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Synthesis of 1-(4-Butoxyphenyl)-1-cyclohexyl-3-(4-arylpiperazin-1-yl)-2-phenylpropan-1-ols and Their Dihydrochlorides

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Abstract—Aminomethylation of 1-(4-butoxyphenyl)-2-phenylethanone with paraformaldehyde and substituted piperazines in ethanol medium results in 1-(4-butoxyphenyl)-3-(4-R-piperazin-1-yl)-2-phenylpropan-1-ones. The latter react with cyclohexylmagnesium halide to give 1-(4-butoxyphenyl)-1-cyclohexyl-3-(4-arylpiperazin-1-yl)-2-phenylpropan-1-ols. Reduction of the prepared β-aminoketones with lithium aluminum hydride in absolute diethyl ether leads to the secondary aminopropanols. The prepared compounds could be converted into the corresponding dihydrochlorides.

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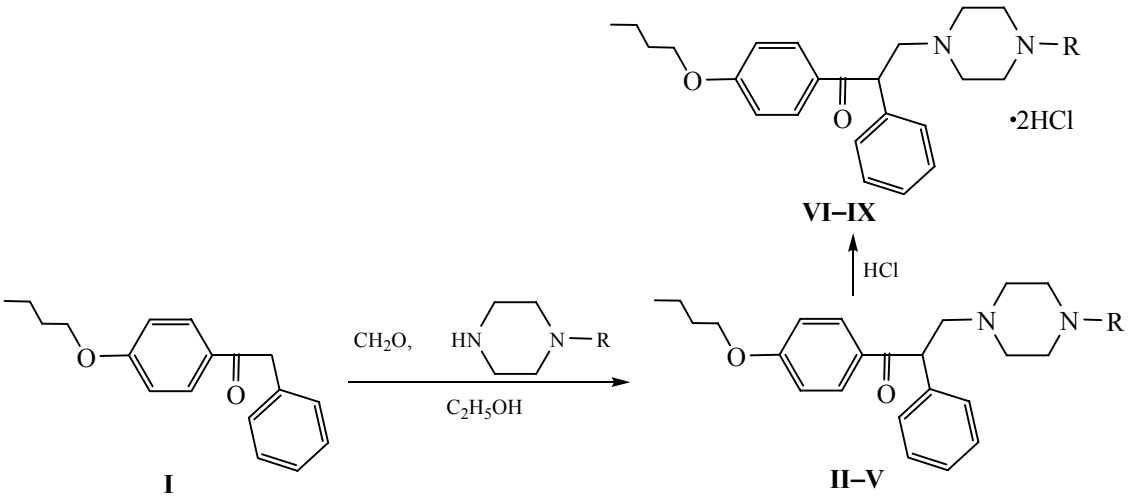
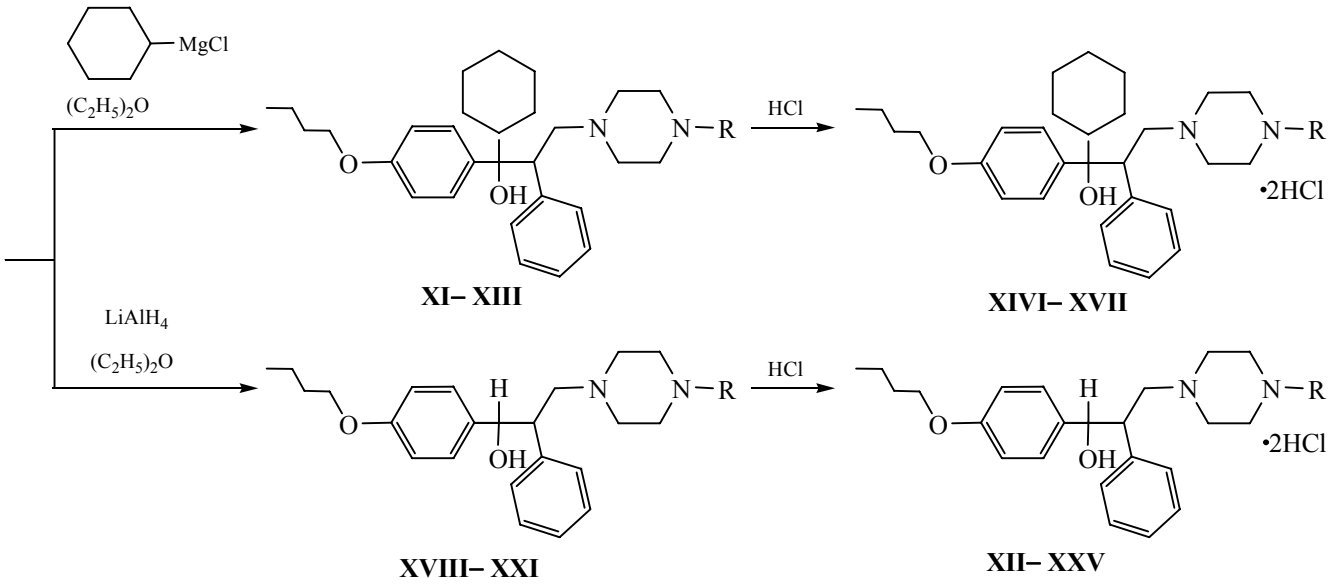
Extending the structure–activity relationship studies of Cyclodolum (1-cyclohexyl-1-phenyl-3-piperidinopropan-1-ol) [1–3] analogs, we performed aminomethylation of 1-(4-butoxyphenyl)-2-phenylethanone **I** with paraformaldehyde and substituted piperazines in ethanol medium to obtain 1-(4-butoxyphenyl)-3-(4-R-piperazine-1-yl)-2-phenylpropan-1-ones **II**–**V**, which were converted into dihydrochlorides **VI**–**IX**.

