Supporting Information

Design, synthesis, spectroscopic characterization, computational analysis, in vitro α-amylase and α-glucosidase evaluation of 3-aminopyridin-2(1*H*)-ones based novel monothioxamides and 1,3,4-thiadiazoles

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Experimental Procedures

1. Materials and Methods

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX400 (400 and 100 MHz, respectively) and Bruker AVANCE 500 (500 and 125 MHz, respectively) instruments using DMSO-d6 the internal standard was TMS or residual solvent signals (2.49 and 39.9 ppm ^{1}H and for ^{13}C nuclei in DMSO-d6).

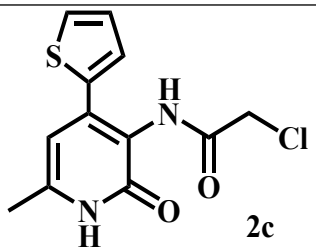
Sample were analyzed by HPLC-MS on an Agilent 1260 Infinity II chromatograph coupled to an Agilent 6545 LC/Q-TOF high-resolution mass spectrometer with a Dual AJS ESI ionization source operating in positive ion mode using the following parameters: capillary voltage: 4000 V; spray pressure: 20 (psi); drying gas: 10 *l*/min; gas temperature: 325ºC; sheathed gas flow: 12 *l*/min; shielding gas temperature: 400°C; nozzle voltage: 0 V, fragmentation voltage: 180 V; skimmer voltage: 45 V; octopole RF: 750 V. Mass spectra with LC/MS accuracy were recorded in the range 100-1000 m/z, scan rate 1.5 spectrum/s.
Chromatographic separation was carried out on columns: ZORBAX RRHD Eclipse Plus C18 (2.1 x 50 mm, particle size 1.8 μm). The column temperature during the analysis was maintained at 35°C. The mobile phase was formed by eluents A and B. In the positive ionization mode, 0.1% formic acid solution in deionized water was used as eluent A, and 0.1% formic acid solution in acetonitrile was used as eluent B. Chromatographic separation was performed with elution according to the following scheme: 0-10 min 95% A, 10-13 min 100% B, 13-15 min 95% A. The flow of the mobile phase was maintained at 400 μL/min throughout the analysis. In all experiments, the sample injection volume was 1 μL. The sample was prepared by dissolving the entire sample (in 1000 μL) in methanol (for HPLC). Sample dilution was carried out immediately before analysis.
The recorded data were processed using Agilent MassHunter 10.0 software.
Melting points were determined using a Stuart SMP10 hot bench. Monitoring of the reaction course and the purity of the products was carried out by TLC on Sorbfil plates and visualized using iodine vapor or UV light.

2-Chloro-N-(6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)acetamide was prepared by similar a literature procedure [A.S. Fisyuk, I.V. Kulakov, D.S. Goncharov, O.S. Nikitina, Y.P. Bogza, A.L. Shatsauskas, Synthesis of 3-Aminopyridin-2(1*H*)-ones and 1*H*-Pyrido[2,3-b][1,4]Oxazin-2(3*H*)-ones, Chem. Heterocycl. Compd., 50 (2014) 217-224, doi:10.1007/s10593-014-1464-9]**.**

Synthesis of 2-chloro-N-(6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)acetamide (2c).

Pyridine (0.08 ml, 1 mmol) was added to a solution of 3-amino-6-methyl-4-(thiophen-2-yl)pyridin-2(1*H*)-one (**1c**) (206 mg, 1 mmol) in dichloromethane (20 ml), the mixture was cooled to 5°C, and chloroacetyl chloride (1.0 ml, 1.2 mmol) was added dropwise. The mixture was stirred at room temperature for 15 h. The solvent was removed by evaporation, and the residue was treated with ice-cold water. The precipitate formed was filtered off, washed with distilled water, and recrystallized from 2-propanol.

Characterization data of products 2c



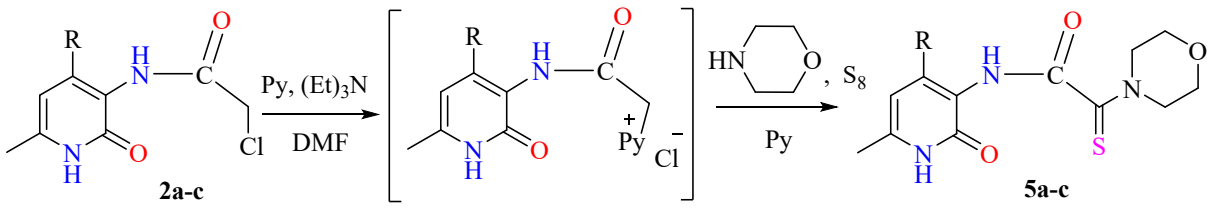
2c

Chemical Formula: $C_{12}H_{11}ClN_2O_2S$
Molecular Weight: 282,7420

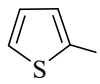
2-Chloro-N-(6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)acetamide.
Beige powder, yield 240 mg, 85%. M.p. 230-232°C. ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 2.20 (s, 3H, CH_3); 4.26 (s, 2H, CH_2Cl); 6.42 (s, 1H, H-5); 7.15 (bs, 1H, H-4 Th); 7.64 (bs, 1H, H-3 Th); 7.72 (bs, 1H, H-5 Th) 9.44 (s, 1H, NHCO'); 11.75 (bs., 1H, NH). ^{13}C NMR (100 MHz, DMSO-d6) δ ppm 18.4 (CH_3); 42.9 (CH_2Cl); 102.8 (C-5); 118.8, 127.2 (C-3 Th); 128.9 (C-4 Th); 129.7 (C-5 Th); 137.1; 140.8; 143.2; 160.6; 165.8. HRMS m/z: calcd for $C_{13}H_{18}N_3O_3S^+$ [M + H]$^+$: 283.0303; found: 283.0309.

Synthesis of 2-morpholino-2-thioxoacetamides derivatives 5a-c

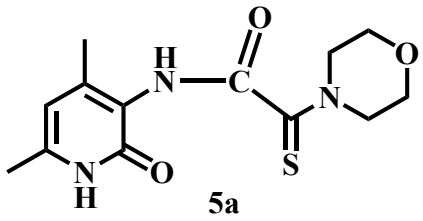
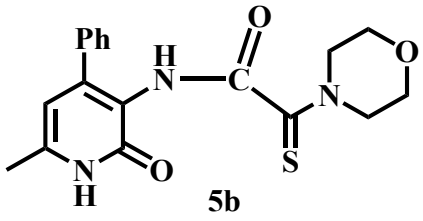
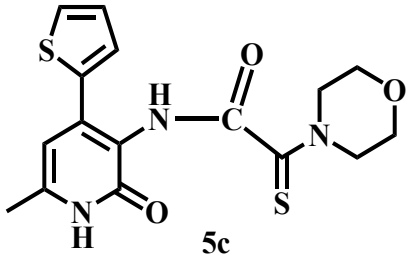
To a mixture (1 mmol) of 2-chloro-N-methylacetamide **2a-c** and 1.5 ml of pyridine in 4 ml of DMF was added a previously prepared solution of 0.2 ml (2.3 mmol) of morpholine and 140 mg (4.4 mmol) of sulfur in 1 ml of triethylamine and 2 ml DMF. The reaction mixture was stirred at t = 20 ° C for 12 hours, then diluted with 25 ml of water, the precipitated were filtered off. The resulting products were recrystallized from a mixture of 2-propanol: DMF (3:1).



2a-c **5a-c**

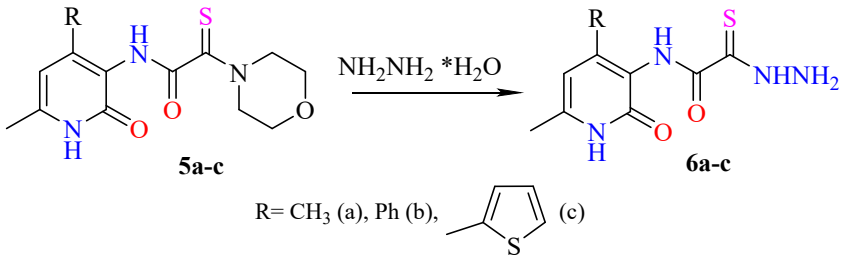
R= CH_3 (a), Ph (b),  (c)

Characterization data of products 5a-c

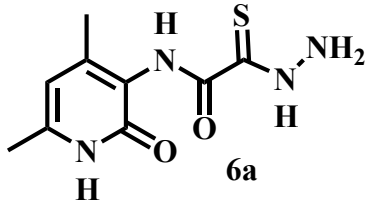
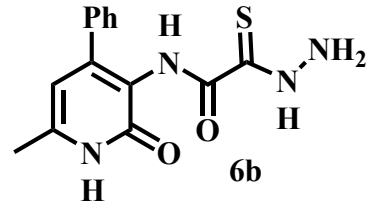
 **5a** Chemical Formula: $C_{13}H_{17}N_3O_3S$ Molecular Weight: 295,3570	**N-(4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2-morpholino-2-thioxoacetamide (5a).** White powder, yield 165 mg, 56%. M.p. 279-281 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 2.02 (s, 3H, CH_3); 2.13 (s, 3H, CH_3); 3.72 (s, 4H, $O(CH_2)_2$); 3.98 (bs, 2H, $N(CH_2)_a$); 4.09 (bs, 2H, $N(CH_2)_b$); 5.89 (s, 1H, H-5); 9.57 (s, 1H, NHCO'); 11.54 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d6) δ ppm 17.41 (CH_3); 18.20 (CH_3); 46.97 ($N(CH_2)_a$); 52.08 ($N(CH_2)_b$); 65.48 ($O(CH_2)_b$); 66.16 ($O(CH_2)_a$); 106.39 (H-5); 120.77; 142.69; 147.60; 159.92; 164.19; 192.03. HRMS m/z: calcd for $C_{13}H_{18}N_3O_3S^+$ [M + H]$^+$: 296.1063; found: 296.1070.
 **5b** Chemical Formula: $C_{18}H_{19}N_3O_3S$ Molecular Weight: 357,4280	**N-(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)-2-morpholino-2-thioxoacetamide (5b)** Yellow powder, yield 214 mg, 60%. M.p. 282-284 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 2.22 (s, 3H, CH_3); 3.60 (br. t, *J*=4.6, 2H, $O(CH_2)_a$); 3.66 (br. t, *J*=4.6, 2H, $O(CH_2)_b$); 3.93 (br. t, *J*=4.3, 2H, $N(CH_2)_a$); 4.04 (br. t, *J*=4.6, 2H, $N(CH_2)_b$); 6.07 (s, 1H, H-5); 7.38-7.45 (m, 5H, Ph); 9.58 (s, 1H, NHCO') 11.84 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d6) δ ppm 18.49 (CH_3); 46.97 ($N(\underline{C}H_2)_a$); 51.88 ($N(\underline{C}H_2)_b$); 65.52 ($O(\underline{C}H_2)_a$); 66.25 ($O(\underline{C}H_2)_b$); 99.50 (H-5); 105.50; 119.70; 128.26 (2C Ph); 128.37 (2C Ph); 128.58; 136.64; 144.03; 149.61; 160.51; 164.45; 191.74. HRMS m/z: calcd for $C_{18}H_{20}N_3O_3S^+$ [M + H]$^+$: 358.1220; found: 358.1228.
 **5c** Chemical Formula: $C_{16}H_{17}N_3O_3S_2$ Molecular Weight: 363,4500	**N-(6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)-2-morpholino-2-thioxoacetamide (5c).** Beige powder, yield 260 mg, 75%. M.p. 286-288 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 2.22 (s, 3H, CH_3); 3.72 (bs, 4H, $O(CH_2)_2$); 4.12 (bs, 2H, $N(CH_2)_a$); 4.21 (bs, 2H, $N(CH_2)_b$); 6.39 (s, 1H, H-5); 7.18 (t, ^3J=4.6 Hz, 1H, H-4' Th); 7.78 (d, ^3J=4.6 Hz, 1 H, H-3' Th); 7.80 (d, ^3J=4.6 Hz, 1 H, H-5' Th); 9.72 (s, 1H, NHCO'); 11.69 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d6) δ ppm 18.52 (CH_3); 47.11 ($N(CH_2)_a$); 52.06 ($N(CH_2)_b$); 65.60 ($O(CH_2)_a$); 66.43 ($O(CH_2)_b$); 103.23 (H-5); 118.12; 127.89; 129.62; 129.82; 137.14; 141.51; 143.83; 160.58; 164.19; 191.87. HRMS m/z: calcd for $C_{16}H_{18}N_3O_3S_2^+$ [M + H]$^+$: 364.0784; found: 364.0788.

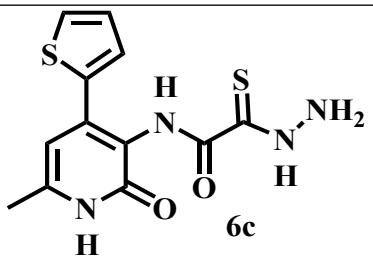
Synthesis of (1,2-dihydropyridin-3-yl)-2-morpholino-2-thioxoacetamide derivatives 6a-c

To 0.1 mmol of monothiooxamide **5a-c** was added 30 mmol of hydrazine hydrate, and the mixture was left standing at room temperature. On completion of reaction (TLC monitoring) the reaction mixture was poured into 100 ml of water, the solution was acidified by hydrochloric acid to pH 5. The separated precipitate was filtered off and dried in air to obtain analytically pure compounds **6a-c.**



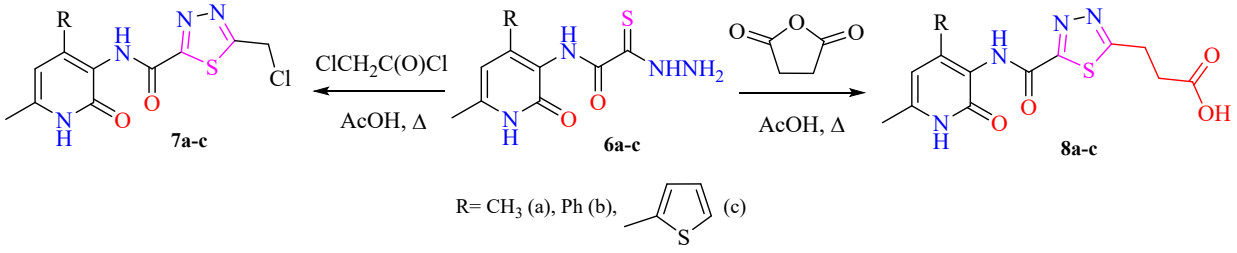
Characterization data of products 6a-c

 **6a** Chemical Formula: $C_9H_{12}N_4O_2S$ Molecular Weight: 240,2810	**N-(4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2-hydrazinyl-2-thioxoacetamide (6a).** Beige powder, yield 163 mg, 68%. M.p. 230-232 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 1.98 (s, 3H, CH_3); 2.13 (s, 3H, CH_3); 5.92 (s, 1H, H-5); 6.48 (bs, 2H, NH_2); 9.46 (s, 1H, NHCO'); 11.76 (s, 1H, 1-NH); 12.93 (bs., 1H, C(S)NH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.14 (CH_3); 18.70 (CH_3); 106.90 (C-5); 121.35; 141.82; 144.97; 157.18; 159.52; 166.27. HRMS m/z: calcd for $C_9H_{13}N_4O_2S^+$ $[M + H]^+$: 241.0261; found: 241.0260.
 **6b** Chemical Formula: $C_{14}H_{14}N_4O_2S$ Molecular Weight: 302,3520	**2-Hydrazinyl-N-(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)-2-thioxoacetamide (6b).** White powder, yield 175 mg, 58%. M.p. 148-150 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.21 (s, 3H, CH_3); 6.06 (s, 1H, H-5); 6.27 (bs, 2H, NH_2); 7.31-7.41 (m, 5H, Ph); 9.50 (s, 1H, NHCO'); 11.99 (bs, 1H, 1-NH); 12.77 (bs, 1H, C(S)NH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.37 (CH_3); 105.85 (C-5); 120.23; 127.33 (2C, Ph); 128.24 (3C, Ph); 137.80; 142.96; 147.19; 157.25; 160.11; 166.11. HRMS m/z: calcd for $C_{14}H_{15}N_4O_2S^+$ $[M + H]^+$: 303.0910; found: 303.0921

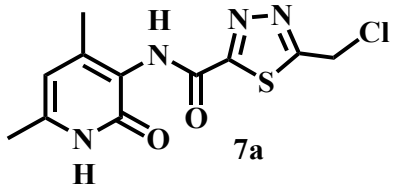
 6c Chemical Formula: $C_{12}H_{12}N_4O_2S_2$ Molecular Weight: 308,3740	**2-Hydrazinyl-N-(6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)-2-thioxoacetamide (6c).** Beige powder, yield 203 mg, 66%. M.p. 249-251 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.2 (s, 3H, CH_3); 6.38 (bs, 2H, NH_2); 6.42 (s, 1H, H-5); 7.12 (dd, *J*=4.9, 3.5, 1H, H-4' Th); 7.62 (d, *J*=3.5, 1H, H-3' Th); 7.69 (d, *J*=4.9, 1H, H-5' Th); 9.5 (s, 1 H, NHCO'); 11.81 (bs, 1 H, 1-NH); 12.89 (bs, 1H, C(S)NH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.44 (CH_3); 103.11 (C-5); 118.77; 127.29 (C-3 Th); 128.83 (C-4 Th); 129.71 (C-5, Th); 137.38; 140.39; 143.16; 158.47; 160.15; 166.38. HRMS m/z: calcd for $C_{12}H_{13}N_4O_2S_2^+$ [M + H]$^+$: 309.0475; found: 309.0480.

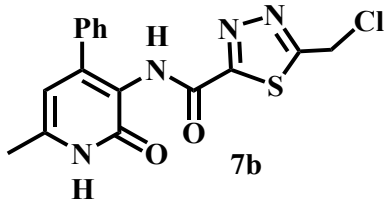
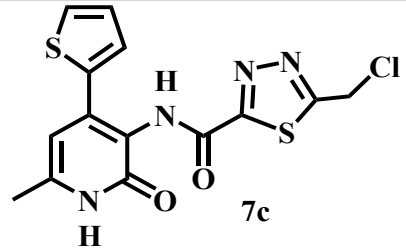
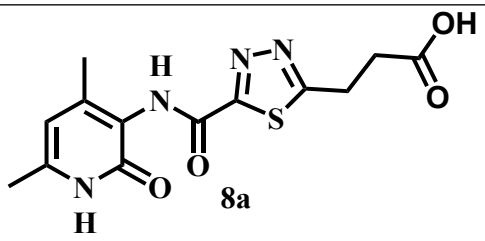
Synthesis of thiadiazoles derivatives 7a-c, 8a-c

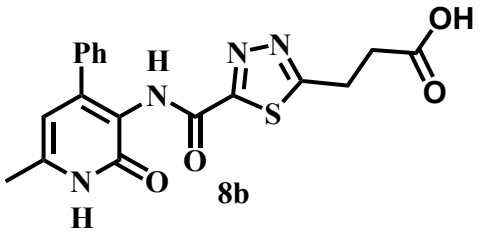
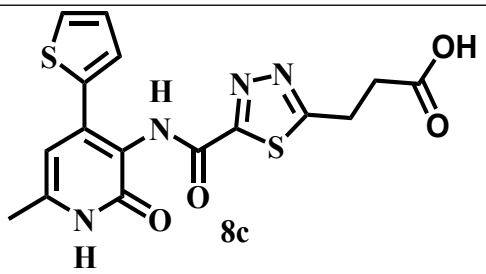
To (1 mmol) of oxamic acid thiohydrazide **6 a-c** in 3 ml of acetic acid was added 0.97 (1.2 mmol) monochloroacetyl chloride (for compounds **7a-c**) or 0.3 (3.0 mmol) succinic anhydride (for compounds **8a-c**). The reaction mixture was heated at reflux temperature on vigorous stirring over 4 h, cooled down and poured into water (25 mL). The precipitates formed was filtered off and air-dried to deliver analytically pure compounds **7a-c** and **8a-c** in yields indicated.



Characterization data of products 7a-c and 8a-c

 7a Chemical Formula: $C_{11}H_{11}ClN_4O_2S$ Molecular Weight: 298,7450	**5-(chloromethyl)-N-(4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-1,3,4-thiadiazole-2-carboxamide (7a)**. White powder, yield 173 mg, 58%. M.p. 246-248 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.03 (s, 3H, CH_3); 2.14 (s, 3H, CH_3); 5.32 (s, 2H, CH_2Cl); 5.93 (s, 1H, H-5); 10.09 (s, 1H, NHCO'); 11.72 (s, 1H, 1-NH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 17.99 (CH_3); 18.19 (CH_3); 37.94 (CH_2); 106.47 (C-5); 121.10; 142.92; 147.34; 155.98; 159.66; 167.12; 170.76. HRMS m/z: calcd for $C_{11}H_{12}ClN_4O_2S^+$ [M +H]$^+$: 299.0364; found: 299.0371.

 **7b** Chemical Formula: $C_{16}H_{13}ClN_4O_2S$ Molecular Weight: 360,8160	**5-(chloromethyl)-N-(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)-1,3,4-thiadiazole-2-carboxamide (7b)**. Beige powder, yield 170 mg, 47%. M.p. 224-226 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.25 (s, 3H, CH_3); 5.28 (s, 2H, CH_2Cl); 6.09 (s, 1H, H-5); 7.34-7.40 (m, 3H, H-3,4,5 Ph); 7.46 (d, *J*=7.3 Hz, 2H, H-5,6 Ph); 10.23 (s, 1H, NHCO'); 12.01 (s, 1H, 1-NH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.43 (CH_3); 37.89 (CH_2); 105.54 (C-5); 119.88; 127.68 (2C Ph); 128.24 (2C Ph); 128.44; 137.17; 144.22; 149.80; 156.70; 160.28; 166.85; 170.71. HRMS m/z: calcd for $C_{16}H_{14}ClN_4O_2S^+$ [M+ H]$^+$: 361.0521; found: 361.0531.
 **7c** Chemical Formula: $C_{14}H_{11}ClN_4O_2S_2$ Molecular Weight: 366,8380	**5-(chloromethyl)-N-(6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)-1,3,4-thiadiazole-2-carboxamide (7c).** Beige powder, yield 286 mg, 78%. M.p. 236-238 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.24 (s, 3H, CH_3); 5.34 (s, 2H, CH_2Cl); 6.51 (s, 1H, H-5); 7.15 (t, *J*=4.9, 1H, H-4' Th); 7.70-7.72 (m, 2H, H-3',5' Th); 10.46 (s, 1H, NHCO'); 11.85 (s, 1H, 1-NH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.49 (CH_3); 37.95 (CH_2Cl); 102.69 (C-5); 118.19; 127.26 (1C Th); 129.20 (1C Th); 130.20 (1C Th); 136.94; 141.46; 143.84; 157.44; 160.29; 166.98; 170.85. HRMS m/z: calcd for $C_{14}H_{12}ClN_4O_2S_2^+$ [M+ H]$^+$: 367.0085; found: 367.0099.
 **8a** Chemical Formula: $C_{13}H_{14}N_4O_4S$ Molecular Weight: 322,3390	**3-(5-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)carbamoyl)-1,3,4-thiadiazol-2-yl)propanoic acid (8a).** Beige powder, yield 251 mg, 78%. M.p. 210-212 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.03 (s, 3H, CH_3); 2.15 (s, 3H, CH_3); 2.82 (bs, 2H, CH_2CO); 3.37 (bs, 2H, 3-CH_2); 5.94 (s, 1H, H-5); 9.95 (s, 1H, 1-NHCO'); 11.73 (bs, 1H, 1-NH); 12.40 (bs, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.03 (CH_3); 18.19 (CH_3); 25.21 (CH_2); 32.73 (CH_2CO); 106.47(C-5); 121.23; 142.75; 147.17; 156.34; 159.71; 165.29; 172.92; 173.36. HRMS m/z: calcd for $C_{13}H_{15}N_4O_4S^+$ [M + H]$^+$: 323.0809; found: 323.0817.

 Chemical Formula: $C_{18}H_{16}N_4O_4S$ Molecular Weight: 384,4100	**3-(5-((6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)carbamoyl)-1,3,4-thiadiazol-2-yl)propanoic acid (8b).** White powder, yield 304 mg, 79%. M.p. 271-273 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.24 (s, 3H, CH_3); 2.79 (t, 2H, *J*=7.0 CH_2CO); 3.33 (t, 2H, *J*=7.1, 3-CH_2); 6.08 (s, 1H, H-5); 7.33-7.39 (m, 3H, H-3,4,5 Ph); 7.46 (d, 2H, *J*=7.3, H-2,6 Ph); 10.06 (s, 1H, NHCO'); 12.04 (bs, 1H, 1-NH); 12.33 (bs, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.42 (CH_3); 25.17 (CH_2); 32.64 (CH_2CO); 105.54 (C-5); 120.04; 127.68 (2C Ph); 128.22 (2C Ph); 128.40 (1C Ph); 137.26; 144.06; 149.69; 157.06; 160.35; 165.09; 172.90; 173.27. HRMS m/z: calcd for $C_{18}H_{17}N_4O_4S^+$ $[M+H]^+$: 385.0965; found: 385.0968.
 Chemical Formula: $C_{16}H_{14}N_4O_4S_2$ Molecular Weight: 390,4320	**3-(5-((6-methyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridin-3-yl)carbamoyl)-1,3,4-thiadiazol-2-yl)propanoic acid (8c).** White powder, yield 323 mg, 83%. M.p. 273-275 °C. ^{1}H NMR (500 MHz, DMSO-d6) δ ppm 2.24 (s, 3H, CH_3); 2.83 (t, 2H, *J*=6.9 CH_2CO); 3.39 (t, *J*=6.9, 2H, 3-CH_2); 6.48 (s, 1H, H-5); 7.15 (t, *J*=4.4, 1H, H-4' Th); 7.68 (d, 2H, *J*=4.4, H-3',5' Th); 10.25 (s, 1H, 1-NHCO'); 11.81 (bs, 1H, 1-NH); 12.38 (bs, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d6) δ ppm 18.44 (CH_3); 25.20 (3-CH_2); 32.63 (CH_2CO); 102.64 (C-5); 118.38; 127.17 (1C Th); 129.05 (1C Th); 130.07 (1C Th); 137.02; 141.36; 143.64; 157.76; 160.31; 165.20; 172.88; 173.34. HRMS m/z: calcd for $C_{16}H_{15}N_4O_4S_2^+$ $[M+H]^+$: 391.0529; found: 391.0533.

