Design and synthesis of novel diamide derivatives of glycine as anti-hyperglycemic agents

Radhika Sharma and Shubhangi S Soman*

Department of Chemistry, Faculty of Science, The M. S. University of Baroda, Vadodara, 390 002, India.

*Corresponding Author's e-mail address: shubhangiss@rediffmail.com

Telephone number: +91 256 2795552

First Author's e-mail address: radhika.naudiyal@gmail.com

Experimental

Reagent grade chemicals and solvents were purchased from commercial supplier and used after purification. TLC was performed on silica gel F254 plates (Merck). Merck silica gel (60-120 mesh) was used for column chromatographic purification. All reactions were carried out in nitrogen atmosphere. Melting points are uncorrected and were measured in open capillary tubes, using a Rolex melting point apparatus. IR spectra were recorded as KBr pellets on Perkin Elmer RX 1 spectrometer and the wave numbers reported in cm^{-1} . ^1H NMR and ^{13}C NMR spectral data were recorded on Advance Bruker 400 spectrometer (^1H 400 MHz/ ^{13}C 100 MHz) with CDCl_3 or DMSO-d_6 as solvent and TMS as internal standard and reported in δ (ppm). J values are in Hz. Mass spectra were determined by ESI-MS, using a Shimadzu LCMS 2020 apparatus. Elemental analyses were recorded on ThermoFinnigan Flash 11-12 series EA. All reactions were carried out under nitrogen atmosphere. Purity of all the tested compounds was greater than 97%.

General procedure for the preparation of compounds (2a-k)

A mixture of boc-glycine **1** (1.11 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI) (1.67 mmol), 1-hydroxybenzotriazole (HOBt) (1.11 mmol), 4-dimethylaminopyridine (DMAP) (1.34 mmol) and amine (**1⁰** and **2⁰**) (1.22 mmol) in dichloromethane (DCM) (50 mL) was stirred at room temperature for 16 hours. The reaction was monitored using TLC. On completion of the reaction, it was washed with water (2X20 mL), brine (1X10 mL), dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to give the crude product which was then purified by column chromatography using silica gel as stationary phase and methanol:dichloromethane (5:95) as eluent to yield desired *N*-boc glycine amide **2a-k**, as white solid.

1-(phenylsulfonyl)piperidine-3-carboxylic acid (5)

To a mixture of piperidine-3-carboxylic acid **4** (1.0 mmol) and sodium carbonate (3.0 mmol) in 25 mL DCM:water (1:1) benzene sulfonyl chloride (1.1 mmol) was added and the reaction mixture stirred at room temperature for 16 hours or till the completion of reaction, as monitored by TLC. On completion of reaction, the reaction mixture was washed with petroleum ether (20 mL) and then acidified with conc. HCl, till pH 2. The white solid thus separated was filtered, washed with water several times and then dried to yield the desired product as white solid.

Yield: 91%; white solid; m.p.: 115-117 °C; IR (KBr): 2940, 1693, 1352 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.41-1.50 (m, 1H), 1.65-1.73 (m, 1H), 1.80-1.85 (m, 1H), 1.99-2.04 (m, 1H), 2.41 (dt, 1H, *J*₁ = 2.8 Hz, *J*₂ = 11.2 Hz), 2.57 (t, 1H, *J* = 10.8 Hz), 2.65-2.71 (m, 1H), 3.59 (br d, 1H, *J* = 11.6 Hz), 3.83 (dd, 1H, *J*₁ = 3.2 Hz, *J*₂ = 7.2 Hz), 7.54-7.58 (m, 2H), 7.61-7.63 (m, 1H), 7.77-7.79 (m, 2H), 8.98 (br s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 23.88, 26.21, 40.73, 46.26, 47.35, 127.62, 129.18, 132.94, 135.96, 178.63.

General procedure for the preparation of compounds (6a-k)

Compounds **2a-k** were de-protected by stirring in 10% trifluoroacetic acid (TFA) in DCM. On completion of the reaction after an hour or as monitored by TLC, the solvent was evaporated under reduced pressure and once again the product was dissolved in DCM to give solution of compounds **3a-k**. To a solution of compound **5** (1.0 mmol) in DCM (20 mL), EDCI (1.5 mmol), HOBt (1.0 mmol) and DMAP (1.0 mmol) were added at 0-5 °C, followed by the solution of compound **3a-k** in DCM (5 mL) and the reaction mixture was then stirred at room temperature for 10 hours or till the completion of the reaction as detected by TLC. After completion of the reaction, it was washed with water (2X20 mL), brine (1X10 mL), dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to give the crude product which was then purified by column chromatography using silica gel, employing ethylacetate:petroleum ether (70:30) as eluent to give pure product **6a-k** as white solid.

