Electronic Supplementary Information (ESI)

Pd-Catalyzed site selective C(sp^2)-H chalcogenation of amino acids and peptides using picolinamide auxiliary

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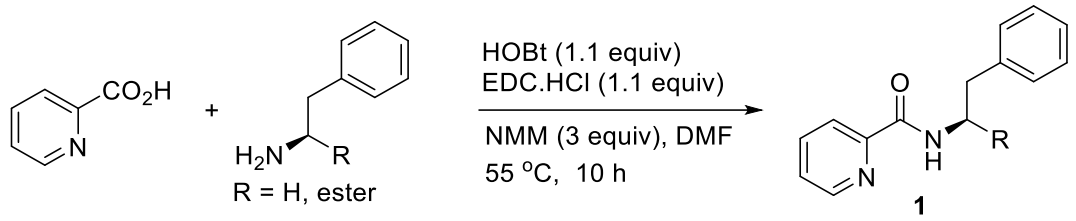
1. General Information

Material and Instrumentation. All required materials were purchased from commercial suppliers and used without further purification. Reactions were monitored by thin layer chromatography, visualized by UV and Ninhydrin. Column chromatography was performed in 100- 200 mesh silica. ^{1}H NMR spectra were recorded on Bruker AV-400 instrument (400 MHz) or Bruker AV-700 instrument (700 MHz). ^{13}C NMR spectra were recorded on Bruker AV-400 instrument (100 MHz) or Bruker AV-700 instrument (176 MHz). ^{1}H and ^{13}C NMR chemical shifts (δ) were recorded in ppm downfield from tetramethyl silane or relative to the residual solvent ($CDCl_3$) signal. Splitting patterns are abbreviated as: br s broad singlet; s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; m, multiplet. Mass spectra were obtained from Waters XEVO-G2XSQTOF Spectrometer. Chiral HPLC analyses were carried out using Waters 2998 with Chiral ART Cellulose-SZ S-5um column using 2-propanol and hexane as eluent.

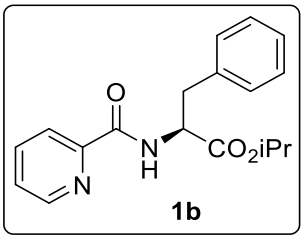
2. Synthesis and Characterization of Starting Materials

The substrates **1a**, **1a**$_1$, **1a**$_2$, **1a**$_3$, **1h-o**, were synthesized by following the literature reported procedure.[1] **2a-i and 2j-k** were synthesized by following the literature reported procedure.[2,3]

Synthesis of Picolinamide-protected amino acid Derivatives

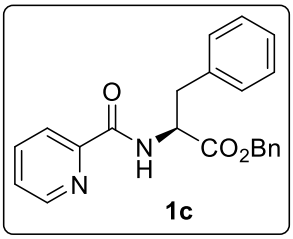


To a solution of Picolinic acid (2 mmol) and L-amino acid ester/amine (2.2 mmol) in anhydrous DMF, NMM (0.66 mL, 6 mmol) was added and the resulting mixture was cooled to 0 °C for 5 minutes with continuous stirring. HOBt (297 mg, 2.2 mmol) was then added to this solution. After 5 minutes, EDC. HCl (420.2 mg, 2.2 mmol) was added to this and stirred for 10 minutes at 0 °C. The reaction mixture was then heated at 55 °C for 10 h. After stipulated time, the mixture was cooled at room temperature and DMF was evaporated in vacuo. Water was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to give picolinamide-protected amino acid derivatives **1** as colorless oil.



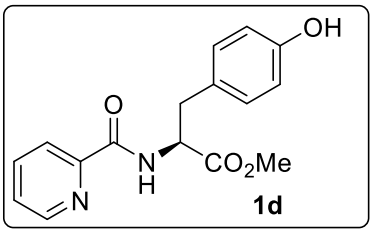
Isopropyl picolinoylphenylalaninate 1b: Following the above-mentioned procedure, the compound **1b** was obtained as colorless oil (487mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56-8.51 (m, 2H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.85-7.79 (m, 1H), 7.43-7.39 (m, 1H), 7.29-7.20 (m,

5H), 5.05-4.99 (m, 2H), 3.27-3.18 (m, 2H), 1.23 (d, *J* = 6.4 Hz, 3H), 1.18 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.87, 163.89, 149.36, 148.28, 137.19, 136.09, 129.40, 128.42, 126.94, 126.28, 122.16, 69.23, 53.50, 38.39, 21.73, 21.62. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{20}N_2O_3Na$ 335.1372; found 335.1356.



1c

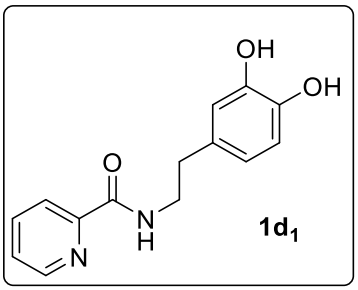
Benzyl picolinoylphenylalaninate 1c: Following the above-mentioned procedure, the compound **1c** was obtained as colorless oil (554 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.0 Hz, 1H), 8.49-8.48 (m, 1H), 8.14 (d, *J* = 7.6 Hz, 1H), 7.76 (td, *J* = 7.6, 1.2 Hz, 1H), 7.36-7.30 (m, 4H), 7.29-7.26 (m, 2H), 7.21-7.18 (m, 3H), 7.10-7.08 (m, 2H), 5.19-5.09 (m, 3H), 3.28-3.18 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.04, 163.85, 149.04, 148.13, 137.08, 135.69, 135.02, 129.15, 128.39, 128.38, 128.33, 128.25, 126.84, 126.22, 122.04, 66.99, 53.32, 38.04. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{22}H_{20}N_2O_3Na$ 383.1372; found 383.1370.



1d

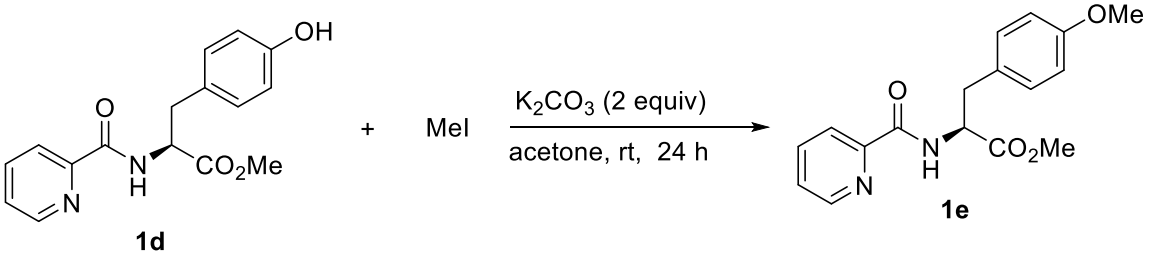
Methyl picolinoyltyrosinate 1d: Following the above-mentioned procedure, the compound **1d** was obtained as colorless oil (540 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.4 Hz, 1H), 8.51 (d, *J* = 4.0 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.04-4.99 (m, 1H), 3.71 (s, 3H), 3.20-3.07 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.95, 164.34, 155.53, 148.72,

148.29, 137.41, 130.19, 126.90, 126.56, 122.29, 115.57, 53.74, 52.40, 37.37. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{16}H_{16}N_2O_4Na$ 323.1008; found 323.1002.



***N*-(3,4-Dihydroxyphenethyl)picolinamide 1d1:** Following the above-mentioned procedure, the compound **1d1** was obtained as colorless oil (402 mg, 78 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 8.31 (t, *J* = 6.0 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.72-7.68 (m, 1H), 7.45 (br s, 1H), 7.31-7.26 (m, 1H), 6.78-6.77 (m, 2H), 6.52 (d, *J* = 7.6 Hz, 1H), 3.58 (d, *J* = 6.4 Hz, 2H), 3.12 (br s, 1H), 2.69 (t, *J* = 6.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.99, 149.03, 148.17, 144.24, 142.95, 137.54, 130.72, 126.42, 122.27, 120.61, 115.73, 115.48, 41.08, 34.85. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{14}H_{15}N_2O_3$ 259.1083; found 259.1078.

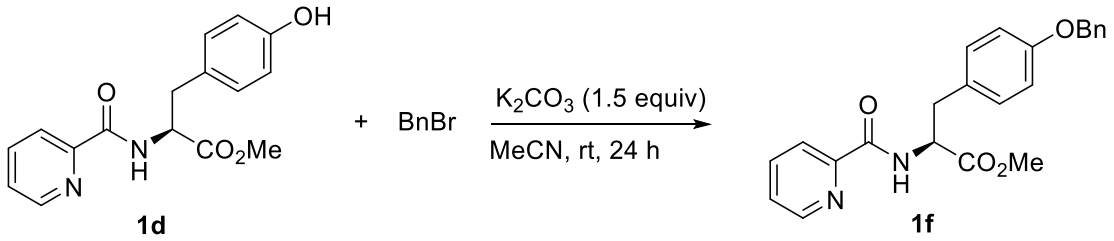
Preparation of methyl 3-(4-methoxyphenyl)-2-(picolinamido)propanoate 1e[1]



To a stirred solution of **1d** (300 mg, 1 mmol) and K_2CO_3 (276 mg, 2 mmol) in acetone (3 mL), MeI (124 μL, 2 mmol) was added dropwise at room temperature. Progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was concentrated in vacuo. Water was added to this residue and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The

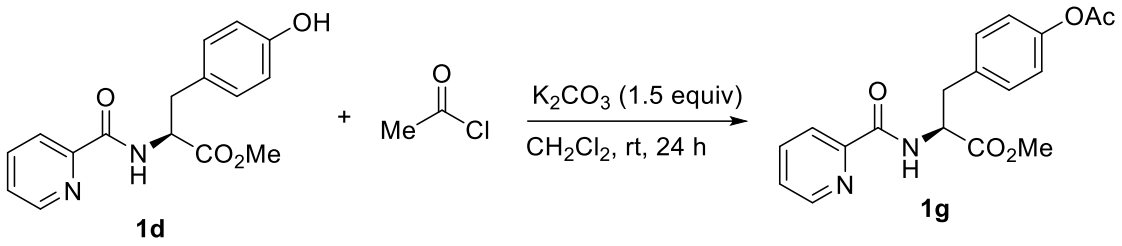
resulting residue was purified by silica gel column chromatography to give compound **1e** as colorless oil (180 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55-8.54 (m, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.43-7.40 (m, 1H), 7.11-7.08 (m, 2H), 6.83-6.80 (m, 2H), 5.05-5.00 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.23-3.14 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.80, 163.91, 158.57, 149.20, 148.25, 137.20, 130.21, 127.88, 126.31, 122.17, 113.92, 55.10, 53.53, 52.25, 37.33. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{17}H_{18}N_2O_4Na$ 337.1164; found 337.1184.

Synthesis of methyl 3-(4-(benzyloxy)phenyl)-2-(picolinamido)propanoate 1f



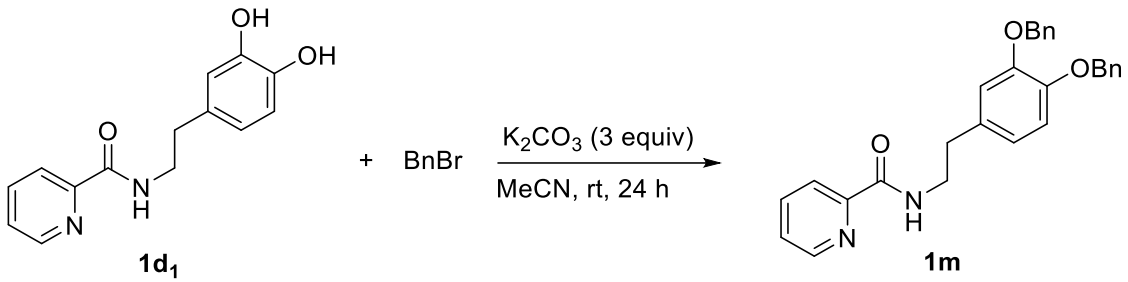
To a stirred solution of **1d** (300 mg, 1 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in anhydrous MeCN (3 mL) at 0 °C, BnBr (178 μL, 1.5 mmol) was added dropwise. The mixture was stirred at room temperature for 24 h. Water was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to obtain the pure compound of **1f** as colorless oil (330 mg, 85%). Eluent: ethyl acetate/hexane (1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53-8.48 (m, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 8.0, 1.6 Hz, 1H), 7.41-7.34 (m, 5H), 7.32-7.28 (m, 1H), 7.11-7.08 (m, 2H), 6.90-6.87 (m, 2H), 5.05-5.02 (m, 1H), 5.00 (s, 2H), 3.71 (s, 3H), 3.23-3.13 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.75, 163.88, 157.78, 149.15, 148.21, 137.17, 136.86, 130.21, 128.45, 128.18, 127.84, 127.40, 126.29, 122.14, 114.82, 69.83, 53.49, 52.22, 37.31. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{23}H_{22}N_2O_4Na$ 413.1477; found 413.1485.

Preparation of Methyl 3-(4-acetoxyphenyl)-2-(picolinamido)propanoate 1g



To a stirred solution of **1d** (300 mg, 1 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in anhydrous CH_2Cl_2 (3 mL), acetyl chloride (178 μL, 1.5 mmol) was added dropwise. The mixture was stirred at room temperature for 24 h. After completion, water was added and the mixture was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to obtain the pure compound of **1g** as colorless oil (212 mg, 62%). Eluent: ethyl acetate/hexane (1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.8 Hz, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 7.86-7.81 (m, 1H), 7.44-7.41 (m, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 5.07 (q, *J* = 8.4 Hz, 1H), 3.73 (s, 3H), 3.29-3.19 (m, 2H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.61, 169.39, 163.98, 149.66, 149.12, 148.28, 137.25, 133.62, 130.22, 126.40, 122.21, 121.60, 53.32, 52.35, 37.57, 21.08. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{18}N_2O_5Na$ 365.1113; found 365.1097.

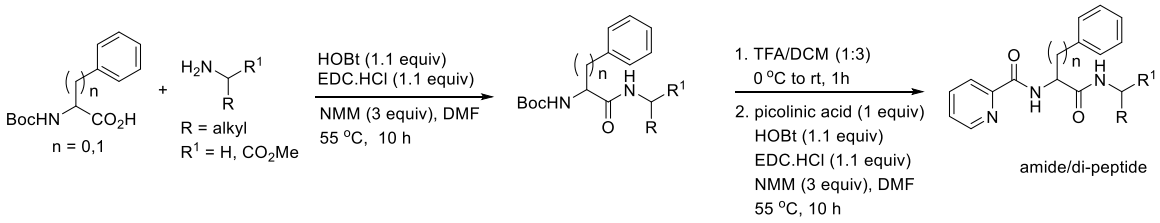
Synthesis of methyl (S)-3-(3,4-bis(benzyloxy)phenyl)-2-(picolinamido)propanoate 1m



To a stirred solution of **1d$_1$** (300 mg, 1 mmol) and K_2CO_3 (414 mg, 3 mmol) in anhydrous MeCN (4 mL) at 0 °C, BnBr (356 μL, 3 mmol) was added dropwise. The mixture was stirred

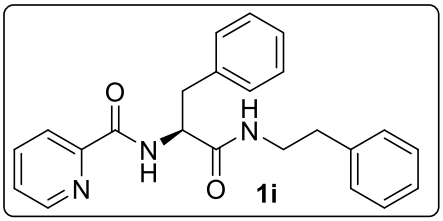
at room temperature for 24 h. Water was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to obtain the pure compound of **1m** as colorless oil (381 mg, 81%). Eluent: ethyl acetate/hexane (1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.4 Hz, 1H), 8.21 (d, *J* = 7.6 Hz, 1H), 8.11 (s, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.44-7.38 (m, 5H), 7.36-7.28 (m, 6H), 6.90-6.86 (m, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 5.13 (d, *J* = 6.8 Hz, 4H), 3.67 (q, *J* = 6.8 Hz, 2H), 2.84 (t, *J* = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.25, 149.96, 149.11, 148.05, 147.65, 137.45, 137.34, 137.30, 132.46, 128.44, 127.77, 127.73, 127.36, 127.32, 126.11, 122.18, 121.63, 115.81, 115.54, 71.51, 71.35, 40.77, 35.42. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{28}H_{26}N_2O_3Na$ 461.1841; found 461.1826.

General Procedure for the synthesis of amides/di-peptides.

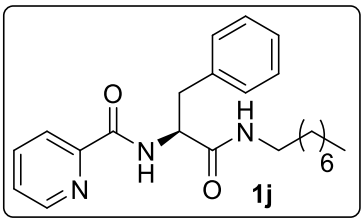


To a solution of Boc-protected L-amino acid (2 mmol) and amino acid methyl ester/amine derivative (2.2 mmol) in anhydrous DMF, NMM (0.66 mL, 6 mmol) was added and the resulting mixture was cooled to 0 °C for 5 minutes with continuous stirring. HOBt (297 mg, 2.2 mmol) was then added to this solution. After 5 minutes, EDC. HCl (420.2 mg, 2.2 mmol) was added and stirred for 10 minutes at 0 °C. The reaction mixture was then heated at 55 °C for 10 h. After stipulated time, the mixture was cooled at room temperature and DMF was evaporated in vacuo. The mixture was dissolved in DCM and treated with trifluoroacetic acid (TFA) for 3 h and then concentrated in vacuo. The crude mixture was dissolved in anhydrous DMF followed by the addition of picolinic acid (1 equiv.) and NMM (3 equiv.). Later, HOBt

(1.1 equiv.) and EDC. HCl (1.1 equiv.) were added within 5 minutes interval at 0 ^{o}C. The reaction mixture was then heated at 55 ^{o}C for 10 h. After cooling, DMF was removed under reduced pressure. Water was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to give desired amides/di-peptides as colorless oil.

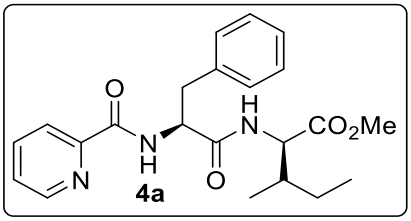


***N*-(1-Oxo-1-(phenethylamino)-3-phenylpropan-2-yl)picolinamide 1i:** Following the above-mentioned procedure, the compound **1i** was obtained as colorless oil (448 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) 8.56-8.52 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.84 (td, *J* = 7.6, 1.6 Hz, 1H), 7.45-7.42 (m, 1H), 7.31-7.21 (m, 5H), 7.18-7.10 (m, 3H), 7.00-6.98 (m, 2H), 5.98 (br s, 1H), 4.76 (q, *J* = 8.4 Hz, 1H), 3.48-3.36 (m, 2H), 3.21 (d, *J* = 7.6 Hz, 2H), 2.73-2.58 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.38, 164.29, 149.11, 148.30, 138.56, 137.29, 136.80, 129.39, 128.66, 128.50, 126.95, 126.46, 126.38, 122.22, 54.89, 40.62, 38.18, 35.49. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{23}H_{23}N_3O_2Na$ 396.1688; found 396.1680.

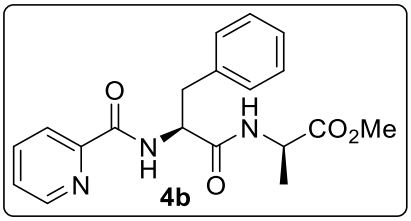


***N*-(1-(Octylamino)-1-oxo-3-phenylpropan-2-yl)picolinamide 1j:** Following the above-mentioned procedure, the compound **1j** was obtained as colorless oil (439 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61-8.56 (m, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.84 (td, *J* = 8.0, 1.6 Hz, 1H),

7.45-7.42 (m, 1H), 7.31-7.28 (m, 4H), 7.25-7.20 (m, 1H), 5.91 (br s, 1H), 4.78 (q, *J* = 8.0 Hz, 1H), 3.26-3.07 (m, 4H), 1.36-1.13 (m, 12H), 0.86 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.34, 164.35, 149.19, 148.34, 137.29, 136.89, 129.36, 128.62, 126.90, 126.45, 122.20, 55.04, 39.55, 38.39, 31.74, 29.27, 29.16, 29.12, 26.74, 22.62, 14.08. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{23}H_{31}N_3O_2Na$ 404.2314; found 404.2293.

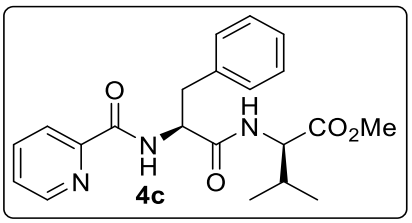


Methyl 3-methyl-2-(3-phenyl-2-(picolinamido)propanamido)pentanoate 4a: Following the above-mentioned procedure, the compound **4a** was obtained as colorless oil (580 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.4 Hz, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 7.83 (td, *J* = 7.6, 1.2 Hz, 1H), 7.44-7.41 (m, 1H), 7.28-7.18 (m, 5H), 6.77 (br s, 1H), 4.99-4.93 (m, 1H), 4.53-4.50 (m, 1H), 3.69 (s, 3H), 3.22 (d, *J* = 6.8 Hz, 2H), 1.86-1.76 (m, 1H), 1.39-1.29 (m, 1H), 1.13-1.02 (m, 1H), 0.84-0.78 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.71, 170.58, 164.39, 149.04, 148.29, 137.27, 136.53, 129.31, 128.52, 126.81, 126.43, 122.23, 56.59, 54.61, 51.99, 38.16, 37.67, 25.06, 15.23, 11.42. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{28}N_3O_4$ 398.2080; found 398.2094.



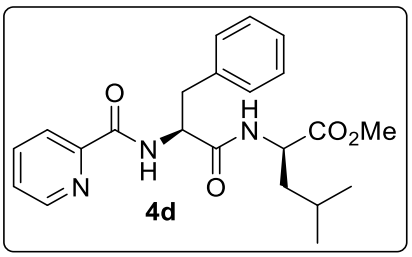
Methyl picolinoylphenylalanylalaninate 4b: Following the above-mentioned procedure, the compound **4b** was obtained as colorless oil (504 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60-8.54 (m, 2H), 8.15 (d, *J* = 7.6 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.44-7.41 (m, 1H),

7.29-7.27 (m, 4H), 7.25-7.19 (m, 1H), 6.70 (d, *J* = 7.2 Hz, 1H), 4.93-4.87 (m, 1H), 4.56-4.48 (m, 1H), 3.70 (s, 3H), 3.25-3.20 (m, 2H), 1.34 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.85, 170.22, 164.37, 149.09, 148.30, 137.29, 136.53, 129.36, 128.56, 126.90, 126.45, 122.25, 54.52, 52.40, 48.17, 38.24, 18.16. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{19}H_{22}N_3O_4$ 356.1610; found 356.1605.



4c

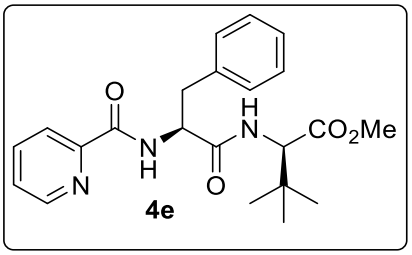
Methyl picolinoylphenylalanylvalinate 4c: Following the above-mentioned procedure, the compound **4c** was obtained as colorless oil (613 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59-8.56 (m, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.45-7.42 (m, 1H), 7.30 (d, *J* = 4.4 Hz, 4H), 7.24-7.21 (m, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 4.88 (q, *J* = 7.6 Hz, 1H), 4.48-4.44 (m, 1H), 3.69 (s, 3H), 3.24 (d, *J* = 7.6 Hz, 2H), 2.13-2.05 (m, 1H), 0.82 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.77, 170.77, 164.38, 149.02, 148.27, 137.25, 136.53, 129.29, 128.48, 126.77, 126.40, 122.24, 57.33, 54.61, 52.01, 38.13, 31.04, 18.75, 17.72. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{21}H_{25}N_3O_4Na$ 406.1743; found 406.1759.



4d

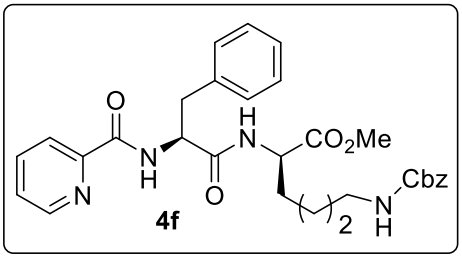
Methyl picolinoylphenylalanylleucinate 4d: Following the above-mentioned procedure, the compound **4d** was obtained as colorless oil (611 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.55-8.54 (m, 1H), 8.14 (d, *J* = 7.6 Hz, 1H), 7.84-7.80 (m, 1H), 7.43-7.40 (m, 1H), 7.29-7.18 (m, 5H), 6.93-6.84 (m, 1H), 5.03-4.95 (m, 1H), 4.59-4.54 (m, 1H), 3.69 (s,

3H), 3.27-3.17 (m, 2H), 1.59-1.44 (m, 3H), 0.84-0.81 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.86, 170.56, 164.31, 149.01, 148.25, 137.22, 136.51, 129.33, 128.42, 126.74, 126.38, 122.17, 54.36, 52.15, 50.81, 41.17, 38.22, 24.61, 22.50, 21.83. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{28}N_3O_4$ 398.2080; found 398.2094.



4e

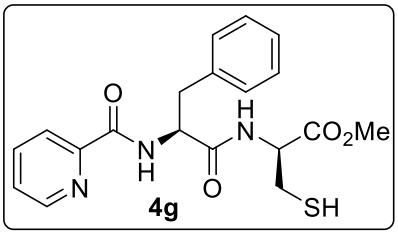
Methyl 3,3-dimethyl-2-(3-phenyl-2-(picolinamido)propanamido)butanoate 4e: Following the above-mentioned procedure, the compound **4e** was obtained as colorless oil (508 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 8.56 (d, *J* = 4.8 Hz, 1H), 8.18 (d, *J* = 7.6 Hz, 1H), 7.83 (td, *J* = 8.0, 1.2 Hz, 1H), 7.44-7.41 (m, 1H), 7.28-7.18 (m, 5H), 6.93-6.83 (m, 1H), 4.98 (s, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 3.67 (s, 3H), 3.24-3.15 (m, 2H), 0.88 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.24, 170.59, 164.38, 149.05, 148.26, 137.26, 136.56, 129.29, 128.48, 126.76, 126.40, 122.28, 60.21, 54.72, 51.66, 38.09, 34.56, 26.37. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{28}N_3O_4$ 398.2080; found 398.2053.



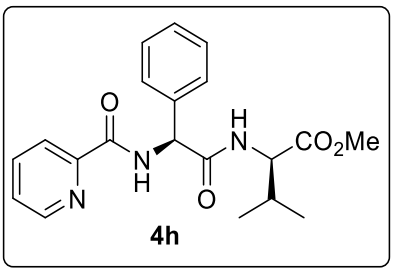
4f

Methyl N^6-((benzyloxy)carbonyl)-N^2-(picolinoylphenylalanyl)lysinate 4f: Following the above-mentioned procedure, the compound **4f** was obtained as colorless oil (622 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 7.6 Hz, 1H), 8.52 (d, *J* = 4.4 Hz, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.38-7.19 (m, 11H), 6.92-6.86 (m, 1H), 5.30 (br s, 1H), 5.12-

5.03 (m, 2H), 4.93-4.88 (m, 1H), 4.54-4.49 (m, 1H), 3.67 (s, 3H), 3.26-3.14 (m, 2H), 3.07-3.06 (m, 2H), 1.79-1.75 (m, 1H), 1.65-1.56 (m, 1H), 1.43-1.40 (m, 2H), 1.28-1.21 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.28, 170.77, 164.60, 156.59, 149.04, 148.36, 137.34, 136.75, 136.58, 129.34, 128.58, 128.49, 128.08, 128.02, 126.90, 126.50, 122.30, 66.52, 54.76, 52.36, 52.13, 40.45, 38.07, 31.67, 29.13, 22.20. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{30}H_{35}N_4O_6$ 547.2557; found 547.2516.



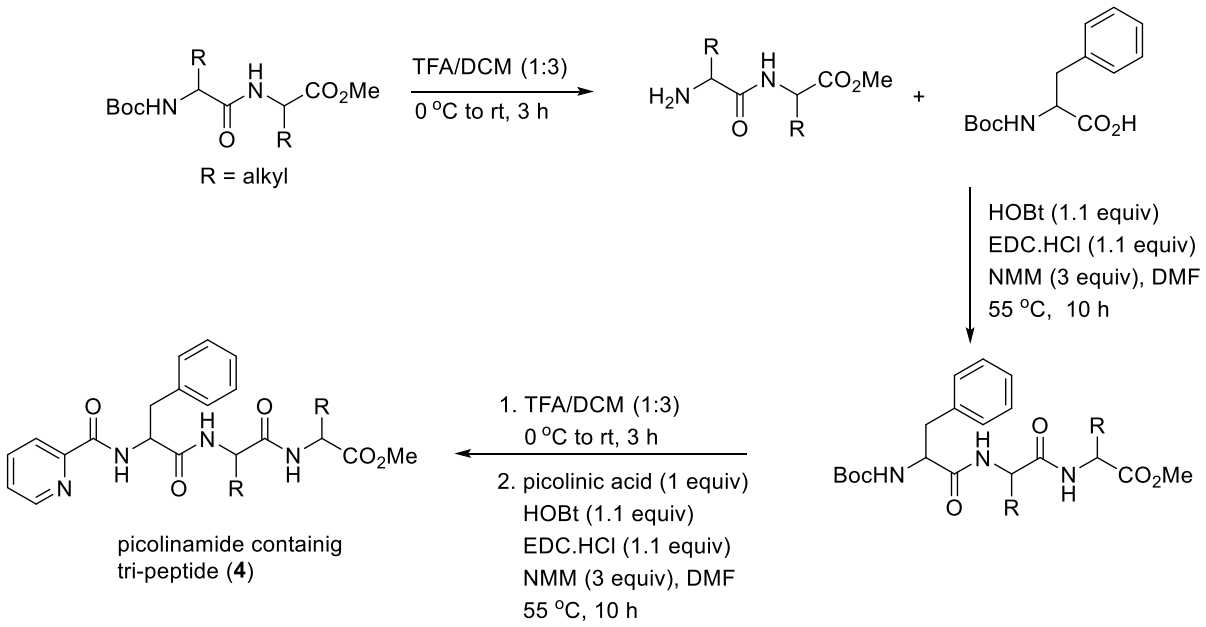
Methyl picolinoylphenylalanylcysteinate 4g: Following the above-mentioned procedure, the compound **4g** was obtained as colorless oil (418 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.0 Hz, 1H), 8.52-8.51 (m, 1H), 8.10-8.05 (m, 1H), 7.81-7.76 (m, 1H), 7.74-7.69 (m, 1H), 7.41-7.38 (m, 1H), 7.27-7.24 (m, 2H), 7.21-7.14 (m, 3H), 5.12 (q, *J* = 6.8 Hz, 1H), 4.87-4.82 (m, 1H), 3.66 (s, 3H), 3.34-3.29 (m, 1H), 3.20-3.14 (m, 1H), 3.06-2.93 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.24, 170.32, 164.62, 149.09, 148.33, 137.23, 136.66, 129.35, 128.52, 126.75, 126.44, 122.43, 54.71, 52.62, 52.51, 39.83, 38.29. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{19}H_{22}N_3O_4S$ 388.1331; found 388.1355.



Methyl (2-phenyl-2-(picolinamido)acetyl)valinate 4h: Following the above-mentioned procedure, the compound **4h** was obtained as colorless oil (465 mg, 63%). ^{1}H NMR (400 MHz,

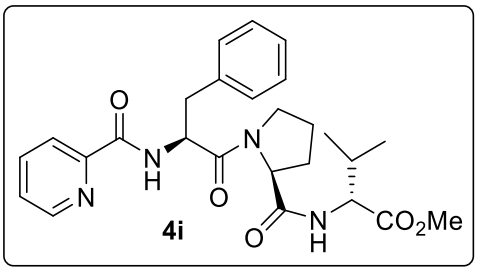
$CDCl_3$) δ 9.18 (d, *J* = 7.6 Hz, 1H), 8.58 (d, *J* = 4.0 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.82 (td, *J* = 8.0, 1.6 Hz, 1H), 7.53-7.50 (m, 2H), 7.44-7.40 (m, 1H), 7.36-7.29 (m, 3H), 6.92 (d, *J* = 8.4 Hz, 1H), 5.91 (d, *J* = 7.6 Hz, 1H), 4.57-4.54 (m, 1H), 3.66 (s, 3H), 2.19-2.14 (m, 1H), 0.94-0.88 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.90, 169.88, 163.99, 149.29, 148.31, 137.34, 137.20, 128.89, 128.33, 127.33, 126.37, 122.30, 57.58, 57.08, 52.06, 31.17, 18.87, 17.86. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{20}H_{23}N_3O_4Na$ 392.1586.; found 392.1577.

General Procedure for the synthesis of tri-peptides.



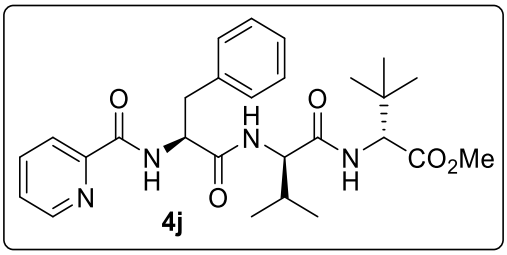
A solution of Boc-protected di-peptide (2 mmol) in DCM was treated with trifluoroacetic acid at 0 °C. The mixture was stirred at room temperature for 3 h and then concentrated in vacuo. The residue was dissolved in anhydrous DMF and Boc protected L-alanine (2 mmol) and NMM (0.66 mL, 6 mmol) was added and the resulting mixture was cooled to 0 °C for 5 minutes with continuous stirring. HOBt (297 mg, 2.2 mmol) was then added to this solution. After 5 minutes, EDC. HCl (420.2 mg, 2.2 mmol) was added to this solution and stirred for 10 minutes at 0 °C. The reaction mixture was then heated at 55 °C for 10 h. After stipulated time, the mixture was cooled at room temperature and DMF was evaporated in vacuo. The mixture dissolved in DCM

was treated with trifluoroacetic acid for 3 h and then concentrated in vacuo. The crude oil was dissolved in anhydrous DMF followed by the addition of picolinic acid (1 equiv.) and NMM (3 equiv.). Later, HOBt (1.1 equiv.) and EDC. HCl (1.1 equiv.) were added within 5 minutes interval at 0 ^{o}C. The reaction mixture was then heated at 55 ^{o}C for 10 h. After cooling, DMF was removed under reduced pressure. Water was added and the mixture was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to give desired tri-peptides **4** as colorless oil.



4i

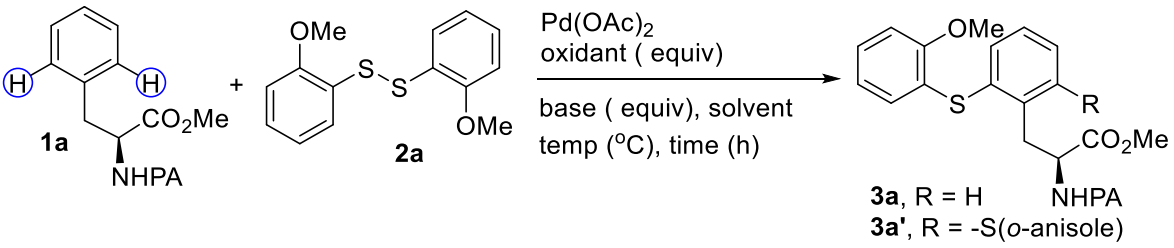
Methyl picolinoylphenylalanylprolylvalinate 4i: Following the above-mentioned procedure, the compound **4i** was obtained as colorless oil (490 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 8.4 Hz, 1H), 8.57 (d, *J* = 4.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.43-7.40 (m, 1H), 7.34-7.20 (m, 6H), 5.16 (q, *J* = 8.4 Hz, 1H), 4.62 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.47-4.44 (m, 1H), 3.75 (m, 3H), 3.73-3.55 (m, 1H), 3.21-3.04 (m, 2H), 2.33-2.28 (m, 1H), 2.23-2.15 (m, 1H), 2.04-1.83 (m, 4H), 0.99 (t, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.16, 171.50, 170.60, 163.93, 149.25, 148.33, 137.21, 136.24, 129.27, 128.59, 127.01, 126.32, 122.14, 60.05, 57.71, 52.31, 52.07, 47.55, 39.27, 31.03, 27.21, 25.10, 19.09, 18.08. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{26}H_{33}N_4O_5$ 481.2451; found 481.2461.



Methyl 3,3-dimethyl-2-(3-methyl-2-(3-phenyl-2-(picolinamido)propanamido)butanamido)butanoate 4j: Following the above-mentioned procedure, the compound **4j** was obtained as colorless oil (545 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55-8.53 (m, 2H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.45-7.41 (m, 1H), 7.27-7.26 (m, 4H), 7.23-7.18 (m, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.53 (d, *J* = 9.2 Hz, 1H), 4.91 (q, *J* = 8.0 Hz, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 4.25-4.22 (m, 1H), 3.72 (s, 3H), 3.29-3.19 (m, 2H), 2.14-2.05 (m, 1H), 0.98 (s, 9H), 0.85-0.81 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.69, 170.93, 170.45, 164.61, 149.03, 148.34, 137.35, 136.51, 129.30, 128.68, 126.96, 126.52, 122.32, 60.22, 58.96, 54.70, 51.83, 37.68, 34.58, 30.53, 26.61, 19.10, 17.99. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{27}H_{37}N_4O_5$ 497.2764; found 497.2760.

3. Optimization of the reaction conditions

Table 1: Optimization of the reaction conditions



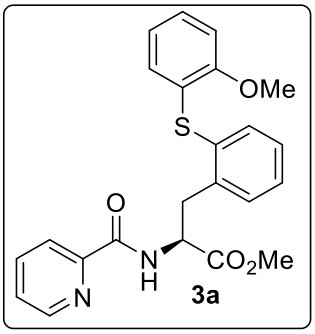
Entry	Catalyst (10 mol%)	Oxidant (2 equiv)	Base (2 equiv)	Solvent	Temp (°C)	Yield (%)[b]
1	$Pd(OAc)_2$	AgOAC	Na_2CO_3	DCE	120	60 (m/d = 2.6:1)[c]
2	$Pd(OAc)_2$	AgOAC	Na_2CO_3	MeCN	120	40 (m/d = 2.3:1)[c]
3	$Pd(OAc)_2$	AgOAC	Na_2CO_3	1,4-dioxane	120	54 (m/d = 2.2:1)[c]
4	$Pd(OAc)_2$	AgOAC	Na_2CO_3	tBuOH	120	47 (m/d = 2.2:1)[c]
5	$Pd(OAc)_2$	AgOAC	Na_2CO_3	benzene	120	59 (m/d = 2.5:1)[c]

6	$Pd(OAc)_2$	AgOAC	Na_2CO_3	DMF	120	n.r.
7	$Pd(OAc)_2$	AgOAC	Na_2CO_3	DMSO	120	n.r.
8	**$Pd(OAc)_2$**	**AgOAC**	**Na_2CO_3**	**toluene**	**120**	**70 (m/d = 2.7:1)[c]**
9	$Pd(OAc)_2$	AgOAC	Na_2CO_3	THF	120	47 (m/d = 2.7:1)[c]
10	$Pd(OAc)_2$	Ag_2CO_3	Na_2CO_3	toluene	120	68 (m/d = 1.3:1)[c]
11	$Pd(OAc)_2$	$Cu(OAc)_2$	Na_2CO_3	toluene	120	trace
12	$Pd(OAc)_2$	$Co(OAC)_2$	Na_2CO_3	toluene	120	trace
13	$Pd(OAc)_2$	AgOAC	NaOAc	toluene	120	63 (m/d = 1.3:1)[c]
14	$Pd(OAc)_2$	AgOAC	$NaHCO_3$	toluene	120	66 (m/d = 2.3:1)[c]
15	$Pd(OAc)_2$	AgOAC	$KHCO_3$	toluene	120	58 (m/d = 1.5:1)[c]
16	$Pd(OAc)_2$	AgOAC	K_2CO_3	toluene	120	64 (m/d = 1.7:1)[c]
17	$Pd(OAc)_2$	AgOAC	KOtBu	toluene	120	n.r.
18	$Pd(OAc)_2$	AgOAC	Na_2CO_3	toluene	120	68 (m/d = 1:1.4)[c,d]
19	$Pd(OAc)_2$	AgOAC	Na_2CO_3	toluene	120	44 (m/d = 1:1.1)[c,e]
20	$Pd(OAc)_2$	AgOAC	Na_2CO_3	toluene	120	65 (m/d = 1:1.3)[c,f]
21	$Pd(OAc)_2$	AgOAC	Na_2CO_3	toluene	100	34 (m/d = 3.3:1)[c,g]
22	$Pd(OAc)_2$	AgOAC	Na_2CO_3	toluene	110	52 (m/d = 2:1)[c,h]
23	$Pd(OAc)_2$	AgOAC	-------	toluene	120	56 (m/d = 2.6:1)[c]
24	$Pd(OAc)_2$	----	Na_2CO_3	toluene	120	trace
25	------	AgOAC	Na_2CO_3	toluene	120	n.r.

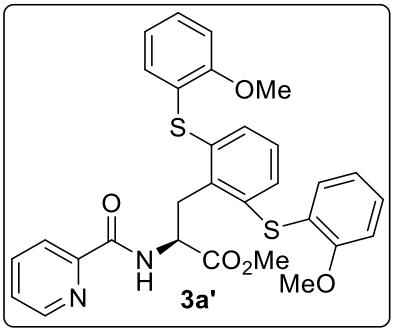
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), AgOAc (2 equiv.), and Na_2CO_3 (2 equiv.) in toluene (3 mL) at 120 ^oC for 24 h under Air. [b]Isolated yield. [c]Ratio of mono- and di-thiolated products. n.r. = no reaction. [d]3 equiv. of AgOAc. [e]3 equiv. of Na_2CO_3. [f]3 equiv. of **2a**. [g]100 ^oC temperature. [h]110 ^oC temperature.

4. General Procedure for C(sp^2)-H-Chalcogenation of amino acids/amines

To a clean, oven-dried 15 mL sealed reaction tube with previously placed magnetic stir-bar was charged with amine derivative (amino acid/amine) **1** (0.2 mmol), diaryl disulfide/ diaryl diselenide **2** (0.4 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol %), AgOAc (67 mg, 0.4 mmol), sodium carbonate (42.4 mg, 0.4 mmol) in toluene. The mixture was then vigorously stirred at 120 °C for 24 h. After completion, the reaction mixture was cooled to room temperature and filtered through a short pad of celite using ethyl acetate as the eluent (30 mL). Evaporation of solvent under vacuum provided a crude mixture which was purified by silica gel column chromatography using ethyl acetate/hexane solvent system to afford the desired chalcogenated products **3** and **3'**.

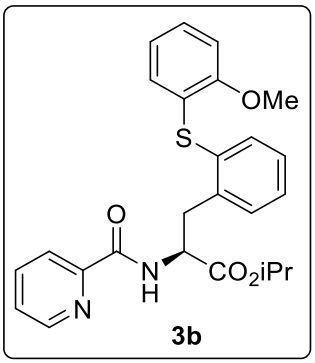


Methyl 3-(2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3a. Thiolated compound **3a** was prepared according to the general procedure with starting materials **1a** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as eluent. **3a** was obtained as a colorless oil (44 mg, 51%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.59 (d, *J* = 7.7 Hz, 1H), 8.54 (d, *J* = 6.6 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 7.82 (t, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 6.3 Hz, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.19 (q, *J* = 7.7 Hz, 2H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 6.81 (t, *J* = 7.7 Hz, 1H), 5.14 (q, *J* = 5.6 Hz, 1H), 3.88 (s, 3H), 3.74 (s, 3H), 3.51-3.48 (m, 1H), 3.44-3.40 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.04, 164.20, 156.91, 149.34, 148.22, 138.69, 137.16, 134.01, 133.57, 130.51, 130.22, 128.13, 128.07, 127.74, 126.26, 124.65, 122.25, 121.29, 110.77, 55.87, 53.14, 52.41, 36.00. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}N_2O_4S$ 423.1378; found 423.1353.



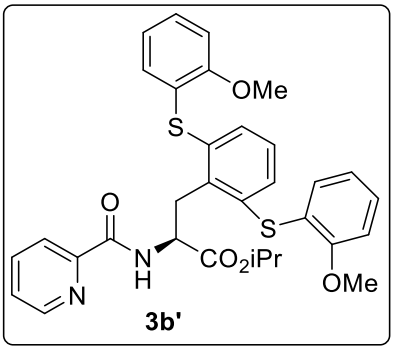
Methyl 3-(2,6-bis((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3a': Thiolated compound **3a'** was prepared according to the general procedure with starting materials **1a** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase.

3a' was obtained as a colorless oil (22 mg, 19%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 8.4 Hz, 1H), 8.53-8.51 (m, 1H), 8.58 (d, *J* = 7.6 Hz, 1H), 7.78-7.74 (m, 1H), 7.38-7.35 (m, 1H), 7.25-7.21 (m, 2H), 7.07-6.97 (m, 5H), 6.90 (d, *J* = 7.6 Hz, 2H), 6.85-6.81 (m, 2H), 5.45-5.39 (m, 1H), 3.84 (s, 6H), 3.75 (s, 3H), 3.70-3.67 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.13, 164.46, 157.65, 149.56, 148.18, 138.65, 136.98, 136.37, 131.88, 131.59, 128.64, 128.30, 126.07, 123.58, 122.23, 121.30, 111.01, 55.91, 52.56, 52.46, 33.58. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{30}H_{28}N_2O_5S_2Na$ 583.1337; found 583.1363.



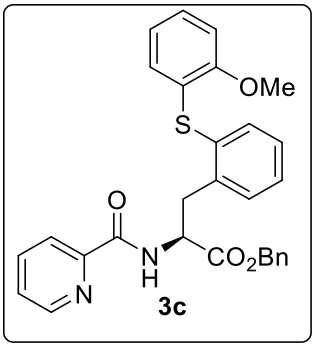
3b

Isopropyl 3-(2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3b: Thiolated compound **3b** was prepared according to the general procedure with starting materials **1b** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3b** was obtained as a colorless oil (40 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57-8.52 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.81-7.77 (m, 1H), 7.40-7.36 (m, 2H), 7.30-7.21 (m, 2H), 7.18-7.14 (m, 2H), 6.87-6.76 (m, 3H), 5.12-5.06 (m, 1H), 5.04-4.98 (m, 1H), 3.86 (s, 3H), 3.46-3.36 (m, 2H), 1.24 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.19, 164.12, 156.85, 149.45, 148.21, 138.96, 137.13, 134.14, 133.50, 130.56, 130.06, 128.13, 127.99, 127.61, 126.20, 124.85, 122.21, 121.27, 110.73, 69.18, 55.86, 53.22, 36.27, 21.77, 21.58. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{25}H_{27}N_2O_4S$ 451.1692; found 451.1663.



3b'

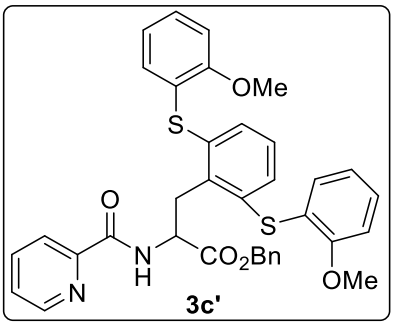
Isopropyl 3-(2,6-bis((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3b': Thiolated compound **3b'** was prepared according to the general procedure with starting materials **1b** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3b'** was obtained as a colorless oil (35 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 8.4 Hz, 1H), 8.53-8.52 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.78-7.74 (m, 1H), 7.38-7.35 (m, 1H), 7.24-7.20 (m, 2H), 7.09-7.07 (m, 2H), 7.04-6.98 (m, 3H), 6.90-6.88 (m, 2H), 6.85-6.81 (m, 2H), 5.41-5.35 (m, 1H), 5.07-5.01 (m, 1H), 3.85 (s, 6H), 3.71-3.61 (m, 2H), 1.26 (d, *J* = 6.4 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.26, 164.33, 157.56, 149.68, 148.16, 139.18, 136.93, 136.27, 131.85, 131.65, 128.45, 128.23, 125.98, 123.87, 122.19, 121.28, 110.94, 69.03, 55.89, 52.66, 33.91, 21.79, 21.64. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{32}H_{32}N_2O_5S_2$ 589.1831; found 589.1837.



3c

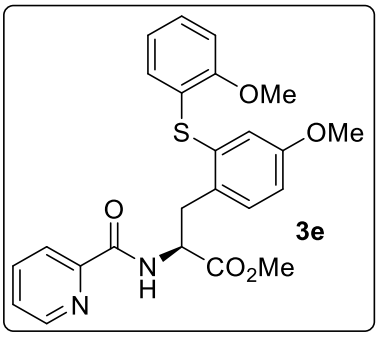
Benzyl 3-(2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3c: Thiolated compound **3c** was prepared according to the general procedure with starting materials **1c** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3c** was obtained

as a colorless oil (29 mg, 29%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.0 Hz, 1H), 8.45-8.44 (m, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.75-7.70 (m, 1H), 7.34-7.30 (m, 1H), 7.24-7.21 (m, 4H), 7.19-7.16 (m, 3H), 7.13-7.05 (m, 3H), 6.78-6.73 (m, 2H), 6.69-6.65 (m, 1H), 5.14-5.04 (m, 3H), 3.74 (s, 3H), 3.42-3.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.50, 164.20, 156.88, 149.36, 148.22, 138.62, 137.15, 135.38, 134.10, 133.56, 130.60, 130.17, 128.47, 128.20, 128.15, 128.07, 127.68, 126.25, 124.67, 122.25, 121.27, 110.74, 67.14, 55.82, 53.16, 36.14. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{29}H_{27}N_2O_4S$ 499.1692; found 499.1714.

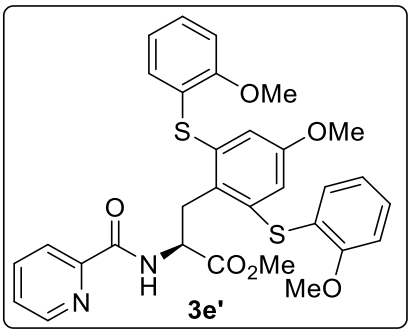


3c'

Benzyl 3-(2,6-bis((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3c': Thiolated compound **3c'** was prepared according to the general procedure with starting materials **1c** and **2a**, purified using ethyl acetate and hexane (1:2) as the mobile phase. **3c'** was obtained as a colorless oil (38 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.4 Hz, 1H), 8.45-8.43 (m, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.71-7.67 (m, 1H), 7.30-7.27 (m, 1H), 7.17-7.12 (m, 7H), 7.00-6.98 (m, 2H), 6.95-6.89 (m, 3H), 6.80 (d, *J* = 8.4 Hz, 2H), 6.73 (t, *J* = 7.6 Hz, 2H), 5.44-5.38 (m, 1H), 5.12 (s, 2H), 3.72 (s, 6H), 3.68-3.57 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.56, 164.44, 157.59, 149.59, 148.17, 138.86, 136.98, 136.33, 135.70, 131.83, 131.74, 128.54, 128.38, 128.30, 127.92, 127.83, 126.06, 123.68, 122.23, 121.28, 110.97, 66.98, 55.87, 52.61, 33.78. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{36}H_{32}N_2O_5S_2Na$ 659.1650; found 659.1641.

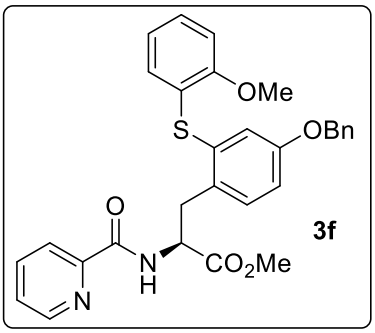


Methyl 3-(4-methoxy-2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3e: Thiolated compound **3e** was prepared according to the general procedure with starting materials **1e** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3e** was obtained as a colorless oil (17 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55-8.53 (m, 2H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.83-7.78 (m, 1H), 7.42-7.38 (m, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.20-7.16 (m, 1H), 6.89-6.86 (m, 2H), 6.82-6.86 (m, 3H), 5.09-5.04 (m, 1H), 3.87 (s, 3H), 3.73 (s, 3H), 3.68 (s, 3H), 3.42-3.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.12, 164.19, 158.95, 156.96, 149.39, 148.22, 137.15, 134.59, 131.32, 130.46, 127.90, 126.24, 124.28, 122.26, 121.34, 118.54, 114.09, 110.78, 55.88, 55.25, 53.29, 52.39, 35.18. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{24}H_{25}N_2O_5S$ 453.1484; found 453.1460.

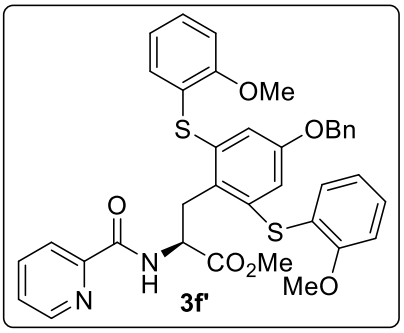


Methyl 3-(4-methoxy-2,6-bis((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3e': Thiolated compound **3e'** was prepared according to the general procedure with starting materials **1e** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3e'** was obtained as a colorless oil (24 mg, 40%). ^{1}H NMR

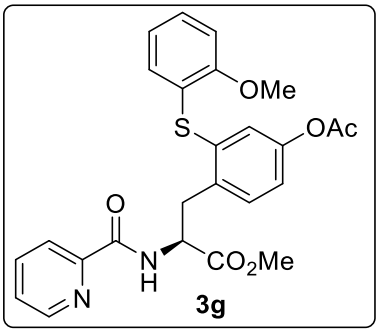
(400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 8.0 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.80-7.76 (m, 1H), 7.40-7.36 (m, 1H), 7.25-7.22 (m, 2H), 7.08-7.06 (m, 2H), 6.91-6.82 (m, 4H), 6.61 (s, 2H), 5.39-5.34 (m, 1H), 3.86 (s, 6H), 3.75 (s, 3H), 3.63-3.56 (m, 2H), 3.52 (s 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.23, 164.47, 158.66, 157.68, 149.63, 148.17, 137.17, 136.97, 132.07, 130.57, 128.76, 126.04, 123.26, 122.27, 121.35, 116.85, 111.00, 55.93, 55.14, 52.74, 52.43, 32.77. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{31}H_{31}N_2O_6S_2$ 591.1624; found 591.1650.



Methyl 3-(4-(benzyloxy)-2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3f: Thiolated compound **3f** was prepared according to the general procedure with starting materials **1f** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3f** was obtained as a colorless oil (50 mg, 47%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.56-8.51 (m, 2H), 8.13 (d, *J* = 7.6 Hz, 1H), 7.82-7.78 (m, 1H), 7.41-7.38 (m, 1H), 7.35-7.28 (m, 5H), 7.23-7.17 (m, 2H), 6.92-6.90 (m, 1H), 6.87-6.78 (m, 4H), 5.10-5.04 (m, 1H), 4.91 (s, 2H), 3.83 (s, 3H), 3.72 (s, 3H), 3.45-3.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.12, 164.21, 158.15, 157.14, 149.39, 148.23, 137.16, 136.63, 134.93, 131.35, 130.90, 130.45, 128.56, 128.09, 128.00, 127.55, 126.25, 123.95, 122.27, 121.36, 119.02, 114.92, 110.88, 70.00, 55.87, 53.27, 52.39, 35.22. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{30}H_{29}N_2O_5S$ 529.1797; found 529.1772.

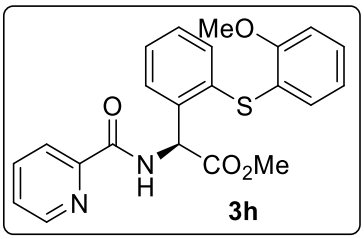


Methyl 3-(4-(benzyloxy)-2,6-bis((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3f': Thiolated compound **3f'** was prepared according to the general procedure with starting materials **1f** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3f'** was obtained as a colorless oil (32 mg, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 8.4 Hz, 1H), 8.53 (d, *J* = 4.4 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.80-7.76 (m, 1H), 7.39-7.36 (m, 1H), 7.28-7.22 (m, 5H), 7.19-7.16 (m, 2H), 7.10-7.07 (m, 2H), 6.89-6-82 (m, 4H), 6.64 (s, 2H), 5.39-5.33 (m, 1H), 4.74 (s, 2H), 3.82 (s, 6H), 3.75 (s, 3H), 3.64-3.53 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.24, 164.51, 157.87, 157.83, 149.64, 148.18, 137.43, 136.97, 136.34, 132.46, 130.21, 128.92, 128.52, 127.98, 127.57, 126.04, 122.93, 122.27, 121.36, 117.24, 111.08, 69.91, 55.90, 52.72, 52.43, 32.73. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{37}H_{35}N_2O_6S_2$ 667.1937; found 667.1908.

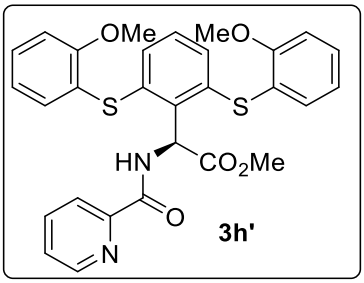


Methyl 3-(4-acetoxy-2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3g: Thiolated compound **3g** was prepared according to the general procedure with starting materials **1g** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase.

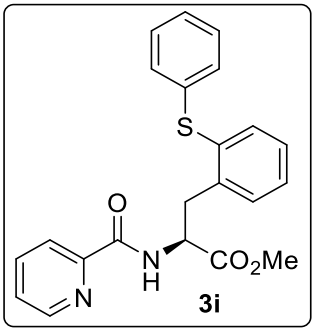
3g was obtained as a colorless oil (49 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.0 Hz, 1H), 8.55-8.54 (m, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.85-7.81 (m, 1H), 7.44-7.41 (m, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.28-7.20 (m, 1H), 7.08-7.02 (m, 1H), 6.96-6.85 (m, 4H), 5.17-5.12 (m, 1H), 3.84 (s, 3H), 3.75 (s, 3H), 3.50-3.37 (m, 2H), 2.22 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.96, 169.05, 164.24, 157.64, 149.93, 149.30, 148.23, 137.19, 136.00, 134.88, 131.97, 131.05, 128.79, 126.30, 124.98, 122.82, 122.29, 121.37, 120.65, 111.07, 55.86, 52.92, 52.45, 35.44. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{25}H_{25}N_2O_6S$ 481.1433; found 481.1443.



Methyl 2-(2-((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)acetate 3h: Thiolated compound **3h** was prepared according to the general procedure with starting materials **1h** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3h** was obtained as a colorless oil (30 mg, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 6.8 Hz, 1H), 8.51 (d, *J* = 4.8 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.81-7.77 (m, 1H), 7.56-7.54 (m, 1H), 7.44-7.33 (m, 3H), 7.30-7.28 (m, 1H), 7.13-7.09 (m, 1H), 6.91-6.89 (m, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 3.86 (s, 3H), 3.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02, 163.75, 156.84, 149.32, 148.17, 139.47, 137.10, 135.57, 133.82, 130.62, 129.31, 129.23, 128.71, 127.67, 126.22, 125.06, 122.27, 121.10, 110.72, 55.90, 55.34, 52.77. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{21}N_2O_4S$ 409.1222; found 409.1202.

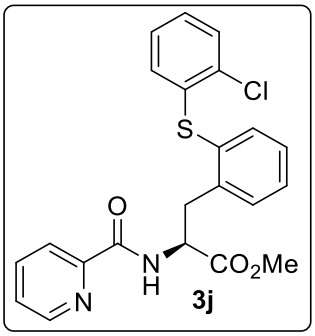


Methyl 2-(2,6-bis((2-methoxyphenyl)thio)phenyl)-2-(picolinamido)acetate 3h': Thiolated compound **3h'** was prepared according to the general procedure with starting materials **1h** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as eluent. **3h'** was obtained as a colorless oil (27 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, *J* = 8.0 Hz, 1H), 8.38-8.37 (m, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.75 (td, *J* = 7.6, 1.6 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 2H), 7.34-7.30 (m, 1H), 7.22-7.17 (m, 2H), 7.15-7.11(m, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.75 (t, *J* = 7.6 Hz, 2H), 3.85 (s, 6H), 3.60 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.69, 163.71, 156.93, 149.62, 148.02, 142.28, 136.84, 135.11, 130.91, 129.35, 127.91, 125.85, 125.05, 122.33, 121.07, 110.81, 55.91, 54.18, 52.77. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{29}H_{26}N_2O_5S_2Na$ 569.1181; found 569.1155.

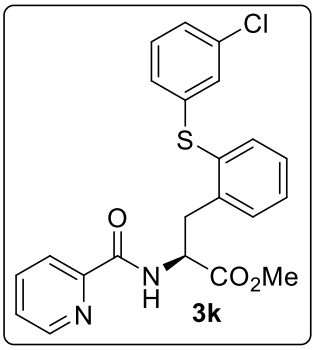


Methyl 3-(2-(phenylthio)phenyl)-2-(picolinamido)propanoate 3i: Thiolated compound **3i** was prepared according to the general procedure with starting materials **1a** and **2b**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3i** was obtained as a colorless oil (43 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.4 Hz, 1H), 8.54 (d, *J* = 4.8 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.83-7.78 (m, 1H), 7.42-7.39 (m, 1H), 7.32-7.28 (m, 2H), 7.25-

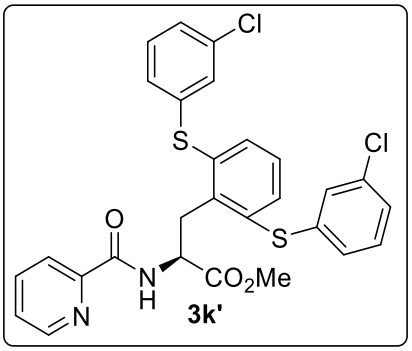
7.16 (m, 7H), 5.15-5.09 (m, 1H), 3.73 (s, 3H), 3.48-3.43 (m, 1H), 3.39-3.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.99, 164.17, 149.32, 148.23, 137.93, 137.20, 136.09, 134.82, 133.49, 130.71, 130.03, 129.16, 128.12, 127.99, 126.64, 126.30, 122.28, 77.35, 77.03, 76.71, 53.19, 52.44, 36.18. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{22}H_{20}N_2O_3SNa$ 415.1092; found 415.1075.



Methyl 3-(2-((2-chlorophenyl)thio)phenyl)-2-(picolinamido)propanoate 3j: Thiolated compound **3j** was prepared according to the general procedure with starting materials **1a** and **2c**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3j** was obtained as a colorless oil (49 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55-8.53 (m, 2H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 8.0, 1.6 Hz, 1H), 7.42-7.29 (m, 5H), 7.24-7.21 (m, 1H), 7.09-7.00 (m, 2H), 6.73 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.12-5.06 (m, 1H), 3.74 (s, 3H), 3.49-3.43 (m, 1H), 3.37-3.31 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.84, 164.16, 149.26, 148.25, 139.86, 137.19, 136.62, 135.56, 132.51, 132.06, 131.06, 129.67, 129.30, 128.92, 128.46, 127.23, 126.82, 126.31, 122.26, 53.19, 52.49, 36.22. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}ClN_2O_3S$ 427.0883; found 427.0881.

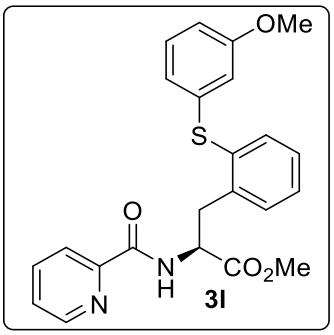


Methyl 3-(2-((3-chlorophenyl)thio)phenyl)-2-(picolinamido)propanoate 3k: Thiolated compound **3k** was prepared according to the general procedure with starting materials **1a** and **2d**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3k** was obtained as a colorless oil (28 mg, 32%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49-8.45 (m, 2H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.73 (td, *J* = 7.6, 1.6 Hz, 1H), 7.35-7.32 (m, 1H), 7.28-7.26 (m, 2H), 7.22-7.18 (m, 1H), 7.16-7.12 (m, 1H), 7.09-7.03 (m, 3H), 6.97-6.92 (m, 1H), 5.06-5.00 (m, 1H), 3.65 (s, 3H), 3.39-3.34 (m, 1H), 3.30-3.24 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.87, 164.12, 149.21, 148.24, 138.95, 138.88, 137.21, 134.89, 134.68, 133.07, 131.00, 130.06, 128.90, 128.52, 128.39, 127.00, 126.40, 126.33, 122.26, 53.21, 52.45, 36.33. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}ClN_2O_3S$ 427.0883; found 427.0881.

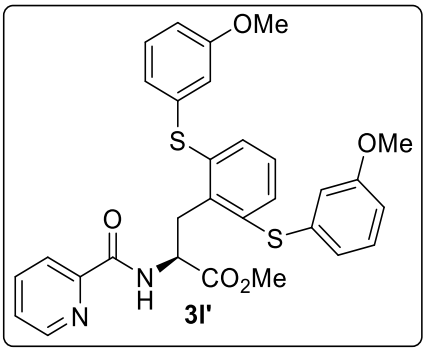


Methyl 3-(2,6-bis((3-chlorophenyl)thio)phenyl)-2-(picolinamido)propanoate 3k': Thiolated compound **3k'** was prepared according to the general procedure with starting materials **1a** and **2d**, purified using ethyl acetate and hexane mixture (1:5) as the mobile phase. **3k'** was obtained as a colorless oil (45 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* =

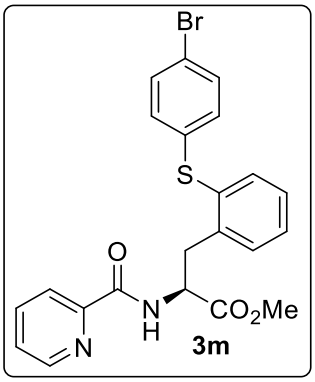
8.8 Hz, 1H), 8.52-8.51 (m, 1H), 8.08-8.05 (m, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.22-7.21 (m, 2H), 7.20-7.17 (m, 6H), 7.14-7.09 (m, 3H), 5.41-5.35 (m, 1H), 3.77 (s, 3H), 3.59-3.57 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.80, 164.27, 149.22, 148.20, 139.09, 137.58, 137.11, 136.30, 135.03, 133.03, 130.28, 129.79, 128.88, 128.24, 127.18, 126.25, 122.30, 52.60, 52.34, 33.90. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{23}Cl_2N_2O_3S_2$ 569.0527; found 569.0546.



Methyl 3-(2-((3-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3l: Thiolated compound **3l** was prepared according to the general procedure with starting materials **1a** and **2e**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3l** was obtained as a colorless oil (48 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.4 Hz, 1H), 8.54-8.52 (m, 1H), 8.11-8.09 (m, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.33-7.30 (m, 2H), 7.24-7.13 (m, 3H), 6.78-6.70 (m, 3H), 5.14-5.09 (m, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.48-3.43 (m, 1H), 3.38-3.32 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.92, 164.10, 160.00, 149.24, 148.19, 138.23, 137.55, 137.15, 134.22, 133.95, 130.71, 129.87, 128.21, 128.10, 126.25, 122.20, 121.87, 114.91, 112.29, 55.19, 53.15, 52.38, 36.19. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}N_2O_4S$ 423.1378; found 423.1395.

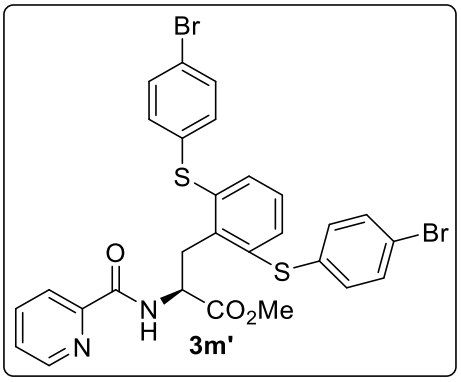


Methyl 3-(2,6-bis((3-methoxyphenyl) thio)phenyl)-2-(picolinamido)propanoate 3l': Thiolated compound **3l'** was prepared according to the general procedure with starting materials **1a** and **2e**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3l'** was obtained as a colorless oil (23 mg, 20%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 8.8 Hz, 1H), 8.54-8.52 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.40-7.37 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.13-7.11 (m, 2H), 7.05-7.01 (m, 1H), 6.87-6.83 (m, 4H), 6.78-6.76 (m, 2H), 5.43-5.37 (m, 1H), 3.76 (s, 3H), 3.74 (s, 6H), 3.62-3.60 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.99, 164.35, 160.13, 149.40, 148.21, 138.05, 137.06, 137.03, 136.47, 131.94, 130.04, 128.43, 126.14, 123.02, 122.24, 115.99, 113.03, 55.29, 52.53, 52.38, 33.64. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{30}H_{29}N_2O_5S_2$ 561.1518; found 561.1524.

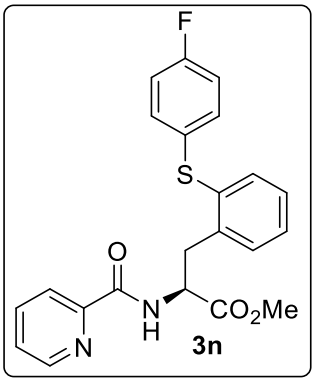


Methyl 3-(2-((4-bromophenyl)thio)phenyl)-2-(picolinamido)propanoate 3m: Thiolated compound **3m** was prepared according to the general procedure with starting materials **1a** and

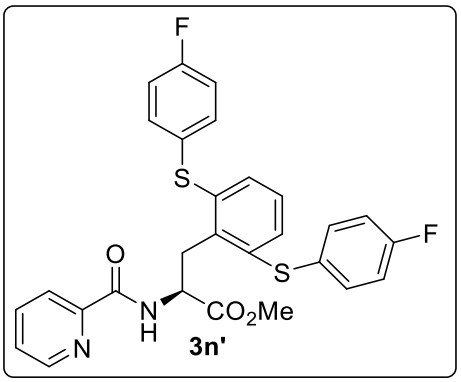
2f, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3m** was obtained as a colorless oil (30 mg, 31%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58-8.53 (m, 2H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.45-7.42 (m, 1H), 7.36-7.32 (m, 3H), 7.31-7.28 (m, 1H), 7.26-7.18 (m, 2H), 7.07-7.04 (m, 2H), 5.17-5.11 (m, 1H), 3.75 (s, 3H), 3.49-3.44 (m, 1H), 3.38-3.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.88, 164.13, 149.21, 148.21, 138.44, 137.21, 135.83, 134.04, 133.82, 132.14, 130.94, 130.90, 128.53, 128.30, 126.34, 122.27, 120.32, 53.16, 52.47, 36.27. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{22}H_{19}BrN_2O_3SNa$ 493.0197; found 493.0211.



Methyl 3-(2,6-bis((4-bromophenyl)thio)phenyl)-2-(picolinamido)propanoate 3m': Thiolated compound **3m'** was prepared according to the general procedure with starting materials **1a** and **2f**, purified using ethyl acetate and hexane mixture (1:5) as the mobile phase. **3m'** was obtained as a colorless oil (28 mg, 21%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 9.2 Hz, 1H), 8.49-8.47 (m, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.44-7.38 (m, 5H), 7.18-7.15 (m, 4H), 7.10-7.06 (m, 3H), 5.47-5.41 (m, 1H), 3.79 (s, 3H), 3.63-3.59 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.84, 164.31, 149.24, 148.11, 137.72, 137.10, 137.08, 134.37, 132.42, 132.39, 131.60, 128.64, 126.26, 122.30, 121.36, 52.63, 52.17, 33.74. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{23}Br_2N_2O_3S_2$ 658.9517; found 658.9542.

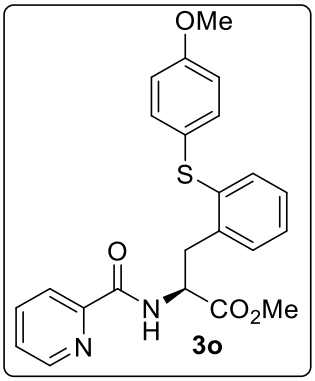


Methyl 3-(2-((4-fluorophenyl)thio)phenyl)-2-(picolinamido)propanoate 3n: Thiolated compound **3n** was prepared according to the general procedure with starting materials **1a** and **2g**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3n** was obtained as a colorless oil (20 mg, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 8.4 Hz, 1H), 8.47-8.45 (m, 1H), 8.05-8.03 (m, 1H), 7.74 (td, J = 7.6, 2.0 Hz, 1H), 7.36-7.32 (m, 1H), 7.20-7.17 (m, 3H), 7.12-7.06 (m, 3H), 6.92-6.87 (m, 2H), 5.10-5.04 (m, 1H), 3.66 (s, 3H), 3.40-3.35 (m, 1H), 3.30-3.24 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.95, 164.15, 163.36 ($J_{C\text{-}F}$ = 248.5 Hz), 149.27, 148.20, 137.23, 136.99, 135.72, 133.08 ($J_{C\text{-}F}$ = 8.1 Hz), 132.20, 130.71, 130.51 ($J_{C\text{-}F}$ = 3.0 Hz), 128.12, 127.59, 126.33, 122.30, 116.49 ($J_{C\text{-}F}$ = 22.2 Hz), 53.04, 52.45, 36.16. ^{19}F NMR (377 MHz, $CDCl_3$) δ -114.62. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}FN_2O_3S$ 411.1179; found 411.1194.

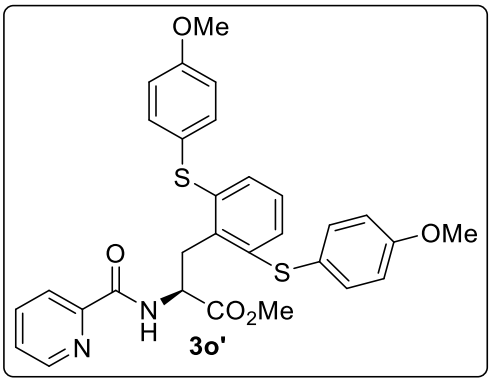


Methyl 3-(2,6-bis((4-fluorophenyl)thio)phenyl)-2-(picolinamido)propanoate 3n': Thiolated compound **3n'** was prepared according to the general procedure with starting

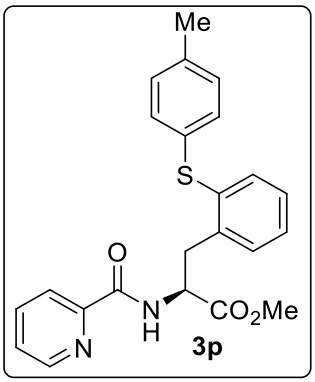
materials **1a** and **2g**, purified using ethyl acetate and hexane mixture (1:5) as the mobile phase. **3n'** was obtained as a colorless oil (47 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 8.8 Hz, 1H), 8.51-8.50 (m, 1H), 8.11-8.08 (m, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.38-7.32 (m, 4H), 7.03-7.93 (m, 5H), 6.86-6.84 (m, 2H), 5.50-5.40 (m, 1H), 3.80 (s, 3H), 3.63 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.96, 164.37, 163.77 (J_{C-F} = 249.5 Hz), 149.37, 148.11, 138.50, 137.13, 135.08, 134.43 (J_{C-F} = 8.1 Hz), 129.28 (J_{C-F} = 3.0 Hz), 129.05, 128.31, 126.23, 122.35, 116.68 (J_{C-F} = 22.2 Hz), 52.60, 52.03, 33.27. ^{19}F NMR (377 MHz, $CDCl_3$) δ -113.38. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{23}F_2N_2O_3S_2$ 537.1118; found 537.1099.



Methyl 3-(2-((4-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3o: Thiolated compound **3o** was prepared according to the general procedure with starting materials **1a** and **2h**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3o** was obtained as a colorless oil (36 mg, 42%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.62 (d, *J* = 7.7 Hz, 1H), 8.55 (d, *J* = 4.2 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 6.3 Hz, 1H), 7.33 (d, *J* = 9.1 Hz, 2H), 7.22-7.21 (m, 1H), 7.10-7.06 (m, 2H), 6.99-6.98 (m, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.17-5.13 (m, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.47-3.44 (m, 1H), 3.37-3.34 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.07, 164.22, 159.64, 149.38, 148.22, 137.86, 137.21, 135.27, 134.71, 130.39, 129.98, 127.87, 126.37, 126.29, 124.44, 122.33, 115.0355.37, 53.02, 52.45, 35.91. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}N_2O_4S$ 423.1378; found 324.1395.

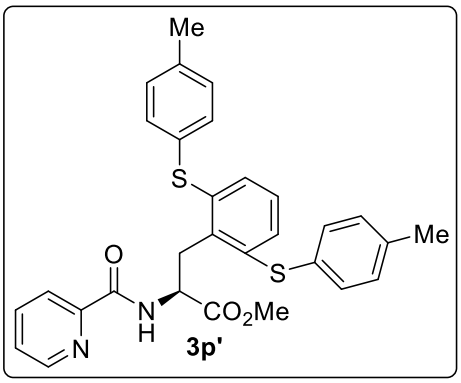


Methyl 3-(2,6-bis((4-methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoate 3o': Thiolated compound **3o'** was prepared according to the general procedure with starting materials **1a** and **2h**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3o'** was obtained as a colorless oil (38 mg, 33%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.01 (d, *J* = 8.4 Hz, 1H), 8.54 (d, *J* = 4.2 Hz, 1H), 8.12 (d, *J* = 7.7 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.41-7.37 (m, 5H), 6.88-6.84 (m, 5H), 6.67 (d, *J* = 8.4 Hz, 2H), 5.44 (q, *J* = 7.7 Hz, 1H), 3.81 (s, 9H), 3.64 (d, *J* = 7.7 Hz, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.21, 164.58, 159.96, 149.60, 148.16, 139.92, 137.08, 135.54, 132.44, 127.91, 126.45, 126.15, 123.63, 122.41, 115.10, 55.38, 52.58, 52.13, 32.69. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{30}H_{28}N_2O_5S_2Na$ 583.1337; found 583.1313.

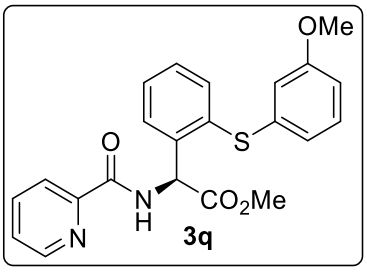


Methyl 2-(picolinamido)-3-(2-(p-tolylthio)phenyl)propanoate 3p: Thiolated compound **3p** was prepared according to the general procedure with starting materials **1a** and **2i**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3p** was obtained as a colorless

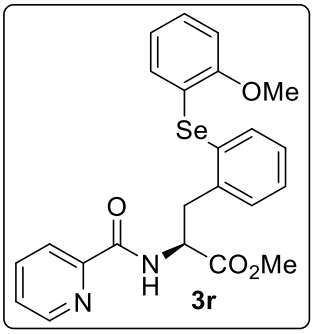
oil (21 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.4 Hz, 1H), 8.55-8.53 (m, 1H), 8.13-8.10 (m, 1H), 7.81 (td, *J* = 8.4, 1.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.28-7.25 (m, 1H), 7.19-7.11 (m, 5H), 7.09 (, *J* = 8.4 Hz, 2H), 5.15-5.10 (m, 1H), 3.73 (s, 3H), 3.48-3.43 (m, 1H), 3.38-3.33 (m, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.02, 164.18, 149.33, 148.21, 137.18, 136.81, 136.14, 132.02, 131.31, 130.53, 130.03, 129.28, 128.58, 127.97, 127.24, 126.26, 122.28, 53.13, 52.42, 36.04, 21.08. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}N_2O_3S$ 407.1429; found 407.1409.



Methyl 3-(2,6-bis(p-tolylthio)phenyl)-2-(picolinamido)propanoate 3p': Thiolated compound **3p'** was prepared according to the general procedure with starting materials **1a** and **2i**, purified using ethyl acetate and hexane mixture (1:5) as the mobile phase. **3p'** was obtained as a colorless oil (39 mg, 36%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 8.4 Hz, 1H), 8.53-8.51 (m, 1H), 8.11-8.08 (m, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.40-7.37 (m, 1H), 7.26-7.24 (m, 4H), 7.12 (d, *J* = 8.0 Hz, 4H), 6.94-6.85 (m, 3H), 5.44-5.38 (m, 1H), 3.79 (s, 3H), 3.64 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.12, 164.49, 149.51, 148.15, 138.61, 137.82, 137.04, 135.12, 132.41, 130.59, 130.16, 128.97, 128.11, 126.10, 122.34, 52.55, 52.30, 33.13, 21.16. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{30}H_{29}N_2O_3S_2$ 529.1620; found 529.1611.

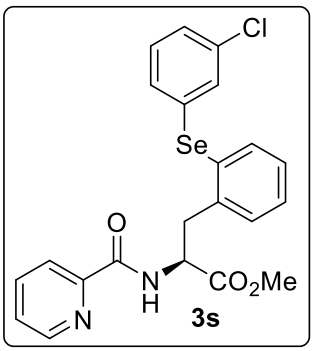


Methyl 2-(2-((3-methoxyphenyl)thio)phenyl)-2-(picolinamido)acetate 3q: Thiolated compound **3q** was prepared according to the general procedure with starting materials **2a** and **2e**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3q** was obtained as a colorless oil (57 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 8.0 Hz, 1H), 8.52-8.50 (m, 1H), 8.12-8.10 (m, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.55 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.48 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.41-7.37 (m, 1H), 7.35 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.32-7.27 (m, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.84-6.79 (m, 2H), 6.66-6.63 (m, 1H), 6.34 (d, *J* = 7.6 Hz, 1H), 3.69 (s, 3H), 3.68 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.98, 163.69, 159.88, 149.24, 148.19, 139.41, 137.88, 137.13, 135.71, 134.08, 129.71, 129.34, 129.25, 128.93, 126.27, 122.23, 121.95, 114.92, 112.42, 55.29, 55.17, 52.81. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{21}N_2O_4S$ 409.1222; found 409.1197.

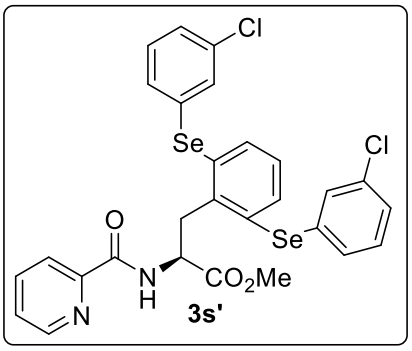


Methyl 3-(2-((2-methoxyphenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3r: The compound **3r** was prepared according to the general procedure with starting materials **1a** and **2j**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3r** was obtained as a colorless oil (57 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54-8.52 (m, 2H), 8.11 (d, *J* =

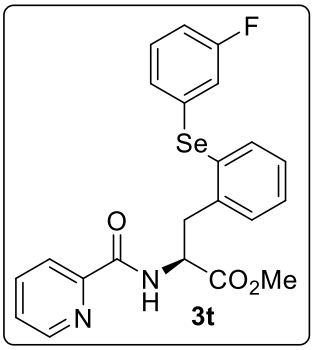
8.0 Hz, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.41-7.38 (m, 2H), 7.31 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18-7.13 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 5.11-5.06 (m, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 3.51-3.38 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.96, 164.15, 156.60, 149.28, 148.24, 140.54, 137.69, 137.16, 130.33, 130.10, 129.48, 129.15, 128.22, 127.50, 126.27, 122.24, 121.93, 121.70, 110.39, 55.87, 53.46, 52.41, 38.16. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}N_2O_4Se$ 471.0850; found 471.0826.



Methyl 3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3s: The compound **3s** was prepared according to the general procedure with starting materials **1a** and **2k**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3s** was obtained as a colorless oil (20 mg, 19%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56-8.54 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1H), 7.46-7.40 (m, 2H), 7.34-7.32 (m, 1H), 7.28-7.25 (m, 2H), 7.19-7.10 (m, 4H), 5.14-5.08 (m, 1H), 3.73 (s, 3H), 3.48-3.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.87, 164.12, 149.22, 148.26, 139.07, 137.24, 136.05, 134.99, 133.65, 131.20, 130.97, 130.69, 130.25, 129.67, 128.92, 128.40, 127.09, 126.36, 122.31, 53.32, 52.47, 38.34. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{19}ClN_2O_3SeNa$ 497.0175; found 497.0183.

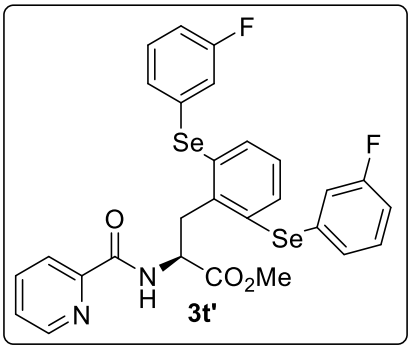


Methyl 3-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3s': The compound **3s'** was prepared according to the general procedure with starting materials **1a** and **2k**, purified using ethyl acetate and hexane mixture (1:5) as the mobile phase. **3s'** was obtained as a colorless oil (50 mg, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 8.8 Hz, 1H), 8.55-8.53 (m, 1H), 8.07-8.05 (m, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.42-7.38 (m, 1H), 7.36 (t, *J* = 1.6 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.27-7.20 (m, 4H), 7.19-7.15 (m, 2H), 6.98 (t, *J* = 7.6 Hz, 1H), 5.42-5.35 (m, 1H), 3.78 (s, 3H), 3.66-3.55 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.72, 164.20, 149.18, 148.21, 139.78, 137.14, 135.07, 135.00, 133.50, 132.84, 132.04, 130.50, 130.43, 129.19, 127.62, 126.28, 122.32, 52.63, 52.49, 38.08. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{23}Cl_2N_2O_3Se_2$ 664.9382; found 664.9384.

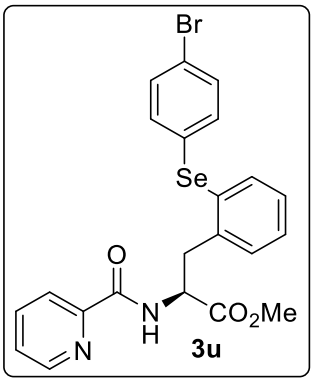


Methyl 3-(2-((3-fluorophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3t: The compound **3t** was prepared according to the general procedure with starting materials **1a** and **2l**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3t** was obtained as a colorless oil (32 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55-8.53 (m, 2H), 8.12 (d, *J* =

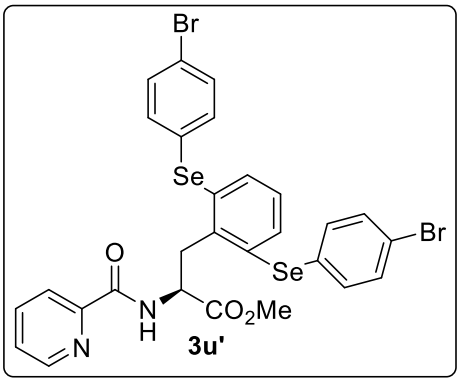
8.0 Hz, 1H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1H), 7.49 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.43-7.40 (m, 1H), 7.35 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.30-7.25 (m, 1H), 7.20-7.13 (m, 2H), 7.10-7.07 (m, 1H), 6.98-6.95 (m, 1H), 6.91-6.86 (m, 1H), 5.14-5.08 (m, 1H), 3.72 (s, 3H), 3.48-3.43 (m, 1H), 3.38-3.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.86, 164.20 (J_{C-F} = 250.5 Hz), 164.11, 149.22, 148.24, 139.23, 137.24, 136.29, 130.85, 130.66, 130.47 (J_{C-F} = 8.1 Hz), 129.00, 128.38, 126.98 (J_{C-F} = 3.0 Hz), 126.35, 122.30, 118.34 (J_{C-F} = 23.2 Hz), 113.93 (J_{C-F} = 21.2 Hz), 113.72, 53.31, 52.45, 38.32. ^{19}F NMR (377 MHz, $CDCl_3$) δ -111.77. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}FN_2O_3Se$ 459.0650; found 459.0634.



Methyl 3-(2,6-bis((3-fluorophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3t': The compound **3t'** was prepared according to the general procedure with starting materials **1a** and **2l**, purified using ethyl acetate and hexane mixture (1:5) as the mobile phase. **3t'** was obtained as a colorless oil (40 mg, 31%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 8.8 Hz, 1H), 8.55-8.53 (m, 1H), 8.07-8.05 (m, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.24-7.19 (m, 2H), 7.17-7.14 (m, 2H), 7.07-7.04 (m, 2H), 7.01-6.91 (m, 3H), 5.42-5.35 (m, 1H), 3.77 (s, 3H), 3.67-3.55 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.74, 164.19 (J_{C-F} = 252.5 Hz), 164.18, 149.23, 148.18, 140.06, 137.15, 135.26, 133.44, 133.10 (J_{C-F} = 7.1 Hz), 130.67 (J_{C-F} = 8.1 Hz), 129.16, 127.86, 126.29, 122.33, 119.25 (J_{C-F} = 23.2 Hz), 114.54 (J_{C-F} = 21.2 Hz), 52.61, 52.50, 38.12. ^{19}F NMR (377 MHz, $CDCl_3$) δ -111.40. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{23}F_2N_2O_3Se_2$ 632.9997; found 633.0024

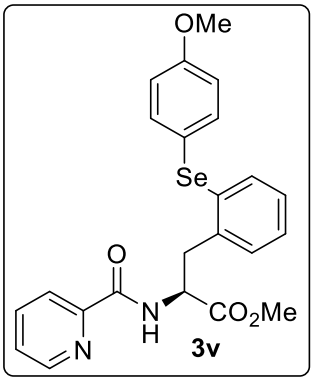


Methyl 3-(2-((4-bromophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3u: The compound **3u** was prepared according to the general procedure with starting materials **1a** and **2m**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3u** was obtained as a colorless oil (50 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58-8.54 (m, 2H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.45-7.40 (m, 2H), 7.34-7.31 (m, 3H), 7.28-7.24 (m, 1H), 7.22-7.18 (m, 2H), 7.14 (td, *J* = 8.8, 1.6 Hz, 1H), 5.17-5.12 (m, 1H), 3.75 (s, 3H), 3.50-3.45 (m, 1H), 3.39-3.34 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.83, 164.08, 149.18, 148.19, 138.74, 137.21, 135.51, 133.53, 132.35, 131.46, 130.65, 130.56, 128.61, 128.30, 126.34, 122.27, 121.19, 53.23, 52.45, 38.23. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}BrN_2O_3Se$ 518.9851; found 518.9863.

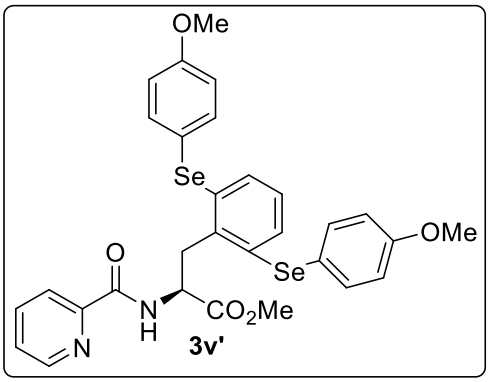


Methyl 3-(2,6-bis((4-bromophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3u': The compound **3u'** was prepared according to the general procedure with starting materials **1a** and

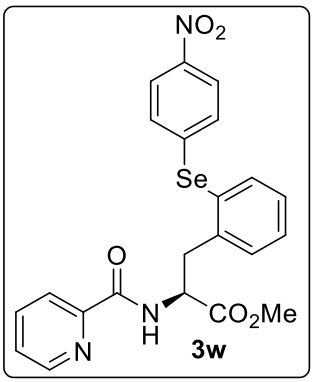
2m, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3u'** was obtained as a colorless oil (25 mg, 16%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.8 Hz, 1H), 8.43 (d, *J* = 4.8 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.35-7.32 (m, 1H), 7.29 (d, *J* = 8.0 Hz, 4H), 7.20-7.18 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.85 (t, *J* = 8.0 Hz, 1H), 5.36-5.30 (m, 1H), 3.71 (s, 3H), 3.57-3.51 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.77, 164.26, 149.25, 148.16, 138.88, 137.15, 134.63, 134.14, 133.91, 132.58, 129.86, 129.02, 126.31, 122.35, 122.00, 52.68, 52.38, 37.93. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{23}Br_2N_2O_3Se_2$ 752.8372; found 752.8362.



Methyl 3-(2-((4-methoxyphenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3v: The compound **3v** was prepared according to the general procedure with starting materials **1a** and **2n**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3v** was obtained as a colorless oil (51 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60-8.55 (m, 2H), 8.14-8.12 (m, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.44-7.40 (m, 3H), 7.23 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.17-7.10 (m, 2H), 7.03 (td, *J* = 7.6, 1.6 Hz, 1H), 6.84-6.81 (m, 2H), 5.17-5.11 (m, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.47-3.42 (m, 1H), 3.36-3.31 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.99, 164.18, 159.72, 149.32, 148.22, 137.22, 136.67, 136.23, 134.28, 132.52, 130.20, 127.97, 127.06, 126.31, 122.32, 119.95, 115.20, 55.29, 53.09, 52.46, 37.83. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{23}H_{22}N_2O_4SeNa$ 493.0670; found 493.0658.

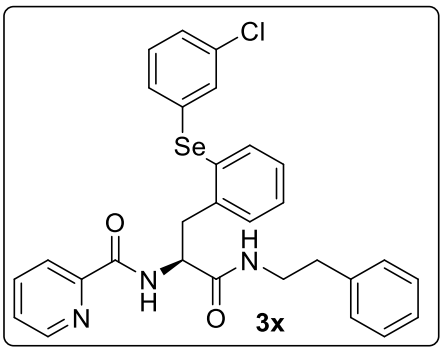


Methyl 3-(2,6-bis((4-methoxyphenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3v': The compound **3v'** was prepared according to the general procedure with starting materials **1a** and **2n**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3v'** was obtained as a colorless oil (21 mg, 16%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, *J* = 8.4 Hz, 1H), 8.57-8.56 (m, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.47-7.39 (m, 5H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.85-6.82 (m, 4H), 6.80-6.76 (m, 1H), 5.44-5.38 (m, 1H), 3.81 (s, 3H), 3.80 (s, 6H), 3.64-3.53 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.05, 164.46, 159.96, 149.54, 148.19, 137.10, 136.81, 136.23, 135.50, 130.13, 128.41, 126.19, 122.42, 119.72, 115.28, 55.32, 52.63, 52.30, 37.01. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{30}H_{28}N_2O_5Se_2Na$ 679.0217; found 679.0211.

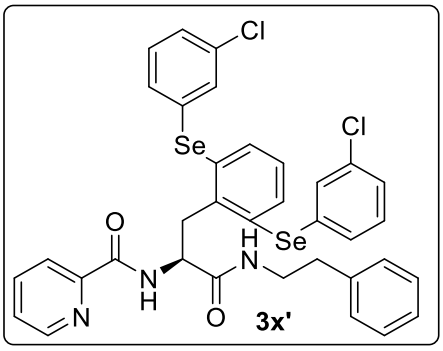


Methyl 3-(2-((4-nitrophenyl)selanyl)phenyl)-2-(picolinamido)propanoate 3w: The compound **3w** was prepared according to the general procedure with starting materials **1a** and **2o**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3w** was obtained

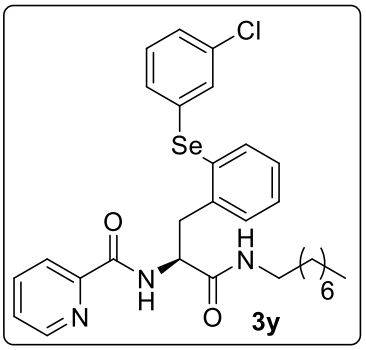
as a colorless oil (50 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50-8.47 (m, 2H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.97-7.93 (m, 2H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1H), 7.63 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.45-7.39 (m, 3H), 7.26-7.23 (m, 3H), 5.14-5.08 (m, 1H), 3.72 (s, 3H), 3.50-3.45 (m, 1H), 3.39-3.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.70, 164.05, 149.07, 148.21, 146.08, 143.98, 140.69, 138.11, 137.29, 131.08, 130.32, 129.25, 128.82, 128.66, 126.41, 123.96, 122.29, 53.34, 52.54, 38.66. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}N_3O_5Se$ 486.0595; found 486.0569.



***N*-(3-(2-((3-Chlorophenyl)selanyl)phenyl)-1-oxo-1-(phenethylamino)propan-2-yl)picolinamide 3x:** The compound **3x** was prepared according to the general procedure with starting materials **1i** and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3x** was obtained as a colorless oil (50 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.4 Hz, 1H), 8.50 (d, *J* = 4.8 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.82 (td, *J* = 8.0, 1.6 Hz, 1H), 7.44-7.41 (m, 2H), 7.38-7.36 (m, 1H), 7.28-7.23 (m, 2H), 7.19-7.10 (m, 7H), 7.06-7.04 (m, 2H), 6.10 (t, *J* = 5.6 Hz, 1H), 4.83-4.77 (m, 1H), 3.51-3.40 (m, 3H), 3.31-3.25 (m, 1H), 2.77-2.63 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.40, 164.41, 149.07, 148.27, 139.67, 138.60, 137.24, 135.84, 135.04, 133.40, 131.21, 131.02, 130.77, 130.35, 129.73, 128.97, 128.72, 128.66, 128.53, 128.30, 127.20, 126.42, 122.27, 54.55, 40.71, 38.11, 35.53. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{29}H_{27}ClN_3O_2Se$ 564.0984; found 564.0952.

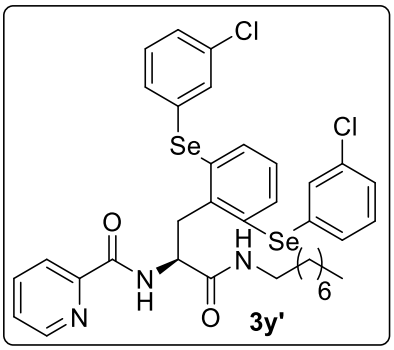


N-(3-(2,6-Bis((3-chlorophenyl)selanyl)phenyl)-1-oxo-1-(phenethylamino)propan-2-yl)picolinamide 3x': The compound **3x'** was prepared according to the general procedure with starting materials **1i** and **2k**, purified using ethyl acetate and hexane mixture (1:1) as the mobile phase. **3x'** was obtained as a colorless oil (25 mg, 17%). ^{1}H NMR (400 MHz, $CDCl_3$) 8.95 (d, *J* = 8.8 Hz, 1H), 8.52-8.50 (m, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.80 (td, *J* = 7.6, 1.6 Hz, 1H), 7.43-7.39 (m, 1H), 7.32 (t, *J* = 2.0 Hz, 2H), 7.27-7.26 (m, 4H), 7.23-7.22 (m, 1H), 7.213-7.208 (m, 2H), 7.18-7.16 (m, 3H), 7.14-7.12 (m, 3H), 6.96 (t, *J* = 4.0 Hz, 1H), 6.30 (t, *J* = 6.0 Hz, 1H), 5.09-5.04 (m, 1H), 3.65-3.59 (m, 1H), 3.55-3.50 (m, 3H), 2.79 (t, *J* = 7.2 Hz, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.50, 164.76, 149.07, 148.30, 140.56, 138.68, 137.15, 135.14, 134.98, 133.36, 132.75, 132.03, 130.50, 129.13, 128.81, 128.57, 127.71, 126.45, 126.38, 122.33, 54.00, 40.76, 37.62, 35.57. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{35}H_{30}Cl_2N_3O_2Se_2$ 754.0013; found 753.9975.



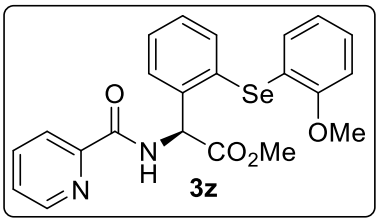
***N*-(3-(2-((3-Chlorophenyl)selanyl)phenyl)-1-(octylamino)-1-oxopropan-2-yl)picolinamide 3y:** Thie compound **3y** was prepared according to the general procedure with

starting materials **1j** and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3y** was obtained as a colorless oil (47 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.8 Hz, 1H), 8.55-8.54 (m, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.46-7.34 (m, 3H), 7.30-7.27 (m, 1H), 7.26-7.24 (m, 1H), 7.22-7.12 (m, 4H), 5.97 (t, *J* = 5.6 Hz, 1H), 4.85-4.80 (m, 1H), 3.47-3.41 (m, 1H), 3.35-3.29 (m, 1H), 3.22-3.12 (m, 2H), 1.41-1.34 (m, 2H), 1.28-1.16 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.31, 164.47, 149.15, 148.31, 139.79, 137.26, 135.96, 135.07, 133.50, 131.15, 131.07, 130.71, 130.36, 129.69, 129.01, 128.28, 127.19, 126.42, 122.26, 54.60, 39.64, 38.26, 31.76, 29.33, 29.18, 29.15, 26.79, 22.63, 14.09. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{29}H_{35}ClN_3O_2Se$ 572.1611; found 572.1599.

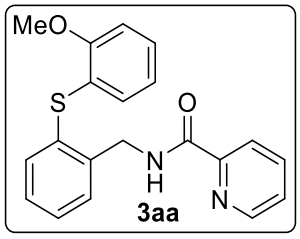


***N*-(3-(2,6-Bis((3-chlorophenyl)selanyl)phenyl)-1-(octylamino)-1-oxopropan-2-yl)picolinamide 3y':** The compound **3y'** was prepared according to the general procedure with starting materials **1j** and **2k**, purified using ethyl acetate and hexane mixture (1:1) as the mobile phase. **3y'** was obtained as a colorless oil (27 mg, 18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, *J* = 8.8 Hz, 1H), 8.52-8.51 (m, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 8.0, 1.6 Hz, 1H), 7.42-7.38 (m, 1H), 7.34 (t, *J* = 2.0 Hz, 2H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.26-7.25 (m, 1H), 7.24-7.21 (m, 3H), 7.19-7.15 (m, 2H), 6.97 (t, *J* = 8.0 Hz, 1H), 6.25 (d, *J* = 5.6 Hz, 1H), 5.13-5.07 (m, 1H), 3.70-3.64 (m, 1H), 3.60-3.55 (m, 1H), 3.31-3.18 (m, 2H), 1.48-1.43 (m, 2H), 1.25-1.21 (m, 10H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.41, 164.83, 149.12,

148.32, 140.67, 137.16, 135.15, 135.04, 133.38, 132.78, 132.01, 130.50, 130.48, 129.11, 127.71, 126.37, 122.28, 54.04, 39.71, 37.70, 31.76, 29.42, 29.20, 29.17, 26.85, 22.63, 14.09. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{35}H_{37}Cl_2N_3O_2Se_2Na$ 784.0458; found 784.0419.

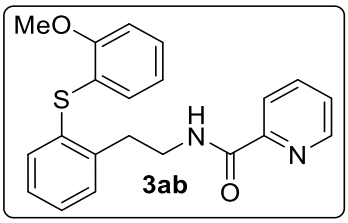


Methyl 2-(2-((2-methoxyphenyl)selanyl)phenyl)-2-(picolinamido)acetate 3z: The compound **3z** was prepared according to the general procedure with starting materials **1** and **2j**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3z** was obtained as a colorless oil (55 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 7.2 Hz, 1H), 8.43-8.41 (m, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.72 (td, *J* = 7.6, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.50 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35-7.30 (m, 2H), 7.22-7.18 (m, 1H), 7.04-6.99 (m, 1H), 6.77-6.72 (m, 2H), 6.60 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.29 (d, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 3.57 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.08, 163.68, 156.68, 149.30, 148.19, 141.05, 138.70, 137.11, 130.92, 129.70, 129.46, 129.42, 128.81, 127.49, 126.23, 122.26, 121.50, 110.31, 57.22, 55.90, 52.78. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{21}N_2O_4Se$ 457.0694 found 457.0687.

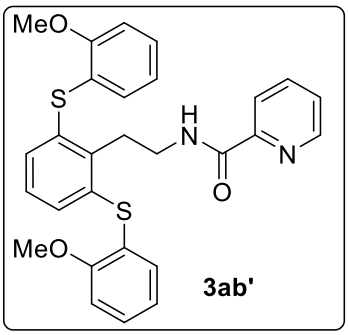


***N*-(2-((2-Methoxyphenyl)thio)benzyl)picolinamide 3aa:** Thiolated compound **3aa** was prepared according to the general procedure with starting materials **1k** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3aa** was obtained as a colorless oil (35 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48-8.47 (m, 2H), 8.19 (d, *J* = 7.6 Hz, 1H), 7.82

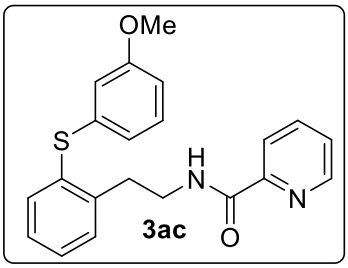
(td, *J* = 7.6, 1.6 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.40-7.37 (m, 2H), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H), 7.26-7.23 (m, 1H), 7.18-7.14 (m, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.83-6.77 (m, 2H), 4.83 (d, *J* = 6.4 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.26, 156.61, 149.86, 148.03, 140.76, 137.21, 134.85, 132.16, 129.75, 129.62, 128.79, 128.51, 127.57, 126.04, 124.79, 122.24, 121.39, 110.74, 55.90, 41.87. ESI-HRMS m/z: $[M+K]^+$ Calcd. for $C_{20}H_{18}N_2O_2SK$ 389.0726; found 389.0735.



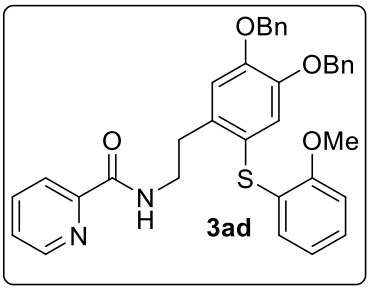
***N*-(2-((2-Methoxyphenyl)thio)phenethyl)picolinamide 3ab:** Thiolated compound **3ab** was prepared according to the general procedure with starting materials **1l** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3ab** was obtained as a colorless oil (28 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51-8.50 (m, 1H), 8.20-8.15 (m, 2H), 7.83 (td, *J* = 8.0, 1.6 Hz, 1H), 7.41-7.28 (m, 4H), 7.22-7.16 (m, 2H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.83-6.81 (m, 2H), 3.89 (s, 3H), 3.77-3.72 (m, 2H), 3.14 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.30, 156.65, 149.95, 148.01, 141.35, 137.26, 134.35, 132.59, 130.42, 129.70, 128.40, 127.67, 127.51, 126.03, 124.99, 122.13, 121.32, 110.68, 55.88, 39.91, 34.07. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{21}H_{20}N_2O_2SNa$ 387.1143; found 387.1125.



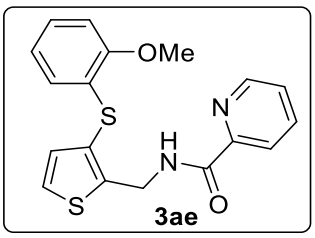
***N*-(2,6-Bis((2-Methoxyphenyl)thio)phenethyl)picolinamide 3ab':** Thiolated compound **3ab'** was prepared according to the general procedure with starting materials **1l** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3ab'** was obtained as a colorless oil (39 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51-8.49 (m, 1H), 8.26 (br s, 1H), 8.19-8.16 (m, 1H), 7.81 (td, *J* = 8.0, 1.6 Hz, 1H), 7.39-7.36 (m, 1H), 7.25-7.21 (m, 2H), 7.12-7.10 (m, 2H), 7.05-7.01 (m, 3H), 6.90-6.84 (m, 4H), 3.85 (s, 6H), 3.83-3.79 (m, 2H), 3.46-3.42 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.21, 157.47, 150.15, 147.89, 141.03, 137.13, 135.76, 131.76, 131.62, 128.44, 127.87, 125.85, 123.88, 122.14, 121.28, 110.93, 55.85, 39.31, 31.91. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{27}N_2O_3S_2$ 503.1463; found 503.1482.



***N*-(2-((3-Methoxyphenyl)thio)phenethyl)picolinamide 3ac:** Thiolated compound **3ac** was prepared according to the general procedure with starting materials **1l** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3ac** was obtained as a colorless oil (46 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51-8.50 (m, 1H), 8.20-8.15 (m, 2H), 7.85-7.80 (m, 1H), 7.41-7.34 (m, 3H), 7.29-7.25 (m, 1H), 7.22-7.14 (m, 2H), 6.85-6.71 (m, 3H), 3.75-3.70 (m, 5H), 3.13 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.33, 160.08, 148.03, 140.91, 137.90, 137.30, 134.18, 133.44, 130.51, 129.95, 128.49, 127.68, 126.07, 122.16, 121.63, 115.97, 114.68, 112.17, 55.24, 39.98, 34.10. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{21}H_{21}N_2O_2S$ 365.1324; found 365.1310.

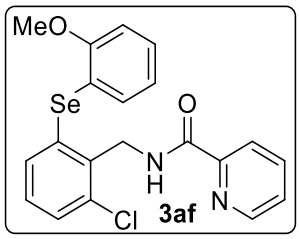


***N*-(4,5-Bis(benzyloxy)-2-((2-methoxyphenyl)thio)phenethyl)picolinamide 3ad:** Thiolated compound **3ad** was prepared according to the general procedure with starting materials **1m** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3ad** was obtained as a colorless oil (55 mg, 42%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.2 Hz, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 8.11 (s, 1H), 7.83 (t, *J* = 7.7 Hz, 1H), 7.42-7.38 (m, 3H), 7.36-7.34 (m, 4H), 7.32-7.27 (m, 4H), 7.10-7.08 (m, 2H), 7.00 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.74 (t, *J* = 7.7 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 5.11 (s, 2H), 5.06 (s, 2H), 3.89 (s, 3H), 3.64 (q, *J* = 7.0 Hz, 2H), 3.02 (t, *J* = 7.0 Hz, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 164.27, 155.48, 150.02, 150.00, 148.04, 147.89, 137.34, 136.88, 136.70, 128.52, 128.46, 127.91, 127.83, 127.39, 127.35, 127.14, 126.93, 126.32, 126.11, 122.69, 122.18, 121.90, 121.37, 116.37, 110.32, 71.31, 71.13, 55.85, 40.16, 33.90. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{35}H_{33}N_2O_4S$ 577.2161; found 577.2143.

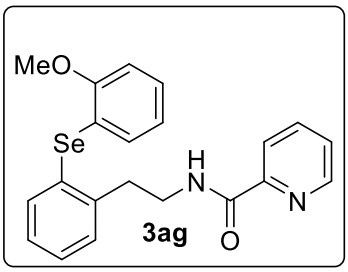


***N*-((3-((2-Methoxyphenyl)thio)thiophen-2-yl)methyl)picolinamide 3ae:** Thiolated compound **3ae** was prepared according to the general procedure with starting materials **1n** and **2a**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3ae** was obtained as a colorless oil (25 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47-8.45 (m, 1H), 8.39 (br s,

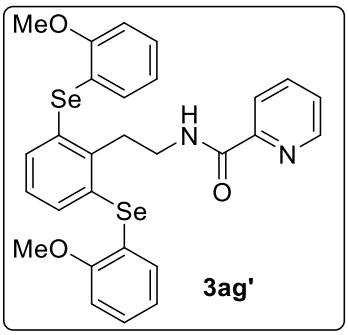
1H), 8.20 (d, *J* = 7.6 Hz, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.37 (m, 1H), 7.30 (d, *J* = 5.2 Hz, 1H), 7.13-7.08 (m, 1H), 7.02 (d, *J* = 5.2 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.78 (td, *J* = 8.0, 1.2 Hz, 1H), 6.71 (dd, *J* = 7.6, 1.6 Hz, 1H), 4.91 (d, *J* = 6.4 Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.13, 155.70, 149.51, 148.04, 144.87, 137.23, 132.95, 127.25, 126.60, 126.19, 126.08, 125.20, 124.85, 122.30, 121.37, 110.46, 55.87, 36.64. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{16}N_2O_2S_2Na$ 379.0551; found 379.0573.



N-(2-Chloro-6-((2-methoxyphenyl)selanyl)benzyl)picolinamide 3af: The compound **3af** was prepared according to the general procedure with starting materials **1o** and **2a**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3af** was obtained as a colorless oil (62 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44-8.43 (m, 1H), 8.21 (br s, 1H), 8.18-8.16 (m, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.41 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.38-7.34 (m, 1H), 7.20-7.12 (m, 2H), 6.97 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.84 (dd, *J* = 8.0, 0.8 Hz, 1H), 6.77 (td, *J* = 7.6, 1.2 Hz, 1H), 5.06 (d, *J* = 5.6 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.70, 157.14, 149.75, 147.91, 138.01, 137.13, 135.78, 135.12, 133.28, 131.83, 130.03, 129.63, 128.48, 125.95, 122.22, 121.74, 120.91, 110.70, 55.88, 42.06. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{20}H_{18}ClN_2O_2Se$ 433.0249; found 433.0233.

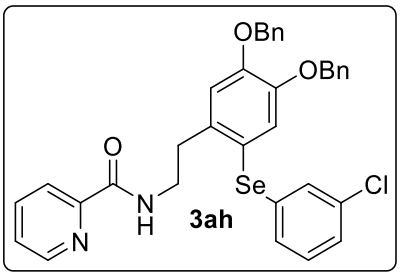


***N*-(2-((2-Methoxyphenyl)selanyl)phenethyl)picolinamide 3ag:** The compound **3ag** was prepared according to the general procedure with starting materials **1l** and **2a**, purified using ethyl acetate and hexane mixture (1:3) as the mobile phase. **3ag** was obtained as a colorless oil (39.5 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51-8.50 (m, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 8.12 (br s, 1H), 7.83 (td, *J* = 8.0, 1.6 Hz, 1H), 7.60 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.42-7.33 (m, 3H), 7.21-7.14 (m, 2H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.76-6.74 (m, 2H), 3.91 (s, 3H), 3.74-3.69 (m, 2H), 3.15 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.29, 156.55, 149.96, 148.03, 142.95, 137.77, 137.29, 130.30, 129.97, 129.30, 128.67, 127.83, 127.46, 126.06, 122.16, 122.00, 121.76, 110.37, 55.89, 40.33, 36.22. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{21}H_{21}N_2O_2Se$ 413.0796; found 413.0778.



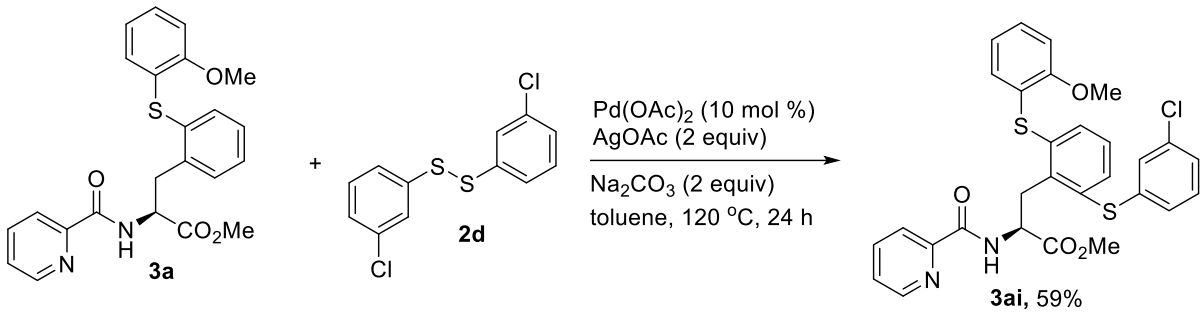
N-(2,6-bis((2-Methoxyphenyl)selanyl)phenethyl)picolinamide 3ag': Thiolated compound **3ag'** was prepared according to the general procedure with starting materials **1l** and **2a**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **3ag'** was obtained as a colorless oil (21.5 mg, 18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51-8.49 (m, 1H), 8.18-8.16 (m, 2H), 7.81 (td, *J* = 8.0, 1.6 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.40-7.36 (m, 1H), 7.24-7.19 (m, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (dd, *J* = 7.6, 1.6 Hz, 2H), 6.87-6.85 (m, 2H), 6.81 (td, *J* = 7.6, 1.2 Hz, 2H), 3.87 (s, 6H), 3.79-3.74 (m, 2H), 3.46-3.42 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.18, 157.10, 150.12, 147.94, 144.69, 137.20, 136.79, 131.45, 131.39, 128.62,

128.18, 125.92, 122.21, 121.72, 121.46, 110.60, 55.90, 40.02, 36.63. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{27}N_2O_3Se_2$ 599.0342; found 599.0377.



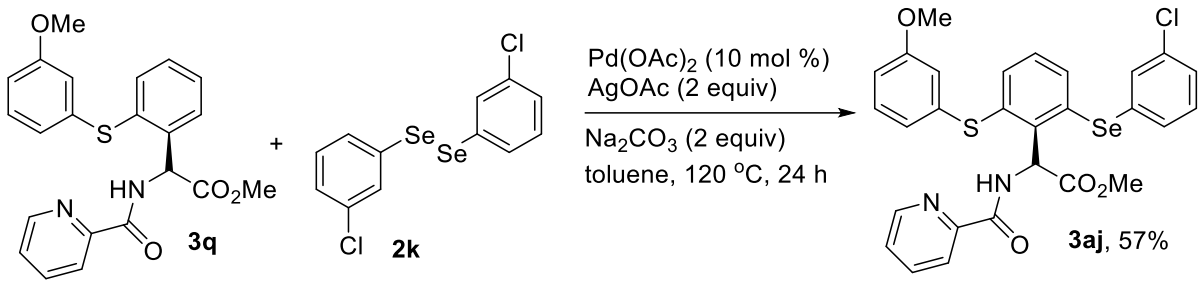
***N*-(4,5-Bis(benzyloxy)-2-((3-chlorophenyl)selanyl)phenethyl)picolinamide 3ah:** The compound **3ah** was prepared according to the general procedure with starting materials **1m** and **2a**, purified using ethyl acetate and hexane mixture (1:4) as the mobile phase. **3ah** was obtained as a colorless oil (72 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 6.0 Hz, 1H), 8.19 (d, *J* = 11.4 Hz, 1H), 8.10 (s, 1H), 7.83 (t, *J* = 11.4 Hz, 1H), 7.42-7.27 (m, 11H), 7.16 (s, 2H), 7.13-7.05 (m, 2H), 7.01-6.99 (m, 2H), 5.10 (s, 2H), 5.07 (s, 2H), 3.61 (q, *J* = 9.6 Hz, 2H), 3.03 (t, *J* = 10.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.30, 150.22, 149.93, 148.06, 147.78, 137.38, 136.83, 136.79, 136.18, 135.00, 130.20, 129.57, 128.55, 128.50, 128.05, 127.99, 127.97, 127.90, 127.37, 126.46, 126.17, 123.87, 122.21, 119.75, 116.22, 71.47, 71.15, 40.42, 35.94. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{34}H_{30}ClN_2O_3Se$ 629.1138; found 629.1157.

Procedure for thiolation of 3a with 2d



To a 15 mL sealed reaction tube containing a magnetic stir-bar, mono-thiolated derivative **3a** (42.2 mg, 0.1 mmol), disulfide **2d** (57.4 mg, 0.2 mmol), $Pd(OAc)_2$ (2.3 mg, 10 mol %), AgOAc (33.2 mg, 0.2 mmol), sodium carbonate (21.2 mg, 0.2 mmol) were added. Toluene was added and the mixture was then stirred at 120 °C for 24 h. After cooling at room temperature, the reaction mixture was filtered through a short pad of celite using ethyl acetate as the eluent (30 mL). Evaporation of solvent under vacuum provided a crude residue which was purified by silica gel column chromatography to afford the desired dichalcogenated product **3ai** as a colorless oil (33 mg, 59%). Eluent: ethyl acetate/hexane mixture (1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 8.4 Hz, 1H), 8.53-8.52 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.6, 1.6 Hz, 1H), 7.40-7.37 (m, 1H), 7.28-7.24 (m, 2H), 7.18-7.15 (m, 3H), 7.14-7.05 (m, 4H), 6.91-6.85 (m, 2H), 5.42-5.36 (m, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 3.65-3.62 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.99, 164.37, 157.93, 149.41, 148.20, 138.89, 138.35, 137.50, 137.05, 135.15, 134.98, 132.64, 132.52, 132.03, 130.15, 129.20, 129.08, 128.58, 127.74, 126.82, 126.15, 122.87, 122.29, 121.37, 111.12, 55.91, 52.54, 52.47, 33.75. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{29}H_{26}ClN_2O_4S_2$ 565.1022; found 565.1019.

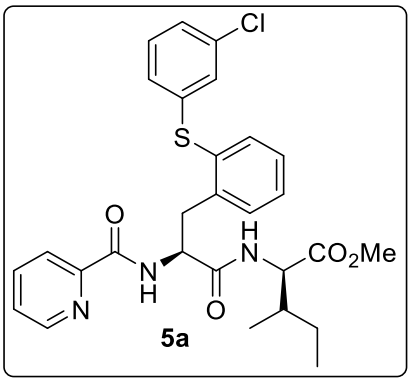
Procedure for Selenoarylation of 3q with 2k



To a 15 mL sealed reaction tube containing a magnetic stir-bar was charged with mono thiolated compound **3q** (40.8 mg, 0.1 mmol), diselenide **2k** (76.2 mg, 0.2 mmol), $Pd(OAc)_2$ (2.3 mg, 10 mol %), AgOAc (33.2 mg, 0.2 mmol), sodium carbonate (21.2 mg, 0.2 mmol) in dry toluene (2 mL). The mixture was then allowed to stir at 120 °C for 24 h. After cooling at room temperature, the reaction mixture was filtered through a short pad of Celite using ethyl acetate as the eluent (30 mL). Evaporation of solvent under reduced pressure gave a crude mixture which was purified by silica gel column chromatography to afford the desired dichalcogenated product **3aj** as a colorless oil (34 mg, 57%). Eluent: ethyl acetate/hexane mixture (1:2). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.2 Hz, 1H), 8.09 (d, *J* = 7.7 Hz, 1H), 7.78-7.76 (m, 1H), 7.59 (d, *J* = 7.0 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.37-7.34 (m, 2H), 7.29 (br s, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.14-7.10 (m, 4H), 6.82-6.77 (m, 2H), 6.67 (d, *J* = 7.0 Hz, 1H), 5.15-5.09 (m, 1H), 3.70 (s, 3H), 3.60 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.45, 163.74, 159.96, 149.20, 148.23, 143.15, 137.74, 137.71, 137.00, 136.62, 136.60, 134.87, 134.39, 131.43, 130.12, 129.96, 129.82, 129.74, 127.06, 126.12, 122.15, 121.78, 114.77, 112.65, 56.81, 55.21, 52.92. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{24}ClN_2O_4SSe$ 599.0338; found 599.0359.

5. General Procedure for the C(sp^2)-H Chalcogenation of peptides

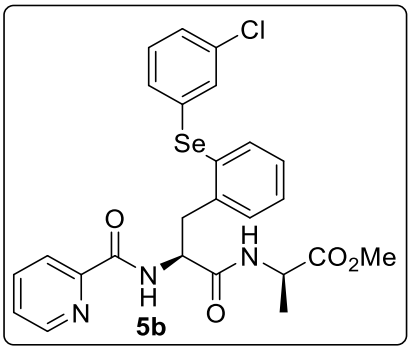
To a clean, oven-dried 15 mL sealed reaction tube containing a magnetic stir-bar was charged with peptides **4** (0.13 mmol), diaryl disulfide/diaryl diselenide **2** (0.26 mmol), $Pd(OAc)_2$ (3 mg, 10 mol %), AgOAc (44 mg, 0.26 mmol), sodium carbonate (28 mg, 0.26 mmol) in toluene. The mixture was then vigorously stirred at 120 °C for 24 h. After completion, the reaction mixture was cooled to room temperature and filtered through a short pad of celite using ethyl acetate as the eluent (30 mL). Evaporation of solvent under vacuum gave a crude mixture which was purified by silica gel column chromatography using ethyl acetate/hexane solvent system to afford the desired chalcogenated peptide **5** and **5'**.



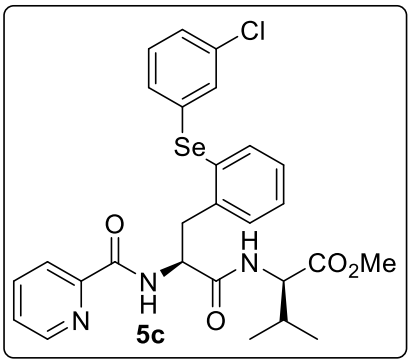
5a

Methyl 2-(3-(2-((3-chlorophenyl)thio)phenyl)-2-(picolinamido)propanamido)-3-methylpentanoate 5a: Thiolated compound **5a** was prepared according to the general procedure with starting materials **4a** and **2d**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5a** was obtained as a colorless oil (30 mg, 42%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.65 (d, *J* = 7.7 Hz, 1H), 8.53 (d, *J* = 4.2 Hz, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 7.0 Hz, 1H), 7.37 (t, *J* = 8.4 Hz, 2H), 7.26-7.25 (m, 1H), 7.22-7.20 (m, 1H), 7.17-7.12 (m, 3H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 4.92-4.89 (m, 1H), 4.54-4.52 (m, 1H), 3.69 (s, 3H), 3.44-3.41 (m, 1H), 3.33-3.29 (m, 1H), 1.85-1.83 (m, 1H), 1.40-1.35 (m, 1H), 1.15-1.09 (m, 1H), 0.85 (t, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 7.0 Hz, 3H). ^{13}C

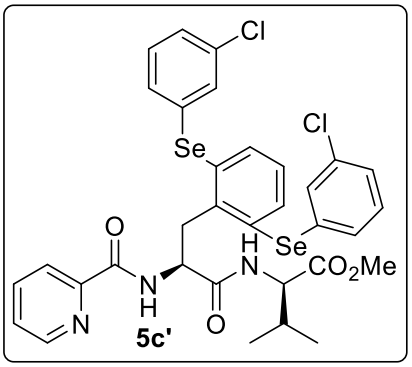
NMR (176 MHz, $CDCl_3$) δ 171.75, 170.44, 164.58, 149.11, 148.31, 139.53, 138.85, 137.25, 134.97, 134.80, 132.71, 131.25, 130.15, 129.05, 128.45, 128.29, 126.89, 126.47, 126.41, 122.25, 56.66, 54.40, 52.07, 37.90, 36.08, 25.16, 15.32, 11.54. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{31}ClN_3O_4S$ 540.1724; found 540.1708.



Methyl (3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)alaninate 5b: The compound **5b** was prepared according to the general procedure with starting materials **4b** and **2k**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5b** was obtained as colorless oil (40 mg, 56%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.55-8.53 (m, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 7.6, 2.0 Hz, 1H), 7.47 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.43-7.40 (m, 1H), 7.38 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.31 (t, *J* = 1.6 Hz, 1H), 7.25-7.22 (m, 1H), 7.21-7.12 (m, 4H), 6.69 (d, *J* = 7.2 Hz, 1H), 4.95-4.89 (m, 1H), 4.58-4.51 (m, 1H), 3.71 (s, 3H), 3.48-3.43 (m, 1H), 3.33-3.27 (m, 1H), 1.38 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.87, 170.15, 164.49, 149.10, 148.30, 139.57, 137.27, 136.08, 135.03, 133.51, 131.13, 130.98, 130.68, 130.35, 129.62, 129.03, 128.31, 127.16, 126.44, 122.33, 54.41, 52.48, 48.27, 38.28, 18.33. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{25}H_{25}ClN_3O_4Se$ 546.0726; found 546.0718.

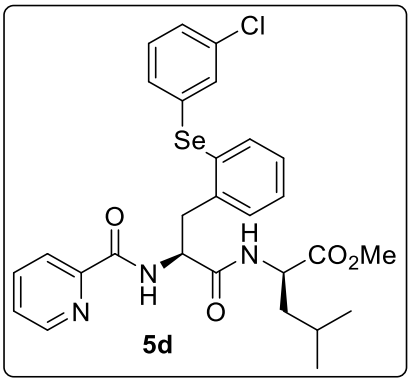


Methyl (3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)valinate 5c: The compound **5c** was prepared according to the general procedure with starting materials **4c** and **2k**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5c** was obtained as a colorless oil (31 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 8.4 Hz, 1H), 8.48 (d, *J* = 4.4 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.37-7.34 (m, 1H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.21-7.06 (m, 6H), 6.66 (d, *J* = 8.8 Hz, 1H), 4.91-4.86 (m, 1H), 4.46-4.42 (m, 1H), 3.64 (s, 3H), 3.42-3.37 (m, 1H), 3.29-3.23 (m, 1H), 2.10-2.02 (m, 1H), 0.81 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.80, 170.61, 164.56, 149.09, 148.31, 139.66, 137.26, 136.12, 135.03, 133.52, 131.10, 130.93, 130.65, 130.33, 129.56, 129.05, 128.28, 127.13, 126.43, 122.28, 57.38, 54.54, 52.12, 38.04, 31.28, 18.84, 17.79. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{27}H_{29}ClN_3O_4Se$ 574.1039; found 574.1003.



Methyl (3-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)valinate 5c': The compound **5c'** was prepared according to the general procedure with starting materials

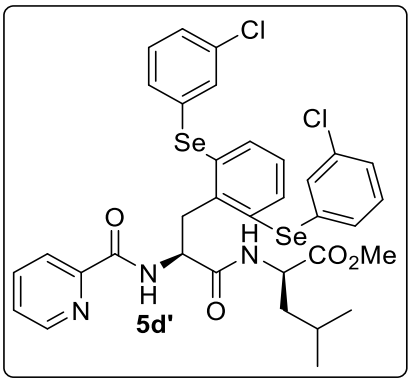
4c and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **5c'** was obtained as a colorless oil (28 mg, 28%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (d, *J* = 8.8 Hz, 1H), 8.51 (d, *J* = 4.4 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.6, 1.6 Hz, 1H), 7.40-7.37 (m, 1H), 7.35 (t, *J* = 1.6 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.24-7.19 (m, 4H), 7.18-7.14 (m, 2H), 6.99 (t, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 5.19-5.13 (m, 1H), 4.56-4.52 (m, 1H), 3.72 (s, 3H), 3.70-3.63 (m, 1H), 3.58-3.53 (m, 1H), 2.27-2.13 (m, 1H), 0.90 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.97, 170.66, 164.81, 149.12, 148.33, 140.71, 137.16, 135.34, 135.13, 133.25, 132.77, 131.94, 130.49, 130.38, 129.19, 127.68, 126.35, 122.28, 57.43, 54.16, 52.18, 37.82, 31.27, 18.91, 17.81. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{33}H_{32}Cl_2N_3O_4Se_2$ 764.0068; found 764.0092.



