Supplementary data for the article:

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Supporting Information – I

New Steroidal 4-Aminoquinolines Antagonize Botulinum Neurotoxin Serotype A in Mouse Embryonic Stem Cell Derived Motor Neurons in Post-intoxication Model

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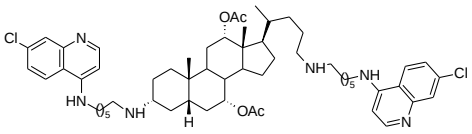
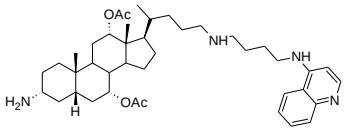
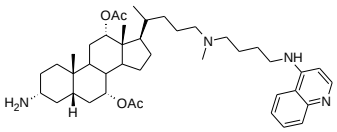
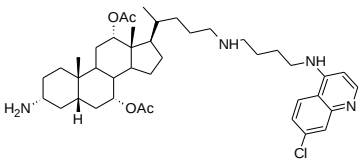
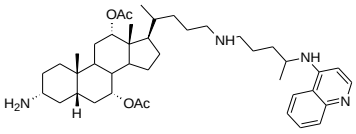
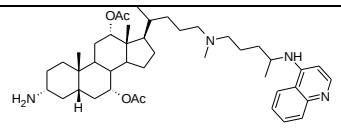
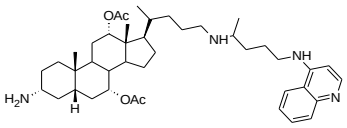
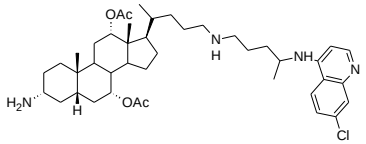
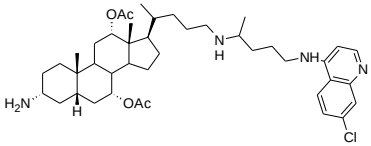
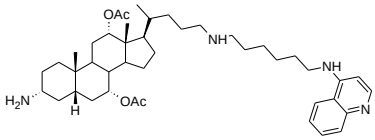
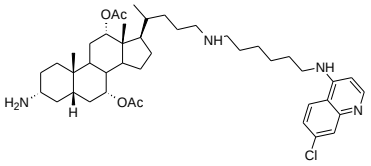
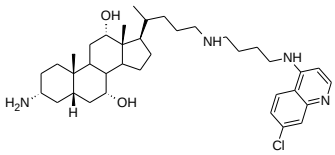
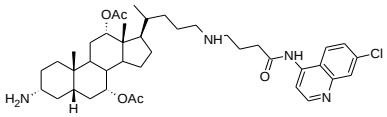
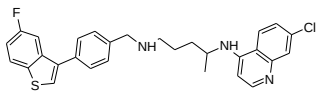
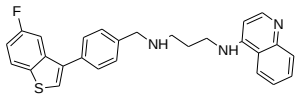
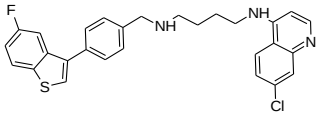
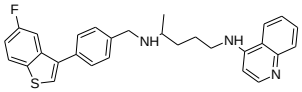
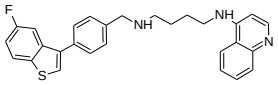
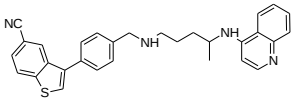
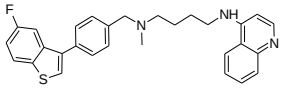
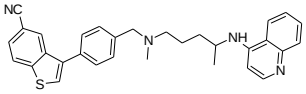
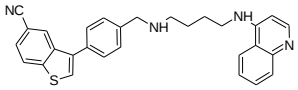
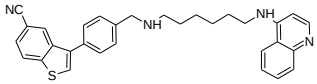
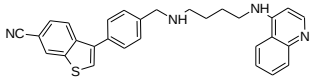
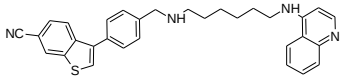
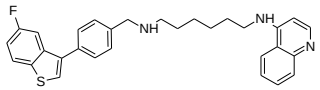
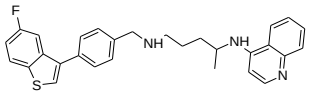
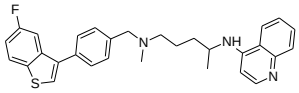
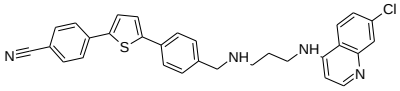
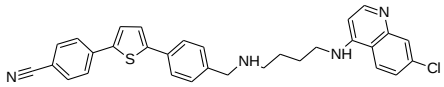
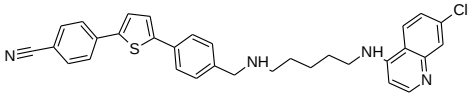
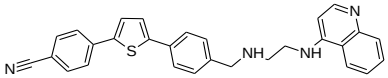
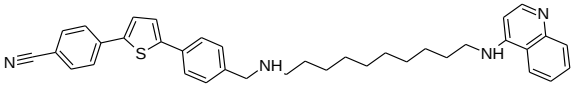
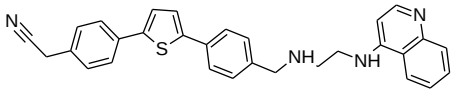
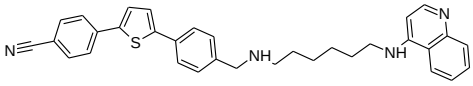
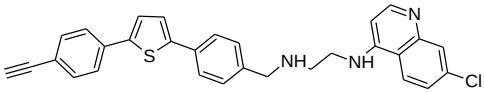
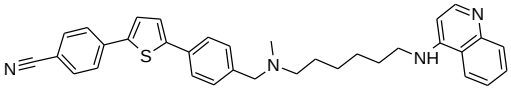
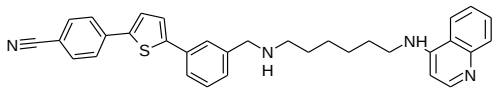
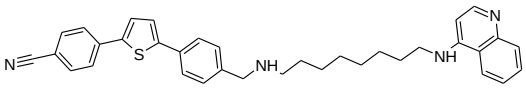
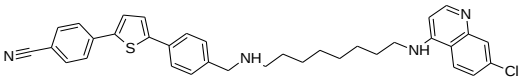
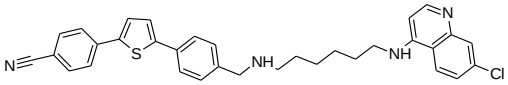
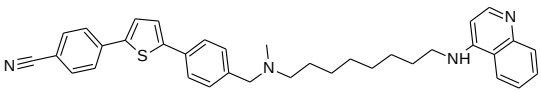
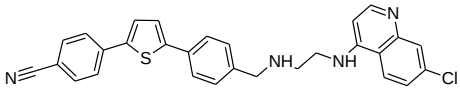
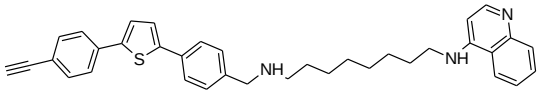
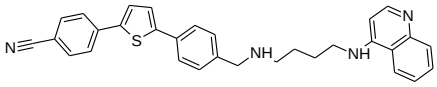
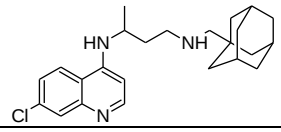
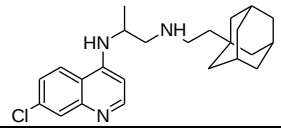
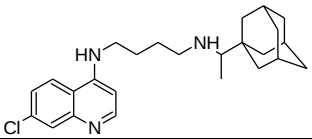
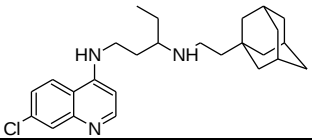
Table S1. Inhibitory activities against BoNT/A LC and holotoxin in proteolytic and cell-based assay

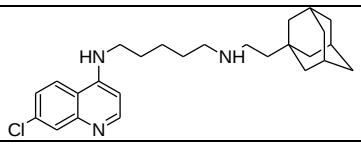
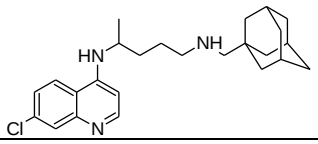
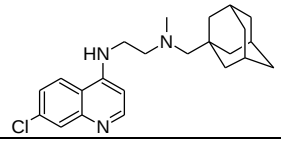
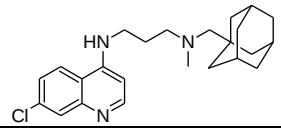
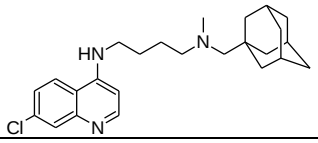
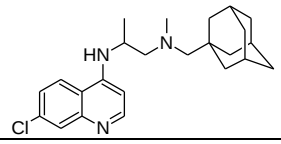
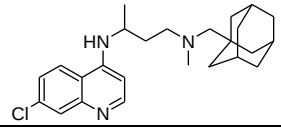
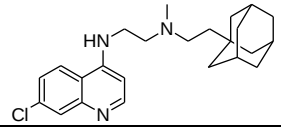
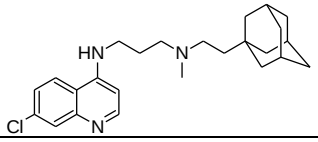
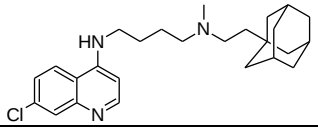
Compound	*In vitro* proteolytic assay % inh BoNT/A LC at 20 µM	*In vitro* proteolytic assay IC_{50} (µM)	mES-MNs pre intoxication % of full length SNAP-25 (10 µM; 20 µM)	mES-MNs post intoxication at 20 µM % of full length SNAP-25 (30 min; 60 min)
1 	90	12.4	70; 84	36; 20
14 	80	5.7	28; 67	48; 49
15 	52	1.5	70; 69	/
16 	66	4.5	72; 88	64; 45
17 	71	2.7	67; 69	38; 22
18	85	0.7	20; 41	/

				
19 	75	3.0	86; 87	50; 22
20 	77	2.4	/	/
21 	54	/	/	/
22 	64	7.1	/	/
23 	67	3.5	/	/
24 	48	/	46; 58[a]	49; [a] /
30 	37	/	/	/
S1 	55	6.6	/	/

S2 	42	/	/	/
33 	69	/	/	/
34 	75	7.4	58; 68	16; 17
35 	34	/	/	/
36 	61	10.2	34; 53	/
37 	46	/	44; 55	/
38 	27	/	59; 64	/
86 	84	4.6	21; 26	/
87 	75	3.3	36; 43	/
88 	23	/	/	/
89 	8	/	/	/

90 	56	5.9	/	/
91 	69	8.8	62; 62	/
92 	48	/	/	/
S3 	49	/	/	/
S4 	47	/	/	/
S5 	63	2.2	/	/
42 	63	2.1	/	/
43 	53	6.4	/	/
44 	49	/	/	/
46 	70-80	3.4	22; 48	/
47 	19	/	/	/
48 	55	/	/	/
50	68	8.7	46; 71	/

				
93 	77	6.8	31; 70	20; 19
94 	14	/	/	/
95 	30	/	/	/
96 	35	/	54; 60	34; 22
97 	36	/	/	/
98 	53	12.3	/	/
101 	67	9.3	18; 39	/
S6 	55	15.7	/	/
S7 	55	16.6	/	/
S8 	46	/	/	/
S9 	44	/	/	/
S10	41	/	/	/

				
S11 	39	/	/	/
56 	3	/	/	/
57 	71	8.8	51; 56	46; 39
58 	24	/	/	/
59 	23	/	/	/
60 	67	11.7	63; 72	15; 16
61 	17	/	/	/
62 	61	21.1	/	/
63 	63	43.3	/	/
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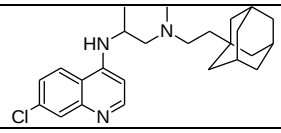
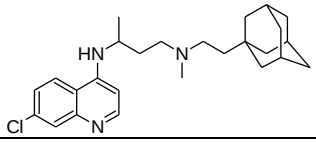
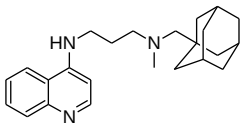
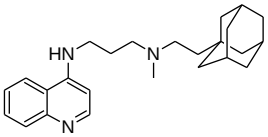
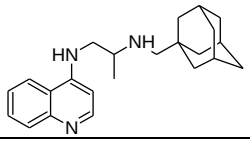
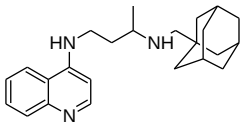
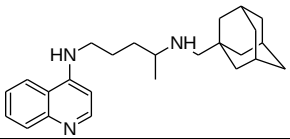
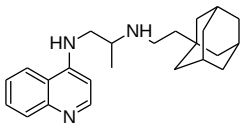
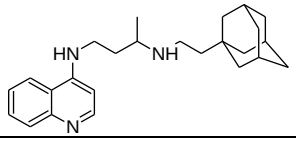
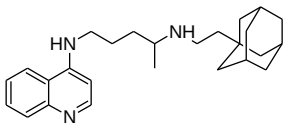
				
65 	48	/	/	/
68 	30	/	30; 31	/
69 	31	/	/	/
77 	20	/	/	/
78 	46	/	/	/
79 	24	/	/	/
80 	59	3.2	/	/
81 	/	/	23; 24	/
82 	41	/	/	/
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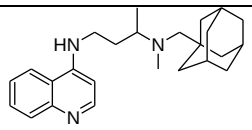
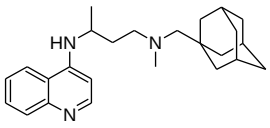
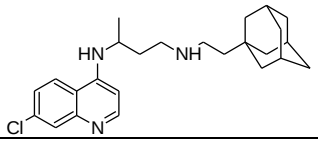
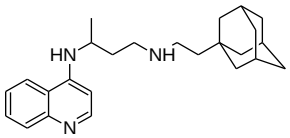
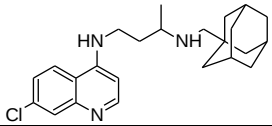
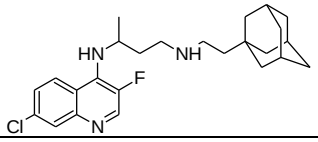
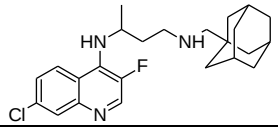
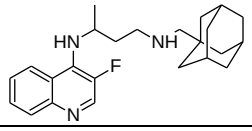
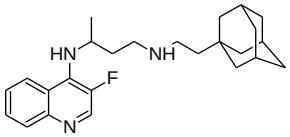
				
85 	51	5.2	47; 46	/
99 	64	9.1	/	/
100 	42	/	/	/
102 	65	2.7	29; 30	/
103 	2	/	30; 29	/
104 	15	/	31; 35	/
105 	/	/	24; 23	/
106 	/	/	30; 32	/

[a]Compound **24** was tested at 8 and 16 μM in pre-intoxication model and at 16 μM in 30 minutes post-intoxication model.

Synthesis of compound **1** was published in our previous work.[1] Syntheses of compounds **S1**-**S5**, **36**, **46**, **86**-**98**, **101** were published in our previous work.[2] Synthesis of compound **35** was published in our previous work.[3] Syntheses of compounds **99**, **100**, **102**-**106, S6**-**S9**, **S11** were published in our previous work.[4] Synthesis of

compound **S10** was published in our previous work.[5]

Table S2. Protection of SNAP-25 in mES-MNs in pre-intoxication model at five concentrations 0.1 → 20 μM (results are given as mean value of three independent experiments).

Compound	Concentration (μM)	% of full length SNAP-25	SEM
No toxin	/	100	0
Toxin only	500 pM	16.6	3.3
1	0.1	23.1	6.8
	1	23.3	4.8
	5	36.4	9.8
	10	55.5	12.9
	20	78.2	5.0
14	0.1	25.8	8.1
	1	23.3	7.1
	5	25.5	5.2
	10	40.1	11.4
	20	60.2	11.3
16	0.1	19.4	3.8
	1	21.1	4.2
	5	25.1	3.4
	10	50.6	14.6
	20	80.7	9.7
17	0.1	19.5	4.3
	1	19.7	4.1
	5	21.9	4.3
	10	31.7	1.3
	20	61.4	6.0
19	0.1	20.0	6.1
	1	22.1	6.1
	5	22.4	3.7
	10	36.1	6.0
	20	79.3	3.4
34	0.1	18.1	4.7
	1	17.6	4.9
	5	27.0	8.4
	10	40.9	4.1
	20	72.7	8.5
38	0.1	24.1	4.2
	1	24.1	7.2
	5	28.5	8.4

	10	45.2	12.6
	20	69.3	11.4
50	0.1	21.1	7.0
	1	24.3	4.3
	5	26.5	2.2
	10	33.9	3.2
	20	57.3	4.2
57	0.1	28.5	7.0
	1	15.9	4.4
	5	20.7	5.9
	10	33.4	4.6
	20	75.6	14.6
60	0.1	19.6	3.8
	1	21.1	3.3
	5	26.9	6.5
	10	60.6	9.0
	20	89.8	4.5
93	0.1	21.3	6.1
	1	25.6	6.8
	5	26.3	2.0
	10	40.4	2.4
	20	75.9	4.2
96	0.1	23.7	6.3
	1	30.1	11.1
	5	42.2	15.3
	10	60.0	15.7
	20	69.7	11.7

Table S3. Protection of SNAP-25 in mES-MNs in 30/60 minutes post-intoxication model at 20 μM (results are given as mean value of three independent experiments)

Compound	% of full length SNAP-25 (30 min)	SEM	% of full length SNAP-25 (60 min)	SEM
No toxin	100	0	100	0
Toxin only	14.8	2.7	16.2	3.7
1	35.9	6.0	19.9	3.5
14	48.4	9.1	48.9	24.1
16	64.4	6.1	44.9	9.6
17	38.5	8.0	21.9	2.4
19	49.5	12.0	22.5	1.8
34	16.3	2.4	16.6	2.2
57	46.4	9.8	39.4	9.8
60	15.2	3.0	16.2	3.0
93	19.8	3.1	18.9	3.0
96	34.3	5.9	22.3	4.1

Table S4. Protection of SNAP-25 in mES-MNs by compounds **16** and **24** administered 30 min post-intoxication – dose response experiment 0.25 to 64 μM (results are given as mean value of two independent experiments)

Compound	Concentration (μM)	% of full length SNAP-25	SEM
No toxin	/	100	0
Toxin only	500 pM	29.6	3.7
16	0.25	33.2	1.8
	0.5	33.9	3.0
	1	38.8	0.3
	2	37.9	0.9
	4	47.3	6.7
	8	48.2	4.3
	16	71.9	4.0
	32	89.4	2.2
	64	100	0
24	0.25	33.0	3.3
	0.5	36.6	0.9
	1	38.6	5.3
	2	41.0	5.5
	4	44.0	2.5
	8	50.3	5.3
	16	49.2	2.1
	32	52.7	4.3
	64	69.2	4.1

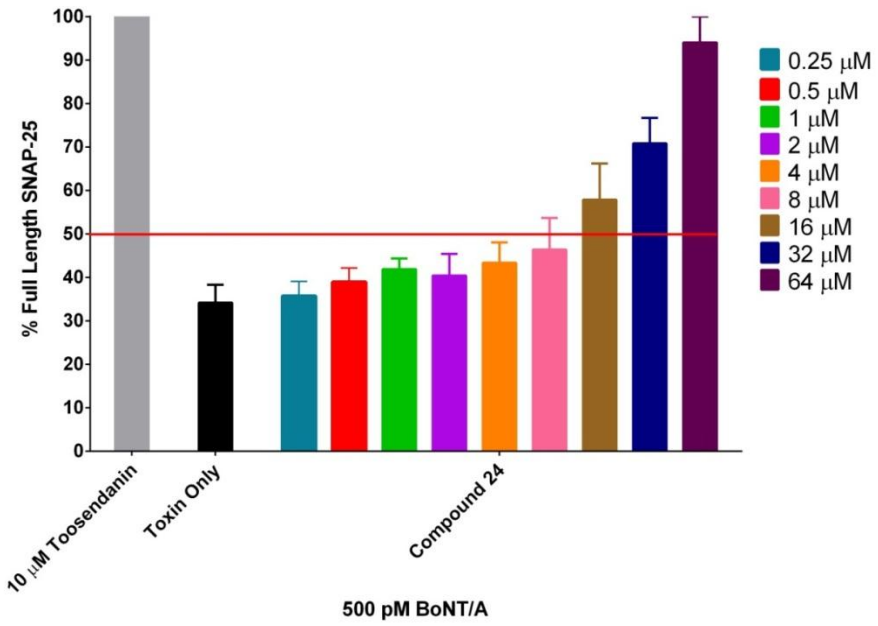


Figure S1. Protection of SNAP-25 in mES-MNs by compound **24** administered 30 min pre-intoxication – dose response experiment 0.25 to 64 μM (results are given as mean value of two independent experiments +/- SEM). IC_{50} =8-16 μM.

Table S5. Protection of SNAP-25 in mES-MNs by compound **24** administered 30 min pre-intoxication – dose response experiment 0.25 to 64 μM (results are given as mean value of two independent experiments).

Compound	Concentration (μM)	% of full length SNAP-25	SEM
Toosendanin	10	100	0
Toxin only	500 pM	34.2	4.1
24	0.25	35.8	3.3
	0.5	38.9	3.2
	1	41.9	2.4
	2	40.4	5.0
	4	43.4	4.7
	8	46.4	7.3
	16	57.9	8.3
	32	70.8	5.8
	64	94.0	6.0

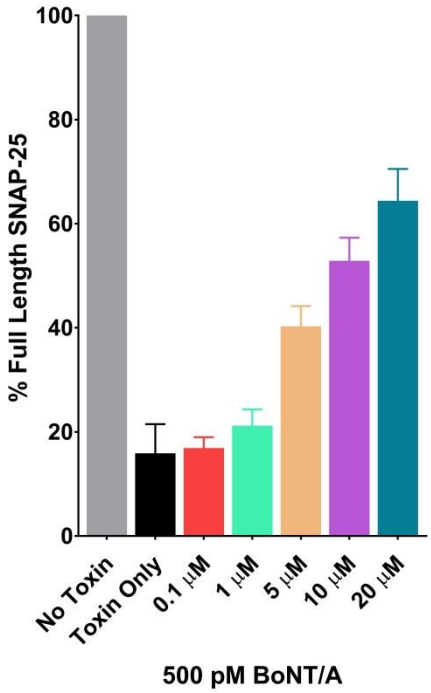


Figure S2. Protection of SNAP-25 in mES-MNs by compound **16** administered 30 min post-intoxication – dose response experiment 0.1 to 20 μM (results are given as mean value of four independent experiments +/- SEM). IC_{50} =5-10 μM.

Table S6. Protection of SNAP-25 in mES-MNs by compound **16** administered 30 min post-intoxication – dose response experiment 0.1 to 20 μM (results are given as mean value of four independent experiments).

Compound	Concentration (μM)	% of full length SNAP-25	SEM
No toxin	/	100	0
Toxin only	500 pM	15.9	5.6
16	0.1	16.9	2.1
	1	21.2	3.1
	5	40.3	3.9
	10	52.9	4.4
	20	64.4	6.1

Fluorescence and UV-Vis spectra of binding 16 to HSA and AGP

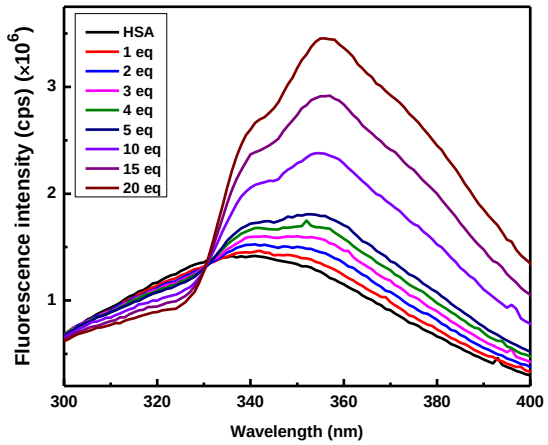


Figure S3. Changes in HSA (c=5×10^{-7} M) fluorescence emission spectra upon addition of **16** (1-20 molar equivalents); T =298 K, 1X PBS, pH=7.34.

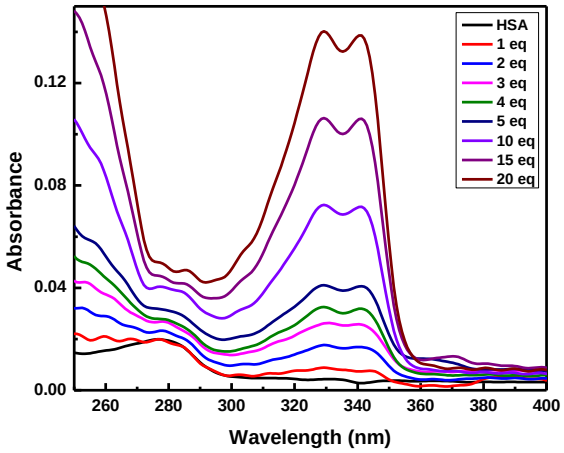


Figure S4. Changes in HSA (c=5×10^{-7} M) UV-Vis spectra upon addition of **16** (1-20 molar equivalents); T=298 K; 1X PBS, pH = 7.34, scan speed 500 nm/min

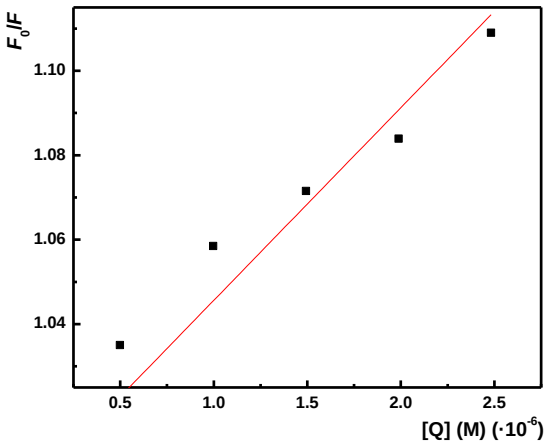


Figure S5. The Stern-Volmer plot for binding of **16** to HSA (c=5×10^{-7} M), T=298 K; pH = 7.34; λ=323 nm; linear equation: y=1+45628.8x (For the calculation of binding constants, only points within linear dependence were used (1-5 molar equivalents).)

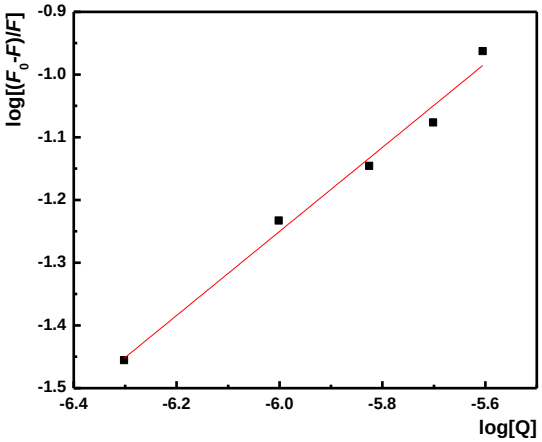


Figure S6. Log-log plot for the determination of binding constants K_b, and the number of binding sites n for binding of **16** to HSA (c=5×10^{-7} M) T=298 K; pH = 7.34; λ=323 nm; linear equation: y=2.77+0.67x (For the calculation of binding constants, only points within linear dependence were used (1-5 molar equivalents).)

K_{sv}=(4.56±0.27)×10^4 M^{-1} logK_b=2.77±0.26; n=0.670

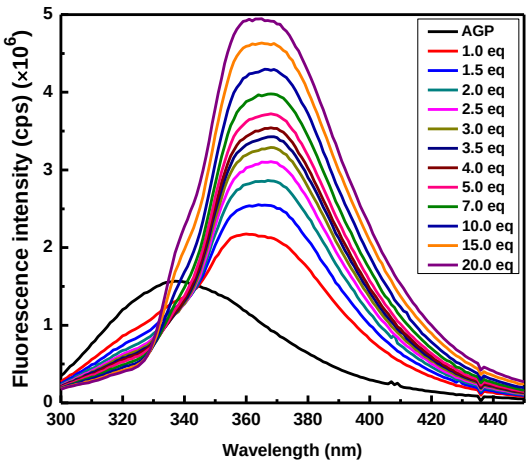


Figure S7. Changes in AGP (c=5×10^{-7} M) fluorescence emission spectra upon addition of **16** (1-20 molar equivalents); T =298 K, 30 mM PBS, pH=7.34.

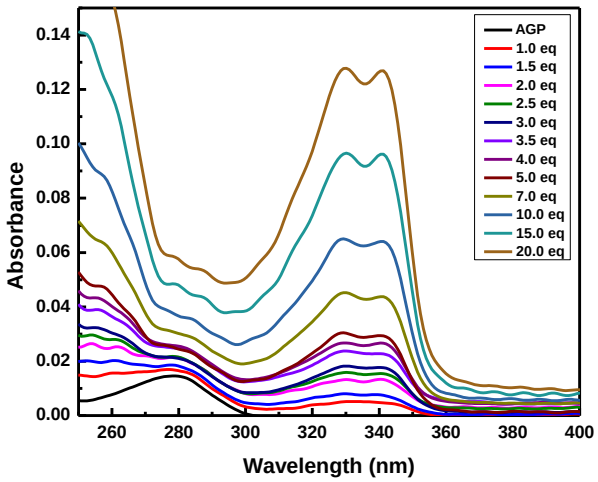


Figure S8. Changes in AGP (c=5×10^{-7} M) UV-Vis spectra upon addition of **16** (1-20 molar equivalents); T=298 K; 1X PBS, pH = 7.34, scan speed 500 nm/min.

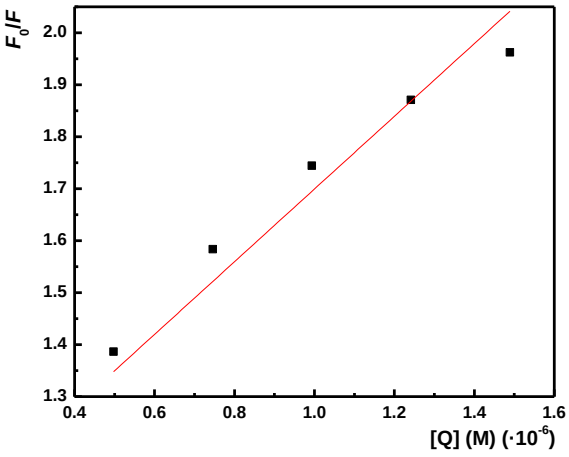


Figure S9. The Stern-Volmer plot for binding of **16** to AGP (c=5×10^{-7} M), T=298 K; pH = 7.34; λ=323 nm; linear equation: y=1+699439.2x (For the calculation of binding constants, only points within linear dependence were used (1-3 molar equivalents).)