N-(2-(4-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6a).

Yield: 70%; white solid; m.p.: 196-198 °C; IR (KBr): 3324, 3298, 2967, 2934, 2843, 2865, 1677, 1654, 1643, 1355 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 1.23-1.27 (m, 1H), 1.46-1.49 (m, 1H), 1.72-1.79 (m, 2H), 2.10-2.20 (m, 2H), 2.50-2.51 (m, 1H), 3.58-3.63 (m, 1H), 3.66-3.72 (m, 1H), 3.82-3.85 (m, 2H), 7.15 (t, 2H, *J* = 8.8 Hz), 7.56-7.60 (m, 2H), 7.66 (t, 2H, *J* = 8.4 Hz), 7.72-7.74 (m, 3H), 8.39 (br s, 1H), 10.05 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆): δ 24.14, 27.00, 41.93, 42.85, 46.52, 48.62, 115.68, 115.90, 121.31, 121.39, 127.85, 129.94, 133.70, 135.59, 135.67, 157.23, 159.61, 168.00, 173.16; Anal. Calc. for C₂₀H₂₂FN₃O₄S: C, 57.27; H, 5.29; N, 10.02; found: C, 57.42; H, 4.90; N, 9.97%; ESI-MS: *m/z* 420.0 [M+H]⁺.

N-(2-(4-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6b).

Yield: 55%; white solid; m.p.: 178-180 °C; IR (KBr): 3329, 3303, 2931, 2863, 2843, 1679, 1644, 1614, 1355, 1334 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 1.22-1.27 (m, 1H), 1.46-1.49

(m, 1H), 1.75 (t, 2H, $J = 15$ Hz), 2.10-2.20 (m, 2H), 2.50-2.54 (m, 1H), 3.60-3.69 (m, 2H), 3.84-3.86 (m, 2H), 7.36 (d, 2H, $J = 8.8$ Hz), 7.59-7.67 (m, 4H), 7.72-7.74 (m, 3H), 8.41 (t, 1H, $J = 8.0$ Hz), 10.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 24.14, 27.01, 41.93, 42.95, 46.52, 48.63, 121.10, 127.25, 127.85, 129.13, 129.93, 133.68, 135.62, 138.25, 168.26, 173.16; Anal. Calc. for $\text{C}_{20}\text{H}_{22}\text{ClN}_3\text{O}_4\text{S}$: C, 55.11; H, 5.09; N, 9.64; found: C, 55.22; H, 5.01; N, 9.58%; ESI-MS: m/z 435.9 $[\text{M}+\text{H}]^+$.

***N*-(2-oxo-2-(*p*-tolylamino)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6c).**

Yield: 85%; white solid; m.p.: 194-196 °C; IR (KBr): 3331, 3327, 2956, 2929, 2846, 1678, 1657, 1644, 1358, 1332 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6): δ 1.23-1.27 (m, 1H), 1.46-1.49 (m, 1H), 1.72-1.79 (m, 2H), 2.10-2.20 (m, 2H), 2.24 (s, 3H), 2.50-2.56 (m, 1H), 3.66-3.69 (m, 2H), 3.77-3.85 (m, 2H), 7.10 (d, 2H, $J = 8.0$ Hz), 7.45 (d, 2H, $J = 8.0$ Hz), 7.64-7.68 (m, 2H), 7.72-7.75 (m, 3H), 8.36 (m, 1H), 9.90 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 20.89, 24.15, 27.01, 41.94, 42.87, 46.53, 48.64, 119.58, 127.86, 129.59, 129.94, 132.64, 133.69, 135.60, 136.76, 167.80, 173.10; Anal. Calc. for $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_4\text{S}$: C, 60.70; H, 6.06; N, 10.11; found: C, 60.78; H, 6.18; N, 9.90%; ESI-MS: m/z 416.1 $[\text{M}+\text{H}]^+$.

