Supporting Information

Structure-based design of novel boronic acid-based inhibitors of autotaxin

Harald M.H.G. Albers,[‡,§] Loes J.D. Hendrickx,[‡,†] Rob J.P. van Tol,[‡] Jens Hausmann,[▽] Anastassis Perrakis[▽] and Huib Ovaa*[,‡,§]

[‡]Division of Cell Biology, [§]Netherlands Proteomics Centre, [▽]Division of Biochemistry, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

[†]Deceased

*Correspondence:

Huib Ovaa, Division of Cell Biology, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands. Phone: +31-20-5121979. E-mail: h.ovaa@nki.nl

Table of Contents

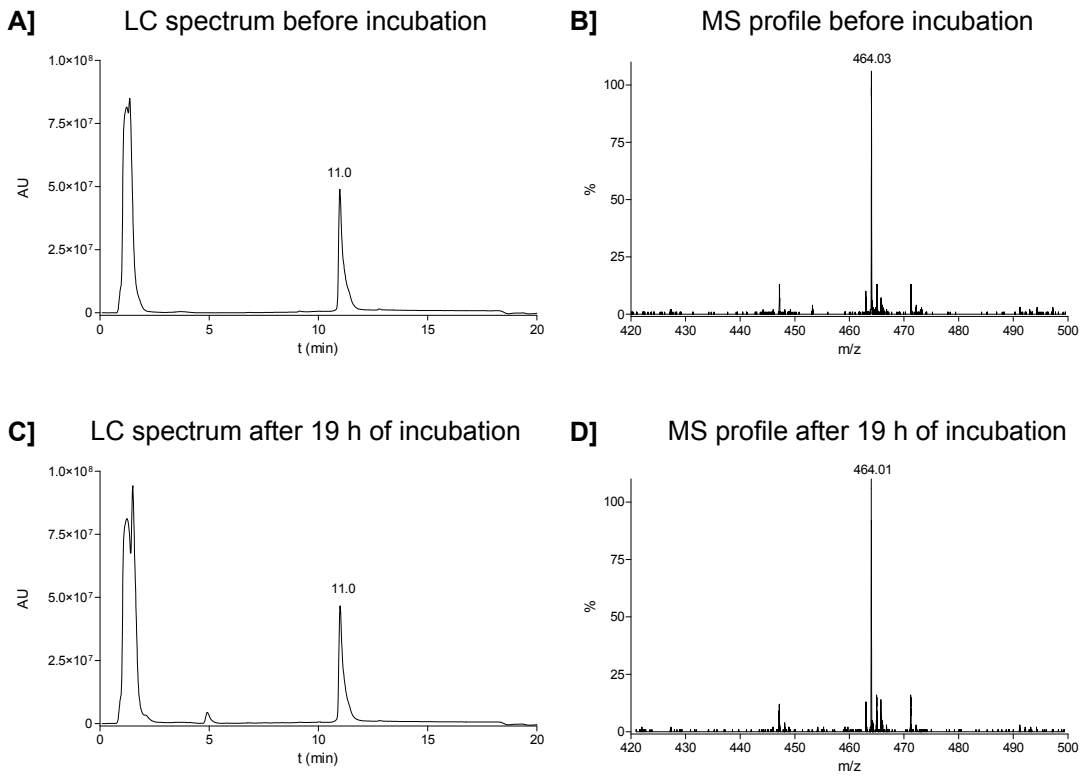


Figure S1. Michael acceptor study of inhibitor **1**. We incubated 100 μM of inhibitor **1** ($(M+H^+)$ = 464.11) with 10 mM of *l*-glutathione (reduced) in a Tris-HCl buffer (50 mM, pH 7.4) at 310 K for 19 h. *L*-glutathione is a natural occurring reducing agent which is abundantly present in blood (1 mM) and can act as a Michael donor. After 19 h of incubation no Michael addition was observed (compare LC spectrum and MS profile in A] and B] with C] and D]).

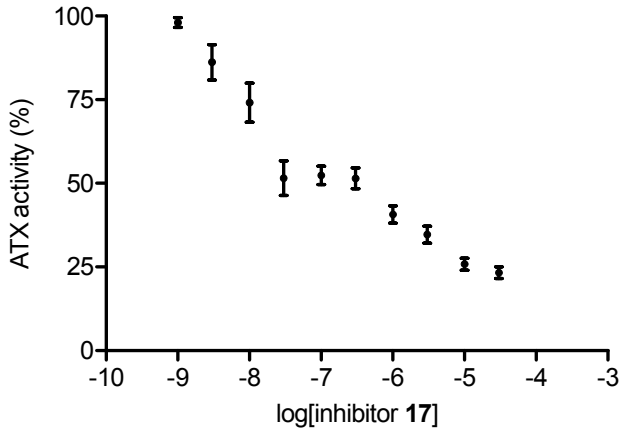


Figure S2. Dose-response curve for inhibitor **17** (n=5).

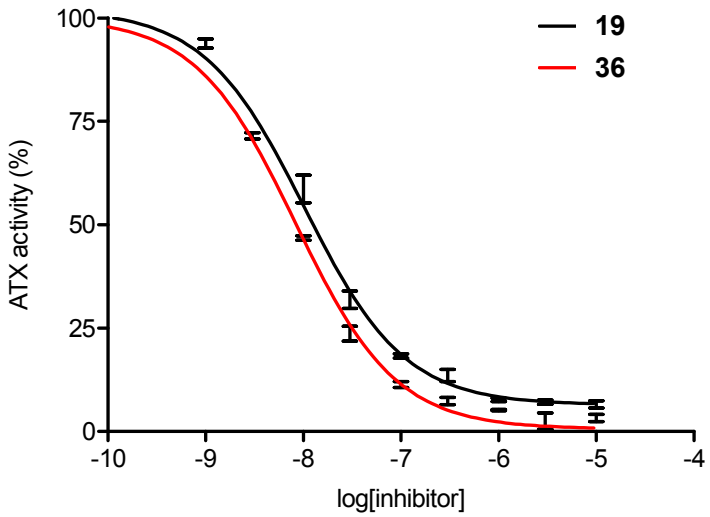


Figure S3. Dose-response curves for inhibitors **19** and **36**.

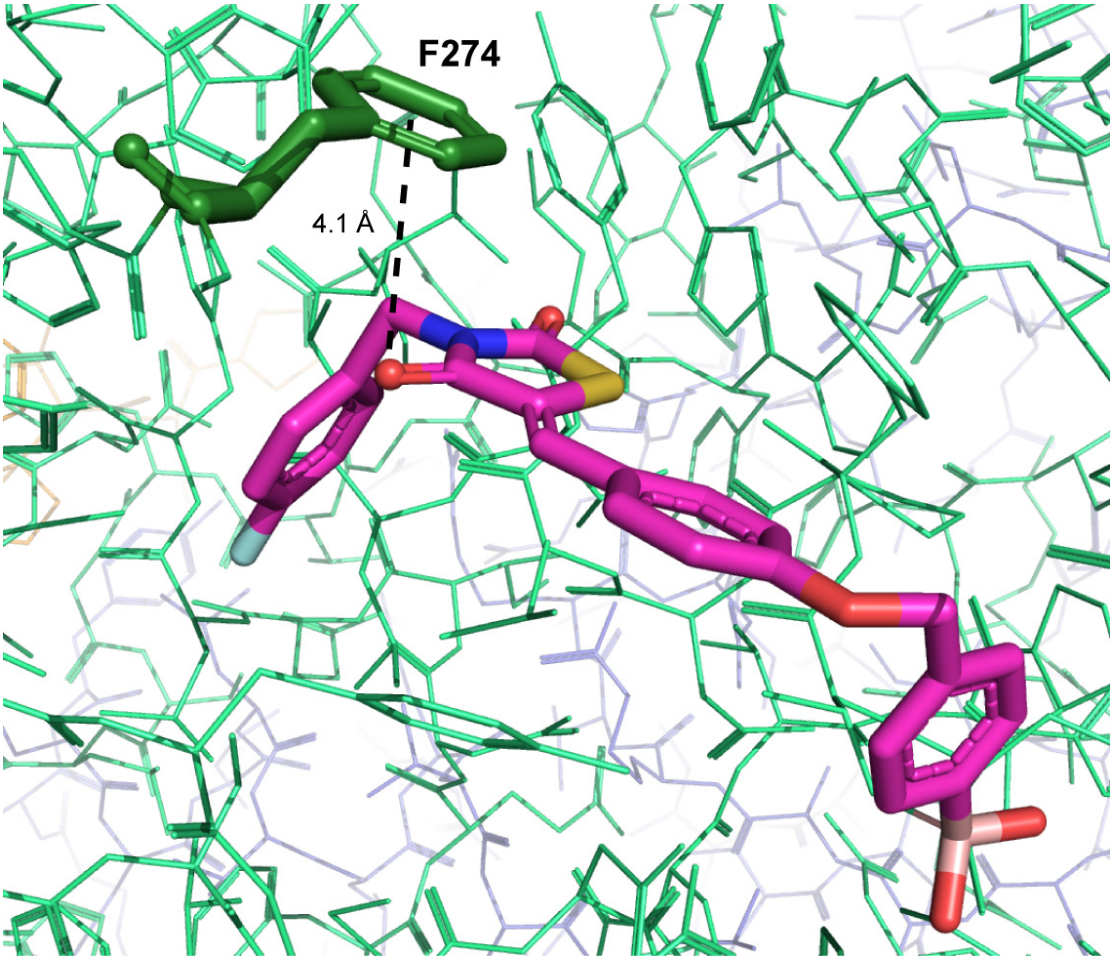


Figure S4. The distance between the oxygen of the carbonyl moiety in inhibitor **1** and the center of the aromatic ring of ATX residue F274 is 4.1 Å, suggesting π-stacking between these two moieties.

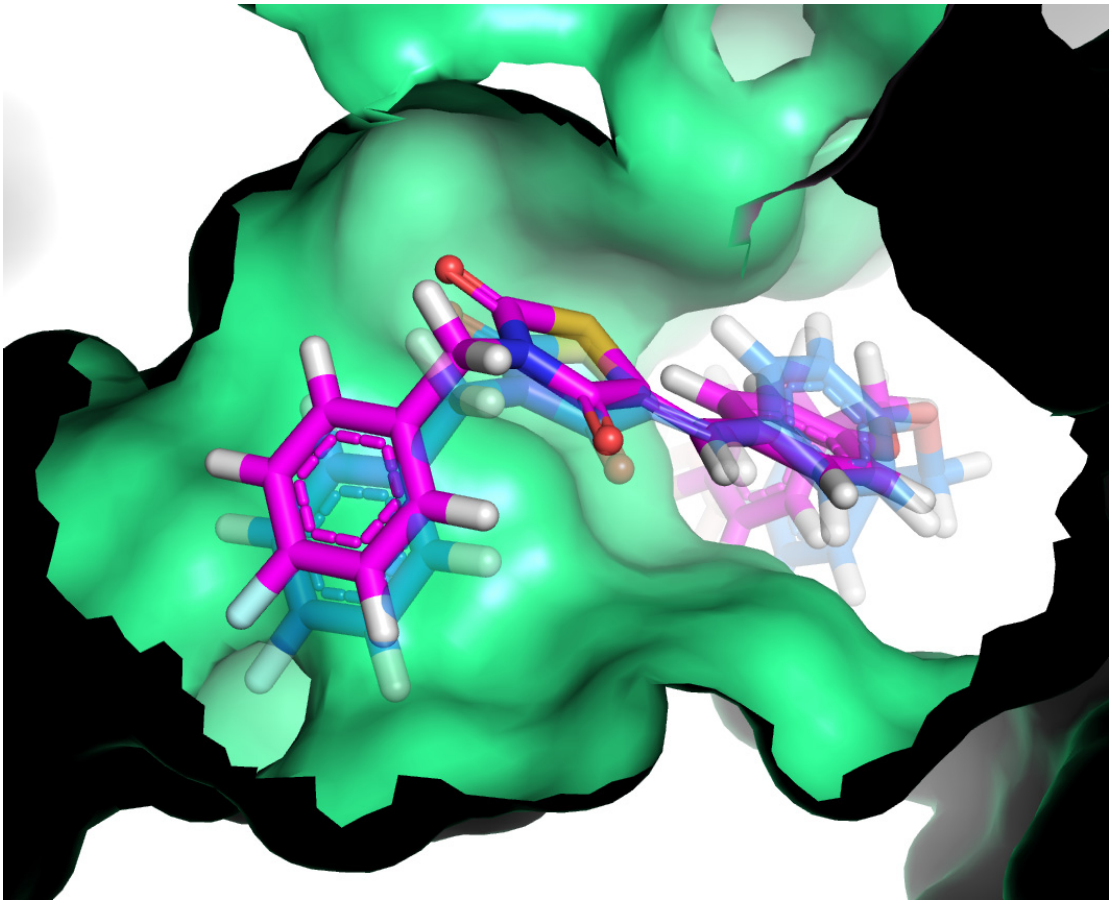
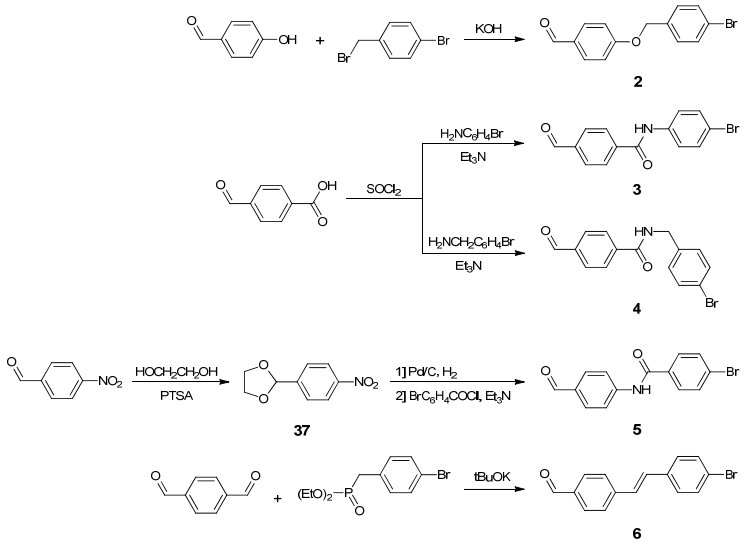


Figure S5. Docked (transparent blue) and X-ray (magenta) pose of inhibitor **1**.

Syntheses aldehydes 2-6



4-((4-bromobenzyl)oxy)benzaldehyde (2). To a solution of 4-hydroxybenzaldehyde (1.02 g, 8.33 mmol) and potassium hydroxide (0.533 g, 9.50 mmol) in dimethyl sulfoxide (13 mL), 4-(bromomethyl)phenyl bromide (1.38 g, 5.51 mmol) was added. The reaction mixture was stirred at room temperature and after 1 h the precipitate was isolated by centrifugation, washed with water (3x15 mL), and lyophilized resulting in the title compound. **Yield:** 1.5 g, 91% **^{1}H NMR:** δ = 9.87 (s, 1H), 7.87 (d, *J* = 8.8, 2H), 7.60 (d, *J* = 8.5, 2H), 7.43 (d, *J* = 8.5, 2H), 7.20 (d, *J* = 8.7, 2H), 5.22 (s, 2H). **^{13}C NMR:** δ = 191.23, 163.02, 135.77 ($\underline{C}_{Ar}$-Br+$\underline{C}_{Ar}$COH), 131.74, 131.40, 129.89, 121.16, 115.27, 68.79. **MS:** m/z $[M+H]^+$ calc. 291.00, 293.00, obs. 291.01, 293.02.

***N*-(4-bromophenyl)-4-formylbenzamide (3).** Thionyl chloride (0.75 mL, 10.3 mmol) was added to a suspension of 4-carboxy benzaldehyde (0.517 g, 3.44 mmol) in dry toluene (15 mL). The reaction mixture became clear after 4 h of refluxing. Concentrating the solution resulted in a light brown solid. The crude product was dissolved in dichloromethane (12.5 mL) and 4-bromo aniline (0.607 g, 3.53 mmol) and triethylamine (1.3 mL, 9.3 mmol) were added. After 1 h 30 of refluxing under an atmosphere of argon the reaction mixture was diluted with ethyl acetate (40 mL) and washed with 1 M hydrochloric acid (40 mL) and saturated bicarbonate solution (40 mL). The organic layer was dried over magnesium sulfate and was concentrated resulting in a yellow solid. **Yield:** 707.1 mg, 68%. **^{1}H NMR:** δ = 10.58 (s, 1H), 10.12 (s, 1H), 8.13 (d, *J* = 8.5, 2H), 8.06 (d, *J* = 8.5, 2H), 7.77 (d, *J* = 8.9, 2H), 7.56 (d, *J* = 8.9, 2H). **^{13}C NMR:** δ = 192.89, 164.81, 139.64, 138.26, 138.04, 131.49, 129.42, 128.43, 122.28, 115.69. **MS:** m/z $[M+H]^+$ calc. 304.00, 306.00, obs. 303.96, 305.96.

***N*-(4-bromobenzyl)-4-formylbenzamide (4).** In a dry flask, thionyl chloride (3.3 mL, 45.2 mmol) was added to a suspension of 4-carboxy benzaldehyde (1.07 g, 7.13 mmol) in dry toluene (30 mL). The reaction mixture was refluxed for 5 h and concentrated *in vacuo*. The crude product was dissolved in dichloromethane (25 mL) and 4-bromobenzyl amine (1.0 mL, 7.92 mmol) and triethylamine (1.3 mL, 7.17 mmol) were added. The reaction mixture was refluxed for 2 h. Finally, the mixture was diluted

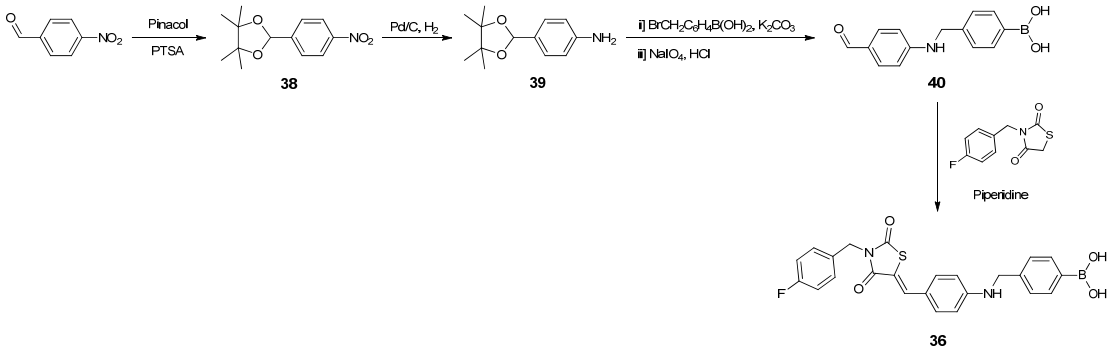
with ethyl acetate (60 mL) and washed with 1 M hydrochloric acid (40 mL) and bicarbonate solution (40 mL). The organic layer was dried over magnesium sulfate and concentrated *in vacuo*. **Yield:** 1.65 g, 73%. **^{1}H NMR:** δ = 10.08 (s, 1H), 9.30 (t, *J* = 5.9, 1H), 8.08 (d, *J* = 8.3, 2H), 8.00 (d, *J* = 8.5, 2H), 7.52 (d, *J* = 8.5, 2H), 7.30 (d, *J* = 8.5, 2H), 4.47 (d, *J* = 5.9, 2H). **^{13}C NMR:** δ = 192.85, 165.45, 139.15, 138.79, 137.84, 131.15, 129.53, 128.81, 127.98, 119.82, 42.19. **MS:** m/z $[M+H]^+$ calc. 318.01, 320.01, obs. 317.95, 319.96.

2-(4-nitrophenyl)-1,3-dioxolane (37). To a solution of 4-Nitrobenzaldehyde (3.95 g, 26.1 mmol) in dry toluene (10 mL), molecular sieves (4 Å, 2 g), dry ethylene glycol (10.0 mL, 179 mmol), and *p*-toluenesulfonic acid monohydrate (2.04 g, 10.7 mmol) were added was refluxed for 25 h using a Dean-Stark apparatus. Toluene (50 mL) and water (50 mL) were added and the water layer was extracted with toluene (2x50 mL). The organic layers were combined and washed with brine (3x100 mL), dried over magnesium sulfate and finally concentrating *in vacuo*. **Yield:** 3.87 g, 76%. **^{1}H NMR:** δ = 8.25 (d, *J* = 8.8, 2H), 7.71 (d, *J* = 8.5, 2H), 5.89 (s, 1H), 4.05-3.97 (m, 4H). **^{13}C NMR:** δ = 147.91, 145.20, 127.79, 123.45, 101.38, 65.02. **MS:** m/z $[M+H]^+$ calc. 196.06, obs. 196.06.

4-bromo-*N*-(4-formylphenyl)benzamide (5). Compound **37** (3.87 g, 19.8 mmol) was dissolved in degassed tetrahydrofuran (250 mL) and 10 wt% Pd/C (480 mg) was added. After stirring the reaction mixture for 16 h under a hydrogen atmosphere it was filtered over Hyflo Super Cel® medium and was concentrated. The crude product was used without any further purification and was dissolved in dry dichloromethane (75 mL) and 4-bromobenzoyl chloride (3.57 g, 16.3 mmol) was added. The solution was stirred for 2 h and triethylamine (0.4 mL, 2.87 mmol) was added. Additional triethyl amine (2.8 ml, 20 mmol) was added over 2 h with time intervals of 30 min. After stirring for another 1 h 30 the solution was diluted with ethyl acetate (200 mL) and washed with 1 M hydrochloric acid (100 mL) and brine (100 mL). The solution was dried over magnesium sulfate and concentrated *in vacuo*. Crude product (922 mg) was deprotected in dichloromethane (100 mL) using perchloric acid (50 mL). After stirring the mixture for 2 h it was diluted with ethyl acetate (100 mL) and neutralized with 30 wt% sodium hydroxide solution which initiated separation. The oranic layer was dried over magnesium sulfate and the solvent was concentrated *in vacuo* which resulted in an orange solid. **Yield:** 464.1 mg, 66%. **^{1}H NMR:** δ = 10.69 (s, 1H), 9.92 (s, 1H), 8.02 (d, *J* = 8.3, 2H), 7.93 (d, *J* = 8.5, 2H), 7.90 (d, *J* = 8.5, 2H), 7.77 (d, *J* = 8.5, 2H). **^{13}C NMR:** δ = 191.62, 165.13, 144.61, 133.55, 131.68, 131.46, 130.59, 129.94, 125.74, 119.92. **MS:** m/z $[M+H]^+$ calc. 304.00, 306.00, obs. 304.03, 306.04.

(*E*)-4-(4-bromostyryl)benzaldehyde (6). To a solution of terephthalaldehyde (8.06 g, 60.1 mmol) in tetrahydrofuran (420 mL) were added diethyl(4-bromobenzyl)phosphonate (5.10 g, 16.6 mmol) and potassium tert-butoxide (2.92 g, 26.0 mmol). After 40 min stirring under an argon atmosphere additional potassium tert-butoxide (2.92 g, 26.0 mmol) was added and stirred for another 30 min. The reaction mixture was filtered and concentrated *in vacuo* and the resulting solid was purified using column chromatography (hexane-dichloromethane, 1:1) to provide compound **6**. **Yield:** 2.1 g, 43%. **^{1}H NMR ($CDCl_3$):** δ = 9.98 (s, 1H), 7.86 (d, *J* = 8.4, 2H), 7.63 (d, *J* = 8.3, 2H), 7.50 (d, *J* = 8.6, 2H), 7.39 (d, *J* = 8.5, 2H), 7.14 (dd, *J* = 16.4, 23.2, 2H). **^{13}C NMR ($CDCl_3$):** δ = 191.75, 143.23, 135.78, 135.74, 132.22, 131.10, 130.49, 128.55, 128.28, 127.20, 122.60. **MS:** m/z $[M+H]^+$ calc. 287.01, 289.01, obs. 286.97, 288.97.

Synthesis amine linker-based inhibitor 36



4,4,5,5-tetramethyl-2-(4-nitrophenyl)-1,3-dioxolane (38). A mixture of 4-nitrobenzaldehyde (6.07 g, 40.2 mmol), pinacol (6.31 g, 53.4 mmol) and *p*-toluenesulfonic acid monohydrate (0.225 g, 1.18 mmol) was refluxed in dry toluene (65 mL) for 4 h using a Dean-Stark apparatus. After cooling to room temperature, sodium hydroxide (0.216 g, 5.40 mmol) in ethanol (3 mL) was added to the mixture and stirred for 30 min. The suspension was filtered and the residue was washed with toluene (125 mL). The filtrate was washed with brine (3x100 mL), dried over sodium sulfate and finally concentrated *in vacuo* to provide the title compound. **Yield:** 9.3 g, 92%. **^{1}H NMR:** δ = 8.23 (d, *J* = 8.8, 2H), 7.70 (d, *J* = 8.4, 2H), 6.00 (s, 0H), 1.27 (s, 6H), 1.17 (s, 6H). **^{13}C NMR:** δ = 147.54, 147.04, 127.37, 123.40, 97.76, 82.75, 23.84, 21.89. **MS:** m/z $[M+H]^+$ calc. 252.12, obs. 252.11.

4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)aniline (39). A mixture of compound **38** (0.498 g, 1.98 mmol) and 10 wt% Pd/C in degassed tetrahydrofuran (15 mL) under a hydrogen atmosphere was stirred for 7 h. The mixture was filtrated over Hyflo Super Cel® medium and the filtrate was concentrated *in vacuo*. **Yield:** 438 mg, 100%. **^{1}H NMR:** δ = 7.06 (d, *J* = 8.4, 2H), 6.51 (d, *J* = 8.5, 2H), 5.71 (s, 1H), 5.10 (s, 2H), 1.21 (s, 6H), 1.19 (s, 6H). **^{13}C NMR:** δ =149.04, 127.44, 126.39, 113.12, 99.75, 81.47, 24.34, 22.00. **MS:** m/z $[M+H]^+$ calc. 222.15, obs. 222.14.

(4-(((4-formylphenyl)amino)methyl)phenyl)boronic acid (40). To a solution of amine **39** (1.06 g, 4.79 mmol) in dry dimethylformamide (10 mL), potassium carbonate (0.612 g, 4.43 mmol) and 4-bromomethylphenylboronic acid (0.880 g, 4.10 mmol) were added. After stirring overnight under an argon atmosphere the reaction mixture was diluted with ethyl acetate (100 mL). The mixture was washed with 0.1 M hydrochloric acid (3x50 mL), dried over magnesium sulfate and concentrated *in vacuo*. The resulting mixture of mono- and dialkylated products was purified using column chromatography (dichloromethane-methanol, 95:5) to isolate the monoalkylated compound **40** (0.661 g, 45%).

The pinacol protecting group was removed as follows: To a solution of monoalkylated compound **40** (0.140 g, 0.394 mmol) in tetrahydrofuran (3 mL), sodium periodate (0.107 g, 0.500 mmol) and water (0.424 mL) were added. After 30 min of stirring under an atmosphere of argon, 1 M hydrochloric acid (0.284 mL) was added and stirred for one night. The reaction mixture was diluted with ethyl acetate (13 mL) and washed with brine (11 mL). The water layer was extracted with ethyl acetate and the combined organic layers were washed with brine (8 mL), dried over magnesium sulfate and

concentrated *in vacuo* to afford the title compound in quantitative yield. **Overall yield:** 100 mg, 45% (two steps). **^{1}H NMR:** δ = 9.58 (s, 1H), 7.97 (s, 2H), 7.74 (d, *J* = 8.1, 2H), 7.58 (d, *J* = 8.8, 2H), 7.42 (t, *J* = 6.0, 1H), 7.30 (d, *J* = 8.0, 2H), 6.67 (d, *J* = 8.7, 2H), 4.39 (d, *J* = 6.0, 2H), . **^{13}C NMR:** δ = 189.55, 153.95, 140.88, 134.23, 131.77, 126.15, 125.05, 111.59, 45.79 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 256.11, obs. 256.17.

(*Z*)-(4-(((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)amino) methyl)phenyl)boronic acid (36). To a solution of 3-(4-fluorobenzyl)thiazolidine-2,4-dione (18.8 mg, 0.0835 mmol) in ethanol (0.2 mL), piperidine (8.2 μL, 0.0835 mmol) and aldehyde **40** (19.7 mg, 0.0772 mmol) were added and the solution was refluxed for 4 h. Upon cooling to room temperature the product precipitated out of solution. Pure compound was obtained after preparative HPLC purification. **Yield:** 10 mg, 29%. **^{1}H NMR:** δ = 7.99 (s, 2H), 7.76 (s, 1H), 7.74 (d, *J* = 8.1, 2H), 7.47 – 7.23 (m, 7H), 7.20 – 7.14 (m, 2H), 6.70 (d, *J* = 8.8, 2H), 4.79 (s, 2H), 4.37 (d, *J* = 5.8, 2H). **^{13}C NMR:** δ = 167.54, 165.66, 161.59 (d, $^1J_{CF}$ = 244), 151.27, 141.03, 134.76, 134.24, 132.67, 132.01 (d, $^4J_{CF}$ = 3), 129.84 (d, $^3J_{CF}$ = 8), 126.17, 119.94, 115.40 (d, $^2J_{CF}$ = 21), 112.57, 112.37, 45.84, 43.66 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 463.13, obs. 463.20.

Experimental details compounds 13-20, 26 and *E*-28

(4-(4-formylbenzamido)phenyl)boronic acid (13). Yield: 81%. **^{1}H NMR:** δ = 10.47 (s, 1H), 10.12 (s, 1H), 8.13 (d, *J* = 8.3, 2H), 8.06 (d, *J* = 8.5, 2H), 7.95 (s, 2H), 7.80 (d, *J* = 8.7, 2H), 7.75 (d, *J* = 8.7, 2H). **^{13}C NMR**: δ = 192.86, 164.74, 140.64, 139.93, 137.94, 134.70, 129.37, 128.38, 119.08 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 270.09, obs. 270.11.

(4-((4-formylbenzamido)methyl)phenyl)boronic acid (14). Yield: 72%. **^{1}H NMR:** δ = 10.09 (s, 1H), 9.25 (t, *J* = 5.9, 1H), 8.08 (d, *J* = 8.3, 2H), 8.01 (d, *J* = 8.5, 2H), 7.75 (d, *J* = 8.1, 2H), 7.29 (d, *J* = 8.1, 2H), 4.51 (d, *J* = 5.9, 2H). **^{13}C NMR:** δ = 192.85, 165.39, 141.10, 139.33, 137.74, 134.14, 129.39, 127.96, 126.21, 42.78 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 284.11, obs. 284.11.

(4-((4-formylphenyl)carbamoyl)phenyl)boronic acid (15). Yield: 72%. **^{1}H NMR:** δ = 10.62 (s, 1H), 9.92 (s, 1H), 8.26 (bs, 2H), 8.05-7.90 (m, 8H). **^{13}C NMR:** δ = 191.61, 166.22, 144.79, 135.65, 134.00, 131.57, 130.59, 126.66, 119.82 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 270.09, obs. 270.11.

(*E*)-(4-(4-formylstyryl)phenyl)boronic acid (16). Yield: 75%. **^{1}H NMR:** δ = 9.99 (s, 1H), 8.06 (s, *2*H), 7.97 – 7.57 (m, 8H), 7.45 (dd, *J* = 16, 1H). **^{13}C NMR:** δ = 192.34, 143.05, 137.94, 135.08, 134.53, 131.97, 129.98, 127.72, 127.02, 125.91 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 253.10, obs. 253.13.

(*Z*)-(4-(4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido) phenyl)boronic acid (17). Upon cooling the reaction mixture to room temperature the product precipitated out of solution. Crude compound was recrystallized from a dichloromethane/methanol mixture (4:1). **Yield:** 60%. **^{1}H NMR:** δ = 10.39 (s, 1H), 8.10-8.04 (m, 3H), 7.94 (s, 2H), 7.80-7.76 (m, 6H), 7.40-7.37 (m, 2H), 7.22-7.16 (m, 2H), 4.84 (s, 2H). **^{13}C NMR:** δ = 167.12, 165.34, 164.66, 161.66 (d, $^1J_{CF}$ = 244), 140.57, 136.23, 135.68, 134.69, 132.23, 131.60 (d, $^4J_{CF}$ = 3), 129.95 (d, $^3J_{CF}$ = 8), 129.94, 128.53, 123.04, 119.01, 115.42 (d, $^2J_{CF}$ = 21), 44.04 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 477.11, obs. 477.08.

(*Z*)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido) methyl)phenyl) boronic acid (18). Title compound was purified using preparative HPLC. **Yield:** 5%. **^{1}H NMR:** δ = 9.17 (t, *J* 6.0, 1H), 8.04-8.00 (m, 3H), 7.97 (s, 2H), 7.74-7.70 (m, 4H), 7.41-7.16 (m, 6H), 4.83 (s, 2H), 4.50 (d, *J* 5.8, 2H). **^{13}C NMR:** δ = 167.15, 165.35, 165.32, 161.66 (d, $^1J_{CF}$ = 244), 141.21, 135.64,

135.41, 134.13, 132.30, 131.58 (d, $^4J_{CF}$ = 3), 129.94 (d, $^3J_{CF}$ = 8), 129.89, 128.11, 126.17, 122.82, 115.42 (d, $^2J_{CF}$ = 21), 44.02, 42.72 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 491.12, obs. 491.17.

(*Z*)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)carbamoyl)phenyl) boronic acid (19). Title compound was purified using preparative HPLC. **Yield:** 21%. **^{1}H NMR:** δ =10.56 (s, 1H), 8.25 (s, 2H), 8.00 (d, *J* 8.8, 2H), 7.93 (m, 5H), 7.66 (d, *J* = 8.8, 2H), 7.40-7.35 (m, 2H), 7.22-7.16 (m, 2H), 4.83 (s, 2H). **^{13}C NMR:** δ = 167.38, 166.05, 165.58, 161.64 (d, $^1J_{CF}$ = 244), 141.53, 135.73, 134.00, 132.20, 131.76 (d, $^4J_{CF}$ = 3), 131.20, 129.92 (d, $^3J_{CF}$ = 8), 127.84, 126.61, 120.39, 118.97), 115.44 (d, $^2J_{CF}$ = 21), 43.89 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 477.11, obs. 477.18.

(4-((*E*)-4-((*Z*)-(3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)styryl)phenyl)boronic acid (20). Upon cooling the reaction mixture to room temperature the product precipitated out of solution. Dissolving the product in dimethyl sulfoxide and precipitating it with 0.5 M hydrochloric acid resulted in pure compound. **Yield:** 47%. **^{1}H NMR:** δ = δ 8.04 (s, 2H), 7.96 (s, 1H), 7.88 – 7.52 (m, 8H), 7.49 – 7.12 (m, 6H), 4.83 (s, 2H). **^{13}C NMR:** δ = 167.20, 165.48, 161.64 (d, $^1J_{CF}$ = 244), 139.43, 138.09, 134.52, 133.01, 131.94, 131.69 (d, $^4J_{CF}$ = 3), 130.93, 130.71, 129.91 (d, $^3J_{CF}$ = 8), 127.78, 127.29, 125.77, 120.38, 115.42 (d, $^2J_{CF}$ = 21), 43.94 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 460.10, obs. 460.06.

(*Z*)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy)methyl)phenyl) boronic acid (26). Final product was isolated by using preparative HPLC. *Z*-configuration confirmed by the chemical shift of the vinyl and amine proton reported in literature.[1] **Yield:** 15%. **^{1}H NMR:** δ = 10.68 (s, 1H), 8.06 (s, 2H), 7.80 (d, *J* = 8.1, 2H), 7.62 (d, *J* = 8.9, 2H), 7.41 (d, *J* = 8.1, 2H), 7.39 – 7.28 (m, 2H), 7.24 – 7.10 (m, 2H), 7.04 (d, *J* = 8.9, 2H), 6.54 (s, 1H), 5.17 (s, 2H), 4.65 (s, 2H). **^{13}C NMR:** δ = 164.02, 161.49 (d, $^1J_{CF}$ = 244), 158.72, 154.89, 138.54, 134.22, 132.83 (d, $^4J_{CF}$ = 3), 131.30, 129.63 (d, $^3J_{CF}$ = 8), 126.55, 125.43, 115.35 (d, $^2J_{CF}$ = 21), 110.30, 69.28, 40.60 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 447.15, obs. 447.25.

(*E*)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy)methyl) phenyl)boronic acid (*E*-28). Title compound was purified using preparative HPLC. ***E*-28** contains 20% of the *Z*-isomers which could not be separated. *E*-configuration confirmed by the chemical shift of the vinyl and methyl proton reported in literature.[1] **Yield:** 28%. **^{1}H NMR:** $\delta_{E\text{-isomer}}$ = 8.04 (s, 2H), 8.01

(d, J = 9.0, 2H), 7.80 (d, J = 8.0, 2H), 7.41 (d, J = 7.9, 2H), 7.38 – 7.32 (m, 2H), 7.23 – 6.98 (m, 4H), 6.52 (s, 1H), 5.16 (s, 2H), 4.65 (s, 2H), 3.15 (s, 3H), . **^{13}C NMR:** $\delta_{E\text{-isomer}}$ = 161.49 (d, $^{1}J_{CF}$ = 244), 161.18, 158.80, 152.62, 138.54, 134.20, 132.74 (d, $^{4}J_{CF}$ = 3), 132.08, 129.83 (d, $^{3}J_{CF}$ = 8), 127.23, 126.59, 125.57, 117.51, 115.31 (d, $^{2}J_{CF}$ = 21), 114.41, 69.23, 40.78, 26.36 (C-B(OH)$_2$ not visible). **MS:** m/z $[M+H]^+$ calc. 461.17, obs. 461.19.

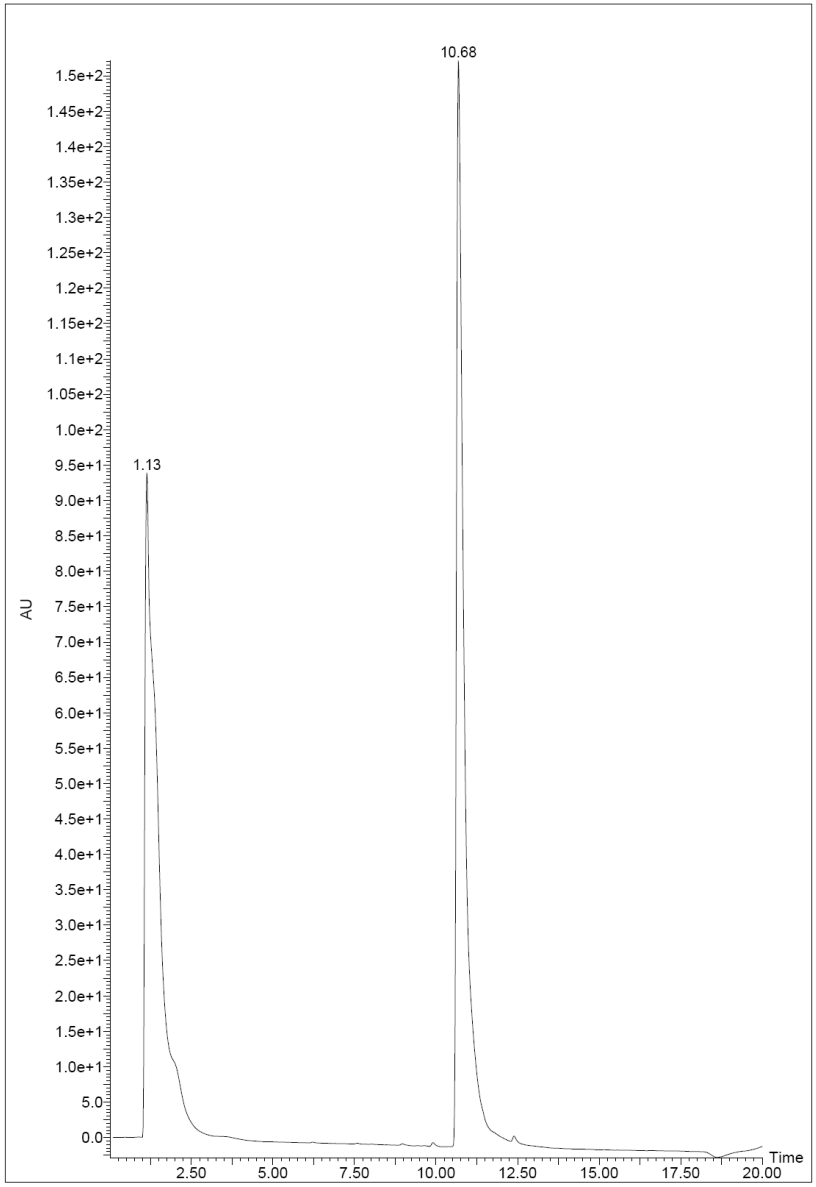
Reference

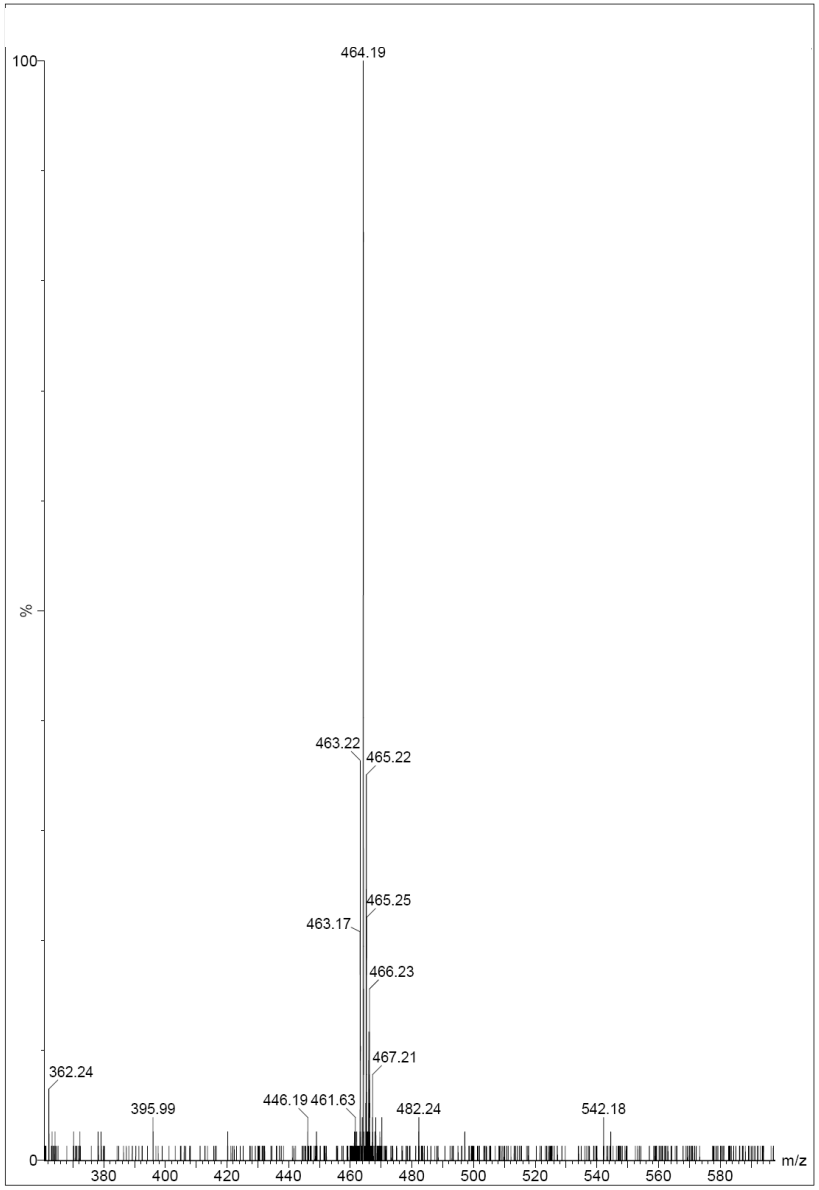
1. Tan, S.; Ang, K.; Fong, Y. (Z)- and (E)-5-Arylmethylenehydantoins: spectroscopic properties and configuration assignment. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1941-1944.

Spectral data on intermediates and inhibitors

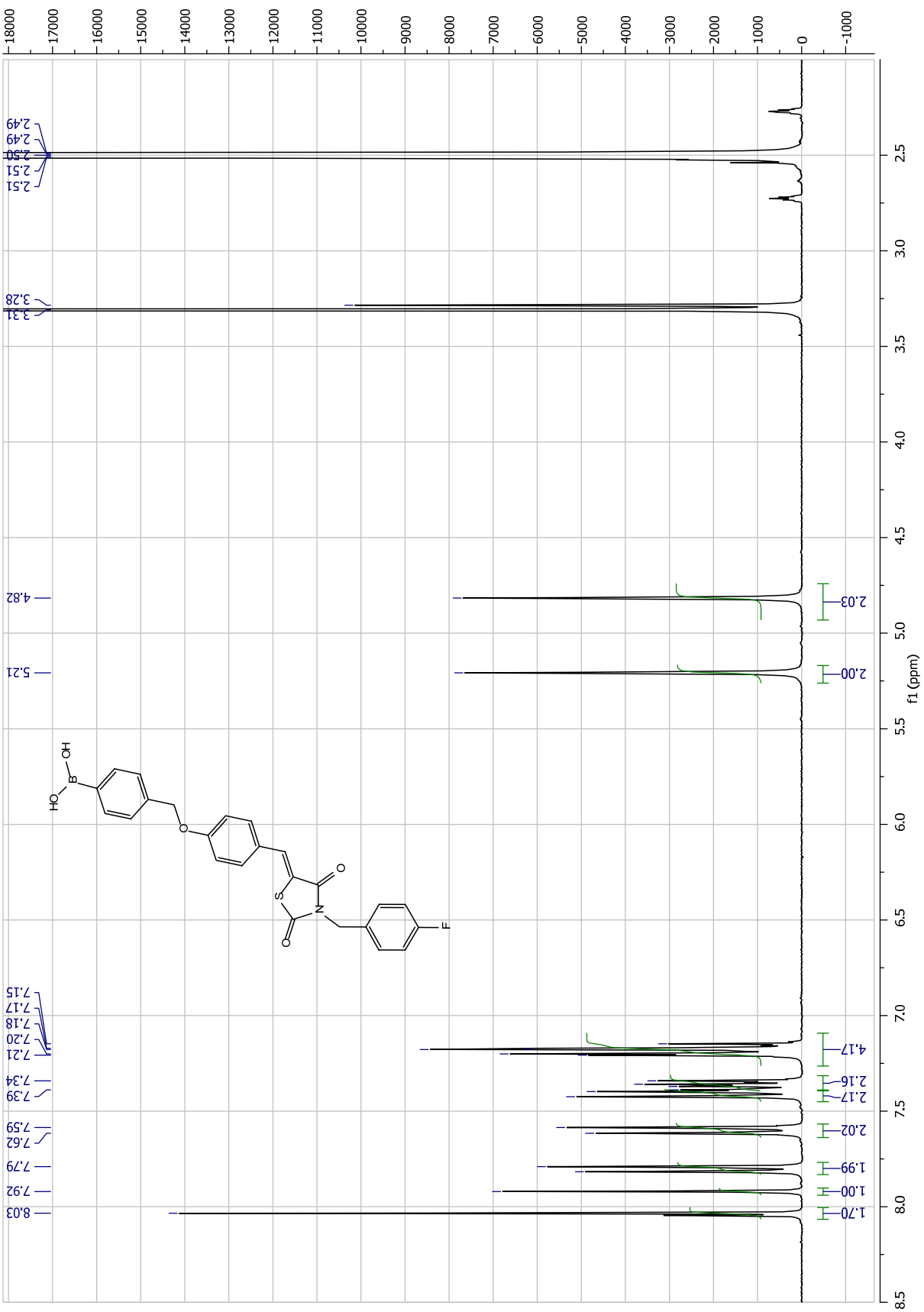
(HPLC-MS, ^{1}H and ^{13}C NMR)

4-[(4-{[3-(4-fluorobenzyl)-2,4-dioxo-1,3-thiazolan-5-yliden]methyl}phenoxy)methyl] benzene boronic acid (**1**); LC-MS

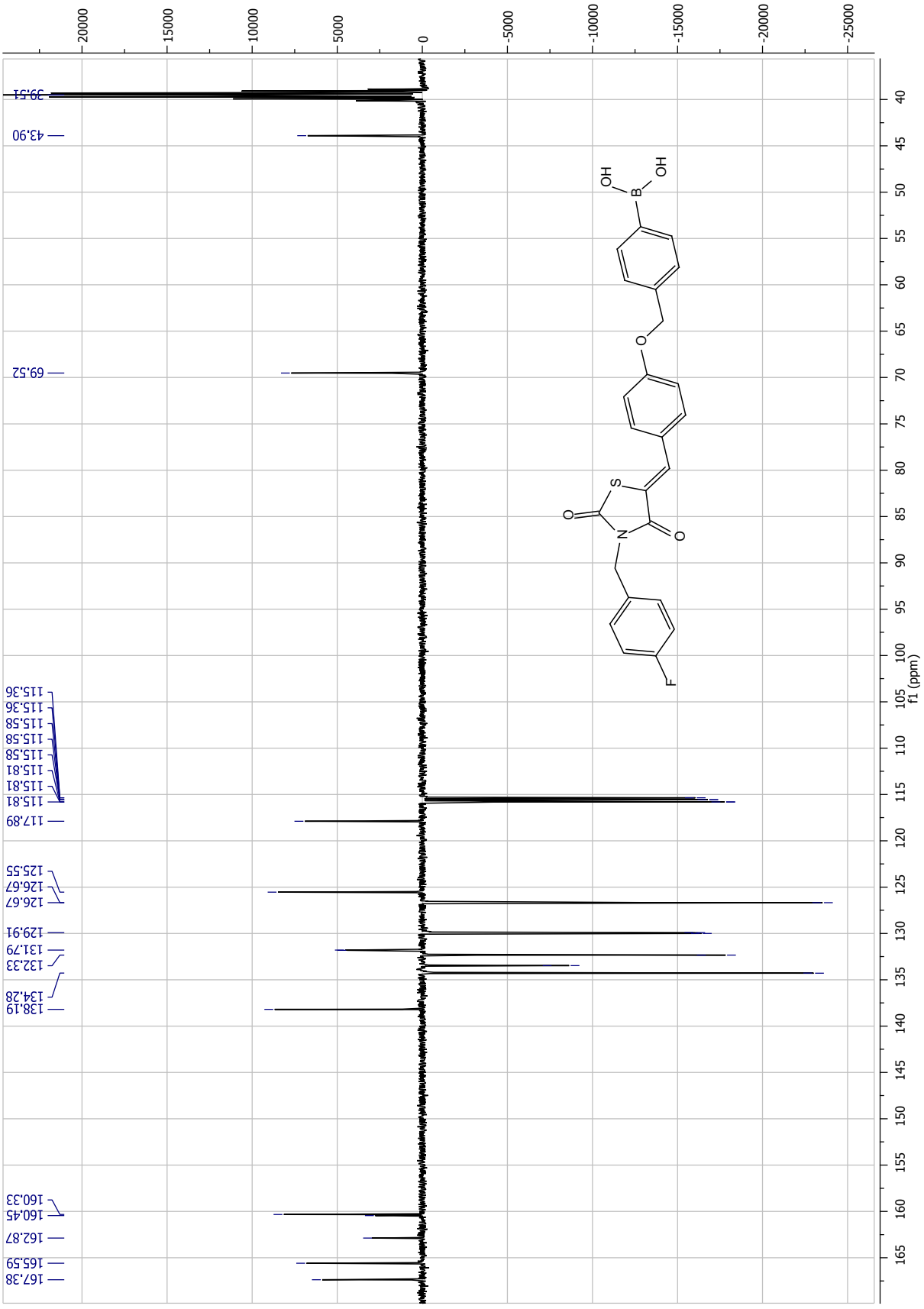




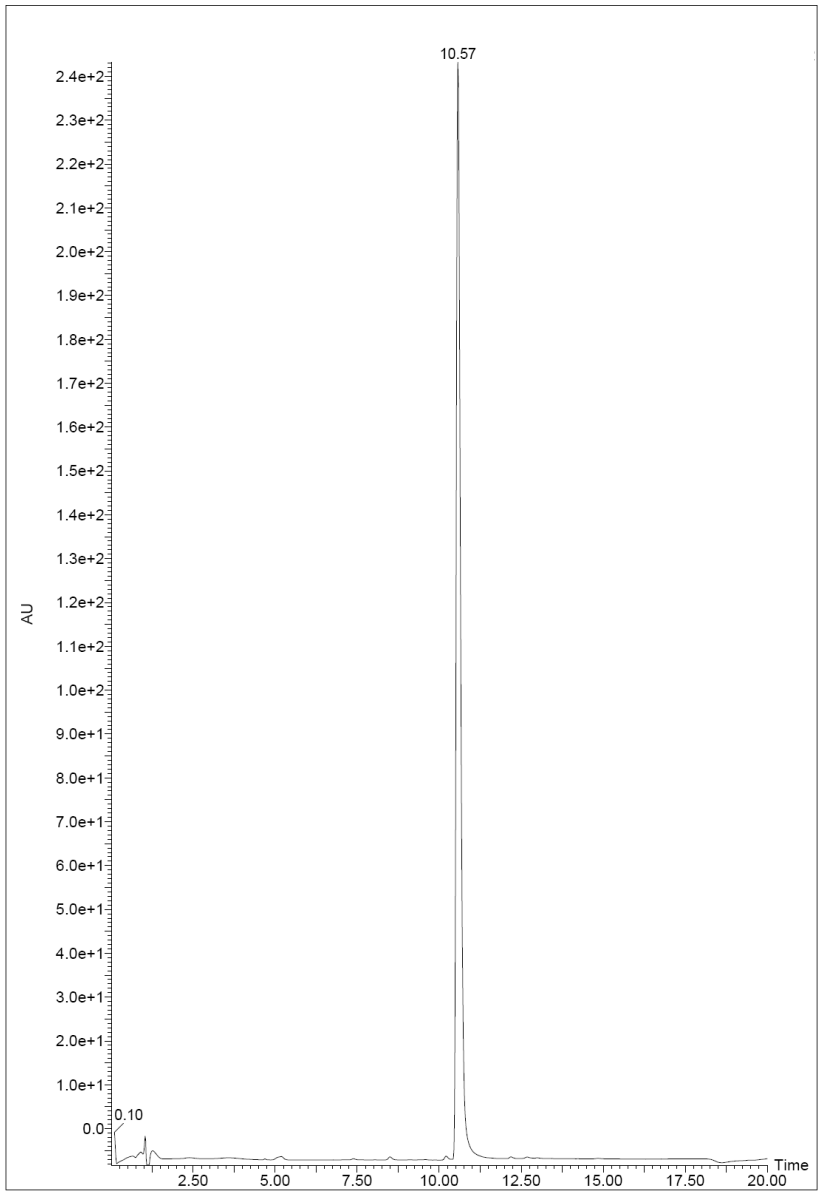
4-[(4-{[3-(4-fluorobenzyl)-2,4-dioxo-1,3-thiazolan-5-yliden]methyl}phenoxy)methyl] benzene boronic acid (**1**); ^{1}H NMR

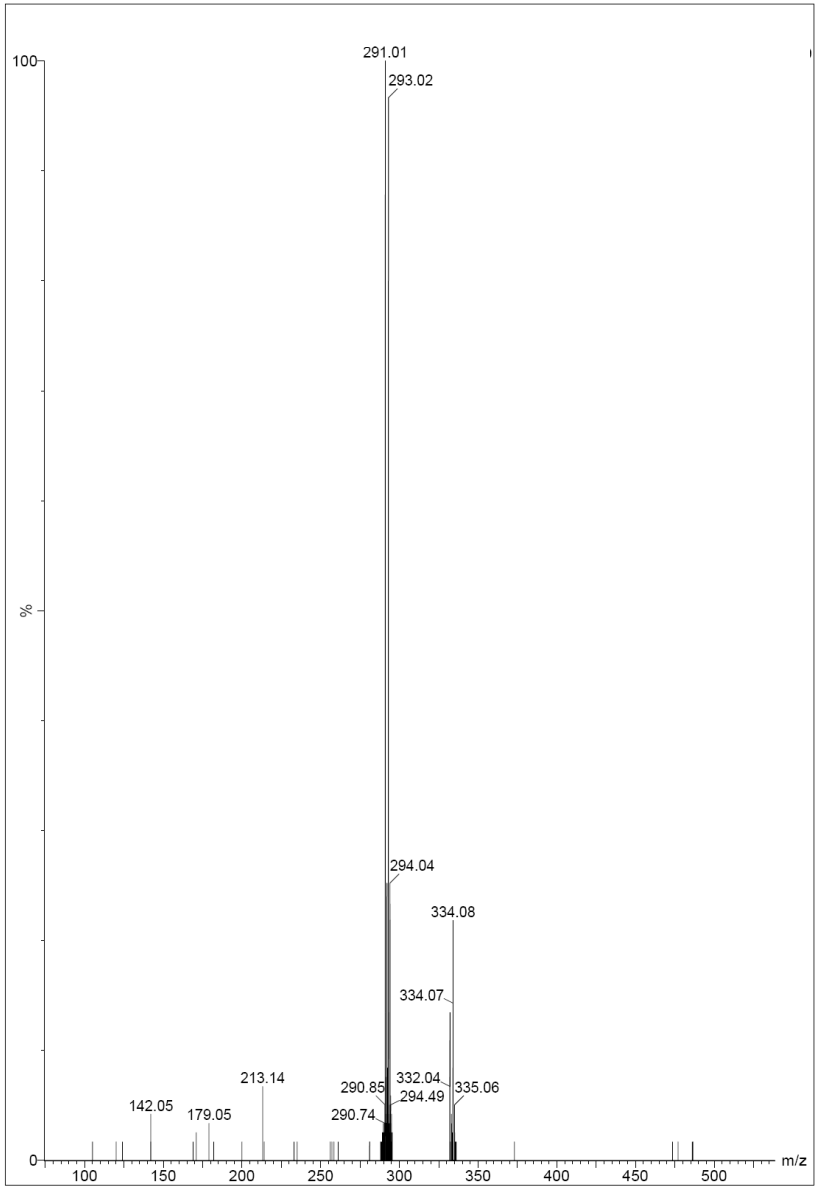


4-[(4-{[3-(4-fluorobenzyl)-2,4-dioxo-1,3-thiazolan-5-yliden]methyl}phenoxy)methyl] benzene boronic acid (**1**); ^{13}C NMR

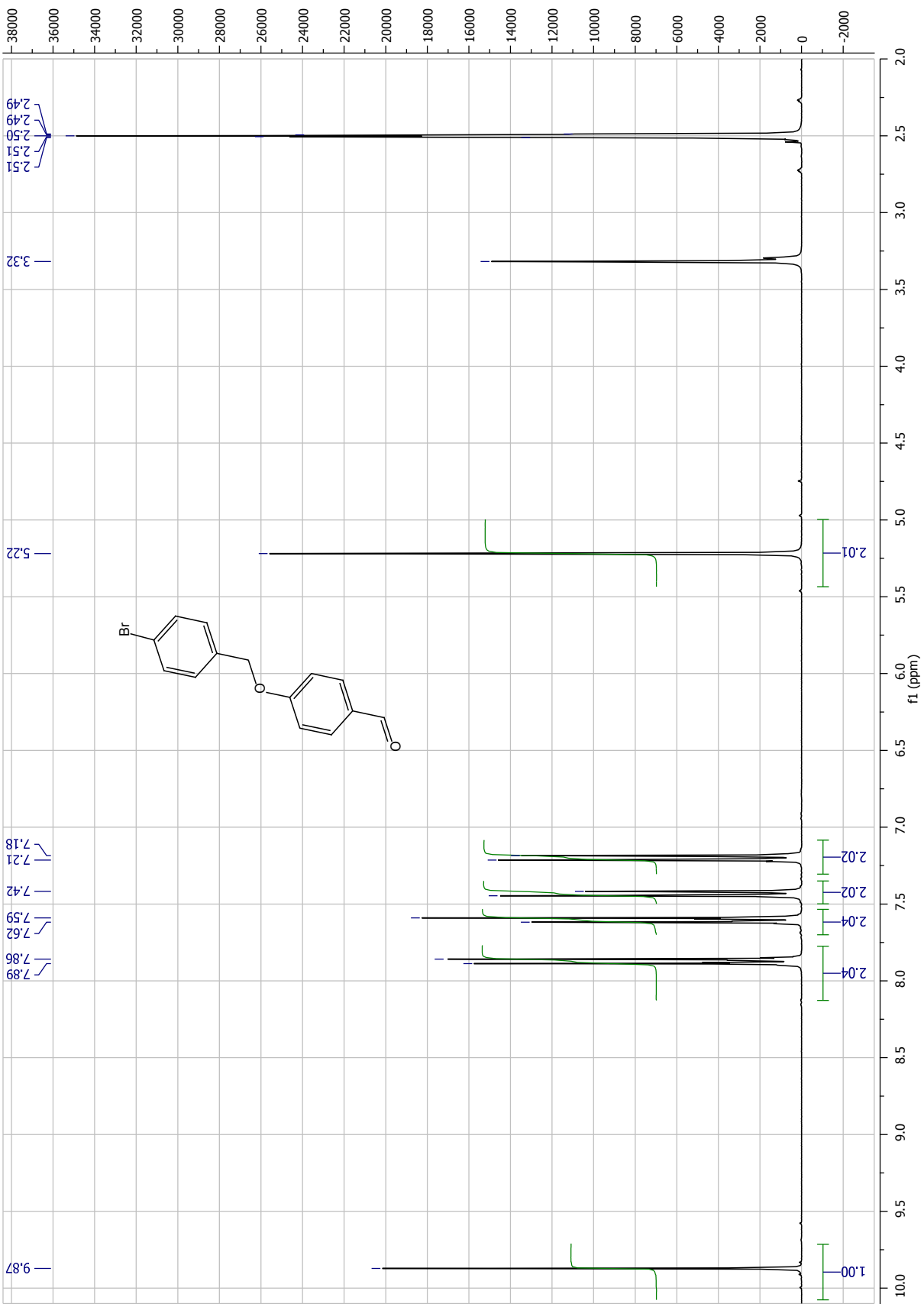


4-((4-bromobenzyl)oxy)benzaldehyde (**2**); LC-MS

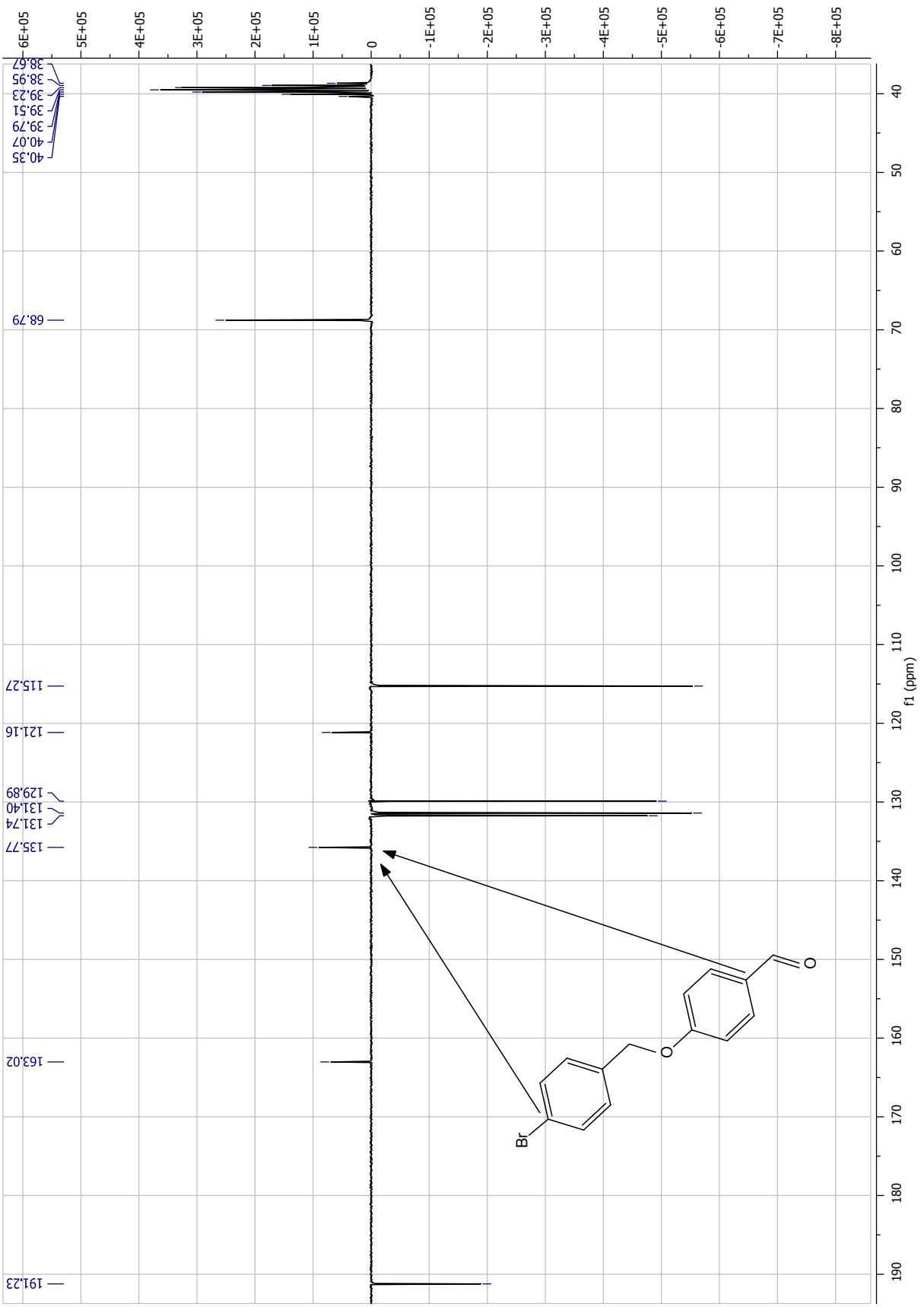




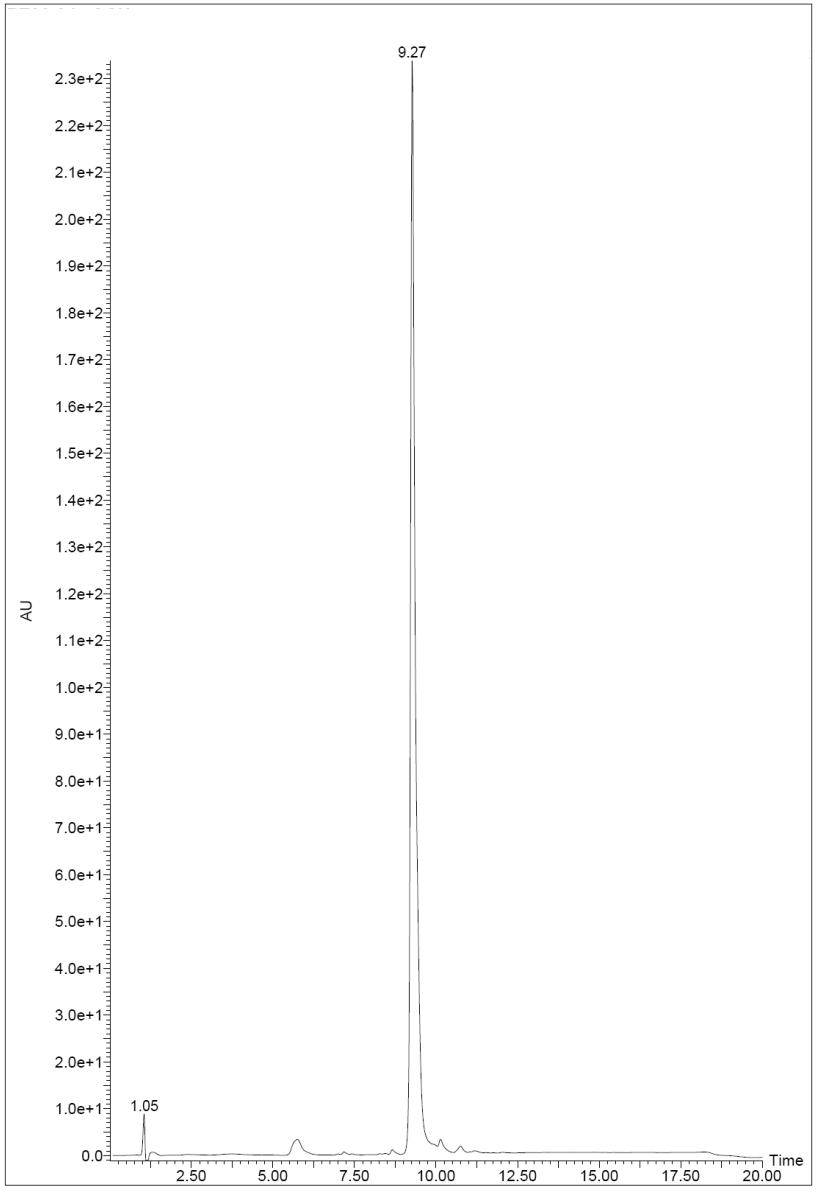
4-((4-bromobenzyl)oxy)benzaldehyde (**2**); ^{1}H NMR

