1. Experimental Details

General: The organic solutions were concentrated by rotary evaporation at 40 ◦C under 15 Torr. Melting points were taken using a Büchi 510 apparatus (Büchi Labortechnik AG, Flawil, Switzerland) and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ or DMSO-*d*6 on a 400 MHz Brüker Avance spectrometer (Brüker BioSpin GmbH, Rheinstetten, Germany). ^{1}H chemical shifts are reported in ppm from an internal standard TMS, residual $CHCl_3$ (7.26 ppm), or DMSO (2.50 ppm). ^{13}C NMR chemical shifts are reported in ppm from an internal standard TMS, residual $CHCl_3$ (77.00 ppm), or DMSO (39.43 ppm). High resolution ESI mass spectra were measured on a Thermo Fisher Scientific Orbitrap XL system (Thermo Fisher Scientific, Waltham, MA, USA). IR spectra were acquired on an Agilent Cary 630 FTIR spectrophotometer (Agilent Technologies, 5301 Stevens Creek Blvd. CA, USA) as solids and are reported in wave numbers (cm^{-1}). Analytical thin layer chromatography (TLC) was performed with TLC plates (Merck 70–230 mesh silica gel). TLC visualization took place under a 254 nm UV light source. Purification of the reaction products was generally conducted by flash column chromatography using Merck silica gel 60. Solvents, reagents, and catalysts were used as received from the manufacturers, Thermo Scientific™ (Paisely, U.K.), Sigma-Aldrich (St. Louis, MO, USA), and Merck Chemicals GmbH (Darmstadt, Germany), except for DCM, EtOAc, and hexane, which were dried and purified according to the recommended procedures.

Synthetic Procedures

Synthesis of 2-bromo-1-(3-nitrophenyl)ethanone 2.[1,2] A solution of 1-(3-nitrophenyl)ethanone **1** (5.02 g, 28 mmol) in dry chloroform (12.5 mL) was placed in a flame dried three-necked round-bottom flask, which is connected to a hydrogen bromine trap (supersaturated aqueous solution of potassium carbonate). Subsequently, under nitrogen atmosphere, a bromine solution (4.47 g, 1.5 mL, 28 mmol) in chloroform (25 mL) was added dropwise, at a rate of one drop per second (approximately 30 minutes). The reaction mixture was stirred at room temperature for 1 hour. The solvent was removed under reduced pressure and the crude oily residue, was treated with cold ethanol 95% (20 mL) to yield **2** as a colorless microcrystalline product (6.49 g, Yield: 95%). m.p.: 90-91 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.81 (t, 1H, J = 1.9 Hz, H-2), 8.47 (ddd, 1H, J = 8.2, 2.2, 1.0 Hz, H-4), 8.33 (dt, 1H, J = 7.9, 1.3 Hz, H-6), 7.73 (t, 1H, J = 8.0 Hz, H-5), 4.48 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 189.5 (C=O), 148.5, 135.2, 134.5, 130.3, 128.2, 123.8, 30.3.

Synthesis of 1-(3-nitrophenyl)-2-(1*H*-pyrazol-1-yl)ethanone 3. A solution of compound **2** (1.0 g, 4,1 mmol) in anhydrous *N,N*-dimethylformamide (5 mL), was cooled to 0 ˚C in an ice bath. Subsequently, a solution of 1*H*-pyrazole (0.279 g, 4.1 mmol), in anhydrous *N,N*-dimethylformamide (3 mL) was added very slowly to the above solution maintaining the temperature at about 5 ˚C. After the completion of the addition, the reaction mixture was stirred for 90 hours at room temperature. The reaction quenched by the addition of a cold aqueous solution of potassium carbonate (0.285 g, 2.06 mmol, 50 mL) to set pH to 6-7. The reaction mixture was stirred for 1 hour and then extracted with ethyl acetate (3 x 5 mL). The organic phase was dried over anhydrous sodium sulfate and after the solvent was removed in vacuo, the product was purified by medium pressure column chromatography (elution solvent system: ethyl acetate/hexane, (1:3), (1:2), (1:1)) and **3** was obtained as a yellow-colored amorphous solid (0.70 g, 74%). m.p.: 125-127 °C (lit.[276] m.p. = 135-136 °C). ^{1}H NMR (400 MHz,

$CDCl_3$) *δ*: 8.79 (t, 1H, *J* = 1.7 Hz, H-2´), 8.48 (ddd, 1H, *J* = 8.2, 2.1, 1.0 Hz, H-4´), 8.31 (ddd, 1H, *J* = 7.7, 1.7, 1.1 Hz, H-6´), 7.73 (t, 1H, *J* = 8.00 Hz, H-5´), 7.61 (d, 1H, *J* = 1.6 Hz, H-5), 7.53 (d, 1H, *J* = 2.6 Hz, H-4), 6.40 (t, 1H, *J* = 2.2 Hz, H-3), 5.64 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) *δ*: 192.6 (C=O), 148.1 (C-3´), 139.1, 135.8, 134.3, 131.5, 130.7, 127.9, 122.4, 106.7, 57.9. LRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{11}H_9N_3O_3$ $[M+H]^+$: 232.06. found 231.8, m/z $[M+Na]^+$ calcd: 254.2. found: 253.8.

Synthesis of 1-(3-aminophenyl)-2-(1*H*-pyrazol-1-yl)ethanone 4. To a solution of **3** (0.66 g, 2.84 mmol) in 95% ethanol (30 mL), a suspension of iron sulfate heptahydrate (6.6 g, 28.4 mmol) in water (25 mL) was added, followed by addition of a 25% v/v aqueous ammonia solution (13 mL). The reaction mixture was refluxed for 2 hours, while additional portions of aqueous ammonia (2 x 15 mL) were added intermittently. Subsequently, the reaction mixture was filtered through a Celite pad, which further washed with hot ethanol and water. The filtrate was evaporated under reduced pressure to remove ethanol and the aqueous residue was extracted with dichloromethane (3 x 15 mL). The organic phase was washed with saturated sodium bicarbonate solution and brine and then dried over anhydrous sodium sulfate. The resulting yellow oil was recrystallized from dichloromethane and hexane to afford the amine **4** as an orange amorphous solid (549.6 mg, 96%). m.p.: 111-114 °C. IR V_{max} (cm^{-1}): 3415 (N–H, m), 3228 (=C–H, m), 2922 (C–H, m), 1695 (C=O, s), 1599 (C=C, m), 1457 (N–O, s), 1394 (C-N, s). ^{1}H NMR (400 MHz, CDCl3) *δ*: 7.59 (d, 1H, J = 1.9, H-5), 7.50 (d, 1H, J = 2.4 Hz, H-3), 7.34 (d, 1H, J = 7.7 Hz, H-6´), 7.30–7.23 (m, 2H, H-2´, H-5´), 6.92 (dd, 1H, J = 7.5, 2.0 Hz, H-4´) 6.37 (t, 1H, J = 2.1 Hz, H-4), 5.56 (s, 2H, CH2), 3.85 (s, 2H, NH2). ^{13}C NMR (100.6 MHz, DMSO-*d*6) *δ*: 193.7 (C=O), 149.2, 138.8, 135.3, 131.5, 129.3, 119.2, 115.6, 112.2, 105.4, 57.5. LRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{11}H_{11}N_{30}$ [M+H]+: 202.098, found 201.80, m/z [M+Na]+ calcd: 224.07, found 223.8.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-phenylurea 6a. In a flame dried two-necked round-bottom flask, compound **4** (50.0 mg, 0.25 mmol) was dissolved in anhydrous tetrahydrofuran (5 mL). Subsequently, freshly distilled triethylamine (0.07 mL, 0.5 mmol) was added and the reaction mixture was stirred at 0 °C for 15 min. Then, a solution of triphosgene (24.5 mg, 0.082 mmol) in anhydrous tetrahydrofuran (3 mL) was added dropwise. The reaction mixture was stirred at the same temperature for 2 hours and then, a solution of freshly distilled aniline (45.2 µL, 46.5 mg, 0.5 mmol) in anhydrous tetrahydrofuran (3 mL) was added. The resulting mixture was stirred at room temperature for 1.5 hours. Then, the mixture was added to saturated sodium bicarbonate solution (18 mL, pH = 8-9) and extracted with dichloromethane (3 x 5 mL). The organic phase was dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The oily residue was treated with cold isopropanol to afford **6a** as colorless amorphous solid (46.53 mg, 58,1 %). ^{1}H NMR (250 MHz, DMSO-*d*6) *δ*: 8.96 (s, 1H, NH, N_a), 8.75 (s, 1H, NH, N_b), 8.08 (s, 1H, H-2'), 7.72 (multiple, H-6', H-4', H-5), 7.49 (multiple, H-5', H-5'', H-4'', H-3''), 7.29 (multiple, H-2'', H-6''), 6.99 (t, 1H, J = 7,4 Hz, H-3), 6.32 (s, 1H, H-4), 5.81 (s, 2H, CH_2). ^{13}C NMR (250 MHz, DMSO-*d*6) *δ*: 193.9 (C=O), 153.0 (C=O),140.8, 139.9, 135.6, 132.0, 129.8, 129.6, 123.9, 122.5, 122.1,118.8, 117.5,105.9, 58.1 (CH_2).

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea 6b. Compound **6b** was prepared similarly to **6a**, from **4** (0.05 g, 0.25 mmol) and 4-methoxyaniline (0.062 g, 0.5 mmol), as a beige amorphous solid (0.0622 g, 71 %). m.p.: 200 – 202 °C. IR V_{max} (cm^{-1}): 3273 (N–H, m), 3003 (=C–H, m), 2933 (C–H, m), 1692 (C=O, s), 1633 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 8.85 (s, 1H, N_b–H), 8.52 (s, 1H, N_a–

H), 8.05 (s, 1H, H-2′), 7.76–7.73 (m, 2H, H-5, H-6′), 7.66 (d, 1H, *J* = 7.6 Hz, H-4′), 7.49–7.45 (m, 2H, H-3, H-5′), 7.36 (dd, 2H, *J* = 8.9, 2.0 Hz, H-2′′, H-6′′), 6.87 (dd, 2H, *J* = 9.0, 2.0 Hz, H-3′′, H-5′′), 6.31 (t, 1H, *J* = 2.0 Hz, H-4), 5.79 (s, 1H, CH_2), 3.71 (s, 3H, OMe). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.5 (C=O), 154.6 (C-4′′), 152.7 ($(NH)_2C$=O), 140.5, 138.9, 135.1, 132.5, 131.6, 129.4, 123.4, 121.5, 120.3 (2C, C-3′′, C-5′′), 116.9, 114.0 (2C, C-2′′, C-6′′), 105.5, 57.6, 55.2. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{19}H_{18}N_4O_3$ $[M+H]^+$: 351.1452. found: 351.1432, m/z $[M+Na]^+$ calcd: 373.1271. found: 373.1249, m/z $[2M+H]^+$ calcd: 701.2831. found: 701.2798.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-fluorophenyl)urea 6c. Compound **6c** was prepared similarly to **6a**, from **4** (0.1 g, 0.497 mmol) and 4-fluoroaniline (95.9 µL, 0.994 mmol) after stirring for 60 h at room temperature, as an amorphous light yellow solid (0.142 g, 85 %). m.p.: 186-189 °C. IR V_{max} (cm^{-1}): 3301 (N–H, m), 3106 (=C–H, m), 2925 (C–H, m), 1691 (C=O, s), 1654 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 8.96 (s, 1H, N_b–H), 8.79 (s, 1H, N_a–H), 8.07 (t, 1H, *J* = 1.9 Hz, H-2′), 7.78–7.74 (m, 2H, H-5, H-6′), 7.68 (dt, 1H, *J* = 7.8, 1.2 Hz, H-4′), 7.50–7.47 (m, 4H, H-3, H-5′, H-2′′, H-6′′), 7.13 (m, 2H, H-3′′, H-5′′), 6.31 (t, 1H, *J* = 2.1 Hz, H-4), 5.80 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.4 (C=O), 156.3 (C-4′′), 152.6 ($(NH)_2C$=O), 140.3, 138.9, 135.8, 135.1, 131.5, 129.4, 123.5, 121.7, 120.2, 120.2, 117.1, 115.4, 115.2, 105.5, 57.6. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{18}H_{15}FN_4O_2$ $[M+H]^+$: 339.1252. found: 339.1239, m/z $[M+Na]^+$ calcd: 361.1071. found: 361.1056, m/z $[2M+Na]^+$ calcd: 699.2250. found: 699.2236, m/z $[2M+H]^+$ calcd: 677.2430. found: 699.2420.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea 6d. Compound **6d** was prepared similarly to **6a**, from **4** (0.2 g, 0.994 mmol) and 4-chloroaniline (0.254 g, 1.988 mmol) after stirring for 60 h at room temperature, as an amorphous yellow solid (0.303 g, 86 %). m.p.: 207-209 °C. IR V_{max} (cm^{-1}): 3299 (N–H, m), 3107 (=C–H, m), 2922 (C–H, m), 1691 (C=O, s), 1632 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 8.98 (s, 1H, N_b–H), 8.88 (s, 1H, N_a–H), 8.06 (t, 1H, *J* = 2.0 Hz, H-2′), 7.77–7.74 (m, 2H, H-5, H-6′), 7.69 (d, 1H, *J* = 7.5 Hz, H-4′), 7.51–7.48 (m, 4H, H-3, H-5′, H-3′′, H-5′′), 7.33 (d, 2H, *J* = 8.8 Hz, H-2′′, H-6′′), 6.31 (t, 1H, *J* = 2.1 Hz, H-4), 5.80 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.41 (C=O), 152.4 ($(NH)_2C$=O), 140.2, 138.9, 138.5, 135.1, 131.5, 129.4, 128.6 (2C, C-3′′, C-5′′), 125.6, 123.6, 121.9, 119.9 (2C, C-2′′, C-6′′), 117.2, 105.5, 57.9. HRMS (ESI) (0.1% HCOOH σε MeOH): m/z calcd $C_{18}H_{15}ClN_4O_2$ $[M+H]^+$: 355.0957. found: 355.0950, m/z $[M+Na]^+$ calcd: 377.0776. found: 377.0768, m/z $[2M+Na]^+$ calcd: 731.1660. found: 731.1655.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea 6e. Compound **6e** was prepared similarly to **6a**, from **4** (0.08 g, 0.398 mmol) and 4-bromoaniline (0.137 g, 0.796 mmol) after stirring for 68 h at room temperature, as an amorphous beige solid (0.087 g, 64 %). m.p.: 216-218 °C. IR V_{max} (cm^{-1}): 3300 (N–H, m), 3110 (=C–H, m), 2927 (C–H, m), 1691 (C=O, s), 1635 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 9.05 (s, 1H, N_b–H), 8.95 (s, 1H, N_a–H), 8.08 (s, 1H, H-2′), 7.78–7.68 (m, 3H, H-5, H-4′, H-6′), 7.51–7.46 (m, 6H, H-3, H-5′, H-2′′, H-3′′, H-5′′, H-6′′), 6.31 (s, 1H, H-4), 5.81 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.4 (C=O), 152.4 ($(NH)_2C$=O), 140.2, 139.0, 138.9, 135.1, 131.5, 131.5 (2C, C-3′′, C-5′′), 129.4, 123.6, 121.9, 120.3 (2C, C-2′′, C-6′′), 117.2, 113.4, 105.5, 57.6. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{18}H_{15}BrN_4O_2$ $[M+H]^+$: 399.0451. found: 399.0432.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea 6f. Compound **6f** was prepared similarly to **6a**, from **4** (0.2 g, 0.994 mmol) and 4-morpholinoaniline (0.354 g, 1.988 mmol) after stirring for 60 h at room temperature, as an amorphous oil-colored solid (0.299 g, 74 %). m.p.: 204-205 °C. IR V_{max} (cm^{-1}): 3278 (N–H, m), 3127 (=C–H, m), 2995 (C–H, m), 1701 (C=O, s), 1636 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.84 (s, 1H, N_b–H), 8.47 (s, 1H, N_a–H), 8.05 (t, 1H, J = 2.0 Hz, H-2´), 7.76–7.74 (m, 2H, H-5, H-6´), 7.66 (d, 1H, J = 7.7 Hz, H-4´), 7.49–7.45 (m, 2H, H-3, H-5´), 7.32 (d, 2H, J = 8.9 Hz, H-2´´, H-6´´), 6.89 (d, 2H, J = 9.0 Hz, H-3´´, H-5´´), 6.31 (t, 1H, J = 2.1 Hz, H-4), 5.80 (s, 2H, CH_2) 3.73 (t, 4H, J = 4.8 Hz, H-3´´´, H-5´´´), 3.03 (t, 4H, J = 4.9 Hz, H-2´´´, H-6´´´). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.5 (C=O), 152.7 ($(NH)_2C$=O), 146.6, 140.6, 138.9, 155.1, 131.7, 131.5, 129.3, 123.3, 121.4, 119.8 (2C, C-2´´, C-6´´), 116.9, 115.8 (2C, C-3´´, C-5´´), 105.5, 66.1, 57.6 (2C, C-3´´´, C-5´´´), 49.2 (2C, C-2´´´, C-6´´´). HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{22}H_{23}N_5O_3$ $[M+H]^+$: 406.1874. found: 4061858, m/z $[M+Na]^+$ calcd: 428.1693. found: 428.1677, m/z $[2M+Na]^+$ calcd: 833.3494. found: 833.3474.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-fluorophenyl)urea 6g. Compound **6g** was prepared similarly to **6a**, from **4** (0.1 g, 0.497 mmol) and 2-fluoroaniline (95.9 µL, 0.994 mmol) after stirring for 60 h at room temperature, as an amorphous light yellow solid (0.073 g, 43 %). m.p.: 186-189 °C. IR V_{max} (cm^{-1}): 3310 (N–H, m), 3114 (=C–H, m), 2964 (C–H, m), 1697 (C=O, s), 1652 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.39 (s, 1H, N_a–H), 8.60 (s,1H, N_b–H), 8.14 (td, 1H, J = 8.6, 1.6 Hz, H-6´´), 8.07 (t, 1H, J = 2.0 Hz, H-2´), 7.77–7.74 (m, 2H, H-5, H-6´), 7.71 (ddd, 1H, J = 7.6, 1.8, 1.0 Hz, H-4´), 7.53–7.48 (m, 2H, H-3, H-5´), 7.24 (ddd, 1H, J = 8.2, 3.6, 1.6 Hz, H-4´´), 7.15 (t, 1H, J = 7.7 Hz, H-5´´), 7.05-7.00 (m, 1H, H-3´´), 6.32 (t, 1H, J = 2.0 Hz, H-4), 5.81 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.4 (C=O), 153.3 (C-2´´), 152.2 ($(NH)_2C$=O), 140.0, 138.9, 135.2, 131.5, 129.5, 127.2, 124.5, 123.3, 122.8, 121.9, 120.8, 116.9, 115.1 105.5, 57.5. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{18}H_{15}FN_4O_2$ $[M+H]^+$: 339.1252. found: 339.1236, m/z $[M+Na]^+$ calcd: 361.1071. found: 361.1052, m/z $[2M+Na]^+$ calcd: 699.2250. found: 699.2224. m/z $[2M+H]^+$ calcd: 677.2431. found: 677.2408.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-cyanophenyl)urea 6h. Compound **6h** was prepared similarly to **6a**, from **4** (0.08 g, 0.398 mmol) and 2-cyanoaniline (0.094 g, 0.796 mmol) after stirring for 68 h at room temperature, as an amorphous beige solid (0.021 g, 15 %). m.p.: 198-201 °C. IR V_{max} (cm^{-1}): 3339 (N–H, m), 3048 (=C–H, m), 2930 (C–H, m), 2229 (CN nitrile, m), 1686 (C=O, s). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.68 (s, 1H, N_a–H), 8.80 (s, 1H, N_b–H), 8.13–8.03 (m, 2H, H-2´, H-6´), 7.80–7.72 (m, 4H, H-6´´ H-5, H-4´, H-5´´), 7.66 (t, 1H, J = 8.0 Hz, H-5´), 7.54–7.48 (m, 2H, H-3´´, H-3), 7.21 (t, 1H, J = 7.3 Hz, H-4´´), 6.31 (s, 1H, H-4), 5.82 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.4 (C=O), 152.1 ($(NH)_2C$=O), 141.7, 139.9, 138.9, 135.2, 134.0, 133.2, 131.6, 129.6, 123.6, 123.4, 122.3, 121.6, 117.2, 116.9, 105.6, 102.5, 57.6. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{19}H_{15}N_5O_2$ $[M+H]^+$: 346.1299. found: 346.1289, m/z $[M+Na]^+$ calcd: 368.1118. found: 368.1107, m/z $[M+K]^+$ calcd: 384.0858. found: 384.0846.

Synthesis of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methyl-3-nitrophenyl)urea 6i. Compound **6i** was prepared similarly to **6a**, from **4** (0.08 g, 0.398 mmol) and 2-cyanoaniline (0.121 g, 0.796 mmol) after stirring for 68 h at room temperature, as an amorphous mustard-colored solid (0.066 g, 48 %). m.p.: 210-212 °C. IR V_{max} (cm^{-1}): 3349 (N–H, m), 3064 (=C–H, m), 2927 (C–H, m), 1684 (C=O, s), 1522 (N–O asym, s), 1308 (N–O sym,

s). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.30 (s, 1H, N_a–H), 9.26 (s, 1H, N_b–H), 8.31 (s, 1H, H-2´), 8.11 (s, 1H, H-2´´), 7.75–7.71 (m, 3H, H-5, H-6´, H-6´´), 7.59–7.37 (m, 4H, H-3, H-4´, H-5´, H-5´´), 6.32 (s, 1H, H-4), 5.82 (s, 2H, CH_2), 2.45 (s, 3H, Me). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 193.4 (C=O), 152.5 ($(NH)_2C$=O), 148.8 (C-3´´), 140.1, 138.9, 138.6, 135.2, 133.0, 131.6, 129.4, 125.7, 123.7, 123.0, 122.0, 117.3, 113.4, 105.5, 57.6, 19.1 (Me). HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{19}H_{17}N_5O_4$ $[M+H]^+$: 380.1353. calcd: 380.1332, m/z $[M+Na]^+$ calcd: 402.1173. calcd: 402.1149, m/z $[M+K]^+$ calcd: 418.0913. Βρέθηκε: 418.0888.

Synthesis of 1-(3-nitrophenyl)-2-(2*H*-1,2,3-triazol-1-yl)ethanone 7a and 1-(3-nitrophenyl)-2-(1*H*-1,2,3-triazol-1-yl)ethanone 7b. In a flame dried two-necked round-bottom flask under nitrogen atmosphere, 1*H*-1,2,3-triazole (235.2 µL, 3.932 mmol) and *N,N*-diisopropylethylamine (680 µL, 3.932 mmol) were stirred at room temperature for 30 min. Then, a solution of **2** (800 mg, 3.276 mmol) in anhydrous acetonitrile (4 mL) was added and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was extracted with ethyl acetate (3 x 15 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was treated with cold ethyl acetate to precipitate the 1*H*-isomer **7b** as a colorless amorphous solid (279.8 mg, 37%). The filtrate was further purified by medium pressure column chromatography [eluent system: ethyl acetate/hexane, (1:2), (1:1), (EtOAc)], which gave the 2*H*-isomer **7a**, which was further recrystallized from ethyl acetate and hexane to yield yellow needle-like crystals of **7a** (122.7 mg, 16%).
7a: m.p.: 125-126 ^{o}C. IR V_{max} (cm^{-1}): 3095 (C–H triazole, m), 2973 (=C–H, m), 2933 (C–H, m), 1699 (C=O, s), 1615 (C=C, m), 1541 (N–O asym, s), 1348 (N–O sym, s). ^{1}HNMR (400 MHz, DMSO-d_6) δ: 8.73 (t, 1H, J = 2.0 Hz, H-2'), 8.54 (ddd, 1H, J = 8.2, 2.3, 1.0 Hz, H-4´), 8.45 (dt, 1H, J = 7.8, 1.7 Hz, H-6´), 7.92–7.88 (m, 3H, H-5´, H-4, H-5), 6.38 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 191.6 (C=O), 148.1, 135.3, 135.2 (2C, C-3, C-4), 134.4, 130.7, 128.2, 122.7, 60.6.
7b: m.p.: 161-162 ^{o}C. IR V_{max} (cm^{-1}): 3158 (C–H triazole, m), 3093 (=C–H, m), 2984 (C–H, m), 1713 (C=O, s), 1611 (C=C, m), 1529 (N–O asym, s), 1357 (N–O sym, s). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.77 (t, 1H, J = 2.0 Hz, H-2´), 8.56 (ddd, 1H, J = 8.2, 2.4, 1.0 Hz, H-4´), 8.49 (dt, 1H, J = 7.8, 1.6 Hz, H-6´), 8.11 (d, 1H, J = 1.0 Hz, H-5), 7.92 (t, 1H, J = 8.0 Hz, H-5´), 7.82 (d, 1H, J = 0.9 Hz, H-4), 6.33 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 191.2 (C=O), 148.1, 135.4, 134.4, 133.4, 130.8, 128.2, 126.5, 122.6, 55.9.

Synthesis of 1-(3-aminophenyl)-2-(2*H*-1,2,3-triazol-1-yl)ethanone 8a. In a two-necked round-bottom flask, compound **7a** (146 mg, 0.629 mmol) was dissolved in isopropanol (15 mL). A suspension of ferric sulfate heptahydrate (1.75 g, 6.29 mmol) in water (7 mL) was added to the stirred solution, followed by the addition of a solution of 25% v/v aqueous ammonia (3 mL). The resulting mixture was heated to reflux for 2 h, while additional portions of 25% v/v aqueous ammonia (2 x 4 mL) were added intermittently. The excess of ammonia was neutralized with a trap of 2N aqueous hydrochloric acid under vacuum. Subsequently, the reaction mixture was filtered through a Celite pad, which further washed with hot methanol. The filtrate was evaporated under reduced pressure to remove ethanol and the aqueous residue was extracted with ethyl acetate (3 x 5 mL). The organic phase was washed with saturated sodium bicarbonate solution and brine and then dried over anhydrous sodium sulfate. The desiccant was removed by filtration and after evaporation of the solvent under reduced pressure, amine **8a** was obtained as a beige amorphous solid (118.4 mg, 93%); m.p.: 155-157 ^{o}C. IR V_{max} (cm^{-1}): 3433 (N–H, m), 3341 (C–H triazole, m), 3206, 3123 (=C–H, m), 2978 (C–H, m), 1701 (C=O, s), 1602 (C=C, m).

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.85 (s, 2H, H-4, H-5), 7.22–7.19 (m, 2H, H-5´, H-6´), 7.14 (d, 1H, J = 1.5 Hz, H-2´), 6.88 (dt, 1H, J = 5.4, 2.5 Hz, H-4´), 6.09 (s, 2H, NH_2), 5.42 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.8 (C=O), 149.2, 135.0, 134.9 (2C, C-3, C-4), 129.3, 119.5, 115.9, 112.1, 60.3.

Synthesis of 1-(3-aminophenyl)-2-(1*H*-1,2,3-triazol-1-yl)ethanone 8b. In a two-necked round-bottom flask, compound **7b** (100 mg, 0.43 mmol) was dissolved in methanol (5 mL) and then stannous chloride dihydrate (0.485 mg, 2.15 mmol) was added. The reaction mixture was heated at 55-60 °C under nitrogen for 3 h. Then, the solvent was evaporated under reduced pressure and the residue was treated with saturated aqueous sodium carbonate solution to pH 8. The aqueous solution was extracted with ethyl acetate (3 x 5 mL) and dried with anhydrous sodium sulfate. Finally, the desiccant was removed by filtration and after evaporation of the solvent under reduced pressure, amine **8a** was obtained, as a salmon-colored amorphous solid (76 mg, 87%). m.p.: 142-144 °C. IR V_{max} (cm^{-1}): 3458 (N–H, m), 3368 (C–H triazole, m), 3223, 3127 (=C–H, m), 2984 (C–H, m), 1691 (C=O, s), 1635 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.09 (s, 1H, H-4), 7.78 (s, 1H, H-5), 7.29–7.21 (m, 2H, H-5´, H-6´), 7.20 (t, 1H, J = 1.9 Hz, H-2´), 6.90 (dt, 1H, J = 7.0, 2.1 Hz, H-4´), 6.08 (s, 2H, CH_2), 5.45 (s, 2H, NH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.3 (C=O), 149.3, 134.9, 133.1, 129.4, 126.5, 119.5, 115.8, 112.2, 55.5.

Synthesis of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea 11a. In a flame dried two-necked round-bottom flask, compound **8a** (0.050 g, 0.247 mmol) was dissolved in anhydrous tetrahydrofuran (2 mL). Subsequently, freshly distilled triethylamine (69 µL, 0.495 mmol) was added and the reaction mixture was stirred at 0 °C for 15 min. Then, a solution of triphosgene (24.4 mg, 0.082 mmol) in anhydrous tetrahydrofuran (3 mL) was added dropwise. The reaction mixture was stirred at the same temperature for 2 hours and then, a solution of 4-methoxyaniline (61.0 mg, 0.495 mmol) in anhydrous tetrahydrofuran (3 mL) was added. The resulting mixture was stirred at room temperature for 48 hours. Then, the mixture was added to saturated sodium bicarbonate solution (18 mL, pH = 8-9) and extracted with ethyl acetate (3 x 5 mL). The organic phase was dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The oily residue was treated with cold isopropanol to afford **11a** as a brown amorphous solid (58.8 mg, 68 %), m.p.: 203-205 °C. IR V_{max} (cm^{-1}): 3282 (N–H, m), 3132 (=C–H, m), 2940 (C–H, m), 1697 (C=O, s), 1636 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.02 (s, 1H, N_b–H), 8.70 (s, 1H, N_a–H), 8.04 (s, 1H, H-2´), 7.88 (s, 2H, H-4, H-5), 7.79 (d, 1H, J = 7.8 Hz, H-6´), 7.68 (d, 1H, J = 7.4 Hz, H-4´), 7.48 (t, 1H, J = 7.8 Hz, H-5´), 7.37 (d, 2H, J = 8.6 Hz, H-2´´, H-6´´), 6.87 (d, 2H, J = 8.6 Hz, H-3´´, H-5´´), 6.20 (s, 2H, CH_2), 3.71 (s, 3H, OMe). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.5 (C=O), 154.6 (C-4´´), 152.8 ((NH)$_2$C=O), 140.7, 135.0 (2C, C-4, C-5), 134.8, 132.5, 129.4, 123.7, 121.8, 120.2 (2C, C-2´´, C-6´´), 116.6, 114.0 (2C, C-3´´, C-5´´), 66.4, 55.2. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd: $C_{18}H_{17}O_3N_5$ [M+H]$^+$: 352.1404. found: 352.1412, m/z [M+Na]$^+$ calcd: 374.1224. found: 374.1230, m/z [M+2K+H]$^+$ calcd: 428.0521. found: 428.1713.

Synthesis of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea 11b. Compound **11b** was prepared similarly to **11a**, from **8b** (0.100 g, 0.495 mmol) and 4-methoxyaniline (0.122 g, 0.99 mmol), as a brown amorphous solid (0.0599 g, 35 %). m.p.: 195-197 °C. IR V_{max} (cm^{-1}): 3283 (N–H, m), 3098 (=C–H, m), 2940 (C–H, m), 1696 (C=O, s), 1636 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.91 (s, 1H, N_b–H), 8.57 (s, 1H, N_a–H), 8.12 (m, 2H, H-2´, H-5), 7.80–7.71 (m, 3H, H-4, H-4´, H-6´), 7.51 (t, 1H, J = 7.6 Hz, H-5´), 7.38 (d,

2H, *J* = 8.1 Hz, H-2′′, H-6′′), 6.88 (d, 2H, *J* = 8.1 Hz, H-3′′, H-5′′), 6.18 (s, 2H, CH_2), 3.72 (s, 3H, OMe). ^{13}C NMR (100.6 MHz, DMSO-d_6) *δ*: 192.1 (C=O), 154.7 (C-4′′), 152.2 ($(NH)_2C$=O), 140.6, 134.7, 133.21, 132.4, 129.4, 126.5, 123.7, 121.7, 120.3 (2C, C-2′′, C-6′′), 117.0, 114.0 (2C, C-3′′, C-5′′), 55.6, 55.2. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{18}H_{17}N_5O_3$ [M+H]$^+$: 352.1404. Βρέθηκε: 352.1390, m/z [M+Na]$^+$ calcd: 374.1223. found: 374.1207, m/z [2M+Na]$^+$ calcd: 725.2554. found: 725.2528, m/z [2M+H]$^+$ calcd: 703.2735. found: 703.2709.

Synthesis of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea 11c. Compound **11c** was prepared similarly to **11a**, from **8a** (0.080 g, 0.396 mmol) and 4-chloroaniline (0.101 g, 0.792 mmol), as a brown amorphous solid (0.0634 g, 45 %). m.p.: 220-222 °C. IR V_{max} (cm^{-1}): 3283 (N–H, m), 3117 (=C–H, m), 2946 (C–H, m), 1697 (C=O, s), 1637 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 8.99 (s, 1H, N_b–H), 8.90 (s, 1H, N_a–H), 8.04 (s, 1H, H-2′), 7.87 (s, 2H, H-4, H-5), 7.79 (d, 1H, *J* = 8.2 Hz, H-6′), 7.71 (d, 1H, *J* = 7.0 Hz, H-4′), 7.51–7.48 (m, 3H, *J* = 7.6 Hz, H-5′, H-2′′, H-6′′), 7.33 (d, 2H, *J* = 8.3 Hz, H-3′′, H-5′′), 6.20 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) *δ*: 192.5 (C=O), 152.4 ((NH2C=O), 140.2, 138.5, 135.0 (2C, C-4, C-5), 134.7, 129.4, 128.6 (2C, C-3′′, C-5′′), 125.6, 123.9, 122.2, 119.9 (2C, C-2′′, C-6′′), 117.2, 60.4. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{17}H_{14}ClN_5O_2$ [M+H]$^+$: 356.0909. found: 356.0898, m/z [M+Na]$^+$ calcd: 378.0728. found: 378.0717, m/z [M+K]$^+$ calcd: 394.0468. found: 394.3495, m/z [2M+Na]$^+$ calcd: 733.1564. found: 733.1545.

Synthesis of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea 11d. Compound **11d** was prepared similarly to **11a**, from **8b** (0.100 g, 0.495 mmol) and 4-chloroaniline (0.126 g, 0.99 mmol), as a colorless amorphous solid (0.0717 g, 41 %). m.p.: > 220 °C, IR V_{max} (cm^{-1}): 3319 (N–H, m), 3282, 3195 (C–H triazole, m), 3117 (=C–H, m), 2938 (C–H, m), 1691 (C=O, s), 1603 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 9.70 (s, 1H, N_b–H), 9.63 (s, 1H, N_a–H), 8.18–8.12 (m, 2H, H-2′, H-5), 7.80–7.73 (m, 3H, H-4, H-4′, H-6′), 7.53–7.51 (m, 3H, H-5′, H-2′′, H-6′′), 7.33 (d, 2H, *J* = 8.7 Hz, H-3′′, H-5′′), 6.18 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) *δ*: 192.1 (C=O), 152.7 ($(NH)_2C$=O), 140.5, 138.7, 134.8, 133.2, 129.5, 128.7 (2C, C-3′′, C-5′′), 126.6, 125.4, 123.6, 122.0, 119.6 (2C, C-2′′, C-6′′), 115.9, 55.6. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{17}H_{14}ClN_5O_2$ [M+H]$^+$: 356.0909. found: 356.0892, m/z [M+Na]$^+$ calcd: 378.0728. found: 378.0709, m/z [2M+H]$^+$ calcd: 711.1745. found: 711.1716.

Synthesis of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea 11e. Compound **11e** was prepared similarly to **11a**, from **8a** (0.080 g, 0.396 mmol) and 4-bromoaniline (0.136 g, 0.792 mmol), as a brown amorphous solid (0.101 g, 64 %). m.p.: > 220 °C, IR V_{max} (cm^{-1}): 3293 (N–H, m), 3125 (=C–H, m), 2945 (C–H, m), 1697 (C=O, s), 1633 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.21 (s, 1H, N_b–H), 9.13 (s, 1H, N_a–H), 8.05 (s, 1H, H-2′), 7.87 (s, 2H, H-4, H-5), 7.78 (d, 1H, *J* = 8.5 Hz, H-6′), 7.70 (d, 1H, *J* = 7.1 Hz, H-4′), 7.52–7.45 (m, 5H, H-5′, H-2′′, H-6′′, H-3′′, H-5′′), 6.20 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.5 (C=O), 152.5 ((NH_2C=O), 140.3, 139.0, 135.0 (2C, C-4, C-5), 134.8, 131.5 (2C, C-3′′, C-5′′), 129.4, 123.9, 123.8, 122.1, 120.2 (2C, C-2′′, C-6′′), 117.1, 113.4, 60.4. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{17}H_{14}BrN_5O_2$ [M+H]$^+$: 400.0404. found: 400.0383, m/z [M+Na]$^+$ calcd: 422.0223. found: 422.0202.

Synthesis of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea 11f. Compound **11f** was prepared similarly to **11a**, from **8b** (0.100 g, 0.495 mmol) and 4-bromoaniline (0.170 g, 0.99 mmol), as a colorless amorphous solid (0.0763 g, 39 %). m.p.: 220-222 °C. IR V_{max} (cm^{-1}): 3317 (N–H, m), 3280, 3199 (C–H triazole,

m), 3117 (=C–H, m), 2938 (C–H, m), 1691 (C=O, s), 1604 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.34 (s, 1H, N_b–H), 9.23 (s, 1H, N_a–H), 8.15–8.10 (m, 2H, H-2′, H-5), 7.79–7.75 (m, 3H, H-4, H-4′, H-6′), 7.54–7.46 (m, 5H, H-5′, H-2′′, H-6′′, H-3′′, H-5′′), 6.17 (s, 2H, CH_2). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.0 (C=O), 152.5 ($(NH)_2C$=O), 140.4, 139.1, 134.7, 133.2, 131.5 (2C, C-3′′, C-5′′), 129.5, 126.5, 123.8, 121.9, 120.2 (2C, C-2′′, C-6′′), 117.1, 113.3, 55.6. HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{17}H_{14}BrN_5O_2$ $[M+H]^+$: 400.0404. found: 400.0382.

