

Supplementary data for the article:

Penjišević, J. Z.; Šukalović, V. V.; Andrić, D. B.; Roglić, G. M.; Novaković, I. T.; Šoškić, V.; Kostić-Rajačić, S. V. Synthesis, Biological Evaluation and Docking Analysis of Substituted Piperidines and (2-Methoxyphenyl)Piperazines. *Journal of the Serbian Chemical Society* **2016**, *81* (4), 347–356. <https://doi.org/10.2298/JSC151021097P>



SUPPLEMENTARY MATERIAL TO

Synthesis, biological evaluation and docking analysis of substituted piperidines and (2-methoxyphenyl)piperazines

JELENA Z. PENJIŠEVIĆ¹, VLADIMIR V. ŠUKALOVIĆ¹, DEANA B. ANDRIĆ^{2*},
GORAN M. ROGLIĆ², IRENA T. NOVAKOVIĆ¹, VUKIĆ ŠOŠKIĆ³
and SLADANA V. KOSTIĆ-RAJACIĆ¹

¹ICTM – Center of Chemistry, University of Belgrade, Njegoševa 12, Belgrade, Serbia,

²Faculty of Chemistry, University of Belgrade, Studentski trg 12–16, Belgrade, Serbia and

³ORGENTEC Diagnostica GmbH, Carl-Zeiss-Straße 49–51, Mainz, Germany

J. Serb. Chem. Soc. 81 (4) (2016) 347–356

ANALYTICAL AND SPECTRAL DATA FOR THE SYNTHESIZED COMPOUNDS

Ethyl 4-[4-(2-methoxyphenyl)piperazin-1-yl]piperidine-1-carboxylate (3). Yield: 88 %; oil; IR (ATR, cm⁻¹): 1698.2 (C=O), 1590.7, 1501.4 (C=C), 1236.0 (C–N), 1025.7 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.25 (3H, *t*, *J* = 6.8 Hz, CH₂–CH₃), 1.46 (2H, *qd*, *J*₁ = 4 Hz, *J*₂ = 12 Hz, C3-H & C5-H piperidine), 1.87 (2H, *d*, *J* = 12.4 Hz, C3-H & C5-H piperidine), 2.45 (1H, *tt*, *J*₁ = 11.2 Hz, *J*₂ = 3.4 Hz, C4-H), 2.76–2.83 (6H, *m*, C2-H & C6-H piperidine and C2-H₂ & C6-H₂ piperazine), 3.02–3.15 (4H, *m*, C3-H₂ & C5-H₂ piperazine), 3.85 (3H, *s*, OCH₃), 4.12 (2H, *q*, *J* = 6.8 Hz, *J* = 7.2 Hz, CH₃–CH₂), 4.21–4.24 (2H, *m*, C2-H & C6-H piperidine), 6.83–7.04 (4H, *m*, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 14.4 (1C, CH₂–CH₃), 27.9 (2C, C3 & C5 piperidine), 43.1 (2C, C2 & C6 piperidine), 49.0 (2C, C2 & C6 piperazine), 50.7 (2C, C3 & C5 piperazine), 55.1 (1C, OCH₃), 61.6 (1C, CH₂–CH₃), 66.9 (1C, C4 piperidine), 110.8 (1C, C3 2-methoxyphenyl group), 117.9 (1C, C5 2-methoxyphenyl group), 120.8 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 140.9 (1C, C2 2-methoxyphenyl group), 152.0 (1C, C1 2-methoxyphenyl group), 155.3 (–C=O); MS (*m/z*): [M+H]⁺ calculated for C₁₉H₂₉N₃O₃: 348.2282. Found: 348.2284.

1-(2-Methoxyphenyl)-4-(piperidin-4-yl)piperazine (4). Yield: 50 %, oil; IR (ATR, cm⁻¹): 3254.4 (N–H), 1585.6, 1502.6 (C=C), 1241.1 (C–N), 1018.0 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.76 (2H, *qd*, *J* = 3.5 Hz & 10.5 Hz, C3-H & C5-H piperidine), 1.98 (2H, *d*, *J* = 11.5 Hz, C3-H & C5-H piperidine), 2.49 (1H, *tt*, *J* = 3.5 Hz & 10.5 Hz, C4-H piperidine), 2.75–2.82 (6H, *m*, C2-H & C6-H piperidine and C2-H₂ & C6-H₂ piperazine), 3.09 (4H, *s*, C3-H₂

* Corresponding author. E-mail: deanad@chem.bg.ac.rs

& C5-H₂ piperazine), 3.37 (2H, *d*, *J* = 12.5 Hz, C2-H & C6-H piperidine), 3.86 (3H, *s*, OCH₃), 6.82–7.02 (4H, *m*, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 27.2 (2C, C3 & C5 piperidine), 44.4 (2C, C2 & C6 piperidine), 49.1 (2C, C2 & C6 piperazine), 50.8 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 60.2 (1C, C4 piperidine), 111.0 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 122.9 (1C, C6 2-methoxyphenyl group), 141.1 (1C, C2 2-methoxyphenyl group), 152.2 (1C, C1 2-methoxyphenyl group); MS (*m/z*): [M+H]⁺ calculated for C₁₆H₂₅N₃O: 276.2070. Found 276.2066.