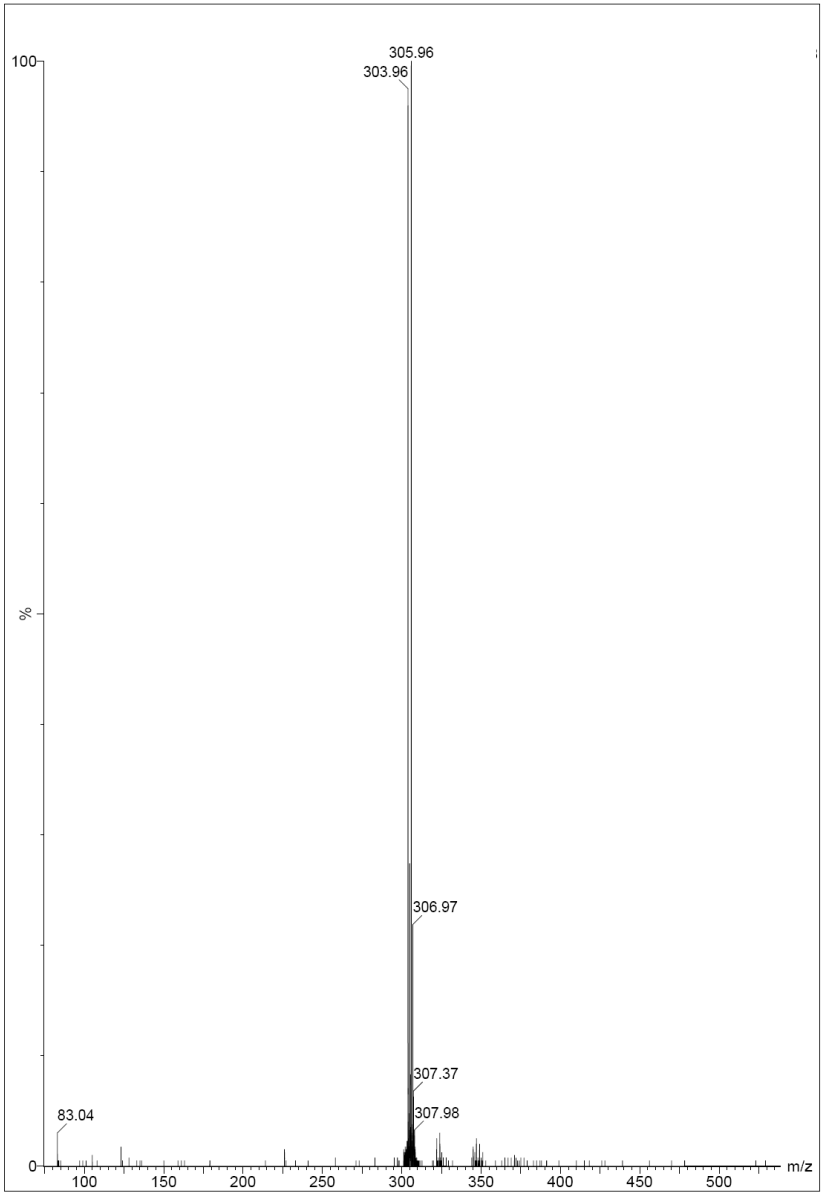


4-((4-bromobenzyl)oxy)benzaldehyde (**2**); ^{13}C NMR

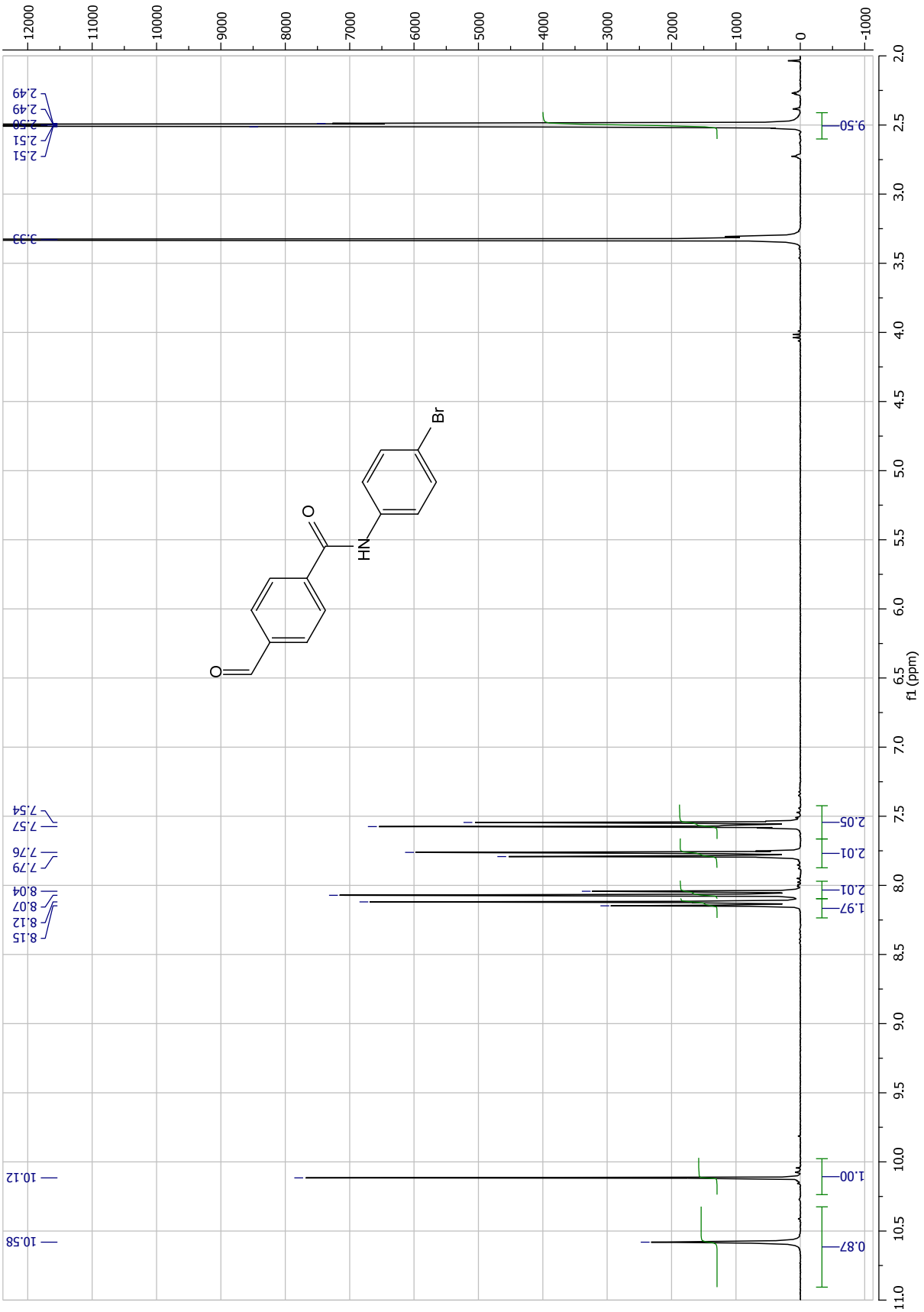


N-(4-bromophenyl)-4-formylbenzamide (**3**); LC-MS

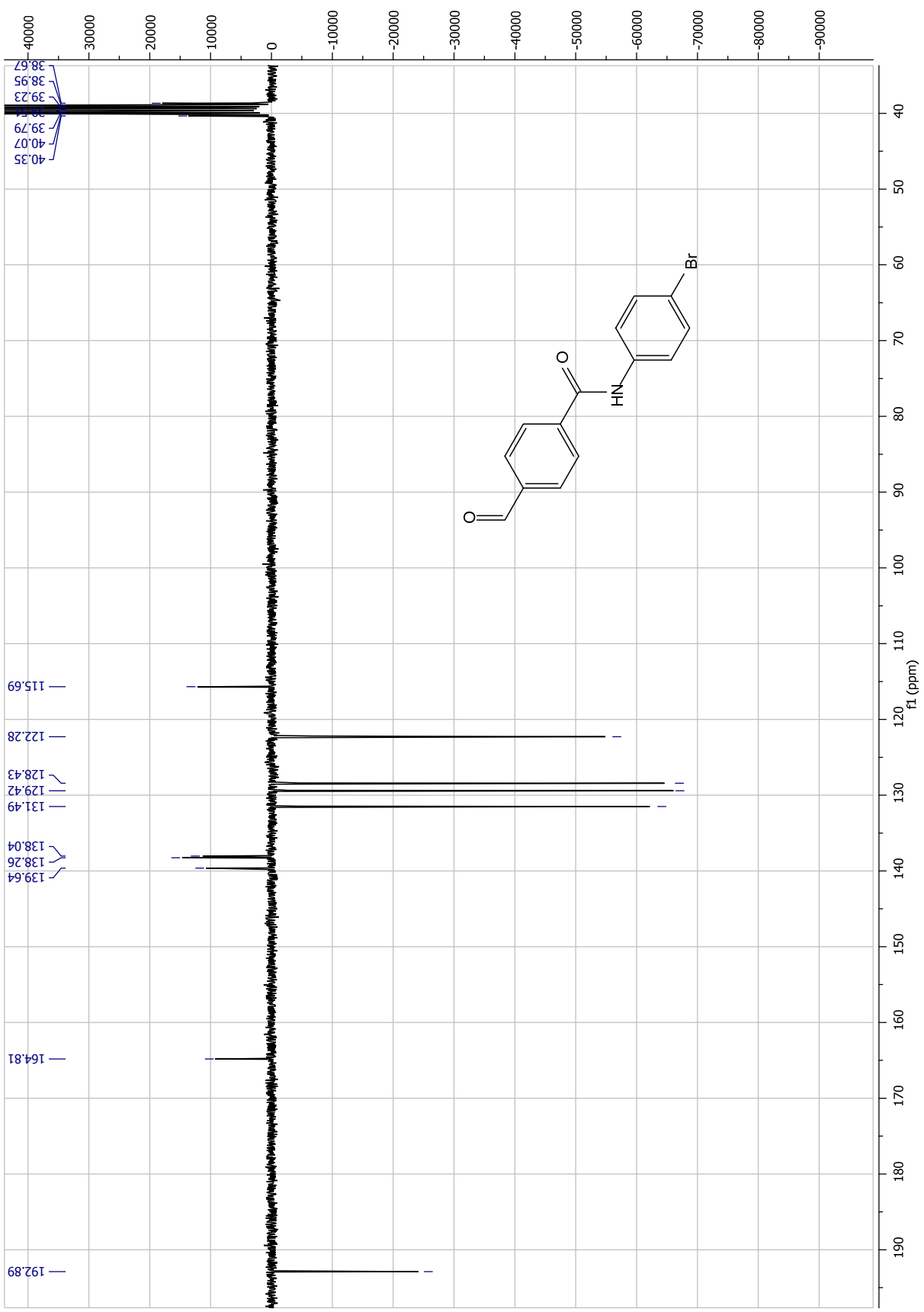




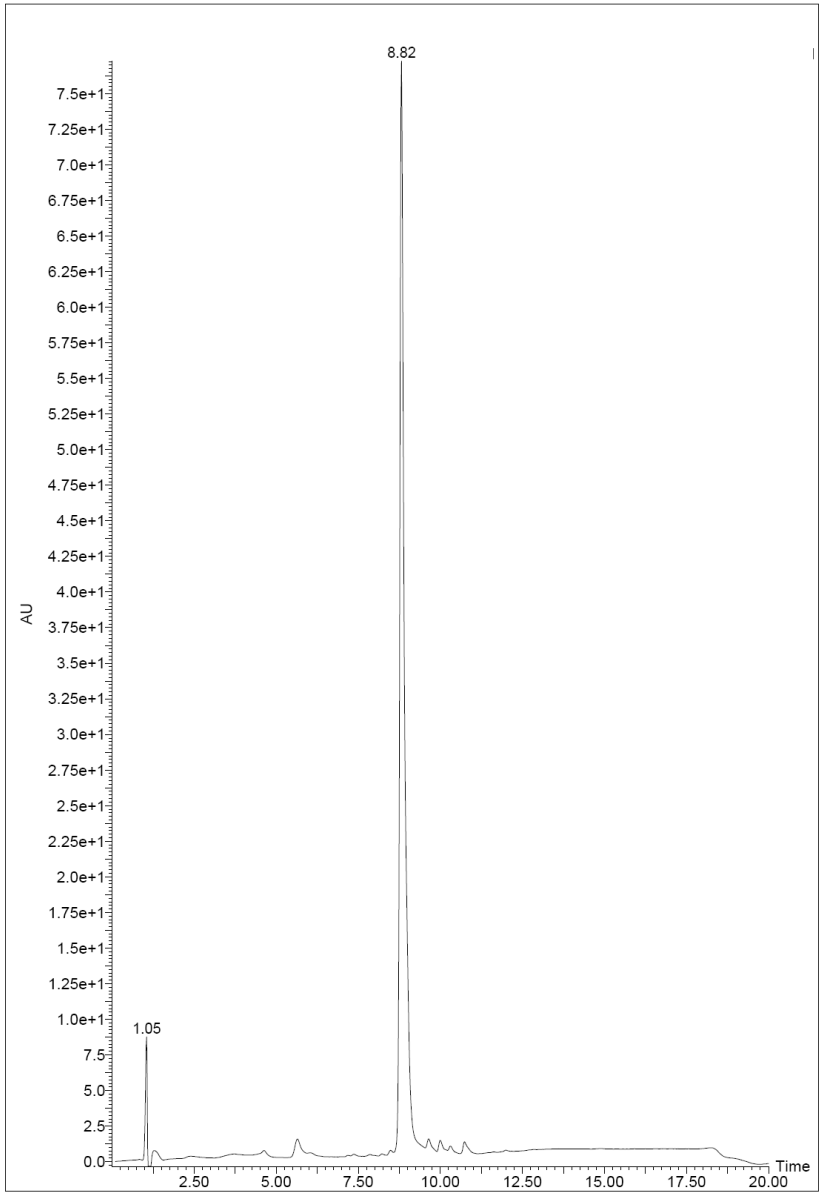
N-(4-bromophenyl)-4-formylbenzamide (**3**); ^{1}H NMR

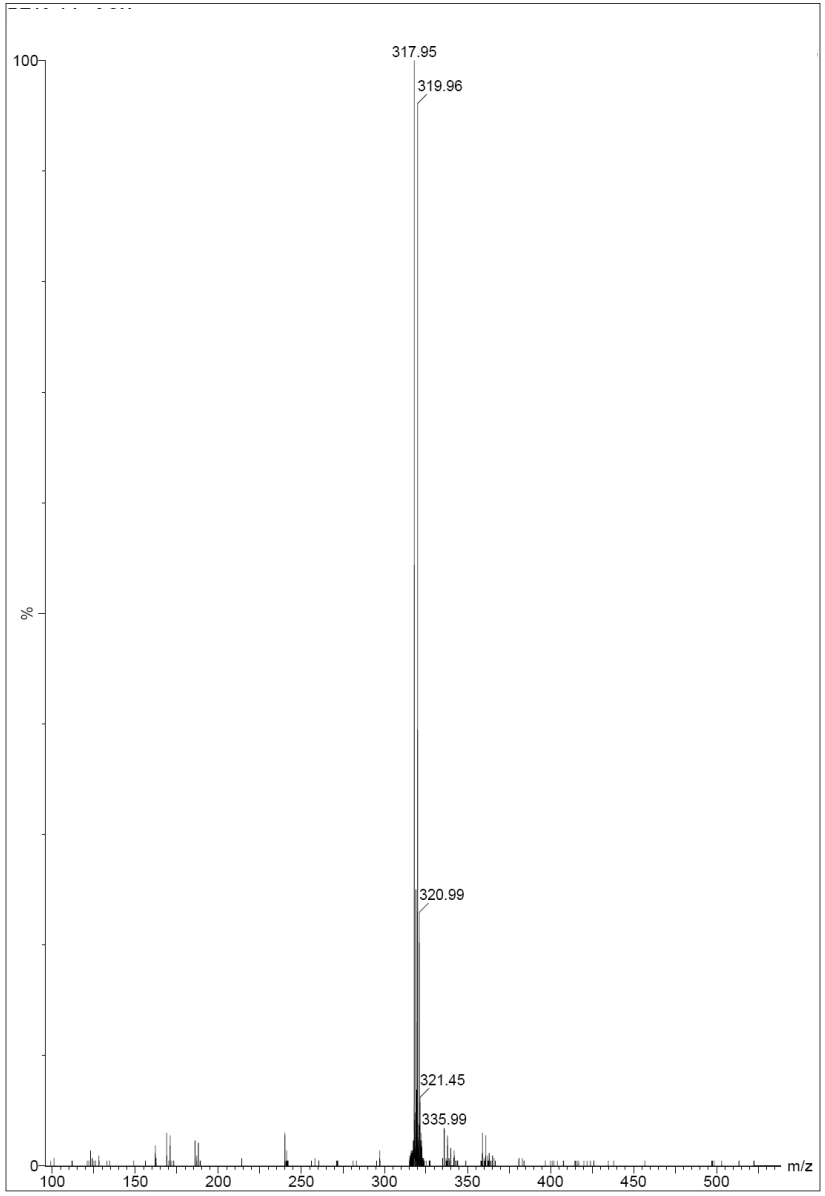


N-(4-bromophenyl)-4-formylbenzamide (**3**); ^{13}C NMR

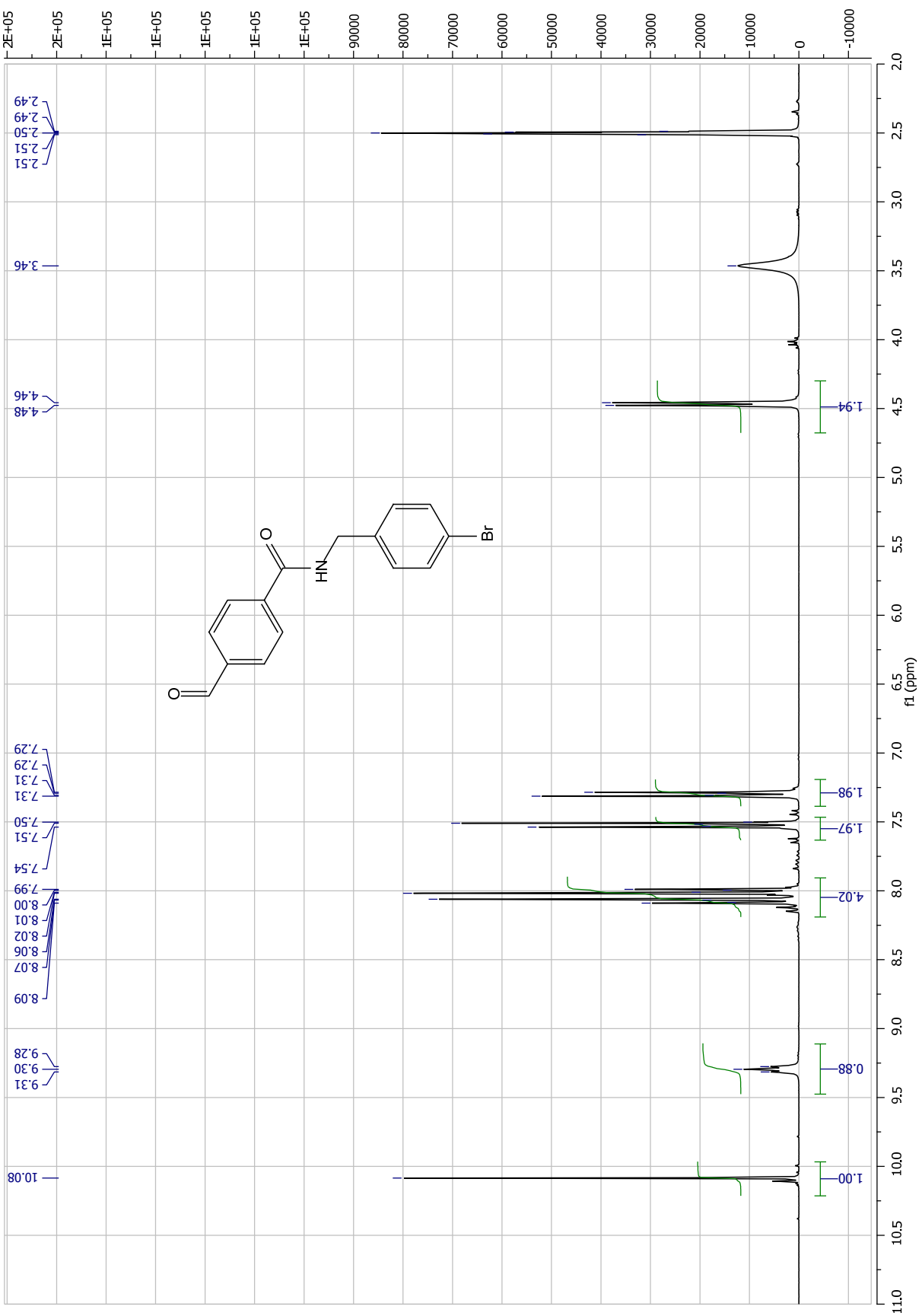


N-(4-bromobenzyl)-4-formylbenzamide (**4**); LC-MS

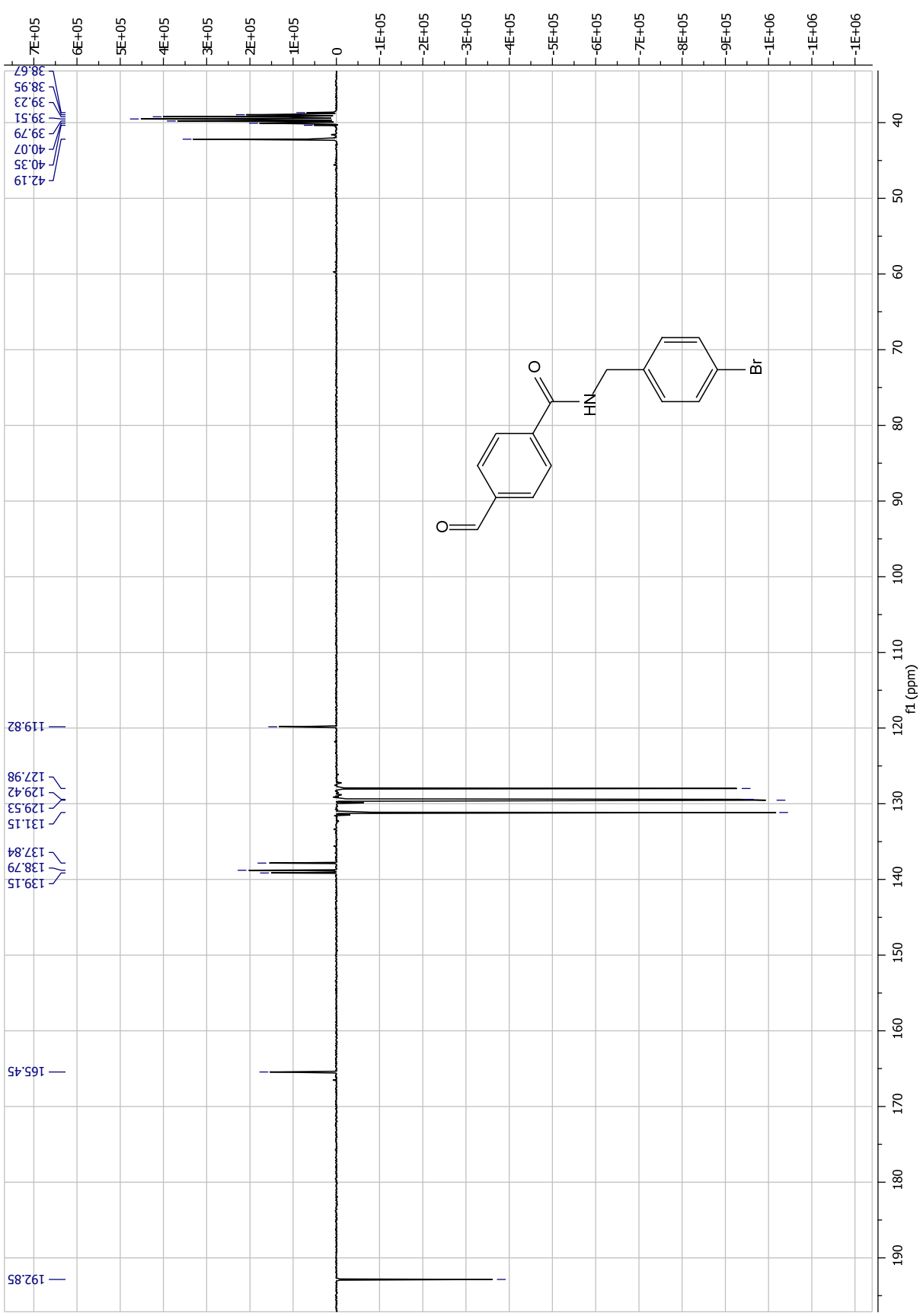




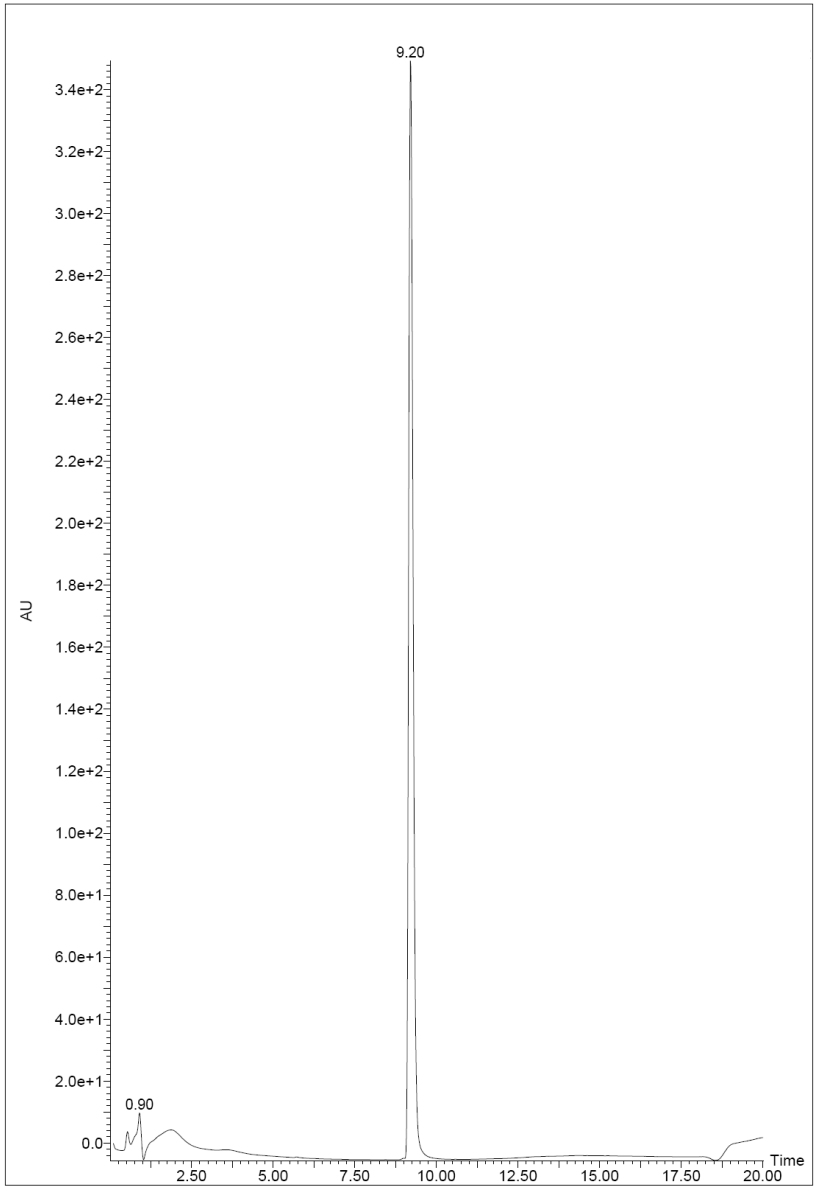
N-(4-bromobenzyl)-4-formylbenzamide (**4**); ^{1}H NMR

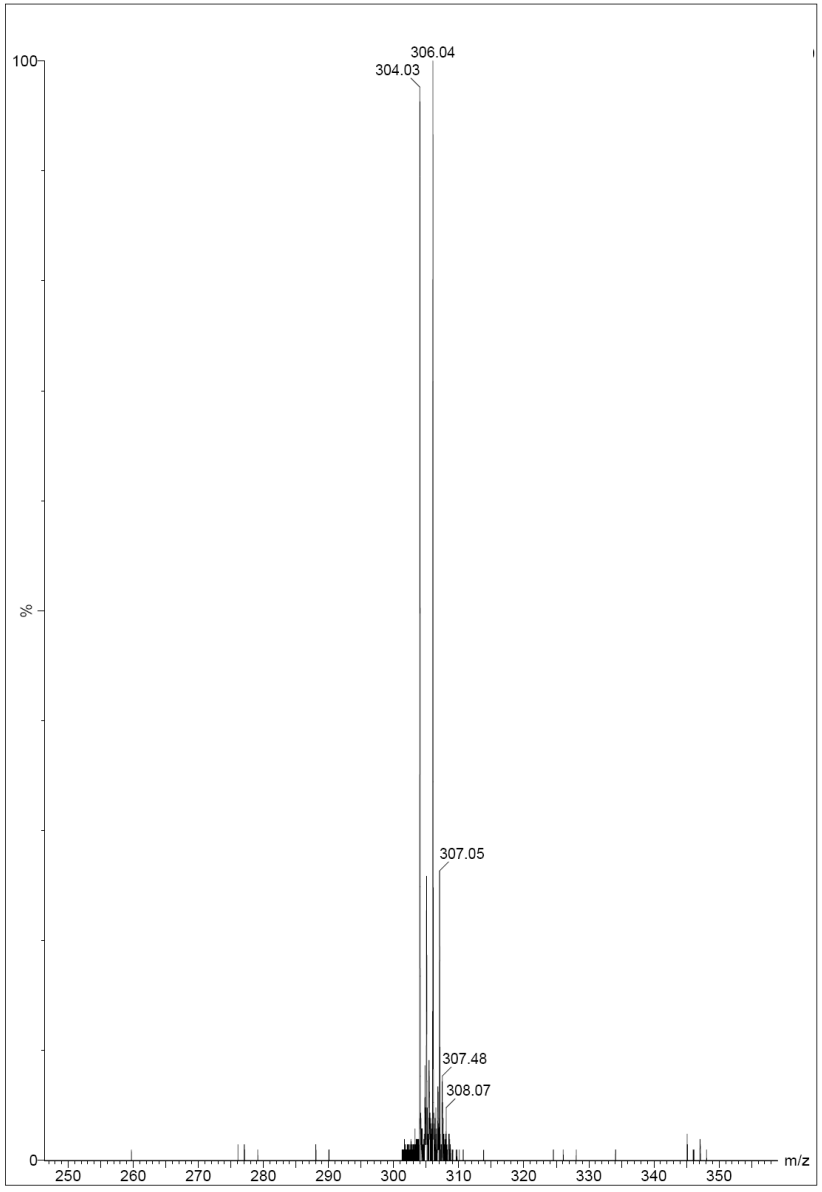


N-(4-bromobenzyl)-4-formylbenzamide (**4**); ^{13}C NMR

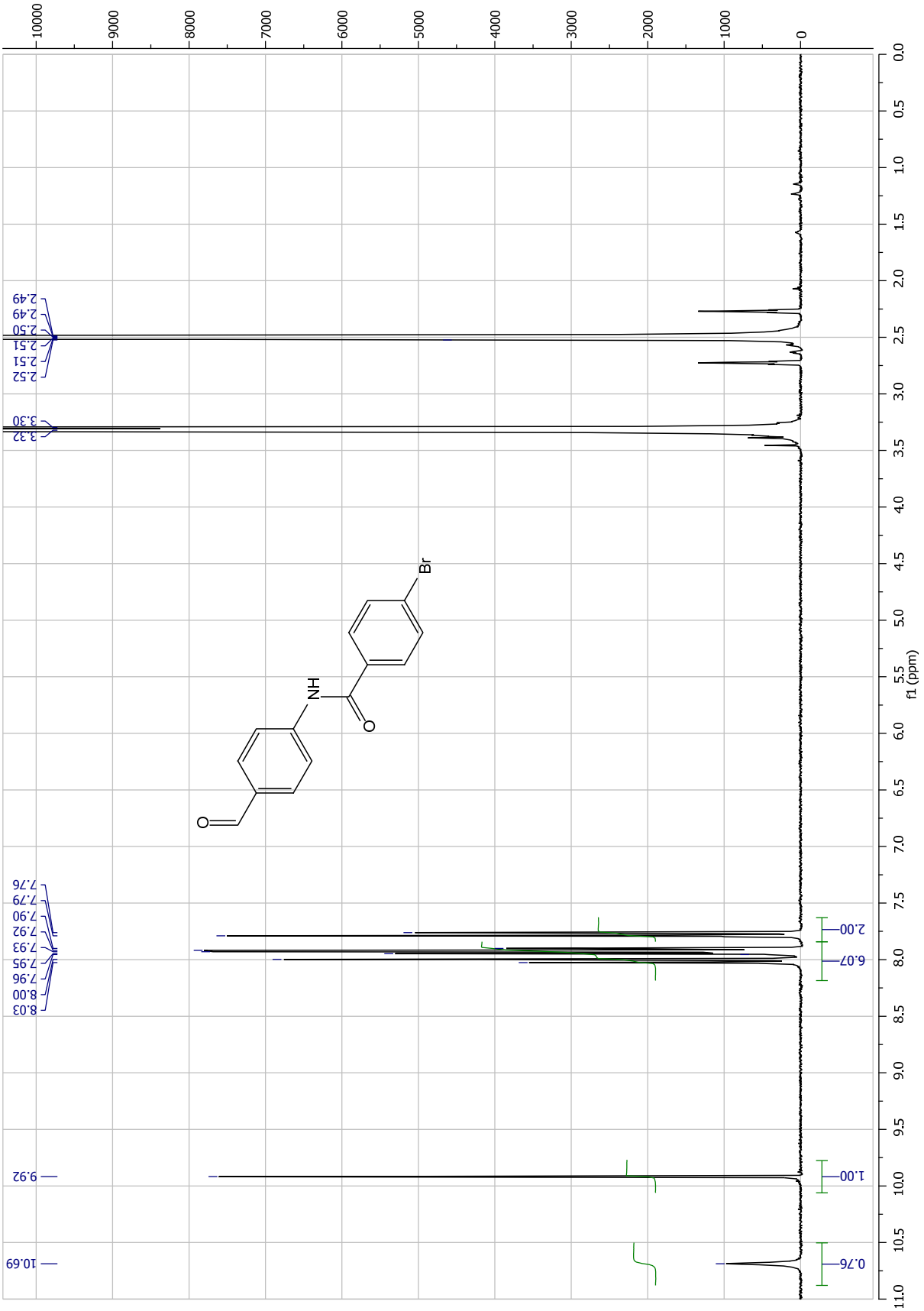


4-bromo-*N*-(4-formylphenyl)benzamide (**5**); LC-MS

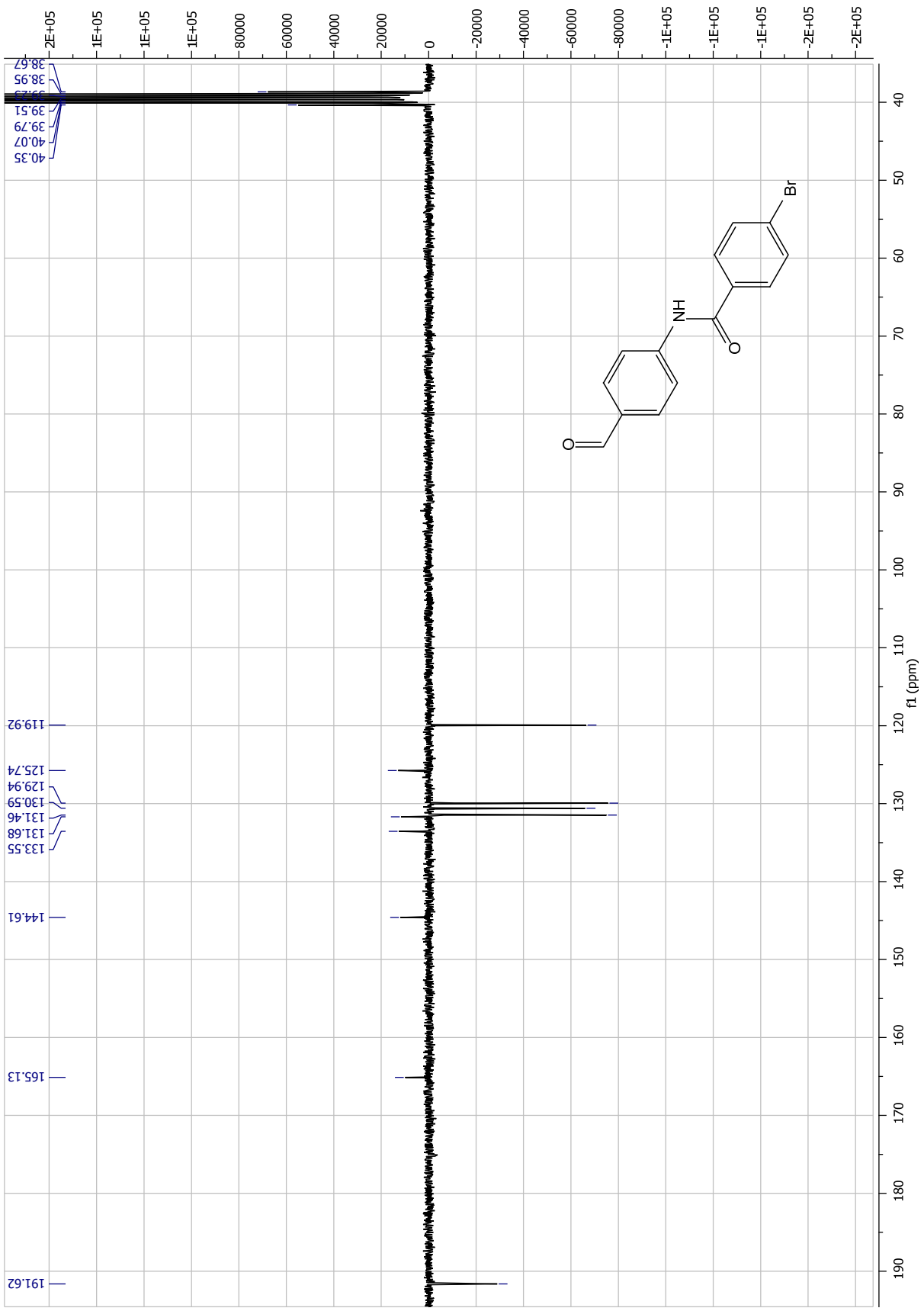




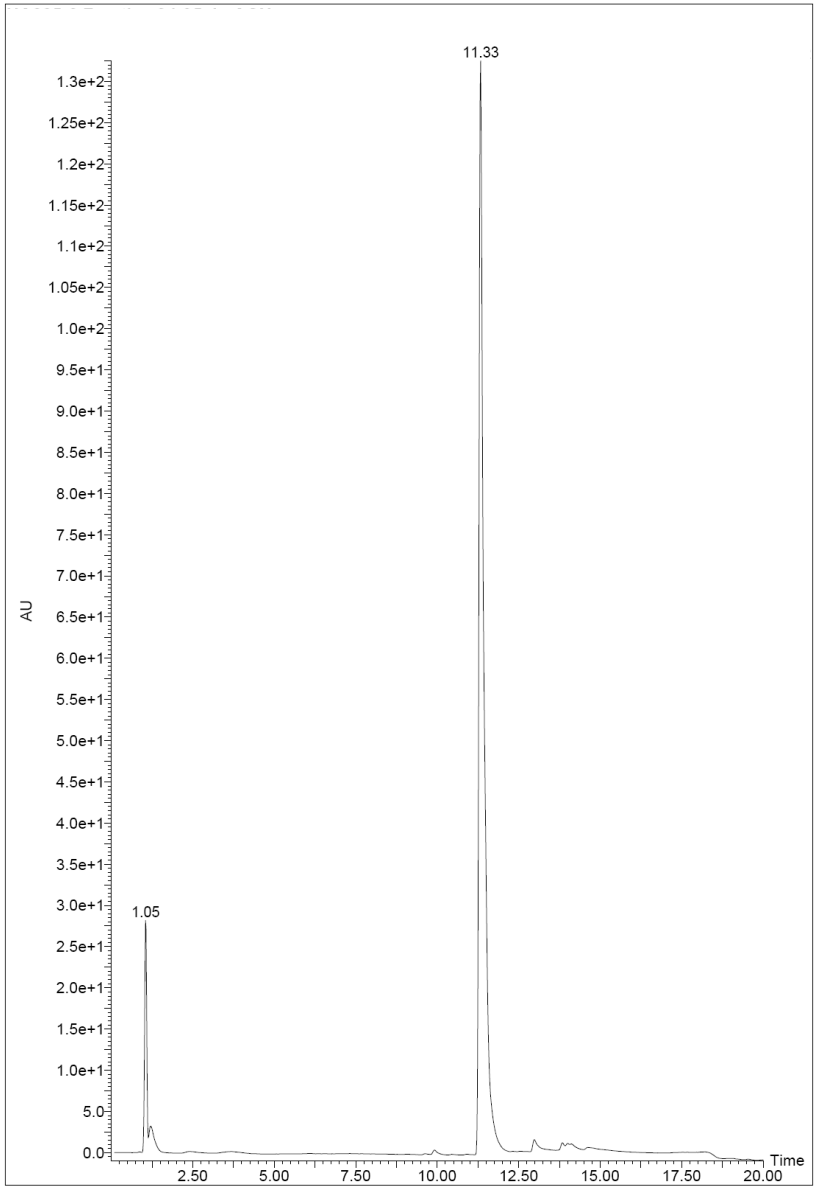
4-bromo-*N*-(4-formylphenyl)benzamide (**5**); ^{1}H NMR

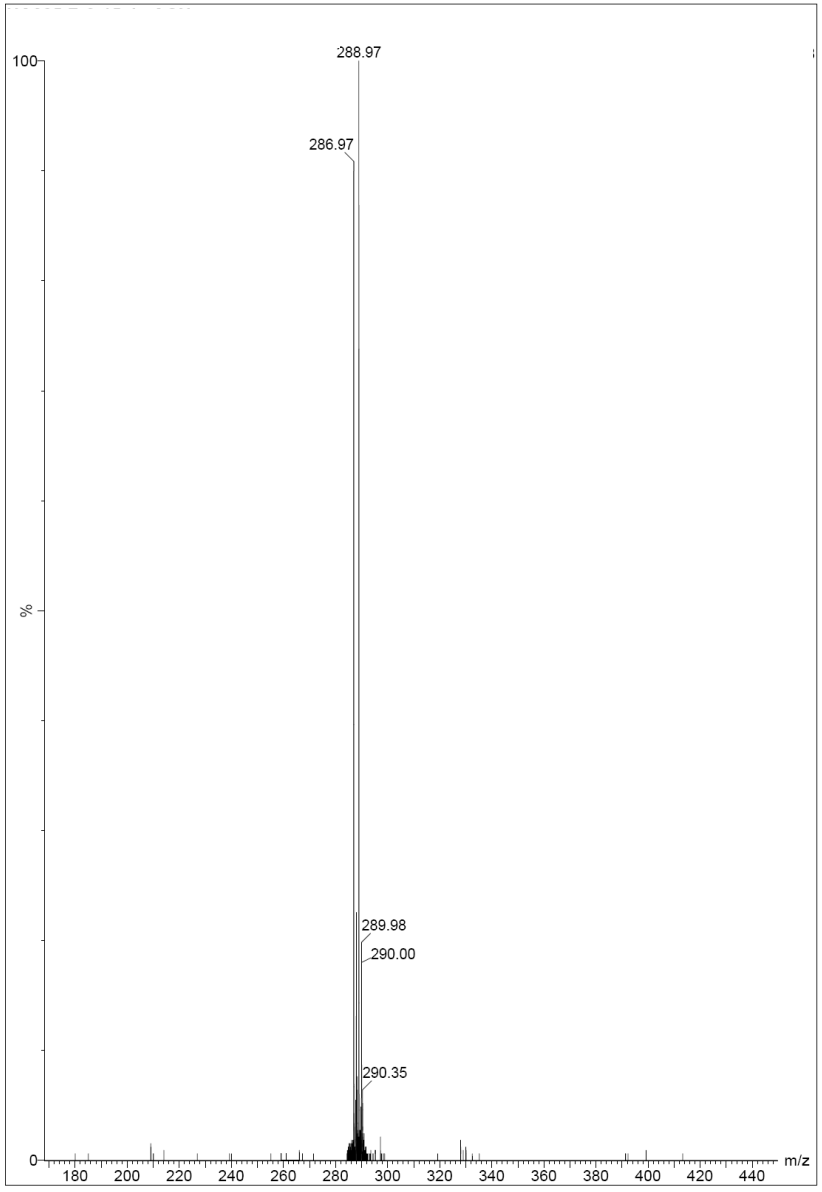


4-bromo-*N*-(4-formylphenyl)benzamide (**5**); ^{13}C NMR

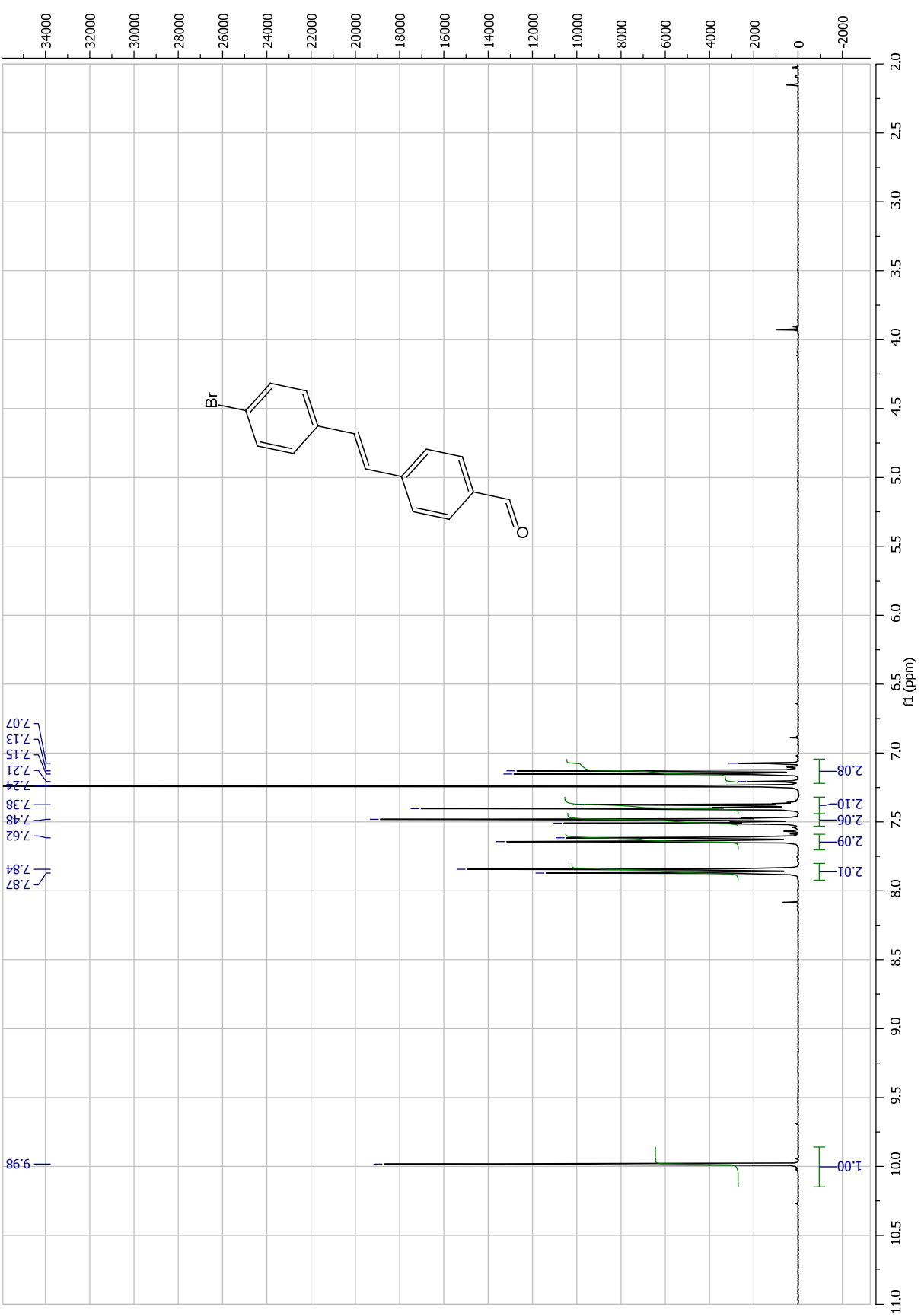


(*E*)-4-(4-bromostyryl)benzaldehyde (**6**); LC-MS

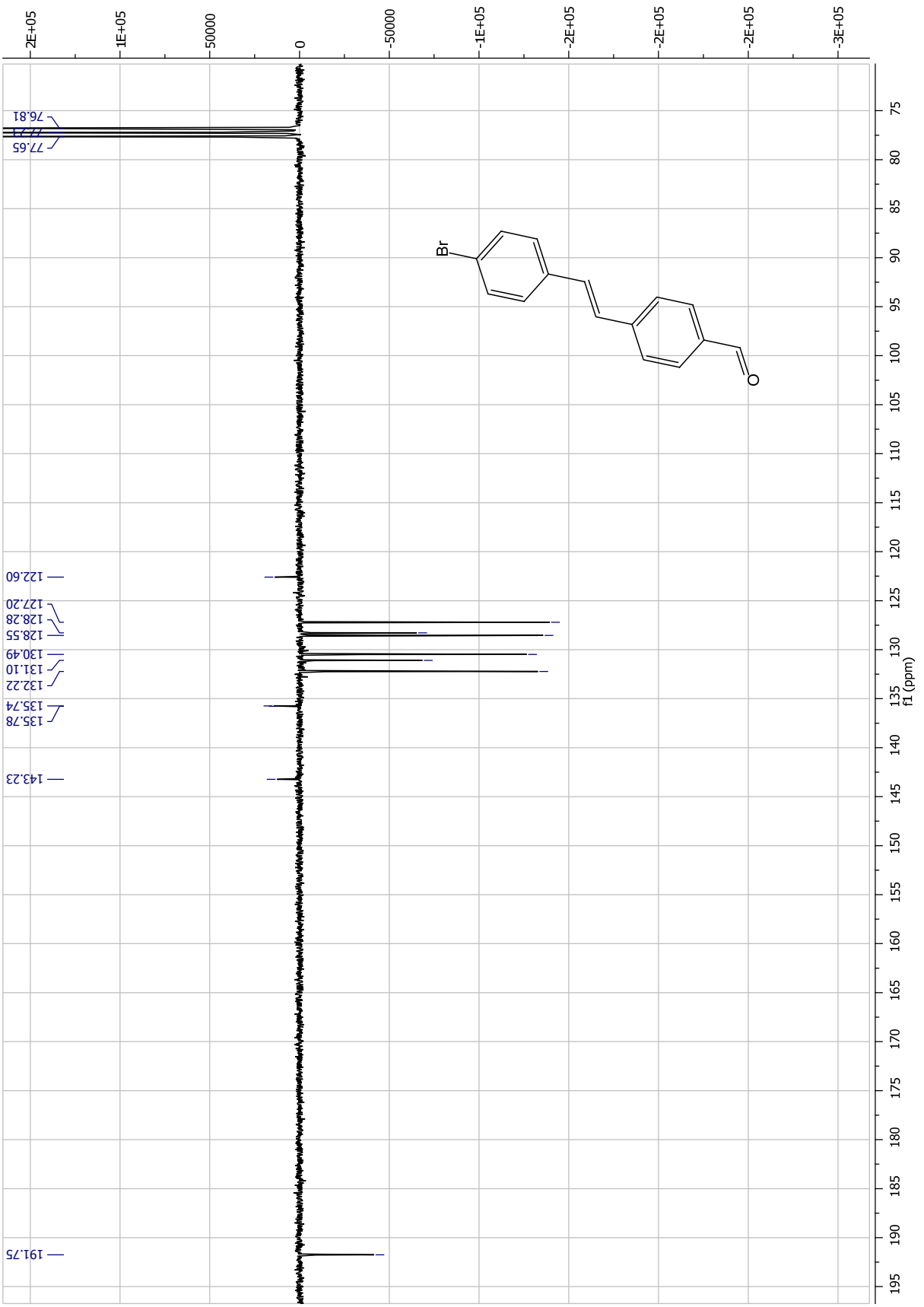




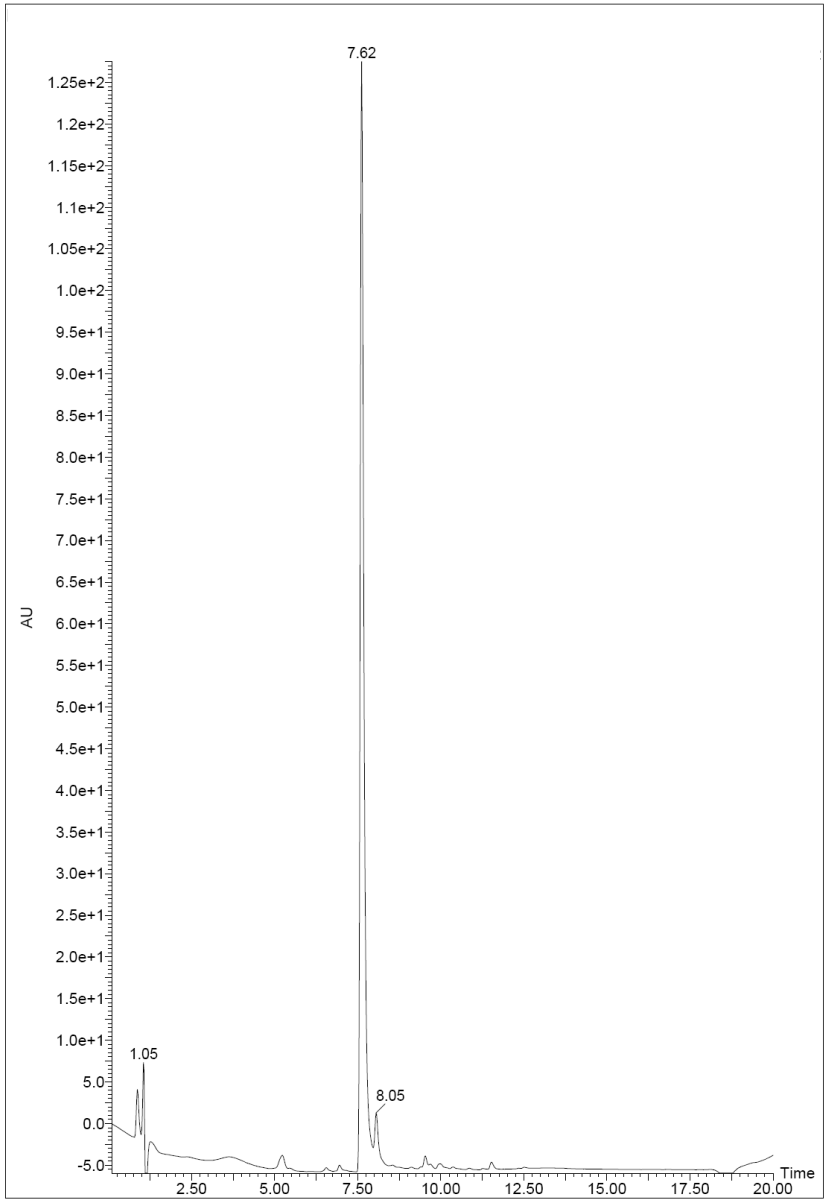
(*E*)-4-(4-bromostyryl)benzaldehyde (**6**); ^{1}H NMR ($CDCl_3$)

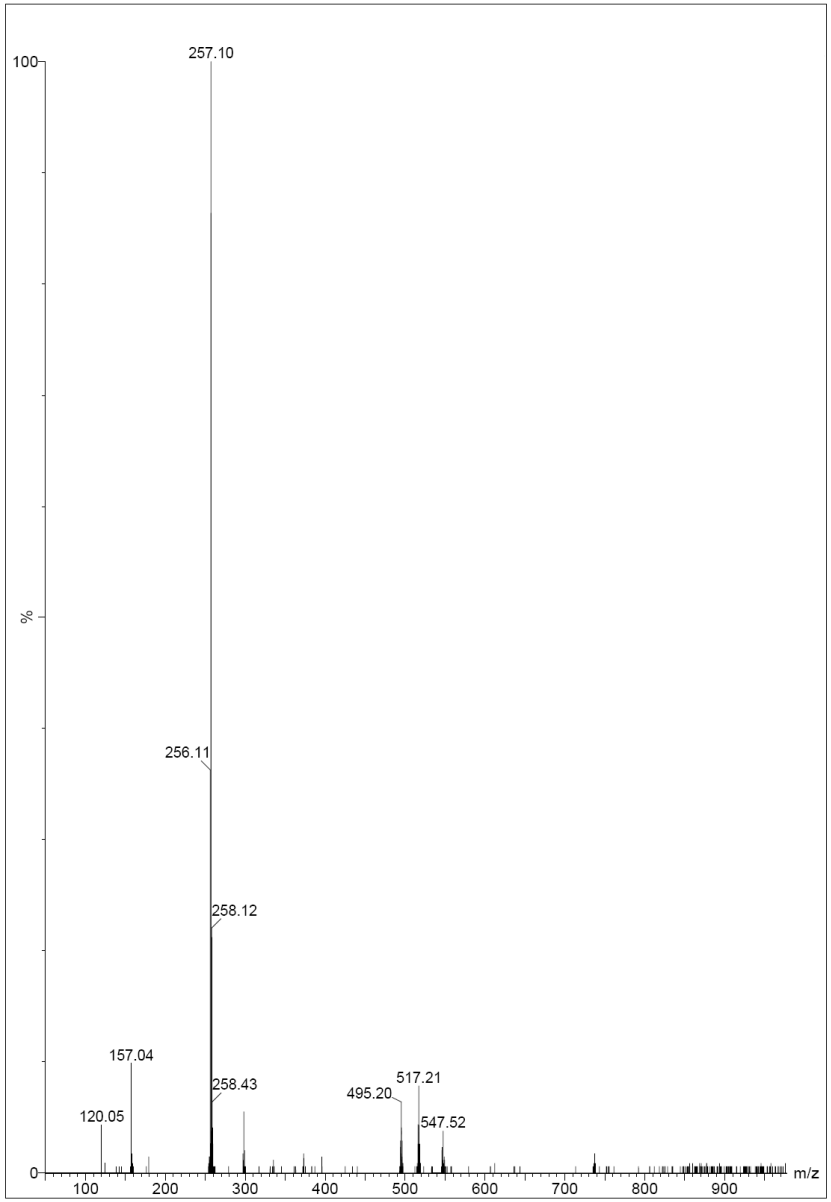


(*E*)-4-(4-bromostyryl)benzaldehyde (**6**); ^{13}C NMR ($CDCl_3$)

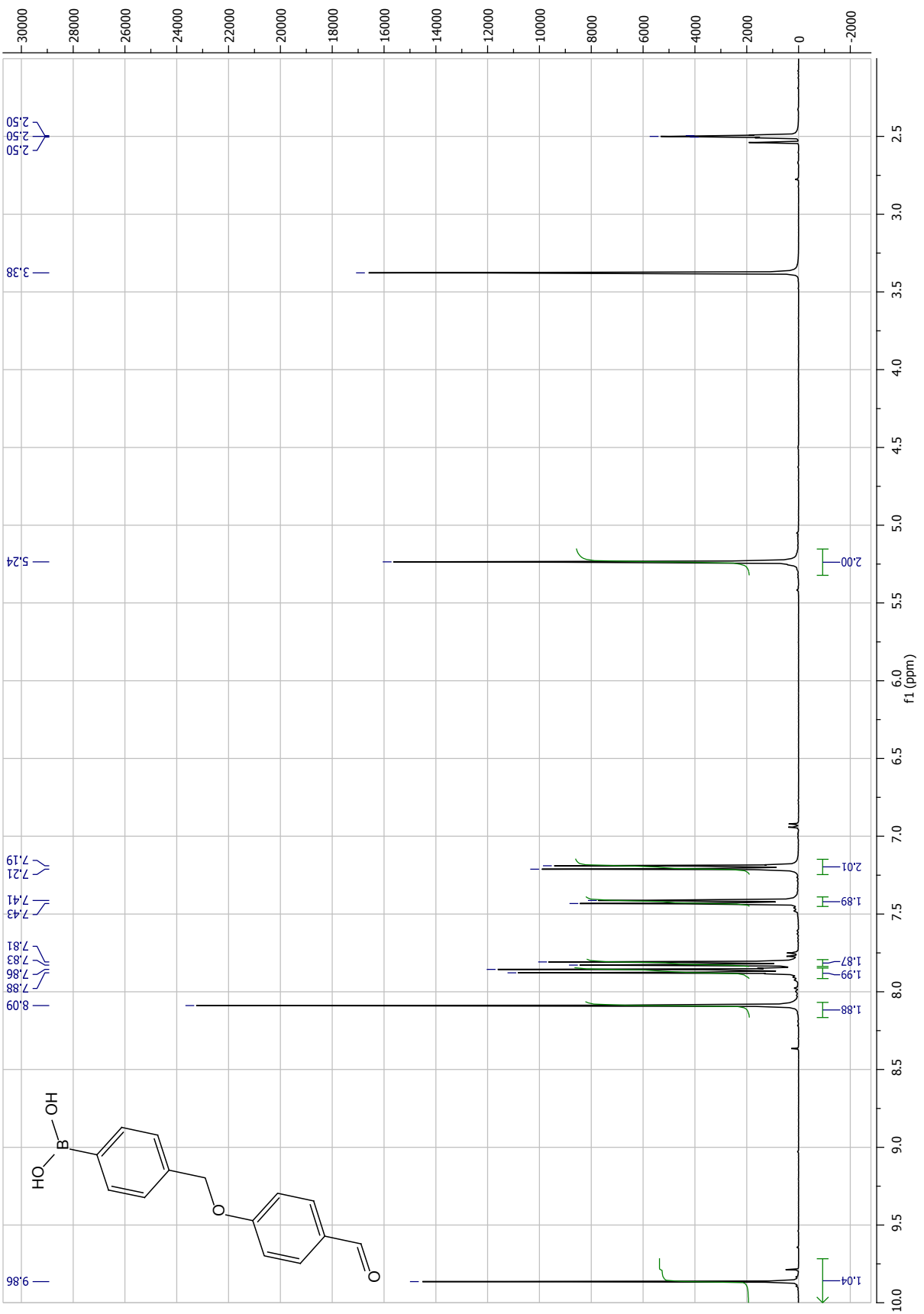


(4-((4-formylphenoxy)methyl)phenyl)boronic acid (**12**); LC-MS

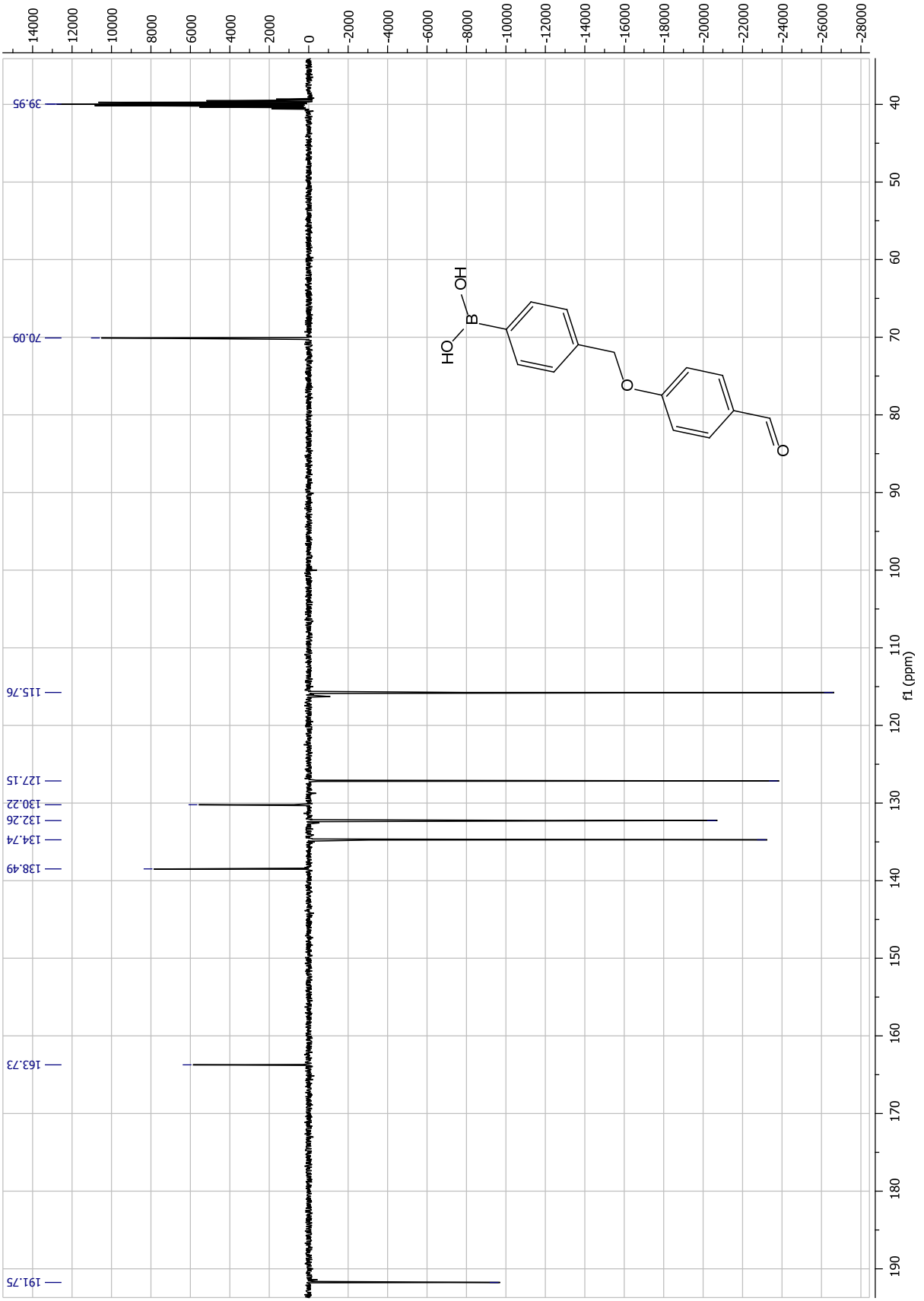




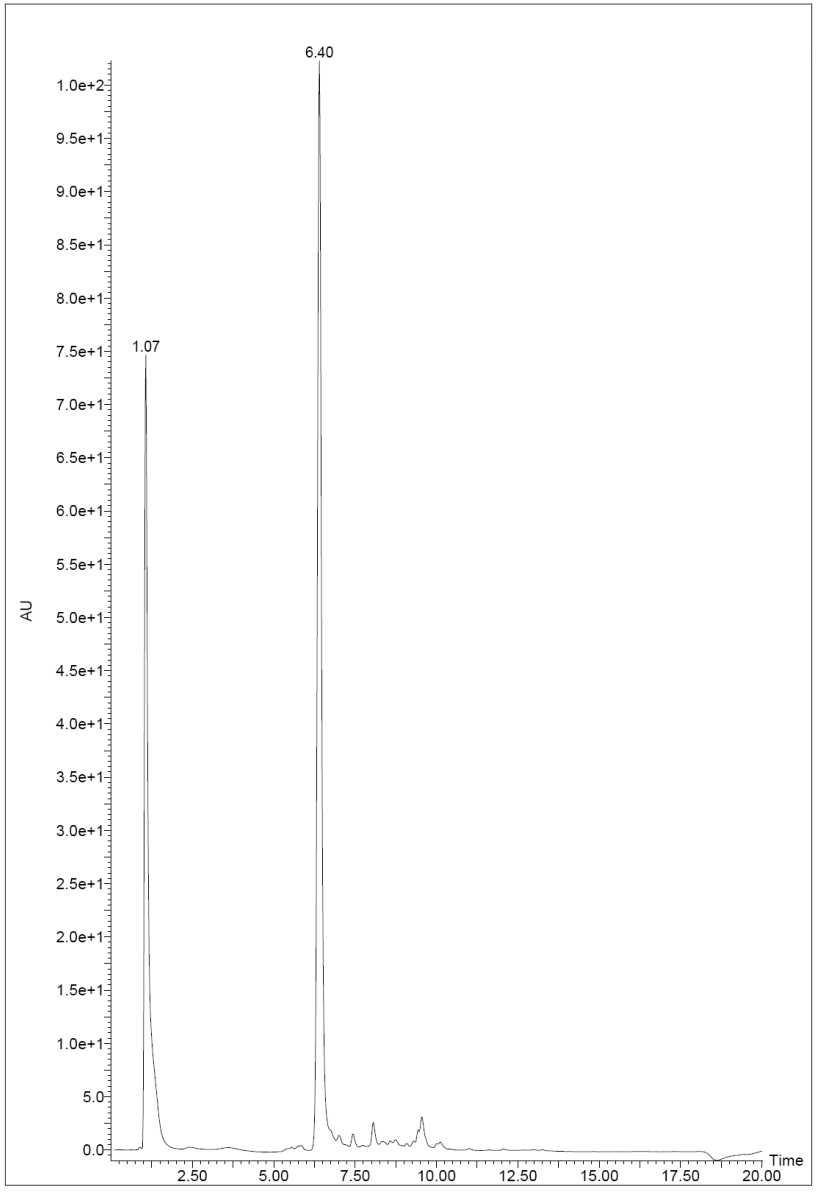
(4-((4-formylphenoxy)methyl)phenyl)boronic acid (**12**); ^{1}H NMR

