Supplementary data

All commercially available chemicals were of analytical quality, and the solvents were partly of analytical quality and partly used after further purification. The reactions were monitored by thin-layer chromatography using a Merck type silica gel 60 GF 254 thin-layer plate, with the developed chromatograms visualised under 254 nm UV light. The silica gel used in the column chromatography procedures was Merck type Kieselgel (0.040–0.063 mm particle size).

Melting point determinations were performed using a Büchi M-560 melting point apparatus and data are given in ºC.

NMR spectra were recorded on a Varian Mercury Plus (^{1}H: 400 MHz, ^{13}C: 100 MHz) and a Bruker Avance III (^{1}H: 500 MHz, ^{13}C: 125 MHz) spectrometer equipped with a standard and a cryogenic head, respectively.

The NMR spectra were recorded at room temperature using the ^{2}H signal of the solvent as lock and tetramethylsilane as internal standard (TMS = 0 ppm). The solvent was given in the characterization of the compound. Chemical shift values (δ) are given in ppm and coupling constants (J) in Hz. The multiplicity is given using designations commonly used in spectroscopy. The same coupling constant values for different signal fine structures (e.g. J_{AB} and J_{BA}) were measured twice, but the values are given only once.

In several cases, ^{1}H-^{13}C heteronuclear correlation measurements and DEPT measurements were also performed to prove the structure. HRMS measurements were performed on a Sciex 5600+ Triple TOF mass spectrometer. The instrument was equipped with a DuoSpray ion source and measurements were performed under electrospray conditions with positive ion detection. The resolution of the instrument is >30000 over the full mass range. Samples were dissolved in methanol and were injected into the ion source of the mass spectrometer at a flow rate of 0.2 mL/min methanol. The source temperature was 350 °C. The mass range was 100–1000, with an accumulation time of 1 second. The instrument was controlled using Analyst 1.7 software and data were evaluated using PeakView 2.2 software.

IR instrument: Jasco FT/IR-4600. Jasco ATR PRO ONE with PKS-Z1 ZnSe prism kit. Spectrum registration parameters: Scan: 32 Resolution 4 cm^{-1}, Range: 4000–500 $cm^{-1.}$ During the spectrum registration the following parameters were presetted: Automatic H_2O, CO_2

reduction; auto baseline correction, auto smoothing-moving means (with=5); automatic ATR correction.

General procedure for the synthesis of substituted thiourea derivatives (3a–f) from acyl chlorides (4a–f) (Scheme 3)

Synthesis of benzoyl isothiocyanates (**2a–f**): To a solution of the appropriate acyl chlorides (**4a–f**, 2 mmol) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (3 mmol) in dry acetone (3 ml) through a dropping funnel. A white precipitate was formed. After the addition the mixture was treated under reflux conditions for 30 minutes (monitored by TLC). The mixture was filtered and the filtrate was used in the next step without any purification.

Synthesis of thiourea derivatives (**3a–f**): 2-Amino-5-bromobenzoic acid (**1a**) (1.6 mmol) was added to the acetone solution of the corresponding isothiocyanate derivative and the mixture was stirred at room temperature until the reaction was completed according to the TLC analysis. For the different derivatives various work-up procedures were used.

Yields were calculated on the basis of the amount of 2-amino-5-bromobenzoic acid (**1a**).

Synthesis of 5-bromo-2-{[(phenylformamido)methanethioyl]amino}benzoic acid (3a): To a solution of benzoyl chloride (2 mmol, 232 μl) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (3 mmol, 228 mg) in dry acetone (3 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered and the filtrate was used without any purification in the next step. To this solution (**2a**) 1.6 mmol (346 mg) 2-amino-5-bromobenzoic acid (**1a**) was added and stirred at room temperature, monitored by TLC. After the reaction was completed, the mixture was poured over 30 ml ice-cold water forming a pale yellow precipitate, which was filtered, washed with *n*-hexane, and dried at room temperature. (0.48 g, 75%) Mp.: 239–240 °C. R_f (dichloromethane/methanol 10:1): 0.4. IR ν_{max}: 3485, 3263, 3102, 1710, 1675, 1597, 1575, 1287, 1160, 945, 761, 598 cm^{-1}. ^{1}H-NMR (DMSO-d_6+CD_3OD) δ: 8.28 (d, J=8.8Hz, 1H, H-1), 8.04 (d, J=2.3Hz, 1H, H-6), 7.92 (d, J=7.5 Hz, 2H. H-2', H-6'), 7.61-7.50 (m, 2H), 7.43 (t, J=7.5Hz, 2H. H-3', H-5'). δC (100 MHz, DMSO-d_6): 179.2 (*C*S), 166.6 (*C*O), 165.9 (*C*OOH), 137.4 (C-2), 134.0 (C-4), 132.8 (C-6), 132.6 (C-3), 131.7 (C-1'), 128 (2C, C-2', C-6'), 128 (2C, C-3', C-5'), 128.0 (C-4'),

117.9 (C-5), 125.1 (C-1). HRMS (ESI) $C_{15}H_{12}N_2O_3SBr$ $[M+H]^+$: calculated: 377.9673, measured: 378.9752, deviation: -1.6003 ppm, -4.22 mDa, DBE: 10.5.

Synthesis of 5-bromo-2-({[(2,6-difluorophenyl)formamido]methanethioyl}amino)benzoic acid (3b): To a solution of 2,6-difluorobenzoyl chloride (2 mmol, 250 μl) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (3 mmol, 228 mg) in dry acetone (3 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered and the filtrate was used without any purification in the next step. To this solution (**2b**) 1.6 mmol (346 mg) 2-amino-5-bromobenzoic acid (**1a**) was added and stirred at room temperature, monitored by TLC. After the reaction was completed, the mixture was evaporated, and the residue was crystallized by acetonitrile/water. The pale yellow precipitate was filtered, washed with diethyl ether and dried at room temperature. (0.04 g, 7%) Mp.: 189–190 °C. R_f (dichloromethane/methanol 10:1): 0.5. IR ν_{max}: 3150, 3020, 1691, 1623, 1589, 1522, 1281, 1176, 943, 762, 592 cm^{-1} ^{1}H-NMR (DMSO-d_6) δ: 13.70 (brs, 1H, COO*H*), 12.84 (s, 1H, N*H*-C2), 12.35 (s, 1H, N*H*-CO), 8.16 (d, J=8.8Hz, 1H, H-3), 8.04 (d, J=2.2Hz,1H, H-6), 7.83 (dd, J=8.8, 2.2Hz, 1H, H-4), 7.64 (m, 1H, H-4'), 7.26 (m, 2H, H-3', H-5'). δC (100 MHz, DMSO-d_6): 178.8 (*C*S), 165.9 (*C*OOH), 137.4 (C-2), 134.7 (C-4), 133.5 (C-4'), 132.7 (C-6), 129.4 (C-3), 126.5 (C-1), 118.5 (C-5), 113.1 (C-1'), 112.1 (2C, C-3', C-5'). HRMS (ESI) $C_{15}H_{11}NO_5F_2SBr$ $[M+H]^+$: calculated: 413.9485, measured: 414.9525, deviation: 1.8662 ppm, 4.4973 mDa, DBE: 10.

Synthesis of 5-bromo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3c): To a solution of 4-fluorobenzoyl chloride (2 mmol, 236 μl) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (3 mmol, 228 mg) in dry acetone (3 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered, and the filtrate was used without any purification in the next step. To this solution (**2c**) 1.6 mmol (346 mg) 2-amino-5-bromobenzoic acid (**1a**) was added and stirred at room temperature, monitored by TLC. White precipitate appeared in the mixture. When the reaction was completed, the product was filtered. The filtrate was poured over ice-water and the residue of the product was precipitated. The pale yellow crystals were filtered, washed with *n*-hexane and dried at room temperature. (0.55 g, 87%) Mp.: 237–238°C. R_f (*n*-hexane): 0.2. IR ν_{max}: 3726, 3467, 3249, 3053, 1711, 1673, 1598, 1574, 1502, 1289, 1155, 943, 757, 593 cm^{-1}.

^{1}H-NMR (DMSO-d_6) δ: 13.75 (brs, 1H, COO*H*), 13.10 (s, 1H, N*H*-C2), 11.75 (s, 1H, N*H*-CO), 8.12 (d, J=8.7Hz, 1H, 3), 8.06 (m, 2H, H-2', H-6'), 8.02 (d, J=2.4Hz, 1H, H-6), 7.82 (dd, J=8.7, 2.4Hz, 1H, H-4), 7.38 (m, 2H, H-3', H-5'). δC (100 MHz, DMSO-d_6): 179.9 (*C*S), 166.6 (*C*O), 165.8 (*C*OOH), 165.1 (*C*F), 137.5 (C-2), 134.6 (C-4), 132.7 (C-6), 131.8 (2C, C-2', C-6'), 129.6 (C-3), 128.6 (C-1'), 126.7 (C-1), 118.3 (C-5), 115.6 (2C, C-3', C-5'). HRMS (ESI) $C_{15}H_{11}N_2O_3FSBr$ $[M+H]^+$: calculated: 395.9579, measured: 396.9657, deviation: -4.4803 ppm, -1.7785 mDa, DBE: 10.5.

Synthesis of 5-bromo-2-({[(3,5-dimethoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3d): To a solution of 3,5-dimethoxybenzoyl chloride (2 mmol, 401 mg) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (3 mmol, 228 mg) in dry acetone (3 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered, and the filtrate was used without any purification in the next step. To this solution (**2d**) 1.4 mmol (302 mg) 2-amino-5-bromobenzoic acid (**1a**) was added and stirred at room temperature, monitored by TLC. Yellow precipitate appeared in the mixture. When the reaction was completed, the product was filtered, washed with *n*-hexane and dried at room temperature. (0.53 g, 87%) Mp.: 221–222 °C. R_f (dichloromethane/methanol 10:1): 0.6. IR ν_{max}: 3259, 2938, 2837, 1678, 1594, 1570, 1509, 1570, 1285, 1155, 741 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 13.75 (brs, 1H, COO*H*), 13.15 (s, 1H, N*H*-C2), 11.69 (s, 1H, N*H*-CO), 8.12 (d, J=8.8Hz, 1H, H-3), 8.02 (d, J=2.4Hz, 1H, H-6), 7.82 (dd, J=8.8, 2.4Hz, 1H, H-4), 7.15 (d, J=2.2Hz, 2H, H-2', H-6'), 6.77 (t, J=2.2Hz, 1H, H-4'), 3.83 (s, 6H, OCH_3-C3', OCH_3-C5'). δC (100 MHz, DMSO-d_6): 179.9 (*C*S), 167.2 (*C*O), 165.8 (*C*OOH), 160.3 (2C, C-3', C-5'), 137.5 (C-2), 134.6 (C-4), 133.9 (C-2'), 132.7 (C-6), 129.6 (C-3), 126.8 (C-1), 118.3 (C-5), 106.3 (2C, C-2', C-6'), 105.6 (C-4'), 55.6 (2C, C3'-O*C*H$_3$, C5'-O*C*H$_3$). HRMS (ESI) $C_{17}H_{16}N_2O_5SBr$ $[M+H]^+$: calculated: 437.9885, measured: 438.9963, deviation: -4.8514 ppm, -2.1297 mDa, DBE: 10.5.

Synthesis of 5-bromo-2-[({[2-(chloromethyl)phenyl]formamido}methanethioyl)amino]benzoic acid (3e): To a solution of 2-(chloromethyl)benzoyl chloride (0.5 mmol, 72 μl) in dry acetone (3 ml) was added under reflux a solution of ammonium thiocyanate (0.5 mmol, 38 mg) in dry acetone (2 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered, and the filtrate was used without any purification in the next step. To this solution (**2e**) 0.45 mmol (97 mg) 2-

amino-5-bromobenzoic acid (**1a**) was added and stirred at room temperature, monitored by TLC. White precipitate appeared in the mixture. When the reaction was completed, the product was filtered, washed with dry acetone and dried at room temperature. (0.14 g, 65%) Mp.: 208–209 °C. R_f (dichloromethane/methanol 10:1): 0.5. IR ν_{max}: 3727, 3704, 3624, 3597, 3264, 3061, 1699, 1674, 1599, 1572, 1287, 1163, 943, 691, 593 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 13.84 (brs, 1H, COO*H*), 13.08 (s, 1H, N*H*-C2), 12.00 (s, 1H, N*H*-CO), 8.21 (d, J=8.8Hz, 1H, H-3), 8.03 (d, J=2.4Hz, 1H, H6), 7.83 (dd, J=8.8, 2.4Hz, 1H, H-4), 7.63 (d, J=7.6Hz, 1H, H-6'), 7.61-7.54 (m, 2H, H-3', H-4'), 7.48 (m, 1H, H-5'), 4.95 (s, 2H, CH_2-C2'), δC (100 MHz, DMSO-d_6): 179.6 (*C*S), 168.7 (*C*O), 165.9 (*C*OOH), 137.6 (C-2), 136.2 (C-2'), 134.6 (C-4), 133.4 (C-1'), 132.7 (C-6), 131.6 (C-4'), 130.5 (C-3'), 129.3 (C-3), 129.1 (C-6'), 128.4 (C-5'), 126.3 (C-1), 118.1 (C-5), 43.3 (*C*H_2). HRMS (ESI) $C_{16}H_{13}N_2O_3SClBr$ $[M+H]^+$: calculated: 425.9440, measured: 426.9518, deviation: -4.3988 ppm, -1.878 mDa, DBE: 10.5.

Synthesis of 5-bromo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3f): To a solution of 4-nitrobenzoyl chloride (1 mmol, 186 mg) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (1.5 mmol, 114 mg) in dry acetone (3 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered, and the filtrate was used without any purification in the next step. To this solution (**2f**) 1.4 mmol (302 mg) 2-amino-5-bromobenzoic acid (**1a**) was added and stirred at room temperature, monitored by TLC. When the reaction was completed, the mixture was evaporated and the residue was recrystallized from ethanol. Yellow crystals were produced. (0.1 g, 23%) Mp.: 220–222 °C. R_f (dichloromethane/methanol 10:1): 0.6. IR ν_{max}: 3187, 3001, 1702, 1679, 1597, 1577, 1341, 1292, 1155, 945, 758, 593 cm^{-1}. ^{1}H-NMR (DMSO-d_6+CD_3OD) δ: 13.04 (brs, 1H, in exchange with CD_3OD, N*H*-C2), 12.01 (brs, 1H, in exchange with CD_3OD, N*H*-CO), 8.33 (d, J=8.8Hz, 2H, H-3', H-5'), 8.20-8.13 (m, 3H, H-3, H-3', H-5'), 8.03 (d, J=2.3Hz, 1H, H-6), 7.80 (dd, J=8.7, 2.3Hz, 1H, H-4). δC (100 MHz, DMSO-d_6): 179.6 (*C*S), 166.3 (*C*O), 165.8 (*C*OOH), 149.9 (C-4'), 137.9 (C-1'), 137.5 (C-2), 134.7 (C-4), 132.7 (C-6), 130.4 (2C, C-2', C-6'), 129.5 (C-3)*, 126.6 (C-5)*, 123.4 (2C, C-3', C-5'), 118.4 (C-1). * These signals are interchangeable with each other. HRMS (ESI) $C_{15}H_{11}N_3O_5SBr$ $[M+H]^+$: calculated: 422.9524, measured: 423.9602, deviation: -4.9027 ppm, -2.0785 mDa, DBE: 11.5.

Synthesis of 5-iodo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3k): To the solution of 4-nitrobenzoyl chloride (1.5 mmol, 278 mg) in dry acetone (5 ml) was added under reflux a solution of ammonium thiocyanate (1.5 mmol, 114 mg) in dry acetone (3 ml) through a dropping funnel. White precipitate appeared. After the addition the mixture was treated under reflux conditions for 30 minutes monitored by TLC. The mixture was filtered, and the filtrate was used without any purification in the next step. To this solution (**2f**) 1.2 mmol (315 mg) 2-amino-5-iodobenzoic acid (**1b**) was added and stirred at room temperature, monitored by TLC. When the reaction was completed, the mixture was evaporated and the residue was recrystallized from ethanol. Yellow crystals were produced. (0.4 g, 73%) Mp.: 218–219 °C. R_f (dichloromethane/methanol 10:1): 0.5. IR ν_{max}: 3186, 2994, 2858, 1698, 1678, 1591, 1512, 1337, 1169, 755. ^{1}H-NMR (DMSO-d_6) δ: 13.76 (brs, 1H, O*H*), 13.06 (s, 1H, N*H*-C2), 12.10 (s, 1H, N*H*-CO), 8.35 (d, J=8.8Hz, 2H, H-3', H-5'), 8.20 (d, J=2.0Hz, 1H, H-6), 8.16 (d, J=8.8Hz, 2H, H-2', H-6'), 8.01 (d, J=8.6Hz, 1H, H-3), 7.96 (dd, J=8.6, 2.0Hz, 1H, H-4). δC (100 MHz, DMSO-d_6): 179.4 (*C*S), 166.3 (*C*O-C1'), 165.9 (*C*OOH), 149.9 (C-4'), 140.4 (C-4), 138.6 (C-6), 138.0 (C-1'), 137.9 (C-2), 130.4 (C-6'), 129.3 (C-3), 126.5 (C-1), 123.4 (C-5'), 91.1 (C-5). HRMS (ESI) $C_{15}H_{11}N_3O_5SI$ $[M+H]^+$: calculated: 470.93859, measured: 471.9458, deviation: -2.4809 ppm, -1.1708 mDa, DBE: 11.5.

General procedure for the synthesis of substituted thiourea derivatives (3g–j) from carboxylic acids (5g–j) (Scheme 4)

Synthesis of benzoyl isothiocyanates (**2g–j**): The reactions were carried out by using 1.0/0.3/0.8/2.5 molar ratio of TPP/TCCA/RCOOH/NH_4SCN. To the cold solution of triphenylphosphine /TPP/ (262 mg, 1 mmol) in dichloromethane (3 mL), trichloroisocyanuric acid /TCCA/ (69 mg, 0.3 mmol) was added under continuous stirring, followed by adding benzoic acid (97 mg, 0.8 mmol) and stirring was continued for 15 min. Then ammonium thiocyanate (190 mg, 2.5 mmol) was added and the temperature was raised up to room temperature. It was stirred at room temperature monitored by TLC. The mixture was evaporated, and the residue passed through to a short silicagel column using *n*-hexane or *n*-hexane/ethyl acetate 10:1 as eluent.

Synthesis of thiourea derivatives (**3g–j**): 2-amino-5-bromobenzoic acid (**1a**) (0.9 moleq.) was added to the acetone solution of the corresponding isothiocyanate derivative and the mixture

was stirred at room temperature until the reaction was completed according to the TLC analysis. For the different derivatives various working up procedures were used.

Yields were calculated based on the amount of 2-amino-5-bromobenzoic acid (**1a**)

Synthesis of 5-bromo-2-({[(2-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3g):

Synthesis of 2-nitrobenzoyl isothiocyanate (**2g**): To the cold solution of triphenylphosphine (984 mg, 3.75 mmol) in dichloromethane (9 mL), trichloroisocyanuric acid (261 mg, 1.125 mmol) was added under continuous stirring, then 2-nitrobenzoic acid (501 mg, 3 mmol) was added and stirring was continued for 15 min. After that ammonium thiocyanate (714 mg, 9.375 mmol) was added and the temperature was raised up to room temperature. It was stirred at room temperature monitored by TLC. White suspension was produced. The mixture was filtered, evaporated and the residue was passed through to a short silicagel column using *n*-hexane/ethyl acetate 10:1 as eluent. Pale yellow crystals were produced (0.124 g, 20%).

2-Amino-5-bromobenzoic acid (**1a**) (93 mg, 0.43 mmol) was added to the acetone solution of the 2-nitrobenzoyl isothiocyanate (**2g**) (100 mg, 0.48 mmol) and the mixture was stirred at room temperature until the reaction was completed according to the TLC analysis. Most of the acetone from the mixture was evaporated, and then water was added to the residue. Yellow crystals appeared, which were filtered and washed with diethyl ether. (0.07 g, 36%). Mp.: 192–194 °C. R_f (dichloromethane/methanol 10:1): 0.4. IR (KBr) ν_{max}: 3727, 3703, 3625, 3598, 3164, 3022, 1688, 1600, 1579, 1523, 1350, 1172, 949, 753 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 12.92 (s, 1H, N*H*), 12.21 (s, 1H, N*H*-CO), 8.25 (d, J=8.8Hz, 1H, H-3), 8.23 (m, 1H, H-5'), 8.04 (d, J=2.4Hz, 1H, H-6), 7.90 (m, 1H, H-3'), 7.84 (dd, J=8.8, 2.4Hz, H-4), 7.80 (m, 1H, H-4'), 7.77 (m, 1H, H-2'). δC (100 MHz, DMSO-d_6): 178.9 (*C*S), 166.5 (*C*O), 165.8 (*C*OOH), 145.5 (C-6'), 137.3 (C-2), 134.7 (C-4, C-3'), 132.7 (C-6), 131.8 (C-4'), 130.6 (C-1'), 129.4 (C-2'), 129.1 (C-3), 126.1 (C-1), 124.3 (C-5'), 118.2 (C-5). HRMS (ESI) $C_{15}H_{11}N_3O_5SBr$ $[M+H]^+$: calculated: 422.9524, measured: 423.9602, deviation: -3.4845 ppm, -1.4785 mDa, DBE: 11.5.

Synthesis of 5-bromo-2-({[(4-methoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3h): *Synthesis of 4-methoxybenzoyl isothiocyanate* (**2h**): To the cold solution of triphenylphosphine (525 mg, 2 mmol) in dichloromethane (6 mL), trichloroisocyanuric acid (139 mg, 0.6 mmol) was added under continuous stirring, than 4-methoxybenzoic acid (243

mg, 1.6 mmol) was added and stirring was continued for 15 min. After that ammonium thiocyanate (380 mg, 5 mmol) was added and the temperature was raised up to room temperature. It was stirred at room temperature monitored by TLC. White suspension was produced. The mixture was filtered, evaporated and the residue was passed through to a short silicagel column using *n*-hexane/ethyl acetate 3:2 as eluent. Colourless oil was produced. (0.23 g, 74%). R_f: 0.2.

2-Amino-5-bromobenzoic acid (**1a**) (230 mg, 1.1 mmol) was added to the acetone solution of the 4-methoxybenzoyl isothiocyanate (**2h**) (230 mg, 1.2 mmol) and the mixture was stirred at room temperature until the reaction was completed according to the TLC analysis. Most of the acetone was evaporated from the mixture, and to the residue water was added. White crystals appeared, which were filtered and washed with *n*-hexane. (0.18 g, 39%). Mp.: 230–232 °C. R_f (toluene/methanol/chloroform 5:1:1): 0.6. IR ν_{max}: 3389, 3025, 2983, 1679, 1602, 1491, 1281, 1171, 687, 595 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 13.17 (brs, 1H, N*H*-C2), 11.49 (brs, 1H, N*H*-CO), 8.10 (d, J=8.7Hz, 1H, H-3), 8.07-7.96 (m, 3H, H-6, H-2', H-6'), 7.81 (dd, J=8.7, 2.4Hz, 1H, H-4), 7.07 (d, J=8.9Hz, 2H, H-3', H-5'), 3.85 (s, 3H, OCH_3). δC (100 MHz, DMSO-d_6): 180.1 (*C*S), 166.9 (*C*O-C1'), 165.8 (*C*OOH), 163.3 (C-4'), 137.6 (C-2), 134.6 (C-4), 132.7 (C-6), 131.1 (C-6'), 129.8 (C-3), 126.9 (C-1), 123.8 (C-1'), 118.3 (C-5), 113.9 (C-5'), 55.7 (O*C*H$_3$). HRMS (ESI) $C_{16}H_{12}N_2O_4SBr$ $[M+H]^+$: calculated: 407.9779, measured: 406.9701, deviation: -5.6883 ppm, -2.3149 mDa, DBE: 11.5.

Synthesis of 5-bromo-2-({[(4-cyanophenyl)formamido]methanethioyl}amino)benzoic acid (3i): *Synthesis of 4-cyanobenzoyl isothiocyanate* (**2i**): To the cold solution of triphenylphosphine (984 mg, 3.75 mmol) in dichloromethane (9 mL), trichloroisocyanuric acid (261 mg, 1.125 mmol) was added under continuous stirring, than 4-cyanobenzoic acid (441 mg, 3 mmol) was added and stirring was continued for 15 min. After that ammonium thiocyanate (714 mg, 9.375 mmol) was added and the temperature was raised up to room temperature. It was stirred at room temperature monitored by TLC. White suspension was produced. The mixture was filtered, evaporated and the residue was passed through to a short silicagel column using *n*-hexane as eluent. White crystals were produced. (0.12 g, 20%). R_f: 0.2.

2-Amino-5-bromobenzoic acid (**1a**) (100 mg, 0.48 mmol) was added to the acetone solution of the 4-cyanobenzoyl isothiocyanate (**2i**) (100 mg, 0.53 mmol) and the mixture was stirred at room temperature until the reaction was completed according to the TLC analysis. Some of

the acetone was evaporated from the mixture, and the mixture was filtered. Pale yellow crystals were produced. (0.06 g, 30%). Mp.: 233–234 °C. R_f (dichloromethane/methanol 10:1): 0.4. IR ν_{max}: 3228, 3005, 2233, 1706, 1680, 1597, 1578, 1523, 1289, 1156, 944, 763, 591 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 13.01 (s, 1H, N*H*), 11.99 (s, 1H, N*H*-CO), 8.14 (d, J=8.8Hz, 1H, H-3), 8.08 (m, 2H, H-2', H-6'), 8.03 (d, J=2.5Hz, 1H, H-6), 8.01 (m, 2H, H-3', H-5'), 7.83 (dd, J=8.8, 2.5Hz, 1H, H-4). δC (100 MHz, DMSO-d_6): 179.4 (*C*S), 166.4 (*C*O), 165.7 (*C*OOH), 137.3 (C-2), 136.3 (C-1'), 134.8 (C-4), 132.7 (C-6), 132.4 (C-3', C-5'), 129.6 (C-2', C-6'), 129.5 (C-3), 126.5 (C-1), 118.4 (C-5), 118.1 (*C*N), 115.1 (C-4'). HRMS (ESI) $C_{16}H_{11}N_3O_3SBr$ $[M+H]^+$: calculated: 402.9626, measured: 403.9704, deviation: -3.5876 ppm, -1.4492 mDa, DBE: 12.5.

Synthesis of 5-bromo-2-({[(2-bromophenyl)formamido]methanethioyl}amino)benzoic acid (3j): *Synthesis of 2-bromobenzoyl isothiocyanate* (**2j**): To the cold solution of triphenylphosphine (656 mg, 2.5 mmol) in dichloromethane (9 mL), trichloroisocyanuric acid (174 mg, 0.75 mmol) was added under continuous stirring, than 2-bromobenzoic acid (402 mg, 2 mmol) was added and stirring was continued for 15 min. After that ammonium thiocyanate (380 mg, 5 mmol) was added and the temperature was raised up to room temperature. It was stirred at room temperature monitored by TLC. White suspension was produced. The mixture was filtered, evaporated and the residue was passed through to a short silicagel column using *n*-hexane as eluent. Yellow oil was produced. (0.26 g, 48%). R_f: 0.2.

2-Amino-5-bromobenzoic acid (**1a**) (120 mg, 0.44 mmol) was added to the acetone solution of the 2-bromobenzoyl isothiocyanate (**2j**) (76 mg, 0.35 mmol) and the mixture was stirred at room temperature until the reaction was completed according to the TLC analysis. The mixture was filtered and the residue was washed with *n*-hexane. White crystals were produced. (0.11 g, 67%). Mp.: 223–223.5 °C. R_f (dichloromethane/methanol 10:1): 0.4. IR ν_{max}: 3261, 3006, 1710, 1688, 1596, 1573, 1518, 1292, 1154, 944, 754 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 13.89 (brs, 1H, COO*H*), 13.00 (s, 1H, N*H*-C2), 12.09 (s, 1H, N*H*-CO), 8.21 (d, J=8.8Hz, 1H, H-3), 8.03 (d, J=2.4Hz, 1H, H-6), 7.83 (dd, J=8.8, 2.4Hz, 1H, H-4), 7.72 (dd, J=7.6, 1.2Hz, 1H, H-5'), 7.58 (dd, J=7.4, 1.8Hz, 1H, H-2'), 7.54-7.41 (m, 2H, H-3', H-4'). δC (100 MHz, DMSO-d_6): 179.3 (*C*S), 167.8 (*C*O-C1'), 166.0 (*C*OOH), 137.5 (C-2), 136.5 (C-1'), 134.7 (C-4), 132.7 (C-6), 132.7 (C-5'), 132.2 (C-4'), 129.3 (C-3), 129.2 (C-2'), 127.6 (C-3'), 126.4 (C-1), 118.9 (C-6'), 118.2 (C-5). HRMS (ESI) $C_{15}H_{11}N_2O_3SBr_2$ $[M+H]^+$: calculated: 455.8778, measured: 456.8857, deviation: -3.7457 ppm, -1.7113 mDa, DBE: 10.5.

Synthesis of 5-iodo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3l): *Synthesis of 4-fluorobenzoyl isothiocyanate* (**2c**): To the cold solution of triphenylphosphine (980 mg, 3.75 mmol) in dichloromethane (9 mL), trichloroisocyanuric acid (260 mg, 1.125 mmol) was added under continuous stirring, then 4-fluorobenzoic acid (420 mg, 3 mmol) was added and stirring was continued for 15 min. After that ammonium thiocyanate (700 mg, 9.375 mmol) was added and the temperature was raised up to room temperature. It was stirred at room temperature monitored by TLC. White suspension was produced. The mixture was filtered, evaporated and the residue was passed through a short silicagel column using *n*-hexane as eluent. Yellow oil was produced (0.26 g, 48%). R_f: 0.2.

2-Amino-5-iodobenzoic acid (**1b**) (302 mg, 1.15 mmol) was added to the acetone solution of the 4-fluorobenzoyl isothiocyanate (**2c**) (260 mg, 1.44 mmol) and the mixture was stirred at room temperature until the reaction was completed according to the TLC analysis. The mixture was filtered, and the residue was washed with *n*-hexane. White crystals were produced. (0.32 g, 63%). Mp.: 221–223 °C. R_f (dichloromethane/methanol 10:1): 0.3. IR ν_{max}: 3255, 2977, 1682, 1520, 1497, 1415 1151, 937, 752, 600. ^{1}H-NMR (DMSO-d_6) δ:13.73 (brs, 1H, COO*H*), 13.11 (s, 1H, N*H*-C2), 11.76 (s, 1H, N*H*-CO), 8.19 (d, J=1.4Hz, 1H, H-6), 8.05 (m, 2H, H-2', H-6'), 8.01-7.92 (m, 2H, H-3, H-4), 7.38 (m, 2H, H-3', H-5'). δC (100 MHz, DMSO-d_6): 179.7 (*C*S), 166.6 (*C*O-C1'), 165.8 (*C*OOH), 165.0 (C-4'), 140.4 (C-4), 138.6 (C-6), 138.0 (C-2), 131.9 (C-6'), 129.4 (C-3), 128.6 (C-1'), 126.6 (C-1), 115.6 (C-5'), 91.0 (C-5). HRMS (ESI) $C_{15}H_{11}N_2O_3FSI$ $[M+H]^+$: calculated: 443.94409, measured: 444.9513, deviation: -2.1819 ppm, -0.9708 mDa, DBE: 10.5.

Synthesis of benzothiazonines from substituted thiourea derivatives (11a–d) (Scheme 5.)

General procedure: To the corresponding substituted thiourea derivative (**3a**, **3c**, **3k**, **3l**) concentrated sulphuric acid was added and stirred at room temperature, monitored by TLC. The mixture was poured into ice/water, the precipitate was filtered, washed with water and *n*-hexane.

Synthesis of *N*-(6-bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11a) To the substituted thiourea derivative (**3a**) (100 mg, 0.26 mmol) 0.5 ml concentrated sulphuric acid was added and stirred at room temperature, monitored by TLC. The mixture was poured into ice/water, the precipitate was filtered, washed with water and *n*-hexane. White crystals were produced. (0.78 g, 83%) Mp.: 227–228 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.8. IR ν_{max}: 3272, 3043, 2517, 1685, 1657, 1622, 1566, 1263, 1187, 753. ^{1}H-NMR (DMSO-d_6) δ: 12.32

(brs, 1H, N*H*), 8.11 (d, J=2.1Hz, 1H, H-5), 8.07-8.00 (m, 3H, H-7, H-2', H-6'), 7.66 (t, J=7.4Hz, 1H, H-4'), 7.60 (d, J=8.7Hz, 1H, H-8), 7.54 (t, J=7.4Hz, 2H, H-3', H-5'). δC (100 MHz, DMSO-d_6): 183.8 (C-4), 167.6 (*C*O), 154.8 (C-1), 146.3 (C-8a), 138.8 (C-7), 133.1 (C-4'), 131.9 (C-1'), 130.8 (C-8), 128.6 (C-2', C-6'), 128.5 (C-3', C-5'), 126.4 (C-5), 120.6 (C-4a). HRMS (ESI) $C_{15}H_{10}N_2O_2SBr$ $[M+H]^+$: calculated: 359.956812, measured: 360.964, deviation: -1.0721 ppm, -0.387 mDa, DBE: 11.5.

Synthesis of 4-fluoro-*N*-(6-bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11b) To the substituted thiourea derivative (**3c**) 60 mg (0.15 mmol) 0.5 ml concentrated sulphuric acid was added and stirred at room temperature, monitored by TLC. The mixture was poured into ice/water, the precipitate was filtered, washed with water and *n*-hexane. White crystals were produced. (0.03 g, 53%) Mp.: 228–229 °C. R_f (dichloromethane/methanol 10:1): 0.9. IR ν_{max}: 3272, 3043, 2517, 1685, 1657, 1622, 1566, 1263, 1187, 753. ^{1}H-NMR (DMSO-d_6) δ: 12.08 (brs, 1H, N*H*), 8.18-8.07 (m, 3H, H-5, H-2', H-6'), 8.02 (d, J=8.6Hz, 1H, H-7), 7.59 (J=8.6Hz, 1H, H-8), 7.37 (m, 2H, H-3', H-5'). δC (100 MHz, DMSO-d_6): 183.7 (C-4), 166.7 (CO), 165.0 (C-4'), 154.9 (C-2), 146.4 (C-8a), 138.8 (C-7), 131.6 (C-2', C-6'), 130.7 (C-8), 128.5 (C-1'), 126.5 (C-5), 120.6 (C-4a), 119.4 (C-6), 115.6 (C-3', C-5'). HRMS (ESI) C15 H9 N2 O2 F S Br $[M+H]^+$: calculated: 377.947390, measured: 378.9546, deviation: -1.4915 ppm, -0.5652 mDa, DBE: 11.5.

Synthesis of 4-nitro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11c) To the substituted thiourea derivative (**3k**) (370 mg, 0.83 mmol) 0.5 ml concentrated sulphuric acid was added and stirred at room temperature, monitored by TLC. The mixture was poured into ice/water, the precipitate was filtered, washed with water and *n*-hexane. White crystals were produced. (0.26 g, 70%) Mp.: 232–233 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.6. IR ν_{max}: 3287, 3103, 1675, 1620, 1576, 1516, 1347, 1263, 1188. ^{1}H-NMR (DMSO-d_6) δ: 12.20 (brs, 1H, N*H*), 8.34 (d, J=8.8Hz, 2H, H-3', H-5'), 8.26 (d, J=1.6Hz, 1H, H-5), 8.23 (d, J=8.8Hz, 2H, H-2', H-6'), 8.17 (dd, J=8.6, 1.6Hz, 1H, H-7), 7.43 (d, J=8.6Hz, 1H, H-8). δC (100 MHz, DMSO-d_6): 183.3 (C-4), 166.8 (*C*O), 149.9 (C-4'), 145.9 (C-8a), 144.6 (C-7), 138.0 (C-1'), 132.6 (C-5), 130.2 (C-2', C-6'), 130.0 (C-8), 123.6 (C-3', C-5'), 120.7 (C-4a), 92.2 (C-6). HRMS (ESI) $C_{15}H_9N_3O_4SI$ $[M+H]^+$: calculated: 452.92802, measured: 453.9353, deviation: -1.3353 ppm, -0.6061 mDa, DBE: 12.5.

Synthesis of 4-fluoro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11d) To the substituted thiourea derivative (**3l**) (370 mg, 0.83 mmol) 0.5 ml concentrated sulphuric acid

was added and stirred at room temperature, monitored by TLC. The mixture was poured into ice/water, the precipitate was filtered, washed with water and *n*-hexane. White crystals were produced. (0.24 g, 68%) Mp.: 236–238 °C. R_f (dichloromethane/methanol 10:1): 0.6. IR ν_{max}: 3264, 3072, 2515, 1676, 1621, 1564, 1266, 1187, 754. ^{1}H-NMR (DMSO-d_6) δ: 11.27 (brs, 1H, N*H*), 8.27 (d, J=1.9Hz, 1H, H-5), 8.19-8.08 (m, 3H, H-7, H-2', H-6'), 7.43 (d, J=8.6Hz, 1H, H-8), 7.41-7.33 (m, 2H, H-3', H-5'). δC (100 MHz, DMSO-d_6): 183.6 (C-4), 166.7 (*C*O), 164.9 (C-4'), 154.9 (C-2), 146.4 (C-8a), 144.4 (C-7), 132.4 (C-5), 131.6 (C-2', C-6'), 130.4 (C-8), 128.6 (C-1'), 120.7 (C-4a), 115.6 (C-3', C-5'), 92.1 (C-6). HRMS (ESI) $C_{15}H_9N_2O_2FSI$ $[M+H]^+$: calculated: 425.93352, measured: 426.9408, deviation: -3.5277 ppm, -1.5061 mDa, DBE: 11.5.

Synthesis of amino acid containing thiourea derivatives (9a–f)

Preparation of (2*S*)-*N*-(2-aminobenzoyl)-2-alkyl-aminoacetic acids (**8a–c**) (Scheme 6.)

General procedure: To the stirred solution of L-amino acids (**7a–c**) (22 mmol) in and triethyl amine (22 mmol) in water (60 mL), isatoic anhydride /**6**/ (20 mmol) was added and stirred at 40°C, monitored by TLC. The stirring was continued for 18 h at room temperature. After completion of the reaction, the mixture was cooled, acidified with HCl solution (2 mol/L) to pH 5 and extracted with dichloromethane, then dried on Na_2SO_4 and evaporated. Brown oils were produced, which were used in the next step without any purification.

(2*S*)-*N*-(2-aminobenzoyl)-2-isopropylaminoacetic acid (**8a**): (5.2 g, 91%)

(2*S*)-*N*-(2-aminobenzoyl)-2-isobutylaminoacetic acid (**8b**): (5.3 g, 96%)

(2*S*)-*N*-(2-aminobenzoyl)-2-(2-methylbutyl)aminoacetic acid (**8c**): (5.1 g, 93%)

Preparation of (2*S*)-*N*-(2-aminobenzoyl)-2-alkyl-aminoacetic acid methyl esters (**9a–c**) (**Scheme 7**)

General procedure: 20 mmol of (2*S*)-*N*-(2-aminobenzoyl)-2-alkyl-aminoacetic acid (**8a–c**) was dissolved in 30 ml methanol, cooled with ice/water and 40 mmol sulfinyl chloride was added dropwise via a dropping funnel. After the addition of sulfinyl chloride, the mixture was stirred at room temperature for 20 hours, monitored by TLC.

Working up: the pH of the mixture was adjusted to neutral with saturated $NaHCO_3$ solution, extracted with ethyl acetate, dried with anhydrous Na_2SO_4 and evaporated. The residue was crystallized, the crystals was filtered and washed with *n*-hexane.

(2*S*)-*N*-(2-aminobenzoyl)-2-isopropylaminoacetic acid methyl ester (**9a**): Light brown crystals. (2.3 g, 53%) Mp.: 82–82.5. IR ν_{max}: 3451, 3351, 2970, 2922, 1734, 1624, 1519, 1209, 1158, 747. ^{1}H-NMR ($CDCl_3$) δ: 7.42 (dd, J=7.9, 1.2Hz, 1H), 7.22 (td, J=7.9, 1.2Hz, 1H), 6.73-6.64 (m, 2H), 6.54 (d, J=8.6Hz, 1H), 5.51 (brs, 2H), 4.73 (dd, J=8.6, 4.9Hz, 1H), 3.77 (s, 3H), 2.32-2.19 (m, 1H), 1.01 (d, J=7.0Hz, 3H), 0.99 (d, J=6.9Hz, 3H). δC (100 MHz, $CDCl_3$): 18,0 (C-5'), 19,0 (*C*H_3), 31,5 (C-4'), 52,2 (O*C*H_3), 57,0 (C-3'), 115,6 (C-1), 116,7 (C-5), 117,3 (C-3), 127,4 (C-6), 132,6 (C-4), 148,7 (C-2), 169,0 (C-1'), 172,7 (*C*O). HRMS (ESI) C13H19N2O3 $[M+H]^+$: calculated: 250.131742, measured: 251.13902, deviation: -4.3 ppm, -1.07 mDa, DBE: 6.0.

(2*S*)-*N*-(2-aminobenzoyl)-2-isobutylaminoacetic acid methyl ester (**9b**): Light brown crystals. (2.7 g, 64%) Mp.:67–69 °C. IR ν_{max}: 3473, 3339, 2955, 2870, 1731, 1631, 1520, 1223, 746. ^{1}H-NMR ($CDCl_3$) δ: 7.39 (d, J=7.9Hz, 1H), 7.22 (t, J=7.9Hz, 1H), 6.71-6.63 (m, 2H), 6.41 (d, J=8.6Hz, 1H), 5.48 (brs, 2H), 4.85-4.76 (m, 1H), 3.76 (s, 3H), 1.80-1.59 (m, 3H), 1.02-0.94 (m, 6H). δC (100 MHz, $CDCl_3$): 22,1 (*C*H_3), 22,8 (C-6'), 25,1 (C-5'), 41,8 (C-4'), 50,9 (C-3'), 52,1 (O*C*H_3), 120,2 (C-3), 124,5 (C-5), 127,1 (C-1), 131,5 (C-6), 132,1 (C-4), 152,7 (C-2), 166,0 (C-1'), 173,8 (*C*O). HRMS (ESI) C14H21N2O3 $[M+H]^+$: calculated: 264.14739, measured: 265.1546, deviation: -2.9009 ppm, -0.7691 mDa, DBE: 5.5.

(2*S*)-*N*-(2-aminobenzoyl)-2-(2-methylbutyl)aminoacetic acid methyl ester (**9c**): Light brown crystals.(2.2 g, 74%). Mp.: 59–60 °C. IR ν_{max}: 3415, 3303, 2963, 2876, 1732, 1618, 1523, 1202, 746. ^{1}H-NMR ($CDCl_3$) δ: 7.40 (dd, J=8.2, 1.2Hz, 1H), 7.22 (tm, J=8.2Hz, 1H), 6.72-6.64 (m, 2H), 6.56 (d, J=8.4Hz, 1H), 5.51 (brs, 2H), 4.76 (dd, J=8.4, 5.0Hz, 1H), 3.77 (s, 3H), 2.05-1.93 (m, 1H), 1.60-1.45 (m, 1H), 1.33-1.18 (m, 1H), 1.01-0.93 (m, 6H). δC (100 MHz, DMSO-d_6): 11,6 (C-6'), 15,5 (*C*H_3), 25,3 (C-5'), 38,2 (C-4'), 52,2 (O*C*H_3), 56,4 (C-3'), 115,6 (C-1), 116,7 (C-5), 117,3 (C-3), 127,4 (C-6), 132,6 (C-4), 148,7 (C-2), 168,9 (C-1'), 172,7 (*C*O). HRMS (ESI) C14H21N2O3 $[M+H]^+$: calculated: 264.14739, measured: 265.1546, deviation: -3.278 ppm, -0.8691 mDa, DBE: 5.5.

Synthesis of amino acid containing thiourea derivatives (10a–c) from 4-nitrobenzoyl chloride (4f) *via* 4-nitrobenzoyl isothiocyanate (2f) (Scheme 8)

To the acetone solution of 4-nitrobenzoyl isothiocyanate (**2f**) (prepared according to the procedure described before, see Scheme 2) 0.5 mmol of the corresponding amine (**10a–c**) was added and stirred at room temperature, monitored by TLC. The mixture was evaporated, and the residue was purified by column chromatography using *n*-hexane/ethyl acetate 3:2 as eluent.

Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}butanoate (**10a**)
Yellow crystals. (0.12 g, 50%) Mp.: 170–171 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.4. IR ν_{max}: 3727, 3703, 3626, 3599, 3210, 3053, 2966, 1738, 1643, 1603, 1524, 1498, 1342, 1267, 1152, 860, 637 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 12.83 (brs, 1H, N*H*-C1), 9.27 (brs, 1H, CO-N*H*-CS), 8.37 (d, J=8.8Hz, 2H, H-3’’, H-5”’), 8.16 (dm, J=7.7Hz, 1H, H-6), 8.12 (d, J=8.8Hz, 2H, H-2”’, H-6’”), 7.64 (dd, J=7.7, 1.1Hz, 1H, H-3), 7.56 (td, J=7.7, 1.2Hz, 1H, H-4), 7.39 (tm, J=7.7Hz, 1H, H-3), 6.77 (d, J=8.8Hz, 1H, N*H*-CO), 4.80 (dd, J=8.8, 4.8Hz, 1H, H-3’), 3.70 (s, 3H, OCH_3), 2.26 (m, 1H, H-4’), 0.99 (d, J=6.8Hz, 3H, CH_3), 0.95 (d, J=6.9Hz, 3H, CH_3). δC (100 MHz, DMSO-d_6): 178.9 (*C*S), 172.2 (*C*O-C3’), 167.0 (C1’), 163.9 (*C*O-C1’’), 150.6 (C-4’’), 136.1 (C-2), 131.2 (C-4), 129.6 (C-1), 129.0 (C-2’’, C-6’’), 127.7 (C-6), 127.2 (C-3, C-5), 124.2 (C-3’’, C-5’’), 57.1 (C-3’), 52,3 (O*C*H_3), 31.5 (C-4’), 19.0 (C-5’), 17.8 (*C*H_3). HRMS (ESI) $C_{21}H_{21}N_4O_6S$ $[M+H]^+$: calculated: 458.1260, measured: 457.1181, deviation: -3.6785 ppm, -1.6815 mDa, DBE: 13.5.

Methyl (2*S*)-4-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (**10b**)
Yellow crystals. (0.18 g, 61%) Mp.: 92.5–94 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.5. IR ν_{max}: 3296, 2955, 2870, 1739, 1683, 1601, 1506, 1334, 1256, 1145, 866, 638 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 12.81 (brs, 1H, N*H*-C2), 9.22 (brs, 1H, CO-N*H*-CS), 8.37 (d, J=8.8Hz, 2H, H-3’’, H-5’’), 8.16-8.08 (m, 3H, H-2’’, H-4’’, H-3), 7.62 (dd, J=7.7, 1.2Hz, 1H, H-6), 7.54 (td, J=7.7, 1.2Hz, 1H, H-4), 7.37 (td, J=7.7, 1.2Hz, 1H, H-5), 6.69 (d, J=8.4Hz, 1H, H-2’), 4.85 (m, 1H, H-3’), 3.69 (s, 3H, OCH_3), 1.80-1.58 (m, 3H, H-4’, H-5’), 0.95 (d, J=6.0Hz, 3H, H-6’), 0.93 (d, J=6.1Hz, 3H, CH_3). δC (100 MHz, DMSO-d_6): 179.0 (*C*S), 173.2 (CO-C3’), 166.9 (C-1’), 164.0 (*C*O-C1’’), 150.6 (C-4’’), 137.3 (C-1’’), 129.7 (C-1), 129.0 (C-2’’, C-6’’), 136.0 (C-2), 131.2 (C-4), 127.7 (C-6), 127.3 (C-5), 127.2 (C-3), 124.2 (C-3’’, C-5’’), 52.4

(O*C*H3), 51.1 (C-3'), 41.5 (C-4'), 25.0 (C-5'), 22.9 (CH_3), 22.1 (C-6'). HRMS (ESI) $C_{22}H_{25}N_4O_6S$ $[M+H]^+$: calculated: 472.1416, measured: 473.1494, deviation: -2.9201 ppm, -1.3816 mDa, DBE: 12.5, $C_{22}H_{25}N_4O_6NaS$ $[M+H]^+$: calculated: 495.1313, measured: 495.1314, deviation: -3.0826 ppm, -1.5263 mDa, DBE: 12.5.

Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (**10c**) Yellow crystals. (0.18 g, 58%) Mp.: 145–146 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.5. IR ν_{max}: 3373, 3275, 3071, 2962, 2876, 1734, 1685, 1601, 1504, 1326, 1257, 1144, 866, 748 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 12.83 (brs, 1H, N*H*-C2), 9.23 (brs, 1H, CO-N*H*-CS), 8.37 (d, J=8.7Hz, 2H, H-3'', H-5''), 8.15 (dm, J=7.6Hz, 1H, H-3), 8.11 (d, J=8.7Hz, 2H, H-2'', H-6''), 7.63 (dd, J=7.6, 1.0Hz, 1H, H-6), 7.55 (td, J=7.6, 1.0Hz, 1H, H-4), 7.37 (td, J=7.6, 1.0Hz, 1H, H-5), 6.78 (d, J=8.7Hz, 1H, H-2'), 4.83 (dd, J=8.7, 4.8Hz, 1H, H-3'), 3.69 (s, 3H, OCH_3), 1.99 (m, 1H, H-4'), 1.47 (m, 1H, H-5'), 1.23 (m, 1H, H-5'), 0.96 (d, J=6.8Hz, 3H, CH_3), 0.91 (t, J=7.5Hz, 3H, H-6'). δC (100 MHz, DMSO-d_6): 178.9 (*C*S), 172.2 (CO-C3'), 166.9 (C-1'), 164.0 (CO-C1''), 150.5 (C-4''), 137.4 (C-1''), 136.0 (C-2), 131.1 (C-4), 129.6 (C-1), 129.0 (2C, C-2'', C-6''), 127.8 (C-6), 127.2 (2C, C-3, C-5), 124.1 (2C, C-3'', C-5''), 56.7 (C-3'), 52.1 (O*C*H3), 38.1 (C-4'), 25.2 (C-5'), 15.4 (CH_3), 11.7 (C-6'). HRMS (ESI) $C_{22}H_{25}N_4O_6S$ $[M+H]^+$: calculated: 472.1416, measured: 473.1494, deviation: -2.9201 ppm, -1.3816 mDa, DBE: 12.5, $C_{22}H_{25}N_4O_6NaS$ $[M+H]^+$: calculated: 495.1313, measured: 495.1314, deviation: -2.6787 ppm, -1.3263 mDa, DBE: 12.5.

Synthesis of amino acid containing thiourea derivatives (10d–f) from 4-fluorbenzoic acid (5h) via 4-fluorobenzoyl isothiocyanate (2h) (Scheme 9)

To the acetone solution of 4-fluorobenzoyl isothiocyanate (**2h**) (prepared according to the procedure described before, see Scheme 3.) 1.1 mmol (0.8 moleq.) of the corresponding amine (**9a–c**) was added and stirred at room temperature, monitored by TLC. For the different derivatives various working up procedures were used.

Methyl-

(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylbutanoate (**10d**) White precipitate appeared. The mixture was filtered, then the crystals were washed with *n*-hexane and dried at room temperature. White crystals were

produced. (0.32 g, 66%) Mp.: 160–161 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.5. IR ν_{max}: 3341, 3229, 2948, 1741, 1640, 1601, 1528, 1498, 1212, 1154, 849, 741 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 12.85 (brs, 1H, N*H*-C2), 9.10 (brs, 1H, CO-N*H*-CS), 8.09 (dm, J=7.8Hz, 1H, H-3), 7.96 (m, 2H, H-2'', H-6''), 7.64 (dd, J=7.8, 1.1Hz, 1H, H-6), 7.54 (td, J=7.8 Hz, 1.1Hz, 1H, H-4), 7.37 (td, J=7.8Hz, 1H, H-5), 7.21 (m, 2H, H-3'', H-5''), 6.79 (d, J=8.8Hz, 1H, H-2'), 4.80 (dd, J=8.8, 4.8Hz, 1H, H-3'), 3.69 (s, 3H, OCH_3), 2.25 (m, 1H, H-4'), 0.98 (d, J=6.9Hz, 3H, H-5'), 0.94 (d, J=6.9Hz, 3H, CH_3). δC (100 MHz, DMSO-d_6): 179.7 (*C*S), 172.1 (*C*O-C3'), 167.0 (C-1'), 164.9 (*C*O-C1''), 136.1 (C-2), 131.0 (C-4), 130.3 (2C, C-2'', C-6''), 130.2 (C-1), 128.0 (C-1''), 127.8 (C-6), 127.5 (C-3), 127.2 (C-5), 116.4 (2C, C-3'', C-5''), 57.2 (C-3'), 52.2 (O*C*H3), 31.4 (C-4'), 18.9 (C-5'), 17.8 (CH_3). HRMS (ESI) $C_{21}H_{23}N_3O_4FS$ $[M+H]^+$: calculated: 431.1315, measured: 432.1393, deviation: -2.387 ppm, -1.0315 mDa, DBE: 11.5, $C_{21}H_{23}N_4O_4FNaS$ $[M+H]^+$: calculated: 454.1212, measured: 454.1212, deviation: -1.0762 ppm, -1.3263 mDa, DBE: 11.5.

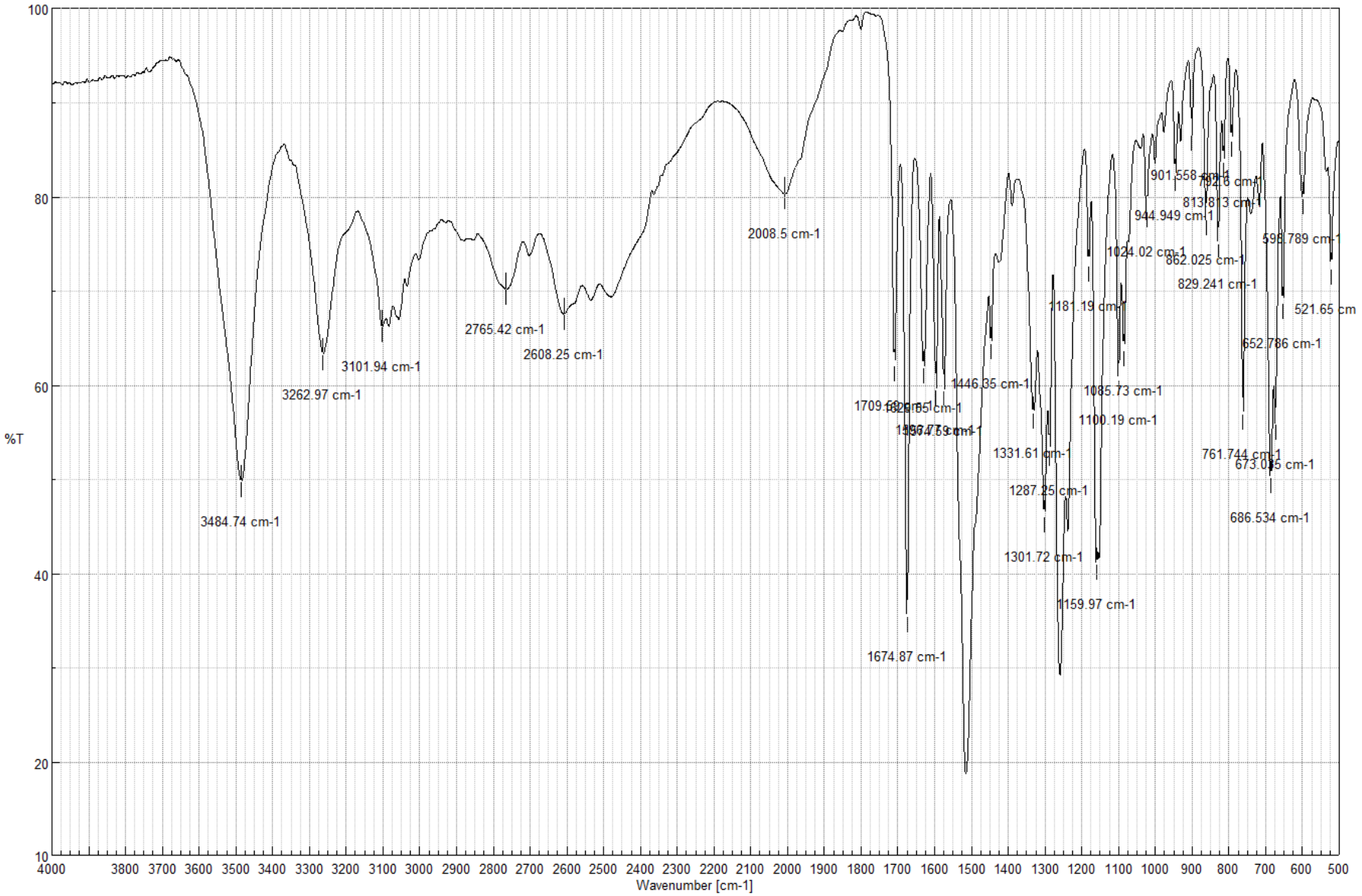
Methyl-
(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-4-

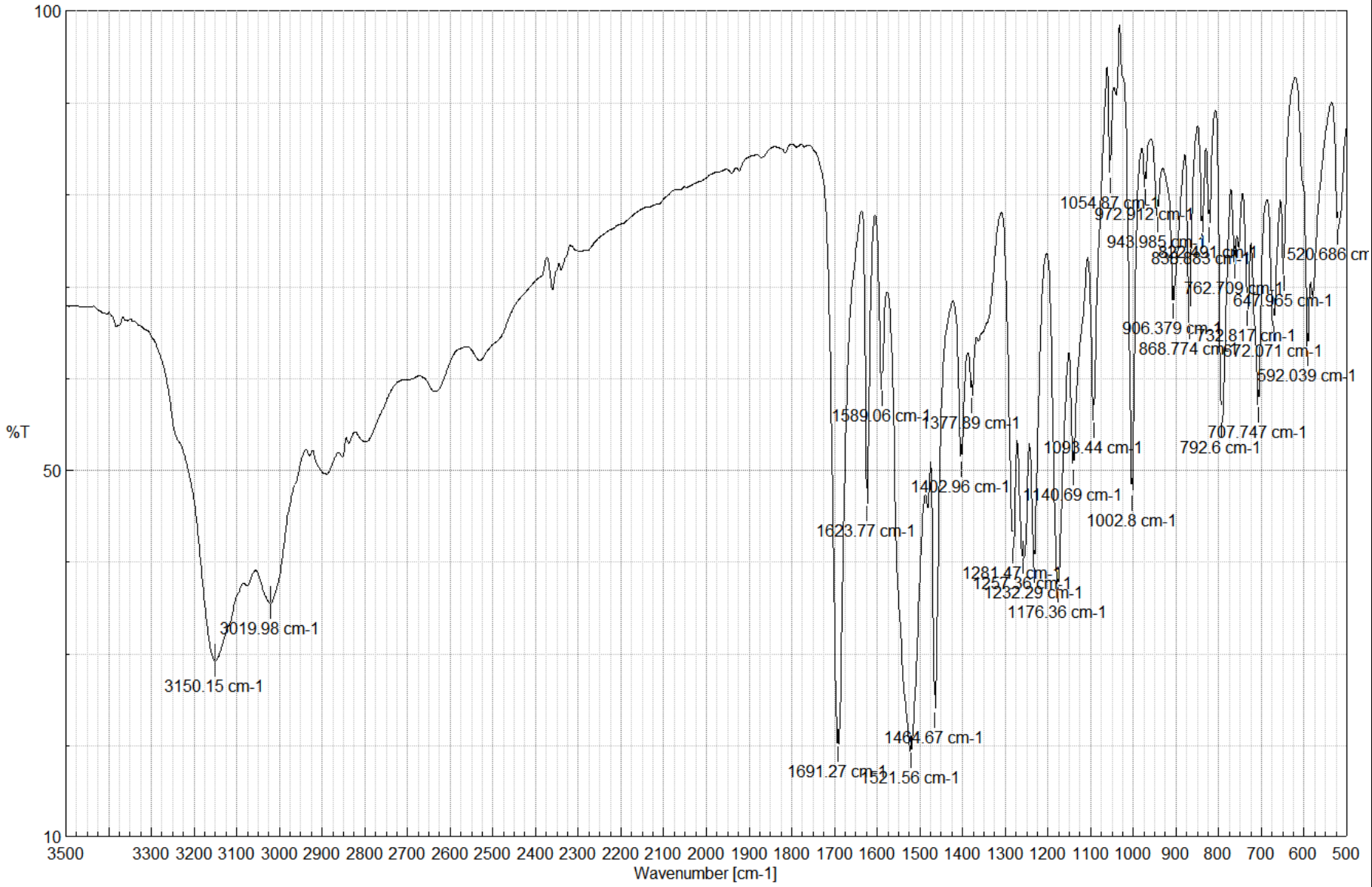
methylpentanoate (**10e**) The mixture was poured into ice/water and the precipitate was filtered, washed with *n*-hexane. It was purified by column chromatography using *n*-hexane/ethyl acetate 3:2 as eluent. Pale yellow crystals were produced. (0.28 g, 58%) Mp.: 90.8–92 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.6. IR ν_{max}: 3301, 2955, 2870, 1718, 1684, 1628, 1602, 1601, 1496, 1330, 1235, 1144, 849, 749 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 12.79 (brs, 1H, N*H*-C2), 9.11 (brs, 1H, CO-N*H*-CS), 8.04 (dm, J=8.1 Hz, 1H, H-3), 7.96 (m, 2H, H-2'', H-6''), 7.62 (dd, J=7.7, 1.1Hz, 1H, H-6), 7.53 (td, J=7.7, 1.1Hz, 1H, H-4), 7.37 (tm, J=7.7Hz, 1H, H-5), 7.21 (m, 2H, H-3'', H-5''), 6.74 (d, J=8.4 Hz, H-2'), 4.84 (m, 1H, H-3'), 3.68 (s, 3H, OCH_3), 1.77-1.57 (m, 3H, H-4', H-5'), 0.94 (d, J=5.9Hz, 3H, H-6'), 0.91 (d, J=6.0Hz, 3H, CH_3). δC (100 MHz, DMSO-d_6): 179.8 (*C*S), 173.1 (*C*O-C3'), 166.9 (C-1'), 165.9 (C-4''), 164.9 (*C*O-C1''), 135.9 (C-2), 131.0 (C-4), 130.5 (C-1), 130.3 (2C, C-2'', C-5''), 127.9 (C-6), 127.6 (C-3), 127.3 (C-5), 116.4 (2C, C-3'', C-6''), 52.3 (OCH_3), 51.0 (C-3'), 41.5 (C-4'), 24.9 (C-5'), 22.8 (CH_3), 22.0 (C-6'). HRMS (ESI) $C_{22}H_{25}N_3O_4FS$ $[M+H]^+$: calculated: 445.1471, measured: 446.1549, deviation: -2.2002 ppm, -0.9816 mDa, DBE: 11.5, $C_{22}H_{25}N_3O_4FNaS$ $[M+H]^+$: calculated: 468.1369, measured: 468.1369, deviation: -1.9786 ppm, -0.9262 mDa, DBE: 11.5.

Methyl

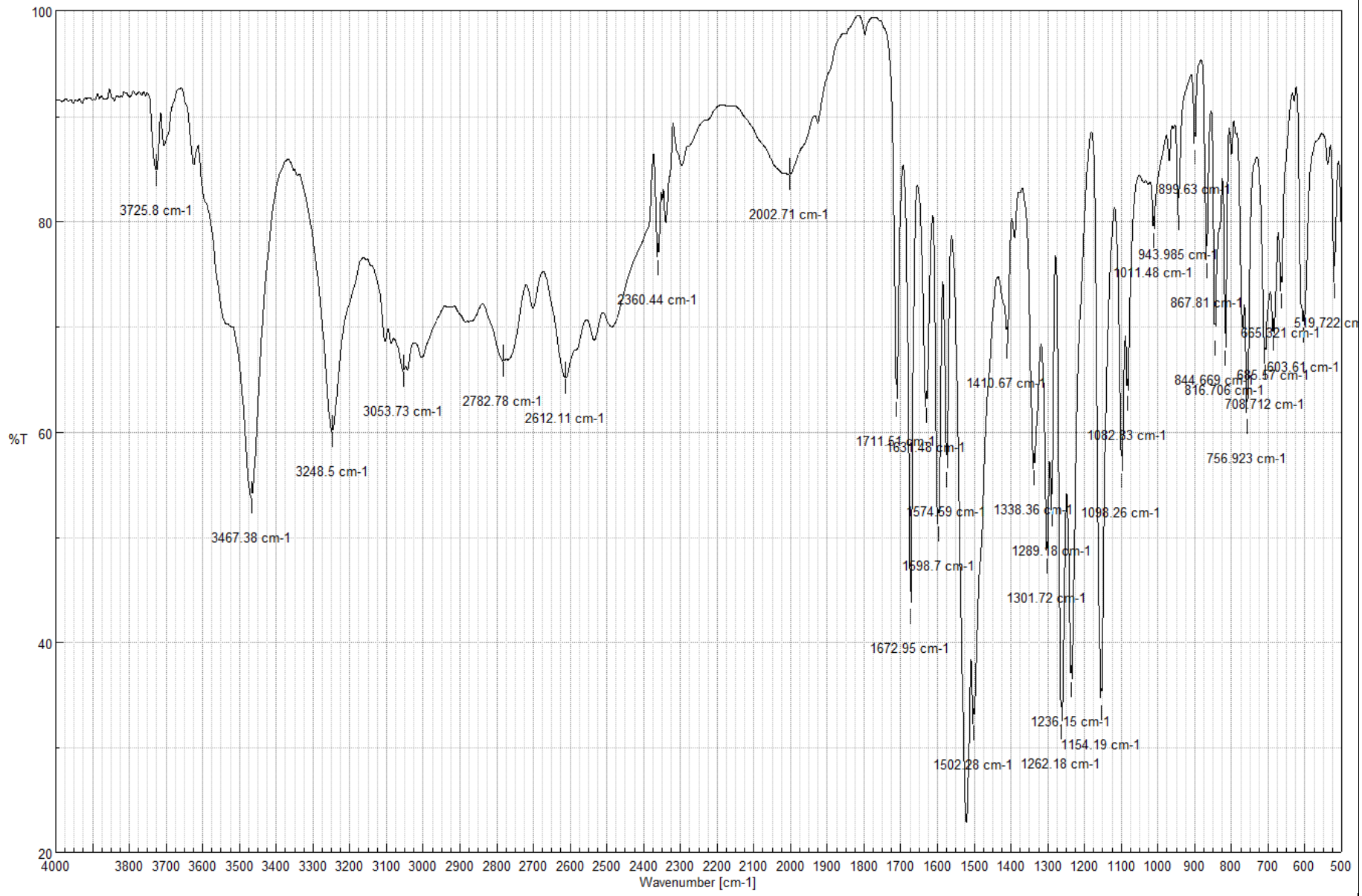
(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-

methylpentanoate (10f) White precipitate appeared. The mixture was filtered, the crystals were washed with *n*-hexane and dried at room temperature. White crystals were produced. (0.16 g, 32%) Mp.: 116–117 °C. R_f (*n*-hexane/ethyl acetate 3:2): 0.5. IR ν_{max}: 3344, 3310, 2960, 2928, 2876, 1713, 1688, 1625, 1601, 1525, 1498, 1341, 1237, 1142, 847, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 12.82 (brs, 1H, H-C2), 9.12 (brs, 1H, CO-N*H*-CS), 8.07 (dm, J=7.7Hz, 1H, H-3), 7.96 (m, 2H, H-2'', H-6''), 7.63 (dd, J=7.7, 1.0Hz, 1H, H-6), 7.54 (td, J=7.7, 1.0Hz, 1H, H-4), 7.37 (tm, J=7.7Hz, 1H, H-5), 7.21 (m, 2H, H-3'', H-5''), 6.81 (d, J=8.8 Hz, 1H, H-2'), 4.82 (dd, J=8.8, 4.8Hz, 1H, H-3'), 3.68 (s, 3H, OCH_3), 1.97 (m, 1H, H-4'), 1.47 (m, 1H, H-5'), 1.21 (m, 1H, H-5'), 0.95 (d, J=6.9 Hz, 3H, H-6'), 0.90 (t, J=7.4Hz, 3H, CH_3). δC (100 MHz, DMSO-d_6): 179.7 (*C*S), 172.1 (*C*O-C3') 165.9 (C-4''), 166.9 (C-1'), 164.9 (*C*O-C1''), 136.0 (C-2), 131.0 (C-4), 130.3 (C-1), 130.3 (2C, C-2'', C-6''), 127.9 (C-6), 127.9 (C-1''), 127.6 (C-3), 127.3 (C-5), 116.4 (2C, C-3'', C-5''), 56.8 (C-3'), 52.1 (OCH_3), 38.1 (C-4'), 25.2 (C-5'), 15.4 (CH_3), 11.7 (C-6'). HRMS (ESI) $C_{22}H_{25}N_3O_4FS$ $[M+H]^+$: calculated: 445.1471, measured: 446.1549, deviation: -4.2174 ppm, -1.8816 mDa, DBE: 11.5, $C_{22}H_{25}N_4O_4FNaS$ $[M+H]^+$: calculated: 468.1369, measured: 468.1369, deviation: -2.6195 ppm, -1.2262 mDa, DBE: 11.5.

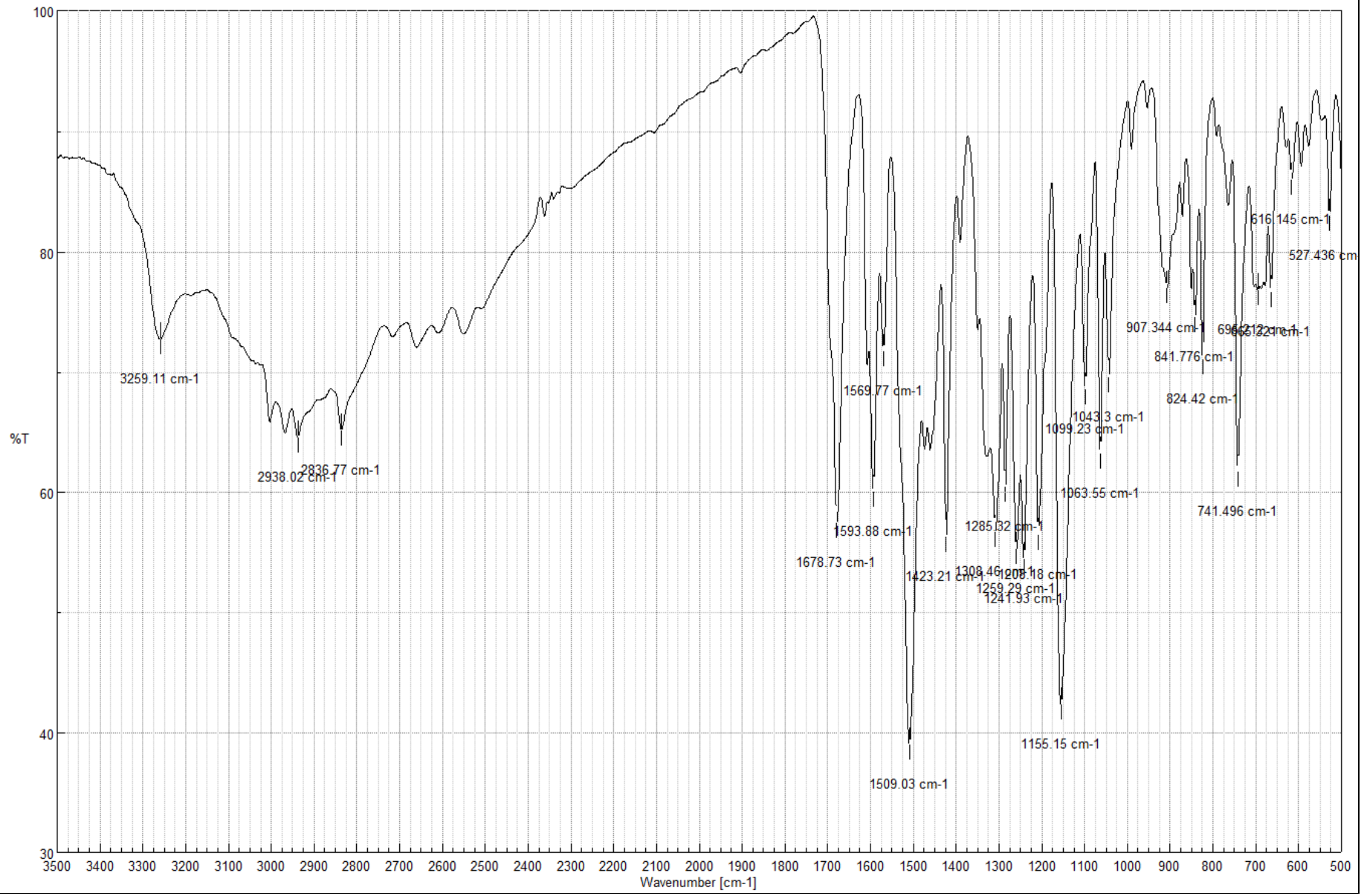
Wavenumber [cm-1]	**5-Bromo-2-{[(phenylformamido)methanethioyl]amino}benzoic acid (3a)**
3484.74	
3262.97	
3101.94	
2765.42	
2608.25	
2008.5	
1709.59	
1674.87	
1629.55	
1596.77	
1574.59	
1446.35	
1331.61	
1301.72	
1287.25	
1181.19	
1159.97	
1100.19	
1085.73	
1024.02	
944.949	
901.558	
862.025	
829.241	
813.813	
792.6	
761.744	
686.534	
673.035	
652.786	
598.789	
521.65	

Wavenumber [cm-1]	**5-Bromo-2-({[(2,6-difluorophenyl)formamido]methanethioyl}amino)benzoic acid (3b)**
3150.15	
3019.98	
1691.27	
1623.77	
1589.06	
1521.56	
1464.67	
1402.96	
1377.89	
1281.47	
1257.36	
1232.29	
1176.36	
1140.69	
1093.44	
1054.87	
1002.8	
972.912	
943.985	
906.379	
868.774	
838.883	
822.491	
792.6	
762.709	
732.817	
707.747	
672.071	
647.965	
592.039	
520.686	

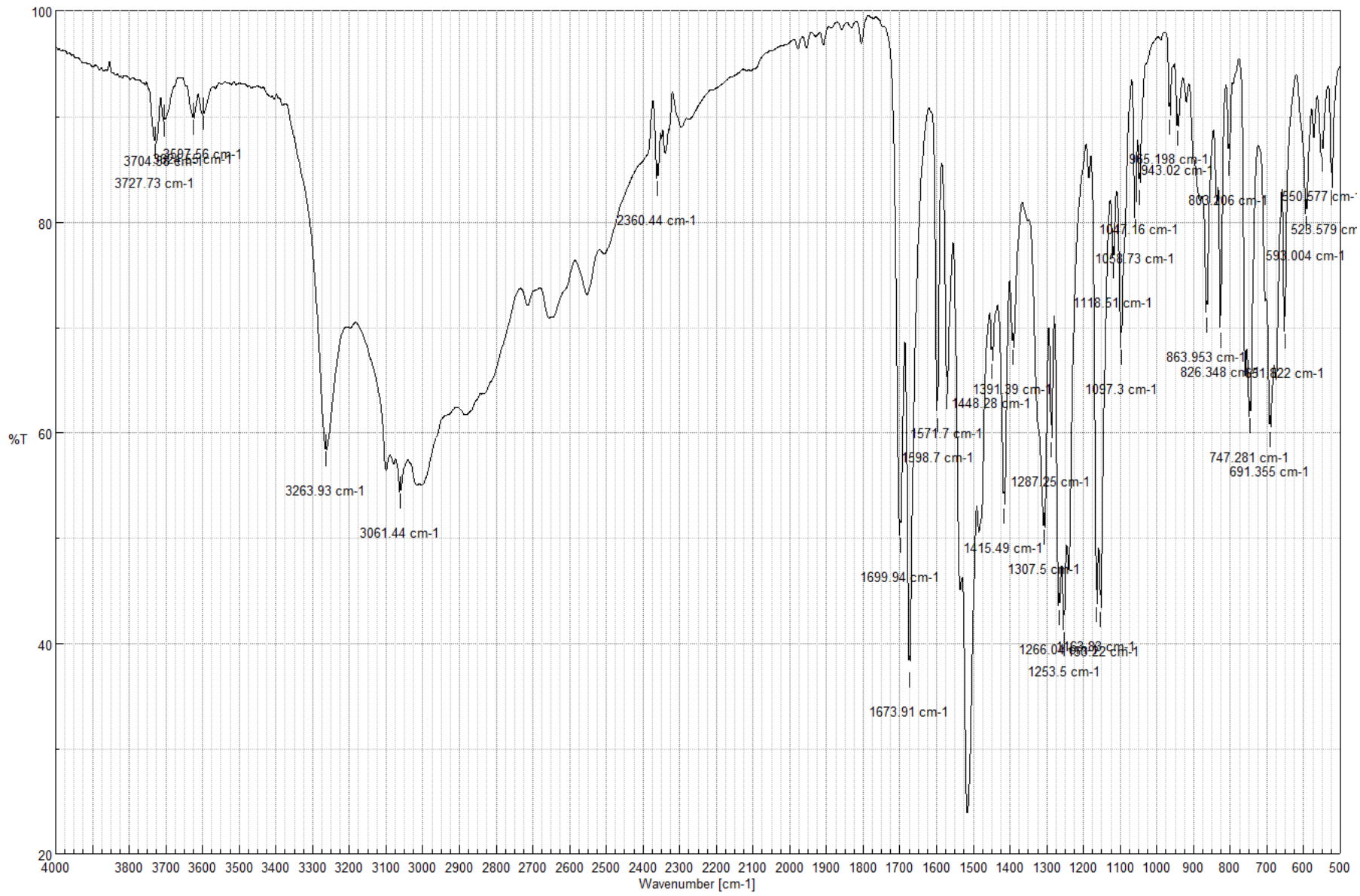
Wavenumber [cm-1]	**5-Bromo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3c)**
3725.8	
3467.38	
3248.5	
3053.73	
2782.78	
2612.11	
2360.44	
2002.71	
1711.51	
1672.95	
1631.48	
1598.7	
1574.59	
1502.28	
1410.67	
1338.36	
1301.72	
1289.18	
1262.18	
1236.15	
1154.19	
1098.26	
1082.83	
1011.48	
943.985	
899.63	
867.81	
844.669	
816.706	
756.923	
708.712	
685.57	
665.321	



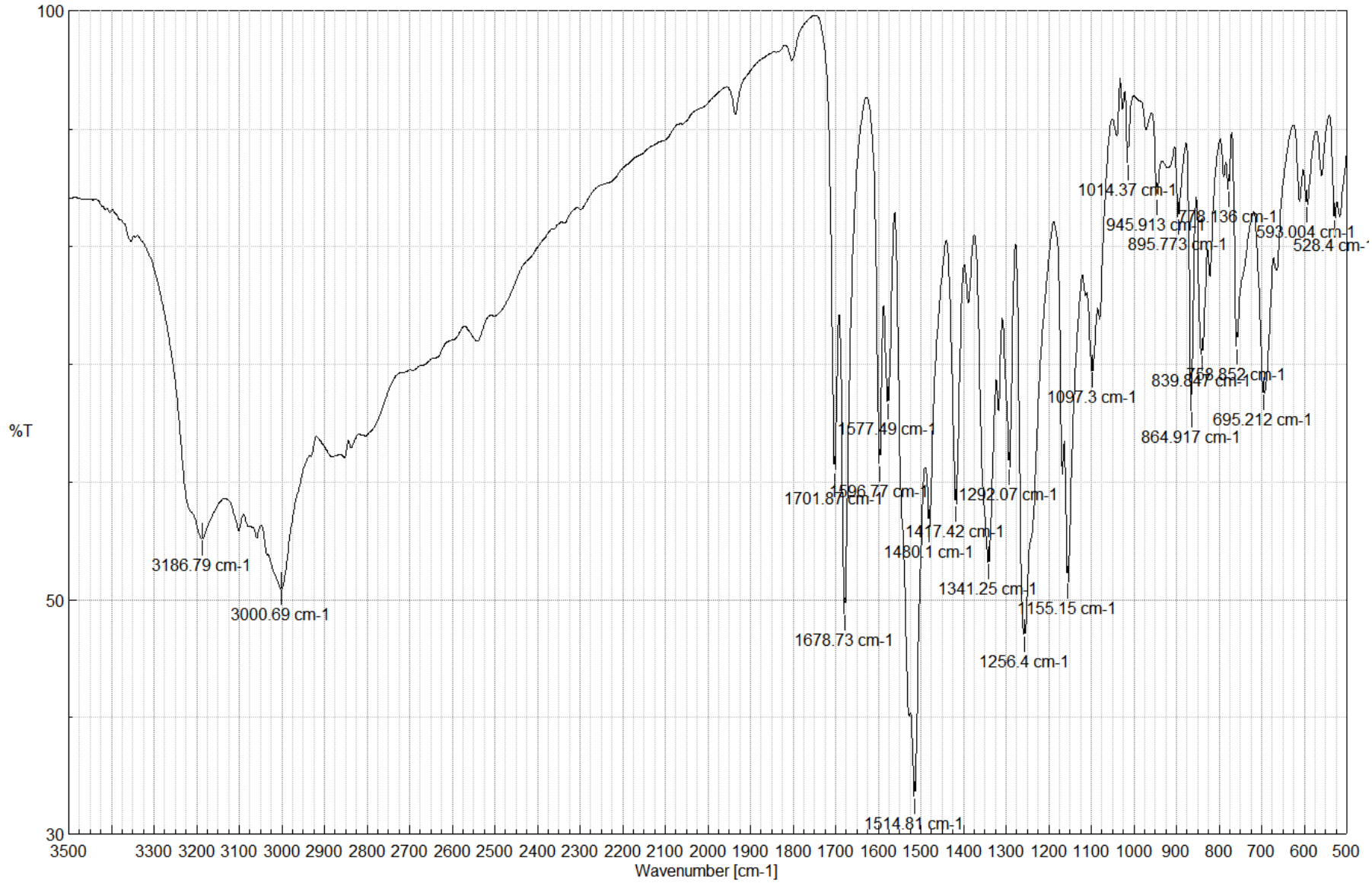
603.61 519.722	

Wavenumber [cm-1]	**5-Bromo-2-({[(3,5-dimethoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3d)**
3259.11	
2938.02	
2836.77	
1678.73	
1593.88	
1569.77	
1509.03	
1423.21	
1308.46	
1285.32	
1259.29	
1241.93	
1208.18	
1155.15	
1099.23	
1063.55	
1043.3	
907.344	
841.776	
824.42	
741.496	
695.212	
665.321	
616.145	
527.436	

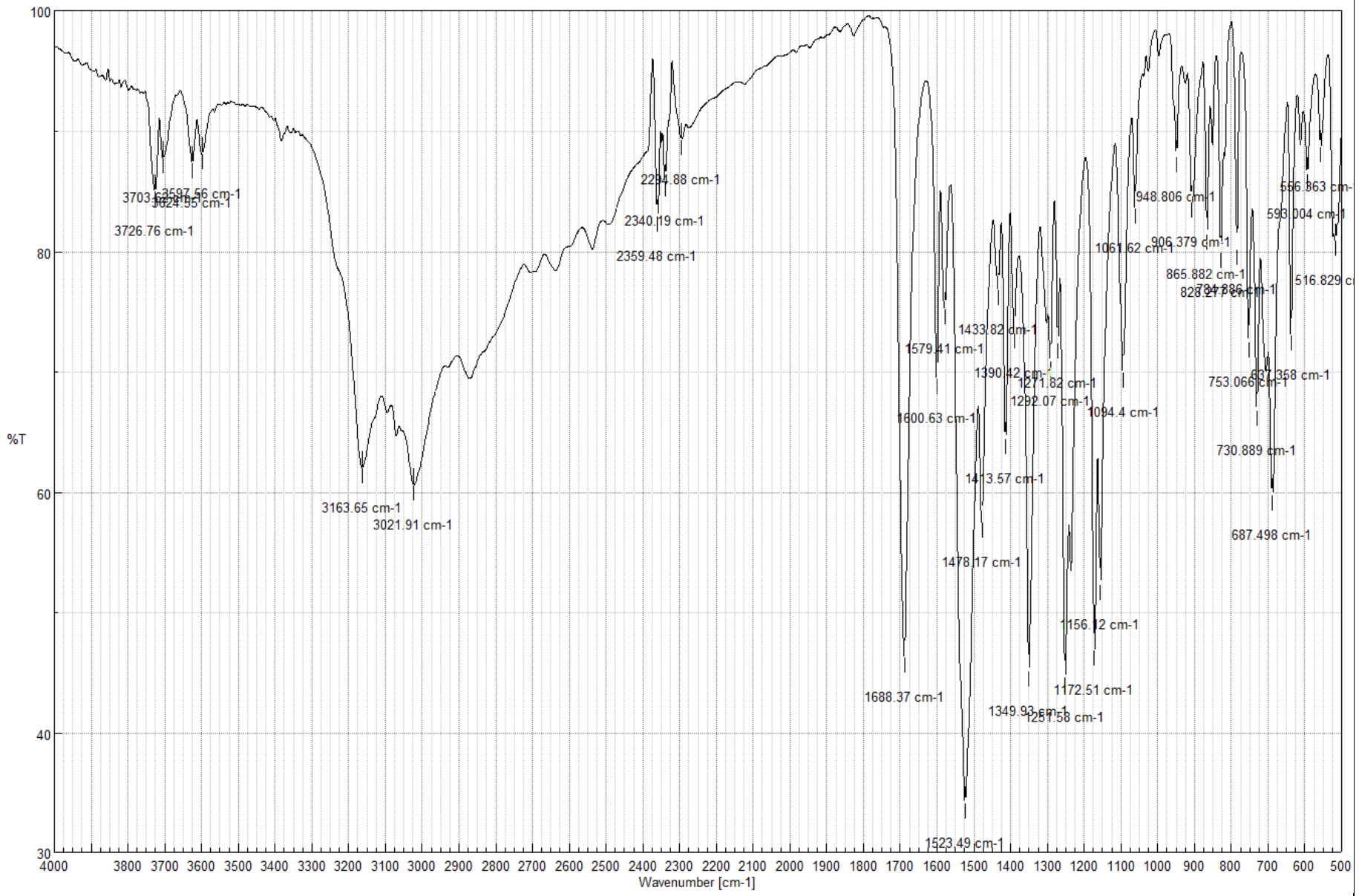
Wavenumber [cm-1]	**5-Bromo-2-[({[2-(chloromethyl)phenyl]formamido}methanethioyl)amino]benzoic acid (3e)**
3727.73	
3704.58	
3624.55	
3597.56	
3263.93	
3061.44	
2360.44	
1699.94	
1673.91	
1598.7	
1571.7	
1448.28	
1415.49	
1391.39	
1307.5	
1287.25	
1266.04	
1253.5	
1163.83	
1153.22	
1118.51	
1097.3	
1058.73	
1047.16	
965.198	
943.02	
863.953	
826.348	
803.206	
747.281	
691.355	
651.822	
593.004	



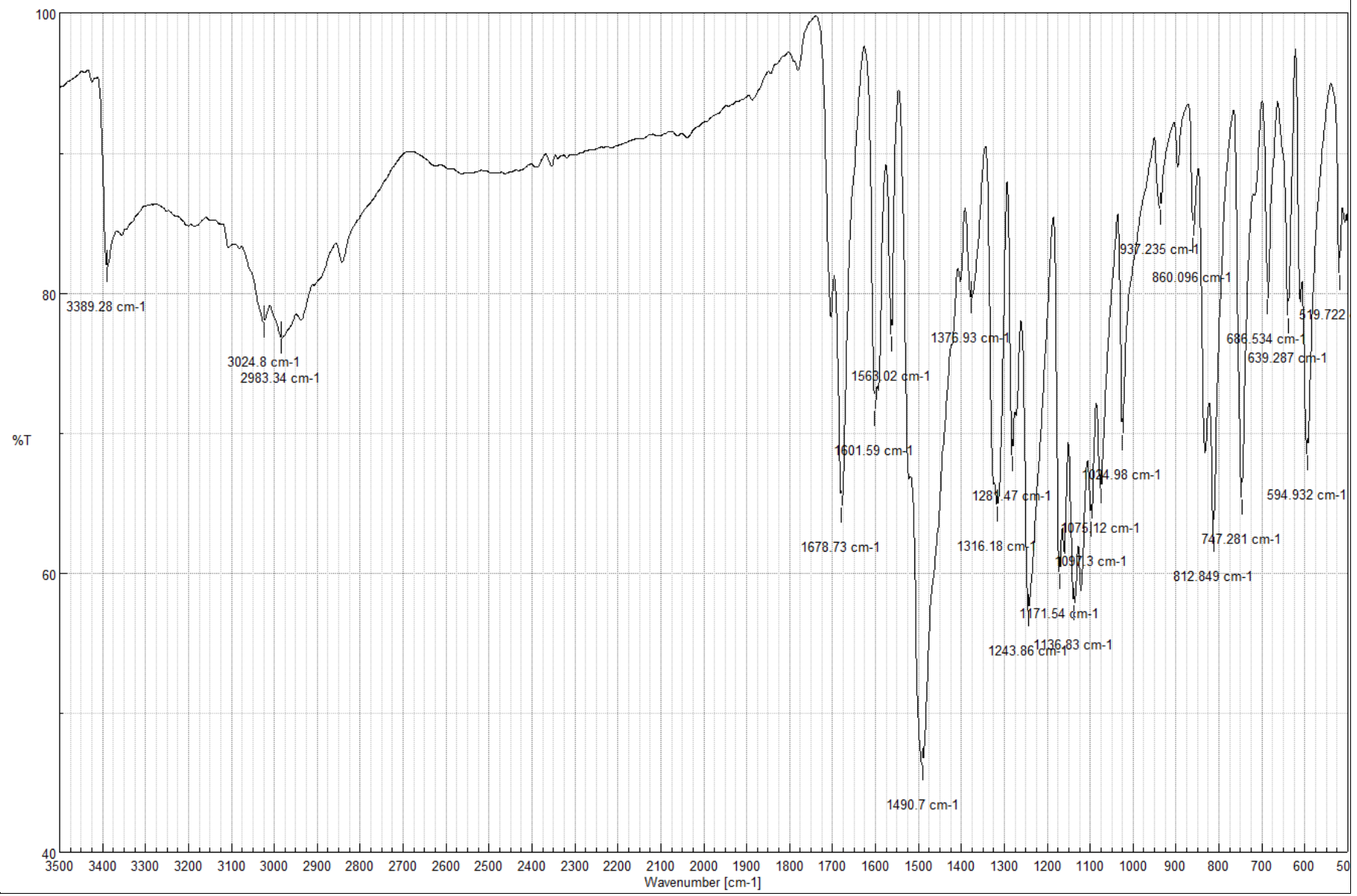
550.577 523.579 556.363 516.829	

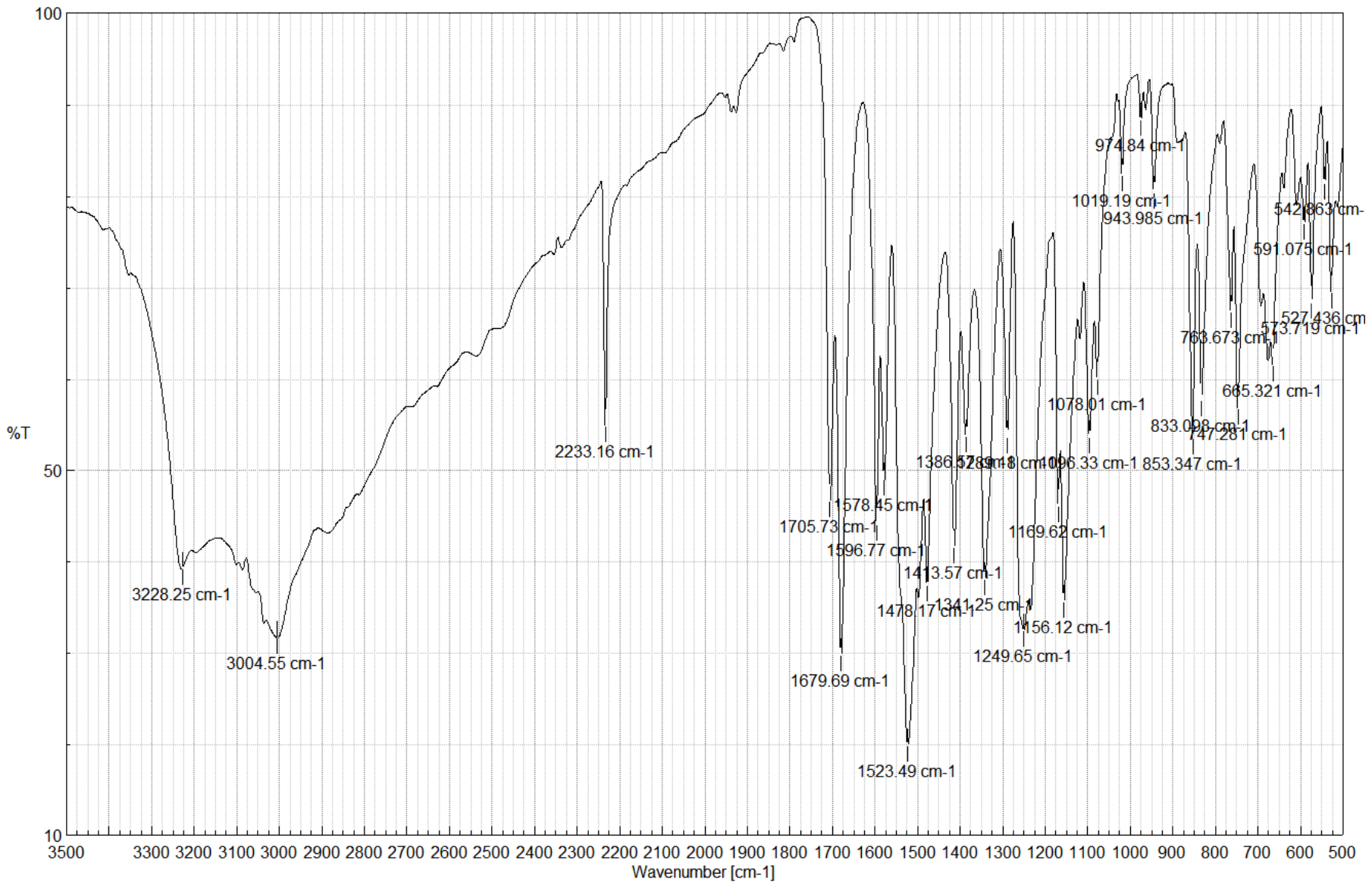
Wavenumber [cm-1]	**5-Bromo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3f)**
3186.79	
3000.69	
1701.87	
1678.73	
1596.77	
1577.49	
1514.81	
1480.1	
1417.42	
1341.25	
1292.07	
1256.4	
1155.15	
1097.3	
1014.37	
945.913	
895.773	
864.917	
839.847	
778.136	
758.852	
695.212	
593.004	
528.4	