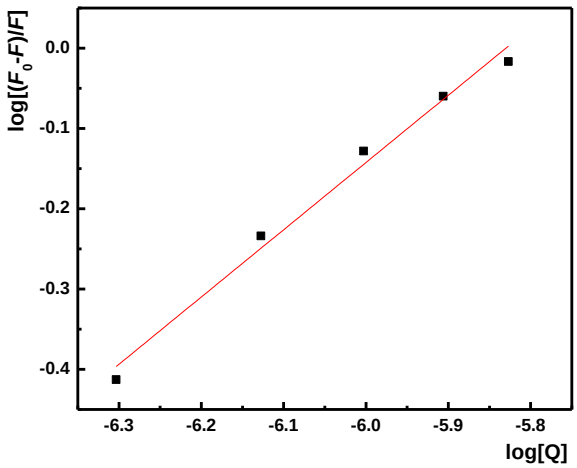


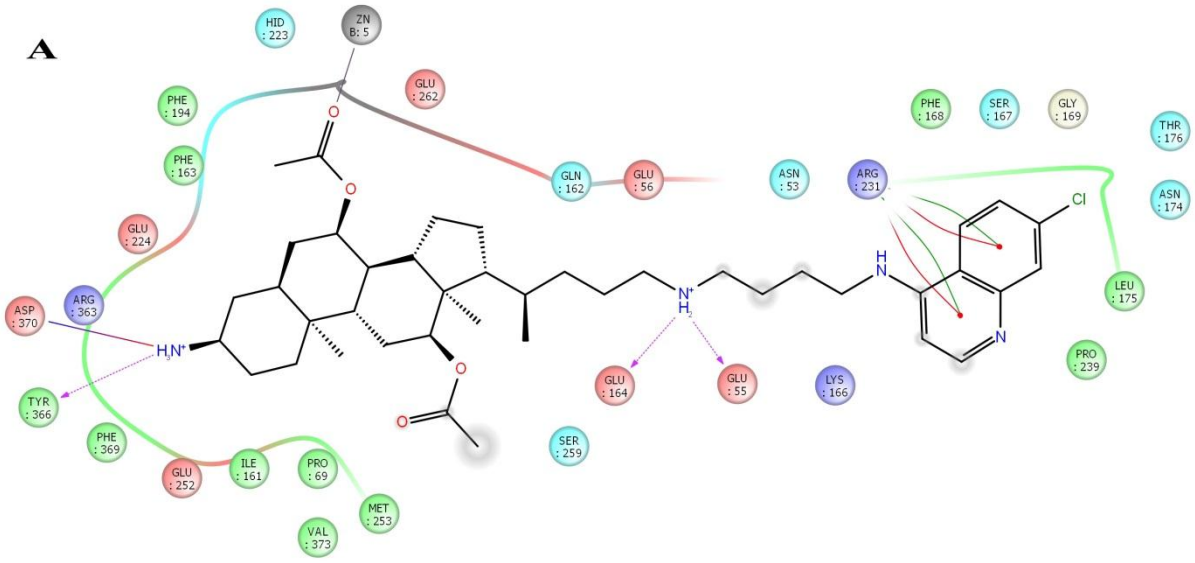
Figure S10. Log-log plot for the determination of binding constants K_b, and the number of binding sites n for binding of **16** to HSA (c=5×10^{-7} M) T=298 K; pH = 7.34; λ=323 nm; linear equation: y=4.88+0.3x (For the calculation of binding constants, only points within linear dependence were used (1-3 molar equivalents).)

K_{sv}=(6.99±0.25)×10^5 M^{-1}

logK_b=4.88±0.32; n=0.838

Ligand interaction diagrams

All ligand structures were built, optimized and their ionization states determined using Schrödinger Suite 2016-4 (Schrödinger, LLC: New York, NY, 2016) in the same manner it was performed before.[1] Docking of the ligands were performed using grid docking from Glide ligand docking module (Glide, Schrödinger, LLC: New York, NY, 2017), using standard precision and flexible ligand sampling, without no additional constraints. All modeling was performed within a pH range of 7.0 ± 1.0, which corresponds to the pH of in vitro experiments (i.e., pH 7.3), according to our previously published studies.[1] The structure of BoNT/A LC and its binding site (BS) corresponds with those used in aforementioned publication.



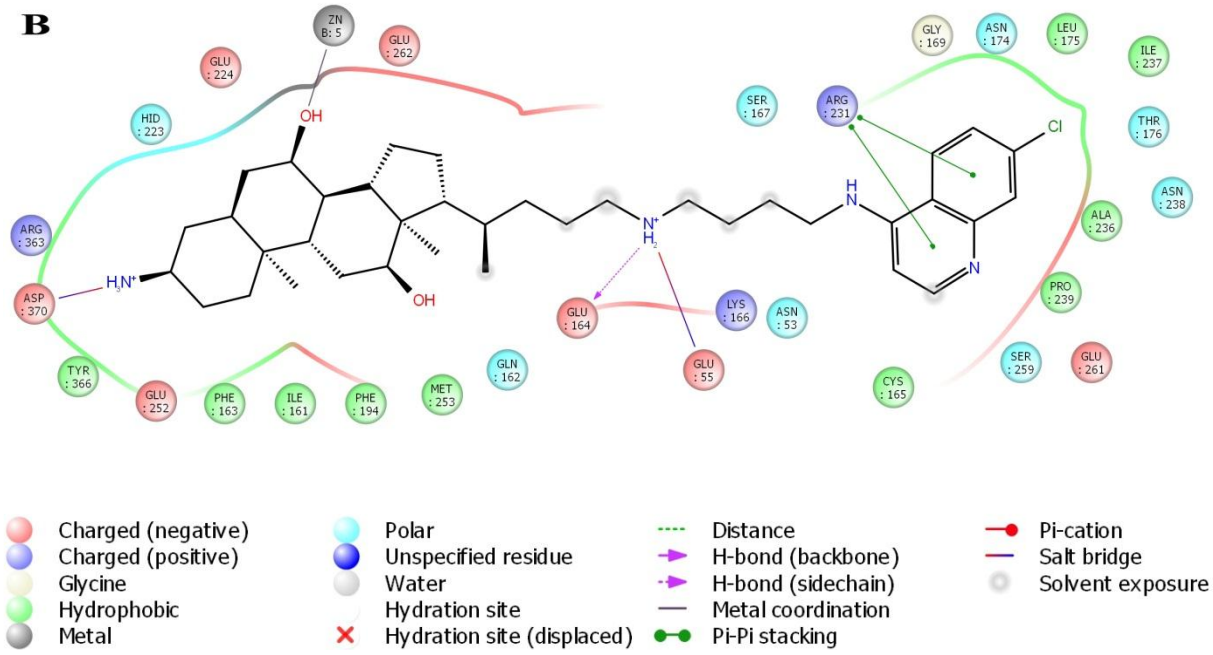


Figure S11. Compounds **16** (A) and **24** (B) docked in the catalytic cleft of BoNT/A LC at pH 7.0±1.0.

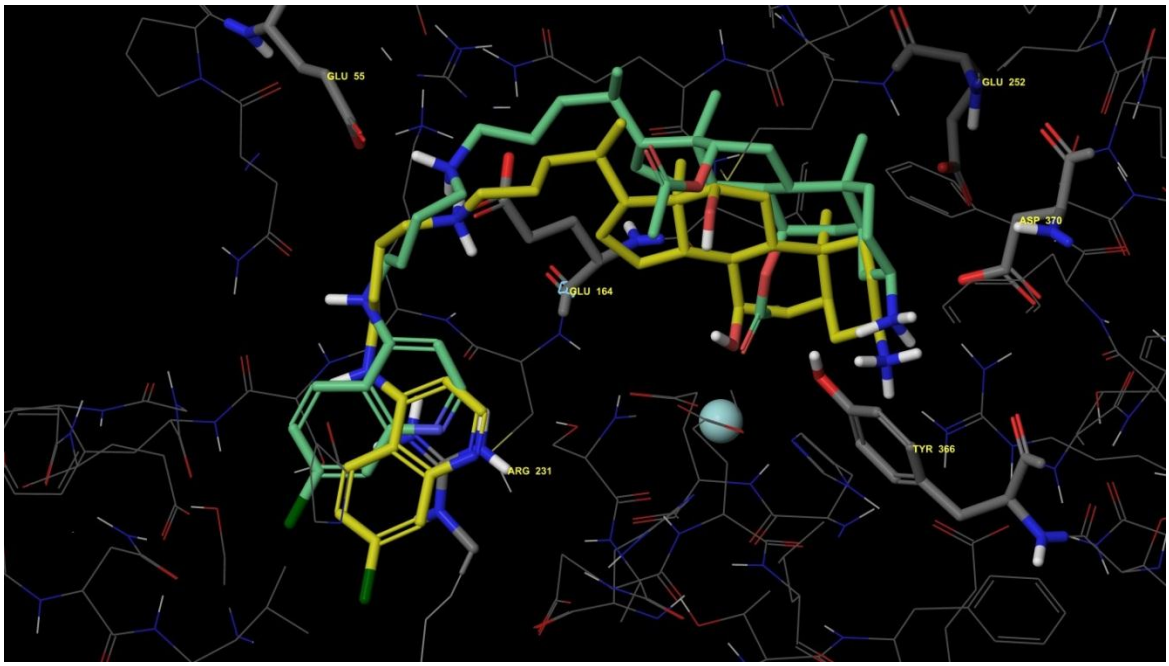


Figure S12. Overlapped docked structures of **16** (green) and **24** (yellow) in the catalytic cleft of the BoNT/A LC at pH 7.0±1.0.

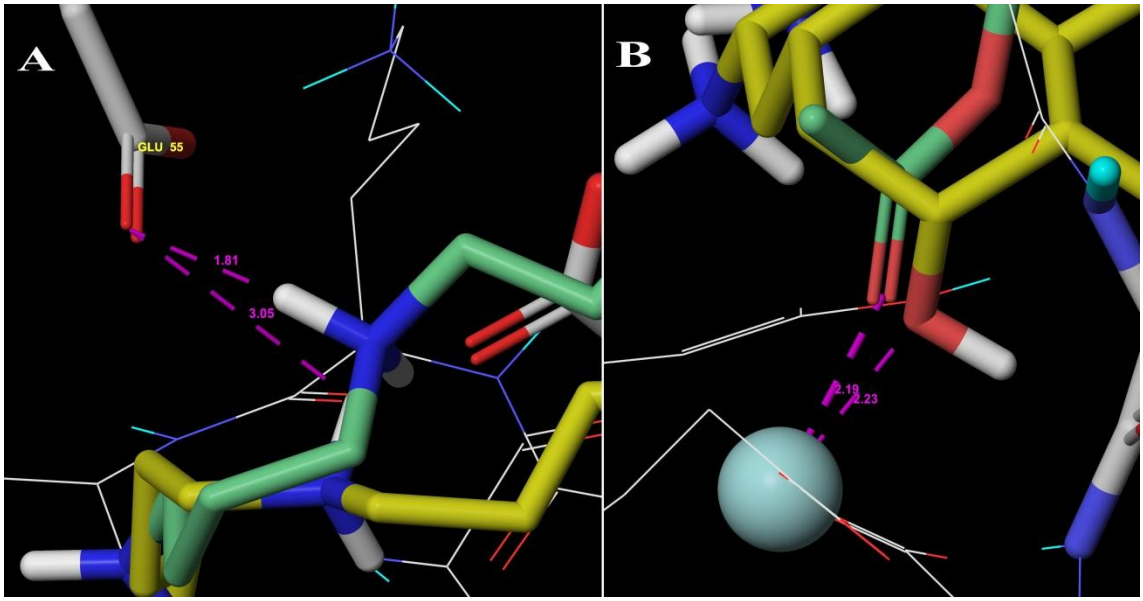


Figure S13. A: **16**-Glu55 distance (1.81 Å) and **24**-Glu55 distance (3.05 Å); B: **16**-Zn^{2+} distance (2.19 Å) and **24**-Zn^{2+} distance (2.23 Å) at pH 7.0±1.0.

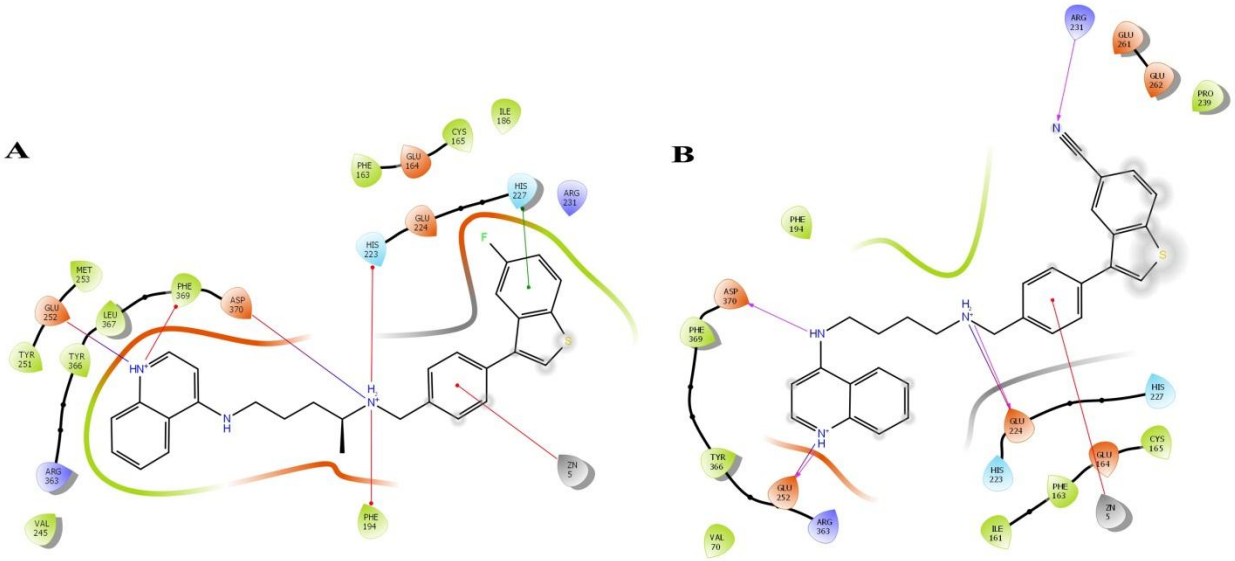


Figure S14. Compounds **34** (A) and **86** (B) docked in the catalytic cleft of BoNT/A LC at pH 7.0±1.0.

Docking scores

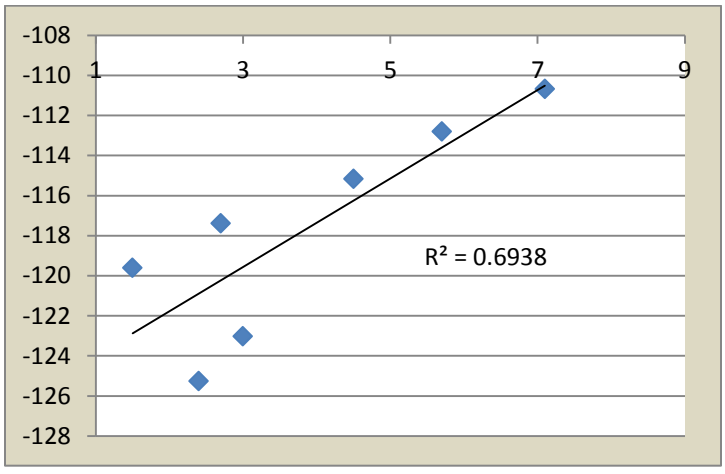
Table S7. Docking scores for **16** and **24**[a]

Compound/score	16	24
Docking score	-10.685	-9.697
Glide score	-10.685	-9.697
Model energy	-110.664	-99.034
Asp:370 Eint	-54.216	-50.774
Tyr:366 Eint	-8.81	-8.36
Glu:252 Eint	-48.758	-37.488
Arg:231 Eint	23.86	25.911
Glu:164 Eint	-70.57	-63.814
Glu:55 Eint	-65.916	-56.733

[a]A lower score indicates better binding of a given ligand in the substrate cleft

Docking-in vitro inhibitory activity correlations

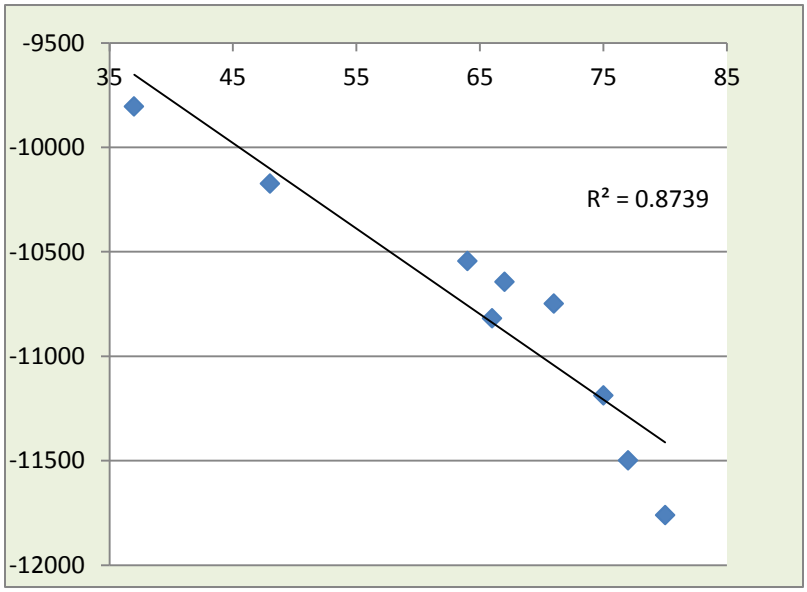
From the Figure S15, it can be seen that there is a certain correlation of IC_{50} and Glide emodel values generated after docking procedure (Emodel represents quantitative representation of the combination of a version of the GlideScore, the internal ligand strain and the coulomb and van der Waals energy).



Compound	IC_{50} (μM)	Glide eModel
14	5.7	-112.811
15	1.5	-119.614
16	4.5	-115.169
17	2.7	-117.385
19	3.0	-123.03
20	2.4	-125.266
22	7.1	-110.686

Figure S15. Correlation of IC_{50} and Glide emodel values

Same structures show relatively good correlation with total potential energy of minimized structure of the ligand-protein complex (Figure S16). This energy was generated by further minimization of docking poses, using MacroModel module (Schrödinger Release 2017-2: MacroModel, Schrödinger, LLC, New York, NY, 2017.). Minimizations were performed using OPLS-2005 force field with water solvent effects (solvent effect was applied using the analytical Generalized-Born/Surface-Area (GB/SA) model), using Polak-Ribier Conjugate Gradient method with 2500 steps or 0.05 convergence threshold. In the model, the structure of ligand and all of the amino acid residues within 6 Å were freely moving, with the exception of His 227, His 223, Glu 262 and Zn^{2+}, that were held frozen.



Compound	% inh	E_{pot} (kJ/mol)
14	80	-11760.4
16	66	-10819.3
17	71	-10748.6
19	75	-11187.9
20	77	-11498.8
22	64	-10544.5
23	67	-10643.5
24	48	-10174.3
30	37	-9805.05

Figure S16. Correlation of % of inhibition with total potential energy

Chemistry

Melting points were determined on a Boetius PMHK apparatus and were not corrected. IR spectra were recorded on a Thermo-Scientific Nicolet 6700 FT-IR diamond crystal spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 spectrometer (at 200 and 50 MHz, respectively), and a Bruker Ultrashield Advance III spectrometer (at 500 and 125 MHz, respectively) in the indicated solvent (vide infra) using TMS as the internal standard. Chemical shifts are expressed in ppm (δ) values and coupling constants (J) in Hz. ESI–MS (HRMS) spectra of the synthesized compounds were acquired on a Agilent Technologies 1200 Series instrument equipped with Zorbax Eclipse Plus C18 (100 × 2.1 mm i.d. 1.8 μm) column and DAD detector (190-450 nm) in combination with a 6210 Time-of-Flight LC/MS instrument in positive and negative ion mode. The samples were dissolved in MeOH (HPLC grade). The selected values were as follows: capillary voltage 4 kV; gas temperature 350 °C; drying gas 12 L min^{-1}; nebulizer pressure 45 psig; fragmentator voltage: 70 V. Mass spectral analyses were done using electrospray ionization in positive ion mode on a Surveyor separations module coupled to a ThermoFinnigan TSQ AM triple quadrupole mass spectrometer. Gas chromatography tandem mass spectrometry (GC-MS) analyses were performed on an Agilent 7890A GC (Agilent) system equipped with a 5975C inert XL EI/CI MSD and a flame ionization detector (FID) connected by capillary flow technology through a 2-way splitter with make-up gas. An HP-5 MS capillary column (Agilent Technologies, 25 mm i.d., 30 m length, 0.25 μm film thickness) was used. The flash chromatography was performed on Biotage SP1 system equipped with UV detector and FLASH 12+, FLASH 25+ or FLASH 40+ columns charged with KP-SIL (40 – 63 μm, pore diameter 60 Å), KP-C18-HS (40 – 63 μm, pore diameter 90 Å) or KP-NH (40 – 63 μm, pore diameter 100 Å) as an adsorbent. Elemental analyses were realized with

an Elemental Vario EL III microanalyser. Compounds were analyzed for purity (HPLC) using a Agilent 1200 HPLC system equipped with Quat Pump (G1311B), Injector (G1329B) 1260 ALS, TCC 1260 (G1316A) and Detector 1260 DAD VL+ (G1315C). Compound **42** was analyzed for purity (HPLC) using Waters 1525 HPLC dual pump system equipped with an Alltech, Select degasser system, and dual λ 2487 UV-VIS detector. HPLC analysis was performed in two diverse systems for each compound. **Method A:** Zorbax Eclipse Plus C18 4.6 × 150 mm, 1.8µ, S.N. USWKY01594 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis were performed at the UV max of the compounds (at 330 nm for compounds **14-16**, **18**, **19**, **22**, **23**, **34**, **37**, **38**, **50**, **56-65**, **66-69**, **77-82**, **84**, **85** and **93**, and at 254 nm for compound **17**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.5 mL/min. Compounds **14**, **16**, **22**, **23**, **56-65**, **66-69**, **77-82**, **84** and **85** were eluted using gradient protocol: 0-1.5 min 95%A, 1-5 min 95%A→ 5%A, 5-16 min 5%A, 16-18 min 5%A→ 95%A. Compounds **15**, **17-19**, **34**, **37** and **50** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-15 min 95%A. Compound **38** was eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-13 min 5%A→ 95%A. Compound **93** was eluted using gradient protocol: 0-2 min 95%A, 2-6 min 95%A→ 5%A, 6-17 min 5%A, 17-19 min 5%A→ 95%A, 19-21 min 95%A. **Method B**: Zorbax Eclipse Plus C18 4.6 x 150 mm, 1.8µ, S.N. USWKY01594 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis were performed at the UV max of the compounds (at 330 nm for compounds **14-19**, **22**, **23**, **34**, **37**, **38**, **44**, **50**, **56-65**, **66-69**, **77-82**, **84**, **85** and **93**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow

rate was 0.5 mL/min. Compounds **14**, **16**, **22** and **23** were eluted using gradient protocol: 0-1.5 min 95%A, 1-5 min 95%A→ 5%A, 5-16 min 5%A, 16-18 min 5%A→ 95%A. Compounds **15**, **17**, **19**, **34**, **37**, **38** and **50** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-15 min 95%A. Compound **18** was eluted using gradient protocol: 0-1 min 95%A, 1-4 min 95%A→ 5%A, 4-11 min 5%A, 11-14 min 5%A→ 95%A, 14-15 min 95%A. Compound **44** was eluted using gradient protocol: 0-1.5 min 95%A, 1-5 min 95%A→ 5%A, 5-17 min 5%A, 17-19 min 5%A→ 95%A. Compounds **56**-**65**, **66**-**69**, **77**-**82**, **84** and **85** were eluted using gradient protocol: 0-1.5 min 95%A, 1-5 min 95%A→ 5%A, 5-16 min 5%A, 16-18 min 5%A→ 95%A, 18-20 min 95%A. Compound **93** was eluted using gradient protocol: 0-1.5 min 95%A, 1-5 min 95%A→ 5%A, 5-14 min 5%A, 14-15 min 5%A→ 95%A, 15-16 min 95%. **Method C**: Zorbax Eclipse Plus C18 2.1 x 100 mm, 1.8µ, S.N. USUXU04444 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis was performed at the UV max of the compound (at 330 nm for compounds **20**, **21**, **24**, **43**, **44**, **47**; at 270 nm for compound **30**, and at 254 nm for compound **33**) to maximize selectivity. Compound was dissolved in methanol, final concentration was ~1 mg/mL. Flow rate was 0.2 mL/min. Compound **20** was eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-15 min 5%A→ 95%A, 15-20 min 95%A. Compounds **21** and **30** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-20 min 95%A. Compound **24** was eluted using gradient protocol: 0-1 min 95%A, 1-2 min 95%A→ 5%A, 2-11 min 5%A, 11-14 min 5%A→ 95%A, 14-18 min 95%A. Compound **33** was eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-18 min 95%A. Compounds **43**, **44** and **47** were eluted using gradient protocol: 0-1 min 95%A, 1-

6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-15 min 95%A. **Method D**: Zorbax Eclipse Plus C18 2.1 x 100 mm, 1.8µ, S.N. USUXU04444 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis was performed at the UV max of the compound (at 254 nm for compounds **20**, **24**, **33**; at 270 nm for compound **30** and at 330 nm for compounds **21, 43** and **47**) to maximize selectivity. Compound was dissolved in methanol, final concentration was ~1 mg/mL. Flow rate was 0.2 mL/min. Compounds **20** and **21** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-20 min 95%A. Compounds **24** and **33** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-18 min 95%A. Compound **30** was eluted using gradient protocol: 0-1 min 95%A, 1-8 min 95%A→ 5%A, 8-12 min 5%A, 12-16 min 5%A→ 95%A, 16-20 min 95%A. Compounds **43** and **47** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-15 min 95%A. **Method E:** Poroshell 120 EC-C18, 4.6 x 50mm, 2.7µ, S.N. USCFU07797 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis was performed at the UV max of the compound (330 nm for compound **48**) to maximize selectivity. Compound was dissolved in methanol, final concentration was ~1 mg/mL. Flow rate was 0.5 mL/min. Compound **48** was eluted using gradient protocol: 0-1 min 95%A, 1-1.5 min 95%A→ 5%A, 1.5-8 min 5%A, 8-10 min 5%A→ 95%A, 10-11 min 95%A. **Method F:** Poroshell 120 EC-C18, 4.6 x 50mm, 2.7µ, S.N. USCFU07797 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis was performed at the UV max of the compound (330 nm for compound **48**) to maximize selectivity. Compound was dissolved in

methanol, final concentration was ~1 mg/mL. Flow rate was 0.5 mL/min. Compound **48** was eluted using gradient protocol: 0-1 min 95%A, 1-1.5 min 95%A→ 5%A, 1.5-8 min 5%A, 8-10 min 5%A→ 95%A, 10-11 min 95%A. **Method G:** Symmetry C18, 4.6 x 150 mm, 5 μm, S.N. 021336278136 37 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis was performed at the UV max of the compound (340 nm for compound **42**) to maximize selectivity. Compound was dissolved in methanol, final concentration was ~1 mg/mL. Compound **42** was eluted using gradient protocol: 0-2 min 10%A→ 20 %A, 2-4 min 20%A, 4-8 min 20%A→ 10 %A. **Method H:** Nucleosil C18, 4 x 150 mm, 5 μm was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis was performed at the UV max of the compound (340 nm for compound **42)** to maximize selectivity. Compound was dissolved in methanol, final concentration was ~1 mg/mL. Compound **42** was eluted using gradient protocol: 0-2 min 6%A→ 12 %A, 2-4 min 12%A→ 30 %A, 4-8 min 30%A→ 6 %A, 8-9 min 6%A.

Procedure A: General procedure for the synthesis of *N*-Cbz protected aminoquinolines 107 and 109.[5] The mixture of 4,7-dichloroquinoline/4-chloroquinoline (1 equiv) and mono-Cbz protected diaminoalkane (1.1 – 1.2 equiv) was slowly heated to 80 °C for 1 h, and the mixture was continued for 6-8 h at 120-130 °C. After cooling to r.t., reaction mixture was transferred to the separation funnel using CH_2Cl_2/1M NaOH. The organic layer was washed with 1M NaOH, water and brine. The organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated under reduced pressure. Crude product was purified using column chromatography.

Procedure B: General procedure for the obtainment of steroidal derivatives 4-11 and 29.[1] Alcohol (1 equiv) was dissolved in CH_2Cl_2. PCC (1.5 equiv) was added, and the mixture was stirred at r.t. for 3.5 h. Reaction mixture was filtered through a short column of SiO_2 (eluent CH_2Cl_2/EtOAc = 7/3). Crude aldehyde was dissolved in dry MeOH, aminoquinoline (1.5 equiv) was added, and mixture was stirred at r.t. overnight. $NaBH_4$ (2 equiv) was added, and stirring was continued at r.t. for 12 h. Solvent was removed under reduced pressure and crude mixture was prepared for column purification.

Procedure C: General procedure for the removal of the Boc-protecting groups with TFA for compounds 14-23 and 30. A solution of the *N*-Boc-protected amine in TFA/CH_2Cl_2 (v:v; 1:10), was stirred at r.t. for 6 h. Solvents were evaporated under reduced pressure and the residue was treated with CH_2Cl_2/2.5M NaOH. The organic layer was dried over $MgSO_4$, and the solvent was evaporated under reduced pressure.

Procedure D: General procedure for N-methylated aminoquinolines 12, 13, 37, 38, 48, 56-65, 68, 69 and 84, 85.[6] To a stirred solution of aminoquinolines (1 equiv) in MeOH containing 37% aqueous formaldehyde (2 equiv), the mixture of $ZnCl_2$ (2 equiv) and $NaHB_3CN$ (4 equiv) in MeOH was added. After the reaction mixture was stirred at r.t. for 4 h, the solution was taken up in 0.1 M NaOH and most of MeOH was evaporated under reduced pressure. Aqueous solution was extracted with CH_2Cl_2, the combined extracts were washed with water and brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure.

