Supplementary data

General

All experiments were carried out under air, using glassware. All starting materials were obtained from commercial suppliers and used without further purification unless otherwise noted. Melting points were determined on a Büchi B-540 apparatus and are uncorrected. Mass spectra were performed by the Spectropole of the Université Paul Cézanne. ^{1}H and ^{13}C NMR spectra were determined on a Bruker ARX 200 spectrometer. The ^{1}H chemical shifts were referenced to the solvent peak: $CDCl_3$ (7.26 ppm), and the ^{13}C chemical shifts were referenced to the solvent peak: $CDCl_3$ (77.0 ppm). Solvents were dried by conventional methods and mixtures were dried with drying oven Heraeus Vacutherm VT 6025 coupled with KNF LABOPORT diaphragm pump. Activated neutral alumina (50-200 mesh) was used as additive. The following adsorbent was used for column chromatography: silica gel 60 (Merck, particle size 0.063–0.200 mm, 70–230 mesh ASTM). TLC was performed on 5 cm x 10 cm aluminium plates coated with silica gel 60F-254 (Merck) in an appropriate solvent.

Microwave instrumentation

The multimode reactor used was an ETHOS Synth Lab station (Ethos start, Milestone Inc.). The multimode microwave has a twin magnetron (2 x 800 W, 2.45 GHz) with a maximum delivered power of 1000 W in 10 W increments (pulsed irradiation). The multimode microwave features a built-in magnetic stirrer (Teflon-coated stirring bar), direct temperature control of the reaction mixture with the aid of IR-sensor on the reactor wall and software that enables on line temperature control by regulation of microwave power output.

General procedure : *Microwaves heating.* To a mixture of arylpiperazine (1 eq), sodium iodide (0.3 eq), sodium sulfate (0.8 g) and cesium hydroxide (2 eq) was added 4-haloalkane (3-5 eq). The reaction mixture was stirred and irradiated in a microwave oven (Ethos start) for an appropriate time and temperature. After being cooled down, the mixture was then taken up in 1N NaOH and then extracted with AcOEt (3 x 30 mL). The organic layers were washed with water (2 x 30 mL), with brine (30 mL) and dried over anhydrous sodium sulphate. Concentration of the solvent under reduced pressure and the drying mixture in a oven under reduced pressure afforded the desired alkylarylpiperazine.

For the reactions carried on with 4-chorobutanol **2a**, the corresponding desired product was isolated and separated to secondary products with chromatographic column with AcOEt/*n*-hexane as eluent.

Experimental data

4-[4-(3,4-Dichlorophenyl)piperazin-1-yl]butan-1-ol **3a**
Orange paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.26 (d, J = 9.0 Hz, 1H), 6.95 (d, J = 2.9 Hz, 1H), 6.75–6.69 (dd, J = 9.0 and 2.8 Hz, 1H), 3.64–3.56 (m, 2H), 3.47–3.41 (m, 1H), 3.27–3.22 (m, 4H), 2.74–2.69 (m, 4H), 2.55–2.50 (m, 2H), 1.72–1.63 (m, 4H); NMR ^{13}C (50 MHz, $CDCl_3$) 150.7, 132.7, 130.4, 122.0, 117.1, 115.2, 70.6, 58.3, 52.8, 48.6, 27.7, 23.6; HRMS (EI): calc. for $C_{14}H_{20}N_2OCl_2$ (M+) 303.1025, found 303.1023.

4-[4-(3,4-Dichlorophenyl)piperazin-1-yl]butanenitrile **3b**
White solid, mp 61°C (recrist *n*-Hexane), NMR ^{1}H (200 MHz, $CDCl_3$) 7.23 (d, J = 8.9 Hz, 1H), 6.95 (d, J = 2.9 Hz, 1H), 6.76-6.70 (dd, J = 2.9 et 8.9 Hz, 1H), 3.20-3.15 (m, 4H), 2.62-2.43 (m, 8H), 1.87 (t, J = 6.9 Hz, 2H); NMR ^{13}C (50 MHz, $CDCl_3$) 146.7, 145.5, 141.6, 133.6, 130.4, 128.6, 127.1, 123.4, 74.1, 45.3; HRMS (EI): calc. for $C_{14}H_{17}N_3Cl_2$ (M+) 298.0872, found 298.0872. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.

3-[4-(3,4-Dichlorophenyl)piperazin-1-yl]propanenitrile **3c**
Yallow paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.27 (d, J = 8.9 Hz, 1H), 6.96-6.93 (m, 1H), 6.76-6.70 (m, 1H), 3.20-3.01 (m, 6H), 2.78-2.48 (m, 6H); NMR ^{13}C (50 MHz, $CDCl_3$) 150.5, 132.8, 130.4, 122.4, 117.4, 115.4, 53.2, 52.4, 48.6, 16.0; HRMS (EI): calc. for $C_{13}H_{15}N_3Cl_2$ (M+) 284.0716, found 284.0715.