Wavenumber [cm-1]	**5-Bromo-2-({[(2-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3g)**
3726.76	
3703.62	
3624.55	
3597.56	
3163.65	
3021.91	
2359.48	
2340.19	
2294.88	
1688.37	
1600.63	
1579.41	
1523.49	
1478.17	
1433.82	
1413.57	
1390.42	
1349.93	
1292.07	
1271.82	
1251.58	
1172.51	
1156.12	
1094.4	
1061.62	
948.806	
906.379	
865.882	
828.277	
784.886	
753.066	
730.889	
687.498	

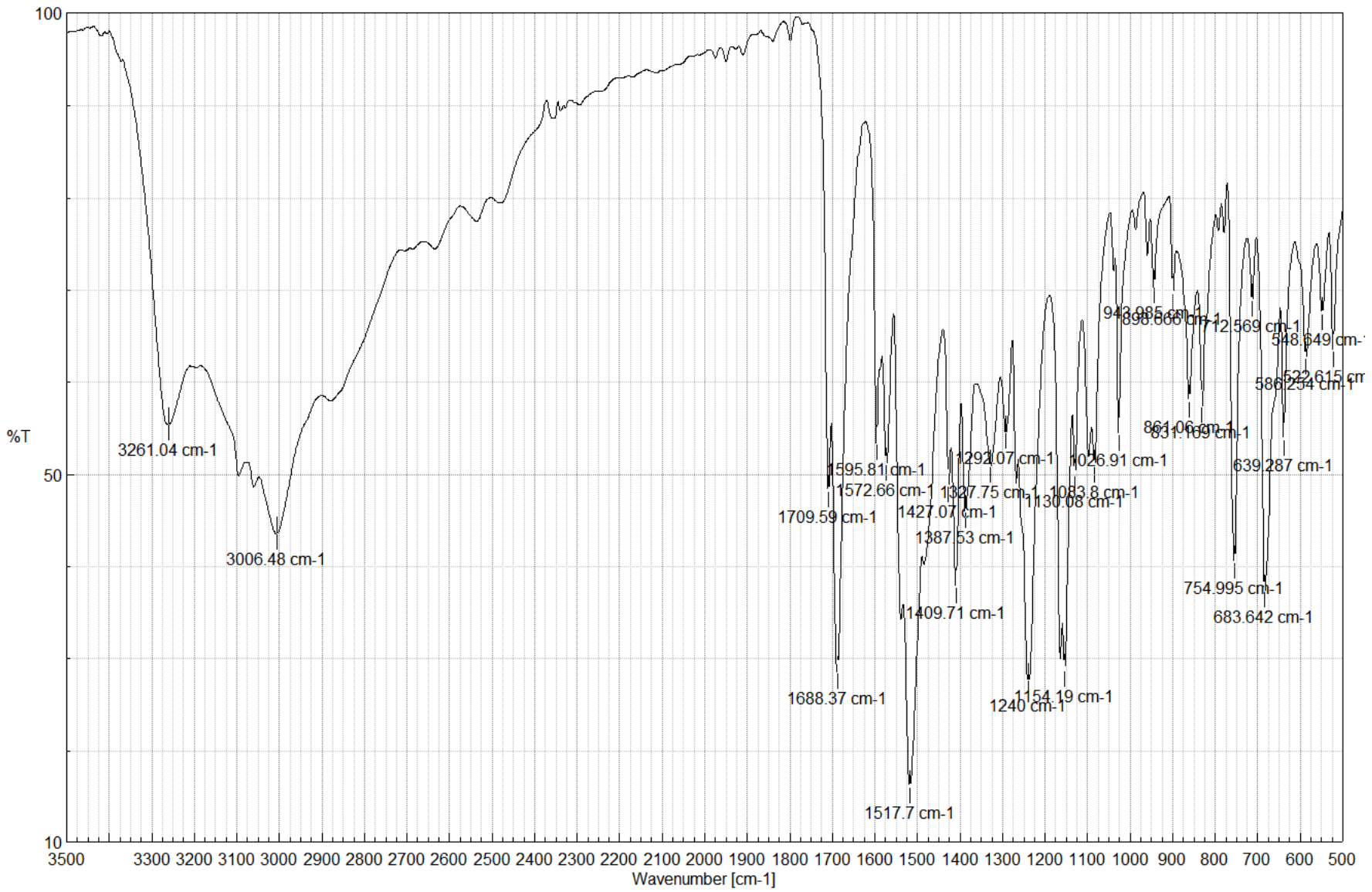


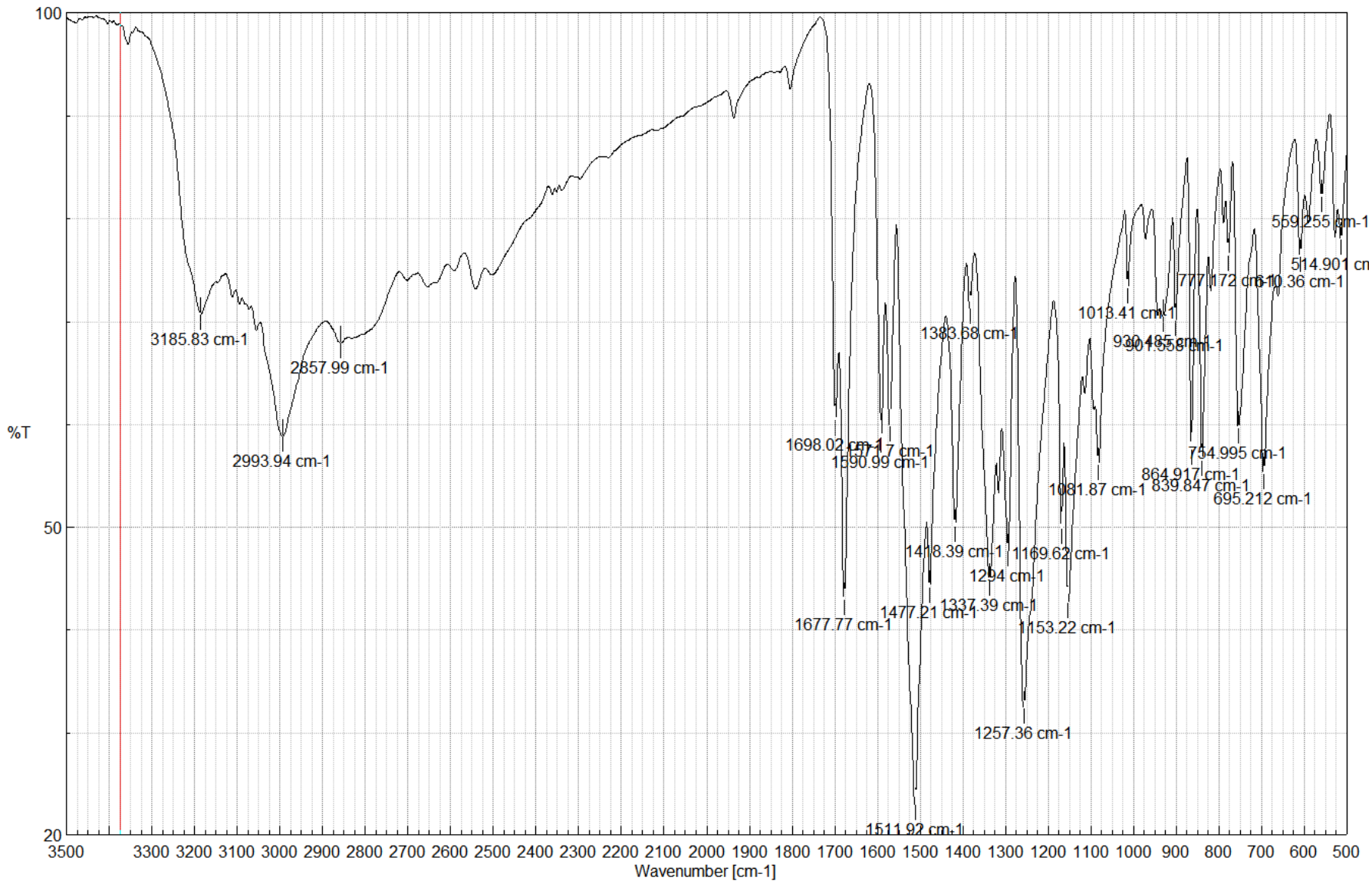
637.358 593.004 556.363 516.829	

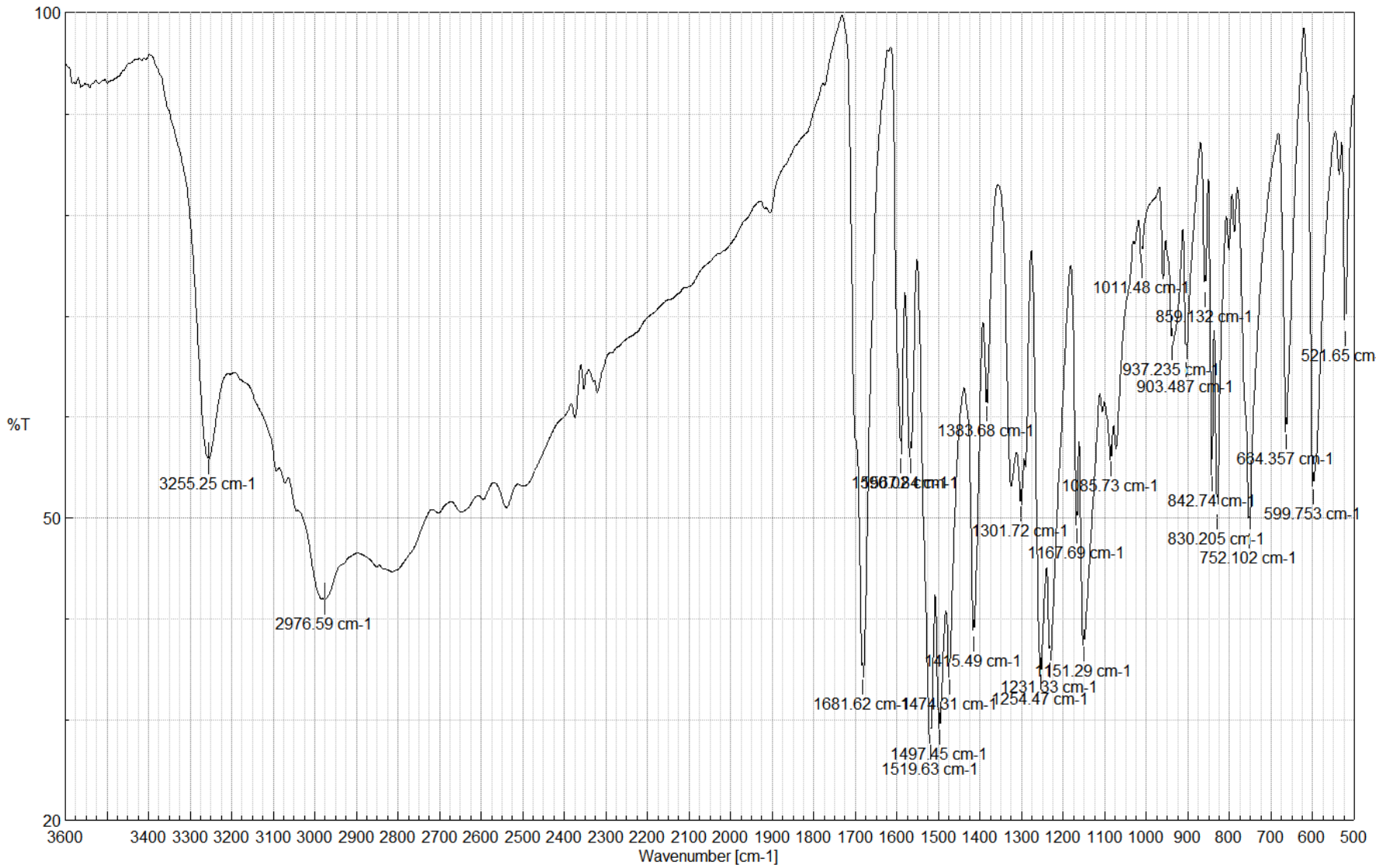
Wavenumber [cm-1]	**5-Bromo-2-({[(4-methoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3h)**
3389.28	
3024.80	
2983.34	
1678.73	
1601.59	
1563.02	
1490.7	
1376.93	
1316.18	
1281.47	
1243.86	
1171.54	
1136.83	
1097.3	
1075.12	
1024.98	
937.235	
860.096	
812.849	
747.281	
686.534	
639.287	
594.932	
519.722	

Wavenumber [cm-1]	**5-Bromo-2-({[(4-cyanophenyl)formamido]methanethioyl}amino)benzoic acid (3i)**
3228.25 3004.55 2233.16 1705.73 1679.69 1596.77 1578.45 1523.49 1478.17 1413.57 1386.57 1341.25 1289.18 1249.65 1169.62 1156.12 1096.33 1078.01 1019.19 974.84 943.985 853.347 833.098 763.673 747.281 665.321 591.075 573.719 542.863 527.436	

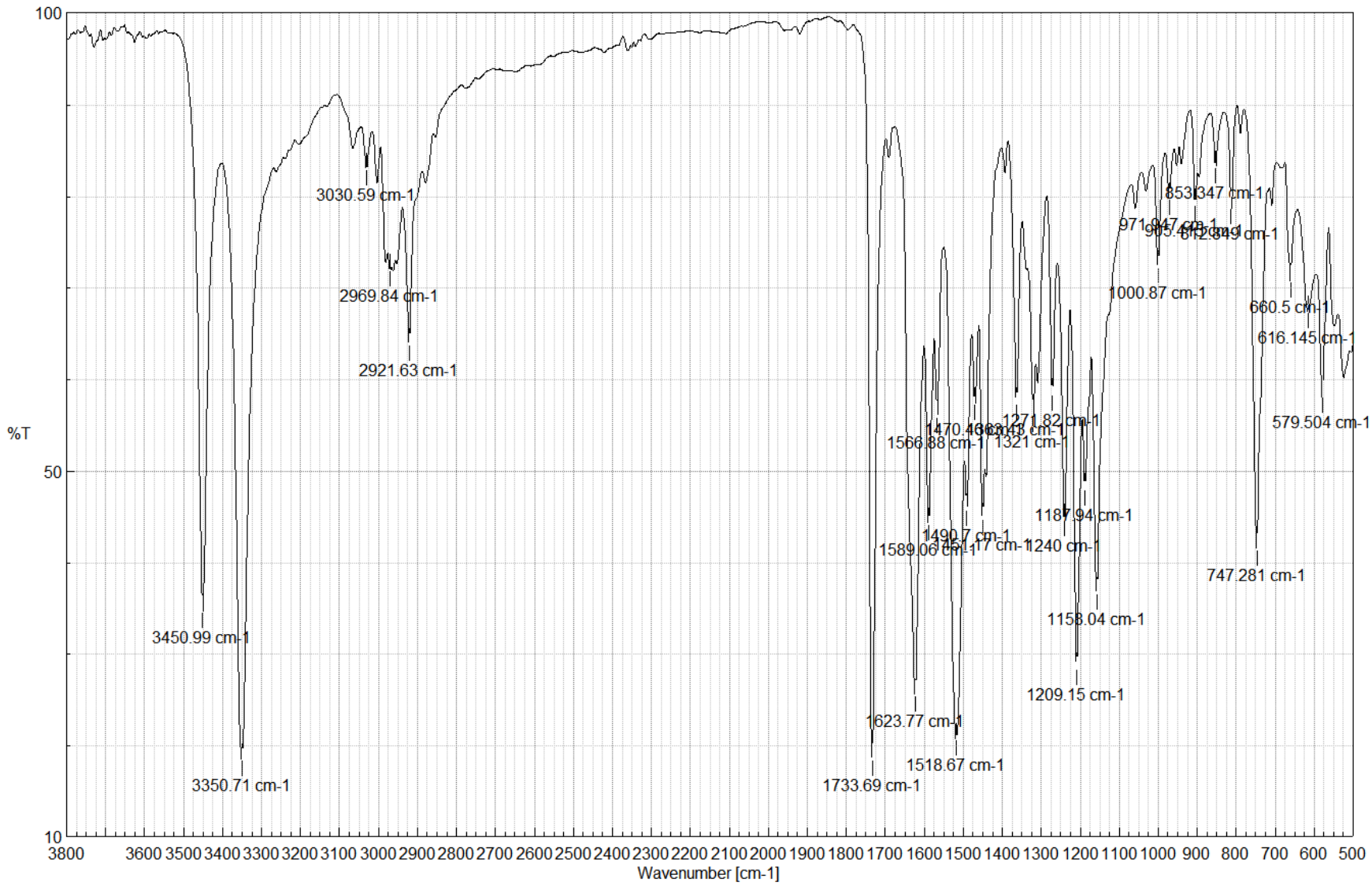
Wavenumber [cm-1]	**5-Bromo-2-({[(2-bromophenyl)formamido]methanethioyl}amino)benzoic acid (3j)**
3261.00	
3006.48	
1709.59	
1688.37	
1595.81	
1572.66	
1517.7	
1427.07	
1409.71	
1387.53	
1327.75	
1292.07	
1240.0	
1154.19	
1130.08	
1083.8	
1026.91	
943.985	
898.666	
861.06	
831.169	
754.995	
712.569	
683.642	
639.287	
586.254	
548.649	
522.615	

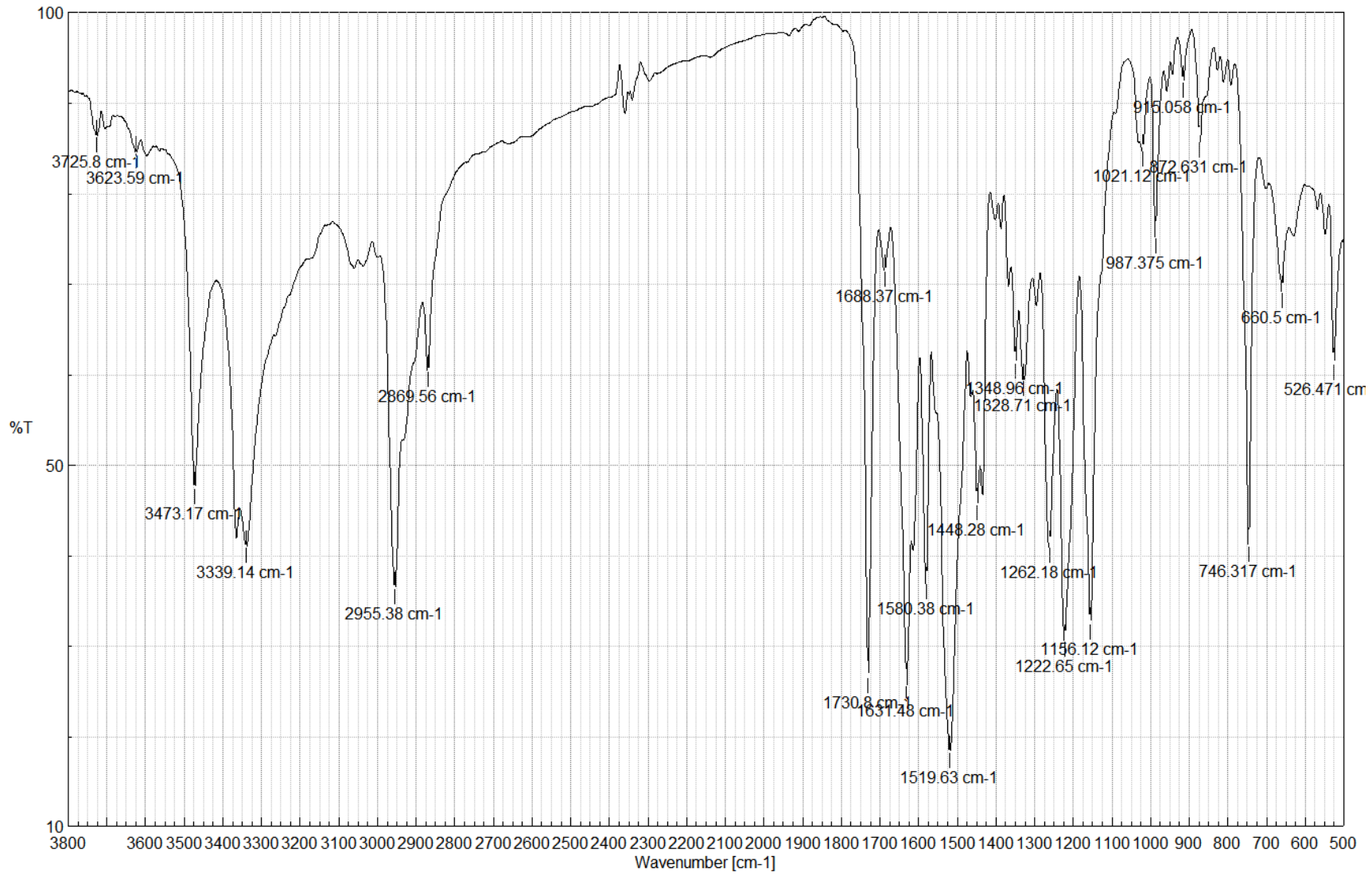


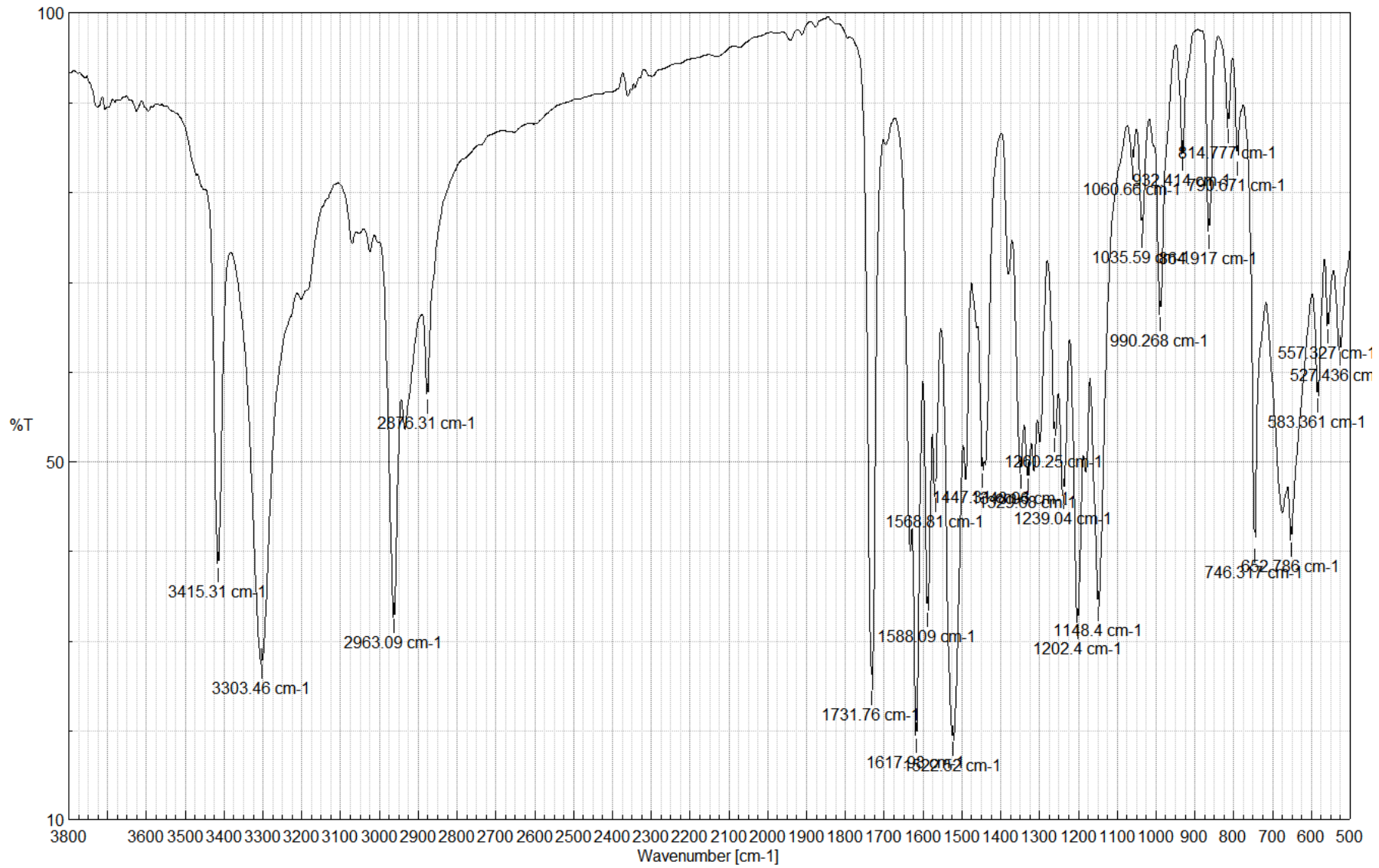
Wavenumber [cm-1]	**5-Iodo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3k)**
3185.83	
2993.94	
2857.99	
1698.02	
1677.77	
1590.99	
1571.7	
1511.92	
1477.21	
1418.39	
1383.68	
1337.39	
1294.0	
1257.36	
1169.62	
1153.22	
1081.87	
1013.41	
930.485	
901.558	
864.917	
839.847	
777.172	
754.995	
695.212	
610.36	
559.255	
514.901	

Wavenumber [cm-1]	**5-Iodo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3l)**
3255.25	
2976.59	
1681.62	
1590.02	
1567.84	
1519.63	
1497.45	
1474.31	
1415.49	
1383.68	
1301.72	
1254.47	
1231.33	
1167.69	
1151.29	
1085.73	
1011.48	
937.235	
903.487	
859.132	
842.74	
830.205	
752.102	
664.357	
599.753	
521.65	

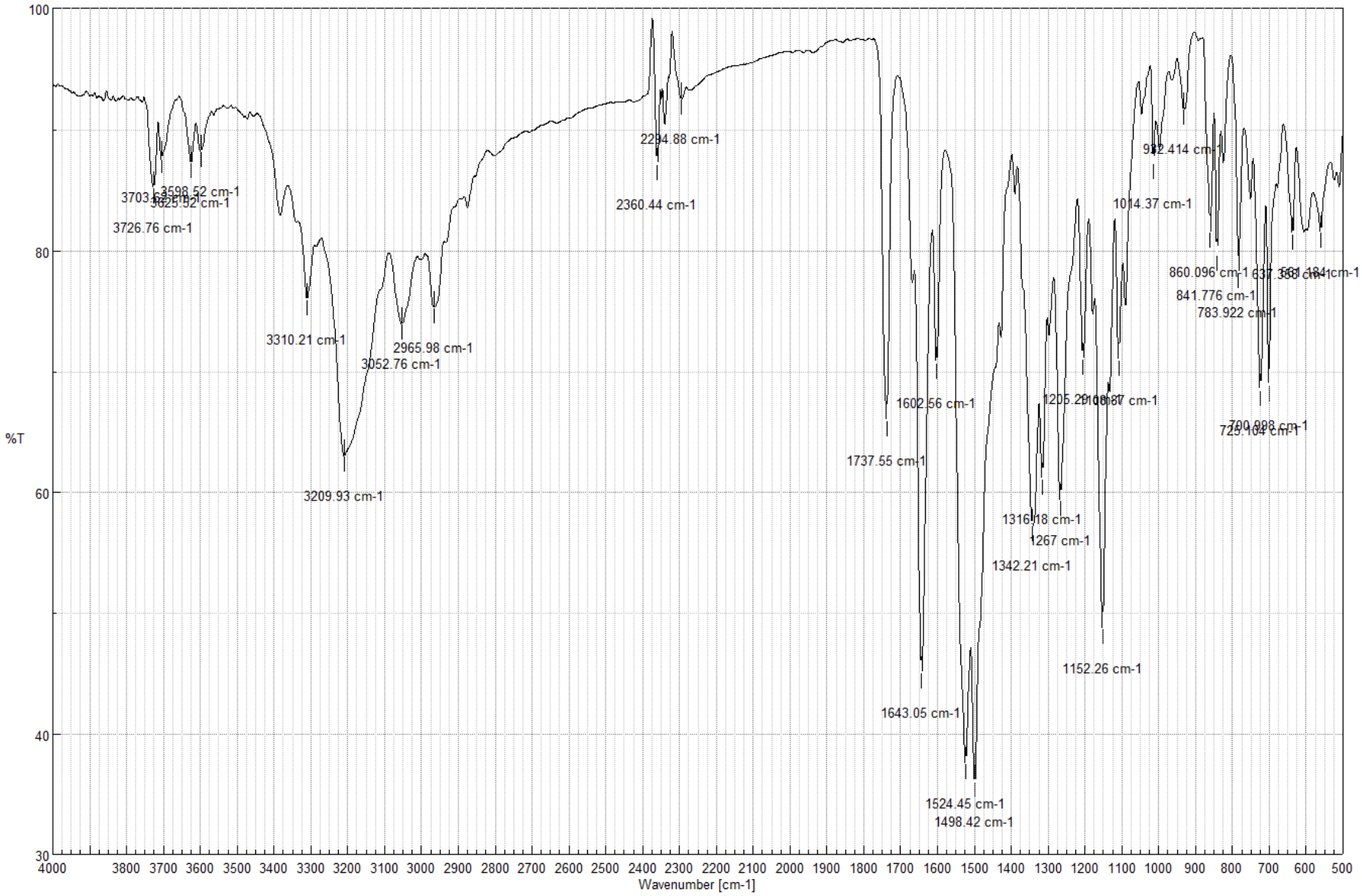
Wavenumber [cm-1]	**(2*S*)-*N*-(2-Aminobenzoyl)-2-isopropylaminoacetic acid methyl ester (9a)**
3450.99	
3350.71	
3030.59	
2969.84	
2921.63	
1733.69	
1623.77	
1589.06	
1566.88	
1518.67	
1490.7	
1470.46	
1451.17	
1363.43	
1321.0	
1271.82	
1240.0	
1209.15	
1187.94	
1158.04	
1000.87	
971.947	
905.415	
853.347	
812.849	
747.281	
660.5	
616.145	
579.504	

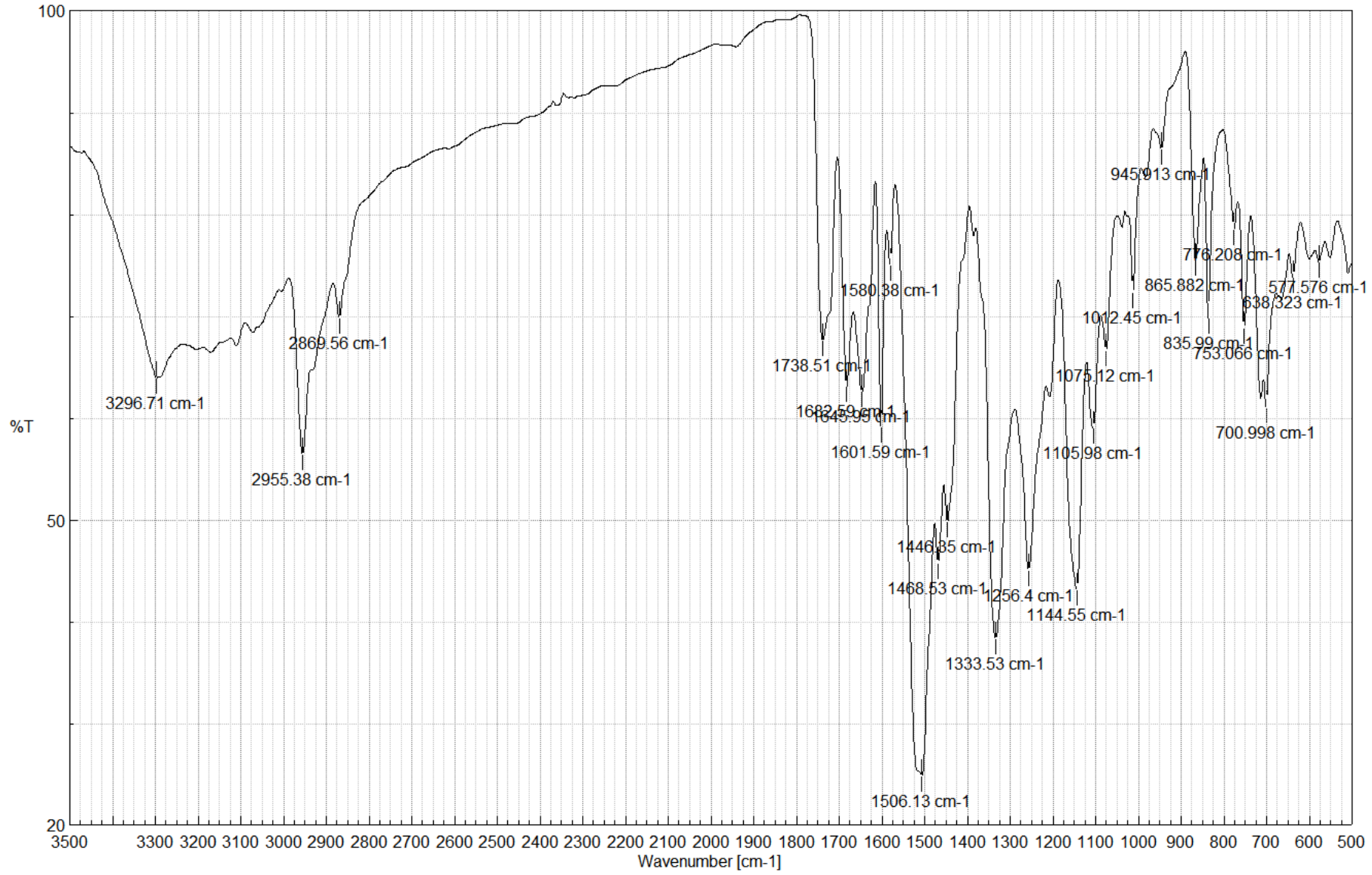


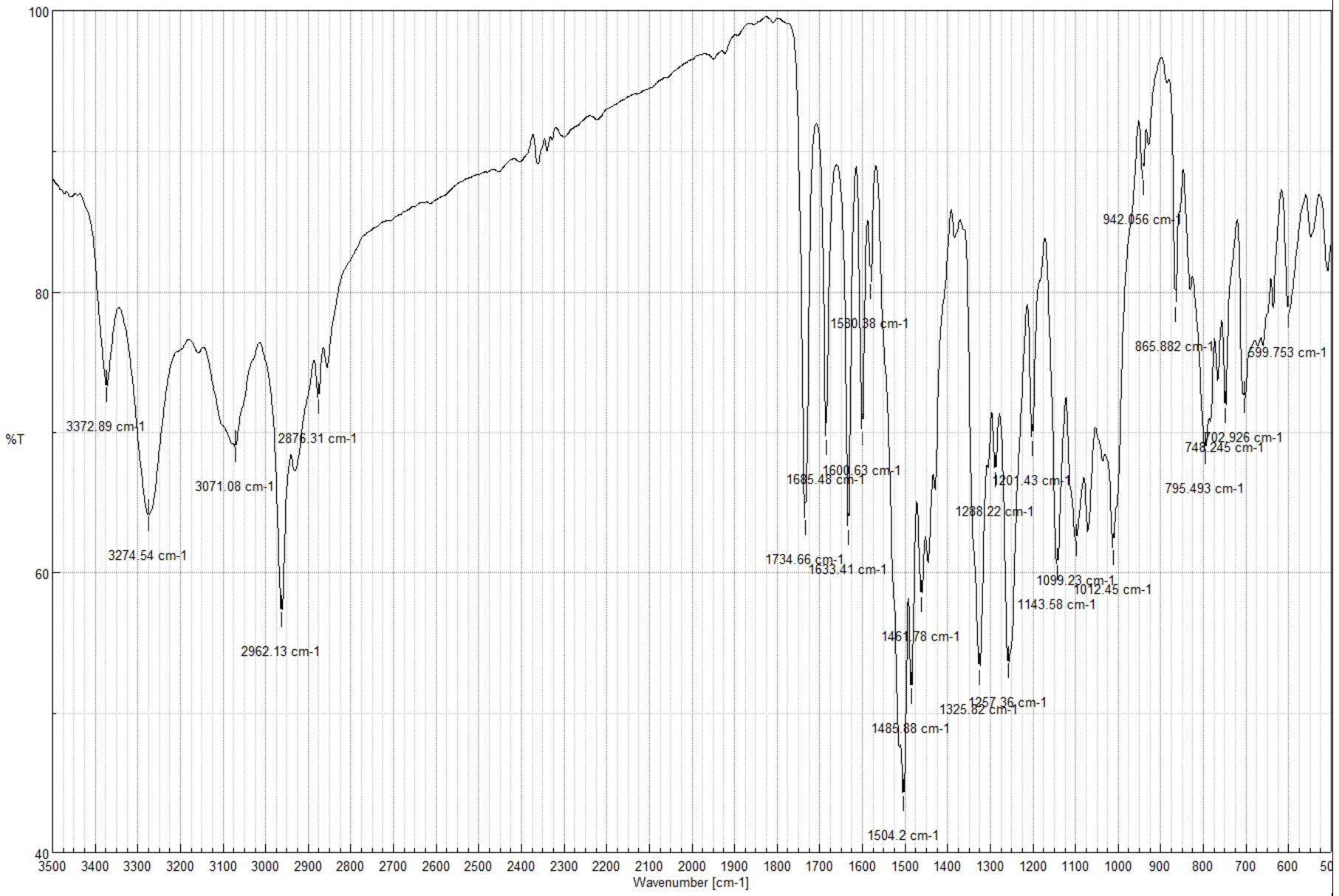
Wavenumber [cm-1]	**(2*S*)-*N*-(2-Aminobenzoyl)-2-isobutylaminoacetic acid methyl ester (9b)**
3725.8 3623.59 3473.17 3339.14 2955.38 2869.56 1730.8 1688.37 1631.48 1580.38 1519.63 1448.28 1348.96 1328.71 1262.18 1222.65 1156.12 1021.12 987.375 915.058 872.631 746.317 660.5 526.471	

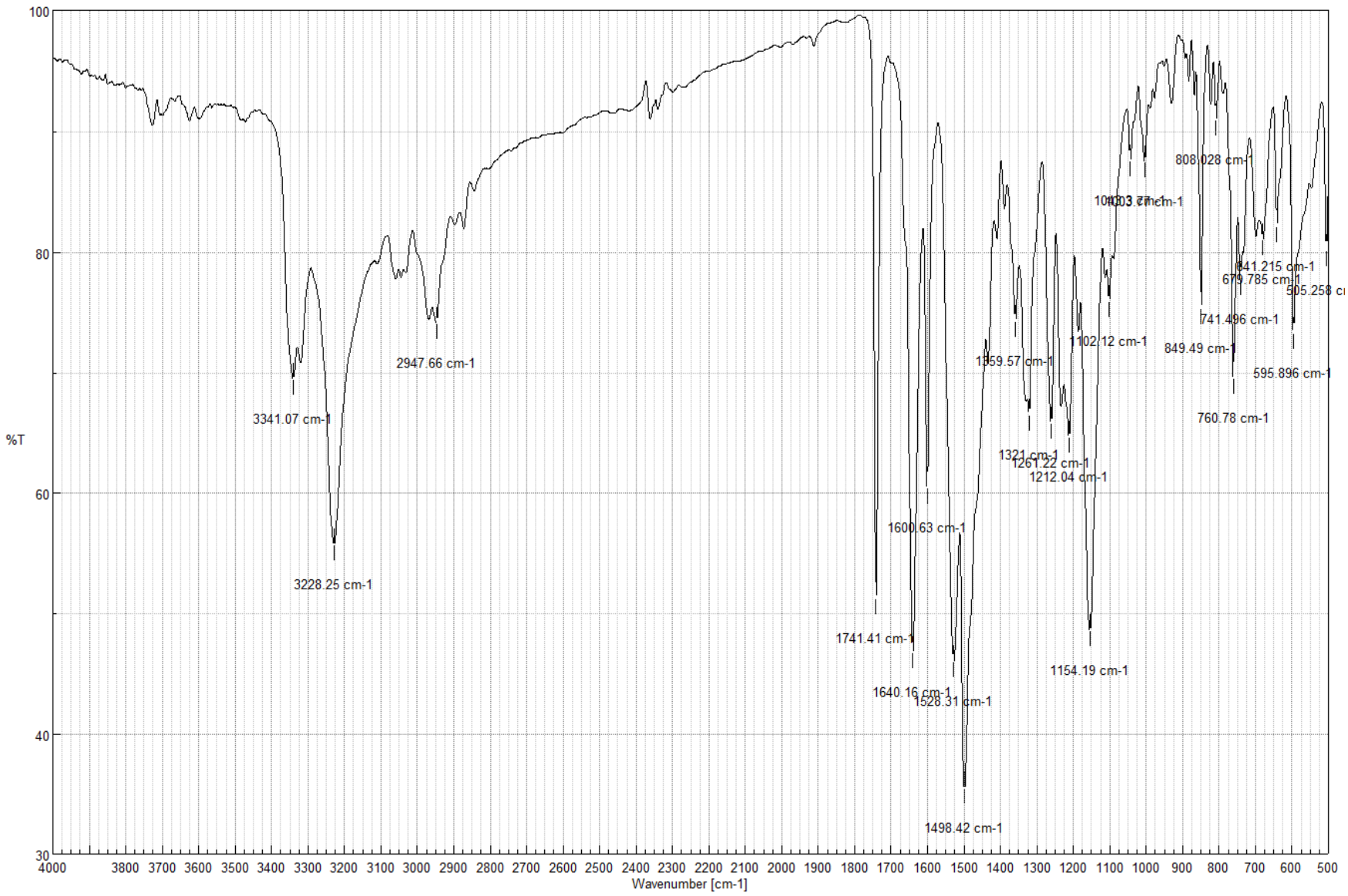
Wavenumber [cm-1]	**(2*S*)-*N*-(2-Aminobenzoyl)-2-(2-methylbutyl)aminoacetic acid methyl ester (9c)**
3415.31 3303.46 2963.09 2876.31 1731.76 1617.98 1588.09 1568.81 1522.52 1447.31 1348.96 1329.68 1260.25 1239.04 1202.4 1148.4 1060.66 1035.59 990.268 932.414 864.917 814.777 790.671 746.317 652.786 583.361 557.327 527.436	

