Supplementary data

Preparation of compounds

All chemicals and solvents were obtained from commercial suppliers and used without further purification. Reactions were monitored by thin layer chromatography. Melting points were determined on a Büchi 530 apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer 833 spectrophotometer. ^{1}H NMR spectra were taken in Deuteriochloroform and recorded on a Bruker DRX 400 (400 MHz) spectrometer, and the spectra are reported in δ. ^{13}C NMR spectra were taken at 100 MHz Bruker DRX 400 spectrometer, respectively. Tetramethylsilane was used as internal standard. Microanalyses were carried out by the NCSR Demokritos, Greece, and the results obtained had a maximum deviation of ±0.4% from the theoretical value.

3-Cyclopentyl-1-adamantanecarboxylic acid (**9**) was prepared by the method we have previously described[20]. 3-Pheny-1-adamantanecarboxylic acid (**11**) was prepared by a modified Stetter and Mayer method[21], using aluminum chloride instead of aluminum bromide.

Compound 10: 3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decanemethanol

To a stirred suspension of $LiAlH_4$ (4.0 g, 0.11 mol) in anhydrous THF (150 mL) a solution of carboxylic acid **9**[20] (6.3 g, 0.03 mol) in anhydrous THF (40 mL) was added dropwise. The reaction mixture was stirred for three hours at room temperature and then hydrolyzed, under cooling, by the careful sequential addition of ethanol, water and sodium hydroxide solution. The inorganic materials formed were removed by filtration and the filtrate was concentrated *in vacuo*. Water was added to the residue and the mixture was extracted with ether. The combined ethereal extracts were washed with water, dried over Na_2SO_4 and evaporated to give 6.1 g (yield 96%) of alcohol **10** as an oil. Bp 115-117 ^{o}C/0.03 mm Hg; IR (film): ν(OH) 3350-3200 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.12-1.58 (m, 22H, 2,4,6,8,9,10-H, 1,2,3,4,5-H$_c$, OH), 1.92-2.02 (m, 2H, 5,7-H), 3.12 (s, 2H, *a*-H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 25.58 (3,4-C$_c$), 25.82 (2,5-C$_c$), 28.35 (5,7-C), 34.54 (3-C), 35.29 (1-C), 37.13 (6-C), 39.06 (4,10-C), 40.18 (8,9-C), 42.09 (2-C), 51.42 (1-C$_c$), 73.95 (*a*-C); Anal. Calcd. for $C_{16}H_{26}O$ (%): C, 81.99; H: 11.18; found, C: 81.72, H: 11.23.

Compound 8a: 3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decanecarboxaldehyde

To a stirred solution of pyridinium chlorochromate (PCC) (5.5 g, 20 mmol) in dry dichloromethane (35 mL) a solution of alcohol **10** (4 g, 17 mmol) in dry dichloromethane (10 mL) was added in one portion. The reaction mixture was stirred under argon atmosphere at room temperature for 1.5 h, then dry ether (100 mL) was added and the mixture was treated and filtrated through a short column of silica gel. The filtrate was concentrated under vacuum and a mixture of dry ether (100 mL) and *n*-pentane (50 mL) was added into the residue. The solution thus obtained was filtrated through another short column of silica gel and the filtrate was evaporated to give 3.2 g (yield 88%) of carboxaldehyde **6a** as a pale oil, which was used without further purification for the next step. ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.74-1.05 (br. m, 4H, 3,4-H$_c$), 1.18-1.35 (br. m, 4H, 2,5-H$_c$), 1.39-1.72 (dm, 13H, 2,4,6,8,9,10-H, 1-H$_c$), 2.13 (br. s, 2H, 5,7-H), 9.34 (s, 1H, *a*-H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 25.51 (3,4-C$_c$), 25.75 (2,5-C$_c$), 28.02 (5,7-C), 34.14 (3-C), 35.94 (4,10-C), 36.53 (6-C), 37.13 (1-C), 38.79 (2-C), 39.69 (8,9-C), 51.25 (1-C$_c$), 206.16 (C=O); IR (film): ν(C=O) 1722 cm^{-1}.

Compound 12: 3-Phenyl-1-tricyclo[3.3.1.1^{3,7}]decanemethanol

Alcohol **12** was prepared by reduction of carboxylic acid **11**[21] with the aid of $LiAlH_4$ following the same procedure for the preparation of alcohol **10** from carboxylic acid **9**. Yield almost quantitative. Mp 67-68 ^{o}C; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.42-1.50 (m, 5H, 4,10-H, OH), 1.59 (br. s, 2H, 2-H), 1.62-1.65 (complex m, 2H, 6-H), 3.21 (s, 2H, *a*-H), 7.08-7.09 (m, 1H, 4-H$_{ar}$), 7.11-7.39 (m, 4H, 2,3,5,6-H$_{ar}$); ^{13}C-NMR ($CDCl_3$) δ (ppm): 28.87 (5,7-C), 35.60 (3-C), 36.28 (6-C), 36.60 (1-C), 38.26 (4,10-C), 42.71 (8,9-C), 44.69 (2-C), 73.52 (*a*-C), 124.82 (3,5-C$_{ar}$), 125.62 (4-C$_{ar}$), 128.10 (2,6-C$_{ar}$), 156.56 (1-C$_{ar}$); IR (nujol): ν(OH) 3325 cm^{-1}; Anal. Calcd. for $C_{17}H_{22}O$ (%): C, 84.25; H, 9.15; found (%) C, 84.35; H, 9.26.

Compound 8b: 3-Phenyl-1-tricyclo[3.3.1.1^{3,7}]decanecarboxaldehyde

Carboxylaldehyde **8b** was prepared by oxidation of alcohol **12** with the aid of PCC in a similar manner as for the preparation of aldehyde **8a**. Yield 70% of a pale crystalline solid, which was used without further purification. Mp 57-58 ^{o}C; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.65-1.73 (m, 6H, 4,6,10-H), 1.78-1.90 (m, 4H, 8,9-H), 1.80 (br. s, 2H, 2-H), 2.21-2.22 (m, 2H, 5,7-H), 7.11-7.15 (m, 1H, 4-H$_{ar}$), 7.25-7.30 (m, 4H, 2,3,5,6-H$_{ar}$), 9.33 (s, 1H, *a*-H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 27.89 (5,7-C), 35.24 (4,10-C), 35.71 (6-C), 36.03 (3-C), 40.94 (2-C), 41.88 (8,9-C), 45.73 (1-C), 124.59 (3,5-C$_{ar}$), 125.82 (4-C$_{ar}$), 128.07 (2,6-C$_{ar}$), 149.74 (1-C$_{ar}$), 205.05 (C=O); IR (nujol): ν(C=O) 1721 cm^{-1}.

Compound 6a: *a*-Amino-3-cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decaneacetonitrile hydrochloride

A mixture of carboxaldehyde **8a** (1.8 g, 7.6 mmol), trimethylsilylcyanide (944 mg, 9.5 mmol) and a catalytical amount of zinc iodide was stirred until the appearance of a yellow cloud. Then chloroform (3 mL) and a saturated solution of methanol in gaseous ammonia (6.5 mL) were added. Dry gaseous ammonia was bubbled into the mixture for ten minutes and the stirring was continued in a sealed tube at 70-75 ^{o}C for 20 h. The solvents were evaporated, water was added into the residue and the mixture was extracted with ether. The combined ethereal extracts were washed with water, dried over Na_2SO_4 and evaporated. The residue was transformed to hydrochloride. Yield 1.38 g (61%) of hydrochloride. Mp 198-199 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.16 (br. s, 2H, 3,4-H$_{c,ax}$), 1.25-1.50 (complex m, 19H, 2,4,6,8,9,10-H, 3,4-H$_{c,eq}$, 1,2,5-H$_c$), 1.99 (s, 2H, 5,7-H), 4.27 (s, 1H, *a*-H), 9.25 (br. s, 3H, NH_3); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.88 (3,4-C$_c$), 25.03 (2,5-C$_c$), 27.47 (5,7-C), 34.07 (3-C), 35.31 (6-C), 35.53 (1-C), 36.78 (4-C), 36.95 (10-C), 38.53 (1-C), 39.78 (2-C), 50.03 (1-C$_c$), 50.41 (*a*-C), 115.23 (CN); Anal. Calcd. for $C_{17}H_{27}ClN_2$ (%): C, 69.25; H, 9.23; N, 9.50; found (%) C, 69.34; H, 9.36; N, 9.46.

