Supplementary data for the article:

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Supporting information-I

Reinvestigating Old Pharmacophores: Are 4-Aminoquinolines and Tetraoxanes Potential Two-Stage Antimalarials?

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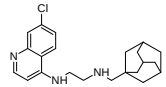
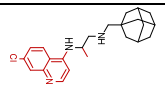
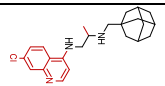
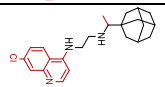
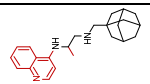
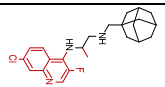
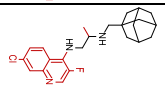
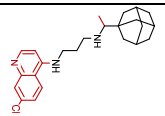
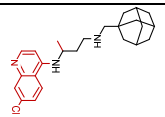
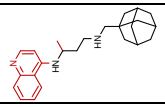
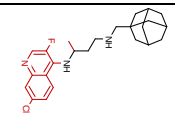
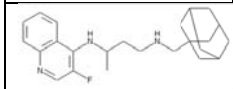
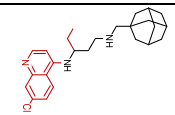
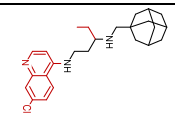
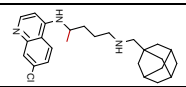
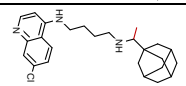
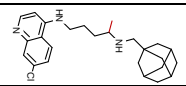
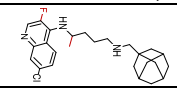
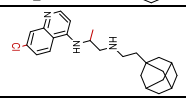
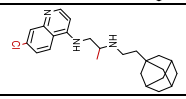
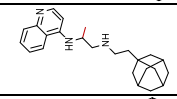
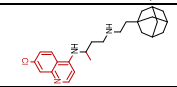
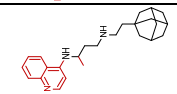
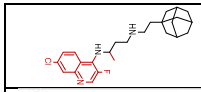
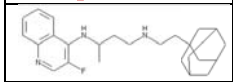
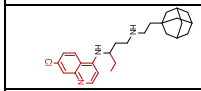
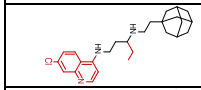
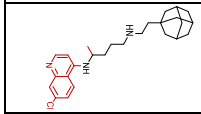
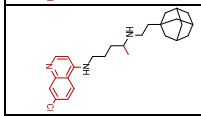
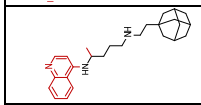
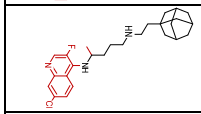
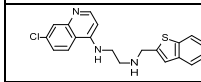
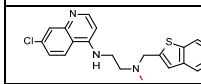
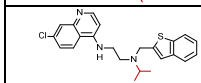
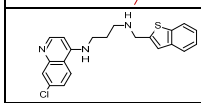
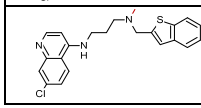
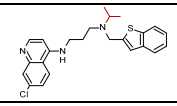
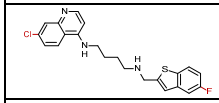
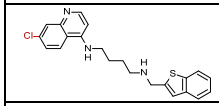
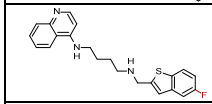
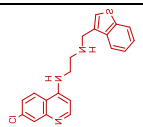
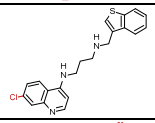
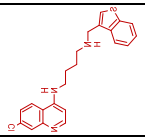
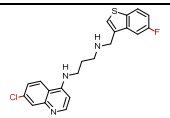
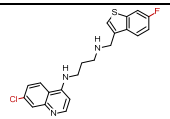
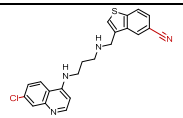
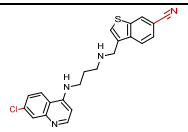
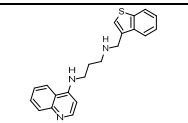
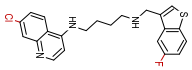
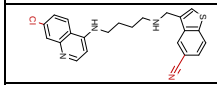
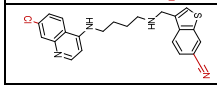
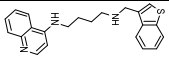
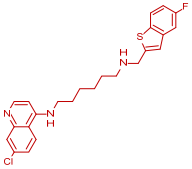
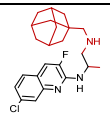
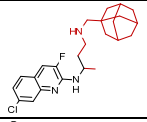
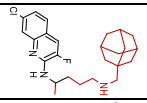
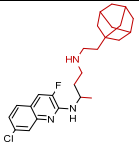
Table S1. Relevant data and activity of synthesized antiplasmodials.