1-(2-Methoxyphenyl)-4-[(piperidin-4-yl)methyl]piperazine (10). Yield: 54 %; oil; IR (ATR, cm⁻¹): 3432.4 (N–H), 1534.8, 1499.6 (C=C), 1237.1 (C–N), 1021.9 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.03–1.23 (2H, *m*, C3-H & C5-H piperidine), 1.62–1.69 (1H, *m*, C4-H piperidine), 1.78 (2H, *d*, *J* = 13 Hz, C3-H & C5-H piperidine), 2.24 (2H, *d*, *J* = 6.8 Hz, CH₂–N), 2.60–2.67 (6H, *m*, C2-H & C6-H piperidine and C2-H₂ & C6-H₂ piperazine), 3.05–3.10 (4H, *m*, C3-H₂ & C5-H₂ piperazine), 3.86 (3H, *s*, OCH₃), 3.38–3.48 (2H, *m*, C2-H & C6-H piperidine), 6.83–7.02 (4H, *m*, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 31.4 (2C, C3 & C5 piperidine), 33.3 (1C, C4 piperidine), 45.9 (2C, C2 & C6 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.7 (2C, C3 & C5 piperazine), 55.2 (1C, OCH₃), 65.0 (1C, CH₂–N), 111.1 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 141.5 (1C, C2 2-methoxyphenyl group), 152.3 (1C, C1 2-methoxyphenyl group); MS (*m/z*): [M+H]⁺ calculated for C₁₇H₂₇N₃O: 290.2227. Found; 290.2222.

1-(Ethoxycarbonyl)piperidine-4-carboxylic acid (6). Yield: 78 %; oil; IR (ATR, cm⁻¹): 1732.7 (C=O), 1673.5 (C=O), 1033.2 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.26 (3H, *t*, *J* = 7.4 Hz, CH₂–CH₃), 1.66 (2H, *qd*, *J* = 10.4 Hz & 4.4 Hz, C3-H & C5-H piperidine), 1.93 (2H, *d*, *J* = 13.5 Hz, C3-H & C5-H piperidine), 2.51 (1H, *tt*, *J* = 4 Hz & 10.6 Hz, C4-H piperidine), 2.85–2.99 (2H, *m*, C2-H & C6-H piperidine), 4.03–4.19 (4H, *m*, C2-H & C6-H piperidine and CH₂–CH₃), 8.43 (1H, *s*, COOH); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 14.6 (1C, CH₂–CH₃), 27.6 (2C, C3 & C5 piperidine), 40.6 (1C, C4 piperidine), 43.0 (2C, C2 & C6 piperidine), 61.5 (1C, CH₃–CH₂), 155.6 (1C, C=O), 179.9 (1C, COOH); MS (*m/z*): [M+H]⁺ calculated for C₉H₁₅NO₄: 202.1073. Found: 202.1069.

Ethyl 4-{[4-(2-methoxyphenyl)piperazine-1-yl]carbonyl}piperidine-1-carboxylate (8). Yield: 85 %; oil; IR (ATR, cm⁻¹): 1690.4 (C=O), 1622.2 (C=O), 1503.3, 1430.7 (C=C), 1243.3 (C–N), 1015.6 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.26 (3H, *t*, *J* = 7.2 Hz, CH₂–CH₃), 1.70–1.88 (4H, *m*, C3-H₂ & C5-H₂ piperidine), 2.63–2.90 (3H, *m*, C4-H, C2-H & C6-H piperidine), 3.00–3.09 (4H, *m*, C3-H₂ & C5-H₂ piperazine), 3.67–3.83 (4H, *m*, C2-H₂ & C6-H₂

piperazine), 3.88 (3H, *s*, OCH₃), 4.08–4.24 (4H, *m*, CH₂–CH₃ and C2-H & C6-H piperidine), 6.83–7.09 (4H, *m*, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 14.6 (1C, CH₂–CH₃), 28.2 (2C, C3 & C5 piperidine), 38.1 (1C, C4 piperidine), 43.2 (2C, C2 & C6 piperidine), 50.5 (2C, C2 & C6 piperazine), 51.1 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 61.2 (1C, CH₂–CH₃), 111.2 (1C, C3 2-methoxyphenyl group), 118.3 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 123.6 (1C, C6 2-methoxyphenyl group), 140.3 (1C, C2 2-methoxyphenyl group), 152.1 (1C, C1 2-methoxyphenyl group), 155.4 (1C, O–C=O), 172.7 (1C, C=O); MS (*m/z*): [M+H]⁺ calculated for C₂₀H₂₉N₃O₄: 376.2228. Found: 376.2231.

Ethyl 4-{[4-(2-methoxyphenyl)piperazin-1-yl]methyl}piperidine-1-carboxylate (9). Yield: 85 %; oil; IR (ATR, cm⁻¹): 1691.3 (C=O), 1499.0, 1432.0 (C=C–), 1225.4 (C–N), 1017.0 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.00–1.14 (2H, *m*, C3-H & C5-H piperidine), 1.25 (3H, *t*, *J* = 6.6 Hz, CH₂–CH₃), 1.57–1.81 (3H, *m*, C4-H, C3-H & C5-H piperidine), 2.24 (2H, *d*, *J* = 6.6 Hz, CH₂–N), 2.58–2.63 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.67–2.80 (2H, *m*, C2-H & C6-H piperidine), 3.07 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.86 (3H, *s*, OCH₃), 4.00–4.17 (4H, *m*, CH₂–CH₃ and C2-H & C6-H piperidine), 6.84–7.04 (4H, *m*, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 14.7 (1C, CH₂–CH₃), 30.7 (2C, C3 & C5 piperidine), 33.5 (1C, C4 piperidine), 43.9 (2C, C2 & C6 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 61.1 (1C, CH₂–CH₃), 64.6 (1C, CH₂–N), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 141.4 (1C, C2 2-methoxyphenyl group), 152.3 (1C, C1, 2-methoxyphenyl group), 155.7 (1C, O–C=O); MS (*m/z*): [M+H]⁺ calculated for C₂₀H₃₁N₃O₃: 362.2438. Found: 362.2437.

