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Chemistry & Drug Discovery

Supporting Information

Discovery of novel non-cyclam polynitrogenated CXCR4 coreceptor inhibitors

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Supporting Information

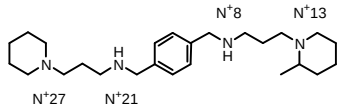
Blind docking and binding pocket docking analyses for the calculated CXCR4-compound **1**{*8,8*} complex and experimental details and spectral data for compounds **1**{*5,5*}, **1**{*6,6*}, **1**{*7,7*}, **1**{*9,9*}, **1**{*10,10*}, **1**{*11,11*}, **2**{*2,2*}, **2**{*3,3*}, **7**{*5*}, **7**{*7*}, **7**{*9*}, **7**{*10*}, **7**{*11*}, **6**{*3*}, **8**{*2,6*}, **8**{*2,8*}, **8**{*2,9*}, **8**{*2,11*}, **8**{*3,4*}, **1**{*4,5*}, **1**{*4,6*}, **1**{*4,9*}, **1**{*4,11*}, **1**{*5,6*}, **1**{*5,7*}, **1**{*5,8*}, **1**{*5,9*}, **1**{*5,10*}, **1**{*5,11*}, **1**{*6,7*}, **1**{*6,9*}, **1**{*6,10*}, **1**{*6,11*}, **1**{*7,9*}, **1**{*7,11*}, **1**{*8,10*}, **1**{*8,11*}, **1**{*9,10*}, **1**{*9,11*}, **1**{*10,11*}, **8**{*1,5*}, **8**{*1,6*}, **8**{*1,8*}, **8**{*1,9*}, **8**{*1,11*}, **8**{*2,5*}, **8**{*3,5*}, **8**{*3,6*}, **8**{*3,8*}, **8**{*3,9*} and **8**{*3,11*}.

Table. Blind docking and binding pocket docking analyses for the calculated CXCR4-compound **1**{8,8} complex. This table shows the distances from the carboxylic oxygens of the three key binding residues Asp171, Asp262, and Glu288, to the four nitrogens (N27, N21, N8, N13) of **1**{8,8}. The lowest interaction distances are shown in bold. The nitrogen atoms of **1**{8,8} are charged according to physiological pH.

	Blind docking [a]	Binding pocket docking [b]
Distance to O^- (sp3) Asp^{171} (Å)	10.11 (N+27) 9.36 (N+13) 12.84 (N+27) 11.06 (N+27) 7.98 (N+13) 9.08 (N+N+27)	10.25 (N+8) 7.22 (N+27) 8.00 (N+13) 8.98 (N+27) 9.70 (N+8)
Average	10.07	8.83
Distance to O (sp2) Asp^{171} (Å)	8.22 (N+21) 7.18 (N+13) 10.82 (N+27) 8.93 (N+27) **6.88 (N+13)** **6.97 (N+27)**	8.08 (N+8) **5.87 (N+27)** **5.81 (N+13)** **6.80 (N+27)** 7.51 (N+8)
Average	8.17	6.81
Distance to O^- (sp3) Asp^{262} (Å)	8.02 (N+27) **5.42 (N+21)** **3.74 (N+21)** **4.45 (N+21)** 6.72 (N+8) 6.74 (N+21)	**4.80 (N+21)** 8.63 (N+13) 7.39 (N+21) **3.86 (N+21)** 4.87 (N+21)
Average	5.85	5.91
Distance to O (sp2) Asp^{262} (Å)	6.64 (N+27) 5.83 (N+21) **4.88 (N+21)** **4.72 (N+21)** **5.24 (N+8)** 5.28 (N+21)	**4.90 (N+21)** 6.86 (N+27) 6.23 (N+8) **5.43 (N+21)** **4.81 (N+21)**
Average	**5.43**	**5.65**
Distance to O^- (sp3) Glu^{288} (Å)	6.28 (N+27) **4.10 (N+8)** **4.75 (N+27)** 6.31 (N+21) **3.95 (N+8)** 5.37 (N+8)	4.93 (N+13) **3.90 (N+8)** **4.34 (N+27)** 7.86 (N+13) **4.04 (N+13)**
Average	**5.13**	**4.96**
Distance to O (sp2) Glu^{288} (Å)	**3.83 (N+8)** 5.84 (N+21) **4.94 (N+8)** 5.09 (N+8) **3.06 (N+21)** **3.63 (N+8)**	4.83 (N+13) **3.01 (N+8)** **4.05 (N+27)** 8.60 (N+13) **4.30 (N+13)**
Average	**4.42**	**4.96**

[a] For blind docking analysis all distances refer to the AUTODOCK pose with the lowest overall distance between the compound nitrogens and the three key binding residues.

[b] For binding pocket docking analysis all distances refer to the lowest energy AUTODOCK pose.



***N*-(4-((3-(pyrrolidin-1-yl)propylamino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (1{*5,5*}).** The procedure was the same as that stated for **1**{*4,4*} but using terephthalaldehyde (**3**) (1.47 g, 11.1 mmol), 1-(3-aminopropyl)pyrrolidine **4**{*5*} (1.47 g, 11.1 mmol) and $NaBH_4$ (0.43 g, 11.1 mmol) to give **1**{*5,5*} as a yellow oil (1.98 g, 99%). IR (film): *n*=3282 (N-H), 2936, 2789 (C-H), 1458 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.26 (s, 4H; Ph), 3.77 (s, 4H; C$\underline{H}_2$-Ph), 2.69 (t, ^3J (H,H)=7.0 Hz, 4H; C$\underline{H}_2$-NH), 2.49 (m, 12H; CH_2-N), 2.08 (br, 2H; NH), 1.75 ppm (m, 12H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.5 (Cq), 128.0 (CH), 54.6 (CH_2), 54.1 (CH_2), 53.5 (CH_2), 47.9 (CH_2), 28.8 (CH_2), 23.4 ppm (CH_2); MS (EI): *m/z* (%): 359.2 (1) [M^++H], 84.0 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for ($C_{22}H_{39}N_4$): 359.3175. Found: 359.3169.

***N*-(4-((3-(1*H*-imidazol-1-yl)propylamino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (1{*6,6*}).** The procedure was the same as that stated for **1**{*4,4*} but using terephthalaldehyde (**3**) (0.54 g, 3.9 mmol), 1-(3-aminopropyl)imidazole **4**{*6*} (1.00 g, 7.8 mmol) and $NaBH_4$ (0.30 g, 7.8 mmol) to afford **1**{*6,6*} as a yellow oil (1.38 g, 100%). IR (film): *n*=3277 (N-H), 3103, 2935, 2815 (C-H), 1508 (imidazol), 1453 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.41 (s, 2H; CH-N), 7.26 (s, 4H; Ph), 7.02 (s, 2H; CH-N), 6.88 (s, 2H; CH-N), 4.04 (t, ^3J (H,H)=6.9 Hz, 4H; CH_2-N), 3.74 (s, 4H; C$\underline{H}_2$-Ph), 2.60 (t, ^3J (H,H)=6.9 Hz, 4H; C$\underline{H}_2$-NH), 2.05 (s, 2H; NH), 1.92 ppm (quint, ^3J (H,H)=6.9 Hz, 4H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.8 (CH), 137.1 (Cq), 129.2 (CH), 128.2 (CH), 118.7 (CH), 53.6 (CH_2), 45.6 (CH_2), 44.6 (CH_2), 31.3 ppm (CH_2); MS (EI): *m/z* (%): 353.0 (1) [M^++H], 228.9 (100) [$C_{14}H_{18}N_3^+$]; HRMS: Calcd for $C_{20}H_{28}N_6$ [M+1H]$^+$: 352.2454. Found: 353.2448.

***N*-(4-((2-(piperidin-1-yl)ethylamino)methyl)benzyl)-2-(piperidin-1-yl)ethanamine (1{*7,7*}).** The procedure was the same as that stated for **1**{*4,4*} but using terephthalaldehyde (**3**) (0.29 g, 2.1 mmol), 1-(2-aminoethyl)piperidine **4**{*7*} (0.56 g, 4.3 mmol) and $NaBH_4$ (0.16 g, 4.3 mmol) to give **1**{*7,7*}as a yellow oil (0.76 g, 100%). IR (film): *n*=3310 cm^{-1} (N-H); ^{1}H-NMR (300MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.32 (s, 4H; Ph), 3.75 (s, 4H; C$\underline{H}_2$-Ph), 2.69 (t, ^3J (H,H)=7.0 Hz, 4H; C$\underline{H}_2$-NH), 2.47 (t, ^3J (H,H)=7.0 Hz, 4H; CH_2-N), 2.39 (m, 8H; CH_2-N), 1.62-1.39 ppm (m, 12H; CH_2); ^{13}C-NMR (75.5MHz, $CDCl_3$, 25 ºC): *d*=139.4 (Cq), 129.6 (CH), 59.0 (CH_2), 55.7 (CH_2), 54.1 (CH_2), 46.1 (CH_2), 26.7 (CH_2), 25.2 ppm (CH_2); Anal. ($C_{22}H_{38}N_4$) C, H, N.

***N*-(4-((3-(4-methylpiperazin-1-yl)propylamino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (1{*9,9*}).** The procedure was the same as that stated for **1**{*4,4*} but using terephthalaldehyde (**3**) (0.48 g, 3.5 mmol), 1-(3-aminopropyl)-4-methylpiperazine **4**{*9*} (1.14 g, 7.0 mmol) and $NaBH_4$ (0.27 g, 7.0 mmol) to give **1**{*9,9*} as a brown oil (1.28 g, 87%). IR (film): *n*=3281 (N-H), 2935, 2793 (C-H), 1458 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.26 (s, 4H; Ph), 3.76 (s, 4H; C$\underline{H}_2$-Ph), 2.66 (t, ^3J (H,H)=6.9 Hz, 4H; C$\underline{H}_2$-NH), 2.42 (m, 22H; CH_2-N, NH), 2.27 (s, 6H; CH_3), 1.70 ppm (quint, ^3J (H,H)=6.9 Hz, 4H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.8 (Cq), 128.0 (CH), 57.0 (CH_2), 55.1 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 46.0 (CH_3), 26.9 ppm (CH_2); MS (EI): *m/z* (%): 417.0 (9) [M^++H], 416.0 (28) [M^+], 113.0 (100) [$C_6H_{13}N_2^+$]; HRMS: Calcd for $C_{24}H_{44}N_6$ [M+1H]$^+$: 417.3706. Found: 417.3700.

