SUPPLEMENTARY MATERIAL

Screening, Synthesis and Biochemical Characterization of SARS-CoV-2 Protease Inhibitors

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1. Synthetic details for the preparation of new compounds.

*3-(Naphthalen-1-ylamino)propanoic acid (**1**)*

1-Naphthylamine (20 g, 140 mmol), acrylic acid (12 g, 168 mmol), acetic acid (13 ml), and water (3 ml) were heated for 10 h. Sodium hydroxide solution (10%, 150 ml) was added to the cooled mixture and the residue of amine was extracted with diethyl ether (3 x 50 ml). The basic solution was acidified with acetic acid to pH 6. Obtained product **1** were filtered off, and washed with water, hexane and dried. Yield 9.45 g (31%), white solid, m. p. 190–191 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ: 2.68 (t, *J* = 7.0 Hz, 2H, CH_2CO); 3.46 (t, *J* = 7.0 Hz, 2H, NCH_2); 6.15 (br. s., 1H, NH); 6.54 (d, *J* = 7.7 Hz, 1H, H_{Ar}); 7.13 (d, *J* = 8.1 Hz, 1H, H_{Ar}); 7.30 (t, *J* = 7.9 Hz, 1H, H_{Ar}); 7.35–7.50 (m, 2H, H_{Ar}); 7.76 (d, *J* = 7.8 Hz, 1H, H_{Ar}); 8.13 (d, *J* = 8.2 Hz, 1H, H_{Ar}); 12.33 (br. s., 1H, COOH). ^{13}C BMR (101 MHz, DMSO-*d*$_6$) δ: 33.37 (CH_2CO); 39.21 (NCH_2); 103.02, 115.67, 121.59, 123.12, 124.00, 125.64, 126.86, 127.97, 134.06, 143.81 (C_{Ar}); 173.44 (COOH). IR (KBr): ν, cm^{-1}: 3340 (NH); 3040 (OH); 1721 (CO). Calcd. for $C_{13}H_{13}NO_2$, %: C 72.54; H 6.09; N 6.51. Found, %: C 72.50; H 6.00; N 6.47.

*3-(1-(Naphthalen-1-yl)thioureido)propanoic acid (**2**)*

A mixture of the β-alanine **1** (3 g, 14 mmol), KSCN (1.75 g, 18 mmol), and acetic acid (10 ml) was heated at reflux for 12 h, acidified with conc. HCl to pH 1and heated at reflux for 20 min, and diluted with water (30 ml). The obtained crystals were filtered off, washed with water, hexane and dried. The crystals were dissolved in the 5% NaOH solution (15 ml) by heating. The basic solution was acidified with acetic acid to pH 6. Obtained product **2** was filtered off, and washed with water, hexane and dried. Yield 1.99 g (52%), white solid, m. p. 171–172 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ: 2.53–2.73 (m, 2H, CH_2CO); 3.84 and 4.73 (2m, 2H, NCH_2); 6.33 (br. s., 2H, NH_2); 7.39–7.52 (m, 1H, H_{Ar}); 7.53–7.80 (m, 4H, H_{Ar}); 7.92–8.13 (m, 2H, H_{Ar}); 12.29 (br. s., 1H, COOH). ^{13}C BMR (101 MHz, DMSO-*d*$_6$) δ: 32.68 (CH_2CO); 50.51 (NCH_2); 122.10, 126.30, 126.60, 127.29, 128.68, 128.80, 128.94, 129.05, 134.64, 157.64 (C_{Ar}); 172.47 (COOH); 182.19 (S=CNH_2). IR (KBr): ν, cm^{-1}: 3485 (NH); 3441 (OH); 1702 (CO). Calcd. for $C_{14}H_{14}N_2O_2S$, %: C 61.29; H 5.14; N 10.21. Found, %: C 61.50; H 5.42; N 10.50.

*3-(Naphthalen-1-yl(thiazol-2-yl)amino)propanoic acid (**3**)*

Was synthesized according to the described procedure [1].

*3-((4-methylthiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**4**)*

Was synthesized according to the described procedure [1].

*3-(naphthalen-1-yl(4-oxo-4,5-dihydrothiazol-2-yl)amino)propanoic acid (**5**)*

Was synthesized according to the described procedure [1].

*3-((4-(4-bromophenyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**6a**)*

Was synthesized according to the described procedure [1].

*3-((4-(4-chlorophenyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**6b**)*

Was synthesized according to the described procedure [2].

*3-((4-(4-fluorophenyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**6c**)*

Was synthesized according to the described procedure [2].

*3-(naphthalen-1-yl(4-(4-nitrophenyl)thiazol-2-yl)amino)propanoic acid (**6d**)*

Was synthesized according to the described procedure [1].

*3-((4-(4-cyanophenyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**6e**)*

Was synthesized according to the described procedure [1].

3-((4-(3,4-dichlorophenyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (7)

A mixture of thioureido acid **2** (2.3 g, 8.4 mmol), the 2-bromo-3′,4′-dichloroacetophenone (2.79 g, 10.4 mmol) and acetone (40 mL) was refluxed for 3 h. The formed *N*,*N*-disubstituted aminothiazole hydrobromide was filtered off, washed with plenty of acetone and then boiled in 4% aqueous sodium acetate for 5 min. The obtained appropriate product 7 was filtered off, washed with water and dried. Yield 2.23 g (60%), white solid, m. p. 157–158 ºC. ^{1}H BMR (700 MHz, DMSO-*d*$_6$) δ: 2.60–2.82 (m, 2H, CH_2CO); 3.97–4.18 and 4.44–4.62 (2m, 2H, NCH_2); 7.31 (s, 1H, SCH); 7.53–7.78 (m, 5H, H_{Ar}); 7.80–7.96 (m, 2H, H_{Ar}) 8.03–8.19 (m, 3H, H_{Ar}). ^{13}C BMR (176 MHz, DMSO-*d*$_6$) δ: 32.60 (CH_2CO); 48.78 (NCH_2); 105.49; 122.31; 125.81; 126.49; 126.80; 127.25; 127.30; 127.44; 128.81; 129.21; 129.71; 130.84; 131.40; 134.83; 136.08; 140.11; 147.62 (C_{Ar}, S−CH=C); 170.20 (C=N); 172.62 (COOH). IR (KBr): ν, cm^{-1}: 3048 (OH); 1721 (CO); 1532 (C=N). Calcd. for $C_{22}H_{16}Cl_2N_2O_2S$, %: C 59.60; H 3.64; N 6.32. Found, %: C 59.74; H 3.54; N 6.22.

*3-(naphthalen-1-yl(4-(naphthalen-2-yl)thiazol-2-yl)amino)propanoic acid (**8**)*

Was synthesized according to the described procedure [1].

*3-((4-(chloromethyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**9**)*

Was synthesized according to the described procedure [4].

*3-((4-(hydroxymethyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**10**)*

Was synthesized according to the described procedure [4].

*3-((4-(2-ethoxy-2-oxoethyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**11**)*

Was synthesized according to the described procedure [4].

*3-(naphthalen-1-yl(4-((phenylamino)methyl)thiazol-2-yl)amino)propanoic acid (**12**)*

Was synthesized according to the described procedure [4].

*3-(((5Z)-5-(4-Bromobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl)(naphthalen-1 yl)amino)propanoic acid (**13a**)*

Was synthesized according to the described procedure [1].

*(((5Z)-5-(4-Chlorobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**13b**)*

Was synthesized according to the described procedure [1].

*3-(((5Z)-5-(4-Fluorobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**13c**)*

Was synthesized according to the described procedure [1].

General synthetic procedure for **14−16**.

A mixture of compound **5** (0.57 g, 1.8 mmol), the corresponding aldehyde (1.98 mmol), sodium carbonate (1.01 g, 9.5 mmol), and water (10 mL) was refluxed for 3 h. The cooled reaction mixture was acidified with acetic acid to pH 6, the formed solid was filtered off, washed with water, dried. Purification was performed by dissolving crystals in 5% aqueous sodium carbonate (10 ml H_2O, 0,5 g Na_2CO_3), filtering and acidifying the filtrate with acetic acid to pH 6 to give **14−16** as solids.

*(Z)-3-((5-(2,4-dihydroxybenzylidene)-4-oxo-4,5-dihydrothiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**14**)*

Yield 0.58 g (74%), greenish solid, m. p. 205–206 ºC. ^{1}H BMR (700 MHz, DMSO-*d*$_6$) δ: 2.64 (t, 2H, *J* = 7.8 Hz, CH_2CO); 3.87–3.93 and 4.57–4.61 (2m, 2H, NCH_2); 6.24–6.52 (m, 1H, H_{Ar}); 6.61–6.78 (m, 1H, H_{Ar}); 7.22–7.45 (m, 2H, H_{Ar}); 7.55–7.68 (m, 2H, H_{Ar}); 7.72–7.92 (m, 2H, H_{Ar}); 8.06–8.41 (m, 3H, H_{Ar}, CH); 10.16 (s, 1H, OH); 10.27 (s, 1H, OH); 12.24 (br. s., 1H, COOH). ^{13}C BMR (176 MHz, DMSO-*d*$_6$) δ: 32.41 (CH_2CO); 50.32 (NCH_2); 121.86, 122.67, 125.71, 126.17, 126.31, 126.86, 127.07, 127.21, 127.27, 127.68, 128.07, 128.49, 128.89, 129.08, 130.33, 134.27, 136.13, 164.954 (C_{Ar}, SC=CH); 173.43 (COOH); 177.11 (C=N); 179.24 (CO). IR (KBr), ν, cm^{-1}: 3388 (OH); 1692 (CO); 1526 (C=N). Calcd. for $C_{23}H_{18}N_2O_5S$, %: C 63.58; H 4.18; N 6.45. Found, %: C 63.50; H 4.08; N 6.38.

*(Z)-3-((5-(2-hydroxybenzylidene)-4-oxo-4,5-dihydrothiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**15**)*

Yield 0.41 g (54 %), greenish solid, m. p. 203–204 ºC. ^{1}H BMR (400 MHz, DMSO-*d*$_6$) δ: 2.73 (t, 2H, *J* = 7.8 Hz, CH_2CO); 3.97–4.04 ir 4.68–4.75 (2m, 2H, NCH_2); 6.70 (t, 2H, *J* = 7.6 Hz, H_{Ar}); 6.85 (d, 2H, *J* = 7.8 Hz, H_{Ar}); 6.96 (t, 2H, *J* = 7.9 Hz, H_{Ar}); 7.14 (t, 2H, *J* = 7.8 Hz, H_{Ar}); 7.49–7.89 (m, 5H, H_{Ar}); 7.92 (s, 1H, CH); 8.05–8.31 (m, 2H, H_{Ar}); 10.31 (s, 1H, OH); 12.42 (pl. s, 1H, COOH). ^{13}C BMR (101 MHz, DMSO-*d*$_6$) δ: 32.16 (CH_2CO); 49.71 (NCH_2); 115.91; 119.53; 120.50; 121.81; 125.88; 126.04; 127.22; 127.77; 127.91; 127.98; 128.28; 128.89; 129.11; 130.72; 131.51; 134.25; 136.80; 156.82 (C_{Ar}, SC=CH); 171.93 (COOH); 177.39 (C=N); 179.80 (CO). IR (KBr), ν, cm^{-1}: 3060 (OH); 1723 (CO); 1534 (C=N). Calcd. for $C_{23}H_{18}N_2O_4S$, %: C 66.02; H 4.34; N 6.69. Found, %: C 66.26; H 4.28; N 6.75.

*(Z)-3-(naphthalen-1-yl(4-oxo-5-(thiophen-2-ylmethylene)-4,5-dihydrothiazol-2-yl)amino)propanoic acid (**16**)*

Yield 0,53 g (72 %), yellowis solid, m. p. 207–208 ºC.^{1}H BMR (400 MHz, DMSO-*d*$_6$) δ: 2.63–2.68 (m, 2H, CH_2CO); 3.95–4.02 and 4.65–4.72 (2m, 2H, NCH_2); 7.10–8.18 (m, 11H, H_{Ar}, CH). ^{13}C BMR (101 MHz, DMSO-*d*$_6$) δ: 32.73 (CH_2CO); 50.23 (NCH_2); 121.79; 123.58; 125.83; 127.21; 127.30; 128.00; 128.28; 128.79; 128.88; 129.09; 130.75; 131.36; 133.31; 134.22; 135.80; 138.25 (C_{Ar}, SC=CH); 172.19 (COOH); 176.21 (CO); 179.29 (C=N). IR (KBr), ν, cm^{-1}: 3397 (OH); 1725 (CO); 1526 (C=N). Calcd. for $C_{21}H_{16}N_2O_3S_2$, %: C 61.75; H 3.95; N 6.86. Found, %: C 61.61; H 3.88; N 6.58.

*3-((5-(2-Methoxy-2-oxoethylidene)-4-oxo-4,5-dihydrothiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**17**)*

Was synthesized according to the described procedure [4].

*2-((2-Carboxyethyl)(naphthalen-1-yl)amino)-4-methylthiazole-5-carboxylic acid (**18**)*

Was synthesized according to the described procedure [4].

*3-[(5-Acetyl-4-methyl-1,3-thiazol-2-yl)(naphthalen-1-yl)amino]propanoic acid (**19**)*

Was synthesized according to the described procedure [1].

3-((5-(Ethoxycarbonyl)-4-methylthiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**20**)

Was synthesized according to the described procedure [4].

*N-(4-Methyl-5-((E)-3-phenyl-2-propenoyl)-1,3-thiazol-2-yl)-N-(1-naphthyl)-β-alanine (**21a**)*

Was synthesized according to the described procedure [4].

*N-(5-((E)-3-(4-Chlorophenyl)-2-propenoyl)-4-methyl-1,3-thiazol-2-yl)-N-(1-naphthyl)-β-alanine (**21b**)*

Was synthesized according to the described procedure [1].

*N-(5-((E)-3-(4-Fluorophenyl)-2-propenoyl)-4-methyl-1,3-thiazol-2-yl)-N-(1-naphthyl)-β-alanine (**21c**)*

Was synthesized according to the described procedure [1].

*(E)-3-((4-methyl-5-(3-(naphthalen-1-yl)acryloyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**22**)*

To a solution of compound **19** (0.2 g, 0.56 mmol) in 10% NaOH (10 mL) 2-propanol (10 mL) was poured and then 1-naphthaldehyde (0.11 g, 0.67 mmol) was added dropwise. The reaction mixture was heated under reflux for 3 h, then diluted with water (10 mL) and acidified with 30% acetic acid to pH 6. The formed precipitate was filtered off, washed with water, dried and purified by column chromatography. Eluent – chloroform : methanol 100 : 5; R_f = 0.58. Yield 0.14 g (50%), yellow solid, m. p. 111−112 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ: 2.59–2.79 (m, 5H, CH_2CO, CH_3); 3.98–4.10 and 4.48–4.61 (2m, 2H, NCH_2); 7.20 and 7.23 (2s, 1H, CHCO); 7.37–7.87 (m, 15H, H_{Ar}, C<u>H</u>=CHCO); 12.43 (br. s., 1H, COOH). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ: 19.17 (CH_3); 32.51 (CH_2CO); 48.54 (NCH_2); 121.98 (CCH); 122.79, 122.92, 124.12, 125.29, 125.69, 126.48, 127.11, 127.73, 128.72, 128.90, 129.04, 129.72, 130.47, 131.02, 131.17, 133.28, 134.81, 136.80, 137.68, 139.03 (CAr); 158.96 (SC=C); 171.52 (C=N); 172.35 (COOH); 180.19 (CHCO). IR (KBr), ν, cm^{-1}: 3058 (OH); 1721 (C=O); 1639 (C=O); 1519 (C=N). Calcd. for $C_{30}H_{24}N_2O_3S$, %: C 73.15; H 4.91; N 5.69. Found, %: C 73.10; H 4.88; N 5.65.

*(Z)-3-((4-methyl-5-(1-(2-phenylhydrazineylidene)ethyl)thiazol-2-yl)(naphthalen-1-yl)amino)propanoic acid (**23**)*

A mixture of compound **19** (0.5 g, 1.4 mmol), phenylhydrazine (0.46 g, 4.2 mmol) and 3 drops of glacial acetic acid in methanol (30 mL) was refluxed for 5 h. Then the reaction mixture was cooled down to room temperature and diluted with water (20 mL). The precipitate was filtered off, washed with water, dried and purified by dissolving it in 5% aqueous sodium carbonate solution (2.5 g Na_2CO_3, 47.5 mL H_2O), filtering the solution and acidifying the filtrate with glacial acetic acid to pH 6. The obtained precipitate was filtered off, washed with water and dried. Yield 0.52 g (83%), yellow solid, m. p. 207–208°C. ^{1}H BMR (400 MHz, DMSO-*d*$_6$) δ: 2.13 (s, 3H, CH_3C=N-N); 2.43 (s, 3H, CH_3); 2.67 (t, 2H, *J* = 7.4 Hz, CH_2CO); 3.80–4.07 ir 4.32–4.56 (2m, 2H, NCH_2); 6.64 (t, 1H, *J* = 7.3 Hz, H_{Ar}); 6.64 (d, 2H, *J* = 8.0 Hz, H_{Ar}); 7.09 (t, 2H, *J* = 7.7 Hz, H_{Ar}); 7.54–7.69 (m, 4H, H_{Ar}); 7.76–7.85 (m, 1H, H_{Ar}); 8.01–8.13 (m, 2H, H_{Ar}); 8.98 (s, 1H, NH); 12,27 (s, 1H, COOH). ^{13}C BMR (101 MHz, DMSO-*d*$_6$) δ: 15.69 (CH_3); 18.24 (CH_3C=N-N); 32.60 (CH_2CO); 48.12 (NCH_2); 118.40; 122.30; 122.33; 126.43; 126.75; 127.29; 127.39; 128.79; 129.04; 129.77; 134.77; 137.77; 140.06 (C_{Ar}); 144.81 (SC=C); 112.35 (<u>C</u>CH_3); 145.83 (C=N); 166.62 ($NCCH_3$); 172.54 (COOH). IR (KBr), ν, cm^{-1}: 3054 (OH); 1712 (CO); 1512 (C=N). Calcd. for $C_{25}H_{24}N_4O_2S$, %: C 67.55; H 5.44; N 12.60. Found, %: C 67.54; H 5.45; N 12.65.

*3,3'-((((1Z,1'Z)-hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(4-methylthiazole-5,2-diyl))bis(naphthalen-1-ylazanediyl))dipropionic acid (**24**)*

A mixture of compound **19** (0.5 g, 1.4 mmol), hydrazine monohydrate (0.42 g, 8.4 mmol) and 3 drops of glacial acetic acid in methanol (20 mL) was refluxed for 5 h. Then the reaction mixture was cooled down to room temperature and diluted with water (30 mL). The precipitate was filtered off, washed

with water, dried and purified by dissolving it in 5% aqueous sodium carbonate solution (2.5 g Na_2CO_3, 47.5 mL H_2O), filtering the solution and acidifying the filtrate with glacial acetic acid to pH 6. The obtained precipitate was filtered off, washed with water and dried. Yield 0.4 g (40%), yellow solid, m. p. 247–248 ºC. ^{1}H BMR (400 MHz, DMSO-*d*$_6$) δ: 2.06 (s, 6H, 2x CH_3C=N-N); 2.41 (s, 6H, 2x CCH_3); 2.65 (t, 4H, *J* = 7.3 Hz, 2x CH_2CO); 3.87–3.94 and 4.40–4.47 (2m, 4H, 2x NCH_2); 7.50–7.66 (m, 8H, H_{Ar}); 7.70–7.81 (m, 2H, H_{Ar}); 7.98–8.11 (m, 4H, H_{Ar}); 12.19 (s, 2H, 2x COOH). ^{13}C BMR (101 MHz, DMSO-*d*$_6$) δ: 16.11 (CH_3); 18.76 (CH_3C=N-N); 32.58 (CH_2CO); 48.10 (NCH_2); 122.13; 122.19; 126.40; 126.78; 127.23; 127.47; 128.79; 129.22; 129.47; 134.72; 139.63; 150.30 (C_{Ar}) 156.57 ($NCCH_3$); 168.61 (C=N); 172.42 (COOH). IR (KBr), ν, cm^{-1}: 3057 (OH); 1706 (CO); 1516 (C=N). Calcd. for $C_{38}H_{36}N_6O_4S_2$, %: C 64.75; H 5.15; N 11.92. Found, %: C 64.80; H 5.03; N 11.98.

*3-((5-Cinnamoyl-4-methylthiazol-2-yl)(p-tolyl)amino)propanoic acid (**25a**)*

Was synthesized according to the described procedure [5].

*3-((5-(3-(4-Chlorophenyl)acryloyl)-4-methylthiazol-2-yl)(p-tolyl)amino)propanoic acid (**25b**)*

Was synthesized according to the described procedure [5].