1-(1-Benzylpiperidin-4-yl)-4-(2-methoxyphenyl)piperazine (15). Yield: 76 %, oil; IR (ATR, cm⁻¹): 1590.7, 1450.5 (C=C), 1237.0 (C–N), 1019.6 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.65 (2H, *qd*, *J* = 3.2 Hz & 11.8 Hz, C3-H & C5-H piperidine), 1.86 (2H, *d*, *J* = 11.2 Hz, C3-H & C5-H piperidine), 2.01 (2H, *t*, *J* = 11.2 Hz, C2-H & C6-H piperidine), 2.36 (1H, *tt*, *J* = 4 Hz & 11.4 Hz, C4-H piperidine), 2.76–2.81 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.97 (2H, *d*, *J* = 11.8 Hz, C2-H & C6-H piperidine), 3.09–3.14 (4H, *m*, C3-H₂ & C5-H₂ piperazine), 3.51 (2H, *s*, CH₂–N), 3.85 (3H, *s*, OCH₃), 6.83–7.04 (4H, *m*, Ar-H), 7.22–7.33 (5H, *m*, aromatic); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 27.8 (2C, C3 & C5 piperidine), 49.2 (2C, C2 & C6 piperidine), 50.7 (2C, C2 & C6 piperazine), 53.0 (2C, C3 & C5 piperazine), 55.2 (1C, OCH₃), 62.1 (1C, CH₂–N), 62.9 (1C, C4 piperidine), 111.0 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.9 (1C, C6 2-methoxyphenyl group), 127.0 (1C, C4 phenyl group), 128.2 (2C, C3 & C5

phenyl group), 129.1 (2C, C2 & C6 phenyl group), 138.1 (1C, C1 phenyl group), 141.2 (1C, C2 2-methoxyphenyl group), 152.2 (1C, C1 2-methoxyphenyl group); MS (m/z): $[M+H]^+$ calculated for $C_{23}H_{31}N_3O$: 366.2540. Found: 366.2547.

1-(2-Methoxyphenyl)-4-[1-(2-nitrobenzyl)piperidin-4-yl]piperazine (16).
Yield: 80 %; m.p.: 145–147 °C; IR (ATR, cm^{-1}): 1589.7, 1454.5 (C=C), 1526.0 (N–O), 1369.8 (N–O), 1237.5 (C–N), 1022.6 (C–N); 1H -NMR (200 MHz, $CDCl_3$, δ / ppm): 1.56 (2H, *qd*, $J = 3.2$ Hz & 11.8 Hz, C3-H & C5-H piperidine), 1.82 (2H, *d*, $J = 11.8$ Hz, C3-H & C5-H piperidine), 2.01–2.12 (2H, *m*, C2-H & C6-H piperidine), 2.29 (1H, *tt*, $J = 3.4$ Hz, & 11.2 Hz, C4-H piperidine), 2.74–2.78 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.86 (2H, *d*, $J = 11.8$ Hz, C2-H & C6-H piperidine), 3.1 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.76 (2H, *s*, CH₂-N), 3.85 (3H, *s*, OCH₃), 6.83–7.04 (4H, *m*, Ar-H), 7.37 (1H, *t*, $J = 7.8$ Hz, Ar-H), 7.53 (1H, *t*, $J = 7.2$ Hz, Ar-H), 7.63 (1H, *d*, $J = 6.8$ Hz, Ar-H), 7.81 (1H, *d*, $J = 6.8$ Hz, Ar-H); ^{13}C -NMR (50 MHz, $CDCl_3$, δ / ppm): 28.3 (2C, C3 & C5 piperidine), 49.3 (2C, C2 & C6 piperidine), 50.9 (2C, C2 & C6 piperazine), 53.3 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 58.8 (1C, CH₂-N), 61.8 (1C, C4, piperidine), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.9 (1C, C6 2-methoxyphenyl group), 124.3 (1C, C1 2-nitrophenyl group), 127.7 (1C, C3 2-nitrophenyl group), 130.8 (1C, C4 2-nitrophenyl group), 132.4 (1C, C5 2-nitrophenyl group), 134.3 (1C, C6 2-nitrophenyl group), 141.3 (1C, C2 2-methoxyphenyl group), 149.7 (1C, C2 2-nitrophenyl group), 152.2 (1C, C1, 2-methoxyphenyl group); MS (m/z): $[M+H]^+$ calculated for $C_{23}H_{30}N_4O_3$: 411.2391. Found: 411.2402.

1-(2-Methoxyphenyl)-4-[1-(3-nitrobenzyl)piperidin-4-yl]piperazine (17).
Yield: 86 %; oil; IR (ATR, cm^{-1}): 1588.3, 1499.4 (C=C), 1530.8 (N–O), 1346.9 (N–O), 1237.5 (C–N), 1027.6 (C–N); 1H -NMR (200 MHz, $CDCl_3$, δ / ppm): 1.63 (2H, *qd*, $J = 3.2$ Hz & 10.7 Hz, C3-H & C5-H piperidine), 1.86 (2H, *d*, $J = 11.8$ Hz, C5-H & C5-H piperidine), 2.05 (2H, *t*, $J = 11.8$ Hz, C2-H & C6-H piperidine), 2.34 (1H, *tt*, $J = 3.8$ Hz & 11.8 Hz, C4-H piperidine), 2.76–2.80 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.92 (2H, *d*, $J = 11.2$ Hz, C2-H & C6-H piperidine), 3.08–3.11 (4H, *m*, C3-H₂ & C5-H₂ piperazine), 3.57 (2H, *s*, CH₂-N), 3.86 (3H, *s*, OCH₃), 6.83–7.04 (4H, *m*, Ar-H), 7.47 (1H, *t*, $J = 7.8$ Hz, Ar-H), 7.67 (1H, *d*, $J = 7.2$ Hz, Ar-H), 8.11 (1H, *d*, $J = 8.4$ Hz, Ar-H), 8.2 (1H, *s*, Ar-H); ^{13}C -NMR (50 MHz, $CDCl_3$, δ / ppm): 28.2 (2C, C3 & C5 piperidine), 49.3 (2C, C2 & C6 piperidine), 50.9 (2C, C2 & C6 piperazine), 55.2 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 62.0 (2C, CH₂-N & C4 piperidine), 111.0 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 120.3 (2C, C4 2-methoxyphenyl group & C4 3-nitrophenyl group), 122.1 (1C, C6 2-methoxyphenyl group), 122.9 (1C, C2 3-nitrophenyl group), 123.6 (1C, C5 3-nitrophenyl group), 129.1 (1C, C6 3-nitrophenyl group), 134.9 (1C, C1 3-nitrophenyl group),

141.3 (1C, C2 2-methoxyphenyl group), 149.8 (1C, C3 3-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group); MS (m/z): $[M+H]^+$ calculated for $C_{23}H_{30}N_4O_3$: 411.2391. Found: 411.2389.

1-(2-Methoxyphenyl)-4-[1-(4-nitrobenzyl)piperidin-4-yl]piperazine (18). Yield: 76 %; m.p.: 144–146 °C; IR (ATR, cm^{-1}): 1599.4, 1445.6 (C=C), 1513.8 (N–O), 1344.2 (N–O), 1236.8 (C–N), 1020.3 (C–N); 1H -NMR (200 MHz, $CDCl_3$, δ / ppm): 1.65 (2H, *qd*, $J = 3.4$ Hz & 12.2 Hz, C3-H & C5-H piperidine), 1.89 (2H, *d*, $J = 11.8$ Hz, C3-H & C5-H piperidine), 2.00–2.11 (2H, *m*, C2-H & C6-H piperidine), 2.39 (1H, *tt*, $J = 4$ Hz & 11.2 Hz, C4-H piperidine), 2.80–2.84 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.92 (2H, *d*, $J = 11.8$ Hz, C2-H & C6-H piperidine), 3.12–3.14 (4H, *m*, C3-H₂ & C5-H₂ piperazine), 3.58 (2H, *s*, CH₂-N), 3.86 (3H, *s*, OCH₃), 6.84–7.05 (4H, *m*, Ar-H), 7.59 (2H, *d*, $J = 9.0$ Hz, Ar-H), 8.17 (2H, *d*, $J = 8.4$ Hz, Ar-H); ^{13}C -NMR (50 MHz, $CDCl_3$, δ / ppm): 28.1 (2C, C3 & C5 piperidine), 49.3 (2C, C2 & C6 piperidine), 50.7 (2C, C2 & C6 piperazine), 53.2 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 62.0 (2C, CH₂-N & C4 piperidine), 111.0 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 123.0 (1C, C6 2-methoxyphenyl group), 123.5 (2C, C3 & C5 4-nitrophenyl group), 129.3 (2C, C2 & C6 4-nitrophenyl group), 141.1 (1C, C2 2-methoxyphenyl group), 146.8 (2C, C1 & C4 4-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group); MS (m/z): $[M+H]^+$ calculated for $C_{23}H_{30}N_4O_3$: 411.2391. Found: 411.2409.

1-[(1-Benzylpiperidin-4-yl)methyl]-4-(2-methoxyphenyl)piperazine (19). Yield: 80 %; m.p.: 104–105 °C; IR (ATR, cm^{-1}): 1588.4, 1447.5 (C=C), 1238.7 (C–N), 1024.9 (C–N); 1H -NMR (200 MHz, $CDCl_3$, δ / ppm): 1.25 (2H, *qd*, $J = 2.8$ Hz & 12 Hz, C3-H & C5-H piperidine), 1.46–1.59 (1H, *m*, C4-H piperidine), 1.74 (2H, *d*, $J = 13$ Hz, C3-H & C5-H piperidine), 1.89–2.00 (2H, *m*, C2-H & C6-H piperidine), 2.41 (2H, *d*, $J = 6.8$ Hz, CH₂-N), 2.52 (4H, *s*, C2-H₂ & C6-H₂ piperazine), 2.89 (2H, *d*, $J = 11.8$ Hz, C2-H & C6-H piperidine), 3.07 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.50 (2H, *s*, CH₂-N), 3.86 (3H, *s*, OCH₃), 6.83–7.04 (4H, *m*, Ar-H), 7.23–7.33 (5H, *m*, Ar-H); ^{13}C -NMR (50 MHz, $CDCl_3$, δ / ppm): 31.0 (2C, C3 & C5 piperidine), 33.1 (1C, C4 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.8 (2C, C2 & C6 piperidine), 53.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 62.5 (1C, CH₂-N), 64.8 (1C, CH₂-N), 111.1 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 126.9 (1C, C4 phenyl group), 128.1 (2C, C3 & C5 phenyl group), 129.2 (2C, C2 & C6 phenyl group), 138.5 (1C, C1 phenyl group), 141.5 (1C, C2 2-methoxyphenyl group), 152.3 (1C, C1 2-methoxyphenyl group); MS (m/z): $[M+H]^+$ calculated for $C_{24}H_{33}N_3O$: 380.2696. Found: 380.2692.

1-(2-Methoxyphenyl)-4-[[1-(2-nitrobenzyl)piperidin-4-yl]methyl]piperazine (20). Yield: 82 %; m.p.: 99–101 °C; IR (ATR, cm^{-1}): 1589.1, 1499.5 (C=C),

1532.6 (N–O), 1314.2 (N–O), 1236.1 (C–N), 1026.4 (C–N); $^1\text{H-NMR}$ (200 MHz, CDCl_3 , δ / ppm): 1.21 (2H, *qd*, $J_1 = 11.5$ Hz, $J_2 = 3$ Hz, C3-H & C5-H piperidine), 1.45–1.58 (1H, *m*, C4-H piperidine), 1.72 (2H, *d*, $J = 11.5$ Hz, C3-H & C5-H piperidine), 1.96–2.07 (2H, *m*, C2-H & C6-H piperidine), 2.23 (2H, *d*, $J = 6.8$ Hz, $\text{CH}_2\text{-N}$), 2.59–2.61 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.78 (2H, *d*, $J = 11.2$ Hz, C2-H & C6-H piperidine), 3.07 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.76 (2H, *s*, $\text{CH}_2\text{-N}$), 3.86 (3H, *s*, OCH_3), 6.83–7.03 (4H, *m*, Ar-H), 7.32–7.83 (4H, *m*, Ar-H); $^{13}\text{C-NMR}$ (50 MHz, CDCl_3 , δ / ppm): 31.1 (2C, C3 & C5 piperidine), 33.1 (1C, C4 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.9 (4C, C2 & C6 piperidine and C3 & C5 piperazine), 55.3 (1C, OCH_3), 63.5 (1C, $\text{CH}_2\text{-N}$), 64.9 (1C, $\text{CH}_2\text{-N}$), 111.1 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 124.3 (1C, C1 2-nitrophenyl group), 127.6 (1C, C3 2-nitrophenyl group), 130.8 (1C, C4 2-nitrophenyl group), 132.4 (1C, C5 2-nitrophenyl group), 134.7 (1C, C6 2-nitrophenyl group), 141.5 (1C, C2 2-methoxyphenyl group), 149.8 (1C, C2 2-nitrophenyl group), 152.3 (1C, C1 2-methoxyphenyl group); MS (*m/z*): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{32}\text{N}_4\text{O}_3$: 425.2547. Found: 425.2540.

