

Solvent-free one-pot four-component synthesis of 2-aminomorpholines: Access to related diaminoalcohols

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Supporting Information

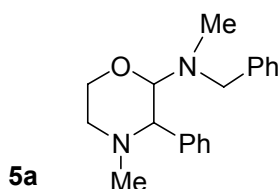
1. General information

Reactions were performed using a CEM Discover (300W) microwave oven controlled by Chemdriver Version 3.5.9 software. ^1H NMR spectra (300 MHz) and ^{13}C NMR (75 MHz) were recorded on a Bruker AC 300 spectrometer, in CDCl_3 solutions with Me_4Si as internal reference. Chemical shifts are given in ppm and coupling constants J in Hz. Infrared spectra were recorded on a Bruker IFS 28 spectrometer. Elemental analyses were performed by the Micro analytical Laboratory of the Centre Regional de Mesures Physiques de l'Ouest. High-resolution mass (HRMS) data spectra were recorded on a Varian MAT 311 spectrometer from the Centre Regional de Mesures Physiques de l'Ouest. Analytical thin layer chromatography was performed on Merck Silica Gel 60 F254 plates. Amino alcohols, amines and boronic acids are commercially available.

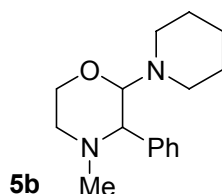
2. General procedure for the synthesis of 2-aminomorpholines **5**

To a mixture of an appropriate boronic acid **3** (1 mmol) and 1,2-aminoalcohol **1** (1 mmol) was added dropwise under stirring glyoxal (1 mmol). An exothermic reaction immediately occurred causing the temperature inside the vessel to rise to $>40^\circ\text{C}$. After 10 mn, the amine (1.5 mmol) was added and the mixture was irradiated, without any solvent, in a 10 mL sealed microwave-reactor for 15 min. For 2-(methylamino)-2-phenylethanol and 1-

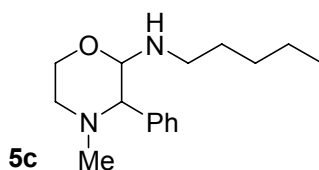
(allylamino)propan-2-ol, the 2-hydroxymorpholines was separately prepared as reported previously.⁶ The temperature was set to 110°C and automatically controlled (15 min.) . After cooling to room temperature, the product was isolated by flash chromatography using 30% ethyl acetate in heptane to give 2-aminomorpholines.



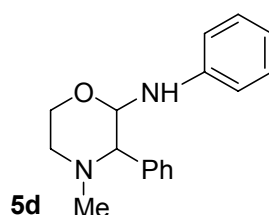
N-benzyl-N,4-dimethyl-3-phenylmorpholin-2-amine (5a). This compound was obtained according to the general procedure in 76% yield (single diastereoisomer). ¹H-NMR (300 MHz, CDCl₃) δ 2.06 (s, 3H), 2.33 (s, 3H), 2.43 (tdd, *J* = 0.9, 2.4, 11.7 Hz, 1H), 2.82 (d, *J* = 11.6 Hz, 1H), 3.14 (d, *J* = 8.6 Hz, 1H), 3.71 (d, *J* = 14.0 Hz, 1H), 3.83 (d, *J* = 14.0 Hz, 1H), 3.88 (t, *J* = 11.4 Hz, 1H), 4.02 (dd, *J* = 3.4, 11.4 Hz, 1H), 4.20 (d, *J* = 8.7 Hz, 1H), 6.79-6.82 (m, 2H), 7.15-7.17 (m, 3H), 7.28-7.47 (m, 5H). ¹³C-NMR (75 MHz, CDCl₃) δ 35.7, 43.9, 55.1, 57.9, 65.1, 71.15, 94.75, 126.3, 127.2, 127.7, 127.8, 127.85, 127.9, 139.2, 139.7. IR : 3060, 3025, 2857, 1653, 1600, 1558, 1491, 1138, 1081, 964, 735, 699 cm⁻¹. MS (EI) calcd. for C₁₉H₂₄N₂O [M]⁺ : 296.1888; found 296.1876.



