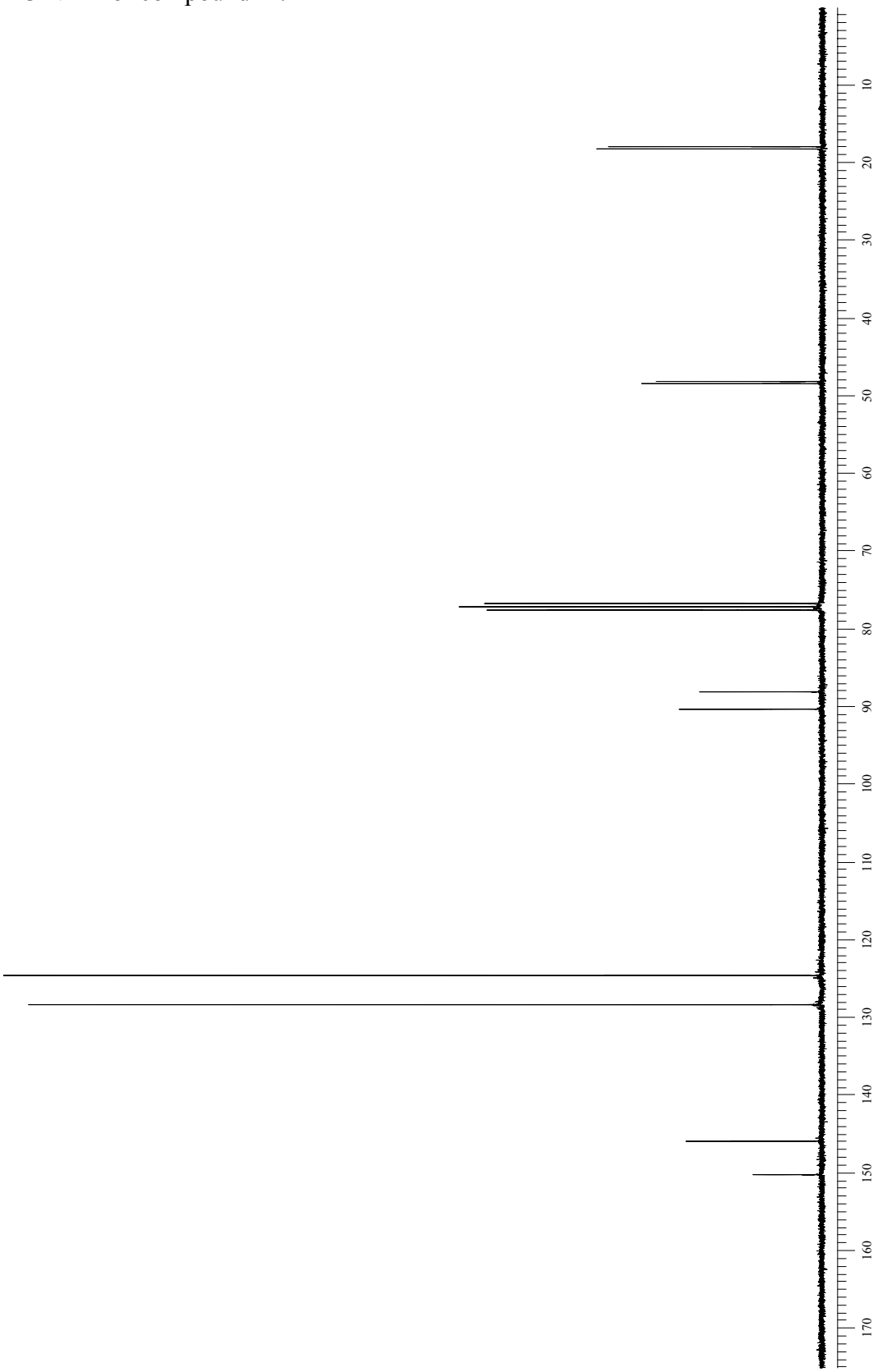
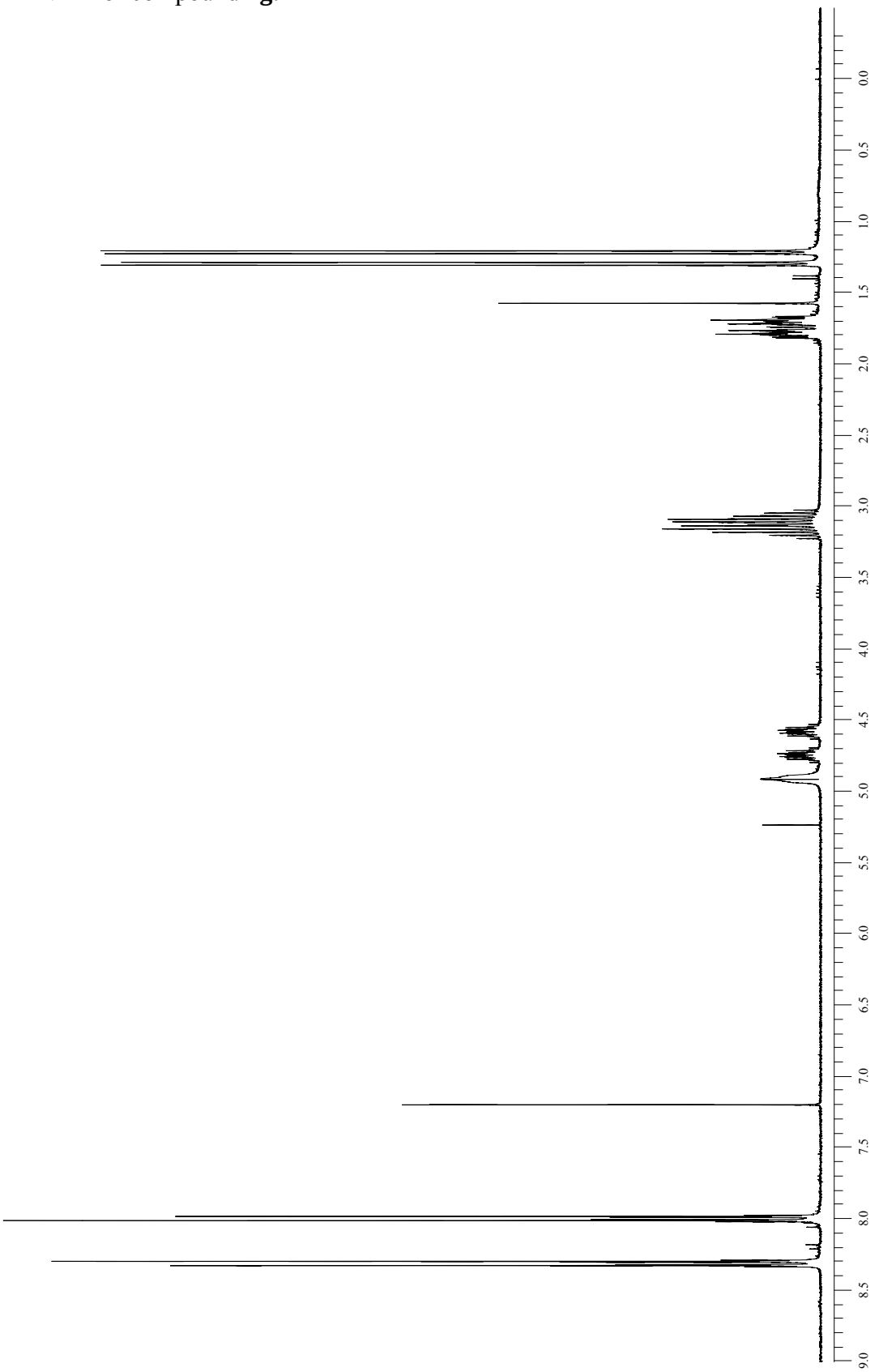


^{1}H NMR of compound **4g**:



^{13}C NMR of compound **4g**: