Supporting Information

A Chimeric Ligand Approach Leading to Potent Anti-Prion Active Acridine Derivatives: Design, Synthesis and Biological Investigation

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Content: Experimental and analytical data of compounds **2b-f**, **2i-k**, **2m-q**, **4a-c**, **5b,d,f,h,i, 6b,d,f,h,i**, elementary analysis data, HRMS data, HPLC purity data

1. Experimental and Analytical Data

5-(3-Chloropropyl)-10,11-dihydro-5H-dibenzo[b,f]azepine (4a) [12]

A solution of iminodibenzyl (6.0 g, 30.7 mmol) in dry toluene (30 mL) was added to a suspension of $NaNH_2$ (3.0 g, 76.9 mmol) in dry toluene (20 mL). After stirring at room temperature for 30 min, 1-bromo-3-chloropropane (9.70 g, 61.5 mmol) was added and stirring was continued for 21 h. The mixture was cooled in an ice bath and brine was added. Extraction with hexane (3 x 50 mL), drying (Na_2SO_4) and evaporation of the organic layer gave crude **4a** (8.30 g) as an oil, which was used without further purification. Analytical data of **4a**, see ref. [12]

10-(3-Chloropropyl)phenothiazine (4b) [13]

To an ice-cooled suspension of NaH (60%, 1.21 g, 30.3 mmol) in dry DMF (10 mL) was added phenothiazine (2.06 g, 10.34 mmol) and 1-bromo-3-chloropropane (3.42 g, 21.7 mmol). The suspension was stirred at room temperature for 4 h. The mixture was cooled in an ice bath and brine was added. Extraction with diethylether (3 x 50 mL), drying (Na_2SO_4) and evaporation of the organic layer was followed by purification of the resulting residue by flash chromatography (hexane) to give 1.94 g (90 %) of **4b** as a colorless solid. ^{1}H NMR (360 MHz) δ 2.24 (quint, J = 6.2 Hz, 2H); 3.66 (t, J = 6.2 Hz, 2H); 3.98-4.18 (m, 2H); 6.81-7.01 (m, 4H); 7.09-7.21 (m, 4H).

(3-Bromopropyl)diphenylamine (4c) [15]

This compound was synthesized starting from *N*-allyldiphenylamine which was readily prepared by allylation of diphenylamine in 83 % yield.[11] Thus, a solution of *N*-allyldiphenylamine (88 mg, 0.42 mmol) and 9-BBN (0.5 M in THF, 1.68 ml, 0.84 mmol) in THF (3 mL) was stirred at room temperature. for 18 h. The reaction mixture was treated with of 2N NaOH (0.35 mL) and aq. H_2O_2 (30%, 0.2 mL) followed by a saturated sodium bicarbonate solution (50 mL). The mixture was extracted with diethylether (3 x 20 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography (hexane/ethyl acetate 8/2) to give 67.3 mg (71 %) of *N*-(3-hydroxypropyl)diphenylamine as an oil. For analytical data, see ref.[14] Subsequent Appel-reaction was performed according to ref [15] to give **4c** in 80% yield. For analytical data, see ref. [15]

General procedure for preparation of piperazinylalkylnitriles.

To a suspension of 1-benzyloxycarbonylpiperazine (10.4 mmol) and Na_2CO_3 (20.8 mmol) in acetonitrile (10 mL) was added 4-bromobutyronitrile or 2-bromoacetonitrile (20.8 mmol), respectively. The mixture was heated to reflux temperature for 18 h and allowed to cool to room temperature. The salts were separated by filtration and the solvent was evaporated. Adding a saturated sodium bicarbonate solution (50 mL) to the residue was followed by extraction with dichloromethane (3 x 20 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. Only in case of benzyloxycarbonyl-protected 3-cyanopropylpiperazine the crude product was purified by flash chromatography. A solution of the alkylation products in MeOH was treated with $Pd(OH)_2$/C (10%) and stirred under H_2 atmosphere for 1h at ambient temperature. The mixture was filtrated (Celite®) and evaporated to obtain the crude cyanoalkyl piperazines.

4-Piperazin-1-yl-butyronitrile [16]

4-(3-Cyanopropyl)-1-benzyloxycarbonylpiperazine was prepared according to the general procedure and purified by flash chromatography (ethyl acetate/hexane 9/1) to give 87 % as a yellow oil. ^{1}H NMR (360 MHz) δ 1.82 (quint, *J* = 6.0 Hz, 2H); 2.34-2.49 (m, 8H); 3.46-3.54 (m, 4H); 5.13 (s, 2H); 7.29-7.37 (m, 5H). Cleavage of the protecting group as described above gave the title compound in 80% yield as a solid. ^{1}H NMR (360 MHz) δ 1.82 (quint, *J* = 6.9 Hz, 2H); 2.32-2.61 (m, 8H); 2.92-3.02 (m, 4H); 3.82 (bs, 1H).