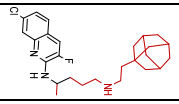
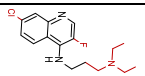
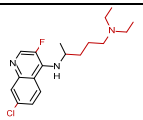
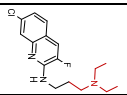
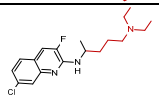
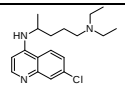
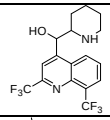
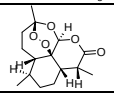
Structure	Compound	MW	$logP_{ow}$ exp.	pK_{a1}±SD	pK_{a2}±SD	Dipole[a]	BHIA[b]	In vitro antimalarial activity[c, d] (*P. falciparum*, IC_{50}, nM)			HepG2[h](RAW 264.7)[i] IC_{50},nM	MLM[j] (min)	HLM[k] (min)	SI HepG2(RAW)/D6
								D6[e]	C235[f]	W2[g]				
	**1**[#]	369.93	3.09					4	9	8	3437			859
	**9**	383.97	3.40	6.75± 0.03	8.18± 0.03			1	1	3	(2901)	10	11	(2901)
	**10**	383.97	3.17	6.51± 0.01	8.13± 0.01			2	9	10	(3771)	10	13	(1886)
	**11**	383.97	3.55					4	19	44	(1809)			(452)
	**12**	349.51	3.70					584	934	1713	4111			7
	**20**	401.96	3.02					585	948	1367	4252			7
	**21**	401.96	3.09					1261	3082	2269	6436	6	13	5
	**22**	398.00	3.93					4	15	22	(3161)	11	16	(790)
	**23**	398.00	3.85	6.96± 0.15	9.22± 0.14	6.04	1.84± 0.08	10	10	10	3045	60	60	305
	**24**	363.54	4.09	7.33± 0.09	9.21± 0.05	4.79	1.22± 0.09	17	135	185	2317	60	60	136

	**25**	415.99	3.25	4.92± 0.11	9.20± 0.20	3.10	0.61± 0.07	135	197	238	3967	21 (79^{l})	13 (78^{m})	29
	**26**	381.53	3.09	5.47± 0.05	8.16± 0.09	4.01	0.61± 0.05	60	259	157				0
	**27**	412.02	3.40					3	12	9	(5257)	13	34	(1752)
	**28**	412.02	3.78					7	19	25	2010	15	14	287
	**29**	412.02	4.16					21	23	22	24271	57	49	1156
	**30**	412.02	4.16					7	19	25	3090			441
	**31**	412.02	3.55					51	165	282	1612			32
	**32**	430.01	3.47					198	342	488	3549			18
	**33**	398.00	4.41	6.81± 0.04	8.63± 0.08	3.84		1	1	4	(2910)	60	57	(2910)
	**34**	398.00	3.78			3.47		6	7	7	25127	60	27	4188
	**35**	363.54	4.33					9	86	97	2345			261
	**36**	412.02	5.16			4.27		13	13	13	24271	60	60	1867
	**37**	377.57	4.85	7.13± 0.06	9.54± 0.03	3.39		7	102	126	1590			227

	**38**	430.01	4.33			2.87		143	171	203	3212			22
	**39**	395.56	4.13			2.96		154	546	394				0
	**40**	426.05	4.59					11	32	18	1767	22	16	161
	**41**	426.05	4.59					43	69	79	23472			546
	**42**	426.05	5.87			4.88		7	14	26	13273	60	60	1896
	**43**	426.05	4.85					9	47	81	2598			289
	**44**	391.59	5.37	7.24± 0.05	9.69± 0.09			12	286	393	1593			133
	**45**	444.04	4.67					288	590	547	2608			9
	**46**	367.90	1.97					55	48	97	33438			608
	**47**	381.90	2.69					120	257	296	5741	9	9	48
	**48**	410.00	3.12					34	56	68	7305	9	9	215
	**49**	381.90	2.38				0.85± 0.06	44	64	87	1906			43
	**50**	396.00	2.76					86	119	177	7336	9	6	85