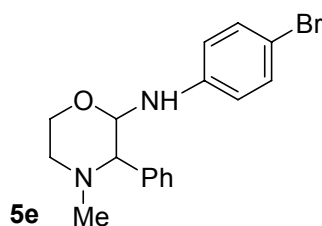
4-Methyl-3-phenyl-2-piperidin-1-ylmorpholine (5b). This compound was obtained according to the general procedure in 77% yield (single diastereoisomer). ¹H-NMR (300 MHz, CDCl₃) δ 1.26 (s, 6H), 1.98 (s, 3H), 2.30-2.41 (m, 3H), 2.72 (d, *J* = 11.7 Hz, 1H), 2.80-2.85 (m, 2H), 3.05 (d, *J* = 8.7 Hz, 1H), 3.82 (t, *J* = 11.6 Hz, 1H), 3.90 (t, *J* = 12.4 Hz, 1H), 3.97 (d, *J* = 8.8 Hz, 1H), 7.26 (s, 5H). ¹³C-NMR (75 MHz, CDCl₃) δ 24.8, 26.2, 44.2, 49.5, 55.4, 65.6, 70.7, 97.0, 127.0, 127.9, 128.3, 140.2. IR : 3062, 3029, 2978, 2936, 2817, 1652, 1600, 1555, 1493, 1095, 958, 752, 699 cm⁻¹. MS (EI) calcd. for C₁₆H₂₄N₂O [M]⁺ : 260.1888; found 260.1882.



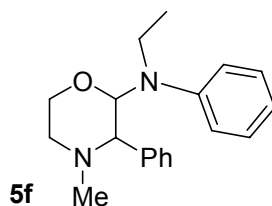
4-Methyl-*N*-pentyl-3-phenylmorpholin-2-amine (5c). This compound was obtained according to the general procedure in 55% yield as a mixture of 2 diastereoisomers (ratio: 93/7). Major diastereoisomer : $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.77 (t, $J = 7.3$ Hz, 3H), 0.93-1.04 (m, 2H), 1.06-1.27 (m, 4H), 1.57 (s, broad, 1H), 2.00 (s, 3H), 2.39 (dd, $J = 1.8$, 7.05 Hz, 1H), 2.44 (t, $J = 5.7$ Hz, 1H), 2.68 (t, $J = 7.3$ Hz, 1H), 2.71 (d, $J = 7.9$ Hz, 1H), 2.79 (d, $J = 11.6$ Hz, 1H), 3.88 (td, $J = 2.2$, 11.5 Hz, 1H), 3.93 (dd, $J = 1.2$, 3.9 Hz, 1H), 4.04 (d, $J = 8.1$ Hz, 1H), 7.32 (s, 5H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 13.9, 22.3, 28.9, 29.6, 43.9, 45.8, 54.95, 64.7, 73.95, 91.1, 127.6, 128.3, 128.4, 139.6. Minor diastereoisomer (characteristic signals) : $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 0.82 (t, $J = 6.7$ Hz, 3H), 2.07 (s, 3H), 4.41 (d, $J = 3.1$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 13.95, 22.4, 29.3, 29.7, 43.6, 45.2, 87.9. MS (EI) calcd. for $\text{C}_{10}\text{H}_{12}\text{N}[\text{M}-\text{C}_6\text{H}_{14}\text{NO}]^+$: 146.0969; found: 146.0964.



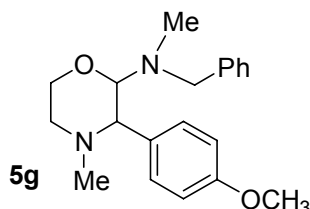
4-Methyl-*N*,3-diphenylmorpholin-2-amine (5d). This compound was obtained according to the general procedure in 50% yield as a white solid (single diastereoisomer), m.p. = 100-102°C (diisopropylether). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 2.07 (s, 3H), 2.46-2.55 (m, 1H), 2.88 (d, $J = 11.6$ Hz, 1H), 2.93 (d, $J = 8.1$ Hz, 1H), 4.02 (d, $J = 6.5$ Hz, 2H), 4.03 (s, broad, 1H), 4.77 (t, $J = 7.9$, 8.2 Hz, 1H), 6.59 (d, $J = 7.8$ Hz, 2H), 6.73 (t, $J = 7.3$ Hz, 1H), 7.12 (t, $J = 7.4$ Hz, 2H), 7.26-7.40 (m, 5H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 43.9, 54.7, 64.5, 73.45, 86.1, 114.1, 118.9, 128.0, 128.3, 128.65, 129.0, 138.5, 145.5. Anal. calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}$: C, 76.09; H, 7.51; N, 10.44; found : C, 76.40; H, 7.39; N, 10.53.