Synthesis of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea 11g. Compound **11g** was prepared similarly to **11a**, from **8a** (0.050 g, 0.247 mmol) and 4-morpholinoaniline (0.088 g, 0.495 mmol), as an oil-colored amorphous solid (0.085 g, 85 %). m.p.: 213-215 °C. IR V_{max} (cm^{-1}): 3389 (C–H triazole, m), 3276 (N–H, m), 3133 (=C–H, m), 2963 (C–H, m), 1697 (C=O, s), 1648 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.09 (s, 1H, N_b–H), 8.71 (s, 1H, N_a–H), 8.04 (s, 1H, H-2′), 7.88 (s, 2H, H-4, H-5), 7.78 (d, 1H, J = 7.7 Hz, H-6′), 7.67 (d, 1H, J = 7.3 Hz, H-4′), 7.48 (t, 1H, J = 7.7 Hz, H-5′), 7.33 (d, 2H, J = 8.4 Hz, H-2′′, H-6′′), 6.89 (d, 2H, J = 8.4 Hz, H-3′′, H-5′′), 6.20 (s, 2H, CH_2), 3.73 (t, 4H, J = 4.8 Hz, H-2′′′, H-6′′′), 3.02 (t, 4H, J = 4.9 Hz H-3′′′, H-5′′′). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.5 (C=O), 152.7 ($(NH)_2C$=O), 146.6, 140.7, 135.0 (2C, C-4, C-5), 134.8, 131.8, 129.4, 123.5, 121.7, 119.7 (2C, C-2′′, C-6′′), 116.8, 115.8 (2C, C-3′′, C-5′′), 66.2, 49.2 (2C, C-3′′′, C-5′′′). HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd for $C_{21}H_{22}N_6O_3$ $[M+H]^+$: 407.1826. found: 407.1804, m/z $[M+Na]^+$ calcd: 429.1645. found: 429.1623.

Synthesis of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea 11h. Compound **11h** was prepared similarly to **11a**, from **8b** (0.100 g, 0.495 mmol) and 4-morpholinoaniline (0.176 g, 0.99 mmol), as an oil-colored amorphous solid (0.105 g, 52 %). m.p.: 211-216 °C. IR V_{max} (cm^{-1}): 3285 (N–H, m), 3099 (=C–H, m), 2950 (C–H, m), 1697 (C=O, s), 1647 (C=C, m). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.38 (s, 1H, N_b–H), 8.96 (s, 1H, N_a–H), 8.16–8.12 (m, 2H, H-2′, H-5), 7.80–7.70 (m, 3H, H-4, H-4′, H-6′), 7.50 (t, 1H, J = 8.1 Hz, H-5′), 7.35 (d, 2H, J = 8.5 Hz, H-2′′, H-6′′), 6.89 (d, 2H, J = 8.5 Hz, H-3′′, H-5′′), 6.18 (s, 2H, CH_2), 3.72 (s, 4H, H-2′′′, H-6′′′), 3.02 (s, 4H, H-3′′′, H-5′′′). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ: 192.1 (C=O), 152.8 ($(NH)_2C$=O), 146.6, 140.9, 134.7, 133.2, 131.9, 129.4, 126.6, 123.5, 121.5, 119.7 (2C, C-4, C-5), 116.7, 115.9 (2C, C-2′′, C-6′′), 66.2 (2C, C-3′′, C-5′′), 55.6, 49.2 (2C, C-3′′′, C-5′′′). HRMS (ESI) (0.1% HCOOH in MeOH): m/z calcd $C_{21}H_{22}N_6O_3$ $[M+Na]^+$: 429.1645. found: 429.1628, m/z $[M+MeOH+H]^+$ calcd: 439.2088. found: 439.2069, m/z $[2M+Na]^+$ calcd: 725.2554. found: 725.2528.

2. NMR and MS Spectra

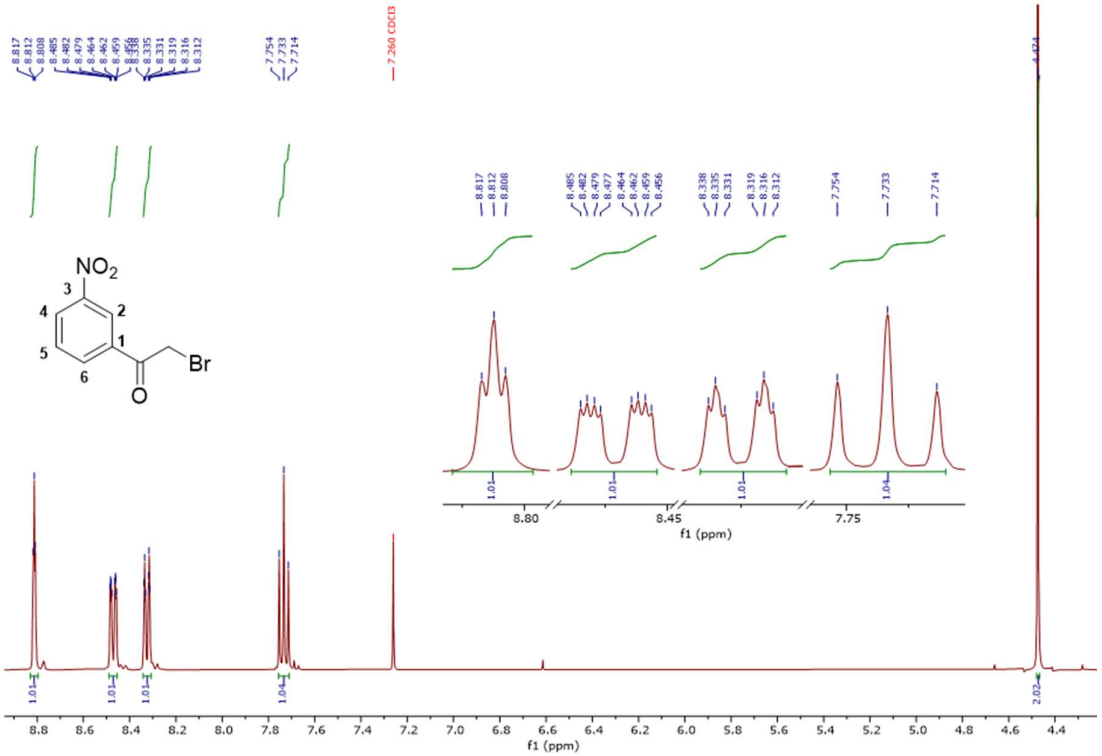

Figure S1. ^{1}H-NMR spectrum of 2-bromo-1-(3-nitrophenyl)ethanone **2**

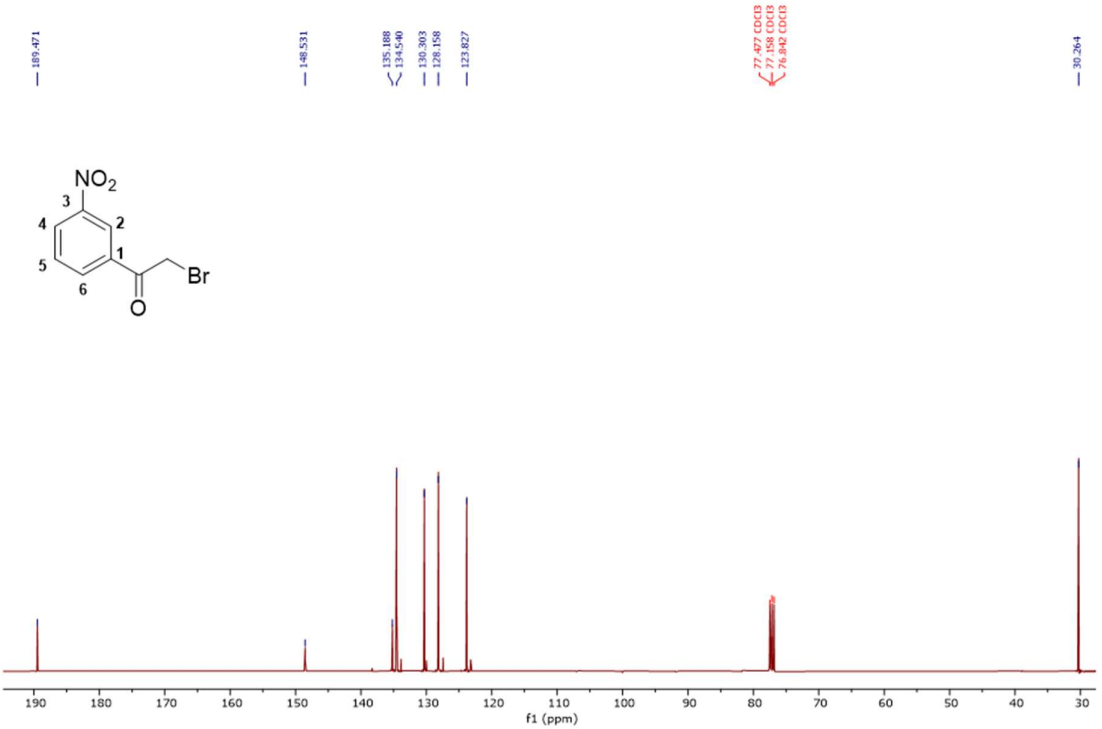

Figure S2. ^{13}C-NMR spectrum of 2-bromo-1-(3-nitrophenyl)ethanone **2**

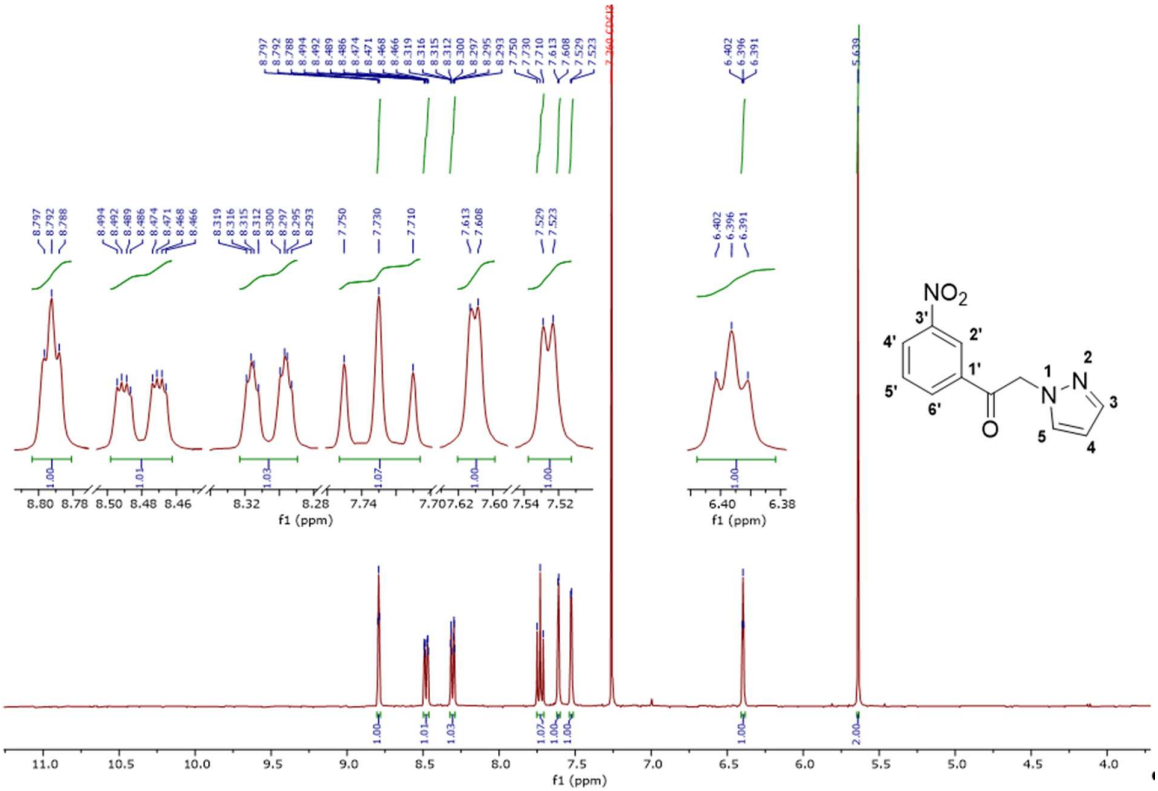

Figure S3. ^{1}H-NMR spectrum of 1-(3-nitrophenyl)-2-(1*H*-pyrazol-1-yl)ethanone **3**

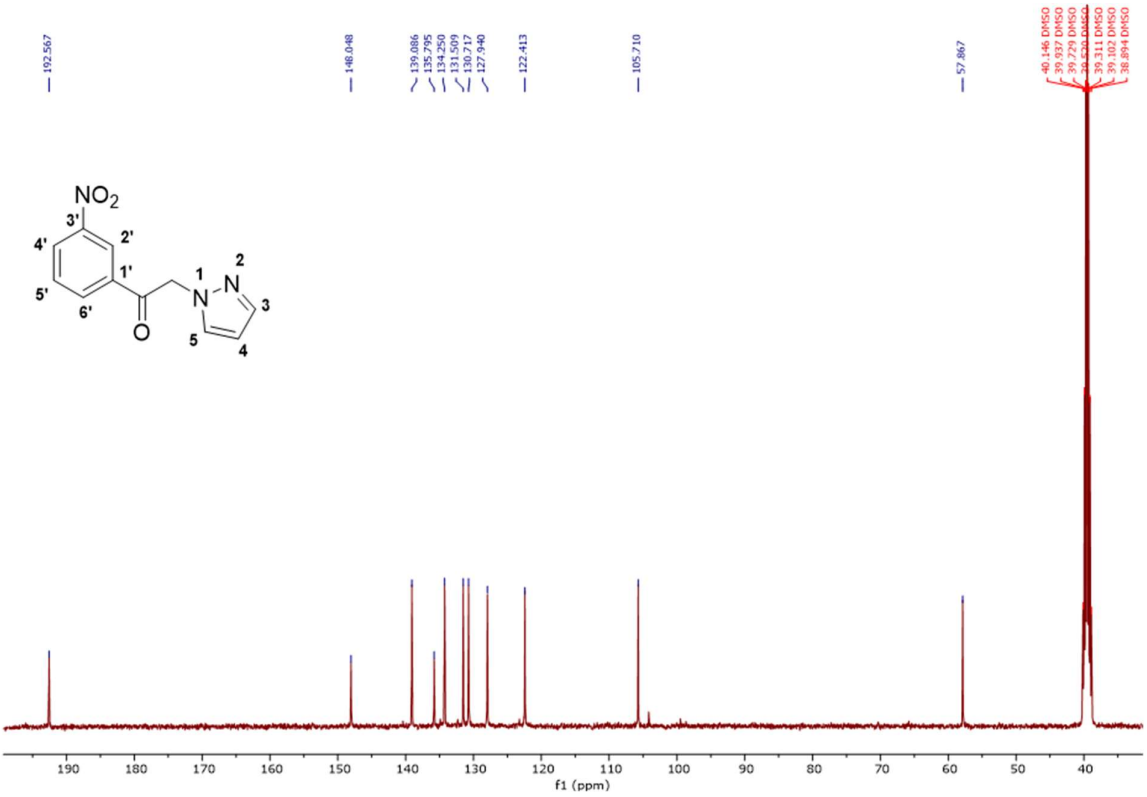

Figure S4. ^{13}C-NMR spectrum of 1-(3-nitrophenyl)-2-(1*H*-pyrazol-1-yl)ethanone **3**

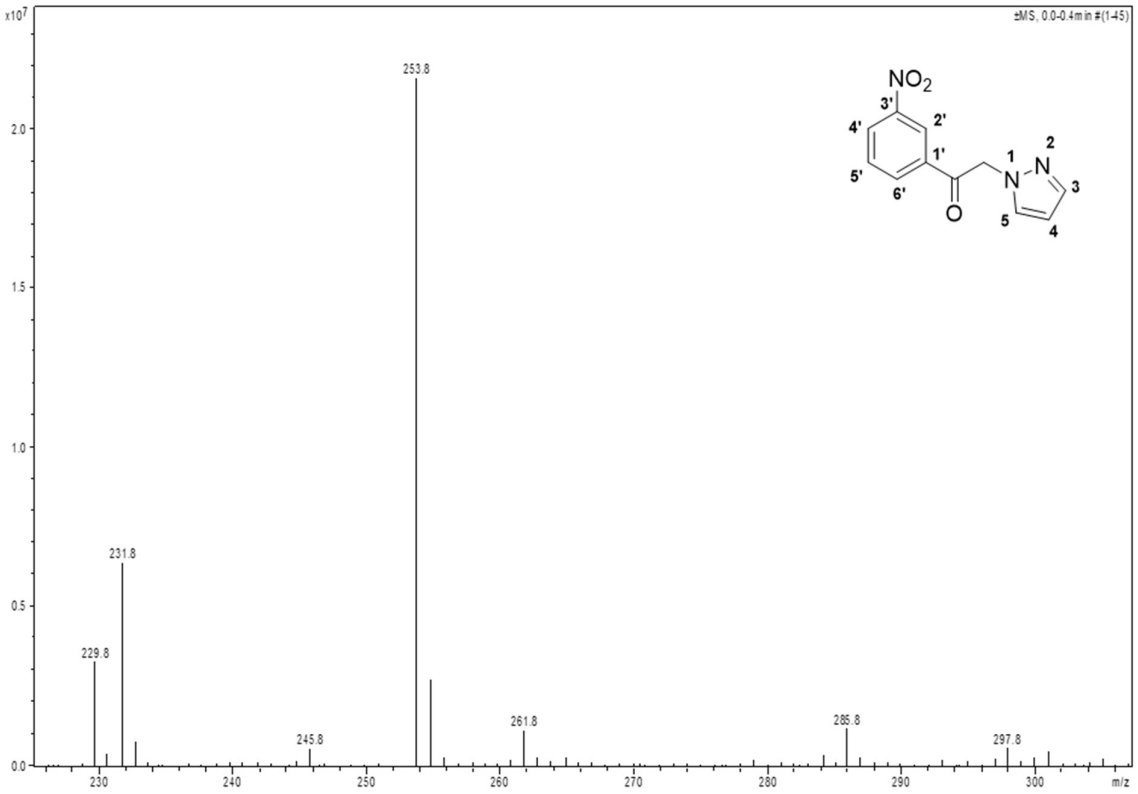

Figure S5. LRMS spectrum of 1-(3-nitrophenyl)-2-(1*H*-pyrazol-1-yl)ethanone **3** in 0.1% HCOOH in MeOH.

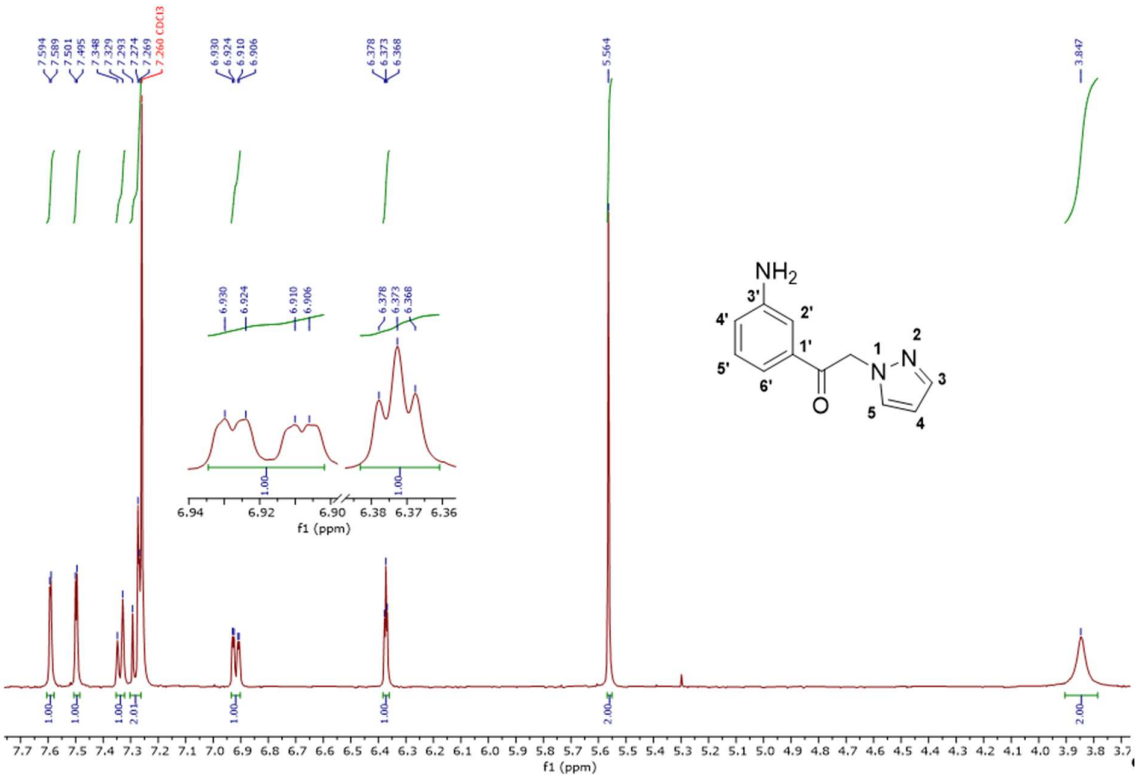

Figure S6. ^{1}H-NMR spectrum of 1-(3-aminophenyl)-2-(1*H*-pyrazol-1-yl)ethanone **4**

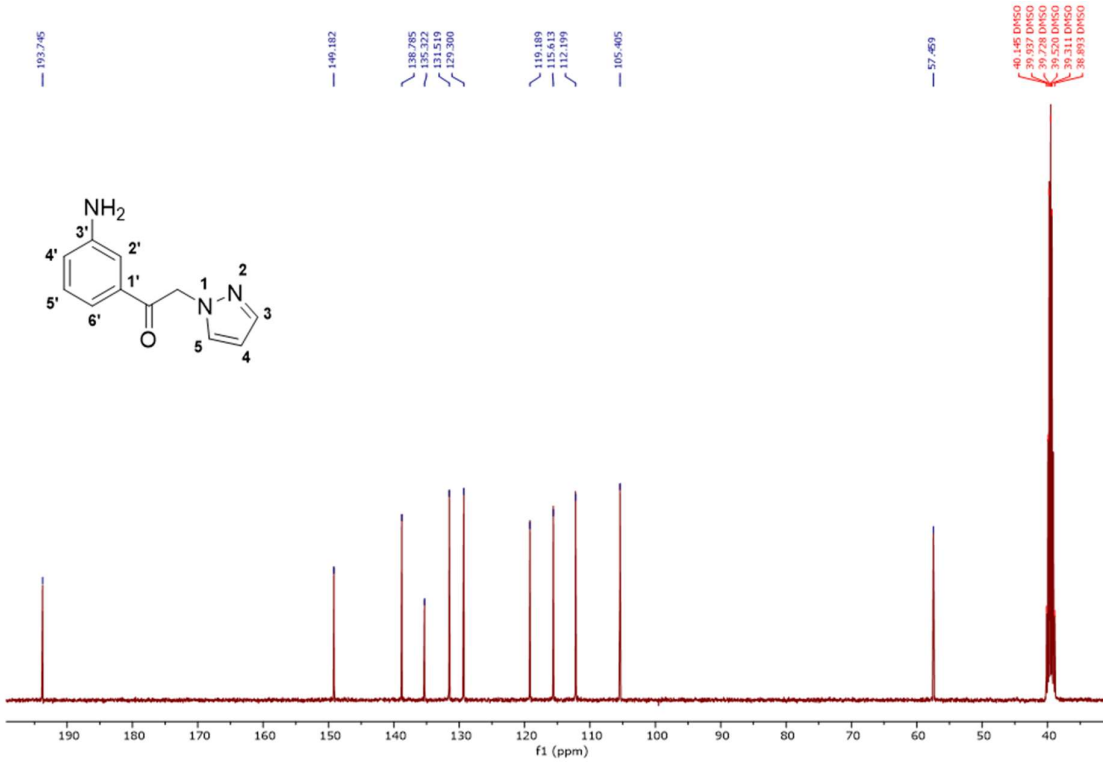

Figure S7. ^{1}H-NMR spectrum of 1-(3-aminophenyl)-2-(1*H*-pyrazol-1-yl)ethanone **4**

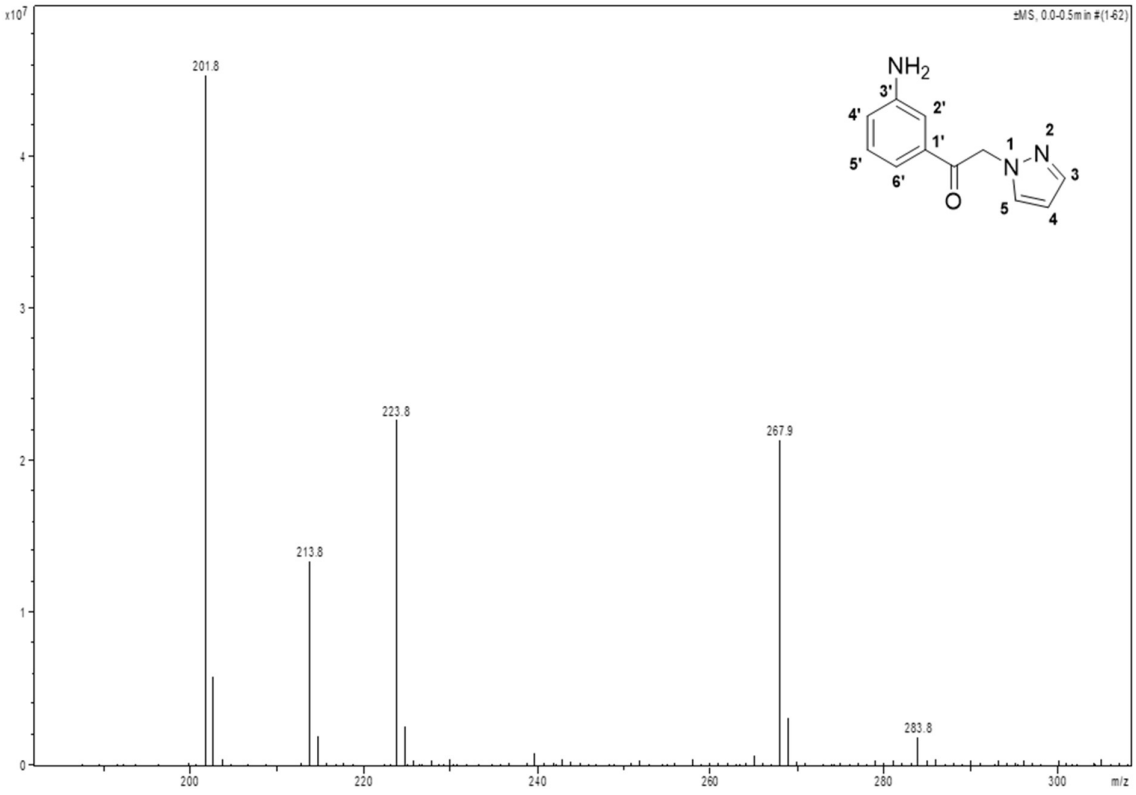

Figure S8. LRMS spectrum of 1-(3-aminophenyl)-2-(1*H*-pyrazol-1-yl)ethanone **4** in 0.1% HCOOH in MeOH.

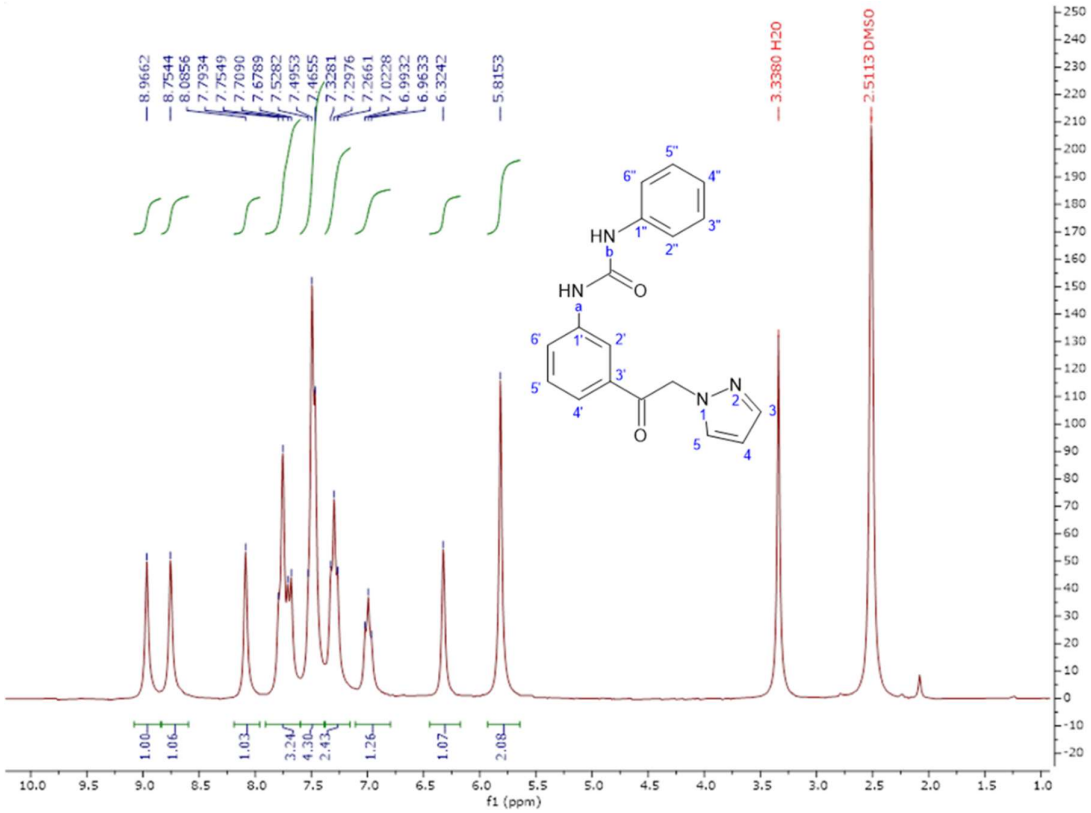

Figure S9. ^{1}H-NMR spectrum of 1-{3-[2-(1H-pyrazol-1-yl)acetyl]phenyl}-3-phenylurea **6a**.

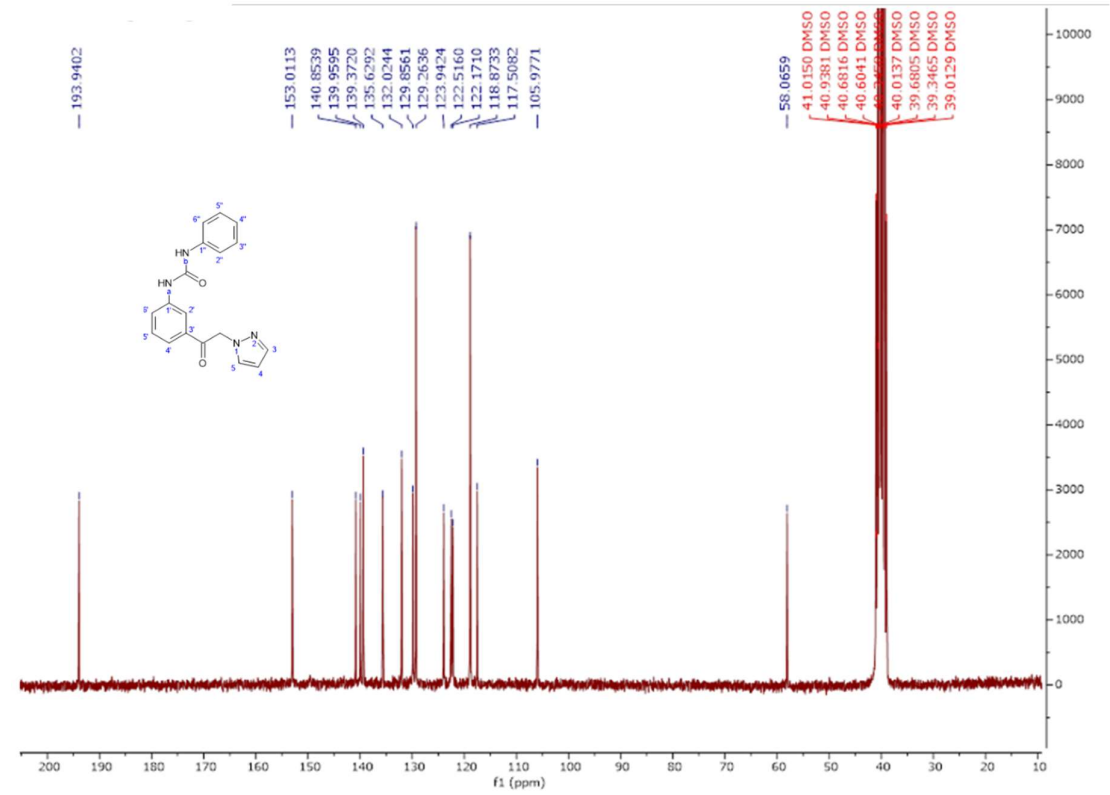

Figure S10. ^{13}C-NMR spectrum of 1-{3-[2-(1H-pyrazol-1-yl)acetyl]phenyl}-3-phenylurea **6a**.

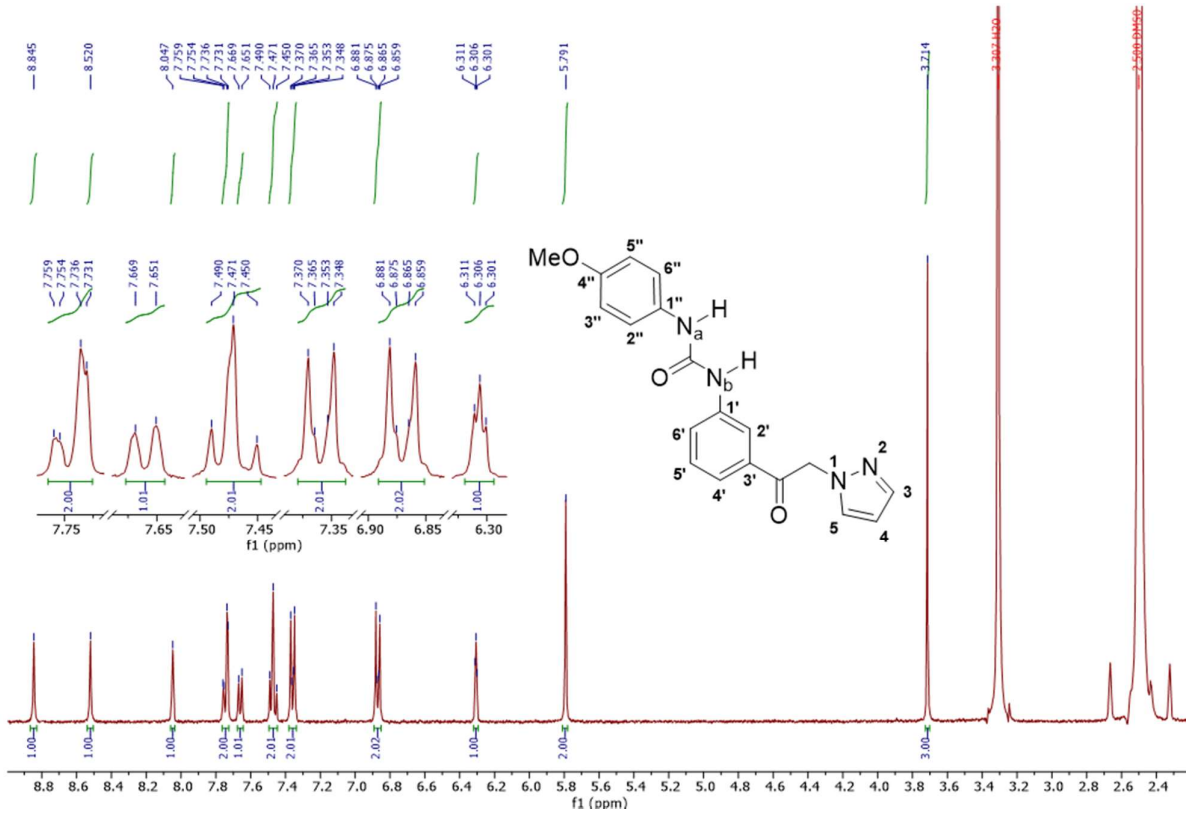

Figure S11. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **6b**.