Reactions of β-aminoketones **II**–**V** with cyclohexylmagnesium halide resulted in a series of new tertiary aminopropanols **X**–**XIII**. Their treatment with hydrochloric acid gave the corresponding dihydrochlorides **XIV**–**XVII**.

Reduction of β-aminoketones **II**–**V** with lithium aluminum hydride in absolute diethyl ether results in





R = 2,3-dimethylphenyl (**II**, **VI**, **X**, **XIV**, **XVIII**, **XXII**); 2,5-dimethylphenyl (**III**, **VII**, **XI**, **XV**, **XIX**, **XXIII**); 2-methyl-5-chlorophenyl (**IV**, **VIII**, **XII**, **XVI**, **XX**, **XXIV**); benzo[1,3]dioxol-5-ylmethyl (**V**, **IX**, **XIII**, **XVII**, **XXI**, **XXV**).

the secondary aminopropanols **XVIII**–**XXI** converted into the dihydrochlorides **XXII**–**XXV**.

Structure of the prepared compounds obtained was confirmed by IR and ^{1}H NMR spectroscopy methods.

EXPERIMENTAL

IR spectra were recorded with Nicolet Avatar 330 FT-IR spectrophotometer. ^{1}H NMR spectra were Registered with Mercury VX-300 spectrometer (300.08 MHz) in DMSO-d_6, relative to internal standard TMS. Melting points were determined with Boetius instrument. Purity of the prepared products was confirmed by TLC using Silufol UV-254 plates, eluting with butanol–ethanol–acetic acid–water mixture (8 : 2 : 1 : 3) and detecting with iodine vapors.

1-(4-Butoxyphenyl)-2-phenylethanone **I** was prepared according to [4].

1-(4-Butoxyphenyl)-3-(4-R-piperazin-1-yl)-2-phenylpropan-1-ones II–V *(general procedure)*. A mixture of 0.08 mol of 1-(4-butoxyphenyl)-2-phenylethanone, 2.7 g (0.09 mol) of paraformaldehyde and 0.08 mol of a substituted piperazine in 50 mL of ethanol was heated (70–80°C) on a water bath during 6–7 h. Then ethanol was distilled off, water and dilute hydrochloric acid were then added to the residue, to pH 1–2. The unreacted ketone was extracted with diethyl ether or benzene. The aqueous layer was alkalized with 40% sodium hydroxide solution to pH 8–9 and extracted with diethyl ether or benzene (3×100 mL). The extracts were dried over anhydrous sodium sulfate, and the solvent was evaporated. The residue was recrystallized from ethanol.