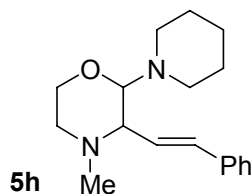
***N*-(4-bromophenyl)-4-methyl-3-phenylmorpholin-2-amine (5e).** This compound was obtained according to the general procedure in 63% yield (single diastereoisomer). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 2.07 (s, 3H), 2.45-2.54 (m, 1H), 2.87 (d, $J = 11.6$ Hz, 1H), 2.93 (d, $J = 7.75$ Hz, 1H), 4.00 (d, $J = 7.7$ Hz, 2H), 4.13 (d, $J = 8.4$ Hz, NH), 4.72 (t, $J = 8.3$ Hz, 1H), 6.48 (d, $J = 8.1$ Hz, 2H), 7.20 (d, $J = 8.8$ Hz, 2H), 7.29-7.40 (m, 5H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 43.7, 54.5, 64.4, 73.2, 86.0, 110.6, 115.7, 128.05, 128.2, 128.7, 131.6, 138.25, 144.5. MS (EI) calcd. for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{OBr}[\text{M}]^+$: 346.0681; found: 346.0680.



***N*-ethyl-4-methyl-*N*,3-diphenylmorpholin-2-amine (5f).** This compound was obtained according to the general procedure in 62% (single diastereoisomer). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.93 (t, $J = 7.1$ Hz, 3H), 2.07 (s, 3H), 2.52 (td, $J = 3.7, 11.7$ Hz, 1H), 2.83 (d, $J = 11.7$ Hz, 1H), 3.18-3.28 (m, 1H), 3.36 (q, $J = 6.9$ Hz, 2H), 3.95 (td, $J = 2.25, 11.3$ Hz, 1H), 4.00-4.08 (m, 1H), 4.80 (d, $J = 9.1$ Hz, 1H), 6.81 (d, $J = 8.4$ Hz, 3H), 7.15 (t, $J = 7.5$ Hz, 2H), 7.26 (s, 5H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 13.9, 29.7, 44.1, 55.0, 66.0, 70.8, 93.8, 118.9, 119.7, 127.5, 128.1, 128.5, 129.3, 139.1, 147.9. MS (EI) calcd. for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}$ $[\text{M}]^+$: 296.1888; found : 296.1906.

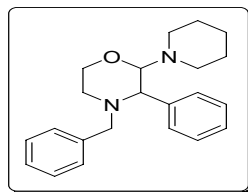


***N*-benzyl-3-(4-methoxyphenyl)-*N*,4-dimethylmorpholin-2-amine (5g).** This compound was obtained according to the general procedure in 76% yield as a white solid (single diastereoisomer), m.p. = 98-100°C (diisopropylether). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 2.04 (s, 3H), 2.33 (s, 3H), 2.40 (td, $J = 3.7, 11.6$ Hz, 1H), 2.78 (d, $J = 11.5$ Hz, 1H), 3.08 (d, $J = 8.7$ Hz, 1H), 3.71 (d, $J = 14.0$ Hz, 1H), 3.83 (d, $J = 14.0$ Hz, 1H), 3.84-3.88 (m, 1H), 3.85 (s, 3H), 3.99 (dd, $J = 2.8, 11.3$ Hz, 1H), 4.14 (d, $J = 8.7$ Hz, 1H), 6.86-6.92 (m, 4H), 7.16-7.38 (m, 5H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 36.0, 43.9, 55.0, 55.3, 57.8, 65.3, 70.5, 94.8, 113.3, 126.3, 127.7, 128.0, 129.2, 131.9, 139.3, 158.7. Anal. calcd. for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_2$: C, 73.59; H, 8.03; N, 8.58; found: C, 73.50; H, 7.83; N, 8.52.

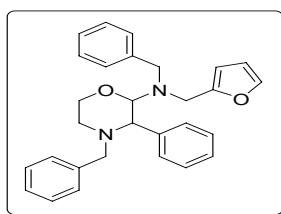


4-Methyl-3-[(*E*)-2-phenylvinyl]-2-piperidin-1-ylmorpholine (5h). This compound was obtained according to the general procedure in 43% yield (single diastereoisomer). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.40-1.55 (m, 6H), 2.24-2.33 (m, 1H), 2.28 (s, 3H), 2.56-2.62 (m, 2H), 2.74 (d, $J = 11.7$ Hz, 1H), 2.76 (t, $J = 8.5$ Hz, 1H), 2.85-2.91 (m, 2H), 3.76 (td, $J = 2.4, 11.6$

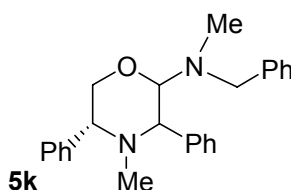
Hz, 1H), 3.91 (dd, $J = 2.5, 11.7$ Hz, 1H), 3.92 (d, $J = 8.4$ Hz, 1H), 6.00 (dd, $J = 9.0, 16.0$ Hz, 1H), 6.53 (d, $J = 16.0$ Hz, 1H), 7.23-7.43 (m, 5H); ^{13}C -NMR (75 MHz, CDCl_3) δ 24.8, 26.3, 43.0, 49.3, 55.0, 65.5, 68.6, 95.6, 126.3, 127.3, 128.2, 128.5, 132.9, 139.2. MS (EI) calcd. for $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}$ $[\text{M}]^+$: 286.2045; found: 286.2051.