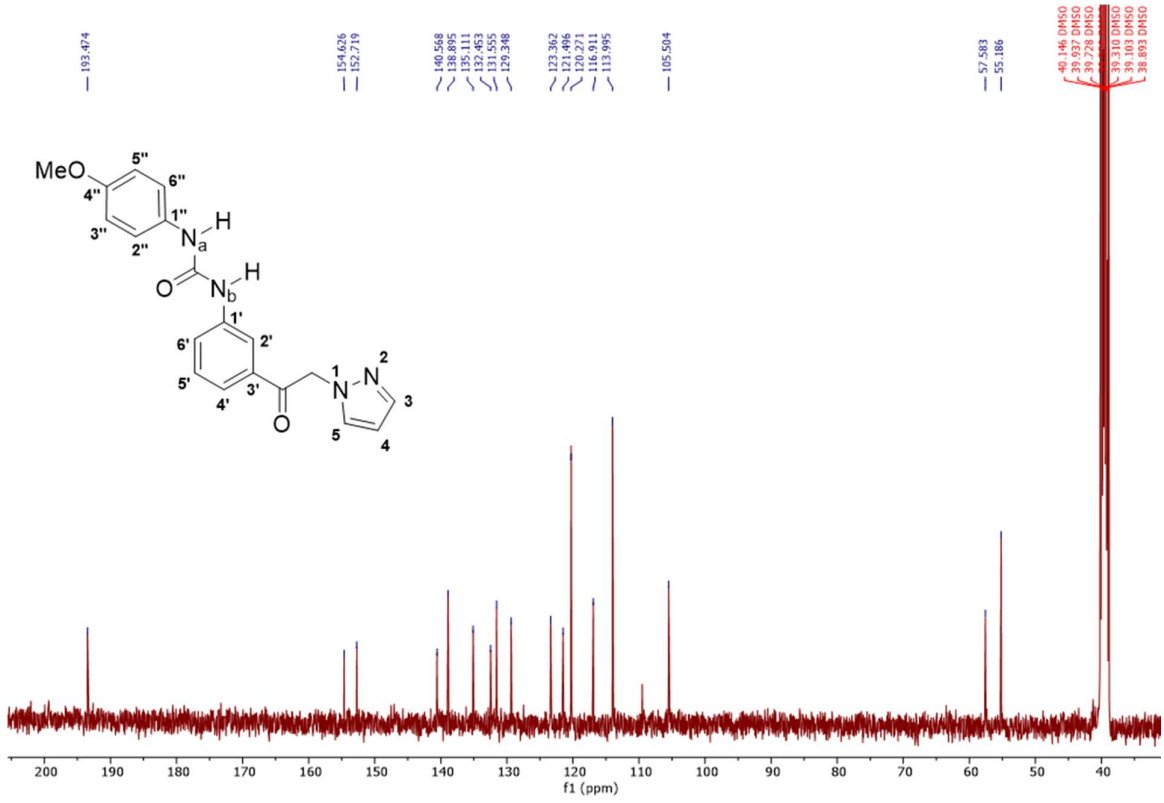

Figure S12. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **6b**.

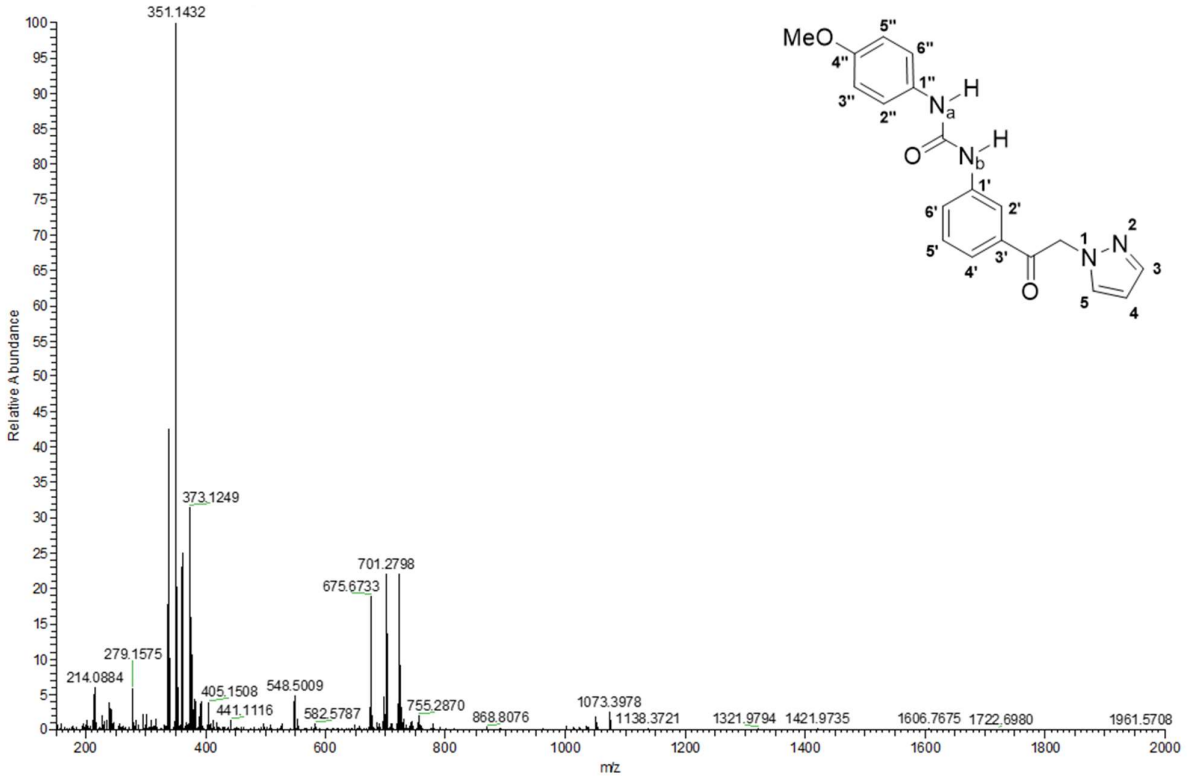

Figure S13. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **6b** in 0.1% HCOOH in MeOH.

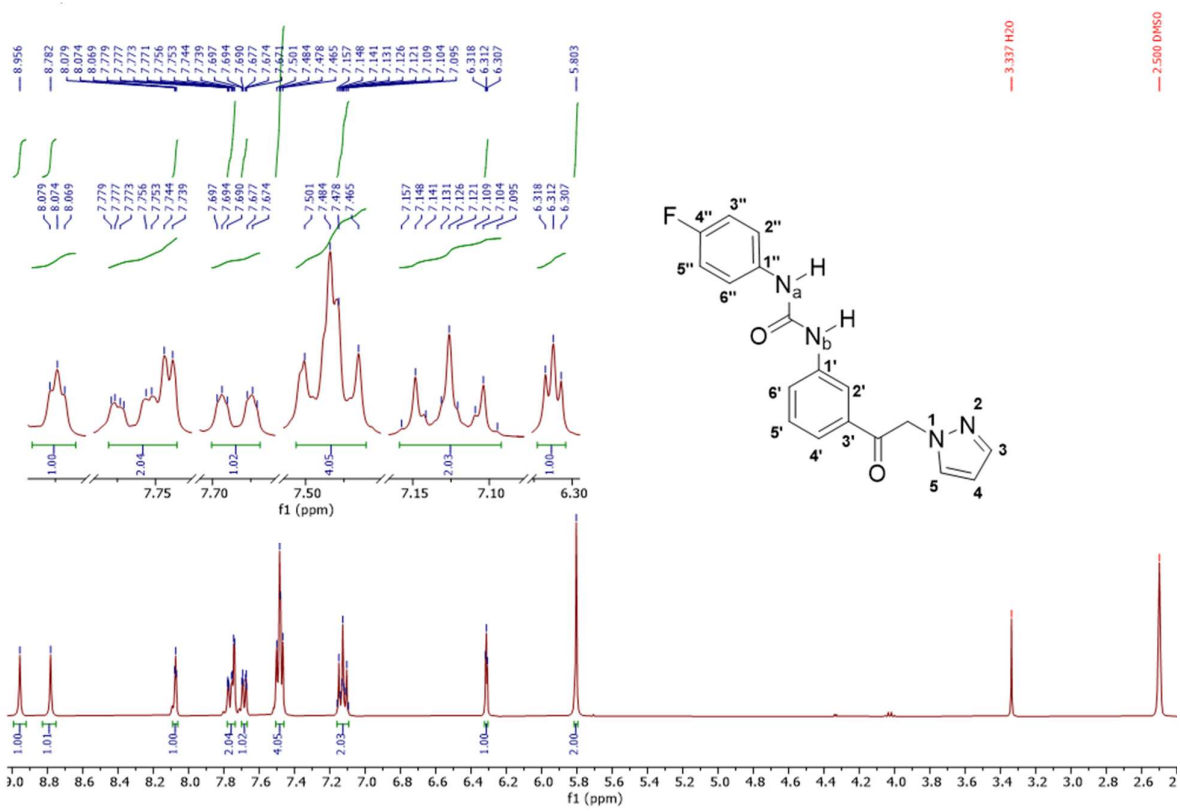

Figure S14. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-fluorophenyl)urea **6c**.

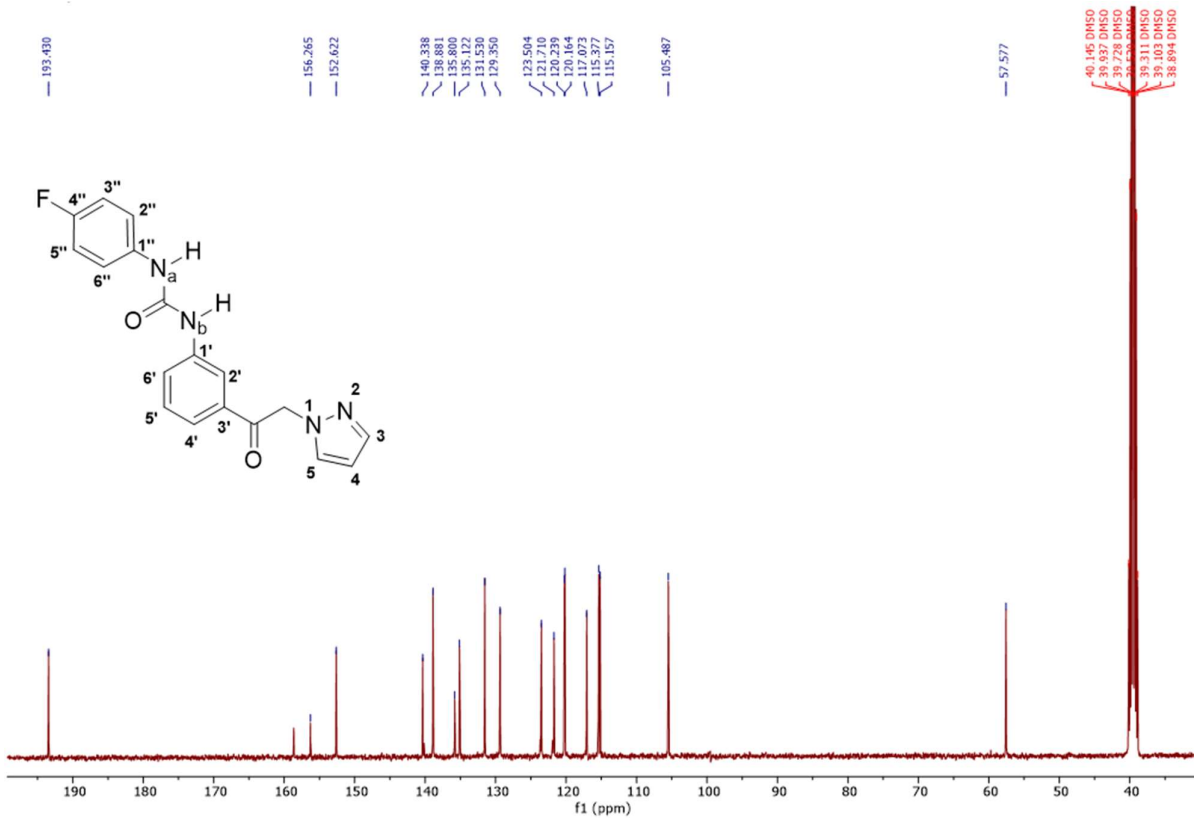

Figure S15. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-fluorophenyl)urea **6c**.

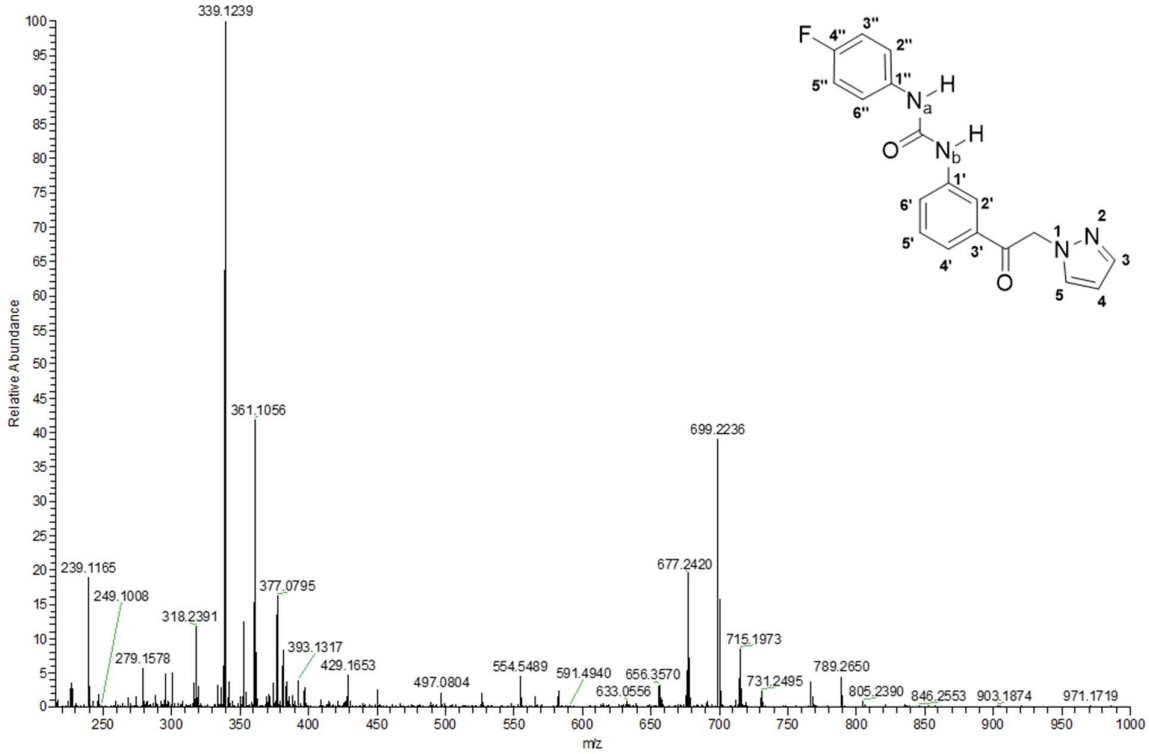

Figure S16. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-fluorophenyl)urea **6c** in 0.1% HCOOH in MeOH.

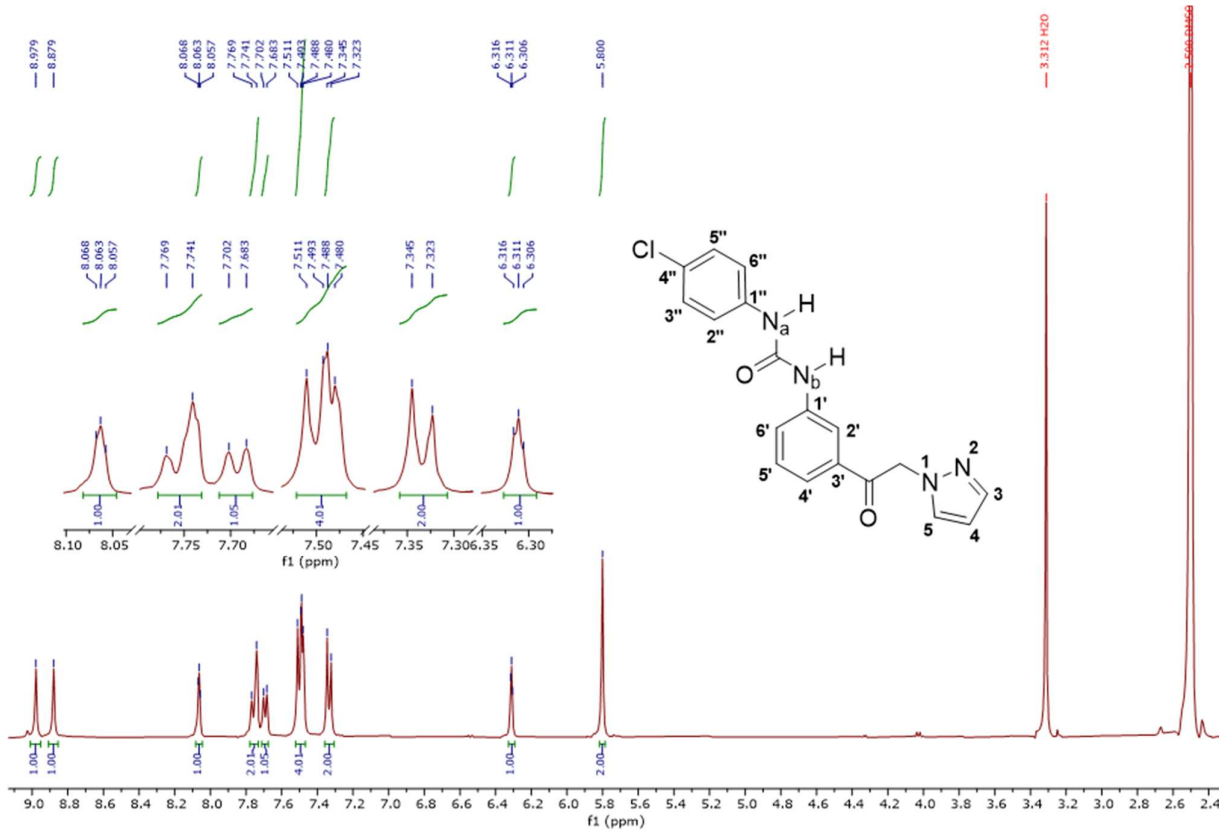

Figure S17. [1]H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **6d**.

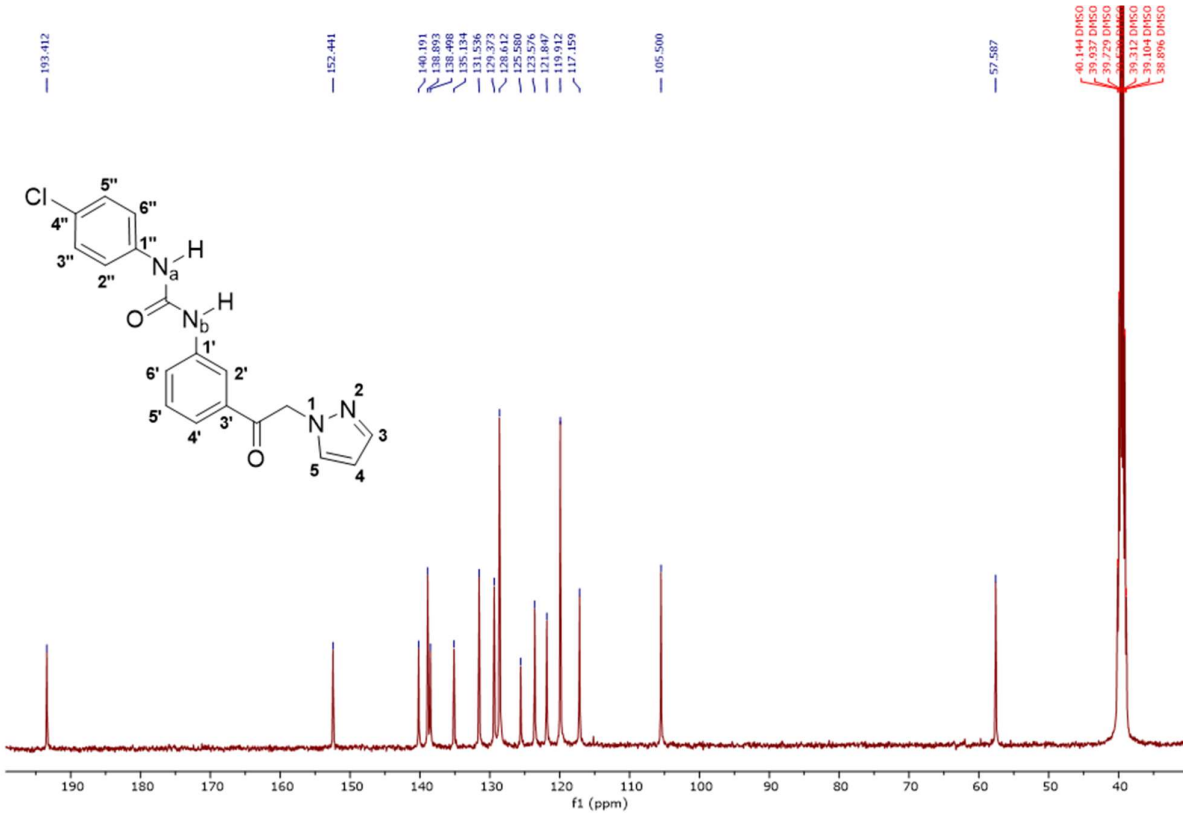

Figure S18. [13]C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **6d**.

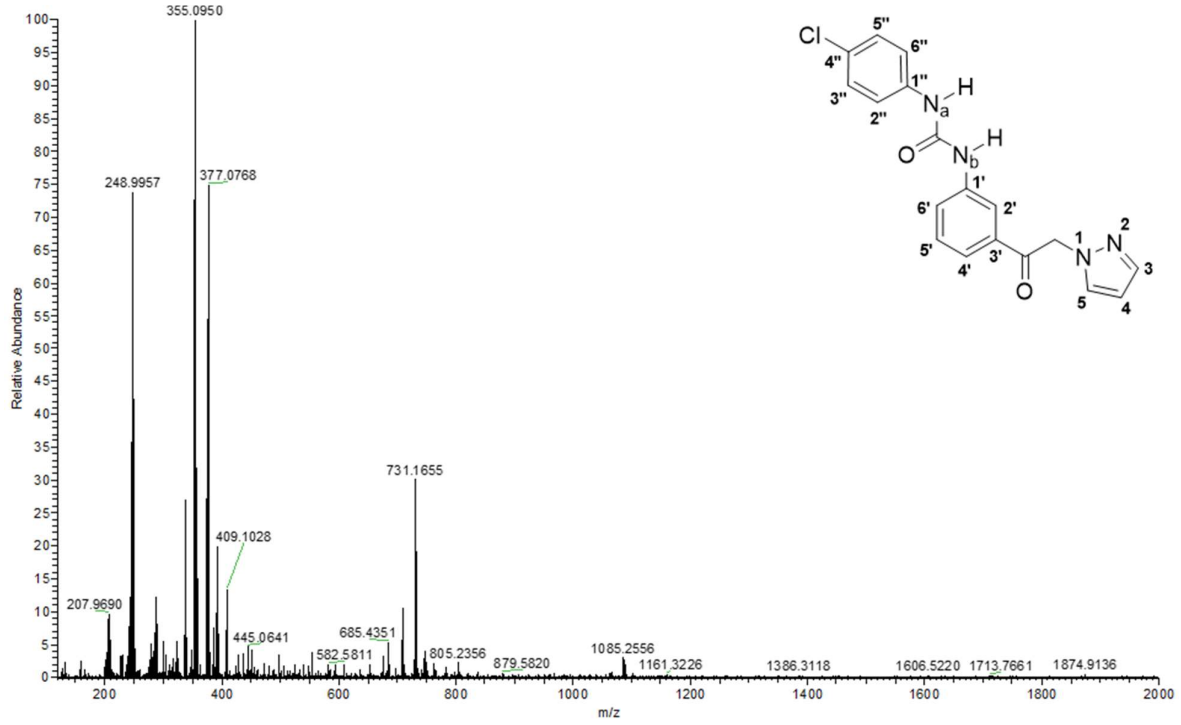

Figure S19. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **6d** in 0.1% HCOOH in MeOH.

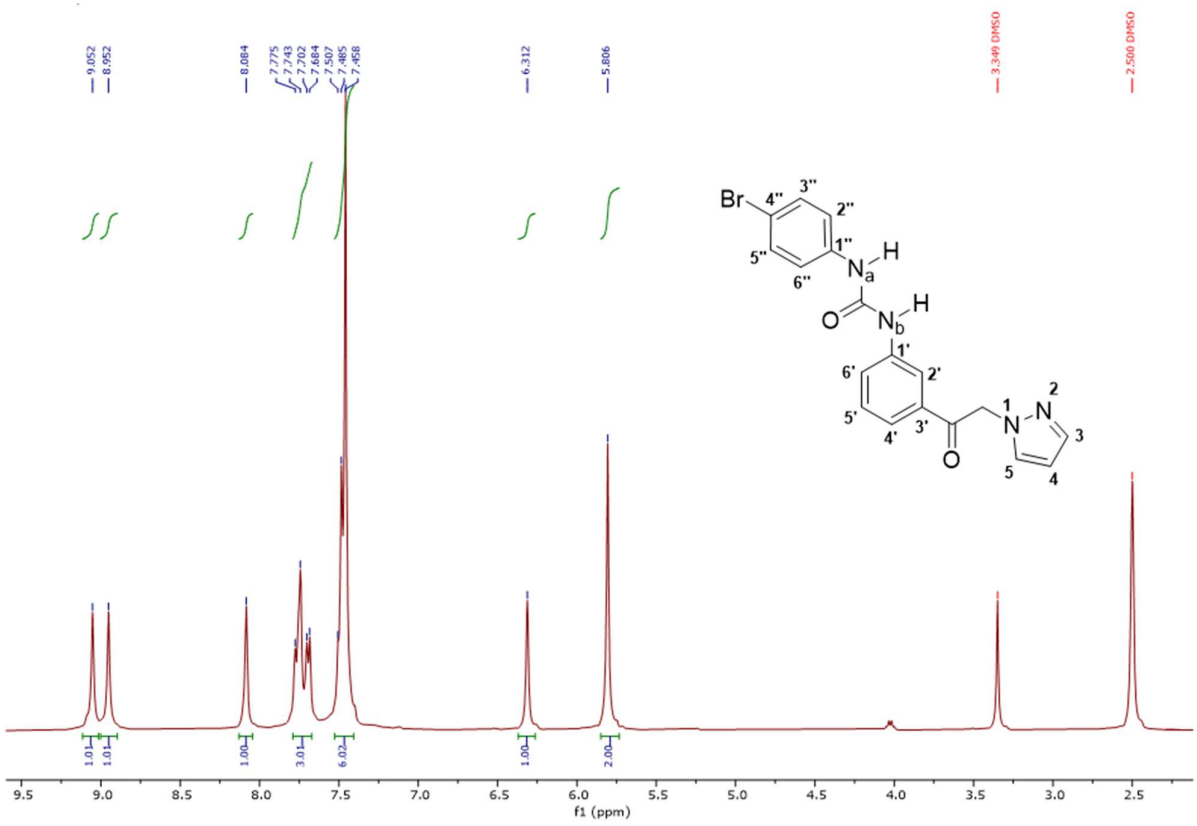

Figure S20. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **6e**.

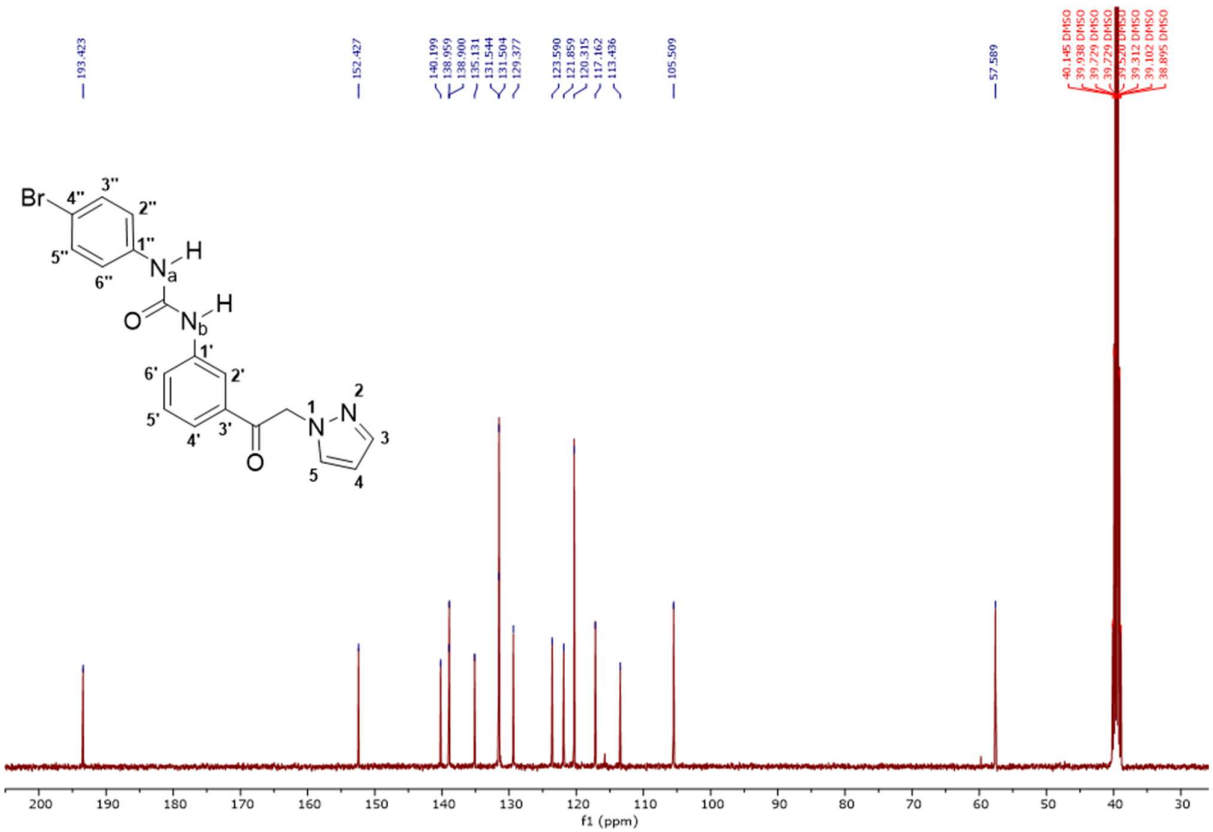

Figure S21. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **6e**.

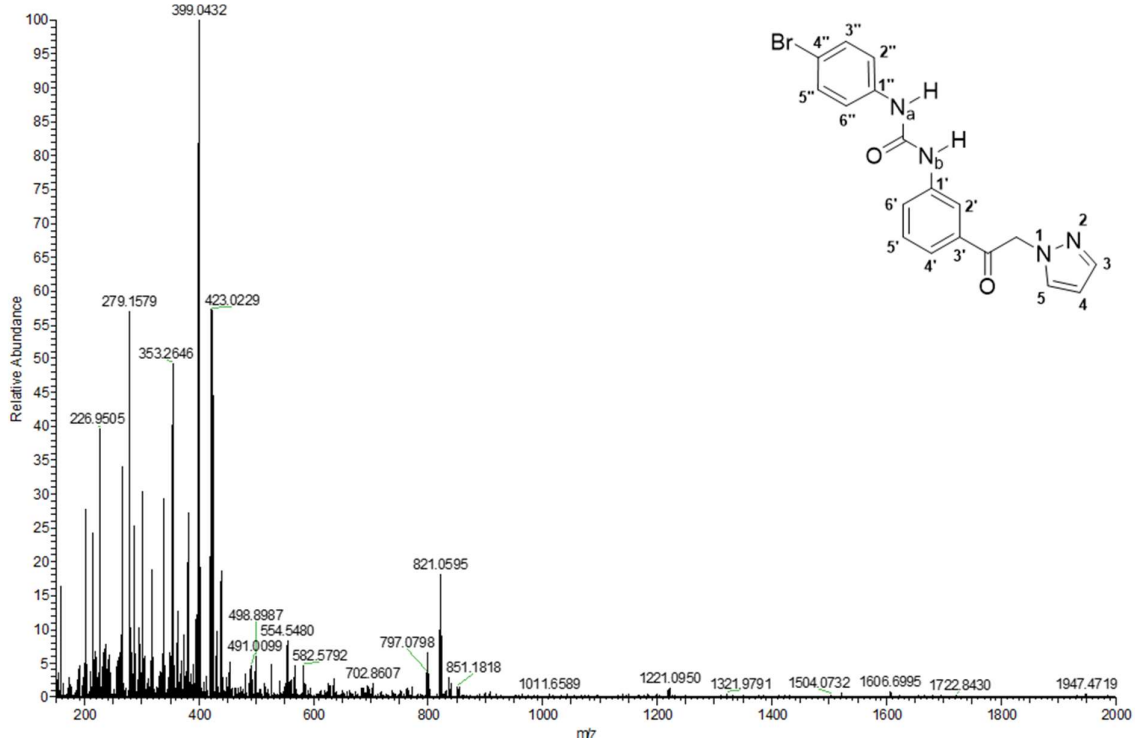

Figure S22. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **6e** in 0.1% HCOOH in MeOH.

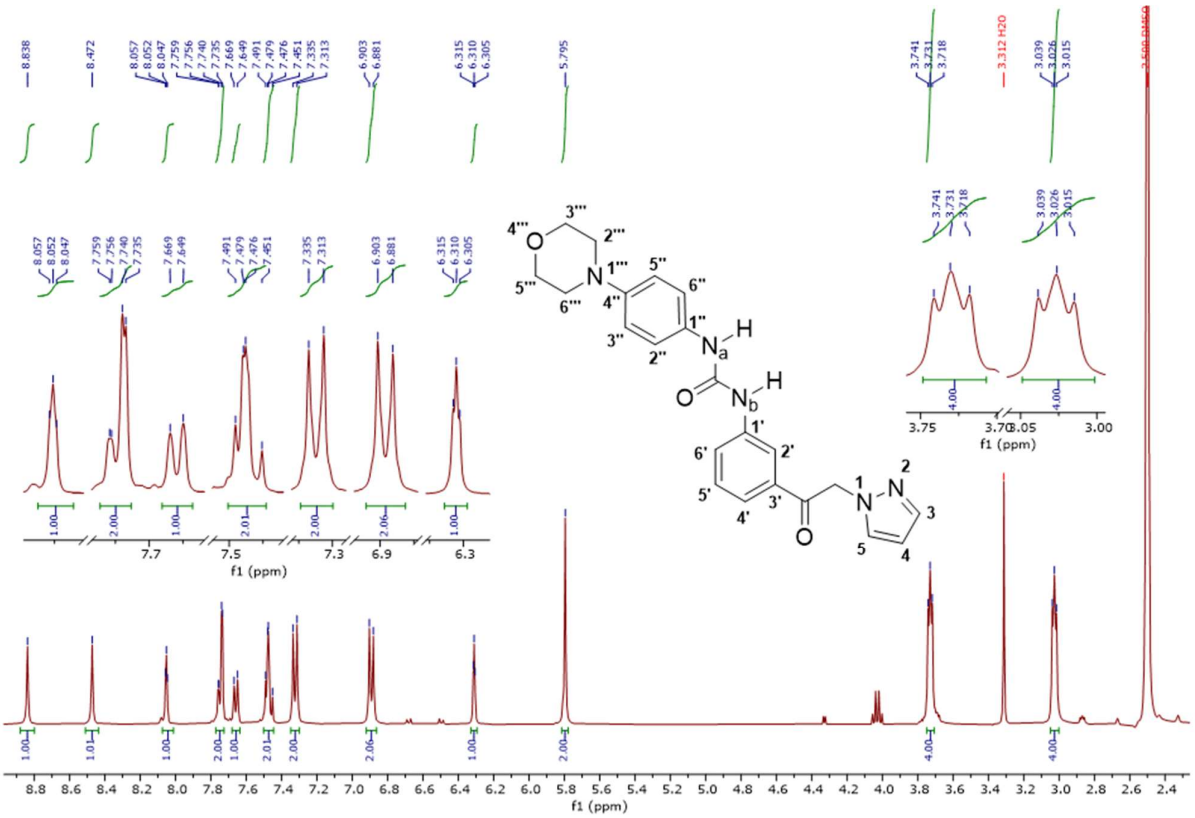

Figure S23. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **6f**.

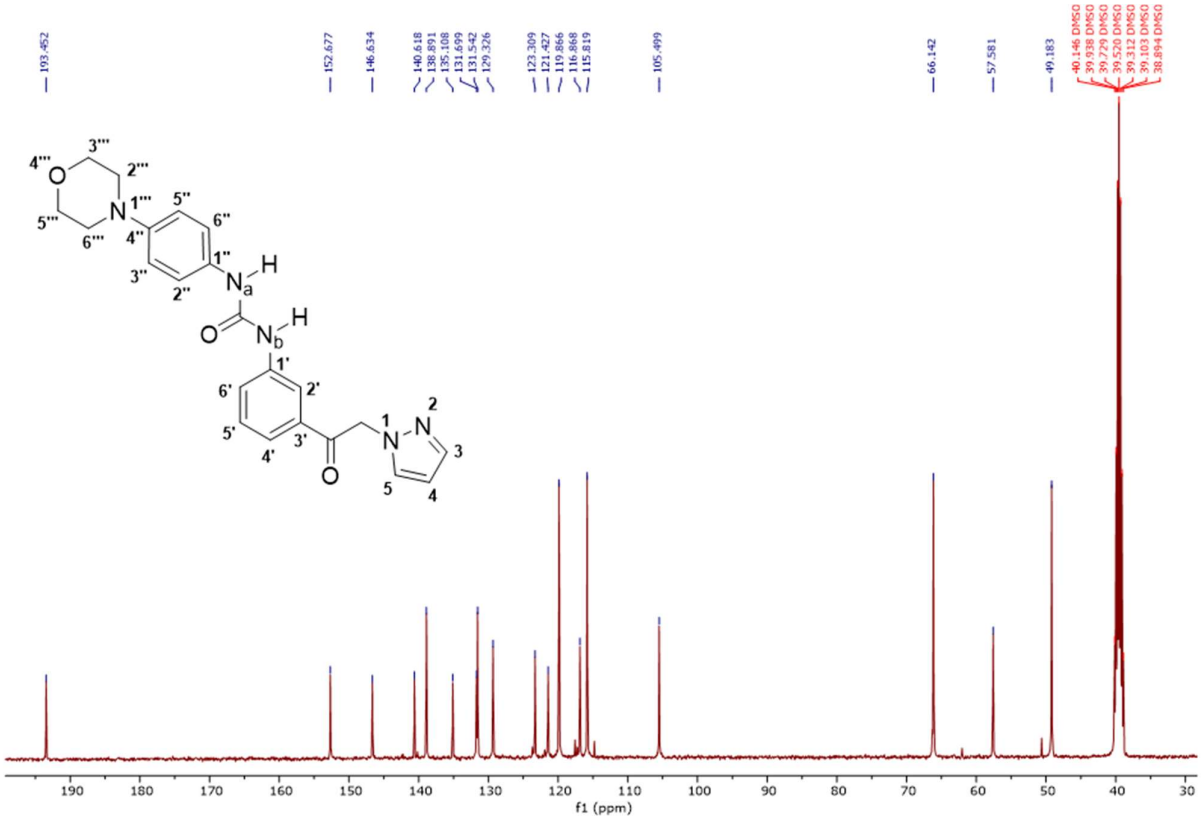

Figure S24. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **6f**.