***N*-(2-(3-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6d).**

Yield: 62%; white solid; m.p.: 186-188 °C; IR (KBr): 3308, 3104, 2930, 2851, 1709, 1670, 1616, 1351, 1317 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6): δ 1.23-1.27 (m, 1H), 1.46-1.49 (m, 1H), 1.72-1.79 (m, 2H), 2.10-2.20 (m, 2H), 2.50-2.51 (m, 1H), 3.61 (d, 1H, $J = 10.8$ Hz), 3.68 (d, 1H, $J = 10.8$ Hz), 3.84-3.87 (m, 2H), 6.88-6.90 (m, 1H), 7.26-7.36 (m, 2H), 7.55-7.75 (m, 6h), 8.41 (br s, 1H), 10.22 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 24.14, 27.00, 41.92, 42.97, 46.52, 48.62, 106.18, 106.44, 110.08, 110.29, 115.27, 127.86, 129.93, 130.85, 130.95, 133.69, 135.61, 140.95, 141.06, 161.38, 163.78, 168.49, 173.17; Anal. Calc. for $\text{C}_{20}\text{H}_{22}\text{FN}_3\text{O}_4\text{S}$: C, 57.27; H, 5.29; N, 10.02; found: C, 57.42; H, 4.90; N, 9.97%. ESI-MS: m/z 420.2 $[\text{M}+\text{H}]^+$.

***N*-(2-(3-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6e).**

Yield: 59%; white solid; m.p.: 140-142 °C; IR (KBr): 3412, 3303, 2948, 2843, 1692, 1666, 1650, 1350, 1333 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.67-1.71 (m, 1H), 1.75 (s, 1H), 1.82-1.91 (m, 2H), 2.45-2.55 (m, 1H), 2.64-2.74 (m, 2H), 3.57 (d, 1H, *J* = 11.6 Hz), 3.74 (d, 1H, *J* = 9.2 Hz), 4.14 (d, 2H, *J* = 5.2 Hz), 7.01-7.10 (m, 1H), 7.16-7.24 (m, 2H), 7.40-7.42 (m, 1H), 7.52-7.56 (m, 2H), 7.60-7.64 (m, 2H), 7.75-7.77 (m, 2H), 8.82 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 23.76, 26.90, 42.39, 44.34, 46.35, 48.22, 117.84, 119.92, 124.44, 127.56, 129.25, 130.03, 133.10, 134.51, 135.59, 138.78, 167.04, 173.90; Anal. Calc. for C₂₀H₂₂ClN₃O₄S: C, 55.11; H, 5.09; N, 9.64; found: C, 55.26; H, 4.98; N, 9.52%; ESI-MS: *m/z* 436.00 [M+H]⁺.

***N*-(2-(2-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6f).**

Yield: 48%; white solid; m.p.: 162-164 °C; IR (KBr): 3373, 3257, 2953, 2936, 2863, 1707, 1649, 1583, 1386, 1323 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.58-1.76 (m, 2H), 1.80-1.93 (m, 2H), 2.41-2.48 (m, 1H), 2.63-2.70 (m, 2H), 3.61-3.64 (m, 1H), 3.75-3.82 (m, 1H), 4.13-4.14 (m, 2H), 7.01-7.10 (m, 2H), 7.26-7.30 (m, 1H), 7.36-7.39 (m, 1H), 7.53-7.57 (m, 2H), 7.61-7.65 (m, 1H), 7.76-7.78 (m, 2H), 8.30-8.35 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 23.84, 26.93, 42.59, 44.53, 46.33, 48.21, 121.86, 123.18, 125.16, 127.61, 127.75, 129.17, 129.25, 133.07, 134.06, 135.54, 167.23, 173.79; Anal. Calc. for C₂₀H₂₂ClN₃O₄S: C, 55.11; H, 5.09; N, 9.64; found: C, 55.25; H, 5.12; N, 9.58%; ESI-MS: *m/z* 436.05 [M+H]⁺.

***N*-(2-(dimethylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6g).**

Yield: 80%; white solid; m.p.: 128-130 °C; IR (KBr): 3351, 3274, 2978, 2940, 1720, 1677, 1635, 1365, 1338 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.46-1.50 (m, 1H), 1.65-1.85 (m, 2H), 1.89-1.93 (m, 1H), 2.28-2.35 (m, 1H), 2.48-2.60 (m, 2H), 3.02 (d, 6H, *J* = 9.6 Hz), 3.73 (d, 1H, *J* = 11.6 Hz), 3.85 (d, 1H, *J* = 9.6 Hz), 4.03 (d, 2H, *J* = 8.4 Hz), 6.82 (br s, 1H), 7.53-7.57 (m, 2H), 7.60-7.64 (m, 1H), 7.77 (d, 2H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 24.02, 27.16,

35.68, 35.95, 41.22, 42.84, 46.26, 48.24, 127.66, 129.13, 132.85, 135.92, 167.65, 172.54; Anal. Calc. for C₁₆H₂₃N₃O₄S: C, 54.37; H, 6.56; N, 11.89; found: C, 54.45; H, 6.62; N, 11.81%; ESI-MS: m/z 354.0 [M+H]⁺.