1-(2-Methoxyphenyl)-4-([1-(3-nitrobenzyl)piperidin-4-yl]methyl)piperazine (**21**). Yield: 80 %; m.p.: 131–133 °C; IR (ATR, cm^{-1}): 1594.7, 1444.9 (C=C), 1534.2 (N–O), 1342.3 (N–O), 1251.5 (C–N), 1030.8 (C–N); $^1\text{H-NMR}$ (200 MHz, CDCl_3 , δ / ppm): 1.32 (2H, *qd*, $J = 3.4$ Hz & 12 Hz, C3-H & C5-H piperidine), 1.48–1.64 (1H, *m*, C4-H piperidine), 1.76 (2H, *d*, $J = 12$ Hz, C3-H & C5-H piperidine), 1.95–2.06 (2H, *m*, C2-H & C6-H piperidine), 2.25 (2H, *d*, $J = 7.4$ Hz, $\text{CH}_2\text{-N}$), 2.60 (4H, *s*, C2-H₂ & C6-H₂ piperazine), 2.85 (2H, *d*, $J = 11.8$ Hz, C2-H & C6-H piperidine), 3.07 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.57 (2H, *s*, $\text{CH}_2\text{-N}$), 3.86 (3H, *s*, OCH_3), 6.83–7.04 (4H, *m*, Ar-H), 7.47 (1H, *t*, $J = 7.8$ Hz, Ar-H), 7.67 (1H, *d*, $J = 8$ Hz, Ar-H), 8.10 (1H, *d*, $J = 8.4$ Hz, Ar-H) 8.2 (1H, *s*, Ar-H); $^{13}\text{C-NMR}$ (50 MHz, CDCl_3 , δ / ppm): 31.0 (2C, C3 & C5 piperidine), 33.1 (1C, C4 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.8 (2C, C2 & C6 piperidine), 53.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH_3), 62.5 (1C, $\text{CH}_2\text{-N}$), 64.8 (1C, $\text{CH}_2\text{-N}$), 111.1 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 120.9 (2C, C4 3-nitrophenyl group & C4 2-methoxyphenyl group), 122.1 (1C, C6 2-methoxyphenyl group), 122.8 (1C, C2 3-nitrophenyl group), 123.7 (1C, C5 3-nitrophenyl group), 129.1 (1C, C6 3-nitrophenyl group), 135.0 (1C, C1 3-nitrophenyl group), 141.3 (1C, C2 2-methoxyphenyl group), 149.3 (1C, C3 3-nitrophenyl group), 152.3 (1C, C1 2-methoxyphenyl group); MS (*m/z*): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{32}\text{N}_4\text{O}_3$: 425.2547. Found: 425.2552.

1-(2-Methoxyphenyl)-4-([1-(4-nitrobenzyl)piperidin-4-yl]methyl)piperazine (**22**). Yield: 87 %; m.p.: 120–121 °C; IR (ATR, cm^{-1}): 1598.2, 1447.6 (C=C–),

1507.9 (N–O), 1343.0 (N–O), 1242.9 (C–N), 1026.6 (C–N); $^1\text{H-NMR}$ (200 MHz, CDCl_3 , δ / ppm): 1.26 (2H, *qd*, $J = 3.8$ Hz & 10.6 Hz, C3-H & C5-H piperidine), 1.47–1.66 (1H, *m*, C4-H piperidine), 1.76 (2H, *d*, $J = 11.8$ Hz, C3-H & C5-H piperidine), 1.95–2.05 (2H, *m*, C2-H & C6-H piperidine), 2.26 (2H, *d*, $J = 6.4$ Hz, $\text{CH}_2\text{-N}$), 2.60–2.62 (4H, *m*, C2-H₂ & C6-H₂ piperazine), 2.84 (2H, *d*, $J = 11.2$ Hz, C2-H & C6-H piperidine), 3.07 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.57 (2H, *s*, $\text{CH}_2\text{-N}$), 3.86 (3H, *s*, OCH_3), 6.83–7.04 (4H, *m*, Ar-H), 7.50 (2H *d*, $J = 8.4$ Hz, Ar-H), 8.17 (2H, *d*, $J = 8.4$ Hz, Ar-H); $^{13}\text{C-NMR}$ (50 MHz, CDCl_3 , δ / ppm): 31.0 (2C, C3 & C5 piperidine), 33.0 (1C, C4 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.8 (4C, C2 & C6 piperidine and C3 & C5 piperazine), 55.3 (1C, OCH_3), 62.5 (1C, $\text{CH}_2\text{-N}$), 64.8 (1C, $\text{CH}_2\text{-N}$), 111.0 (1C, C3, 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 123.4 (2C, C3 & C5 4-nitrophenyl group), 129.4 (2C, C2 & C6 4-nitrophenyl group), 141.4 (1C, C2 2-methoxyphenyl group), 146.9 (2C, C1 & C4 4-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group); MS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{32}\text{N}_4\text{O}_3$: 425.2547. Found: 425.2561.