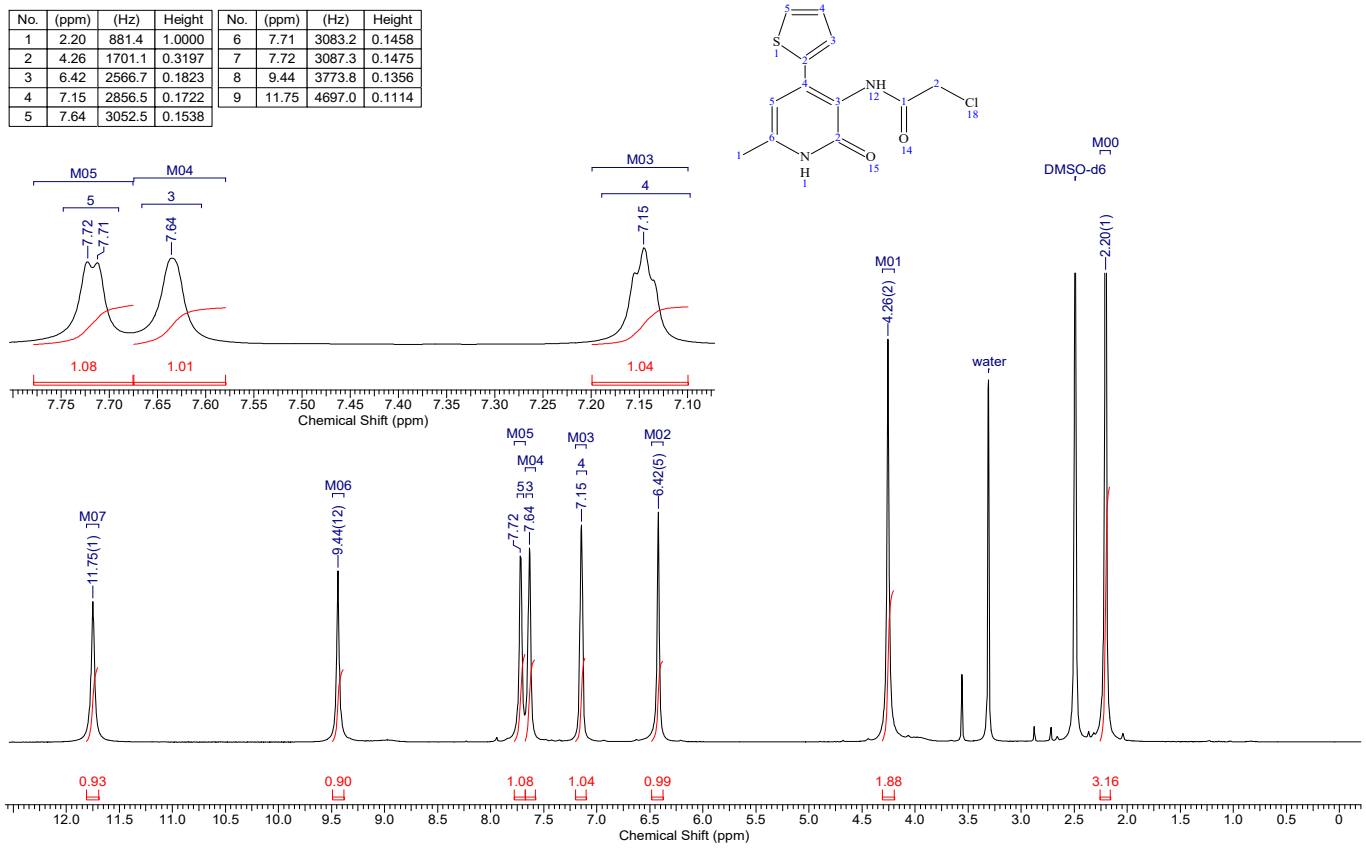
Author Contributions

Spectrophotometric studies were performed on the basis of the Research Resource Center “Natural Resource Management and Physico-Chemical Research” Institute of Chemistry, Tyumen State University.

Copies of NMR Spectra of Products

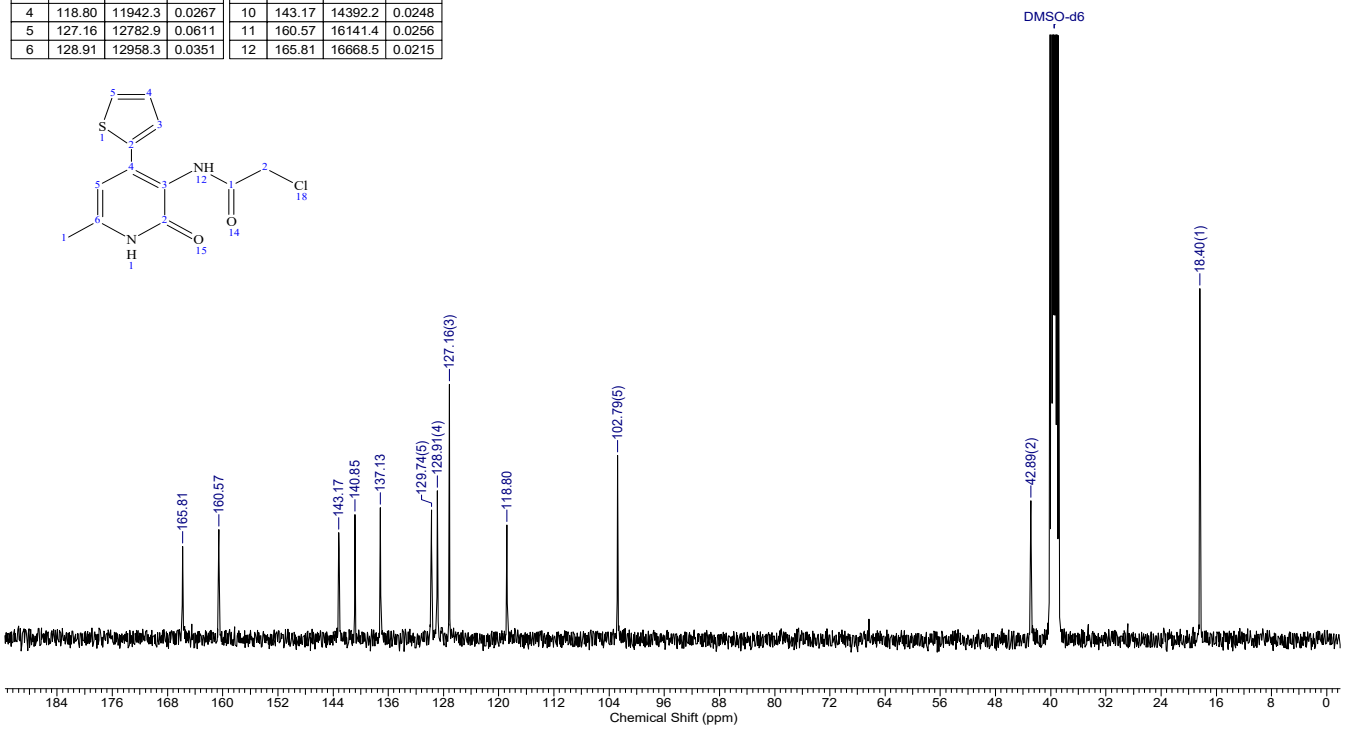
No.	(ppm)	(Hz)	Height
1	2.20	881.4	1.0000
2	4.26	1701.1	0.3197
3	6.42	2566.7	0.1823
4	7.15	2856.5	0.1722
5	7.64	3052.5	0.1538

No.	(ppm)	(Hz)	Height
6	7.71	3083.2	0.1458
7	7.72	3087.3	0.1475
8	9.44	3773.8	0.1356
9	11.75	4697.0	0.1114



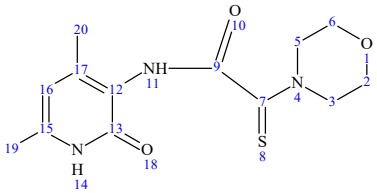
No.	(ppm)	(Hz)	Height
1	18.40	1849.7	0.0845
2	42.89	4312.0	0.0326
3	102.79	10333.1	0.0438
4	118.80	11942.3	0.0267
5	127.16	12782.9	0.0611
6	128.91	12958.3	0.0351

No.	(ppm)	(Hz)	Height
7	129.74	13042.6	0.0305
8	137.13	13785.4	0.0310
9	140.85	14159.3	0.0293
10	143.17	14392.2	0.0248
11	160.57	16141.4	0.0256
12	165.81	16668.5	0.0215



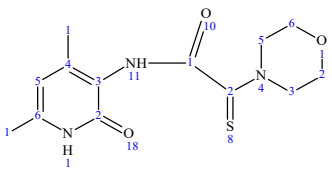
^{1}H (400 MHz, DMSO-d6) and ^{13}C (100 MHz, DMSO-d6) NMR Spectra of **2c**

No.	(ppm)	(Hz)	Height
1	2.02	806.3	0.6124
2	2.13	851.7	0.6110
3	3.72	1486.4	0.4779
4	3.98	1593.1	0.2693
5	4.09	1637.0	0.2684
6	5.89	2356.0	0.2037
7	9.57	3825.6	0.1805
8	11.54	4614.2	0.1236

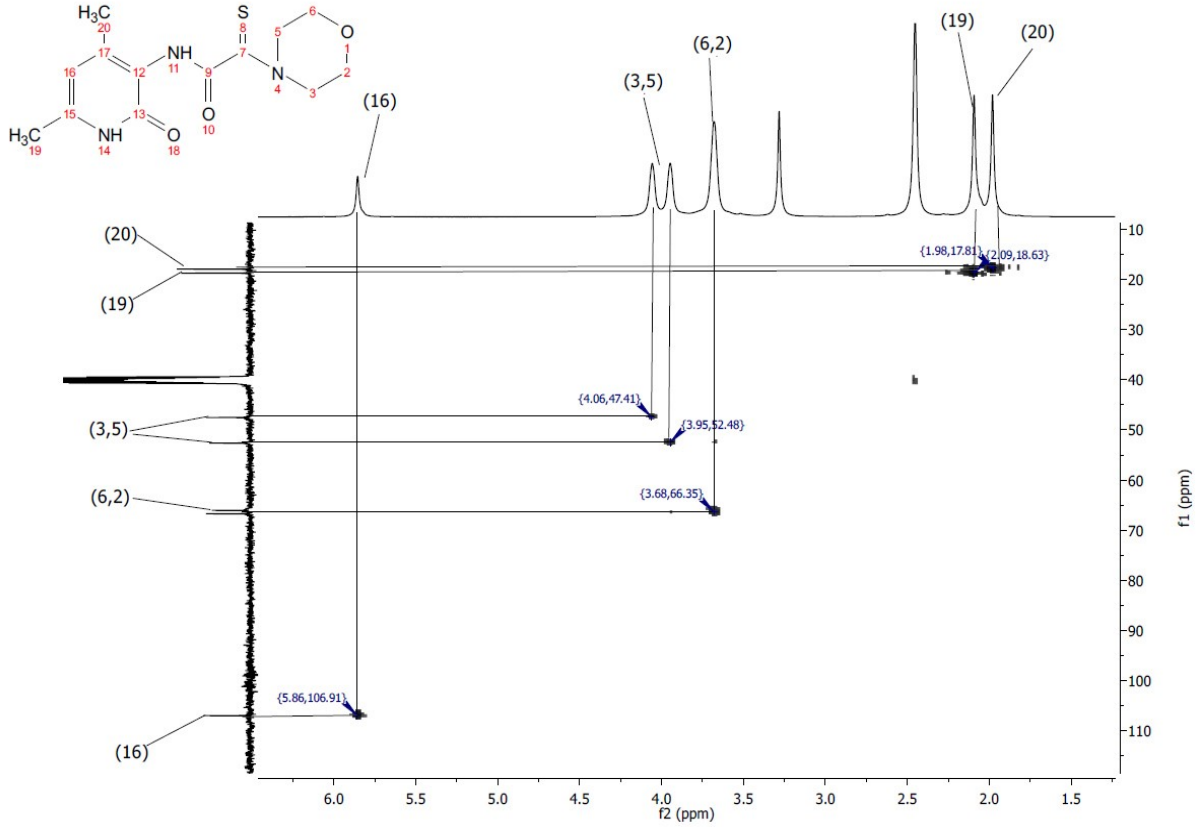


No.	(ppm)	(Hz)	Height
1	17.41	1750.0	0.0604
2	18.20	1829.5	0.0567
3	46.97	4721.2	0.0357
4	52.08	5235.0	0.0329
5	65.48	6582.6	0.0309
6	66.16	6650.6	0.0357
7	106.39	10695.4	0.0379

No.	(ppm)	(Hz)	Height
8	120.77	12140.7	0.0303
9	142.69	14344.2	0.0317
10	147.60	14837.8	0.0295
11	159.92	16076.2	0.0327
12	164.19	16505.6	0.0338
13	192.03	19304.3	0.0232



^{1}H (400 MHz, DMSO-d6) and ^{13}C (100 MHz, DMSO-d6) NMR Spectra of **5a**

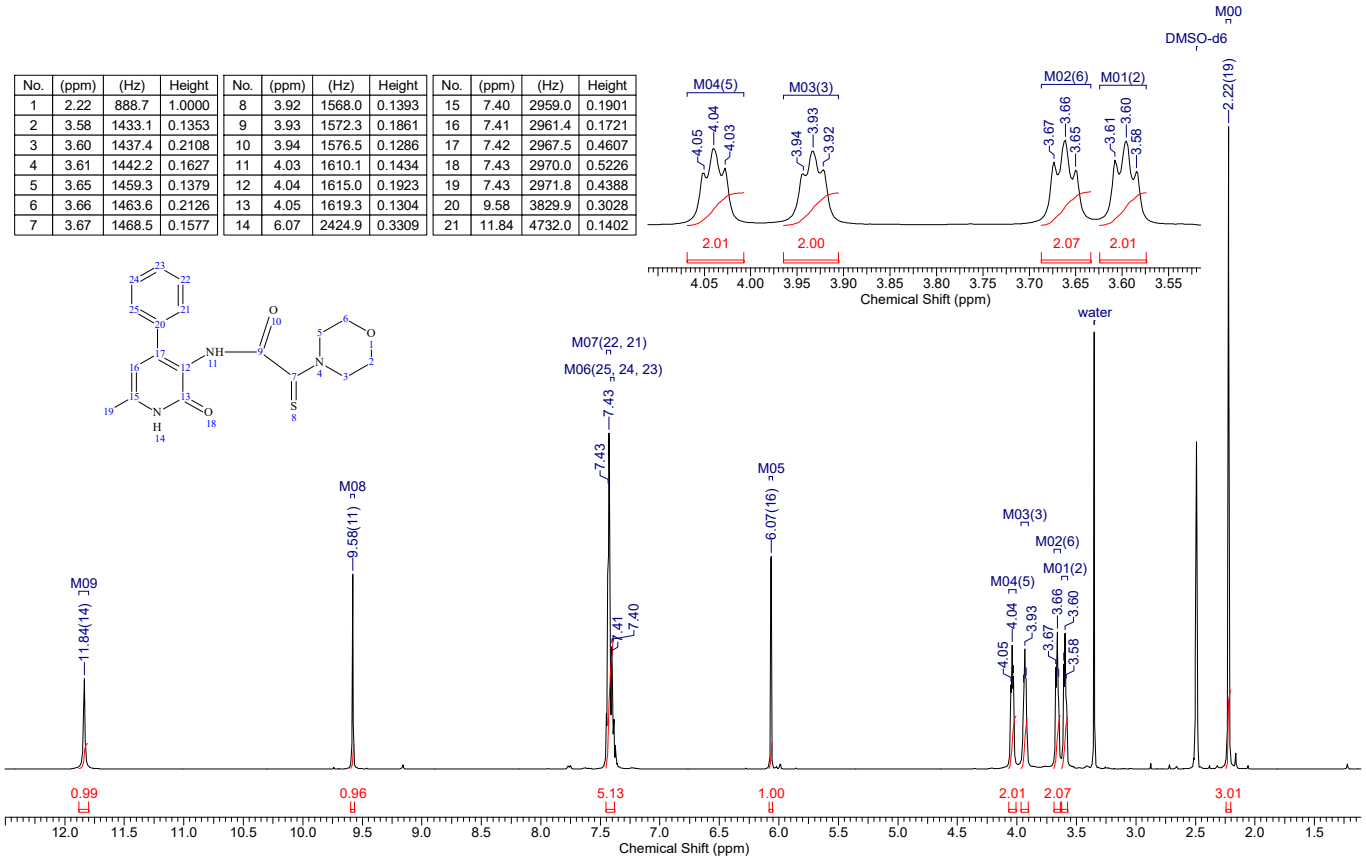


HMQC NMR Spectra of **5a**

No.	(ppm)	(Hz)	Height
1	2.22	888.7	1.0000
2	3.58	1433.1	0.1353
3	3.60	1437.4	0.2108
4	3.61	1442.2	0.1627
5	3.65	1459.3	0.1379
6	3.66	1463.6	0.2126
7	3.67	1468.5	0.1577

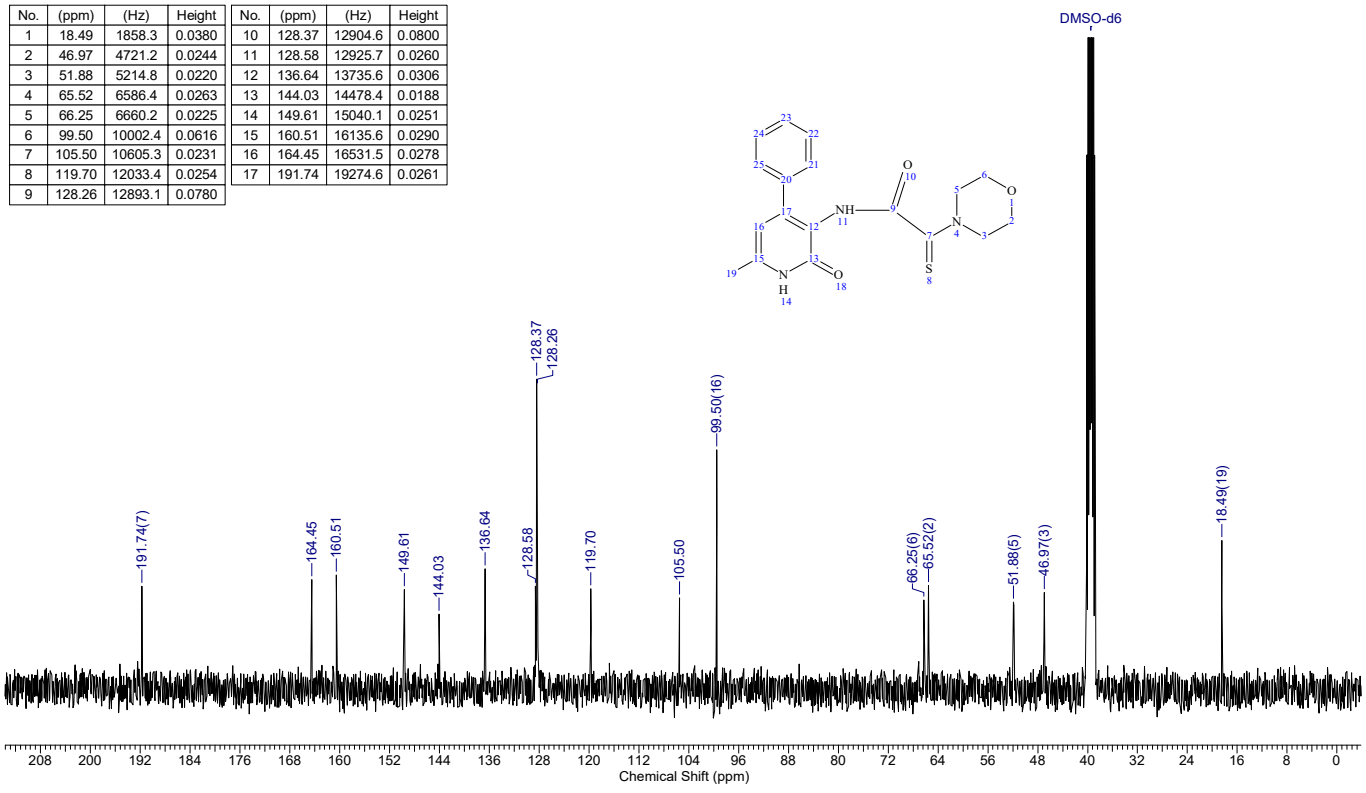
No.	(ppm)	(Hz)	Height
8	3.92	1568.0	0.1393
9	3.93	1572.3	0.1861
10	3.94	1576.5	0.1286
11	4.03	1610.1	0.1434
12	4.04	1615.0	0.1923
13	4.05	1619.3	0.1304
14	6.07	2424.9	0.3309

No.	(ppm)	(Hz)	Height
15	7.40	2959.0	0.1901
16	7.41	2961.4	0.1721
17	7.42	2967.5	0.4607
18	7.43	2970.0	0.5226
19	7.43	2971.8	0.4388
20	9.58	3829.9	0.3028
21	11.84	4732.0	0.1402



No.	(ppm)	(Hz)	Height
1	18.49	1858.3	0.0380
2	46.97	4721.2	0.0244
3	51.88	5214.8	0.0220
4	65.52	6586.4	0.0263
5	66.25	6660.2	0.0225
6	99.50	10002.4	0.0616
7	105.50	10605.3	0.0231
8	119.70	12033.4	0.0254
9	128.26	12893.1	0.0780

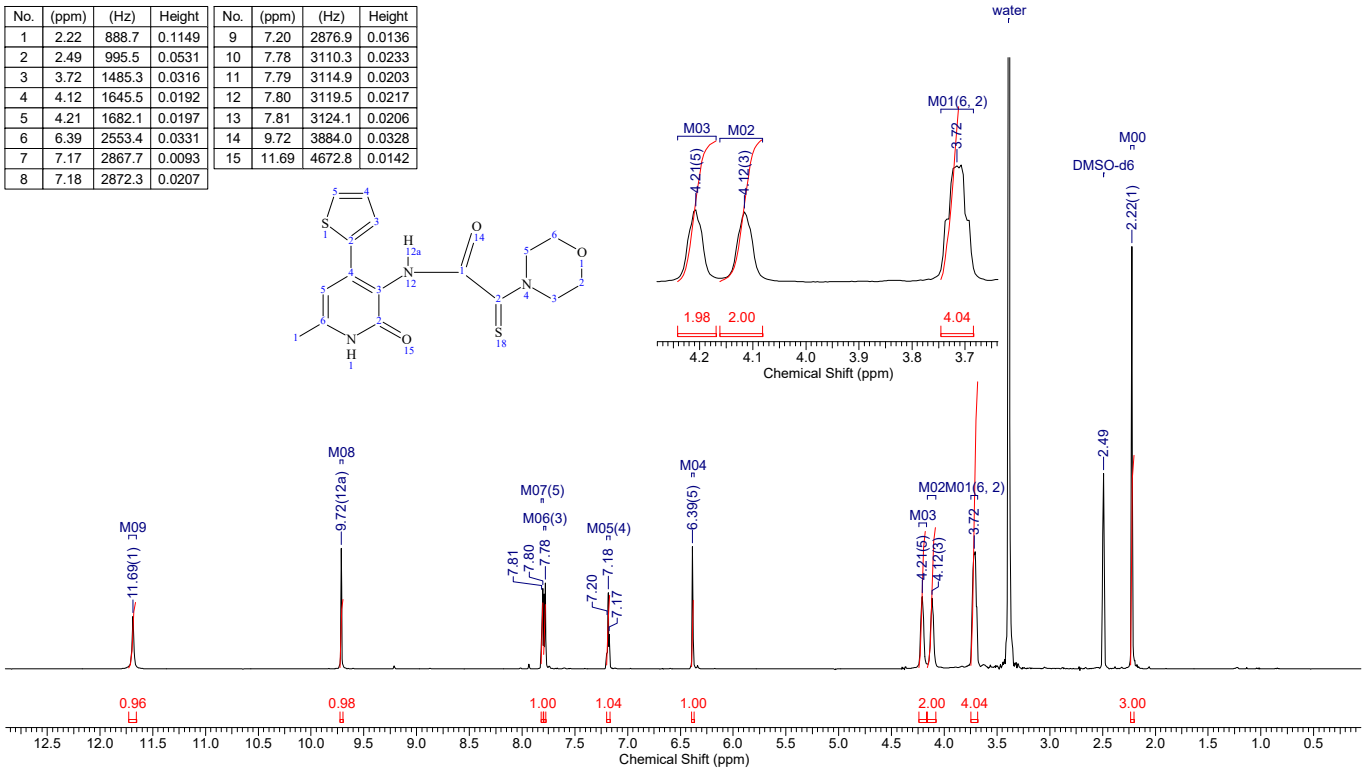
No.	(ppm)	(Hz)	Height
10	128.37	12904.6	0.0800
11	128.58	12925.7	0.0260
12	136.64	13735.6	0.0306
13	144.03	14478.4	0.0188
14	149.61	15040.1	0.0251
15	160.51	16135.6	0.0290
16	164.45	16531.5	0.0278
17	191.74	19274.6	0.0261



^{1}H (400 MHz, DMSO-d6) and ^{13}C (100 MHz, DMSO-d6) NMR Spectra of **5b**

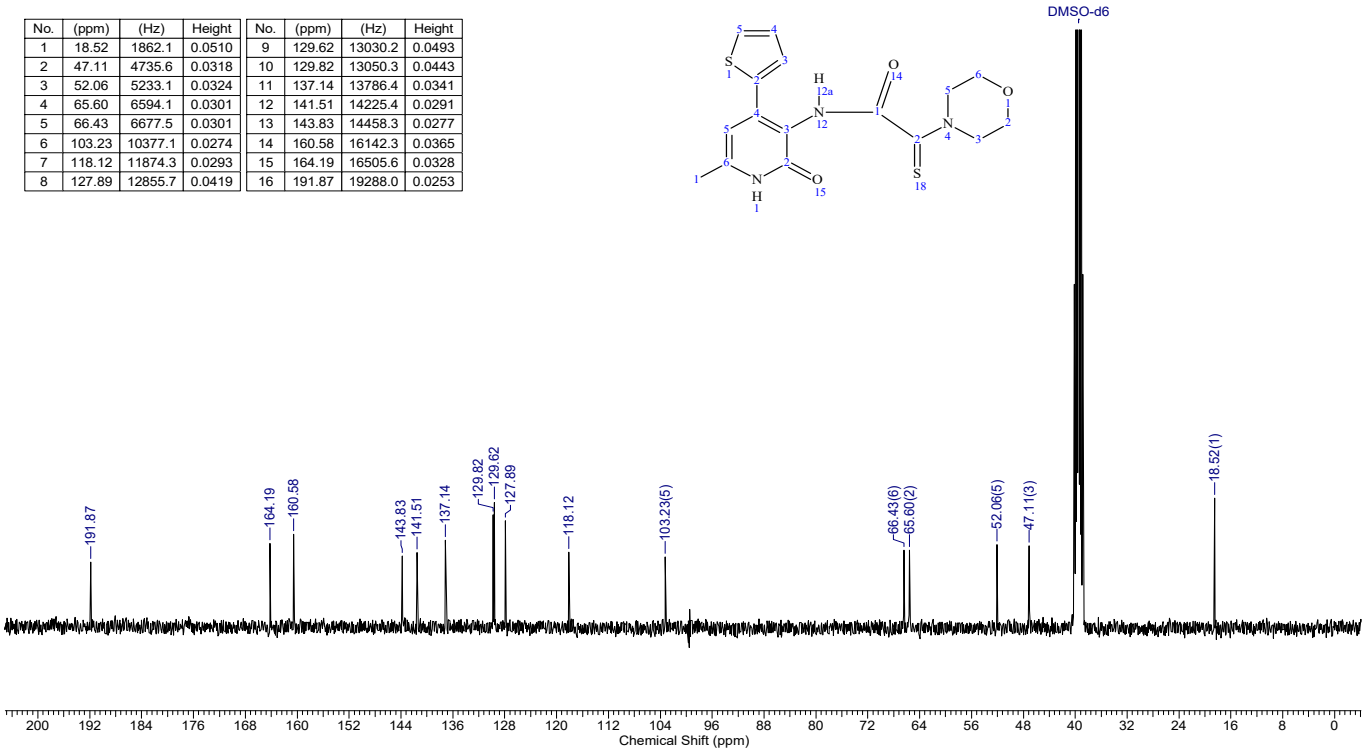
No.	(ppm)	(Hz)	Height
1	2.22	888.7	0.1149
2	2.49	995.5	0.0531
3	3.72	1485.3	0.0316
4	4.12	1645.5	0.0192
5	4.21	1682.1	0.0197
6	6.39	2553.4	0.0331
7	7.17	2867.7	0.0093
8	7.18	2872.3	0.0207