***N*-(4-((2-morpholinoethylamino)methyl)benzyl)-2-morpholinoethylamine (1{*10,10*}).** The procedure was the same as that stated for **1**{*4,4*} but using terephthalaldehyde (**3**) (0.54 g, 4.0 mmol), 2-morpholinoethylamine **4**{*10*} (1.05 g, 8.0 mmol) and $NaBH_4$ (0.31 g, 8.0 mmol) to give **1**{*10,10*} as a white solid (0.93 g, 64%). IR (film): *n*=3341 (N-H), 2968, 2930, 2817 (C-H), 1446 (C-H), 1117, 830 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 4H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.6 Hz, 8H; CH_2-O), 2.70 (t, ^3J (H,H)=6.0 Hz, 4H; C$\underline{H}_2$-NH), 2.50 (t, ^3J (H,H)=6.0 Hz, 4H; CH_2-N), 2.403 (t, ^3J (H,H)=4.6 Hz, 8H; CH_2-N), 1.82 ppm (s, 2H; NH); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 128.0 (CH), 67.0 (CH_2), 58.3 (CH_2), 53.7 (CH_2), 45.3 ppm (CH_2); Anal. ($C_{20}H_{34}N_4O_2$) C, H, N. MS (EI): *m/z* (%) 363.4 (5) [M^++H], 362.4 (6) [M^+], 100.0 (100) [$C_5H_{10}NO^+$].

***N*-(4-((3-morpholinopropylamino)methyl)benzyl)-3-morpholinopropan-1-amine (1{*11,11*}).** The procedure was the same as that stated for **1**{*4,4*} but using terephthalaldehyde (**3**) (0.47 g, 3.5 mmol), 3-morpholinopropylamine **4**{*11*} (1.00 g, 7.0 mmol) and $NaBH_4$ (0.27 g, 7.0 mmol) to give **1**{*11,11*} as a yellow oil (1.16 g, 85%). IR (film): *n*=3301(N-H), 2948, 2852, 2806 (C-H), 1456 (C-H), 1118, 862 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 4H; C$\underline{H}_2$-Ph), 3.70 (t, ^3J (H,H)=4.6 Hz, 8H; CH_2-O), 2.68 (t, ^3J (H,H)=7.0 Hz, 4H; C$\underline{H}_2$-NH), 2.41 (m, 12H; CH_2-N), 1.81 (s, 2H; NH), 1.70 ppm (quint, ^3J (H,H)=7.0 Hz, 4H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 128.0 (CH), 67.0 (CH_2), 57.4 (CH_2), 53.8 (CH_2), 48.0 (CH_2), 26.8 ppm (CH_2). MS (EI): *m/z* (%) 390.3 (2) [M^+], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{22}H_{38}N_4O_2$: 390.2995. Found: 390.3007.

((4-(*N*-(2,6-dimethylpiperidin-1-yl)imino)methyl)phenyl)-*N*-(2,6-dimethylpiperidin-1-yl)methanamine (2{*2,2*}). The procedure was the same as that stated for **2**{*1,1*} but using terephthalaldehyde (**3**) (0.57 g, 4.2 mmol) and 1-amino-2,6-dimethylpiperidine **4**{*2*} (1.20 g, 8.4 mmol) to give **2**{*2,2*} as a yellow solid (1.05 g, 65%). IR (film): *n*=1684 cm^{-1} (C=N); ^{1}H-NMR (300MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.87 (s, 2H; CH=N), 7.64 (s, 4H; Ph), 3.31-3.27 (m, 4H; C$\underline{H}$-CH_3), 1.83-1.51 (m, 12H; CH_2), 1.03 ppm (d, ^3J (H,H)=6.0 Hz, 12H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=146.6 (CH), 136.0 (Cq), 126.8 (CH), 56.1 (CH), 32.4 (CH_2), 20.0 (CH_3), 19.9 ppm (CH_2); Anal. ($C_{22}H_{34}N_4$) C, H, N.

((4-(*N*-(4-methylpiperazin-1-yl)imino)methyl)phenyl)-*N*-(4-methylpiperazin-1-yl)methanamine (2{*3,3*}). The procedure was the same as that stated for **2**{*1,1*} but using terephthalaldehyde (**3**) (0.37 g, 2.7 mmol) and 1-amino-4-methylpiperazine **4**{*3*} (0.64 g, 5.4 mmol) to give **2**{*3,3*} as a yellow solid (0.67 g, 75%). IR (film): *n*=1579 cm^{-1} (C=N); ^{1}H-NMR (300MHz, $CDCl_3$): *d*=7.57 (s, 4H; Ph), 7.53 (s, 2H; CH=N), 3.23 (m, 8H; CH_2-N), 2.62 (m, 8H; CH_2-N), 2.36 ppm (s, 6H; CH_3); ^{13}C-NMR (75.5MHz, $CDCl_3$, 25 ºC): *d*=135.8 (Cq), 135.4 (CH), 126.2 (CH), 54.5 (CH_2), 51.0 (CH_2), 46.0 ppm (CH_3); Anal. ($C_{18}H_{28}N_6$) C, H, N.

4-((3-(pyrrolidin-1-yl)propylamino)methyl)benzaldehyde (7{*5*}). The procedure was the same as that stated for **7**{*4*} but using 4-(diethoxymethyl)benzaldehyde (**5**) (6.01 g, 28.0 mmol), 1-(3-aminopropyl)pyrrolidine **4**{*5*} (3.70 g, 28.0 mmol) and $NaBH_4$ (1.07 g, 28.0 mmol). The intermediate aminoacetal was obtained as a yellow oil (8.01 g, 89%). This acetal (7.98 g, 24.9 mmol) was deprotected to afford **7**{*5*} (4.59 g, 75%) as a red oil. IR (film): *n*=3276 (N-H), 2934, 2874, 2790 (C-H), 1700 (C=O), 1606 (C-C), 1458 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=10.00 (s, 1H; CHO), 7.84 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.50 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.88 (s, 2H; C$\underline{H}_2$-Ph), 2.70 (t, ^3J (H,H)=7.0 Hz, 2H; C$\underline{H}_2$-NH), 2.51 (m, 6H; CH_2-N), 1.87 (br, 1H; NH), 1.75 ppm (m, 6H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=191.8 (CH), 147.7 (Cq), 135.2 (Cq), 129.8 (CH), 128.3 (CH), 54.7 (CH_2), 54.3 (CH_2), 53.7 (CH_2), 48.2 (CH_2), 29.2 (CH_2), 23.5 ppm (CH_2); Anal. ($C_{15}H_{22}N_2O$) C, H, N; MS (EI): *m/z* (%): 247.2 (2) [M^++H], 246.2 (21) [M^+], 84.1 (100) [$C_5H_{10}N^+$].

4-((2-(piperidin-1-yl)ethylamino)methyl)benzaldehyde (7{*7*}). The procedure was the same as that stated for **7**{*4*} but using 4-(diethoxymethyl)benzaldehyde (**5**) (2.01 g, 9.4 mmol), 1-(2-aminoethyl)piperidine **4**{*7*} (1.23 g, 9.4 mmol) and $NaBH_4$ (0.36 g, 9.4 mmol). The intermediate aminoacetal was obtained as a yellow oil (2.79 g, 93%). This acetal (2.75 g, 8.6 mmol) was deprotected to afford **7**{*7*} (2.11 g, quantitative) as a yellow oil. IR (film): *n*=3308 (N-H), 3050, 2934, 2851, 2809 (C-H), 1701 (C=O), 1606 (C-C), 1453 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=10.00 (s, 1H; CHO), 7.84 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.50 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.89 (s, 2H; C$\underline{H}_2$-Ph), 2.70 (t, ^3J (H,H)=6.2 Hz, 2H; C$\underline{H}_2$-NH), 2.47 (t, ^3J (H,H)=6.2 Hz, 2H, CH_2-N), 2.36 (br, 4H; CH_2-N), 2.18 (br, 1H; NH), 1.57 (quint, ^3J (H,H)=5.7 Hz, 4H; CH_2), 1.43 ppm (m, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=191.8 (CH), 147.7 (Cq), 135.2 (Cq), 129.8 (CH), 128.4 (CH), 58.4 (CH_2), 54.7 (CH_2), 53.7 (CH_2), 45.9 (CH_2), 25.9 (CH_2), 24.4 ppm (CH_2); Anal. ($C_{15}H_{22}N_2O$) C, H, N; MS (EI): *m/z* (%): 246.2 (8) [M^+], 98.1 (100) [$C_6H_{12}N^+$]; HRMS: Calcd for $C_{15}H_{22}N_2O$: 246.1732. Found: 246.1731.

4-((3-(4-methylpiperazin-1-yl)propylamino)methyl)benzaldehyde (7{*9*}). The procedure was the same as that stated for **7**{*4*} but using 4-(diethoxymethyl)benzaldehyde (**5**) (2.00 g, 9.3 mmol), 1-(3-aminopropyl)-4-methylpiperazine **4**{*9*} (1.49 g, 9.3 mmol) and $NaBH_4$ (0.36 g, 9.3 mmol). The intermediate aminoacetal was obtained as a yellow oil (2.94 g, 90%). This acetal (2.93 g, 8.4 mmol) was deprotected to afford **7**{*9*} (2.31 g, quantitative) as a brown oil. IR (film): *n*=3276 (N-H), 2936, 2875, 2794, 2769, 2740 (C-H), 1700 (C=O), 1606 (C-C), 1458 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=10.00 (s, 1H; CHO), 7.85 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.50 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.87 (s, 2H; C$\underline{H}_2$-Ph), 2.69 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.45 (br, 8H; CH_2-N), 2.42 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 2.27 (s, 3H; CH_3), 2.08 (br, 1H; NH), 1.72 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=191.8 (CH), 147.7 (Cq), 135.2 (Cq), 129.8 (CH), 128.3 (CH), 57.0 (CH_2), 55.1 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.3 (CH_2), 46.0 (CH_3), 27.0 ppm (CH_2); MS (EI): *m/z* (%): 276.2 (4) [M^++H], 275.2 (26) [M^+], 231.2 (100) [$C_{14}H_{21}N_3^+$]; HRMS: Calcd for $C_{16}H_{25}N_3O$: 275.1998. Found: 275.2001.