Dihydrochlorides VI–IX *(general procedure)*. Ethereal solution of hydrogen chloride was added dropwise to ethereal solution of 1-(4-butoxyphenyl)-3-(4-R-piperazin-1-yl)-2-phenylpropan-1-one. The precipitate formed was filtered off and recrystallized from anhydrous acetone or from anhydrous diethyl ether–acetone mixture (1 : 1).

1-(4-Butoxyphenyl)-3-[4-(2,3-dimethylphenyl)piperazin-1-yl]-2-phenylpropan-1-one (II). Yield 65%, mp 85–86°C, R_f 0.81. IR spectrum, ν, cm^{-1}: 1668 (C=O). ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.98 t (3H, CH_3, Bu, *J* 7.4), 1.42–1.55 m (2H, $\underline{CH_2}CH_3$), 1.70–1.80 m (2H, $\underline{CH_2}CH_2CH_3$), 2.15 s (3H, CH_3-Ar), 2.21 s (3H, CH_3-Ar), 2.59 d.d (1H, CH_2, J_1 12.5, J_2 4.6), 2.55–2.70 m (4H) and 2.72–2.77 m (4H, $C_4H_8N_2$), 3.37 d.d (1H, CH_2, J_1 12.5, J_2 8.8), 4.00 t (2H, OCH_2, *J* 6.4), 4.88 d.d (1H, CH, J_1 8.8, J_2 4.6), 6.74–6.78 m (2H, C_6H_3), 6.85–6.89 m (2H) and 7.92–7.97 m (2H, C_6H_4), 6.91 t (1H, C_6H_3, *J* 7.7), 7.15 t (1H, H^4, Ph, *J* 7.0), 7.21–7.27 m (2H, C_6H_5), 7.28–7.33 m (2H, C_6H_5). Found, %: C 79.08; H 8.15; N 5.93. $C_{31}H_{38}N_2O_2$. Calculated, %: C 79.11; H 8.14; N 5.95. **Dihydrochloride VI**. Mp 250–252°C. Found, %: N 5.15; Cl 13.05. $C_{31}H_{38}N_2O_2 \cdot 2HCl$. Calculated, %: N 5.16; Cl 13.08.

1-(4-Butoxyphenyl)-3-[4-(2,5-dimethylphenyl)piperazin-1-yl]-2-phenylpropan-1-one (III). Yield 72%, mp 88–89°C, R_f 0.83. IR spectrum, ν, cm^{-1}: 1673 (C=O). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.98 t (3H, CH_3, Bu, *J* 7.4), 1.42–1.55 m (2H, $\underline{CH_2}CH_3$), 1.70–1.80 m (2H, $\underline{CH_2}CH_2CH_3$), 2.18 s (3H, CH_3-Ar), 2.23 s (3H, CH_3-Ar), 2.51–2.73 m (5H) and 2.74–2.80 m (4H, CH_2, CH_2 $C_4H_8N_2$), 3.31–3.41 m (1H, CH_2), 4.00 t (2H, OCH_2, *J* 6.4), 4.87 br.s (1H, CH), 6.65 d.d (1H, C_6H_3, J_1 7.7, J_2 1.5), 6.70 d (1H, C_6H_3, *J* 1.5), 6.84–6.89 m (2H) and 7.92–7.99 m (2H, C_6H_4O), 6.91 d (1H, C_6H_3, *J* 7.7), 7.15 t (1H, H^4, C_6H_5, *J* 7.1), 7.21–7.28 m (2H) and 7.29–7.33 m (2H, C_6H_5). Found, %: C 79.15; H 8.09; N 5.91. $C_{31}H_{38}N_2O_2$. Calculated, %: C 79.11; H 8.14; N 5.95. **Dihydrochloride VII.** Mp 193–195°C. Found, %: N 5.21; Cl 13.00. $C_{31}H_{38}N_2O_2 \cdot 2HCl$. Calculated, %: N 5.16; Cl 13.08.

