Synthesis of Aryl Enopyranones Directly Accessed From Glycals and Aromatic Halides Enroute Toward 2-Deoxy-β-C-Aryl Glycosides

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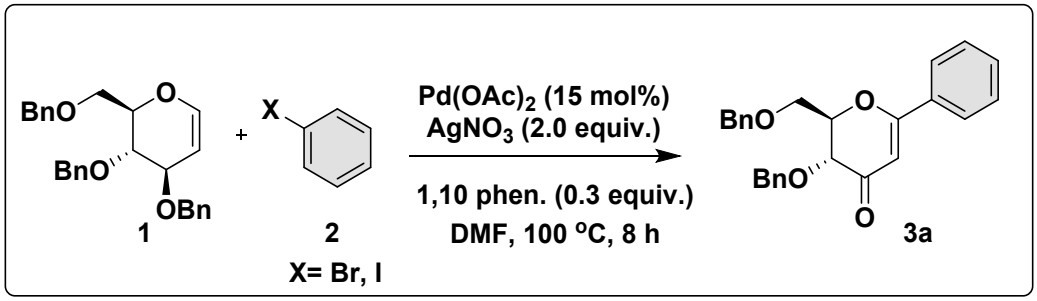
1. General Information

All compounds were characterized by spectroscopic data. The ^{1}H and ^{13}C NMR spectra were obtained using 400 and 500 MHz spectrometers with TMS as internal standard. Chemical shift (∂) is expressed in ppm, J values are given in Hz and deuterated $CDCl_3$ was used as solvent. All the reactions were monitored by thin layer chromatography (TLC). Column chromatography was performed on silica gel (60-120 mesh). All the chemicals used in experiments were purchased from commercial source mostly from sigma Aldrich and were used without further purification.

2. Experimental

2.1. General procedures

2.1.1 General procedure for the synthesis of C-1 aryl enopyranones 3 a-q and 4 a-c



A mixture of tri-*O*-benzyl-glucal **1** (50 mg, 0.12, 1.0 equiv.), iodo benzene **2** (29.4 mg, 0.14 mmol, 1.2 equiv.), $Pd(OAc)_2$ (4.0 mg, 0.018 mmol, 15 mol %), $AgNO_3$ (40.8 mg, 0.24 mmol, 2.0 equiv.) and 1,10 phenanthroline (32.4 mg, 0.18 mmol,0.3 equiv.) were loaded into a Schlenk tube with magnetic bead and flashed several times with N_2. Then DMF (3mL) was added into the mixture and the resulting mixture was stirred for 8 h at 100 °C in an oil bath (oil bath temperature 100 °C). After completion of reaction, the reaction mixture was cooled to room temperature and then filtered through a small bed of celite. The filtrate was washed with ethyl acetate and water. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using petroleum ether and hexane to acquire a pure product **3a** in 68% yield.

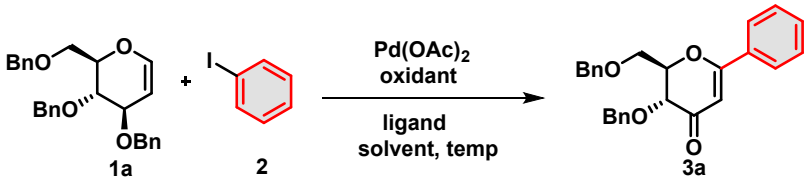
2.1.2 General procedure for the synthesis of β-aryl-2-deoxy C-glycosides (7)

Aryl enopyranone **3d** (20 mg, 0.046 mmol, 1.0 equiv.) was stirred in 2 mL methanol at room temperature in the presence of 10% Pd/C (10 mg). The round bottom flask was flushed with H_2 two times and further stirred for 2 h under H_2-balloon. After completion of the reaction, the reaction mixture was filtered through a small bed of celite. The filtrate was washed with ethyl acetate and water. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using petroleum ether and hexane to acquire a pure product **7** in 80% yield.

2.1.3 General procedure for selective reduction of aryl enopyranone (8)

Compound **8** was synthesized using **4a** (20 mg, 0.032 mmol, 1.0 equiv.) in MeOH:THF (1:1), sodium borohydride (1.5 mg , 0.038 mmol, 1.2 equiv.) and $CeCl_3.7H_2O$ (18 mg, 0.048 mmol, 1.5 equiv.) were added slowly at -10 ^oC temperature. Stirred the reaction mixture until complete consumption of starting material was observed by TLC analysis. Then the reaction mixture was diluted with 5 mL of ethyl acetate and quenched by addition of saturated aqueous NH4Cl solution (1 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (90:10) as eluent to obtain compound **8** as white gummy liquid (18.0 mg, 90%).

Table 1a: Optimization



entry	Ligand	Oxidant	solvent	Temp	Yield[b]
1.	1,10-Phen (0.1 equiv.)	$AgNO_3$ (1.0 equiv.)	DMF	100 °C	30
2.	1,10-Phen (0.2 equiv.)	$AgNO_3$ (1.0 equiv.)	DMF	100 °C	40
3.	1,10-Phen (0.3 equiv.)	$AgNO_3$ (1.0 equiv.)	DMF	100 °C	60
4.	1,10-Phen (0.3 equiv.)	$AgNO_3$ (2.0 equiv.)	DMF	100 °C	68
5.	1,10-Phen (0.3 equiv.)	$AgNO_3$ (2.0 equiv.)	DMF	>80 °C	0
6.	1,10-Phen (0.3 equiv.)	$Cu(OAc)_2$ (2.0 equiv.) + pyridine (10 mol%)	DMF	100 °C	30

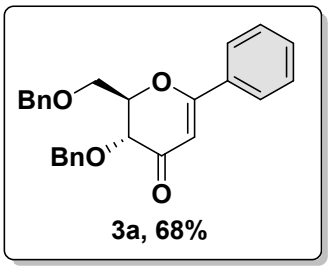
[a]Reaction were carried out by using **1** (1.0 equiv.), **2** (1.2 equiv.) and $Pd(OAc)_2$ (15 mol %) in 3 mL of DMF for 8 h.
[b]Yield was calculated after column chromatography.

We conducted a series of reactions to optimize the catalyst and oxidant loadings. Reacting compounds **1a** and **2** with palladium acetate (15 mol%), a ligand (0.1 equiv.), and $AgNO_3$ (1.0 equiv.) in DMF at 100°C yielded only 30%, with some starting material recovered. Increasing the ligand to 0.2 equiv. while keeping $AgNO_3$ at 1.0 equiv. improved the yield to 40%. Further enhancement was observed using 1,10-phenanthroline (0.3 equiv.) and Ag_2NO_3 (1.0 equiv.). The best yield, up to 68%, was achieved by increasing the $AgNO_3$ loading to 2.0 equiv. (entry 4). It was also noted that the reaction did not proceed at temperatures below 80°C. Additionally, reacting **1a** and **2** with palladium acetate (15 mol%) and 1,10-phenanthroline (0.3 equiv.), in the presence of copper acetate (2.0 equiv.) and pyridine (10 mol%), resulted in a yield of 30% for the desired product **3a**.

3. Characterization Data

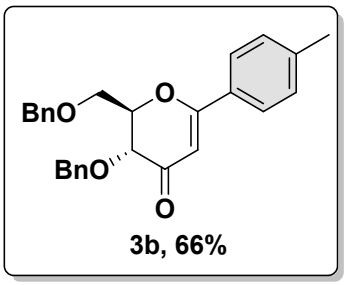
3.1. Characterization Data of C-1 aryl enopyranones

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (3a)



The compound **3a** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (68% yield, 33.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.62 (m, 2H), 7.44 – 7.38 (m, 1H), 7.35 (ddd, *J* = 8.4, 2.4, 0.9 Hz, 2H), 7.31 – 7.20 (m, 10H), 5.90 (s, 1H), 5.06 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.1 Hz, 1H), 4.58 – 4.47 (m, 3H), 4.23 (d, *J* = 11.4 Hz, 1H), 3.90 – 3.80 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.1, 169.5, 137.8, 137.6, 132.3, 131.9, 128.7, 128.5, 128.4, 128.0, 127.9, 127.8, 126.7, 100.4, 80.9, 74.6, 73.8, 73.5, 68.0. **HRMS** (ESI), m/z calcd. for $C_{26}H_{24}O_4$ $[M+H]^+$ 401.1753, found 401.1759.

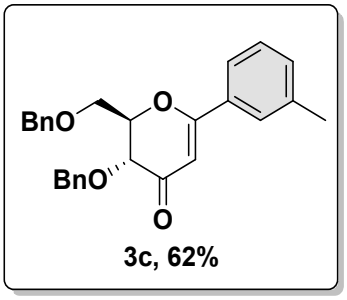
(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(p-tolyl)-2,3-dihydro-4H-pyran-4-one (3b)



The compound **3b** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (66% yield, 33.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.32 – 7.21 (m, 10H), 7.15 (d, *J* = 8.0 Hz, 2H), 5.88 (s, 1H), 5.07 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.1 Hz, 1H), 4.57 – 4.46 (m, 3H), 4.21 (d, *J* = 11.3 Hz, 1H), 3.89 – 3.79 (m, 2H), 2.33 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.0, 169.7, 142.5, 137.8, 137.6,

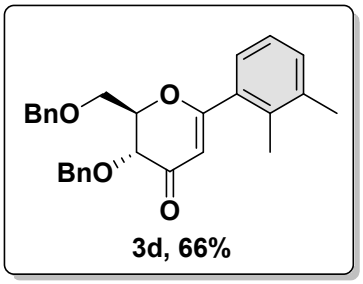
129.4, 128.5, 128.4, 128.4, 127.9, 127.8, 127.7, 126.7, 99.8, 80.8, 74.6, 73.8, 73.5, 68.0, 21.6. **HRMS** (ESI), m/z calcd. for $C_{27}H_{26}O_4$ $[M+H]^+$ 415.1909, found 415.1919.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(m-tolyl)-2,3-dihydro-4H-pyran-4-one (3c)



The compound **3c** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (62% yield, 31.0 mg). **^{1}H NMR** (400 MHz, CDCl3) δ 7.44 (dd, *J* = 6.9, 2.6 Hz, 2H), 7.30 – 7.23 (m, 8H), 7.23 – 7.18 (m, 4H), 5.87 (s, 1H), 5.05 (d, *J* = 11.1 Hz, 1H), 4.58 (dd, *J* = 11.2, 8.3 Hz, 2H), 4.54 – 4.49 (m, 2H), 4.20 (d, *J* = 11.3 Hz, 1H), 3.88 – 3.74 (m, 2H), 2.30 (s, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.1, 169.8, 138.4, 137.8, 137.6, 132.6, 132.2, 128.6, 128.6, 128.5, 128.4, 128.0, 127.9, 127.7, 127.3, 127.0, 123.9, 100.3, 80.9, 74.6, 73.9, 73.5, 68.0, 21.5. **HRMS** (ESI), m/z calcd. for $C_{27}H_{27}O_4$ $[M+H]^+$ 415.1909, found 415.1910.

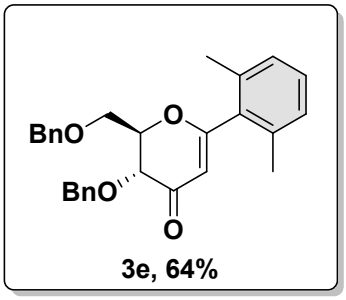
(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(2,3-dimethylphenyl)-2,3-dihydro-4H-pyran-4-one (3d)



The compound **3d** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (66% yield, 34.0 mg). **^{1}H NMR** (400 MHz, CDCl3) δ 7.38 – 7.26 (m, 11H), 7.21 (dd, *J* = 10.6, 7.0 Hz, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 5.55 (s, 1H), 5.14 (d, *J* = 11.1 Hz, 1H), 4.68 (d, *J* = 8.3 Hz, 1H), 4.56 (dt, *J* = 25.4, 7.9 Hz, 3H), 4.34 (d, *J* = 11.5 Hz, 1H), 3.91 – 3.81 (m, 2H), 2.29 (s, 3H), 2.26 (s, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ 193.9, 173.8,

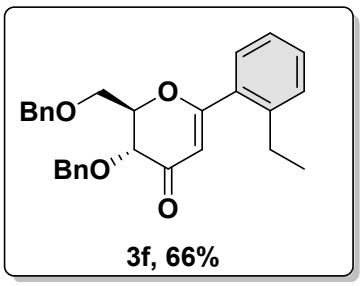
137.8, 137.7, 137.7, 135.2, 134.0, 132.1, 128.5, 128.4, 128.4, 128.0, 127.8, 127.7, 127.0, 126.7, 125.6, 105.1, 81.1, 74.6, 73.9, 73.6, 68.2, 20.4, 17.0. **HRMS** (ESI), m/z calcd. for $C_{28}H_{29}O_4$ $[M+H]^+$ 429.2066, found 429.2076.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(2,6-dimethylphenyl)-2,3-dihydro-4H-pyran-4-one (3e)



The compound **3e** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (64% yield, 33.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 13H), 7.10 (s, 1H), 5.94 (s, 1H), 5.14 (d, *J* = 11.1 Hz, 1H), 4.67 (d, *J* = 8.8 Hz, 1H), 4.64 – 4.52 (m, 3H), 4.27 (d, *J* = 11.3 Hz, 1H), 3.91 (qd, *J* = 11.1, 3.3 Hz, 2H), 2.33 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.1, 170.0, 138.3, 137.9, 137.7, 133.6, 132.2, 128.5, 128.4, 128.0, 127.9, 127.7, 124.5, 100.3, 80.9, 74.6, 73.9, 73.5, 68.0, 21.4. **HRMS** (ESI), m/z calcd. for $C_{28}H_{29}O_4$ $[M+H]^+$ 429.2066, found 429.2058.

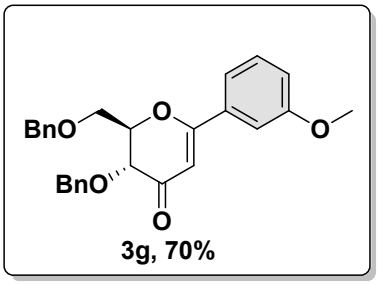
(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(2-ethylphenyl)-2,3-dihydro-4H-pyran-4-one (3f)



The compound **3f** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (66% yield, 34.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.18 (m, 15H), 5.59 (s, 1H), 5.15 (d, *J* = 11.1 Hz, 1H), 4.68 (d, *J* = 11.1 Hz, 1H), 4.62 – 4.57 (m, 1H), 4.57 – 4.50 (m, 2H), 4.35 (d, *J* = 11.5 Hz, 1H), 3.92 – 3.83 (m, 2H), 2.83 – 2.65 (m, 2H), 1.20

(t, J = 7.5 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.9, 173.6, 143.1, 137.7, 137.6, 132.9, 130.8, 129.6, 129.2, 128.4, 128.4, 128.4, 127.9, 127.8, 127.7, 125.9, 104.7, 81.2, 74.6, 73.8, 73.6, 68.1, 26.9, 15.8. **HRMS** (ESI), m/z calcd. for $C_{28}H_{29}O_4$ $[M+H]^+$ 429.2066, found 429.2057.

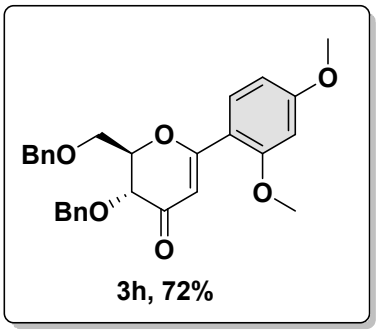
(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(3-methoxyphenyl)-2,3-dihydro-4H-pyran-4-one (3g)



3g, 70%

The compound **3g** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained white gummy liquid (70% yield, 36.0 mg). **^{1}H NMR** (400 MHz, CDCl3) δ 7.40 – 7.23 (m, 14H), 7.00 (s, 1H), 5.96 (s, 1H), 5.13 (d, J = 11.1 Hz, 1H), 4.67 (d, J = 11.1 Hz, 1H), 4.64 – 4.54 (m, 3H), 4.28 (d, J = 11.2 Hz, 1H), 3.96 – 3.86 (m, 2H), 3.79 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.0, 169.3, 159.8, 137.8, 137.6, 133.7, 129.7, 128.5, 128.4, 128.0, 127.9, 127.7, 119.2, 117.6, 111.9, 100.6, 81.0, 74.6, 73.9, 73.5, 68.0, 55.4. **HRMS** (ESI), m/z calcd. for $C_{27}H_{27}O_5$ $[M+H]^+$ 431.1858, found 431.1848.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(2,4-dimethoxyphenyl)-2,3-dihydro-4H-pyran-4-one (3h)

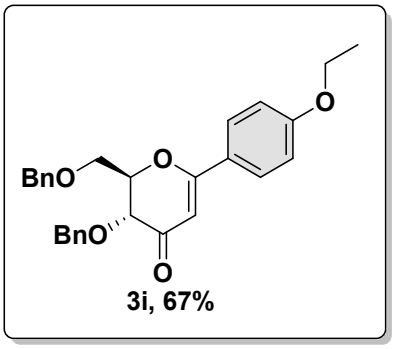


3h, 72%

The compound **3h** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (93:07) as eluent to obtained white gummy liquid (72% yield, 40.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.8 Hz, 1H), 7.30 – 7.18 (m, 11H), 6.44 (dd, J = 8.8, 2.4 Hz, 1H), 6.38 (d, J = 2.3 Hz, 1H),

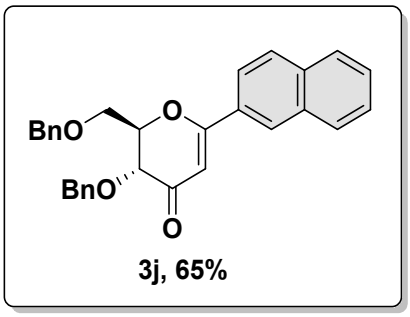
6.24 (s, 1H), 5.06 (d, *J* = 11.2 Hz, 1H), 4.60 (d, *J* = 11.2 Hz, 1H), 4.51 (q, *J* = 12.1 Hz, 2H), 4.43 (ddd, *J* = 11.5, 4.0, 2.8 Hz, 1H), 4.18 (d, *J* = 11.5 Hz, 1H), 3.85 – 3.78 (m, 2H), 3.75 (d, *J* = 2.3 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.8, 166.5, 163.4, 160.1, 137.9, 137.8, 130.9, 128.5, 128.4, 128.4, 127.9, 127.8, 127.7, 113.9, 105.0, 104.3, 98.7, 80.4, 74.5, 73.9, 73.5, 68.3, 55.6, 55.5. **HRMS** (ESI), m/z calcd. for $C_{28}H_{29}O_6$ $[M+H]^+$ 461.1964, found 461.1960.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(4-ethoxyphenyl)-2,3-dihydro-4H-pyran-4-one (3i)



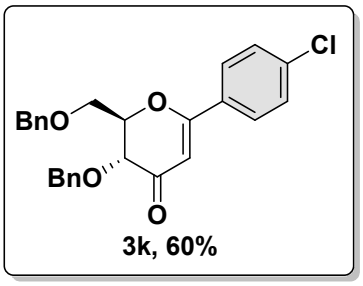
The compound **3i** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (67% yield, 33.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.9 Hz, 2H), 7.30 – 7.17 (m, 11H), 6.84 – 6.77 (m, 2H), 5.81 (d, *J* = 0.7 Hz, 1H), 5.05 (d, *J* = 11.2 Hz, 1H), 4.59 (d, *J* = 11.2 Hz, 1H), 4.55 – 4.44 (m, 3H), 4.17 (d, *J* = 11.2 Hz, 1H), 3.97 (q, *J* = 7.0 Hz, 2H), 3.85 – 3.76 (m, 2H), 1.33 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.8, 169.5, 162.0, 137.8, 137.7, 128.6, 128.5, 128.4, 128.4, 127.9, 127.8, 127.7, 124.3, 114.5, 98.9, 80.8, 74.5, 73.8, 73.5, 68.1, 63.7, 14.7. **HRMS** (ESI), m/z calcd. for $C_{28}H_{29}O_5$ $[M+H]^+$ 445.2015, found 445.2013.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(naphthalen-2-yl)-2,3-dihydro-4H-pyran-4-one (3j)



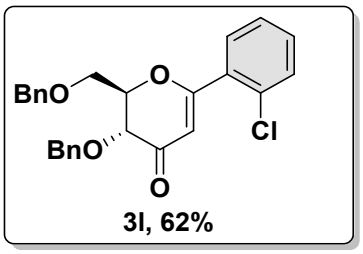
The compound **3j** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (65% yield, 35.0 mg). **^{1}H NMR** (400 MHz, CDCl3) δ 8.20 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.64 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.48 (ddd, *J* = 15.4, 7.9, 4.3 Hz, 3H), 7.43 – 7.28 (m, 11H), 5.80 (s, 1H), 5.17 (d, *J* = 11.2 Hz, 1H), 4.78 – 4.70 (m, 2H), 4.56 (q, *J* = 12.0 Hz, 2H), 4.43 (d, *J* = 11.3 Hz, 1H), 3.93 (d, *J* = 3.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.8, 172.3, 137.8, 137.6, 133.7, 131.6, 131.3, 130.4, 128.6, 128.6, 128.5, 128.4, 128.0, 127.8, 127.7, 127.5, 127.2, 127.0, 126.4, 125.3, 124.9, 105.6, 81.4, 74.6, 73.9, 73.6, 68.2. **HRMS** (ESI), m/z calcd. for $C_{30}H_{27}O_4$ $[M+H]^+$ 451.1909, found 451.1915.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(4-chlorophenyl)-2,3-dihydro-4H-pyran-4-one (3k)



The compound **3k** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (60% yield, 29.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 2H), 7.40 – 7.28 (m, 13H), 5.94 (s, 1H), 5.12 (d, *J* = 11.1 Hz, 1H), 4.67 (d, *J* = 11.0 Hz, 1H), 4.64 – 4.54 (m, 3H), 4.28 (d, *J* = 11.3 Hz, 1H), 3.95 – 3.86 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.9, 168.2, 137.9, 137.7, 137.5, 130.7, 129.0, 128.5, 128.4, 128.0, 127.9, 127.9, 127.8, 100.5, 81.0, 74.6, 73.7, 73.5, 67.9. **HRMS** (ESI), m/z calcd. for $C_{26}H_{24}ClO_4$ $[M+H]^+$ 435.1363, found 435.1353.

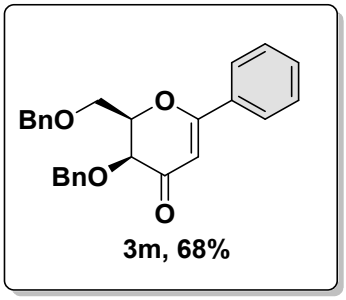
(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(2-chlorophenyl)-2,3-dihydro-4H-pyran-4-one (3l)



3l, 62%

The compound **3l** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (62% yield, 30.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.30 – 7.18 (m, 13H), 5.67 (s, 1H), 5.05 (d, *J* = 11.0 Hz, 1H), 4.61 – 4.49 (m, 3H), 4.44 (d, *J* = 12.1 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 3.82 (d, *J* = 3.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.0, 169.5, 137.7, 137.6, 132.8, 132.6, 131.7, 130.7, 130.4, 128.5, 128.4, 128.4, 128.0, 127.9, 127.8, 126.8, 105.9, 81.6, 74.7, 73.9, 73.6, 68.0. **HRMS** (ESI), m/z calcd. for $C_{26}H_{24}ClO_4$ $[M+H]^+$ 435.1363, found 435.1346.

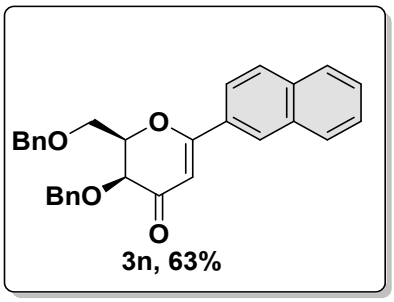
(2R,3S)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (3m)



3m, 68%

The compound **3m** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (68% yield, 33 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 2H), 7.39 – 7.34 (m, 1H), 7.33 – 7.16 (m, 12H), 5.94 (d, *J* = 1.3 Hz, 1H), 4.68 (d, *J* = 11.9 Hz, 1H), 4.58 – 4.43 (m, 4H), 3.95 (dd, *J* = 10.2, 6.9 Hz, 1H), 3.81 (dd, *J* = 10.2, 5.6 Hz, 1H), 3.70 (dd, *J* = 2.4, 1.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.4, 169.8, 137.8, 137.2, 132.4, 131.9, 128.7, 128.6, 128.4, 128.4, 128.0, 127.9, 127.8, 126.8, 100.3, 80.6, 73.7, 72.1, 67.8. **HRMS** (ESI), m/z calcd. for $C_{26}H_{25}O_4$ $[M+H]^+$ 401.1753, found 401.1747.

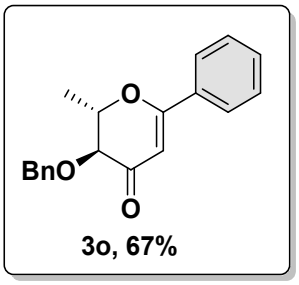
(2R,3S)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(naphthalen-2-yl)-2,3-dihydro-4H-pyran-4-one (3n)



3n, 63%

The compound **3n** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (63% yield, 34 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.73 (m, 1H), 7.56 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.30 – 7.17 (m, 11H), 5.75 (d, *J* = 1.1 Hz, 1H), 4.81 – 4.70 (m, 2H), 4.59 – 4.40 (m, 3H), 3.95 (dd, *J* = 10.3, 7.0 Hz, 1H), 3.84 (dd, *J* = 10.3, 5.4 Hz, 1H), 3.80 – 3.78 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.3, 172.6, 137.7, 137.4, 133.7, 131.6, 131.5, 130.5, 128.6, 128.5, 128.5, 128.3, 128.0, 127.9, 127.7, 127.6, 127.2, 126.4, 125.4, 124.9, 105.5, 81.1, 73.8, 73.7, 72.0, 67.8. **HRMS** (ESI), m/z calcd. for $C_{30}H_{26}O_4$ $[M+H]^+$ 451.1909, found 451.1895.

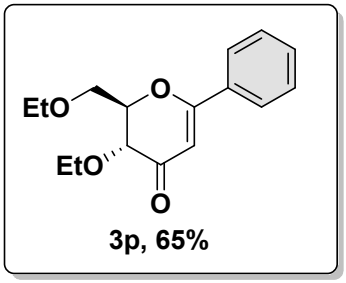
(2S,3S)-3-(benzyloxy)-2-methyl-6-phenyl-2,3-dihydro-4H-pyran-4-one (3o)



3o, 67%

The compound **3o** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (97:03) as eluent to obtained yellow gummy liquid (67% yield, 32.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.60 (m, 2H), 7.39 – 7.20 (m, 8H), 5.88 (s, 1H), 5.01 (d, *J* = 11.5 Hz, 1H), 4.66 – 4.60 (m, 1H), 4.53 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.71 (d, *J* = 10.0 Hz, 1H), 1.44 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.8, 169.3, 137.5, 132.4, 131.7, 128.7, 128.5, 128.5, 128.0, 126.6, 100.3, 78.4, 78.3, 74.0, 17.4. **HRMS** (ESI), m/z calcd. for $C_{19}H_{19}O_3$ $[M+H]^+$ 295.1334, found 295.1325.

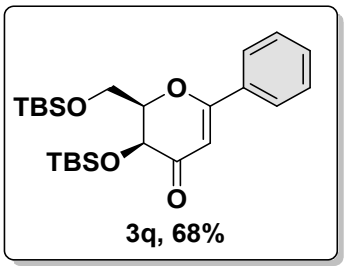
(2R,3R)-3-ethoxy-2-(ethoxymethyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (3p)



3p, 65%

The compound **3p** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained yellow gummy liquid (65% yield, 39 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.61 (m, 2H), 7.43 – 7.28 (m, 3H), 5.87 (s, 1H), 4.42 (ddd, *J* = 11.4, 3.9, 2.6 Hz, 1H), 4.07 (d, *J* = 11.4 Hz, 1H), 4.04 – 3.97 (m, 1H), 3.83 (qd, *J* = 11.2, 3.3 Hz, 2H), 3.65 – 3.47 (m, 3H), 1.18 (t, *J* = 6.8 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.3, 169.4, 132.3, 131.7, 128.6, 126.6, 100.3, 81.2, 74.6, 68.5, 68.4, 67.2, 15.3, 15.1. **HRMS** (ESI), m/z calcd. for $C_{16}H_{21}O_4$ $[M+H]^+$ 277.1440, found 277.1448.