*3-((5-(3-(4-Fluorophenyl)acryloyl)-4-methylthiazol-2-yl)(p-tolyl)amino)propanoic acid (**25c**)*

Was synthesized according to the described procedure [5].

*3-(Naphthalen-1-yl(4-((phenylamino)methyl)thiazol-2-yl)amino)propanoic acid (**26**)*

Was synthesized according to the described procedure [4].

*3-((4-(4-Chlorophenyl)-5-((2-phenylhydrazono)methyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid (**27a**)*

Was synthesized according to the described procedure [4].

*3-((4-(4-Fluorophenyl)-5-((2-phenylhydrazono)methyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid (**27b**)*

Was synthesized according to the described procedure [4].

*3-((4-(4-Cyanophenyl)-5-((2-phenylhydrazono)methyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid (**27c**)*

Was synthesized according to the described procedure [4].

*3-((5-((2-Carbamothioylhydrazono)methyl)-4-(4-cyanophenyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid (**28**)*

Was synthesized according to the described procedure [4].

*3-((4-(4-Cyanophenyl)-5-formylthiazol-2-yl)(p-tolyl)amino)propanoic acid (**29**)*

Was synthesized according to the described procedure [4].

*3-((4-Aminophenyl)(4-(4-chlorophenyl)-1,3-thiazol-2-yl)amino)propanoic acid (**30a**)*

Was synthesized according to the described procedure [6].

*3-{(4-Aminophenyl)[4-(4-fluorophenyl)-1,3-thiazol-2-yl]amino}propanoic acid (**30b**)*

Was synthesized according to the described procedure [6].

*3-{(4-Aminophenyl)[4-(4-cianophenyl)-1,3-thiazol-2-yl]amino}propanoic acid (**30c**)*

Was synthesized according to the described procedure [6].

*3-((4-Aminophenyl){4-[4-(trifluoromethyl)phenyl]thiazol-2-yl}amino)propanoic acid (**30d**)*

Was synthesized according to the described procedure [6].

*N-(1-Naphthyl)-N-(4-((E)-2-phenylethyl)-5-((E)-3-phenyl-2-propenoyl)-1,3-thiazol-2-yl)-β-alanine (**31**)*

Was synthesized according to the described procedure [1].
The synthesis and characterization of disulfides **32-38** are described in the paper submitted recently [7]

2. 1H and 13C NMR spectra for new compounds

Supplemental Figures S1–S18, representing ^{1}H and ^{13}C NMR spectra of the newly synthesized compounds **1**, **2, 7, 14–16, 22–24**.

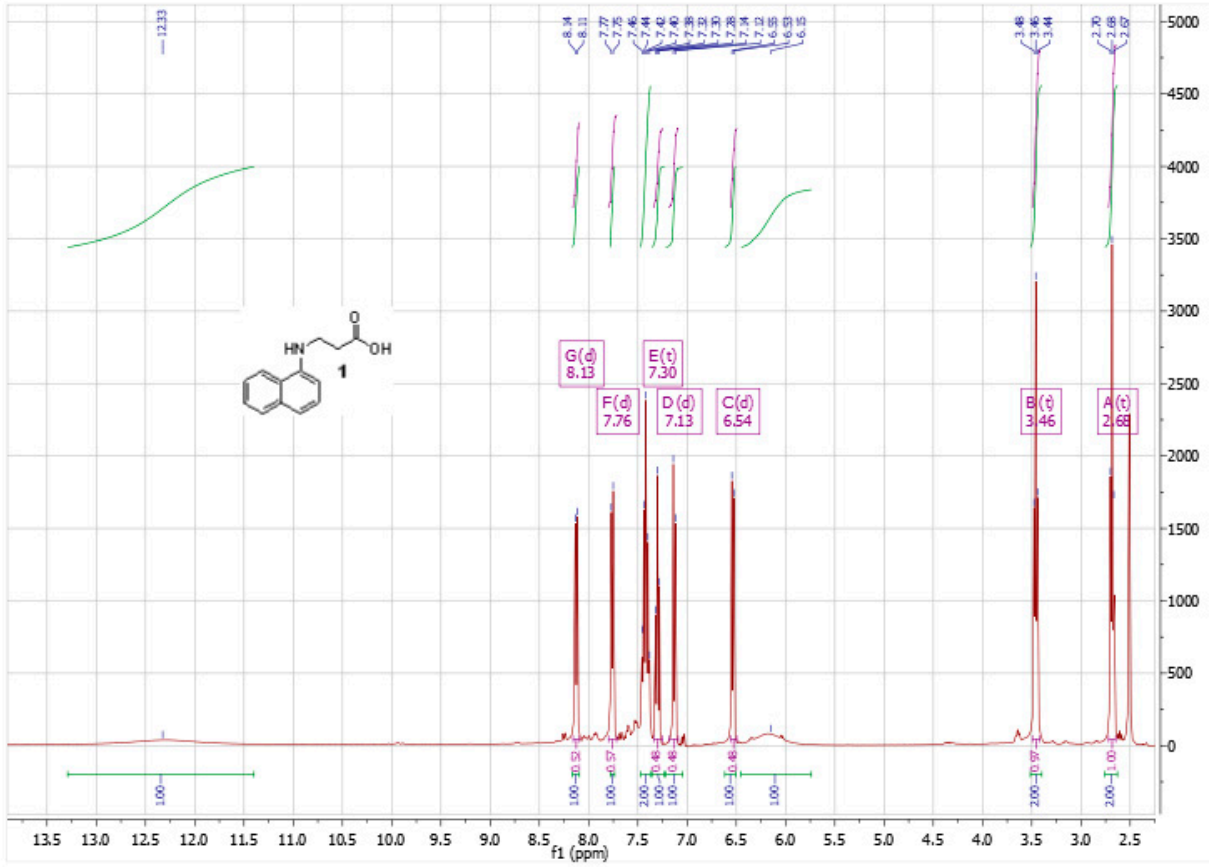


Figure S1: ^{1}H-NMR spectrum of compound **1**.

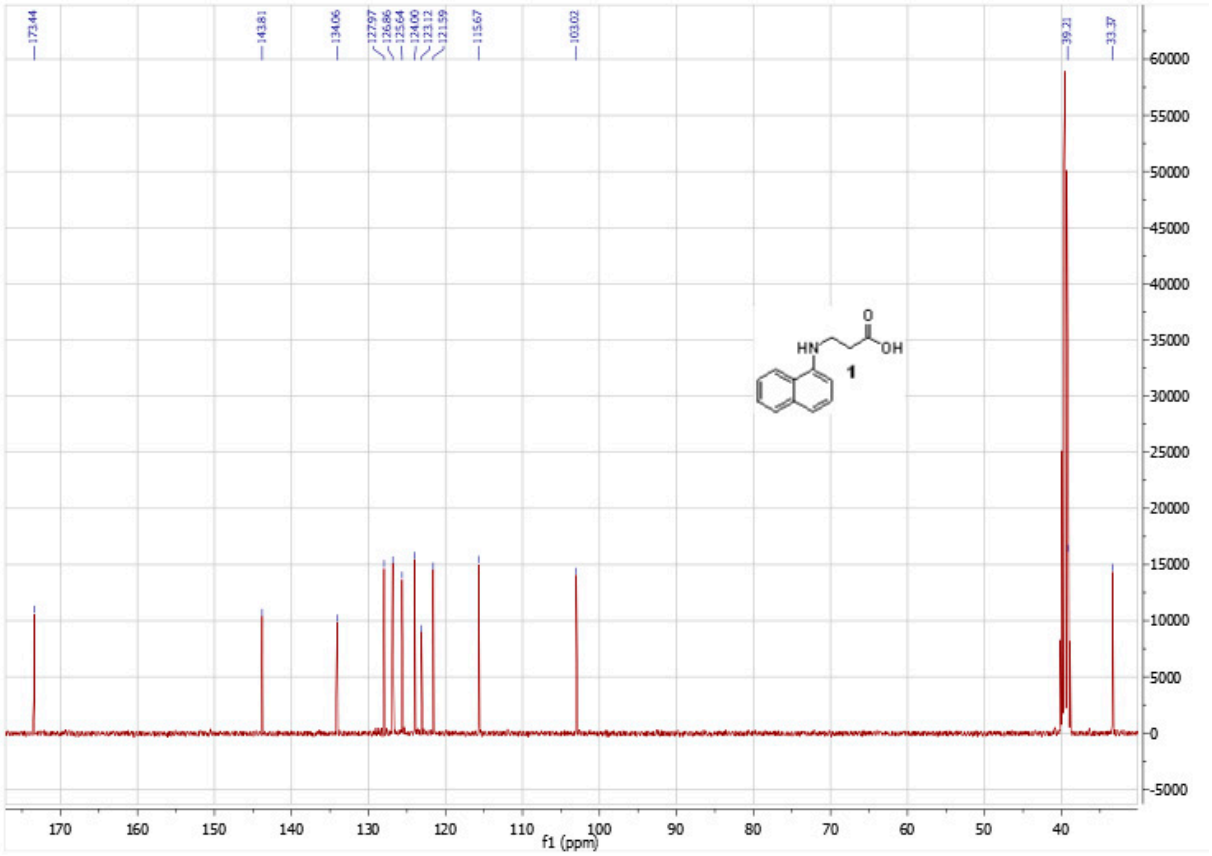


Figure S2: ^{13}C-NMR spectrum of compound **1**.

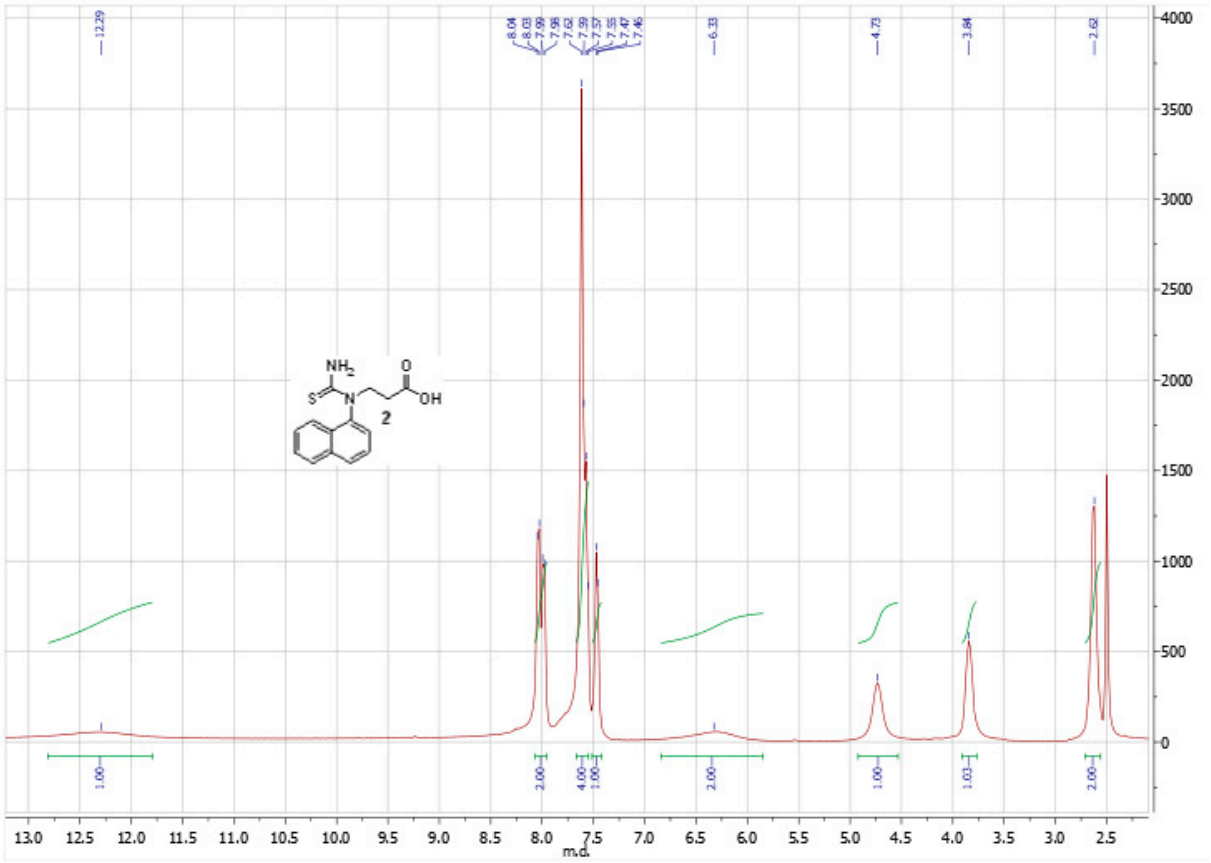


Figure S3: ^{1}H-NMR spectrum of compound **2**.

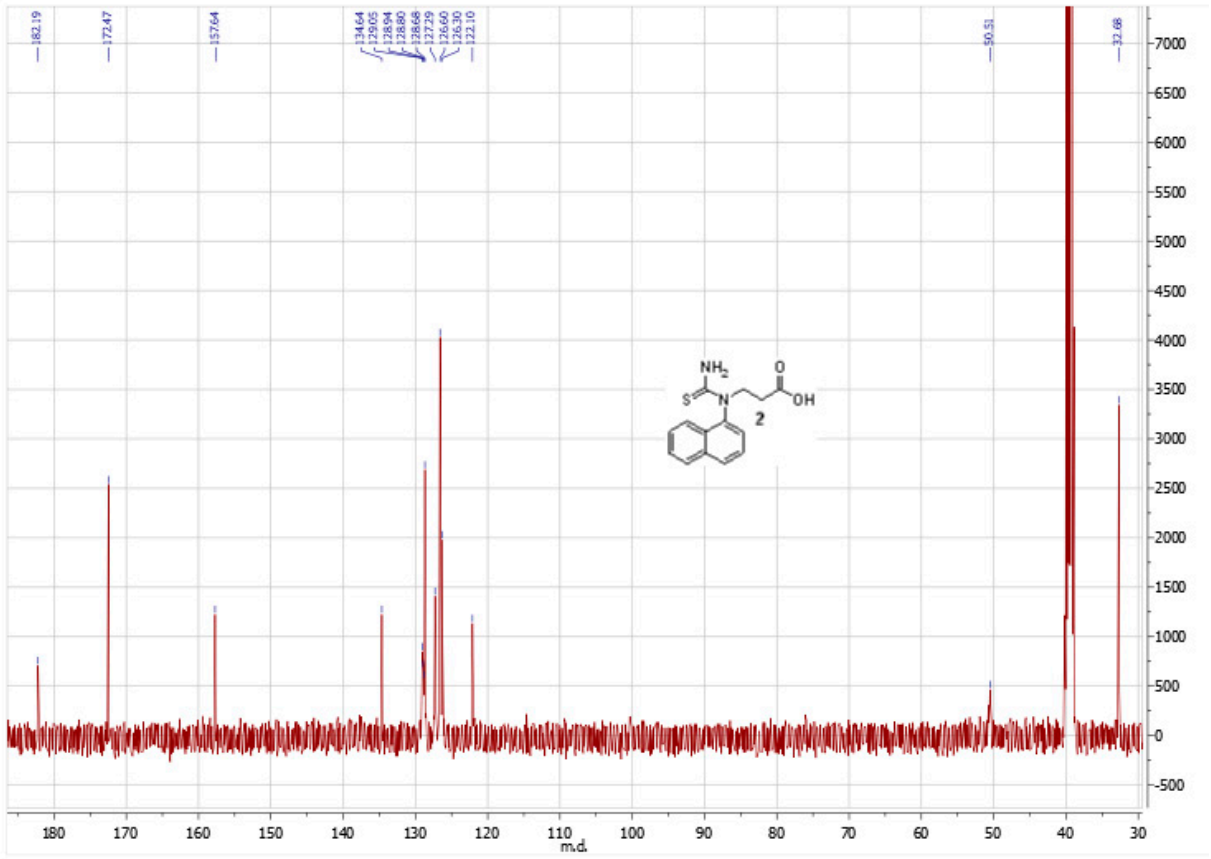


Figure S4: ^{13}C-NMR spectrum of compound **2**.

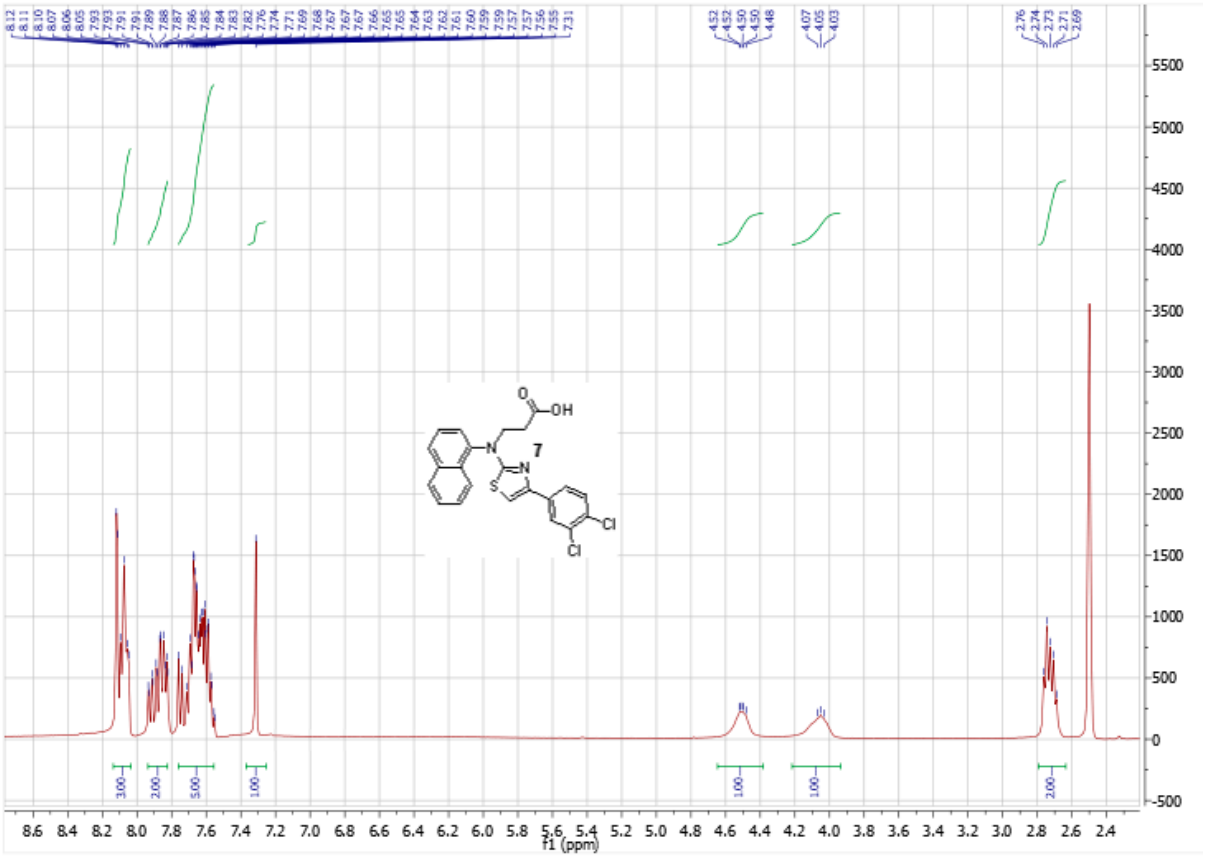


Figure S5: ^{1}H-NMR spectrum of compound **7**.