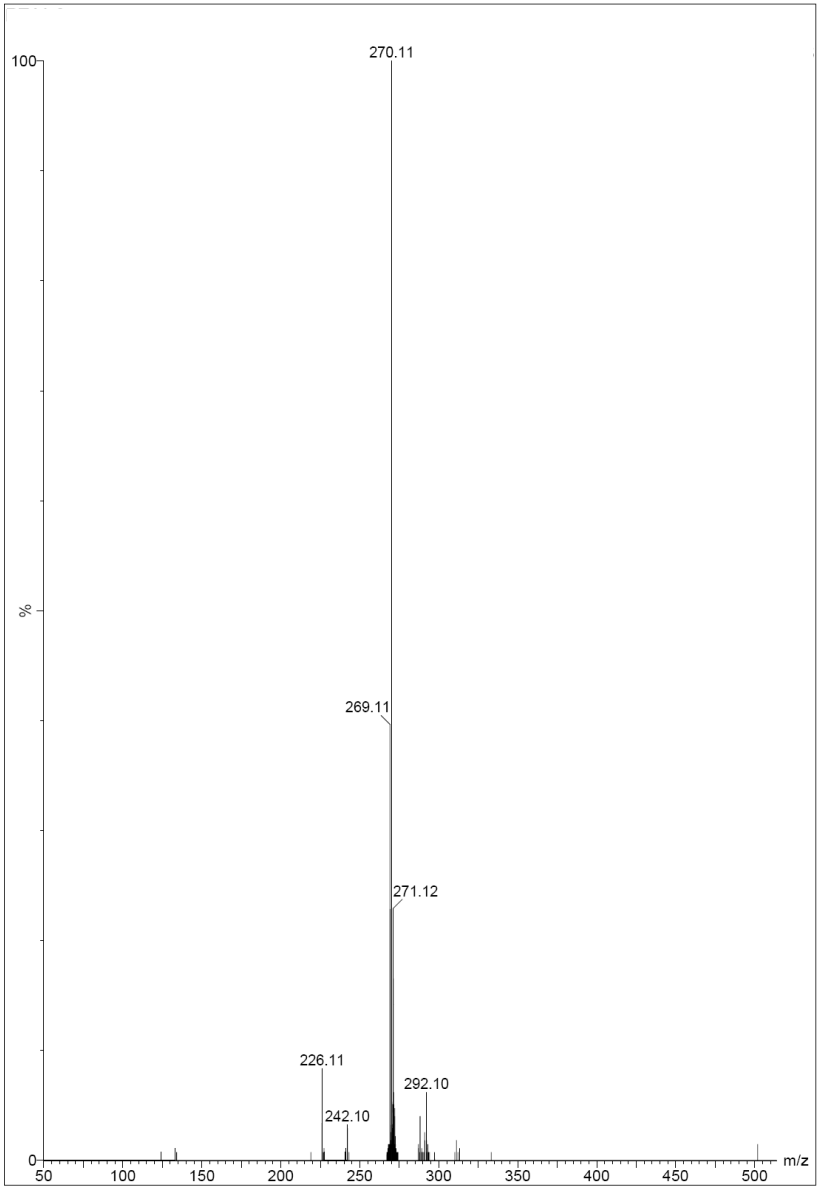


(4-((4-formylphenoxy)methyl)phenyl)boronic acid (**12**); ^{13}C NMR

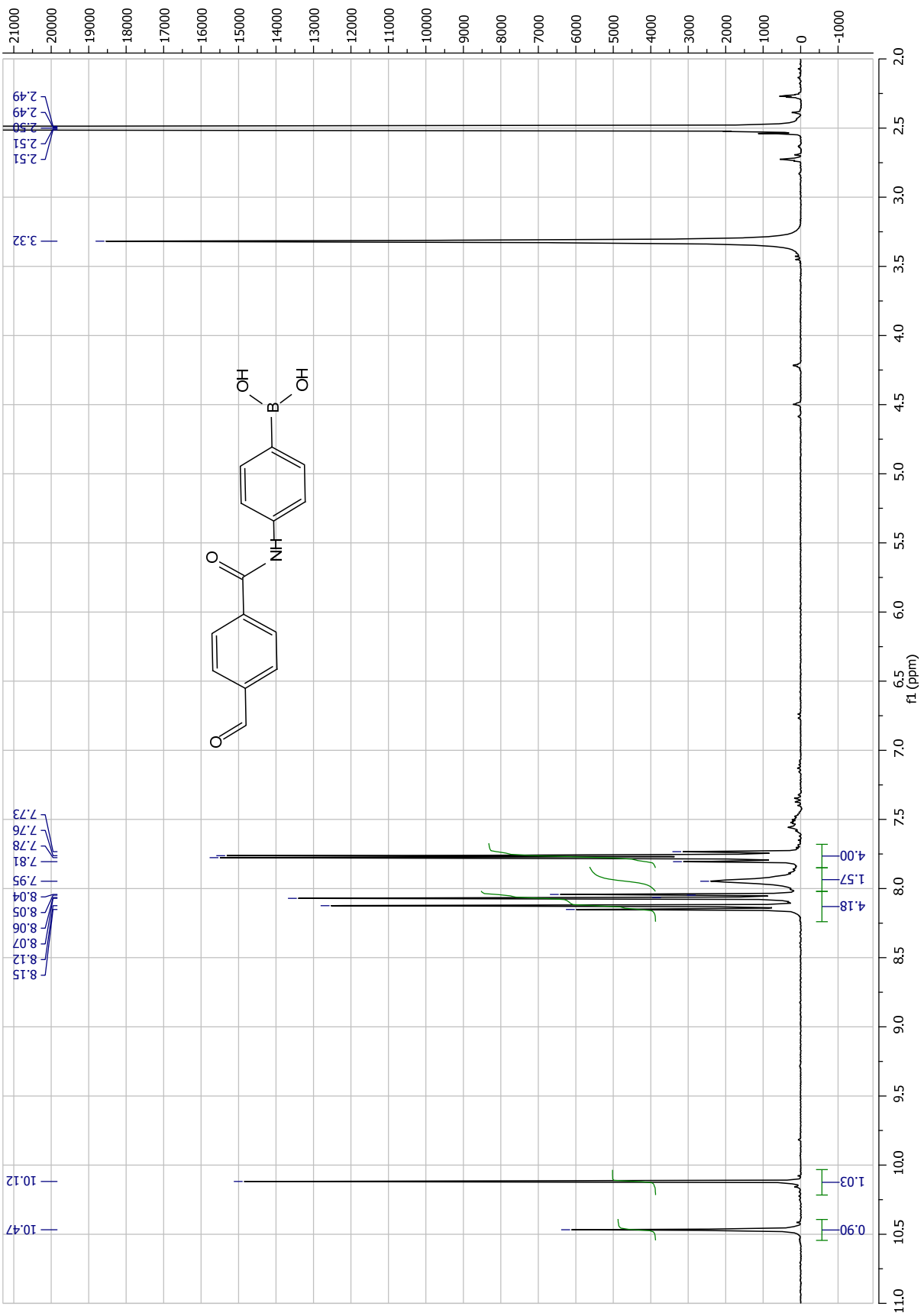


(4-(4-formylbenzamido)phenyl)boronic acid (**13**); LC-MS

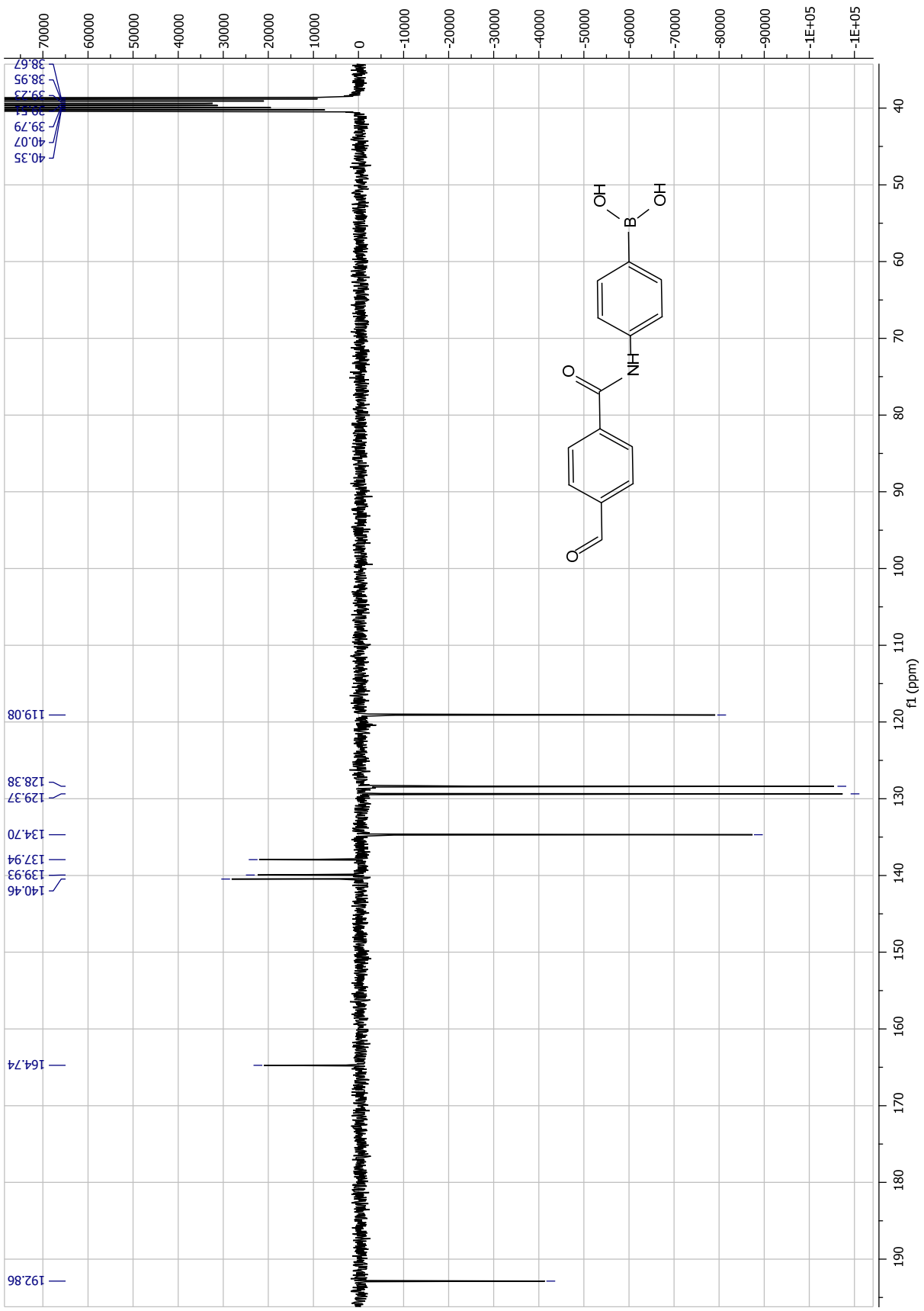




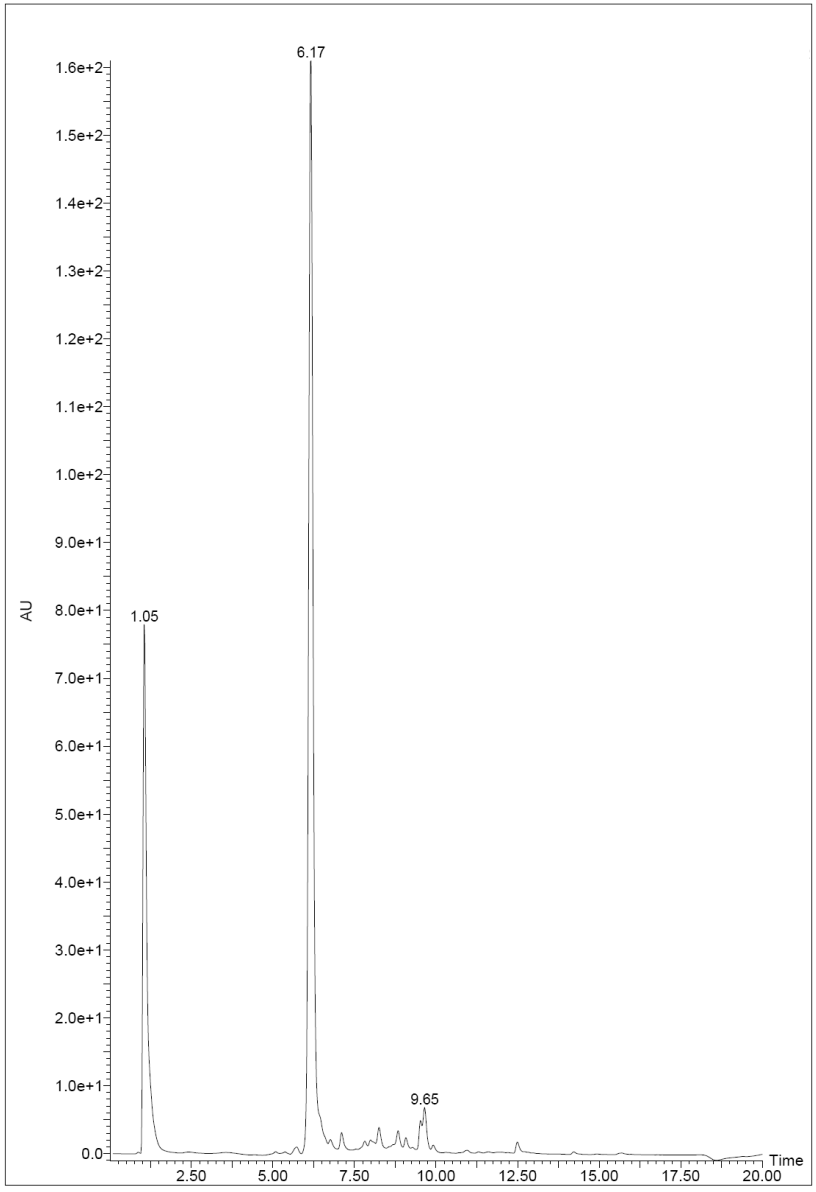
(4-(4-formylbenzamido)phenyl)boronic acid (**13**); ^{1}H NMR

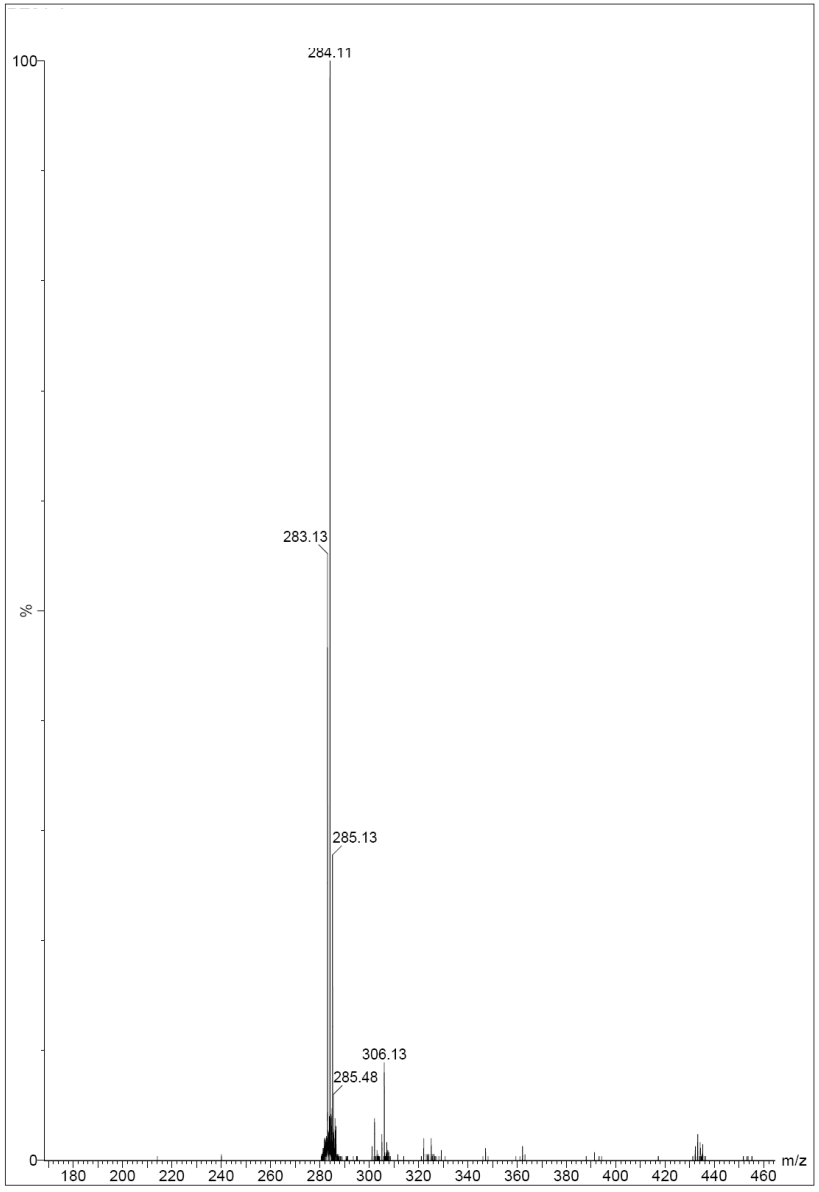


(4-(4-formylbenzamido)phenyl)boronic acid (**13**); ^{13}C NMR

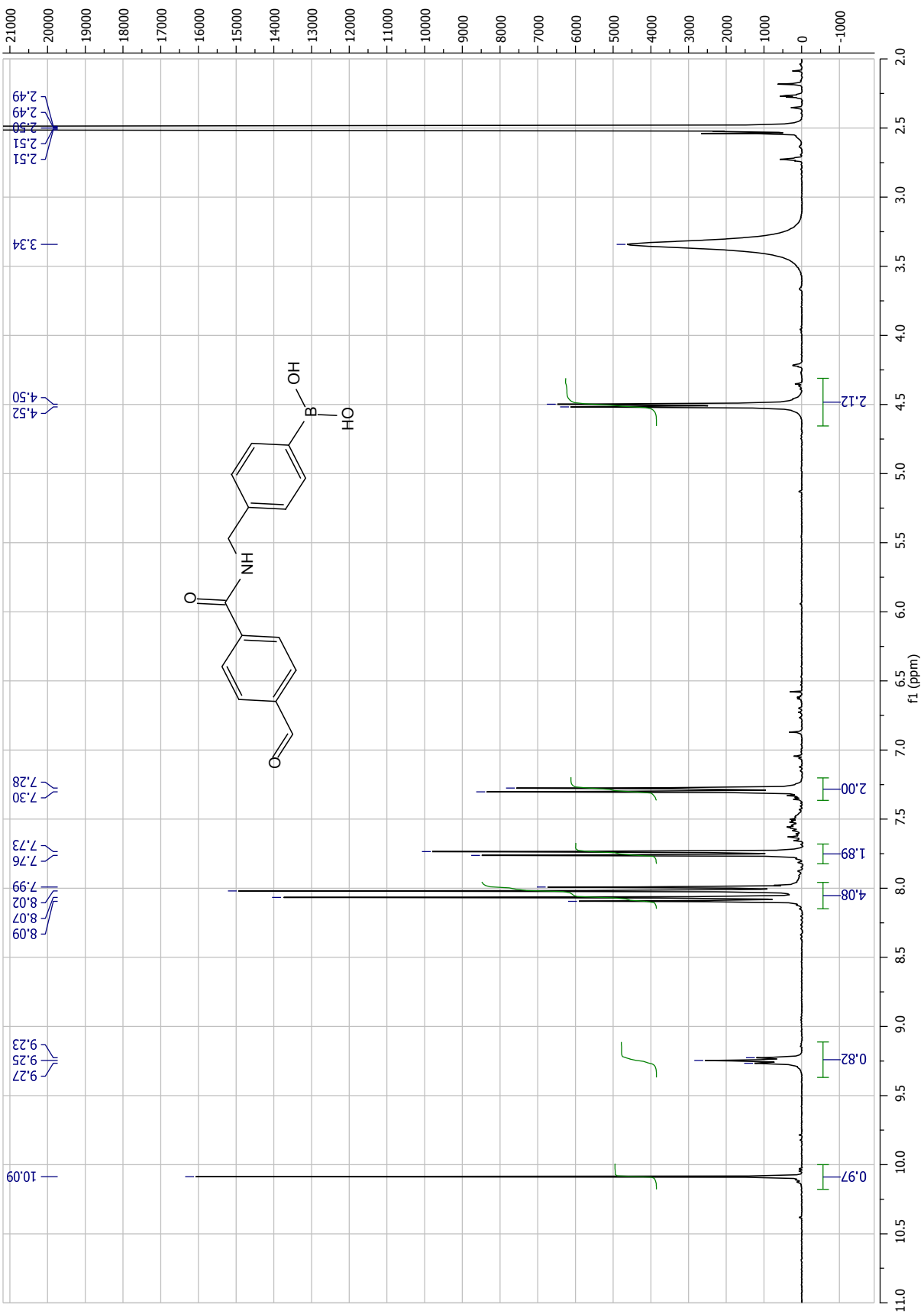


(4-((4-formylbenzamido)methyl)phenyl)boronic acid (**14**); LC-MS

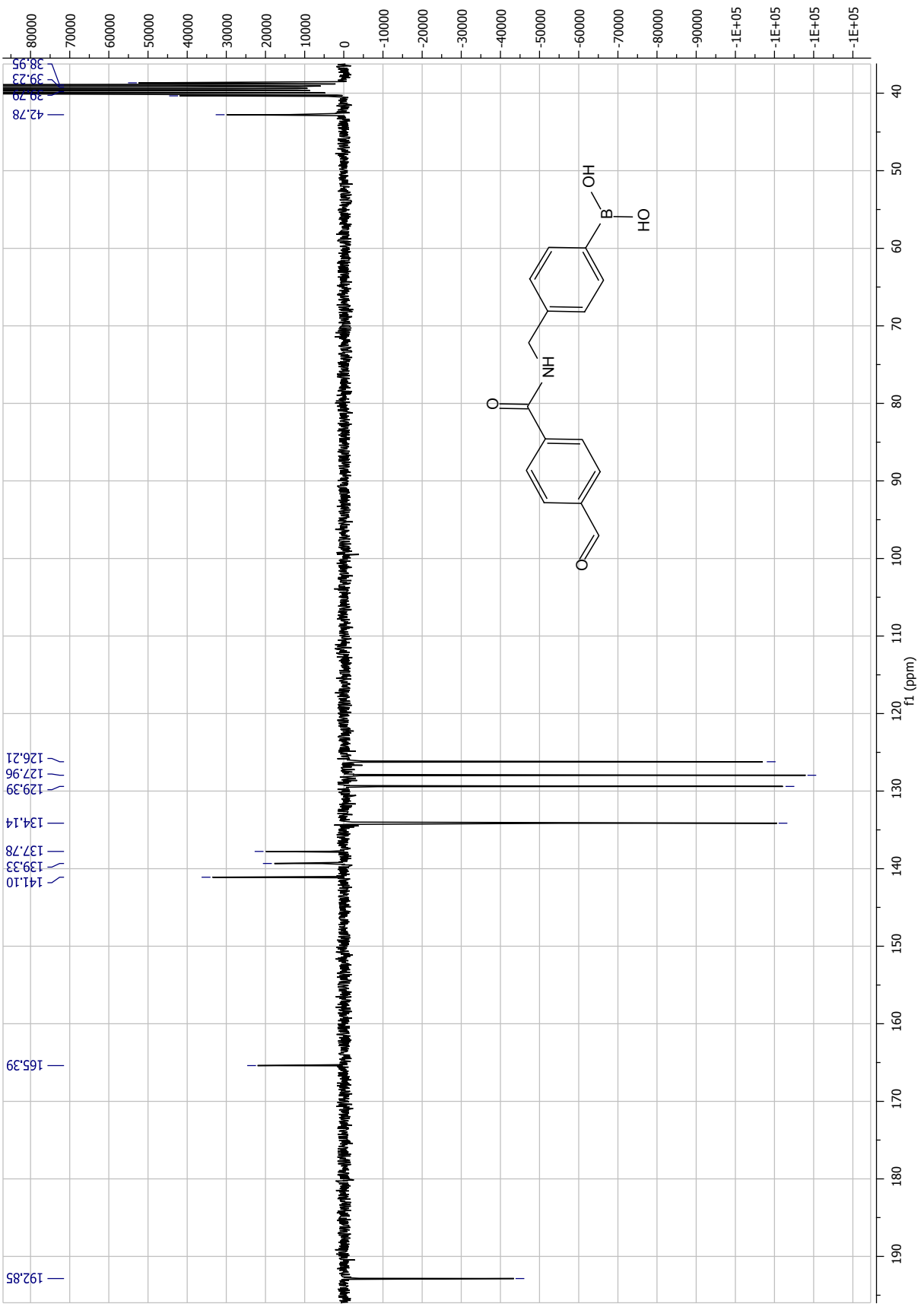




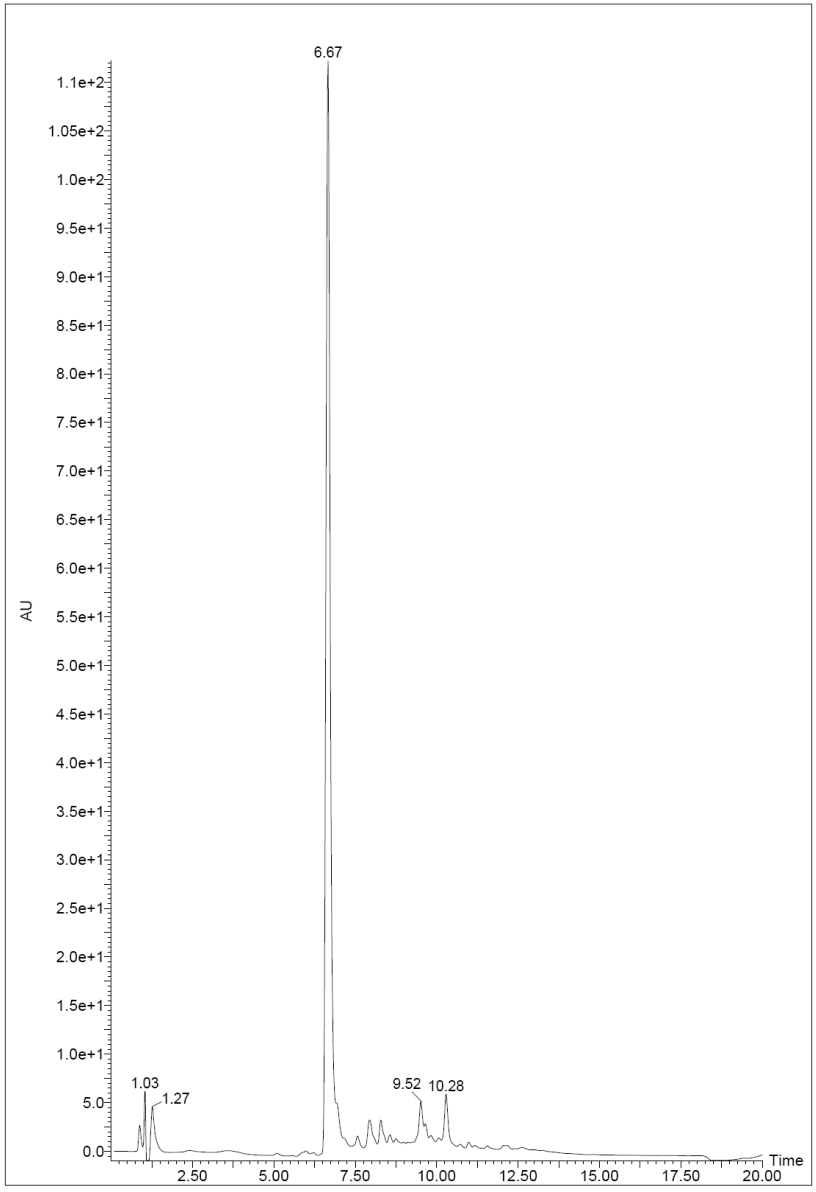
(4-((4-formylbenzamido)methyl)phenyl)boronic acid (**14**); ^{1}H NMR

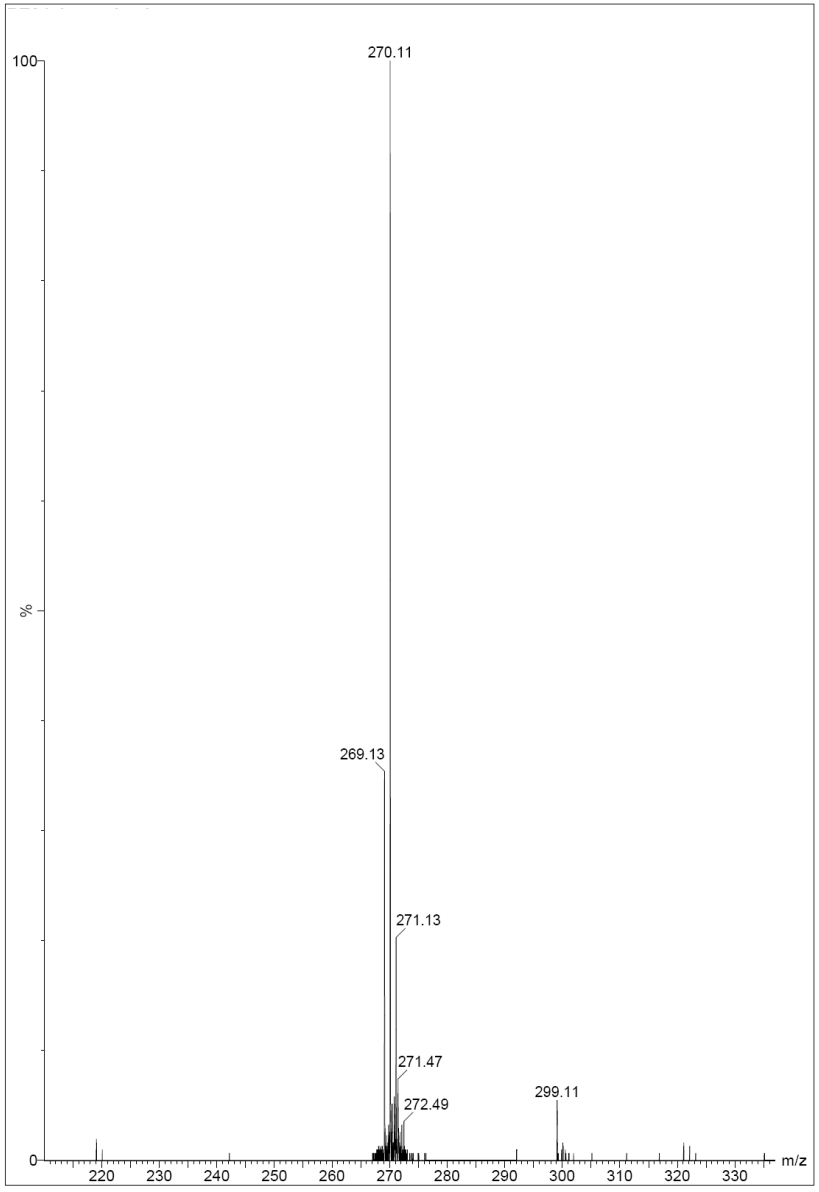


(4-((4-formylbenzamido)methyl)phenyl)boronic acid (**14**); ^{13}C NMR

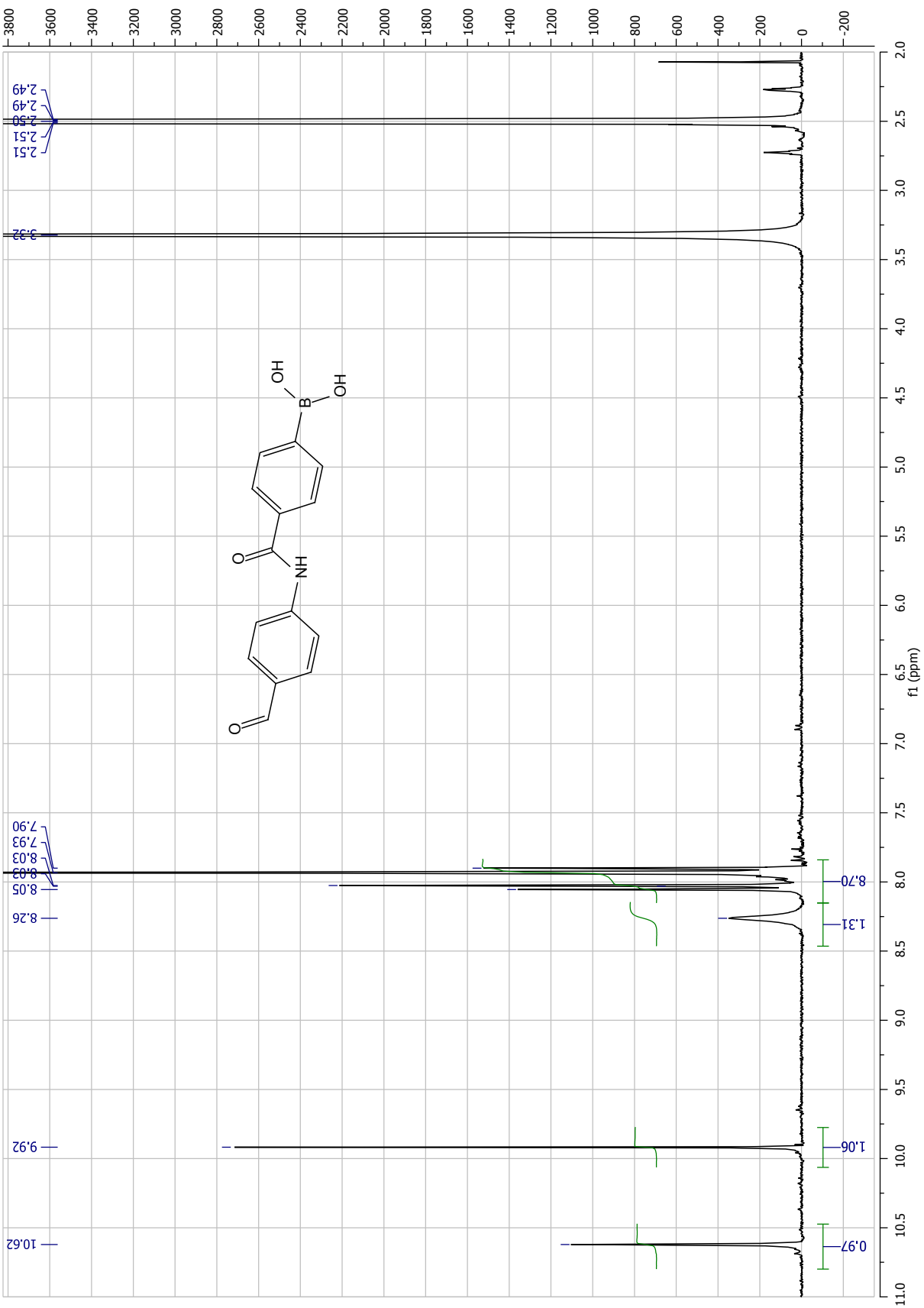


(4-((4-formylphenyl)carbamoyl)phenyl)boronic acid (**15**); LC-MS

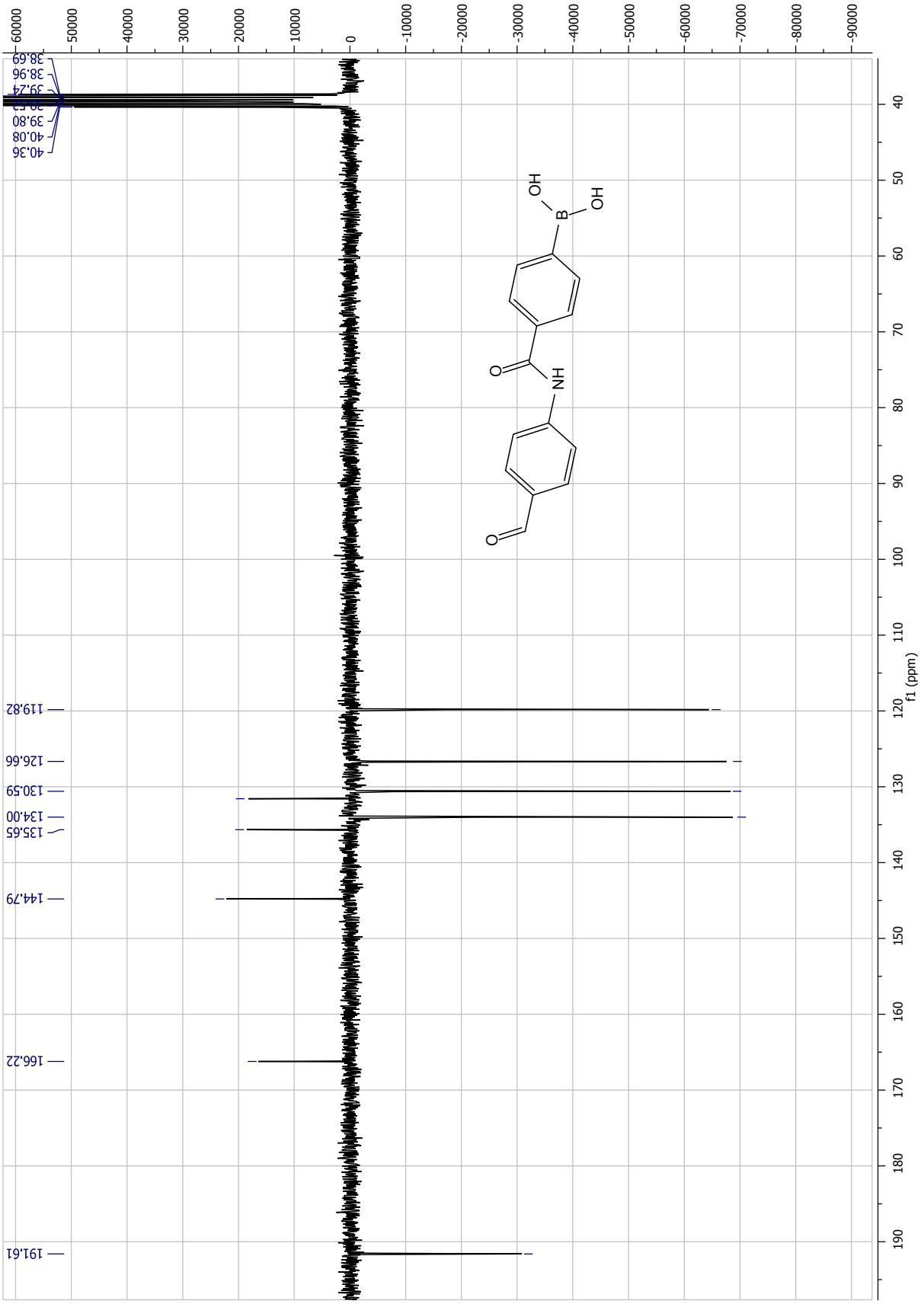




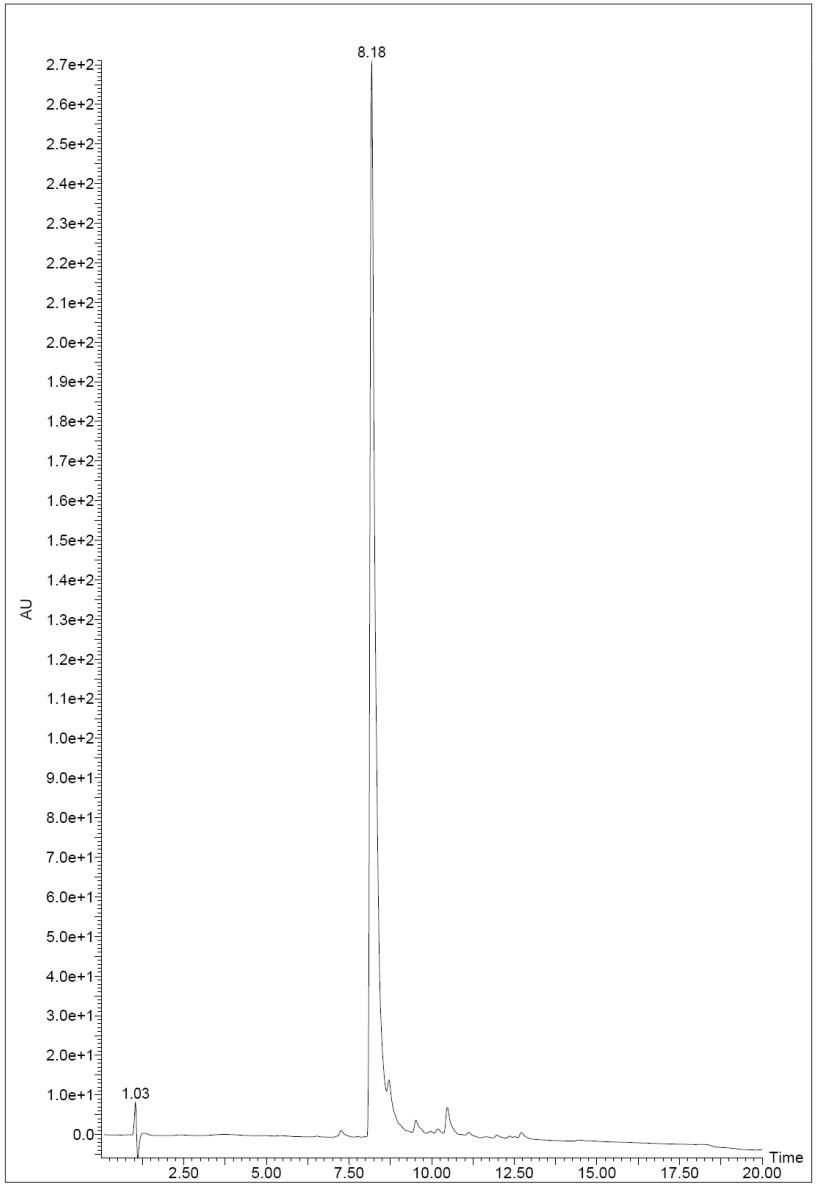
(4-((4-formylphenyl)carbamoyl)phenyl)boronic acid (**15**); ^{1}H NMR

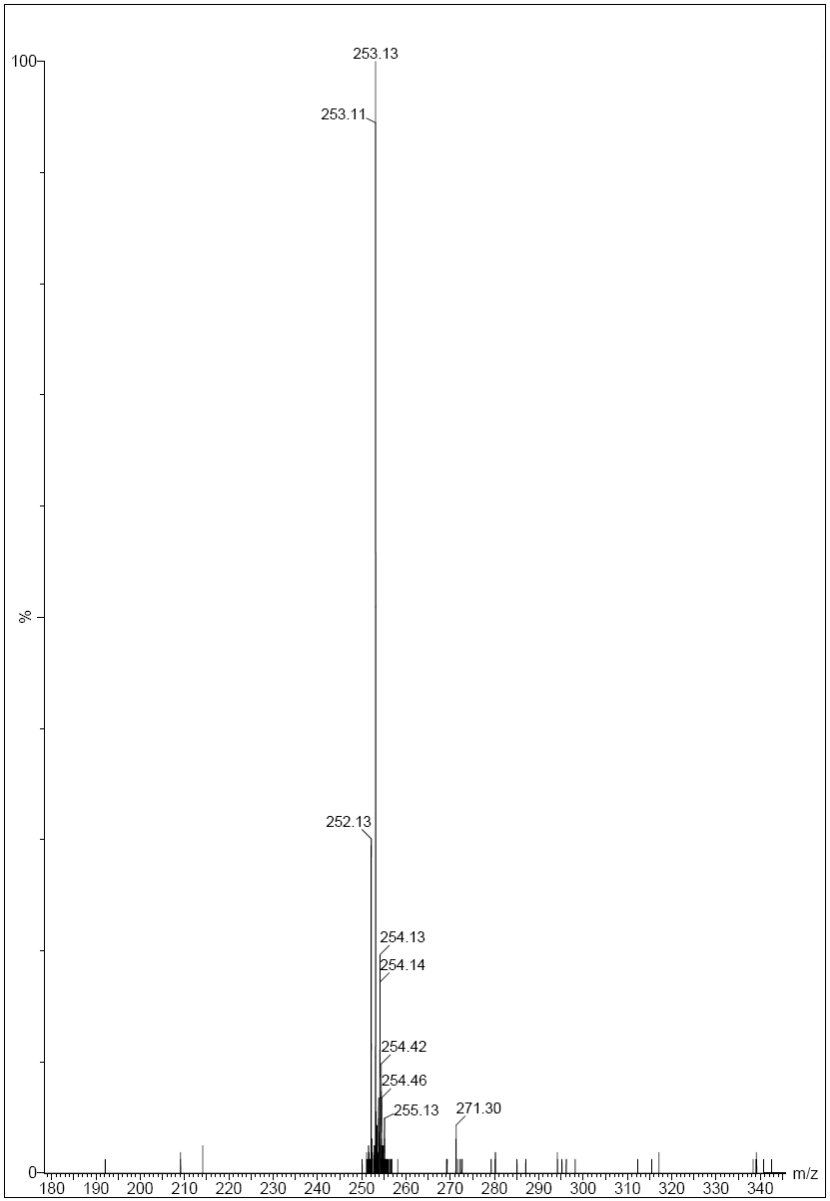


(4-((4-formylphenyl)carbamoyl)phenyl)boronic acid (**15**); ^{13}C NMR

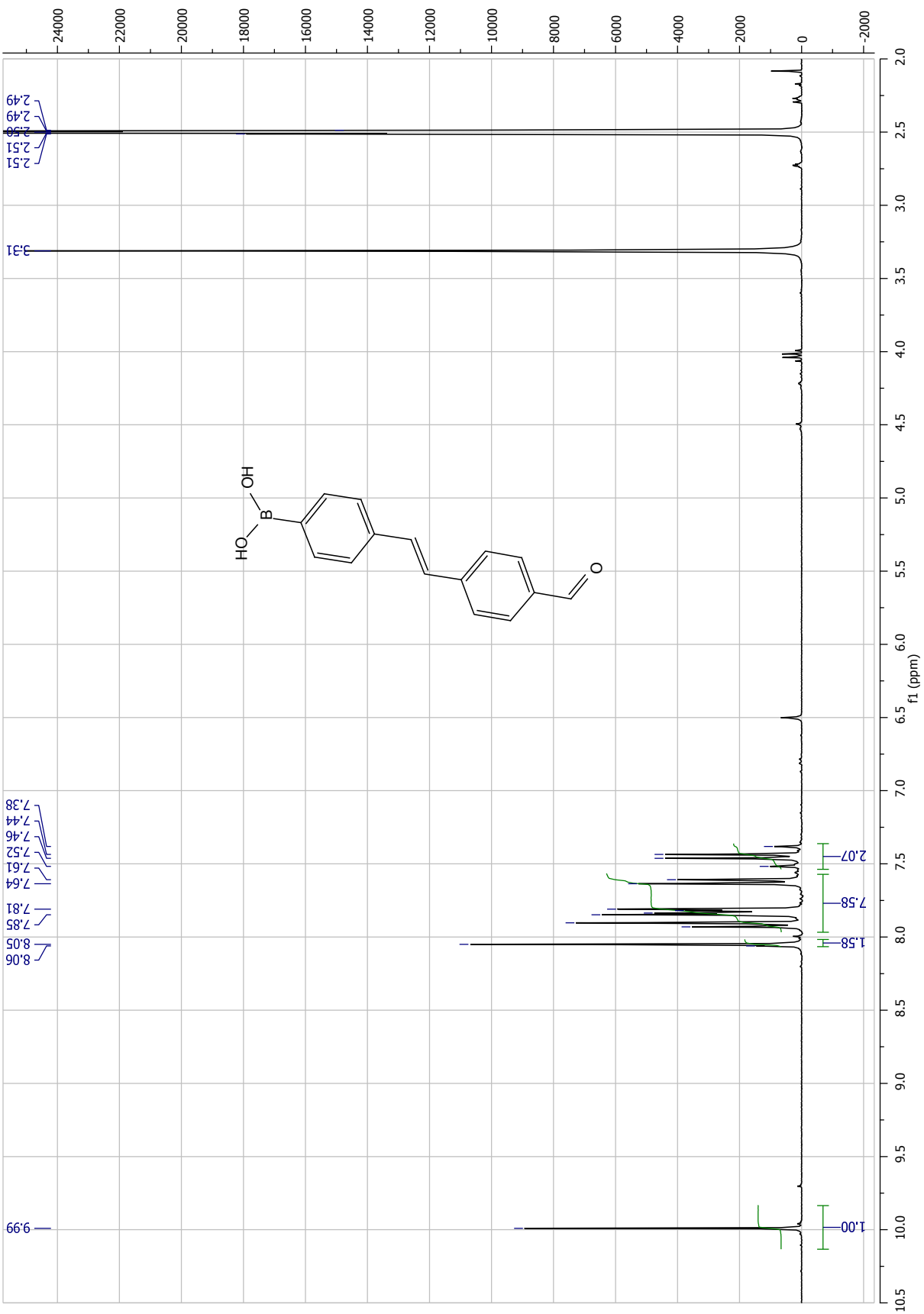


(*E*)-(4-(4-formylstyryl)phenyl)boronic acid (**16**); LC-MS

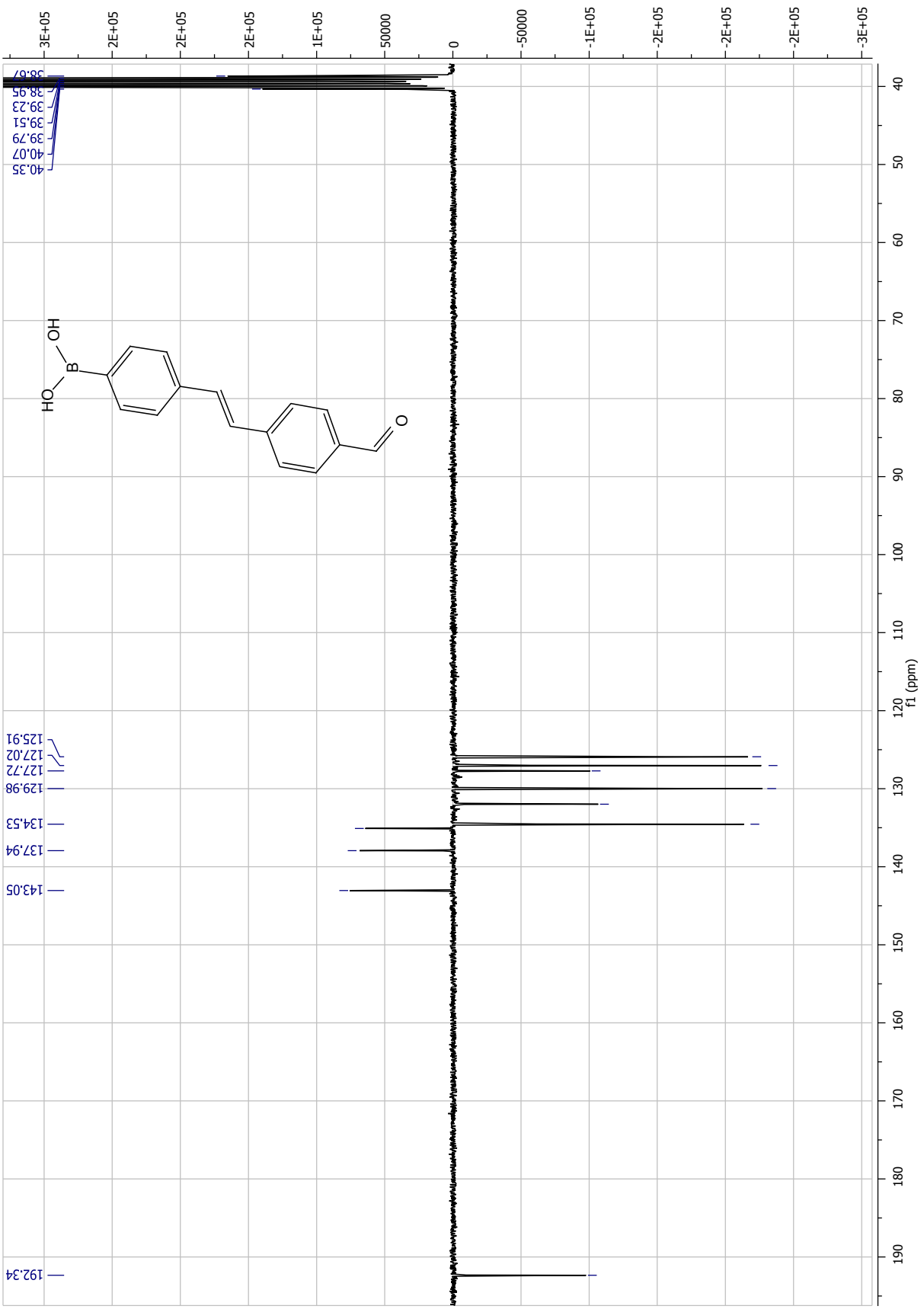




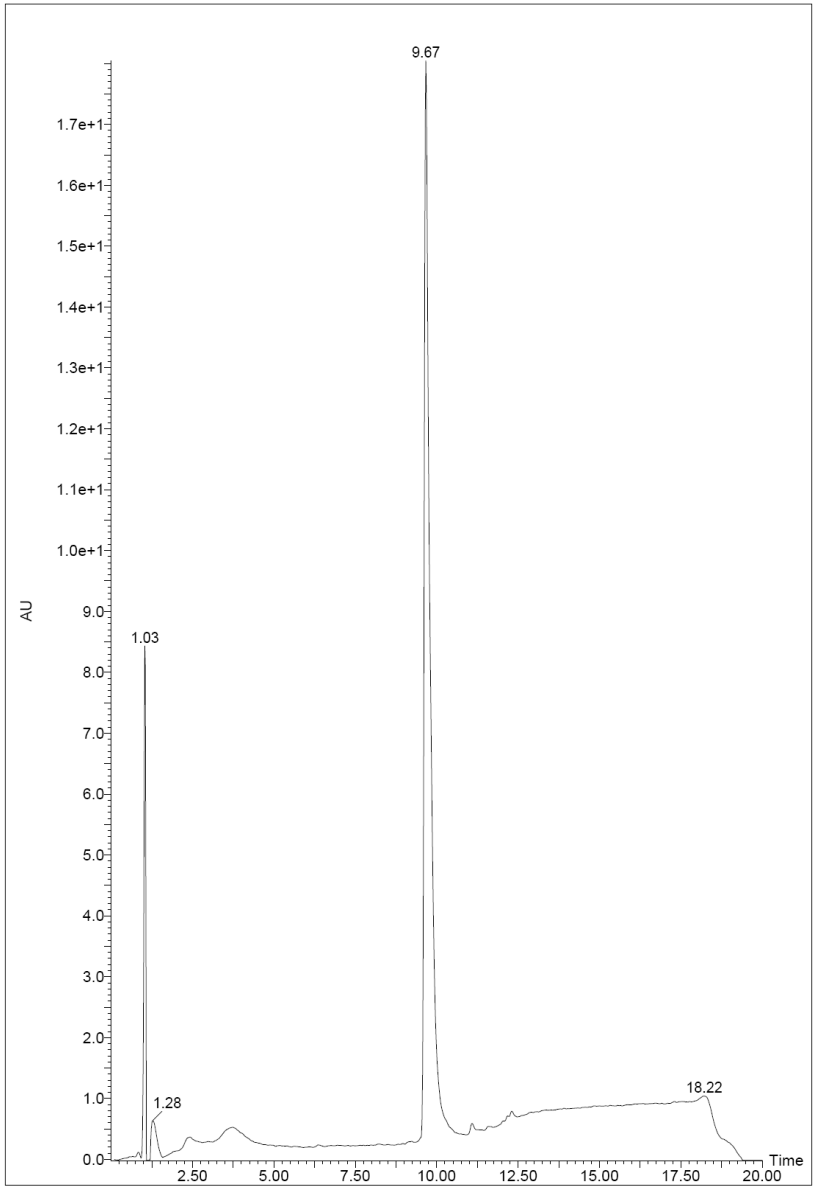
(*E*)-(4-(4-formylstyryl)phenyl)boronic acid (**16**); ^{1}H NMR

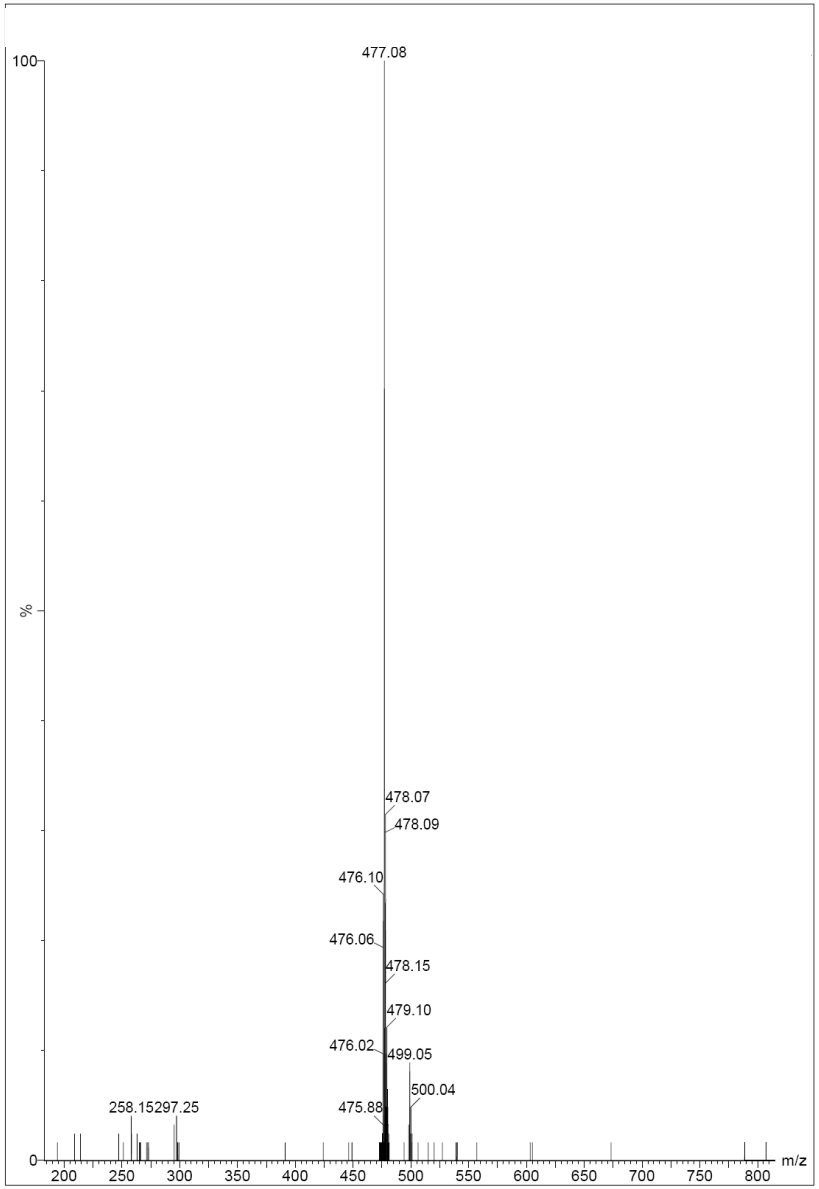


(*E*)-(4-(4-formylstyryl)phenyl)boronic acid (**16**); ^{13}C NMR

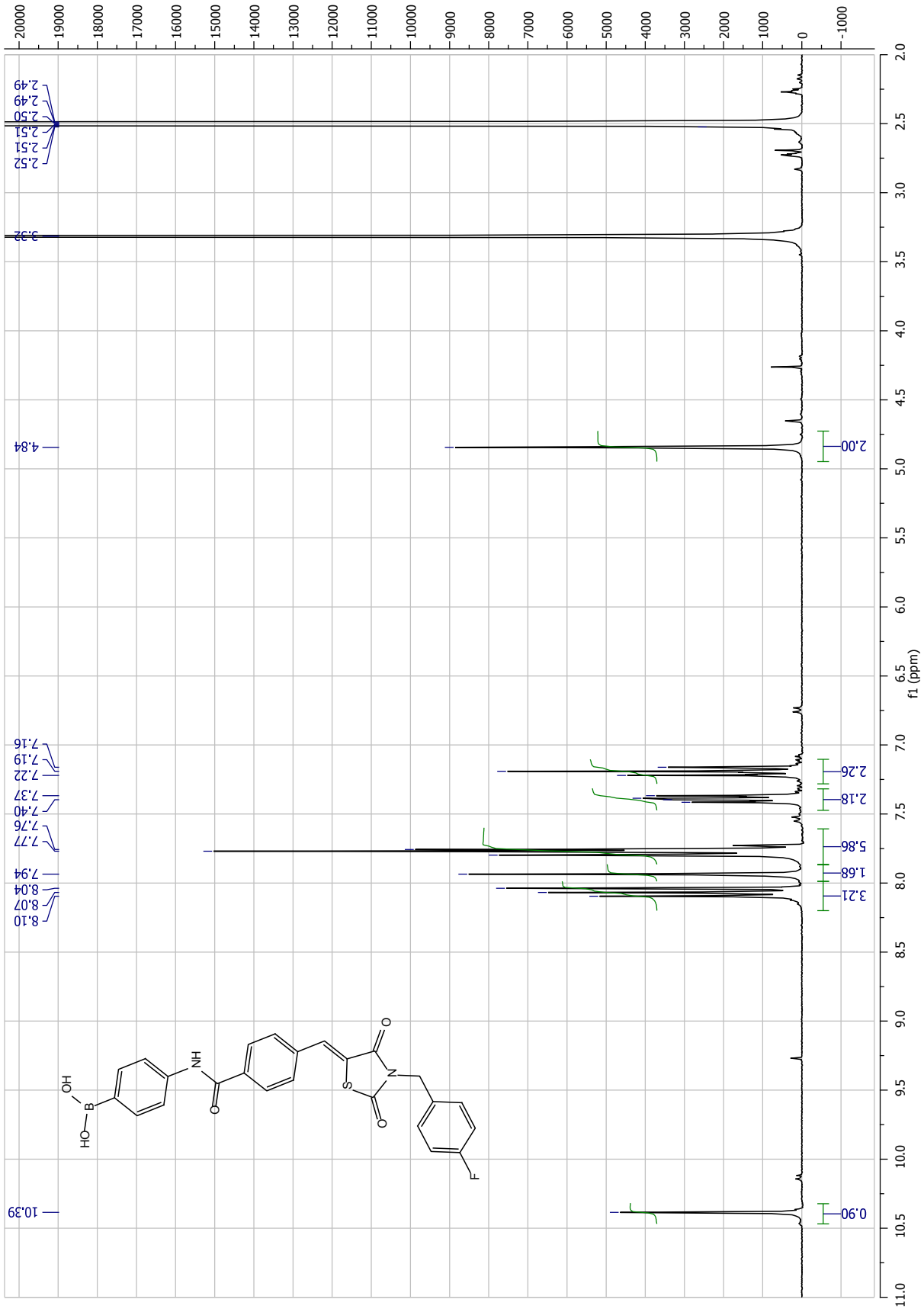


(*Z*)-(4-(4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido)phenyl)boronic acid (**17**); LC-MS