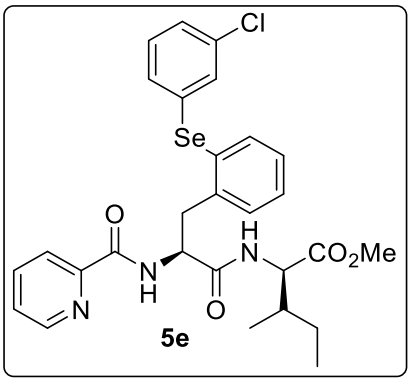
5d

Methyl (3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)leucinate 5d: The compound **5d** was prepared according to the general procedure with starting materials **4d** and **2k**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5d** was obtained as a colorless oil (31 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.4 Hz, 1H), 8.54-8.53 (m, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1H), 7.47 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.43-7.40 (m, 1H), 7.38 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.31 (t, *J* = 1.2 Hz, 1H), 7.25 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.21-7.12 (m, 4H), 6.55 (d, *J* = 8.0 Hz, 1H), 4.95-4.85 (m, 1H), 4.60-4.55 (m, 1H), 3.69 (s, 3H), 3.49-3.44 (m, 1H), 3.33-3.27 (m, 1H), 1.62-1.48 (m, 3H), 0.86 (dd, *J* = 6.0, 2.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.83, 170.39, 164.55, 149.10,

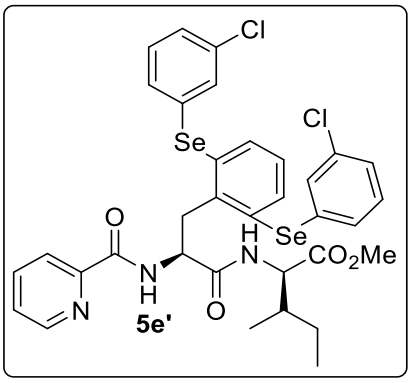
148.30, 139.66, 137.26, 136.13, 135.04, 133.56, 131.07, 130.97, 130.64, 130.34, 129.57, 129.06, 128.29, 127.13, 126.43, 122.27, 54.37, 52.29, 50.96, 41.54, 38.03, 24.78, 22.64, 22.00. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{31}ClN_3O_4Se$ 588.1196; found 588.1169.



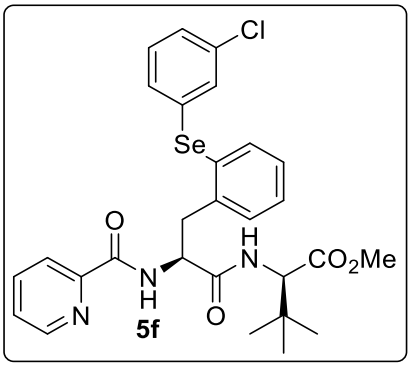
Methyl (3-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)leucinate 5d': The compound **5d'** was prepared according to the general procedure with starting materials **4d** and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **5d'** was obtained as a colorless oil (18 mg, 18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, *J* = 8.8 Hz, 1H), 8.52-8.51 (m, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.79 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.35 (t, *J* = 1.6 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.25-7.20 (m, 4H), 7.18-7.14 (m, 2H), 6.99 (t, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.19-5.12 (m, 1H), 4.64-4.59 (m, 1H), 3.72 (s, 3H), 3.69-3.63 (m, 1H), 3.58-3.54 (m, 1H), 1.67-1.63 (m, 2H), 1.59-1.54 (m, 1H), 0.88 (d, *J* = 5.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.99, 170.46, 164.77, 149.12, 148.31, 140.66, 137.14, 135.31, 135.13, 133.26, 132.80, 131.93, 130.49, 130.39, 129.18, 127.67, 126.34, 122.28, 53.95, 52.33, 51.05, 41.57, 37.83, 24.84, 22.68, 22.04. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{34}H_{34}Cl_2N_3O_4Se_2$ 778.0224; found 778.0217.



Methyl 2-(3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanamido)-3-methylpentanoate 5e: The compound **5e** was prepared according to the general procedure with starting materials **4a** and **2k**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5e** was obtained as a colorless oil (30 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.4 Hz, 1H), 8.55-8.53 (m, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 8.0, 1.6 Hz, 1H), 7.48 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.43-7.40 (m, 1H), 7.38 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.32 (t, *J* = 1.6 Hz, 1H), 7.25-7.12 (m, 5H), 6.67 (d, *J* = 8.4 Hz, 1H), 4.95-4.89 (m, 1H), 4.55-4.52 (m, 1H), 3.69 (s, 3H), 3.47-3.42 (m, 1H), 3.33-3.28 (m, 1H), 1.88-1.81 (m, 1H), 1.43-1.33 (m, 1H), 1.17-1.06 (m, 1H), 0.87-081 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.74, 170.42, 164.54, 149.11, 148.32, 139.67, 137.27, 136.15, 135.05, 133.51, 131.09, 130.94, 130.63, 130.34, 129.55, 129.06, 128.29, 127.14, 126.43, 122.27, 56.66, 54.51, 52.08, 38.13, 37.90, 25.17, 15.32, 11.54. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{31}ClN_3O_4Se$ 588.1196; found 588.1169.



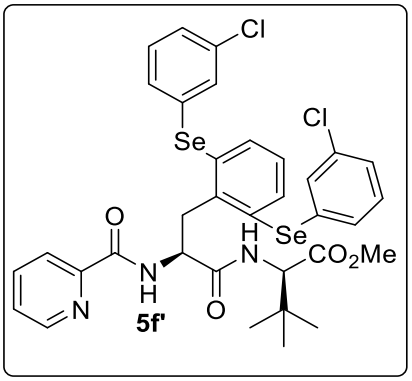
Methyl 2-(3-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanamido)-3-methylpentanoate 5e': The compound **5e'** was prepared according to the general procedure with starting materials **4a** and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **5e'** was obtained as a colorless oil (22 mg, 22%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (d, *J* = 8.4 Hz, 1H), 8.52 (d, *J* = 4.0 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.35-7.31 (m, 4H), 7.24-7.14 (m, 6H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.19-5.13 (m, 1H), 4.60-4.57 (m, 1H), 3.72 (s, 3H), 3.70-3.64 (m, 1H), 3.58-3.53 (m, 1H), 1.94-1.87 (m, 1H), 1.45-1.39 (m, 1H),1.20-1.12 (m, 1H), 0.90-0.85 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.92, 170.49, 164.77, 149.13, 148.33, 140.74, 137.15, 135.37, 135.13, 133.22, 132.79, 131.91, 130.49, 130.35, 129.20, 127.66, 126.34, 122.28, 56.73, 54.11, 52.13, 37.94, 37.89, 25.23, 15.42, 11.60. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{34}H_{34}Cl_2N_3O_4Se_2$ 778.0224; found 778.0217.



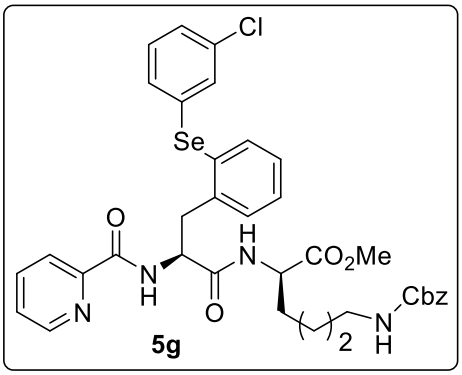
5f

Methyl 2-(3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanamido)-3,3-dimethylbutanoate 5f: The compound **5f** was prepared according to the general procedure with starting materials **4e** and **2k**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5f** was obtained as a colorless oil (34 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.4 Hz, 1H), 8.54-8.53 (m, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1H), 7.47 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.43-7.40 (m, 1H), 7.37 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.31 (t,

J = 1.6 Hz, 1H), 7.26-7.22 (m, 1H), 7.20-7.11 (m, 4H), 6.77 (d, *J* = 9.2 Hz, 1H), 4.94-4.89 (m, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 3.68 (s, 3H), 3.45-3.40 (m, 1H), 3.35-3.30 (m, 1H), 0.90 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.32, 170.40, 164.60, 149.09, 148.32, 139.66, 137.28, 136.15, 135.05, 133.52, 131.10, 130.93, 130.65, 130.33, 129.54, 129.05, 128.28, 127.14, 126.44, 122.29, 60.31, 54.63, 51.78, 37.91, 34.79, 26.48. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{28}H_{31}ClN_3O_4Se$ 588.1196; found 588.1180.

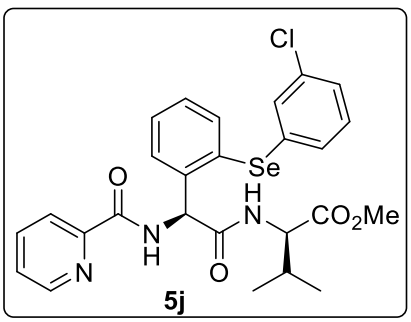


Methyl 2-(3-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanamido)-3,3-dimethylbutanoate 5f': The compound **5f'** was prepared according to the general procedure with starting materials **4e** and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **5f'** was obtained as a colorless oil (26 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (d, *J* = 8.8 Hz, 1H), 8.51-8.50 (m, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.79 (td, *J* = 8.0, 1.6 Hz, 1H), 7.41-7.38 (m, 1H), 7.35 (t, *J* = 1.6 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.25-7.20 (m, 4H), 7.18-7.15 (m, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 9.2 Hz, 1H), 5.17-5.11 (m, 1H), 4.45 (d, *J* = 9.2 Hz, 1H), 3.71 (s, 3H), 3.68-3.64 (m, 1H), 3.57-3.52 (m, 1H), 0.94 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.51, 170.42, 164.88, 149.12, 148.34, 140.68, 137.17, 135.31, 135.13, 133.25, 132.75, 131.96, 130.49, 130.39, 129.19, 127.68, 126.36, 122.28, 60.41, 54.20, 51.83, 37.63, 34.79, 26.55. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{34}H_{34}Cl_2N_3O_4Se_2$ 778.0224; found 778.0217.



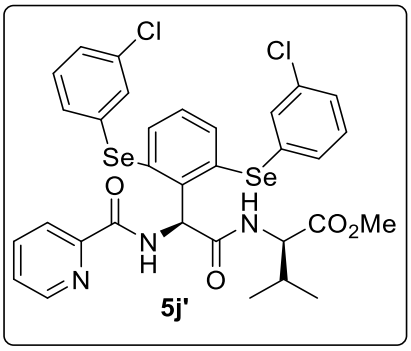
5g

Methyl N^6-((benzyloxy)carbonyl)-N^2-(3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)lysinate 5g: The compound **5g** was prepared according to the general procedure with starting materials **4f** and **2k**, purified using ethyl acetate and hexane mixture (3:2) as the mobile phase. **5g** was obtained as a colorless oil (39.2 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 8.52-8.50 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.47 (dd, *J* = 8.0,1.2 Hz, 1H), 7.39-7.27 (m, 8H), 7.26-7.22 (m, 1H), 7.20-7.10 (m, 4H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.21 (br s, 1H), 5.13-5.03 (m, 2H), 4.88-4.83 (m, 1H), 4.58-4.53 (m, 1H), 3.69 (s, 3H), 3.45-3.40 (m, 1H), 3.32-3.27 (m, 1H), 3.12-3.03 (m, 2H), 1.86-1.79 (m, 1H), 1.68-1.59 (m, 1H), 1.48-1.41 (m, 2H), 1.36-1.26 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.22, 170.49, 164.71, 156.53, 148.98, 148.31, 139.53, 137.30, 136.75, 136.15, 135.05, 133.49, 131.11, 130.98, 130.63, 130.37, 129.60, 129.06, 128.49, 128.34, 128.10, 128.02, 127.18, 126.47, 122.32, 66.53, 54.70, 52.42, 52.09, 40.47, 37.96, 31.83, 29.12, 22.12. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{36}H_{38}ClN_4O_6Se$ 737.1673; found 737.1649.



5j

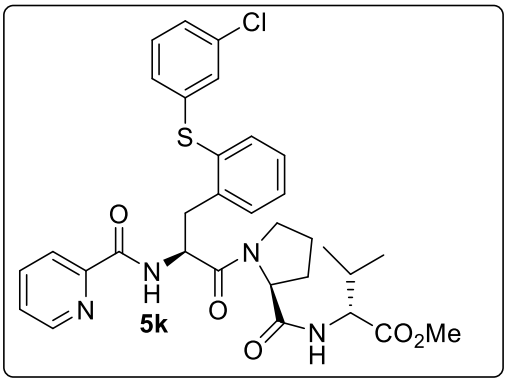
Methyl (2-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)acetyl)valinate 5j: The compound **5j** was prepared according to the general procedure with starting materials **4h** and **2k**, purified using ethyl acetate and hexane mixture (2:3) as the mobile phase. **5j** was obtained as a colorless oil (25 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (d, *J* = 6.8 Hz, 1H), 8.55 (d, *J* = 4.4 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.43-7.37 (m, 3H), 7.32-7.28 (m, 2H), 7.13-7.10 (m, 2H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.23 (d, *J* = 6.8 Hz, 1H), 4.52-4.49 (m, 1H), 3.63 (s, 3H), 2.18-2.10 (m, 1H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.59, 169.44, 163.90, 149.28, 148.34, 140.33, 137.17, 136.91, 135.09, 133.35, 131.38, 130.38, 129.95, 129.92, 129.68, 129.64, 128.70, 127.31, 126.35, 122.23, 57.70, 57.38, 52.16, 31.13, 18.97, 17.76. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{26}H_{26}ClN_3O_4Se$ Na 582.0702; found 582.0662.



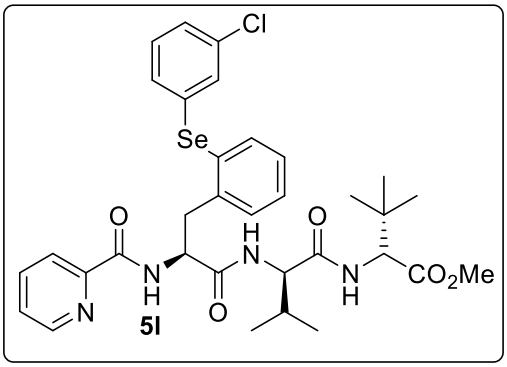
5j'

Methyl (2-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)acetyl)valinate 5j': The compound **5j'** was prepared according to the general procedure with starting materials **4h** and **2k**, purified using ethyl acetate and hexane mixture (1:2) as the mobile phase. **5j'** was obtained as a colorless oil (14 mg, 14%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, *J* = 6.4 Hz, 1H), 8.44-8.42 (m, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.42 (s, 2H), 7.39-7.35 (m, 1H), 7.29-7.27 (m, 2H), 7.16-7.08 (m, 5H), 6.89 (d, *J* = 6.4 Hz, 1H), 6.34 (d, *J* = 8.4 Hz, 1H), 4.59-4.55 (m, 1H), 3.71 (s, 3H), 2.17-2.09 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.88, 168.86,

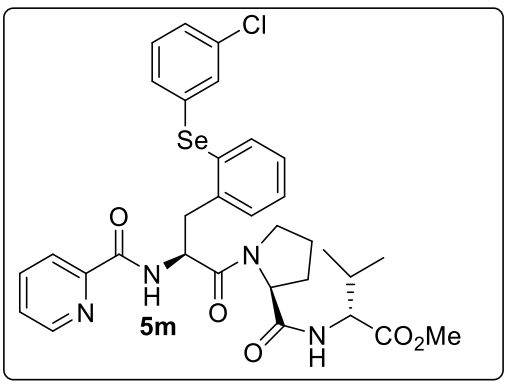
164.26, 148.98, 148.34, 141.09, 137.04, 136.91, 135.02, 133.58, 132.01, 130.48, 130.33, 127.50, 126.23, 122.13, 58.87, 57.59, 52.30, 31.41, 18.98, 17.68. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{32}H_{30}Cl_2N_3O_4Se_2$ 749.9911; found 749.9901.



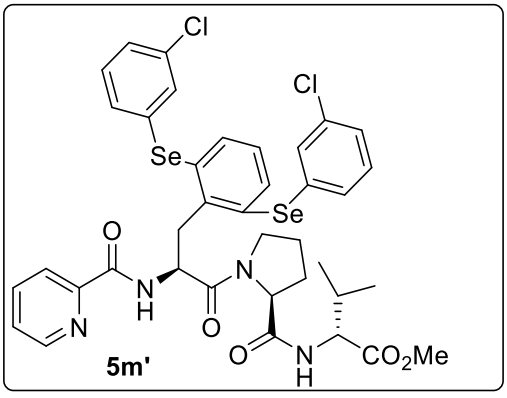
Methyl (3-(2-((3-chlorophenyl)thio)phenyl)-2-(picolinamido)propanoyl)prolylvalinate 5k: Thiolated compound **5k** was prepared according to the general procedure with starting materials **4i** and **2d**, purified using ethyl acetate and hexane mixture (3:2) as the mobile phase. **5k** was obtained as a colorless oil (25 mg, 31%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.8 Hz, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 8.03-8.00 (m, 1H), 7.78 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41-7.34 (m, 4H), 7.23-7.21 (m, 2H), 7.19-7.15 (m, 1H), 7.14-7.12 (m, 2H), 7.06-7.03 (m, 1H), 5.29-5.23 (m, 1H), 4.65 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.46-4.43 (m, 1H), 3.79-3.75 (m, 1H), 3.73 (s, 3H), 3.65-3.60 (m, 1H), 3.37 (dd, *J* = 14.0, 4.8 Hz, 1H), 3.19-3.13 (m, 1H), 2.40-2.35 (m, 1H), 2.18-2.06 (m, 2H), 2.04-1.96 (m, 1H), 1.89-1.80 (m, 1H), 0.90 (dd, *J* = 6.8, 1.6 Hz, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.13, 171.69, 170.61, 163.98, 149.23, 148.33, 138.95, 137.16, 135.04, 132.37, 131.60, 131.55, 130.23, 129.49, 129.01, 128.56, 128.17, 126.66, 126.42, 126.28, 122.16, 57.51, 52.10, 51.33, 47.56, 37.27, 31.04, 26.93, 25.18, 19.05, 17.82. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{32}H_{36}ClN_4O_5S$ 623.2095; found 623.2084.



Methyl 2-(2-(3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanamido)-3-methylbutanamido)-3,3-dimethylbutanoate 5l: The compound **5l** was prepared according to the general procedure with starting materials **4j** and **2k**, purified using ethyl acetate and hexane mixture (3:2) as the mobile phase. **5l** was obtained as a colorless oil (30 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 8.54-8.52 (m, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 7.6, 2.0 Hz, 1H), 7.46-7.40 (m, 2H), 7.38-7.36 (m, 1H), 7.30 (t, *J* = 1.6 Hz, 1H), 7.24-7.22 (m, 1H), 7.20-7.11 (m, 4H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.45 (d, *J* = 9.2 Hz, 1H), 4.94-4.88 (m, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 4.24-4.20 (m, 1H), 3.71 (s, 3H), 3.51-3.46 (m, 1H), 3.33-3.27 (m, 1H), 2.18-2.13 (m, 1H), 0.96 (s, 9H), 0.88 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.69, 170.96, 170.42, 164.80, 148.98, 148.34, 139.62, 137.33, 136.14, 135.07, 133.51, 131.13, 130.83, 130.68, 130.36, 129.58, 129.14, 128.36, 127.16, 126.53, 122.35, 60.22, 59.03, 54.73, 51.85, 37.57, 34.62, 30.50, 26.63, 19.18, 18.00. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{33}H_{39}ClN_4O_5SeNa$ 709.1700; found 709.1685.



Methyl (3-(2-((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)prolylvalinate 5m: The compound **5m** was prepared according to the general procedure with starting materials **4i** and **2k**, purified using ethyl acetate and hexane mixture (3:2) as the mobile phase. **5m** was obtained as a colorless oil (32 mg, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.8 Hz, 1H), 8.57-8.55 (m, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 8.0, 1.6 Hz, 1H), 7.48 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.42-7.40 (m, 1H), 7.39-7.33 (m, 2H), 7.29-7.27 (m, 1H), 7.25-7.23 (m, 1H), 7.21-7.12 (m, 4H), 5.30-5.22 (m, 1H), 4.66 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.46-4.43 (m, 1H), 3.79-3.74 (m, 1H), 3.73 (s, 3H), 3.62-3.57 (m, 1H), 3.37-3.32 (m, 1H), 3.26-3.20 (m, 1H), 2.39-2.34 (m, 1H), 2.19-1.95 (m, 3H), 1.90-1.83 (m, 1H), 0.92 (dd, *J* = 6.8, 2.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.13, 171.61, 170.60, 163.95, 149.21, 148.32, 139.07, 137.18, 136.38, 135.12, 133.62, 131.30, 130.79, 130.40, 130.27, 129.29, 129.03, 128.53, 127.07, 126.29, 122.17, 59.99, 57.54, 52.10, 51.44, 47.65, 39.16, 31.05, 26.96, 25.19, 19.08, 17.86. ESI-HRMS m/z: $[M+H]^+$ Calcd. for $C_{32}H_{36}ClN_4O_5Se$ 671.1567; found 671.1562.

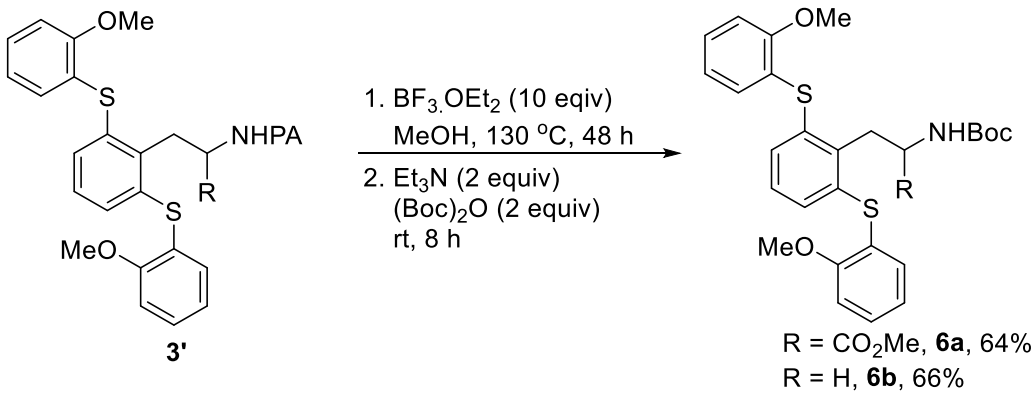


Methyl (3-(2,6-bis((3-chlorophenyl)selanyl)phenyl)-2-(picolinamido)propanoyl)prolylvalinate 5m': Thiolated compound **5m'** was prepared according to the general procedure with starting materials **4i** and **2k**, purified using ethyl acetate and hexane mixture (1:1) as the mobile phase. **5m'** was obtained as a colorless oil (29 mg, 26%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 9.6 Hz, 1H), 8.56-8.55 (m, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.77 (td, *J* = 7.6, 1.6 Hz, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.41-7.37 (m, 1H), 7.32-

7.29 (m, 4H), 7.23-7.15 (m, 6H), 6.99 (d, *J* = 8.0 Hz, 1H), 5.57-5.51 (m, 1H), 4.73 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.45-4.42 (m, 1H), 4.03-3.90 (m, 2H), 3.71 (s, 3H), 3.69-3.65 (m, 1H), 3.39-3.34 (m, 1H), 2.47-2.40 (m, 1H), 2.23-2.02 (m, 3H), 1.90-1.81 (m, 1H), 0.81 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.09, 171.59, 170.61, 164.07, 149.17, 148.38, 140.01, 137.09, 135.49, 135.19, 133.31, 132.99, 131.62, 130.51, 130.08, 129.40, 127.57, 126.27, 122.15, 59.87, 57.38, 52.08, 51.27, 47.90, 38.24, 30.95, 26.63, 25.28, 19.04, 17.56. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{38}H_{38}Cl_2N_4O_5Se_2Na$ 883.0416; found 883.0394.

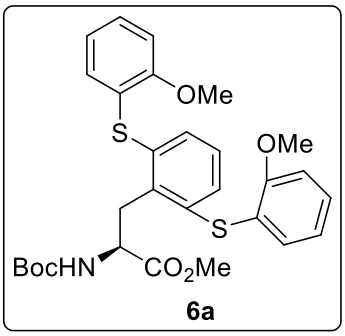
6. Synthetic Applications of the Chalcogenated Compounds

General procedure for the removal of directing group[4]



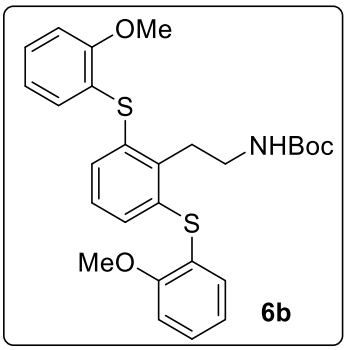
To a 15 mL sealed reaction tube, dithiolated compound **3'** (0.2 mmol) and MeOH (3 mL) were added under air. The reaction mixture was allowed to stir at room temperature for 5 mins and $BF_3{\cdot}Et_2O$ (0.246 mL, 20 mmol) was then added dropwise to the solution with continuous stirring. A teflon-coated cap was fitted with the tube and the reaction was vigorously stirred at 130 ℃ for 48 h. After completion, the reaction was cooled at room temperature and saturated Na_2CO_3 was added slowly to this reaction for quenching. The reaction mixture was extracted with ethyl acetate (3 x 15 mL) washed with brine. The combined organic layers were next dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was then dissolved in DCM (3 mL). Et_3N (0.056 mL, 0.4 mmol) and Boc_2O (0.092 mL, 0.4

mmol) were then added and the mixture was stirred for 8 h at room temperature. After evaporation of solvent, the crude mixture was purified by silica gel column chromatography using ethyl acetate/hexane as the eluent to gain the product **6**.



6a

Methyl 3-(2,6-bis((2-methoxyphenyl)thio)phenyl)-2-((tert-butoxycarbonyl)amino)propanoate 6a: Following the above-mentioned procedure, using compound **3a'** (0.2 mmol, 112 mg) provided the compound **6a** as a colourless liquid (71 mg, 64% yield). Eluent: ethyl acetate/hexane (1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.24 (m, 2H), 7.10-7.02 (m, 5H), 6.92-6.86 (m, 4H), 5.58 (d, *J* = 8.8 Hz, 1H), 4.96-4.90 (m, 1H), 3.86 (s, 6H), 3.74 (s, 3H), 3.55-3.50 (m, 1H), 3.44-3.38 (m, 1H), 1.34 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.00, 157.60, 155.39, 138.74, 136.37, 131.87, 131.66, 128.69, 128.21, 123.52, 121.35, 111.05, 79.47, 55.92, 53.65, 52.30, 33.48, 28.30. ESI-HRMS m/z: $[M+Na]^+$ Calcd. for $C_{29}H_{33}NO_6S_2Na$ 578.1647; found 578.1634.

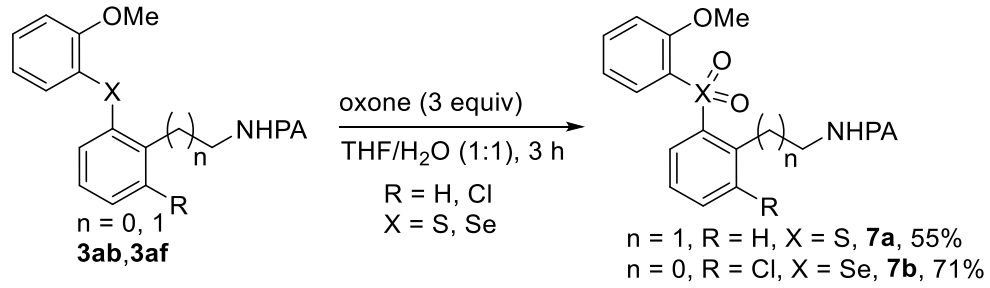


6b

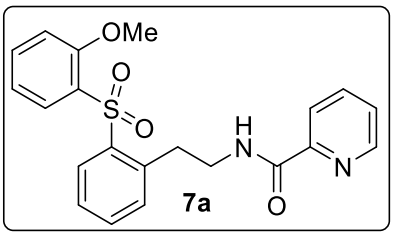
***Tert*-butyl (2,6-bis((2-methoxyphenyl)thio)phenethyl)carbamate 6b:** Following the above mentioned procedure, using compound **3ab'** (0.2 mmol, 110 mg) provided the compound **6b**

as a colourless liquid (66 mg, 66% yield). Eluent: ethyl acetate/hexane (1:4). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.26-7.23 (m, 2H), 7.09-7.08 (m, 2H), 7.02-7.01 (m, 3H), 6.90-6.86 (m, 4H), 4.85 (br s, 1H), 3.85 (s, 6H), 3.50-3.49 (m, 2H), 3.27 (s, 2H), 1.41 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 157.46, 155.84, 141.32, 135.82, 131.71, 131.66, 128.50, 127.80, 123.94, 121.35, 110.97, 78.85, 55.89, 40.60, 32.08, 28.48. ASAP-HRMS m/z: $[M]^+$ Calcd. for $C_{27}H_{31}NO_4S_2$ 497.1695; found 497.1696.

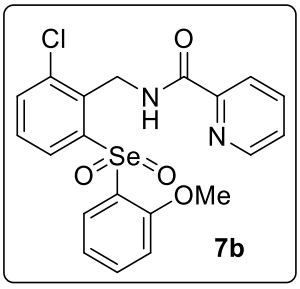
Oxone mediated Oxidation of chalcogenated compounds



To a solution of compound **3** (0.1 mmol) in THF (1 mL) and H_2O (1 mL) was added Oxone monopersulfate (90.1 mg, 0.3 mmol). The mixture was stirred for 3 h at room temperature. After completion, the reaction mixture was extracted with ethyl acetate (3 x 10 mL) and washed with saturated brine. The organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. Pure product was obtained by silica gel column chromatography using ethyl acetate/hexane as eluent to yield pure oxygenated compound **7**.



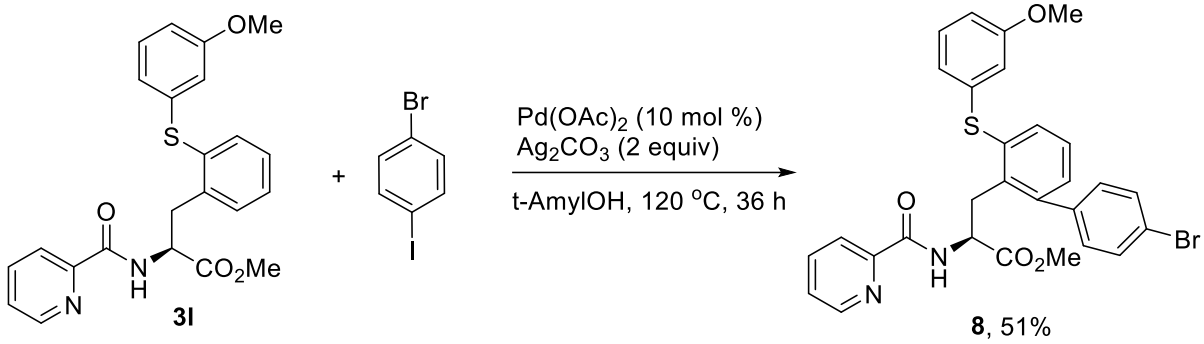
***N*-(2-((2-Methoxyphenyl)sulfonyl)phenethyl)picolinamide 7a:** Following the above-mentioned procedure, using compound **3ab** (0.1 mmol, 36.5 mg) provided the compound **7a** as a colourless liquid (22 mg, 55% yield). Eluent: ethyl acetate/hexane (3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.4 Hz, 1H), 8.23-8.21 (m, 2H), 8.17 (d, *J* = 7.8 Hz, 2H), 7.86-7.82 (m, 1H), 7.58-7.49 (m, 2H), 7.44-7.39 (m, 2H), 7.37-7.35 (m, 1H), 7.17-7.13 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 3.65 (s, 3H), 3.56-3.50 (m, 2H), 3.14 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.44, 157.14, 148.17, 139.66, 138.65, 137.31, 136.94, 135.63, 133.26, 131.85, 131.18, 129.71, 129.36, 126.38, 126.15, 122.13, 120.61, 112.71, 55.81, 40.50, 32.55. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{21}H_{21}N_2O_4S$ 397.1222; found 397.1234.



7b

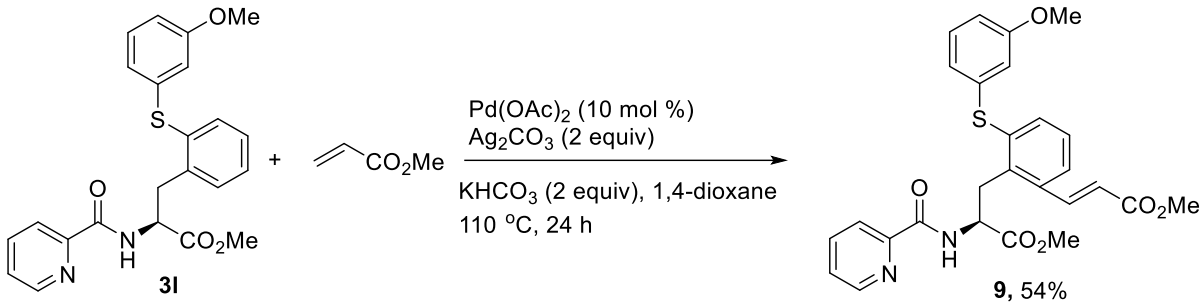
***N*-(2-Chloro-6-((2-methoxyphenyl)selenonyl)benzyl)picolinamide 7b:** Following the above-mentioned procedure, using compound **3af** (0.1 mmol, 43 mg) provided the compound **7b** as a colourless liquid (33 mg, 71% yield). Eluent: ethyl acetate/hexane (3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60-8.58 (m, 1H), 8.52 (d, *J* = 4.8 Hz, 1H), 8.29 (dd, *J* = 7.2, 0.8 Hz, 1H), 8.23 (dd, *J* = 6.8, 1.2 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.8, 1.6 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.57-7.51 (m, 2H), 7.40-7.37 (m, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 5.00 (d, *J* = 6.0 Hz, 2H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.67, 156.93, 149.56, 148.25, 145.59, 137.76, 137.12, 136.43, 135.39, 135.00, 130.49, 129.55, 128.97, 127.85, 126.13, 122.33, 122.07, 113.09, 56.32, 37.64. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{20}H_{18}ClN_2O_4Se$ 465.0148; found 465.0106.

Pd-Catalyzed arylation of 3l with 4-bromo-1-iodobenzene



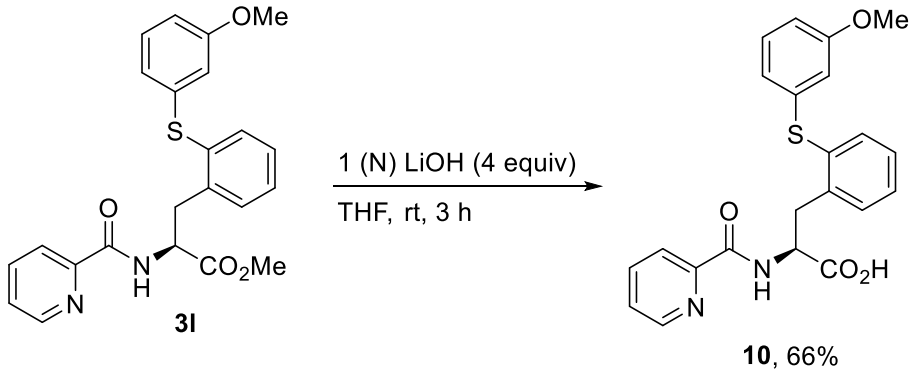
To a 15 mL sealed reaction tube having a magnetic stir-bar, the compound **3l** (84.5 mg, 0.2 mmol), 4-bromo-1-iodobenzene (170 mg, 0.6 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (137.5 mg, 0.5 mmol) and *t*-AmylOH (4 mL) were added in presence of atmospheric air. The mixture was then stirred for 36 h at 120 °C. After completion, the reaction was cooled at room temperature and filtered through a celite pad using ethyl acetate as eluent. After evaporation of solvent under vacuo, the residue was purified by column chromatography on silica gel to afford the desired product **8** as a colorless oil (59 mg, 51%). Eluent: ethyl acetate/hexane (1:4). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.2 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 7.7 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 7.0 Hz, 1H), 7.23-7.13 (m, 5H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.91-6.89 (m, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 5.05-5.01 (m, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 3.47-3.45 (m, 1H), 3.38-3.34 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.79, 164.05, 160.14, 149.24, 148.07, 143.14, 140.03, 137.14, 136.75, 136.40, 135.00, 132.24, 131.51, 131.20, 130.04, 129.62, 127.58, 126.25, 123.06, 122.28, 121.60, 116.09, 112.91, 77.23, 77.05, 76.86, 55.32, 52.42, 32.63. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{29}H_{26}BrN_2O_4S$ 577.0797; found 577.0761.

Pd-Catalyzed olefination of 3l with methyl acrylate



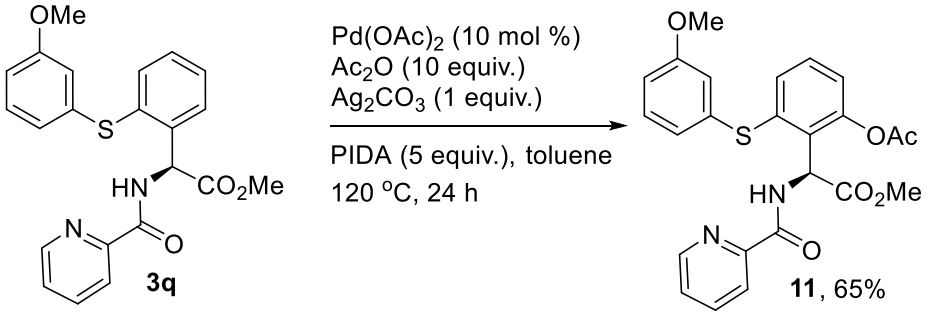
To a 15 mL oven dried sealed reaction tube, compound **3l** (42.2 mg, 0.1 mmol), methyl acrylate (18 μL, 0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol %), Ag_2CO_3 (55.2 mg, 0.2 mmol), $KHCO_3$ (20 mg, 0.2 mmol) and 1,4-dioxane (2 mL) were added under air. The reaction mixture was stirred for 24 h at 110 °C followed by cooling at room temperature. The mixture was then filtered through a short pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford desired olefinated product **9** as a colorless oil (27.3 mg, 54%). Eluent: ethyl acetate/hexane (1:3). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.52 (d, *J* = 4.2 Hz, 1H), 8.14 (d, *J* = 15.4 Hz, 1H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.42-7.38 (m, 2H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.18 (q, *J* = 7.7 Hz, 2H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.81 (s, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.26 (d, *J* = 8.4 Hz, 1H), 5.10-5.07 (m, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.73 (s, 3H), 3.65-3.62 (m, 1H), 3.56-3.52 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.60, 166.79, 164.11, 160.14, 149.18, 148.17, 141.91, 137.08, 136.93, 136.78, 136.62, 135.81, 134.39, 130.08, 128.20, 126.64, 126.22, 122.83, 122.22, 121.49, 115.88, 112.91, 55.30, 52.96, 52.64, 51.79, 32.69. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{27}H_{27}N_2O_6S$ 507.1590; found 507.1590.

Ester hydrolysis of 3l



To a 10 mL round bottom flask, compound **3l** (42.2 mg, 0.1 mmol) was dissolved in THF and 1 (N) LiOH (19 μL, 0.4 mmol) solution was added to the reaction at room temperature. The mixture was allowed to stir for 3 h at ambient temperature. Progress of the reaction was monitored by TLC and upon completion the reaction was concentrated in vacuo. The crude reaction mixture was purified by silica gel column chromatography using ethyl acetate/hexane (4:1) solvent system to give the desired free acid product **10** as a colorless oil (26.9 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 7.6 Hz, 1H), 8.52 (d, *J* = 4.4 Hz, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.83-7.78 (m, 1H), 7.42-7.39 (m, 1H), 7.37-7.31 (m, 2H), 7.24-7.11 (m, 3H), 6.77-6.69 (m, 3H), 5.09-5.04 (m, 1H), 3.70 (s, 3H), 3.57-3.52 (m, 1H), 3.39-3.33 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 174.43, 164.99, 160.04, 148.90, 148.29, 138.22, 137.46, 137.34, 134.23, 134.06, 130.85, 129.94, 128.42, 128.21, 126.51, 122.45, 121.91, 114.91, 112.41, 55.24, 53.59, 35.53. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{21}N_2O_4S$ 409.1222; found 409.1197.

Pd-Catalyzed acetoxylation of 3q with Ac_2O



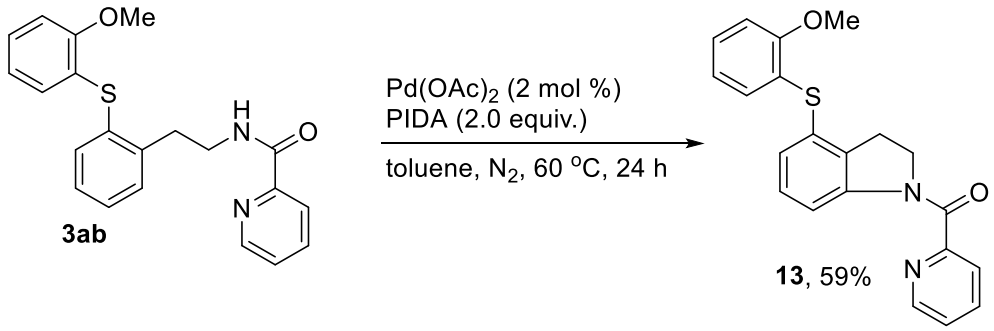
To a 15 mL oven dried sealed reaction tube containing a stirring bar, compound **3q** (40.8 mg, 0.1 mmol), Ac_2O (94 μL, 1 mmol), $PhI(OAc)_2$ (166 mg, 0.5 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol %), Ag_2CO_3 (27.6 mg, 0.1 mmol) and toluene (2 mL) were added under atmospheric air. The reaction was stirred for 24 h at 120 °C followed by cooling at room temperature. The mixture was diluted with ethyl acetate and filtered through a celite pad and concentrated under vacuum. The residue was purified by silica gel column chromatography with ethyl acetate/hexane (1:2) solvent system to provide the desired product **11** as a colorless oil (30.3 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (d, *J* = 8.0 Hz, 1H), 8.54-8.52 (m, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 7.8, 1.6 Hz, 1H), 7.42-7.38 (m, 1H), 7.36-7.33 (m, 1H), 7.31-7.28 (m, 1H), 7.16-7.10 (m, 2H), 6.90-6.85 (m, 2H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.71-6.68 (m, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.62, 169.11, 163.68, 159.97, 149.45, 149.37, 148.23, 137.16, 137.13, 137.04, 132.48, 131.69, 129.85, 129.50, 126.26, 123.19, 122.68, 122.41, 115.57, 112.95, 55.24, 52.84, 50.82, 20.96. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{24}H_{23}N_2O_6S$ 467.1277; found 467.1258.

Pd-Catalyzed bromination of 3q with NBS

A mixture of compound **3q** (40.8 mg, 0.1 mmol), NBS (26.7 mg, 0.15 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol %) were placed in a 15 mL oven dried sealed reaction tube. 1,2-Dichloroethane (DCE) (2 mL) was added and the mixture was stirred for 24 h at 110 °C. After stipulated time, the mixture was cooled and filtered through a celite pad using dichloromethane as eluent and

concentrated under vacuum. The crude reaction mixture was purified by column chromatography on silica gel (eluent: ethyl acetate/hexane (1:3) solvent system) to afford the desired brominated product **12** as yellowish liquid (20.4 mg, 42%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.97 (d, *J* = 6.3 Hz, 1H), 8.49 (s, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.39-7.34 (m, 3H), 6.45 (d, *J* = 9.1 Hz, 1H), 6.29-7.28 (m, 2H), 3.68 (s, 3H), 3.50 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.76, 163.59, 159.01, 149.18, 148.19, 140.87, 139.74, 137.13, 137.10, 133.13, 132.17, 130.08, 129.73, 129.70, 126.23, 122.15, 114.87, 113.07, 112.67, 55.47, 55.16, 52.90. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{22}H_{20}BrN_2O_4S$ 487.0327; found 487.0315.

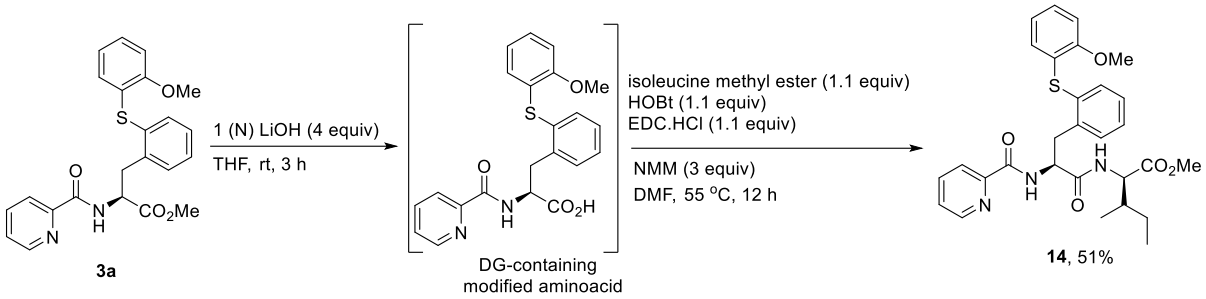
Pd-Catalyzed synthesis of indoline derivative 13



To a 15 mL sealed reaction tube, a mixture of compound **3ab** (36.2 mg, 0.3 mmol), $Pd(OAc)_2$ (1.3 mg, 2 mol %) and $PhI(OAc)_2$ (199.2 mg, 0.6 mmol) were added in toluene (4 mL) under N_2 atmosphere. The mixture was heated at 60 °C for 24 h. The reaction mixture was cooled to room temperature, filtered through a celite pad and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to provide the cyclized indoline derivative **13** as colorless oil (21.3 mg, 59%). Eluent: ethyl acetate/hexane (1:3). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.29 (d, *J* = 7.0 Hz, 1H), 7.87-7.85 (m, 2H), 7.39 (s, 1H), 7.25-7.19 (m, 2H), 7.05 (d, *J* = 7.0 Hz, 1H), 6.90-6.89 (m, 2H), 6.86-6.84 (m, 1H), 4.34 (t, *J* = 7.7 Hz, 2H), 3.88 (s, 3H), 3.09 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 166.33, 156.87, 154.36,

148.08, 143.94, 137.14, 135.11, 129.84, 129.45, 128.58, 128.56, 127.80, 125.13, 124.22, 123.50, 121.37, 117.43, 110.81, 55.94, 50.44, 28.34. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{21}H_{19}N_2O_2S$ 363.1167; found 363.1158.

Sequential One pot synthesis of peptide 14



To a 25 mL round bottom flask, compound **3a** (139.2 mg, 0.33 mmol) was dissolved in THF and 1 (N) LiOH (62.7 μL, 1.32 mmol) solution was added to the reaction at room temperature. The mixture was allowed to stir for 3 h. Progress of the reaction was monitored by TLC and upon completion the reaction was concentrated in vacuo. The crude reaction mixture was then dissolved in anhydrous DMF. L-Isoleucine methyl ester (52.6 mg, 0.36 mmol) and NMM (108 μL, 0.99 mmol) were added and the resulting mixture was cooled to 0 °C. HOBt (49 mg, 0.36 mmol) was added to this solution. After 5 minutes, EDC. HCl (69.3 mg, 0.36 mmol) was added and stirred at 0 °C for 10 minutes. The reaction mixture was then heated at 55 °C for 12 h. After stipulated time, the mixture was cooled at room temperature and DMF was evaporated in vacuo. Water was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to give the desired di-peptide **14** as colorless oil (90.3 mg, 51%). Eluent: ethyl acetate/hexane (1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.55-8.53 (m, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.80 (td, *J* = 8.0, 1.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.35-7.33 (m, 1H), 7.29-7.27 (m, 1H), 7.22-7.13 (m, 3H), 6.94-6.88 (m, 2H), 6.85-6.81 (m, 1H), 6.72 (d, *J* = 8.8 Hz, 1H), 5.02-4.96 (m, 1H), 4.53-

4.50 (m, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 3.48-3.43 (m, 1H), 3.35-3.30 (m, 1H), 1.89-1.83 (m, 1H), 1.41-1.33 (m, 1H), 1.15-1.06 (m, 1H), 0.86-0.81 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.67, 170.76, 164.53, 157.05, 149.25, 148.28, 139.11, 137.20, 133.90, 133.39, 130.85, 130.65, 128.12, 128.01, 127.98, 126.33, 124.32, 122.20, 121.34, 110.92, 56.68, 55.93, 54.14, 51.98, 37.82, 36.30, 25.13, 15.32, 11.55. ASAP-HRMS m/z: $[M+H]^+$ Calcd. for $C_{29}H_{34}N_3O_5S$ 536.2219; found 536.2183.

7. X-Ray Crystallography Data and structure

Crystal Data and Structure Refinement for 3af

Single crystal of ***N*-(2-Chloro-6-((2-methoxyphenyl)selanyl)benzyl)picolinamide (3af)** was obtained in solvent mixture ethyl acetate and hexane by slow evaporation method. The crystal data was collected on a Rigaku Oxford diffractometer at 293 K. Selected-collection parameters and other crystallographic results are summarized below in Table 1. The program package SHELXTL1 and Olex2 was used for structure solution and ORTEP diagram carried out by DIAMOND 3.2.

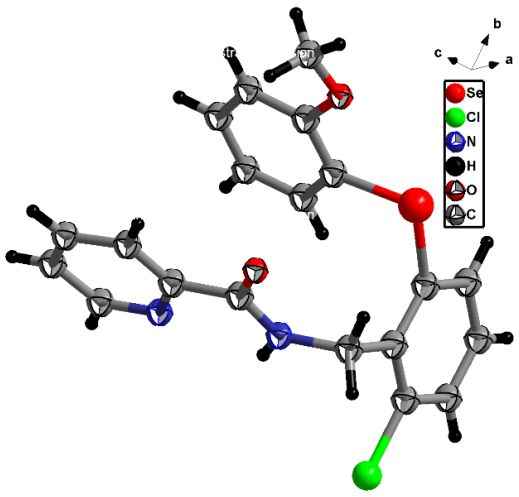


Figure 1. ORTEP diagram of **N-(2-chloro-6-((2-methoxyphenyl)selanyl)benzyl)picolinamide (3af)** with 50% ellipsoid. (CCDC 2220553)

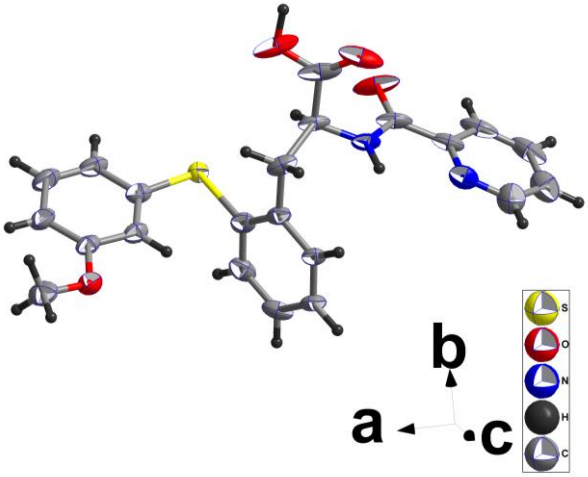
Table 2. Crystal data and structure refinement for 3af

Identification code	NKS-RNB-197 B_auto
Empirical formula	$C_{3.64}H_{3.09}Cl_{0.18}N_{0.36}O_{0.36}Se_{0.18}$
Formula weight	78.50
Temperature/K	295(4)
Crystal system	triclinic
Space group	P-1
a/Å	7.9413(5)
b/Å	8.6162(7)
c/Å	15.5382(11)
α/°	89.406(6)
β/°	81.894(6)
γ/°	62.946(7)
Volume/Å^3	935.64(13)
Z	11
ρ_{calc}g/cm^3	1.533
μ/mm^{-1}	2.166
F(000)	436.0
Crystal size/mm^3	0.01 × 0.01 × 0.001
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.628 to 60.812
Index ranges	$-11 \leq h \leq 10$, $-10 \leq k \leq 12$, $-21 \leq l \leq 17$
Reflections collected	16304
Independent reflections	4500 [R_{int} = 0.0745, R_{sigma} = 0.0717]
Data/restraints/parameters	4500/0/236
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0696, wR_2 = 0.1674
Final R indexes [all data]	R_1 = 0.1220, wR_2 = 0.1865
Largest diff. peak/hole / e Å^{-3}	0.56/-0.41

Crystal Data and Structure Refinement for 10

Single crystal of **3-(2-((3-Methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoic acid (10)** was obtained in solvent mixture ethyl acetate and hexane by slow evaporation method. The crystal data was collected on a Rigaku Oxford diffractometer at 293 K. Selected-collection

parameters and other crystallographic results are summarized below in Table 2. The program package SHELXTL1 and Olex2 was used for structure solution and ORTEP diagram carried out by DIAMOND 3.2.



1.

Figure 2. ORTEP diagram of **3-(2-((3-Methoxyphenyl)thio)phenyl)-2-(picolinamido)propanoic acid (10)** with 50% ellipsoid. (CCDC 2220554)

Table 3. Crystal data and structure refinement for 10.

Identification code	NKS-RNB-164 A_auto
Empirical formula	$C_{3.14}H_{2.86}N_{0.29}O_{0.57}S_{0.14}$
Formula weight	58.35
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	14.7554(11)
b/Å	13.0587(7)
c/Å	10.6435(7)
α/°	90
β/°	103.754(7)
γ/°	90
Volume/Å^3	1992.0(2)
Z	28
ρ_{calc}g/cm^3	1.362
μ/mm^{-1}	0.194

F(000)	856.0
Crystal size/mm^3	0.01 × 0.01 × 0.001
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.486 to 62.982
Index ranges	$-21 \leq h \leq 20$, $-16 \leq k \leq 17$, $-14 \leq l \leq 13$
Reflections collected	21495
Independent reflections	5507 [R_{int} = 0.0813, R_{sigma} = 0.0633]
Data/restraints/parameters	5507/0/267
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0940, wR_2 = 0.2407
Final R indexes [all data]	R_1 = 0.1362, wR_2 = 0.2628
Largest diff. peak/hole / e $Å^{-3}$	1.06/-0.66

8. Determination of *ee* by Chiral HPLC Analysis

Chiral ART Cellulose-SZ S-5um; sHexane : isopropanol = 45:55; 1 mL/min, λ = 245 nm.

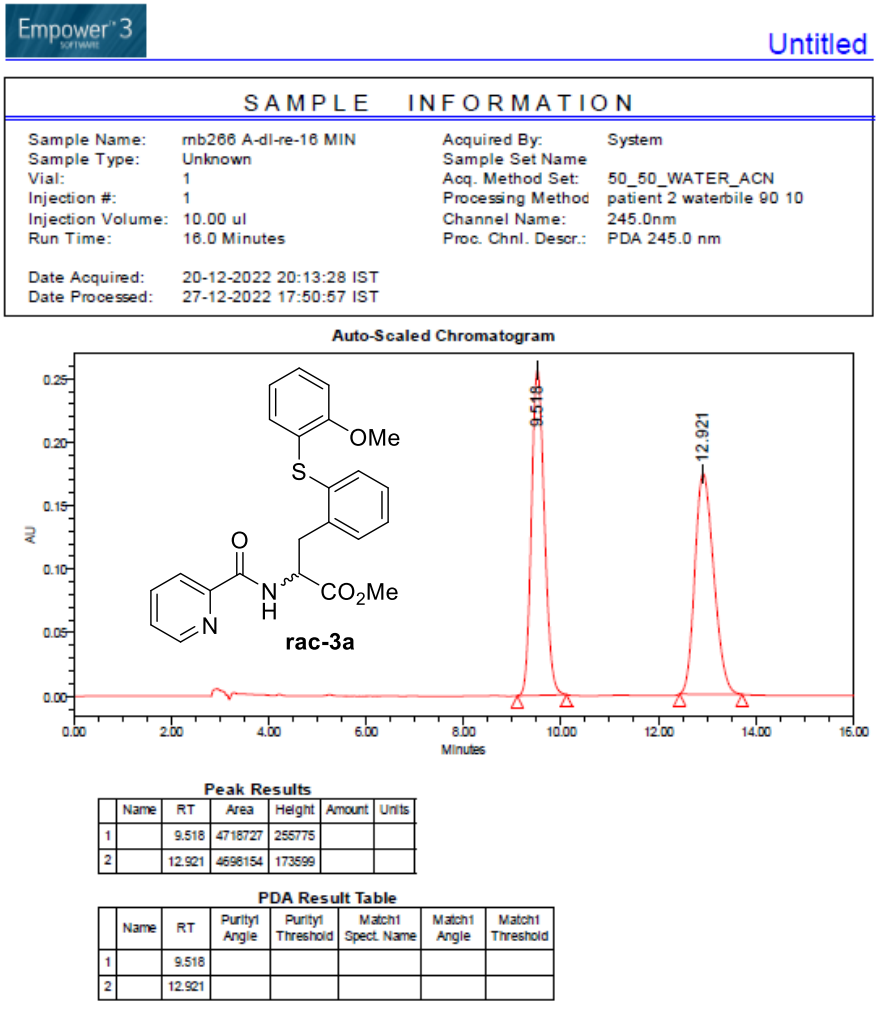


Fig SA. HPLC of compound **rac-3a**

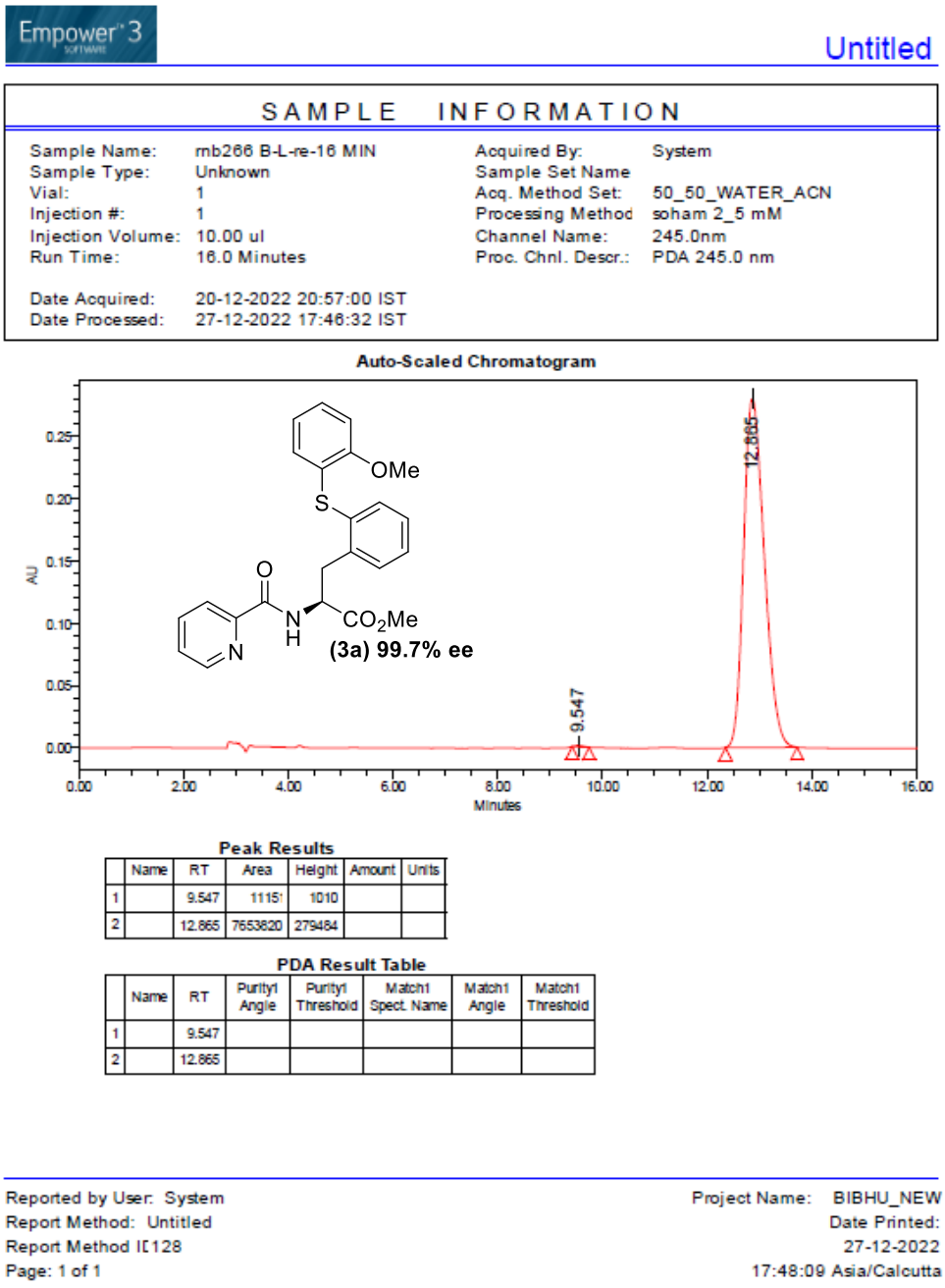


Fig SB. HPLC of compound **3a**

9. References

1. P. Andrade-Sampedro, J. M. Matxain and A. Correa, *Chem. Eur. J.*, 2021, **27**, 5782-5789.
2. (a) P. Natarajan, H. Sharma, M. Kaur, P. Sharma, *Tetrahedron Lett*., 2015, **56**, 5578-5582; (b) P. Sun, D. Yang, W. Wei, L. Jiang, Y. Wang, T. Dai and H. Wang, *Org. Chem. Front*., 2017, **4**, 1367-1371.
3. D. Singh, A. M. Deobald, L. R. S. Camargo, G. Tabarelli, O. E. D. Rodrigues and A. L. Braga, *Org. Lett*., 2010, **12**, 3288-3291.
4. K. Li, Q. Wu, J. Lan and J. You, *Nat. Commun*., 2015, **6**, 8404.

10. NMR and HRMS Spectra

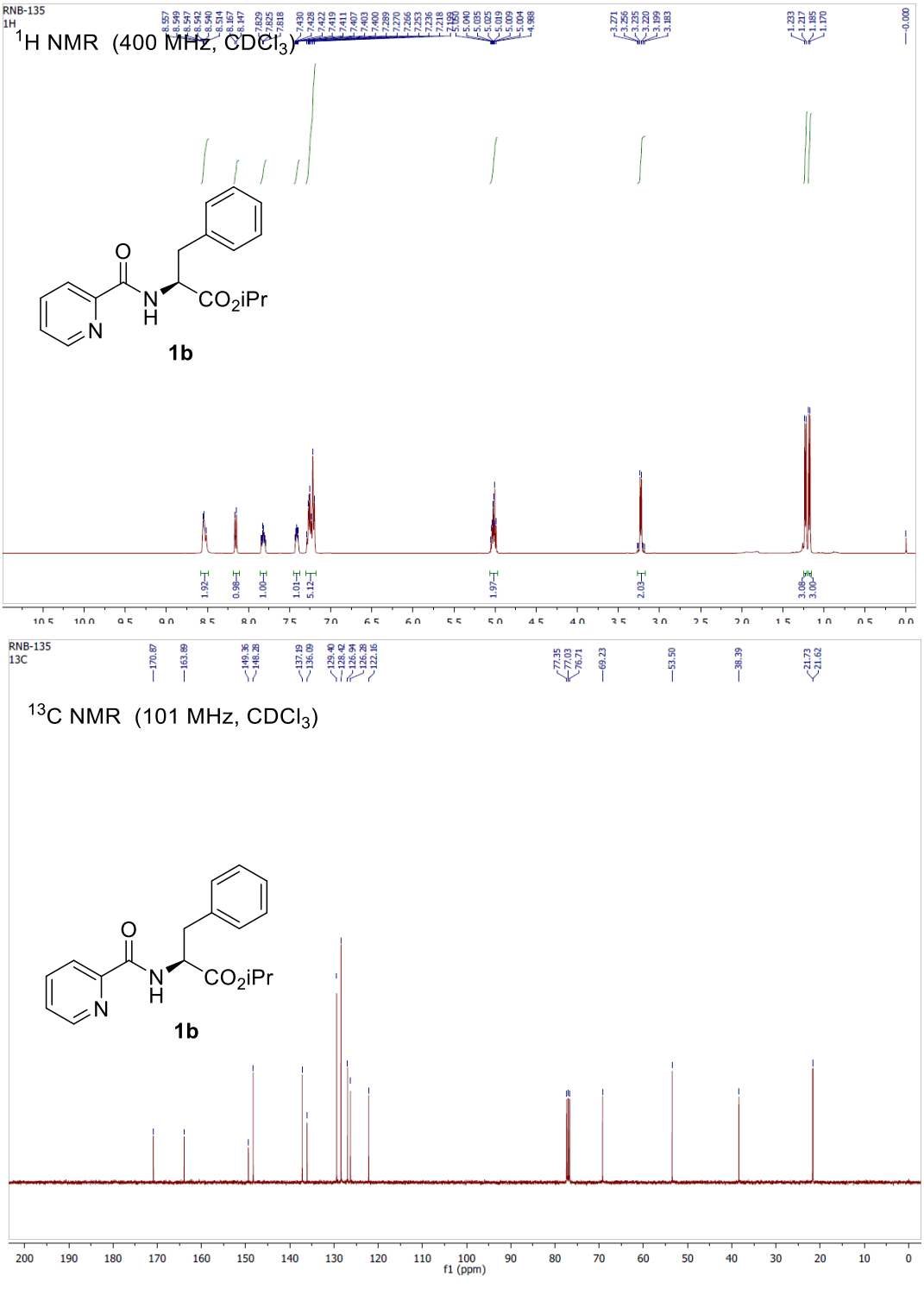


Fig S1. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1b**

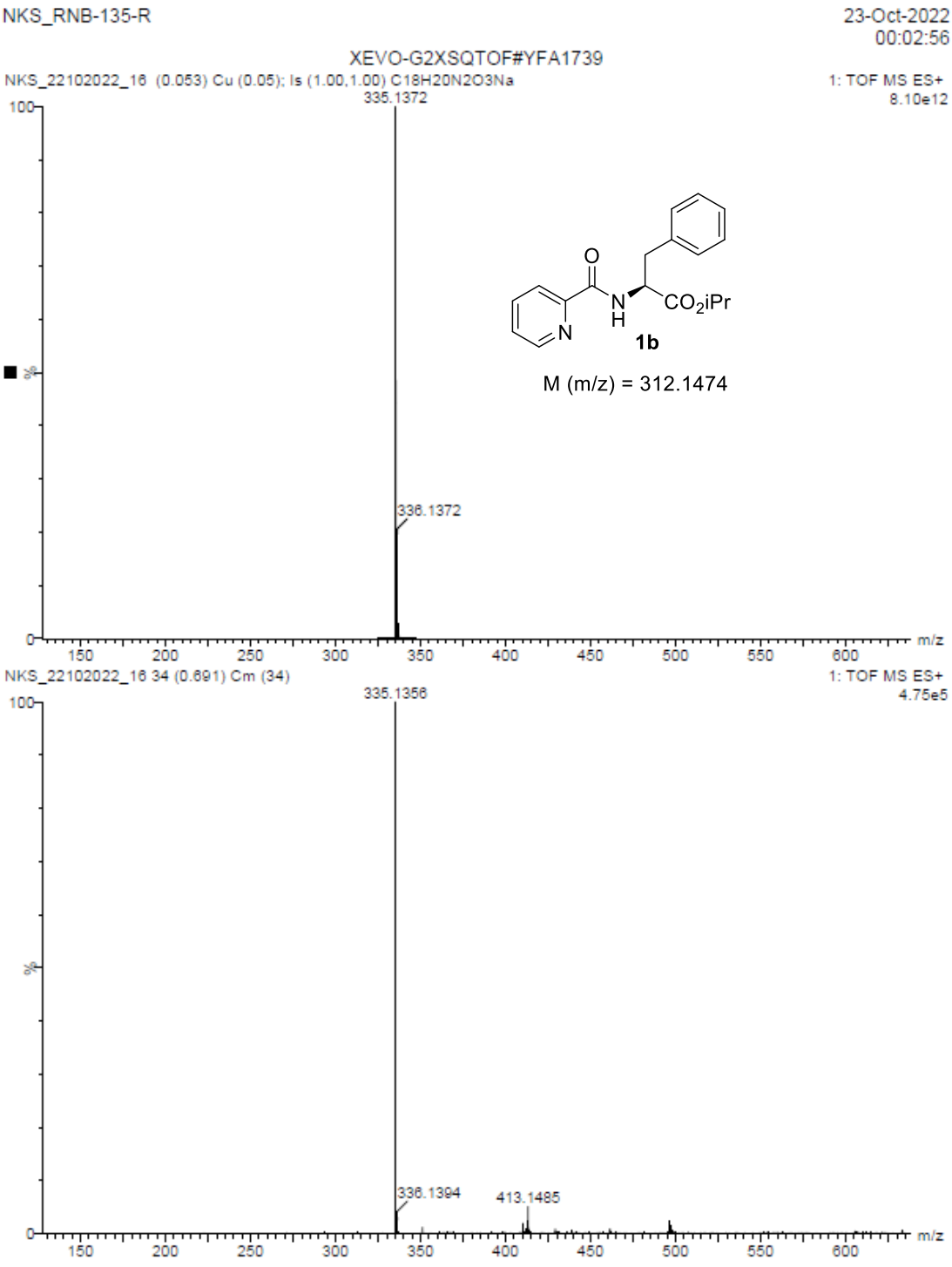


Fig S2. ESI-HRMS spectra of compound **1b**

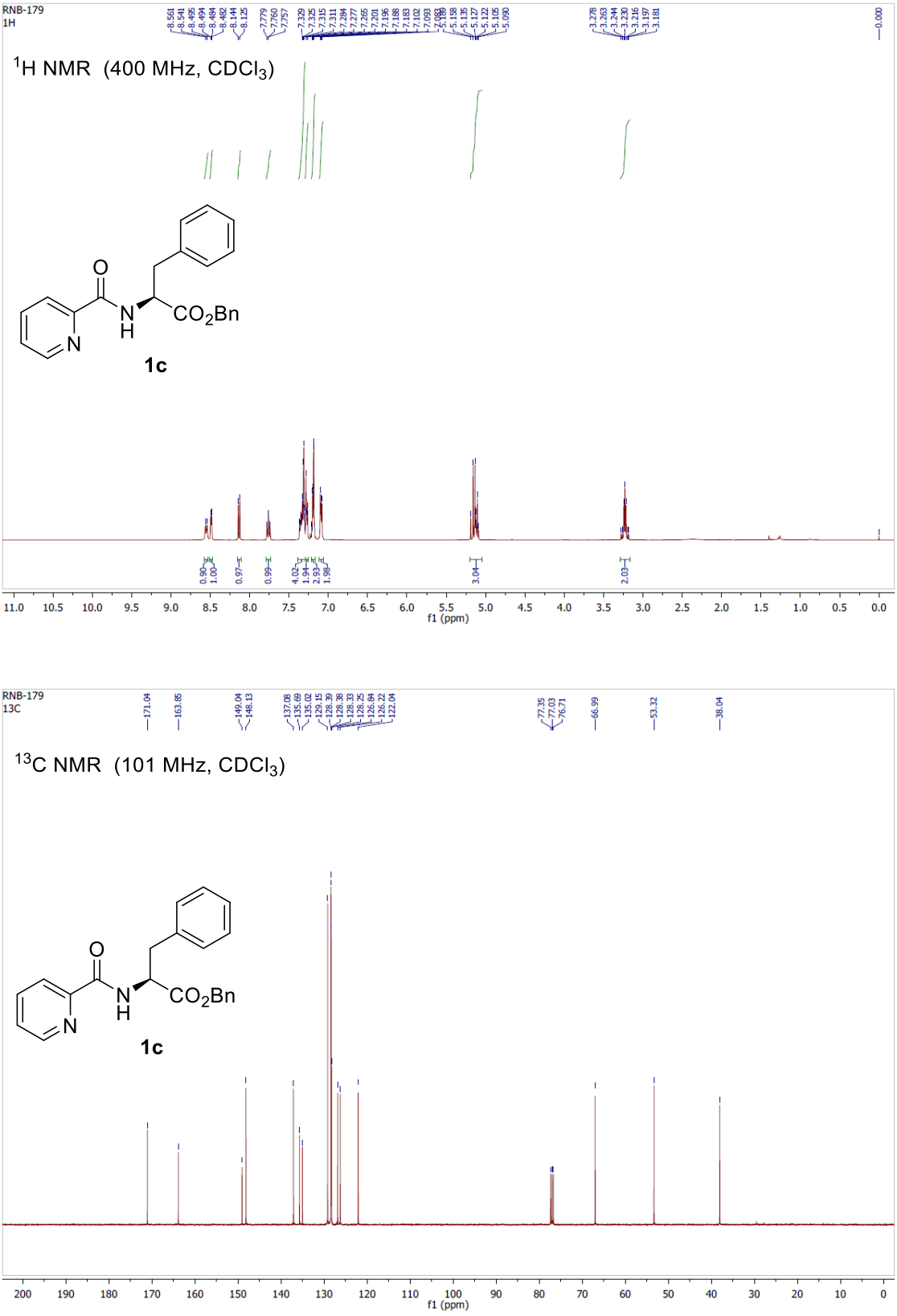


Fig S3. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1c**

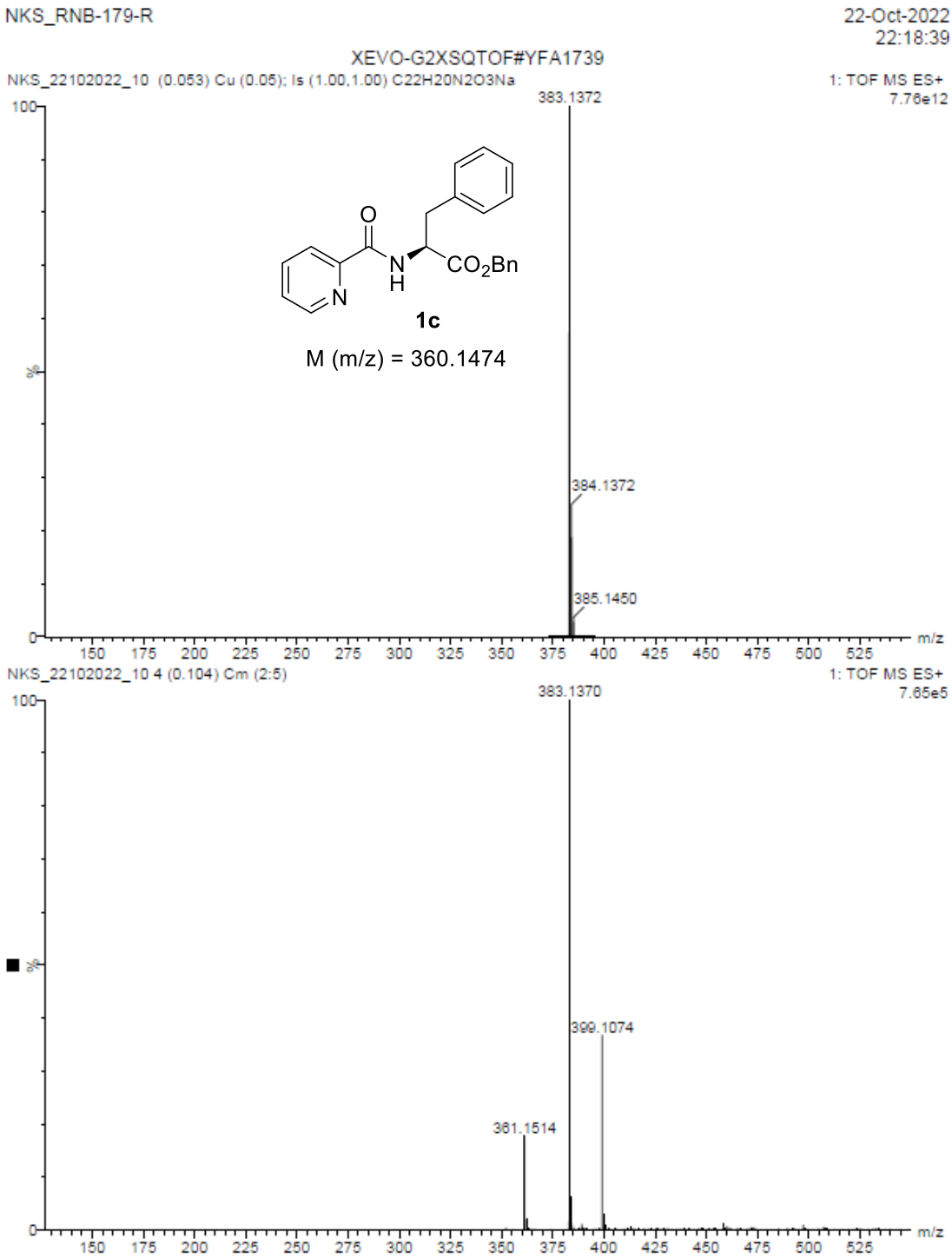


Fig S4. ESI-HRMS spectra of compound **1c**

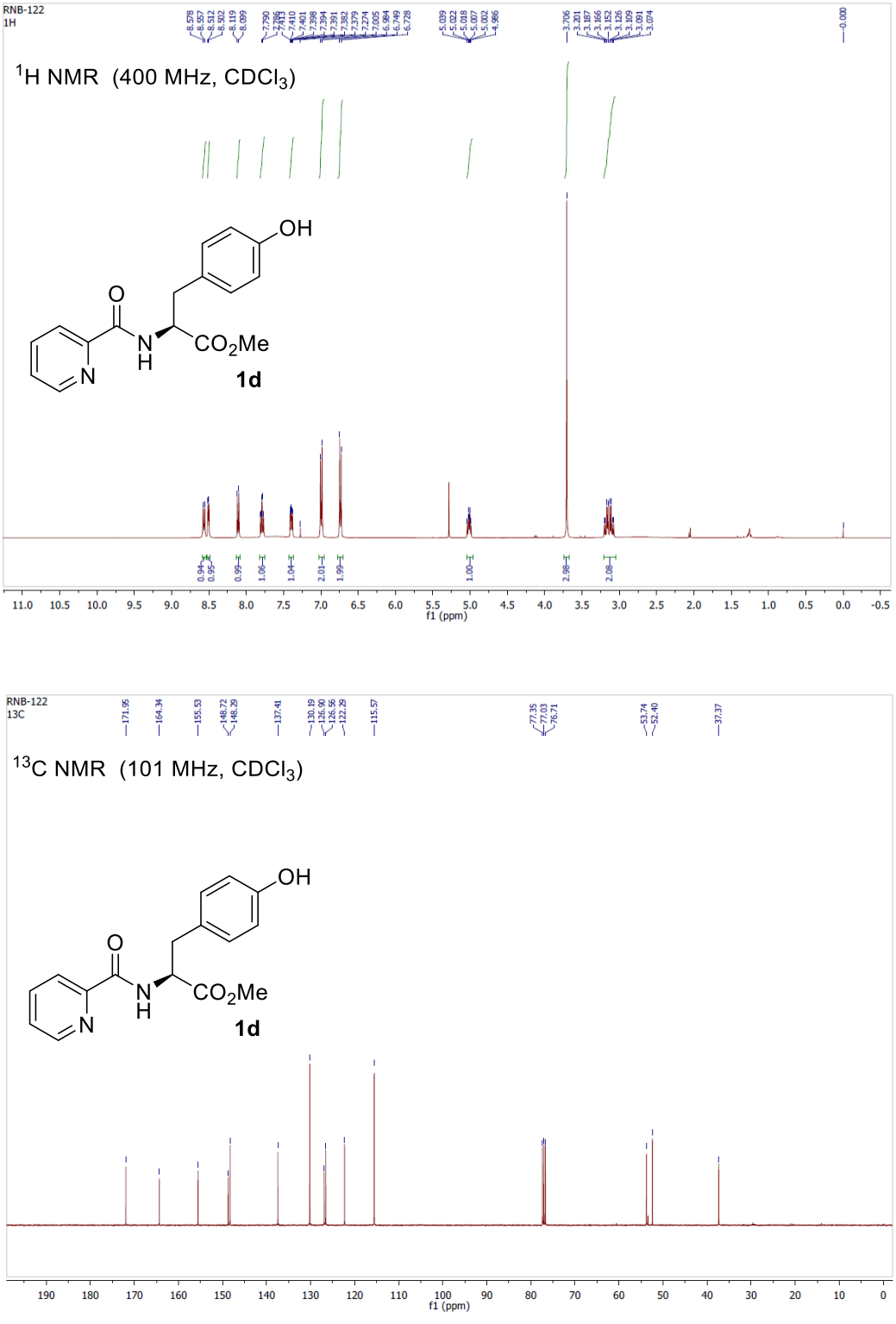


Fig S5. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1d**

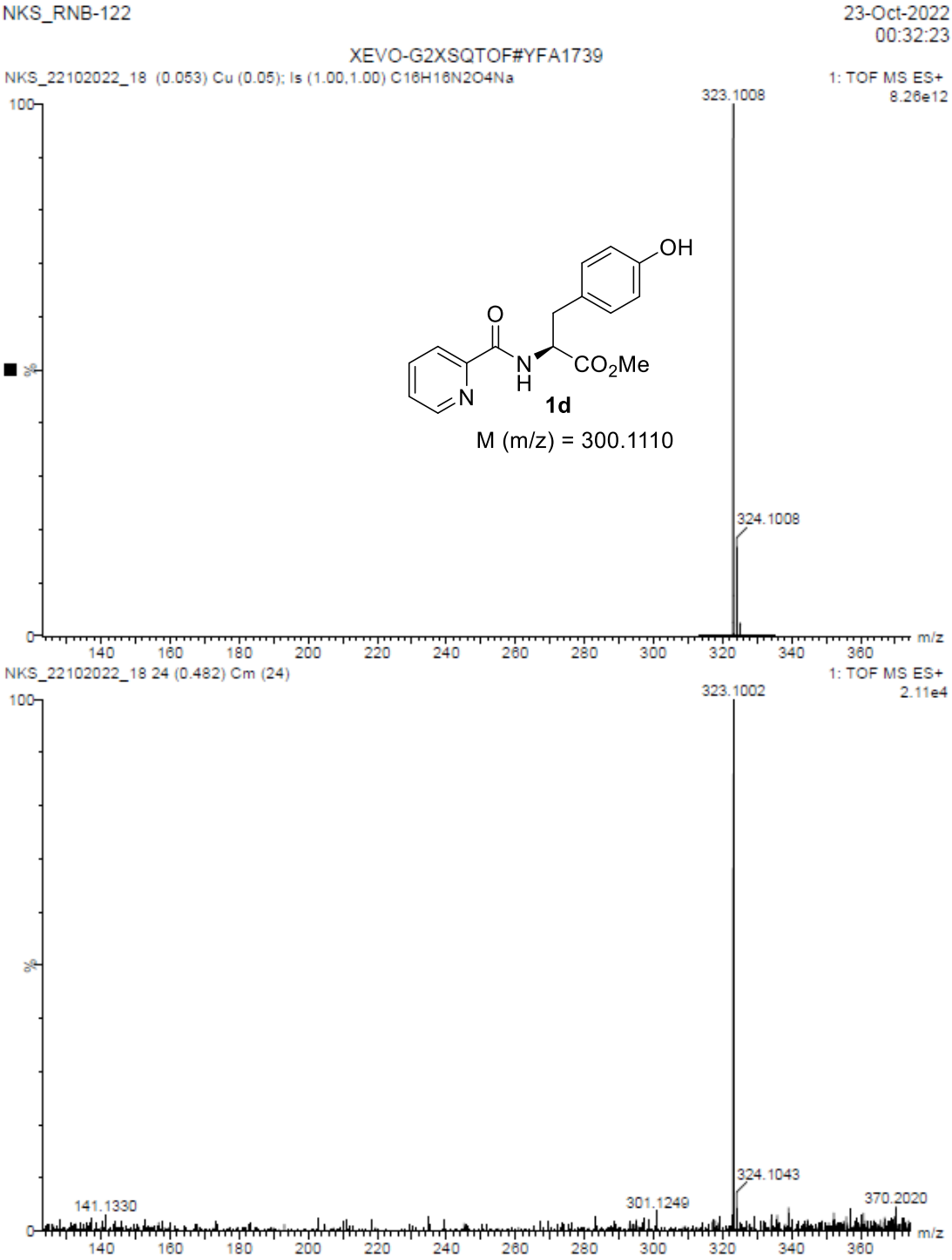


Fig S6. ESI-HRMS spectra of compound **1d**

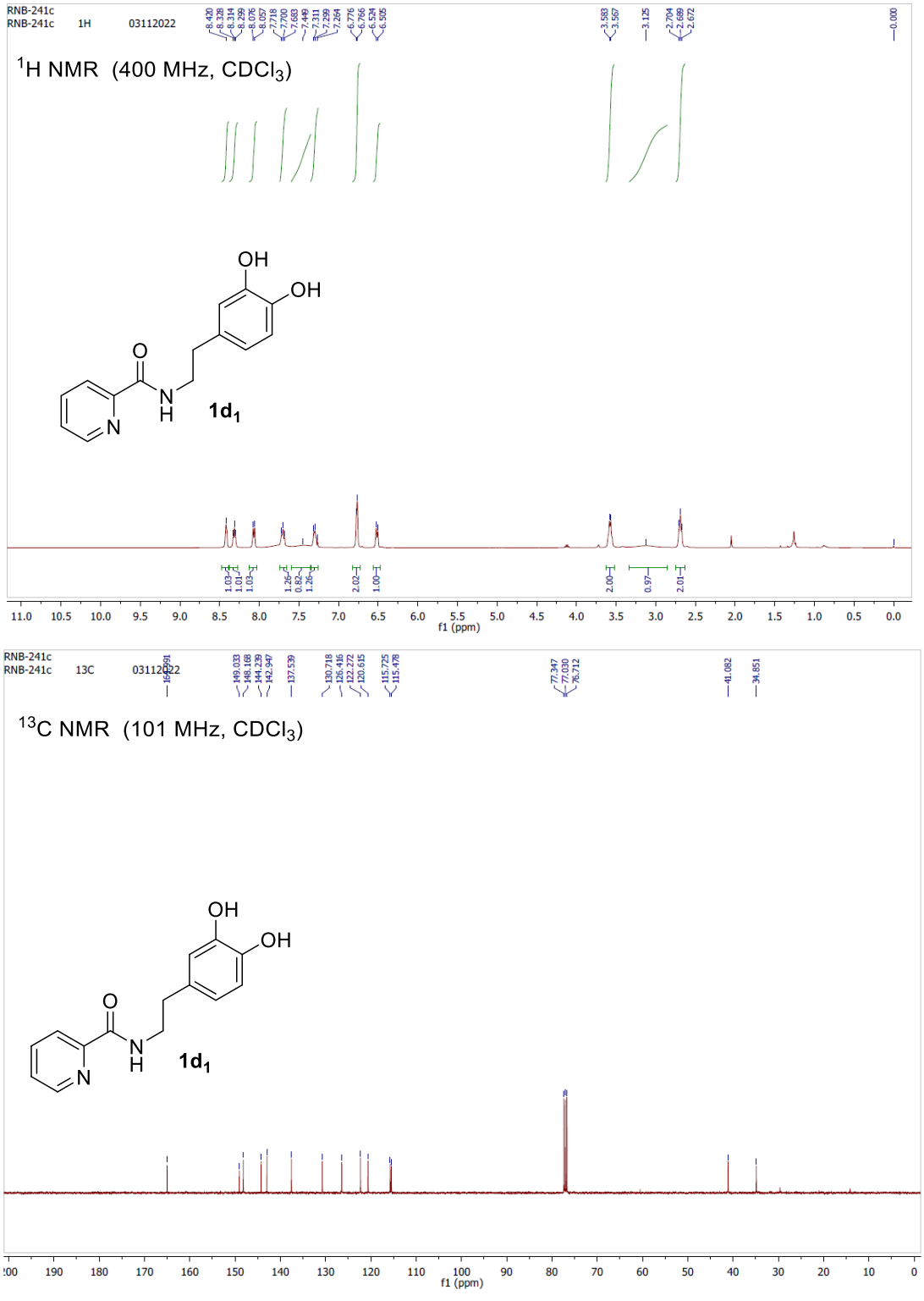


Fig S7. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1d$_1$**

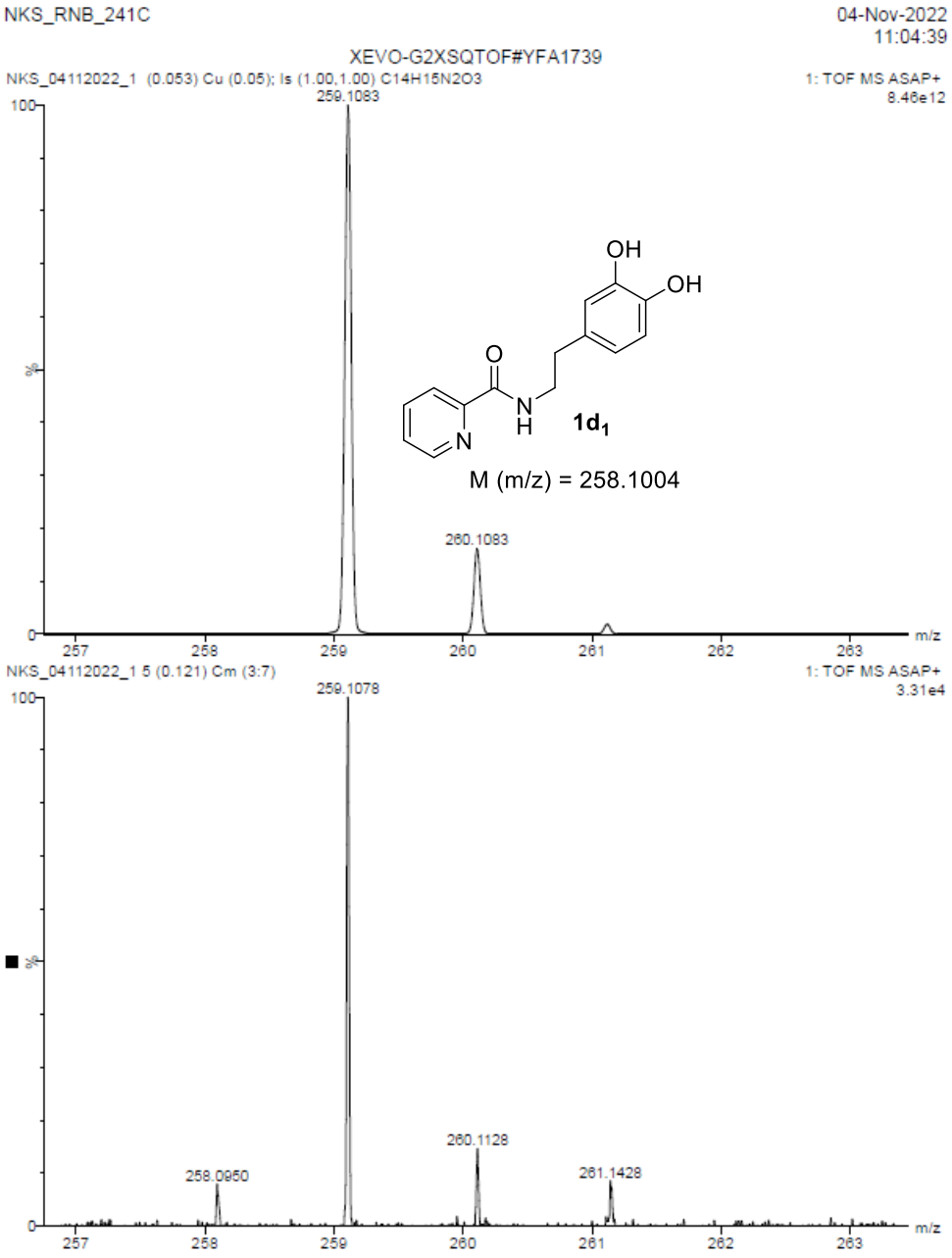
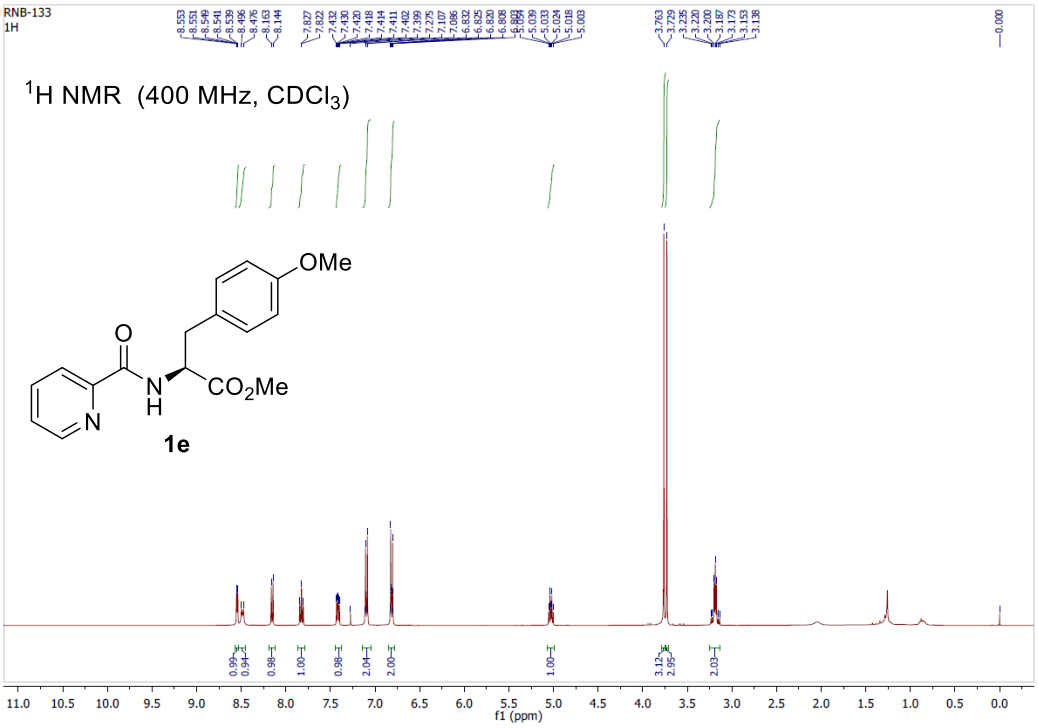


Fig S8. ASAP-HRMS spectra of compound **1d$_1$**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^{1}H NMR (400 MHz, $CDCl_3$)
OMe
O
N
H
CO_2Me
N
1e
f1 (ppm)

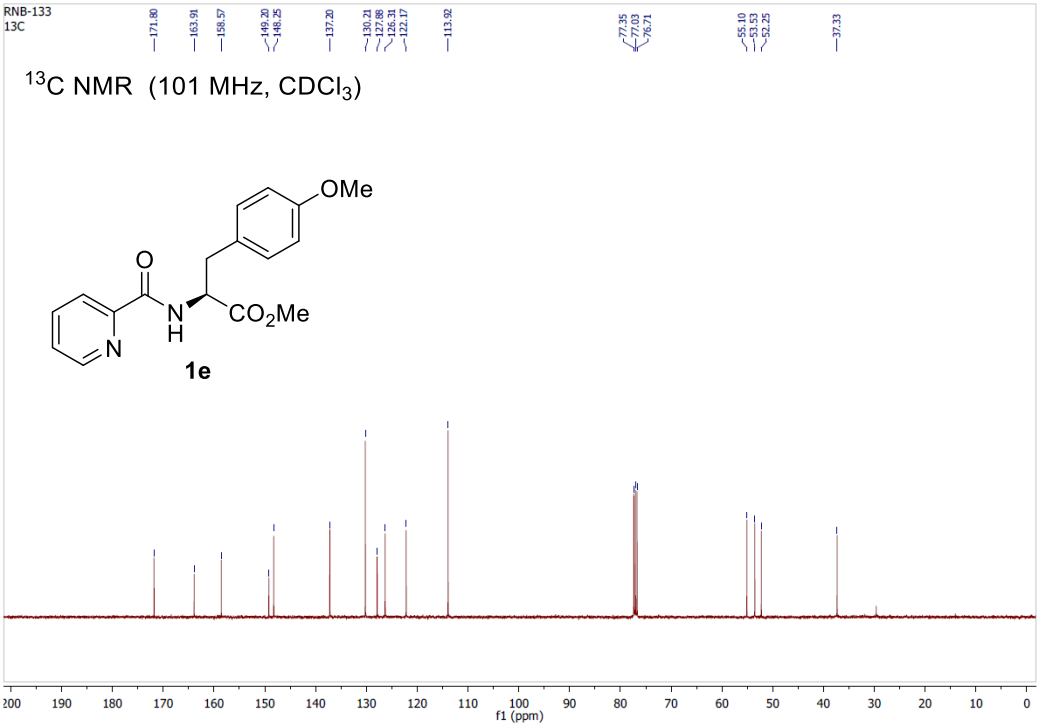

RNB-133
13C
^{13}C NMR (101 MHz, $CDCl_3$)
OMe
O
N
H
CO_2Me
N
1e
f1 (ppm)

Fig S9. ^{1}H, ^{13}C $\{^{1}H\}$ NMR spectra of compound **1e**

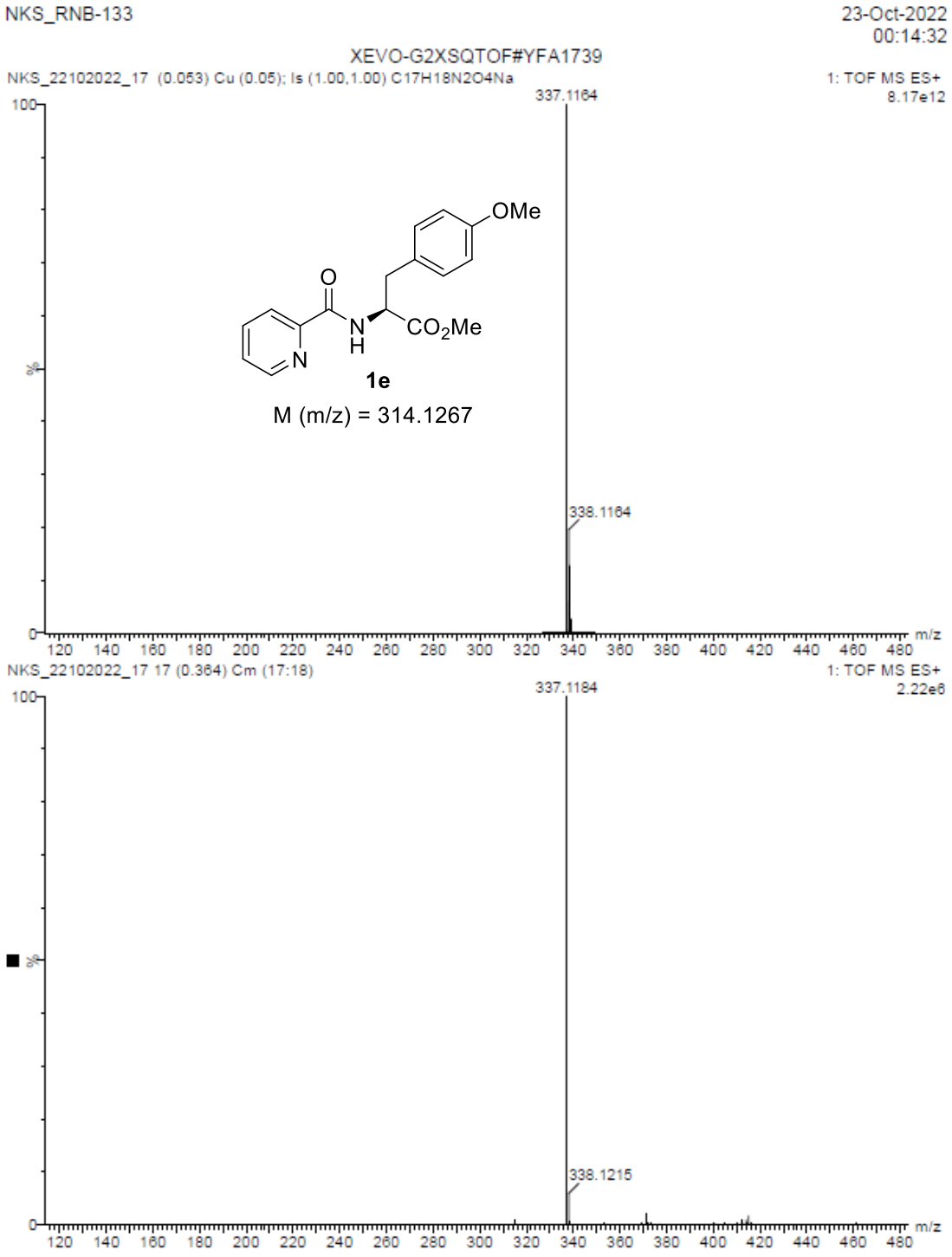
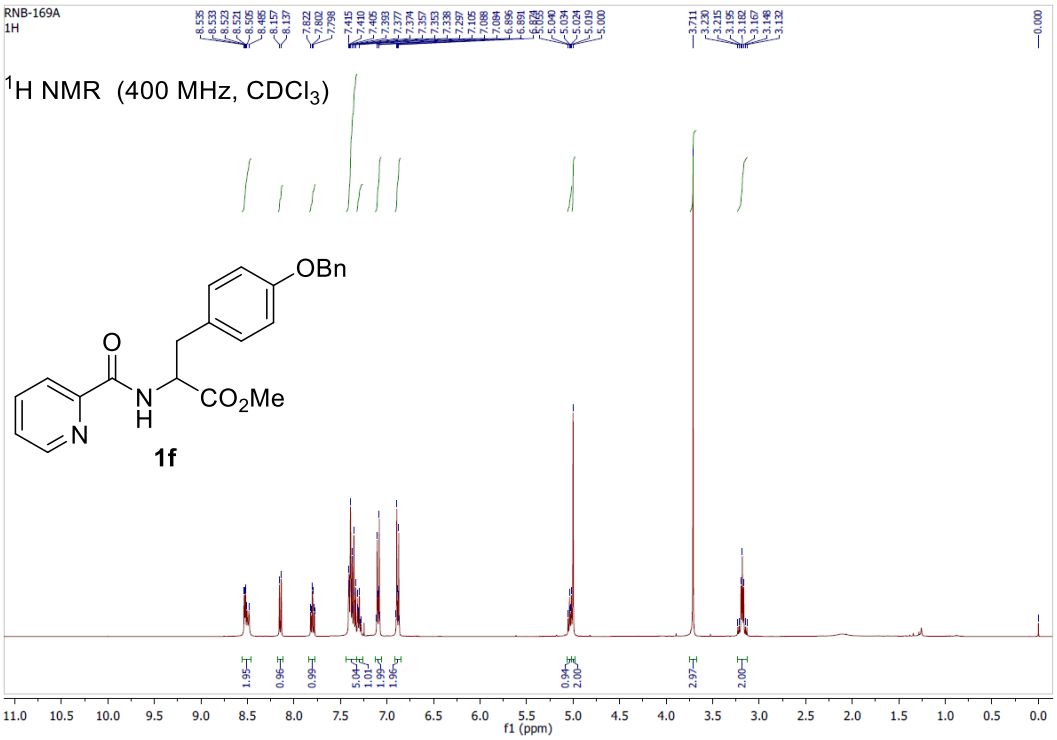


Fig S10. ESI-HRMS spectra of compound **1e**



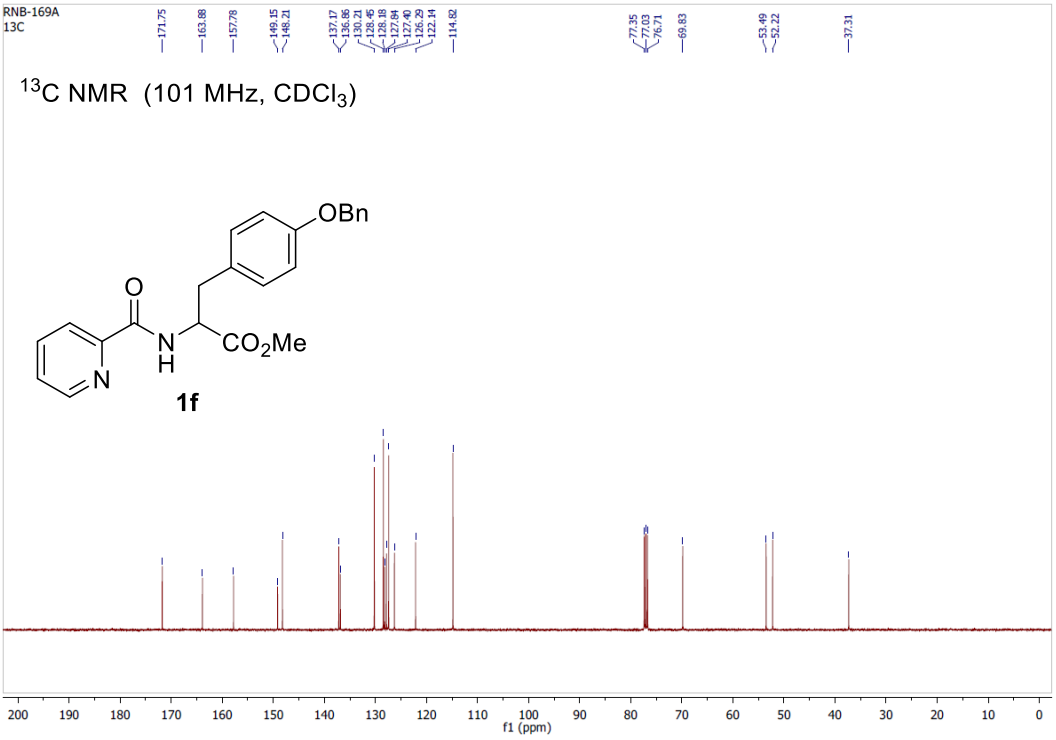


Fig S11. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1f**

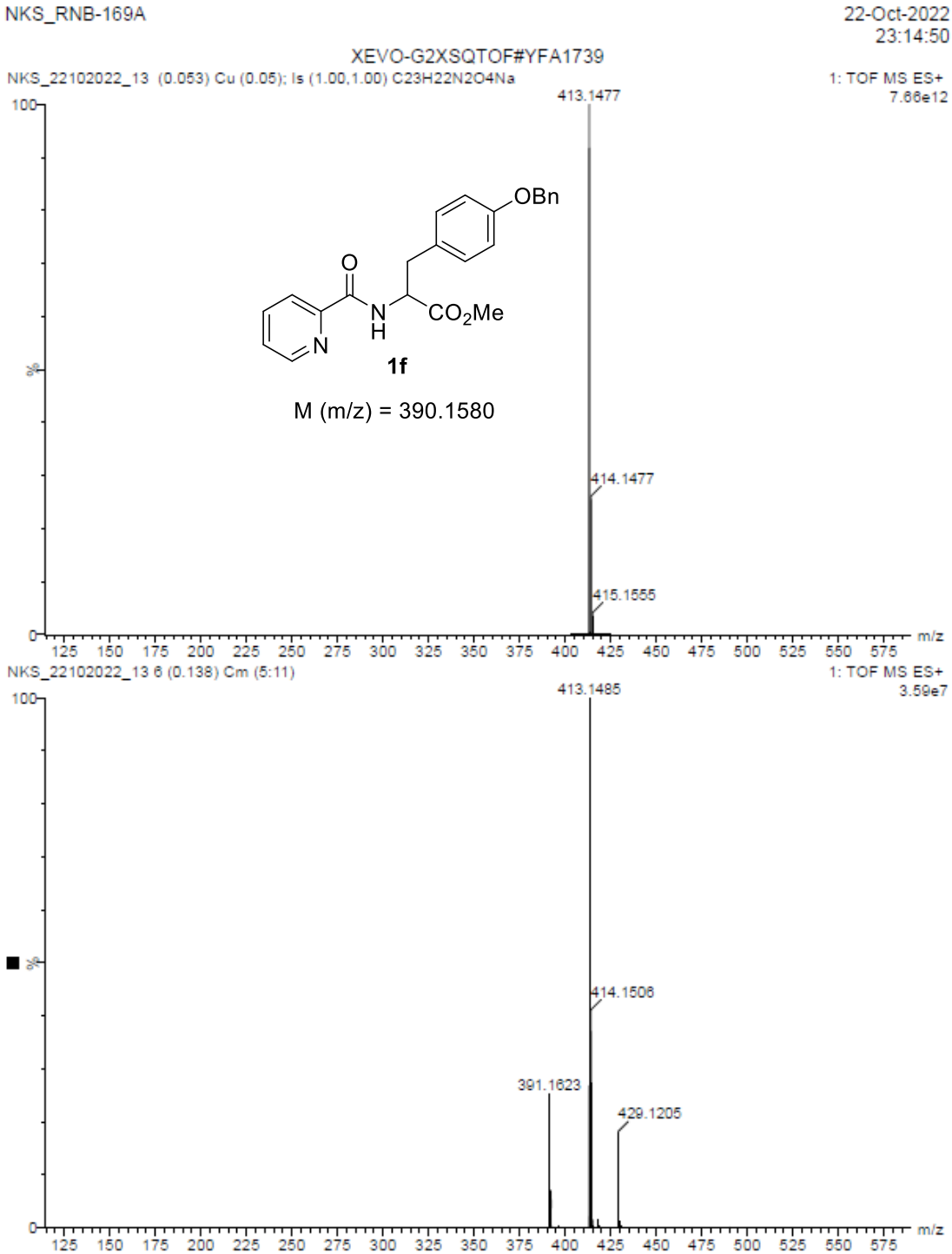
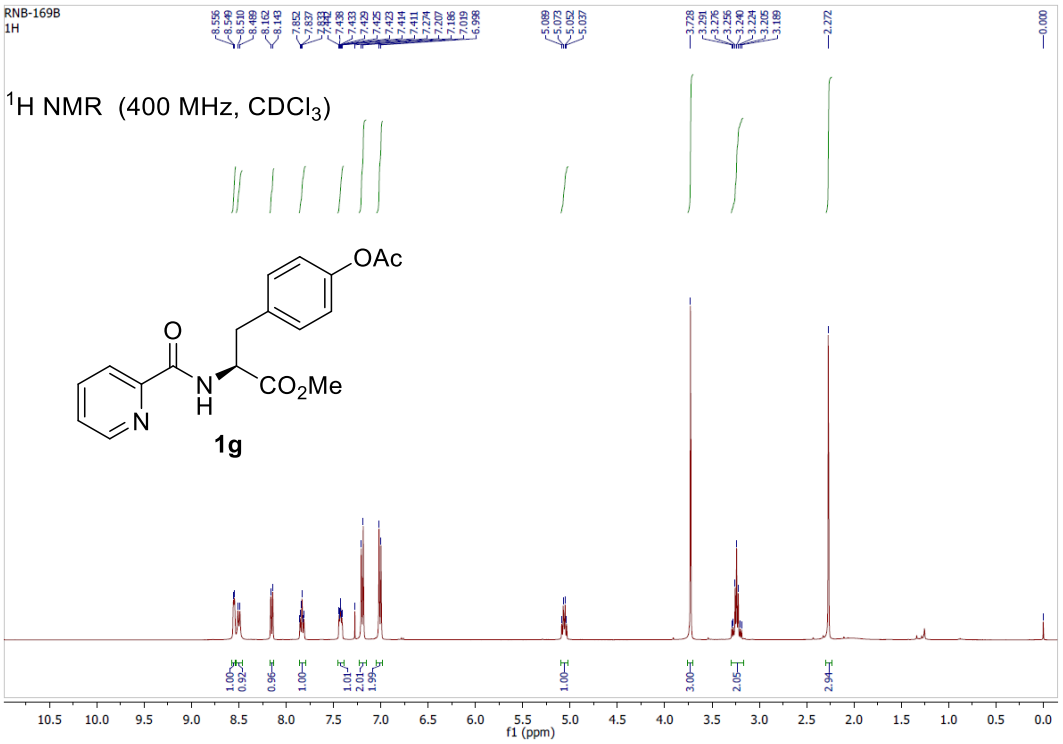


Fig S12. ESI-HRMS spectra of compound **1f**



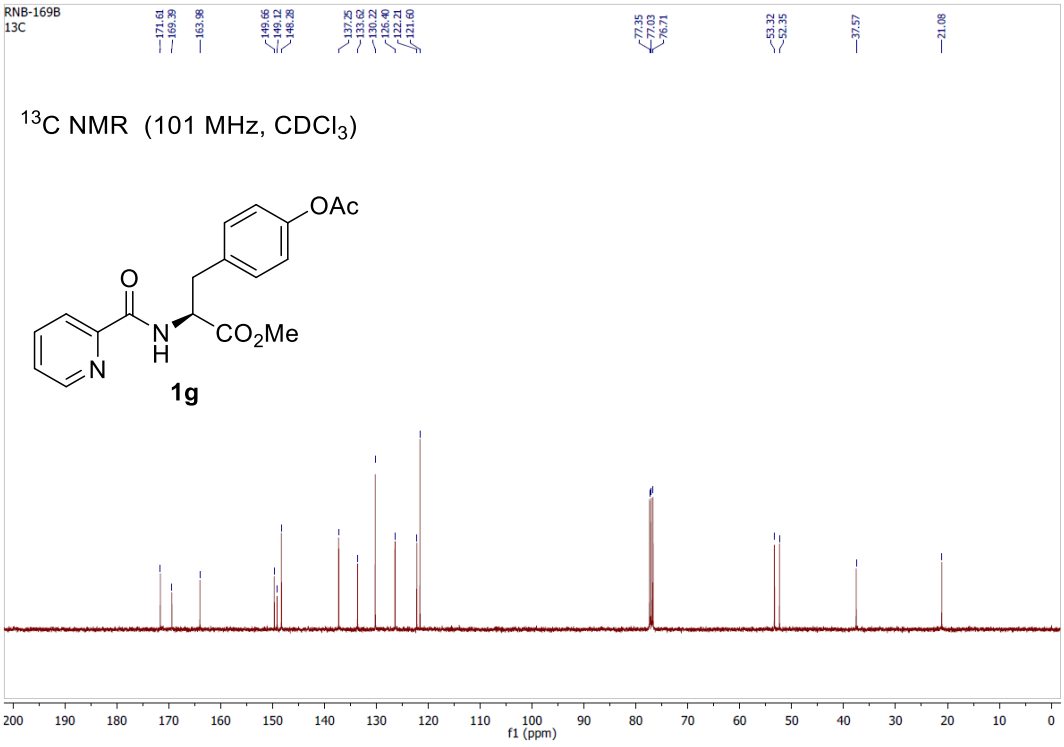


Fig S13. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1g**

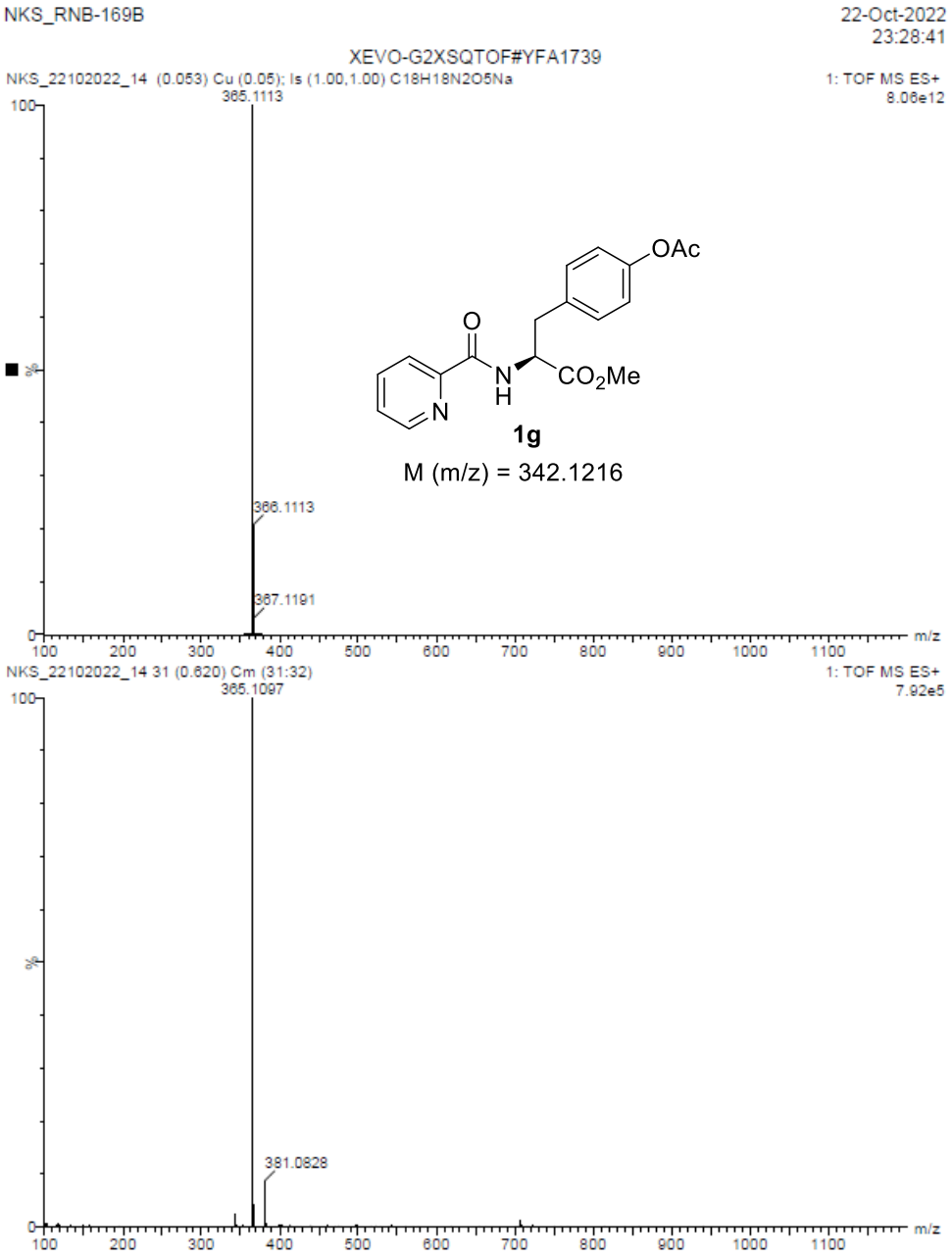
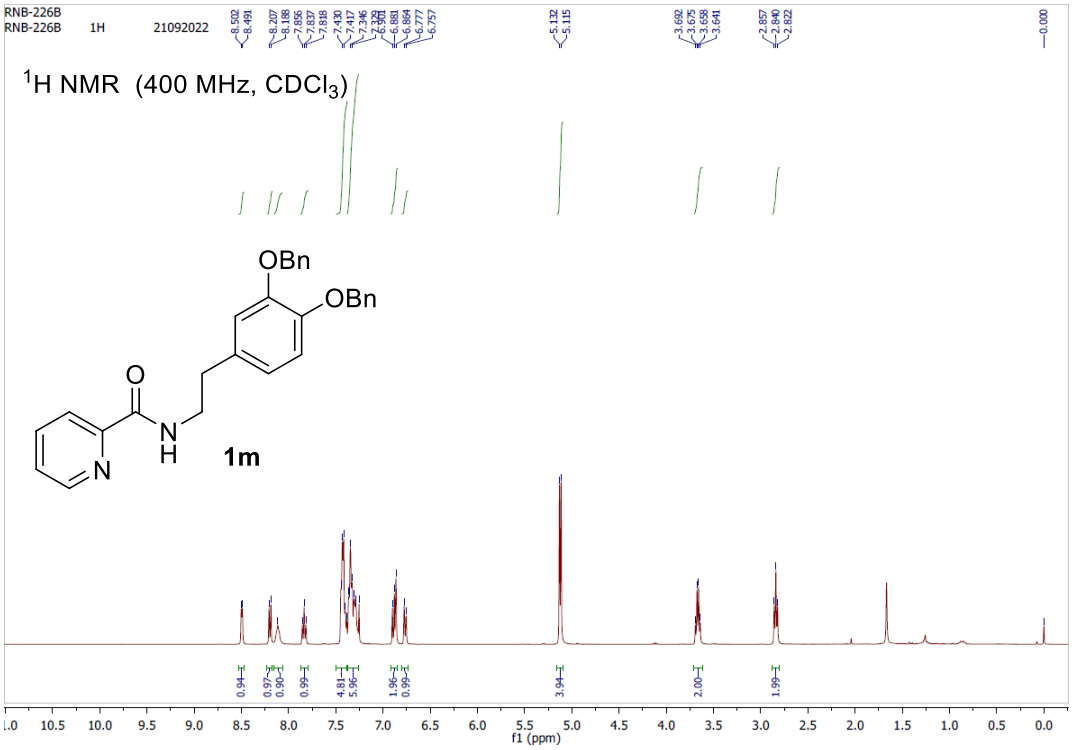


Fig S14. ESI-HRMS spectra of compound **1g**



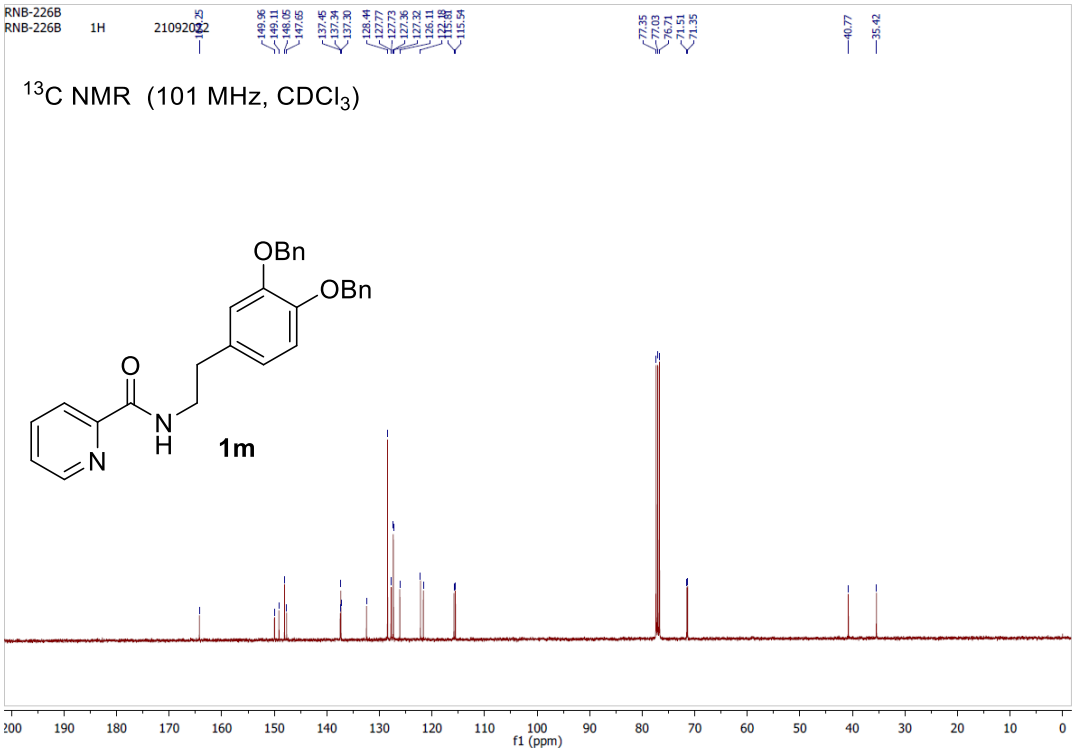


Fig S15. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1m**

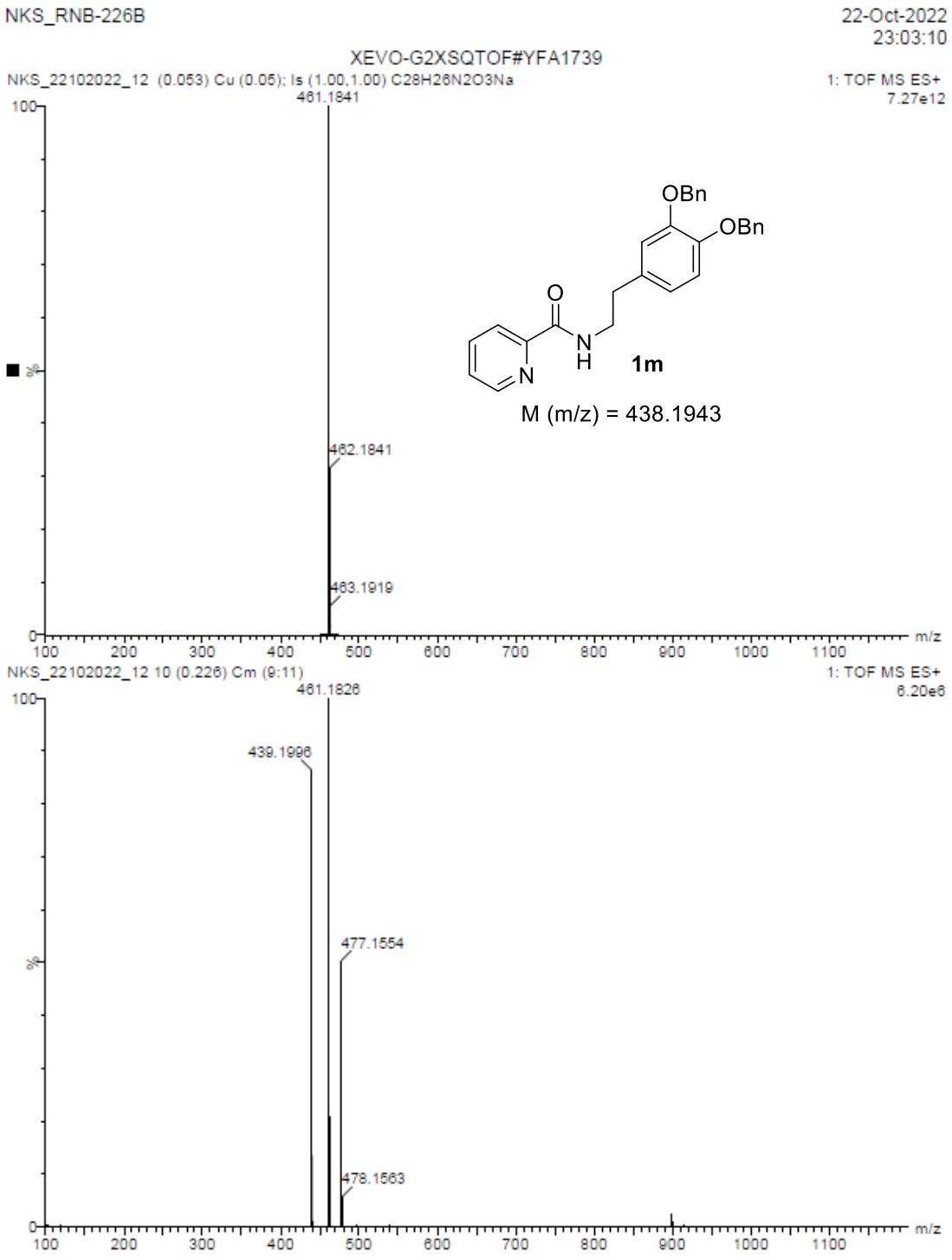
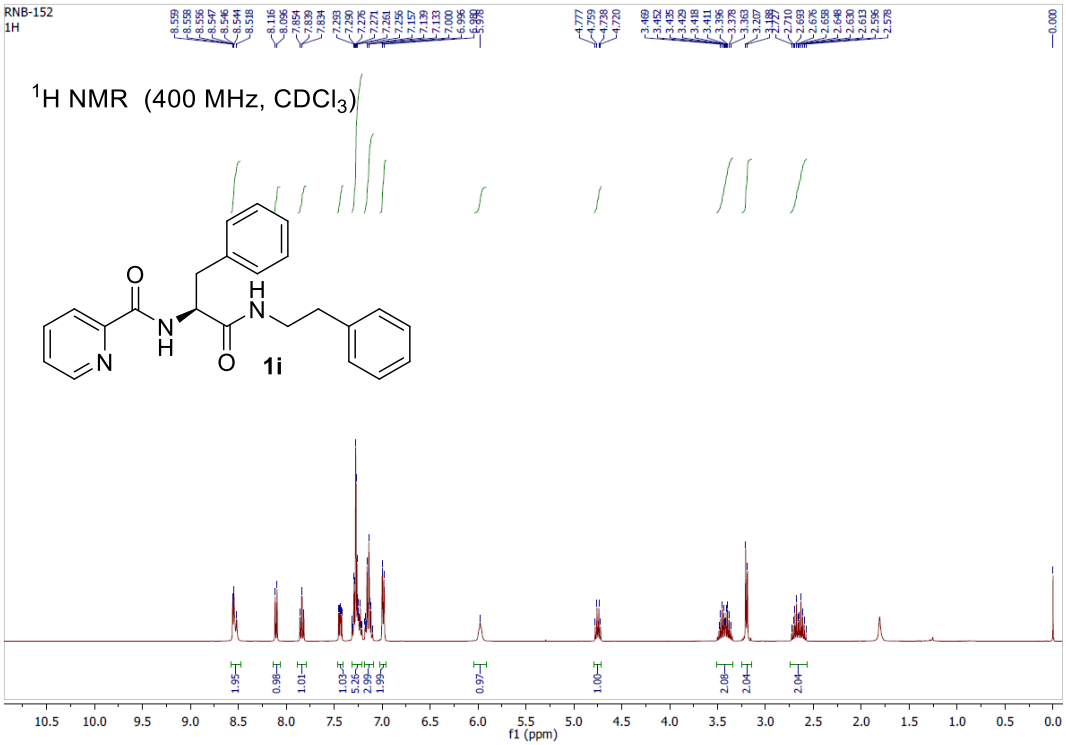