1-(4-Butoxyphenyl)-3-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-2-phenylpropan-1-one (IV). Yield 55%, mp 87–89°C, R_f 0.95. IR spectrum, ν, cm^{-1}: 1680 (C=O). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.98 t (3H, CH_3, Bu, *J* 7.4), 1.43–1.55 m (2H, $\underline{CH_2}CH_3$), 1.71–1.80 m (2H, $\underline{CH_2}CH_2CH_3$), 2.21 s (3H, CH_3-Ar), 2.56–2.70 m [5H, $N(CH_2)_2$], 2.77–2.81 m (4H, NCH_2), 3.36 d.d (1H, CH_2, J_1 12.5, J_2 8.8), 4.00 t (2H, OCH_2, *J* 6.4), 4.88 d.d (1H, CH, J_1 8.8, J_2 4.9), 6.83–6.90 m (4H, C_6H_4), 7.03 d (1H, C_6H_3, *J* 8.6), 7.12–7.18 m (1H), 7.22–7.33 m (4H) and 7.92– 7.98 m (2H, C_6H_5). Found, %: C 73.31; H 7.21; N 5.77. $C_{30}H_{35}ClN_2O_2$. Calculated, %: C 73.38; H 7.18; N 5.70. **Dihydrochloride VIII.** Mp 179–181°C. Found, %: N 4.91; Cl 12.66. $C_{30}H_{35}ClN_2O_2 \cdot 2HCl$. Calculated, %: N 4.97; Cl 12.60.

3-(4-Benzo[1,3]dioxol-5-ylmethylpiperazin-1-yl)-1-(4-butoxyphenyl)-2-phenylpropan-1-one (V). Yield 65%, mp 105–106°C, R_f 0.60. IR spectrum, ν, cm^{-1}: 1671 (C=O). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.98 t (3H, CH_3, Bu, *J* 7.4), 1.42–1.55 m (2H, $\underline{CH_2}CH_3$), 1.70–1.79 m (2H, $\underline{CH_2}CH_2CH_3$), 2.26–2.34 m (4H) and 2.38–2.48 m (4H, $C_4H_8N_2$), 2.52 d.d (1H, CH_2, J_1 12.4, J_2 4.3), 3.29 s (2H, CH_2-Ar), 3.30 d.d (1H, CH_2, J_1 12.4, J_2 8.5), 3.99 t (2H, OCH_2, *J* 6.4), 4.81 d.d (1H, CH, J_1 8.5, J_2 4.3), 5.91 s (2H, OCH_2O), 6.64 br.s (2H) and 6.75 br.s (1H, C_6H_3), 6.83–6.88 m (2H) and 7.89–7.94 m (2H, C_6H_4), 7.13 t (1H, H^4, Ph, 7.0), 7.19–7.23 m (2H) and 7.24–7.30 m (4H, C_6H_5). Found, %: C 74.38; H 7.15; N 5.65. $C_{31}H_{36}N_2O_4$. Calculated, %: C 74.37; H 7.25; N 5.60. **Dihydrochloride IX.** Mp 188–189°C. Found, %: N 4.91; Cl 12.36. $C_{31}H_{36}N_2O_4 \cdot 2HCl$. Calculated, %: N 4.89; Cl 12.39.

1-(4-Butoxyphenyl)-1-cyclohexyl-3-(4-arypiperazin-1-yl)-2-phenylpropan-1-ols (X–XIII) *(general procedure).* The Grignard reagent was prepared from 1 g (0.04 mol) of metal magnesium and 0.06 mol cyclohexylhalide. 0.004 mol of 1-(4- butoxyphenyl)-3-(4-R-piperazin-1-yl)-2-phenylpropan-1-one **II–V** in 20 mL of absolute diethyl ether was added dropwise to the Grignard reagent solution in 30 mL of absolute diethyl ether. The reaction mixture was heated during 6 h, cooled, and poured slowly into cold water. The ether layer was decanted, and the residue was washed twice with diethyl ether (2×20 mL). The combined ether extracts were dried over anhydrous sodium sulfate. Then the solvent was distilled off to give the target compound **X–XIII**. **Dihydrochlorides XIV–XVII** were prepared similarly to β-aminoketones dihydrochlorides.