4-Piperazin-1-yl-acetonitrile [17, 18]

1-Benzyloxycarbonyl-4-cyanomethylpiperazine was prepared according to the general procedure in 96 % yield. ^{1}H NMR (360 MHz) δ 2.52-2.60 (m, 4H); 3.53 (s, 2H); 3.54-3.60 (m, 4H); 5.14 (s, 2H); 7.31-7.39 (m, 5H). Cleavage of the protecting group as described above gave the title compound in 65 % yield as an oil. For analytical data, see ref. [17, 18]

4-Piperazin-1-yl-priopionitrile

4-Piperazin-1-yl-priopionitrile was purchased from Fluka, Riedel-de Haen®.

3-{4-[3-(10,11-Dihydrodibenzo[b,f]azepin-5-yl)propyl]piperazin-1-yl}propionitrile (5b).

The title compound was prepared according to the general procedure to give 5b (74 %) as oil. No further purification was necessary. 1H NMR (360 MHz) 1.74 (quint, J = 7.0 Hz, 2H); 2.30-2-56 (m, 12H); 2.66 (t, J = 7.0 Hz); 3.15 (s, 4H); 3.76 (t, J = 7.0 Hz, 2H); 6.90 (ddd, J = 7.2 Hz, 6.8 Hz, 1.4 Hz); 7.06 (dd, J = 8.0 Hz, 1.4 Hz, 2H); 7.08 (dd, J = 7.2 Hz, 1.6 Hz, 2H); 7.11 (ddd, J = 8.0 Hz, 6.8 Hz, 1.6 Hz, 2H). EIMS: m/z 374 (M+).

[4-(3-Phenothiazin-10-ylpropyl)piperazin-1-yl]acetonitrile (5d).[19]

The title compound was prepared according to the general procedure. The crude product was purified by flash chromatography (hexane/ethyl acetate/methanol 7/2/1) to give **5d** (54 %) as a yellow solid. ^{1}H NMR (360 MHz) δ 1.93 (quint, *J* = 6.8 Hz, 2H); 2.39-2.59 (m, 10H); 3.47 (s, 2H); 3.94 (t, *J* = 6.8 Hz, 2H); 6.86-6.94 (m, 4H); 7.09-7.17 (m, 4H). Further analytical data, see ref. [19]

4-[4-(3-Phenothiazin-10-ylpropyl)piperazin-1-yl]butyronitrile (5f).

The title compound was prepared according to the general procedure. The crude product was purified by flash chromatography (hexane/ethyl acetate/methanol 5/4/1 + 0.5 % triethylamine) to give **5f** (72 %) as a yellow solid. ^{1}H NMR (600 MHz) δ 1.79 (quint, *J* = 6.7 Hz, 2H); 1.95 (quint, *J* = 7.0 Hz, 2H); 2.35-2.49 (m, 14H); 3.91 (t, *J* = 7.0 Hz, 2H); 6.87-6.92 (m, 4H); 7.11-7.15 (m, 4H). EIMS *m/z* 392 (M^+).

3-[4-(3-Diphenylaminopropyl)piperazin-1-yl]propionitrile (5h).

The title compound was prepared according to the general procedure. The crude product was purified by flash chromatography (hexane/ethyl acetate/methanol 7/2/1 + 0.5 % triethylamine) to give **5h** (77 %) as a yellow oil. ^{1}H NMR (600 MHz) δ 1.82 (quin, *J* = 7.2 Hz, 2H); 2.33-2.62 (m, 12H); 2.69 (t, *J* = 7.2 Hz, 2H); 3.76 (t, *J* = 7.2 Hz, 2H); 6.89-7.06 (m, 6H); 7.20-7.31 (m, 4H). EIMS *m/z* 348 (M^+).

4-[4-(3-Diphenylaminopropyl)piperazin-1-yl]butyronitrile (5i).

The title compound was prepared according to the general procedure. The crude product was purified by flash chromatography (hexane/ethyl acetate 7/3 + 0.5 % triethylamine) to give **5i** (50 %) as a yellow oil. ^{1}H NMR (360 MHz) δ 1.77-1.84 (m, 4H); 2.33-2.53 (m, 14H); 3.76 (t, *J* = 7.4 Hz, 2H); 6.90-6.96 (m, 2H); 6.98-7.03 (m, 4H); 7.22-7.27 (m, 4H). EIMS *m/z* 362 (M^+).