Fig S16. ESI-HRMS spectra of compound **1m**



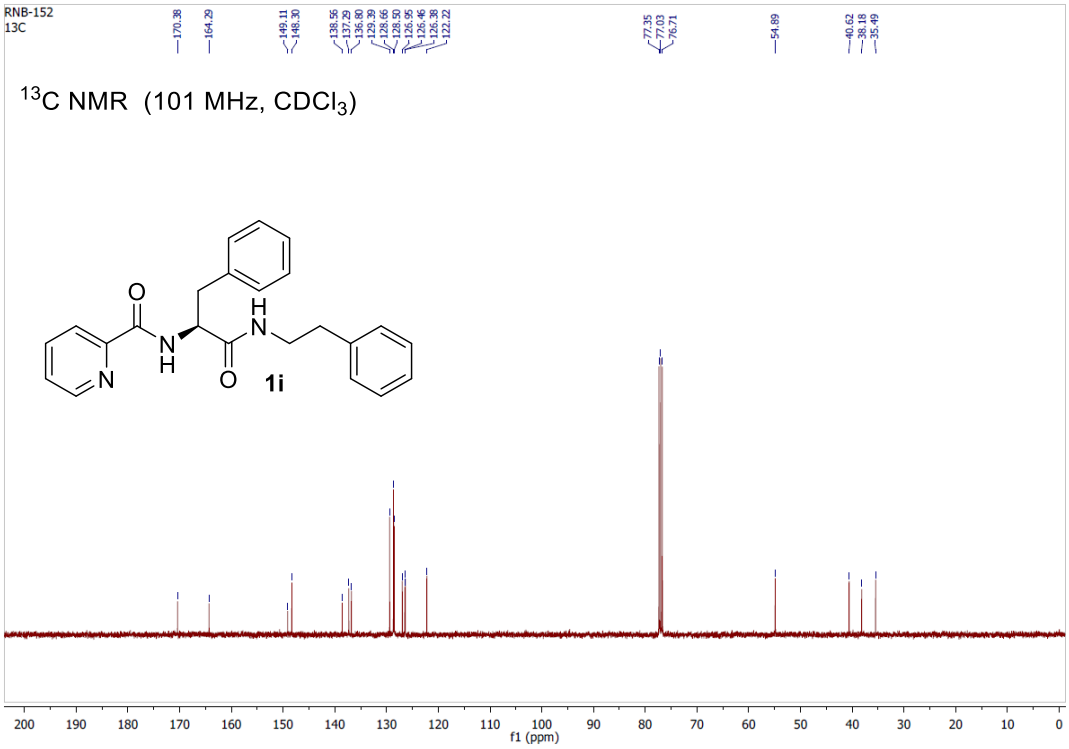


Fig S17. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1i**

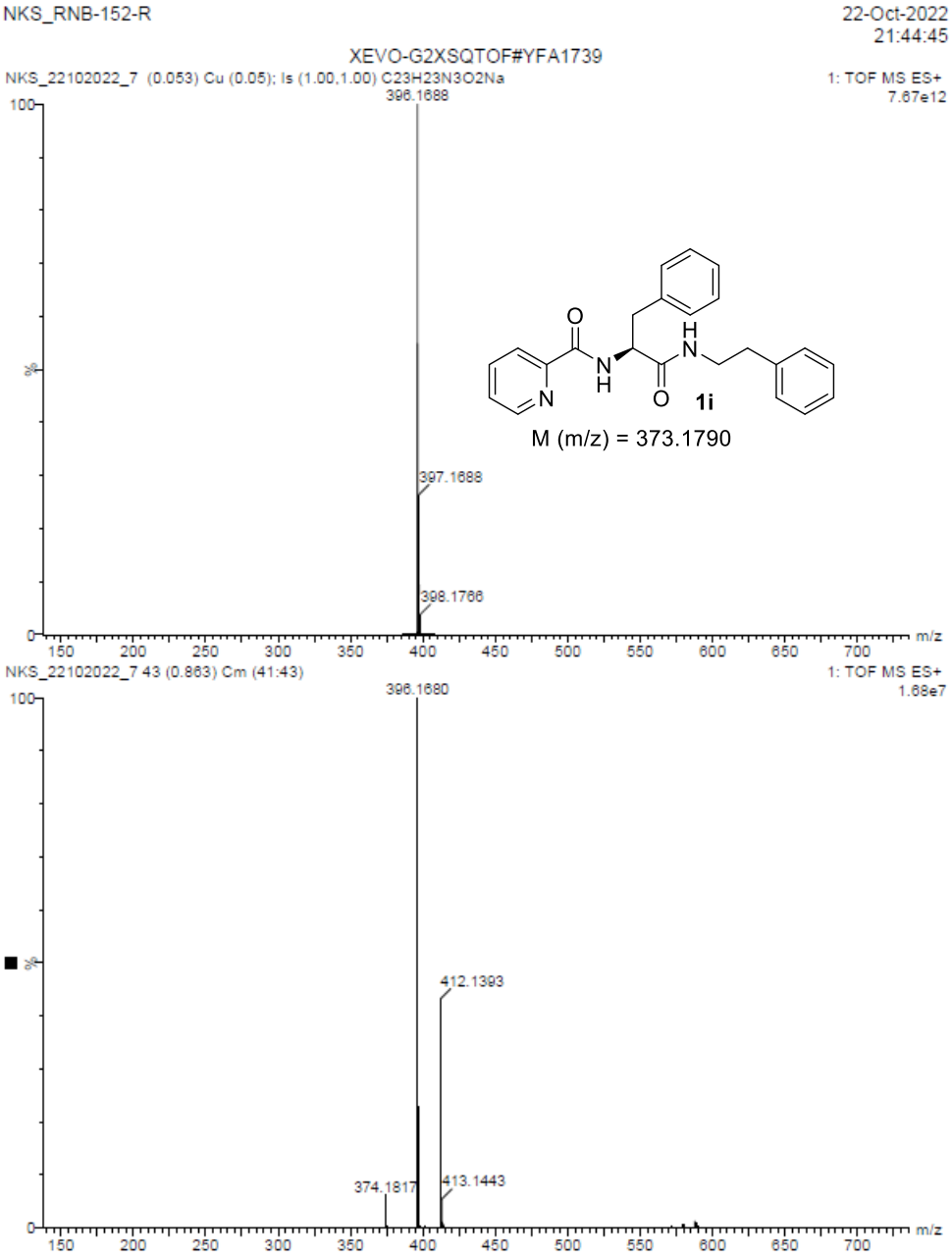
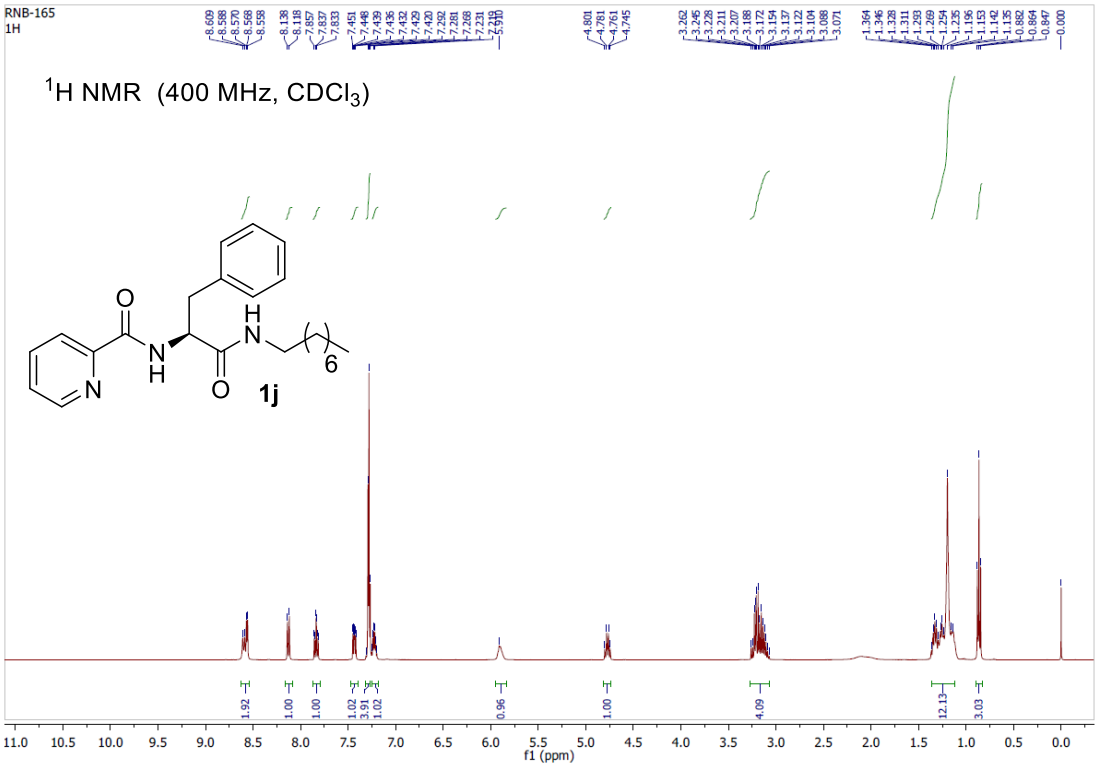


Fig S18. ESI-HRMS spectra of compound **1i**



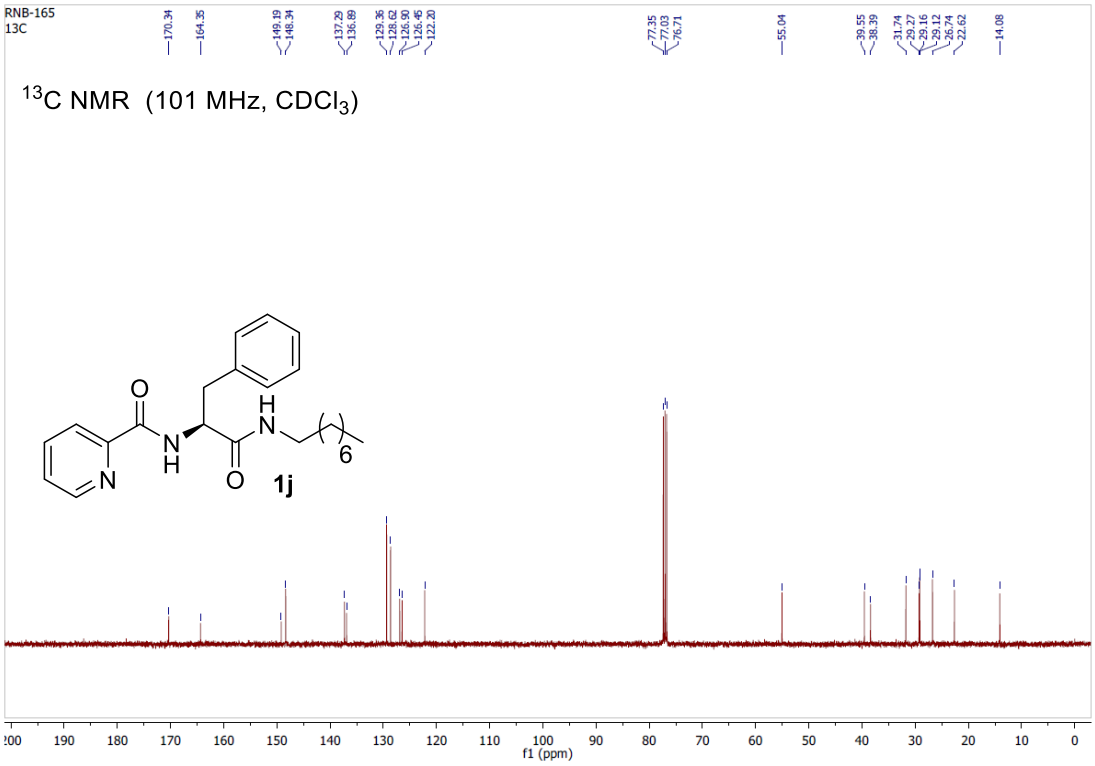


Fig S19. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **1j**

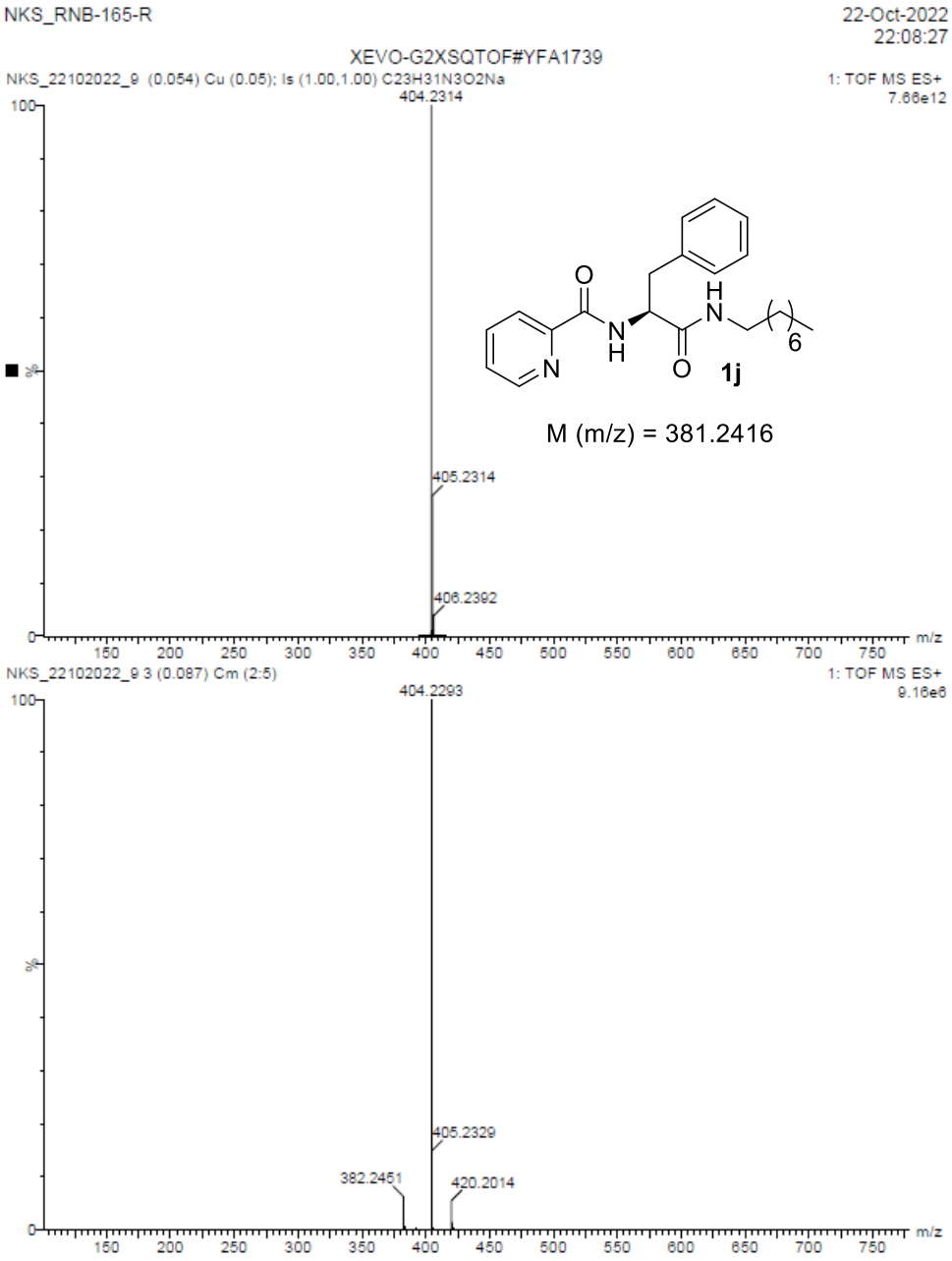
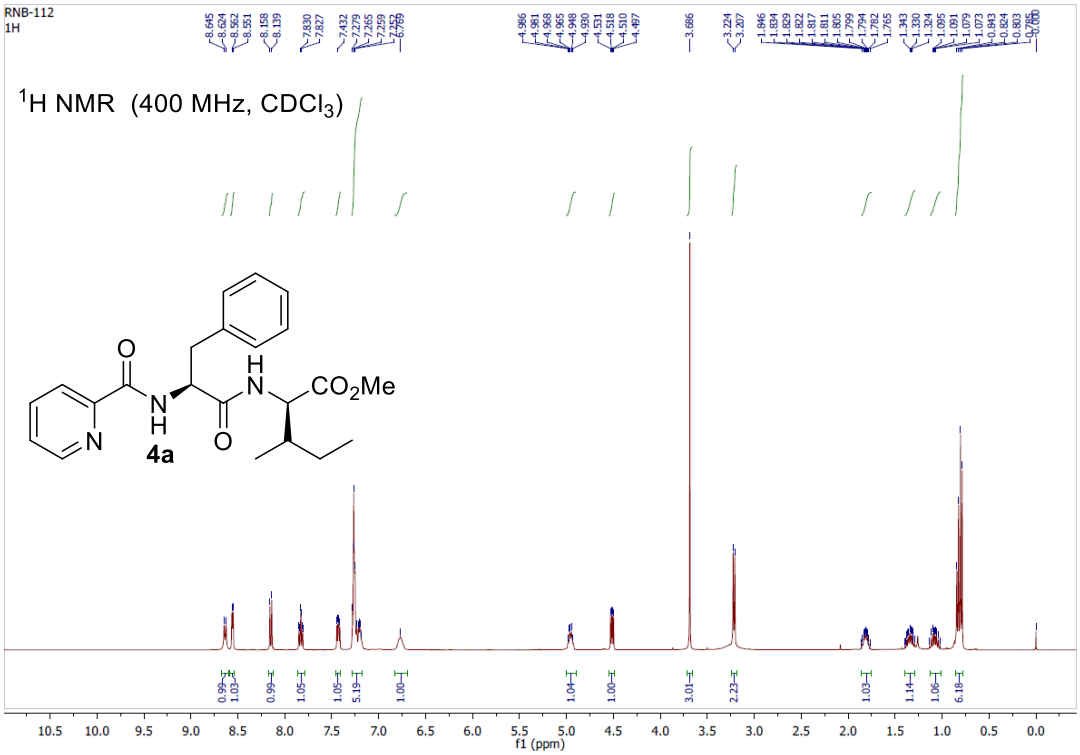


Fig S20. ESI-HRMS spectra of compound **1j**



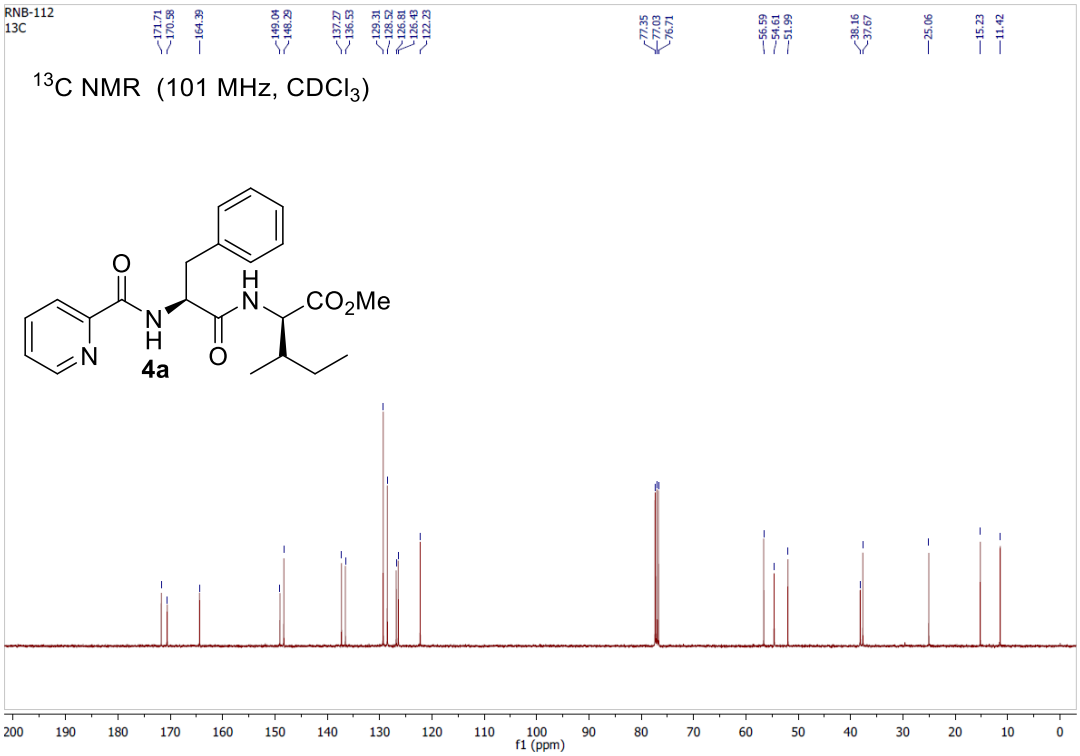


Fig S21. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4a**

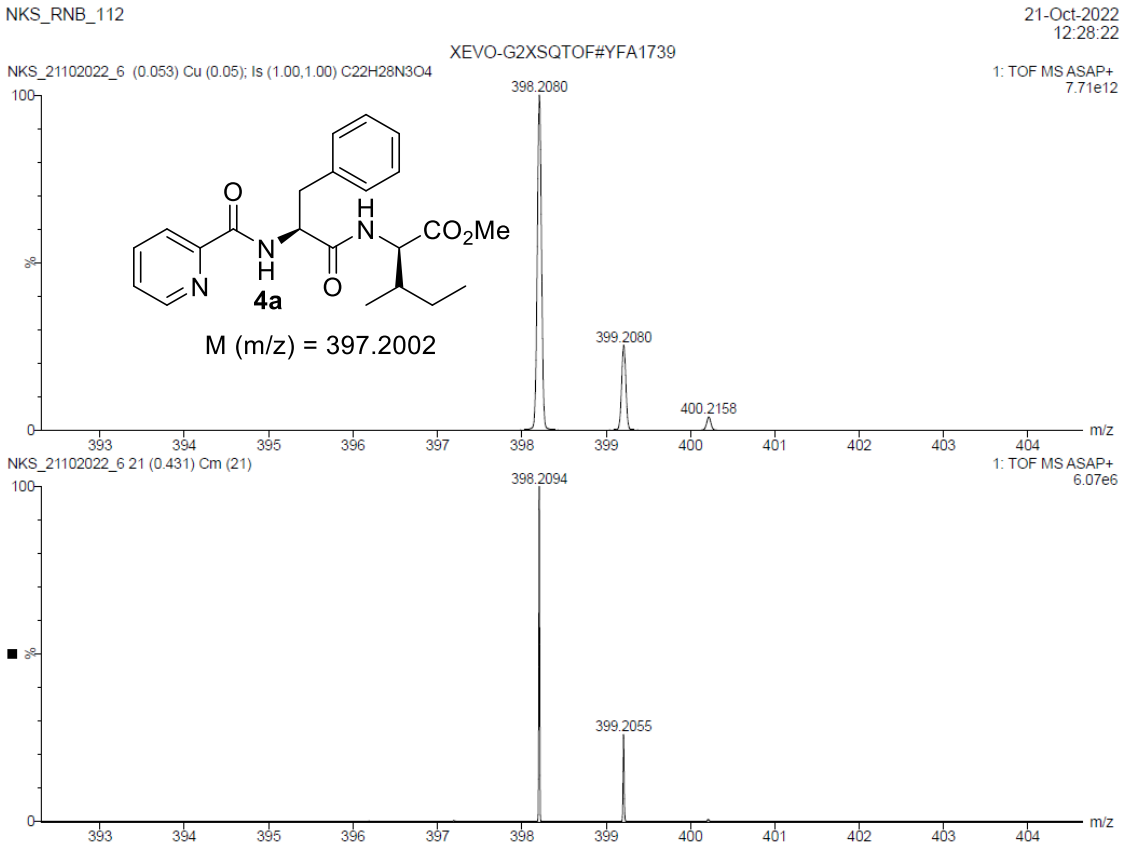
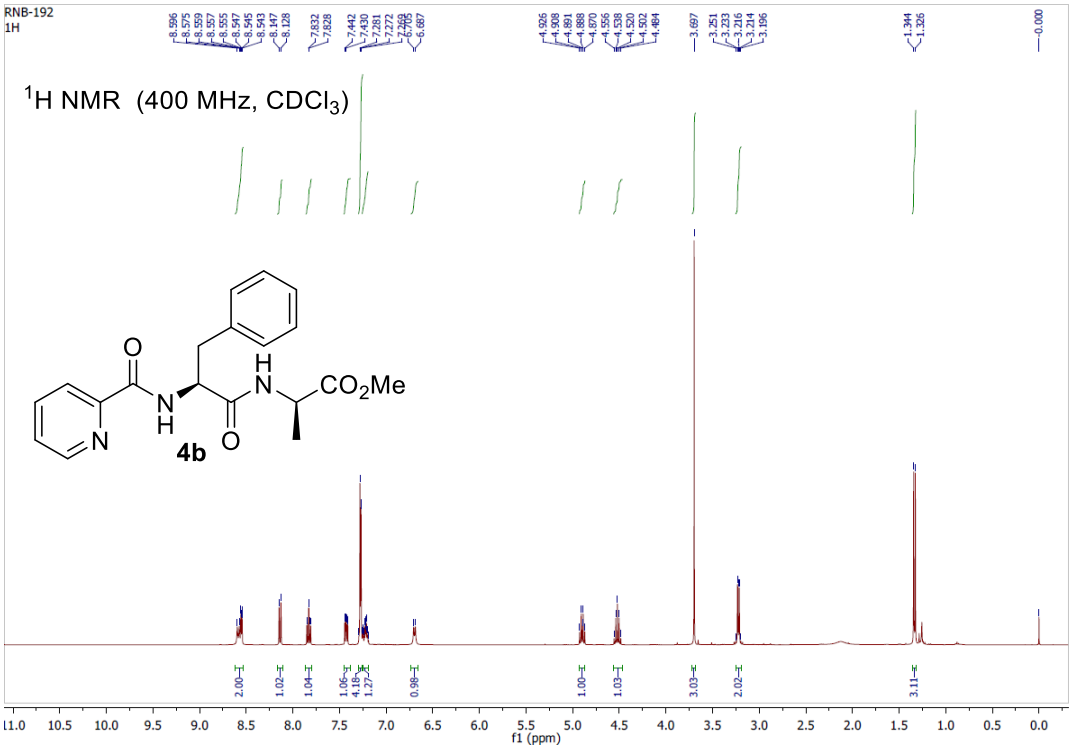


Fig S22. ASAP-HRMS spectra of compound **4a**



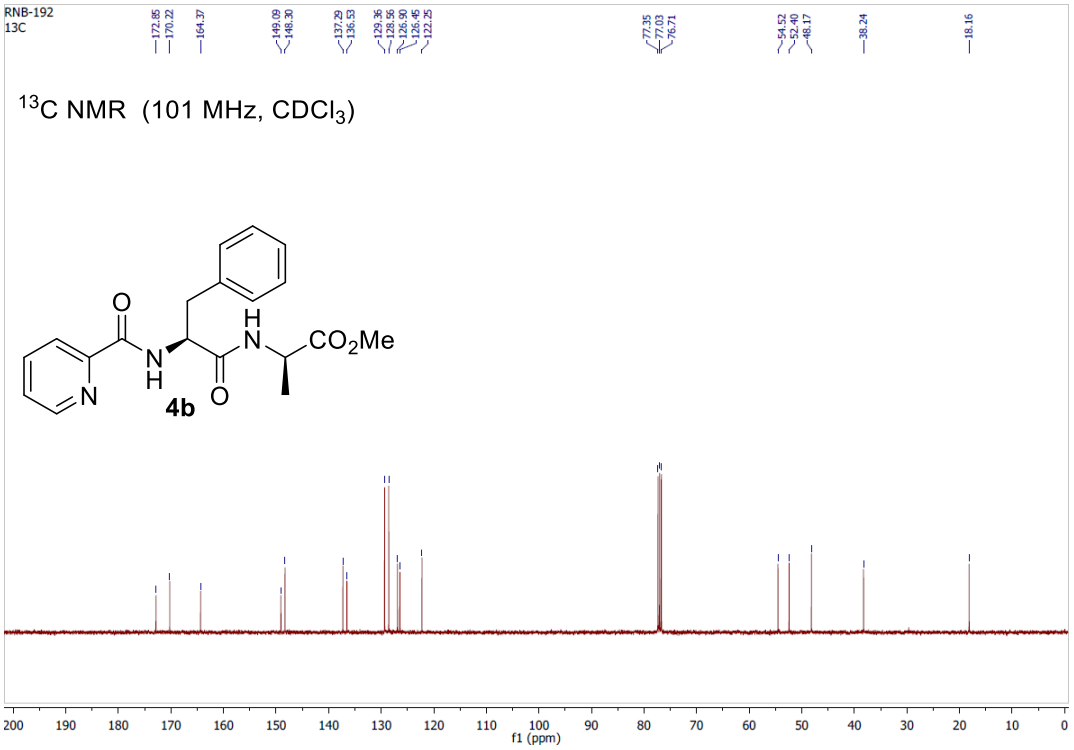


Fig S23. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4b**

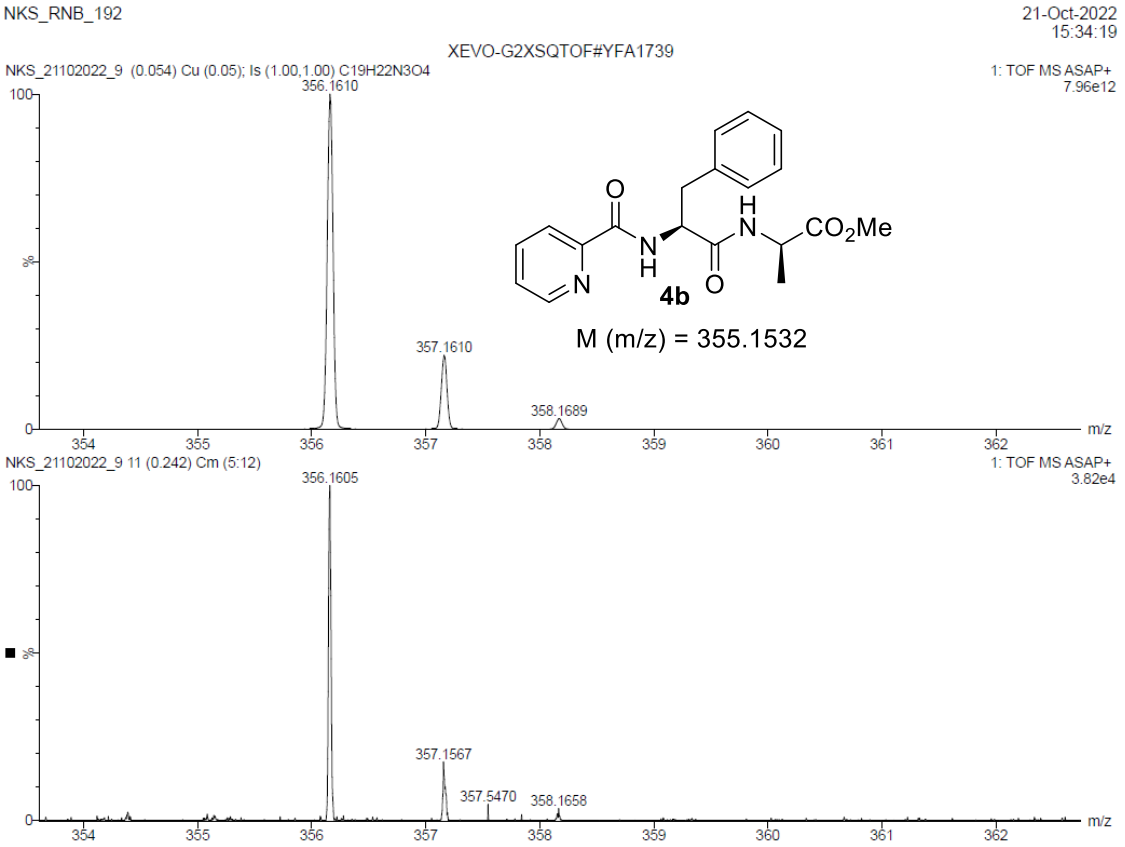
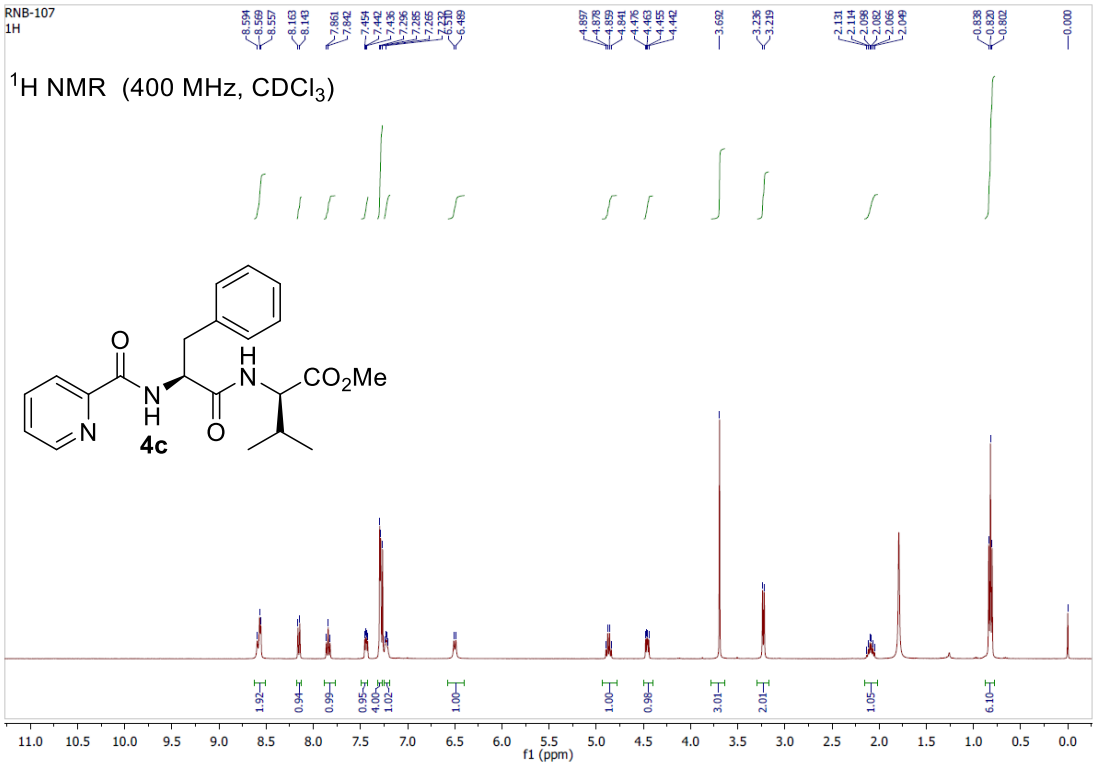


Fig S24. ASAP-HRMS spectra of compound **4b**



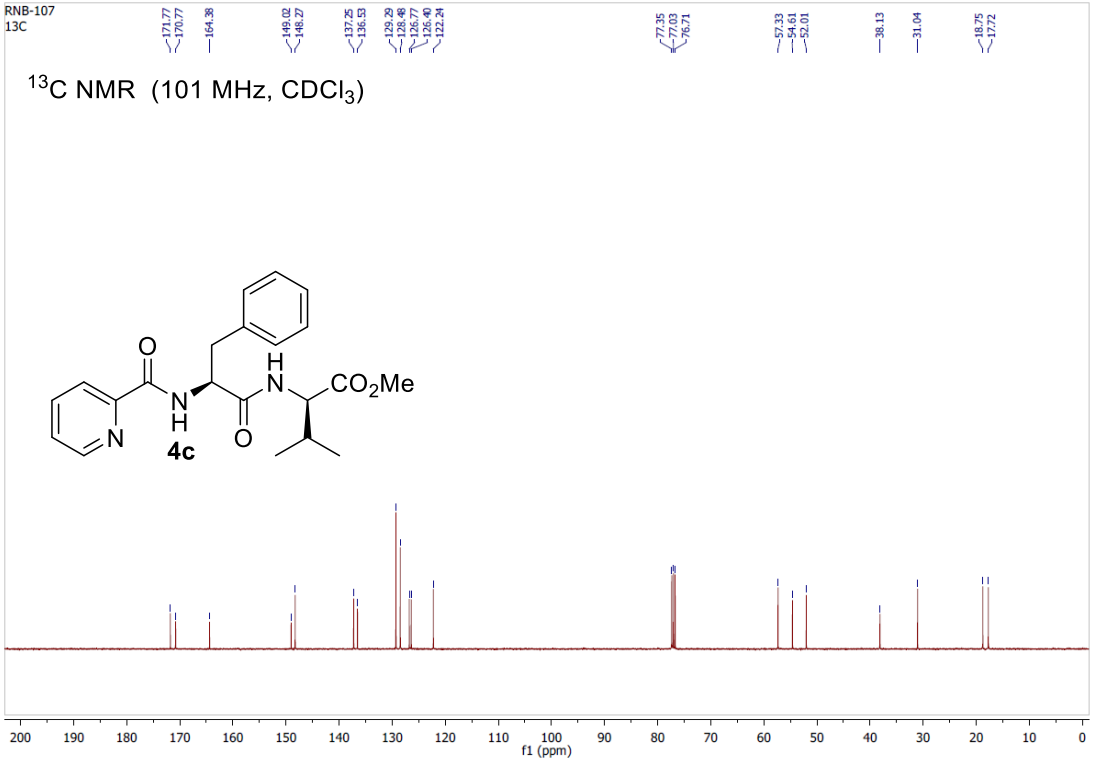


Fig S25. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4c**

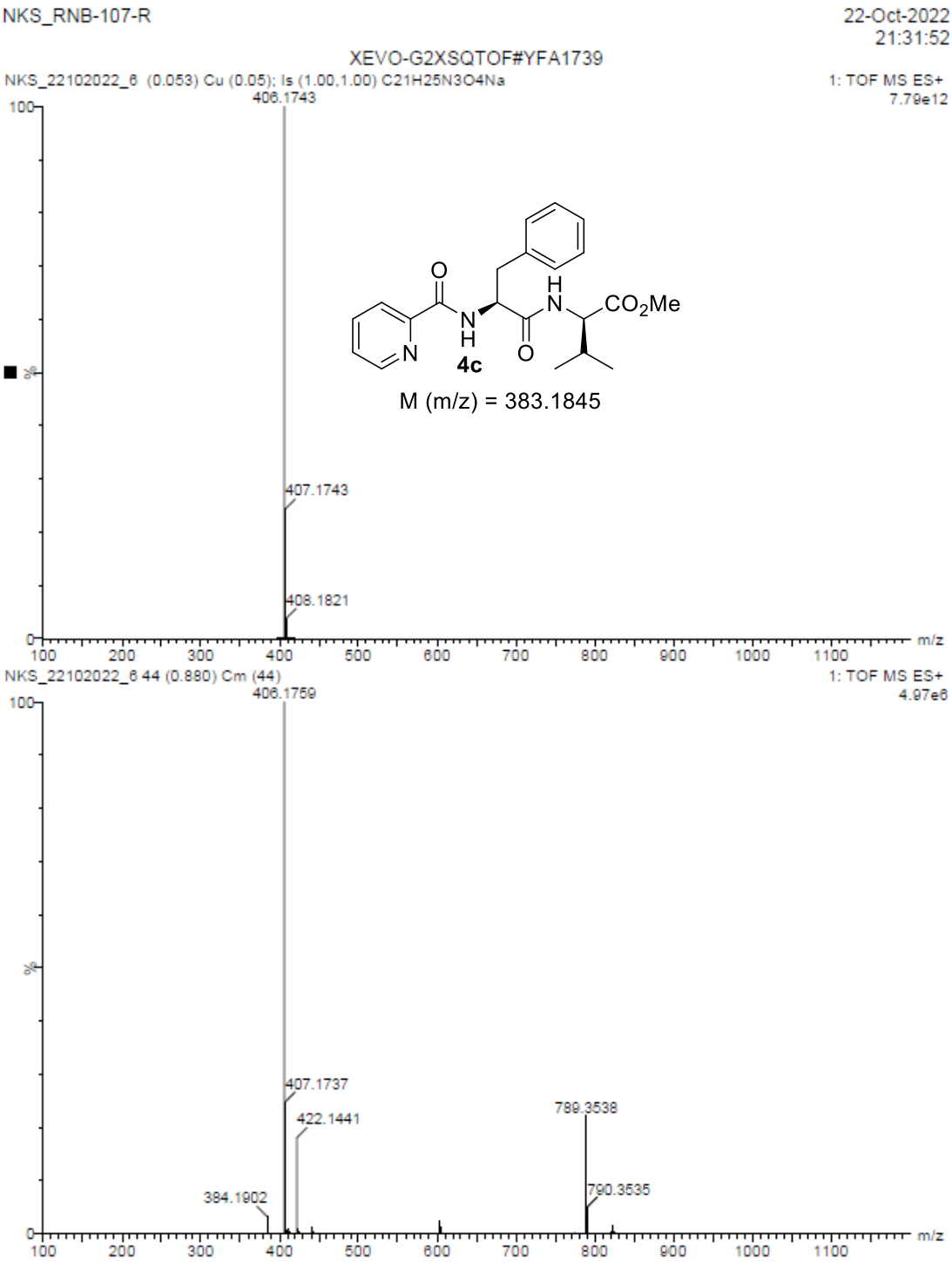


Fig S26. ESI-HRMS spectra of compound **4c**

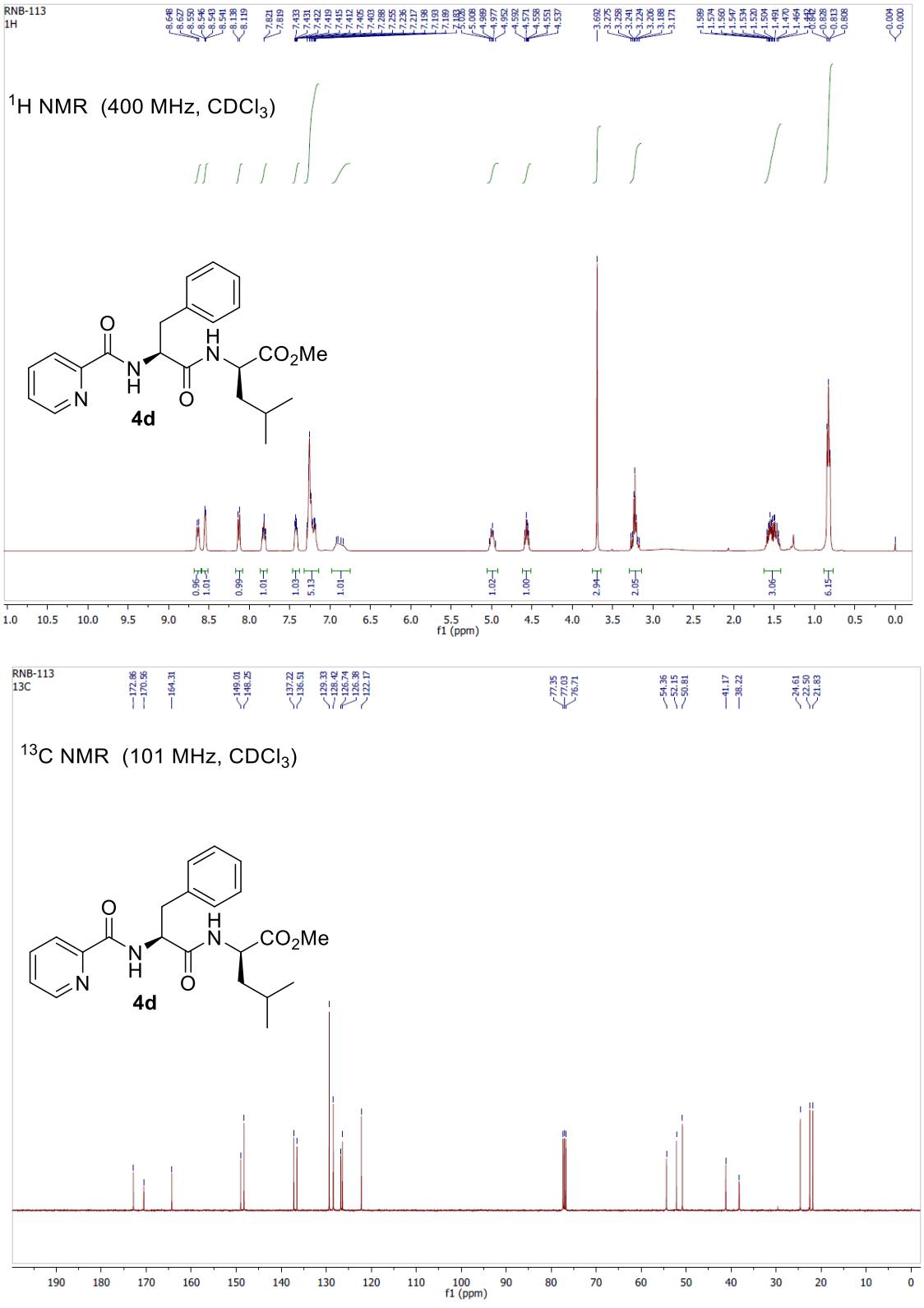


Fig S27. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4d**

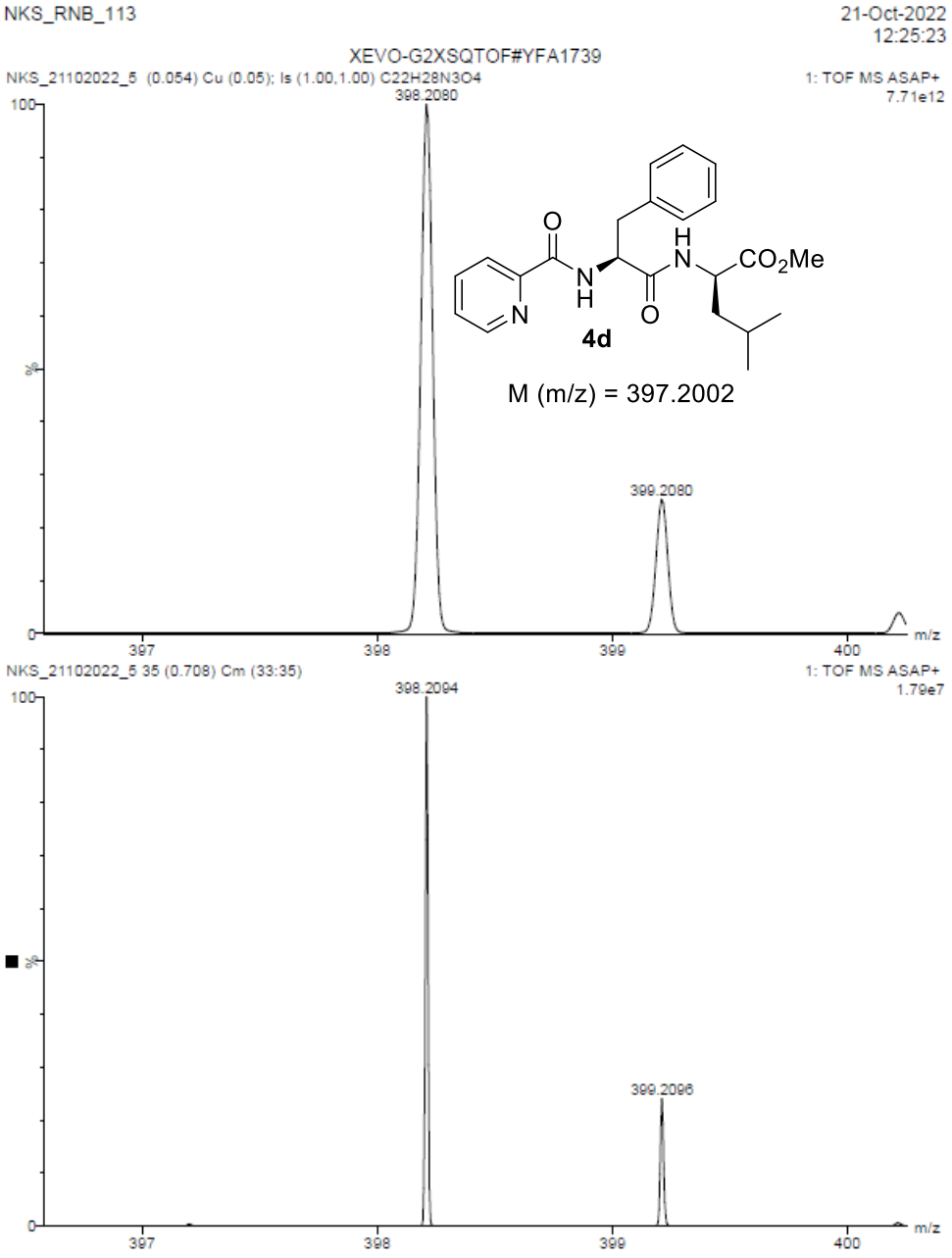
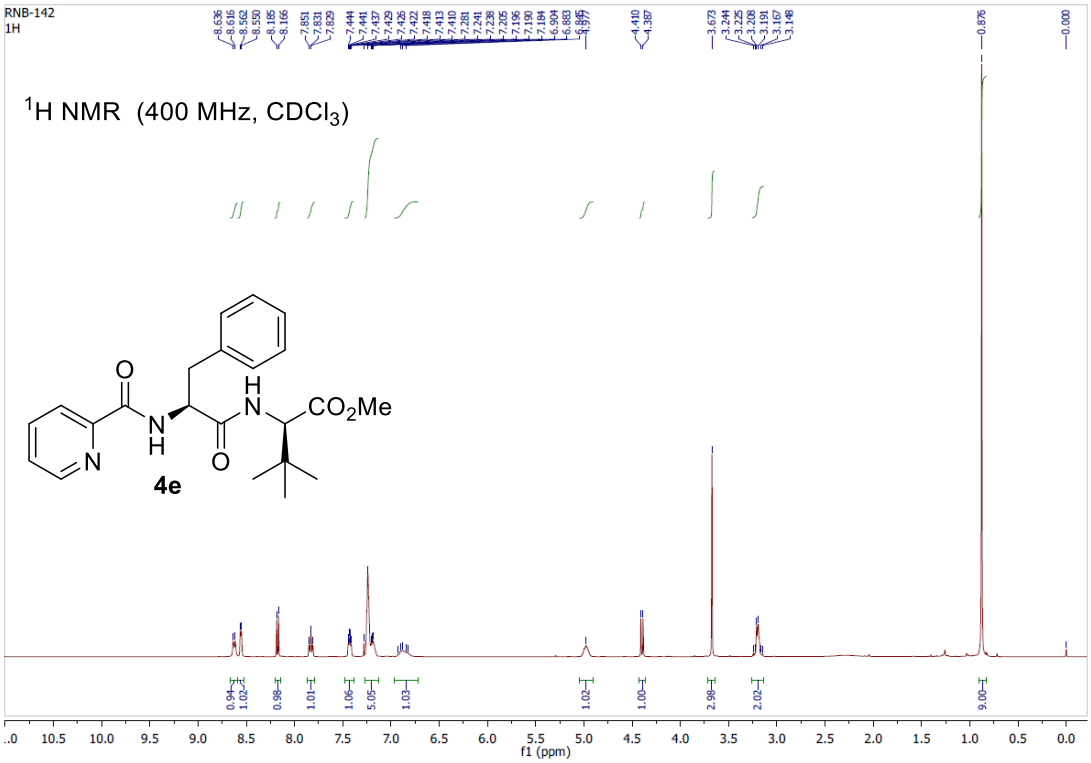


Fig S28. ASAP-HRMS spectra of compound **4d**



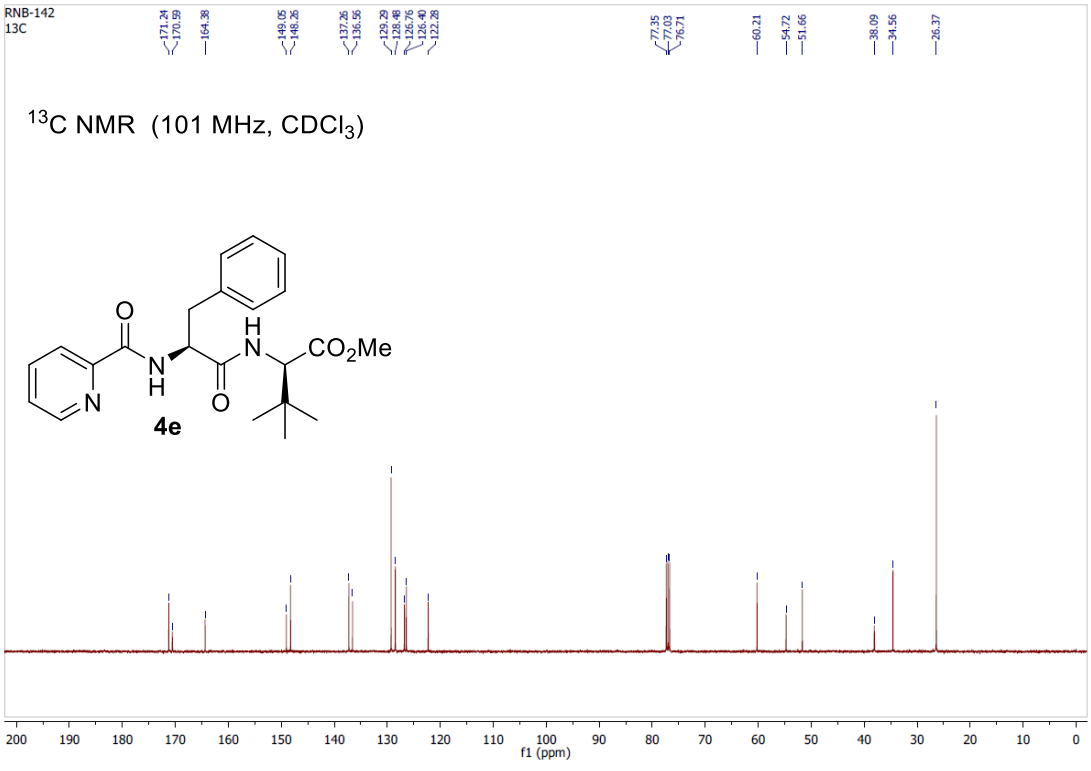


Fig S29. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4e**

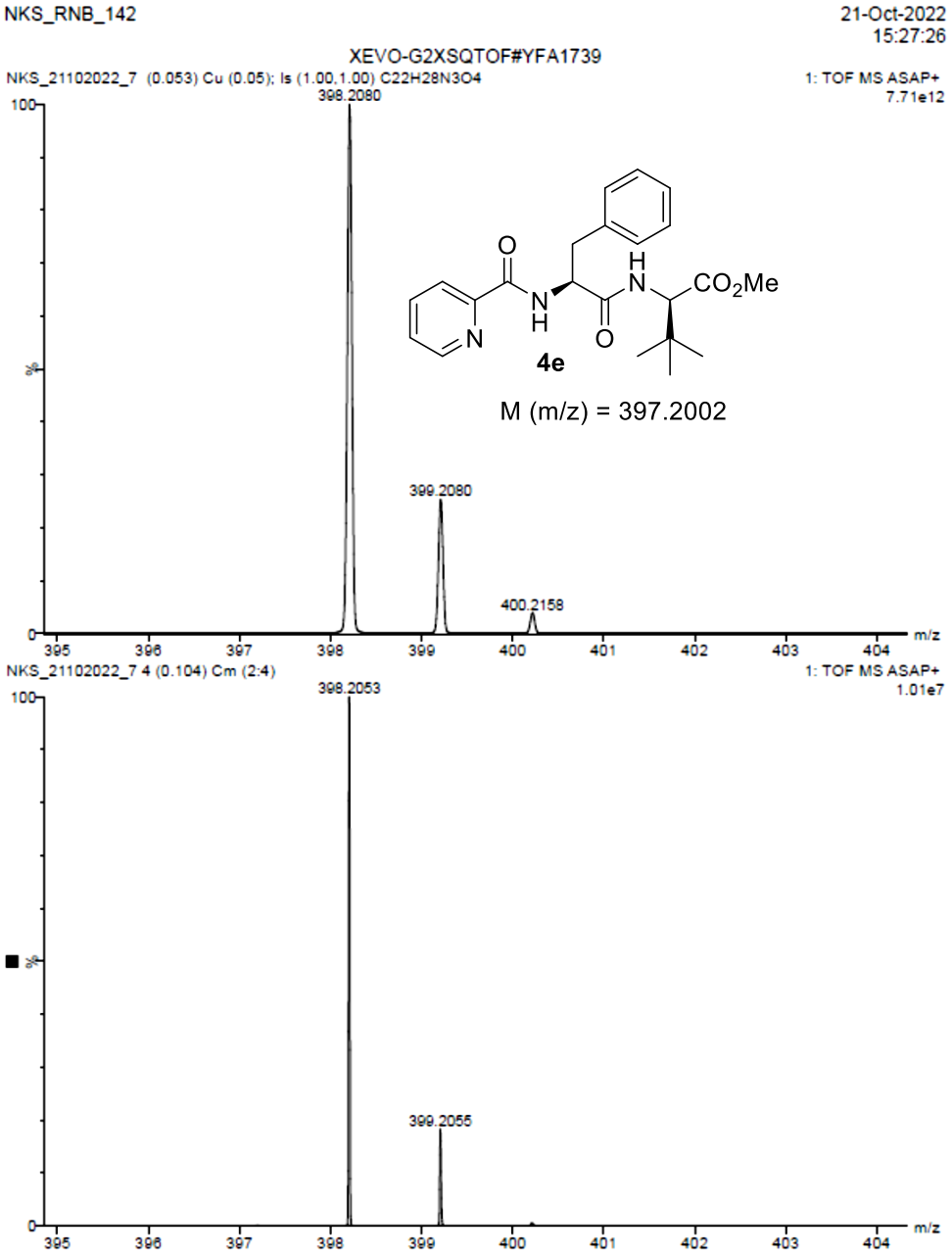


Fig S30. ASAP-HRMS spectra of compound **4e**

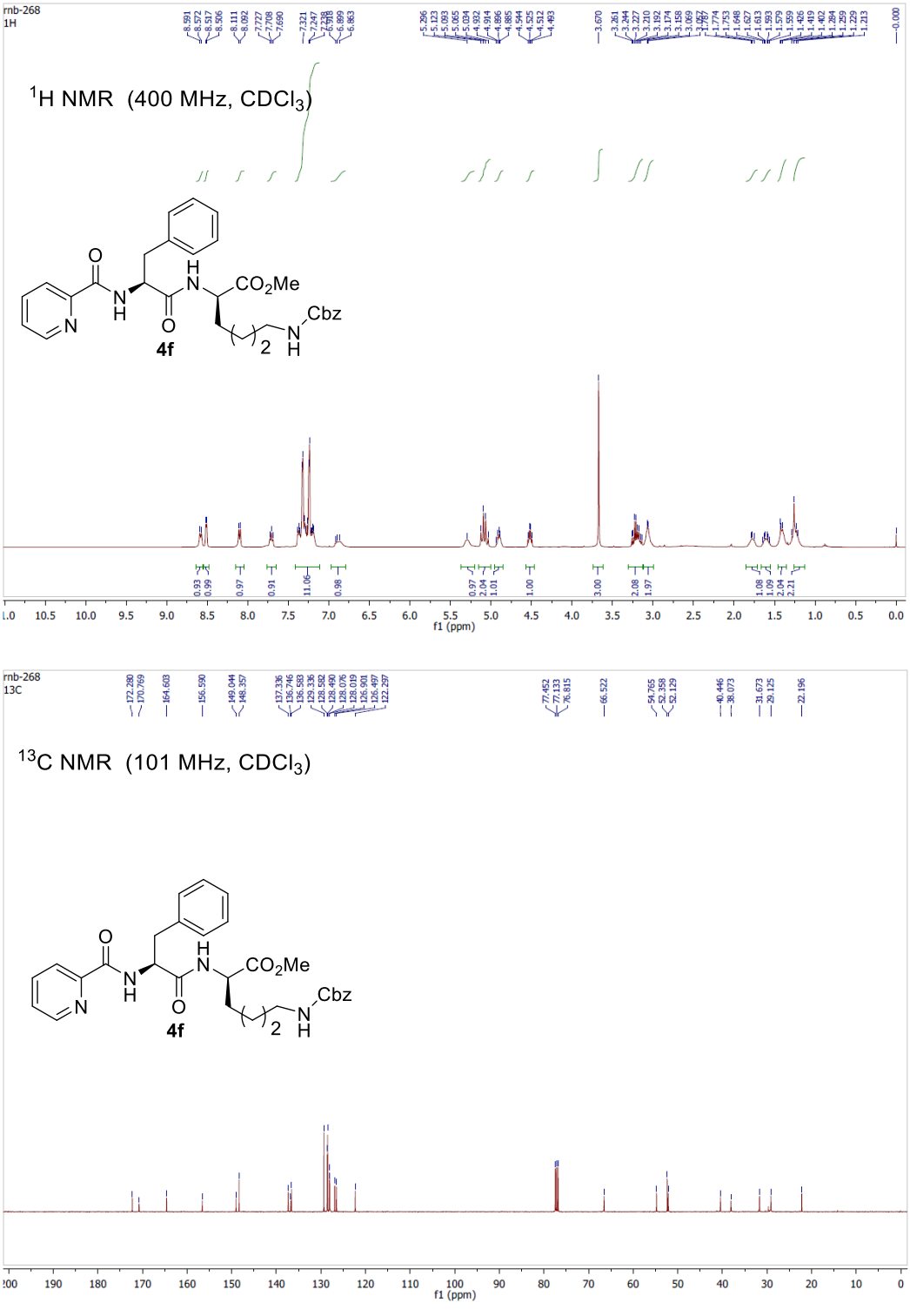


Fig S31. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4f**

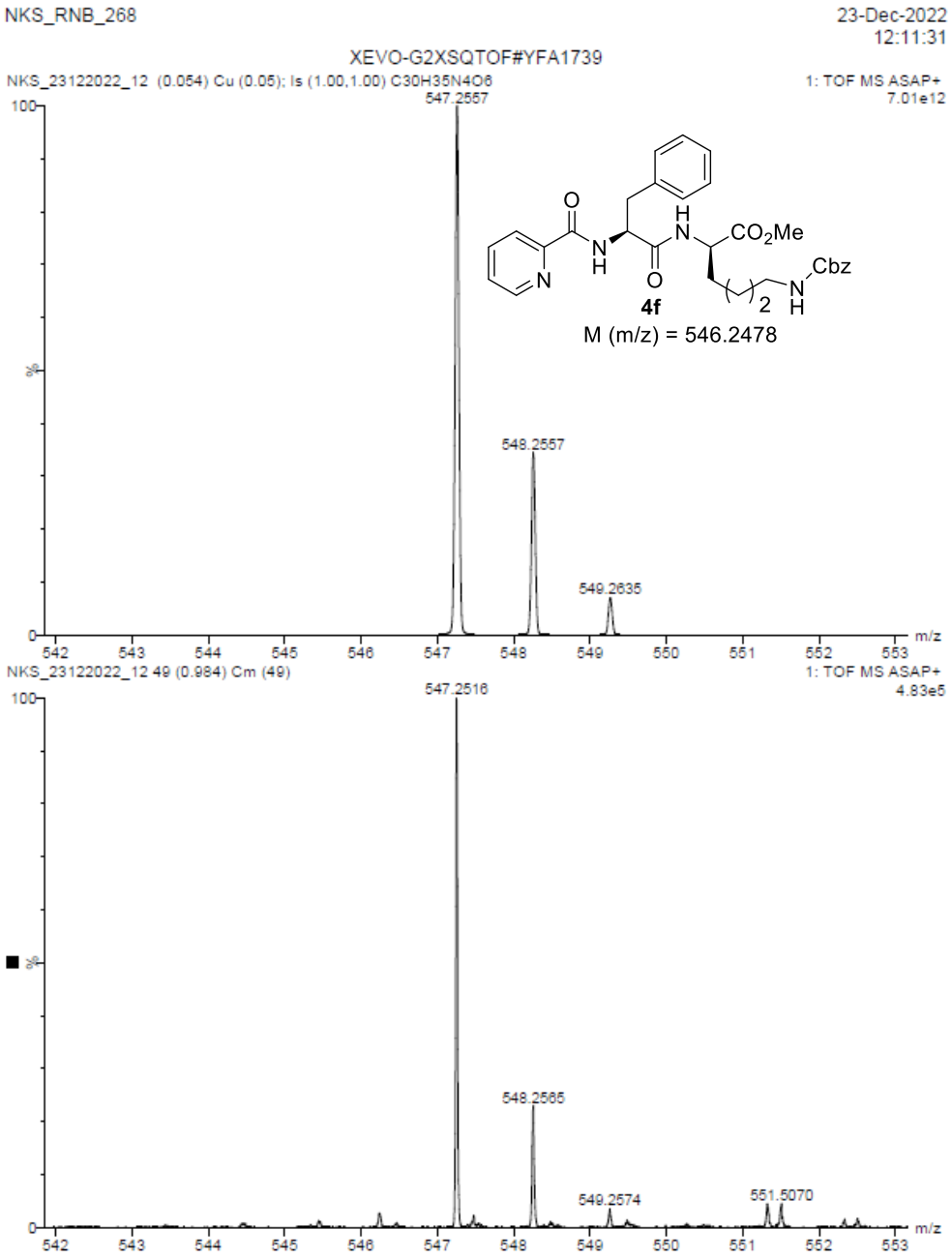
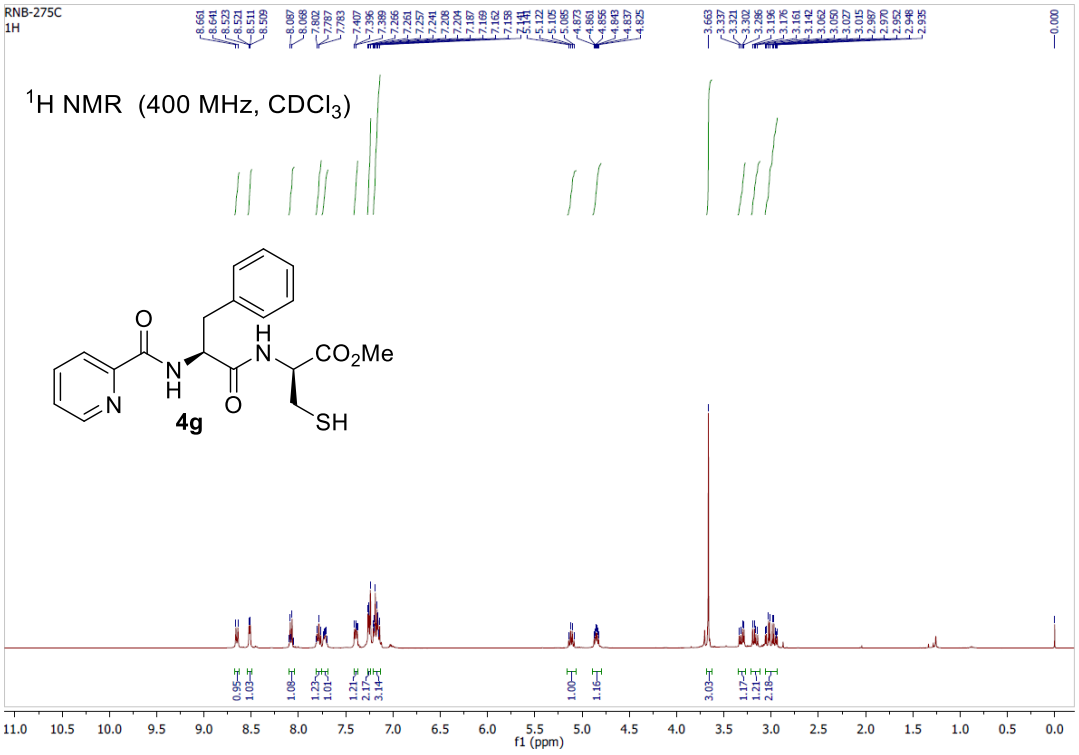


Fig S32. ASAP-HRMS spectra of compound **4f**



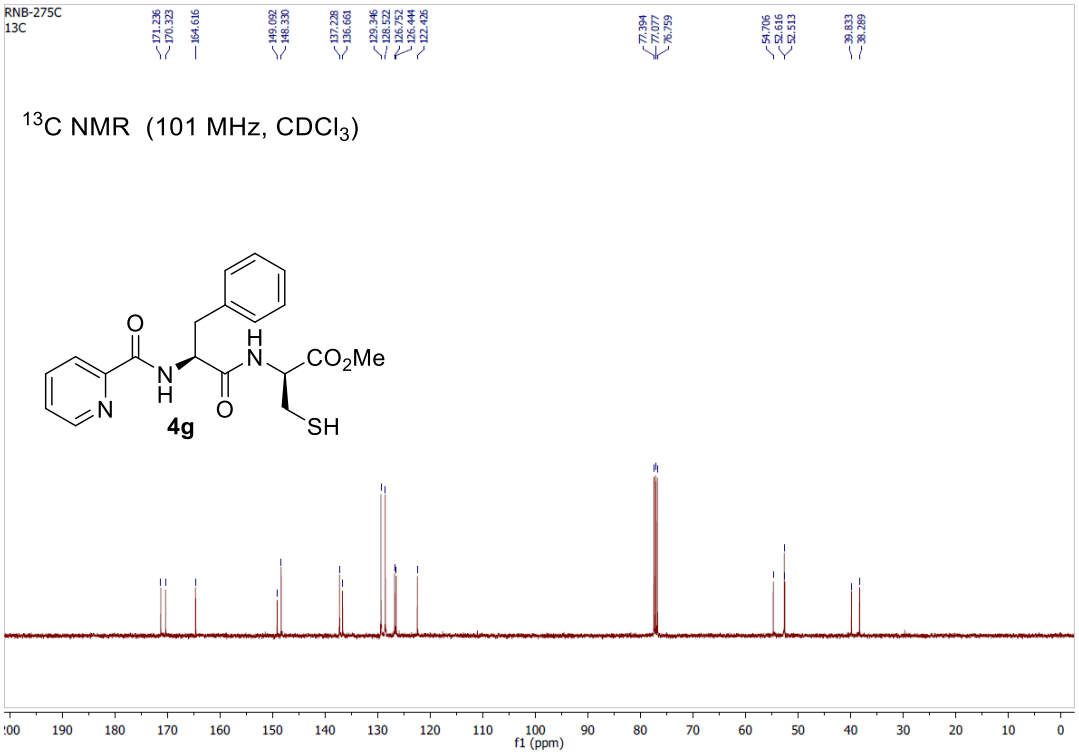


Fig S33. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4g**

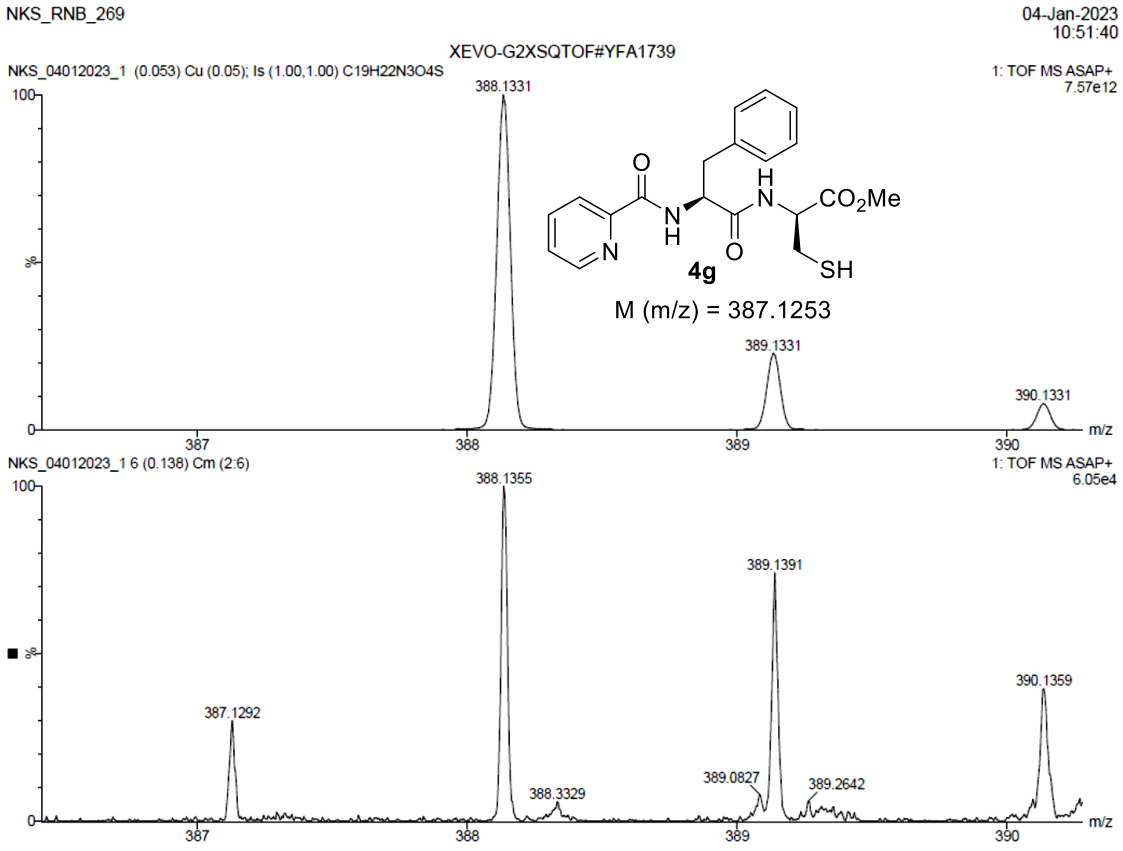


Fig S34. ASAP-HRMS spectra of compound **4g**

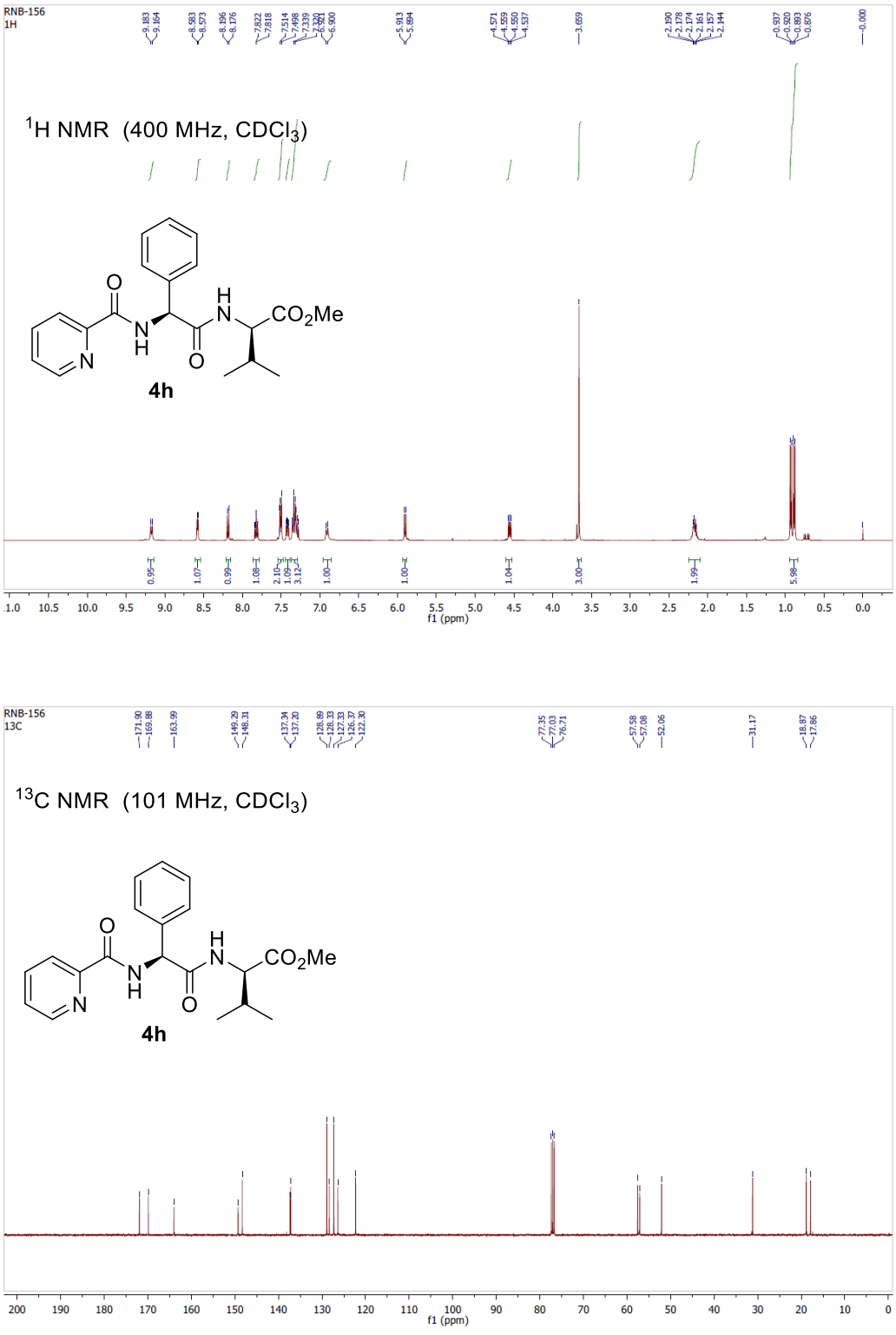


Fig S35. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4h**

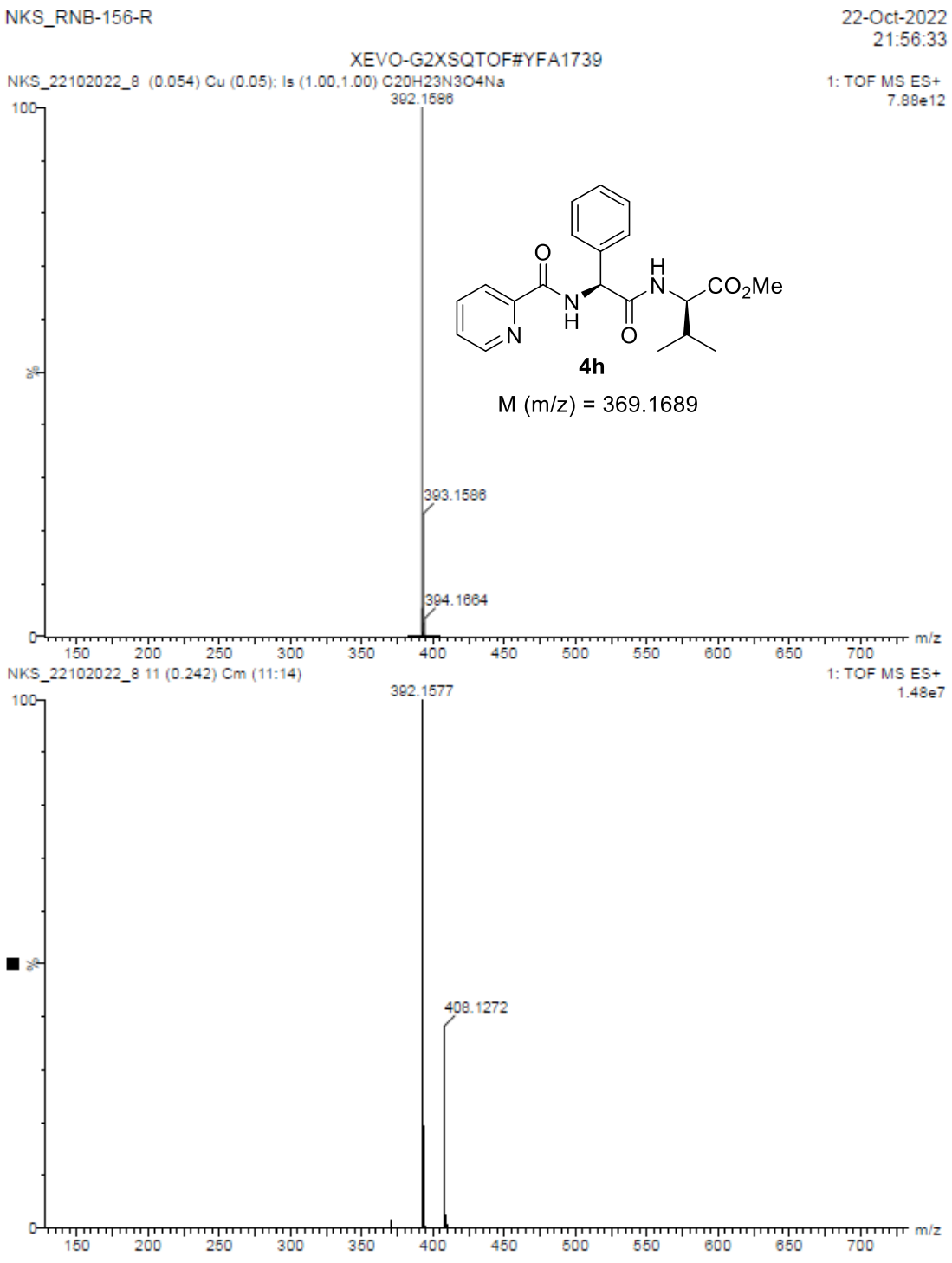
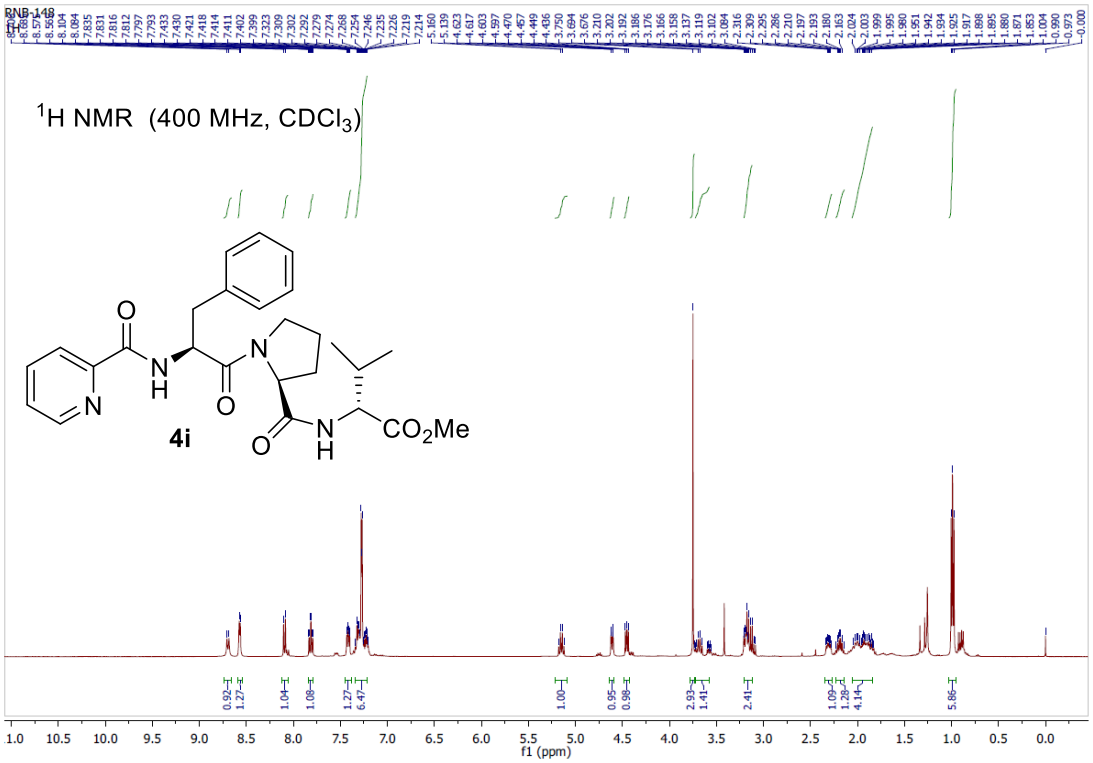


Fig S36. ESI-HRMS spectra of compound **4h**



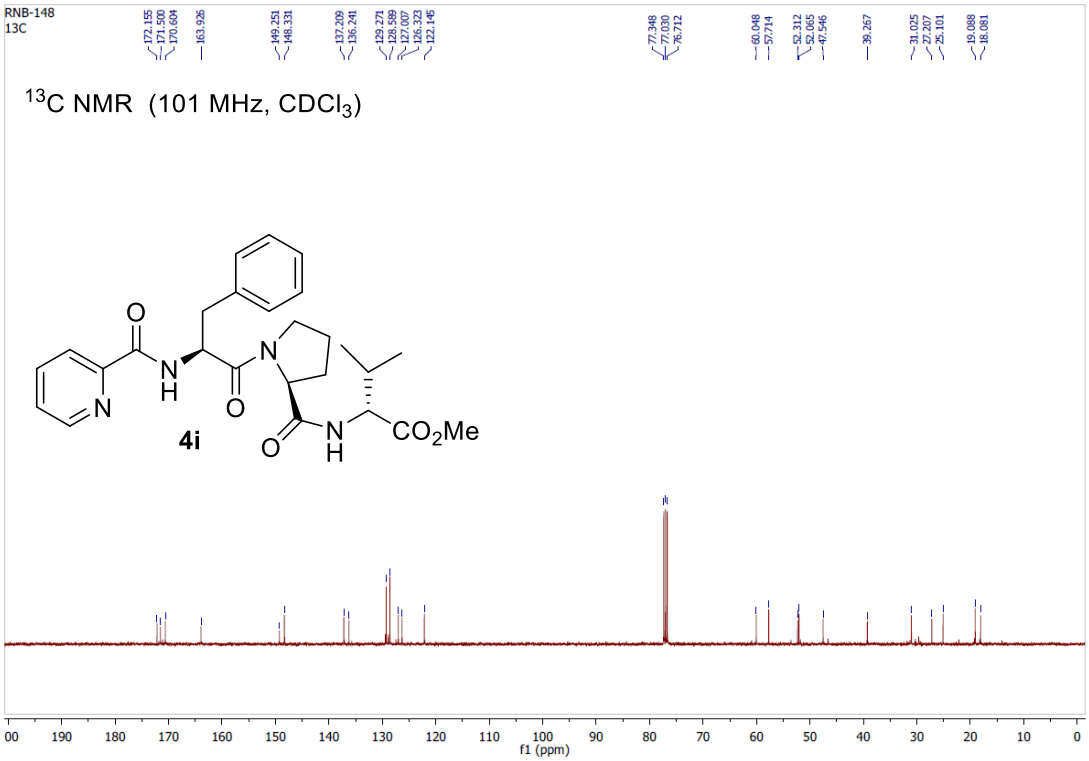


Fig S37. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4i**

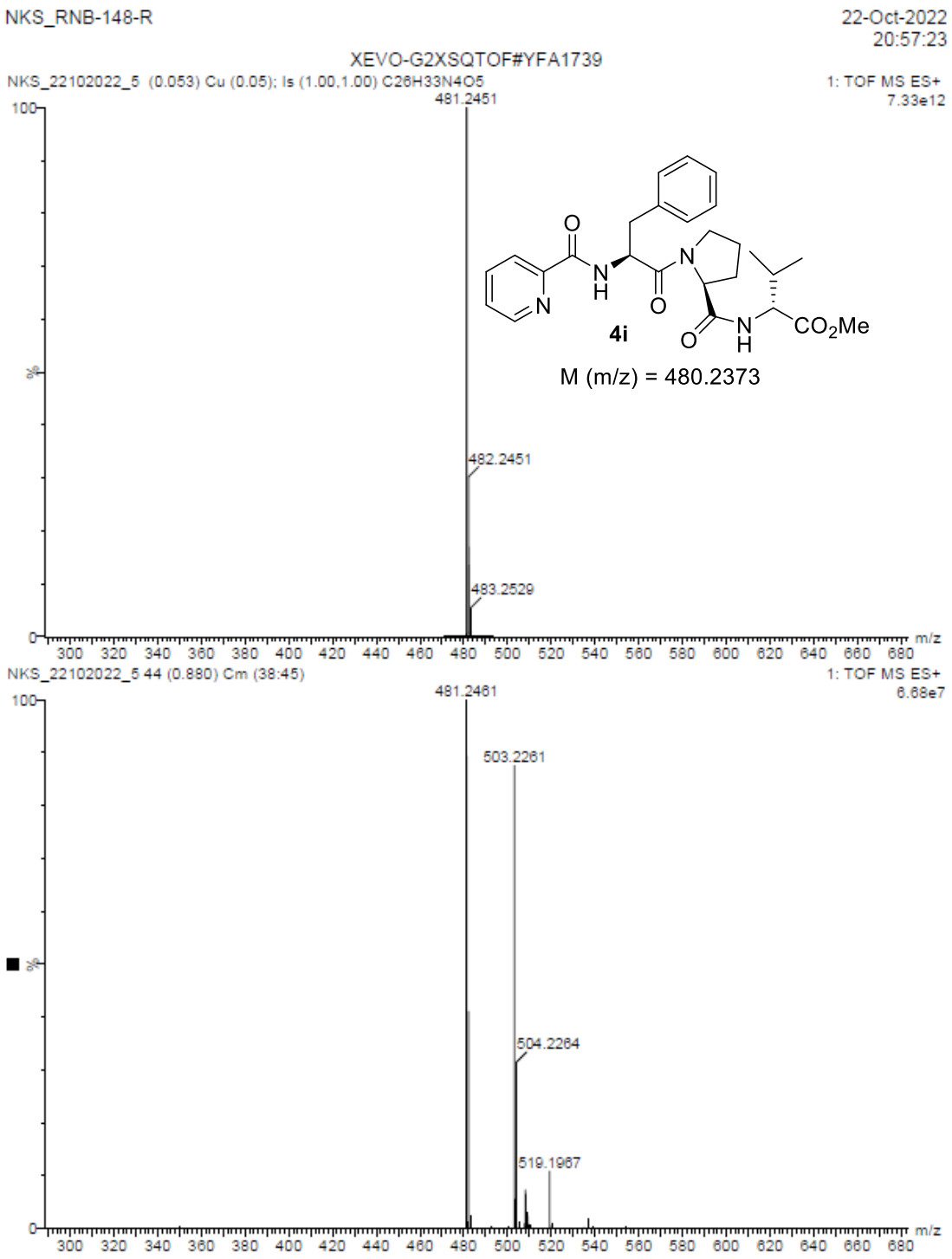
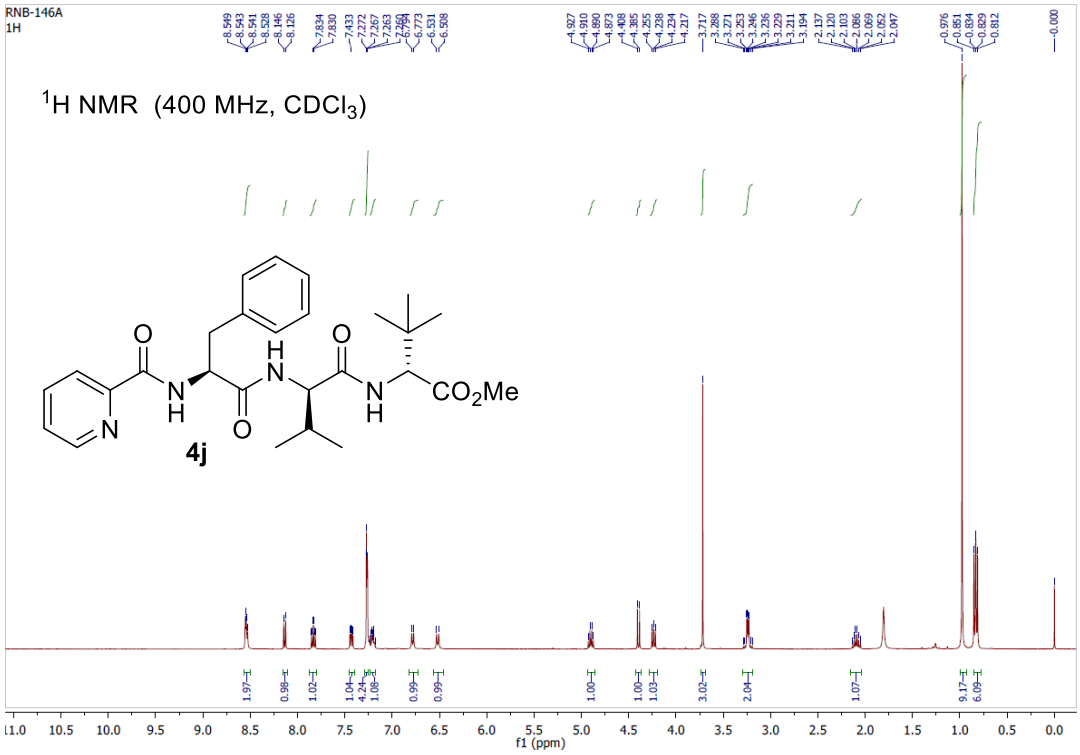


Fig S38. ESI-HRMS spectra of compound **4i**



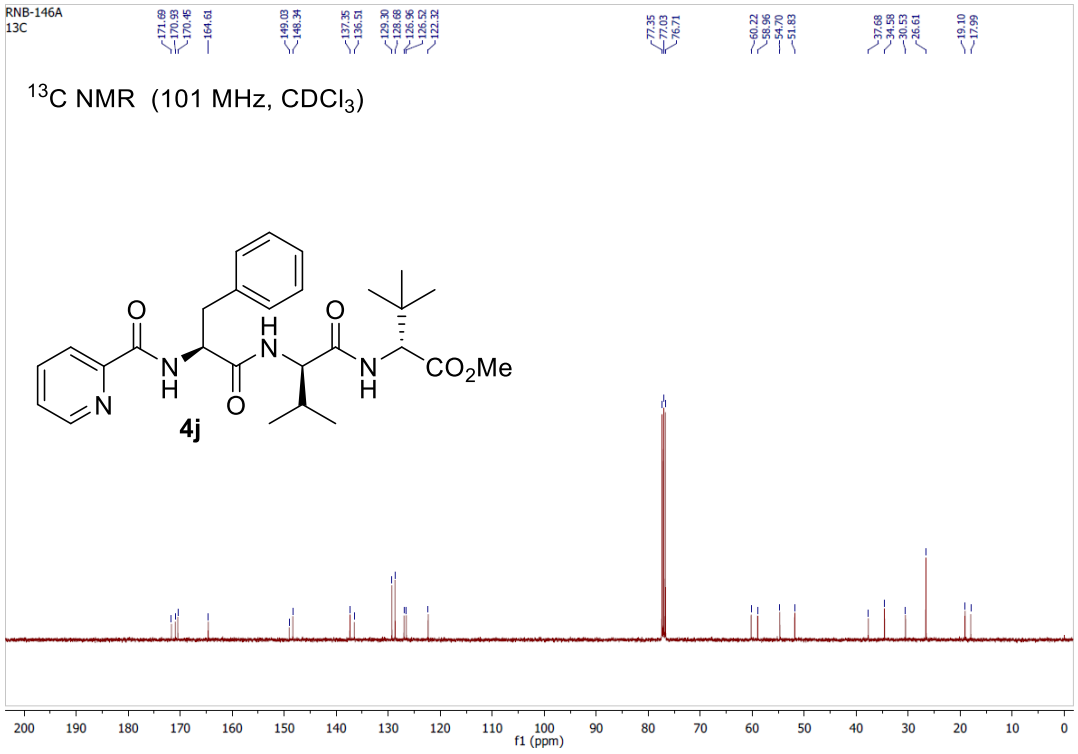


Fig S39. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **4j**

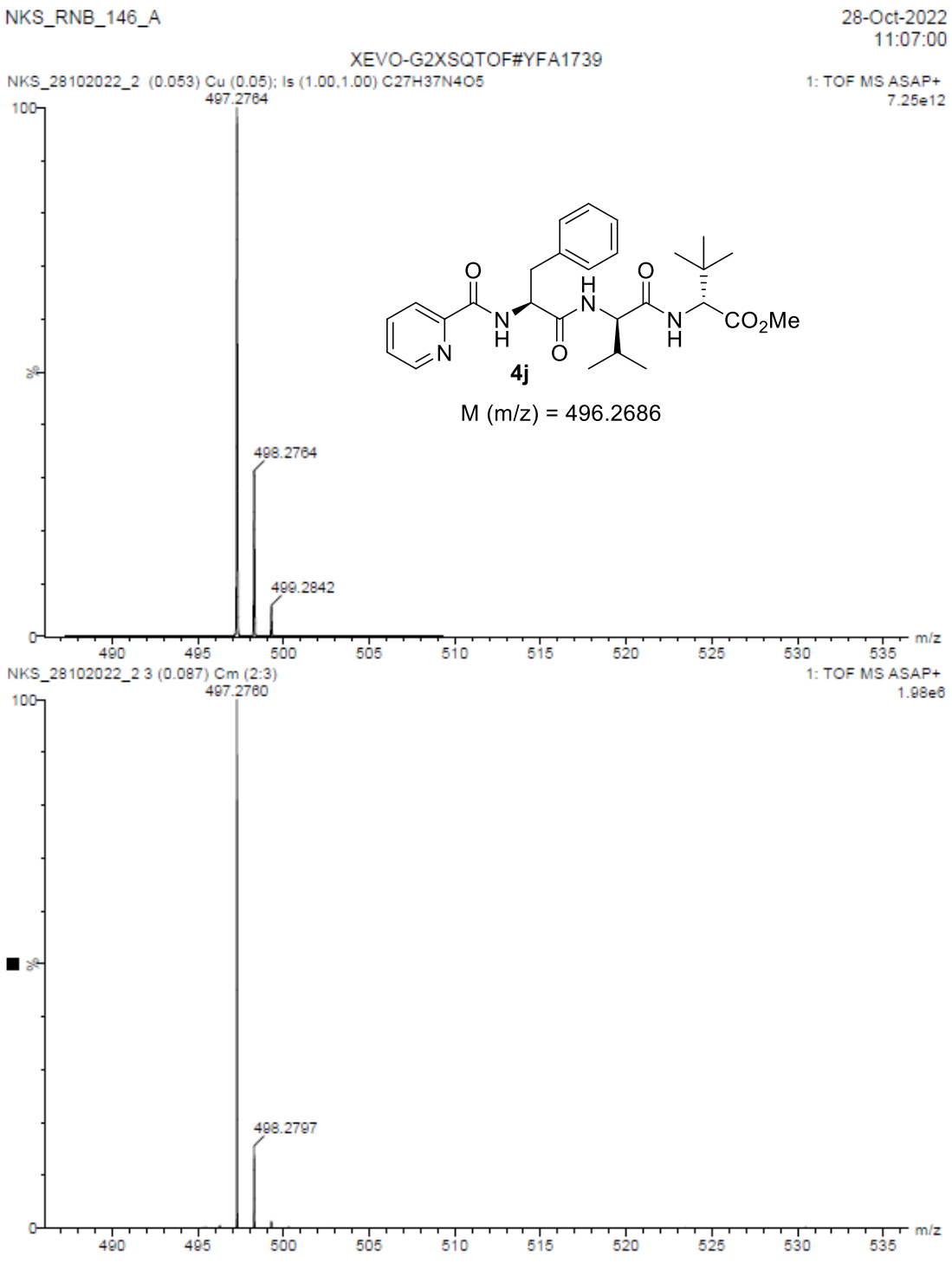
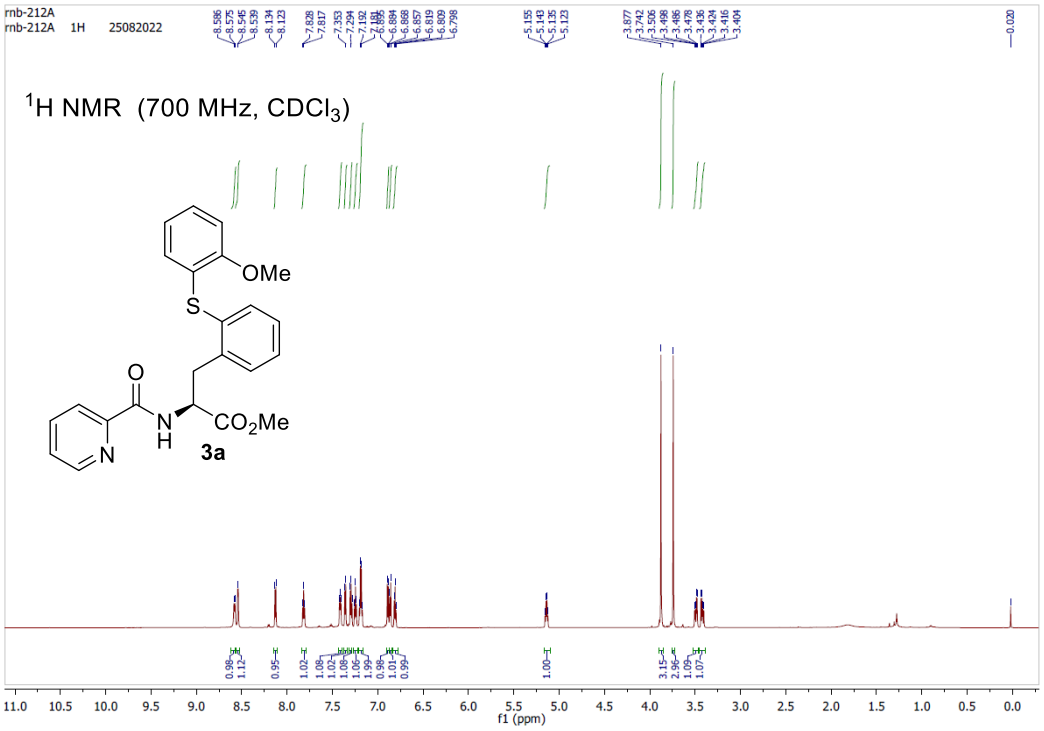


Fig S40. ASAP-HRMS spectra of compound **4j**



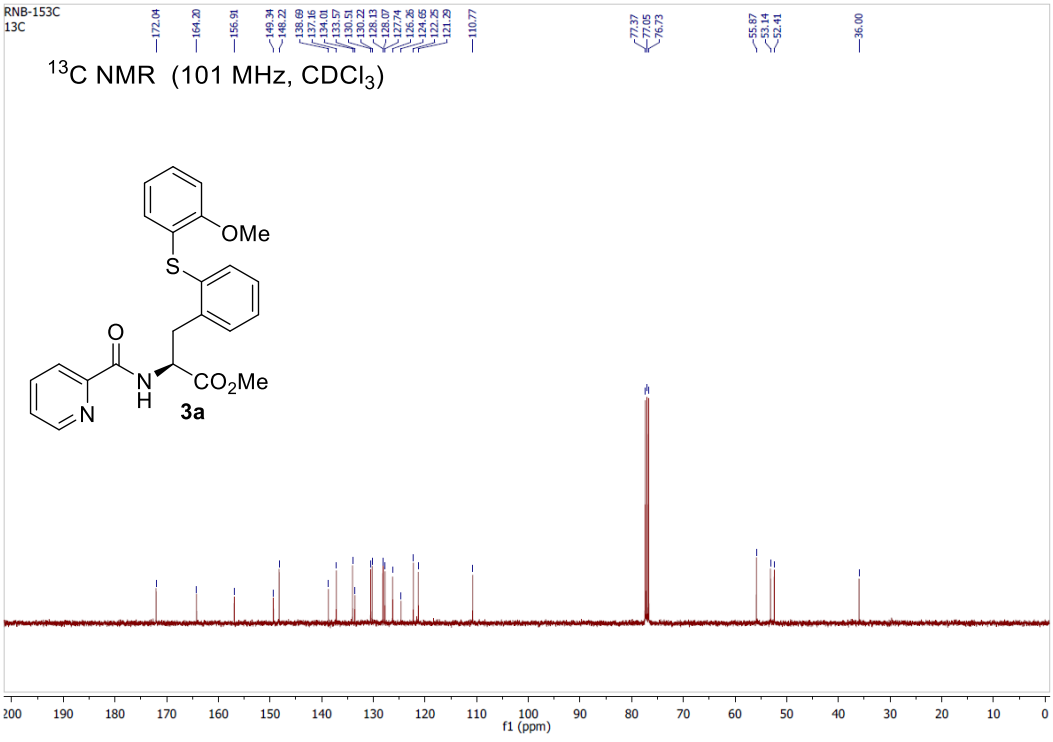


Fig S41. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3a**

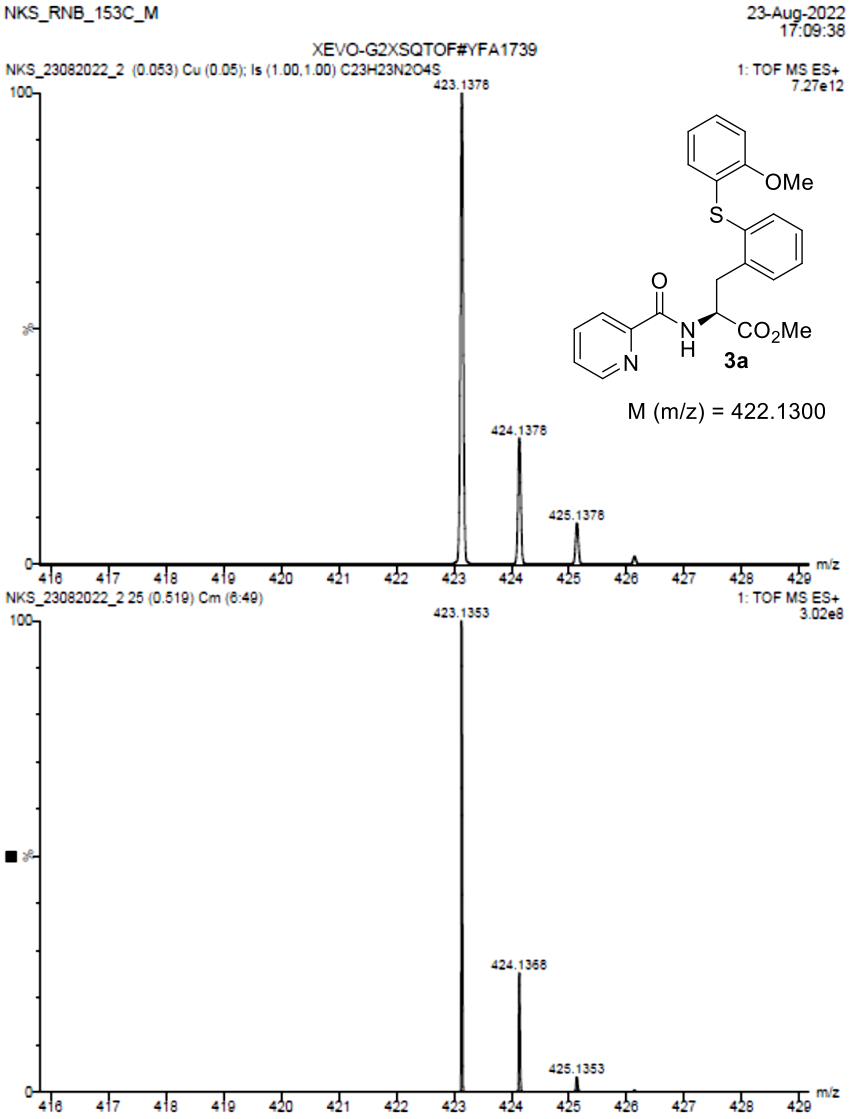


Fig S42. ESI-HRMS spectra of thiolated compound **3a**

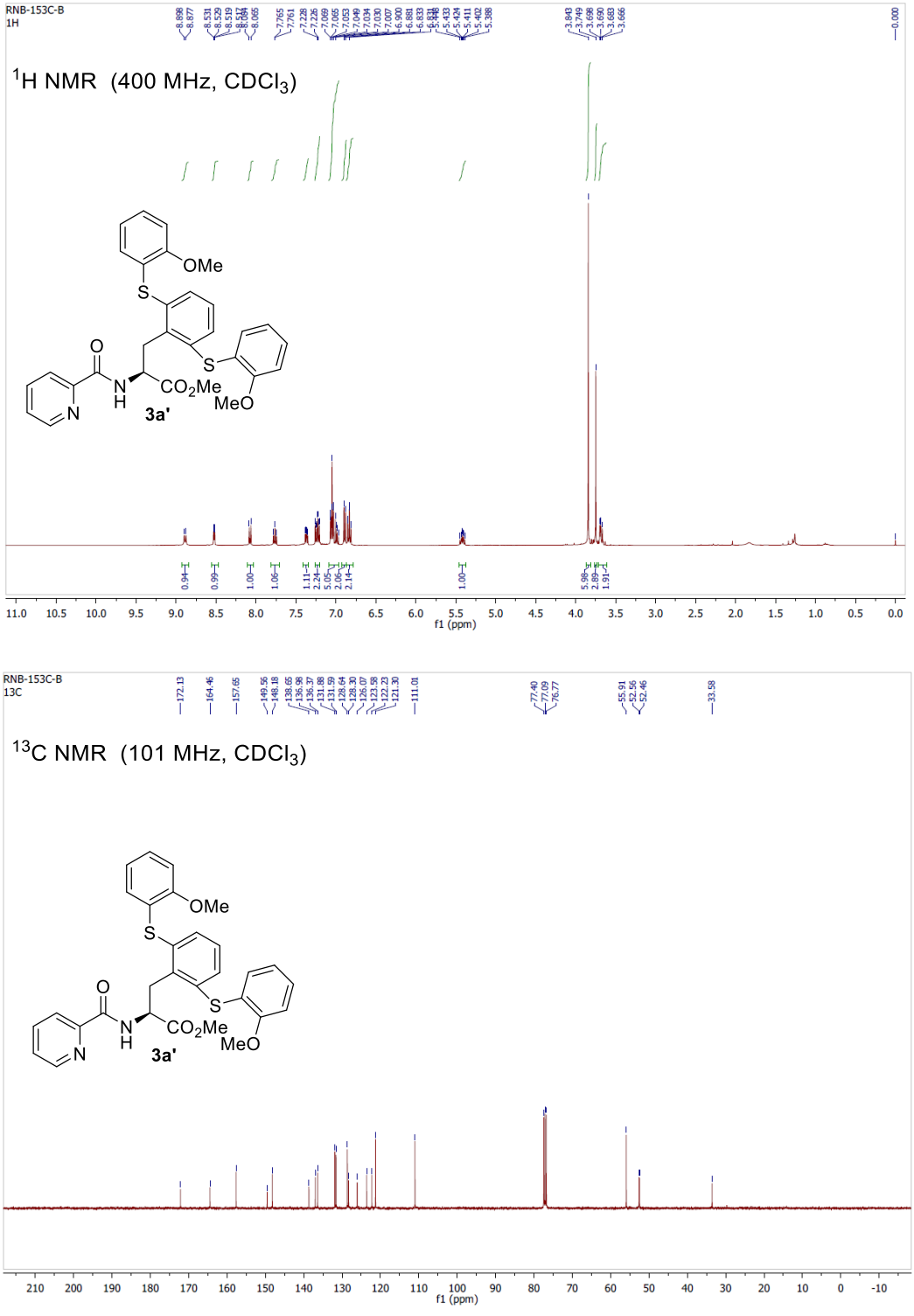


Fig S43. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3a'**

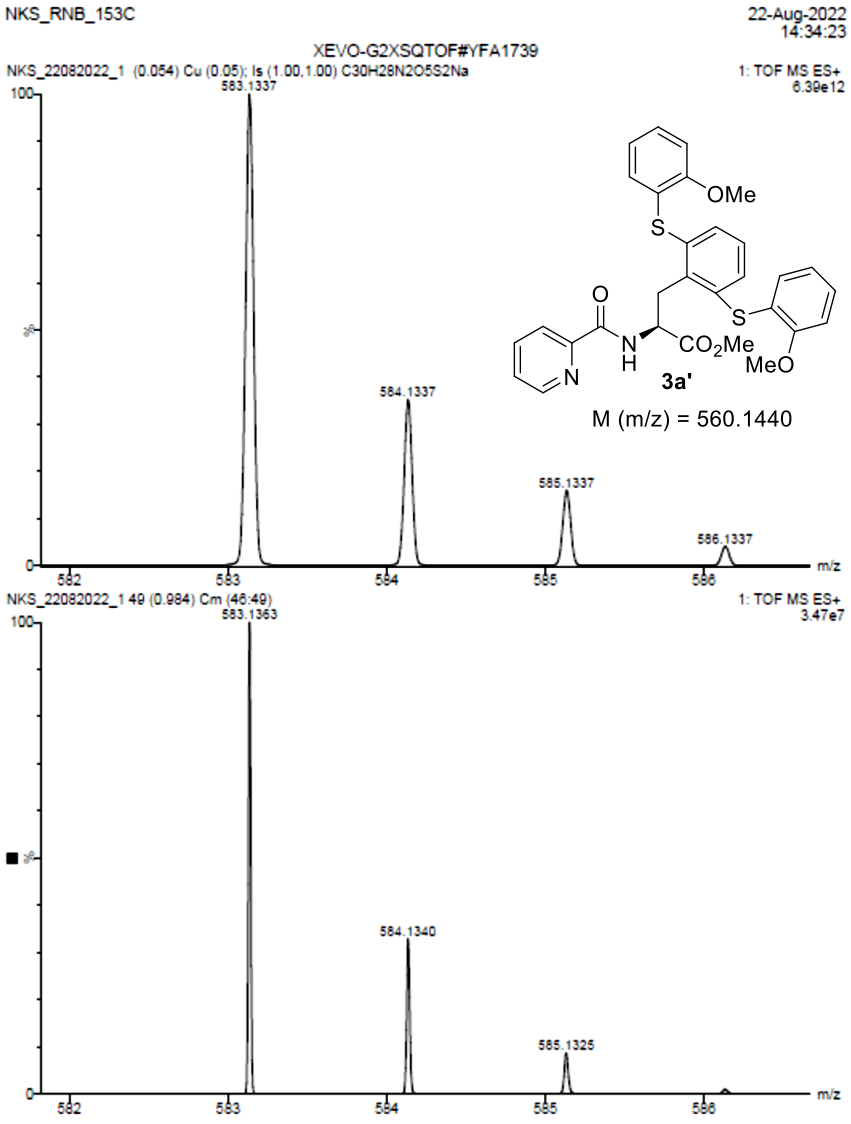
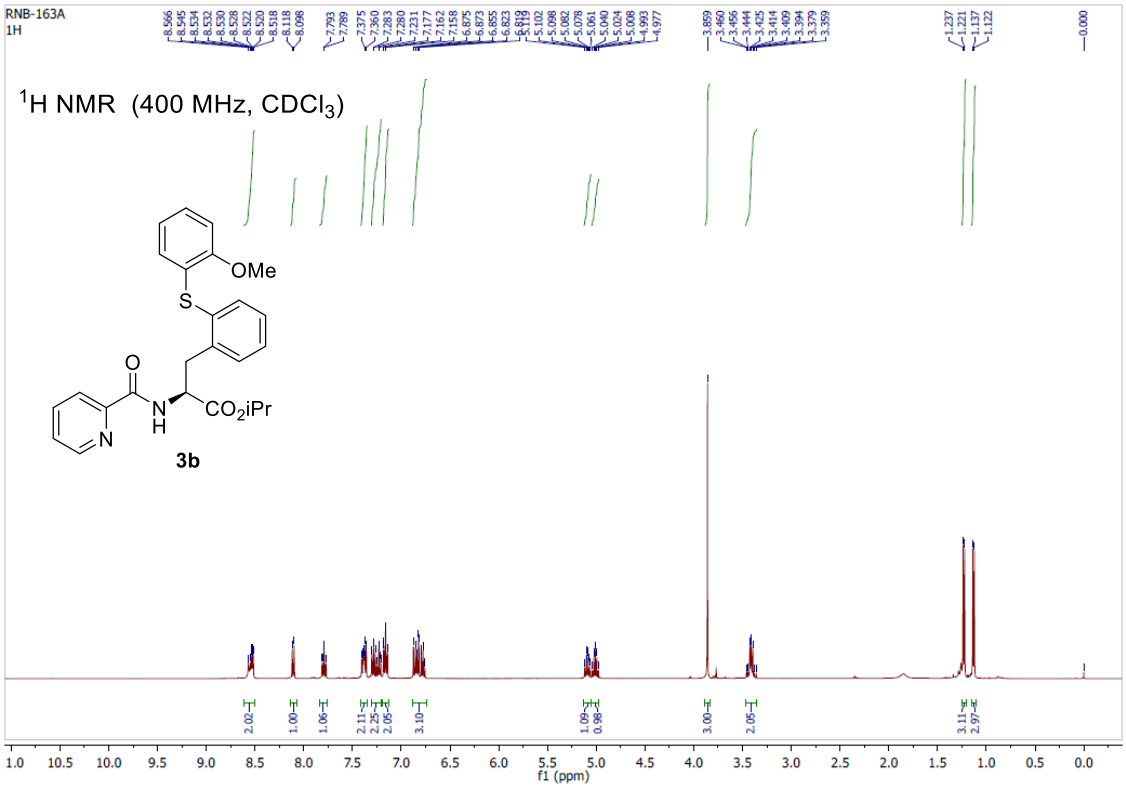


Fig S44. ESI-HRMS spectra of thiolated compound **3a'**



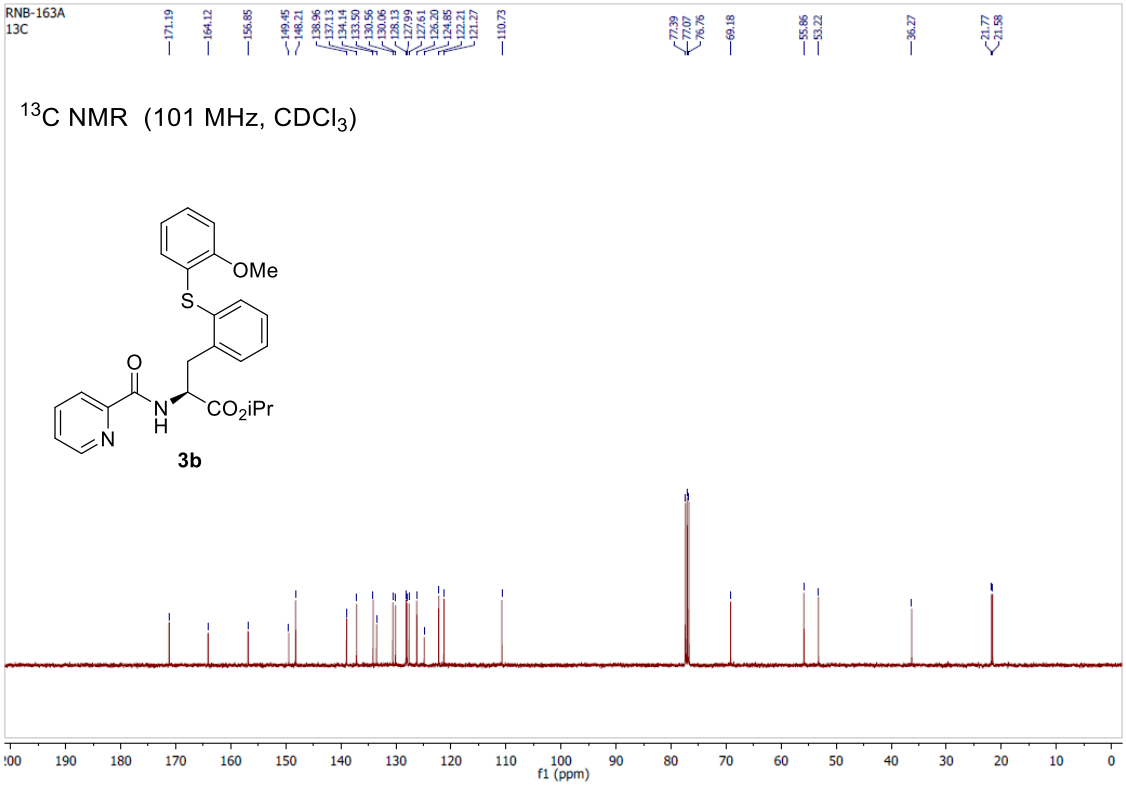


Fig S45. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3b**

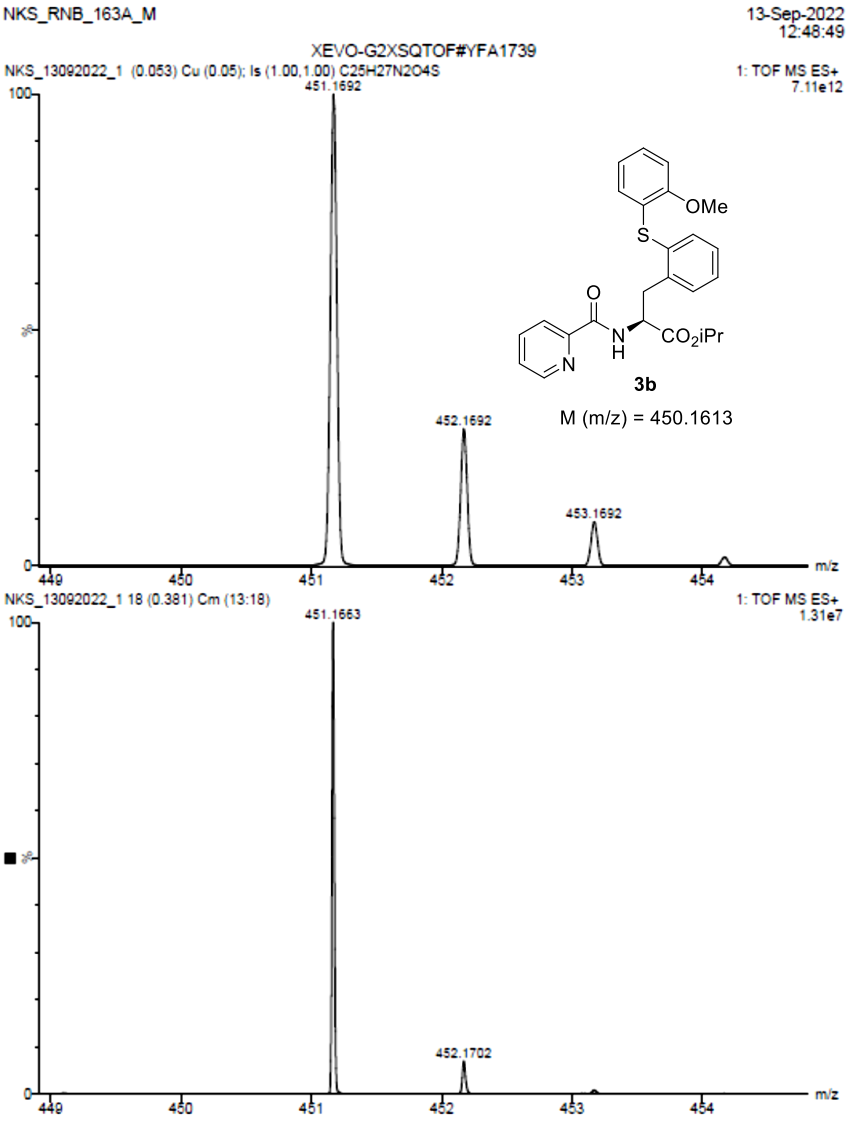
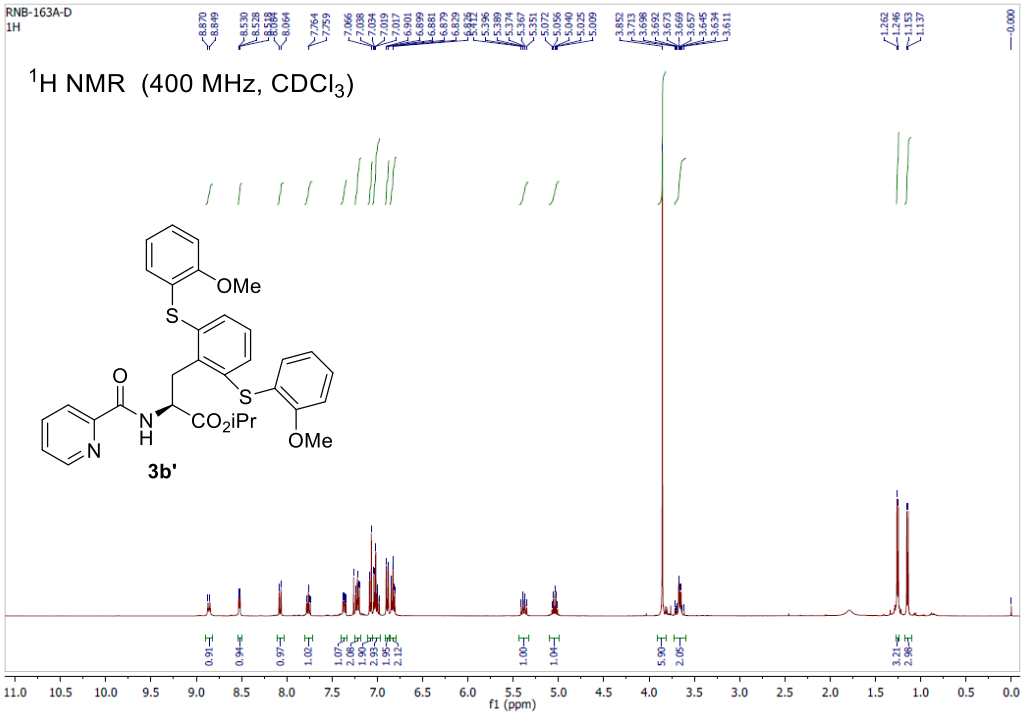