	**51**	424.00	2.94					75	137	231	3054	8	5	41
	**52**	414.00	2.57					14	29	41	4435			317
	**53**	396.00	2.63					20	37	45	866			43
	**54**	379.50	2.94					32	177	240	3227			101
	**55**	367.90	2.44					30	19	22	6120	23	24	204
	**56**	381.90	2.82				0.66± 0.04	7	17	24	7780			1111
	**57**	396.00	3.06					8	68	31	2258			282
	**58**	399.90	2.63				0.41± 0.04	28	78	50	2463			88
	**59**	399.90	2.76				0.50± 0.05	33	20	28	5543			168
	**60**	406.90	2.11				0.99± 0.07	5	25	32	3971			794

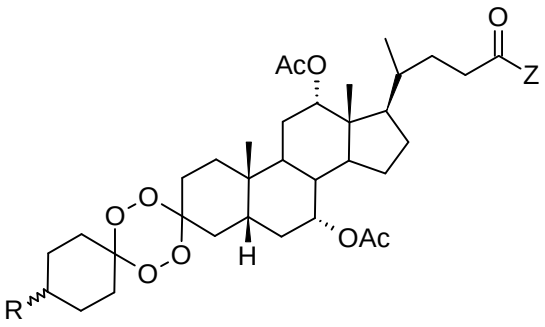
	**61**	406.90	2.24				0.78± 0.06	17	52	47	3880			228
	**62**	347.50	3.18				1.54± 0.10	89	280	283	5144			58
	**63**	414.00	2.82				0.38± 0.03	10	19	27	1649			165
	**64**	421.00	2.31					12	36	40	2929			244
	**65**	421.00	2.51				1.07± 0.08	10	24	40	3808			381
	**66**	361.50	3.30					65	299	275	4673			72
	**67**	442.00	2.88					20	32	36	3871			194
	**68**	401.96	3.40					3192	2918	1577	4048			1
	**69**	415.99	3.70					731	990	950	5481			7
	**70**	430.01	4.01					751	963	588	3639	60	60	5
	**71**	430.01	5.37					2821	2763	1884	8930	60	24	3

	**72**	444.04	5.26					2241	3432	1212	22992			10
	**73**	309.82	3.32	5.16± 0.09	9.25± 0.19		0.78± 0.08	1601	1354	1797	34983			22
	**74**	337.87	4.01	5.17± 0.12	9.46± 0.04		1.07± 0.09	405	412	565	18815			46
	**75**	309.82	4.01					800	626	423	30948			39
	**76**	337.87	4.16	3.77± 0.14	9.48± 0.18		2.42± 0.11	6772	3362	571	18712			3
	**CQ**	319.87		7.48± 0.02	9.58± 0.03		1.23± 0.10	12	139	456				
	**MFQ**	378.31						16	36	5				
	**ART**	282.33						9	13	7				

[a] QikProp, version 3.5, Schrödinger, Inc., New York, NY, 2012.[b]aIC50 values represent molar equivalents of compound, relative to hemin, that inhibit β-hematin formation by 50% (data expressed as means ± SD from an experiment done in triplicates, except for CQ which was tested 6 times).[c]Antiplasmodial IC_{50} values (nM) ([^{3}H]hypoxanthine incorporation method) for isolates and clones of *P. falciparum*. [d] All in vitro experiments were done as technical triplicates with R2 within 0.96–1. [e] CQ susceptible *P. falciparum* African D6 clone. [f]*P. falciparum* multidrug resistant C235 strain (Thailand). [g] CQ resistant *P. falciparum* Indochina W2 clone. [h] Hepatocellular carcinoma. [i]Rat Macrophage Cell Line. [j] Mouse liver microsomes. [k] Human liver microsomes. [l] Mouse hepatocytes. [m] Human hepatocytes.

[#] Šolaja, B.; Opsenica, D.; Smith, K. S.; Milhous, W. K.;Terzić, N.; Opsenica, I.; Burnett, J. C.; Nuss, J.; Gussio, R.; Bavari, S. Novel 4-Aminoquinolines Active againstChloroquine-Resistant and Sensitive *P. falciparum* Strains that also InhibitBotulinum Serotype A., *J. Med. Chem.* **2008**, *51*, 4388-4391.