Ethyl 4-[4-(3,4-dichlorophenyl)piperazin-1-yl]butanoate **3d**
Orange solid, mp 48°C (recrist *n*-Hexane), NMR ^{1}H (200 MHz, $CDCl_3$) 7.26 (d, J = 8.9 Hz, 1H), 6.92 (d, J = 2.8 Hz, 1H), 6.71 (dd, J = 8.9 and 2.8 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.17–3.12 (m, 4H), 3.12–2.59 (m, 4H), 2.45–2.31 (m, 4H), 1.90–1.76 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); NMR ^{13}C (50 MHz, $CDCl_3$) 173.3, 150.5, 132.6, 130.3, 121.9, 117.0, 115.1, 60.2, 57.4, 52.6, 48.4, 32.1, 21.9, 14.2; HRMS (EI): calc. for $C_{16}H_{22}N_2O_2Cl_2$ (M+) 345.1131, found 345.1131.

4-[4-(2-Methoxyphenyl)piperazin-1-yl]butan-1-ol **5a**
Translucent paste, NMR ^{1}H (200 MHz, $CDCl_3$) 6.99-6.82 (m, 4H), 3.85 (s, 3H), 3.59-3.56 (m, 2H), 3.48-3.42 (m, 1H), 3.15-3.08 (m, 4H), 2.75-2.66 (m, 4H), 2.50-2.44 (m, 2H), 1.72-1.67 (m, 4H); NMR ^{13}C (50 MHz, $CDCl_3$) 150.9, 136.2, 130.7, 129.3, 124.0, 120.1, 62.6, 58.5, 53.5, 51.2, 32.6, 25.2, 21.1, 17.3; The ^{1}H NMR, ^{13}C NMR were identical to those of the known compound.

4-[4-(2-Methoxyphenyl)piperazin-1-yl]butanenitrile **5b**
White needles, mp 82°C (recrist *n*-Hexane), NMR ^{1}H (200 MHz, $CDCl_3$) 7.04-6.90 (m, 3H), 6.85 (d, J = 7.2 Hz, 1H), 3.86 (s, 3H), 3.10-3.06 (m, 4H), 2.66-2.61 (m, 4H), 2.56-2.41 (m, 4H), 1.92-1.79 (m, 2H); NMR ^{13}C (50 MHz, $CDCl_3$) 152.2, 141.2, 122.9, 120.9, 119.7, 118.1, 112.2, 56.3, 55.3, 53.2, 50.5, 22.7, 14.9; HRMS (EI): calc. for $C_{15}H_{21}N_3O$ (M+) 260.1757, found 260.1756. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.

4-[4-(4-Fluorophenyl)piperazin-1-yl]butan-1-ol **7a**
White solid, mp 73°C (recrist *n*-Hexane), NMR ^{1}H (200 MHz, $CDCl_3$) 7.01-6.82 (m, 4H), 3.64-3.54 (m, 2H), 3,46 (bs, 1H), 3,17-3,12 (m, 8H), 2.70-2.63 (m, 2H), 1.73-1.67 (m, 4H); NMR ^{13}C (50 MHz, $CDCl_3$) 157.3 (d, J = 238.8 Hz), 147.7 (d, J = 2.2 Hz), 118.1 (d. J = 7.8 Hz), 115.4 (d. J = 21.9 Hz), 62.5, 58.4, 52.9, 49.8, 32.3, 25.0; HRMS (EI): calc. for

$C_{14}H_{21}N_2OF$ (M+) 253.1711, found 253.1711.

4-[4-(4-Fluorophenyl)piperazin-1-yl]butanenitrile **7b**
White solid, mp 120°C (recrist *n*-Hexane), NMR ^{1}H (200 MHz, $CDCl_3$) 6.99-6.81 (m, 4H), 3.12-3.07 (m, 4H), 2.61-2.40 (m, 8H), 1.84 (t, *J* = 7.0 Hz, 2H); NMR ^{13}C (50 MHz, $CDCl_3$) 157.0 (d, *J* = 238.9 Hz), 147.8 (d, *J* = 2.2 Hz), 119.6, 117.7 (d, *J* = 7.7 Hz), 115.4 (d, *J* = 22.3 Hz), 56.1, 52.9, 50.0, 22.6, 14.8; HRMS (EI): calc. for $C_{14}H_{18}N_3F$ (M+) 248.1558, found 248.1555.

3-[4-(4-Fluorophenyl)piperazin-1-yl]propanenitrile **7c**
White solid, mp 90°C (recrist *n*-Hexane), NMR ^{1}H (200 MHz, $CDCl_3$) 7.01–6.83 (m, 4H), 3.17–3.12 (m, 4H), 2.81–2.54 (m, 8H); NMR ^{13}C (50 MHz, $CDCl_3$) 157.3 (d, *J* = 238.9 Hz), 147.8, 118.6, 118.0 (d, *J* = 7.7 Hz), 115.6 (d, *J* = 21.9 Hz), 53.3, 52.7, 50.1, 16.0; HRMS (EI): calc. for $C_{13}H_{16}FN_3$ (M+) 234.1401, found 234.1400. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.