Fig S46. ESI-HRMS spectra of thiolated compound **3b**



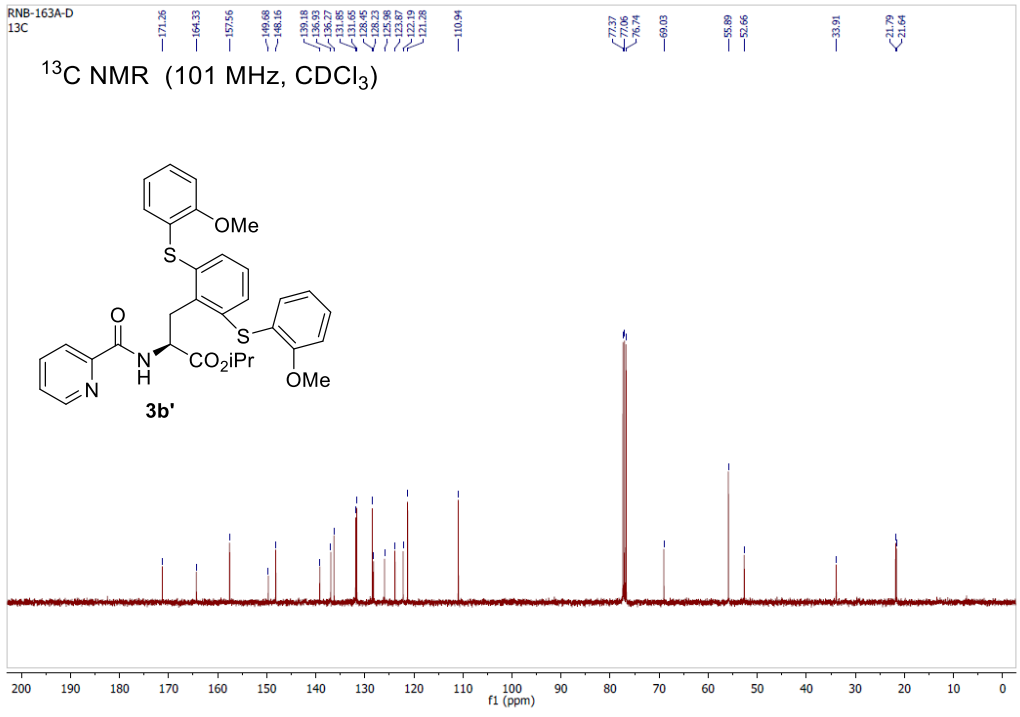


Fig S47. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3b'**

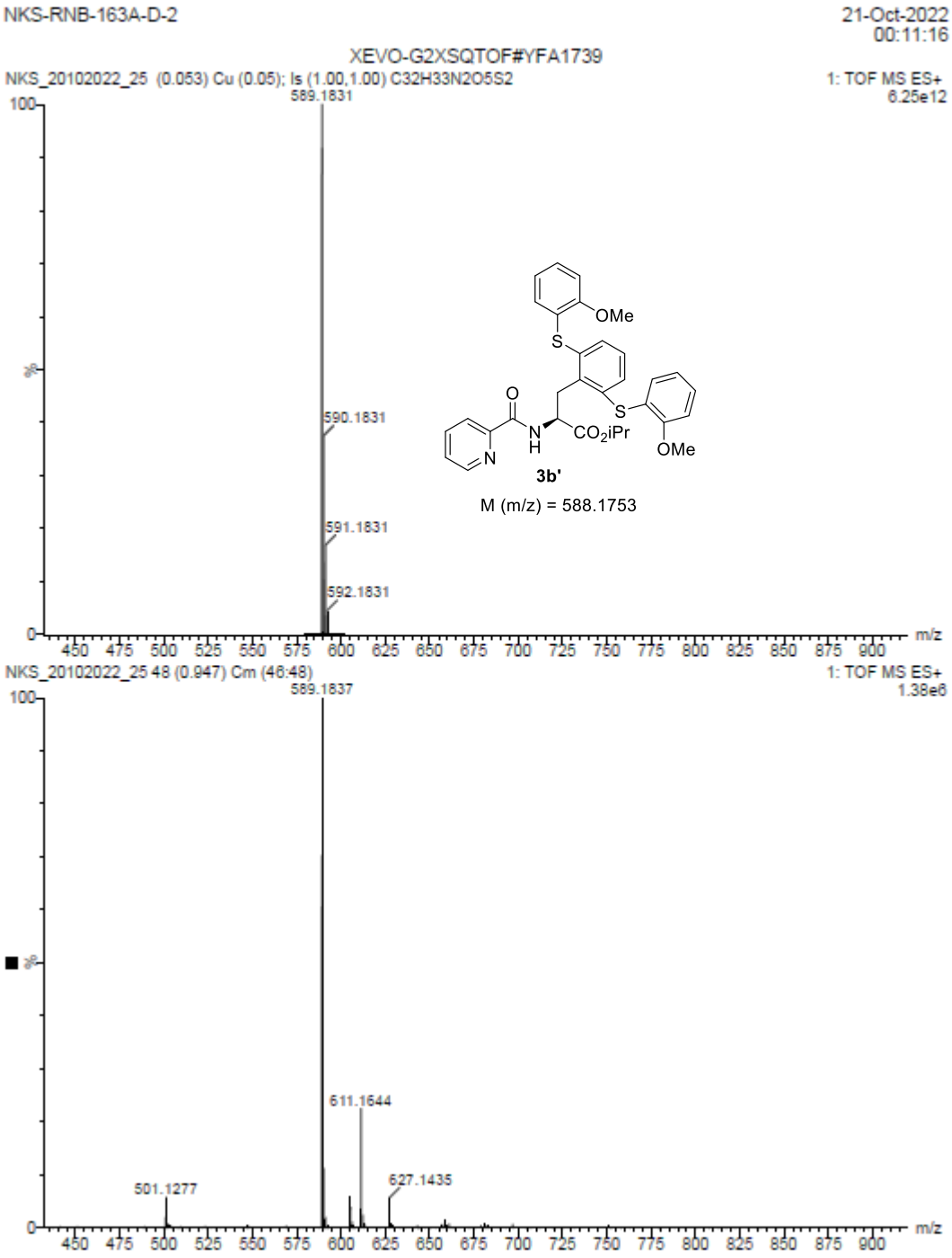


Fig S48. ESI-HRMS spectra of thiolated compound **3b'**

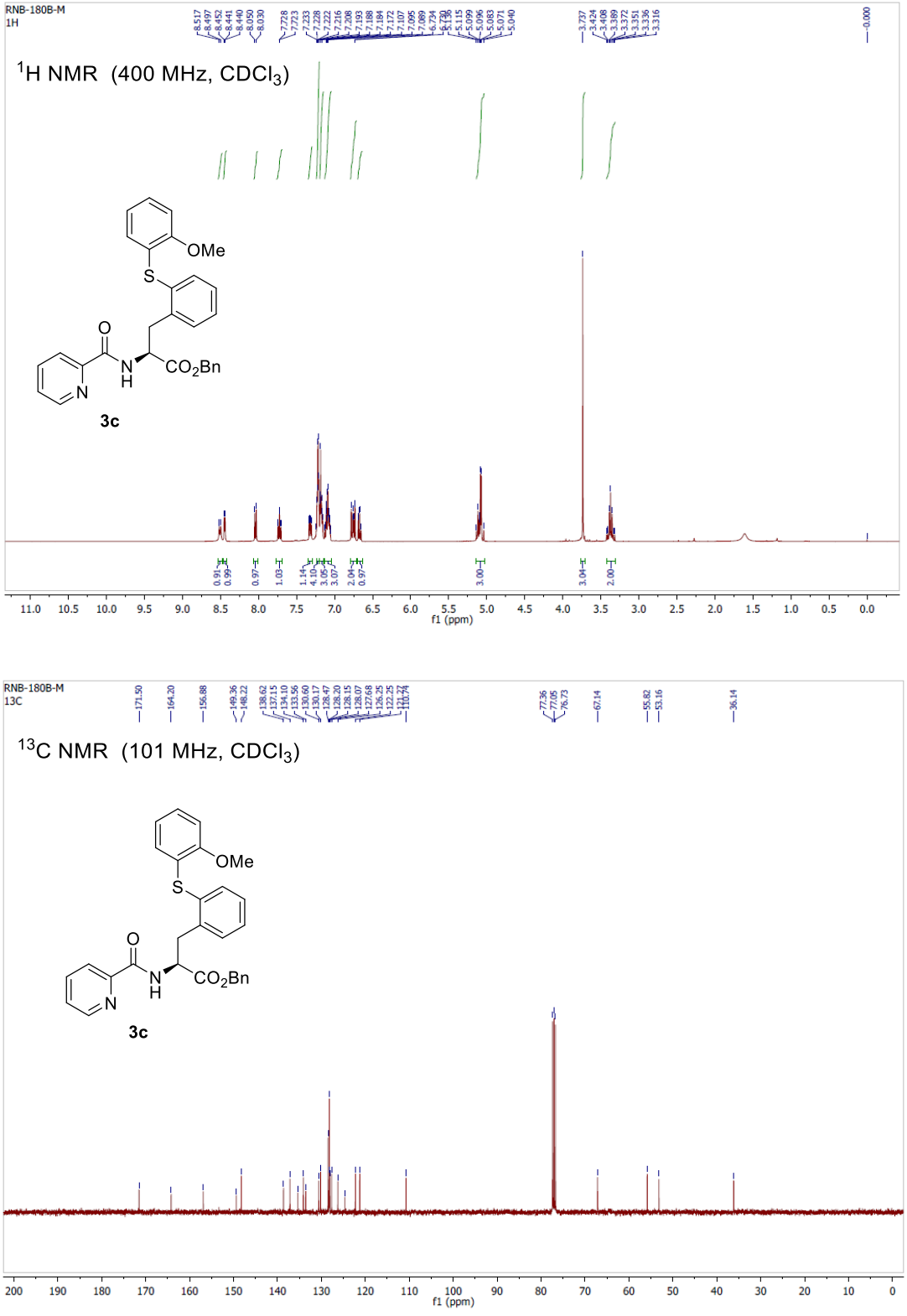


Fig S49. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3c**

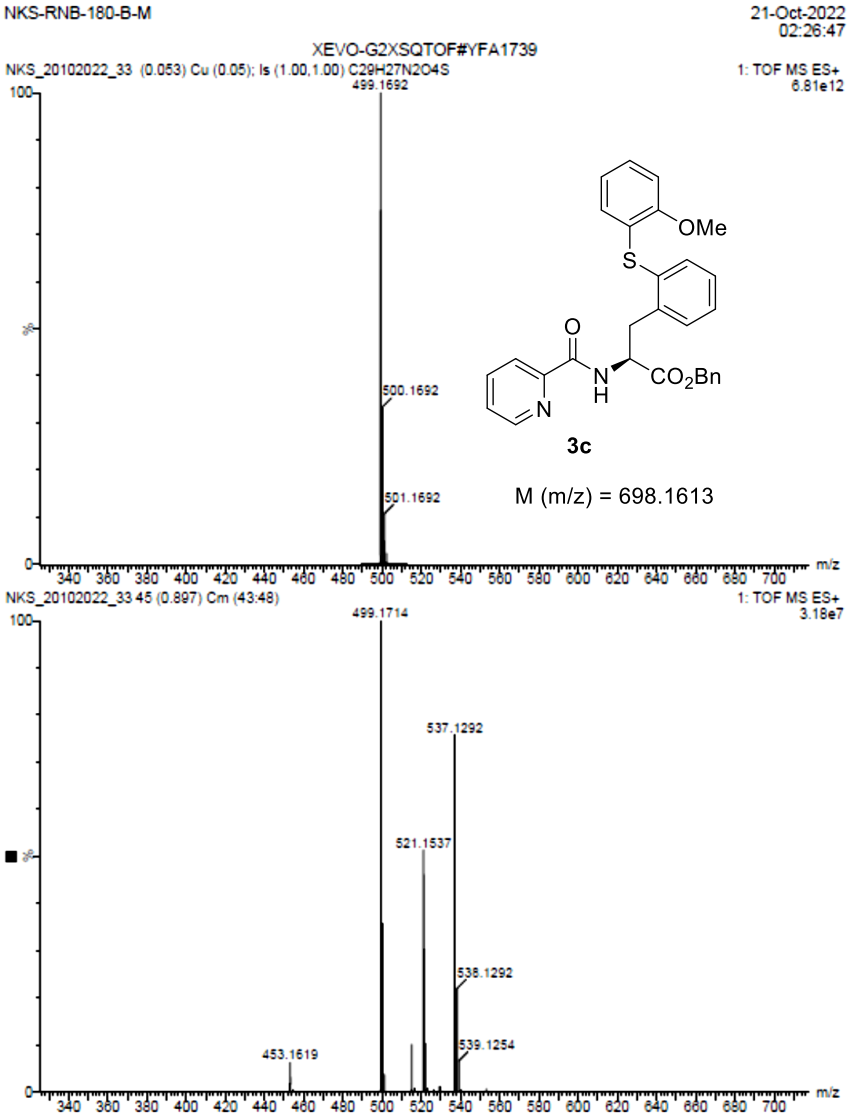


Fig S50. ESI-HRMS spectra of thiolated compound **3c**

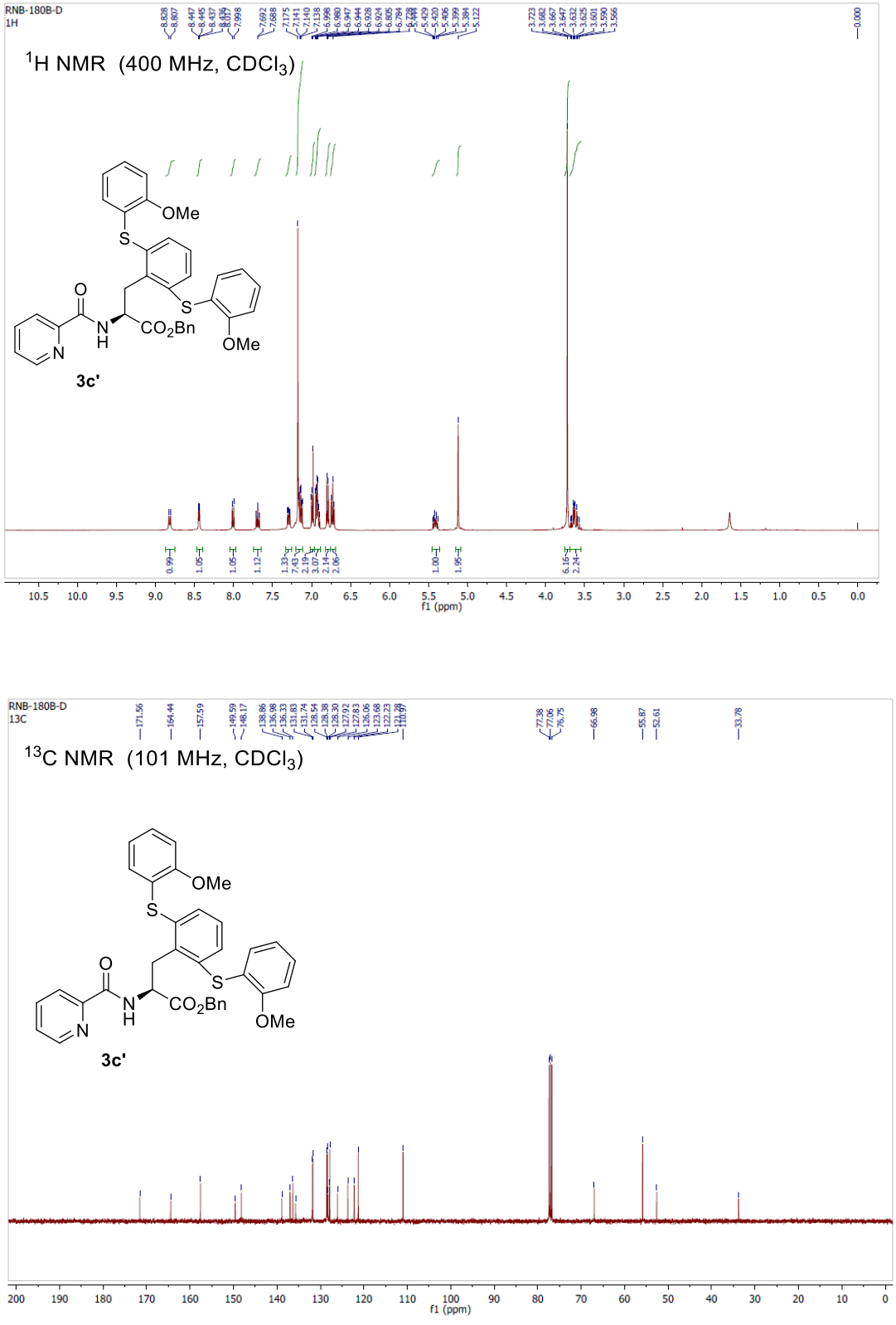


Fig S51. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3c'**

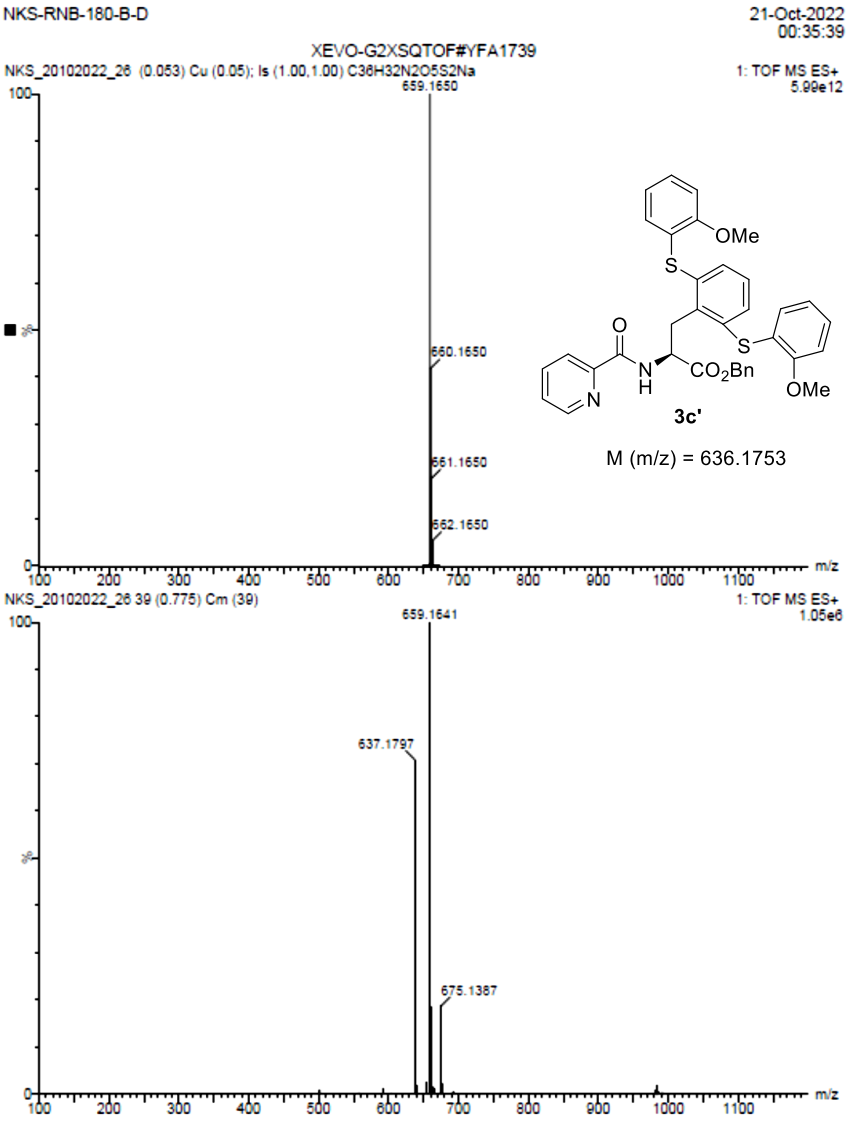
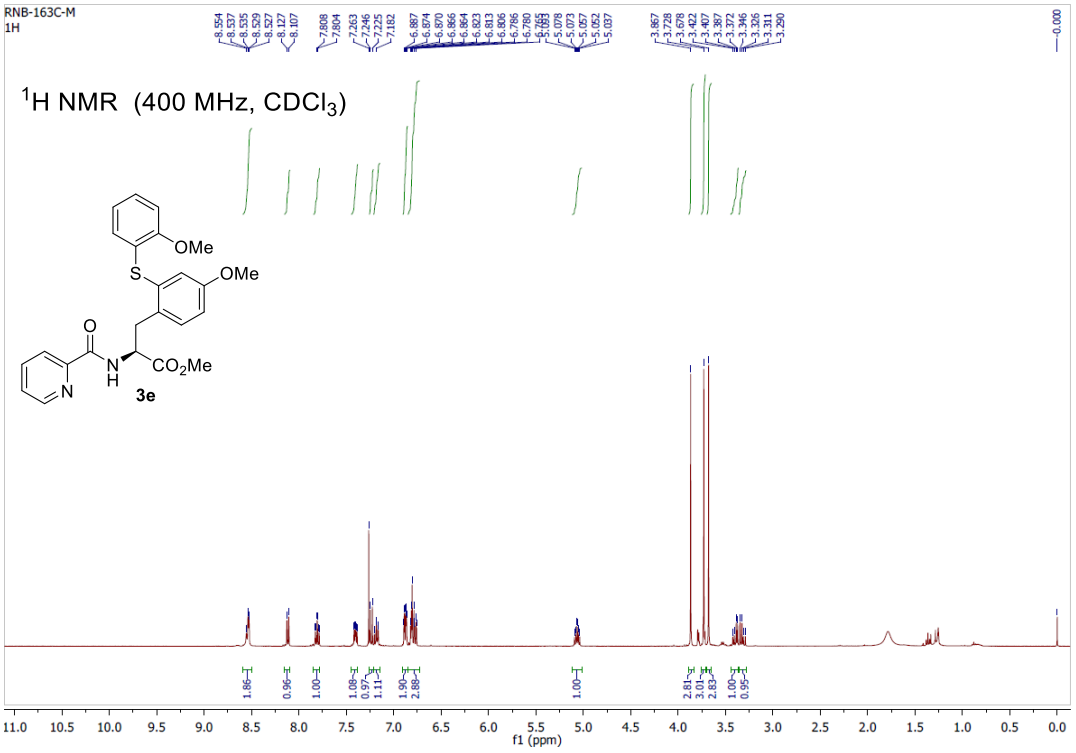


Fig S52. ESI-HRMS spectra of thiolated compound **3c'**



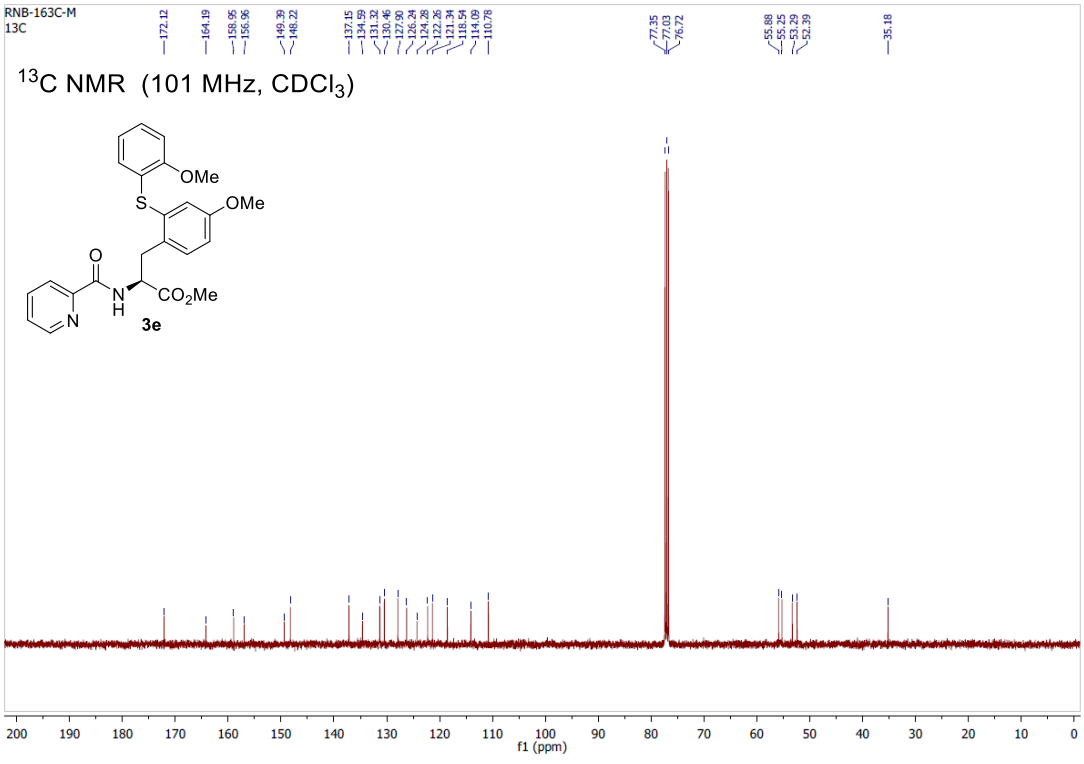


Fig S53. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3e**

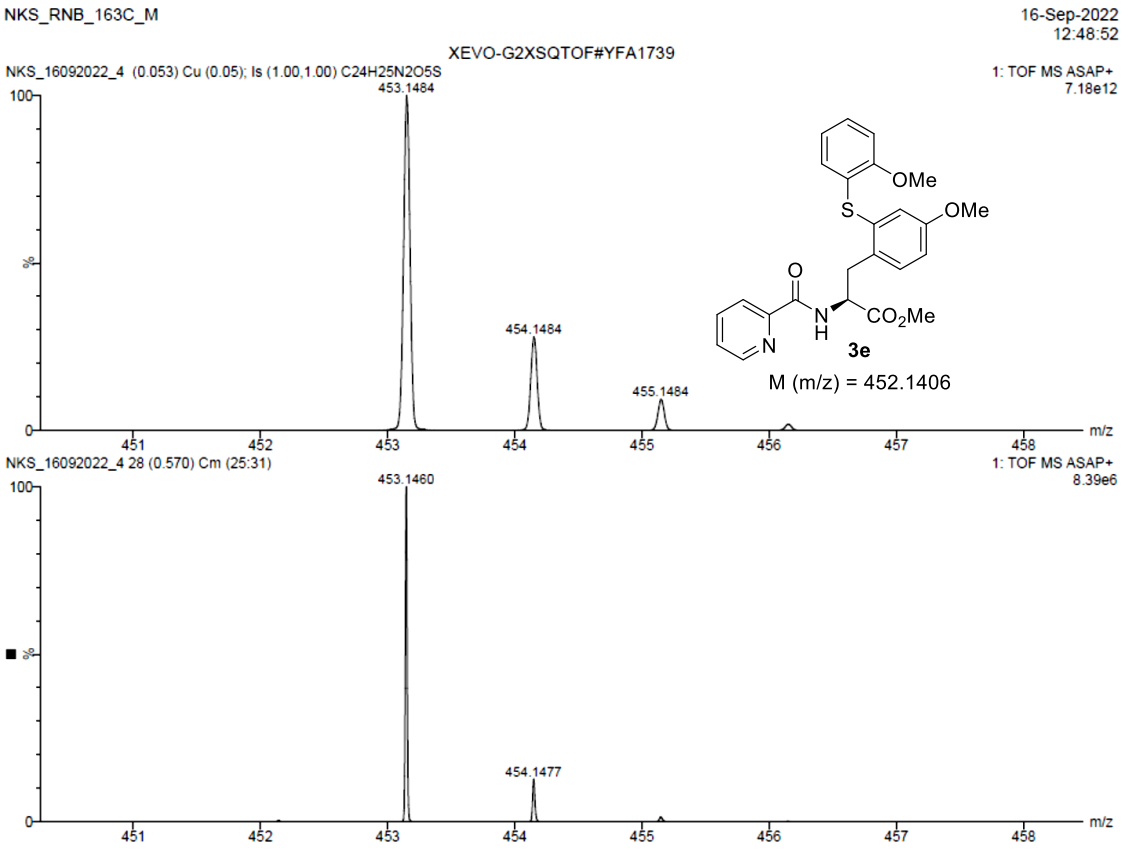
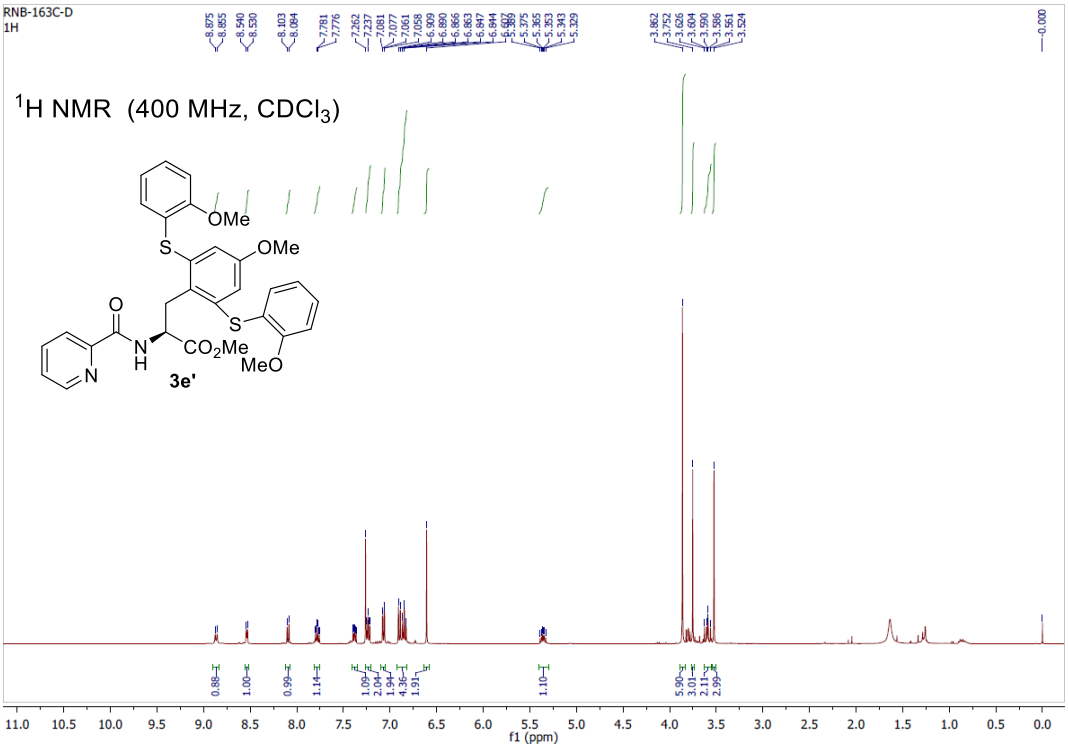


Fig S54. ESI-HRMS spectra of thiolated compound **3e**



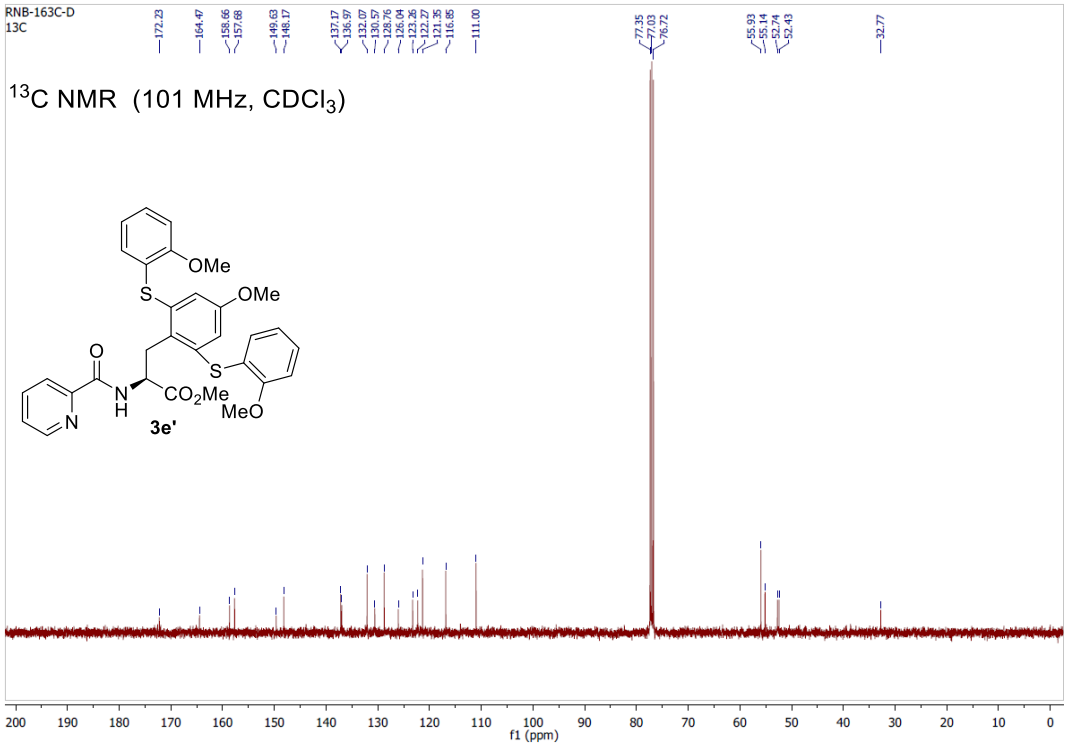


Fig S55. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3e'**

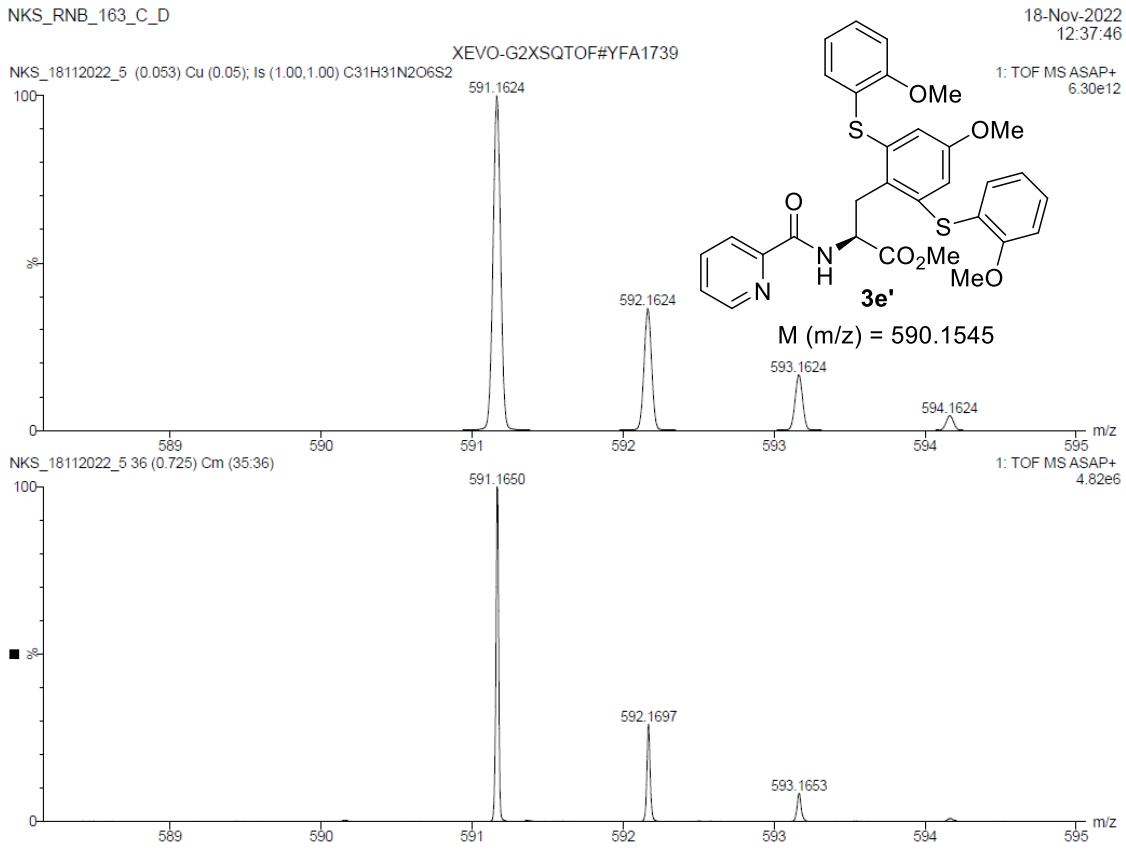


Fig S56. ASAP-HRMS spectra of thiolated compound **3e'**

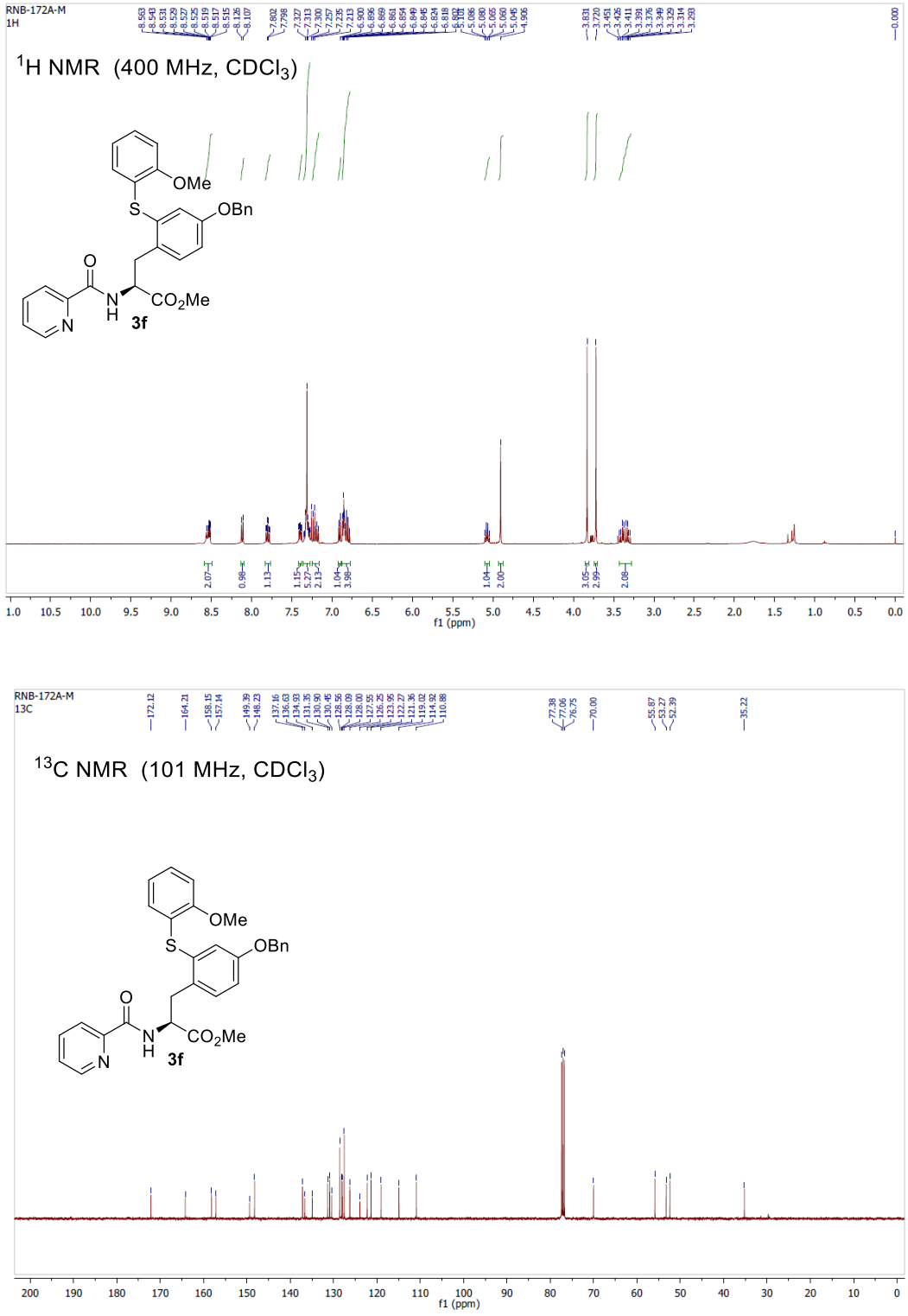


Fig S57. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3f**

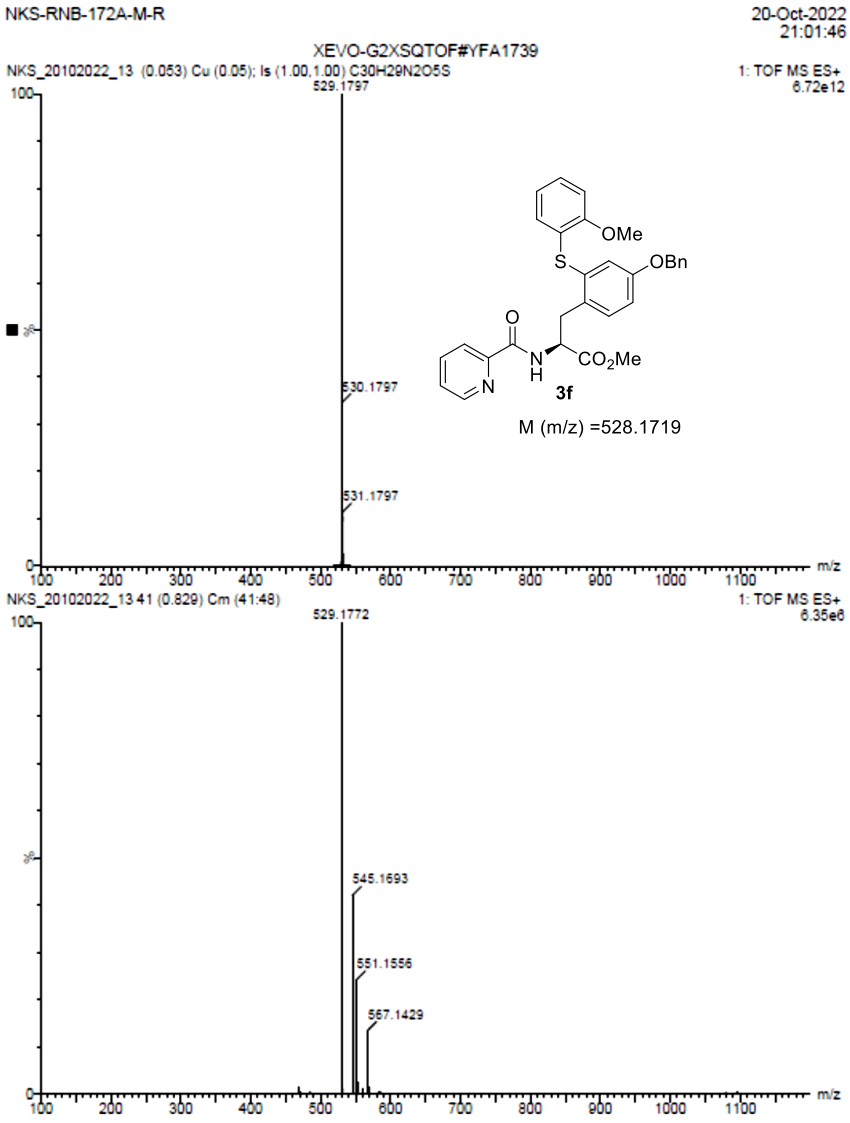
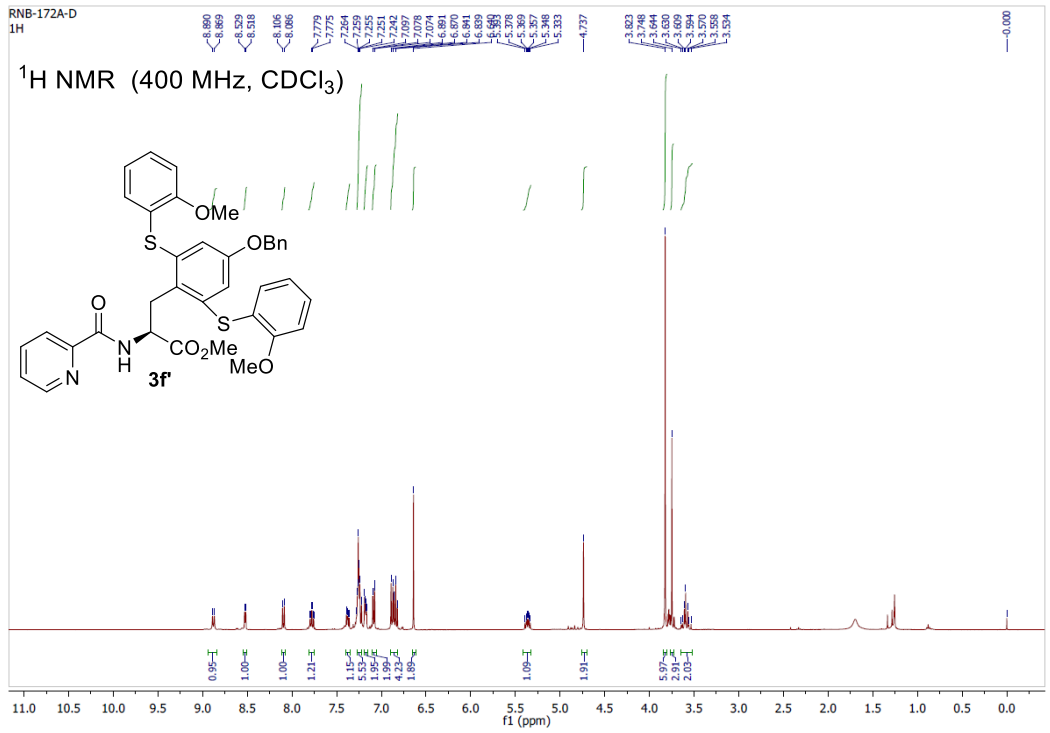


Fig S58. ESI-HRMS spectra of thiolated compound **3f**



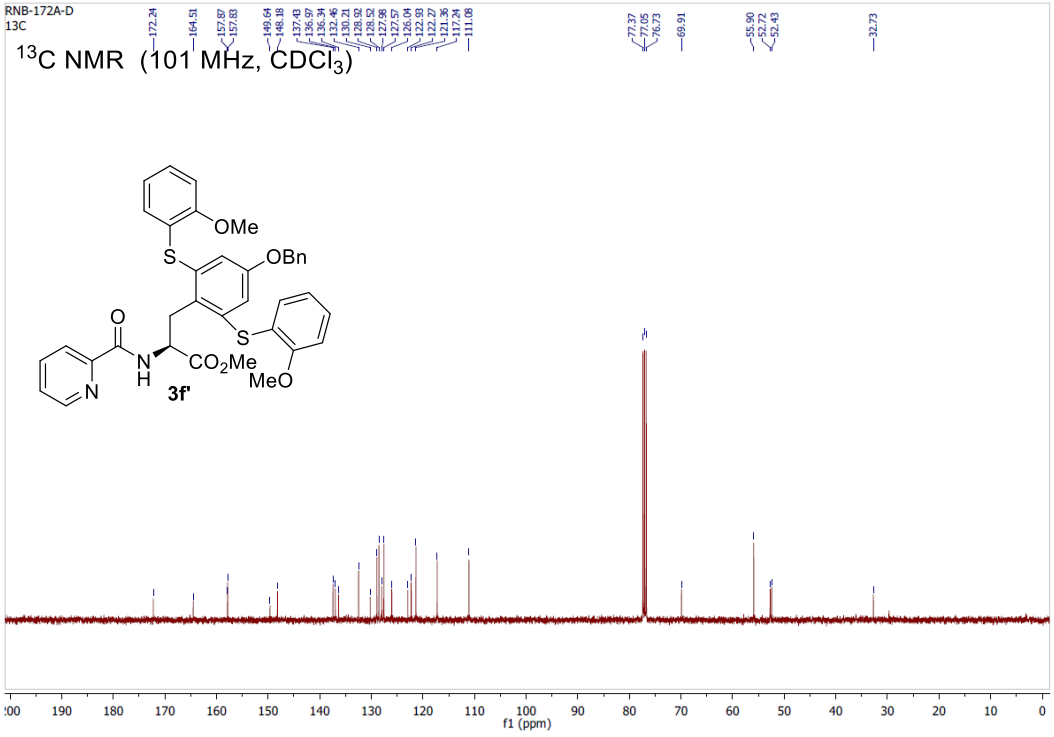


Fig S59. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3f'**

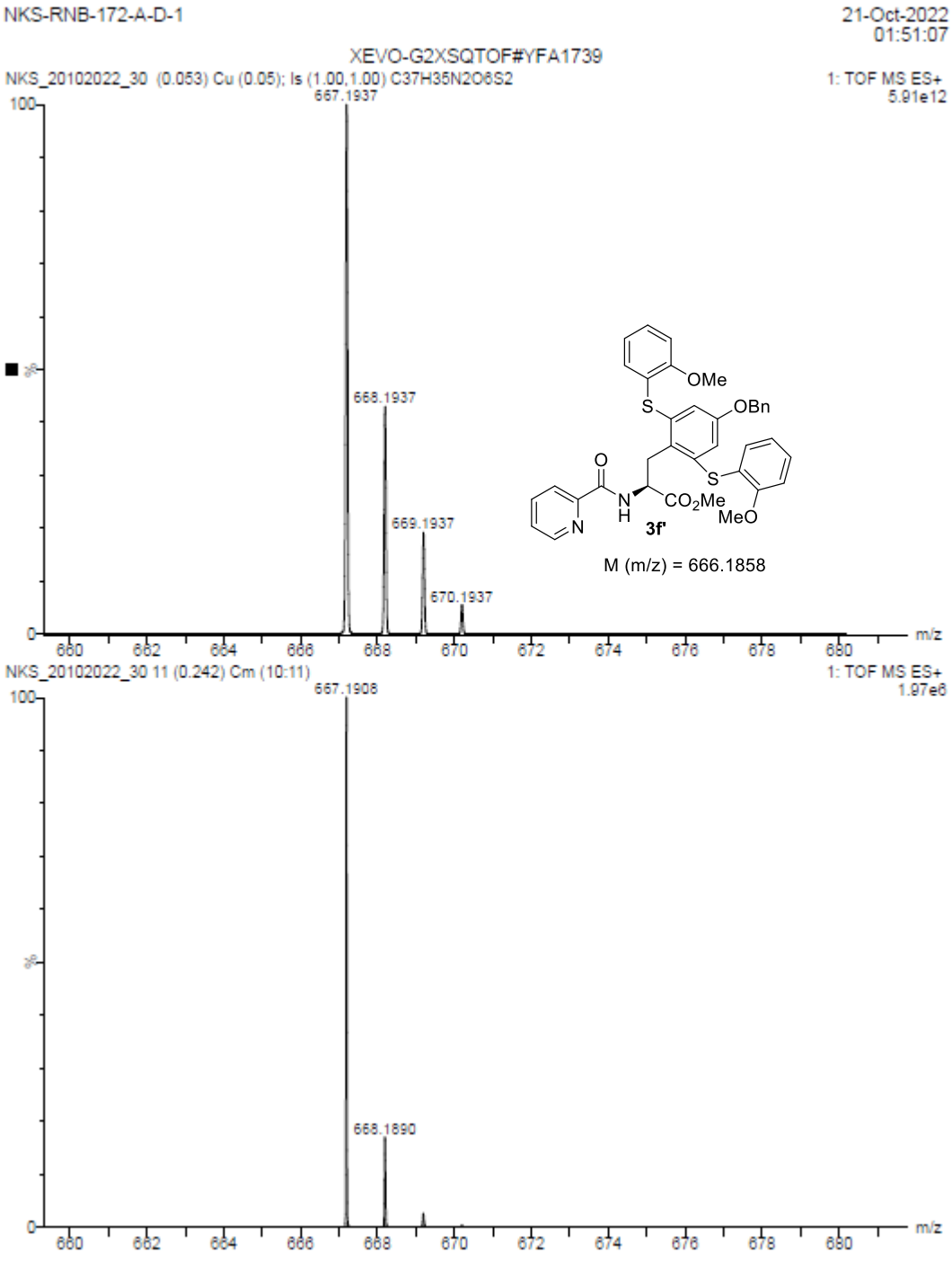


Fig S60. ESI-HRMS spectra of thiolated compound **3f'**

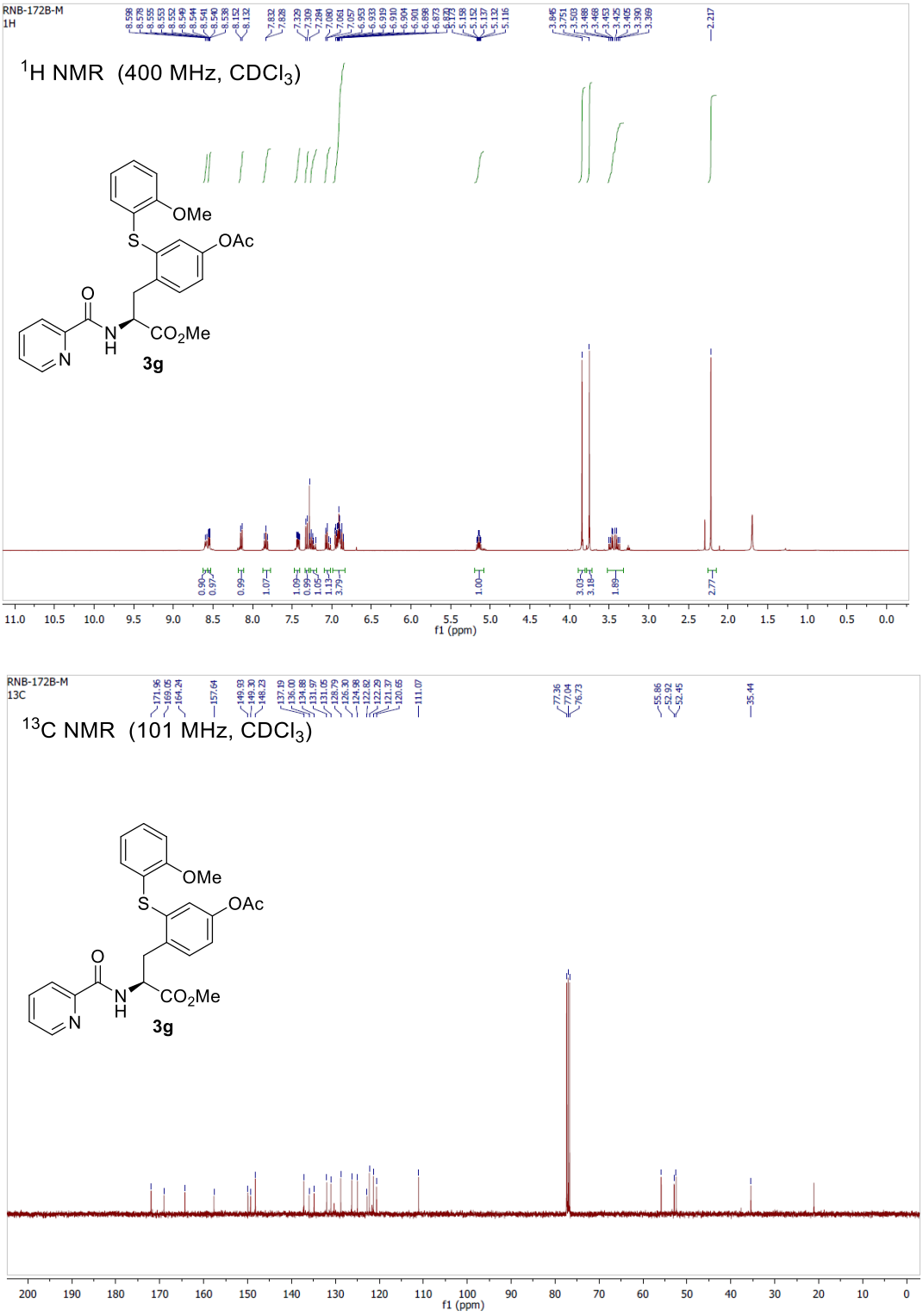


Fig S61. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3g**

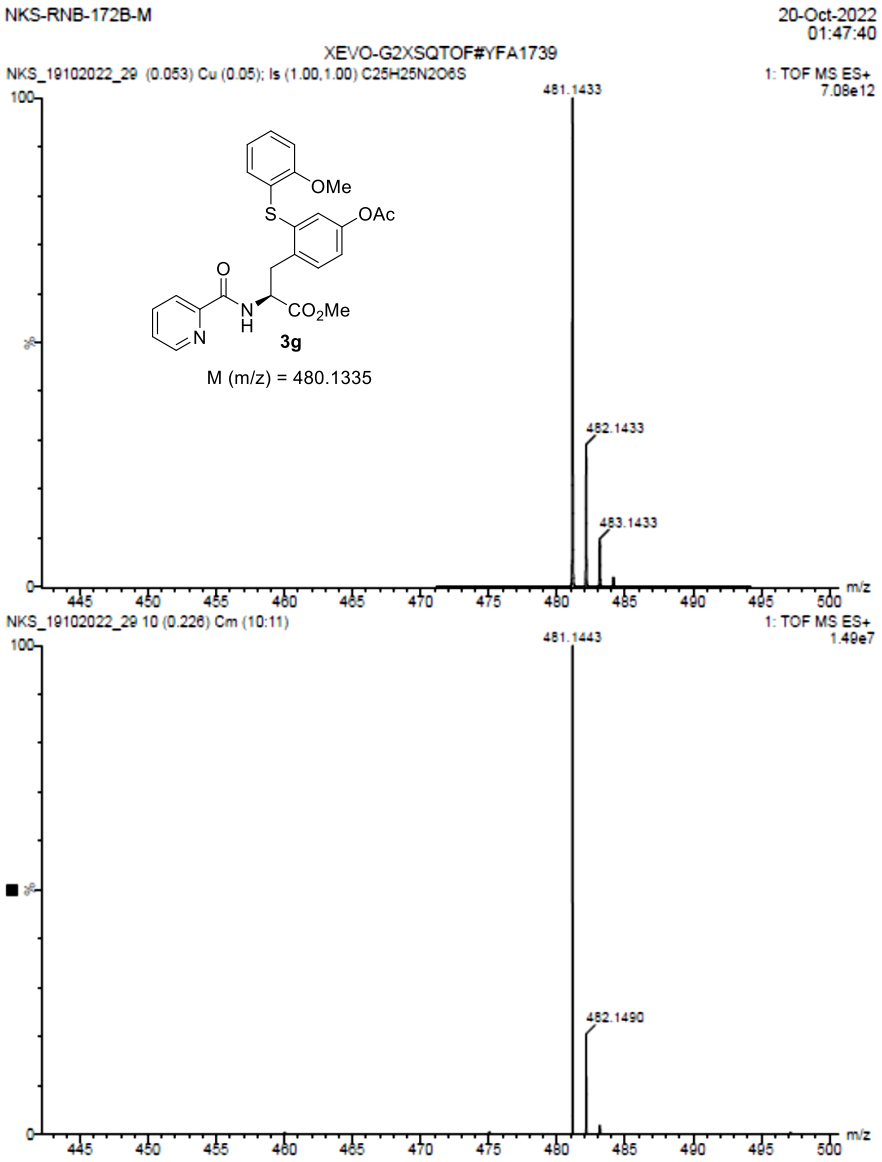
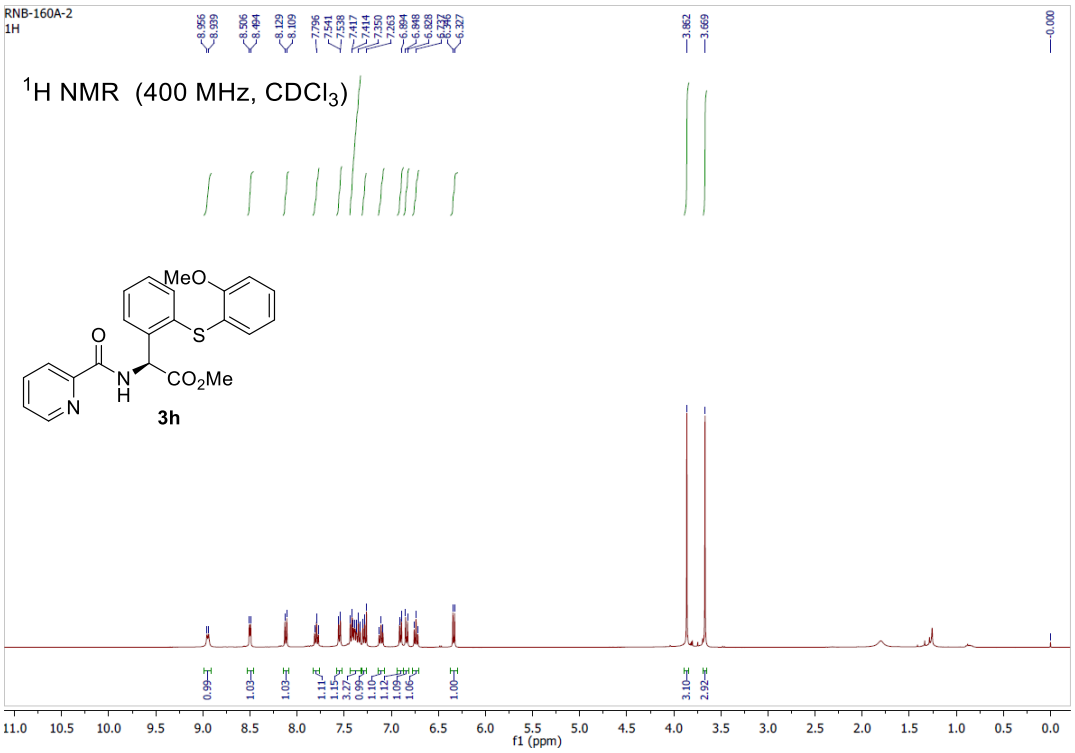


Fig S62. ESI-HRMS spectra of thiolated compound **3g**



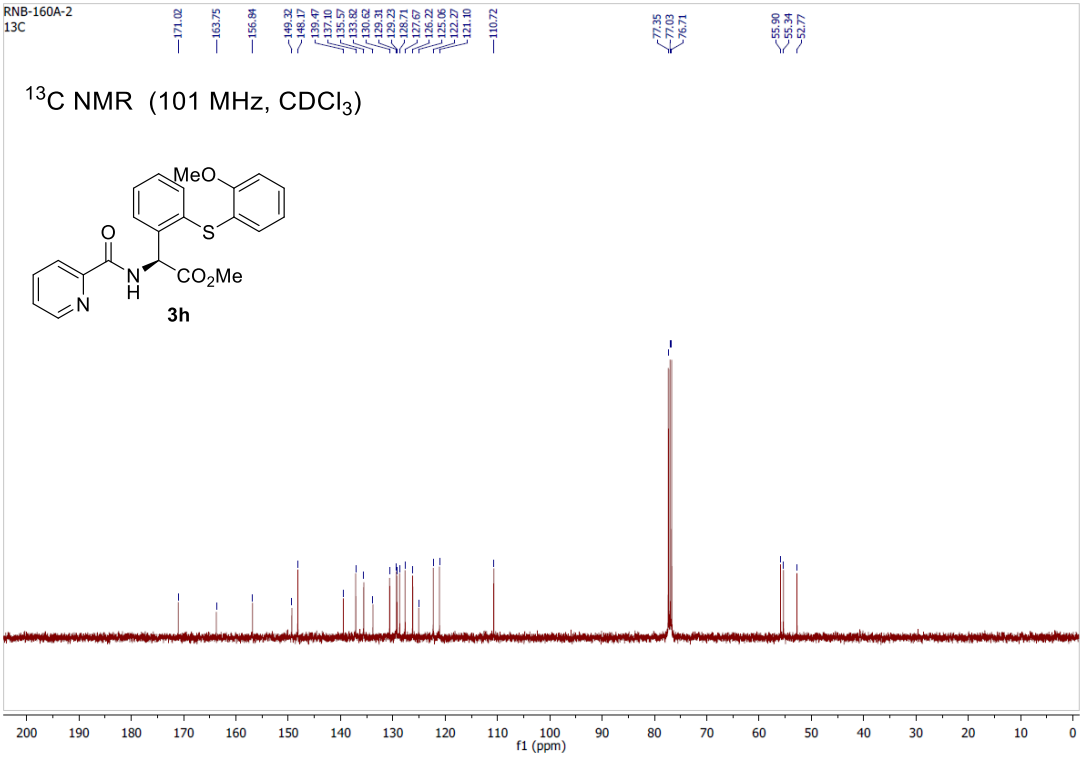


Fig S63. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3h**

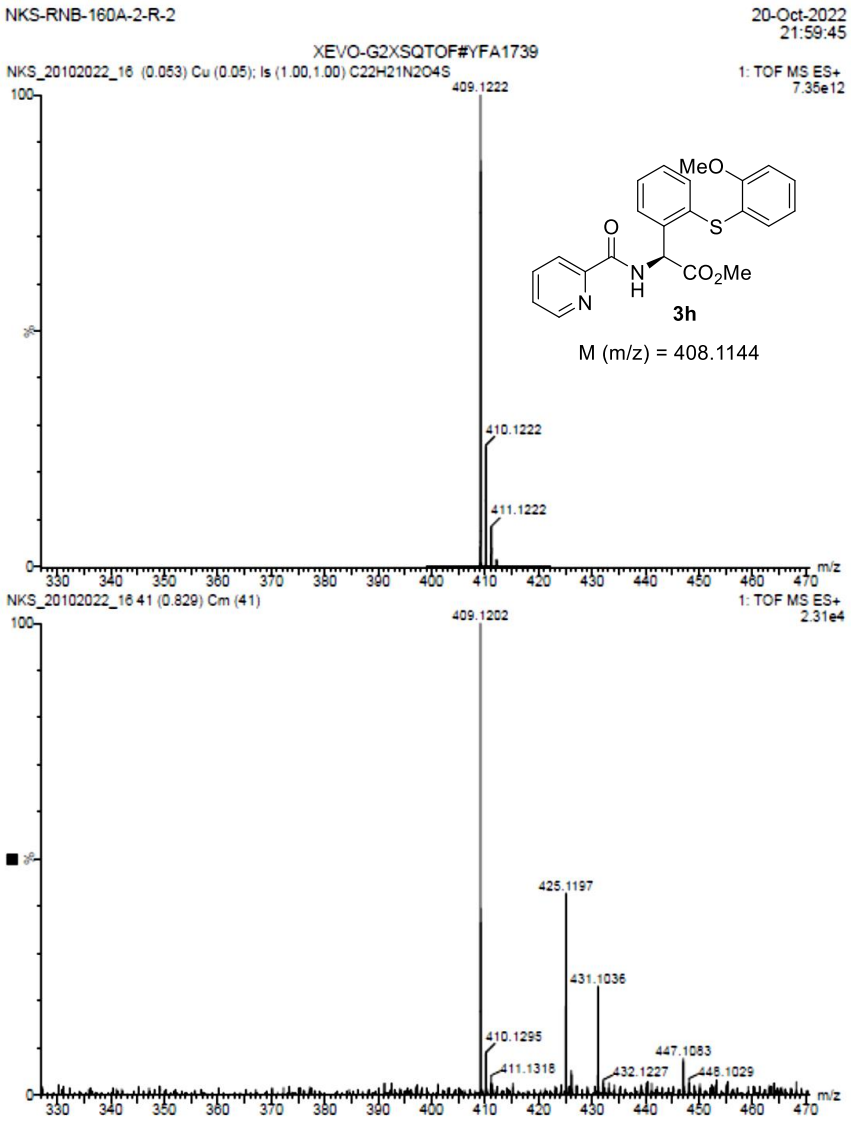


Fig S64. ESI-HRMS spectra of thiolated compound **3h**

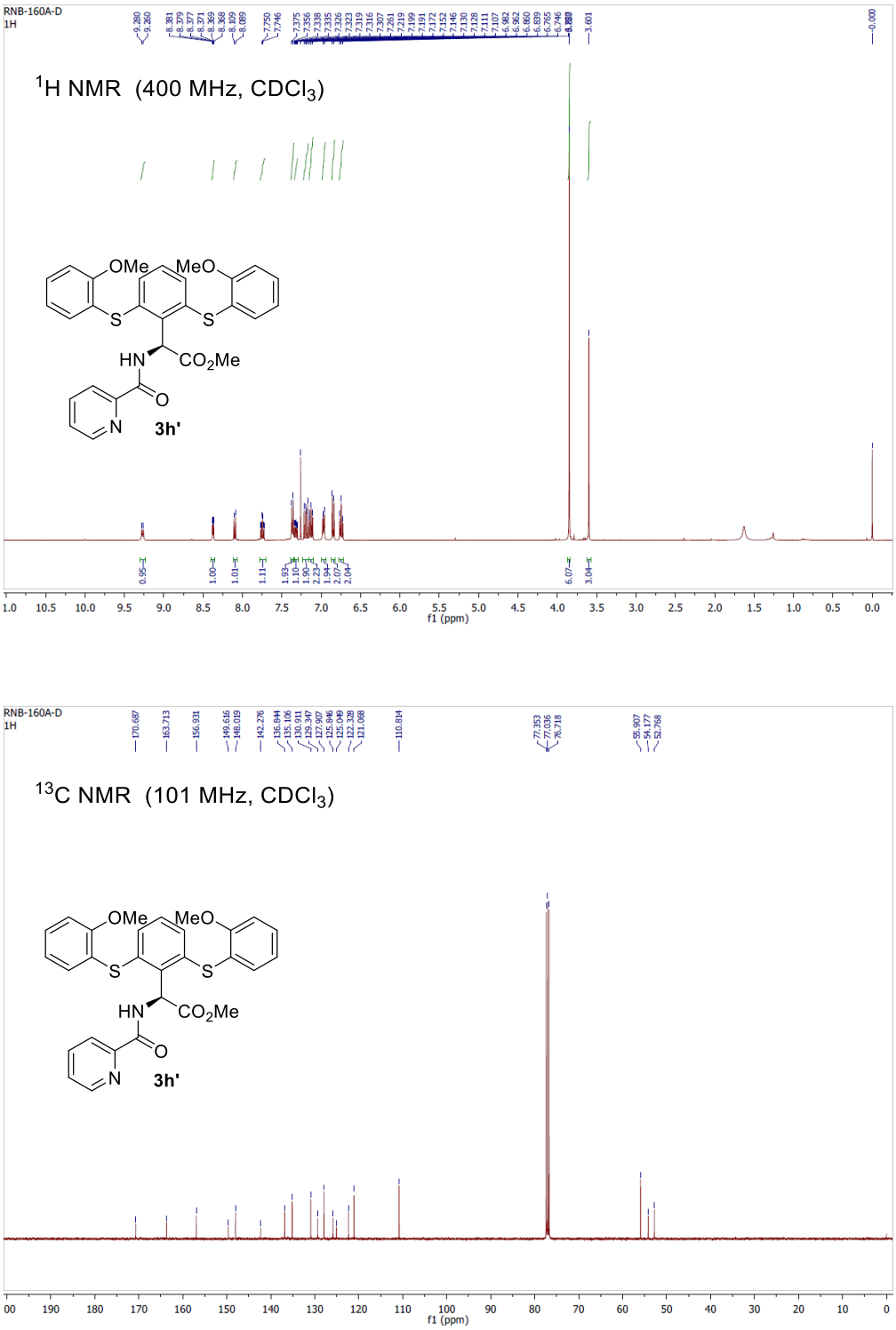


Fig S65. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3h'**

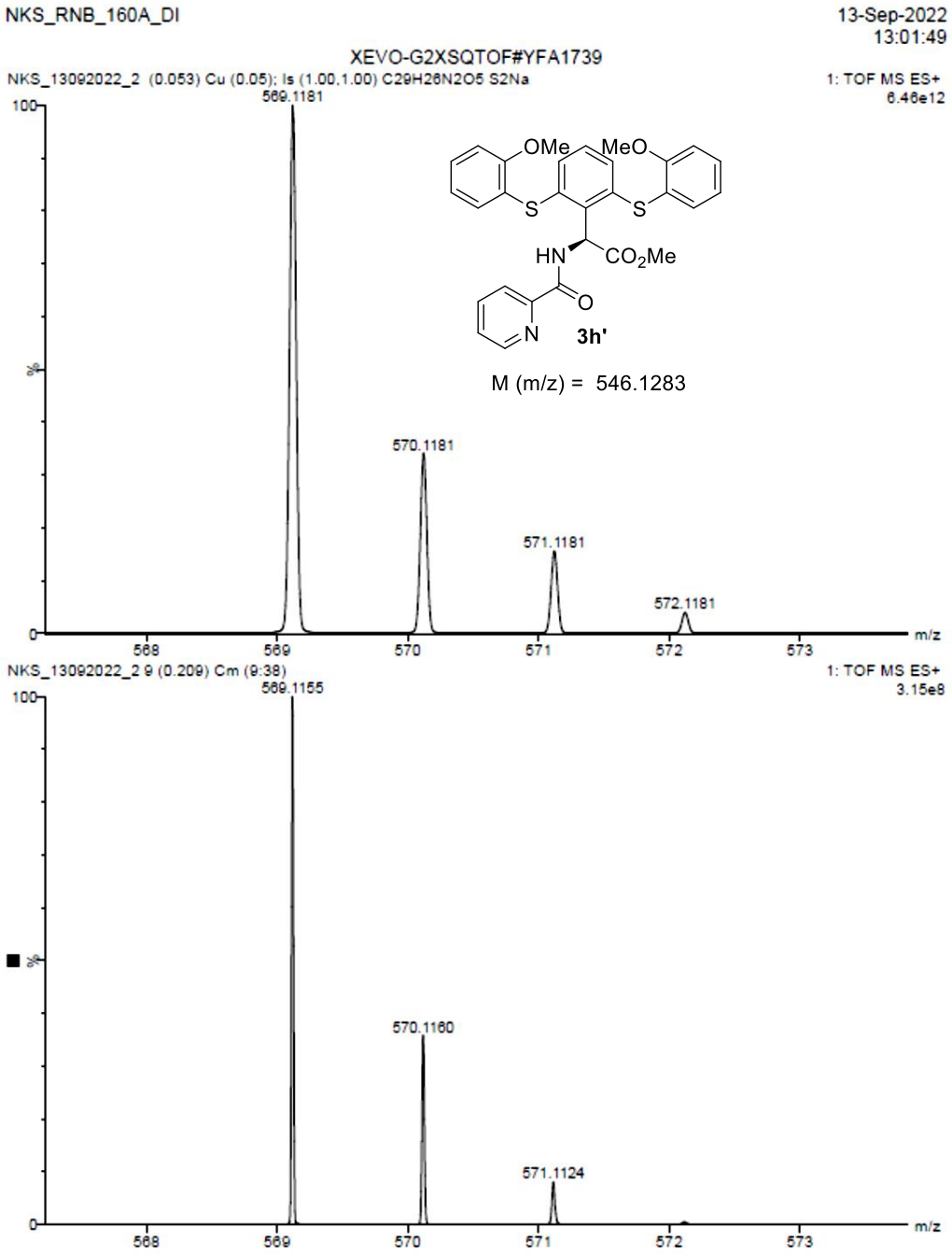
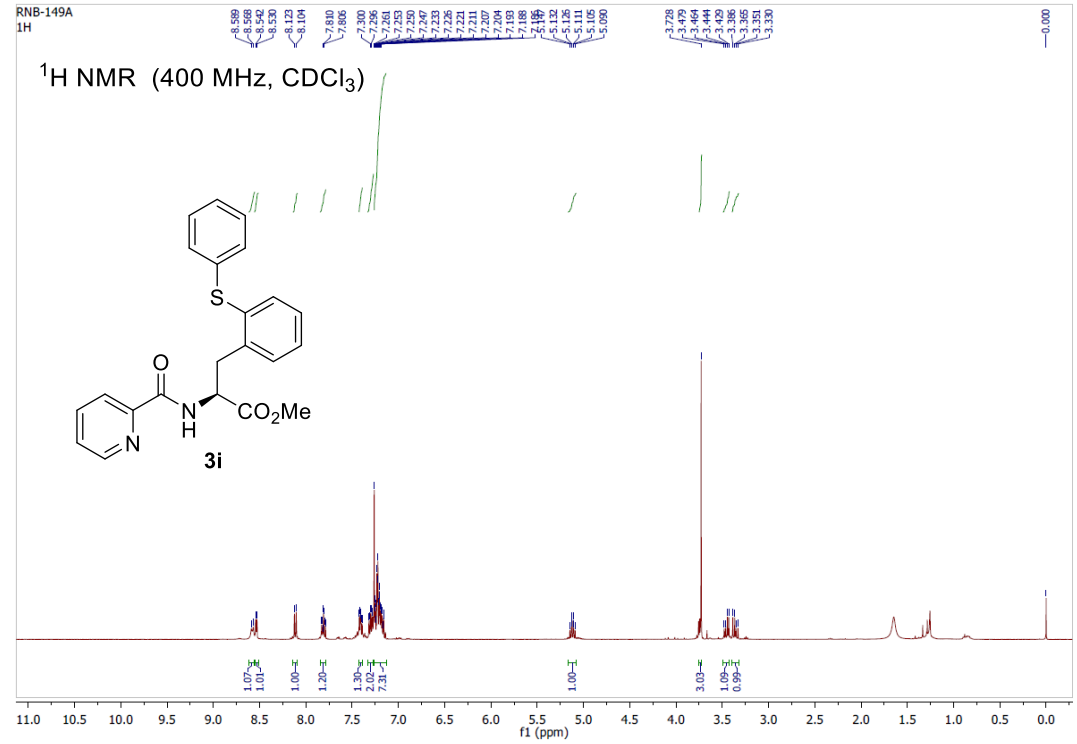


Fig S66. ESI-HRMS spectra of thiolated compound **3h'**



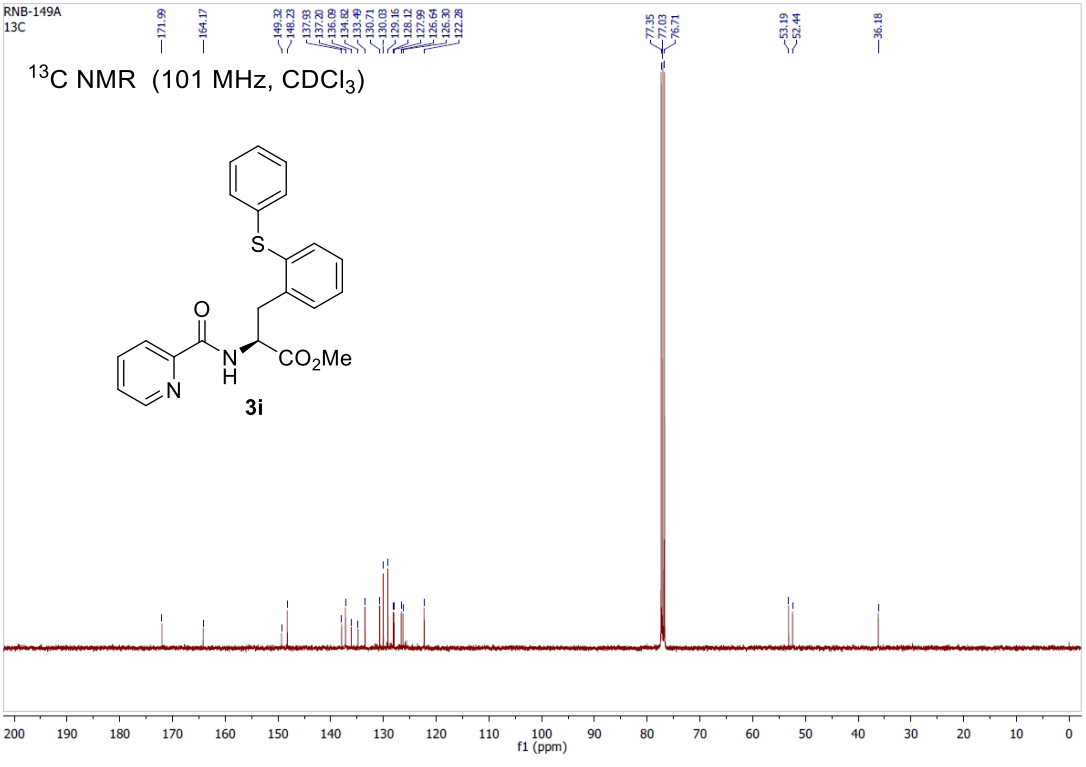


Fig S67. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3i**

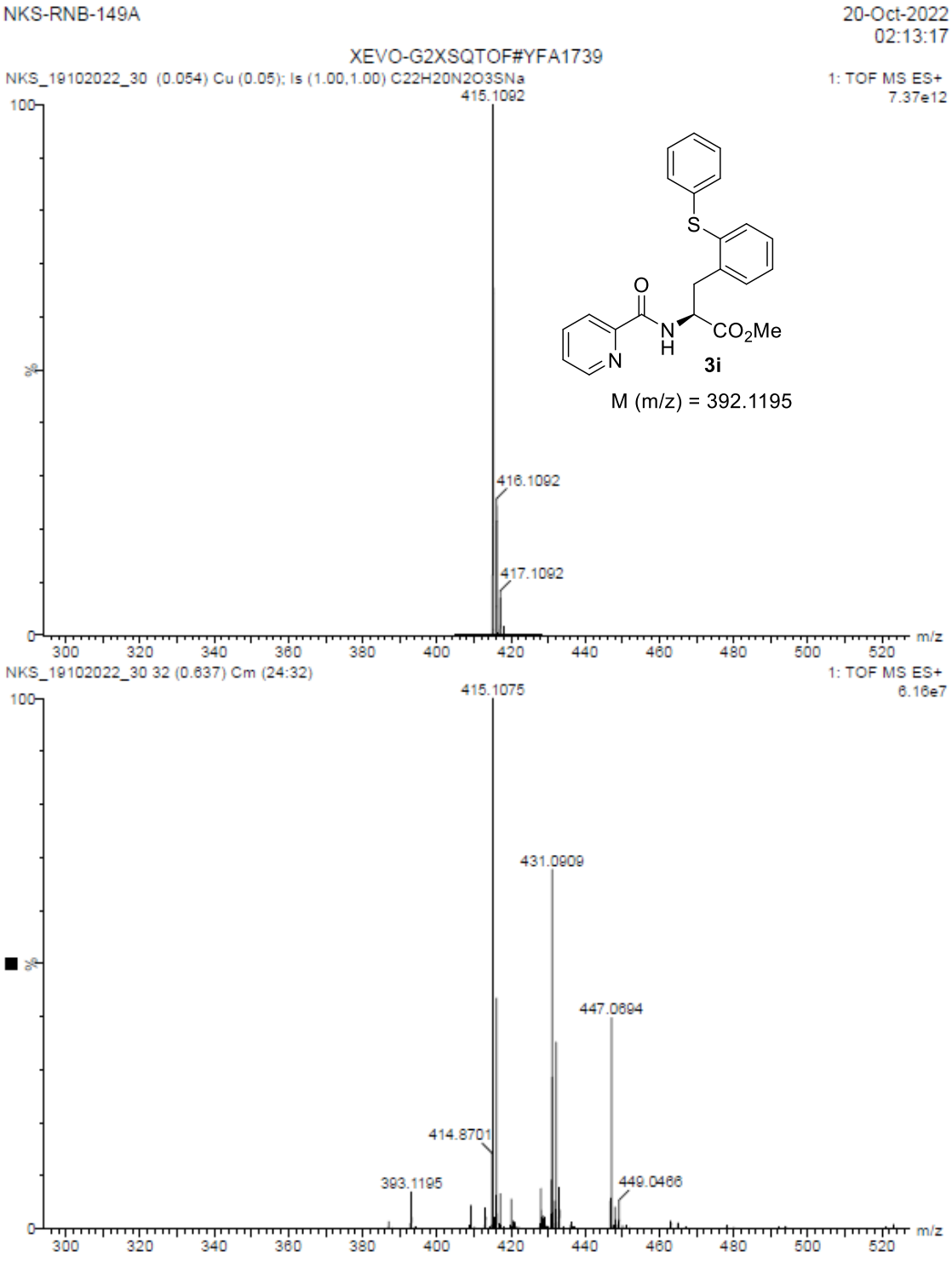


Fig S68. ESI-HRMS spectra of thiolated compound **3i**

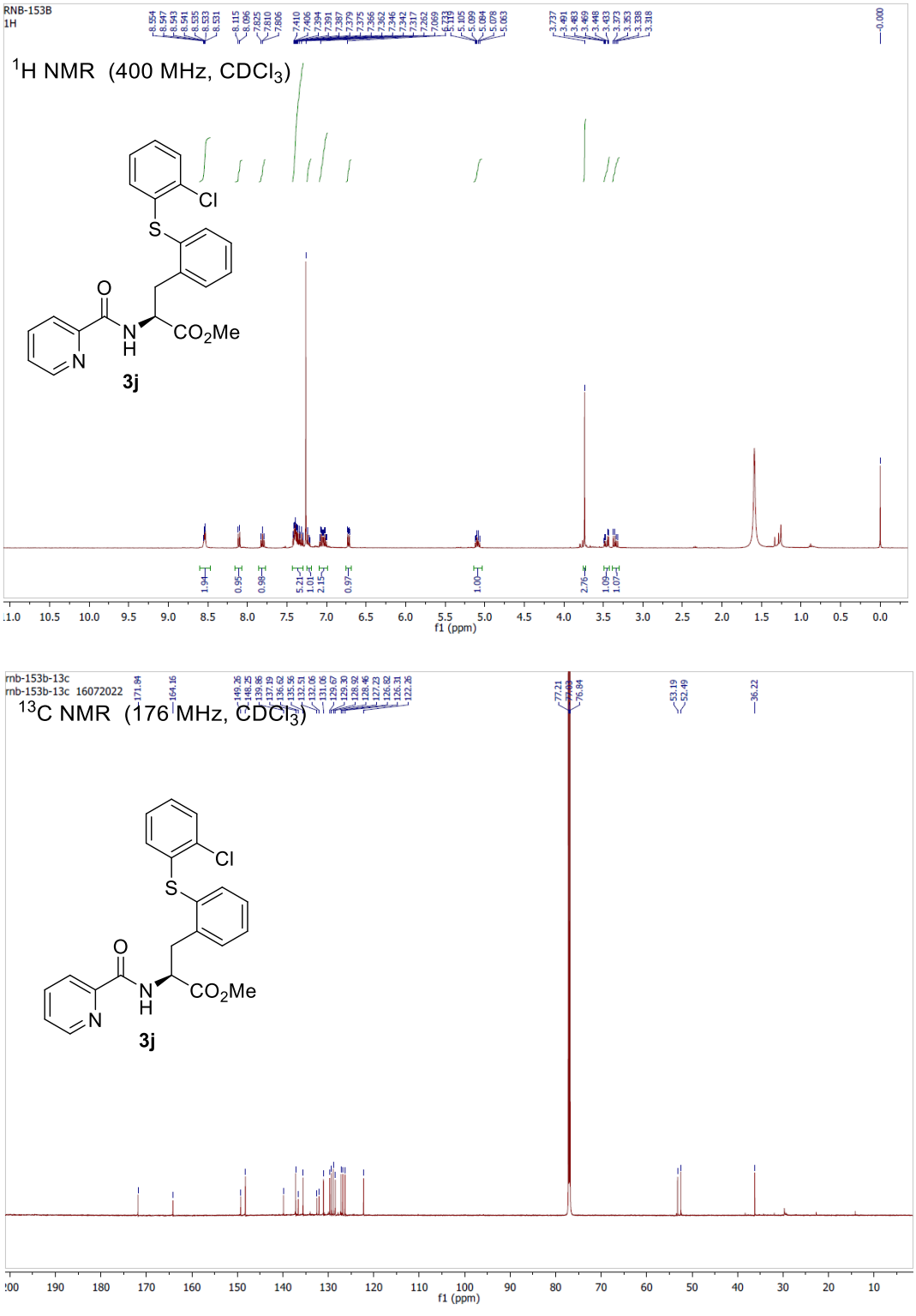


Fig S69. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3j**

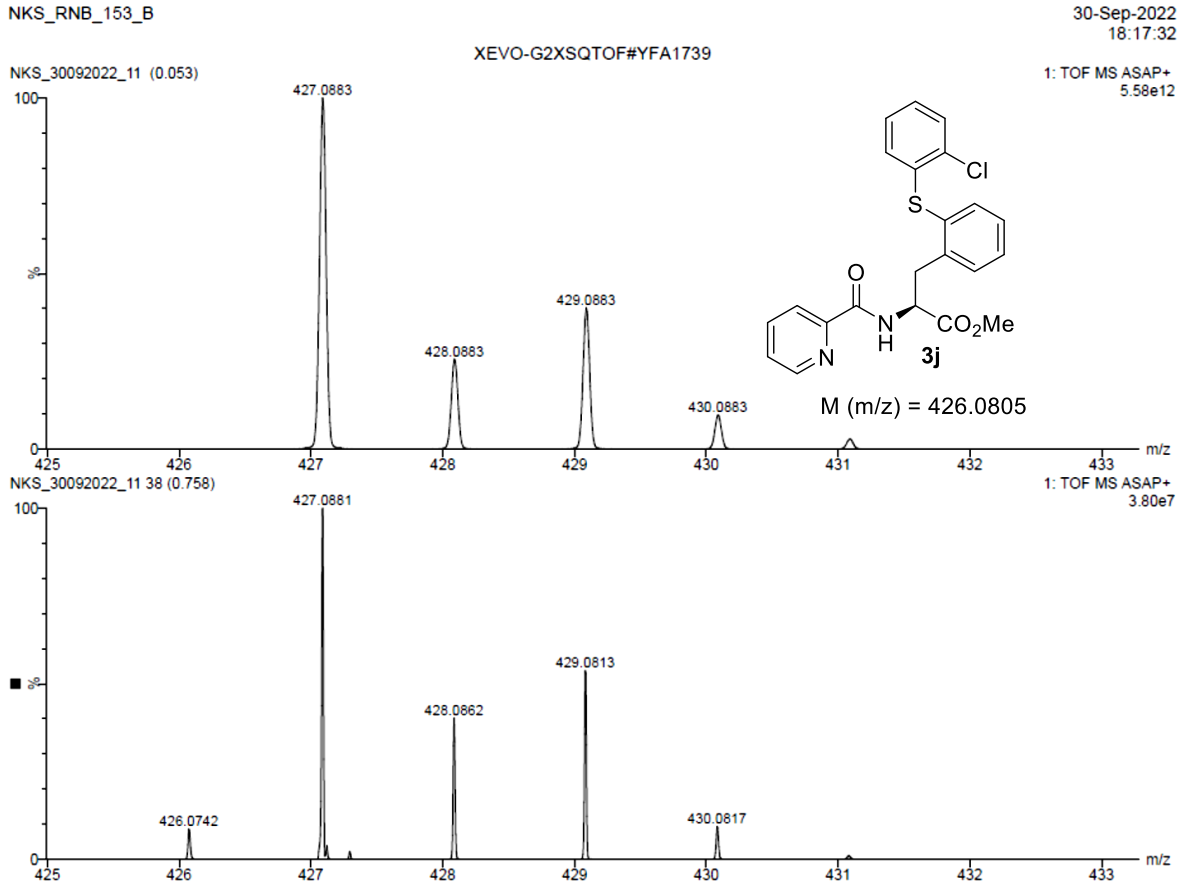


Fig S70. ASAP-HRMS spectra of thiolated compound **3j**

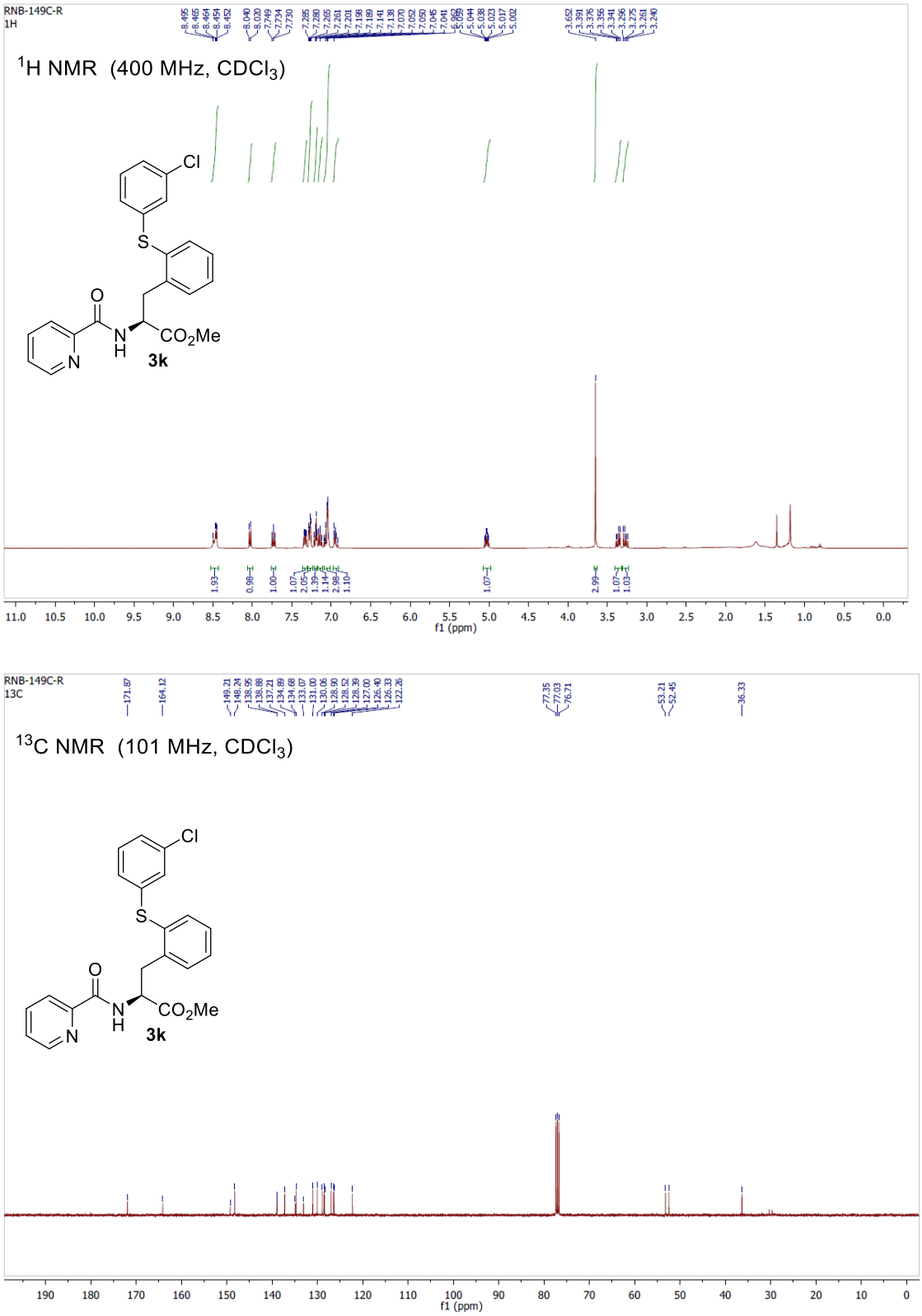


Fig S71. ^{1}H, ^{13}C $\{^{1}H\}$ NMR spectra of thiolated compound **3k**

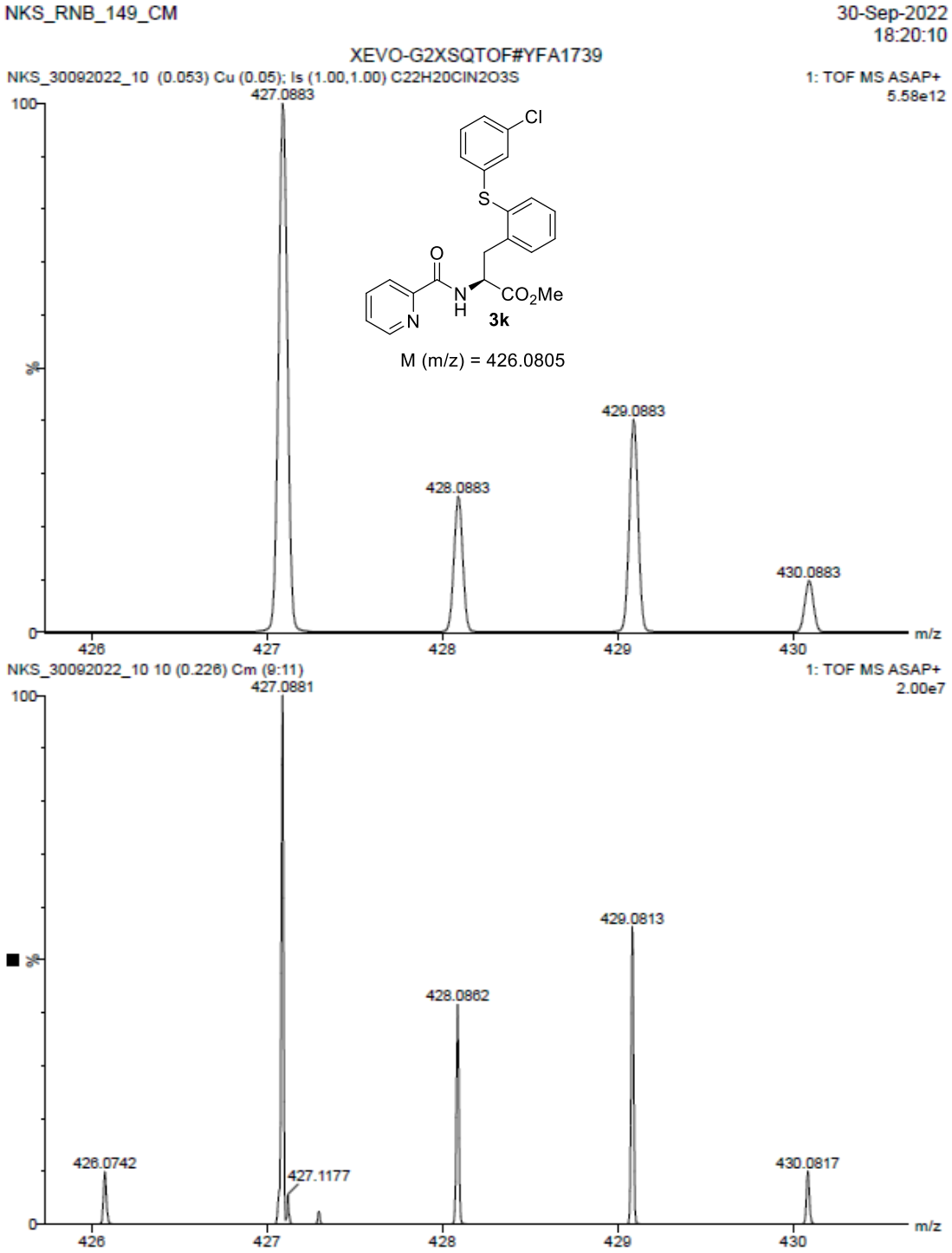
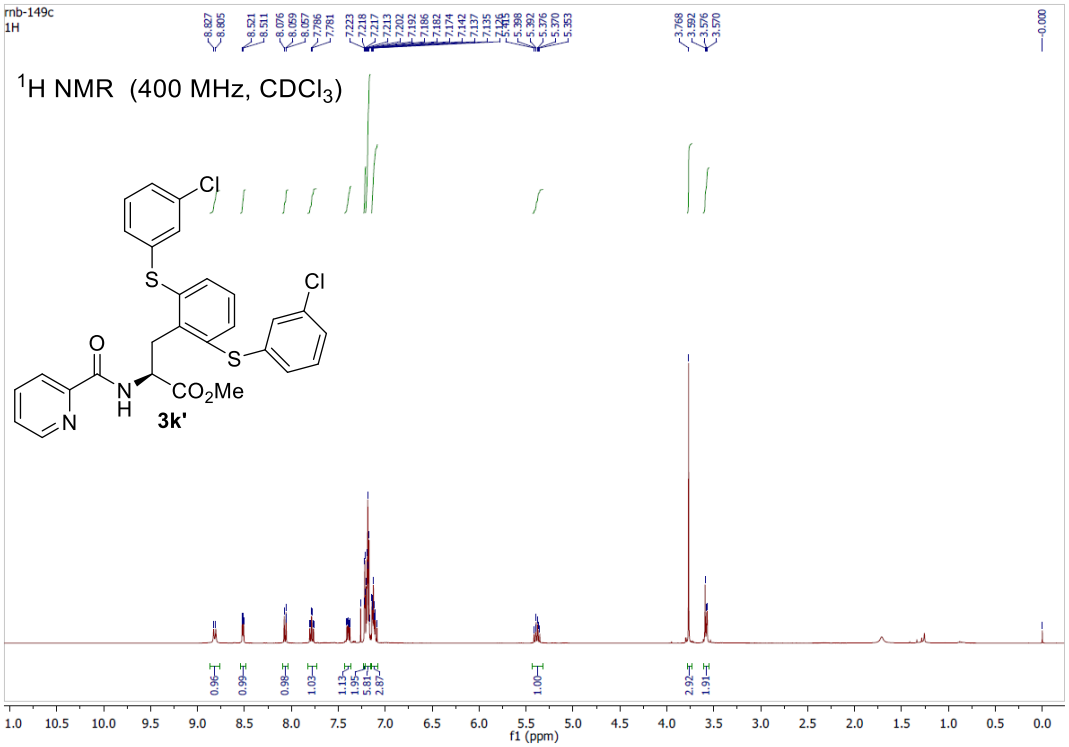