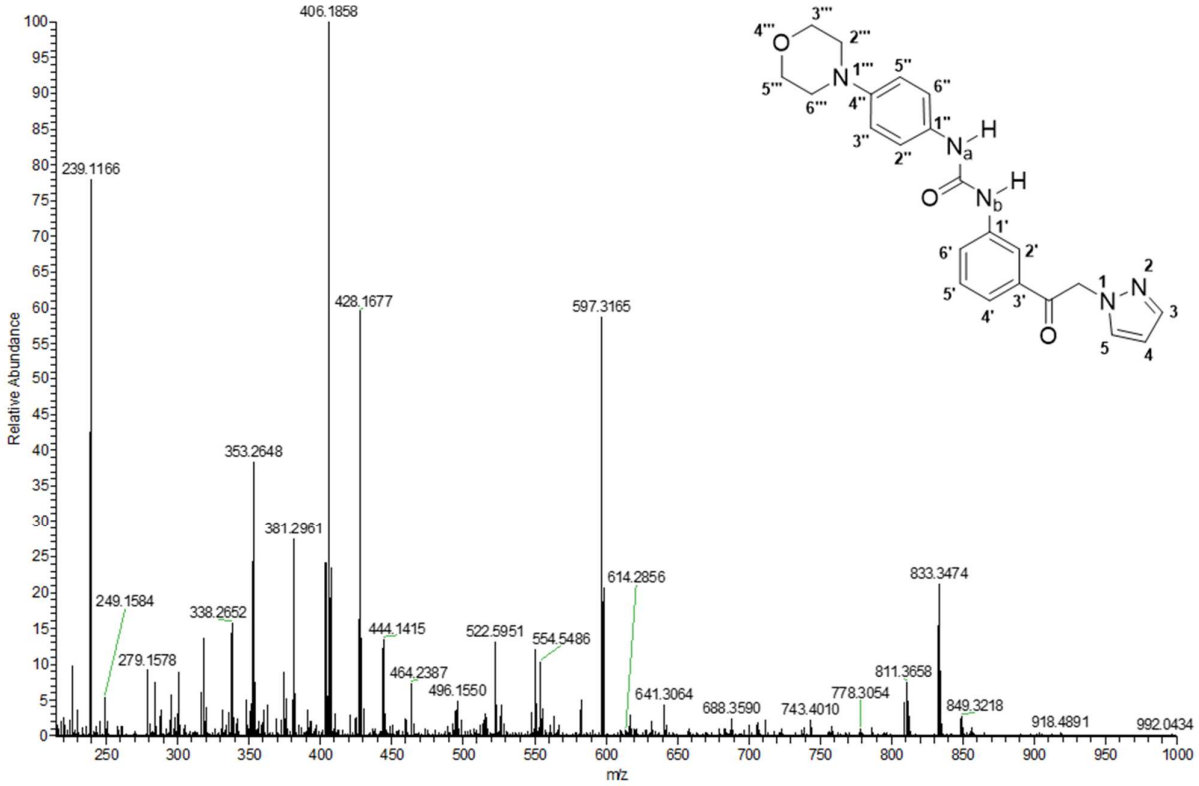

Figure S25. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **6f** in 0.1% HCOOH in MeOH.

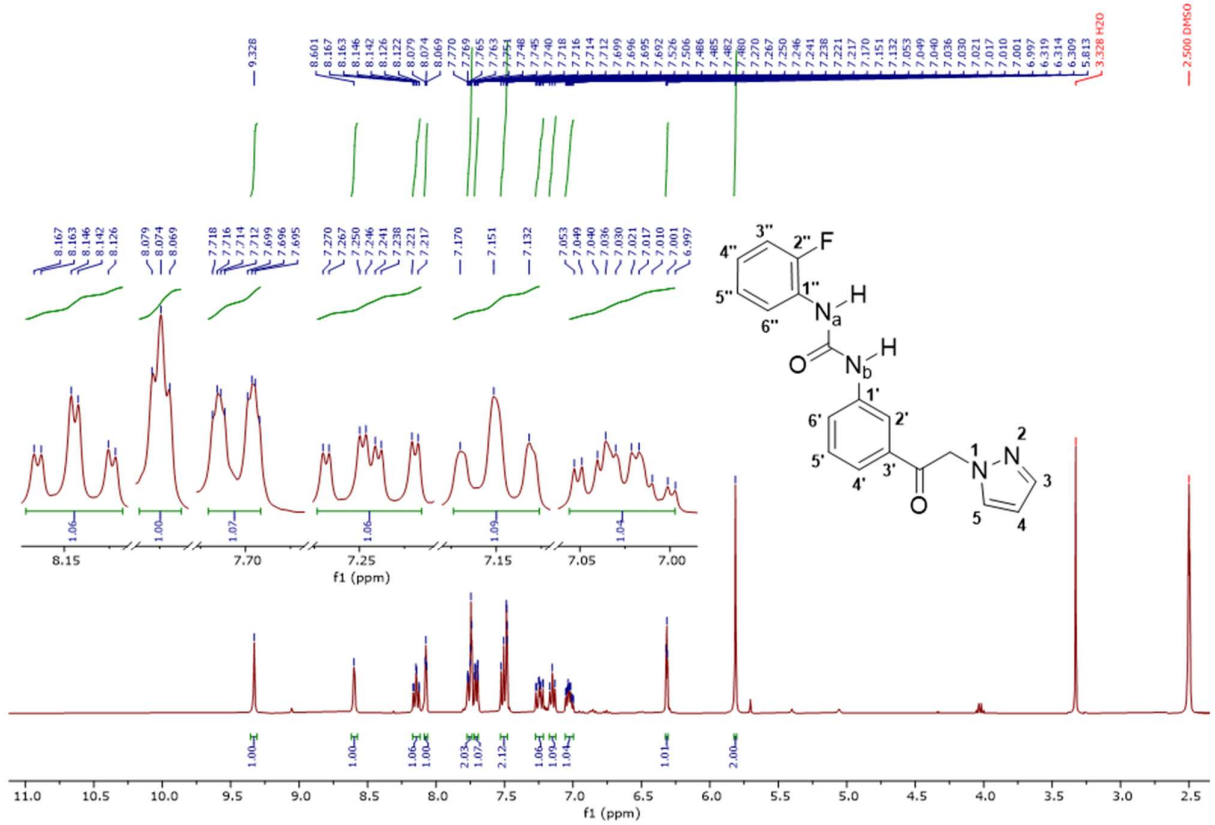

Figure S26. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-fluorophenyl)urea **6g**.

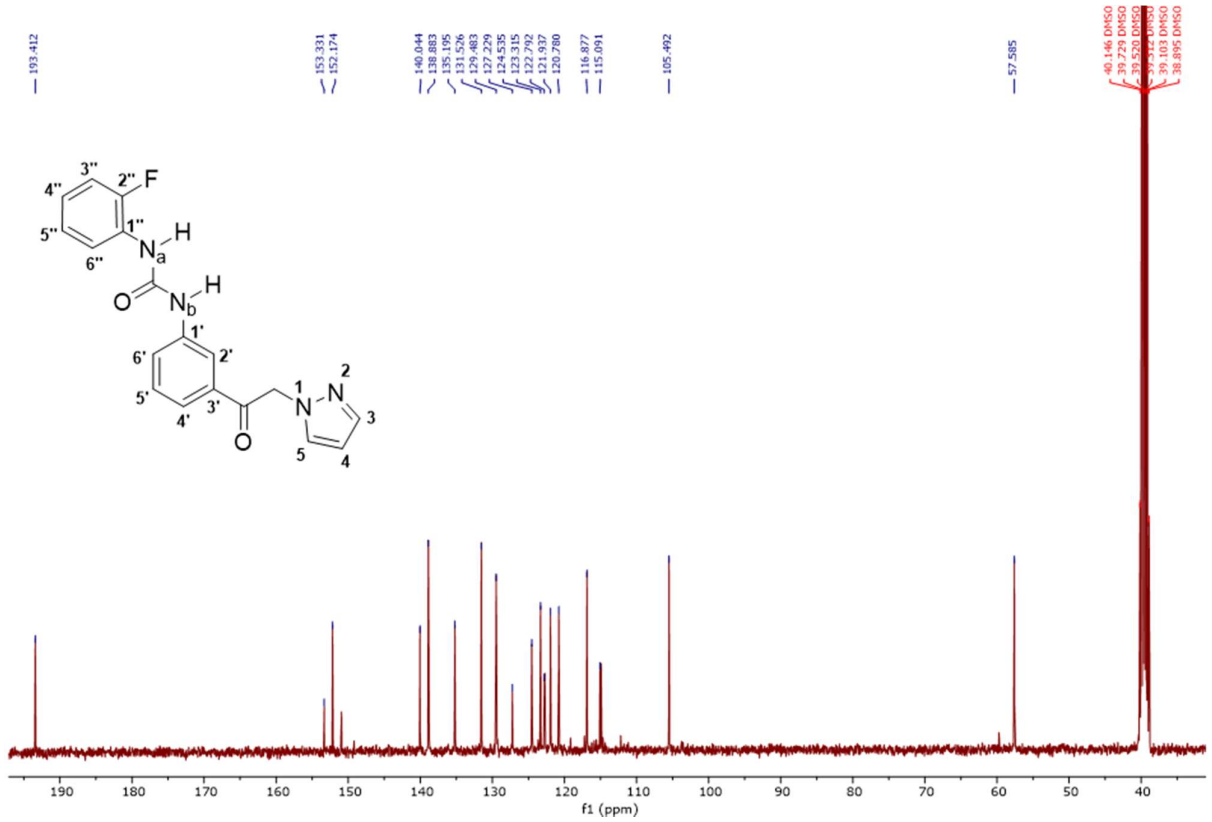

Figure S27. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-fluorophenyl)urea **6g**.

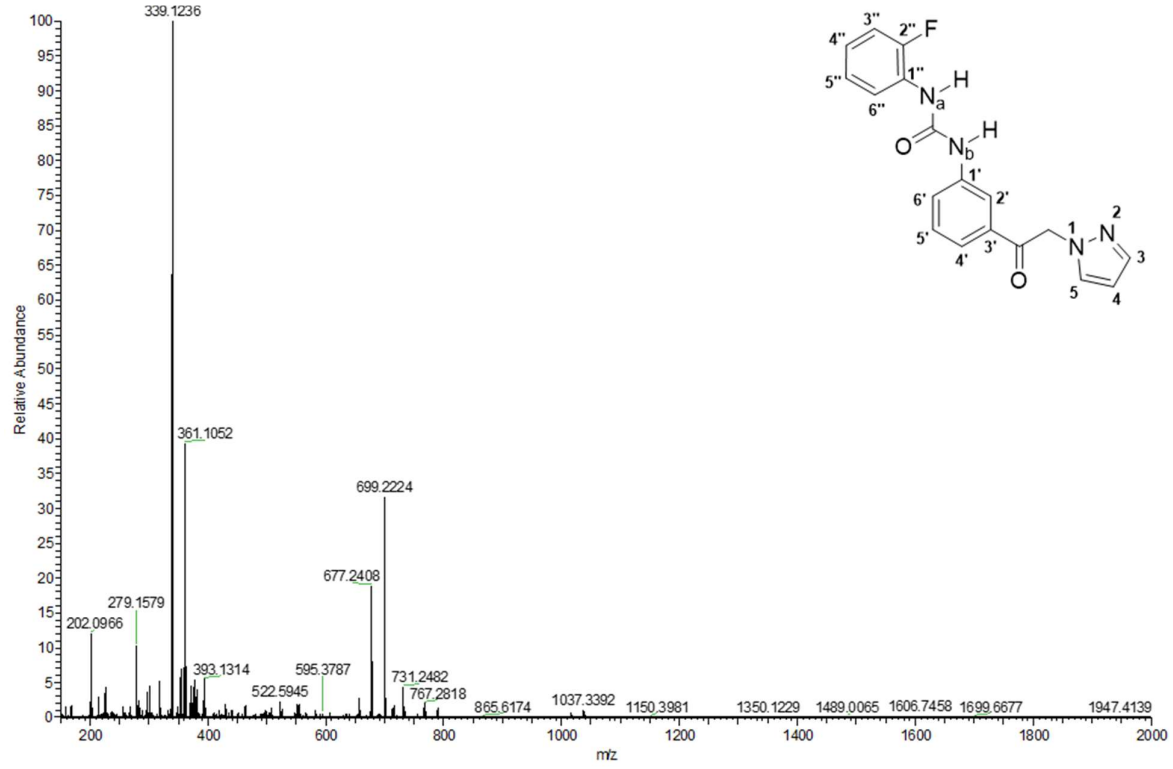

Figure S28. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-fluorophenyl)urea **6g** in 0.1% HCOOH in MeOH.

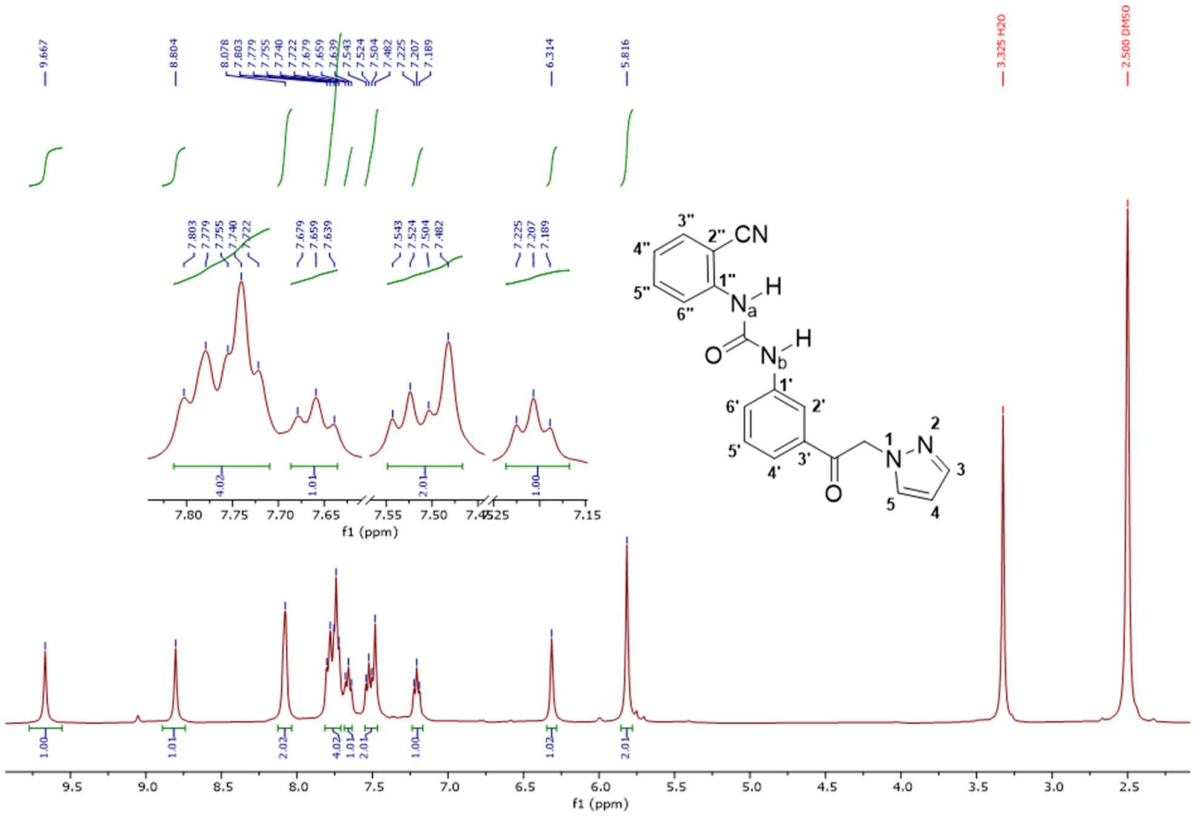

Figure S29. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-cyanophenyl)urea **6h**.

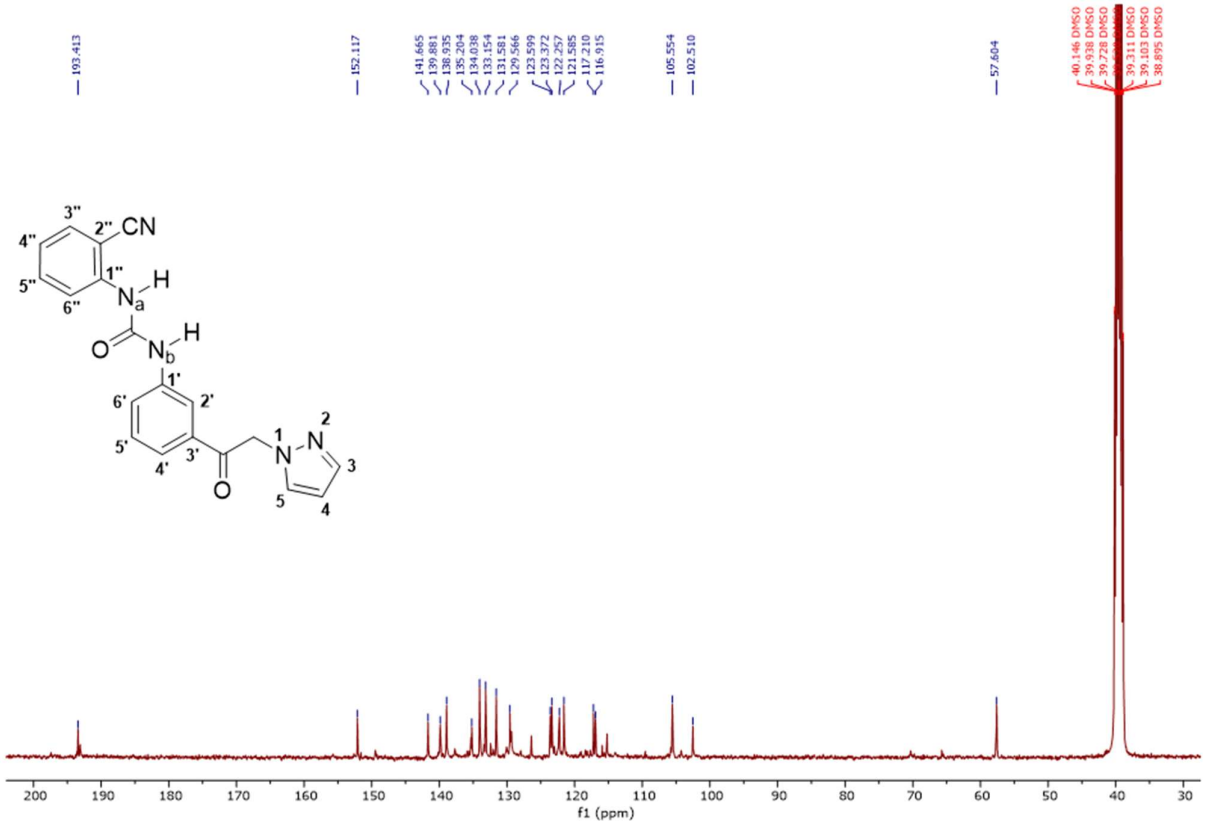

Figure S30. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-cyanophenyl)urea **6h**.

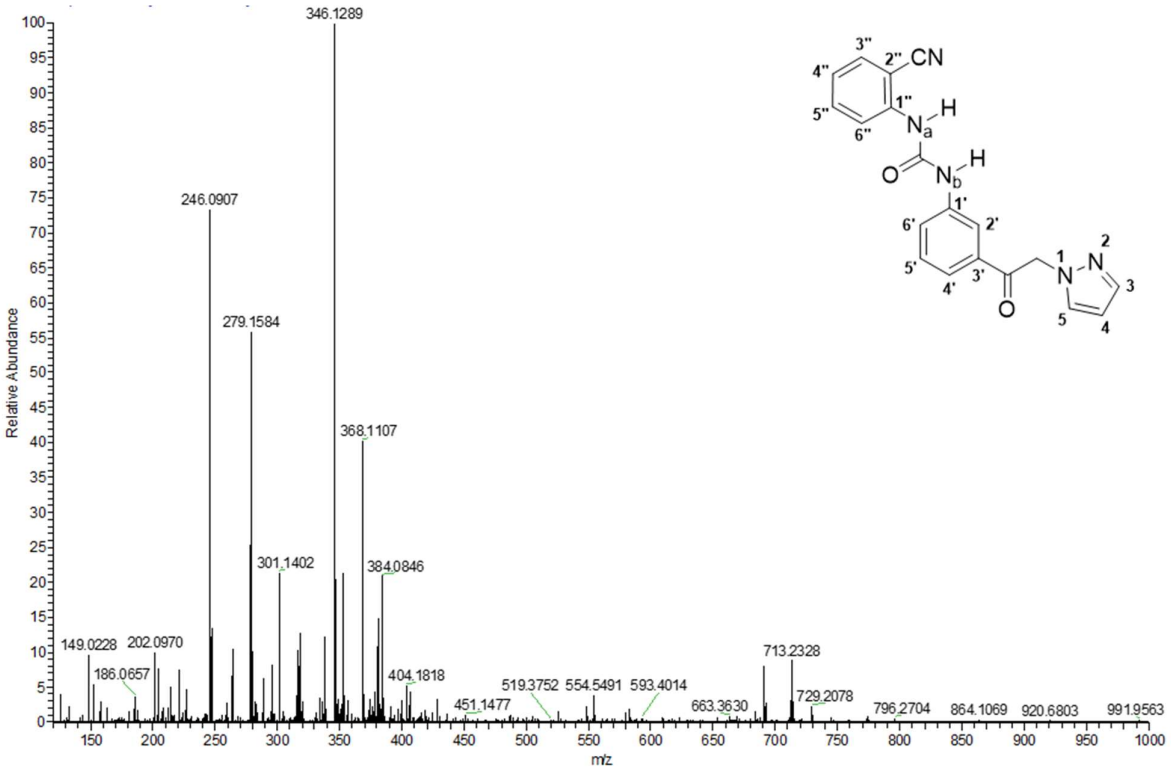

Figure S31. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(2-cyanophenyl)urea **6h** in 0.1% HCOOH in MeOH.

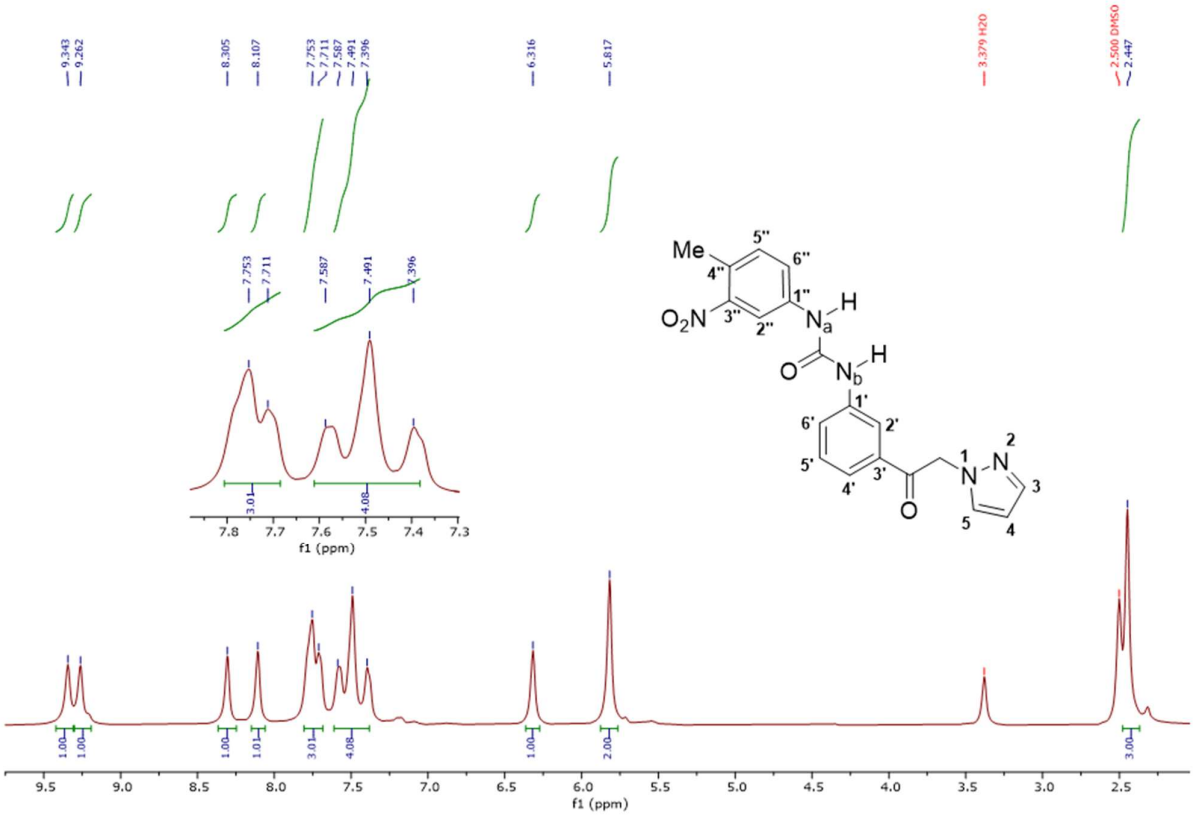

Figure S32. [1]H-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methyl-2-nitrophenyl)urea **6i**.

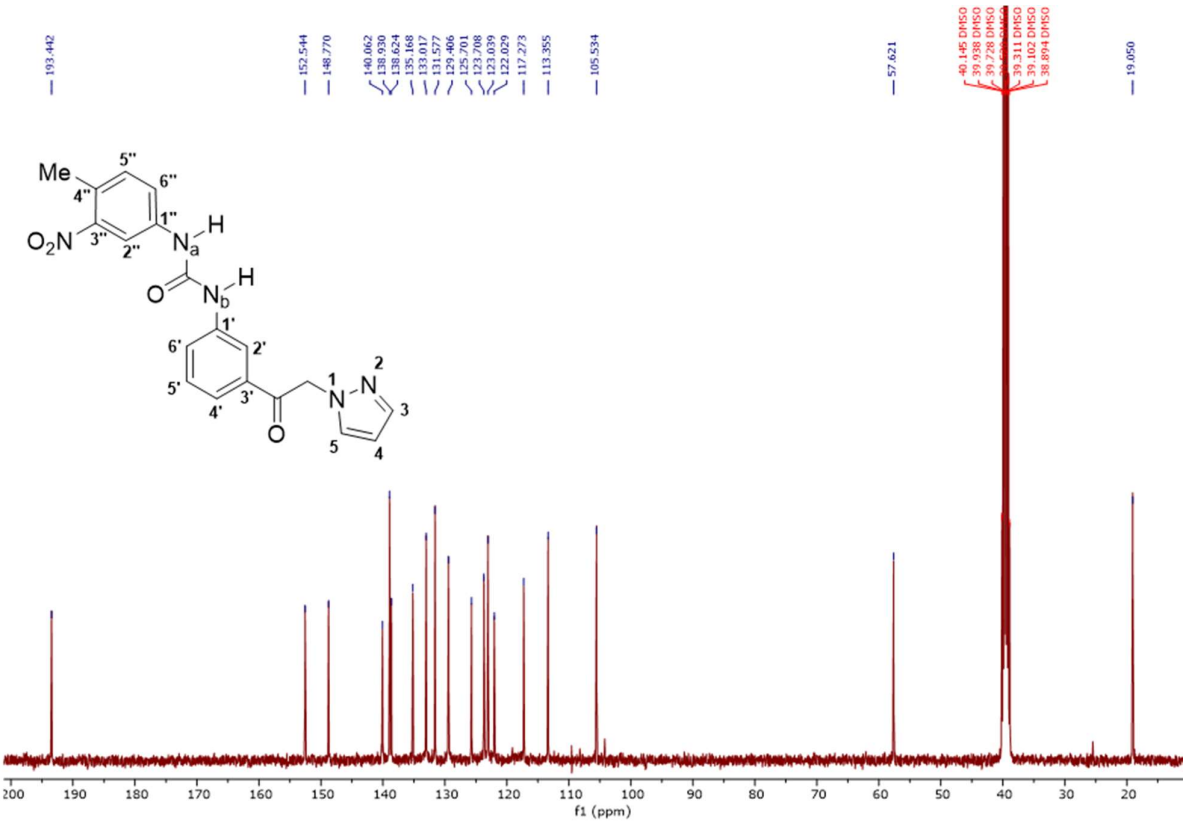

Figure S33. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methyl-2-nitrophenyl)urea **6i**.

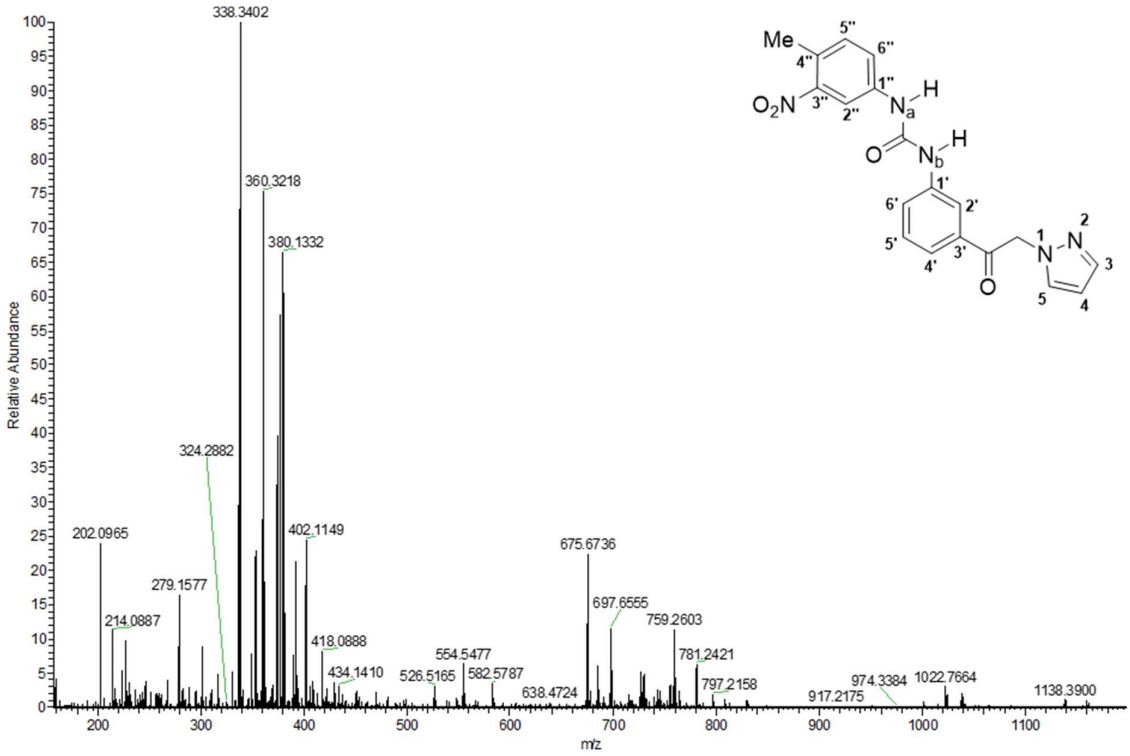

Figure S34. HRMS spectrum of 1-{3-[2-(1*H*-pyrazol-1-yl)acetyl]phenyl}-3-(4-methyl-2-nitrophenyl)urea **6i** in 0.1% HCOOH in MeOH.

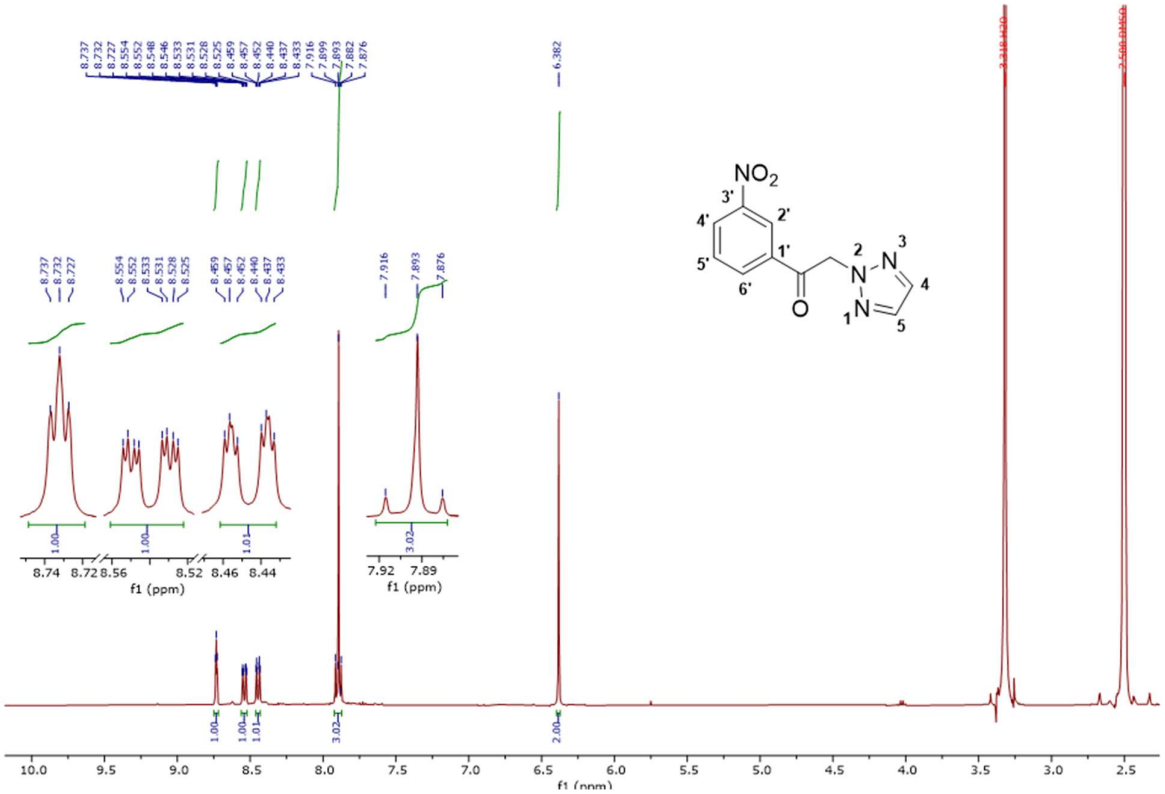

Figure S35. ^{1}H-NMR spectrum of 1-(3-nitrophenyl)-2-(2*H*-1,2,3-triazol-1-yl)ethanone **7a**.

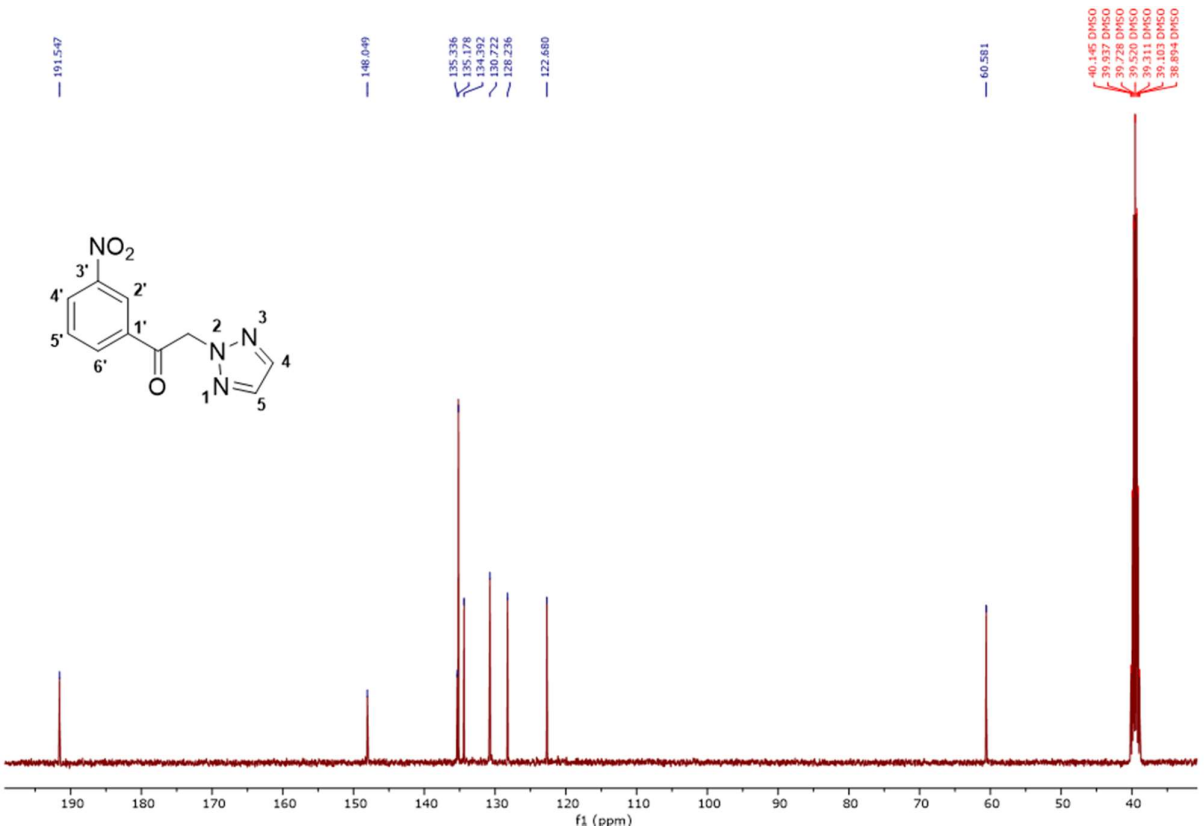

Figure S36. ^{13}C-NMR spectrum of 1-(3-nitrophenyl)-2-(2*H*-1,2,3-triazol-1-yl)ethanone **7a**.