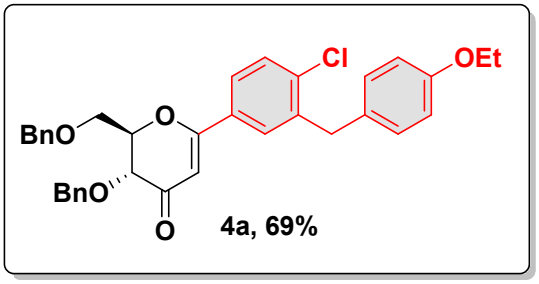
(2R,3S)-3-((tert-butyldimethylsilyl)oxy)-2-(((tert-butyldimethylsilyl)oxy)methyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (3q)



3q, 68%

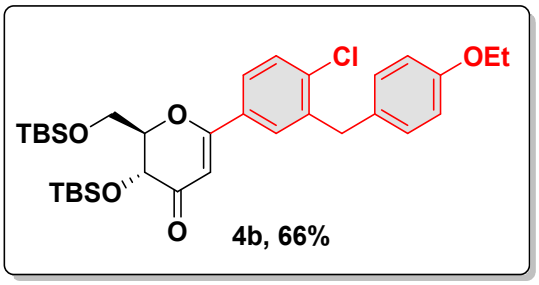
The compound **3q** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (97:03) as eluent to obtained yellow gummy liquid (68% yield, 42 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.7 Hz, 2H), 7.43 – 7.30 (m, 3H), 5.83 (s, 1H), 4.43 (d, *J* = 12.1 Hz, 1H), 4.25 (d, *J* = 12.0 Hz, 1H), 4.13 – 3.95 (m, 2H), 0.85 (d, *J* = 11.6 Hz, 18H), 0.19 (s, 3H), 0.05 (s, 6H), 0.02 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.4, 169.2, 132.5, 131.5, 128.6, 126.5, 99.8, 83.6, 69.2, 61.6, 25.9, 25.9, -3.9, -5.1, -5.2, -5.6. **HRMS** (ESI), m/z calcd. for $C_{24}H_{40}O_4Si_2$ $[M+H]^+$ 449.2543, found 449.2543.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(4-chloro-3-(4-ethoxybenzyl)phenyl)-2,3-dihydro-4H-pyran-4-one (4a)



The compound **4a** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained white gummy liquid (68% yield, 47 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 9.5 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.38 – 7.28 (m, 10H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 5.87 (s, 1H), 5.11 (d, *J* = 11.2 Hz, 1H), 4.67 (d, *J* = 11.1 Hz, 1H), 4.63 – 4.52 (m, 3H), 4.26 (d, *J* = 11.1 Hz, 1H), 4.09 – 3.94 (m, 4H), 3.88 (d, *J* = 2.8 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.7, 168.4, 157.7, 139.8, 137.9, 137.7, 137.5, 131.0, 130.5, 129.9, 129.8, 128.9, 128.5, 128.4, 127.9, 127.8, 127.7, 125.7, 114.7, 100.5, 81.1, 74.5, 73.8, 73.6, 68.0, 63.4, 38.4, 14.9. **HRMS** (ESI), m/z calcd. for $C_{35}H_{33}ClO_5$ $[M+H]^+$ 569.2095, found 569.2103.

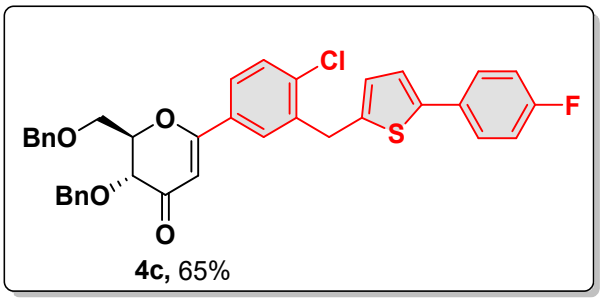
(2R,3R)-3-((tert-butyldimethylsilyl)oxy)-2-(((tert-butyldimethylsilyl)oxy)methyl)-6-(4-chloro-3-(4-ethoxybenzyl)phenyl)-2,3-dihydro-4H-pyran-4-one (4b)



The compound **4b** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (97:03) as eluent to obtained white gummy liquid (66% yield, 41 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 9.1 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 5.85 (s, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.34 (d, *J* = 12.1 Hz, 1H), 4.08 (dt, *J* = 13.9, 11.4 Hz, 6H), 1.45 (t, *J* = 7.0 Hz, 3H), 0.98 (s, 9H), 0.95 (s, 9H), 0.31 (s, 3H), 0.16 (d, *J* = 8.0 Hz, 6H), 0.12 (s,

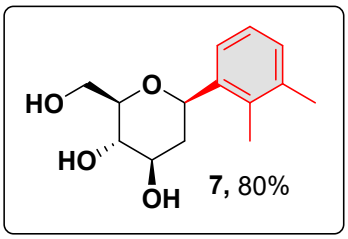
3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.3, 168.1, 157.7, 139.8, 137.7, 131.2, 130.6, 129.9, 128.8, 125.5, 114.7, 99.9, 83.6, 69.2, 63.4, 61.6, 38.4, 26.0, 25.9, 18.6, 18.4, 14.9, -3.9, -5.1, -5.2, -5.6. **HRMS** (ESI), m/z calcd. for $C_{33}H_{49}ClO_5Si_2$ $[M+H]^+$ 617.2885, found 617.2890.

(2R,3R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(4-chloro-3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)phenyl)-2,3-dihydro-4H-pyran-4-one (4c)



The compound **4c** was synthesized according to the general procedure (2.1.1) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (97:03) as eluent to obtained white gummy liquid (65% yield, 41 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, J = 1.9 Hz, 1H), 7.67 (dd, J = 8.1, 1.9 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.31 – 7.12 (m, 13H), 7.08 – 7.00 (m, 2H), 5.89 (s, 1H), 5.04 (d, J = 11.1 Hz, 1H), 4.60 (d, J = 11.1 Hz, 1H), 4.54 – 4.44 (m, 3H), 4.21 (d, J = 11.2 Hz, 1H), 3.87 – 3.76 (m, 2H), 2.36 (s, 2H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.8, 189.1, 168.5, 164.6, 162.1, 153.4, 142.9, 140.7, 138.8, 137.6, 137.5, 136.8, 131.6, 129.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 126.0, 124.2, 116.4, 116.2, 100.3, 81.1, 74.6, 73.7, 73.5, 67.9. **HRMS** (ESI), m/z calcd. for $C_{37}H_{30}ClFO_4S$ $[M+H]^+$ 625.1616, found 625.1620.

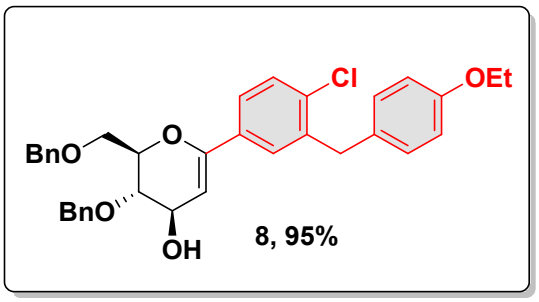
(2R,3S,4R,6R)-6-(2,3-dimethylphenyl)-2-(hydroxymethyl)tetrahydro-2H-pyran-3,4-diol (7)



The compound **7** was synthesized according to the general procedure (2.1.2) and purified using column chromatography over silica gel (60-120 mesh) using pet DCM/MeOH (98:02) as eluent to obtained white foamy liquid (80% yield, 9.5 mg). **^{1}H NMR** (400 MHz, MeOD) δ 7.22 (t, J = 4.6 Hz, 1H), 6.95 (d, J = 5.1 Hz, 2H), 4.62 (dd, J = 11.3, 1.3 Hz, 1H), 3.80 (dd, J = 11.9, 2.2 Hz, 1H),

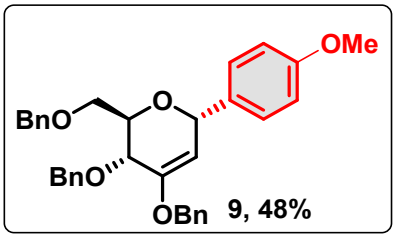
3.67 – 3.57 (m, 2H), 3.29 (ddd, *J* = 9.3, 5.8, 2.2 Hz, 1H), 3.23 – 3.18 (m, 1H), 2.16 (s, 3H), 2.13 (s, 3H), 2.03 (ddd, *J* = 12.9, 4.9, 1.6 Hz, 1H), 1.59 – 1.48 (m, 1H). **^{13}C NMR** (101 MHz, MeOD) δ 139.2, 136.3, 133.2, 128.6, 125.1, 123.1, 80.9, 74.6, 72.9, 72.1, 61.9, 39.7, 19.3, 13.5. **HRMS** (ESI), m/z calcd. for $C_{14}H_{21}O_4$ $[M+H]^+$ 253.1440, found 253.1449. **$[\alpha]_D$** = +22.30 (c = 0.5, MeOH).

(2R,3S,4R)-3-(benzyloxy)-2-((benzyloxy)methyl)-6-(4-chloro-3-(4-ethoxybenzyl)phenyl)-3,4-dihydro-2H-pyran-4-ol (8)



The compound **8** was synthesized according to the general procedure (2.1.3) and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained white gummy liquid (95% yield, 44 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.26 (m, 14H), 7.09 (d, *J* = 8.2 Hz, 2H), 6.81 (d, *J* = 8.2 Hz, 2H), 5.25 (d, *J* = 2.6 Hz, 1H), 4.79 (dd, *J* = 26.9, 11.6 Hz, 2H), 4.63 (q, *J* = 12.1 Hz, 2H), 4.47 (d, *J* = 3.1 Hz, 1H), 4.15 (d, *J* = 8.7 Hz, 1H), 4.06 – 3.88 (m, 6H), 3.82 – 3.73 (m, 1H), 1.40 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5, 151.7, 138.8, 138.3, 138.0, 134.6, 133.1, 131.2, 129.8, 129.3, 128.6, 128.4, 128.0, 127.9, 127.7, 124.4, 114.5, 98.9, 73.7, 73.6, 69.7, 68.9, 63.4, 38.5, 14.9. **HRMS** (ESI), m/z calcd. for $C_{35}H_{35}ClO_5$ $[M+H]^+$ 571.2251, found 571.2255. **$[\alpha]_D$** = +38.20 (c = 0.5, $CHCl_3$).

(2R,3R,6S)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-(4-methoxyphenyl)-3,6-dihydro-2H-pyran (9)

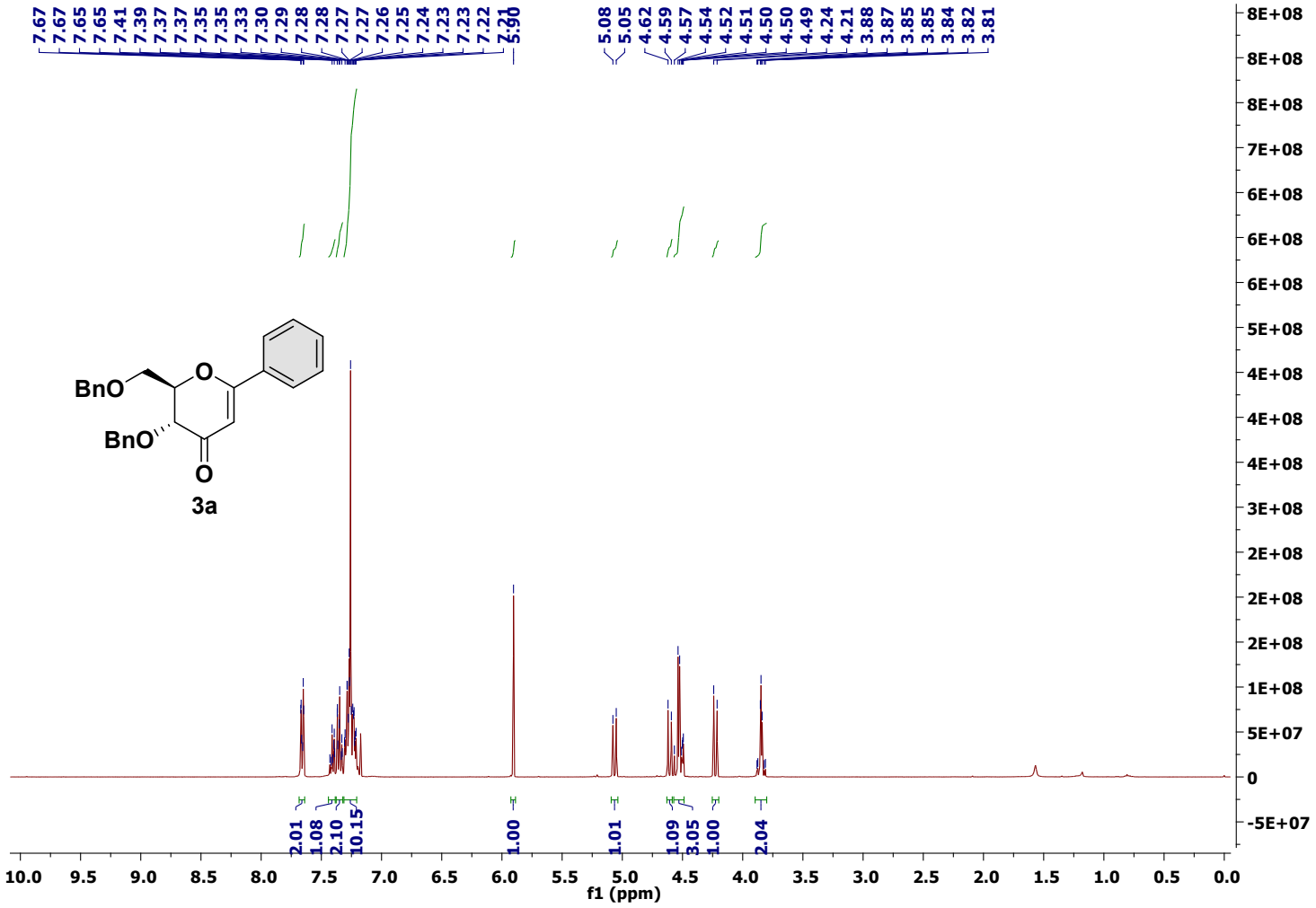


The compound 8 was synthesized and purified using column chromatography over silica gel (60-120 mesh) using pet ether/ethyl acetate (95:05) as eluent to obtained white gummy liquid (48% yield, 60 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 12H), 7.26 – 7.22 (m, 5H), 7.12 (d,

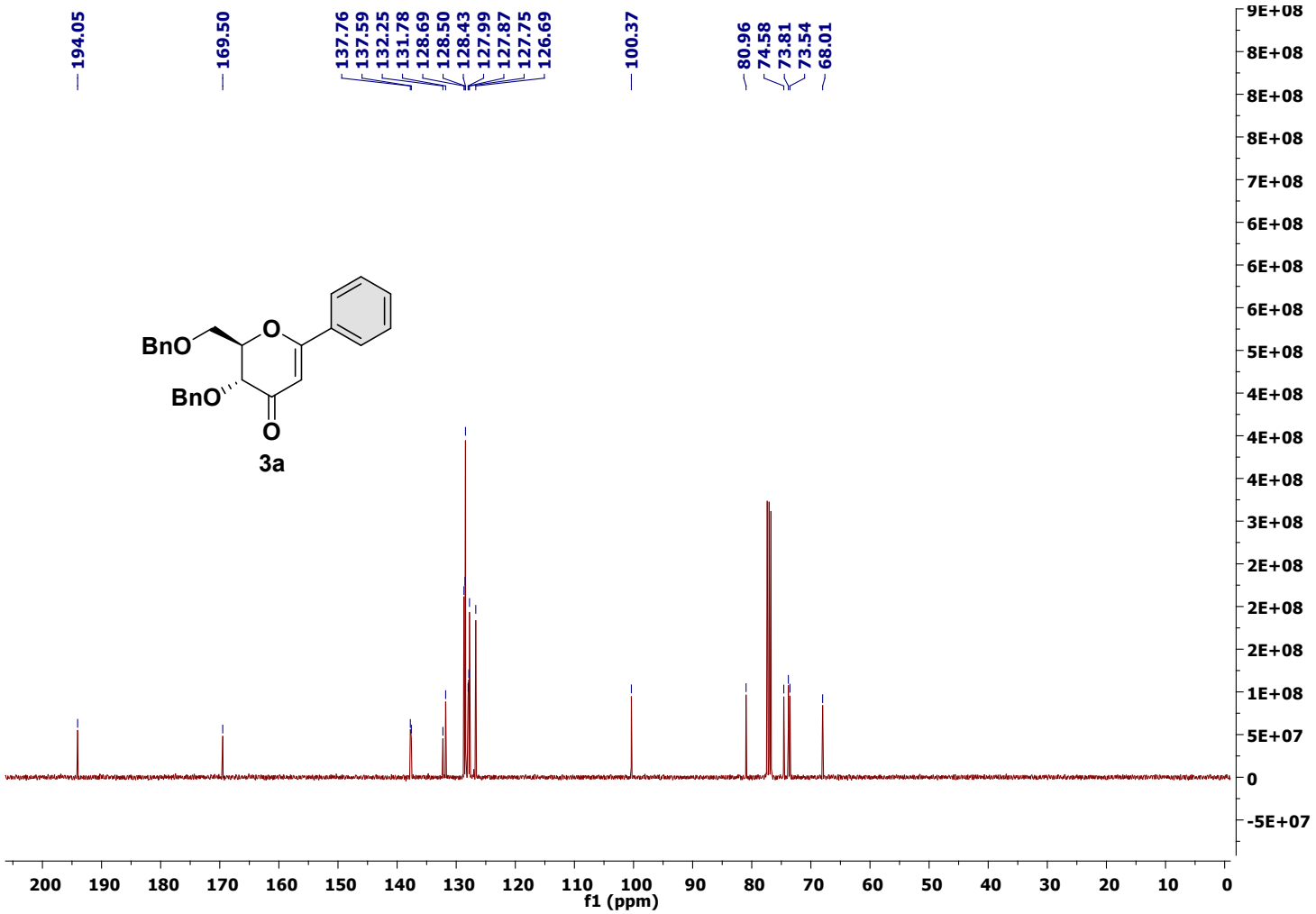
J = 7.9 Hz, 2H), 5.35 (d, *J* = 3.2 Hz, 1H), 5.01 (d, *J* = 3.6 Hz, 1H), 4.94 – 4.82 (m, 3H), 4.56 (s, 1H), 4.53 (s, 1H), 4.42 (d, *J* = 12.1 Hz, 1H), 4.23 (dd, *J* = 6.7, 1.1 Hz, 1H), 3.88 (dt, *J* = 6.8, 4.1 Hz, 1H), 3.65 (dd, *J* = 10.4, 4.6 Hz, 1H), 3.54 (dd, *J* = 10.4, 3.6 Hz, 1H), 2.32 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.28, 138.46, 138.17, 137.71, 137.66, 136.91, 128.95, 128.53, 128.36, 128.28, 128.26, 128.23, 127.94, 127.87, 127.65, 127.62, 127.43, 98.97, 73.57, 73.56, 73.23, 72.08, 71.39, 69.15, 68.83, 21.19. **HRMS** (ESI), m/z calcd. for $C_{34}H_{34}O_5$ $[M+H]^+$ 523.2484, found 523.2490.

4. NMR Spectra

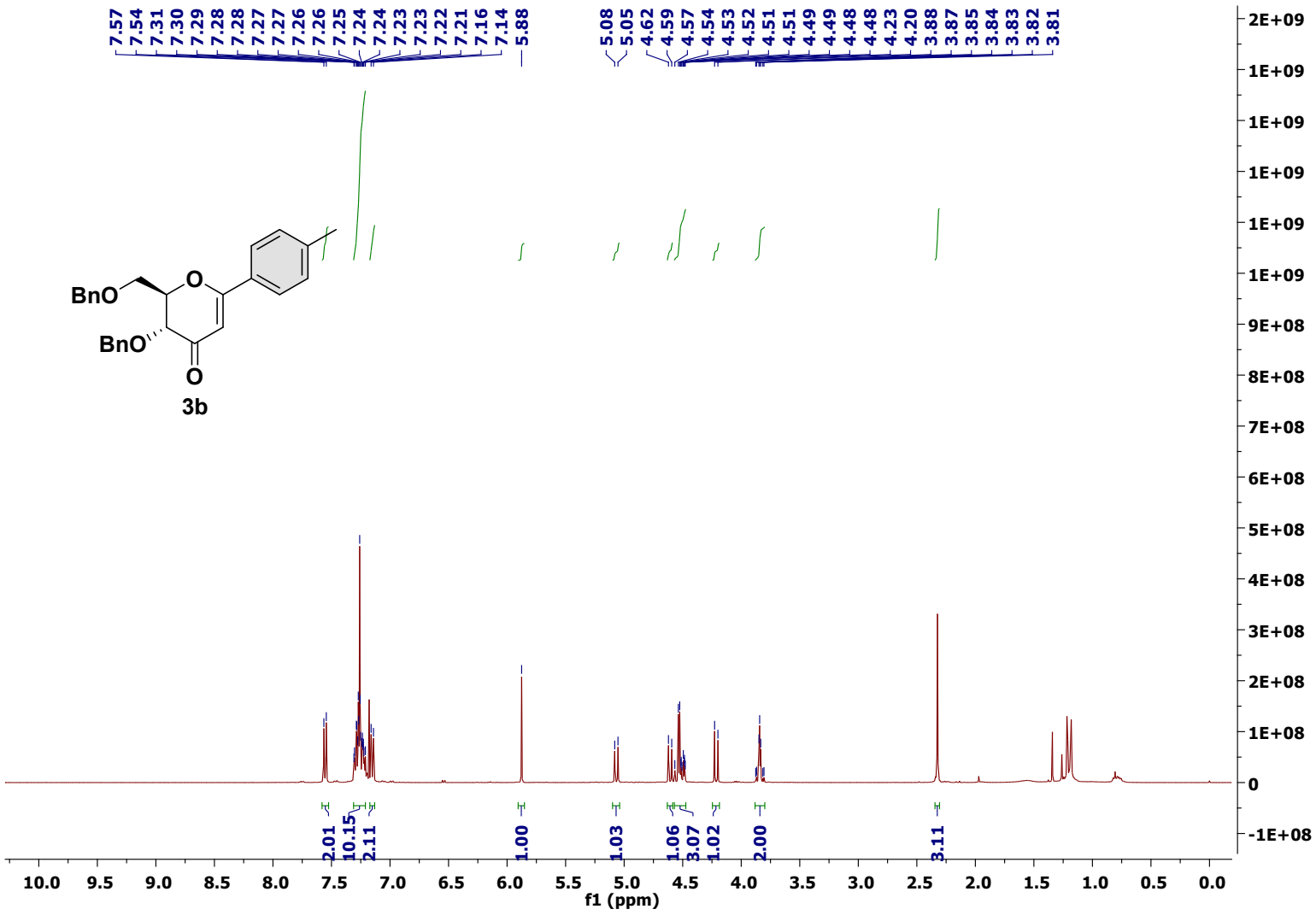
^{1}H NMR (400 MHz) of **3a** in $CDCl_3$



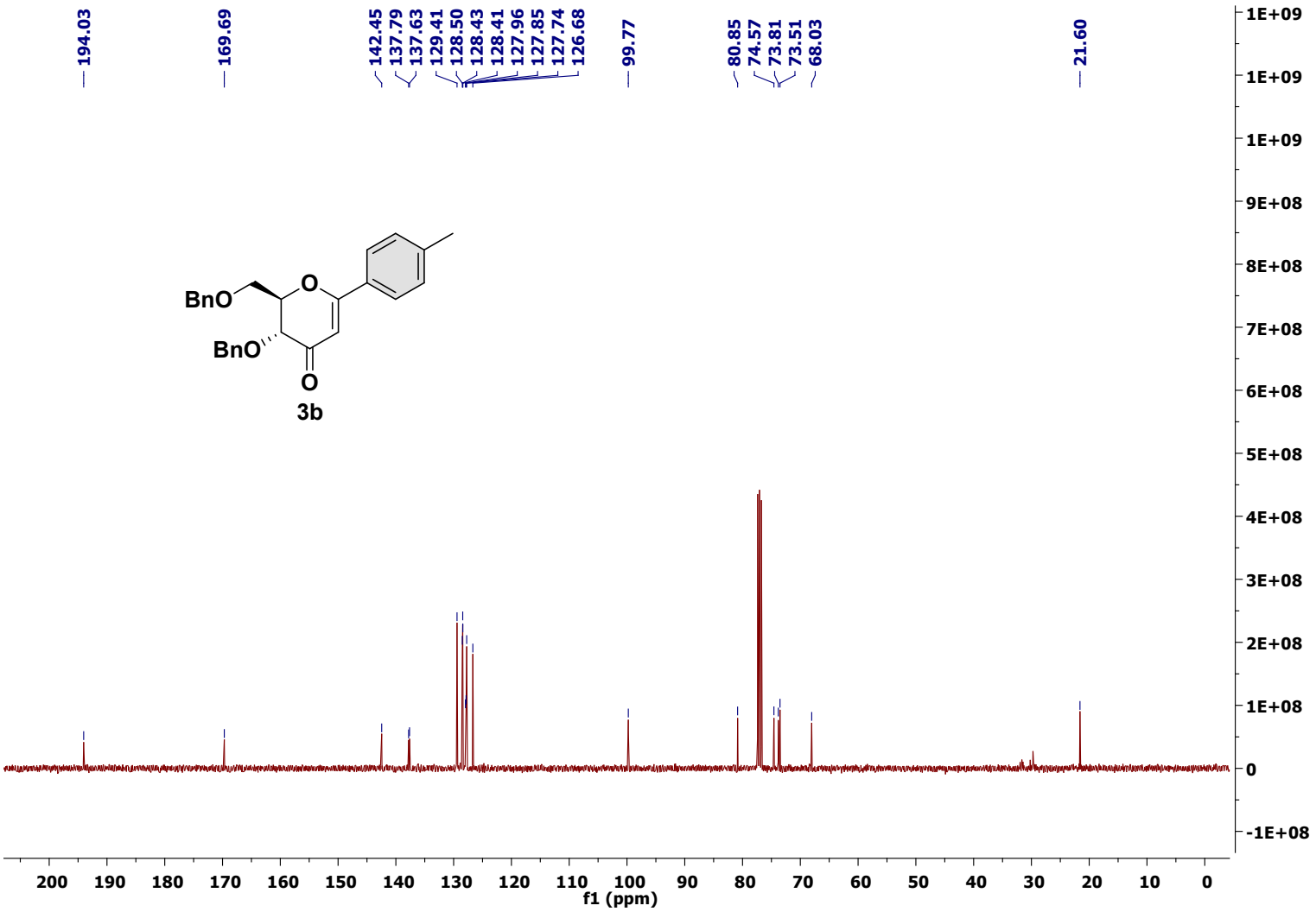
^{13}C NMR {^{1}H} (101 MHz) of **3a** in $CDCl_3$