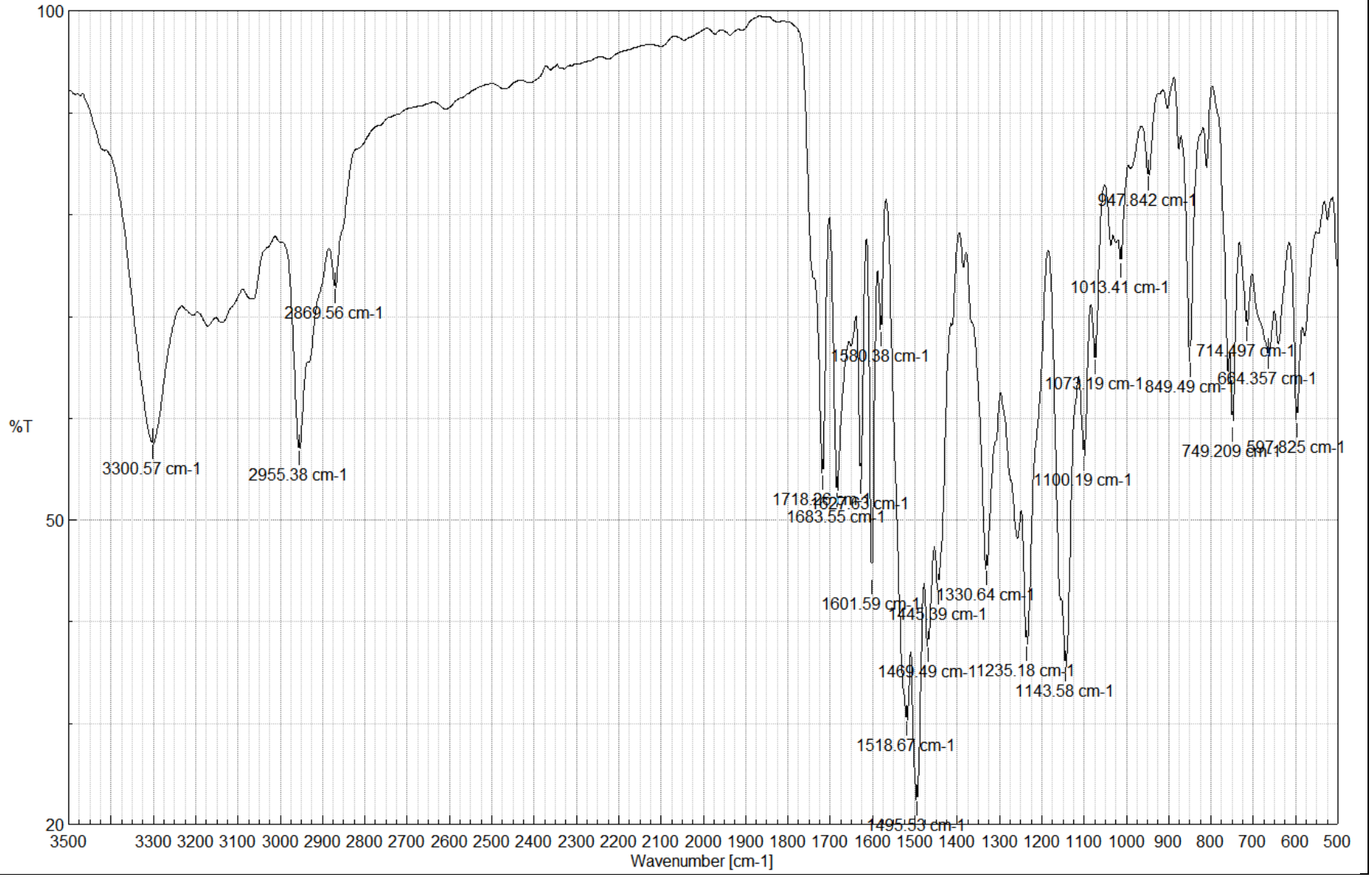
Wavenumber [cm-1]	**Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}butanoate (10a)**
3726.76	
3703.62	
3625.52	
3598.52	
3310.21	
3209.93	
3052.76	
2965.98	
2360.44	
2294.88	
1737.55	
1643.05	
1602.56	
1524.45	
1498.42	
1342.21	
1316.18	
1267.0	
1205.29	
1152.26	
1108.87	
1014.37	
932.414	
860.096	
841.776	
783.922	
725.104	
700.998	
637.358	
561.184	



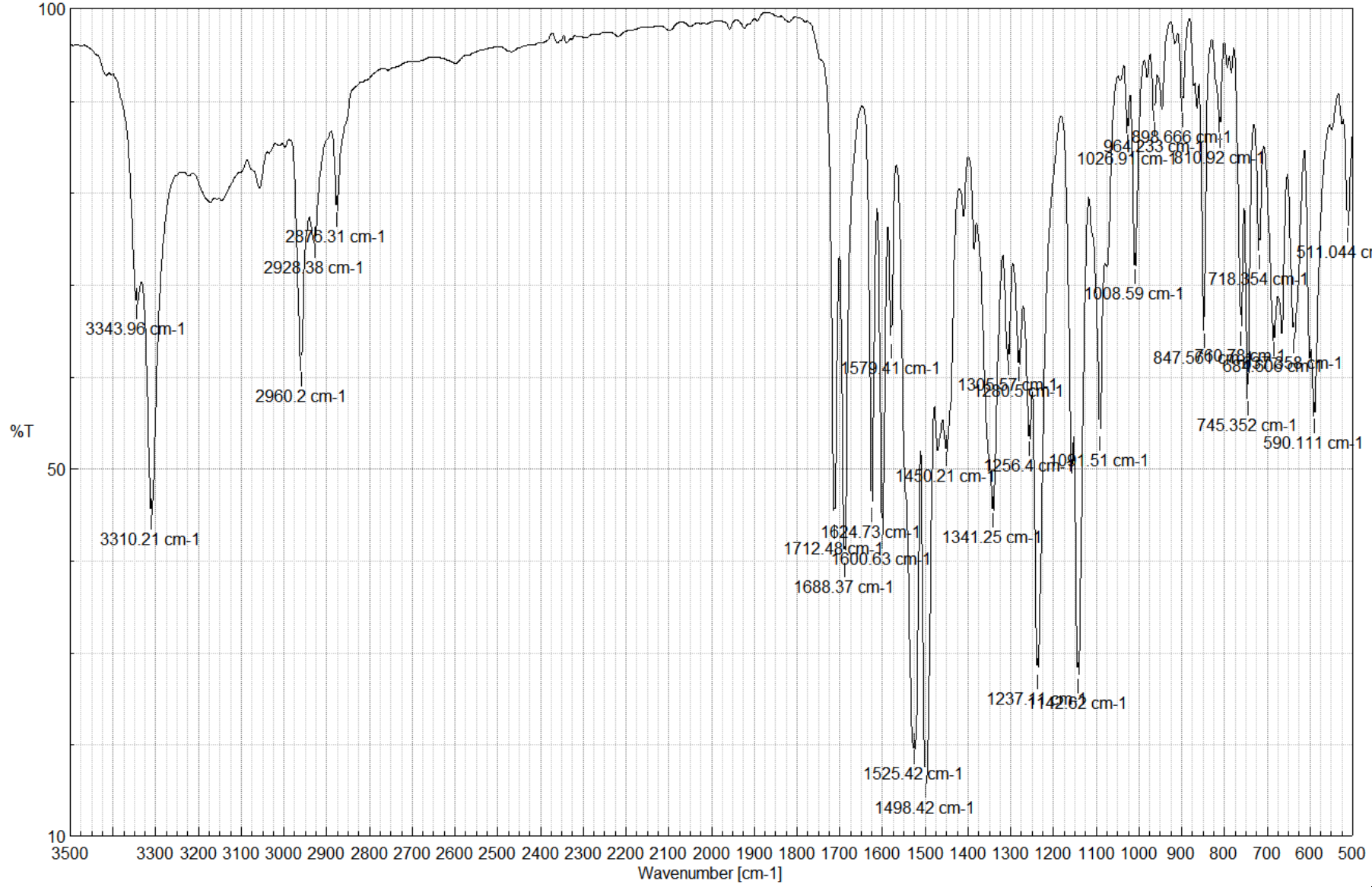
Wavenumber [cm-1]	**Methyl (2*S*)-4-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (10b)**
3296.71 2955.38 2869.56 1738.51 1682.59 1645.95 1601.59 1580.38 1506.13 1468.53 1446.35 1333.53 1256.4 1144.55 1105.98 1075.12 1012.45 945.913 865.882 835.99 776.208 753.066 700.998 638.323 577.576	

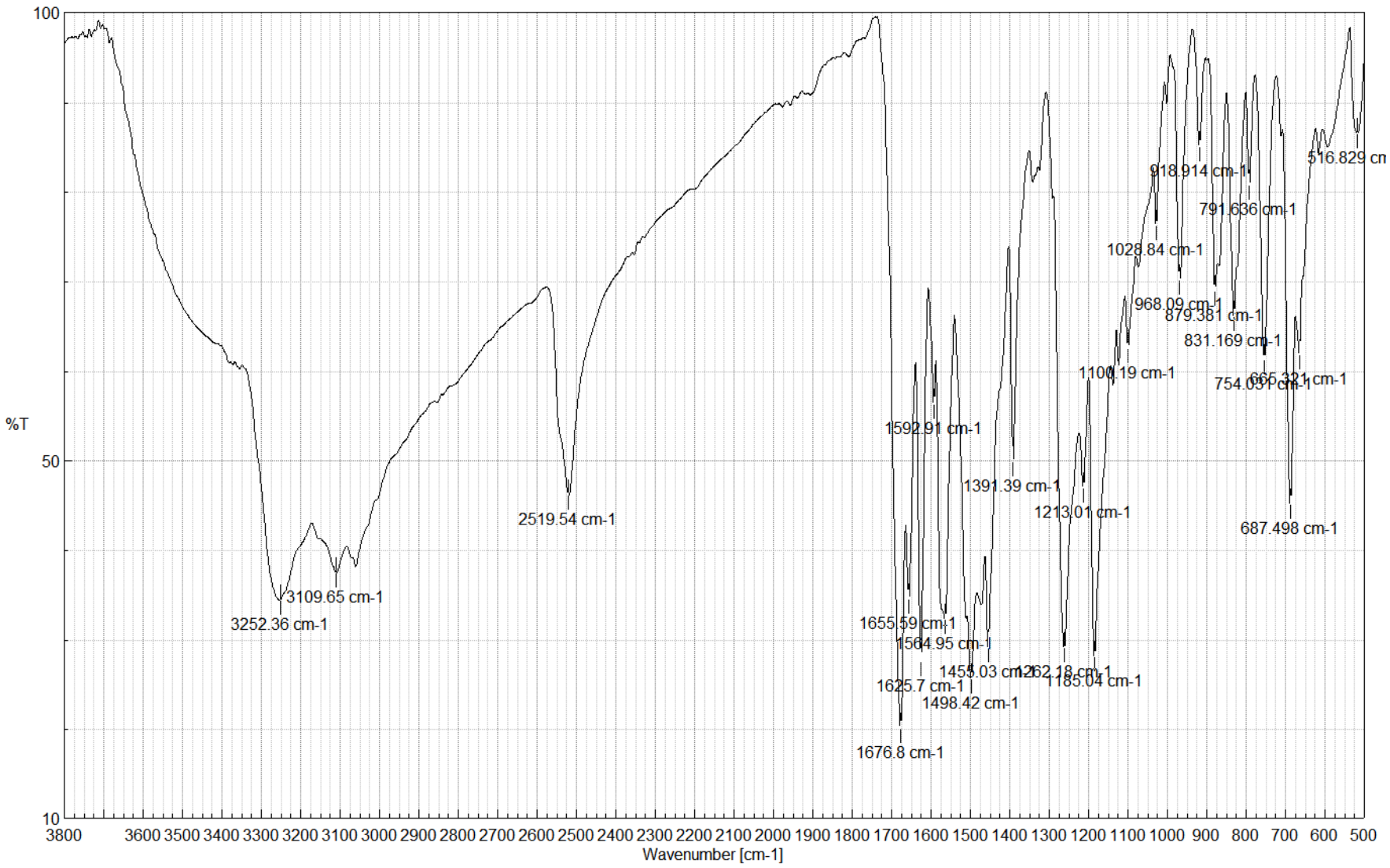
Wavenumber [cm-1]	**Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (10c)**
3372.89 3274.54 3071.08 2962.13 2876.31 1734.66 1685.48 1633.41 1600.63 1580.38 1504.2 1485.88 1461.78 1325.82 1288.22 1257.36 1201.43 1143.58 1099.23 1012.45 942.056 865.882 795.493 748.245 702.926 599.753	

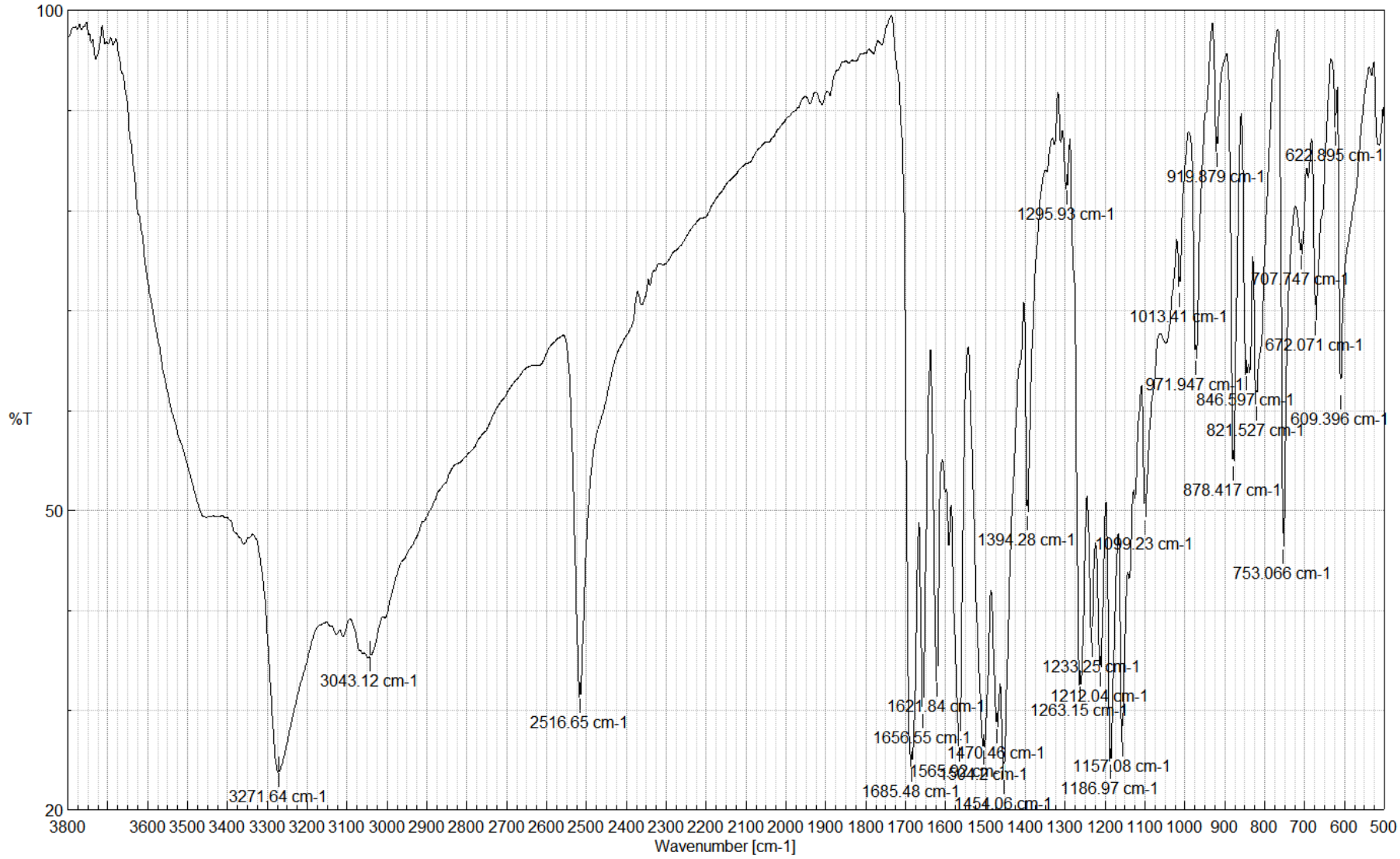
Wavenumber [cm-1]	**Methyl-(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylbutanoate (10d)**
3341.07	
3228.25	
2947.66	
1741.41	
1640.16	
1600.63	
1528.31	
1498.42	
1359.57	
1321	
1261.22	
1212.04	
1154.19	
1102.12	
1043.3	
1003.77	
849.49	
808.028	
760.78	
741.496	
679.785	
641.215	
595.896	
505.258	

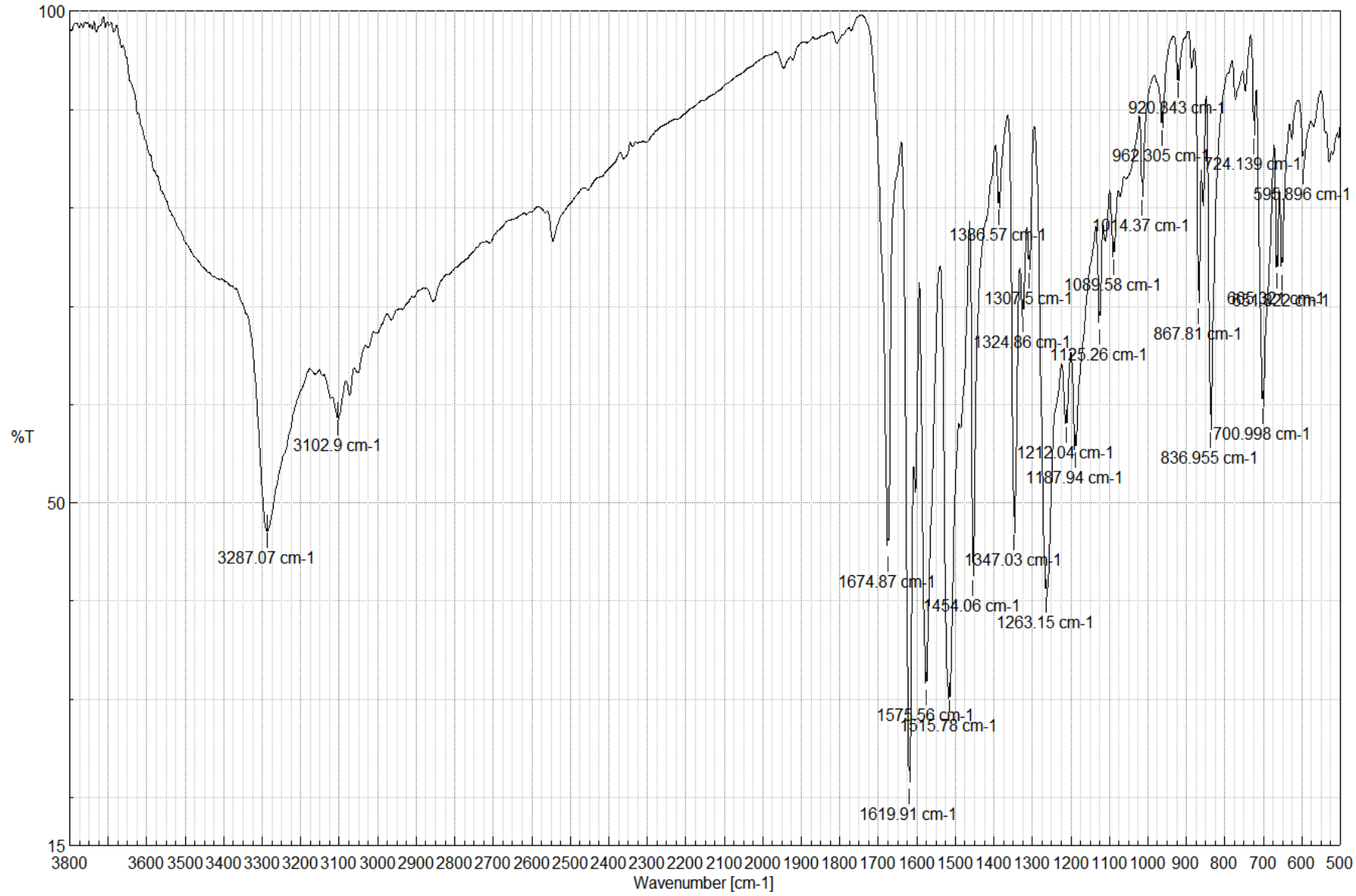
Wavenumber [cm-1]	**Methyl-(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-4-methylpentanoate (10e)**
3300.57 2955.38 2869.56 1718.26 1683.55 1627.63 1601.59 1580.38 1518.67 1495.53 1469.49 1445.39 1330.64 1235.18 1143.58 1100.19 1073.19 1013.41 947.842 849.49 749.209 714.497 664.357 597.825	

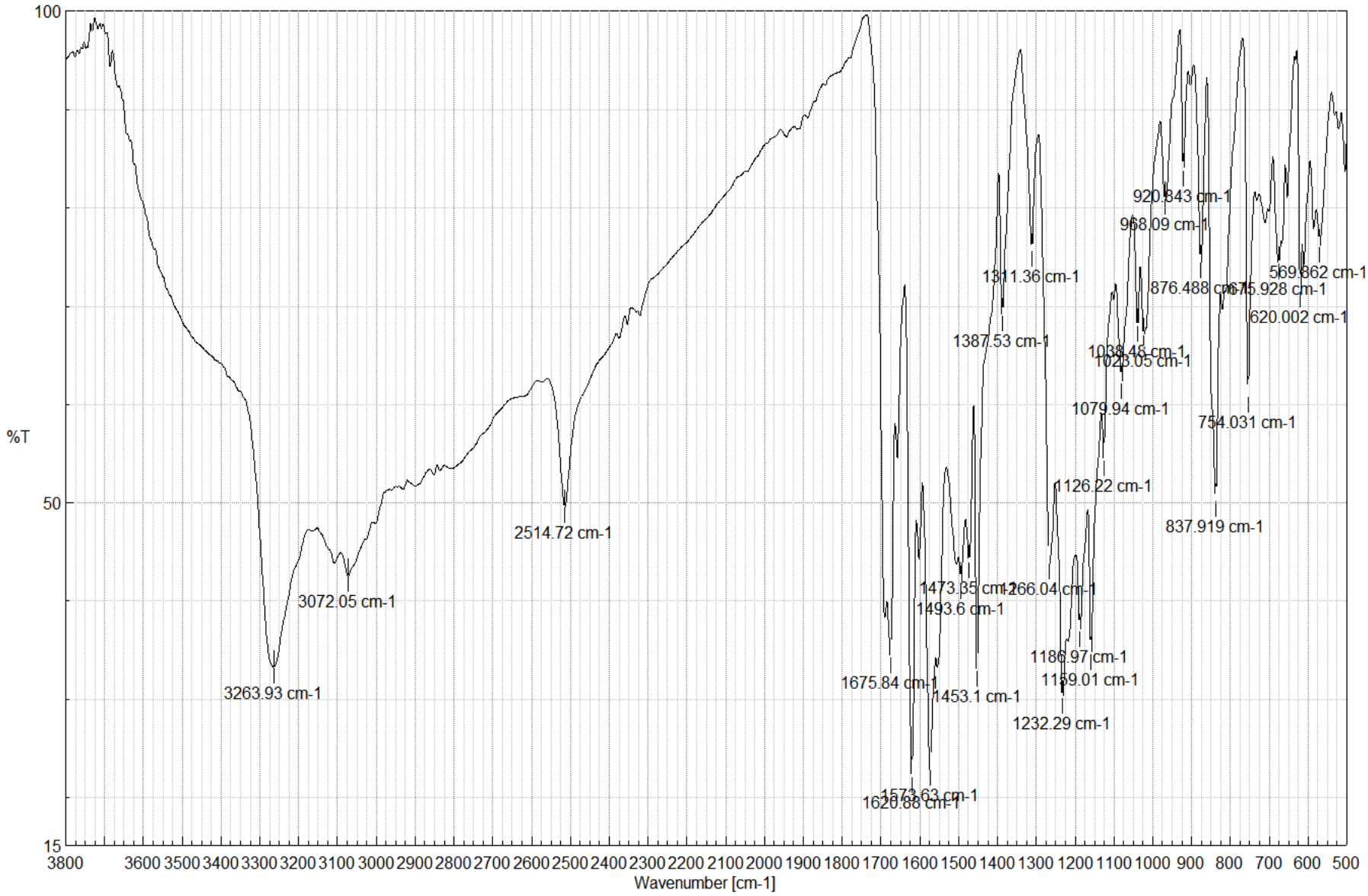
Wavenumber [cm-1]	**Methyl (2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylpentanoate (10f)**
3343.96	
3310.21	
2960.20	
2928.38	
2876.31	
1712.48	
1688.37	
1624.73	
1600.63	
1579.41	
1525.42	
1498.42	
1450.21	
1341.25	
1305.57	
1280.5	
1256.4	
1237.11	
1142.62	
1091.51	
1026.91	
1008.59	
964.233	
898.666	
847.561	
810.92	
760.78	
745.352	
718.354	
684.606	
637.358	
590.111	
511.044	



Wavenumber [cm-1]	***N*-(6-Bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11a)**
3252.36 3109.65 2519.54 1676.8 1655.59 1625.7 1592.91 1564.95 1498.42 1455.03 1391.39 1262.18 1213.01 1185.04 1100.19 1028.84 968.09 918.914 879.381 831.169 791.636 754.031 687.498 665.321 516.829	

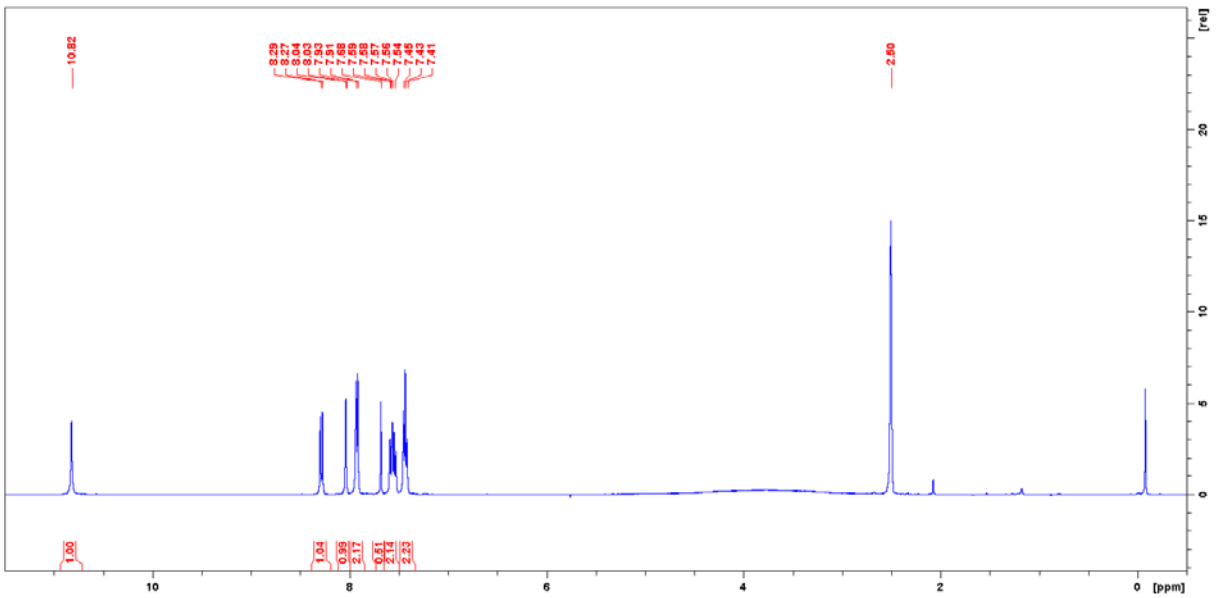
Wavenumber [cm-1]	**4-Fluoro-*N*-(6-bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11b)**
3271.64	
3043.12	
2516.65	
1685.48	
1656.55	
1621.84	
1565.92	
1504.2	
1470.46	
1454.06	
1394.28	
1295.93	
1263.15	
1233.25	
1212.04	
1186.97	
1157.08	
1099.23	
1013.41	
971.947	
919.879	
878.417	
846.597	
821.527	
753.066	
707.747	
672.071	
622.895	
609.396	

Wavenumber [cm-1]	**4-Nitro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11c)**
3287.07	
3102.9	
1674.87	
1619.91	
1575.56	
1515.78	
1454.06	
1386.57	
1347.03	
1324.86	
1307.5	
1263.15	
1212.04	
1187.94	
1125.26	
1089.58	
1014.37	
962.305	
920.843	
867.81	
836.955	
724.139	
700.998	
665.321	
651.822	
595.896	

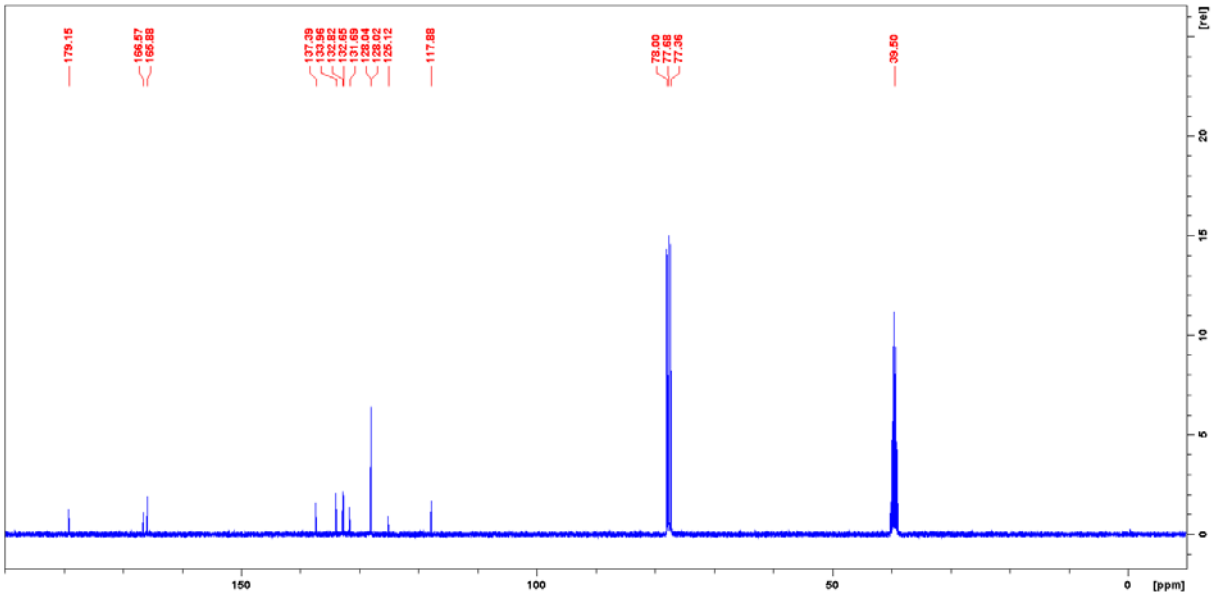
Wavenumber [cm-1]	**4-Fluoro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11d)**
3263.93	
3072.05	
2514.72	
1675.84	
1620.88	
1573.63	
1493.6	
1473.35	
1453.1	
1387.53	
1311.36	
1266.04	
1232.29	
1186.97	
1159.01	
1126.22	
1079.94	
1038.48	
1023.05	
968.09	
920.843	
876.488	
837.919	
754.031	
675.928	
620.002	
569.862	

5-Bromo-2-{[(phenylformamido)methanethioyl]amino}benzoic acid (3a)

1H

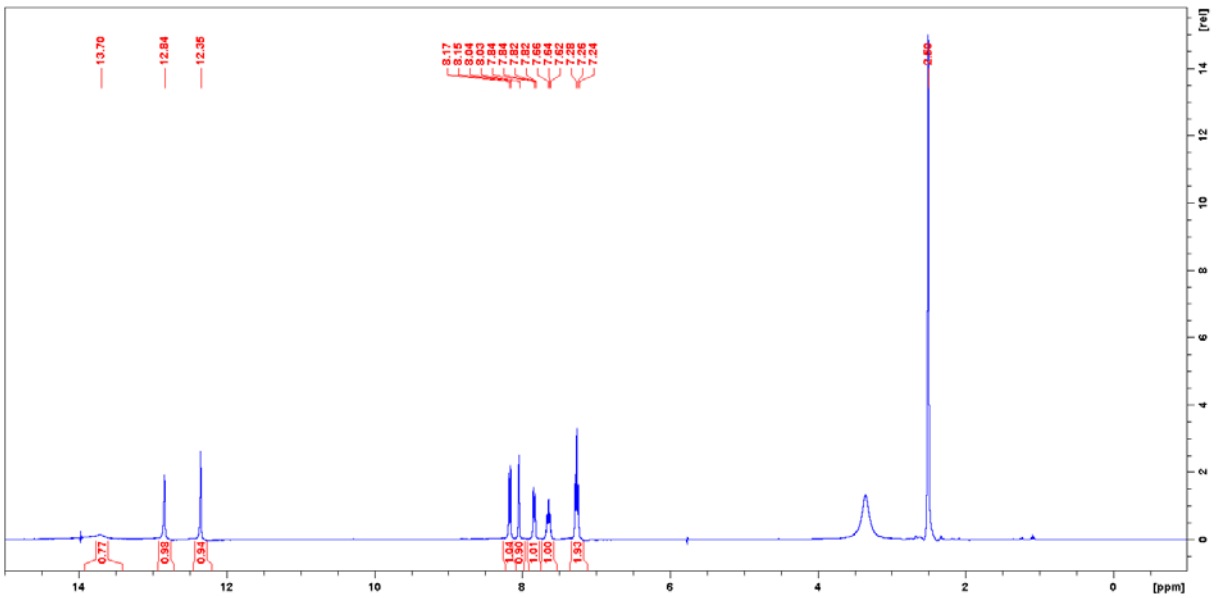


13C

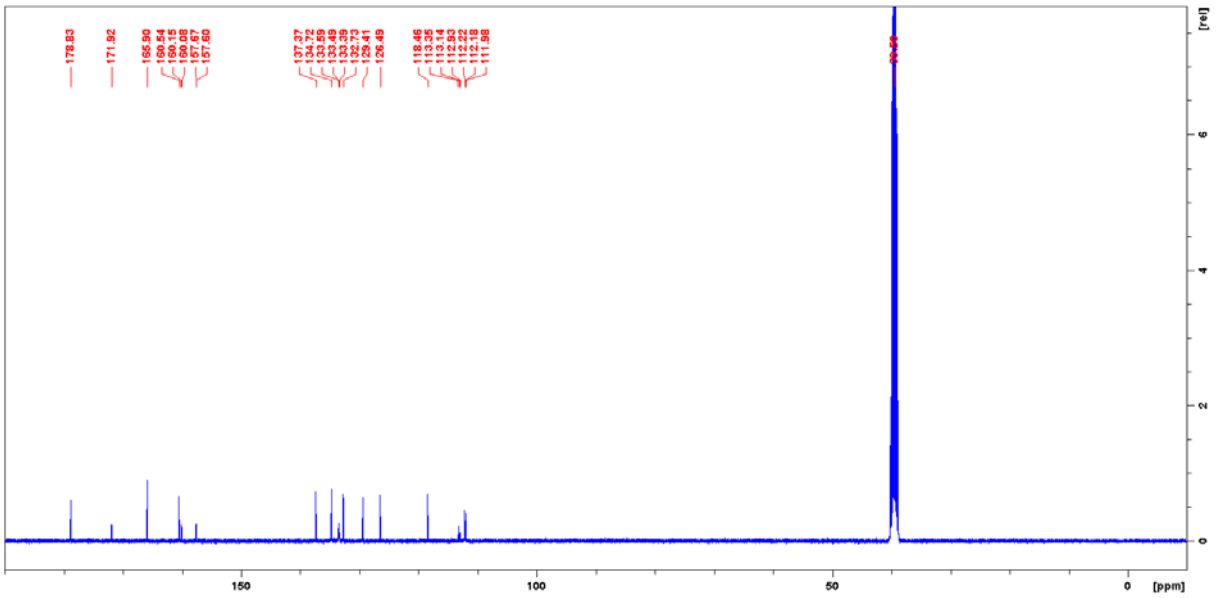


5-Bromo-2-({[(2,6-difluorophenyl)formamido]methanethioyl}amino)benzoic acid (3b)

1H

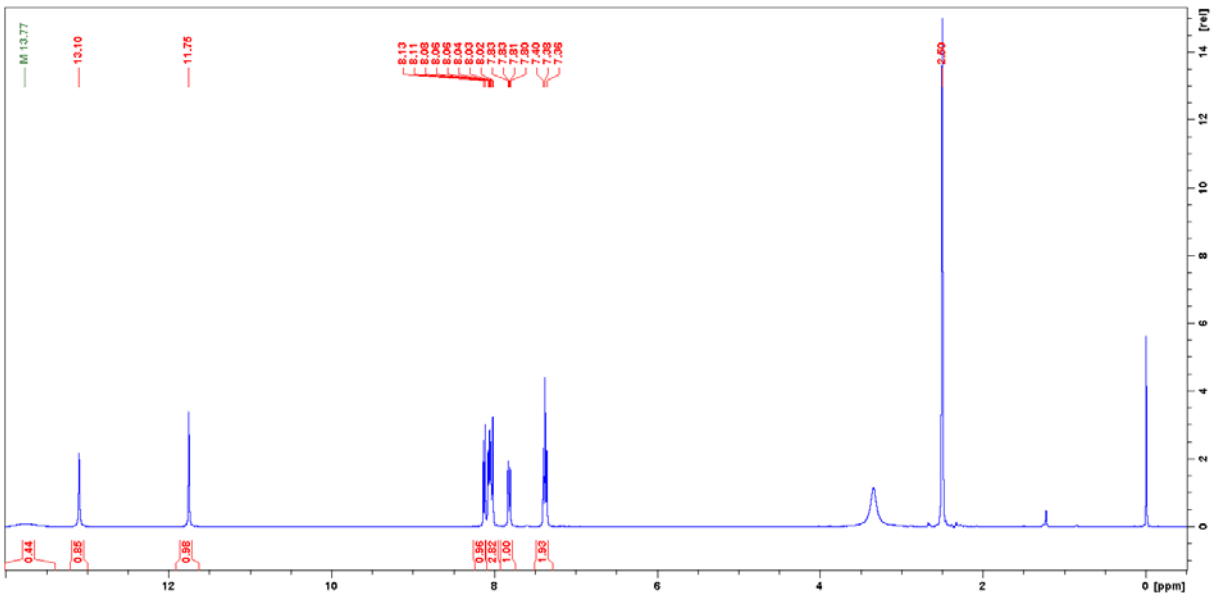


13C

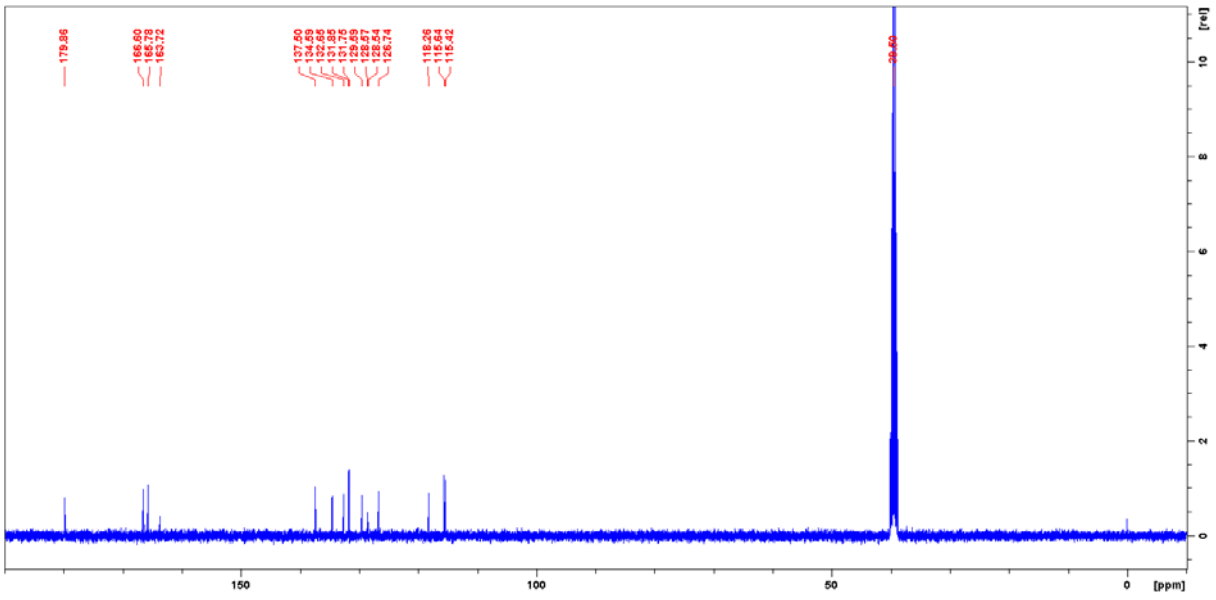


5-Bromo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3c)

1H

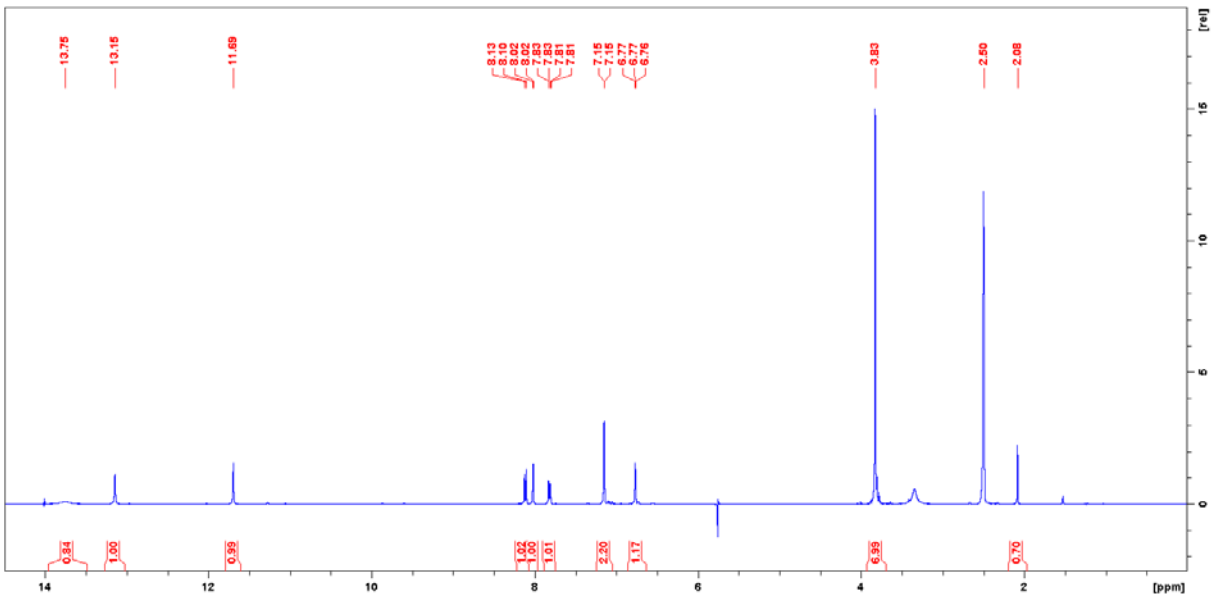


13C

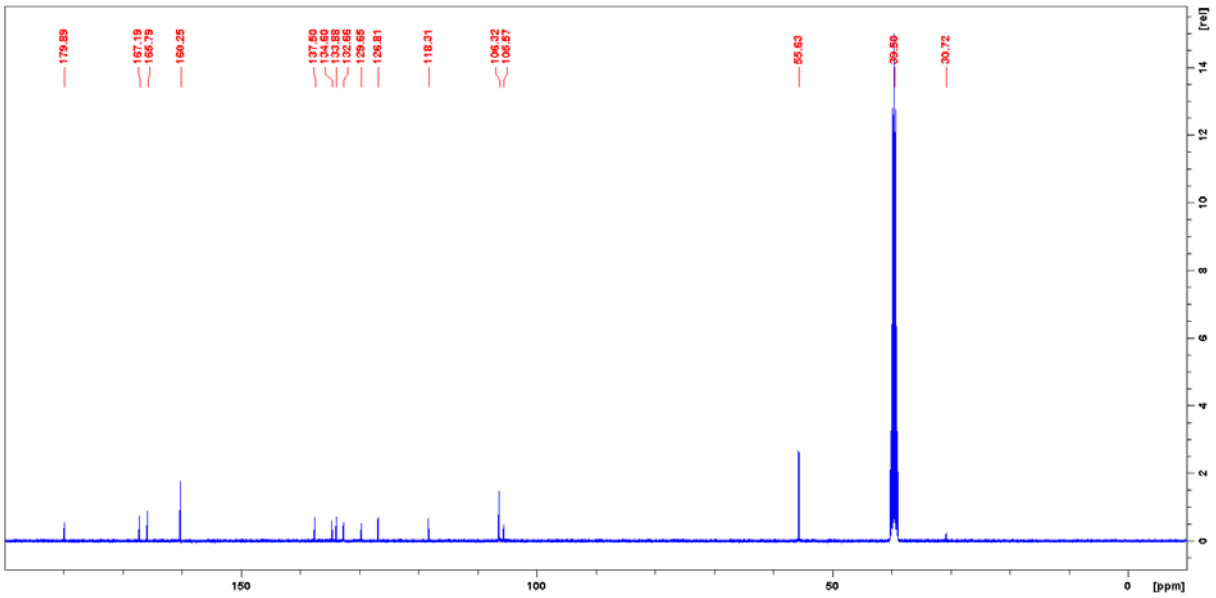


5-Bromo-2-({[(3,5-dimethoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3d)