Figure S1



77: R=H, Z=OCH_3[5]

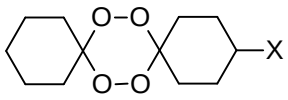
79: R=H, Z=NH_2[5,8]

80: R=α-CH_3, Z=NH_2[5]

81: R=β-CH_3, Z=NH_2[5]

78: R=H, Z=NHPr[5,8]

82: R=H, Z=$NHCH_2CH_2N(CH_3)$[7]



83: X=CONHPr[3]

84: X=$CONHCH_2CH_2NH$-4'-(7'-chloroquinoline)[4]

85: X=CH_2OH[3]

86: X=CH_2N_3[3]

87: X=CH_2NH_2[3]

88: X=CH_2NHCy[3]

89: X=$CH_2NHCH_2CH_2NH$-4'-(7'-chloroquinoline)[4]

Figure S1. Tetraoxanes tested for activity in the liver stage.

Table S2: Liver stage activity of tetraoxane antiplasmodials.

Compound	% LS infection (5 µM)[a]	LS IC_{50} (µM)[b]	LS in vivo, (mg/kg/day)[c]	IC_{50} (nM)[d]		RBC in vivo cure[d,e] (Thompson test, mg/kg/day)
				W2	D6	
77	31	<1		27.67	39.14	
78	0.55	0.33 ±0.05	40 (50); 9 (100)	4.74	11.83	50
79	13	1-5		0.58	1.17	50
80	16	1-5		14.10	20.04	50
81	6	1-5		6.80	14.76	200
82	11	3-4		14.49	28.16	40
83	21	1-5		7.54	9.40	37.5
84	~1	~1		2.00	2.33	80
85	100			6.54	15.18	
86	90			6.07	9.87	150
87	N.A.			7.79	12.84	37.5
88	28	1-5		6.17	11.18	37.5
89	~1	1-5		5.76	9.05	80
PQ	62 (10µM)					
CQ		ca. 9[1]				
ART	>75[2]	ca. 121				
Artemisone		ca. 0.041				
ATQ		22 nM1				

[a] 10 000 Huh7 cells/well seeded 24 h before infection. 10 000 PbA-LuciGFPcon spz/well. Confluency measured by a fluorimetric assay. Infection measured by a bioluminescence assay.

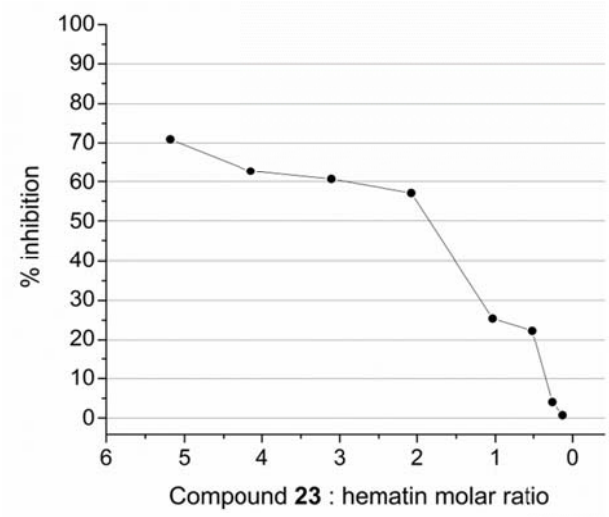
[b] All dose-responses with at least 5 dosages.

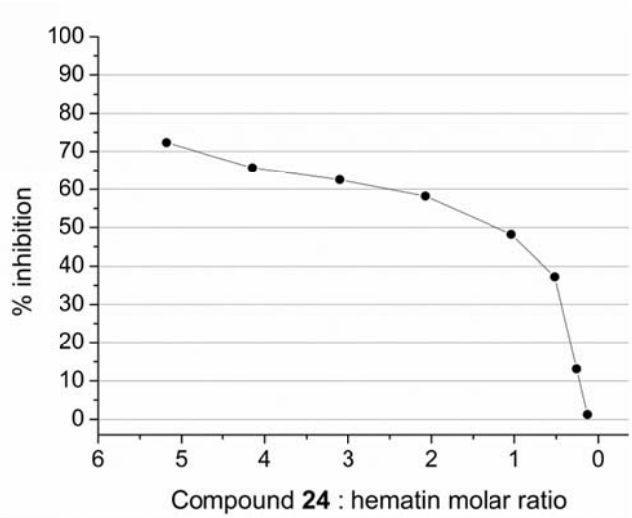
[c] Measurement of liver load by qRT-PCR. Mean of 2 independent experiments. All mice were infected by i.v. injection of 10,000 *P. berghei* sporozoites. Control groups were treated by oral gavage with vehicle (equivalent % of DMSO, in sunflower oil). Experimental groups were treated by oral gavage administration of **78** at 50 and 100 mg/kg.