Compound 6b: *a*-Methylamino-3-cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decaneacetonitrile hydrochloride

To a stirred suspension of sodium cyanide (588 mg, 12 mmol) and methylamine hydrochloride (810 mg, 12 mmol) in a mixture of DMSO:H_2O, 9:1 (5 mL), a solution of carboxaldehyde **8a** (1.4 g, 6 mmol) in DMSO (10 mL) was added and the reaction mixture was stirred at room temperature, under an argon atmosphere for 48 h and then at 60 ^{o}C for 7 h. Then, water was added and the mixture was extracted with ether. The combined ethereals were washed with water, dried over Na_2SO_4 and evaporated. The residue was transformed to hydrochloride. Yield 1.11 g (60%) of hydrochloride. Mp 179-182 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.21-1.32 (br. s, 2H, 3,4-H$_{c,ax}$), 1.35-1.70 (very complex m, 19H, 2,4,6,8,9,10-H, 3,4-H$_{c,eq}$, 5,6-H$_c$), 2.08 (s, 2H, 5,7-H), 2.68 (s, 3H, CH_3), 3.26-3.78 (very br. s, 1H, NH), 4.51 (s, 1H, *a*-H), 9.55-10.50 (very br. s, 1H, NH);

^{13}C-NMR (DMSO-d_6) δ (ppm): 25.00 (3,4-C_c), 25.12 (2,5-C_c), 27.61 (5,7-C), 33.38 (CH_3), 34.23 (3-C), 35.38 (6-C), 36.13 (1-C), 37.43 (4-C), 37.70 (10-C), 38.61 (8,9-C), 40.48 (2-C), 50.53 (1-C_c), 59.64 (*a*-C), 114.21 (CN); Anal. Calcd. for $C_{18}H_{29}ClN_2$ (%): C, 69.99; H, 9.46; N, 9.07; found (%) C, 70.32; H, 9.32; N, 9.10.

Compound 6c: *a*-Amino-3-phenyl-1-tricyclo[3.3.1.1^{3,7}] decaneacetonitrile hydrochloride

Aminonitrile **6c** was synthesized from carboxaldehyde **8b** in a similar method as for the preparation of nitrile **6a**. Yield 78%. Mp 200-202 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.56-1.64 (m, 2H, 6-H), 1.66-1.76 (complex m, 6H, 2,4,10-H), 1.78-1.88 (complex m, 4H, 8,9-H), 2.21 (br. s, 2H, 5,7-H), 4.46 (s, 1H, *a*-H), 7.18-7.20 (m, 1H, 4-H_{ar}), 7.31-7.33 (m, 2H, 2,6-H_{ar}), 7.38-7.39 (m, 2H, 3,5-H_{ar}), 9.10 (s, 3H, NH_3); ^{13}C-NMR (DMSO-d_6) δ (ppm): 27.96 (5,7-C), 34.72 (6-C), 36.09 (1-C), 36.26 (3-C), 36.34 (4-C), 36.54 (10-C), 41.30 (8-C), 41.38 (9-C), 42.40 (2-C), 50.05 (*a*-C), 115.25 (CN), 124.76 (3,5-C_{ar}), 125.90 (4-C_{ar}), 128.18 (2,6-C_{ar}), 149.35 (1-C_{ar}); Anal. Calcd. for $C_{18}H_{23}ClN_2$ (%): C, 71.39; H, 7.66; N, 9.25; found (%) C, 71.45; H, 7.73; N, 9.51.

Compound 6d: *a*-Methylamino-3-phenyl-1-tricyclo [3.3.1.1^{3,7}]decaneacetonitrile hydrochloride

Aminonitrile 5d was prepared from carboxaldehyde **8b** in a similar way as for aminonitrile **6b**. Yield 90%. Mp 154-155 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.61-1.70 (m, 2H, 6-H), 1.74-1.77 (m, 4H, 4,10-H), 1.84-1.87 (m, 4H, 8,9-H), 1.94-1.97 (m, 2H, 2-H), 2.22 (br. s, 2H, 5,7-H), 2.71 (s, 3H, CH_3), 4.62 (s, 1H, *a*-H), 7.18-7.21 (m, 1H, 4-H_{ar}), 7.30-7.34 (m, 2H, 2,6-H_{ar}), 7.40-7.42 (m, 2H, 3,5-H_{ar}), 10.13 (br. s, 2H, NH_2); ^{13}C-NMR (DMSO-d_6) δ (ppm): 27.99 (5,7-C), 33.38 (CH_3), 34.68 (6-C), 36.40 (1-C), 36.58 (3-C), 36.79 (4-C), 37.18 (10-C), 41.26 (8-C), 41.33 (9-C), 42.87 (2-C), 59.51 (*a*-C), 114.11 (CN), 124.78 (3,5-C_{ar}), 125.90 (4-C_{ar}), 128.17 (2,6-C_{ar}), 149.27 (1-C_{ar}); Anal. Calcd. for $C_{19}H_{25}ClN_2$ (%): C, 72.02; H, 7.95; N, 8.84; found (%) C, 72.22; H, 8.06; N, 8.79.

Compound 6e: 3-Cyclopentyl-*a*-phenylamino-1-tricyclo[3.3.1.1^{3,7}]decaneacetonitrile

A mixture of carboxaldehyde **8a** (1.1 g, 4.7 mmol), aniline (338 mg, 4.7 mmol) and trimethylsilylcyanide (482 mg, 4.9 mmol) in acetonitrile (8 mL) was stirred under argon, at room temperature for 45 h. Then a saturated solution of ammonium chloride was added and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with water, dried over Na_2SO_4 and evaporated. The residue was treated with ether-*n*-pentane and the mixture was kept in refrigeration overnight. Nitrile **6e** was obtained by filtration and triturated with cold *n*-pentane. Yield 1.1 g (70%). Mp 120-122 ^{o}C (Et_2O-*n*-pentane); ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.27-1.72 (very complex m, 22H, 1,2,3,4,5-H_c, 2,4,6,8,9,10-H, NH), 2.15 (s, 2H, 5,7-H), 3.85 (s, 1H, *a*-H), 6.72-6.74 (m, 2H, 2,6-H_{ar}), 6.83-6.87 (m, 1H, 4-H_{ar}), 7.22-7.26 (m, 2H, 3,5-H_{ar}); ^{13}C-NMR ($CDCl_3$) δ (ppm): 25.61 (3,4-C_c), 25.71 (2,5-C_c), 28.59 (5,7-C), 34.96 (3-C), 36.50 (6-C), 37.09 (1-C), 38.68 (4,10-C), 39.53 (8-C), 39.58 (9-C), 41.99 (2-C), 51.22 (1-C_c), 57.27 (*a*-C), 114.41 (2,6-C_{ar}), 118.49 (CN), 120.03 (4-C_{ar}), 129.65 (3,5-C_{ar}), 145.73 (1-C_{ar}); Anal. Calcd. for $C_{23}H_{30}N_2$ (%): C, 82.59; H, 9.04; N, 8.37; found (%) C, 82.76; H, 9.13; N, 8.46.