4-((2-morpholinoethylamino)methyl)benzaldehyde (7{*10*}). The procedure was the same as that stated for **7**{*4*} but using 4-(diethoxymethyl)benzaldehyde (**5**) (2.00 g, 9.3 mmol), 2-morpholinoethylamine **4**{*10*} (1.23 g, 9.3 mmol) and $NaBH_4$ (0.36 g, 9.3 mmol). The intermediate aminoacetal was obtained as a yellow oil (2.55 g, 85%). This acetal (2.52 g, 7.8 mmol) was deprotected to afford **7**{*10*} (1.94 g, quantitative) as a brown oil. IR (film): *n*=3309 (N-H), 2954, 2917, 2894, 2852, 2818 (C-H), 1698 (C=O), 1607 (C-C), 1455 (C-H), 1117, 852 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=10.00 (s, 1H; CHO), 7.86 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.50 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.90 (s, 2H; C$\underline{H}_2$-Ph), 3.70 (t, ^3J (H,H)=4.5 Hz, 4H; CH_2-O), 2.71 (t, ^3J (H,H)=6.0 Hz, 2H; C$\underline{H}_2$-NH), 2.51 (t, ^3J (H,H)=6.0 Hz, 2H; CH_2-N), 2.42 (t, ^3J (H,H)=4.5 Hz, 4H; CH_2-N), 1.93 ppm (br, 1H; NH); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=191.7 (CH), 147.5 (Cq), 135.2 (Cq), 129.8 (CH), 128.4 (CH), 66.9 (CH_2), 58.2 (CH_2), 53.7 (CH_2), 45.4 ppm (CH_2); MS (IE): *m/z* (%) 249.2 (0.3) [M^++H], 248.2 (8) [M^+], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{14}H_{20}N_2O_2$: 248.1525. Found: 248.1531.

4-((3-morpholinopropylamino)methyl)benzaldehyde (7{*11*}). The procedure was the same as that stated for **7**{*4*} but using 4-(diethoxymethyl)benzaldehyde (**5**) (2.01 g, 9.3 mmol), 3-morpholinopropylamine **5**{*11*} (1.35 g, 9.3 mmol) and $NaBH_4$ (0.36 g, 9.3 mmol). The intermediate aminoacetal was obtained as a yellow oil (2.91 g, 92%). This acetal (2.86 g, 8.5 mmol) was deprotected to afford **7**{*11*} (1.60 g, 72%) as a yellow oil. IR (film): *n*=3307 (N-H), 2950, 2892, 2853, 2814 (C-H), 1698 (C=O), 1607 (C-C), 1457 (C-H), 1117, 861 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=10.00 (s, 1H; CHO), 7.85 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.50 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.88 (s, 2H; C$\underline{H}_2$-Ph), 3.70 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.70 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.45-2.39 (m, 6H; CH_2-N), 1.81 (br, 1H; NH), 1.72 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=191.2 (CH), 147.6 (Cq), 135.2 (Cq), 129.8 (CH), 128.3 (CH), 66.9 (CH_2), 57.3 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 48.1 (CH_2), 26.7 ppm (CH_2); MS (EI): *m/z* (%) 262.2 (3) [M^+], 84.0 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{15}H_{22}N_2O_2$: 262.1681. Found: 262.1682.

4-((4-methylpiperazin-1-ylimino)methyl)benzaldehyde (6{*3*}). The procedure was the same as that stated for **6**{*1*} but using terephthalaldehyde (**3**) (1.14 g, 8.4 mmol) and 1-amino-4-methylpiperazine **4**{*3*} (0.50 g, 4.2 mmol). Upon removal of the solvent, the residue was chromatographed on silica gel, eluting with DCM/MeOH (gradient from 10:0 to 9:1) to afford **6**{*3*} (0.80 g, 82%) as a yellow solid. IR (film): *n*= 2941, 2843, 2799, 2728 (C-H), 1692 (C=O), 1605 (C-C), 1581 (C=N), 1551 (C-C), 1451, 1364 cm^{-1} (C-H); ^{1}H-NMR (300MHz, $CDCl_3$, 25 ºC, TMS): *d*=9.98 (s, 1H; CHO), 7.84 (d, ^3J (H,H)=7.7 Hz, 2H; Ph), 7.72 (d, ^3J (H,H)=7.7 Hz, 2H; Ph), 7.50 (s, 1H; CH=N), 3.30 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.62 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.37 ppm (s, 3H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=191.6 (CH), 142.1 (Cq), 135.3 (Cq), 132.6 (CH), 130.0 (CH), 126.1 (CH), 54.3 (CH_2), 50.6 (CH_2), 46.0 ppm (CH_3); MS (EI): *m/z* (%): 232.1 (12) [M^++H], 99.0 (100) [$C_5H_{11}N_2^+$]; HRMS: Calcd for $C_{13}H_{17}N_3O$: 231.1372. Found: 231.1376.

***N*-(4-((2,6-dimethylpiperidin-1-ylimino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (8{*2,6*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)imidazole **4**{*6*} (0.26 g, 2.0 mmol), **6**{*2*} (0.26 g, 2.0 mmol) and $NaBH_4$ (0.08 g, 2.0 mmol) to give **8**{*2,6*} (0.70 g, 100%) as a yellow oil. IR (film): *n*=3284 (N-H), 3106, 2961, 2931, 2867, 2856, 2824 (C-H), 1624 (C-C), 1582 (C=N), 1552 (C-C), 1508 (imidazol), 1449, 1369 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=8.04 (s, 1H; CH=N), 7.65 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.46 (s, 1H; CH-N), 7.31 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.04 (s, 1H; CH-N), 6.89 (s, 1H; CH-N), 4.05 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.77 (s, 2H; CH_2-Ph), 3.10 (m, 2H; C$\underline{H}$-CH_3), 2.61 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 1.93 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.85 (br, 1H; NH), 1.77 (m, 4H; CH_2), 1.51 (m, 2H; CH_2), 1.00 ppm (d, ^3J (H,H)=6.6 Hz, 6H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=151.7 (CH), 141.4 (Cq), 137.0, (CH) 134.0 (Cq), 129.2 (CH), 128.2 (CH), 127.3 (CH), 118.7 (CH), 57.2 (CH), 53.7 (CH_2), 45.7 (CH_2), 44.7 (CH_2), 32.8 (CH_2), 31.4 (CH_2), 21.2 (CH_2), 20.5 ppm (CH_3); MS (EI): *m/z* (%): 354.2 (5) [M^++H], 112.1 (100) [$C_7H_{14}N^+$]; HRMS: Calcd for $C_{21}H_{32}N_5$ [M+1H]$^+$: 354.2658. Found: 354.2666.

***N*-(4-((2,6-dimethylpiperidin-1-ylimino)methyl)benzyl)-3-(2-methylpiperidin-1-yl)propan-1-amine (8{*2,8*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)-2-methyl-piperidine **4**{*8*} (0.35 g, 2.1 mmol), **6**{*2*} (0.52 g, 2.1 mmol) and $NaBH_4$ (0.08 g, 2.1 mmol) to give **8**{*2,8*} (0.77 g, 93%) as a yellow oil. IR (film): *n*=3281 (N-H), 2961, 2930, 2855, 2808 (C-H), 1625 (C-C), 1584 (C=N), 1554 (C-C),

1449, 1370 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=8.06 (s, 1H; CH=N), 7.64 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.34 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.81 (s, 2H; C$\underline{H}_2$-NH), 3.08 (m, 2H; C$\underline{H}$-CH_3), 2.88 (m, 1H; CH_{eq}-N), 2.76 (m, 1H; CH_{eq}-N), 2.65 (t, ^3J (H,H)=6.8 Hz, 4H; C$\underline{H}_2$-NH), 2.35 (br, 1H; NH), 2.34 (m, 1H; CH_{ax}-N), 2.25 (m, 1H; C$\underline{H}$-CH_3), 2.10 (m, 1H; CH_{ax}-N), 1.79-1.32 (cs, 12H; CH_2), 1.27 (m, 2H; CH_{ax}), 1.06 (d, ^3J (H,H)=6.3 Hz, 3H; CH_3), 1.00 ppm (d, ^3J (H,H)=6.3 Hz, 6H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=152.3 (CH), 141.6 (Cq), 133.8 (Cq), 128.2 (CH), 127.2 (CH), 57.3 (CH), 56.0 (CH), 53.7 (CH_2), 52.3 (CH_2), 52.0 (CH_2), 48.3 (CH_2), 34.6 (CH_2), 32.9 (CH_2), 26.1 (CH_2), 25.6 (CH_2), 23.9 (CH_2), 21.4 (CH_2), 20.6 (CH_3), 19.0 ppm (CH_3).

***N*-(4-((2,6-dimethylpiperidin-1-ylimino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (8{*2,9*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)-4-methylpiperazine **4**{*9*} (0.31 g, 1.9 mmol), **6**{*2*} (0.47 g, 1.9 mmol) and $NaBH_4$ (0.07 g, 1.9 mmol) to give **8**{*2,9*} (0.72 g, 97%) as a yellow oil. IR (film): *n*=3286 (N-H), 2932, 2872, 2837, 2794 (C-H), 1625 (C-C), 1584 (C=N), 1554 (C-C), 1458, 1370 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=8.05 (s, 1H; CH=N), 7.65 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.34 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.81 (s, 2H; C$\underline{H}_2$-Ph), 3.08 (m, 2H; C$\underline{H}$-CH_3), 2.69 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.44 (br, 8H; CH_2-N), 2.41 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 2.30 (br, 1H; NH), 2.27 (s, 3H; CH_3-N), 1.81-1.68 (m, 6H; CH_2), 1.51 (m, 2H; CH_2), 1.00 ppm (d, ^3J (H,H)=6.3 Hz, 6H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=152.1 (CH), 141.3 (Cq), 133.8 (Cq), 128.2 (CH), 127.3 (CH), 57.2 (CH), 57.0 (CH_2), 55.1 (CH_2), 53.6 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 46.0 (CH_3), 32.9 (CH_2), 26.7 (CH_2), 21.4 (CH_2), 20.6 ppm (CH_3); MS (EI): *m/z* (%): 386.3 (1) [M^++H], 385.3 (1) [M^+], 113.0 (100) [$C_6H_{13}N^+$]; HRMS: Calcd for $C_{23}H_{39}N_5$: 385.3205. Found: 385.3211.