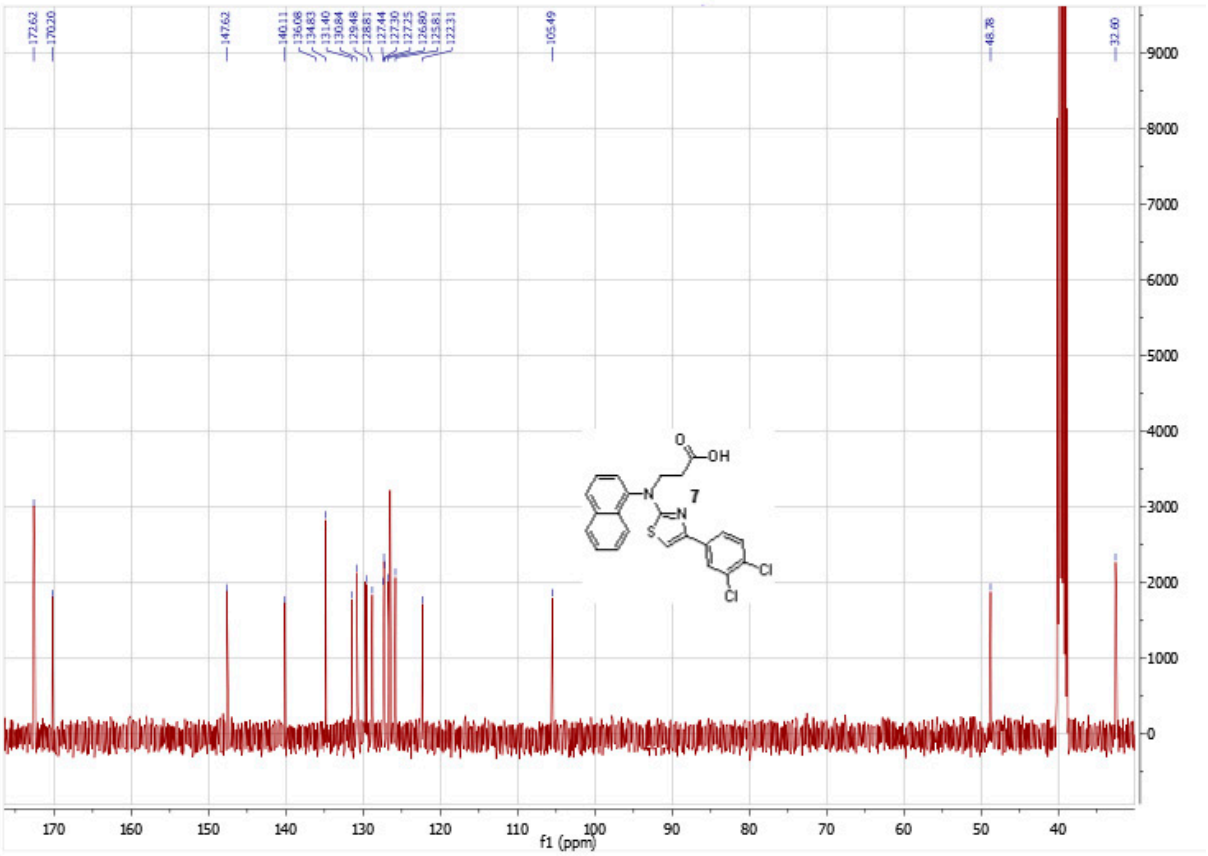


Figure S6: ^{13}C-NMR spectrum of compound **7**.

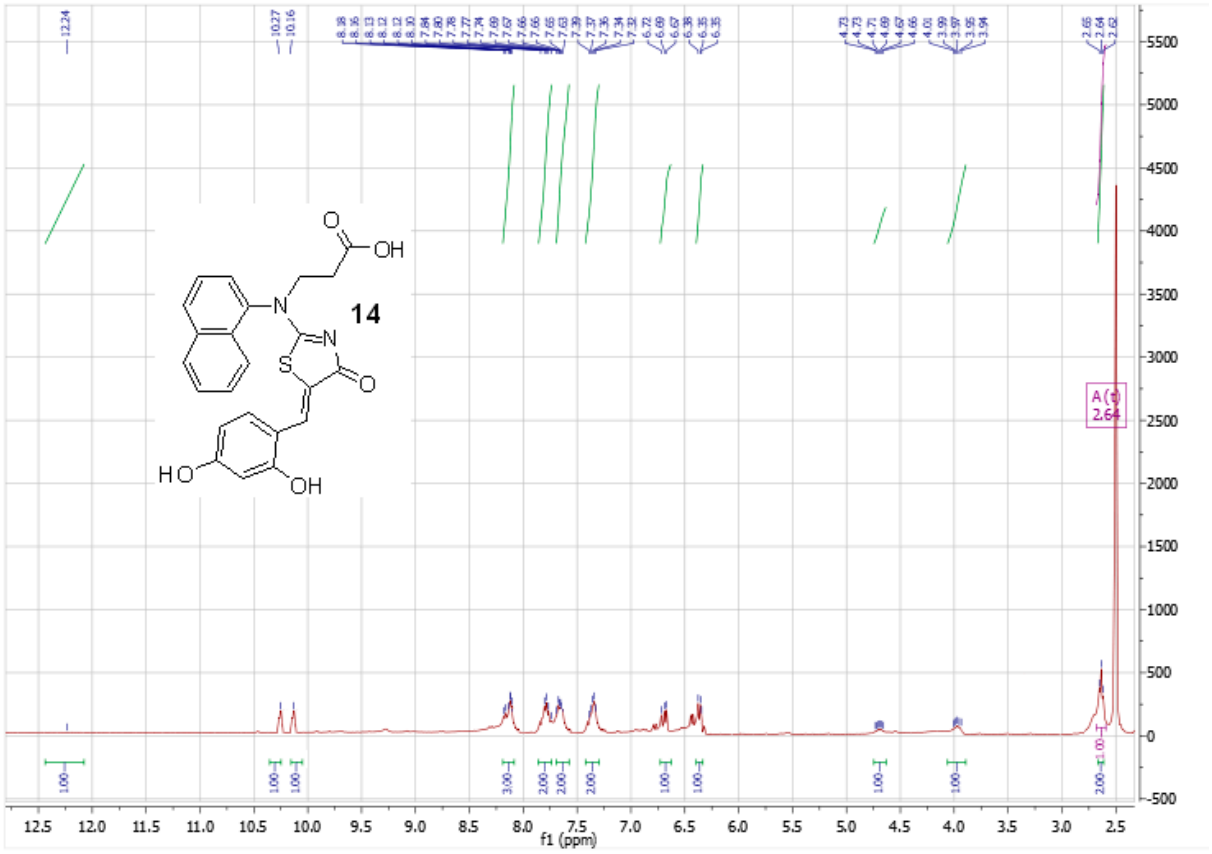


Figure S7: ^{1}H-NMR spectrum of compound **14**.

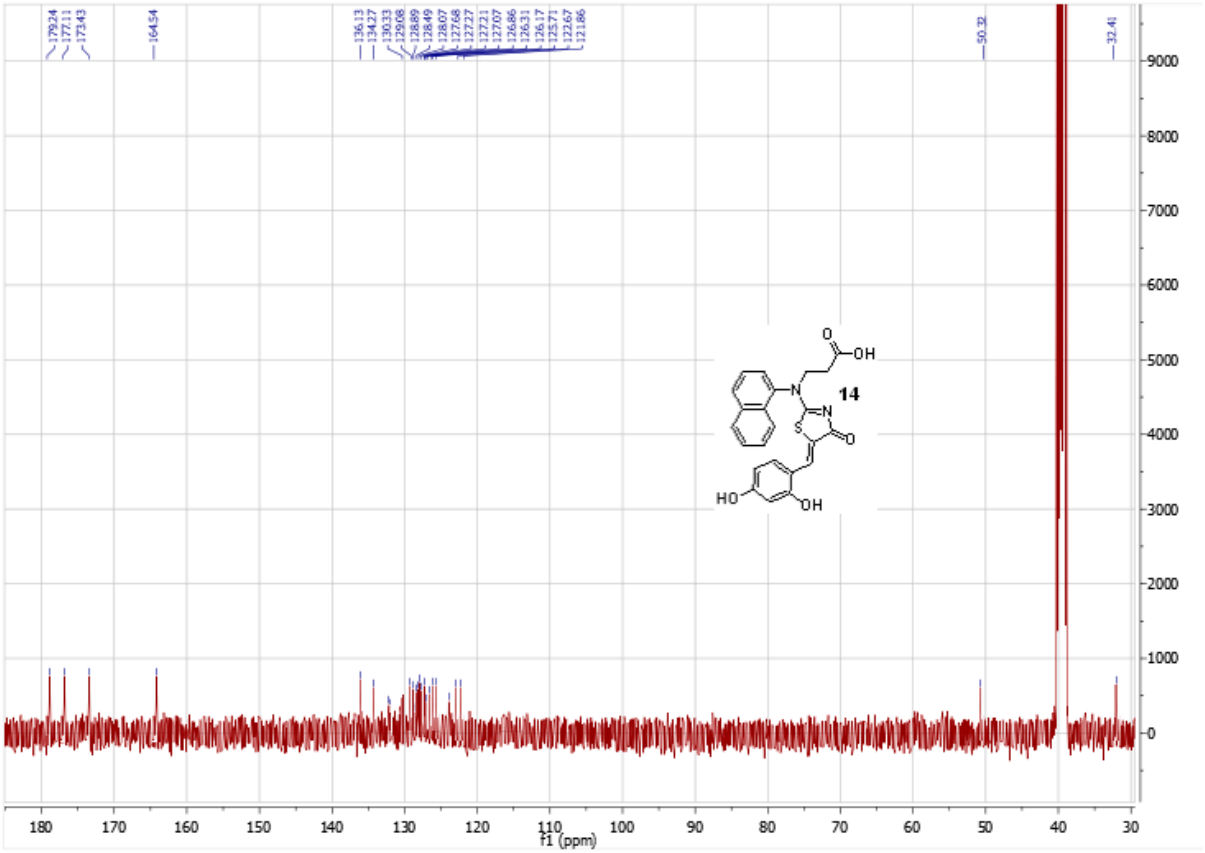


Figure S8: ^{13}C-NMR spectrum of compound **14**.

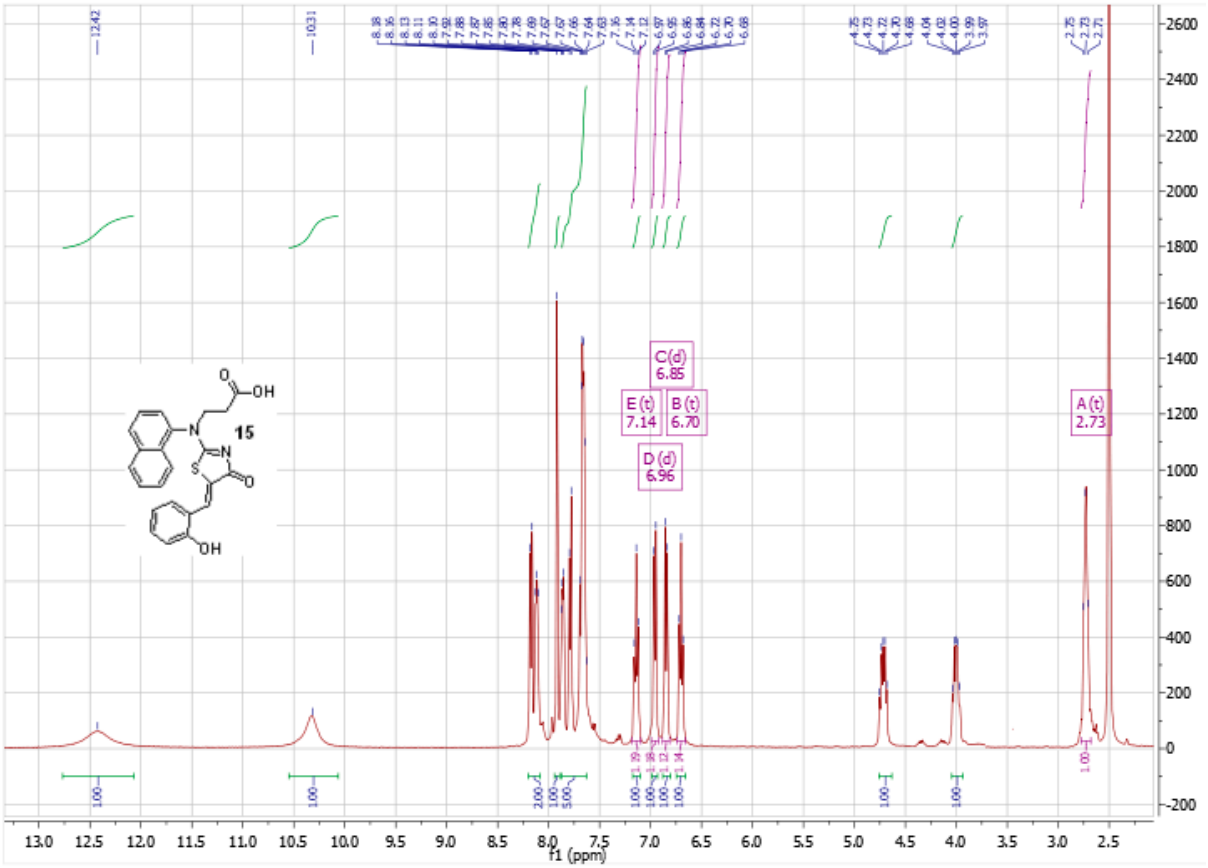


Figure S9: ^{1}H-NMR spectrum of compound **15**.

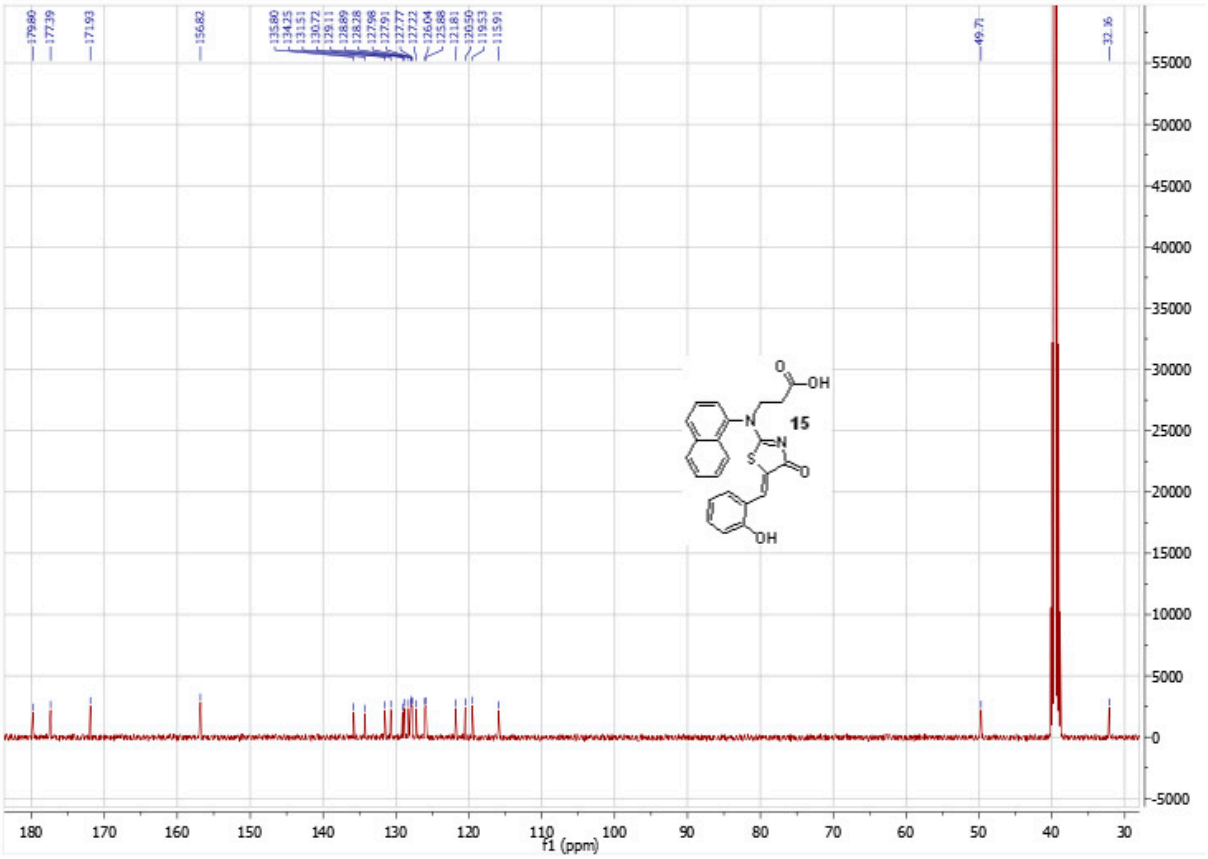


Figure S10: ^{13}C-NMR spectrum of compound **15**.

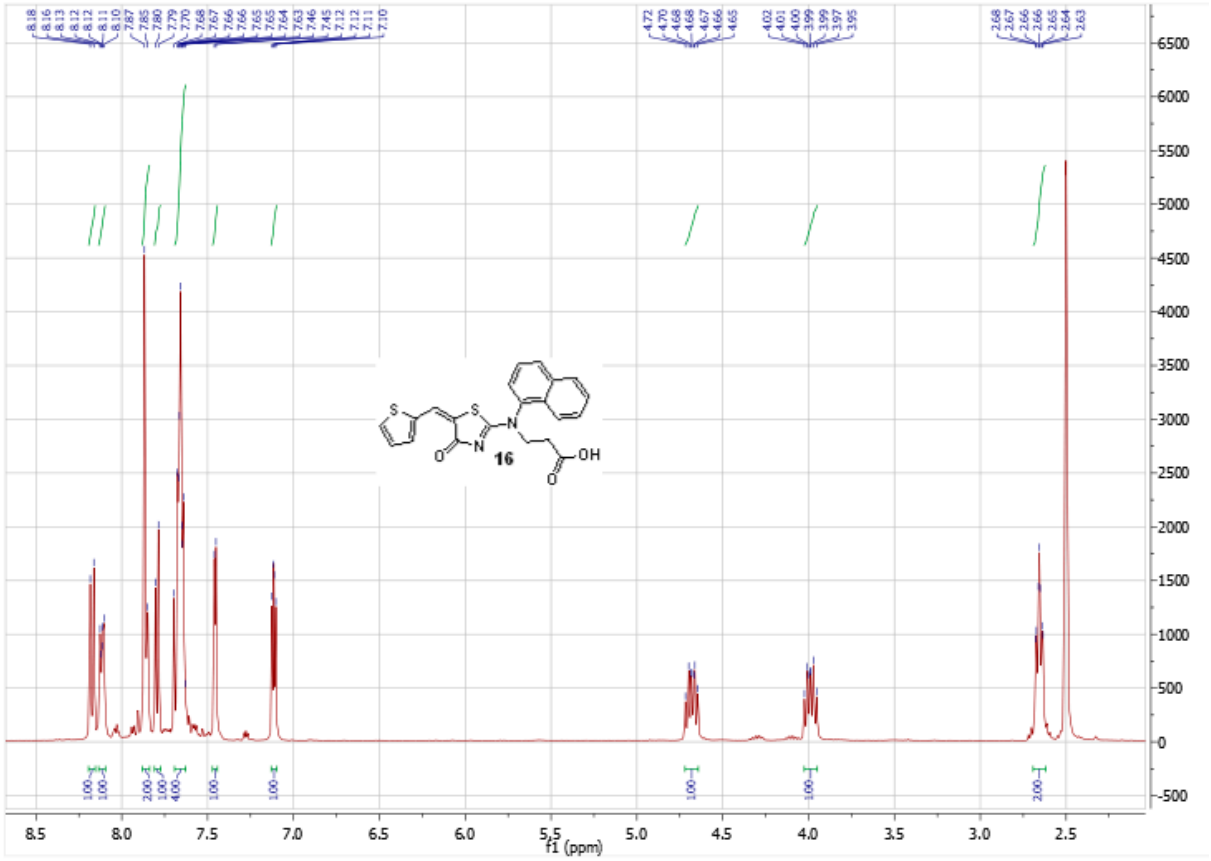


Figure S11: ^{1}H-NMR spectrum of compound **16**.