Compound 5a: 1-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-1,2-ethanediamine dihydrochloride

To a solution of aminonitrile hydrochloride **6a** (2 g, 6.8 mmol) in methanol (80 mL) and saturated ethanolic hydrogen chloride (3 mL), Adams-type PtO_2 (200 mg) was added and the mixture was hydrogenated at 60 ^{o}C under a pressure of 50-60 psi for 4 h. Then, the catalyst was filtered off and the filtrate was evaporated under vacuum to give 2.3 g of the diamine dihydrochloride **5a**. Yield almost quantitative. Mp 248-250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.24-1.61 (complex m, 21H, 2,4,6,8,9,10-H, 1,2,3,4,5-H_c), 2.01 (s, 2H, 5,7-H), 2.92 (m, 1H, *a*-H), 3.05 (m, 1H, *a*-H), 3.27 (m, 1H, *b*-H), 8.52 (s, 3H, NH_3), 8.74 (s, 3H, NH_3); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.89 (3,4-C_c), 25.08 (2,5-C_c), 27.59 (5,7-C), 33.93 (3-C), 35.10 (1-C), 35.52 (6-C), 36.41 (4-C), 36.67 (10-C), 37.94 (*b*-C), 38.62 (8-C), 38.72 (9-C), 39.72 (2-C), 50.60 (1-C_c), 57.97 (*a*-C). Dihydrochloride **5a** was treated with 50% until strong alkaline reaction and the mixture was extracted with ether. The combined ethereal extracts were washed with brine, dried over Na_2SO_4 and evaporated to dryness. The base was used as such to the next step immediately.

Compound 5b: 1-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-*N*^{1}-methyl-1,2-ethanediamine dihydrochloride

Diamine dihydrochloride **5b** was prepared by hydrogenation of nitrile **6b**, in a similar manner as for the preparation of diamine dihydrochloride **5a**. Yield almost quantitative. Mp 192-194 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.27-1.63 (complex m, 21H, 2,4,6,8,9,10-H, 1,2,3,4,5-H_c), 2.01 (s, 2H, 5,7-H), 2.68 (s, 3H, CH_3), 2.99 (m, 1H, *a*-H), 3.10-3.22 (dm, 2H, *b*-H), 8.00-9.20 (very br. s, 5H, NH_3,NH_2) ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.00 (3,4-C_c), 25.19 (2,5-C_c), 27.73 (5,7-C), 34.08 (3-C), 34.74 (CH_3), 35.52 (6-C), 35.10 (1-C), 36.52 (4-C, *b*-C),), 36.76 (10-C), 38.23 (8,9-C), 39.69 (2-C), 50.71 (1-C_c), 67.07 (*a*-C).

Compound 5c: 1-(3-Cyclohexyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-1,2-ethanediamine dihydrochloride

Diamine dihydrochloride **5c** was prepared by hydrogenation of aminonitrile hydrochloride **6c** in methanol, in the presence of saturated ethanolic hydrogen chloride and Adams-type PtO_2, at 60 ^{o}C under a pressure of 55 psi for 8 h. Yield almost quantitative. Mp 210-212 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.80-0.92 (m, 3H, 1,3,5-$H_{cx,ax}$), 1.03-1.16 (m, 3H, 2,4,6-$H_{cx,ax}$), 1.21-1.24 (~d, 1H, 2-H_{ax}), 1.36-1.44 (m, 5H, 2-H_{eq},8,9-H), 1.52 (br. s, 6H, 4,6,10-H), 1.58-1.62 (~d, 2H, 2,6-$H_{cx,eq}$), 1.72-1.74(~d, 3H, 3,4,5-$H_{cx,eq}$), 2.02 (br. s, 2H, 5,7-H), 2.92-2.95 (m, 1H, *b*-H), 3.03 (m, 1H, *a*-H), 3.25-3.28 (m, 1H, *b*-H), 8.49 (br. s, 3H, NH_3), 8.70 (br. s, 3H, NH_3); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.63 (3,5-C_x), 26.37 (4-C_x), 26.65 (2,6-C_x), 27.83 (5,7-C), 34.53 (3-C), 35.32 (1-C), 35.67 (6-C), 36.48 (4-C), 36.74 (10-C), 37.86 (8-C), 38.04 (9-C, *b*-C), 39.46 (2-C), 47.88 (1-C_x), 58.16 (*a*-C).

Compound 5d: 1-(3-Cyclohexyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-*N*^{1}-methyl-1,2-ethanediamine dihydrochloride

Diamine dihydrochloride **5d** was prepared by hydrogenation of aminonitrile hydrochloride **6d** in a similar manner and under the same conditions as for diamine hydrochloride **5c**. Yield almost quantitative. Mp 176-177 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.85-1.06 (m, 3H, 1,3,5-$H_{cx,ax}$), 1.08-1.11 (m, 3H, 2,4,6-$H_{cx,ax}$) 1.37-1.74 (very complex m, 17H, 2,3,4,5,6-$H_{cx,eq}$, 2,4,6,8,9,10-H), 2.03 (s, 2H, 5,7-H), 2.70 (s, 3H, CH_3), 3.10 (m, 1H, *a*-H), 3.15-3.17 (m, 1H, *b*-H), 3.25 (m, 1H, *b*-H), 7.80-8.23 (br. s, 1H, NH), 8.73 (br. s, 3H, NH_3), 9.62 (br. s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.64 (3,5-C_x), 26.34 (4-C_x), 27.32 (2,6-C_x), 27.84 (5,7-C), 34.39 (3-C), 36.54 (1-C), 35.47 (CH_3), 36.47 (6-C), 37.24 (4-C), 37.53 (10-C), 38.76 (8,9-C, *b*-C), 40.17 (2-C), 47.86 (1-C_x), 67.06 (*a*-C).

Compound 5e: 1-(3-Phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1,2-ethanediamine dihydrochloride

Diamine hydrochloride **5e** was prepared by hydrogenation of methanolic solution of aminonitrile hydrochloride **6c**, in the presence of saturated ethanolic hydrogen chloride and Adams-type PtO_2 at ambient temperature under a pressure of 40-50 psi for 2h. Yield almost quantitative. Mp>250 ^{o}C

(EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.51-1.82 (very complex m, 12H, 2,4,6,8,9,10-H), 2.16 (s, 2H, 5,7-H), 2.95-3.00 (m, 1H, β-H), 3.12-3.13 (m, 1H, *a*-H), 3.33-3.37 (m, 1H, β-H), 7.16-7.20 (m, 1H, 4-H_{ar}), 7.29-7.33 (m, 2H, 2,6-H_{ar}), 7.37-7.42 (m, 2H, 3,5-H_{ar}), 8.52 (br. s, 3H, NH_3), 8.63 (br. s, 3H, NH_3); ^{13}C-NMR (DMSO-d_6) δ (ppm): 27.93 (5,7-C), 35.63 (1-C), 35.80 (6-C) 35.90 (4-C), 36.02 (10-C), 36.23 (3-C), 36.78 (β-C), 41.35 (8-C), 41.49 (9-C), 42.24 (2-C), 58.08 (*a*-C), 124.73 (3-C_{ar}), 124.87 (5-C_{ar}), 125.75 (4-C_{ar}), 128.04 (2-C_{ar}), 128.18 (6-C_{ar}), 149.49 (1-C_{ar}).

Compound 5f: N^1-Methyl-1-(3-phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1,2-ethanediamine dihydrochloride

Diamine dihydrochloride **5f** was prepared by hydrogenation of aminonitrile hydrochloride **6d** in a similar manner and under the same conditions as diamine dihydrochloride **4e**. Yield almost quantitative. Mp 177-178 °C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.40-1.86 (very complex m, 12H, 2,4,6,8,9,10-H), 2.03 (s, 2H, 5,7-H), 2.73 (s, 3H, CH_3), 3.05-3.10 (m, 1H, *a*-H), 3.15-3.28 (m, 1H, β-H), 3.30-3.38 (m, 1H, β-H), 7.16-7.19 (m, 1H, 4-H_{ar}), 7.29-7.32 (m, 2H, 2,6-H_{ar}), 7.42-7.44 (m, 2H, 3,5-H_{ar}), 8.68 (br. s, 3H, NH_3), 8.87 (br. s, 1H, NH), 9.63 (br. s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm): 27.91 (5,7-C), 34.74 (CH_3), 35.79 (1-C), 36.01 (6-C) 36.26 (β-C), 36.37 (3-C), 36.68 (4,10-C), 41.16 (8-C), 41.22 (9-C), 41.96 (2-C), 66.97 (*a*-C), 125.00 (3,5-C_{ar}), 125.65 (4-C_{ar}), 128.02 (2,6-C_{ar}), 146.66 (1-C_{ar}).

Compound 5g: N^1-Cyclohexyl-1-(3-cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1,2-ethanediamine dihydrochloride

Diamine dihydrochloride **5g** was prepared by hydrogenation of aminonitrile hydrochloride **6e** in a similar manner and under the same conditions as for the preparation of diamine dihydrochloride **5e** from aminonitrile hydrochloride **5c**. Yield almost quantitative. Mp 223-225 °C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.27-1.74 (very complex m, 26H, 2,4,6,8,9,10-H, 1,2,3,4,5-H_c, 2,3,4,5,6-$H_{cx,ax}$), 2.02 (s, 2H, 5,7-H), 2.09 (br. s, 2H, 3,5-$H_{cx,eq}$), 2.28-2.30 (m, 1H, 4-$H_{cx,eq}$), 2.41-2.52 (br. s, 2H, 2,6-$H_{cx,eq}$), 3.19-3.38 (complex m, 4H, *a*-H, β-H, 1-$H_{cx,ax}$), 7.75 (br. s, 1H, NH), 8.62 (br. s, 3H, NH_3), 9.57 (br. s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.08 (3-C_{cx}), 24.30 (5-C_{cx}), 24.70 (4-C_{cx}), 25.02 (3,4-C_c), 25.21 (2,5-C_c), 27.71 (5,7-C), 27.98 (2-C_{cx}), 28.96 (6-C_{cx}), 34.12 (3-C), 35.42 (6-C), 35.92 (1-C), 36.44 (4-C), 36.71 (10-C), 38.28 (*a*-C), 38.67 (8-C), 39.15 (9-C), 39.55 (2-C), 50.68 (1-C_c), 57.44 (β-C), 62.24 (1-C_{cx}).

Compound 5h: 1-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-N^1-phenyl-1,2-ethanediamine

To a stirred solution of aminonitrile **6e** (1 g, 3 mmol) in anhydrous THF (15 mL) a solution of borane in THF (18 mL, 1M, 18 mmol) was added dropwise, under cooling and argon atmosphere. The reaction mixture was refluxed gently under argon for 2 h. Then, water was added dropwise into the mixture at 0 °C until no foaming was further formed. The organic solvent was removed *in vacuo* and HCl 18% (30 mL) was added into the residue. The mixture was refluxed for 4h to hydrolyze the borazine complex, which was formed. Then, the mixture was cooled and alkalined by dropwise addition of NaOH 40%. The liberated base **5h** was extracted with ether, the combined ethereals were washed with water, dried over Na_2SO_4 and evaporated to give 800 mg (yield 79%) 5**h** as a pale viscous oil, which was used as such to the next step. ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.18-1.54 (very complex m, 24H, 2,4,6,8,9,10-H, 1,2,3,4,5-H_c, NH_2, NH), 1.98 (br. s, 2H, 5,7-H), 2.74 (s, 2H, β-H), 3.48-3.51 (s, 1H, *a*-H), 6.54-6.60 (m, 3H, 2,4,6-H_{ar}), 7.06-7.10 (m, 2H, 3,5-H_{ar}); ^{13}C-NMR ($CDCl_3$) δ (ppm): 25.59 (3,4-C_c), 25.80 (2,5- C_c), 28.89 (5,7-C), 34.57 (3-C), 34.74 (1-C), 37.02 (6-C), 40.05 (4,10-C), 40.79 (8,9-C), 43.96 (2-C), 51.40 (*a*-C, 1-C_c), 56.41 (β-C), 112.73 (2,6-C_{ar}), 116.87 (4-C_{ar}), 129.30 (3,5-C_{ar}), 149.37 (1-C_{ar}).

Compound 7: 3-Cyclopentyl-*N*-phenyl-1-tricyclo[3.3.1.1^{3,7}]decanemethanamine

To a stirred suspension of $LiAlH_4$ (160 mg, 4.2 mmol) in anhydrous THF (10 mL) a solution of aminonotrile **6e** (700 mg, 2.1 mmol) in anhydrous THF (10 mL) was added dropwise at 0 °C. The mixture was stirred at 0 °C for 1 h and then was hydrolyzed under cooling. The inorganic materials were removed by filtration and the filtrate was concentrated *in vacuo*. Water was added to the residue and the resulting mixture was extracted with ether. The combined ethereals were washed with water, dried over Na_2SO_4 and evaporated to give 690 mg of aniline **7** (yield almost quantitative) as a pale viscous oil. ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.28-1.31 (m, 4H, 3,4-H_c), 1.42-1.63 (complex m, 18H, 1,2,5-H_c, 2,4,6,8,9,10-H, NH), 2.07 (s, 2H, 5,7-H), 2.82 (s, 2H, *a*-H), 6.62-6.69 (m, 3H, 2,4,6-H_{ar}), 7.15-7.19 (m, 2H, 3,5-H_{ar}).

Compound 4a: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-4,5-dihydro-1*H*-imidazole

Diamine **5a** (340 mg, 1.3 mmol) was dissolved in absolute ethanol (10 mL) and formamidine acetate (170 mg, 1.7 mmol) was added into the solution. The mixture was stirred under an argon atmosphere at ambient temperature for 24 h and at 50 °C for another 24 h. The solvent was then evaporated under vacuum, the residue was treated with HCl 4% (30 mL) and the resulting mixture was washed with ethyl acetate. The aqueous phase was made alkaline with NaOH 4% and extracted with ethyl acetate. The organic phase was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give 251 mg (71%) of **4a**, which was then converted to its fumarate. Mp 202-204 °C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.76-0.85 (m, 1H, 2-H_{ax}), 1.05-1.10 (m, 2H, 3,4-$H_{c,ax}$), 1.23-1.55 (complex m, 18H, 1,2,5-H_c, 3,4- $H_{c,eq}$, 2-H_{eq}, 4,6,8,9,10-H), 2.01 (s, 2H, 5,7-H), 3.69-3.73 (m, 2H, 4-H_{im}), 3.79-3.84 (m, 1H, 5-H_{im}), 6.49 (s, 2H, CH=, fumarate), 8.44 (s, 1H, 2-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.01 (3,4-C_c), 25.18 (2,5-C_c), 27.64 (5,7-C), 33.83 (3-C), 35.47 (1-C), 36.04 (6-C), 36.23 (4-C), 36.42 (10-C), 39.09 (8-C), 39.30 (9-C), 39.74 (2-C), 43.97 (4-C_{im}), 50.68 (1-C_c), 66.03 (5-C_{im}), 135.00 (CH=, fumarate), 156.99 (2-C_{im}), 167.72 (CO_2H, fumarate); Anal. Calcd. for $C_{22}H_{32}N_2O_4$ (%): C, 68.01; H, 8.30; N, 7.21; found (%) C, 68.05; H, 8.17; N, 6.97.