***N*-(4-((2,6-dimethylpiperidin-1-ylimino)methyl)benzyl)-3-morpholinopropan-1-amine (8{*2,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 3-morpholinopropylamine **4**{*11*} (0.27 g, 1.9 mmol), **6**{*2*} (0.46 g, 1.9 mmol) and $NaBH_4$ (0.07 g, 1.9 mmol) to give **8**{*2,11*} (0.63 g, 91%) as a yellow oil. IR (film): *n*=3293 (N-H), 2930, 2854, 2808 (C-H), 1625 (C-C), 1584 (C=N), 1554 (C-C), 1456, 1369 (C-H), 1118, 863 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=8.06 (s, 1H; CH=N), 7.65 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.33 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.81 (s, 2H; C$\underline{H}_2$-Ph), 3.70 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 3.08 (m, 2H; C$\underline{H}$-CH_3), 2.69 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.45-2.38 (m, 6H; CH_2-N), 2.06 (br, 1H; NH), 1.81-1.66 (m, 6H; CH_2), 1.51 (m, 2H; CH_2), 1.00 ppm (d, ^3J (H,H)=6.3 Hz, 6H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=152.2 (CH), 141.6 (Cq), 133.8 (Cq), 128.1 (CH), 127.3 (CH), 66.9 (CH_2), 57.4 (CH_2), 57.3 (CH), 53.8 (CH_2), 53.7 (CH_2), 47.9 (CH_2), 32.9 (CH_2), 26.6 (CH_2), 21.4 (CH_2), 20.6 ppm (CH_3); MS (EI): *m/z* (%): 372.2 (2) [M^+], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{22}H_{36}N_4O$: 372.2889. Found: 372.2895.

***N*-(4-((4-methylpiperazin-1-ylimino)methyl)benzyl)-2-(pyrrolidin-1-yl)ethanamine (8{3,4}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)pyrrolidine **4**{*4*} (1.16 g, 1.4 mmol), **6**{*3*} (0.32 g, 1.4 mmol) and $NaBH_4$ (0.053 g, 1.4 mmol) to give **8**{*3,4*} (0.42 g, 92%) as a yellow oil. IR (film): *n*=3309 (N-H), 2935, 2875, 2795 (C-H), 1592 (C=N), 1452 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.0 Hz, 2H; Ph), 7.55 (s, 1H; CH=N), 7.29 (d, ^3J (H,H)=8.0 Hz, 2H; Ph), 3.80 (s, 2H; C$\underline{H}_2$-Ph), 3.21 (t, ^3J (H,H)=5.0 Hz, 4H; CH_2-N), 2.73 (t, ^3J (H,H)=6.0 Hz, 2H; C$\underline{H}_2$-NH), 2.61 (m, 6H; CH_2-N), 2.48 (m, 4H; CH_2-N), 2.36 (s, 3H; CH_3), 1.87 (s, 1H; NH), 1.75 ppm (m, 4H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=140.4 (Cq), 135.8 (CH), 134.8 (Cq), 128.2 (CH), 126.0 (CH), 55.9 (CH_2), 54.5 (CH_2), 54.2 (CH_2), 53.8 (CH_2), 51.1 (CH_2), 47.8 (CH_2), 46.0 (CH_3), 23.5 ppm (CH_2); Anal. ($C_{19}H_{31}N_5$) C, H, N; MS (EI): *m/z* (%): 330.4 (4) [M^++H], 329.3 (12) [M^+], 84.0 (100) [$C_5H_{10}N^+$].

***N*-(4-((2-(pyrrolidin-1-yl)ethylamino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (1{*4,5*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)pyrrolidine **4**{*5*} (0.46 g, 3.5 mmol), **7**{*4*} (0.46 g, 3.5 mmol) and $NaBH_4$ (0.13 g, 3.5 mmol) to give **1**{*4,5*} (1.11 g, 92%) as a yellowish oil. IR (film): *n*=3281 (N-H), 2961, 2930, 2874, 2790 (C-H), 1458, 1445 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 2.73 (m, 4H; C$\underline{H}_2$-NH), 2.61 (t, ^3J (H,H)=6.0 Hz, 2H; CH_2-N), 2.49 (m, 10H; CH_2-N), 2.14 (br, 2H; NH), 1.79-1.71 ppm (m, 10H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.8 (Cq), 128.1 (CH), 128.0 (CH), 55.9 (CH_2), 54.7 (CH_2), 54.2 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 48.0 (CH_2), 29.2 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 345.3 (0.3) [M^++H], 84.1 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{21}H_{37}N_4$ [M^++H]: 345.3018. Found: 345.3022.

***N*-(4-((2-(pyrrolidin-1-yl)ethylamino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (1{*4,6*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)pyrrolidine **4**{*4*} (0.43 g, 3.7 mmol), **7**{*6*} (0.89 g, 3.7 mmol) and $NaBH_4$ (0.14 g, 3.7 mmol) to give **1**{*4,6*} (1.14 g, 91%) as a yellow oil. IR (film): *n* =3279 (N-H), 3104, 2929, 2875, 2799 (C-H), 1508 (imidazol), 1458, 1446 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.44 (s, 1H; CH-N), 7.27 (s, 4H; Ph), 7.03 (s, 1H; CH-N), 6.88 (s, 1H; CH-N), 4.04 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.73 (s, 2H; C$\underline{H}_2$-Ph), 2.74 (t, ^3J (H,H)=5.9 Hz, 2H; C$\underline{H}_2$-NH), 2.61 (m, 4H; C$\underline{H}_2$-NH, CH_2-N), 2.48 (m, 4H; CH_2-N), 2.18 (br, 2H; NH), 1.92 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.76 ppm (quint, ^3J (H,H)=3.3 Hz, 4H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.1 (Cq), 138.6 (Cq), 137.0 (CH), 129.2 (CH), 128.2 (CH), 128.0 (CH), 118.7 (CH), 55.9 (CH_2), 54.2 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 47.9 (CH_2), 45.6 (CH_2), 44.7 (CH_2), 31.4 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 342.2 (4) [M^++H], 257.2 (100) [$C_{15}H_{21}N_4^+$]; HRMS: Calcd for $C_{20}H_{32}N_5$ [M^++H]: 342.2658. Found: 342.2666.

***N*-(4-((2-(pyrrolidin-1-yl)ethylamino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (1{*4,9*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)pyrrolidine **4**{*4*} (0.39 g, 3.3 mmol), **7**{*9*} (0.91 g, 3.3 mmol) and $NaBH_4$ (0.13 g, 3.3 mmol) to give **1**{*4,9*} (0.96 g, 77%) as a yellow oil. IR (film): *n*=3288 (N-H), 2934, 2875, 2793 (C-H), 1458, 1447, 1372, 1354 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.76 (s, 2H; C$\underline{H}_2$-Ph), 2.74 (t, ^3J (H,H)=6.5 Hz, 2H; C$\underline{H}_2$-NH), 2.67 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.61 (t, ^3J (H,H)=6.5 Hz, 2H; CH_2-N), 2.50-2.38 (m, 14H; CH_2-N), 2.27 (s, 3H; CH_3), 2.11 (br, 2H; NH), 1.77-1.66 ppm (m, 6H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.8 (Cq), 128.1 (CH), 128.0 (CH), 57.0 (CH_2), 55.9 (CH_2), 55.1 (CH_2), 54.2 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 47.9 (CH_2), 46.0 (CH_3), 27.0 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 374.3 (0.4) [M^++H], 84.0 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{22}H_{40}N_5$ [M^++H]: 374.3284. Found: 374.3276.

***N*-(4-((2-(pyrrolidin-1-yl)ethylamino)methyl)benzyl)-3-morpholinopropan-1-amine (1{*4,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)pyrrolidine **4**{*4*} (0.37 g, 3.2 mmol), **7**{*11*} (0.84 g, 3.2 mmol) and $NaBH_4$ (0.12 g, 3.2 mmol) to give **1**{*4,11*} (1.05 g, 91%) as a yellow oil. IR (film): *n*=3305 (N-H), 2953, 2932, 2872, 2852, 2802 (C-H), 1457, 1446 (C-H), 1118, 862 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph'), 3.69 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.74 (t, ^3J (H,H)=5.9 Hz, 2H; C$\underline{H}_2$-NH), 2.68 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.61 (t, ^3J (H,H)=5.9 Hz, 2H; CH_2-N), 2.50-2.37 (m, 10H; CH_2-N), 2.04 (br, 2H; NH), 1.80-1.68 ppm (m, 6H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.7 (Cq), 128.1 (CH), 128.0 (CH), 67.0 (CH_2), 57.4

(CH_2), 55.9 (CH_2), 54.2 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 48.0 (CH_2), 47.9 (CH_2), 26.7 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 361.2 (0.5) [M^++H], 84.0 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{21}H_{37}N_4O$ [M^++H]: 361.2967. Found: 361.2965.

***N*-(4-((3-(1*H*-imidazol-1-yl)propylamino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (1{*5,6*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)pyrrolidine **4**{*5*} (0.49 g, 3.7 mmol), **7**{*6*} (0.91 g, 3.7 mmol) and $NaBH_4$ (0.14 g, 3.7 mmol) to give **1**{*5,6*} (1.33 g, 100%) as a yellow oil. IR (film): *n*=3281 (N-H), 3104, 2931, 2875, 2794 (C-H), 1508 (imidazol), 1458 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.43 (s, 1H; CH-N), 7.27 (s, 4H; Ph), 7.03 (s, 1H; CH-N), 6.88 (s, 1H; CH-N), 4.04 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.74 (s, 2H; C$\underline{H}_2$-Ph), 2.70 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.60 (t, ^3J (H,H)=6.6 Hz, 2H; C$\underline{H}_2$-NH), 2.50 (m, 6H; CH_2-N), 2.05 (br, 2H; NH), 1.92 (quint, ^3J (H,H)=6.6 Hz, 2H; CH_2), 1.79-1.10 ppm (m, 6H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.1 (Cq), 138.6 (Cq), 137.0 (CH), 129.2 (CH), 128.1 (CH), 128.0 (CH), 118.7 (CH), 54.7 (CH_2), 54.2 (CH_2), 53.7 (CH_2), 48.0 (CH_2), 45.6 (CH_2), 44.7 (CH_2), 31.4 (CH_2), 29.2 (CH_2), 23.4 ppm (CH_2). MS (EI): *m/z* (%): 357.4 (0.2) [M^++2H], 356.4 (1), 355.5 (0.2) [M^+], 84.2 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{21}H_{33}N_5$: 355.2736. Found: 355.2740.

***N*-(4-((2-(piperidin-1-yl)ethylamino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (1{*5,7*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)pyrrolidine **4**{*5*} (0.46 g, 3.5 mmol), **7**{*7*} (0.85 g, 3.5 mmol) and $NaBH_4$ (0.13 g, 3.5 mmol) to give **1**{*5,7*} (1.13 g, 92%) as a yellowish oil. IR (film): *n*=3298 (N-H), 2933, 2876, 2851, 2792 (C-H), 1454, 1443 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph),3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 2.69 (t, ^3J (H,H)=6.3 Hz, 4H; C$\underline{H}_2$-NH), 2.52 (m, 6H; CH_2-N), 2.44 (t, ^3J (H,H)=6.3 Hz, 2H; CH_2-N), 2.33 (br, 4H; CH_2-N), 2.08 (br, 2H; NH), 1.79-1.70 (m, 6H; CH_2), 1.55 (m, 4H; CH_2), 1.42 ppm (m, 2H; CH_2). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.7 (Cq), 128.0 (CH), 58.5 (CH_2), 54.7 (CH_2), 54.2 (CH_2), 53.7 (CH_2), 53.6 (CH_2), 48.0 (CH_2), 45.9 (CH_2), 29.2 (CH_2), 26.0 (CH_2), 24.5 (CH_2), 23.4 ppm (CH_2); MS (EI): *m/z* (%): 359.3 (1) [M^++H], 98.2 (100) [$C_6H_{12}N^+$]; HRMS: Calcd for $C_{22}H_{39}N_4$ [M^++H]: 359.3175. Found: 359.3175.