3-{4-[3-(10,11-Dihydrodibenzo[b,f]azepin-5-yl)propyl]piperazin-1-yl}propylamine (6b).
The title compound was prepared according to the general procedure yielding 70 % of **6b** as a yellow oil. ^{1}H NMR (360 MHz) δ: 1.62 (quint, *J* = 6.9 Hz, 2H); 1.74 (quint, *J* = 7.0 Hz, 2H); 2.24-2.60 (m, 14H); 2.74 (t, *J* = 6.9 Hz, 2H); 3.15 (s, 4H); 3.75 (t, *J* = 7.0 Hz, 2H); 6.88-6.92 (m, 2H); 7.03-7.13 (m, 6H). EIMS *m/z* 378 (M^+).

2-[4-(3-Phenothiazin-10-ylpropyl)-piperazin-1-yl]ethylamine (6d).
The title compound was prepared according to the general procedure to give 35 % of **6d** as a solid. ^{1}H NMR (600 MHz) δ 1.89-1.98 (m, 2H); 1.71 (bs, 2H); 2.76 (t, *J* = 6.2 Hz, 2H); 2.34-2.56 (m, 12H); 3.91 (t, *J* = 7.2 Hz, 2H); 6.84-6.93 (m, 4H); 7.09-7.16 (m, 4H). EIMS *m/z* 368 (M^+).

4-[4-(3-Phenothiazin-10-ylpropyl)piperazin-1-yl]-butylamine (6f).
The title compound was prepared according to the general procedure to give 73 % of **6f** as a solid. ^{1}H NMR (360 MHz) δ 1.44-1.55 (m, 4H); 1.74 (bs, 2H); 1.95 (quint, *J* = 7.0 Hz, 2H); 2.26-2.55 (m, 12H); 2.70 (t, *J* = 6.9 Hz, 2H); 3.91 (t, *J* = 7.0 Hz, 2H); 6.85-6.94 (m, 4H); 7.09-7.16 (m, 4H,). EIMS *m/z* 396 (M^+).

3-[4-(3-Diphenylaminopropyl)piperazin-1-yl]propylamine (6h).
The title compound was prepared according to the general procedure yielding 53 % of **6h** as a yellow oil. ^{1}H NMR (600 MHz) δ 1.77-1.89 (m, 4H); 2.00 (bs, 2H); 2.31-2.60 (m, 12H); 2.69 (t, *J* = 7.2 Hz, 2H); 3.76 (t, *J* = 7.2 Hz, 2H); 6.93-7.12 (m, 6H); 7.23-7.37 (m, 4H). EIMS *m/z* 352 (M^+).

4-[4-(3-Diphenylaminopropyl)piperazin-1-yl]butylamine (6i).
The title compound was prepared according to the general procedure yielding 91 % of **6i** as a yellow oil. ^{1}H NMR (360 MHz) δ 1.41−1.76 (m, 6H); 1.82 (quint, *J* = 7.3 Hz, 2H); 2.20-2.62 (m, 12H); 2.71 (t, *J* = 6.6 Hz, 2H); 3.75 (t, *J* = 7.3 Hz, 2H); 6.88-7.06 (m, 6H); 7.18-7.30 (m, 4H). EIMS *m/z* 366 (M^+).

***N*-Acridin-9-yl-*N*-(3-{4-[3-(10,11-dihydrodibenzo[b,f]azepin-5-yl)propyl]piperazin-1-yl}propyl)amine (2b).**
The title compound was prepared according to the general procedure from compound **6b** (53.4 mg, 0.141mmol) and 9-chloroacridine (30.1 mg, 0.141 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2b** (43.1 mg, 55 %) as yellow crystals; mp 147 °C. ^{1}H NMR (600 MHz) δ 1.81 (quint, *J* = 6.9 Hz, 2H), 1.92 (quint, *J* = 5.6 Hz, 2H), 2.44-2.75 (m, 12H), 3.17 (s, 4H), 3.81 (t, *J* = 6.9 Hz, 2H), 4.04 (t, *J* = 5.6 Hz, 2H), 6.93-6.89 (m, 2H), 7.09-7.14 (m, 6H), 7.25 (ddd, *J* = 8.7 Hz, 7.2 Hz, 1.2 Hz, 2H), 7.64 (ddd, *J* = 8.7 Hz, 7.2 Hz, 1.2 Hz, 2H), 8.08 (d, *J* = 8.7 Hz, 2H), 8.22 (d, *J* = 7.2 Hz, 2H). EIMS *m/z* 555 (M^+). Anal. ($C_{37}H_{41}N_5$) C, H, N.