No.	(ppm)	(Hz)	Height
9	7.20	2876.9	0.0136
10	7.78	3110.3	0.0233
11	7.79	3114.9	0.0203
12	7.80	3119.5	0.0217
13	7.81	3124.1	0.0206
14	9.72	3884.0	0.0328
15	11.69	4672.8	0.0142



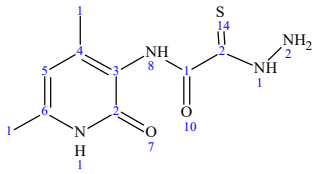
No.	(ppm)	(Hz)	Height
1	18.52	1862.1	0.0510
2	47.11	4735.6	0.0318
3	52.06	5233.1	0.0324
4	65.60	6594.1	0.0301
5	66.43	6677.5	0.0301
6	103.23	10377.1	0.0274
7	118.12	11874.3	0.0293
8	127.89	12855.7	0.0419

No.	(ppm)	(Hz)	Height
9	129.62	13030.2	0.0493
10	129.82	13050.3	0.0443
11	137.14	13786.4	0.0341
12	141.51	14225.4	0.0291
13	143.83	14458.3	0.0277
14	160.58	16142.3	0.0365
15	164.19	16505.6	0.0328
16	191.87	19288.0	0.0253



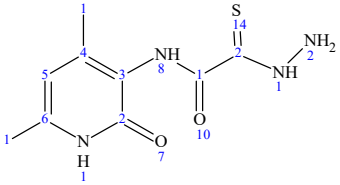
^{1}H (400 MHz, DMSO-d6) and ^{13}C (100 MHz, DMSO-d6) NMR Spectra of **5c**

No.	(ppm)	(Hz)	Height
1	1.98	989.5	1.0000
2	2.13	1065.1	0.8729
3	5.92	2960.4	0.2771
4	6.48	3241.2	0.0038
5	9.46	4729.6	0.2101
6	11.76	5882.5	0.0181
7	12.93	6464.4	0.0010



No.	(ppm)	(Hz)	Height
1	18.14	2281.0	0.1637
2	18.70	2351.7	0.1800
3	106.90	13443.5	0.1561
4	121.35	15260.2	0.0818
5	141.82	17835.0	0.0878

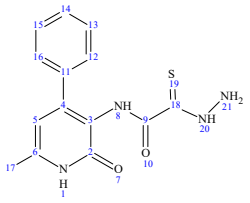
No.	(ppm)	(Hz)	Height
6	144.97	18231.7	0.0906
7	157.18	19766.5	0.0595
8	159.52	20061.2	0.0867
9	166.27	20910.1	0.0155



^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **6a**

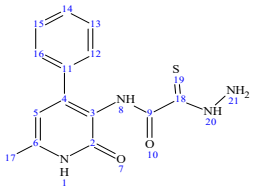
No.	(ppm)	(Hz)	Height
1	2.21	1106.1	1.0000
2	6.06	3028.6	0.3354
3	6.27	3135.3	0.0546
4	7.31	3654.5	0.1445
5	7.32	3661.3	0.1553
6	7.34	3669.3	0.1977
7	7.35	3677.0	0.3336

No.	(ppm)	(Hz)	Height
8	7.37	3684.2	0.1817
9	7.39	3696.3	0.3996
10	7.41	3703.7	0.2187
11	9.50	4753.0	0.2934
12	11.99	5995.9	0.0354
13	12.77	6388.7	0.0227



No.	(ppm)	(Hz)	Height
1	18.37	2309.9	0.0930
2	105.85	13311.8	0.0705
3	120.23	15119.7	0.0448
4	127.33	16012.7	0.1876
5	128.24	16127.6	0.2630
6	137.80	17329.8	0.0510

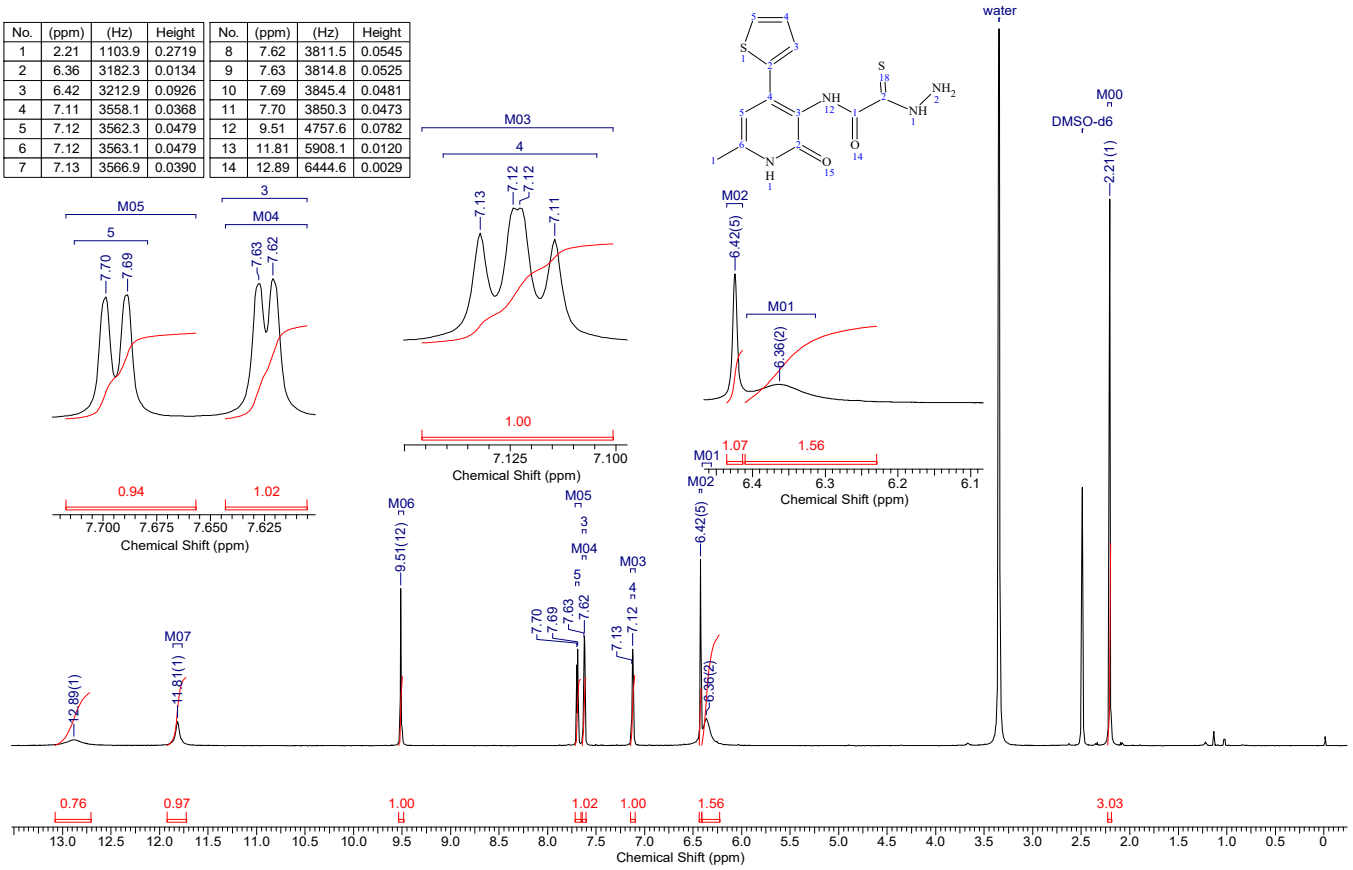
No.	(ppm)	(Hz)	Height
7	142.96	17978.0	0.0413
8	147.19	18510.4	0.0452
9	157.25	19775.3	0.0409
10	160.11	20135.1	0.0503
11	166.11	20889.3	0.0270



^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **6b**

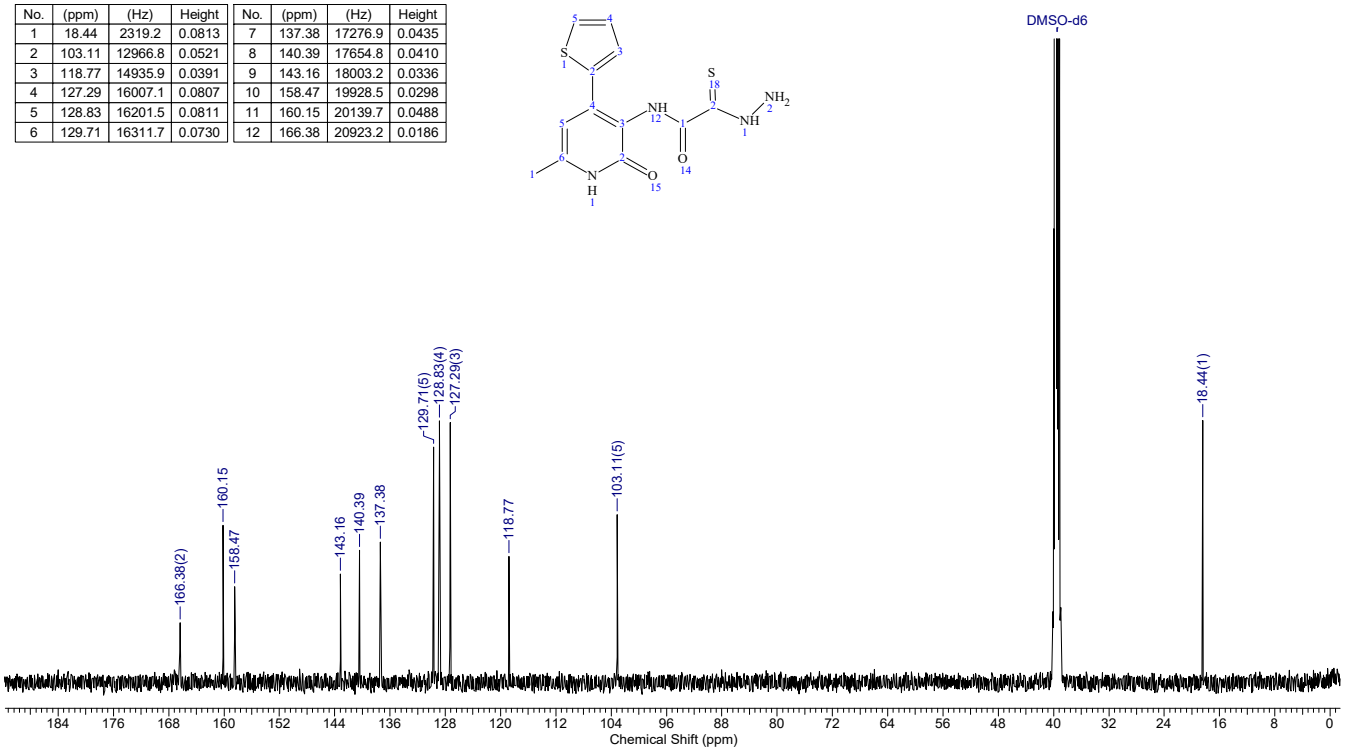
No.	(ppm)	(Hz)	Height
1	2.21	1103.9	0.2719
2	6.36	3182.3	0.0134
3	6.42	3212.9	0.0926
4	7.11	3558.1	0.0368
5	7.12	3562.3	0.0479
6	7.12	3563.1	0.0479
7	7.13	3566.9	0.0390

No.	(ppm)	(Hz)	Height
8	7.62	3811.5	0.0545
9	7.63	3814.8	0.0525
10	7.69	3845.4	0.0481
11	7.70	3850.3	0.0473
12	9.51	4757.6	0.0782
13	11.81	5908.1	0.0120
14	12.89	6444.6	0.0029



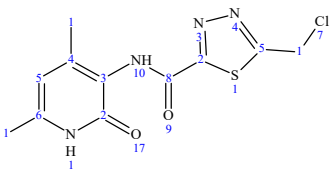
No.	(ppm)	(Hz)	Height
1	18.44	2319.2	0.0813
2	103.11	12966.8	0.0521
3	118.77	14935.9	0.0391
4	127.29	16007.1	0.0807
5	128.83	16201.5	0.0811
6	129.71	16311.7	0.0730

No.	(ppm)	(Hz)	Height
7	137.38	17276.9	0.0435
8	140.39	17654.8	0.0410
9	143.16	18003.2	0.0336
10	158.47	19928.5	0.0298
11	160.15	20139.7	0.0488
12	166.38	20923.7	0.0186



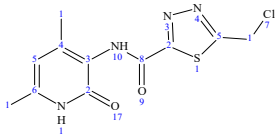
^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **6c**

No.	(ppm)	(Hz)	Height
1	2.03	1013.5	0.7564
2	2.14	1072.0	0.8037
3	5.32	2658.8	0.5389
4	5.93	2966.6	0.3015
5	10.09	5048.4	0.1747
6	11.72	5860.3	0.1152



No.	(ppm)	(Hz)	Height
1	17.99	2262.5	0.1646
2	18.19	2287.4	0.1317
3	37.94	4771.5	0.1498
4	106.47	13389.7	0.0838
5	121.10	15229.7	0.0416
6	142.92	17973.1	0.0420

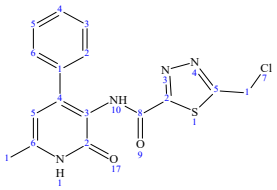
No.	(ppm)	(Hz)	Height
7	147.34	18528.9	0.0445
8	155.98	19616.3	0.0458
9	159.66	20078.1	0.0735
10	167.12	21016.2	0.0645
11	170.76	21473.9	0.0461



^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **7a**

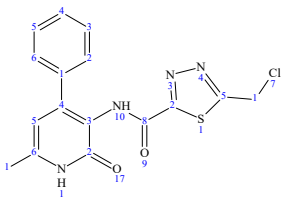
No.	(ppm)	(Hz)	Height
1	2.25	1123.2	0.5747
2	5.28	2642.5	0.4541
3	6.09	3044.3	0.2268
4	7.34	3671.3	0.0795
5	7.35	3678.3	0.0879
6	7.37	3685.9	0.1208

No.	(ppm)	(Hz)	Height
7	7.39	3693.5	0.1792
8	7.40	3700.6	0.0829
9	7.45	3727.3	0.1946
10	7.47	3734.6	0.1354
11	10.23	5115.0	0.1297
12	12.01	6005.1	0.0777



No.	(ppm)	(Hz)	Height
1	18.43	2317.1	0.1054
2	37.89	4765.5	0.1471
3	105.54	13272.9	0.0454
4	119.88	15075.5	0.0300
5	127.68	16056.6	0.1637
6	128.24	16127.5	0.2425
7	128.44	16152.9	0.1017

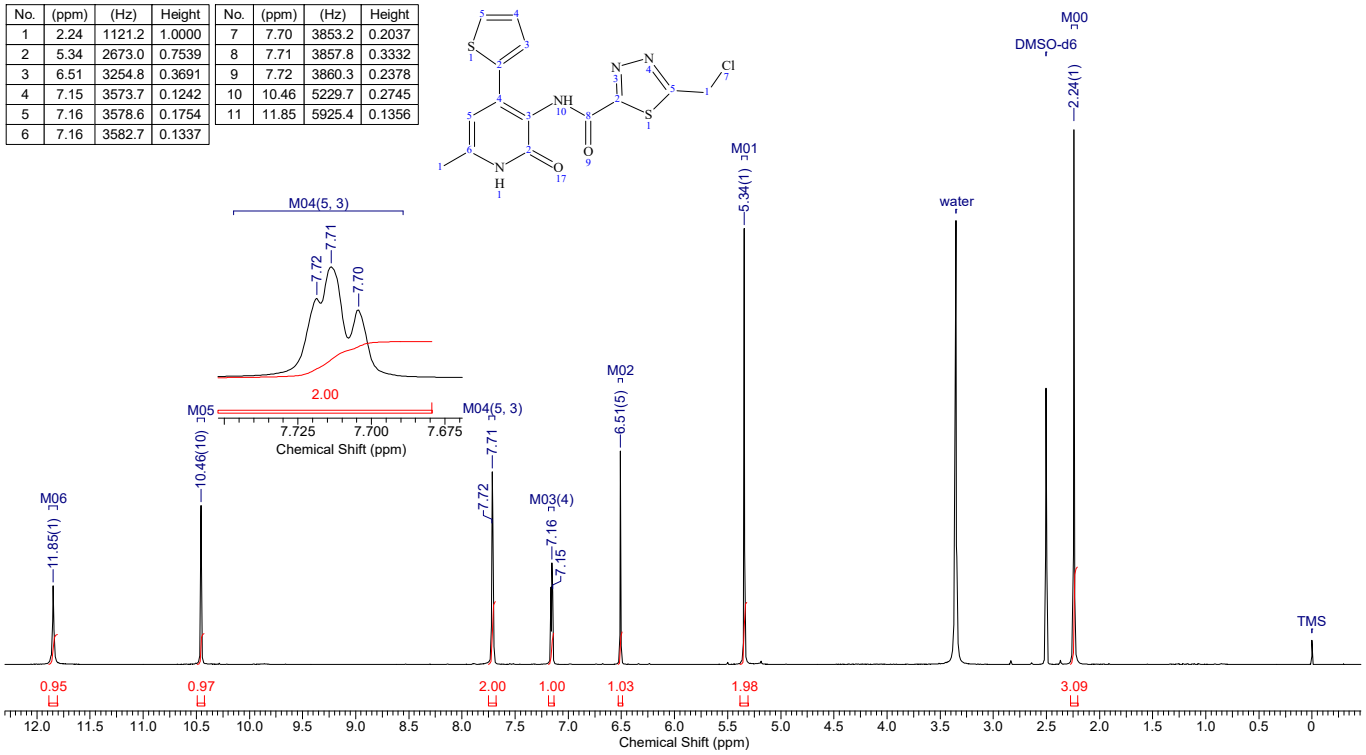
No.	(ppm)	(Hz)	Height
8	137.17	17249.6	0.0879
9	144.22	18136.6	0.0275
10	149.80	18837.9	0.0354
11	156.70	19705.7	0.0390
12	160.28	20156.6	0.0520
13	166.85	20982.7	0.0437
14	170.71	21468.2	0.0369



^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **7b**

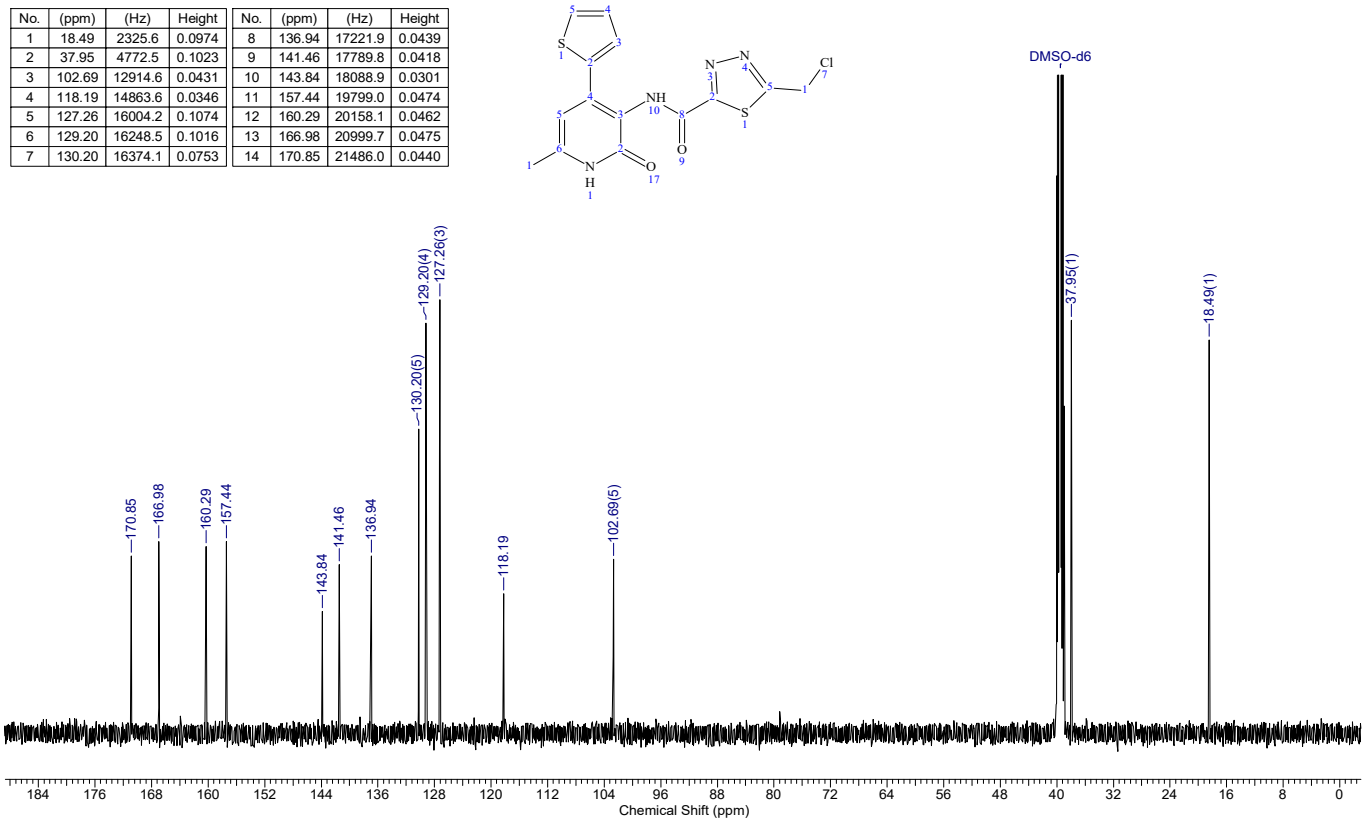
No.	(ppm)	(Hz)	Height
1	2.24	1121.2	1.0000
2	5.34	2673.0	0.7539
3	6.51	3254.8	0.3691
4	7.15	3573.7	0.1242
5	7.16	3578.6	0.1754
6	7.16	3582.7	0.1337

No.	(ppm)	(Hz)	Height
7	7.70	3853.2	0.2037
8	7.71	3857.8	0.3332
9	7.72	3860.3	0.2378
10	10.46	5229.7	0.2745
11	11.85	5925.4	0.1356



No.	(ppm)	(Hz)	Height
1	18.49	2325.6	0.0974
2	37.95	4772.5	0.1023
3	102.69	12914.6	0.0431
4	118.19	14863.6	0.0346
5	127.26	16004.2	0.1074
6	129.20	16248.5	0.1016
7	130.20	16374.1	0.0753

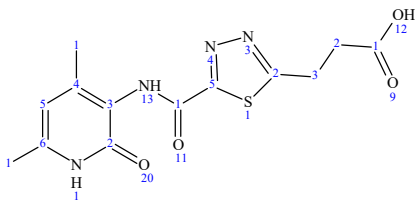
No.	(ppm)	(Hz)	Height
8	136.94	17221.9	0.0439
9	141.46	17789.8	0.0418
10	143.84	18088.9	0.0301
11	157.44	19799.0	0.0474
12	160.29	20158.1	0.0462
13	166.98	20999.7	0.0475
14	170.85	21486.0	0.0440



^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **7c**

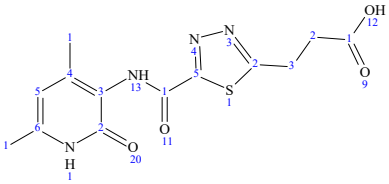
No.	(ppm)	(Hz)	Height
1	2.03	1014.3	0.5848
2	2.15	1077.1	0.6053
3	2.50	1252.0	1.0000
4	2.82	1410.5	0.2735
5	3.37	1687.2	0.2337

No.	(ppm)	(Hz)	Height
6	5.94	2970.6	0.2090
7	9.95	4976.1	0.1433
8	11.73	5867.8	0.0197
9	12.40	6201.7	0.0096



No.	(ppm)	(Hz)	Height
1	18.03	2267.0	0.0471
2	18.19	2287.0	0.0454
3	25.21	3170.2	0.0309
4	32.73	4115.8	0.0348
5	106.47	13389.3	0.0340
6	121.23	15245.9	0.0149
7	142.75	17952.4	0.0157

No.	(ppm)	(Hz)	Height
8	147.17	18508.1	0.0150
9	156.34	19661.0	0.0169
10	159.71	20084.9	0.0214
11	165.29	20787.0	0.0217
12	172.92	21746.5	0.0305
13	173.36	21801.9	0.0156