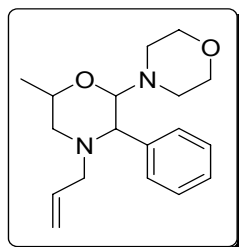
4-Benzyl-3-phenyl-2-piperidin-1-ylmorpholine (5i). This compound was obtained according to the general procedure in 65% yield (single diastereoisomer). ^1H -NMR (200 MHz, CDCl_3) δ 1.34 (s, 6H), 2.20 (td, $J = 3.6, 11.6$ Hz, 1H), 2.41-2.52 (m, 2H), 2.70 (d, $J = 11.7$ Hz, 1H), 2.90 (d, $J = 13.2$ Hz, 1H), 2.91-3.00 (m, 2H), 3.47 (d, $J = 8.6$ Hz, 1H), 3.77 (d, $J = 12.9$ Hz, 2H), 3.91 (td, $J = 2.3, 11.8$ Hz, 1H), 4.07 (d, $J = 8.6$ Hz, 1H), 7.23-7.53 (m, 10H). ^{13}C NMR (75 MHz) δ 24.8, 26.3, 49.6, 51.4, 59.6, 65.7, 68.9, 97.4, 126.7, 127.0, 127.9, 128.0, 128.5, 128.6, 138.9, 140.7. IR : 3061, 3027, 2942, 2907, 2853, 1601, 1559, 1492, 1183, 1108, 1081, 988, 761 and 700 cm^{-1} . MS (EI) calcd. for $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}$ $[\text{M}]^+$: 336.2202, found: 336.2179.



4-Dibenzyl-N-((2-furylmethyl)-3-phenylmorpholin-2-amine (5j). This compound was obtained according to the general procedure in 52% yield (single diastereoisomer). ^1H -NMR (200 MHz, CDCl_3) δ 2.25 (td, $J = 2, 7.8$ Hz, 1H), 2.70 (d, $J = 7.8$ Hz, 1H), 2.88 (d, $J = 9.0$ Hz, 1H), 3.51 (d, $J = 5.8$ Hz, 1H), 3.68-4.21 (m, 7H), 4.23 (d, $J = 8.5$ Hz, 1H), 5.9 (s, broad, 1H), 6.3 (s, broad, 1H), 6.8 (d, $J = 3.3.0$ Hz, 1H), 7.16-7.42 (m, 15H). ^{13}C NMR (75 MHz) δ 46.7, 51.4, 53.7, 59.6, 65.9, 69.5, 92.1, 107.5, 110.0, 126.4, 126.8, 127.3, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.7, 129.2, 139.1, 141.3, 153.4. MS (EI) calcd. for $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}-\text{C}_7\text{H}_7]^+$: 347.1759; found 347.1747.

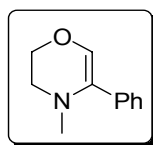


***N*-Benzyl-*N*,4-dimethyl-3,5-diphenylmorpholin-2-amine (5k).** This compound was obtained according to the general procedure in 63% yield as a mixture of 3 isomers (ratio : 60/30/10). Major diastereoisomer : $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.88 (s, 3H), 2.43 (s, 3H), 3.41 (dd, $J = 3.6, 10.6$ Hz, 1H), 3.47 (d, $J = 8.9$ Hz, 1H), 3.67 (t, $J = 11.3$ Hz, 1H), 3.78 (d, $J = 14.2$ Hz, 1H), 3.90 (d, $J = 14.0$ Hz, 1H), 3.96 (dd, $J = 3.5, 11.5$ Hz, 1H), 4.31 (d, $J = 8.9$ Hz, 1H), 6.84-6.87 (m, 2H), 7.18-7.22 (m, 3H), 7.34-7.52 (m, 10H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 36.0, 41.5, 58.2, 68.1, 70.1, 72.1, 95.5, 126.4, 127.1, 127.5, 127.8, 127.85, 128.0, 128.1, 128.4, 130.2, 139.35, 139.7, 140.6. Second diastereoisomer (characteristic signals) : $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.87 (s, 3H), 2.46 (s, 3H), 3.72 (d, $J = 4.0$ Hz, 1H), 3.80 (d, $J = 8.9$ Hz, 1H), 3.84 (s, broad, 2H), 3.88 (d, $J = 13.8$ Hz, 1H), 4.32 (d, $J = 2.2$ Hz, 1H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 35.9, 40.6, 58.3, 62.3, 63.3, 69.8, 95.9, 126.5, 127.15, 127.25, 138.2, 139.3, 140.0. Third diastereoisomer (characteristic signals) : $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 2.42 (s, 3H), 3.45 (dd, $J = 3.6, 10.5$ Hz, 1H), 4.35 (d, $J = 9.1$ Hz, 1H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 52.9, 60.7, 97.9. MS (EI) calcd. for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}$ $[\text{M}]^+$: 372.22015; found: 372.2214.