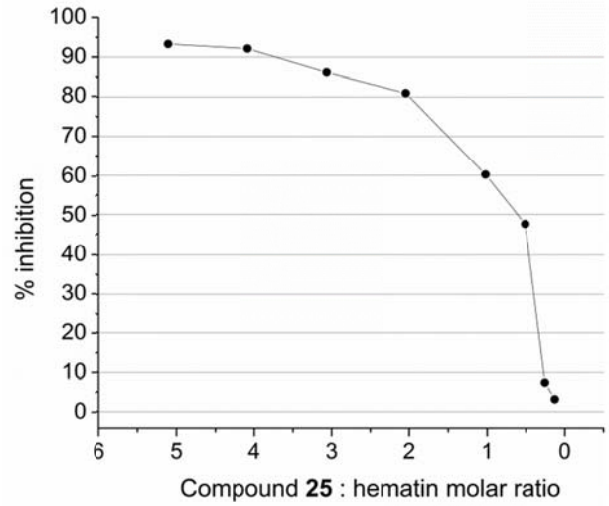
[d] Taken from refs. 3, 4, 5, 6, 7, 8.

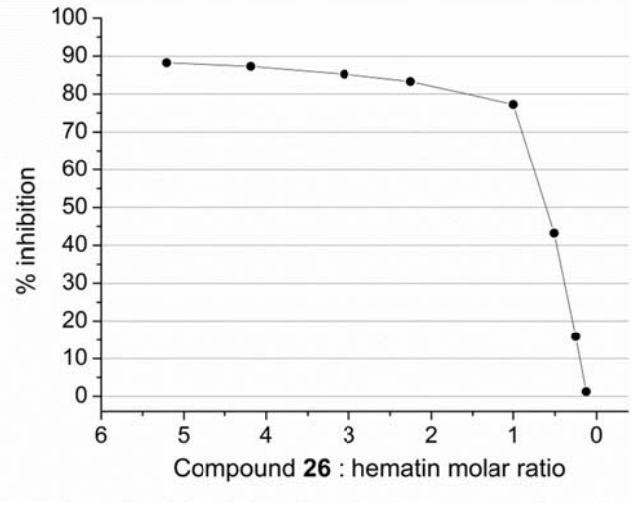
[e] Lowest dose that cured mice in Thompson test (no parasitemia on D31).

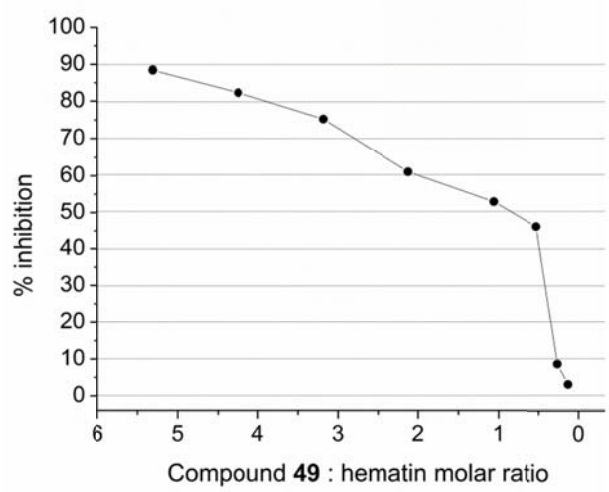
BHIA plots. Plots of the dose-dependent inhibition of β-hematin formation by studied compounds.