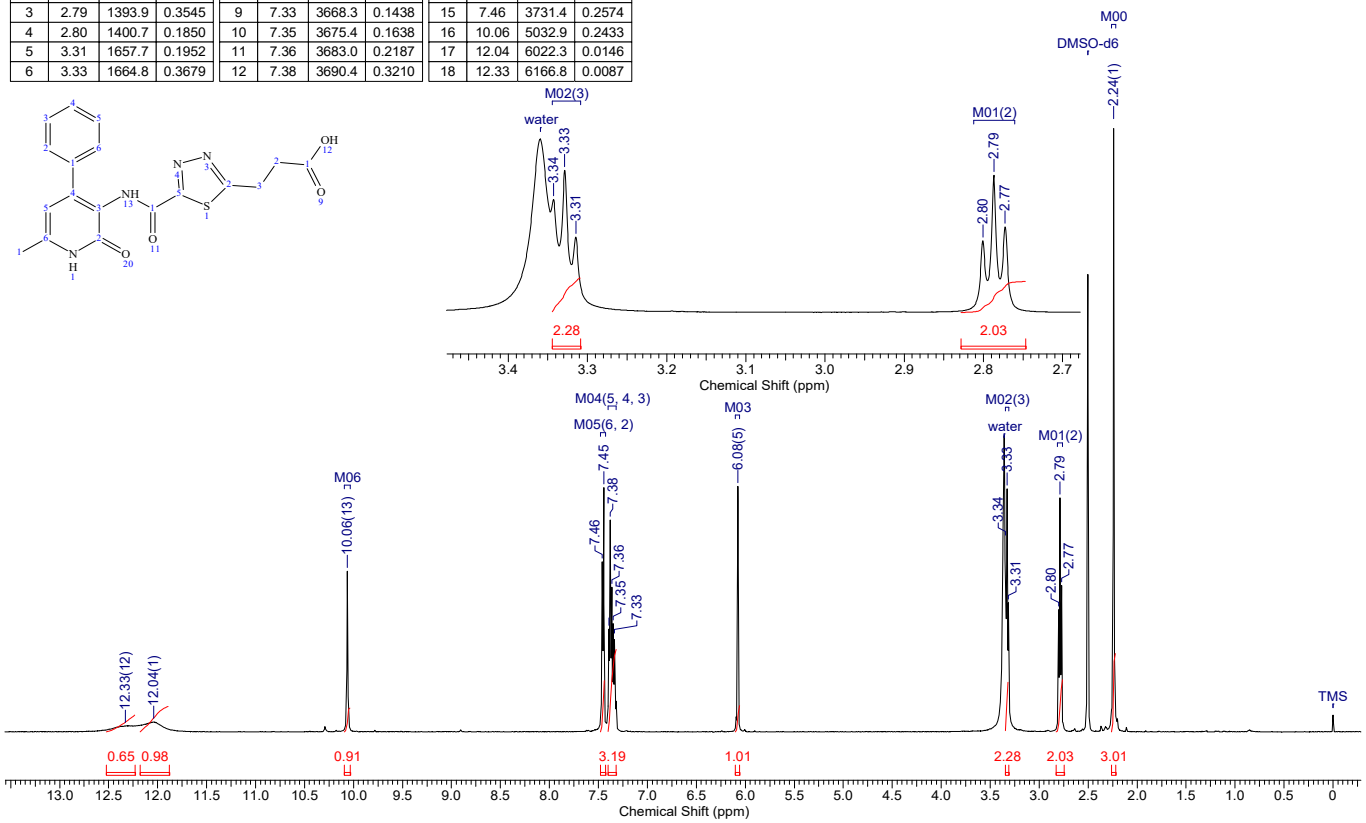


^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **8a**

No.	(ppm)	(Hz)	Height
1	2.24	1120.7	1.0000
2	2.77	1386.8	0.2212
3	2.79	1393.9	0.3545
4	2.80	1400.7	0.1850
5	3.31	1657.7	0.1952
6	3.33	1664.8	0.3679

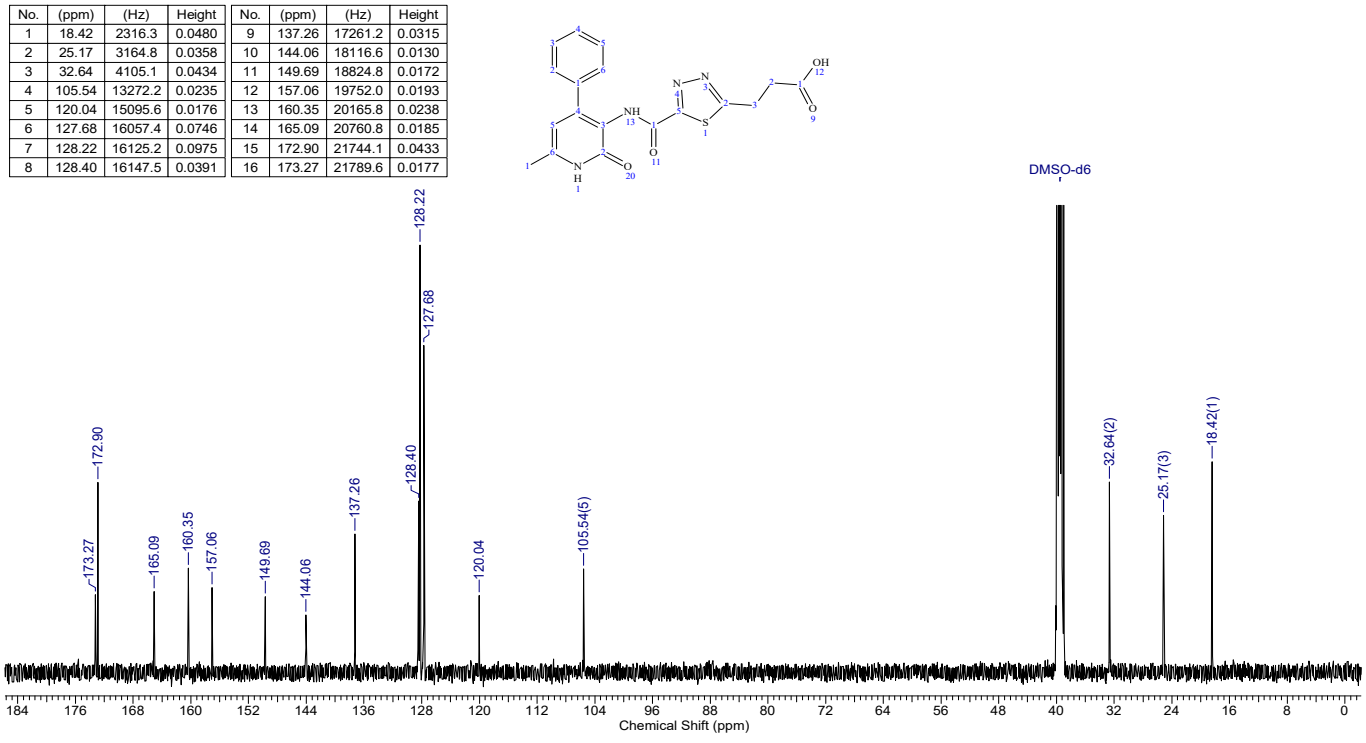
No.	(ppm)	(Hz)	Height
7	3.34	1671.9	0.2922
8	6.08	3038.4	0.3715
9	7.33	3668.3	0.1438
10	7.35	3675.4	0.1638
11	7.36	3683.0	0.2187
12	7.38	3690.4	0.3210

No.	(ppm)	(Hz)	Height
13	7.39	3697.4	0.1555
14	7.45	3724.1	0.3697
15	7.46	3731.4	0.2574
16	10.06	5032.9	0.2433
17	12.04	6022.3	0.0146
18	12.33	6166.8	0.0087



No.	(ppm)	(Hz)	Height
1	18.42	2316.3	0.0480
2	25.17	3164.8	0.0358
3	32.64	4105.1	0.0434
4	105.54	13272.2	0.0235
5	120.04	15095.6	0.0176
6	127.68	16057.4	0.0746
7	128.22	16125.2	0.0975
8	128.40	16147.5	0.0391

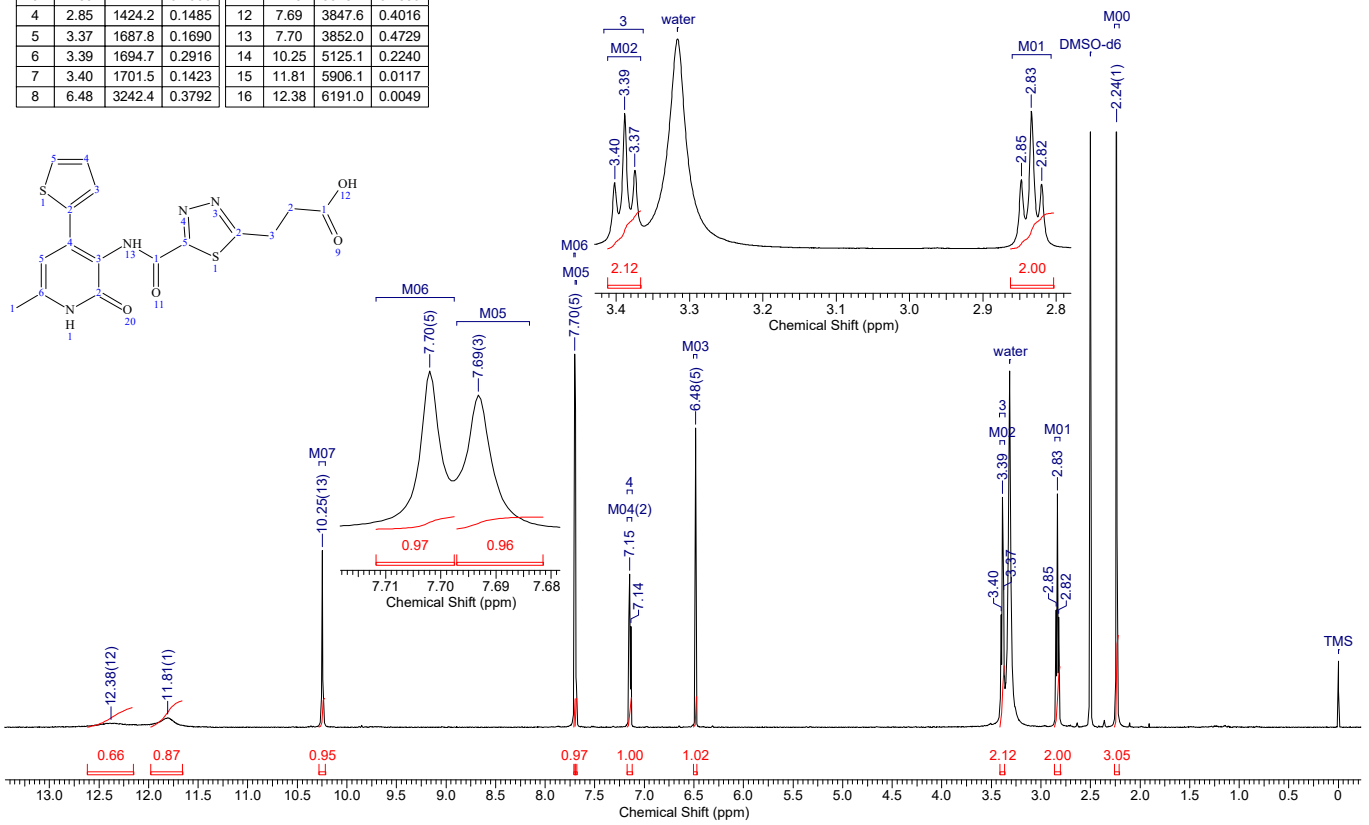
No.	(ppm)	(Hz)	Height
9	137.26	17261.2	0.0315
10	144.06	18116.6	0.0130
11	149.69	18824.8	0.0172
12	157.06	19752.0	0.0193
13	160.35	20165.8	0.0238
14	165.09	20760.8	0.0185
15	172.90	21744.1	0.0433
16	173.27	21789.6	0.0177



^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **8b**

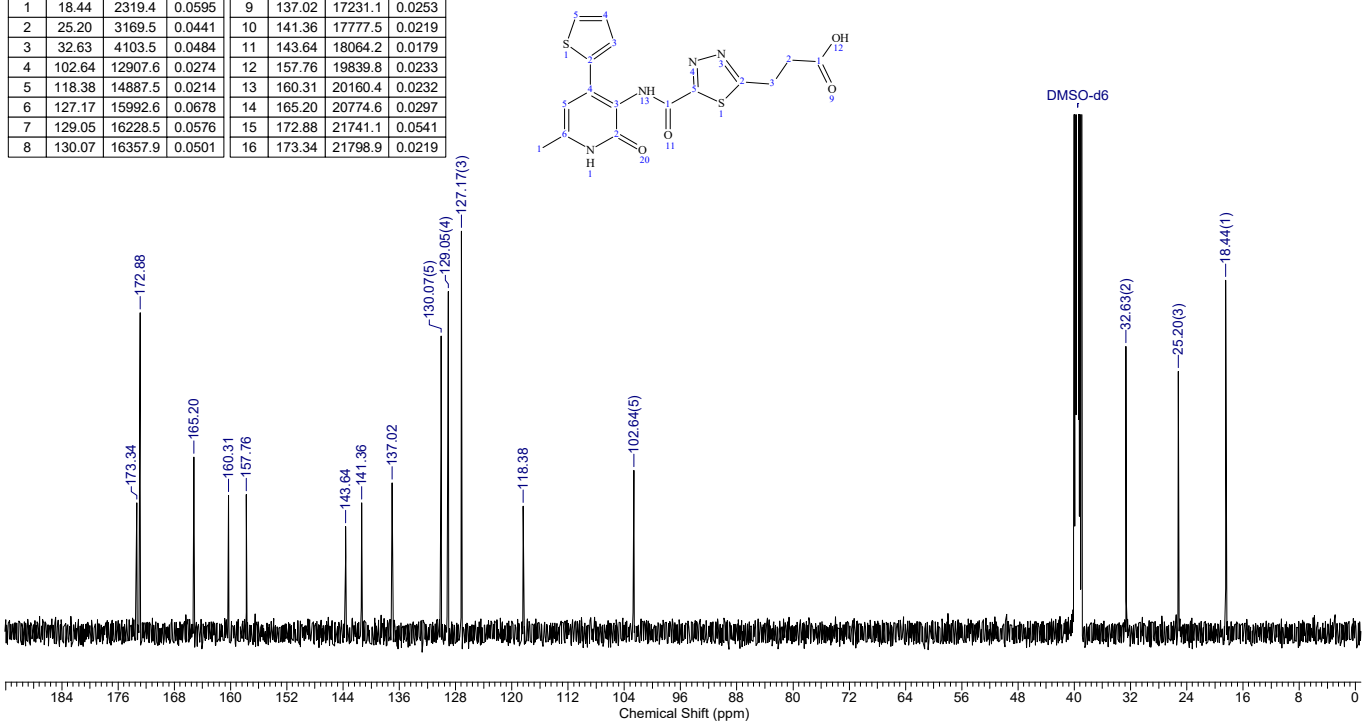
No.	(ppm)	(Hz)	Height
1	2.24	1118.5	1.0000
2	2.82	1410.3	0.1392
3	2.83	1417.4	0.2956
4	2.85	1424.2	0.1485
5	3.37	1687.8	0.1690
6	3.39	1694.7	0.2916
7	3.40	1701.5	0.1423
8	6.48	3242.4	0.3792

No.	(ppm)	(Hz)	Height
9	7.14	3569.6	0.1274
10	7.15	3574.0	0.1939
11	7.15	3578.4	0.1359
12	7.69	3847.6	0.4016
13	7.70	3852.0	0.4729
14	10.25	5125.1	0.2240
15	11.81	5906.1	0.0117
16	12.38	6191.0	0.0049



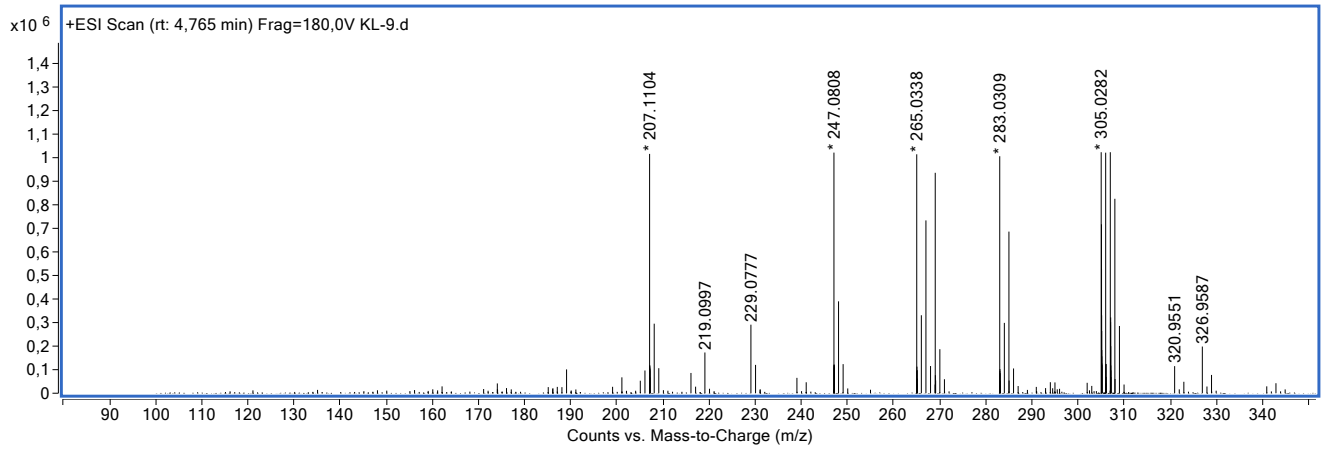
No.	(ppm)	(Hz)	Height
1	18.44	2319.4	0.0595
2	25.20	3169.5	0.0441
3	32.63	4103.5	0.0484
4	102.64	12907.6	0.0274
5	118.38	14887.5	0.0214
6	127.17	15992.6	0.0678
7	129.05	16228.5	0.0576
8	130.07	16357.9	0.0501

No.	(ppm)	(Hz)	Height
9	137.02	17231.1	0.0253
10	141.36	17777.5	0.0219
11	143.64	18064.2	0.0179
12	157.76	19839.8	0.0233
13	160.31	20160.4	0.0232
14	165.20	20774.6	0.0297
15	172.88	21741.1	0.0541
16	173.34	21798.9	0.0219

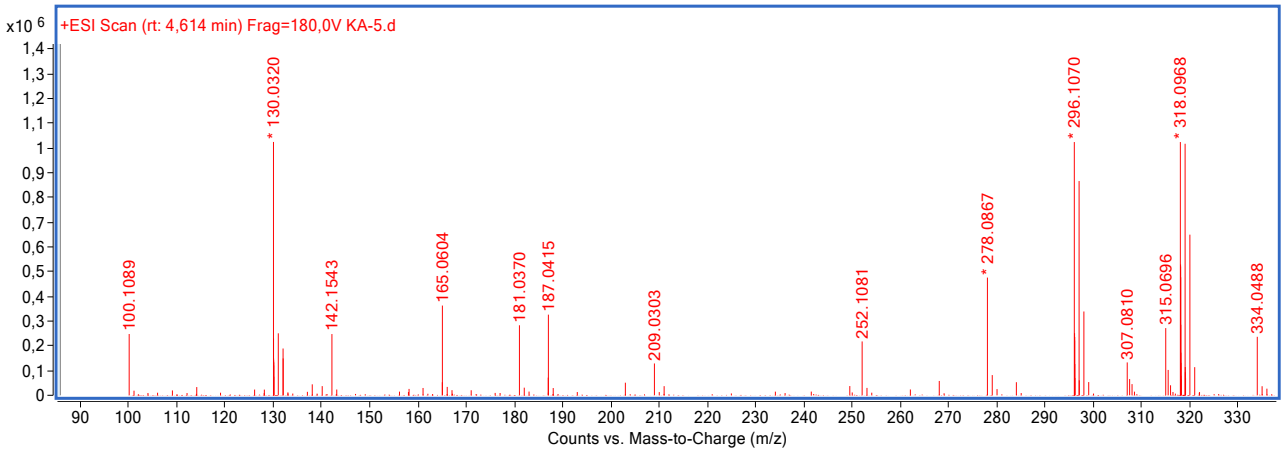


^{1}H (500 MHz, DMSO-d6) and ^{13}C (125 MHz, DMSO-d6) NMR Spectra of **8c**

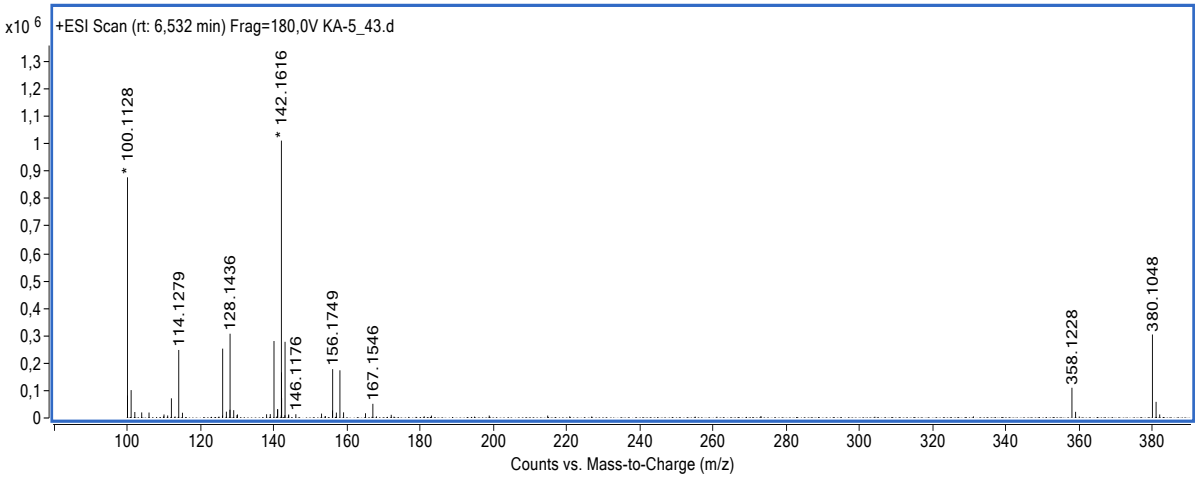
Copies of MS Spectra of Products



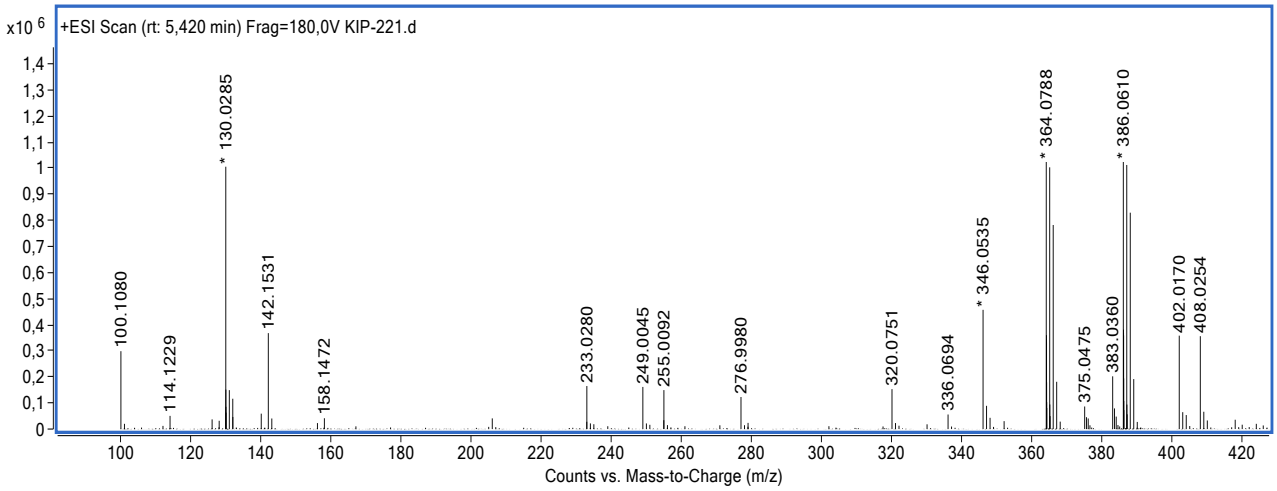
Mass spectrum (LC/Q-TOF) of (**2c**)



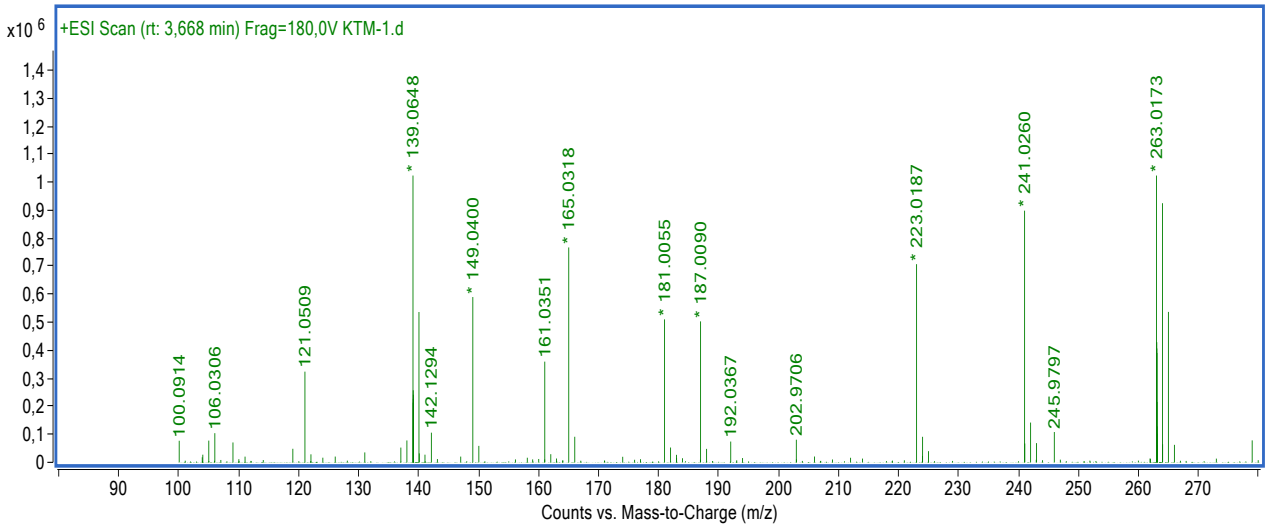
Mass spectrum (LC/Q-TOF) of (**5a**)



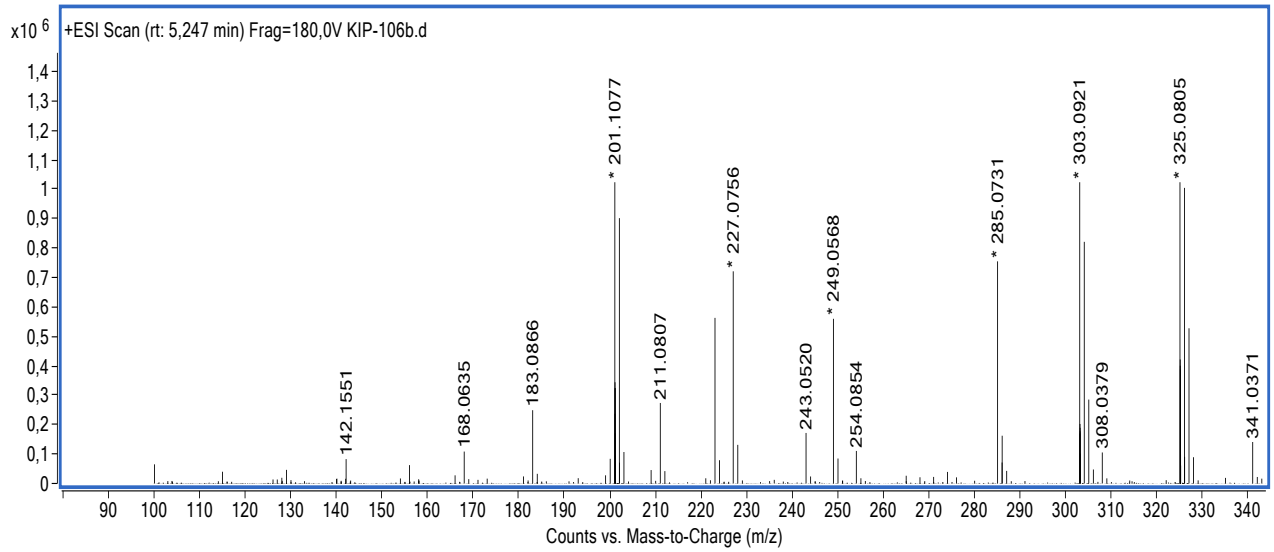
Mass spectrum (LC/Q-TOF) of (**5b**)