1H

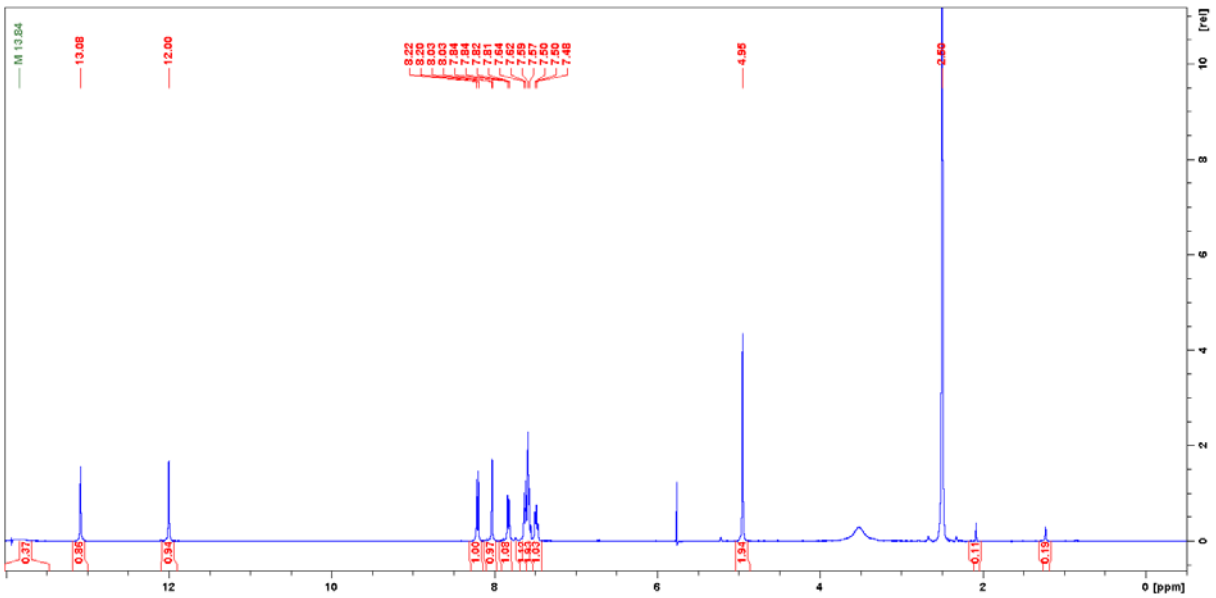


13C



5-bromo-2-[({[2-(chloromethyl)phenyl]formamido}methanethioyl)amino]benzoic acid (3e)

1H



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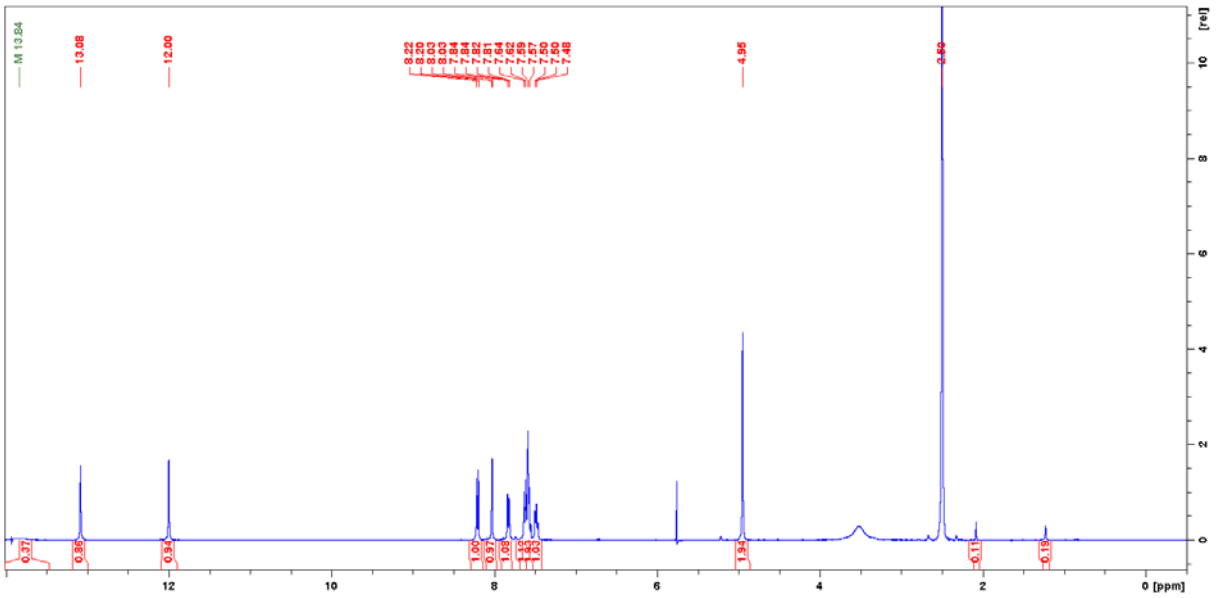
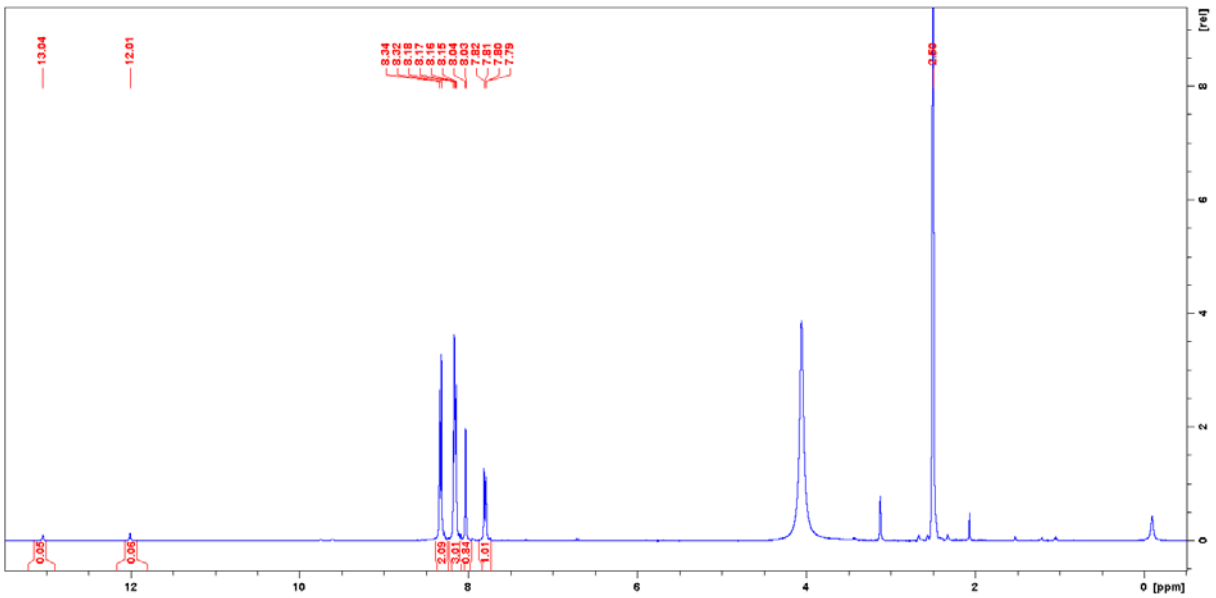


5-Bromo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3f)

1H



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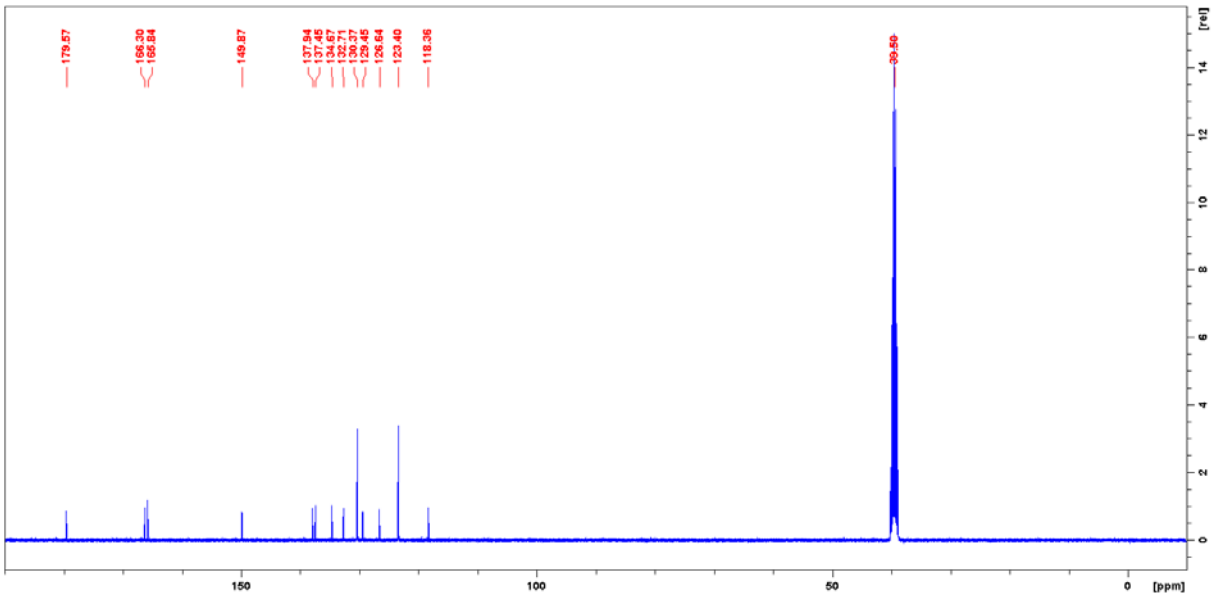
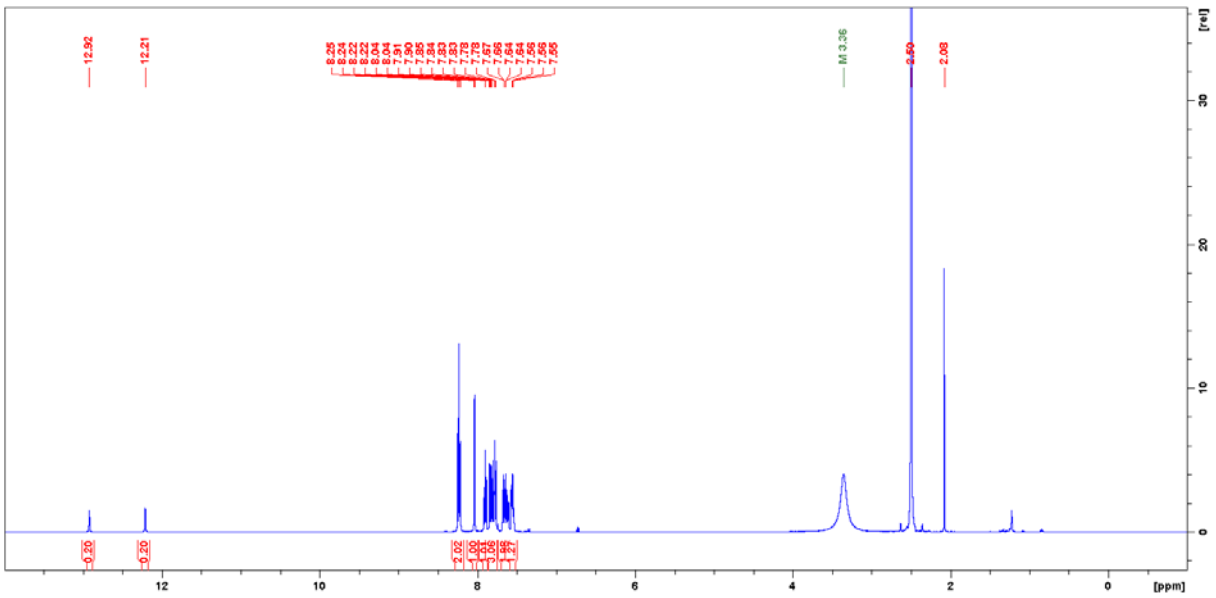
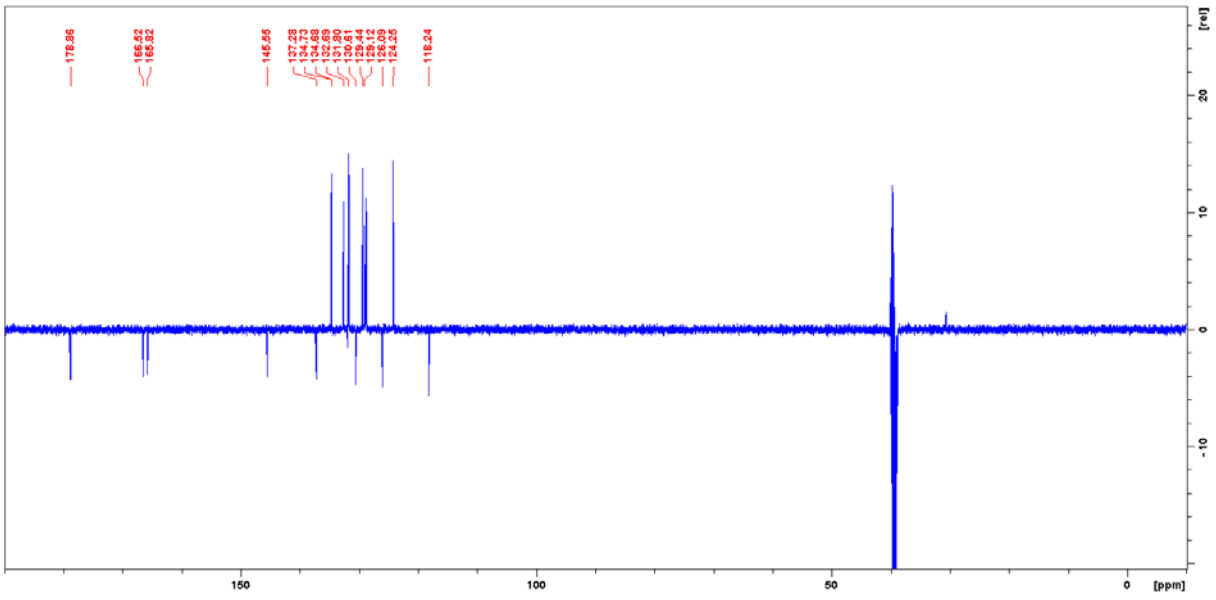


5-Bromo-2-({[(2-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3g)

1H

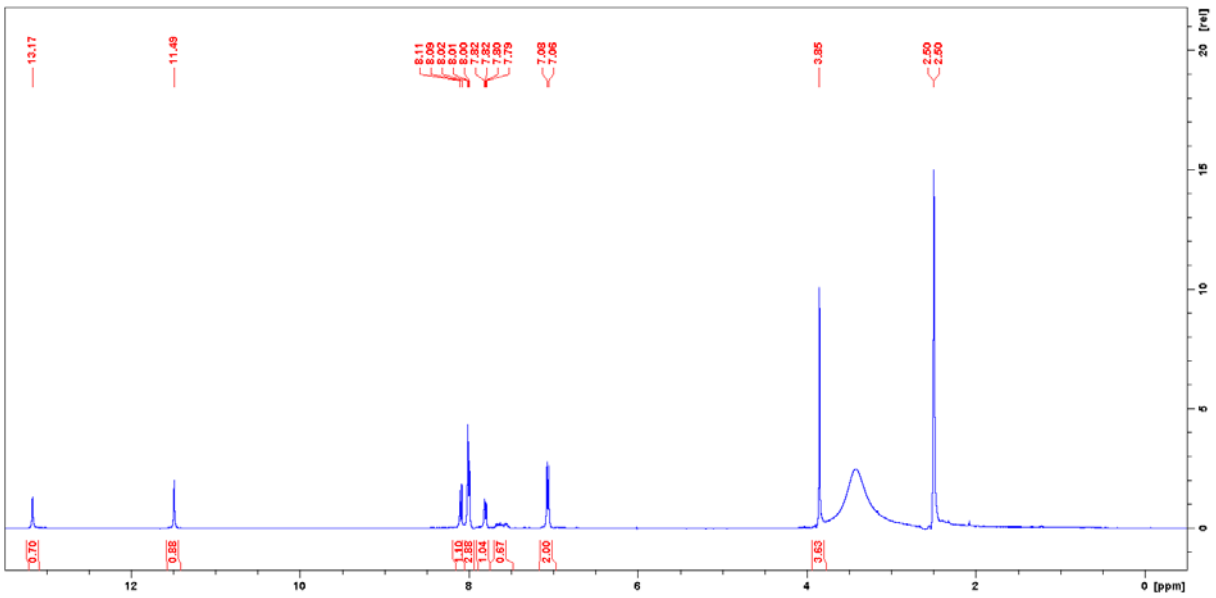


13C

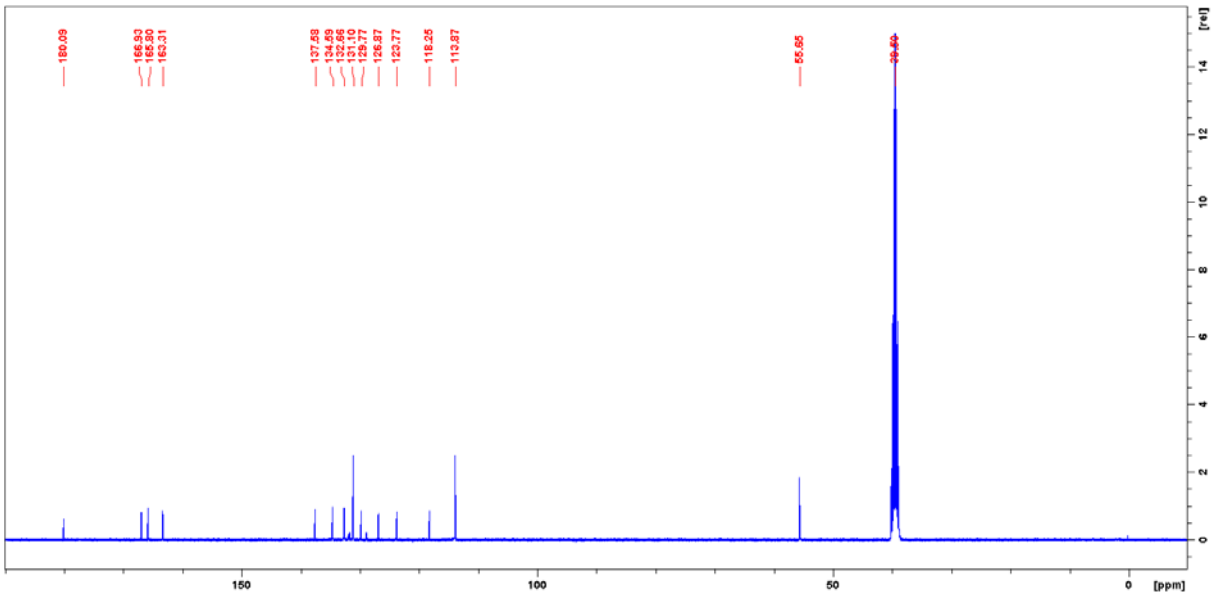


5-Bromo-2-({[(4-methoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3h)

1H

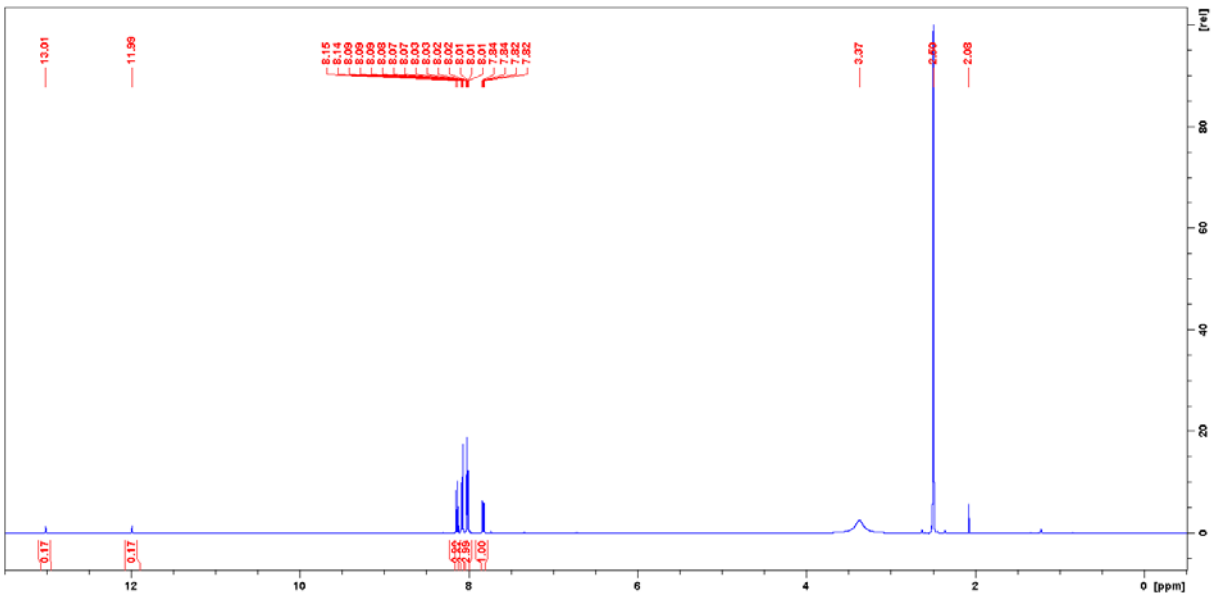


13C

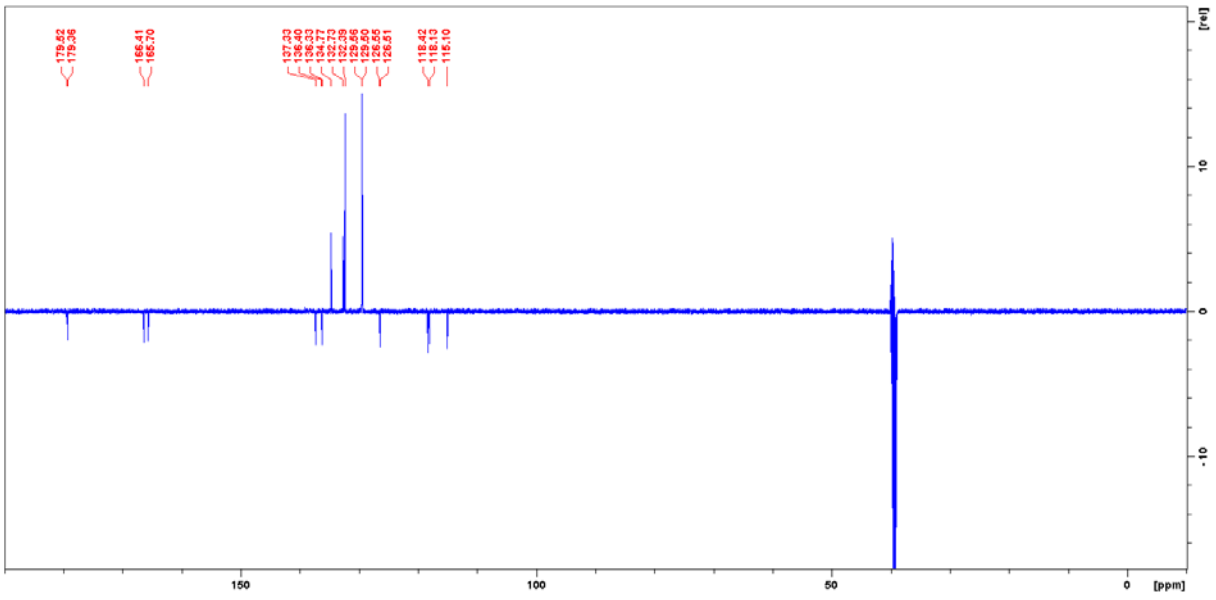


5-Bromo-2-({[(4-cyanophenyl)formamido]methanethioyl}amino)benzoic acid (3i)

1H

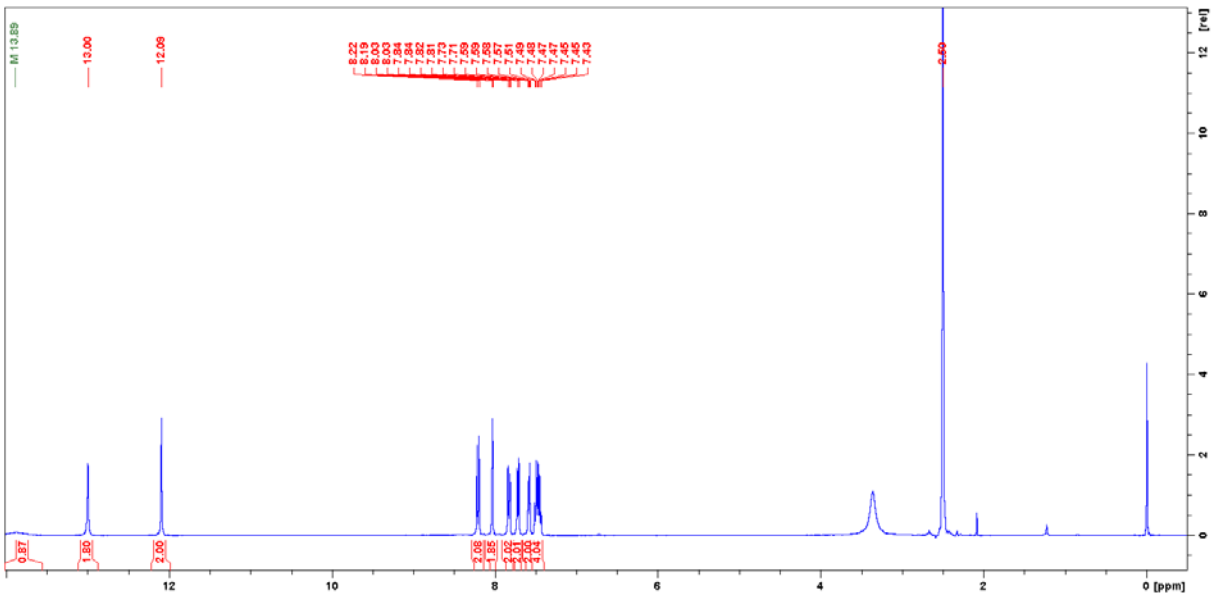


13C

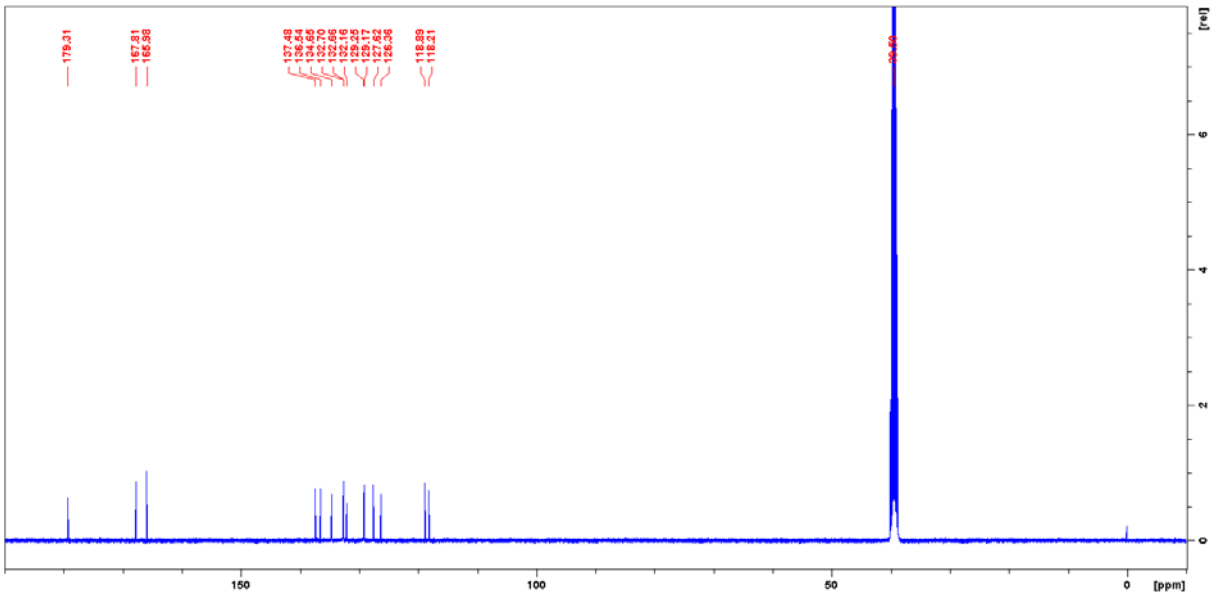


5-Bromo-2-({[(2-bromophenyl)formamido]methanethioyl}amino)benzoic acid (3j)

1H

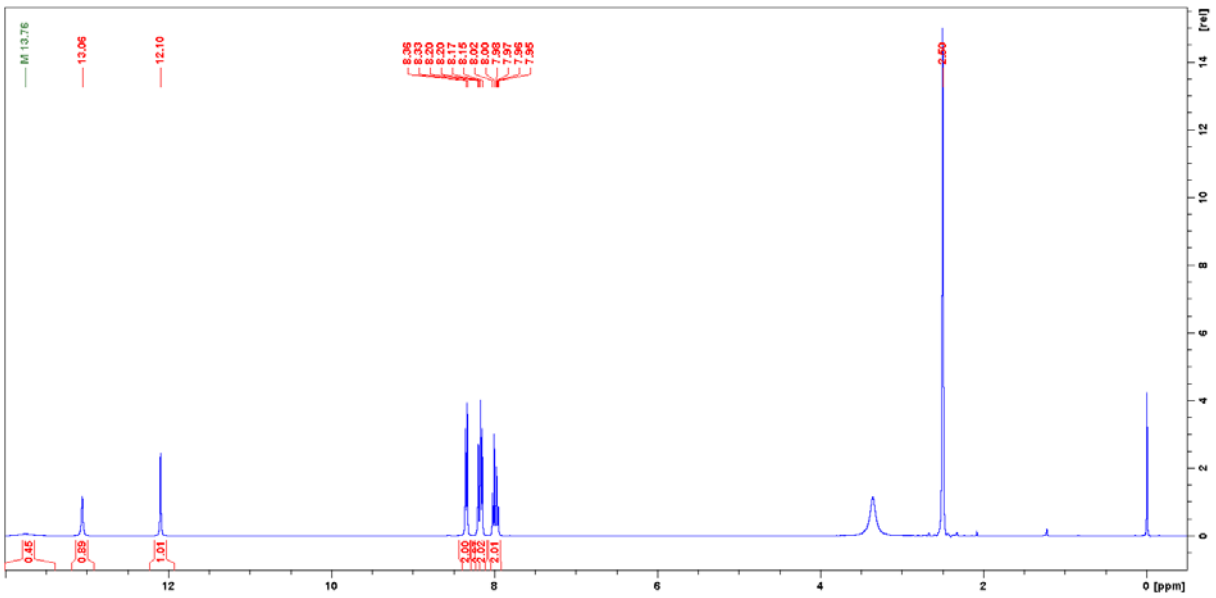


13C

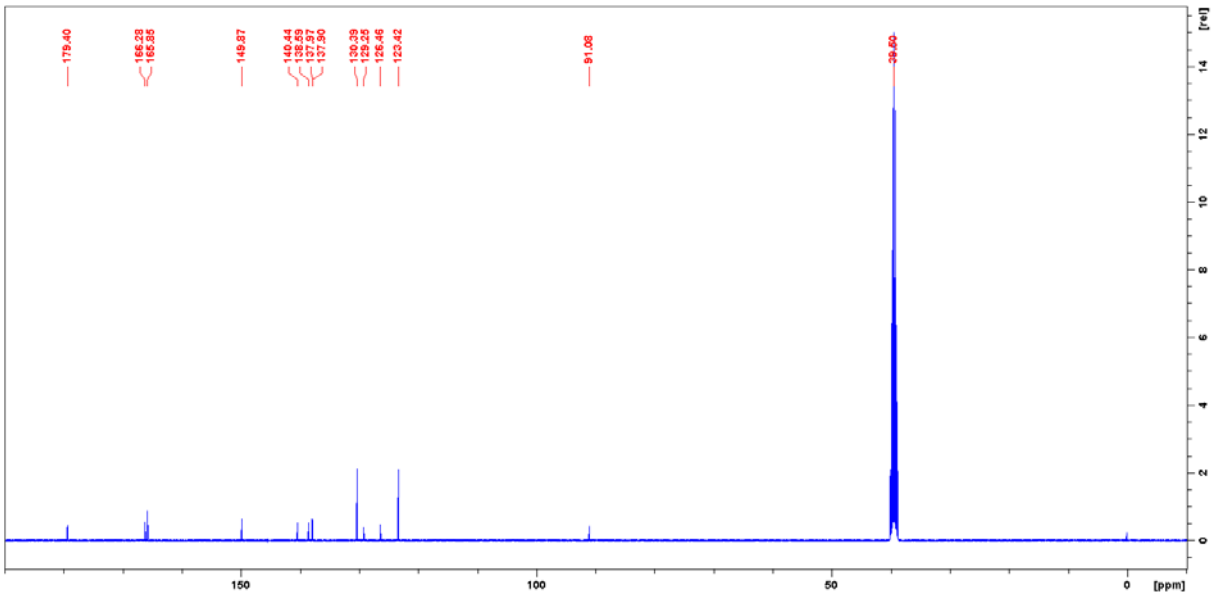


5-Iodo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3k)

1H

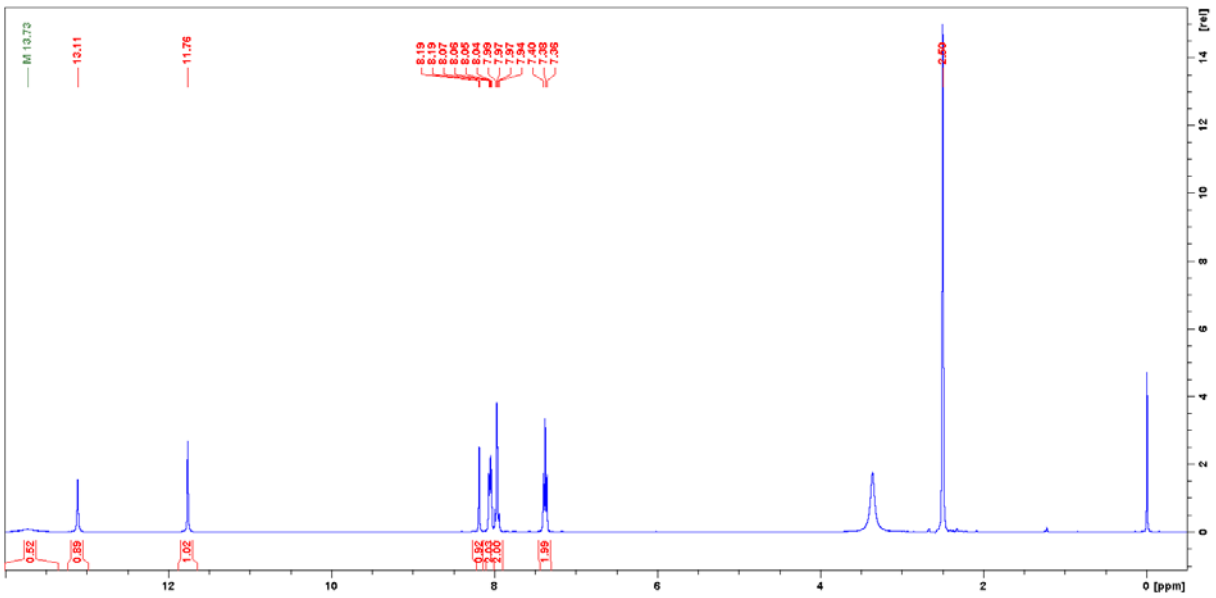


13C

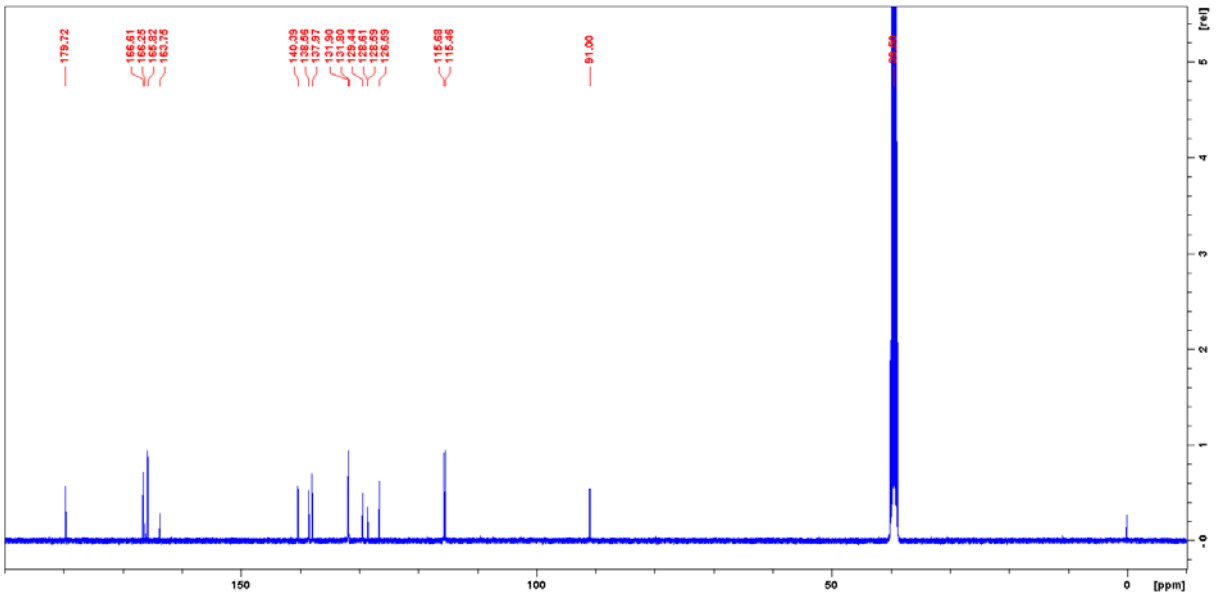


5-Iodo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3l)

1H

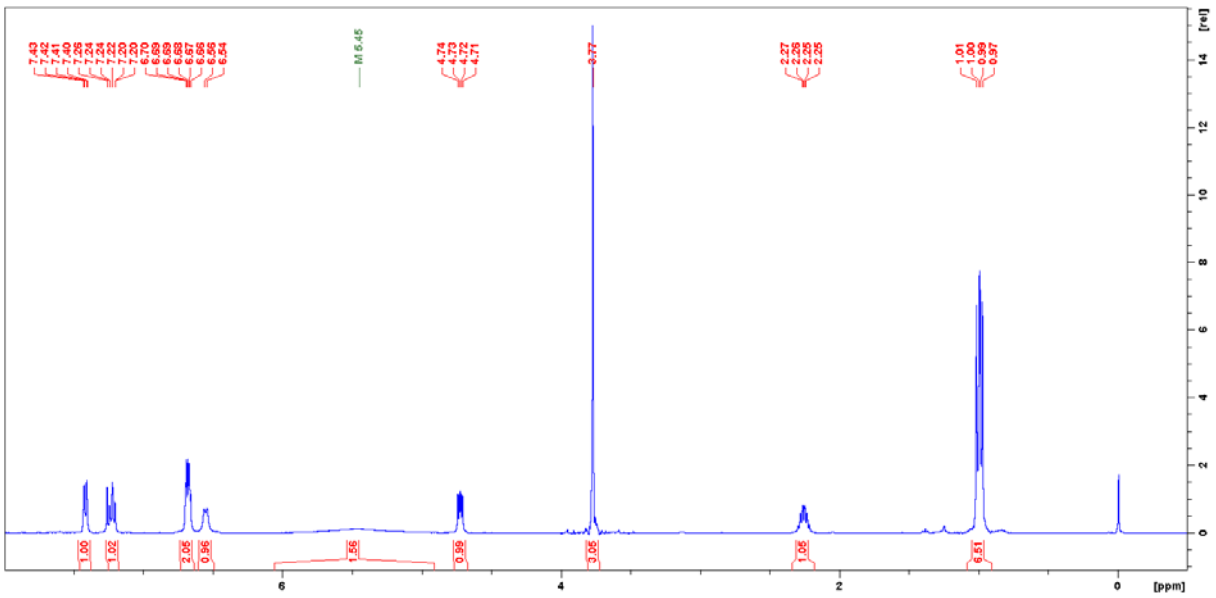


13C



(2*S*)-*N*-(2-aminobenzoyl)-2-isopropylaminoacetic acid methyl ester (9a)

1H



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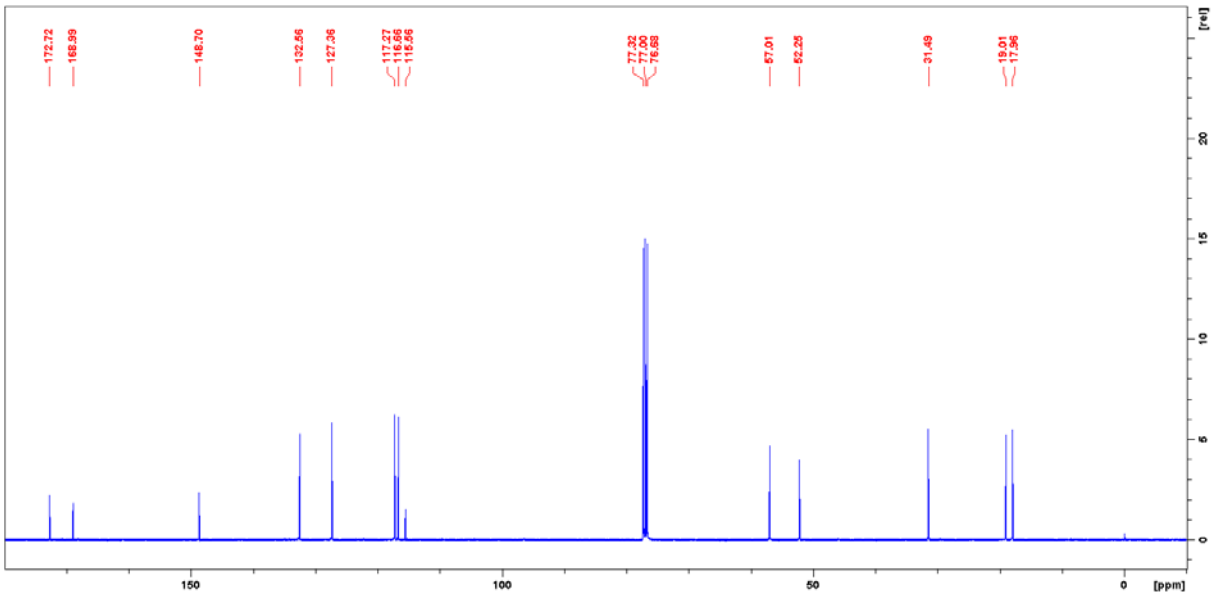
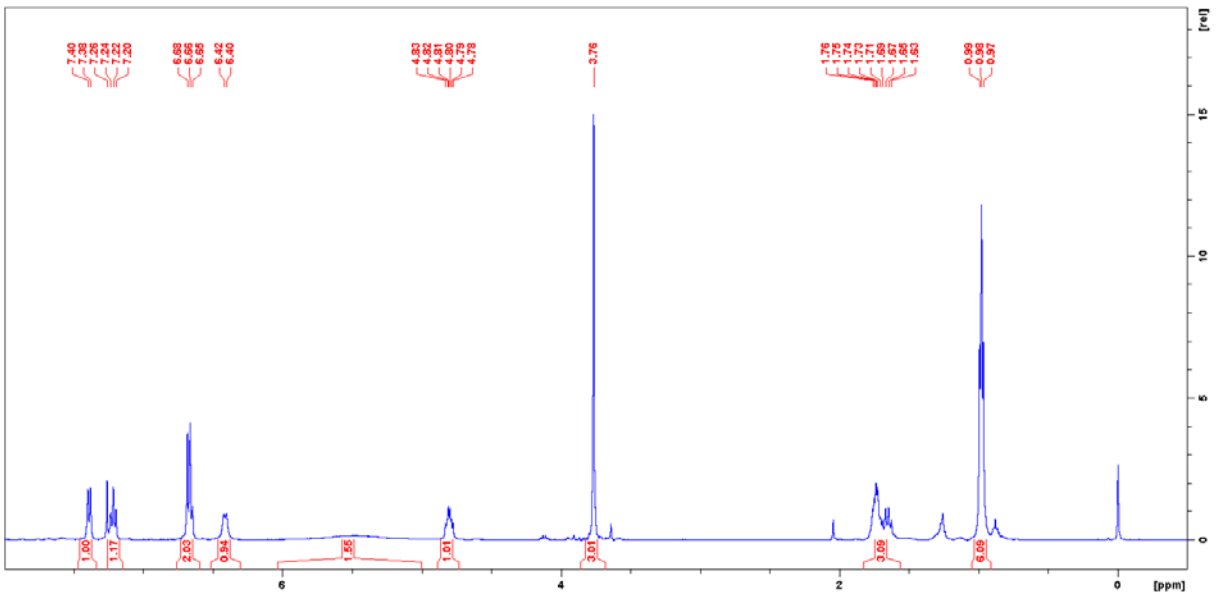


(2*S*)-*N*-(2-aminobenzoyl)-2-isobutylaminoacetic acid methyl ester (9b)