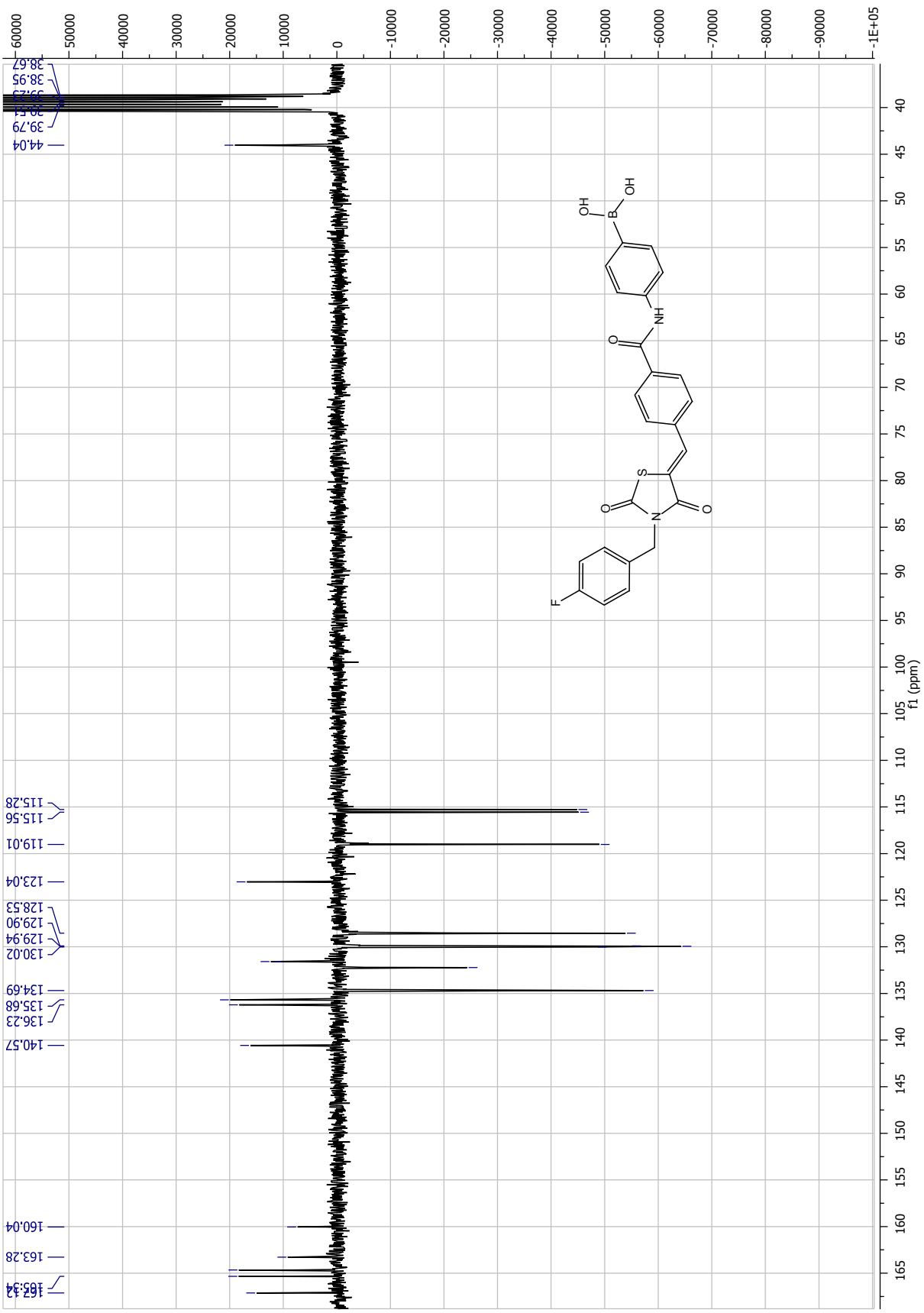




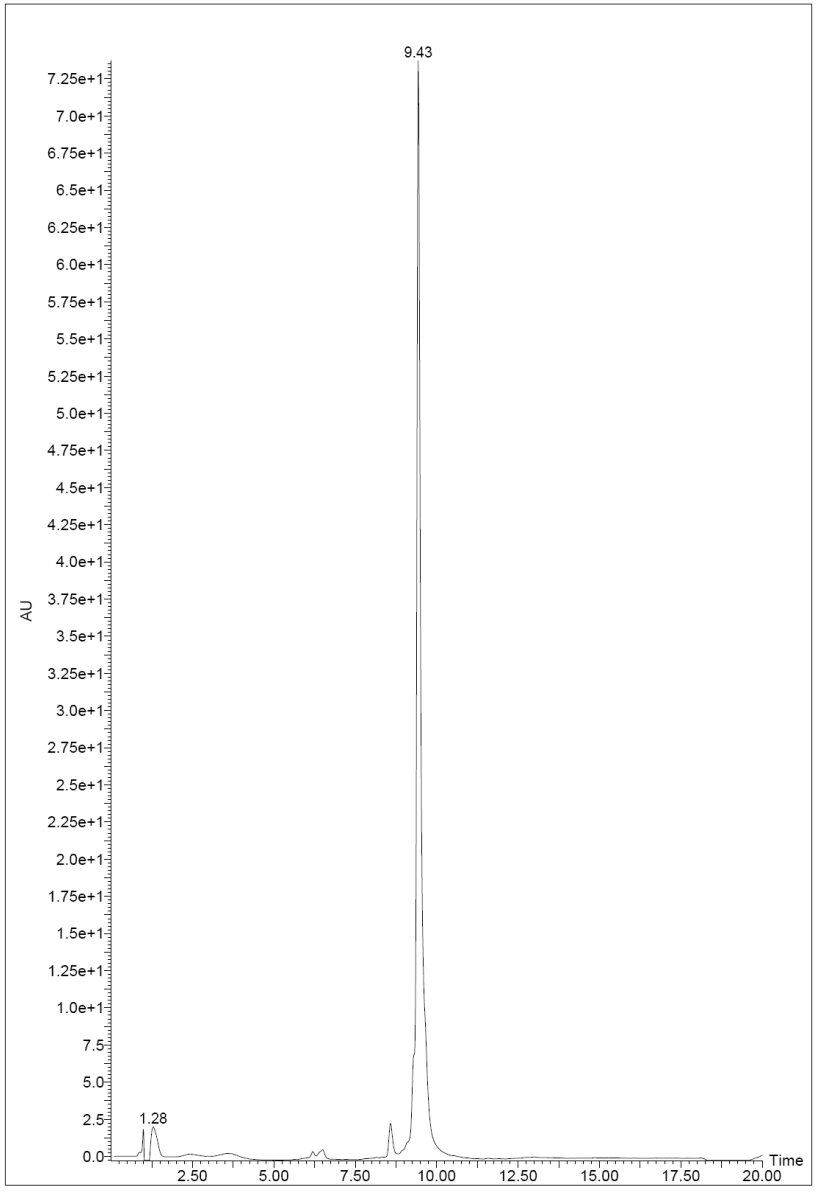
(*Z*)-(4-(4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido)phenyl)boronic acid (**17**); ^{1}H NMR

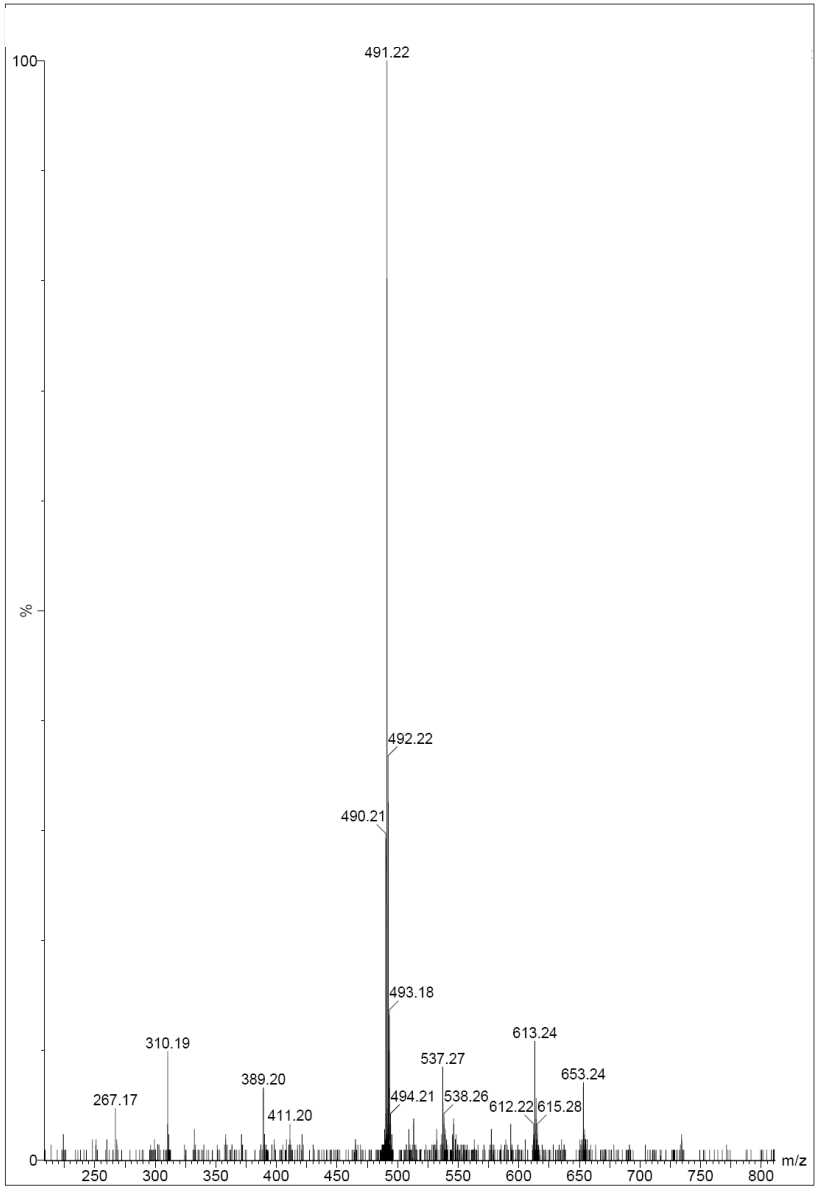


(Z)-(4-(4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido)phenyl)boronic acid (**17**); ^{13}C NMR

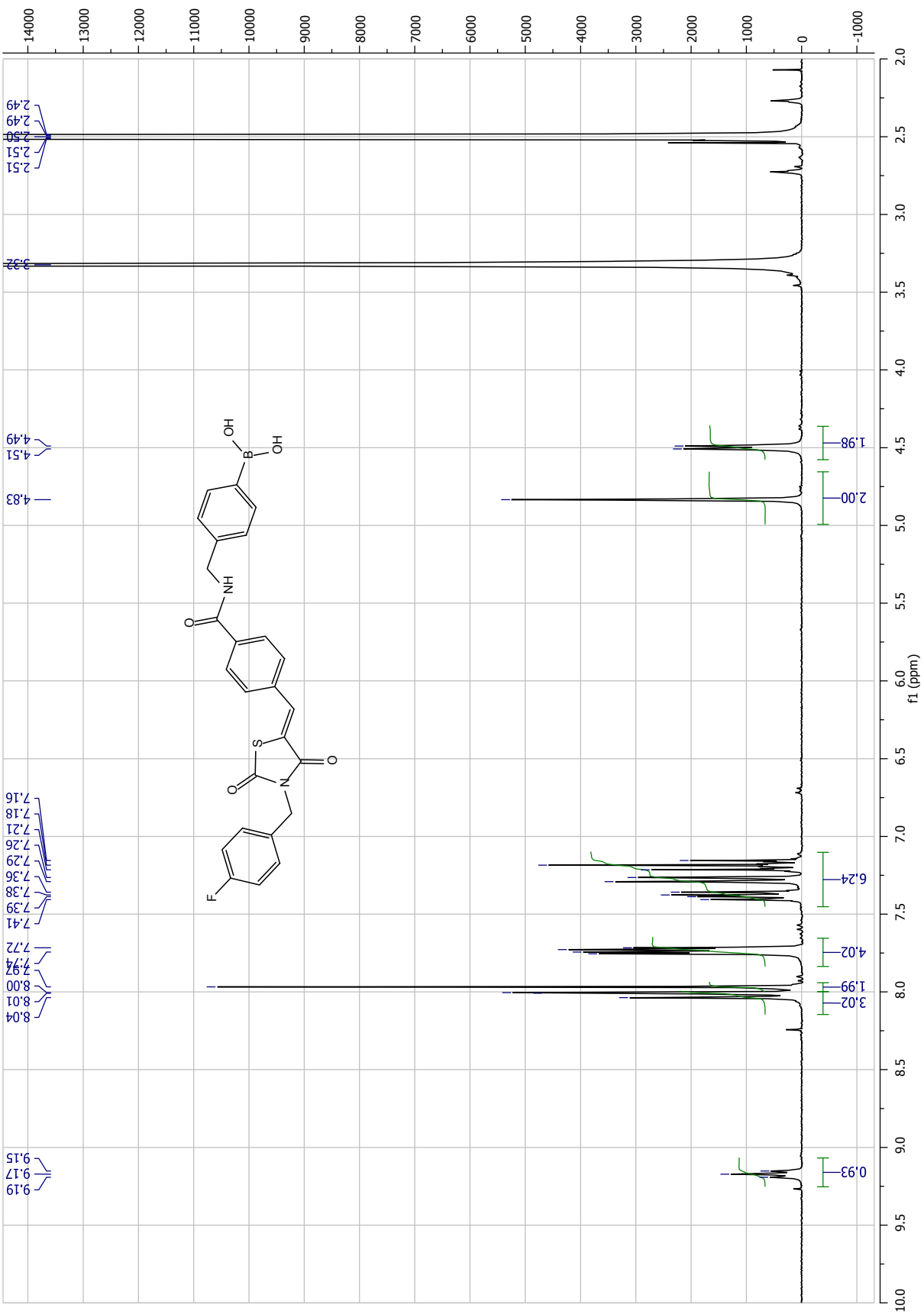


(*Z*)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido)methyl)phenyl) boronic acid (**18**); LC-MS

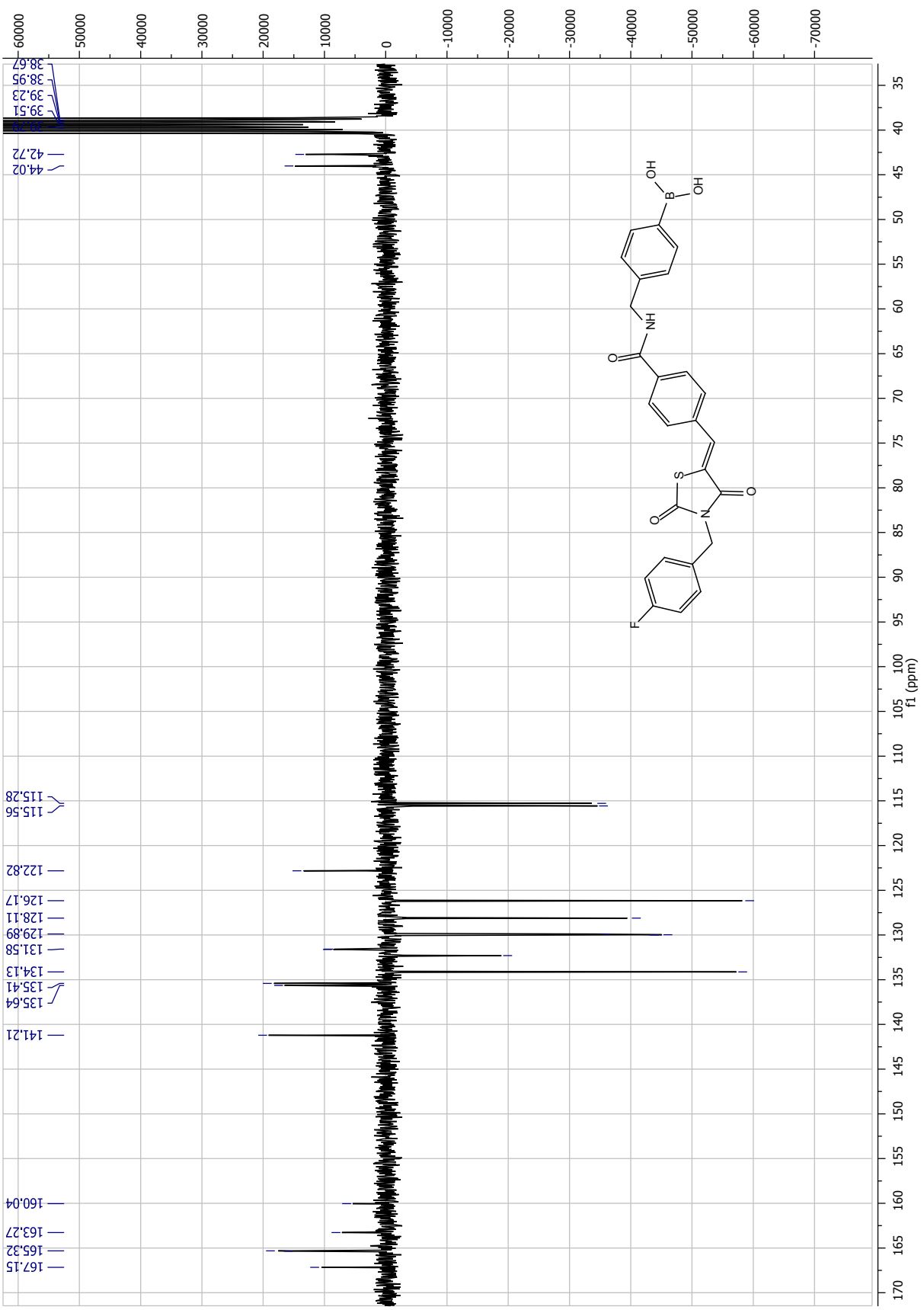




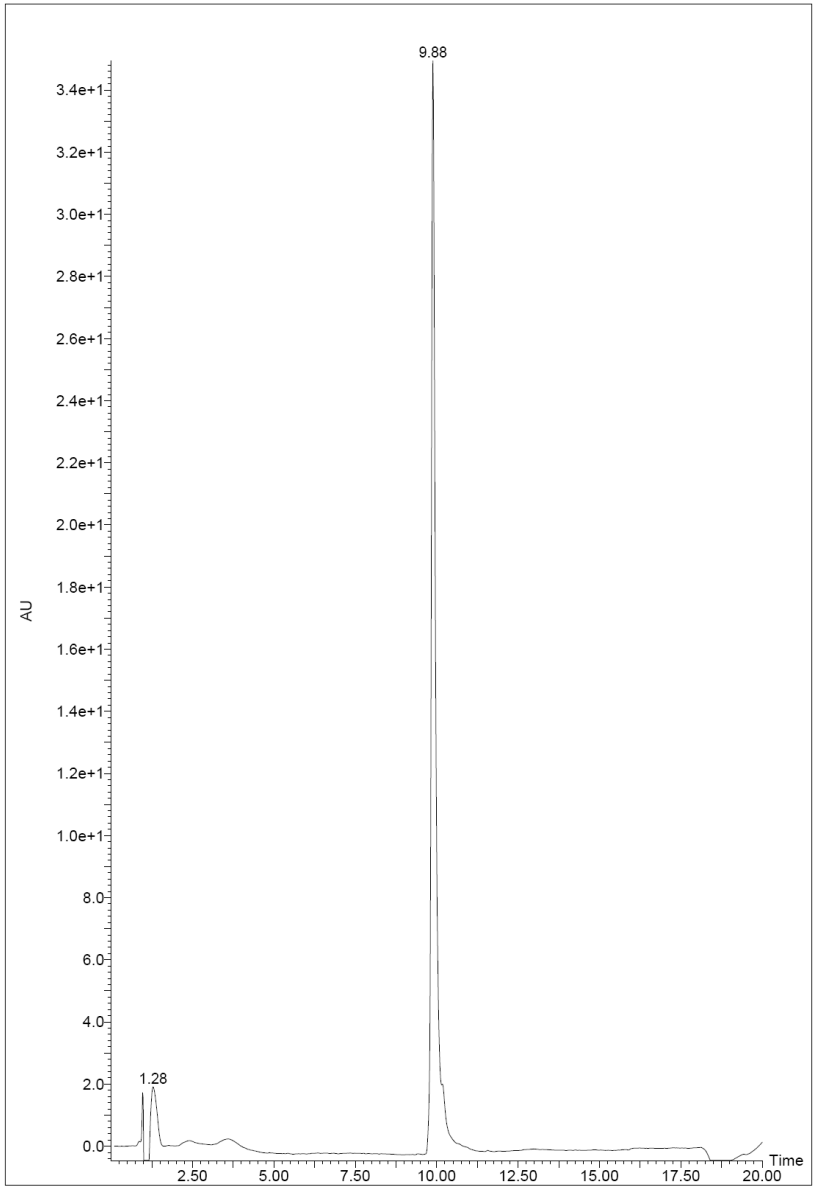
(Z)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido)methyl)phenyl) boronic acid (**18**); ^{1}H NMR

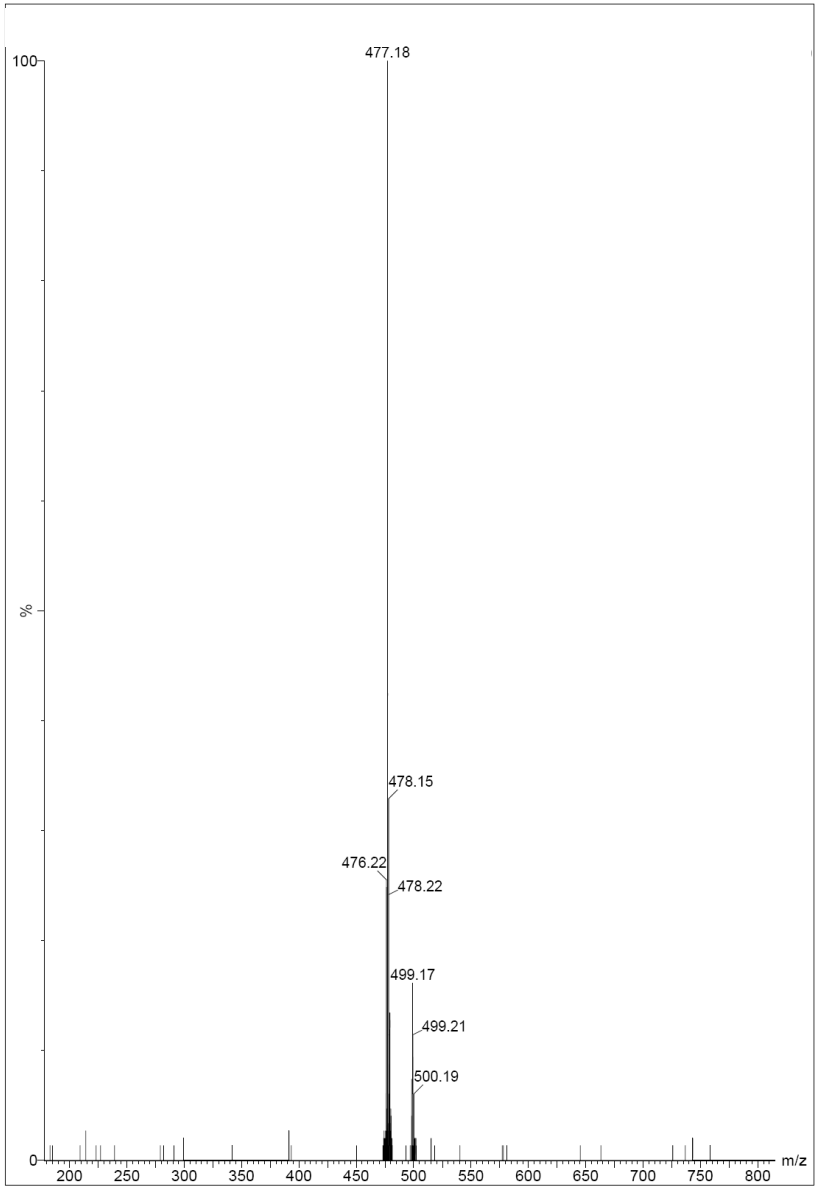


(*Z*)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)benzamido)methyl)phenyl) boronic acid (**18**); ^{13}C NMR

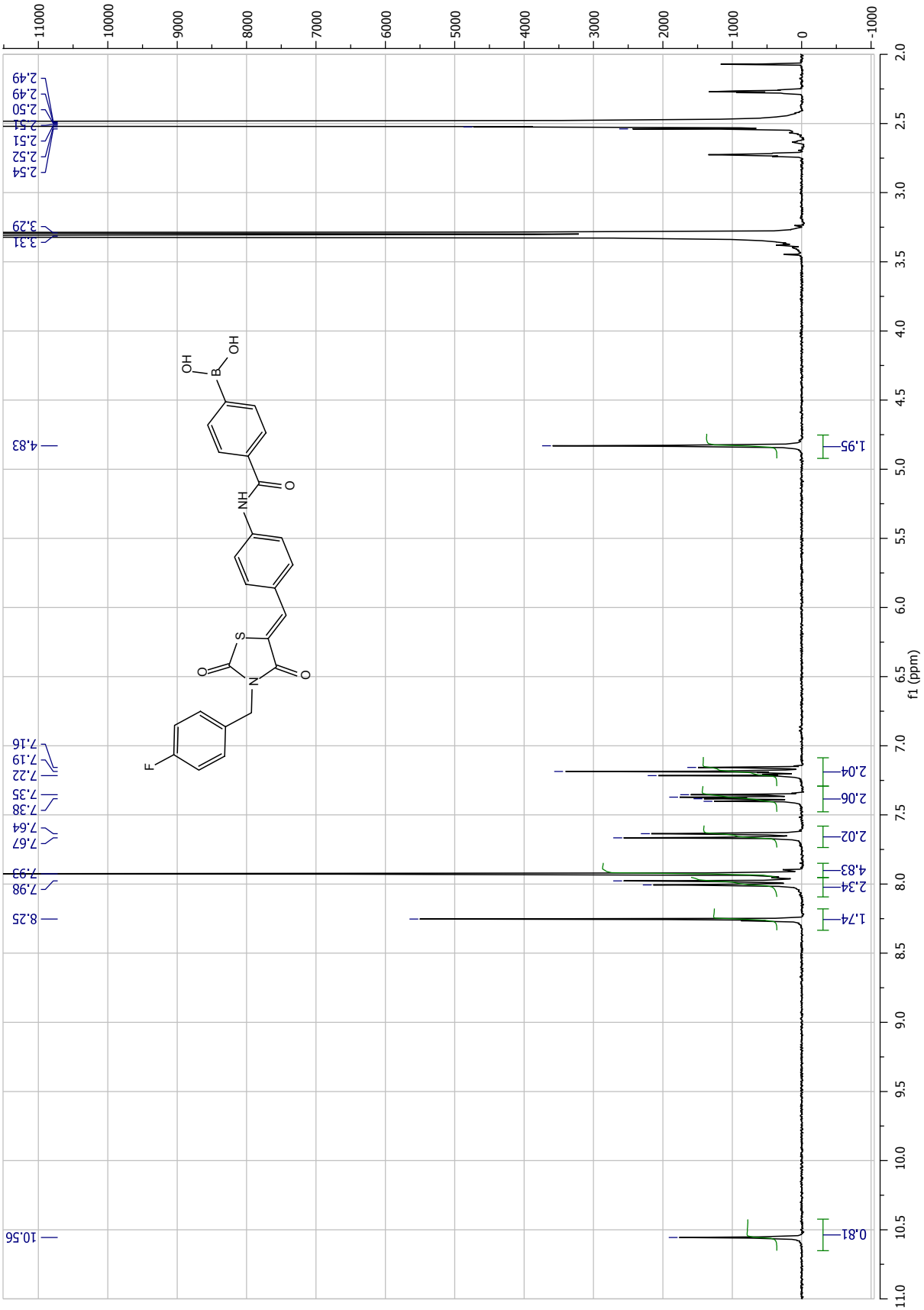


(*Z*)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)carbamoyl)phenyl)boronic acid (**19**); LC-MS

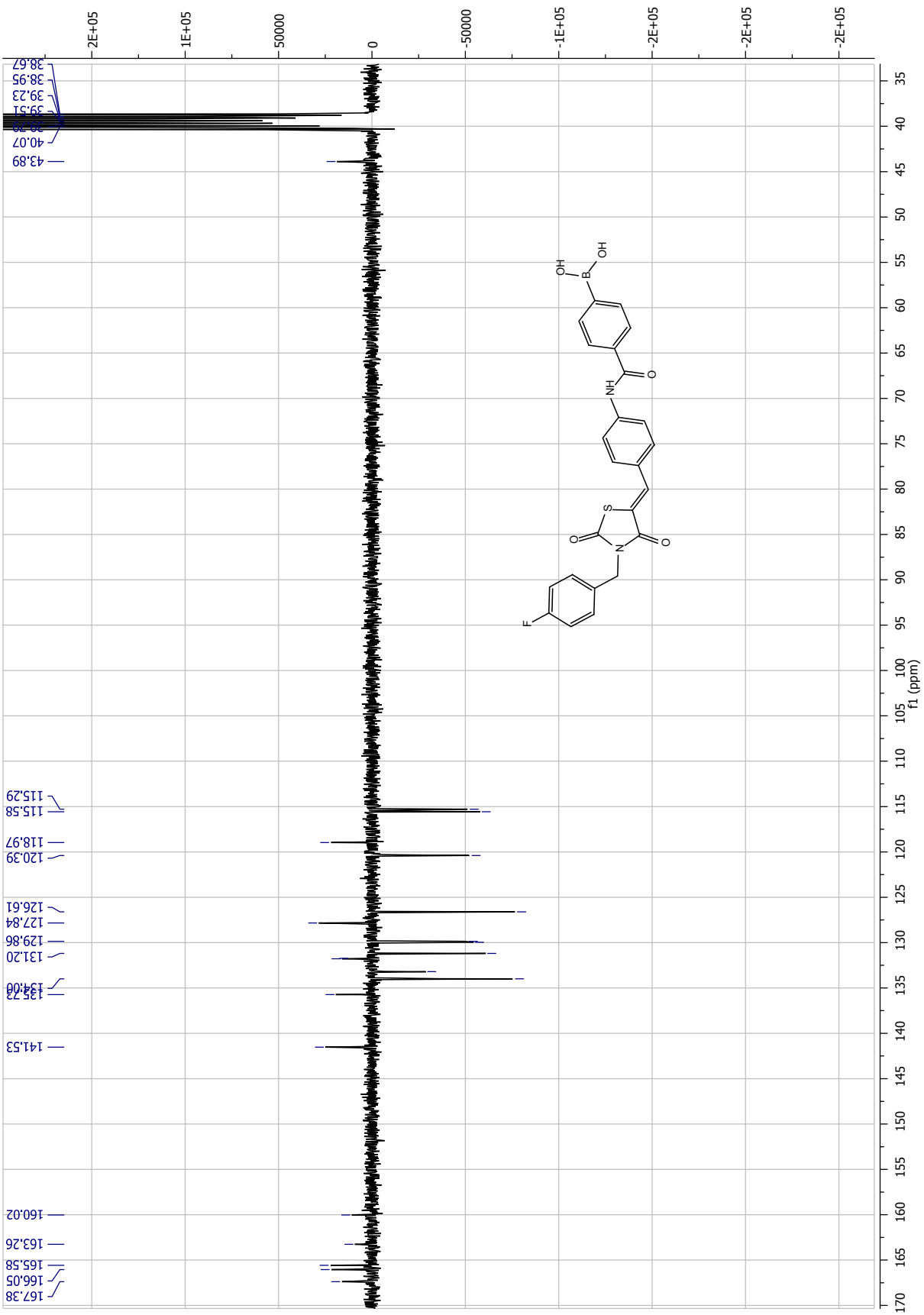




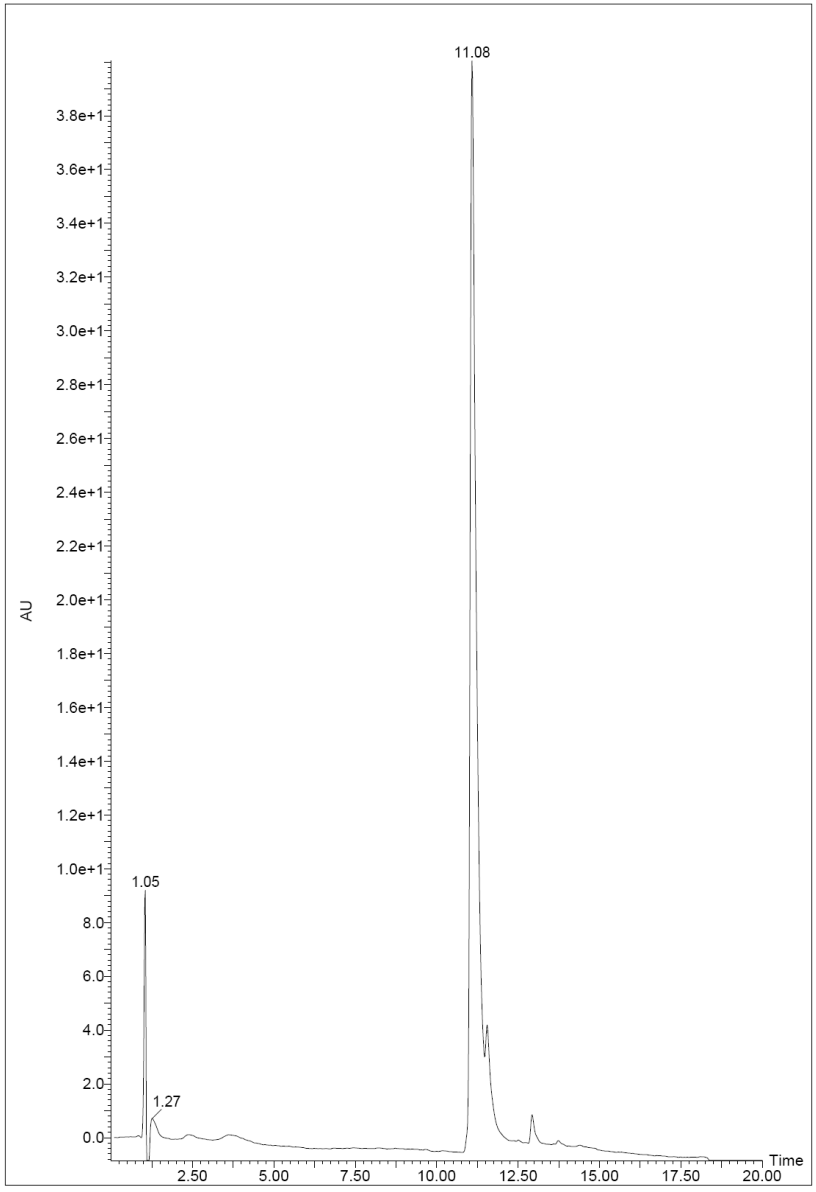
(Z)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)carbamoyl)phenyl)boronic acid (**19**); ^{1}H NMR

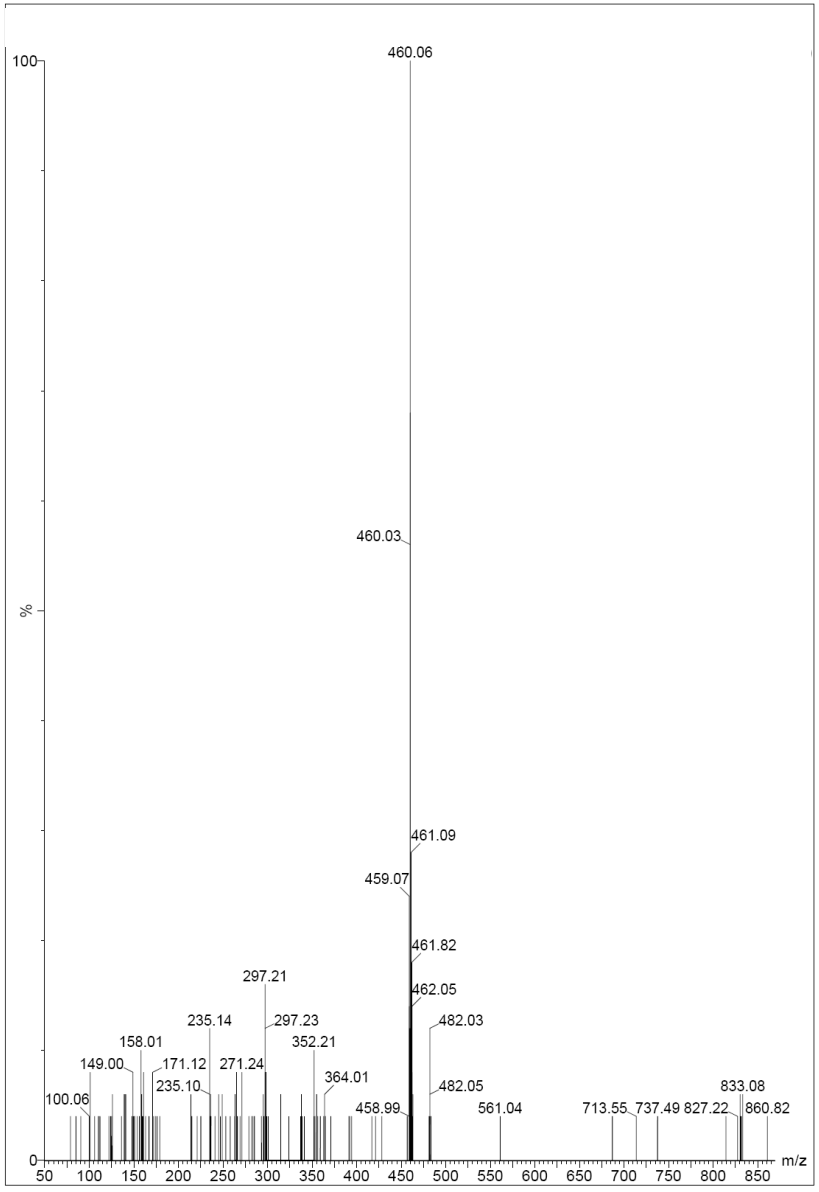


(Z)-(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)carbamoyl)phenyl)boronic acid (**19**); ^{13}C NMR

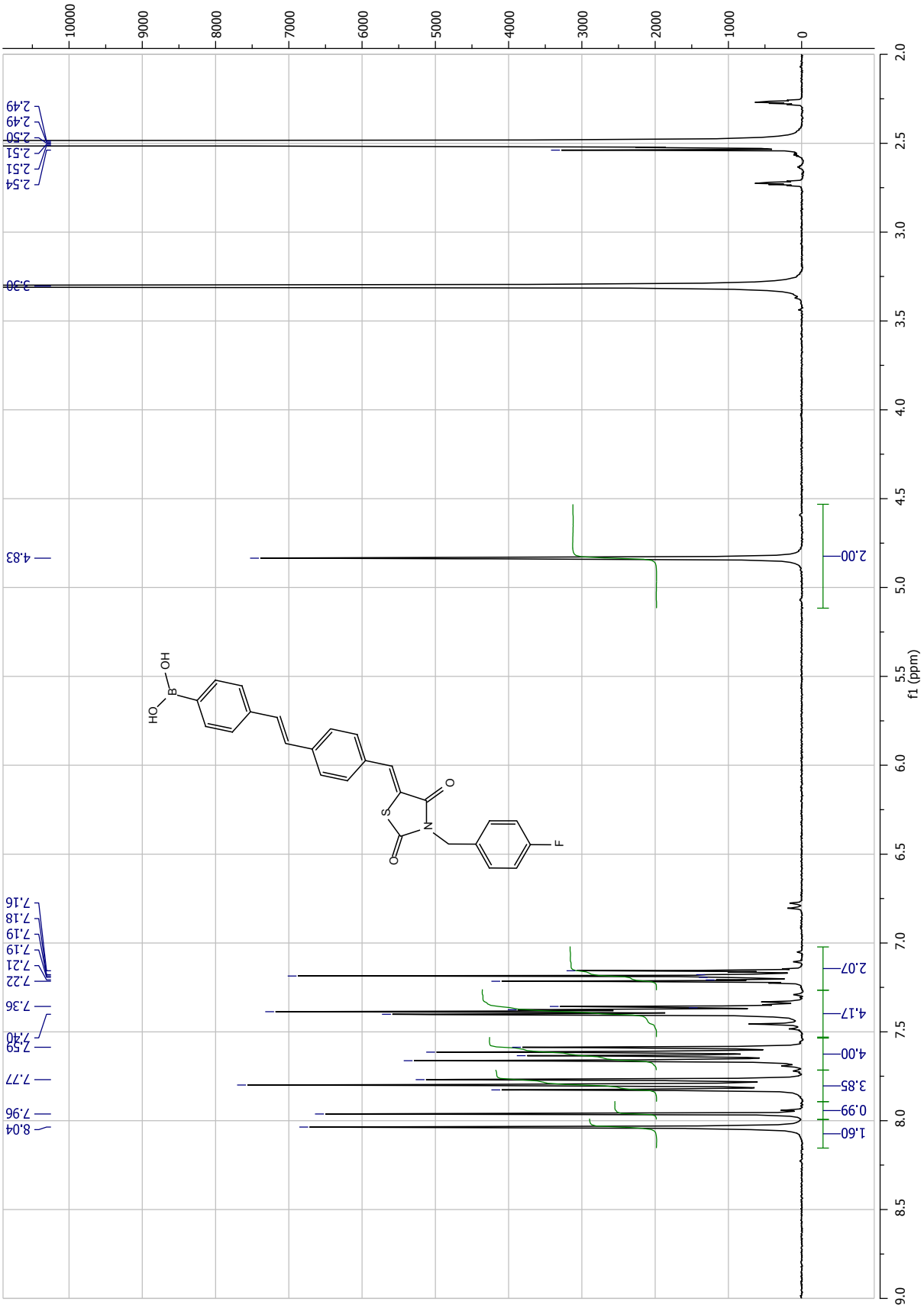


(4-((*E*)-4-((*Z*)-(3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)styryl)phenyl)boronic acid (**20**); LC-MS

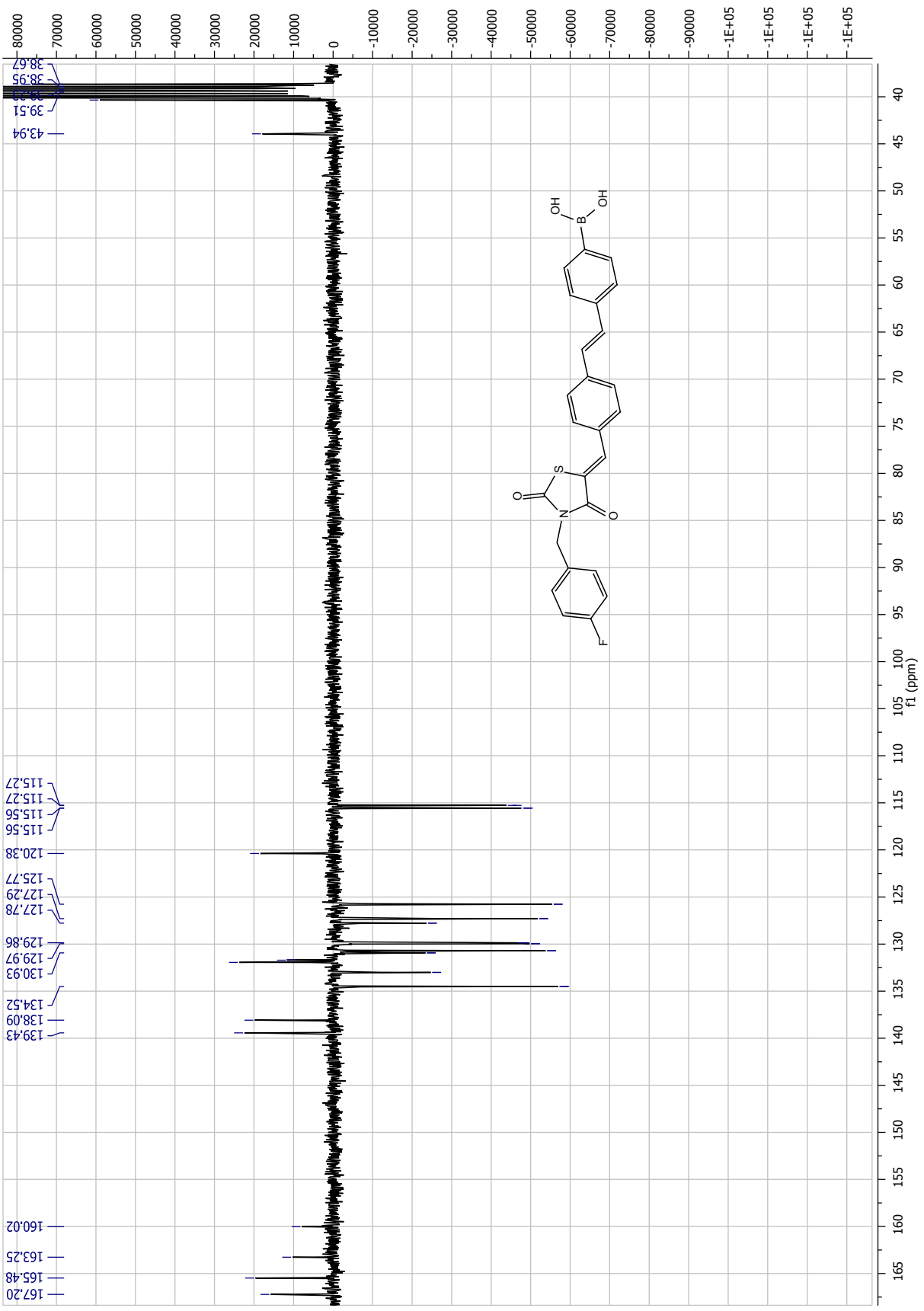




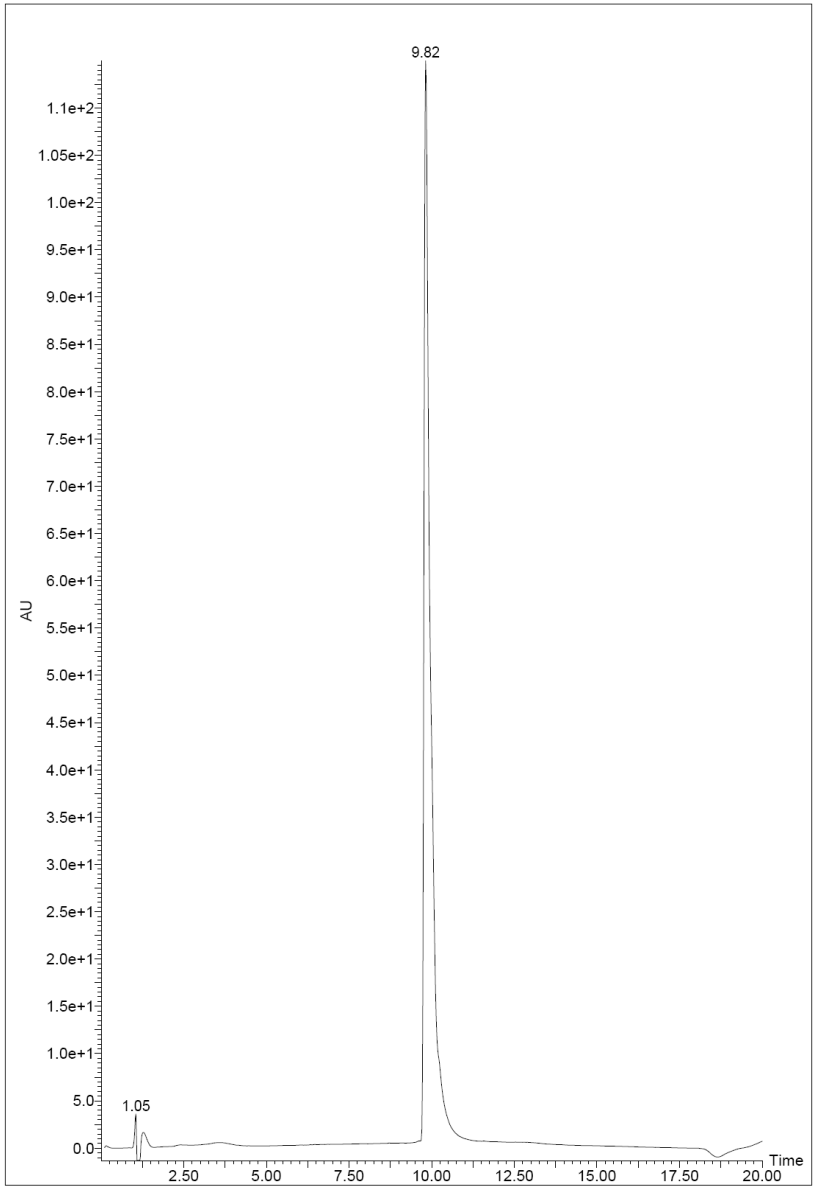
(4-((*E*)-4-((*Z*)-(3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)styryl)phenyl)boronic acid (**20**); ^{1}H NMR

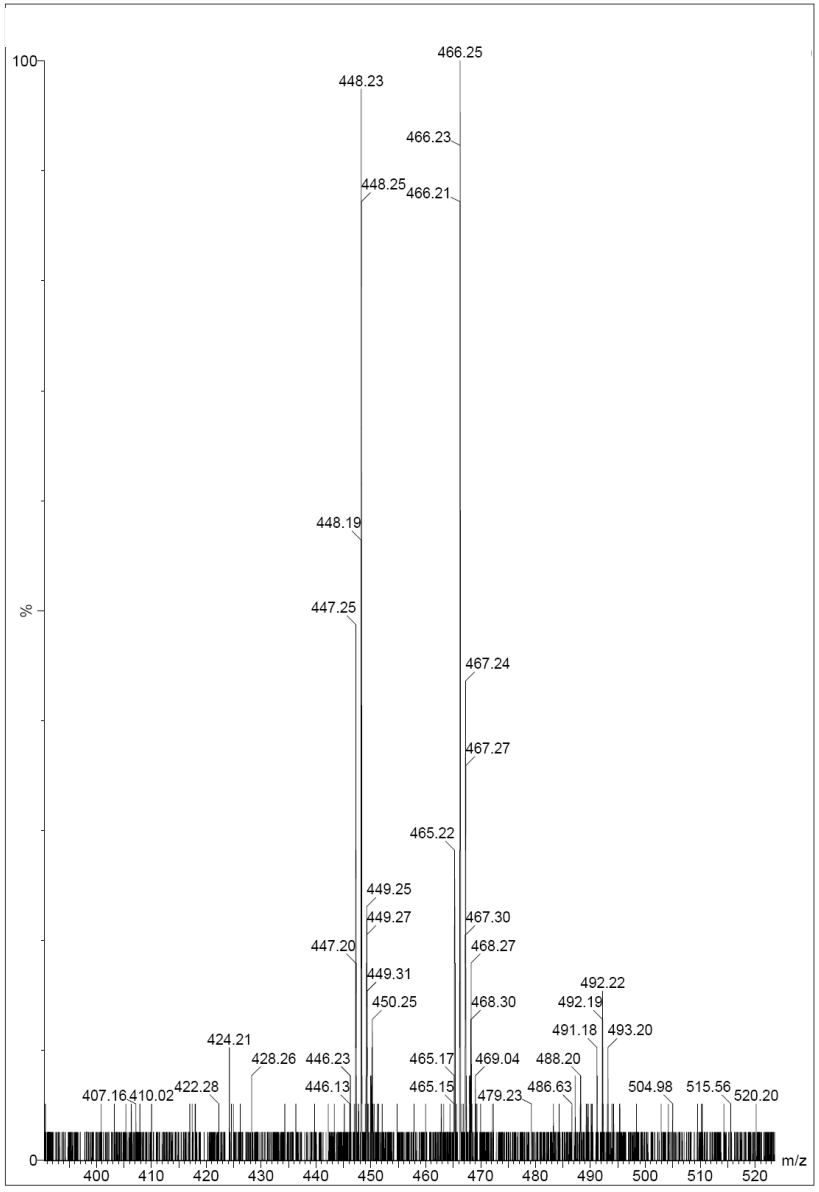


(4-((*E*)-4-((*Z*)-(3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)styryl)phenyl)boronic acid (**20**); ^{13}C NMR

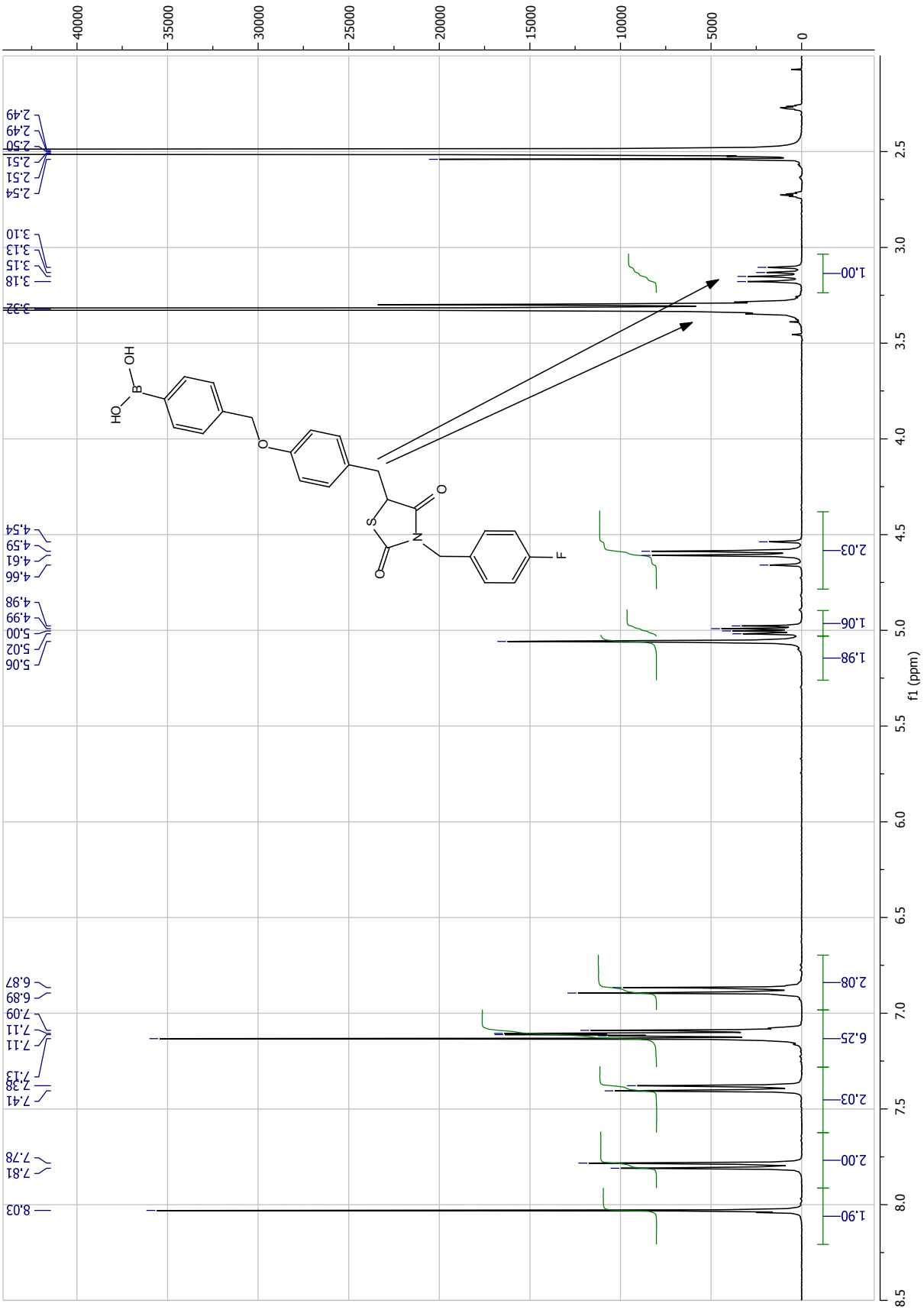


(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**21**); LC-MS

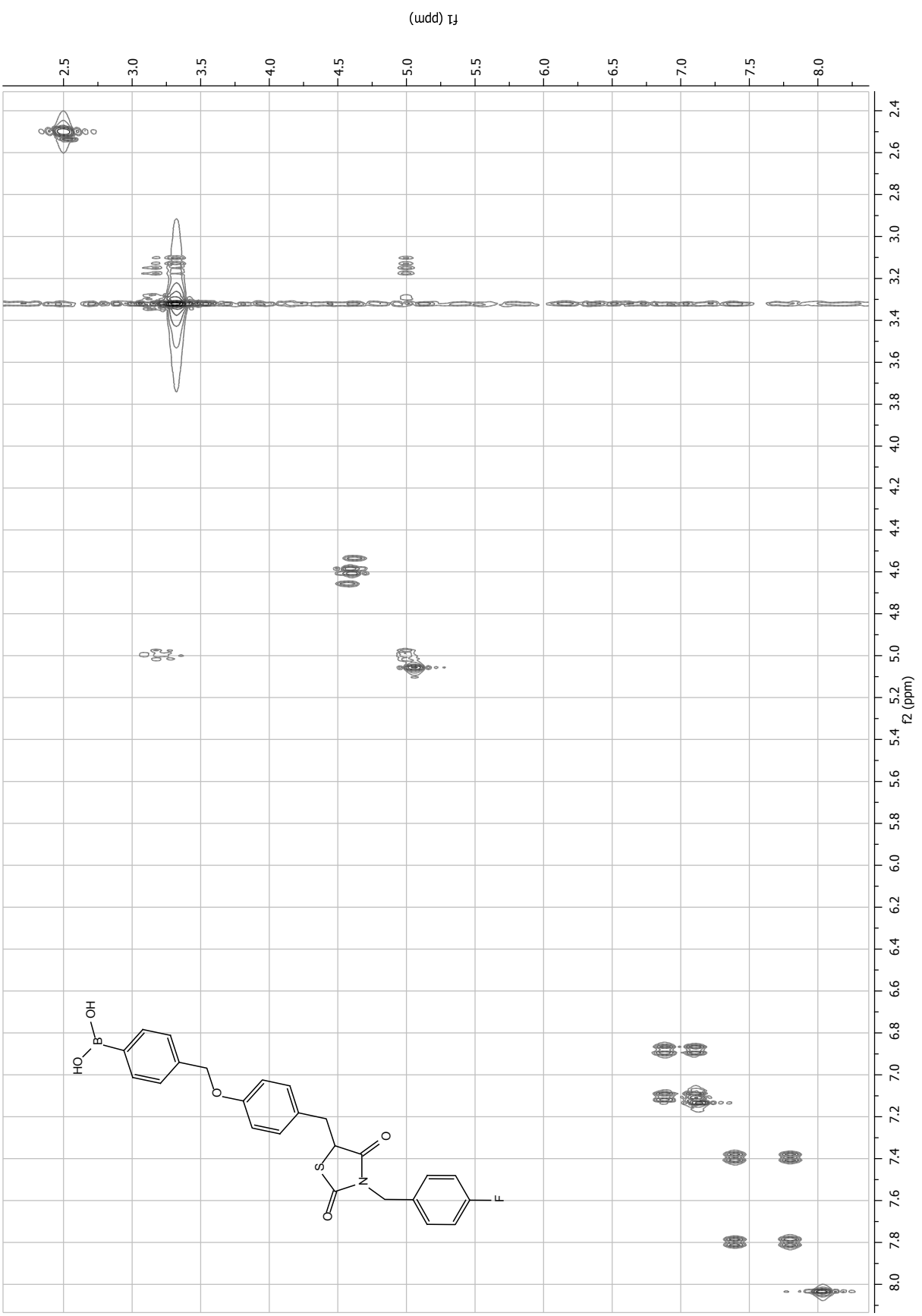




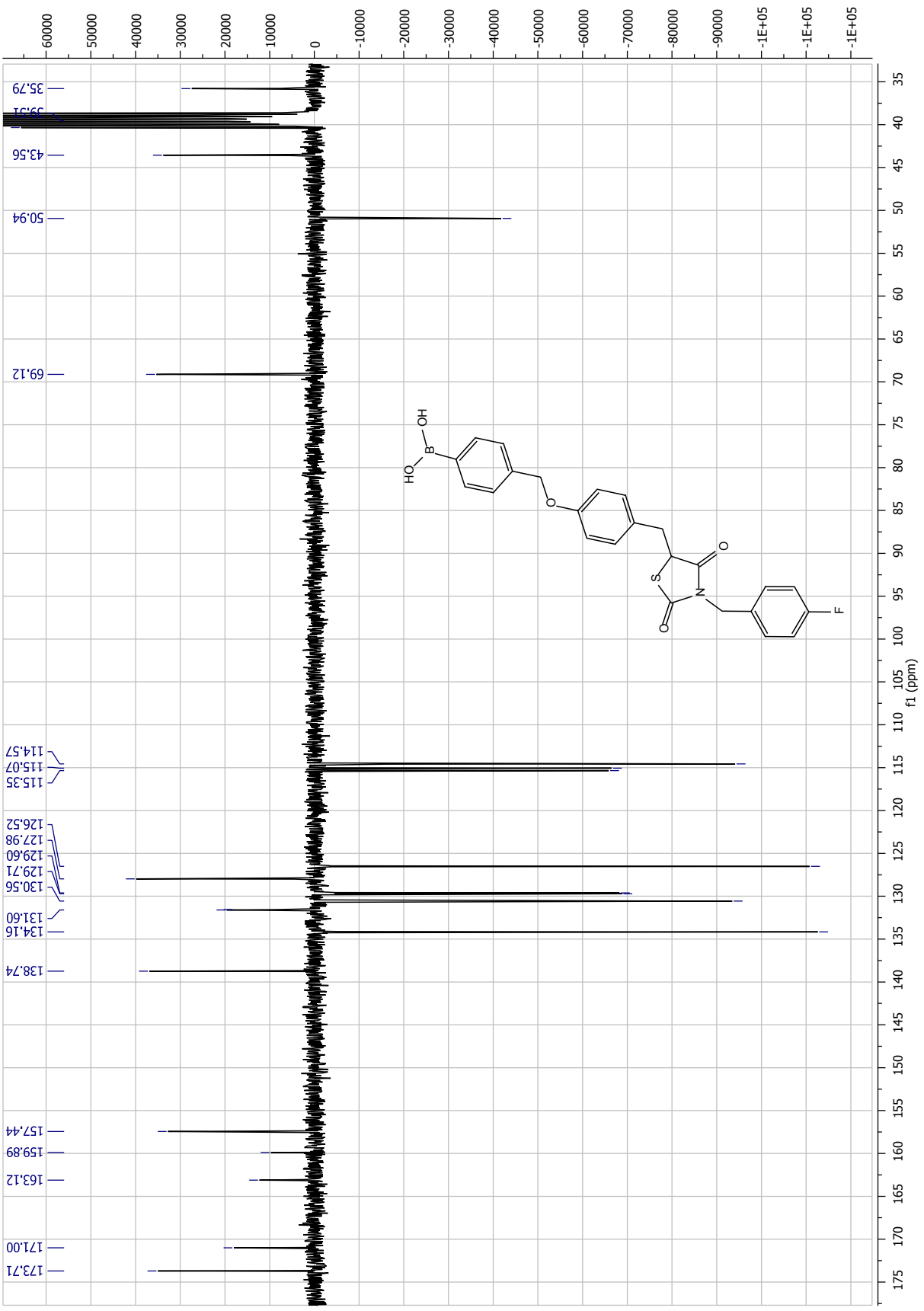
(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**21**); ^{1}H NMR



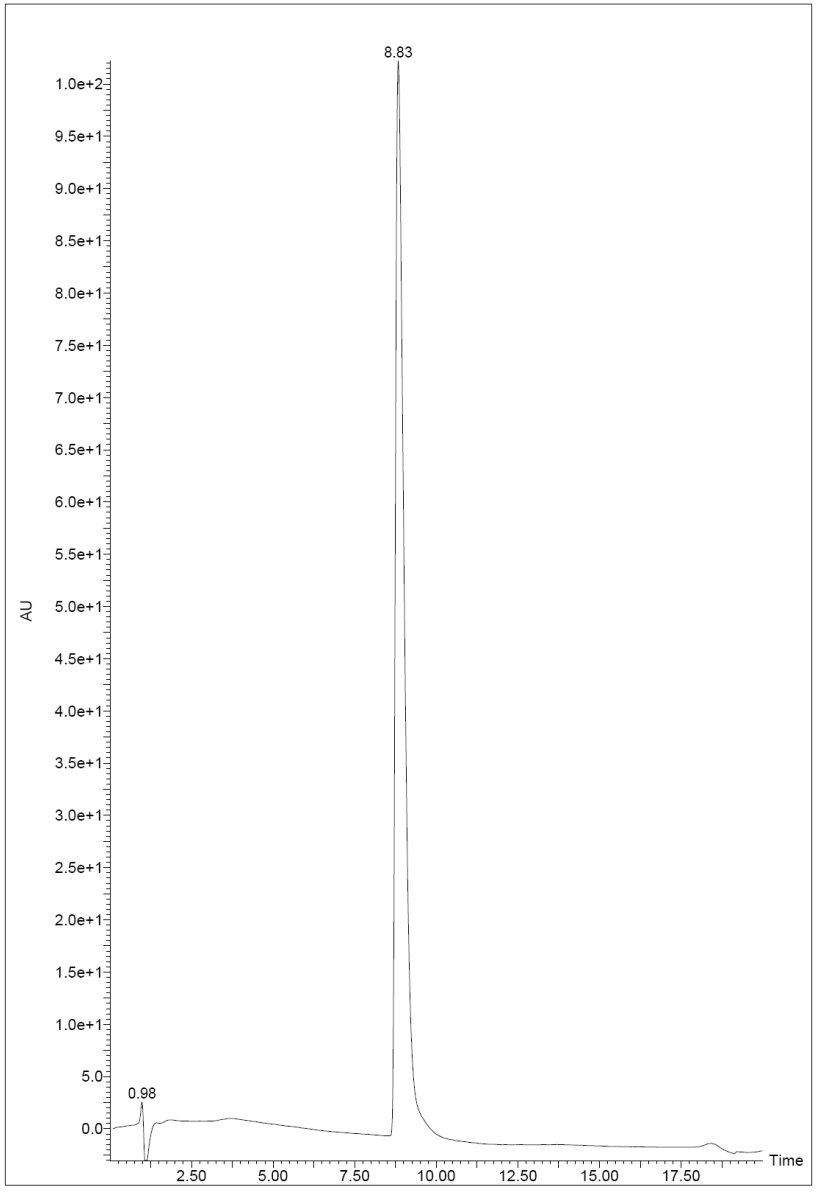
(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**21**); COSY