Fig S72. ASAP-HRMS spectra of thiolated compound **3k**



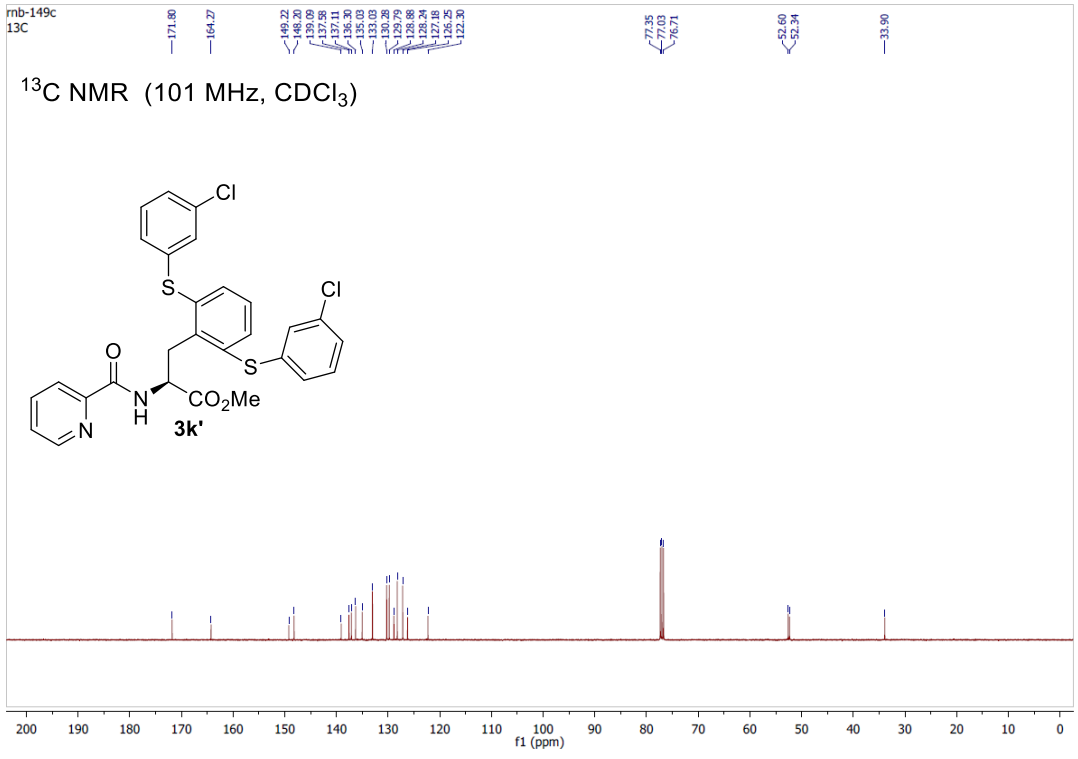


Fig S73. ^{1}H, ^{13}C $\{^{1}H\}$ NMR spectra of thiolated compound **3k'**

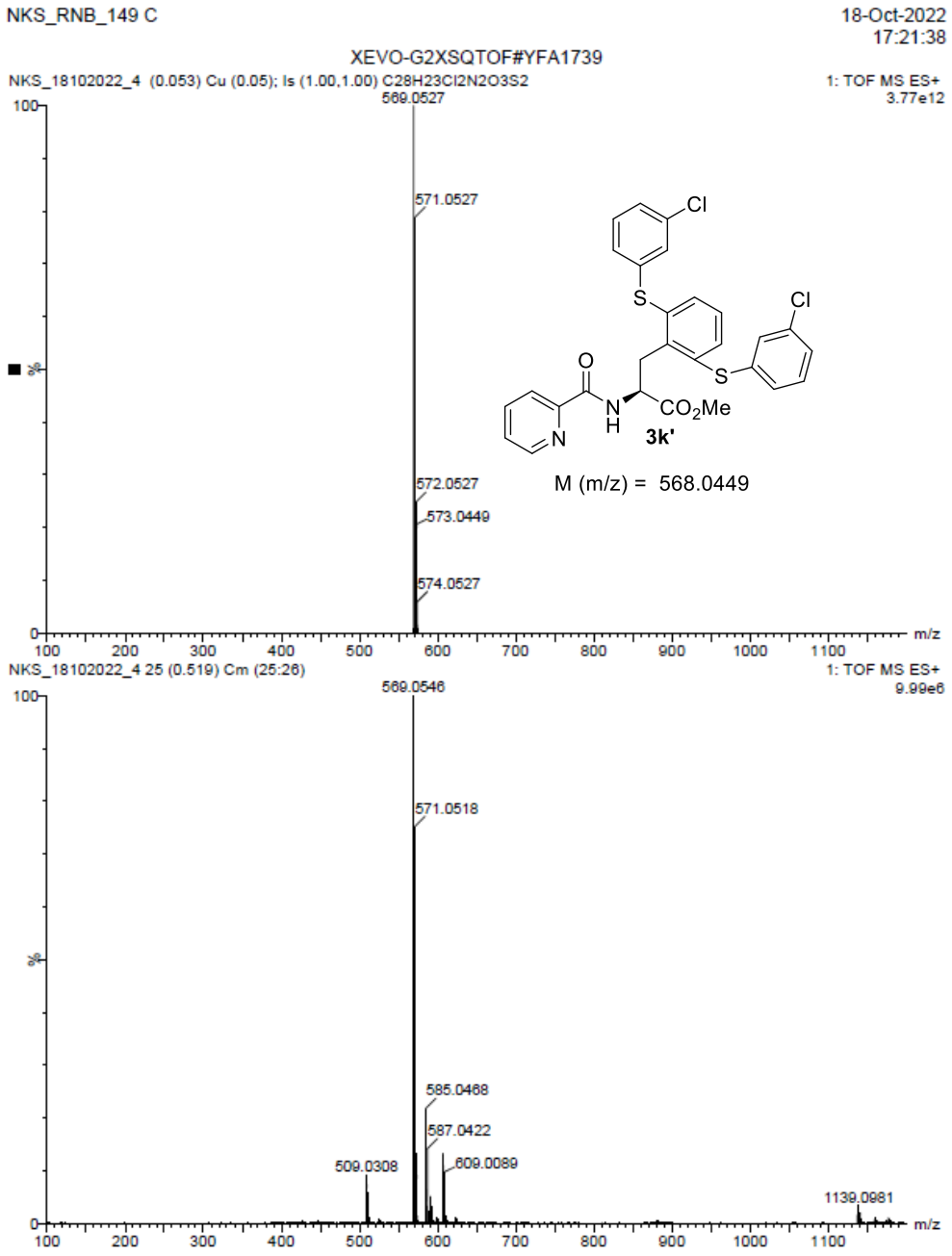


Fig S74. ESI-HRMS spectra of thiolated compound **3k'**

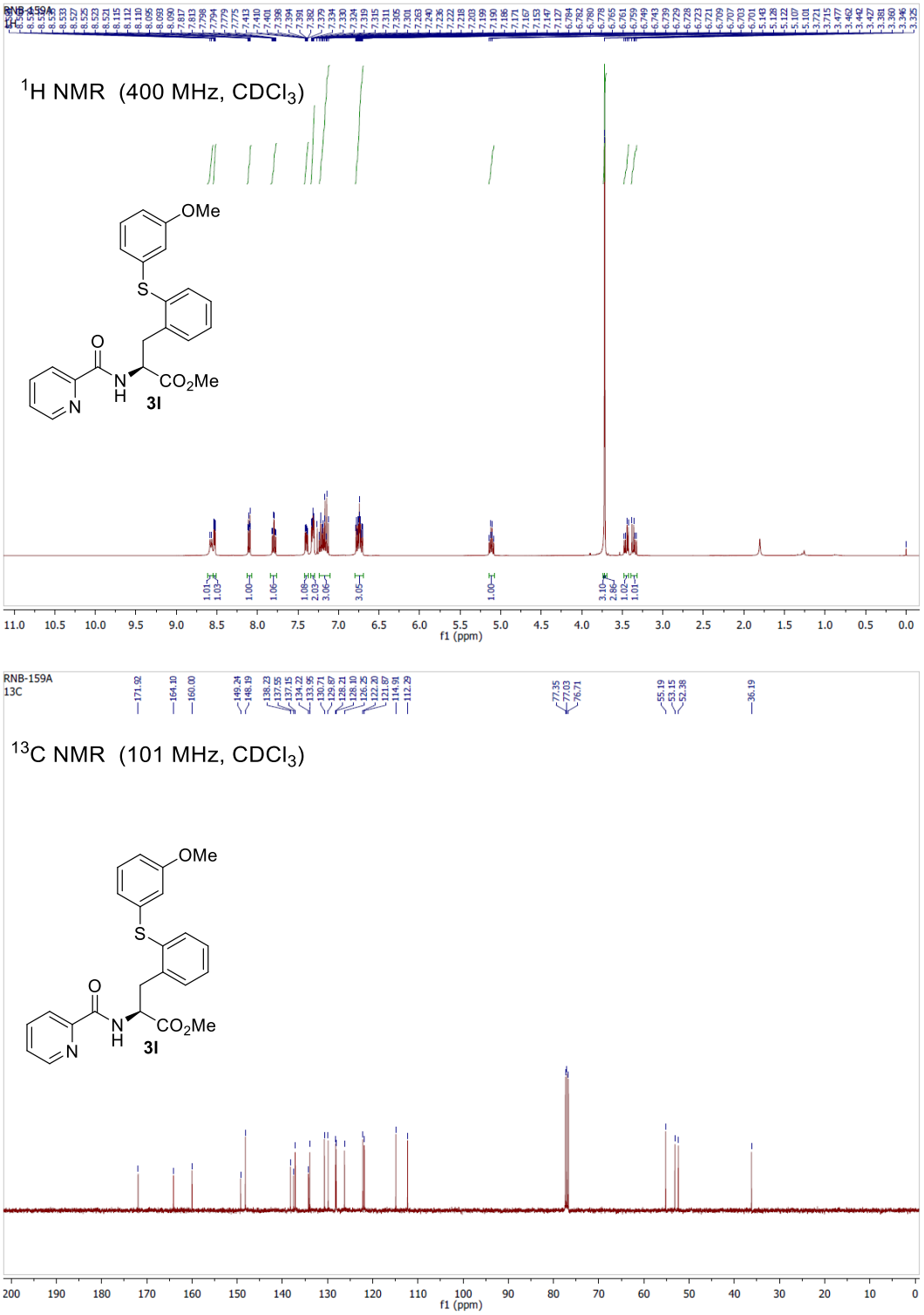


Fig S75. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3l**

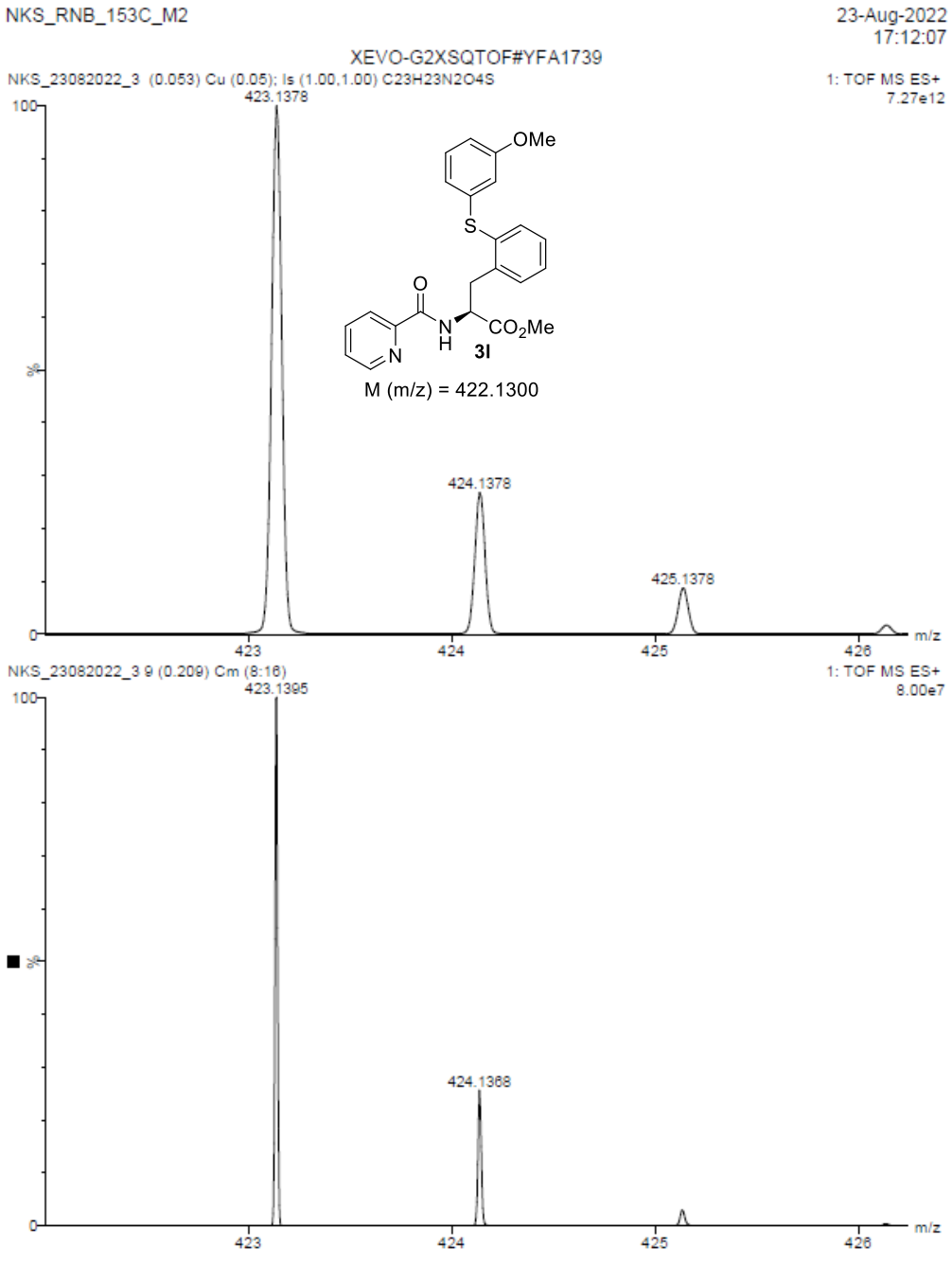


Fig S76. ESI-HRMS spectra of thiolated compound **3l**

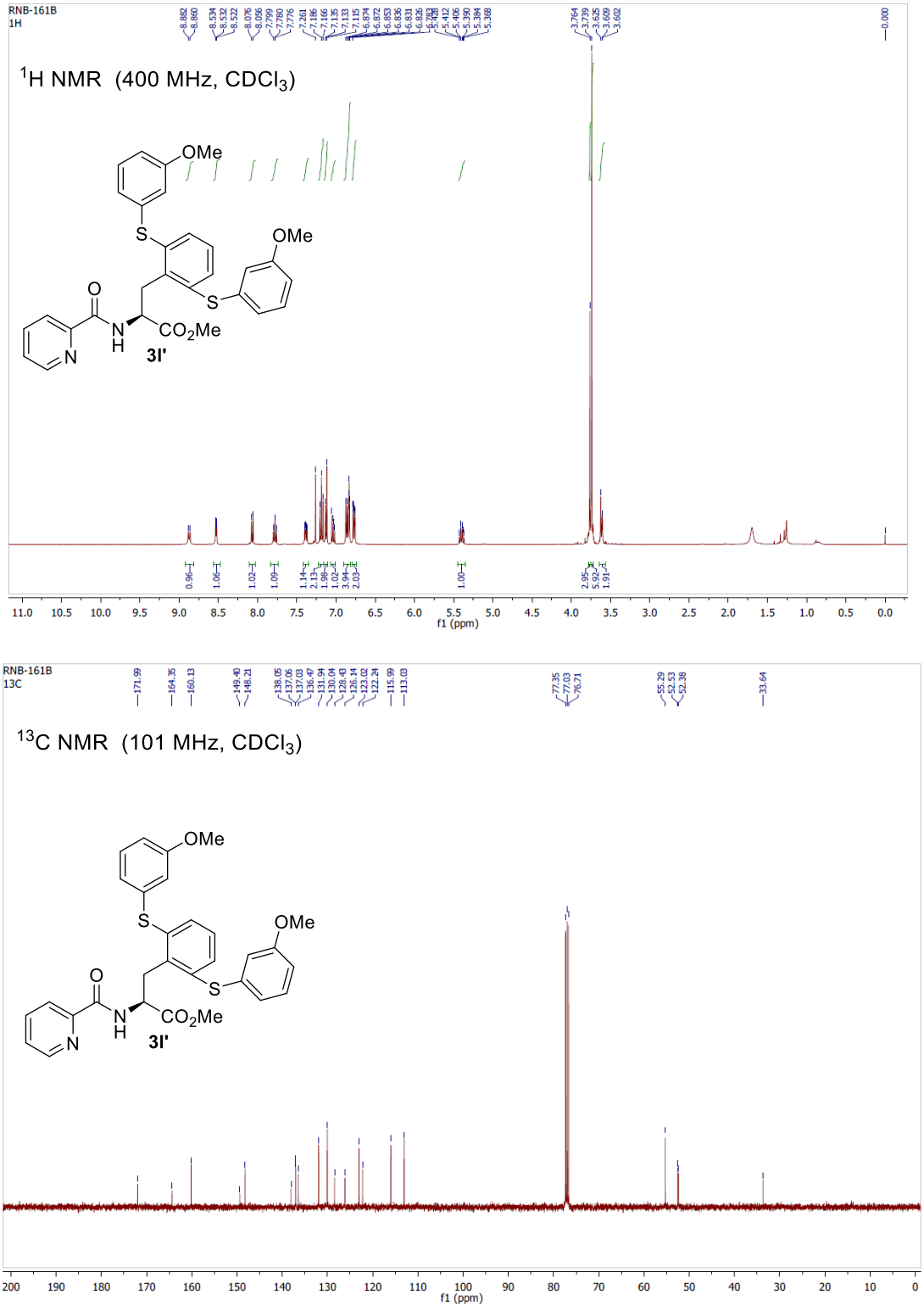


Fig S77. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3l'**

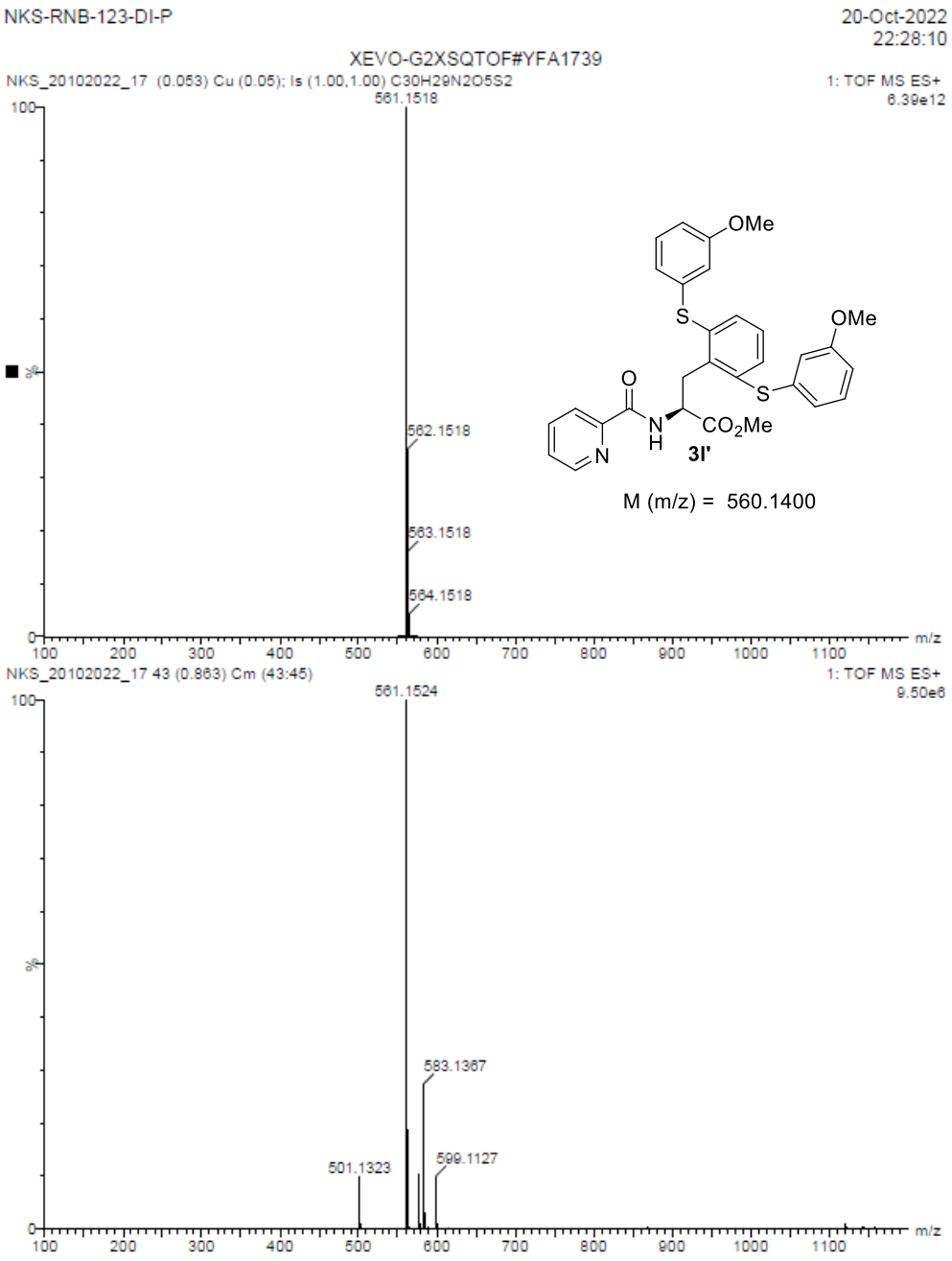


Fig S78. ESI-HRMS spectra of thiolated compound **3l'**

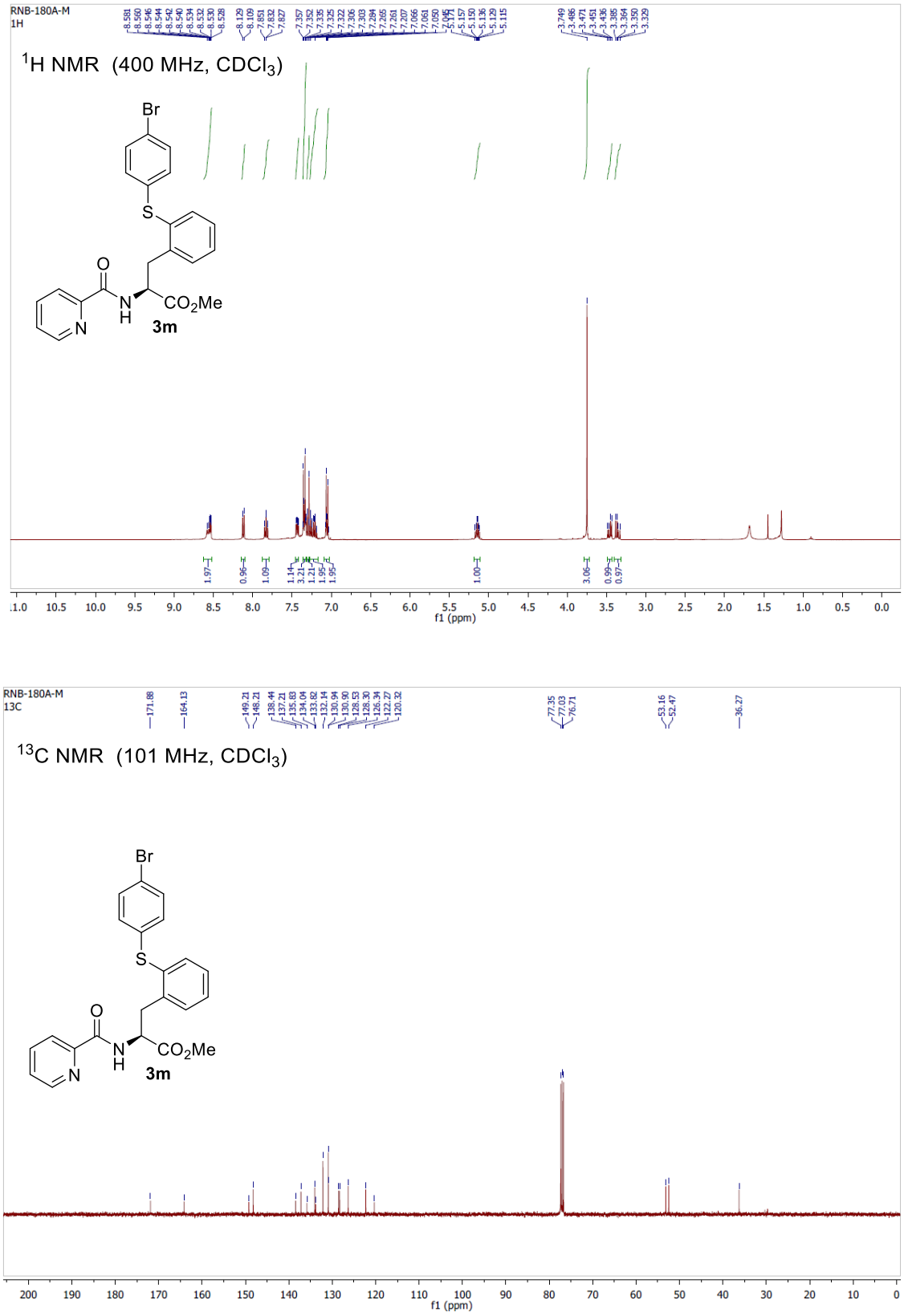


Fig S79. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3m**

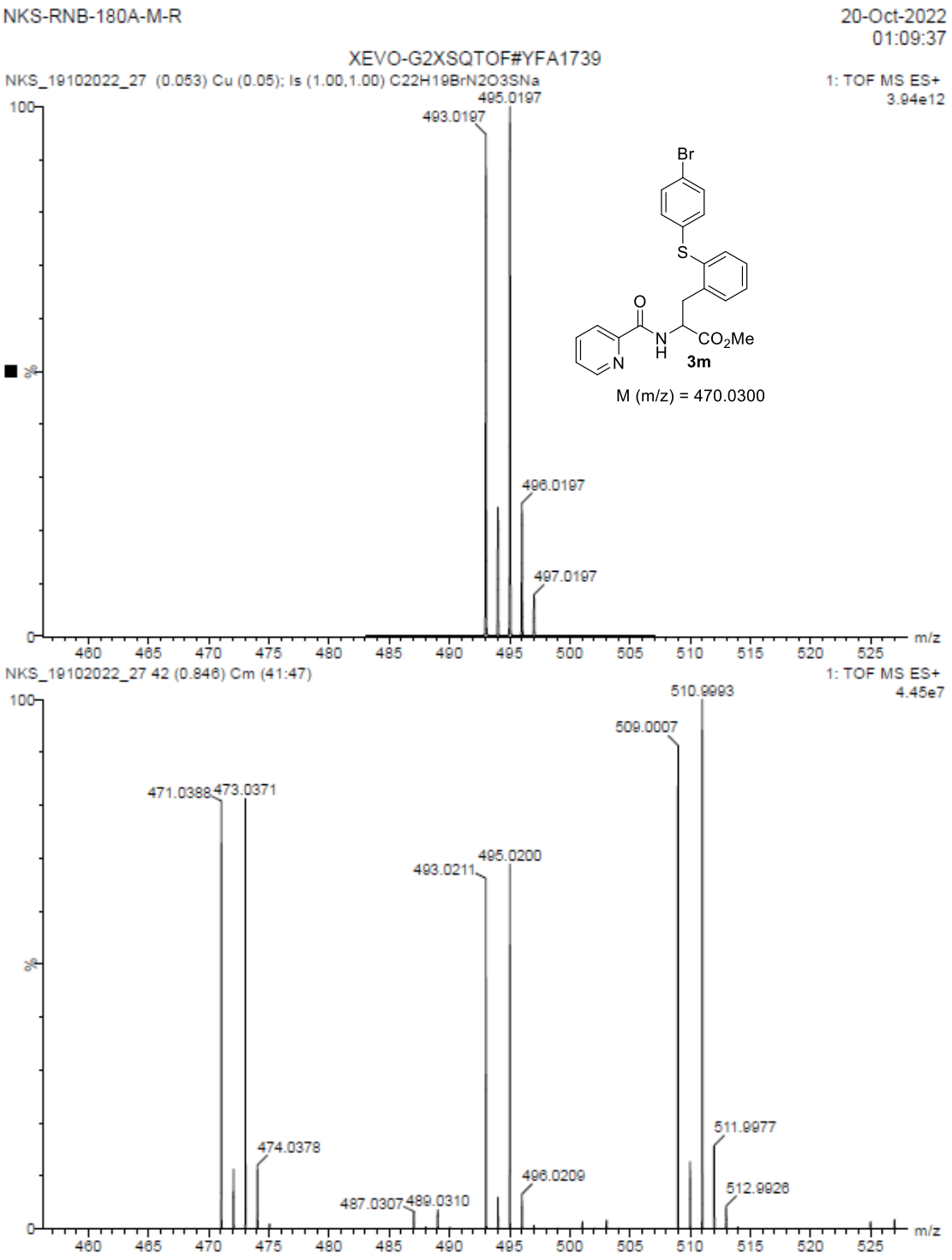


Fig S80. ESI-HRMS spectra of thiolated compound **3m**

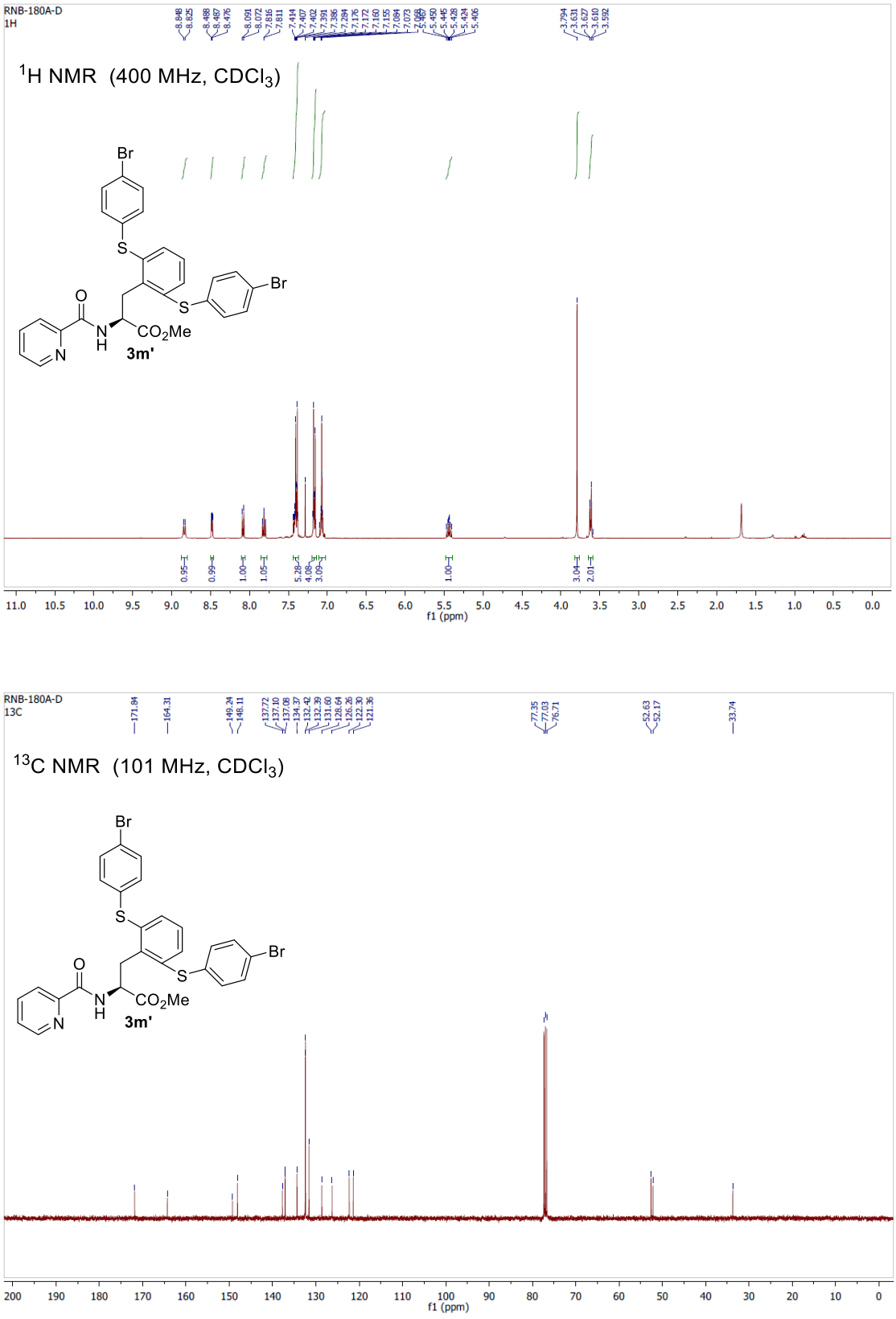


Fig S81. ^{1}H, ^{13}C $\{^{1}H\}$ NMR spectra of thiolated compound **3m'**

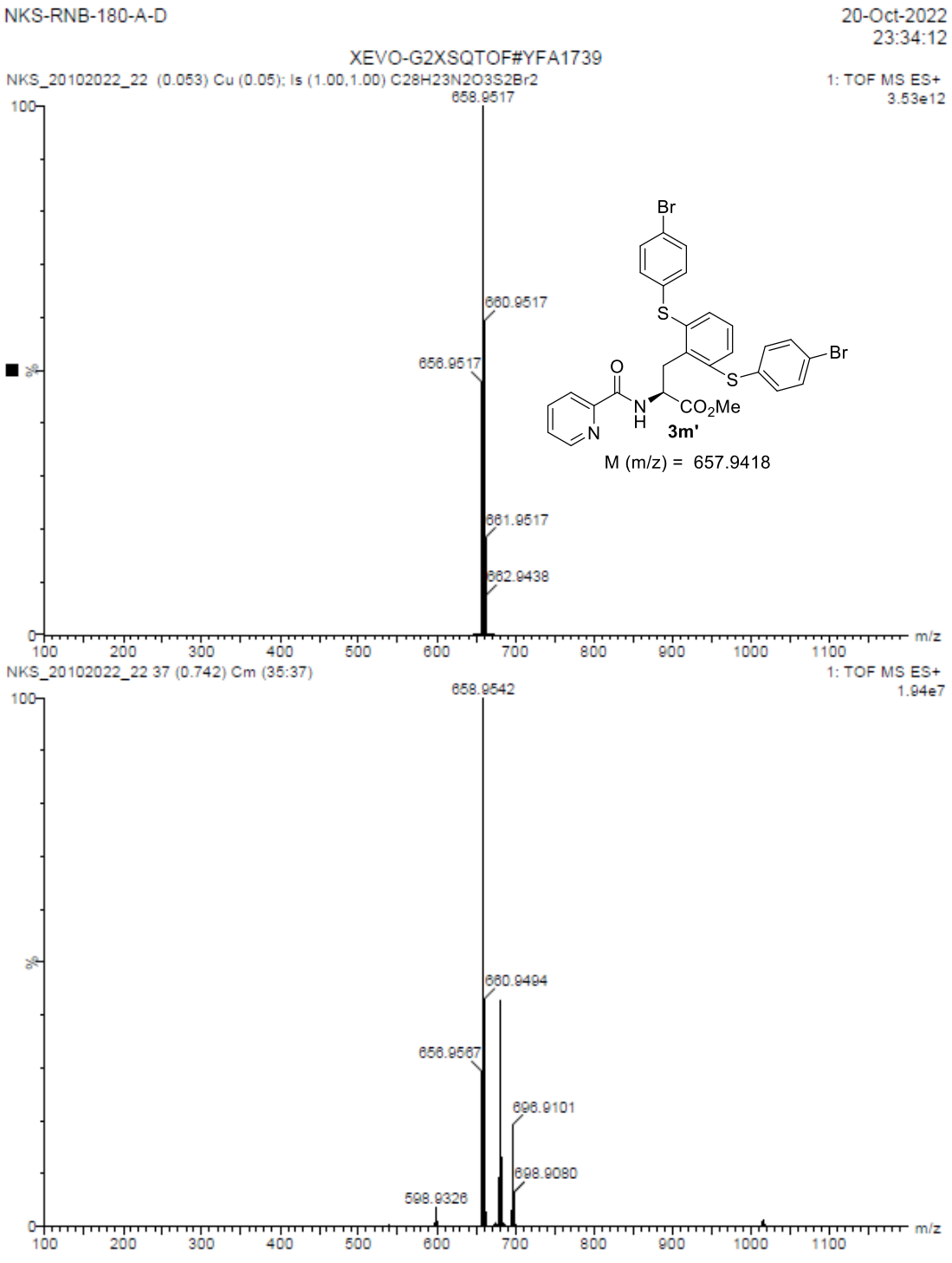


Fig S82. ESI-HRMS spectra of thiolated compound **3m'**

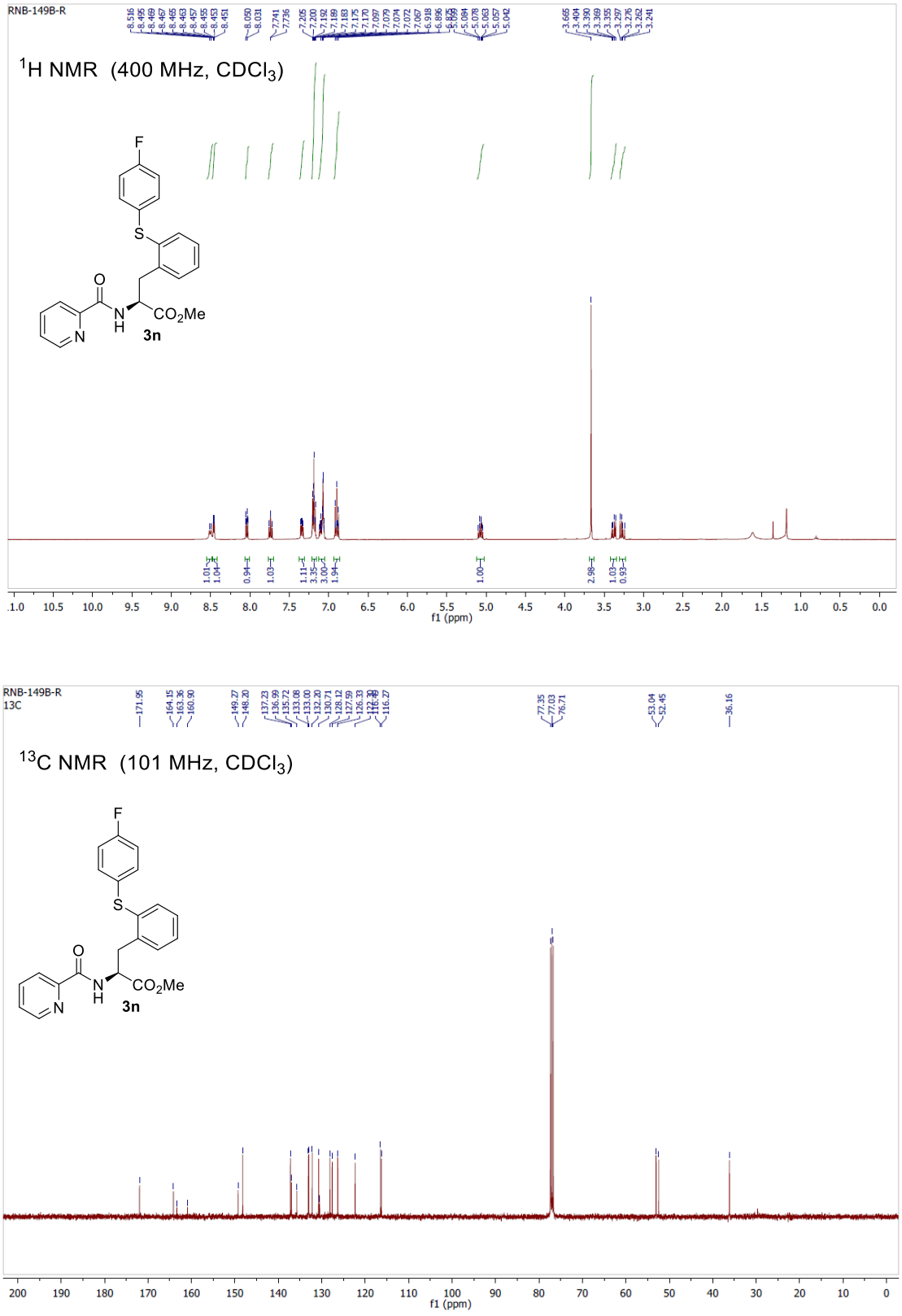


Fig S83. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3n**

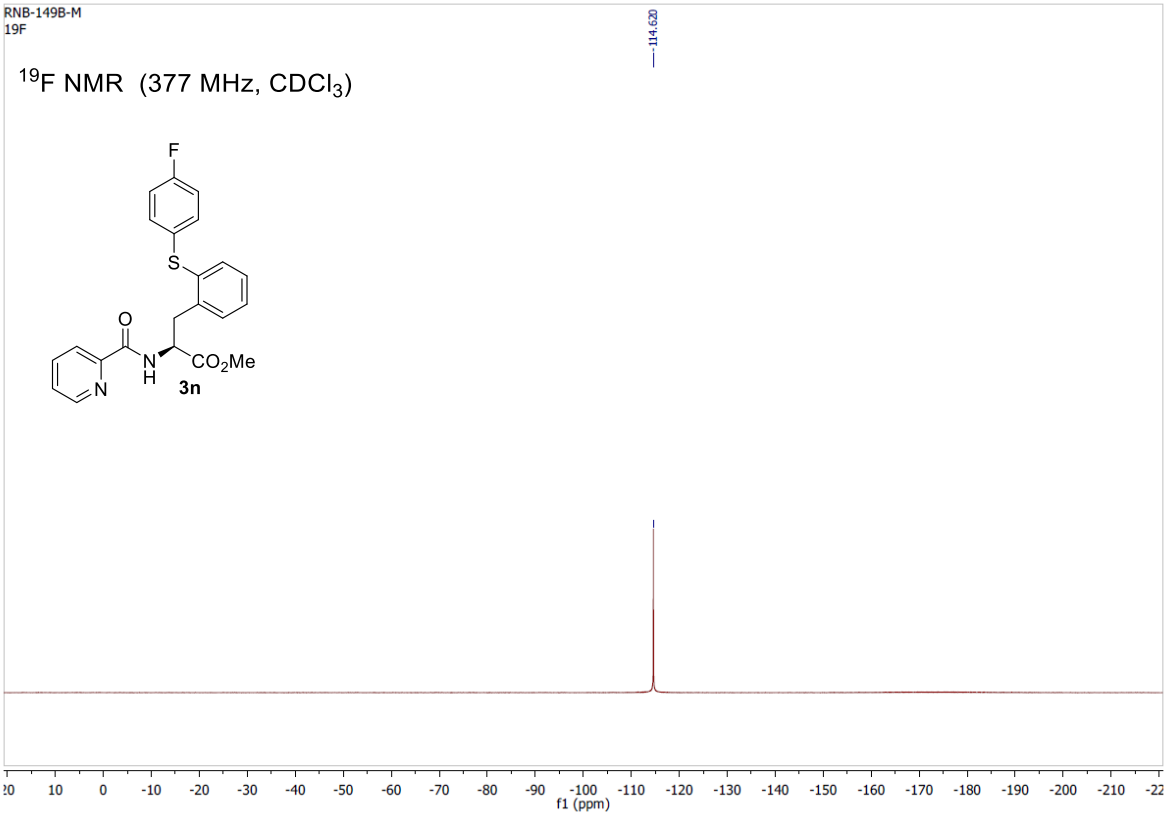


Fig S84. ^{19}F {^{1}H} NMR spectra of thiolated compound **3n**

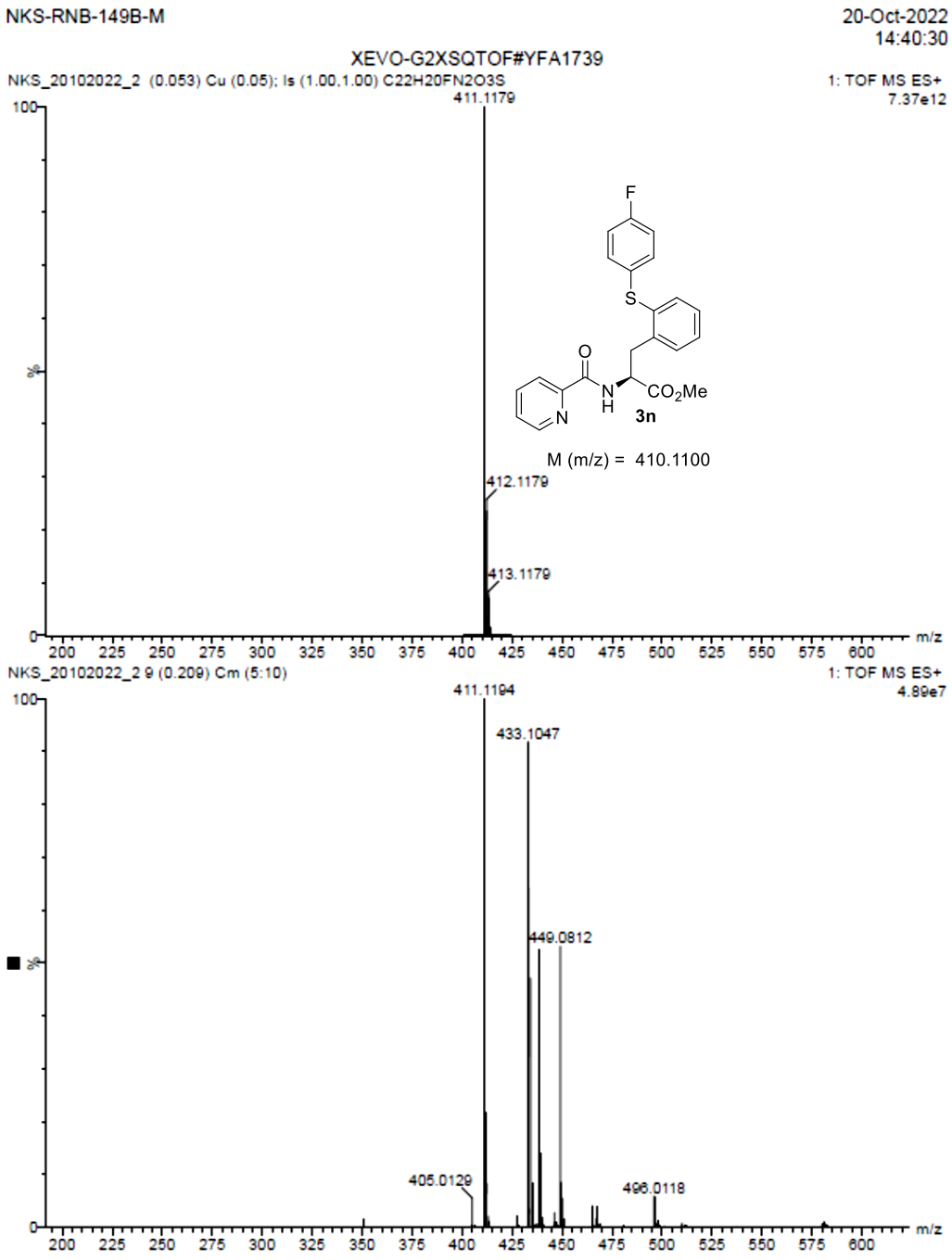


Fig S85. ESI-HRMS spectra of thiolated compound **3n**

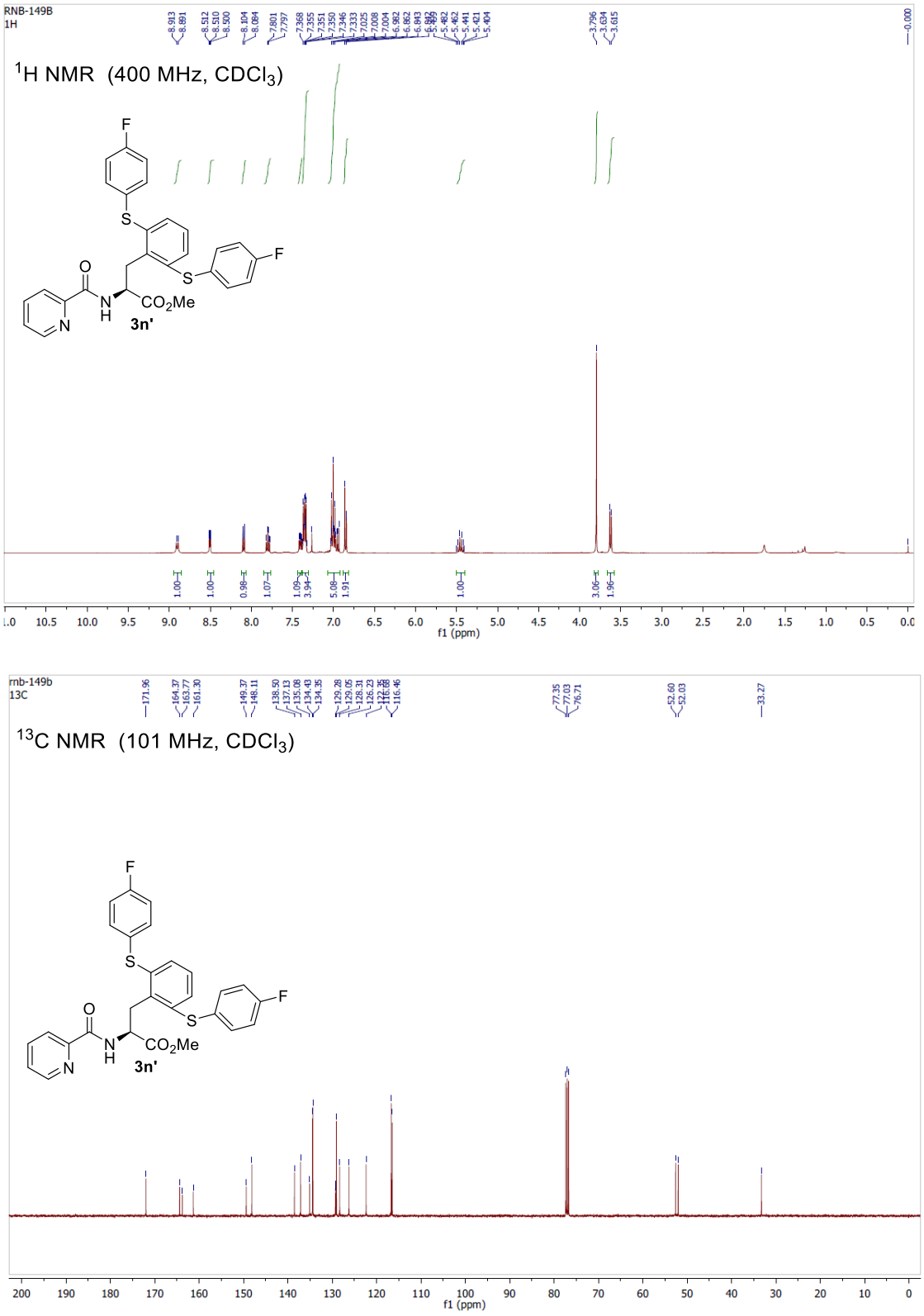


Fig S86. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3n'**

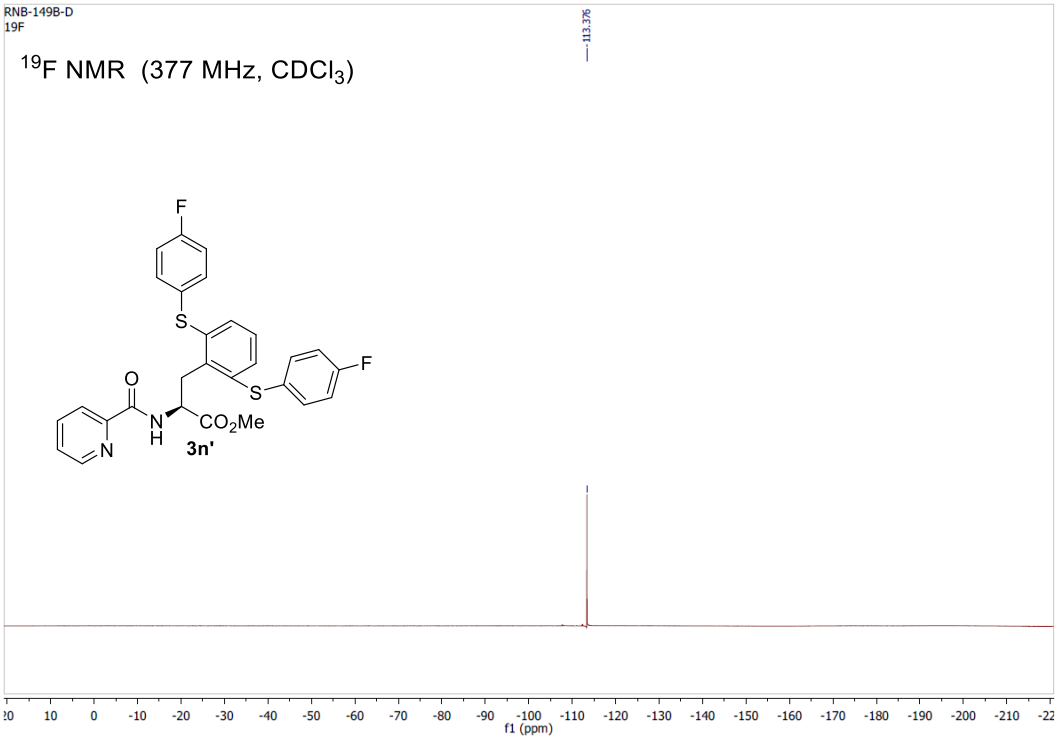


Fig S87. ^{19}F {^{1}H} NMR spectra of thiolated compound **3n'**

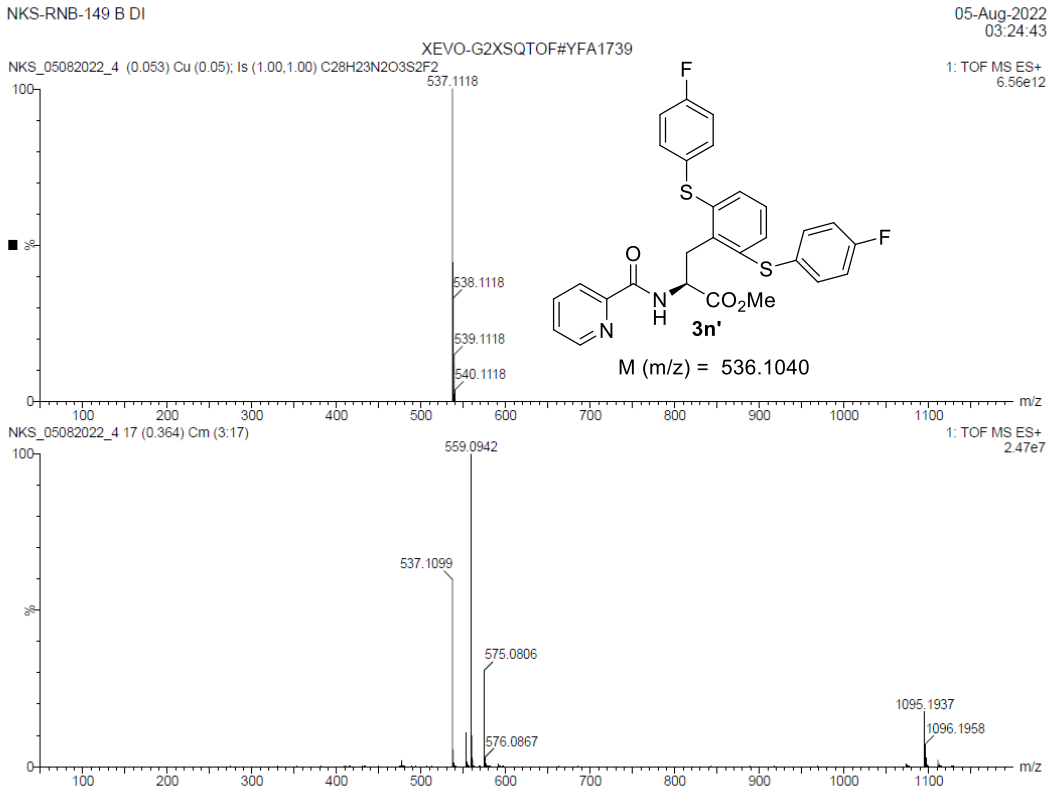


Fig S88. ESI-HRMS spectra of thiolated compound **3n'**

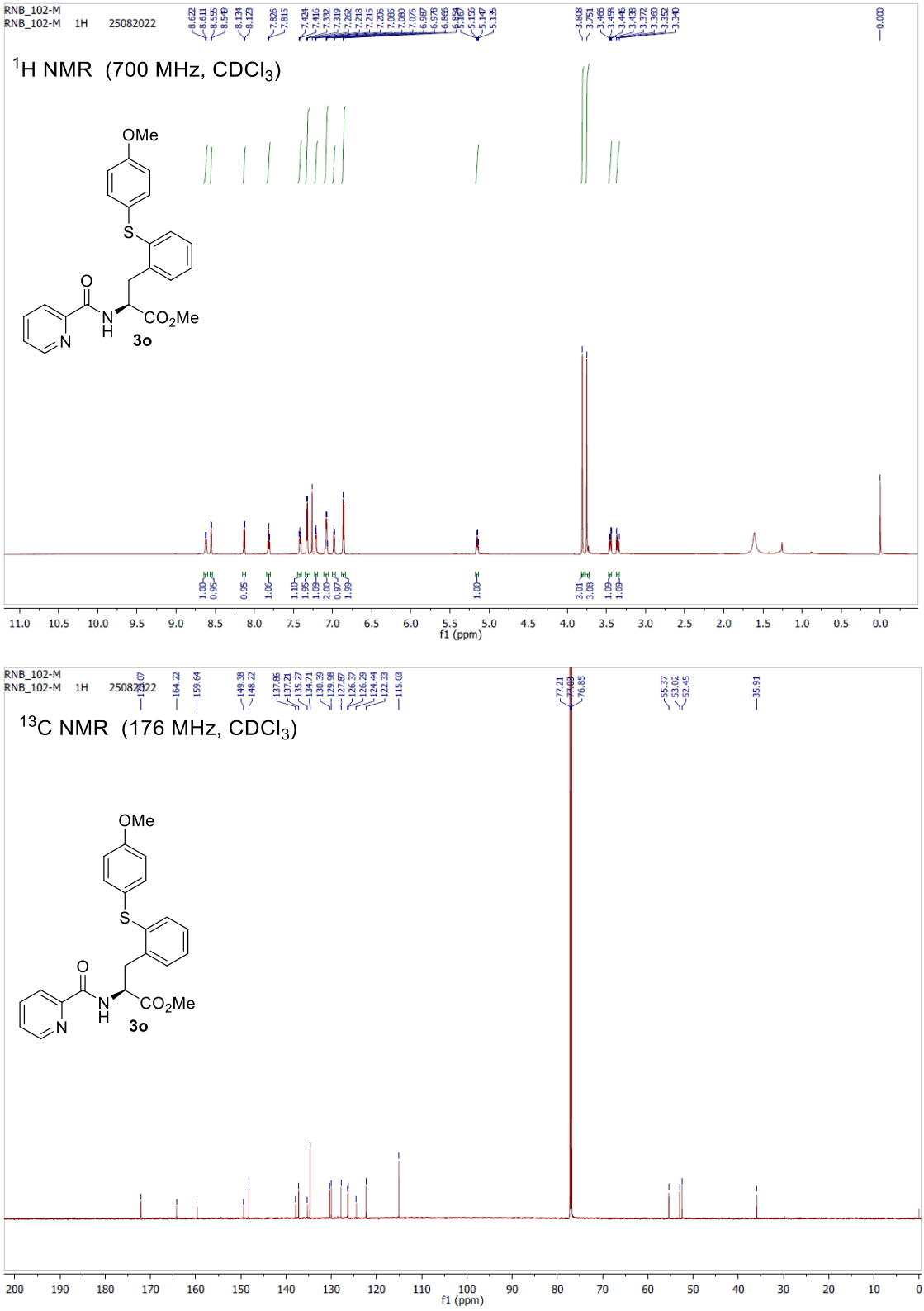


Fig S89. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3o**

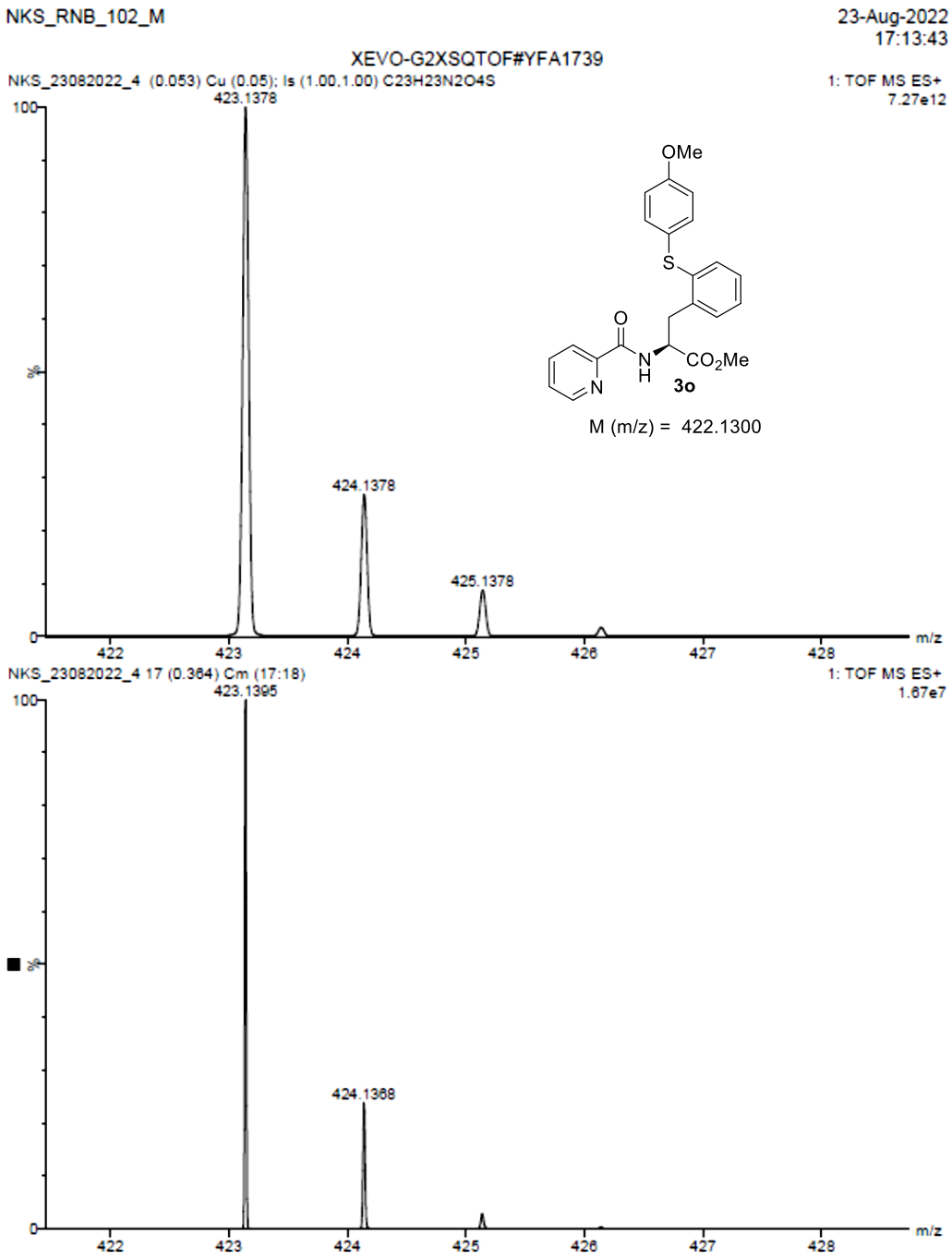
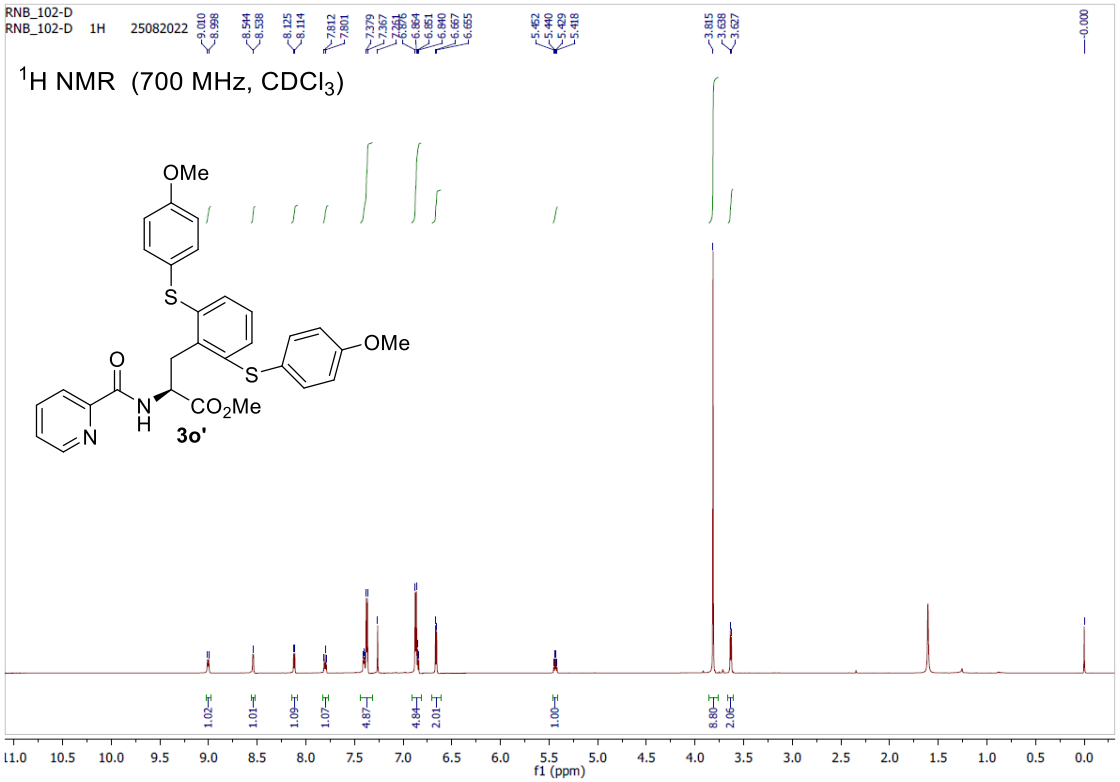


Fig S90. ESI-HRMS spectra of thiolated compound **3o**



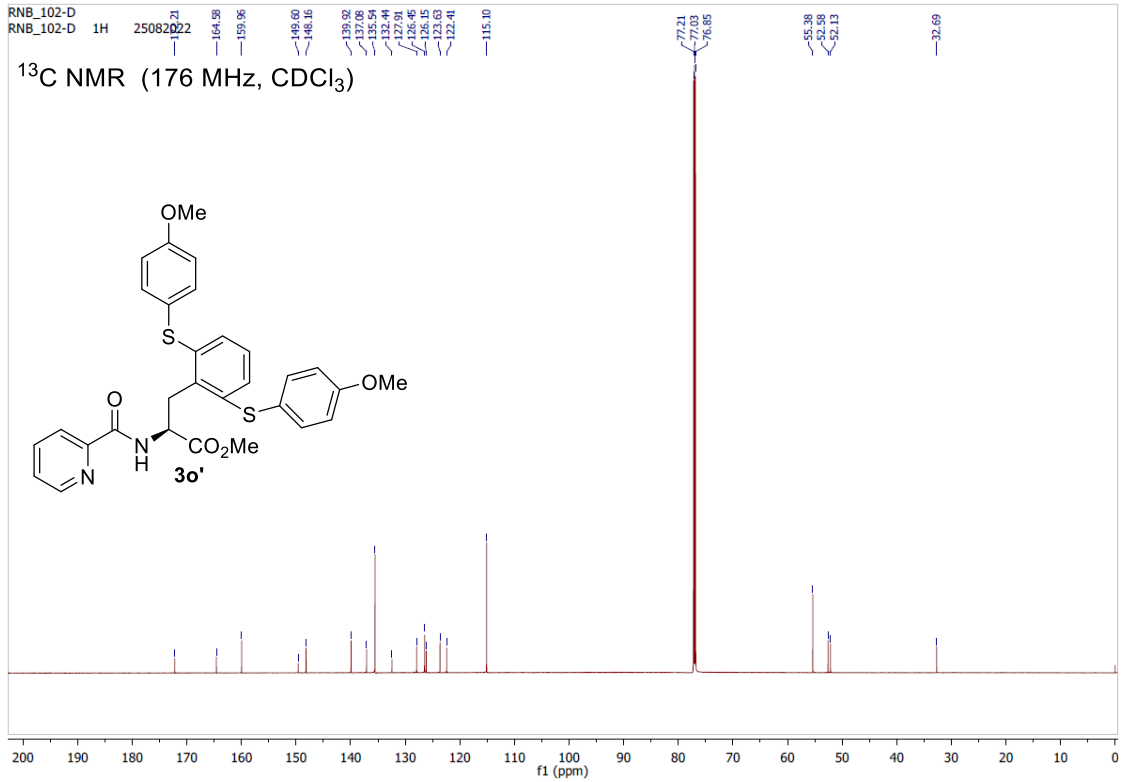


Fig S91. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3o'**

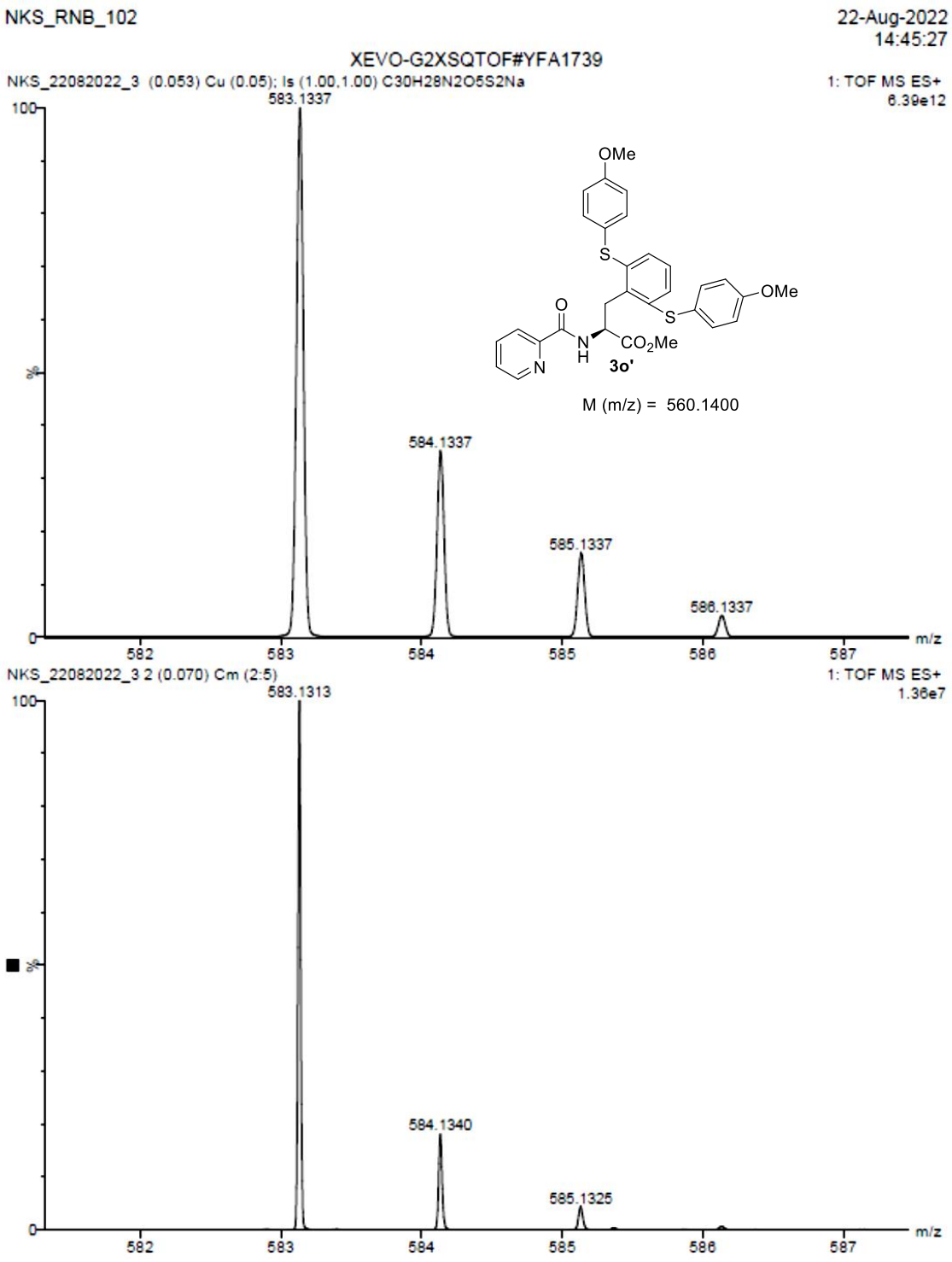


Fig S92. ESI-HRMS spectra of thiolated compound **3o'**

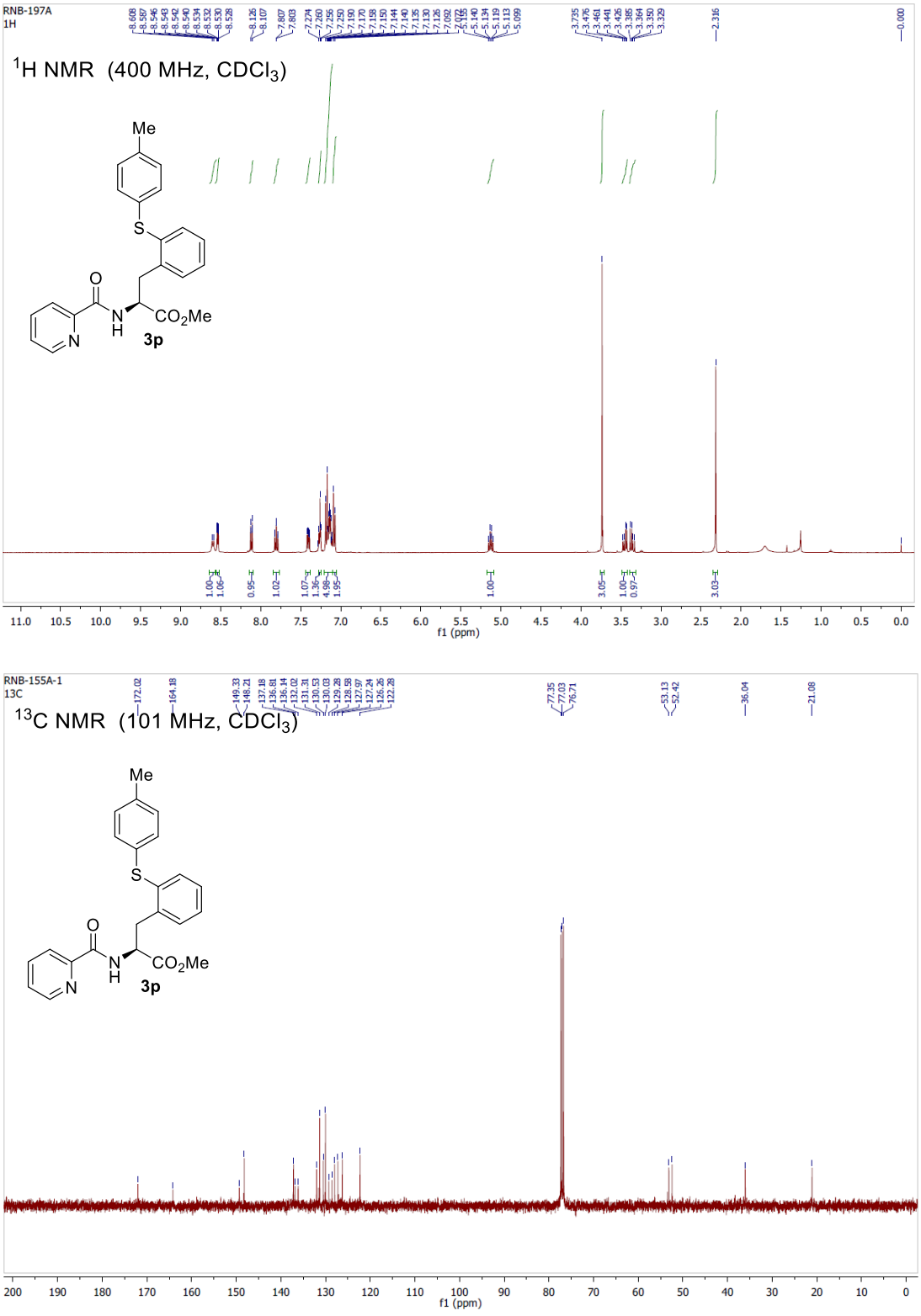


Fig S93. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3p**

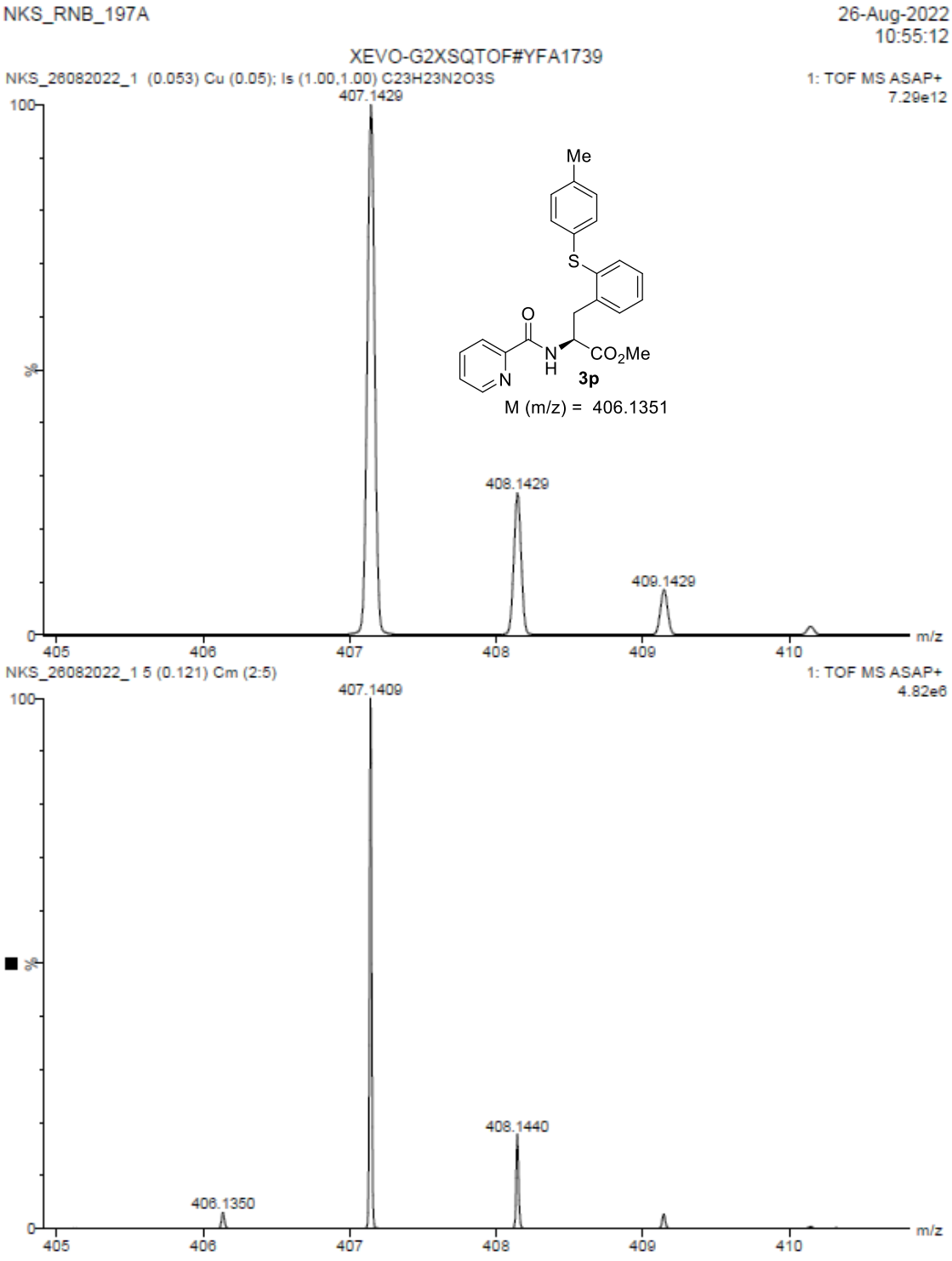


Fig S94. ASAP-HRMS spectra of thiolated compound **3p**

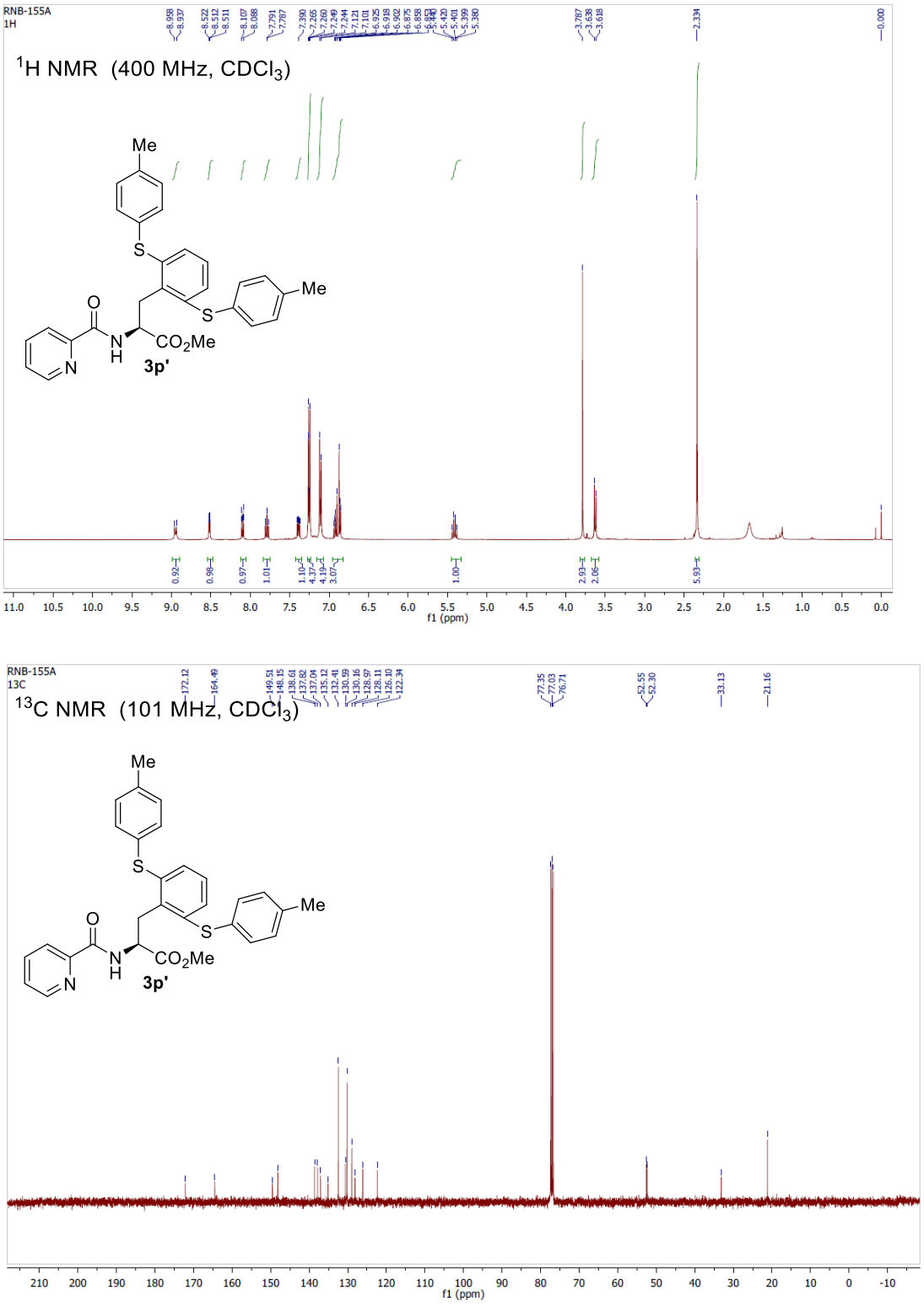


Fig S95. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3p'**

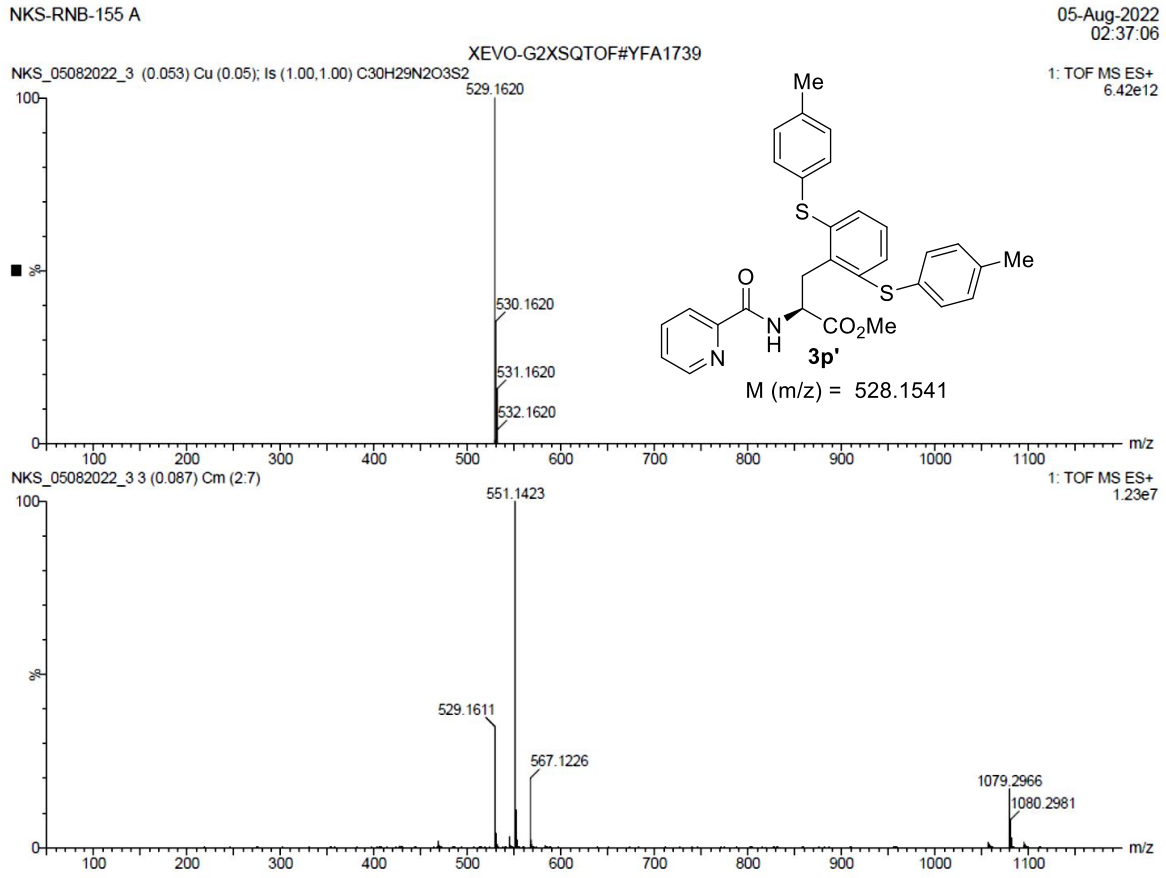
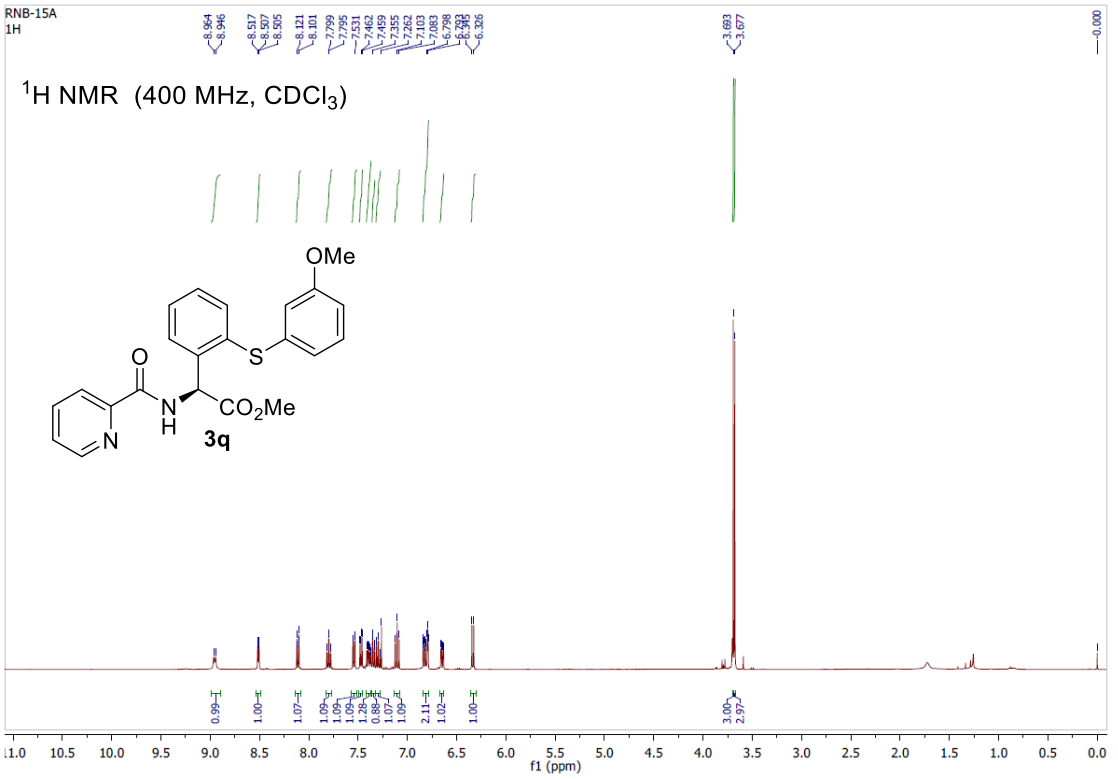


Fig S96. ESI-HRMS spectra of thiolated compound **3p'**



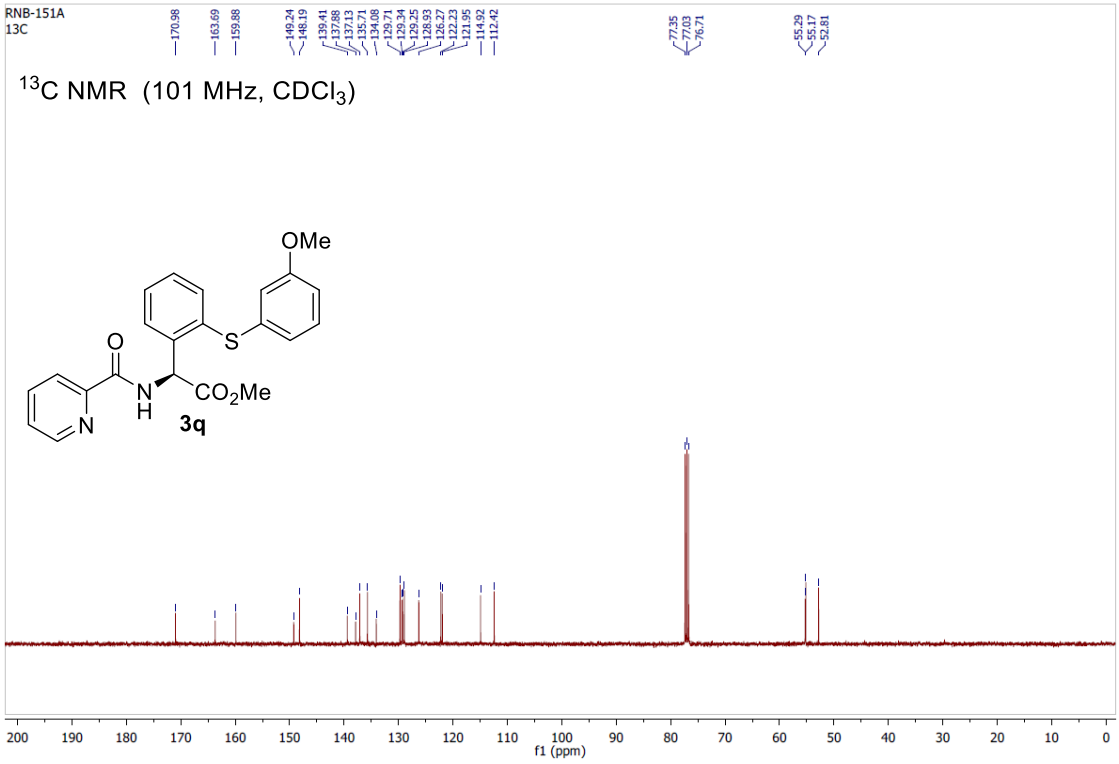


Fig S97. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3q**

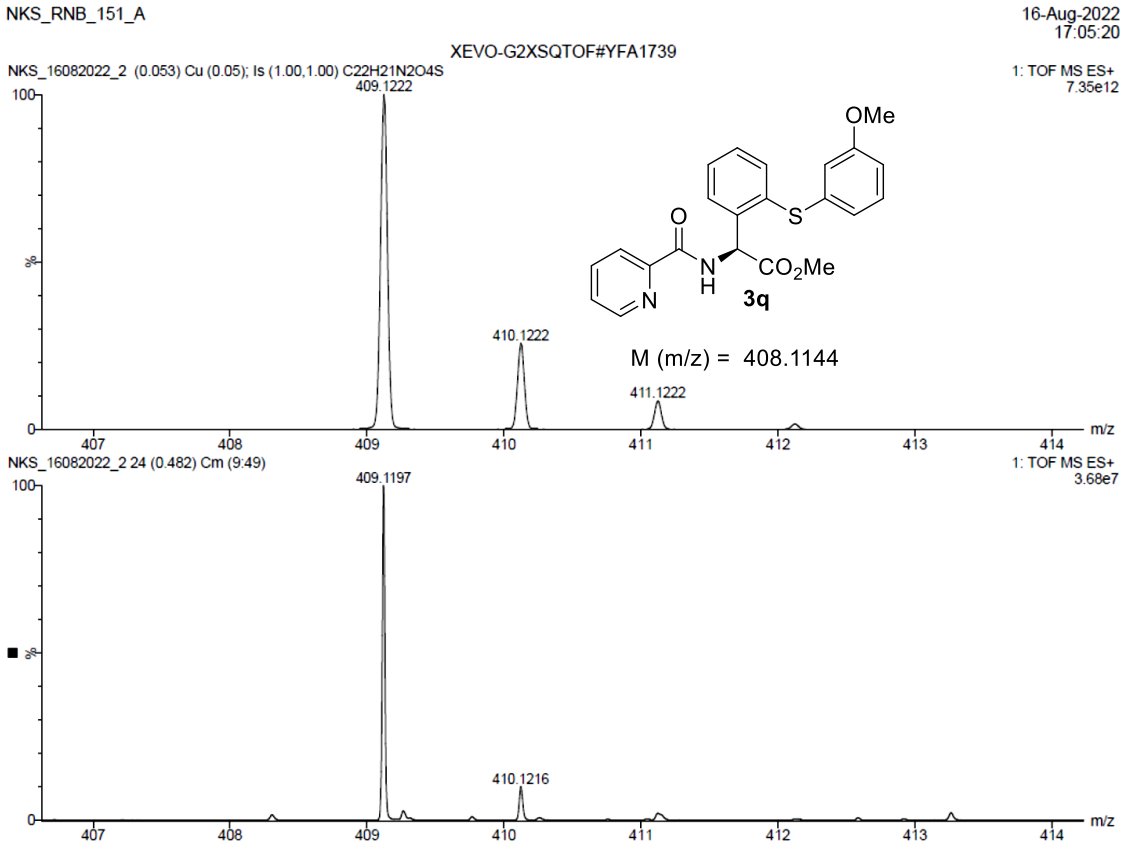
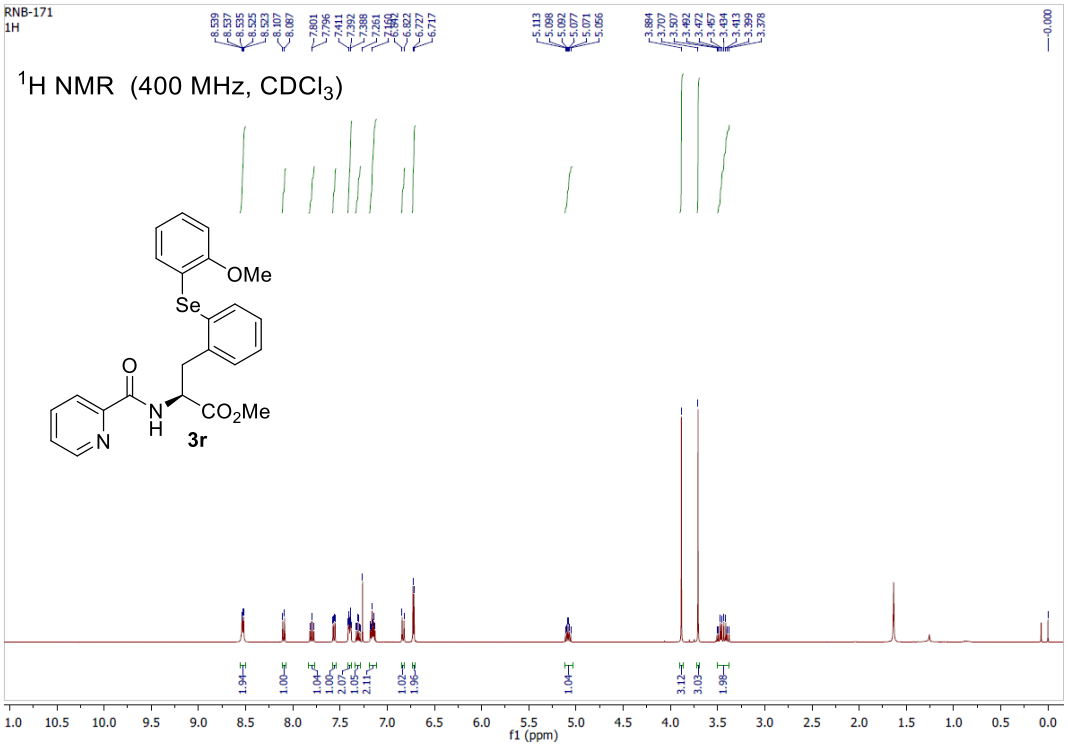


Fig S98. ESI-HRMS spectra of thiolated compound **3q**



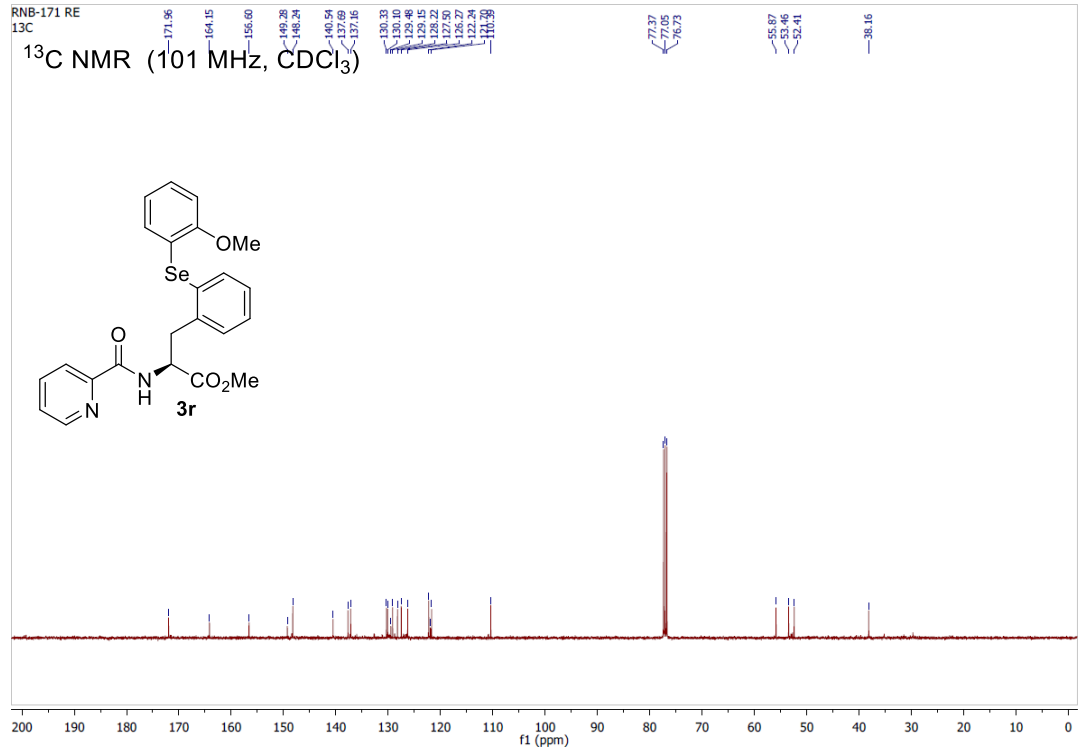


Fig S99. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3r**

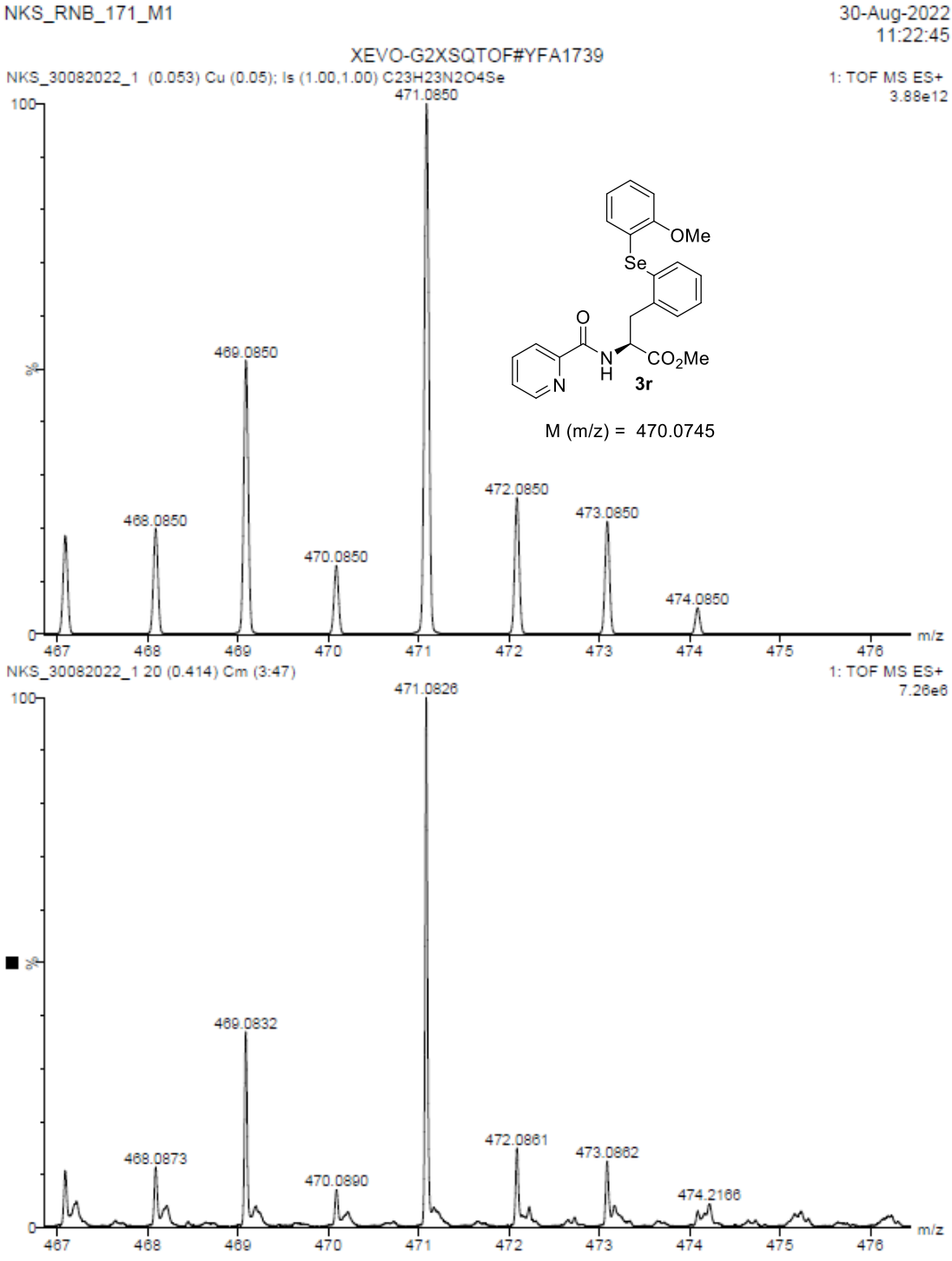


Fig S100. ESI-HRMS spectra of compound **3r**

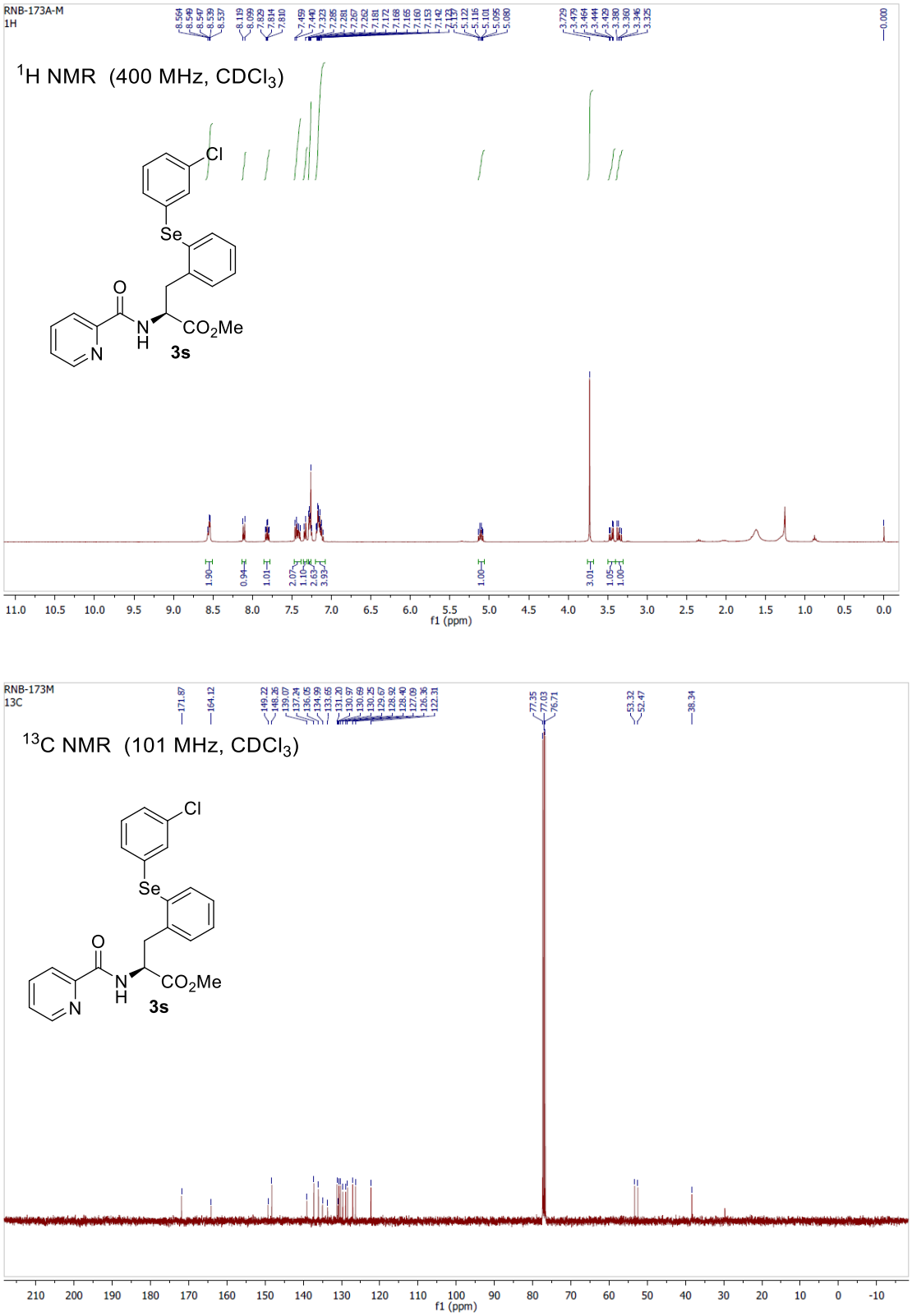


Fig S101. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3s**

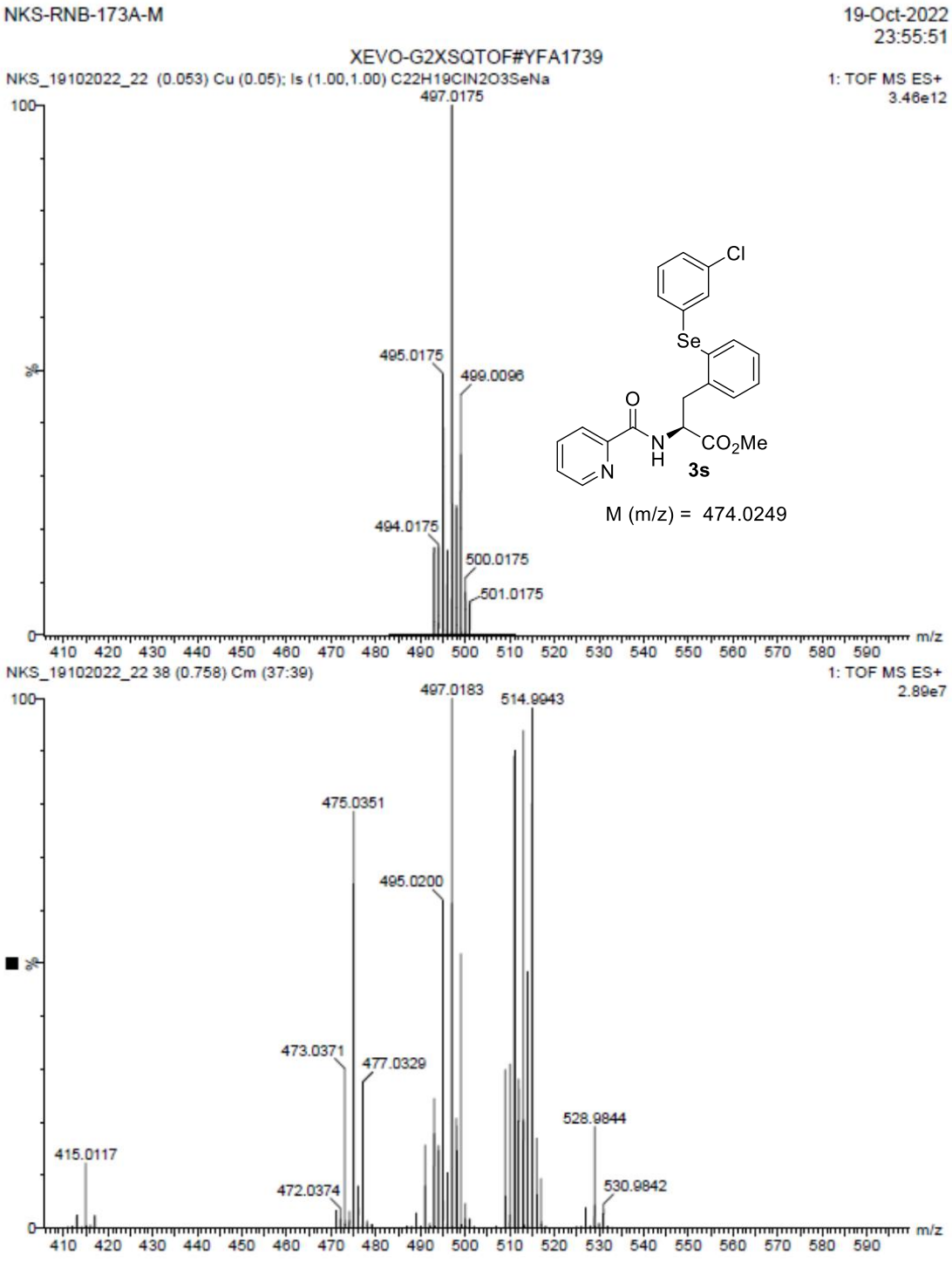


Fig S102. ESI-HRMS spectra of compound **3s**

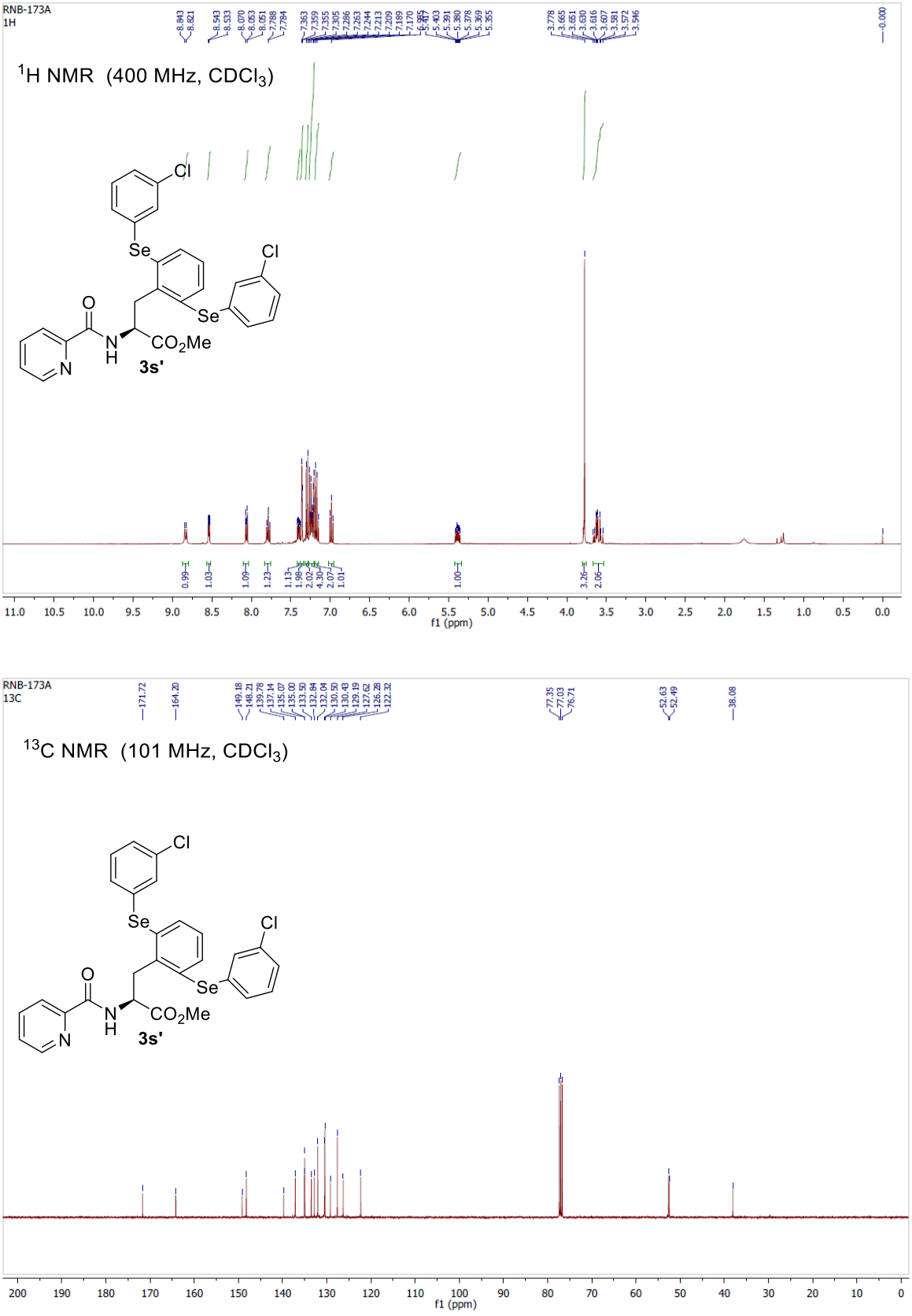


Fig S103. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3s'**

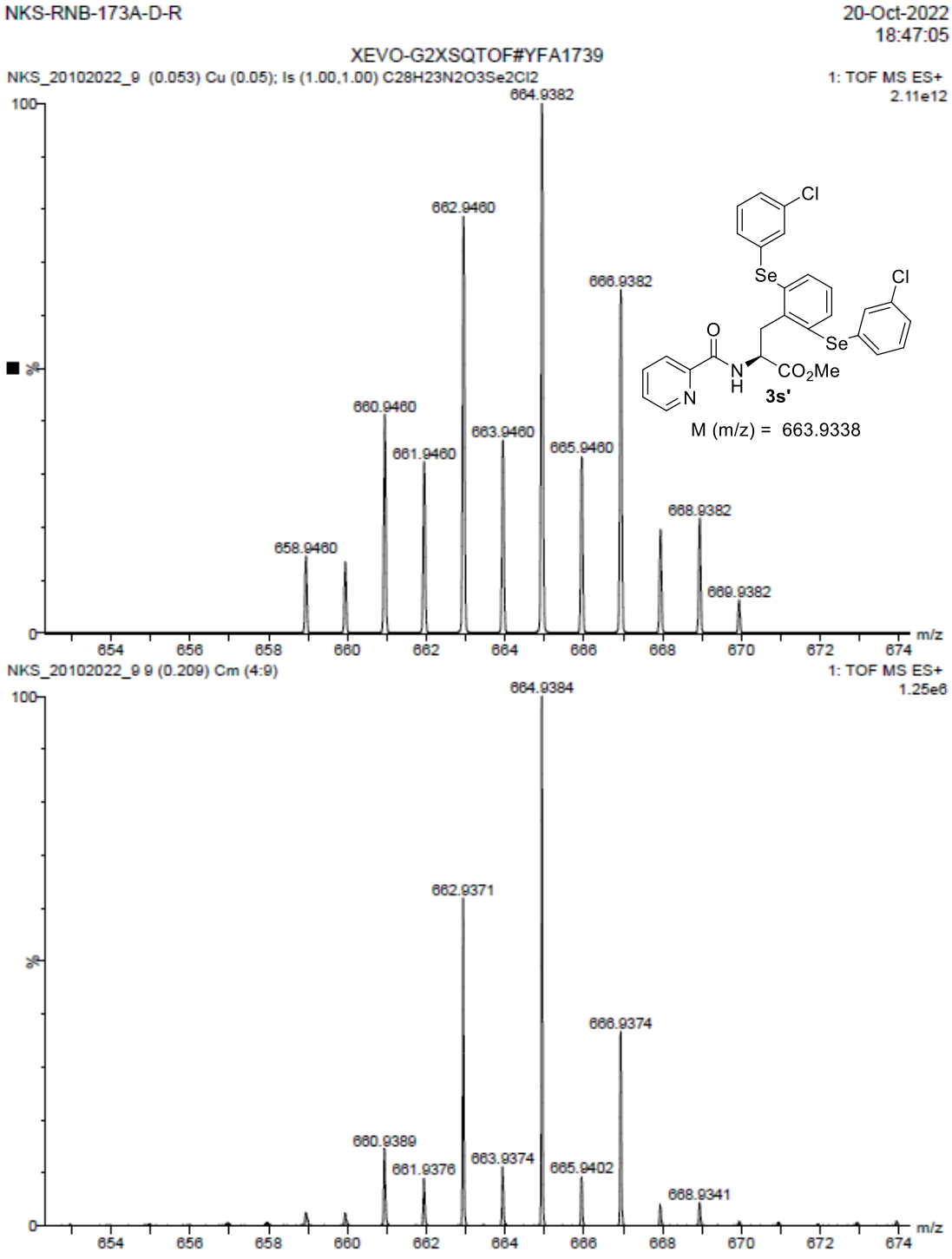


Fig S104. ESI-HRMS spectra of compound **3s'**

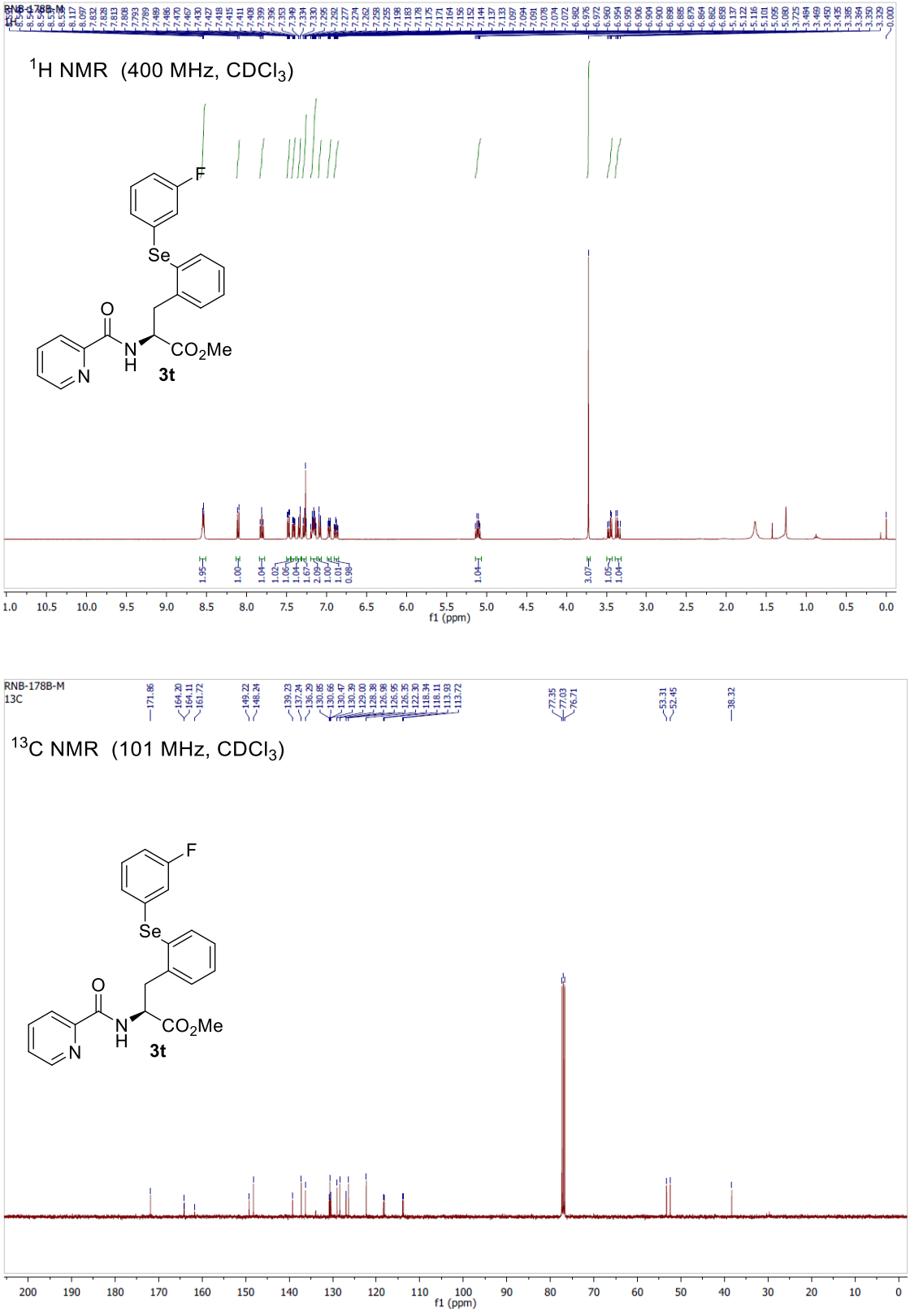


Fig S105. ^{1}H, ^{13}C $\{^{1}H\}$ NMR spectra of compound **3t**

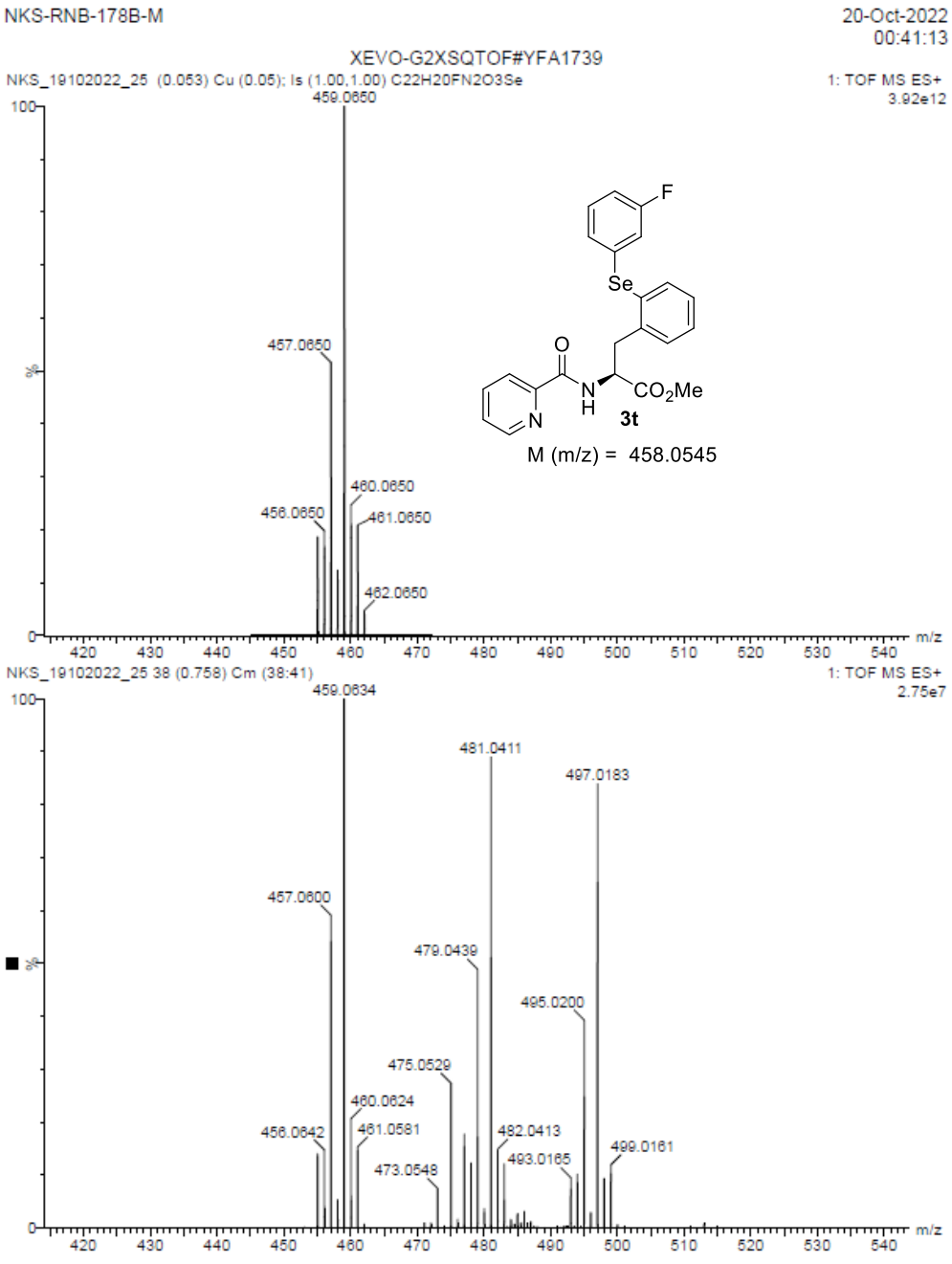
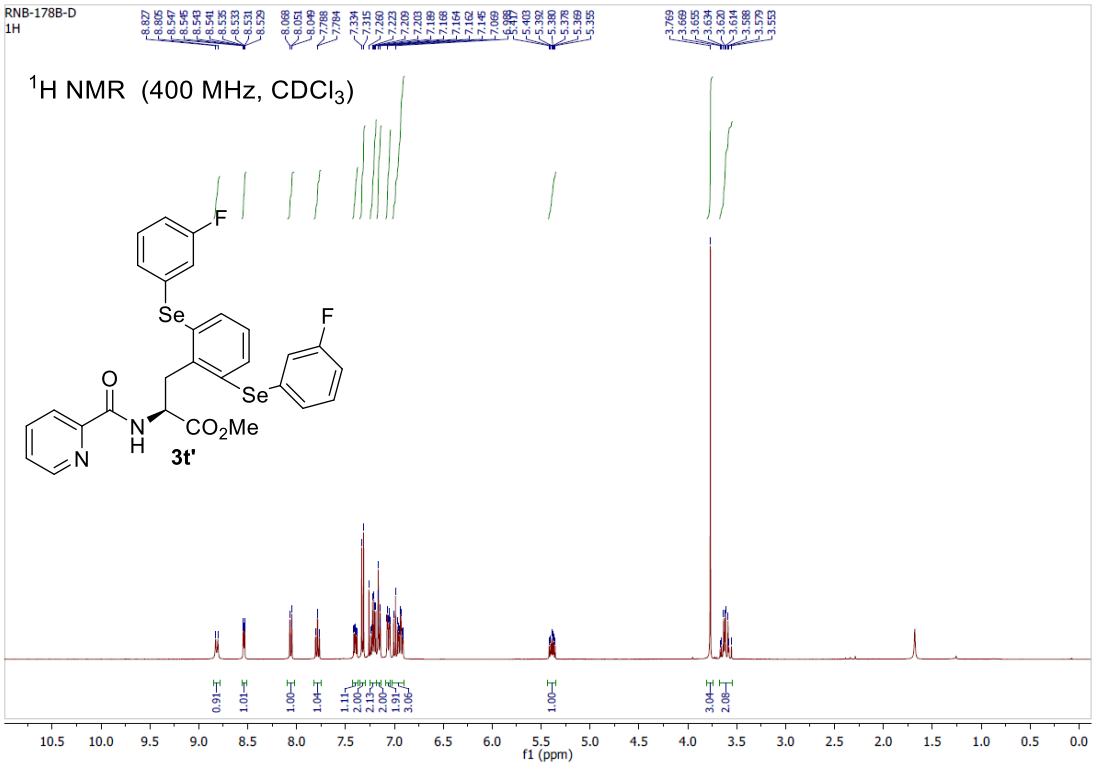


Fig S106. ESI-HRMS spectra of compound **3t**



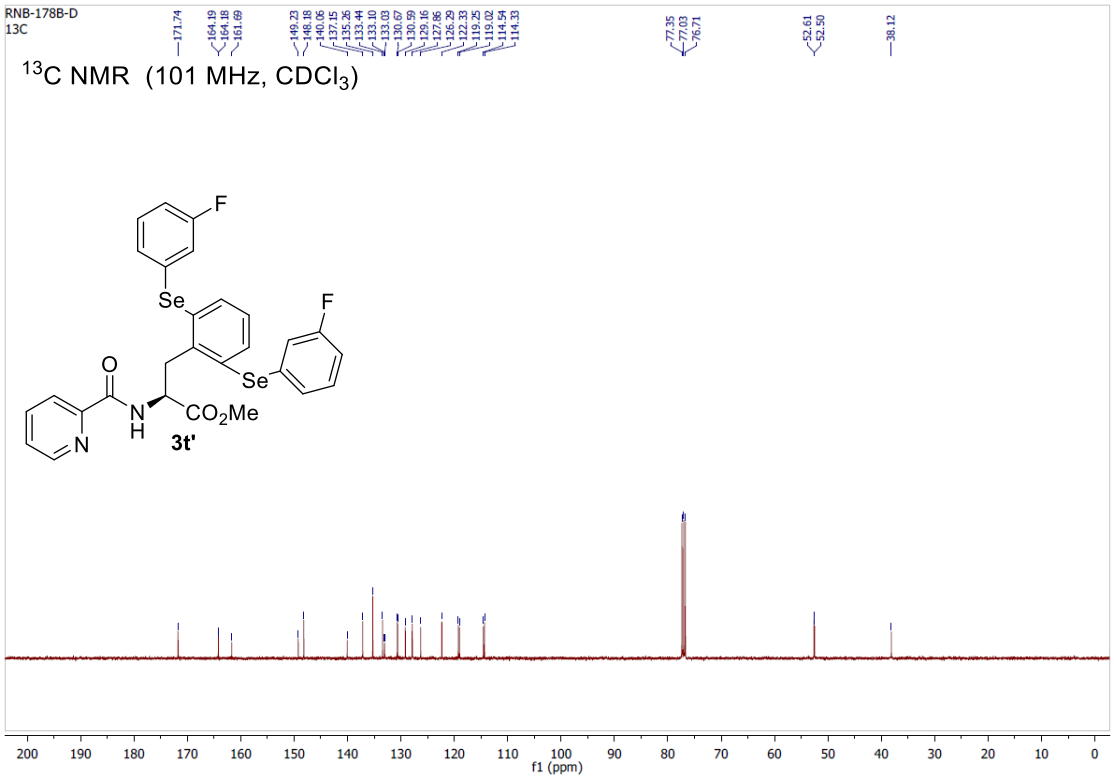


Fig S107. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3t'**

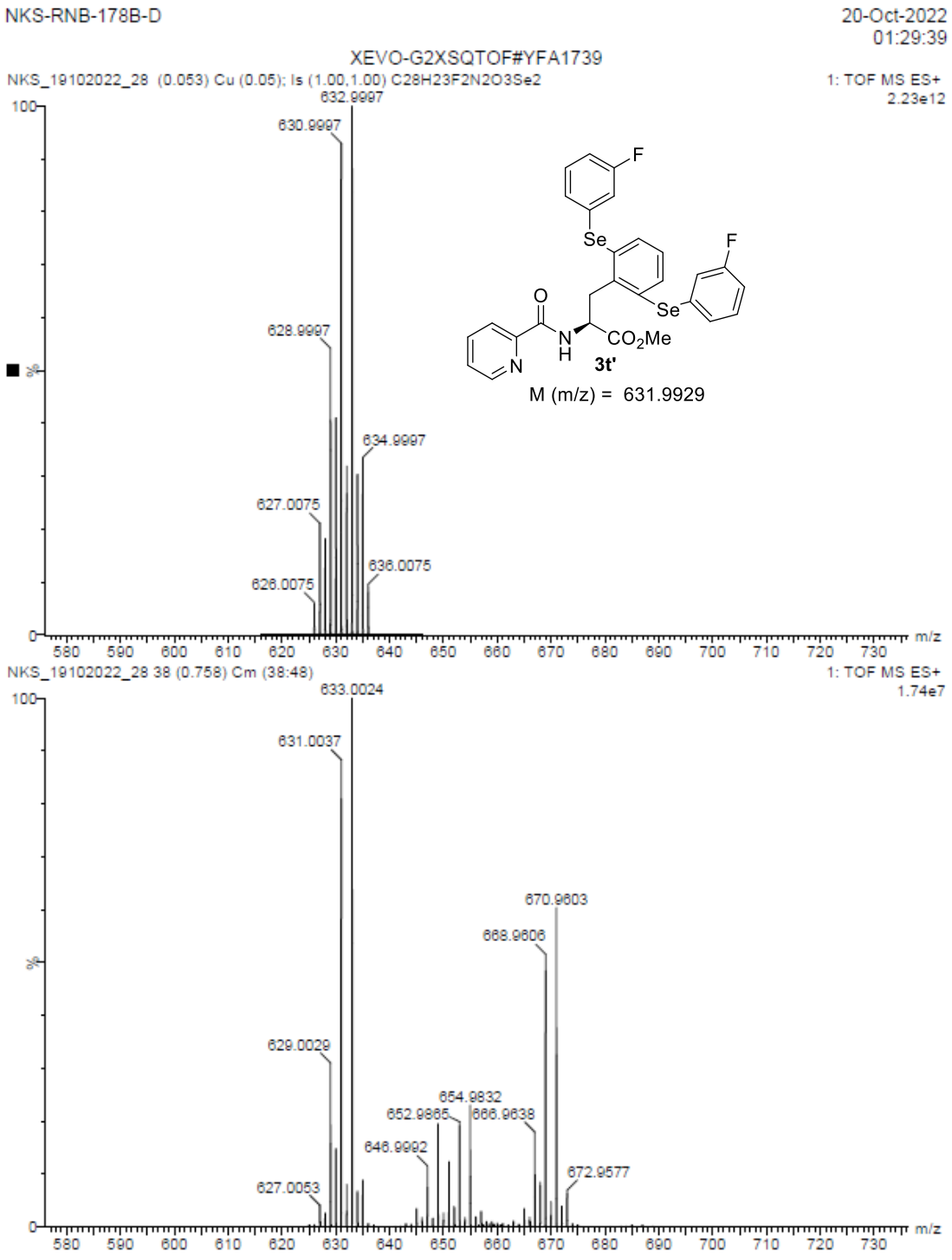
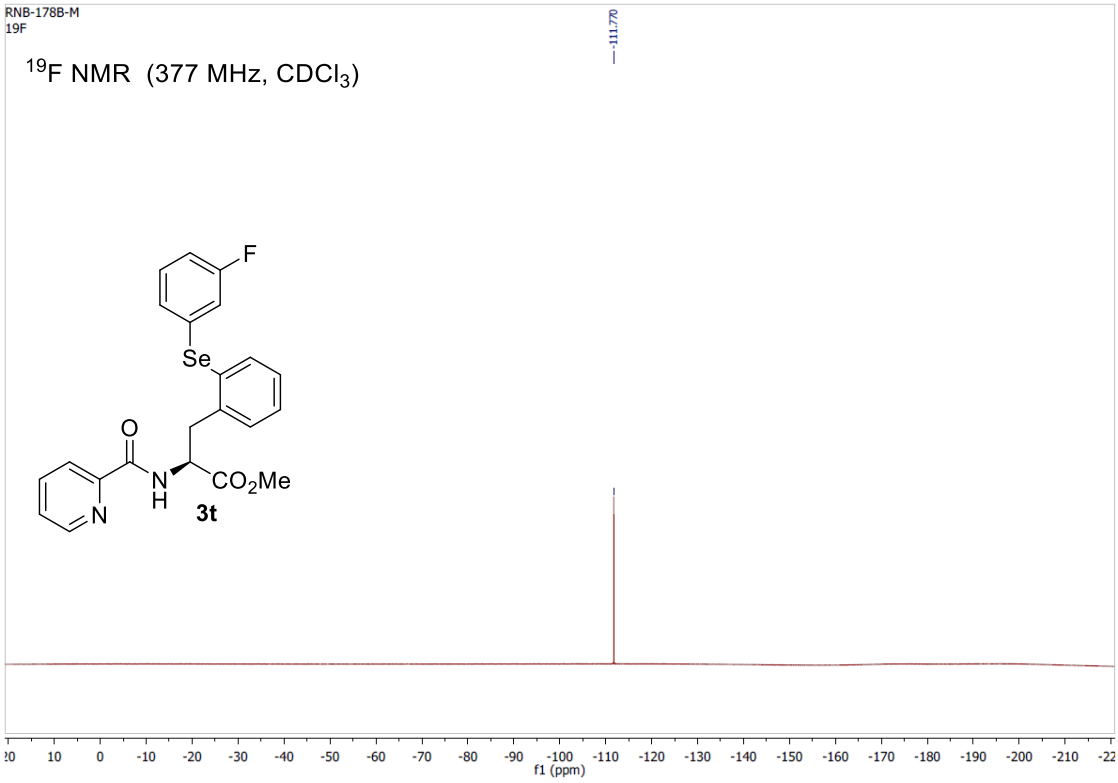


Fig S108. ESI-HRMS spectra of compound **3t'**



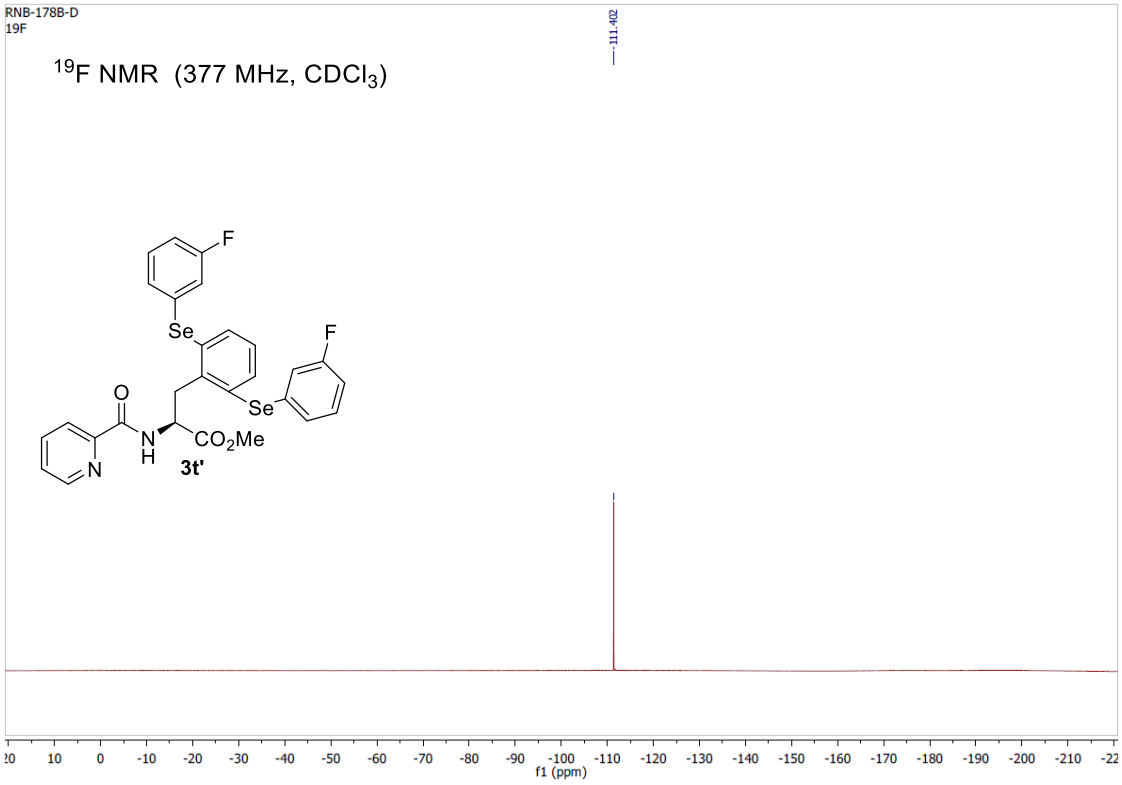


Fig S109. ^{19}F {^{1}H} NMR spectra of compounds **3t** and **3t'**

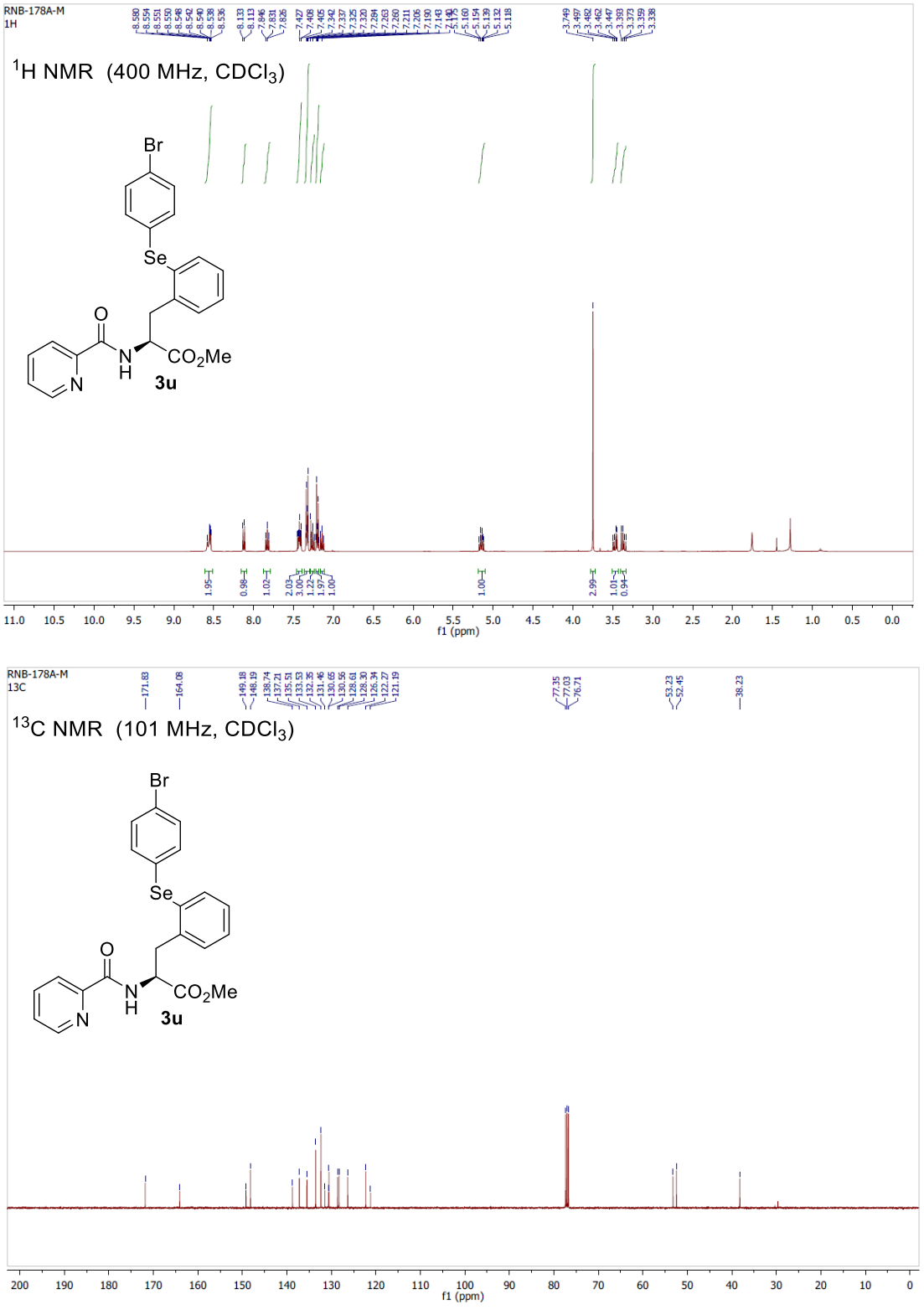


Fig S110. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3u**

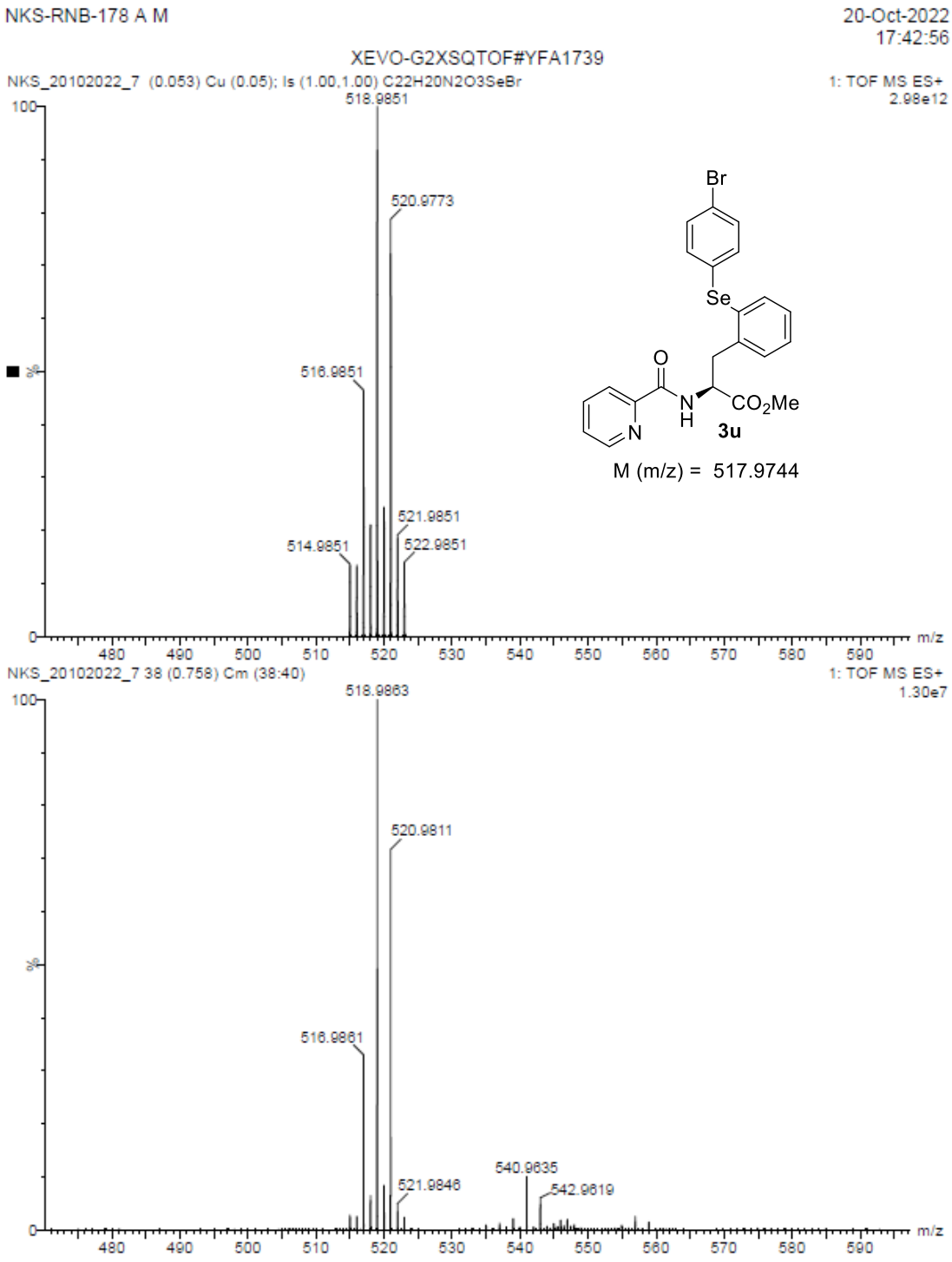


Fig S111. ESI-HRMS spectra of compound **3u**

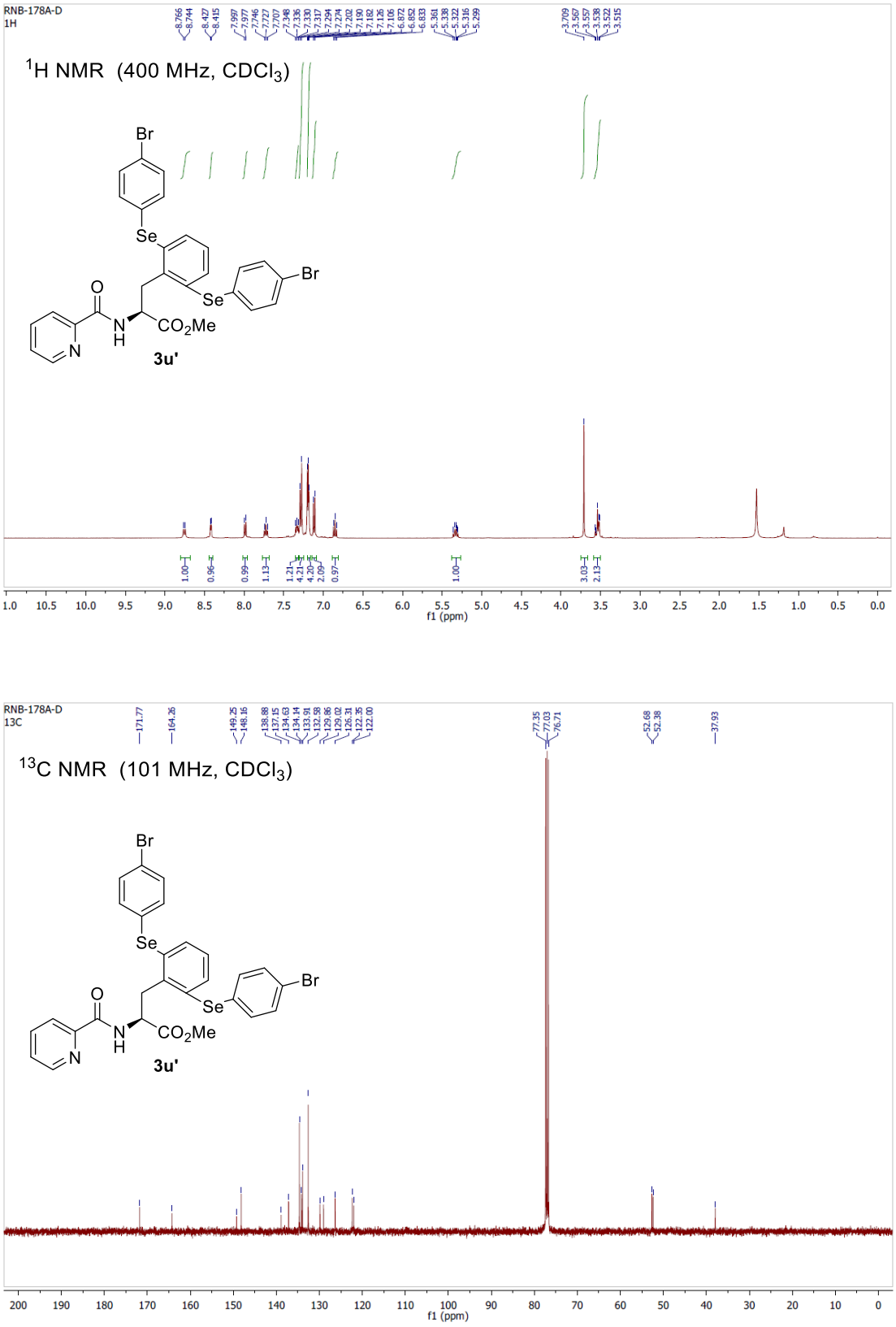


Fig S112. ^{1}H, ^{13}C $\{^{1}H\}$ NMR spectra of compound **3u'**

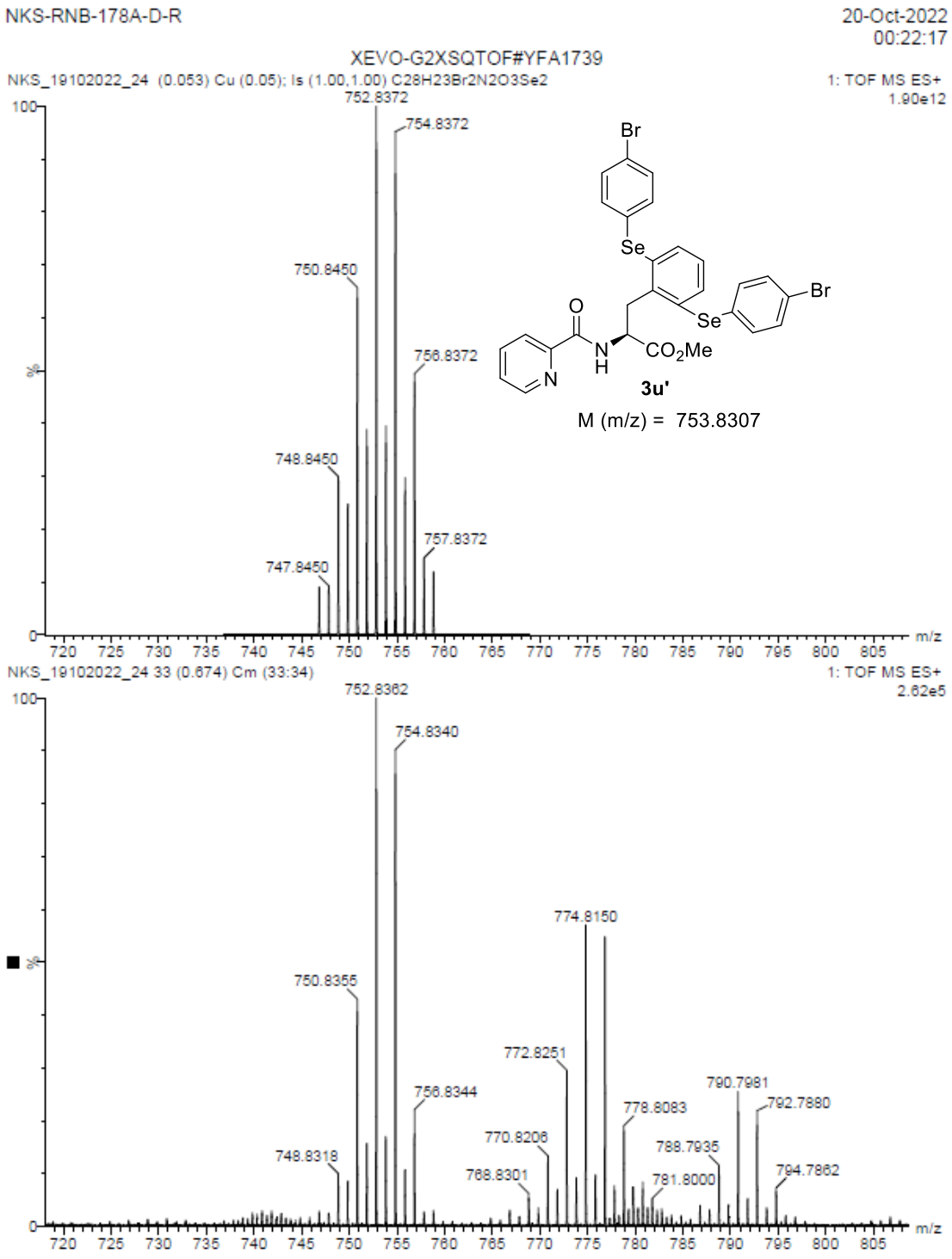


Fig S113. ESI-HRMS spectra of compound **3u'**

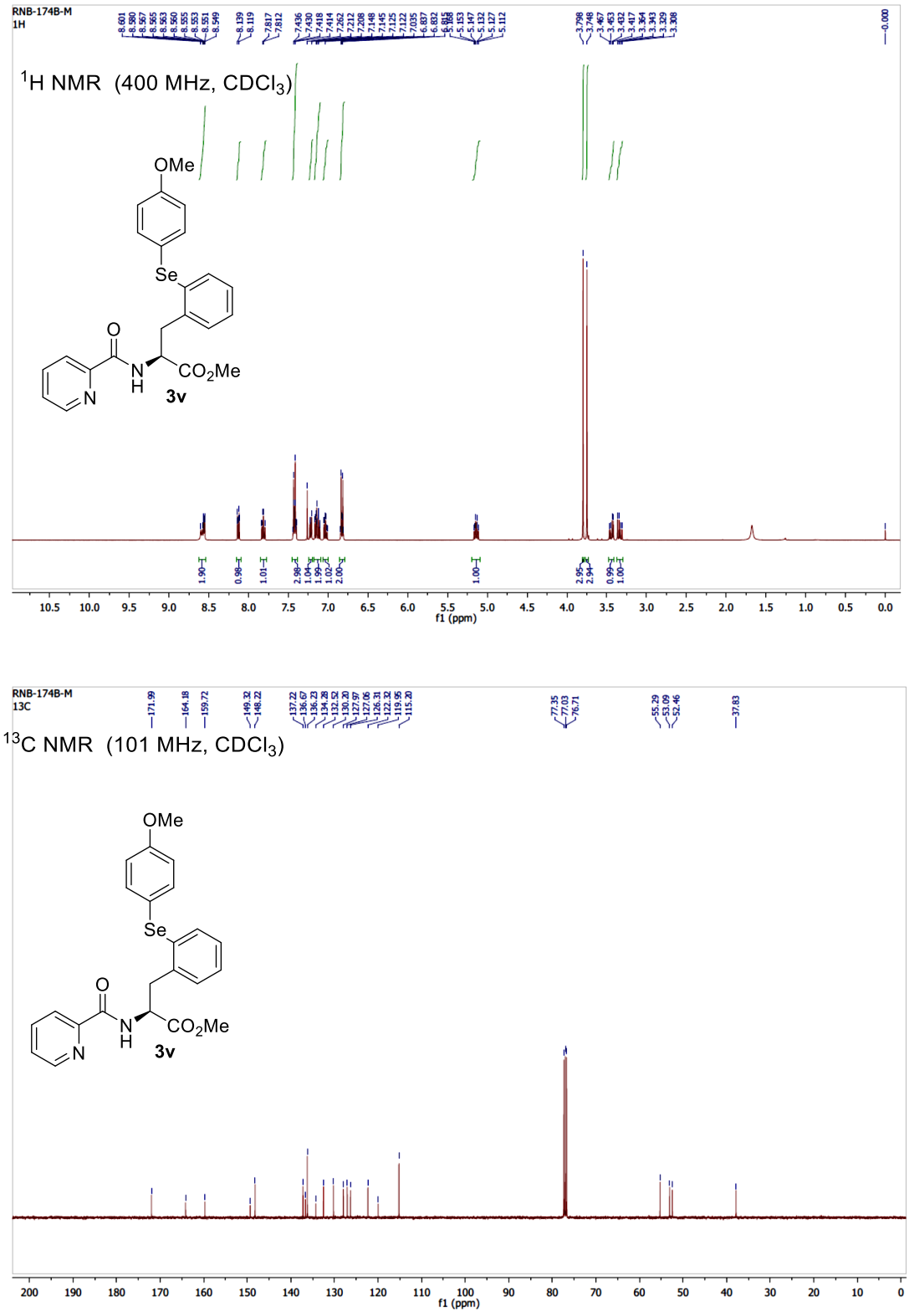


Fig S114. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3v**

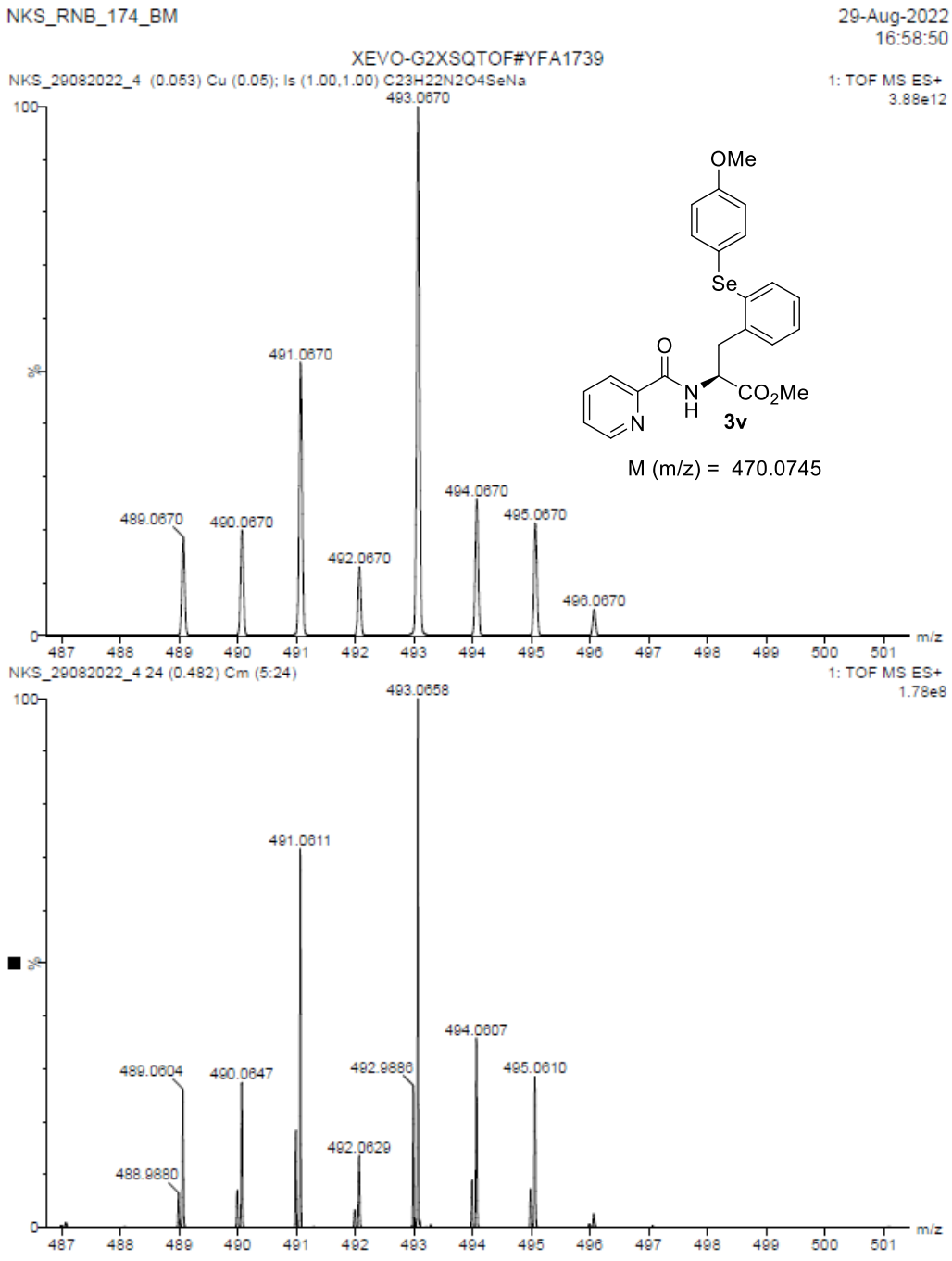


Fig S115. ESI-HRMS spectra of compound **3v**

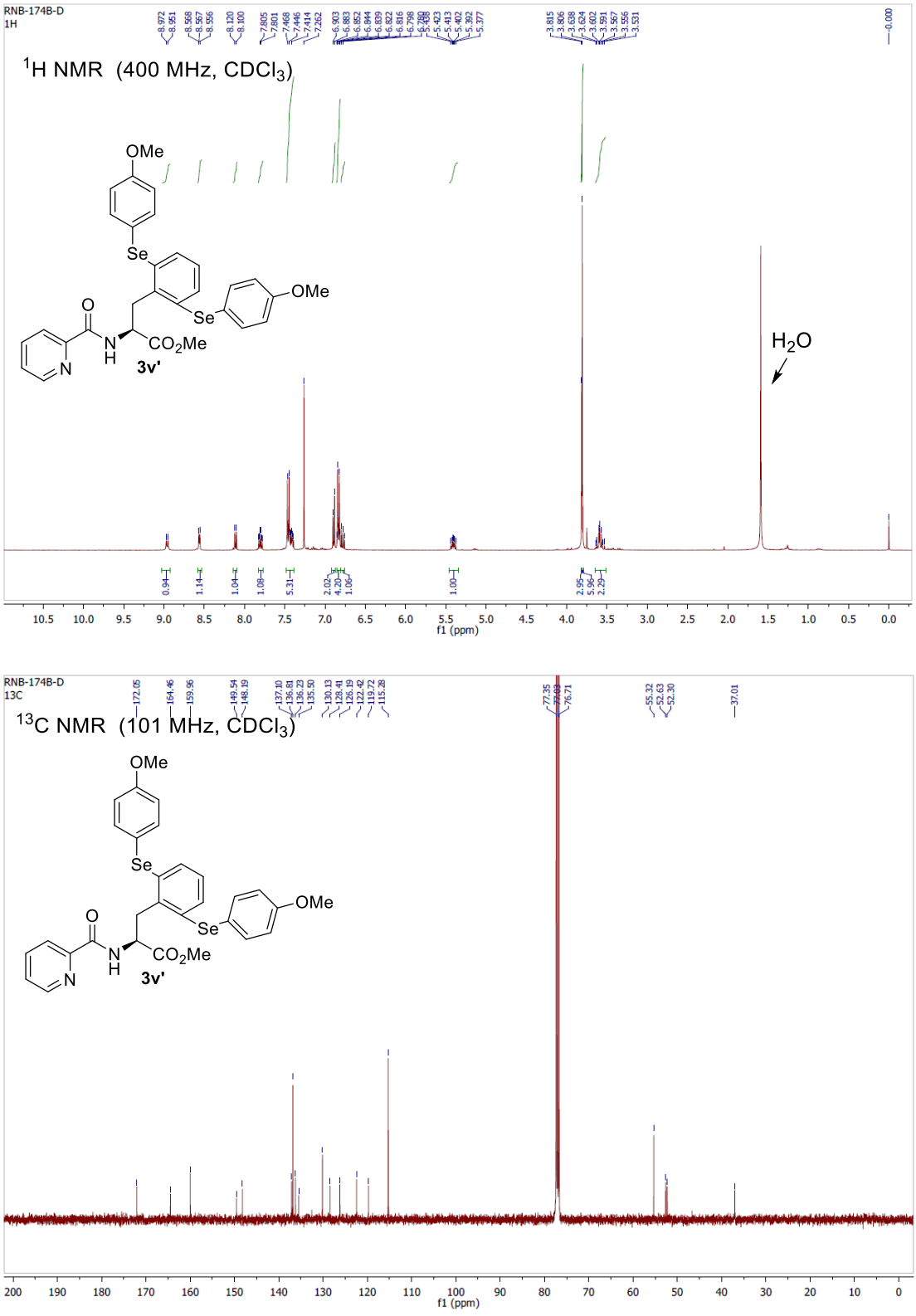


Fig S116. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3v'**

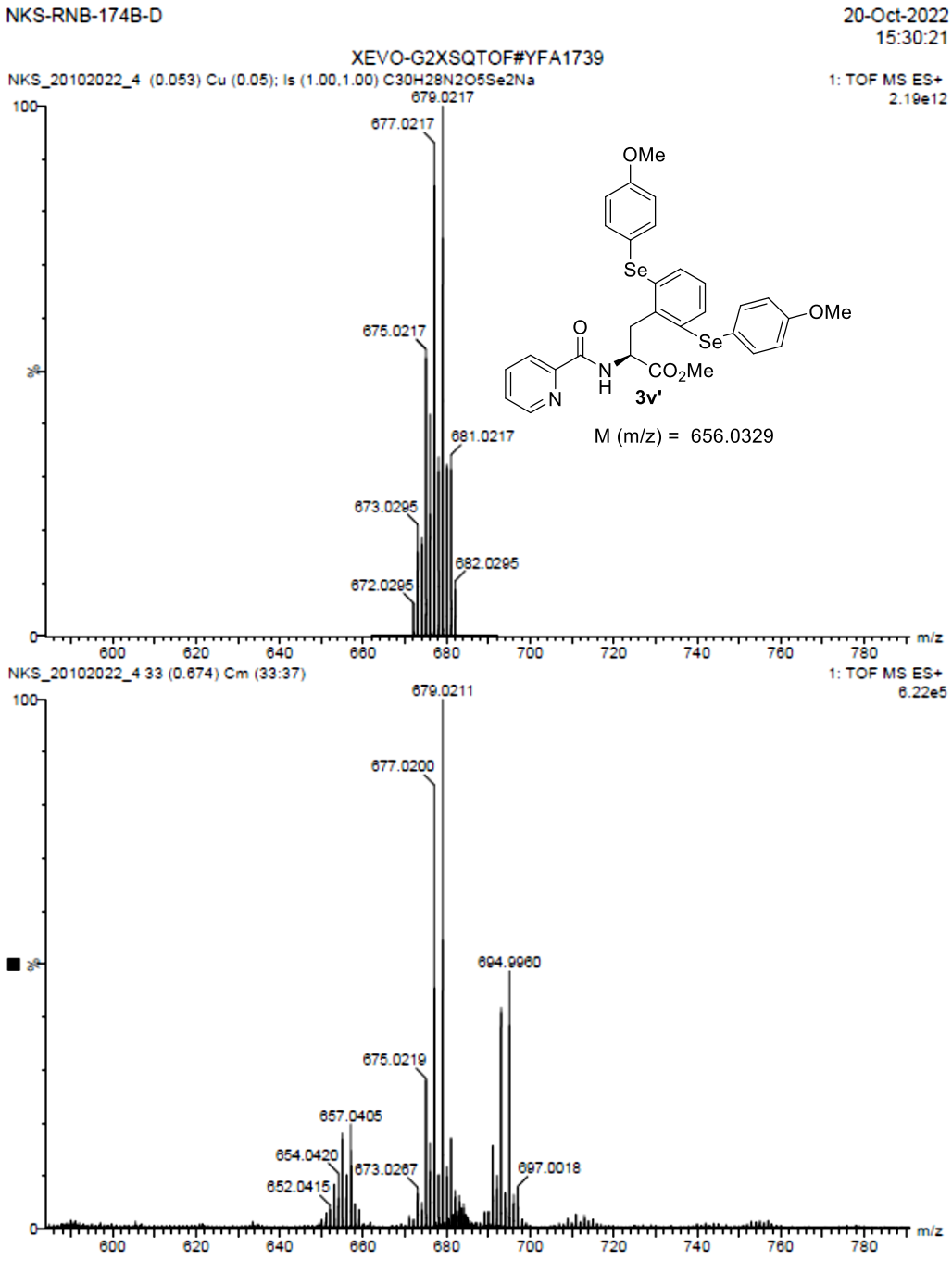
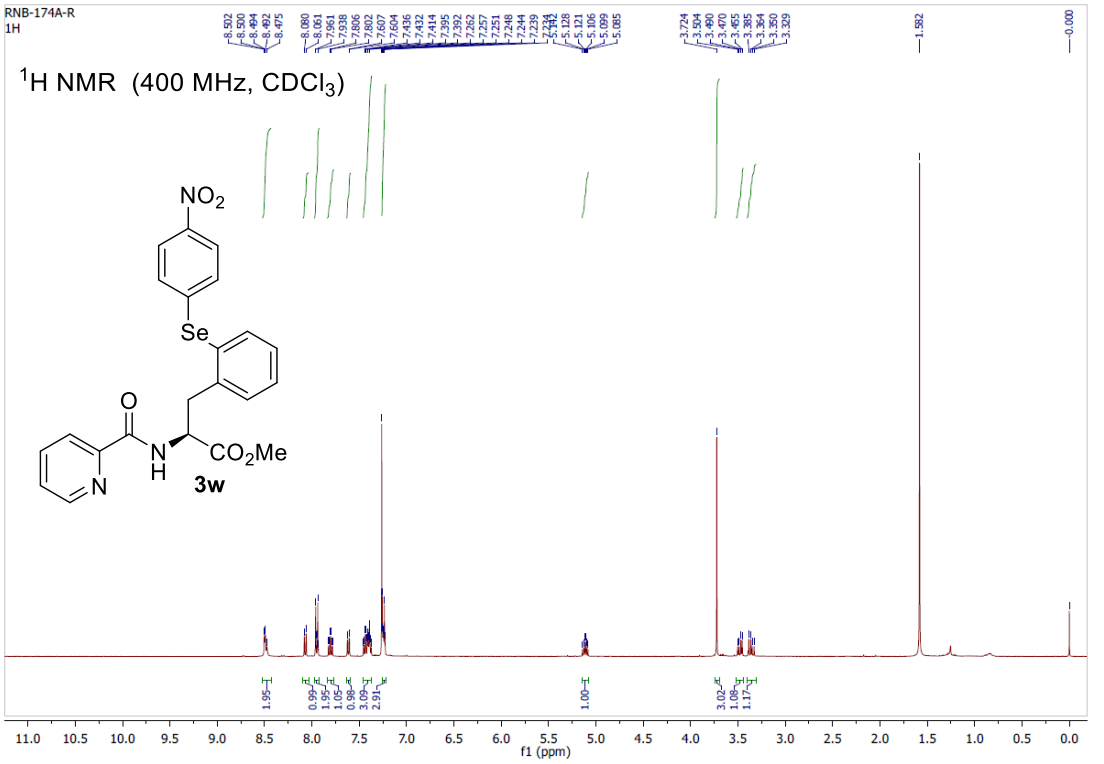