1H



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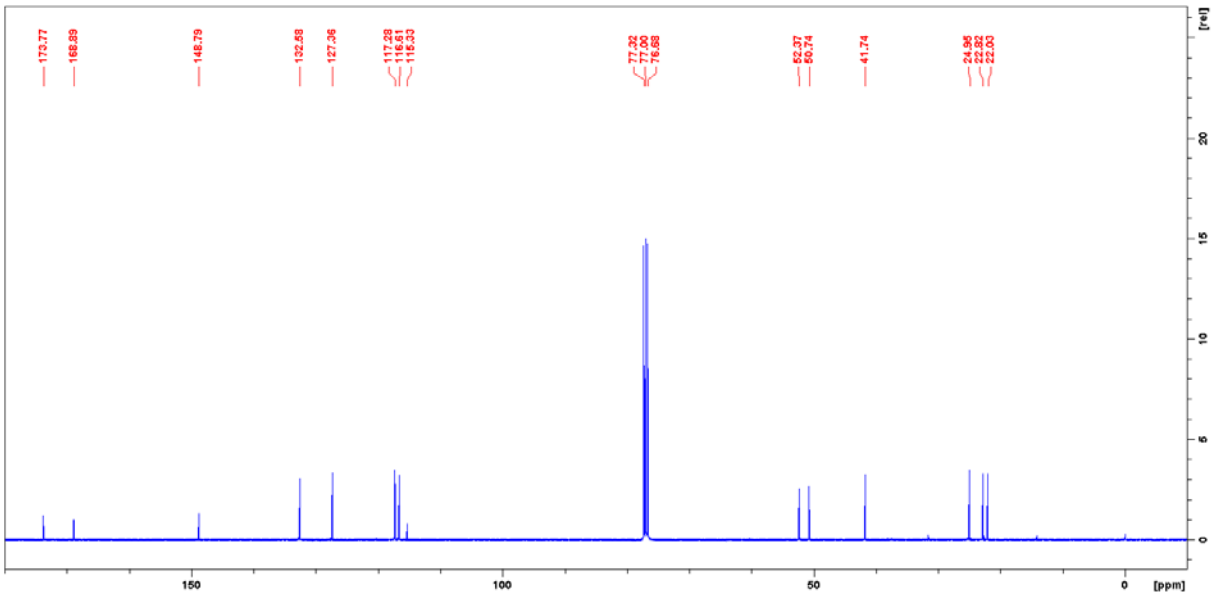
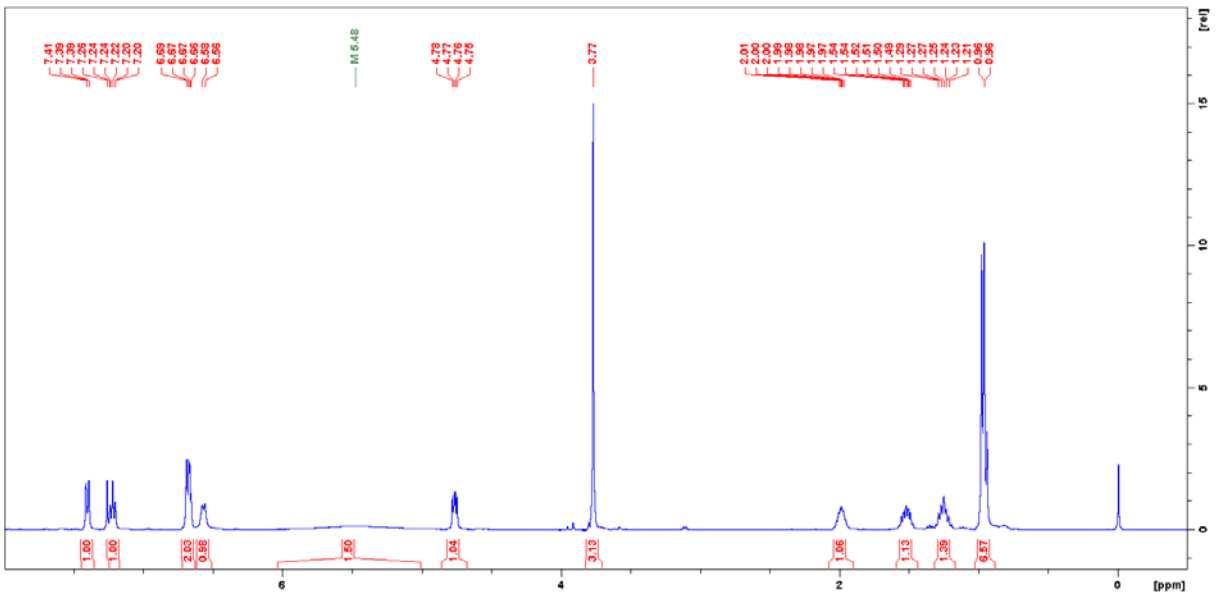


(2*S*)-*N*-(2-aminobenzoyl)-2-(2-methylbutyl)aminoacetic acid methyl ester (9c)

1H



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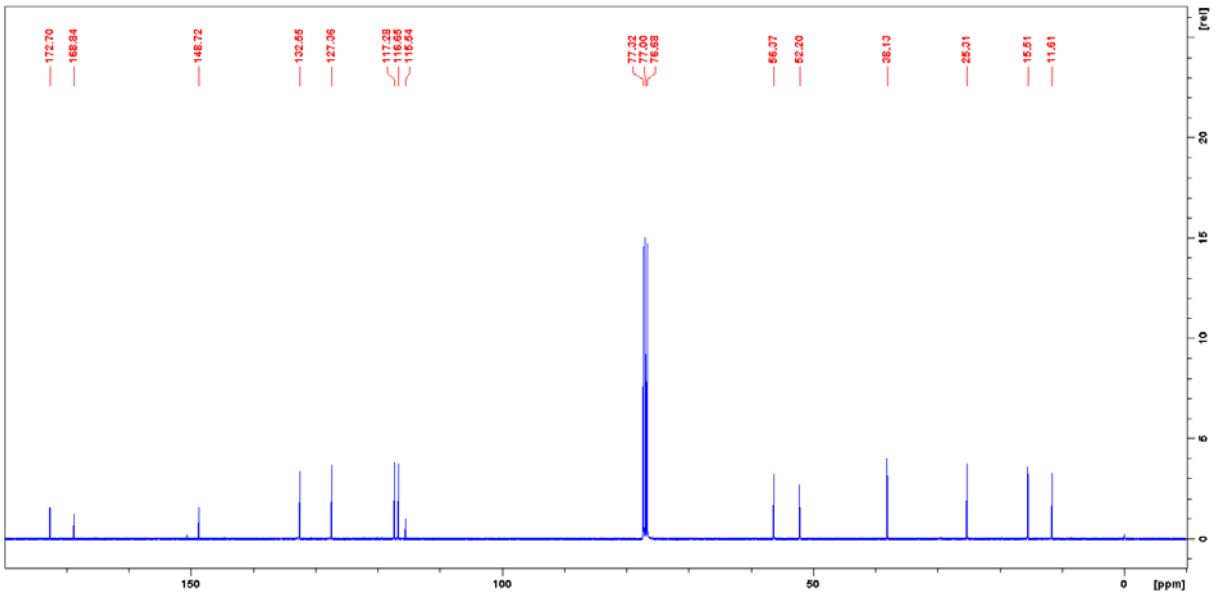
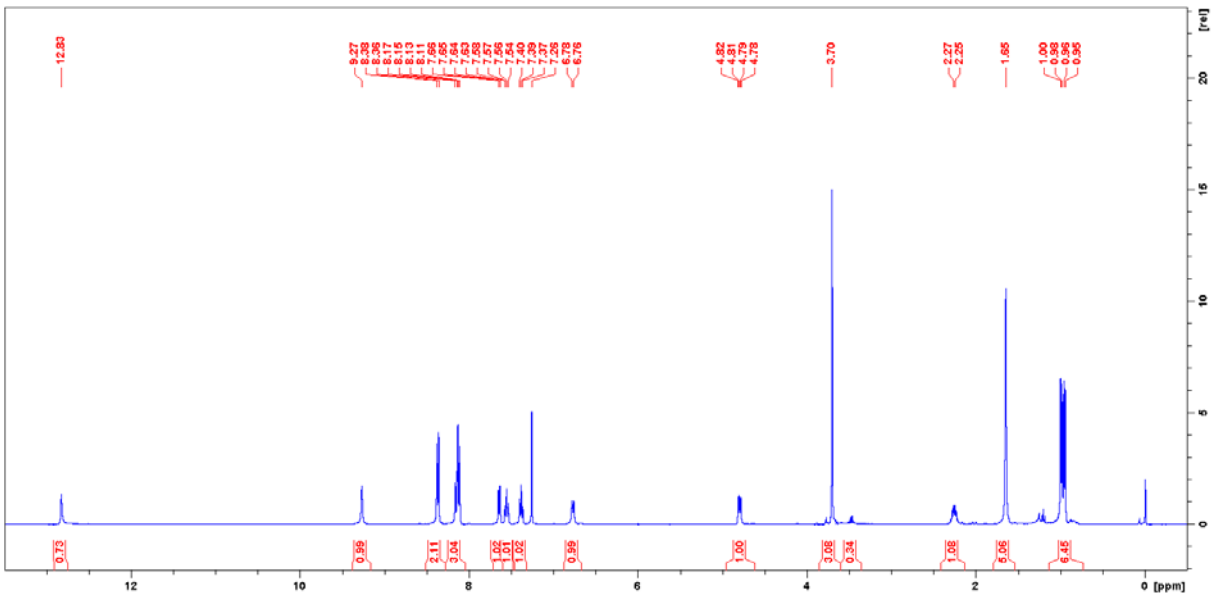


Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}butanoate (10a)

1H



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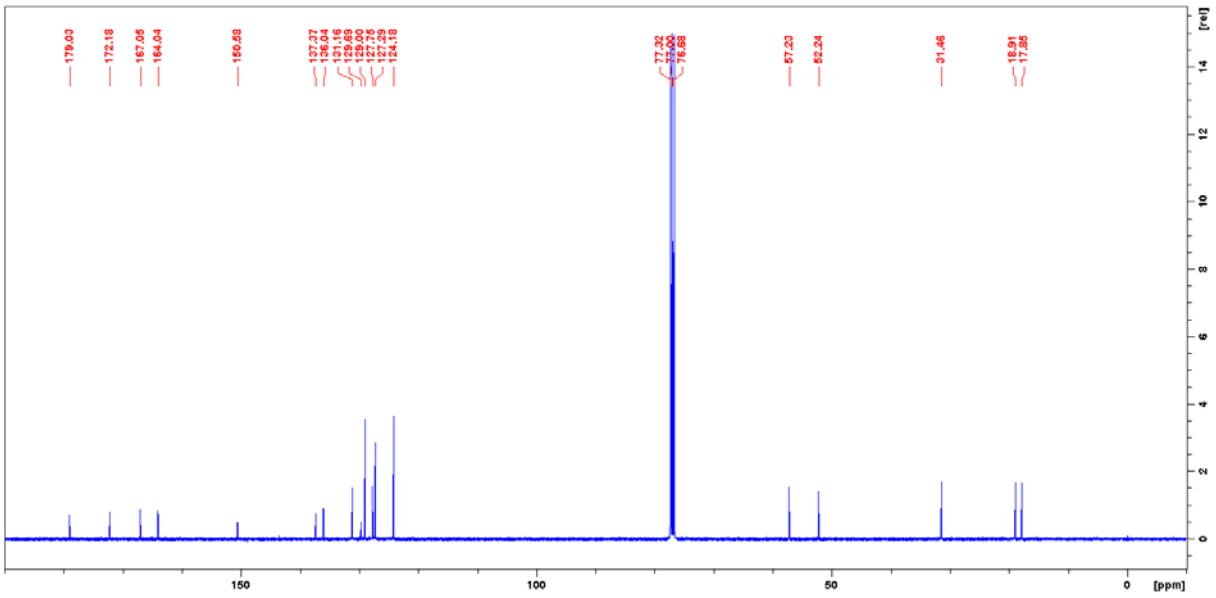
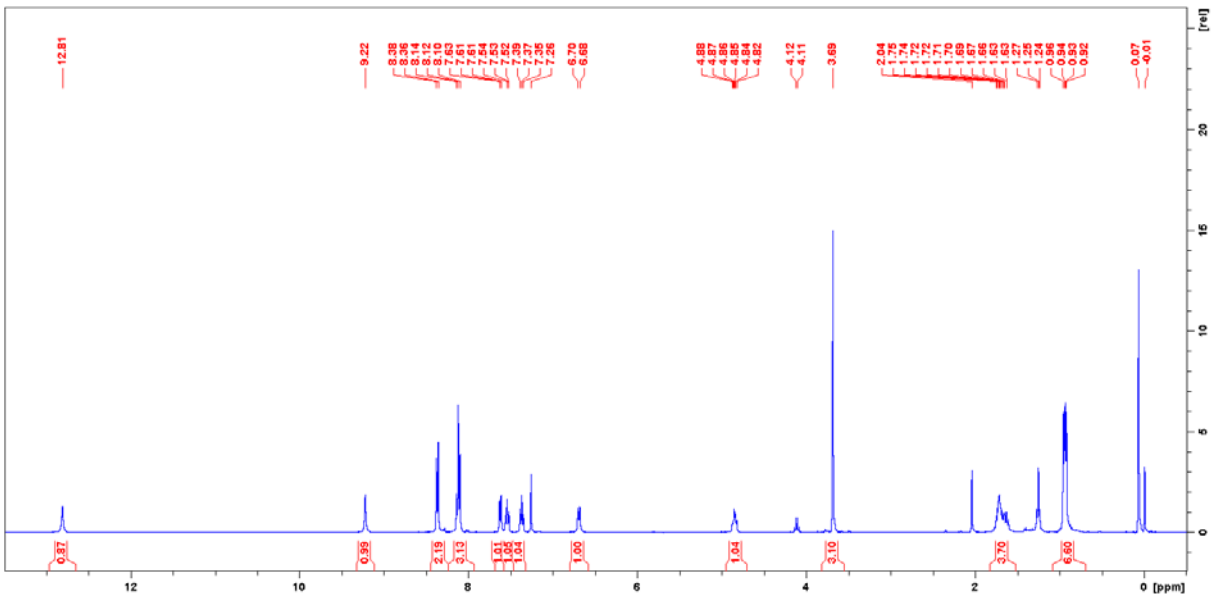


Methyl (2*S*)-4-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (10b)

1H



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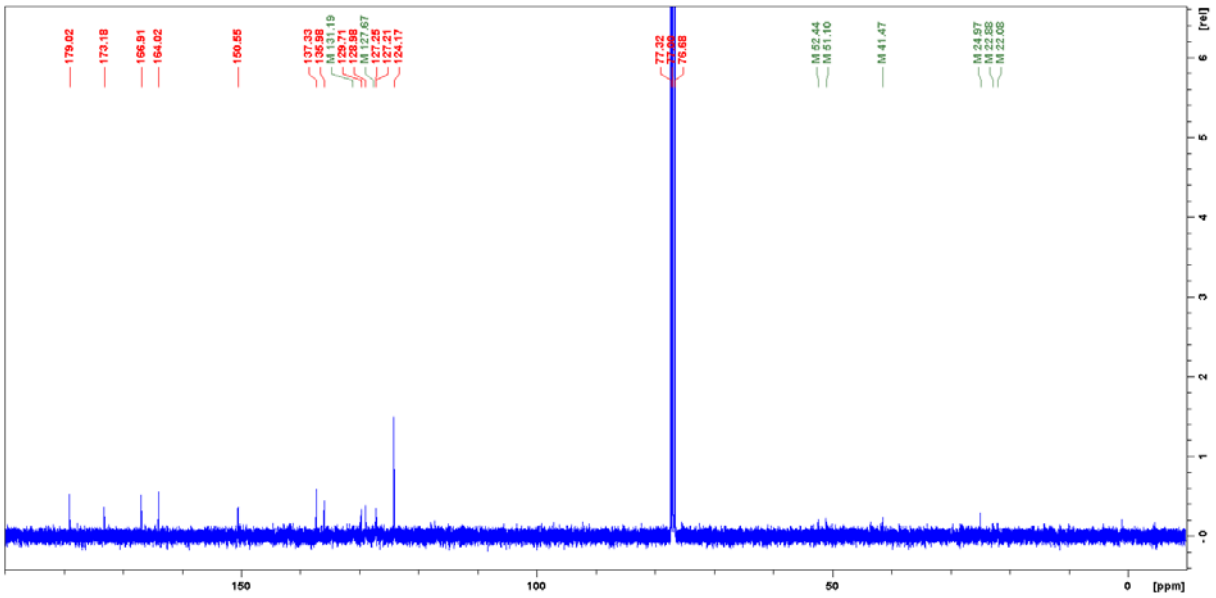
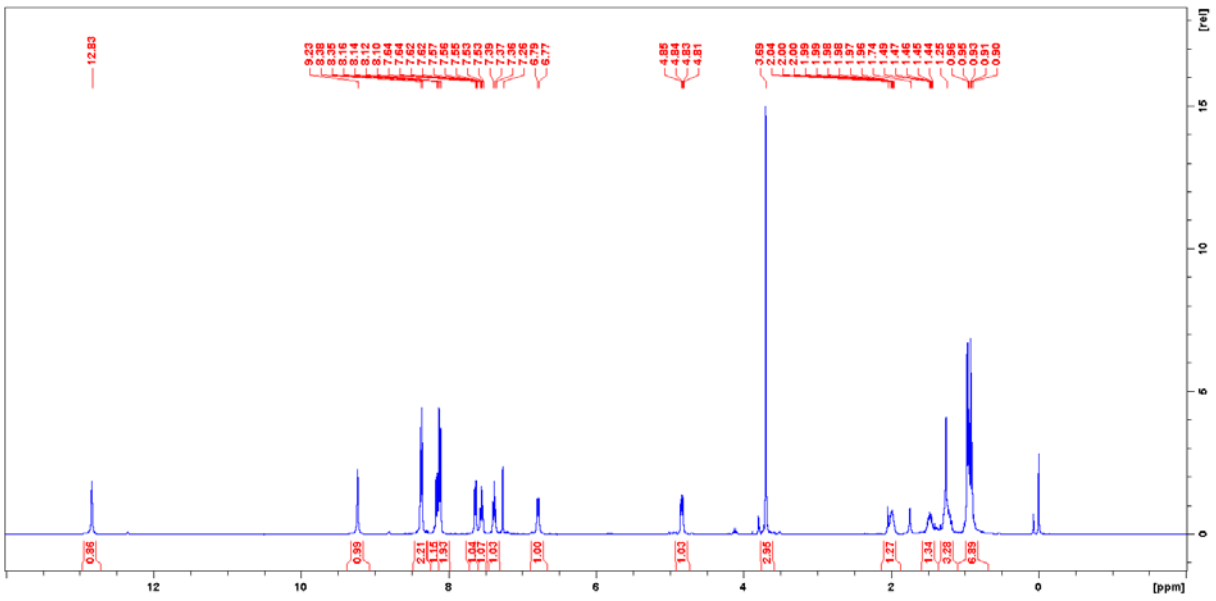


Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (10c)

1H



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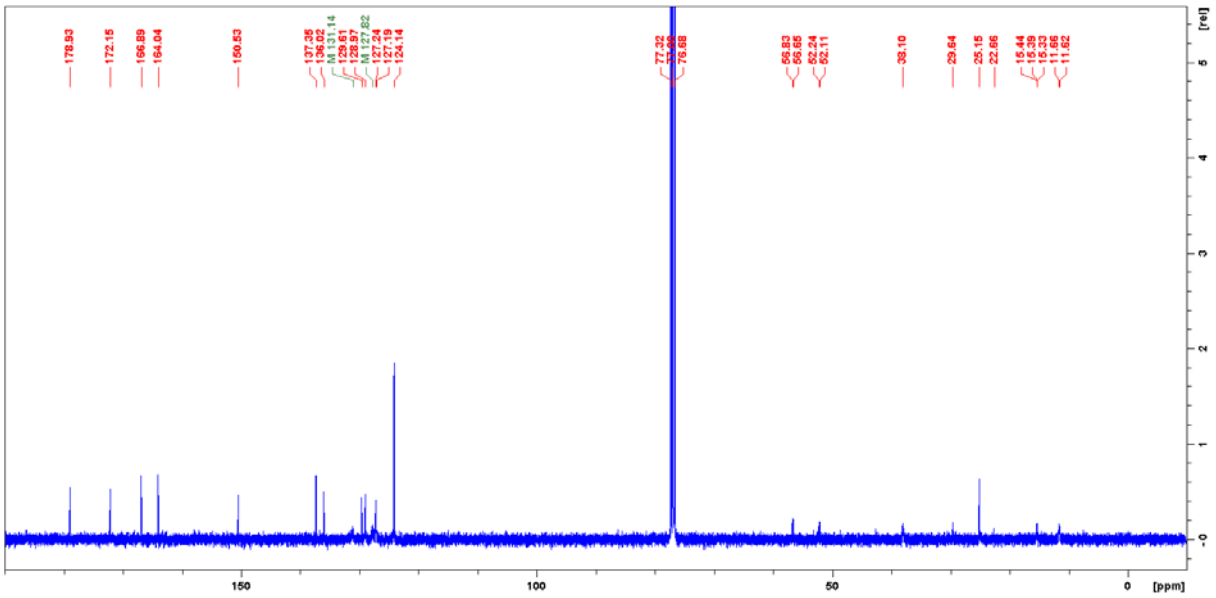
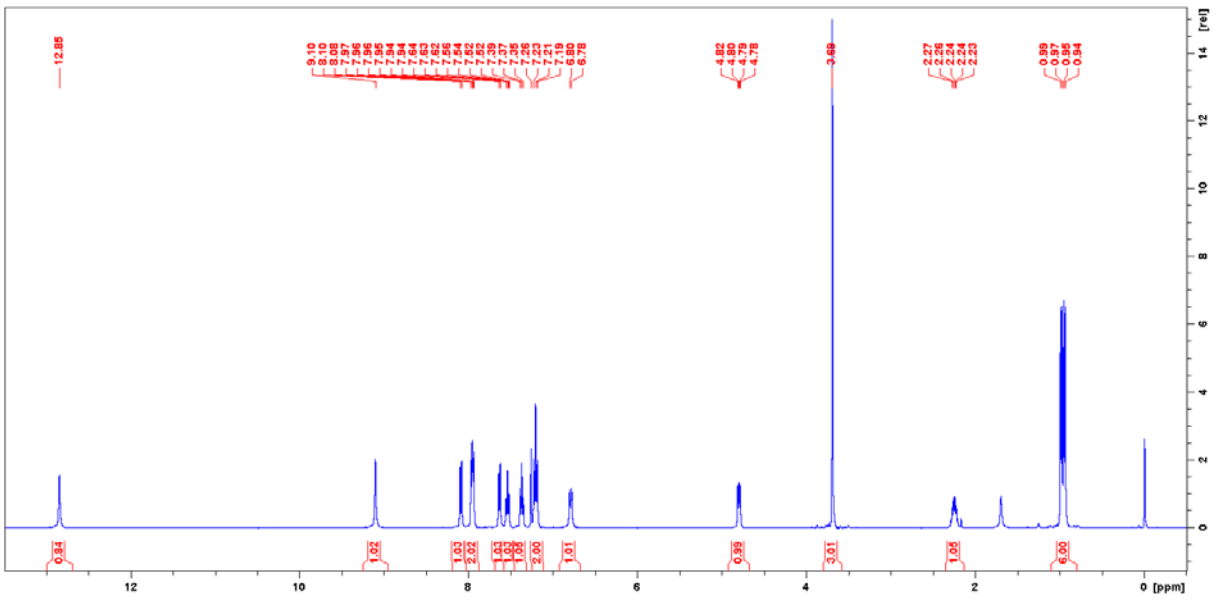


Methyl-(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylbutanoate (10d)

1H



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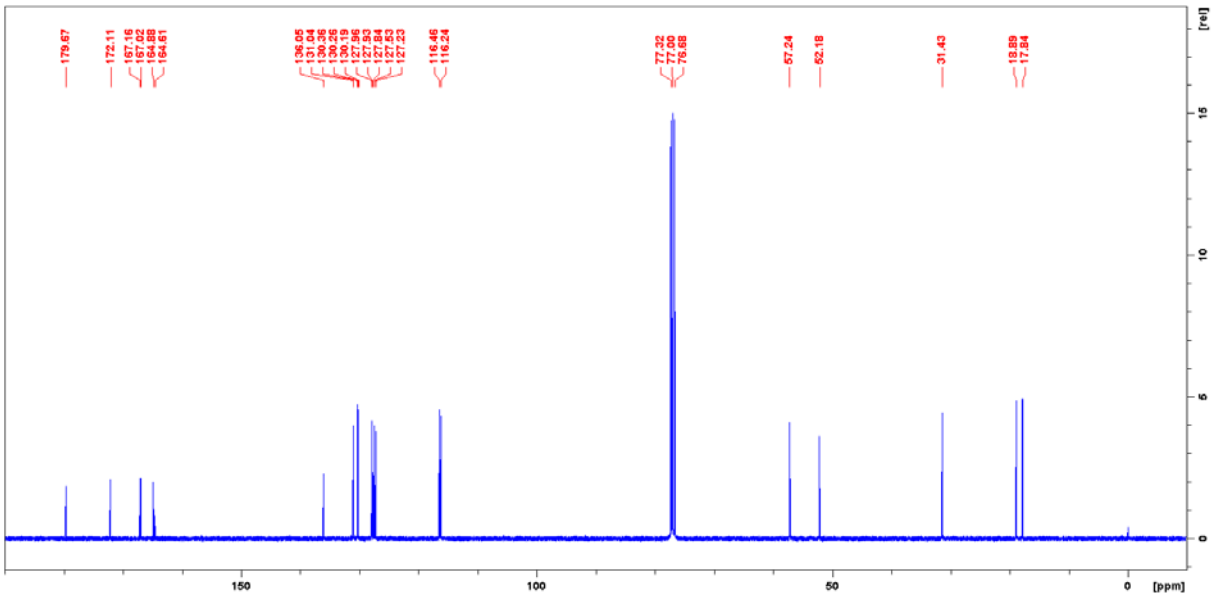
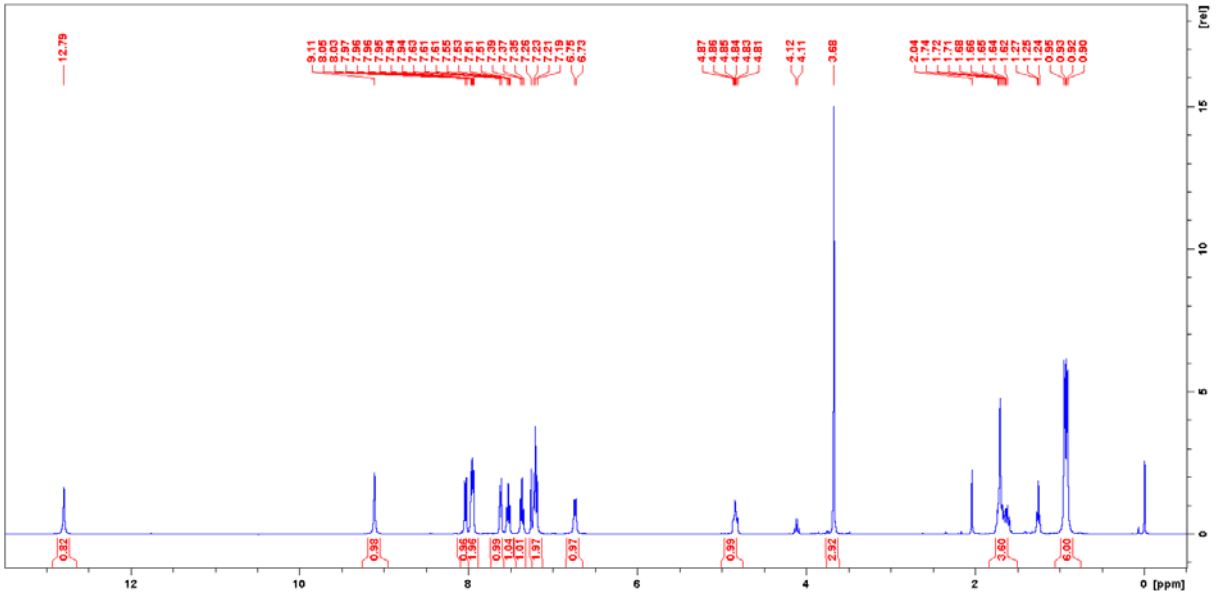


Methyl-(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-4-methylpentanoate (**10e**)

1H



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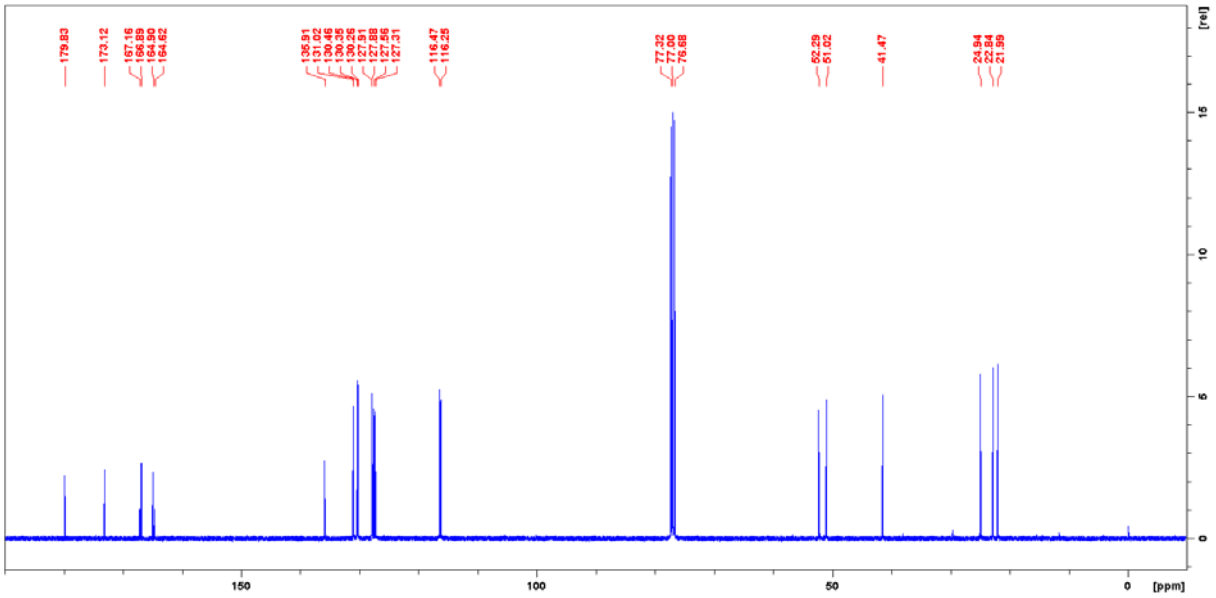
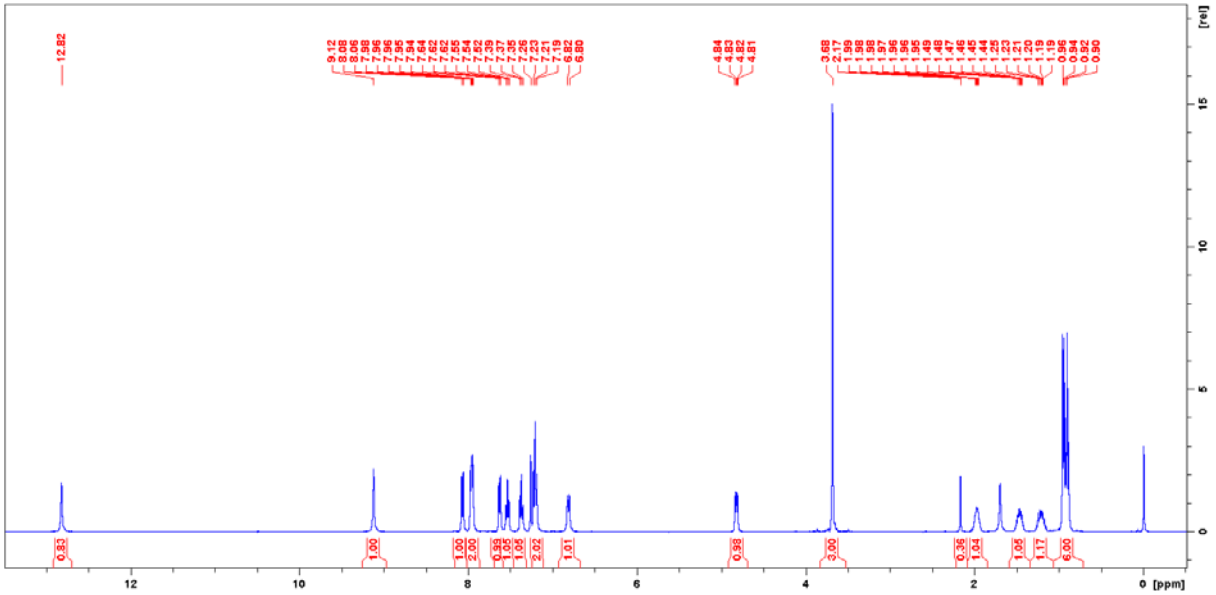


Methyl (2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylpentanoate (10f)

1H



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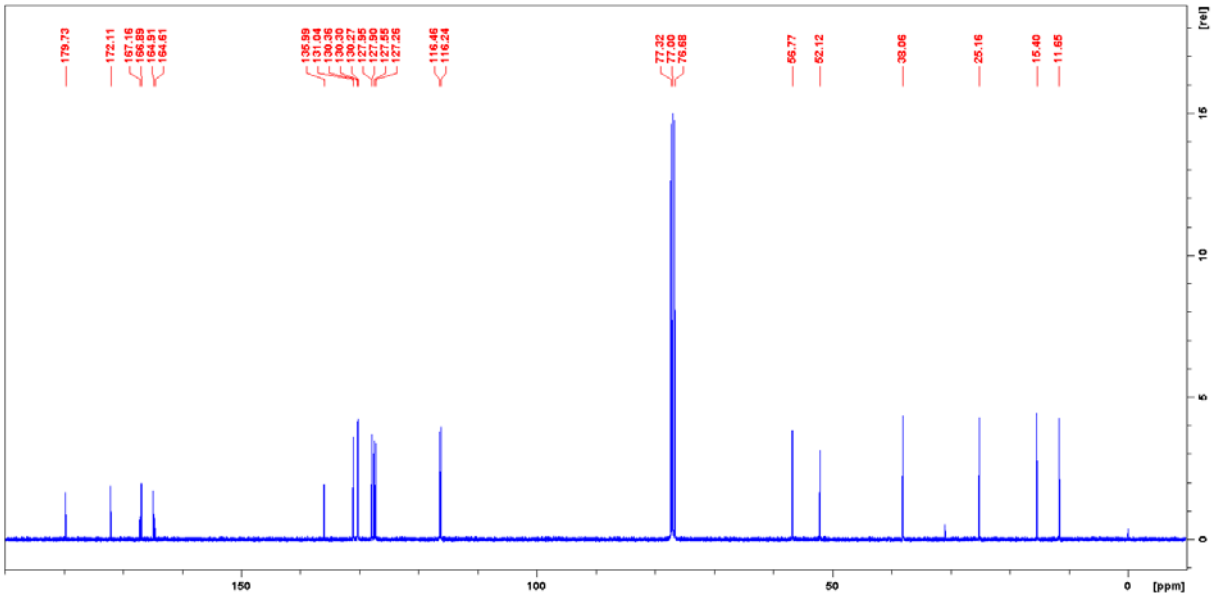
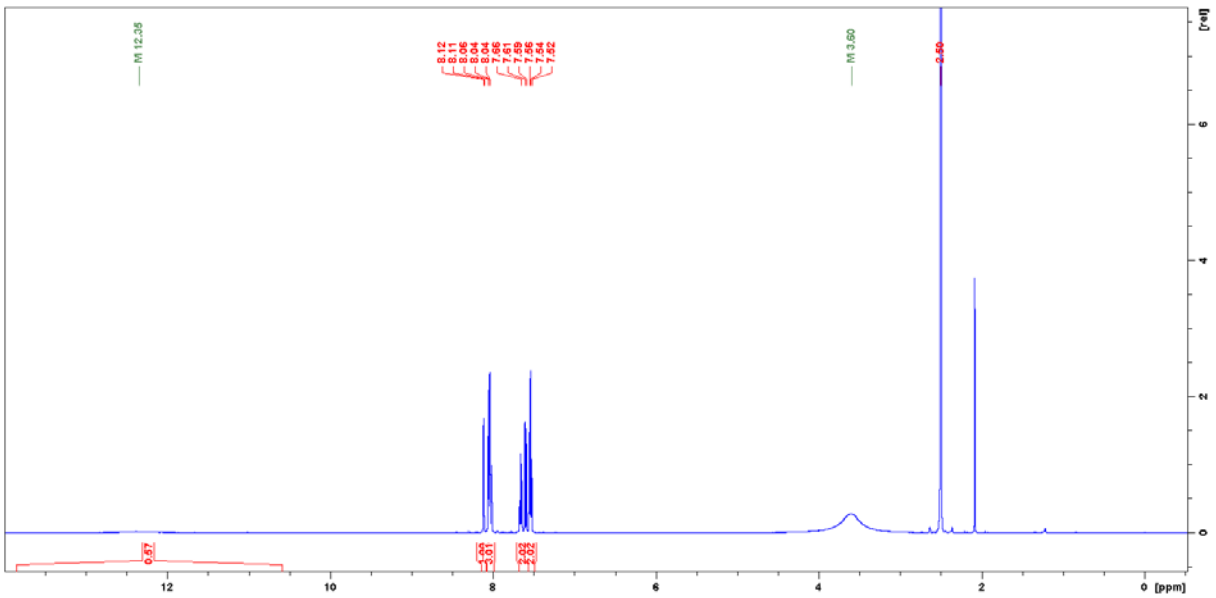


***N*-(6-Bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11a)**

1H



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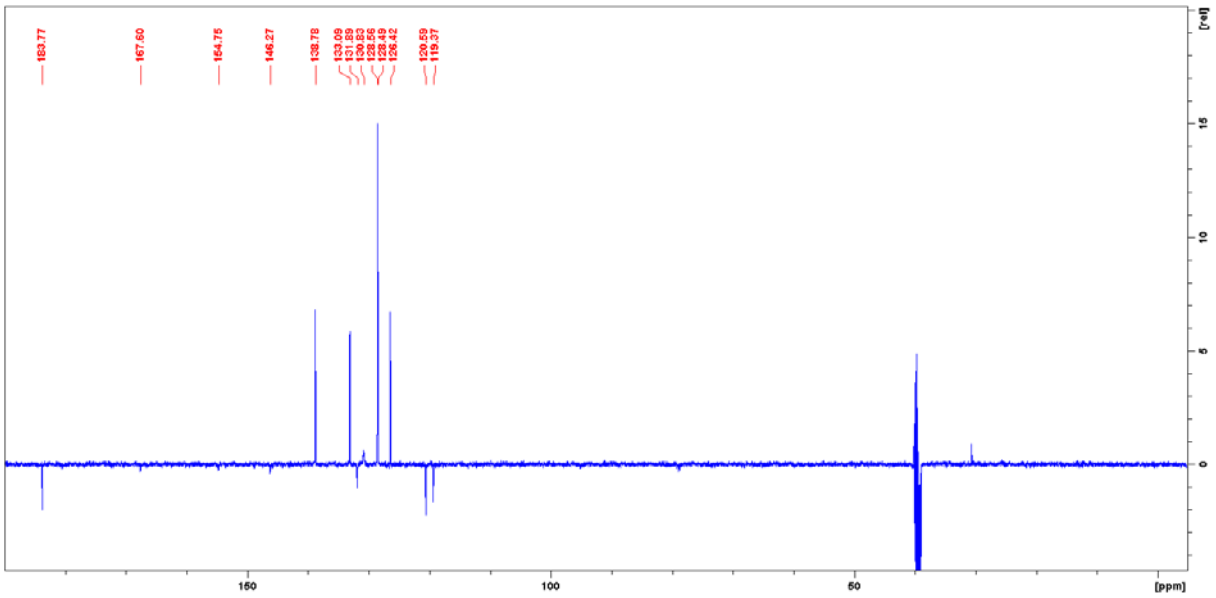
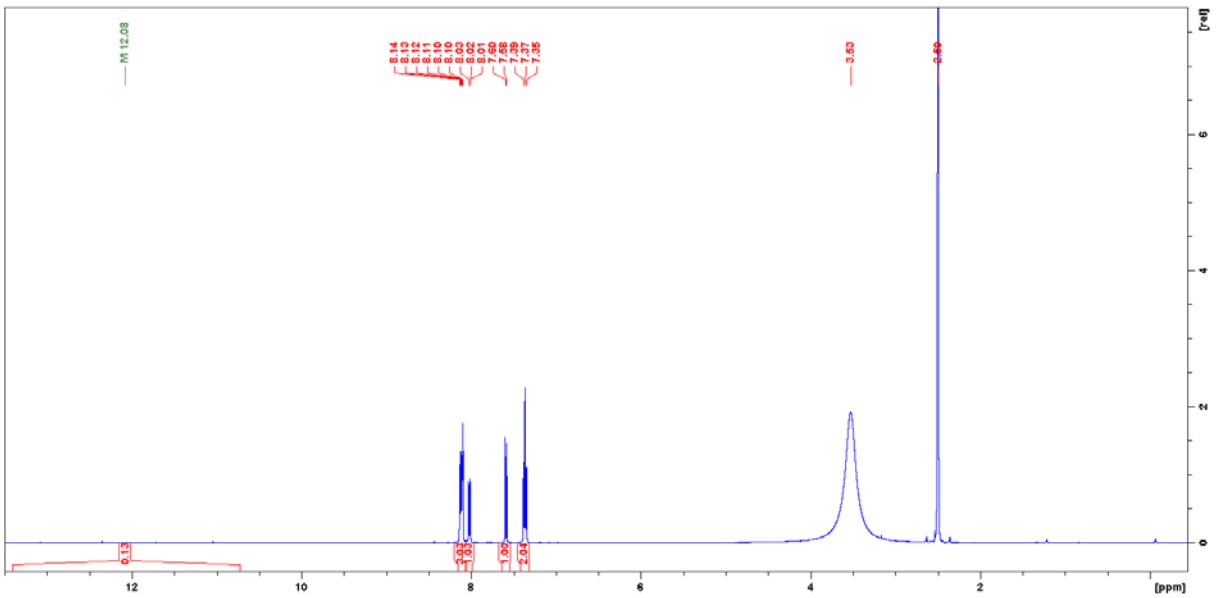


4-Fluoro-*N*-(6-bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11b)

1H



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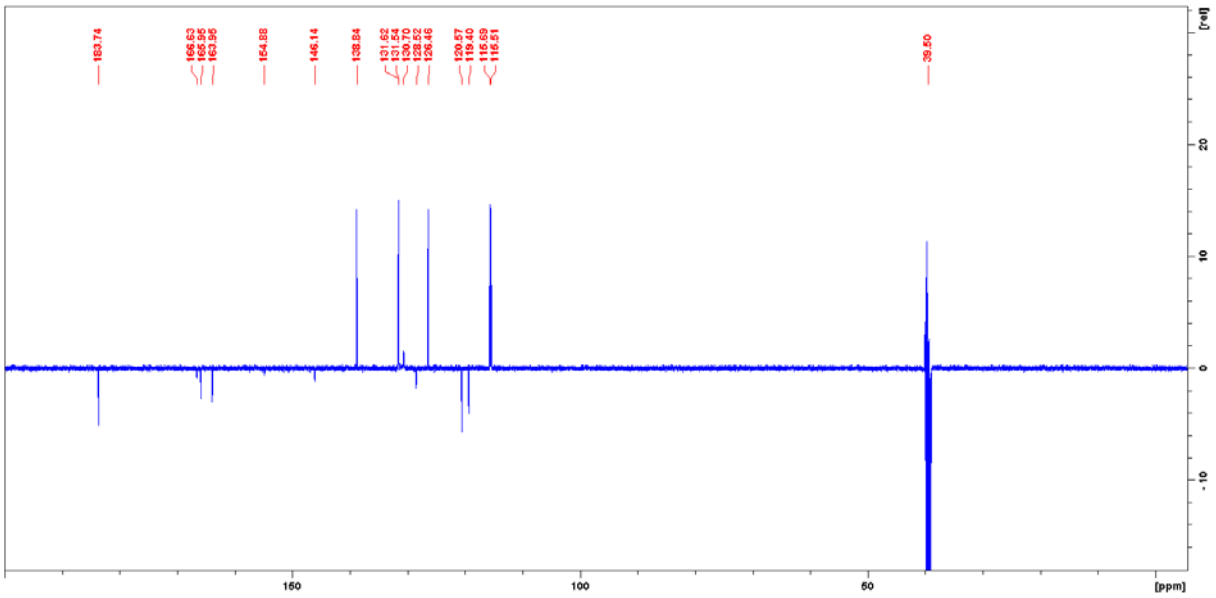
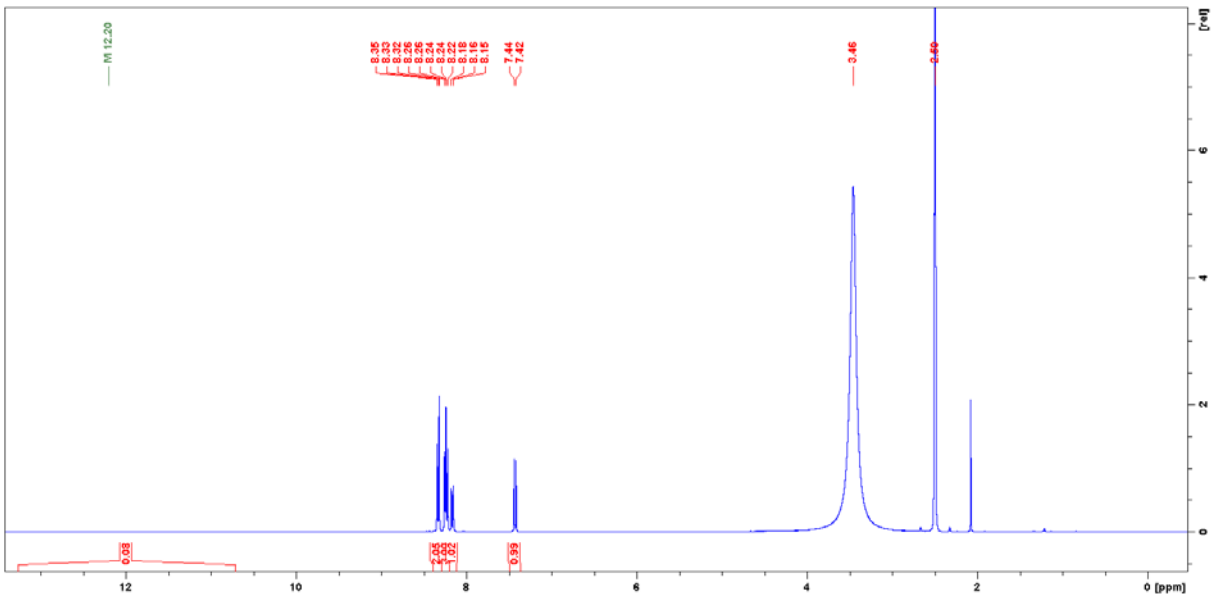


4-Nitro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11c)