Compound 4b: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-4,5-dihydro-1-methyl-1*H*-imidazole

Imidazoline **4b** was prepared by following the procedure used for the synthesis of **4a** by reacting diamine **5b** with formamidine acetate. Yield 70%. Fumarate Mp 173-175 °C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.15-1.18 (d, 1H, 2-H_{ax}), 1.25-1.65 (complex m, 20H, 2-H_{eq}, 1,2,3,4,5-H_c, 4,6,8,9,10-H), 2.01 (s, 2H, 5,7-H), 3.11 (s, 3H, CH_3), 3.49-3.54 (m, 1H, 5-H_{im}), 3.75-3.78 (~d, 2H, 4-H_{im}), 6.46 (s, 2H, CH=, fumarate), 8.02 (s, 1H, 2-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.47 (3,4-C_c), 24.66 (2,5-C_c), 27.19 (5-C), 27.25 (7-C), 33.33 (3-C), 35.42 (6-C), 36.31 (4-C), 36.56 (1-C, CH_3), 36.63 (10-C), 38.34 (8-C), 38.48 (9-C), 39.81 (2-C), 47.73 (4-C_{im}), 50.28 (1-C_c), 70.42 (5-C_{im}), 134.62 (CH=, fumarate), 159.89 (2-C_{im}), 177.21 (CO_2H, fumarate); Anal. Calcd. for $C_{23}H_{34}N_2O_4$ (%): C, 68.63; H, 8.51; N, 6.96; found (%) C, 68.35; H, 9.02; N, 6.93.

Compound 4c: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-2-methyl-1*H*-imidazole

Imidazoline **4c** was prepared by following the procedure used for the synthesis of **4a** by reacting diamine **5a** with acetamidine hydrochloride. Yield 67%. Mp 133-135 °C (Et_2O), hydrochloride 239-241 °C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.05-1.10 (m, 1H, 2-H_{ax}), 1.22-1.56 (complex m, 20H, 1,2,3,4,5-H_c, 2-H_{eq}, 4,6,8,9,10-H), 2.02 (br. s, 2H, 5,7-H), 2.19 (s, 3H, CH_3), 3.68-3.71 (m, 2H, 4-H_{im}), 3.77-3.81 (m, 1H, 5-H_{im}), 10.38 (s, 2H, 2xNH); ^{13}C-NMR (DMSO-d_6) δ (ppm): 11.84 (CH_3), 25.02 (3,4-C_c), 25.17 (2,5-

C_c), 27.61 (5,7-C), 33.83 (3-C), 35.48 (1-C), 36.00 (6-C), 36.24 (4,10-C), 39.04 (8-C), 39.26 (9-C), 39.93 (2-C), 43.96 (4-C_{im}), 50.70 (1-C_c), 66.10 (5-C_{im}), 167.33 (2-C_{im}); Anal. Calcd. for $C_{19}H_{31}ClN_2$ (%): C, 70.67; H, 9.68; N, 8.68; found (%) C, 70.32; H, 9.98; N, 8.54.

Compound 4d: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1,2-dimethyl-1*H*-imidazole

Imidazoline **4d** was prepared by following the procedure used for the synthesis of **4a** by reacting diamine **5b** with acetamidine hydrochloride. Yield 52%. ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.07-1.10 (~d, 1H, 2-H_{ax}), 1.16-1.20 (m, 4H, 2,3,4,5-$H_{c,ax}$), 1.26-1.43 (complex m, 14H, 1-H_c, 2,3,4,5- $H_{c,eq}$, 2-H_{eq}, 4,8,9,10-H), 1.52 (br. s, 2H, 6-H), 1.87 (s, 3H, 2-CH_3), 1.97 (br. s, 2H, 5,7-H), 2.80 (s, 3H, 1-CH_3), 2.86-2.91 (~t, 1H, 5-H_{im}), 3.52-3.56 (m, 2H, 4-H_{im}); ^{13}C-NMR ($CDCl_3$) δ (ppm): 14.73 (2-CH_3), 24.96 (3,4-C_c), 25.37 (2,5-C_c), 28.47 (5,7-C), 34.26 (3-C), 36.89 (6-C), 37.29 (1-CH_3), 37.60 (1-C), 38.11 (4-C), 38.35 (10-C), 39.73 (8-C), 39.90 (9-C), 41.58 (2-C), 51.33 (1-C_c), 53.70 (4-C_{im}), 73.34 (5-C_{im}), 166.20 (2-C_{im}); Hydrochloride, Mp 244-245 ^{o}C (EtOH-Et_2O); Anal. Calcd. for $C_{20}H_{33}ClN_2$ (%): C, 71.29; H, 9.87; N, 8.31; found (%) C, 71.45; H, 10.01; N, 8.35.

Compound 4e: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1*H*-2-imidazolamine

To a stirred solution of diamine **5a** (770 mg, 2.9 mmol) in dry dichloromethane (10 mL) a solution of cyanogen bromide (375 mg, 3.52 mmol) in dry dichloromethane (5 mL) was added dropwise and under cooling. Stirring was continued at ambient temperature and under an argon atmosphere for 48 h. The solvent was then evaporated under vacuum to leave a residue that was crystallized upon treating with anhydrous ether as hydrobromide. Yield 77%. Mp 224-225 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.03-1.06 (d, 1H, 2-H_{ax}), 1.19-1.46 (complex m, 18H, 1,2,3,4,5-H_c, 2-H_{eq}, 4,8,9,10-H), 1.54 (s, 2H, 6-H), 2.00 (s, 2H, 5,7-H), 3.35-3.55 (m, 3H, 4,5-H_{im}), 7.53 (s, 2H, NH_2), 7.85 (s, 1H, 1-H_{im}), 8.26 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.49 (3-C_c), 25.52 (4-C_c), 25.66 (2,5-C_c), 28.14 (5,7-C), 34.29 (3-C), 35.99 (1-C), 36.63 (6-C), 36.94 (4-C), 37.11 (10-C), 39.65 (8-C), 39.78 (9-C), 40.49 (2-C), 42.78 (4-C_{im}), 51.19 (1-C_c), 64.16 (5-C_{im}), 159.87 (2-C_{im}); Anal. Calcd. for $C_{18}H_{30}BrN_3$ x H_2O (%): C, 55.95; H, 8.35; N, 10.88; found (%) C, 55.78; H, 8.54; N, 10.73.

Compound 4f: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1-methyl-1*H*-2-imidazolamine

2-Aminoimidazoline **4f** was prepared by following the procedure used for the synthesis of **4e** by reacting diamine **5b** with cyanogen bromide. Hydrobromide, yield 57%. Mp 252-254 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.15-1.24 (m, 3H, 3,4-$H_{c,ax}$, 2-H_{ax}), 1.34-1.55 (complex m, 16H, 1,2,5-H_c, 3,4-$H_{c,eq}$, 2-H_{eq}, 4,8,9,10-H), 1.55 (s, 2H, 6-H), 2.01 (s, 2H, 5,7-H), 3.40-3.43 (m, 1H, 5-H_{im}), 3.48-3.50 (m, 2H, 4-H_{im}), 7.86 (s, 1H, 3-H_{im}), 7.90 (s, 2H, NH_2); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.88 (3,4-C_c), 25.05 (2,5-C_c), 27.54 (5-C), 27.59 (7-C), 33.67 (3-C), 35.60 (CH_3), 35.90 (6-C), 36.49 (4-C), 36.84 (10-C), 37.51 (1-C), 38.79 (8-C), 38.99 (9-C), 40.09 (2-C), 41.58 (4-C_{im}), 50.52 (1-C_c), 69.86 (5-C_{im}), 159.66 (2-C_{im}); Anal. Calcd. (%) for $C_{19}H_{32}BrN_3$: C, 59.68; H, 8.44; N, 10.99; Found (%) C, 59.31; H, 8.55; N, 10.87.