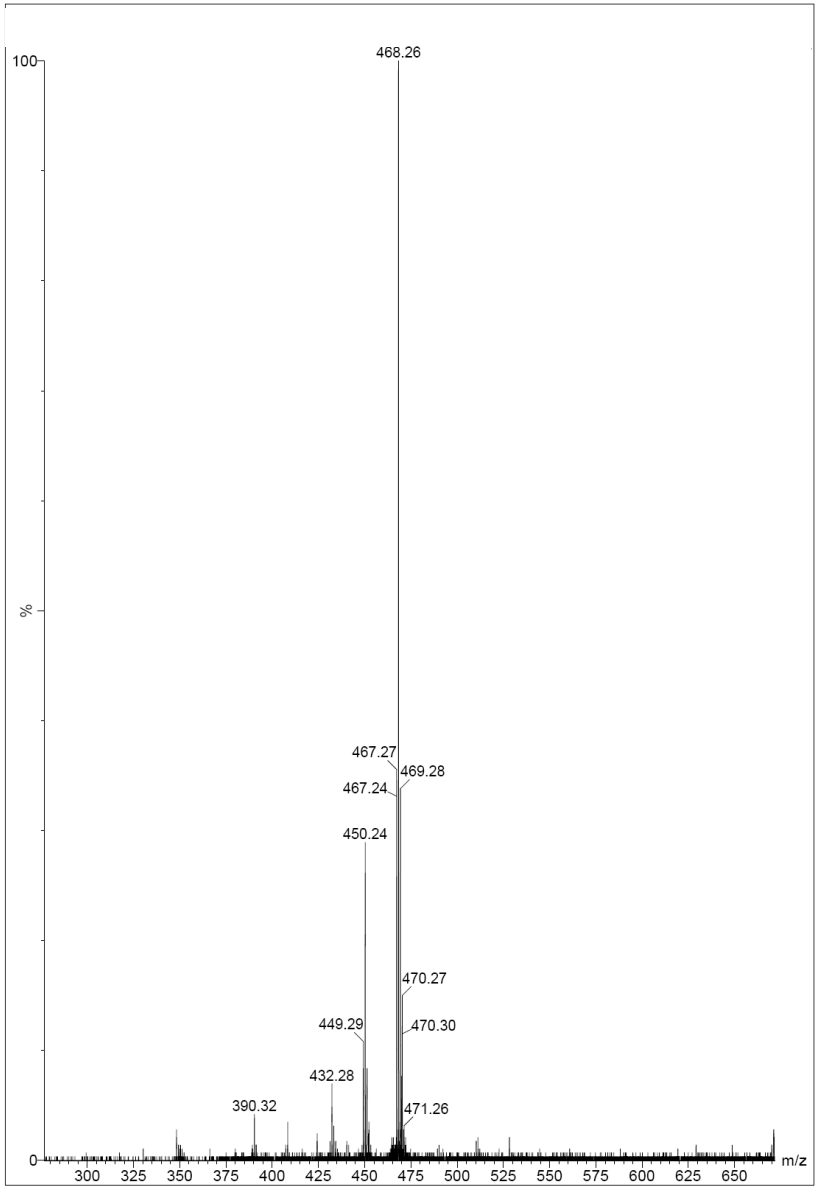


(4-((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**21**); ^{13}C NMR

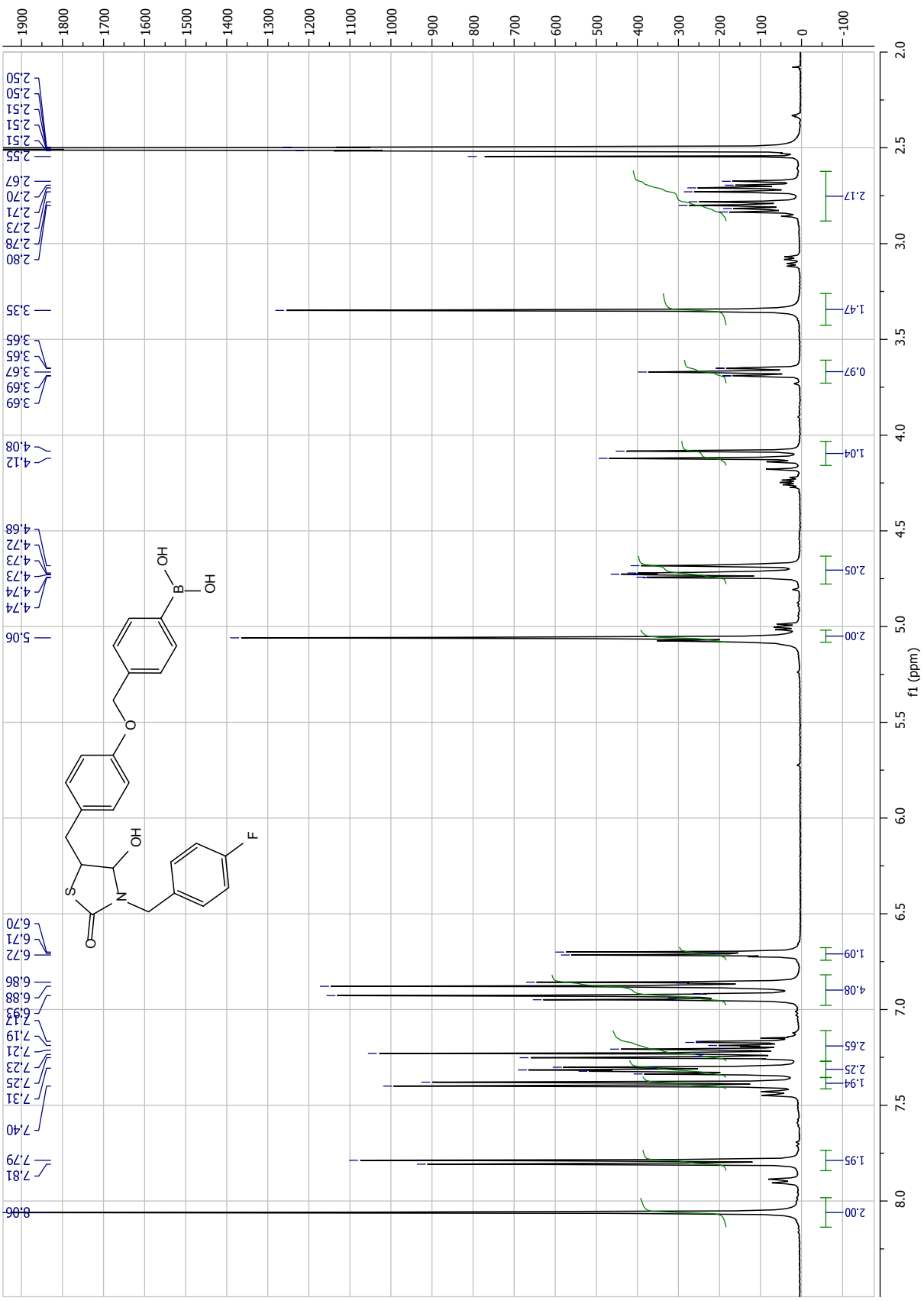


(4-((4-((3-(4-fluorobenzyl)-4-hydroxy-2-oxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**22**): LC-MS

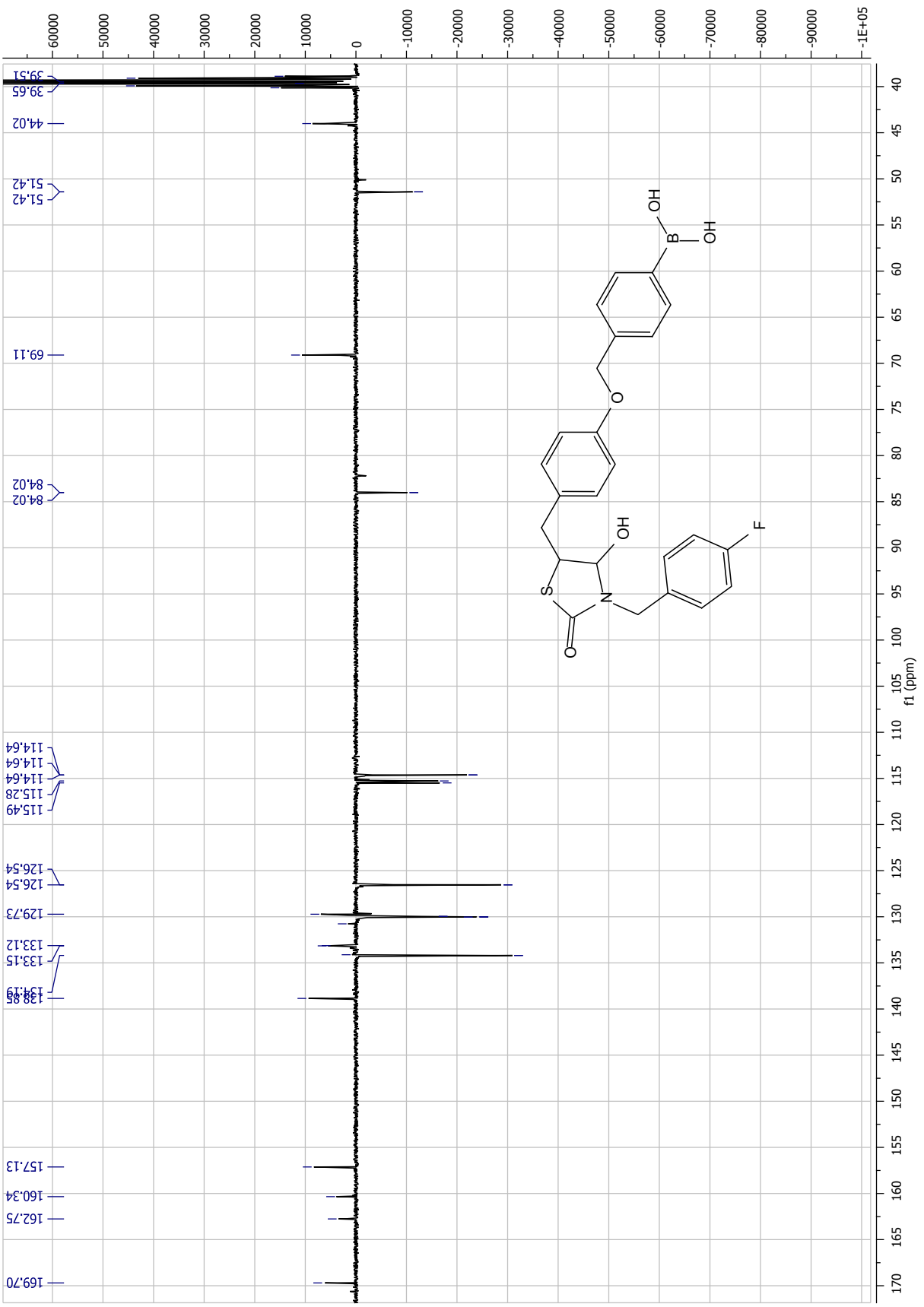




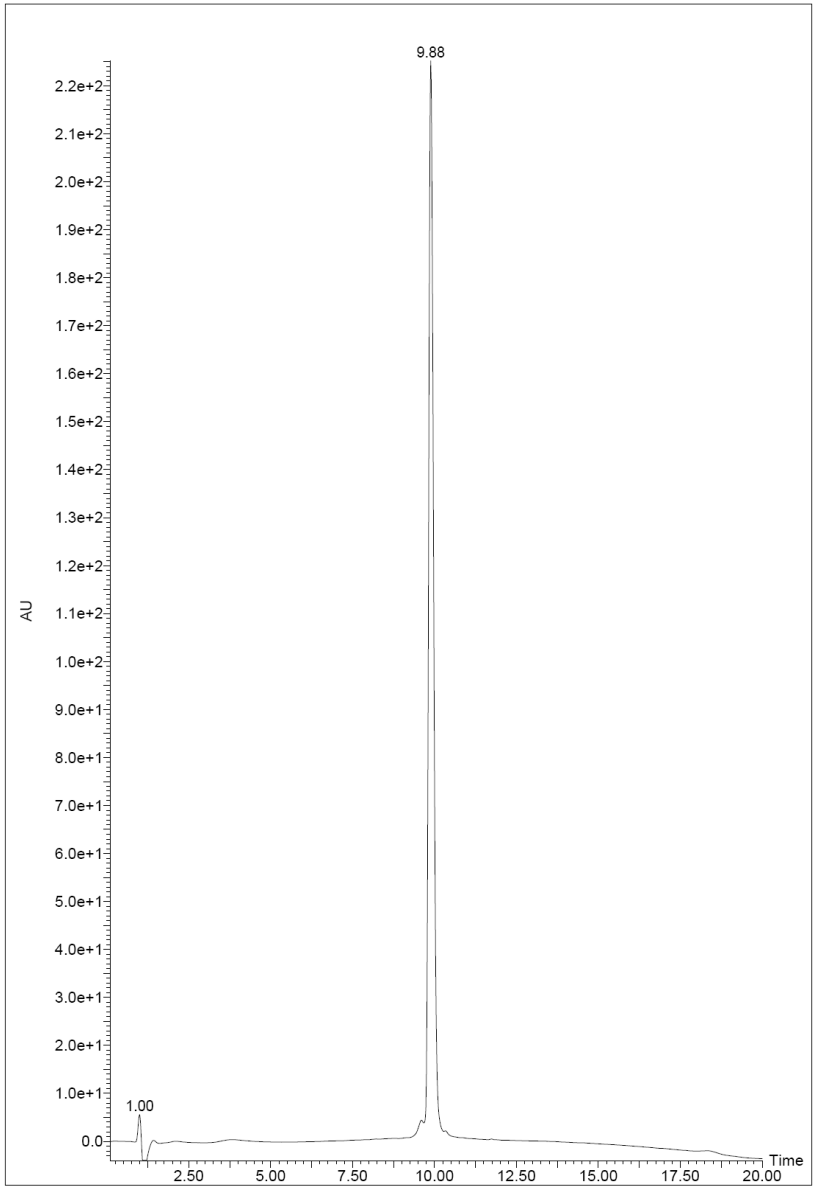
(4-((4-((3-(4-fluorobenzyl)-4-hydroxy-2-oxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**22**): ^{1}H NMR

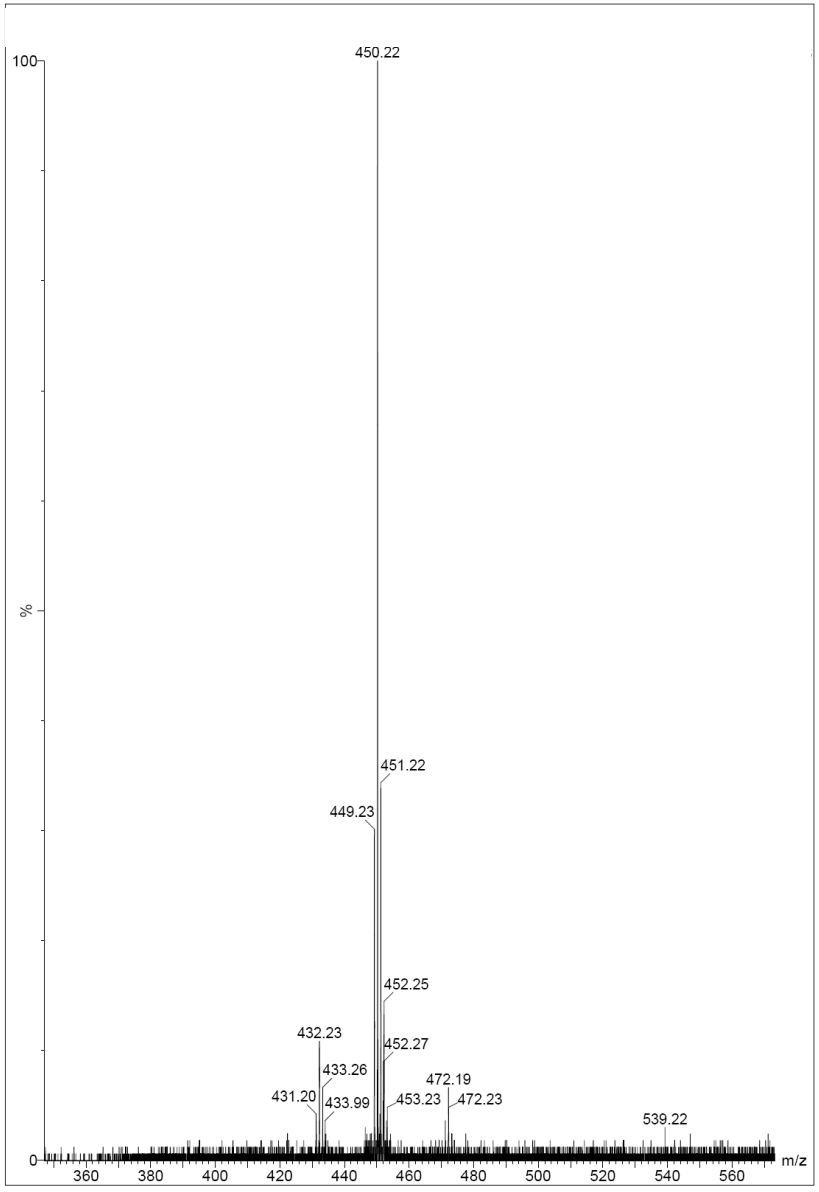


(4-((4-((3-(4-fluorobenzyl)-4-hydroxy-2-oxothiazolidin-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**22**): ^{13}C NMR

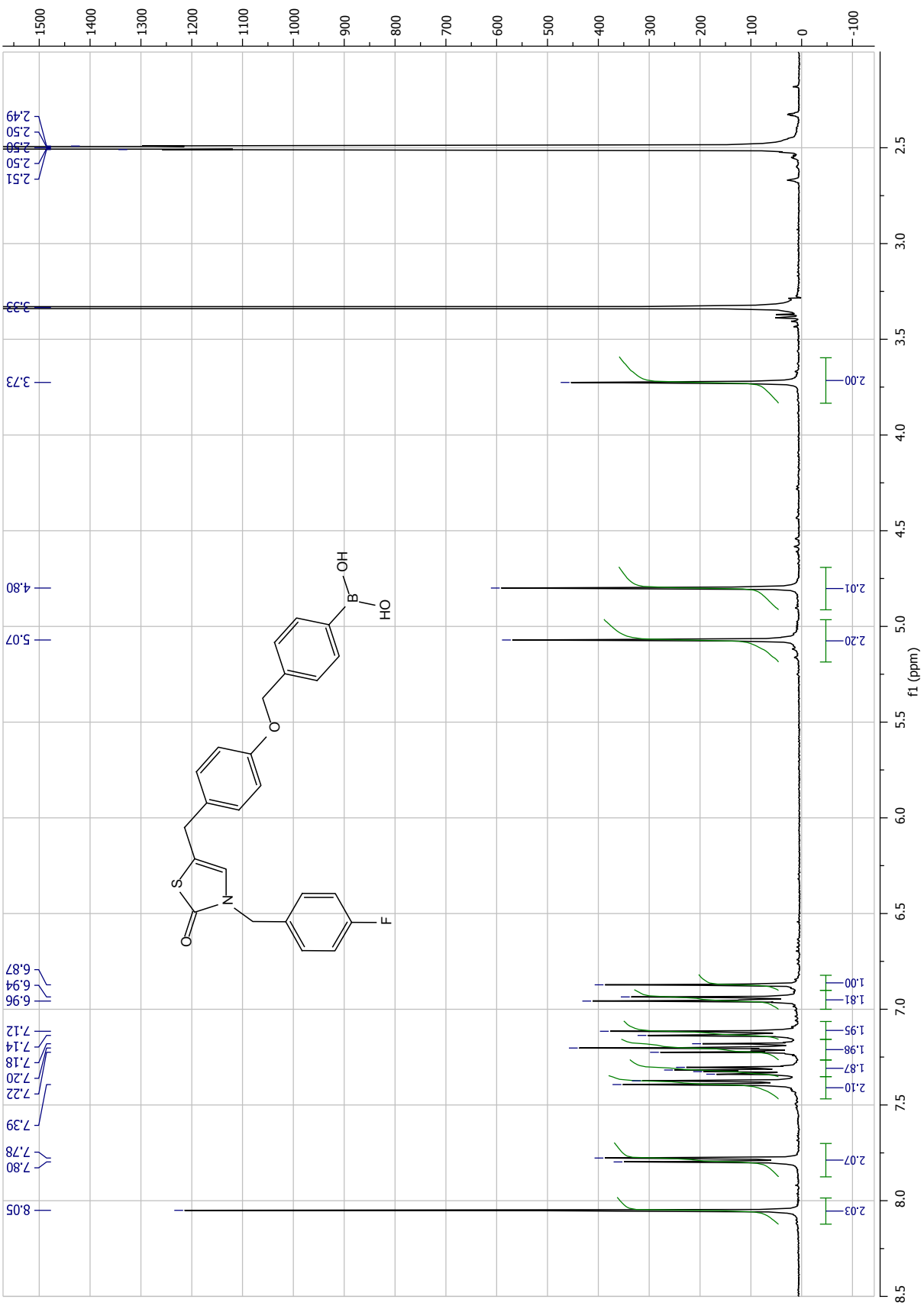


(4-((4-((3-(4-fluorobenzyl)-2-oxo-2,3-dihydrothiazol-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**23**): LC-MS

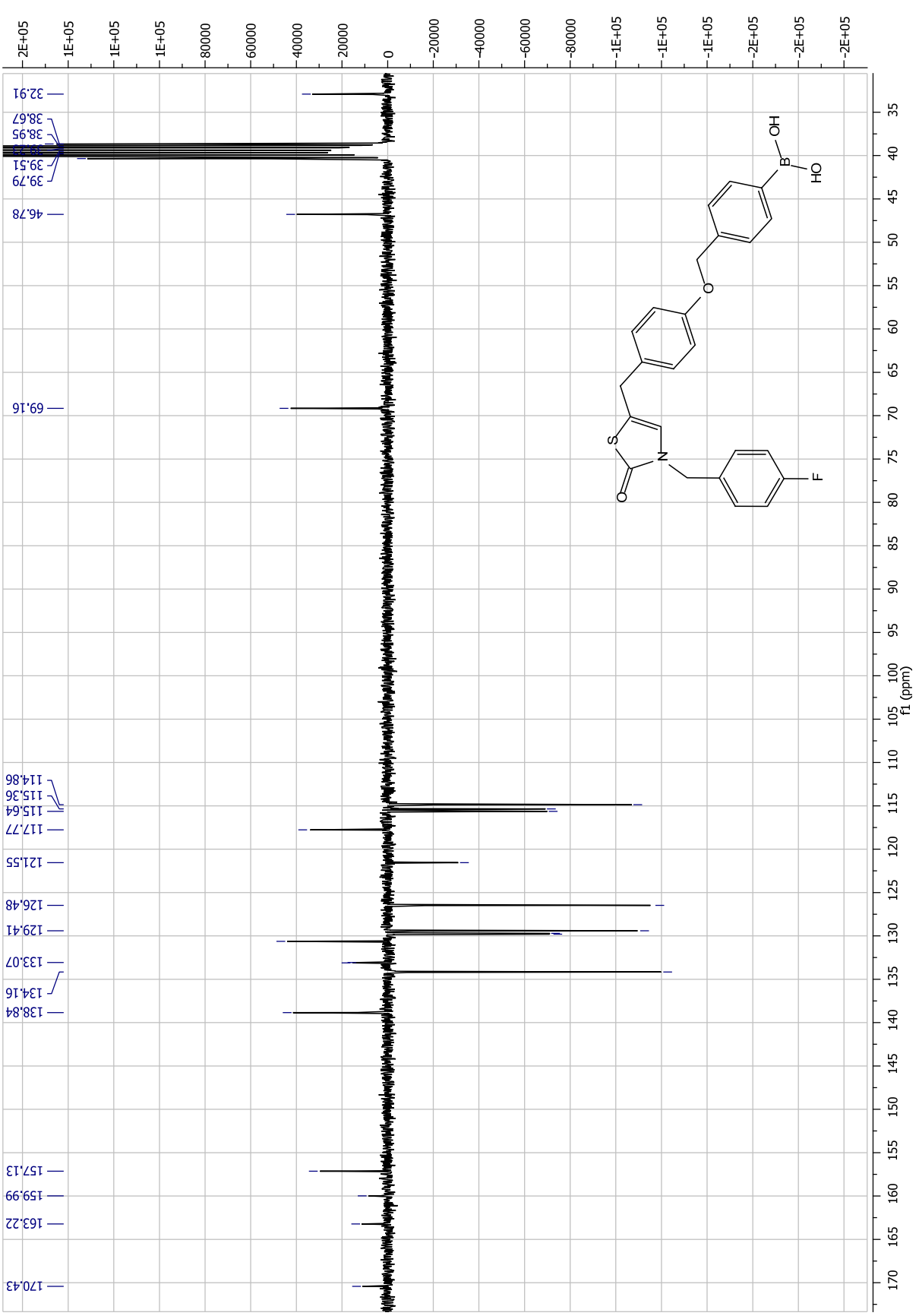




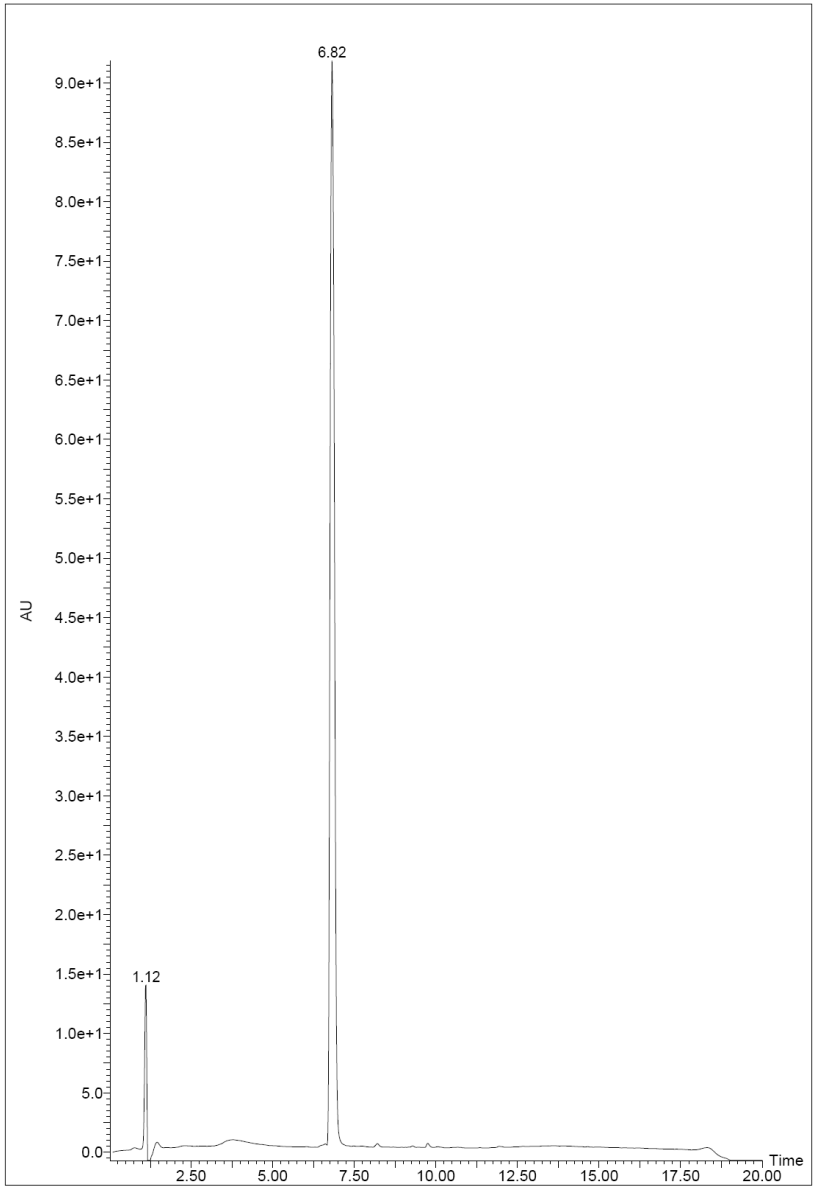
(4-((4-((3-(4-fluorobenzyl)-2-oxo-2,3-dihydrothiazol-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**23**): ^{1}H NMR

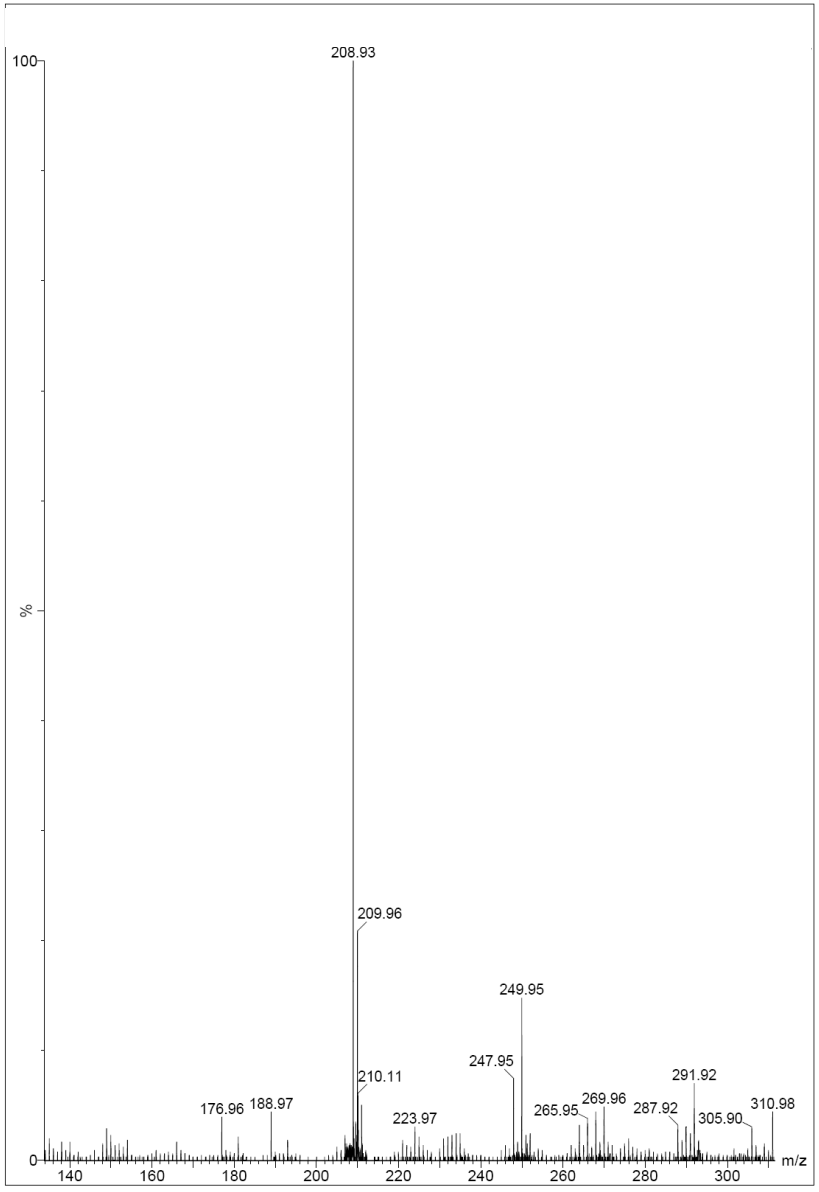


(4-((4-((3-(4-fluorobenzyl)-2-oxo-2,3-dihydrothiazol-5-yl)methyl)phenoxy)methyl)phenyl)boronic acid (**23**): ^{13}C NMR

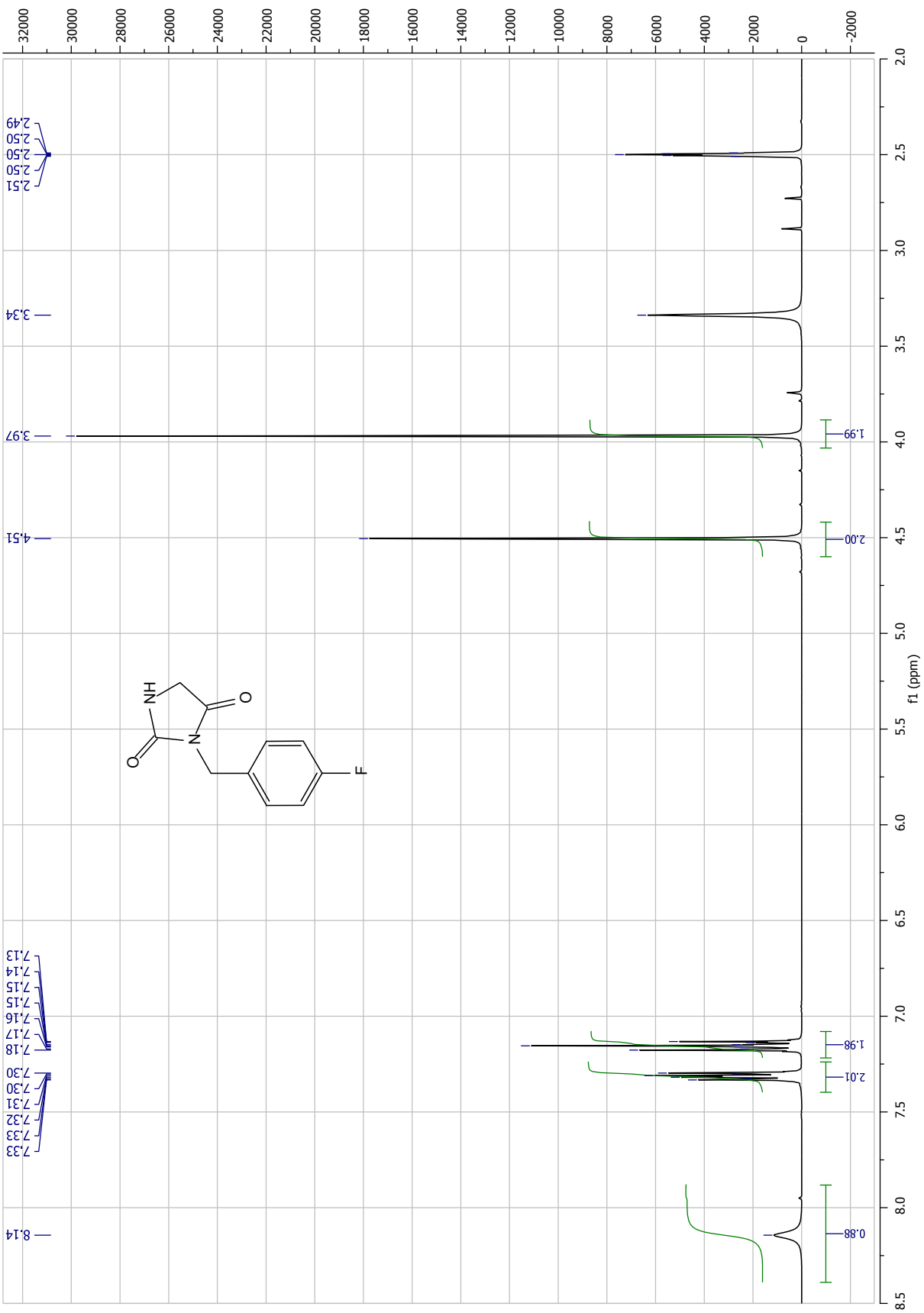


3-(4-fluorobenzyl)imidazolidine-2,4-dione (**25**): LC-MS

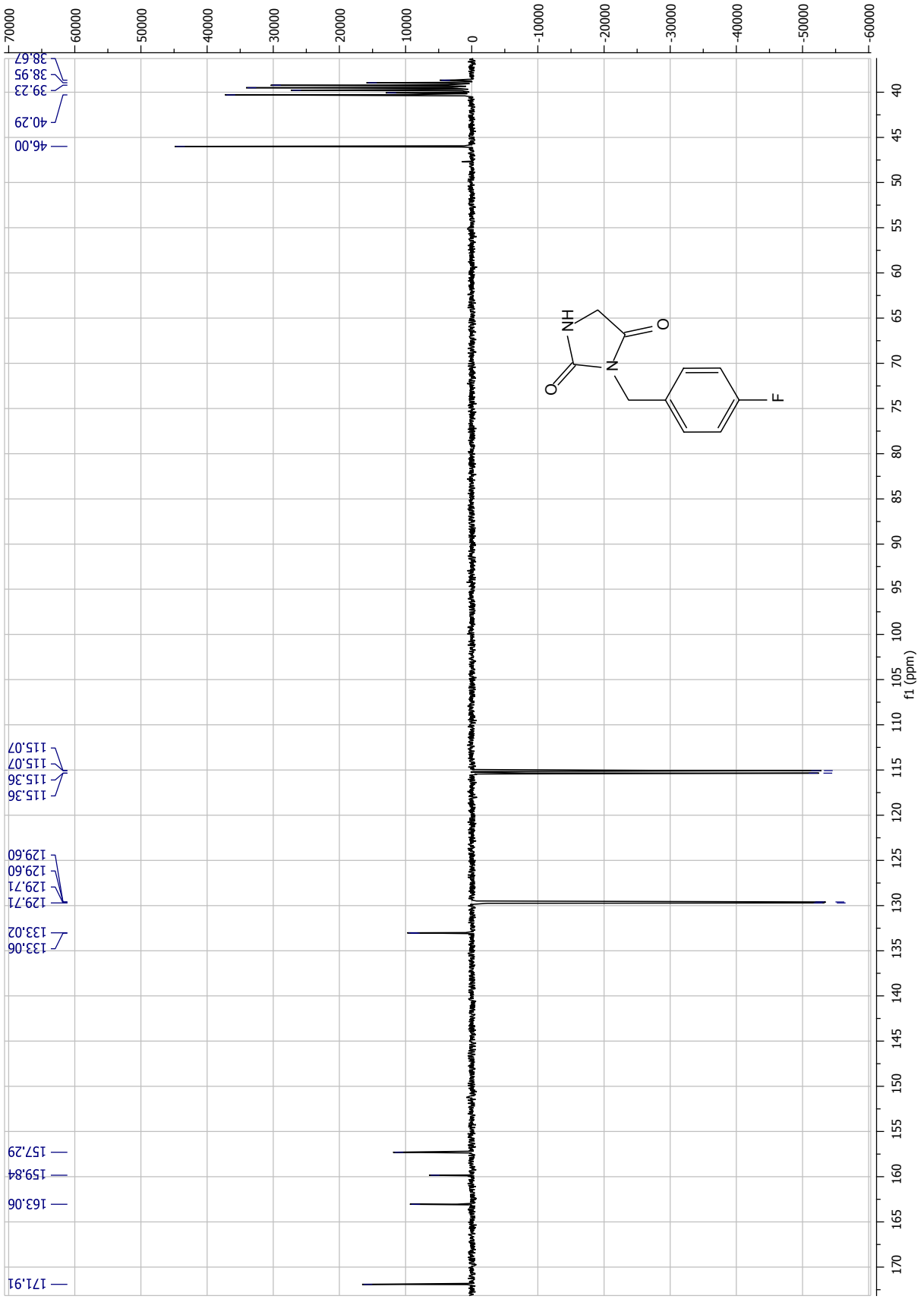




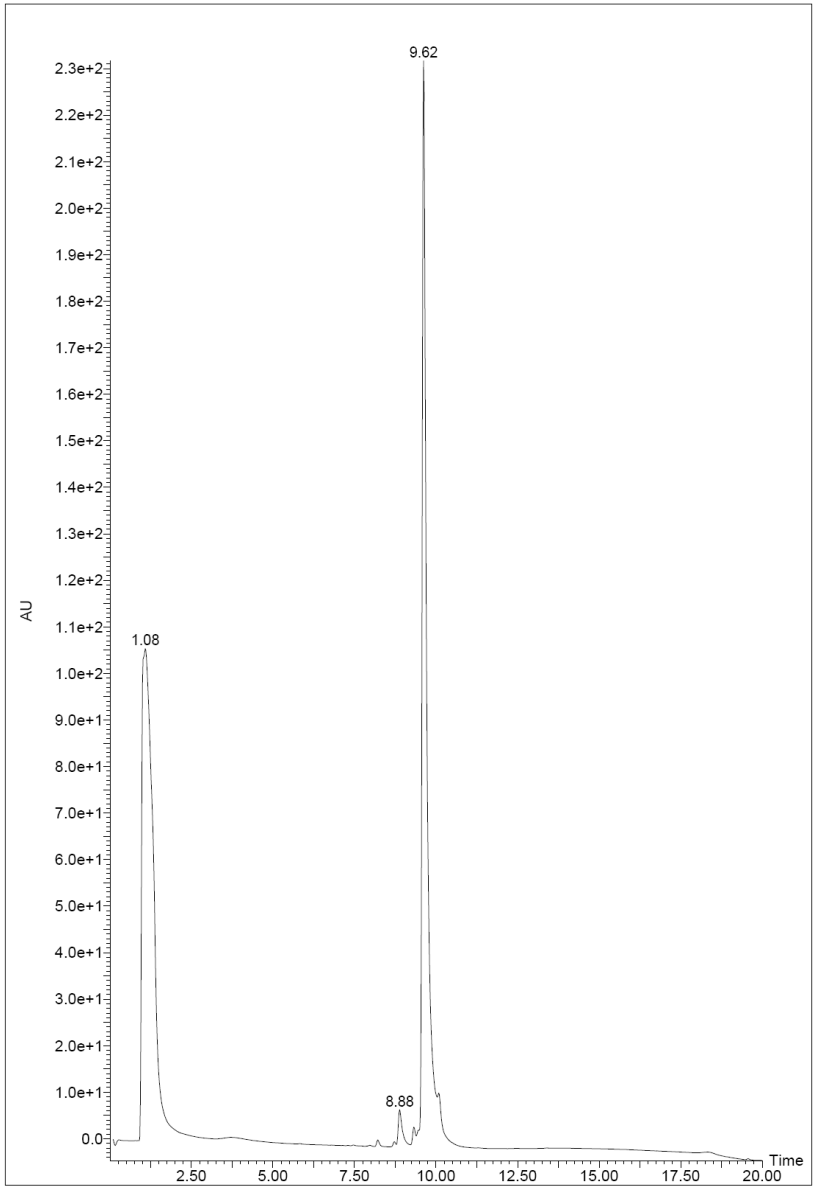
3-(4-fluorobenzyl)imidazolidine-2,4-dione (**25**): ^{1}H NMR

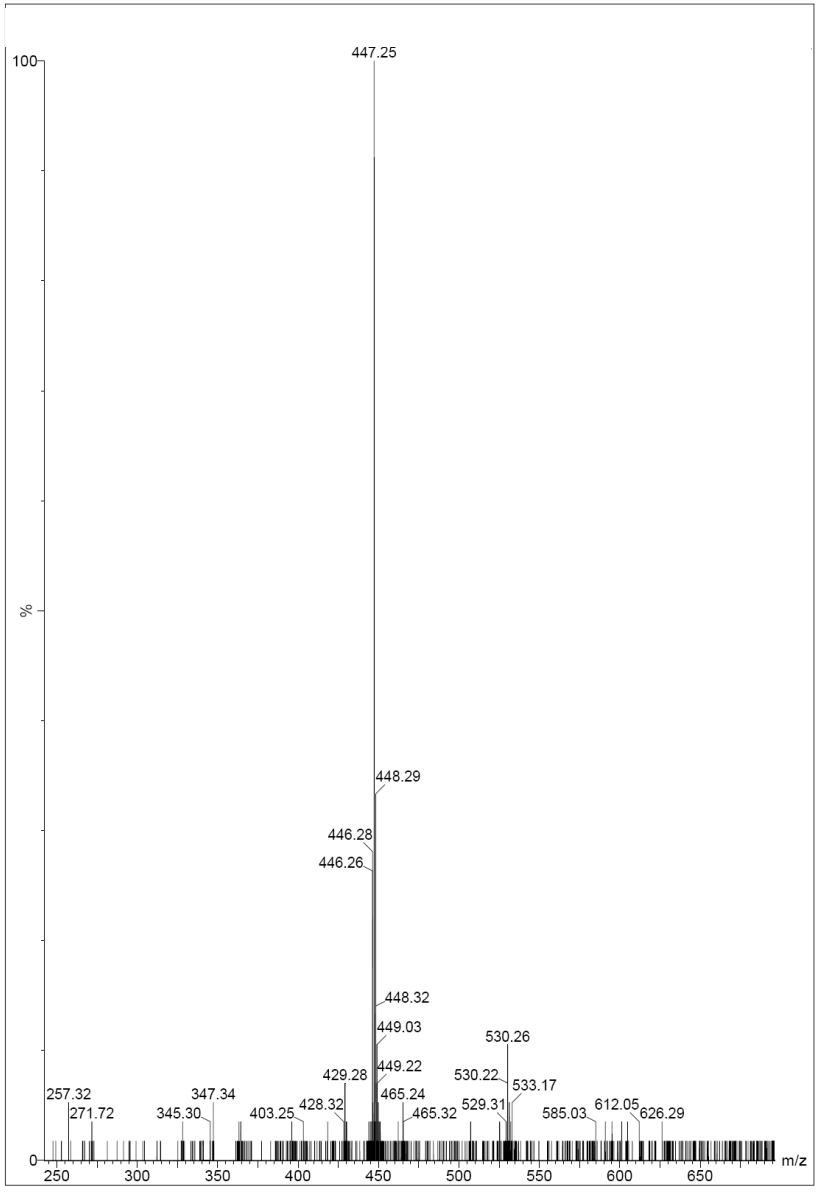


3-(4-fluorobenzyl)imidazolidine-2,4-dione (**25**): ^{13}C NMR

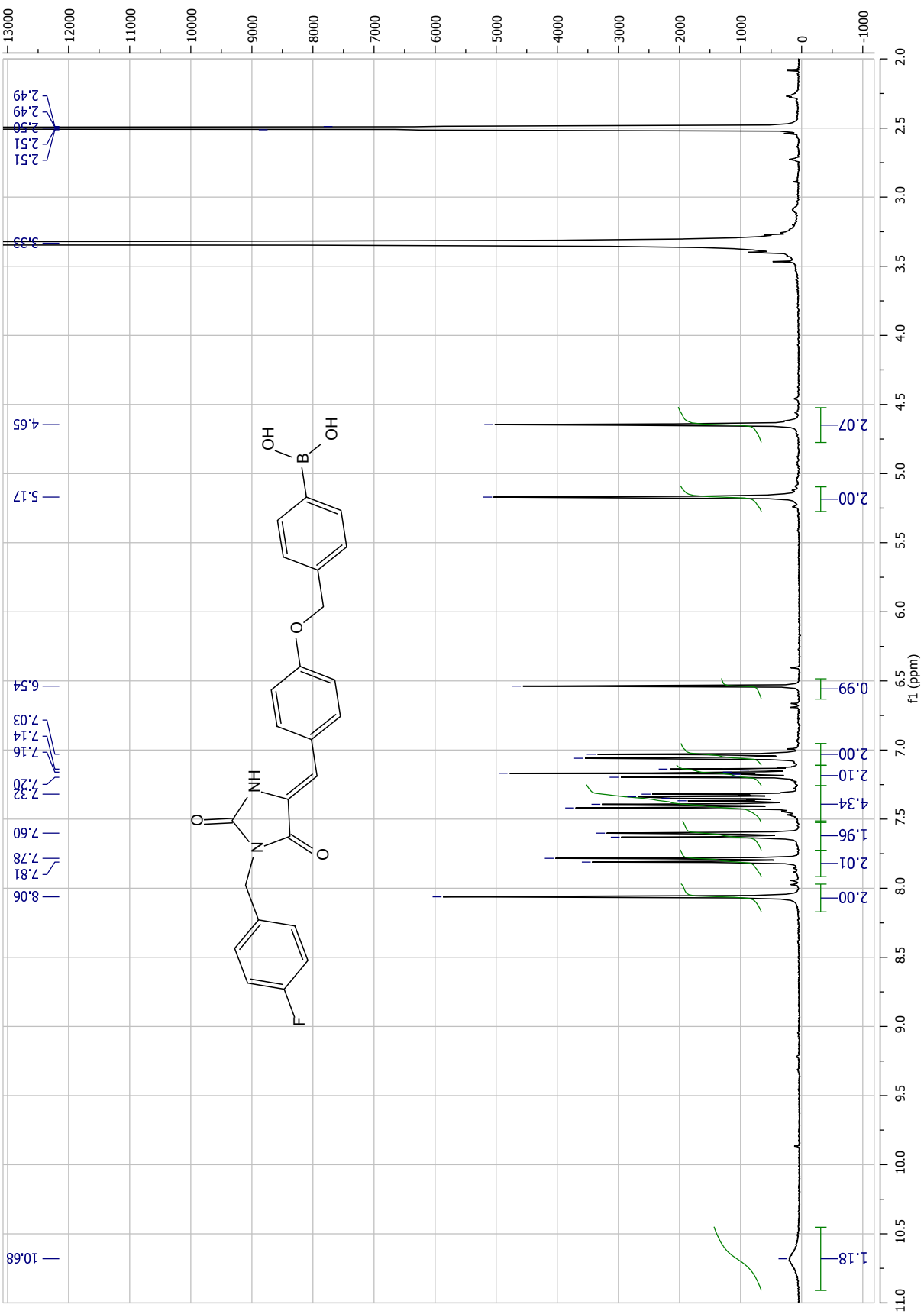


(*Z*)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**26**): LC-MS

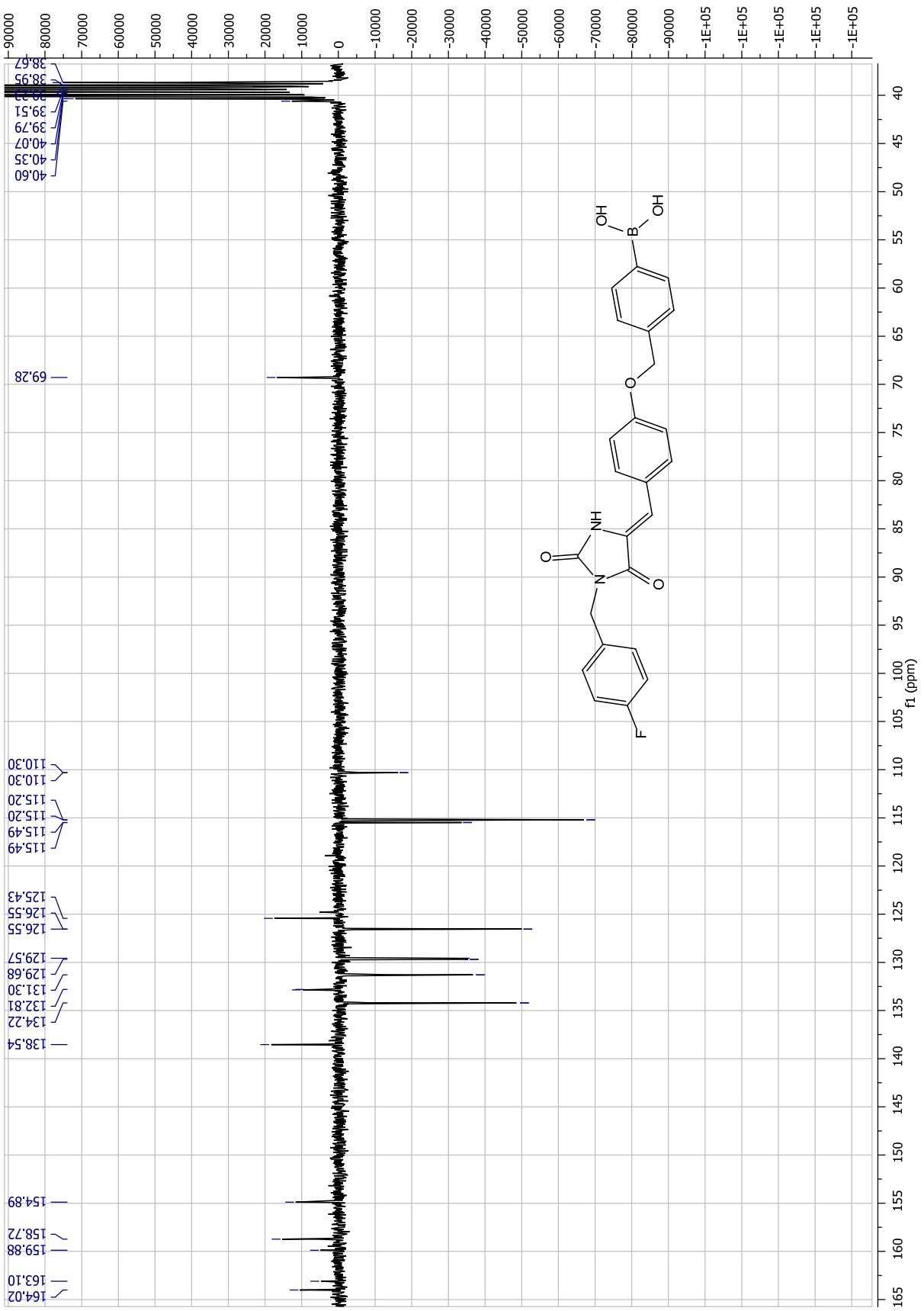




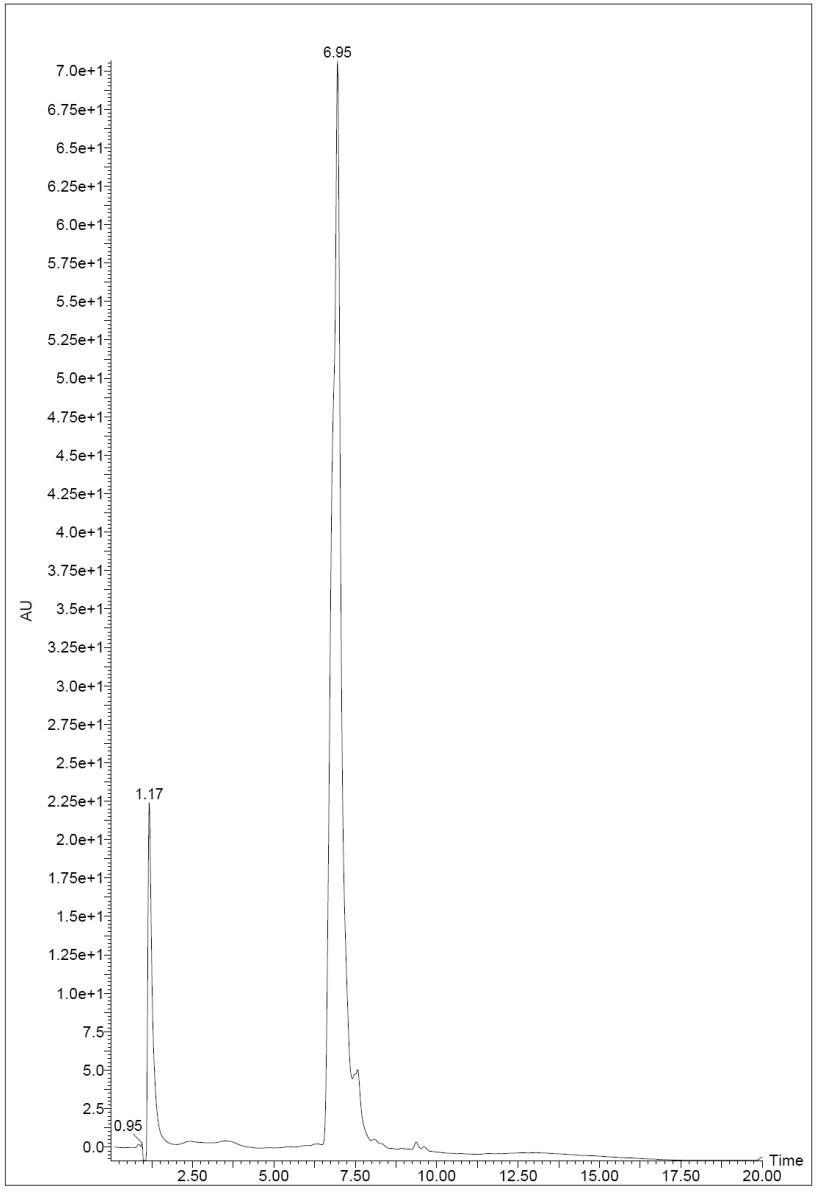
(Z)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**26**): ^{1}H NMR

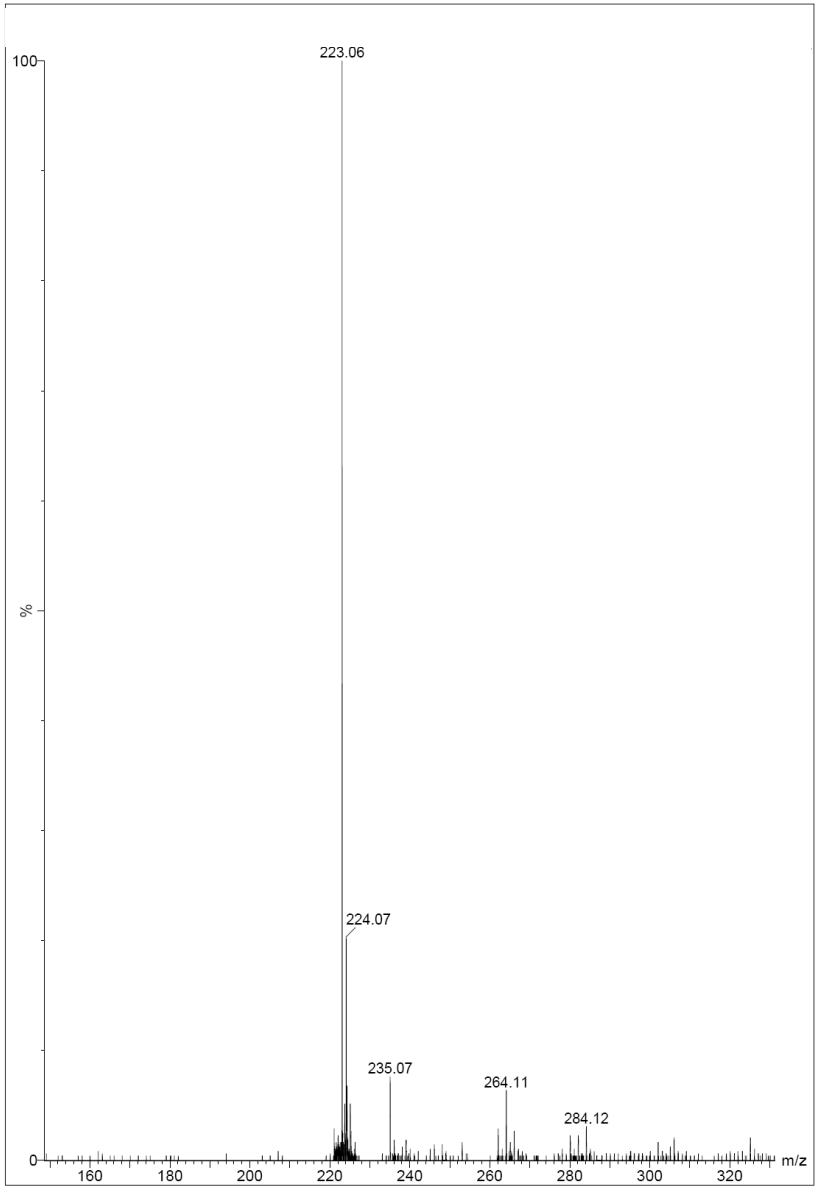


(Z)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**26**): ^{13}C NMR

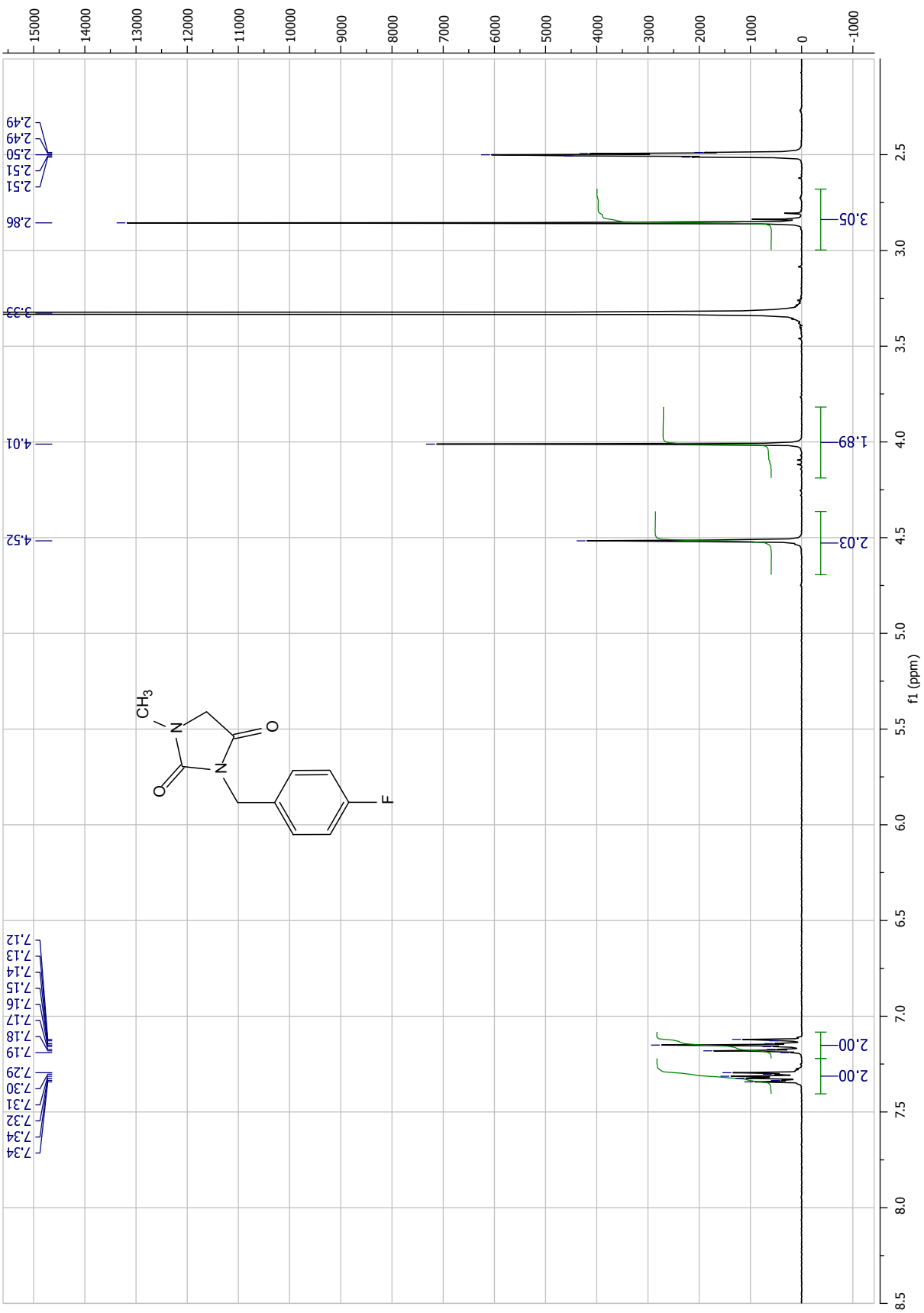


3-(4-fluorobenzyl)-1-methylimidazolidine-2,4-dione (**27**): LC-MS

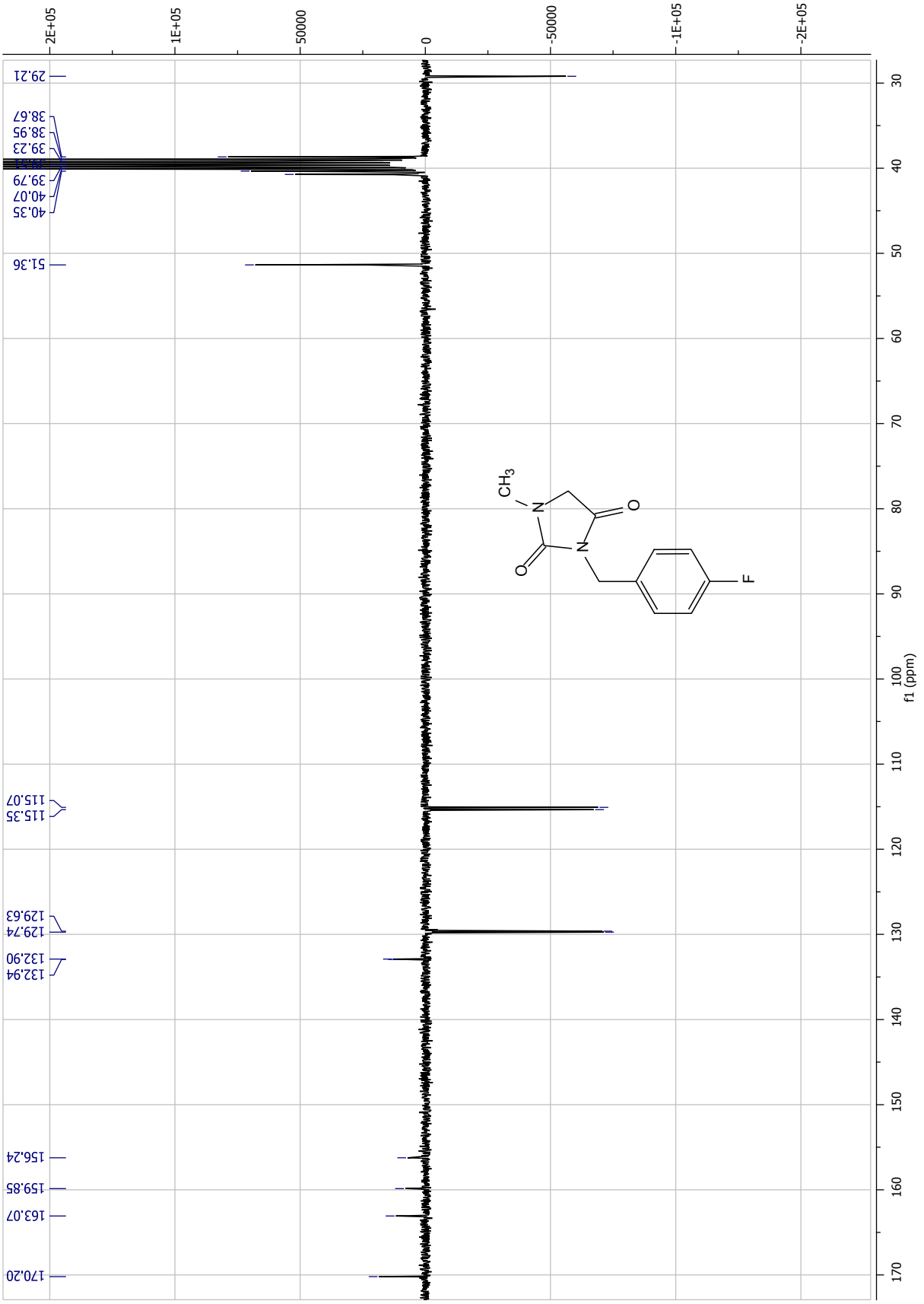




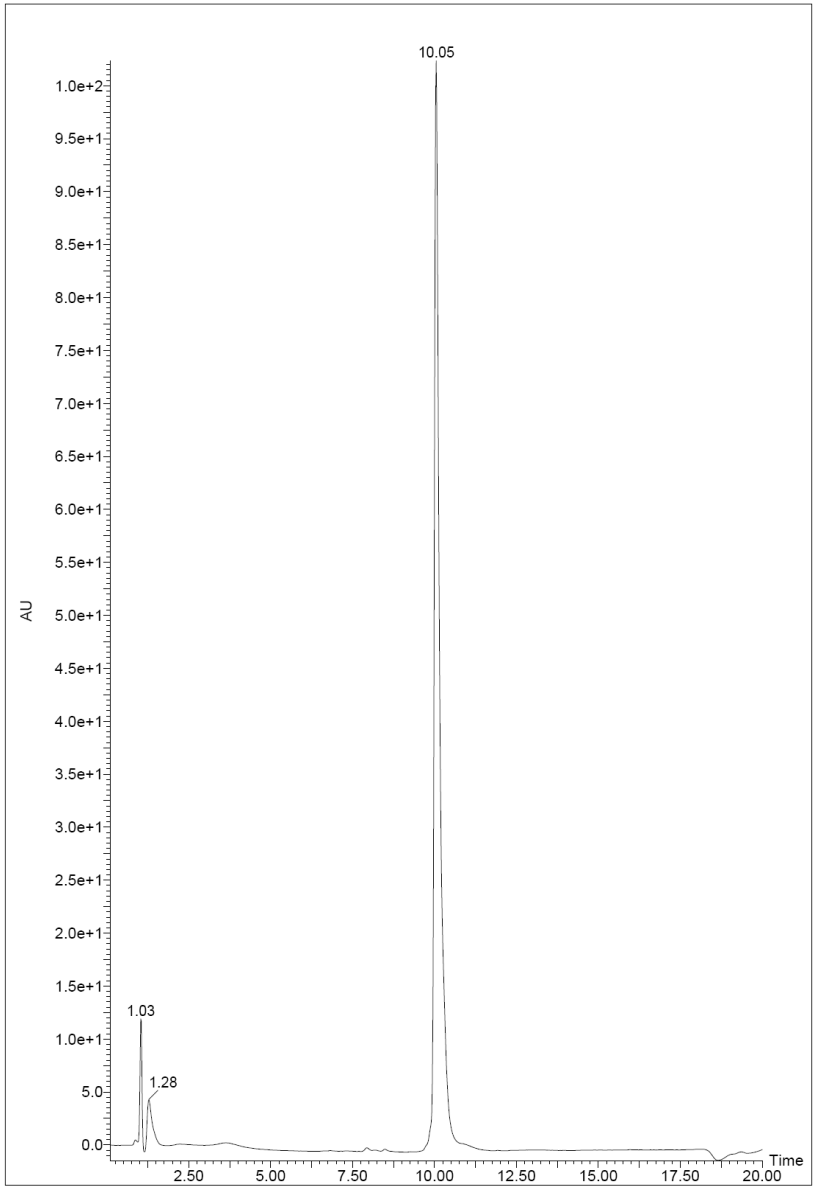
3-(4-fluorobenzyl)-1-methylimidazolidine-2,4-dione (**27**): ^{1}H NMR