1H



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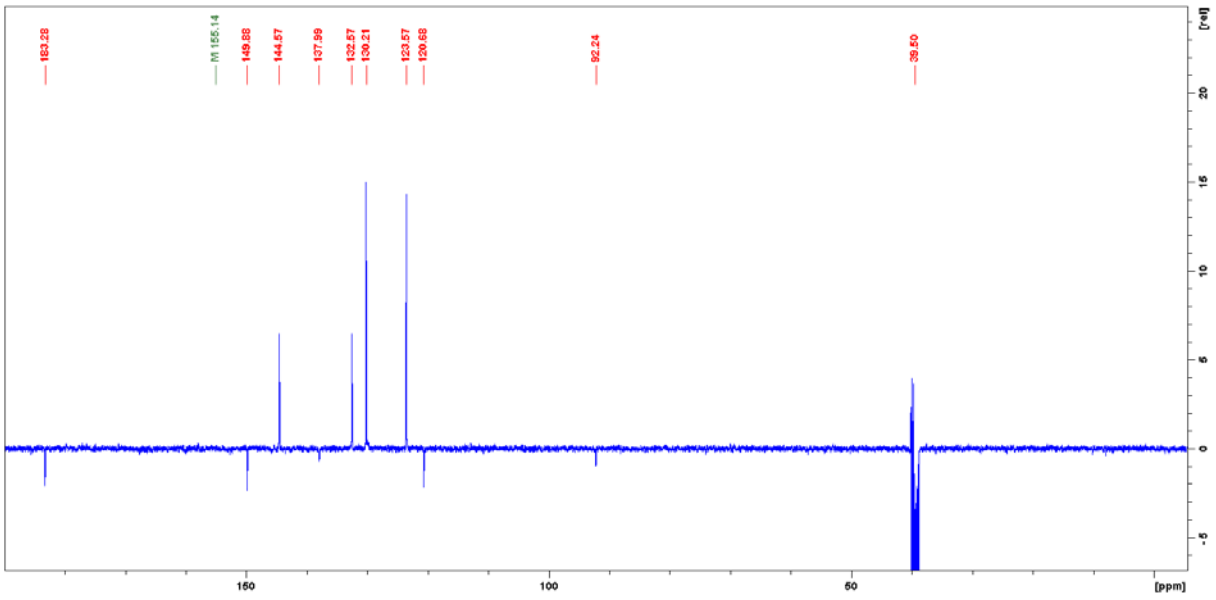
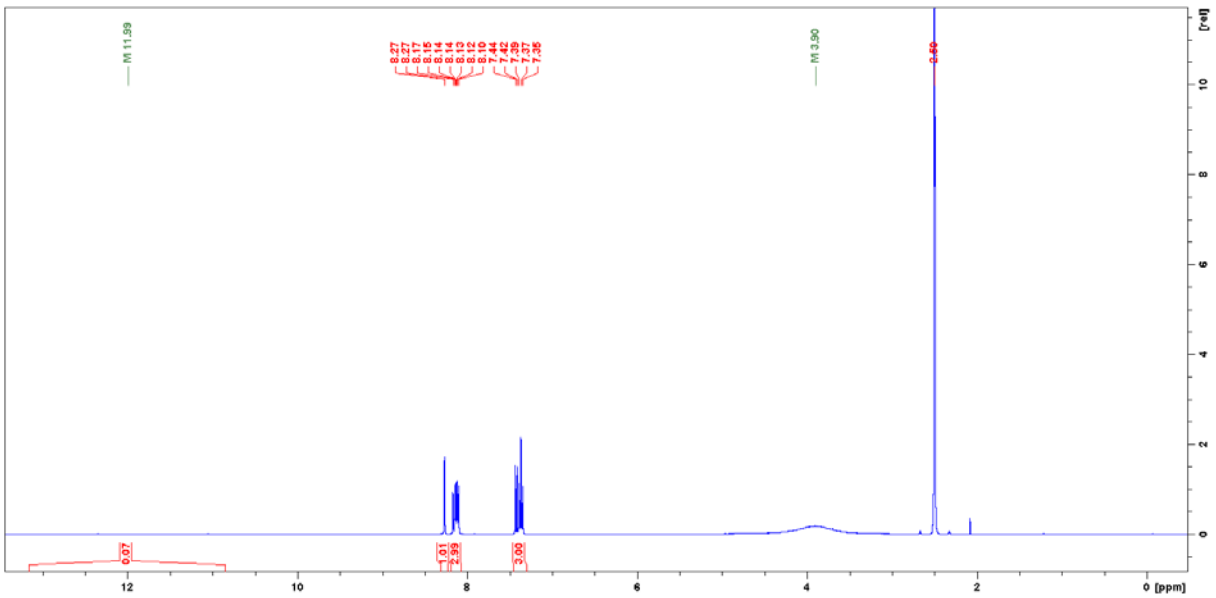


4-Fluoro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11d)

1H



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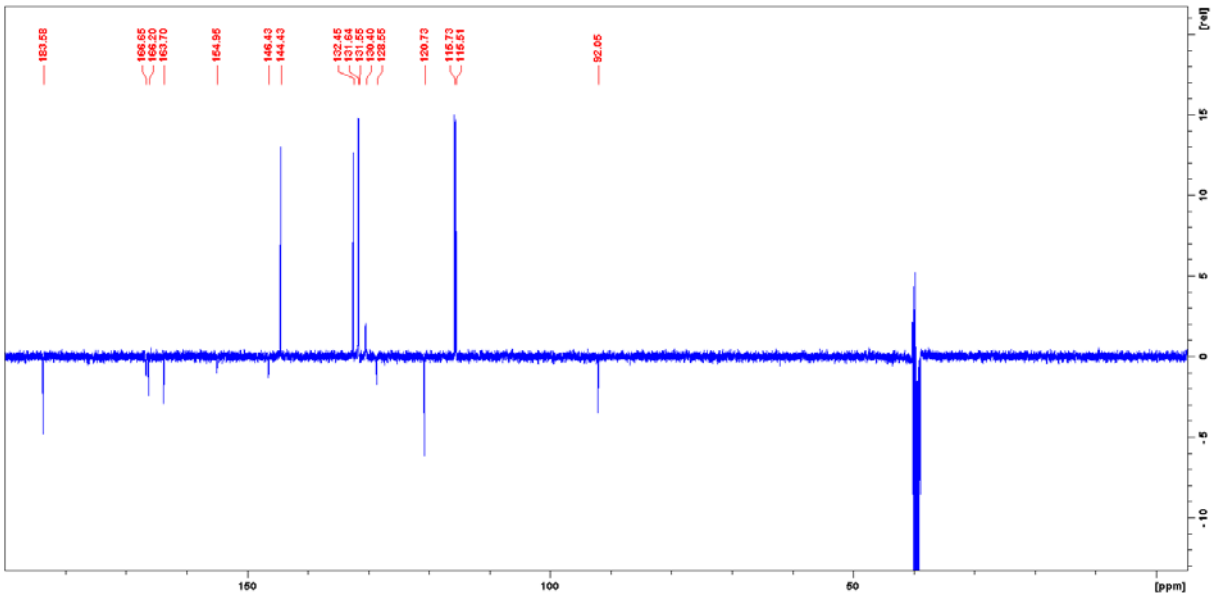
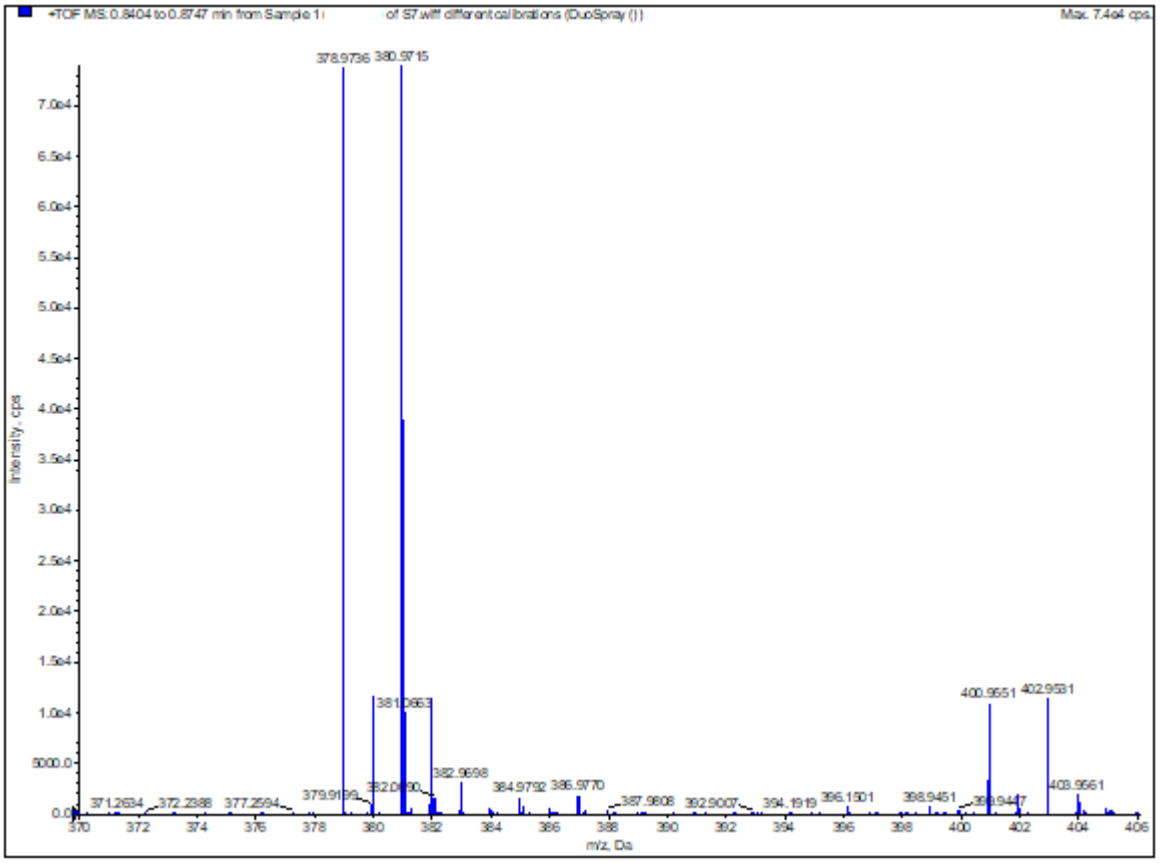
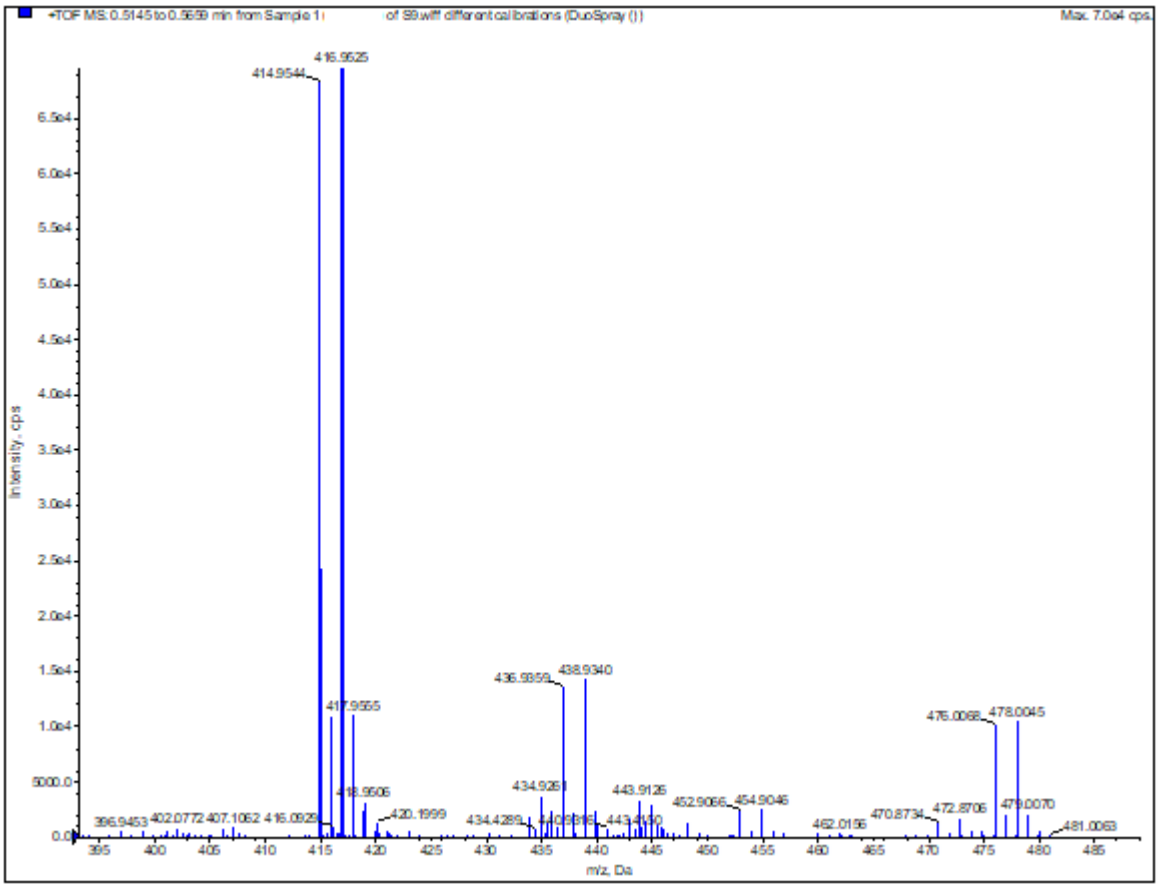


5-Bromo-2-{[(phenylformamido)methanethioyl]amino}benzoic acid (3a)



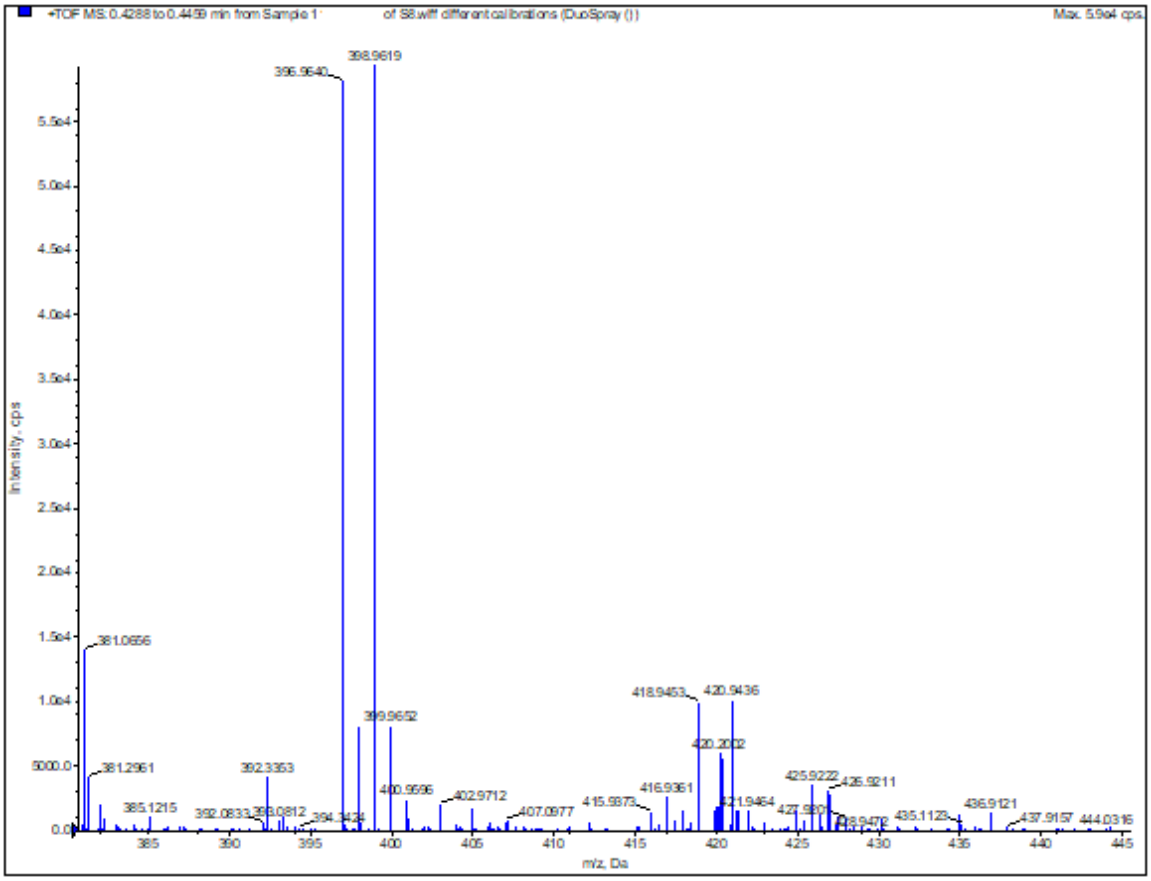
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H12 N2 O3 S Br	378.9752	-1.6003	-4.2227	10.5

5-Bromo-2-({[(2,6-difluorophenyl)formamido]methanethioyl}amino)benzoic acid (3b)



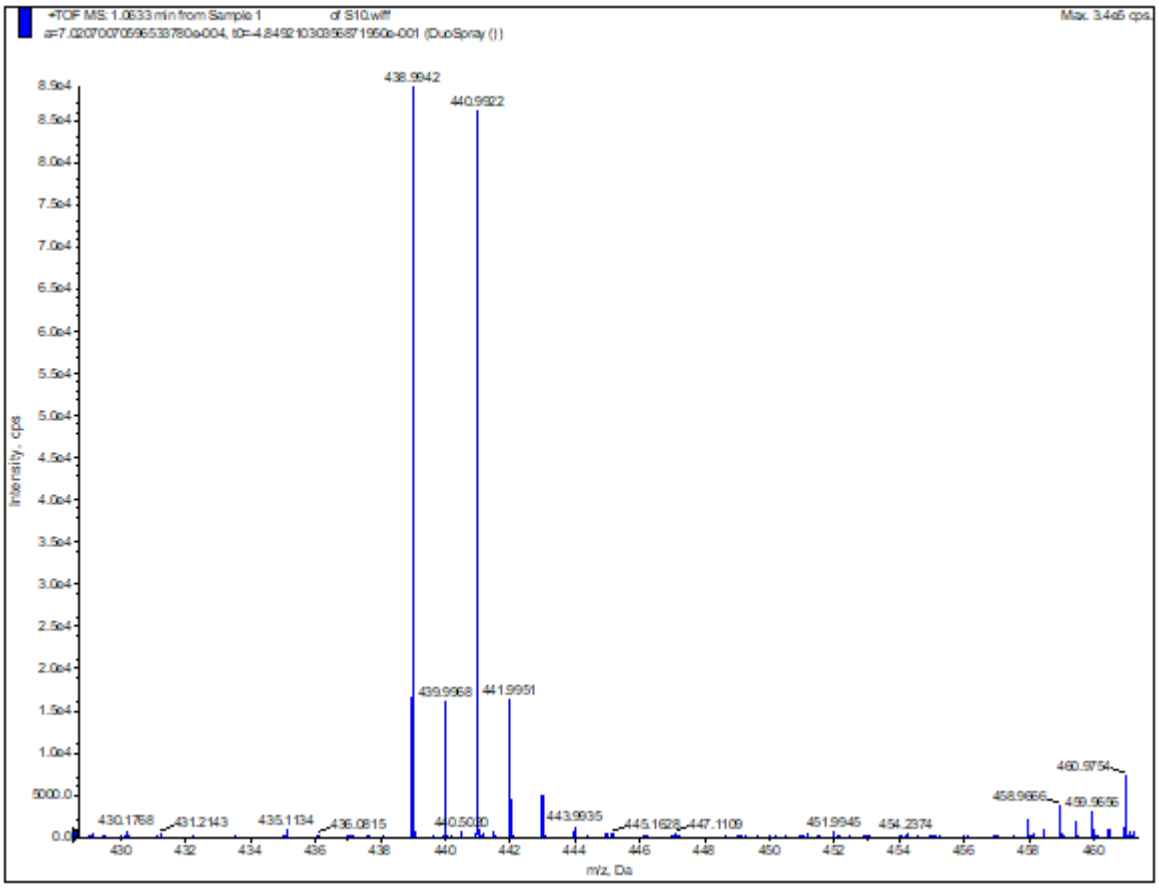
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N O5 F S Br	414.9525	1.8662	4.4973	10

5-Bromo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3c)



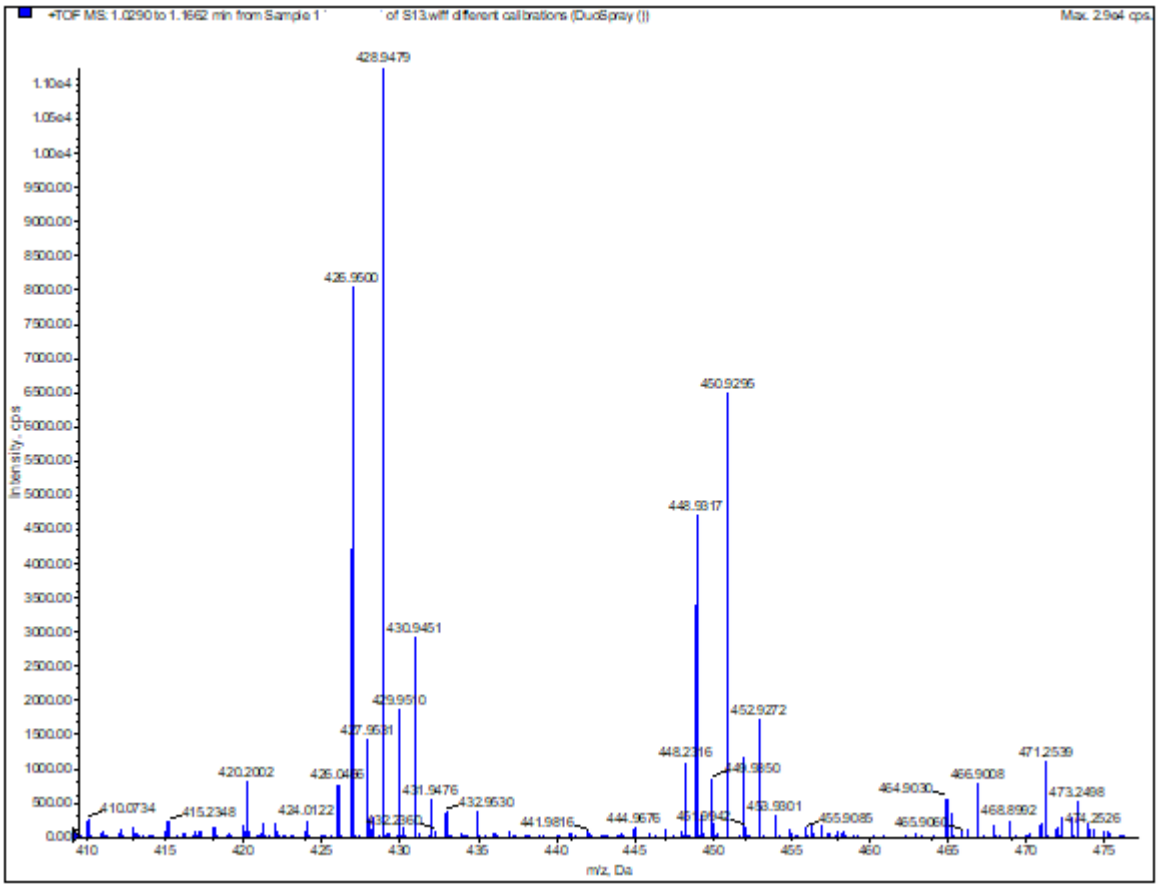
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N2 O3 F S Br	396.9657	-1.7785	-4.4803	10.5

5-Bromo-2-({[(3,5-dimethoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3d)



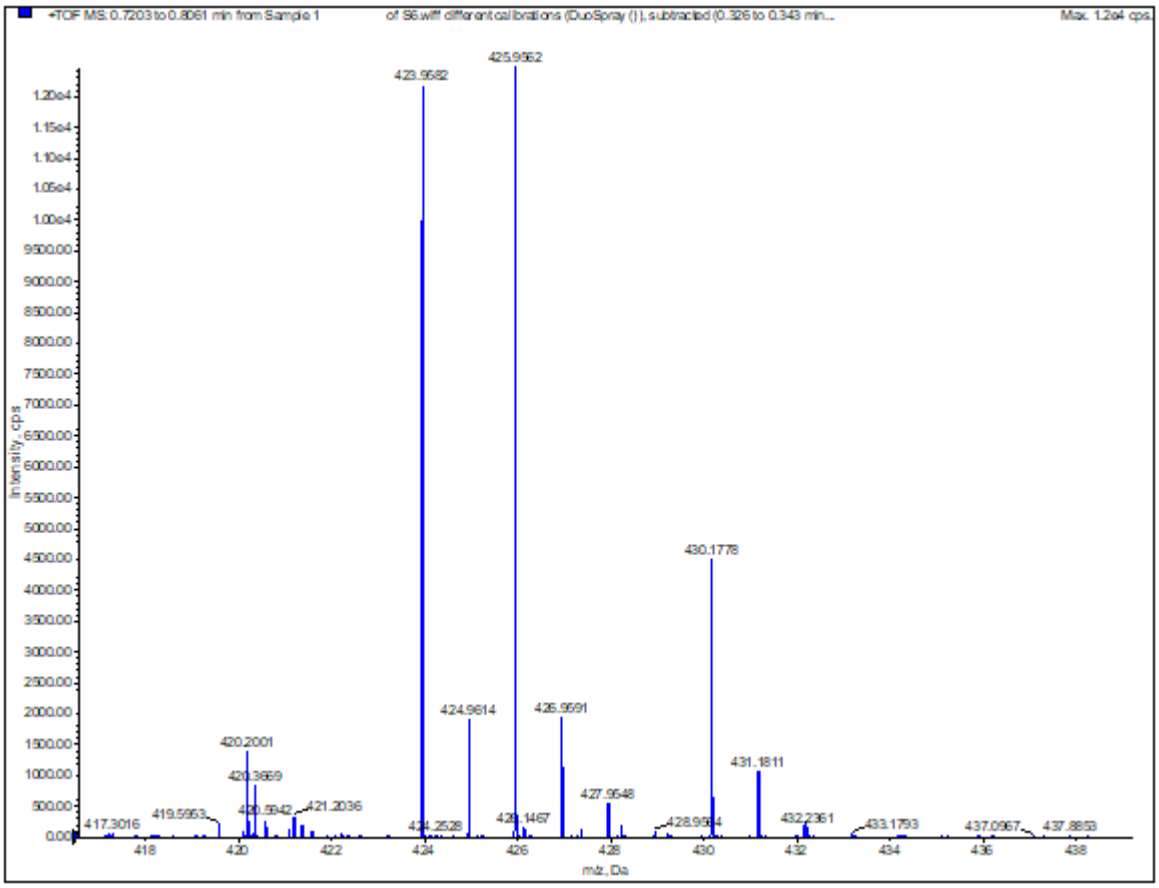
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C17 H16 N2 O5 S Br	438.9963	-2.1297	-4.8514	10.5

5-Bromo-2-[({[2-(chloromethyl)phenyl]formamido}methanethioyl)amino]benzoic acid (3e)



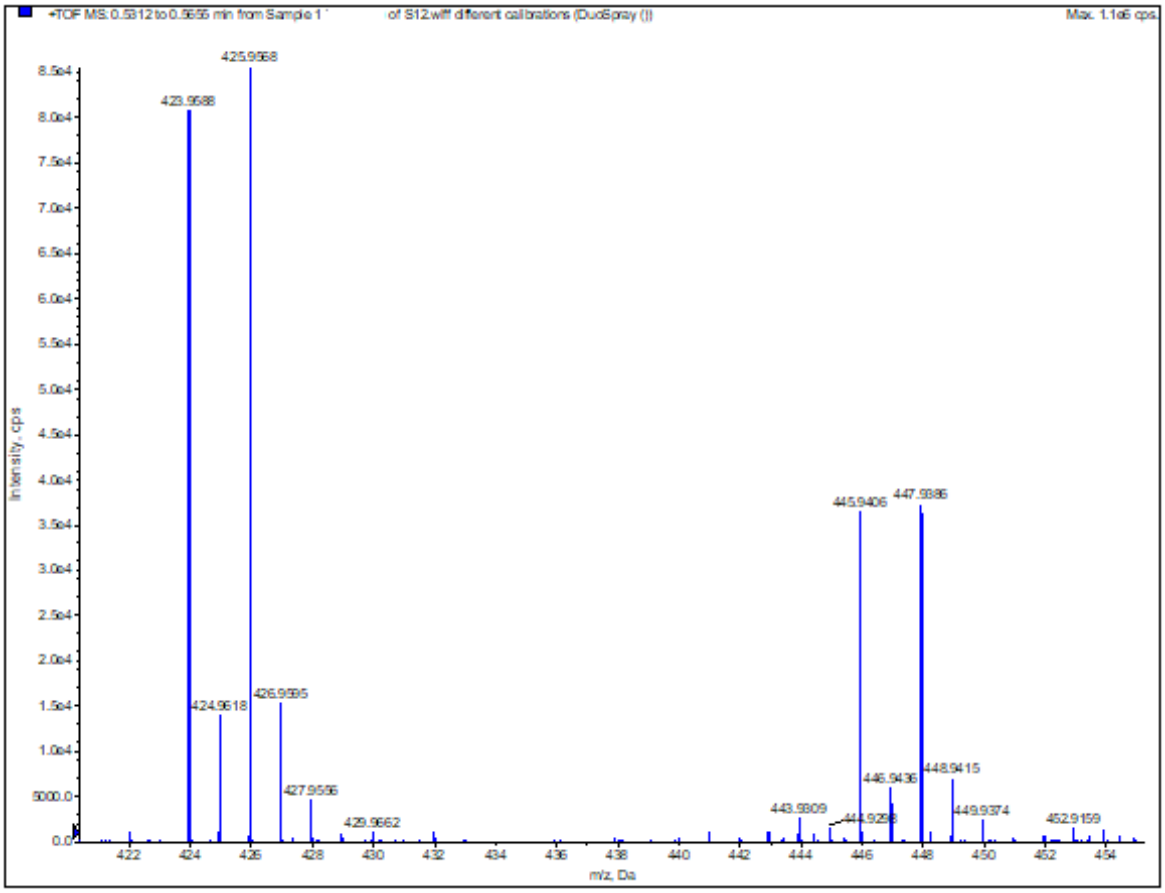
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C16 H13 N2 O3 S Cl Br	426.9518	-1.878	-4.3988	10.5

5-Bromo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3f)



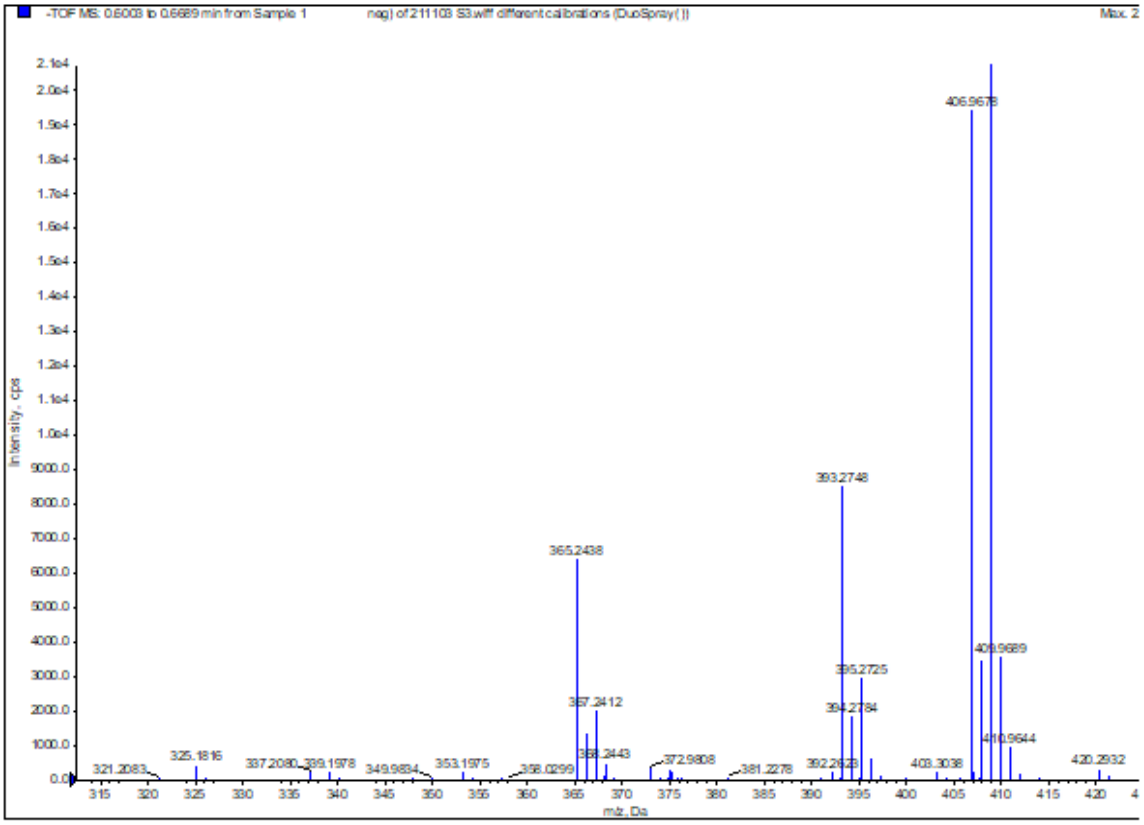
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N3 O5 S Br	423.9602	-2.0785	-4.9027	11.5

5-Bromo-2-({[(2-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3g)



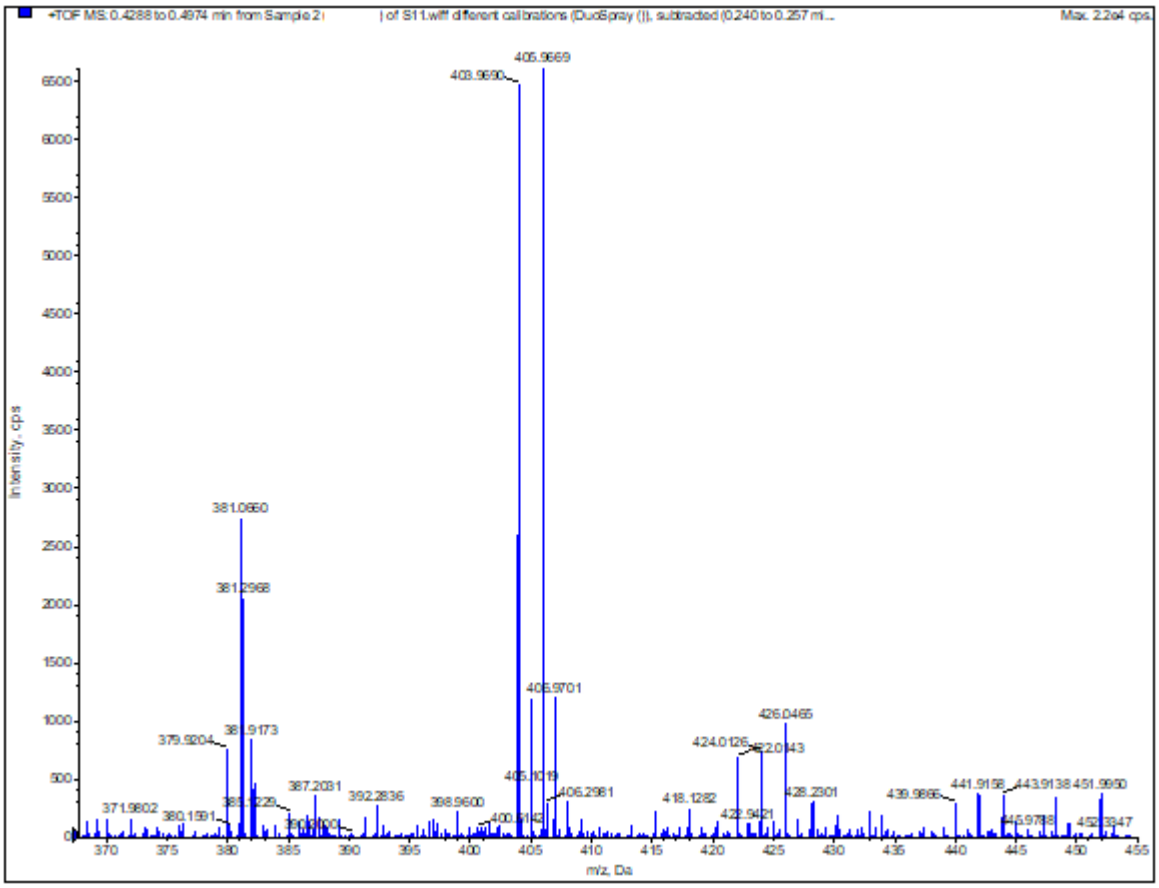
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N3 O5 S Br	423.9602	-1.4785	-3.4875	11.5

5-Bromo-2-({[(4-methoxyphenyl)formamido]methanethioyl}amino)benzoic acid (3h)
(neg)



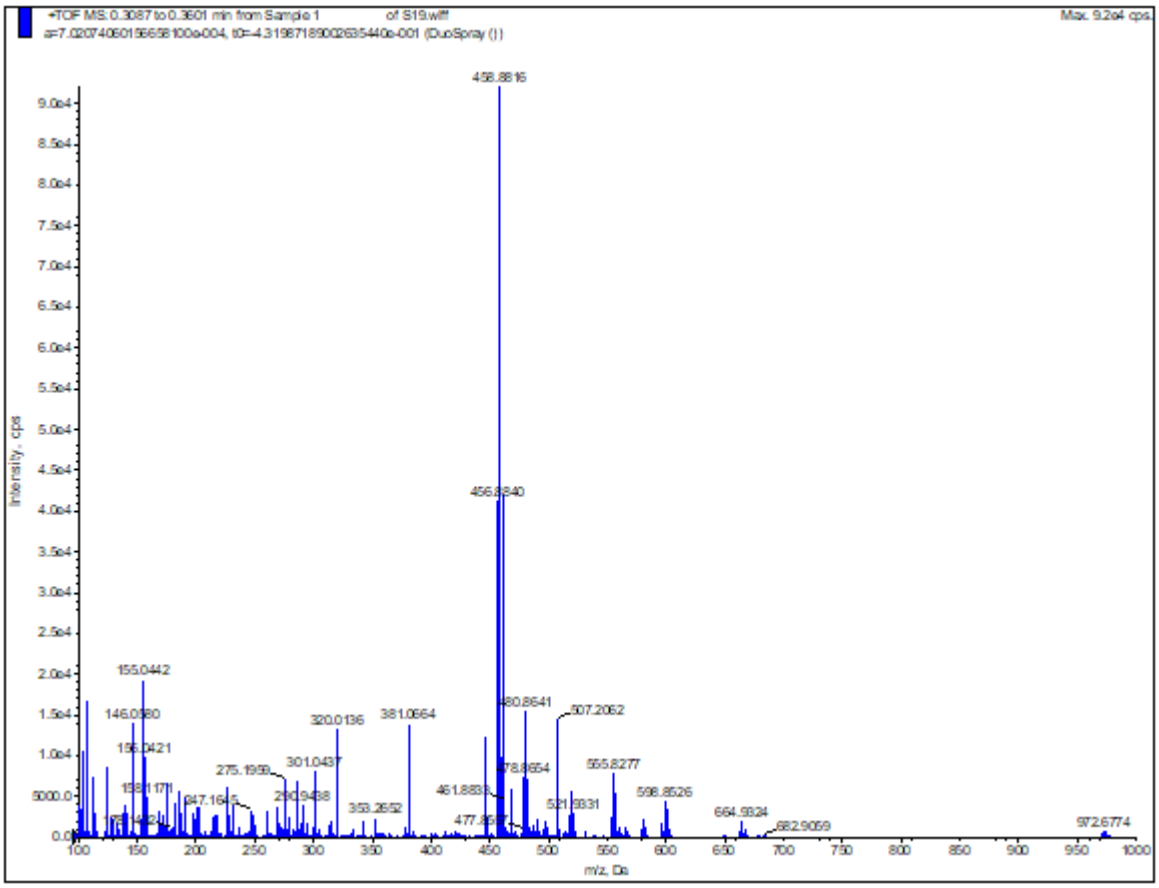
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C16 H12 N2 O4 S Br	406.9701	-2.3149	-5.6883	11.5

5-Bromo-2-({[(4-cyanophenyl)formamido]methanethioyl}amino)benzoic acid (3i)



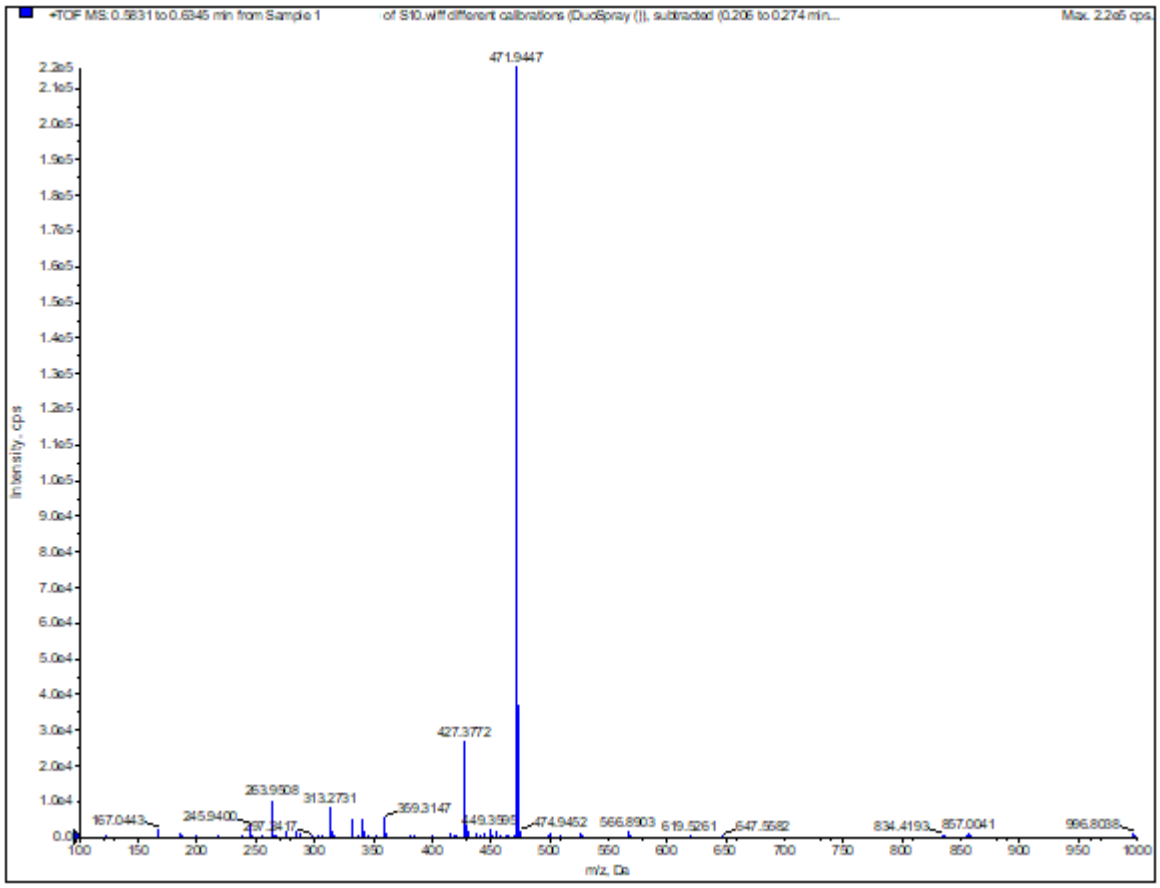
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C16 H11 N3 O3 S Br	403.9704	-1.4492	-3.5876	12.5

5-Bromo-2-({[(2-bromophenyl)formamido]methanethioyl}amino)benzoic acid (3j)



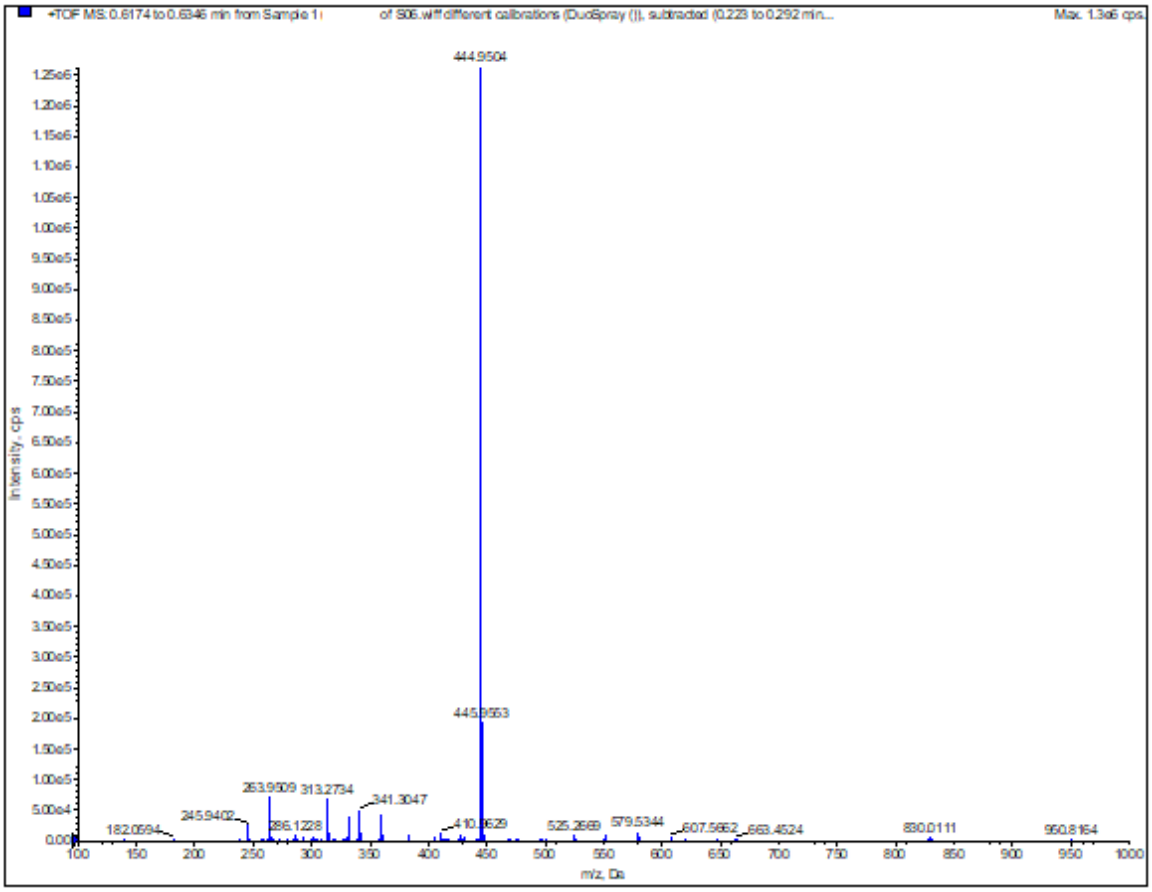
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N2 O3 S Br2	456.8857	-1.7113	-3.7457	10.5