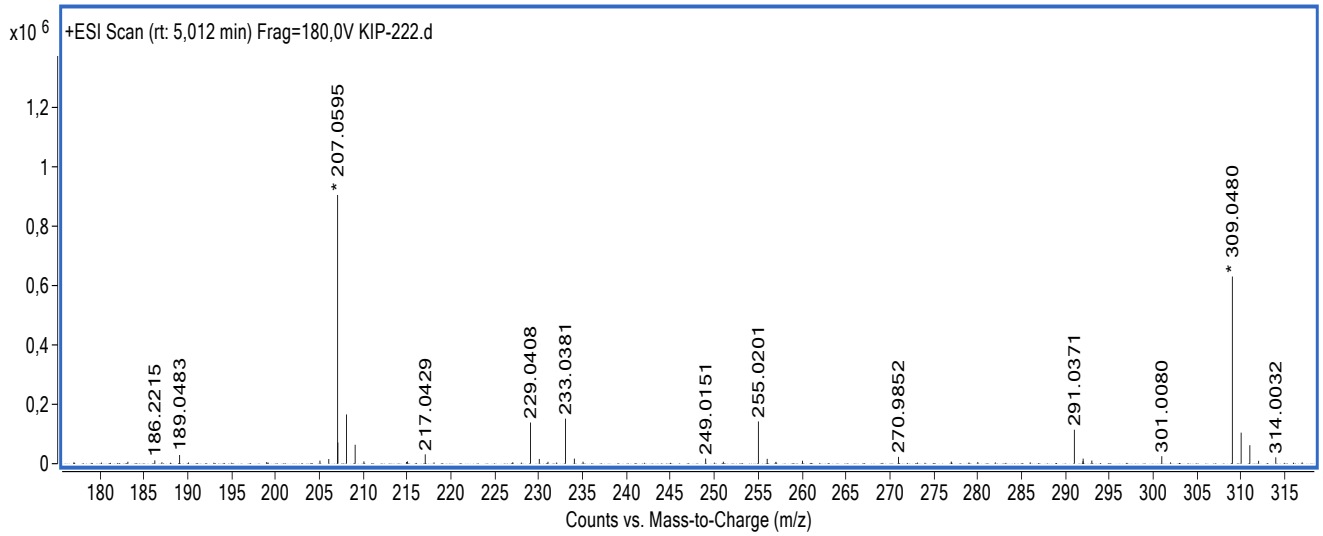
Mass spectrum (LC/Q-TOF) of (**5c**)



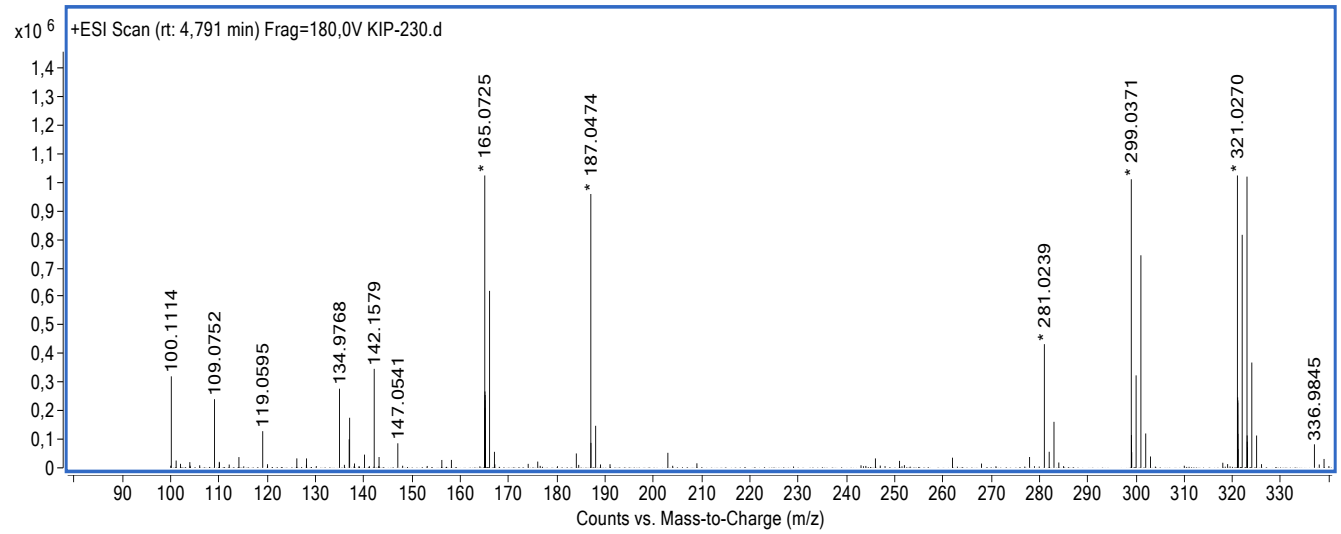
Mass spectrum (LC/Q-TOF) of (**6a**)



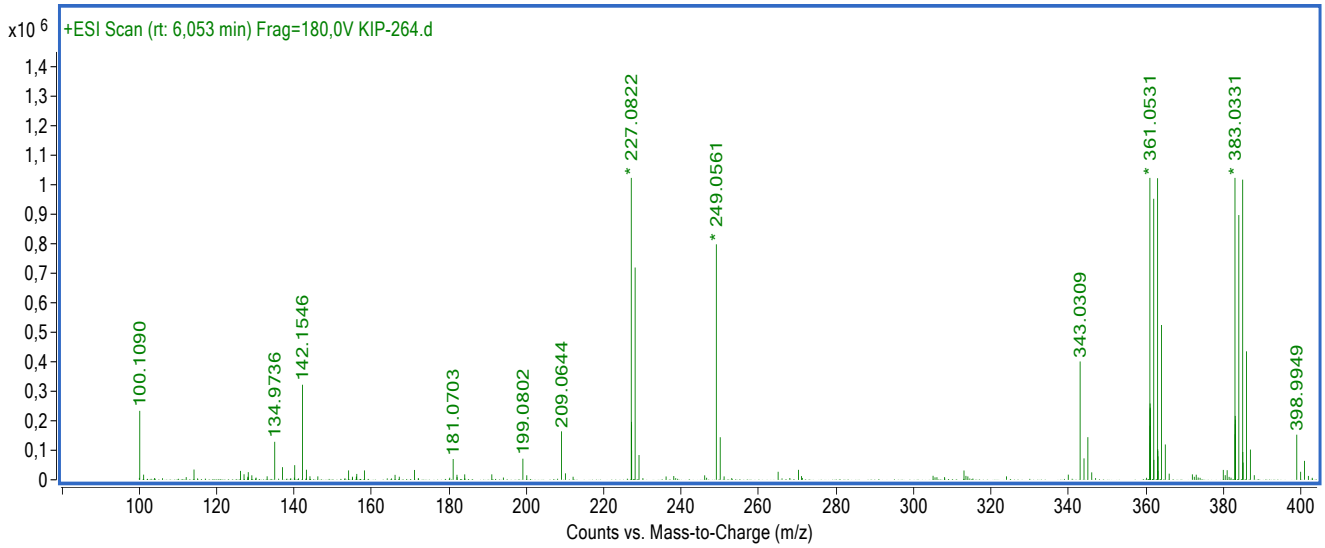
Mass spectrum (LC/Q-TOF) of (**6b**)



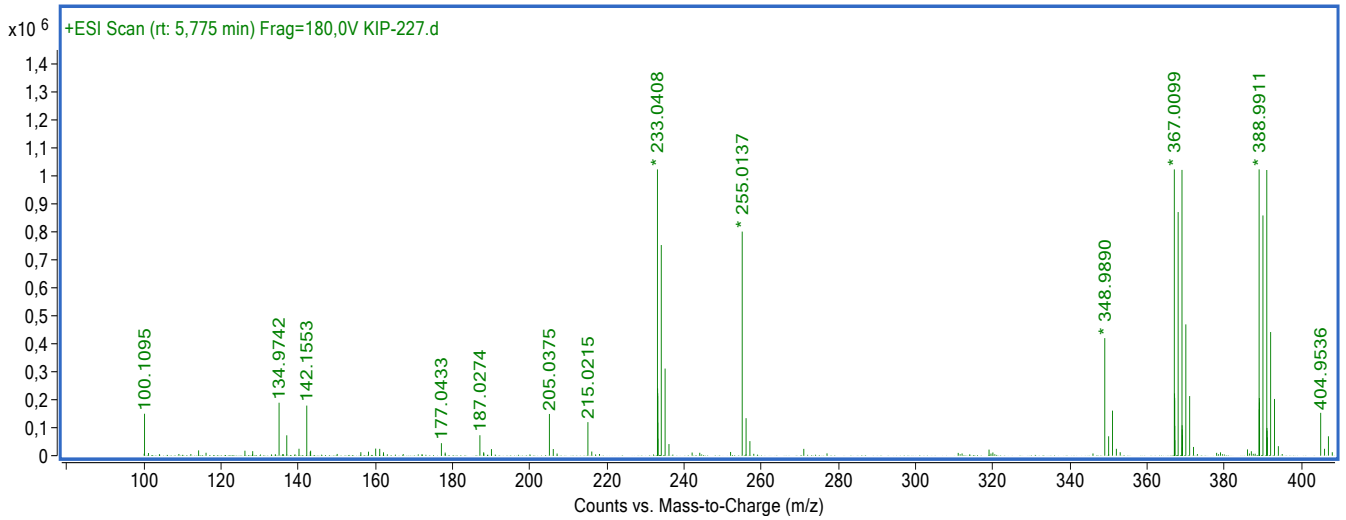
Mass spectrum (LC/Q-TOF) of (**6c**)



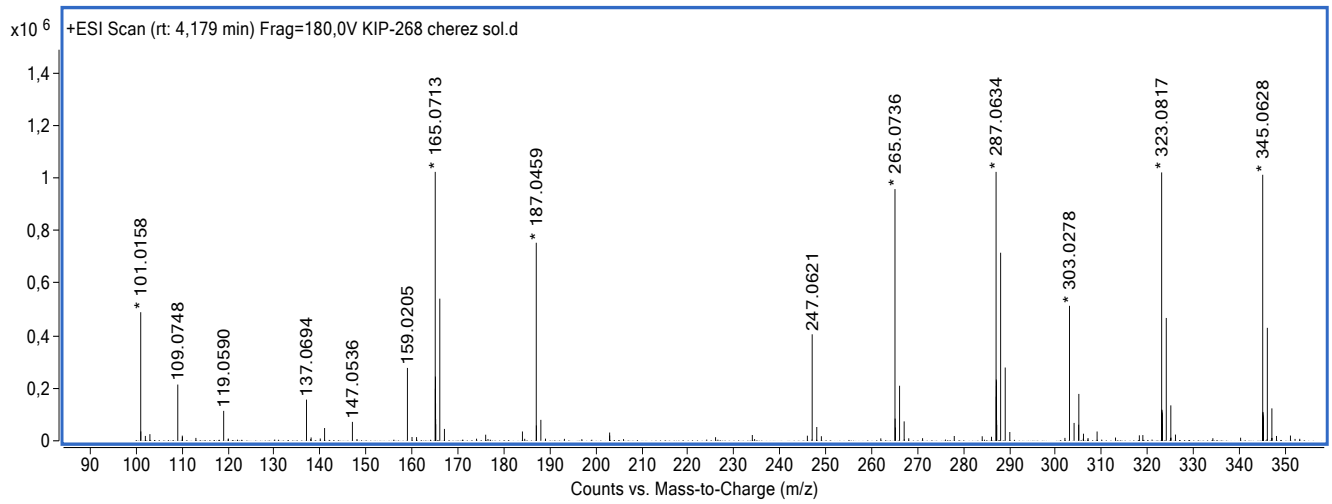
Mass spectrum (LC/Q-TOF) of (**7a**)



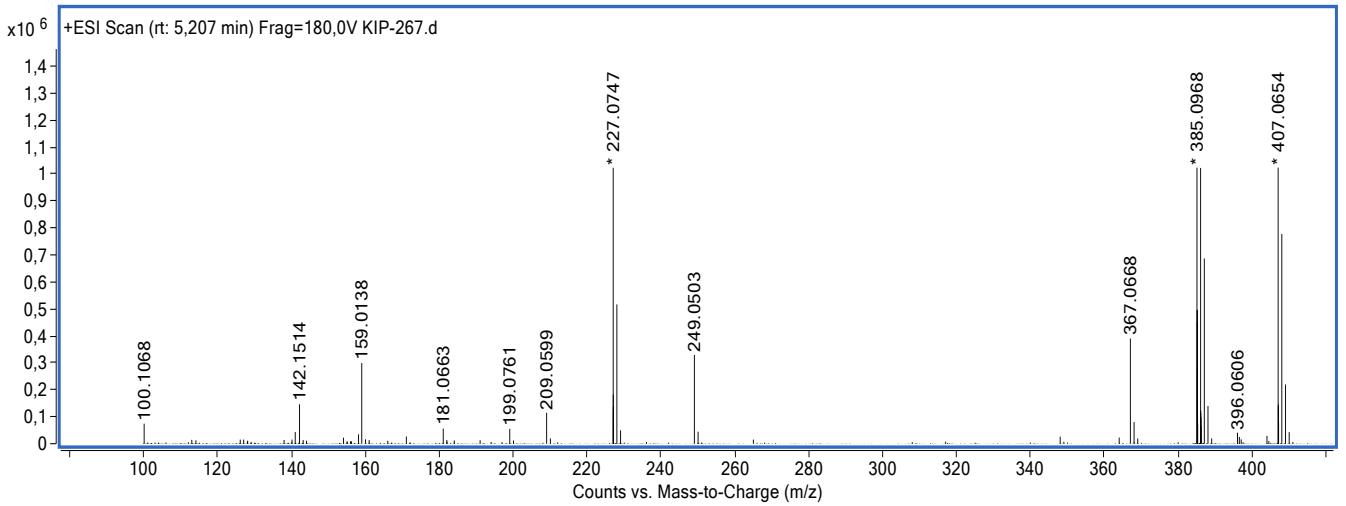
Mass spectrum (LC/Q-TOF) of (**7b**)



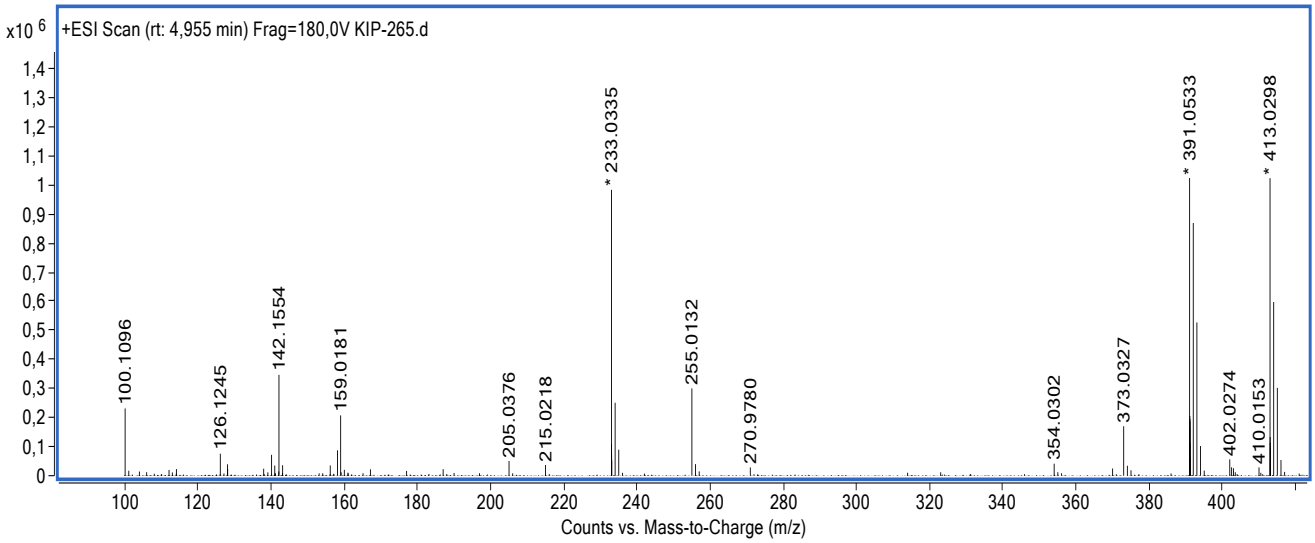
Mass spectrum (LC/Q-TOF) of (**7c**)



Mass spectrum (LC/Q-TOF) of (**8a**)

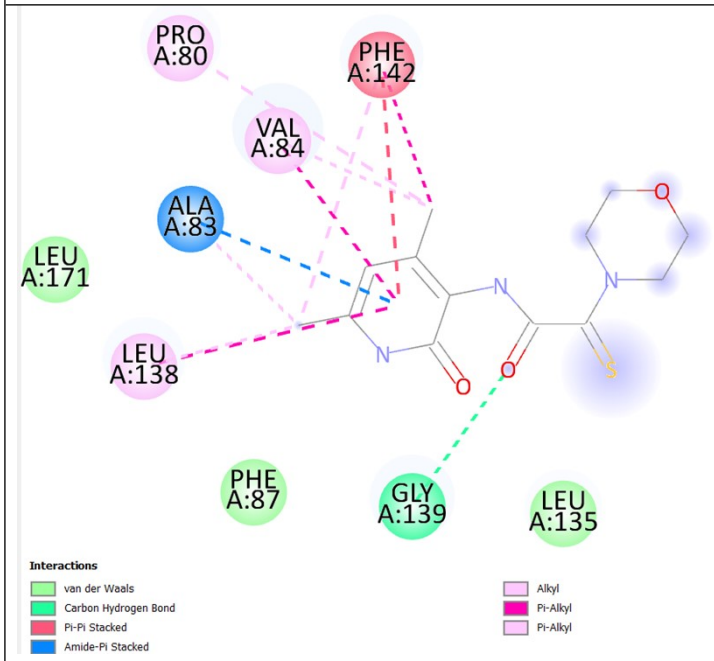
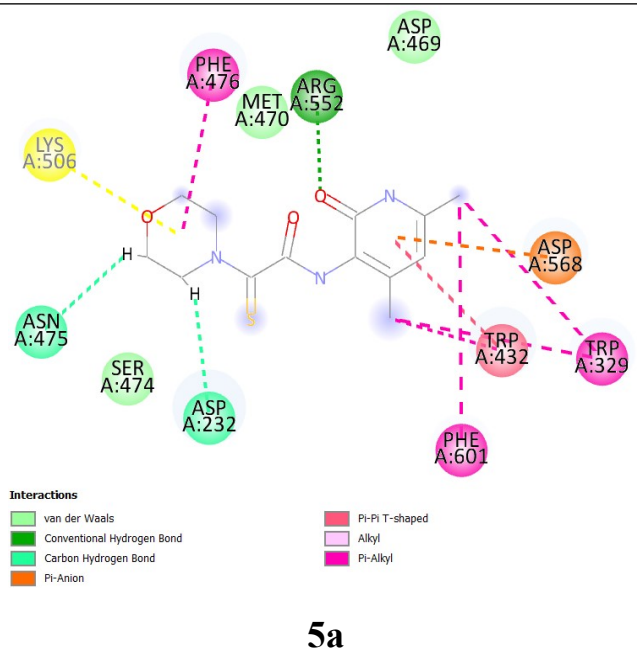
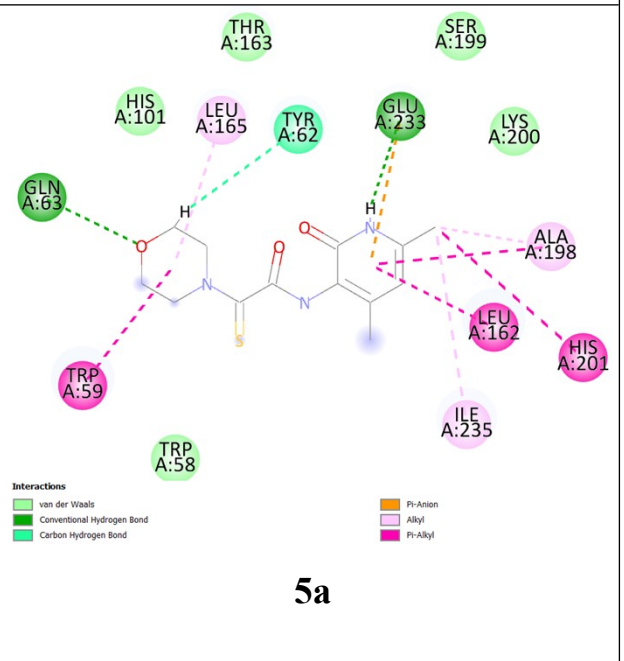


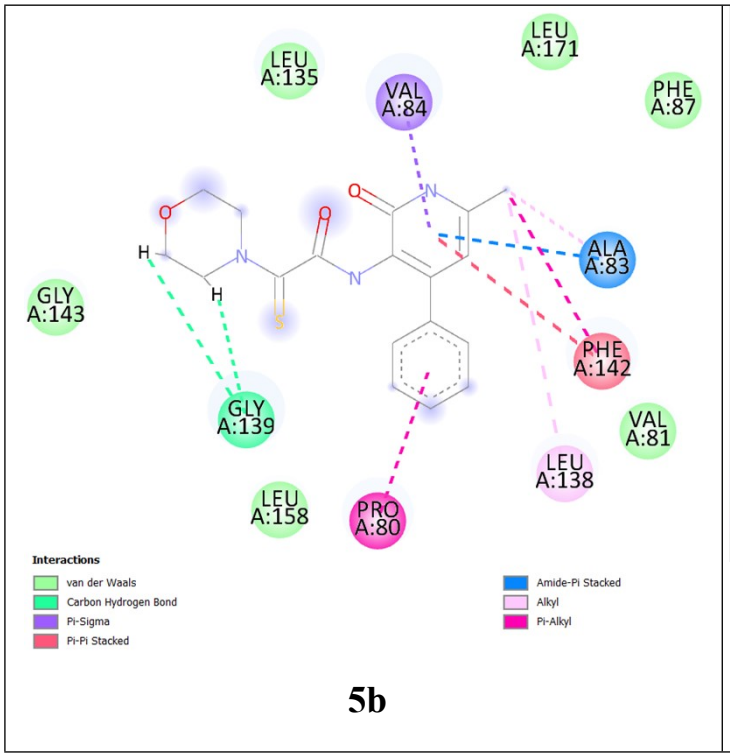
Mass spectrum (LC/Q-TOF) of (**8b**)



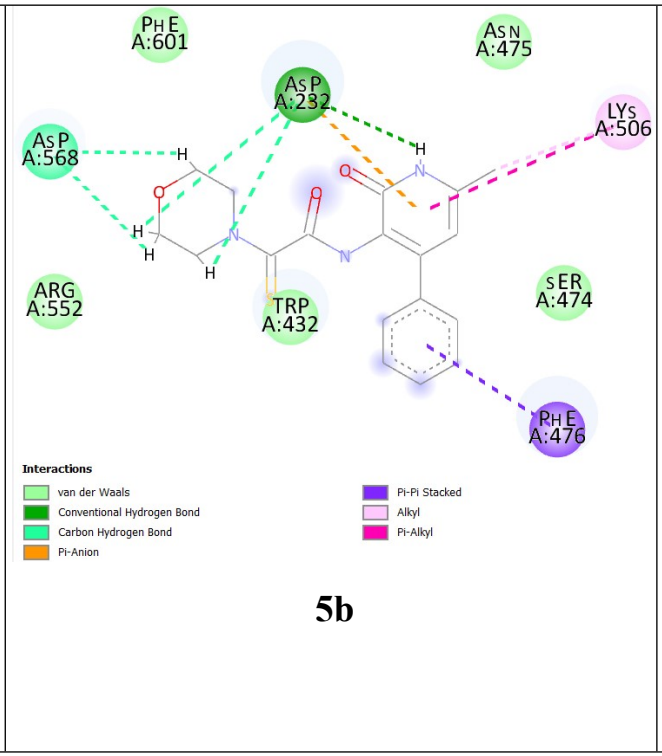
Mass spectrum (LC/Q-TOF) of (**8c**)

Table 1. Complexes between synthesized derivatives **5-8(a-c)** and active sites of proteins (PDB: 5TZR, 3W37, 2QV4, 5NN8)

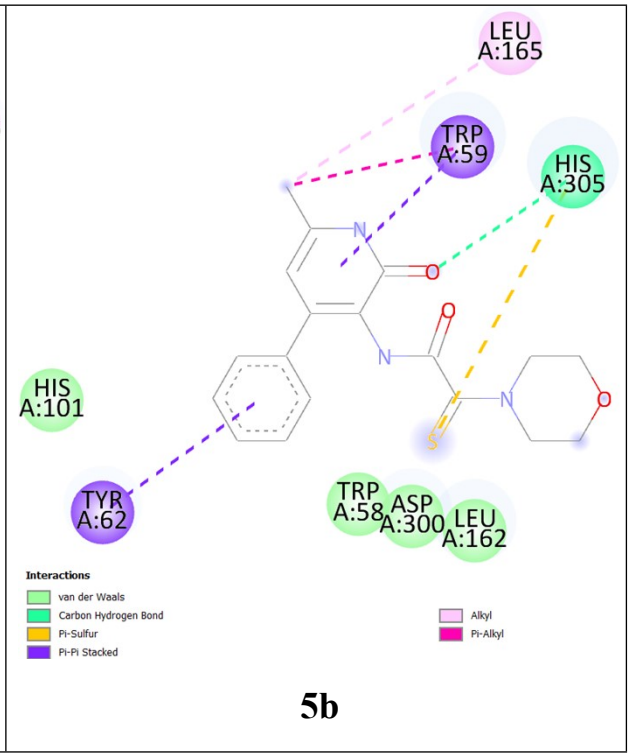
5TZR	3W37	2QV4
 **5a**	 **5a**	 **5a**


LEU A:135
LEU A:171
VAL A:84
PHE A:87
ALA A:83
GLY A:143
PHE A:142
GLY A:139
VAL A:81
LEU A:138
LEU A:158
PRO A:80
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Sigma
Pi-Pi Stacked
Amide-Pi Stacked
Alkyl
Pi-Alkyl