***N*-(4-((3-(pyrrolidin-1-yl)propylamino)methyl)benzyl)-3-(2-methylpiperidin-1-yl)propan-1-amine (1{*5,8*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)-2-methyl-piperidine **4**{*8*} (0.63 g, 3.9 mmol), **7**{*5*} (0.96 g, 3.9 mmol) and $NaBH_4$ (0.15 g, 3.9 mmol) to give **1**{*5,8*} (1.24 g, 83%) as a yellowish oil. IR (film): *n*=3281 (N-H), 2930, 2874, 2855, 2790 (C-H), 1448, 1372 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.76 (s, 2H; C$\underline{H}_2$-Ph), 2.86 (m, 1H; CH_{eq}-N), 2.68 (m, 5H; CH_{eq}-N, C$\underline{H}_2$-NH), 2.49 (m, 6H; CH_2-N), 2.36 (m, 1H; CH_{ax}-N), 2.26 (m, 1H; C$\underline{H}$-CH_3), 2.11 (m, 1H; CH_{ax}-N), 2.02 (br, 2H; NH), 1.79-1.58 (m, 12H; CH_2), 1.27 (m, 2H; CH_{ax}), 1.05 ppm (d, ^3J (H,H)=6.3 Hz, 3H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.8 (Cq), 128.1 (CH), 128.0 (CH), 56.0 (CH), 54.8 (CH_2), 54.3 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 52.3 (CH_2), 52.1 (CH_2), 48.3 (CH_2), 48.0 (CH_2), 34.7 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 25.8 (CH_2), 24.0 (CH_2), 23.5 (CH_2), 19.1 ppm (CH_3); MS (EI): *m/z* (%): 387.3 (8) [M^++H]. 386.3 (6) [M^+], 112.1 (100) [$C_7H_{14}N^+$]; HRMS: Calcd for $C_{24}H_{42}N_4$: 386.3409. Found: 386.3412.

***N*-(4-((3-(4-methylpiperazin-1-yl)propylamino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (1{*5,9*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)pyrrolidine **4**{*5*} (0.45 g, 3.4 mmol), **7**{*9*} (0.93 g, 3.4 mmol) and $NaBH_4$ (0.13 g, 3.4 mmol) to give **1**{*5,9*} (1.25 g, 95%) as a yellowish oil. IR (film): *n*=3284 (N-H), 2935, 2875, 2792 (C-H), 1458, 1372, 1353 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.76 (s, 2H; C$\underline{H}_2$-Ph), 2.68 (m, 4H; C$\underline{H}_2$-NH), 2.53-2.38 (m, 16H; CH_2-N), 2.27 (s, 3H; CH_3), 1.91 (br, 2H; NH), 1.79-1.68 ppm (m, 8H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 128.0 (CH), 56.9 (CH_2), 55.1 (CH_2), 54.7 (CH_2), 54.2 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 48.0 (CH_2), 46.0 (CH_3), 29.3 (CH_2), 27.0 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 387.4 (1) [M^+], 259.2 (100) [$C_{16}H_{25}N_3^+$]; HRMS: Calcd for $C_{23}H_{41}N_5$: 387.3362. Found: 387.3347.

***N*-(4-((2-morpholinoethylamino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (1{*5,10*}).** The procedure was the same as that stated for **8**{*2,4*} but using 2-morpholinoethylamine **4**{*10*} (0.51 g, 3.9 mmol), **7**{*5*} (0.96 g, 3.9 mmol) and $NaBH_4$ (0.15 g, 3.9 mmol) to give **1**{*5,10*} (1.27 g, 90%) as a yellowish oil. IR (film): *n*=3304 (N-H), 2935, 2872, 2852, 2800 (C-H), 1454 (C-H), 1118, 868 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.28 (s, 4H; Ph), 3.79 (s, 4H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.5 Hz, 4H; CH_2-O), 2.71 (m, 4H; C$\underline{H}_2$-NH), 2.51 (m, 8H; CH_2-N), 2.40 (t, ^3J (H,H)=4.5 Hz, 4H; CH_2-N), 2.18 (br, 2H; NH), 1.78 ppm (m, 6H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.6 (Cq), 128.1 (CH), 67.0 (CH_2), 58.2 (CH_2), 54.8 (CH_2), 54.2 (CH_2), 53.7 (CH_2), 53.6 (CH_2), 48.0 (CH_2), 45.3 (CH_2), 28.9 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 361.3 (3) [M^++H], 360.3 (4) [M^+], 230.3 (100) [$C_{15}H_{22}N_2^+$]; HRMS: Calcd for $C_{21}H_{36}N_4O$: 360.2889. Found: 360.2879.

***N*-(4-((3-(pyrrolidin-1-yl)propylamino)methyl)benzyl)-3-morpholinopropan-1-amine (1{*5,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 3-morpholinopropylamine **4**{*11*} (0.55 g, 3.8 mmol), **7**{*5*} (0.94 g, 3.8 mmol) and $NaBH_4$ (0.15 g, 3.8 mmol) to give **1**{*5,11*} (1.33 g, 93%) as a yellow oil. IR (film): *n*=3288 (N-H), 2935, 2872, 2853, 2802 (C-H), 1457, 1447 (C-H), 1118, 862 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.8 Hz, 4H; CH_2-O), 2.70 (m, 4H; C$\underline{H}_2$-NH), 2.51 (m, 6H; CH_2-N), 2.41 (m, 6H; CH_2-N), 2.04 (br, 2H; NH), 1.73 ppm (m, 8H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 128.0 (CH), 67.0 (CH_2), 57.4 (CH_2), 54.8 (CH_2), 54.3 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 48.1 (CH_2), 48.0 (CH_2), 29.3 (CH_2), 26.8 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 374.3 (18) [M^++H], 373.2 (19) [M^+], 230.2 (100) [$C_{15}H_{22}N_2^+$]; HRMS: Calcd for $C_{22}H_{38}N_4O$: 388.3202. Found: 388.3202.

***N*-(4-((2-(piperidin-1-yl)ethylamino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (1{*6,7*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)piperidine **4**{*7*} (0.48 g, 3.7 mmol), **7**{*6*} (0.90 g, 3.7 mmol) and $NaBH_4$ (0.14 g, 3.7 mmol) to give **1**{*6,7*} (1.23 g, 94%) as a yellow oil. IR (film): *n*=3279 (N-H), 2935, 2850, 2793 (C-H), 1508 (imidazol), 1446 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.43 (s, 1H; CH-N), 7.28 (m, 4H; Ph), 7.03 (s, 1H; CH-N), 6.89 (s, 1H; CH-N), 4.04 (t, ^3J (H,H)=6.8 Hz, 2H; CH_2-N), 3.81 (s, 2H; C$\underline{H}_2$-Ph), 3.74 (s, 2H; C$\underline{H}_2$-Ph), 2.73 (t, ^3J (H,H)=5.9 Hz, 2H; C$\underline{H}_2$-NH), 2.60 (t, ^3J (H,H)=6.8 Hz, 2H; C$\underline{H}_2$-NH), 2.48 (t, ^3J (H,H)=5.9 Hz, 2H; CH_2-N), 2.46 (br, 2H; NH), 2.37 (m, 4H; CH_2-N), 1.92 (quint, ^3J (H,H)=6.8 Hz, 2H; CH_2), 1.56 (m, 4H; CH_2), 1.43 ppm (m, 2H; CH_2); ^{13}C-NMR (75.5 MHz, DMSO-d_6, 25 ºC): *d*=137.0 (Cq, CH), 128.6 (CH), 128.3 (CH), 128.1 (CH), 119.1 (CH), 55.8 (CH_2), 53.7 (CH_2), 51.8 (CH_2), 51.3 (CH_2), 44.8 (CH_2), 43.9 (CH_2), 43.7 (CH_2), 29.9 (CH_2), 25.0 (CH_2), 23.6 ppm (CH_2); MS (EI): *m/z* (%): 356.1 (0.05) [M^++H], 98.0 (100) [$C_6H_{12}^+$]; HRMS: Calcd for $C_{21}H_{34}N_5$: 356.2814. Found: 356.2809.

***N*-(4-((3-(4-methylpiperazin-1-yl)propylamino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (1{*6,9*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)imidazole **4**{*6*} (0.35 g, 2.8 mmol), **7**{*9*} (0.76 g, 2.8 mmol) and $NaBH_4$ (0.11 g, 2.8 mmol) to give **1**{*6,9*} (0.36 g, 34%) as a yellow oil. IR (film): *n*=3278 (N-H), 3102, 2934, 2875, 2795 (C-H), 1508 (imidazol), 1458, 1372, 1356 cm^{-1} (C-H);

^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.43 (s, 1H; CH-N), 7.27 (s, 4H; Ph), 7.03 (s, 1H; CH-N), 6.88 (s, 1H; CH-N), 4.04 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.74 (s, 2H; C$\underline{H}_2$-Ph), 2.68 (t, ^3J (H,H)=7.2 Hz, 2H; C$\underline{H}_2$-NH), 2.61 (t, ^3J (H,H)=6.6 Hz, 2H; C$\underline{H}_2$-NH), 2.43 (br, 8H; CH_2-N), 2.41 (t, ^3J (H,H)=7.2 Hz, 2H; CH_2-N), 2.27 (s, 3H; CH_3), 1.93 (br, 2H; NH), 1.92 (quint, ^3J (H,H)=6.6 Hz, 2H; CH_2), 1.71 ppm (quint, ^3J (H,H)=7.2 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.7 (Cq), 137.1 (CH), 129.2 (CH), 128.1 (CH), 128.0 (CH), 118.7 (CH), 56.9 (CH_2), 55.1 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 46.0 (CH_3), 45.7 (CH_2), 44.7 (CH_2), 31.4 (CH_2), 26.9 ppm (CH_2); MS (EI): *m/z* (%): 385.3 (2) [M^++H], 70.0 (100) [$C_4H_8N^+$]; HRMS: Calcd for $C_{22}H_{36}N_6$: 384.3001. Found: 384.3004.