Ethyl 4-[4-(4-fluorophenyl)piperazin-1-yl]butanoate **7d**
Yellow paste, NMR ^{1}H (200 MHz, $CDCl_3$) 6.97–6.80 (m, 4H), 4.10 (q, *J* = 7.2 Hz, 2H), 3.12–3.07 (m, 4H), 2.62–2.57 (m, 4H), 2.54–2.30 (m, 4H), 1.91–1.76 (m, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); NMR ^{13}C (50 MHz, $CDCl_3$) 173.3, 157.0 (d, *J* = 238.6 Hz), 147.8 (d, *J* = 2.2 Hz), 117.6 (d, *J* = 7.7 Hz), 115.3 (d, *J* = 22.0 Hz), 60.2, 57.4, 53.0, 49.9, 32.1, 21.1, 14.1; HRMS (EI): calc. for $C_{16}H_{23}N_2O_2F$ (M+) 295.1816, found 295.1815. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.

4-[4-(2,5-Dimethylphenyl)piperazin-1-yl]butanenitrile **9b**
Yellow paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.06 (d, *J* = 7.4 Hz, 1H), 6.83-6.79 (m, 2H), 2.97-2.94 (m, 4H), 2.69-2.57 (m, 6H), 2.49 (t, *J* = 7.0 Hz, 2H), 2.30 (s, 3H), 2.24 (s, 3H), 1.94 (t, *J* = 6.9 Hz, 2H); NMR ^{13}C (50 MHz, $CDCl_3$) 151.2, 136.0, 130.8, 129.2, 123.7, 119.7, 62.4, 56.3, 53.6, 51.6, 22.7, 21.1, 17.4, 14.8; HRMS (EI): calc. for $C_{16}H_{23}N_3$ (M+) 258.1965, found 258.1964.

3-[4-(2,5-Dimethylphenyl)piperazin-1-yl]propanenitrile **9c**
Orange paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.04 (d, *J* = 7.3 Hz, 1H), 6.81–6.86 (m, 2H), 3.06-2.52 (m, 12H), 2.34 (s, 3H); 2.28 (s, 3H); NMR ^{13}C (50 MHz, $CDCl_3$) 151.0, 136.1, 130.8, 129.2, 123.9, 119.8, 118.7, 53.4, 53.2, 51.4, 21.1, 17.4, 15.8; HRMS (EI): calc. for $C_{15}H_{21}N_3$ (M+) 244.1808, found 244.1807. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.

Ethyl 4-[4-(2,5-dimethylphenyl)piperazin-1-yl]butanoate **9d**
Yellow paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.05 (d, *J* = 7.3 Hz, 1H), 6.85–6.77 (m, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.95–2.91 (m, 4H), 2.70–2.59 (m, 4H), 2.49–2.25 (m, 10H), 1.94–1.83 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); NMR ^{13}C (50 MHz, $CDCl_3$) 173.5, 151.3, 136.0, 130.8, 129.2, 123.6, 119.7, 60.2, 57.7, 53.6, 51.6, 32.2, 22.1, 21.1, 17.4, 14.2; HRMS (EI): calc. for $C_{18}H_{28}N_2O_2$ (M+) 305.2224, found 305.2221.

3-[4-(3-(Trifluoromethyl)phenyl)piperazin-1-yl]propanenitrile **11c**
Translucent paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.38–7.26 (m, 1H), 7.10–7.04 (m, 3H), 3.27–3.16 (m, 4H), 3.06–3.01 (m, 4H), 2.78–2.51 (m, 4H); NMR ^{13}C (50 MHz, $CDCl_3$) 151.2, 131.4 (q, *J* = 31.8 Hz), 129.6, 124.3 (q, *J* = 272.2 Hz), 118.8, 118.5, 115.9 (q, *J* = 4.0 Hz), 112.2 (q, *J* = 3.7 Hz), 53.2, 52.5, 48.6, 15.9; HRMS (EI): calc. for $C_{14}H_{16}N_3F_3$ (M+) 284.1369, found 284.1373. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.

Ethyl 4-[4-(3-(trifluoromethyl)phenyl)piperazin-1-yl]butanoate **11d**
Translucent paste, NMR ^{1}H (200 MHz, $CDCl_3$) 7.36–7.28 (1H, m), 7.09–7.02 (3H, m), 4.12 (q, *J* = 7.17 Hz, 2H),3.20–3.25 (4H, m), 2.63–2.58 (4H, m), 2.47–2.32 (4H, m), 1.92–1.81 (2H, m), 1.24 (t, *J* = 7.17 Hz, 3H); NMR ^{13}C (50 MHz, $CDCl_3$) 173.4, 151.3, 131.3 (q, *J* = 31.6 Hz), 129.4, 124.3 (q, *J* = 272.6 Hz), 118.5, 115.6 (q, *J* = 3.8 Hz), 112.0 (q, *J* = 4.0 Hz), 60.2, 57.4, 58.8, 48.4, 32.1, 21.9, 14.15; HRMS (EI): calc. for $C_{17}H_{23}N_2O_2F_3$ (M+) 345.1784, found 345.1783. The ^{1}H NMR, ^{13}C NMR, and MS were identical to those of the known compound.