Fig S117. ESI-HRMS spectra of compound **3v'**



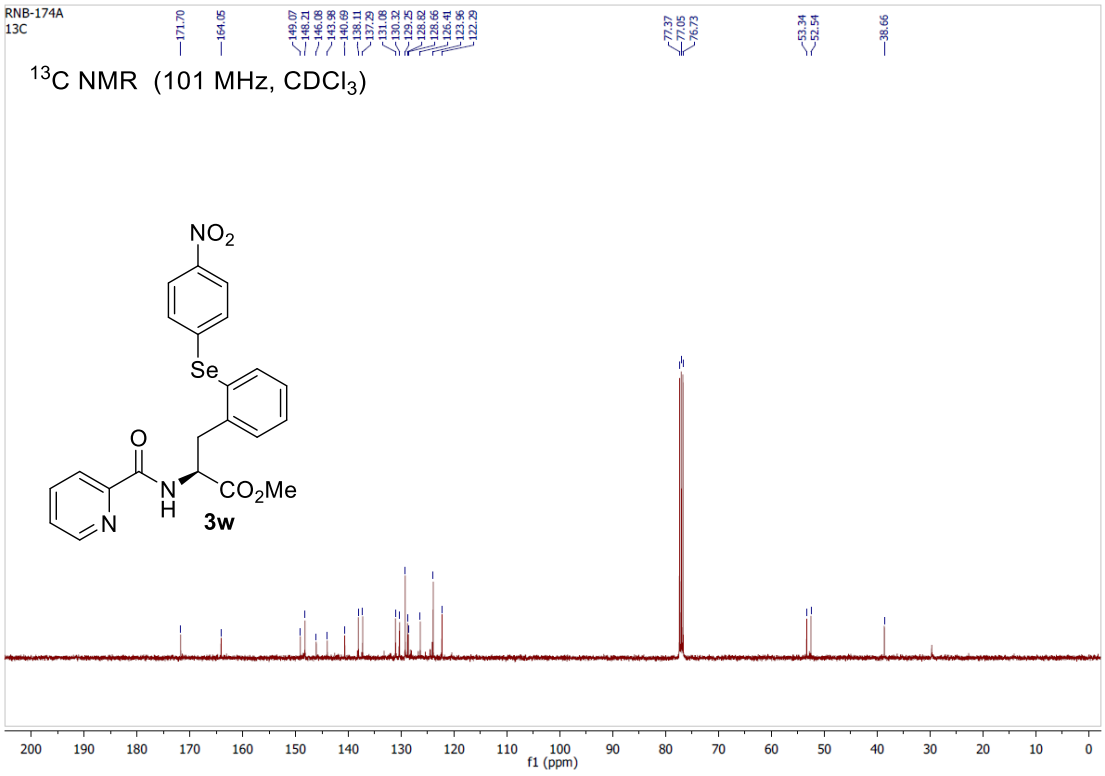


Fig S118. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3w**

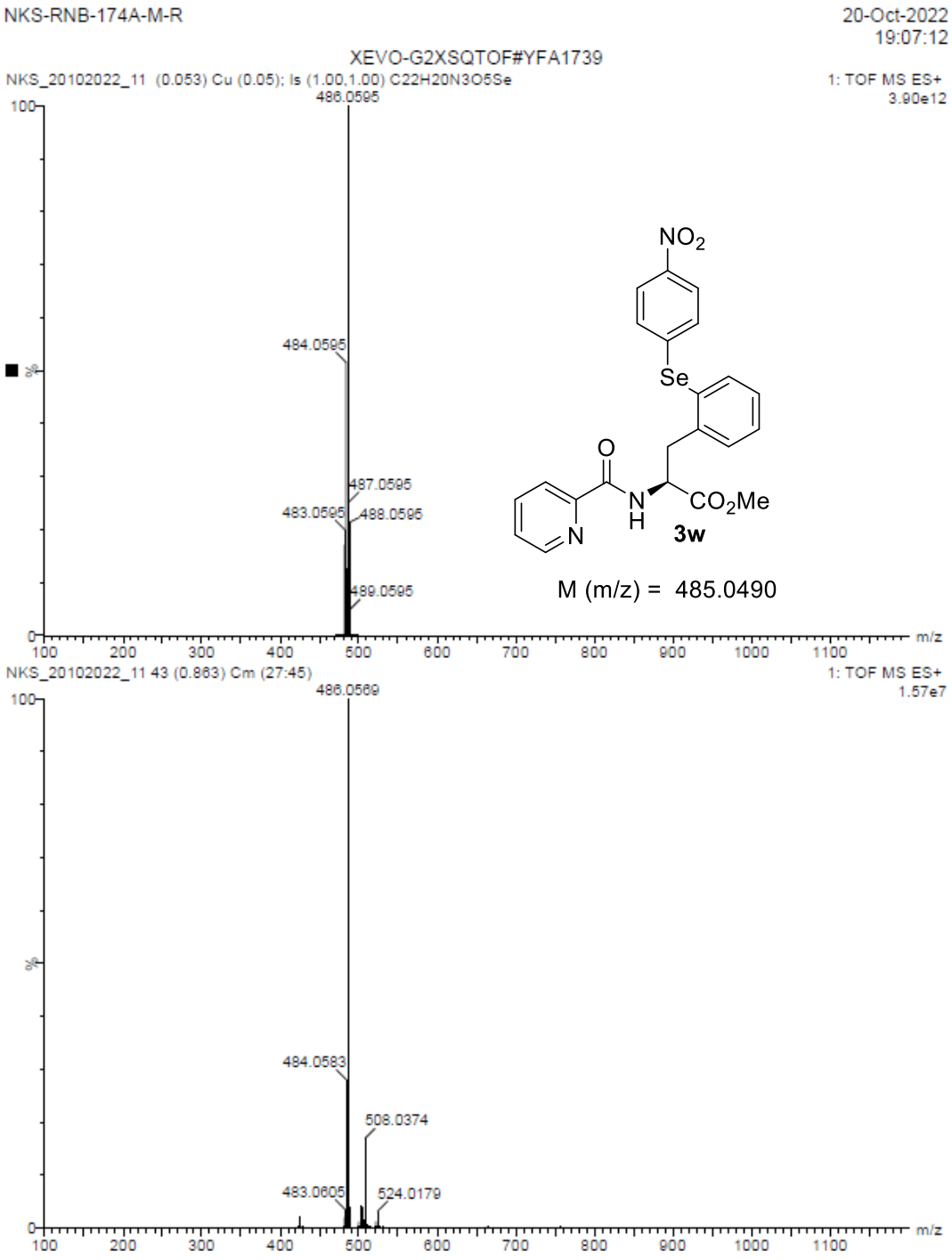


Fig S119. ESI-HRMS spectra of compound **3w**

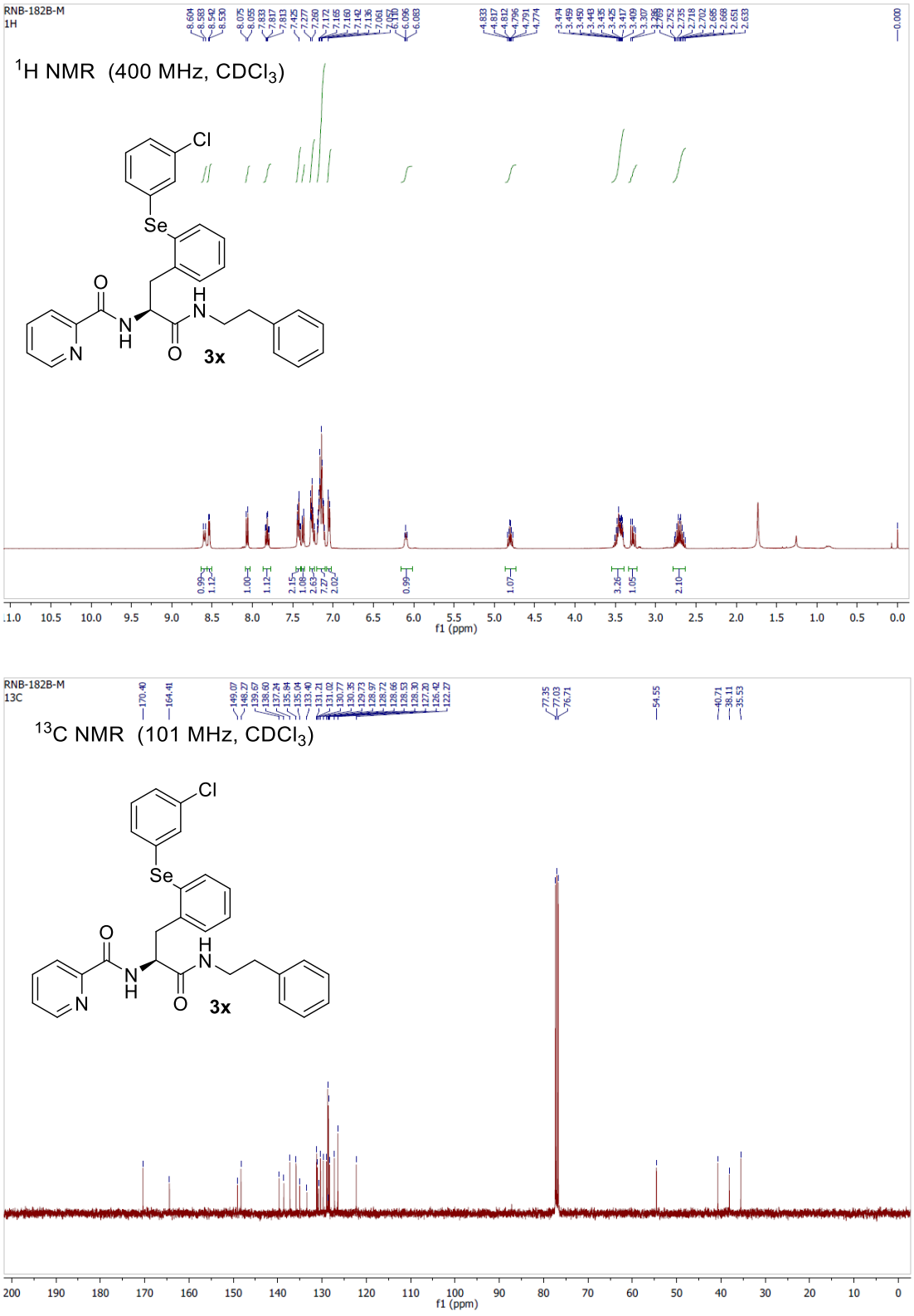


Fig S120. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3x**

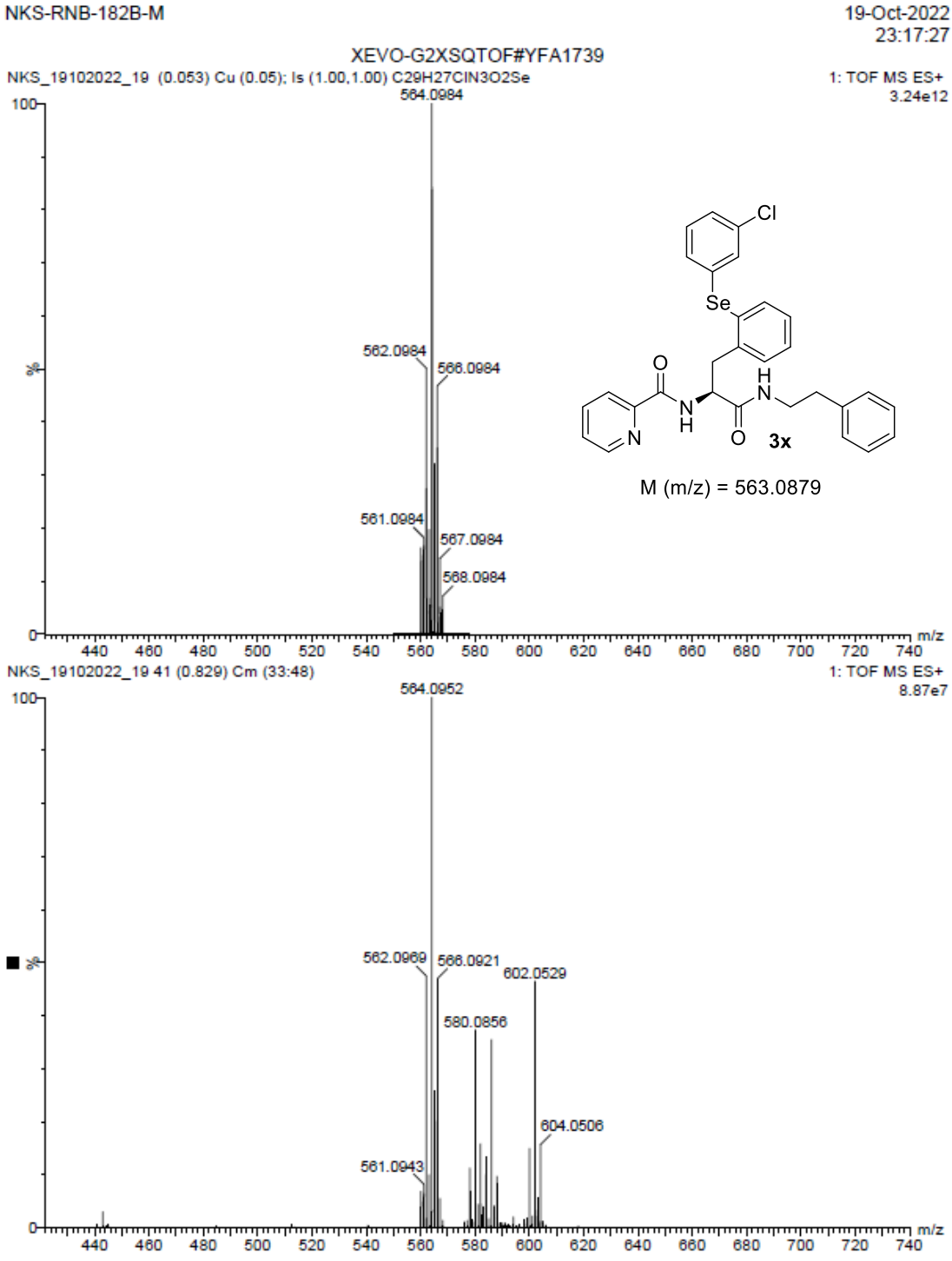


Fig S121. ESI-HRMS spectra of compound **3x**

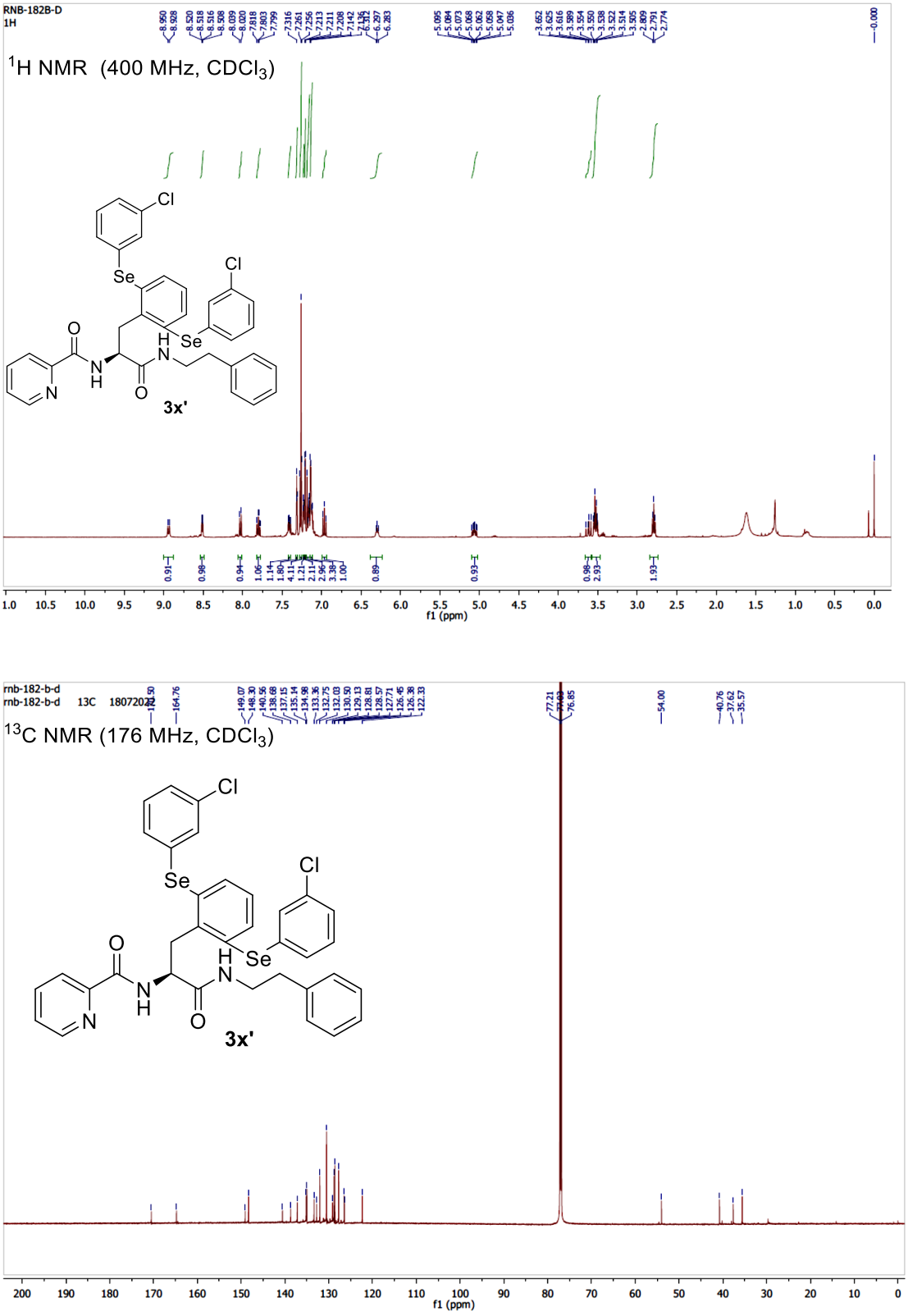


Fig S122. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3x'**

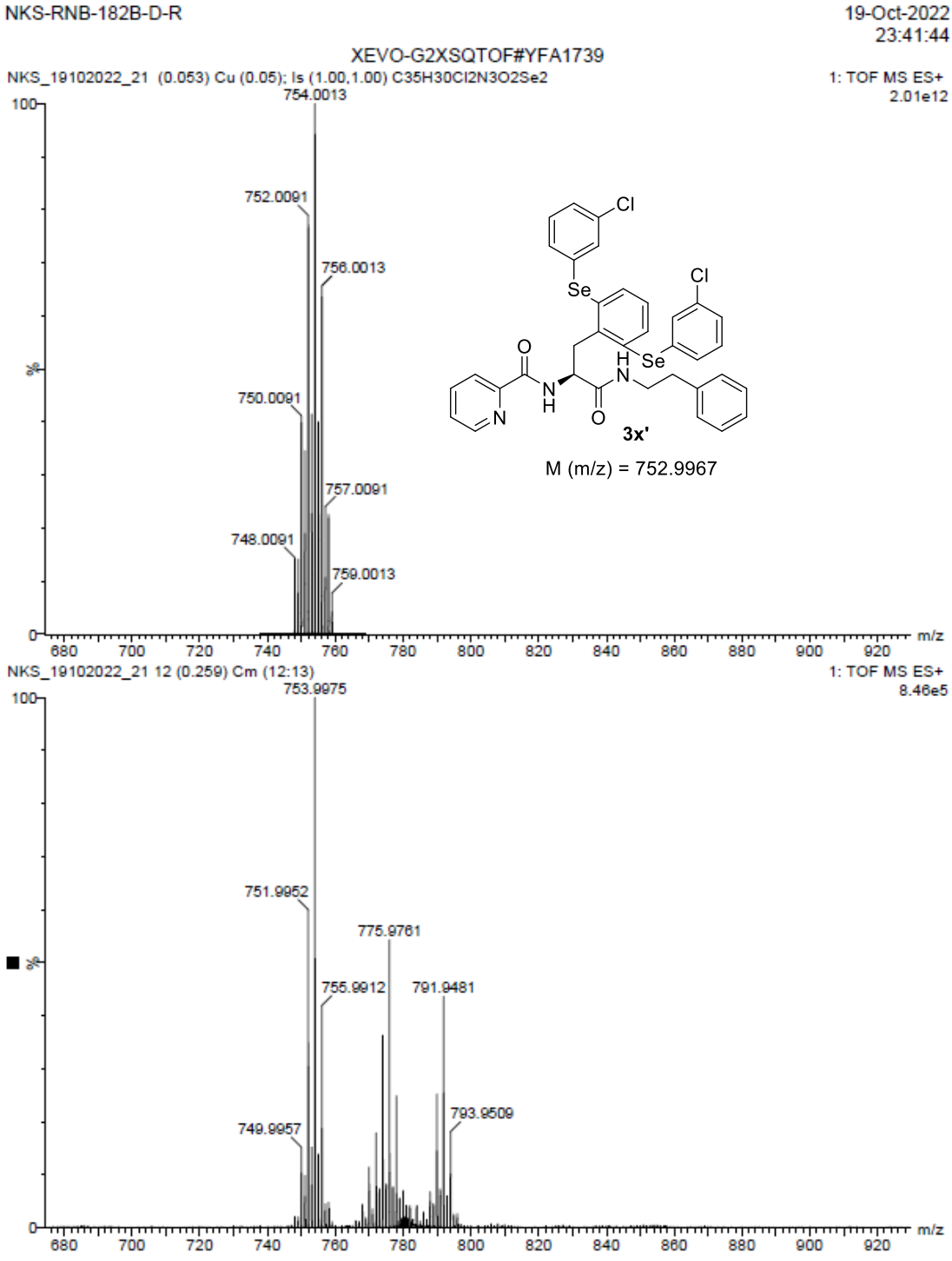


Fig S123. ESI-HRMS spectra of compound **3x'**

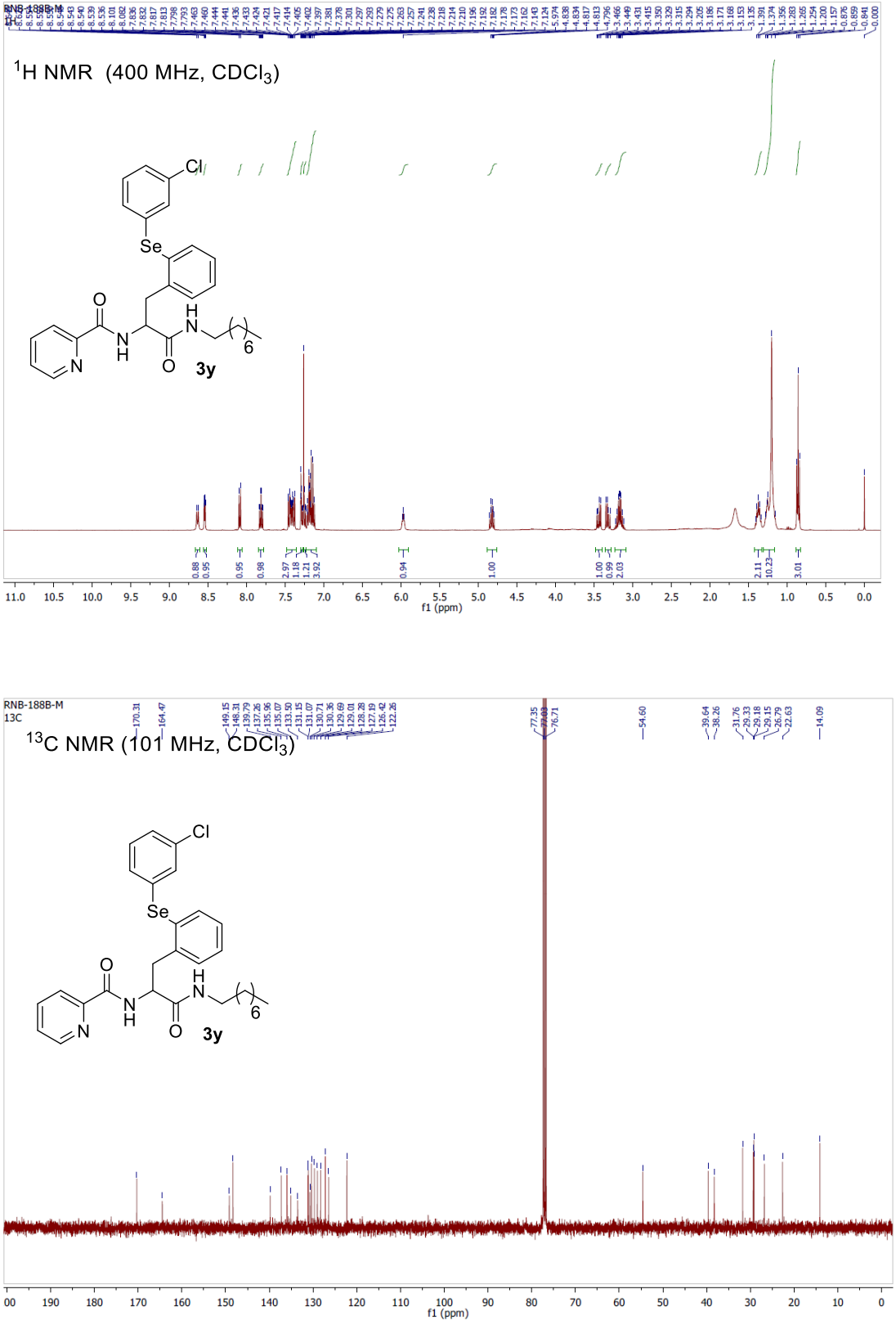


Fig S124. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3y**

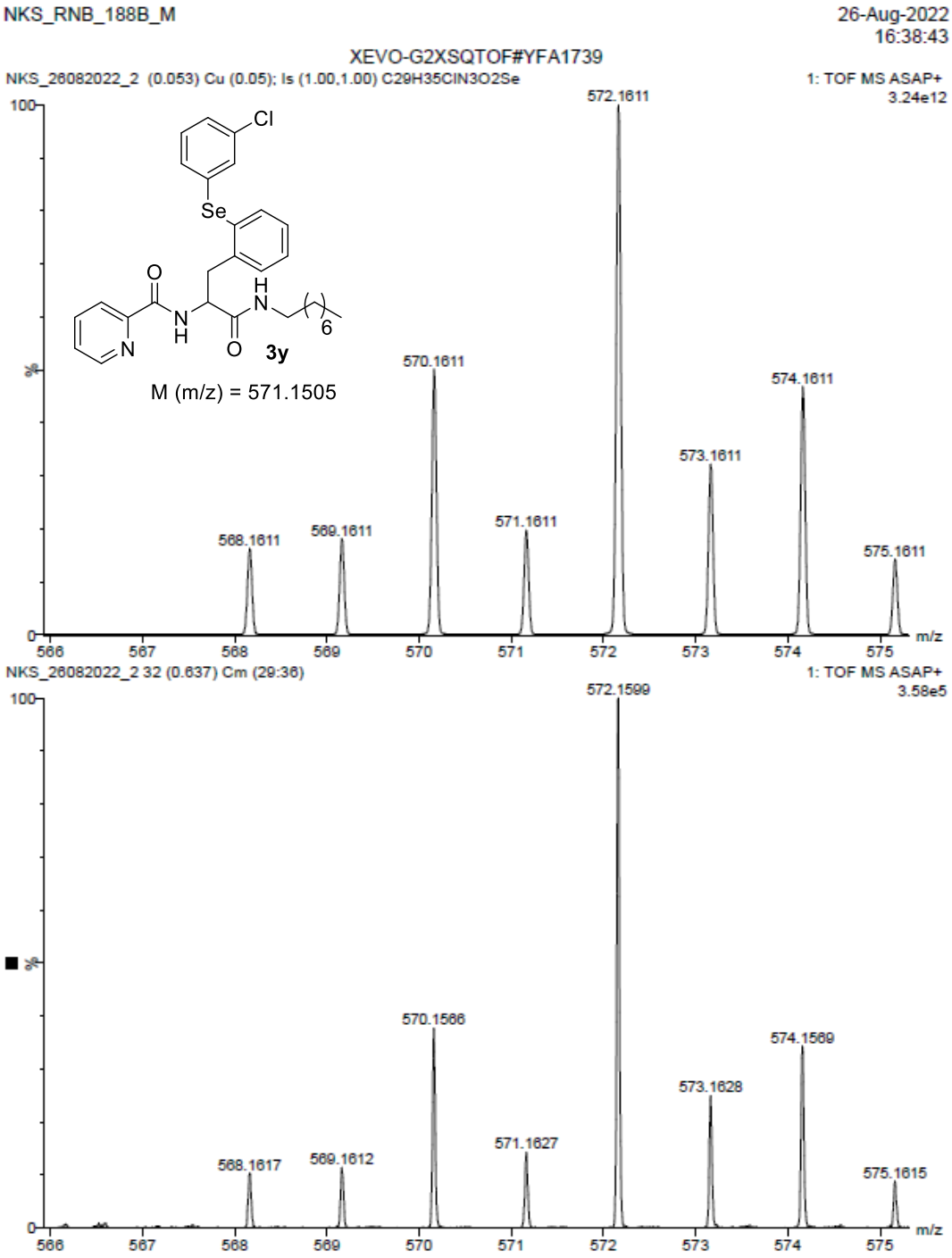


Fig S125. ASAP-HRMS spectra of compound **3y**

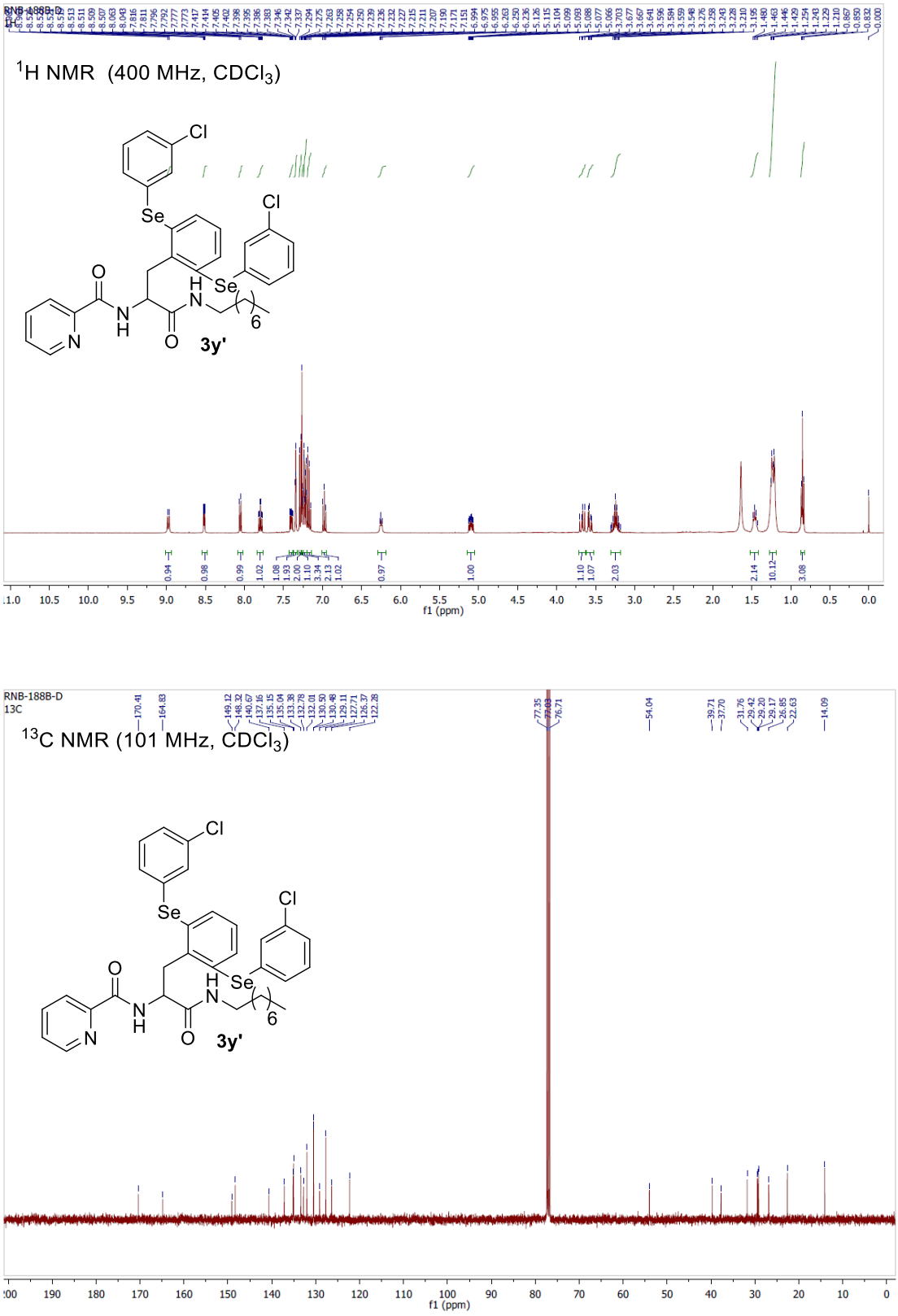


Fig S126. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3y'**

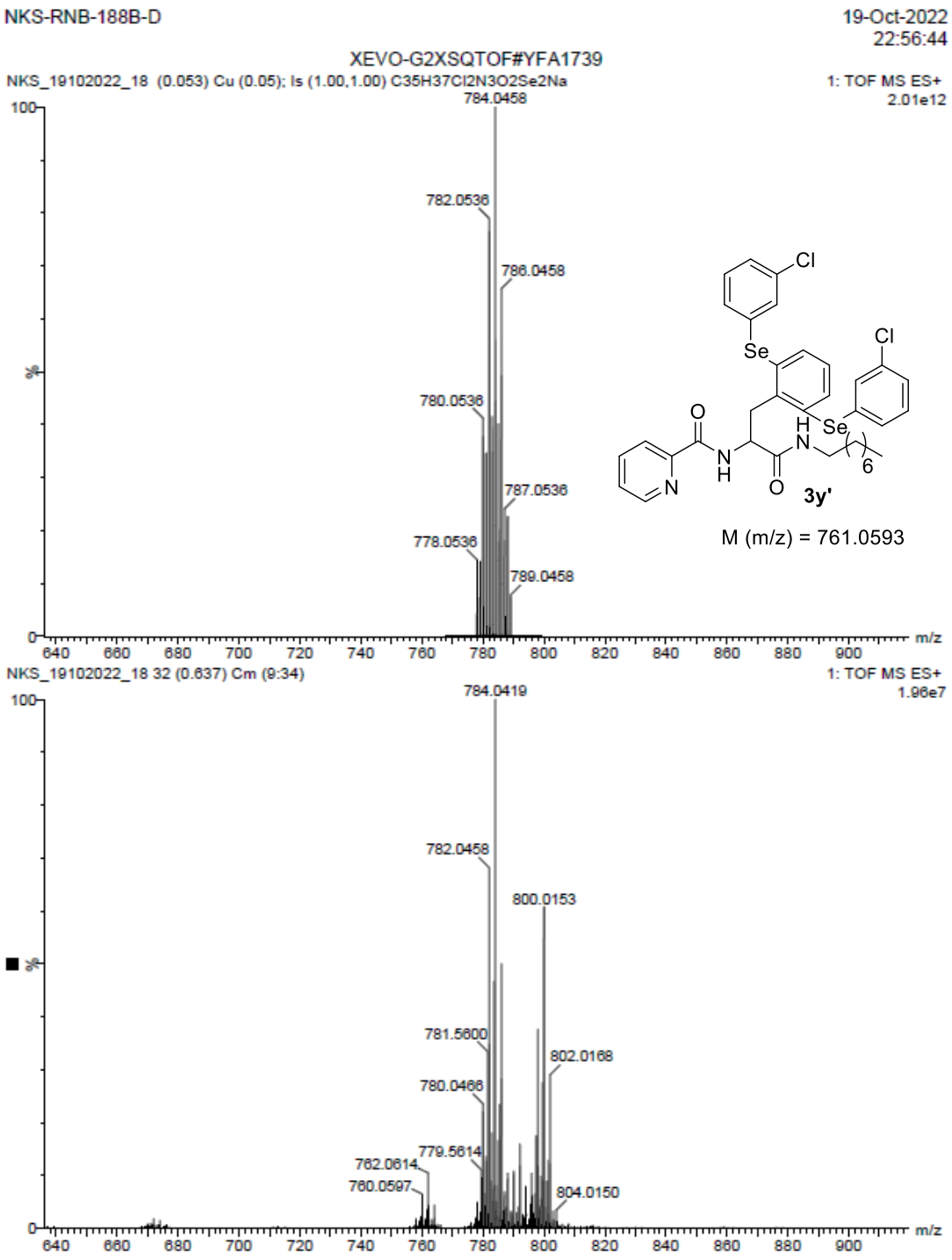


Fig S127. ESI-HRMS spectra of compound **3y'**

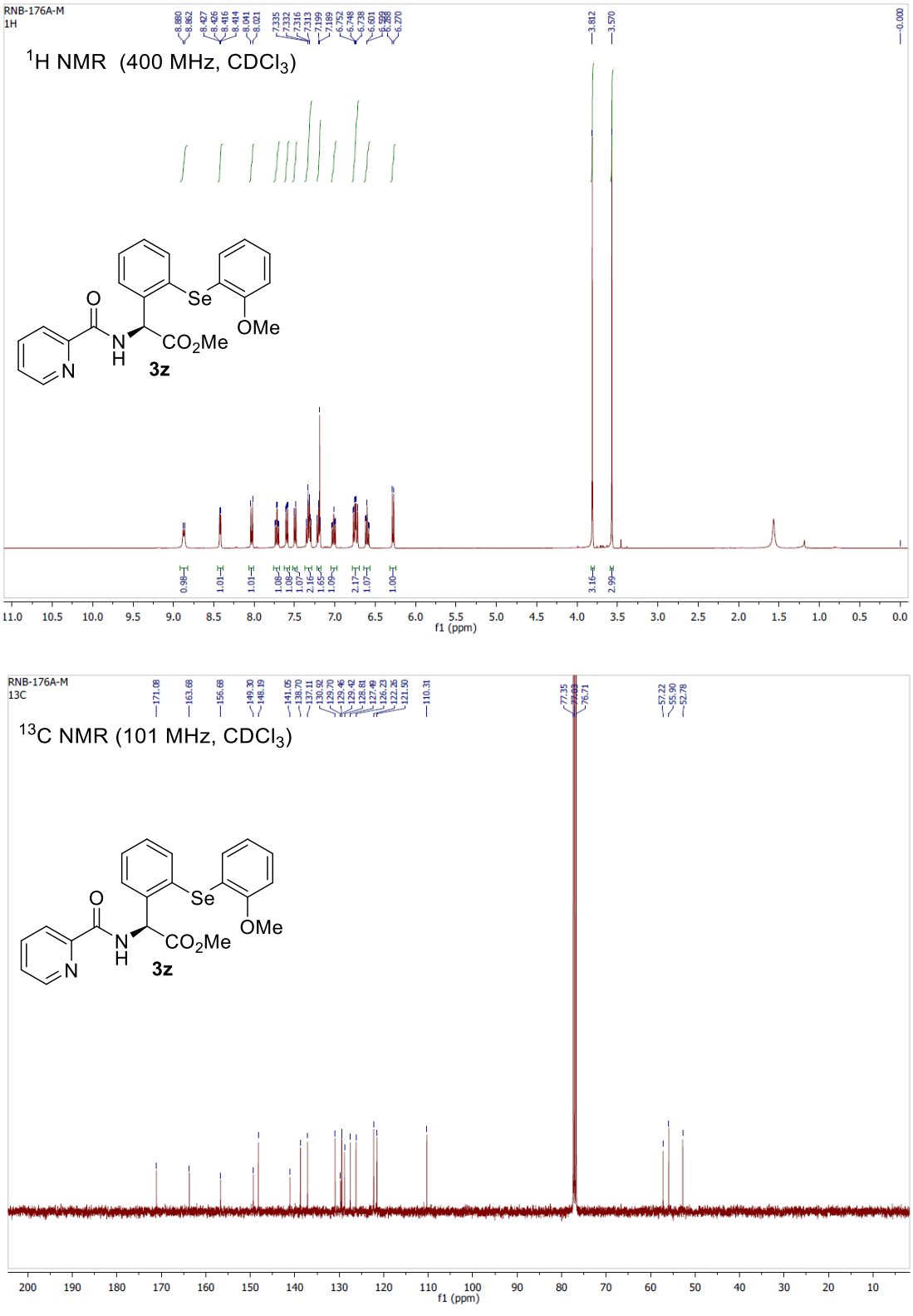


Fig S128. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3z**

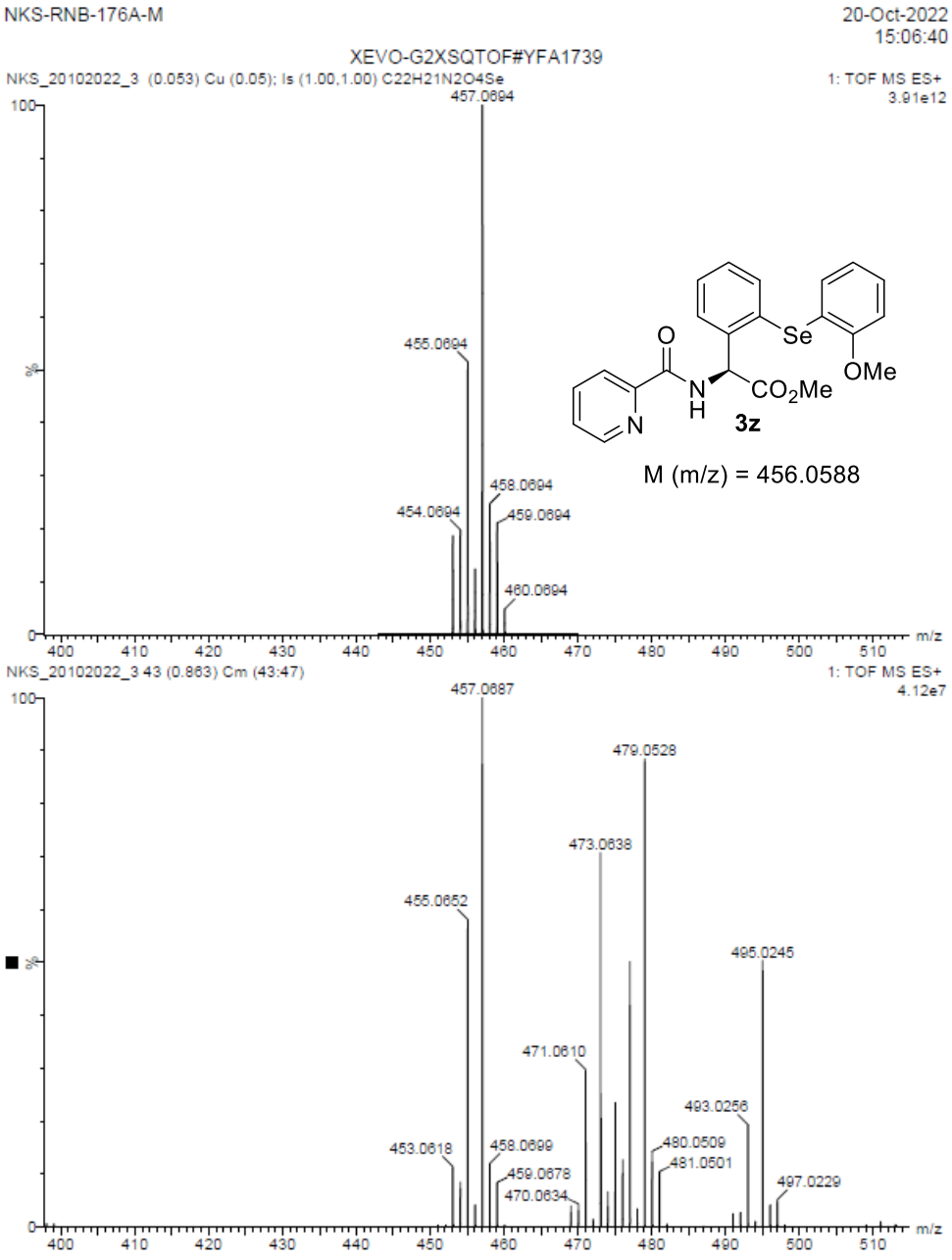


Fig S129. ESI-HRMS spectra of compound **3z**

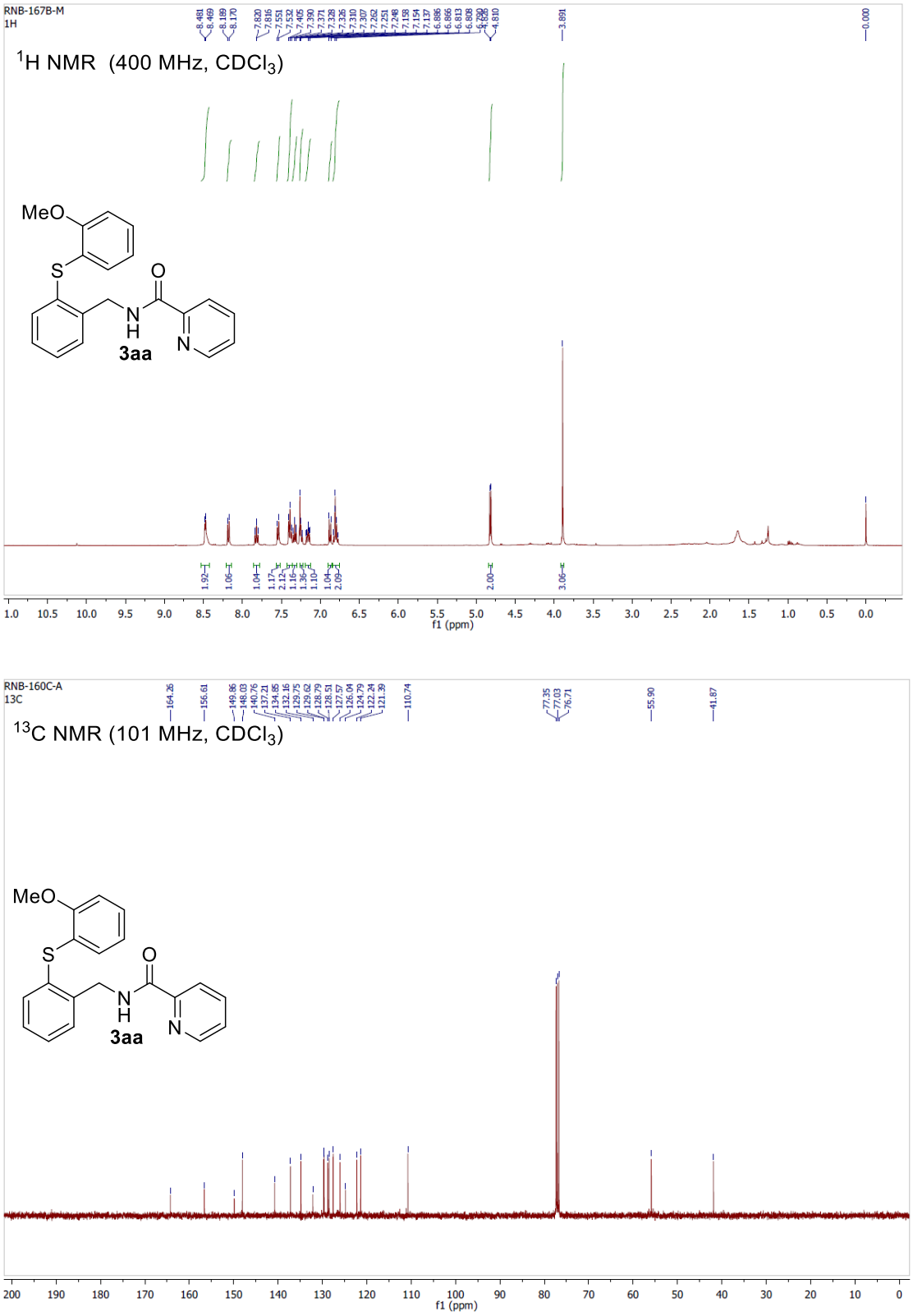


Fig S130. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3aa**

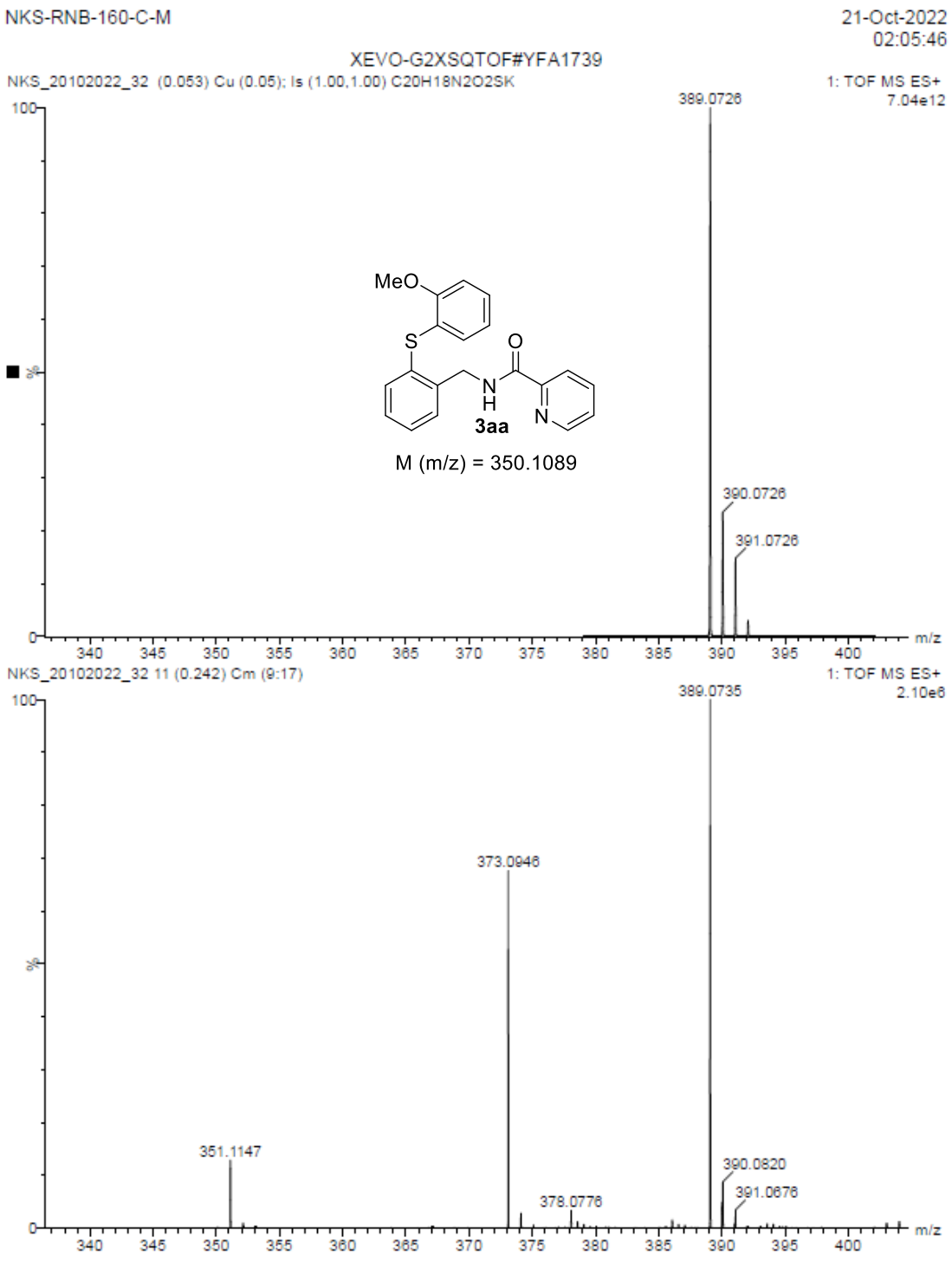
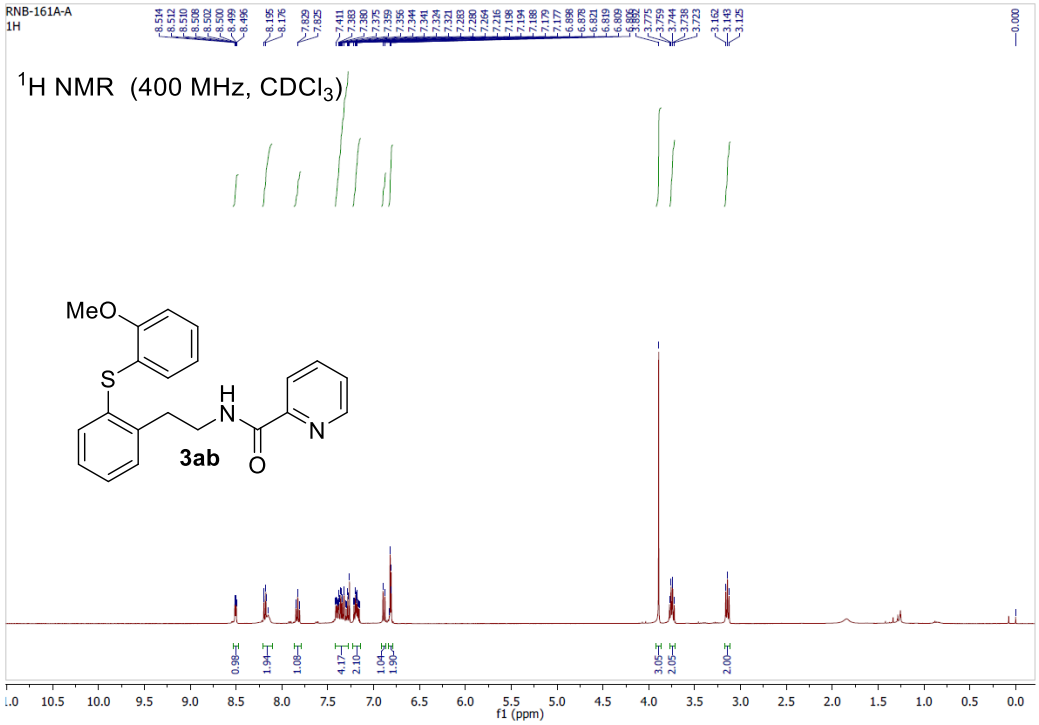


Fig S131. ESI-HRMS spectra of thiolated compound **3aa**



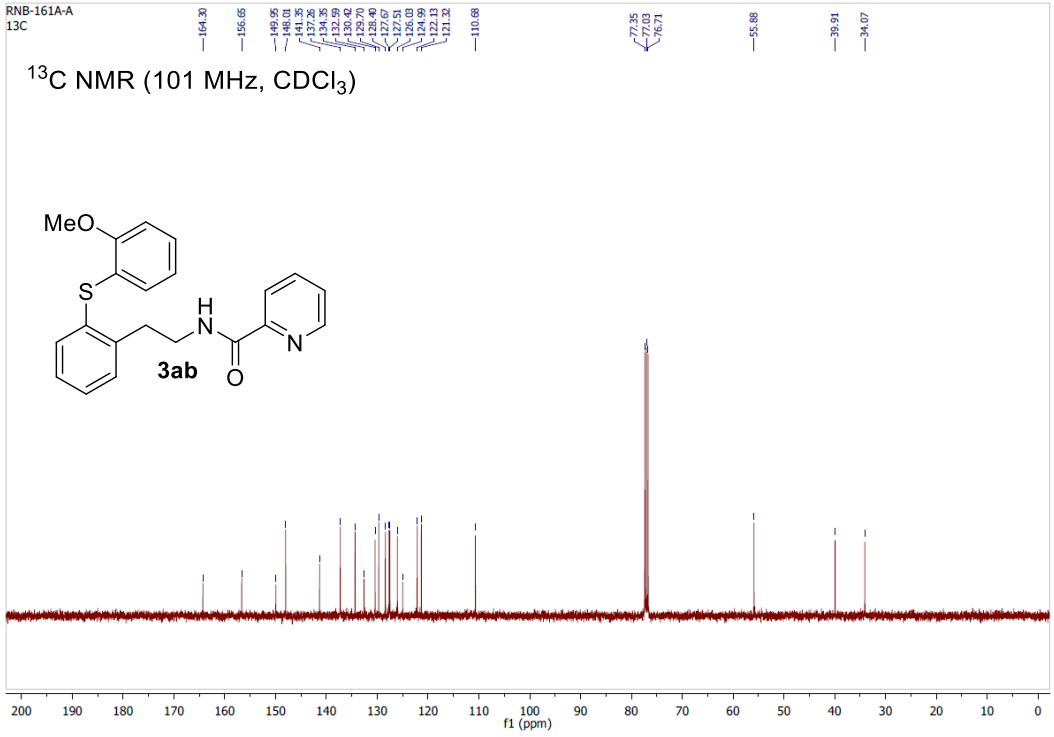


Fig S132. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3ab**

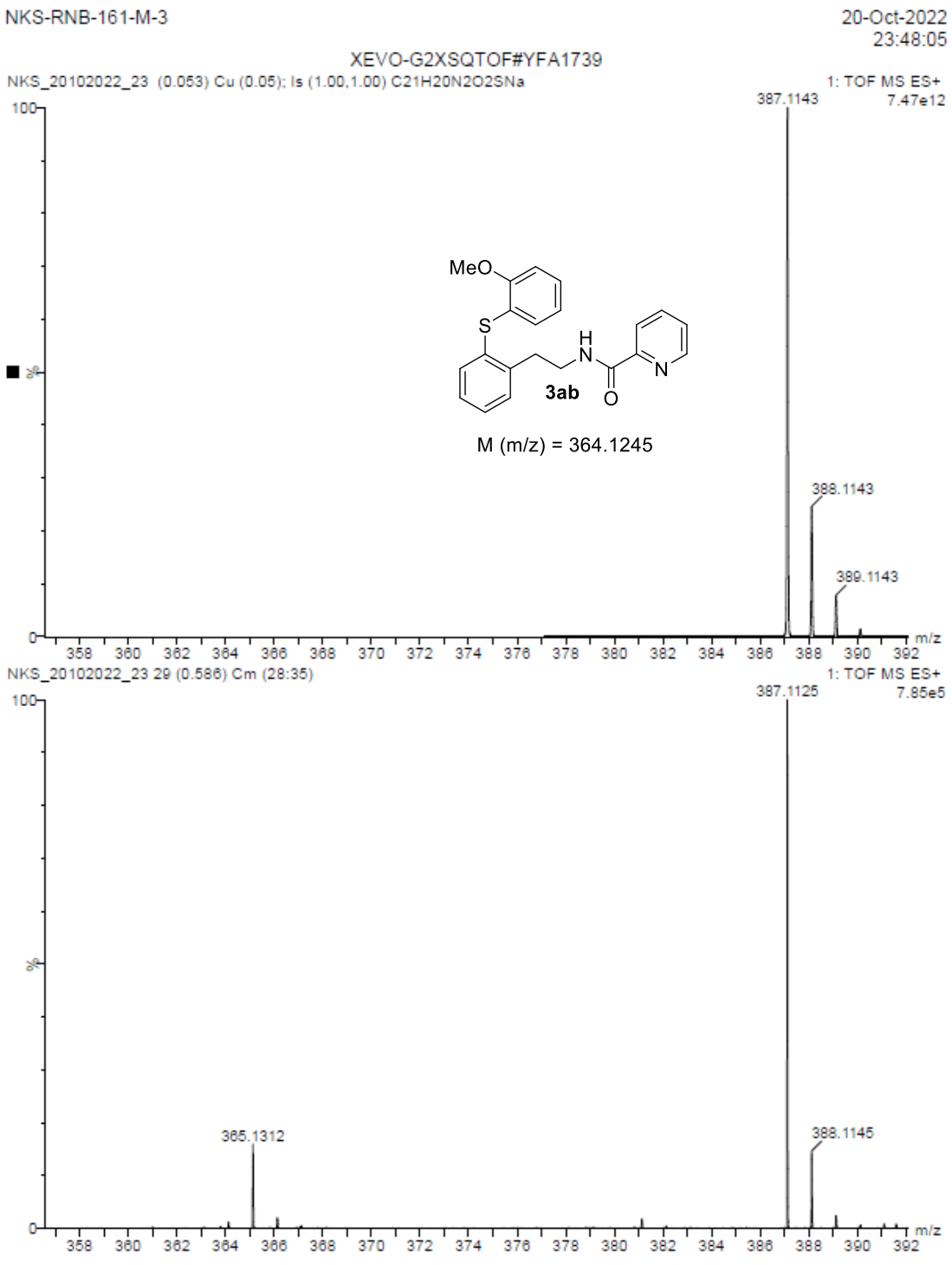
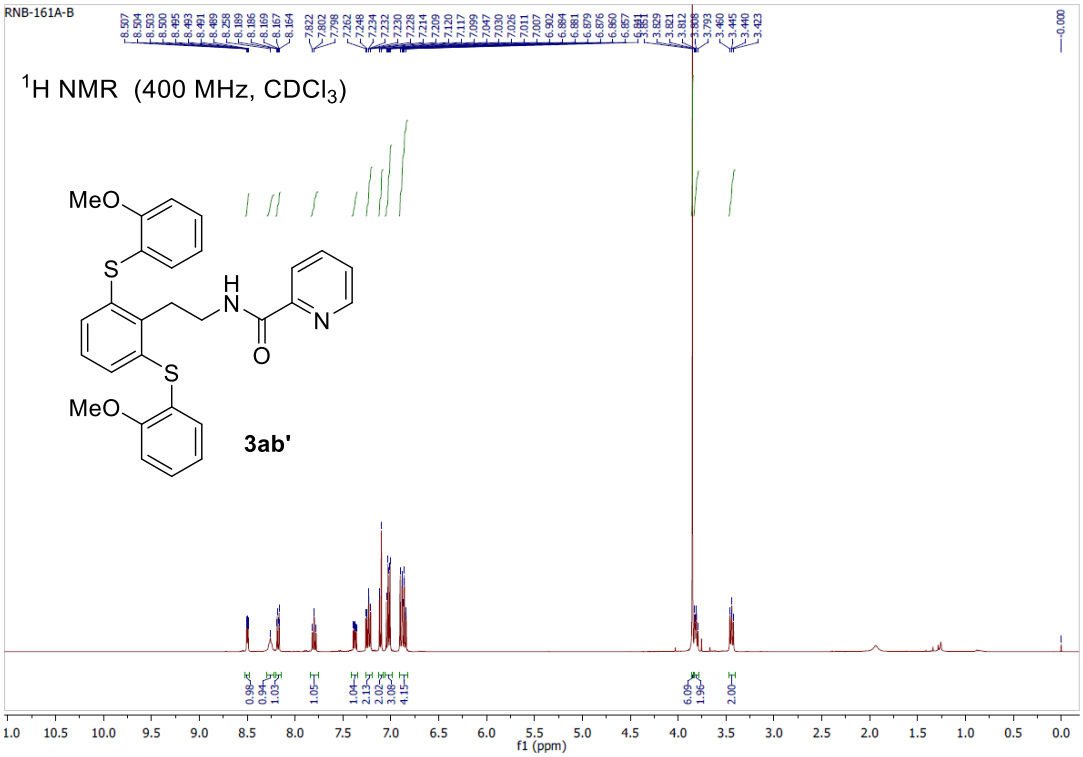


Fig S133. ESI-HRMS spectra of thiolated compound **3ab**



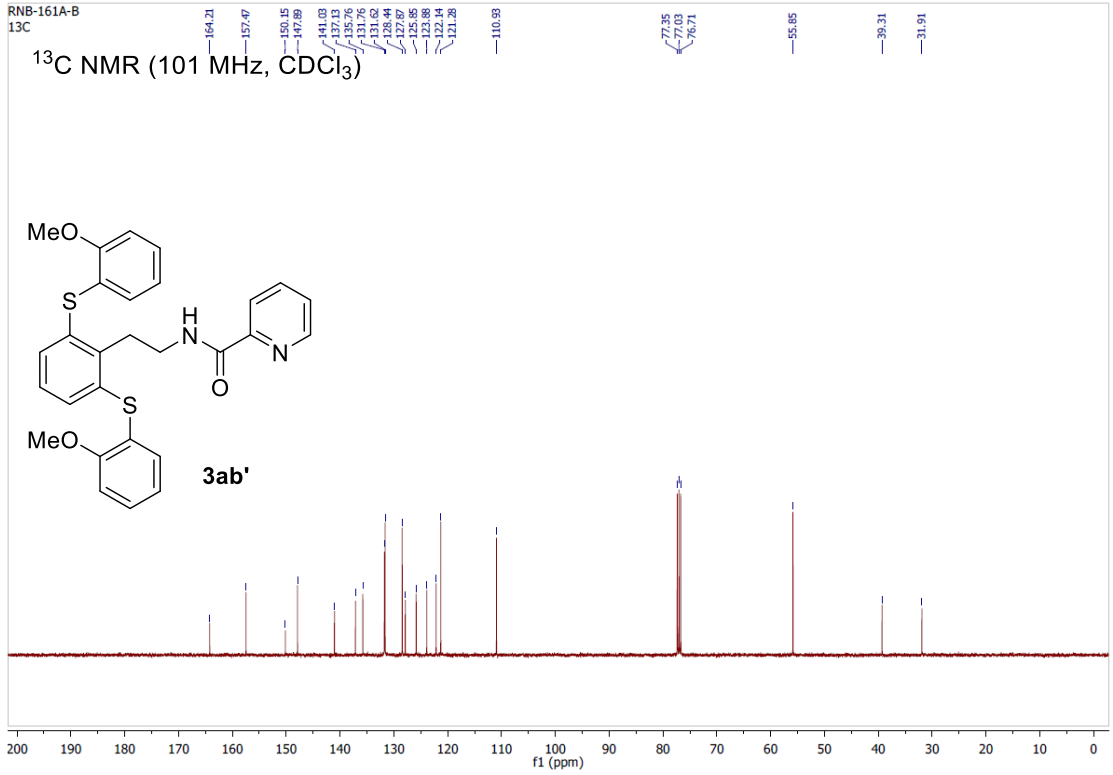


Fig S134. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3ab'**

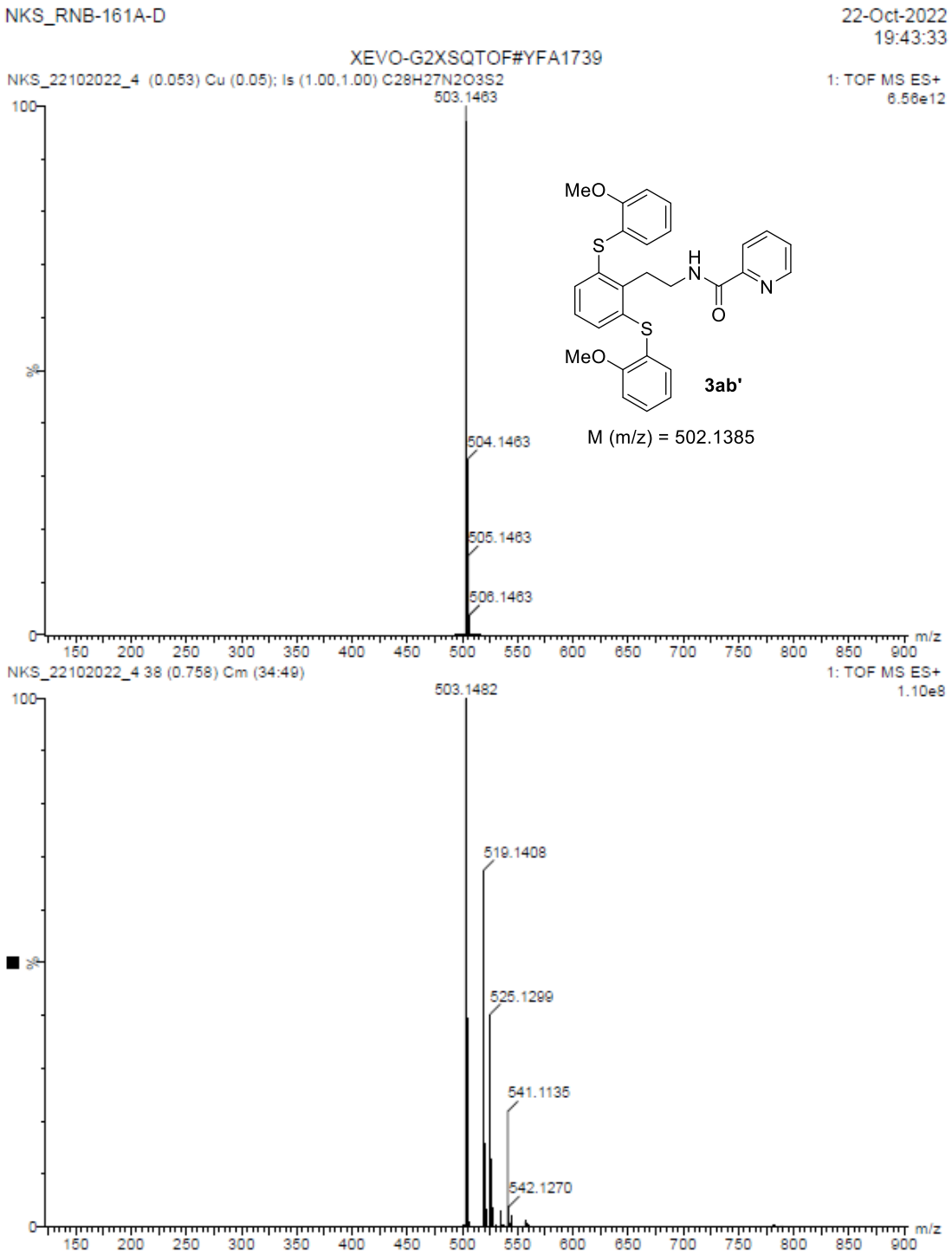


Fig S135. ESI-HRMS spectra of thiolated compound **3ab'**

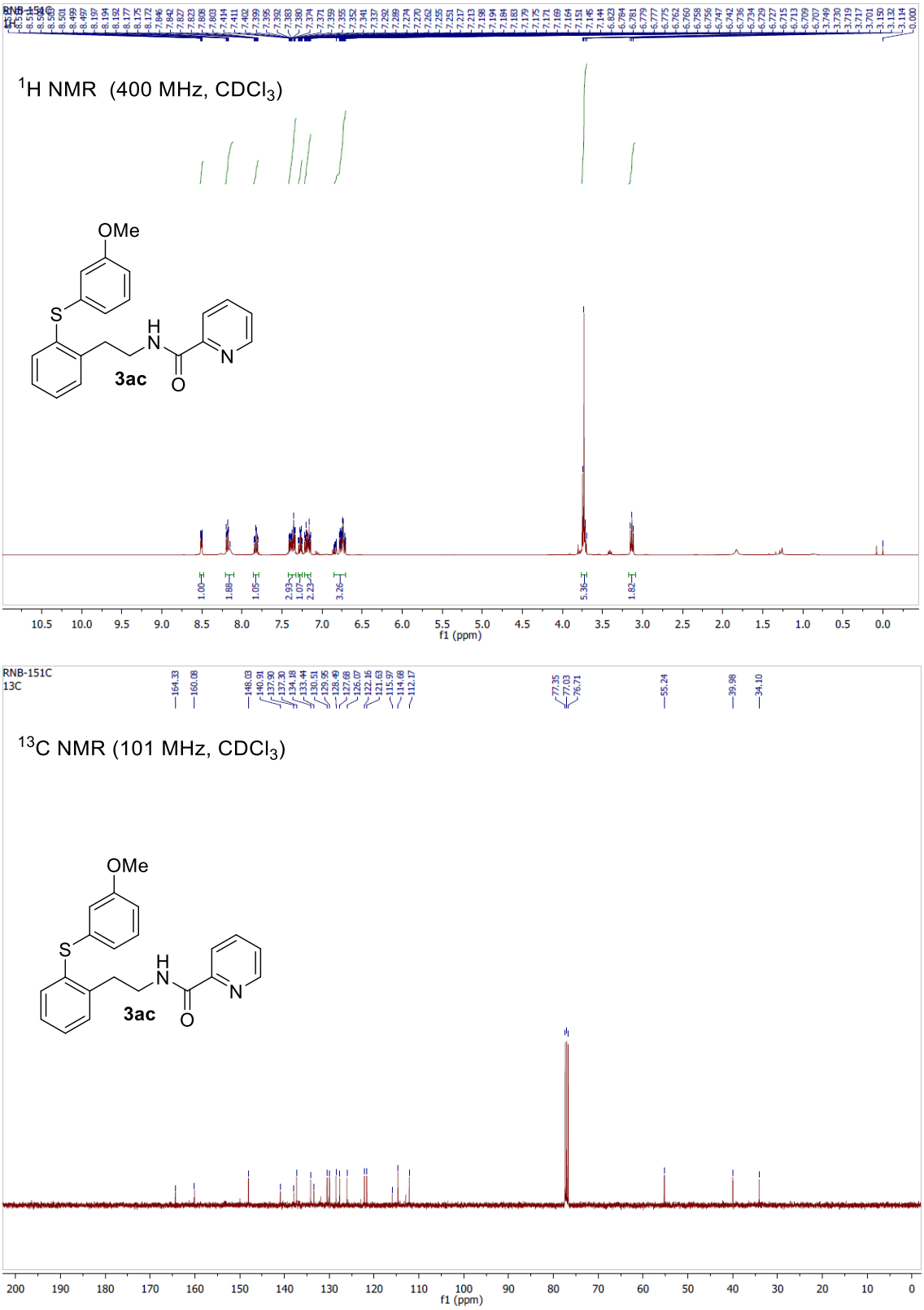


Fig S136. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3ac**

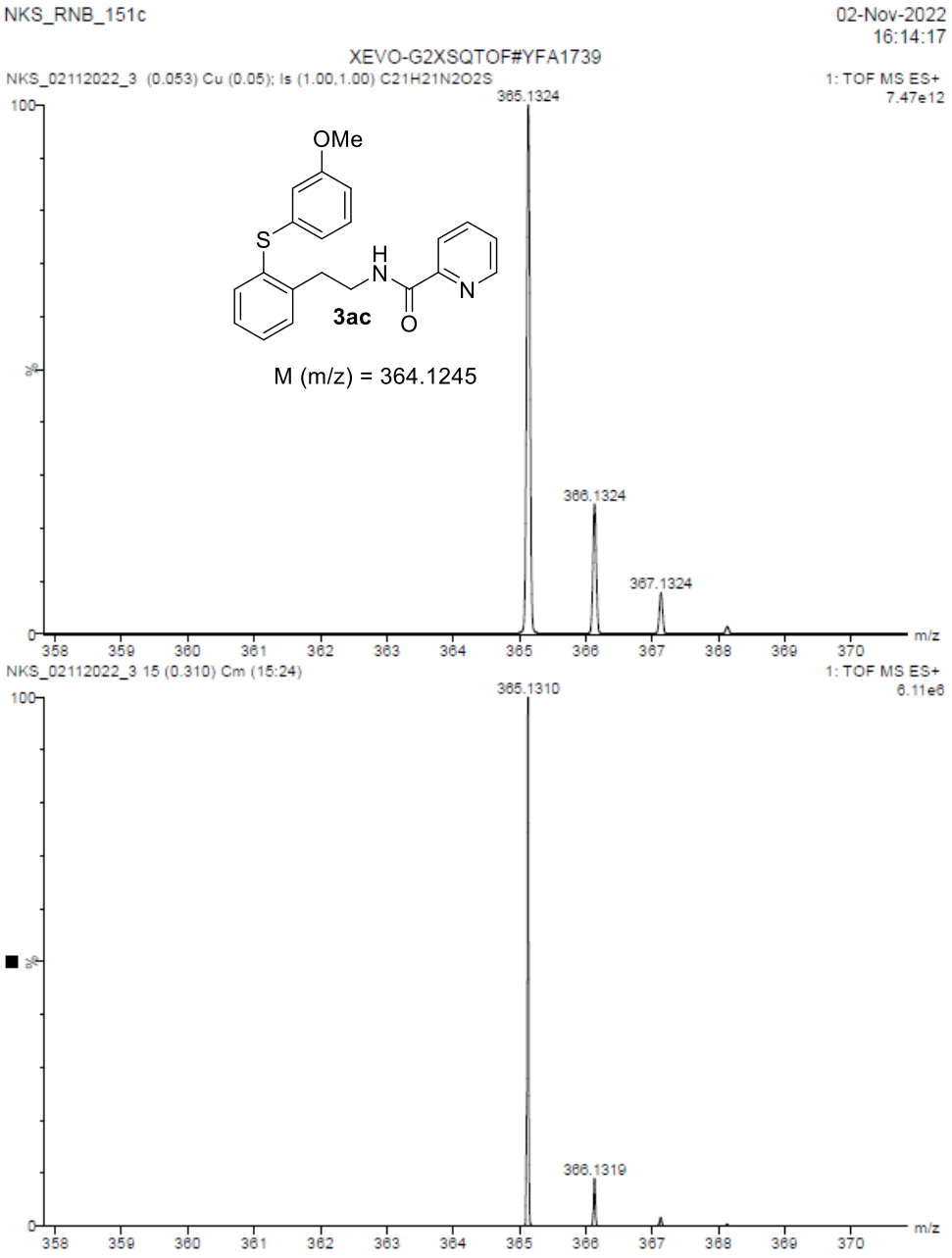


Fig S137. ESI-HRMS spectra of thiolated compound **3ac**

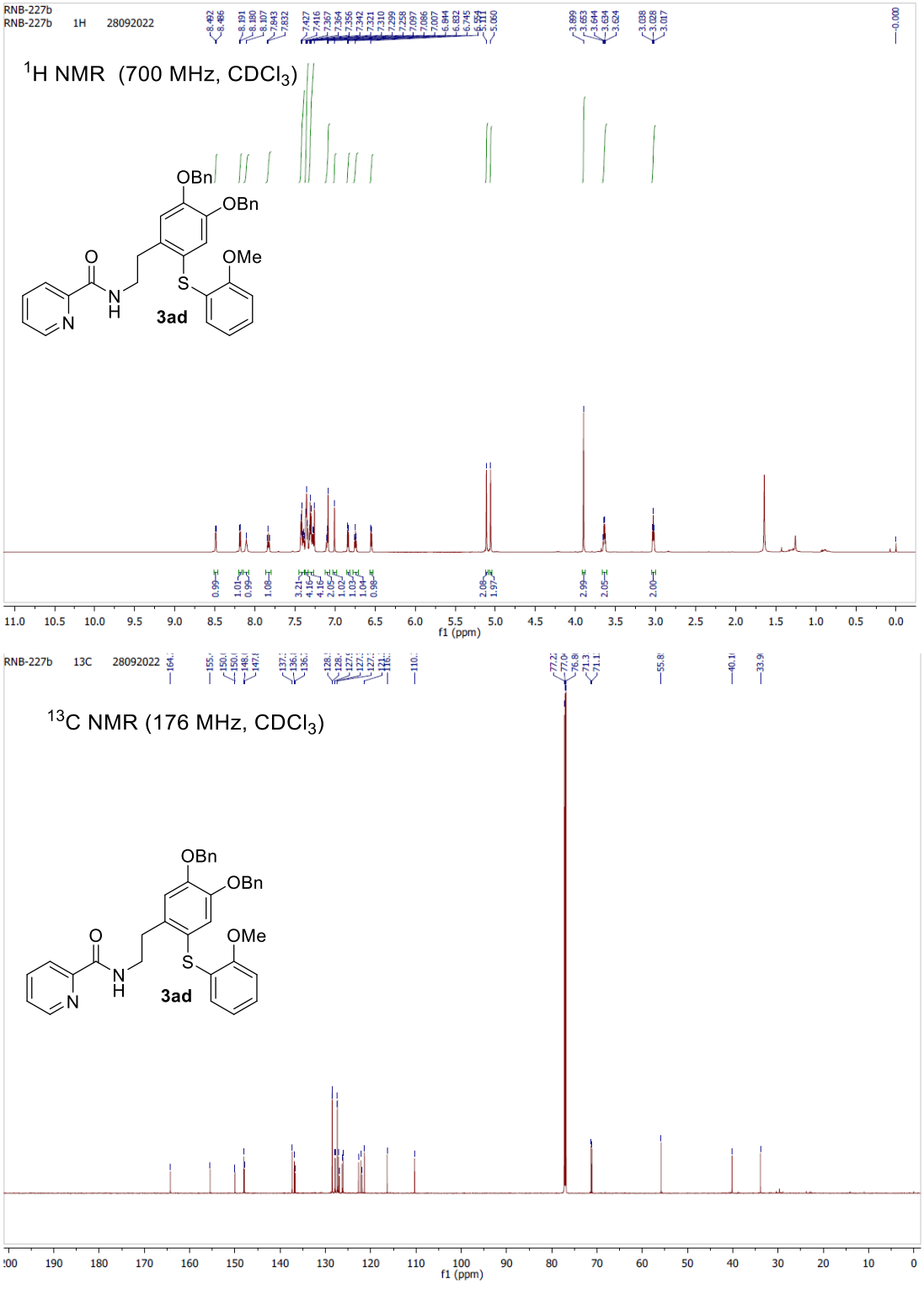


Fig S138. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3ad**

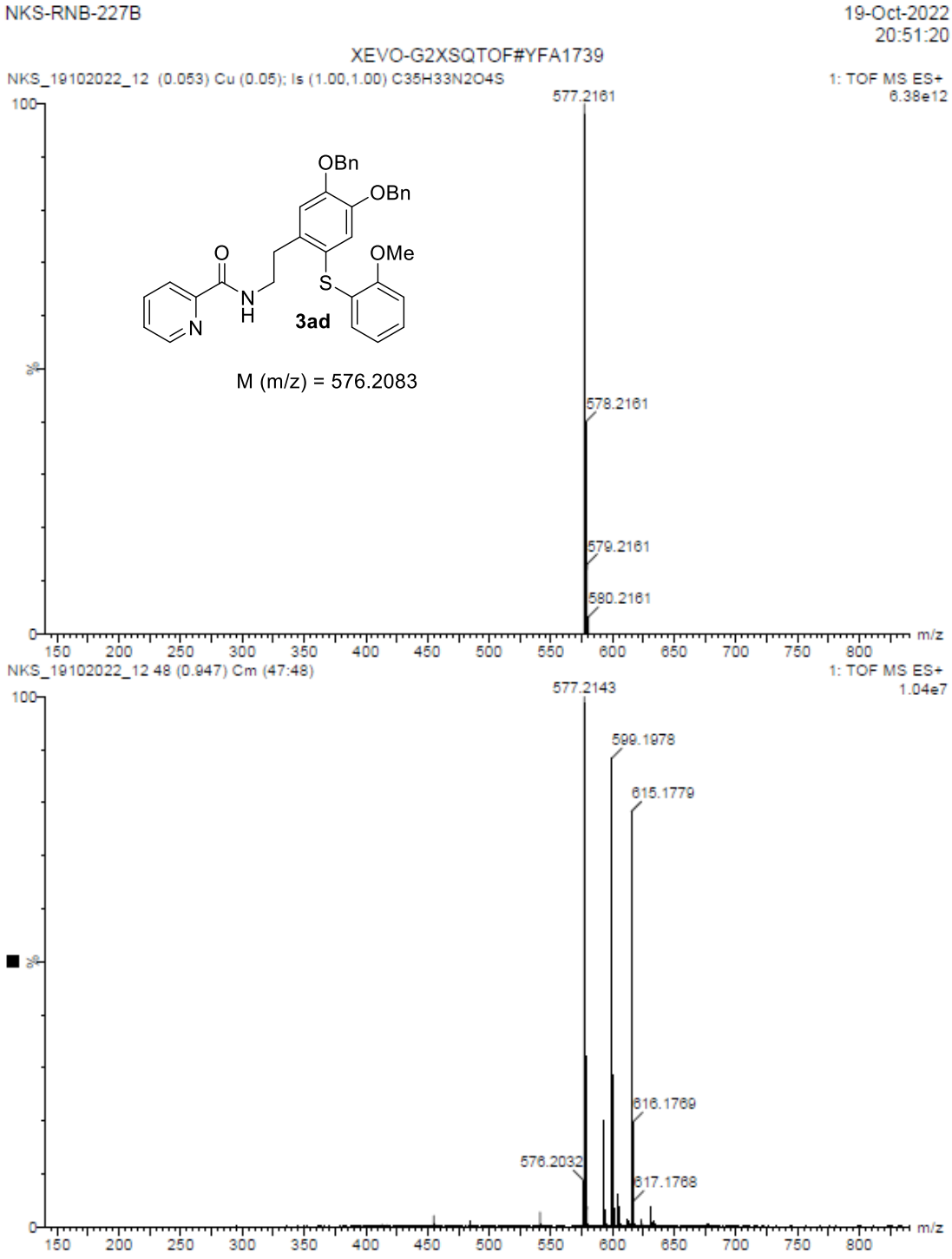
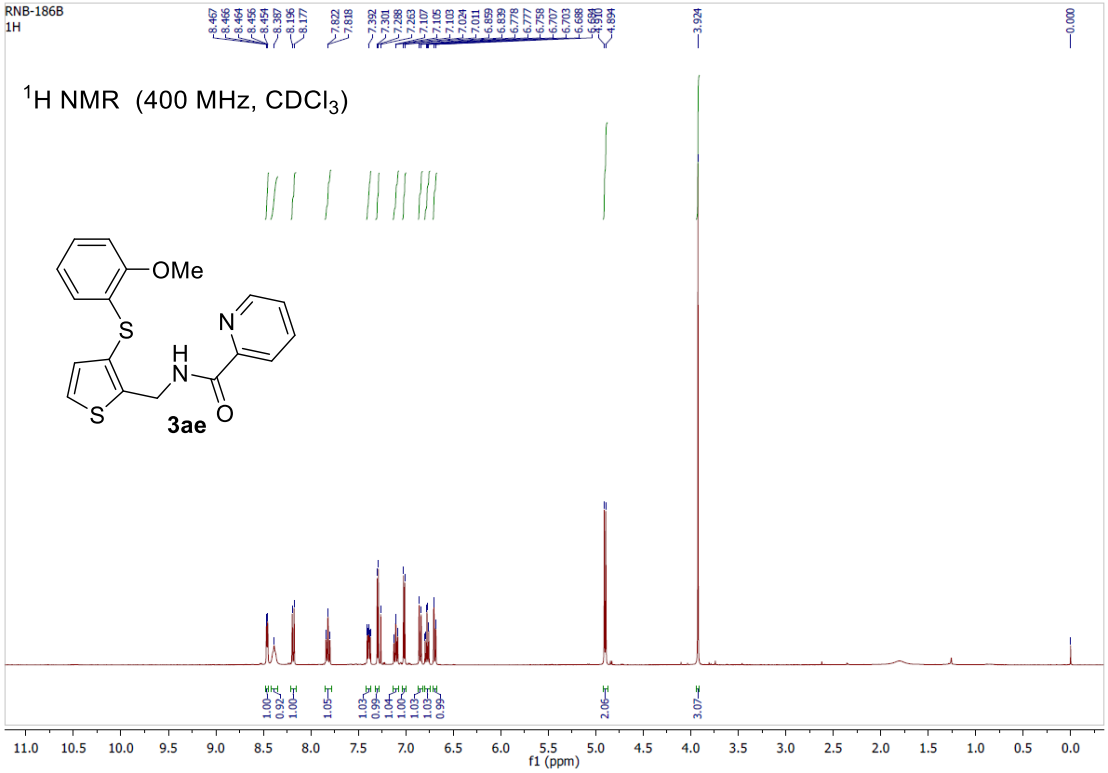


Fig S139. ESI-HRMS spectra of thiolated compound **3ad**



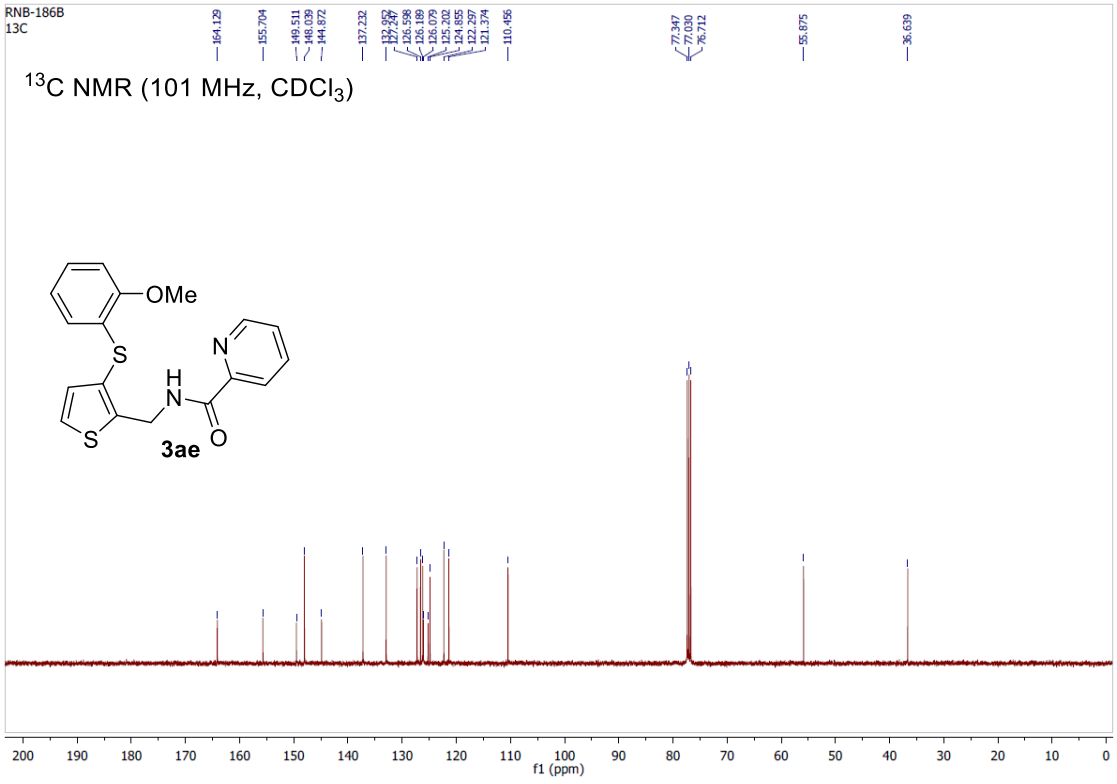


Fig S140. ^{1}H, ^{13}C {^{1}H} NMR spectra of thiolated compound **3ae**

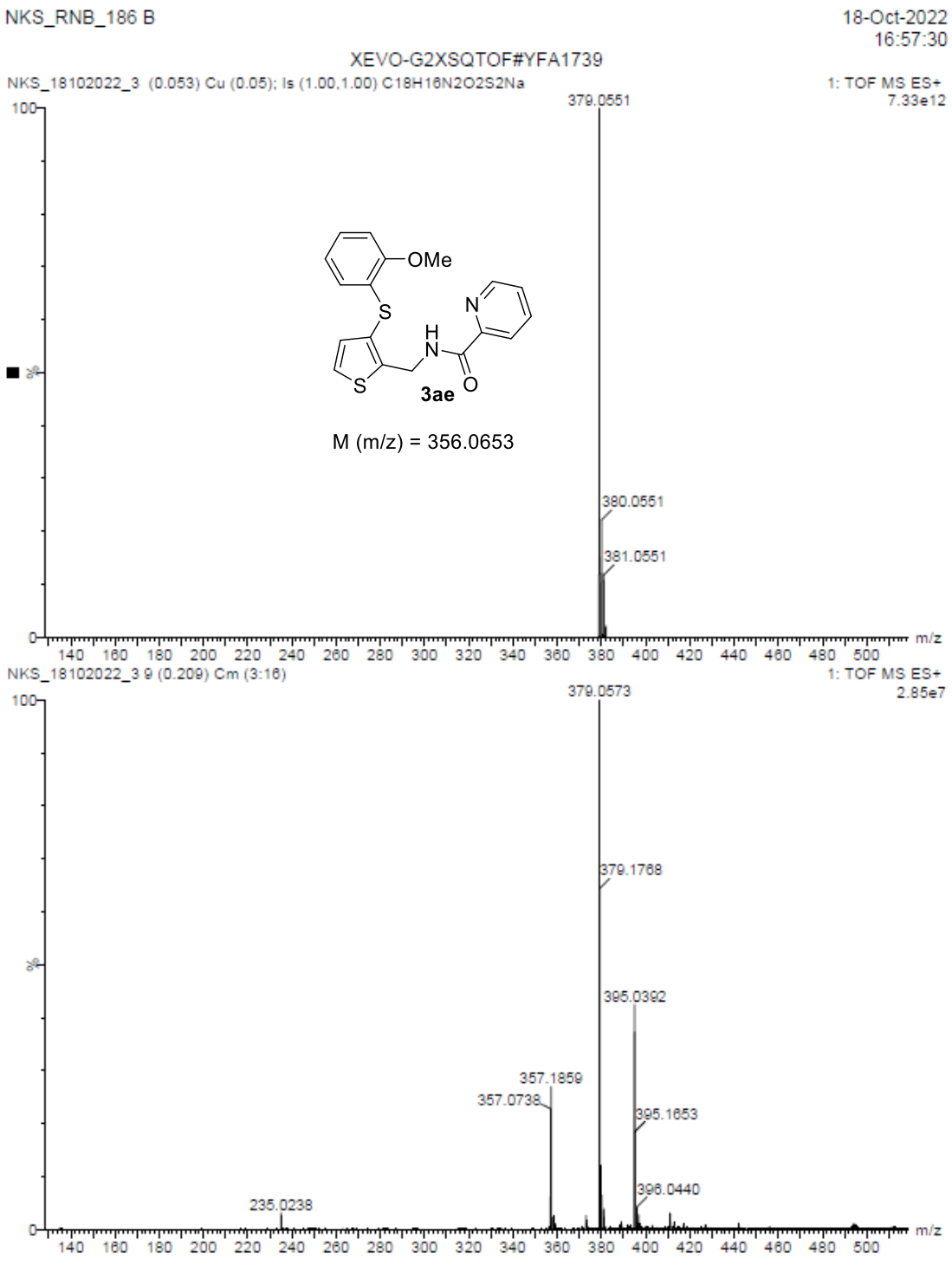
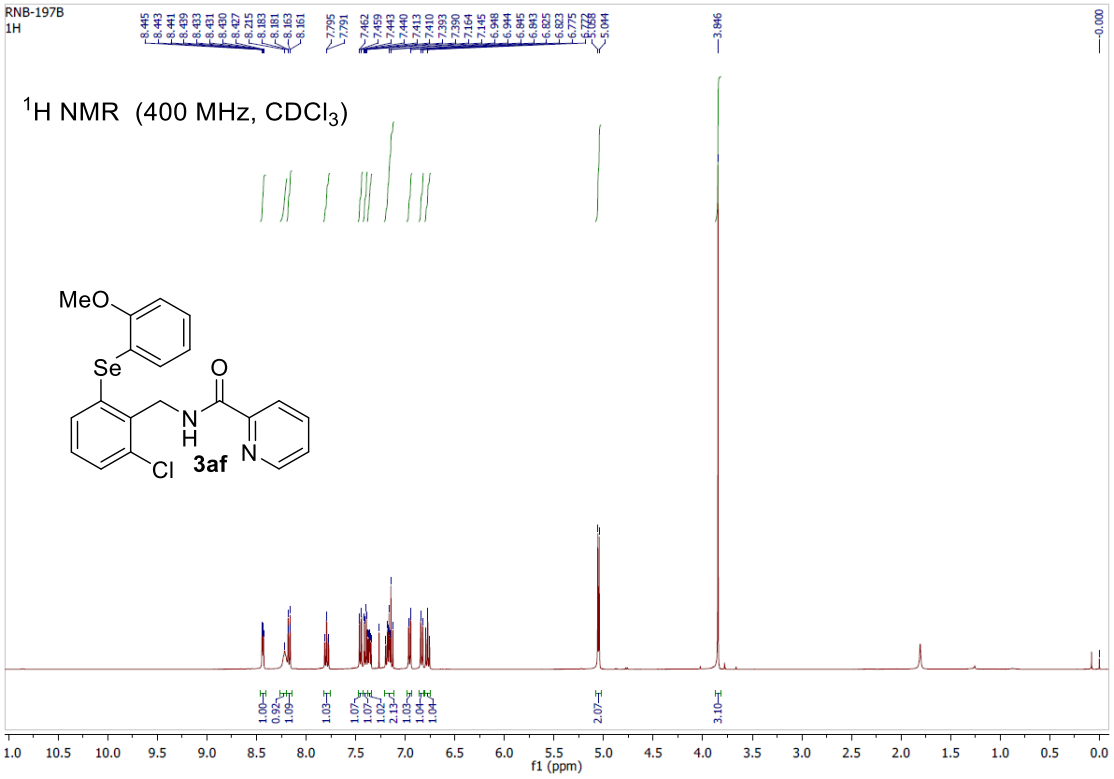


Fig S141. ESI-HRMS spectra of thiolated compound **3ae**



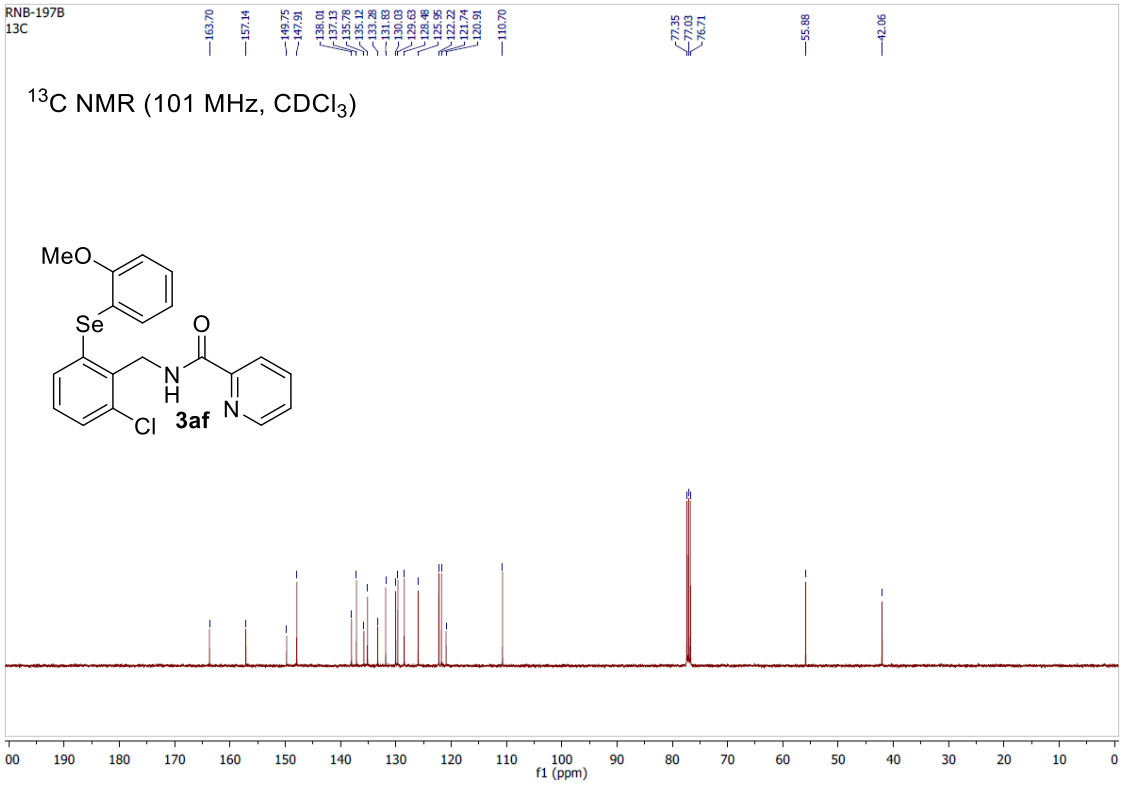


Fig S142. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3af**

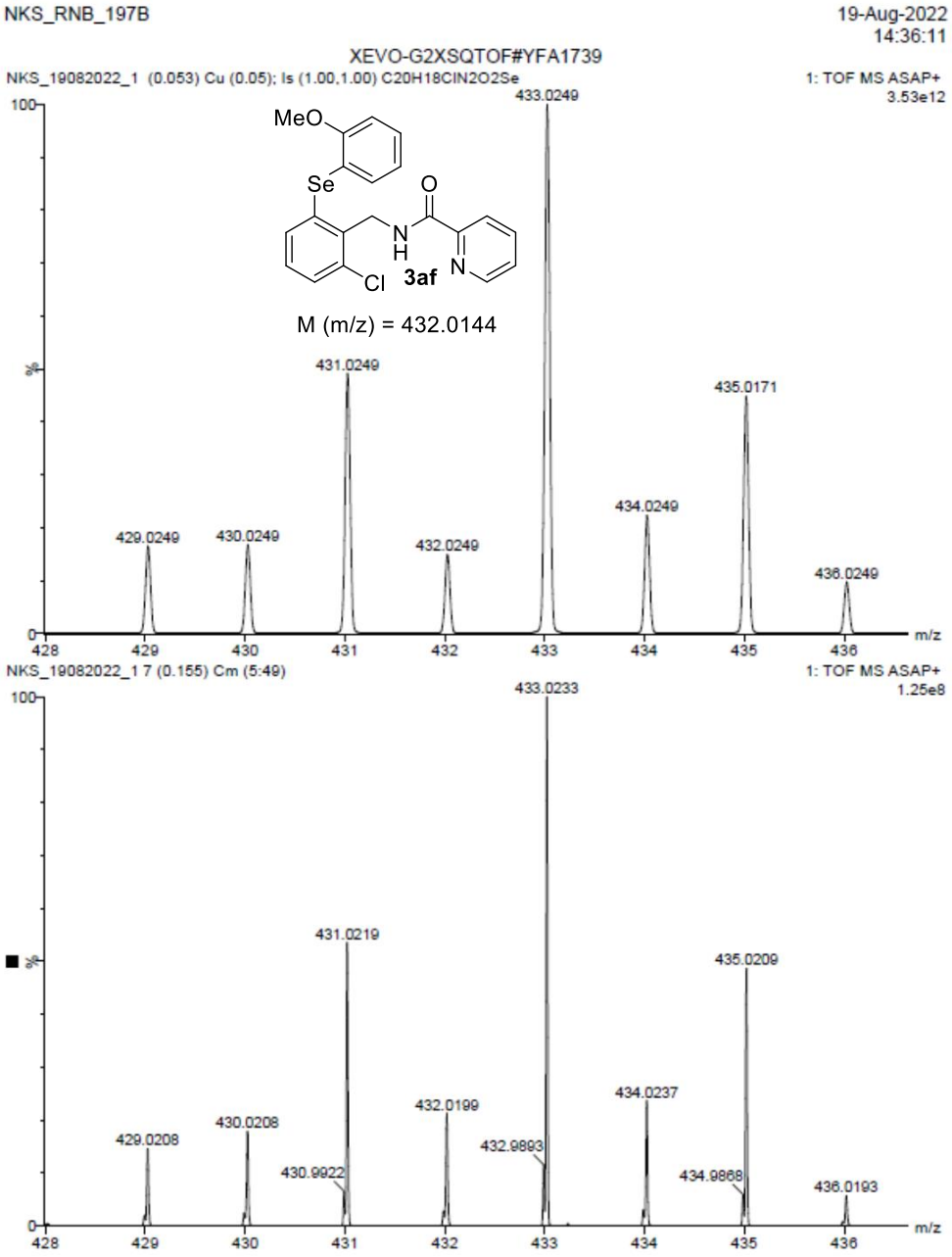


Fig S143. ASAP-HRMS spectra of compound **3af**

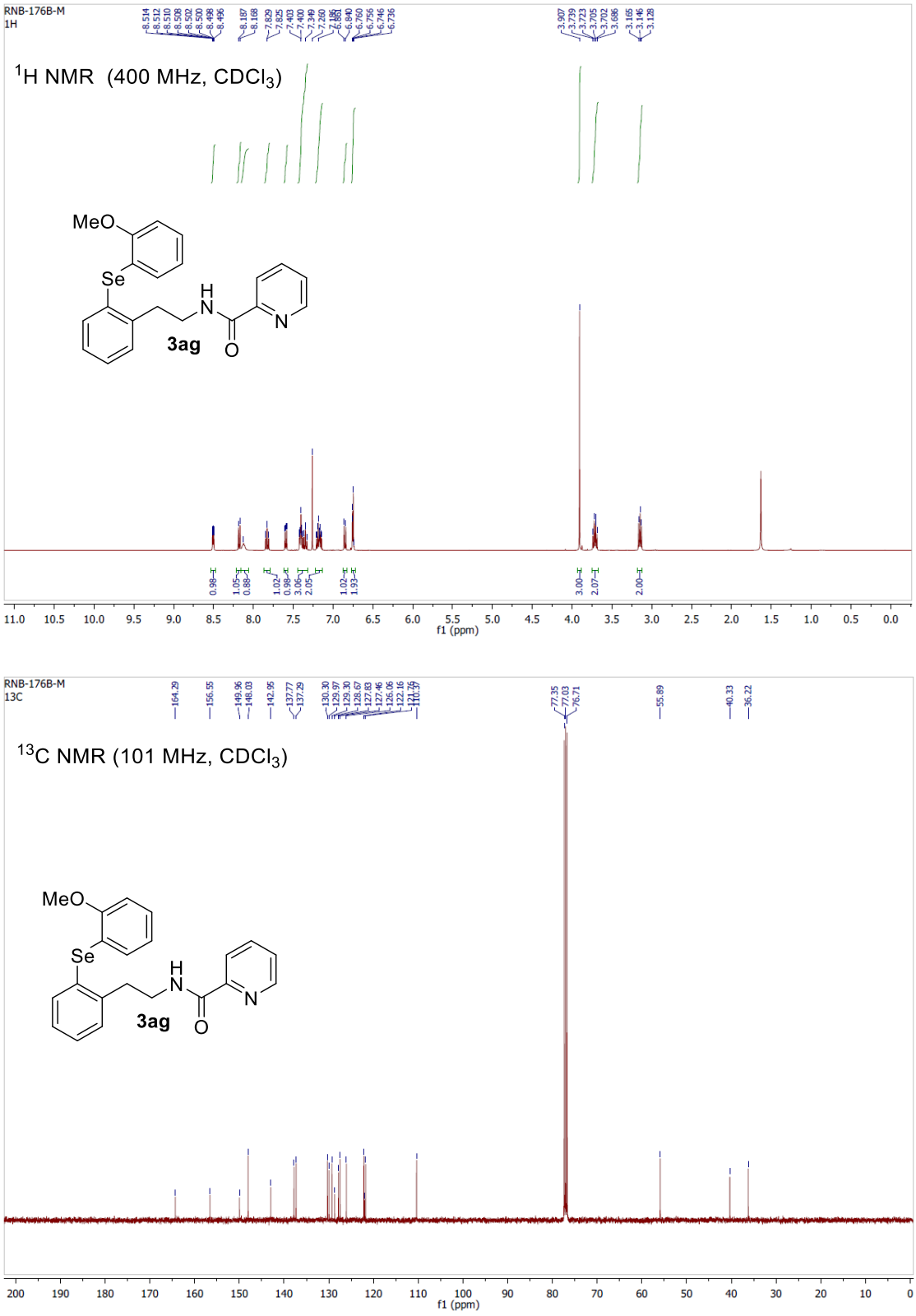


Fig S144. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3ag**

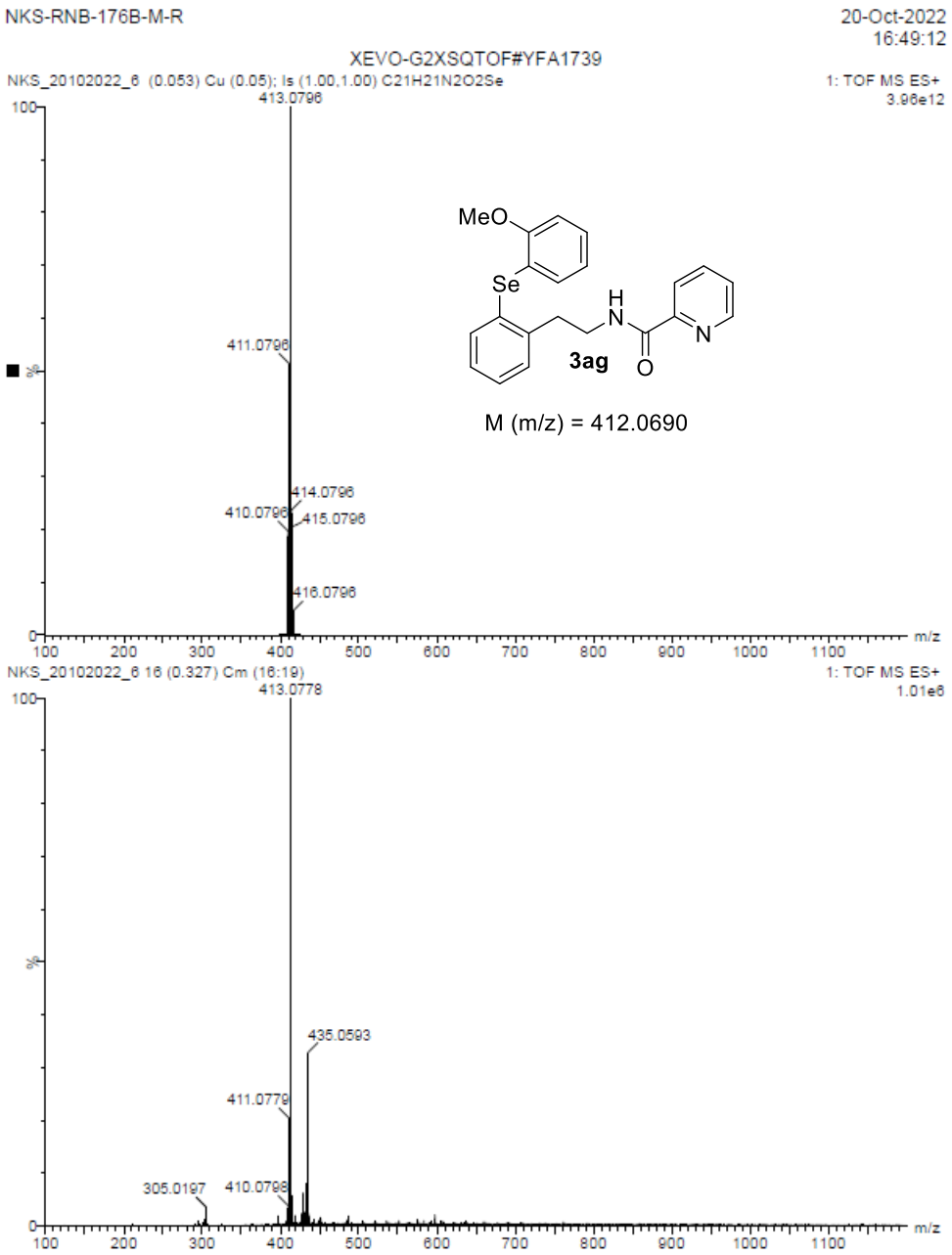
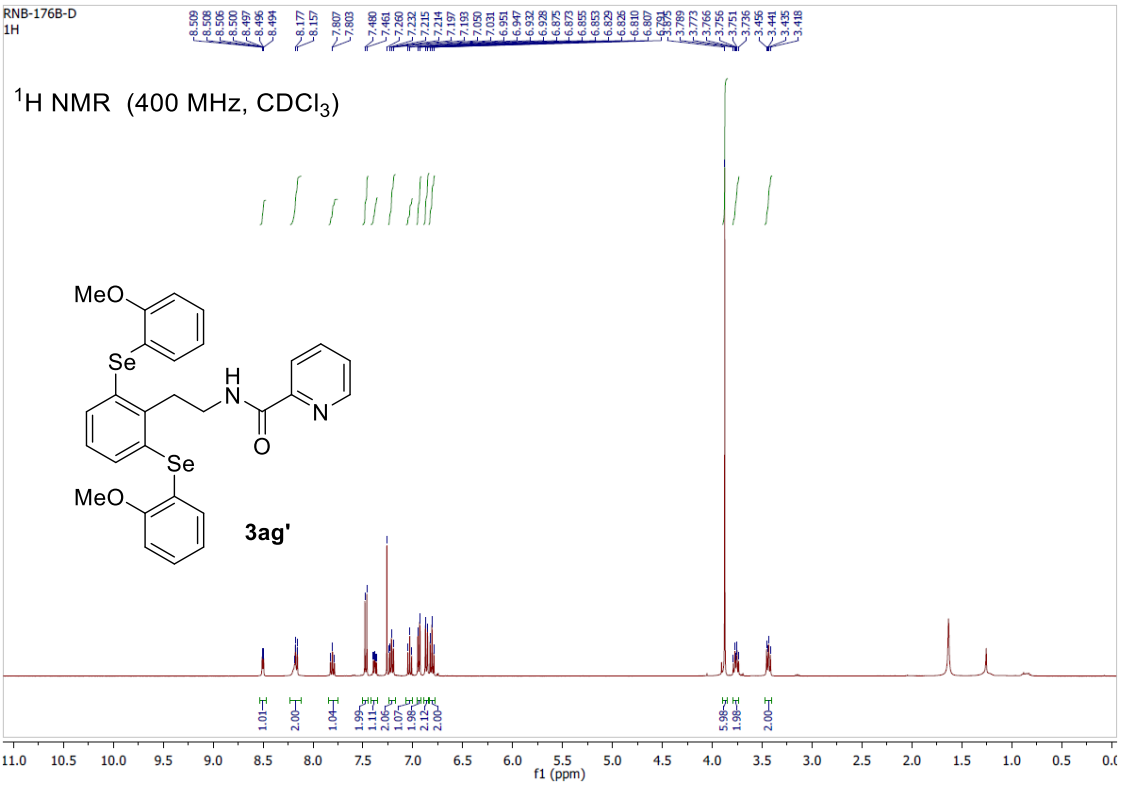


Fig S145. ESI-HRMS spectra of compound **3ag**



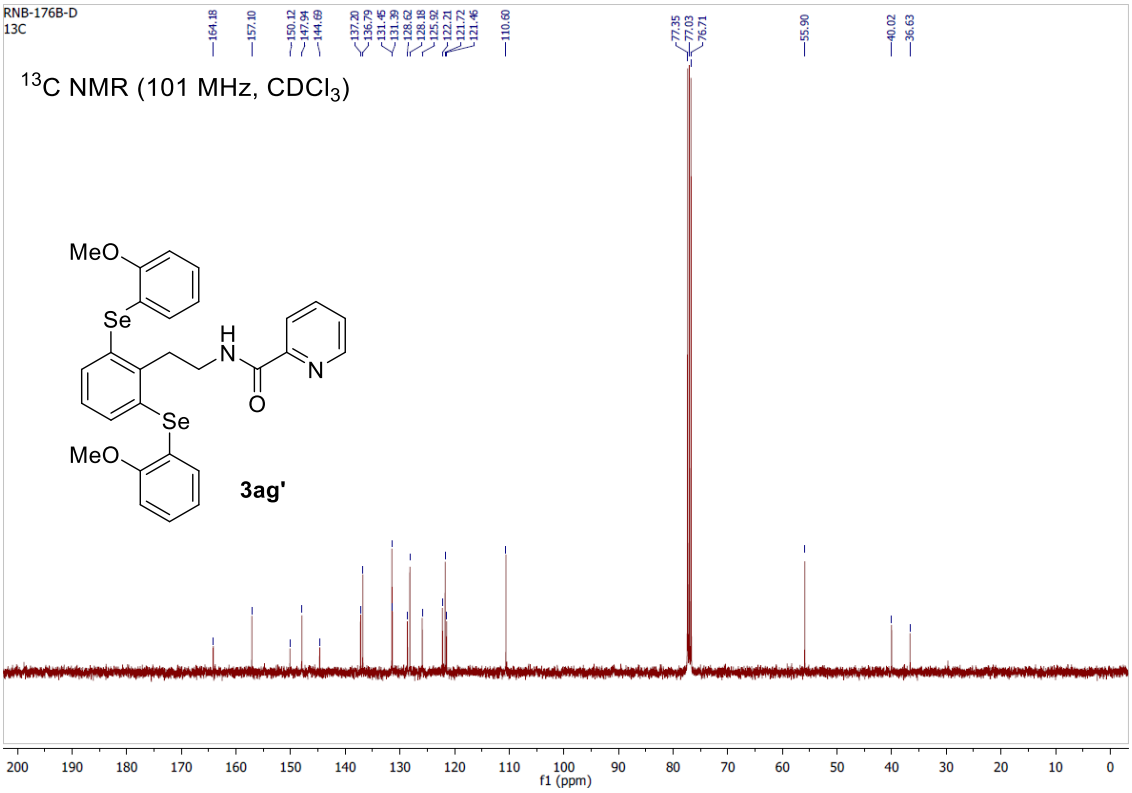


Fig S146. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3ag'**

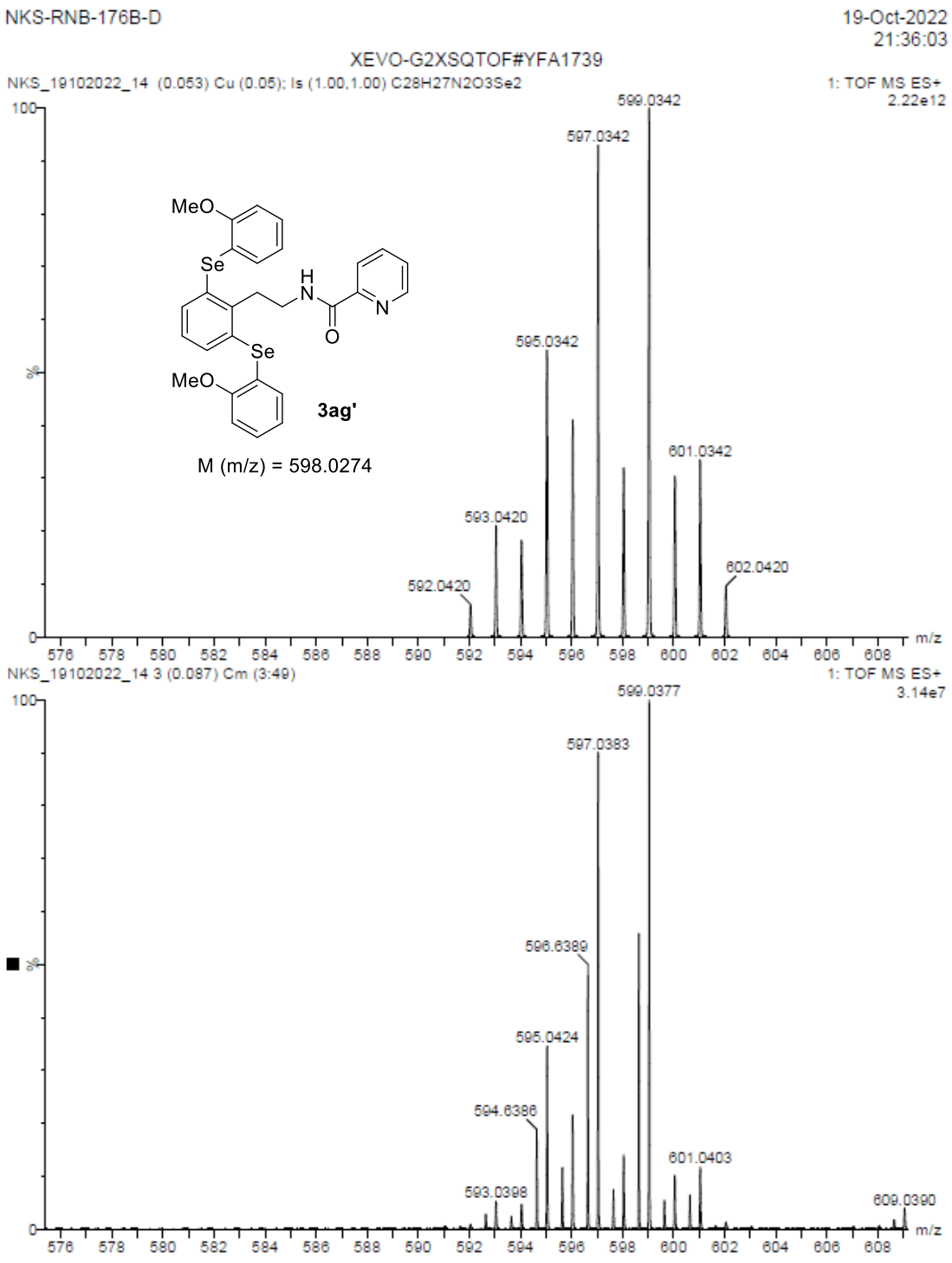
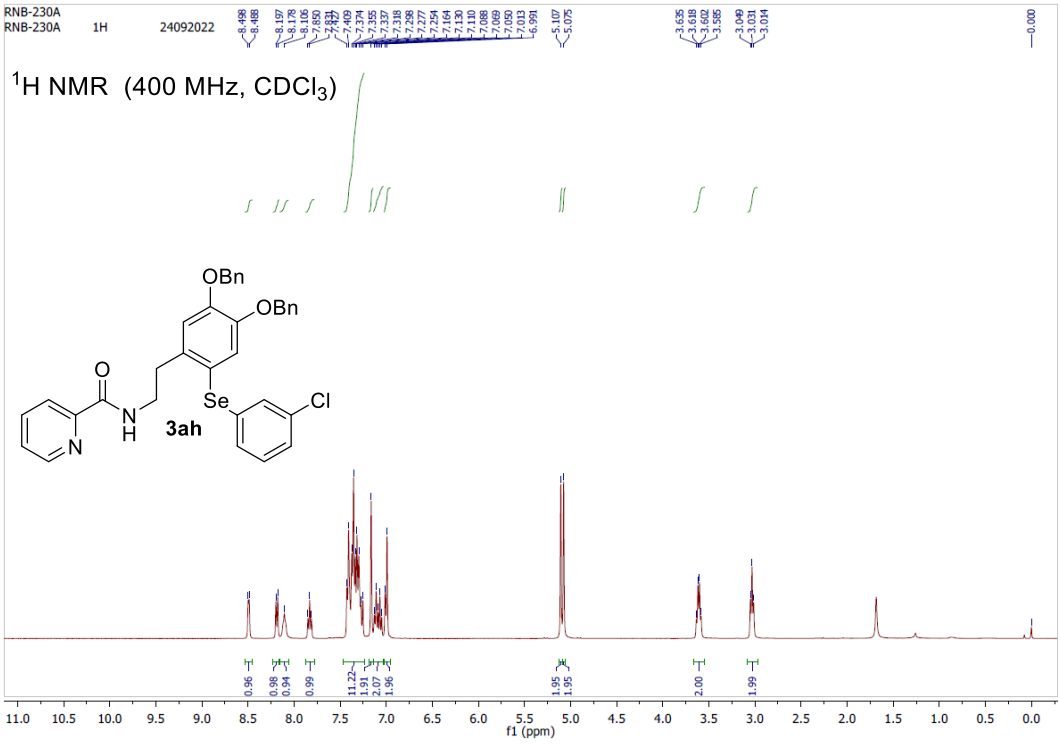