Procedure E: General procedure for reductive amination to produce compounds 33, 34, 42-45, 50, 66 and 67. Amine (1.5 equiv) and appropriate aldehyde (1 equiv) were dissolved in MeOH/CH_2Cl_2 mixture (v:v; 2:1), glac. AcOH (1.5 equiv) was added, and the mixture was

stirred under Ar atmosphere at r.t. After 3 h, $NaBH_4$ (6 equiv) was added, and stirring was continued for another 18 h. Solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2. The organic layer was washed with 2M NH_4OH, water and then extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over anh. Na_2SO_4. Finally, the solvent was evaporeted under reduced pressure.

Procedure F: General procedure for the Suzuki coupling reaction using PdO × 1.4 H_2O for compounds 40 and 113.[7] An appropriate aryl-bromide (1 equiv) was added to the mixture of arylboronic acid (1.2 equiv), catalyst PdO × 1.4 H_2O (0.1 equiv), K_2CO_3 (1.2 equiv) and EtOH/H_2O (3:1, v/v). The mixture was stirred at 60 °C for 5 h, then diluted with water and extracted with CH_2Cl_2. Combined organic layers were washed with brine and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The product was purified using silica gel flash chromatography.

Procedure G: General procedure for the Suzuki coupling reaction using $Pd(OAc)_2$ and PPh_3 for compounds 49 and 111. The solution of $Pd(OAc)_2$ (0.1 equiv) and PPh_3 (0.4 equiv) in DME was purged with argon and stirred at r. t. for 10 min. An appropriate arylboronic acid (1 equiv) and 2M aq. Na_2CO_3 were added. After 5 min, aryl-bromide (1 equiv) was added. The mixture is once more purged with Ar and heated in a sealed vessel in microwave reactor at 80 °C for 3h. The reaction mixture was cooled and extracted with ethyl-acetate. The combined organic layers were washed with brine and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The crude product was further purified in a manner provided for each compound.

Procedure H: General procedure for palladium catalyzed amination of quinolones to produce compounds 78, 79, 81 and 82. Vial was charged with mixture of $Pd(OAc)_2$ (4 mol %) and DPEphos (8 mol %)/SPhos (8 mol %) in dioxne and stirred for a few minutes in Ar atmosphere on room temperature. Subsequently, haloquinoline (1.0 equiv), amine (1.2 equiv) and K_3PO_4 (2.5 equiv) were added in to reaction mixture.The resulting suspension was sparged with argon for several minuties. The vial was quickly capped, heated to 85 ^oC over the night and then cooled down to room temperature. The mixture was adsorbed onto silica gel and purified.

N-(quinolin-4-yl)ethane-1,2-diamine **(AQ11)**, *N*-(7-chloroquinolin-4-yl)butane-1,4-diamine (**AQ4**), *N*-(7-chloroquinolin-4-yl)hexane-1,6-diamine (**AQ6**), *N*-(quinolin-4-yl)propane-1,3-diamine (**AQ7**), *N*-(quinolin-4-yl)butane-1,4-diamine (**AQ8**), *N*-(quinolin-4-yl)hexane-1,6-diamine (**AQ9**), *N*-quinolin-4-yldecane-1,10-diamine (**AQ12**) were prepared according to known procedures.[8-11]

***N*-quinolin-4-yldecane-1,10-diamine (AQ12).**

The mixture of 4-chloroquinoline (37.9 mg, 0.232 mmol) and 1,10-diaminodecane (200 mg, 1.16 mmol) were subjected to microwave irradiation using Biotage Initiator 2.5 apparatus for 10 min at 80 °C, followed by 1h at 140 °C. After cooling to room temperature 0.1 M aqueous NaOH was added and then extracted with dichloromethane. Combined organic layers were dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The crude product was purified using column chromatography (dry-flash, SiO_2, eluent CH_2Cl_2/MeOH). Final product was obtained as yellow oil (19.9 mg, 53%). IR (ATR): 3329m, 2924s, 2854s, 1651m, 1581s, 1492m, 1465m, 1390m, 1342m, 1317m, 1158w, 767w, 722w. ^1H NMR (500 MHz,

CD_3OD, δ): 8.33 (d, 1H, *J* = 5.5, H-C(2)), 8.10 (d, 1H, *J* = 7.6, H-C(8)), 7.81 (d, 1H, *J* = 7.8, H-C(5)), 7.65 – 7.55 (m, 1H, H-C(7)), 7.48 – 7.36 (m, 1H, H-C(6)), 6.44 (d, 1H, *J* = 5.5, H-C(3)), 3.35 – 3.26 (m, 2H, ArNH*CH*$_2$-), 2.70 – 2.48 (m, 2H, -*CH*$_2$-NH_2), 1.77 – 1.65 (m, 2H, $ArNHCH_2$*CH*$_2$-), 1.50 – 1.08 (m, 14 H, -$(CH_2)_7$-). ^{13}C NMR (125 MHz, CD_3OD, δ): 152.77, 151.38, 149.12, 130.52, 129.03, 125.63, 122.42, 120.49, 99.25, 44.19, 42.73, 33.97, 30.84, 30.78, 30.69, 29.63, 28.42, 28.19. HRMS: *m/z* 150.62467 corresponds to molecular formula $C_{19}H_{29}N_3H_2^{2+}$ (error in ppm -4.51).

(3α,5β,7α,12α)-3-[(*Tert*-butoxycarbonyl)amino]-24-{[4-(quinolin-4-ylamino)butyl]amino}cholane-7,12-diyl diacetate (4).

According to general procedure B, alcohol **3** (445 mg, 0.770 mmol) was transformed into aldehyde using PCC (239 mg, 1.10 mmol) in CH_2Cl_2 (35 mL), which was further transformed into **4** using amine **AQ8**[4] (211.5 mg, 0.9823 mmol), $NaBH_4$ (49.5 mg, 1.31 mmol) and MeOH (20 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) = 9/1). Final product **4** was obtained as colorless oil (360 mg, 60%). $[\alpha]_D^{20}$ = +38.9 (MeOH). IR (ATR): 3320w, 3052w, 2935s, 2866m, 1724s, 1618w, 1582s, 1540m, 1441w, 1375m, 1342w, 1310w, 1250s, 1171m, 1126w, 1064w, 1023w, 999w, 965w, 884w, 854w, 808w, 765w, 736m, 702w, 610w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.54 (d, 1H, *J* = 5.3, H-C(2')), 7.97 (d, 1H, *J* = 8.2, H-C(8')), 7.76 (d, 1H, *J* = 8.2, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.42-7.37 (m, 1H, H-C(6')), 6.40 (d, 1H, *J* = 5.2, H-C(3')), 5.77 (bs, 1H, H-N, exchangeable with D_2O), 5.10-5.07 (m, 1H, H-C(12)), 4.92-4.88 (m, 1H, H-C(7)), 4.42 (bs, 1H, H-N, exchangeable with D_2O), 3.35-3.21 (m, 3H, ArNHC*H*$_2$- and H-C(3)), 2.73-2.66 (m, 2H, $ArNHCH_2CH_2CH_2CH_2$-), 2.65-2.54 (m, 2H-

C(24)), 2.10 (s, 3H, C*H*$_3$COO-C(12)), 2.05 (s, 3H, C*H*$_3$COO-C(7)), 2.00-1.44 (m, 20H, H-steroid), 1.44 (s, 9H, -NHCOOC(C*H*$_3$)$_3$), 1.41-0.97 (m, 9H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.82 (d, 3H, *J* = 6.6, C*H*$_3$-C(20)), 0.71 (s, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.39, 170.27, 155.12, 151.05, 149.85, 148.42, 129.87, 128.87, 124.32, 119.57, 118.83, 98.58, 79.16, 75.48, 70.86, 50.55, 49.29, 47.49, 44.99, 43.36, 43.18, 41.53, 37.70, 36.39, 35.48, 34.90, 34.24, 33.36, 31.29, 28.85, 28.40, 27.85, 27.26, 26.46, 26.43, 25.49, 22.80, 22.68, 21.60, 21.37, 17.91, 12.18. HRMS: *m/z* 775.53542 corresponds to molecular formula $C_{46}H_{70}N_4O_6H^+$ (error in ppm -1.79).

(3α,5β,7α,12α)-3-[(*tert*-butoxycarbonyl)amino]-24-({4-[(7-chloroquinolin-4-yl)amino]butyl}amino)cholane-7,12-diyl diacetate (5).

According to general procedure B, alcohol **3** (430.0 mg, 0.7442 mmol) was transformed into aldehyde using PCC (230 mg, 1.1 mmol) in CH_2Cl_2 (35 mL), which was further transformed into **5** using amine **AQ4** (230.8 mg, 0.9242 mmol), $NaBH_4$ (46.7 mg, 1.23 mmol) and MeOH (20 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) = 9/1). Final product **5** was obtained as colorless oil (396.3 mg, 66%). $[\alpha]_D^{20}$ = +62.2 (MeOH). IR (ATR): 3311w, 3054w, 2935s, 2866m, 2157w, 1724s, 1610w, 1581s, 1535w, 1450w, 1370m, 1331w, 1248s, 1170w, 1135w, 1064w, 1022w, 999w, 965w, 880w, 851w, 808w, 768w, 736w, 702w, 647w, 609w, 411sl cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.51 (d, 1H, *J* = 5.5, H-C(2')), 7.96-7.92 (m, 1H, H-C(8')), 7.71 (d, 1H, *J* = 8.9, H-C(5')), 7.34-7.30 (m, 1H, H-C(6')), 6.37 (d, 1H, *J* = 5.2, H-C(3')), 6.03 (bs, 1H, H-N, exchangeable with D_2O), 5.11-5.07 (m, 1H, H-C(12)), 4.92-4.88 (m, 1H, H-C(7)), 4.43 (bs, 1H, H-N, exchangeable with D_2O), 3.34-3.24 (m, 3H,

ArNHCH_2- and H-C(3)), 2.73-2.67 (m, 2H, ArNHCH$_2$CH$_2$CH$_2$CH_2-), 2.64-2.52 (m, 2H-C(24)), 2.10 (s, 3H, CH_3COO-C(12)), 2.06 (s, 3H, CH_3COO-C(7)), 2.02-1.45 (m, 20H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.41-0.98 (m, 9H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.84-0.81 (m, 3H, CH_3-C(20)), 0.72 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.38, 170.26, 155.13, 152.08, 149.95, 149.19, 134.64, 128.71, 124.88, 121.38, 117.31, 98.83, 79.17, 75.46, 70.84, 50.53, 49.15, 47.52, 44.98, 43.36, 43.19, 41.52, 37.68, 36.37, 35.47, 34.93, 34.22, 33.36, 31.28, 28.84, 28.39, 27.87, 27.26, 26.52, 26.28, 25.48, 22.77, 22.67, 21.59, 21.36, 17.91, 12.18. HRMS: *m/z* 809.49621 corresponds to molecular formula $C_{46}H_{69}ClN_4O_6H^+$ (error in ppm -2.01).

(3α,5β,7α,12α)-3-[(*tert*-butoxycarbonyl)amino]-24-{[4-(quinolin-4-ylamino)pentyl]amino}cholane-7,12-diyl diacetate (6) (Mixture of diastereomers).

According to general procedure B, alcohol **3** (493.6 mg, 0.8543 mmol) was transformed into aldehyde using PCC (265.2 mg, 1.230 mmol) in CH_2Cl_2 (35 mL), which was further transformed into **6** using amine N^4-(quinolin-4-yl)pentane-1,4-diamine[2] (238.9 mg, 1.042 mmol), $NaBH_4$ (52.6 mg, 1.39 mmol) and MeOH (10 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) = 9/1, flash, Biotage SP1, RP column 40+M, eluent MeOH/H_2O gradient 7/3 → MeOH). Final product **6** was obtained as mixture of diastereomers. Colorless foam (398 mg, 59%). M.p. = 101 – 103 °C. $[\alpha]_D^{20}$ = +48.0 (MeOH). IR (ATR): 3356w, 3260w, 3233w, 3192w, 3122w, 2934s, 2868m, 1718s, 1622w, 1580s, 1533s, 1450m, 1374s, 1168s, 1062w, 1023m, 965w, 890w, 857w, 809w, 764m, 691w, 655w, 609w, 533w, 500w, 474w, 435w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.55-8.52 (m, 1H, H-C(2')), 7.98-7.95 (m, 1H, H-C(8')), 7.73 (d, 1H, *J* = 8.4, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.42-7.37 (m, 1H, H-C(6')),

6.42 (d, 1H, *J* = 5.5, H-C(3')), 5.29-5.23 (m, 1H, H-N, exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.91-4.88 (m, 1H, H-C(7)), 4.42 (bs, 1H, H-N), 3.77-3.68 (m, 1H, ArNHC*H*(CH_3)-), 3.27 (bs, 1H, H-C(3)), 2.69-2.61 (m, 2H, ArNHCH(CH_3)$CH_2CH_2CH_2$-), 2.61-2.49 (m, 2H-C(24)), 2.10 and 2.09 (s and s, overlap, 3H, C*H*$_3$COO-C(12)), 2.06 and 2.05 (s and s, overlap, 3H, C*H*$_3$COO-C(7)), 2.00-1.45 (m, 20H, H-steroid), 1.44 (s, 9H, -NHCOOC(C*H*$_3$)$_3$), 1.40-1.33 (m, 3H, H-steroid), 1.32 (d, 3H, *J* = 6.4, ArNHCH(C*H*$_3$)-), 1.25-0.75 (m, 6H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.81 (d, 3H, *J* = 6.6, C*H*$_3$-C(20)), 0.71 and 0.70 (s and s, overlap, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.39, 170.28, 155.12, 151.00, 148.89, 148.63, 129.98, 128.87, 124.32, 119.35, 118.83, 98.86, 79.21, 75.48, 70.87, 50.58, 50.54, 49.67, 48.18, 47.45, 44.98, 43.37, 41.54, 37.70, 36.40, 35.49, 34.87, 34.23, 33.32, 31.29, 28.85, 28.40, 27.26, 26.59, 26.56, 26.47, 25.49, 22.79, 22.69, 21.60, 21.38, 20.27, 17.90, 12.18. HRMS: *m/z* 789.55312 corresponds to molecular formula $C_{47}H_{72}N_4O_6H^+$ (error in ppm 0.84).

(3α,5β,7α,12α)-3-[(*tert*-butoxycarbonyl)amino]-24-{[1-methyl-4-(quinolin-4-ylamino)butyl]amino}cholane-7,12-diyl diacetate (7) (Mixture of diastereomers).

According to general procedure B, alcohol **3** (440.0 mg, 0.7615 mmol) was transformed into aldehyde using PCC (236 mg, 1.09 mmol) in CH_2Cl_2 (35 mL), which was further transformed into **7** using amine **108** (221 mg, 0.964 mmol), $NaBH_4$ (48.6 mg, 1.28 mmol) and MeOH (20 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) gradient 9/1 → 7/3). Final product **7** was obtained as mixture of diastereomers. Colorless oil (390 mg, 65%). $[\alpha]_D^{20}$ = +40.0 (MeOH). IR (ATR): 3337m, 3190m, 2932s, 2866s, 2654w, 1729s, 1582s, 1537s, 1444m, 1374s, 1244s, 1170s, 1063w, 1024m, 966w, 940w, 885w, 856w, 807w,

764m, 656w, 611w, 532w, 406w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.55 (d, 1H, *J* = 5.3, H-C(2')), 7.99-7.96 (m, 1H, H-C(8')), 7.78-7.74 (m, 1H, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.43-7.38 (m, 1H, H-C(6')), 6.40 (d, 1H, *J* = 5.5, H-C(3')), 5.60 (bs, 1H, H-N, exchangeable with D_2O), 5.09-5.06 (m, 1H, H-C(12)), 4.91-4.87 (m, 1H, H-C(7)), 4.46 (bs, 1H, H-N), 3.38-3.20 (m, 3H, ArNHCH_2- and H-C(3)), 2.77-2.69 (m, 1H, ArNHCH$_2$CH$_2$CH$_2$C*H*(CH_3)-), 2.67-2.47 (m, 2H-C(24)), 2.09 and 2.08 (s and s, overlap, 3H, CH_3COO-C(12)), 2.05 and 2.04 (s and s, overlap, 3H, CH_3COO-C(7)), 2.00-1.45 (m, 20H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.42-1.20 (m, 6H, H-steroid), 1.09 (d, 3H, *J* = 6.2, ArNHCH$_2$CH$_2$CH$_2$CH(CH_3)-), 1.08-1.01 (m, 3H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.81 (d, 3H, *J* = 6.4, CH_3-C(20)), 0.70 and 0.69 (s and s, overlap, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.38, 170.26, 155.17, 151.02, 149.78, 148.40, 129.88, 128.88, 124.37, 119.47, 118.78, 98.62, 79.17, 75.46, 70.84, 52.68, 47.65, 47.62, 47.44, 47.41, 44.95, 43.46, 43.35, 41.52, 37.67, 36.37, 35.47, 34.82, 34.64, 34.58, 34.21, 33.39, 33.36, 31.27, 28.84, 28.38, 27.23, 26.70, 25.47, 25.11, 22.76, 22.66, 21.57, 21.35, 20.46, 20.40, 17.88, 12.16. HRMS: *m/z* 789.54993 corresponds to molecular formula $C_{47}H_{72}N_4O_6H^+$ (error in ppm -3.21); *m/z* 395.27922 corresponds to molecular formula $C_{47}H_{72}N_4O_6H_2^{2+}$ (error in ppm -1.64).

(3α,5β,7α,12α)-3-[(*tert*-butoxycarbonyl)amino]-24-({4-[7-(chloroquinolin-4-ylamino)pentyl}amino)cholane-7,12-diyl diacetate (8) (Mixture of diastereomers).

According to general procedure B, alcohol **3** (150.0 mg, 0.2596 mmol) was transformed into aldehyde using PCC (80.6 mg, 0.374 mmol) in CH_2Cl_2 (15 mL), which was further transformed into **8** using amine N^4-(7-chloroquinolin-4-yl)pentane-1,4-diamine[4] (80.4 mg, 0.305 mmol), $NaBH_4$ (15.4 mg, 0.406 mmol) and MeOH (10 mL). The product was purified using column

chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) = 9/1). Final product **8** was obtained as mixture of diastereomers. Colorless oil (142.9 mg, 67%). $[\alpha]_D^{20}$ = +51.1 (MeOH). IR (ATR): 3364w, 3317w, 2934s, 2868m, 1716s, 1612w, 1578s, 1535m, 1450m, 1374s, 1335w, 1246s, 1170m, 1064w, 1024m, 965w, 940w, 880w, 852w, 810w, 767w, 605w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.52-8.49 (m, 1H, H-C(2')), 7.95-7.92 (m, 1H, H-C(8')), 7.68 (d, 1H, *J* = 8.9, H-C(5')), 7.34-7.30 (m, 1H, H-C(6')), 6.40 (d, 1H, *J* = 5.5, H-C(3')), 5.48-5.43 (m, 1H, H-N, exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.91-4.87 (m, 1H, H-C(7)), 4.43 (bs, 1H, H-N, exchangeable with D_2O), 3.75-3.66 (m, 1H, ArNHC*H*(CH_3)-), 3.27 (bs, 1H, H-C(3)), 2.67-2.61 (m, 2H, ArNHCH(CH_3)$CH_2CH_2CH_2$-), 2.60-2.48 (m, 2H-C(24)), 2.10 and 2.09 (s and s, overlap, 3H, C*H*$_3$COO-C(12)), 2.06 (s, 3H, C*H*$_3$COO-C(7)), 2.00-1.45 (m, 20H, H-steroid), 1.44 (s, 9H, -NHCOOC(C*H*$_3$)$_3$), 1.40-1.32 (m, 3H, H-steroid), 1.31 (d, 3H, *J* = 6.4, ArNHCH(C*H*$_3$)-), 1.26-0.99 (m, 6H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.82 (d, 3H, *J* = 6.6, C*H*$_3$-C(20)), 0.72 and 0.71 (s and s, overlap, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.38, 170.27, 155.12, 151.99, 149.37, 149.02, 134.68, 128.79, 124.91, 121.17, 117.32, 99.13, 79.18, 75.47, 70.85, 53.39, 50.56, 50.53, 49.51, 48.28, 47.48, 44.97, 43.35, 41.52, 37.69, 36.38, 35.47, 34.90, 34.87, 34.22, 34.07, 33.32, 31.28, 28.84, 28.39, 27.25, 26.49, 26.48, 25.48, 22.77, 22.67, 21.59, 21.36, 20.14, 17.89, 12.17. HRMS: *m/z* 823.51447 corresponds to molecular formula $C_{47}H_{71}ClN_4O_6H^+$ (error in ppm 1.19); *m/z* 412.26065 corresponds to molecular formula $C_{47}H_{71}ClN_4O_6H_2^{2+}$ (error in ppm 0.66).

(3α,5β,7α,12α)-3-[(*Tert*-butoxycarbonyl)amino]-24-({4-[(7-chloroquinolin-4-yl)amino]-1-methylbutyl}amino)cholane-7,12-diyl diacetate (9) (Mixture of diastereomers).

According to general procedure B, alcohol **3** (120.0 mg, 0.2077 mmol) was transformed into aldehyde using PCC (64.5 mg, 0.299 mmol) in CH_2Cl_2 (12 mL), which was further transformed into **9** using amine **110** (67.3 mg, 0.255 mmol), $NaBH_4$ (12.9 mg, 0.340 mmol) and MeOH (8 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) gradient 95/5 → 8/2). Final product **9** was obtained as mixture of diastereomers. Colorless oil (132.4 mg, 77%). $[\alpha]_D^{20}$ = +44.6 (MeOH). IR (ATR): 3341w, 3055w, 2935s, 2866m, 1723s, 1610w, 1581s, 1538m, 1451m, 1371m, 1332w, 1249s, 1171m, 1065w, 1023w, 999w, 852w, 809w, 737m cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.52 (d, 1H, *J* = 5.2, H-C(2')), 7.96-7.94 (m, 1H, H-C(8')), 7.71-7.68 (m, 1H, H-C(5')), 7.35-7.32 (m, 1H, H-C(6')), 6.38 (d, 1H, *J* = 5.5, H-C(3')), 5.82-5.77 (m, 1H, H-N exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.91-4.88 (m, 1H, H-C(7)), 4.45 (bs, 1H, H-N), 3.35-3.20 (m, 3H, ArNHCH_2- and H-C(3)), 2.76-2.69 (m, 1H, ArNHCH$_2$CH$_2$CH$_2$C*H*(CH$_3$)-), 2.67-2.46 (m, 2H-C(24)), 2.09 and 2.09 (s and s, overlap, 3H, CH_3COO-C(12)), 2.05 i 2.04 (s and s, overlap, 3H, CH_3COO-C(7)), 2.02-1.45 (m, 20H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.40-1.20 (m, 6H, H-steroid), 1.09 (d, 3H, *J* = 6.4, ArNHCH$_2$CH$_2$CH$_2$CH(CH_3)-), 1.07-0.97 (m, 3H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.81 (d, 3H, *J* = 6.6, CH_3-C(20)), 0.71 i 0.70 (s and s, overlap, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.37, 170.27, 155.11, 151.08, 149.86, 149.20, 134.69, 128.78, 124.99, 121.23, 117.26, 98.91, 79.17, 75.47, 70.84, 52.59, 50.78, 47.62, 47.58, 47.47, 44.98, 43.50, 43.37, 41.52, 37.68, 36.38, 35.47, 34.87, 34.69, 34.62, 34.22, 33.41, 33.39, 31.28, 28.85, 28.40, 27.24, 26.80,

25.49, 24.98, 22.77, 22.67, 21.58, 21.36, 20.50, 20.46, 17.89, 12.18. HRMS: *m/z* 823.51237 corresponds to molecular formula $C_{47}H_{71}N_4ClO_6H^+$ (error in ppm -1.36).

(3α,5β,7α,12α)-3-[(*Tert*-butoxycarbonyl)amino]-24-{[6-(quinolin-4-ylamino) hexyl]amino}cholane-7,12-diyl diacetate (10).

According to general procedure B, alcohol **3** (207.4 mg, 0.3590 mmol) was transformed into aldehyde using PCC (111.4 mg, 0.5170 mmol) in CH_2Cl_2 (17 mL), which was further transformed into **10** using amine **AQ9**[2] (115.4 mg, 0.4742 mmol), $NaBH_4$ (23.9 mg, 0.632 mmol) and MeOH (5 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) = 9/1 → 6/4; flash, Biotage SP1, RP column 25+M, eluent MeOH/H_2O gradient 75/25 → MeOH). Final product **10** was obtained as a pale yellow oil (157 mg, 54%). $[\alpha]_D^{20}$ = +22.6 (MeOH). IR (ATR): 3325w, 2932s, 2862m, 1725s, 1619w, 1582s, 1540m, 1460w, 1376m, 1342w, 1249s, 1172w, 1127w, 1065w, 1024w, 965w, 885w, 810w, 765w, 736w, 608w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.57-8.54 (m, 1H, H-C(2')), 7.98 (d, 1H, *J* = 8.2, H-C(8')), 7.73 (d, 1H, *J* = 8.2, H-C(5')), 7.65-7.60 (m, 1H, H-C(7')), 7.45-7.39 (m, 1H, H-C(6')), 6.44-6.40 (m, 1H, H-C(3')), 5.10-5.06 (m, 1H, H-C(12)), 5.05-5.00 (m, 1H, H-N, exchangeable with D_2O), 4.92-4.87 (m, 1H, H-C(7)), 4.44 (bs, 1H, H-N), 3.36-3.22 (m, 3H, ArNHCH_2- and H-C(3)), 2.65-2.48 (m, 4H, ArNHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH_2- and 2H-C(24)), 2.10 (s, 3H, CH_3COO-C(12)), 2.06 (s, 3H, CH_3COO-C(7)), 2.00-1.45 (m, 24H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.40-0.98 (m, 9H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.82 (d, 3H, *J* = 6.4, CH_3-C(20)), 0.71 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.39, 170.27, 155.14, 151.02, 149.60, 148.40, 129.96, 128.90, 124.50, 119.12, 118.66, 98.72, 79.17, 75.48, 70.85, 53.38, 50.58, 49.96,

47.40, 44.95, 43.35, 43.14, 41.51, 37.68, 36.38, 35.47, 34.82, 34.21, 33.31, 31.28, 30.07, 28.85, 28.38, 27.22, 27.12, 27.07, 26.41, 25.47, 22.78, 22.66, 21.58, 21.36, 17.88, 12.16. HRMS: *m/z* 803.56820 corresponds to molecular formula $C_{48}H_{74}N_4O_6H^+$ (error in ppm 0.11).

(3α,5β,7α,12α)-3-[(*Tert*-butoxycarbonyl)amino]-24-({6-[(7-chloroquinolin-4-yl)amino]hexyl}amino)cholane-7,12-diyl diacetate (11).

According to general procedure B, alcohol **3** (121.4 mg, 0.2101 mmol) was transformed into aldehyde using PCC (65.2 mg, 0.302 mmol) in CH_2Cl_2 (10 mL), which was further transformed into **11** using amine **AQ6** (82.2 mg, 0.296 mmol), $NaBH_4$ (15.0 mg, 0.39 mmol) and MeOH (4 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc = 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) = 9/1; flash, Biotage SP1, RP column 25+M, eluent MeOH/H_2O gradient 75/25 → MeOH). Final product **11** was obtained as a colorless oil (103 mg, 58%). $[\alpha]_D^{20}$ = +87.5 (MeOH). IR (ATR): 3344w, 3054w, 2933s, 2862m, 1724s, 1610w, 1580s, 1536w, 1451w, 1371m, 1331w, 1249s, 1171m, 1065w, 1023w, 965w, 884w, 851w, 808w, 737m, 703w, 613w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.53 (d, 1H, *J* = 5.3, H-C(2')), 7.97-7.94 (m, 1H, H-C(8')), 7.66 (d, 1H, *J* = 8.9, H-C(5')), 7.37-7.34 (m, 1H, H-C(6')), 6.41 (d, 1H, *J* = 5.5, H-C(3')), 5.10-5.07 (m, 1H, H-C(12)), 5.04-4.99 (m, 1H, H-N, exchangeable with D_2O), 4.92-4.88 (m, 1H, H-C(7)), 4.43 (bs, 1H, H-N), 3.35-3.22 (m, 3H, ArNHCH_2- and H-C(3)), 2.65-2.48 (m, 4H, ArNHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH_2- and 2H-C(24)), 2.10 (s, 3H, CH_3COO-C(12)), 2.06 (s, 3H, CH_3COO-C(7)), 2.00-1.45 (m, 23H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.41-0.98 (m, 10H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.82 (d, 3H, *J* = 6.4, CH_3-C(20)), 0.71 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.40, 170.28, 155.12, 152.04, 149.64, 149.14, 134.77, 128.86, 125.20, 120.78, 117.08,

99.04, 79.19, 75.49, 70.86. 50.60, 49.96, 47.41, 44.96, 43.36, 43.17, 41.52, 37.69, 36.39, 35.47, 34.83, 34.22, 33.32, 31.29, 30.09, 28.84, 28.81, 28.40, 27.24, 27.11, 27.05, 26.44, 25.48, 22.79, 22.67, 21.60, 21.37, 17.90, 12.17. HRMS: *m/z* 837.52879 corresponds to molecular formula $C_{48}H_{73}ClN_4O_6H^+$ (error in ppm -0.42).

(3α,5β,7α,12α)-3-[(*Tert*-butoxycarbonyl)amino]-24-{methyl[4-(quinolin-4-ylamino)butyl]amino}cholane-7,12-diyl diacetate (12).