Compound 4g: 5-(3-Cyclohexyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1*H*-imidazole

Imidazoline **4g** was prepared by following the procedure used for the synthesis of **4a** by reacting diamine **5c** with formamidine acetate. Yield 45%. Hydrochloride, Mp 253-255 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.84-0.89 (m, 3H, 1,3,5-$H_{cx,ax}$), 1.04-1.14 (m, 3H, 2,4,6-$H_{cx,ax}$), 1.23-1.28 (~d, 1H, 2-H_{ax}), 1.31-1.41 (m, 5H, 2-H_{eq},8,9-H), 1.46-1.49 (~d, 2H, 2,6-$H_{cx,eq}$), 1.53 (br. s, 6H, 4,6,10-H), 1.58-1.72(m, 3H, 3,4,5-$H_{cx,eq}$), 2.01 (br. s, 2H, 5,7-H), 3.70-3.73 (m, 2H, 4-H_{im}), 3.80-3.85 (m, 1H, 5-H_{im}), 8.60 (s, 1H, 2-H_{im}), 10.63 (s, 1H, 1-H_{im}), 10.64 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.67 (3,5-C_x), 26.34 (4-C_x), 26.63 (2,6-C_x), 27.76 (5,7-C), 34.28 (3-C), 35.56 (1-C), 36.02 (6-C), 36.21 (4-C), 36.38 (10-C), 38.17 (8-C), 38.42 (9-C), 39.15 (2-C), 43.69 (4-C_{im}), 47.85 (1-C_x), 65.91 (5-C_{im}), 156.91 (2-C_{im}); Anal. Calcd. for $C_{19}H_{31}ClN_2$ (%): C, 70.67; H, 9.68; N, 8.68; found (%) C, 70.83; H, 9.78; N, 8.80.

Compound 4h: 5-(3-Cyclohexyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1*H*-2-imidazolamine

2-Aminoimidazoline **5h** was prepared by following the procedure used for the synthesis of **4e** by reacting diamine **5c** with cyanogen bromide. Hydrobromide, yield 85%. Mp 244-245 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.84-0.89 (m, 3H, 1,3,5-$H_{cx,ax}$), 1.04-1.14 (m, 3H, 2,4,6-$H_{cx,ax}$), 1.21-1.24 (~d, 1H, 2-H_{ax}), 1.32-1.42 (m, 5H, 2-H_{eq},8,9-H), 1.53 (br. s, 2H, 2,6-$H_{cx,eq}$), 1.58-1.61(m, 3H, 3,4,5-$H_{cx,eq}$), 1.71 (br. s, 6H, 4,6,10-H), 2.01 (s, 2H, 5,7-H), 3.44-3.50 (m, 3H, 4,5-H_{im}), 7.52 (br. s, 2H, NH_2), 7.83 (br. s, 1H, 1-H_{im}), 8.23 (br. s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.68 (3,5-C_x), 26.10 (4-C_x), 26.63 (2,6-C_x), 27.79 (5,7-C), 34.46 (3-C), 35.28 (1-C), 35.92 (6-C), 36.12 (4-C), 36.40 (10-C), 38.10 (8-C), 38.24 (9-C), 39.17 (2-C), 42.03 (4-C_{im}), 47.62 (1-C_x), 63.47 (5-C_{im}), 159.02 (2-C_{im}); Anal. Calcd. for $C_{19}H_{32}BrN_3$ (%): C, 59.68; H, 8.44; N, 10.99; found (%) C, 59.55; H, 8.79; N, 11.01.

Compound 4i: 5-(3-Cyclohexyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4.5-dihydro-1-methyl-1*H*-2-imidazolamine

2-Aminoimidazoline **4i** was prepared with the same procedure as for the synthesis of **4e** by the action of cyanogen bromide on the diamine **5d**. Hydrobromide, yield 77%. Mp>250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.82-0.90 (m, 3H, 1,3,5-$H_{cx,ax}$), 1.03-1.23 (m, 5H, 2,4,6-$H_{cx,ax}$, 2-H), 1.28-1.70 (very complex m, 15H, 2,3,4,5,6-$H_{cx,eq}$, 4,6,8,9,10-H), 2.08 (br. s, 2H, 5,7-H), 2.99 (s, 3H, CH_3), 3.38-3.50 (complex m, 3H, 4,5-H_{im}), 7.86 (s, 1H, 3-H_{im}) 7.91 (s, 2H, NH_2); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.84 (3,5-C_x), 26.50 (4-C_x), 26.80 (2,6-C_x), 27.98 (5,7-C), 34.41 (3-C), 35.88 (CH_3), 36.20 (6-C), 36.82 (4-C), 37.15 (10-C), 37.91 (1-C), 38.37 (8-C), 38.48 (9-C), 39.47 (2-C), 41.82 (4-C_{im}), 48.01 (1-C_x), 70.21 (5-C_{im}), 159.95 (2-C_{im}); Anal. calcd. for $C_{20}H_{34}BrN_3$ (%): C, 60.60; H: 8.65; N: 10.60; found (%) C, 60.46; H, 8.95; N, 10.37.

Compound 4j: 4,5-Dihydro-5-(3-phenyl-1-tricyclo [3.3.1.1^{3,7}]decyl)-1*H*-imidazole

Imidazoline **4j** was synthesized by the same method as for imidazoline **4a** by reacting diamine **5e** with formamidine acetate. Yield 60%. Hydrochloride Mp>250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.37-1.82 (very complex m, 12H, 2,4,6,8,9,10-H), 2.16 (s, 2H, 5,7-H), 3.70-3.74 (m, 1H, 5-H_{im}), 3.77-3.93 (m, 2H, 4-H_{im}), 7.15-7.19 (m, 1H, 4-H_{ar}), 7.29-7.32 (m, 2H, 2,6-H_{ar}), 7.37-7.39 (m, 2H, 3,5-H_{ar}), 8.60 (s, 1H, 2-H_{im}), 10.57 (s, 1H, 1-H_{im}), 10.68 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 27.96 (5,7-C), 35.27 (6-C), 35.57 (4-C) 35.73 (10-C), 35.93 (3-C), 36.01 (1-C), 41.60 (8-C), 41.89 (9-C), 42.33 (2-C), 43.73 (4-C_{im}), 65.75 (5-C_{im}), 124.75 (3,5-C_{ar}), 125.67 (4-C_{ar}), 128.05 (2,6-C_{ar}), 149.96 (1-C_{ar}), 157.01 (2-C_{im}); Anal. Calcd. for $C_{19}H_{25}ClN_2$ (%): C, 72.02; H, 7.95; N: 8.84; found (%) C, 72.32; H, 8.25; N, 8.90.

Compound 4k: 4,5-Dihydro-1-methyl-5-(3-phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1*H*-imidazoline

Imidazoline **4k** was synthesized by the same method as for imidazoline **4a** by reacting diamine **5f** with formamidine acetate. Yield 71%. Hydrochloride Mp>250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.40-1.88 (very complex m, 12H, 2,4,6,8,9,10-H), 2.16 (br. s, 2H, 5,7-H), 3.26 (s, 3H, CH_3), 3.78-3.87 (m, 2H, 4-H_{im}), 3.92-3.96 (m, 1H, 5-H_{im}),

7.16-7.19 (m, 1H, 4-H_{ar}), 7.29-7.32 (m, 2H, 2,6-H_{ar}), 7.38-7.40 (m, 2H, 3,5-H_{ar}), 8.58 (s, 1H, 2-H_{im}), 10.68 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 28.04 (5,7-C), 35.08 (6-C), 36.06 (4-C), 36.24 (10-C), 37.05 (CH_3), 37.36 (3-C), 38.26 (1-C), 41.43 (8,9-C), 42.19 (2-C), 45.52 (4-C_{im}), 70.54 (5-C_{im}), 124.79 (3,5-C_{ar}), 125.68 (4-C_{ar}), 128.08 (2,6-C_{ar}), 150.00 (1-C_{ar}), 159.73 (2-C_{im}); Anal. Calcd. for $C_{20}H_{27}ClN_2$ (%): C, 72.60; H, 8.22; N, 8.47; found (%) C, 72.80; H, 8.76; N, 8.42

Compound 4l: 4,5-Dihydro-2-methyl-5-(3-phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1*H*-imidazole