1-(4-Butoxyphenyl)-1-cyclohexyl-3-[4-(2,3-dimethylphenyl)piperazin-1-yl]-2-phenylpropan-1-ol (X). Yield 86%, mp 130–133°C, R_f 0.82. IR spectrum, ν, cm^{-1}: 3360–3350–3052 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.01 t (3H, CH_3, Bu, *J* 7.3), 0.90–1.35 m (5H, C_6H_{11}), 1.46–1.58 m (2H, $\underline{CH_2}CH_3$), 1.44–1.65 m (4H, C_6H_{11}), 1.71–1.80 m (2H, $\underline{CH_2}CH_2O$), 1.89 br.d (1H, C_6H_{11}, *J* 12.5), 2.16 s (3H, CH_3-Ar), 2.24 s (3H, CH_3-Ar), 2.28 d.d (1H, $CHCH_2N$, J_1 12.6, J_2 2.1), 2.35 br.d (1H, C_6H_{11}, *J* 11.8), 2.55 br.s (2H), 2.79–3.03 m (7H), 3.69 d.d (1H, $\underline{CH}CH_2N$, J_1 11.6, J_2 1.8), 3.92 t (2H, OCH_2, *J* 6.4), 6.60–6.67 m (2H), 6.75 br.s (2H, C_6H_4O), 6.73–6.80 m (2H) and 7.10–7.18 m (3H, C_6H_5), 6.82 d (1H, *J* 7.2), 6.91 d.d (1H, J_1 8.0, J_2 1.1), 6.99 d.d (1H, C_6H_3, J_1 8.0, J_2 7.2), 7.58 s (1H, OH). Found, %: C 80.19; H 9.17; N 5.01. $C_{37}H_{50}N_2O_2$. Calculated, %: C 80.10; H 9.08; N 5.05. **Dihydrochloride XIV.** Mp 142–145°C. Found, %: N 4.45; Cl 11.30. $C_{37}H_{50}N_2O_2 \cdot 2HCl$. Calculated, %: N 4.47; Cl 11.32.

1-(4-Butoxyphenyl)-1-cyclohexyl-3-[4-(2,5-dimethylphenyl)piperazin-1-yl]-2-phenylpropan-1-ol (XI). Yield 95%, mp 165–168°C, R_f 0.86. IR spectrum, ν, cm^{-1}: 3350–3050 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.03 t (3H, CH_3, Bu, *J* 7.3), 0.91–1.35 m (5H, C_6H_{11}), 1.46–1.59 m (2H, $\underline{CH_2}CH_3$), 1.53–1.65 m (4H, C_6H_{11}), 1.71–1.80 m (2H, $\underline{CH_2}CH_2$), 1.85–1.93 m (1H, C_6H_{11}), 2.19 s (3H, CH_3-Ar), 2.29 s (3H, CH_3-Ar), 2.28 d.d (2H, J_1 12.5, J_2 2.2) and 2.35 br.d (2H, *J* 12.5), 2.54 br.s (2H), 2.84 t (1H, *J* 12.3), 2.85 br.s (2H), 2.94–3.04 m (4H), 3.69 d.d (1H, J_1 11.5, J_2 1.9), 3.92 t (2H, OCH_2, *J* 6.3), 6.60–6.67 m (2H), 6.72 d.d (1H, C_6H_3-4, J_1 7.6, J_2 1.2), 6.74–6.79 m (2H) and

7.10–7.18 m (3H, C_6H_5), 6.85 d (1H, C_6H_3-6, *J* 1.2), 6.96 d (1H, C_6H_3-3, *J* 7.6), 7.62 s (1H, OH). Found, %: C 80.17; H 9.16; N 4.98. $C_{37}H_{50}N_2O_2$. Calculated, %: C 80.10; H 9.08; N 5.05. **Dihydrochloride** XV. Mp 215–217°C. Found, %: N 4.43; Cl 11.35. $C_{37}H_{50}N_2O_2$·2HCl. Calculated, %: N 4.47; Cl 11.32.