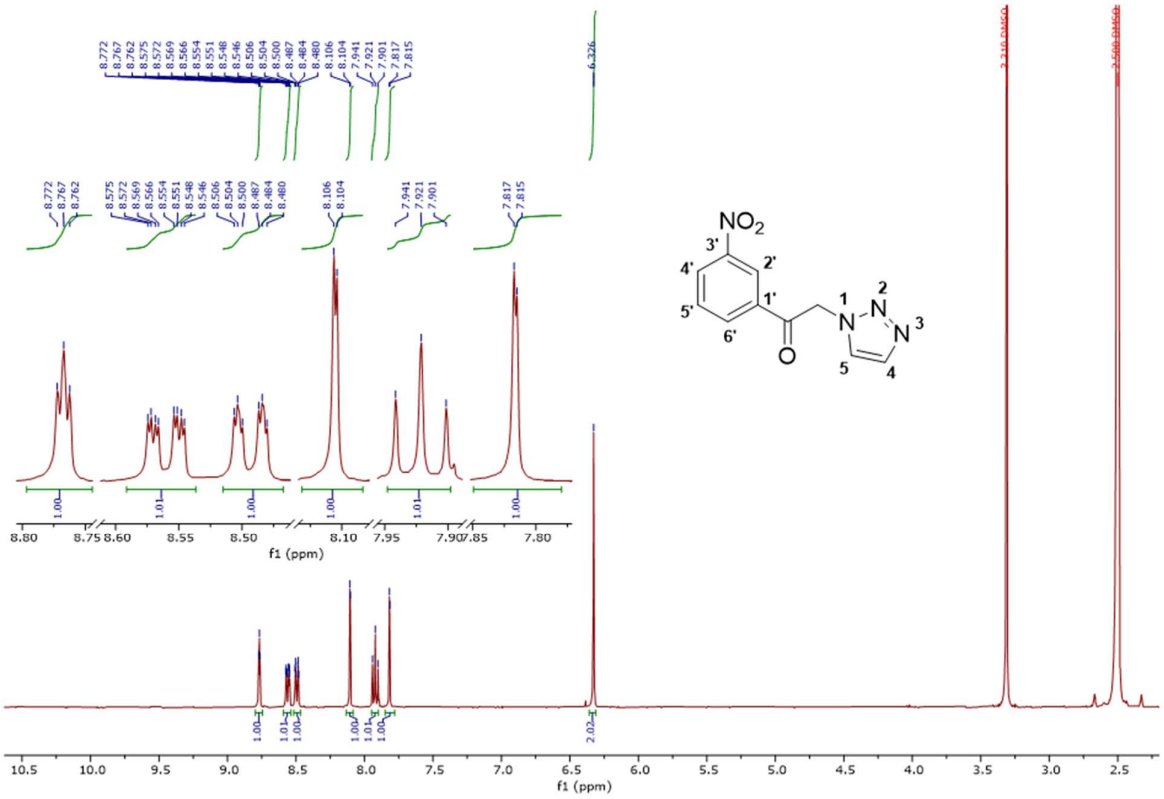

Figure S37. ^{1}H-NMR spectrum of 1-(3-nitrophenyl)-2-(1*H*-1,2,3-triazol-1-yl)ethanone **7b**.

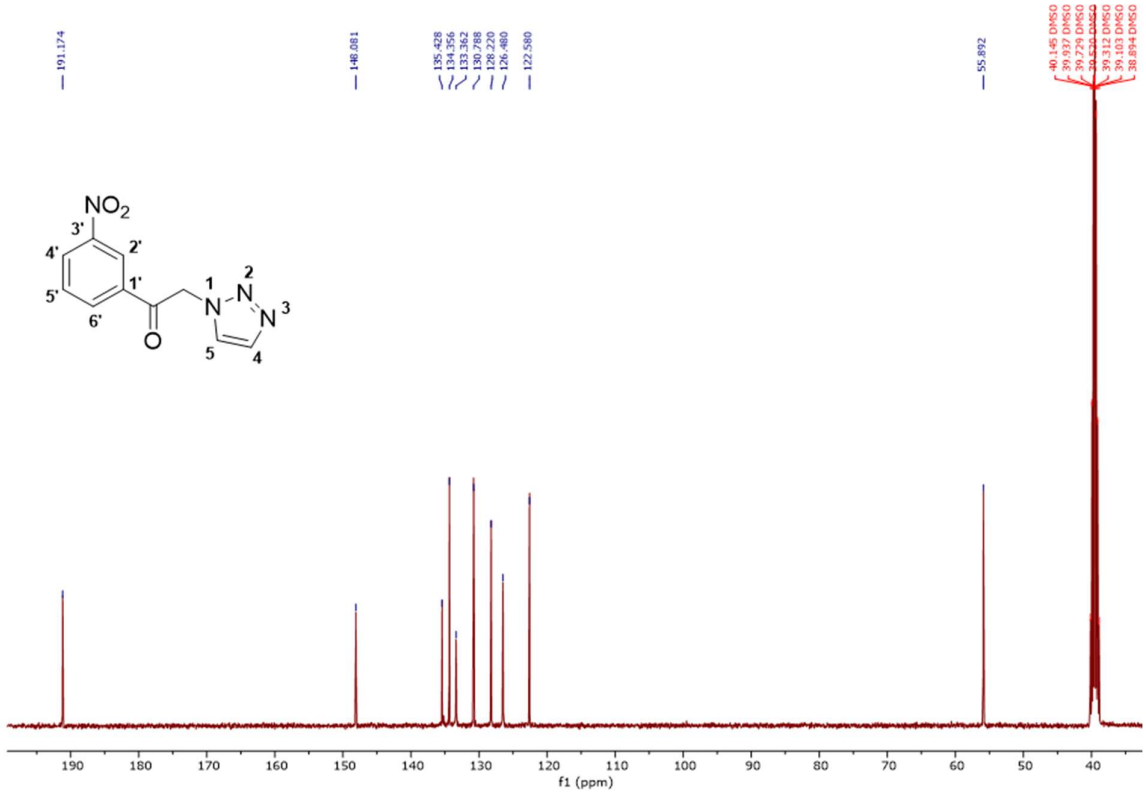

Figure S38. ^{13}C-NMR spectrum of 1-(3-nitrophenyl)-2-(1*H*-1,2,3-triazol-1-yl)ethanone **7b**.

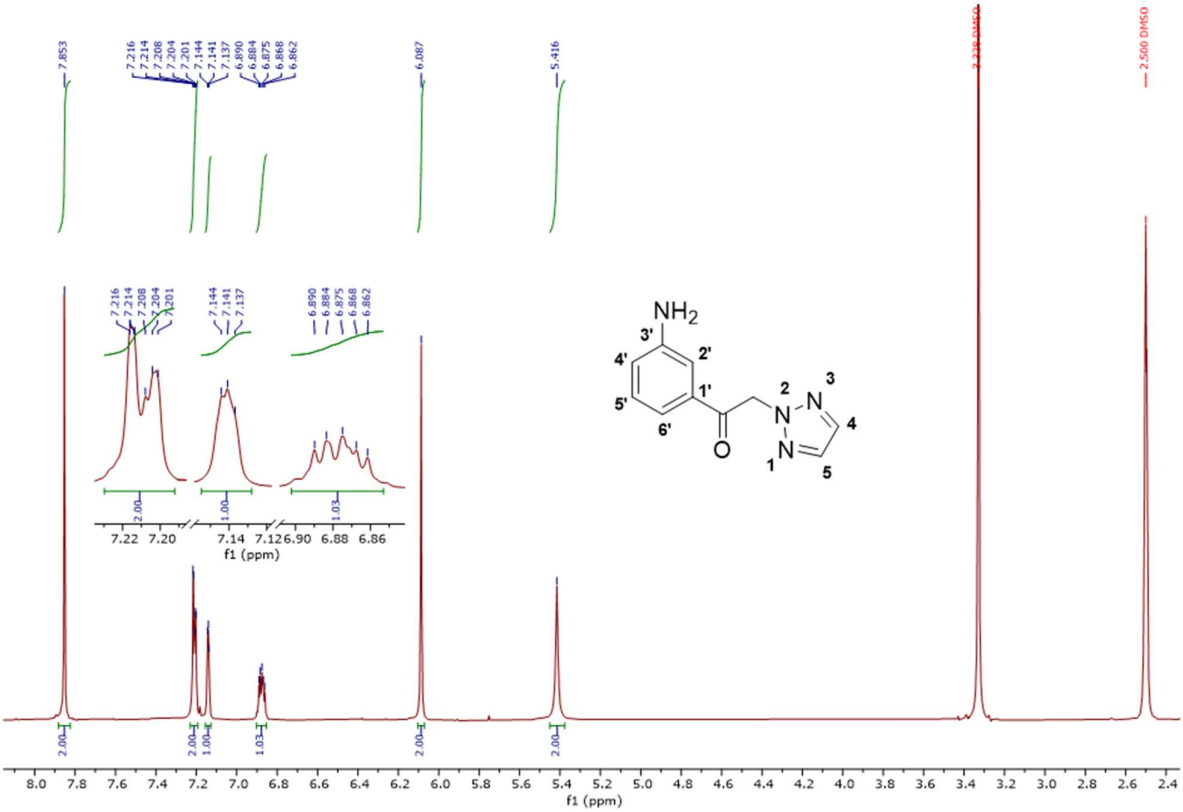

Figure S39. ^{1}H-NMR spectrum of 1-(3-aminophenyl)-2-(2*H*-1,2,3-triazol-1-yl)ethanone **8a**.

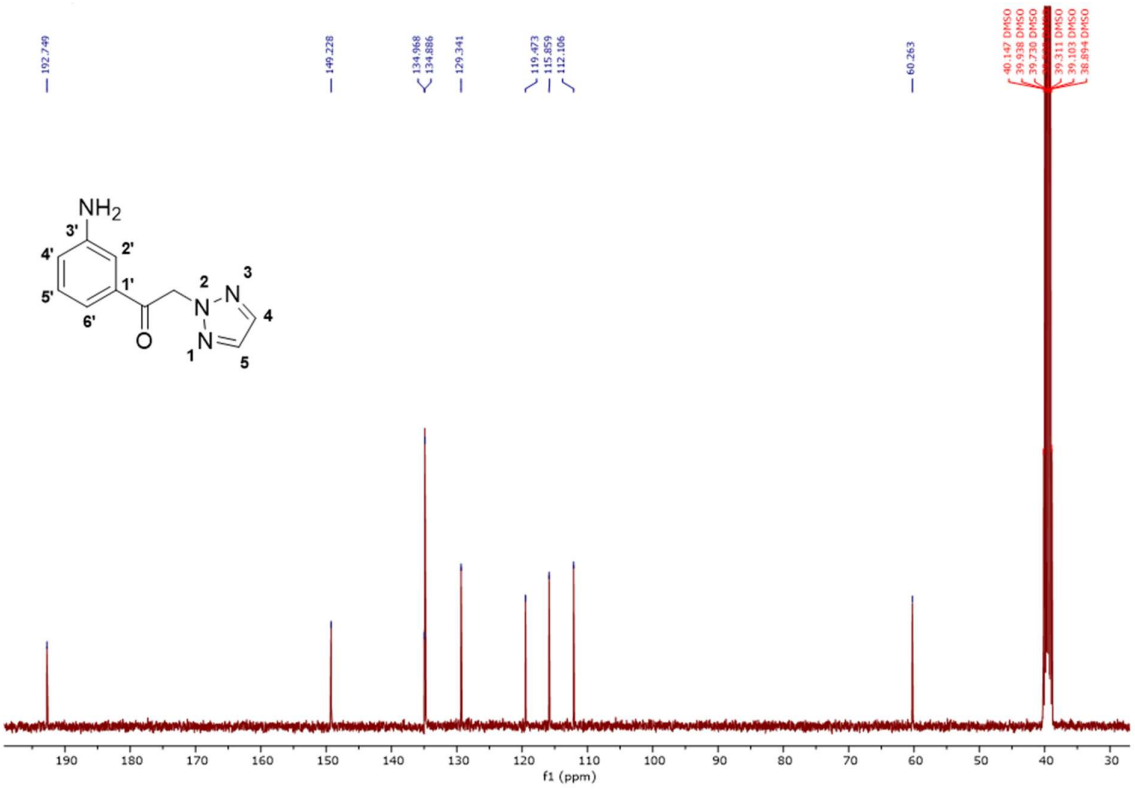

Figure S40. ^{13}C-NMR spectrum of 1-(3-aminophenyl)-2-(2*H*-1,2,3-triazol-1-yl)ethanone **8a**.

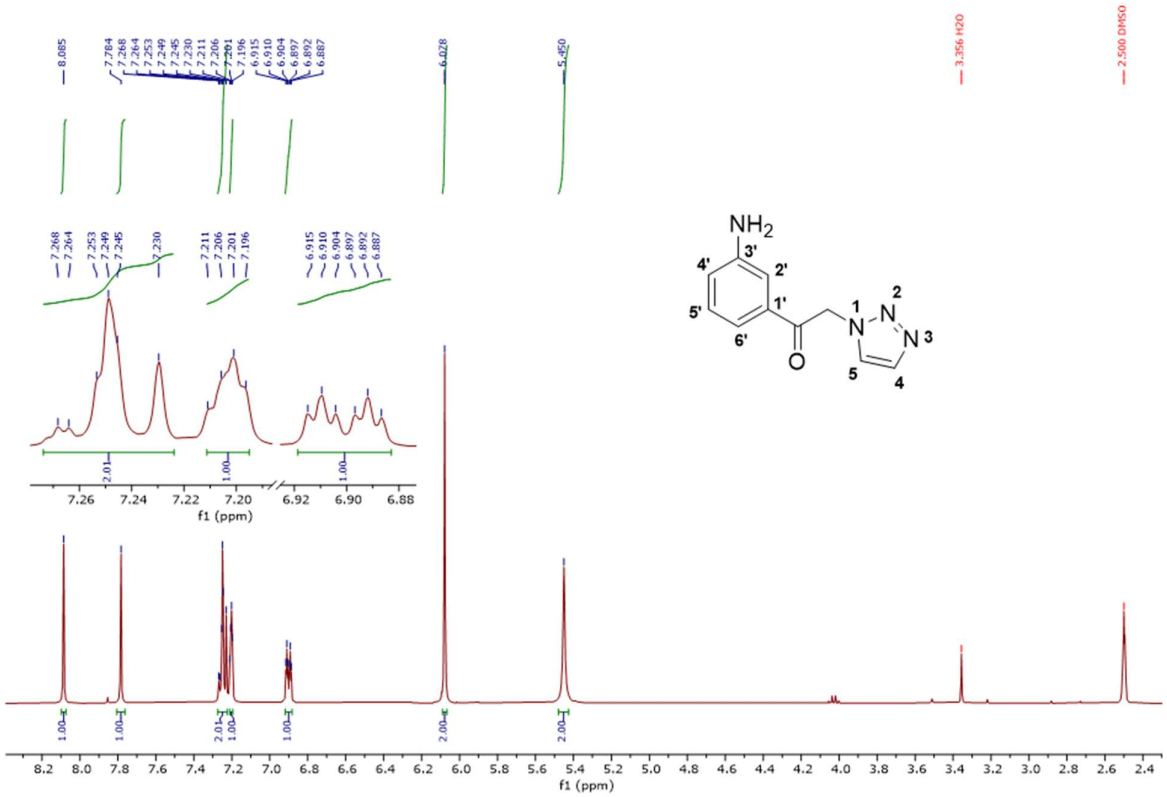

Figure S41. ^{1}H-NMR spectrum of 1-(3-aminophenyl)-2-(1*H*-1,2,3-triazol-1-yl)ethanone **8b**.

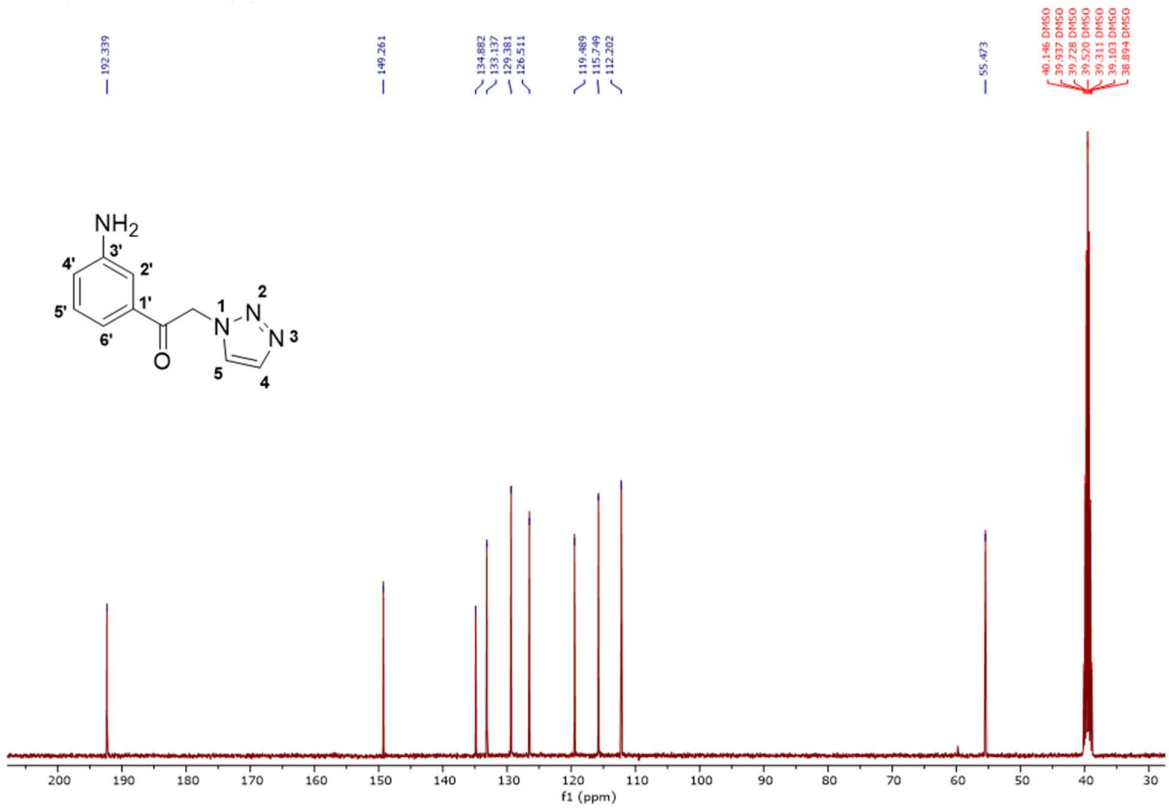

Figure S42. ^{13}C-NMR spectrum of 1-(3-aminophenyl)-2-(1*H*-1,2,3-triazol-1-yl)ethanone **8b**.

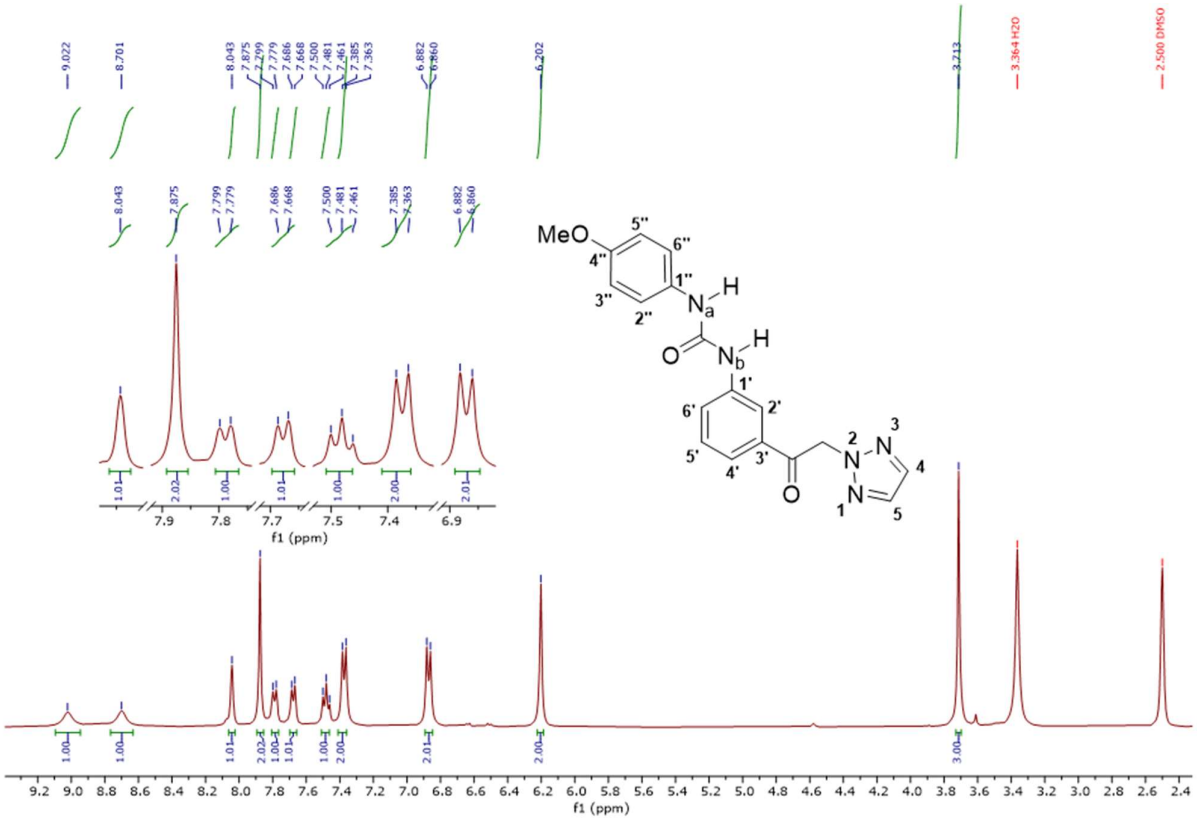

Figure S43. ^{1}H-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **11a**.

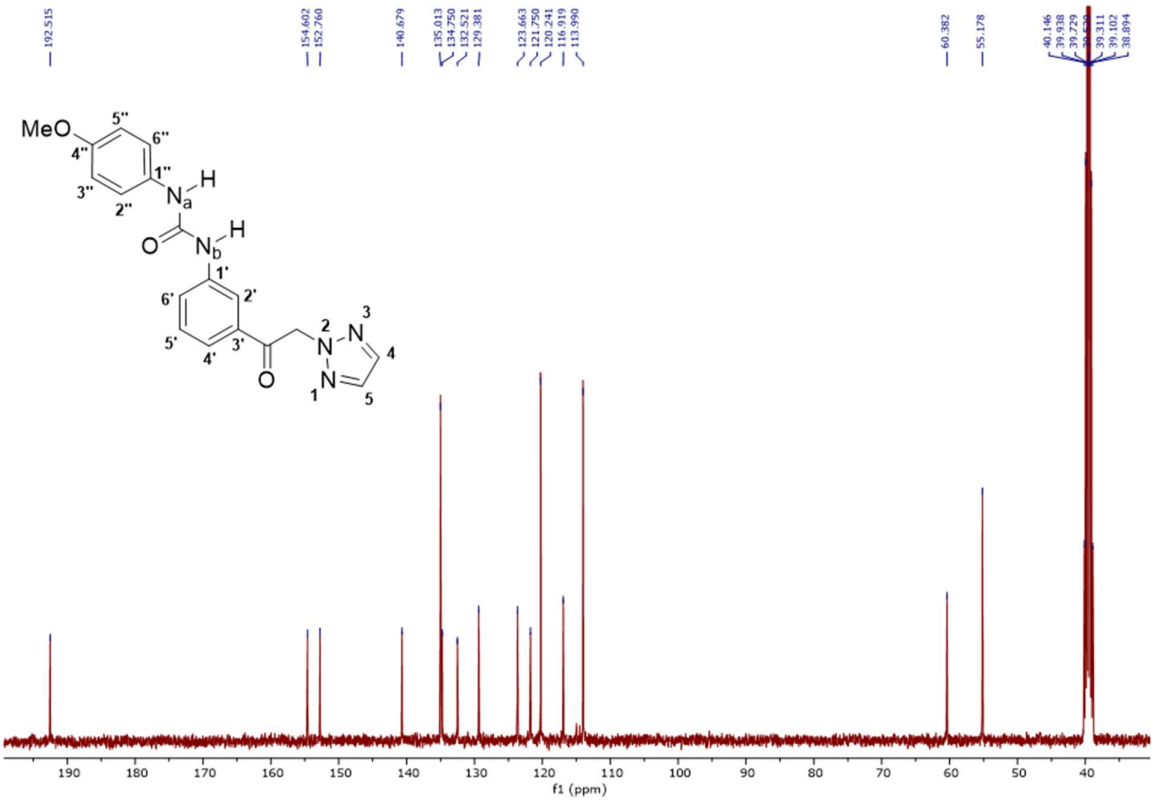

Figure S44. ^{13}C-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **11a**.

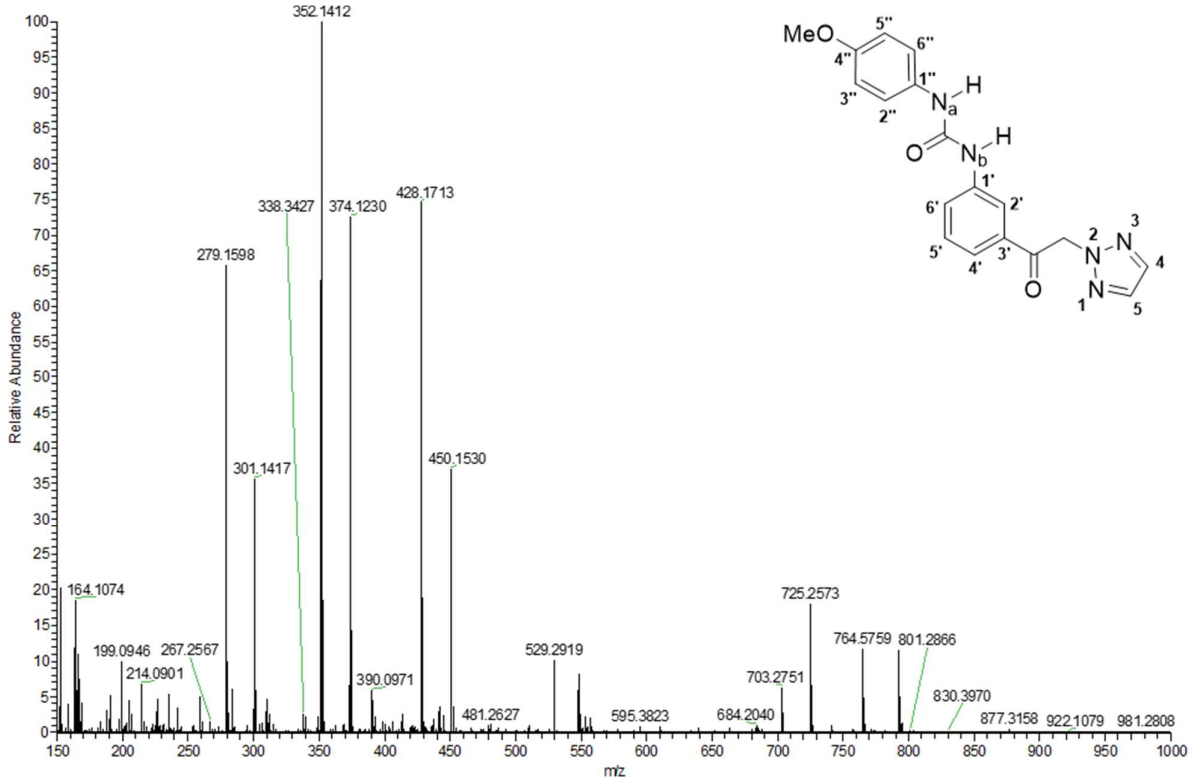

Figure S45. HRMS spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **11a** in 0.1% HCOOH in MeOH.

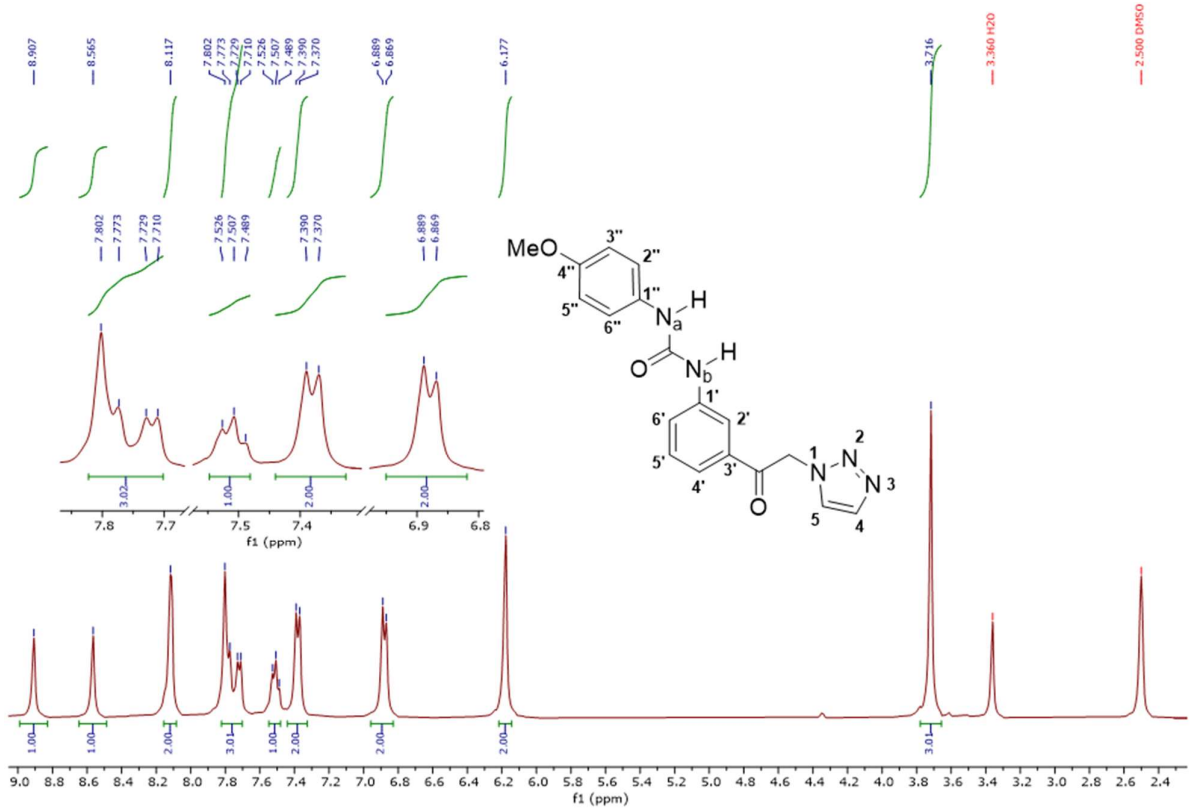

Figure S46. [1]H-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **11b**.

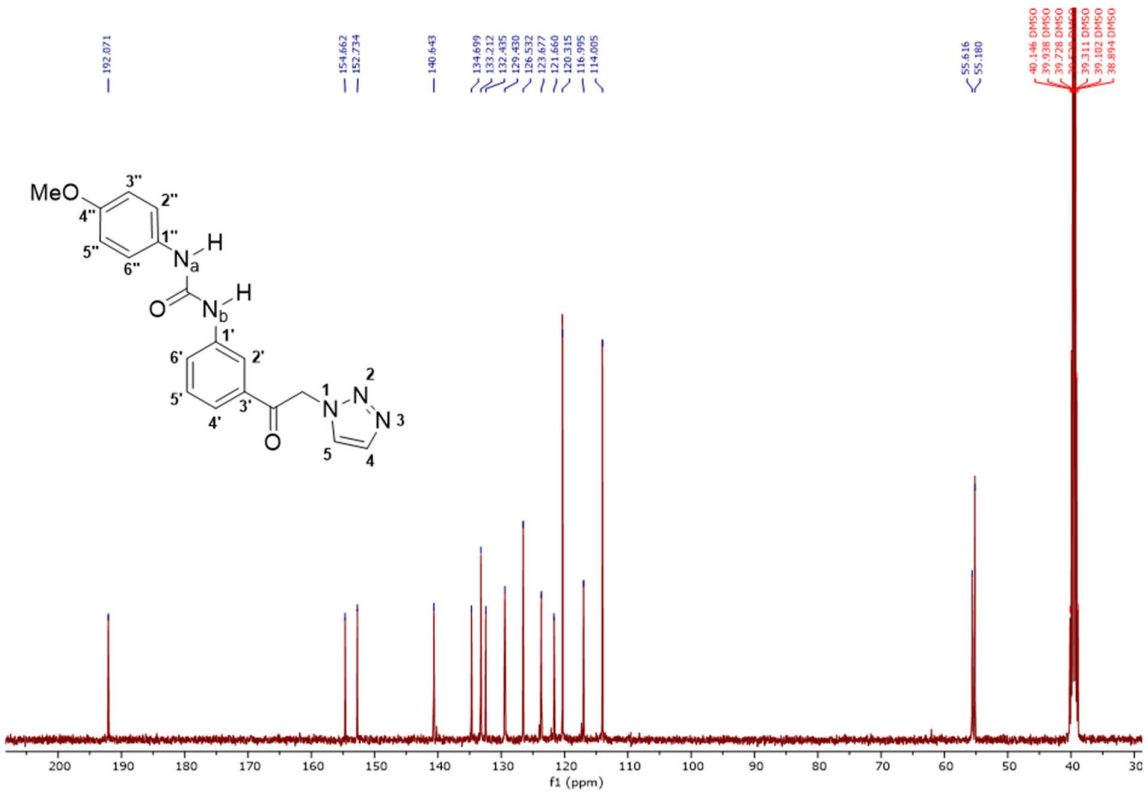

Figure S47. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **11b**.

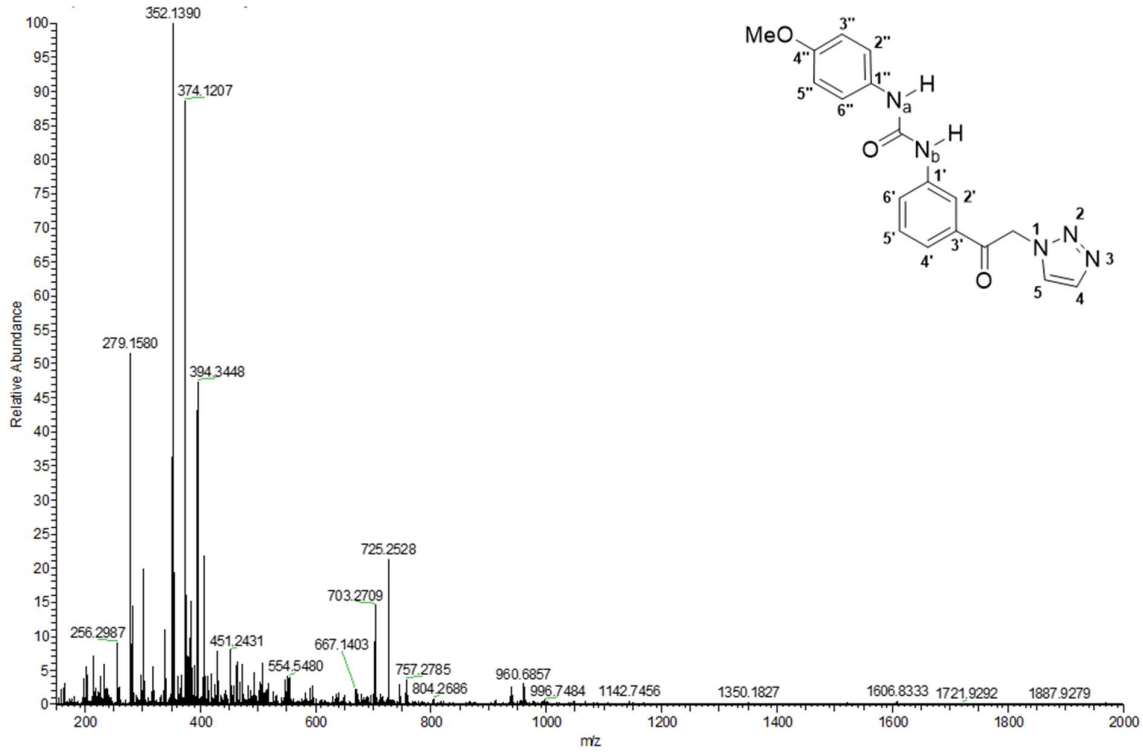

Figure S48. HRMS spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-methoxyphenyl)urea **11b** in 0.1% HCOOH in MeOH.