4-Allyl-6-methyl-3-phenyl-2,4'-bimorpholine (5l). This compound was obtained according to the procedure in 42% yield (single diastereoisomer). $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ 1.21 (d, $J = 6.2$ Hz, 3H), 1.90 (t, $J = 10.4$ Hz, 1H), 2.46-2.53 (m, 3H), 2.86-2.94 (m, 3H), 3.10 (dd, $J = 2.7, 13.7$ Hz, 1H), 3.22 (d, $J = 8.6$ Hz, 1H), 3.44 (t, $J = 4.8$ Hz, 4H), 3.78-3.89 (m, 1H), 4.02 (d, $J = 8.6$ Hz, 1H), 5.04 (d, $J = 7.7$ Hz, 1H), 5.11 (s, broad, 1H), 5.64-5.89 (m, 1H), 7.31 (s, broad, 5H). ^{13}C NMR (75 MHz) δ 18.8, 48.6, 57.9, 58.0, 67.2 (2C), 70.4, 96.2, 117.6, 127.2, 128.1, 128.5, 134.9, 139.1. MS (EI) calcd. for $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_2$ $[\text{M}]^+$: 302.19943; found: 302.2010.

3. Synthesis of 4-methyl-5-phenyl-2,3-dihydro-2H-1,4-oxazine (7).

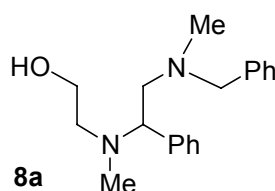


Phenyl boronic acid (610 mg, 5 mmol), *N*-methylethanolamine (401 μL , 5 mmol) and glyoxal (575 μL , 5 mmol) were irradiated, without any solvent, in a 10 mL sealed microwave-reactor for 30 minutes. The temperature was set to 110°C and automatically controlled. After cooling to room temperature, the product was isolated by flash chromatography using 40% ethyl

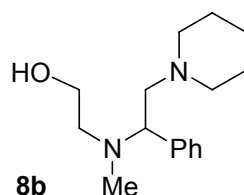
acetate in heptane to give the pure compound with 85% yield. ^1H -NMR (200 MHz, CDCl_3) δ 2.72 (s, 3H), 3.13 (t, $J = 4.8$ Hz, 2H), 4.27 (t, $J = 4.2$ Hz, 2H), 5.98 (s, 1H), 7.15 (t, $J = 7.2$ Hz, 1H), 7.29 (t, $J = 7.5$ Hz, 2H), 7.41 (d, $J = 7.5$ Hz, 2H). ^{13}C NMR (75 MHz) δ 43.1, 49.5, 64.0, 122.1, 125.9, 127.4, 128.2, 128.8, 135.1. MS (EI) calcd. for $\text{C}_{11}\text{H}_{13}\text{NO}$ $[\text{M}]^+$: 175.0997; found: 175.0985.

4 General procedure for the synthesis of diaminoalcohols 8

A solution of 2-aminomorpholine **5** (1 mmol) in dry diethylether (4 mL) was added dropwise to a 1M solution of LiAlH_4 (1.5 mmol) in dry diethylether at 0°C . The mixture was stirred at room temperature for 5 h, cooled to 0°C , and quenched with water. Aqueous phase was extracted with CHCl_3 (3x10 mL) and the combined organic phases were dried over MgSO_4 , filtered and concentrated to give crude aminodiols which were purified by flash chromatography using 5% methanol in dichloromethane.