Compound **12** was prepared by procedure D, using **4** (340.0 mg, 0.4387 mmol), 37% aqueous formaldehyde (65 μL, 0.88 mmol), $ZnCl_2$ (30.0 mg, 0.219 mmol), $NaHB_3CN$ (28.0 mg, 0.439 mmol) and MeOH (5 mL + 5 mL). Final product **12** was obtained as colorless foam (300 mg, 87%). M.p. = 85 – 86 °C. $[\alpha]_D^{20}$= +60.0 (MeOH). IR (ATR): 3356w, 2939s, 2865m, 2789w, 1729s, 1711s, 1582s, 1541m, 1444w, 1372m, 1308w, 1239s, 1170m, 1123w, 1063w, 1024m, 763w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.59-8.50 (m, 1H, H-C(2')), 8.05-7.94 (m, 1H, H-C(8')), 7.81-7.75 (m, 1H, H-C(5')), 7.65-7.58 (m, 1H, H-C(7')), 7.44-7.36 (m, 1H, H-C(6')), 6.42-6.37 (m, 1H, H-C(3')), 5.94 (bs, 1H, H-N, exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.92-4.86 (m, 1H, H-C(7)), 4.54 (bs, 1H, H-N), 3.34-3.22 (m, 3H, ArNHCH_2- and H-C(3)), 2.44-2.39 (m, 2H, ArNHCH$_2$CH$_2$CH$_2$CH_2-), 2.36-2.30 (m, 2H-C(24)), 2.22 (s, 3H, CH_3-N), 2.07 (s, 3H, CH_3COO-C(12)), 2.03 (s, 3H, CH_3COO-C(7)), 2.00-1.45 (m, 19H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.40-0.97 (m, 9H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.83-0.80 (m, 3H, CH_3-C(20)), 0.70 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.36, 170.26, 155.16, 150.87, 150.02, 148.24, 129.67, 128.90, 124.29, 119.71, 118.78, 98.52, 79.13, 75.45, 70.83, 58.11, 57.00, 53.37, 50.71, 47.57, 44.98, 43.35, 43.24, 42.44, 41.52, 37.66, 36.35, 35.47, 34.94, 34.20, 33.54, 31.26, 28.86, 28.38, 27.24, 26.63, 25.48, 25.19, 23.56, 22.76, 22.66, 21.57, 21.33,

17.91, 12.16. HRMS: *m/z* 789.55095 corresponds to molecular formula $C_{47}H_{72}N_4O_6H^+$ (error in ppm -1.91); *m/z* 395.27983 corresponds to molecular formula $C_{47}H_{72}N_4O_6H_2^{2+}$ (error in ppm -0.09).

(3α,5β,7α,12α)-3-[(*tert*-butoxycarbonyl)amino]-24-{methyl[4-(quinolin-4-ylamino)pentyl]amino}cholane-7,12-diyl diacetate (13) (Mixture of diastereomers).

Compound **13** was prepared by procedure D, using **6** (223.0 mg, 0.2826 mmol), 37% aqueous formaldehyde (42 μL, 0.56 mmol), $ZnCl_2$ (19.3 mg, 0.141 mmol), $NaHB_3CN$ (17.8 mg, 0.283 mmol) and MeOH (4 mL + 4 mL). Final product **13** was obtained as mixture of diastereomers. Colorless foam (186 mg, 82%). M.p. = 85 – 87 °C. $[\alpha]_D^{20}$ = +32.8 (MeOH). IR (ATR): 3354m, 2939s, 2869m, 2789m, 1715s, 1639w, 1579s, 1534s, 1447m, 1374s, 1241s, 1168m, 1063w, 1022m, 965w, 897w, 857w, 809w, 763w, 612w, 533w, 478w, 426w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.56-8.51 (m, 1H, H-C(2')), 8.01-7.95 (m, 1H, H-C(8')), 7.77-7.72 (m, 1H, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.42-7.38 (m, 1H, H-C(6')), 6.45-6.41 (m, 1H, H-C(3')), 5.38-5.31 (m, 1H, H-N, exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.91-4.87 (m, 1H, H-C(7)), 4.55 and 4.45 (bs and bs, 1H, H-N), 3.77-3.68 (m, 1H, ArNHC*H*(CH_3)-), 3.28 (bs, 1H, H-C(3)), 2.40-2.34 (m, 2H, ArNHCH(CH_3)$CH_2CH_2CH_2$-), 2.32-2.25 (m, 2H-C(24)), 2.20-2.17 (m, 3H, C*H*$_3$-N), 2.09 and 2.07 (s and s, overlap, 3H, C*H*$_3$COO-C(12)), 2.05 and 2.03 (s and s, overlap, 3H, C*H*$_3$COO-C(7)), 2.00-1.46 (m, 20H, H-steroid), 1.44 (s and s, overlap, 9H, -NHCOOC(C*H*$_3$)$_3$), 1.40-1.33 (m, 3H, H-steroid), 1.32 (d, 3H, *J* = 6.4, ArNHCH(C*H*$_3$)-), 1.27-0.95 (m, 5H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.81 (d, 3H, *J* = 6.4, C*H*$_3$-C(20)), 0.70 and 0.69 (s and s, overlap, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.37, 170.27, 155.11, 150.80, 149.05, 148.44, 129.78, 128.92, 124.32, 124.30, 119.48, 119.44, 118.82, 118.81, 98.86,

79.13, 75.47, 70.85, 58.27, 58.20, 57.47, 57.34, 50.74, 48.18, 48.12, 47.61, 47.52, 44.97, 43.38, 43.32, 42.33, 42.30, 41.52, 37.68, 37.66, 36.37, 35.47, 34.92, 34.89, 34.44, 34.22, 34.20, 33.50, 33.45, 31.26, 28.87, 28.83, 28.39, 27.24, 25.48, 23.86, 23.75, 23.70, 23.59, 22.76, 22.67, 21.59, 21.57, 21.35, 21.34, 20.22, 20.20, 17.91, 12.17, 12.15. HRMS: *m/z* 803.56681 corresponds to molecular formula $C_{48}H_{74}N_4O_6H^+$ (error in ppm -1.62).

(3α,5β,7α,12α)-3-Amino-24-{[4-(quinolin-4-ylamino)butyl]amino}cholane-7,12-diyl diacetate (14).

Compound **14** was prepared by procedure C using **4** (178 mg, 0.230 mmol) and TFA/CH_2Cl_2 (5,5 mL). The product was purified using column chromatography (flash, Biotage SP1, RP column 25+M, eluent MeOH/H_2O gradient 75/25 → MeOH). Final product **14** was obtained as a colorless foam (75 mg, 48%). M.p. = 67 – 70 °C. $[\alpha]_D^{20}$= +50.0 (MeOH). IR (ATR): 3279w, 2937s, 2864m, 1727s, 1582s, 1543w, 1440w, 1377m, 1342w, 1248s, 1126w, 1024w, 964w, 806w, 766w, 733w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.56-8.52 (m, 1H, H-C(2')), 7.98-7.95 (m, 1H, H-C(8')), 7.79-7.75 (m, 1H, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.42-7.36 (m, 1H, H-C(6')), 6.41-6.38 (m, 1H, H-C(3')), 5.79 (bs, 1H, H-N, exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.91-4.86 (m, 1H, H-C(7)), 3.36-3.28 (m, 2H, ArNHCH_2-), 2.72-2.67 (m, 2H, ArNHCH$_2$CH$_2$CH$_2$CH_2-), 2.65-2.52 (m, 3H, 2H-C(24) and H-C(3)), 2.11 (s, 3H, CH_3COO-C(12)), 2.07 (s, 3H, CH_3COO-C(7)), 2.05-0.95 (m, 31H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.84-0.80 (m, 3H, CH_3-C(20)), 0.71 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.64, 170.61, 151.01, 149.84, 148.38, 129.80, 128.84, 124.28, 119.57, 118.81, 98.55, 75.50, 70.90, 51.62, 50.53, 49.27, 47.48, 44.98, 43.38, 43.15, 41.48, 39.48, 37.74, 35.50, 34.89, 34.34, 33.34, 31.42, 31.22, 28.96, 27.84, 27.24, 26.48, 26.39, 25.55, 22.77, 21.62, 21.46, 17.86, 12.17.

HRMS: *m/z* 675.48325 corresponds to molecular formula $C_{41}H_{62}N_4O_4H^+$ (error in ppm -1.68); *m/z* 338.24629 corresponds to molecular formula $C_{41}H_{62}N_4O_4H_2^{2+}$ (error in ppm 1.36). HPLC purity (λ = 330 nm): method A: RT 9.070, area 98.83%; method B: RT 7.811, area 96.95%.

(3α,5β,7α,12α)-3-Amino-24-{methyl[4-(quinolin-4-ylamino)butyl]amino}cholane-7,12-diyl diacetate (15).

Compound **15** was prepared by procedure C, using **12** (230 mg, 0.33 mmol) and TFA/CH_2Cl_2 (8 mL). The product was purified using column chromatography (flash, Biotage SP1, RP column 25+M, eluent MeOH/H_2O gradient 75/25 → MeOH). Final product **15** was obtained as a colorless foam (110 mg, 56%). M.p. = 77 – 80 °C. $[\alpha]_D^{20}$ = +59.1 (MeOH). IR (ATR): 3308m, 2946s, 2867s, 2795m, 1730s, 1664w, 1642w, 1619w, 1583s, 1544m, 1460m, 1377s, 1343m, 1246s, 1156w, 1126w, 1026m, 966w, 767m cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.53 (d, 1H, *J* = 5.5, H-C(2')), 7.99-7.95 (m, 1H, H-C(8')), 7.79-7.74 (m, 1H, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.42-7.37 (m, 1H, H-C(6')), 6.39 (d, 1H, *J* = 5.2, H-C(3')), 5.94 (bs, 1H, H-N, exchangeable with D_2O), 5.10-5.05 (m, 1H, H-C(12)), 4.90-4.85 (m, 1H, H-C(7)), 3.34-3.28 (m, 2H, ArNHCH_2-), 2.64-2.55 (m, 1H, H-C(3)), 2.43-2.38 (m, 2H, ArNHCH$_2$CH$_2$CH$_2$CH_2-), 2.35-2.30 (m, 2H-C(24)), 2.22 (s, 3H, CH_3-N), 2.09 (s, 3H, CH_3COO-C(12)), 2.07 (s, 3H, CH_3COO-C(7)), 2.05-0.94 (m, 30H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.81 (d, 3H, *J* = 6.6, CH_3-C(20)), 0.70 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.64, 150.89, 150.02, 148.25, 129.65, 128.89, 124.26, 119.70, 118.80, 98.53, 75.50, 70.90, 58.12, 57.11, 51.61, 47.64, 44.99, 43.35, 43.24, 42.38, 41.47, 39.44, 37.73, 35.50, 34.98, 34.33, 33.56, 31.41, 31.18, 28.95, 27.24, 26.66, 25.54, 25.26, 23.66, 22.76, 21.63, 21.43, 17.88, 12.16. HRMS: *m/z* 689.49878 corresponds to molecular formula $C_{42}H_{64}N_4O_4H^+$ (error in ppm -1.82); *m/z* 345.25311

corresponds to molecular formula $C_{42}H_{64}N_4O_4H_2^{2+}$ (error in ppm -1.56). HPLC purity (λ = 330 nm): method A: RT 7.549, area 95.60%; method B: RT 7.483, area 97.51%.

(3α,5β,7α,12α)-3-Amino-24-({4-[(7-chloroquinolin-4-yl)amino]butyl}amino)cholane-7,12-diyl diacetate (16).

Compound **16** was prepared by procedure C using **5** (590.0 mg, 0.7288 mmol) and TFA/CH_2Cl_2 (25 mL). Final product **16** was obtained as a colorless foam (502.4 mg, 97%). M.p. = 79 – 82 °C. $[\alpha]_D^{20}$ = +78.2 (MeOH). IR (ATR): 3554w, 3401w, 3329w, 2935s, 2863m, 1941w, 1727s, 1647w, 1610w, 1580s, 1542w, 1448w, 1374w, 1332w, 1246m, 1134w, 1078w, 1026w, 969w, 930w, 891w, 848w, 809w, 773w, 721w, 570w, 537w, 455w, 423w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.53-8.49 (m, 1H, H-C(2')), 7.96-7.92 (m, 1H, H-C(8')), 7.72 (d, 1H, *J* = 8.9, H-C(5')), 7.34-7.30 (m, 1H, H-C(6')), 6.38-6.35 (m, 1H, H-C(3')), 6.03 (bs, 1H, H-N, exchangeable with D_2O), 5.10-5.06 (m, 1H, H-C(12)), 4.91-4.86 (m, 1H, H-C(7)), 3.33-3.27 (m, 2H, ArNHCH_2-), 2.73-2.68 (m, 2H, ArNHCH$_2$CH$_2$CH$_2$CH_2-), 2.65-2.53 (m, 3H, 2H-C(24) and H-C(3)), 2.11 (s, 3H, CH_3COO-C(12)), 2.07 (s, 3H, CH_3COO-C(7)), 2.06-1.95 (m, 31H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.82 (d, 3H, *J* = 6.4, CH_3-C(20)), 0.72 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.65, 170.62, 152.06, 149.96, 149.17, 134.65, 128.70, 124.88, 121.38, 117.30, 98.83, 75.51, 70.91, 51.64, 50.52, 49.14, 47.54, 45.01, 43.40, 43.18, 41.50, 39.51, 37.76, 35.51, 34.95, 34.36, 33.36, 31.43, 31.25, 28.98, 27.85, 27.26, 26.53, 26.27, 25.58, 22.78, 21.63, 21.47, 17.88, 12.19. HRMS: *m/z* 709.44393 corresponds to molecular formula $C_{41}H_{61}ClN_4O_4H^+$ (error in ppm -2.08). HPLC purity (λ = 330 nm): method A: RT 9.189, area 95.02%; method B: RT 7.825, area 97.26%.

(3α,5β,7α,12α)-3-amino-24-{[4-(quinolin-4-ylamino)pentyl]amino}cholane-7,12-diyl diacetate (17) (Mixture of diastereomers).

Compound **17** was prepared by procedure C using **6** (150 mg, 0.19 mmol) and TFA/CH_2Cl_2 (5.5 mL). Final product **17** was obtained as mixture of diastereomers. Colorless foam (92.9 mg, 71%). M.p. = 82 – 83 °C. $[\alpha]_D^{20}$ = +31.5 (MeOH). IR (ATR): 3478w, 3275m, 3190m, 3118m, 3078m, 2930s, 2861s, 1725s, 1653w, 1538s, 1496w, 1445m, 1377s, 1342m, 1154w, 1025m, 963w, 892w, 810w, 765m, 656w, 611w, 532w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.53 (d, 1H, *J* = 5.5, H-C(2')), 7.98-7.94 (m, 1H, H-C(8')), 7.74 (d, 1H, *J* = 8.4, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.42-7.37 (m, 1H, H-C(6')), 6.41 (d, 1H, *J* = 5.5, H-C(3')), 5.31-5.26 (m, 1H, H-N, exchangeable with D_2O), 5.09-5.06 (m, 1H, H-C(12)), 4.90-4.86 (m, 1H, H-C(7)), 3.76-3.69 (m, 1H, ArNHC*H*(CH_3)-), 2.67-2.49 (m, 5H, ArNHCH(CH_3)$CH_2CH_2CH_2$- and 2H-C(24) and H-C(3)), 2.11 (s, 3H, C*H*$_3$COO-C(12)), 2.07 (s, 3H, C*H*$_3$COO-C(7)), 2.04-1.33 (m, 25H, H-steroid), 1.32 (d, 3H, *J* = 6.4, ArNHCH(C*H*$_3$)-), 1.28-0.96 (m, 6H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.81 (d, 3H, *J* = 6.6, C*H*$_3$-C(20)), 0.71 and 0.70 (s and s, overlap, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.64, 170.62, 150.94, 148.89, 148.56, 129.90, 128.85, 124.28, 119.37, 118.81, 98.81, 75.50, 70.90, 51.63, 50.54, 50.51; 49.62, 48.16, 47.44, 44.97, 43.37, 41.49, 39.50, 37.74, 35.50, 34.86, 34.84, 34.35, 34.18, 33.31, 31.42, 31.23, 28.96, 27.23, 26.54, 26.52, 26.45, 25.55, 22.77, 21.62, 21.47, 20.23, 17.85, 12.16. HRMS: *m/z* 345.25444 corresponds to molecular formula $C_{42}H_{64}N_4O_4H_2^{2+}$ (error in ppm 2.27). HPLC purity: method A (λ = 254 nm): RT 8.644, area 95.76%; method B (λ = 330 nm): RT 7.455, area 95.83%.

(3α,5β,7α,12α)-3-amino-24-{methyl[4-(quinolin-4-ylamino)pentyl]amino}cholane-7,12-diyl diacetate (18) (Mixture of diastereomers).

Compound **18** was prepared by procedure C using **13** (90 mg, 0.1 mmol) and TFA/CH_2Cl_2 (8 mL). The product was purified using column chromatography (flash, Biotage SP1, RP column 25+M, eluent MeOH/H_2O gradient 8/2 → MeOH). Final product **18** was obtained as mixture of diastereomers. Colorless foam (47 mg, 60%). M.p. = 70 – 72 °C. $[\alpha]_D^{20}$= +39.3 (MeOH). IR (ATR): 3353w, 3278w, 3064w, 2942s, 2863m, 2790w, 1725s, 1579s, 1537m, 1448w, 1376m, 1341w, 1244s, 1152w, 1023w, 765w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.58-8.49 (m, 1H, H-C(2')), 8.00-7.94 (m, 1H, H-C(8')), 7.76-7.71 (m, 1H, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.43-7.38 (m, 1H, H-C(6')), 6.45-6.40 (m, 1H, H-C(3')), 5.33-5.26 (m, 1H, H-N, exchangeable with D_2O), 5.07 (bs, 1H, H-C(12)), 4.90-4.85 (m, 1H, H-C(7)), 3.77-3.68 (m, 1H, ArNHC*H*(CH_3)-), 2.61 (bs, 1H, H-C(3)), 2.39-2.33 (m, 2H, ArNHCH(CH_3)$CH_2CH_2CH_2$-), 2.31-2.24 (m, 2H-C(24)), 2.18 (s, 3H, C*H*$_3$-N), 2.10 (s, 3H, C*H*$_3$COO-C(12)), 2.07 (s, 3H, C*H*$_3$COO-C(7)), 2.04-1.34 (m, 22H, H-steroid), 1.33-1.30 (m, 3H, ArNHCH(C*H*$_3$)-), 1.26-0.94 (m, 6H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.82-0.79 (m, 3H, C*H*$_3$-C(20)), 0.70 and 0.69 (s and s, overlap, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.71, 150.85, 149.01, 148.44, 129.77, 128.92, 124.30, 119.44, 118.80, 98.86, 75.52, 70.93, 58.26, 57.50, 51.59, 48.18, 48.15, 47.62, 44.98, 43.35, 42.29, 41.45, 39.39, 37.71, 35.48, 34.95, 34.48, 34.34, 33.50, 31.40, 31.15, 28.95, 27.24, 25.54, 23.89, 23.88, 23.73, 22.78, 21.67, 21.48, 20.22, 17.87, 12.17. HRMS: *m/z* 345.25306 corresponds to molecular formula $C_{42}H_{64}N_4O_4H_2^{2+}$ (error in ppm -1.72); *m/z* 230.50462 corresponds to molecular formula $C_{42}H_{64}N_4O_4H_3^{3+}$ (error in ppm -1.04). HPLC purity (λ = 330 nm): method A: RT 8.574, area 95.26%; method B: RT 6.961, area 98.08%.

(3α,5β,7α,12α)-3-amino-24-{[1-methyl-4-(quinolin-4-ylamino)butyl]amino}cholane-7,12-diyl diacetate (19) (Mixture of diastereomers).

Compound **19** was prepared by procedure C using **7** (390 mg, 0.49 mmol) and TFA/CH_2Cl_2 (17 mL). Final product was obtained as mixture of diastereomers. Colorless foam (319 mg, 94%). M.p. = 75 – 77 °C. $[\alpha]_D^{20}$ = +45.6 (MeOH). IR (ATR): 3265m, 2938s, 2865s, 1727s, 1623w, 1583s, 1543m, 1505w, 1442m, 1377s, 1342m, 1247s, 1154w, 1127w, 1082w, 1026m, 964w, 890w, 809w, 766m, 609w, 540w, 423w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.54 (d, 1H, *J* = 5.2, H-C(2')), 7.97 (d, 1H, *J* = 8.5, H-C(8')), 7.76 (d, 1H, *J* = 8.2, H-C(5')), 7.64-7.59 (m, 1H, H-C(7')), 7.43-7.37 (m, 1H, H-C(6')), 6.40 (d, 1H, *J* = 5.2, H-C(3')), 5.62 (bs, 1H, H-N, exchangeable with D_2O), 5.09-5.05 (m, 1H, H-C(12)), 4.90-4.86 (m, 1H, H-C(7)), 3.38-3.25 (m, 2H, ArNHCH_2-), 2.77-2.68 (m, 1H, $ArNHCH_2CH_2CH_2CH(CH_3)$-), 2.67-2.47 (m, 3H, 2H-C(24) and H-C(3)), 2.10 and 2.10 (s and s, overlap, 3H, CH_3COO-C(12)), 2.07 (s, 3H, CH_3COO-C(7)), 2.05-1.20 (m, 28H, H-steroid), 1.09 (d, 3H, *J* = 6.2, $ArNHCH_2CH_2CH_2CH(CH_3)$-), 1.07-0.99 (m, 3H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.81 (d, 3H, *J* = 6.4, CH_3-C(20)), 0.70 and 0.69 (s and s, overlap, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.62, 170.60, 150.98, 149.77, 148.36, 129.81, 128.85, 124.34, 119.47, 118.76, 98.58, 75.49, 70.89, 52.72, 51.60, 47.67, 47.60, 47.44, 44.95, 43.44, 43.35, 41.46, 39.47, 37.72, 35.48, 34.84, 34.64, 34.58, 34.32, 33.39, 33.36, 31.40, 31.20, 28.94, 27.21, 26.77, 25.52, 25.08, 22.74, 21.60, 21.44, 20.41, 20.38, 17.83, 12.14. HRMS: *m/z* 689.49852 corresponds to molecular formula $C_{42}H_{64}N_4O_4H^+$ (error in ppm -2.19); *m/z* 345.25324 corresponds to molecular formula $C_{42}H_{64}N_4O_4H_2^{2+}$ (error in ppm -1.21). HPLC purity (λ = 330 nm): method A: RT 7.059, area 98.72%; method B: RT 7.502, area 97.72%.

(3α,5β,7α,12α)-3-amino-24-({4-[(7-chloroquinolin-4-yl)amino)pentyl}amino)cholane-7,12-diyl diacetate (20) (Mixture of diastereomers).

Compound **20** was prepared by procedure C using **8** (130 mg, 0.16 mmol) and TFA/CH_2Cl_2 (11 mL). Final product **20** was obtained as mixture of diastereomers. Colorless foam (110.5 mg, 97%). M.p. = 85 – 87 °C. $[\alpha]_D^{20}$= +44.8 (MeOH). IR (ATR): 3301w, 2937s, 2864m, 2351w, 2327w, 1727s, 1610w, 1578s, 1538w, 1451w, 1377m, 1334w, 1246s, 1154w, 1080w, 1024w, 964w, 878w, 851w, 811w, 766w, 607w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.50 (d, 1H, *J* = 5.4, H-C(2')), 7.94-7.92 (m, 1H, H-C(8')), 7.69 (d, 1H, *J* = 9.0, H-C(5')), 7.34-7.30 (m, 1H, H-C(6')), 6.40 (d, 1H, *J* = 5.4, H-C(3')), 5.51-5.43 (m, 1H, H-N, exchangeable with D_2O), 5.09-5.06 (m, 1H, H-C(12)), 4.91-4.86 (m, 1H, H-C(7)), 3.74-3.67 (m, 1H, ArNHC*H*(CH_3)-), 2.67-2.62 (m, 2H, ArNHCH(CH_3)$CH_2CH_2CH_2$-), 2.62-2.50 (m, 3H, H-C(3) and 2H-C(24)), 2.11 (s, 3H, C*H*$_3$COO-C(12)), 2.07 (s, 3H, C*H*$_3$COO-C(7)), 2.05-1.32 (m, 24H, H-steroid), 1.31 (d, 3H, *J* = 6.4, ArNHCH(C*H*$_3$)-),1.26-0.99 (m, 7H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.81 (d, 3H, *J* = 6.4, C*H*$_3$-C(20)), 0.72 and 0.71 (s and s, overlap, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.64, 170.62, 151.97, 149.34, 149.00, 134.67, 128.75, 124.89, 121.17, 117.30, 99.11, 75.70, 70.90, 51.63, 50.53, 50.50, 49.48, 48.27, 47.49, 44.98, 43.38, 41.49, 39.50, 37.74, 35.50, 34.90, 34.87, 34.35, 34.05, 33.31, 31.42, 31.24, 28.97, 27.24, 26.47, 25.56, 22.77, 21.62, 21.47, 20.13, 17.85, 12.17. HRMS: *m/z* 723.45837 corresponds to molecular formula $C_{42}H_{63}ClN_4O_4H^+$ (error in ppm -3.72). HPLC purity: method C (λ = 330 nm): RT 10.367, area 95.87%; method D (λ = 254 nm): RT 8.879, area 95.63%.

(3α,5β,7α,12α)-3-Amino-24-({4-[(7-chloroquinolin-4-yl)amino]-1-methylbutyl}amino)cholane-7,12-diyl diacetate (21) (Mixture of diastereomers).

Compound **21** was prepared by procedure C using **9** (120 mg, 0.16 mmol) and TFA/CH_2Cl_2 (11 mL). Final product was obtained as mixture of diastereomers. Colorless foam (75.7 mg, 72%). M.p. = 75 – 77 °C. $[\alpha]_D^{20}$ = +46.9 (MeOH). IR (ATR): 3284w, 2931s, 2860s, 1725s, 1652w, 1610w, 1578s, 1539m, 1449m, 1373m, 1331w, 1242s, 1154w, 1135w, 1078w, 1022w, 963w, 937w, 895w, 849w, 806w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.51 (d, 1H, *J* = 5.2, H-C(2')), 7.96-7.92 (m, 1H, H-C(8')), 7.72-7.68 (m, 1H, H-C(5')), 7.35-7.31 (m, 1H, H-C(6')), 6.38 (d, 1H, *J* = 5.5, H-C(3')), 5.79 (bs, 1H, H-N exchangeable with D_2O), 5.09-5.05 (m, 1H, H-C(12)), 4.90-4.86 (m, 1H, H-C(7)), 3.36-3.23 (m, 2H, ArNHCH_2-), 2.76-2.69 (m, 1H, ArNHCH$_2$CH$_2$CH$_2$C*H*(CH$_3$)-), 2.67-2.47 (m, 3H, 2H-C(24) and H-C(3)), 2.11 and 2.10 (s and s, overlap, 3H, CH_3COO-C(12)), 2.07 (s, 3H, CH_3COO-C(7)), 2.05-1.20 (m, 28H, H-steroid), 1.09 (d, 3H, *J* = 6.4, ArNHCH$_2$CH$_2$CH$_2$CH(CH_3)-), 1.07-0.97 (m, 3H, H-steroid), 0.90 and 0.90 (s and s, overlap, 3H, CH_3-C(10)), 0.80 (d, 3H, *J* = 6.6, CH_3-C(20)), 0.71 i 0.70 (s and s, overlap, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.65, 152.04, 149.88, 149.15, 134.70, 128.72, 124.99, 121.23, 117.25, 98.90, 75.51, 70.91, 52.64, 51.63, 47.65, 47.57, 47.52, 44.99, 43.50, 43.39, 41.49, 39.50, 37.75, 35.51, 34.90, 34.69, 34.61, 34.35, 33.42, 33.39, 31.43, 31.23, 28.97, 27.24, 26.87, 26.84, 25.56, 24.95, 22.77, 21.63, 21.47, 20.45, 20.42, 17.86, 12.18. HRMS: *m/z* 723.45968 corresponds to molecular formula $C_{42}H_{63}N_4ClO_4H^+$ (error in ppm -1.91). HPLC purity (λ = 330 nm): method C: RT 10.536, area 95.38%; method D: RT 8.430, area 95.36%.

(3α,5β,7α,12α)-3-Amino-24-{[6-(quinolin-4-ylamino)hexyl]amino}cholane-7,12-diyl diacetate (22).

Compound **22** was prepared by procedure C using **10** (170 mg, 0.21 mmol) and TFA/CH_2Cl_2 (5.5 mL). The product was purified using column chromatography (flash, Biotage SP1, RP column 25+M, eluent MeOH/H_2O gradient 8/2 → MeOH). Final product **22** was obtained as a colorless foam (112.8 mg, 76%). M.p. = 72 – 75 °C. $[\alpha]_D^{20}$= +56.4 (MeOH). IR (ATR): 3294w, 3061w, 2933s, 2860m, 1726s, 1582s, 1542w, 1441w, 1376m, 1341w, 1247s, 1156w, 1125w, 1084w, 1023w, 964w, 891w, 808w, 767w, 734w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.55 (d, 1H, *J* = 5.2, H-C(2')), 8.00-7.95 (m, 1H, H-C(8')), 7.74 (d, 1H, *J* = 7.8, H-C(5')), 7.64-7.60 (m, 1H, H-C(7')), 7.44-7.39 (m, 1H, H-C(6')), 6.42 (d, 1H, *J* = 5.5, H-C(3')), 5.11-5.05 (m, 2H, H-N, exchangeable with D_2O and H-C(12)), 4.90-4.86 (m, 1H, H-C(7)), 3.34-3.28 (m, 2H, ArNHC*H*$_2$-), 2.63-2.49 (m, 5H, ArNHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$- and 2H-C(24) and H-C(3)), 2.11 (s, 3H, C*H*$_3$COO-C(12)), 2.07 (s, 3H, C*H*$_3$COO-C(7)), 2.05-1.99 (m, 35H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.81 (d, 3H, *J* = 6.6, C*H*$_3$-C(20)), 0.71 (s, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.62, 170.59, 150.96, 149.59, 148.34, 129.86, 128.85, 124.44, 119.15, 118.63, 98.67, 75.48, 70.87, 51.59, 50.53, 49.90, 47.35, 44.92, 43.35, 43.09, 41.45, 39.45, 37.70, 35.47, 34.79, 34.30, 33.26, 31.40, 31.19, 30.01, 28.93, 28.79, 27.18, 27.08, 27.02, 26.37, 25.52, 22.74, 21.59, 21.43, 17.82, 12.12. HRMS: *m/z* 703.51463 corresponds to molecular formula $C_{43}H_{66}N_4O_4H^+$ (error in ppm -1.50); *m/z* 352.26200 corresponds to molecular formula $C_{43}H_{66}N_4O_4H_2^{2+}$ (error in ppm 1.49). HPLC purity (λ = 330 nm): method A: RT 9.134, area 98.86%; method B: RT 7.830, area 97.20%.

(3α,5β,7α,12α)-3-amino-24-({6-[(7-chloroquinolin-4-yl)amino]hexyl}amino)cholane-7,12-diyl diacetate (23).