***N*-(4-((2-morpholinoethylamino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (1{*6,10*}).** The procedure was the same as that stated for **8**{*2,4*} but using 2-morpholinoethylamine **4**{*10*} (0.43 g, 3.2 mmol), **7**{*6*} (0.79 g, 3.2 mmol) and $NaBH_4$ (0.12 g, 3.2 mmol) to give **1**{*6,10*} (1.11 g, 96%) as a yellowish oil. IR (film): *n*=3299 (N-H), 3105, 2934, 2890, 2851, 2811 (C-H), 1508 (imidazol), 1454 (C-H), 1117, 854 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.43 (s, 1H; CH-N), 7.28 (s, 4H; Ph), 7.03 (s, 1H; CH-N), 6.88 (s, 1H; CH-N), 4.05 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.74 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.71 (t, ^3J (H,H)=6.0 Hz, 2H; C$\underline{H}_2$-NH), 2.60 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.50 (t, ^3J (H,H)=6.0 Hz, 2H; CH_2-N), 2.41 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-N), 1.95 (br, 2H; NH), 1.93 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.7 (Cq), 137.0 (CH), 129.2 (CH), 128.1 (CH), 128.0 (CH), 118.7 (CH), 67.0 (CH_2), 58.2 (CH_2), 53.7 (CH_2), 45.6 (CH_2), 45.3 (CH_2), 44.6 (CH_2), 31.2 ppm (CH_2). MS (EI): *m/z* (%): 358.2 (1) [M^++H], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{20}H_{31}N_5O$: 357.2529. Found: 357.2517.

***N*-(4-((3-morpholinopropylamino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (1{*6,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)imidazole **4**{*6*} (0.56 g, 4.4 mmol), **7**{*11*} (0.56 g, 4.4 mmol) and $NaBH_4$ (0.17 g, 4.4 mmol) to give **1**{*6,11*} (1.36 g, 85%) as a yellow oil. IR (film): *n*=3282 (N-H), 3104, 2935, 2852, 2808 (C-H), 1509 (imidazol), 1456 (C-H), 1117, 861 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.42 (s, 1H; CH-N), 7.27 (m, 4H; Ph), 7.03 (s, 1H; CH-N), 6.88 (s, 1H; CH-N), 4.04 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.74 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.71 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.60 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.42 (m, 6H; CH_2-N), 1.92 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.88 (s, 2H; NH), 1.72 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.2 (Cq), 137.0 (CH), 129.1 (CH), 128.2 (CH), 118.7 (CH), 66.9 (CH_2), 57.4 (CH_2), 53.7 (CH_2), 53.6 (CH_2), 53.4 (CH_2), 48.0 (CH_2), 45.5 (CH_2), 44.6 (CH_2), 31.3 (CH_2), 26.1 ppm (CH_2); MS (EI): *m/z* (%): 373.0 (2) [M^++2H], 372.0 (8) [M+H$^+$], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{21}H_{34}N_5O$ [M^++H]: 372.2763. Found: 372.2758.

***N*-(4-((2-(piperidin-1-yl)ethylamino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (1{*7,9*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)piperidine **4**{*7*} (0.34 g, 2.6 mmol), **7**{*9*} (0.73 g, 2.6 mmol) and $NaBH_4$ (0.10 g, 2.6 mmol) to give **1**{*7,9*} (0.48 g, 47%) as a yellowish oil. IR (film): *n*=3285 (N-H), 2934, 2878, 2849, 2794 (C-H), 1457, 1446, 1372, 1349 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 2.69 (m, 4H; C$\underline{H}_2$-NH), 2.47-2.34 (m, 16H; CH_2-N), 2.27 (s, 3H; CH_3), 2.22 (br, 2H; NH), 1.72 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.55 (m, 4H; CH_2), 1.42 ppm (m, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.5 (Cq), 128.1 (CH), 128.0 (CH), 58.5 (CH_2), 57.0 (CH_2), 55.1 (CH_2), 54.7 (CH_2), 53.7 (CH_2), 53.6 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 46.0 (CH_3), 45.9 (CH_2), 26.8 (CH_2), 26.0 (CH_2), 24.5 ppm (CH_2); MS (FAB): *m/z* (%) 389.2 (5) [M^++2H], 388.2 (100) [M^++H], 387.2 (17) [M^+]; HRMS: Calcd for $C_{21}H_{34}N_5O$ [M^++H]: 88.3440. Found: 388.3454.

***N*-(4-((2-(piperidin-1-yl)ethylamino)methyl)benzyl)-3-morpholinopropan-1-amine (1{*7,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(2-aminoethyl)piperidine **4**{*7*} (0.44 g, 3.4 mmol), **7**{*11*} (0.89 g, 3.4 mmol) and $NaBH_4$ (0.13 g, 3.4 mmol) to give **1**{*7,11*} (1.24 g, 98%) as a yellow oil. IR (film): *n*=3304 (N-H), 2933, 2852, 2806 (C-H), 1454, 1444 (C-H), 1119, 862 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.69 (m, 4H; C$\underline{H}_2$-NH), 2.47-2-34 (m, 12H; CH_2-N), 2.11 (br, 2H; NH), 1.71 (quint, ^3J (H,H)=7.2 Hz, 2H; CH_2), 1.55 (m, 4H; CH_2), 1.42 ppm (m, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.6 (Cq), 128.1 (CH), 128.0 (CH), 66.9 (CH_2), 58.5 (CH_2), 57.4 (CH_2), 54.7 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 48.0 (CH_2), 45.9 (CH_2), 26.6 (CH_2), 26.0 (CH_2), 24.5 ppm (CH_2); Anal. ($C_{22}H_{38}N_4O$) C, H, N; MS (EI): *m/z* (%): 373.3 (1) [M^+- H], 98.0 (100) [$C_6H_{12}N^+$].

***N*-(4-((2-morpholinoethylamino)methyl)benzyl)-3-(2-methylpiperidin-1-yl)propan-1-amine (1{*8,10*}).** The procedure was the same as that stated for **8**{*2,4*} but using 2-morpholinoethylamine **4**{*10*} (1.12 g, 8.5 mmol), **7**{*8*} (1.35 g, 8.5 mmol) and $NaBH_4$ (0.33 g, 8.5 mmol) to give **1**{*8,10*} (2.46 g, 74%) as a yellow oil. IR (film): *n*=3305 (N-H), 2930, 2853, 2807 (C-H), 1453 (C-H), 1119, 868 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.5 Hz, 4H; CH_2-O), 2.86 (m, 1H; CH_{eq}-N), 2.74 (m, 1H; CH_{eq}-N), 2.70 (t, ^3J (H,H)=6.0 Hz, 2H; C$\underline{H}_2$-NH), 2.63 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.49 (t, ^3J (H,H)=6.0 Hz, 2H; CH_2-N), 2.40 (m, 4H; CH_2-N), 2.34 (m, 1H; CH_{ax}-N), 2.25 (m, 1H; C$\underline{H}$-CH_3), 2.11 (m, 1H; CH_{ax}-N), 1.91 (br, 2H; NH), 1.68 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.63 (m, 4H; CH_2), 1.27 (m, 2H; CH_{ax}) 1.05 ppm (d, ^3J (H,H)=6.0 Hz, 3H; CH_3); ^{3}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.0 (Cq), 138.9 (Cq), 128.0 (CH), 67.0 (CH_2), 58.3 (CH_2), 55.9 (CH), 53.8 (CH_2), 53.7 (CH_2), 52.3 (CH_2), 52.1 (CH_2), 48.4 (CH_2), 45.3 (CH_2), 34.7 (CH_2), 26.2 (CH_2), 25.8 (CH_2), 24.0 (CH_2), 19.2 ppm (CH_3); MS (EI): *m/z* (%): 389.3 (1) [M^++H], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{23}H_{40}N_4O$: 374.3046. Found: 374.3049.

***N*-(4-((3-morpholinopropylamino)methyl)benzyl)-3-(2-methylpiperidin-1-yl)propan-1-amine (1{*8,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)-2-methyl-piperidine **4**{*8*} (0.62 g, 3.8 mmol), **7**{*11*} (1.00 g, 3.8 mmol) and $NaBH_4$ (0.15 g, 3.8 mmol) to give **1**{*8,11*} (1.54 g, 100%) as a yellow oil. IR (film): *n*=3286 (N-H), 2929, 2853, 2806 (C-H), 1448, 1372 (C-H), 1119, 862 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.77 (s, 4H; C$\underline{H}_2$-Ph), 3.70 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.87 (m, 1H; CH_{eq}-N), 2.79-2.62 (m, 5H; C$\underline{H}_2$-NH, CH_{eq}-N), 2.43-2.32 (m, 7H; CH_{ax}-N, CH_2-N), 2.27 (m, 1H; C$\underline{H}$-CH_3), 2.12 (br, 2H; NH), 2.11 (m, 1H; CH_{ax}-N), 1.75-1.52 (m, 8H; CH_2), 1.30 (m, 2H; CH_{ax}), 1.05 ppm (d, ^3J (H,H)=6.0 Hz, 3H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.7 (Cq), 128.1 (CH), 128.0 (CH), 67.0 (CH_2), 57.4 (CH_2), 56.0 (CH), 53.8 (CH_2), 53.7 (CH_2), 52.3 (CH_2), 52.0 (CH_2), 48.3 (CH_2), 48.0 (CH_2), 34.6 (CH_2), 27.0 (CH_2), 26.1 (CH_2), 25.7 (CH_2), 23.9 (CH_2), 19.1 ppm (CH_3); MS (EI): *m/z* (%): 403.4 (0.5) [M^++H], 112.0 (100) [$C_7H_{14}N^+$]; HRMS: Calcd for $C_{24}H_{42}N_4O$: 402.3359. Found: 402.3354.

***N*-(4-((2-morpholinoethylamino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (1{*9,10*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)-4-methylpiperazine **4**{*9*} (0.44 g, 2.7 mmol), **7**{*10*} (0.68 g, 2.7 mmol) and $NaBH_4$ (0.10 g, 2.7 mmol) to give **1**{*9,10*} (0.92 g, 86%) as a yellow oil. IR (film): *n*=3300 (N-H), 2935, 2872, 2796 (C-H), 1456, 1372, 1355 (C-H), 1118, 868 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.68 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 2.69 (m, 4H; C$\underline{H}_2$-NH), 2.52-2.39 (m, 16H; CH_2-N), 2.27 (s, 3H; CH_3), 2.11 (br, 2H; NH), 1.72 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR

(75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.7 (Cq), 128.0 (CH), 67.0 (CH_2), 58.2 (CH_2), 57.0 (CH_2), 55.1 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 46.0 (CH_3), 45.3 (CH_2), 26.9 ppm (CH_2); MS (EI): *m/z* (%): 389.4 (1) [M^+], 100.1 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{22}H_{39}N_5O$: 389.3155. Found: 389.3153.