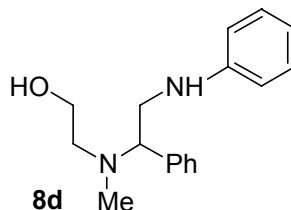


2-[(2-[Benzyl(methyl)amino]-1-phenylethyl)(methyl)amino]ethanol (8a). This compound was obtained according to the general procedure in 87% yield. ^1H -NMR (300 MHz, CDCl_3) δ 2.25 (s, 3H), 2.30 (s, 3H), 2.38 (dt, $J = 3.1, 13.3$ Hz, 1H), 2.43 (dd, $J = 5.1, 12.9$ Hz, 1H), 2.97 (ddd, $J = 3.75, 9.4, 13.4$ Hz, 1H), 3.16 (dd, $J = 10.75, 12.9$ Hz, 1H), 3.55 (d, $J = 12.8$ Hz, 1H), 3.57 (dt, $J = 3.7, 10.6$ Hz, 1H), 3.70 (d, $J = 12.7$ Hz, 1H), 3.73 (dd, $J = 2.75, 10.5$ Hz, 1H), 3.95 (dd, $J = 5.2, 10.65$ Hz, 1H), 4.72 (s, broad, 1H), 7.23 (d, $J = 6.4$ Hz, 2H), 7.31-7.40 (m, 8H); ^{13}C -NMR (75 MHz, CDCl_3) δ 38.9, 41.3, 53.0, 58.5, 59.0, 62.2, 64.2, 127.0, 127.1, 127.9, 128.0, 128.1, 129.35, 137.6, 138.0. MS (EI) calcd. for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}$ $[\text{M}-\text{H}_2\text{O}]^+$: 280.1939; found: 280.1951.

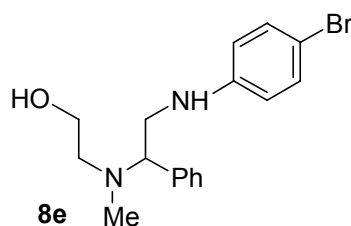


2-[Methyl(1-phenyl-2-piperidin-1-ylethyl)amino]ethanol (8b). This compound was obtained according to the general procedure in 95% yield. ^1H -NMR (300 MHz, CDCl_3) δ 1.39-1.52 (m, 2H), 1.56-1.72 (m, 4H), 2.20-2.38 (m, 4H), 2.25 (s, 3H), 2.62 (s, broad, 2H),

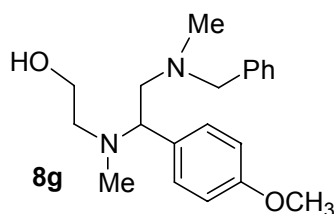
3.00 (t, $J = 12.7$ Hz, 1H), 3.09 (td, $J = 2.8, 10.7$ Hz, 1H), 3.46 (dt, $J = 2.7, 7.9$ Hz, 1H), 3.66 (t, $J = 10.45$ Hz, 1H), 3.90 (dd, $J = 4.5, 11.8$ Hz, 1H), 5.54 (s, broad, 1H), 7.18-7.34 (m, 5H); ^{13}C -NMR (75 MHz, CDCl_3) δ 24.2, 25.4, 40.0, 52.2, 53.8, 59.7, 60.3, 63.1, 127.1, 127.9, 128.0, 148.6. MS (EI) calcd. for $\text{C}_{16}\text{H}_{26}\text{N}_2\text{O}$ $[\text{M}-\text{H}_2\text{O}]^+$: 244.1939; found: 244.1923.



2-[(2-Anilino-1-phenylethyl)(methyl)amino]ethanol (8d). This compound was obtained according to the general procedure in 86% yield. ^1H -NMR (300 MHz, CDCl_3) δ 2.27 (s, 3H), 2.52 (dt, $J = 4.8, 12.8$ Hz, 1H), 2.70 (ddd, $J = 4.7, 7.0, 12.2$ Hz, 1H), 3.17 (s, broad, 2H), 3.43 (dd, $J = 6.2, 12.2$ Hz, 1H), 3.59-3.73 (m, 3H), 3.94 (dd, $J = 6.3, 8.4$ Hz, 1H), 6.67 (d, $J = 8.2$ Hz, 2H), 6.76 (t, $J = 7.3$ Hz, 1H), 7.22 (t, $J = 7.8$ Hz, 2H), 7.28-7.34 (m, 5H); ^{13}C -NMR (75 MHz, CDCl_3) δ 37.3, 45.0, 54.9, 58.6, 66.9, 113.2, 117.6, 127.8, 128.3, 128.65, 129.2, 136.9, 148.0. IR : 3354, 3061, 3025, 2971, 2836, 2797, 1602, 1504, 1068, 1027, 749, 702, 692 cm^{-1} . MS (EI) calcd. for $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}$ $[\text{M}]^+$: 270.1732; found : 270.1728.