***N*-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6h).** Yield: 66%; white solid; m.p.: 138-140 °C; IR (KBr): 3383, 3304, 2949, 2870, 1681, 1651, 1398 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.43-1.53 (m, 1H), 1.66-1.73 (m, 1H), 1.79-1.84 (m, 2H), 1.90-1.94 (m, 2H), 1.98-2.03 (m, 2H), 2.27-2.33 (m, 1H), 2.49 (t, 1H, J = 10.4 Hz) 2.55-2.60 (m, 1H), 3.39 (t, 2H, J = 6.8 Hz), 3.53 (t, 2H, J = 6.8 Hz), 3.84-3.85 (m, 1H), 3.86-3.87 (m, 1H), 3.95-3.99 (m, 2H), 6.86 (br s, 1H), 7.52-7.56 (m, 2H), 7.59-7.63 (m, 1H), 7.75-7.78 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 24.07, 24.14, 25.89, 27.04, 41.96, 42.66, 45.53, 46.13, 46.26, 48.36, 127.62, 129.11, 132.82, 135.88, 166.33, 172.73; Anal. Calc. for C₁₈H₂₅N₃O₄S: C, 56.97; H, 6.64; N, 11.07; found: C, 57.00; H, 6.82; N, 11.30%; ESI-MS: m/z 380.1 [M+H]⁺.

***N*-(2-morpholino-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6i).** Yield: 79%; white solid; m.p.: 178-180 °C; IR (KBr): 3311, 2963, 2922, 2856, 1670, 1655, 1640, 1351, 1332 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.49-1.56 (m, 1H), 1.66-1.74 (m, 1H), 1.80-1.91 (m, 2H), 2.33-2.39 (m, 1H), 2.52-2.58 (m, 2H), 3.41-3.44 (m, 2H), 3.66-3.74 (m, 7H), 3.81 (d, 1H, J = 8.0 Hz), 4.03-4.10 (m, 2H), 6.81 (br s, 1H), 7.53-7.57 (m, 2H), 7.60-7.64 (m, 1H), 7.76-7.78 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 23.95, 27.11, 41.04, 42.34, 42.77, 44.78, 46.28, 48.19, 66.31, 66.69, 127.65, 129.14, 132.87, 135.89, 166.39, 172.62; Anal. Calc. for C₁₈H₂₅N₃O₅S: C, 54.67; H, 6.37; N, 10.63; found: C, 54.75; H, 5.86; N, 10.32%; ESI-MS: m/z 396.1 [M+H]⁺.

***N*-(2-(1,2,3,4-tetrahydroisoquinolin-2(1H)-yl)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6j).** Yield: 62%; white solid; m.p.: 142-144 °C; IR (KBr): 3322, 2948, 2913, 2849, 1664, 1650, 1635, 1351, 1343 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.48-1.51 (m, 1H),

1.67-1.70 (m, 1H), 1.80-1.85 (m, 1H), 1.90-1.93 (m, 1H), 2.30-2.36 (m, 1H), 2.50-2.60 (m, 2H), 2.90-2.96 (m, 2H), 3.64 (t, 1H, $J = 6.0$ Hz), 3.72 (d, 1H, $J = 11.2$ Hz), 3.83-3.89 (m, 2H), 4.11-4.16 (m, 2H), 4.57 (s, 1H), 4.78 (s, 1H), 7.11-7.13 (m, 1H), 7.16-7.20 (m, 2H), 7.22-7.25 (m, 2H), 7.53-7.57 (m, 2H), 7.60-7.64 (m, 1H), 7.76-7.78 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 24.01, 27.14, 28.28, 29.07, 40.24, 41.42, 41.57, 42.13, 42.81, 44.51, 46.01, 46.27, 48.23, 126.16, 126.62, 126.66, 126.85, 126.91, 127.28, 127.66, 128.39, 128.95, 129.13, 131.47, 132.64, 132.85, 133.70, 134.64, 135.90, 166.62, 166.64, 172.56, 172.62; Anal. Calc. for $\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}_4\text{S}$: C, 62.56; H, 6.16; N, 9.52; found: C, 62.46; H, 6.07; N, 9.49%; ESI-MS: m/z 442.2 $[\text{M}+\text{H}]^+$.