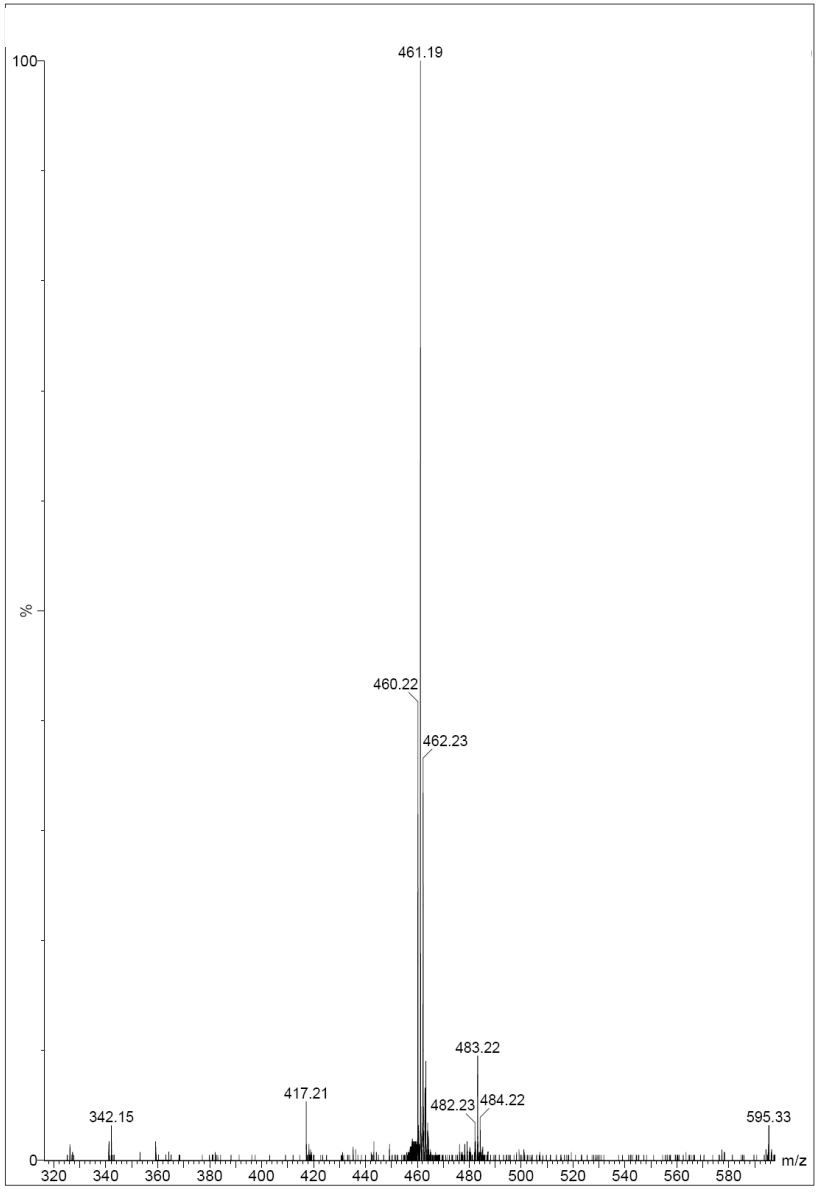


3-(4-fluorobenzyl)-1-methylimidazolidine-2,4-dione (**27**): ^{13}C NMR

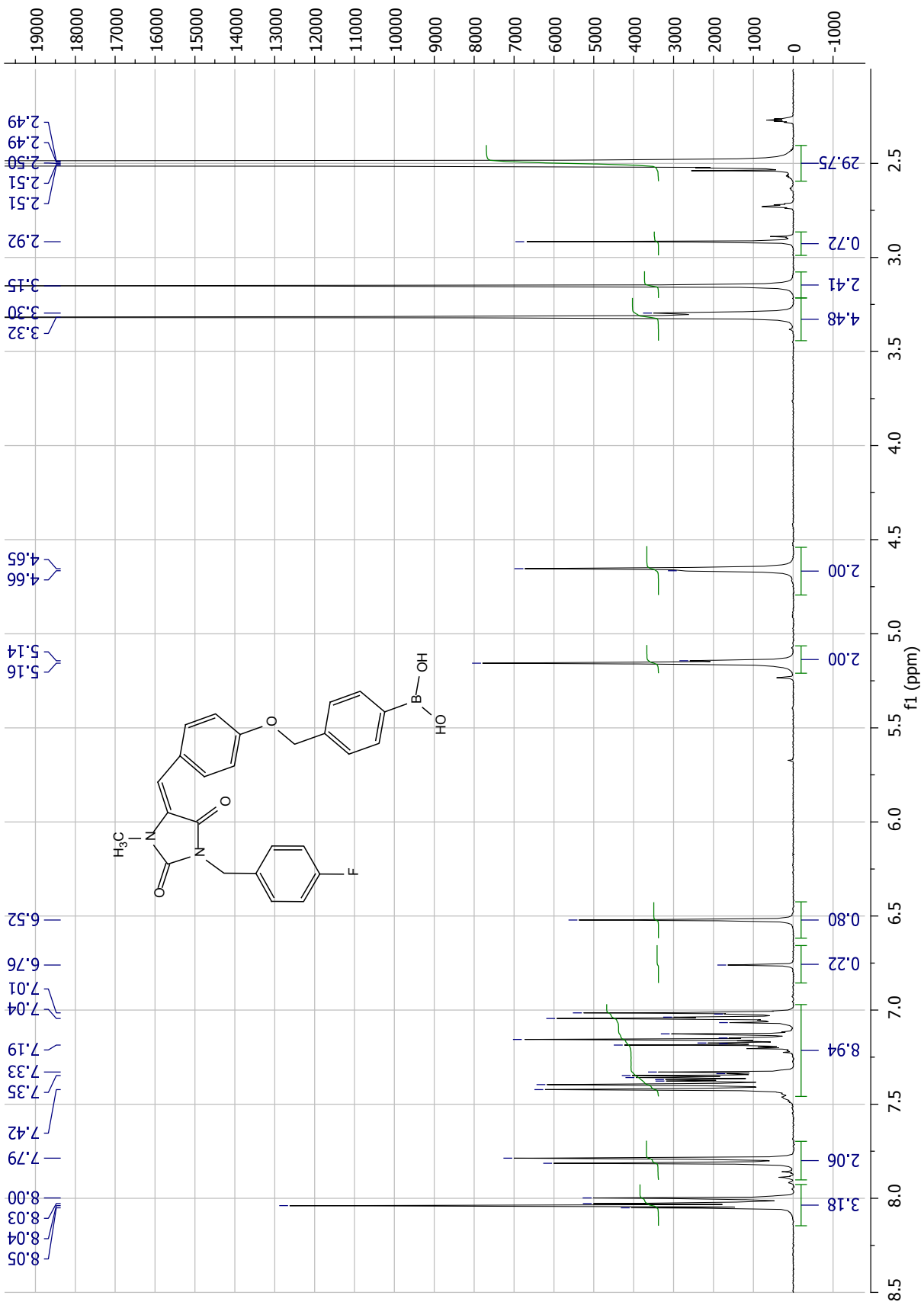


(*E*)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy) methyl)phenyl)boronic acid (*E*-**28**): LC-MS

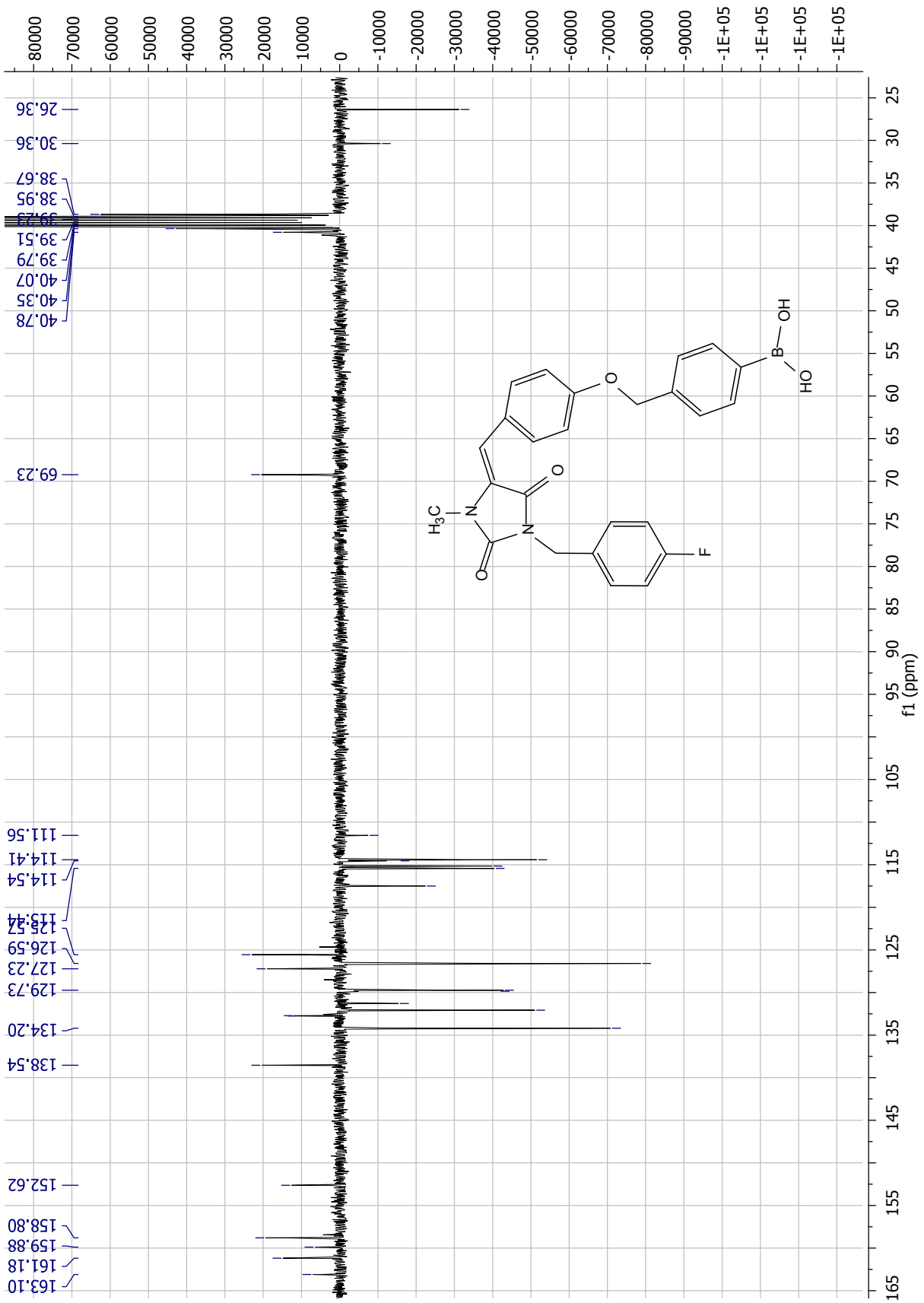




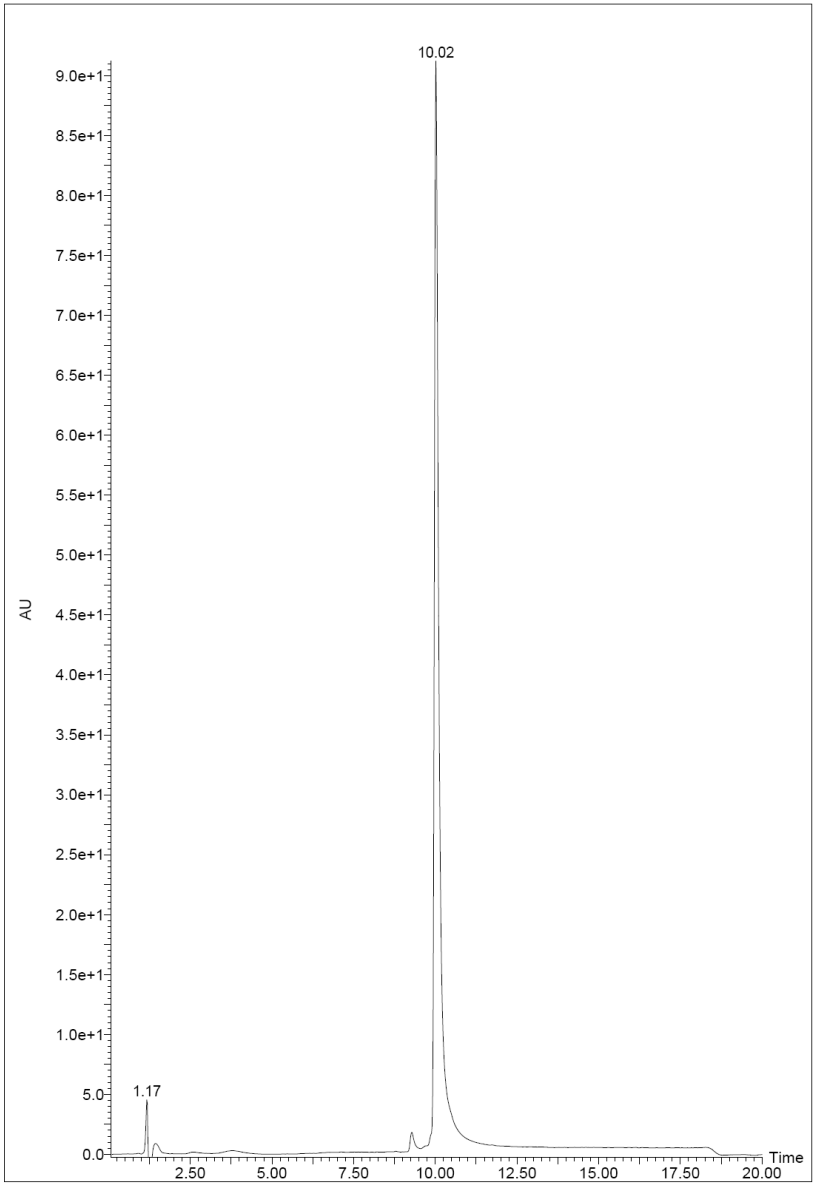
(*E*)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy) methyl)phenyl)boronic acid (*E*-**28**): ^{1}H NMR

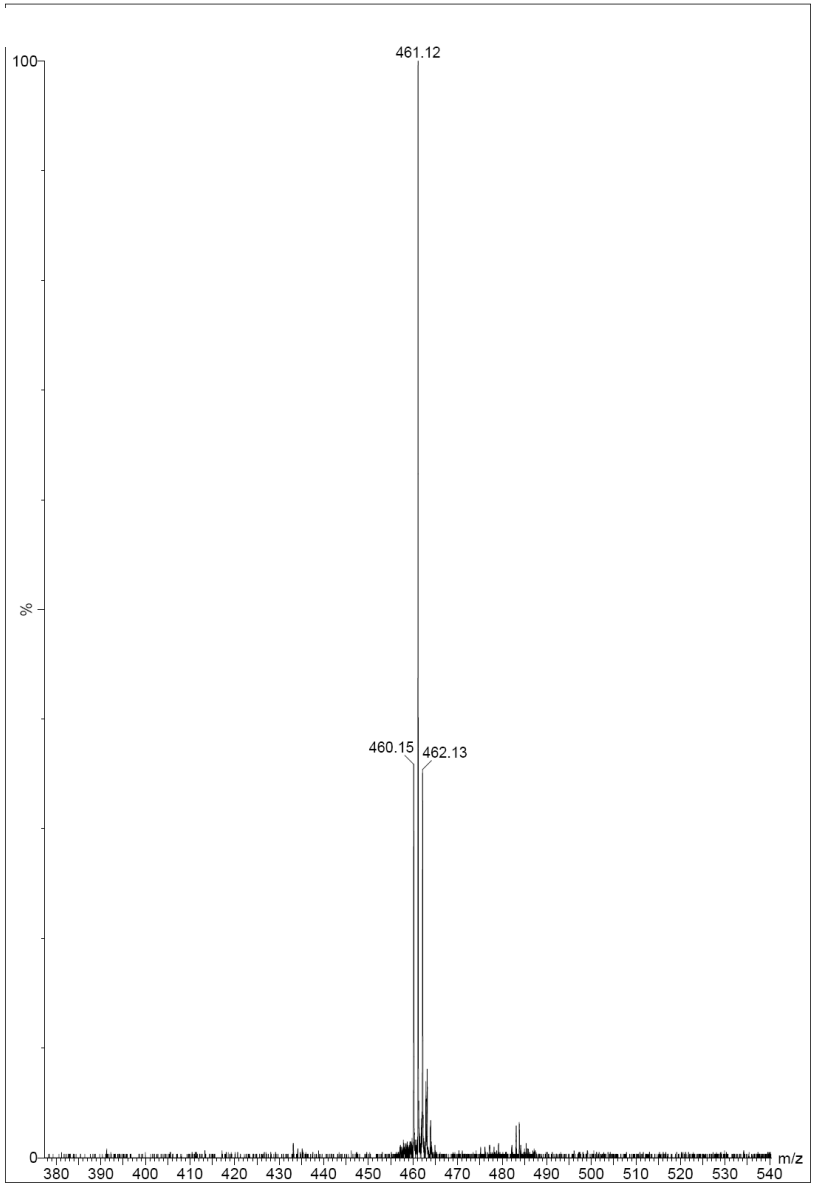


(*E*)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy) methyl)phenyl)boronic acid (*E*-**28**): ^{13}C NMR

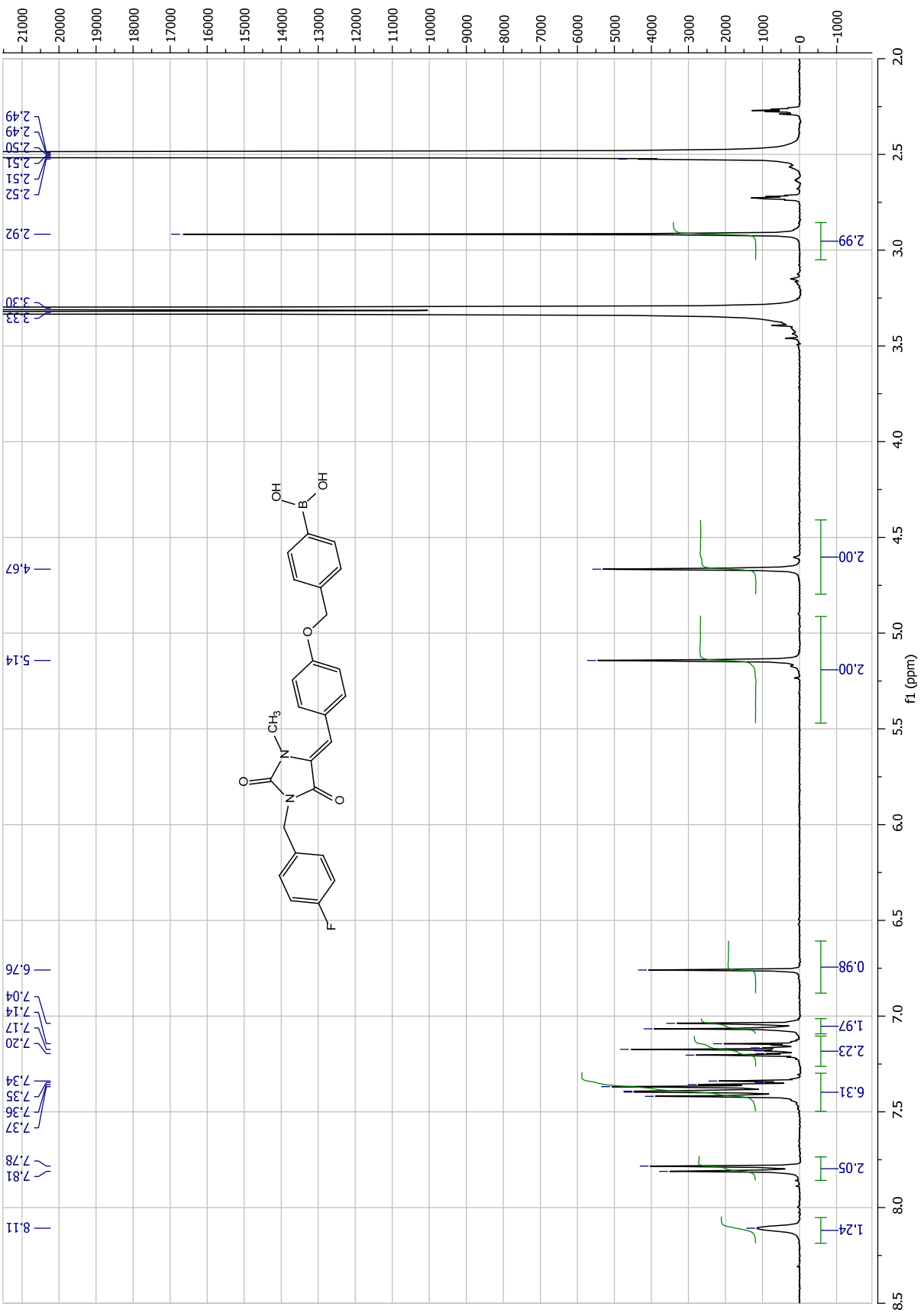


(*Z*)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy) methyl)phenyl)boronic acid (*Z*-**28**): LC-MS

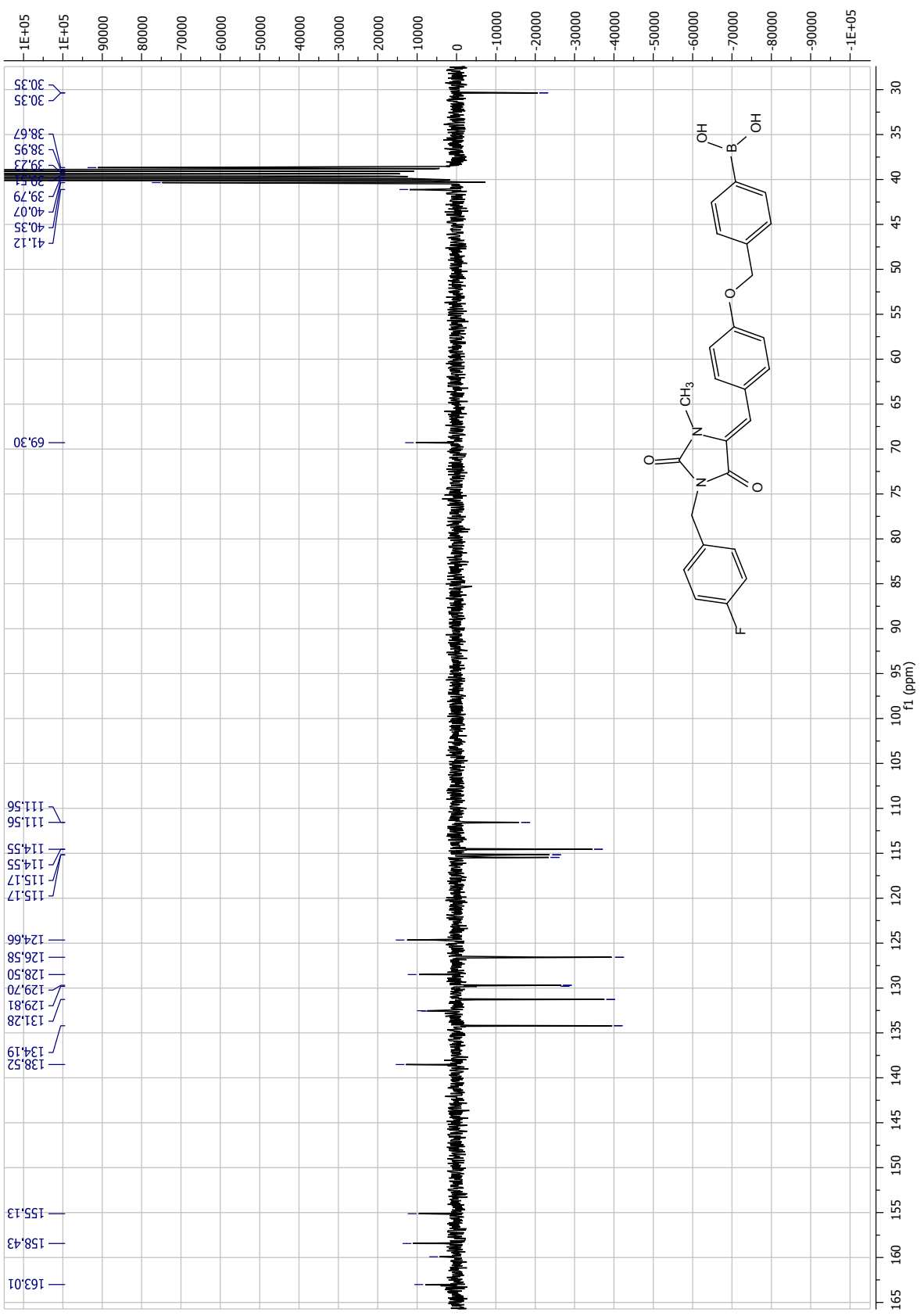




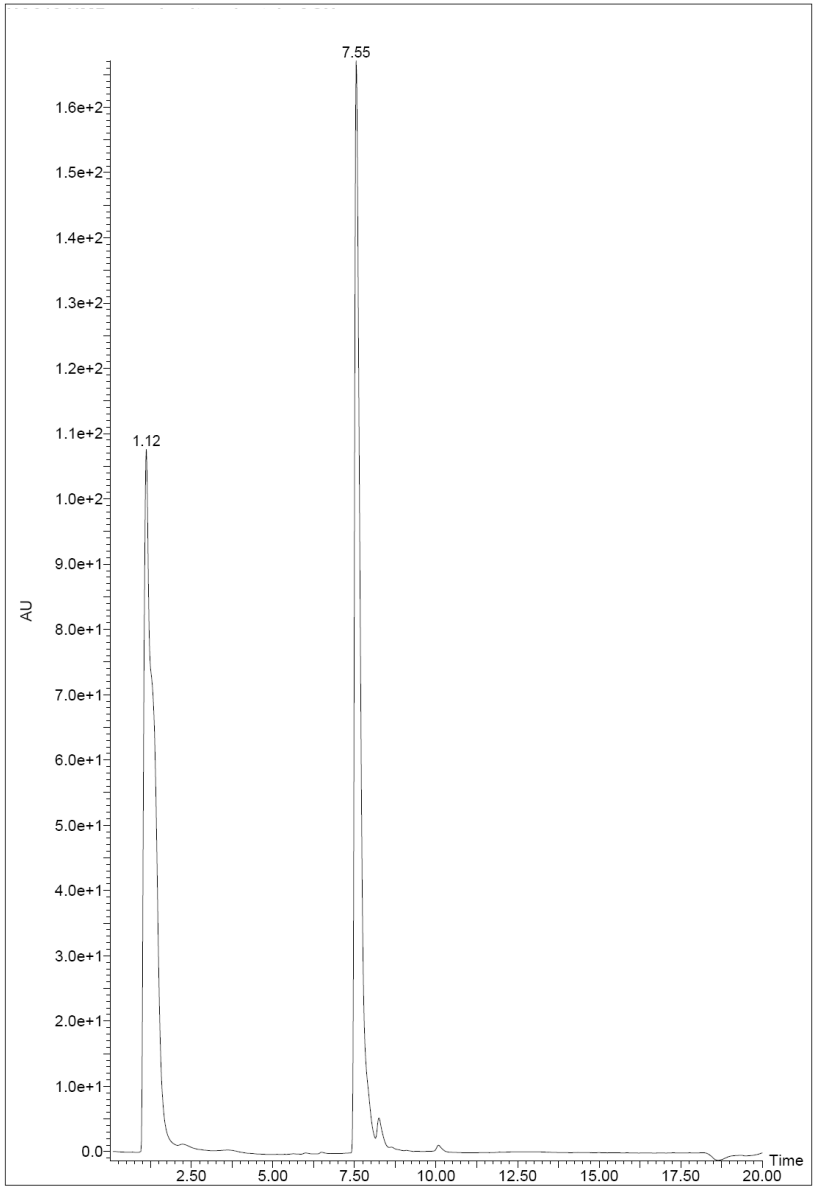
(Z)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy) methyl)phenyl)boronic acid (Z-**28**): ^{1}H NMR

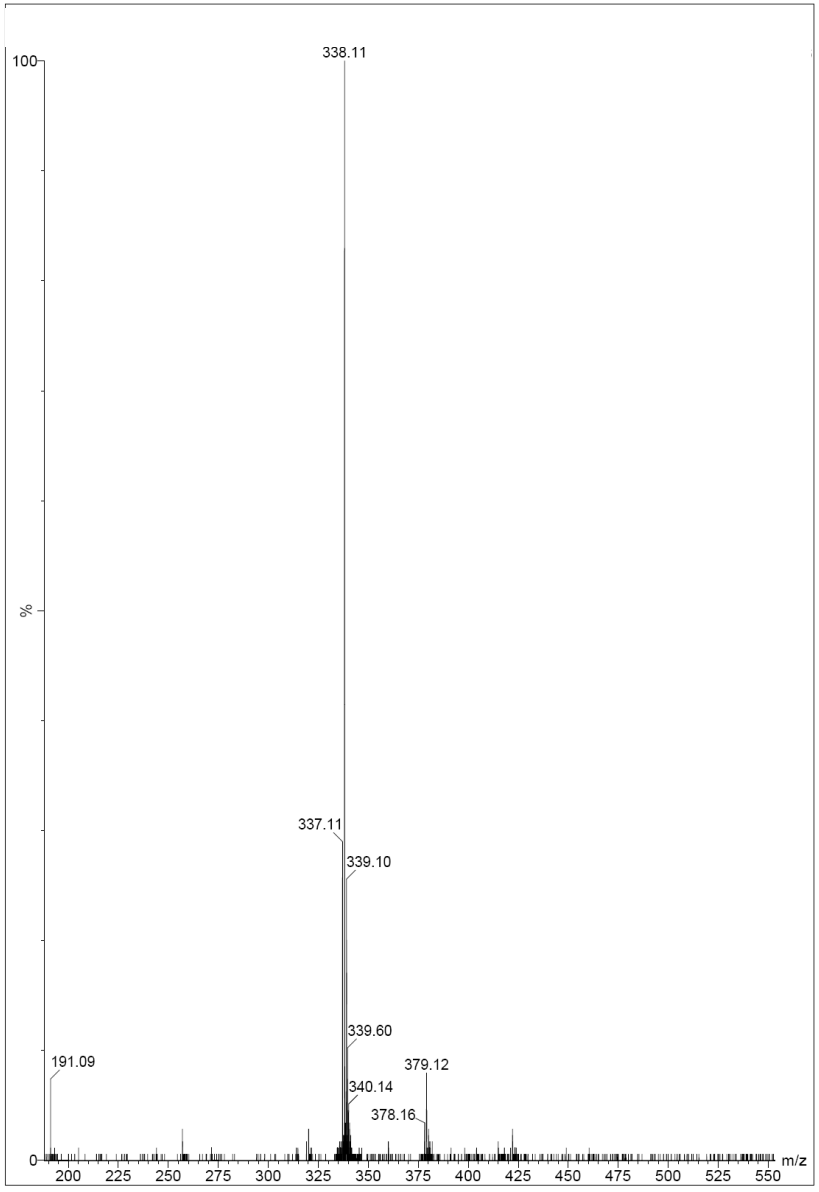


(Z)-(4-((4-((1-(4-fluorobenzyl)-3-methyl-2,5-dioxoimidazolidin-4-ylidene)methyl)phenoxy) methyl)phenyl)boronic acid (*Z*-**28**): ^{13}C NMR

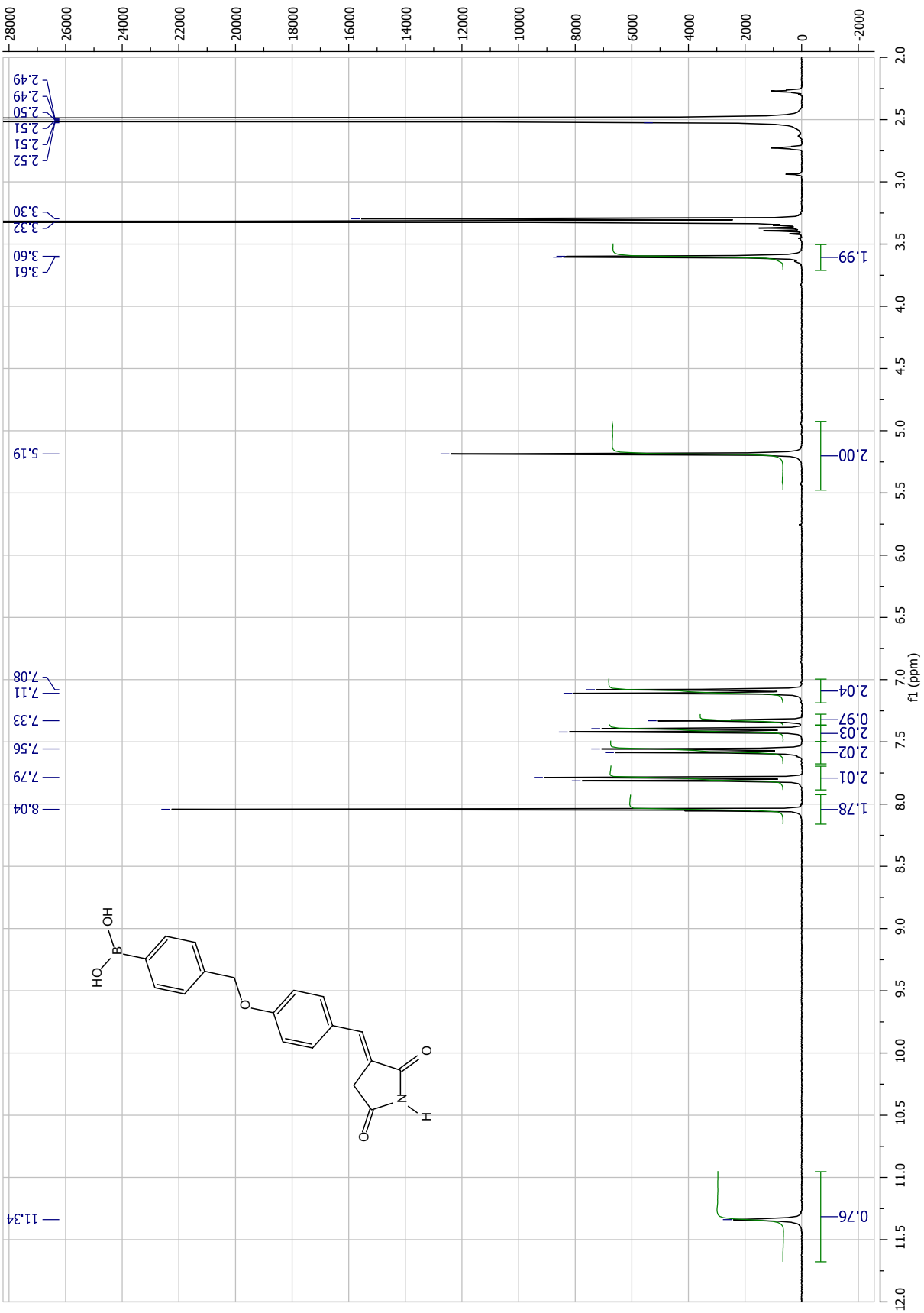


(*E*)-(4-((4-((2,5-dioxopyrrolidin-3-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**31**): LC-MS

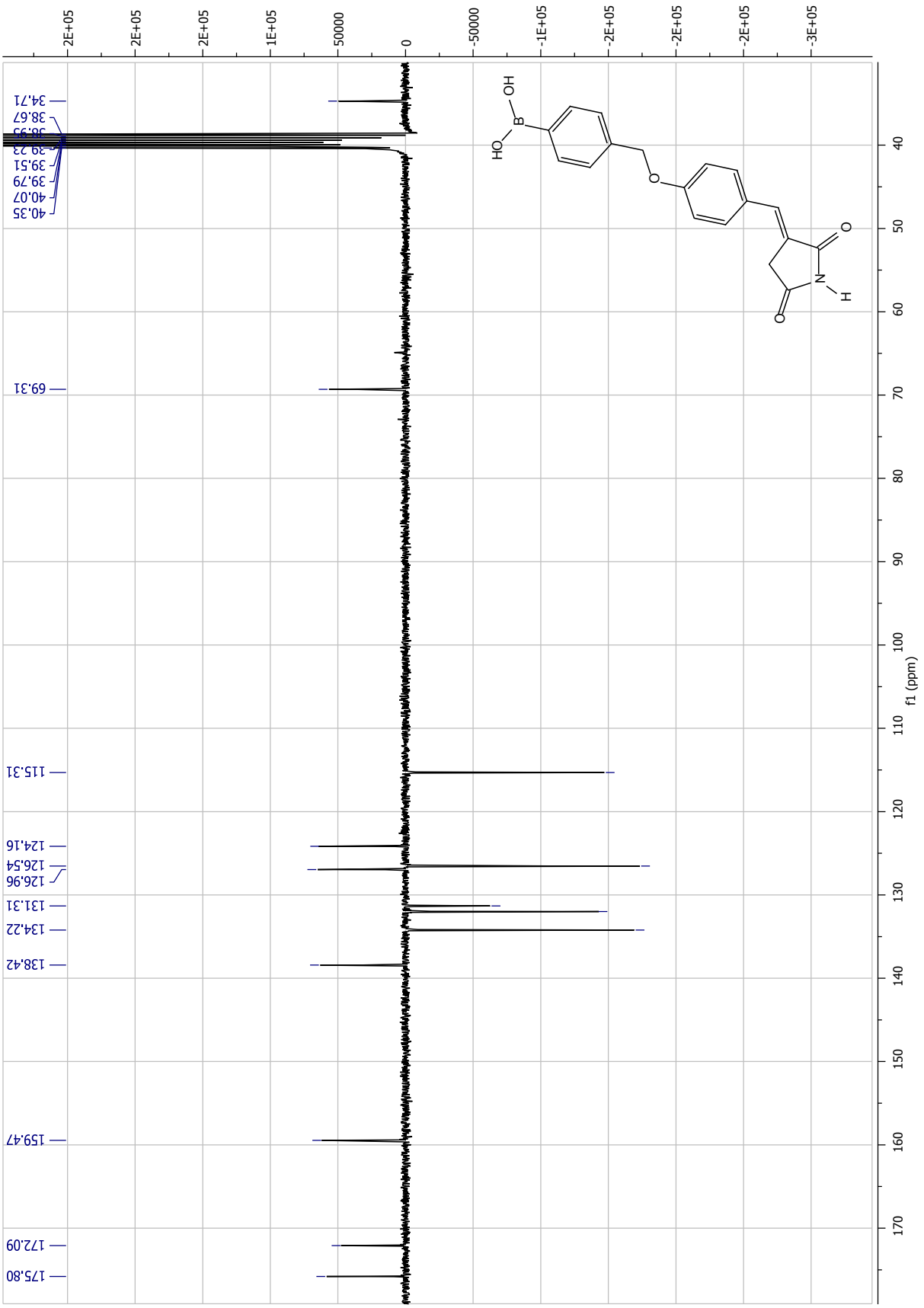




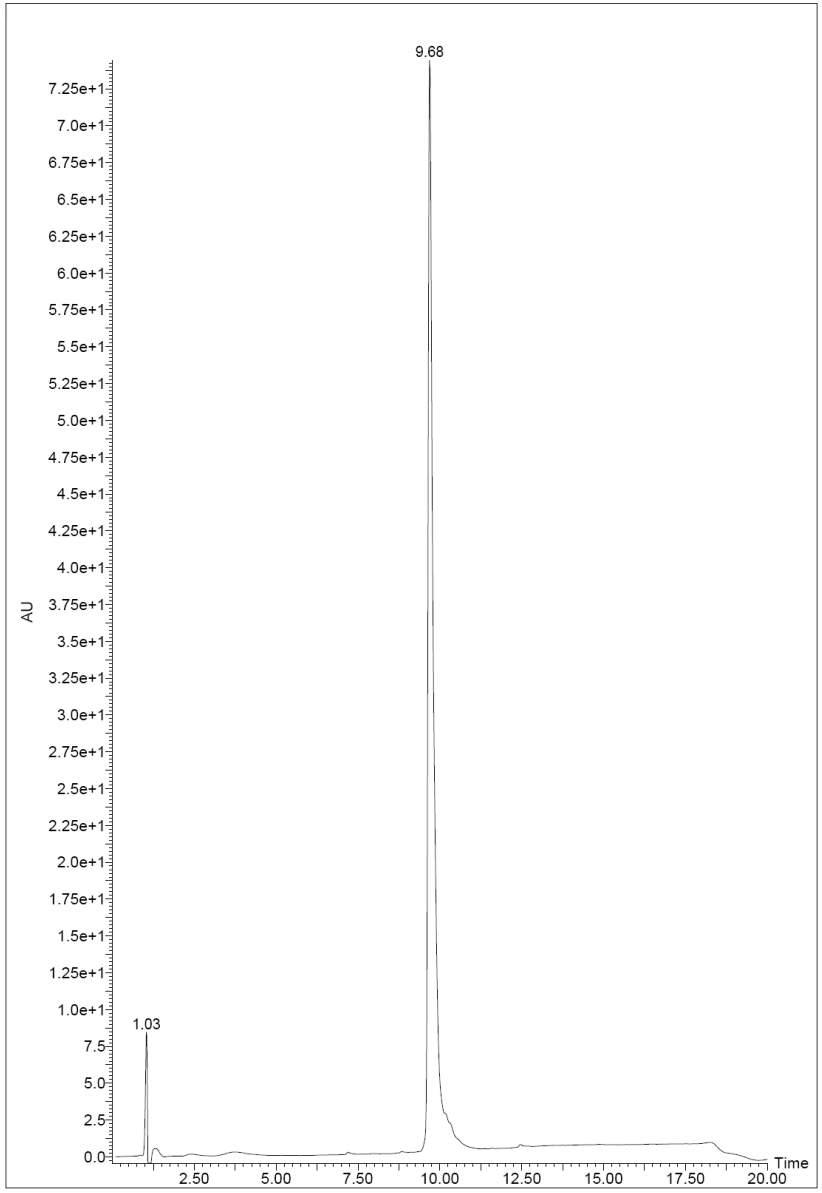
(*E*)-(4-(4-((2,5-dioxopyrrolidin-3-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**31**): ^{1}H NMR

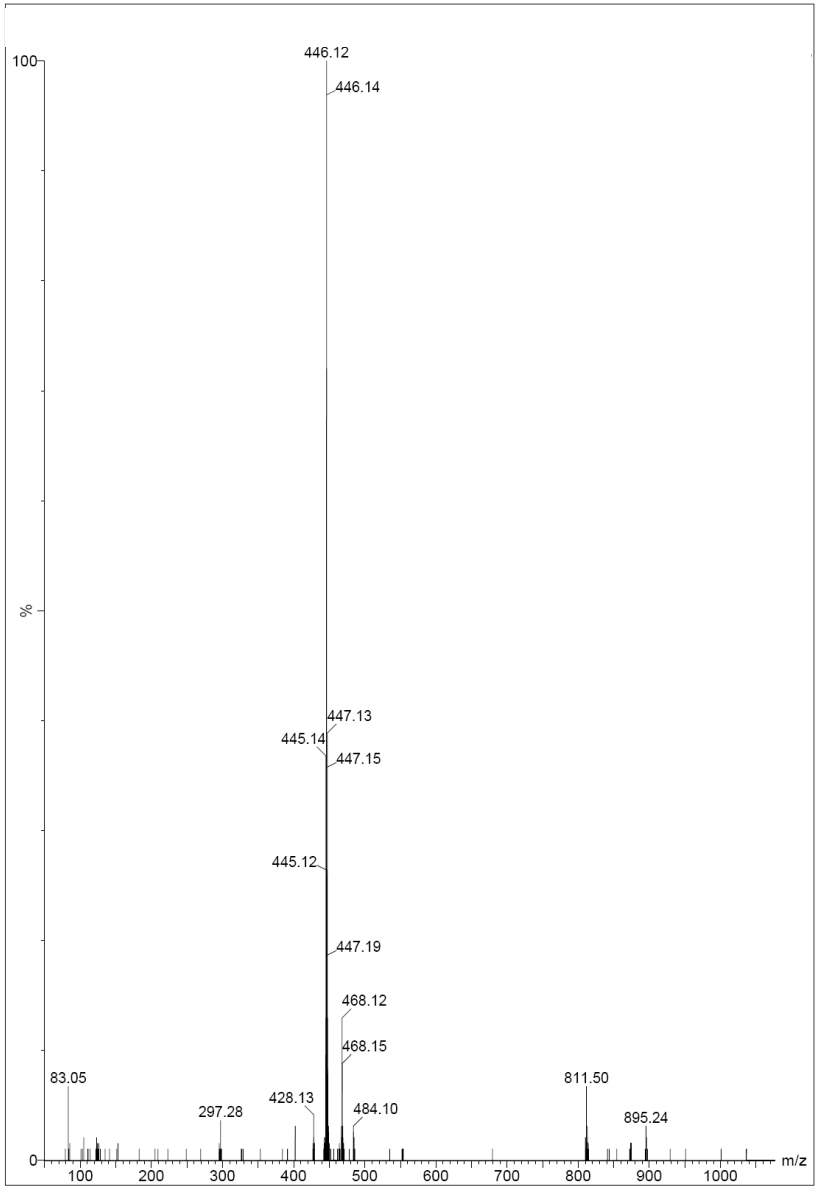


(*E*)-(4-((4-((2,5-dioxopyrrolidin-3-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**31**): ^{13}C NMR

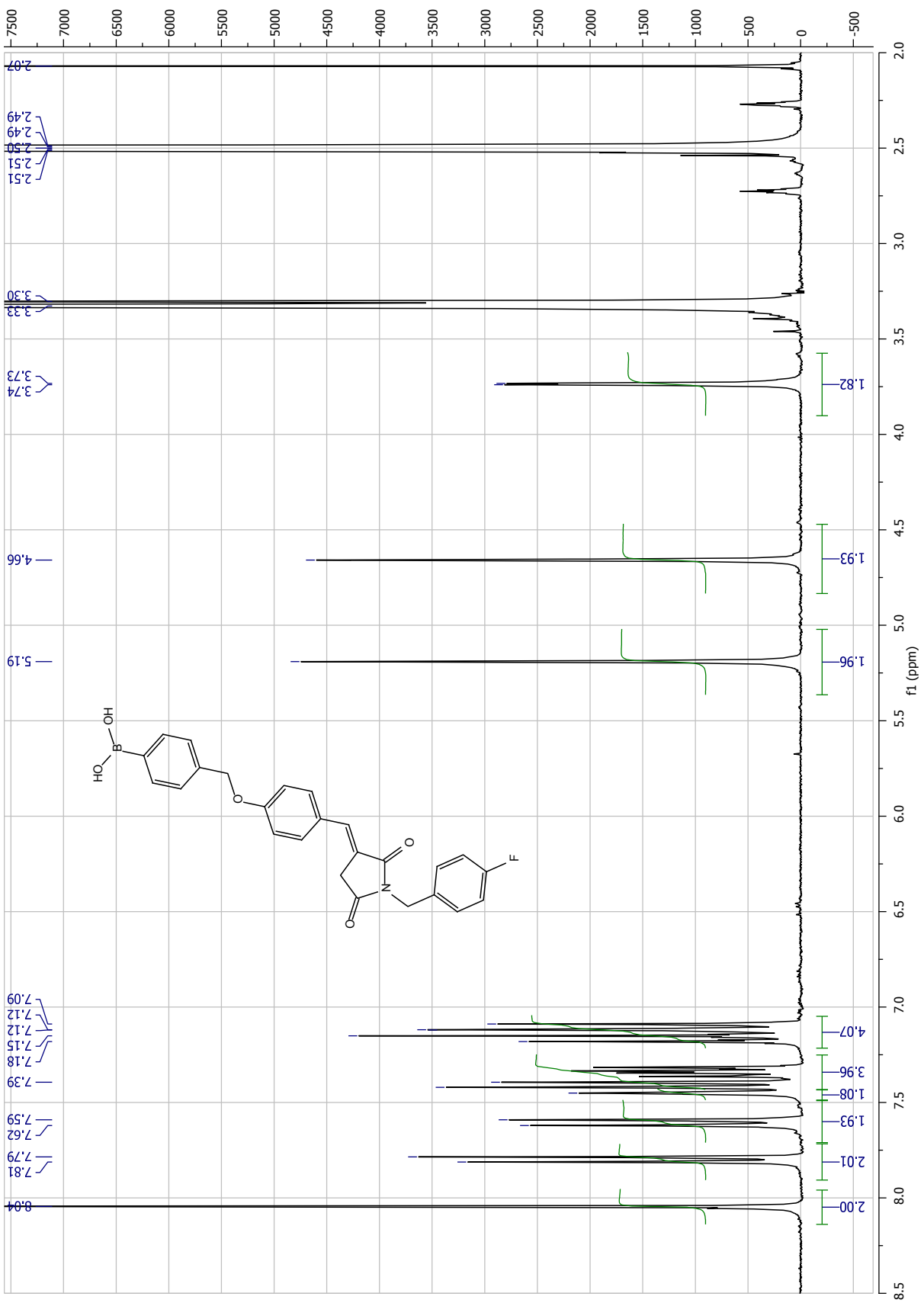


(*E*)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxopyrrolidin-3-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**32**): LC-MS

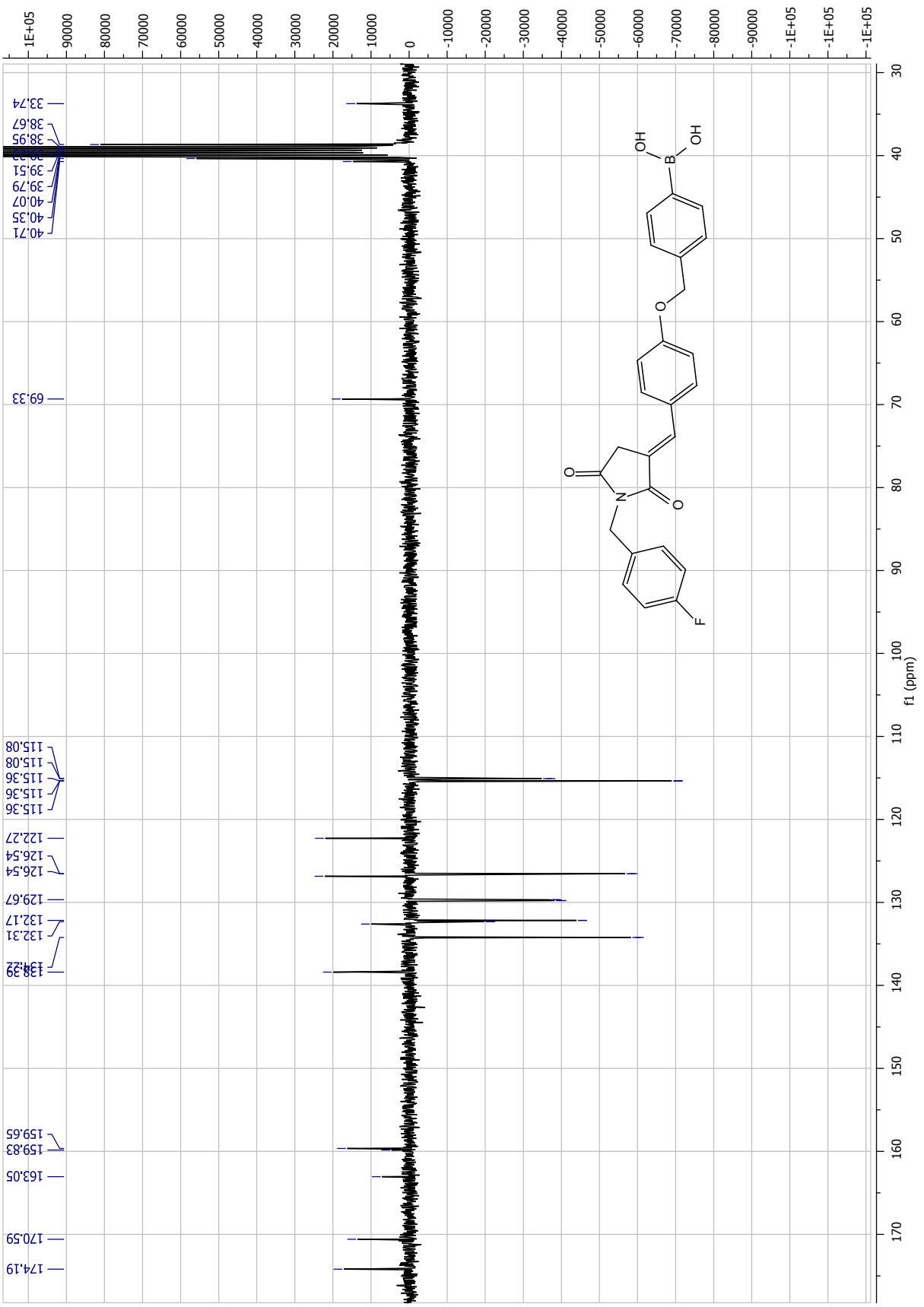




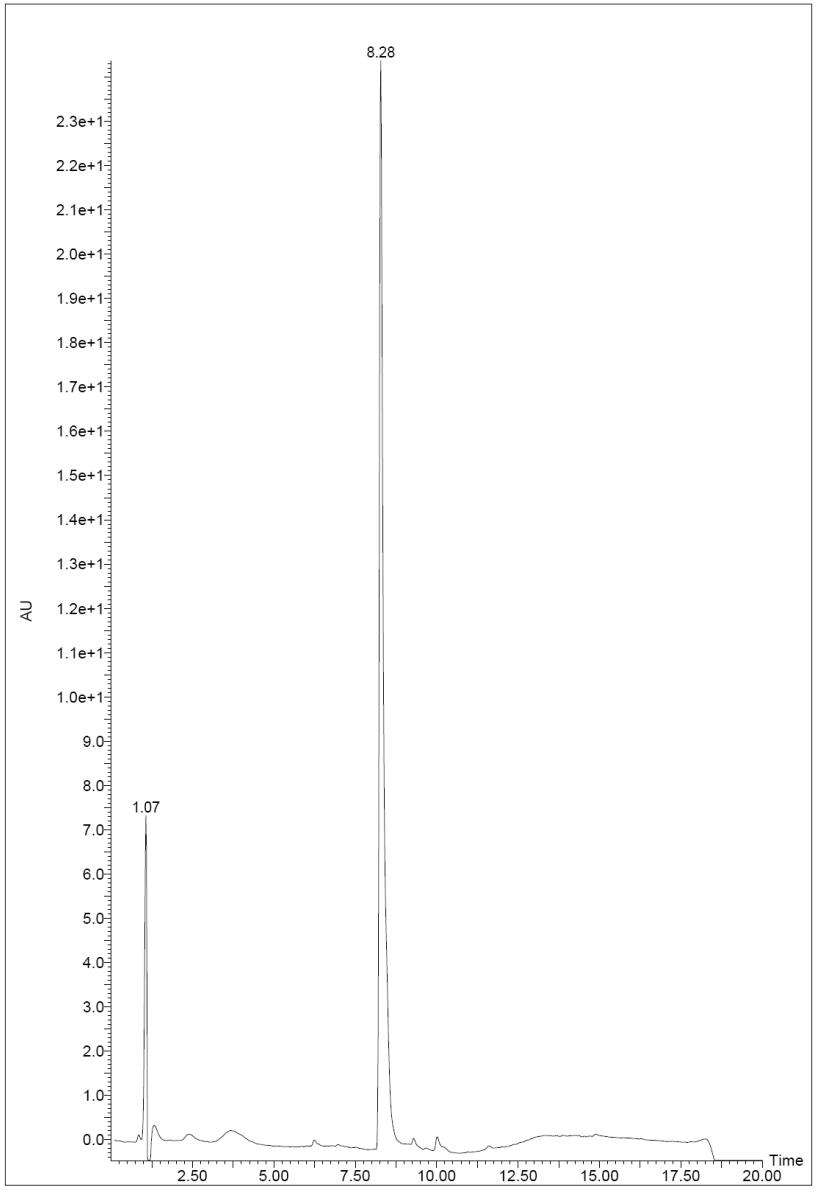
(*E*)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxopyrrolidin-3-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**32**): ^{1}H NMR

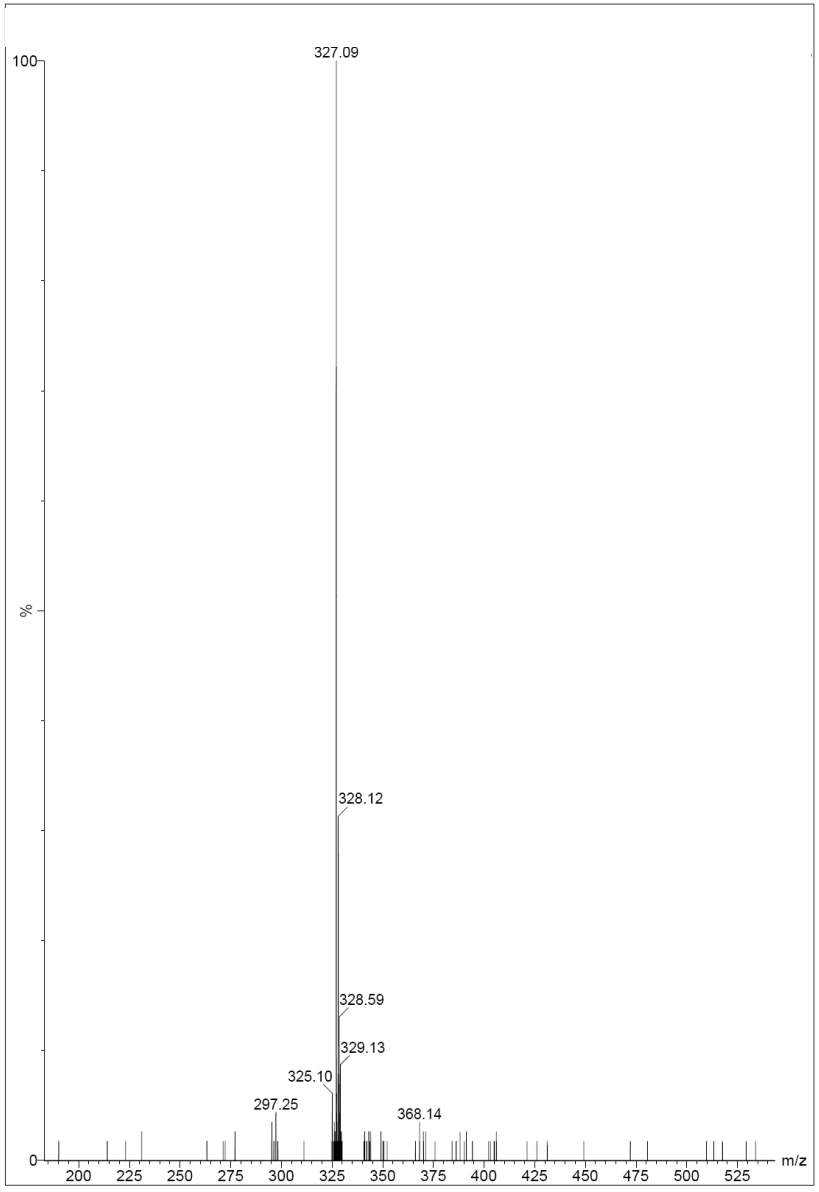


(*E*)-(4-((4-((1-(4-fluorobenzyl)-2,5-dioxopyrrolidin-3-ylidene)methyl)phenoxy)methyl)phenyl)boronic acid (**32**): ^{13}C NMR

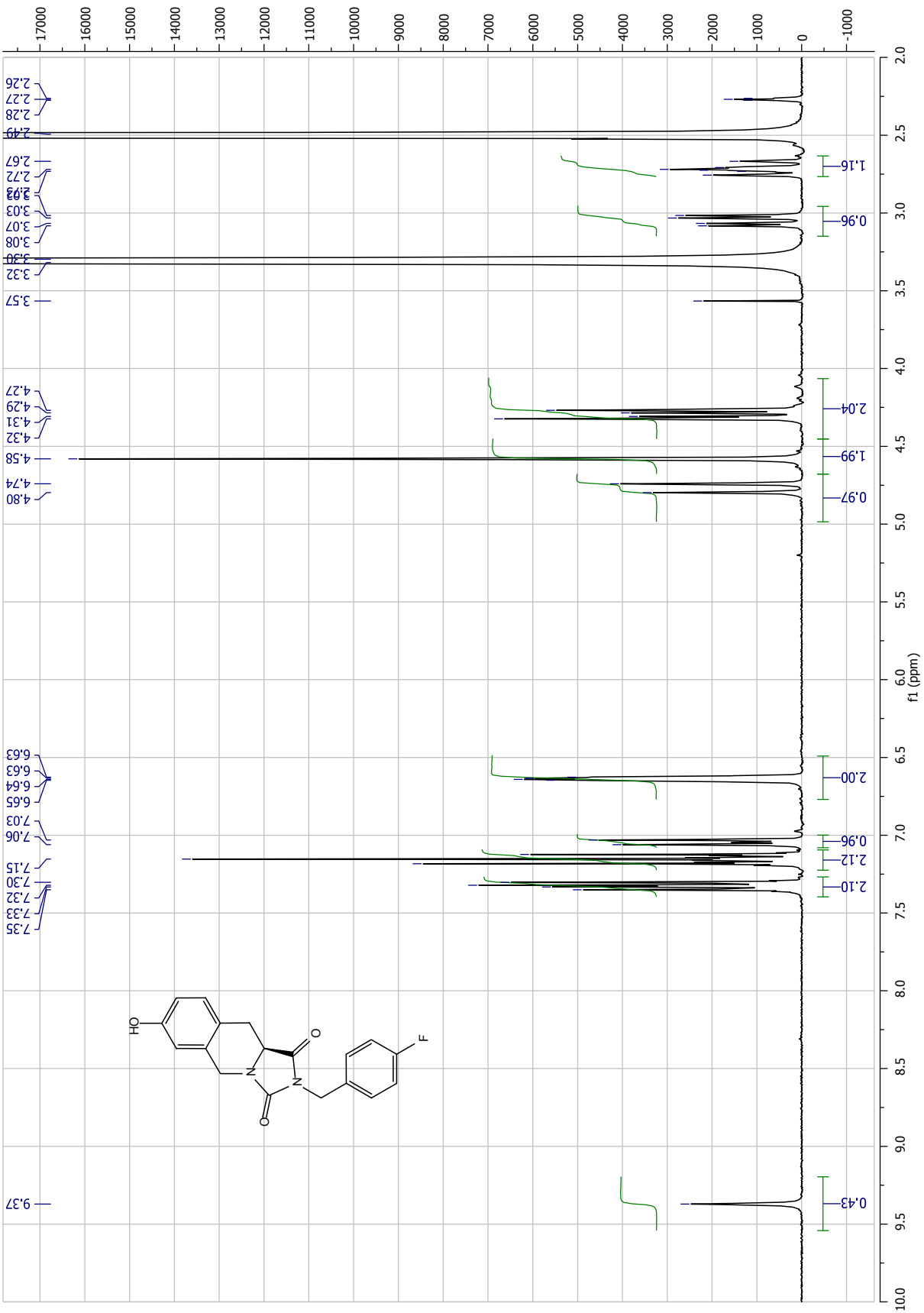


(*S*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(*2H*,*5H*)-dione (*S*-**34**): LC-MS