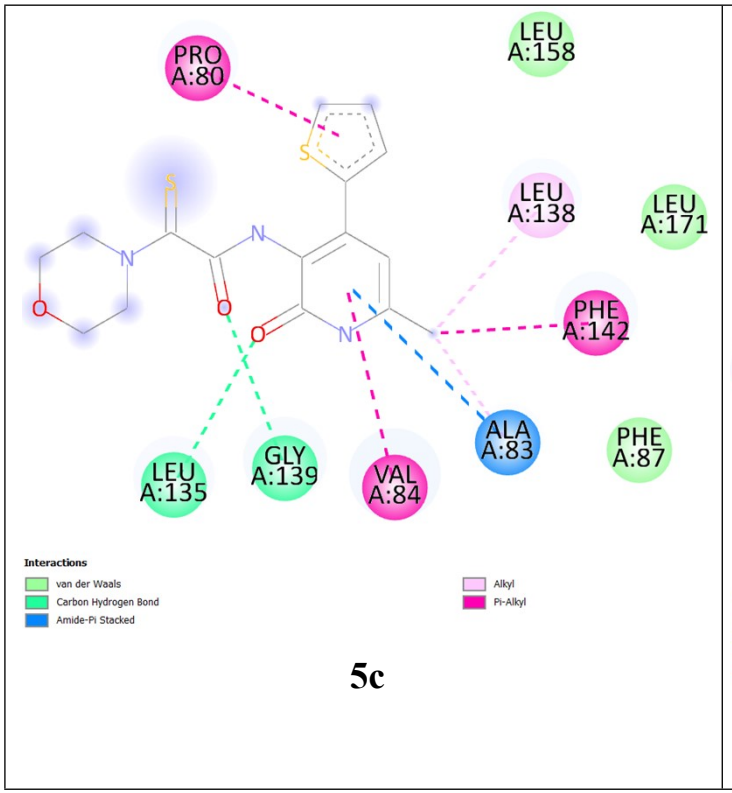
5b


PHE A:601
ASN A:475
ASP A:232
LYS A:506
ASP A:568
ARG A:552
TRP A:432
SER A:474
PHE A:476
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Pi Stacked
Alkyl
Pi-Alkyl

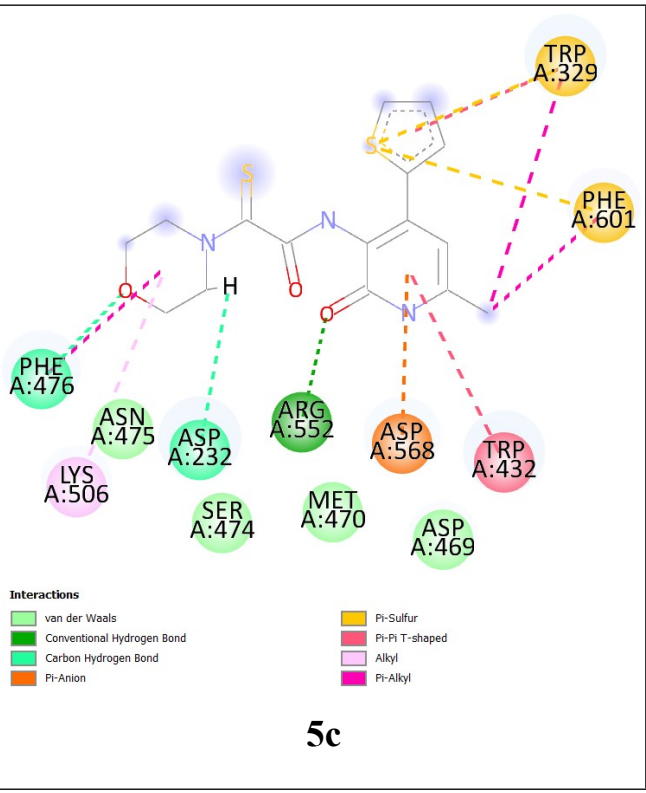
5b


LEU A:165
TRP A:59
HIS A:305
HIS A:101
TYR A:62
TRP A:58
ASP A:300
LEU A:162
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Sulfur
Pi-Pi Stacked
Alkyl
Pi-Alkyl

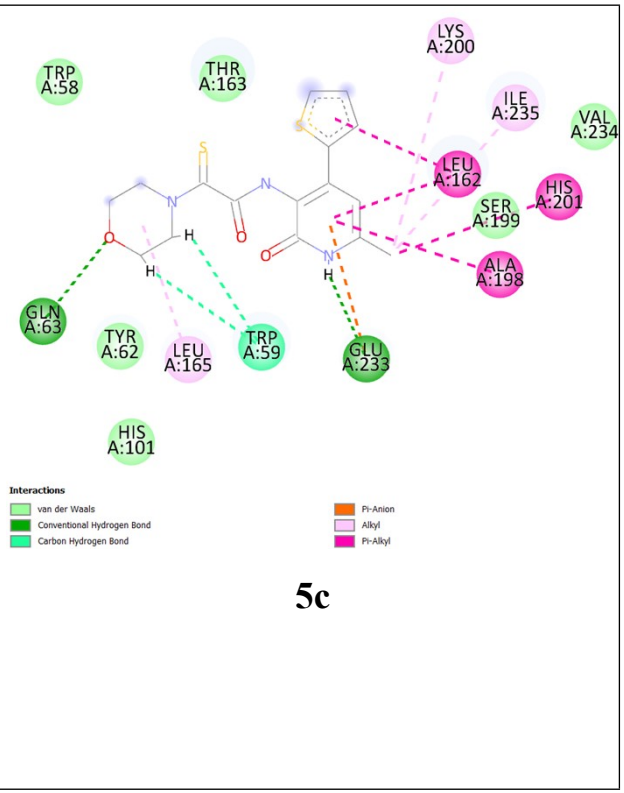
5b


PRO A:80
LEU A:158
LEU A:138
LEU A:171
PHE A:142
ALA A:83
PHE A:87
LEU A:135
GLY A:139
VAL A:84
Interactions
van der Waals
Carbon Hydrogen Bond
Amide-Pi Stacked
Alkyl
Pi-Alkyl

5c


TRP A:329
PHE A:601
PHE A:476
ASN A:475
ASP A:232
ARG A:552
ASP A:568
TRP A:432
LYS A:506
SER A:474
MET A:470
ASP A:469
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

5c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ALA A:198
GLN A:63
TYR A:62
LEU A:165
TRP A:59
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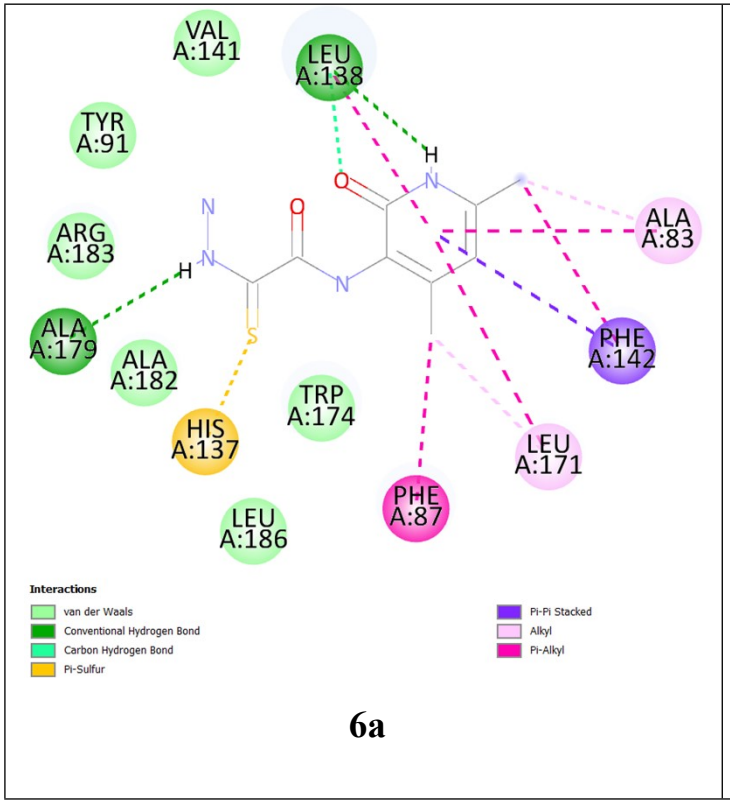
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Alkyl
Pi-Alkyl

5c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PHE A:142
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LEU A:171
PHE A:87
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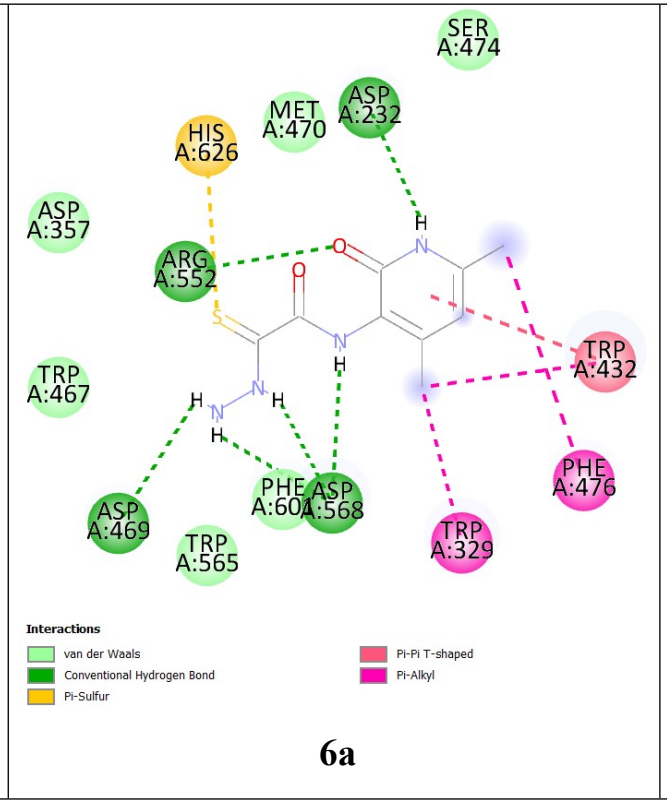
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Sulfur
Pi-Pi Stacked
Alkyl
Pi-Alkyl

6a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PHE A:604
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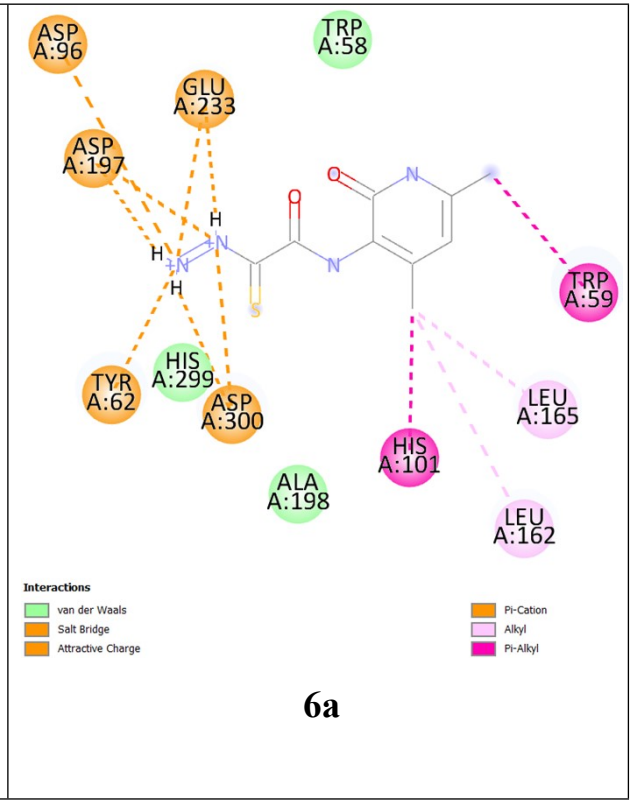
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Sulfur
Pi-Pi T-shaped
Pi-Alkyl

6a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ASP A:300
LEU A:165
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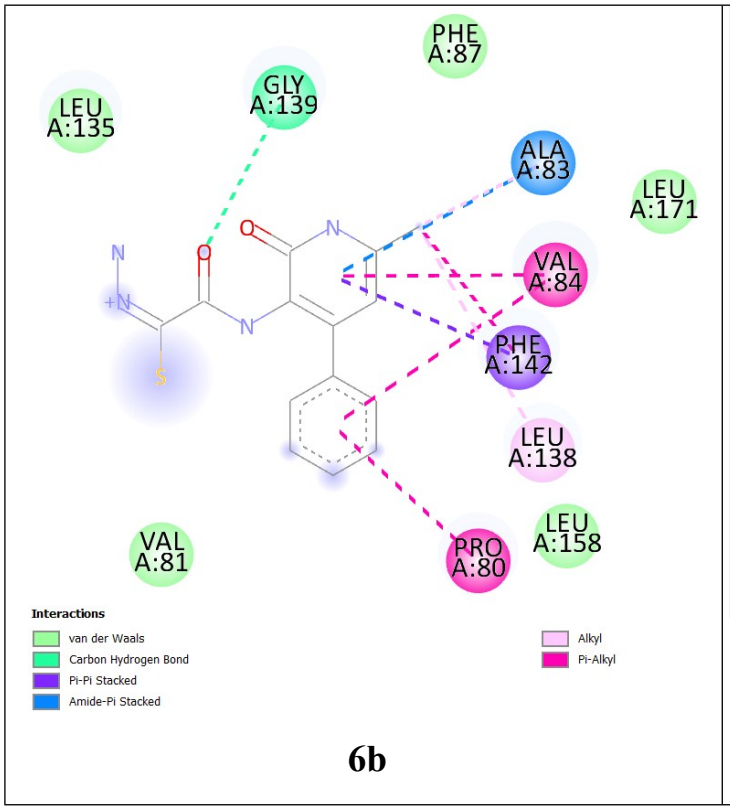
LEU A:162
Interactions
van der Waals
Salt Bridge
Attractive Charge
Pi-Cation
Alkyl
Pi-Alkyl

6a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VAL A:84
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LEU A:158
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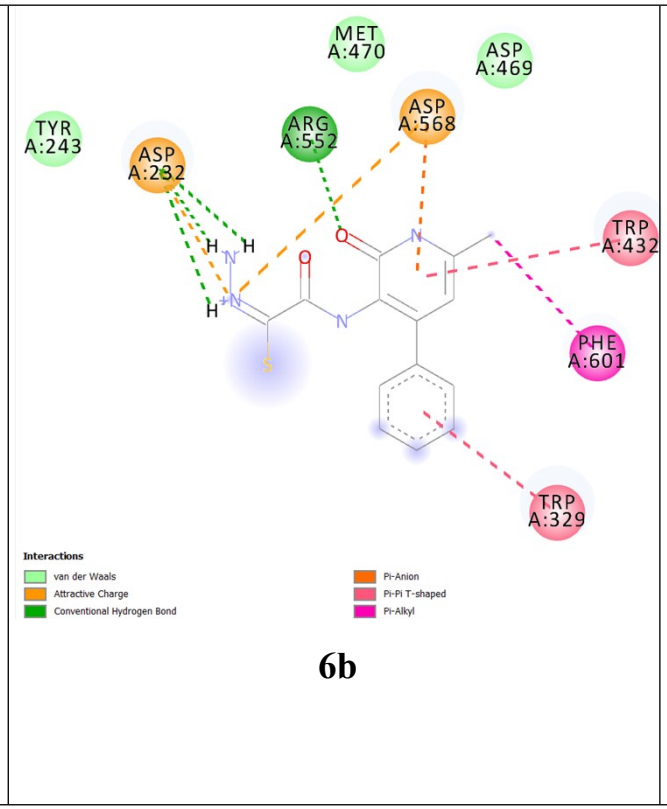
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Pi Stacked
Amide-Pi Stacked
Alkyl
Pi-Alkyl

6b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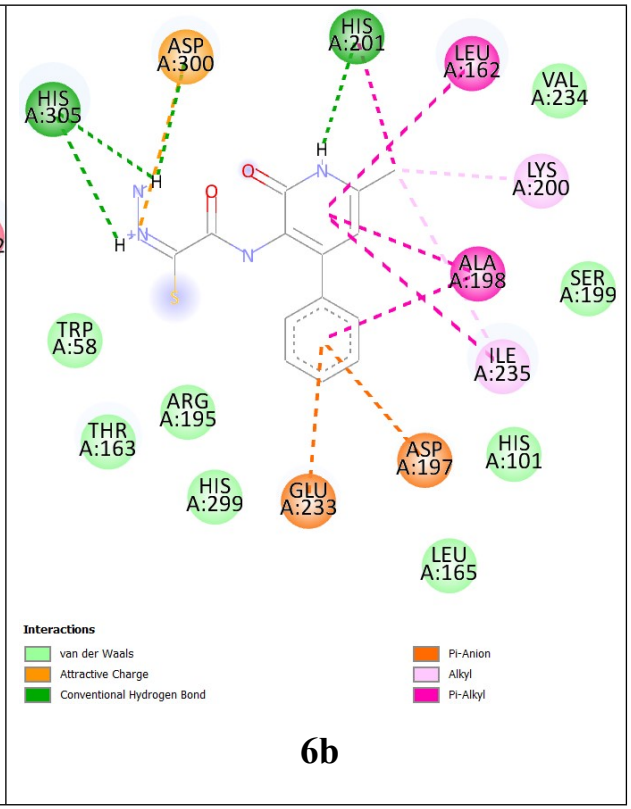
Interactions
van der Waals
Attractive Charge
Conventional Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Pi-Alkyl

6b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ARG A:195
THR A:163
ASP A:197
HIS A:101
HIS A:299
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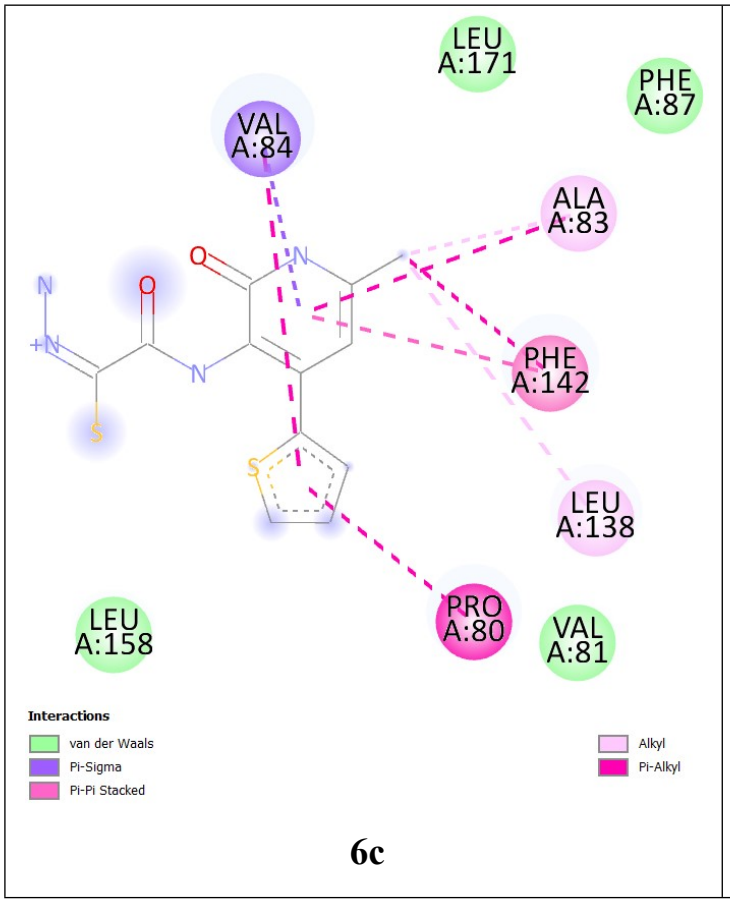
Interactions
van der Waals
Attractive Charge
Conventional Hydrogen Bond
Pi-Anion
Alkyl
Pi-Alkyl

6b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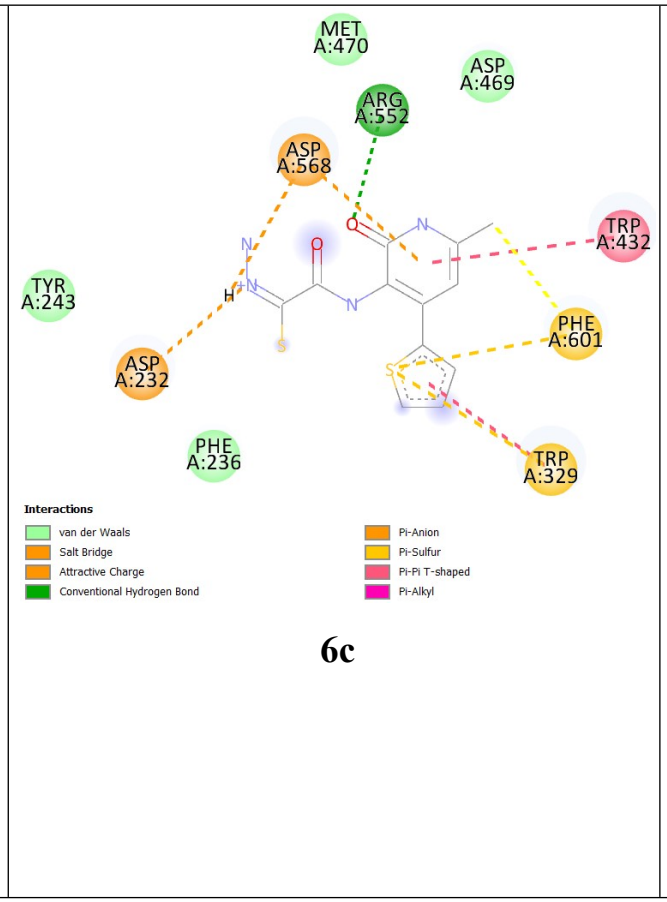
Interactions
van der Waals
Pi-Sigma
Pi-Pi Stacked
Alkyl
Pi-Alkyl

6c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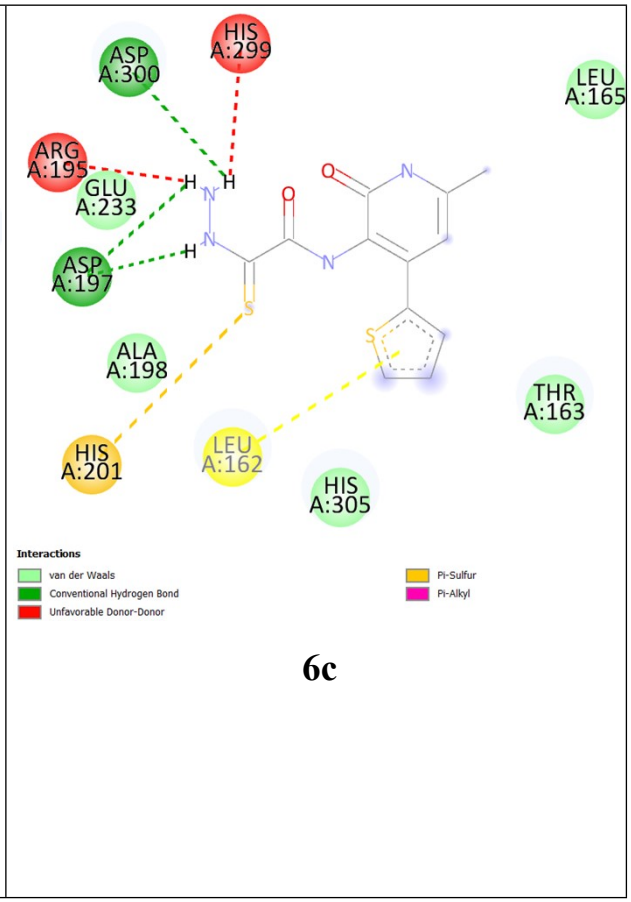
PHE A:601
ASP A:232
PHE A:236
TRP A:329
Interactions
van der Waals
Salt Bridge
Attractive Charge
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Pi-Alkyl

6c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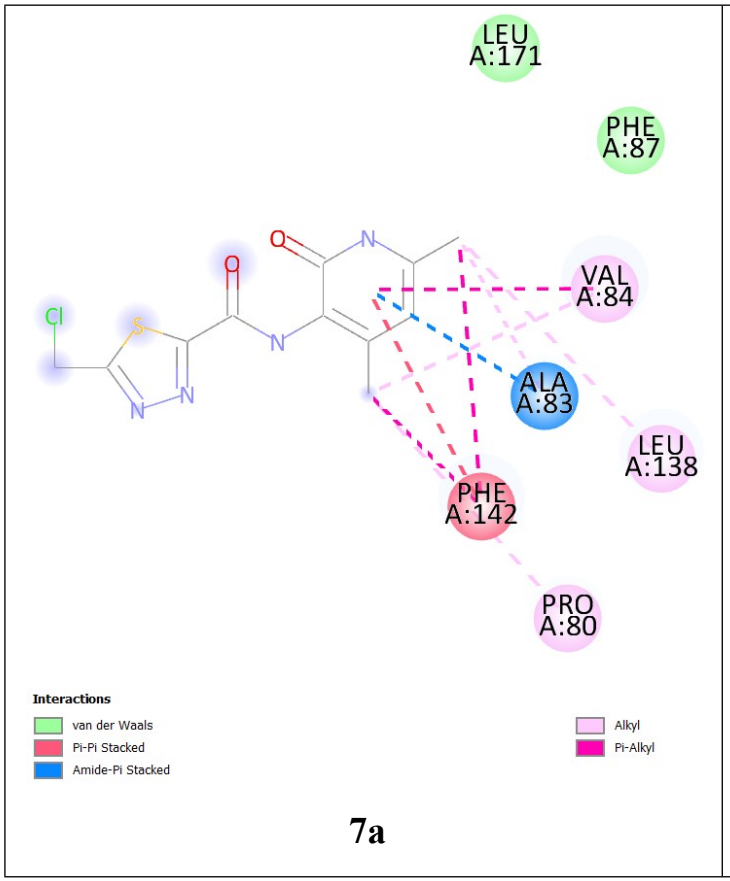
Interactions
van der Waals
Conventional Hydrogen Bond
Unfavorable Donor-Donor
Pi-Sulfur
Pi-Alkyl

6c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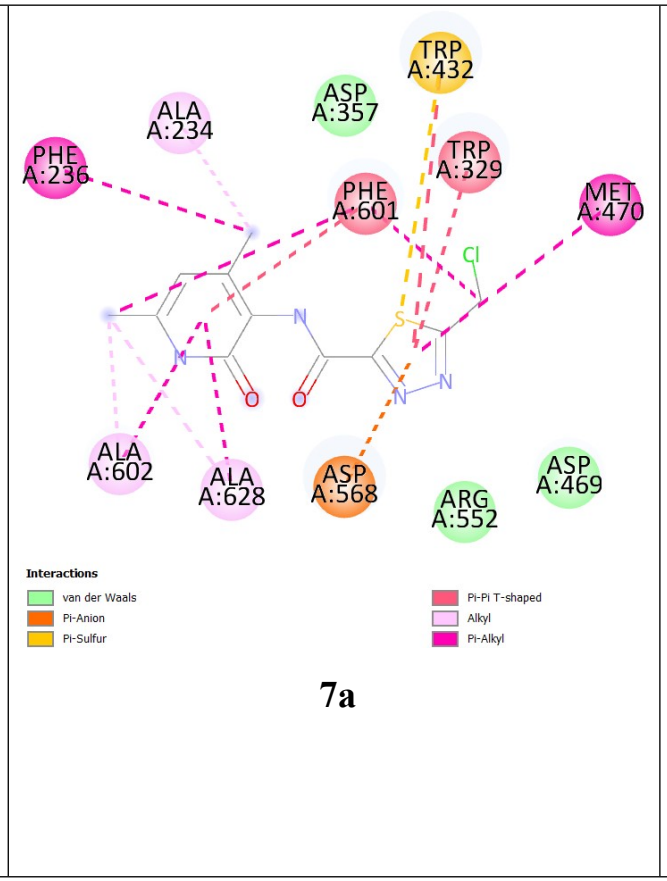
Interactions
van der Waals
Pi-Pi Stacked
Amide-Pi Stacked
Alkyl
Pi-Alkyl