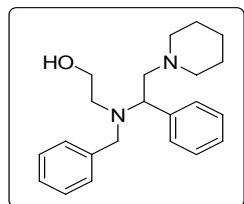


2-[(2-(4-Bromophenyl)amino)-1-phenylethyl](methyl)amino]ethanol (8e). This compound was obtained according to the general procedure in 73% yield. ^1H -NMR (300 MHz, CDCl_3) δ 2.25 (s, 3H), 2.48 (dt, $J = 4.8, 7.9$ Hz, 1H), 2.68 (ddd, $J = 4.7, 6.9, 12.1$ Hz, 1H), 2.85 (s, broad, 2H), 3.36 (dd, $J = 6.1, 12.1$ Hz, 1H), 3.59 (dd, $J = 8.6, 12.5$ Hz, 1H), 3.62-3.68 (m, 2H), 3.90 (dd, $J = 6.2, 8.5$ Hz, 1H), 6.53 (d, $J = 8.7$ Hz, 2H), 7.27 (d, $J = 8.7$ Hz, 2H), 7.28-7.44 (m, 5H); ^{13}C -NMR (75 MHz, CDCl_3) δ 37.3, 44.9, 54.9, 58.6, 66.7, 109.0, 114.6, 127.8, 128.3, 128.6, 131.8, 136.6, 147.0. IR : 3356, 3059, 3024, 2946, 2798, 1596, 1495, 1171, 1071, 752, 703 cm^{-1} . MS (EI) calcd. for $\text{C}_{14}\text{H}_{13}\text{NBr}$ $[\text{M}-\text{C}_3\text{H}_8\text{NO}]^+$: 274.0231; found : 274.0223.

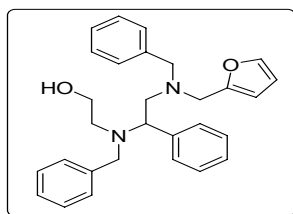


2-[(2-[Benzyl(methyl)amino]-1-(4-methoxyphenyl)ethyl](methyl)amino]ethanol (8g). This compound was obtained according to the general procedure in 76% yield. ^1H -NMR (300

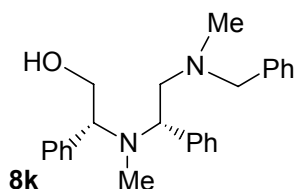
MHz, CDCl₃) δ 2.22 (s, 3H), 2.37 (s, 3H), 2.46 (dd, J = 5.1, 13.0 Hz, 1H), 2.90 (ddd, J = 3.5, 8.9, 13.0 Hz, 1H), 3.49 (s, 1H), 3.59 (dd, J = 3.6, 7.3 Hz, 1H), 3.65-3.77 (m, 5H), 3.82 (s, 3H), 3.93 (dd, J = 5.2, 10.9 Hz, 1H), 6.89 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.5 Hz, 2H), 7.29-7.40 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃) δ 38.7, 41.4, 54.1, 55.3, 57.6, 58.8, 61.9, 63.8, 113.8, 126.8, 127.9, 128.5, 129.7, 130.0, 135.9, 159.3. MS (EI) calcd. for C₁₇H₂₀NO [M-C₃H₈NO]⁺ : 254.1544; found : 254.1534.



2-[N-Benzyl(1-phenyl-2-piperidin-1-ylethyl)amino]ethanol (8i). This compound was obtained according to the general procedure in 82% yield. ¹H-NMR (200 MHz, CDCl₃) δ 1.37 (s, broad, 2H), 1.54 (s, broad, 4H), 2.03 (dd, J = 4.5, 13.2 Hz, 1H), 2.19-2.46 (m, 4H), 2.42 (d, J = 14.1 Hz, 1H), 2.98 (t, J = 12.9 Hz, 1H), 3.25-3.77 (m, 4H), 3.39 (d, J = 13.9 Hz, 1H), 3.61 (d, J = 8.6 Hz, 1H), 5.27 (s, broad, 1H), 7.13-7.65 (m, 10H). ¹³C NMR (75 MHz) δ 24.1, 25.2, 50.6, 53.75, 55.9, 57.5, 60.0, 60.6, 127.0, 127.4, 128.0, 128.3, 128.35, 129.2, 138.5, 140.0. IR : 3352, 3063, 2972, 2789, 1578, 1510, 1080, 1029, 749, 720, 700 cm⁻¹. MS (EI) calcd. for C₂₀H₂₅N₂ [M-C₂H₄OH]⁺ : 293.2018; found 293.2044.