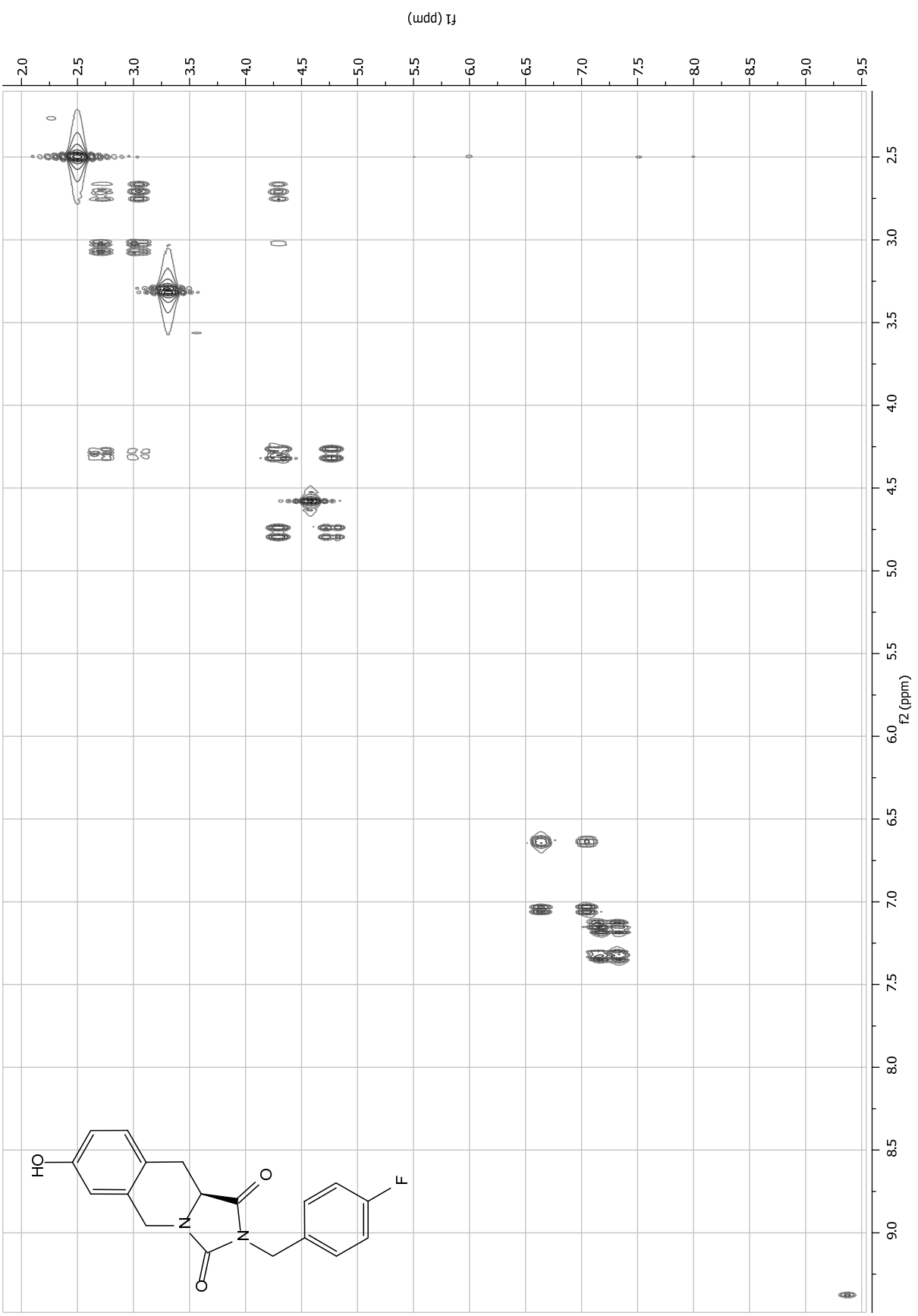




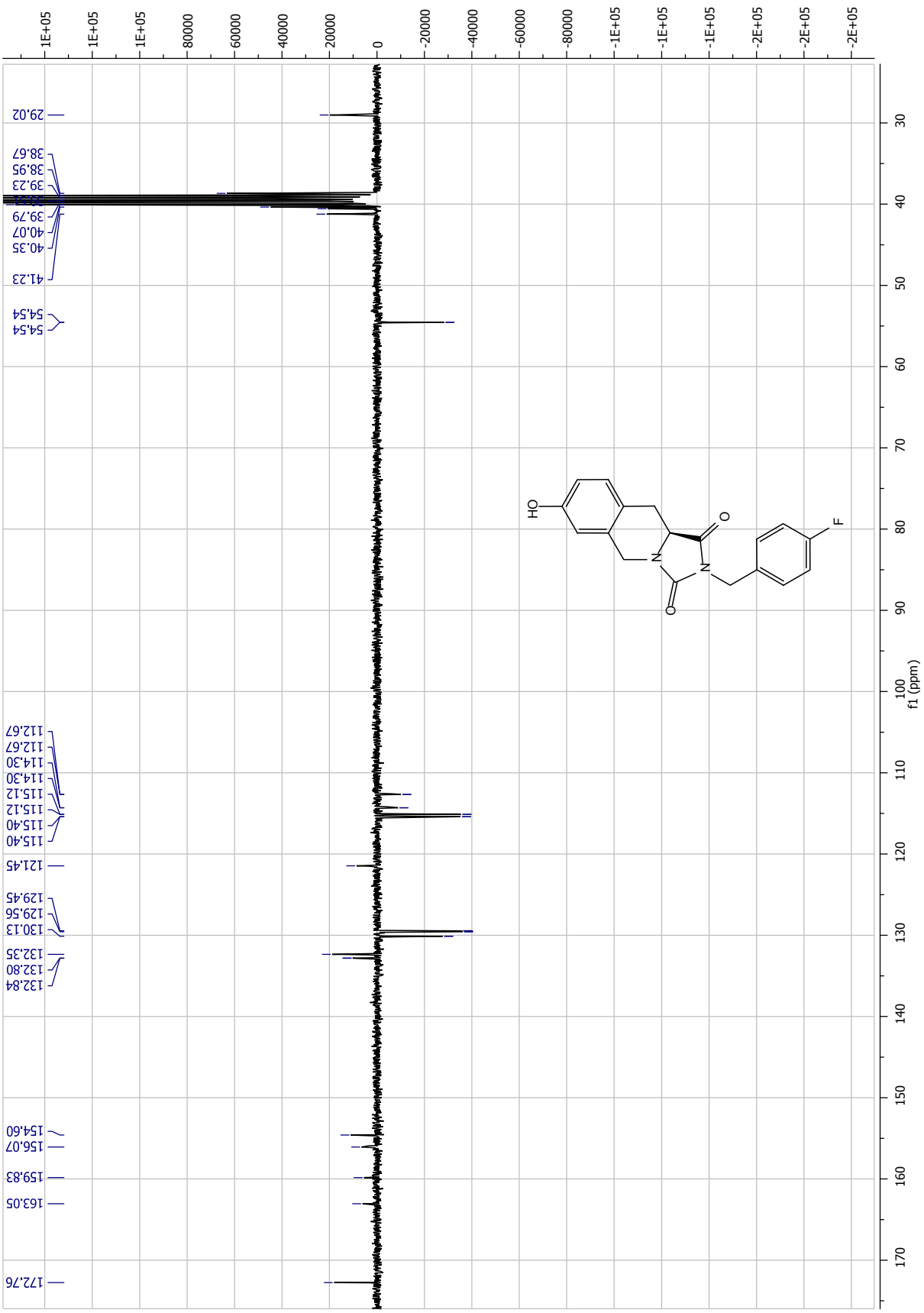
(*S*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(2*H*,5*H*)-dione (*S*-**34**): ^{1}H NMR



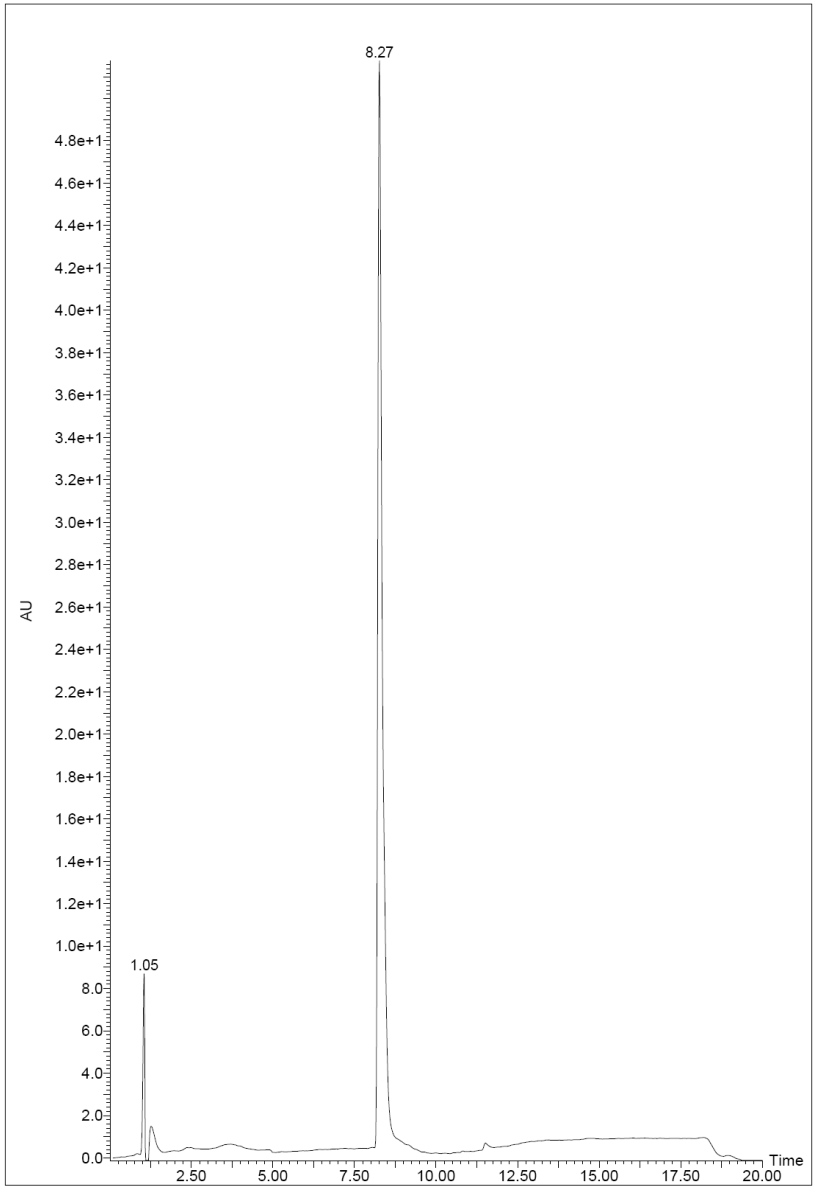
(*S*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(2*H*,5*H*)-dione (*S*-**34**): COSY

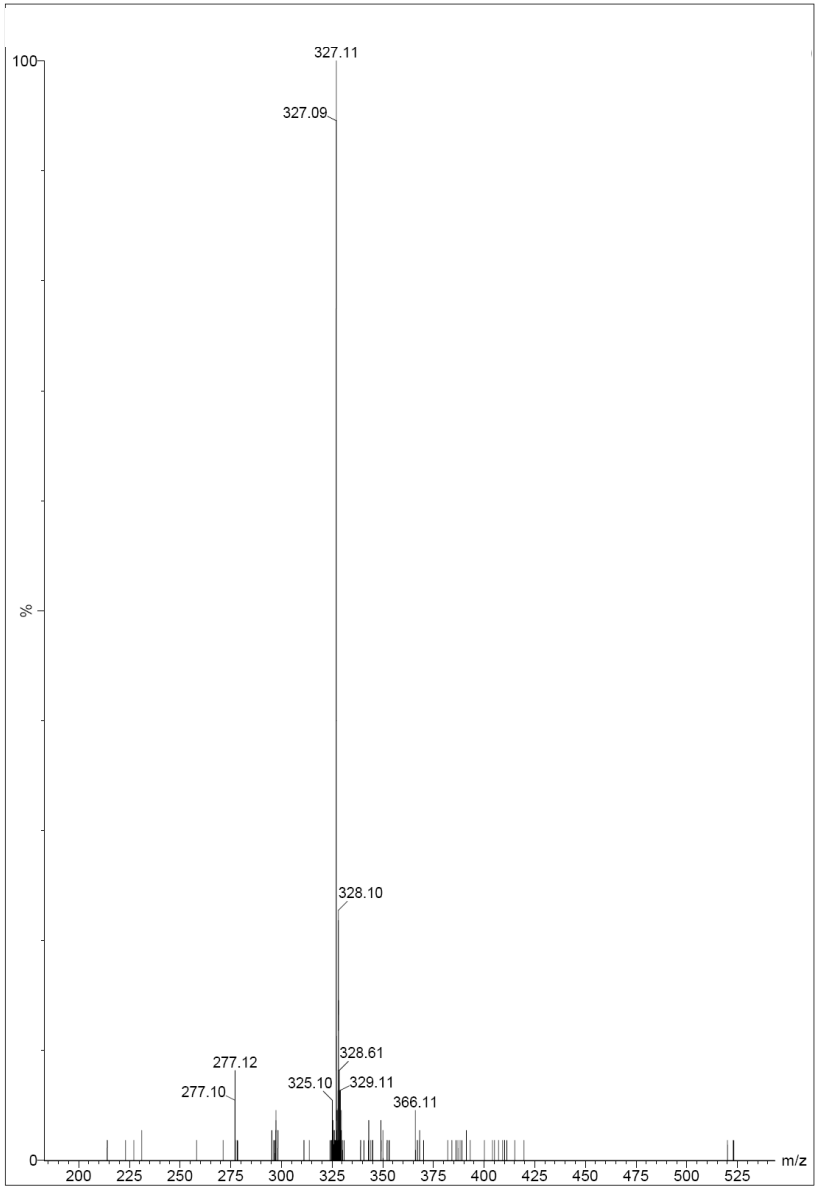


(*S*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(2*H*,5*H*)-dione (*S*-**34**): ^{13}C NMR

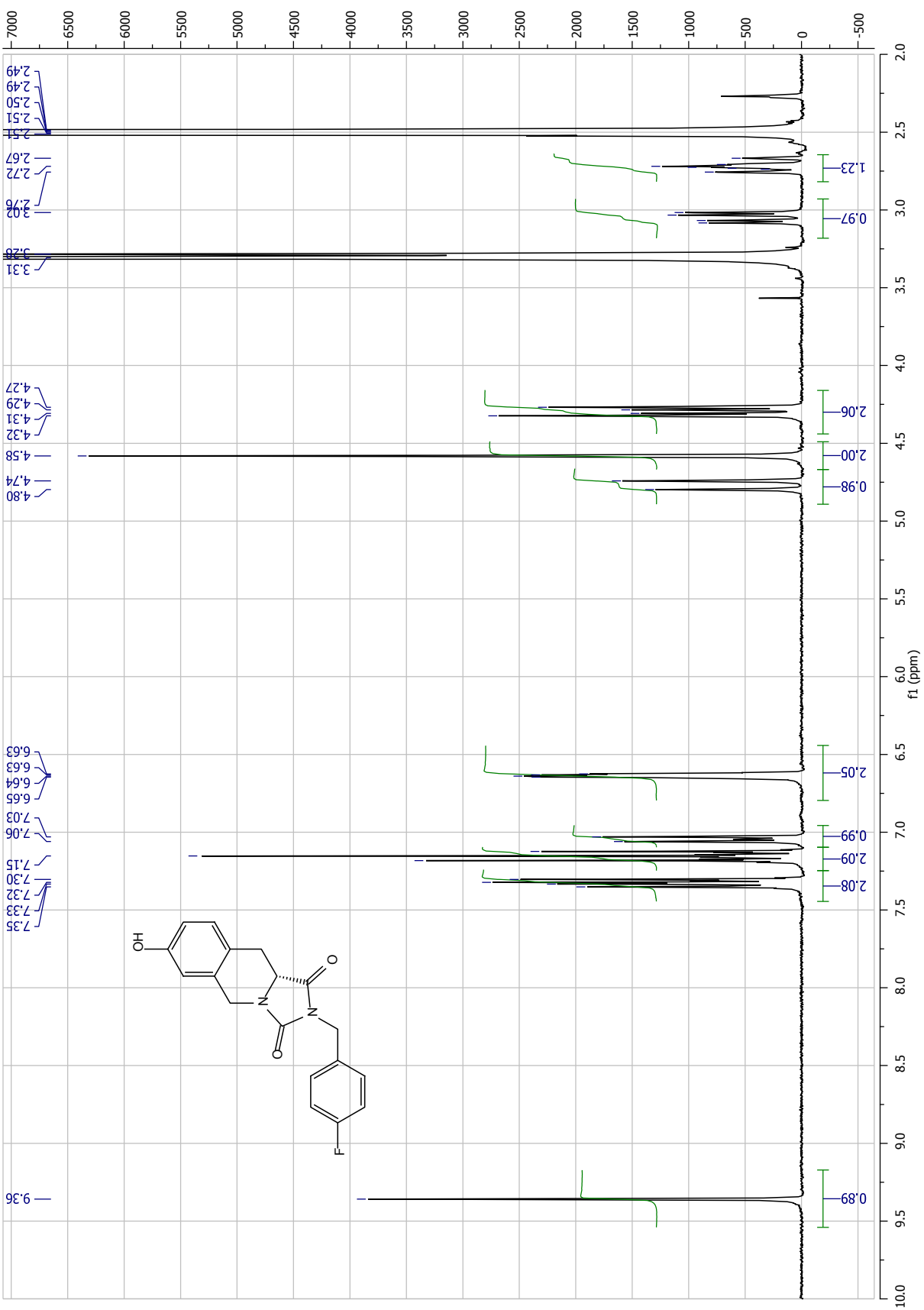


(*R*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(*2H*,*5H*)-dione (*R*-**34**): LC-MS

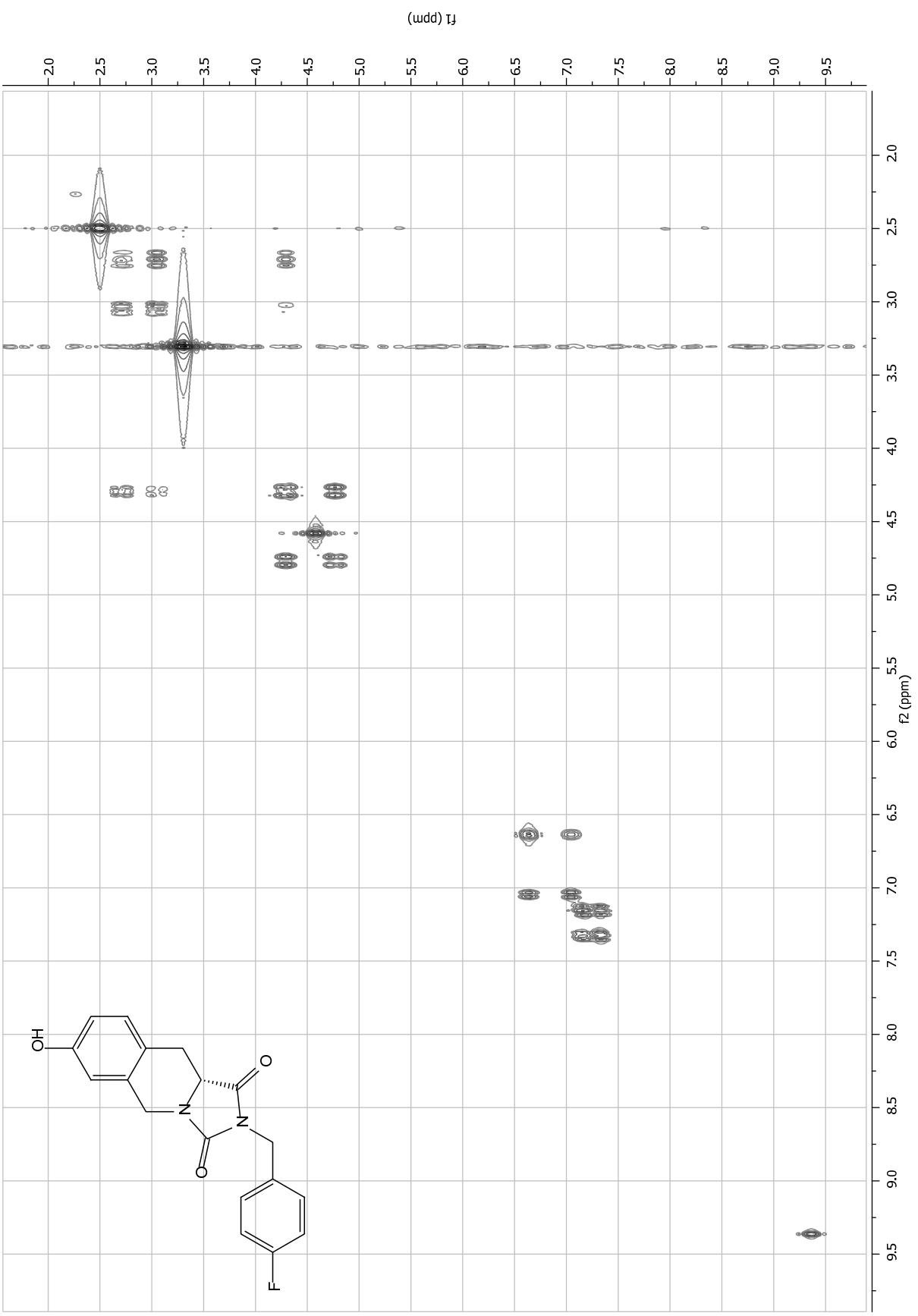




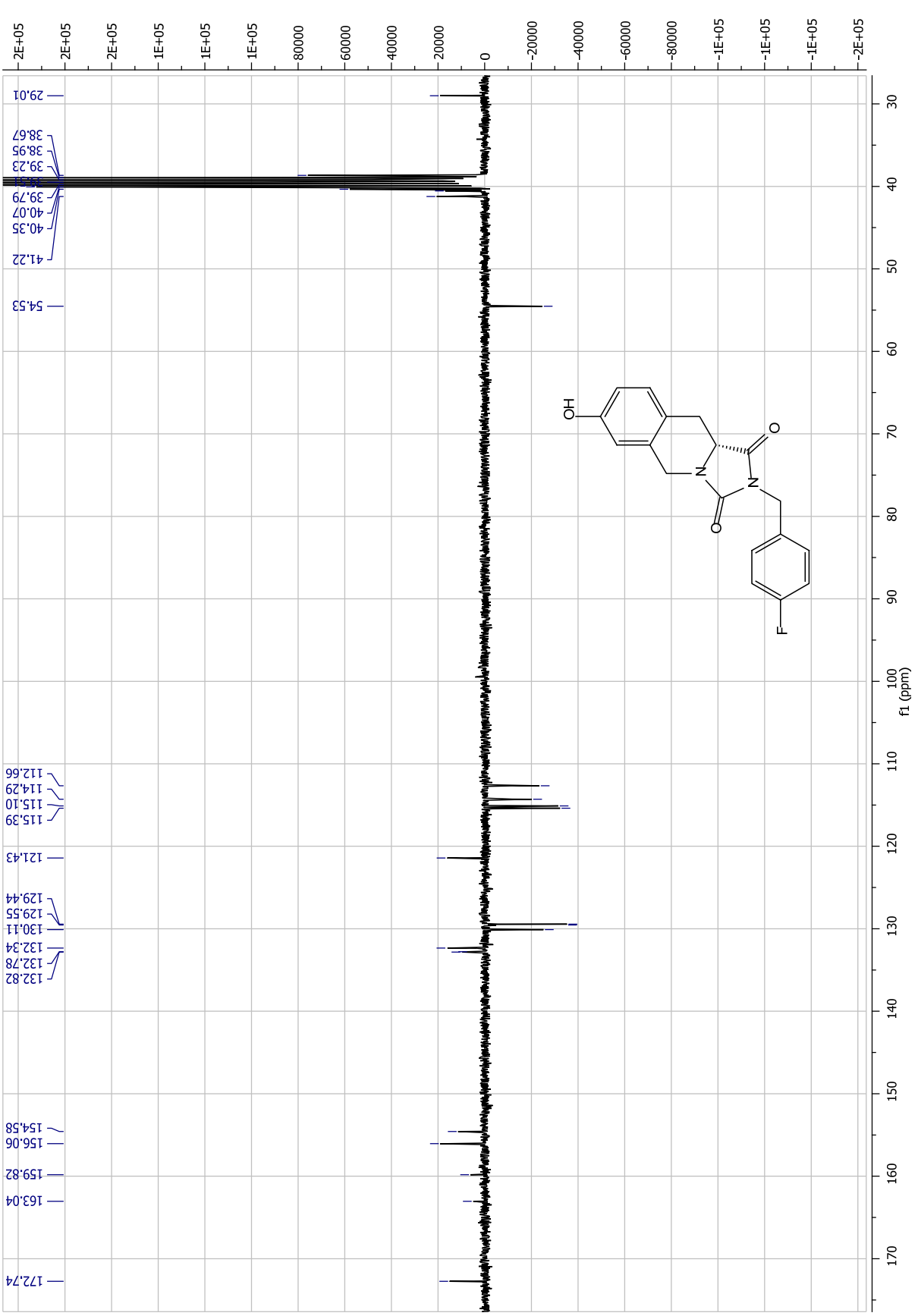
(*R*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(2*H*,5*H*)-dione (*R*-**34**): ^{1}H NMR



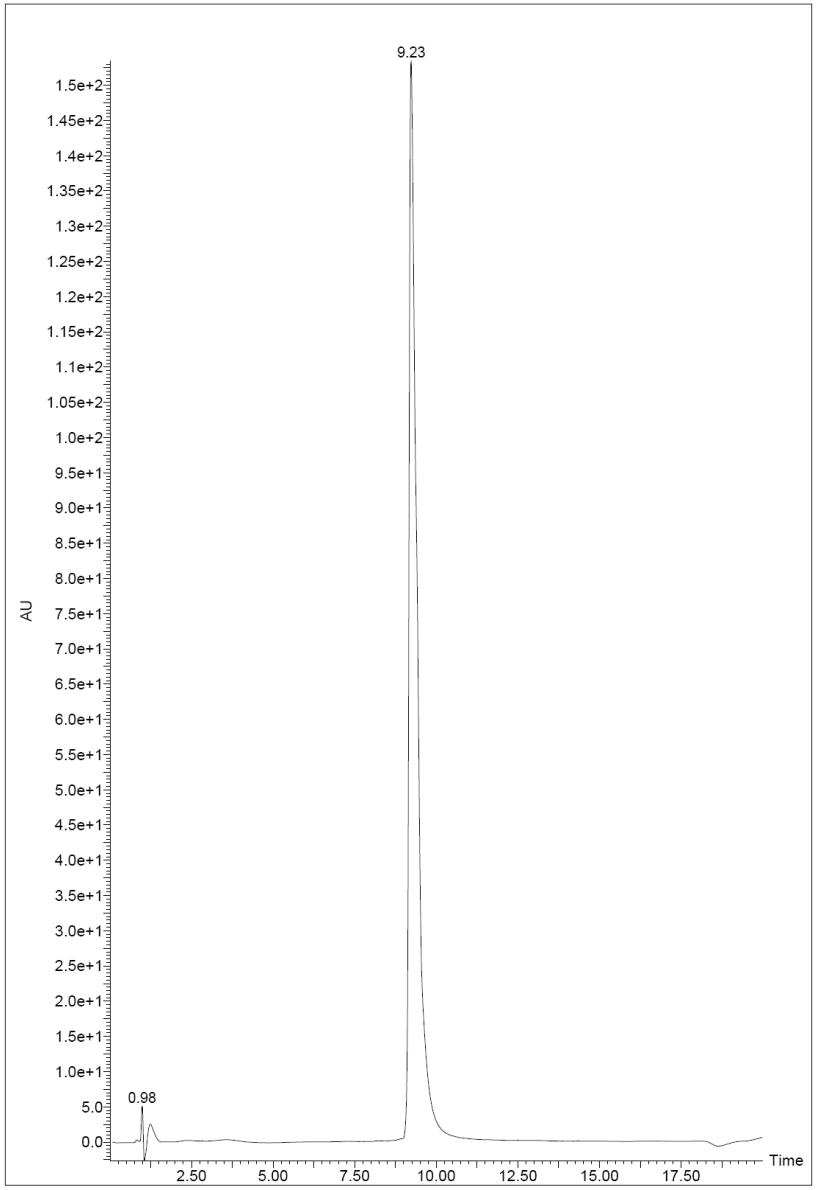
(*R*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(2*H*,5*H*)-dione (*R*-**34**): COSY

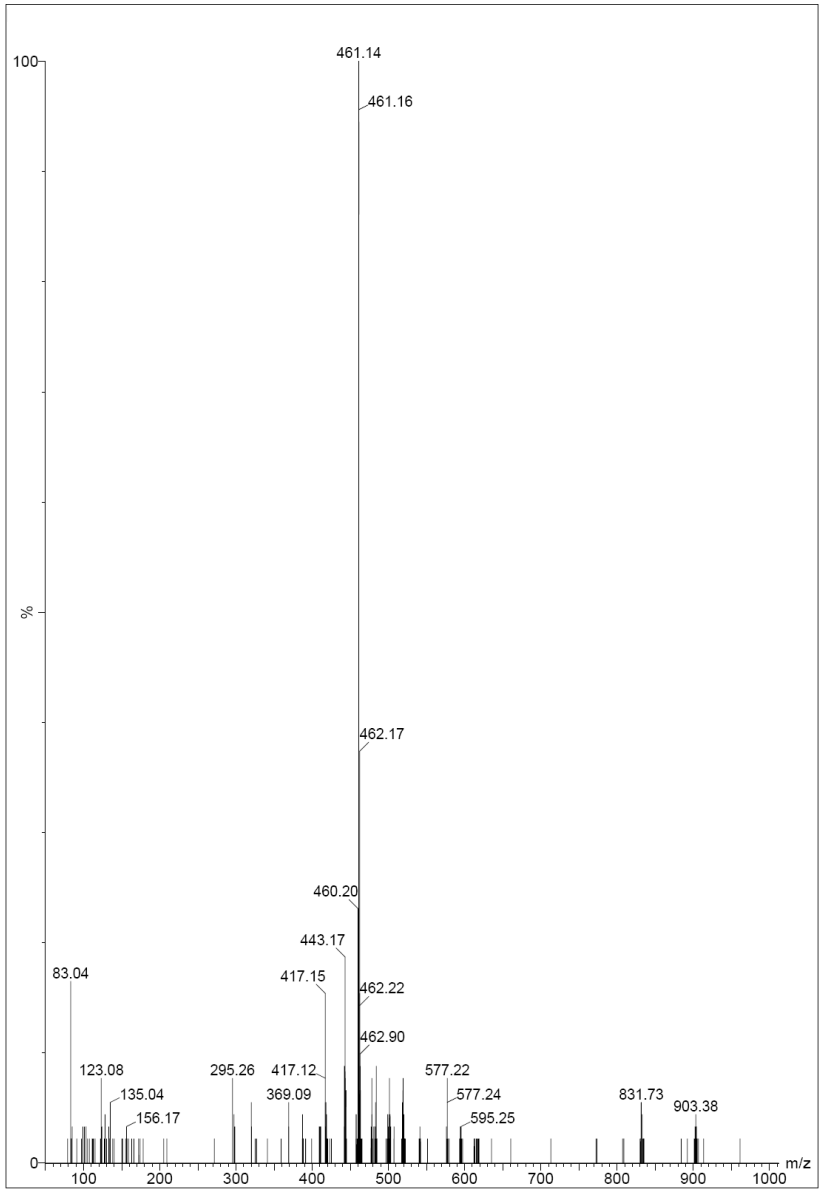


(*R*)-2-(4-fluorobenzyl)-7-hydroxy-10,10a-dihydroimidazo[1,5-*b*]isoquinoline-1,3(2*H*,5*H*)-dione (*R*-**34**): ^{13}C NMR

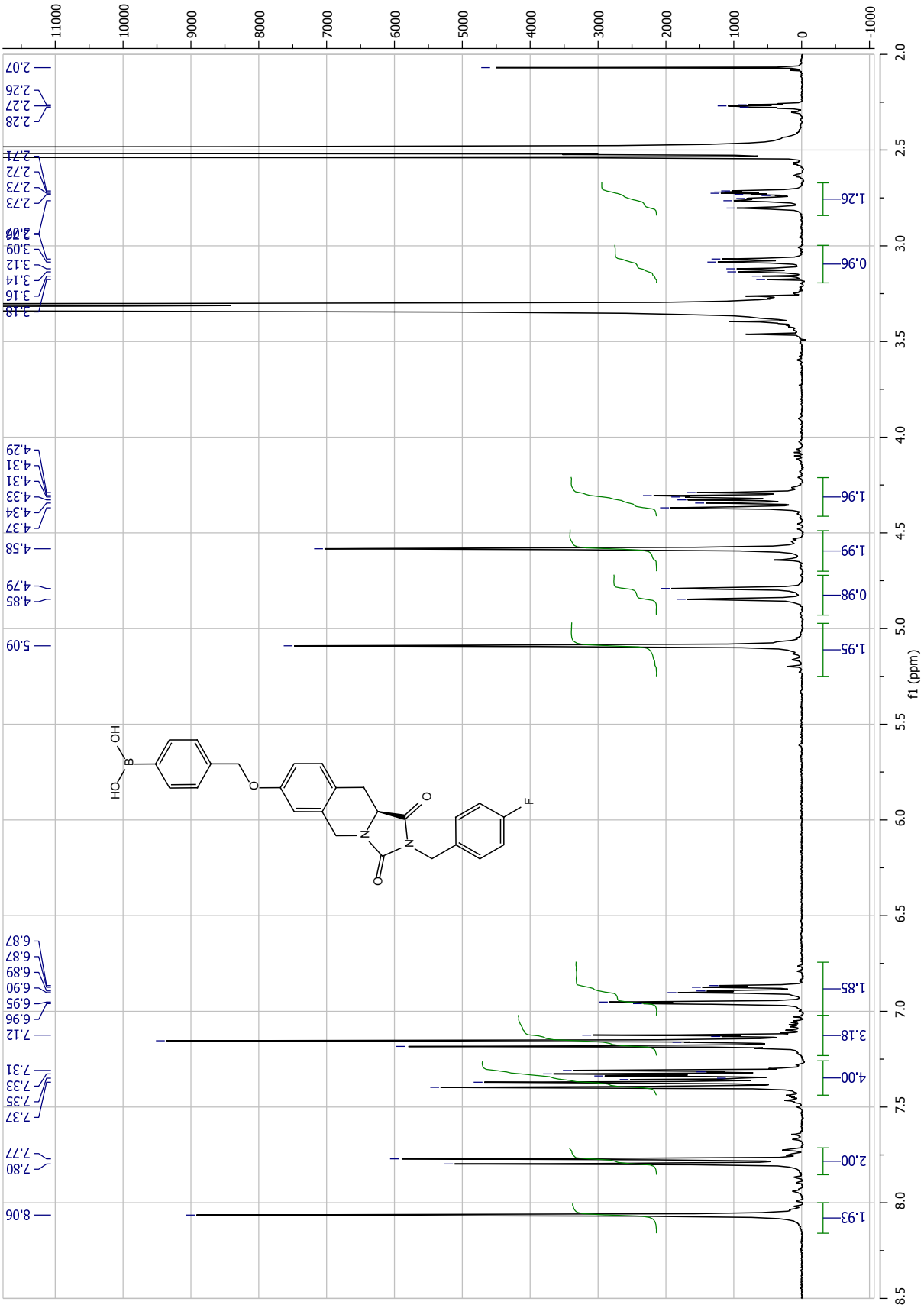


(*S*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*S*-**35**): LC-MS

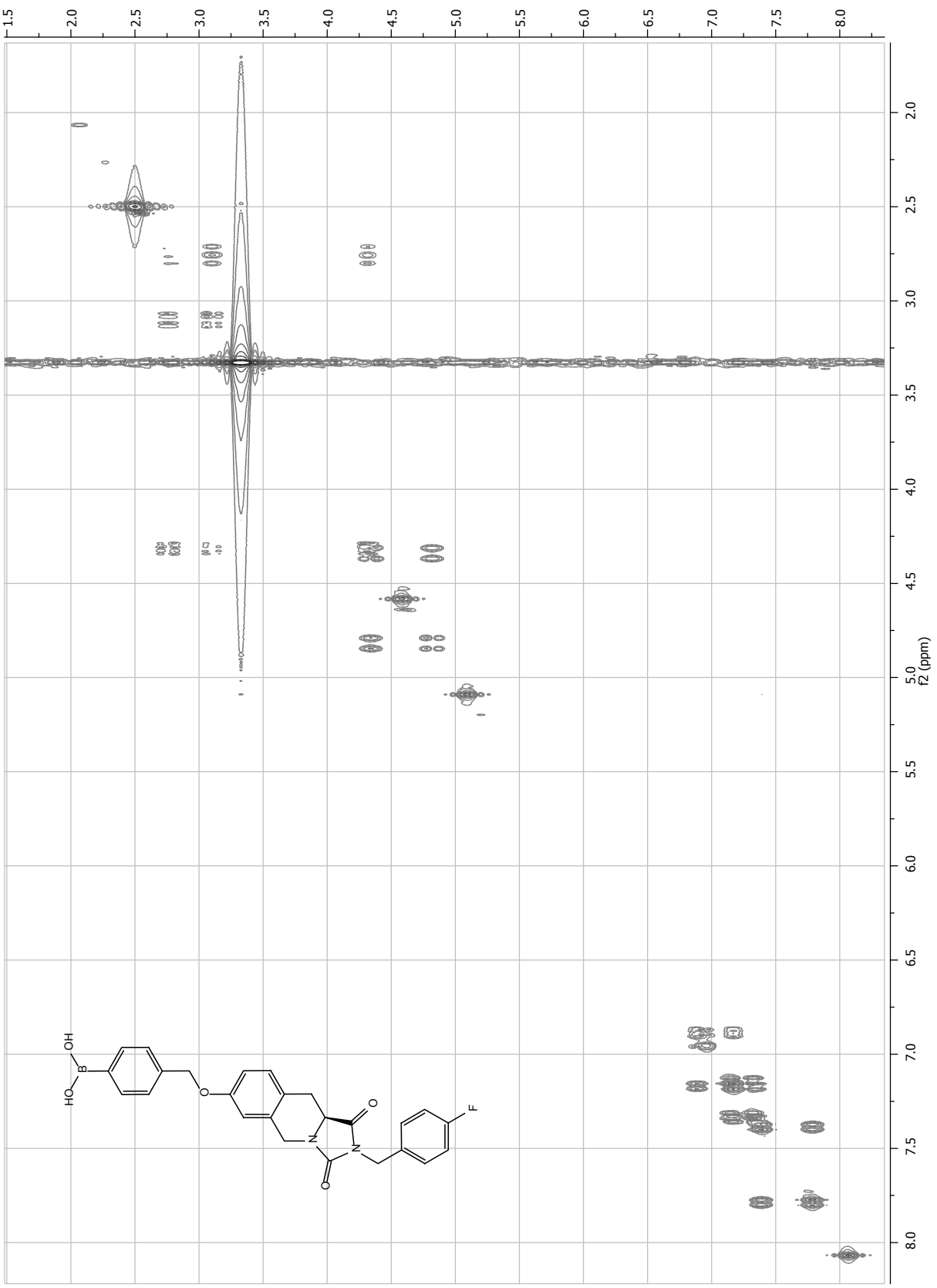




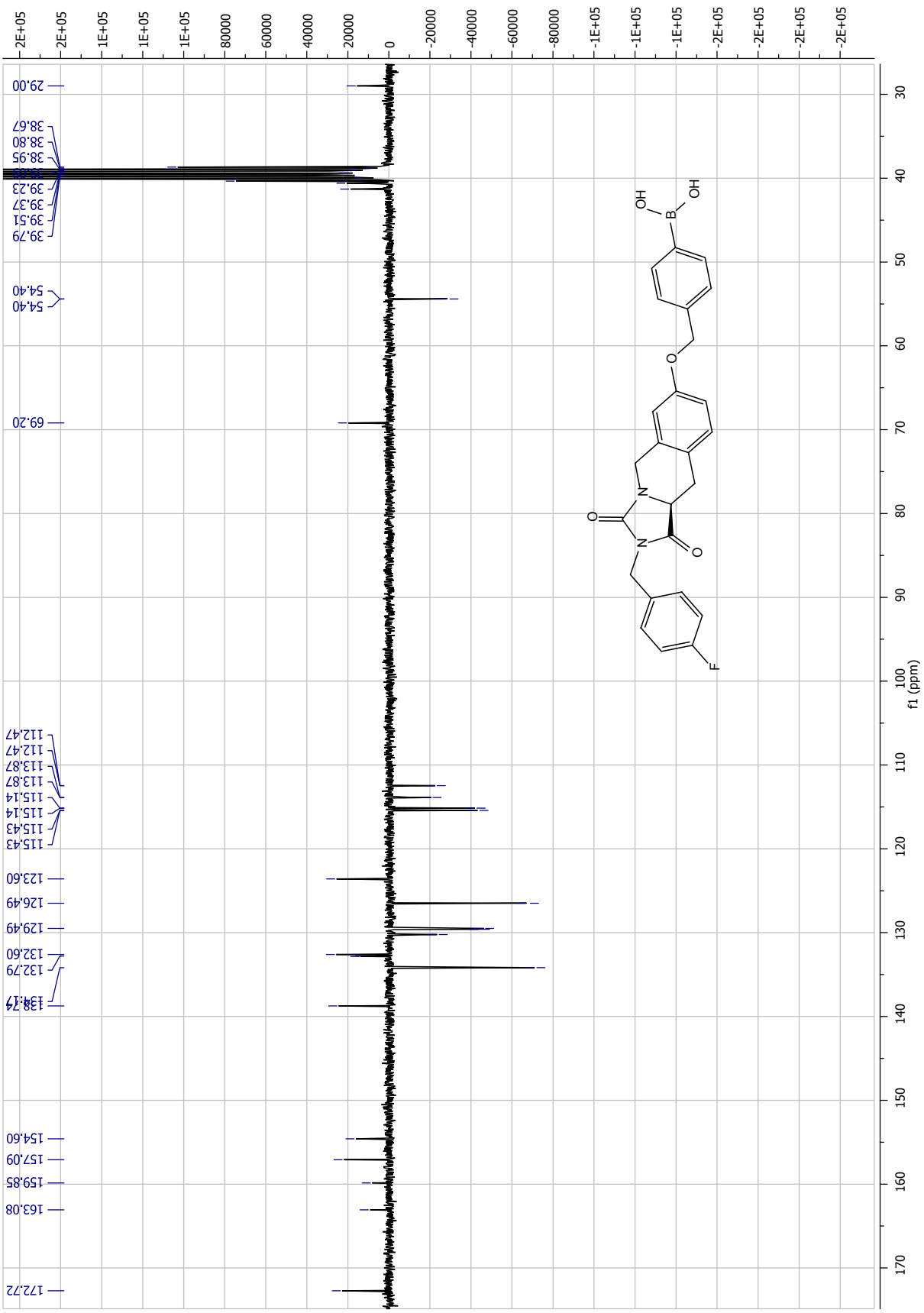
(*S*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*S*-**35**): ^{1}H NMR



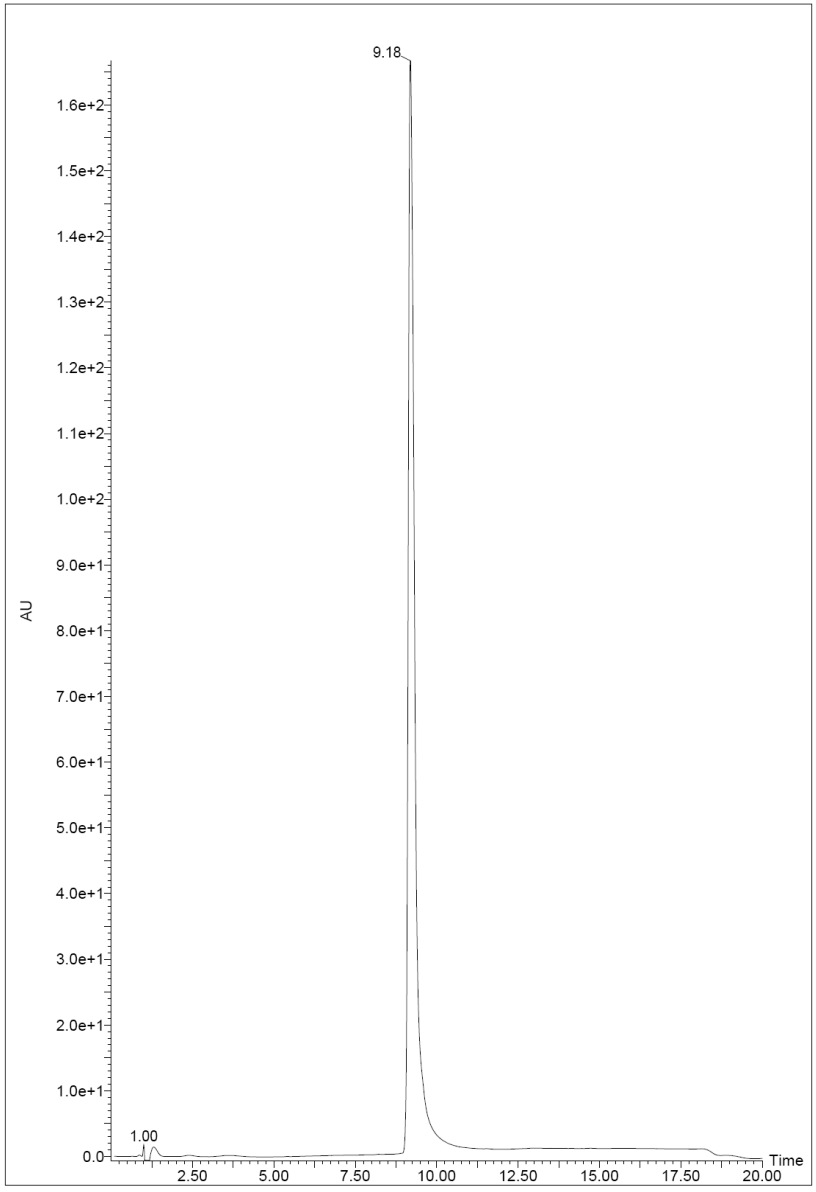
(*S*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*S*-**35**): COSY

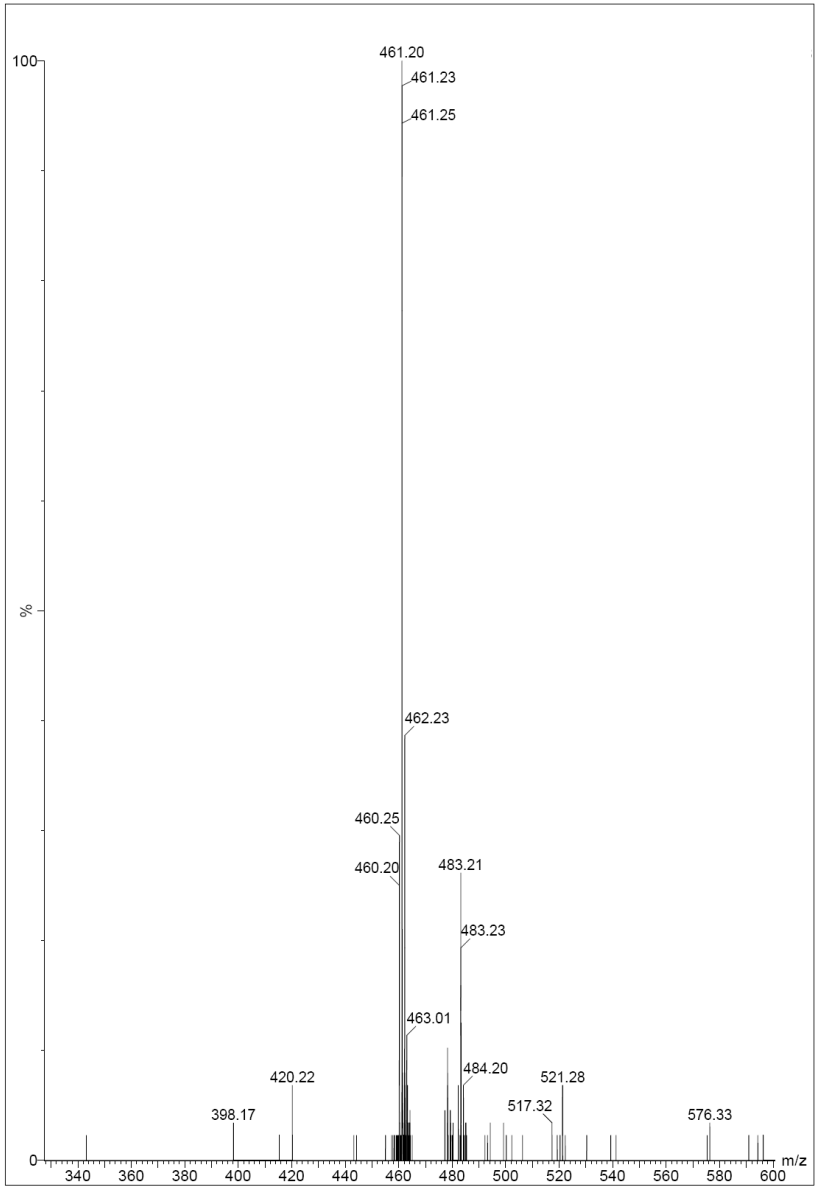


(*S*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*S*-**35**): ^{13}C NMR

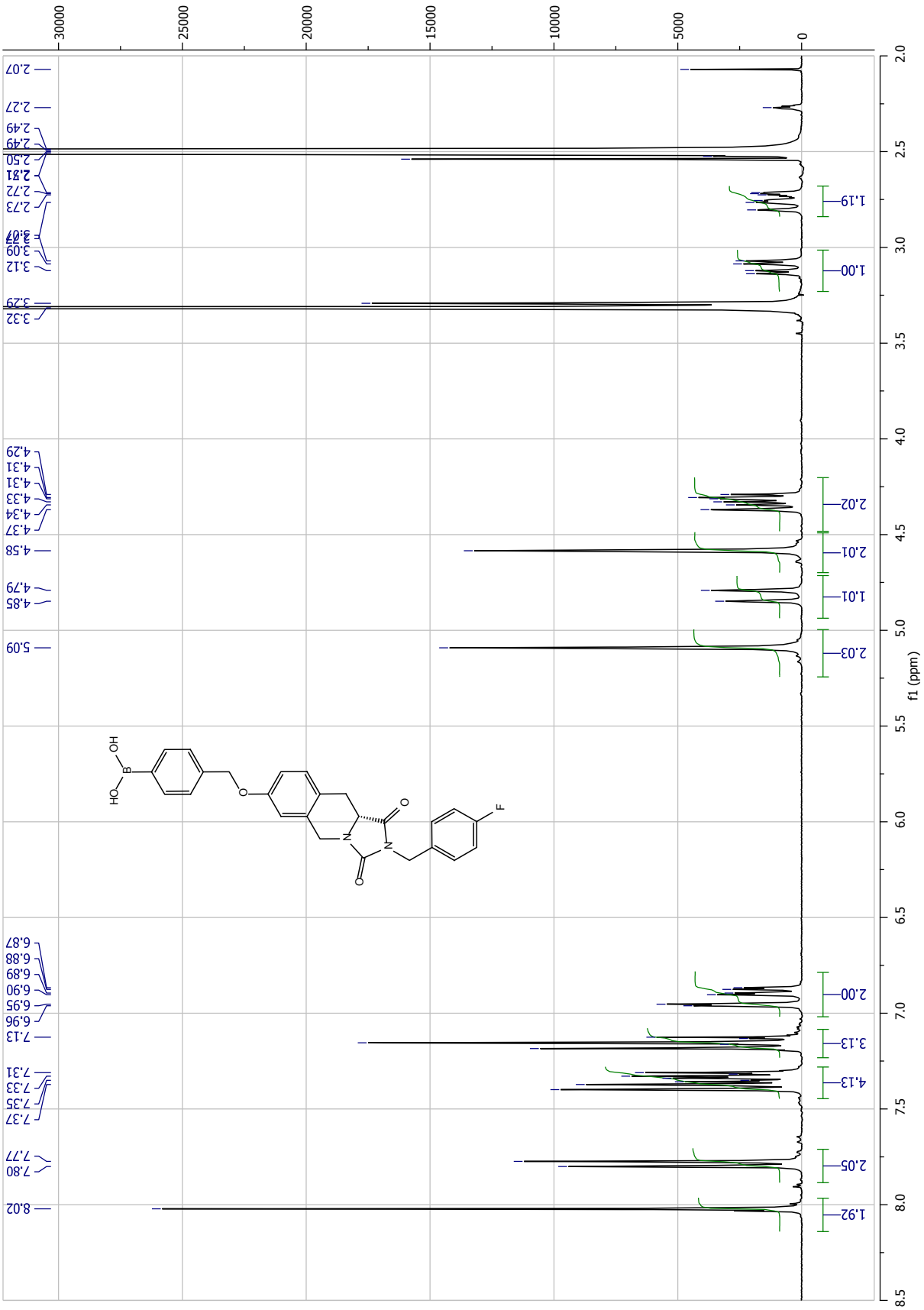


(*R*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*R*-**35**): LC-MS

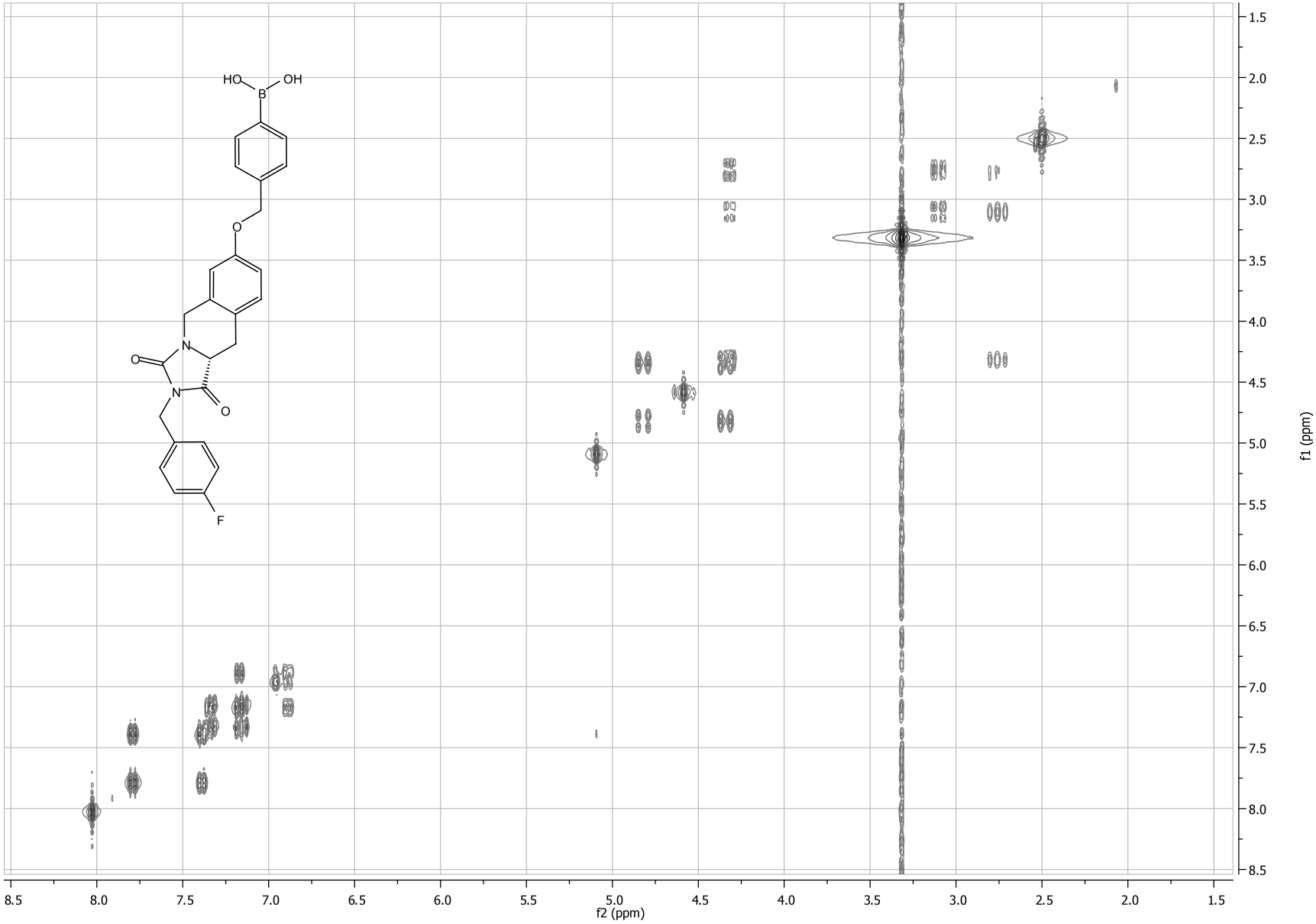




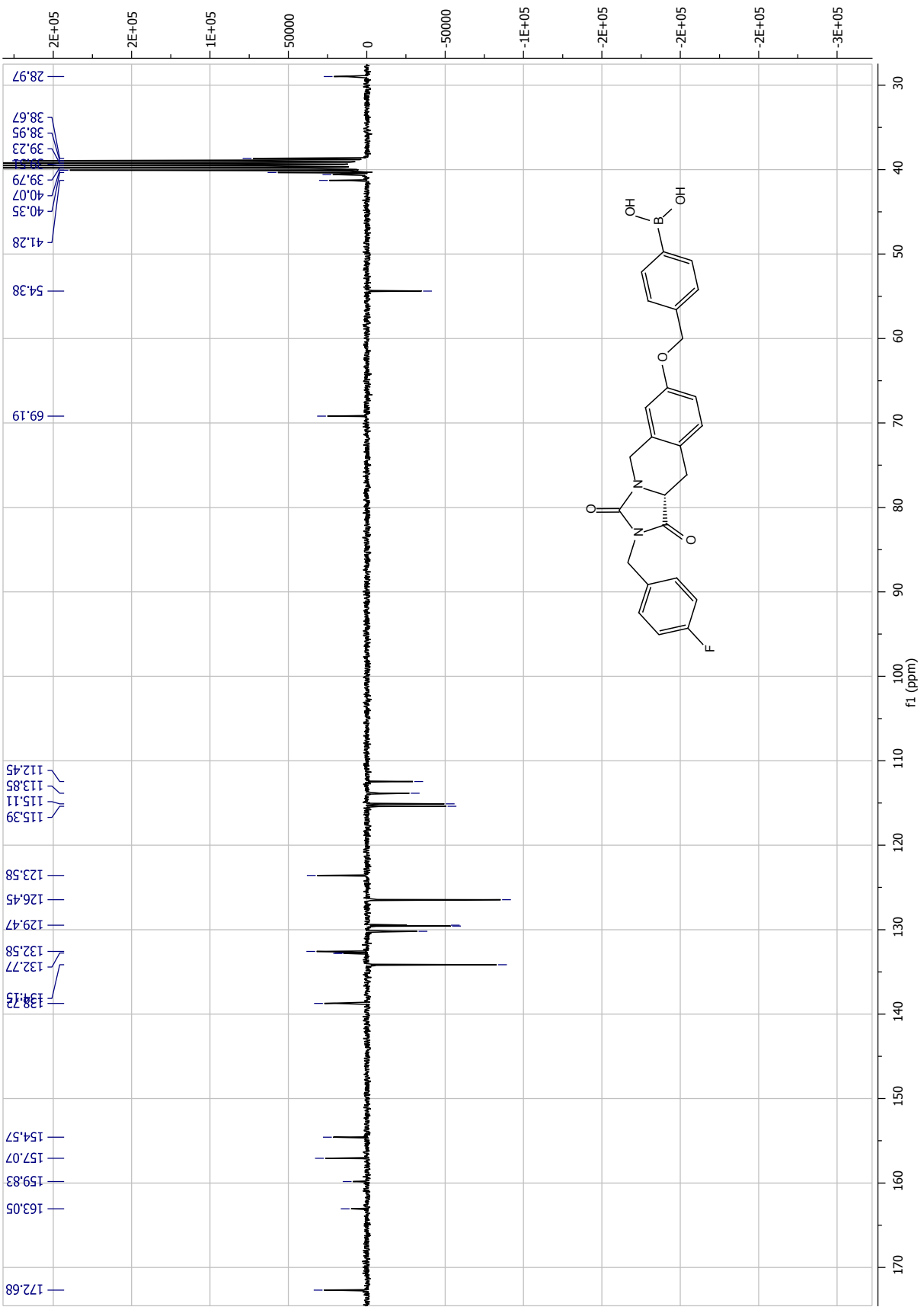
(*R*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*R*-**35**): ^{1}H NMR



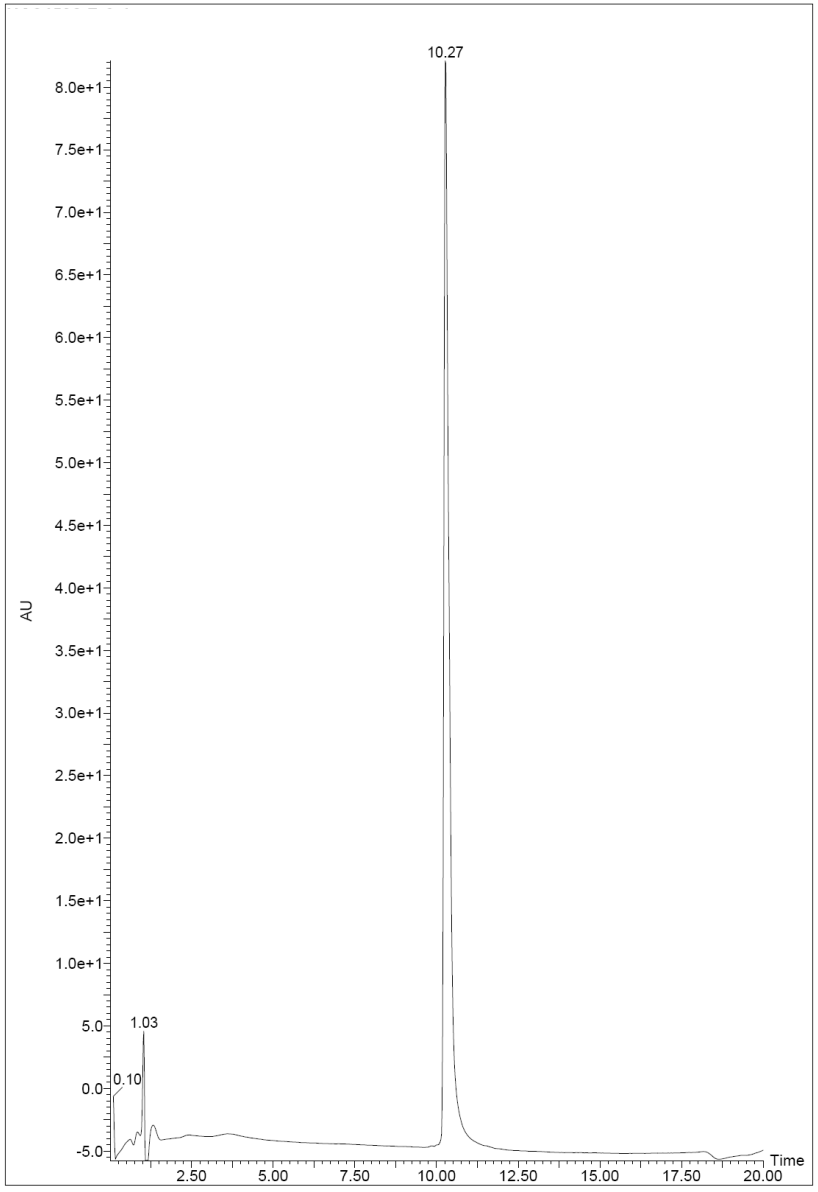
(*R*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*R*-**35**): COSY

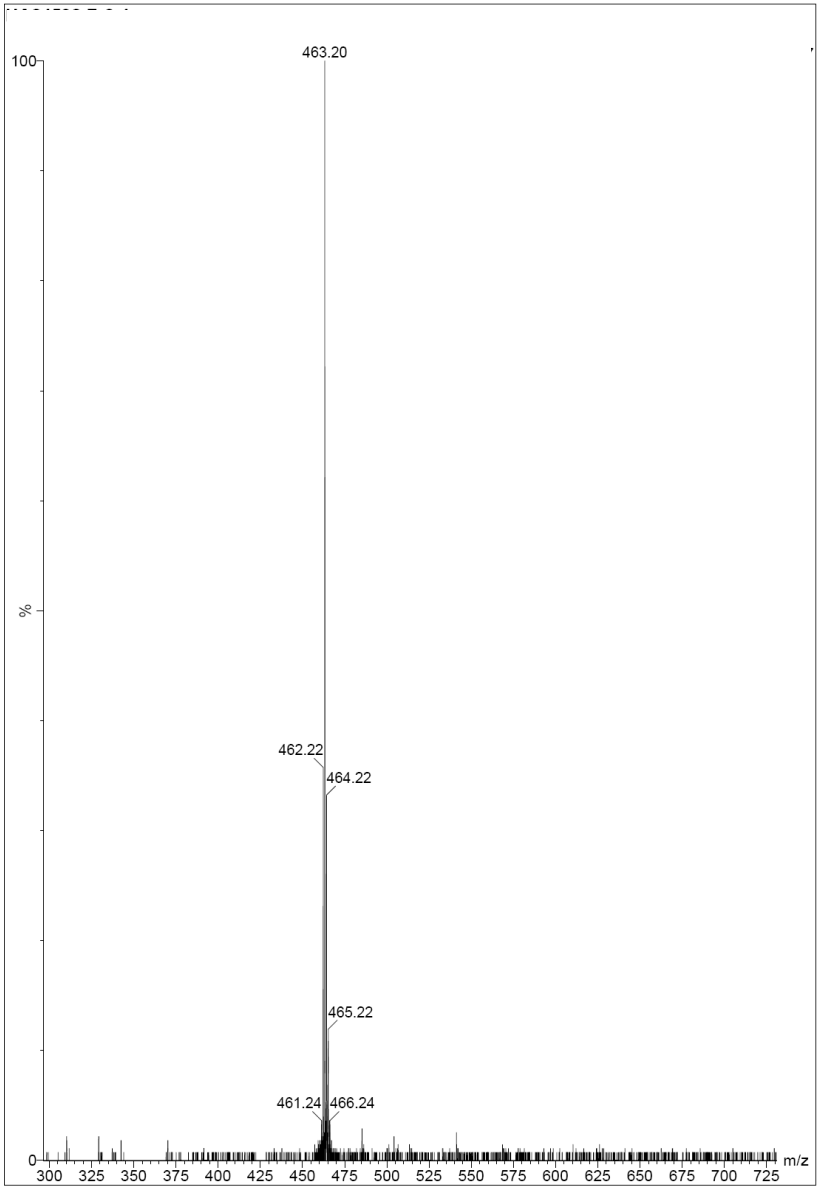


(*R*)-(4-(((2-(4-fluorobenzyl)-1,3-dioxo-1,2,3,5,10,10a-hexahydroimidazo[1,5-*b*]isoquinolin-7-yl)oxy)methyl)phenyl)boronic acid (*R*-**35**): ^{13}C NMR