7a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ASP A:568
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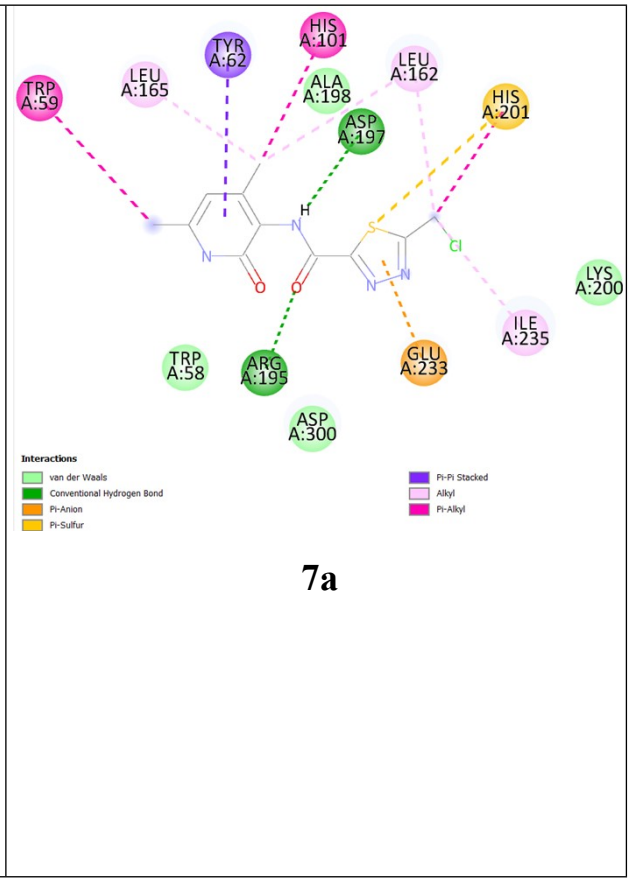
Interactions
van der Waals
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

7a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LEU A:162
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ALA A:198
HIS A:201
ASP A:197
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ARG A:195
GLU A:233
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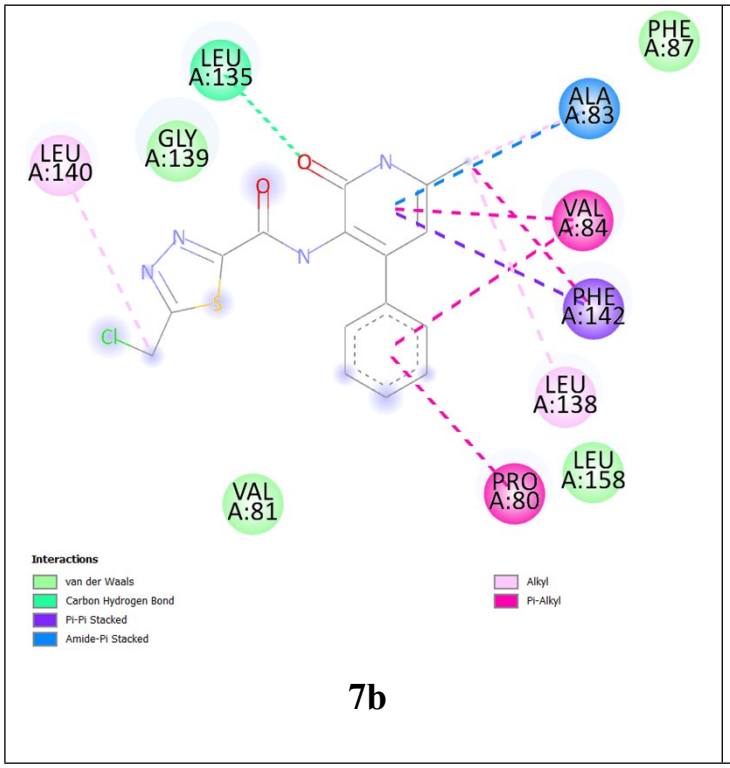
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi Stacked
Alkyl
Pi-Alkyl

7a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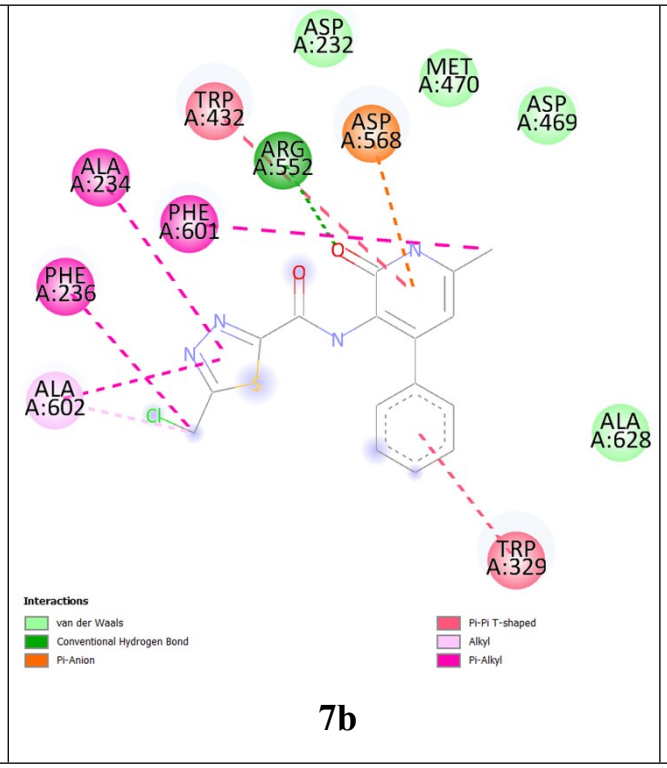
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Pi Stacked
Amide-Pi Stacked
Alkyl
Pi-Alkyl

7b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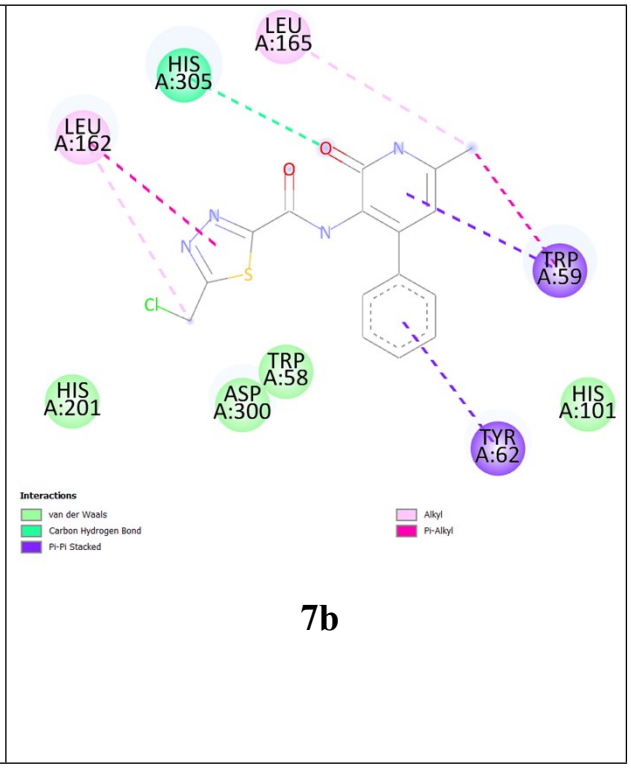
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

7b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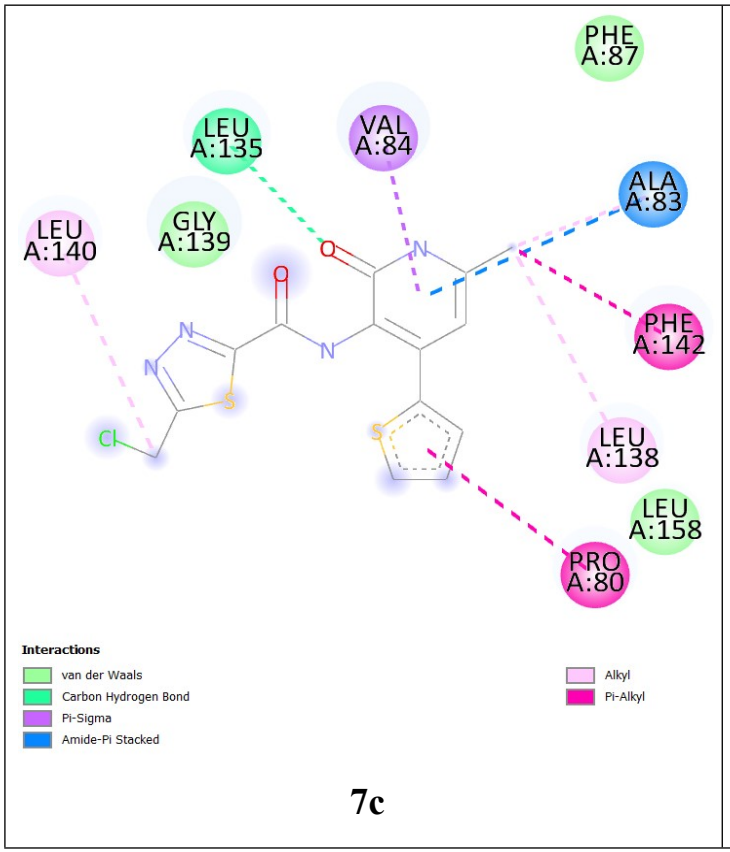
van der Waals
Carbon Hydrogen Bond
Pi-Pi Stacked
Alkyl
Pi-Alkyl

7b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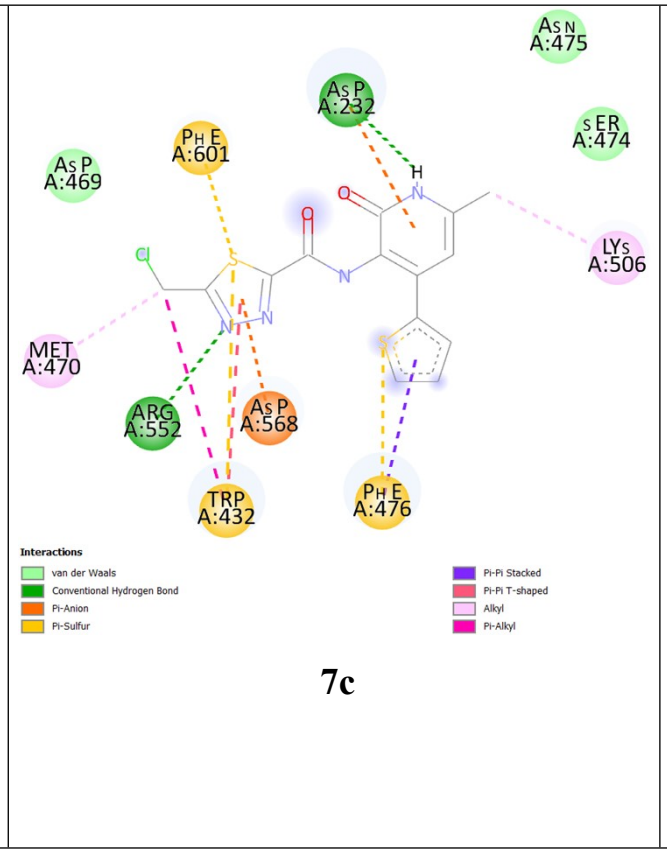
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Sigma
Amide-Pi Stacked
Alkyl
Pi-Alkyl

7c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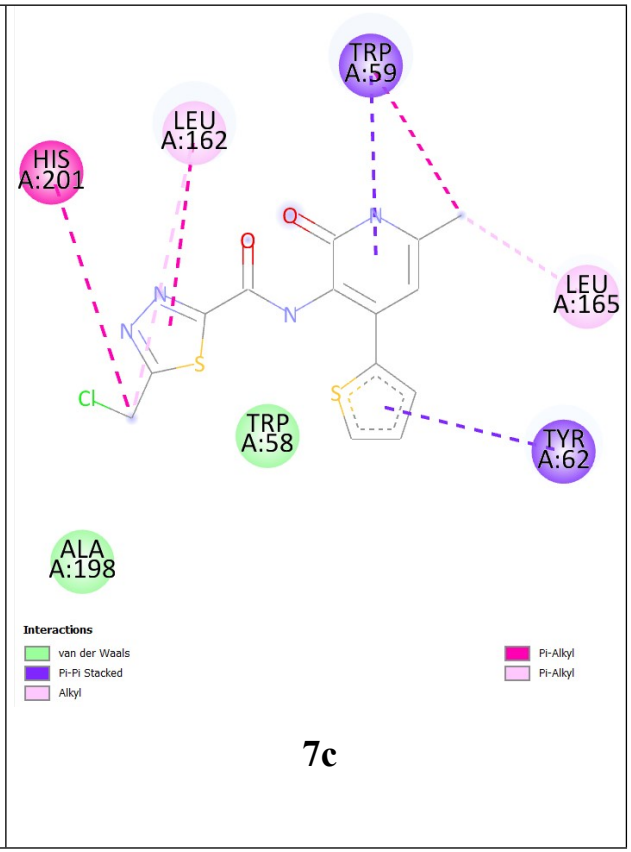
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi Stacked
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

7c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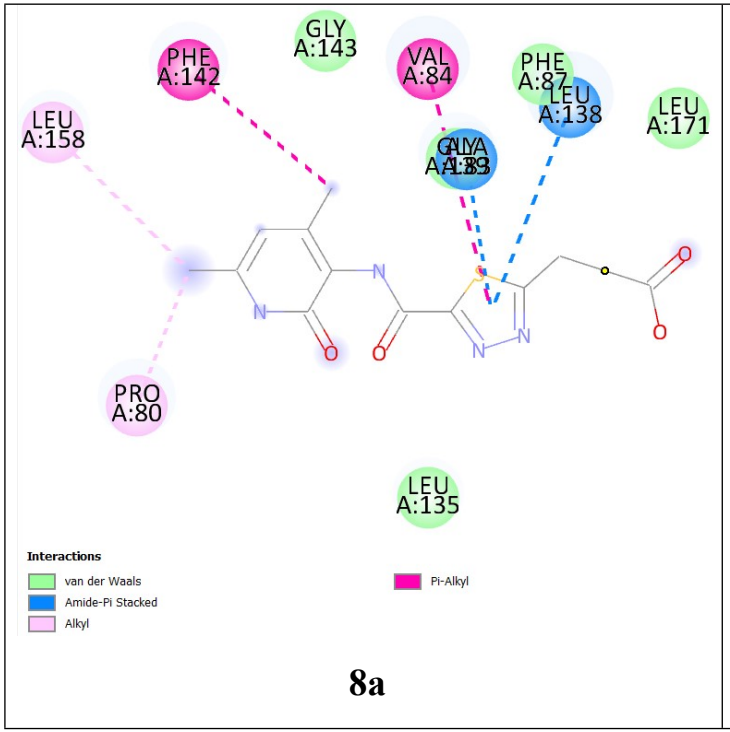
van der Waals
Pi-Pi Stacked
Alkyl
Pi-Alkyl
Pi-Alkyl

7c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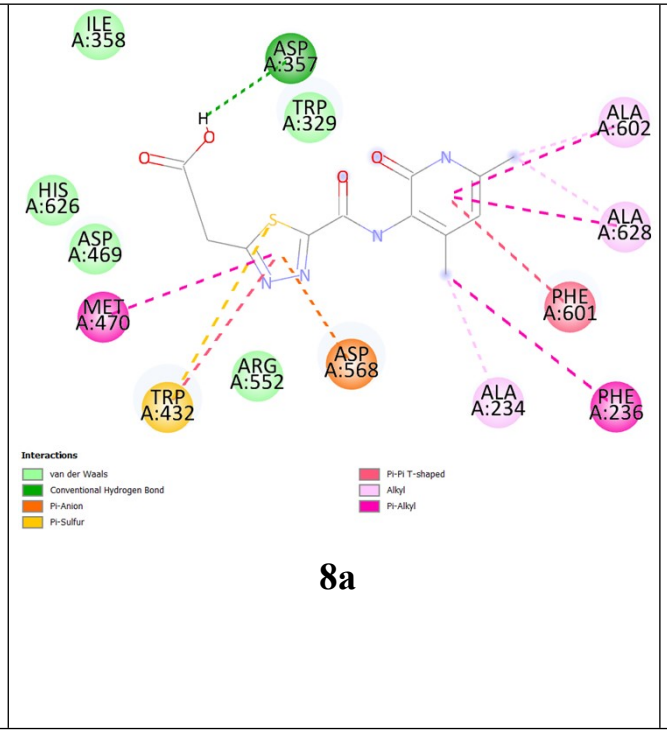
Interactions
van der Waals
Amide-Pi Stacked
Alkyl
Pi-Alkyl

8a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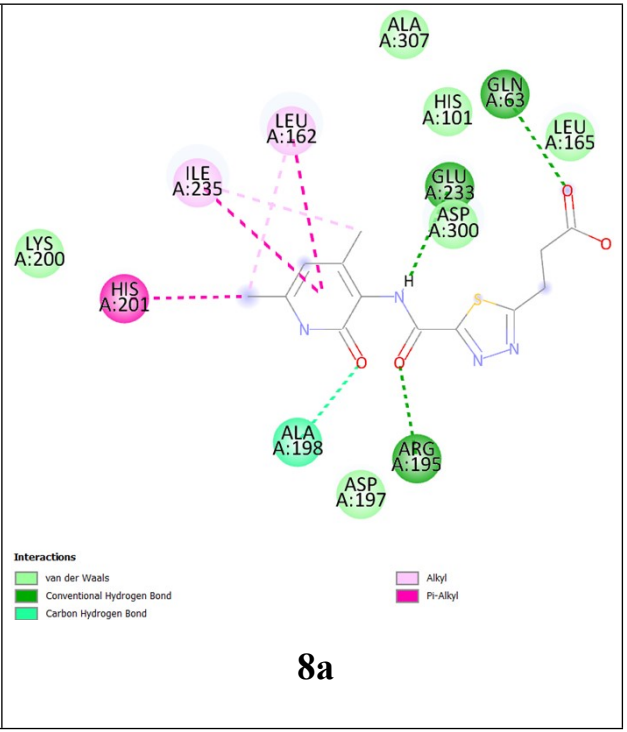
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

8a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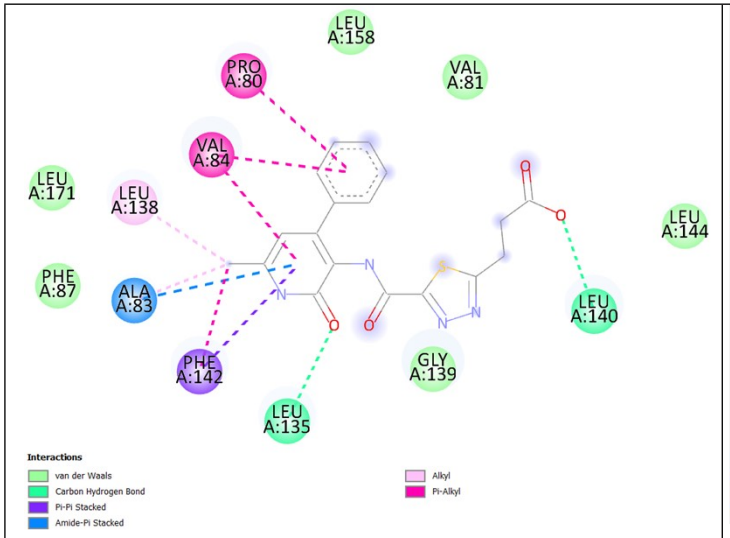
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Alkyl
Pi-Alkyl

8a



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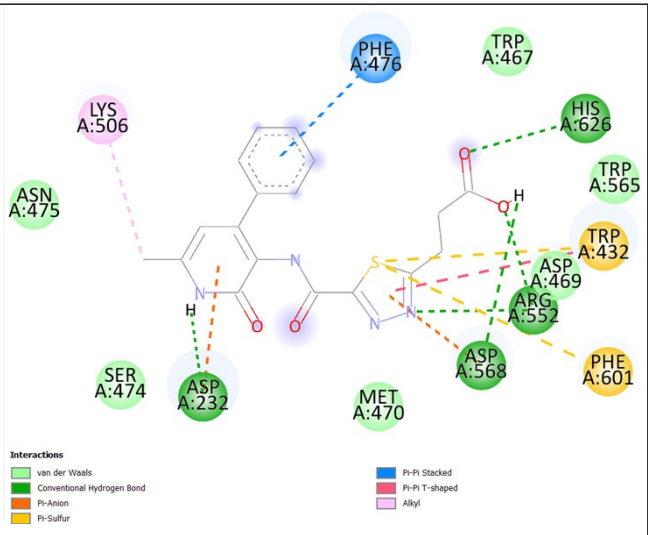

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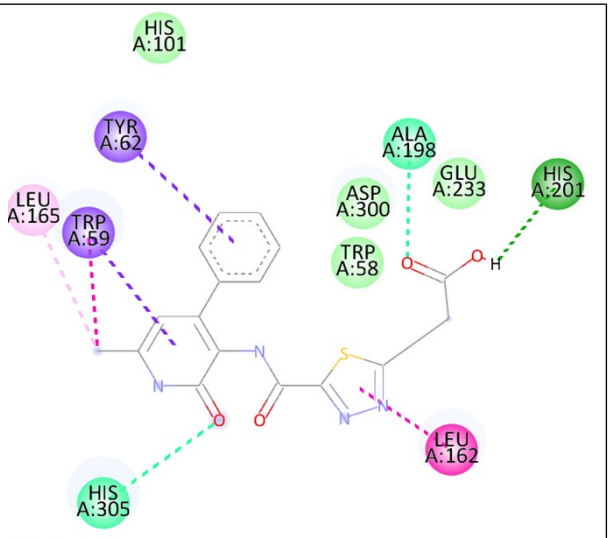

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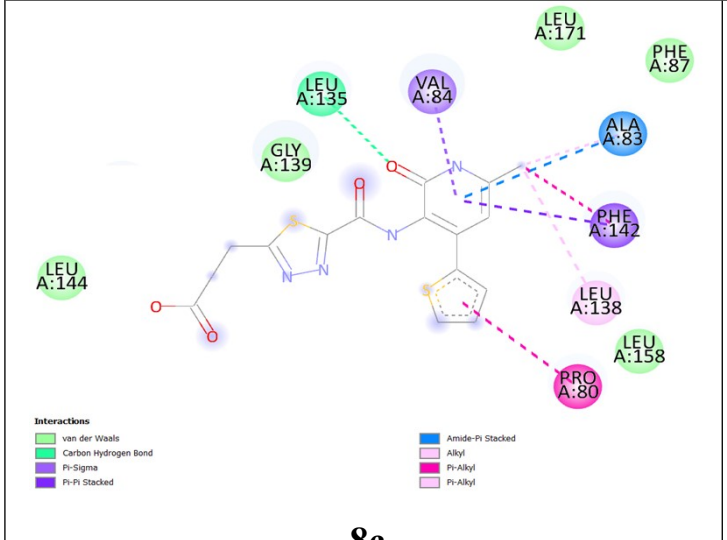

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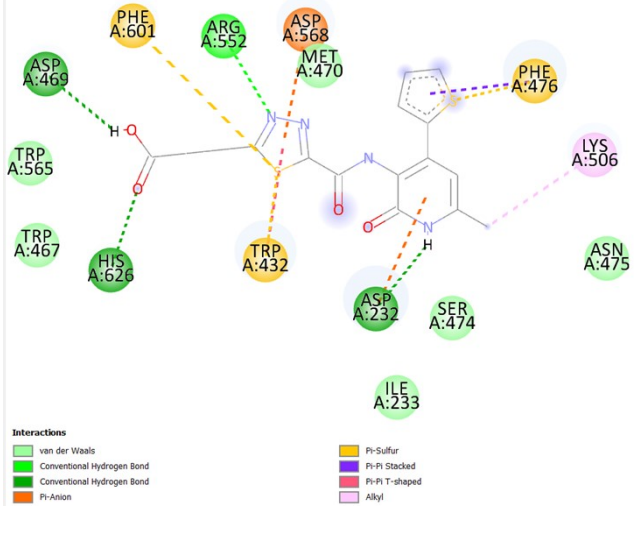

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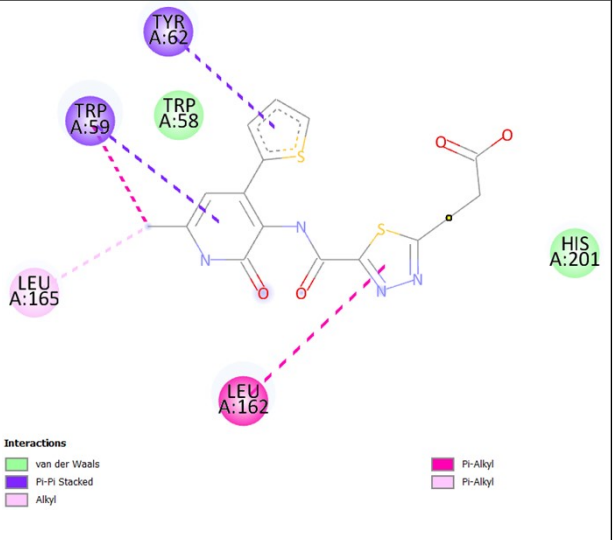