***N*-(2-(methyl(phenyl)amino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide (6k).**

Yield: 65%; white solid; m.p.: 156-158 °C; IR (KBr): 3322, 2944, 1673, 1635, 1347, 1333 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.44-1.50 (m, 1H), 1.66-1.89 (m, 3H), 2.29-2.35 (m, 1H), 2.44-2.56 (m, 2H), 3.31 (s, 3H), 3.66-3.78 (m, 4H), 6.69 (br s, 1H), 7.20-7.23 (m, 2H), 7.38-7.48 (m, 3H), 7.51-7.55 (m, 2H), 7.59-7.63 (m, 1H), 7.73-7.76 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 23.94, 27.00, 37.60, 42.04, 42.72, 46.26, 48.26, 127.18, 127.64, 128.77, 129.12, 130.27, 132.86, 135.78, 141.68, 168.06, 172.47; Anal. Calc. for $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_4\text{S}$: C, 60.70; H, 6.06; N, 10.11; found: C, 60.71; H, 5.85; N, 10.12%; ESI-MS: m/z 416.1 $[\text{M}+\text{H}]^+$.

Figure 1: IR of N-(2-(4-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6a**

Figure 2: ¹H NMR of N-(2-(4-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6a**

Figure 3: ¹³C NMR of N-(2-(4-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6a**

Figure 4: ESI-MS of N-(2-(4-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6a**

Figure 5: IR of N-(2-(4-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6b**

Figure 6: ¹H NMR of N-(2-(4-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6b**

Figure 7: ¹³C NMR of N-(2-(4-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6b**

Figure 8: ESI-MS of N-(2-(4-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6b**

Figure 9: IR of N-(2-oxo-2-(p-tolylamino)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6c**

Figure 10: ¹H NMR of N-(2-oxo-2-(p-tolylamino)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6c**

Figure 11: ¹³C NMR of N-(2-oxo-2-(p-tolylamino)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6c**

Figure 12: ESI-MS of N-(2-oxo-2-(p-tolylamino)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6c**

Figure 13: IR of N-(2-(3-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6d**

Figure 14: ^1H NMR of N-(2-(3-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6d

Figure 15: ^{13}C NMR of N-(2-(3-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6d

Figure 16: ESI-MS of N-(2-(3-fluorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6d**

Figure 17: IR of N-(2-(3-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6e**

Figure 18: ^1H NMR of N-(2-(3-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6e

Figure 19: ^{13}C NMR of N-(2-(3-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6e

Figure 20: ESI-MS of N-(2-(3-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6e**

Figure 21: IR of N-(2-(2-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6f**

Figure 22: ¹H NMR of N-(2-(2-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6f**

Figure 23: ¹³C NMR of N-(2-(2-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6f

Figure 24: ESI-MS of N-(2-(2-chlorophenylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6f**

Figure 25: IR of N-(2-(dimethylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6g**

Figure 26: ¹H NMR of N-(2-(dimethylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6g**

Figure 27: ¹³C NMR of N-(2-(dimethylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6g**

Figure 28: ESI-MS of N-(2-(dimethylamino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6g**

Figure 29: IR of N-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6h**

Figure 30: ¹H NMR of N-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6h**

Figure 31: ¹³C NMR of N-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6h**

Figure 32: ESI-MS of N-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6h**

Figure 33: IR of N-(2-morpholino-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6i**

Figure 34: ¹H NMR of N-(2-morpholino-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6i**

Figure 35: ¹³C NMR of N-(2-morpholino-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6i**

Figure 36: ESI-MS of N-(2-morpholino-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6i**

Figure 37: IR of N-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6j**

Figure 38: ¹H NMR of N-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6j**

Figure 39: ¹³C NMR of N-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6j**

Figure 40: ESI-MS of N-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6j**

Figure 41: IR of N-(2-(methyl(phenyl)amino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6k**

Figure 42: ¹H NMR of N-(2-(methyl(phenyl)amino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6k

Figure 43: ¹³C NMR of N-(2-(methyl(phenyl)amino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide

6k

Figure 44: ESI-MS of N-(2-(methyl(phenyl)amino)-2-oxoethyl)-1-(phenylsulfonyl)piperidine-3-carboxamide **6k**