Fig S147. ESI-HRMS spectra of compound **3ag'**



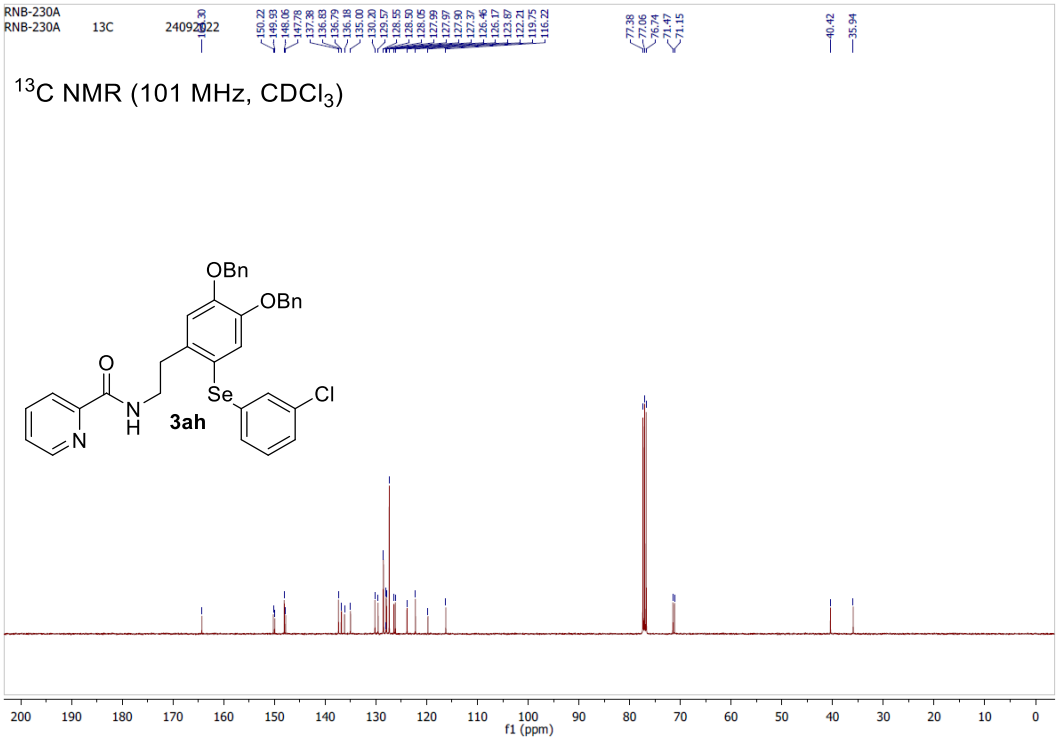


Fig S148. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3ah**

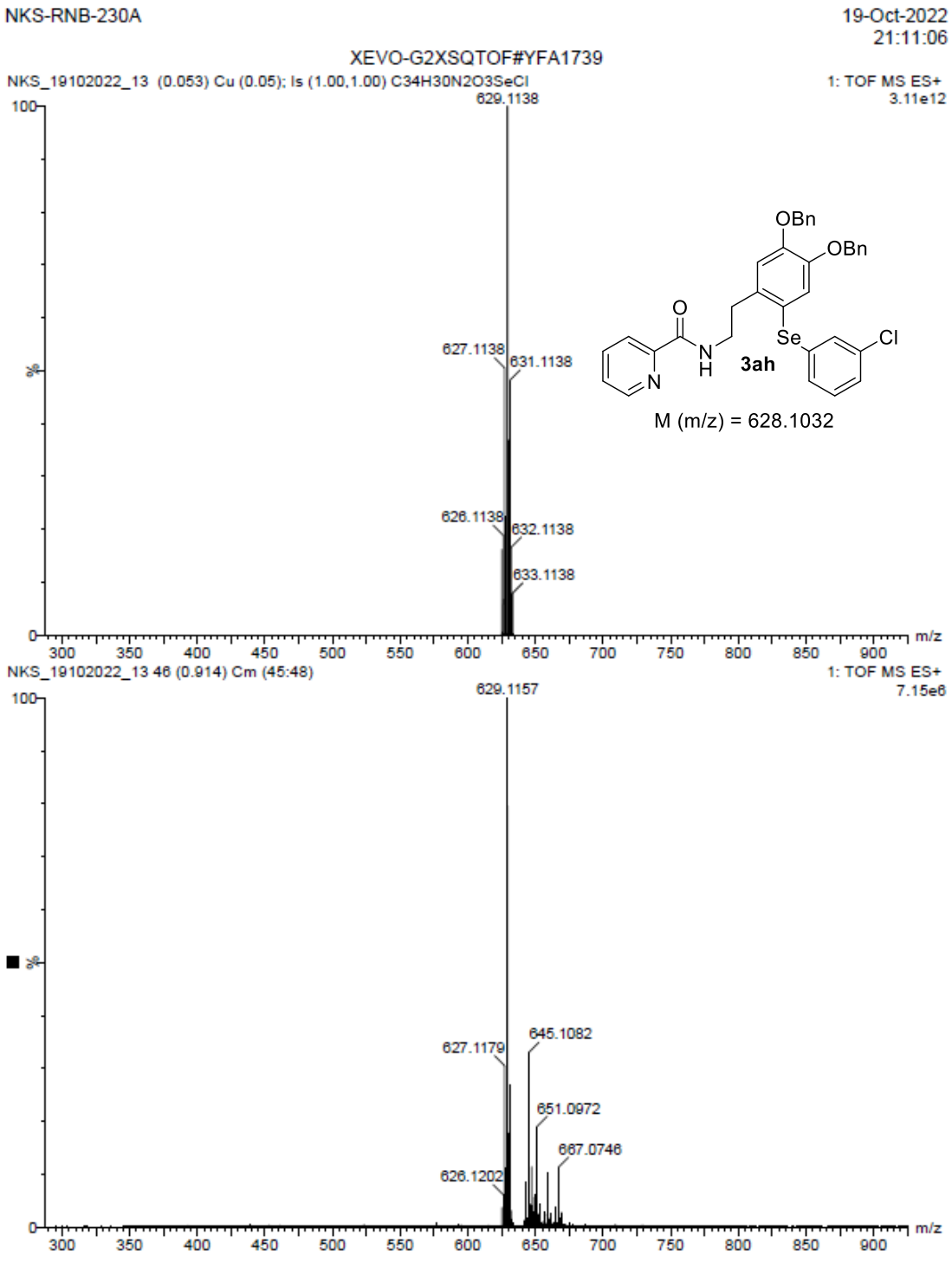
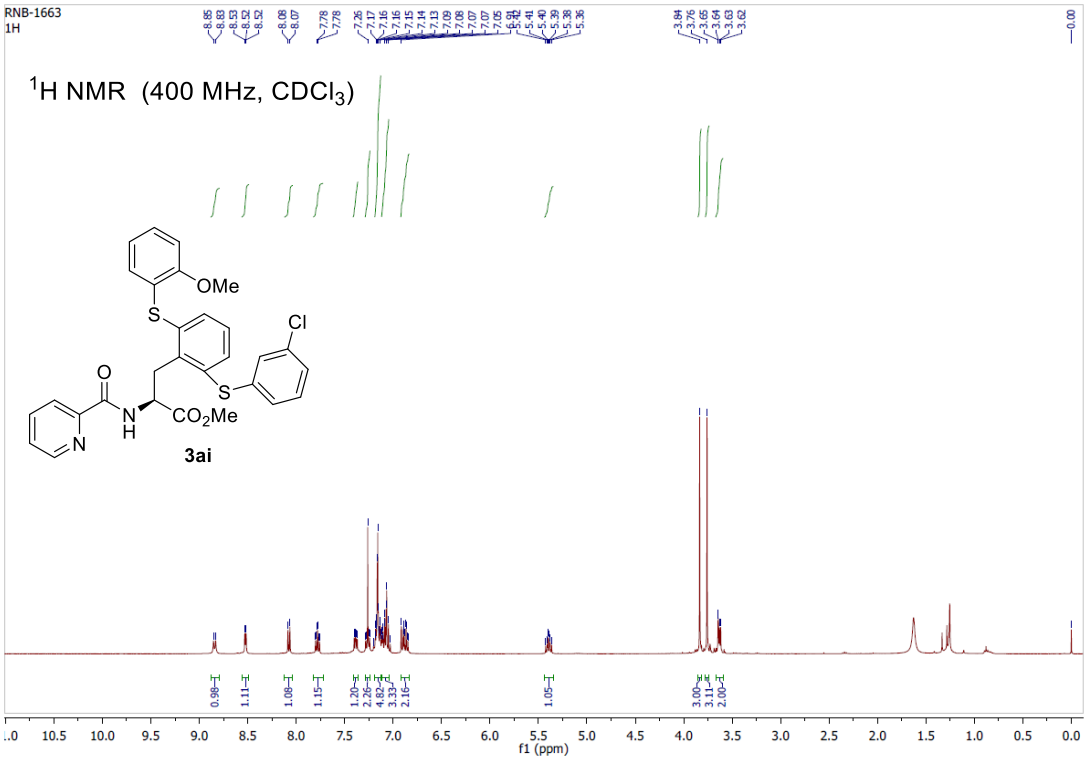


Fig S149. ESI-HRMS spectra of compound **3ah**



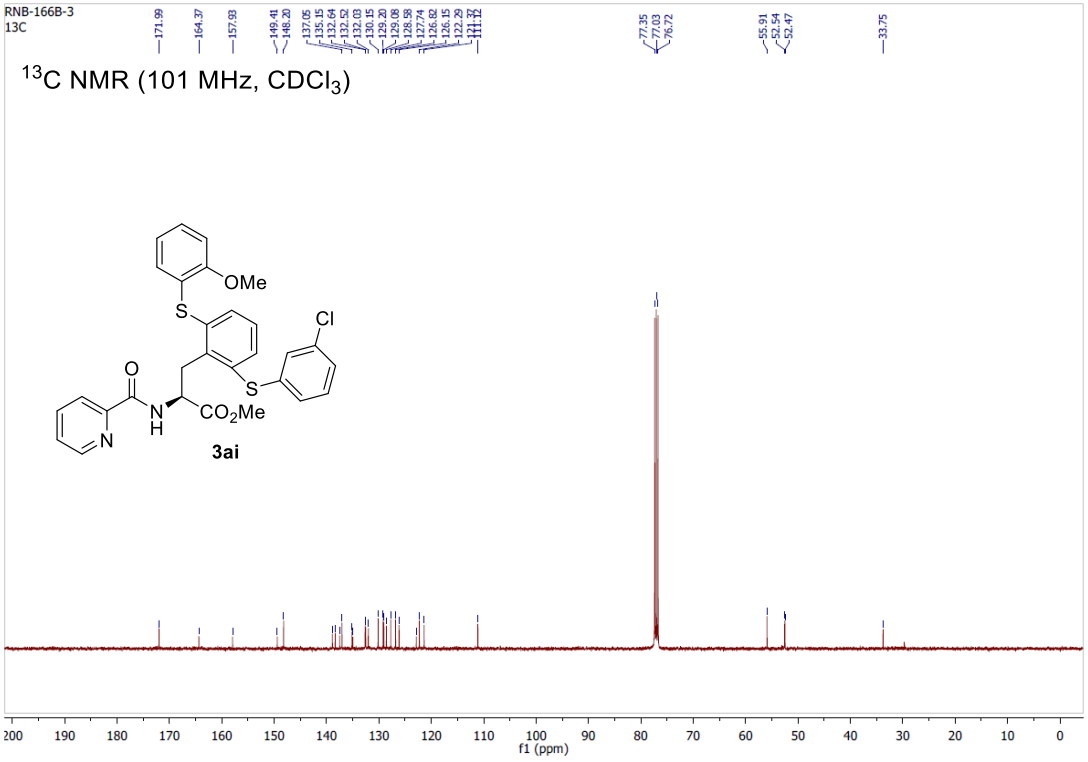


Fig S150. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3ai**

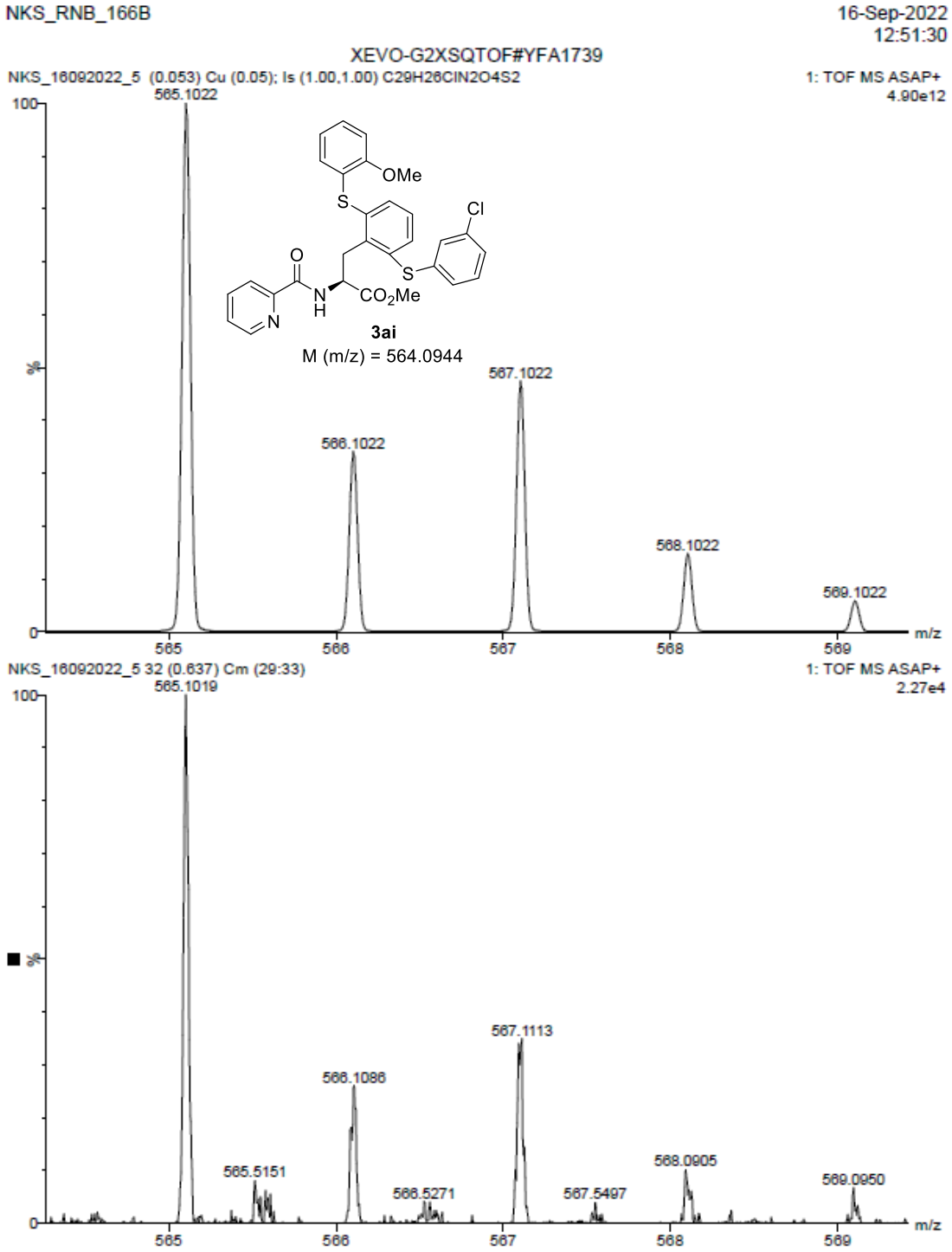
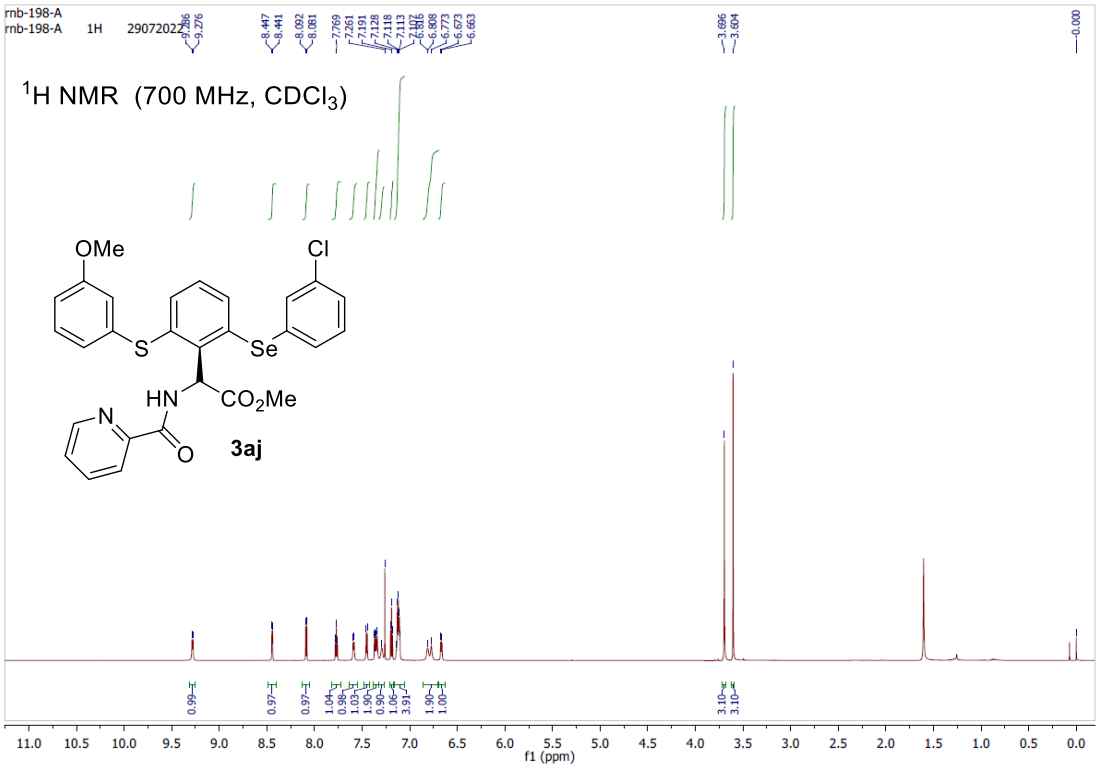


Fig S151. ASAP-HRMS spectra of compound **3ai**



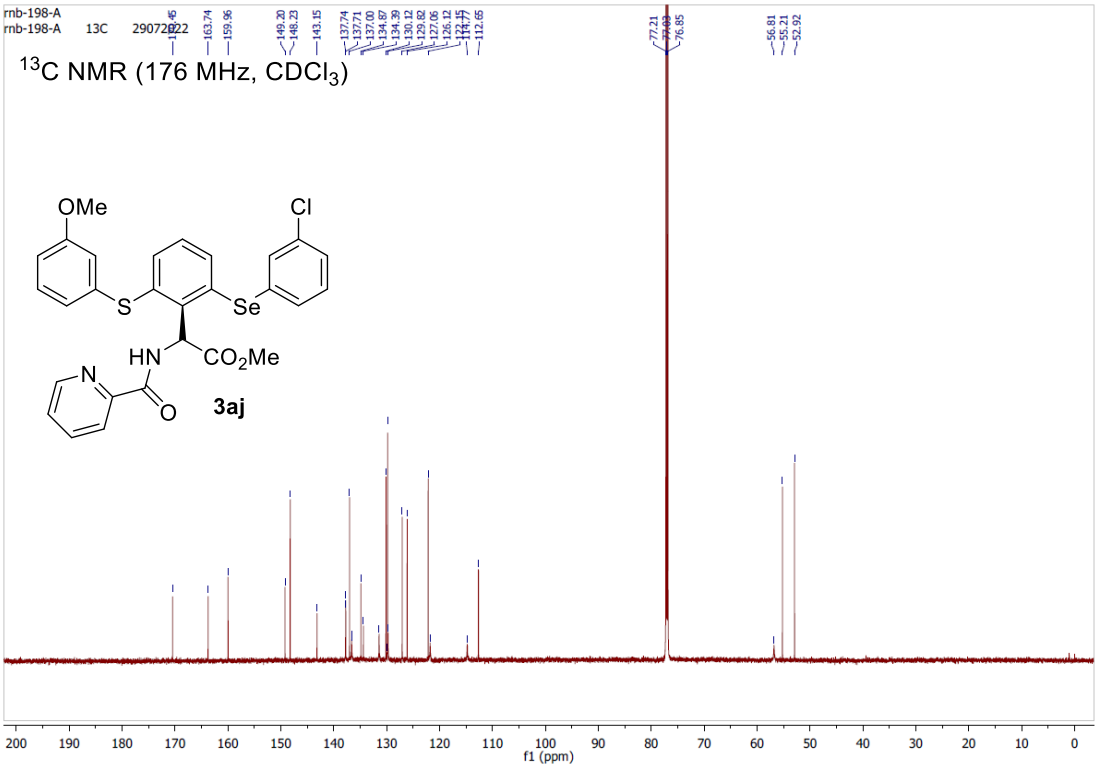


Fig S152. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **3aj**

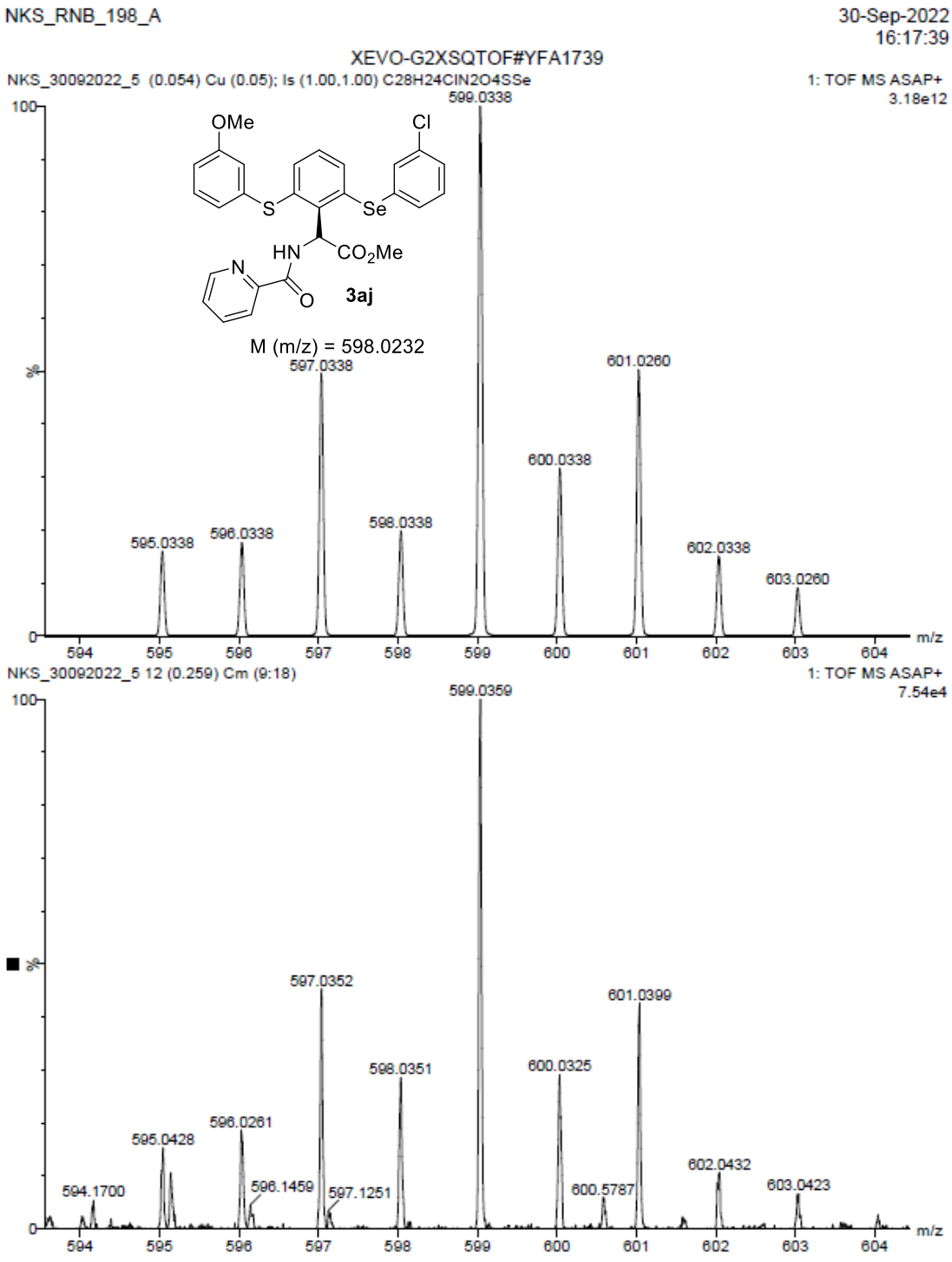


Fig S153. ASAP-HRMS spectra of compound **3aj**

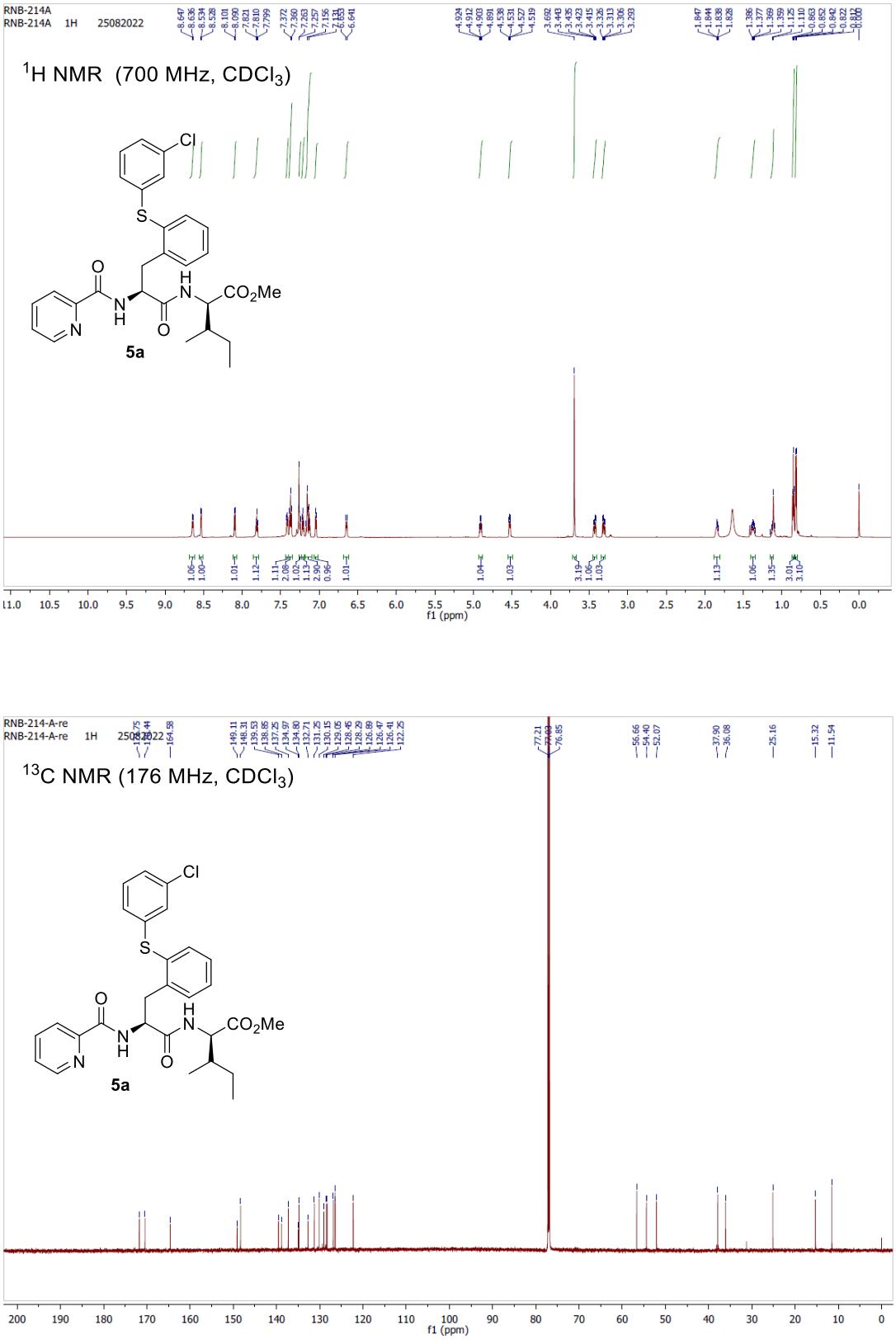


Fig S154. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5a**

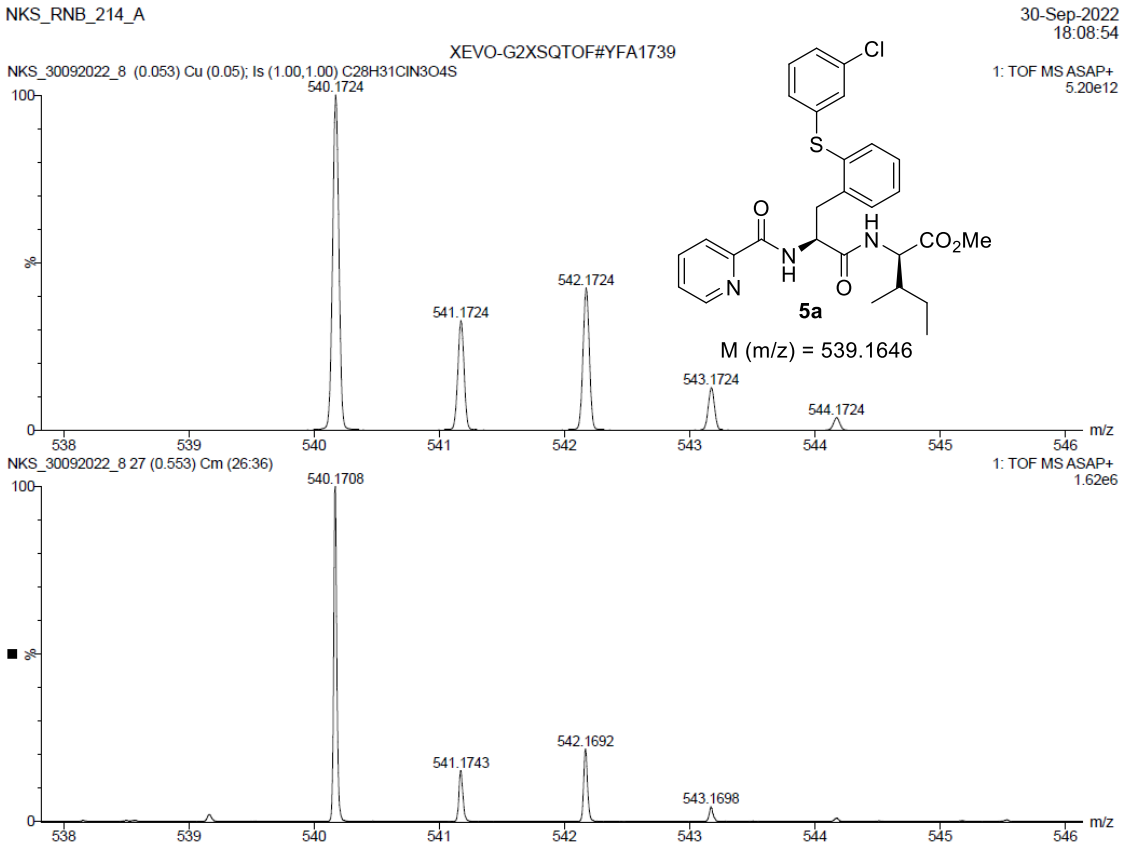


Fig S155. ASAP-HRMS spectra of compound **5a**

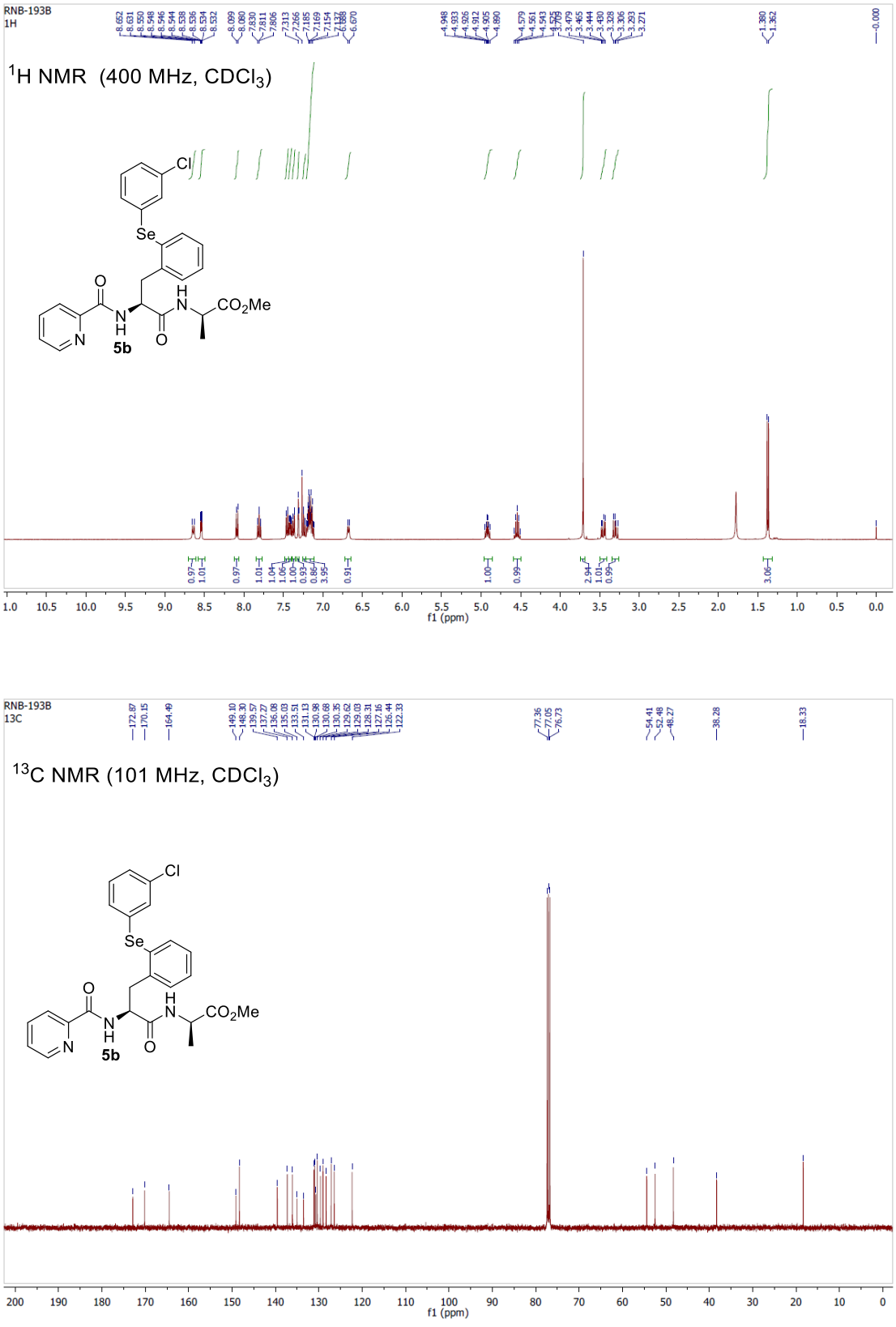


Fig S156. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5b**

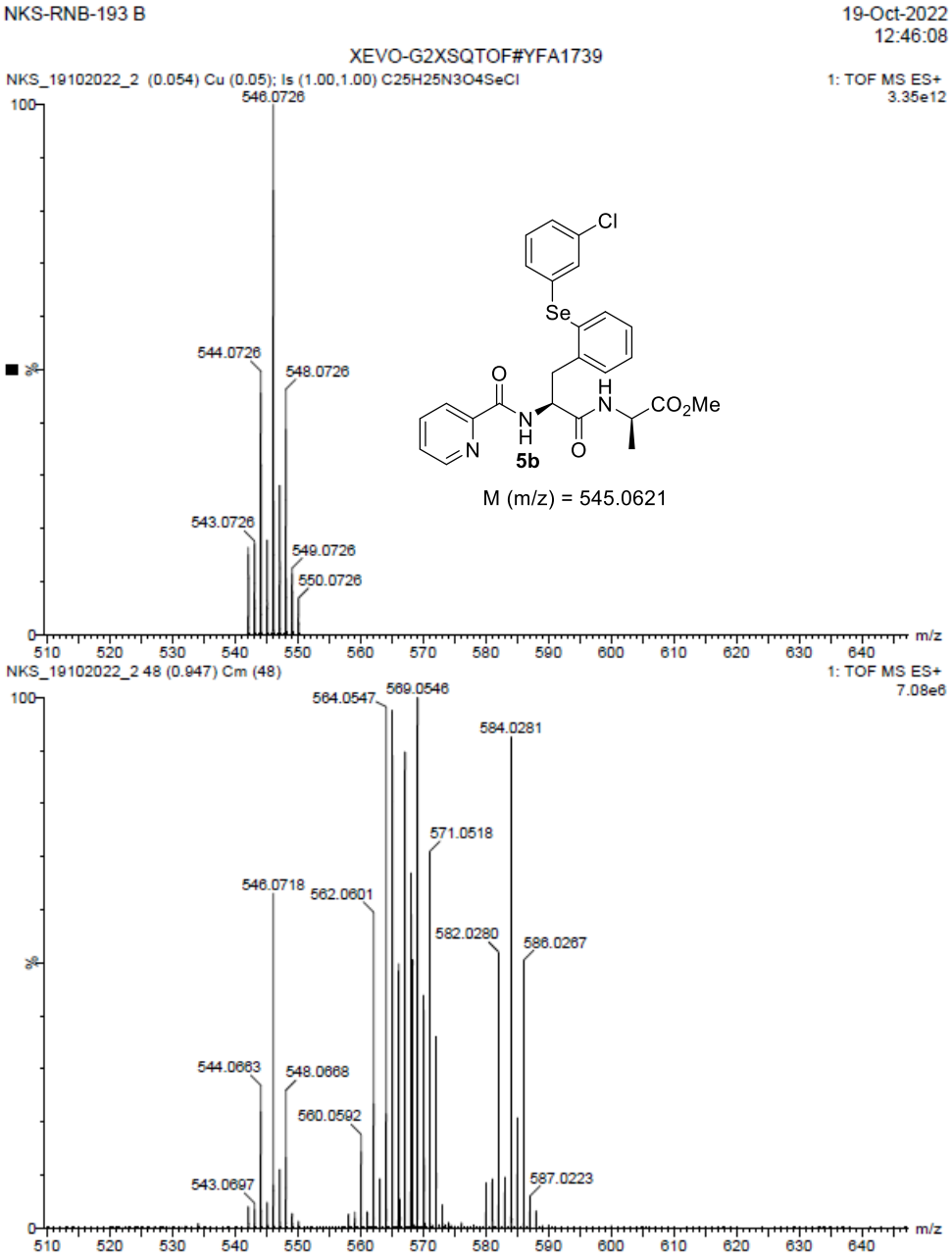


Fig S157. ESI-HRMS spectra of compound **5b**

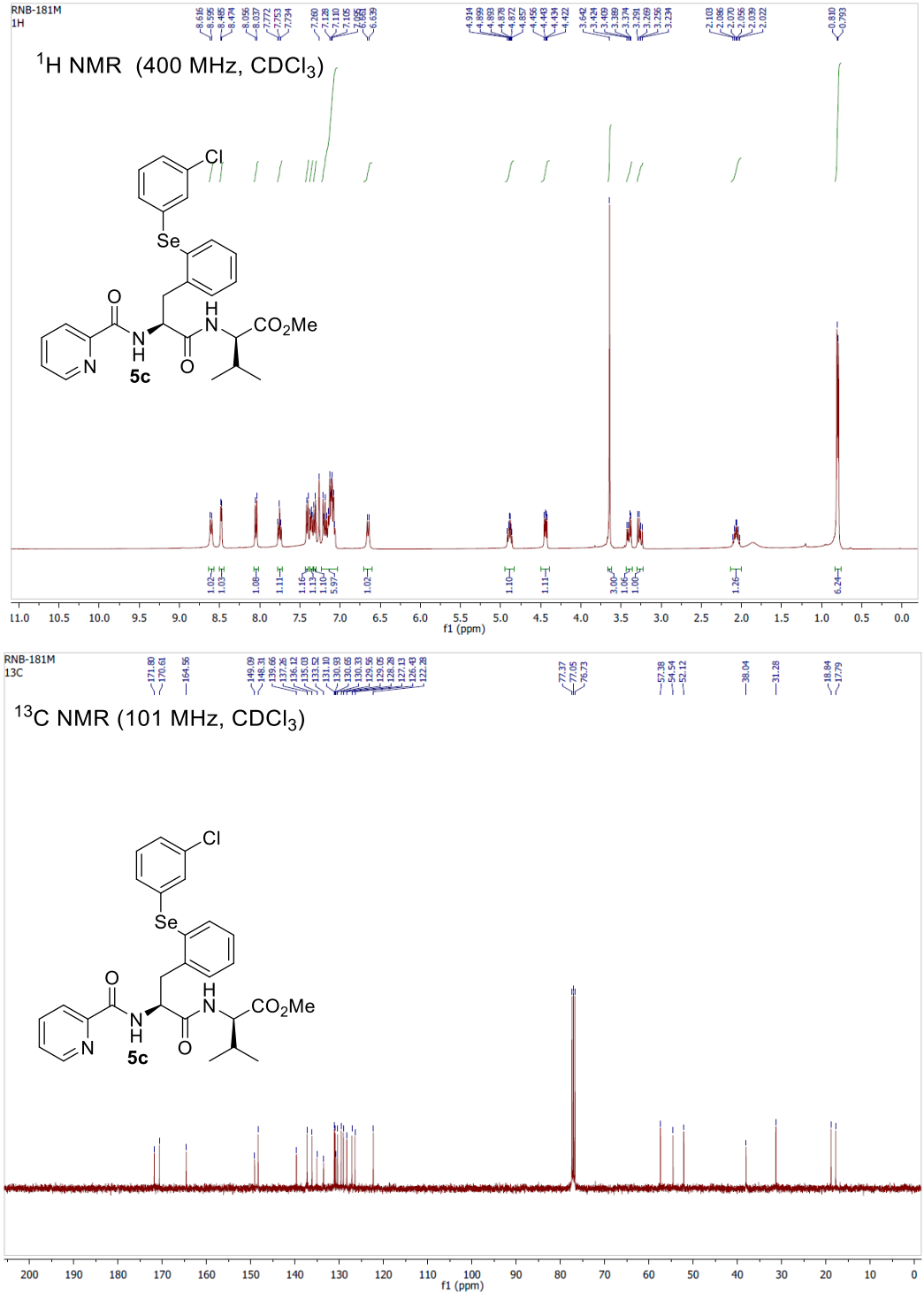


Fig S158. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5c**

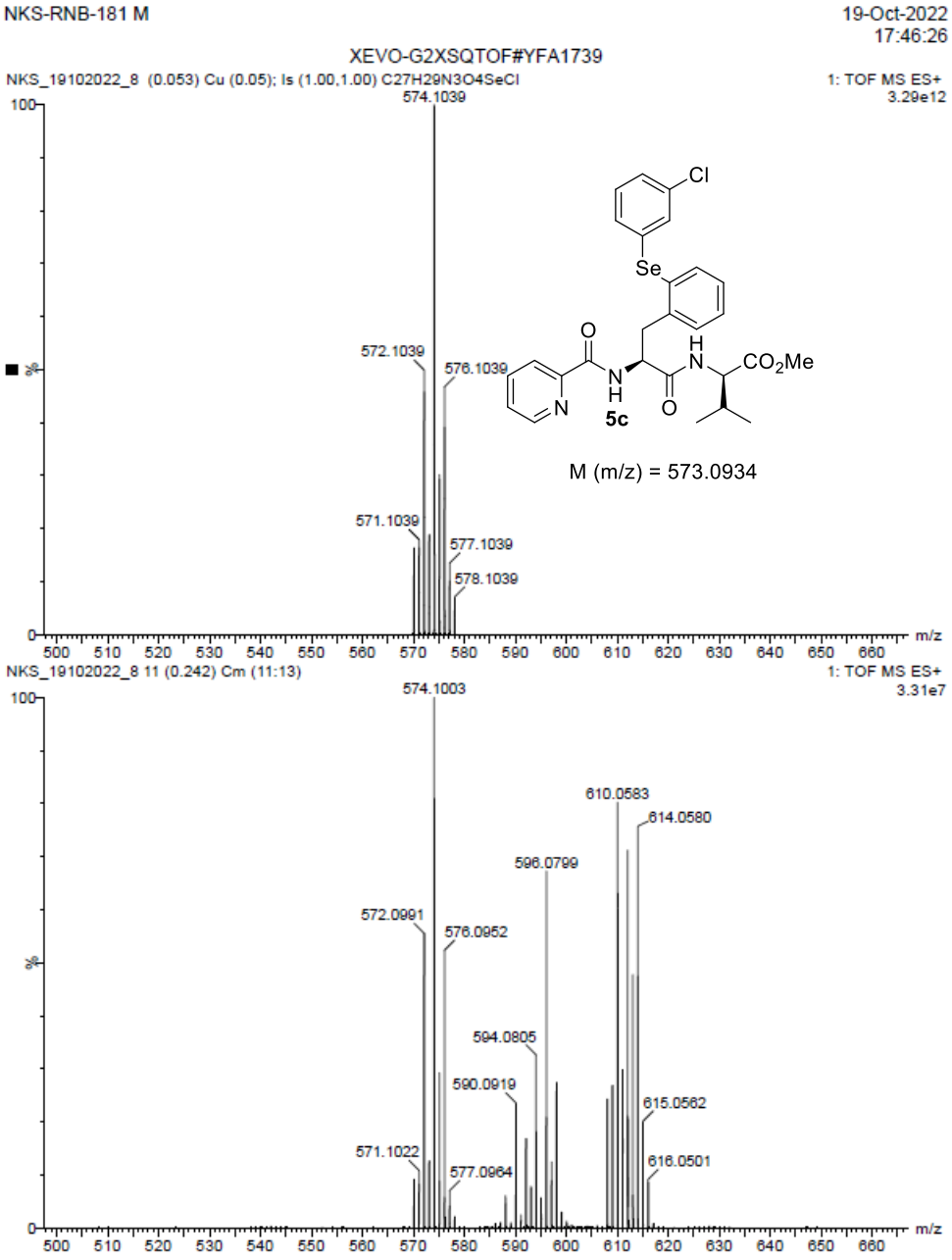
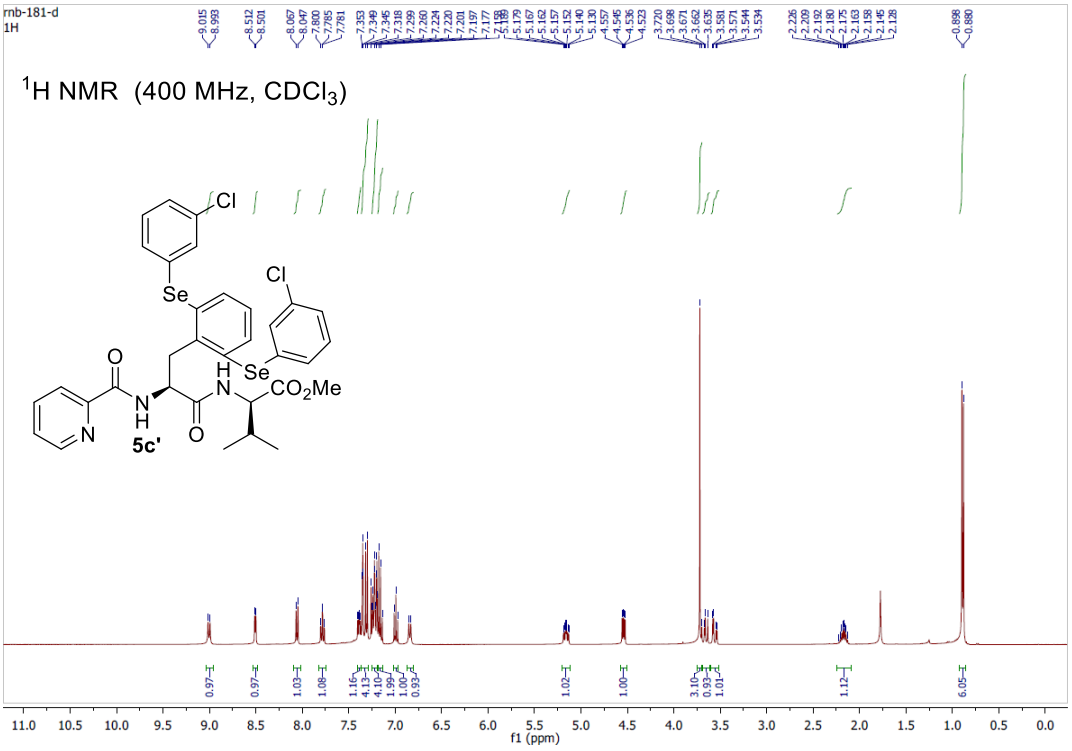


Fig S159. ESI-HRMS spectra of compound **5c**



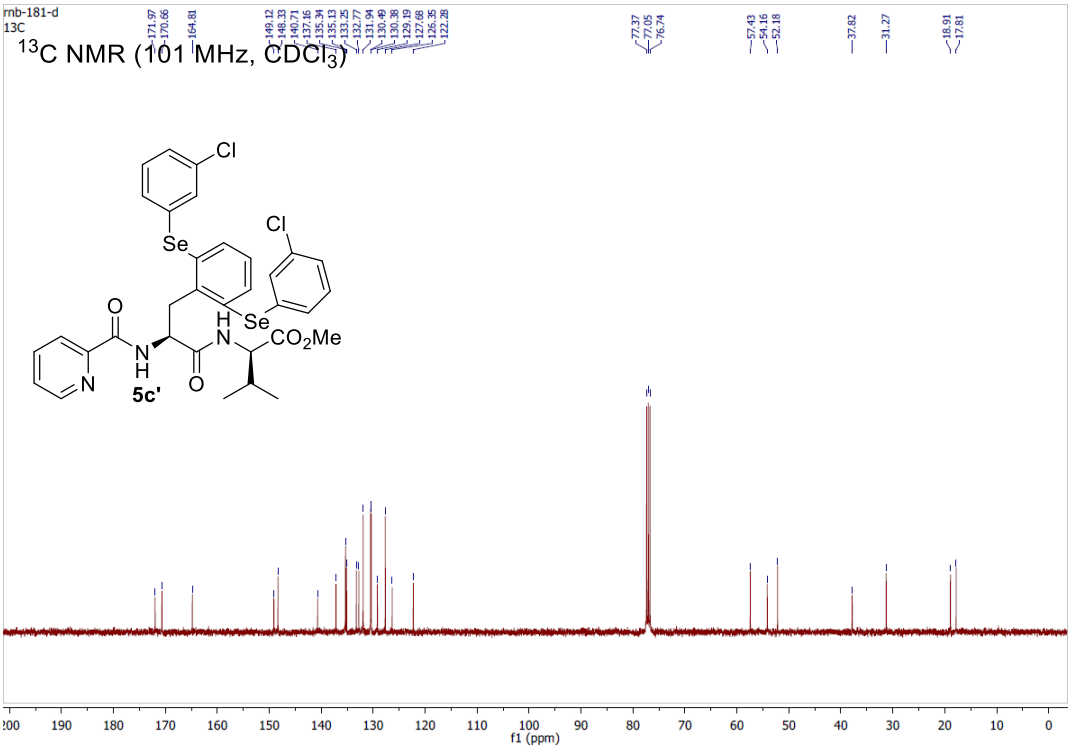


Fig S160. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5c'**

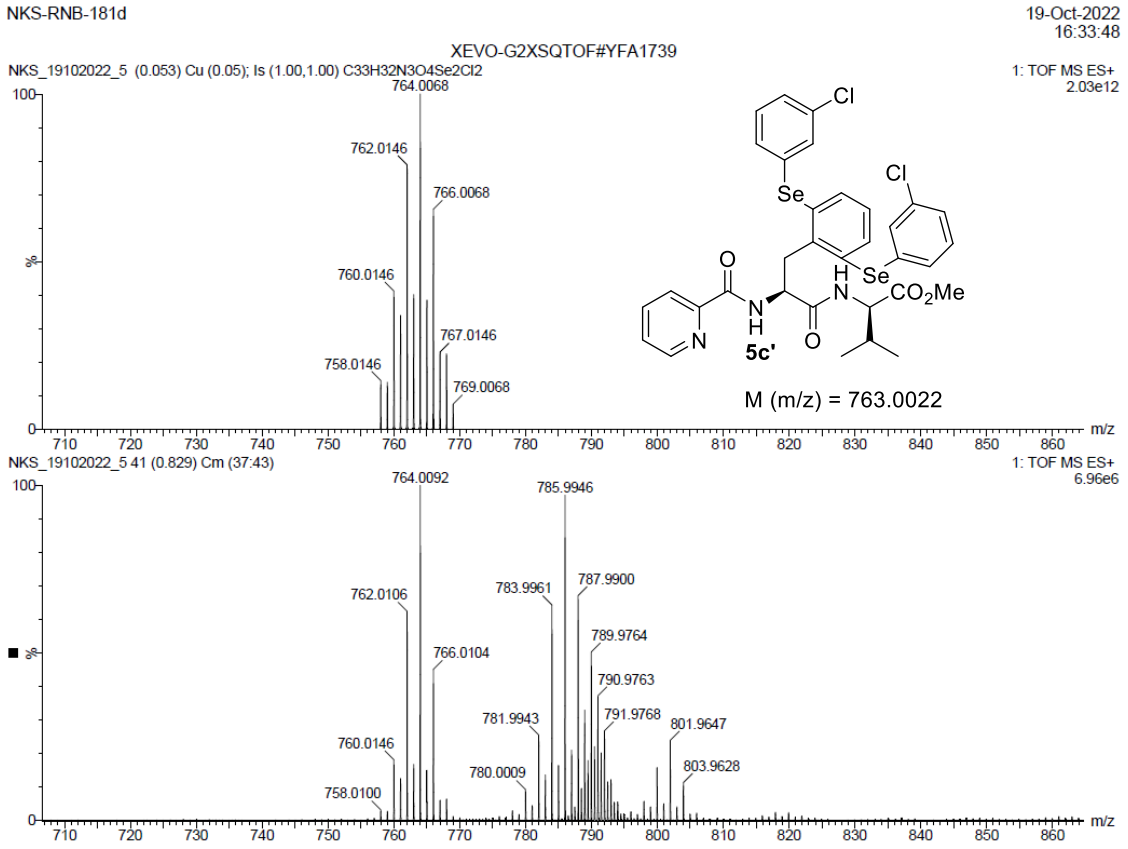
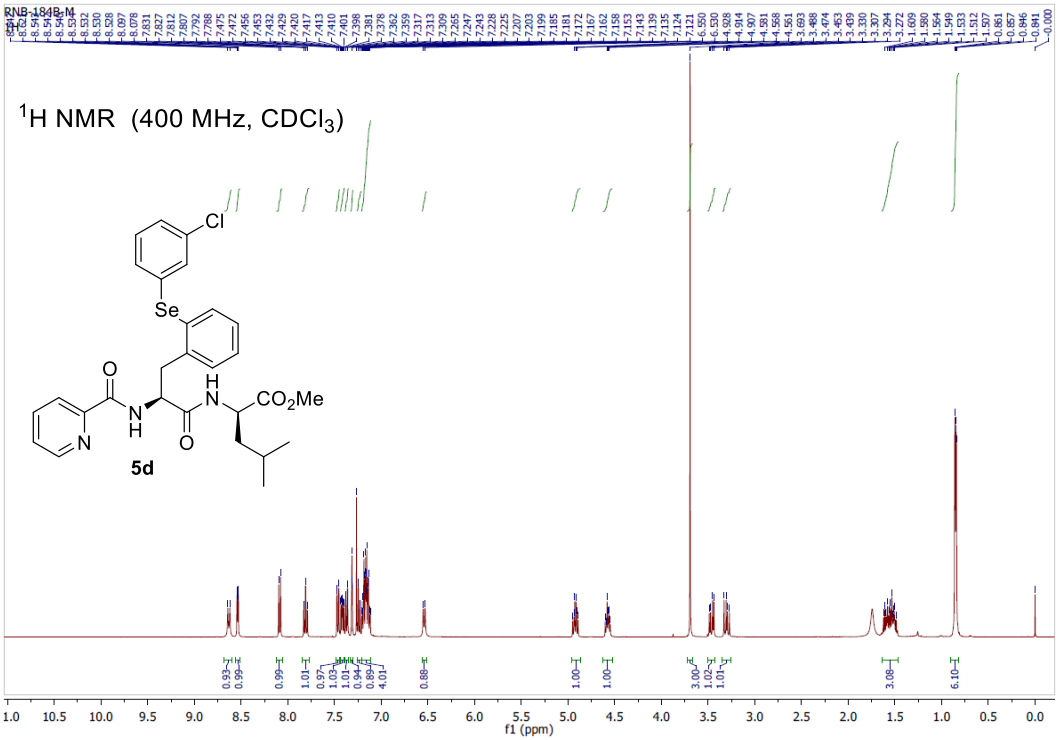


Fig S161. ESI-HRMS spectra of compound **5c'**



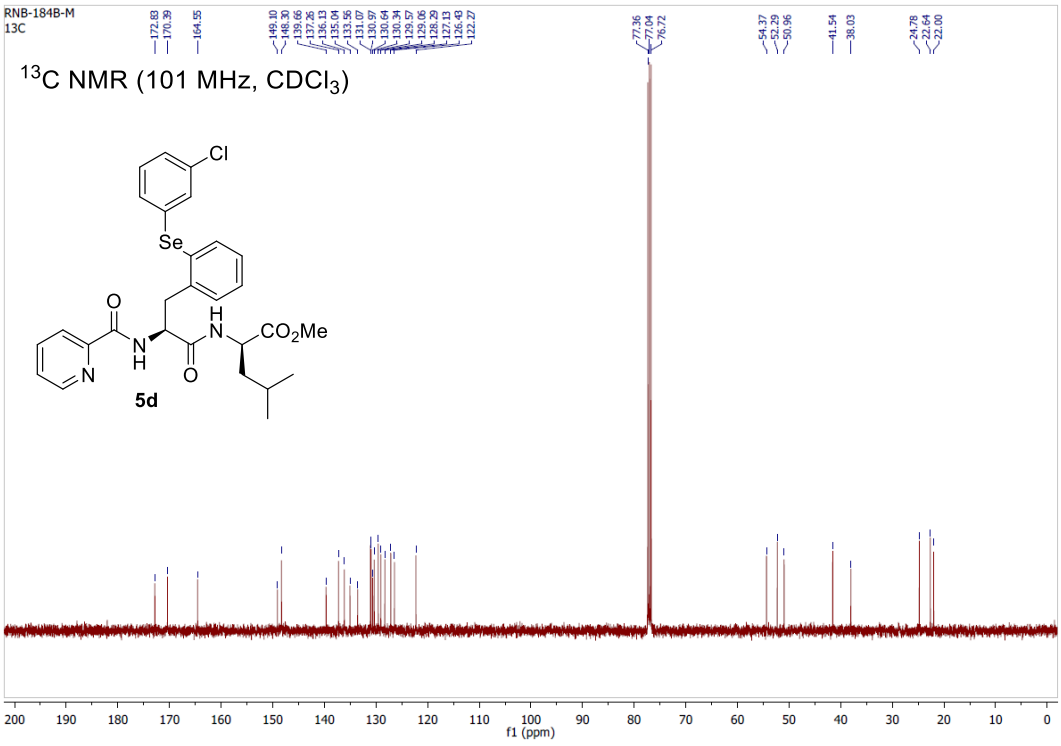


Fig S162. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5d**

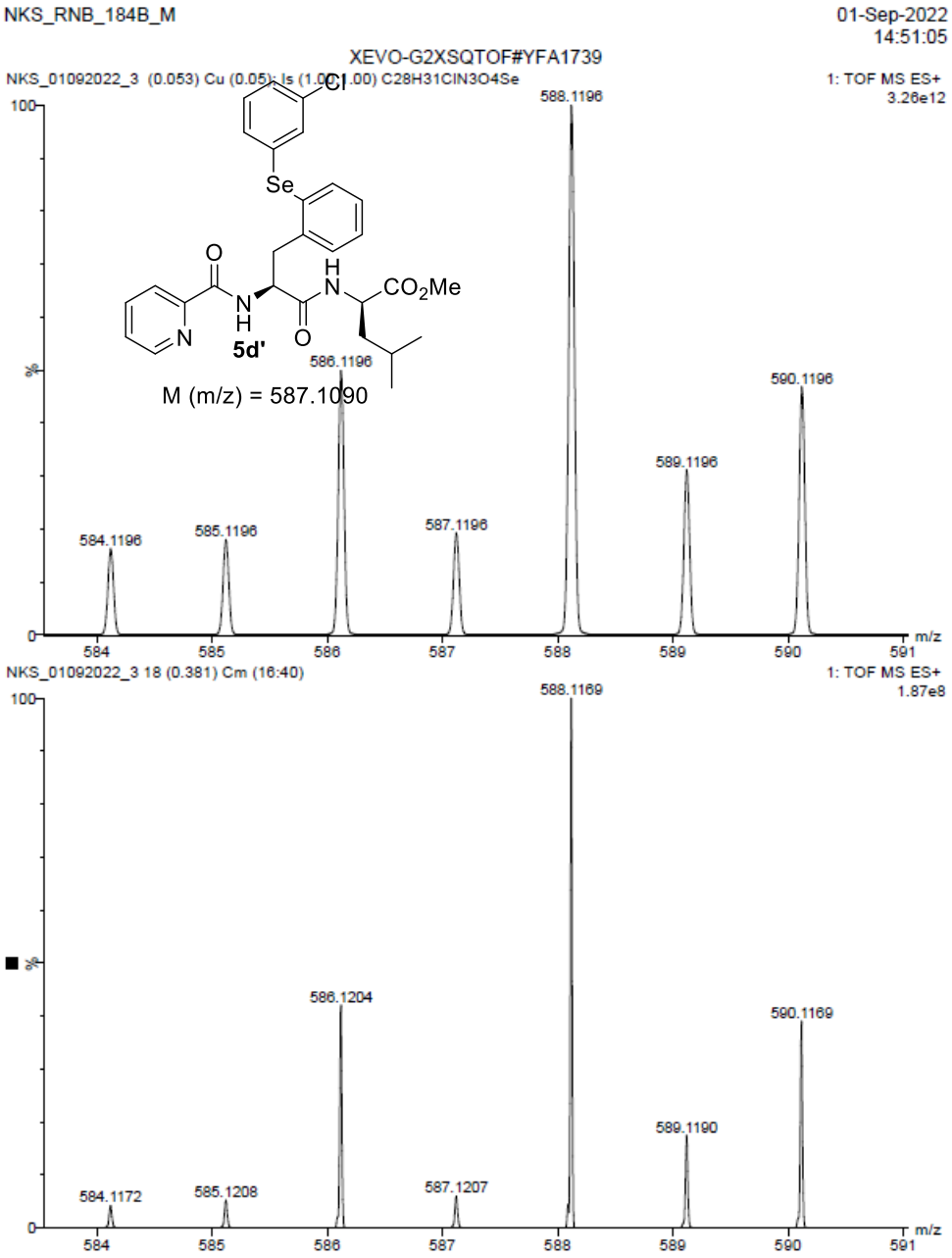
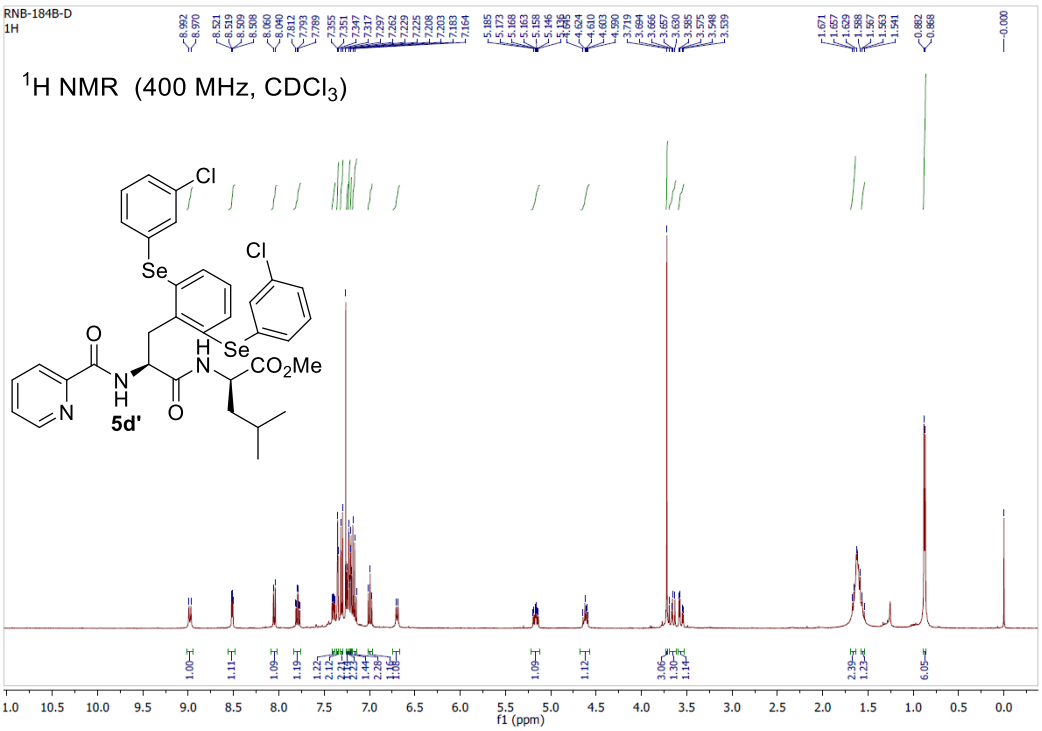


Fig S163. ESI-HRMS spectra of compound **5d**



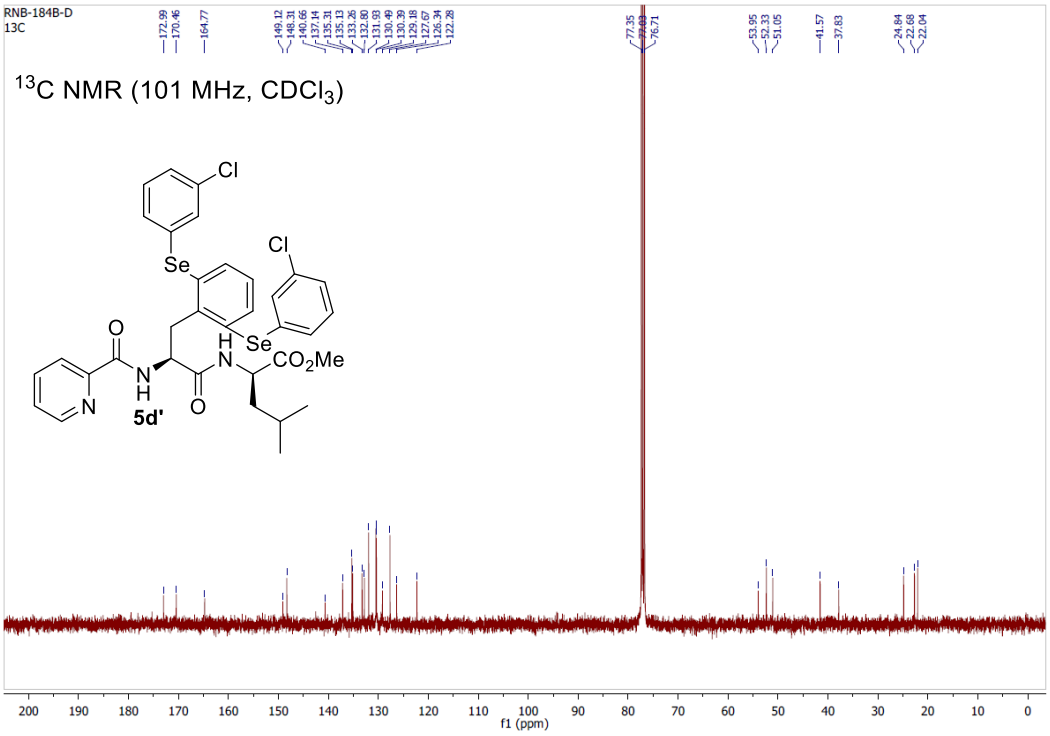


Fig S164. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5d'**

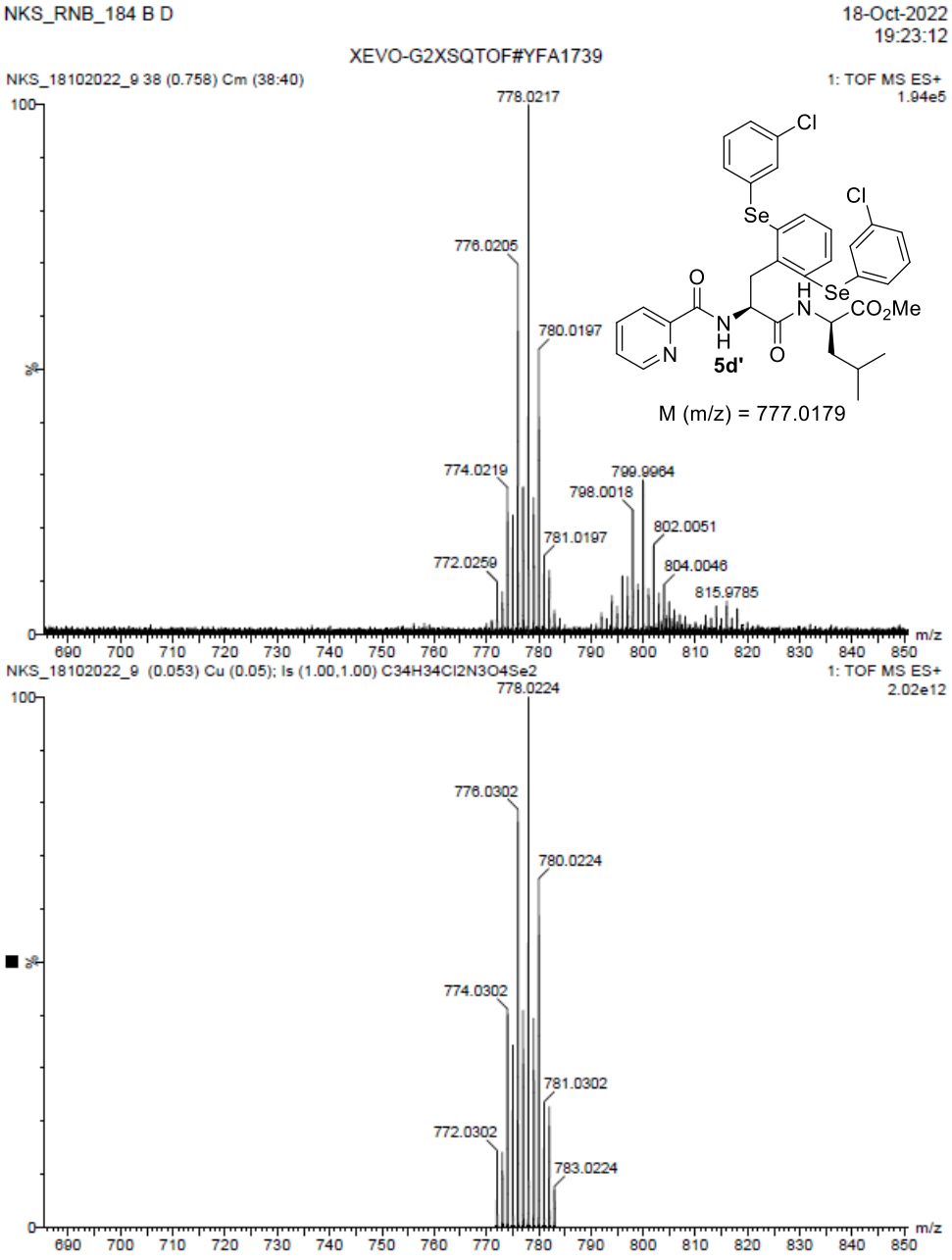
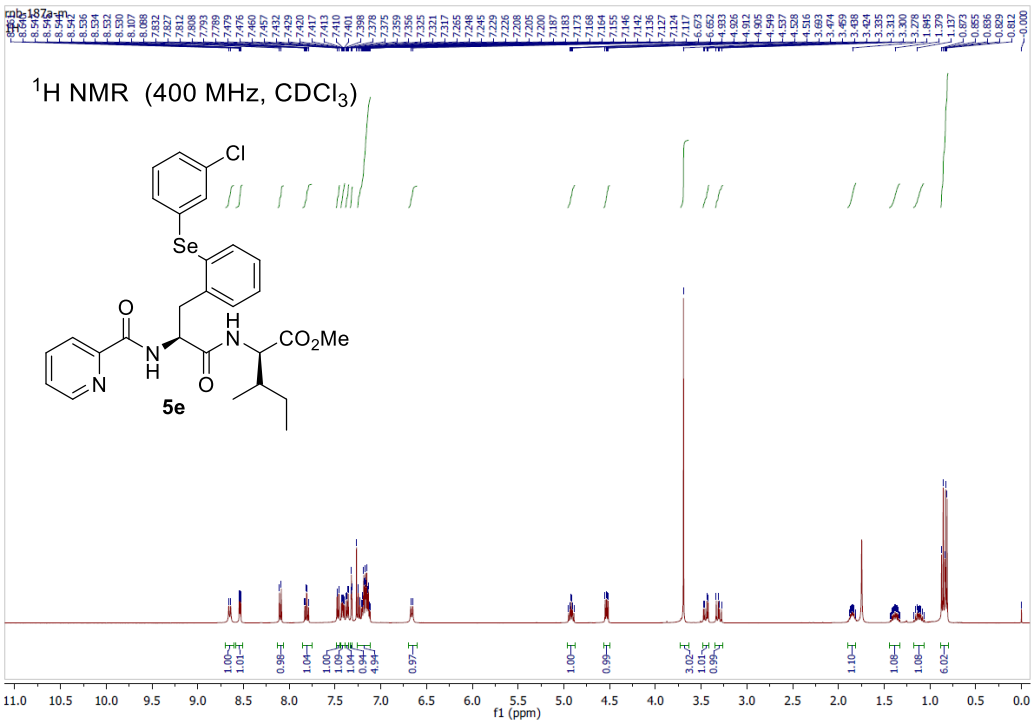


Fig S165. ESI-HRMS spectra of compound **5d'**



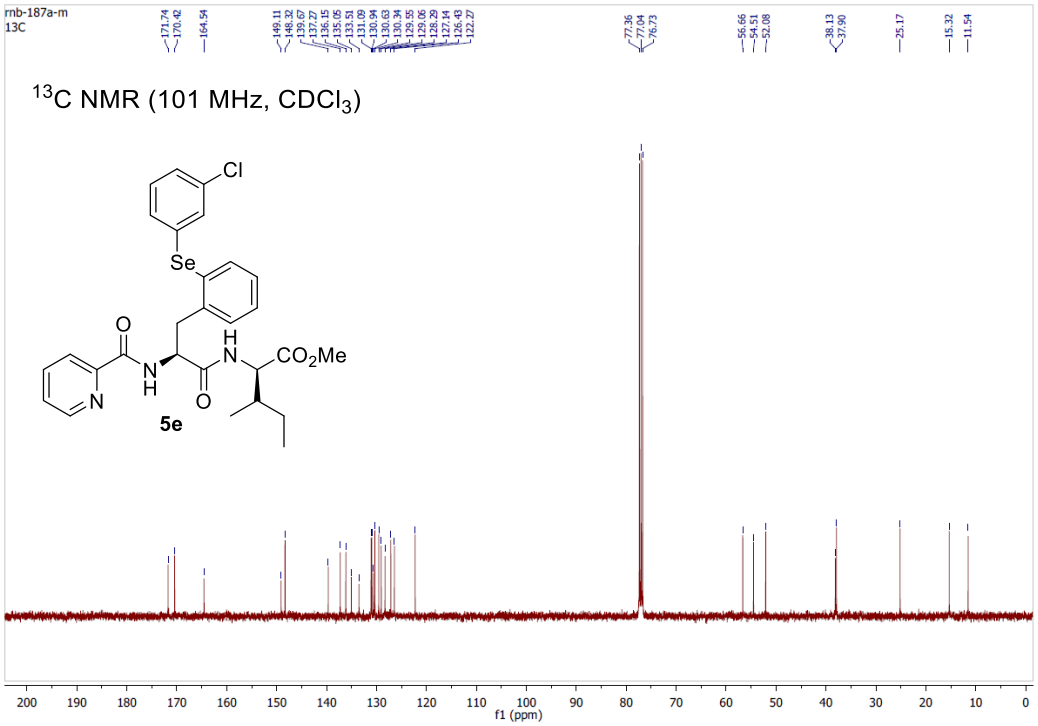


Fig S166. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5e**

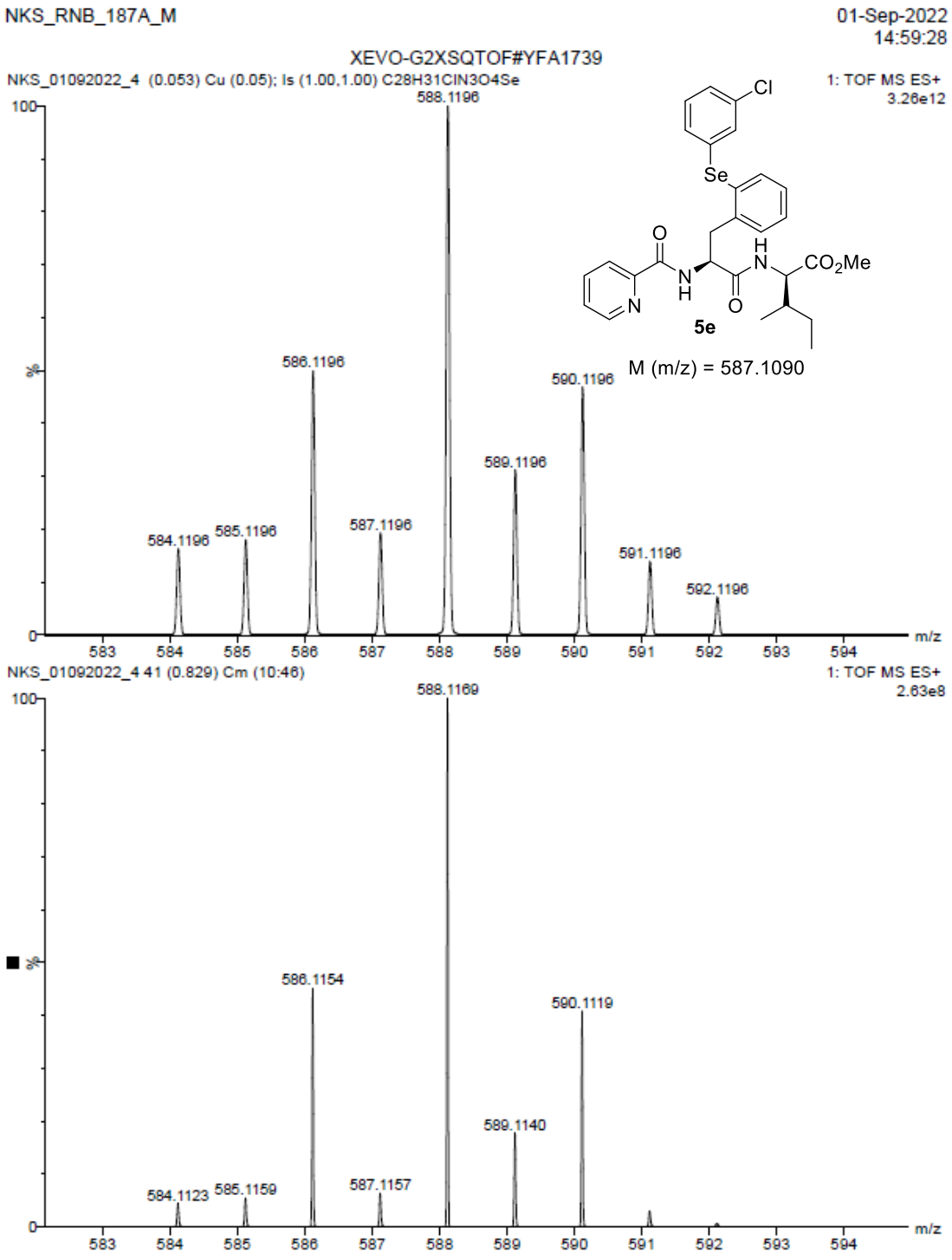
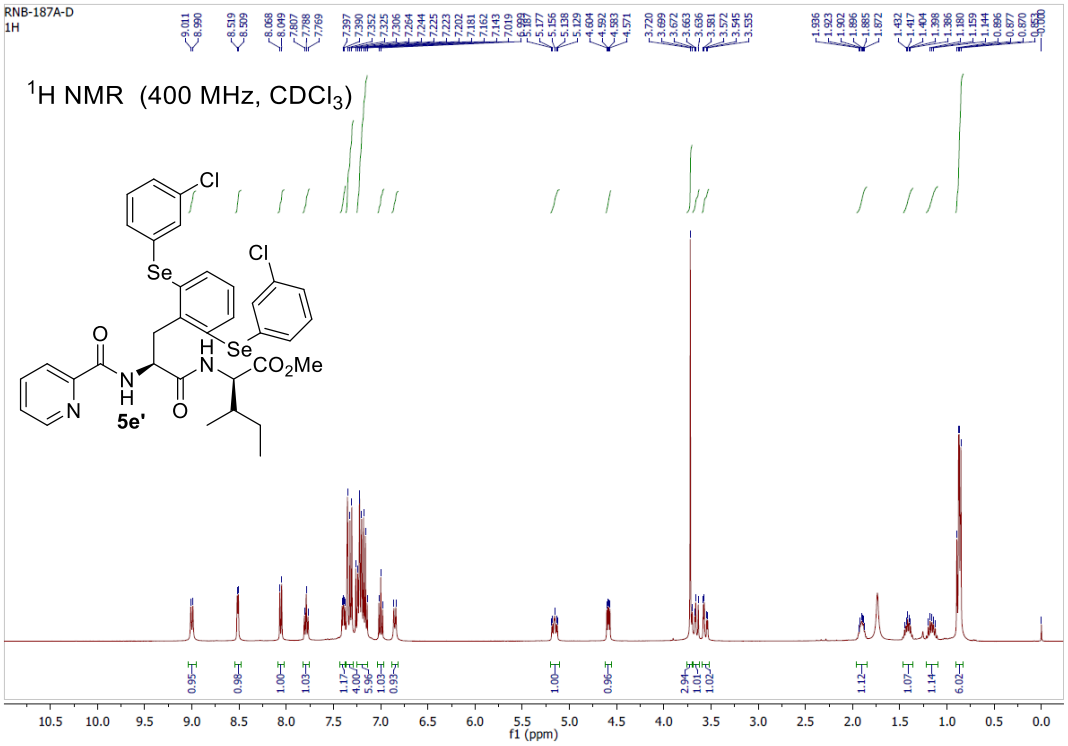


Fig S167. ESI-HRMS spectra of compound **5e**



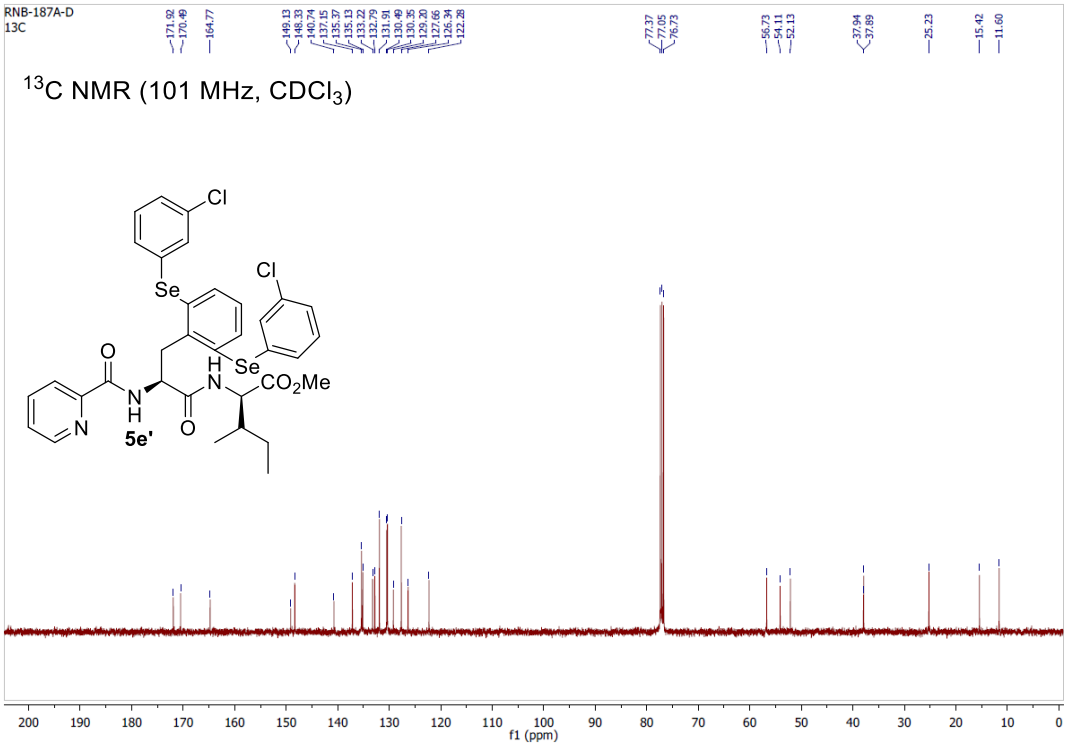


Fig S168. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5e'**

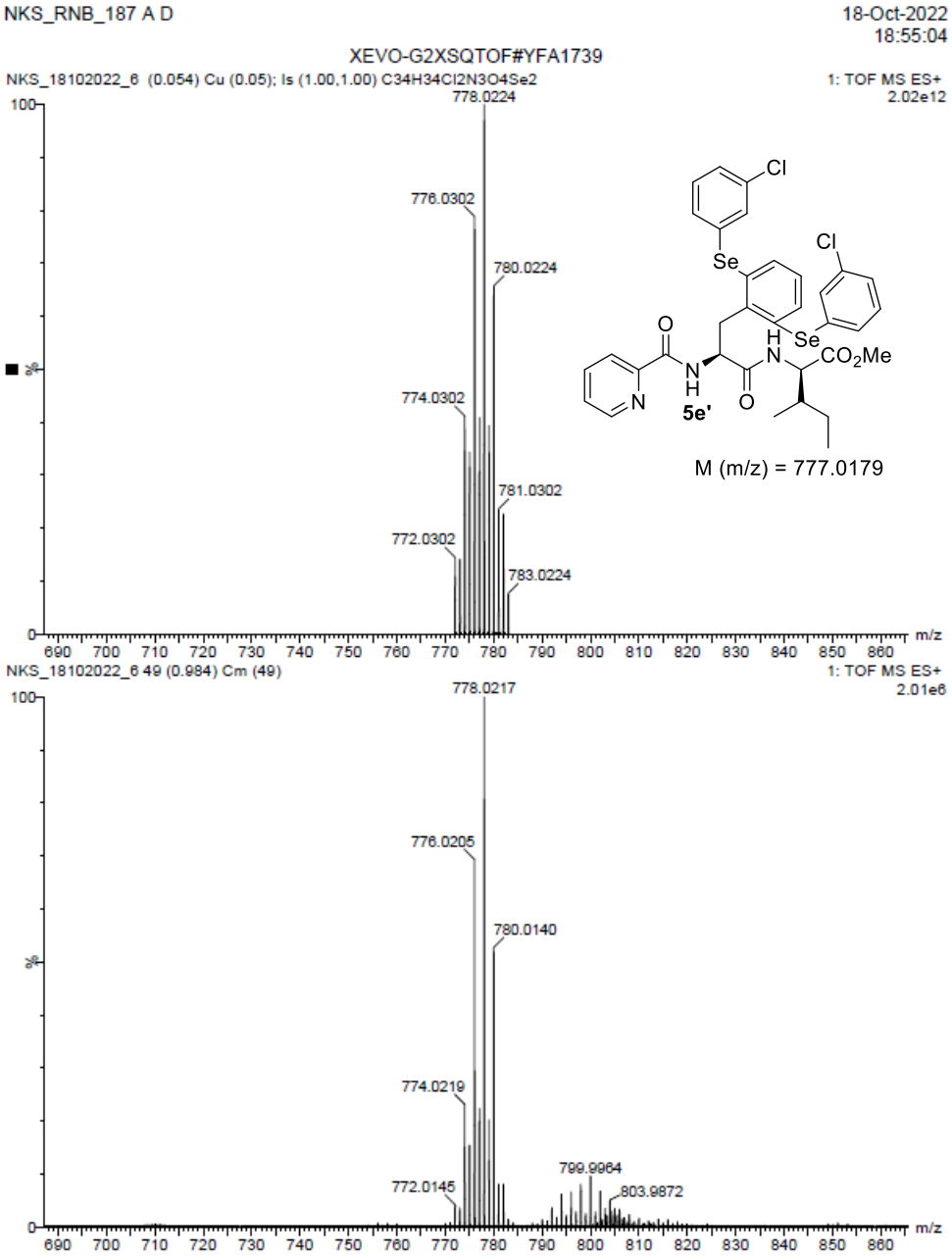
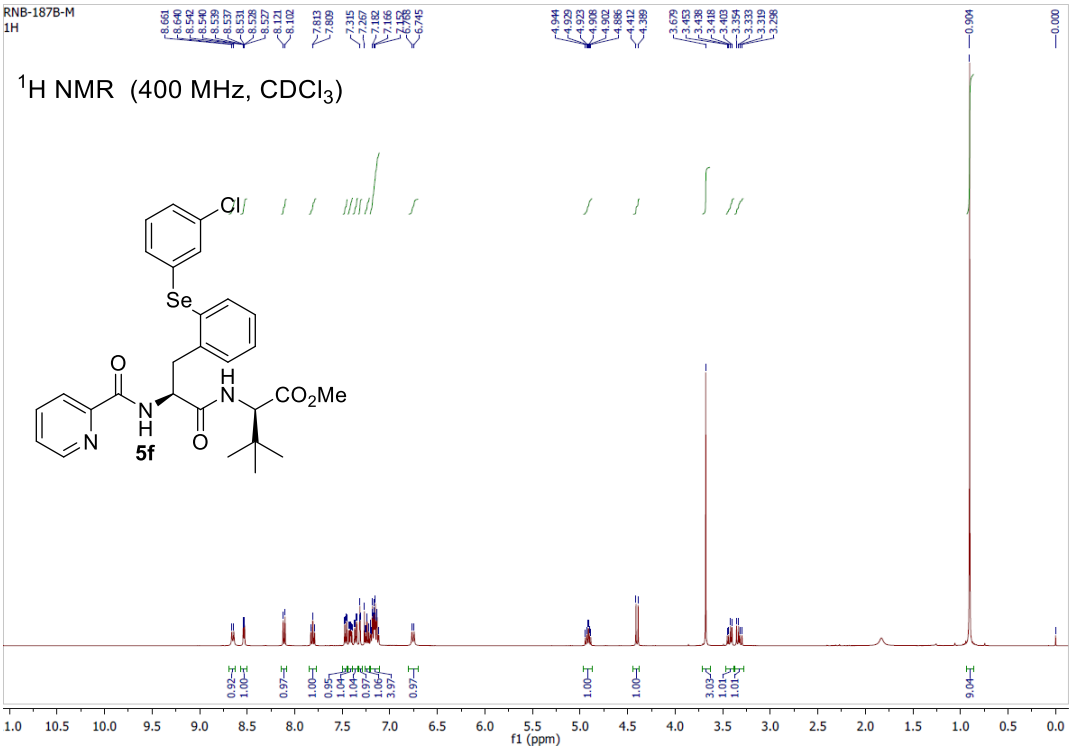


Fig S169. ESI-HRMS spectra of compound **5e'**



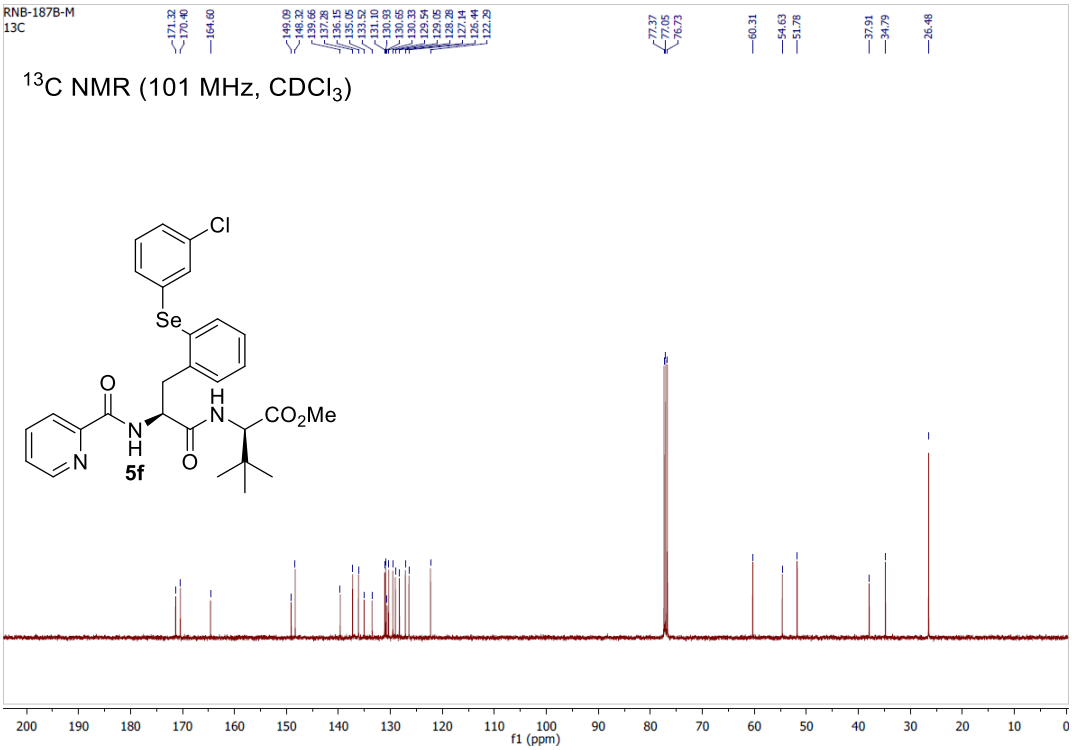


Fig S170. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5f**

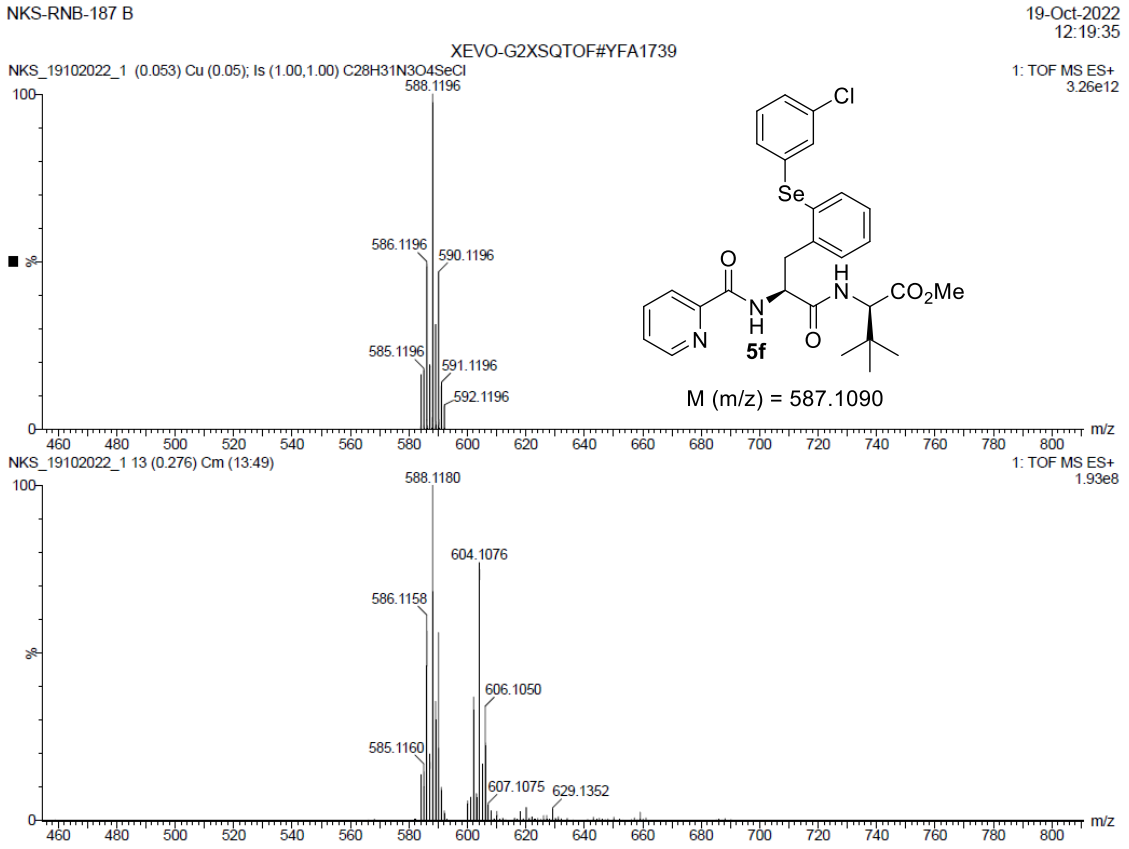
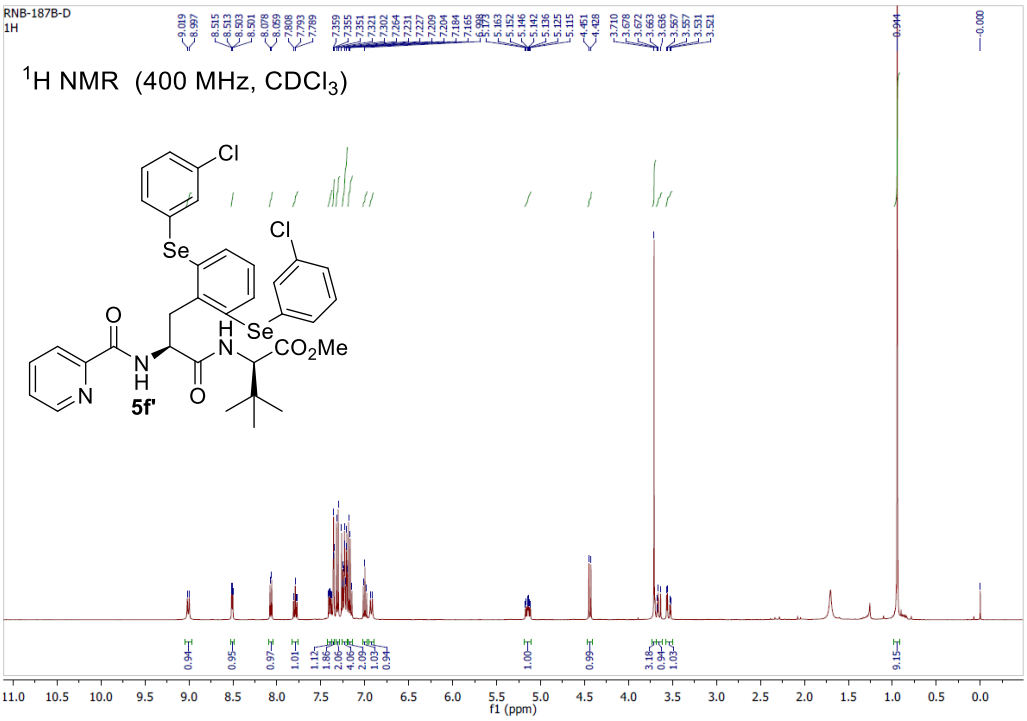


Fig S171. ESI-HRMS spectra of compound **5f**



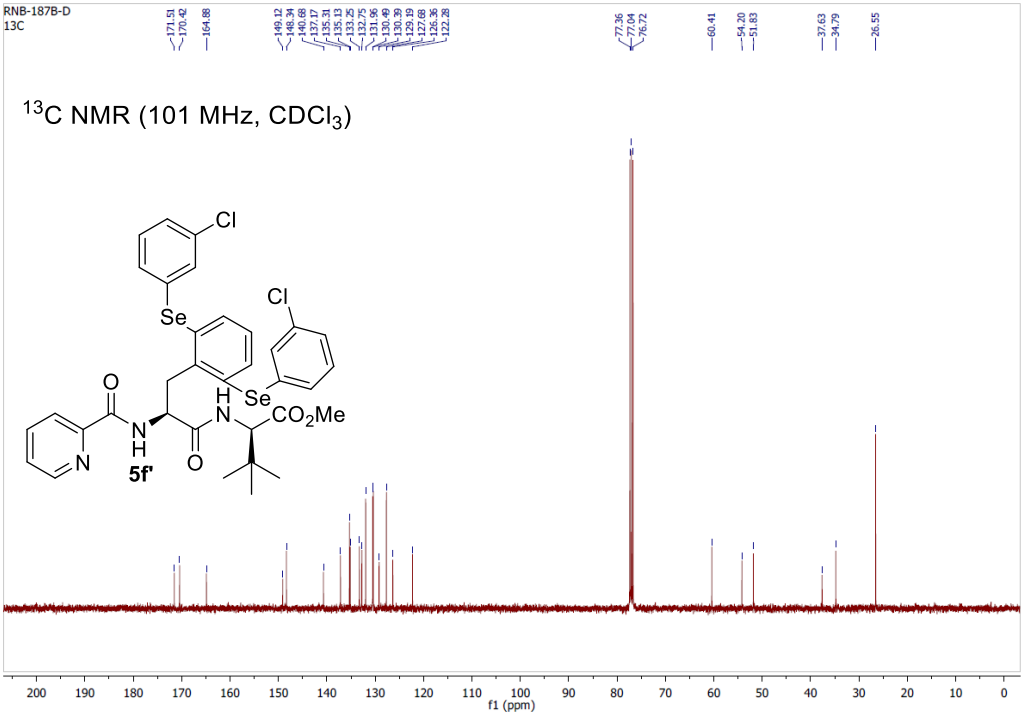


Fig S172. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5f'**

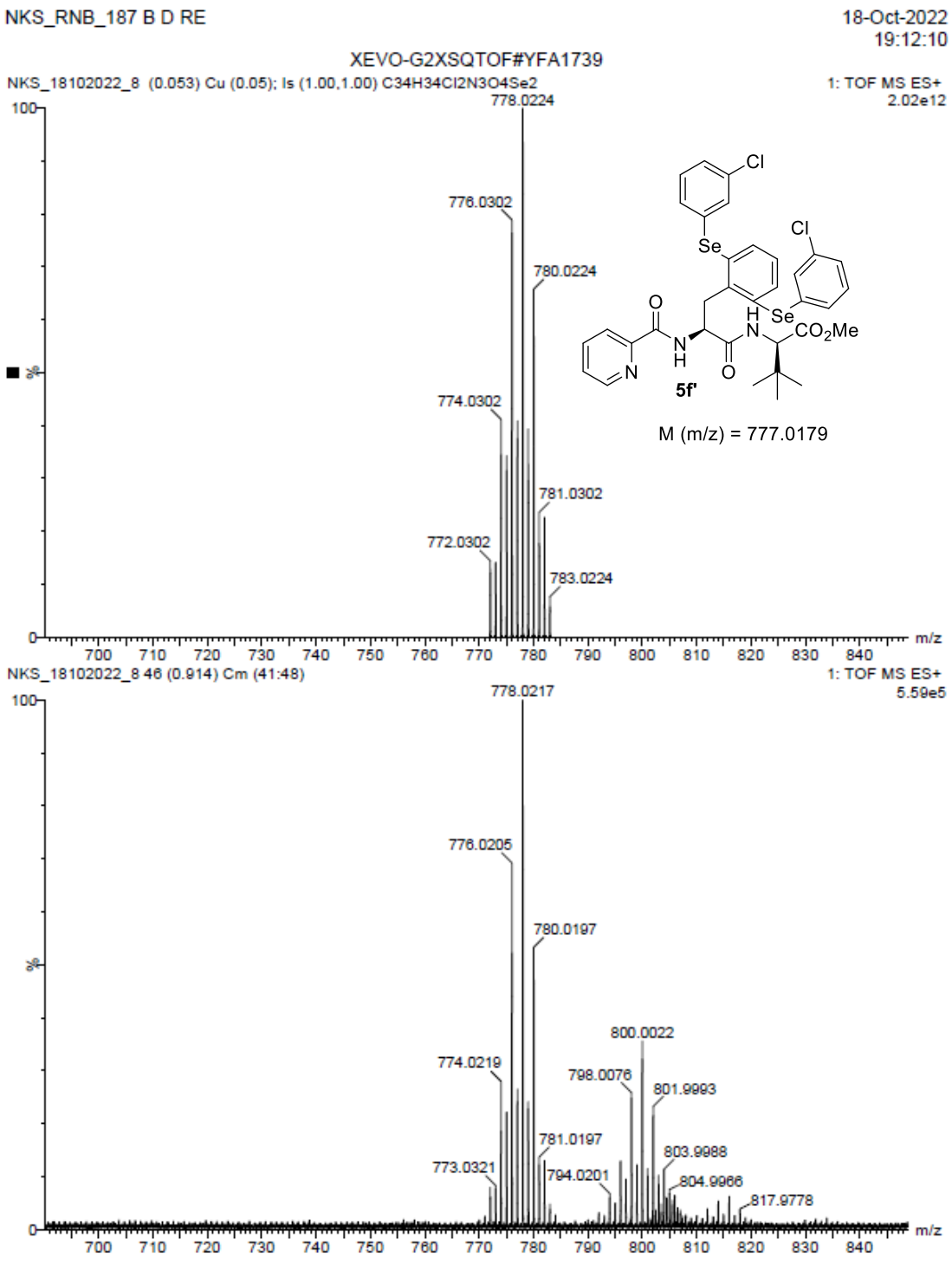
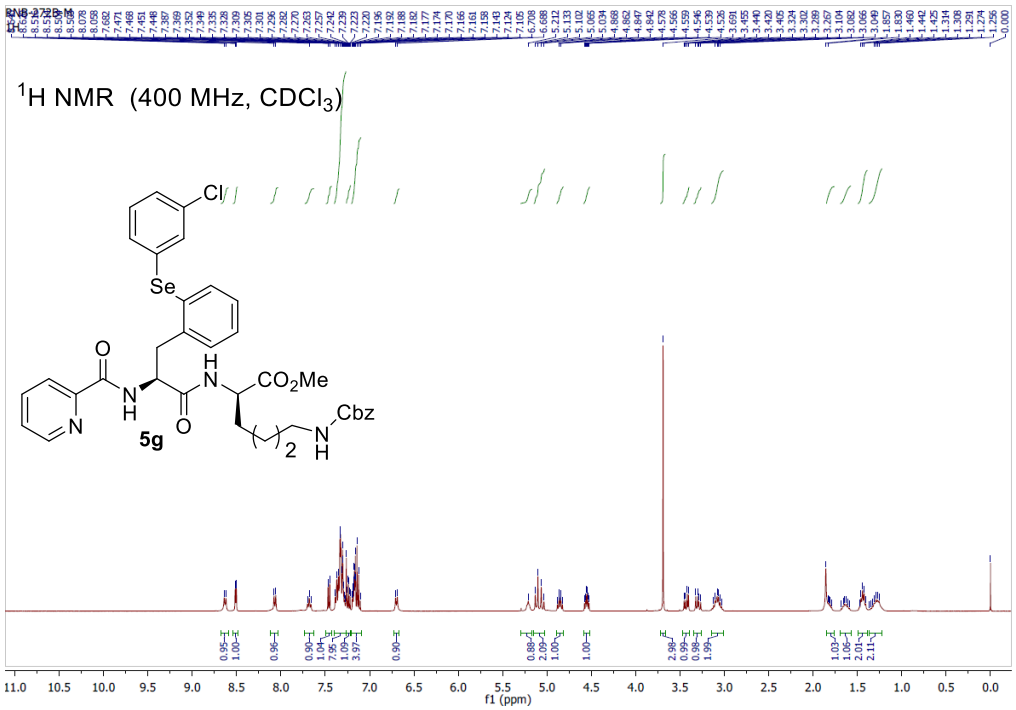


Fig S173. ESI-HRMS spectra of compound **5f'**



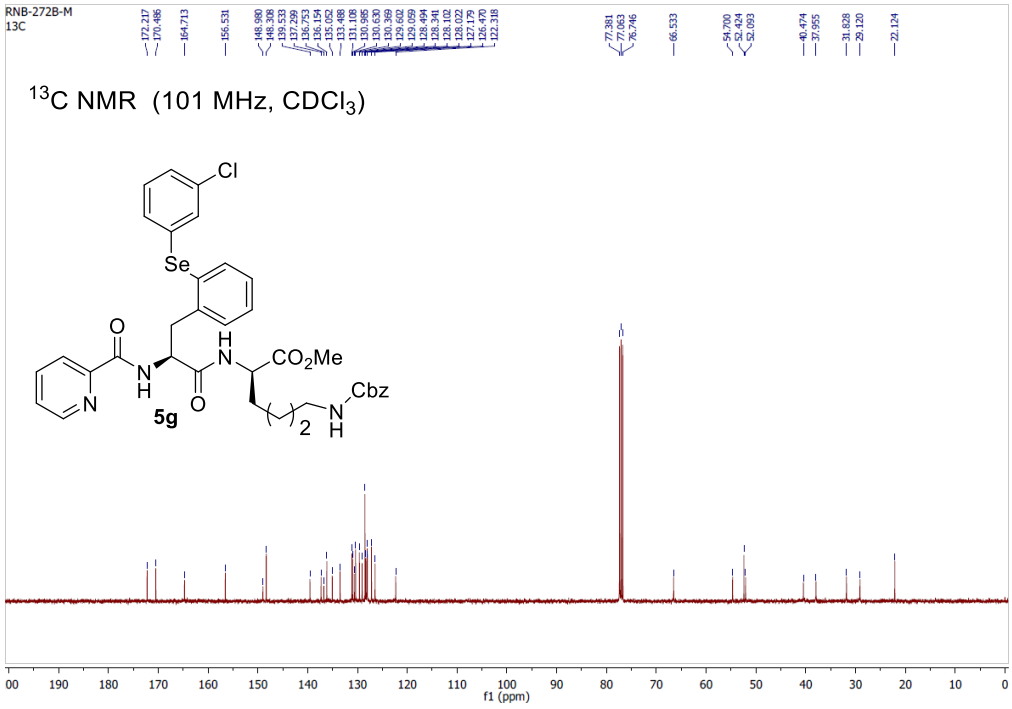


Fig S174. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5g**

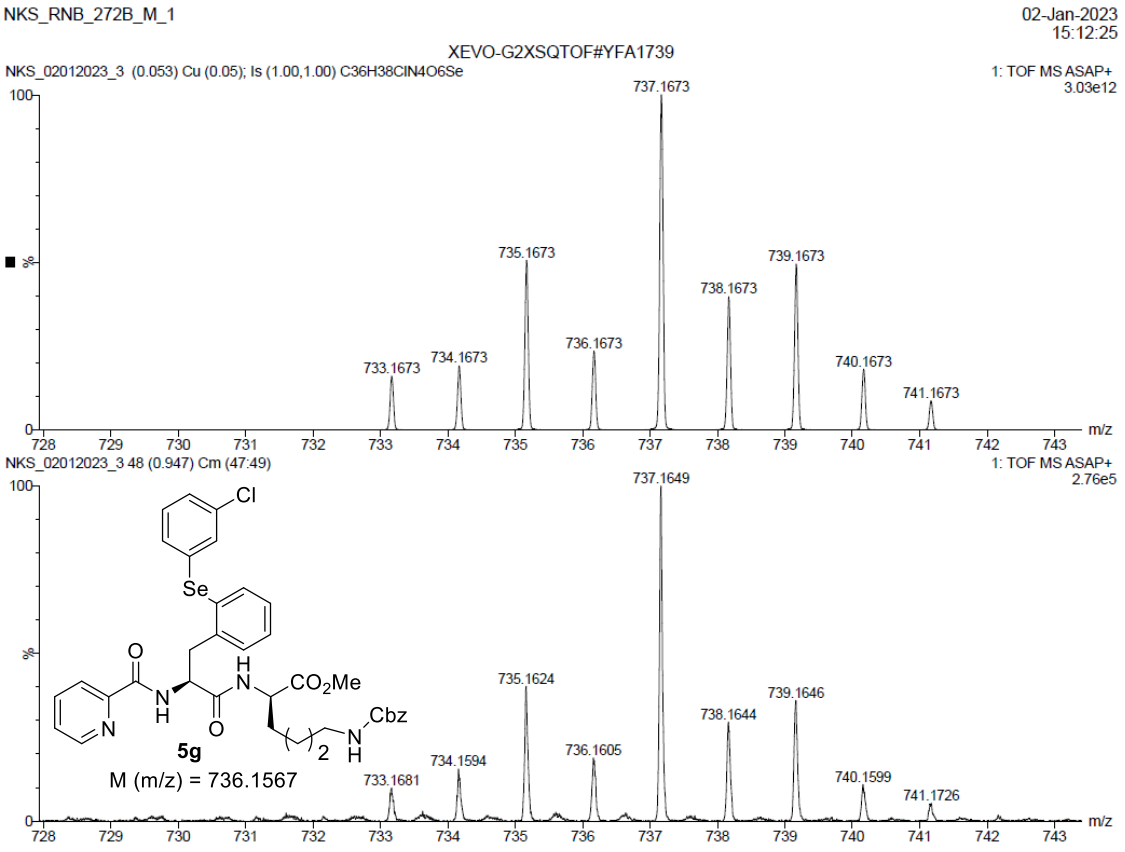
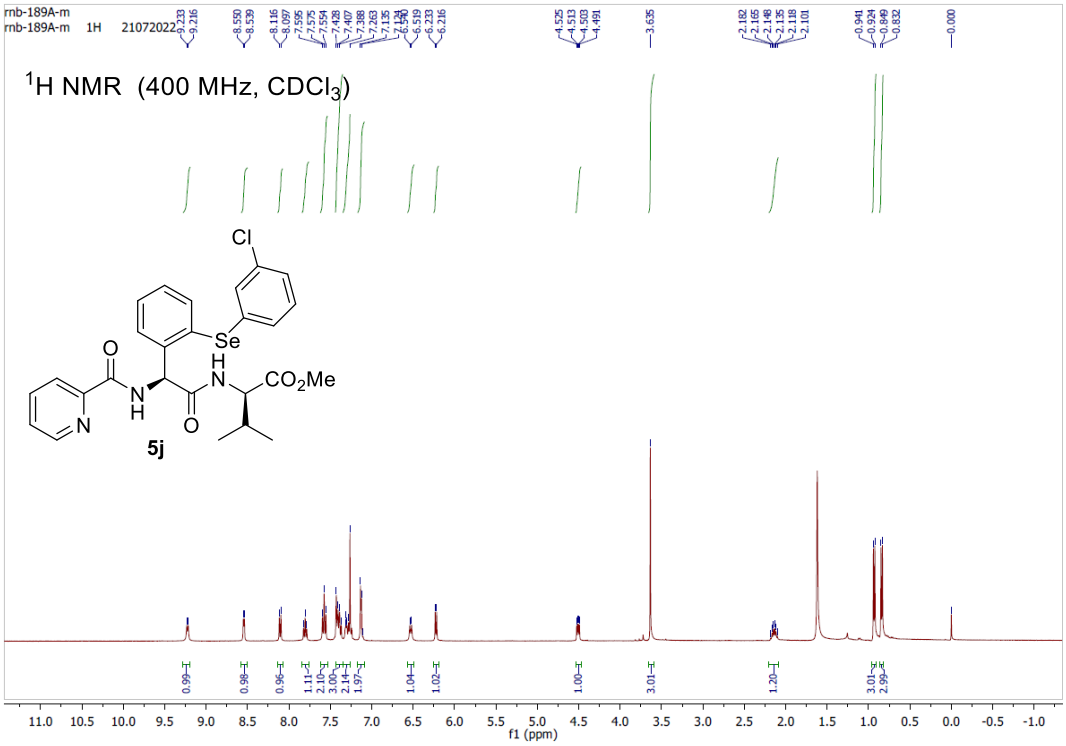


Fig S175. ASAP-HRMS spectra of compound **5g**



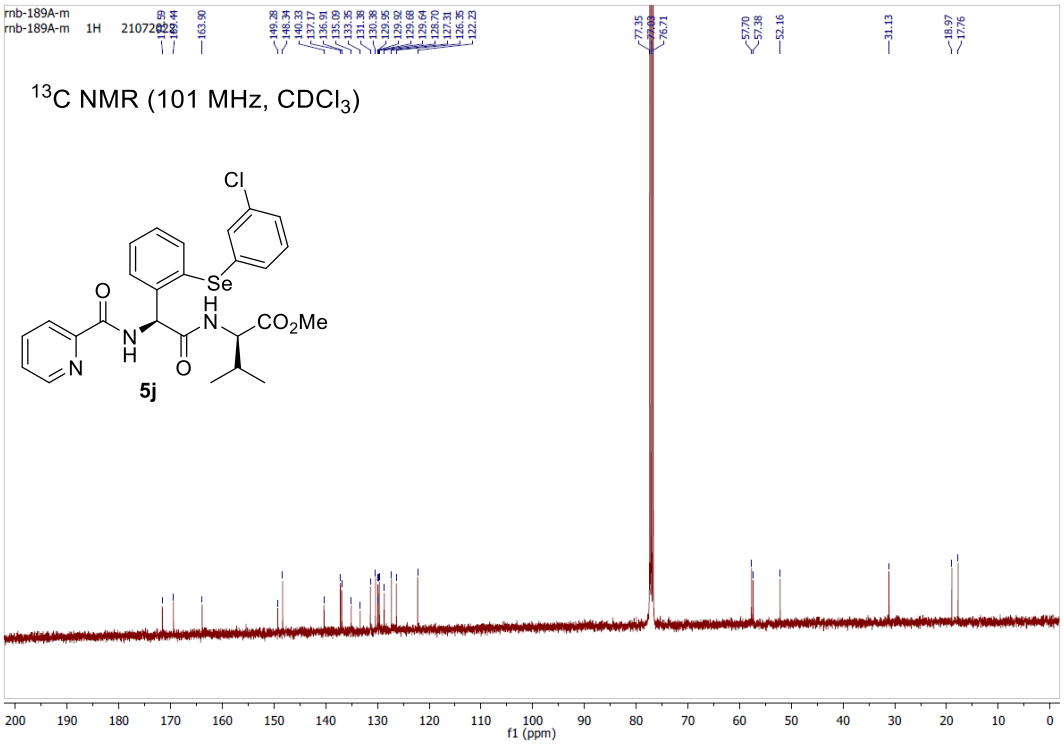


Fig S176. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5j**

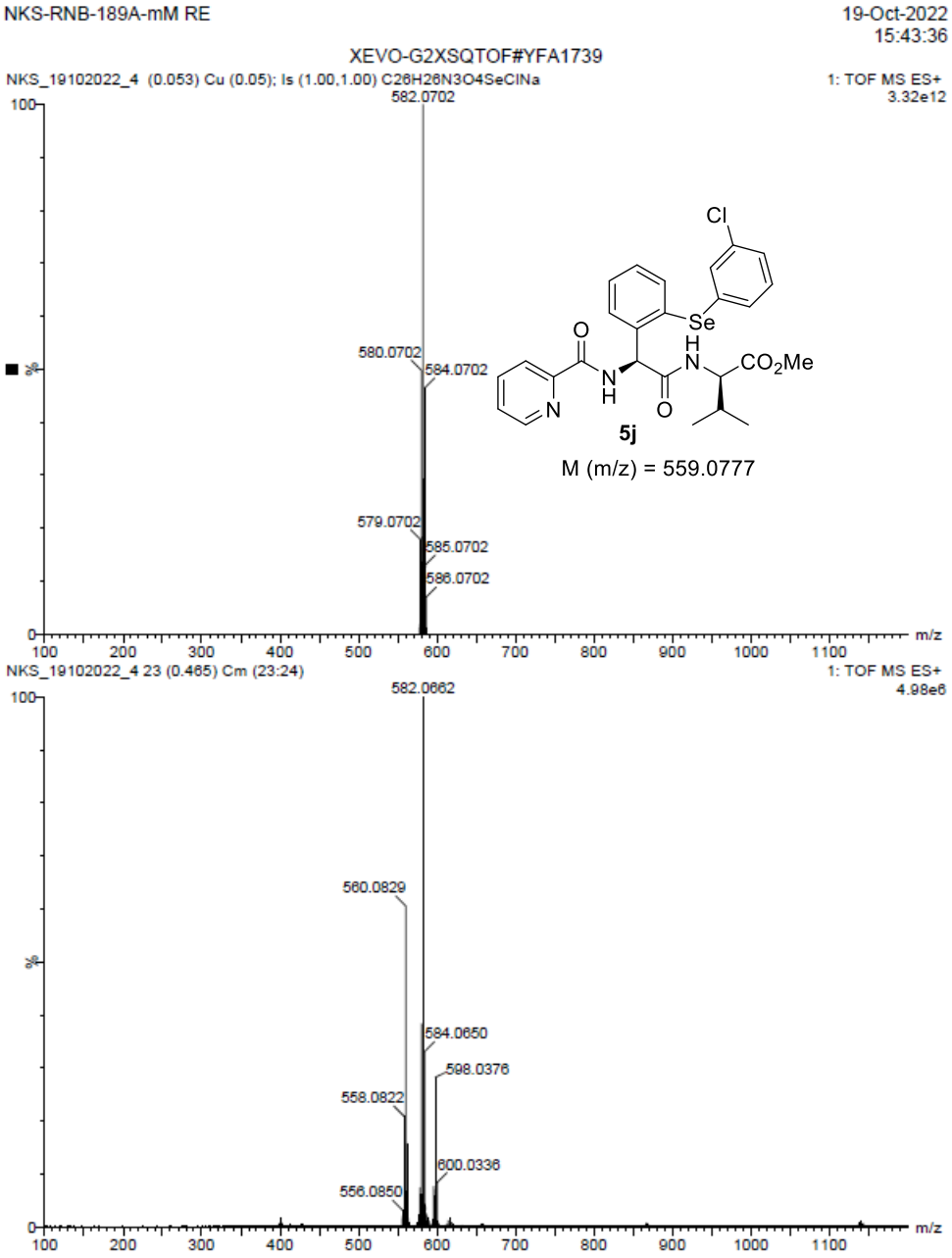
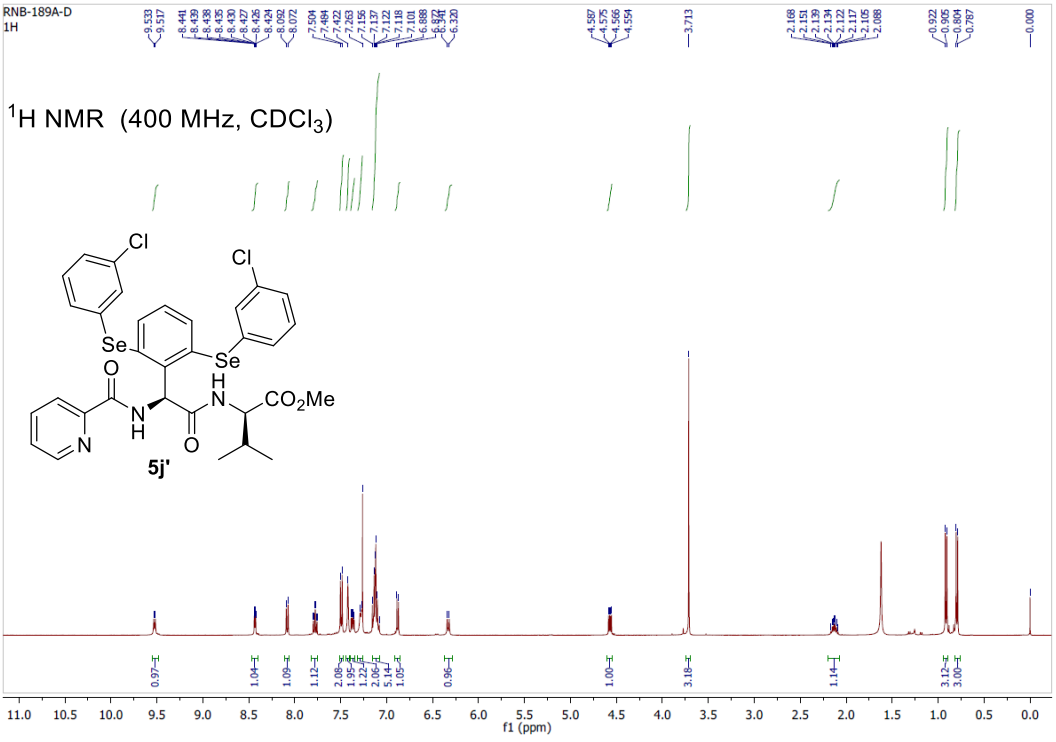


Fig S177. ESI-HRMS spectra of compound **5j**



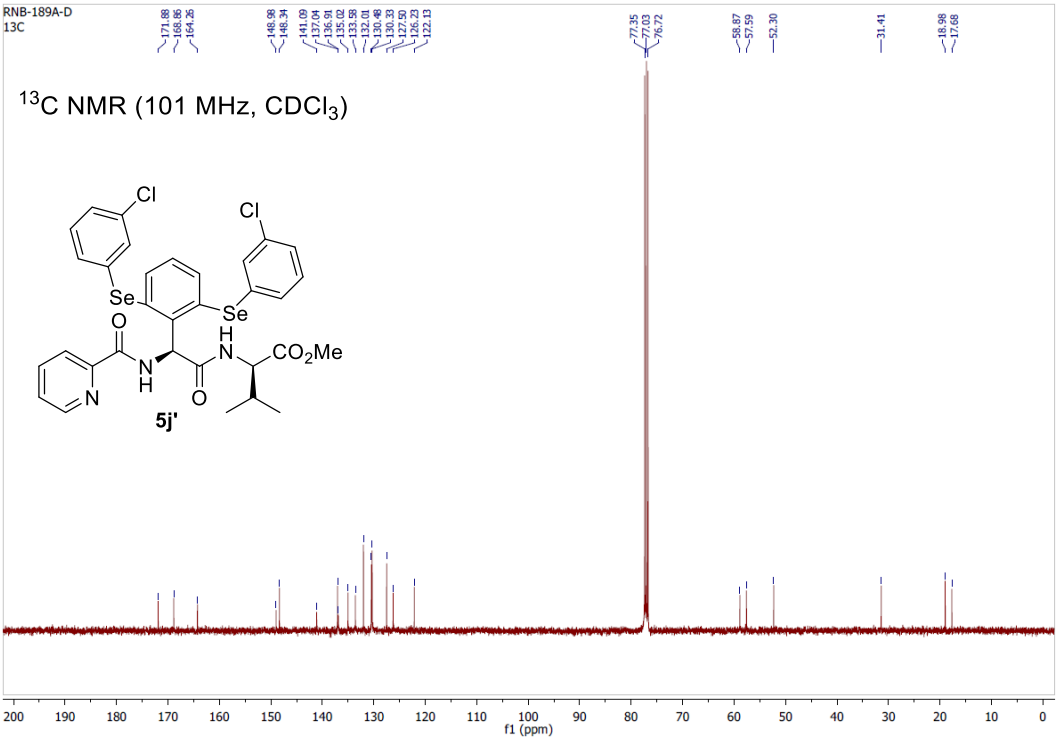


Fig S178. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5j'**

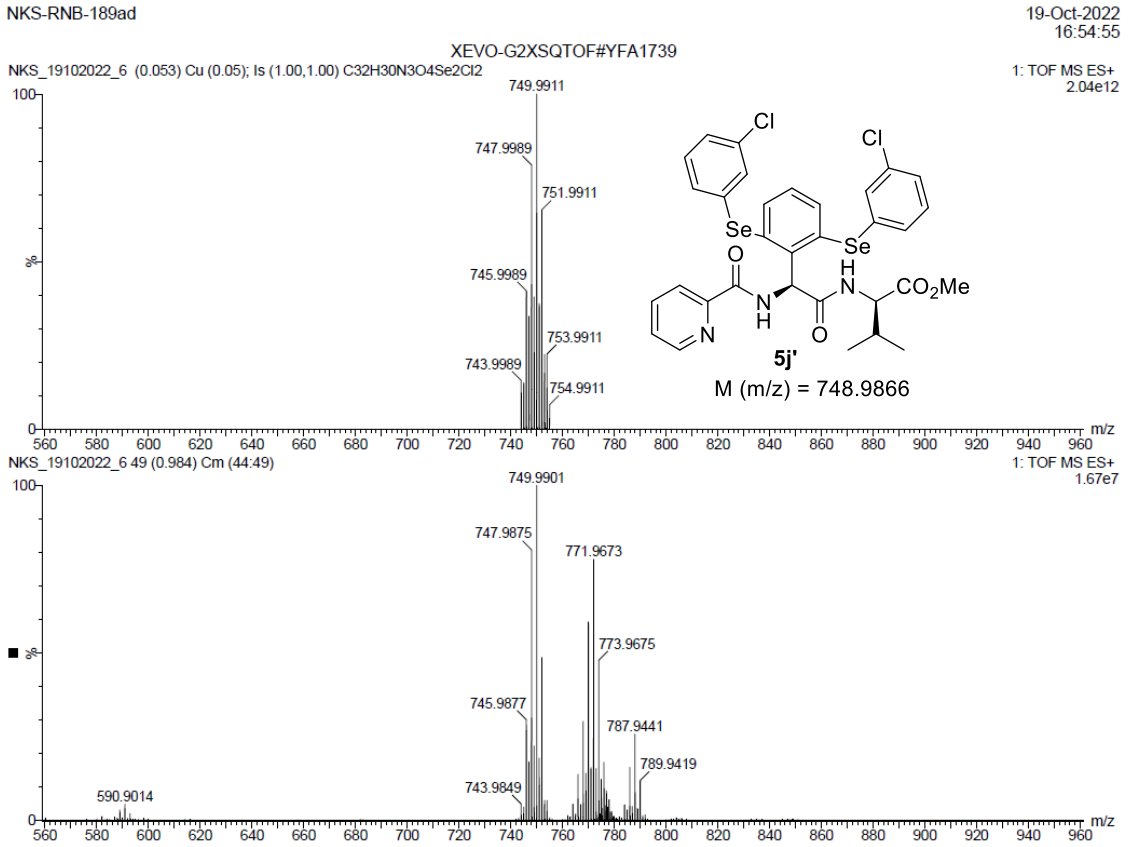
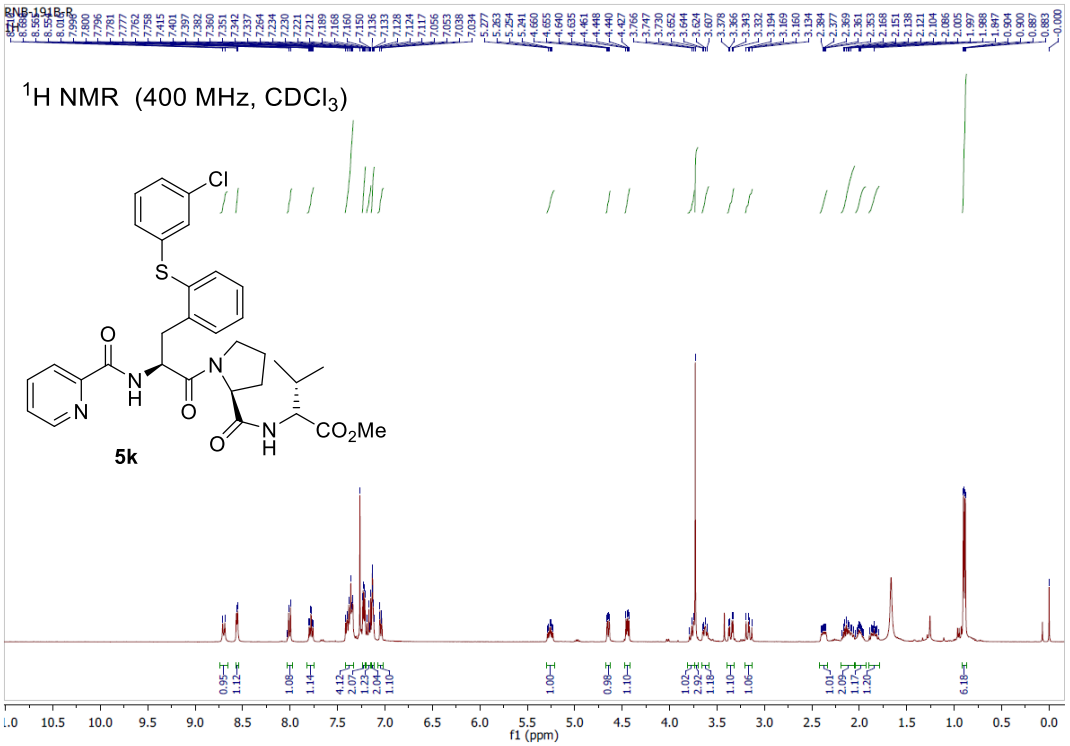