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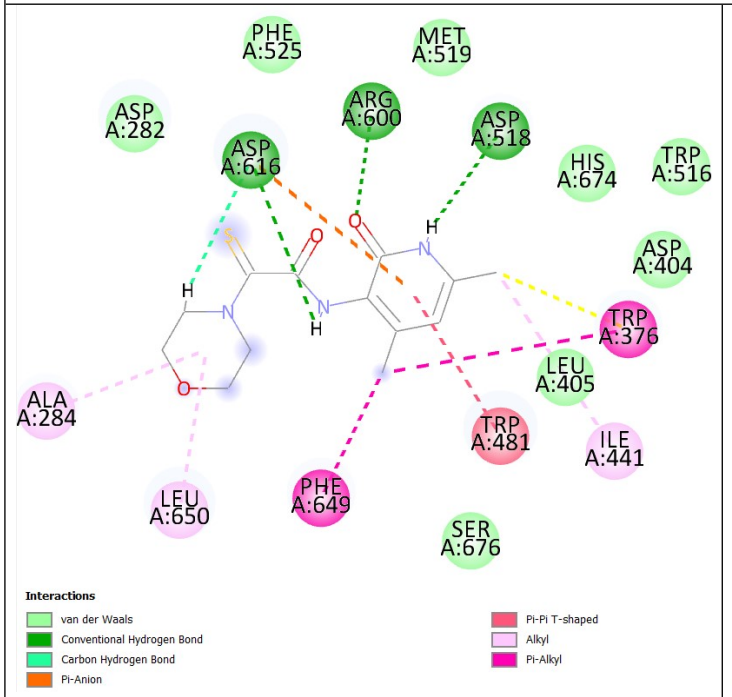
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TRP A:376
LEU A:405
ALA A:284
TRP A:481
ILE A:441
LEU A:650
PHE A:649
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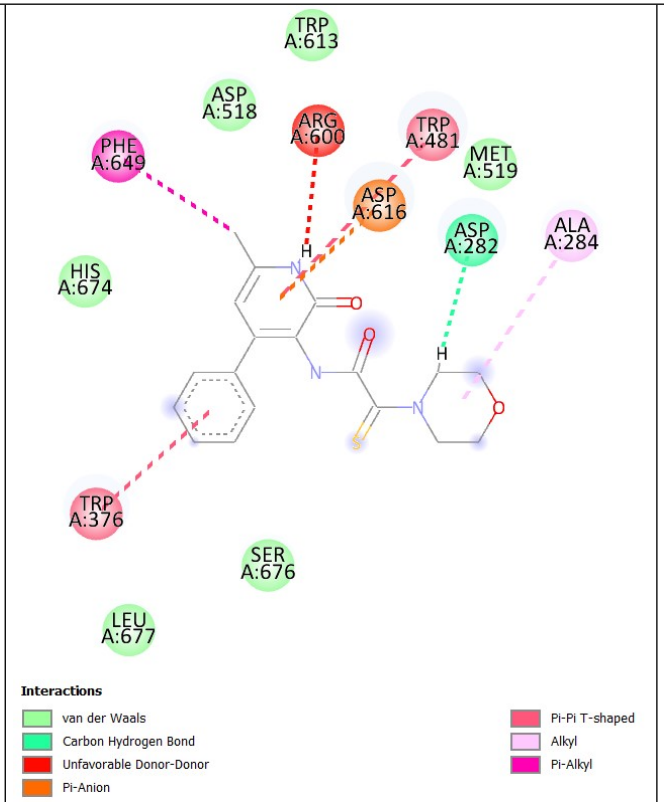
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

5a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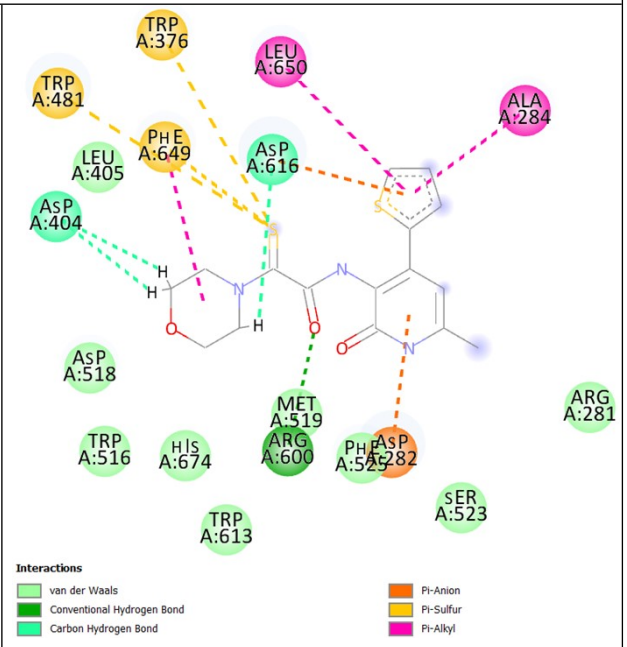
TRP A:376
SER A:676
LEU A:677
Interactions
van der Waals
Carbon Hydrogen Bond
Unfavorable Donor-Donor
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

5b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HIS A:674
ARG A:600
ASP A:282
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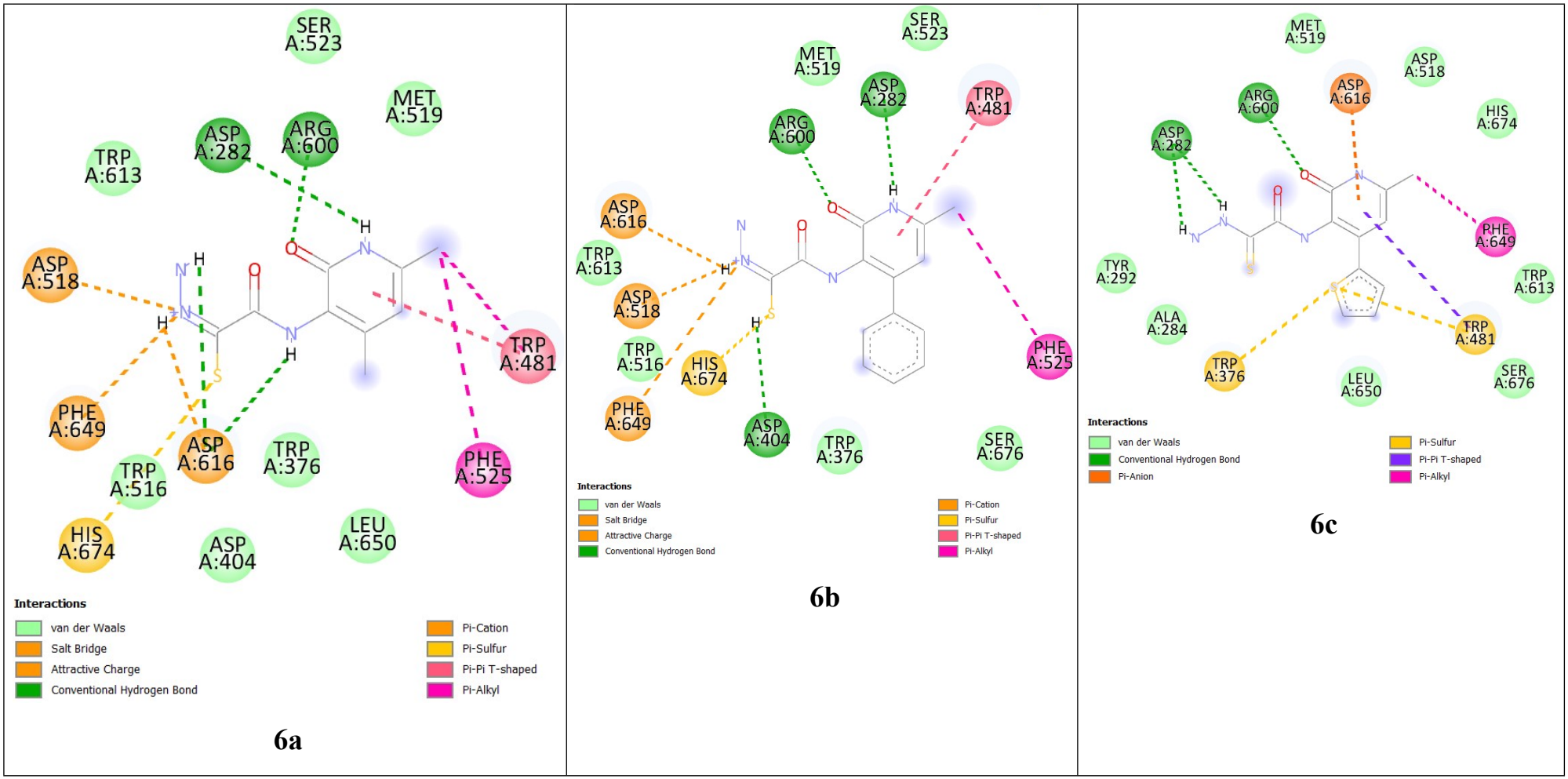
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Alkyl

5c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ASP A:404
LEU A:650
Interactions
van der Waals
Salt Bridge
Attractive Charge
Conventional Hydrogen Bond
Pi-Cation
Pi-Sulfur
Pi-Pi T-shaped
Pi-Alkyl
6a
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ASP A:282
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TRP A:613
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TRP A:516
HIS A:674
PHE A:525
PHE A:649
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TRP A:376
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Interactions
van der Waals
Salt Bridge
Attractive Charge
Conventional Hydrogen Bond
Pi-Cation
Pi-Sulfur
Pi-Pi T-shaped
Pi-Alkyl
6b
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ASP A:518
ASP A:616
ARG A:600
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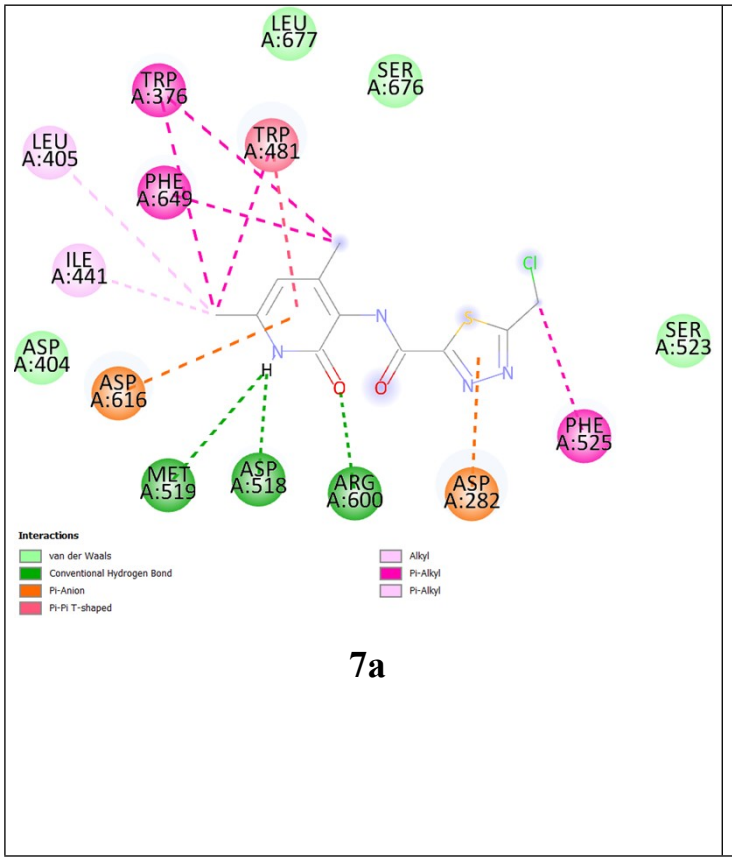
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Pi-Alkyl
6c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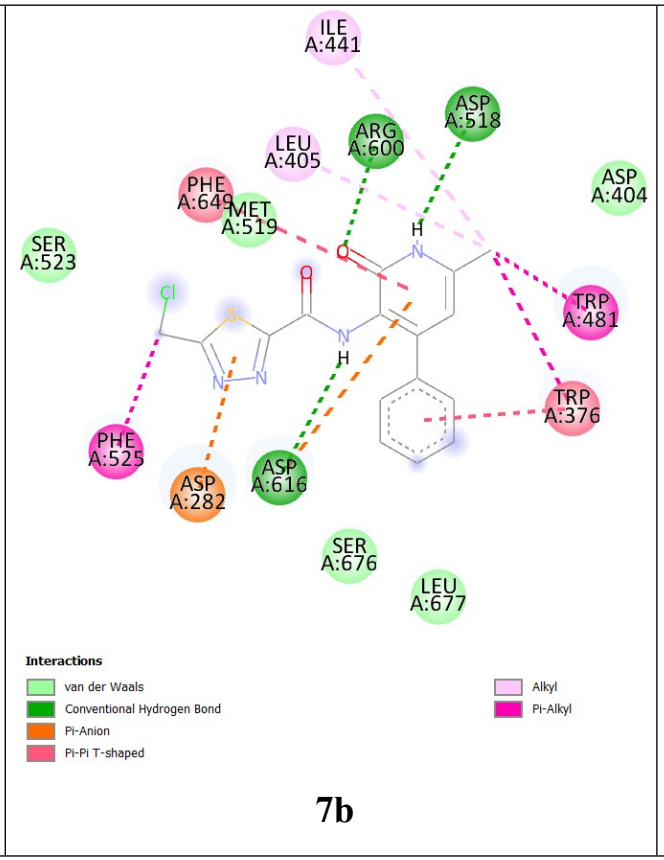
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl
Pi-Alkyl

7a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PHE A:525
ASP A:282
ASP A:616
SER A:676
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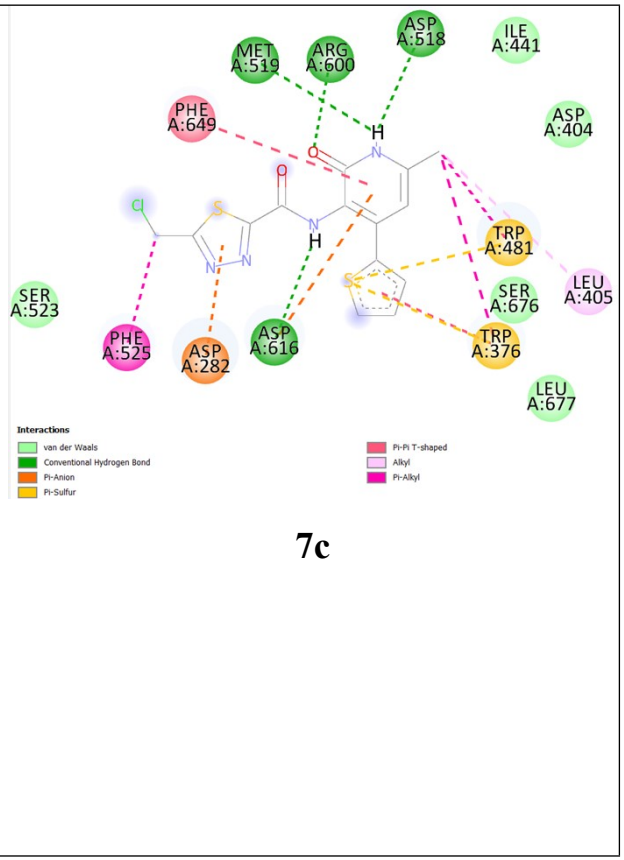
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

7b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TRP A:376
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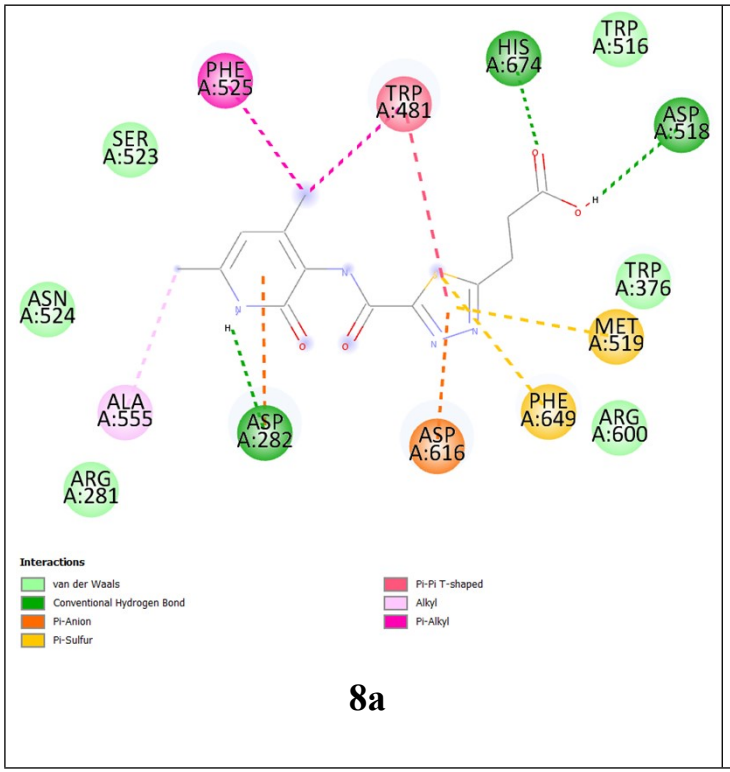
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

7c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ASP A:616
PHE A:649
ARG A:600
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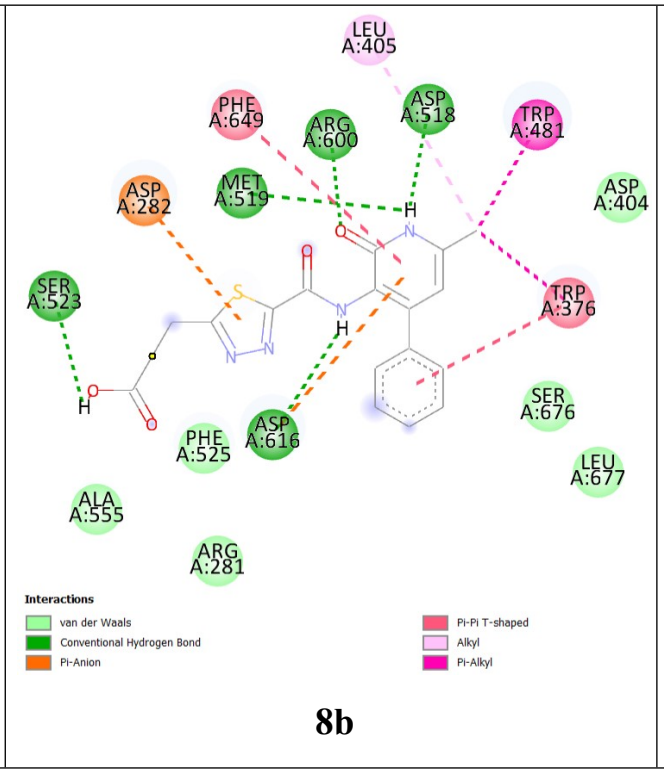
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

8a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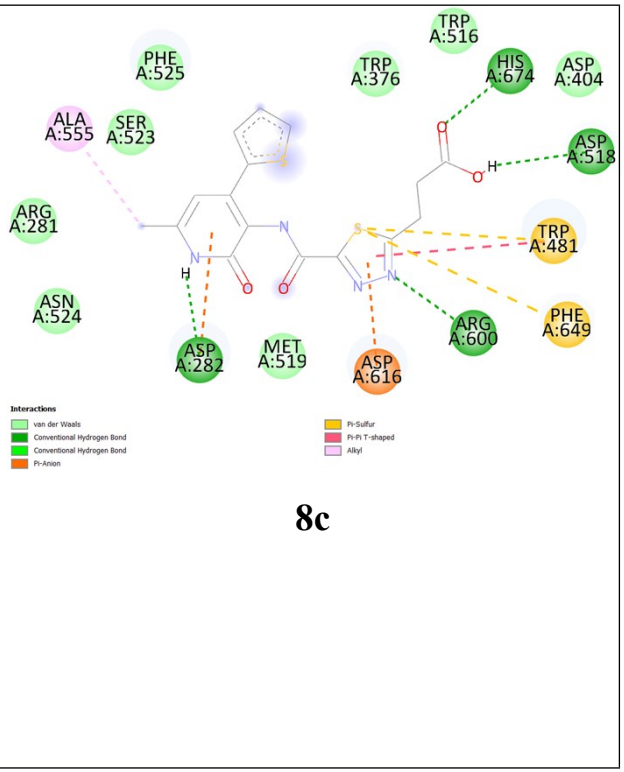
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

8b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ASN A:524
PHE A:649
ARG A:600
ASP A:282
MET A:519
ASP A:616
Interactions
van der Waals
Conventional Hydrogen Bond
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi T-shaped
Alkyl

8c

Table 2. Basic amino acid interactions and H-bonds

Compound	Receptor	H-bond	Residual Amino acid Interactions	
			Pi-Sulfur/ Pi-Anion/Pi-Cation/Pi-Pi Stacked/ Pi-sigma/Pi-Pi T-shaped/Pi-Alkyl/ Alkyl/Amide-Pi Stacked/Pis interactions/Salt Bridge/ Attactive Charge/	Van-der Walls interactions
5a	5TZR	GLY139	PHE142; PRO80; VAL84; ALA83; LEU138	LEU135; LEU171
5b		GLY139	VAL84; PRO80; LEU138; PHE142; ALA83	GLY143; LEU158; LEU135; LEU171; PHE87; VAL81
5c		LEU135; GLY139	PRO80; VAL84; ALA83; PHE142; LEU138	LEU158; LEU171; PHE87
5a	3W37	ASN475; ASP232; ARG532	PHE476; LYS506; PHE601; TRP432; TRP329; ASP568	SER474; MET470; ASP469
5b		ASP568; ASP232	ASP232; LYS506; PHE476	PHE601; ARG552; TRP432; ASN475; SER474
5c		PHE476; ASP232; ARG552	PHE476; LYS506; ASP568; TRP432; PHE601; TRP329	ASN475; SER474; MET470; ASP469
5a	2QV4	GLN63; TYR62; GLU233	TRP59; LEU165; GLU233; ILE235; LEU162; HIS201; ALA198	SER199; LYS200; THR163; HIS101; TRP58
5b		HIS305	TYR62; TRP59; LEU165; HIS305	HIS101; TRP58; ASP300; LEU162
5c		GLN63; TRP59; GLU233	LEU165; GLU233; ALA198; LEU162; HIS201; ILE235; LYS200	TRP58; TYR62; HIS101; THR163; SER199; VAL234
5a	5NN8	ASP616; ARG600; ASP518	ALA284; LEU650; PHE649; ASP616; TRP481; ILE441; TRP376	ASP282; PHE525; MET519; HIS674; TRP516; ASP404; LEU405; SER676
5b		ASP282	PHE649; TRP376; ARG600; ASP616; TRP481; ALA284	HIS674; LEU677; SER676; MET519; TRP613; ASP518
5c		ARG600; ASP616; ASP404	PHE649; TRP481; TRP376; ASP282; ALA284; LEU650; ASP616	ASP518; TRP516; HIS674; TRP613; MET519; PHE525; SER523; ARG281; LEU405
6a	5TZR	LEU138; ALA179	LEU138; HIS137; PHE87; LEU171; PHE142; ALA83	VAL141; TYR91; ARG183; ALA182; LEU186; TRP174
6b		GLY139	ALA83; VAL84; PHE142; LEU138; PRO80	LEU135; VAL81; LEU158; LEU171; PHE87
6c		-	VAL84; PRO80; LEU138; PHE142; ALA83	LEU158; VAL81; LEU171; PHE87
6a	3W37	ARG552; ASP469; ASP568; ASP232;	HIS626; TRP329; PHE476; TRP432	ASP357; TRP467; TRP565;PHE60; MET470; SER474
6b		ASP232; ARG552	ASP232; ASP568; TRP432; PHE601; TRP329	TYR243; MET470; ASP469
6c		ARG552	ASP232; ASP568; TRP329; PHE601; TRP432	TYR243; PHE236; MET470; ASP469
6a	2QV4	-	ASP96; ASP197; TYR62; ASP300; GLU233; HIS101; LEU162; LEU165; TRO59	TRP58; ALA198; HIS299
6b		HIS305; HIS201; ASP300	ASP300; LEU233; ASP197; ILE235; ALA198; LYS200; LEU162; HIS201	TRP58; THR163; ARG195; HIS299; LEU165; HIS101; SER199; VAL234
6c		ASP197; ASP300;	ARG195; HIS299; HIS201; LEU162	GLU233; ALA198; HIS305; THR163; LEU165
6a	5NN8	ASP282; ARG600; ASP616	ASP518; PHE649; HIS674; ASP616; PHE525; TRP481	TRP613; TRP516; ASP604; TRP376; LEU650; MET519; SER523
6b		ASP282; ARG600; ASP404	ASP616; ASP518; PHE649; HIS674; PHE525; TRP481	TRP613; TRP516; TRP376; SER676; SER523; MET519
6c		ASP262; ARG600	TRP376; TRP481; PHE649; ASP616	TYR292; ALA284; LEU650; SER676; TRP613; HIS674; ASP518; MET519
7a	5TZR	-	PHE142; ALA83; VAL84; LEU138; PRO80	LEU171; PHE87

7b		LEU135	LEU 140; PRO80; LEU138; PHE142; VAL84; ALA83	GLY139; VAL81; LEU158; PHE87
7c		LEU135	LEU140; PRO80; LEU138; PHE142; ALA83; VAL84	GLY139; LEU158; PHE87
7a	3W37	-	ALA234; PHE236; ALA602; ALA628; ASP568; PHE601; TRP329; TRP432; MET470	ASP469; ARG552; ASP357
7b		ARG552	PHE234; PHE236; ALA602; TRP329;ASP568; TRP432; PHE601	ASP232; MET470; ASP469; ALA628
7c		ARG552; ASP232	MET470; TRP432; ASP568; PHE476; LYS506; ASP232	ASP469; ASN475; SER474
7a		ARG195; ASP197	TRP59; LEU165; TYR62; HIS101; LEU162; GLU233; ILE235; HIS201	ALA198; LYS200; ASP300; TRP58
7b	2QV4	HIS305	LEU162; TYR62; TRP59; LEU165	HIS201; ASP300; TRP58; HIS101
7c		-	HIS201; LEU162; TYR62; LEU165; TRP59	ALA198; TRP58
7a		MET519; ASP518; ARG600	ASP616; ASP282; PHE525; ILE441; LEU405; PHE649; TRP376; TRP481	LEU677; SER676; ASP404; SER523
7b	5NN8	ARG600; ASP518; ASP616	ASP616; PHE525; ASP282; TRP376; TRP481; ILE441; LEU405; PHE649	SER523; SER676; LEU677; MET519; ASP404
7c		MET519; ARG600; ASP518; ASP616	PHE649; ASP282; PHE525; TRP376; TRP481; LEU405; ASP616	SER523; LEU677; SER676; ASP404; ILE441
8a		-	ALA83, LEU138, VAL84, PRO80, LEU158,	GLY143, GLY139, PHE142, PHE87, LEU171, LEU135
8b	5TZR	LEU140, LEU135	ALA83, LEU138, VAL84, PRO80, PHE142	GLY139, LEU144, LEU158
8c		LEU135	LEU140, LEU138, ALA83, VAL84, PHE142, PRO80,	GLY139, LEU144, LEU158
8a		ASP357	ALA234, ALA602, ALA628, PHE601, PHE236, ASP568, MET470, TRP432	ARG552, HIS626, ASP469, ILE358, TRP329
8b	3W37	ASP232, ASP568, ARG552, HIS626	TRP432, PHE601, PHE476, LYS506	ASP469, TRP565, TRP467, MET470, SER474, ASN475
8c		ASP469, ASP232, ARG552, HIS626	TRP432, PHE601, ASP568, PHE476, LYS506	TRP565, TRP467, MET470, SER474
8a		HIS299, GLU233, ILE235, LYS200, VAL234	ALA198	ARG195, ASP300, SER199, HIS201, HIS101
8b	2QV4	HIS201, HIS305, ALA198	LEU162, TYR62, LEU165, TRP59	ASP300, TRP58, GLU233
8c		HIS305	LEU162, TYR62, LEU165, TRP59, TRP58	ASP300, HIS201,
8a		ASP282; HIS674; ASP518	PHE525; ALA555; ASP282; ASP616; PHE646; MET519; TRP481	SER523; ASN524; ARG281; ARG600; TRP376; TRP516
8b	5NN8	SER523; ASP616; MET519; ARG600; ASP518	ASP282; ASP616; TRP376; TRP481; PHE649; LEU405	ALA555; PHE525; ARG281; SER676; LEU677
8c		ASP282; ARG600; ASP518; HIS674	ALA555; ASP282; ASP616; PHE649; TRP481	PHE525; SER523; ARG281; ASN524; MET519; ASP404; TRP516; TRP376