Compound **23** was prepared by procedure C using **11** (51.5 mg, 0.0698 mmol) and TFA/CH_2Cl_2 (3.5 mL). Colorless foam (41.5 mg, 92%). M.p. = 69 – 71 °C. $[\alpha]_D^{20}$ = +66.9 (MeOH). IR (ATR): 3284w, 2934s, 2860m, 1727s, 1610w, 1581s, 1540w, 1452w, 1376m, 1332w, 1248s, 1136w, 1080w, 1024w, 964w, 899w, 850w, 807w, 735w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.53 (d, 1H, *J* = 5.3, H-C(2')), 7.98-7.93 (m, 1H, H-C(8')), 7.66 (d, 1H, *J* = 8.9, H-C(5')), 7.38-7.33 (m, 1H, H-C(6')), 6.41 (d, 1H, *J* = 5.5, H-C(3')), 5.09-5.06 (m, 1H, H-C(12)), 5.02-4.97 (m, 1H, H-N, exchangeable with D_2O), 4.91-4.86 (m, 1H, H-C(7)), 3.34-3.27 (m, 2H, ArNHCH_2-), 2.64-2.48 (m, 5H, ArNHCH_2CH_2CH_2CH_2CH_2CH_2- and 2H-C(24) and H-C(3)), 2.11 (s, 3H, CH_3COO-C(12)), 2.08 (s, 3H, CH_3COO-C(7)), 2.05-0.99 (m, 35H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.81 (d, 3H, *J* = 6.6, CH_3-C(20)), 0.71 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 170.68, 170.65, 152.06, 149.62, 149.16, 134.76, 128.89, 125.21, 120.76, 117.08, 99.06, 75.54, 70.93, 51.66, 50.63, 49.98, 47.41, 44.99, 43.41, 43.18, 41.51, 39.52, 37.77, 35.52, 34.85, 34.37, 33.33, 31.46, 31.26, 30.13, 28.99, 28.82, 27.25, 27.13, 27.07, 26.48, 25.58, 22.80, 21.65, 21.49, 17.88, 12.18. HRMS: *m/z* 737.47556 corresponds to molecular formula $C_{43}H_{65}ClN_4O_4H^+$ (error in ppm -1.56); *m/z* 246.49683 corresponds to molecular formula $C_{43}H_{65}ClN_4O_4H_3^{3+}$ (error in ppm -1.04). HPLC purity (λ = 330 nm): method A: RT 9.278, area 97.57%; method B: RT 7.853, area 97.20%.

(3α,5β,7α,12α)-3-Amino-24-({4-[(7-chloroquinolin-4-yl)amino]butyl}amino)cholane-7,12-diol (24).

16 (20.0 mg, 0.0282 mmol) was dissolved in MeOH (1 mL), KOH (31.6 mg, 0.564 mmol) was added and the mixture was heated at 60 °C for 5 days. The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2. The organic layer was washed with wather and dried over anh. Na_2SO_4. The product was purified using column chromatography (flash, Biotage SP1, RP column 12+M, eluent MeOH/H_2O gradient 7/3 → MeOH). Pale yellow foam (12 mg, 68%). M.p. = 116 – 119 °C. $[\alpha]_D^{20}$ = +26.2 (MeOH). IR (ATR): 3282m, 2932s, 2861m, 1609w, 1581s, 1541w, 1453m, 1372m, 1333w, 1281w, 1251w, 1201w, 1136w, 1081w, 1038w, 982w, 952w, 908w, 878w, 852w, 807w, 767w, 736w, 645w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 8.49 (d, 1H, *J* = 5.5, H-C(2')), 7.97-7.92 (m, 1H, H-C(8')), 7.78 (d, 1H, *J* = 8.8, H-C(5')), 7.34-7.29 (m, 1H, H-C(6')), 6.44 (bs, 1H, H-N), 6.36 (d, 1H, *J* = 5.4, H-C(3')), 3.97-3.91 (m, 1H, H-C(12)), 3.85-3.79 (m, 1H, H-C(7)), 3.34-3.24 (m, 2H, ArNHCH_2-), 2.75-2.67 (m, 3H, ArNHCH$_2$CH$_2$CH$_2$CH_2- and H-C(3)), 2.65-2.51 (m, 4H, 2H-C(24) and 2 H-O), 2.00-1.00 (m, 31H, H-steroid), 0.98-0.93 (m, 3H, CH_3-C(20)), 0.87 (s, 3H, CH_3-C(10)), 0.64 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.03, 150.24, 149.17, 134.66, 128.53, 124.84, 121.90, 117.48, 98.82, 72.80, 68.13, 51.72, 50.46, 49.10, 46.90, 46.32, 43.26, 41.94, 41.89, 39.60, 35.87, 35.44, 34.68, 34.58, 33.42, 28.29, 27.73, 27.55, 26.59, 26.36, 26.19, 23.21, 22.67, 17.71, 12.48. HRMS: *m/z* 625.42214 corresponds to molecular formula $C_{37}H_{57}ClN_4O_2H^+$ (error in ppm -3.42). HPLC purity: method C (λ = 330 nm): RT 8.685, area 97.90%; method D (λ = 254 nm): RT 8.713, area 96.63%.

7-Chloroquinolin-4-amine (25).[12]

4,7-Dichloroquinoline (2.00 g, 10.1 mmol) was dissolved in phenol (9.50 g, 101 mmol) and the mixture was heated at 110 °C. $(NH_4)_2CO_3$ (4.85 g, 50.5 mmol) was added in portions, and stirring continued for 3 h at 165 °C. After cooling to room temperature, diethyl ether was added (150 mL) and organic layer washed with 10% aqueous NaOH (3 × 50 mL). The solvent was removed under the reduced pressure. The product was purified using column chromatography (dry-flash, SiO_2, eluent CH_2Cl_2, CH_2Cl_2/MeOH = 9/1, MeOH). Final product **25** was obtained as beige powder (1.44 g, 80%). M.p. = 137-139 °C. IR (ATR): 3443w, 3321m, 3098s, 2788w, 2707w, 1683w, 1656m, 1635m, 1612m, 1577s, 1505m, 1444m, 1371w, 1329m, 1285w, 1204w, 1165w, 1125w, 1107w, 1076w, 908w, 877w, 853w, 810m, 766w, 640w, 625w cm^{-1}. ^1H NMR (200 MHz, CD_3OD, δ): 8.22 (d, 1H, *J* = 5.0, H-C(2)), 7.99 (d, 1H, *J* = 9.0, H-C(5)), 7.76-7.78 (m, 1H, H-C(8)), 7.37-7.25 (m, 1H, H-C(6)), 6.57 (d, 1H, *J* = 5.6, H-C(3)). ^{13}C NMR (50 MHz, CD_3OD, δ): 154.44, 151.80, 149.85, 136.56, 127.27, 125.80, 124.96, 118.26, 103.88. HRMS: *m/z* 179.03644 corresponds to molecular formula $C_9H_7ClN_2H^+$ (error in ppm -3.43).

4-Chloro-*N*-(7-chloroquinolin-4-yl)butanamide (26).

25 (500.0 mg, 2.799 mmol) was suspended in CH_2Cl_2 (20 mL), triethyl amine (0.47 mL, 3.4 mmol) was added and the mixture was cooled in an ice bath. 4-Chlorobutanoyl chloride (0.38 mL, 3.4 mmol) in CH_2Cl_2 (5 mL) was slowly added to the mixture, stirring continued for 10 minutes at 0 °C, and 1.5 h at r.t. The solvent was removed under the reduced pressure. The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, hexane/EtOAc gradient 9/1→ 3/7). The final product **26** was obtained as white crystals (707 mg, 89%). M.p. = 89-90 °C. IR (ATR): 3318s, 3101w, 2963w, 2919w, 2815w, 1670s, 1614m,

1571m, 1526s, 1488s, 1443m, 1419w, 1379w, 1349w, 1323m, 1304m, 1275w, 1254w, 1208m, 1190w, 1141w, 1107w, 1076w, 1032w, 967w, 873w, 846w, 819w, 776w, 644w, 598w, 563w, 430w cm^{-1}. ^1H NMR (200 MHz, CD_3OD, δ): 8.72 (d, 1H, *J* = 5.1, H-C(2)), 8.23-8.12 (m, 2H, H-C(5) and H-C(3)), 7.96-7.93 (m, 1H, H-C(8)), 7.60-7.52 (m, 1H, H-C(6)), 3.70 (t, 2H, *J* = 6.5, -C*H*$_2$Cl), 2.79 (t, 2H, *J* = 7.3, ArNHCOC*H*$_2$-), 2.27-2.12 (m, 2H, ArNHCOCH$_2$C*H*$_2$-). ^{13}C NMR (50 MHz, CD_3OD, δ): 174.21, 152.96, 143.98, 136.96, 128.42, 128.25, 124.85, 121.02, 113.83, 97.83, 45.16, 34.72, 29.13. HRMS: *m/z* 283.04012 corresponds to molecular formula $C_{13}H_{12}Cl_2N_2OH^+$ (error in ppm 0.63).

4-Azido-*N*-(7-chloroquinolin-4-yl)butanamide (27).

26 (500.0 mg, 1.766 mmol) was dissolved in DMF (2 mL) in Ar atmosphere, and sodium azide was added (459 mL, 7.06 mmol). Reaction mixture was stirred at 80 °C for 2 h. The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2. Organic layer was washed with water and dried over anh. Na_2SO_4. The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, hexane/EtOAc gradient 9/1 → 1/1). Final product **27** was obtained as white powder (383 mg, 75%). M.p.= 54-55 °C. IR (ATR): 3318s, 2930m, 2670m, 2168w, 2101s, 1946w, 1894w, 1675s, 1613m, 1570m, 1525s, 1485s, 1443m, 1416w, 1375w, 1343w, 1303s, 1253m, 1217m, 1189m, 1161m, 1108w, 1072w, 1040w, 965w, 878w, 847m, 817w, 764w, 642w, 617w, 559w, 475w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, δ): 8.80 (d, 1H, *J* = 5.6, H-C(2)), 8.32 (bs, 1H, H-N), 8.17 (d, 1H, *J* = 5.1, H-C(3)), 8.09-8.03 (m, 1H, H-C(8)), 7.83-7.75 (m, 1H, H-C(5)), 7.51-7.40 (m, 1H, H-C(6)), 3.46 (t, 2H, *J* = 6.5, -C*H*$_2$N$_3$), 2.66 (t, 2H, *J* = 7.3, ArNHCOC*H*$_2$-), 2.15-1.97 (m, 2H, ArNHCOCH$_2$C*H*$_2$-). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 170.95, 152.18, 149.24, 140.47, 135.46, 129.20, 127.34, 120.95, 118.62, 111.74,

50.53, 34.25, 24.29. HRMS: *m/z* 290.08039 corresponds to molecular formula $C_{13}H_{12}ClN_5OH^+$ (error in ppm 0.28).

4-Amino-*N*-(7-chloroquinolin-4-yl)butanamide (28).

Syntesis was conducted according to modified procedure from the literature.[13] **27** (382 mg, 1.32 mmol) was dissolved in THF (6 mL), Ph_3P (380.4 mg, 1.450 mmol) and water (26 μL, 1.4 mmol) was added and reaction mixture was stirred at 65 °C for 48h. The solvent was removed under reduced pressure. Crude product was purified using fast column chromatography (dry-flash, SiO_2, eluent CH_2Cl_2, CH_2Cl_2/MeOH = 9/1, CH_2Cl_2/MeOH (NH_3 satd.) = 7/3) and without characterizaton was used in the next reaction. Yield 230 mg (66%). Product **28** fastly decomposes to amine **25** and pyrrolidin-2-one (confirmed by HRMS).

(3α,5β,7α,12α)-3-[(*Tert*-butoxycarbonyl)amino]-24-({4-[(7-chloroquinolin-4-yl)amino]-4-oxobutyl}amino)cholane-7,12-diyl diacetate (29).

According to general procedure B, alcohol **3** (68 mg, 0.12 mmol) was transformed into aldehyde using PCC (36.5 mg, 0.170 mmol) in CH_2Cl_2 (6 mL), which was further transformed into **29** using amine **28** (30.0 mg, 0.113 mmol), $NaBH_4$ (6.6 mg, 0.17 mmol) and MeOH (3 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, EtOAc/MeOH(NH_3 sat.) gradient 95/5 → 8/2). Final product **29** was obtained as colorless foam (42 mg, 43%). M.p. = 80-84 °C. $[\alpha]_D^{20}$ = +50.5 (MeOH). IR (ATR): 3305w, 2933m, 2866w, 1710m, 1616w, 1567w, 1526m, 1450w, 1373w, 1307w, 1240m, 1167w, 1063w, 1022w, 965w, 881w, 850w, 822w, 768w, 675w cm^{-1}. ^1H NMR (500MHz, $CDCl_3$, δ): 10.26 (bs, 1H, -N*H*CO-), 8.82 (d, 1H, *J* = 5.3, H-C(2')), 8.28 (d, 1H, *J* =

5.2, H-C(3')), 8.11-8.07 (m, 1H, H-C(8')), 7.90 (d, 1H, *J* = 8.9, H-C(5')), 7.48-7.43 (m, 1H, H-C(6')), 5.10-5.05 (m, 1H, H-C(12)), 4.92-4.87 (m, 1H, H-C(7)), 4.41 (bs, 1H, H-N), 3.27 (bs, 1H, H-C(3)), 2.84-2.78 (m, 2H, ArNHCOCH_2-), 2.71-2.65 (m, 2H, ArNHCOCH$_2$CH$_2$CH_2-), 2.63-2.54 (m, 2H-C(24)), 2.10 (s, 3H, CH_3COO-C(12)), 2.06 (s, 3H, CH_3COO-C(7)), 2.01-1.49 (m, 18H, H-steroid), 1.44 (s, 9H, -NHCOOC(CH_3)$_3$), 1.38-0.96 (m, 9H, H-steroid), 0.90 (s, 3H, CH_3-C(10)), 0.77 (d, 3H, *J* = 6.4, CH_3-C(20)), 0.70 (s, 3H, CH_3-C(13)). ^{13}C NMR (125 MHz, CDCl$_3$, δ): 172.46, 170.38, 170.26, 155.12, 152.48, 149.47, 141.47, 135.07, 129.25, 126.69, 121.80, 118.96, 111.26, 79.20, 75.42, 70.84, 53.39, 50.25, 48.30, 47.68, 45.01, 43.34, 41.52, 37.69, 36.38, 36.27, 35.47, 35.07, 34.23, 33.32, 31.28, 28.83, 28.40, 27.27, 26.61, 25.48, 24.76, 22.77, 22.68, 21.60, 21.36, 17.86, 12.18. HRMS: *m/z* 823.47498 corresponds to molecular formula $C_{46}H_{67}ClN_4O_7H^+$ (error in ppm -2.59); *m/z* 845.45727 corresponds to molecular formula $C_{46}H_{67}ClN_4O_7Na^+$ (error in ppm -2.11).

(3α,5β,7α,12α)-3-Amino-24-({4-[(7-chloroquinolin-4-yl)amino]-4-oxobutyl}amino)cholane-7,12-diyl diacetate (30).

Compound **30** was prepared by procedure C using **29** (40.0 mg, 0.0486 mmol) and TFA/CH$_2$Cl$_2$ (3.3 mL). Final product **30** was obtained as colorless foam (28 mg, 80%). M.p. = 65-67 °C. IR (ATR): 3287w, 2940s, 2864m, 1726s, 1616w, 1567w, 1531m, 1491w, 1446w, 1377m, 1307w, 1249s, 1159w, 1120w, 1077w, 1025w, 965w, 883w, 850w, 823w, 735w, 702w, 610w cm^{-1}. ^{1}H NMR (500MHz, CDCl$_3$, δ): 10.28 (bs, 1H, -N*H*CO-), 8.82 (d, 1H, *J* = 5.2, H-C(2')), 8.28 (d, 1H, *J* = 5.0, H-C(3')), 8.10-8.08 (m, 1H, H-C(8')), 7.89 (d, 1H, *J* = 8.9, H-C(5')), 7.47-7.43 (m, 1H, H-C(6')), 5.08-5.05 (m, 1H, H-C(12)), 4.90-4.87 (m, 1H, H-C(7)), 2.84-2.79 (m, 2H, ArNHCOCH_2-), 2.71-2.66 (m, 2H, ArNHCOCH$_2$CH$_2$CH_2-), 2.64-2.54 (m, 3H, 2H-C(24) and H-

C(3)), 2.11 (s, 3H, C*H*$_3$COO-C(12)), 2.07 (s, 3H, C*H*$_3$COO-C(7)), 2.05-0.95 (m, 29H, H-steroid), 0.90 (s, 3H, C*H*$_3$-C(10)), 0.77 (d, 3H, *J* = 6.6, C*H*$_3$-C(20)), 0.70 (s, 3H, C*H*$_3$-C(13)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 172.45, 170.62, 152.48, 149.47, 141.45, 135.07, 129.26, 126.68, 121.78, 118.94, 111.23, 75.48, 70.90, 51.65, 50.24, 48.28, 47.68, 45.04, 43.40, 41.50, 39.51, 37.76, 36.30, 35.51, 35.08, 34.38, 33.32, 31.44, 31.25, 28.98, 27.27, 26.62, 25.58, 24.71, 22.79, 21.65, 21.49, 17.83, 12.20. HRMS: *m/z* 723.42255 corresponds to molecular formula $C_{41}H_{59}ClN_4O_5H^+$ (error in ppm -2.93); *m/z* 362.21612 corresponds to molecular formula $C_{41}H_{59}ClN_4O_5H_2^{2+}$ (error in ppm 0.41). It must be stored under Ar atmosphere at -20 °C, otherwise it decomposes to amine **25** and (3α,5β,7α,12α)-3-amino-24-(2-oxopyrrolidin-1-yl)cholane-7,12-diyl diacetate (confirmed by HRMS). HPLC purity (λ = 270 nm): method C: RT 10.993, area 95.23%; method D: RT 9.394, area 96.81%.

***N*-(7-chloroquinolin-4-yl)-*N*'-[4-(5-fluoro-1-benzothiophene-3-yl)benzyl]butane-1,4-diamine (33).**

Compound **33** was prepared by procedure E, using aldehyde **31**[2] (93.2 mg, 0.364 mmol), amine **AQ4** (136.3 mg, 0.5458 mmol), glac. AcOH (31 μL, 0.54 mmol), $NaBH_4$ (82.6 mg, 2.18 mmol) and MeOH/CH_2Cl_2 (15 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH). Final product **33** was obtained as a white foam (99.1 mg, 56%). M.p. = 112 – 114 ºC. IR (ATR): 3266m, 3068m, 2932m, 2854m, 2565w, 1608m, 1578s, 1535m, 1490w, 1471w, 1435m, 1367m, 1331m, 1280w, 1249m, 1195m, 1135w, 1114w, 1060w, 1019w, 970w, 902w, 881w, 850w, 804w, 781w, 735w, 647w, 619w, 570w, 543w, 517w, 430w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$): 8.51 (d, 1H, *J* = 5.5, H-C(2')), 7.94-7.92 (m, 1H, H-C(8')), 7.85-7.80 (m, 1H, H-C(7)),

7.66-7.62 (m, 1H, H-C(5')), 7.58-7.50 (m, 3H, 2H-Ar and H-C(4)), 7.48-7.42 (m, 3H, 2H-Ar and H-C(2)), 7.23-7.19 (m, 1H, H-C(6')), 7.17-7.12 (m, 1H, H-C(6)), 6.38 (d, 1H, J = 5.5, H-C(3')), 5.88 (s, 1H, H-N exchangeable with D_2O), 3.90 (s, 2H, ArCH_2NH-), 3.35-3.29 (m, 2H, ArNHCH_2-), 2.82-2.77 (m, 2H, ArCH$_2$NHCH_2-), 1.94-1.87 (m, 2H, ArNHCH$_2$CH_2-), 1.78-1.60 (m, 3H, ArCH$_2$NHCH$_2$CH_2- and H-N). ^{13}C NMR (125 MHz, $CDCl_3$): 161.09 (d, J = 241.0), 152.07, 149.90, 149.16, 139.64, 139.06 (d, J = 9.9), 137.52 (d, J = 3.6), 135.98, 134.70, 134.37, 128.73, 128.61, 128.52, 125.68, 125.00, 124.00 (d, J = 9.0), 121.26, 117.25, 113.32 (d, J = 25.3), 108.48 (d, J = 24.4), 98.89, 53.68, 48.68, 43.21, 27.77, 26.37. HRMS: *m/z* 490.15075 corresponds to molecular formula $C_{28}H_{25}ClN_3SFH^+$ (error in ppm -1.43). HPLC purity (λ = 254 nm): method C: RT 10.920, area 96.15%; method D: RT 9.897, area 96.40%.

N^4-[4-(5-fluoro-1-benzothien-3-yl)benzyl]-N^1-quinolin-4-ylpentane-1,4-diamine (34).

Compound **34** was prepared by procedure E, using aldehyde **31**[2] (170 mg, 0.66 mmol), amine **108** (213 mg, 0.929 mmol), glac. AcOH (50 μL, 0.8 mmol), $NaBH_4$ (150.6 mg, 3.980 mmol) and MeOH/CH_2Cl_2 (24 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH, flash, Biotage SP1, NH column, eluent EtOac/hexane gradient 8/2 → EtOAc, EtOAc/MeOH gradient 95/5 → 1/1 and flash, Biotage SP1, SiO_2 column, eluent EtOAc/MeOH+NH_3(9/1) gradient 95/5 → 65/35). Final product **34** was obtained as a white foam (239 mg, 77%). M.p. = 41 – 44 ºC. IR (ATR): 3257m, 3070m, 2958m, 2866m, 1581s, 1540m, 1495w, 1438m, 1374w, 1340w, 1252w, 1196w, 1117w, 1020w, 883w, 862w, 809w, 768w, 652w, 438w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$, δ): 8.53 (d, 1H, J = 5.3, H-C(2')), 7.98-7.95 (m, 1H, H-C(8')), 7.81 (dd, 1H, J_1 = 8.7, J_2 = 4.8, H-C(7)), 7.73-7.70 (m, 1H, H-C(5')), 7.60-7.52 (m,

2H, H-C(7') and H-C(4)), 7.51-7.47 (m, 2H-Ar), 7.46-7.42 (m, 3H, 2H-Ar and H-C(2)), 7.34-7.29 (m, 1H, H-C(6')), 7.16-7.10 (m, 1H, H-C(6)), 6.39 (d, 1H, J = 5.3, H-C(3')), 5.67 (bs, 1H, H-N exchangeable with D_2O), 3.93, 3.82 (ABq, 2H, J_{AB} = 13.0, ArCH_2-), 3.36-3.26 (m, 2H, ArNHCH_2-), 2.88-2.80 (m, 1H, ArNHCH$_2$CH$_2$CH$_2$CH(CH$_3$)-), 2.06 (bs, 1H, H-N exchangeable with D_2O), 1.94-1.78 (m, 2H, ArNHCH$_2$CH_2-), 1.69-1.55 (m, 2H, ArNHCH$_2$CH$_2$CH_2-), 1.18 (d, 3H, J = 6.3, ArNHCH$_2$CH$_2$CH$_2$CH(CH_3)-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 161.08 (d, J = 239.6), 151.02, 149.79, 148.38, 140.15, 139.08 (d, J = 9.0), 137.59 (d, J = 4.1), 135.97, 134.26, 129.87, 128.91, 128.62, 128.57, 125.60, 124.43, 123.98 (d, J = 9.0), 119.42, 118.77, 113.31 (d, J = 25.3), 108.50 (d, J = 23.5), 98.67, 52.17, 50.97, 43.48, 34.60, 25.10, 20.50. HRMS: *m/z* 470.20588 corresponds to molecular formula $C_{29}H_{28}FN_3SH^+$ (error in ppm -0.40). HPLC purity (λ = 330 nm): method A: RT 7.766, area 95.04%; method B: RT 7.737, area 95.17%.

_N_-[4-(5-fluoro-1-benzothiophene-3-yl)benzyl]-_N_-methyl-_N_'-quinolin-4-ylbutane-1,4-diamine (37).

Compound **37** was prepared by procedure D, using **35**[3] (30.0 mg, 0.0658 mmol), 37% aqueous formaldehyde (10 μL, 0.1 mmol), $ZnCl_2$ (17.9 mg, 0.132 mmol), $NaHB_3CN$ (16.6 mg, 0.263 mmol) and MeOH (1 mL + 1 mL). The product was purified using column chromatography (flash, Biotage SP1, NH column, eluent EtOAc/hexane gradient 8/2 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH and flash, Biotage SP1, SiO_2 column, eluent EtOAc/MeOH+NH_3(9/1) gradient 95/5 → 2/8). Final product **37** was obtained as a colorless oil (23 mg, 74%). IR (ATR): 3647w, 3252m, 3069m, 2927s, 2852m, 2793m, 1730w, 1582s, 1541m, 1494w, 1438m, 1374w, 1342m, 1252m, 1195m, 1118w, 969w, 883w, 864w, 807w, 765m, 737w, 653w, 628w, 572w, 543w, 422w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$): 8.53 (d, 1H, J = 5.2, H-C(2')), 7.99-7.95 (m, 1H,

H-C(8')), 7.82 (dd, 1H, J_1 = 4.6, J_2 = 8.8, H-C(7)), 7.74-7.71 (m, 1H, H-C(5')), 7.61-7.54 (m, 2H, H-C(7') and H-C(4)), 7.51-7.48 (m, 2H-Ar), 7.47-7.44 (m, 3H, 2H-Ar and H-C(2)), 7.35-7.30 (m, 1H, H-C(6')), 7.17-7.11 (m, 1H, H-C(6)), 6.40 (d, 1H, J = 5.3, H-C(3')), 5.76 (bs, 1H, H-N exchangeable with D_2O), 3.60 (s, 2H, ArCH_2-), 3.36-3.30 (m, 2H, ArNHCH_2-), 2.52 (t, 2H, J = 6.8, ArCH_2NHCH_2-), 2.27 (s, 3H, CH_3-N), 2.19 (bs, 1H, H-N), 1.89 (quin, 2H, J = 6.8, Ar$NHCH_2$CH_2-), 1.76 (quin, 2H, J = 7.0, Ar$NHCH_2CH_2$CH_2-). ^{13}C NMR (125 MHz, $CDCl_3$): 161.08 (d, J = 240.1), 150.87, 150.00, 148.21, 139.05 (d, J = 9.0), 138.43, 137.58 (d, J = 4.5), 135.98, 134.35, 129.70, 129.57, 128.96, 128.38, 125.61, 124.38, 123.98 (d, J = 9.9), 119.58, 118.76, 113.30 (d, J = 25.3), 108.50 (d, J = 23.5), 98.62, 61.89, 56.75, 43.19, 42.51, 26.48, 25.21. HRMS: *m/z* 470.20631 corresponds to molecular formula $C_{29}H_{28}FN_3SH^+$ (error in ppm 0.50). HPLC purity (λ = 330 nm): method A: RT 9.126, area 97.87%; method B: RT 7.770, area 96.71%.

3-[4-({methyl[4-(quinolin-4-ylamino)pentyl]amino}methyl)phenyl]-1-benzothiophene-5-carbonitrile (38).

Compound **38** was prepared by procedure D, using **36**[2] (15.8 mg, 0.0331 mmol), 37% aqueous formaldehyde (5.1 μL, 0.066 mmol), $ZnCl_2$ (9.0 mg, 0.066 mmol), $NaHB_3CN$ (8.3 mg, 0.283 mmol) and MeOH (1 mL + 1 mL). The product was purified using column chromatography (flash, Biotage SP1, NH column, eluent EtOac/hexane gradient 8/2 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH and flash, Biotage SP1, SiO_2 column, eluent EtOAc/MeOH+NH_3(9/1) gradient 95/5 → 65/35). Final product **38** was obtained as a colorless oil (12.1 mg, 74%). IR (film): 3375s, 3104s, 2971s, 2796m, 2346w, 2306w, 2227m, 1963w, 1703m, 1601s, 1553s, 1498m, 1460s, 1405m, 1342m, 1264m, 1224m, 1146m, 1058m, 1014w, 888w, 860w, 805m,

767m, 735m, 702w, 654m, 614w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, 1H, *J* = 5.2, H-C(2')), 8.21-8.19 (m, 1H, H-C(4)), 8.01-7.98 (m, 1H, H-C(8')), 7.98-7.95 (m, 1H, H-C(7)), 7.74-7.71 (m, 1H, H-C(5')), 7.63-7.57 (m, 2H, H-C(6) and H-C(7')), 7.52 (s, 1H, H-C(2)), 7.49-7.44 (m, 4H-Ar), 7.39-7.35 (m, 1H, H-C(6')), 6.42 (d, 1H, *J* = 5.6, H-C(3')), 5.20-5.16 (m, 1H, H-N exchangeable with D_2O), 3.79-3.70 (m, 1H, ArNHC*H*(CH_3)-), 3.58 (s, 2H, ArCH_2-), 2.50-2.45 (m, 2H, $ArCH_2NHCH_2$-), 2.24 (s, 3H, CH_3-N), 2.10 (bs, 1H, H-N exchangeable with D_2O), 1.84-1.67 (m, 4H, $ArNHCH(CH_3)CH_2CH_2$-), 1.35 (d, 3H, *J* = 6.2, ArNHCH(CH_3)-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 150.77, 149.03, 148.36, 144.78, 139.28, 137.96, 137.92, 133.28, 129.79, 129.64, 129.00, 128.50, 127.76, 126.27, 125.50, 124.42, 123.91, 119.46, 119.32, 118.76, 108.12, 98.91, 62.02, 57.03, 48.14, 42.39, 34.27, 23.90, 20.35. HRMS: *m/z* 491.22662 corresponds to molecular formula $C_{31}H_{30}N_4SH^+$ (error in ppm 0.45). HPLC purity (λ = 330 nm): method A: RT 8.785, area 96.50%; method B: RT 7.734, area 97.90%.

4-{5-[4-({[2-(quinolin-4-ylamino)ethyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (42).

Compound **42** was prepared by procedure E using aldehyde **39**[2] (40 mg, 0.14 mmol), amine **AQ11** (38.8 mg, 0.207 mmol), glac. AcOH (12 μL, 0.21 mmol), $NaBH_4$ (31.3 mg, 0.828 mmol) and MeOH/CH_2Cl_2 (3 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc, EtOAc/MeOH gradient 9/1 → MeOH and flash Biotage SP1, NH column, eluent hexane/EtOAc gradient 36/65 → EtOAc). Final product **42** was obtained as a yellow solid (41.3 mg, 65%). M.p. = 107 – 111 ºC. IR (film): 3296w, 3064w, 2223w, 1581s, 1539m, 1495w, 1452m, 1393w, 1337w, 1278w, 1177w, 1129w, 836m, 800m, 765m, 734w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.54 (d, 1H, *J* = 5.3, H-C(2)), 8.01 – 7.96 (m, 1H, H-C(8)), 7.82 – 7.76 (m, 1H, H-C(5)), 7.72 – 7.67 (m, 2H-ArCN), 7.67 – 7.62 (m, 3H, 2H-ArCN and H-C(7)),

7.61 – 7.56 (m, 2H-Ar), 7.47 – 7.42 (m, 1H, H-C(6)), 7.41 – 7.35 (m, 3H, 2H-Ar and H-thiophene), 7.32 – 7.28 (m, 1H, H-thiophene), 6.40 (d, 1H, *J* = 5.4, H-C(3)), 5.82 (bs, 1H, N-H, exchangeable with D_2O), 3.89 (s, 2H, -Ar*CH*$_2$NH-), 3.40 – 3.36 (m, 2H, -CH_2*CH*$_2$NHAr), 3.10 – 3.06 (m, 2H, -*CH*$_2$$CH_2$NHAr). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 150.93, 149.84, 148.27, 145.70, 140.89, 140.09, 138.48, 132.72, 129.78, 129.03, 128.75, 126.08, 125.91, 125.67, 124.62, 124.32, 119.51, 118.90, 118.82, 110.43, 98.92, 52.99, 46.99, 42.17. HRMS: *m/z* 461.17978 corresponds to molecular formula $C_{29}H_{24}N_4SH^+$ (error in ppm 0.73). HPLC purity (λ = 330 nm): method G: RT 2.132, area 95.55%; method H: RT 1.879, area 95.01%.