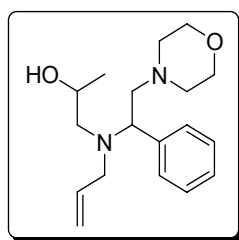


2-(N-Benzyl{2-[benzyl(2-furylmethyl)amino]-1-phenylethyl}amino)ethanol (8j). This compound was obtained according to the general procedure in 30% yield. ¹H-NMR (200 MHz, CDCl₃) δ 2.38 (dd, J = 8.6, 13.4 Hz, 1H), 2.51 (d, J = 13.6 Hz, 1H), 3.12 (dd, J = 11.2, 13.1 Hz, 1H), 3.18 (ddd, J = 3.8, 10.9, 13.9 Hz, 1H), 3.39 (d, J = 11.5 Hz, 1H), 3.43 (d, J = 11.3 Hz, 1H), 3.52 (d, J = 15.2 Hz, 1H), 3.61 (d, J = 15.3 Hz, 1H), 3.56-3.67 (m, 2H), 3.71 (d, J = 13.2 Hz, 1H), 3.76 (d, J = 13.1 Hz, 1H), 3.81 (dd, J = 6.6, 9.0 Hz, 1H), 4.03 (dd, J = 5.2, 11.1 Hz, 1H), 5.95 (d, J = 3.1 Hz, 1H), 6.29 (dd, J = 2.1, 2.7 Hz, 1H), 7.17-7.41 (m, 16H). ¹³C NMR (75 MHz) δ 47.2, 50.7, 55.0, 55.5, 58.0, 59.0, 59.9, 109.5, 110.0, 127.15, 127.2, 127.4, 127.9, 128.3 (2C), 128.6, 129.4, 129.8, 137.7, 138.8, 139.6, 142.1, 151.6. MS (EI) calcd. for C₁₆H₁₈NO [M-C₁₃H₁₄NO]⁺ : 240.1388; found: 240.1400.



(2R)-2-[(1S)-2-[benzyl(methyl)amino]-1-phenylethyl](methylamino)-2-phenylethanol

(8k). This compound was obtained according to the general procedure in 41% yield. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.87 (s, 3H), 2.41 (s, 3H), 2.47 (dd, $J = 4.0, 13.1$ Hz, 1H), 3.21 (dd, $J = 10.0, 13.0$ Hz, 1H), 3.58 (d, $J = 12.8$ Hz, 1H), 3.75 (d, $J = 12.8$ Hz, 1H), 3.95 (d, $J = 6.3$ Hz, 2H), 4.13 (t, $J = 6.3$ Hz, 1H), 4.18 (dd, $J = 3.9, 9.9$ Hz, 1H), 7.18-7.40 (m, 15H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 30.0, 43.3, 58.8, 62.4, 63.6, 64.6, 68.8, 127.0, 127.1, 127.3, 128.1, 128.1, 128.2, 128.3 (2C), 129.7, 138.1, 139.9, 140.7. MS (EI) calcd. for $\text{C}_{16}\text{H}_{18}\text{NO}$ $[\text{M}-\text{C}_9\text{H}_{12}\text{N}]^+$: 240.1388, found 240.1379. $[\alpha]_{\text{D}}^{20} = +6.8^\circ$ (c 0.74, CH_2Cl_2).



1-[N-allyl(2-morpholino-4-yl-1-phenylethyl)amino]propan-2-ol (8l). This compound was obtained according to the general procedure in 78% yield. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ 1.13 (d, $J = 6.3$ Hz, 3H), 2.39-2.60 (m, 4H), 2.67-2.77 (m, 2H), 2.92 (dd, $J = 3.0, 8.6$ Hz, 1H), 2.98-3.07 (m, 3H), 3.23 (ddt, $J = 1.4, 5.5, 14.5$ Hz, 1H), 3.72-3.83 (m, 5H), 4.08 (dd, $J = 4.4, 11.0$ Hz, 1H), 5.10 (d, $J = 9.5$ Hz, 1H), 5.14 (dd, $J = 1.3, 15.8$ Hz, 1H), 5.71-5.85 (m, 1H), 7.24-7.39 (m, 5H). ^{13}C NMR (75 MHz) δ 20.2, 53.9, 55.2, 59.6, 60.4, 62.0, 66.6, 66.8, 116.9, 127.2, 127.9, 128.3, 137.4, 139.1. MS (EI) calcd. for $\text{C}_{13}\text{H}_{18}\text{NO}$ $[\text{M}-\text{CH}_2\text{N}(\text{CH}_2)_4\text{O}]^+$: 204.1388; found 204.1397.