***N*-(4-((3-morpholinopropylamino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (1{*9,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 1-(3-aminopropyl)-4-methylpiperazine **4**{*9*} (0.43 g, 2.7 mmol), **7**{*11*} (0.71 g, 2.7 mmol) and $NaBH_4$ (0.10 g, 2.7 mmol) to give **1**{*9,11*} (0.91 g, 84%) as a yellow oil. IR (film): *n*=3288 (N-H), 2935, 2872, 2851, 2795 (C-H), 1476, 1372, 1356 (C-H), 1118, 862 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.77 (s, 4H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.8 Hz, 4H; CH_2-O), 2.68 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.67 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.45-2.37 (m, 16H; CH_2-N), 2.27 (s, 3H; CH_3), 2.03 (br, 2H; NH), 1.71 ppm (quint, ^3J (H,H)=6.9 Hz, 4H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.8 (Cq), 128.0 (CH), 127.9 (CH), 66.9 (CH_2), 57.3 (CH_2), 56.9 (CH_2), 55.1 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 48.1 (CH_2), 47.9 (CH_2), 46.0 (CH_3), 26.9 (CH_2), 26.7 ppm (CH_2); MS (EI): *m/z* (%): 403.4 (4) [M^+], 100.1 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{23}H_{41}N_5O$: 403.3311. Found: 403.3311.

***N*-(4-((2-morpholinoethylamino)methyl)benzyl)-3-morpholinopropan-1-amine (1{*10,11*}).** The procedure was the same as that stated for **8**{*2,4*} but using 2-morpholinoethylamine **4**{*10*} (0.44 g, 3.3 mmol), **7**{*11*} (0.88 g, 3.3 mmol) and $NaBH_4$ (0.13 g, 3.3 mmol) to give **1**{*10,11*} (1.16 g, 92%) as an orange oil. IR (film): *n*=3307 (N-H), 2950, 2891, 2852, 2808 (C-H), 1455 (C-H), 1118, 863 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.27 (s, 4H; Ph), 3.79 (s, 2H; C$\underline{H}_2$-Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (m, 8H; CH_2-O), 2.69 (m, 4H; C$\underline{H}_2$-NH), 2.50 (t, ^3J (H,H)=6.0 Hz, 2H; CH_2-N), 2.45-2.38 (m, 10H; CH_2-N), 1.96 (br, 2H; NH), 1.71 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=138.9 (Cq), 138.8 (Cq), 128.1 (CH), 128.0 (CH), 67.0 (CH_2), 58.2 (CH_2), 57.4 (CH_2), 53.8 (CH_2), 53.7 (CH_2), 48.0 (CH_2), 45.3 (CH_2), 26.7 ppm (CH_2). MS (EI): *m/z* (%): 376.2 (0.7) [M^+], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{21}H_{36}N_4O_2$: 376.2838. Found: 376.2849.

***N*-(4-((piperidin-1-ylimino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (8{*1,5*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-aminopiperidine **4**{*1*} (0.44 g, 4.2 mmol) and **7**{*5*} (1.04 g, 4.2 mmol) to give **8**{*1,5*} (1.17 g, 84%) as a yellow oil. IR (film): *n*=3287 (N-H), 2935, 2874, 2854, 2793 (C-H), 1591 (C=N), 1450 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.54 (s, 1H; CH=N), 7.27 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.15 (t, ^3J (H,H)=5.7 Hz, 4H; CH_2-N), 2.28 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.50 (m, 6H; CH_2-N), 2.03 (br, 1H; NH), 1.79-1.69 (m, 10H; CH_2), 1.55 ppm (m, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.7 (Cq), 135.3 (Cq), 134.5 (CH), 128.1 (CH), 125.9 (CH), 54.8 (CH_2), 54.2 (CH_2), 53.7 (CH_2), 52.1 (CH_2), 48.0 (CH_2), 29.1 (CH_2), 25.2 (CH_2), 24.2 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 328.3 (0.5) [M^+], 84.1 (100) [$C_5H_{10}N^+$]; HRMS: Calcd $C_{20}H_{32}N_4$: 328.2627. Found: 328.2624.

***N*-(4-((piperidin-1-ylimino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (8{*1,6*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-aminopiperidine **4**{*1*} (0.42 g, 4.0 mmol) and **7**{*6*} (0.98 g, 4.0 mmol) to give **8**{*1,6*} (1.31 g, 100%) as a reddish oil. IR (film): *n*=3282 (N-H), 3105, 2935, 2853, 2809 (C-H), 1590 (C=N), 1508 (imidazol), 1450 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.56 (s, 1H; CH=N), 7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.45 (s, 1H; CH-N), 7.26 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.03 (s, 1H; CH-N), 6.88 (s, 1H; CH-N), 4.03 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.74 (s, 2H; C$\underline{H}_2$-Ph), 3.15 (t, ^3J (H,H)=5.7 Hz, 4H; CH_2-N), 2.60 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.07 (br, 1H; NH), 1.92 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.75 (quint, ^3J (H,H)=5.7 Hz, 4H; CH_2), 1.54 ppm (quint, ^3J (H,H)=5.7 Hz, 2H; CH_2); ^{13}C-NMR (75.5MHz, $CDCl_3$, 25 ºC): *d*=139.5 (Cq), 137.0 (CH), 135.5 (Cq), 134.2 (CH), 129.2 (CH), 128.1 (CH), 125.9 (CH), 118.7 (CH), 53.7 (CH_2), 52.1 (CH_2), 45.6 (CH_2), 44.7 (CH_2), 31.3 (CH_2), 25.2 (CH_2), 24.2 ppm (CH_2); MS (EI): *m/z* (%): 327.2 (4) [M^++2H], 326.2 (18) [M^++H], 243.2 (100) [$C_{15}H_{21}N_3^+$]; HRMS: Calcd for $C_{19}H_{27}N_5$: 325.2266. Found: 325.2277.

***N*-(4-((piperidin-1-ylimino)methyl)benzyl)-3-(2-methylpiperidin-1-yl)propan-1-amine (8{*1,8*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-aminopiperidine **4**{*1*} (0.19 g, 1.9 mmol) and **7**{*8*} (0.51 g, 1.9 mmol) to give **8**{*1,8*} (0.67 g, 100%) as a reddish oil. IR (film): *n*=3282 (N-H), 2932, 2854, 2804 (C-H), 1591 (C=N), 1450, 1364 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.54 (s, 1H; CH=N), 7.28 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.15 (t, ^3J (H,H)=5.4 Hz, 4H; CH_2-N), 2.87 (m, 1H; CH_{eq}-N), 2.74 (m, 1H; CH_{eq}-N), 2.65 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.42 (br, 1H; NH), 2.37 (m, 1H; CH_{ax}-N), 2.28 (m, 1H; C$\underline{H}$-CH_3), 2.13 (m, 1H; CH_{ax}-N), 1.79-1.52 (m, 12H; CH_2), 1.29 (m, 2H; CH_{ax}), 1.05 ppm (d, ^3J (H,H)=6.3 Hz, 3H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.5 (Cq), 135.4 (Cq), 134.4 (CH), 128.2 (CH), 125.9 (CH), 56.0 (CH), 53.7 (CH_2), 52.3 (CH_2), 52.1 (CH_2), 52.0 (CH_2), 48.3 (CH_2), 34.6 (CH_2), 26.1 (CH_2), 25.5 (CH_2), 25.3 (CH_2), 24.2 (CH_2), 23.9 (CH_2), 19.0 ppm (CH_3); MS (EI): *m/z* (%): 356.2 (2) [M^+], 112.0 (100) [$C_7H_{14}N^+$]; HRMS: Calcd for $C_{22}H_{36}N_4$: 356.2940. Found: 356.2942.

***N*-(4-((piperidin-1-ylimino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (8{*1,9*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-aminopiperidine **4**{*1*} (0.36 g, 3.5 mmol) and **7**{*9*} (0.96 g, 3.5 mmol) to give **8**{*1,9*} (1.21 g, 97%) as a yellow oil. IR (film): *n*=3286 (N-H), 2935, 2875, 2853, 2794 (C-H), 1591 (C=N), 1451, 1357 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.54 (s, 1H; CH=N), 7.27 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.15 (t, ^3J (H,H)=5.7 Hz, 4H; CH_2-N), 2.67 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.42 (br, 8H; CH_2-N), 2.40 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 2.27 (s, 3H; CH_3), 2.16 (br, 1H; NH), 1.79-1.66 (m, 6H; CH_2), 1.54 ppm (m, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.7 (Cq), 135.4 (Cq), 134.5 (CH), 128.1 (CH), 125.9 (CH), 57.0 (CH_2), 55.1 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 52.1 (CH_2), 48.1 (CH_2), 46.0 (CH_3), 26.9 (CH_2), 25.3 (CH_2), 24.2 ppm (CH_2); MS (EI): *m/z* (%): 358.3 (2) [M^++H], 201.1 (100) [$C_{13}H_{17}N_2^+$]; HRMS: Calcd for $C_{21}H_{35}N_5$: 357.2892. Found: 357.2903.

***N*-(4-((piperidin-1-ylimino)methyl)benzyl)-3-morpholinopropan-1-amine (8{*1,11*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-aminopiperidine **4**{*1*} (0.37 g, 3.6 mmol) and **7**{*11*} (0.93 g, 3.6 mmol) to give **8**{*1,11*} (1.21 g, 99%) as a yellow oil. IR (film): *n*=3298 (N-H), 2936, 2853, 2807 (C-H), 1591 (C=N), 1451 (C-H), 1118, 861 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.54 (s, 1H; CH=N), 7.27 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 3.15 (t, ^3J (H,H)=5.6 Hz, 4H; CH_2-N), 2.67 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.44-2.37 (m, 6H; CH_2-N), 1.99 (br, 1H; NH), 1.79-1.65 (m, 6H; CH_2), 1.54 ppm (quint, ^3J (H,H)=5.7 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=139.8 (Cq), 135.4 (Cq), 134.4 (CH), 128.1 (CH), 125.9 (CH), 67.0 (CH_2), 57.4 (CH_2), 53.8 (CH_2), 52.1 (CH_2), 47.9 (CH_2), 26.6 (CH_2), 25.3 (CH_2), 24.2 ppm (CH_2); MS (EI): *m/z* (%): 345.2 (2) [M^++H], 344.2 (3) [M^+], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{20}H_{32}N_4O$: 344.2576. Found: 344.2580.