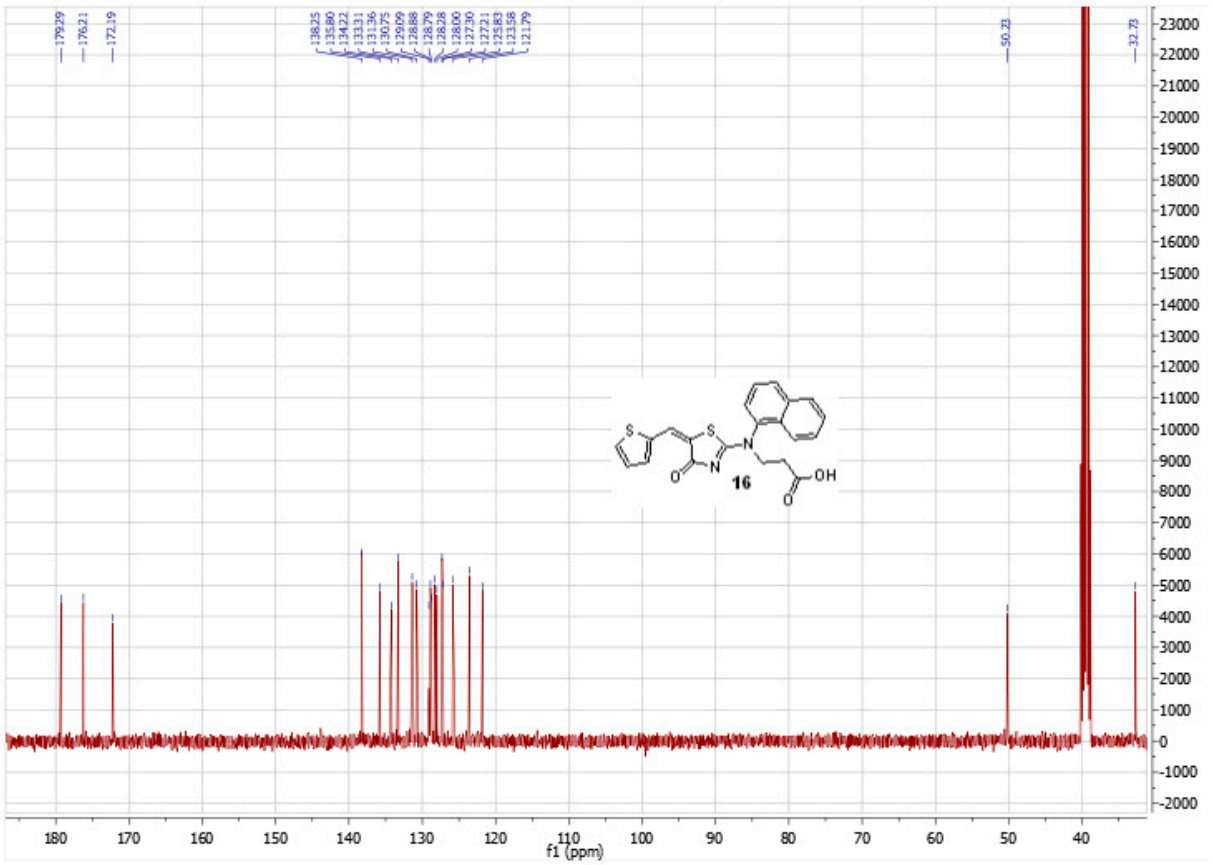


Figure S12: ^{13}C-NMR spectrum of compound **16**.

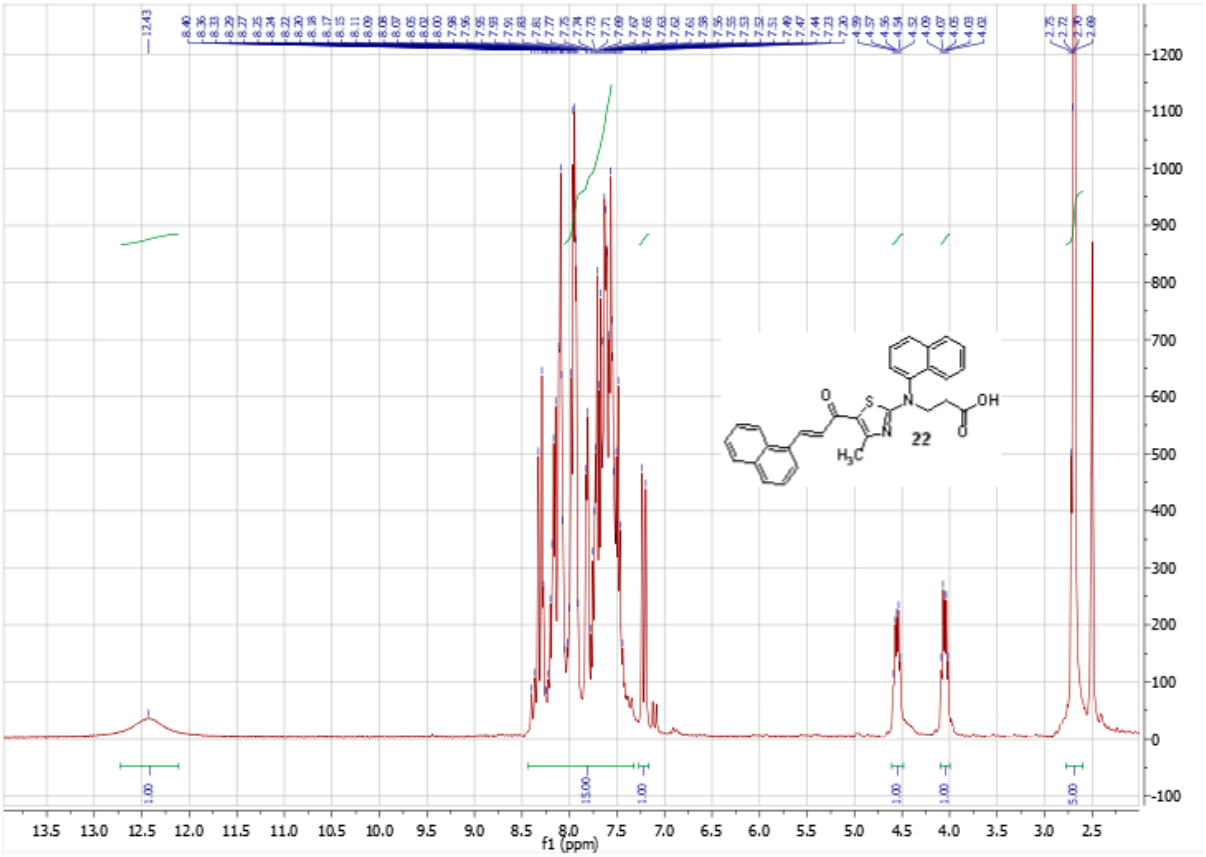


Figure S13: ^{1}H-NMR spectrum of compound **22**.

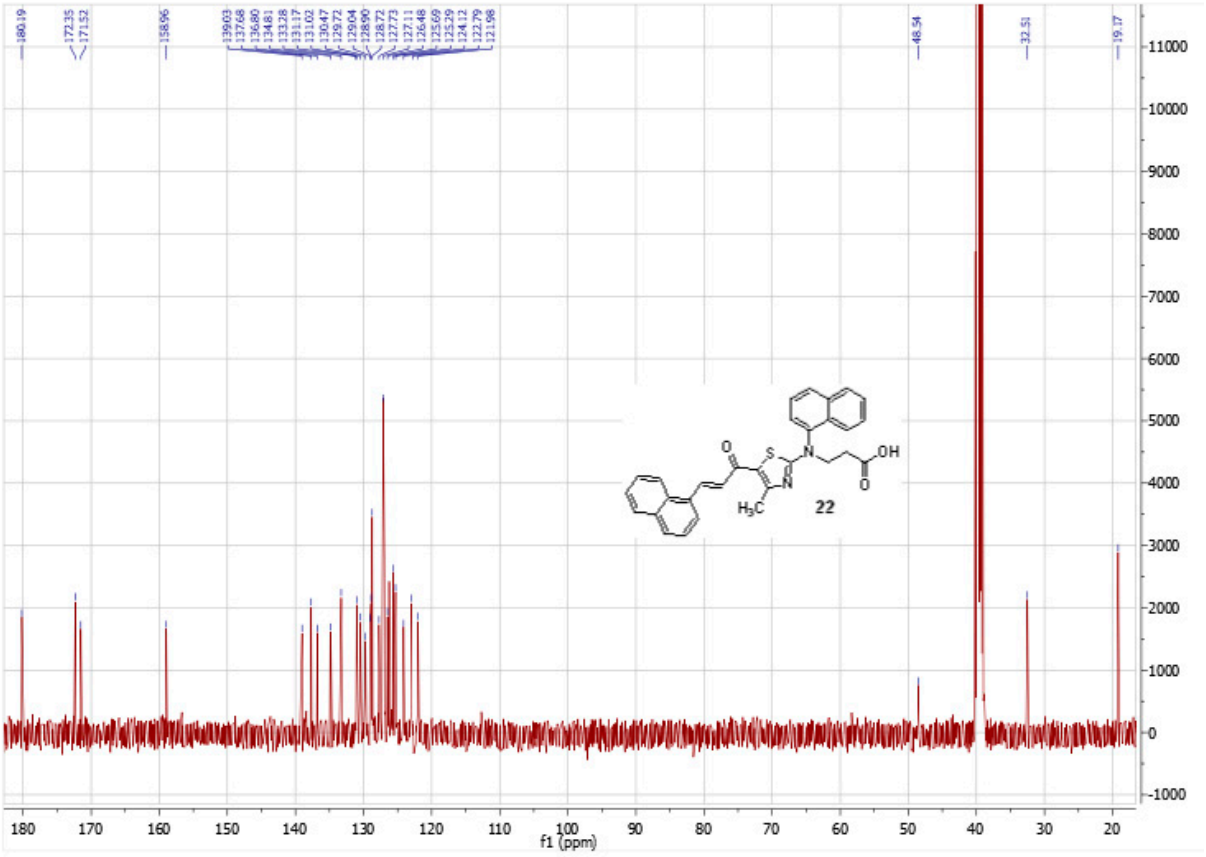


Figure S14: ^{13}C-NMR spectrum of compound **22**.

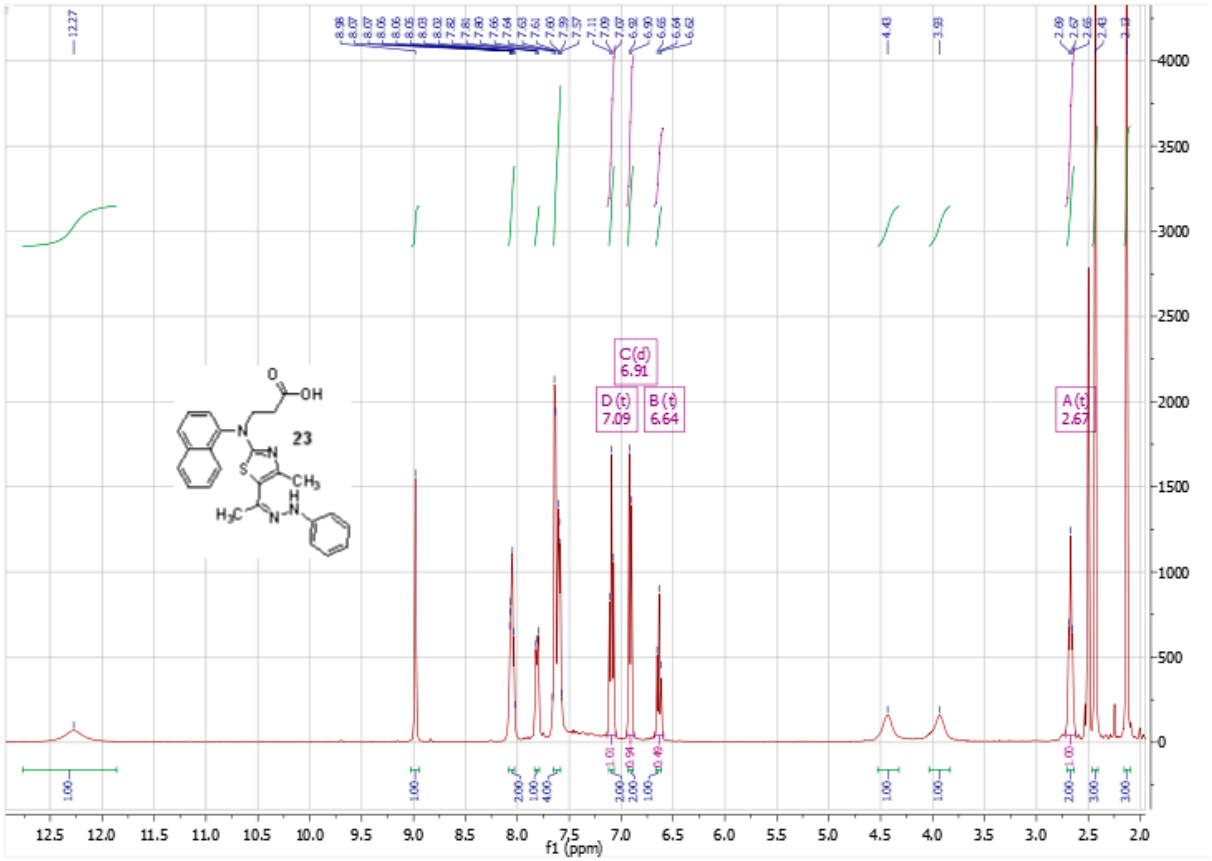


Figure S15: ^{1}H-NMR spectrum of compound **23**.

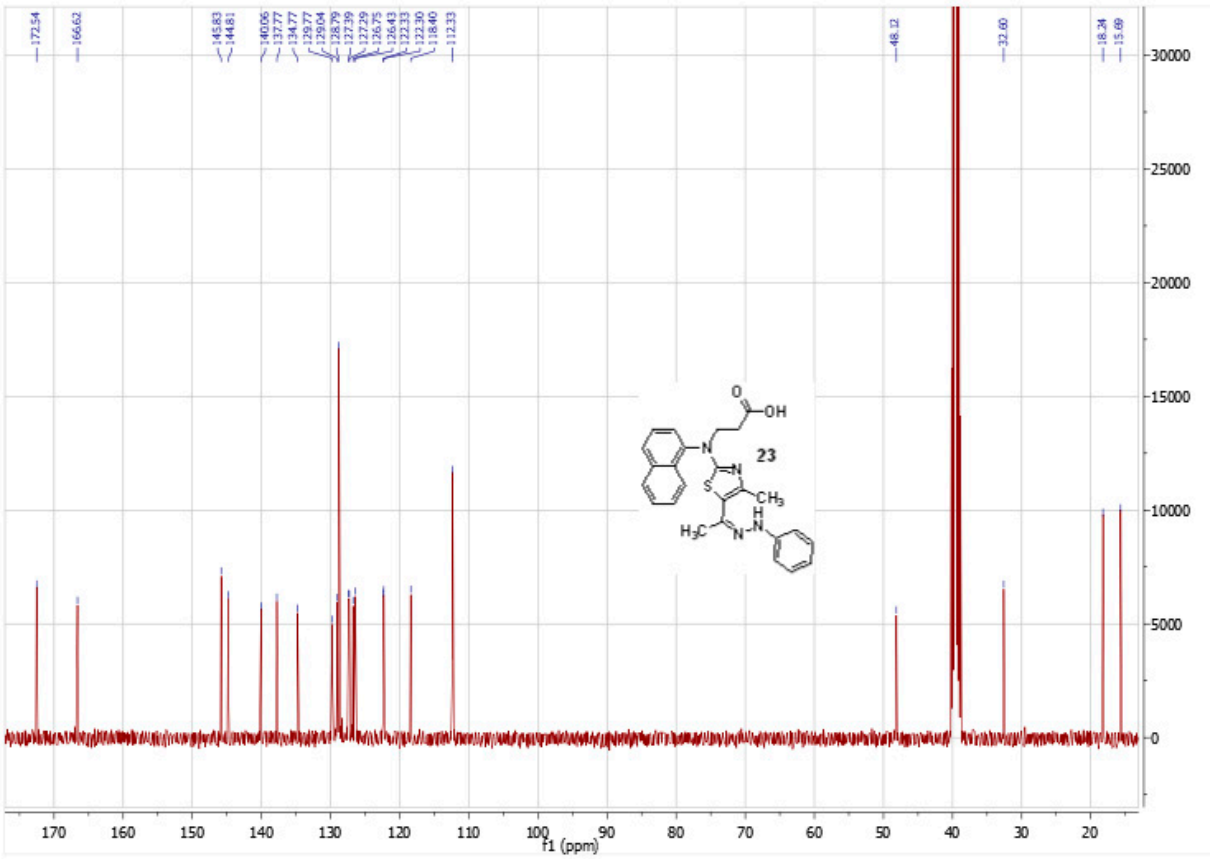


Figure S16: ^{13}C-NMR spectrum of compound **23**.

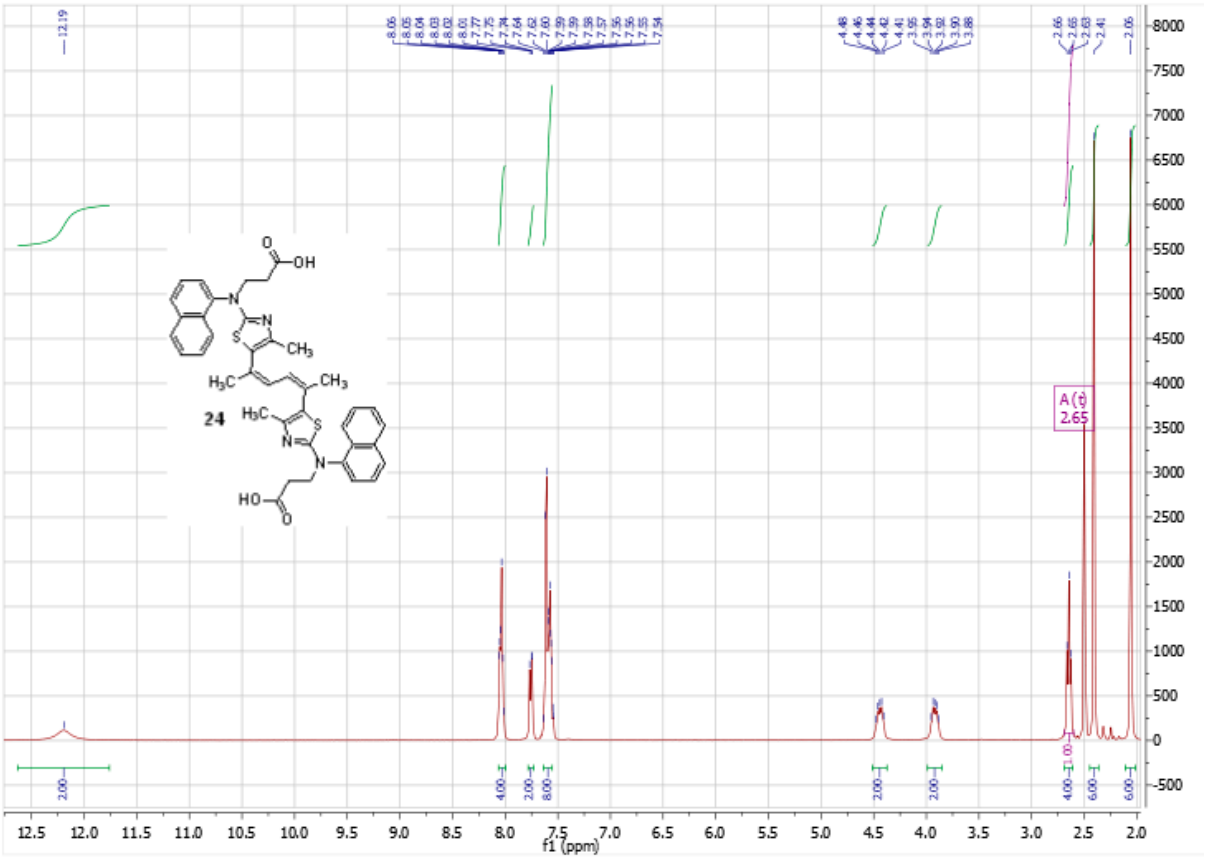


Figure S17: ^{1}H-NMR spectrum of compound **24**.