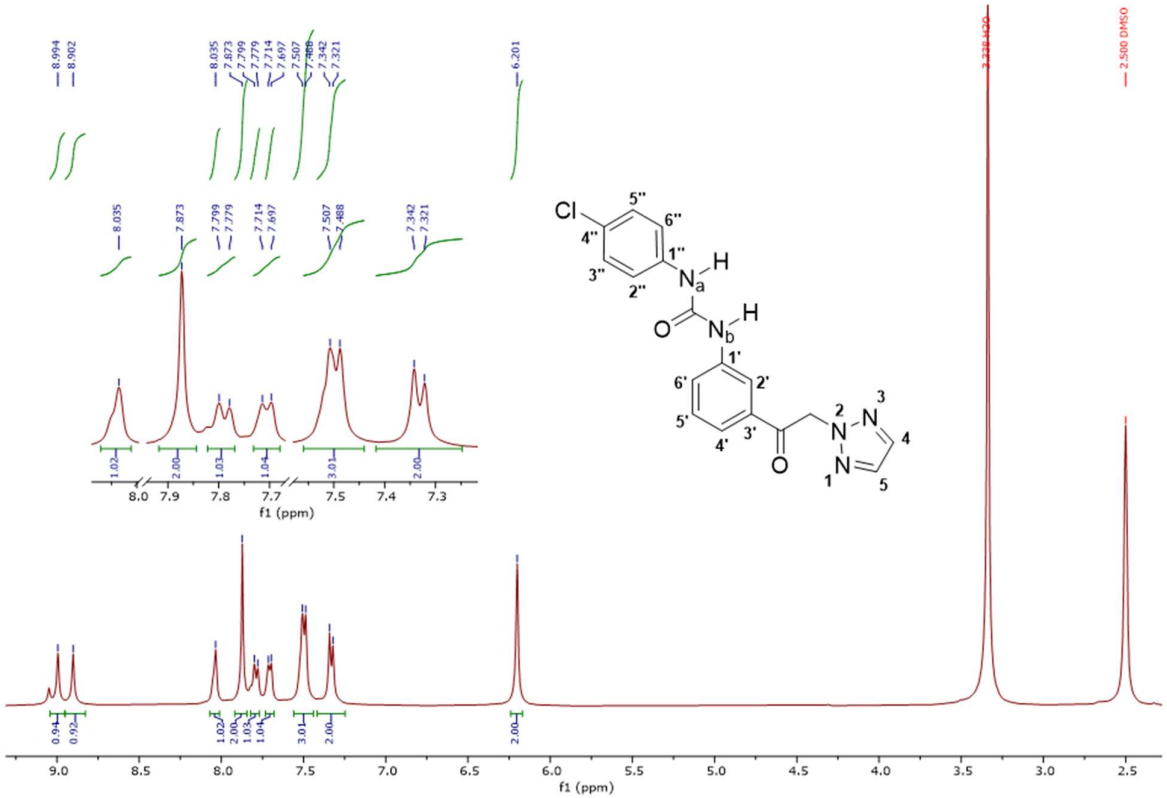

Figure S49. ^{1}H-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **11c**.

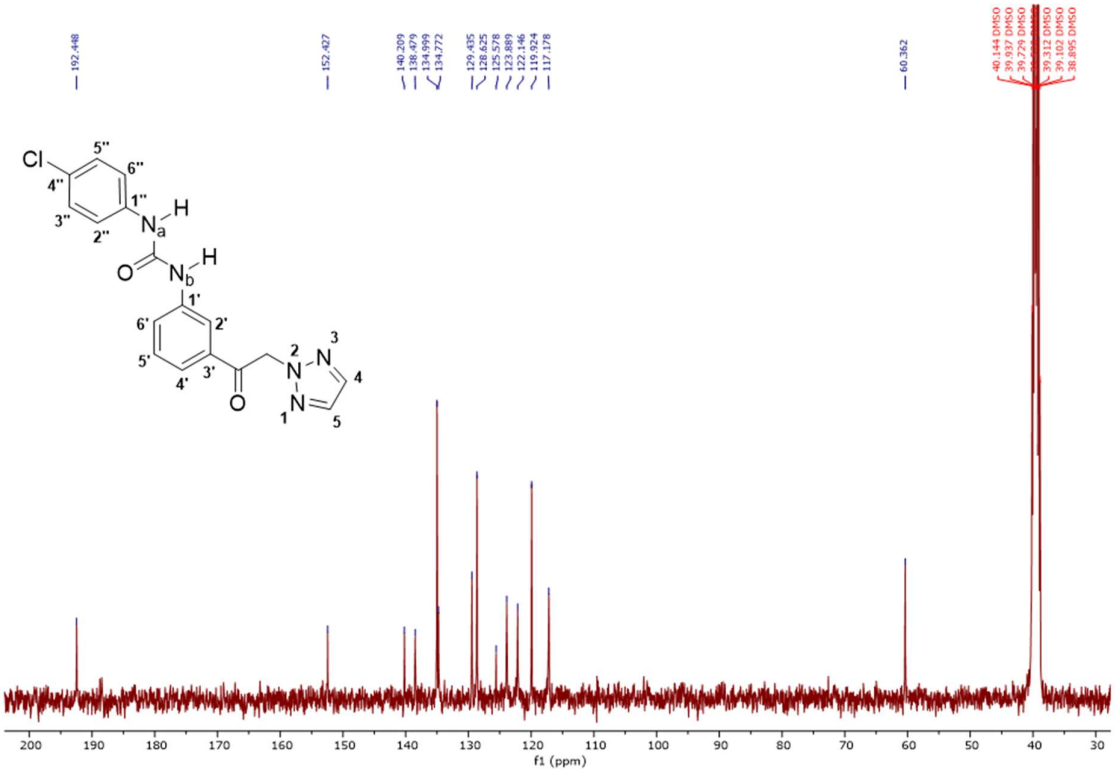

Figure S50. ^{13}C-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **11c**.

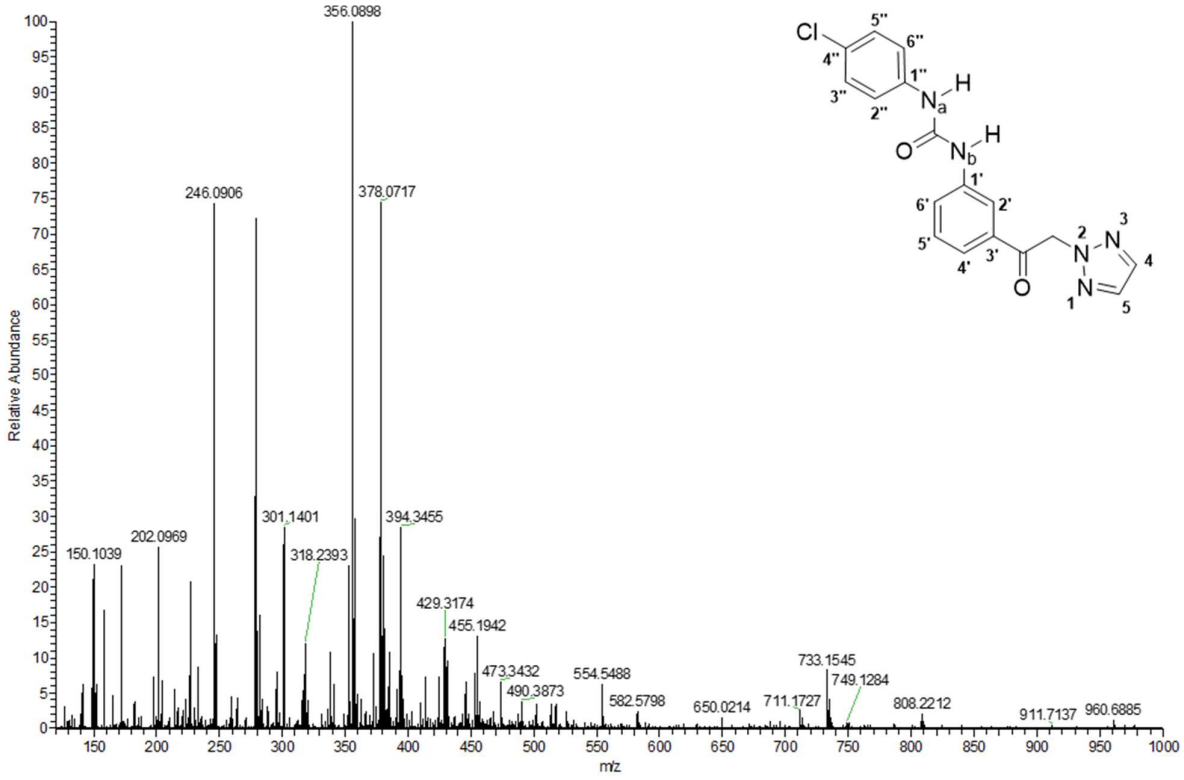

Figure S51. HRMS spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **11c** in 0.1% HCOOH in MeOH.

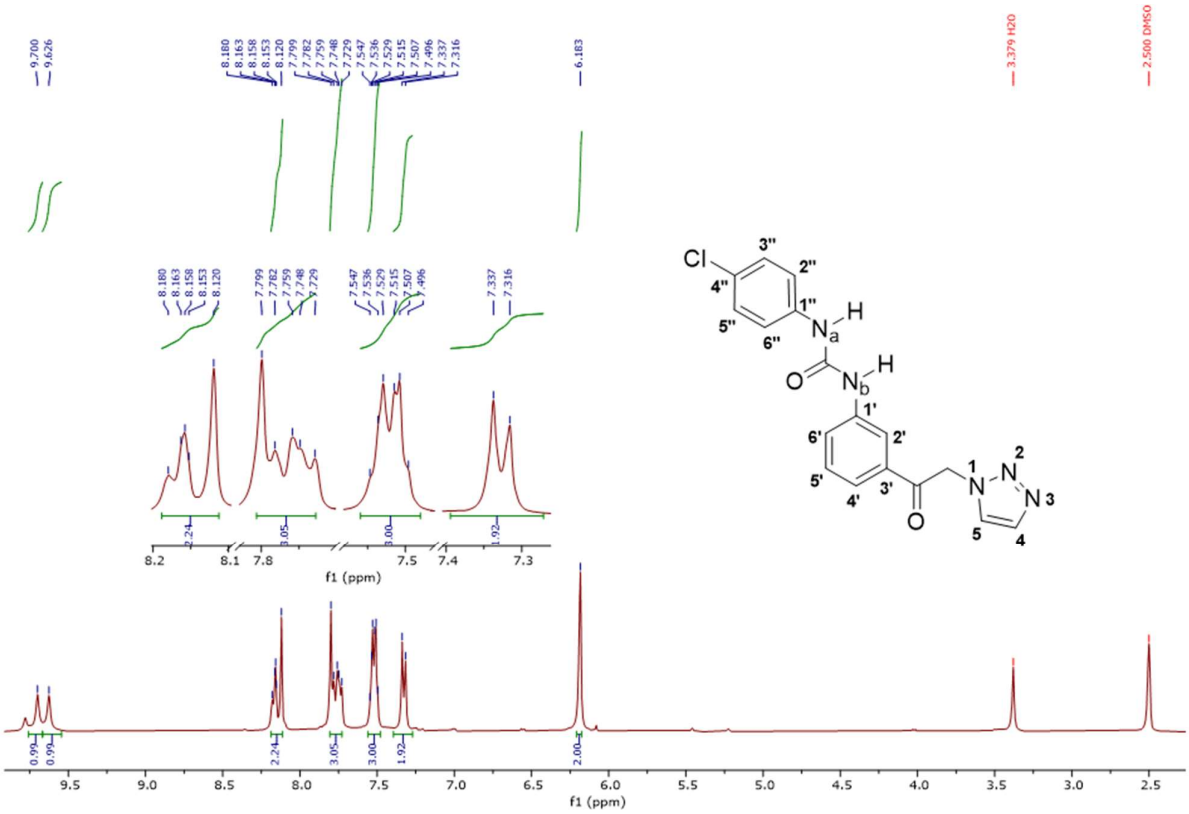

Figure S52. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **11d**.

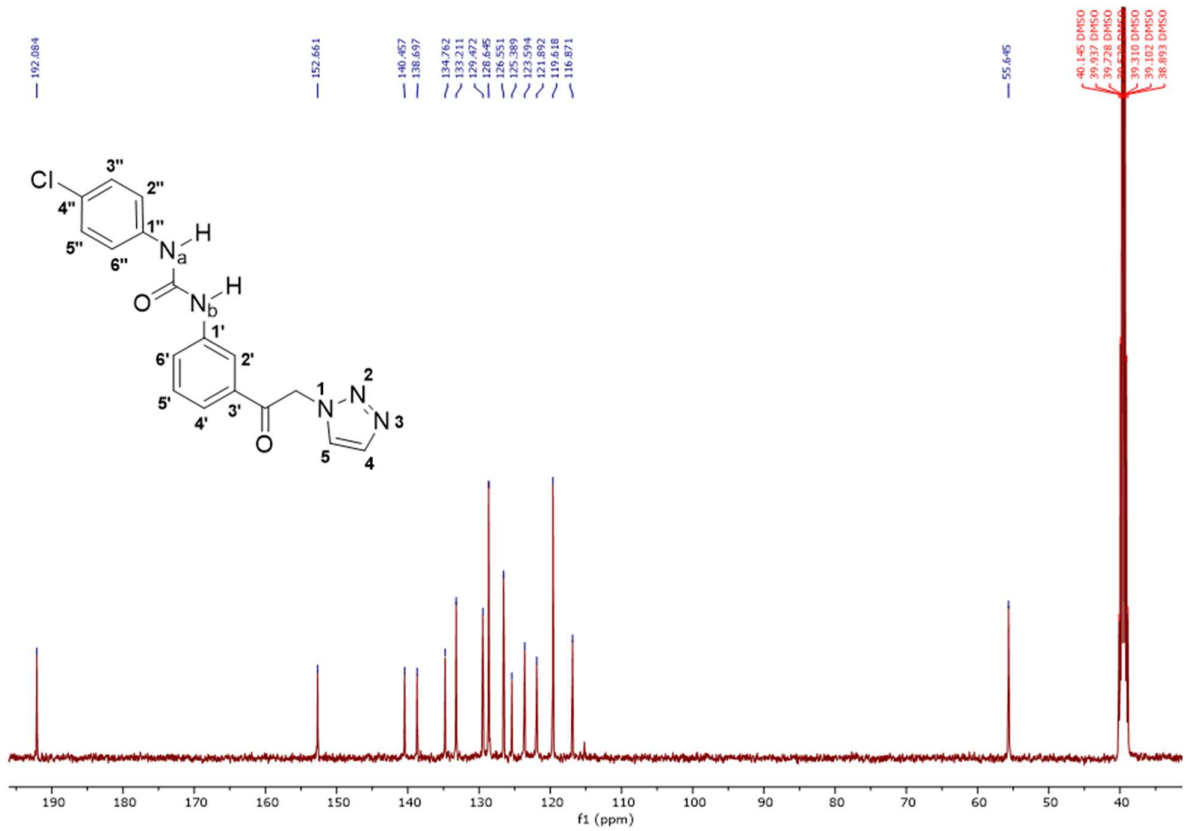

Figure S53. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **11d**.

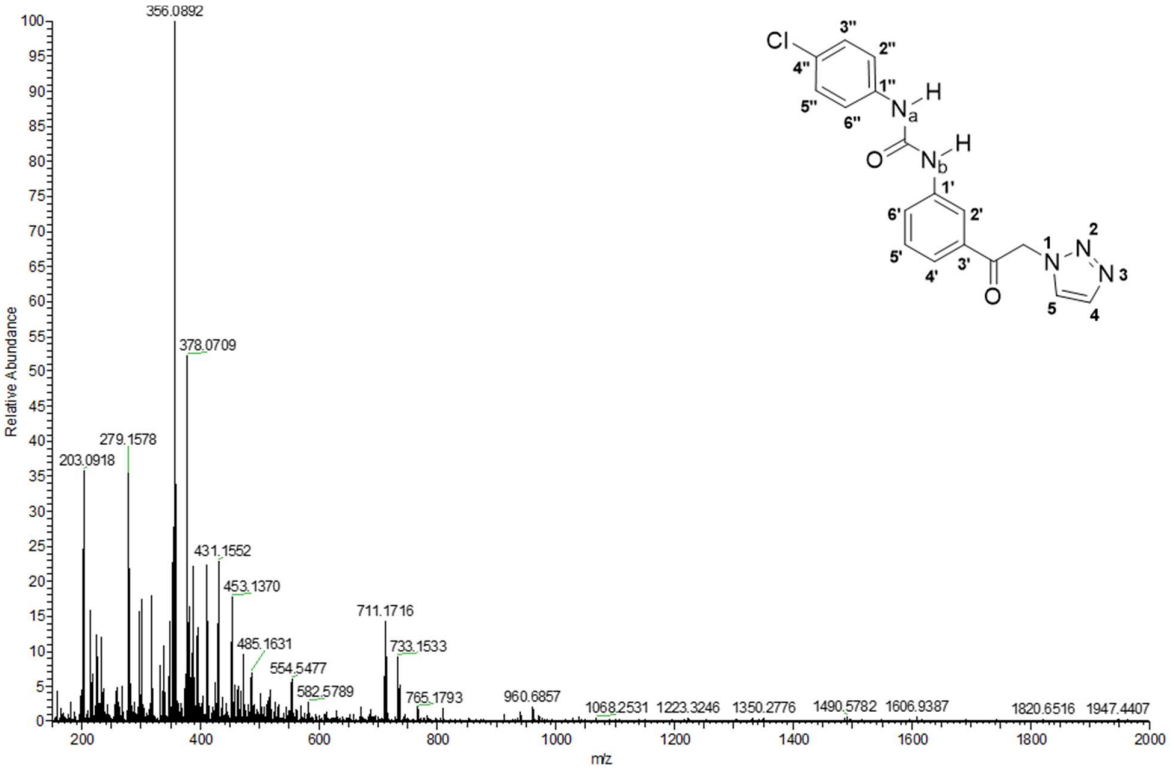

Figure S54. HRMS spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-chlorophenyl)urea **11d** in 0.1% HCOOH in MeOH.

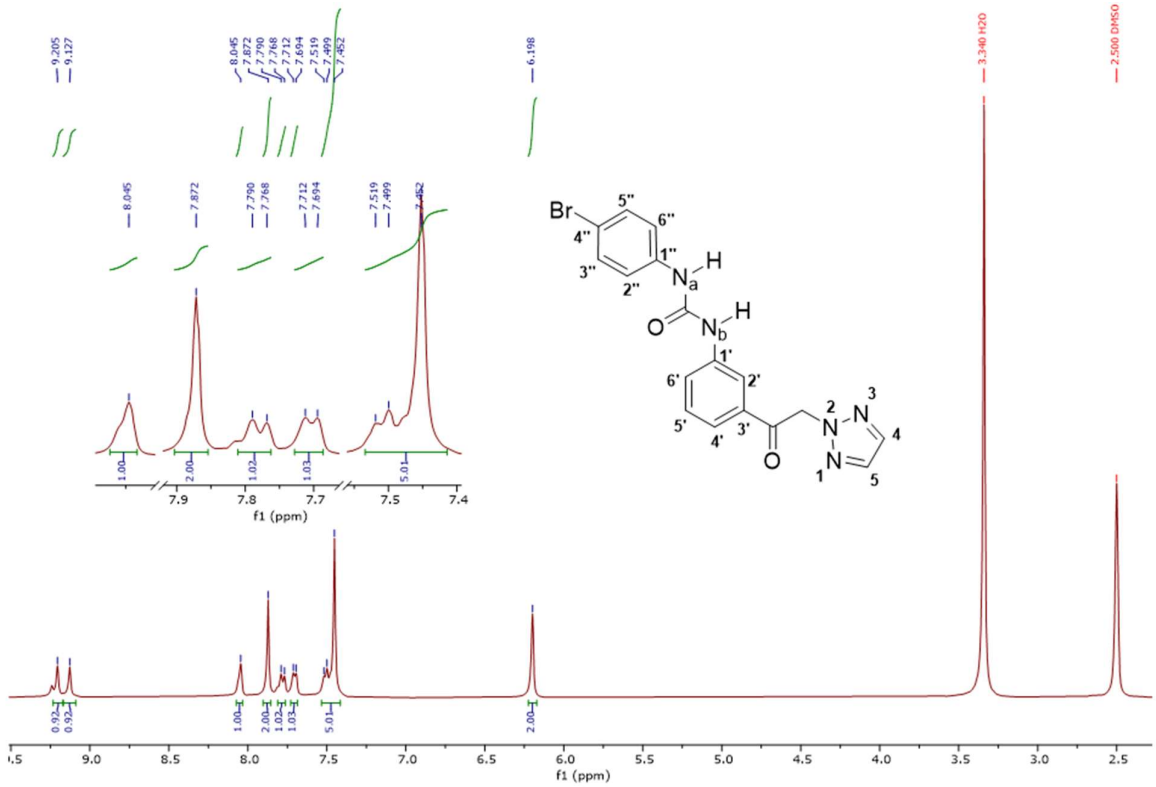

Figure S55. ^{1}H-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **11e**.

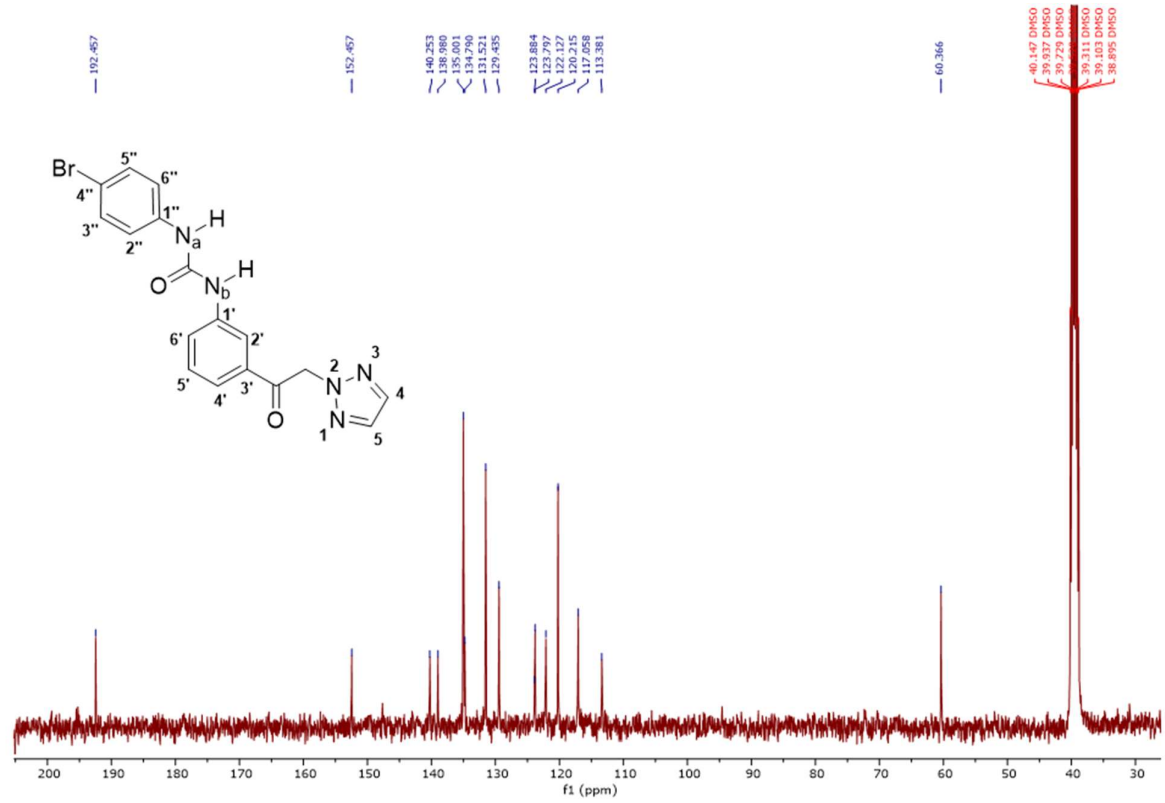

Figure S56. ^{13}C-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **11e**.

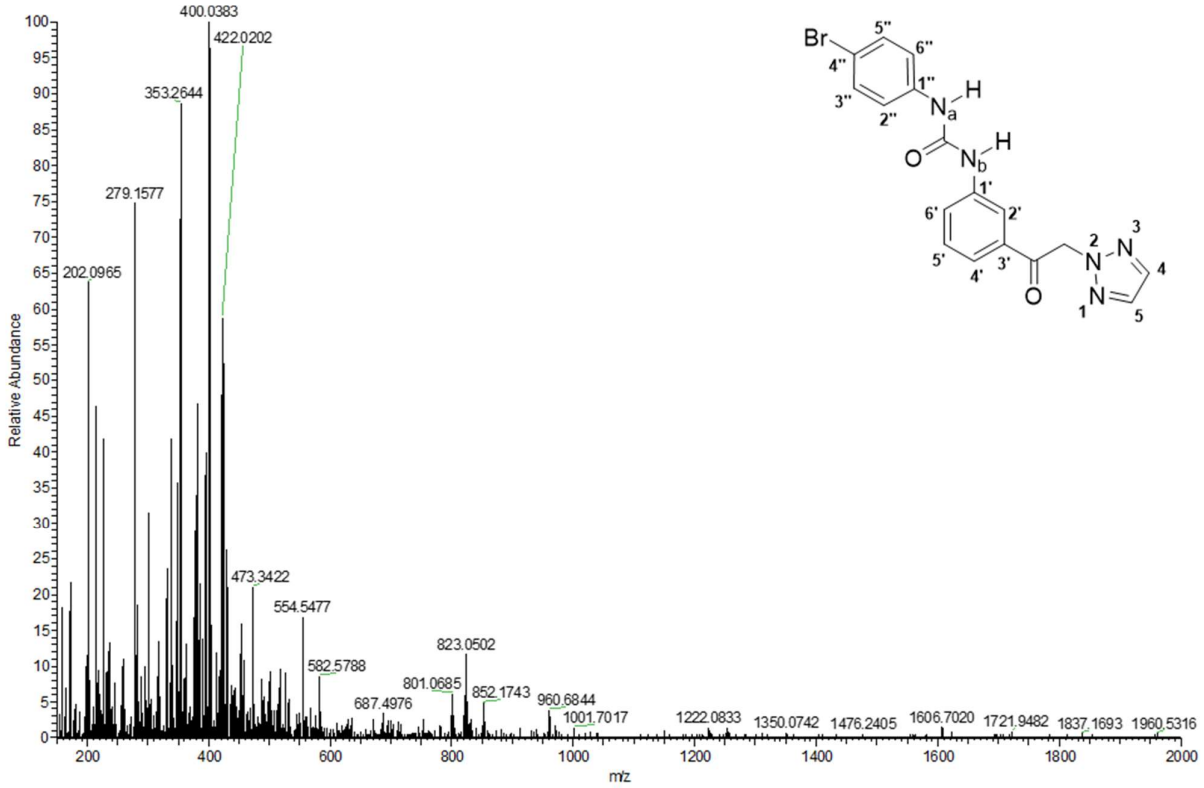

Figure S57. HRMS spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **11e** in 0.1% HCOOH in MeOH.

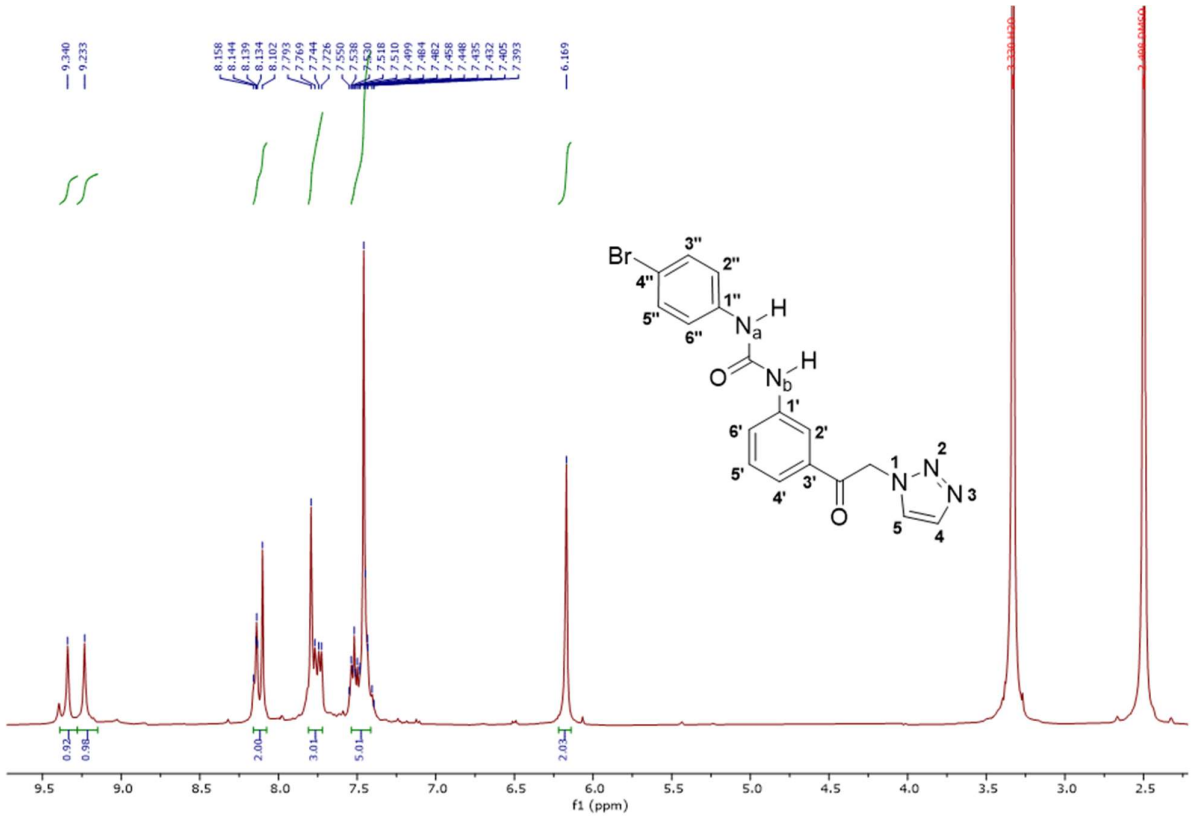

Figure S58. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **11f**.

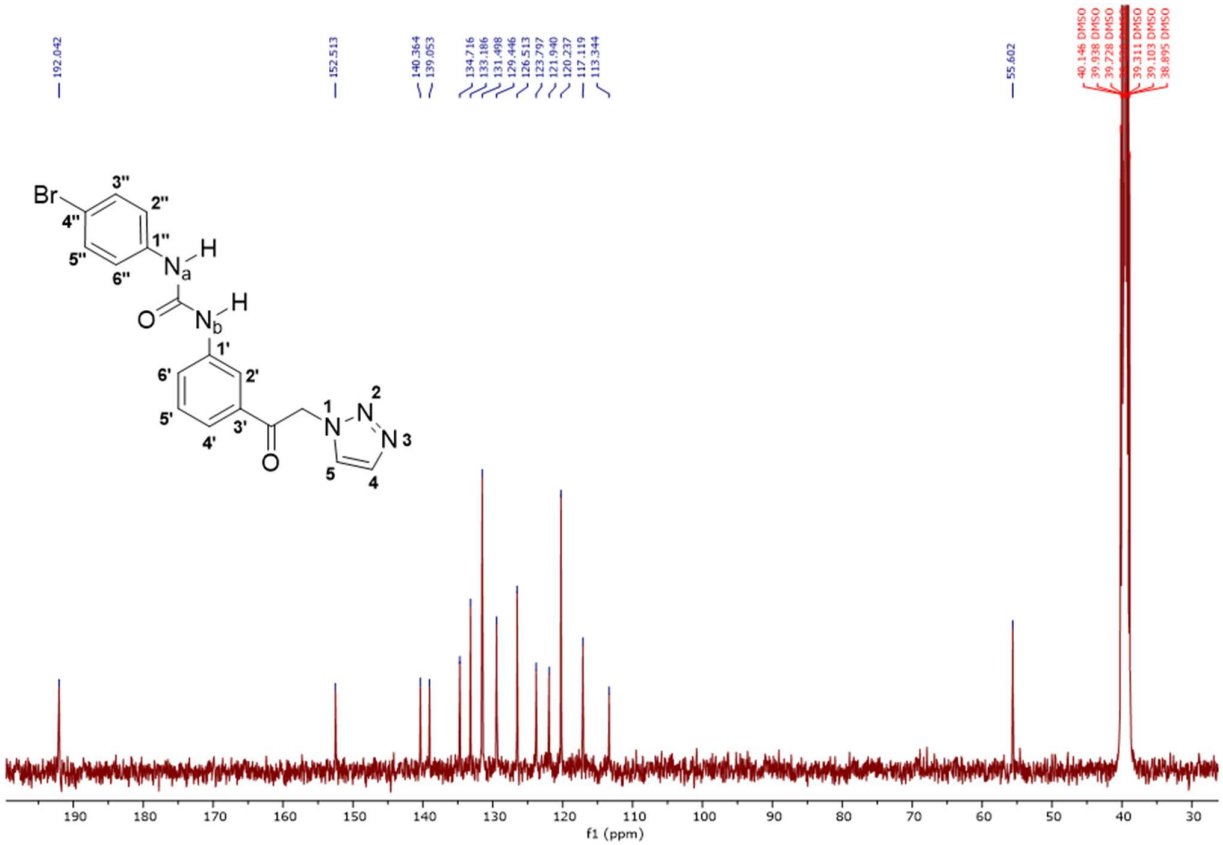

Figure S59. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **11f**.

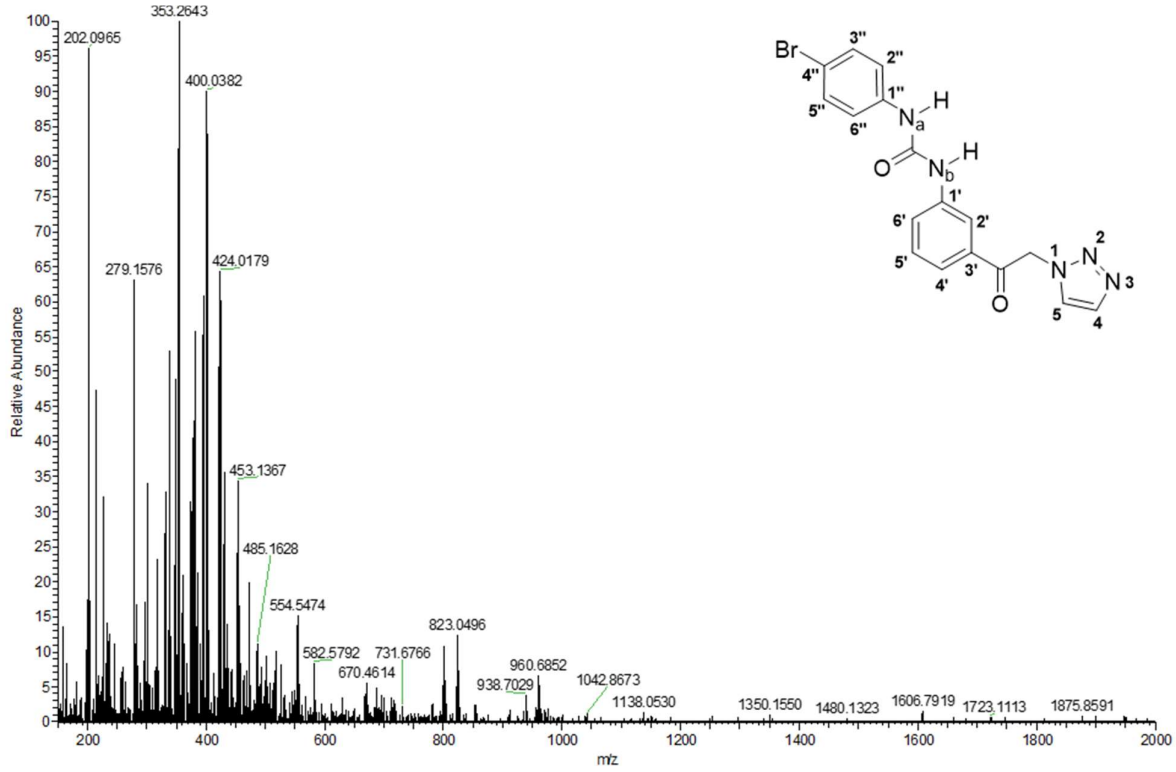

Figure S60. HRMS spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-bromophenyl)urea **11f** in 0.1% HCOOH in MeOH.

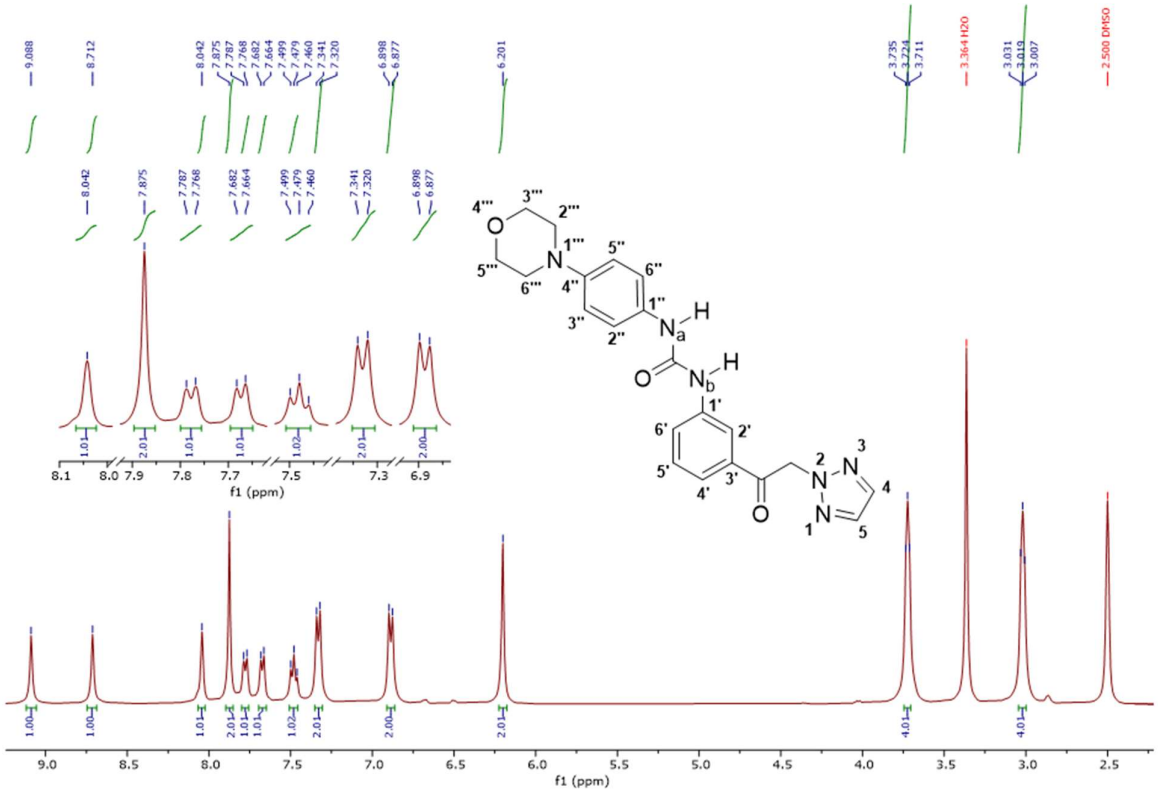

Figure S61. [1]H-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **11g**.