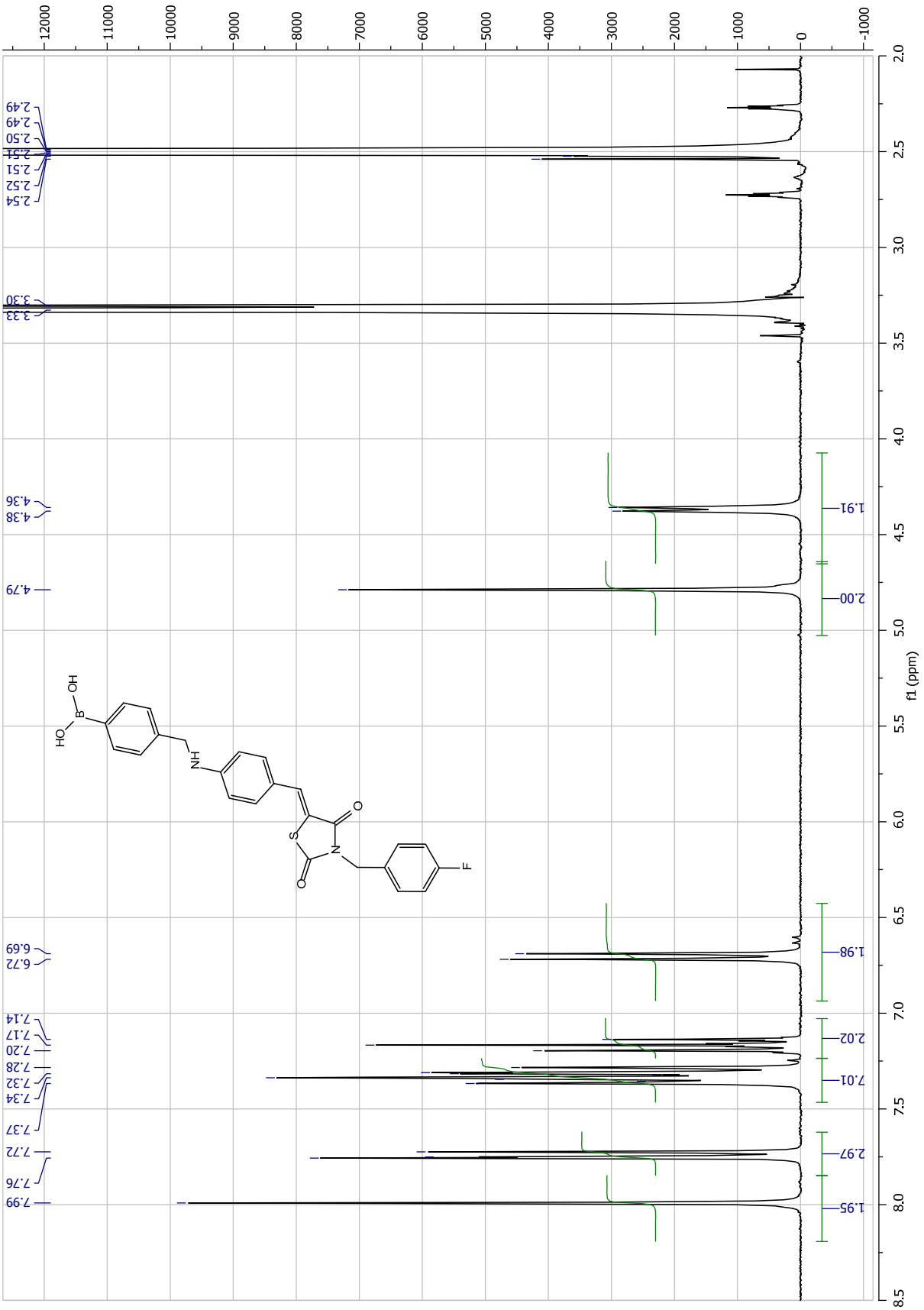


(*Z*)-(4-(((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)amino)methyl) phenyl)boronic acid (**36**); LC-MS

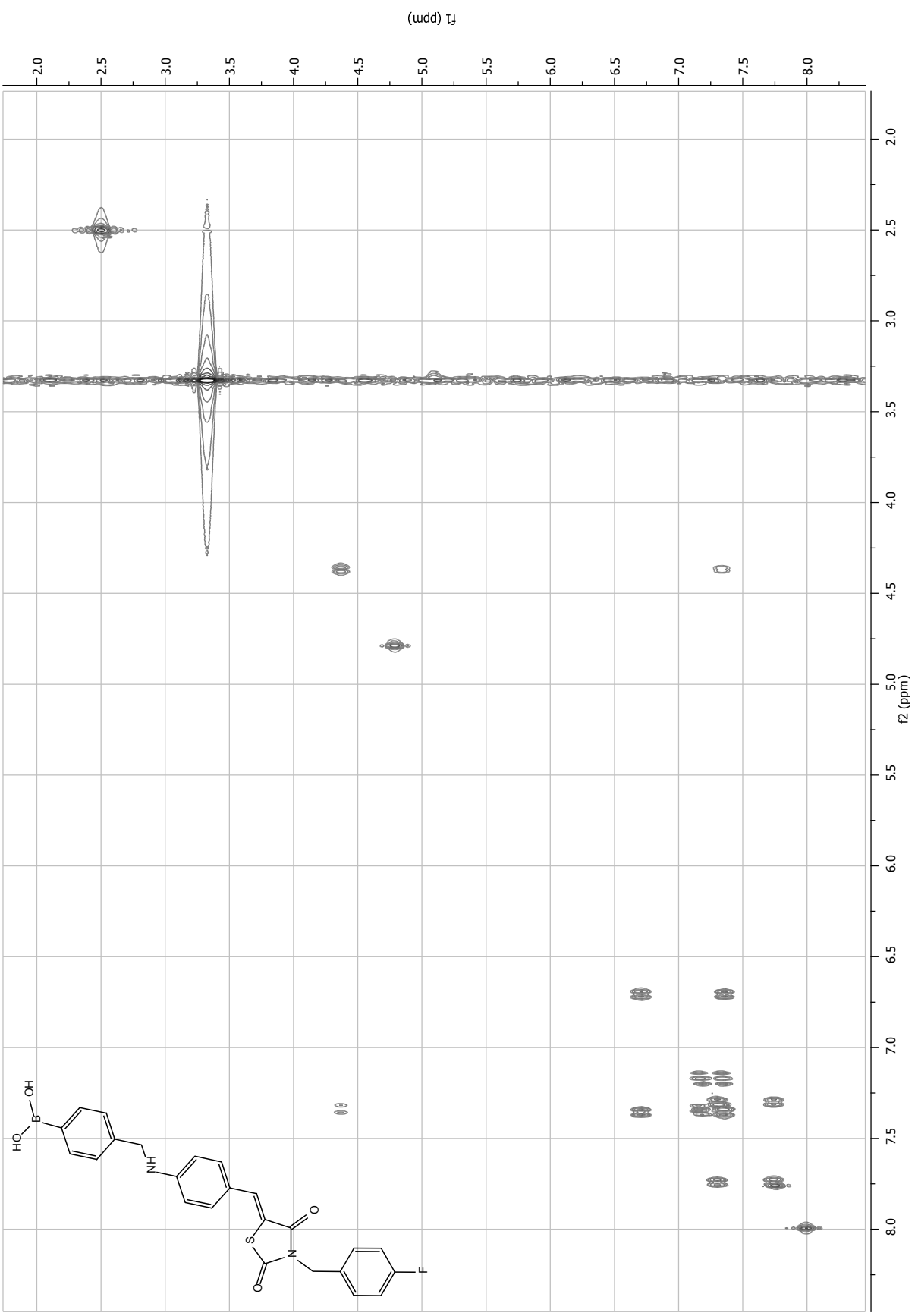




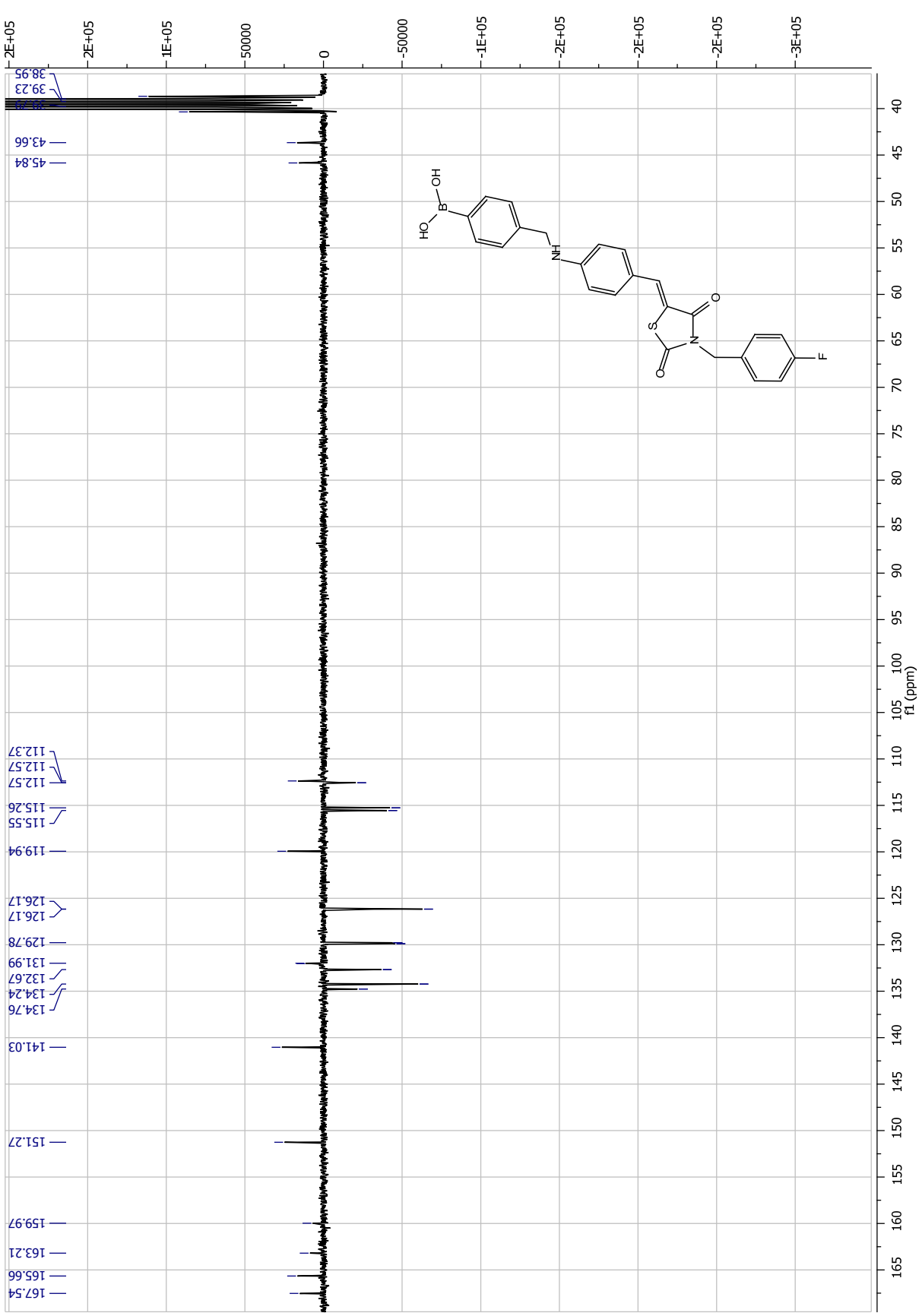
(Z)-(4-((((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)amino)methyl) phenyl)boronic acid (**36**); ^{1}H NMR



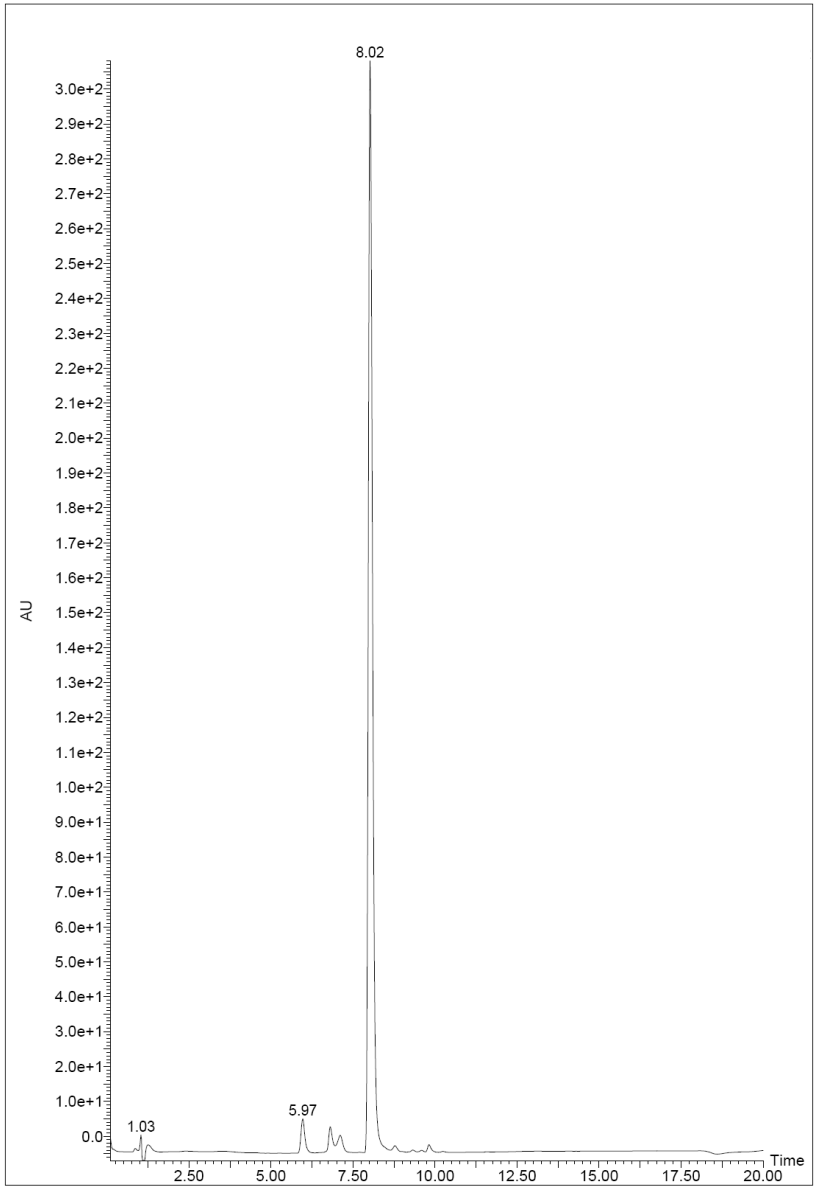
(Z)-(4-((((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)amino)methyl) phenyl)boronic acid (**36**); COSY

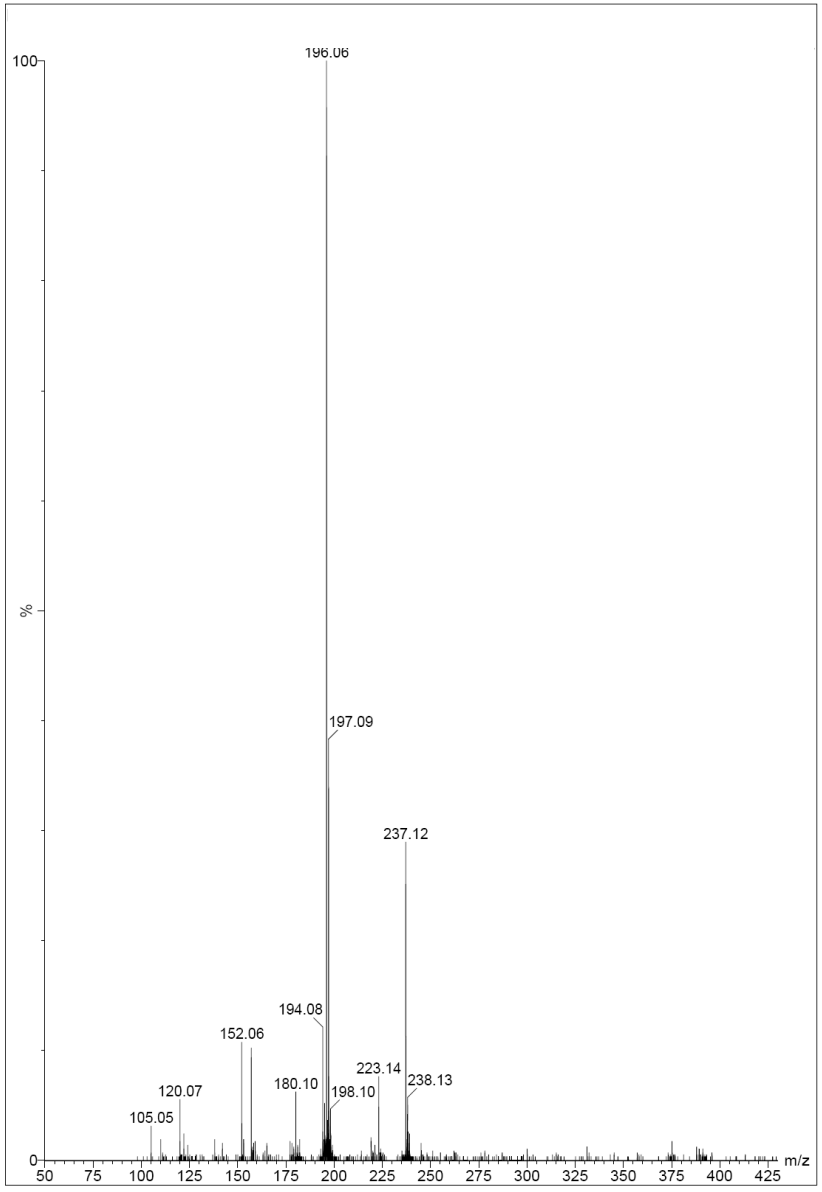


(Z)-(4-((((4-((3-(4-fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)amino)methyl) phenyl)boronic acid (**36**); ^{13}C NMR

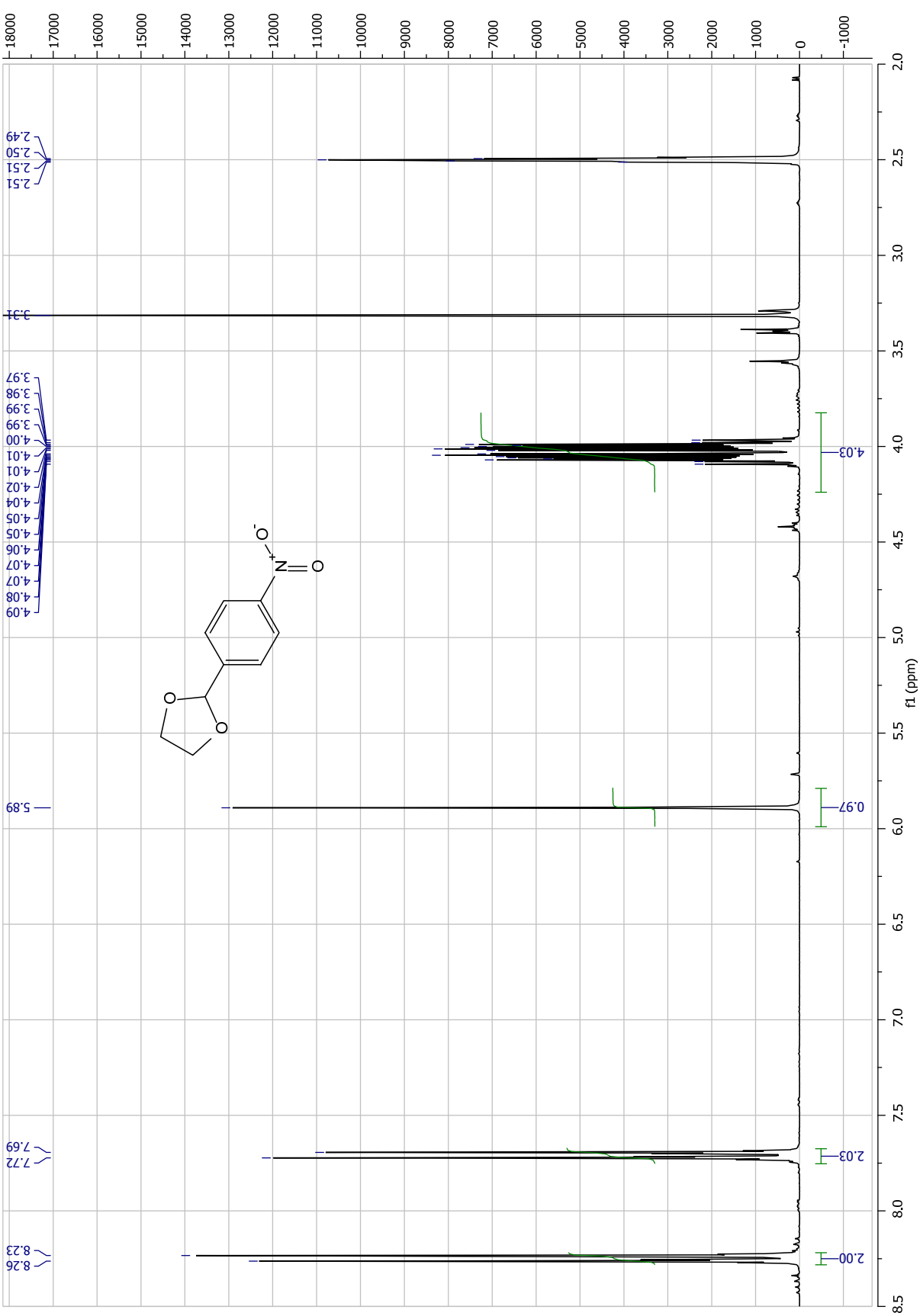


2-(4-nitrophenyl)-1,3-dioxolane (**37**); LC-MS

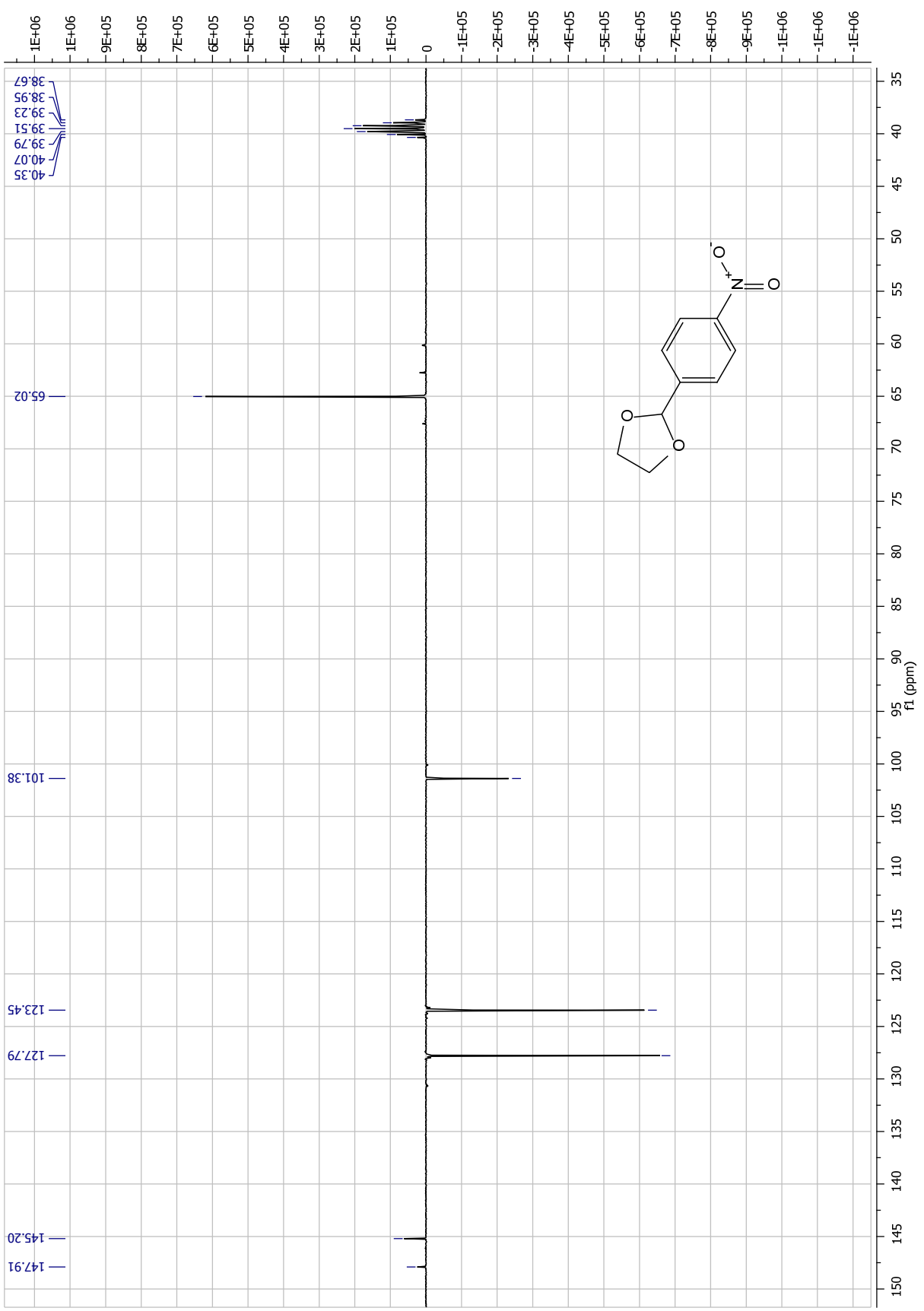




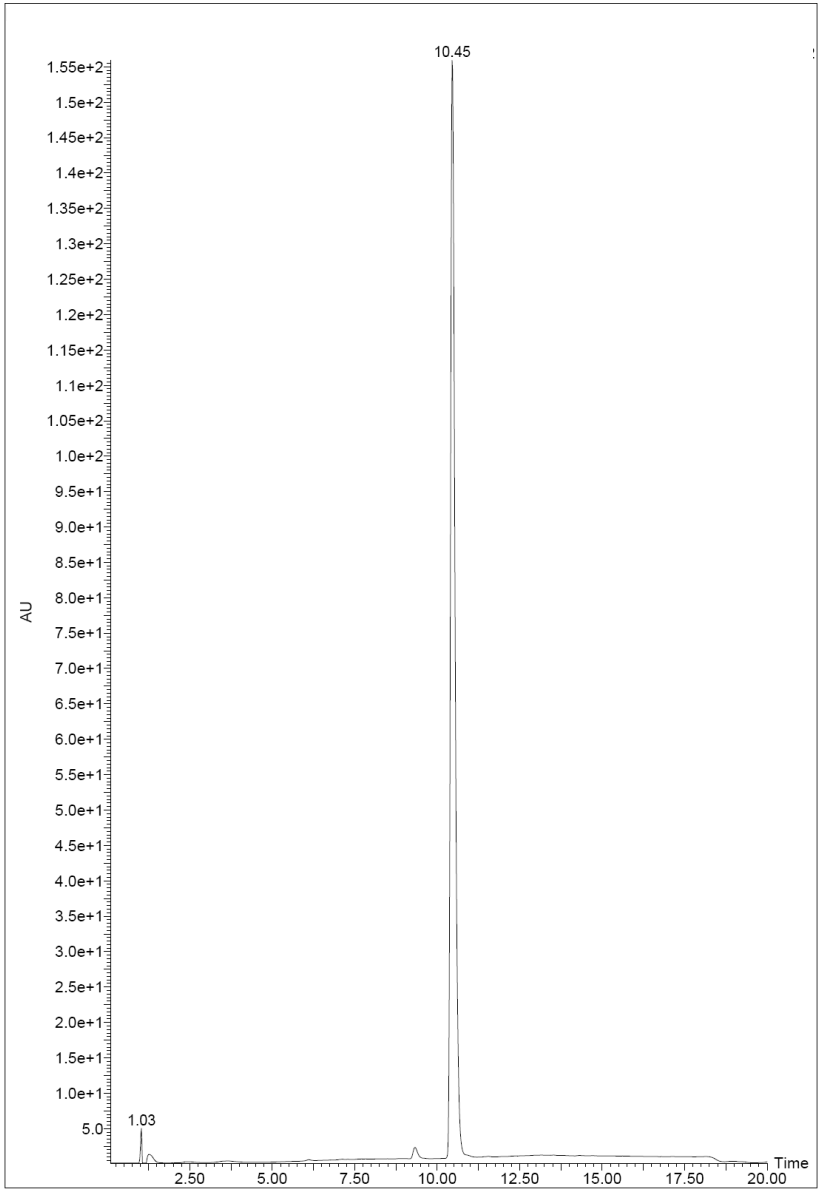
2-(4-nitrophenyl)-1,3-dioxolane (**37**); ^{1}H NMR

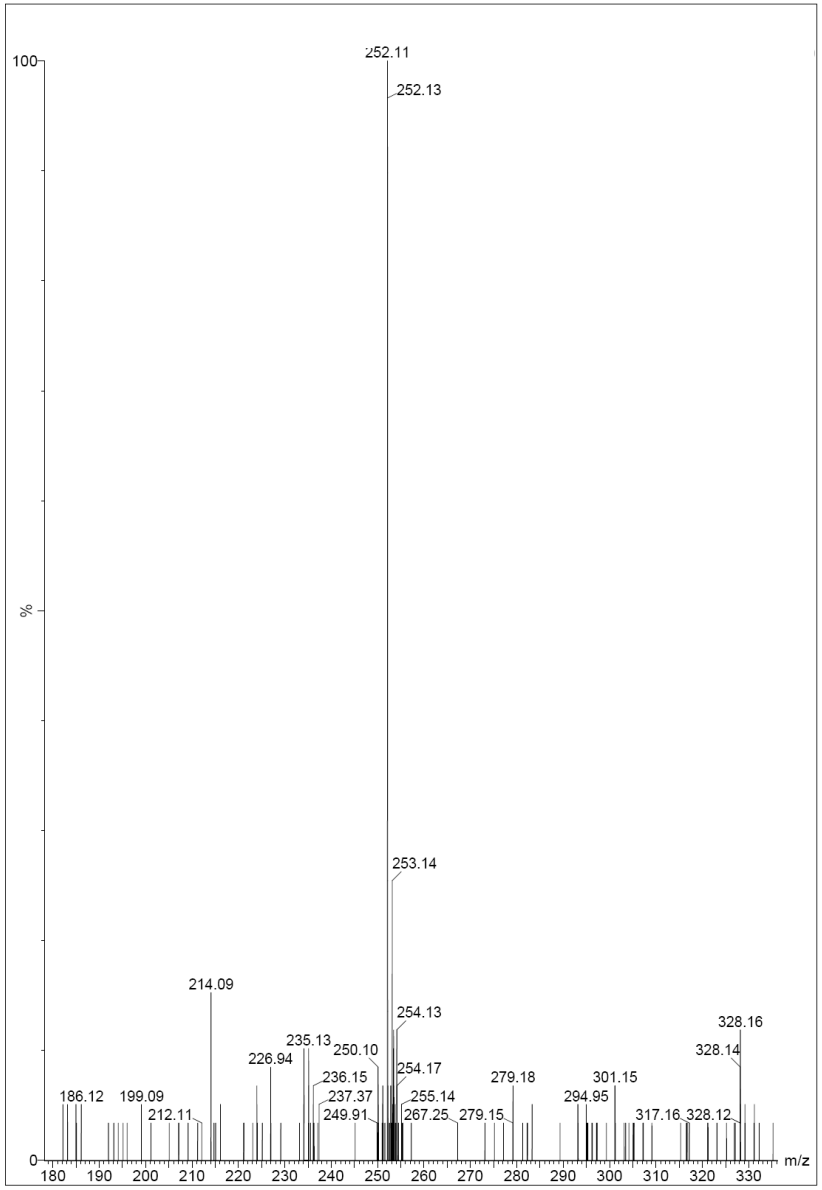


2-(4-nitrophenyl)-1,3-dioxolane (**37**); ^{13}C NMR

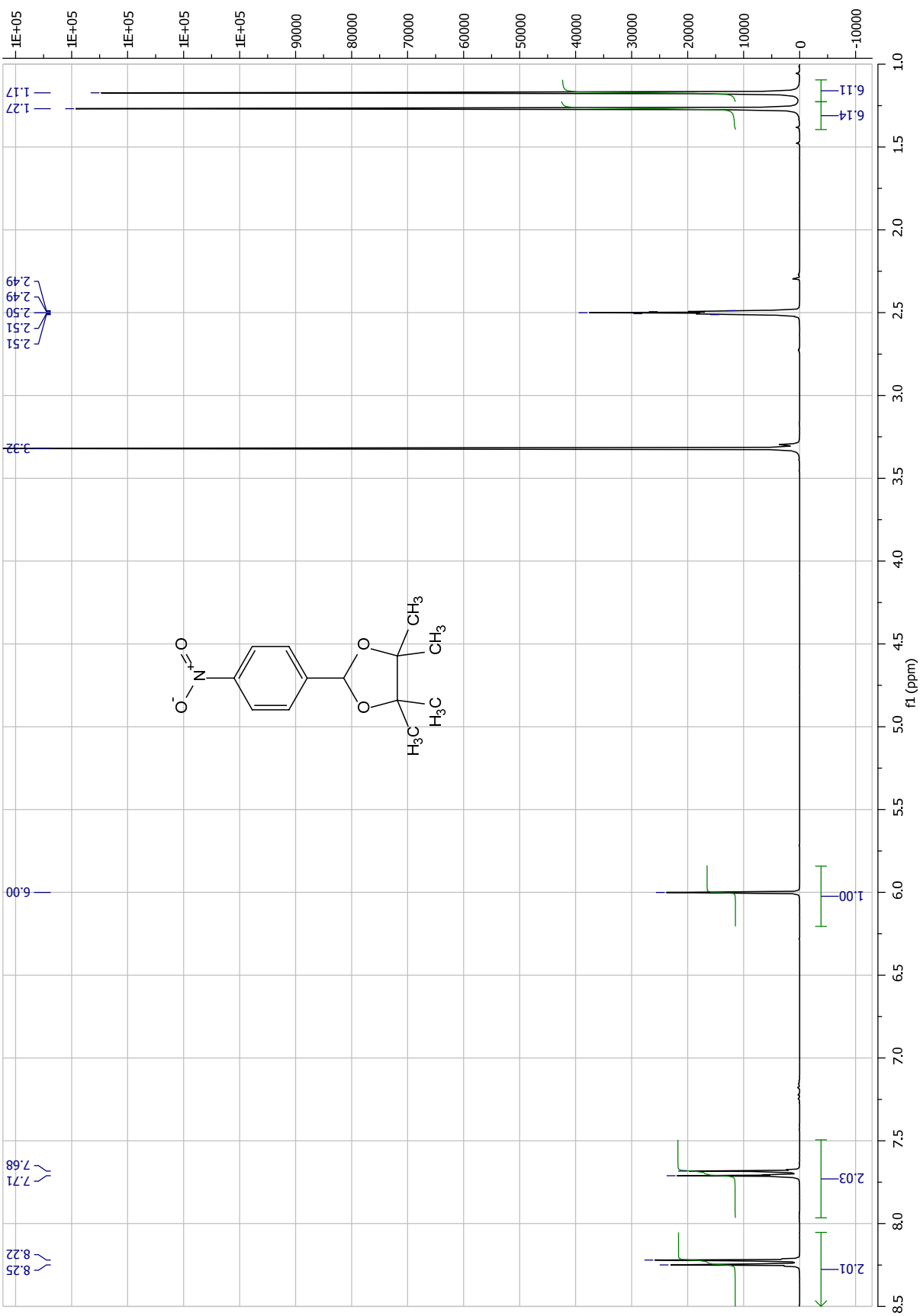


4,4,5,5-tetramethyl-2-(4-nitrophenyl)-1,3-dioxolane (**38**); LC-MS

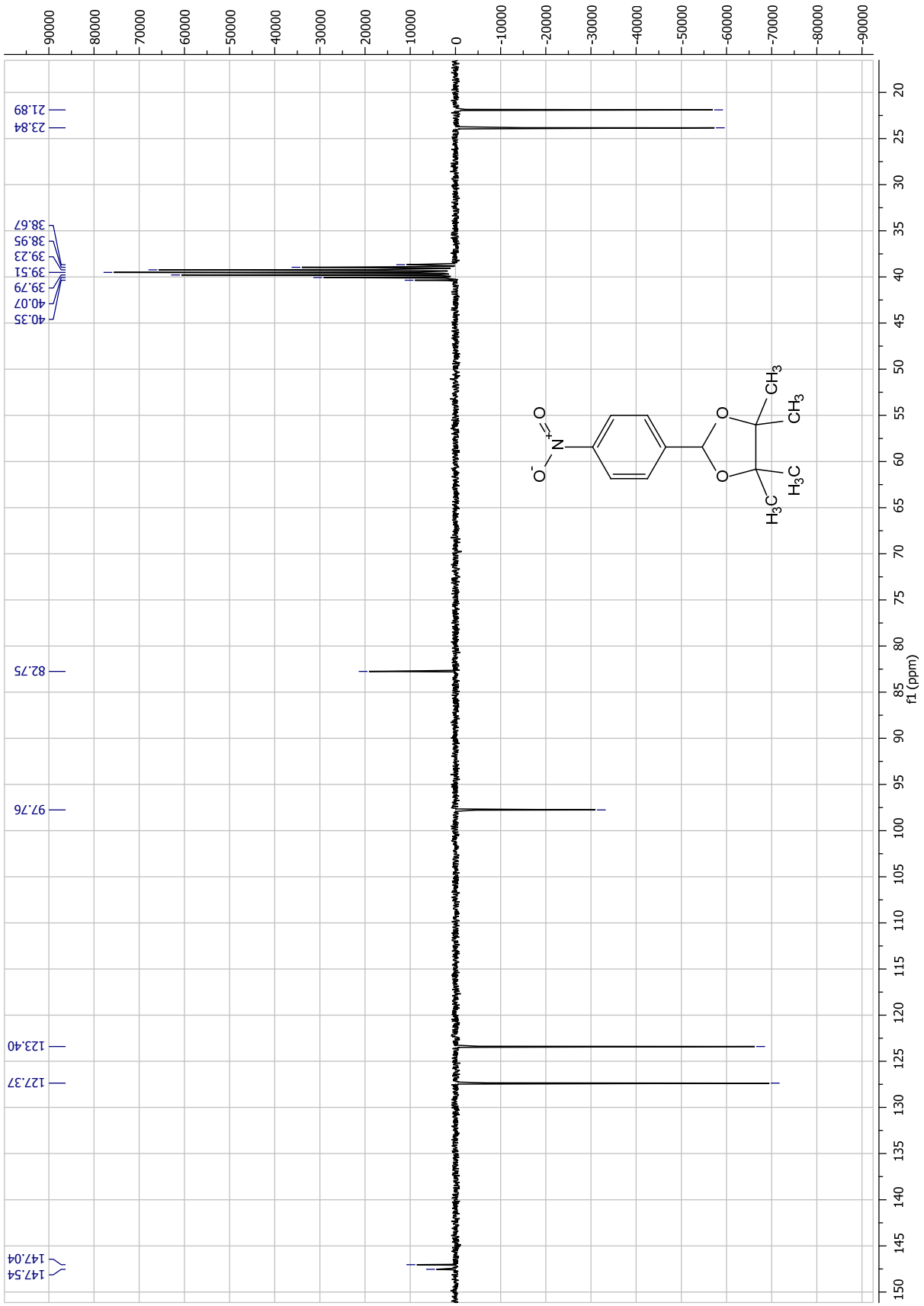




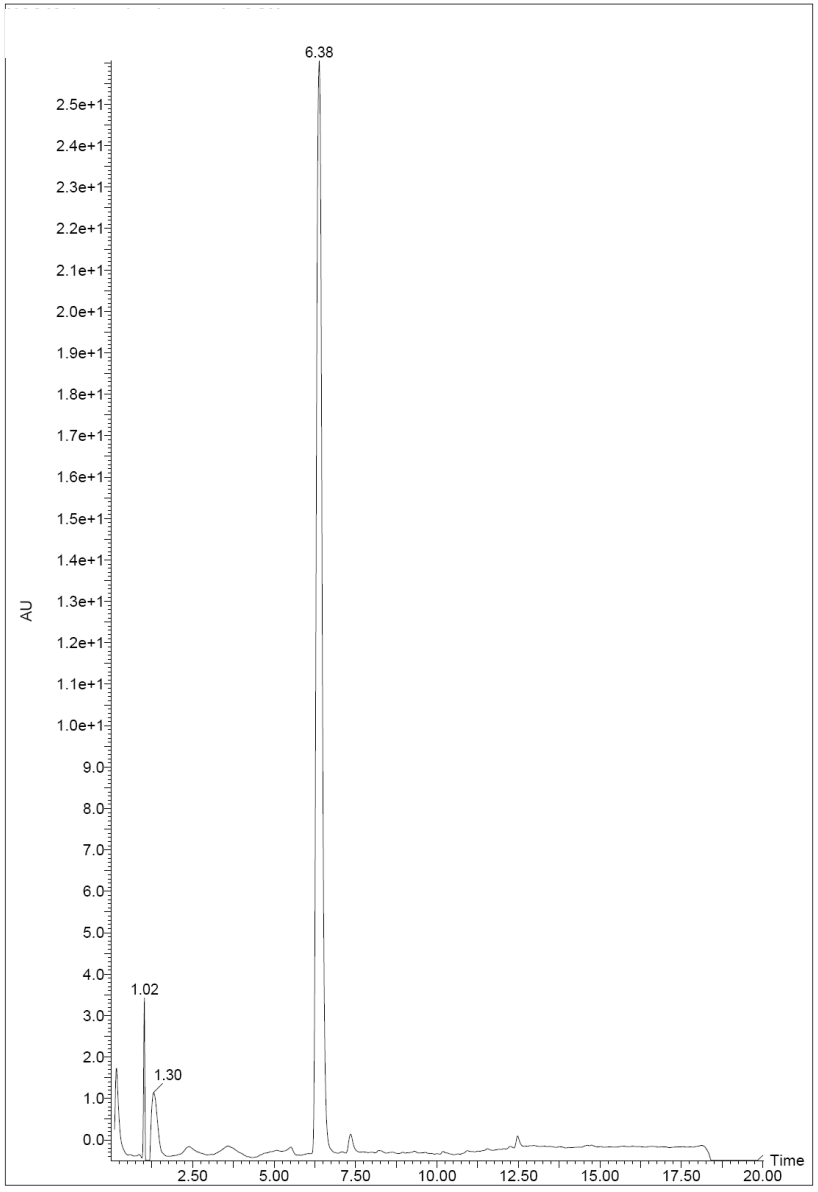
4,4,5,5-tetramethyl-2-(4-nitrophenyl)-1,3-dioxolane (**38**); ^{1}H NMR

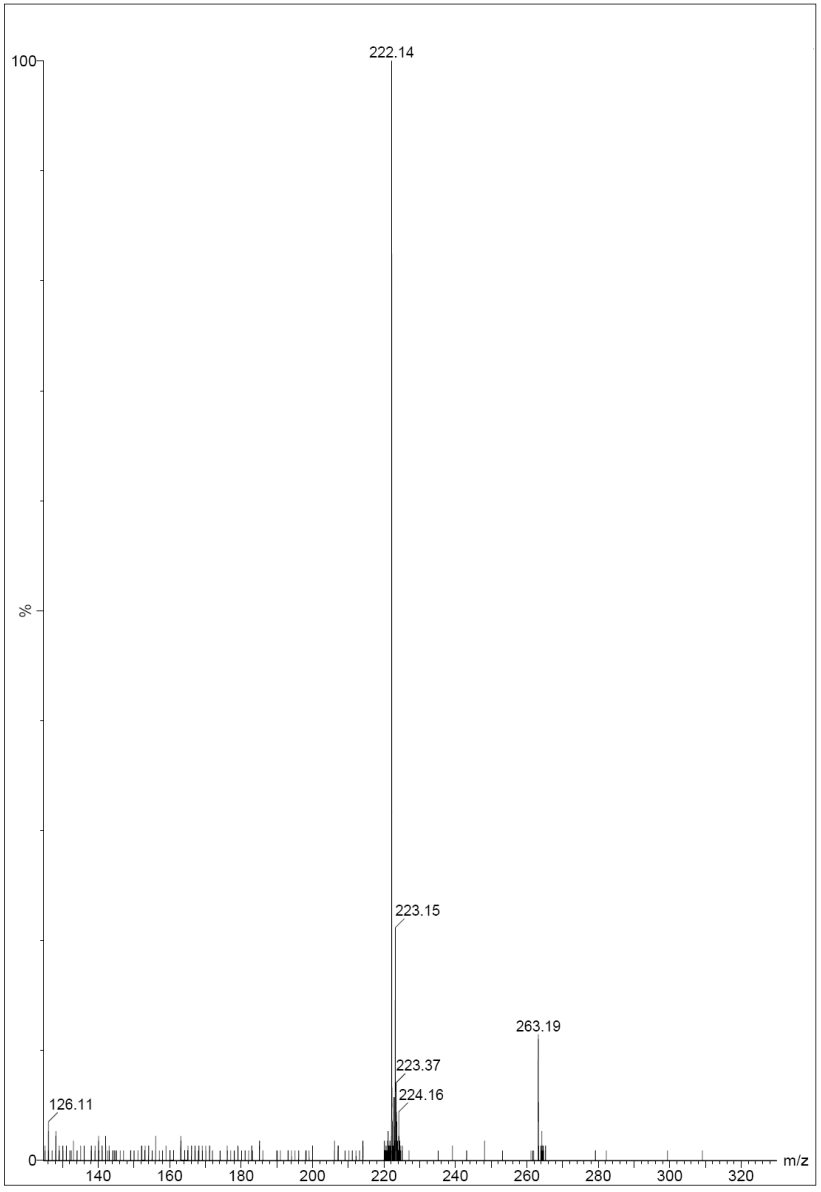


4,4,5,5-tetramethyl-2-(4-nitrophenyl)-1,3-dioxolane (**38**); ^{13}C NMR

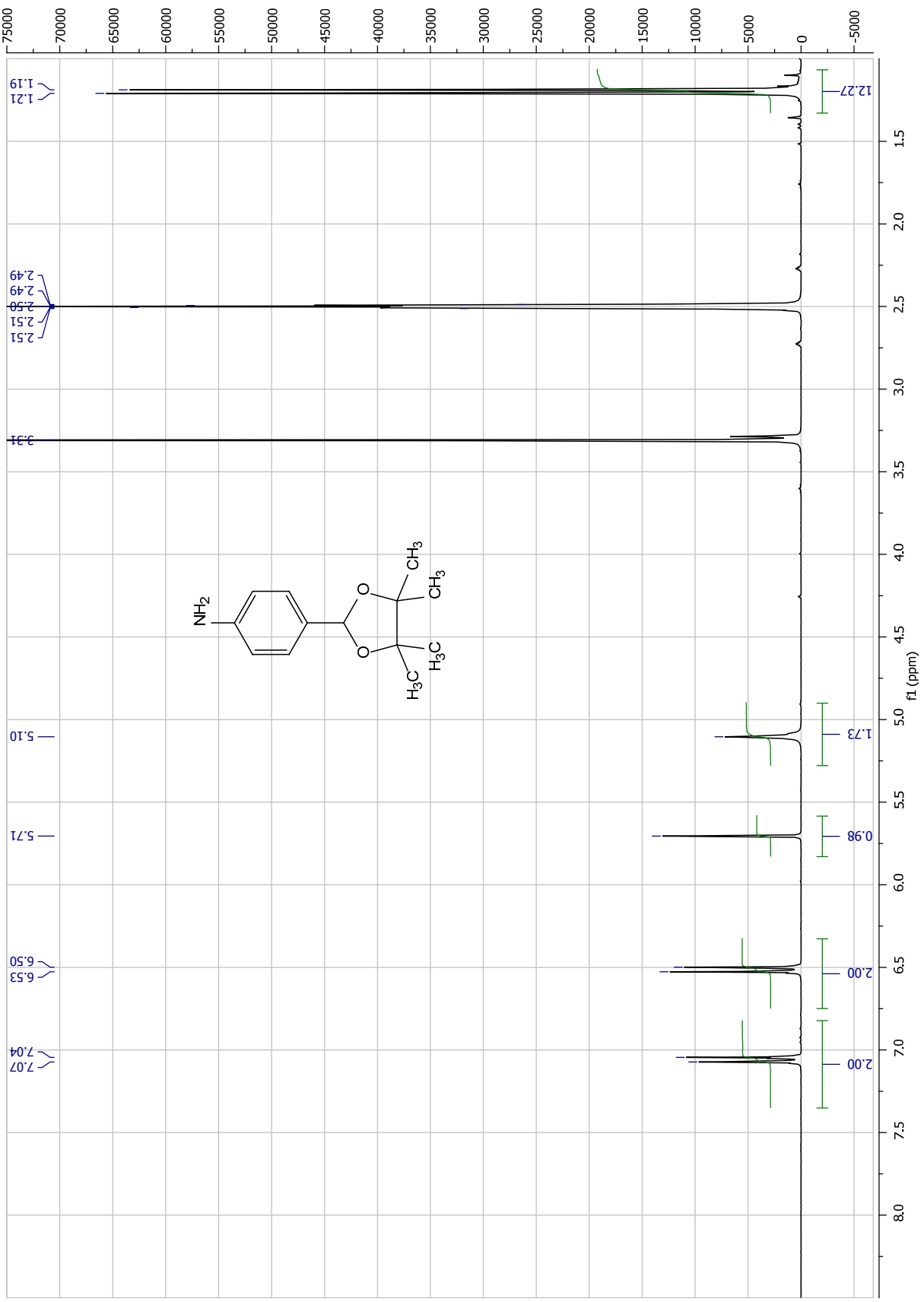


4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)aniline (**39**); LC-MS

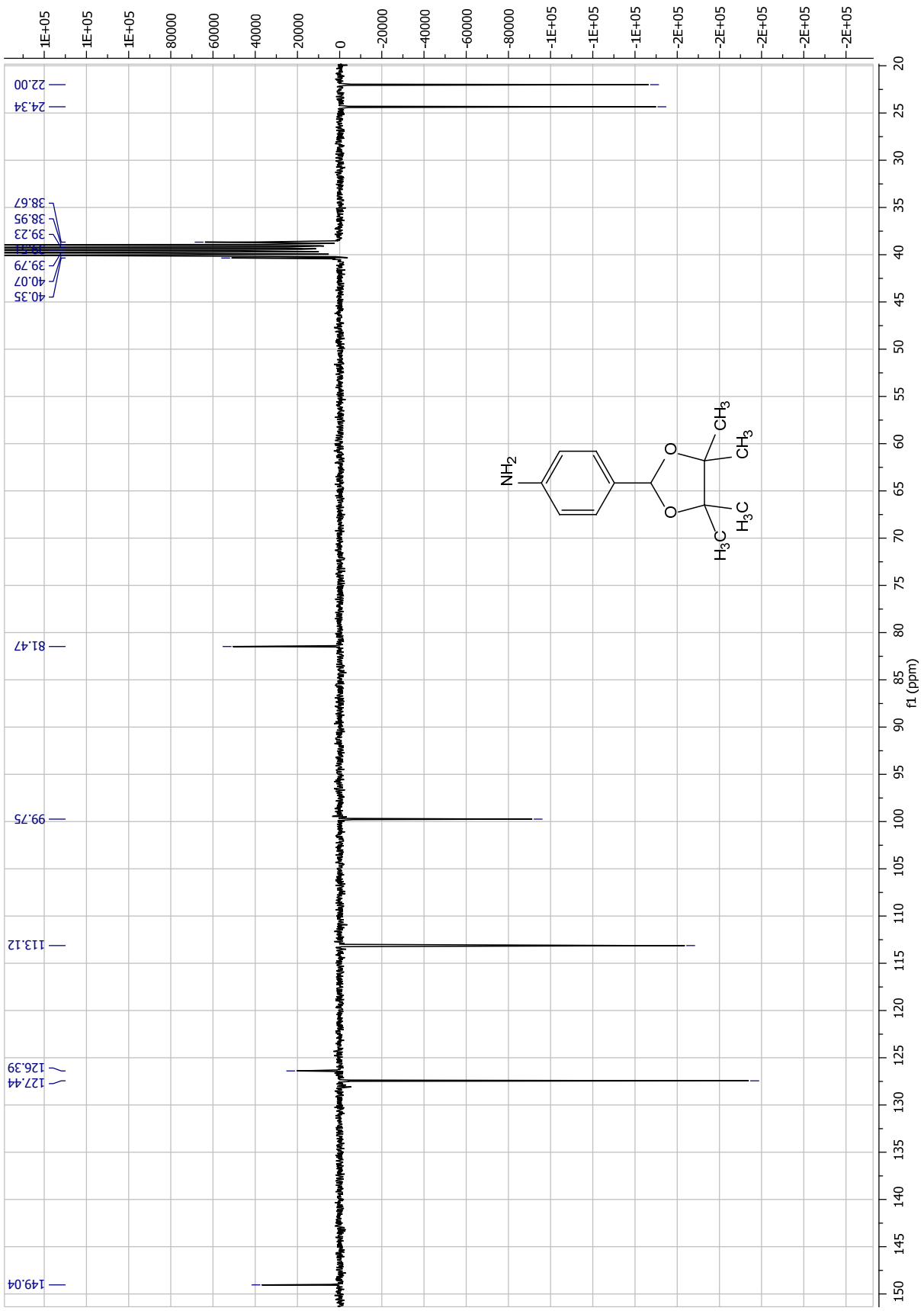




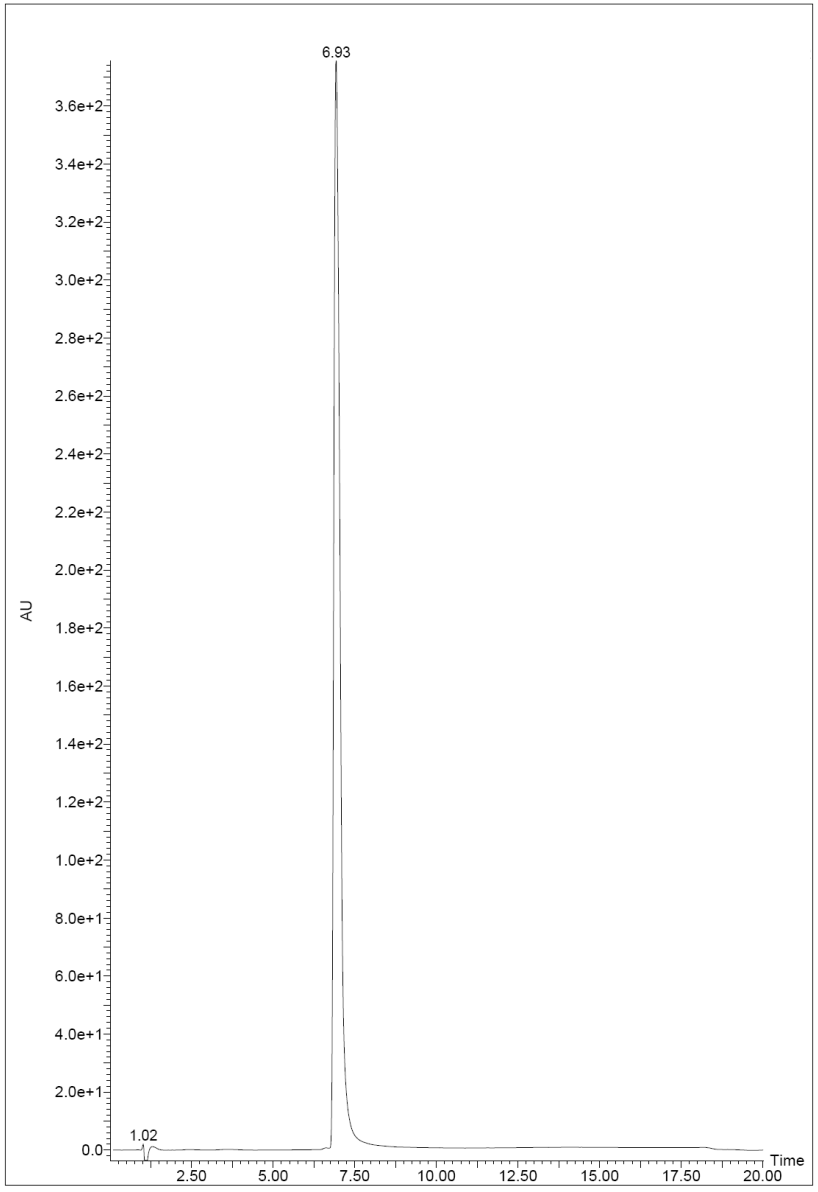
4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)aniline (**39**); ^{1}H NMR

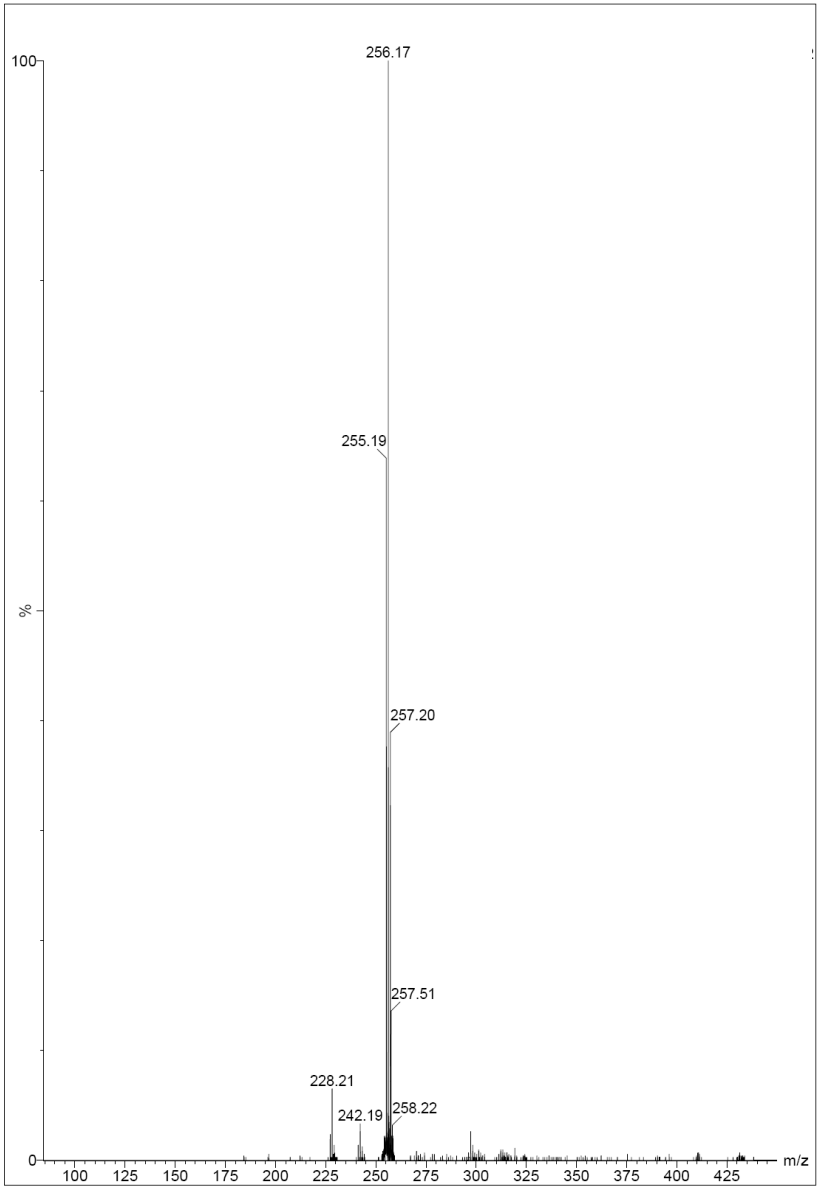


4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)aniline (**39**); ^{13}C NMR

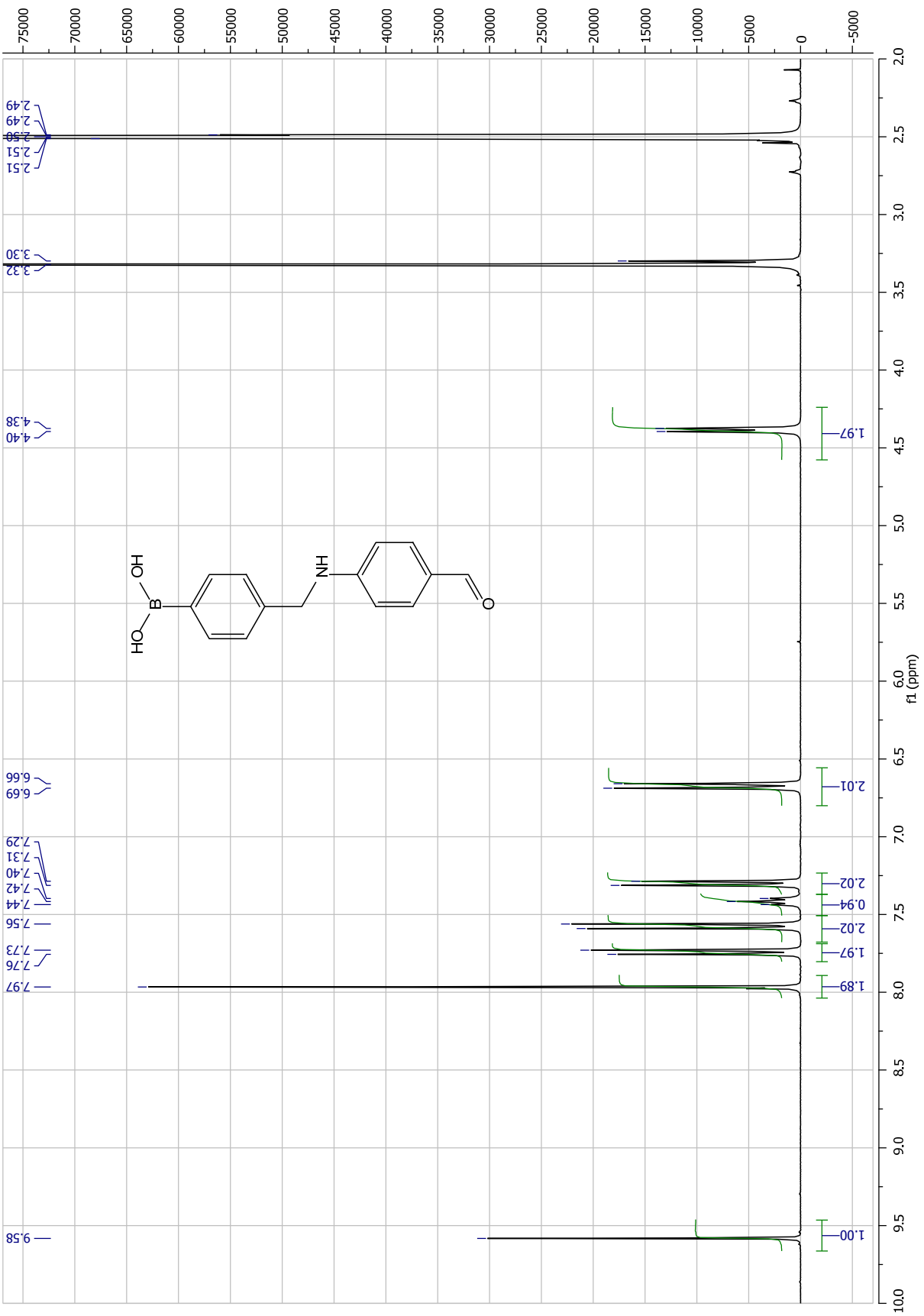


(4-(((4-formylphenyl)amino)methyl)phenyl)boronic acid (**40**); LC-MS

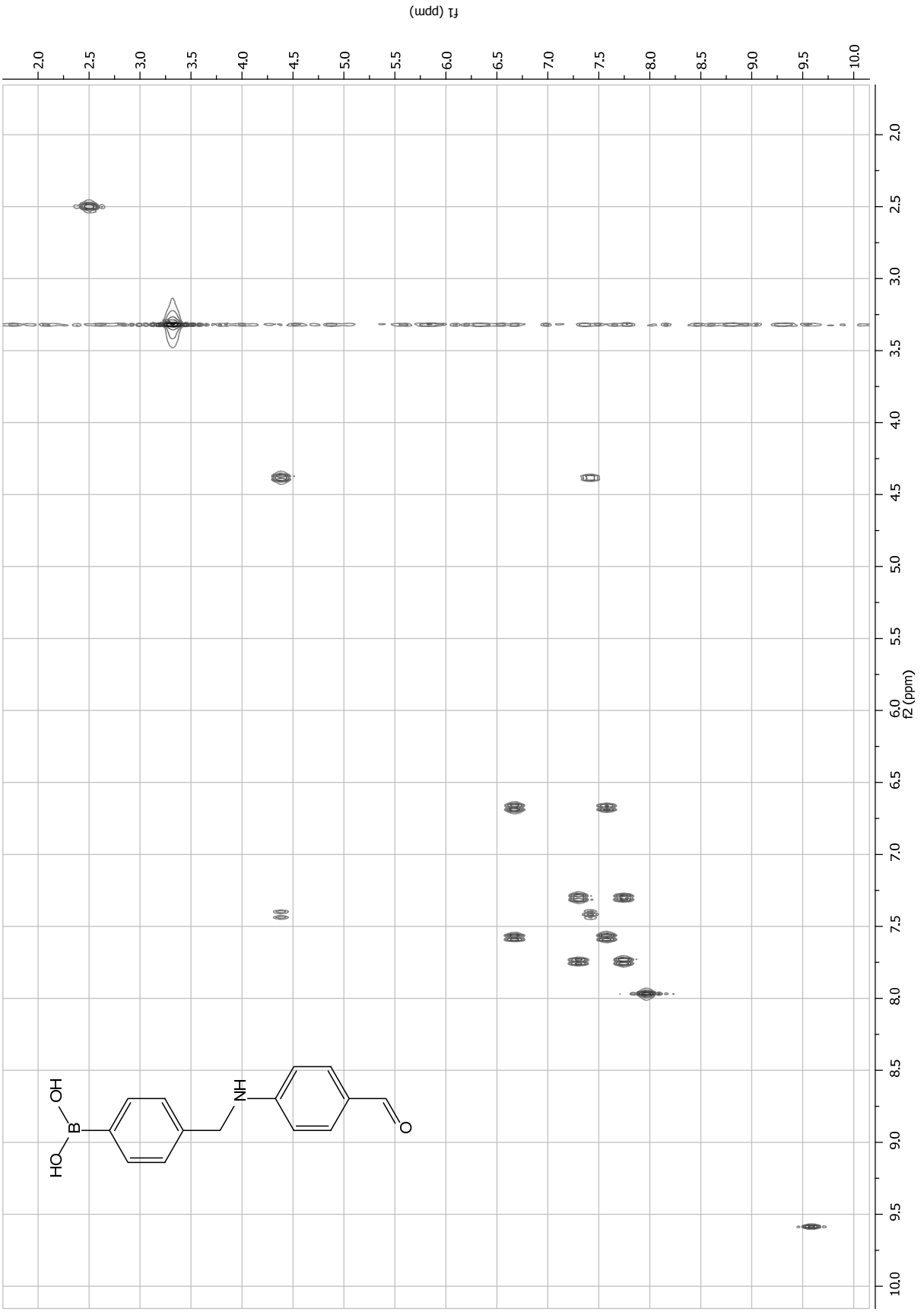




(4-(((4-formylphenyl)amino)methyl)phenyl)boronic acid (**40**); ^{1}H NMR



(4-(((4-formylphenyl)amino)methyl)phenyl)boronic acid (**40**); COSY



(4-(((4-formylphenyl)amino)methyl)phenyl)boronic acid (**40**); ^{13}C NMR