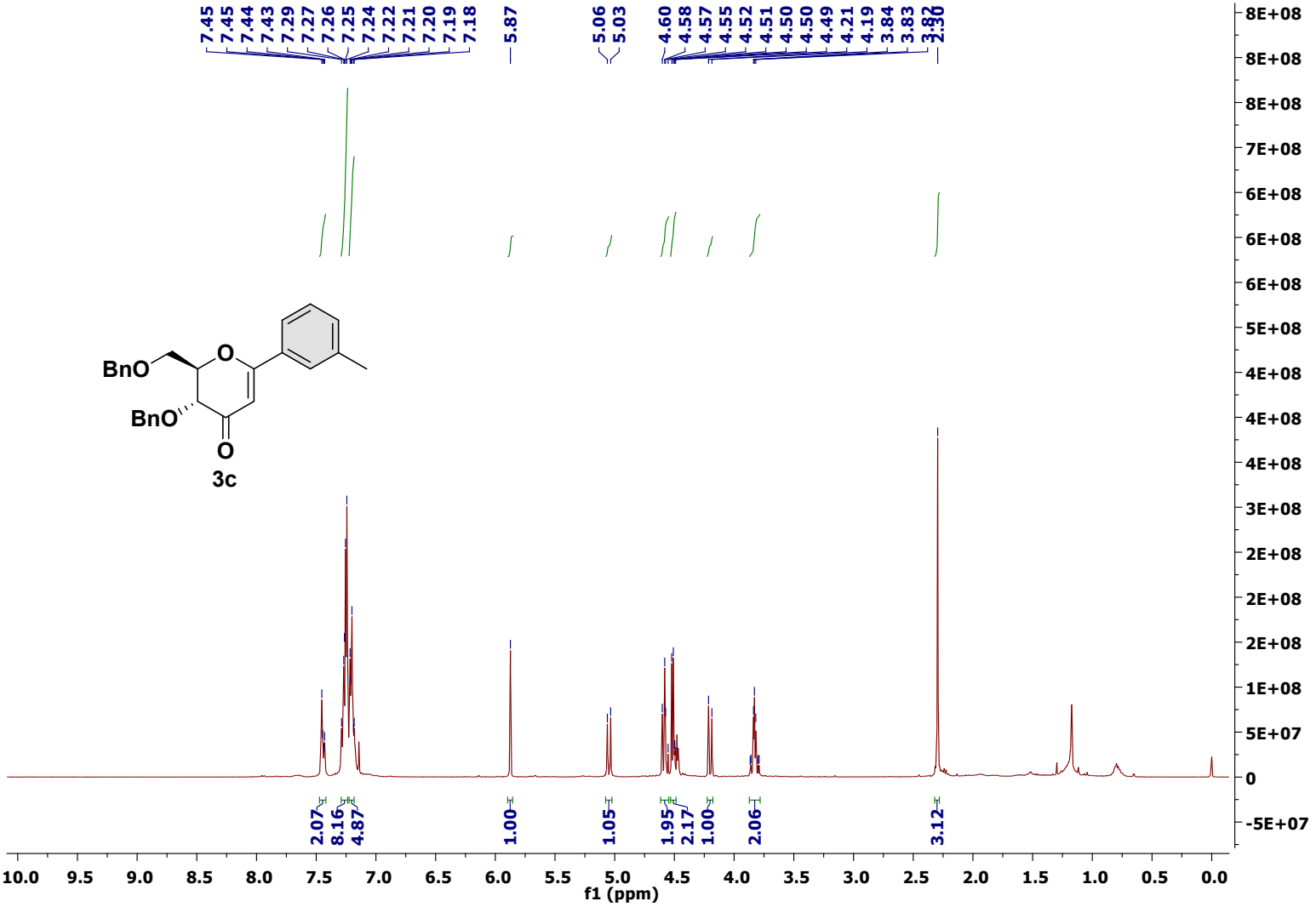
^{1}H NMR (400 MHz) of **3b** in $CDCl_3$



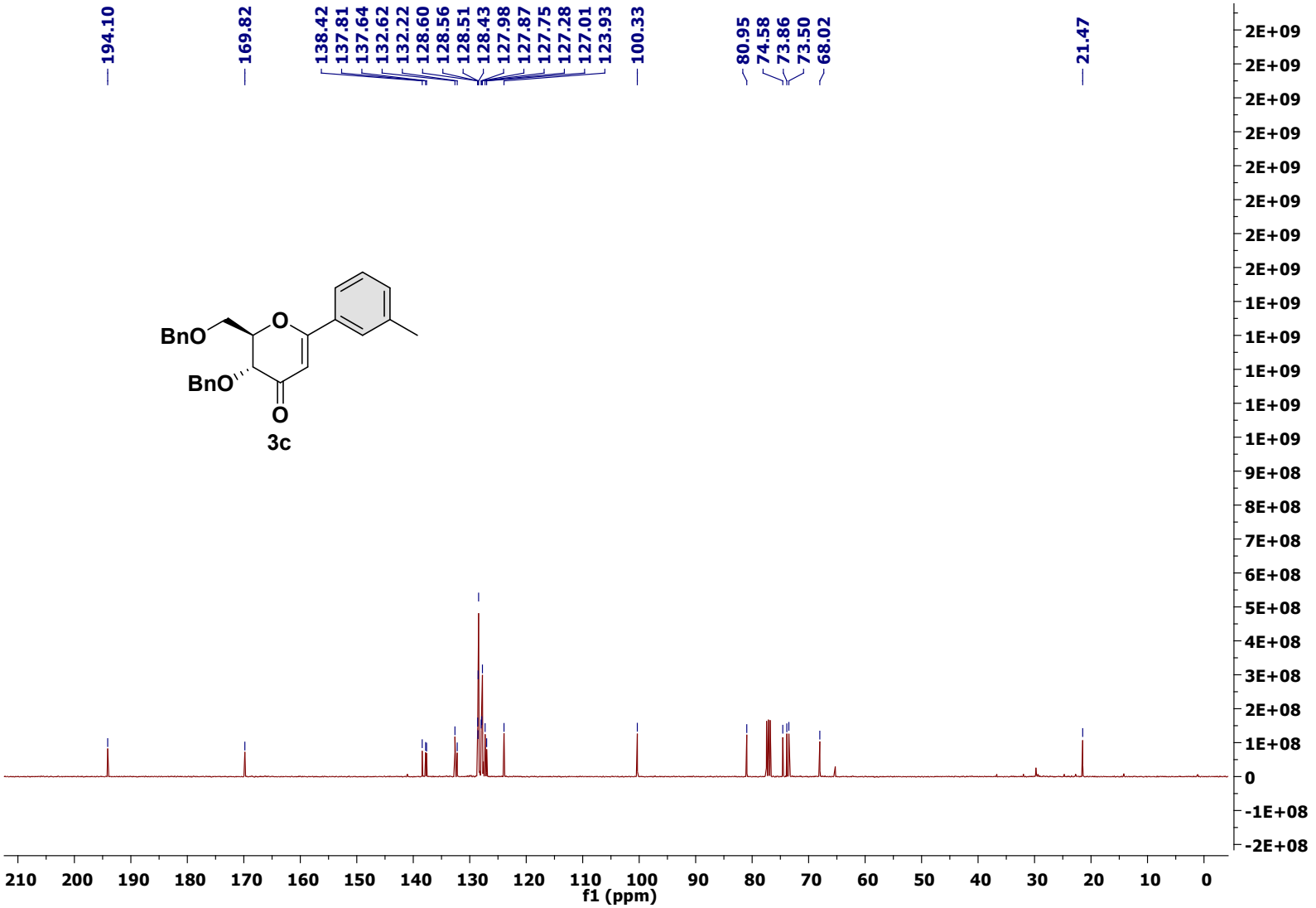
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3b** in $CDCl_3$



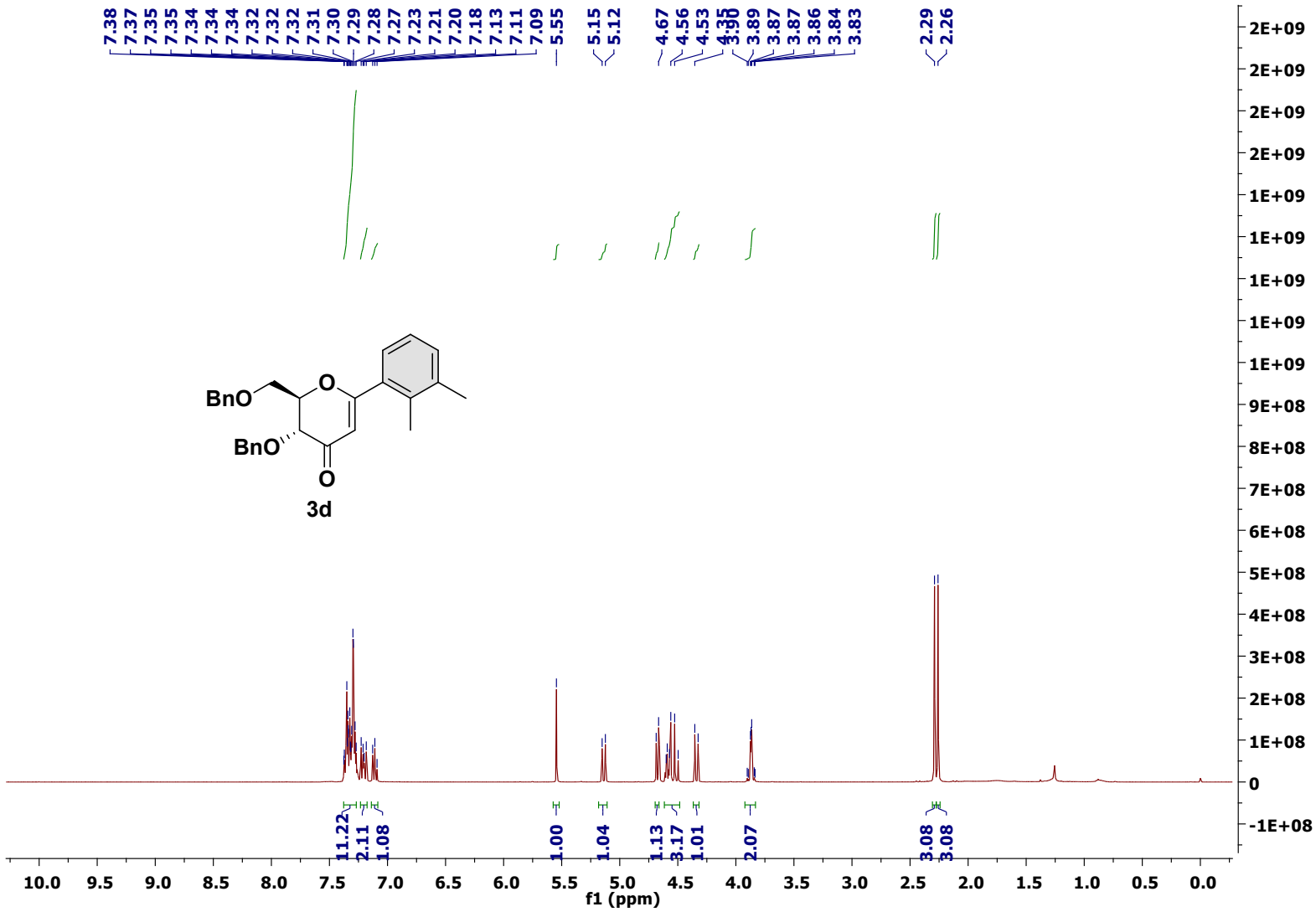
^{1}H NMR (400 MHz) of **3c** in $CDCl_3$



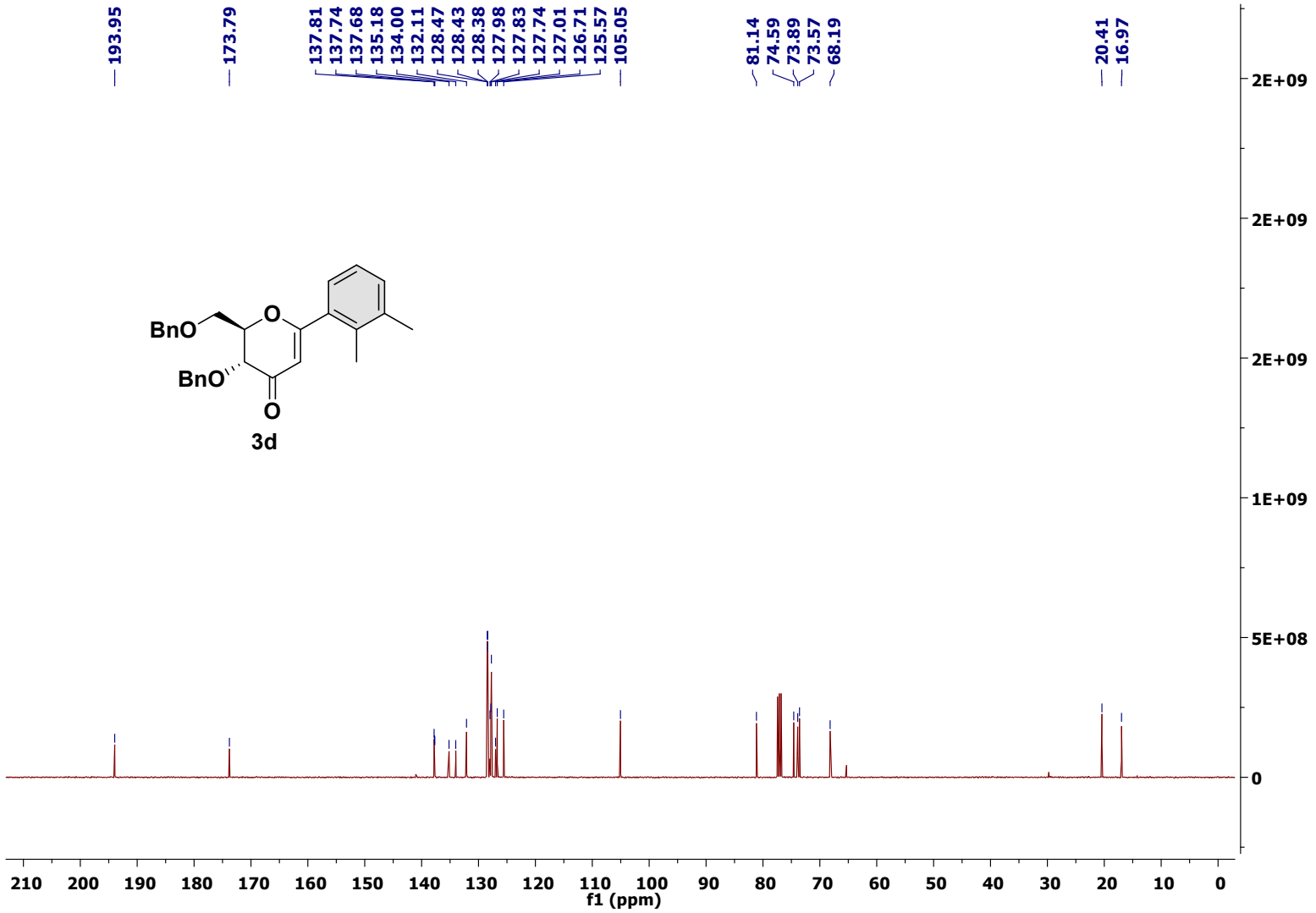
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3c** in $CDCl_3$



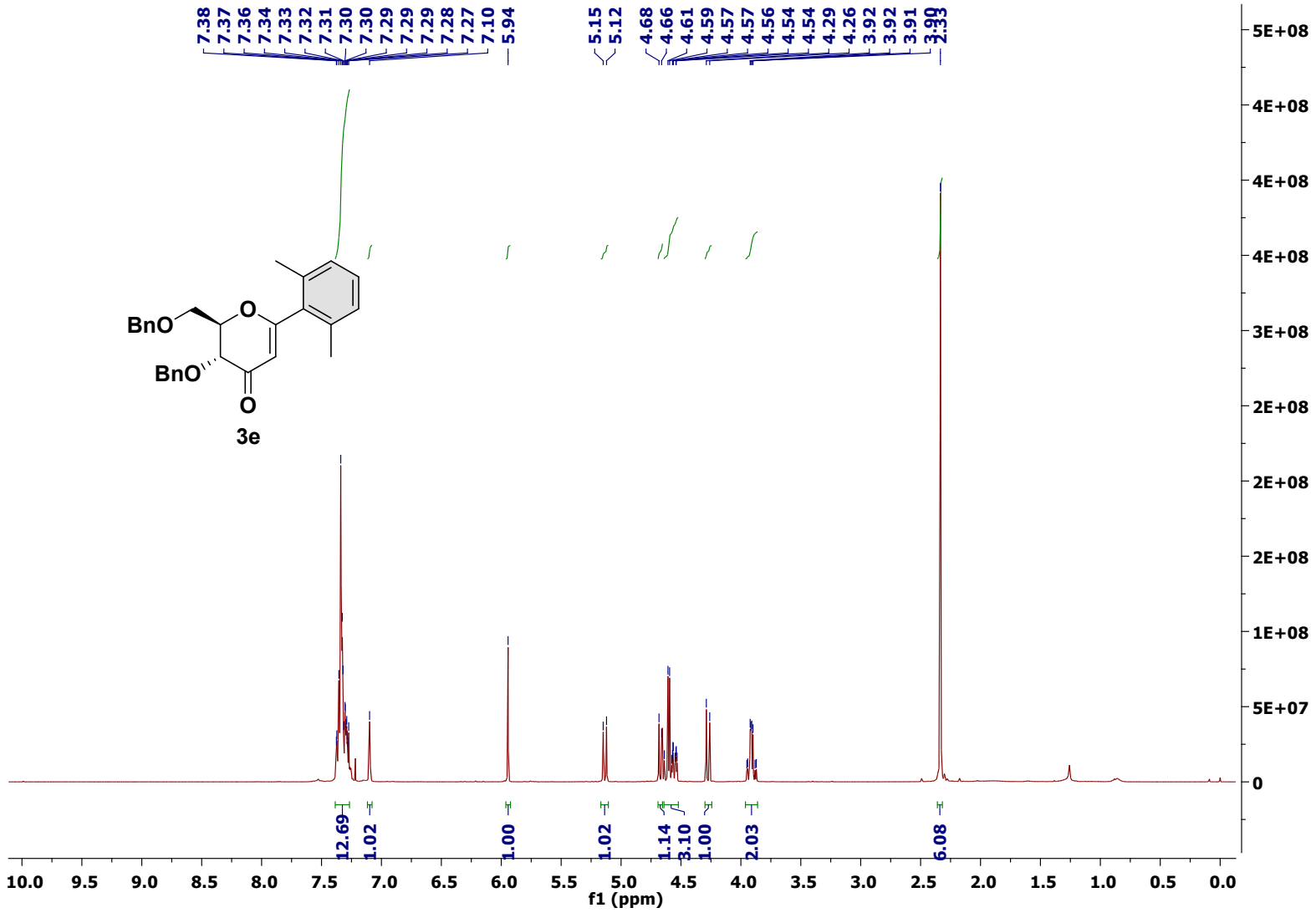
^{1}H NMR (400 MHz) of **3d** in $CDCl_3$



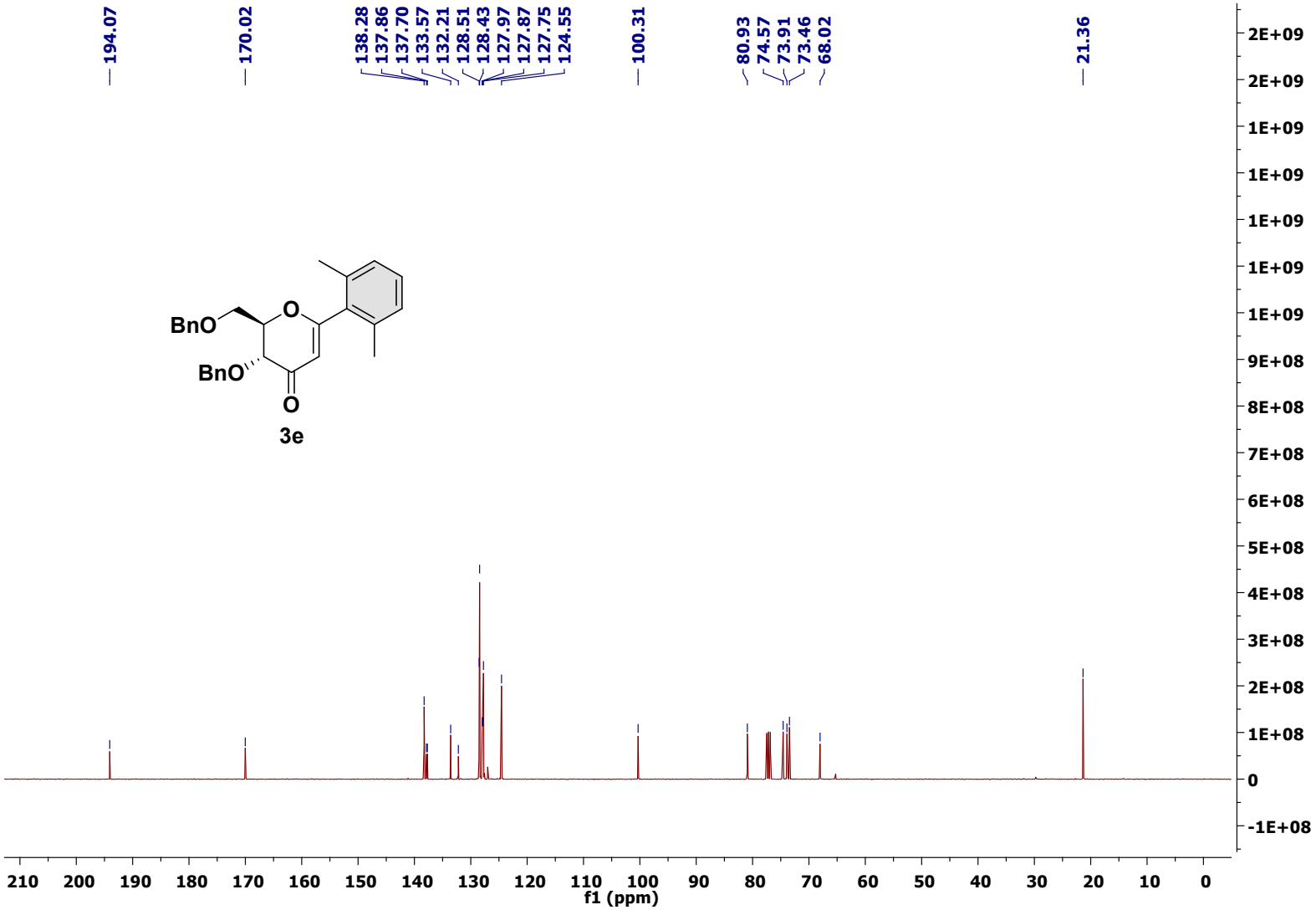
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3d** in $CDCl_3$



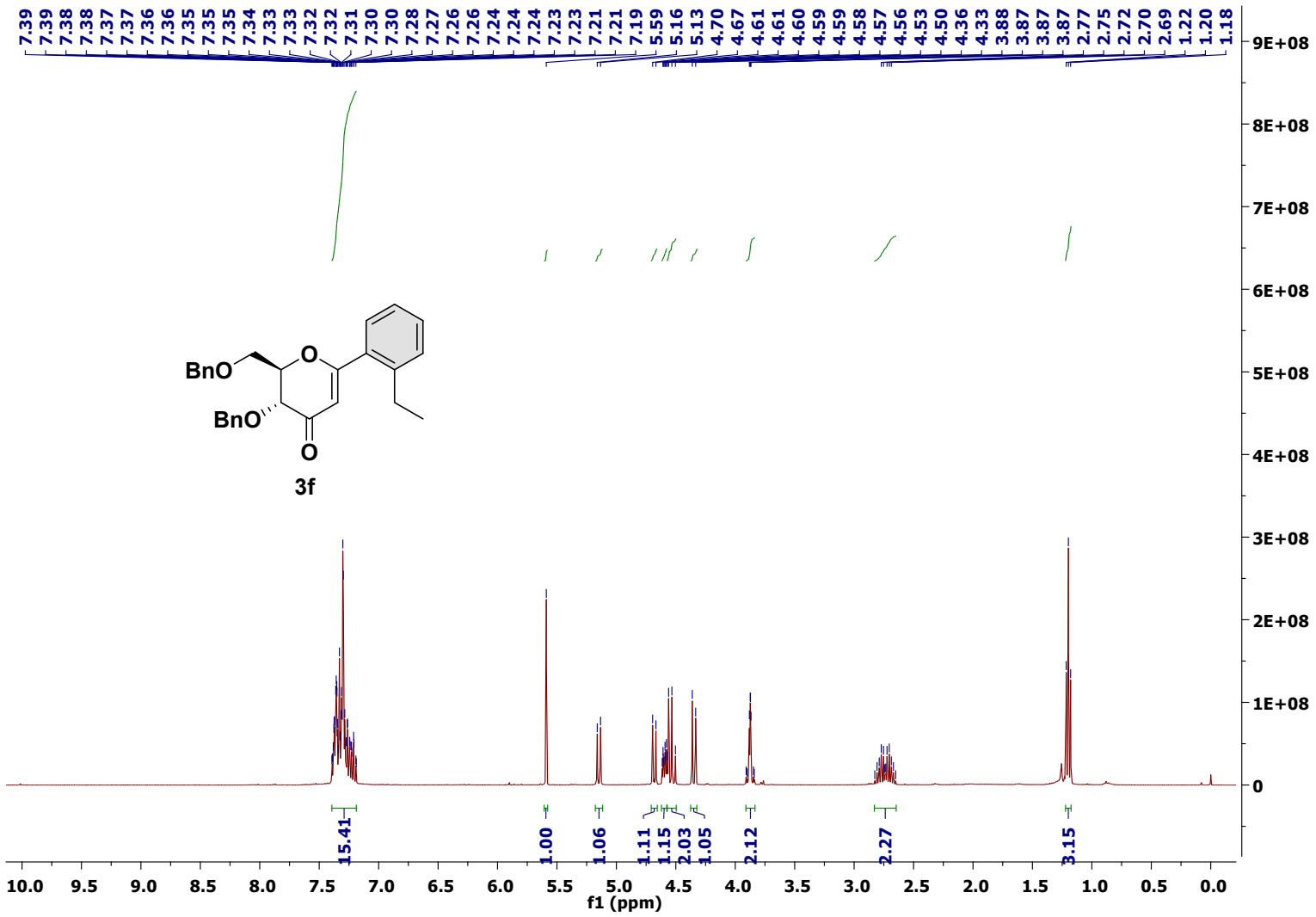
^{1}H NMR (400 MHz) of **3e** in $CDCl_3$



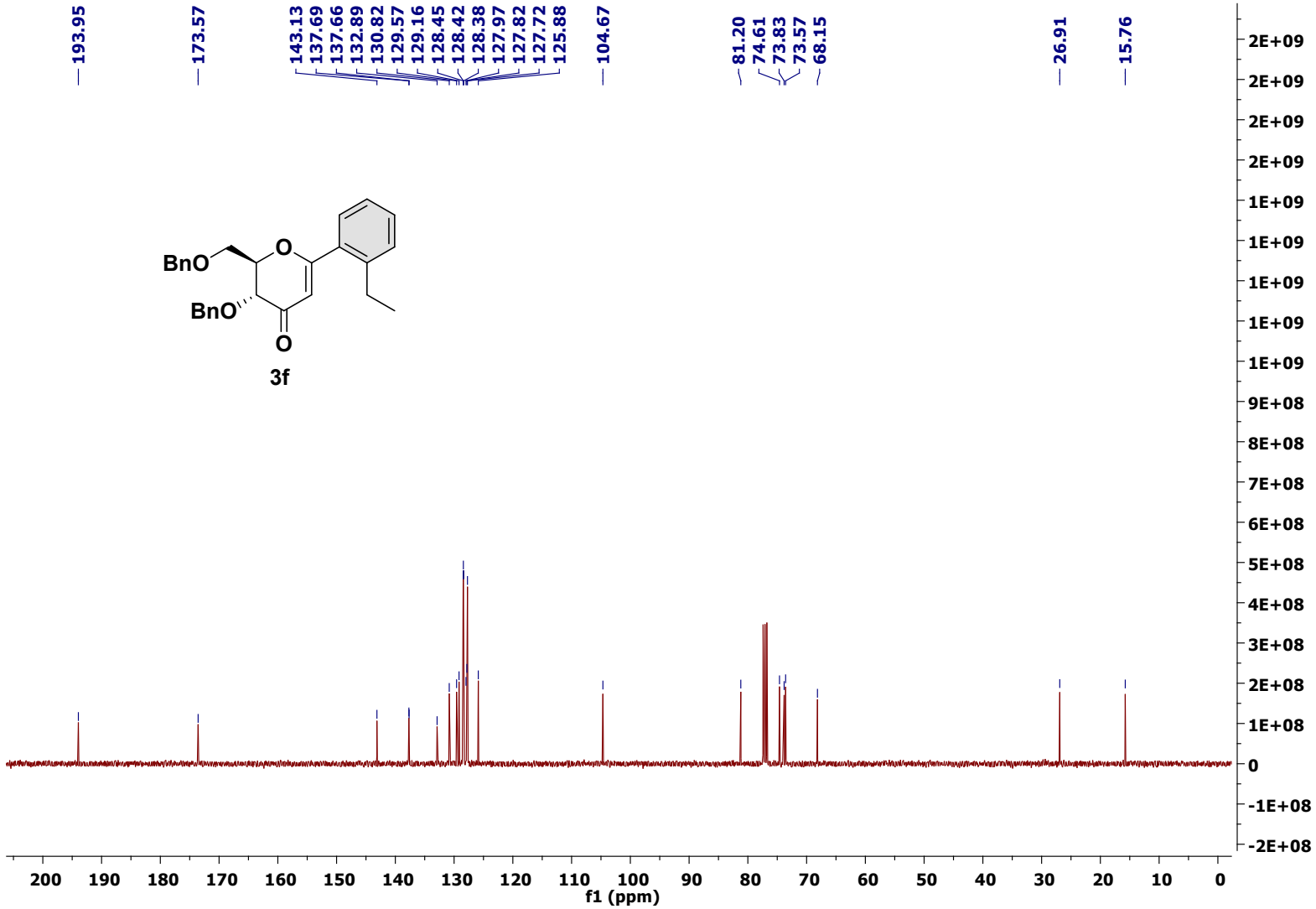
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3e** in $CDCl_3$