5-Iodo-2-({[(4-nitrophenyl)formamido]methanethioyl}amino)benzoic acid (3k)



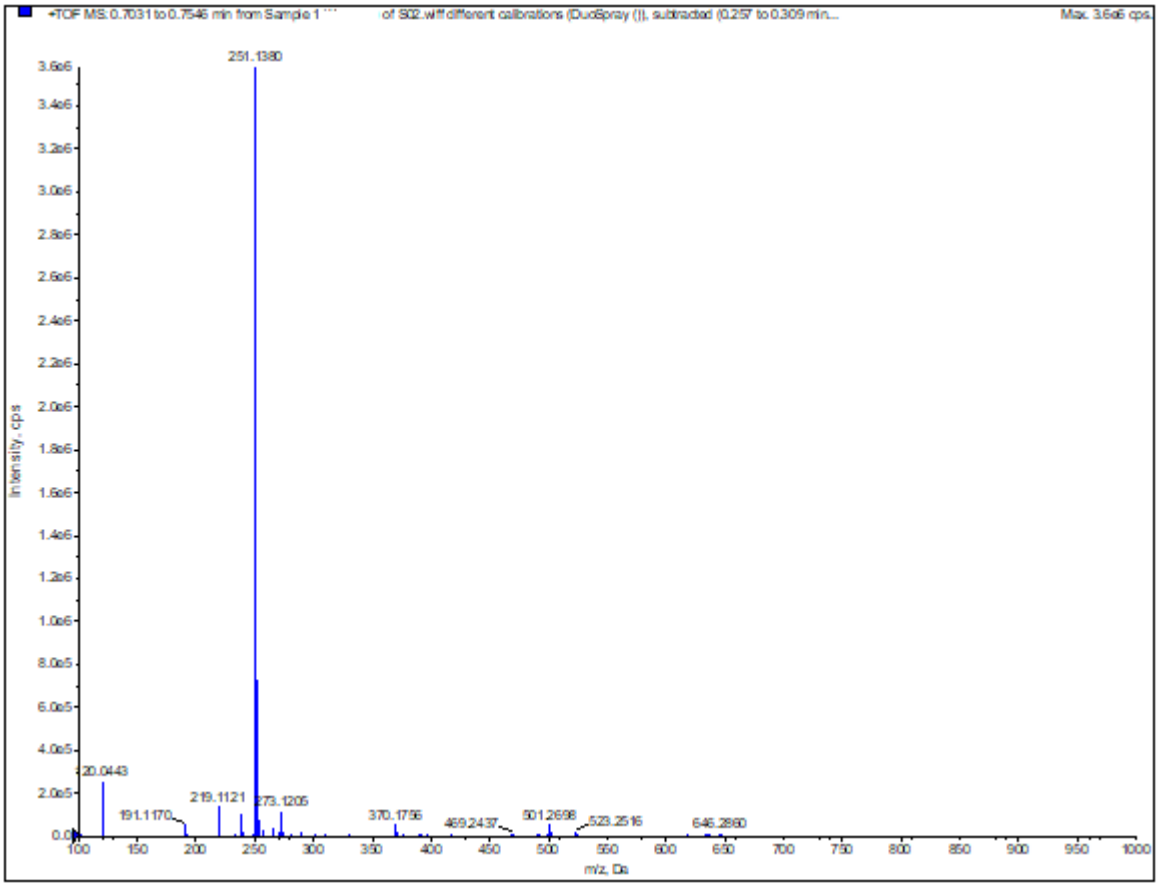
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N3 O5 S I	471.9458	-1.1708	-2.4809	11.5

5-Iodo-2-({[(4-fluorophenyl)formamido]methanethioyl}amino)benzoic acid (3l)



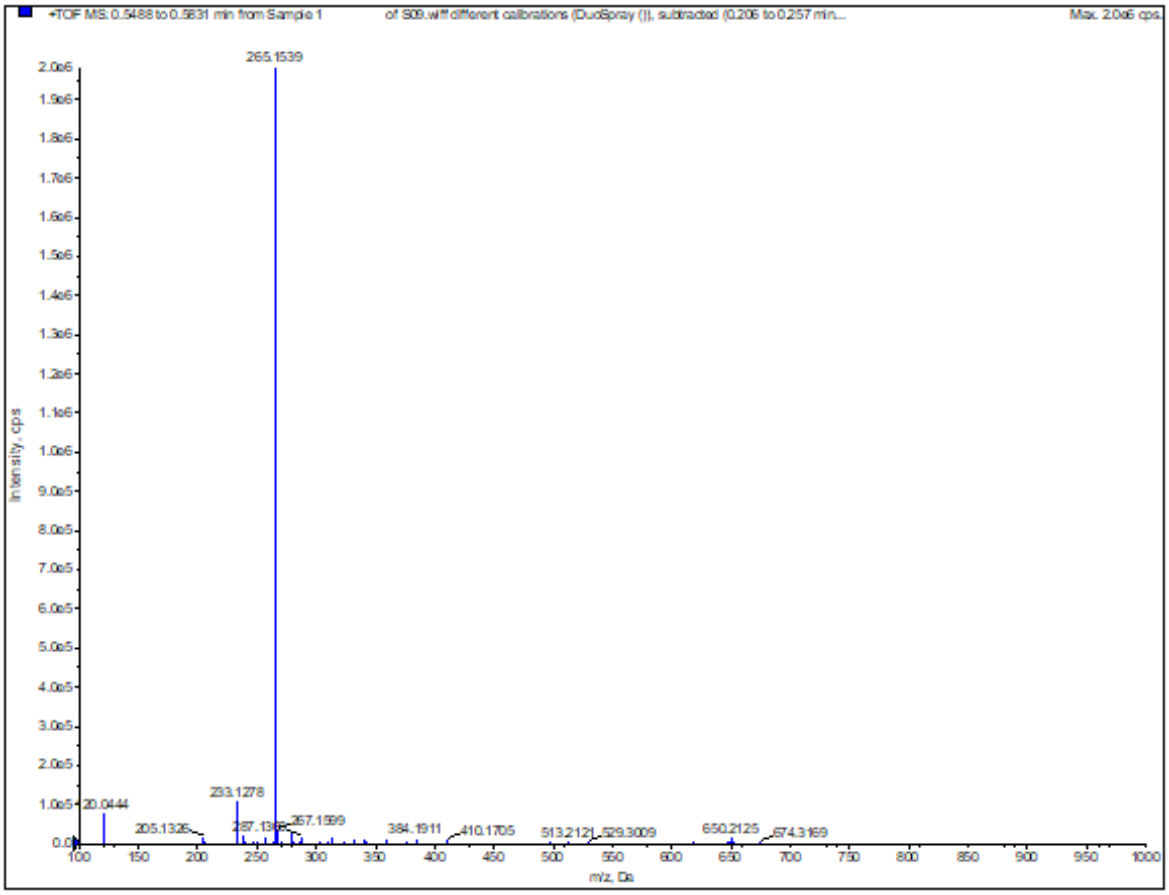
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H11 N2 O3 F S I	444.9513	-0.9708	-2.1819	10.5

(2*S*)-*N*-(2-Aminobenzoyl)-2-isopropylaminoacetic acid methyl ester (9a)



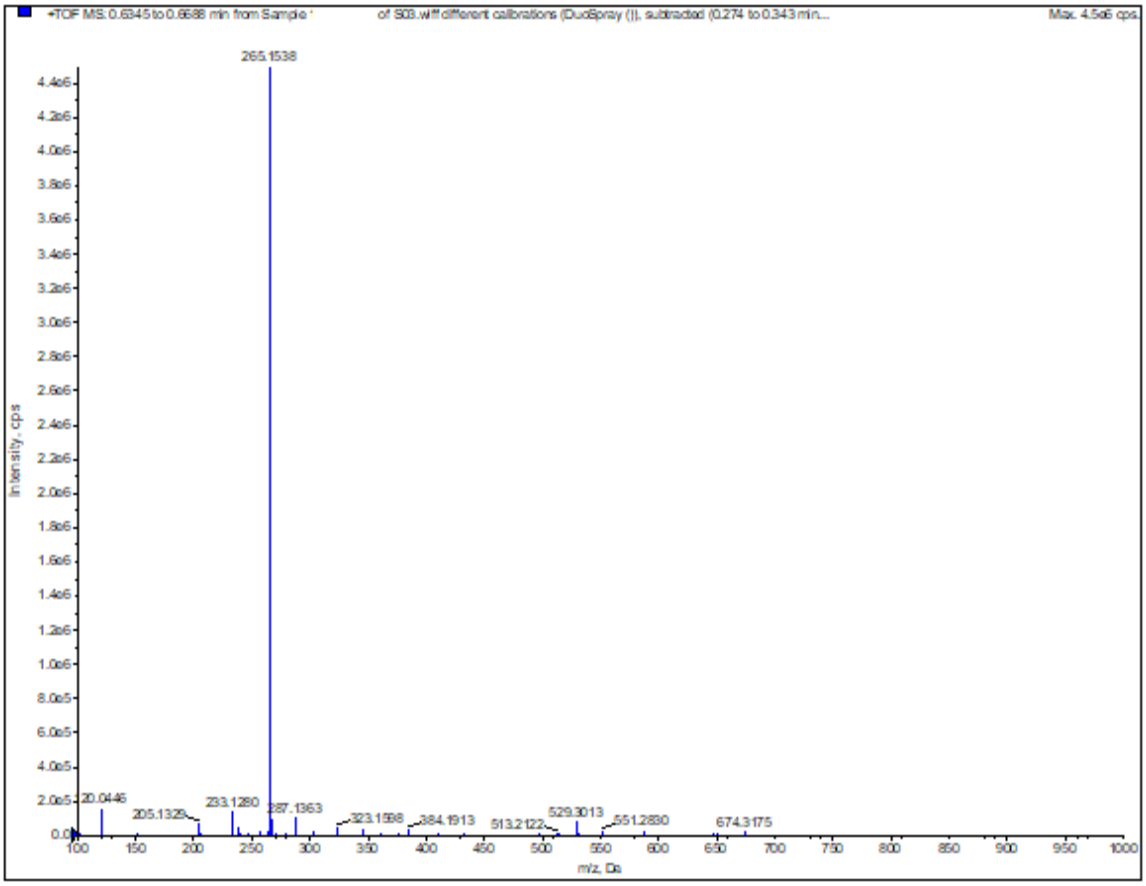
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C13H19N2O3	251.13902	-1.07	-4.3	6.0

(2*S*)-*N*-(2-Aminobenzoyl)-2-isobutylaminoacetic acid methyl ester (9b)



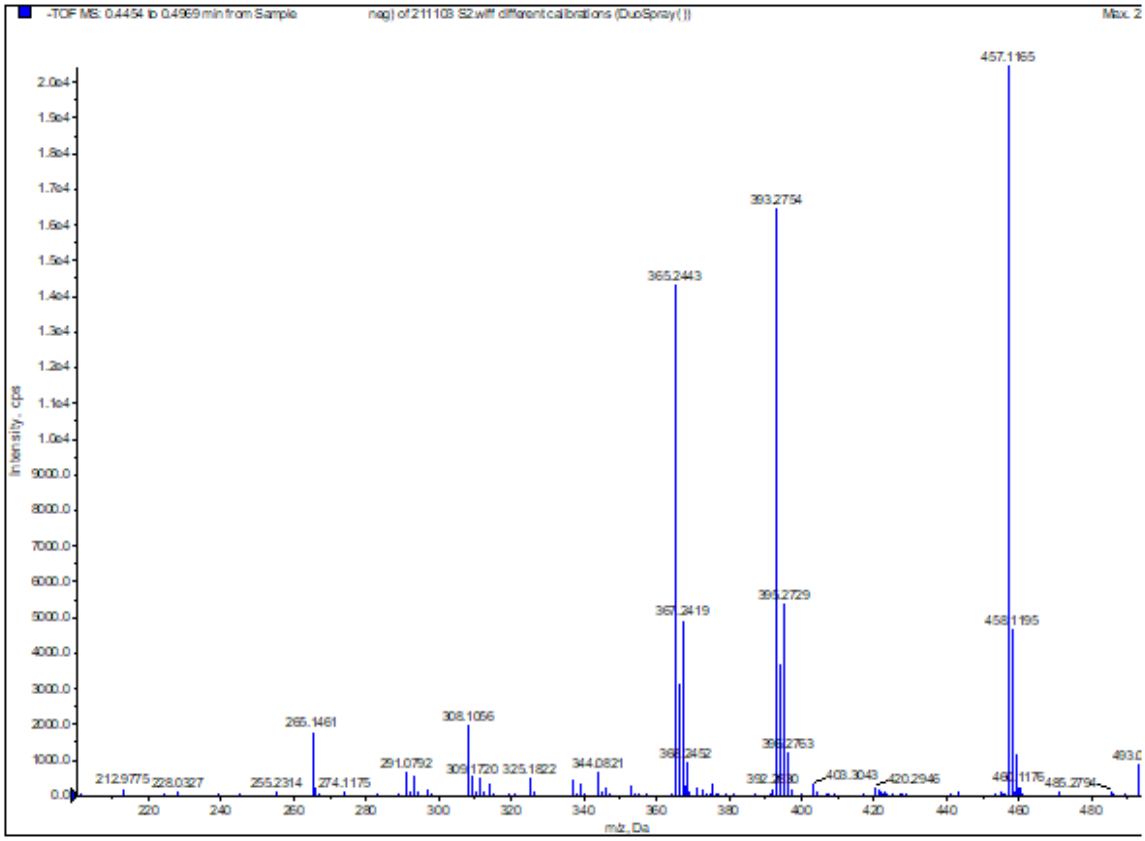
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C14 H21 N2 O3	265.1546	-0.7691	-2.9009	5.5

(2*S*)-*N*-(2-Aminobenzoyl)-2-(2-methylbutyl)aminoacetic acid methyl ester (9c)



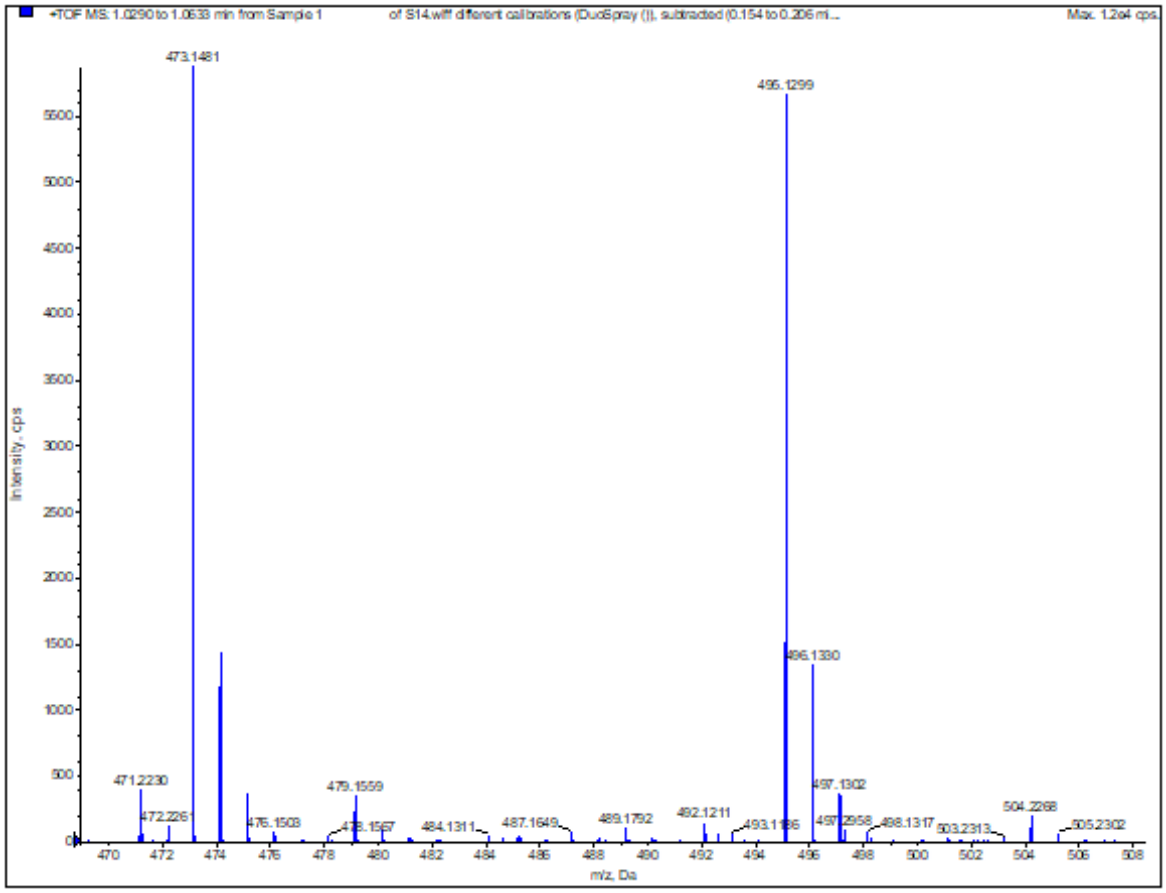
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C14 H21 N2 O3	265.1546	-0.8691	-3.278	5.5

Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}butanoate (10a) (neg)



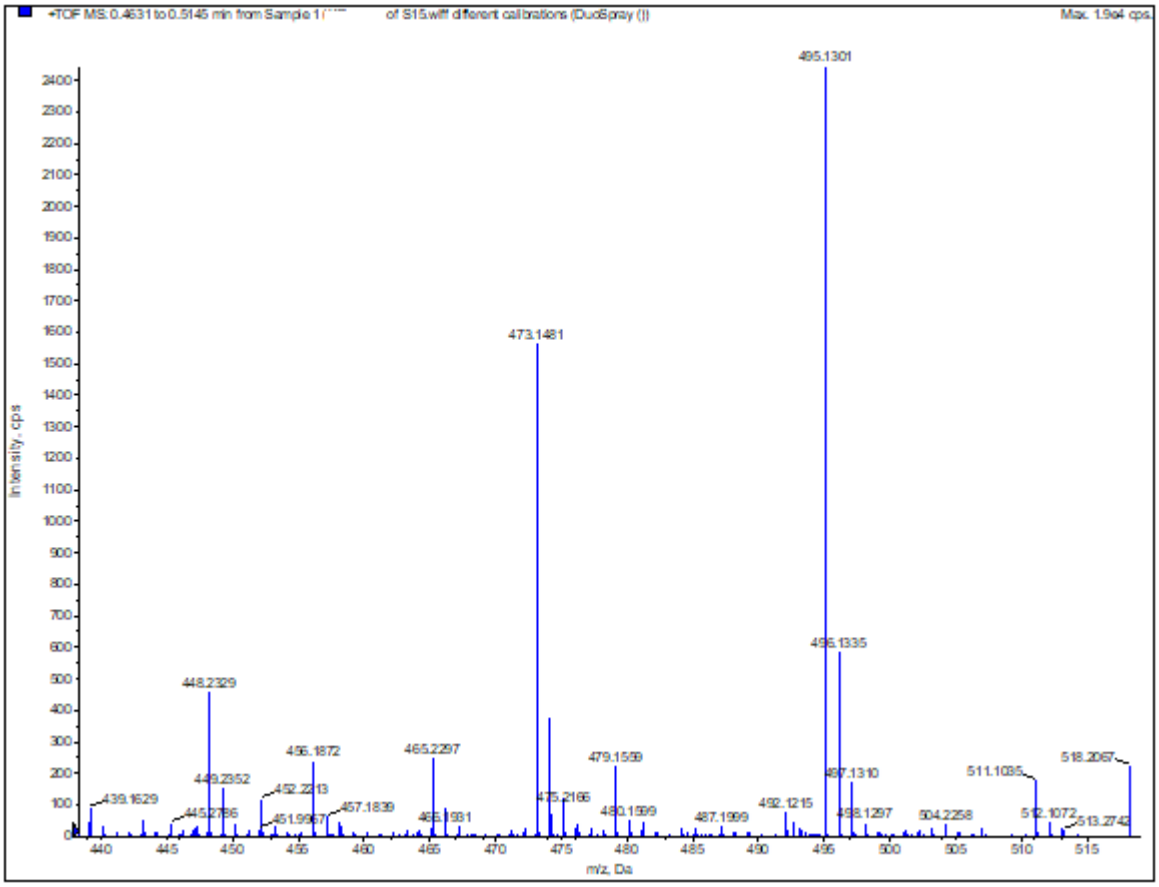
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C21 H21 N4 O6 S	457.1181	-1.6815	-3.6785	13.5

Methyl (2*S*)-4-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (10b)



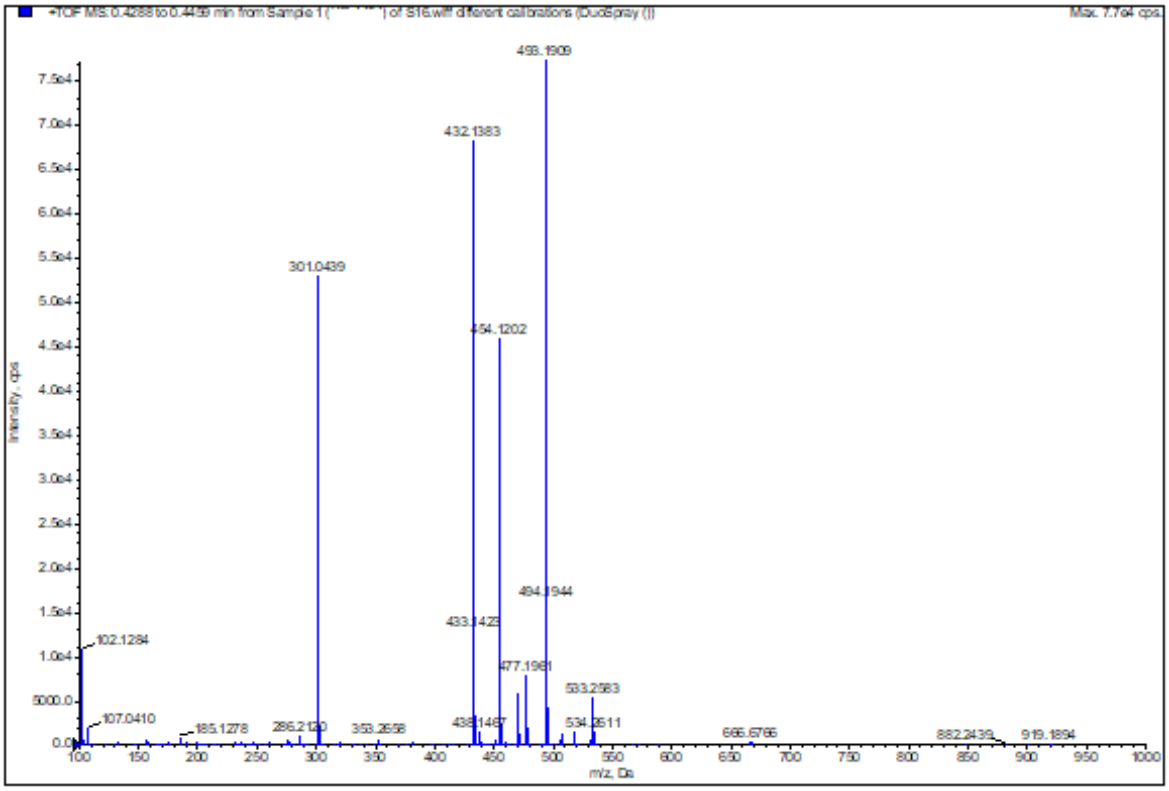
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C22 H25 N4 O6 S	473.1494	-1.3816	-2.9201	12.5
C22 H24 N4 O6 Na S	495.1314	-1.5263	-3.0826	12.5

Methyl (2*S*)-3-methyl-2-{[2-({[(4-nitrophenyl)formamido]methanethioyl}amino)phenyl]formamido}pentanoate (10c)



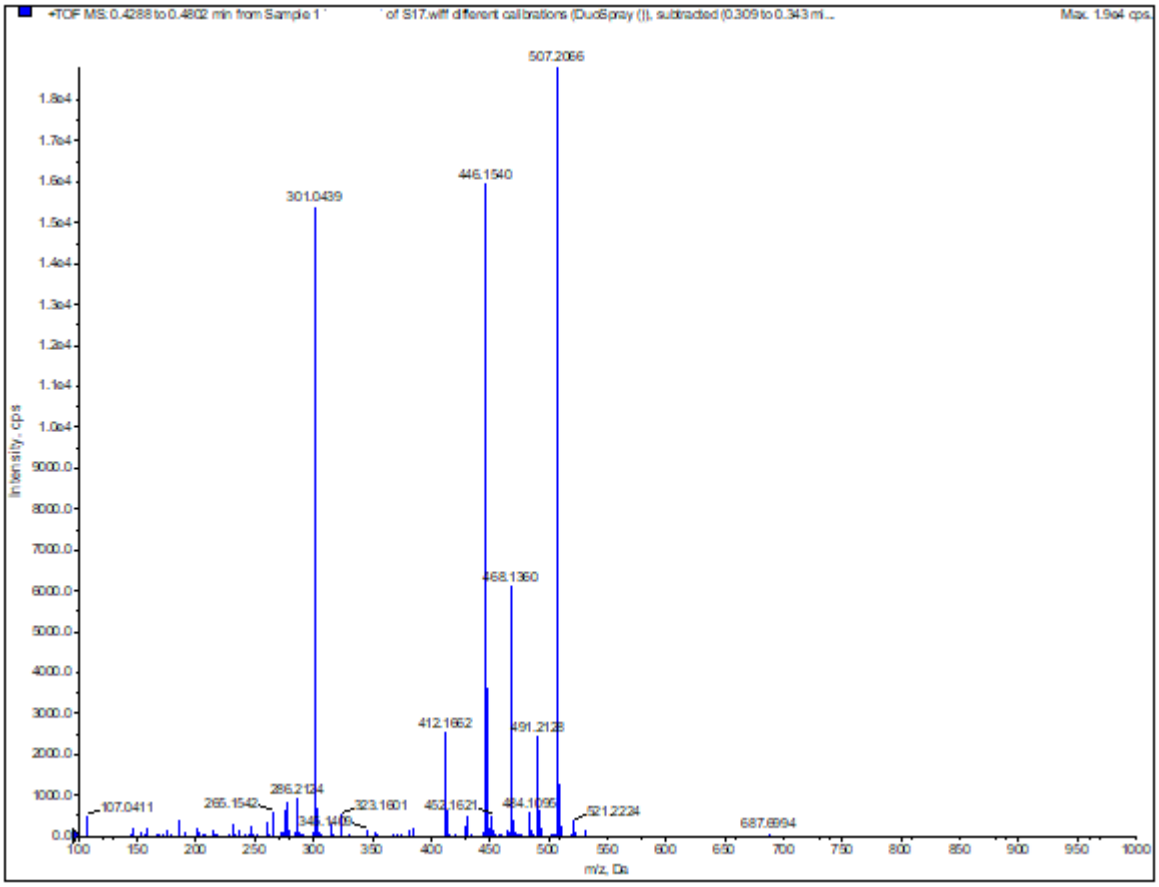
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C22 H25 N4 O6 S	473.1494	-1.3816	-2.9201	12.5
C22 H24 N4 O6 Na S	495.1314	-1.3263	-2.6787	12.5

Methyl-(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylbutanoate (10d)



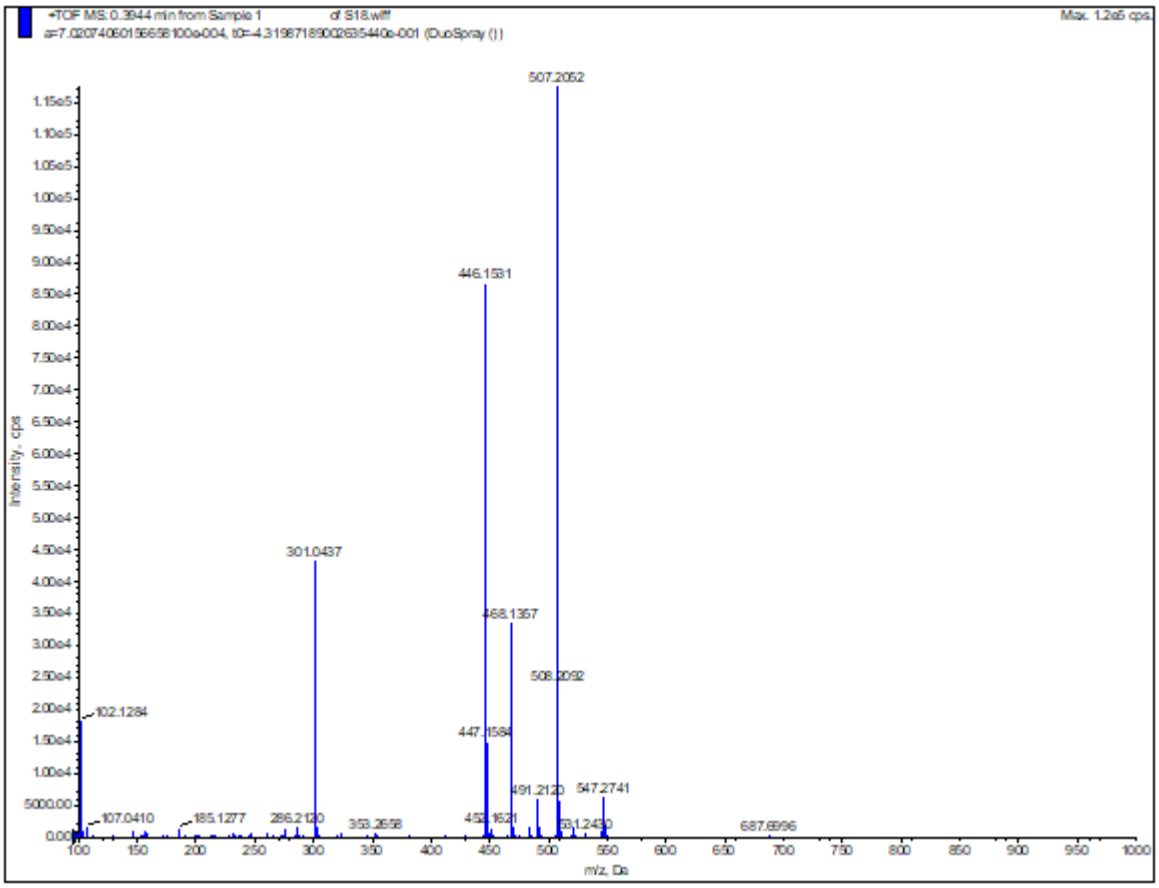
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C21 H23 N3 O4 F S	432.1393	-1.0315	-2.387	11.5
C21 H22 N3 O4 F Na S	454.1212	-1.0762	-2.3698	11.5

Methyl-(2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-4-methylpentanoate (**10e**)



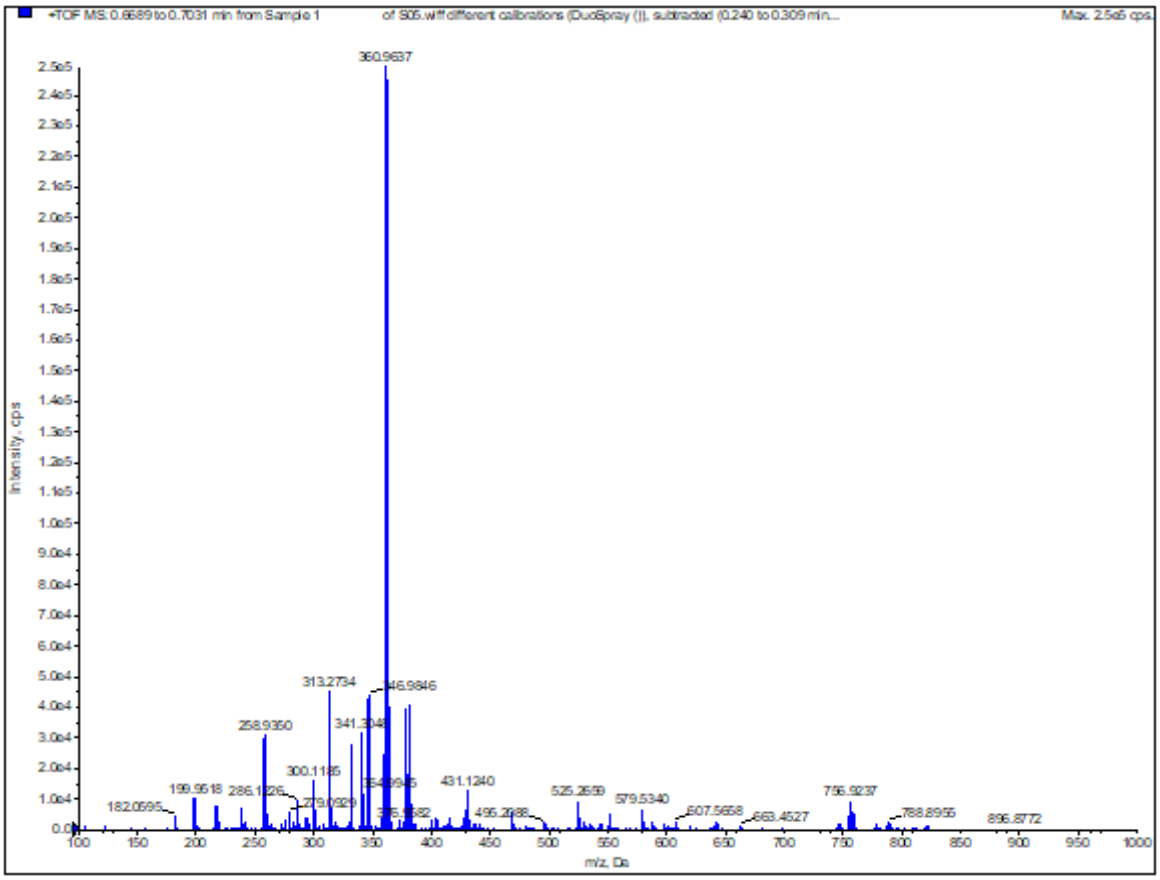
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C22 H25 N3 O4 F S	446.1549	-0.9816	-2.2002	11.5
C22 H24 N3 O4 F Na S	468.1369	-0.9262	-1.9786	11.5

Methyl (2*S*)-2-{[2-({[(4-fluorophenyl)formamido]methanethioyl}amino)phenyl]formamido}-3-methylpentanoate (10f)



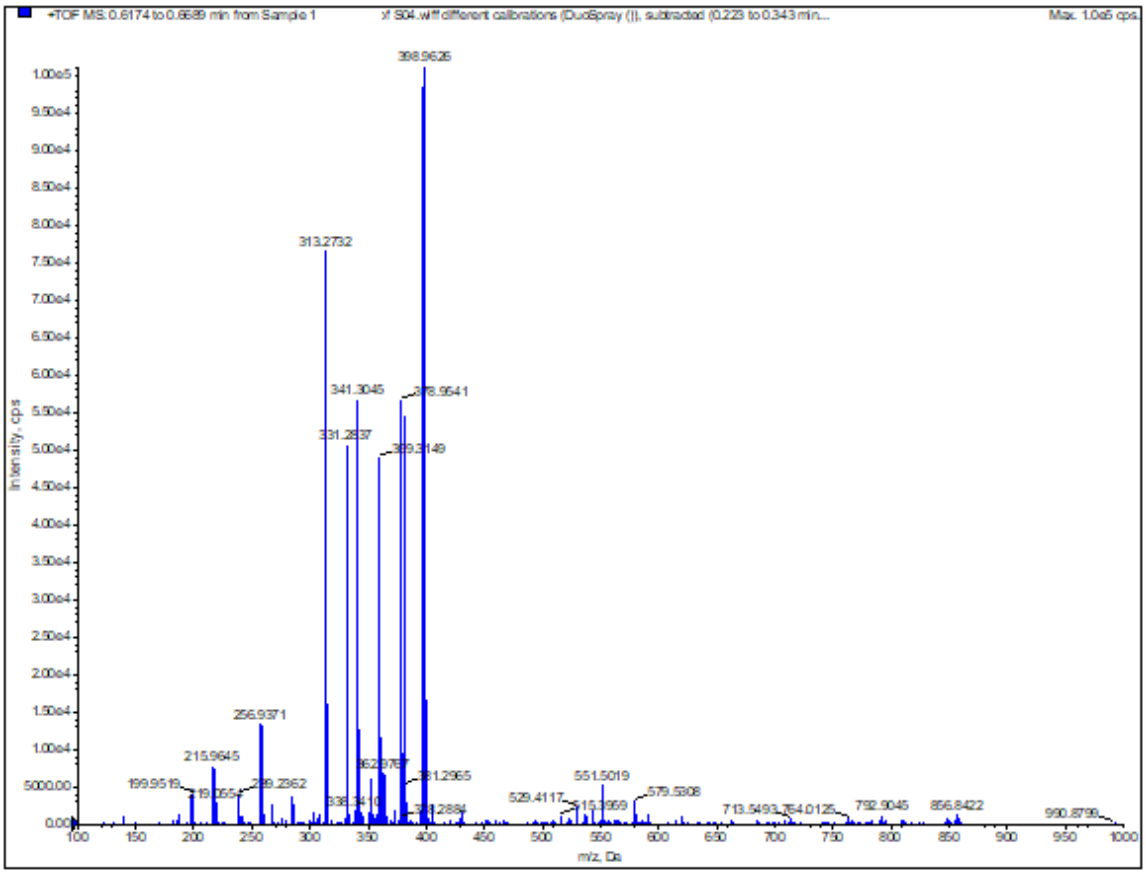
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C22 H25 N3 O4 F S	446.1549	-1.8816	-4.2174	11.5
C22 H24 N3 O4 F Na S	468.1369	-1.2262	-2.6195	11.5

***N*-(6-Bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11a)**



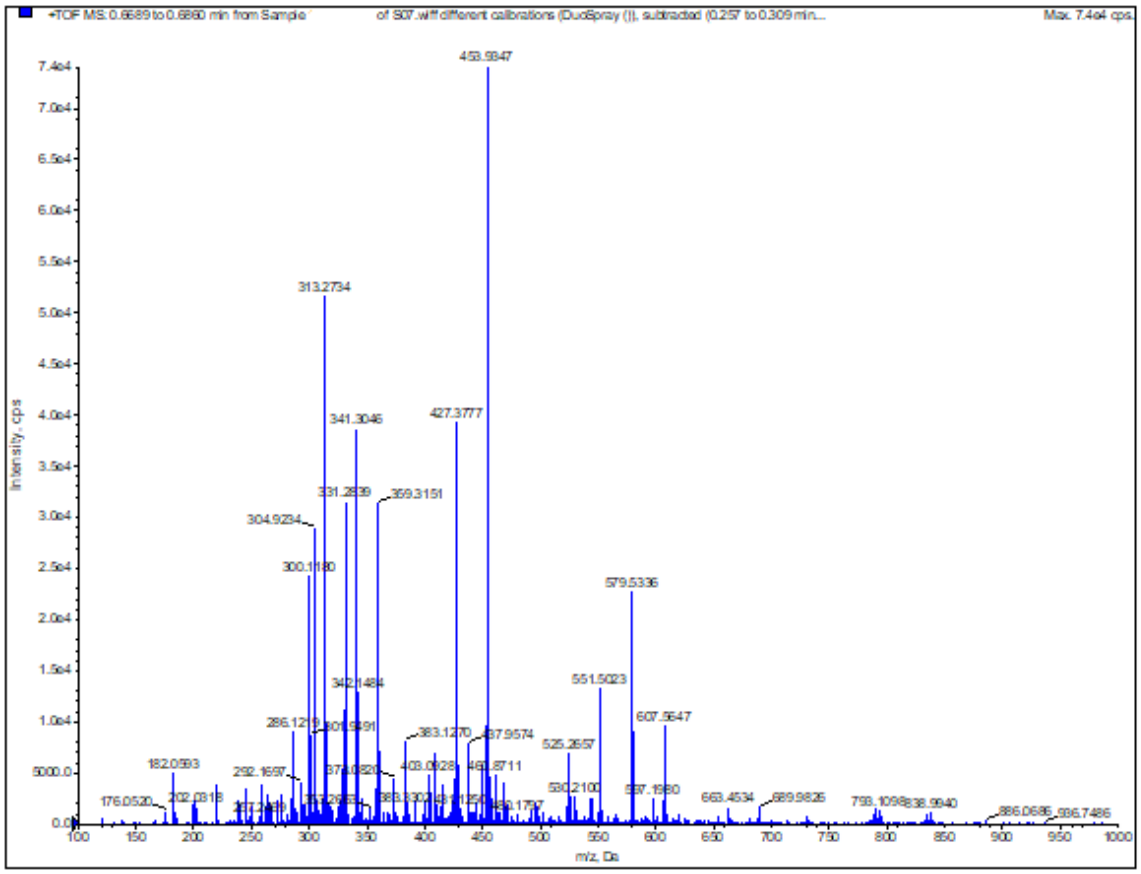
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H10 N2 O2 S Br	360.964	-0.387	-1.0721	11.5
C15 H12 N2 O3 S Br	378.9746	-0.6517	-1.7197	10.5
C15 H10 N2 O3 Br	344.9869	-0.3298	-0.9561	11.5

4-Fluoro-*N*-(6-bromo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11b)



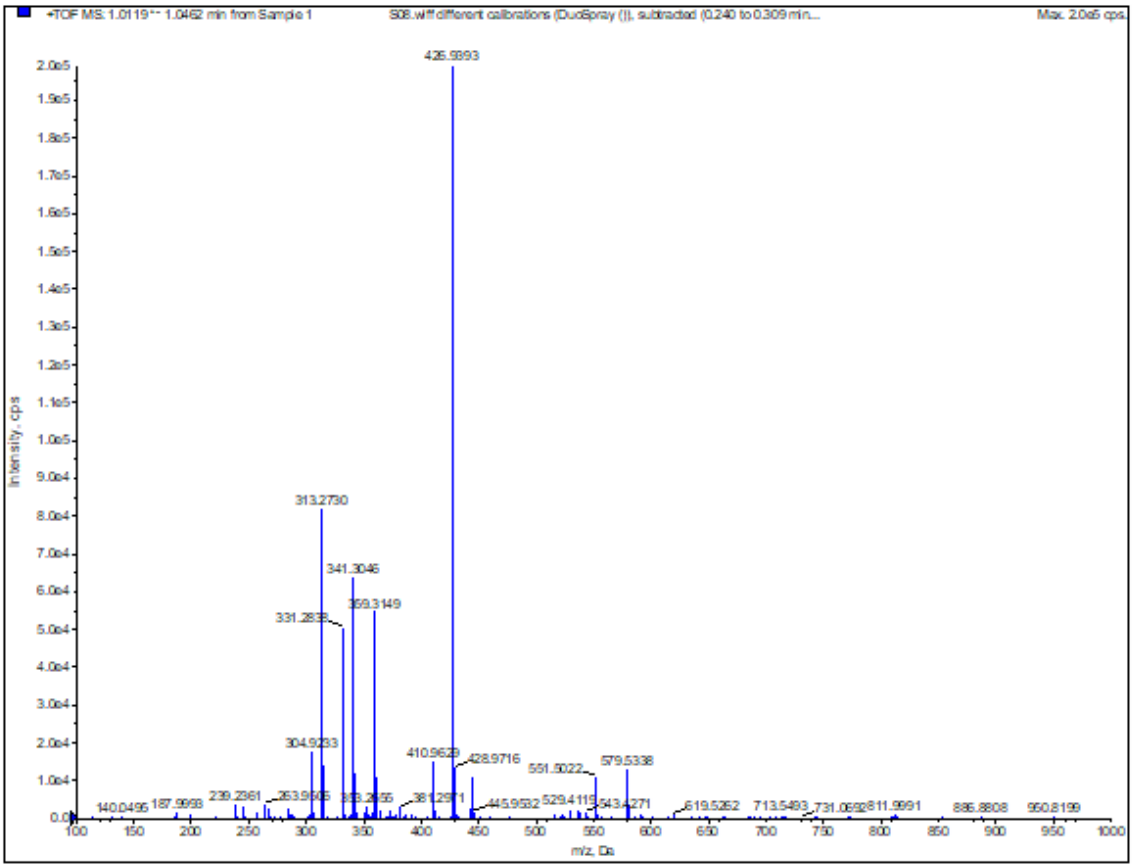
Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H9 N2 O2 F S Br	378.9546	-0.5652	-1.4915	11.5
C15 H11 N2 O3 F S Br	396.9652	-0.7299	-1.8388	10.5

4-Nitro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11c)



Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H9 N3 O4 S I	453.9353	-0.6061	-1.3353	12.5

4-Fluoro-*N*-(6-iodo-4-oxo-4*H*-3,1-benzothiazin-2-yl)benzamide (11d)



Formula	Calculated mass	Error / mDa	Error / ppm	DBE
C15 H9 N2 O2 F S I	426.9408	-1.5061	-3.5277	11.5