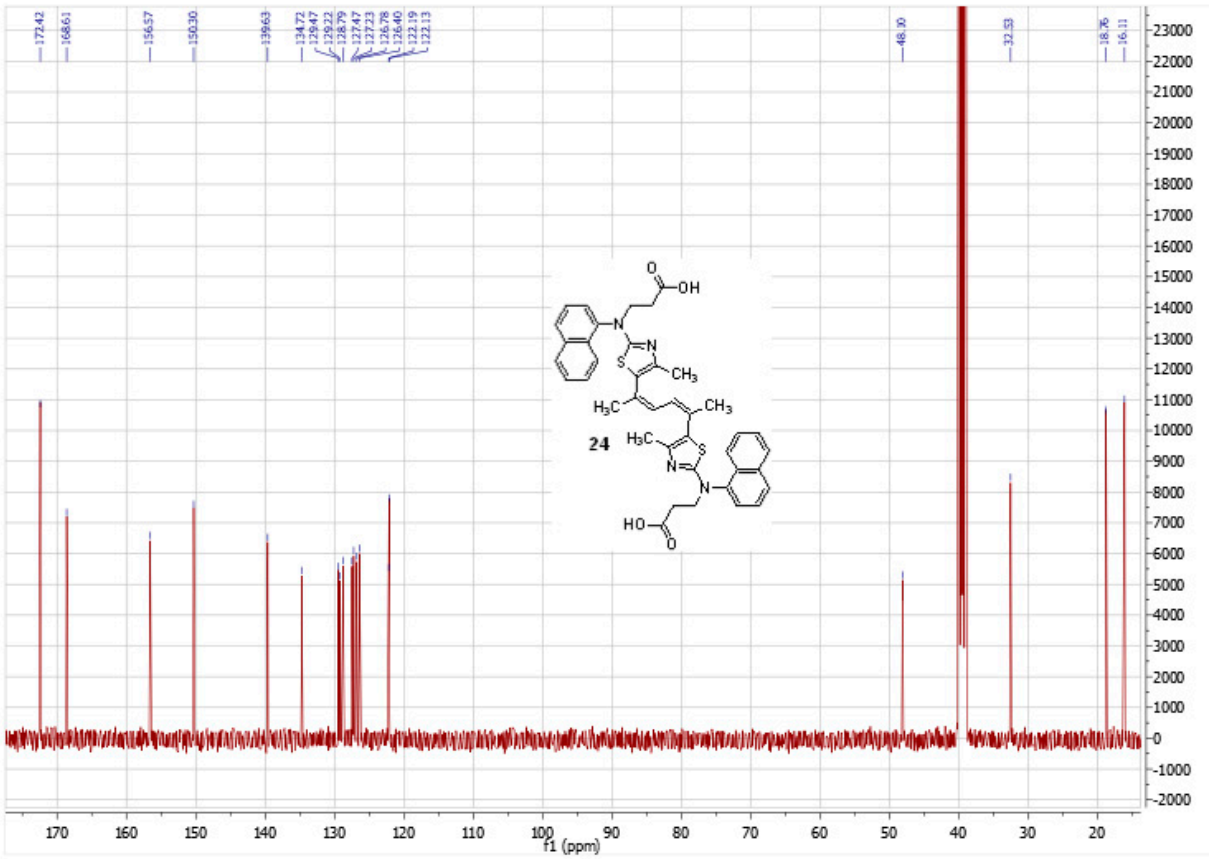
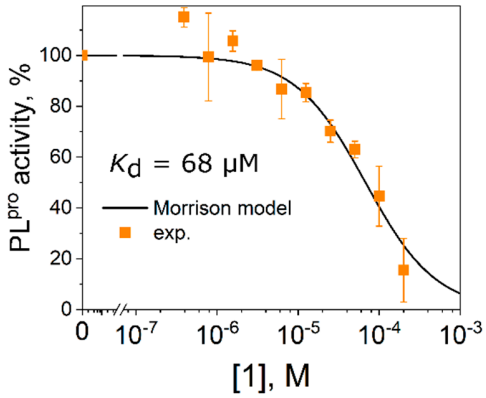
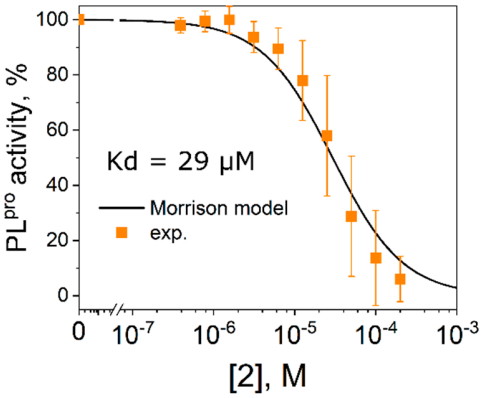
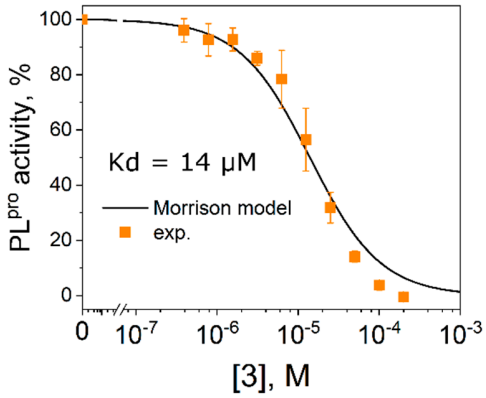


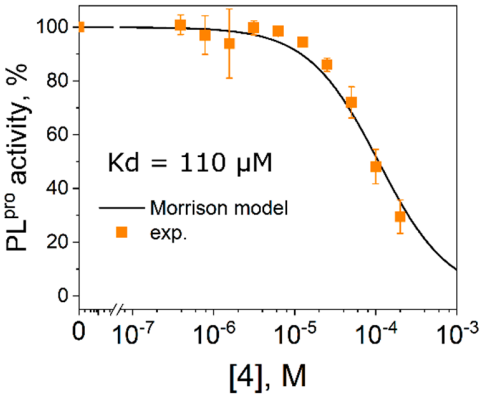
Figure S18: ^{13}C-NMR spectrum of compound **24**.