***N*-Acridin-9-yl-*N*-(4-{4-[3-(10,11-dihydrodibenzo[b,f]azepin-5-yl)propyl]piperazin-1-yl}butyl)amine (2c).**
The title compound was prepared according to the general procedure from compound **6c** (32.8 mg, 0.084 mmol) and 9-chloroacridine (17.8 mg, 0.084mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 5/4/1 + 0.5 % triethylamine) to give **2c** (29.5 mg, 62 %) as yellow crystals; mp 133 °C. ^{1}H NMR (600 MHz) δ 1.65 (quint, *J* = 7.1 Hz, 2H), 1.74 (quint, *J* = 6.0 Hz, 2H), 1.83 (quint, *J* = 7.1 Hz, 2H), 2.29-2.50 (m, 12 H), 3.14 (s, 4H), 3.75 (t, *J* = 6.0 Hz, 2H), 3.85 (t, *J* = 7.1 Hz, 2H), 6.90 (ddd, *J* = 7.3 Hz, 7.3 Hz, 1.2 Hz, 2H), 7.04-7.13 (m, 6H), 7.30 (ddd, *J* = 8.0 Hz, 8.0 Hz, 0.7 Hz, 2H), 7.61 (dd, *J* = 8.0 Hz, 8.0 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 2H), 8.11 (dd, *J* = 8.0 Hz, 2H). EIMS *m/z* 569 (M^+). Anal. ($C_{38}H_{43}N_5$) HRMS. purity HPLC.

***N*-(2-Chloro-6-methoxyacridin-9-yl)-*N*-(2-{4-[3-(10,11-dihydrodibenzo[b,f]azepin-5-yl)propyl]piperazin-1-yl}ethyl)amine (2d).**

The title compound was prepared according to the general procedure from compound **6a** (17.1 mg, 0.047 mmol) and 6,9-dichloro-2-methoxyacridine (13.1 mg, 0.047 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2d** (9.1 mg, 32 %) as yellow crystals; mp 149-150 °C. ^{1}H NMR (600 MHz) δ 1.77 (quint, *J* = 6.4 Hz, 2H), 2.31-2.72 (m, 12H), 3.17 (s, 4H), 3.76 (t, *J* = 6.4 Hz, 2H), 3.79 (t, *J* = 6.8 Hz, 2H), 3.95 (s, 3H), 6.89-6.94 (m, 2H), 7.06-7.15 (m, 6H), 7.24-7.28 (m, 2H), 7.41 (dd, *J* = 9.4 Hz, 2.7 Hz, 1H), 7.98 (d, *J* = 9.4 Hz, 1H), 8.05 (d, *J* = 2.0 Hz, 1H), 8.11 (d, *J* = 9.3 Hz, 1H). EIMS *m/z* 605 (M^+). Anal. ($C_{37}H_{40}ClN_5O$) C, H, N.

***N*-(2-Chloro-6-methoxyacridin-9-yl)-*N*-(3-{4-[3-(10,11-dihydro-dibenzo[b,f]azepin-5-yl)propyl]piperazin-1-yl}propyl)-amine (2e).**

The title compound was prepared according to the general procedure from compound **6b** (52.6 mg, 0.139 mmol) and 6,9-dichloro-2-methoxyacridine (38.6 mg, 0.139 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2e** (44.0 mg, 51 %) as yellow crystals; mp 179-180 °C. ^{1}H NMR (600 MHz) δ 1.78 (quint, *J* = 7.0 Hz, 2H), 1.93 (quint, *J* = 5.8 Hz, 2H), 2.28-2.79 (m, 12H), 3.17 (s, 4H), 3.79 (t, *J* = 7.0 Hz, 2H), 3.86 (t, *J* = 5.8 Hz, 2H), 3.93 (s, 3H), 6.54 (bs, NH), 6.89-6.93 (m, 2H), 7.07-7.14 (m, 6H); 7.24 (dd, *J* = 9.1 Hz, 2.3 Hz, 1H), 7.37 (d, *J* = 2.6 Hz, 1H), 7.41 (dd, *J* = 9.1 Hz, 2.6 Hz, 1H), 7.99 (d, *J* = 9.1 Hz, 1H), 8.05 (d, *J* = 1.9 Hz, 1H), 8.12 (d, *J* = 9.1 Hz, 1H). EIMS *m/z* 619 (M^+). Anal. ($C_{38}H_{42}ClN_5O$) C, H, N.