1-(4-Butoxyphenyl)-3-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1-cyclohexyl-2-phenylpropan-1-ol (XII). Yield 70%, mp 166–169°C, R_f 0.80. IR spectrum, ν, cm^{-1}: 3464 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.01 t (3H, CH_3, Bu, *J* 7.3), 0.92–1.35 m (5H, C_6H_{11}), 1.46–1.66 m (6H, $\underline{CH_2}CH_3$, C_6H_{11}), 1.71–1.81 m (2H, $OCH_2\underline{CH_2}$), 1.88–1.96 m (1H, C_6H_{11}), 2.23 s (3H, CH_3-Ar), 2.32 d.d (1H, J_1 12.6, J_2 2.0), 2.89 d.d (1H, $N\underline{CH_2}CH$, J_1 12.6, J_2 12.1), 2.35–2.45 m (1H, C_6H_{11}), 2.49–2.67 m (2H), 2.80–3.10 m (2H) и 3.00–3.10 m (4H, $C_4H_8N_2$), 3.76 d.d (1H, $\underline{CH}CH_2N$, J_1 12.1, J_2 2.0), 3.95 t (2H, OCH_2, *J* 6.4), 6.60–6.67 m (2H) and 6.61–6.95 m (2H, C_6H_4O), 6.77–6.82 m (2H) and 7.15–7.22 m (3H, C_6H_5), 6.95 d.d (1H, C_6H_3-4, J_1 8.0, J_2 2.1), 7.01 d (1H, C_6H_3-6, *J* 2.1), 7.07 d (1H, C_6H_3-3, *J* 8.0), 8.09 s (1H, OH). Found, %: C 75.28; H 8.34; N 4.82. $C_{36}H_{47}ClN_2O_2$. Calculated, %: C 75.17; H 8.24; N 4.87. **Dihydrochloride XVI.** Mp 223–225°C. Found, %: N 4.35; Cl 11.00. $C_{36}H_{47}ClN_2O_2$·2HCl. Calculated, %: N 4.32; Cl 10.97.

3-(4-Benzo[1,3]dioxol-5-ylmethylpiperazin-1-yl)-1-(4-butoxyphenyl)-1-cyclohexyl-2-phenylpropan-1-ol (XIII). Yield 88%, oil, R_f 0.78. IR spectrum, ν, cm^{-1}: 3431–3056 (OH). Found, %: C 77.11; H 8.38; N 4.69. $C_{37}H_{48}N_2O_4$. Calculated, %: C 77.17; H 8.33; N 5.14. **Dihydrochloride XVII.** Mp 212–215°C. Found, %: N 4.21; Cl 10.82. $C_{37}H_{48}N_2O_4$·2HCl. Calculated, %: N 4.26; Cl 10.80.

1-(4-Aryl)-3-[4-R-piperazin-1-yl]-2-phenylpropan-1-ols (XVIII–XXI) *(general procedure).* 0.005 mol of β-aminoketone in 50 mL of absolute ether was added dropwise to a stirred dispersion of 1.9 g (0.05 mol) of lithium aluminum hydride in 50 mL of absolute diethyl ether. The mixture was refluxed during 1 h and incubated at room temperature during 24 h. After cooling with ice, water was added to the mixture. The organic layer was separated, and the residue was extracted twice with diethyl ether (2×30 mL). The ethereal extracts were washed with water, dried over anhydrous sodium sulfate, and stripped to give target 1-(4-aryl)-3-[4-R-piperazin-1-yl]-2-phenylpropan-1-ols. **Dihydrochlorides XXII–XXV** were prepared similarly to β-aminoketones dihydrochlorides.