Imidazoline **4l** was prepared by following the procedure used for the synthesis of **4a** by reacting diamine **5e** with acetamidine hydrochloride. Yield 59%. Difumarate, Mp 142-143 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.33-1.83 (very complex m, 12H, 2,4,6,8,9,10-H), 2.16 (br. s, 2H, 5,7-H), 2.18 (s, 3H, CH_3), 3.69-3.88 (very complex m, 3H, 4,5-H_{im}), 6.50 (s, 4H, difumarate), 7.15-7.19 (m, 1H, 4-H_{ar}), 7.28-7.32 (m, 2H, 2,6-H_{ar}), 7.37-7.39 (m, 2H, 3,5-H_{ar}), 8.75-11.50 (very br. s, 5H, 4xCOOH,1-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 11.91 (CH_3), 28.01 (5,7-C), 35.37 (6-C), 35.42 (3-C), 35.81 (4,10-C), 38.23 (1-C), 41.62 (8-C), 41.98 (9-C), 42.62 (2-C), 44.20 (4-C_{im}), 66.07 (5-C_{im}), 124.78 (3,5-C_{ar}), 125.69 (4-C_{ar}), 128.08 (2,6-C_{ar}), 134.94 (CH=, difumarate), 150.10 (1-C_{ar}), 167.41 (2-C_{im}), 167.49 (C=O); Anal. Calcd. for $C_{28}H_{34}N_2O_4$ (%): C, 63.87; H, 6.51; N, 5.32; found (%) C, 63.93; H, 6.64; N, 5.48.

Compound 4m: 4,5-Dihydro-1,2-dimethyl-5-(3-phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1*H*-imidazole

Imidazoline **4m** was synthesized by the same method as for imidazoline **4a** by reacting diamine **5f** with acetamidine hydrochloride. Yield 95%. Hydrochloride, Mp 248-250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.45-1.87 (dm, 12H, 2,4,6,8,9,10-H), 2.16 (br. s, 2H, 5,7-H), 2.25 (s, 3H, 2-CH_3), 3.26 (s, 3H, 1-CH_3), 3.69-3.71 (m, 1H, 4-H_{im}), 3.74-3.81 (m, 1H, 5-H_{im}), 3.88-3.96 (m, 1H, 4-H_{im}), 7.16-7.19 (m, 1H, 4-H_{ar}), 7.29-7.33 (m, 2H, 2,6-H_{ar}), 7.38-7.40 (m, 2H, 3,5-H_{ar}), 10.71 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 11.86 (2-CH_3), 28.02 (5,7-C), 35.14 (6-C), 35.63 (1-CH_3), 35.78 (4-C), 36.05 (1,3,10-C), 41.53 (8,9-C), 42.06 (2-C), 43.75 (4-C_{im}), 71.54 (5-C_{im}), 124.77 (3,5-C_{ar}), 125.68 (4-C_{ar}), 128.08 (2,6-C_{ar}), 150.02 (1-C_{ar}), 168.38 (2-C_{im}); Anal. Calcd. for $C_{21}H_{29}ClN_2$ (%): C, 73.13; H, 8.47; N, 8.12; found (%) C, 73.31; H, 8.54; N, 7.98.

Compound 4n: 4,5-Dihydro-5-(3-phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1*H*-2-imidazolamine

2-Aminoimidazoline **4n** was prepared by following the procedure used for the synthesis of **4e** by reacting diamine **5e** with cyanogen bromide. Hydrobromide, yield 82%. Mp>250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.31-1.70 (dm, 10H, 4,6,8,9,10-H), 1.79 (br. s, 2H, 2-H), 2.15 (s, 2H, 5,7-H), 3.46-3.54 (m, 2H, 4-H_{im}), 3.59-3.63 (m, 1H, 5-H_{im}), 7.15-7.19 (m, 1H, 4-H_{ar}), 7.29-7.33 (m, 2H, 2,6-H_{ar}), 7.36-7.38 (m, 2H, 3,5-H_{ar}), 7.52 (s, 2H, NH_2), 7.86 (s, 1H, 1-H_{im}), 8.28 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 28.01 (5,7-C), 35.42 (6-C), 35.71 (4-C), 36.01 (1,3,10-C), 41.73 (2-C), 41.91 (4-C_{im}), 42.33 (8-C), 42.82 (9-C), 63.59 (5-C_{im}), 124.71 (3,5-C_{ar}), 125.63 (4-C_{ar}), 128.10 (2,6-C_{ar}), 150.07 (1-C_{ar}), 159.85 (2-C_{im}); Anal. Calcd. for $C_{19}H_{26}BrN_3$ (%): C, 60.64; H, 6.96; N, 11.17; found (%) C, 60.43; H, 7.23; N, 11.18.

Compound 4o: 4,5-Dihydro-1-methyl-5-(3-phenyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-1*H*-2-imidazolamine

2-Aminoimidazoline **4o** was prepared by the same procedure as for the synthesis of **4e** by the action of cyanogen bromide on the diamine **5f**. Hydrobromide, yield 85%. Mp>270 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.40-1.84 (complex dm, 12H, 2,4,6,8,9,10-H), 2.15 (s, 2H, 5,7-H), 3.02 (s, 3H, 3CH_3), 3.48-3.58 (m, 3H, 4,5-H_{im}), 7.15-7.19 (m, 1H, 4-H_{ar}), 7.29-7.32 (m, 2H, 2,6-H_{ar}), 7.36-7.38 (m, 2H, 3,5-H_{ar}), 7.89 (s, 1H, 3-H_{im}), 7.92 (s, 2H, NH_2); ^{13}C-NMR (DMSO-d_6) δ (ppm): 28.02 (5,7-C), 35.28 (6-C), 35.70 (CH_3), 36.02 (1,3-C), 36.39 (4,10-C), 36.98 (2-C), 41.67 (4-C_{im}), 42.48 (8,9-C), 64.91 (5-C_{im}), 124.70 (3,5-C_{ar}), 125.67 (4-C_{ar}), 128.10 (2,6-C_{ar}), 150.06 (1-C_{ar}), 159.81 (2-C_{im}); Anal. Calcd. for $C_{20}H_{28}BrN_3$ (%): C, 61.54; H, 7.23; N, 10.16; found (%) C, 61.52; H, 7.62; N, 10.54.

Compound 4p: 1-Cyclohexyl-5-(3-cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-4,5-dihydro-1*H*-imidazole

Imidazoline **4p** was prepared by the action of formamidine acetate on diamine **5g** in a similar manner as for the preparation of **4a**.Yield 40%. Hydrochloride, Mp>250 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.22-2.14 (very complex m, 33H, 1,2,3,4,5-H_c, 2,3,4,5,6-H_{cx},2,4,5,6,7,8,9,10-H,), 3.24-3.30 (br. s, 1H, 1-H_{cx}), 3.80-3.83 (m, 1H, 5-H_{im}), 3.91-3.97 (m, 2H, 4-H_{im}), 8.82 (s, 1H, 2-H_{im}), 10.96 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.53 (3,4,5-C_{cx}), 24.57 (3,4-C_c), 25.26 (2,5-C_c), 27.59 (5,7-C), 30.86 (2,6-C_{cx}), 33.78 (3-C), 34.26 (6-C), 35.83 (4-C), 36.10 (10-C), 37.73 (1-C), 38.42 (8-C), 39.31 (9-C), 39.83 (2-C), 45.73 (4-C_{im}), 50.51 (1-C_c), 58.38 (1-C_{cx}), 68.48 (5-C_{im}), 157.19 (2-C_{im}); Anal. Calcd. for $C_{24}H_{39}ClN_2$ (%): C, 73.72; H, 10.05; N, 7.16; found (%) C, 74.01; H, 10.12; N, 7.23.