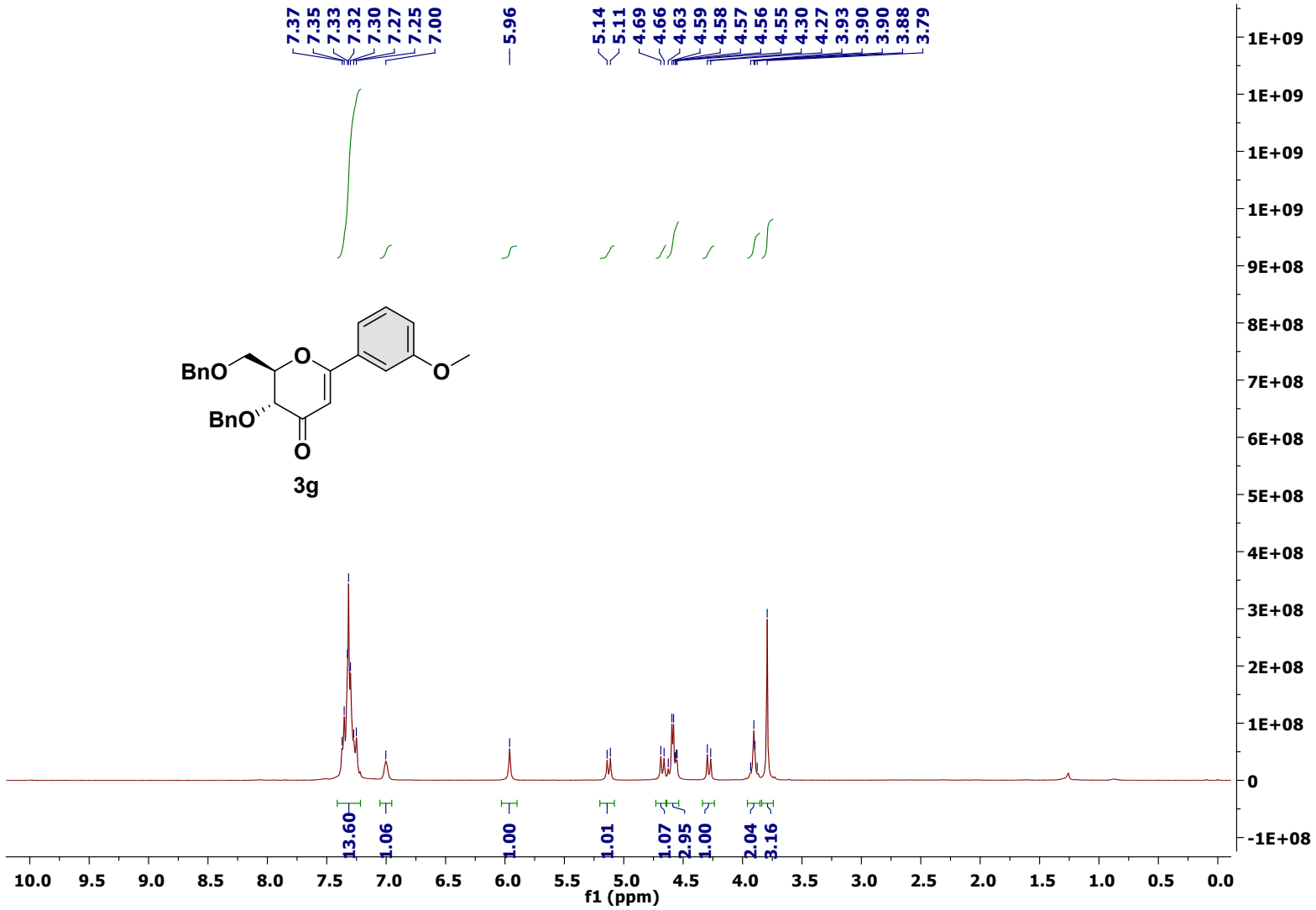
^{1}H NMR (400 MHz) of **3f** in $CDCl_3$



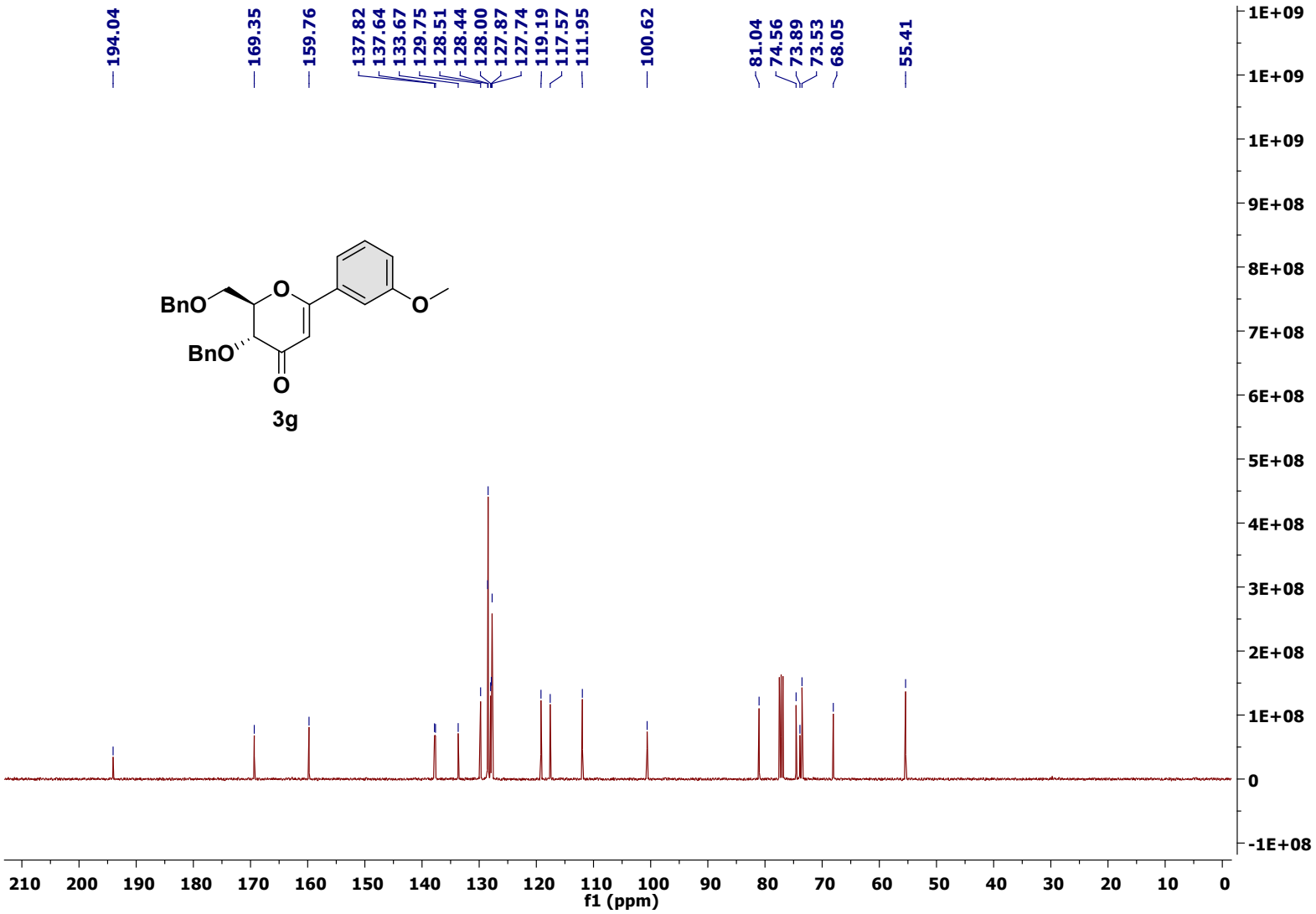
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3f** in $CDCl_3$



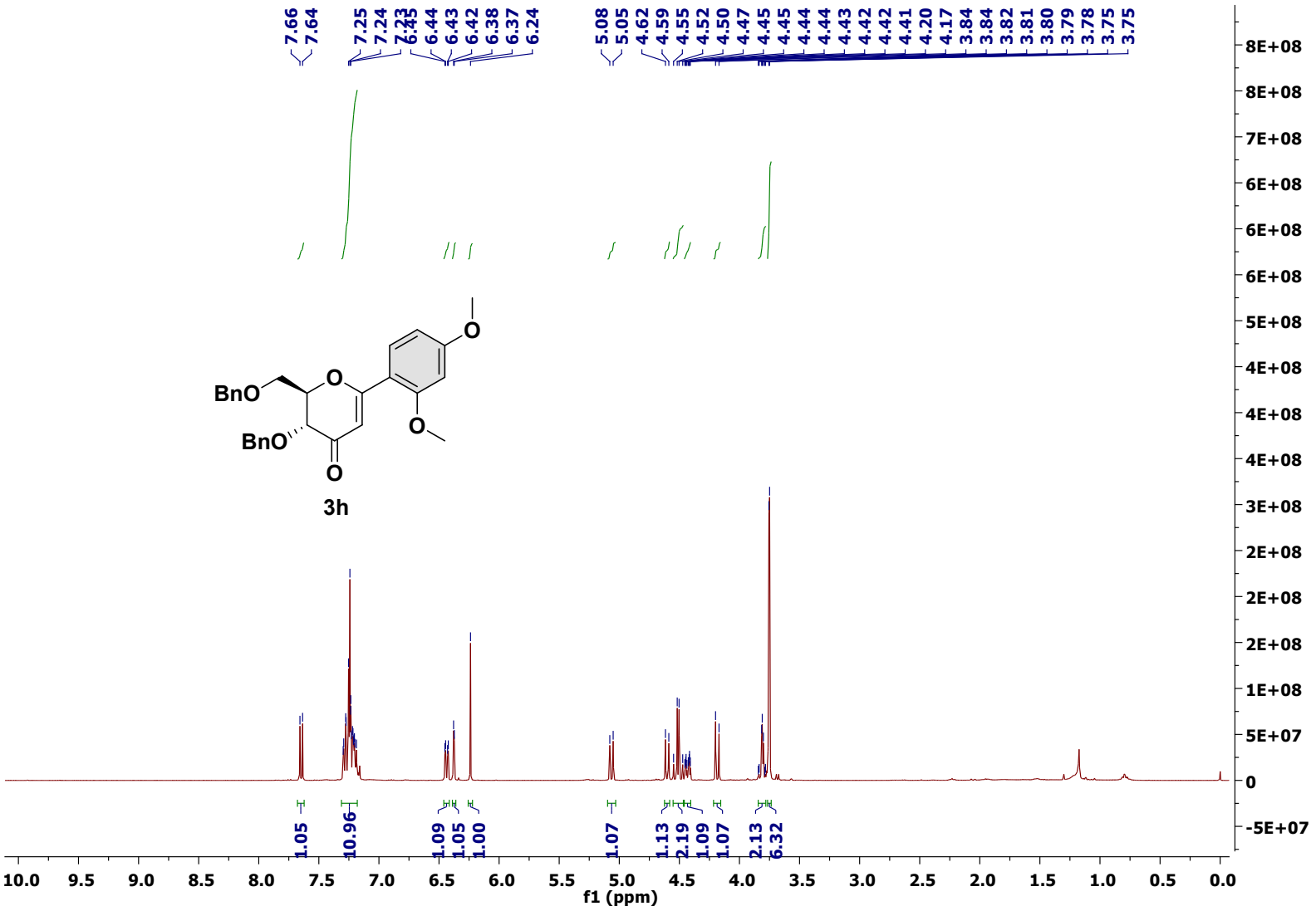
^{1}H NMR (400 MHz) of **3g** in $CDCl_3$



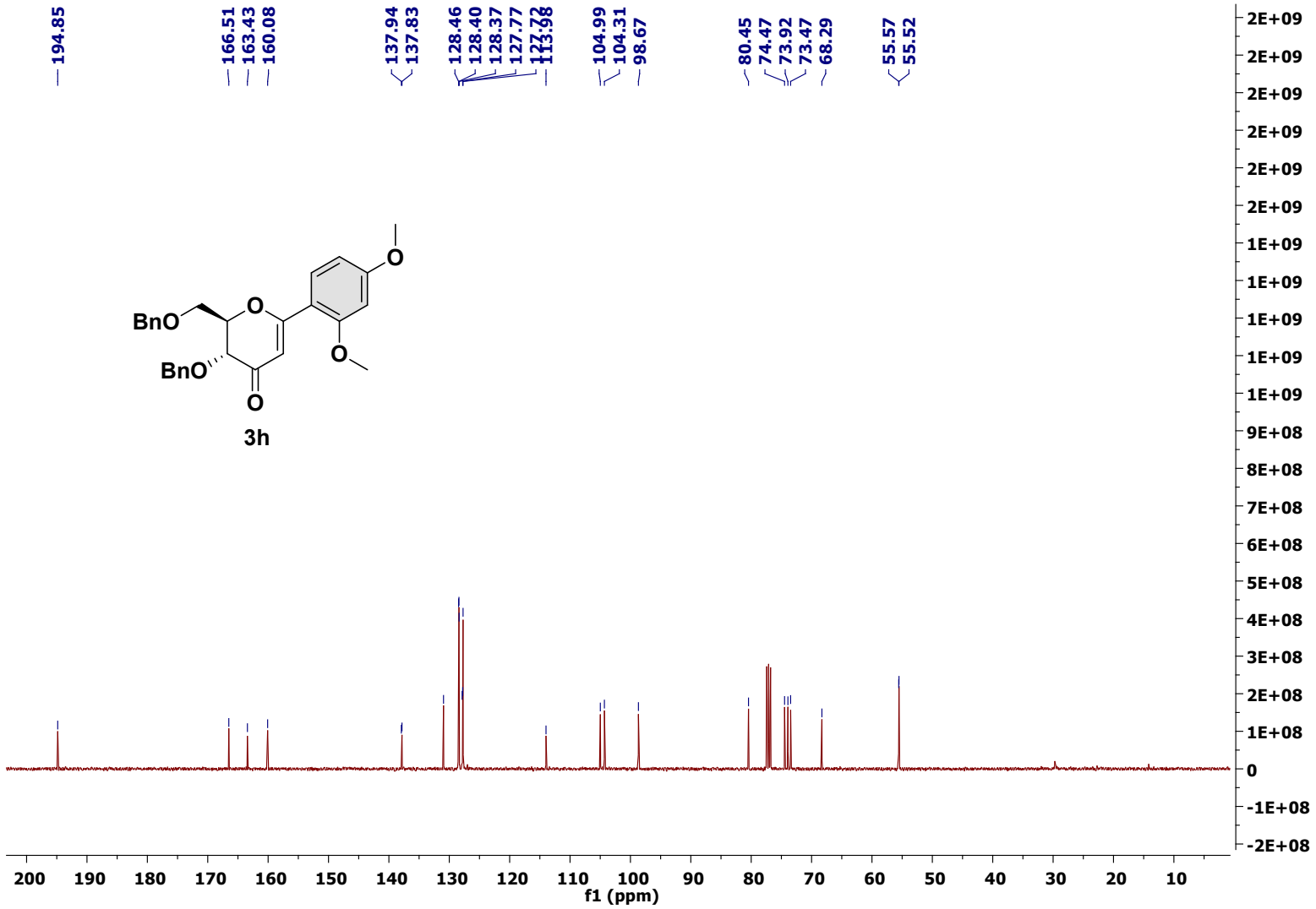
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3g** in $CDCl_3$



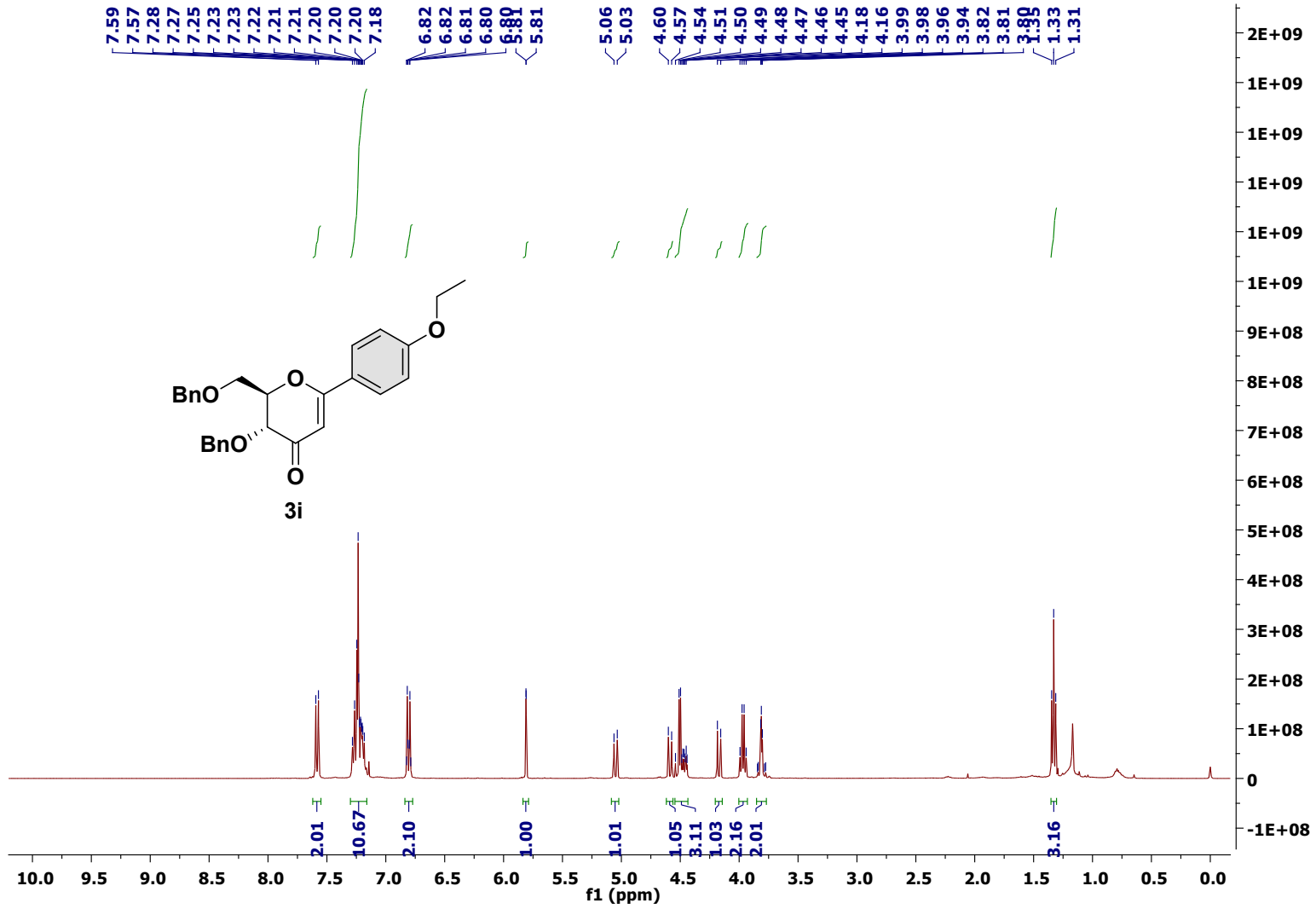
^{1}H NMR (400 MHz) of **3h** in $CDCl_3$



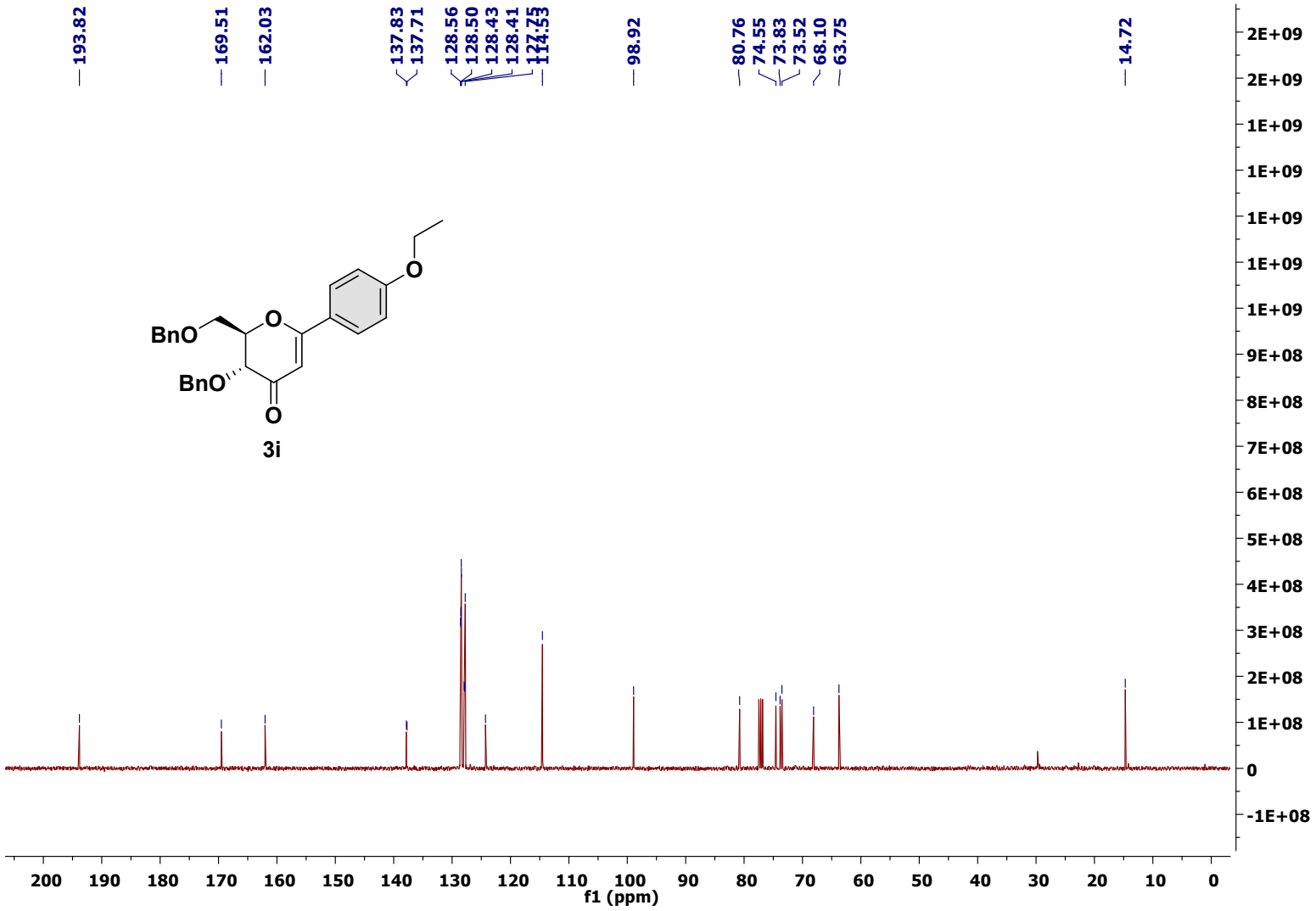
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3h** in $CDCl_3$



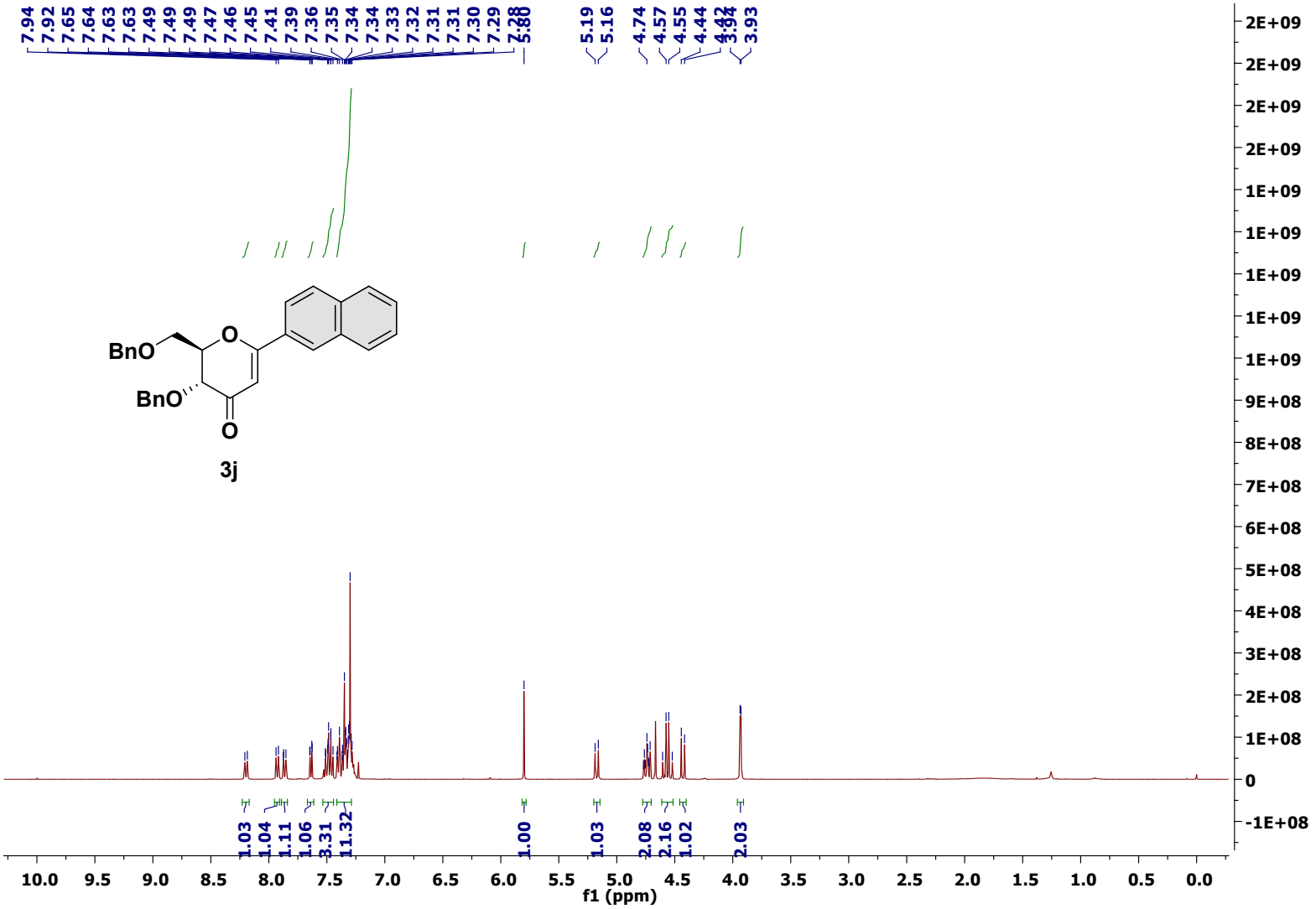
^{1}H NMR (400 MHz) of **3i** in $CDCl_3$