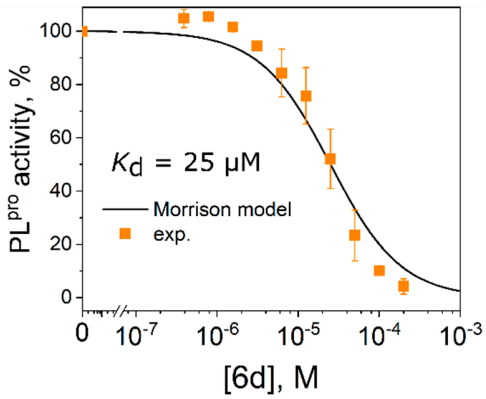
3. Dose-response curves of PL^{pro}

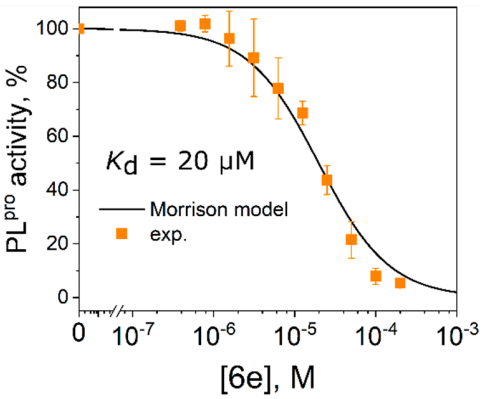

PL^pro activity, %
Kd = 68 μM
Morrison model
exp.
[1], M

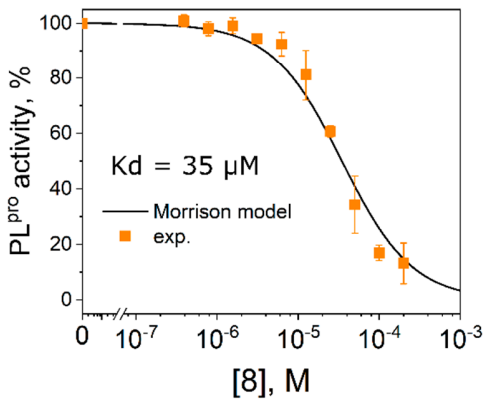

PL^pro activity, %
Kd = 29 μM
Morrison model
exp.
[2], M

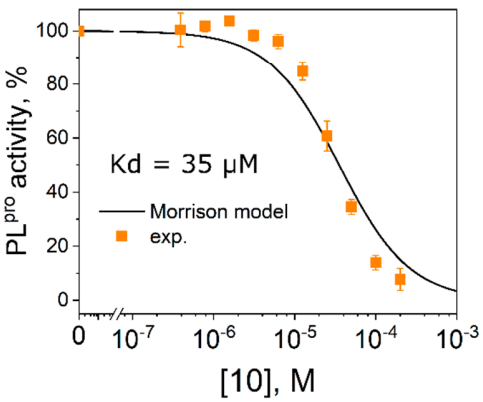

PL^pro activity, %
Kd = 14 μM
Morrison model
exp.
[3], M

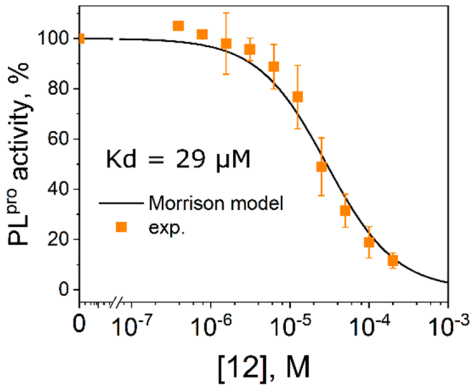

PL^pro activity, %
Kd = 110 μM
Morrison model
exp.
[4], M

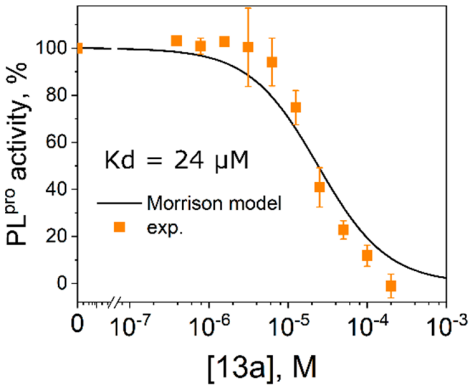

PL^pro activity, %
Kd = 25 μM
Morrison model
exp.
[6d], M

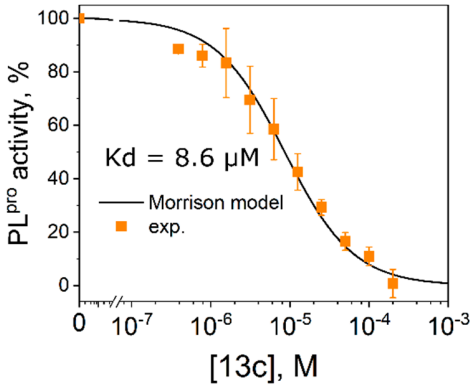

PL^pro activity, %
Kd = 20 μM
Morrison model
exp.
[6e], M

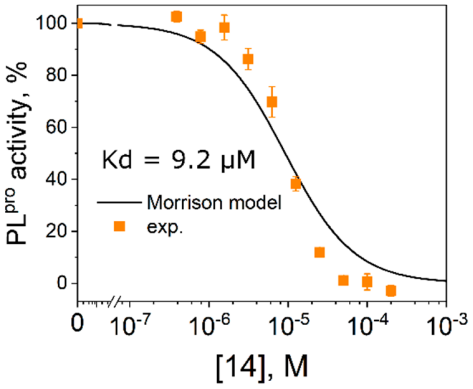

PL^pro activity, %
Kd = 35 μM
Morrison model
exp.
[8], M

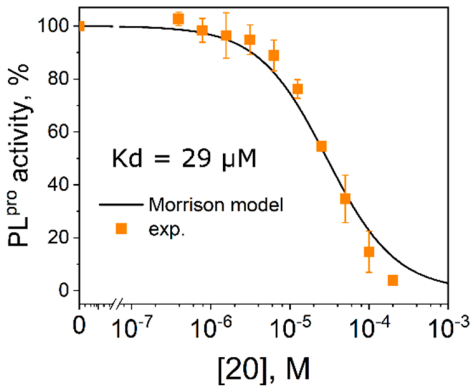

PL^pro activity, %
Kd = 35 μM
Morrison model
exp.
[10], M

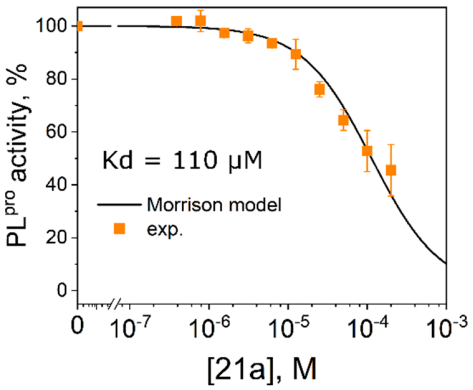

PL^pro activity, %
Kd = 29 μM
Morrison model
exp.
[12], M

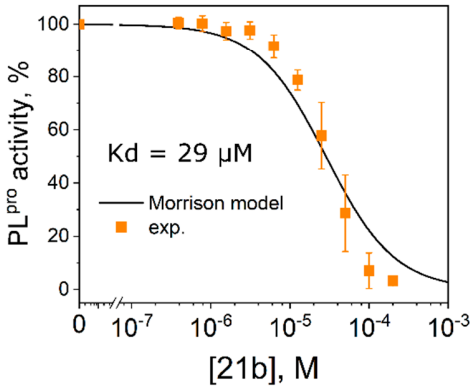

PL^pro activity, %
Kd = 24 μM
Morrison model
exp.
[13a], M

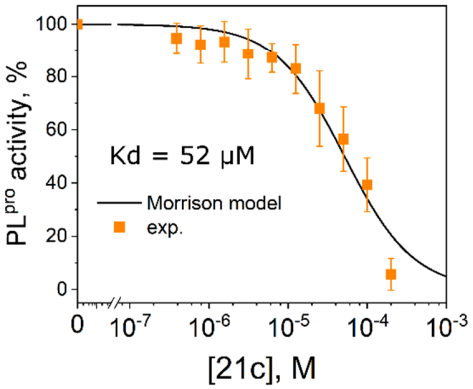

PL^pro activity, %
Kd = 8.6 μM
Morrison model
exp.
[13c], M

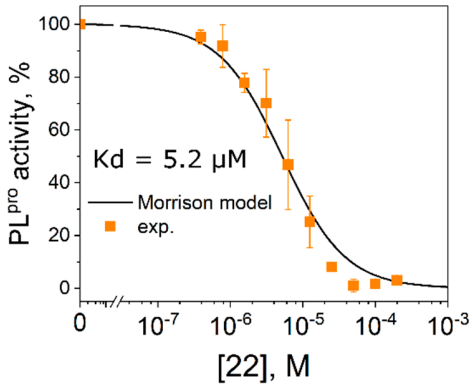

PL^pro activity, %
Kd = 9.2 μM
Morrison model
exp.
[14], M

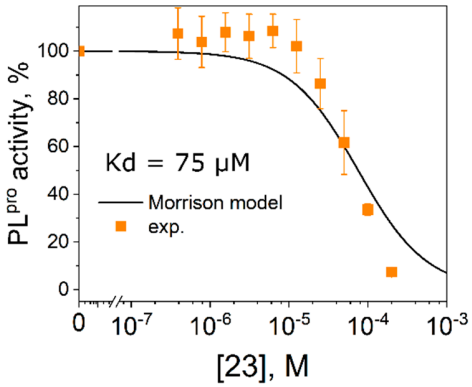

PL^pro activity, %
Kd = 29 μM
Morrison model
exp.
[20], M

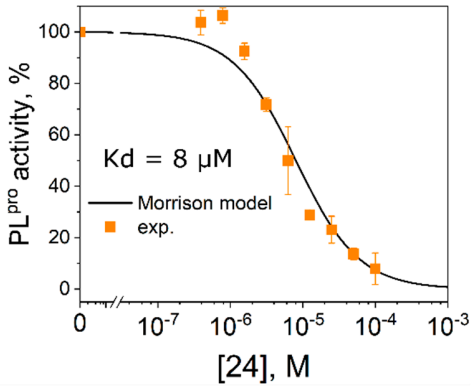

PL^pro activity, %
Kd = 110 μM
Morrison model
exp.
[21a], M

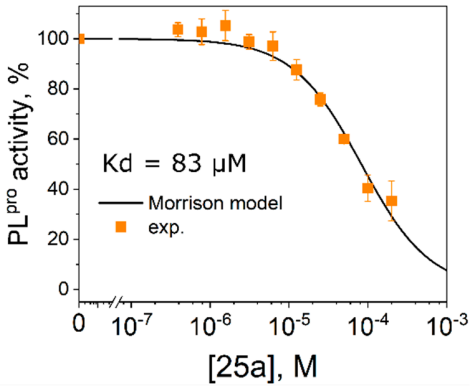

PL^pro activity, %
Kd = 29 μM
Morrison model
exp.
[21b], M

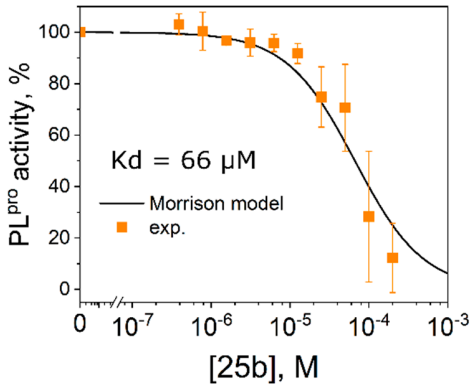

PL^pro activity, %
Kd = 52 μM
Morrison model
exp.
[21c], M

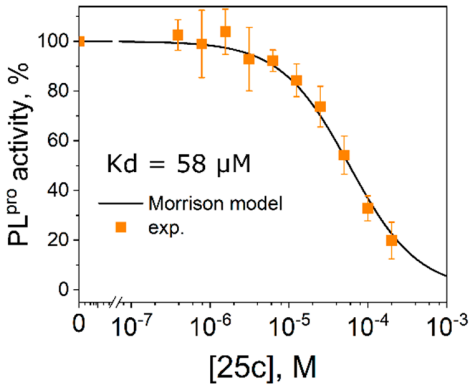

PL^pro activity, %
Kd = 5.2 μM
Morrison model
exp.
[22], M

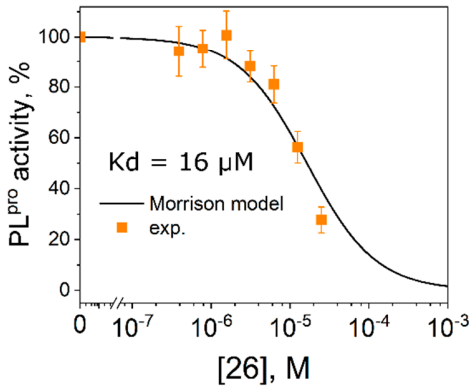

PL^pro activity, %
Kd = 75 μM
Morrison model
exp.
[23], M

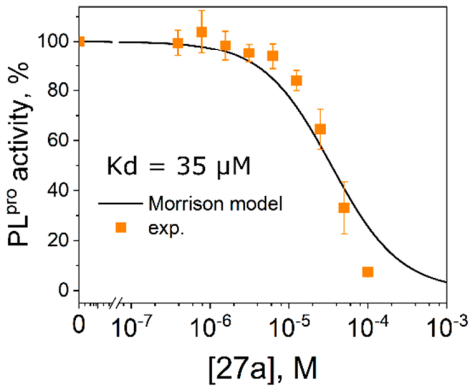

PL^pro activity, %
Kd = 8 μM
Morrison model
exp.
[24], M

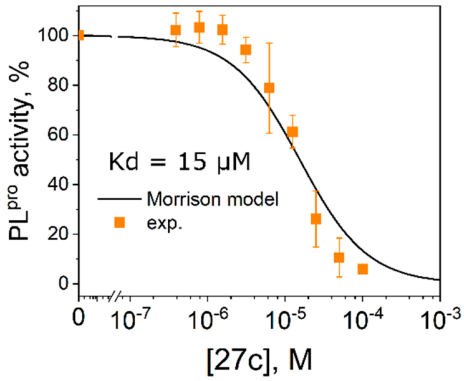

PL^pro activity, %
Kd = 83 μM
Morrison model
exp.
[25a], M

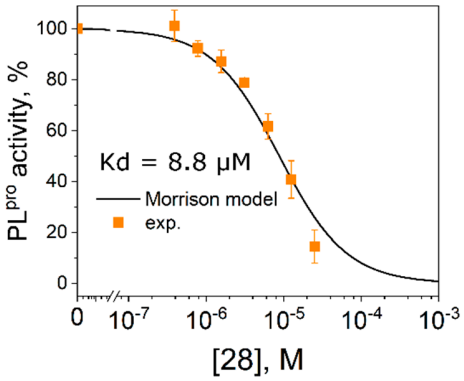

PL^pro activity, %
Kd = 66 μM
Morrison model
exp.
[25b], M

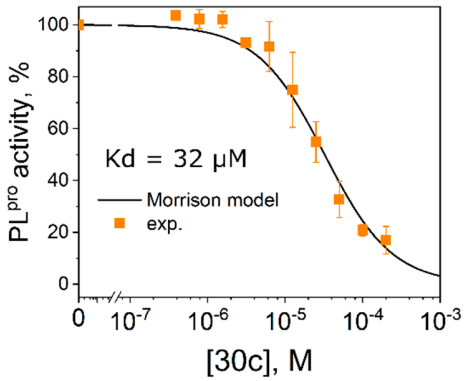

PL^pro activity, %
Kd = 58 μM
Morrison model
exp.
[25c], M

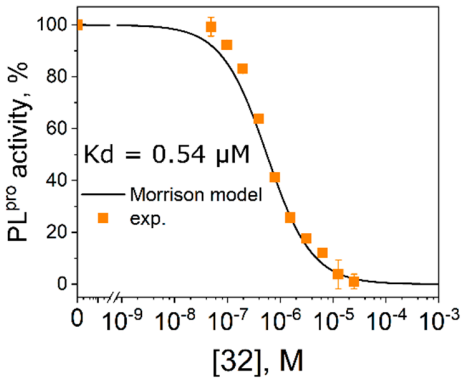

PL^pro activity, %
Kd = 16 μM
Morrison model
exp.
[26], M

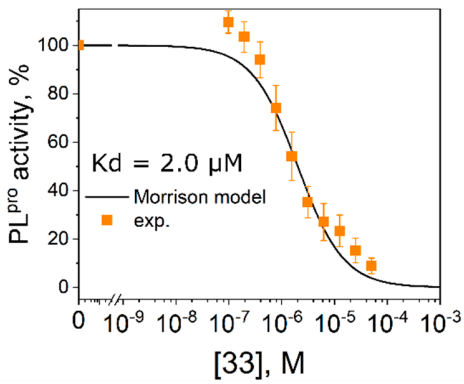

PL^pro activity, %
Kd = 35 μM
Morrison model
exp.
[27a], M

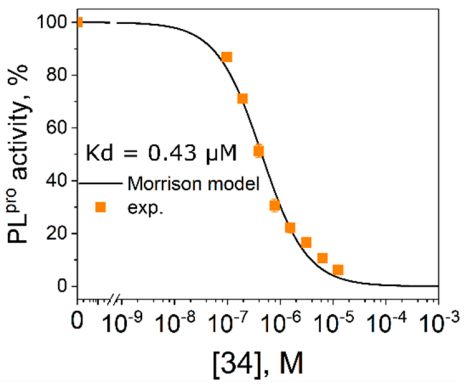

PL^pro activity, %
Kd = 15 μM
Morrison model
exp.
[27c], M

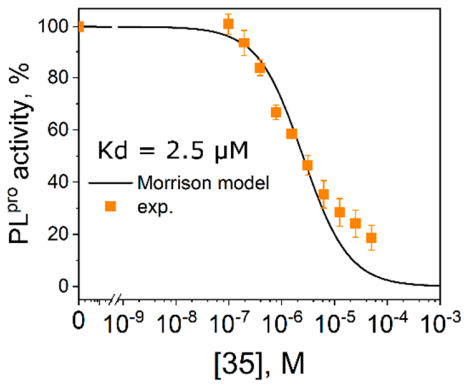

PL^pro activity, %
Kd = 8.8 μM
Morrison model
exp.
[28], M

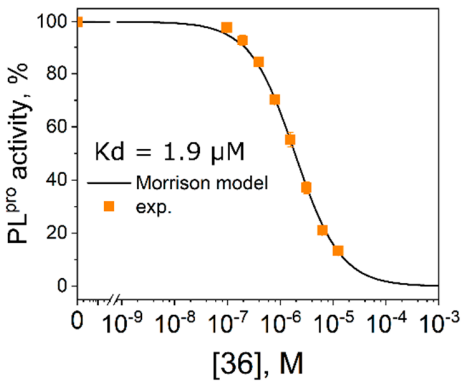

PL^pro activity, %
Kd = 32 μM
Morrison model
exp.
[30c], M


PL^pro activity, %
Kd = 0.54 μM
Morrison model
exp.
[32], M


PL^pro activity, %
Kd = 2.0 μM
Morrison model
exp.
[33], M


PL^pro activity, %
Kd = 0.43 μM
Morrison model
exp.
[34], M


PL^pro activity, %
Kd = 2.5 μM
Morrison model
exp.
[35], M


PL^pro activity, %
Kd = 1.9 μM
Morrison model
exp.
[36], M

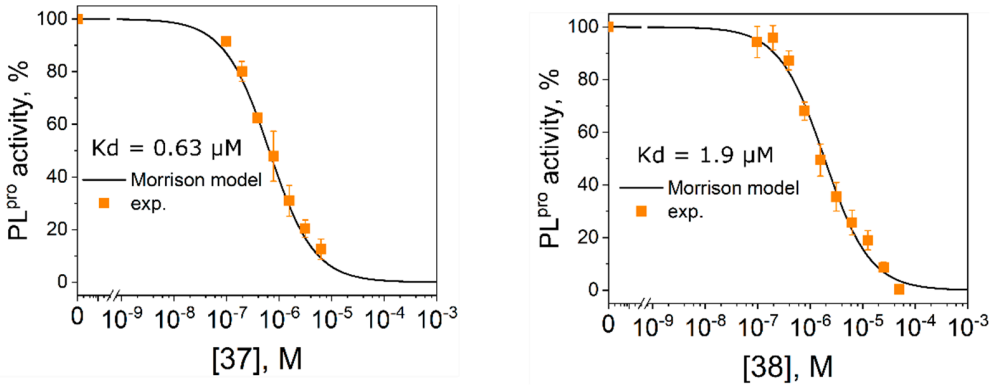


Figure S19. Dose-response curves of PL^{pro} inhibition with naphthalene-based and disulfide compounds.

4. Dose-response curves of M^{pro}.

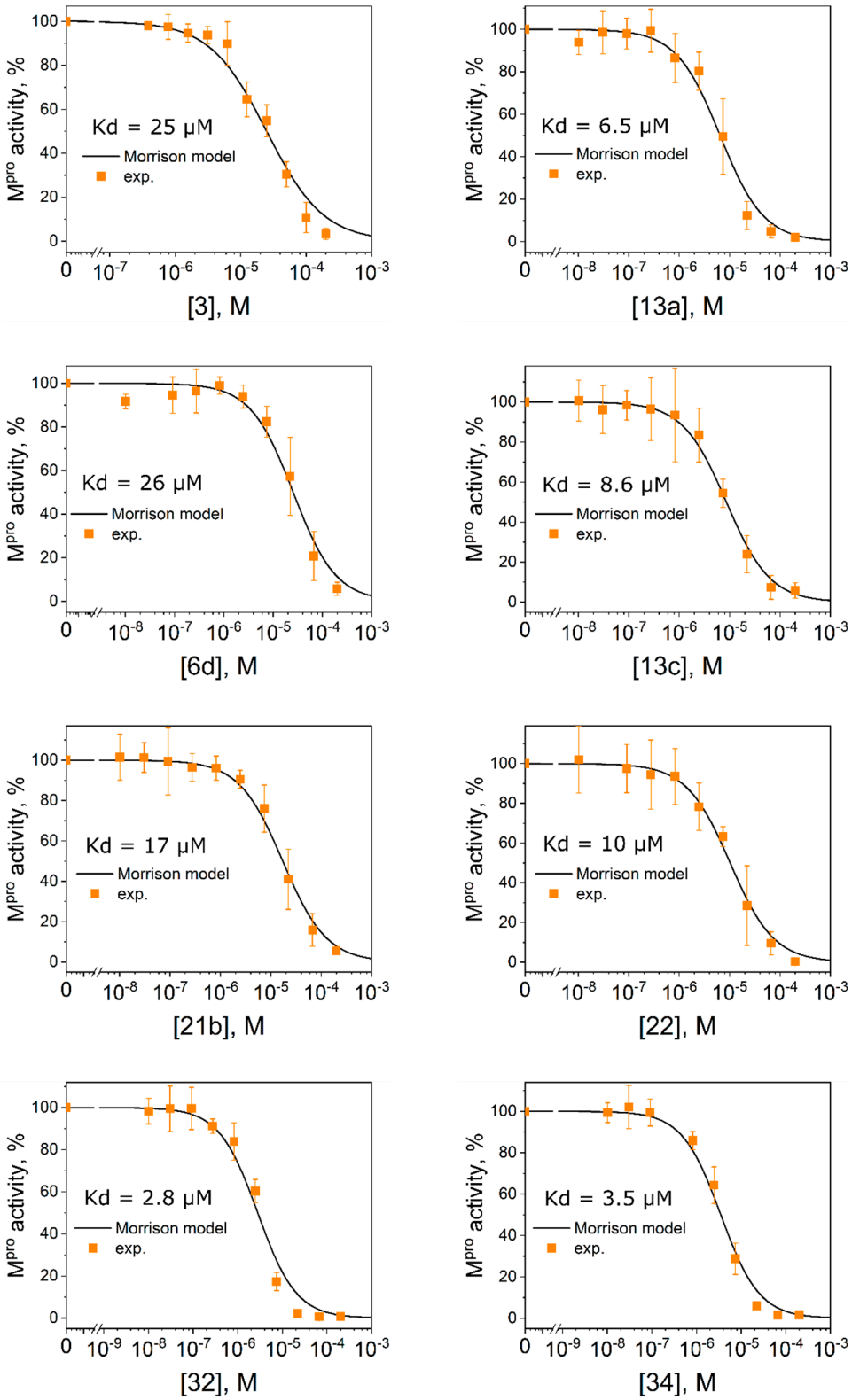


Figure S20. Dose-response curves of M^{pro} inhibition with naphthalene-based and disulfide compounds.

5. **Table S1**. Primers used in PL^{pro}C111S mutagenesis.

Primer name	Sequence
PL^{pro}-C111S_F	5' - gctgataacaattcctacctagctac - 3'
PL^{pro}-C111S_R	5' - ccatttgatgctagtcagacc - 3'

6. Sequencing analysis of PL^{pro} WT and PL^{pro}C111S plasmids.

The only one difference between two plasmids is nucleotide at 5468 position.

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1                                                   50
 PLpro_WT  TGGCGAATGG GACGCGCCCT GTAGCGGCGC ATTAAGCGCG GCGGGTGTGG
PLproC111S TGGCGAATGG GACGCGCCCT GTAGCGGCGC ATTAAGCGCG GCGGGTGTGG
 Consensus TGGCGAATGG GACGCGCCCT GTAGCGGCGC ATTAAGCGCG GCGGGTGTGG

           51                                               100
 PLpro_WT  TGGTTACGCG CAGCGTGACC GCTACACTTG CCAGCGCCCT AGCGCCCGCT
PLproC111S TGGTTACGCG CAGCGTGACC GCTACACTTG CCAGCGCCCT AGCGCCCGCT
 Consensus TGGTTACGCG CAGCGTGACC GCTACACTTG CCAGCGCCCT AGCGCCCGCT

           101                                              150
 PLpro_WT  CCTTTCGCTT TCTTCCCTTC CTTTCTCGCC ACGTTCGCCG GCTTTCCCCG
PLproC111S CCTTTCGCTT TCTTCCCTTC CTTTCTCGCC ACGTTCGCCG GCTTTCCCCG
 Consensus CCTTTCGCTT TCTTCCCTTC CTTTCTCGCC ACGTTCGCCG GCTTTCCCCG

           151                                              200
 PLpro_WT  TCAAGCTCTA AATCGGGGGC TCCCTTTAGG GTTCCGATTT AGTGCTTTAC
PLproC111S TCAAGCTCTA AATCGGGGGC TCCCTTTAGG GTTCCGATTT AGTGCTTTAC
 Consensus TCAAGCTCTA AATCGGGGGC TCCCTTTAGG GTTCCGATTT AGTGCTTTAC

           201                                              250
 PLpro_WT  GGCACCTCGA CCCCAAAAAA CTTGATTAGG GTGATGGTTC ACGTAGTGGG
PLproC111S GGCACCTCGA CCCCAAAAAA CTTGATTAGG GTGATGGTTC ACGTAGTGGG
 Consensus GGCACCTCGA CCCCAAAAAA CTTGATTAGG GTGATGGTTC ACGTAGTGGG

           251                                              300
 PLpro_WT  CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTTGG AGTCCACGTT
PLproC111S CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTTGG AGTCCACGTT
 Consensus CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTTGG AGTCCACGTT

           301                                              350
 PLpro_WT  CTTTAATAGT GGACTCTTGT TCCAAACTGG AACAACACTC AACCCTATCT
PLproC111S CTTTAATAGT GGACTCTTGT TCCAAACTGG AACAACACTC AACCCTATCT
 Consensus CTTTAATAGT GGACTCTTGT TCCAAACTGG AACAACACTC AACCCTATCT

           351                                              400
 PLpro_WT  CGGTCTATTC TTTTGATTTA TAAGGGATTT TGCCGATTTC GGCCTATTGG
PLproC111S CGGTCTATTC TTTTGATTTA TAAGGGATTT TGCCGATTTC GGCCTATTGG
 Consensus CGGTCTATTC TTTTGATTTA TAAGGGATTT TGCCGATTTC GGCCTATTGG

           401                                              450
 PLpro_WT  TTAAAAAATG AGCTGATTTA ACAAAAATTT AACGCGAATT TTAACAAAAT
PLproC111S TTAAAAAATG AGCTGATTTA ACAAAAATTT AACGCGAATT TTAACAAAAT
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 Consensus  TTAAAAAATG AGCTGATTTA ACAAAAATTT AACGCGAATT TTAACAAAAT

            451                                                 500
  PLpro_WT  ATTAACGTTT ACAATTTCAG GTGGCACTTT TCGGGGAAAT GTGCGCGGAA
PLproC111S  ATTAACGTTT ACAATTTCAG GTGGCACTTT TCGGGGAAAT GTGCGCGGAA
 Consensus  ATTAACGTTT ACAATTTCAG GTGGCACTTT TCGGGGAAAT GTGCGCGGAA

            501                                                 550
  PLpro_WT  CCCCTATTTG TTTATTTTTC TAAATACATT CAAATATGTA TCCGCTCATG
PLproC111S  CCCCTATTTG TTTATTTTTC TAAATACATT CAAATATGTA TCCGCTCATG
 Consensus  CCCCTATTTG TTTATTTTTC TAAATACATT CAAATATGTA TCCGCTCATG

            551                                                 600
  PLpro_WT  AATTAATTCT TAGAAAAACT CATCGAGCAT CAAATGAAAC TGCAATTTAT
PLproC111S  AATTAATTCT TAGAAAAACT CATCGAGCAT CAAATGAAAC TGCAATTTAT
 Consensus  AATTAATTCT TAGAAAAACT CATCGAGCAT CAAATGAAAC TGCAATTTAT

            601                                                 650
  PLpro_WT  TCATATCAGG ATTATCAATA CCATATTTTT GAAAAAGCCG TTTCTGTAAT
PLproC111S  TCATATCAGG ATTATCAATA CCATATTTTT GAAAAAGCCG TTTCTGTAAT
 Consensus  TCATATCAGG ATTATCAATA CCATATTTTT GAAAAAGCCG TTTCTGTAAT

            651                                                 700
  PLpro_WT  GAAGGAGAAA ACTCACCGAG GCAGTTCCAT AGGATGGCAA GATCCTGGTA
PLproC111S  GAAGGAGAAA ACTCACCGAG GCAGTTCCAT AGGATGGCAA GATCCTGGTA
 Consensus  GAAGGAGAAA ACTCACCGAG GCAGTTCCAT AGGATGGCAA GATCCTGGTA

            701                                                 750
  PLpro_WT  TCGGTCTGCG ATTCCGACTC GTCCAACATC AATACAACCT ATTAATTTCC
PLproC111S  TCGGTCTGCG ATTCCGACTC GTCCAACATC AATACAACCT ATTAATTTCC
 Consensus  TCGGTCTGCG ATTCCGACTC GTCCAACATC AATACAACCT ATTAATTTCC

            751                                                 800
  PLpro_WT  CCTCGTCAAA AATAAGGTTA TCAAGTGAGA AATCACCATG AGTGACGACT
PLproC111S  CCTCGTCAAA AATAAGGTTA TCAAGTGAGA AATCACCATG AGTGACGACT
 Consensus  CCTCGTCAAA AATAAGGTTA TCAAGTGAGA AATCACCATG AGTGACGACT

            801                                                 850
  PLpro_WT  GAATCCGGTG AGAATGGCAA AAGTTTATGC ATTTCTTTCC AGACTTGTTC
PLproC111S  GAATCCGGTG AGAATGGCAA AAGTTTATGC ATTTCTTTCC AGACTTGTTC
 Consensus  GAATCCGGTG AGAATGGCAA AAGTTTATGC ATTTCTTTCC AGACTTGTTC

            851                                                 900
  PLpro_WT  AACAGGCCAG CCATTACGCT CGTCATCAAA ATCACTCGCA TCAACCAAAC
PLproC111S  AACAGGCCAG CCATTACGCT CGTCATCAAA ATCACTCGCA TCAACCAAAC
 Consensus  AACAGGCCAG CCATTACGCT CGTCATCAAA ATCACTCGCA TCAACCAAAC

            901                                                 950
  PLpro_WT  CGTTATTCAT TCGTGATTGC GCCTGAGCGA GACGAAATAC GCGATCGCTG
PLproC111S  CGTTATTCAT TCGTGATTGC GCCTGAGCGA GACGAAATAC GCGATCGCTG
 Consensus  CGTTATTCAT TCGTGATTGC GCCTGAGCGA GACGAAATAC GCGATCGCTG
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            951                                                 1000
  PLpro_WT  TTAAAAGGAC AATTACAAAC AGGAATCGAA TGCAACCGGC GCAGGAACAC
PLproC111S  TTAAAAGGAC AATTACAAAC AGGAATCGAA TGCAACCGGC GCAGGAACAC
 Consensus  TTAAAAGGAC AATTACAAAC AGGAATCGAA TGCAACCGGC GCAGGAACAC

            1001                                                1050
  PLpro_WT  TGCCAGCGCA TCAACAATAT TTTCACCTGA ATCAGGATAT TCTTCTAATA
PLproC111S  TGCCAGCGCA TCAACAATAT TTTCACCTGA ATCAGGATAT TCTTCTAATA
 Consensus  TGCCAGCGCA TCAACAATAT TTTCACCTGA ATCAGGATAT TCTTCTAATA

            1051                                                1100
  PLpro_WT  CCTGGAATGC TGTTTTCCCG GGGATCGCAG TGGTGAGTAA CCATGCATCA
PLproC111S  CCTGGAATGC TGTTTTCCCG GGGATCGCAG TGGTGAGTAA CCATGCATCA
 Consensus  CCTGGAATGC TGTTTTCCCG GGGATCGCAG TGGTGAGTAA CCATGCATCA

            1101                                                1150
  PLpro_WT  TCAGGAGTAC GGATAAAATG CTTGATGGTC GGAAGAGGCA TAAATTCCGT
PLproC111S  TCAGGAGTAC GGATAAAATG CTTGATGGTC GGAAGAGGCA TAAATTCCGT
 Consensus  TCAGGAGTAC GGATAAAATG CTTGATGGTC GGAAGAGGCA TAAATTCCGT

            1151                                                1200
  PLpro_WT  CAGCCAGTTT AGTCTGACCA TCTCATCTGT AACATCATTG GCAACGCTAC
PLproC111S  CAGCCAGTTT AGTCTGACCA TCTCATCTGT AACATCATTG GCAACGCTAC
 Consensus  CAGCCAGTTT AGTCTGACCA TCTCATCTGT AACATCATTG GCAACGCTAC

            1201                                                1250
  PLpro_WT  CTTTGCCATG TTTCAGAAAC AACTCTGGCG CATCGGGCTT CCCATACAAT
PLproC111S  CTTTGCCATG TTTCAGAAAC AACTCTGGCG CATCGGGCTT CCCATACAAT
 Consensus  CTTTGCCATG TTTCAGAAAC AACTCTGGCG CATCGGGCTT CCCATACAAT

            1251                                                1300
  PLpro_WT  CGATAGATTG TCGCACCTGA TTGCCCGACA TTATCGCGAG CCCATTTATA
PLproC111S  CGATAGATTG TCGCACCTGA TTGCCCGACA TTATCGCGAG CCCATTTATA
 Consensus  CGATAGATTG TCGCACCTGA TTGCCCGACA TTATCGCGAG CCCATTTATA

            1301                                                1350
  PLpro_WT  CCCATATAAA TCAGCATCCA TGTTGGAATT TAATCGCGGC CTAGAGCAAG
PLproC111S  CCCATATAAA TCAGCATCCA TGTTGGAATT TAATCGCGGC CTAGAGCAAG
 Consensus  CCCATATAAA TCAGCATCCA TGTTGGAATT TAATCGCGGC CTAGAGCAAG

            1351                                                1400
  PLpro_WT  ACGTTTCCCG TTGAATATGG CTCATAACAC CCCTTGTATT ACTGTTTATG
PLproC111S  ACGTTTCCCG TTGAATATGG CTCATAACAC CCCTTGTATT ACTGTTTATG
 Consensus  ACGTTTCCCG TTGAATATGG CTCATAACAC CCCTTGTATT ACTGTTTATG

            1401                                                1450
  PLpro_WT  TAAGCAGACA GTTTTATTGT TCATGACCAA AATCCCTTAA CGTGAGTTTT
PLproC111S  TAAGCAGACA GTTTTATTGT TCATGACCAA AATCCCTTAA CGTGAGTTTT
 Consensus  TAAGCAGACA GTTTTATTGT TCATGACCAA AATCCCTTAA CGTGAGTTTT

            1451                                                1500
  PLpro_WT  CGTTCCACTG AGCGTCAGAC CCCGTAGAAA AGATCAAAGG ATCTTCTTGA
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PLproC111S  CGTTCCACTG AGCGTCAGAC CCCGTAGAAA AGATCAAAGG ATCTTCTTGA
 Consensus  CGTTCCACTG AGCGTCAGAC CCCGTAGAAA AGATCAAAGG ATCTTCTTGA