1-(4-Butoxyphenyl)-3-[4-(2,3-dimethylphenyl)piperazin-1-yl]-2-phenylpropan-1-ol (XVIII) (a mixture of two diastereomers, 83.5 : 16.5). Yield 79%, mp 96–98°C, R_{f1} 0.68, R_{f2} 0.59. IR spectrum, ν, cm^{-1}: 3262 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): first isomer, 0.98 t (3H, CH_3, Bu, *J* 7.3), 1.44–1.56 m (2H, $\underline{CH_2}CH_3$), 1.68–1.78 m (2H, $\underline{CH_2}CH_2CH_3$), 2.14 s (3H, CH_3-Ar), 2.21 s (3H, CH_3-Ar), 2.51 d.d (1H, NCH_2, J_1 13.4, J_2 6.0), 2.85 d.d (1H, NCH_2, J_1 13.4, J_2 4.2), 2.53–2.61 m (2H, $C_4H_8N_2$), 2.62–2.71 m (2H, $C_4H_8N_2$), 2.80–2.84 m (4H, $C_4H_8N_2$), 3.13–3.21 m (1H, $\underline{CH}CH_2$), 3.88 t (2H, OCH_2, Bu, *J* 6.4), 4.87 t (1H, OCH, *J* 4.0), 5.23 d (1H, OH, *J* 4.0), 6.62–6.66 m (2H) and 6.82–6.86 m (2H, C_6H_4O), 6.74–6.87 m (2H, H-Ar), 6.90–6.99 m (3H, H-Ar) 7.06–7.17 m (3H, H-Ar); second isomer, 0.96 t (3H, CH_3, Bu, *J* 7.3), 1.44–1.56 m (2H, CH_2CH_3), 1.68–1.78 m (2H, $\underline{CH_2}CH_2CH_3$), 2.17 s (3H, CH_3-Ar), 2.23 c (3H, CH_3-Ar), 2.51 d.d (1H, NCH_2, J_1 13.4, J_2 6.0), 2.85 d.d (1H, NCH_2, J_1 13.4, J_2 4.2), 2.53–2.61 m (2H, $C_4H_8N_2$), 2.62–2.71 m (2H, $C_4H_8N_2$), 2.80–2.84 m (4H, $C_4H_8N_2$), 3.13–3.21 m (1H, $\underline{CH}CH_2$), 3.00–3.08 m (1H, $\underline{CH}CH_2$), 3.84 t (2H, OCH_2, Bu, *J* 6.4), 4.78 d (1H, OCH, *J* 8.2), 6.54–6.59 m (2H) and 6.86–6.92 m (2H, C_6H_4O), 6.74–6.87 m (2H, H-Ar), 6.90–6.99 m (3H, H-Ar), 7.06–7.17 m (3H, H-Ar). Found, %: C 78.70; H 8.60; N 5.97. $C_{31}H_{40}N_2O_2$. Calculated, %: C 78.77; H 8.53; N 5.93. **Dihydrochloride XXII.** Mp 119–121°C. Found, %: N 5.49; Cl 6.95. $C_{31}H_{40}N_2O_2$·2HCl. Calculated, %: N 5.51; Cl 6.98.

1-(4-Butoxyphenyl)-3-[4-(2,5-dimethylphenyl)piperazin-1-yl]-2-phenylpropan-1-ol (XIX) (a mixture of two diastereomers, 80 : 20). Yield 60%, oil, R_{f1} 0.69, R_{f2} 0.57. IR spectrum, ν, cm^{-1}: 3270 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): major isomer, 0.96 t (0.6H) and 0.98 t (2.4H, CH_3, Bu), 1.42–1.54 m (2H, $\underline{CH_2}CH_3$), 1.64–1.76 m (2H, $\underline{CH_2}CH_2CH_3$), 2.17 s (2.4H) and 2.20 c (0.6H, CH_3-Ar), 2.25 s (2.4H) and 2.26 s (0.6H, CH_3-Ar), 2.50–2.69 m (4H), 2.80–2.86 m (4H), 2.88–2.93 m (2H) and 2.99–3.19 m (1H, $C_4H_8N_2$, NCH_2, $\underline{CH}$-Ph), 3.84 t (0.4H) and 3.88 t (1.6H, OCH_2, *J* 6.4), 4.78 d (0.2H, *J* 8.5), 4.87 d.d (0.8H, OCH, J_1 4.8, J_2 3.6), 5.25 d (0.8H, OH, *J* 4.8), 6.54–6.58 m (0.4H) and 6.61–6.66 m (1.6H, C_6H_4O), 6.64–6.68 m (1H, C_6H_3), 6.75 d (1H, C_6H_3, *J* 1.2), 6.79–6.99 m (5H) and 7.06–7.17 m (3H, H-Ar). Found, %: C 78.74; H 8.56; N 5.95. $C_{31}H_{40}N_2O_2$. Calculated, %: C 78.77; H 8.53; N 5.93. **Dihydrochloride XXIII.** Mp 234–236°C. Found, %: N 5.50; Cl 6.93. $C_{31}H_{40}N_2O_2$·2HCl. Calculated, %: N 5.51; Cl 6.98.