***N*-Acridin-9-yl-*N*-{2-[4-(3-phenothiazin-10-yl-propyl)piperazin-1-yl]ethyl}amine (2f).**

The title compound was prepared according to the general procedure from compound **6d** (36.5 mg, 0.099 mmol) and 9-chloroacridine (21.2 mg, 0.099 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5) to give **2f** (27.0 mg, 50 %) as yellow crystals; mp 107 °C. ^{1}H NMR (600 MHz) δ 1.98 (quint, *J* = 6.8 Hz, 2H), 2.39-2.72 (m, 12H), 3.90 (t, *J* = 5.8 Hz, 2H), 3.95 (t, *J* = 6.8 Hz, 2H), 6.87-6.94 (m, 4H), 7.10-7.21 (m, 4H), 7.34 (ddd, *J* = 8.6 Hz, 6.6 Hz, 1.0 Hz, 2H), 7.65 (ddd, *J* = 8.6 Hz, 6.6 Hz, 1.0 Hz, 2H), 8.11 (d, *J* = 8.7 Hz, 2H), 8.15 (d, *J* = 8.7 Hz, 2H). EIMS *m/z* 545 (M^+); Anal. ($C_{34}H_{35}N_5S$) HRMS. purity HPLC.

***N*-Acridin-9-yl-*N*-{4-[4-(3-phenothiazin-10-yl-propyl)piperazin-1-yl]butyl}amine (2h).**

The title compound was prepared according to the general procedure from compound **6f** (51.2 mg, 0.129 mmol) and 9-chloroacridine (57.6 mg, 0.129 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2h** (47.4 mg, 64 %) as yellow crystals; mp 109 °C. ^{1}H NMR (600 MHz) δ 1.67 (quint, *J* = 7.1 Hz, 2H), 1.88 (quint, *J* = 7.1 Hz, 2H), 1.95 (quint, *J* = 7.0 Hz, 2H), 2.17-2.75 (m, 12H), 3.86 (t, *J* = 7.1 Hz, 2H), 3.91 (t, *J* = 7.0 Hz, 2H), 6.87-6.92 (m, 4H), 7.11-7.15 (m, 4H), 7.23-7.29 (m, 2H), 7.52-7.61 (m, 2H), 7.84-7.97 (m, 2H), 8.10 (d, *J* = 8.7 Hz, 2H). EIMS *m/z* 573 (M^+); Anal. ($C_{36}H_{39}N_5S$) HRMS. purity HPLC.

***N*-(6-Chloro-2-methoxyacridin-9-yl)-*N*-{2-[4-(3-phenothiazin-10-ylpropyl)piperazin-1-yl]ethyl}-amine (2i).**

The title compound was prepared according to the general procedure from compound **6d** (87.0 mg, 0.236 mmol) and 6,9-dichloro-2-methoxyacridine (65.6 mg, 0.236 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 7/2/1 + 0.5 % triethylamine) to give **2i** (74 mg, 51 %) as yellow crystals; mp 153 °C. ^{1}H NMR (600 MHz) δ 1.93

(quint, *J* = 7.2 Hz, 2H), 2.29-2.68 (m, 12H), 3.66-3.76 (m, 2H), 3.84-3.96 (m, 5H), 6.76-6.80 (m, 4H), 7.05-7.15 (m, 4H), 7.17 (d, *J* = 2.7 Hz, 1H), 7.20 (dd, *J* = 8.9 Hz, 2.1 Hz, 1H), 7.36 (dd, *J* = 9.3 Hz, 2.7 Hz, 1H), 7.96 (d, *J* = 9.3 Hz, 1H), 8.01 (d, *J* = 8.9 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H). EIMS *m/z* 609 (M^+). Anal. ($C_{35}H_{36}ClN_5OS$) HRMS. purity HPLC.