Fig S179. ESI-HRMS spectra of compound **5j'**



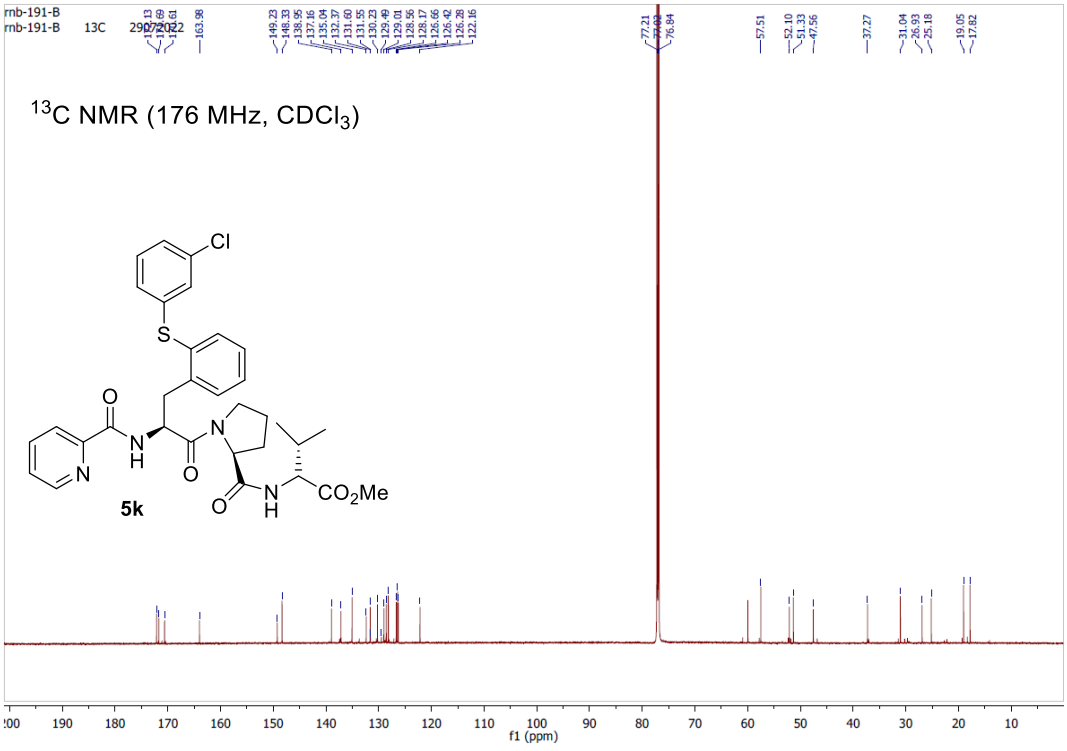


Fig S180. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5k**

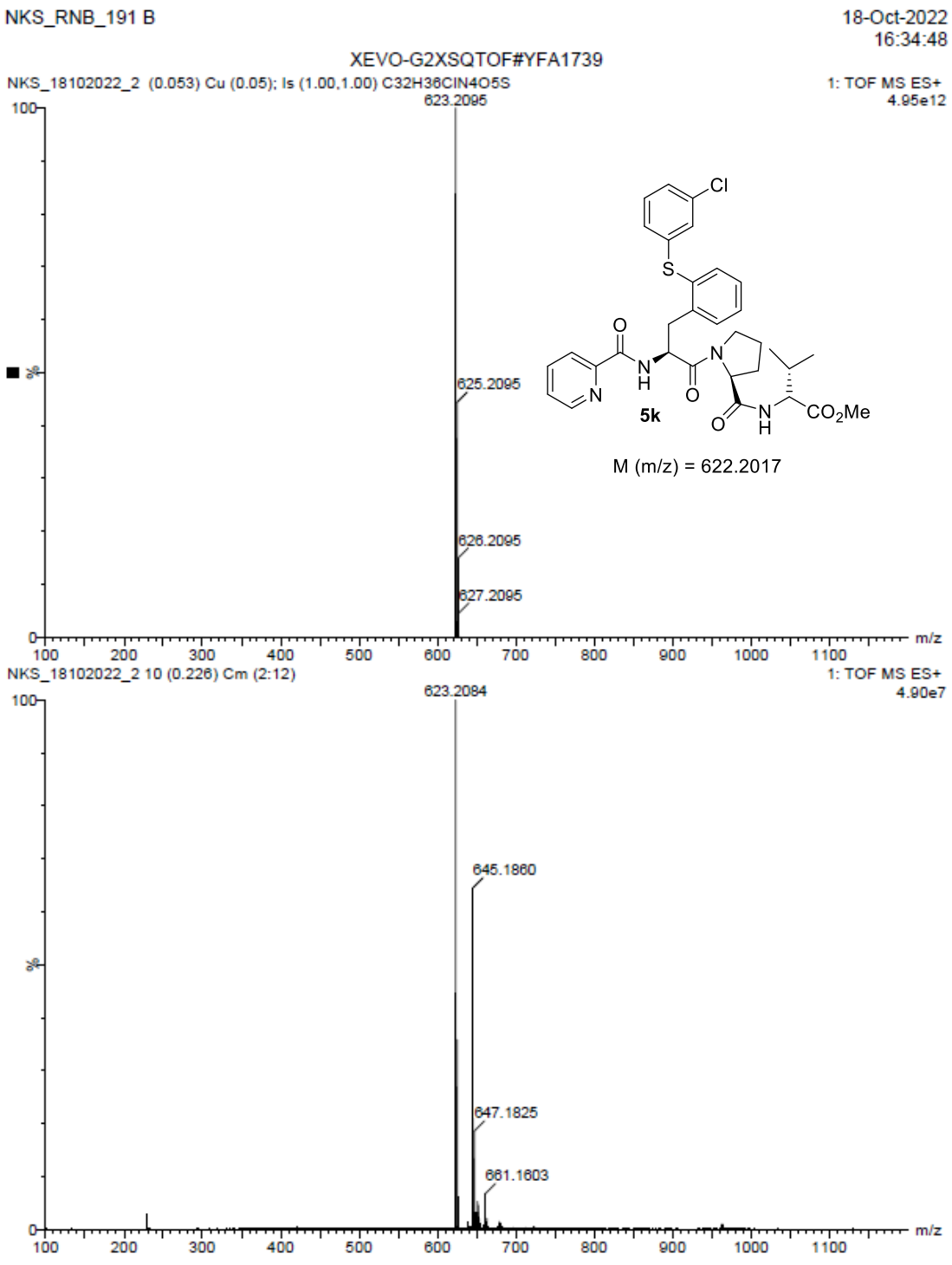
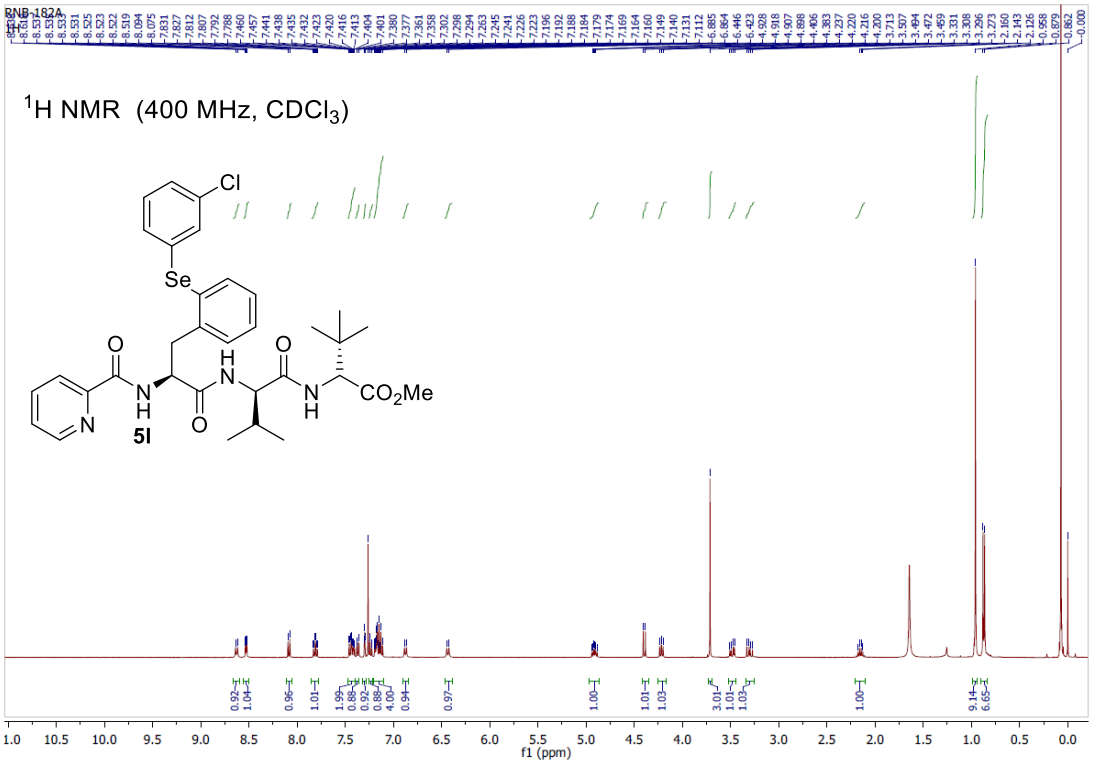


Fig S181. ESI-HRMS spectra of compound **5k**



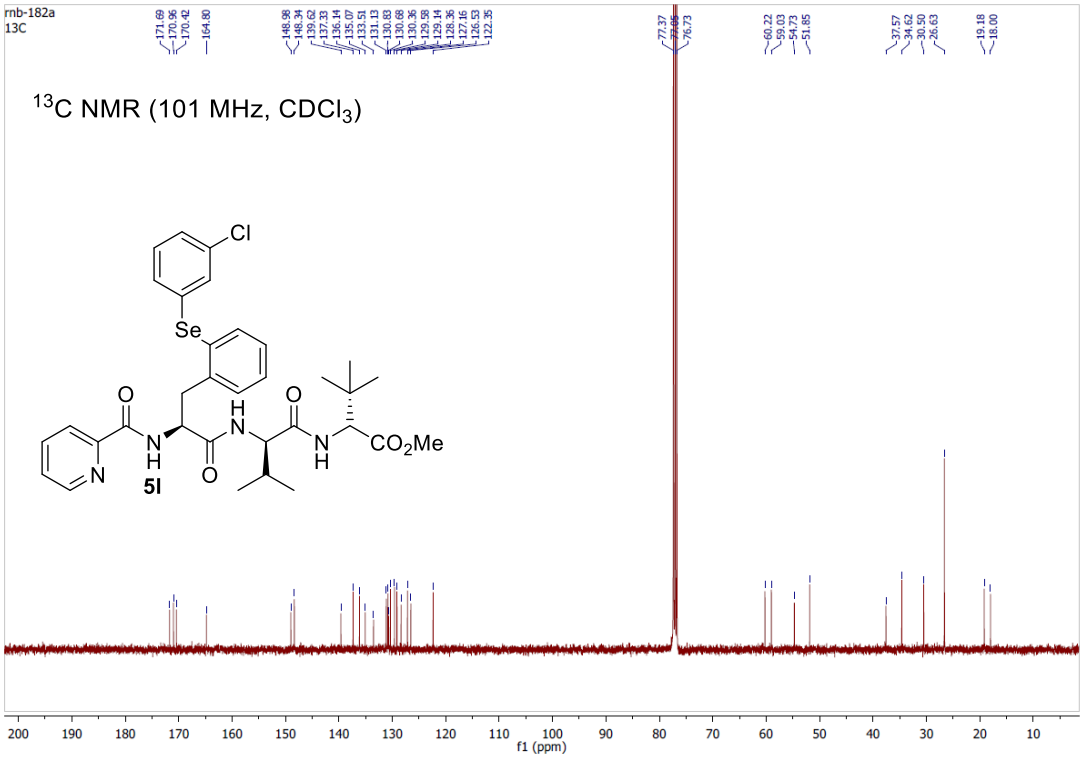


Fig S182. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5l**

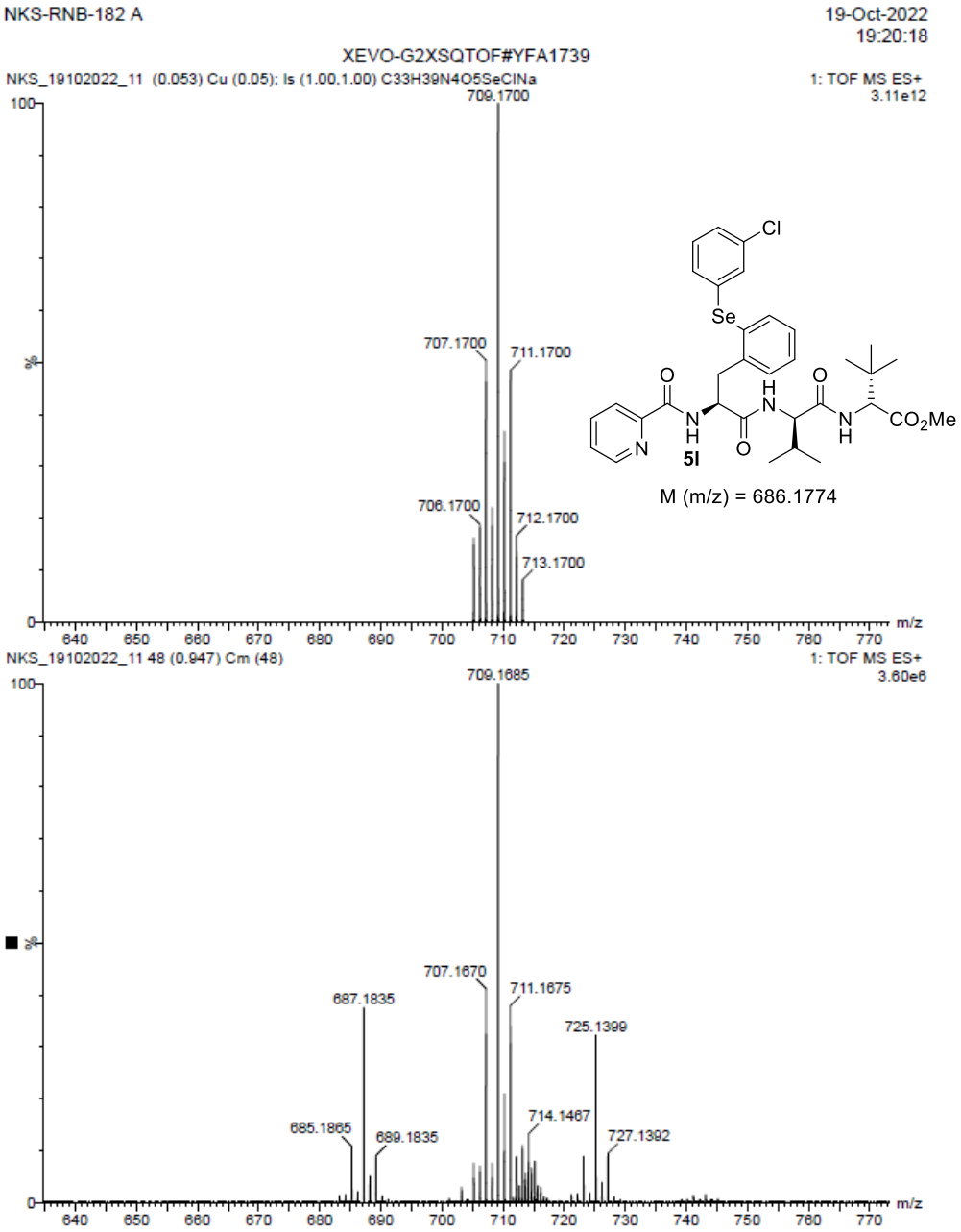
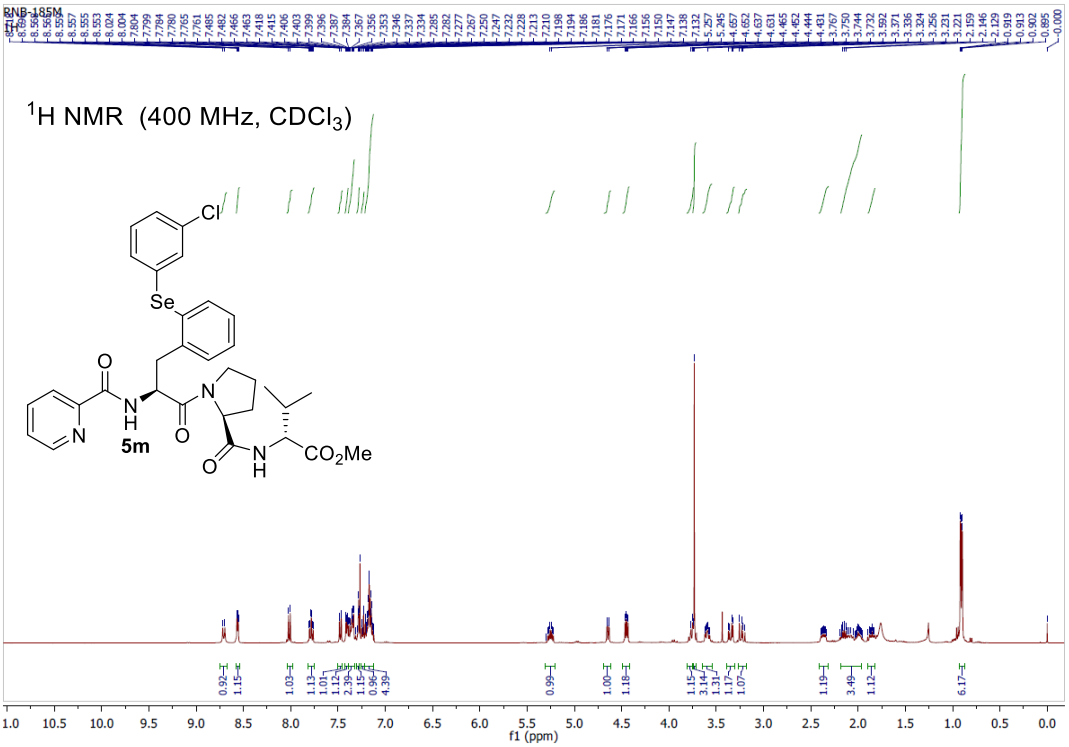


Fig S183. ESI-HRMS spectra of compound **5l**



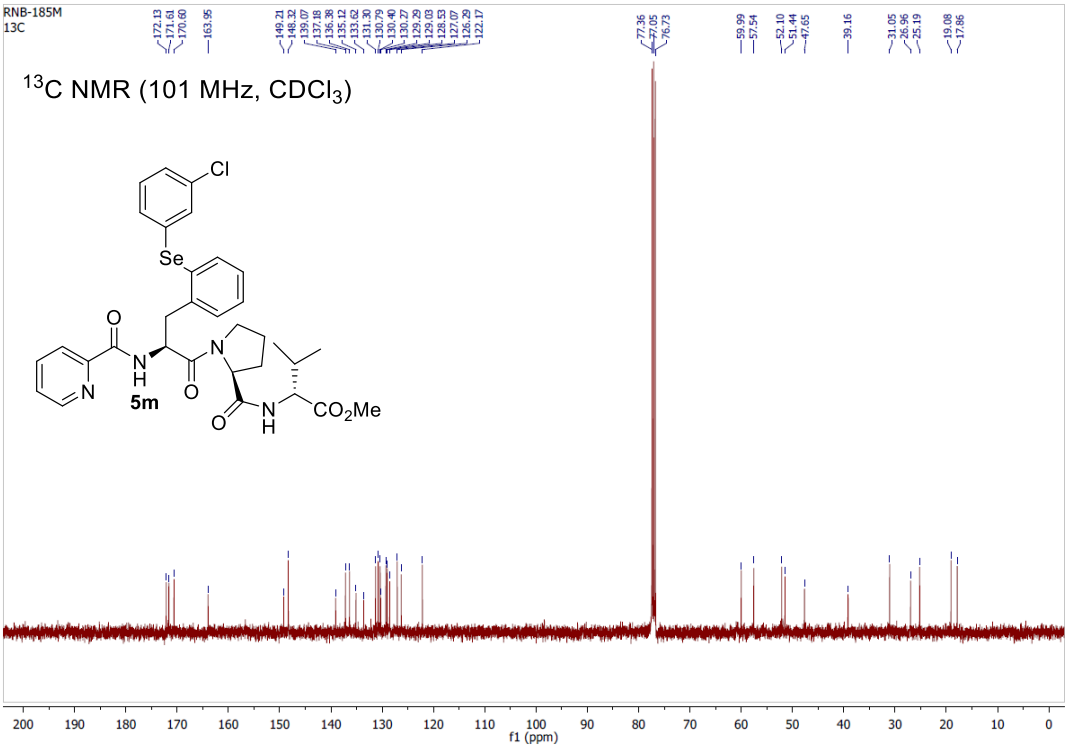


Fig S184. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5m**

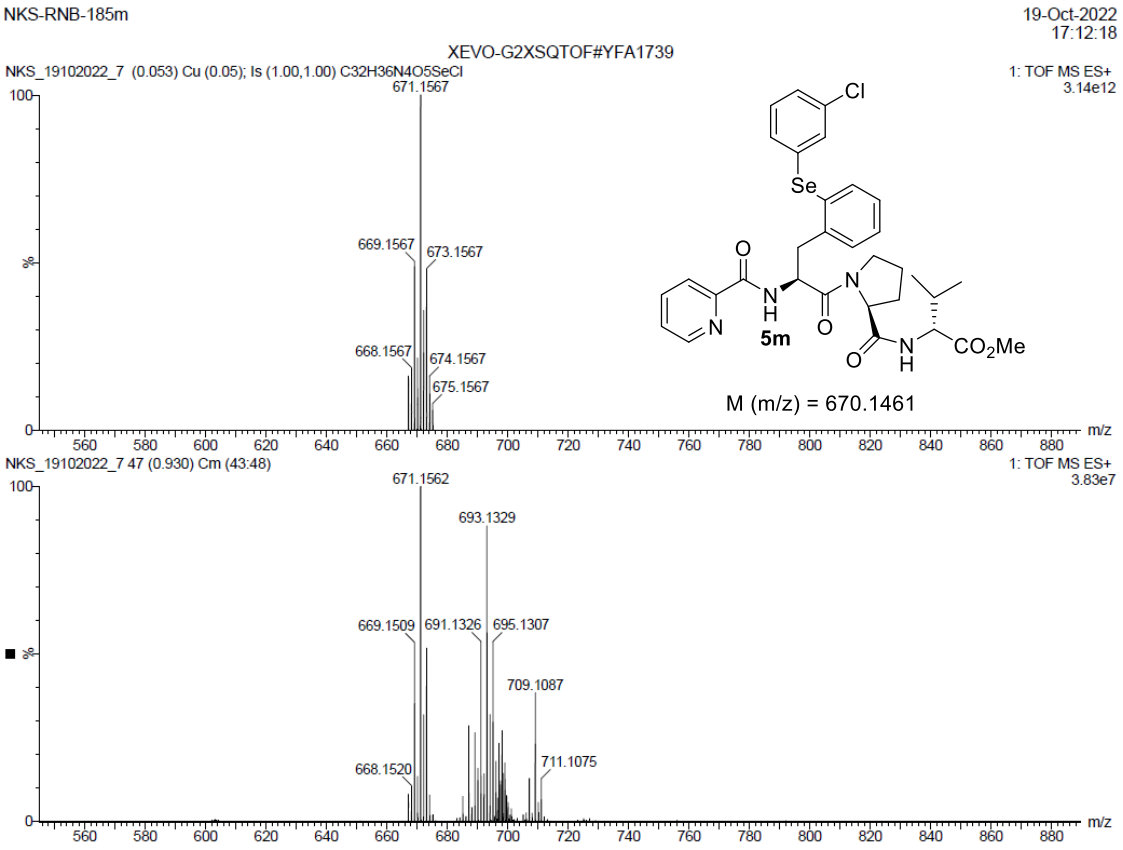
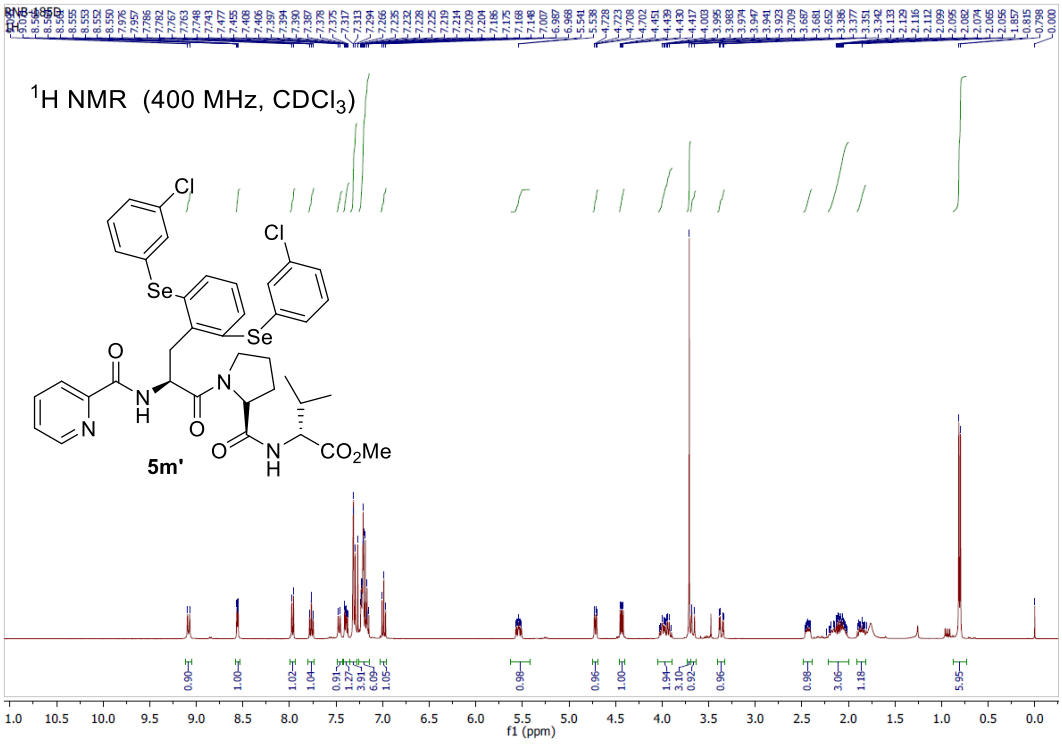


Fig S185. ESI-HRMS spectra of compound **5m**



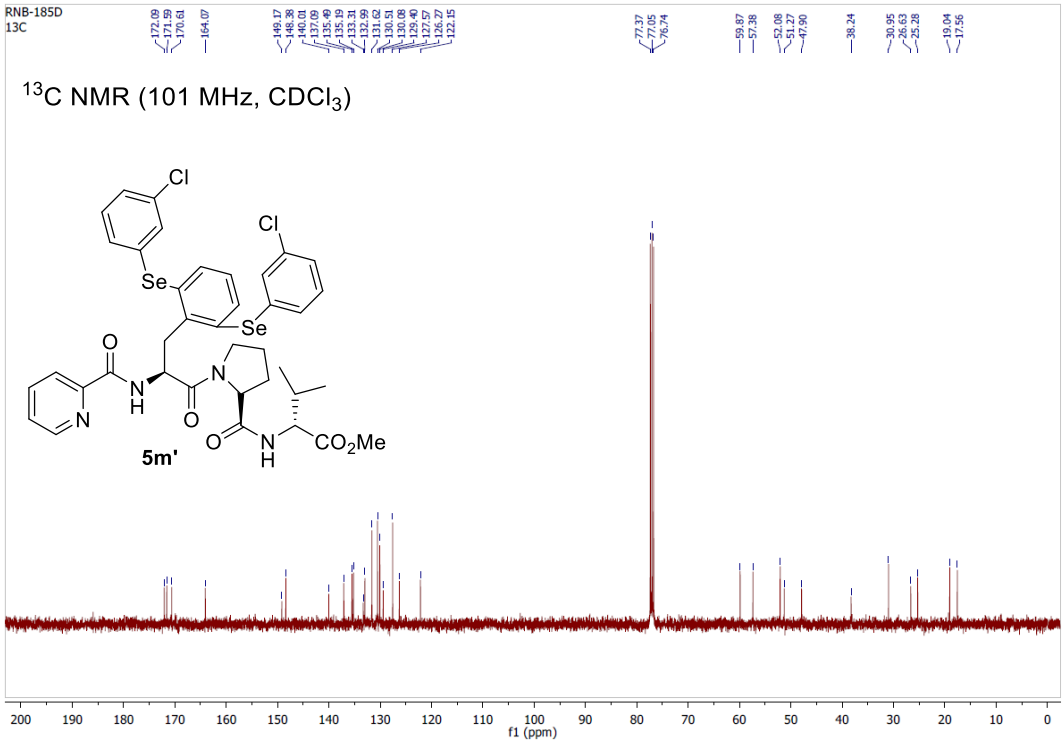


Fig S186. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **5m'**

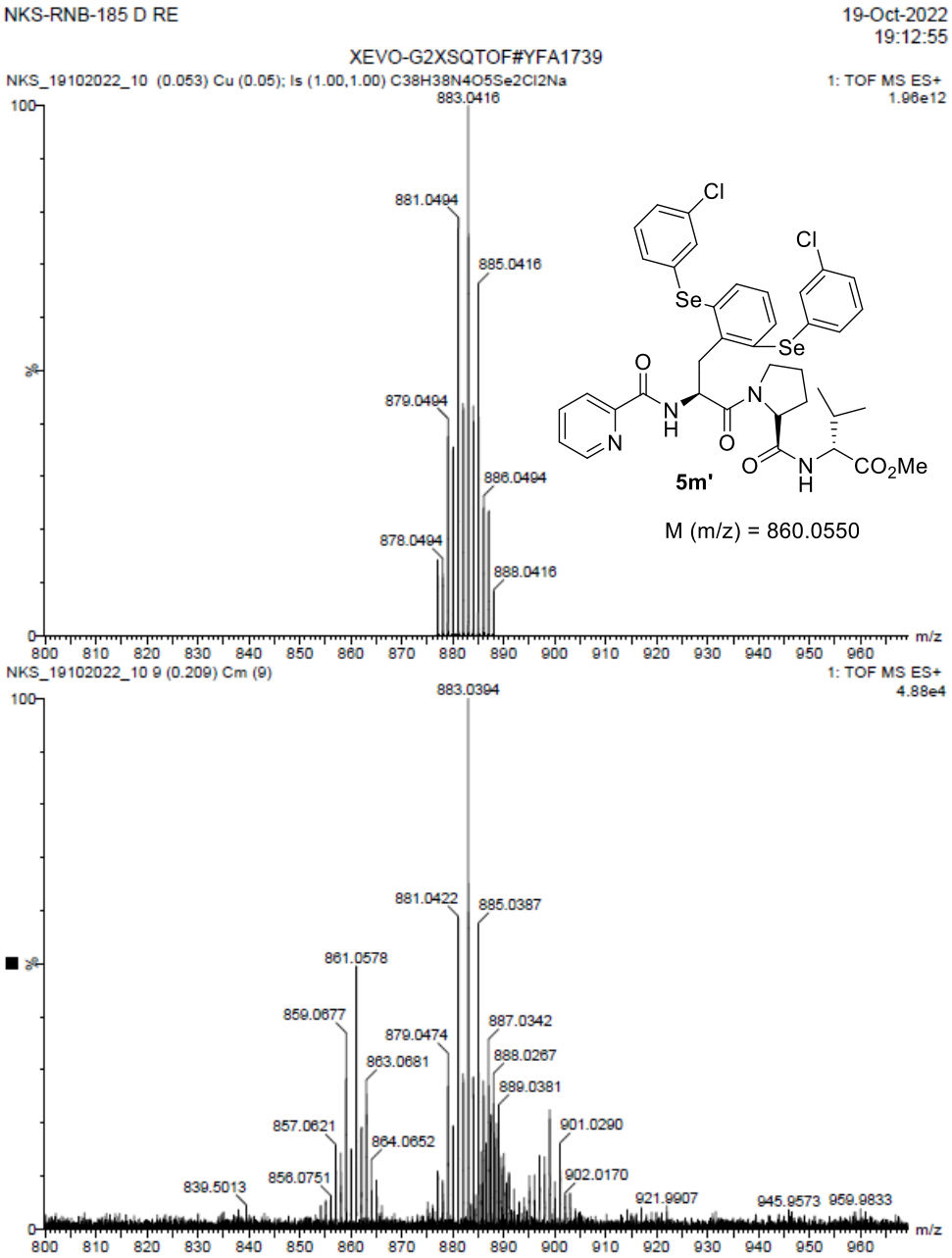
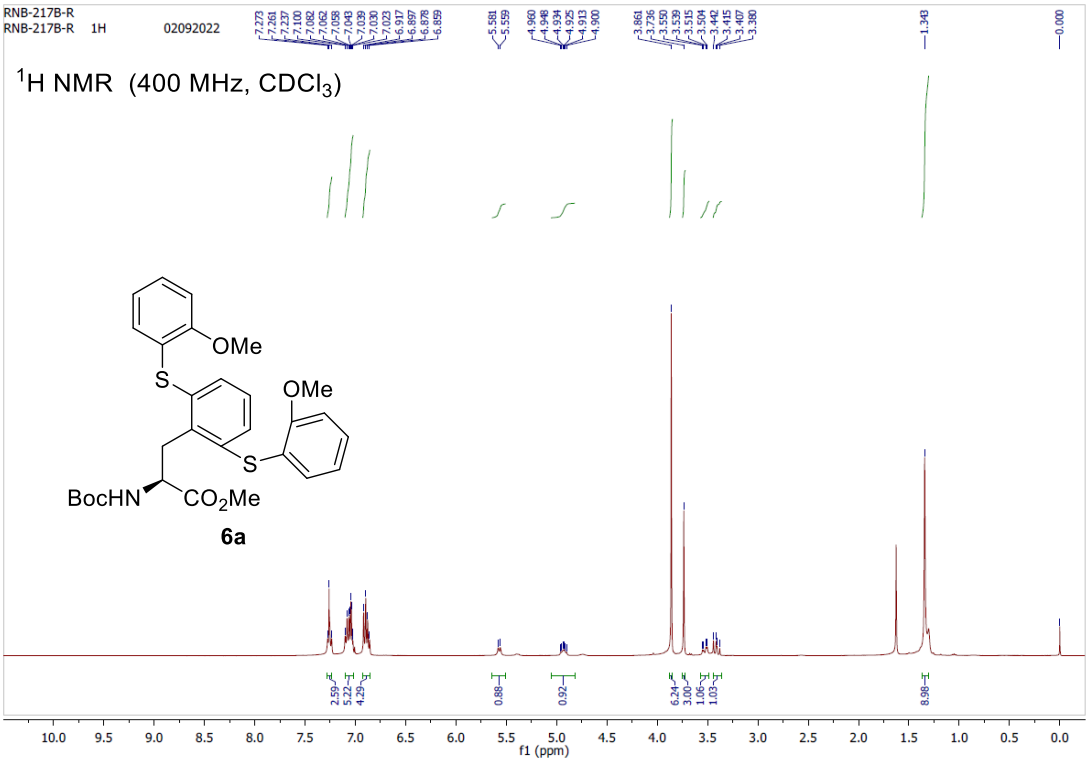


Fig S187. ESI-HRMS spectra of compound **5m'**



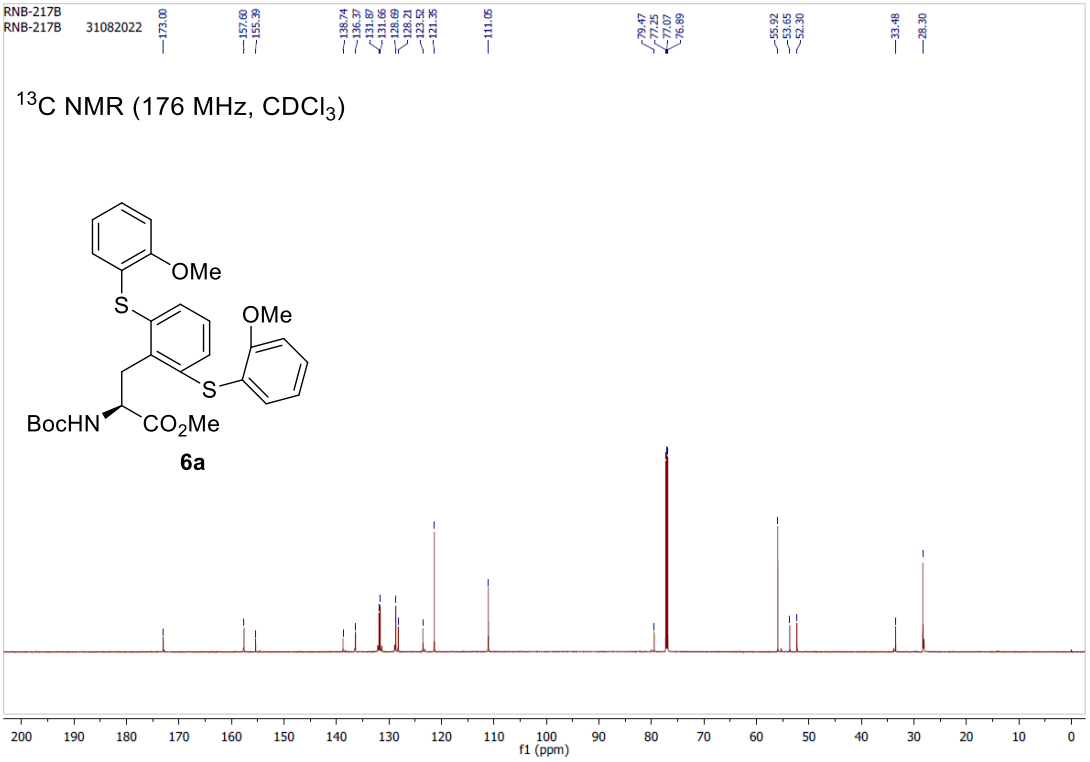


Fig S188. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **6a**

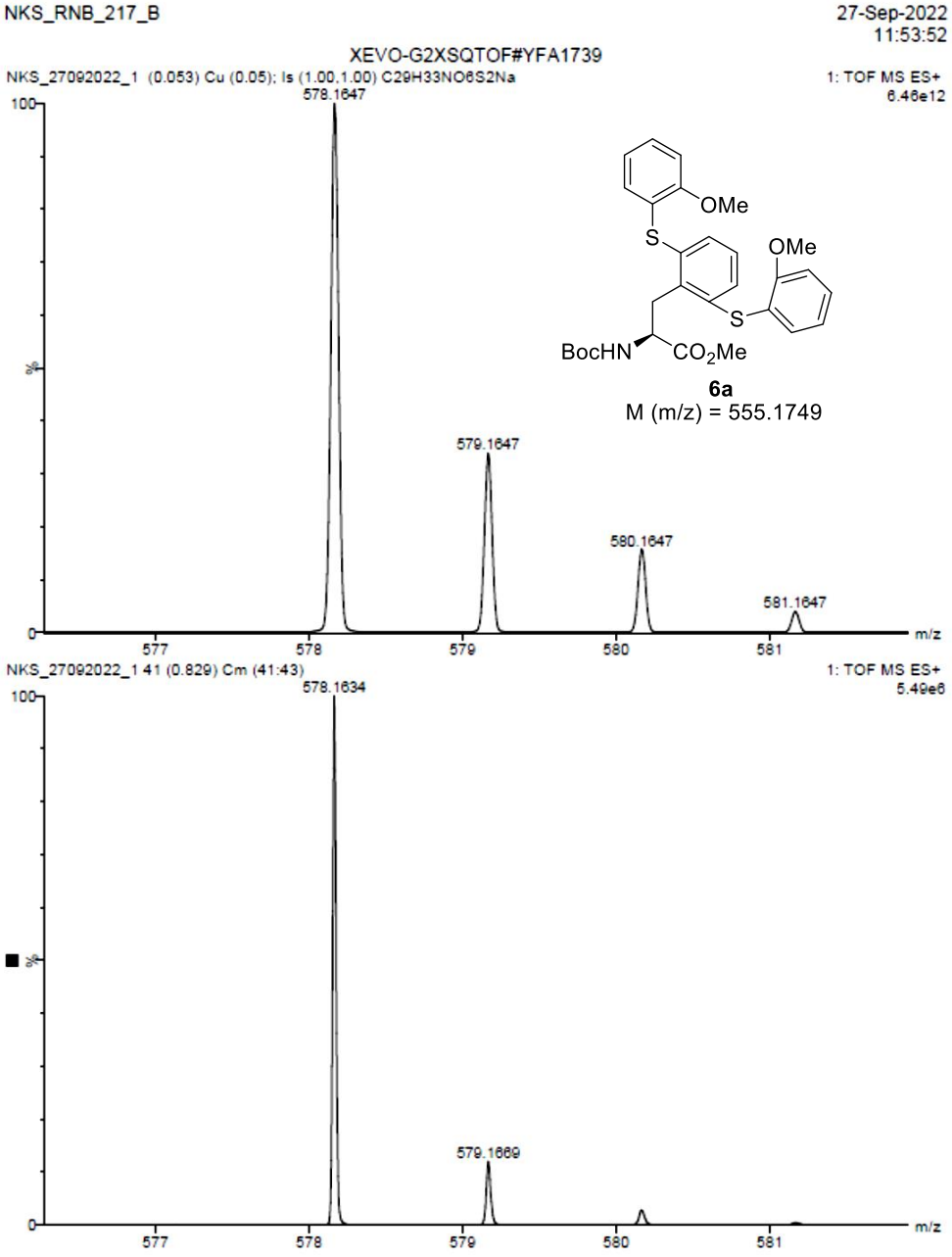
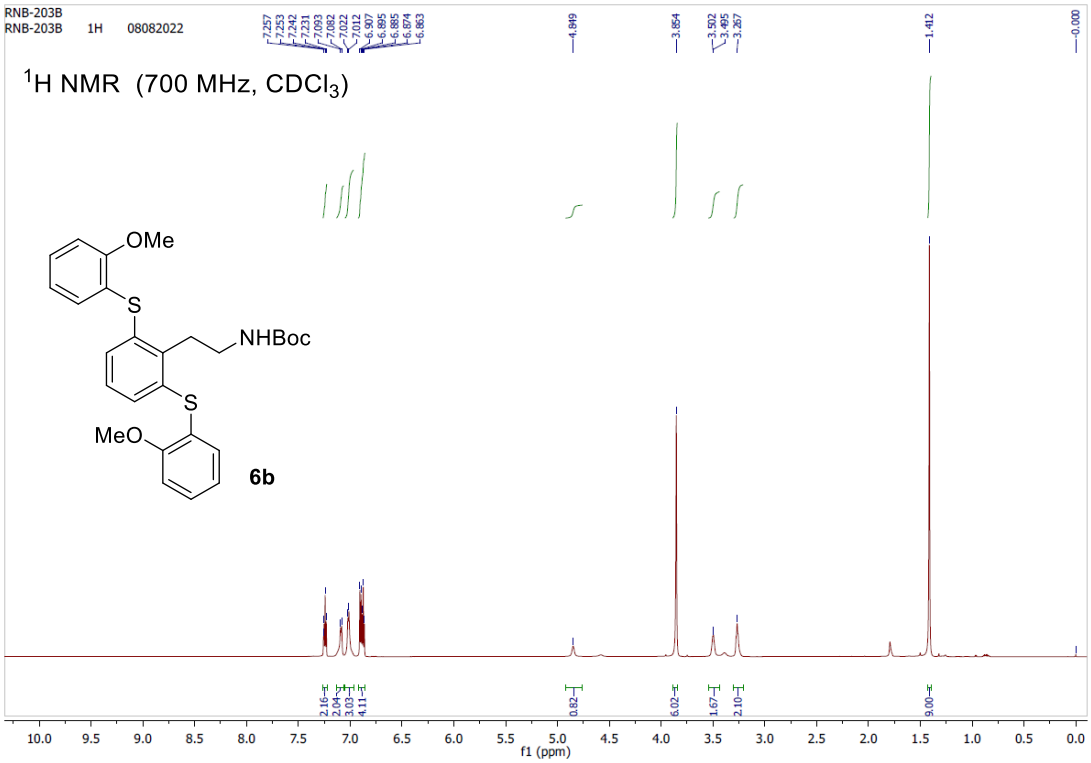


Fig S189. ESI-HRMS spectra of compound **6a**



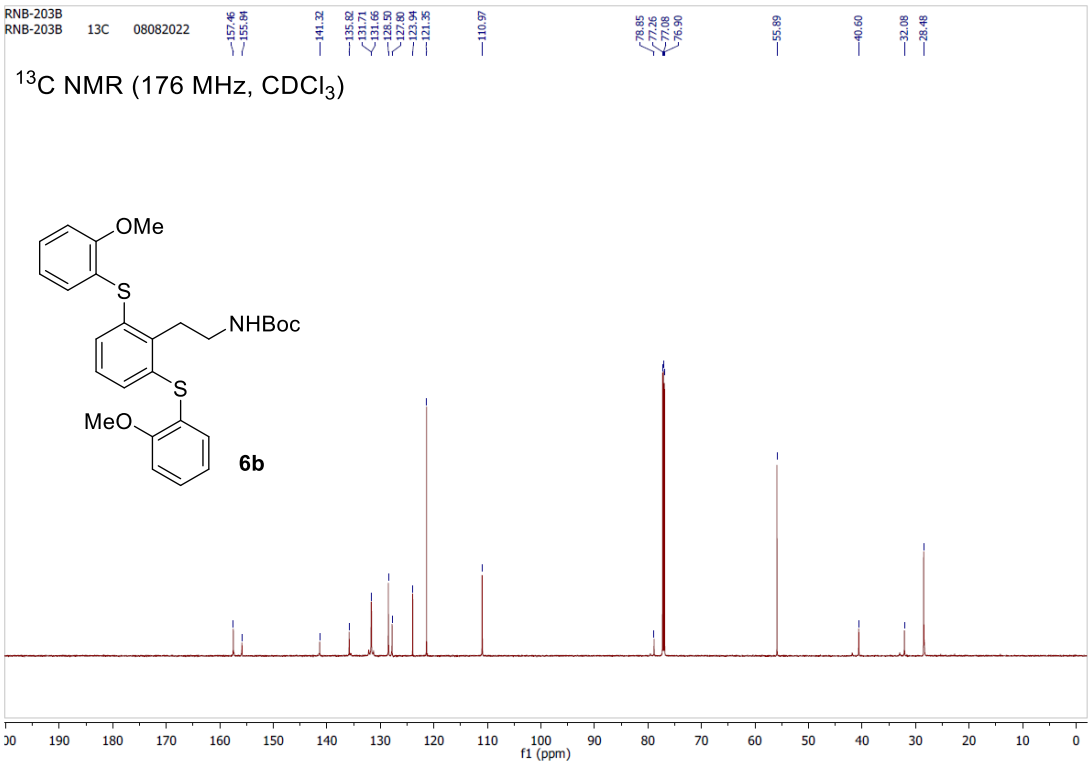


Fig S190. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **6b**

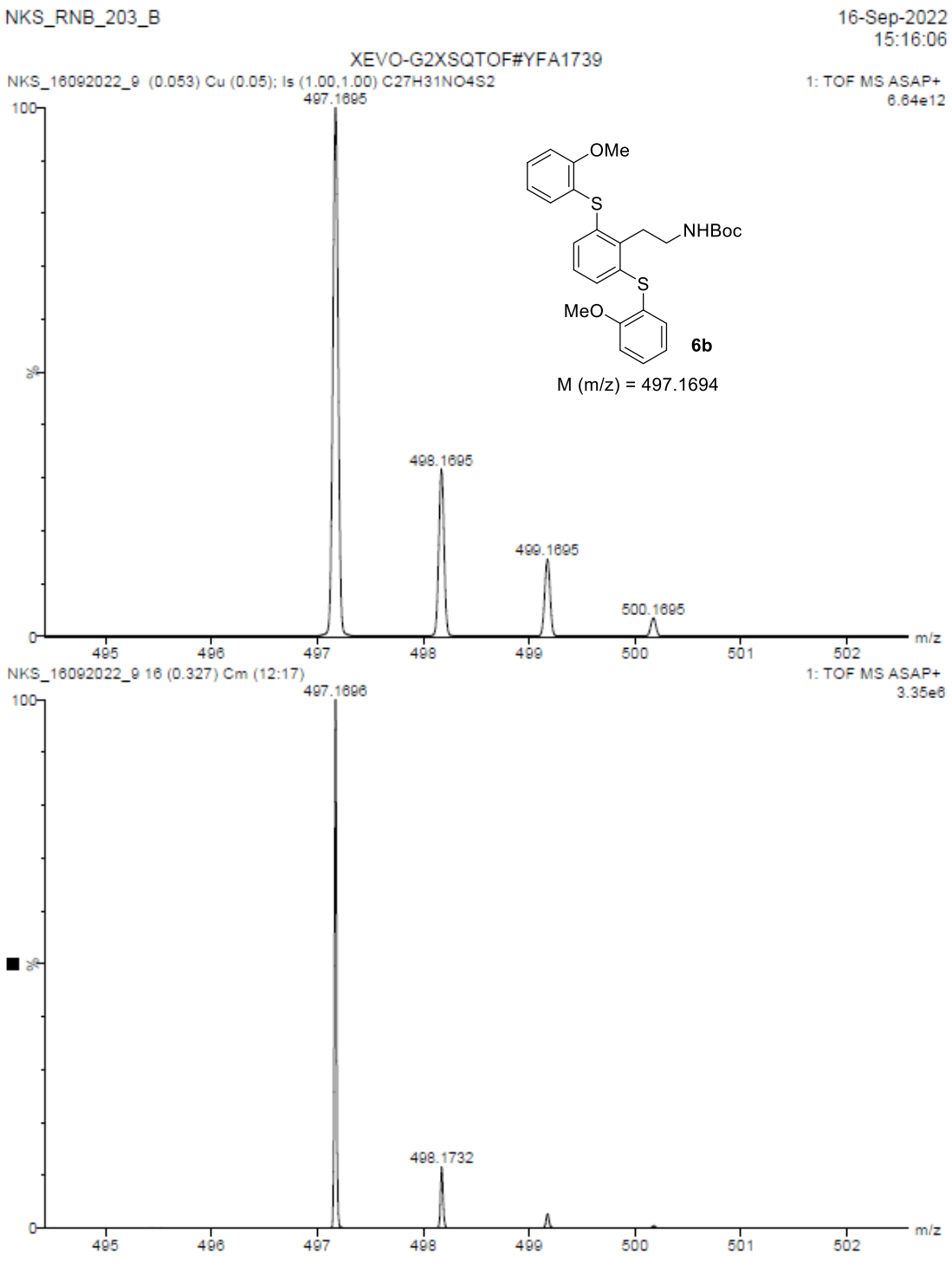
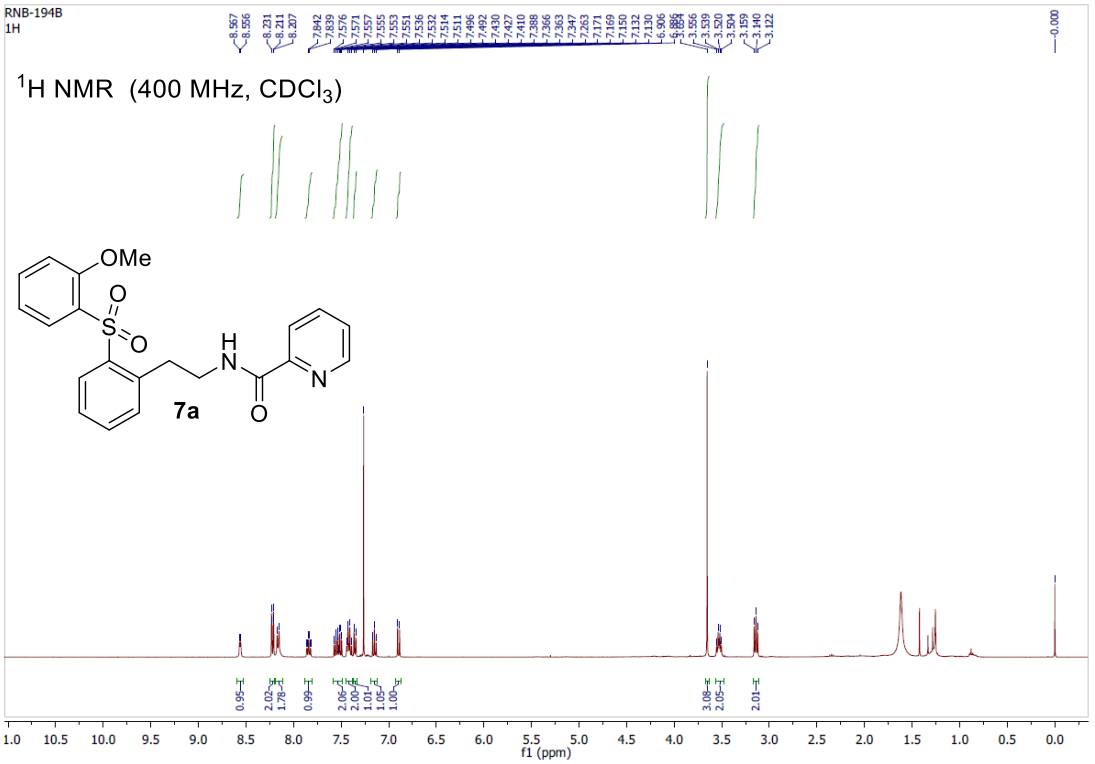


Fig S191. ASAP-HRMS spectra of compound **6b**



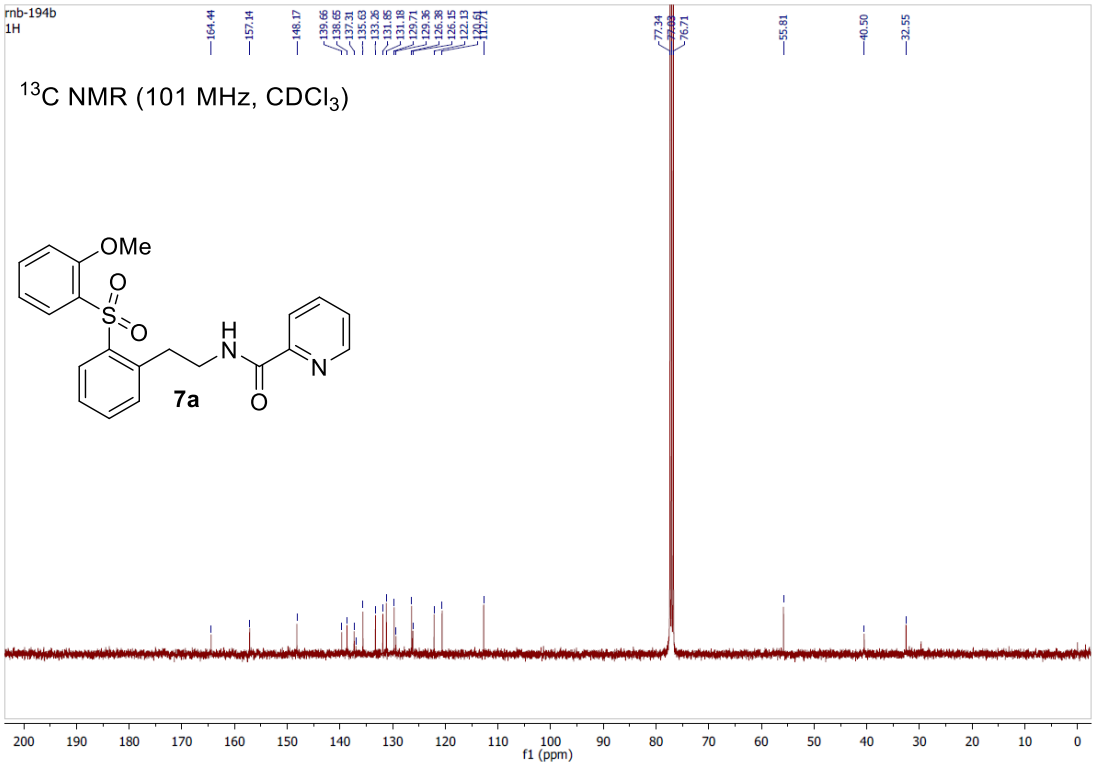


Fig S192. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **7a**

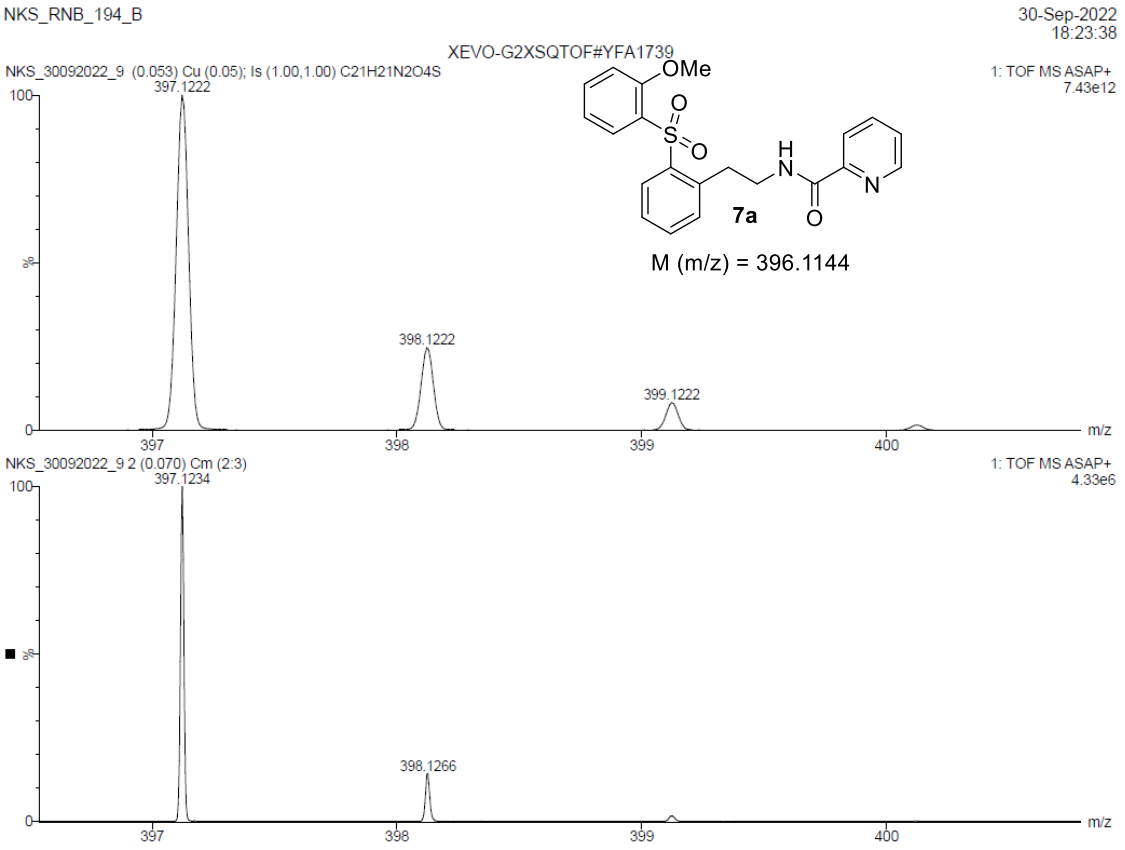
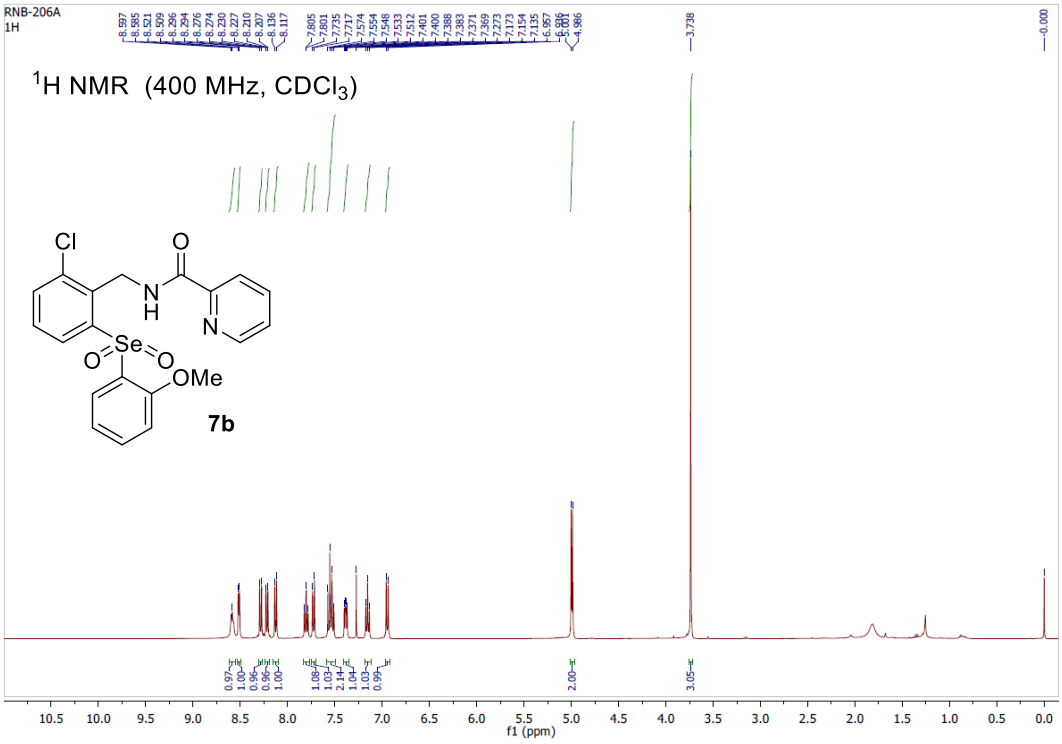


Fig S193. ASAP-HRMS spectra of compound **7a**



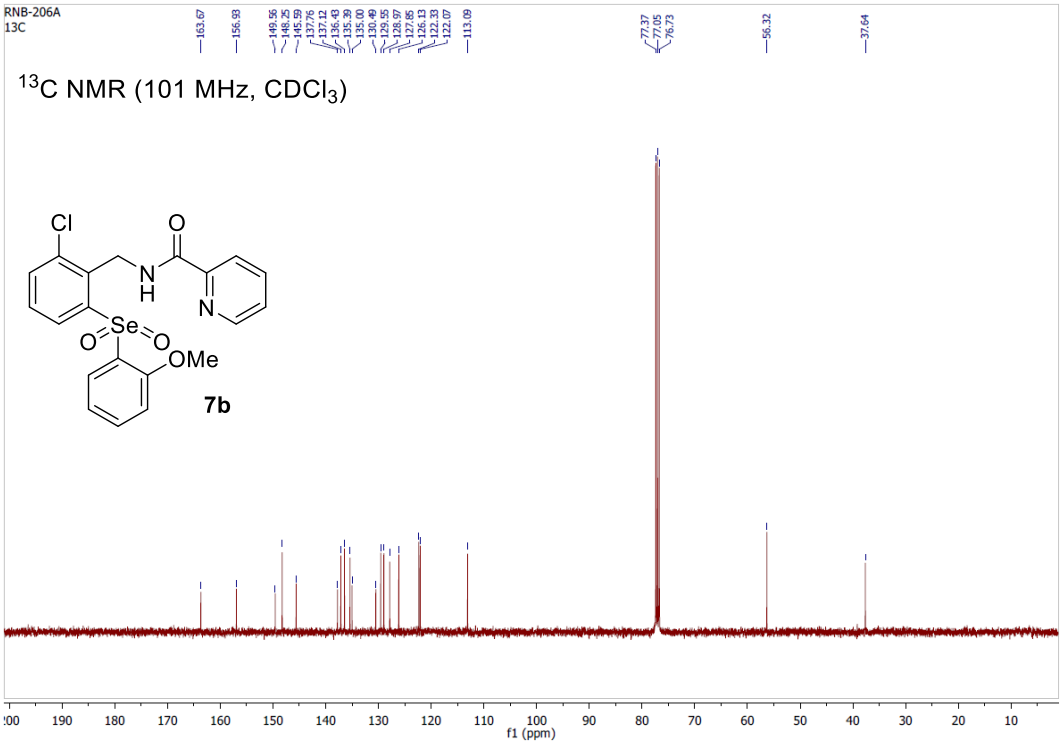


Fig S194. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **7b**

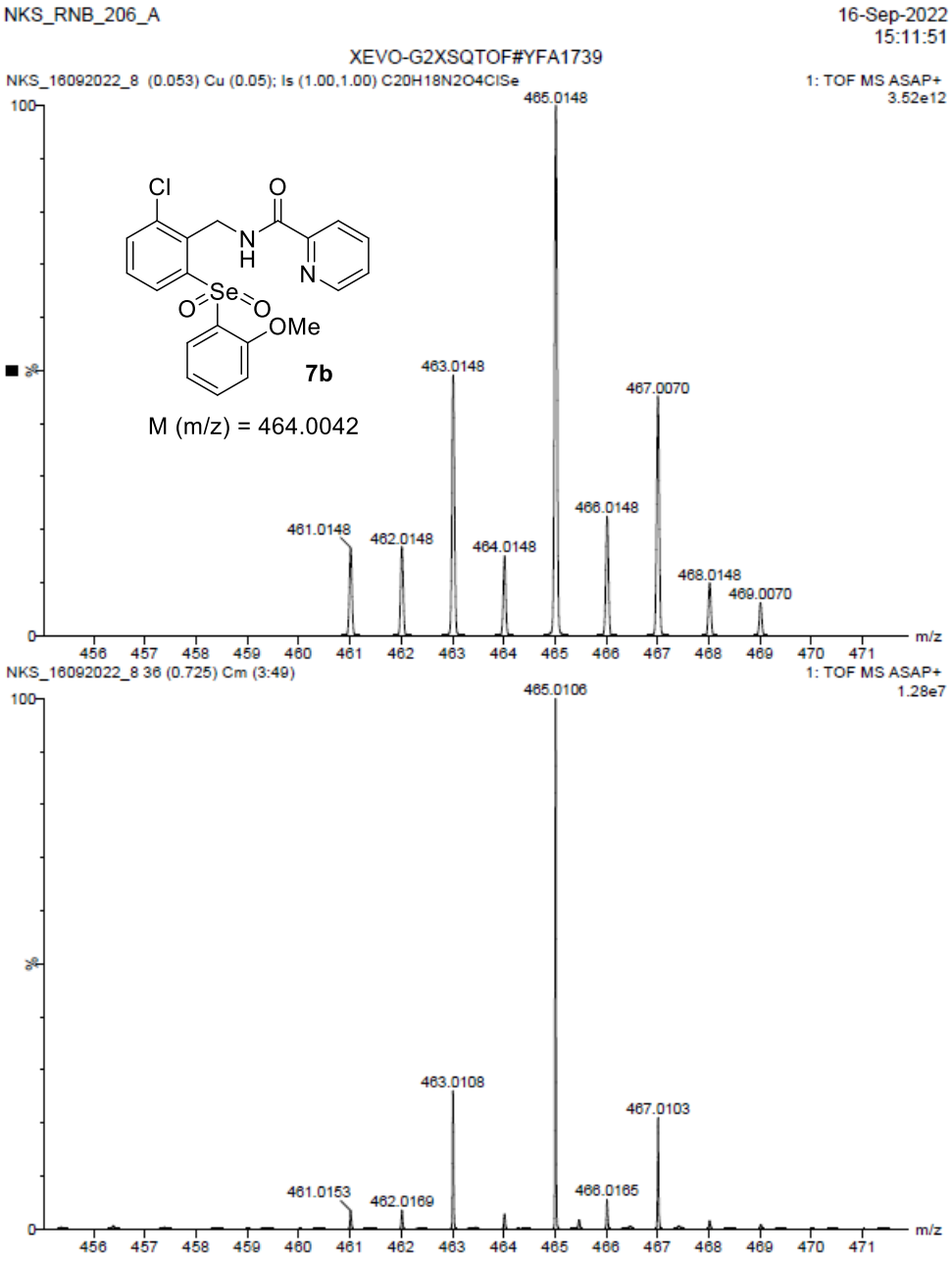
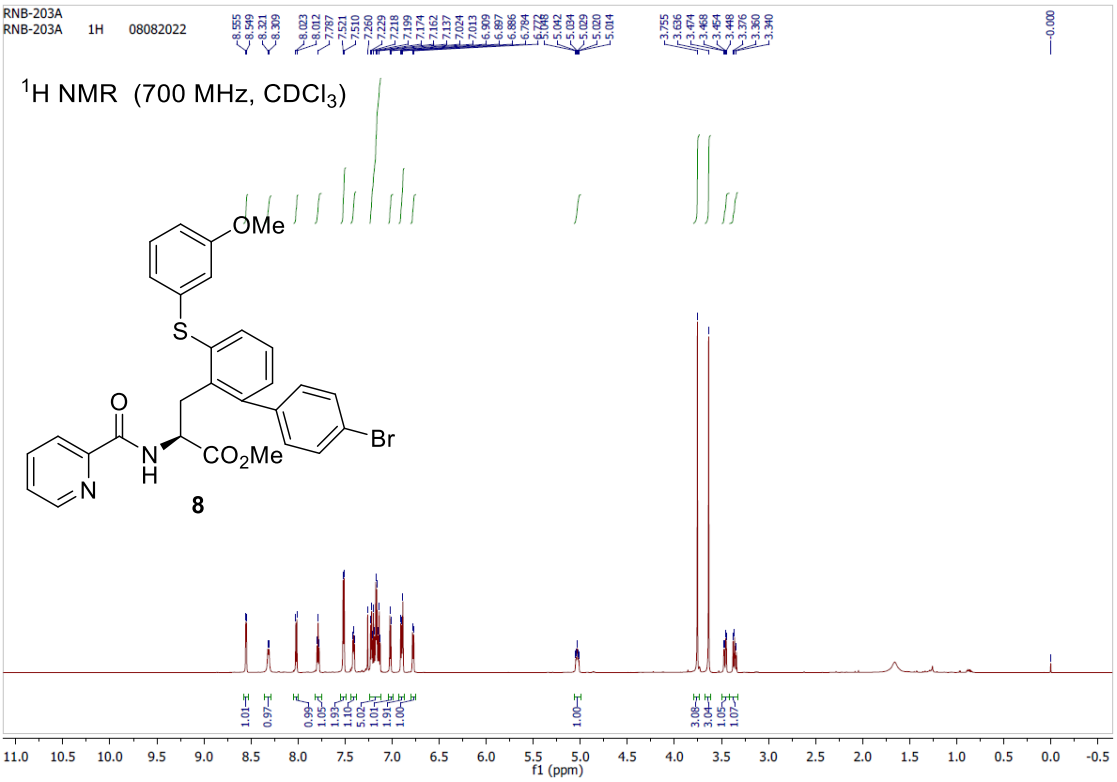


Fig S195. ASAP-HRMS spectra of compound **7b**



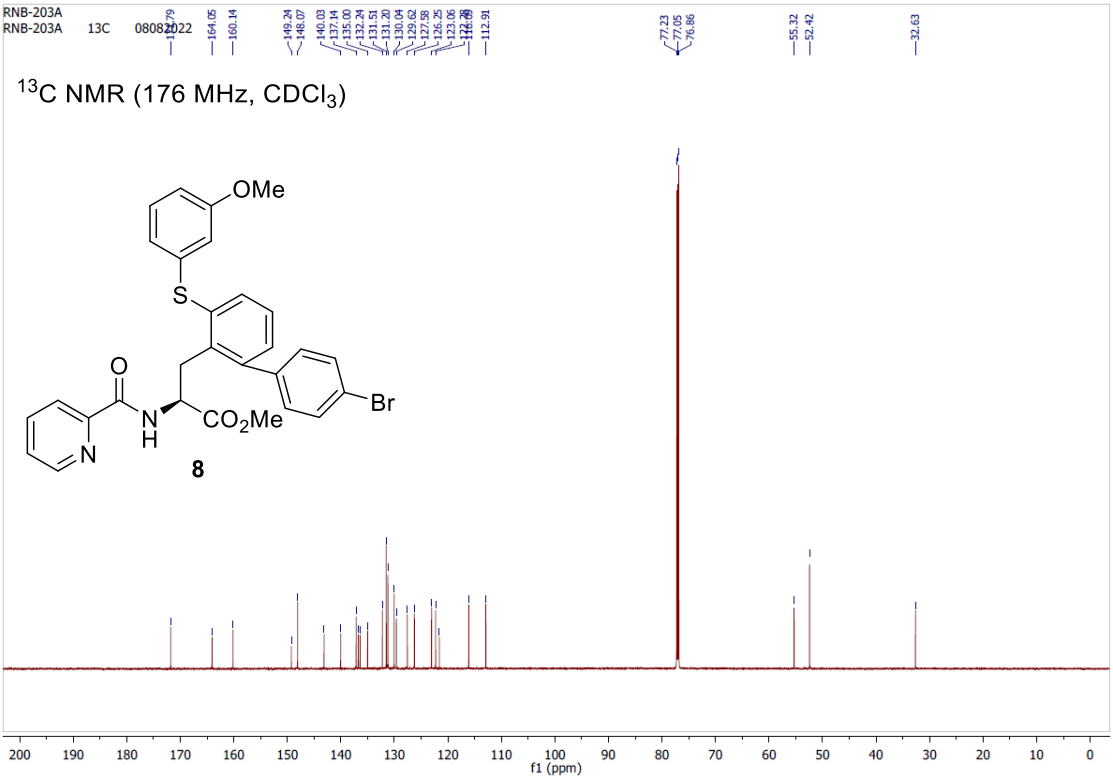


Fig S196. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **8**

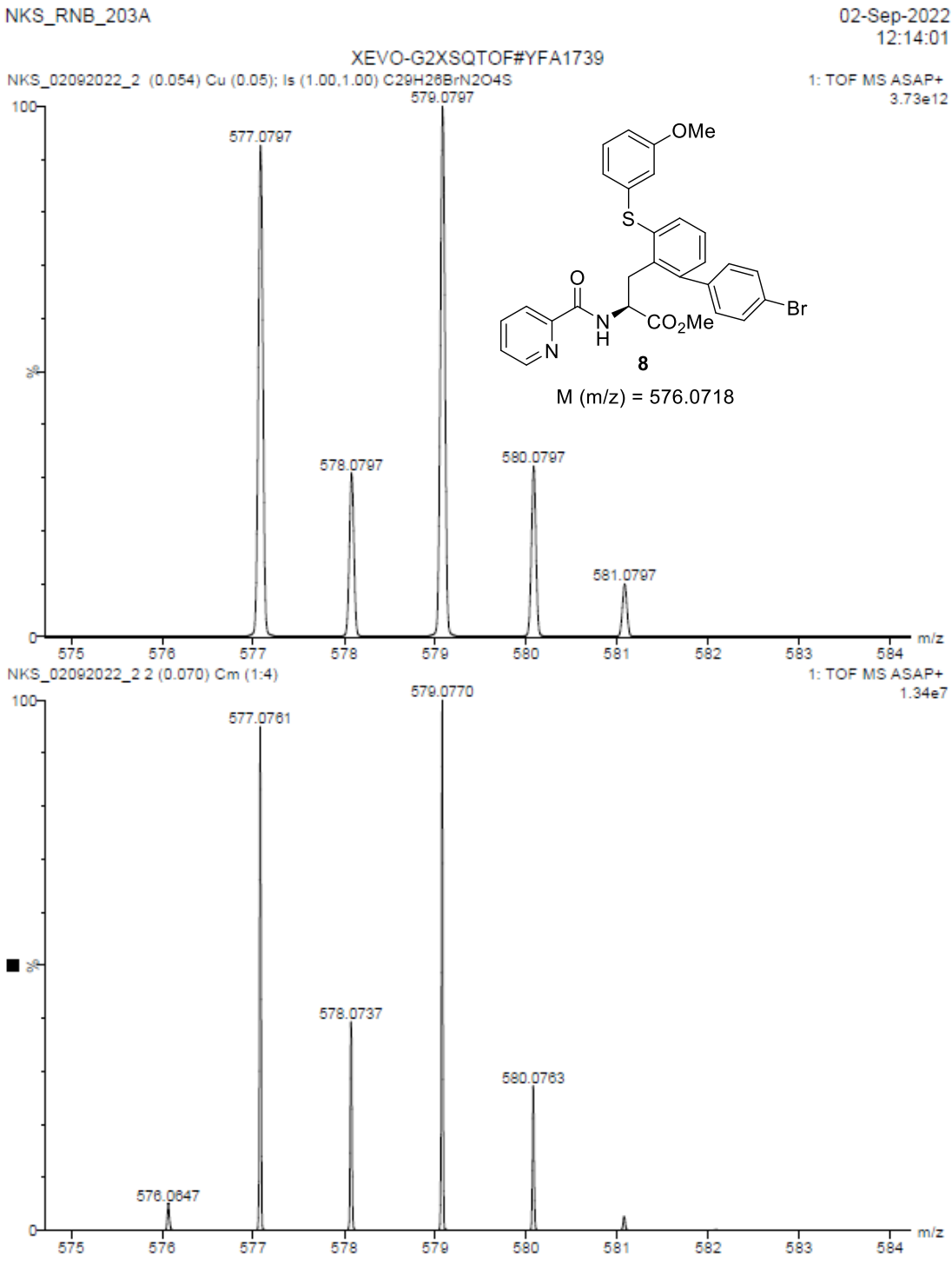
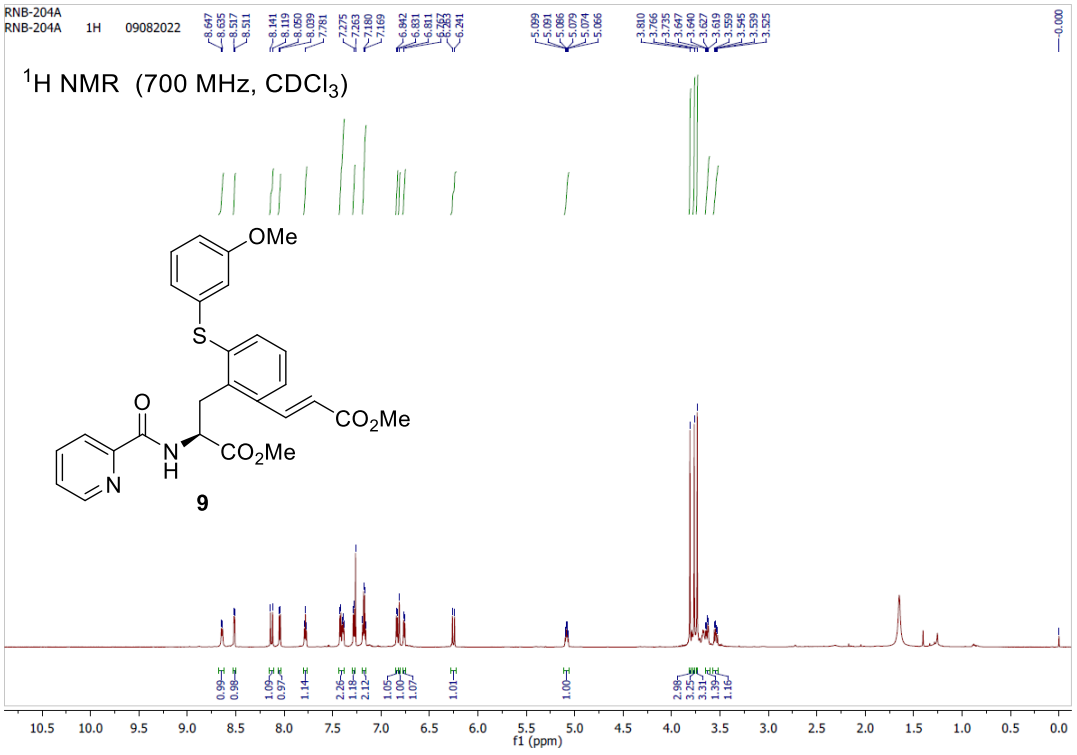


Fig S197. ASAP-HRMS spectra of compound **8**



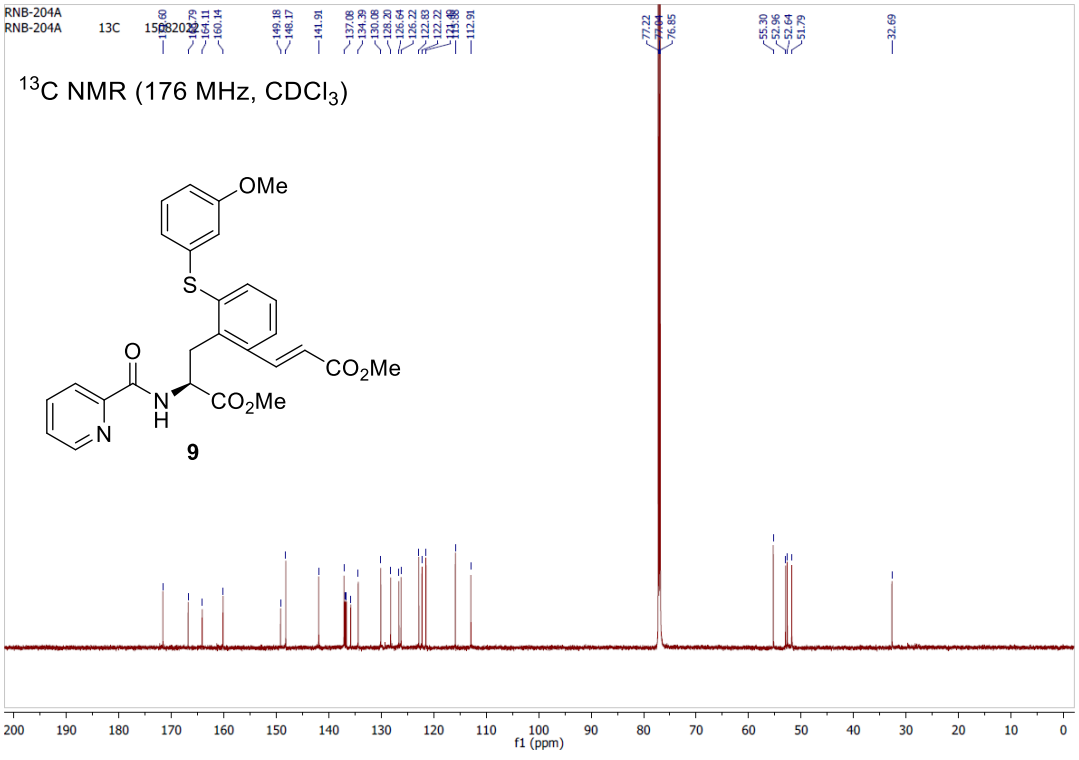


Fig S198. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **9**

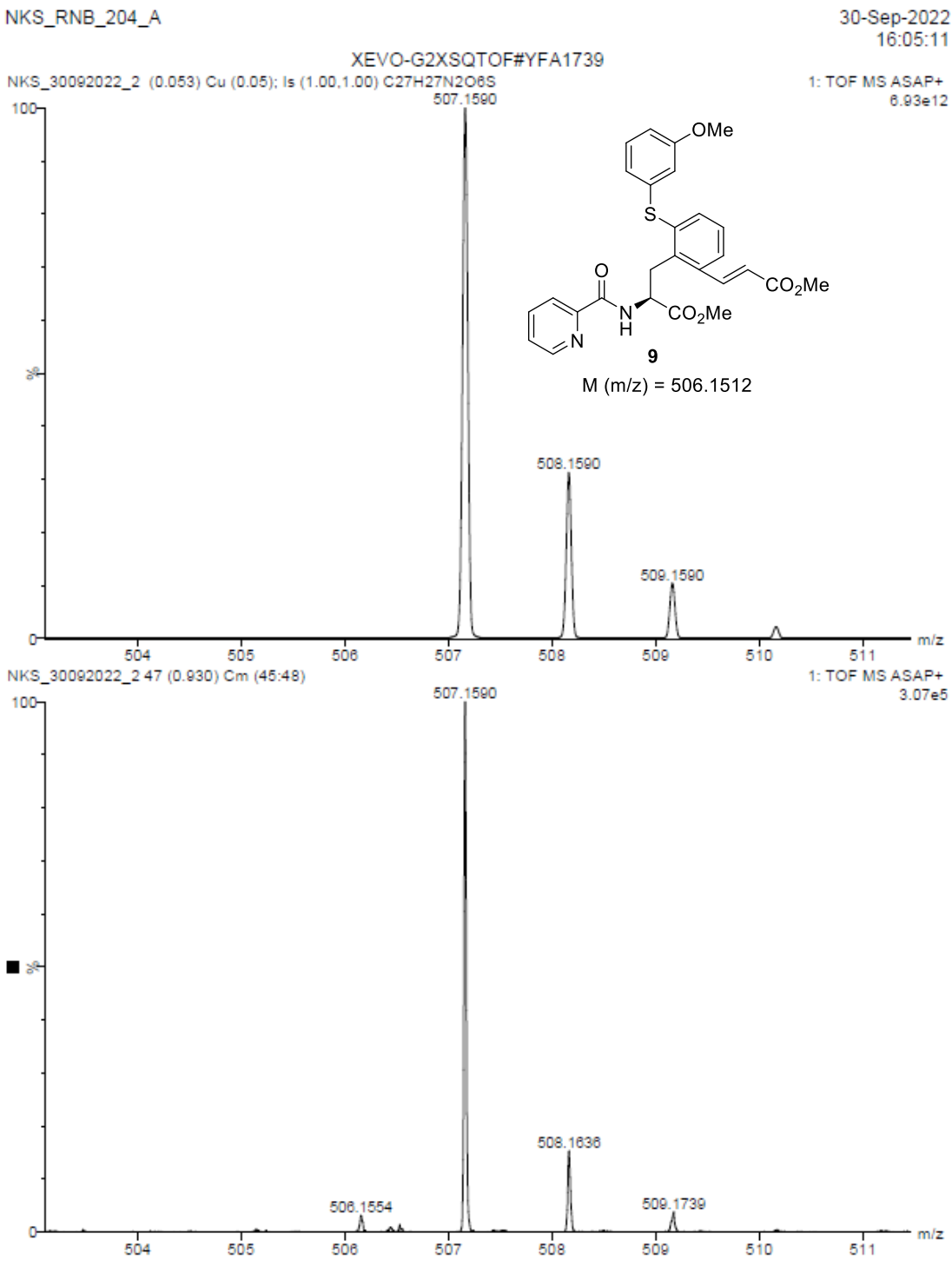
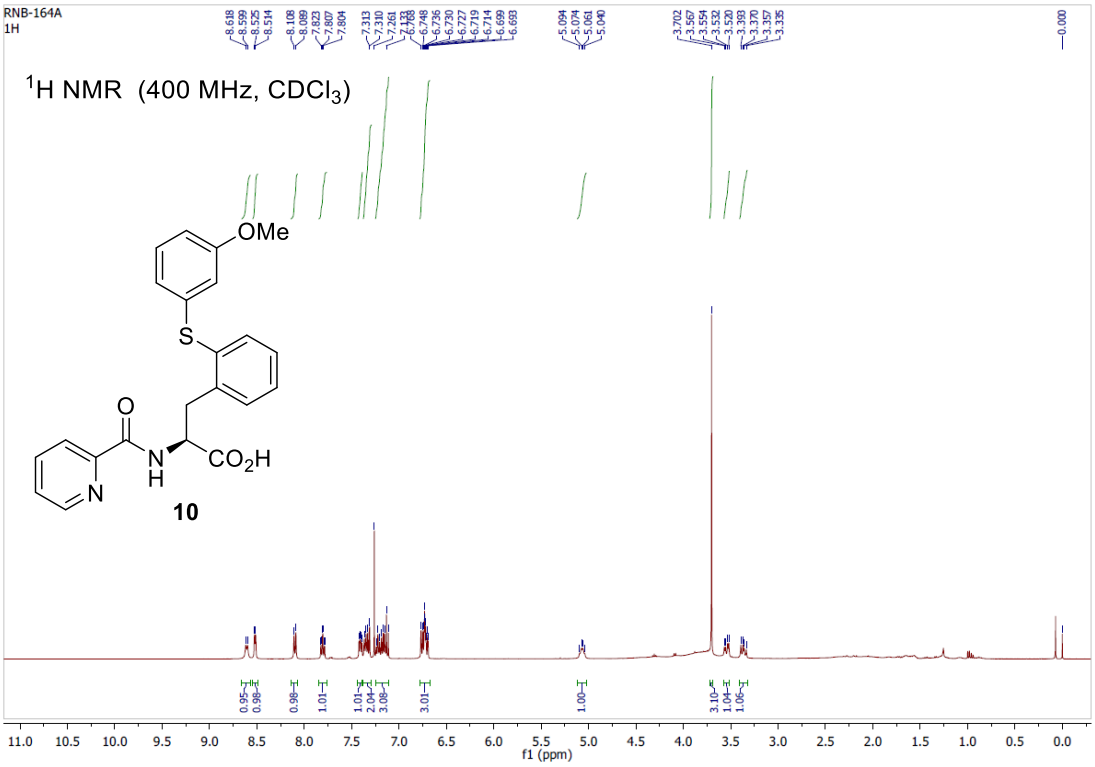


Fig S199. ASAP-HRMS spectra of compound **9**



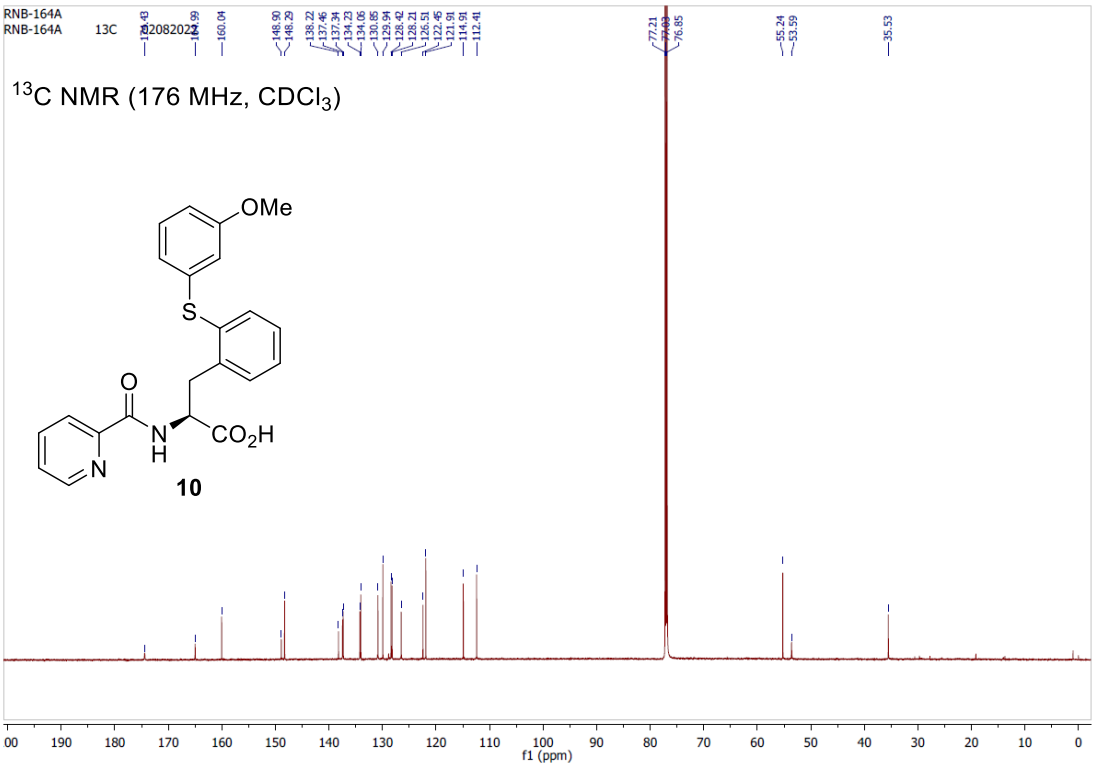


Fig S200. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **10**

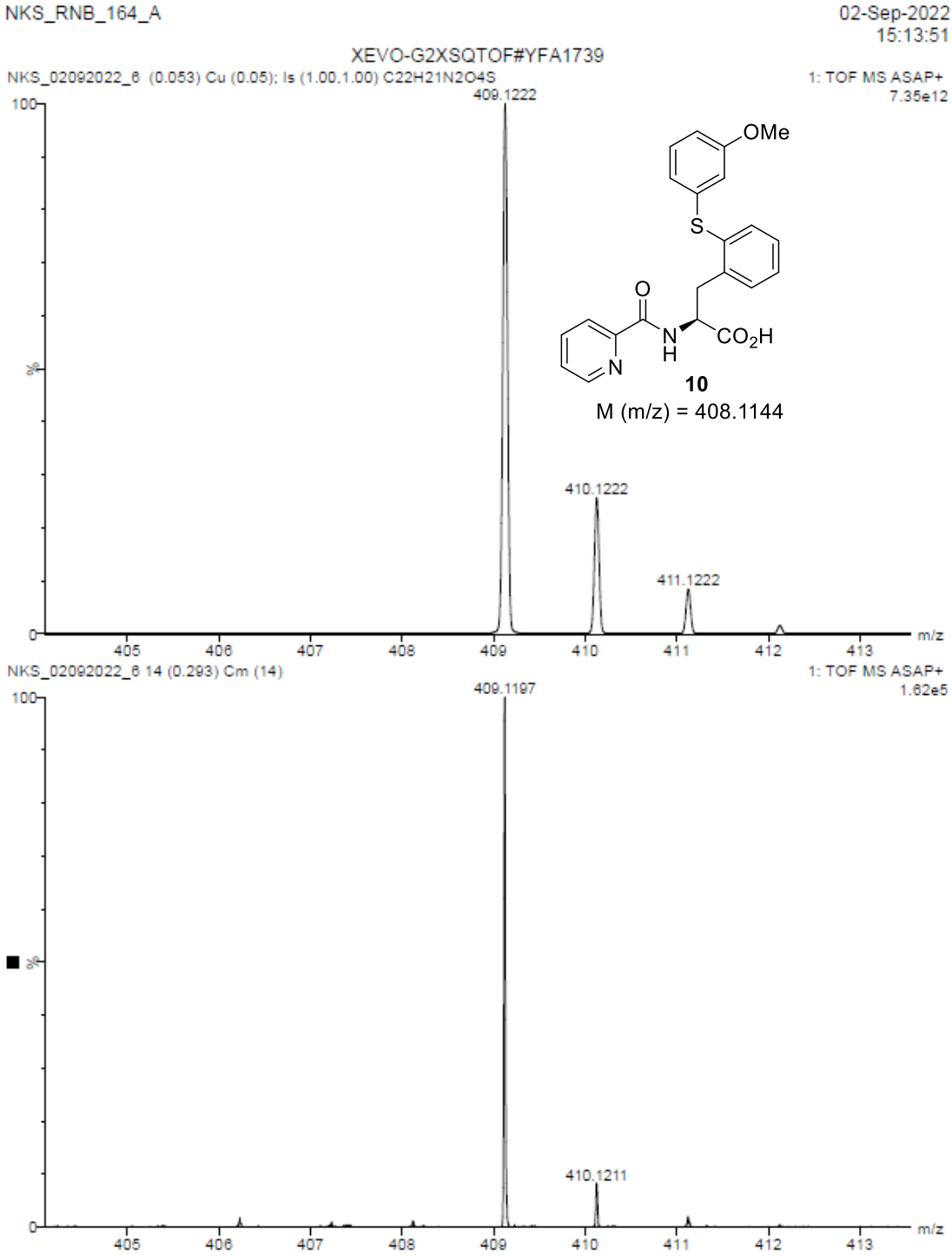
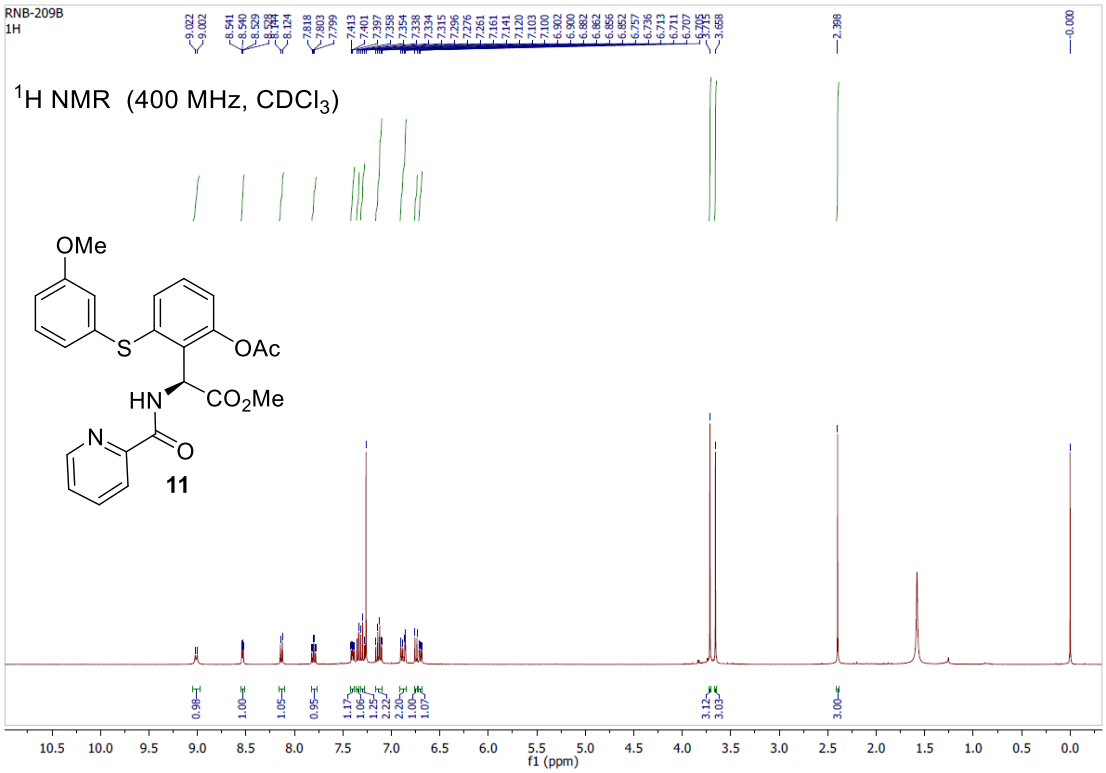


Fig S201. ASAP-HRMS spectra of compound **10**



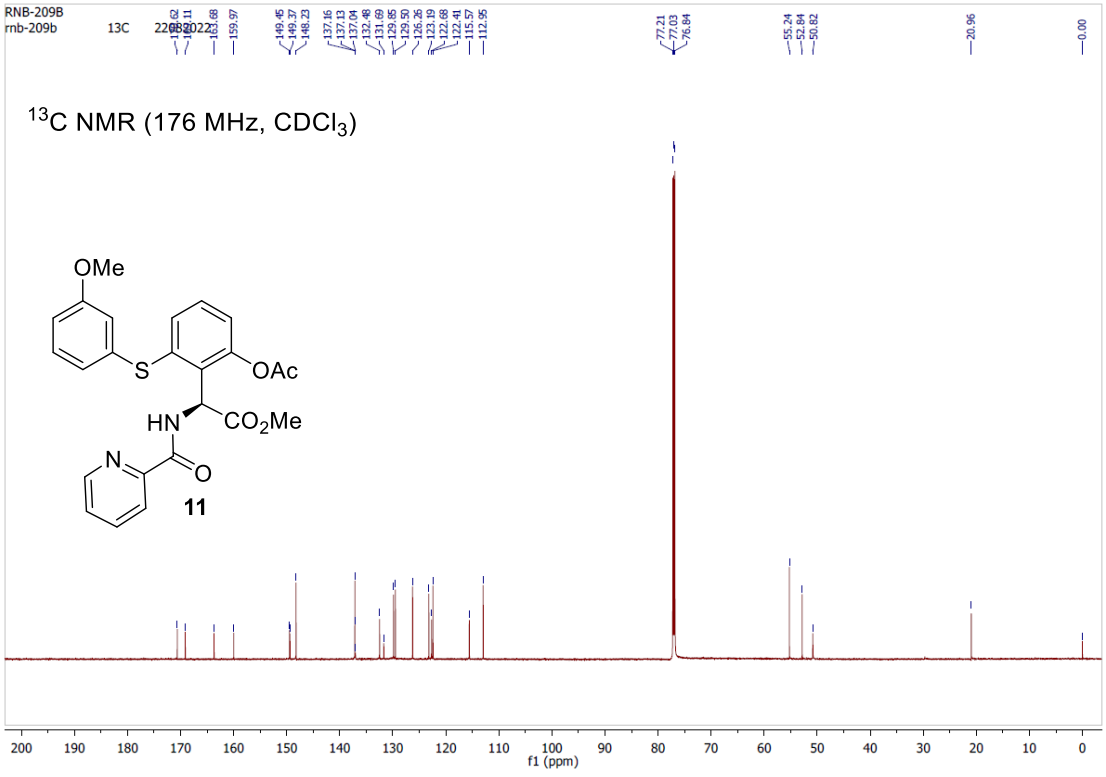


Fig S202. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **11**

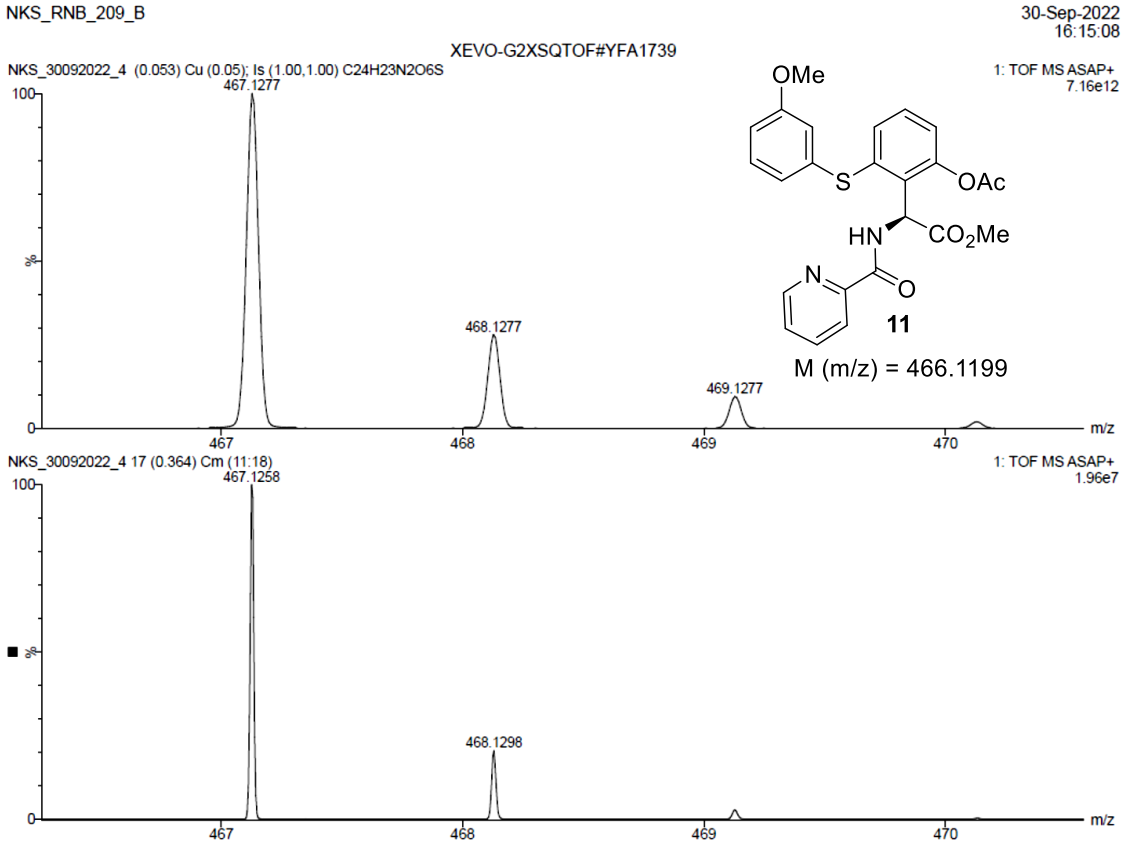
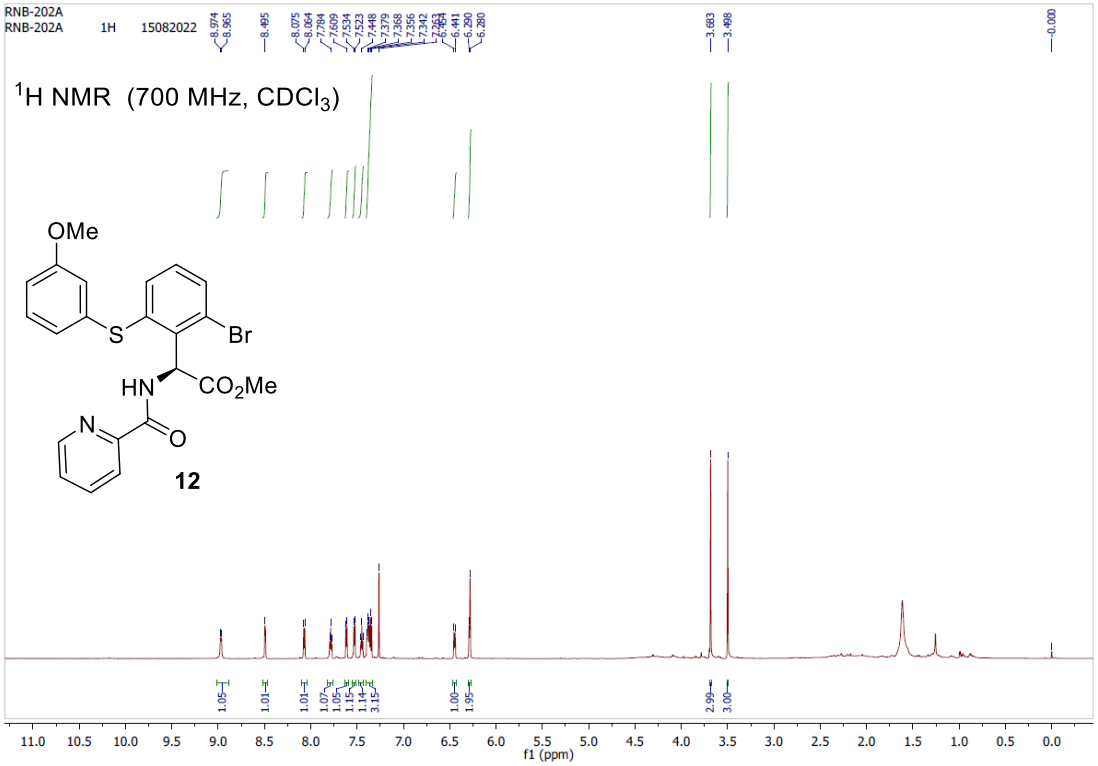


Fig S203. ASAP-HRMS spectra of compound **11**



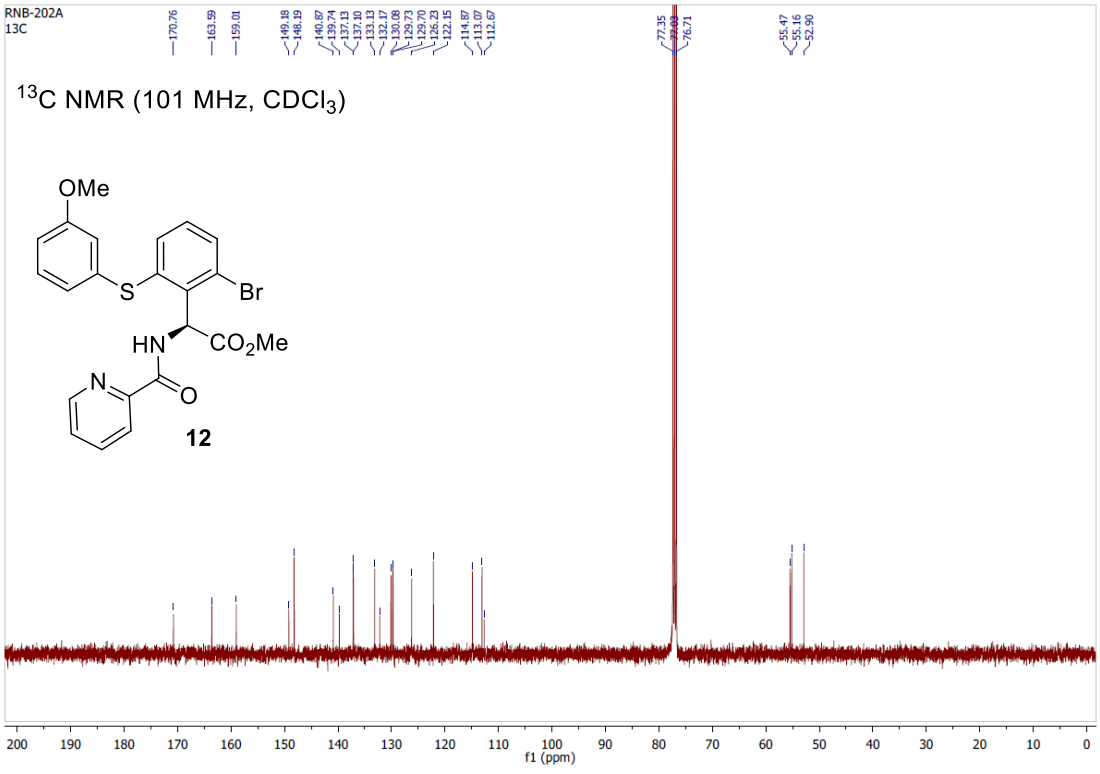


Fig S204. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **12**

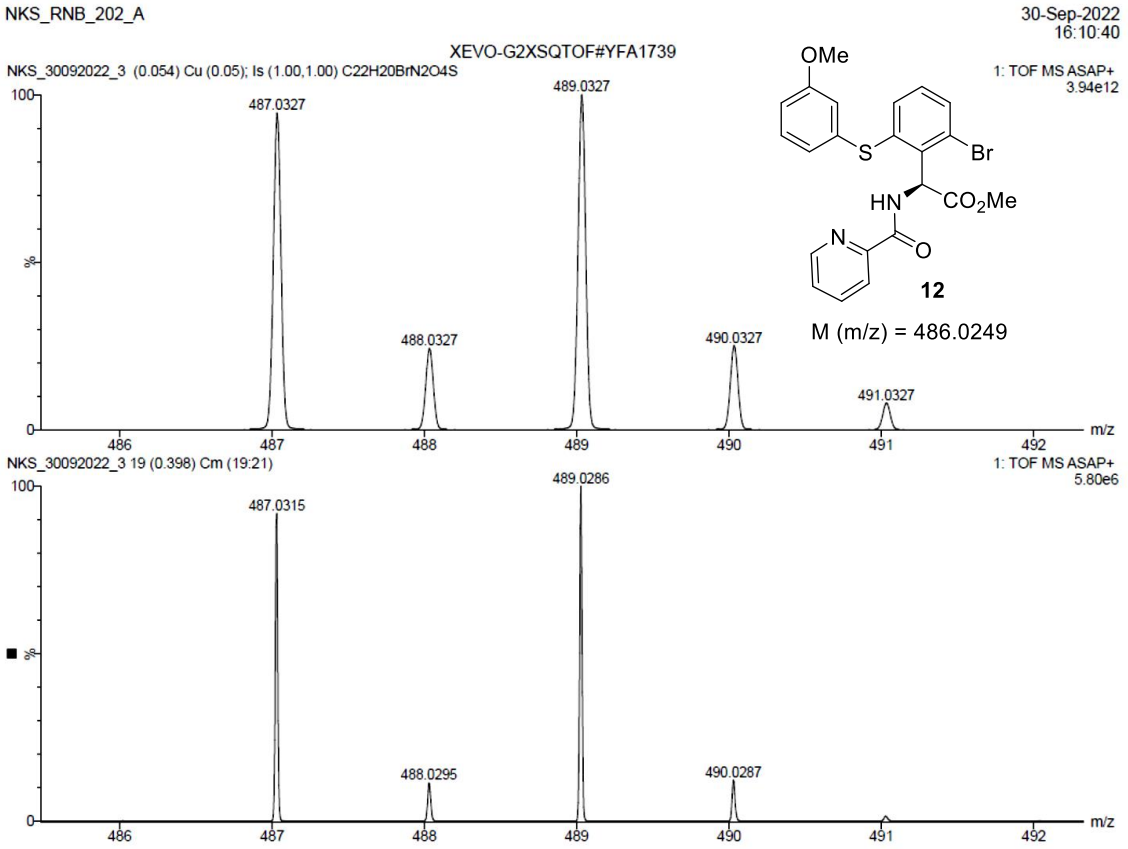
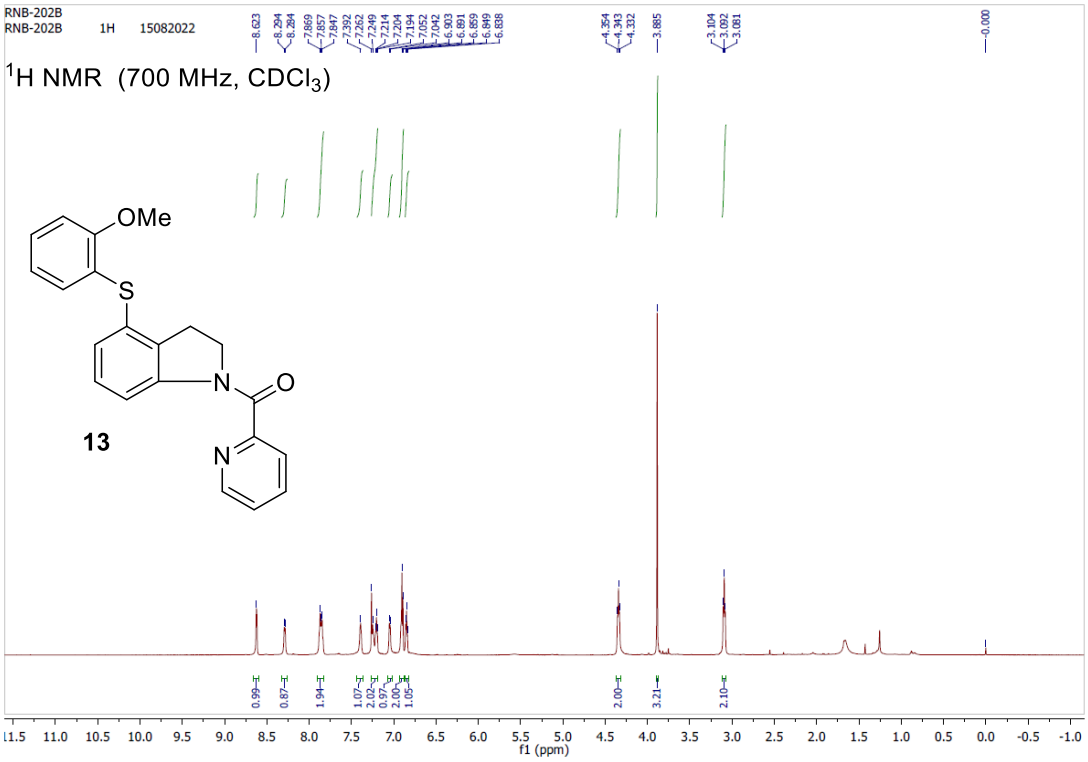


Fig S205. ASAP-HRMS spectra of compound **12**



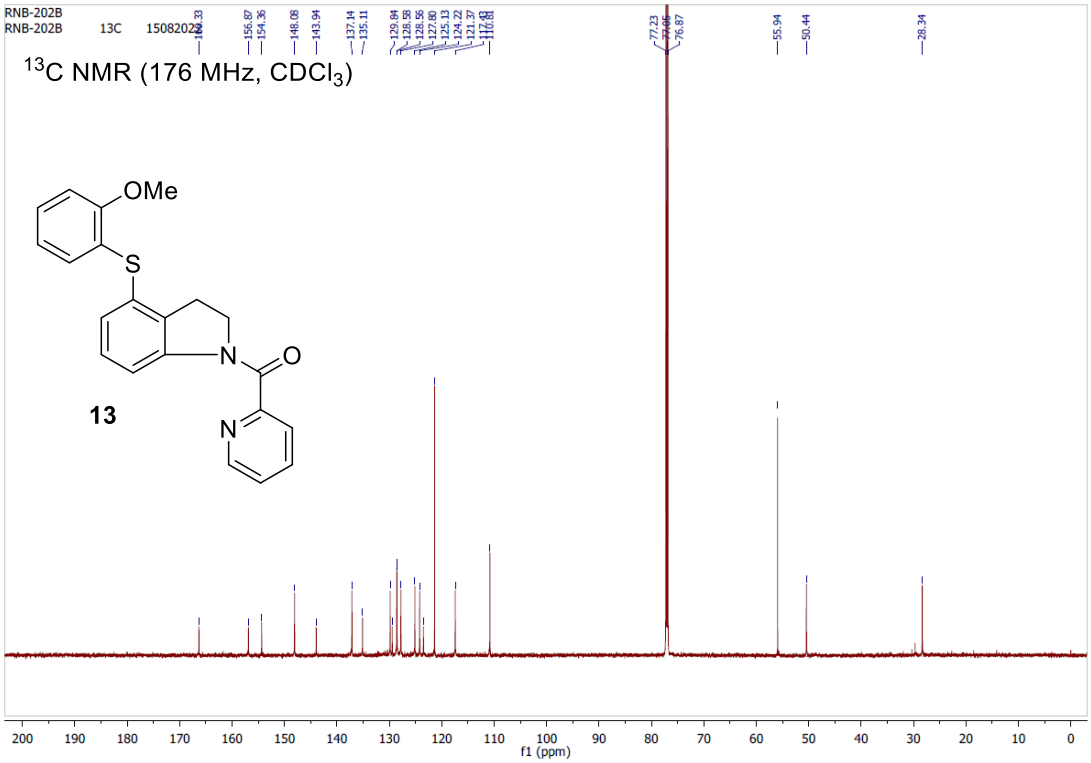


Fig S206. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **13**

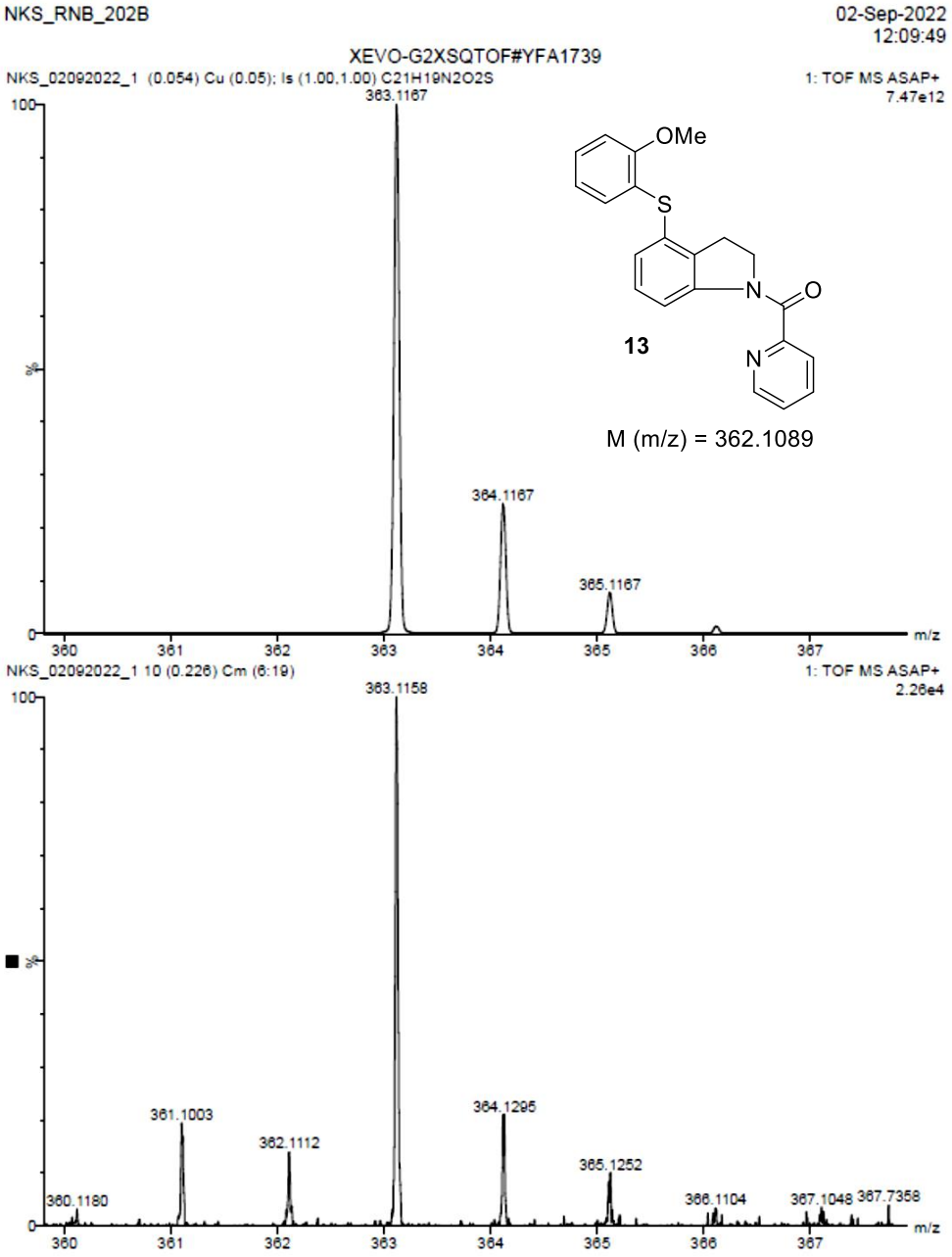
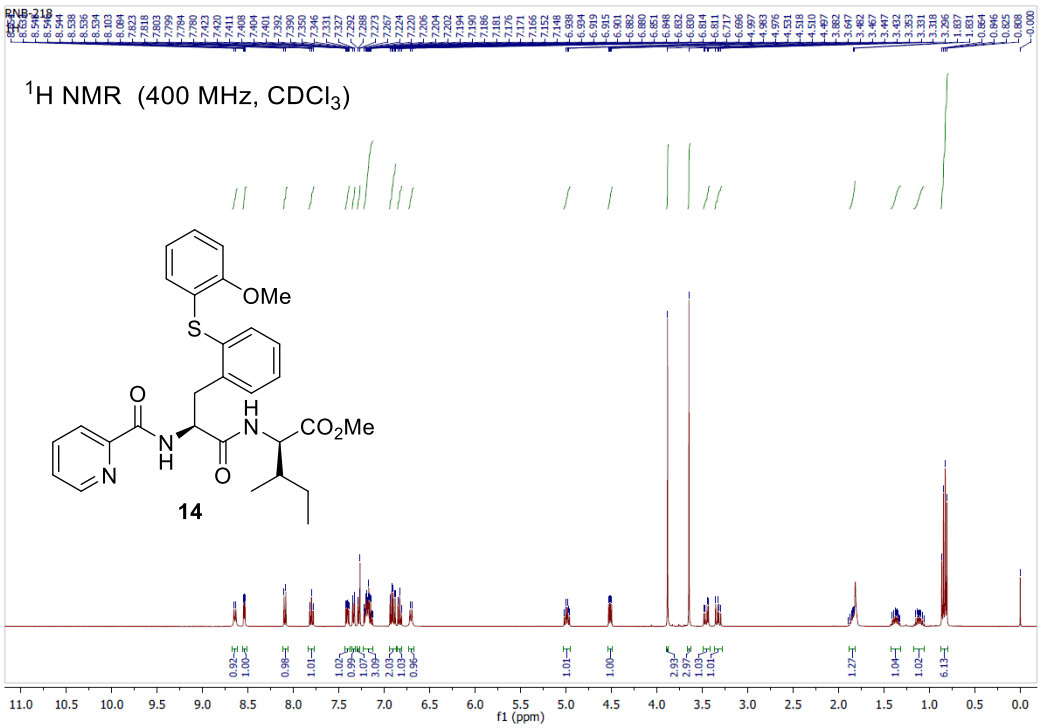


Fig S207. ASAP-HRMS spectra of compound **13**



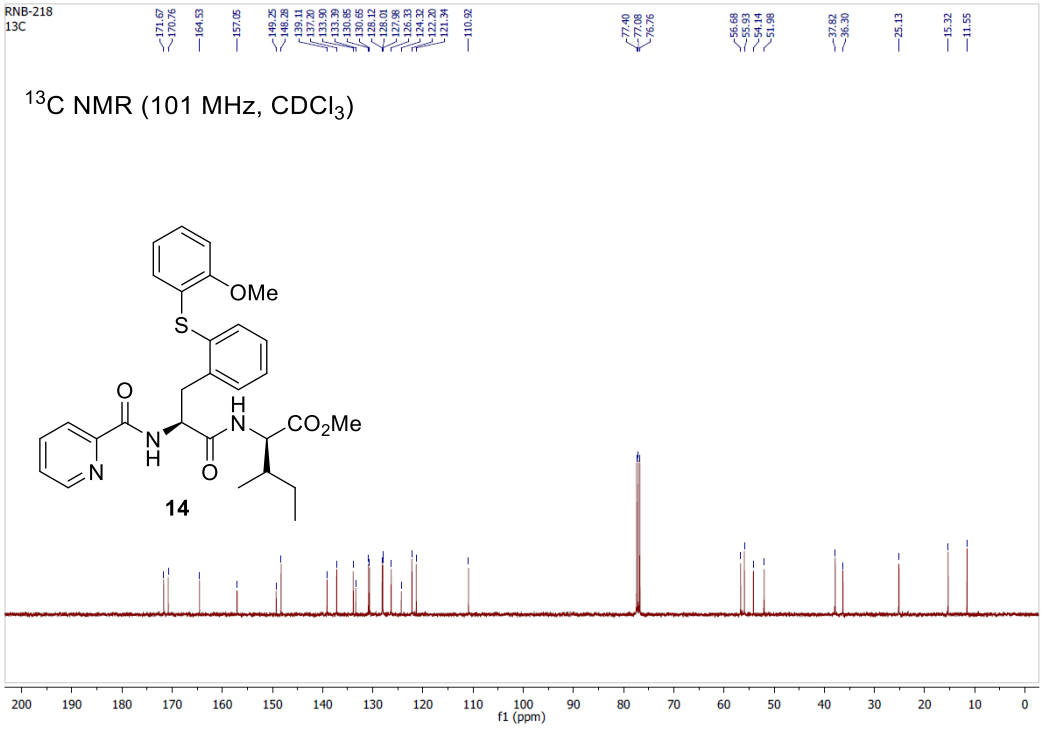


Fig S208. ^{1}H, ^{13}C {^{1}H} NMR spectra of compound **14**

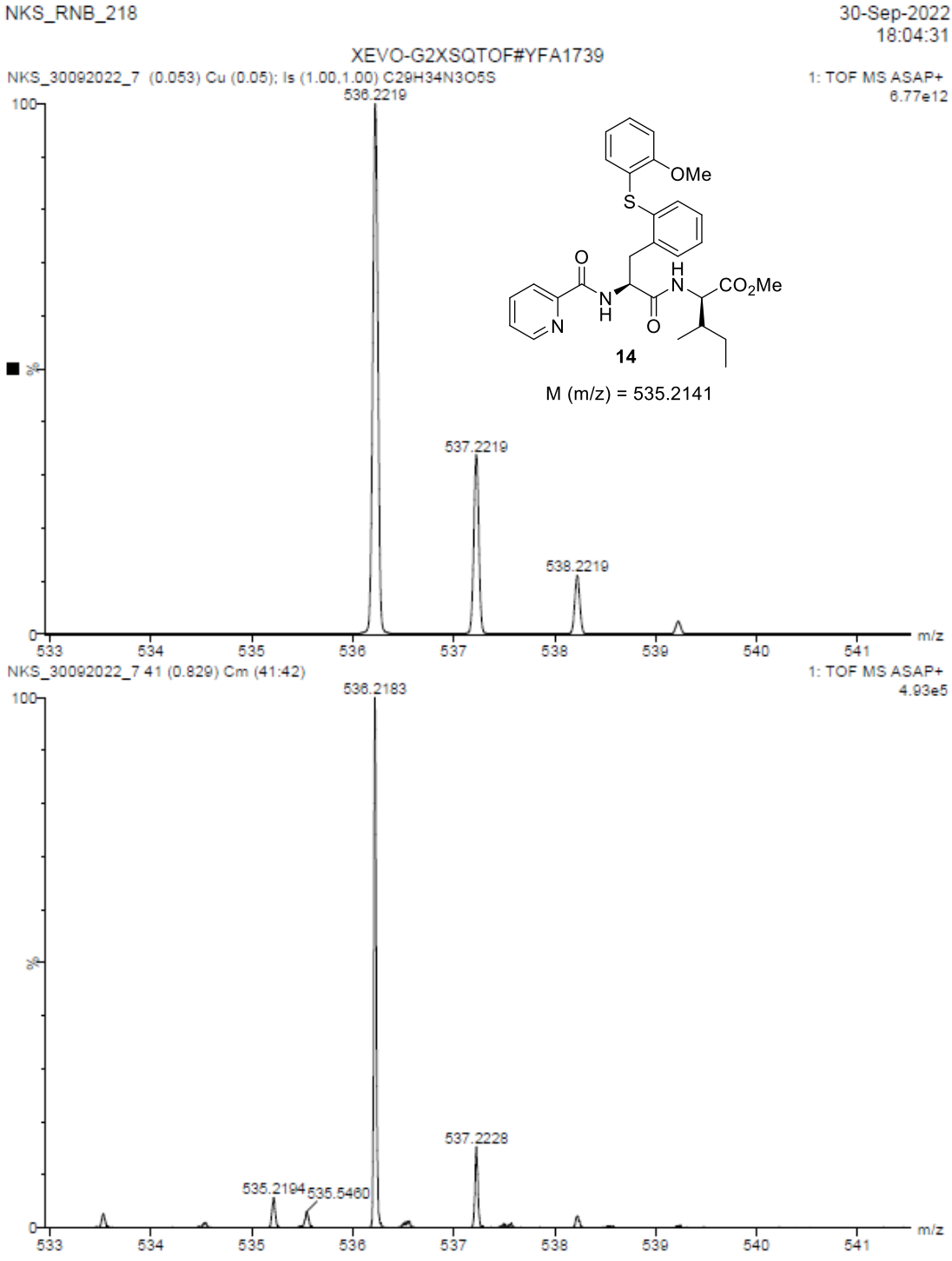


Fig S209. ASAP-HRMS spectra of compound **14**