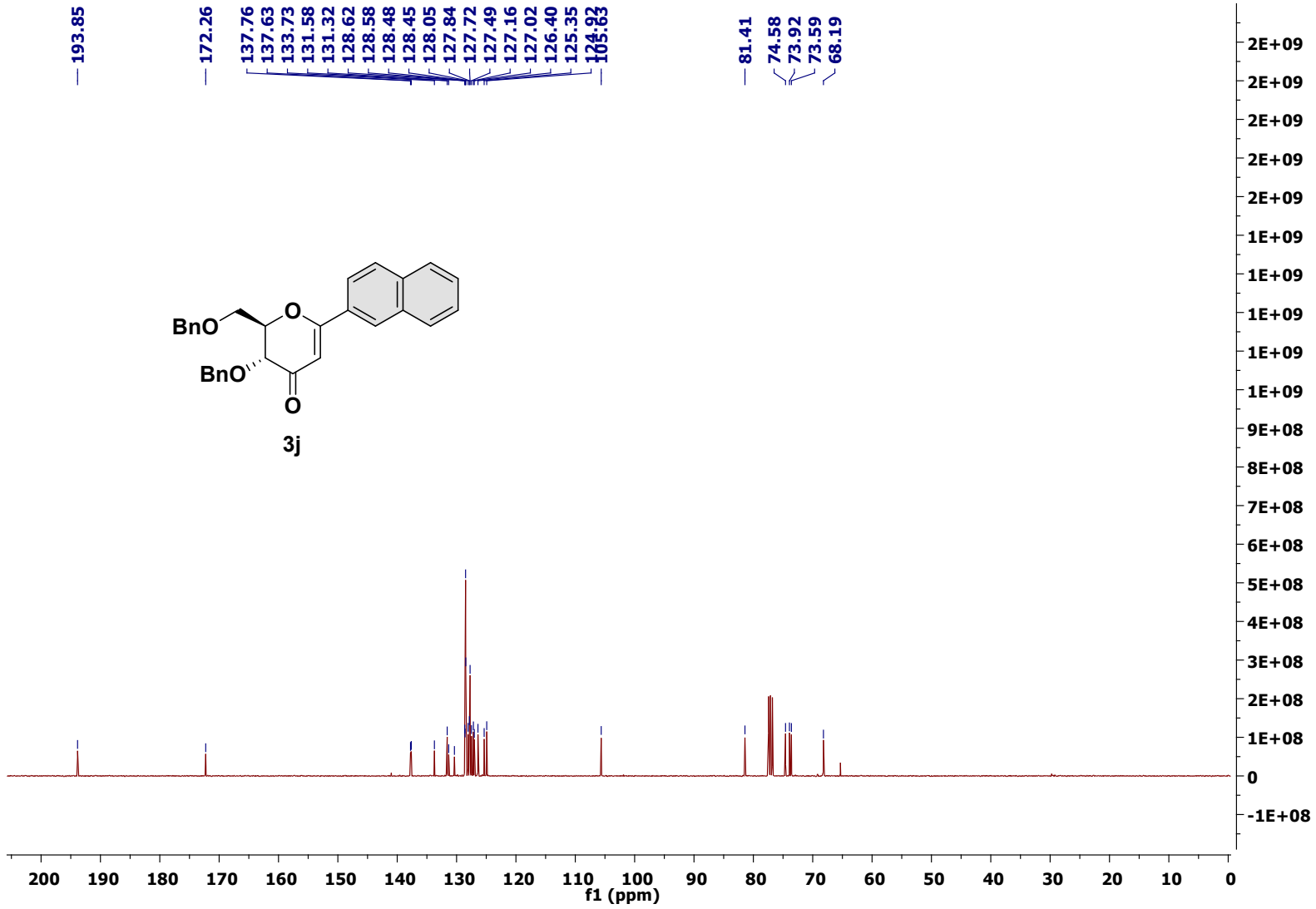
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3i** in $CDCl_3$



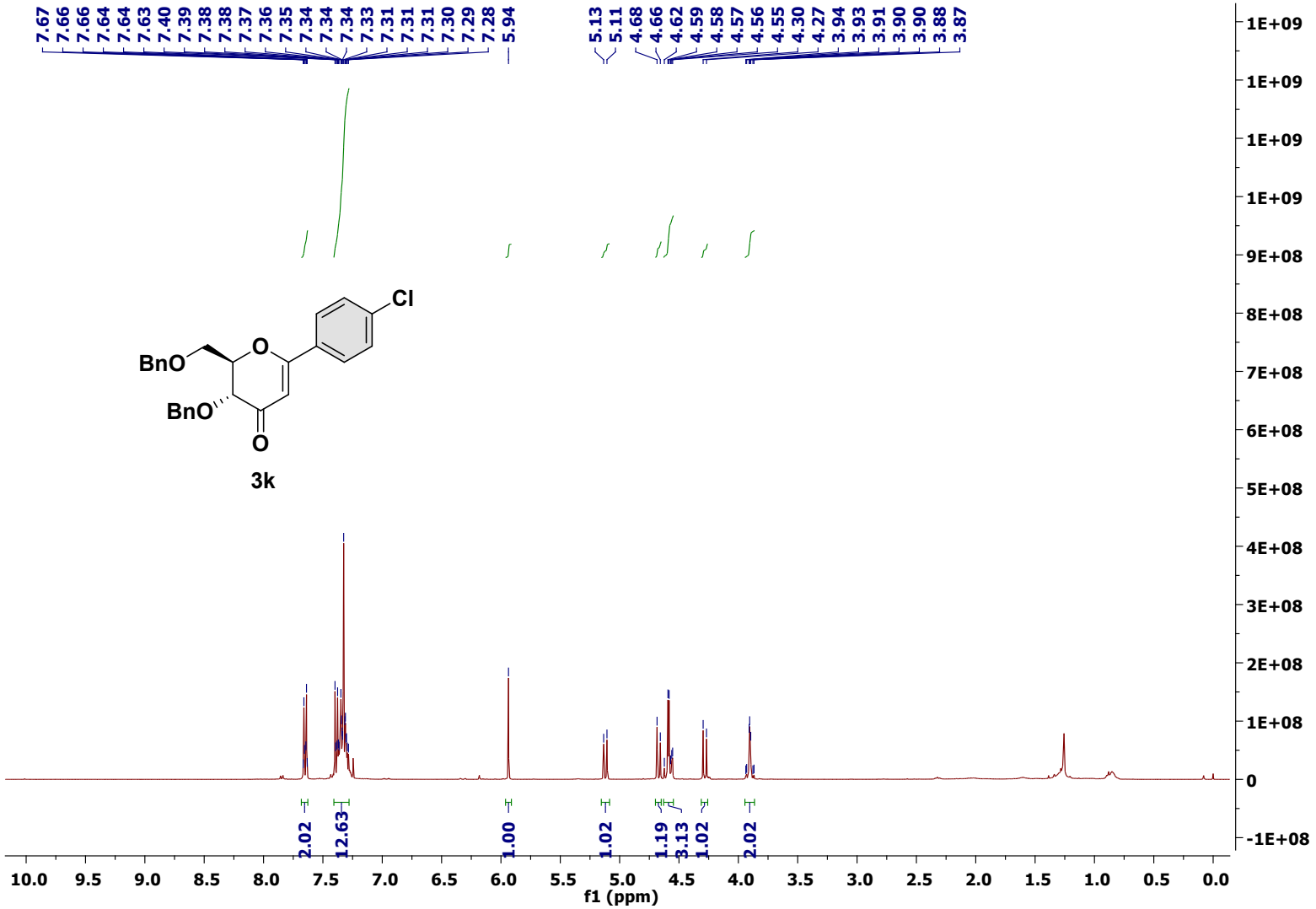
^{1}H NMR (400 MHz) of **3j** in $CDCl_3$



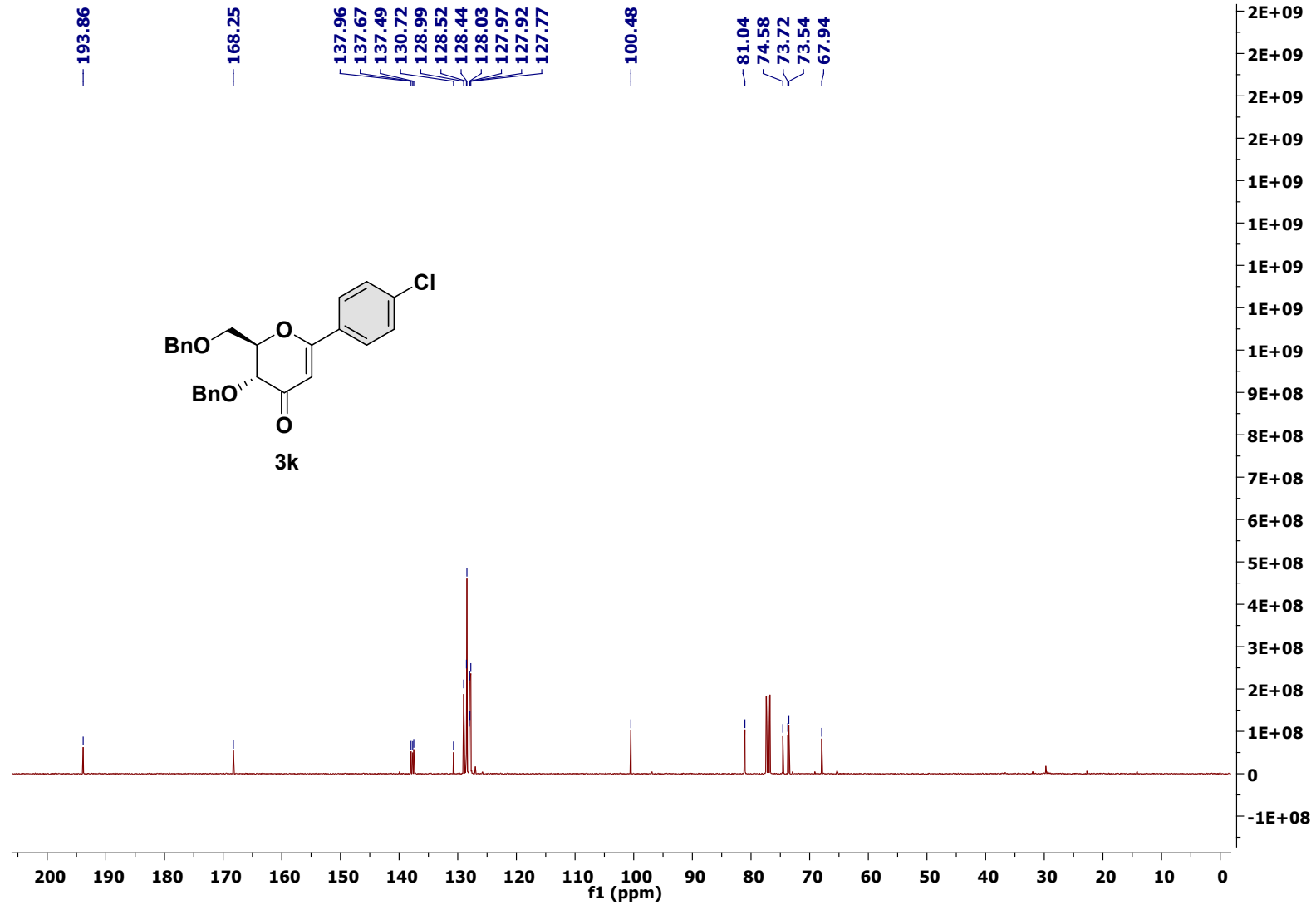
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3j** in $CDCl_3$



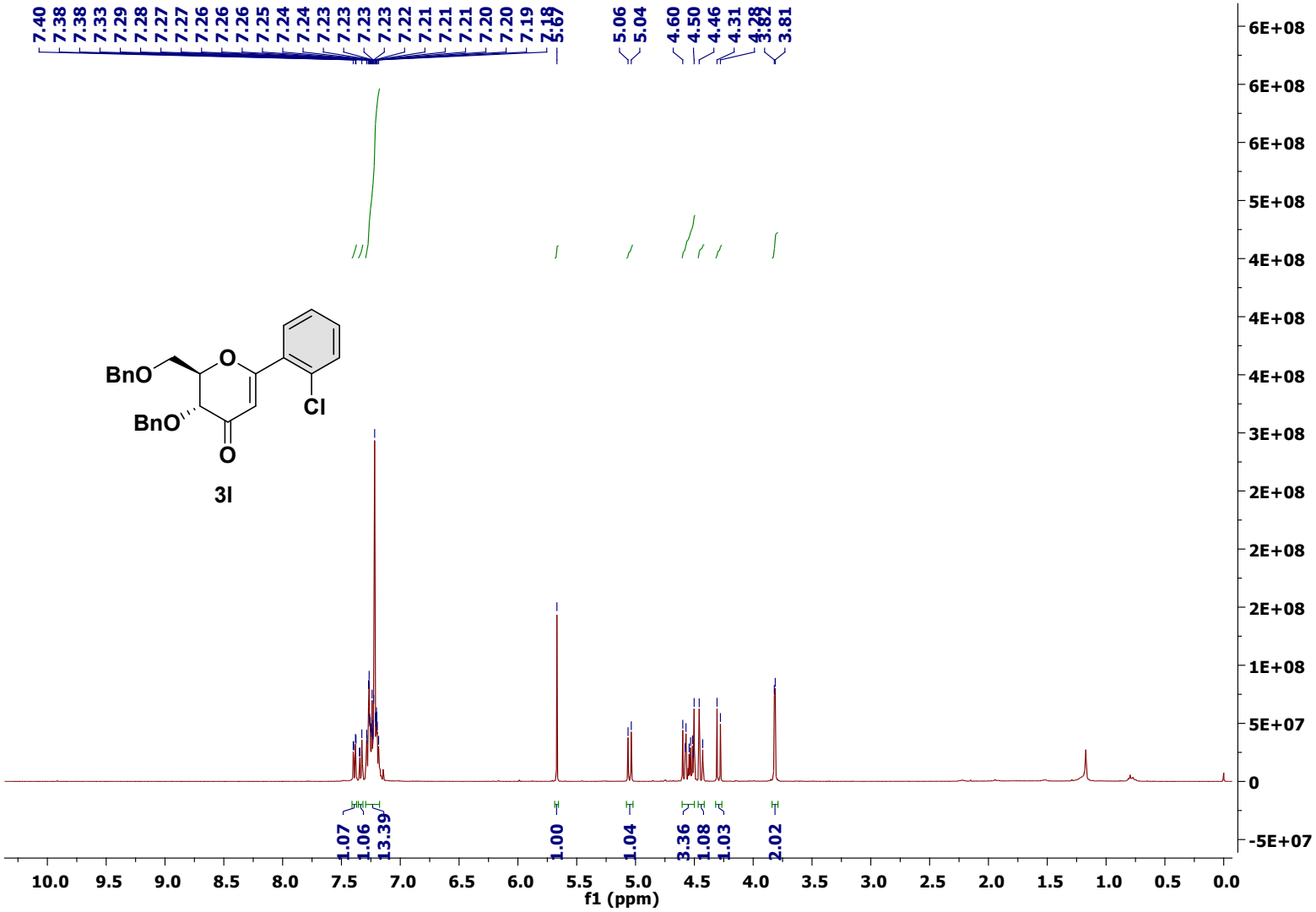
^{1}H NMR (400 MHz) of **3k** in $CDCl_3$



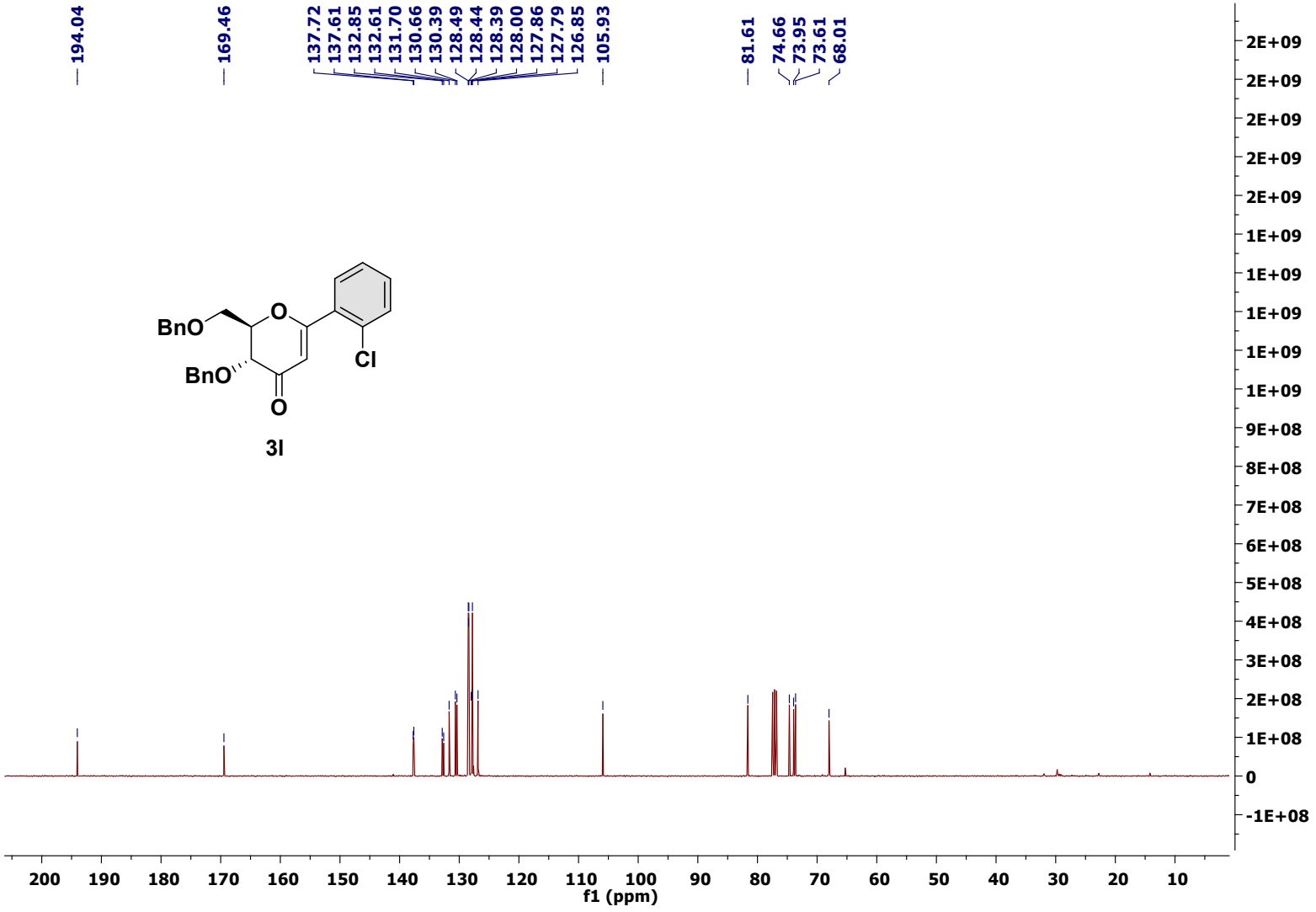
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3k** in $CDCl_3$



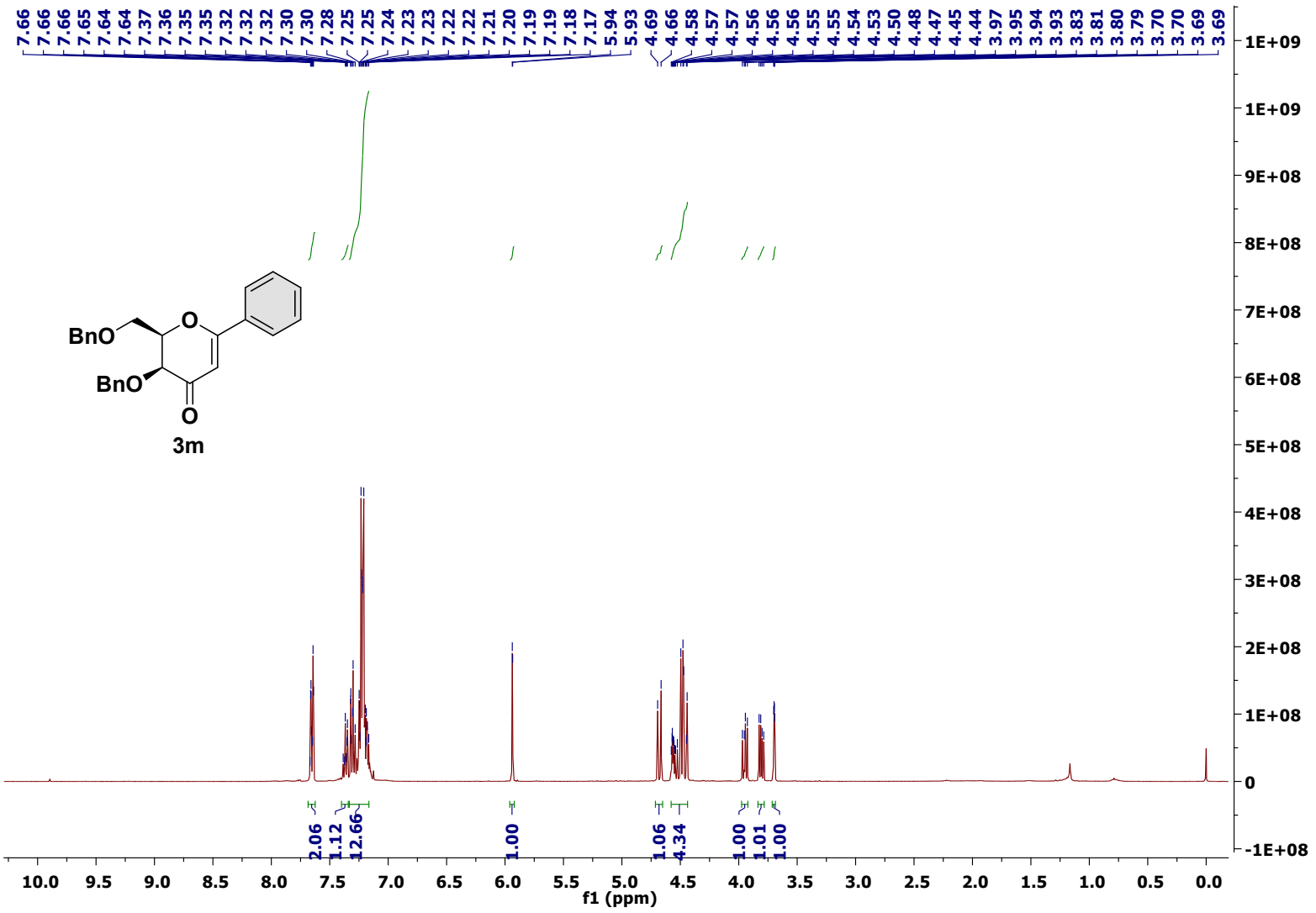
^{1}H NMR (400 MHz) of **3l** in $CDCl_3$



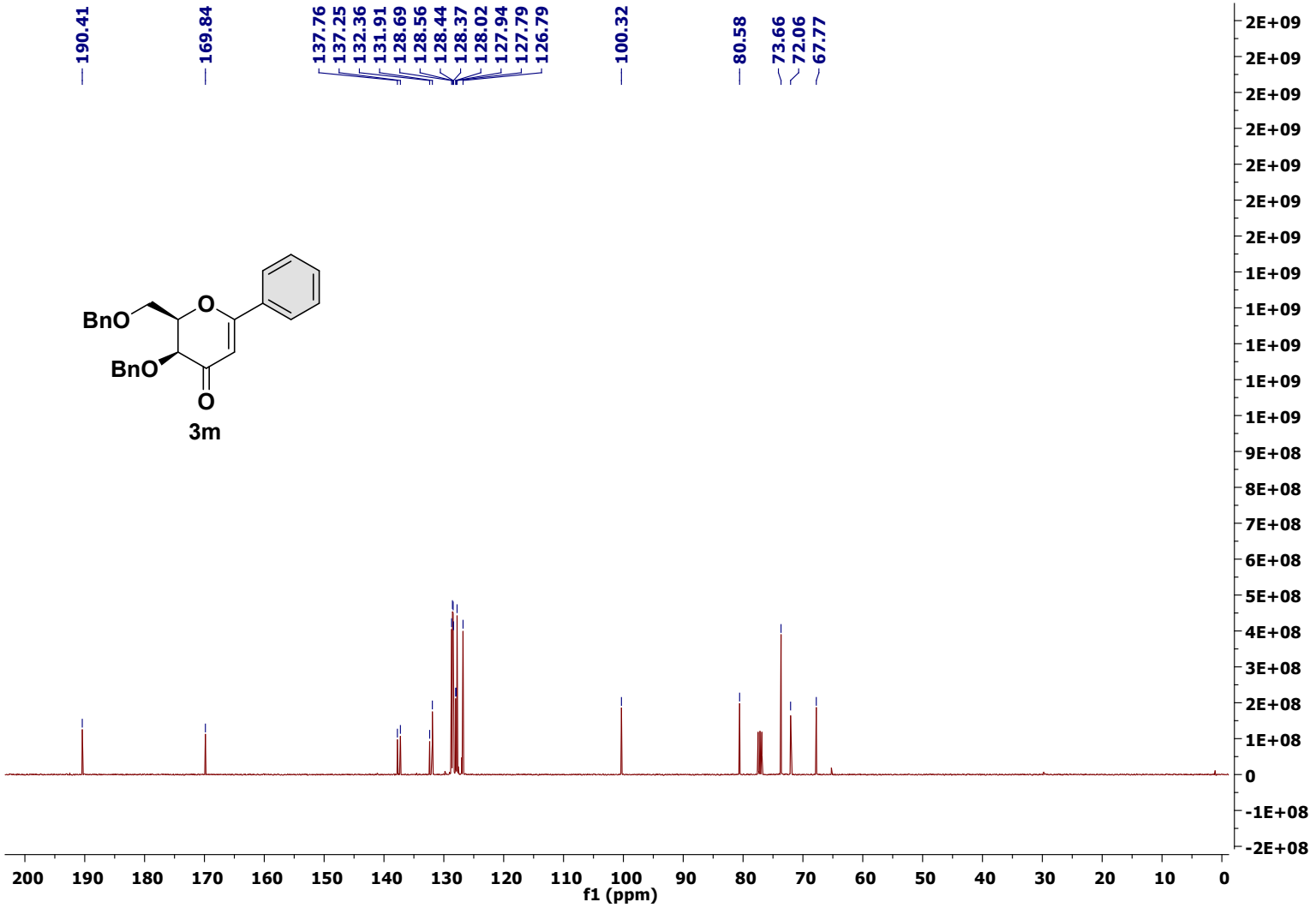
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3l** in $CDCl_3$



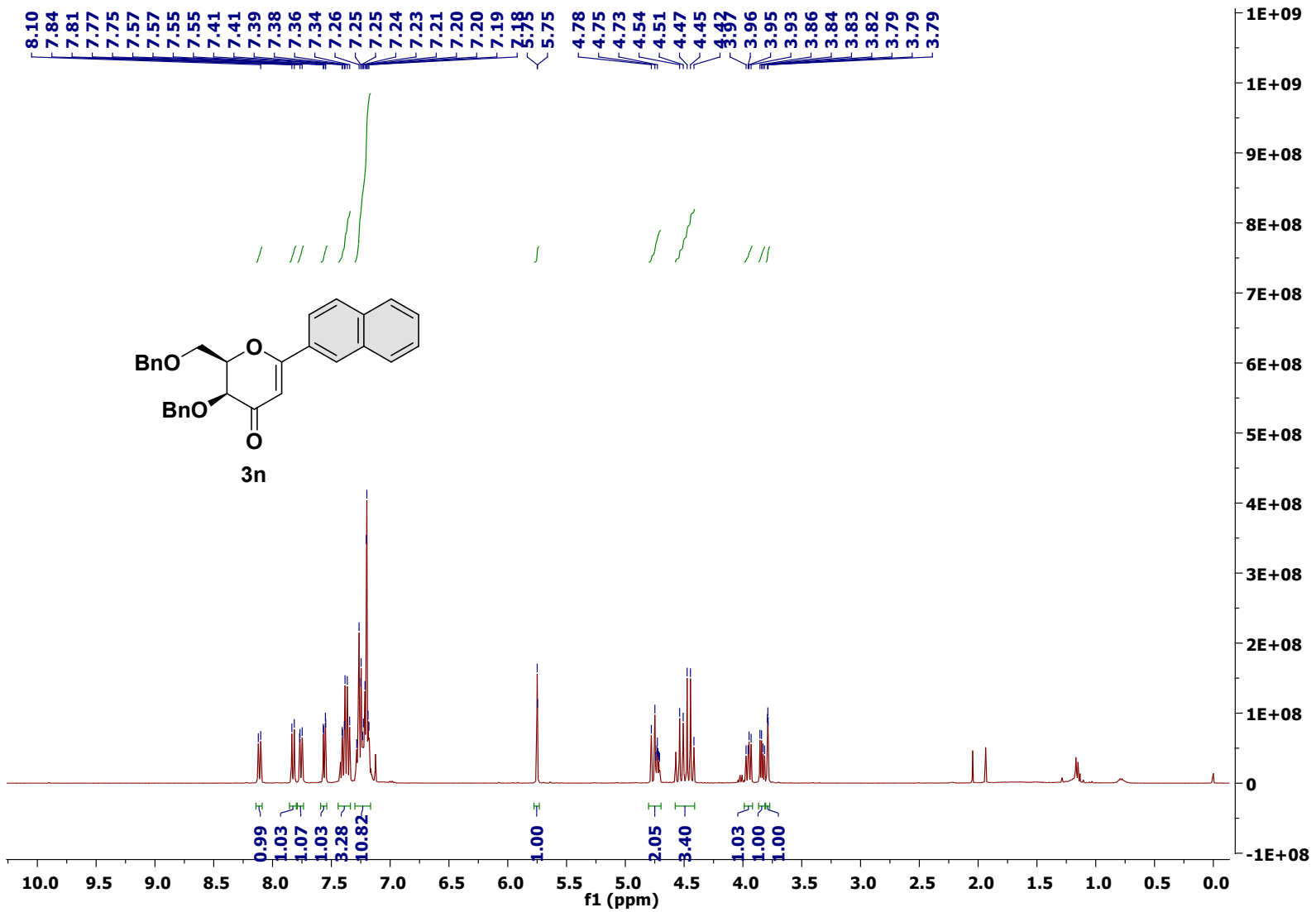
^{1}H NMR (400 MHz) of **3m** in $CDCl_3$