Compound 4q: 1-Cyclohexyl-5-(3-cyclopentyl-1-tricyclo[3.3.1.1^{3,7}]decyl)-4,5-dihydro-1*H*-2-imidazolamine

2-Aminoimidazoline **4q** was prepared by the action of cyanogen bromide on diamine **5g** in a similar manner as for the preparation of **4e**. Hydrobromide, yield 45%. Mp 146-148 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.08-1.68 (very complex m, 27H, 1,2,3,4,5-H_c, 3,4,5-H_{cx},2,4,6,8,9,10-H,), 1.74-1.89 (complex m, 4H, 2,6-H_{cx}), 2.01 (br. s, 2H, 5,7-H), 3.16-3.21 (m, 1H, 1-H_{cx}), 3.46-3.53 (m, 1H, 4,5-H_{im}), 7.95 (br. s, 2H, NH_2), 8.23 (s, 1H, 3-H_{im}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.33 (4-C_{cx}), 25.02 (3,4-C_c), 25.31 (2,5-C_c), 25.53 (3-C_{cx}), 26.00 (5-C_{cx}), 27.65 (5,7-C), 29.27 (2-C_{cx}), 30.24 (6-C_{cx}), 33.78 (3-C), 35.87 (6-C), 36.07 (4-C), 36.50 (10-C), 37.39 (1-C), 38.64 (8-C), 39.63 (9-C), 40.18 (2-C), 42.09 (4-C_{im}), 50.65 (1-C_c), 59.92 (1-C_{cx}), 68.45 (5-C_{im}), 157.75 (2-C_{im}); Anal. Calcd. for $C_{24}H_{40}BrN_3$ (%): C, 63.99; H, 8.95; N, 9.33; found (%) C, 64.06; H, 9.05; N, 9.23.

Compound 4r: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1-phenyl-1*H*-imidazole

Imidazoline **4r** was prepared by the action of cyanogen bromide on diamine **5h** in a similar manner as for the preparation of **4a**. After removal of ethanol from the reaction mixture the residue was dissolved in anhydrous ether and treated with an ethereal solution of hydrogen chloride to give the corresponding hydrochloride. Yield 40%. Mp 184-186 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.26-1.28 (~d, 1H, 2-H_{ax}), 1.37-1.62 (very complex m, 20H, 1,2,3,4,5-H_c, 2-H_{eq}, 4,6,8,9,10-H), 2.02 (s, 2H, 5,7-H), 2.93 (s, 3H, 4,5-H_{im}), 7.21 (br. s, 1H, 2-H_{im}), 7.38-7.40 (m, 5H, 2,3,4,5,6-H_{ar}); ^{13}C-NMR ($CDCl_3$) δ (ppm): 25.42 (3,4-C_c), 25.63 (2,5- C_c), 28.34 (5,7-C), 33.95 (3-C), 34.50 (1-C), 36.35 (6-C), 39.53 (4,10-C), 39.58 (8,9-C), 42.48 (2-C), 51.11 (1-C_c), 62.18 (4,5-C_{im}), 120.76 (4-C_{ar}), 125.56 (2-C_{im}) 129.85 (2,3,5,6-C_{ar}), 141.51 (1-C_{ar}); Anal. Calcd. for $C_{24}H_{33}ClN_2$ (%): C, 74.87; H, 8.64; N, 7.28; found (%) C, 74.48; H, 8.92; N, 7.34.

Compound 4s: 5-(3-Cyclopentyl-1-tricyclo[3.3.1.1^{3,7}] decyl)-4,5-dihydro-1-phenyl-1*H*-2-imidazolamine

2-Aminoimidazoline **4s** was prepared by following the procedure used for the synthesis of **4e** by reacting diamine **5h** with cyanogen bromide. Hydrobromide, yield 82%. Mp 186-188 ^{o}C (EtOH-Et_2O); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.26 (~d, 1H, 2-H_{ax}), 1.35-1.56 (very complex m, 20H, 1,2,3,4,5-H_c, 2-

H_{eq}, 4,6,8,9,10-H), 2.03 (s, 2H, 5,7-H), 2.72, 2.73 (s, s, 3H, 4,5-H_{im} rotamers), 3.26-6.00 (very br. s, 3H, NH_2, H_{im}), 6.64-6.66, 7.09 (~d, br. s, 1H, 4-H_{ar} rotamers), 7.17-7.18 (m, 2H, 2,6-H_{ar}), 7.33-7.37 (m, 2H, 3,5-H_{ar}); ^{13}C-NMR (DMSO-d_6) δ (ppm): 25.03 (3,4-C_c), 25.22 (2,5- C_c), 27.94 (5,7-C), 33.69 (3-C), 34.10 (1-C), 36.03 (6-C), 39.24 (4,8,9,10-C), 42.15 (2-C), 50.72 (1-C_c), 55.84, 60.42 (4,5-C_{im} rotamers), 114.79, 118.73 (4-C_{ar} rotamers), 123.53 (2-C_{im}) 129.46 (2,3,5,6-C_{ar}), 142.22 (1-C_{ar}); Anal. Calcd. for $C_{24}H_{34}BrN_3$ (%): C, 64.86; H, 7.71; N, 9.45; found (%) C, 64.99; H, 64.63; N, 9.46.

Parasite culturing and drug testing

Bloodstream form *Trypanosoma brucei* strain Lister 427 were cultured in HMI-9 medium (Invitrogen) supplemented with 10% v/v fetal bovine serum (BioSera), penicillin/streptomycin (GibcoBRL) and β–mercaptoethanol (Sigma) at 37°C in a 5% CO_2 atmosphere.[22] For inhibition assays, a preliminary screen was carried out to identify the activity range of each of the compounds. Informed by these data, parasites were then seeded into 96-well plates at $2.5x10^4$ ml^{-1} at a range of drug concentrations (at least 5 points per order of magnitude) and the plates incubated at 37 °C for 2 days. 20 µl AlamarBlue™ was then added to each well and the plates incubated at 37 °C overnight. Fluorescence was read in a Gemini Fluorimeter at λ_{ex} 530 nm and λ_{em} 585 nm with a cut-off set at 570 nm (Molecular Devices). To test for cytotoxicity, we used L6 cells, a rat skeletal muscle line. Assays were carried out in microtitre plates using a similar two step approach as outlined above. Cells were seeded at $1x10^4$ ml^{-1} and incubated for 6 days at 37 °C in a range of drug concentrations. 20 µl alamarBlue™ was then added to each well. After 8 h incubation, fluorescence was determined as described.

Table 2. Lipophilicity[a] of 5-(3-substituted-1-adamantyl)-2-imidazolines **4a-s**.

Cmpd	logP	PSA (Å^2)
4a	4.037	24.391
4b	4.281	15.602
4c	4.483	24.391
4d	4.728	15.602
4e	3.505	50.414
4f	3.75	41.625
4g	4.542	24.391
4h	4.011	50.414
4i	4.256	41.625
4j	3.849	24.391
4k	4.093	15.602
4l	4.295	24.391
4m	4.54	15.602
4n	3.317	50.414
4o	3.562	41.625
4p	6.187	15.602
4q	5.655	41.625
4r	5.979	15.602
4s	5.447	41.625

[a]molinspiration cheminformatics WebME 3.81

Notes and references

[a]*Faculty of Pharmacy, Department of Pharmaceutical Chemistry, University of Athens, Panepistimioupoli-Zografou, 157 71 Athens, Greece. Fax: +30 210 7274747; Tel: +30 210 7274527;E-mail: gfosc@pharm.uoa.gr*
[b]*Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, London WC1E 7HT, U.K. Fax : +44 207 6368739 ; Tel :+44 207 9272330 ; E-mail : john.kelly@lshtm.ac.uk*

20 G. Fytas, P. Marakos, N. Kolocouris, G.B. Foscolos, N. Pouli, A.Vamvakides, S. Ikeda and E. De Clercq, *Il Farmaco*, 1994, **49**, 641.
21 H. Stetter and J. Mayer, *Chem. Ber*., 1962, **95**, 667.
22 H. Hirumi and K. Hirumi, *J. Parasitol*, 1989, **75**, 985.