***N*-(6-Chloro-2-methoxyacridin-9-yl)-*N*-{3-[4-(3-phenothiazin-10-ylpropyl)piperazin-1-yl]propyl}amine (2j).**

The title compound was prepared according to the general procedure from compound **6e** (25.9 mg, 0.068 mmol) and 6,9-dichloro-2-methoxyacridine (18.8 mg, 0.068 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2j** (24.1 mg, 57 %) as yellow crystals; mp 161 °C. ^{1}H NMR (360 MHz) δ 1.95 (quint, *J* = 6.0 Hz, 2H), 1.98 (quint, *J* = 7.0 Hz, 2H), 2.34-2.73 (m, 12H), 3.86 (t, *J* = 6.0 Hz, 2H), 3.90 (s, 3H), 3.95 (t, *J* = 7.0 Hz, 2H), 6.87-6.93 (m, 4H), 7.11-7.16 (m, 4H), 7.18 (dd, *J* = 9.3 Hz, 2.2 Hz, 1H), 7.32 (dd, *J* = 9.4 Hz, 2.6 Hz, 1H), 7.37 (d, *J* = 2.6 Hz, 1H), 7.91 (d, *J* = 9.4 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 8.07 (d, *J* = 9.3 Hz, 1H). EIMS *m/z* 623 (M^+). Anal. ($C_{36}H_{38}ClN_5OS$) HRMS. purity HPLC.

***N*-(6-Chloro-2-methoxyacridin-9-yl)-*N*-{4-[4-(3-phenothiazin-10-ylpropyl)piperazin-1-yl]butyl}amine (2k).**

The title compound was prepared according to the general procedure from compound **6f** (65.5 mg, 0.165 mmol) and 6,9-dichloro-2-methoxyacridine (45.9 mg, 0.165 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2k** (65.0 mg, 62 %) as yellow crystals; mp 107-108 °C. ^{1}H NMR (600 MHz) δ 1.63 (quint, *J* = 7.3 Hz, 2H), 1.78 (quint, *J* = 7.3 Hz, 2H), 1.94 (quint, *J* = 7.0 Hz, 2H), 2.15-2.72 (m, 12H), 3.72 (t, *J* = 7.3 Hz, 2H), 3.91 (t, *J* = 7.0 Hz, 2H), 3.95 (s, 3H), 6.85-6.94 (m, 4H), 7.10-7.17 (m, 4H), 7.22 (d, *J* = 2.6 Hz, 1H), 7.29 (dd, *J* = 9.1 Hz, 2.2 Hz, 1H), 7.42 (dd, *J* = 9.3 Hz, 2.6 Hz, 1H), 7.99 (d, *J* = 9.3 Hz, 1H), 8.02 (d, *J* = 9.1 Hz, 1H), 8.06 (d, *J* = 2.2 Hz, 1H). EIMS *m/z* 637 (M^+). Anal. ($C_{37}H_{40}ClN_5OS$) C, H, N.

***N*-Acridin-9-yl-*N*-{3-[4-(3-diphenylaminopropyl)piperazin-1-yl]propyl}amine (2m).**

The title compound was prepared according to the general procedure from compound **6h** (52.6 mg, 0.149 mmol) and 9-chloroacridine (47.8 mg, 0.149 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2m** (40.3 mg, 51 %) as yellow crystals; mp 127-128 °C. ^{1}H NMR (600 MHz) δ 1.87 (quint, *J* = 6.6 Hz, 2H), 1.91 (tt, *J* = 6.2 Hz, 6.2 Hz, 2H), 2.30-2.89 (m, 12H), 3.80 (t, *J* = 6.52 Hz, 2H), 3.99 (t, *J* = 6.6 Hz, 2H), 6.94 (dd, *J* = 7.6 Hz, 7.6 Hz, 2H), 7.03 (d, *J* = 7.8 Hz, 4H); 7.26 (dd, *J* = 7.8 Hz, 7.6 Hz, 4H), 7.26 (dd, *J* = 8.1 Hz, 7.1 Hz, 2H), 7.62 (dd, *J* = 8.4 Hz, 7.1 Hz, 2H), 8.05 (d, *J* = 8.1 Hz, 2H), 8.21 (d, *J* = 8.4 Hz, 2H). EIMS *m/z* 529 (M^+). Anal. ($C_{35}H_{39}N_5$) C, H, N.

***N*-Acridin-9-yl-*N*-{4-[4-(3-diphenylaminopropyl)piperazin-1-yl]butyl}amine (2n).**

The title compound was prepared according to the general procedure from compound **6i** (46.2 mg, 0.126 mmol) and 6-chloroacridine (26.9 mg, 0.126 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2n** (28.7 mg, 42 %) as yellow crystals; mp 123 °C. ^{1}H NMR (600 MHz) δ 1.70 (quint, *J* = 7.1 Hz, 2H), 1.82 (quint, *J* = 7.1 Hz, 2H), 1.89 (quint, *J* = 7.1 Hz, 2H), 2.27-2.64 (m, 12H), 3.76 (t, *J* = 7.1 Hz, 2H), 3.90 (t, *J* = 7.1 Hz, 2H), 6.93 (dd, *J* = 7.3 Hz, 7.3 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 4H); 7.24 (dd, *J* = 8.1 Hz, 7.3 Hz, 4H), 7.31 (dd, *J* =7.9 Hz, 7.4 Hz, 2H), 7.60 (dd, *J* = 7.9 Hz, 7.4 Hz, 2H), 8.04 (d, *J* = 7.9 Hz, 2H), 8.13 (d, *J* = 7.9 Hz, 2H). EIMS *m/z* 543 (M^+). Anal. ($C_{36}H_{41}N_5$) HRMS. purity HPLC.