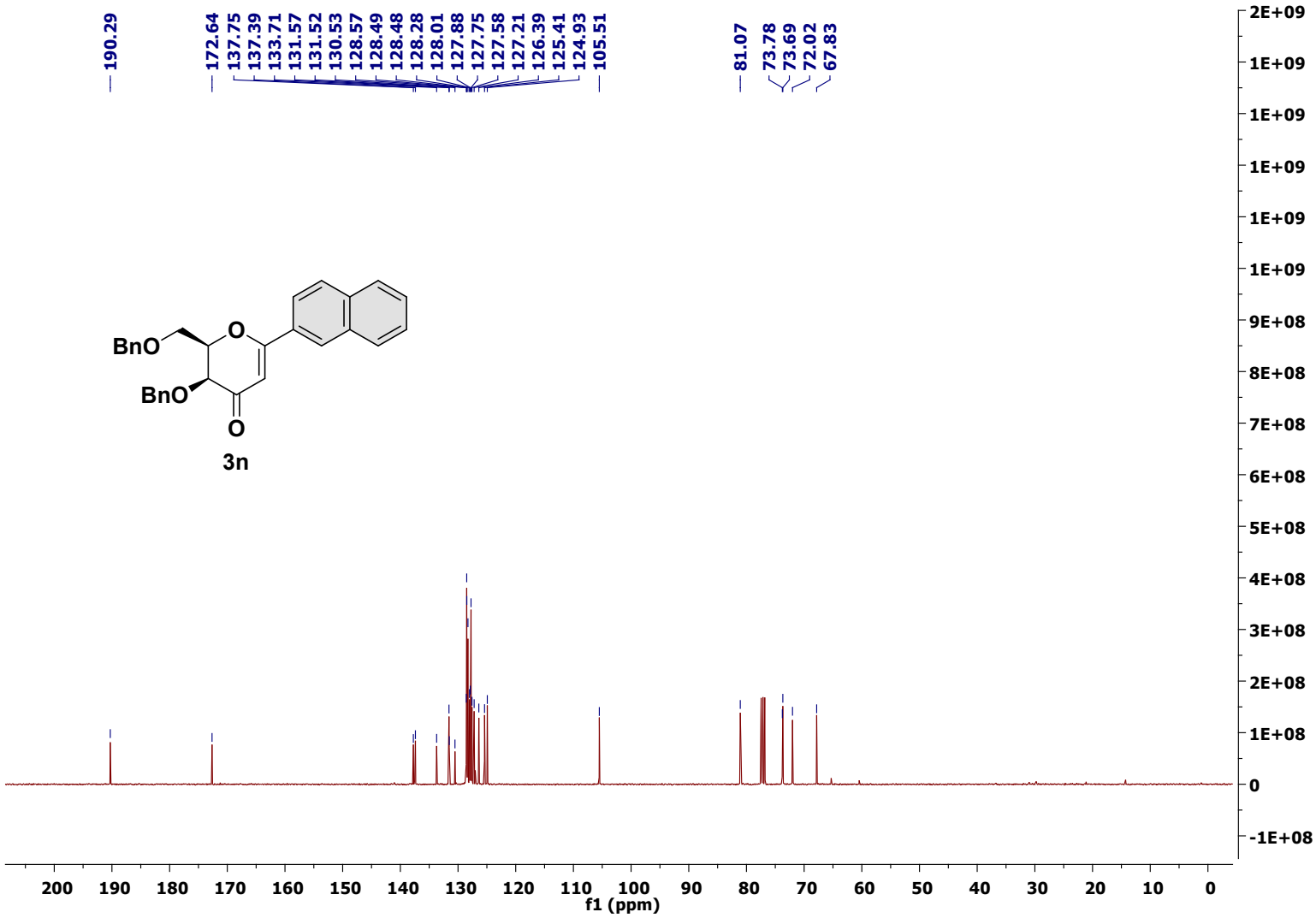
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3m** in $CDCl_3$



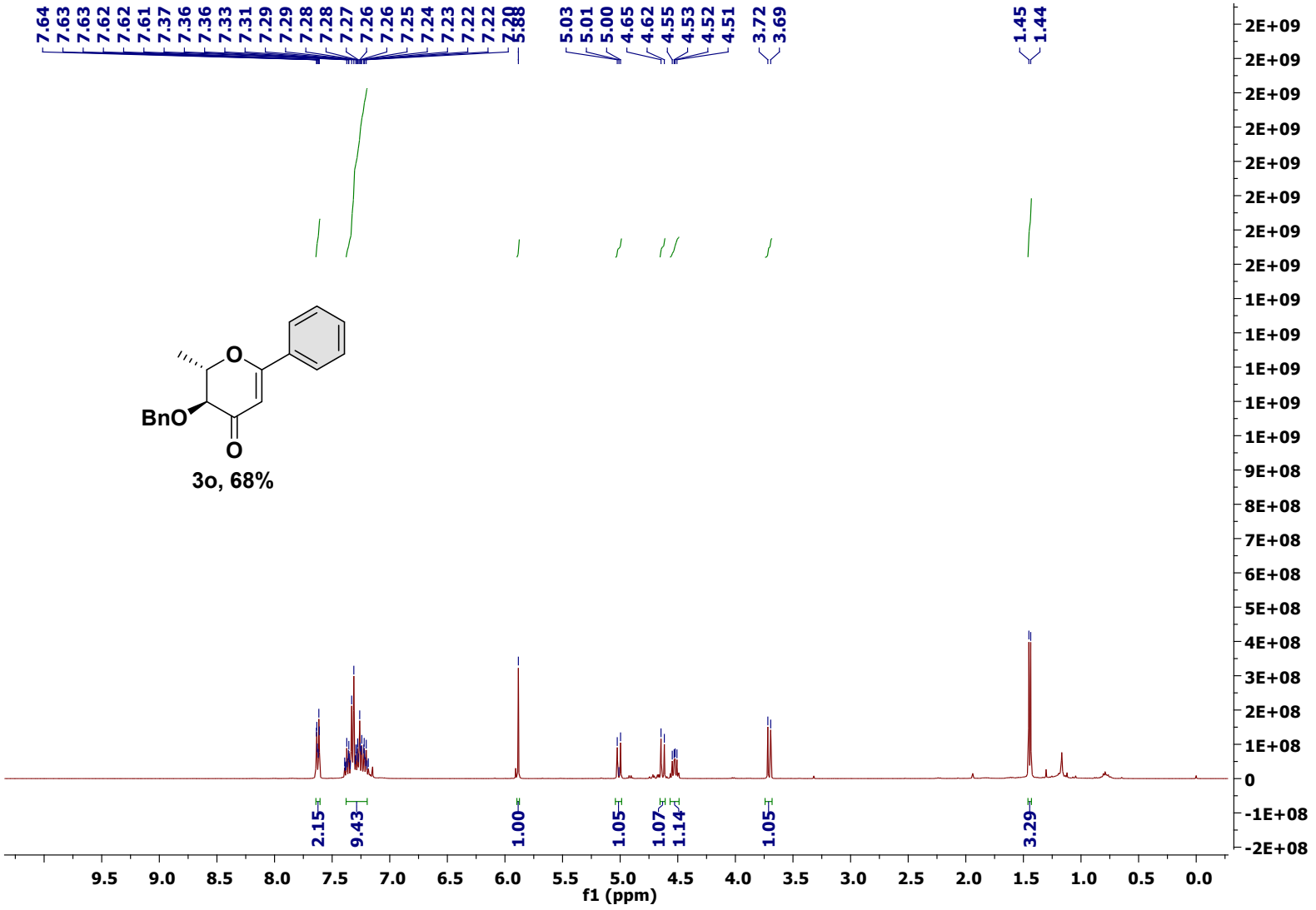
^{1}H NMR (400 MHz) of **3n** in $CDCl_3$



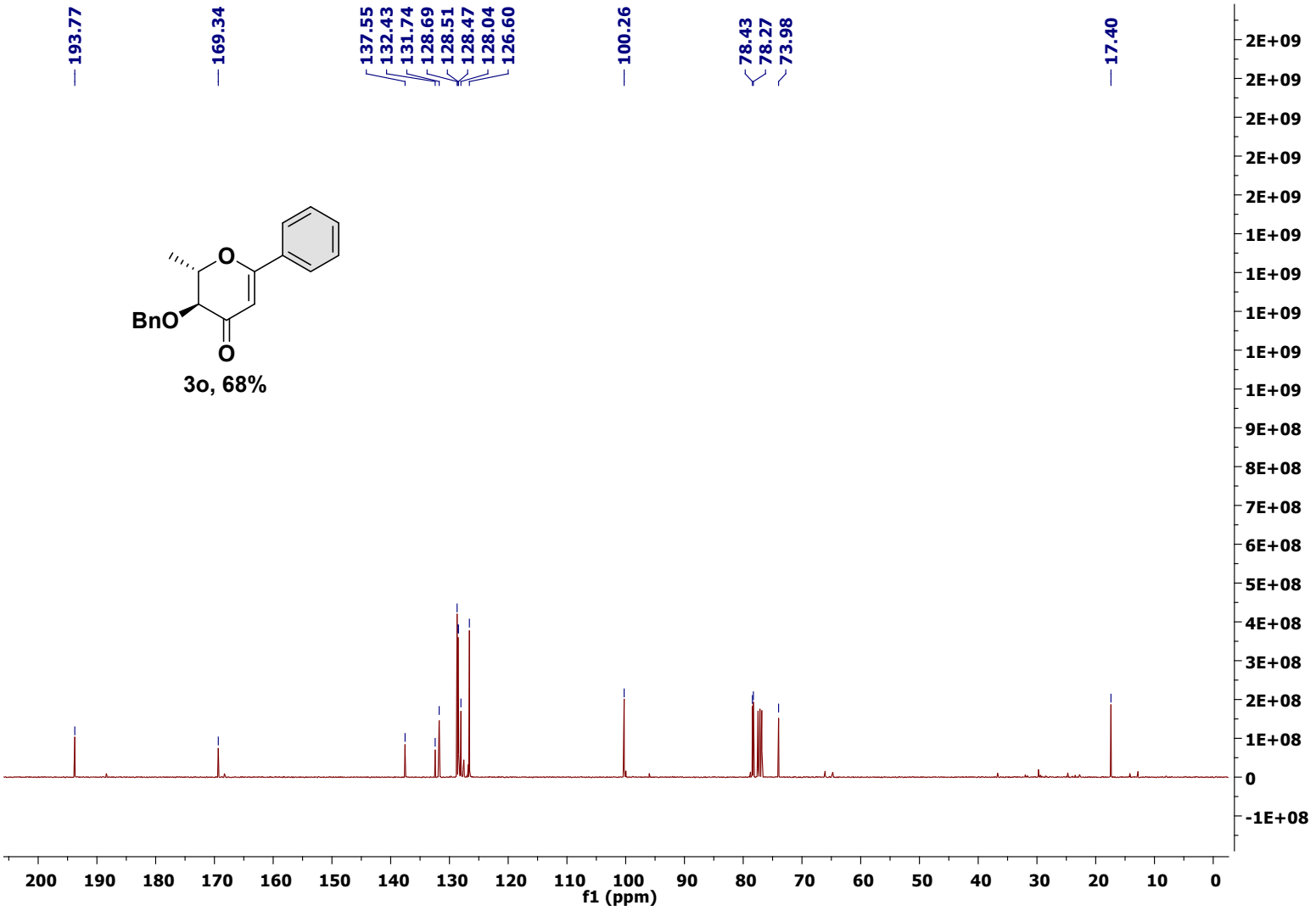
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3n** in $CDCl_3$



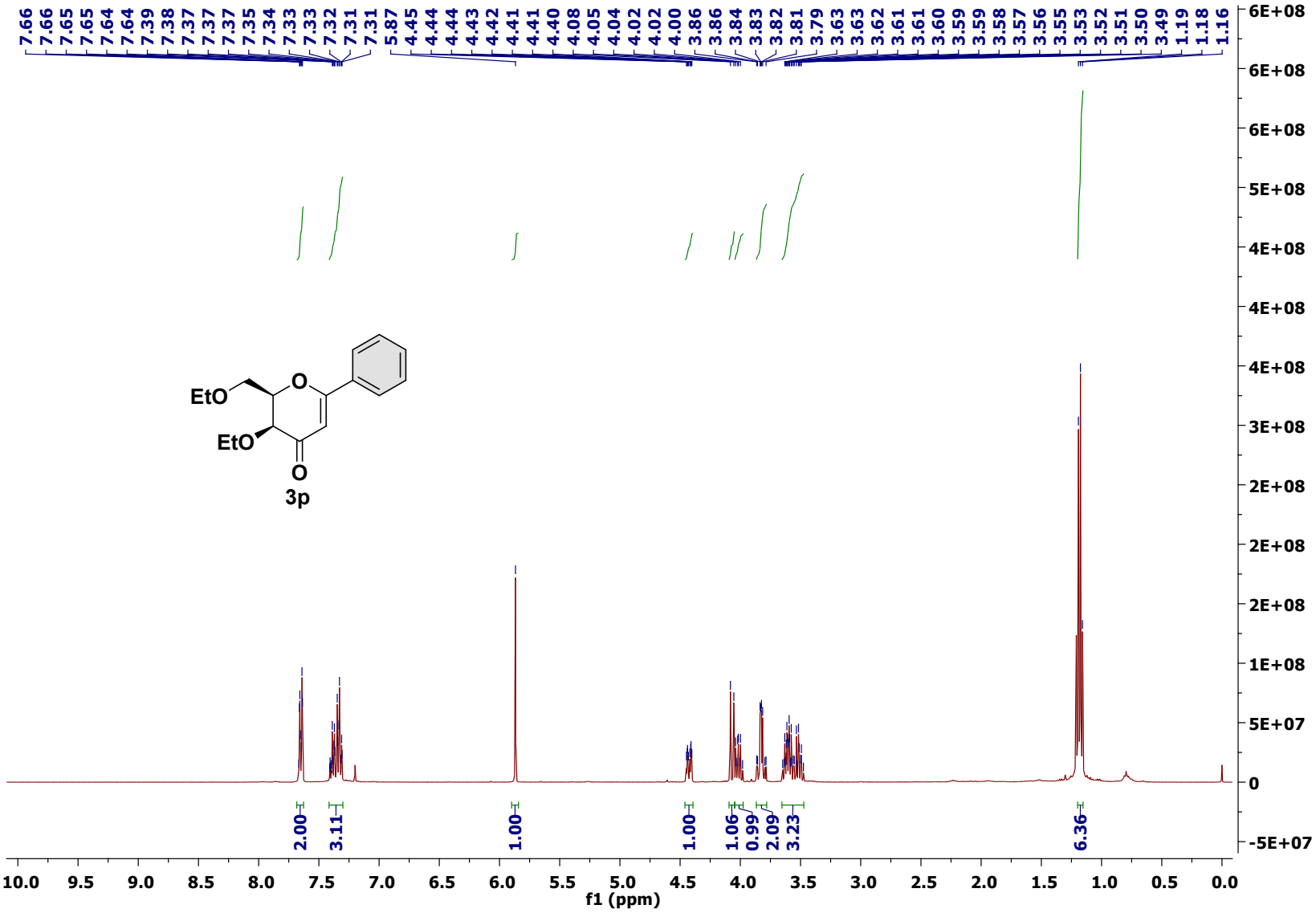
^{1}H NMR (400 MHz) of **3o** in $CDCl_3$



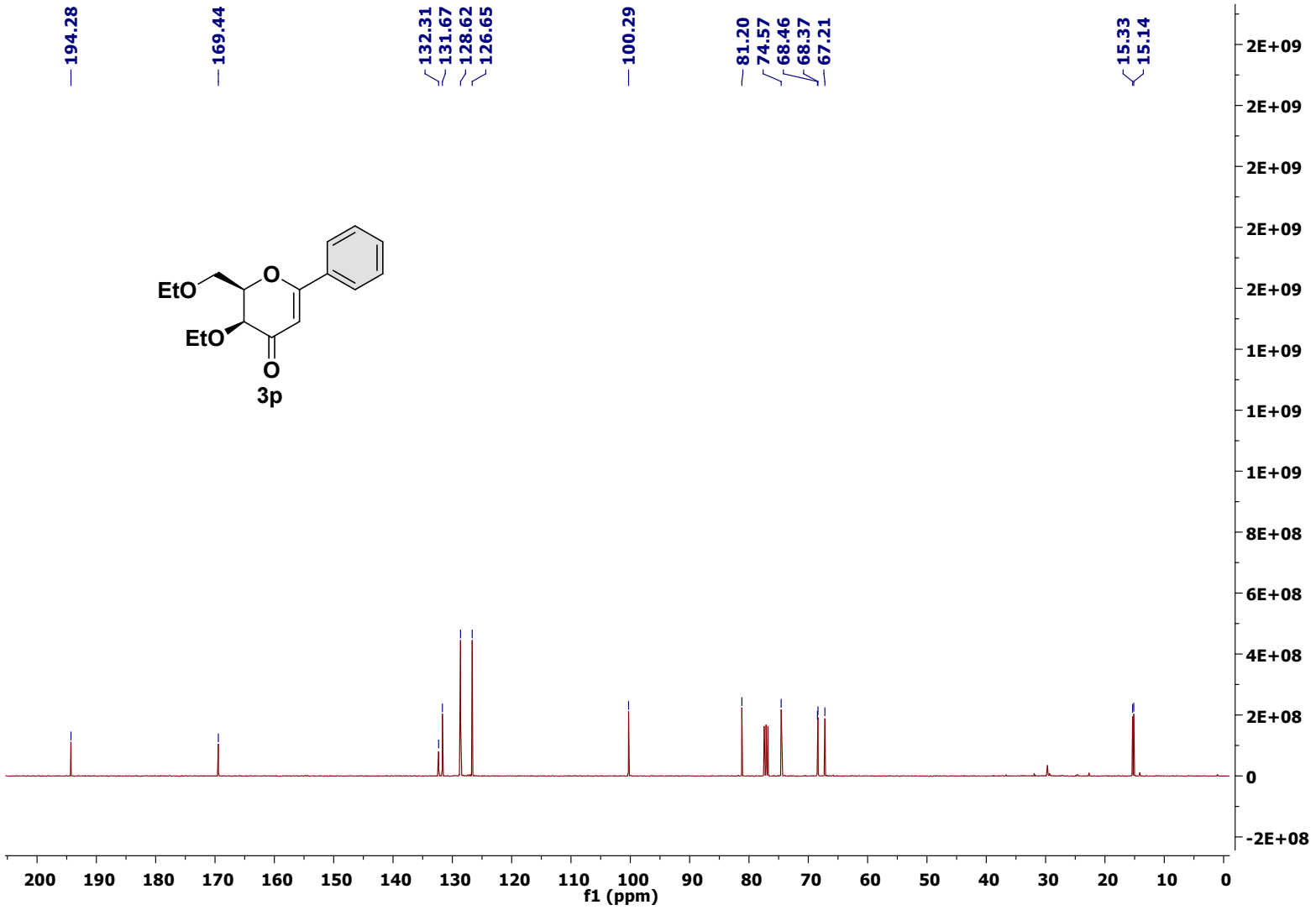
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3o** in $CDCl_3$



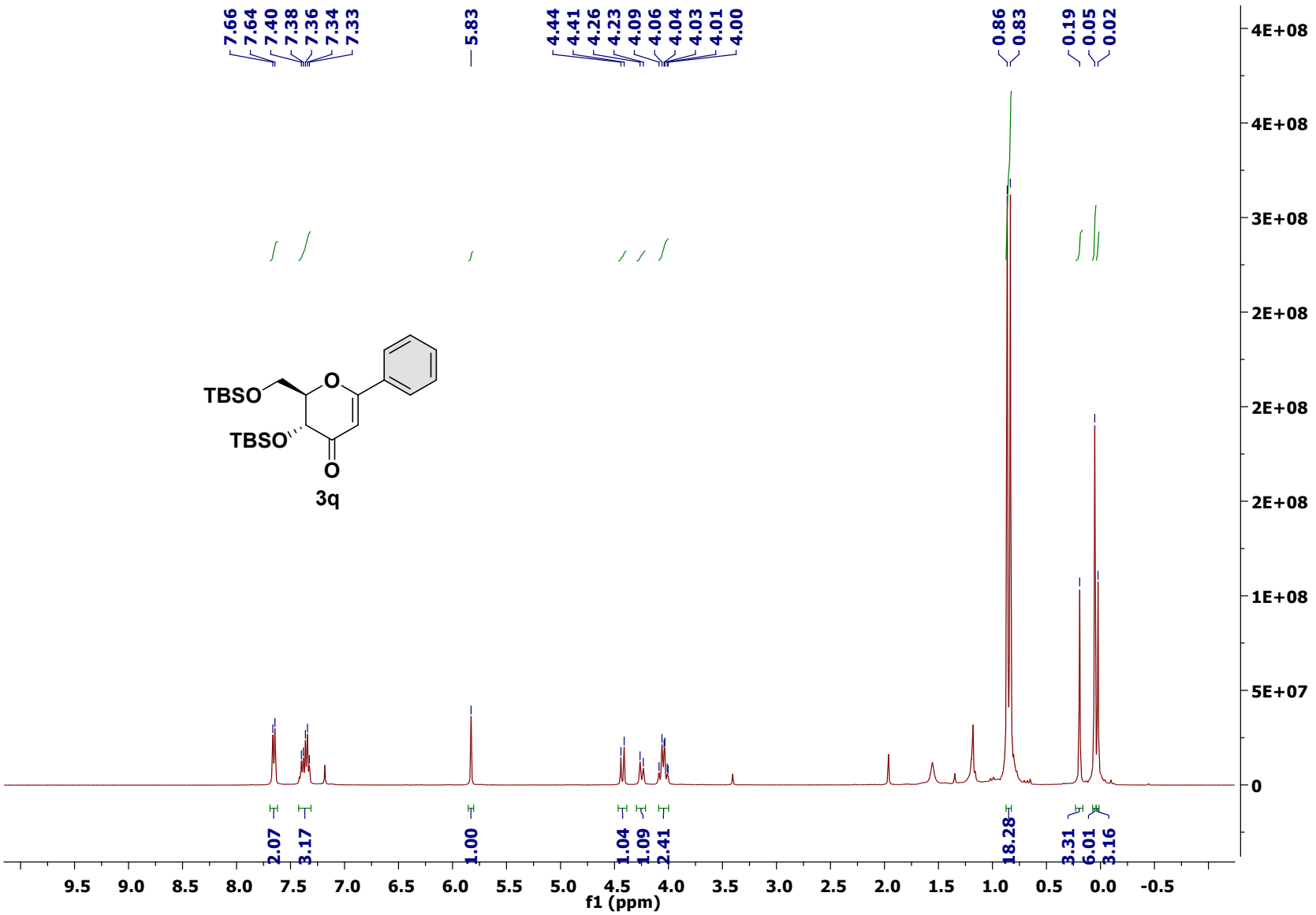
^{1}H NMR (400 MHz) of **3p** in $CDCl_3$



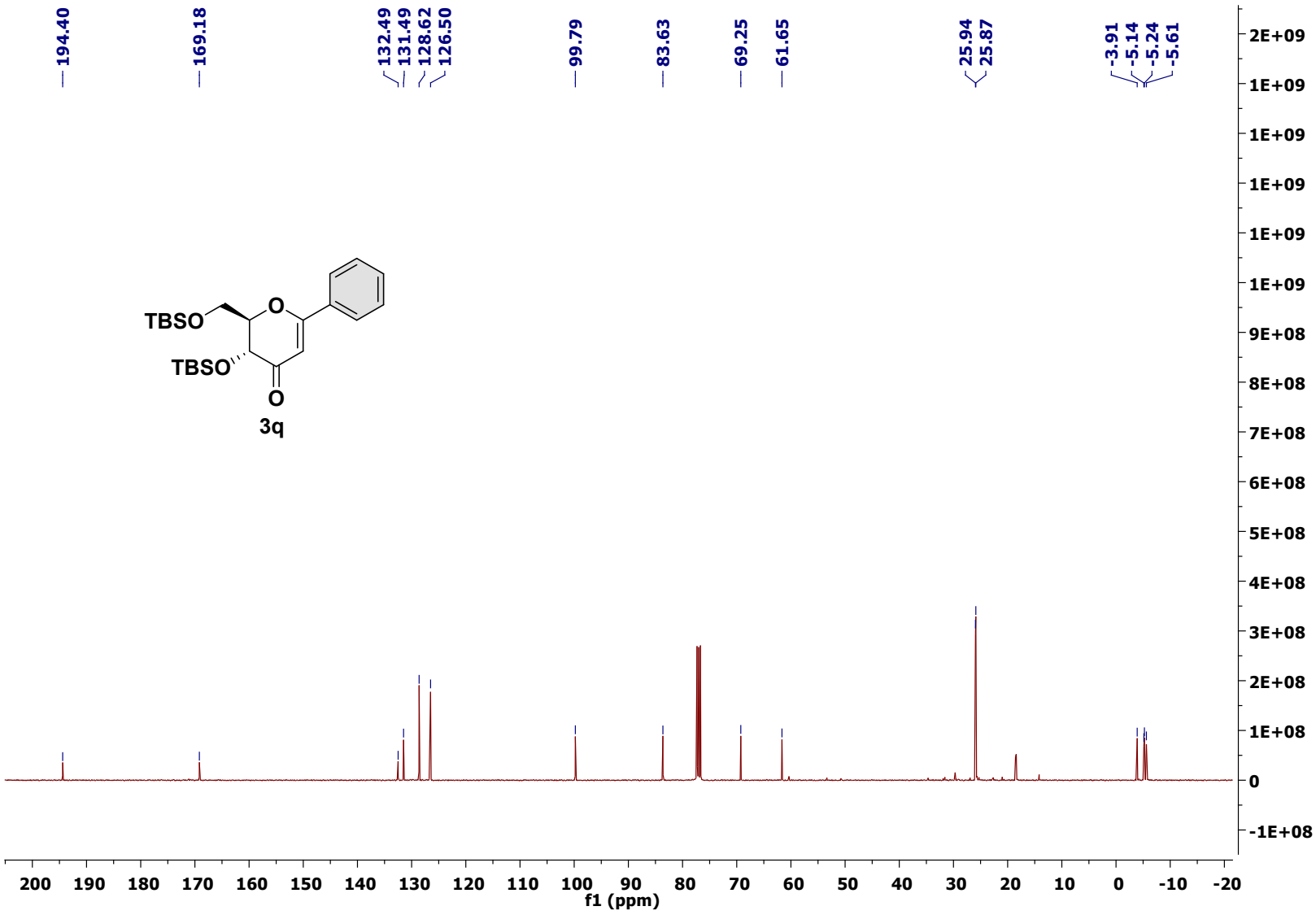
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3p** in $CDCl_3$