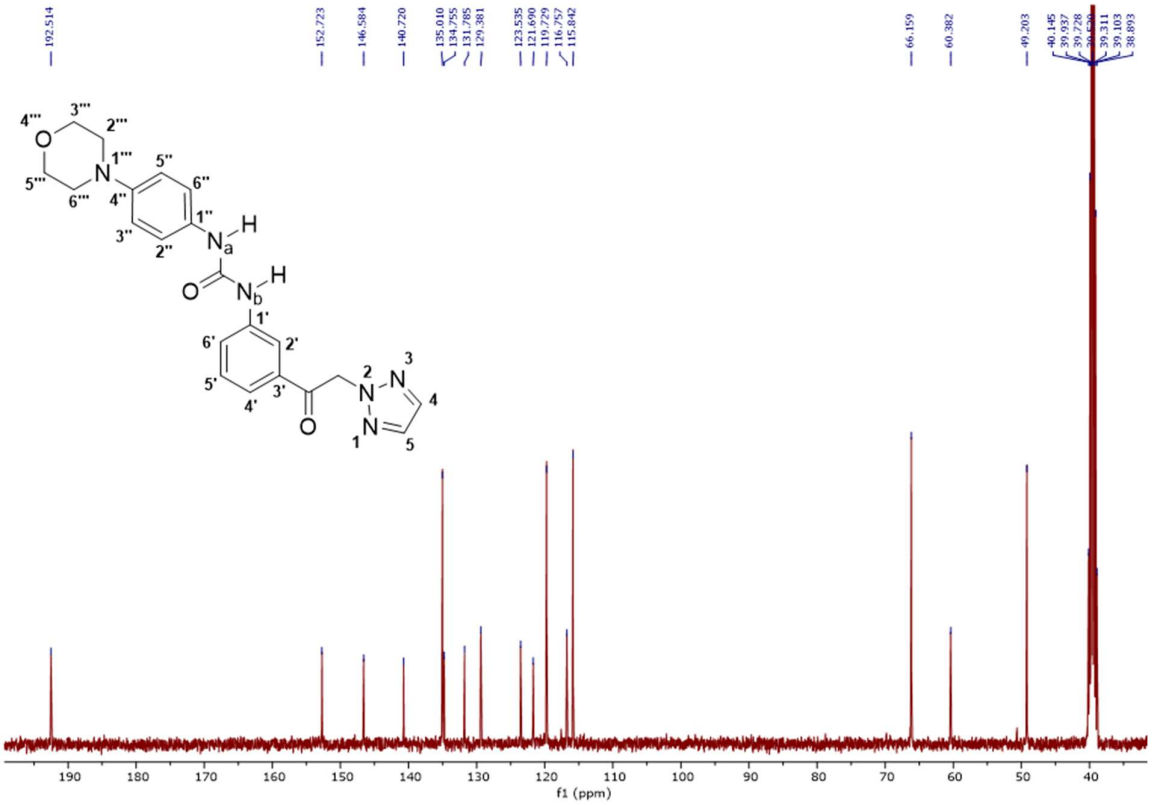

Figure S62. [13]C-NMR spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **11g**.

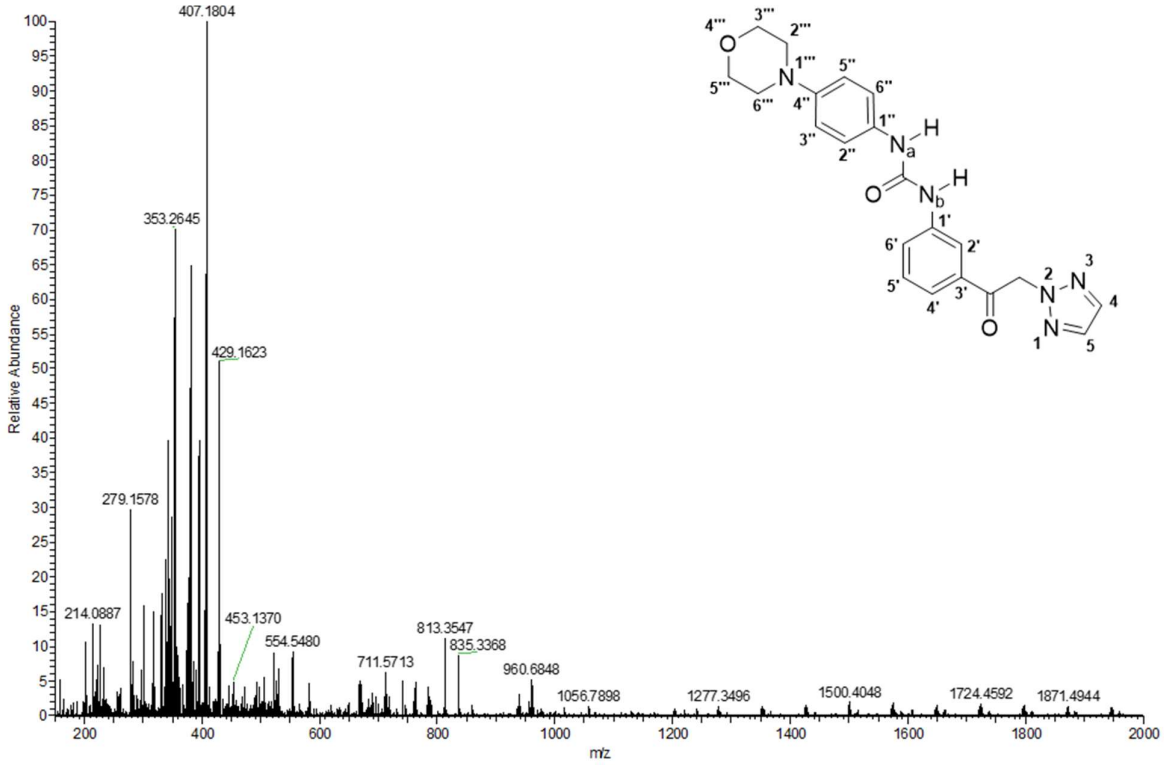

Figure S63. HRMS spectrum of 1-{3-[2-(2*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **11g** in 0.1% HCOOH in MeOH.

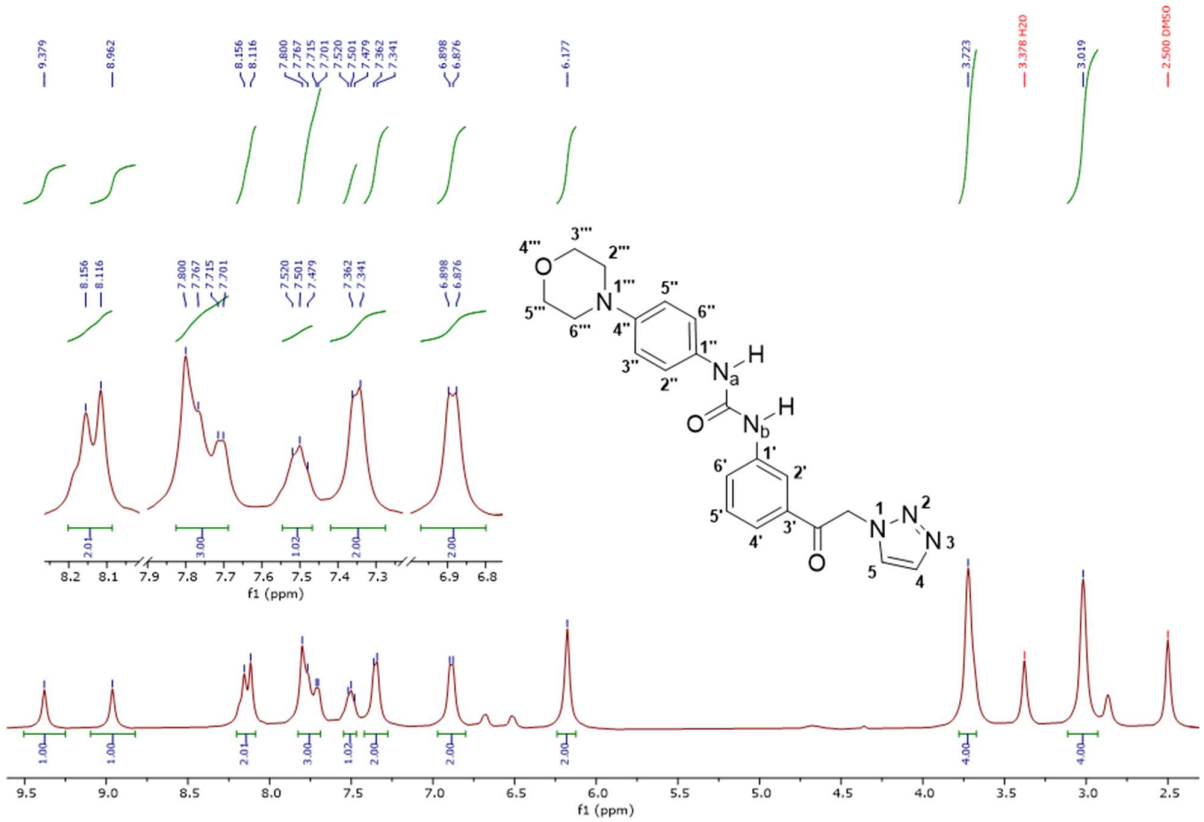

Figure S64. ^{1}H-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **11h**.

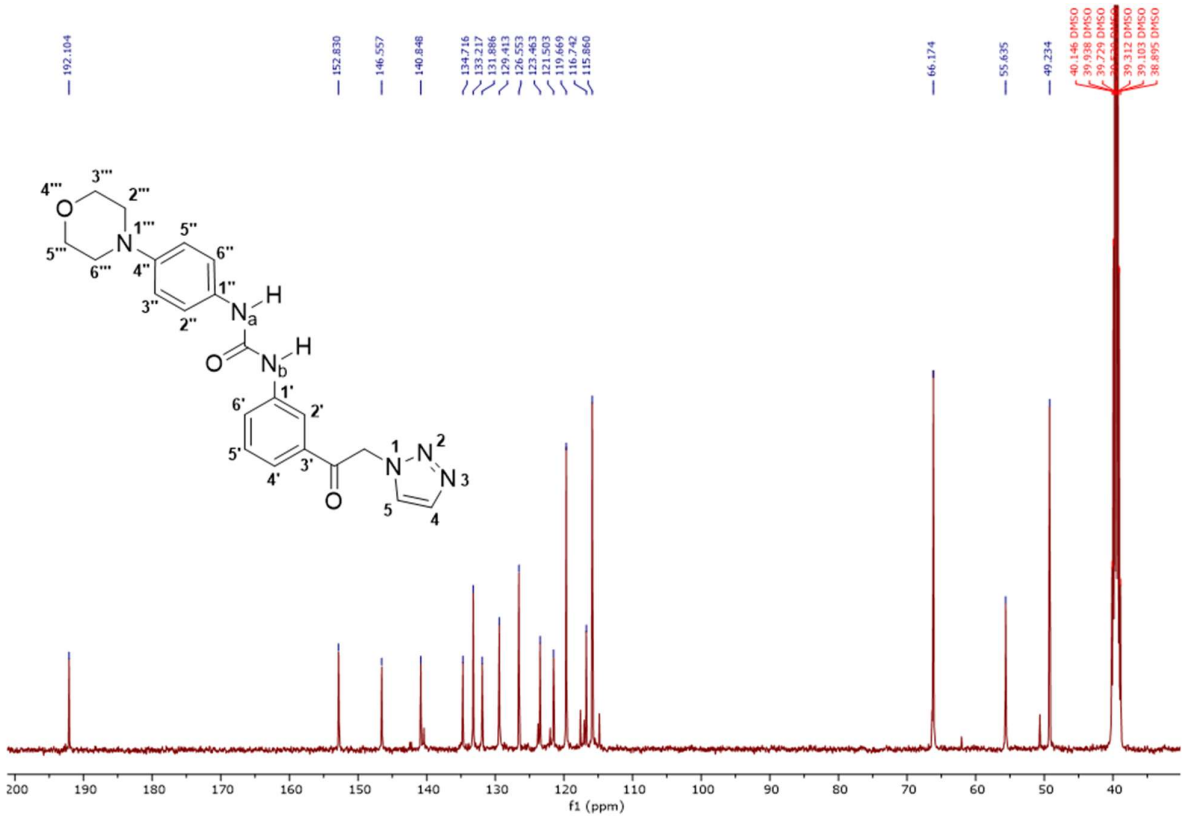

Figure S65. ^{13}C-NMR spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **11h**.

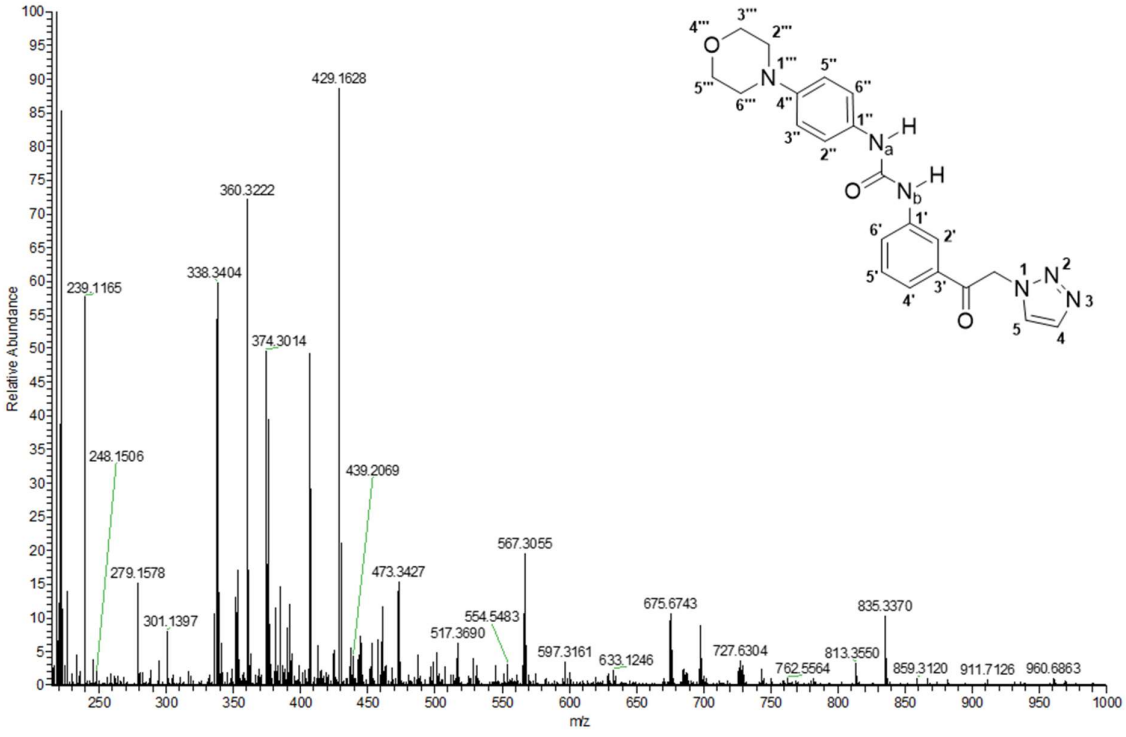

Figure S66. HRMS spectrum of 1-{3-[2-(1*H*-1,2,3-triazol-1-yl)acetyl]phenyl}-3-(4-morpholinophenyl)urea **11h** in 0.1% HCOOH in MeOH.

Computational Details

1. DFT calculations

Seventeen diarylureas **6a-i** and **11a-h** have been studied via Density Functional Theory (DFT). All calculations were carried out using the B3LYP [3-4] functional in conjunction with the 6-311+G(d,p) [5] basis set in THF solvent employing the polarizable continuum model (PCM). [6,7]. This model is divided into a solute part lying inside a cavity, surrounded by the solvent part represented as a material without structure, characterized by its macroscopic properties, i.e., dielectric constants and solvent radius. The B3LYP/6-311+G(d,p) methods has been regarded as an appropriate calculation for the present molecular systems.[8-9]

Conformational analyses were carried out at first. All species were fully geometrically optimized in the ground state with respect to their energy to locate the global minimum structure for each species. The energy convergence criteria for the geometry optimization are set to 1×10^{-8} hartree. All calculations were carried out employing the Gaussian16 code. [10]

2. Molecular Binding (MB)

MB1 methodology: Induced fit docking was employed to investigate potential binding interactions at the allosteric blind site of Cannabinoid receptor 1 (PDB ID: 5XR8).[11] The in silico studies were conducted using the Protein Preparation Wizard in the Schrödinger Suite to process the crystal structures. All compounds were sketched in the Schrödinger's Maestro molecular modeling platform and underwent energy minimization using MacroModel [12] and density functional theory (DFT) calculations. Conformer analysis ensured the identification of stable low-energy geometries through DFT, while molecular mechanics provided further refinement, balancing accuracy and computational efficiency. LigPrep was utilized to generate 3D models, accounting for stereochemistry, and the "add metal binding states" option was applied to optimize ligand binding. Geometry optimization in MacroModel preserved chirality, with the OPLS2005 force field employed for minimization while considering protonation states at physiological pH. Chemically accurate 3D models were generated using the Hammett and Taft methods alongside an ionization tool. Ligand structures were further minimized in a water environment with OPLS2005 [13] as the designated force field. To explore the most stable conformations, a mixed-torsional/low-sampling conformational search was performed, and the lowest-energy conformer was selected for docking studies. The Induced Fit Docking (IFD) approach in the Schrödinger Suite was utilized for docking, with the ligand being docked in five energetically favorable conformations obtained from MacroModel. Prior to docking, protein preparation involved constrained refinement, which included automatic side-chain trimming based on B-factor analysis and Prime-based side-chain optimization. The Glide/XP docking tool was used, with an active-site dielectric constant set to 80, and crystallographic water molecules were retained throughout the docking process

MB2 methodology: Additionally, the molecular binding calculations were performed using AutoDock software,[14] specifically employing the Lamarckian Genetic Algorithm for the binding in the orthosteric position of the CB1. Protein crystal structures were obtained from the online database "Protein Data Bank—PDB" and directly imported into the AutoDock program for analysis.[15] Ligands were designed using the ChemOffice software, which was also used to minimize their energy using an MM2 force field.[16]

3. Molecular Dynamics (MD)

The molecular dynamics (MD) simulations were conducted with SPC/E-modeled water molecules [17] surrounding the drug-protein complex. To neutralize the solution, sodium (Na^+) and chloride (Cl^-) ions were added until the salt concentration reached 0.150 M NaCl. The protein's N-terminal was modified with an acetyl group, while the C-terminal remained uncapped due to its involvement in the active site. The protein-ligand interactions were modeled using the OPLS2005 force field, with long-range electrostatic interactions handled by the particle mesh Ewald (PME) [18,19] method and a grid spacing of 0.8 Å. Van der Waals and

short-range electrostatic interactions were smoothly truncated at 9.0 Å. Temperature was controlled using the Nose-Hoover thermostat, and pressure was regulated using the Martyna-Tobias-Klein method. Periodic boundary conditions were applied, with simulation box dimensions of (10.0 × 10.0 × 10.0) Å. The equations of motion were integrated with the multistep RESPA integrator,[20] using a 2-fs inner time step for bonded and short-range non-bonded interactions (within a 9 Å cutoff), and a 6-fs outer time step for interactions beyond the cutoff. Equilibration followed the default protocol of Desmond,[21] starting with Brownian dynamics in the NVT ensemble at 310 K with restraints on heavy atoms, followed by a relaxation step in the NPT ensemble without restraints for 1.0 ns. The production phase of the MD simulation lasted 200 ns to ensure sufficient data for analyzing the ligand's binding to the protein. These simulations were performed on GPU-accelerated workstations, with performance evaluated by monitoring the RMSD convergence of the protein backbone's Cα atoms and the ligand's RMSD.

The molecular docking of seventeen compounds to CB1 receptor were calculated. The visualization of the results was performed using the AutoDock software. For the creation of the grid box, the coordinates used were those of the ligand bound to macromolecule, provided that the ligand binds to the enzyme's active site. The specific coordinates used for each enzyme were as follows: 5XR8 (CB1) [22]: X=-42.678, Y=-157.964, Z=308.565. For the grid box creation, the dimensions used for all receptors were the same and as follows: number of grid points: X= 40, Y= 40, Z= 40 and grid spacing: 0.430 Å.

1. DFT Calculations

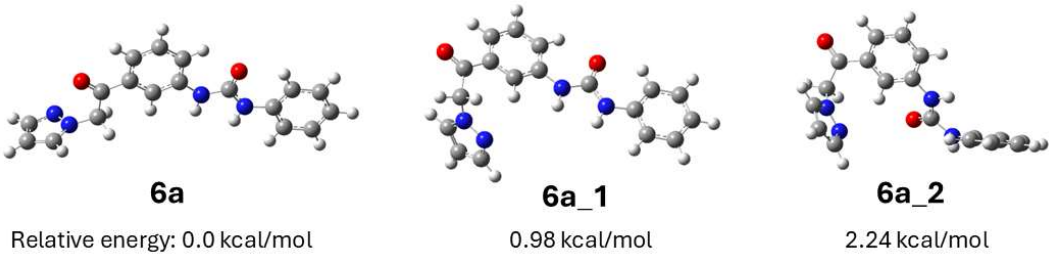

Figure S1: Calculated minima structures of diarylurea **6a** at the B3LYP/6-311+g(d,p) methodology in THF solvent.

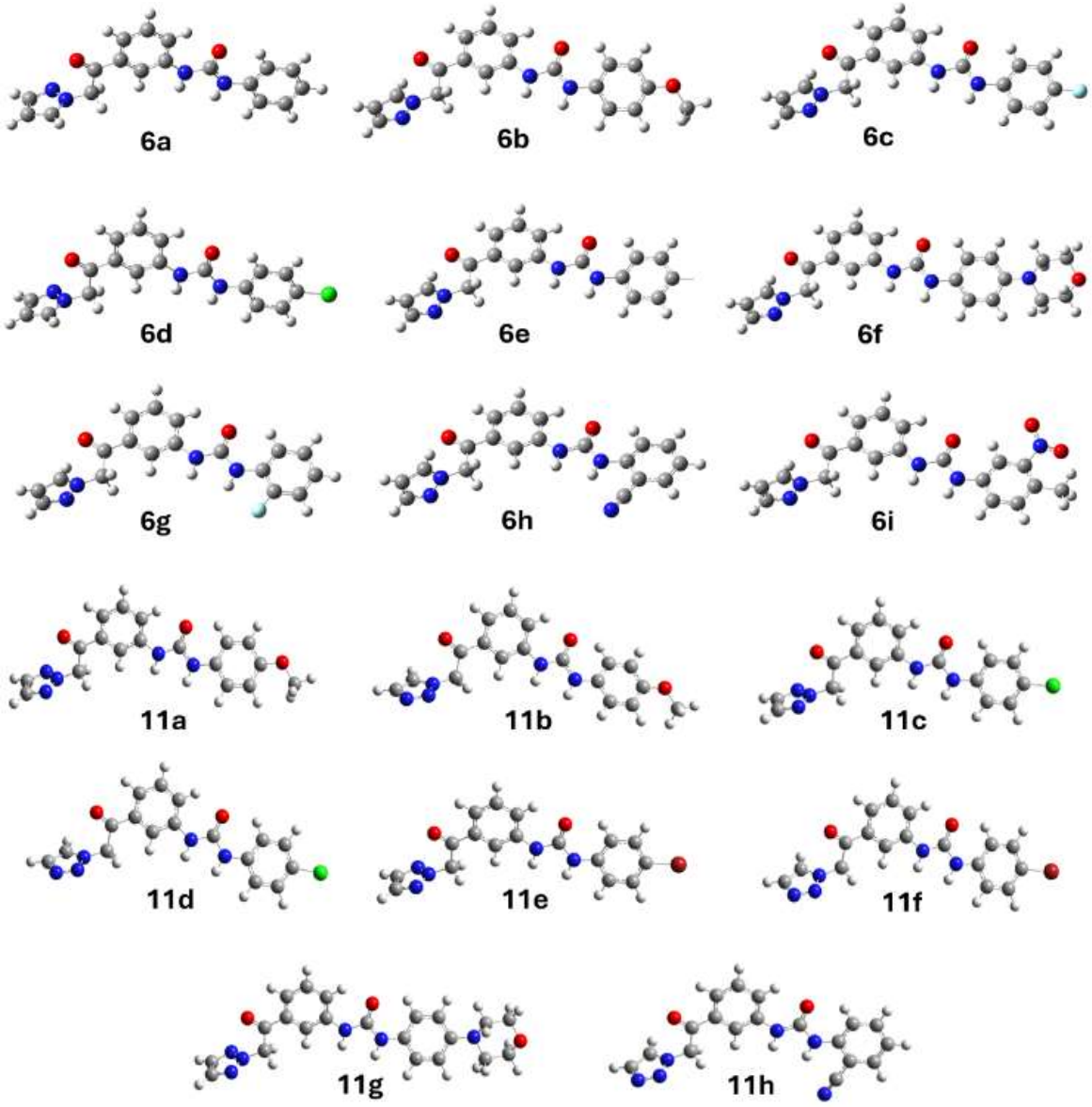

Figure S2: Calculated minima structures of new diarylureas **6a-i** and **11a-h** at the B3LYP/6-311+g(d,p) methodology in THF solvent.

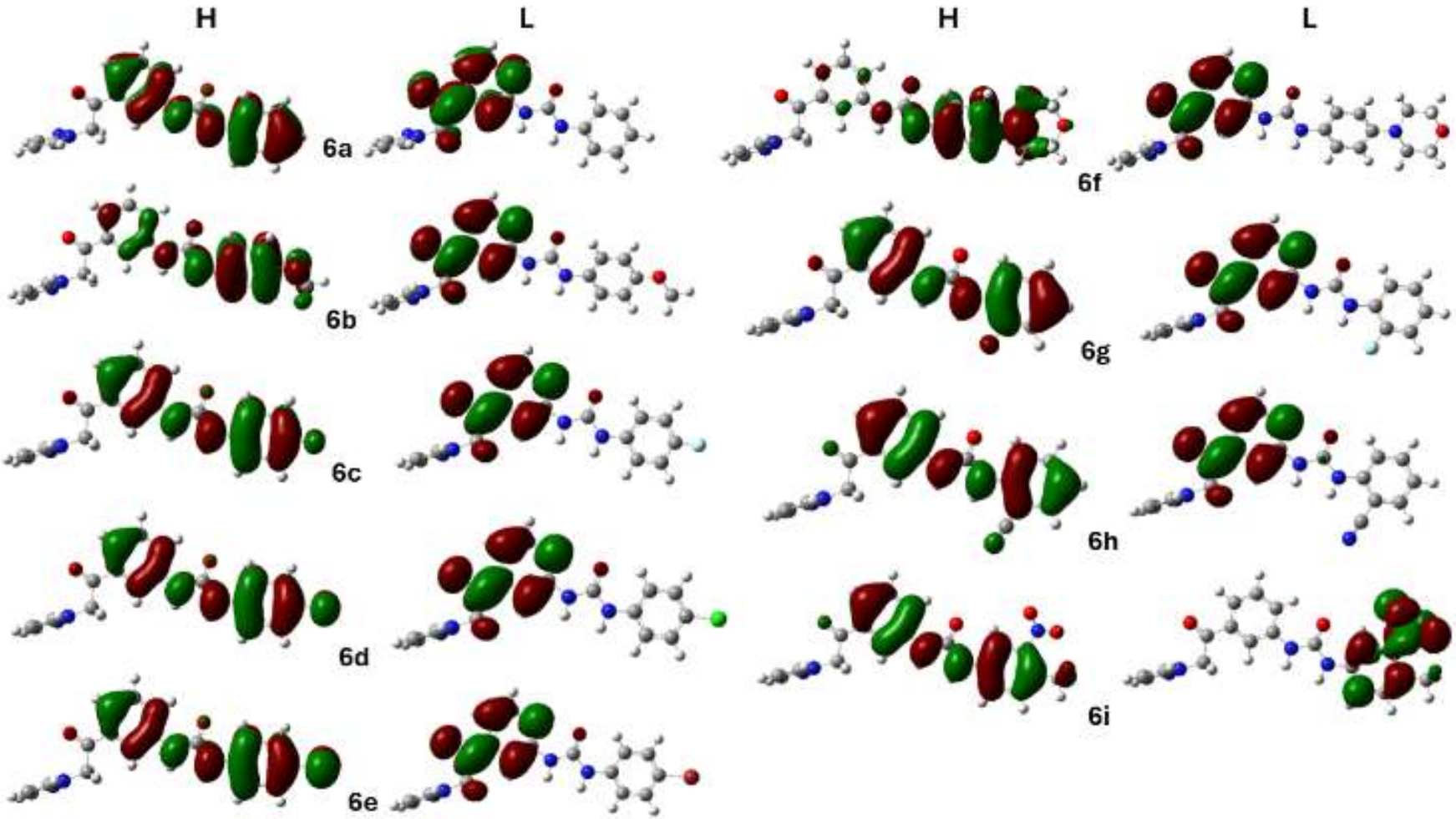

Figure S3: Calculated minima structures of new diarylureas **6a-i** at the B3LYP/6-311+g(d,p) methodology in THF solvent.

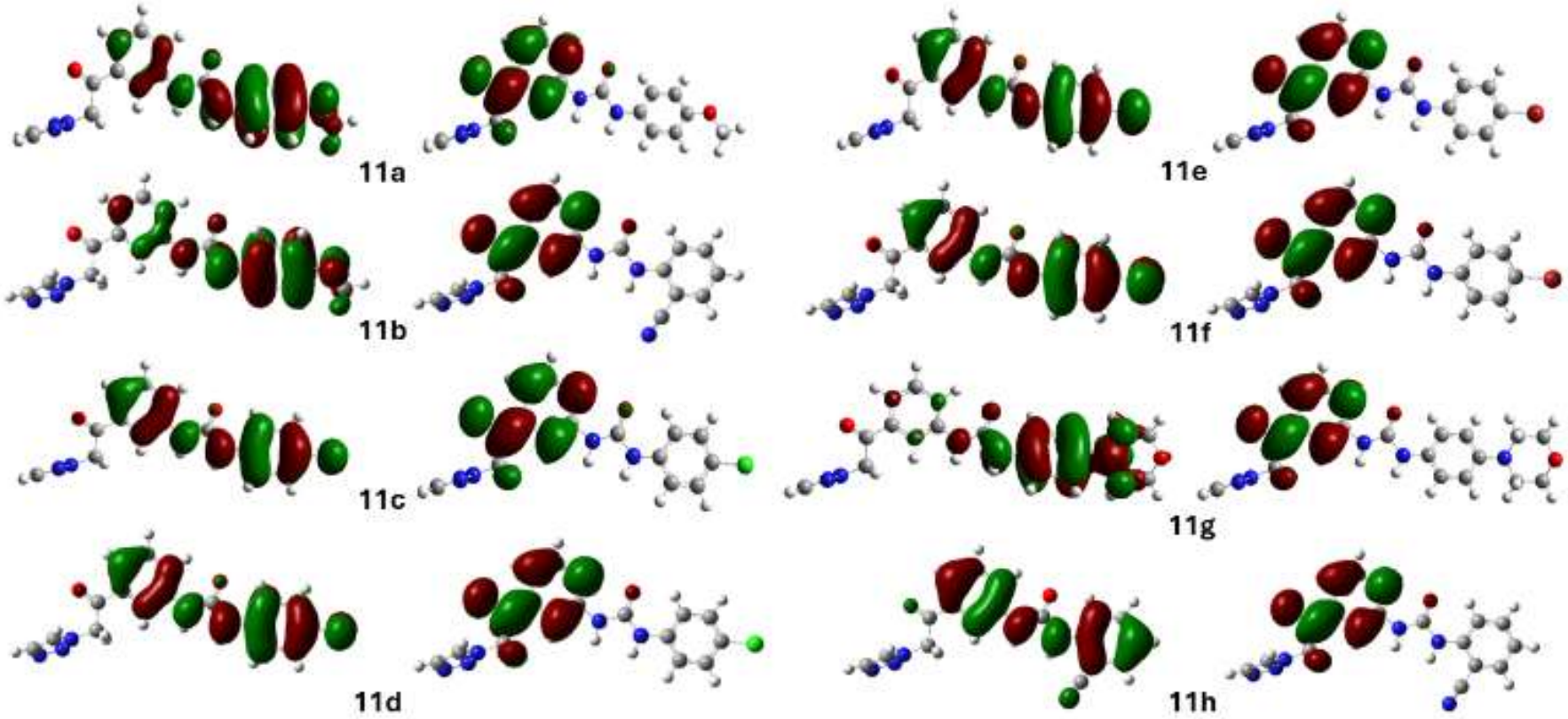

Figure S4: Calculated minima structures of new diarylureas **11a-h** at the B3LYP/6-311+g(d,p) methodology in THF solvent.

Table S1: XYZ geometry of the calculated diarylureas **6a-i** and **11a-h** at the B3LYP/6-311+g(d,p) methodology in THF solvent using the PCM model.