{4-[4-(2-Methoxyphenyl)piperazin-1-yl]piperidin-1-yl}phenylmethanone (**27**). Yield: 76 %; m.p.: 131–132 °C; IR (ATR, cm^{-1}): 1626.6 (C=O), 1234.1 (C–N), 1024.3 (C–N); $^1\text{H-NMR}$ (200 MHz, CDCl_3 , CDCl_3 , δ / ppm): 1.55–2.17 (5H *m*, C3-H₂, C5-H₂ & C2-H piperidine), 2.56 (1H, *tt*, $J = 3.4$ Hz & 7.4 Hz, C4-H piperidine), 2.76–2.80 (5H, *m*, C2-H₂ & C6-H₂ piperazine and C6-H piperidine), 3.11 (5H, *s*, C3-H₂ & C5-H₂ piperazine and C2-H piperidine), 3.86 (3H, *s*, OCH_3), 4.75 (1H, *s*, C6-H piperidine), 6.84–7.05 (4H, *m*, Ar-H), 7.26–7.40 (5H, *m*, Ar-H); $^{13}\text{C-NMR}$ (50 MHz, CDCl_3 , δ / ppm): 28.2 (2C, C3 & C5 piperidine), 47.1 (2C, C2 & C6 piperidine), 49.4 (2C, C2 & C6 piperazine), 50.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH_3), 61.8 (1C, C4 piperidine), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 123.0 (1C, C6 2-methoxyphenyl group), 126.8 (2C, C2 & C6 phenyl group), 128.4 (2C, C3 & C5 phenyl group), 129.5 (1C, C4 phenyl group), 136.2 (1C, C1 phenyl group), 141.2 (1C, C2 2-methoxyphenyl group), 152.2 (1C, C1 2-methoxyphenyl group), 170.2 (1C, C=O); MS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}_2$: 380.2333. Found: 380.2338.

{4-[4-(2-Methoxyphenyl)piperazin-1-yl]piperidin-1-yl}(2-nitrophenyl)-methanone (**28**). Yield: 75 %; m.p.: 159–161 °C; IR (ATR, cm^{-1}): 1638.7 (C=O), 1521.1 (N–O), 1341.8 (N–O), 1236.1 (C–N), 1025.4 (C–N); $^1\text{H-NMR}$ (200 MHz, CDCl_3 , δ / ppm): 1.25–1.99 (5H, *m*, C3-H₂, C5-H₂ & C2-H piperidine), 2.61 (1H, *tt*, $J = 3.4$ Hz & 10 Hz, C4-H piperidine), 2.78–2.83 (5H, *m*, C2-H₂ & C2-H₂ piperazine and C6-H piperidine), 3.10–3.12 (5H, *m*, C3-H₂ & C5-H₂ piperazine and C2-H piperidine), 3.78 (1H, *s*, C6-H piperidine), 3.87 (3H, *s*, OCH_3), 6.85–7.06 (5H, *m*, Ar-H), 7.58–7.66 (1H, *m*, Ar-H), 7.72–7.78 (1H, *m*,

Ar-H), 8.18–8.35 (1H, *m*, Ar-H); ^{13}C -NMR (50 MHz, CDCl_3 , δ / ppm): 28.0 (2C, C3 & C5 piperidine), 47.1 (2C, C2 & C6 piperidine), 49.3 (2C, C2 & C6 piperazine), 50.8 (2C, C3 & C5 piperazine), 55.3 (1C, OCH_3), 61.5 (1C, C4 piperidine), 111.1 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 122.1 (1C, C6 2-methoxyphenyl group), 124.8 (1C, C3 2-nitrophenyl group), 128.0 (1C, C6 2-nitrophenyl group), 129.7 (1C, C4 2-nitrophenyl group), 133.2 (1C, C1 2-nitrophenyl group), 134.3 (1C, C5 2-nitrophenyl group), 141.1 (1C, C2 2-methoxyphenyl group), 145.4 (1C, C2 2-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group), 166.4 (1C, $\text{C}=\text{O}$); MS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{28}\text{N}_4\text{O}_4$: 425.2183. Found: 425.2192.

{4-[4-(2-Methoxyphenyl)piperazin-1-yl]piperidin-1-yl}(3-nitrophenyl)methanone (29). Yield: 72 %; m.p.: 118–119 °C; IR (ATR, cm^{-1}): 1621.8 ($\text{C}=\text{O}$), 1531.0 (N–O), 1351.3 (N–O), 1244.8 (C–N), 1025.3 (C–N); ^1H -NMR (200 MHz, CDCl_3 , δ / ppm): 1.53–1.63 (2H, *m*, C3-H & C5-H piperidine), 1.88–2.16 (2H, *m*, C3-H & C5-H piperidine), 2.62 (1H, *tt*, $J = 3.4$ Hz & 11.4 Hz, C4-H piperidine), 2.73–2.83 (5H, *m*, C2-H₂ & C6-H₂ piperazine and C2-H piperidine), 3.10–3.15 (5H, *m*, C3-H₂ & C5-H₂ piperazine and C6-H piperidine), 3.50–3.73 (1H, *m*, C2-H piperidine), 3.82 (3H, *s*, OCH_3), 4.74–4.79 (1H, *m*, C6-H piperidine), 6.82–7.06 (4H, *m*, Ar-H), 7.46–7.68 (2H, *m*, Ar-H), 8.18–8.39 (2H, *m*, Ar-H); ^{13}C -NMR (50 MHz, CDCl_3 , δ / ppm): 27.9 (2C, C3 & C5 piperidine), 46.8 (2C, C2 & C6 piperidine) 49.3 (2C, C2 & C6 piperazine), 50.7 (2C, C3 & C5 piperazine), 55.3 (1C, OCH_3), 61.5 (1C, C4 piperidine), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 122.1 (1C, C6 2-methoxyphenyl group), 123.0 (1C, C2 3-nitrophenyl group), 124.4 (1C, C4 3-nitrophenyl group), 129.8 (1C, C5 3-nitrophenyl group), 132.9 (1C, C6 3-nitrophenyl group), 137.7 (1C, C1 3-nitrophenyl group), 141.1 (1C, C2 2-methoxyphenyl group), 148.0 (1C, C3 3-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group), 167.5 (1C, $\text{C}=\text{O}$); MS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{28}\text{N}_4\text{O}_4$: 425.2183. Found: 425.2195.