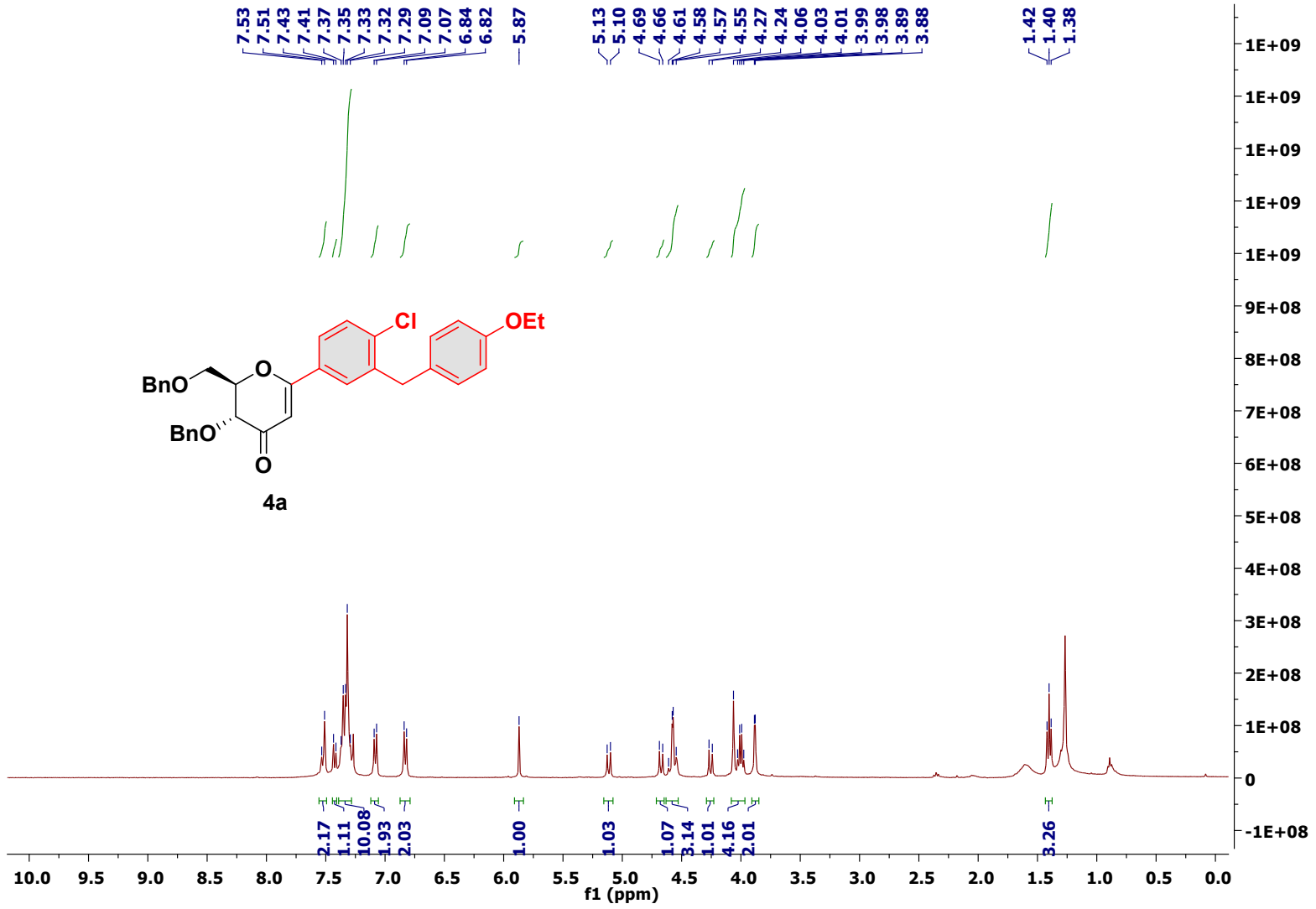
^{1}H NMR (400 MHz) of **3q** in $CDCl_3$



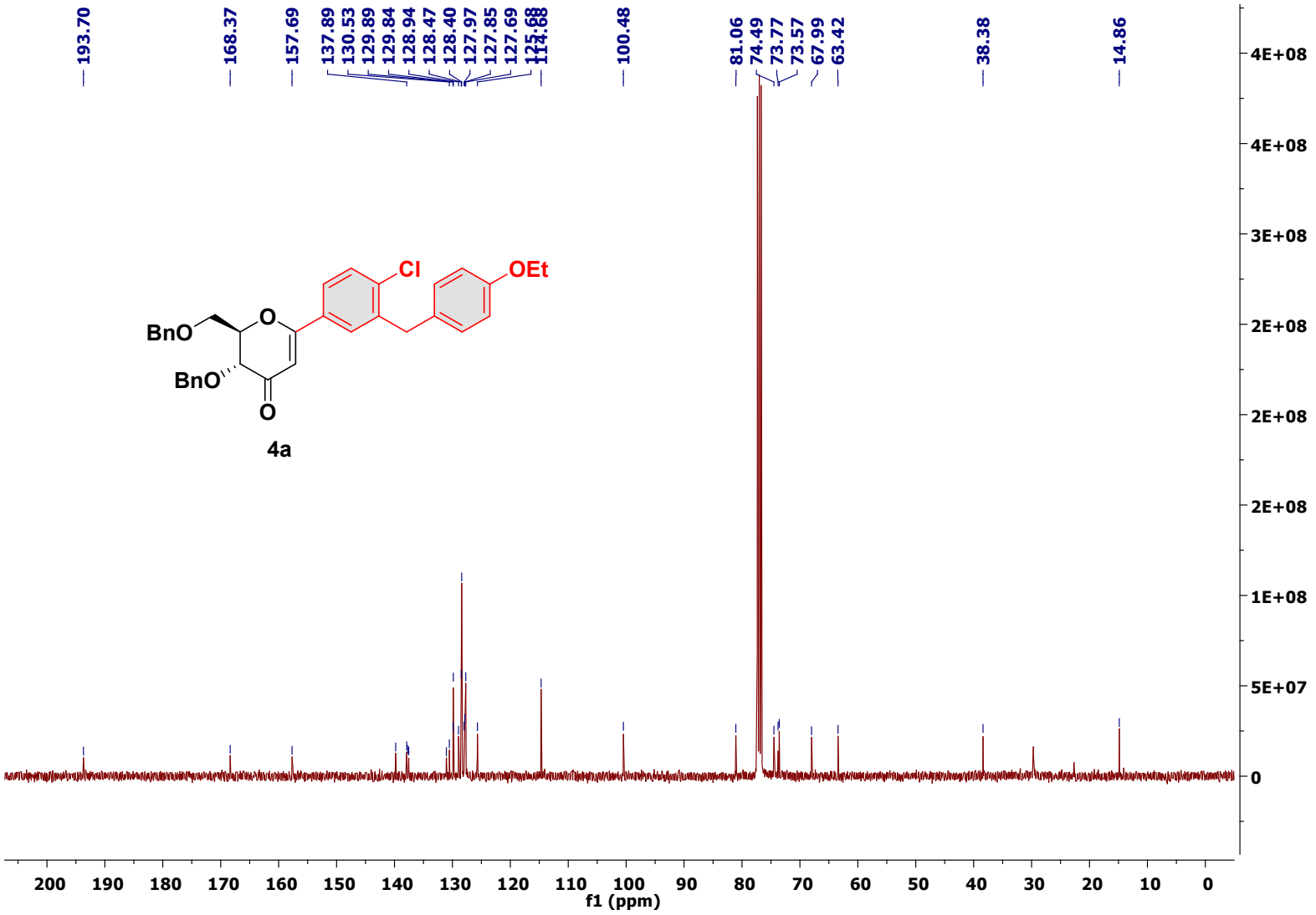
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **3q** in $CDCl_3$



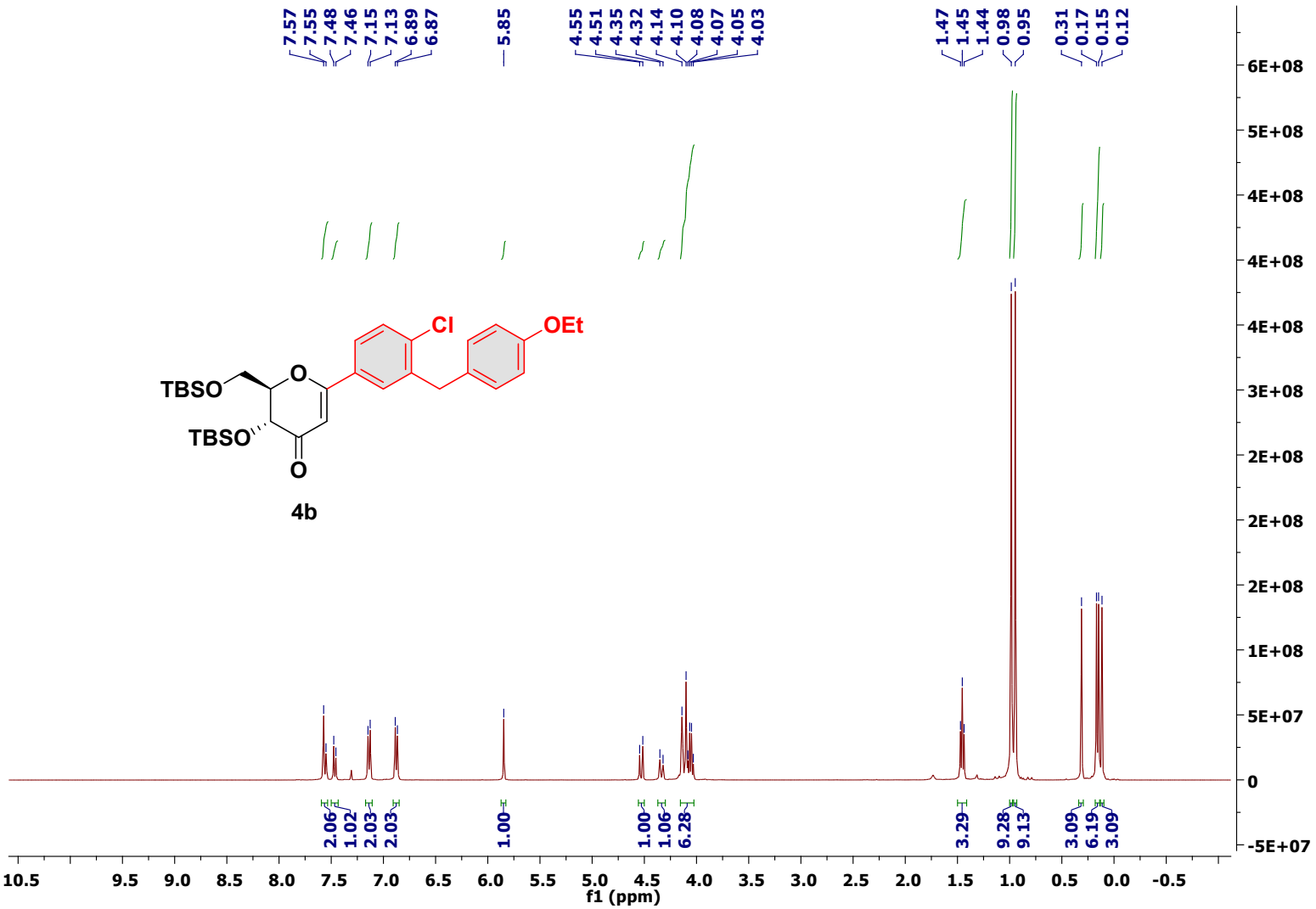
^{1}H NMR (400 MHz) of **4a** in $CDCl_3$



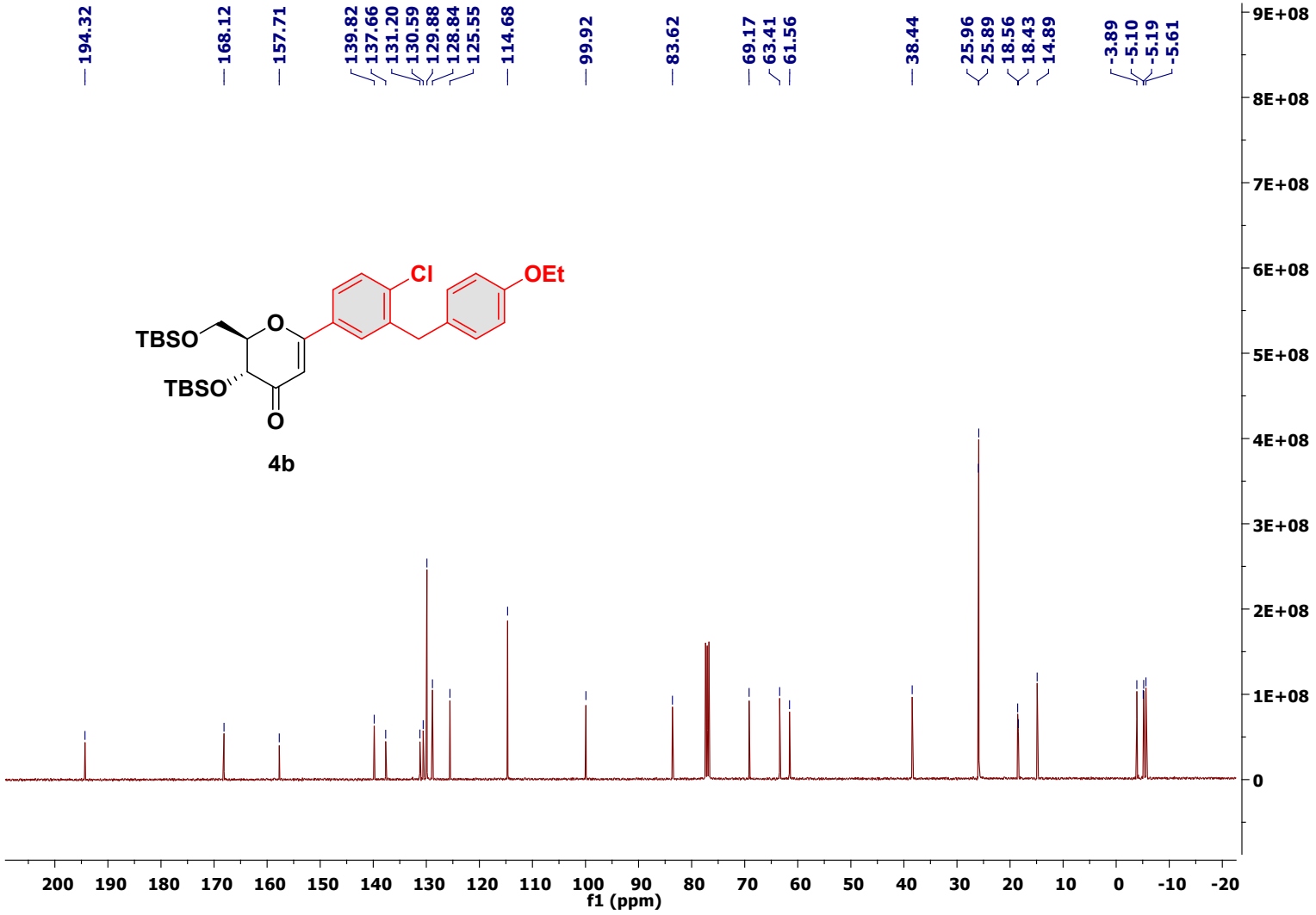
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **4a** in $CDCl_3$



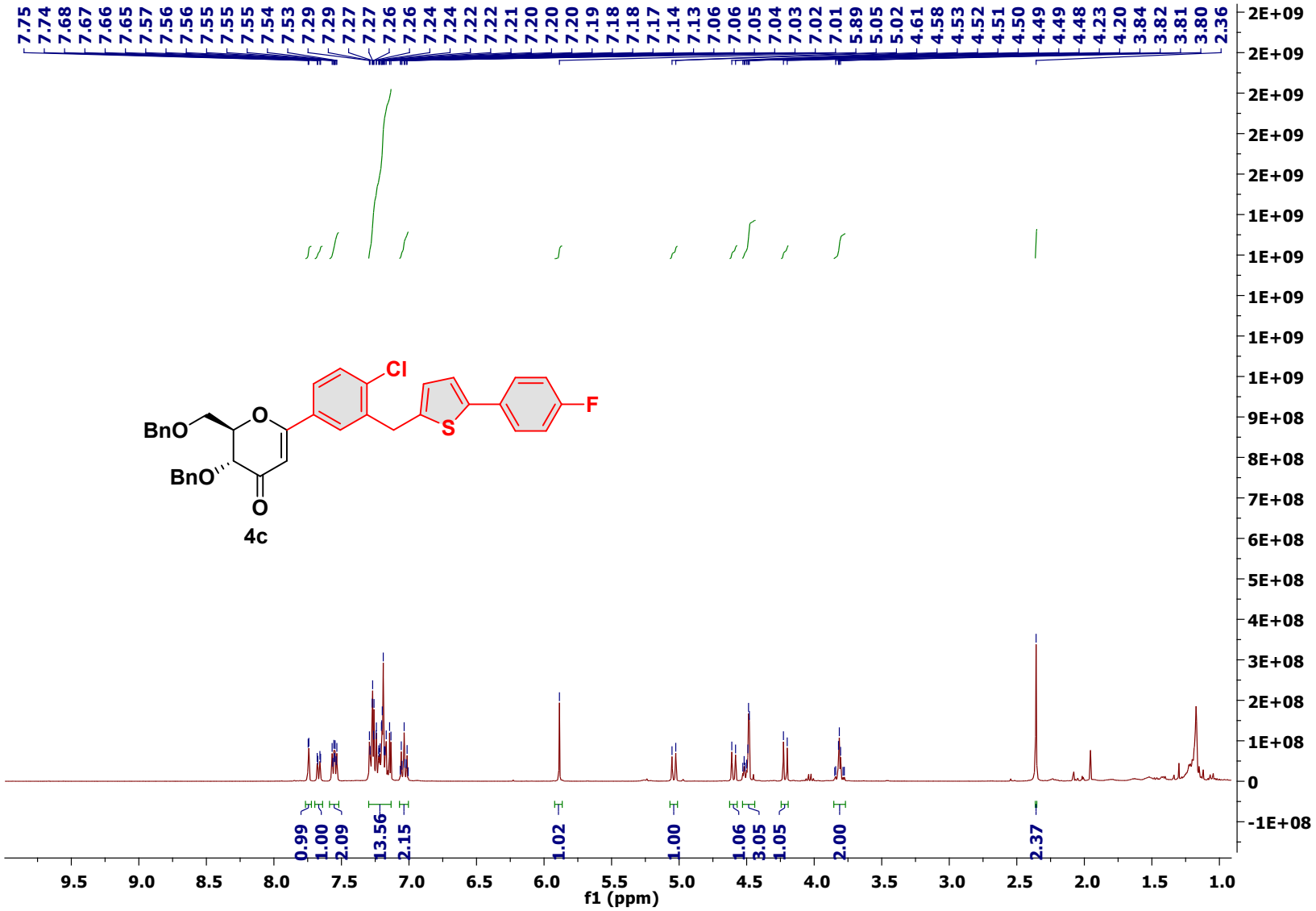
^{1}H NMR (400 MHz) of **4b** in $CDCl_3$



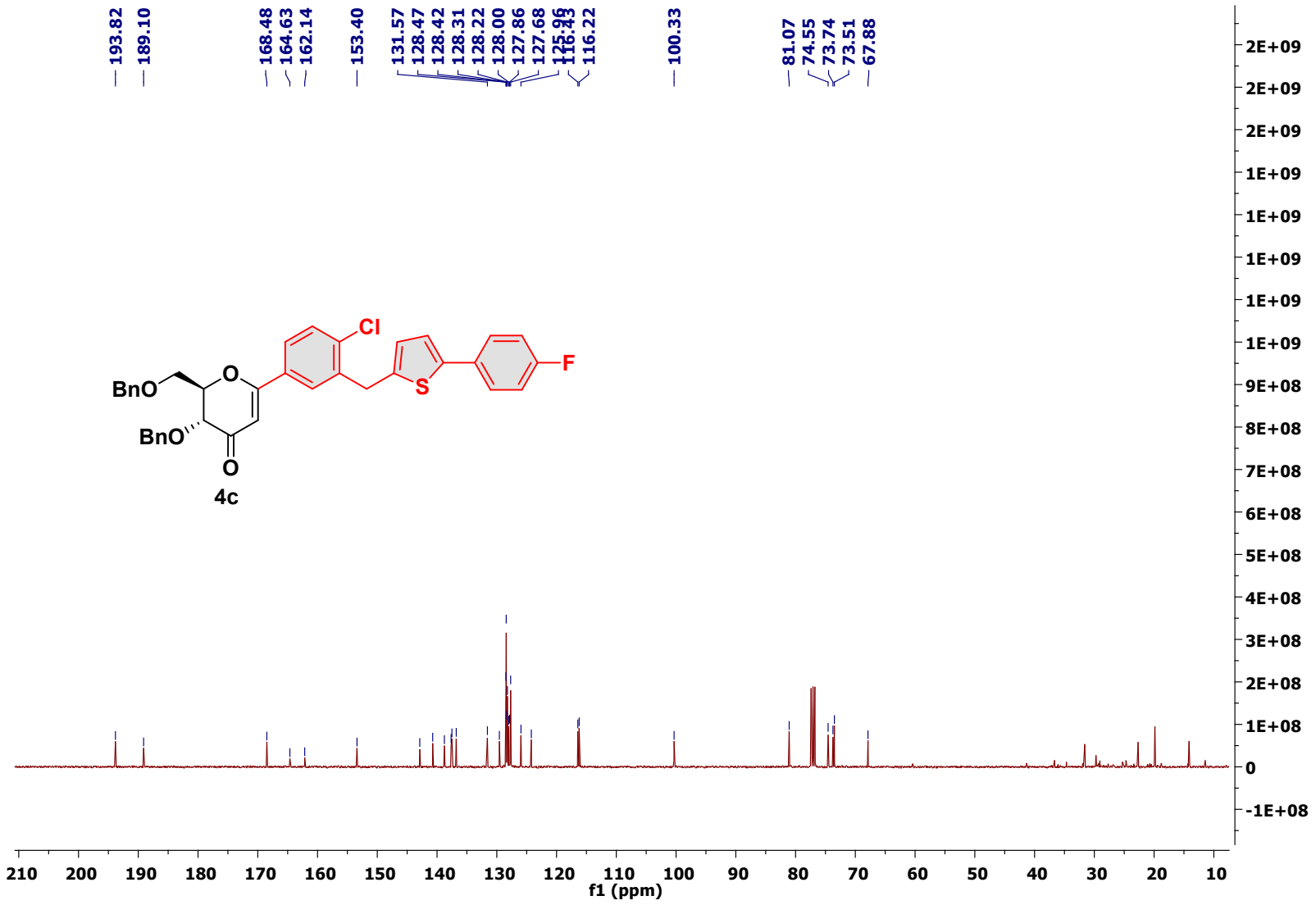
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **4b** in $CDCl_3$



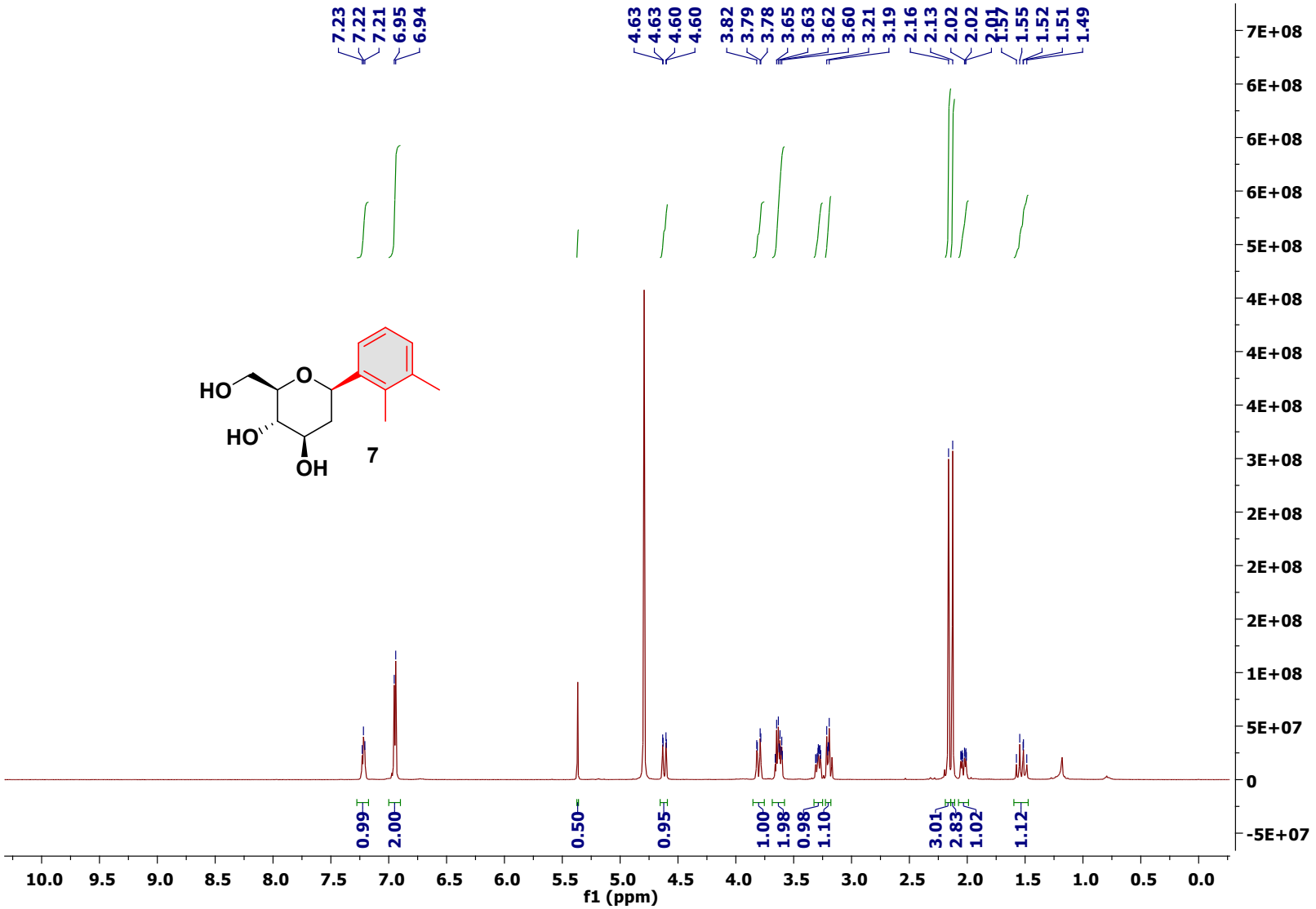
^{1}H NMR (400 MHz) of **4c** in $CDCl_3$



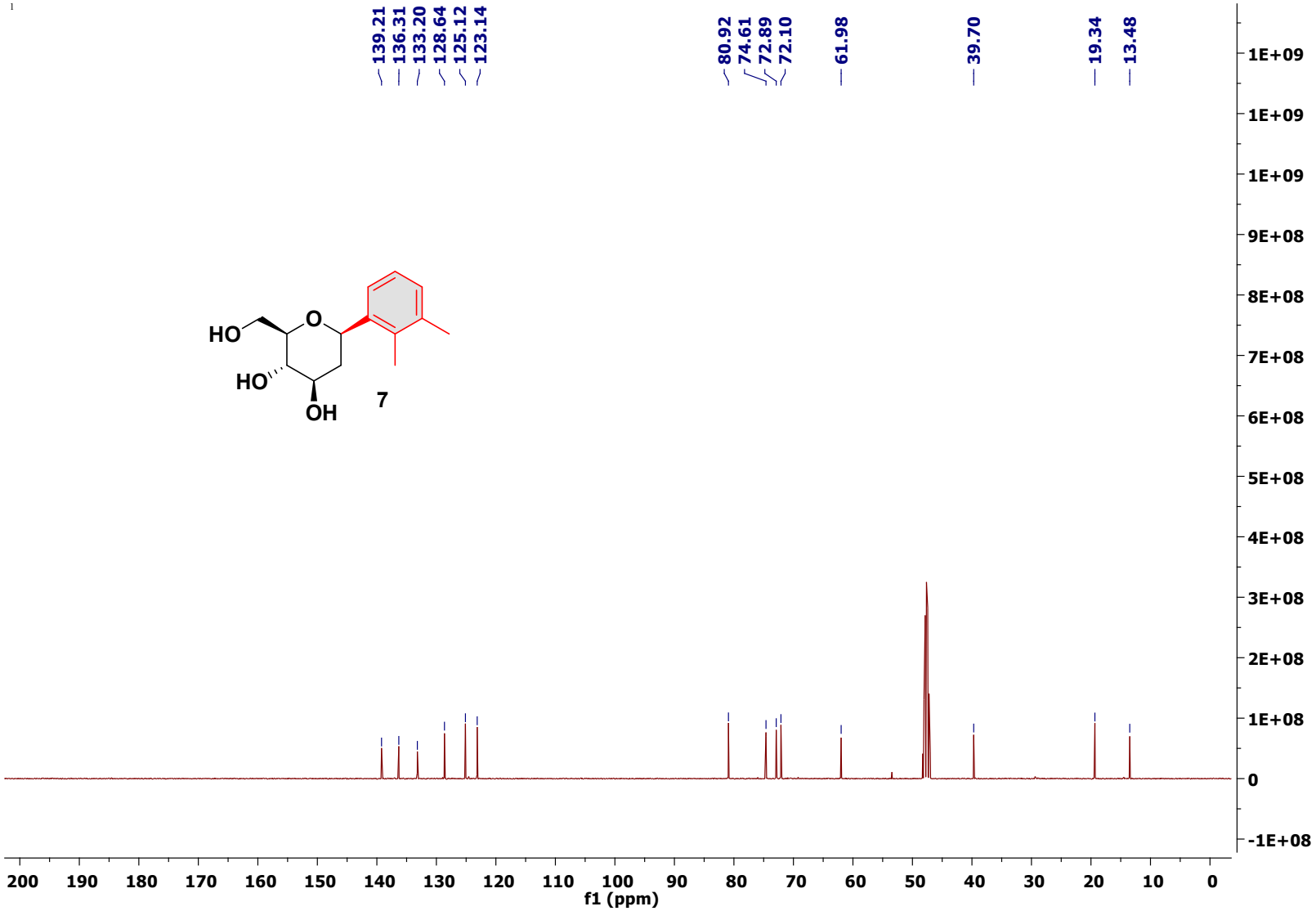
^{13}C NMR $\{^{1}H\}$ (101 MHz) of **4c** in $CDCl_3$