            1501                                                1550
  PLpro_WT  GATCCTTTTT TTCTGCGCGT AATCTGCTGC TTGCAAACAA AAAAACCACC
PLproC111S  GATCCTTTTT TTCTGCGCGT AATCTGCTGC TTGCAAACAA AAAAACCACC
 Consensus  GATCCTTTTT TTCTGCGCGT AATCTGCTGC TTGCAAACAA AAAAACCACC

            1551                                                1600
  PLpro_WT  GCTACCAGCG GTGGTTTGTT TGCCGGATCA AGAGCTACCA ACTCTTTTTC
PLproC111S  GCTACCAGCG GTGGTTTGTT TGCCGGATCA AGAGCTACCA ACTCTTTTTC
 Consensus  GCTACCAGCG GTGGTTTGTT TGCCGGATCA AGAGCTACCA ACTCTTTTTC

            1601                                                1650
  PLpro_WT  CGAAGGTAAC TGGCTTCAGC AGAGCGCAGA TACCAAATAC TGTCCTTCTA
PLproC111S  CGAAGGTAAC TGGCTTCAGC AGAGCGCAGA TACCAAATAC TGTCCTTCTA
 Consensus  CGAAGGTAAC TGGCTTCAGC AGAGCGCAGA TACCAAATAC TGTCCTTCTA

            1651                                                1700
  PLpro_WT  GTGTAGCCGT AGTTAGGCCA CCACTTCAAG AACTCTGTAG CACCGCCTAC
PLproC111S  GTGTAGCCGT AGTTAGGCCA CCACTTCAAG AACTCTGTAG CACCGCCTAC
 Consensus  GTGTAGCCGT AGTTAGGCCA CCACTTCAAG AACTCTGTAG CACCGCCTAC

            1701                                                1750
  PLpro_WT  ATACCTCGCT CTGCTAATCC TGTTACCAGT GGCTGCTGCC AGTGGCGATA
PLproC111S  ATACCTCGCT CTGCTAATCC TGTTACCAGT GGCTGCTGCC AGTGGCGATA
 Consensus  ATACCTCGCT CTGCTAATCC TGTTACCAGT GGCTGCTGCC AGTGGCGATA

            1751                                                1800
  PLpro_WT  AGTCGTGTCT TACCGGGTTG GACTCAAGAC GATAGTTACC GGATAAGGCG
PLproC111S  AGTCGTGTCT TACCGGGTTG GACTCAAGAC GATAGTTACC GGATAAGGCG
 Consensus  AGTCGTGTCT TACCGGGTTG GACTCAAGAC GATAGTTACC GGATAAGGCG

            1801                                                1850
  PLpro_WT  CAGCGGTCGG GCTGAACGGG GGGTTCGTGC ACACAGCCCA GCTTGGAGCG
PLproC111S  CAGCGGTCGG GCTGAACGGG GGGTTCGTGC ACACAGCCCA GCTTGGAGCG
 Consensus  CAGCGGTCGG GCTGAACGGG GGGTTCGTGC ACACAGCCCA GCTTGGAGCG

            1851                                                1900
  PLpro_WT  AACGACCTAC ACCGAACTGA GATACCTACA GCGTGAGCTA TGAGAAAGCG
PLproC111S  AACGACCTAC ACCGAACTGA GATACCTACA GCGTGAGCTA TGAGAAAGCG
 Consensus  AACGACCTAC ACCGAACTGA GATACCTACA GCGTGAGCTA TGAGAAAGCG

            1901                                                1950
  PLpro_WT  CCACGCTTCC CGAAGGGAGA AAGGCGGACA GGTATCCGGT AAGCGGCAGG
PLproC111S  CCACGCTTCC CGAAGGGAGA AAGGCGGACA GGTATCCGGT AAGCGGCAGG
 Consensus  CCACGCTTCC CGAAGGGAGA AAGGCGGACA GGTATCCGGT AAGCGGCAGG

            1951                                                2000
  PLpro_WT  GTCGGAACAG GAGAGCGCAC GAGGGAGCTT CCAGGGGGAA ACGCCTGGTA
PLproC111S  GTCGGAACAG GAGAGCGCAC GAGGGAGCTT CCAGGGGGAA ACGCCTGGTA
 Consensus  GTCGGAACAG GAGAGCGCAC GAGGGAGCTT CCAGGGGGAA ACGCCTGGTA
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            2001                                                2050
  PLpro_WT  TCTTTATAGT CCTGTCGGGT TTCGCCACCT CTGACTTGAG CGTCGATTTT
PLproC111S  TCTTTATAGT CCTGTCGGGT TTCGCCACCT CTGACTTGAG CGTCGATTTT
 Consensus  TCTTTATAGT CCTGTCGGGT TTCGCCACCT CTGACTTGAG CGTCGATTTT

            2051                                                2100
  PLpro_WT  TGTGATGCTC GTCAGGGGGG CGGAGCCTAT GGAAAAACGC CAGCAACGCG
PLproC111S  TGTGATGCTC GTCAGGGGGG CGGAGCCTAT GGAAAAACGC CAGCAACGCG
 Consensus  TGTGATGCTC GTCAGGGGGG CGGAGCCTAT GGAAAAACGC CAGCAACGCG

            2101                                                2150
  PLpro_WT  GCCTTTTTAC GGTTCCTGGC CTTTTGCTGG CCTTTTGCTC ACATGTTCTT
PLproC111S  GCCTTTTTAC GGTTCCTGGC CTTTTGCTGG CCTTTTGCTC ACATGTTCTT
 Consensus  GCCTTTTTAC GGTTCCTGGC CTTTTGCTGG CCTTTTGCTC ACATGTTCTT

            2151                                                2200
  PLpro_WT  TCCTGCGTTA TCCCCTGATT CTGTGGATAA CCGTATTACC GCCTTTGAGT
PLproC111S  TCCTGCGTTA TCCCCTGATT CTGTGGATAA CCGTATTACC GCCTTTGAGT
 Consensus  TCCTGCGTTA TCCCCTGATT CTGTGGATAA CCGTATTACC GCCTTTGAGT

            2201                                                2250
  PLpro_WT  GAGCTGATAC CGCTCGCCGC AGCCGAACGA CCGAGCGCAG CGAGTCAGTG
PLproC111S  GAGCTGATAC CGCTCGCCGC AGCCGAACGA CCGAGCGCAG CGAGTCAGTG
 Consensus  GAGCTGATAC CGCTCGCCGC AGCCGAACGA CCGAGCGCAG CGAGTCAGTG

            2251                                                2300
  PLpro_WT  AGCGAGGAAG CGGAAGAGCG CCTGATGCGG TATTTTCTCC TTACGCATCT
PLproC111S  AGCGAGGAAG CGGAAGAGCG CCTGATGCGG TATTTTCTCC TTACGCATCT
 Consensus  AGCGAGGAAG CGGAAGAGCG CCTGATGCGG TATTTTCTCC TTACGCATCT

            2301                                                2350
  PLpro_WT  GTGCGGTATT TCACACCGCA TATATGGTGC ACTCTCAGTA CAATCTGCTC
PLproC111S  GTGCGGTATT TCACACCGCA TATATGGTGC ACTCTCAGTA CAATCTGCTC
 Consensus  GTGCGGTATT TCACACCGCA TATATGGTGC ACTCTCAGTA CAATCTGCTC

            2351                                                2400
  PLpro_WT  TGATGCCGCA TAGTTAAGCC AGTATACACT CCGCTATCGC TACGTGACTG
PLproC111S  TGATGCCGCA TAGTTAAGCC AGTATACACT CCGCTATCGC TACGTGACTG
 Consensus  TGATGCCGCA TAGTTAAGCC AGTATACACT CCGCTATCGC TACGTGACTG

            2401                                                2450
  PLpro_WT  GGTCATGGCT GCGCCCCGAC ACCCGCCAAC ACCCGCTGAC GCGCCCTGAC
PLproC111S  GGTCATGGCT GCGCCCCGAC ACCCGCCAAC ACCCGCTGAC GCGCCCTGAC
 Consensus  GGTCATGGCT GCGCCCCGAC ACCCGCCAAC ACCCGCTGAC GCGCCCTGAC

            2451                                                2500
  PLpro_WT  GGGCTTGTCT GCTCCCGGCA TCCGCTTACA GACAAGCTGT GACCGTCTCC
PLproC111S  GGGCTTGTCT GCTCCCGGCA TCCGCTTACA GACAAGCTGT GACCGTCTCC
 Consensus  GGGCTTGTCT GCTCCCGGCA TCCGCTTACA GACAAGCTGT GACCGTCTCC

            2501                                                2550
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  PLpro_WT  GGGAGCTGCA TGTGTCAGAG GTTTTCACCG TCATCACCGA AACGCGCGAG
PLproC111S  GGGAGCTGCA TGTGTCAGAG GTTTTCACCG TCATCACCGA AACGCGCGAG
 Consensus  GGGAGCTGCA TGTGTCAGAG GTTTTCACCG TCATCACCGA AACGCGCGAG

            2551                                                2600
  PLpro_WT  GCAGCTGCGG TAAAGCTCAT CAGCGTGGTC GTGAAGCGAT TCACAGATGT
PLproC111S  GCAGCTGCGG TAAAGCTCAT CAGCGTGGTC GTGAAGCGAT TCACAGATGT
 Consensus  GCAGCTGCGG TAAAGCTCAT CAGCGTGGTC GTGAAGCGAT TCACAGATGT

            2601                                                2650
  PLpro_WT  CTGCCTGTTC ATCCGCGTCC AGCTCGTTGA GTTTCTCCAG AAGCGTTAAT
PLproC111S  CTGCCTGTTC ATCCGCGTCC AGCTCGTTGA GTTTCTCCAG AAGCGTTAAT
 Consensus  CTGCCTGTTC ATCCGCGTCC AGCTCGTTGA GTTTCTCCAG AAGCGTTAAT

            2651                                                2700
  PLpro_WT  GTCTGGCTTC TGATAAAGCG GGCCATGTTA AGGGCGGTTT TTTCCTGTTT
PLproC111S  GTCTGGCTTC TGATAAAGCG GGCCATGTTA AGGGCGGTTT TTTCCTGTTT
 Consensus  GTCTGGCTTC TGATAAAGCG GGCCATGTTA AGGGCGGTTT TTTCCTGTTT

            2701                                                2750
  PLpro_WT  GGTCACTGAT GCCTCCGTGT AAGGGGGATT TCTGTTCATG GGGGTAATGA
PLproC111S  GGTCACTGAT GCCTCCGTGT AAGGGGGATT TCTGTTCATG GGGGTAATGA
 Consensus  GGTCACTGAT GCCTCCGTGT AAGGGGGATT TCTGTTCATG GGGGTAATGA

            2751                                                2800
  PLpro_WT  TACCGATGAA ACGAGAGAGG ATGCTCACGA TACGGGTTAC TGATGATGAA
PLproC111S  TACCGATGAA ACGAGAGAGG ATGCTCACGA TACGGGTTAC TGATGATGAA
 Consensus  TACCGATGAA ACGAGAGAGG ATGCTCACGA TACGGGTTAC TGATGATGAA

            2801                                                2850
  PLpro_WT  CATGCCCGGT TACTGGAACG TTGTGAGGGT AAACAACTGG CGGTATGGAT
PLproC111S  CATGCCCGGT TACTGGAACG TTGTGAGGGT AAACAACTGG CGGTATGGAT
 Consensus  CATGCCCGGT TACTGGAACG TTGTGAGGGT AAACAACTGG CGGTATGGAT

            2851                                                2900
  PLpro_WT  GCGGCGGGAC CAGAGAAAAA TCACTCAGGG TCAATGCCAG CGCTTCGTTA
PLproC111S  GCGGCGGGAC CAGAGAAAAA TCACTCAGGG TCAATGCCAG CGCTTCGTTA
 Consensus  GCGGCGGGAC CAGAGAAAAA TCACTCAGGG TCAATGCCAG CGCTTCGTTA

            2901                                                2950
  PLpro_WT  ATACAGATGT AGGTGTTCCA CAGGGTAGCC AGCAGCATCC TGCGATGCAG
PLproC111S  ATACAGATGT AGGTGTTCCA CAGGGTAGCC AGCAGCATCC TGCGATGCAG
 Consensus  ATACAGATGT AGGTGTTCCA CAGGGTAGCC AGCAGCATCC TGCGATGCAG

            2951                                                3000
  PLpro_WT  ATCCGGAACA TAATGGTGCA GGGCGCTGAC TTCCGCGTTT CCAGACTTTA
PLproC111S  ATCCGGAACA TAATGGTGCA GGGCGCTGAC TTCCGCGTTT CCAGACTTTA
 Consensus  ATCCGGAACA TAATGGTGCA GGGCGCTGAC TTCCGCGTTT CCAGACTTTA

            3001                                                3050
  PLpro_WT  CGAAACACGG AAACCGAAGA CCATTCATGT TGTTGCTCAG GTCGCAGACG
PLproC111S  CGAAACACGG AAACCGAAGA CCATTCATGT TGTTGCTCAG GTCGCAGACG
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 Consensus  CGAAACACGG AAACCGAAGA CCATTCATGT TGTTGCTCAG GTCGCAGACG

            3051                                                3100
  PLpro_WT  TTTTGCAGCA GCAGTCGCTT CACGTTCGCT CGCGTATCGG TGATTCATTC
PLproC111S  TTTTGCAGCA GCAGTCGCTT CACGTTCGCT CGCGTATCGG TGATTCATTC
 Consensus  TTTTGCAGCA GCAGTCGCTT CACGTTCGCT CGCGTATCGG TGATTCATTC

            3101                                                3150
  PLpro_WT  TGCTAACCAG TAAGGCAACC CCGCCAGCCT AGCCGGGTCC TCAACGACAG
PLproC111S  TGCTAACCAG TAAGGCAACC CCGCCAGCCT AGCCGGGTCC TCAACGACAG
 Consensus  TGCTAACCAG TAAGGCAACC CCGCCAGCCT AGCCGGGTCC TCAACGACAG

            3151                                                3200
  PLpro_WT  GAGCACGATC ATGCGCACCC GTGGGGCCGC CATGCCGGCG ATAATGGCCT
PLproC111S  GAGCACGATC ATGCGCACCC GTGGGGCCGC CATGCCGGCG ATAATGGCCT
 Consensus  GAGCACGATC ATGCGCACCC GTGGGGCCGC CATGCCGGCG ATAATGGCCT

            3201                                                3250
  PLpro_WT  GCTTCTCGCC GAAACGTTTG GTGGCGGGAC CAGTGACGAA GGCTTGAGCG
PLproC111S  GCTTCTCGCC GAAACGTTTG GTGGCGGGAC CAGTGACGAA GGCTTGAGCG
 Consensus  GCTTCTCGCC GAAACGTTTG GTGGCGGGAC CAGTGACGAA GGCTTGAGCG

            3251                                                3300
  PLpro_WT  AGGGCGTGCA AGATTCCGAA TACCGCAAGC GACAGGCCGA TCATCGTCGC
PLproC111S  AGGGCGTGCA AGATTCCGAA TACCGCAAGC GACAGGCCGA TCATCGTCGC
 Consensus  AGGGCGTGCA AGATTCCGAA TACCGCAAGC GACAGGCCGA TCATCGTCGC

            3301                                                3350
  PLpro_WT  GCTCCAGCGA AAGCGGTCCT CGCCGAAAAT GACCCAGAGC GCTGCCGGCA
PLproC111S  GCTCCAGCGA AAGCGGTCCT CGCCGAAAAT GACCCAGAGC GCTGCCGGCA
 Consensus  GCTCCAGCGA AAGCGGTCCT CGCCGAAAAT GACCCAGAGC GCTGCCGGCA

            3351                                                3400
  PLpro_WT  CCTGTCCTAC GAGTTGCATG ATAAAGAAGA CAGTCATAAG TGCGGCGACG
PLproC111S  CCTGTCCTAC GAGTTGCATG ATAAAGAAGA CAGTCATAAG TGCGGCGACG
 Consensus  CCTGTCCTAC GAGTTGCATG ATAAAGAAGA CAGTCATAAG TGCGGCGACG

            3401                                                3450
  PLpro_WT  ATAGTCATGC CCCGCGCCCA CCGGAAGGAG CTGACTGGGT TGAAGGCTCT
PLproC111S  ATAGTCATGC CCCGCGCCCA CCGGAAGGAG CTGACTGGGT TGAAGGCTCT
 Consensus  ATAGTCATGC CCCGCGCCCA CCGGAAGGAG CTGACTGGGT TGAAGGCTCT

            3451                                                3500
  PLpro_WT  CAAGGGCATC GGTCGAGATC CCGGTGCCTA ATGAGTGAGC TAACTTACAT
PLproC111S  CAAGGGCATC GGTCGAGATC CCGGTGCCTA ATGAGTGAGC TAACTTACAT
 Consensus  CAAGGGCATC GGTCGAGATC CCGGTGCCTA ATGAGTGAGC TAACTTACAT

            3501                                                3550
  PLpro_WT  TAATTGCGTT GCGCTCACTG CCCGCTTTCC AGTCGGGAAA CCTGTCGTGC
PLproC111S  TAATTGCGTT GCGCTCACTG CCCGCTTTCC AGTCGGGAAA CCTGTCGTGC
 Consensus  TAATTGCGTT GCGCTCACTG CCCGCTTTCC AGTCGGGAAA CCTGTCGTGC
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            3551                                                 3600
  PLpro_WT  CAGCTGCATT AATGAATCGG CCAACGCGCG GGGAGAGGCG GTTTGCGTAT
PLproC111S  CAGCTGCATT AATGAATCGG CCAACGCGCG GGGAGAGGCG GTTTGCGTAT
 Consensus  CAGCTGCATT AATGAATCGG CCAACGCGCG GGGAGAGGCG GTTTGCGTAT

            3601                                                 3650
  PLpro_WT  TGGGCGCCAG GGTGGTTTTT CTTTTCACCA GTGAGACGGG CAACAGCTGA
PLproC111S  TGGGCGCCAG GGTGGTTTTT CTTTTCACCA GTGAGACGGG CAACAGCTGA
 Consensus  TGGGCGCCAG GGTGGTTTTT CTTTTCACCA GTGAGACGGG CAACAGCTGA

            3651                                                 3700
  PLpro_WT  TTGCCCTTCA CCGCCTGGCC CTGAGAGAGT TGCAGCAAGC GGTCCACGCT
PLproC111S  TTGCCCTTCA CCGCCTGGCC CTGAGAGAGT TGCAGCAAGC GGTCCACGCT
 Consensus  TTGCCCTTCA CCGCCTGGCC CTGAGAGAGT TGCAGCAAGC GGTCCACGCT

            3701                                                 3750
  PLpro_WT  GGTTTGCCCC AGCAGGCGAA AATCCTGTTT GATGGTGGTT AACGGCGGGA
PLproC111S  GGTTTGCCCC AGCAGGCGAA AATCCTGTTT GATGGTGGTT AACGGCGGGA
 Consensus  GGTTTGCCCC AGCAGGCGAA AATCCTGTTT GATGGTGGTT AACGGCGGGA

            3751                                                 3800
  PLpro_WT  TATAACATGA GCTGTCTTCG GTATCGTCGT ATCCCACTAC CGAGATATCC
PLproC111S  TATAACATGA GCTGTCTTCG GTATCGTCGT ATCCCACTAC CGAGATATCC
 Consensus  TATAACATGA GCTGTCTTCG GTATCGTCGT ATCCCACTAC CGAGATATCC

            3801                                                 3850
  PLpro_WT  GCACCAACGC GCAGCCCGGA CTCGGTAATG GCGCGCATTG CGCCCAGCGC
PLproC111S  GCACCAACGC GCAGCCCGGA CTCGGTAATG GCGCGCATTG CGCCCAGCGC
 Consensus  GCACCAACGC GCAGCCCGGA CTCGGTAATG GCGCGCATTG CGCCCAGCGC

            3851                                                 3900
  PLpro_WT  CATCTGATCG TTGGCAACCA GCATCGCAGT GGGAACGATG CCCTCATTCA
PLproC111S  CATCTGATCG TTGGCAACCA GCATCGCAGT GGGAACGATG CCCTCATTCA
 Consensus  CATCTGATCG TTGGCAACCA GCATCGCAGT GGGAACGATG CCCTCATTCA

            3901                                                 3950
  PLpro_WT  GCATTTGCAT GGTTTGTTGA AAACCGGACA TGGCACTCCA GTCGCCTTCC
PLproC111S  GCATTTGCAT GGTTTGTTGA AAACCGGACA TGGCACTCCA GTCGCCTTCC
 Consensus  GCATTTGCAT GGTTTGTTGA AAACCGGACA TGGCACTCCA GTCGCCTTCC

            3951                                                 4000
  PLpro_WT  CGTTCCGCTA TCGGCTGAAT TTGATTGCGA GTGAGATATT TATGCCAGCC
PLproC111S  CGTTCCGCTA TCGGCTGAAT TTGATTGCGA GTGAGATATT TATGCCAGCC
 Consensus  CGTTCCGCTA TCGGCTGAAT TTGATTGCGA GTGAGATATT TATGCCAGCC