4-{5-[4-({[10-(quinolin-4-ylamino)decyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (43).

Compound **43** was prepared by procedure E using aldehyde **39**[2] (57.9 mg, 0.200 mmol), amine **AQ12** (90 mg, 0.30 mmol), glac. AcOH (18 μL, 0.30 mmol), $NaBH_4$ (45.4 g, 1.20 mmol) and MeOH/CH_2Cl_2 (4.5 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, EtOAc, EtOAc/MeOH gradient 9/1 → MeOH, MeOH (NH_3 sat.) and flash, Biotage SP1 NH column, eluent EtOAc, gradient EtOAc → EtOAc/MeOH 4/6). Final product **43** was obtained as a yellow solid (45.9 mg, 40 %). M. p. = 115 – 116 °C. IR (film): 3266m, 2922s, 2851m, 2221m, 1725w, 1668w, 1580s, 1530m, 1492w, 1445m, 1375m, 1342m, 1278m, 1234w, 970w, 875w, 836w, 799m, 762m cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.55 (d, 1H, *J* = 5.3, H-C(2)), 7.98 (d, 1H, *J* = 7.8, H-C(8)), 7.75 – 7.55 (m, 8H, 4H-ArCN, 2H-Ar, H-C(5) and H-C(7)), 7.45 – 7.34 (m, 4H, H-C(6), H-thiophene, 2H-Ar), 7.30 (d, 1H, *J* = 3.9, H-thiophene), 6.42 (d, 1H, *J* = 5.3, H-C(3)), 4.96 (bs, 1H, H-N), 3.81 (s, 2H, Ar*CH*$_2$NH), 3.35 – 3.27 (m, 2H, -*CH*$_2$NHAr), 2.64 (t, *J* = 7.2, ArCH$_2$NHC*H*$_2$-), 1.80 – 1.25 (m, 16H, -(*CH*$_2$)$_8$-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.10, 149.64, 148.46, 146.04, 140.86, 140.72, 138.56, 132.75,

132.34, 130.05, 128.94, 128.77, 126.09, 125.79, 125.66, 124.55, 124.18, 119.12, 118.88, 118.69, 110.38, 98.79, 53.72, 49.54, 43.27, 30.14, 29.52, 29.49, 29.36, 28.97, 27.33, 27.15. HRMS: *m/z* 573.30186 corresponds to molecular formula $C_{37}H_{40}N_4SH^+$ (error in ppm – 4.85). HPLC purity (λ = 330 nm): method C: RT 8.038, area 96.27%; method D: RT 6.152, area 95.99%.

(4-{5-[4-({[2-(quinolin-4-ylamino)ethyl]amino}methyl)phenyl]-2-thienyl}phenyl)acetonitrile (44).

Compound **44** was prepared in two steps from **114**. The general procedure F was followed using **114** (95 mg, 0.34 mmol), 4-formylphenylboronic acid (118.6 mg, 0.4099 mmol), PdO × 1.4 H_2O (5 mg, 0.03 mmol), K_2CO_3 (56.6 mg, 0.409 mmol), EtOH/H_2O (9.6 mL, 3:1, v/v). The product **40** was roughly purified using column chromatography (flash Biotage SP1, SiO_2 column, eluent toluene, toluene/EtOAc gradient 9/1 → EtOAc). The crude product was subjected to the next reaction step following procedure E using amine **AQ11** (32.3 mg, 0.172 mmol), AcOH (10 µL, 0.172 mmol), $NaBH_4$ (26.1 mg, 0.690 mmol), MeOH/CH_2Cl_2 (3 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc, EtOAc/MeoH gradient 9/1 → 1/1 and flash, Biotage SP1, NH column, eluent hexane/EtOAc gradient 6/4 → EtOAc). The final product **44** was obtained as a yellow solid. (20 mg, 12 %) M. p. = 110 – 112 °C. IR (ATR): 3638m, 3358s, 3315m, 3079m, 3027m, 2934m, 2900m, 2860m, 2815m, 1647w, 1620m, 1581s, 1542s, 1500m, 1458m, 1438m, 1417m, 1402m, 1370m, 1336s, 1277m, 1261m, 1223w, 1126m, 1047w, 1015w, 965w, 912m, 815m, 795s, 766m, 738m, 650w, 476w, 401w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$ + CD_3OD, δ): 8.55 – 8.45 (m, 1H, H-C(2)), 8.02 – 7.95 (m, 1H, H-C(8)), 7.85 – 7.78 (m, 1H, H-C(5)), 7.67 – 7.57 (m, 5H, 2H-Ar, 2H-*Ar*CH_2CN and H-C(7)), 7.47 – 7.42 (m, 1H, H-C(6)), 7.40 – 7.32 (m, 4H, 2H-Ar and 2H-*Ar*CH_2CN), 7.31 – 7.27 (m, 2H-

thiophene), 6.40 (d, 1H, *J* = 5.5, H-C(3)), 4.73 (bs, 1H, H-N), 3.86 (s, 2H, Ar*CH*$_2$NH), 3.77 (s, 2H, CH_2CN), 3.42 – 3.36 (m, 2H, -*CH*$_2$NHAr), 3.13 – 3.03 (m, 2H, $ArCH_2NHCH_2$-). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD, δ): 150.36, 150.21, 147.50, 143.58, 142.38, 138.82, 134.10, 133.23, 129.38, 128.74, 128.60, 128.46, 126.12, 125.76, 124.77, 124.43, 124.04, 119.92, 118.75, 117.71, 98.51, 52.95, 46.78, 42.10, 23.20. HRMS *m/z* 475.19470 corresponds to molecular formula $C_{30}H_{26}N_4SH^+$ (error in ppm -0.82). HPLC purity (λ = 330 nm): method B: RT 7.922, area 95.73%; method C: RT 7.974, area 95.24%.

_N_-(7-chloroquinolin-4-yl)-_N'_-[4-(5-{4-[(trimethylsilyl)ethynyl]phenyl}-2-thienyl)benzyl]ethane-1,2-diamine (45).

Compound **45** was prepared by procedure E using aldehyde **41**[2] (25.9 mg, 0.0718 mmol), amine **AQ2** (23.9 mg, 0.108 mmol), glac. AcOH (7 μL, 0.108 mmol), $NaBH_4$ (16.3 mg, 0.431 mmol) and MeOH/CH_2Cl_2 (3 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc, EtOAc/MeoH gradient 9/1 → MeOH and flash, Biotage SP1, NH column, eluent hexane/EtOAc gradient 6/4 → EtOAc). The final product **45** was obtained as a yellow foam (23.9 mg, 59 %). IR (ATR): 3298m, 3070w, 2958m, 2853w, 2158w, 1608m, 1584s, 1536w, 1495w, 1453w, 1372w, 1332w, 1280w, 1250w, 1139w, 867m, 844m, 802w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$ + D_2O, δ): 8.50 (d, 1H, *J* = 5.5, H-C(2)), 7.96 – 7.94 (m, 1H, H-C(8)), 7.71 – 7.67 (m, 1H, H-C(5)), 7.60 – 7.52 (m, 4H-Ar), 7.52 – 7.44 (m, 2H-Ar), 7.40 – 7.33 (m, 3H, H-C(6) and 2H-Ar), 7.32 – 7.29 (m, 1H, H-thiophene), 7.28 – 7.26 (m, 1H, H-thiophene, overlap with $CHCl_3$), 6.36 (d, 1H, *J* = 5.5, H-C(2)), 3.85 (s, 2H, Ar*CH*$_2$NH-), 3.40 – 3.26 (m, 2H, ArNH*CH*$_2$-), 3.10 – 3.01 (m, 2H, $ArNHCH_2CH_2$-), 0.26 (s, 9H, $(CH_3)_3Si$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.95, 149.86, 148.99, 143.80, 142.72, 139.42, 139.37, 134.88, 134.17, 133.23,

132.66, 132.50, 128.69, 125.78, 125.31, 125.13, 124.69, 124.56, 124.11, 122.04, 121.18, 117.32, 104.86, 99.19, 95.34, 52.95, 46.79, 42.02, 0.04. HRMS *m/z* 566.18315 corresponds to molecular formula $C_{33}H_{32}ClN_3SSiH^+$ (error in ppm -2.83).

_N_-(7-chloroquinolin-4-yl)-_N'_-{4-[5-(4-ethynylphenyl)-2-thienyl]benzyl}ethane-1,2-diamine (47).

Compound **45** (17.8 mg, 0.314 mmol) was dissolved in dry methanol (0.5 mL). Anh. K_2CO_3 (2.2 mg, 0.016 mmol) was added and reaction mixture was stirred at r.t. for 24 h. After extraction with ethyl-acetate, combined organic layers were washed with satd. aqueous solution of $NaHCO_3$ and dried over anh. Na_2SO_4. After filtration, the crude product was purified using column chromatography (flash, Biotage SP1, NH column, eluent CH_2Cl_2, CH_2Cl_2/MeOH gradient 9/1 → 1/1). The final product **47** was obtained as a yellow solid (7.6 mg, 49 %). M.p. = 163 – 167 °C. IR (ATR): 3292m, 2924w, 2854w, 1611m, 1583s, 1539m, 1493w, 1453m, 1372w, 1334w, 1281w, 1246w, 1211w, 1139w, 1113w, 837m, 803m cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$ + CD_3OD, δ): 8.36 (d, 1H, *J* = 5.5, H-C(2)), 7.99 (d, 1H, *J* = 8.9, H-C(5)), 7.90 – 7.80 (m, 1H, H-C(8)), 7.65 – 7.58 (m, 4H-Ar), 7.54 – 7.48 (m, 2H-Ar), 7.43 – 7.40 (m, 1H, H-C(6)), 7.39 – 7.33 (m, 3H, 2H-Ar and H-thiophene), 7.32 – 7.27 (m, 1H, H-thiophene), 6.50 – 6.41 (m, 1H, H-C(3)), 3.88 (s, 2H, $ArCH_2NH$-), 3.54 – 3.46 (m, 2H, $ArNH\mathit{CH_2}$), 3. 26 (s, 1H, CH), 3.12 – 2.98 (m, 2H, $ArNHCH_2\mathit{CH_2}$). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD, δ): 150.97, 150.16, 147.20, 143.47, 142.25, 137.87, 135.42, 134.21, 133.05, 132.29, 128.64, 126.14, 125.44, 125.26, 124.91, 124.42, 123.91, 122.22, 120.76, 116.97, 98.33, 83.04, 77.92, 52.56, 46.24, 41.83. HRMS *m/z* 494.14419 corresponds to molecular formula $C_{30}H_{24}ClN_3SH^+$ (error in ppm -2.09). HPLC purity (λ = 330 nm): method C: RT 8.075, area 96.46%; method D: RT 5.738, area 95.31%.

4-{5-[4-({methyl[6-(quinolin-4-ylamino)hexyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (48).

Compound **48** was prepared by procedure D using **46**[2] (36.5 mg, 0.071 mmol) in methanol (1.5 mL), 37% aqueous formaldehyde (11.5 μL, 0.141 mmol), and solution of $NaBH_3CN$ (17.8 mg, 0.282 mmol) and $ZnCl_2$ (19.2 mg, 0,141 mmol) in methanol (1.5 mL). The crude product was purified using column chromatography (flash, Biotage SP1, NH column, eluent hexane/EtOAc, gradient 1/1 → EtOAc → MeOH). The final product **48** was obtained as a yellow solid (18.6 mg, 50 %). M.p. = 135 – 140 ºC. IR (film): 3271w, 3068w, 2928m, 2853m, 2793w, 2224m, 1734w, 1652w, 1601m, 1581s, 1540m, 1496m, 1455m, 1373w, 1342m, 1279w, 1223w, 1177w, 1123w, 1015w, 837w, 800m, 765m, 730w, 668w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.54 (d, 1H, *J* = 5.3, H-C(2)), 8.05 – 7.95 (m, 1H, H-C(8)), 7.72 – 7.60 (m, 6H, 4H-ArCN, H-C(5)) and H-C(7)), 7.59 – 7.54 (m, 2H-Ar), 7.44 – 7.39 (m, 1H, H-C(6)), 7.38 – 7.33 (m, 3H, 2H-Ar and H-thiophene), 7.31 – 7.28 (m, 1H, H-thiophene), 6.44 – 6.40 (m, 1H, H-C(3)), 4.95 (bs, 1H, H-N), 3.50 (s, 2H, Ar*CH*$_2$N(CH_3)CH_2-), 3.35 – 3.27 (m, 2H, ArNH*CH*$_2$-), 2.44 – 2.35 (m, 2H, ArCH_2N(CH_3)*CH*$_2$-), 2.22 (s, 3H, CH_3-), 1.81 – 1.74 (m, 2H, ArNHCH_2*CH*$_2$-), 1.61 – 1.52 (m, 2H, ArNH$(CH_2)_4$*CH*$_2$-), 1.52 – 1.37 (m, 4H, -$(CH_2)_2$*CH*$_2$*CH*$_2$$(CH_2)_2$-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.34, 151.36, 149.66, 147, 57, 142.27, 141.09, 140.11, 134.42, 134.31, 133.97, 132.11, 131.30, 131.23, 131.17, 130.65, 127.65, 127.51, 127.22, 127.17, 126.20, 125.73, 120.71, 120.44, 120.17, 111.95, 100.30, 63.60, 58.70, 44.80, 43.90, 30.50, 28.84, 28.62, 28.57. HRMS: *m/z* 531.25859 corresponds to molecular formula $C_{34}H_{34}N_4SH^+$ (error in ppm 1.69). HPLC purity (λ = 330 nm): method E: RT 4.358, area 95.79%; method F: RT 4.042, area 95.71%.

4-[5-(3-formylphenyl)thiophen-2-yl]benzonitrile (49).

Compound **49** was prepared by procedure G using $Pd(OAc)_2$ (8.7 mg, 0.039 mmol), PPh_3 (40.7 mg, 0.155 mmol), 4-cyanophenylboronic acid (57.1 mg, 0.388 mmol), aq. 2M Na_2CO_3 (1.5 mL), **112** (103.8 mg, 0.388 mmol) and DME (10 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, hexane/EtOAc gradient 9/1 → 7/3). Final product **49** was precipitated with ethyl acetate as a yellow solid (42.7 mg, 38 %). M.p. = 178 °C. IR (film): 3096m, 3066m, 2873m, 2760w, 2222s, 1685s, 1636m, 1600s, 1581s, 1507m, 1485m, 1458m, 1435m, 1414m, 1389m, 1340m, 1314m, 1286s, 1240m, 1177s, 1092m, 1003w, 883w, 842m, 809m, 786m, 751w, 724m, 696m, 677w, 650w, 542m cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 10.08 (s, 1H, H-CO), 8.13 (bs, 1H, H-C(2')), 7.89 – 7.82 (m, 2H, H-C(4') and H-C(6')), 7.73 – 7.67 (m, 4H, H-ArCN), 7.60 (t, 1H, J = 7.7, H-C(5')), 7.44 – 7.42 (m, 2H, H-C(3) and H-C(4)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 191.81, 144.12, 142.03, 138.18, 137.05, 134.71, 132.81, 131.32, 129.80, 129.40, 126.23, 126.20, 125.83, 125.33, 118.72, 110.84. GC/MS (m/z (%)): 289.0 ([M^+], 100); 259.0 (20).

4-{5-[3-({[6-(quinolin-4-ylamino)hexyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (50).

Compound **50** was prepared by procedure E using aldehyde **49** (37.6 mg, 0.129 mmol), amine **AQ9**[2] (47.4 mg, 0.195 mmol), glac, AcOH (12 μL, 0.195 mmol), $NaBH_4$ (29.3 mg, 0.774 mmol) and MeOH/CH_2Cl_2 (3 mL, 2:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, EtOAc, EtOAc/MeOH gradient 9/1 → MeOH and flash Biotage SP1 NH column eluent hexane/EtOAc gradient 6/4 → EtOAc, MeOH). The final product **50** was obtained as a yellow solid (28.2 mg, 54 %). M.p. = (143 – 146) °C. IR (film): 3402w, 3300w, 3062w, 2930m, 2855m, 2225m, 1602m, 1583s, 1541m, 1505w, 1456w, 1394w, 1372w, 1342w,

1280w, 1176w, 1125w, 837w, 808w, 787w, 766w, 732w, 698w, 542w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.54 (d, 1H, *J* = 5.3, H-C(2")), 7.98 (d, 1H, *J* = 8.5, H-C(8")), 7.71 – 7.60 (m, 7H, H-C(7"), 4H-ArCN, H-C(5") and H-C(2')), 7.51 (d, 1H, *J* = 7.3, H-C(6')), 7.42 – 7.32 (m, 4H, H-C(6"), 2H-ArS and H-C(5')), 7.29 – 7.27 (m, 1H, H-C(4')), 6.40 (d, 1H, *J* = 5.3, H-C(3")), 4.99 (bs, 1H, H-N), 3.84 (s, 2H, Ar-CH_2), 3.31 – 3.28 (m, 2H, ArNHCH_2-), 2.69 – 2.66 (m, 2H, -CH_2NHCH_2CH_2-), 1.79 – 1.73 (m, 2H, ArNHCH$_2CH_2$-), 1.60 – 1.55 (m, 2H, -CH_2NHCH$_2CH_2$-), 1.52 – 1.44 (m, 4H, ArNHCH$_2$CH$_2CH_2CH_2$-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 150.87, 149.68, 148.22, 146.04, 141.41, 140.91, 138.48, 133.79, 132.72, 129.84, 129.09, 129.01, 127.94, 126.04, 125.63, 125.45, 124.58, 124.41, 119.12, 118.83, 118.61, 110.41, 98.72, 53.88, 49.27, 43.17, 29.98, 28.88, 27.05. HRMS *m/z* 517.24204 corresponds to molecular formula $C_{33}H_{32}N_4SH^+$ (error in ppm -1.04). HPLC purity (λ=330 nm): method A: RT 9.390, area 97.66%; method B: RT 7.586, area 95.23%.

_N_-(1-Adamantylmethyl)-_N'_-(7-chloroquinolin-4-yl)-_N_-methylethane-1,2-diamine (56).

Compound **56** was prepared from aminoquinoline *N*-(1-adamantylmethyl)-*N'*-(7-chloroquinolin-4-yl)ethane-1,2-diamine[5] (87 mg, 0.24 mmol) and 37% formaldehyde (35 μL, 0.48 mmol) using $ZnCl_2$ (65 mg, 0.48 mmol) and $NaBH_3CN$ (60 mg, 0.96 mmol) by procedure D and was obtained after column chromatography (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (74 mg, 82%) softenes at 135-137 °C. IR (ATR): 3207w, 3062w, 2901s, 2844m, 2792w, 1612w, 1581s, 1489w, 1453m, 1432w, 1374w, 1339w, 1313w, 1283w, 1243w, 1208m, 1183w, 1166w, 1135w, 1101w, 1080w, 1046w, 986w, 949w, 902w, 874w, 847w, 823w, 804m, 772w, 735w, 645w, 623w, 567w, 488w, 425w cm^{-1}. ^1H-NMR (200 MHz, $CDCl_3$): 8.53 (d, 1H, *J* = 5.0 Hz, H-C(2)), 7.96 (d, 1H, *J* = 2.4 Hz, H-C(8)), 7.77 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.35 (dd, 1H, *J* = 2.2

Hz, *J* = 9.0 Hz, H-C(6)), 6.36 (d, 1H, *J* = 5.6 Hz, H-C(3)), 6.30 (bs, 1H, -N*H*), 3.30-3.15 (m, 2H, ArNHC*H*$_2$-), 2.90-2.70 (m, 2H, ArNHCH$_2$C*H*$_2$-), 2.29 (s, 3H, -N(C*H*$_3$)), 2.14 (s, 2H, -C*H*$_2$Ad), 1.99 (bs, 3H, -Ad), 1.70-1.50 (m, 12H, -Ad). ^{13}C-NMR (50 MHz, $CDCl_3$): 152.09; 149.87; 149.01; 134.74; 128.67; 125.08; 121.24; 117.37; 99.20; 77.41; 57.96; 44.21; 41.31; 40.13; 37.13; 35.03; 28.31. (+)ESI-HRMS (m/z (%)): 384.21997 ([M+H]$^+$, 100); calculated 384.22010 (error in ppm: -0.34). Anal. ($C_{23}H_{30}ClN_3 \times H_2O$) Calcd: C, 70.30; H, 7.95; N, 10.69. Found: C, 70.50; H, 7.97; N, 10.58. HPLC purity (λ=330 nm): method A: RT 7.872, area 98.49%; method B: RT 9.624, area 98.88%.

_N_-(1-Adamantylmethyl)-_N'_-(7-chloroquinolin-4-yl)-_N_-methylpropane-1,3-diamine (57).

Compound **57** was prepared from aminoquinoline *N*-(1-adamantylmethyl)-*N'*-(7-chloroquinolin-4-yl)propane-1,3-diamine[5] (93 mg, 0.24 mmol) and 37% formaldehyde (36 µL, 0.48 mmol) using $ZnCl_2$ (65 mg, 0.48 mmol) and $NaBH_3CN$ (60 mg, 0.96 mmol) by procedure D and was obtained after column chromatography: (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (85 mg, 87%) softenes at 137-139 °C. IR (ATR): 3246m, 3064w, 2900s, 2844m, 1612w, 1580s, 1540w, 1451m, 1429w, 1367, 1330w, 1283w, 1233w, 1202w, 1167w, 1139m, 1103w, 1079w, 1036w, 901w, 876w, 850w, 804m, 766w, 731w, 644w cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.52 (d, 1H, *J* = 5.0 Hz, H-C(2)), 7.94 (d, 1H, *J* = 2.2 Hz, H-C(8)), 7.80 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.32 (dd, 1H, *J* = 2.2 Hz, *J* = 9.0 Hz, H-C(6)), 7.21 (bs, 1H, -N*H*), 6.35 (d, 1H, *J* = 5.2 Hz, H-C(3)), 3.45-3.30 (m, 2H, ArNHC*H*$_2$-), 2.65-2.55 (m, 2H, ArNHCH$_2$CH$_2$C*H*$_2$-), 2.39 (s, 3H, -N(C*H*$_3$)), 2.08 (s, 2H, -C*H*$_2$Ad), 2.00-1.40 (m, 17 H, -Ad, -ArNHCH$_2$C*H*$_2$-). ^{13}C-NMR (50 MHz, $CDCl_3$): 152.09; 150.45; 149.10; 134.61; 128.51; 124.70; 122.06; 117.53; 98.59; 72.47; 60.87; 46.14; 44.06; 41.46; 36.87; 34.69; 28.24; 25.46. (+)ESI-HRMS (m/z (%)):

398.23579 ([M+H]$^+$, 100); calculated 398.23575 (error in ppm: -0.09). Anal. ($C_{24}H_{32}ClN_3 \times 1/2$ H_2O) Calcd: C, 70.83; H, 8.17; N, 10.32. Found: C, 71.01; H, 8.12; N, 10.14. HPLC purity (λ=330 nm): method A: RT 7.834, area 96.12%; method B: RT 9.633, area 96.86%.

***N*-[2-(1-Adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)-*N*-methylpropane-1,3-diamine (58).**

Compound **58** was prepared from aminoquinoline *N*-(1-adamantylmethyl)-*N*'-(7-chloroquinolin-4-yl)butane-1,4-diamine[5] (127 mg, 0.32 mmol) and 37% formaldehyde (48 μL, 0.64 mmol) using $ZnCl_2$ (87 mg, 0.64 mmol) and $NaBH_3CN$ (80 mg, 1.28 mmol) by procedure D and was obtained after column chromatography: (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (123 mg, 93%) softenes at 157-159 °C. IR (ATR): 3234m, 3063w, 2900s, 2844m, 2790w, 1611w, 1578s, 1541w, 1508w, 1489w, 1473w, 1452m, 1429w, 1368m, 1331w, 1281w, 1252w, 1203w, 1164w, 1140m, 1102w, 1080w, 1034w, 898w, 873w, 847m, 804m, 767w, 637w, 564w cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.52 (d, 1H, *J* = 5.6 Hz, H-C(2)), 7.94 (d, 1H, *J* = 2.4 Hz, H-C(8)), 7.71 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.32 (dd, 1H, *J* = 1.7 Hz, *J* = 8.9 Hz, H-C(6)), 6.40 (d, 1H, *J* = 5.6 Hz, H-C(3)), 5.40 (bs, 1H, -N*H*), 3.40-3.20 (m, 2H, ArNHCH_2-), 2.50-2.30 (m, 2H, -CH_2N(CH_3)CH_2Ad), 2.25 (s, 3H, -N(CH_3)), 2.10-1.40 (m, 21H, -CH_2Ad, ArNHCH$_2$CH_2-, ArNHCH$_2$CH$_2$CH_2-, -Ad). ^{13}C-NMR (50 MHz, $CDCl_3$): 152.01; 149.81; 149.14; 134.72; 128.71; 125.03; 121.12; 117.15; 98.98; 71.05; 60.20; 46.41; 43.15; 41.35; 37.11; 34.70; 28.42; 26.42; 25.69. (+)ESI-HRMS (m/z (%)): calculated 412.25123 ([M+H]$^+$, 100); calculated 412.25140 (error in ppm: -0.42). Anal. ($C_{25}H_{34}ClN_3 \times 1/2$ H_2O) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.73; H, 8.77; N, 10.02. HPLC purity (λ=330 nm): method A: RT 7.856, area 99.06%; method B: RT 9.641, area 98.70%.

N^1-(1-Adamantylmethyl)-N^2-(7-chloroquinolin-4-yl)-N^1-methylpropane-1,2-diamine (59).

Compound **59** was prepared from aminoquinoline N^1-(1-adamantylmethyl)-N^2-(7-chloroquinolin-4-yl)propane-1,2-diamine[4] (61 mg, 0.16 mmol) and 37% formaldehyde (24 μL, 0.32 mmol) using $ZnCl_2$ (45 mg, 0.32 mmol) and $NaHB_3CN$ (40 mg, 0.64 mmol) by procedure D and was obtained after dry-flash chromatography: (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 100/2) as white solid (58 mg, 91%) softenes at 134-136 °C. IR (ATR): 3257m, 3067w, 2980w, 2901s, 2844s, 2795w, 2611w, 1574s, 1546m, 1490w, 1453m, 1426w, 1377m, 1332m, 1313w, 1283w, 1250w, 1208m, 1173w, 1152m, 1105w, 1079w, 1038w, 956w, 902w, 874w, 862w, 843w, 824w, 803w, 772w, 757w, 610w, 600w, 567w, 495w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.54 (d, 1H, *J* = 5.0 Hz, H-C(2)), 7.96 (d, 1H, *J* = 2.0 Hz, H-C(8)), 7.82 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.35 (dd, 1H, *J* = 2.2 Hz, *J* = 8.8 Hz, H-C(6)), 6.45 (d, 1H, *J* = 5.5 Hz, H-C(3)), 6.26 (bs, 1H, ArN*H*-), 3.60-3.50 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.60 (m, 1H, ArNHCH(CH_3)CH_2-), 2.60-2.50 (m, 1H, ArNHCH(CH_3)CH_2-), 2.19 (m, 3H, -N(CH_3)), 2.15 (ABq, 1H, H_A, *J* = 14.0 Hz, -CH_2Ad), 2.10 (ABq, 1H, H_B, *J* = 14.0 Hz, -CH_2Ad), 1.98 (m, 3H, -Ad), 1.85-1.60 (m, 6H, -Ad), 1.60-1.50 (m, 6H, -Ad), 1.29 (d, 3H, *J* = 6.0 Hz, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 152.04; 150.24; 149.21; 134.75; 128.79; 125.14; 121.49; 118.21; 99.85; 71.62; 65.98; 46.18, 44.72; 41.37; 37.20; 35.15; 28.40; 18.60. (+)ESI-HRMS (m/z (%)): 398.23694 ($[M+H]^+$, 100); calculated 398.23575 (error in ppm: 2.99). Anal. ($C_{24}H_{32}ClN_3 \times 2/3H_2O$) Calcd: C, 70.31; H, 8.19; N, 10.25. Found: C, 70.29; H, 8.40; N, 10.15. HPLC purity (λ=330 nm): method A: RT 7.838, area 98.86%; method B: RT 9.645, area 99.04%.

N^1-(1-Adamantylmethyl)-N^3-(7-chloroquinolin-4-yl)-N^1-methylbutane-1,3-diamine (60).