1-(4-Butoxyphenyl)-3-[4-(5-chloro-2-methylphenyl)-piperazin-1-yl]-2-phenylpropan-1-ol (XX). Yield 56%, mp 115–118°C, R_{f1} 0.71, R_{f2} 0.62. IR spectrum, ν, cm^{-1}: 3300–3040 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.99 t (3H, CH_3, Bu, *J* 7.3), 1.43–1.56 m (2H, CH_2, Bu), 1.68–1.78 m (2H, β-CH_2, Bu), 2.21 s (3H, CH_3-Ar), 2.50–2.70 m (4H) and 2.82–2.91 m (6H, NCH_2), 3.10–3.18 m (1H, CHPh), 3.89 t (2H, OCH_2, *J* 6.4), 4.88 br.s (1H, OCH), 5.15 br.s (1H, OH), 6.62–6.67 m (2H, C_6H_4), 6.82–7.17 m (10H, H-Ar). Found, %: C 73.62; H 7.50; N 5.65. $C_{30}H_{37}ClN_2O_2$. Calculated, %: C 73.08; H 7.56; N 5.68. **Dihydrochloride XXIV.** Mp 227–230°C. Found, %: N 5.00, Cl 12.60. $C_{30}H_{37}ClN_2O_2 \cdot 2HCl$. Calculated, %: N 4.96, Cl 12.56.

3-(4-Benzo[1,3]dioxol-5-ylmethylpiperazin-1-yl)-1-(4-butoxyphenyl)-2-phenylpropan-1-ol (XXI) (a mixture of two diastereomers, 88 : 12). Yield 55%, oil, R_{f1} 0.65, R_{f2} 0.58. IR spectrum, ν, cm^{-1}: 3360 (OH). ^1H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): first isomer, 0.98 t (3H, CH_3, *J* 7.4), 1.43–1.55 m (2H, $\underline{CH_2}CH_3$), 1.67–1.77 m (2H, $\underline{CH_2}CH_2CH_3$), 2.33–2.57 m (8H, $C_4H_8N_2$), 2.43 d.d (1H, $\underline{CH_2}CH$, *J* 5.7), 2.82 d.d (1H, CH_2CH, J_1 12.5, J_2 9.0), 3.14 d.d. d (1H, $\underline{CH}CH_2$, J_1 9.0, J_2 5.7, J_3 3.8), 3.34 s (2H, NCH_2-Ar), 3.88 t (2H, OCH_2, *J* 6.4), 4.84 d (1H, OCH, *J* 3.8), 5.38 br.s (1H, OH), 5.92 s (2H, OCH_2O), 6.59–6.63 m (2H), 6.66–6.69 m (2H), 6.75–6.80 m (3H), 6.89–6.94 m (2H) and 7.05–7.14 m (3H, H-Ar); second isomer, 0.96 t (3H, CH_3, *J* 7.4), 1.43–1.55 m (2H, $\underline{CH_2}CH_3$), 1.67–1.77 m (2H, $\underline{CH_2}CH_2CH_3$), 2.33–2.57 m (8H, $C_4H_8N_2$), 2.43 d.d (1H, $\underline{CH_2}CH$, *J* 5.7), 2.82 d.d (1H, CH_2CH, J_1 12.5, J_2 9.0), 3.14 d.d.d (1H, $\underline{CH}CH_2$, J_1 9.0, J_2 5.7, J_3 3.8), 3.34 s (2H, NCH_2-Ar), 3.83 t (2H, OCH_2, *J* 6.4), 4.74 d (1H, OCH, *J* 8.5), 5.38 br.s (1H, OH), 5.93 s (2H, OCH_2O), 6.59–6.63 m (2H), 6.66–6.69 m (2H), 6.75–6.80 m (3H), 6.89–6.94 m (2H) and 7.05– 7.14 m (3H, H-Ar). Found, %: C 74.00; H 7.61; N 5.60. $C_{31}H_{38}N_2O_4$. Calculated, %: C 74.08; H 7.62; N 5.57. **Dihydrochloride XXV.** Mp 127–130°C. Found, %: N 5.19; Cl 6.56. $C_{31}H_{38}N_2O_4 \cdot 2HCl$. Calculated, %: N 5.2; Cl 6.59.

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