6a	**6b**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	H 4.75336 -2.94188 -0.07308
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047
H 8.73363 -1.33673 0.06283	C 0.2481 1.05021 -0.04281
C 0.2481 1.05021 -0.04281	C -1.03595 0.48715 -0.00039
C -1.03595 0.48715 -0.00039	C 0.37771 2.44577 -0.08283
C 0.37771 2.44577 -0.08283	C -2.17672 1.29532 0.00138
C -2.19267 1.28575 0.00198	H -1.12475 -0.59255 0.0305
H -1.12475 -0.59255 0.0305	C -0.76528 3.24566 -0.07914
C -0.76528 3.24566 -0.07914	H 1.35955 2.89015 -0.11525
H 1.35955 2.89015 -0.11525	C -2.03589 2.68986 -0.03747
C -2.03589 2.68986 -0.03747	H -0.64861 4.3228 -0.11075
H -0.64861 4.3228 -0.11075	H -2.92142 3.31142 -0.0353
H -2.92142 3.31142 -0.0353	C -3.55632 0.72302 0.05086
C -3.55632 0.72302 0.05086	O -4.54303 1.43183 0.05422
O -4.54303 1.43183 0.05422	C -3.69827 -0.80761 0.11142
C -3.69827 -0.80761 0.11142	H -3.18173 -1.26115 -0.73563
H -3.18173 -1.26115 -0.73563	H -3.22611 -1.17763 1.02498
H -3.22611 -1.17763 1.02498	N -5.07217 -1.24987 0.07619
N -5.07217 -1.24987 0.07619	C -5.93639 -1.36974 1.11667
C -5.93639 -1.36974 1.11667	C -6.92423 -1.82008 -0.80477
C -6.92423 -1.82008 -0.80477	C -7.15384 -1.74613 0.58531
C -7.15384 -1.74613 0.58531	H -5.62518 -1.18401 2.13236
H -5.62518 -1.18401 2.13236	H -7.61672 -2.08791 -1.58912
H -7.61672 -2.08791 -1.58912	H -8.06763 -1.94291 1.12163

H -8.06763 -1.94291 1.12163 N -5.66454 -1.51461 -1.11141	N -5.66454 -1.51461 -1.11141 O 9.0767 -1.38475 0.06893 C 9.38151 -2.70798 -0.37948 H 10.43805 -2.80252 -0.51975 H 9.054 -3.41679 0.35211 H 8.88054 -2.89473 -1.30633
6c	**6d**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	H 4.75336 -2.94188 -0.07308
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047
C 0.2481 1.05021 -0.04281	C 0.2481 1.05021 -0.04281
C -1.03595 0.48715 -0.00039	C -1.03595 0.48715 -0.00039
C 0.37771 2.44577 -0.08283	C 0.37771 2.44577 -0.08283
C -2.17672 1.29532 0.00138	C -2.17672 1.29532 0.00138
H -1.12475 -0.59255 0.0305	H -1.12475 -0.59255 0.0305
C -0.76528 3.24566 -0.07914	C -0.76528 3.24566 -0.07914
H 1.35955 2.89015 -0.11525	H 1.35955 2.89015 -0.11525
C -2.03589 2.68986 -0.03747	C -2.03589 2.68986 -0.03747
H -0.64861 4.3228 -0.11075	H -0.64861 4.3228 -0.11075
H -2.92142 3.31142 -0.0353	H -2.92142 3.31142 -0.0353
C -3.55632 0.72302 0.05086	C -3.55632 0.72302 0.05086
O -4.54303 1.43183 0.05422	O -4.54303 1.43183 0.05422
C -3.69827 -0.80761 0.11142	C -3.69827 -0.80761 0.11142
H -3.18173 -1.26115 -0.73563	H -3.18173 -1.26115 -0.73563
H -3.22611 -1.17763 1.02498	H -3.22611 -1.17763 1.02498
N -5.07217 -1.24987 0.07619	N -5.07217 -1.24987 0.07619

C -5.93639 -1.36974 1.11667	C -5.93639 -1.36974 1.11667
C -6.92423 -1.82008 -0.80477	C -6.92423 -1.82008 -0.80477
C -7.15384 -1.74613 0.58531	C -7.15384 -1.74613 0.58531
H -5.62518 -1.18401 2.13236	H -5.62518 -1.18401 2.13236
H -7.61672 -2.08791 -1.58912	H -7.61672 -2.08791 -1.58912
H -8.06763 -1.94291 1.12163	H -8.06763 -1.94291 1.12163
N -5.66454 -1.51461 -1.11141	N -5.66454 -1.51461 -1.11141
F 8.99749 -1.37366 0.06752	Cl 9.40346 -1.4305 0.07474
6e	**6f**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	H 4.75336 -2.94188 -0.07308
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047
C 0.2481 1.05021 -0.04281	C 0.2481 1.05021 -0.04281
C -1.03595 0.48715 -0.00039	C -1.03595 0.48715 -0.00039
C 0.37771 2.44577 -0.08283	C 0.37771 2.44577 -0.08283
C -2.17672 1.29532 0.00138	C -2.17672 1.29532 0.00138
H -1.12475 -0.59255 0.0305	H -1.12475 -0.59255 0.0305
C -0.76528 3.24566 -0.07914	C -0.76528 3.24566 -0.07914
H 1.35955 2.89015 -0.11525	H 1.35955 2.89015 -0.11525
C -2.03589 2.68986 -0.03747	C -2.03589 2.68986 -0.03747
H -0.64861 4.3228 -0.11075	H -0.64861 4.3228 -0.11075
H -2.92142 3.31142 -0.0353	H -2.92142 3.31142 -0.0353
C -3.55632 0.72302 0.05086	C -3.55632 0.72302 0.05086
O -4.54303 1.43183 0.05422	O -4.54303 1.43183 0.05422
C -3.69827 -0.80761 0.11142	C -3.69827 -0.80761 0.11142
H -3.18173 -1.26115 -0.73563	H -3.18173 -1.26115 -0.73563

H -3.22611 -1.17763 1.02498	H -3.22611 -1.17763 1.02498
N -5.07217 -1.24987 0.07619	N -5.07217 -1.24987 0.07619
C -5.93639 -1.36974 1.11667	C -5.93639 -1.36974 1.11667
C -6.92423 -1.82008 -0.80477	C -6.92423 -1.82008 -0.80477
C -7.15384 -1.74613 0.58531	C -7.15384 -1.74613 0.58531
H -5.62518 -1.18401 2.13236	H -5.62518 -1.18401 2.13236
H -7.61672 -2.08791 -1.58912	H -7.61672 -2.08791 -1.58912
H -8.06763 -1.94291 1.12163	H -8.06763 -1.94291 1.12163
N -5.66454 -1.51461 -1.11141	N -5.66454 -1.51461 -1.11141
Br 9.55199 -1.45129 0.07739	C 9.56364 -2.20896 1.29499
	C 9.62415 -2.09416 -1.20286
	C 11.04754 -2.514 1.31828
	H 8.98557 -3.1703 1.2992
	H 9.28232 -1.64274 2.22067
	C 11.10822 -2.39847 -1.17989
	H 9.04922 -3.04979 -1.32356
	H 9.38757 -1.44472 -2.08531
	H 11.28344 -3.16466 2.20003
	H 11.62254 -1.55864 1.44094
	H 11.38948 -2.96507 -2.1053
	H 11.68568 -1.43671 -1.18506
	N 9.18562 -1.4 0.07087
	O 11.48736 -3.20627 0.04451
6g	**6h**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047

C 0.2481 1.05021 -0.04281 C -1.03595 0.48715 -0.00039 C 0.37771 2.44577 -0.08283 C -2.17672 1.29532 0.00138 H -1.12475 -0.59255 0.0305 C -0.76528 3.24566 -0.07914 H 1.35955 2.89015 -0.11525 C -2.03589 2.68986 -0.03747 H -0.64861 4.3228 -0.11075 H -2.92142 3.31142 -0.0353 C -3.55632 0.72302 0.05086 O -4.54303 1.43183 0.05422 C -3.69827 -0.80761 0.11142 H -3.18173 -1.26115 -0.73563 H -3.22611 -1.17763 1.02498 N -5.07217 -1.24987 0.07619 C -5.93639 -1.36974 1.11667 C -6.92423 -1.82008 -0.80477 C -7.15384 -1.74613 0.58531 H -5.62518 -1.18401 2.13236 H -7.61672 -2.08791 -1.58912 H -8.06763 -1.94291 1.12163 N -5.66454 -1.51461 -1.11141 H 8.72023 -1.33485 0.06259 F 4.59145 -3.15057 -0.08292	C 0.2481 1.05021 -0.04281 C -1.03595 0.48715 -0.00039 C 0.37771 2.44577 -0.08283 C -2.17672 1.29532 0.00138 H -1.12475 -0.59255 0.0305 C -0.76528 3.24566 -0.07914 H 1.35955 2.89015 -0.11525 C -2.03589 2.68986 -0.03747 H -0.64861 4.3228 -0.11075 H -2.92142 3.31142 -0.0353 C -3.55632 0.72302 0.05086 O -4.54303 1.43183 0.05422 C -3.69827 -0.80761 0.11142 H -3.18173 -1.26115 -0.73563 H -3.22611 -1.17763 1.02498 N -5.07217 -1.24987 0.07619 C -5.93639 -1.36974 1.11667 C -6.92423 -1.82008 -0.80477 C -7.15384 -1.74613 0.58531 H -5.62518 -1.18401 2.13236 H -7.61672 -2.08791 -1.58912 H -8.06763 -1.94291 1.12163 N -5.66454 -1.51461 -1.11141 H 8.72023 -1.33485 0.06259 C 4.47506 -3.30058 -0.09 N 3.7727 -4.20588 -0.13269
6i C 2.68994 0.45082 -0.0166 O 3.13527 1.58906 0.02476 N 3.47285 -0.68629 -0.03413 H 2.99607 -1.57497 -0.07534 N 1.3344 0.15693 -0.05125 H 1.07372 -0.8182 -0.06349 C 4.87963 -0.78802 -0.00594 C 5.4184 -2.08468 -0.03265 C 5.74669 0.31191 0.04623 C 6.79436 -2.27928 -0.00819 H 4.75336 -2.94188 -0.07308 C 7.12518 0.09921 0.07031	

H 5.34432 1.31204 0.06663 C 7.66073 -1.18652 0.04374 H 7.1881 -3.28913 -0.0298 C 0.2481 1.05021 -0.04281 C -1.03595 0.48715 -0.00039 C 0.37771 2.44577 -0.08283 C -2.17672 1.29532 0.00138 H -1.12475 -0.59255 0.0305 C -0.76528 3.24566 -0.07914 H 1.35955 2.89015 -0.11525 C -2.03589 2.68986 -0.03747 H -0.64861 4.3228 -0.11075 H -2.92142 3.31142 -0.0353 C -3.55632 0.72302 0.05086 O -4.54303 1.43183 0.05422 C -3.69827 -0.80761 0.11142 H -3.18173 -1.26115 -0.73563 H -3.22611 -1.17763 1.02498 N -5.07217 -1.24987 0.07619 C -5.93639 -1.36974 1.11667 C -6.92423 -1.82008 -0.80477 C -7.15384 -1.74613 0.58531 H -5.62518 -1.18401 2.13236 H -7.61672 -2.08791 -1.58912 H -8.06763 -1.94291 1.12163 N -5.66454 -1.51461 -1.11141 C 9.18562 -1.4 0.07087 H 9.57703 -1.30302 -0.92024 H 9.63717 -0.66679 0.70601 H 9.40216 -2.37853 0.44569 N 8.01887 1.26507 0.12475 O 9.31837 1.4326 -0.23974 O 7.78369 2.59812 -0.00672	
11a C 2.68994 0.45082 -0.0166 O 3.13527 1.58906 0.02476 N 3.47285 -0.68629 -0.03413 H 2.99607 -1.57497 -0.07534	**11b** C 2.68994 0.45082 -0.0166 O 3.13527 1.58906 0.02476 N 3.47285 -0.68629 -0.03413 H 2.99607 -1.57497 -0.07534

N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	H 4.75336 -2.94188 -0.07308
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047
C 0.2481 1.05021 -0.04281	C 0.2481 1.05021 -0.04281
C -1.03595 0.48715 -0.00039	C -1.03595 0.48715 -0.00039
C 0.37771 2.44577 -0.08283	C 0.37771 2.44577 -0.08283
C -2.17672 1.29532 0.00138	C -2.17672 1.29532 0.00138
H -1.12475 -0.59255 0.0305	H -1.12475 -0.59255 0.0305
C -0.76528 3.24566 -0.07914	C -0.76528 3.24566 -0.07914
H 1.35955 2.89015 -0.11525	H 1.35955 2.89015 -0.11525
C -2.03589 2.68986 -0.03747	C -2.03589 2.68986 -0.03747
H -0.64861 4.3228 -0.11075	H -0.64861 4.3228 -0.11075
H -2.92142 3.31142 -0.0353	H -2.92142 3.31142 -0.0353
C -3.55632 0.72302 0.05086	C -3.55632 0.72302 0.05086
O -4.54303 1.43183 0.05422	O -4.54303 1.43183 0.05422
C -3.69827 -0.80761 0.11142	C -3.69827 -0.80761 0.11142
H -3.18173 -1.26115 -0.73563	H -3.18173 -1.26115 -0.73563
H -3.22611 -1.17763 1.02498	H -3.22611 -1.17763 1.02498
N -5.07217 -1.24987 0.07619	N -5.07217 -1.24987 0.07619
C -6.92423 -1.82008 -0.80477	C -5.93639 -1.36974 1.11667
C -7.15384 -1.74613 0.58531	C -7.15384 -1.74613 0.58531
H -7.61672 -2.08791 -1.58912	H -5.62518 -1.18401 2.13236
H -8.06763 -1.94291 1.12163	H -8.06763 -1.94291 1.12163
N -5.66454 -1.51461 -1.11141	N -5.66454 -1.51461 -1.11141
O 9.0767 -1.38475 0.06893	O 9.0767 -1.38475 0.06893
C 9.38151 -2.70798 -0.37948	C 9.38151 -2.70798 -0.37948
H 10.43805 -2.80252 -0.51975	H 10.43805 -2.80252 -0.51975
H 9.054 -3.41679 0.35211	H 9.054 -3.41679 0.35211
H 8.88054 -2.89473 -1.30633	H 8.88054 -2.89473 -1.30633
N -5.93639 -1.36974 1.11667	N -6.92423 -1.82008 -0.80477

11c	**11d**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	H 4.75336 -2.94188 -0.07308
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047
C 0.2481 1.05021 -0.04281	C 0.2481 1.05021 -0.04281
C -1.03595 0.48715 -0.00039	C -1.03595 0.48715 -0.00039
C 0.37771 2.44577 -0.08283	C 0.37771 2.44577 -0.08283
C -2.17672 1.29532 0.00138	C -2.17672 1.29532 0.00138
H -1.12475 -0.59255 0.0305	H -1.12475 -0.59255 0.0305
C -0.76528 3.24566 -0.07914	C -0.76528 3.24566 -0.07914
H 1.35955 2.89015 -0.11525	H 1.35955 2.89015 -0.11525
C -2.03589 2.68986 -0.03747	C -2.03589 2.68986 -0.03747
H -0.64861 4.3228 -0.11075	H -0.64861 4.3228 -0.11075
H -2.92142 3.31142 -0.0353	H -2.92142 3.31142 -0.0353
C -3.55632 0.72302 0.05086	C -3.55632 0.72302 0.05086
O -4.54303 1.43183 0.05422	O -4.54303 1.43183 0.05422
C -3.69827 -0.80761 0.11142	C -3.69827 -0.80761 0.11142
H -3.18173 -1.26115 -0.73563	H -3.18173 -1.26115 -0.73563
H -3.22611 -1.17763 1.02498	H -3.22611 -1.17763 1.02498
N -5.07217 -1.24987 0.07619	N -5.07217 -1.24987 0.07619
C -6.92423 -1.82008 -0.80477	C -5.93639 -1.36974 1.11667
C -7.15384 -1.74613 0.58531	C -7.15384 -1.74613 0.58531
H -7.61672 -2.08791 -1.58912	H -5.62518 -1.18401 2.13236
H -8.06763 -1.94291 1.12163	H -8.06763 -1.94291 1.12163
N -5.66454 -1.51461 -1.11141	N -5.66454 -1.51461 -1.11141
Cl 9.40346 -1.4305 0.07474	Cl 9.40346 -1.4305 0.07474
N -5.93639 -1.36974 1.11667	N -6.92423 -1.82008 -0.80477

11e	**11b**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	H 4.75336 -2.94188 -0.07308
C 7.12518 0.09921 0.07031	C 7.12518 0.09921 0.07031
H 5.34432 1.31204 0.06663	H 5.34432 1.31204 0.06663
C 7.66073 -1.18652 0.04374	C 7.66073 -1.18652 0.04374
H 7.1881 -3.28913 -0.0298	H 7.1881 -3.28913 -0.0298
H 7.78445 0.95926 0.11047	H 7.78445 0.95926 0.11047
C 0.2481 1.05021 -0.04281	C 0.2481 1.05021 -0.04281
C -1.03595 0.48715 -0.00039	C -1.03595 0.48715 -0.00039
C 0.37771 2.44577 -0.08283	C 0.37771 2.44577 -0.08283
C -2.17672 1.29532 0.00138	C -2.17672 1.29532 0.00138
H -1.12475 -0.59255 0.0305	H -1.12475 -0.59255 0.0305
C -0.76528 3.24566 -0.07914	C -0.76528 3.24566 -0.07914
H 1.35955 2.89015 -0.11525	H 1.35955 2.89015 -0.11525
C -2.03589 2.68986 -0.03747	C -2.03589 2.68986 -0.03747
H -0.64861 4.3228 -0.11075	H -0.64861 4.3228 -0.11075
H -2.92142 3.31142 -0.0353	H -2.92142 3.31142 -0.0353
C -3.55632 0.72302 0.05086	C -3.55632 0.72302 0.05086
O -4.54303 1.43183 0.05422	O -4.54303 1.43183 0.05422
C -3.69827 -0.80761 0.11142	C -3.69827 -0.80761 0.11142
H -3.18173 -1.26115 -0.73563	H -3.18173 -1.26115 -0.73563
H -3.22611 -1.17763 1.02498	H -3.22611 -1.17763 1.02498
N -5.07217 -1.24987 0.07619	N -5.07217 -1.24987 0.07619
C -6.92423 -1.82008 -0.80477	C -5.93639 -1.36974 1.11667
C -7.15384 -1.74613 0.58531	C -7.15384 -1.74613 0.58531
H -7.61672 -2.08791 -1.58912	H -5.62518 -1.18401 2.13236
H -8.06763 -1.94291 1.12163	H -8.06763 -1.94291 1.12163
N -5.66454 -1.51461 -1.11141	N -5.66454 -1.51461 -1.11141
Br 9.55199 -1.45129 0.07739	Br 9.55199 -1.45129 0.07739

N -5.93639 -1.36974 1.11667	N -6.92423 -1.82008 -0.80477
11g	**11h**
C 2.68994 0.45082 -0.0166	C 2.68994 0.45082 -0.0166
O 3.13527 1.58906 0.02476	O 3.13527 1.58906 0.02476
N 3.47285 -0.68629 -0.03413	N 3.47285 -0.68629 -0.03413
H 2.99607 -1.57497 -0.07534	H 2.99607 -1.57497 -0.07534
N 1.3344 0.15693 -0.05125	N 1.3344 0.15693 -0.05125
H 1.07372 -0.8182 -0.06349	H 1.07372 -0.8182 -0.06349
C 4.87963 -0.78802 -0.00594	C 4.87963 -0.78802 -0.00594
C 5.4184 -2.08468 -0.03265	C 5.4184 -2.08468 -0.03265
C 5.74669 0.31191 0.04623	C 5.74669 0.31191 0.04623
C 6.79436 -2.27928 -0.00819	C 6.79436 -2.27928 -0.00819
H 4.75336 -2.94188 -0.07308	C 7.12518 0.09921 0.07031
C 7.12518 0.09921 0.07031	H 5.34432 1.31204 0.06663
H 5.34432 1.31204 0.06663	C 7.66073 -1.18652 0.04374
C 7.66073 -1.18652 0.04374	H 7.1881 -3.28913 -0.0298
H 7.1881 -3.28913 -0.0298	H 7.78445 0.95926 0.11047
H 7.78445 0.95926 0.11047	C 0.2481 1.05021 -0.04281
C 0.2481 1.05021 -0.04281	C -1.03595 0.48715 -0.00039
C -1.03595 0.48715 -0.00039	C 0.37771 2.44577 -0.08283
C 0.37771 2.44577 -0.08283	C -2.17672 1.29532 0.00138
C -2.17672 1.29532 0.00138	H -1.12475 -0.59255 0.0305
H -1.12475 -0.59255 0.0305	C -0.76528 3.24566 -0.07914
C -0.76528 3.24566 -0.07914	H 1.35955 2.89015 -0.11525
H 1.35955 2.89015 -0.11525	C -2.03589 2.68986 -0.03747
C -2.03589 2.68986 -0.03747	H -0.64861 4.3228 -0.11075
H -0.64861 4.3228 -0.11075	H -2.92142 3.31142 -0.0353
H -2.92142 3.31142 -0.0353	C -3.55632 0.72302 0.05086
C -3.55632 0.72302 0.05086	O -4.54303 1.43183 0.05422
O -4.54303 1.43183 0.05422	C -3.69827 -0.80761 0.11142
C -3.69827 -0.80761 0.11142	H -3.18173 -1.26115 -0.73563
H -3.18173 -1.26115 -0.73563	H -3.22611 -1.17763 1.02498
H -3.22611 -1.17763 1.02498	N -5.07217 -1.24987 0.07619
N -5.07217 -1.24987 0.07619	C -5.93639 -1.36974 1.11667
C -6.92423 -1.82008 -0.80477	C -7.15384 -1.74613 0.58531
C -7.15384 -1.74613 0.58531	H -5.62518 -1.18401 2.13236
H -7.61672 -2.08791 -1.58912	H -8.06763 -1.94291 1.12163
H -8.06763 -1.94291 1.12163	N -5.66454 -1.51461 -1.11141
N -5.66454 -1.51461 -1.11141	H 8.72023 -1.33485 0.06259

C 9.56364 -2.20896 1.29499	C 4.47506 -3.30058 -0.09
C 9.62415 -2.09416 -1.20286	N 3.7727 -4.20588 -0.13269
C 11.04754 -2.514 1.31828	N -6.92423 -1.82008 -0.80477
H 8.98557 -3.1703 1.2992	
H 9.28232 -1.64274 2.22067	
C 11.10822 -2.39847 -1.17989	
H 9.04922 -3.04979 -1.32356	
H 9.38757 -1.44472 -2.08531	
H 11.28344 -3.16466 2.20003	
H 11.62254 -1.55864 1.44094	
H 11.38948 -2.96507 -2.1053	
H 11.68568 -1.43671 -1.18506	
N 9.18562 -1.4 0.07087	
O 11.48736 -3.20627 0.04451	
N -5.93639 -1.36974 1.11667	

Table S2. HOMO and LUMO energies in Hartree and HOMO-LUMO energy difference of the diarylureas **6a-6i** and **11a-11h** at the B3LYP/6-311+g(d,p) methodology in THF solvent using the PCM model.

	HOMO	LUMO	|HOMO-LUMO|
6a	-0.22324	-0.08008	3.896
6b	-0.21504	-0.07877	3.708
6c	-0.22878	-0.08138	4.011
6d	-0.22940	-0.08160	4.022
6e	-0.22925	-0.08163	4.017
6f	-0.20220	-0.08039	3.315
6g	-0.23223	-0.08144	4.103
6h	-0.23863	-0.08224	4.256
6i	-0.23570	-0.10570	3.537
11a	-0.21615	-0.08210	3.648
11b	-0.21571	-0.08424	3.577
11c	-0.22959	-0.08322	3.983
11d	-0.23018	-0.08523	3.944
11e	-0.22940	-0.08330	3.976
11f	-0.23002	-0.08530	3.938
11g	-0.20159	-0.08206	3.253
11h	-0.23969	-0.08586	4.186

The ordering of the diarylureas **6a-6i** and **11a-11h** starting from the molecule with the smallest H-L energy difference to the largest one:

11g < 6f < 6i < 11b < 11a < 6b < 6a < 11f < 11d < 11e < 11c < 6c < 6e < 6d < 6g < 11h < 6h

Molecular Docking:

The molecular docking of the new *N*,*N*′-diarylureas **6a-i** and **11a-h** and of the known inhibitor PSNCBAM-1 to the orthosteric position in the CB1 receptor have been computed, see Table S3, via the Autodock code. The visualization of the results was performed using AutoDock software.[14] For the creation of the grid box, the coordinates used were those of the diarylurea bound to the macromolecule, provided that the diarylurea binds to the enzyme's active site. The specific coordinates used for each enzyme were as follows: 5XR8 (CB1)[11]: X=-42.678, Y=-157.964, Z=308.565. For the grid box creation, the dimensions used for all receptors were the same and as follows: number of grid points: X= 40, Y= 40, Z= 40 and grid spacing: 0.430 Å. It was found that all *N*,*N*′-diarylureas bind strongly to the active center of the enzyme. The strongest binding seems to have *N*,*N*′-diarylureas **6f** (-10.89 kcal/mol), **6i** (-12.58 kcal/mol), and **11g** (-11.15 kcal/mol), see Table S3. In addition. molecular docking calculations were conducted for the known inhibitor PSNCBAM-1 and it was found that molecular binding is -11.62 kcal/mol which is similar with the other compounds. Thus, we can conclude that **6f**, **6i**, and **11g** present the same strong molecular binding with the known inhibitor PSNCBAM-1 showing that they are the best candidates as inhibitors of the CB1 receptor, among the present calculated *N*,*N*′-diarylureas. Furthermore, it seems that **6i** is a better inhibitor than PSNCBAM-1.

The interactions of each diarylurea with the amino acids of the active center are shown in Figure S5. All new *N*,*N*′-diarylureas bind to the same pocket of the enzyme. Specifically, diarylurea **6i** forms one hydrogen bond with PHE174 amino acid. Furthermore, diarylurea **6f** forms two π-π interactions with TRP279 and two hydrogen bonds with PHE117. Also, diarylurea **11g** forms 5 π-π interactions with TRP279, PHE268, PHE501 and PHE174. Diaryl-urea **6b** forms two π-π interactions with PHE279 and PHE189 and diarylurea **6c** forms one π-π interactions with TRP275. The interactions are similar for each diarylurea. The interactions of selected diaryl ureas with the CB1 are shown in Table S4.

Table S3. Molecular docking results for 17 *N*,*N*′-diarylureas and of the known inhibitor PSNCBAM-1 in the orthosteric pocket of the receptor CB1 via the MB1 methodology.

a/a	Diaryl urea	Docking score kcal/mol)	a/a	Diaryl urea	Docking score kcal/mol)
1	**6a**	-8.98	10	**11a**	-9.86
2	**6b**	-9.37	11	**11b**	-9.47
3	**6c**	-9.07	12	**11c**	-10.19
4	**6d**	-9.69	13	**11d**	-10.04
5	**6e**	-9.90	14	**11e**	-10.26
6	**6f**	-10.89	15	**11f**	-10.18
7	**6g**	-9.65	16	**11g**	-11.15
8	**6h**	-10.26	17	**11h**	-10.76
9	**6i**	-12.58 (-9.85)[a]	18	**PSNCBAM-1**	-11.62

[a] MB2 methodology

Table S4. Interactions of *N*,*N*′-diarylureas and PSNCBAM-1 with CB1 in its orthosteric pocket via the MB1 methodology.

a/a	Diarylurea	Hydrogen Bonding	π-π interaction
1	**6b**		PHE279, PHE189
2	**6c**		TYR275
3	**6f**	PHE177	TRP279
4	**6g**	PHE174	PHE268
5	**6h**	PHE177	PHE177
6	**6i**	PHE174	
7	**11a**	PHE501	PHE170
8	**11b**		PHE268
9	**11c**		TRP279
10	**11d**		TRP475, PHE501, PHE268
11	**11e**	SER505	
12	**11f**		TYR275
13	**11g**		PHE174, PHE268, PHE501, TRP279
14	**11h**	PHE174	
15	**PSNCBAM-1**	PHE174	

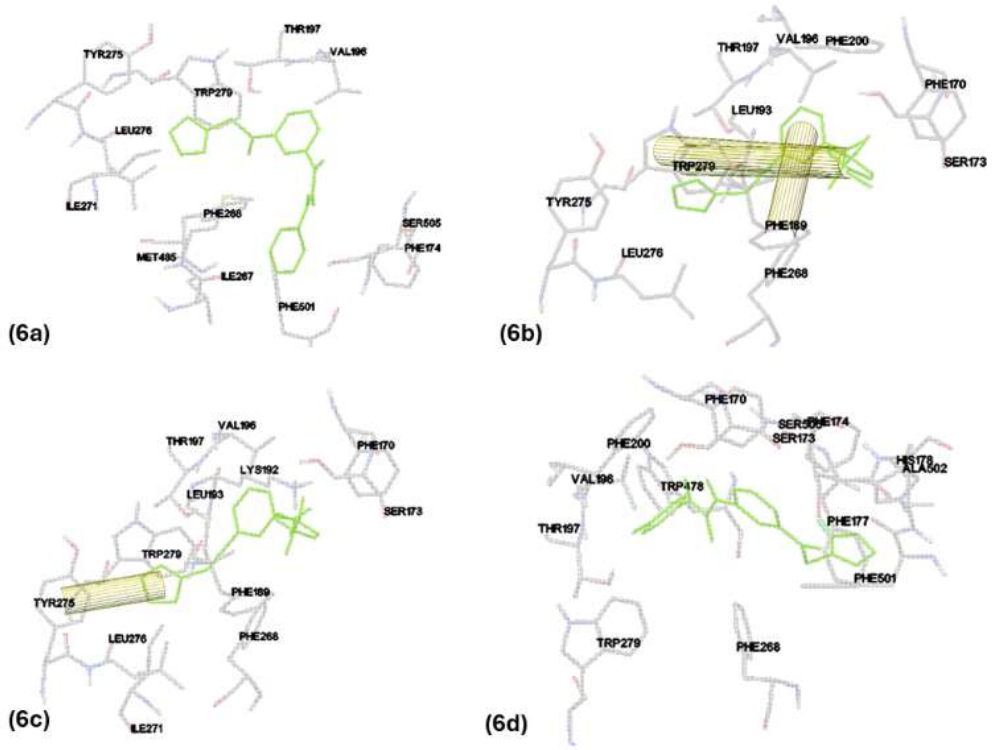

Figure S5 (continues)

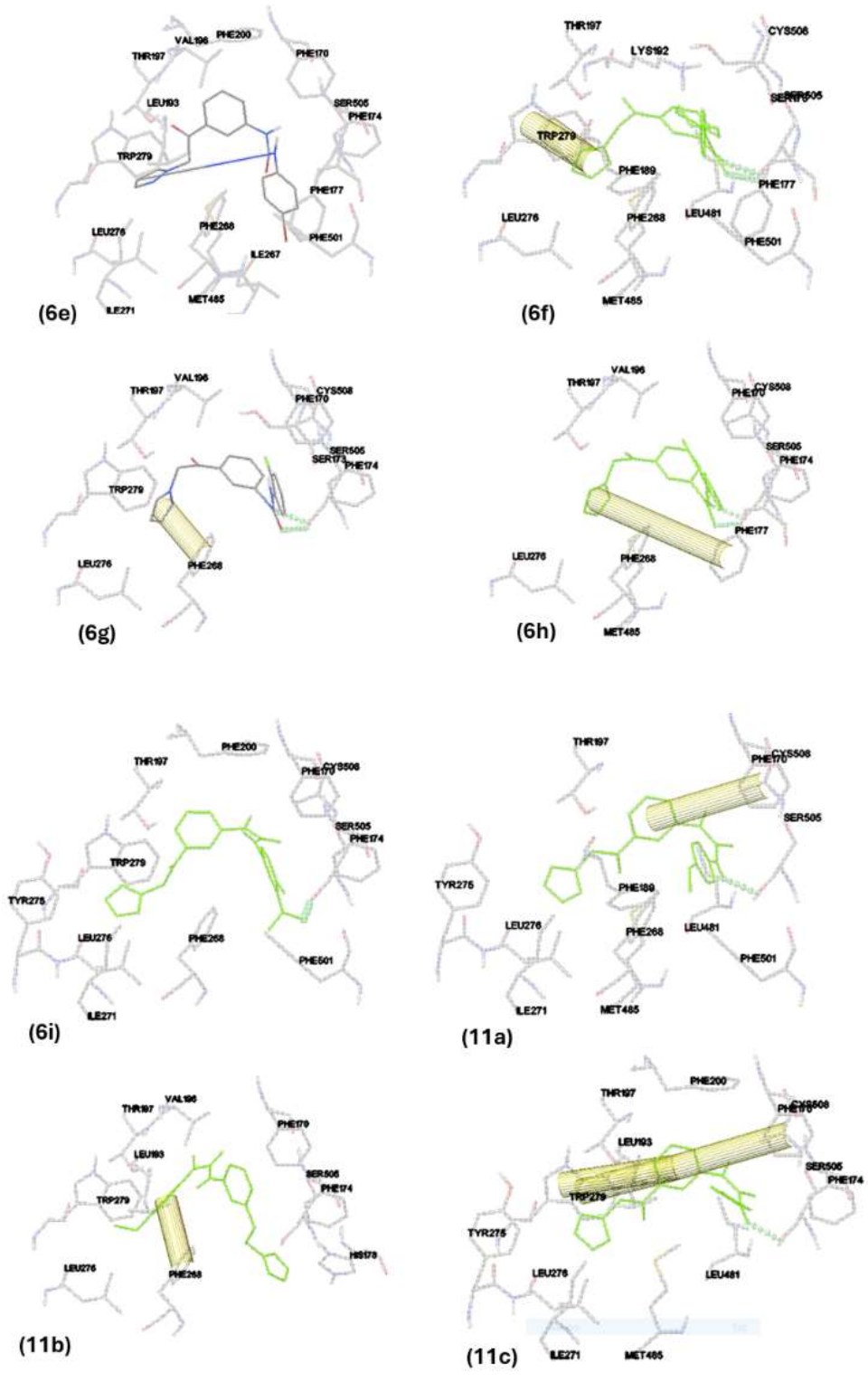

Figure S5 (continues)

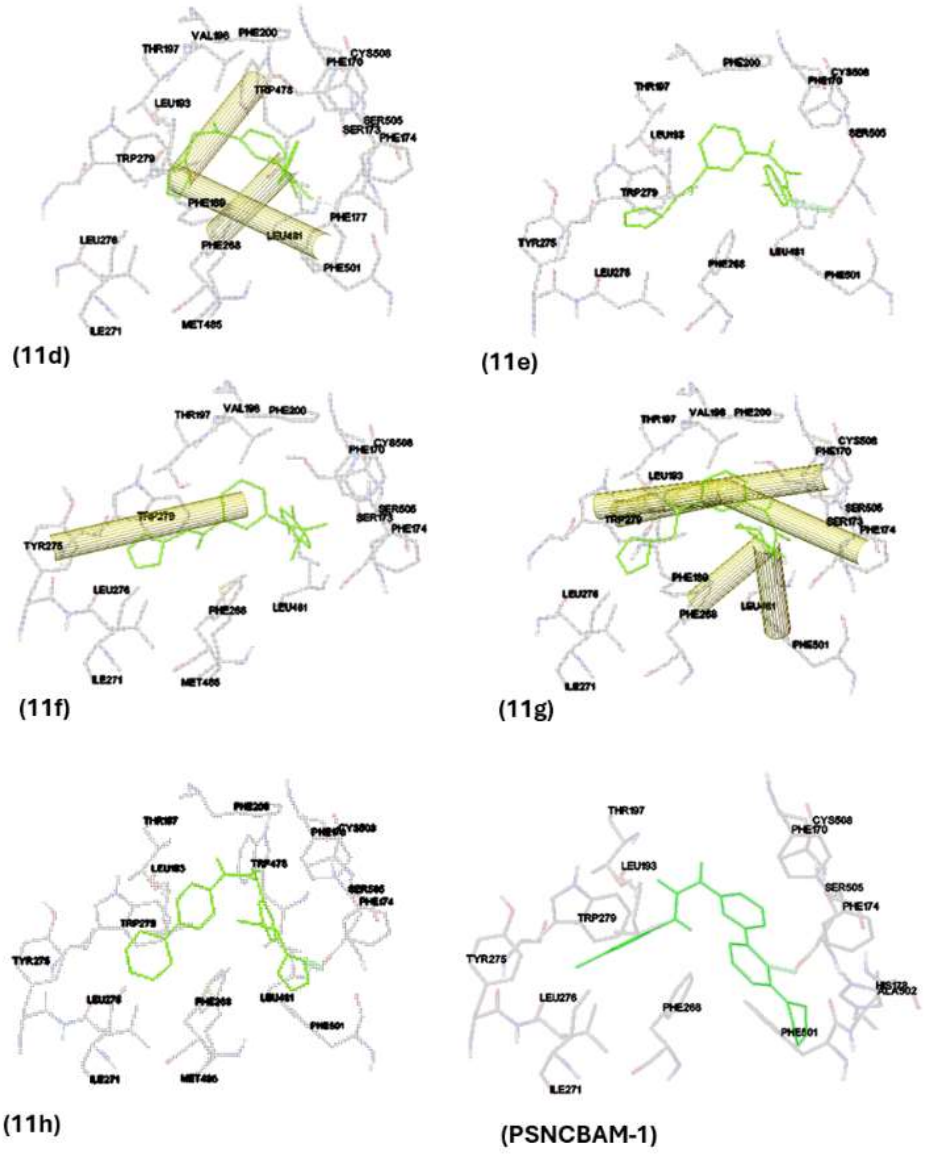

Figure S5: Interactions of *N,N′*-diarylureas **6a-i**, **11a-h**, and known inhibitor PSNCBAM-1 with CB1 in the orthosteric pocket via the MB1 methodology.

2. ***Molecular* Dynamics *Simulations:***

Molecular Dynamics (MD) were carried out for the *N*,*N*´-diarylureas that bind strongly to the active center to investigate if the diarylurea remains stable in the active center of the protein. The Root Mean Square Deviation (RMSD) for both protein and diarylurea was calculated during the MD which is a measure of the average distance between atoms of superimposed protein structures and diaryl urea structures, respectively.

The Cα RMSD stabilizes around 10 Å (Figure S6a). The protein RMSD (blue line) exhibits significant fluctuations, with periodic spikes reaching up to 45 Å. These spikes indicate large conformational shifts in the protein, possibly suggesting flexible regions or domain movements that could be relevant to the binding dynamics. The diarylurea **6f** RMSD (maroon line) also shows fluctuations, though it remains relatively stable compared to the RMSD protein. It generally stabilizes around 5-10 Å, indicating that it retains its binding orientation but may experience slight positional or orientational shifts over time. While the protein undergoes significant conformational flexibility, the diarylurea remains bound in a relatively stable manner, maintaining interaction with the protein.

The protein RMSD (Figure S6b) (blue) shows highly fluctuating values, with several peaks that seem to reach above 20 Å (and some even close to 40 Å). This suggests that the protein undergoes significant conformational changes or that there are regions in the protein that are very flexible during the simulation. The diarylurea **6i** RMSD (red) seems more stable in comparison but also it has noticeable fluctuations. While the diaryl urea starts with low RMSD values (around 2-5 Å), it shows sporadic spikes, but overall, it tends to remain in a narrower range (below 10 Å).

In Figure S6c, the blue line represents the deviation of the protein's Cα atoms (alpha carbon atoms of the amino acids) from their initial position over time. It remains relatively stable, fluctuating around 2-5 Å after an initial equilibration phase. This suggests that the protein maintains structural integrity during the simulation, showing minor deviations. The pink line represents the **11g** diaryl urea's RMSD, and it shows more variation compared to the protein's RMSD. It fluctuates with large peaks and troughs, especially between 10 and 50 Å. These peaks suggest that the diaryl urea undergoes substantial movements or conformational changes within the binding site, possibly detaching or relocating during the simulation. Since the protein's RMSD (blue line) remains low and stable after a brief equilibration phase, the protein structure appears to remain relatively stable throughout the simulation. The frequent fluctuations in the diarylurea's RMSD (red line) indicate that the diarylurea may not be stably bound to the protein during the simulation or could be experiencing significant conformational changes or binding mode shifts.

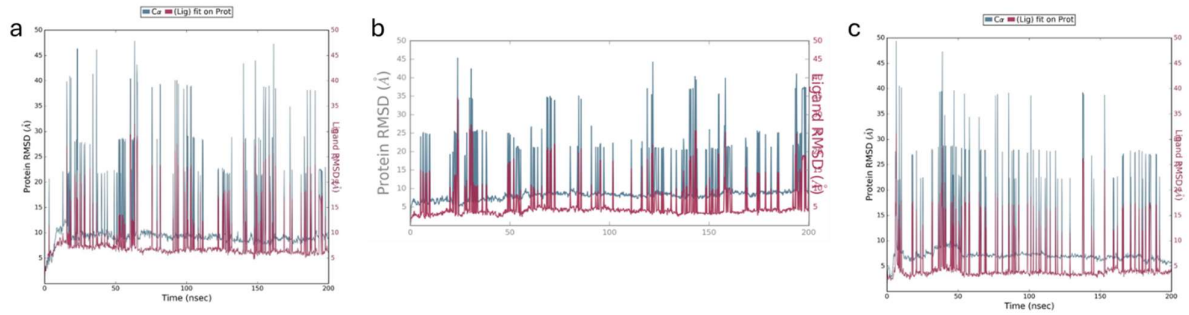

Figure S6. RMSD values for the protein (CB1) (depicted in green) and the diarylureas (a) **6f,** (b) **6i** and (c) **11g** (depicted in magenta) were calculated over a 200 ns simulation period, with the initial docking pose serving as the reference structure.

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