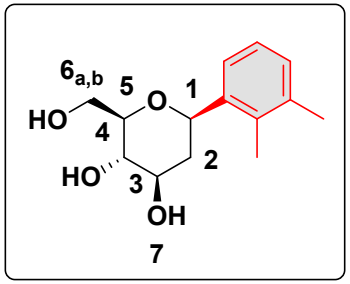
^{1}H NMR (400 MHz) of **7** in $CDCl_3$



^{13}C NMR $\{^{1}H\}$ (101 MHz) of **7** in $CDCl_3$

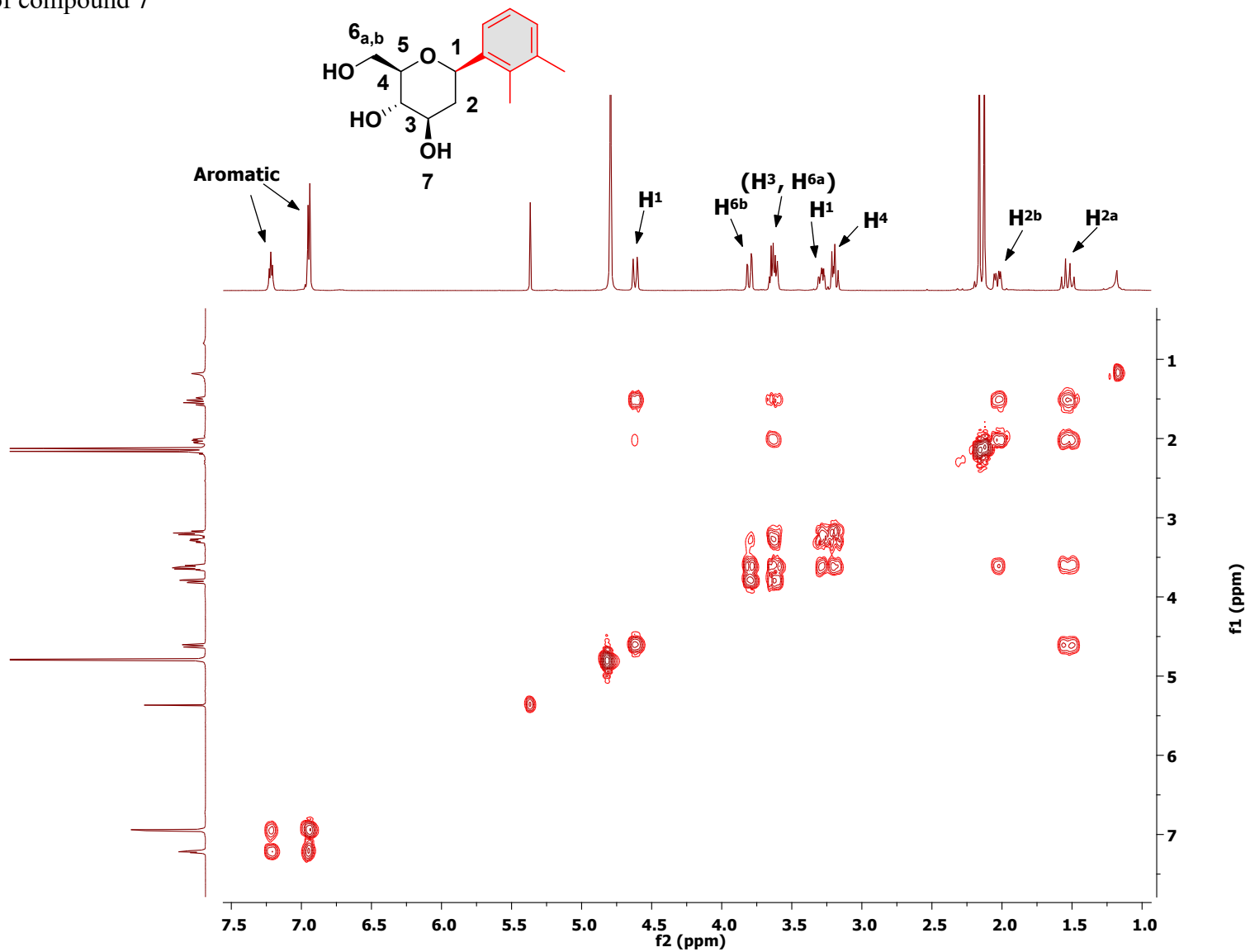


HSQC table of compound 7

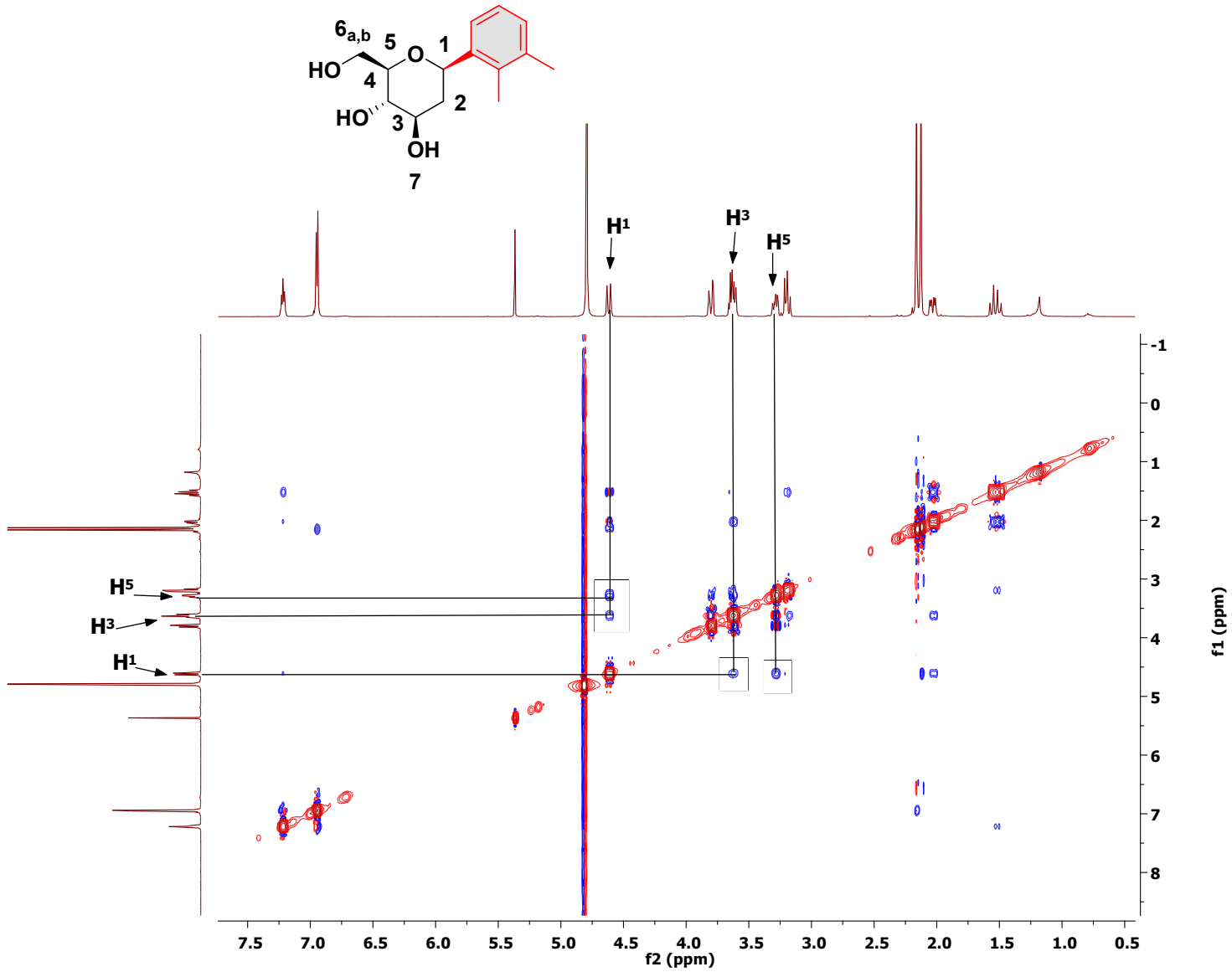


	^{1}H	^{13}C
1.	H_1= 4.62 (dd, *J* = 11.3, 1.3 Hz, 1H)	74.6
2.	H_{2a}= 1.53 (dd, *J* = 24.3, 11.5 Hz, 1H)	39.7
3.	H_{2b}= 2.03 (ddd, *J* = 12.9, 4.9, 1.6 Hz, 1H)	39.7
4.	H_3 and H_{6a} = 3.67 – 3.57 (m, 2H)	72.9 and 62.0
5.	H_4= 3.23 – 3.18 (m, 1H)	72.1
6.	H_5= 3.29 (ddd, *J* = 9.3, 5.8, 2.2 Hz, 1H)	80.9
7.	H_{6b}= 3.80 (dd, *J* = 11.9, 2.2 Hz, 1H)	62.0

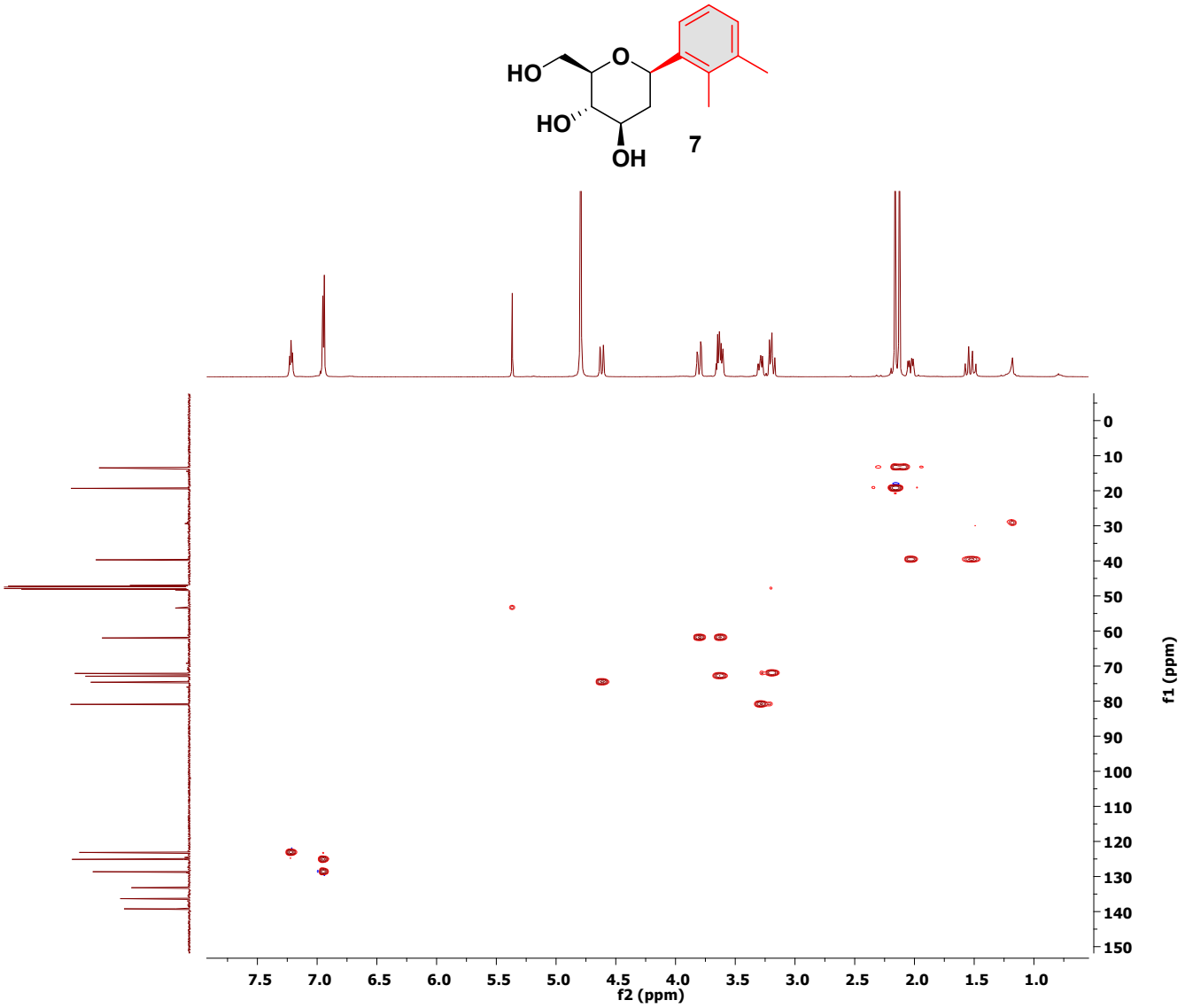
COSY of compound **7**



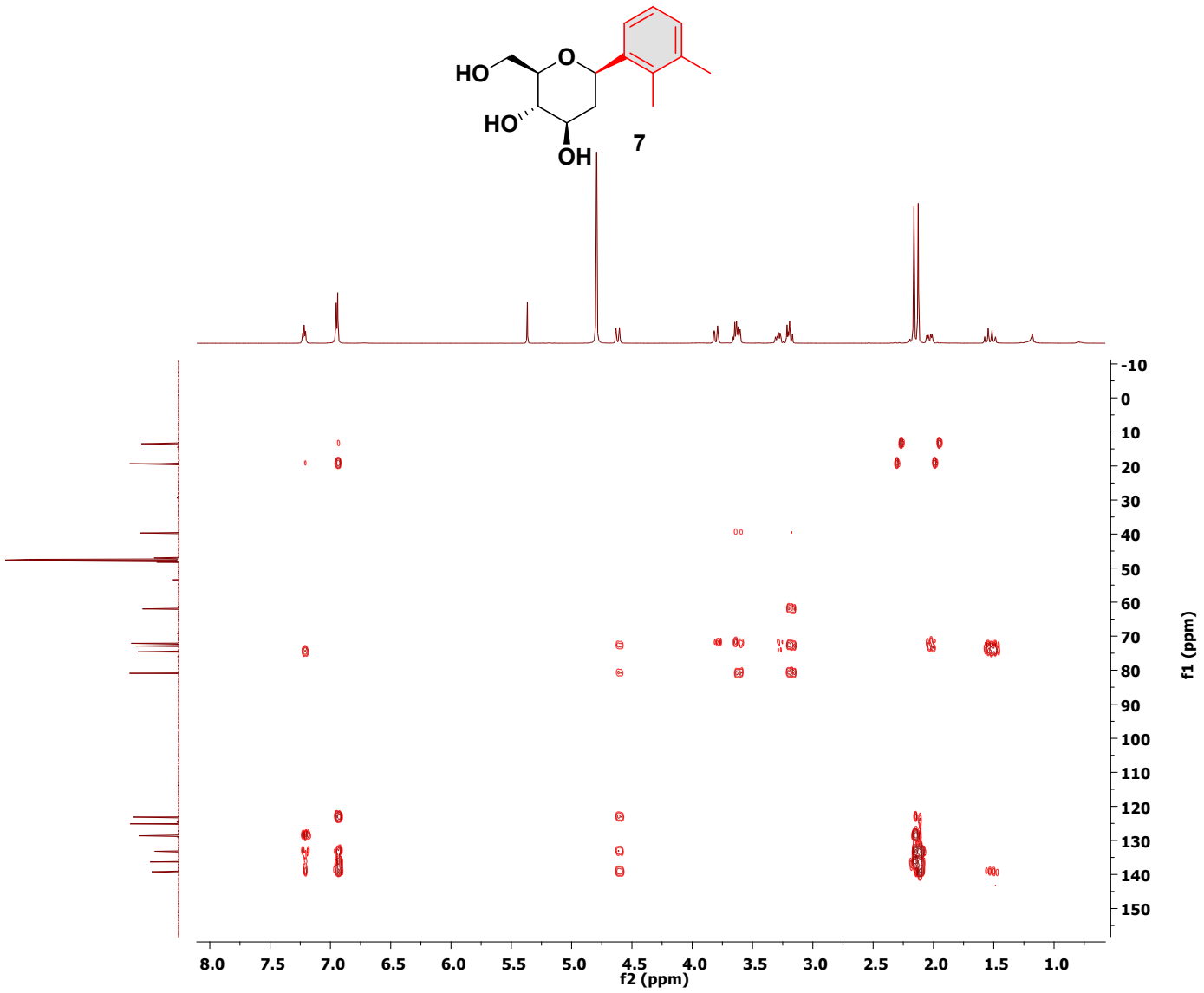
NOESY of compound **7**



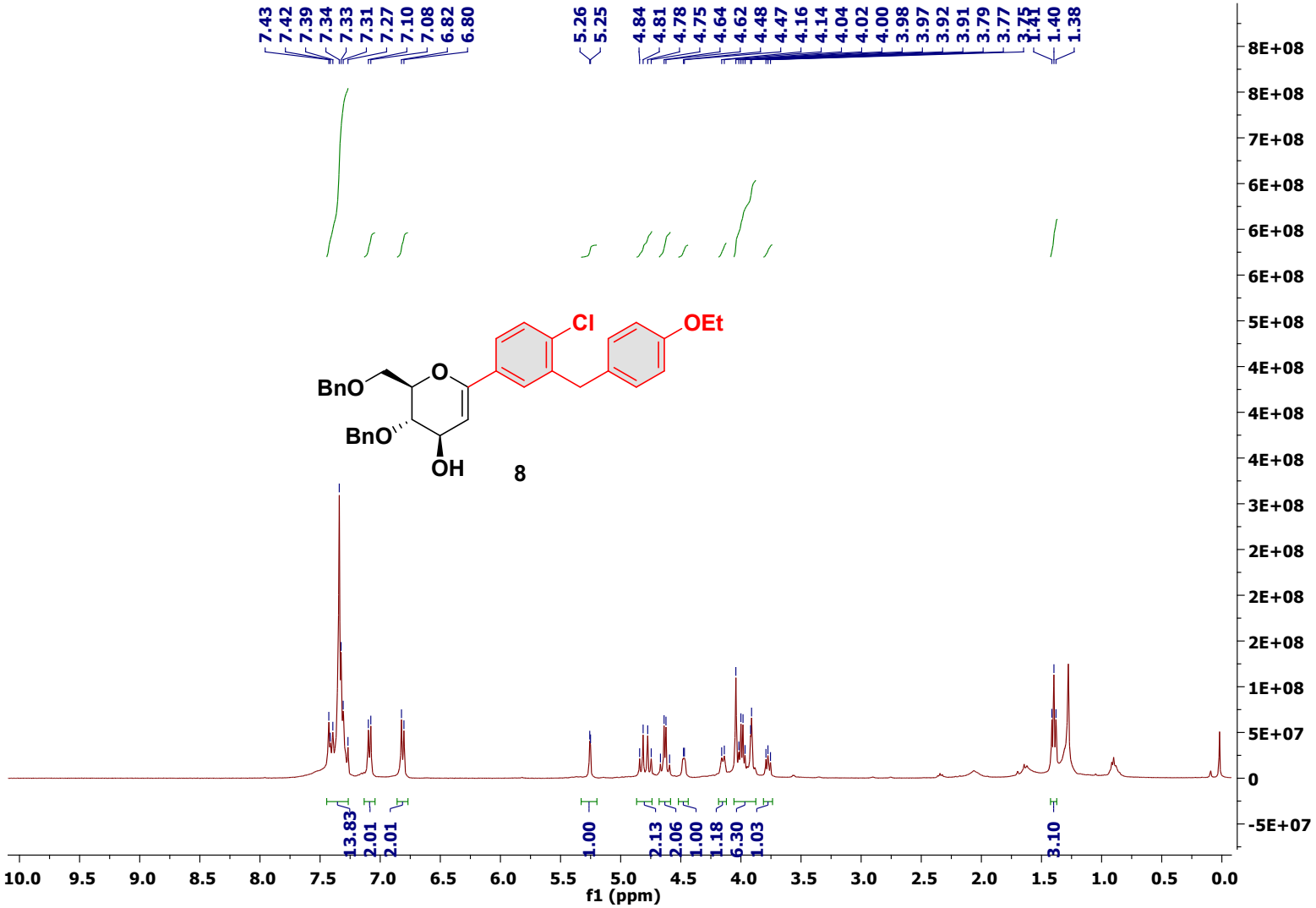
HSQC of compound **7**



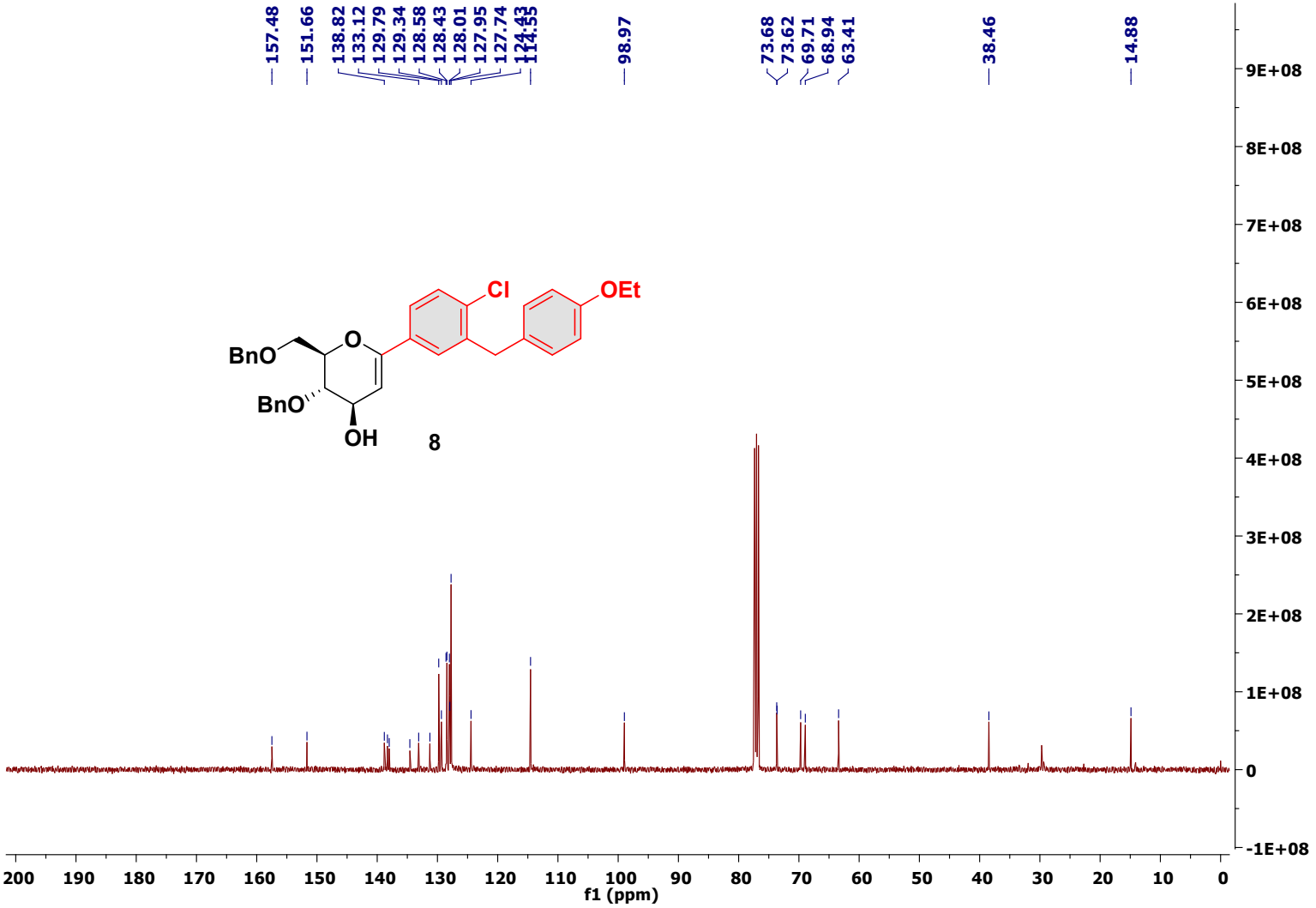
HMBC of compound **7**



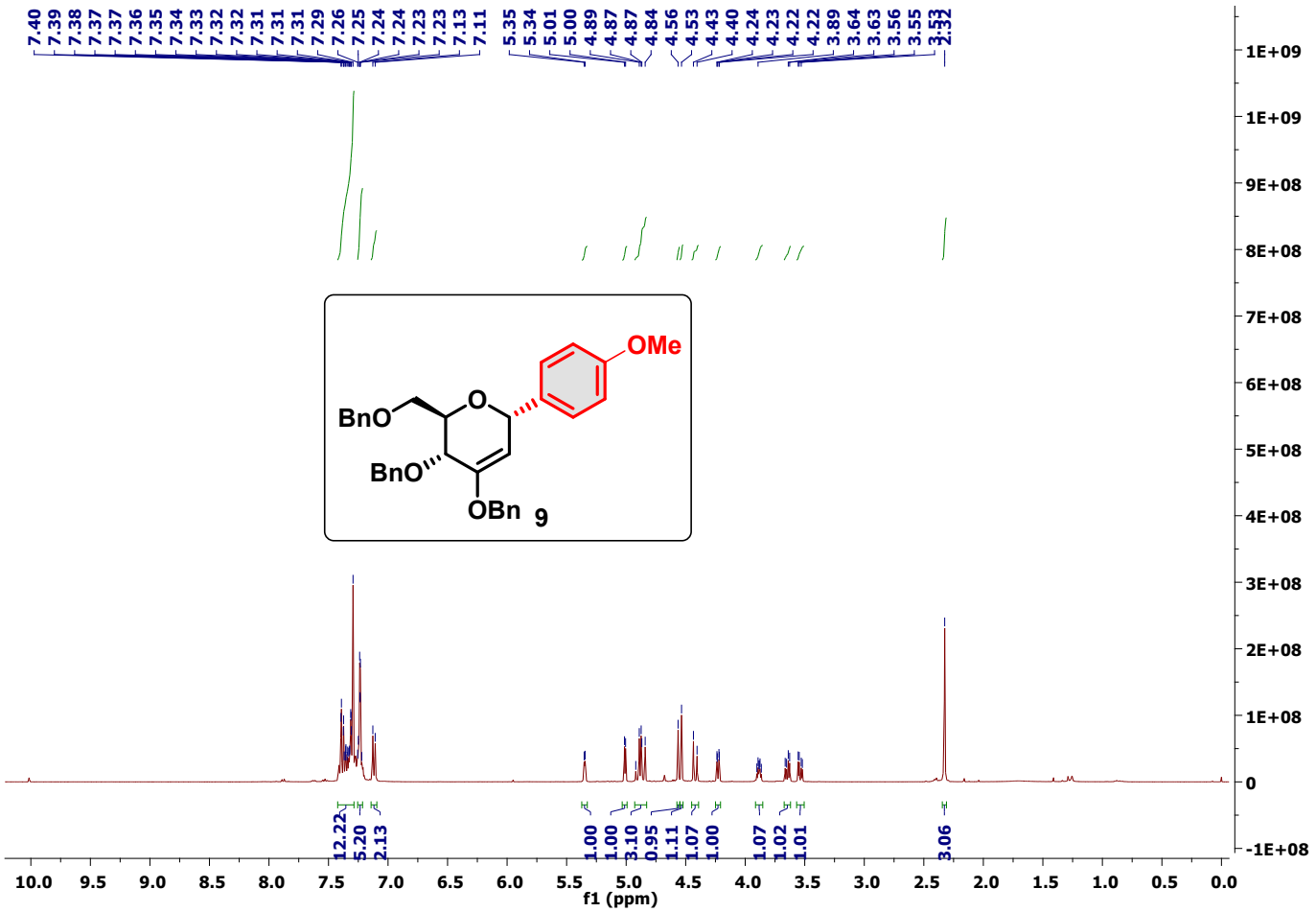
^{1}H NMR (400 MHz) of **8** in $CDCl_3$



^{13}C NMR $\{^{1}H\}$ (101 MHz) of **8** in $CDCl_3$



^{1}H NMR (400 MHz) of **9** in $CDCl_3$



^{13}C NMR $\{^{1}H\}$ (101 MHz) of **9** in $CDCl_3$