***N*-(4-((2,6-dimethylpiperidin-1-ylimino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (8{*2,5*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-amino-2,6-dimethylpiperidine **4**{*2*} (0.58 g, 4.1 mmol) and **7**{*5*} (1.00 g, 4.1 mmol) to give **8**{*2,5*} (1.18 g, 81%) as a yellow oil. IR (film): *n*=3283 (N-H), 2961, 2931, 2872, 2794 (C-H), 1625 (C-C), 1584 (C=N), 1554 (C-C), 1449, 1369 cm^{-1} (C-H); ^{1}H-NMR (300

MHz, $CDCl_3$, 25 ºC, TMS): *d*=8.06 (s, 1H; CH=N), 7.64 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.33 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.81 (s, 2H; C$\underline{H}_2$-Ph), 3.07 (br, 2H; C$\underline{H}$-CH_3), 2.69 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.51 (m, 6H; CH_2-N), 2.08 (br, 1H; NH), 1.79-1.69 (m, 10H; CH_2), 1.53 (m, 2H; CH_2), 1.00 ppm (d, ^3J (H,H)=6.3 Hz, 6H; CH_3); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=152.4 (CH), 141.7 (Cq), 133.7 (Cq), 128.1 (CH), 127.3 (CH), 57.3 (CH), 54.8 (CH_2), 54.2 (CH_2), 53.7 (CH_2), 48.0 (CH_2), 32.9 (CH_2), 29.1 (CH_2), 23.5 (CH_2), 21.5 (CH_2), 20.6 ppm (CH_3); MS (EI): *m/z* (%): 356.3 (1) [M^+], 84.1 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{22}H_{36}N_4$: 356.2940. Found: 356.2934.

***N*-(4-((4-methylpiperazin-1-ylimino)methyl)benzyl)-3-(pyrrolidin-1-yl)propan-1-amine (8{*3,5*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-amino-4-methylpiperazine **4**{*3*} (0.50 g, 4.2 mmol) and **7**{*5*} (1.03 g, 4.2 mmol) to give **8**{*3,5*} (1.43 g, 100%) as a brown oil. IR (film): *n*=3288 (N-H), 2937, 2876, 2794 (C-H), 1592 (C=N), 1452, 1365, 1355 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.54 (s, 1H; CH=N), 7.28 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.78 (s, 2H; C$\underline{H}_2$-Ph), 3.21 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.70 (t, ^3J (H,H)=6.6 Hz, 2H; C$\underline{H}_2$-NH), 2.62 (t, ^3J (H,H)=5.1Hz, 4H; CH_2-N), 2.49 (m, 6H; CH_2-N), 2.35 (s, 3H; CH_3), 2.02 (br, 1H; NH), 1.76 ppm (m, 6H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=140.3 (Cq), 135.8 (CH), 134.8 (Cq), 128.1 (CH), 126.0 (CH), 54.8 (CH_2), 54.5 (CH_2), 54.3 (CH_2), 53.7 (CH_2), 51.0 (CH_2), 48.0 (CH_2), 46.0 (CH_3), 29.2 (CH_2), 23.5 ppm (CH_2); MS (EI): *m/z* (%): 343.2 (1) [M^+], 84.2 (100) [$C_5H_{10}N^+$]; HRMS: Calcd for $C_{20}H_{33}N_5$: 343.2736. Found: 343.2736.

***N*-(4-((4-methylpiperazin-1-ylimino)methyl)benzyl)-3-(1*H*-imidazol-1-yl)propan-1-amine (8{*3,6*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-amino-4-methylpiperazine **4**{*3*} (0.45 g, 3.8 mmol) and **7**{*6*} (0.92 g, 3.8 mmol) to give **8**{*3,6*} (1.23 g, 96%) as a yellow oil. IR (film): *n*=3282 (N-H), 3104, 2937, 2880, 2828, 2797 (C-H), 1592 (C=N), 1508 (imidazol), 1452, 1365, 1356 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.56 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.55 (s, 1H; CH=N), 7.45 (s, 1H; CH-N), 7.27 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.04 (s, 1H; CH-N), 6.89 (s, 1H; CH-N), 4.04 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 3.75 (s, 2H; C$\underline{H}_2$-Ph), 3.22 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.64-2.58 (m, 6H; C$\underline{H}_2$-NH, CH_2-N), 2.36 (s, 3H; CH_3), 1.92 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.70 ppm (br, 1H; NH); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=140.0 (Cq), 137.0 (CH), 135.6 (CH), 135.1 (Cq), 129.2 (CH), 128.1 (CH), 126.1 (CH), 118.7 (CH), 54.5 (CH_2), 53.7 (CH_2), 51.0 (CH_2), 45.9 (CH_3), 45.6 (CH_2), 44.7 (CH_2), 31.4 ppm (CH_2); MS (EI): *m/z* (%): 341.3 (2) [M^++H], 98.2 (100) [$C_5H_{11}N_2^+$]; HRMS: Calcd for $C_{19}H_{28}N_6$: 340.2375. Found: 340.2374.

***N*-(4-((4-methylpiperazin-1-ylimino)methyl)benzyl)-3-(2-methylpiperidin-1-yl)propan-1-amine (8{*3,8*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-amino-4-methylpiperazine **4**{*3*} (0.40 g, 3.4 mmol) and **7**{*8*} (0.93 g, 3.4 mmol) to give **8**{*3,8*} (1.05 g, 84%) as a red oil. IR (film): *n*=3279 (N-H), 2932, 2881, 2841, 2795 (C-H), 1593 (C=N), 1452, 1366 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.56 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.55 (s, 1H; CH=N), 7.29 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.21 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.87 (m, 1H; CH_{eq}-N), 2.73 (m, 1H; CH_{eq}-N), 2.65-2.60 (m, 6H; C$\underline{H}_2$-NH, CH_2-N), 2.36 (s, 3H; CH_3-N), 2.36 (m, 1H; CH_{ax}-N), 2.29 (m, 1H; C$\underline{H}$-CH_3), 2.11 (m, 1H; CH_{ax}-N), 1.95 (br, 1H; NH), 1.67 (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2), 1.61-1.48 (m, 4H; CH_2), 1.27 (m, 2H; CH_{ax}), 1.04 ppm (d, ^3J (H,H)=6.0 Hz, 3H; CH-C$\underline{H}_3$); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=140.3 (Cq), 135.8 (CH), 134.8 (Cq), 128.2 (CH), 126.1 (CH), 56.0 (CH), 54.5 (CH_2), 53.8 (CH_2), 52.3 (CH_2), 52.1 (CH_2), 51.1 (CH_2), 48.3 (CH_2), 46.0 (CH_3), 34.7 (CH_2), 26.2 (CH_2), 25.8 (CH_2), 24.0 (CH_2), 19.1 ppm (CH_3); MS (EI): *m/z* (%): 372.4 (1) [M^++H], 371.4 (2) [M^+], 112.2 (100) [$C_7H_{14}N^+$]; HRMS: Calcd for $C_{22}H_{37}N_5$: 371.3049. Found: 371.3053.

***N*-(4-((4-methylpiperazin-1-ylimino)methyl)benzyl)-3-(4-methylpiperazin-1-yl)propan-1-amine (8{*3,9*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-amino-4-methylpiperazine **4**{*3*} (0.40 g, 3.4 mmol) and **7**{*9*} (0.93 g, 3.4 mmol) to give **8**{*3,9*} (1.25 g, 99%) as a yellowish oil. IR (film): *n*=3283 (N-H), 2936, 2877, 2836, 2794, 2768 (C-H), 1593 (C=N), 1453, 1365, 1356 cm^{-1} (C-H); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.55 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.55 (s, 1H; CH=N), 7.28 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.21 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.66 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.62 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.42 (br, 8H; CH_2-N), 2.40 (t, ^3J (H,H)=6.9 Hz, 2H; CH_2-N), 2.36 (s, 3H; CH_3), 2.27 (s, 3H; CH_3), 1.82 (br, 1H; NH), 1.70 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=140.2 (Cq), 135.8 (CH), 134.8 (Cq), 128.1 (CH), 126.0 (CH), 57.0 (CH_2), 55.1 (CH_2), 54.5 (CH_2), 53.7 (CH_2), 53.2 (CH_2), 51.0 (CH_2), 48.0 (CH_2), 46.0 (CH_3), 45.9 (CH_3), 26.9 ppm (CH_2); MS (EI): *m/z* (%) 373.4 (0.6) [M^++H], 372.3 (0.7) [M^+], 56.0 (100) [$C_4H_8^+$]; HRMS: Calcd for $C_{21}H_{36}N_6$: 372.3001. Found: 372.2990.

***N*-(4-((4-methylpiperazin-1-ylimino)methyl)benzyl)-3-morpholinopropan-1-amine (8{*3,11*}).** The procedure was the same as that stated for **2**{*1,3*} but using 1-amino-4-methylpiperazine **4**{*3*} (0.40 g, 3.4 mmol) and **7**{*11*} (0.89 g, 3.4 mmol) to give **8**{*3,11*} (1.22 g, 100%) as a yellow oil. IR (film): *n*=3293 (N-H), 2939, 2888, 2844, 2799 (C-H), 1592 (C=N), 1453, 1364, 1356 (C-H), 1118, 806 cm^{-1} (C-O-C); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): *d*=7.56 (s, 1H; CH=N), 7.56 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 7.28 (d, ^3J (H,H)=8.1 Hz, 2H; Ph), 3.77 (s, 2H; C$\underline{H}_2$-Ph), 3.69 (t, ^3J (H,H)=4.7 Hz, 4H; CH_2-O), 3.21 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.67 (t, ^3J (H,H)=6.9 Hz, 2H; C$\underline{H}_2$-NH), 2.62 (t, ^3J (H,H)=5.1 Hz, 4H; CH_2-N), 2.44-2.37 (m, 6H; CH_2-N), 2.35 (s, 3H; CH_3), 2.05 (br, 1H; NH), 1.70 ppm (quint, ^3J (H,H)=6.9 Hz, 2H; CH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25 ºC): *d*=140.2 (Cq), 135.7 (CH), 134.9 (Cq), 128.1 (CH), 126.1 (CH), 66.9 (CH_2), 57.4 (CH_2), 54.5 (CH_2), 53.8 (CH_2), 51.0 (CH_2), 47.9 (CH_2), 45.9 (CH_3), 26.6 ppm (CH_2); MS (EI): *m/z* (%): 359.2 (2) [M^+], 100.0 (100) [$C_5H_{10}NO^+$]; HRMS: Calcd for $C_{20}H_{33}N_5O$: 359.2685. Found: 359.2685.