Compound **60** was prepared from aminoquinoline N^1-(1-adamantylmethyl)-N^3-(7-chloroquinolin-4-yl)butane-1,3-diamine[4] (248 mg, 0.62 mmol) and 37% formaldehyde (93 µL, 1.25 mmol) using $ZnCl_2$ (169 mg, 1.24 mmol) and $NaBH_3CN$ (156 mg, 2.48 mmol) by procedure D and was obtained after column chromatography: (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (222 mg, 87%) softenes at 48-50 °C. IR (ATR): 3251m, 3063w, 2902s, 2845s, 1655w, 1611w, 1576s, 1538m, 1489w, 1452m, 1372w, 1332w, 1280w, 1201w, 1149m, 1102w, 1080w, 1045w, 1007w, 983w, 877w, 850w, 806m, 766w, 737w, 648w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.49 (d, 1H, *J* = 5.5 Hz, H-C(2)), 7.95 (d, 1H, *J* = 2.5 Hz, H-C(8)), 7.83 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.31 (dd, 1H, *J* = 9.0 Hz, *J* = 2.0 Hz, H-C(6)), 7.07 (bs, 1H, -N*H*), 6.40 (d, 1H, *J* = 5.5 Hz, H-C(3)), 3.90-3.80 (m, 1H, ArNHC*H*(CH_3)-), 2.75-2.65 (m, 1H, -CH_2N(CH_3)CH_2Ad), 2.65-2.40 (m, 1H, -CH_2N(CH_3)CH_2Ad), 2.34 (m, 3H, -N(CH_3)), 2.12 (ABq, 1H, H_A, *J* = 13.5 Hz, -CH_2Ad), 2.04 (ABq, 1H, H_B, *J* = 13.5 Hz, -CH_2Ad), 1.95-1.85 (m, 4H, -Ad, ArNHCH(CH_3)CH_2-), 1.80-1.45 (m, 14H, ArNHCH(CH_3)CH_2-, -Ad), 1.33 (d, 3H, *J* = 6.5 Hz, ArNHCH(CH_3)-). ^{13}C-NMR (125 MHz, $CDCl_3$): 151.68; 149.87; 149.04; 134.82; 128.39; 124.75; 122.09; 117.68; 98.90; 72.28; 58.14; 48.64; 46.45; 41.61; 36.96; 34.74; 33.28; 28.39; 19.63. (+)ESI-HRMS (m/z (%)): 412.25136 ($[M+H]^+$, 100); calculated 412.25140 (error in ppm: -0.11). Anal. ($C_{25}H_{34}ClN_3 \times 1/2\ H_2O$) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.32; H, 8.20; N, 9.85. HPLC purity (λ=330 nm): method A: RT 7.851, area 96.80%; method B: RT 9.605, area 96.30%.

***N*-[2-(1-Adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)-*N*-methylethane-1,2-diamine (61).**

Compound **61** was prepared from aminoquinoline *N*-[2-(1-adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)ethane-1,2-diamine[5] (54 mg, 0.14 mmol) and 37% formaldehyde (21 µL, 0.28 mmol) using $ZnCl_2$ (38 mg, 0.28 mmol) and $NaBH_3CN$ (35 mg, 0.56 mmol) by procedure D and was obtained after column chromatography (SiO_2, eluent CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (50 mg, 89%) softenes at 157-159 °C. IR (KBr): 3264m, 3064w, 2902s, 2843s, 2787w, 1611w, 1581s, 1550w, 1508w, 1489w, 1451m, 1431w, 1366m, 1355w, 1333m, 1282w, 1248w, 1203w, 1169w, 1145m, 1104w, 1083w, 1059w, 1041w, 1014w, 911w, 876m, 869w, 838m, 818m cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.53 (d, 1H, *J* = 5.6 Hz, H-C(2)), 7.95 (d, 1H, *J* = 2.2 Hz, H-C(8)), 7.68 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.36 (dd, 1H, *J* = 1.9 Hz, *J* = 8.7 Hz, H-C(6)), 6.37 (d, 1H, *J* = 5.6 Hz, H-C(3)), 6.01 (bs, 1H, -N*H*), 3.35-3.20 (m, 2H, ArNHCH_2-), 2.80-2.65 (m, 2H, ArNHCH$_2$CH_2-), 2.55-2.40 (m, 2H, -CH_2CH$_2$Ad), 2.61 (s, 3H, -N(CH_3)), 1.94 (bs, 3H, -Ad), 1.80-1.55 (m, 6H, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.40-1.20 (m, 2H, -CH_2Ad). ^{13}C-NMR (50 MHz, $CDCl_3$): 152.10; 149.85; 149.08; 134.75; 128.65; 125.16; 121.32; 117.35; 99.20; 54.95; 51.93; 42.61; 41.42; 41.31; 39.58; 37.05; 31.86; 28.55. (+)ESI-HRMS (m/z (%)): 398.23665 ($[M+H]^+$, 100); calculated 398.23575 (error in ppm: 2.25). Anal. ($C_{24}H_{32}ClN_3 \times 1/2$ H_2O) Calcd: C, 70.83; H, 8.17; N, 10.32. Found: C, 70.36; H, 8.11; N, 10.30. HPLC purity (λ=330 nm): method A: RT 7.898, area 98.86%; method B: RT 9.851, area 95.82%.

***N*-[2-(1-Adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)-*N*-methylpropane-1,3-diamine (62).**

Compound **62** was prepared from aminoquinoline *N*-[2-(1-adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)propane-1,3-diamine[5] (132 mg, 0.33 mmol) and 37% formaldehyde (50 µL, 0.66 mmol) using $ZnCl_2$ (90 mg, 0.66 mmol) and $NaBH_3CN$ (83 mg, 1.32 mmol) by procedure D

and was obtined after column chromatography (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (113 mg, 84%) softenes at 101-103 °C. IR (ATR): 3245m, 3064w, 2899s, 2844m, 2786w, 1610w, 1578s, 1541w, 1508w, 1497w, 1473w, 1452m, 1430w, 1396w, 1366m, 1331w, 1282w, 1231w, 1202w, 1168w, 1140w, 1098w, 1080w, 1038w, 900w, 870w, 845w, 804w, 769w, 644w cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.49 (d, 1H, *J* = 5.6 Hz, H-C(2)), 8.08 (bs, 1H, -N*H*), 7.92 (d, 1H, *J* = 1.6 Hz, H-C(8)), 7.61 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.31 (dd, 1H, *J* = 2.3 Hz, *J* = 8.9 Hz, H-C(6)), 6.29 (d, 1H, *J* = 5.6 Hz, H-C(3)), 3.45-3.30 (m, 2H, ArNHCH_2-), 2.70-2.55 (m, 2H, ArNHCH$_2$CH$_2$CH_2-), 2.55-2.40 (m, 2H, -CH_2CH$_2$Ad), 2.33 (s, 3H, -N(CH_3)), 1.91 (bs, 3H, -Ad), 1.80-1.50 (m, 8H, ArNHCH$_2$CH_2-, Ad), 1.46 (bs, 6H, -Ad), 1.40-1.30 (m, 2H, -CH_2Ad). ^{13}C-NMR (50 MHz, $CDCl_3$): 152.12; 150.68; 149.14; 134.50; 128.45; 124.67; 122.15; 117.62; 98.19; 58.06; 52.28; 44.37; 42.42; 42.01; 41.48; 37.00; 31.68; 28.48; 24.07. (+)ESI-HRMS (m/z (%)): 412.25106 ([M+H]$^+$, 100); calculated 412.25140 (error in ppm: -0.83). Anal. ($C_{25}H_{34}ClN_3 \times 1/2\ H_2O$) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.54; H, 8.02; N, 10.07. HPLC purity (λ=330 nm): method A: RT 7.999, area 99.74%; method B: RT 9.940, area 99.04%.

_N_-[2-(1-Adamantyl)ethyl]-_N'_-(7-chloroquinolin-4-yl)-_N_-methylbutane-1,4-diamine (63).

Compound **63** was prepared from aminoquinoline *N*-[2-(1-adamantyl)ethyl]-*N'*-(7-chloroquinolin-4-yl)butane-1,4-diamine[5] (194 mg, 0.47 mmol) and 37% formaldehyde (71 µL, 0.94 mmol) using $ZnCl_2$ (128 mg, 0.94 mmol) and $NaBH_3CN$ (118 mg, 1.88 mmol) by procedure D and was obtained after column chromatography (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (172 mg, 86%) softenes at 136-138 °C. IR (ATR): 3232m, 3064w, 2906s, 2844m, 2367w, 1610w, 1580s, 1542w, 1522w, 1508w, 1490w, 1454m, 1430w, 1386w, 1367m,

1331m, 1279w, 1256w, 1225w, 1200w, 1167w, 1139w, 1074w, 1039w, 1028w, 898w, 869w, 852w, 821w, 805w, 770w, 734w, 644w, 637w cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.49 (d, 1H, *J* = 5.6 Hz, H-C(2)), 7.92 (d, 1H, *J* = 2.2 Hz, H-C(8)), 7.73 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.29 (dd, 1H, *J* = 1.9 Hz, *J* = 8.7 Hz, H-C(6)), 6.61 (bs, 1H, -N*H*), 6.34 (d, 1H, *J* = 5.6 Hz, H-C(3)), 3.35-3.15 (m, 2H, ArNHCH_2CH$_2$CH$_2$CH$_2$N(CH$_3$)-), 2.50-2.30 (m, 4H, ArNHCH$_2$CH$_2$CH_2-, -CH_2CH$_2$Ad), 2.19 (s, 3H, -N(CH_3)), 1.94 (bs, 3H, -Ad), 1.80-1.55 (m, 10H, ArNHCH$_2$CH_2-, ArNHCH$_2$CH$_2$CH_2-, -Ad), 1.48 (bs, 6H, -Ad), 1.40-1.20 (m, 2H, -CH_2Ad). ^{13}C-NMR (50 MHz, $CDCl_3$): 151.98; 150.28; 149.10; 134.52; 128.42; 124.67; 121.83; 117.38; 98.72; 56.90; 51.42; 43.28; 42.61; 42.41; 40.99; 37.00; 31.63; 28.50; 26.60; 25.36. (+)ESI-HRMS (m/z (%)): 426.26631 ($[M+H]^+$, 100); calculated 426.26705 (error in ppm: -1.75). Anal. ($C_{26}H_{36}ClN_3 \times 1/3$ H_2O) Calcd: C, 72.28; H, 8.55; N, 9.73. Found: C, 72.17; H, 8.82; N, 9.71. HPLC purity (λ=330 nm): method A: RT 7.898, area 99.37%; method B: RT 9.855, area 99.17%.

N^1-[2-(1-Adamantyl)ethyl]-N^2-(7-chloroquinolin-4-yl)-N^1-methylpropane-1,2-diamine (64).

Compound **64** was prepared from aminoquinoline N^1-[2-(1-adamantyl)ethyl]-N^2-(7-chloroquinolin-4-yl)propane-1,2-diamine[4] (27 mg, 0.07 mmol) and 37% formaldehyde (11 µL, 0.14 mmol) using $ZnCl_2$ (19 mg, 0.14 mmol) and $NaBH_3CN$ (18 mg, 0.28 mmol) by procedure D and was obtained after column chromatography (SiO_2, eluent; CH_2Cl_2/MeOH(NH_3 satd) = 95/5) a white solid (27 mg, 93%) softenes at 138-140 °C. IR (ATR): 3275m, 2964w, 2901s, 2844m, 2799w, 2346w, 1610w, 1575s, 1541m, 1500w, 1490w, 1451m, 1425w, 1381w, 1366w, 1341w, 1331w, 1273w, 1254w, 1198w, 1153w, 1126w, 1104w, 1078w, 1045w, 909w, 872m, 839w, 820w, 802w, 769w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.52 (d, 1H, *J* = 5.0 Hz, H-C(2)), 7.95 (d, 1H, *J* = 2.0 Hz, H-C(8)), 7.71 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.35 (dd, 1H, *J* = 2.5 Hz, *J* = 9.0 Hz,

H-C(6)), 6.44 (d, 1H, *J* = 5.5 Hz, H-C(3)), 5.96 (d, 1H, *J* = 3.0 Hz, ArN*H*-), 3.70-3.55 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.55 (m, 1H, ArNHCH(CH_3)CH_2-), 2.50-2.30 (m, 3H, ArNHCH(CH_3)CH_2-, -C$H_2$$CH_2$Ad), 2.20 (s, 3H, -N(C$H_3$)), 1.90 (bs, 3H, -Ad), 1.75-1.50 (m, 6H, -Ad), 1.45 (bs, 6H, -Ad), 1.30 (d, 3H, *J* = 6.0 Hz, ArNHCH(CH_3)-), 1.30-1.15 (m, 2H, -CH_2Ad). ^{13}C-NMR (125 MHz, $CDCl_3$): 151.98; 149.87; 149.22; 134.68; 128.66; 125.13; 121.44; 118.06; 99.70; 62.58; 52.04; 45.59; 42.55; 42.10; 41.36; 37.06; 31.82; 28.58; 18.69. (+)ESI-HRMS (m/z (%)): 412.25217 ($[M+H]^+$, 100); calculated 412.25140 (error in ppm: 1.86). Anal. ($C_{25}H_{34}ClN_3$ × 1/2 H_2O) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.57; H, 8.72; N, 9.98. HPLC purity (λ=330 nm): method A: RT 7.811, area 98.20%; method B: RT 9.832, area 98.83%.

N^1-[2-(1-Adamantyl)ethyl]-N^3-(7-chloroquinolin-4-yl)-N^1-methylbutane-1,3-diamine (65).

Compound **65** was prepared from aminoquinoline N^1-[2-(1-adamantyl)ethyl]-N^3-(7-chloroquinolin-4-yl)butane-1,3-diamine[4] (140 mg, 0.34 mmol) and 37% formaldehyde (54 µL, 0.68 mmol) using $ZnCl_2$ (93 mg, 0.68 mmol) and $NaBH_3CN$ (85 mg, 1.36 mmol) by procedure D and was obtained after column chromatography (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (116 mg, 80%) softenes at 54-56 °C. IR (ATR): 3236m, 2902s, 2845s, 2611w, 1578s, 1541m, 1488w, 1450m, 1428w, 1375w, 1330w, 1281w, 1243w, 1200w, 1152m, 1098w, 1078w, 1048w. 878w, 849w, 806m, 765w, 644w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.47 (d, 1H, *J* = 5.0 Hz, H-C(2)), 8.00 (d, 1H, *J* = 4.9 Hz, -N*H*), 7.92 (d, 1H, *J* = 2.0 Hz, H-C(8)), 7.65 (d, 1H, *J* = 9.0 Hz, H-C(5)), 7.30 (dd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz, H-C(6)), 6.34 (d, 1H, *J* = 5.5 Hz, H-C(3)), 3.90-3.80 (m, 1H, ArNHC*H*(CH_3)-), 2.85-2.75 (m, 1H, ArNHCH(CH_3)CH_2CH_2-), 2.50-2.40 (m, 3H, ArNHCH(CH_3)CH_2CH_2-, -C$H_2$$CH_2$Ad), 2.31 (s, 3H, -N(C$H_3$)), 2.05-1.95 (m, 1H, ArNHCH(CH_3)CH_2-), 1.92 (bs, 3H, -Ad), 1.75-1.55 (m, 7H, ArNHCH(CH_3)CH_2, -Ad), 1.44 (m,

6H, -Ad), 1.35-1.25 (m, 5H, -C*H*$_2$Ad, -C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$): 151.86; 149.94; 149.27; 134.61; 128.42; 124.65; 122.25; 117.85; 98.50; 54.42; 52.32; 48.65; 42.47; 42.08; 41.37; 37.07; 31.75; 31.50; 28.58; 18.90. (+)ESI-HRMS (m/z (%)): 426.26541 ([M+H]$^+$, 100); calculated 426.26705 (error in ppm: -3.85). Anal. ($C_{26}H_{36}ClN_3 \times H_2O$) Calcd: C, 70.32; H, 8.63; N, 9.46. Found: C, 69.70; H, 9.05; N, 9.38. HPLC purity (λ=330 nm): method A: RT 8.531, area 97.77%; method B: RT 9.909, area 96.78%.

***N*-(1-Adamantylmethyl)-*N*'-quinolin-4-ylpropane-1,3-diamine (66).**

Compound **66** was prepared from **AQ7** (1.4 g, 6.96 mmol) and adamantane-1-carboxaldehyde (952 mg, 5.80 mmol) using AcOH (370 μL, 6.96 mmol) and $NaBH_4$ (1.36 g, 34.80 mmol) by procedure E and was obtained after flash chromatography (SiO_2, gradient: Hex/EtOAc = 4/6→1/9) as a colorless foam (1.21 g, 60%). IR (ATR): 3290m, 2901s, 2846s, 1657w, 1619w, 1584s, 1544m, 1451m, 1372w, 1340w, 1285w, 1225w, 1151w, 1131w, 1100w, 1041m, 807w, 762m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.51 (d, 1H, *J* = 5.3 Hz, H-C(2)), 7.94 (d, 1H, *J* = 8.5 Hz, H-C(8)), 7.89 (d, 1H, *J* = 8.2 Hz, H-C(5)), 7.58 (t, 1H, *J* = 7.7 Hz, H-C(7)), 7.32 (t, 1H, *J* = 7.6 Hz, H-C(6)), 7.14 (bs, 1H, -N*H*), 6.33 (d, 1H, *J* = 5.3 Hz, H-C(3)), 3.36 (s, 2H, ArNHC*H*$_2$-), 2.90-2.78 (m, 2H, -C*H*$_2$NHCH$_2$Ad), 2.29 (s, 2H, -C*H*$_2$Ad), 2.05-1.95 (m, 3H, -Ad), 1.93-1.83 (m, 2H, ArNHCH$_2$*CH*$_2$-), 1.8-1.67 (m, 6H, -Ad), 1.65-1.55(m, 6H, -Ad). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.89; 150.48; 148.11; 129.33; 128.81; 123.94; 120.66; 118.94; 98.13; 63.56; 50.62; 43.86; 41.05; 37.10; 33.24; 28.38; 27.60. (+)ESI-HRMS (m/z (%)): 350.25906 ([M+H]$^+$, 100); calculated 350.25907 (error in ppm: -0.05). HPLC purity (λ=330 nm): method A: RT 7.531, area 95.70%; method B: RT 8.193, area 95.60%.

***N*-[2-(1-Adamantyl)ethyl]-*N*'-quinolin-4-ylpropane-1,3-diamine (67).**

Compound **67** was prepared from **AQ7** (185 mg, 0.92 mmol) and adamantyl-1-acetaldehyde (136mg, 0.77 mmol) using AcOH (63 μL, 1.10 mmol) and $NaBH_4$ (209 mg, 5.52 mmol) by procedure E and was obtained after flash chromatography (SiO_2, gradient: Hex/EtOAc = 4/6→1/9) as a colorless foam (195 mg, 70%). IR (ATR): 3250m, 3072w, 2902s, 2844m, 1612w, 1583s, 1544m, 1446m, 1399w, 1371w, 1339w, 1284w, 1242w, 1131w, 808w, 762w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.52 (d, 1H, *J* = 5.3 Hz, H-C(2)), 7.95 (dd, 1H, *J* = 0.8 Hz, *J* = 8.5 Hz, H-C(8)), 7.82 (dd, 1H, *J* = 0.9 Hz, *J* = 8.4 Hz, H-C(5)), 7.74 (bs, 1H, -N*H*), 7.65-7.58 (m, 1H, H-C(7)), 7.42-7.25 (m, 1H, H-C(6)), 6.32 (d, 1H, *J* = 5.2 Hz, H-C(3)), 3.45-3.35 (m, 2H, ArNHCH_2-), 2.95-2.85 (m, 2H, -CH_2NHCH_2Ad), 2.75-2.60 (m, 2H, -CH_2CH_2Ad), 2.00-1.85 (m, 5H, ArNHCH_2CH_2-, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.45-1.35 (-CH_2Ad). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.99; 150.61; 148.26; 129.40; 128.80; 124.02; 120.61; 119.13; 97.88; 49.61; 44.94; 44.42; 43.84; 42.65; 37.06; 31.83; 28.59; 27.47. HPLC purity (λ=330 nm): method A: RT 7.661, area 96.48%; method B: RT 7.311, area 95.26%

N-(1-Adamantylmethyl)-N-methyl-N'-quinolin-4-ylpropane-1,3-diamine (68).

Compound **68** was prepared from aminoquinoline **66** (1.2 g, 3.43 mmol) and 36% formaldehyde (529 μL, 6.87 mmol) using $ZnCl_2$ (936 mg, 6.87 mmol) and $NaHB_3CN$ (862 mg, 13.72 mmol) by procedure D and was obtained after multiple chromatography: dry-flash (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) and flash chromatography (Biotage SP1 NH column, gradient: Hex/EtOAc = 3/7→1/9) as a white foam. Yield: 900 mg (72%). IR (ATR): 3291m, 3078w, 2901s, 2846s, 1659w, 1619w, 1584s, 1544m, 1454m, 1374w, 1342w, 1229w, 1176w, 1132w, 1104w, 1042m, 984w, 887w, 809w, 764m, 738w, 598w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.55

(d, 1H, *J* = 5.3 Hz, H-C(2)), 7.98 (d, 1H, *J* = 8.5 Hz, H-C(8)), 7.87 (d, 1H, *J* = 7.8 Hz, H-C(5)), 7.65-7.55 (m, 1H, H-C(7)), 7.45-7.33 (m, 1H, H-C(6)), 6.98 (bs, 1H, -N*H*), 6.38 (d, 1H, *J* = 5.3 Hz, H-C(3)), 3.47-3.35 (m, 2H, ArNHCH_2-), 2.68-2.55 (m, 2H, -CH_2NHCH_2Ad), 2.39 (s, 3H, -NCH_3), 2.08 (s, 2H, -CH_2Ad), 1.95-1.83 (m, 5H, ArNHCH$_2$$CH_2$-, -Ad) 1.70-1.40 (m, 12H, -Ad). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.86; 150.50; 148.15; 129.42; 128.90; 124.13; 120.36; 119.04; 98.29; 72.53; 60.76; 46.11; 43.86; 41.47; 36.95; 34.77; 28.35; 25.82. (+)ESI-HRMS (m/z (%)): 364.27455 ($[M+H]^+$, 100); calculated 364.27472 (error in ppm: -0.48). Anal. ($C_{24}H_{33}N_3$ × 1/2H_2O) Calculated: C, 77.37; H, 9.20; N, 11.28 Found: C, 77.49; H, 9.11; N, 11.36. HPLC purity (λ=330 nm): method A: RT 7.800, area 99.24%; method B: RT 9.268, area 98.89%.

_N_-[2-(1-Adamantyl)ethyl]-_N_-methyl-_N'_-quinolin-4-ylpropane-1,3-diamine (69).

Compound **69** was prepared from aminoquinoline **67** (220 mg, 0.60 mmol) and 36% formaldehyde (93 μL, 1.20 mmol) using $ZnCl_2$ (165 mg, 1.20 mmol) and $NaHB_3CN$ (151 mg, 2.4 mmol) by procedure D and was obtained after dry-flash chromatography (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) as a white solid (167 mg, 73%). IR (ATR): 3236m, 3070w, 2901s, 2844s, 1582s, 1544m, 1445m, 1397w, 1372w, 1339w, 1235w, 1133w, 1046w, 857w, 808w, 764w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.53 (d, 1H, *J* = 5.3 Hz, H-C(2)), 7.98 (d, 1H, *J* = 8.4 Hz, H-C(8)), 7.88 (bs, 1H, -N*H*), 7.75 (d, 1H, *J* = 8.2 Hz, H-C(5)), 7.67-7.55 (m, 1H, H-C(7)), 7.45-7.35 (m, 1H, H-C(6)), 6.33 (d, 1H, *J* = 5.3 Hz, H-C(3)), 3.47-3.33 (m, 2H, ArNHCH_2-), 2.70-2.65 (m, 2H, -CH_2NHCH_2CH_2Ad), 2.53-2.40 (m, 2H, -CH_2CH_2Ad), 2.35 (s, 3H, -NCH_3), 2.00-1.85 (m, 5H, ArNHCH$_2$$CH_2$-, -Ad) 1.75-1.65 (m, 6H, -Ad) 1.47 (m, 6H, -Ad), 1.40-1.30 (m, 2H, -CH_2Ad). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.85; 150.69; 147.94; 129.91; 128.92; 124.16; 120.54; 119.10; 97.91; 57.83; 52.29; 44.18; 42.46; 41.98; 41.36; 37.06; 31.74;

28.56; 24.35. (+)ESI-HRMS (m/z (%)): 378.29024 ([M+H]$^+$, 100); calculated 378.29037 (error in ppm: -0.36). Anal. ($C_{25}H_{35}N_3 \times 1/2H_2O$) Calculated: C, 77.67; H, 9.39; N, 10.87. Found: C, 77.22; H, 9.44; N, 11.03. HPLC purity (λ=330 nm): method A: RT 7.931, area 98.67%; method B: RT 9.534, area 96.77%.

N^2-(1-Adamantylmethyl)-N^1-quinolin-4-ylpropane-1,2-diamine (77).

Compound **77** was prepared from amine linker **70**[4] (110 mg, 0.49 mmol) and 4-chloroquinoline (81 mg, 0.49 mmol) in phenol (692 mg, 7.35 mmol). The mixture was heated at 120-130 °C for 24 h, cooled to r.t. and taken up in CH_2Cl_2. The organic layer was washed several times with NaOH and brine. The organic layer was dried over anh. Na_2SO_4 and solvent was removed under reduced pressure. The final product was obtained after multiple chromatography: dry-flash (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 9/1) and flash chromatography (Biotage SP1 RP column, eluent: MeOH/H_2O = 9/1) as a yellow solid (102 mg, 60%). IR (ATR): 3364m, 3303w, 2897s, 2843s, 1589s, 1534s, 1483w, 1453m, 1395w, 1366w, 1300w, 1246w, 1161w, 803w, 757w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.55 (d, 1H, *J* = 5.0 Hz, H-C(2)), 7.99 (d, 1H, *J* = 8.0 Hz, H-C(8)), 7.81 (d, 1H, *J* = 8.0 Hz, H-C(5)), 7.66-7.61 (m, 1H, H-C(7)), 7.46-7.40 (m, 1H, H-C(6)), 6.38 (d, 1H, *J* = 5.5 Hz, H-C(3)), 6.26 (bs, 1H, -N*H*), 3.38-3.31 (m, 1H, ArNHCH$_2$*CH*(CH_3)-), 3.07-3.01 (m, 1H, -(*CH*$_2$CH$_3$)CHNHCH$_2$Ad), 3.00-2.93 (m, 1H, -(*CH*$_2$CH$_3$)CHNHCH$_2$Ad), 2.44 (ABq, 1H, H_A, *J* = 11.4 Hz, -C*H*$_2$Ad), 2.17 (ABq, 1H, H_B, *J* = 11.4 Hz, -C*H*$_2$Ad), 2.00 (s, 3H, -Ad), 1.80-1.49 (m, 12H, -Ad), 1.24 (d, 3H, *J* = 6.2 Hz, -C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.98; 150.12; 148.28; 129.70; 128.93; 124.42; 119.66; 119.04; 98.87; 59.17; 52.29; 46.91; 40.93; 37.22; 33.47; 28.44; 19.53. (+)ESI-HRMS (m/z (%)): 367.25596 ([M+H]$^+$, 100); calculated 367.28562 (error in ppm: +1.28). Anal. ($C_{23}H_{31}N_3 \times 2/3$

H_2O) Calcd.: C, 76,41; H, 9,01; N, 11,62; Found: C, 76,33; H, 8,56; N, 11,34. HPLC purity (λ= 330 nm) method A: RT 7.904 min., area 95.56%; method B: RT 9.308 min., area 95.43%.

N^3-(1-Adamantylmethyl)-N^1-quinolin-4-ylbutane-1,3-diamine (78).

Compound **78** was prepared from amine linker **71**[4] (370 mg, 1.54 mmol) and 4-chloroquinoline (233 mg, 1.42 mmol) using $Pd(OAc)_2$ (12.8 mg, 0.057 mmol), SPhos (51.4 mg, 0.11 mmol) and K_3PO_4 (750 mg, 3.55 mmol) by procedure H and was obtained after dry-flash chromatography (SiO_2, gradient: EtOAc/[MeOH/(NH_3 aq.) = 9/1] = 9/1→7/3). Yield: 473 mg (91%). IR (ATR): 3263s, 3067w, 2900s, 2845m, 1711w, 1582s, 1541m, 1450m, 1373w, 1340w, 1251w, 1224w, 1134w, 808w, 763m, 735w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.53 (d, 1H, *J* = 5.3 Hz, H-C(2)), 7.96 (d, 1H, *J* = 8.5 Hz, H-C(8)), 7.89 (d, 1H, *J* = 8.25 Hz, H-C(5)), 7.60 (t, 1H, *J* = 7.6 Hz, H-C(7)), 7.34 (t, 1H, *J* = 7.6 Hz, H-C(6)), 7.22 (bs, 1H, -N*H*), 6.36 (d, 1H, *J* = 5.5 Hz, H-C(3)), 3.55-3.30 (m, 2H, ArNHCH_2-), 2.93-2.80 (m, 1H, ArNHCH$_2$CH$_2$*CH*(CH$_3$)-), 2.40 (ABq, 1H, H_A, *J* = 11.4 Hz, -CH_2Ad), 2.30 (ABq, 1H, H_B, *J* = 11.4 Hz, -CH_2Ad), 1.99 (s, 3H, -Ad), 1.80-1.68 (m, 6H, -Ad), 1.67-1.50 (m, 8H, ArNHCH$_2$CH_2-, -Ad), 1.17 (d, 3H, *J* = 6.6 Hz, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 151.01; 150.45; 148.25; 129.48; 128.83; 123.97; 120.68; 119.06; 98.24; 60.89; 54.28; 41.52; 41.11; 37.15; 33.41; 33.26; 28.42; 19.82. (+)ESI-HRMS (m/z (%)): 364.27468 ([M+H]$^+$, 100); calculated 364.27472 (error in ppm: -0.12). Anal. ($C_{24}H_{33}N_3 \times H_2O$) Calcd: C, 75.55; H, 9.25; N, 11.01. Found C, 75.20; H, 8.74; N, 10.86. HPLC purity (λ= 330 nm) method A: RT 7.898 min. area 97.80%; method B: RT 9.348 min., area 97.14%.

N^4-(1-adamantylmethyl)-N^1-quinolin-4-ylpentane-1,4-diamine (79).

Compound **79** was prepared from amine linker **72**[4] (389 mg, 1.54 mmol) and 4-chloroquinoline (231 mg, 1.41 mmol) using $Pd(OAc)_2$ (12.7 mg, 0.056 mmol), SPhos (46.3 mg, 0.11 mmol) and

K_3PO_4 (749 mg, 3.52 mmol) by procedure H and was obtained after dry-flash chromatography (SiO_2, gradient: CH_2Cl_2/[MeOH/(NH_3 aq.) = 9/1] = 9/1→7/3). Yield: 235 mg (44%). IR (ATR): 3324m, 3219m, 3057m, 2903s, 2847m, 1582s, 1460m, 1435s, 1396m, 1339w, 1261w, 1220m, 1175m, 1123m, 1072w, 805w, 764m, 696m, 646w, 545m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.54 (d, 1H, *J* = 5.5 Hz, H-C(2)), 7.98 (d, 1H, *J* = 7.8 Hz, H-C(8)), 7.79 (d, 1H, *J* = 7.8 Hz, H-C(5)), 7.60 (t, 1H, *J* = 7.0 Hz, H-C(7)), 7.45-7.35 (m, 1H, H-C(6)), 6.41 (d, 1H, *J* = 5.5 Hz, H-C(3)), 5.54 (bs, 1H, -N*H*), 3.40-3.25 (m, 2H, ArNHCH_2-), 2.75-2.60 (m, 1H, -(CH_3)C*H*NHCH_2Ad), 2.29 (ABq, 1H, H_A, *J* = 11.3 Hz, -CH_2Ad), 2.20 (ABq, 1H, H_B, *J* = 11.3 Hz, -CH_2Ad), 1.96 (s, 3H, -Ad), 1.89-1.76 (m, 2H, ArNHCH$_2$CH_2-), 1.74-1.59 (m, 6H, -Ad), 1.58-1.45 (m, 8H, ArNHCH$_2$CH$_2$CH_2-, -Ad), 1.08 (d, 3H, *J* = 6.4 Hz, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.73; 149.98; 148.08; 129.58; 129.01; 124.44; 119.67; 118.74; 98.59; 59.34; 53.11; 43.40; 40.95; 37.17; 34.08; 33.28; 28.42; 24.95; 20.48. (+)ESI-HRMS (m/z (%)): 378.28996 ([M+H]$^+$, 100); calculated 378.29037 (error in ppm: -1.08). Anal. ($C_{25}H_{35}N_3$x3/2H_2O) Calcd: C, 77.08; H, 9.40; N, 10.79. Found: C, 77.10; H, 8.95; N, 10.87. HPLC purity (λ=330 nm): method A: RT 7.560, area 95.16%; method B: RT 8.832, area 95.67%.