{4-[4-(2-Methoxyphenyl)piperazin-1-yl]piperidin-1-yl}(4-nitrophenyl)methanone (30). Yield: 70 %; m.p.: 156–157 °C; IR (ATR, cm^{-1}): 1630.1 ($\text{C}=\text{O}$), 1522.0 (N–O), 1352.0 (N–O), 1233.0 (C–N), 1024.5 (C–N); ^1H -NMR (200 MHz, CDCl_3 , δ / ppm): 1.47–2.07 (5H, *m*, C3-H₂, C5-H₂ & C2-H piperidine), 2.57–2.61 (1H, *m*, C4-H piperidine), 2.79 (4H, *s*, C2-H₂ & C6-H₂ piperazine), 2.87 (1H, *s*, C6-H piperidine), 3.11 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.66 (1H, *m*, C2-H piperidine), 3.86 (3H, *s*, OCH_3), 4.73–4.76 (1H, *m*, C6-H piperidine), 6.85–7.02 (4H, *m*, Ar-H), 7.56–7.58 (2H, *m*, Ar-H), 8.27–8.29 (2H, *m*, Ar-H); ^{13}C -NMR (50 MHz, CDCl_3 , δ / ppm): 28.1 (2C, C3 & C5 piperidine), 47.0 (2C, C2 & C6 piperidine), 49.4 (2C, C2 & C6 piperazine), 50.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH_3), 61.5 (1C, C4 piperidine), 111.1 (1C, C3

2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 123.1 (1C, C6 2-methoxyphenyl group), 123.9 (2C, C3 & C5 4-nitrophenyl group), 127.9 (2C, C2 & C6 4-nitrophenyl group), 141.1 (1C, C2 2-methoxyphenyl group), 142.29 (1C, C1 4-nitrophenyl group), 148.35 (1C, C4 4-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group), 167.8 (1C, C=O); MS (*m/z*): [M+H]⁺ calculated for C₂₃H₂₈N₄O₄: 425.2183. Found: 425.2186.

(4-{[4-(2-Methoxyphenyl)piperazin-1-yl]methyl}piperidin-1-yl)phenylmethanone (**31**). Yield: 68 %; oil; IR (ATR, cm⁻¹): 1629.3 (C=O), 1239.0 (C–N), 1130.4 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.24–1.25 (2H, *m*, C3-H & C5-H piperidine), 1.80–1.85 (3H, *m*, C3-H, C5-H & C4-H piperidine), 2.28–2.29 (2H, *m*, CH₂–N), 2.62 (5H, *s*, C2-H₂ & C6-H₂ piperazine and C2-H piperidine), 3.07 (5H, *s*, C3-H₂, & C5-H₂ piperazine and C6-H piperidine), 3.70 (1H, *s*, C2-H piperidine), 3.86 (3H, *s*, OCH₃), 4.72 (1H, *s*, C6-H piperidine), 6.84 (1H, *m*, Ar-H), 6.89 (2H, *m*, Ar-H), 6.94 (1H, *m*, Ar-H), 6.97 (5H, *m*, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 30.7 (2C, C3 & C5 piperidine), 33.7 (1C, C4 piperidine), 48.0 (2C, C2 & C6 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 64.4 (1C, CH₂–N), 111.2 (1C, C3 2-methoxyphenyl group), 118.2 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 122.9 (1C, C6 2-methoxyphenyl group), 126.8 (2C, C2 & C6 phenyl group), 128.4 (2C, C3 & C5 phenyl group), 129.4 (1C, C4 phenyl group), 136.5 (1C, C1 phenyl group), 141.4 (1C, C2 2-methoxyphenyl group), 152.3 (1C, C1 2-methoxyphenyl group), 170.3 (1C, C=O); MS (*m/z*): [M+H]⁺ calculated for C₂₄H₃₁N₃O₂: 394.2489. Found: 394.2488.

(4-{[4-(2-Methoxyphenyl)piperazin-1-yl]methyl}piperidin-1-yl)(2-nitrophenyl)methanone (**32**). Yield: 73 %; m.p.: 127–130 °C; IR (ATR, cm⁻¹): 1628.4 (C=O), 1524.2 (N–O), 1343.5 (N–O), 1235.7 (C–N), 1114.5 (C–N); ¹H-NMR (200 MHz, CDCl₃, δ / ppm): 1.06–1.09 (2H, *m*, C3-H & C5-H piperidine), 1.59 (2H, *s*, CH₂–N), 1.68–1.72 (3H, *m*, C3-H, C5-H & C4-H piperidine), 2.24–2.33 (1H, *m*, C2-H piperidine), 2.61 (4H, *s*, C2-H₂ & C6-H₂ piperazine), 2.84–2.88 (1H, *m*, C6-H piperidine), 3.02 (4H, *s*, C3-H₂ & C5-H₂ piperazine), 3.36 (1H, *s*, C2-H piperidine), 3.85 (3H, *s*, OCH₃), 4.73–4.78 (1H, *m*, C6-H piperidine), 6.84 (1H, *d*, *J* = 8.5 Hz, Ar-H), 6.89–6.94 (2H, *m*, Ar-H), 6.97–7.00 (1H, *m*, Ar-H), 7.38 (1H, *s*, Ar-H), 7.55 (1H, *t*, *J* = 8.5 Hz, Ar-H), 7.69 (1H, *t*, *J* = 7.5 Hz, Ar-H), 8.19 (1H, *d*, *J* = 8.5 Hz, Ar-H); ¹³C-NMR (50 MHz, CDCl₃, δ / ppm): 29.9 (2C, C3 & C5 piperidine), 33.6 (1C, C4 piperidine), 46.7 (2C, C2 & C6 piperidine), 50.7 (2C, C2 & C6 piperazine), 53.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 64.2 (1C, CH₂–N), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 121.0 (1C, C4 2-methoxyphenyl group), 122.9 (1C, C6 2-methoxyphenyl group), 124.8 (1C, C3 2-nitrophenyl group), 128.0 (1C, C6 2-nitrophenyl group), 129.6 (1C, C4 2-nitrophenyl group), 133.5 (1C, C1 2-nit-