            4001                                                 4050
  PLpro_WT  AGCCAGACGC AGACGCGCCG AGACAGAACT TAATGGGCCC GCTAACAGCG
PLproC111S  AGCCAGACGC AGACGCGCCG AGACAGAACT TAATGGGCCC GCTAACAGCG
 Consensus  AGCCAGACGC AGACGCGCCG AGACAGAACT TAATGGGCCC GCTAACAGCG

            4051                                                 4100
  PLpro_WT  CGATTTGCTG GTGACCCAAT GCGACCAGAT GCTCCACGCC CAGTCGCGTA
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PLproC111S  CGATTTGCTG GTGACCCAAT GCGACCAGAT GCTCCACGCC CAGTCGCGTA
 Consensus  CGATTTGCTG GTGACCCAAT GCGACCAGAT GCTCCACGCC CAGTCGCGTA

            4101                                                4150
  PLpro_WT  CCGTCTTCAT GGGAGAAAAT AATACTGTTG ATGGGTGTCT GGTCAGAGAC
PLproC111S  CCGTCTTCAT GGGAGAAAAT AATACTGTTG ATGGGTGTCT GGTCAGAGAC
 Consensus  CCGTCTTCAT GGGAGAAAAT AATACTGTTG ATGGGTGTCT GGTCAGAGAC

            4151                                                4200
  PLpro_WT  ATCAAGAAAT AACGCCGGAA CATTAGTGCA GGCAGCTTCC ACAGCAATGG
PLproC111S  ATCAAGAAAT AACGCCGGAA CATTAGTGCA GGCAGCTTCC ACAGCAATGG
 Consensus  ATCAAGAAAT AACGCCGGAA CATTAGTGCA GGCAGCTTCC ACAGCAATGG

            4201                                                4250
  PLpro_WT  CATCCTGGTC ATCCAGCGGA TAGTTAATGA TCAGCCCACT GACGCGTTGC
PLproC111S  CATCCTGGTC ATCCAGCGGA TAGTTAATGA TCAGCCCACT GACGCGTTGC
 Consensus  CATCCTGGTC ATCCAGCGGA TAGTTAATGA TCAGCCCACT GACGCGTTGC

            4251                                                4300
  PLpro_WT  GCGAGAAGAT TGTGCACCGC CGCTTTACAG GCTTCGACGC CGCTTCGTTC
PLproC111S  GCGAGAAGAT TGTGCACCGC CGCTTTACAG GCTTCGACGC CGCTTCGTTC
 Consensus  GCGAGAAGAT TGTGCACCGC CGCTTTACAG GCTTCGACGC CGCTTCGTTC

            4301                                                4350
  PLpro_WT  TACCATCGAC ACCACCACGC TGGCACCCAG TTGATCGGCG CGAGATTTAA
PLproC111S  TACCATCGAC ACCACCACGC TGGCACCCAG TTGATCGGCG CGAGATTTAA
 Consensus  TACCATCGAC ACCACCACGC TGGCACCCAG TTGATCGGCG CGAGATTTAA

            4351                                                4400
  PLpro_WT  TCGCCGCGAC AATTTGCGAC GGCGCGTGCA GGGCCAGACT GGAGGTGGCA
PLproC111S  TCGCCGCGAC AATTTGCGAC GGCGCGTGCA GGGCCAGACT GGAGGTGGCA
 Consensus  TCGCCGCGAC AATTTGCGAC GGCGCGTGCA GGGCCAGACT GGAGGTGGCA

            4401                                                4450
  PLpro_WT  ACGCCAATCA GCAACGACTG TTTGCCCGCC AGTTGTTGTG CCACGCGGTT
PLproC111S  ACGCCAATCA GCAACGACTG TTTGCCCGCC AGTTGTTGTG CCACGCGGTT
 Consensus  ACGCCAATCA GCAACGACTG TTTGCCCGCC AGTTGTTGTG CCACGCGGTT

            4451                                                4500
  PLpro_WT  GGGAATGTAA TTCAGCTCCG CCATCGCCGC TTCCACTTTT TCCCGCGTTT
PLproC111S  GGGAATGTAA TTCAGCTCCG CCATCGCCGC TTCCACTTTT TCCCGCGTTT
 Consensus  GGGAATGTAA TTCAGCTCCG CCATCGCCGC TTCCACTTTT TCCCGCGTTT

            4501                                                4550
  PLpro_WT  TCGCAGAAAC GTGGCTGGCC TGGTTCACCA CGCGGGAAAC GGTCTGATAA
PLproC111S  TCGCAGAAAC GTGGCTGGCC TGGTTCACCA CGCGGGAAAC GGTCTGATAA
 Consensus  TCGCAGAAAC GTGGCTGGCC TGGTTCACCA CGCGGGAAAC GGTCTGATAA

            4551                                                4600
  PLpro_WT  GAGACACCGG CATACTCTGC GACATCGTAT AACGTTACTG GTTTCACATT
PLproC111S  GAGACACCGG CATACTCTGC GACATCGTAT AACGTTACTG GTTTCACATT
 Consensus  GAGACACCGG CATACTCTGC GACATCGTAT AACGTTACTG GTTTCACATT
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            4601                                                4650
  PLpro_WT  CACCACCCTG AATTGACTCT CTTCCGGGCG CTATCATGCC ATACCGCGAA
PLproC111S  CACCACCCTG AATTGACTCT CTTCCGGGCG CTATCATGCC ATACCGCGAA
 Consensus  CACCACCCTG AATTGACTCT CTTCCGGGCG CTATCATGCC ATACCGCGAA

            4651                                                4700
  PLpro_WT  AGGTTTTGCG CCATTCGATG GTGTCCGGGA TCTCGACGCT CTCCCTTATG
PLproC111S  AGGTTTTGCG CCATTCGATG GTGTCCGGGA TCTCGACGCT CTCCCTTATG
 Consensus  AGGTTTTGCG CCATTCGATG GTGTCCGGGA TCTCGACGCT CTCCCTTATG

            4701                                                4750
  PLpro_WT  CGACTCCTGC ATTAGGAAGC AGCCCAGTAG TAGGTTGAGG CCGTTGAGCA
PLproC111S  CGACTCCTGC ATTAGGAAGC AGCCCAGTAG TAGGTTGAGG CCGTTGAGCA
 Consensus  CGACTCCTGC ATTAGGAAGC AGCCCAGTAG TAGGTTGAGG CCGTTGAGCA

            4751                                                4800
  PLpro_WT  CCGCCGCCGC AAGGAATGGT GCATGCAAGG AGATGGCGCC CAACAGTCCC
PLproC111S  CCGCCGCCGC AAGGAATGGT GCATGCAAGG AGATGGCGCC CAACAGTCCC
 Consensus  CCGCCGCCGC AAGGAATGGT GCATGCAAGG AGATGGCGCC CAACAGTCCC

            4801                                                4850
  PLpro_WT  CCGGCCACGG GGCCTGCCAC CATACCCACG CCGAAACAAG CGCTCATGAG
PLproC111S  CCGGCCACGG GGCCTGCCAC CATACCCACG CCGAAACAAG CGCTCATGAG
 Consensus  CCGGCCACGG GGCCTGCCAC CATACCCACG CCGAAACAAG CGCTCATGAG

            4851                                                4900
  PLpro_WT  CCCGAAGTGG CGAGCCCGAT CTTCCCCATC GGTGATGTCG GCGATATAGG
PLproC111S  CCCGAAGTGG CGAGCCCGAT CTTCCCCATC GGTGATGTCG GCGATATAGG
 Consensus  CCCGAAGTGG CGAGCCCGAT CTTCCCCATC GGTGATGTCG GCGATATAGG

            4901                                                4950
  PLpro_WT  CGCCAGCAAC CGCACCTGTG GCGCCGGTGA TGCCGGCCAC GATGCGTCCG
PLproC111S  CGCCAGCAAC CGCACCTGTG GCGCCGGTGA TGCCGGCCAC GATGCGTCCG
 Consensus  CGCCAGCAAC CGCACCTGTG GCGCCGGTGA TGCCGGCCAC GATGCGTCCG

            4951                                                5000
  PLpro_WT  GCGTAGAGGA TCGAGATCTC GATCCCGCGA AATTAATACG ACTCACTATA
PLproC111S  GCGTAGAGGA TCGAGATCTC GATCCCGCGA AATTAATACG ACTCACTATA
 Consensus  GCGTAGAGGA TCGAGATCTC GATCCCGCGA AATTAATACG ACTCACTATA

            5001                                                5050
  PLpro_WT  GGGGAATTGT GAGCGGATAA CAATTCCCCT CTAGAAATAA TTTTGTTTAA
PLproC111S  GGGGAATTGT GAGCGGATAA CAATTCCCCT CTAGAAATAA TTTTGTTTAA
 Consensus  GGGGAATTGT GAGCGGATAA CAATTCCCCT CTAGAAATAA TTTTGTTTAA

            5051                                                5100
  PLpro_WT  CTTTAAGAAG GAGATATACC ATGGGCAGCA GCCATCATCA TCATCATCAC
PLproC111S  CTTTAAGAAG GAGATATACC ATGGGCAGCA GCCATCATCA TCATCATCAC
 Consensus  CTTTAAGAAG GAGATATACC ATGGGCAGCA GCCATCATCA TCATCATCAC

            5101                                                5150
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  PLpro_WT  AGCAGCGGCC TGGTGCCGCG CGGCAGCCAT CATATGGAGG TCCGCACCAT
PLproC111S  AGCAGCGGCC TGGTGCCGCG CGGCAGCCAT CATATGGAGG TCCGCACCAT
 Consensus  AGCAGCGGCC TGGTGCCGCG CGGCAGCCAT CATATGGAGG TCCGCACCAT

            5151                                                5200
  PLpro_WT  CAAAGTTTTC ACTACTGTGG ATAACATCAA CCTGCATACC CAGGTGGTTG
PLproC111S  CAAAGTTTTC ACTACTGTGG ATAACATCAA CCTGCATACC CAGGTGGTTG
 Consensus  CAAAGTTTTC ACTACTGTGG ATAACATCAA CCTGCATACC CAGGTGGTTG

            5201                                                5250
  PLpro_WT  ACATGTCTAT GACATACGGC CAGCAGTTTG GGCCAACTTA CCTGGACGGC
PLproC111S  ACATGTCTAT GACATACGGC CAGCAGTTTG GGCCAACTTA CCTGGACGGC
 Consensus  ACATGTCTAT GACATACGGC CAGCAGTTTG GGCCAACTTA CCTGGACGGC

            5251                                                5300
  PLpro_WT  GCGGACGTTA CCAAAATTAA ACCGCACAAC TCCCATGAAG GGAAAACCTT
PLproC111S  GCGGACGTTA CCAAAATTAA ACCGCACAAC TCCCATGAAG GGAAAACCTT
 Consensus  GCGGACGTTA CCAAAATTAA ACCGCACAAC TCCCATGAAG GGAAAACCTT

            5301                                                5350
  PLpro_WT  CTACGTACTG CCTAACGATG ACACCCTGCG TGTGGAAGCT TTTGAATACT
PLproC111S  CTACGTACTG CCTAACGATG ACACCCTGCG TGTGGAAGCT TTTGAATACT
 Consensus  CTACGTACTG CCTAACGATG ACACCCTGCG TGTGGAAGCT TTTGAATACT

            5351                                                5400
  PLpro_WT  ACCACACGAC CGACCCGAGT TTCCTTGGTC GTTATATGAG CGCTTTGAAC
PLproC111S  ACCACACGAC CGACCCGAGT TTCCTTGGTC GTTATATGAG CGCTTTGAAC
 Consensus  ACCACACGAC CGACCCGAGT TTCCTTGGTC GTTATATGAG CGCTTTGAAC

            5401                                                5450
  PLpro_WT  CACACCAAAA AATGGAAGTA CCCACAAGTG AACGGTCTGA CTAGCATCAA
PLproC111S  CACACCAAAA AATGGAAGTA CCCACAAGTG AACGGTCTGA CTAGCATCAA
 Consensus  CACACCAAAA AATGGAAGTA CCCACAAGTG AACGGTCTGA CTAGCATCAA

            5451                                                5500
  PLpro_WT  ATGGGCTGAT AACAATTGCT ACCTAGCTAC CGCACTGCTG ACACTGCAAC
PLproC111S  ATGGGCTGAT AACAATTCCT ACCTAGCTAC CGCACTGCTG ACACTGCAAC
 Consensus  ATGGGCTGAT AACAATTcCT ACCTAGCTAC CGCACTGCTG ACACTGCAAC

            5501                                                5550
  PLpro_WT  AGATCGAGCT GAAGTTCAAC CCGCCGGCGT TACAGGATGC TTACTACCGT
PLproC111S  AGATCGAGCT GAAGTTCAAC CCGCCGGCGT TACAGGATGC TTACTACCGT
 Consensus  AGATCGAGCT GAAGTTCAAC CCGCCGGCGT TACAGGATGC TTACTACCGT

            5551                                                5600
  PLpro_WT  GCTCGCGCCG GCGAAGCAGC TAACTTTTGC GCACTGATTC TGGCTTATTG
PLproC111S  GCTCGCGCCG GCGAAGCAGC TAACTTTTGC GCACTGATTC TGGCTTATTG
 Consensus  GCTCGCGCCG GCGAAGCAGC TAACTTTTGC GCACTGATTC TGGCTTATTG

            5601                                                5650
  PLpro_WT  TAACAAAACC GTGGGCGAAC TGGGTGATGT TCGTGAAACC ATGAGTTACC
PLproC111S  TAACAAAACC GTGGGCGAAC TGGGTGATGT TCGTGAAACC ATGAGTTACC
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 Consensus  TAACAAAACC GTGGGCGAAC TGGGTGATGT TCGTGAAACC ATGAGTTACC

            5651                                                5700
  PLpro_WT  TTTTCCAGCA CGCTAATCTG GACTCATGCA AACGCGTCCT GAACGTGGTA
PLproC111S  TTTTCCAGCA CGCTAATCTG GACTCATGCA AACGCGTCCT GAACGTGGTA
 Consensus  TTTTCCAGCA CGCTAATCTG GACTCATGCA AACGCGTCCT GAACGTGGTA

            5701                                                5750
  PLpro_WT  TGTAAAACCT GCGGTCAGCA GCAAACCACA CTCAAAGGCG TTGAAGCCGT
PLproC111S  TGTAAAACCT GCGGTCAGCA GCAAACCACA CTCAAAGGCG TTGAAGCCGT
 Consensus  TGTAAAACCT GCGGTCAGCA GCAAACCACA CTCAAAGGCG TTGAAGCCGT

            5751                                                5800
  PLpro_WT  TATGTATATG GGCACTCTGA GTTATGAGCA GTTTAAAAAA GGTGTGCAGA
PLproC111S  TATGTATATG GGCACTCTGA GTTATGAGCA GTTTAAAAAA GGTGTGCAGA
 Consensus  TATGTATATG GGCACTCTGA GTTATGAGCA GTTTAAAAAA GGTGTGCAGA

            5801                                                5850
  PLpro_WT  TCCCGTGTAC TTGCGGCAAA CAGGCTACCA AGTATCTGGT TCAGCAGGAA
PLproC111S  TCCCGTGTAC TTGCGGCAAA CAGGCTACCA AGTATCTGGT TCAGCAGGAA
 Consensus  TCCCGTGTAC TTGCGGCAAA CAGGCTACCA AGTATCTGGT TCAGCAGGAA

            5851                                                5900
  PLpro_WT  TCTCCATTCG TAATGATGAG CGCACCACCG GCGCAGTACG AACTCAAACA
PLproC111S  TCTCCATTCG TAATGATGAG CGCACCACCG GCGCAGTACG AACTCAAACA
 Consensus  TCTCCATTCG TAATGATGAG CGCACCACCG GCGCAGTACG AACTCAAACA

            5901                                                5950
  PLpro_WT  CGGGACTTTT ACTTGCGCGT CTGAATACAC AGGTAATTAC CAGTGTGGTC
PLproC111S  CGGGACTTTT ACTTGCGCGT CTGAATACAC AGGTAATTAC CAGTGTGGTC
 Consensus  CGGGACTTTT ACTTGCGCGT CTGAATACAC AGGTAATTAC CAGTGTGGTC

            5951                                                6000
  PLpro_WT  ACTACAAACA TATTACGTCC AAAGAAACTC TCTATTGCAT CGACGGCGCT
PLproC111S  ACTACAAACA TATTACGTCC AAAGAAACTC TCTATTGCAT CGACGGCGCT
 Consensus  ACTACAAACA TATTACGTCC AAAGAAACTC TCTATTGCAT CGACGGCGCT

            6001                                                6050
  PLpro_WT  CTGCTGACCA AATCGAGCGA ATACAAAGGC CCTATCACGG ATGTCTTCTA
PLproC111S  CTGCTGACCA AATCGAGCGA ATACAAAGGC CCTATCACGG ATGTCTTCTA
 Consensus  CTGCTGACCA AATCGAGCGA ATACAAAGGC CCTATCACGG ATGTCTTCTA

            6051                                                6100
  PLpro_WT  CAAAGAGAAC TCGTACACGA CCACTATCAA ACCGGTTACG TATTAGTCGA
PLproC111S  CAAAGAGAAC TCGTACACGA CCACTATCAA ACCGGTTACG TATTAGTCGA
 Consensus  CAAAGAGAAC TCGTACACGA CCACTATCAA ACCGGTTACG TATTAGTCGA

            6101                                                6150
  PLpro_WT  CAAGCTTGCG GCCGCACTCG AGCACCACCA CCACCACCAC TGAGATCCGG
PLproC111S  CAAGCTTGCG GCCGCACTCG AGCACCACCA CCACCACCAC TGAGATCCGG
 Consensus  CAAGCTTGCG GCCGCACTCG AGCACCACCA CCACCACCAC TGAGATCCGG
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            6151                                                  6200
  PLpro_WT  CTGCTAACAA AGCCCGAAAG GAAGCTGAGT TGGCTGCTGC CACCGCTGAG
PLproC111S  CTGCTAACAA AGCCCGAAAG GAAGCTGAGT TGGCTGCTGC CACCGCTGAG
 Consensus  CTGCTAACAA AGCCCGAAAG GAAGCTGAGT TGGCTGCTGC CACCGCTGAG

            6201                                                  6250
  PLpro_WT  CAATAACTAG CATAACCCCT TGGGGCCTCT AAACGGGTCT TGAGGGGTTT
PLproC111S  CAATAACTAG CATAACCCCT TGGGGCCTCT AAACGGGTCT TGAGGGGTTT
 Consensus  CAATAACTAG CATAACCCCT TGGGGCCTCT AAACGGGTCT TGAGGGGTTT

            6251                        6279
  PLpro_WT  TTTGCTGAAA GGAGGAACTA TATCCGGAT
PLproC111S  TTTGCTGAAA GGAGGAACTA TATCCGGAT
 Consensus  TTTGCTGAAA GGAGGAACTA TATCCGGAT
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7. Mass spectra of native PL^{pro} in complex with compound 34

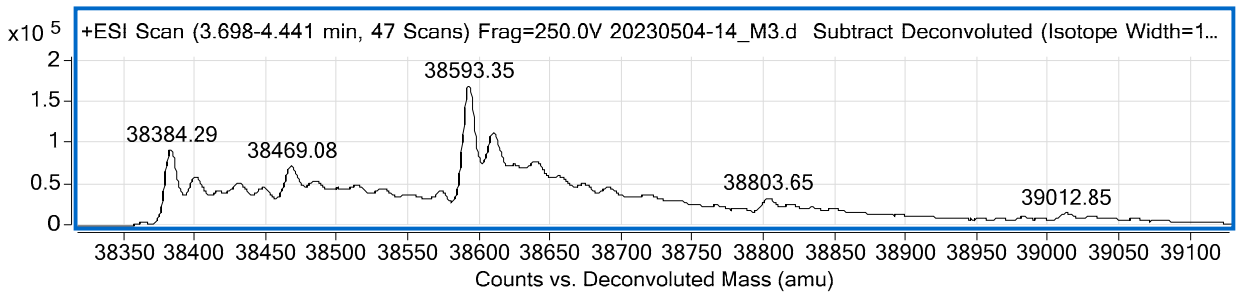

Figure S21. Mass spectra of native PL^{pro} in complex with compound **34**. The difference compared to the molecular weight of native PL^{pro} is equal to 210.11 Da. MW (native PL^{pro}) – MW (PL^{pro}-**34** complex) = 38593.35-38384.29 = 210.28) (corresponds to MW(**34**)/2 = 420.55/2 = 210.28).

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