N^2-[2-(1-Adamantyl)ethyl]-N^1-quinolin-4-ylpropane-1,2-diamine (80).

Amine linker **73**[4] (260 mg, 1.10 mmol) and 4-chloroquinoline (180 mg, 1.10 mmol) were mixed in NMP (1.5 ml) in MW cuvette under argon. The reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*, 1 h, 180 °C. Compound **80** was obtained after multiple chromatography: dry-flash (SiO_2, eluent: EtOAc/MeOH/(NH_3 aq.) 90/9/1 = 95/5) and flash chromatography (Biotage SP1-NH column, eluent: Hex/EtOAc = 6/4; RP column eluent: MeOH/H_2O = 8/2). Yield: 253 mg (63%); mp = 112-113 °C. IR (ATR): 3251 m, 3059 m, 2962

m , 2902 s, 2844 s, 1708 w, 1618 w, 1578 s, 1543 s, 1451 s, 1396 s, 1374 m, 1343 m, 1280 w, 1258 w, 1159 w, 1130 w, 1108 w, 909 w, 807 w, 763 m, 733 w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.53 (d, 1H, *J* = 5.3 Hz, H-C(2)), 7.97 (d, 1H, *J* = 8.0 Hz, H-C(8)), 7.81-7.76 (m, 1H, H-C(5)), 7.65-7.59 (m, 1H, H-C(7)), 7.46-7.37 (m, 1H, H-C(6)), 6.45 (d, 1H, *J* = 5.4 Hz, H-C(3)), 5.69 (bs, 1H, -N*H*), 3.87-3.73 (m, 1H, ArNHC*H*(CH_3)-), 2.91-2.81 (m, 2H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.70-2.61 (m, 2H, -C*H*$_2$CH$_2$Ad), 1.93 (m, 3H, -Ad), 1.73-1.57 (m, 7H, -N*H* -Ad), 1.55-1.44 (m, 6H, -Ad), 1.36-1.24 (m, 2H, -C*H*$_2$Ad), 1.18 (d, 3H, *J* = 6.2 Hz, -C*H*$_3$). ^{13}C-NMR (125 MHz. $CDCl_3$): 150.94; 149.21; 148.52; 129.81; 128.93; 124.45; 119.59;119.12; 99.13; 54.69; 47.52; 44.79; 44.53; 42.69; 37.10; 31.91; 28.63; 18.30. (+)ESI-HRMS (m/z (%)): 364.27554 ($[M+H]^+$, 100); calculated 364.27472 (error in ppm: -0.59). Anal. ($C_{24}H_{33}N_3 \times H_2O$) Calculated: C, 75.55; H, 9.25; N, 11.01. Found: C, 75.91; H, 8.82; N, 11.08. HPLC purity (λ= 330 nm) method A: RT 7.840 min. area 96.96%; method B: RT 9.480 min., area 96.39%.

N^3-[2-(1-Adamantyl)ethyl]-N^1-quinolin-4-ylbutane-1,3-diamine (81).

Compound **81** was prepared from amine linker **74**[4] (22.6 mg, 0.09 mmol) and 4-chloroquinoline (13.4 mg, 0.08 mmol) using $Pd(OAc)_2$ (0.7 mg, 0.003 mmol), SPhos (2.7 mg, 0.007 mmol) and K_3PO_4 (43.5 mg, 0.20 mmol) by procedure H and was obtained after multiple chromatography: dry-flash (SiO_2, gradient: pure EtOAc; gradient: CH_2Cl_2/[MeOH/(NH_3 aq.) = 9/1] =9/1→7/3) and flash chromatography (Biotage SP1-NH column, eluent: Hex/EtOAc = 7/3; RP column eluent: MeOH/H_2O = 9/1). Yield: 6.5 mg (21%). IR (ATR): 3250m, 3065w, 2902s, 2845s, 2675w, 1664w, 1618w, 1584s, 1543m, 1449m, 1372w, 1341w, 1248w, 1134w, 808w, 763w, 734w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.52 (d, 1H, *J* = 5.3 Hz, H-C(2)), 8.08 (bs, 1H, -N*H*), 7.95 (d, 1H, *J* = 8.5 Hz, H-C(8)), 7.82 (dd, 1H, *J* = 0.9 Hz, *J* = 8.4 Hz, H-C(5)), 7.65-7.57 (m,

1H, H-C(7)), 7.40-7.35 (m, 1H, H-C(6)), 6.31 (d, 1H, *J* = 5.2 Hz, H-C(3)), 3.50-3.40 (m, 1H, ArNHC*H*$_2$-), 3.40-3.30 (m, 1H, ArNHC*H*$_2$-), 3.05-2.90 (m, 1H, ArNHCH$_2$CH$_2$(CH$_3$)*CH*-), 2.85-2.70 (m, 1H, -NHC*H*$_2$CH$_2$Ad), 2.70-2.55 (m, 1H, -NHC*H*$_2$CH$_2$Ad), 1.94 (s, 3H, -Ad), 1.80-1.55 (m, 7H, ArNHCH$_2$C*H*$_2$-, -Ad), 1.55-1.40 (m, 7H, ArNHCH$_2$C*H*$_2$-, -Ad), 1.40-1.25 (m, 1H, -C*H*$_2$Ad), 1.20 (d, 3H, *J* = 6.6 Hz, -C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$): 151.18; 150.60; 148.43; 129.59; 128.76; 123.92; 120.80; 119.27; 97.86; 45.51; 42.83; 42.41; 41.90; 41.67 37.10; 33.30; 31.93; 28.63; 20.23. (+)ESI-HRMS (m/z (%)): 378.29011 ([M+H]$^+$, 100); calculated 378.29037 (error in ppm: -0.70). Anal. ($C_{25}H_{33}N_3 \times 1/2H_2O$) Calculated: C, 77.67; H, 9.39; N, 10.87. Found C, 77.62; H, 9.38; N, 10.82. HPLC purity (λ= 330 nm) method A: RT 7.919 min. area 99.19%; method B: RT 8.491 min., area 98.62%.

N^4-[2-(1-Adamantyl)ethyl]-N^1-quinolin-4-ylpentane-1,4-diamine (82).

Compound **82** was prepared from amine linker **75** (410 mg, 1.55 mmol) and 4-chloroquinoline (231 mg, 1.41 mmol) using $Pd(OAc)_2$ (12.7 mg, 0.056 mmol), SPhos (46.3 mg, 0.11 mmol) and K_3PO_4 (749 mg, 3.52 mmol) by procedure H and was obtained after multiple chromatography: dry-flash (SiO_2, eluent: pure EtOAc; gradient: CH_2Cl_2/[MeOH/(NH_3 aq.) = 9/1] = 9/1→7/3) and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc =1/9). Yield: 293 mg (53%). IR (ATR): 3245w, 3067w, 2902s, 2845m, 1616w, 1582s, 1543m, 1448m, 1373w, 1341w, 1130w, 765w, 638w, 596w, 524w, 495w, 410w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.54 (d, 1H, *J* = 5.5 Hz, H-C(2)), 7.98 (d, 1H, *J* = 8.3 Hz, H-C(8)), 7.77 (d, 1H, *J* = 8.3 Hz, H-C(5)), 7.63 (t, 1H, *J* = 7.0 Hz, H-C(7)), 7.42 (t, 1H, *J* = 7.6 Hz, H-C(6)), 6.41 (d, 1H, *J* = 5.5 Hz, H-C(3)), 5.65 (bs, 1H, -N*H*), 3.40-3.27 (m, 2H, ArNHC*H*$_2$-), 2.78-2.73 (m, 1H, -C*H*NHCH$_2$CH$_2$Ad), 2.72-2.64 (m, 1H, -C*H*$_2$CH$_2$Ad), 2.63-2.53 (m, 1H, -C*H*$_2$CH$_2$Ad), 2.05-1.90 (m, 3H, -Ad), 1.89-1.75 (m,

2H, ArNHCH$_2$C*H*$_2$-), 1.73-1.60 (m, 8H, ArNHCH$_2$CH$_2$C*H*$_2$-, -Ad), 1.52-1.45 (m, 6H, -Ad), 1.32-1.24 (m, 2H, -C*H*$_2$Ad), 1.11 (d, 3H, *J* = 6.2 Hz, -C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.93; 149.91; 148.32; 129.72; 128.91; 124.39; 119.73; 118.83; 98.58; 52.91; 44.64; 43.41; 42.59; 41.29; 37.07; 34.43; 31.85; 28.61; 24.96; 20.12. (+)ESI-HRMS (m/z (%)): 392.30476 ([M+H]$^+$, 100); calculated 392.30602 (error in ppm: -0.88). Anal. ($C_{26}H_{37}N_3 \times 2H_2O$) Calcd: C, 73.03; H, 9.56; N, 9.83. Found: C, 73.34; H, 9.30; N, 9.81. HPLC purity (λ=330 nm): method A: RT 7.675, area 97.58%; method B: RT 9.162, area 96.45%.

N^3-(1-Adamantylmethyl)-N^3-methyl-N^1-quinolin-4-ylbutane-1,3-diamine (84).

Compound **84** was prepared from aminoquinoline **78** (260 mg, 0.72 mmol) and 36% formaldehyde (110 μL, 1.43 mmol) using $ZnCl_2$ (195 mg, 1.43 mmol) and $NaBH_3CN$ (180 mg, 2.86 mmol) by procedure D and was obtained after multiple chromatography: dry-flash (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) and flash chromatography (Biotage SP1 NH column, gradient: Hex/EtOAc = 3/7→1/9). Yield: 240 mg (89%). IR (ATR): 3355m, 3055w, 2957m, 2902s, 2845s, 2792w, 1616w, 1578s, 1538m, 1494w, 1455m, 1400w, 1373m, 1346m, 1289w, 1258w, 1233w, 1179w, 1152w, 1125w, 1104w, 1074w, 1046w, 1014w, 984w, 950w, 889w, 871w, 802m, 764m, 470w, 448w, 406w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.55 (d, 1H, *J* = 5.2 Hz, H-C(2)), 7.96 (d, 1H, *J* = 7.8 Hz, H-C(8)), 7.83 (d, 1H, *J* = 7.6 Hz, H-C(5)), 7.65-7.55 (m, 1H, H-C(7)), 7.45-7.35 (m, 1H, H-C(6)), 6.63-6.50 (bs, 1H, -N*H*), 6.40 (d, 1H, *J* = 5.2 Hz, H-C(3)), 3.55-3.45 (m, 1H, ArNHC*H*$_2$-), 3.44-3.30 (m, 1H, ArNHC*H*$_2$-), 2.85-2.75 (m, 1H, ArNHCH$_2$CH$_2$(CH$_3$)*CH*-), 2.33 (s, 3H, -N*CH*$_3$), 2.15-2.05 (m, 2H, -C*H*$_2$Ad), 2.00-1.88 (m, 1H, ArNHCH$_2$*CH*$_2$-), 1.81 (s, 3H, -Ad), 1.72-1.62 (m, 1H, ArNHCH$_2$*CH*$_2$-), 1.60-1.35 (m, 12H, -Ad), 1.00 (d, 3H, *J* = 6.7 Hz, -C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.91; 150.37; 148.24;

129.53; 128.90; 124.16; 120.20; 119.13; 98.57; 69.04; 61.23; 42.94; 41.30; 38.77; 36.97; 35.07; 32.57; 28.35. (+)ESI-HRMS (m/z (%)): 378.28906 ($[M+H]^+$, 100), calculated 378.29037 (error in ppm: -0.12). Anal. ($C_{25}H_{35}N_3 \times 2/3H_2O$) Calculated: C, 77.08; H, 9.40; N, 10.79. Found C, 76.98; H, 9.06; N, 10.78. HPLC purity (λ= 330 nm) method A: RT 7.896 min. area 98.74%; method B: RT 9.244 min., area 97.79%.

N^1-(1-Adamantylmethyl)-N^1-methyl-N^3-quinolin-4-ylbutane-1,3-diamine (85).

Compound **85** was prepared from aminoquinoline N^1-(1-adamantylmethyl)-N^3-quinolin-4-ylbutane-1,3-diamine[4] (169 mg, 0.46 mmol) and 36% formaldehyde (72 μL, 0.93 mmol) using $ZnCl_2$ (126 mg, 0.93 mmol) and $NaBH_3CN$ (117 mg, 1.85 mmol) by procedure D and was obtained after multiple chromatography: dry-flash (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 satd) = 95/5) and flash chromatography (Biotage SP1 NH column, gradient: Hex/EtOAc = 3/7→1/9 and RP column, gradient: MeOH/H_2O = 8/2→9/1) as a white solid (123 mg, 70%). IR (ATR): 3288m, 3073w, 2901s, 2845s, 1618w, 1581s, 1541m, 1451m, 1396w, 1375w, 1342w, 1262w, 1184w, 1150w, 1045m, 983w, 945w, 872w, 809w, 763m, 737w, 603w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.52 (d, 1H, *J* = 5.2 Hz, H-C(2)), 7.96 (d, 1H, *J* = 8.4 Hz, H-C(8)), 7.86 (d, 1H, *J* = 8.4 Hz, H-C(5)), 7.65-7.58 (m, 1H, H-C(7)), 7.43-7.35 (m, 1H, H-C(6)), 6.79 (bs, 1H, -N*H*), 6.42 (d, 1H, *J* = 5.5 Hz, H-C(3)), 3.93-3.80 (m, 1H, ArNHC*H*(CH_3)-), 2.72-2.62 (m, 1H, ArNHCH(CH_3)CH_2*CH_2*-), 2.52-2.42 (m, 1H, ArNHCH(CH_3)CH_2*CH_2*-), 2.33 (s, 3H, -N*CH_3*), 2.08 (ABq, 1H, H_A, *J* = 14.0 Hz, -*CH_2*Ad), 2.03 (ABq, 1H, H_B, *J* = 14.0 Hz, -*CH_2*Ad), 1.95-1.67 (m, 4H, ArNHCH(CH_3)*CH_2*-, -Ad), 1.95-1.85 (m, 1H, ArNHCH(CH_3)C*H_2*-), 1.66-1.50 (m, 12H, -Ad), 1.33 (d, 3H, *J* = 6.4 Hz, -C*H_3*). ^{13}C-NMR (125 MHz, $CDCl_3$):150.06; 149.86; 129.23; 128.98; 124.27; 120.42; 119.03; 98.49; 72.33; 58.07; 48.45; 46.42; 41.56; 36.97; 34.76; 33.44;

28.41; 19.62. (+)ESI-HRMS (m/z (%)): 378.29037 ([M+H]$^+$, 100); calculated 378.29037 (error in ppm: -0.02). Anal. ($C_{25}H_{35}N_3 \times 1/2H_2O$) Calcd: C, 77.67; H, 9.39; N, 10.87. Found: C, 77.20; H, 9.51; N, 10.92. HPLC purity (λ= 330 nm) method A: RT 7.851 min., area 97.80%; method B: RT 9.284 min., area 95.71%.

Benzyl [1-methyl-4-(quinolin-4-ylamino)butyl]carbamate (107).

Compound **107** was prepared by procedure A using 4-chloroquinoline (195 mg, 1.18 mmol) and benzyl (4-amino-1-methylbutyl)carabamate[4] (335 mg, 1.42 mmol). The product was purified using column chromatography (flash, Biotage SP, NH column, 40+M, eluent hexane, hexane/EtOAc gradient 9/1 → EtOAc, EtOAc/MeOH gradient 9/1 → MeOH). Final product **107** was obtained as a yellow oil (320 mg, 72%). IR (ATR): 3344m, 3063w, 3031w, 2964w, 2934w, 2866w, 1696s, 1616w, 1582s, 1539s, 1454m, 1395w, 1374w, 1343m, 1257m, 1081m, 1029w, 808w, 764m, 697w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.54 (d, 1H, *J* = 5.2, H-C(2)), 8.00-7.95 (m, 1H, H-C(8)), 7.84-7.78 (m, 1H, H-C(5)), 7.65-7.59 (m, 1H, H-C(7)), 7.44-7.39 (m, 1H, H-C(6)), 7.37-7.29 (m, 5H, -*Ph*), 6.43-6.36 (m, 1H, H-C(3)), 5.30 (bs, 1H, NH), 5.11 (s, 2H, -C*H*$_2$Ph), 4.73-4.64 (bs, 1H, NH), 3.89-3.80 (m, 1H, CbzNHC*H*(CH_3)), 3.37-3.30 (m, 2H, CbzNHCH(CH_3)$CH_2CH_2CH_2$-), 1.85-1.75 (m, 2H, CbzNHCH(CH_3)C*H*$_2$-), 1.65-1.56 (m, 2H, CbzNHCH(CH_3)CH_2C*H*$_2$-), 1.18 (d, 3H, *J* = 6.5, C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 156.02, 151.00, 149.70, 148.40, 136.45, 129.84, 128.94, 128.53, 128.16, 128.09, 124.54, 119.52, 118.77, 98.70, 66.68, 46.76, 43.07, 35.12, 25.13, 21.37. HRMS: *m/z* 364.20267 corresponds to molecular formula $C_{22}H_{25}N_3O_2H^+$ (error in ppm 1.98).

N^1-(quinolin-4-yl)pentane-1,4-diamine (108).

The Cbz-protected amine **107** (305 mg, 0.839 mmol) was hydrogenated using palladium on carbon 10% (30 mg, 10% mw) as catalyst under 30 psi of hydrogen in MeOH (150 mL). After the mixture was stirred at r.t. for 8 h, the catalyst was removed by filtration and the solvent was evaporated under reduced pressure. Final product **108** was obtained as a yellow oil (192 mg, 99.8%). IR (ATR): 3353m, 3077w, 2958w, 1584s, 1545m, 1441w, 1376w, 1343m, 1258w, 1228w, 1127w, 1037w, 884w, 810w, 766w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.34 (d, 1H, *J* = 5.5, H-C(2)), 8.12-8.07 (m, 1H, H-C(8)), 7.83-7.78 (m, 1H, H-C(5)), 7.65-7.60 (m, 1H, H-C(7)), 7.45-7.41 (m, 1H, H-C(6)), 6.50 (d, 1H, *J* = 5.8, H-C(3)), 3.38 (t, 2H, *J* = 7.1, ArNHCH_2-), 3.03-2.95 (m, 1H, $NH_2CH(CH_3)$-), 1.85-1.74 (m, 2H, $ArNHCH_2CH_2$-), 1.61-1.48 (m, 2H, $ArNHCH_2CH_2CH_2$-), 1.14 (d, 3H, *J* = 6.4, $NH_2CH(CH_3)$-). ^{13}C NMR (125 MHz, CD_3OD, δ): 152.67, 151.14, 148.82, 130.49, 128.72, 125.59, 122.21, 120.28, 99.14, 47.92, 43.87, 36.88, 26.12, 22.28. HRMS: *m/z* 230.16532 corresponds to molecular formula $C_{14}H_{19}N_3H^+$ (error in ppm 0.64); *m/z* 115.58652 corresponds to molecular formula $C_{14}H_{19}N_3H_2^{2+}$ (error in ppm 2.52).

Benzyl {4-[(7-chloroquinolin-4-yl)amino]-1-methylbutyl}carbamate (109).

Compound **109** was prepared by procedure A using 4,7-dichloroquinoline (400.0 mg, 2.019 mmol) and benzyl (4-amino-1-methylbutyl)carbamate[4] (525 mg, 2.22 mmol). The product was purified using column chromatography (flash, Biotage SP, NH column, 40+M, eluent hexane, hexane/EtOAc gradient 9/1 → 1/9, EtOAc/MeOH gradient 9/1 →1/9). Final product **109** was obtained as yellow oil (477 mg, 59%). IR (ATR): 3314m, 3033w, 2938m, 1698s, 1610w, 1581s, 1537m, 1452m, 1370w, 1333w, 1256m, 1139w, 1080w, 1026w, 901w, 878w, 851w, 808w, 738w, 698w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.30 (d, 1H, *J* = 5.5, H-C(2)), 8.10-8.04 (m,

1H, H-C(5)), 7.78-7.75 (m, 1H, H-C(8)), 7.38-7.34 (m, 1H, H-C(6)), 7.34-7.22 (m, 5H, -Ph), 6.50-6.44 (m, 1H, H-C(3)), 5.10-5.01 (s, 2H, -CH_2Ph), 3.76-3.66 (m, 1H, CbzNHCH(CH_3)-), 3.38-3.32 (m, 2H, CbzNHCH(CH_3)$CH_2CH_2CH_2$-), 1.81-1.71 (m, 2H, CbzNHCH(CH_3)CH_2-), 1.63-1.54 (m, 2H, CbzNHCH(CH_3)CH_2CH_2-), 1.15 (d, 3H, J = 6.6, CbzNHCH(CH_3)-). ^{13}C NMR (125 MHz, CD_3OD, δ): 158.44, 152.69, 152.36, 149.64, 138.48, 136.26, 129.42, 128.90, 128.69, 127.54, 125.89, 124.32, 118.75, 99.60, 67.23, 47.92, 43.78, 35.38, 26.04, 21.51. HRMS: *m/z* 398.16435 corresponds to molecular formula $C_{22}H_{24}ClN_3O_2H^+$ (error in ppm 3.43).

N^1-(7-chloroquinolin-4-yl)pentane-1,4-diamine (110).

According to the procedure described in literature,[14] Cbz-protected amine **109** (120 mg, 0.30 mmol) was dissolved in TFA (2 mL) and the mixture was stirring under the reflux for 2 h. TFA was removed under the reduced pressure. Crude product was dissolved in CH_2Cl_2/2.5 M NaOH, organic layer washed twice with 2.5 M NaOH and dried over anh. Na_2SO_4. Final product was obtained as white powder (77 mg, 97%). M.p. = 109 – 111 ºC. IR (ATR): 3294m, 3104w, 3010w, 2959w, 2931m, 2857m, 1610w, 1577s, 1542m, 1473w, 1452m, 1369m, 1331w, 1283w, 1248w, 1197w, 1149w, 1131w, 1085w, 1025w, 953w, 919w, 901m, 850w, 824w, 800m, 767w cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD, δ): 8.32 (d, 1H, J = 5.5, H-C(2)), 8.07 (d, 1H, J = 9.2, H-C(5)), 7.76-7.74 (m, 1H, H-C(8)), 7.38-7.34 (m, 1H, H-C(6)), 6.48 (d, 1H, J = 5.7, H-C(3)), 3.34 (t, 2H, J = 7.2, ArNHCH_2-), 2.89 (sext, 1H, J = 6.4, NH_2CH(CH_3)-), 1.83-1.69 (m, 2H, $ArNHCH_2$CH_2-), 1.54-1.42 (m, 2H, $ArNHCH_2CH_2$CH_2-), 1.09 (d, 3H, J = 6.4, NH_2CH(CH_3)-). ^{13}C NMR (125 MHz, CD_3OD, δ): 152.71, 152.44, 149.71, 136.26, 127.60, 125.90, 124.30, 118.77, 99.61, 47.66, 44.06, 37.79, 26.23, 23.26. HRMS: *m/z* 264.12514 corresponds to molecular formula $C_{14}H_{18}ClN_3H^+$ (error in ppm -4.02).

3-(thiophen-2-yl)benzaldehyde (111).

Compound **111** was prepared by procedure G using $Pd(OAc)_2$ (36.4 mg, 0.162 mmol), PPh_3 (170 mg, 0.648 mmol), 2-thienylboronic acid (207.4 mg, 1.621 mmol), aq. 2M Na_2CO_3 (3.1 mL), 3-bromobenzaldehyde (189 mg, 1.62 mmol) and DME (16 mL). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, hexane/EtOAc gradient 9/1 → 7/3 and flash Biotage SP1, RP column, eluent MeOH/H_2O gradient 7/3 → MeOH). Final product **111** was obtained as a white foam (162 mg, 53 %). IR (ATR): 3370w, 3105w, 3072w, 2924w, 2834w, 2727w, 1699s, 1599w, 1581w, 1532w, 1480w, 1442w, 1387w, 1350w, 1312w, 1270m, 1220w, 1165m, 1119w, 1084w, 1055w, 1000w, 896w, 842w, 793m, 703m, 651w, 544w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 10.06 (s, 1H, H-CO), 8.10 – 8.09 (m, 1H, H-C(2)), 7.87 – 7.85 (m, 1H, H-C(6)), 7.79 – 7.77 (m, 1H, H-C(4)), 7.55 (t, 1H, J = 7.7, H-C(5)), 7.40 (dd, 1H, J_1 = 3.6, J_2 = 1.1, H-C(3')), 7.34 (dd, 1H, J_1 = 5.2, J_2 = 1.1, H-C(5')), 7.12 (dd, 1H, J_1 = 5.0, J_2 = 3.7, H-C(4')). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 192.04, 142.68, 136.95, 135.41, 131.57, 129.59, 128.64, 128.25, 126.61, 125.79, 124.06. GC/MS (m/z (%)): 188.0 ([M^+], 100); 159.0 (36); 115.1 (50).

3-(5-bromothiophen-2-yl)benzaldehyde (112).

According to known procedure,[15] **111** (136 mg, 0.722 mmol) was dissolved in 1,2-dichloroethane (2.5 mL). The solution of Br_2 (41 μL, 0.79 mmol) in 1,2-dichloroethane (2.5 mL) was added slowly at 0 °C, then warmed to r.t. and stirred for 2h. Aqueous $Na_2S_2O_3$ solution was added, and the desired product was extracted with 1,2-dichloroethane. Combined organic layers were washed with brine and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The product was purified using column chromatography (flash, Biotage SP1, RP column, eluent MeOH/H_2O gradient 8/2 → MeOH). The final product **112** was obtained

as a white foam (144 mg, 75 %). M.p. = 58 – 59 °C. IR (ATR): 3357w, 3097w, 3025w, 2857w, 2812w, 2761w, 1738w, 1685s, 1601w, 1480w, 1449w, 1429w, 1398w, 1284w, 1258w, 1183w, 1158w, 1005w, 872w, 783m, 681w, 653w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 10.05 (s, 1H, H-CO), 8.01 – 8.00 (m, 1H, H-Ar), 7.81 – 7.79 (m, 1H, H-Ar), 7.77 – 7.75 (m, 1H, H-Ar), 7.57-7.54 (m, 1H, H-Ar), 7.15 (d, 1H, *J* = 3.9, H-C(thiophene)), 7.07 (d, 1H, *J* = 3.7, H-C(thiophene)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 191.80, 144.08, 137.03, 134.63, 131.20, 131.10, 129.77, 129.10, 126.15, 124.27, 112.61. GC/MS (m/z (%)): 267.9 ([M^+], 100); 158.0 (60).

[4-(2-thienyl)phenyl]acetonitrile (113).

Compound **113** was prepared by procedure F using 2-bromothiophene (200 mg, 1.23 mmol), [4-(cyanomethyl)phenyl]boronic acid (217.2 mg, 1.349 mmol), PdO × 1.4 H_2O (18 mg, 0.12 mmol), K_2CO_3 (186.4 mg, 1.349 mmol) and EtOH/H_2O (12 mL, 3:1, v/v). The product was purified using column chromatography (dry-flash, SiO_2, eluent hexane, hexane/toluene gradient 9/1 → toluene). The final product **113** was obtained as an ocher solid (157.9 mg, 65 %). M.p. = 98 – 102 °C. IR (film): 3120m, 3024w, 2956w, 2906w, 2359w, 2247m, 2171w, 1609w, 1534m, 1500m, 1428m, 1412m, 1353w, 1300w, 1260m, 1211w, 1119w, 1078w, 1055w, 957w, 910w, 851m, 824m, 802s, 702s cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.64 – 7.60 (m, 2H-Ar), 7.35 – 7.31 (m, 3H, 2H-Ar and H-C(2)), 7.30 (dd, 1H, J_1 = 5.1, J_2 =1.2, H-C(4)), 7.11 – 7.07 (m, 1H, H-C(3)), 3.76 (s, 2H, Ar-CH_2-CN). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 143.30, 134.34, 128.85, 128.46, 128.11, 126.54, 125.26, 123.52, 117.65, 23.32. GC/MS (m/z (%)): 199.1 ([M^+], 100); 171.1 (27).

[4-(5-bromo-2-thienyl)phenyl]acetonitrile (114).

N-bromosuccinimide (82.4 mg, 0.463 mmol) was added to the stirring solution of **113** (86.3 mg, 0.433 mmol) in dry THF (9 mL) in the dark, at room temperature. Reaction progress was monitored by TLC (RP, MeOH). After 1h of stirring, an aq. $Na_2S_2O_3$ solution was added, and the desired product was extracted with CH_2Cl_2. Combined organic layers were washed with brine, and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The product was purified using column chromatography (flash Biotage SP1 RP column, eluent MeOH/H_2O gradient 6/4 → MeOH). The final product **114** was obtained as an ocher solid (64.2 mg, 53 %). M.p. = 142 – 145 °C. IR (film): 3094w, 3032w, 2923w, 2315w, 2248m, 1913w, 1749w, 1568w, 1538w, 1500m, 1431s, 1407m, 1330w, 1299w, 1246w, 1209w, 1124w, 1065w, 979w, 946w, 910w, 820w, 794s, 673w, 632w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 7.55 – 7.49 (m, 2H-Ar), 7.37 – 7.32 (m, 2H-Ar), 7.07 – 7.03 (m, 2H-thiophene), 3.76 (s, 2H, Ar-CH_2-CN). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 144.70, 133.56, 130.94, 129.36, 128.60, 126.22, 123.70, 117.51, 111.95, 23.33. GC/MS (m/z (%)): 279.0 ([M^+], 100); 198.1 (40).

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