rophenyl group), 134.4 (1C, C5 2-nitrophenyl group), 141.4 (1C, C2 2-methoxyphenyl group), 145.3 (1C, C2 2-nitrophenyl group), 152.3 (1C, C1 2-methoxyphenyl group), 170.3 (1C, C=O); MS (m/z): $[M+H]^+$ calculated for $C_{24}H_{30}N_4O_4$: 439.2340. Found: 439.2348.

(4-{[4-(2-Methoxyphenyl)piperazin-1-yl]methyl}piperidin-1-yl)(3-nitrophenyl)methanone (**33**). Yield: 80 %; m.p.: 116–118 °C; IR (ATR, cm^{-1}): 1630.6 (C=O), 1533.1 (N–O), 1351.6 (N–O), 1243.6 (C–N), 1109.9 (C–N); 1H -NMR (200 MHz, $CDCl_3$, δ / ppm): 1.15–1.17 (2H, *m*, C3-H & C5-H piperidine), 1.82–1.94 (3H, *m*, C3-H, C5-H & C4-H piperidine), 2.30 (2H, *s*, CH_2-N), 2.62 (4H, *s*, C2-H₂ & C6-H₂ piperazine), 2.84 (1H, *s*, C2-H piperidine), 3.07 (5H, *s*, C2-H₂ & C6-H₂ piperazine and C6-H piperidine), 3.64–3.66 (1H, *m*, C2-H piperidine), 3.86 (3H, *s*, OCH₃), 4.73 (1H, *s*, C6-H piperidine), 6.84–6.86 (1H, *m*, Ar-H), 6.89–6.94 (2H, *m*, Ar-H), 6.97–7.00 (1H, *m*, Ar-H), 7.58–7.62 (1H, *m*, Ar-H), 7.74 (1H, *m*, Ar-H), 8.26–8.28 (2H, *m*, Ar-H); ^{13}C -NMR (50 MHz, $CDCl_3$, δ / ppm): 30.4 (2C, C3 & C5 piperidine), 33.6 (1C, C4 piperidine), 47.9 (2C, C2 & C6 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.8 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 64.2 (1C, CH_2-N), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.8 (1C, C6 2-methoxyphenyl group), 124.2 (1C, C2 3-nitrophenyl group), 128.0 (1C, C4 3-nitrophenyl group), 129.7 (1C, C5 3-nitrophenyl group), 132.9 (1C, C6 3-nitrophenyl group), 137.9 (1C, C1 3-nitrophenyl group), 141.3 (1C, C2 2-methoxyphenyl group), 149.8 (1C, C3 3-nitrophenyl group), 152.3 (1C, C1 2-methoxyphenyl group), 167.2 (1C, C=O); MS (m/z): $[M+H]^+$ calculated for $C_{24}H_{30}N_4O_4$: 439.2340. Found: 439.2357.

(4-{[4-(2-methoxyphenyl)piperazin-1-yl]methyl}piperidin-1-yl)(4-nitrophenyl)methanone (**34**). Yield: 85 %; m.p.: 119–121 °C; IR (ATR, cm^{-1}): 1630.7 (C=O), 1519.0 (N–O), 1347.9 (N–O), 1239.4 (C–N), 1012.9 (C–N); 1H -NMR (200 MHz, $CDCl_3$, δ / ppm): 1.11–1.13 (2H, *m*, C3-H & C5-H piperidine), 1.79–1.87 (2H, *m*, C3-H & C5-H piperidine), 1.95 (1H, *m*, C4-H piperidine), 2.28–2.30 (2H, *m*, CH_2-N), 2.62 (5H, *s*, C2-H₂ & C6-H₂ piperazine and C2-H piperidine), 3.07 (5H, *s*, C3-H₂ & C5-H₂ piperazine and C6-H piperidine), 3.59 (1H, *d*, $J = 12.5$ Hz, C2-H piperidine), 3.86 (3H, *s*, OCH₃), 4.71 (1H, *d*, $J = 12$ Hz, C6-H piperidine), 6.84–6.86 (1H, *m*, Ar-H), 6.89–6.94 (2H, *m*, Ar-H), 6.97–7.01 (1H, *m*, Ar-H), 7.55 (2H, *d*, $J = 9$ Hz, Ar-H), 8.26 (2H, *d*, $J = 9$ Hz, Ar-H); ^{13}C -NMR (50 MHz, $CDCl_3$, δ / ppm): 30.4 (2C, C3 & C5 piperidine), 33.6 (1C, C4 piperidine), 47.8 (2C, C2 & C6 piperidine), 50.6 (2C, C2 & C6 piperazine), 53.9 (2C, C3 & C5 piperazine), 55.3 (1C, OCH₃), 64.2 (1C, CH_2-N), 111.1 (1C, C3 2-methoxyphenyl group), 118.1 (1C, C5 2-methoxyphenyl group), 120.9 (1C, C4 2-methoxyphenyl group), 122.9 (1C, C6 2-methoxyphenyl group), 123.8 (2C, C3 & C5 4-nitrophenyl group), 127.8 (2C, C2 & C6 4-nitrophenyl group), 141.4 (1C, C2 2-methoxyphenyl group), 142.6 (1C, C1 4-nitrophenyl group), 148.2

(1C, C4 4-nitrophenyl group), 152.2 (1C, C1 2-methoxyphenyl group), 167.8 (1C, C=O); MS (*m/z*): [M+H]⁺ calculated for C₂₄H₃₀N₄O₄: 439.2340. Found: 439.2360.