***N*-(6-Chloro-2-methoxyacridin-9-yl)-*N*-{2-[4-(3-diphenylaminopropyl)piperazin-1-yl]ethyl}amine (2o).**

The title compound was prepared according to the general procedure from compound **6g** (31.5 mg, 0.093 mmol) and 6,9-dichloro-2-methoxyacridine (25.9 mg, 0.093 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2o** (31.4 mg, 58 %) as yellow crystals; mp 131-132 °C. ^{1}H NMR (360 MHz) δ 1.86 (quint, *J* = 7.2 Hz, 2H), 2.34-2.77 (m, 12H), 3.78 (t, *J* = 7.2 Hz, 2H), 3.84 (t, *J* = 5.6 Hz, 2H), 3.94 (s, 3H), 6.44 (bs, NH), 6.84-7.04 (m, 8H), 7.16-7.29 (m, 4H), 7.37 (dd, *J* = 9.5 Hz, 2.7 Hz, 1H), 8.00 (d, *J* = 9.5 Hz, 1H), 8.07 (d, *J* = 2.0 Hz, 1H), 8.09 (d, *J* = 9.5 Hz, 1H). EIMS *m/z* 579 (M^+). Anal. ($C_{35}H_{38}ClN_5O$) C, H, N. HRMS. purity HPLC.

***N*-(6-Chloro-2-methoxyacridin-9-yl)-*N*-{3-[4-(3-diphenylaminopropyl)piperazin-1-yl]propyl}amine (2p).**

The title compound was prepared according to the general procedure from compound **6h** (53.5 mg, 0.152 mmol) and 6,9-dichloro-2-methoxyacridine (63.3 mg, 0.152 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2p** (48.7 mg, 54 %) as yellow crystals; mp 148 °C. ^{1}H NMR (600 MHz) δ 1.86 (quint, *J* = 6.5 Hz, 2H), 1.97 (quint, *J* = 6.5 Hz, 2H), 2.29-2.81 (m, 12H), 3.79 (t, *J* = 6.5 Hz, 2H), 3.89 (t, *J* = 6.5 Hz, 2H), 3.91 (s, 3H), 6.93 (dd, *J* = 7.7 Hz, 7.7 Hz, 2H), 7.03 (d, *J* = 7.9 Hz, 4H); 7.16 (dd, *J* = 9.1 Hz, 1.9 Hz, 1H), 7.25 (dd, *J* = 7.9 Hz, 7.7 Hz, 4H), 7.34 (dd, *J* = 9.1 Hz, 2.6 Hz, 1H), 7.37 (d, *J* = 2.6 Hz, 1H), 7.97 (d, *J* = 9.1 Hz, 1H), 8.03 (d, *J* = 1.9 Hz, 1H), 8.07 (d, *J* = 9.1 Hz, 1H). EIMS *m/z* 593 (M^+). Anal. ($C_{36}H_{40}ClN_5O$) HRMS. purity HPLC.

***N*-(6-Chloro-2-methoxyacridin-9-yl)-*N*-{4-[4-(3-diphenylaminopropyl)piperazin-1-yl]butyl}amine (2q).**

The title compound was prepared according to the general procedure from compound **6i** (47.6 mg, 0.130 mmol) and 6,9-dichloro-2-methoxyacridine (36.1 mg, 0.130 mmol). The crude product was purified by gravitation column chromatography (hexane/ethyl acetate/methanol 8/1.5/0.5 + 0.5 % triethylamine) to give **2q** (37.9 mg, 48 %) as yellow crystals; mp 124 °C. ^{1}H NMR (600 MHz) δ 1.65 (quint, *J* = 7.4Hz, 2H), 1.79 (quint, *J* = 7.4 Hz, 2H), 1.82 (quint, *J* = 7.0 Hz, 2H), 2.23-2.65 (m, 12H), 3.73 (t, *J* = 7.0 Hz, 2H), 3.75 (t, *J* = 7.4 Hz, 2H), 3.95 (s, 3H), 6.93 (ddd, *J* = 8.4 Hz, 7.3 Hz, 0.9 Hz, 2H), 7.00 (dd, *J* = 8.7 Hz, 0.9 Hz, 4H); 7.22-7.23 (m, 4H), 7.24 (d, *J* = 1.9 Hz, 1H), 7.28 (dd, *J* = 9.2 Hz, 2.0 Hz, 1H), 7.41 (dd, *J* = 9.4 Hz, 1.9 Hz, 1H), 7.99 (d, *J* = 9.4 Hz, 1H), 8.02 (d, *J* = 9.2 Hz, 1H), 8.06 (d, *J* = 2.0 Hz, 1H). EIMS *m/z* 607 (M^+). Anal. ($C_{37}H_{42}ClN_5O$) C, H, N.

Reference numbers correspond to those mentioned in the article.

2. Elementary Analysis Data

Compound	Formula		C (%)	H (%)	N (%)
2b	$C_{37}H_{41}N_5$	Calcd	79.96	7.44	12.60
		Found	**79.87**	**7.44**	**12.59**
2d	$C_{37}H_{40}ClN_5O$ x 2 H_2O	Calcd	69.20	6.91	10.90
		Found	**68.89**	**6.89**	**10.73**
2e	$C_{38}H_{42}ClN_5O$ x 0.5 H_2O	Calcd	72.53	6.89	11.13
		Found	**72.58**	**6.80**	**10.86**
1	$C_{39}H_{44}ClN_5O$	Calcd	73.85	6.99	11.04
		Found	**74.03**	**7.11**	**10.90**
2g	$C_{35}H_{37}N_5S$ x 2/3 H_2O	Calcd	73.52	6.76	12.25
		Found	**73.22**	**6.60**	**12.12**
2k	$C_{37}H_{40}ClN_5OS$ x 1H_2O	Calcd	67.72	6.45	10.67
		Found	**67.92**	**6.61**	**10.64**
2l	$C_{34}H_{37}N_5$ x 2/3 H_2O	Calcd	77.39	7.32	13.27
		Found	**77.38**	**7.00**	**13.35**
2m	$C_{35}H_{39}N_5$ x 0.5 H_2O	Calcd	78.03	7.48	13.00
		Found	**78.14**	**7.52**	**12.96**
2q	$C_{37}H_{42}ClN_5O$ x 0.5 H_2O	Calcd.	72.00	7.02	11.35
		Found	**72.00**	**6.81**	**10.96**

2. HRMS Data

Compound	Formula	HRMS
2a	$C_{36}H_{39}N_5$	Calcd: 541.3205 **Found: 541.3213**
2c	$C_{38}H_{43}N_5$	Calcd: 569.3518 **Found: 569.3515**
2f	$C_{34}H_{35}N_5S$	Calcd: 545.2613 **Found: 545.2609**
2h	$C_{36}H_{39}N_5S$	Calcd: 573.2926 **Found: 573.2934**
2i	$C_{35}H_{36}ClN_5OS$	Calcd: 609.2329 **Found: 609.2325**
2j	$C_{36}H_{38}ClN_5OS$	Calcd: 623.2510 **Found: 623.2486**
2n	$C_{36}H_{41}N_5$	Calcd: 543.3362 **Found: 543.3368**
2o	$C_{35}H_{38}ClN_5O$	Calcd: 579.2765 **Found: 579.2765**
2p	$C_{36}H_{40}ClN_5O$	Calcd: 593.2927 **Found: 593.2921**

3. HPLC Data

The compounds were reanalyzed in solution (1mM in MeOH) by HPLC with a ZORBAX Eclipse XDB-C8 column (4.6x150 mm, 5µm) using two different elution systems (system A: MeOH/0.1% HCO_2H in H_2O; gradient elution 10/90-90/10; system B: CH_3CN/0.1% HCO_2H in H_2O; gradient elution 0/100-100/0) at a flow rate of 0.5 mL/min. System A it was used in combination with UV (254 nm) detection and APCI-MS. System B we used with UV (254 nm) detection alone.

Compound	System A		System B	
	t_r in min.	purity (%)	t_r in min.	purity (%)
2a	15.3	100	16.1	99.5
2c	15.4	98.8	16.2	100
2f	15.4	98.2	16.3	99.8
2h	15.8	99.0	16.0	100
2i	16.2	95.8	16.5	100
2j	16.8	100	17.4	98.9
2n	16.1	96.1	16.8	99.0
2o	15.6	97.7	16.5	96.0
2p	16.2	100	16.7	98.3