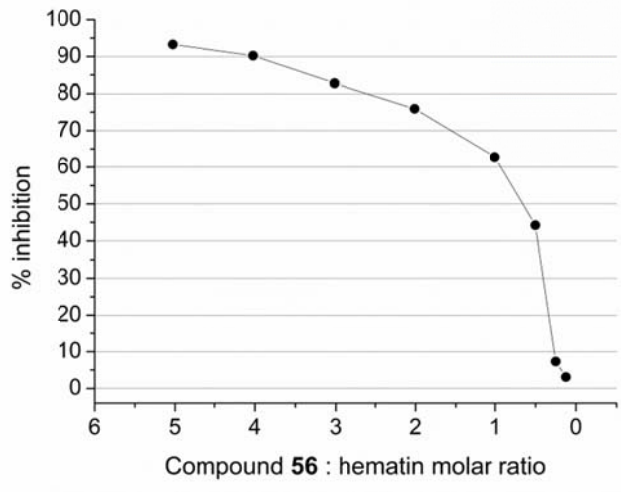


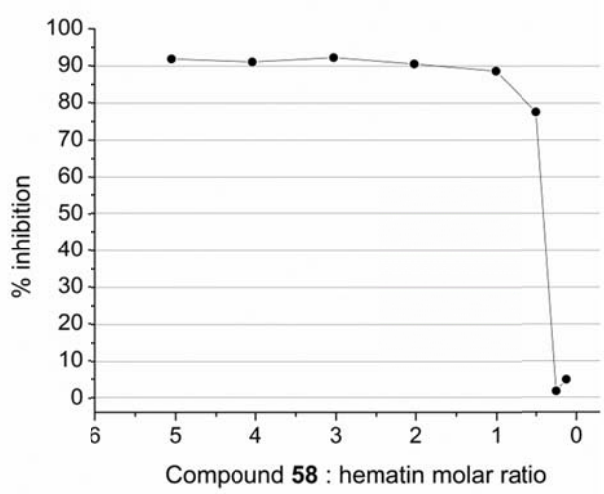


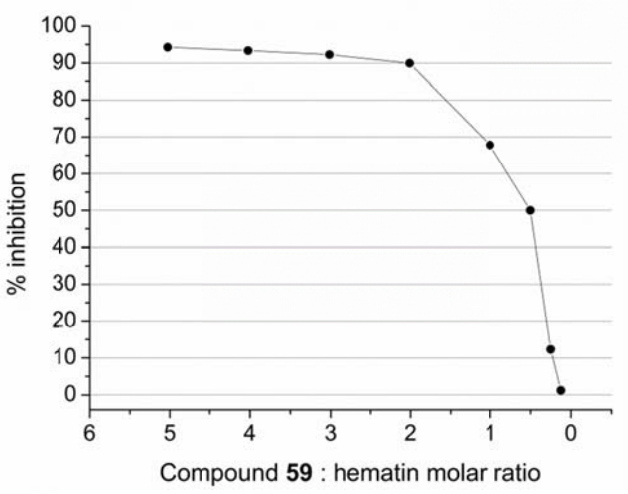


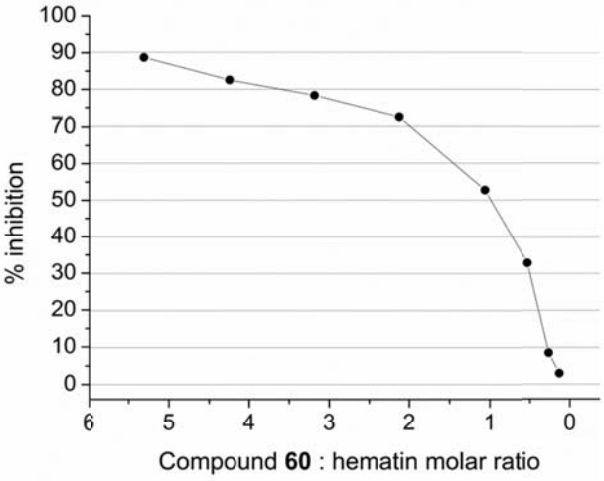


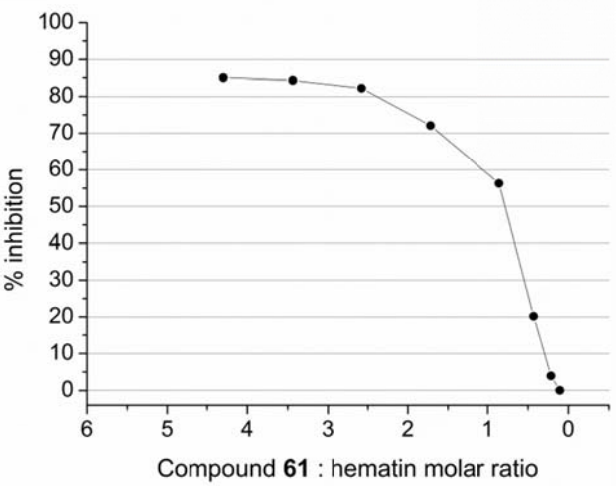


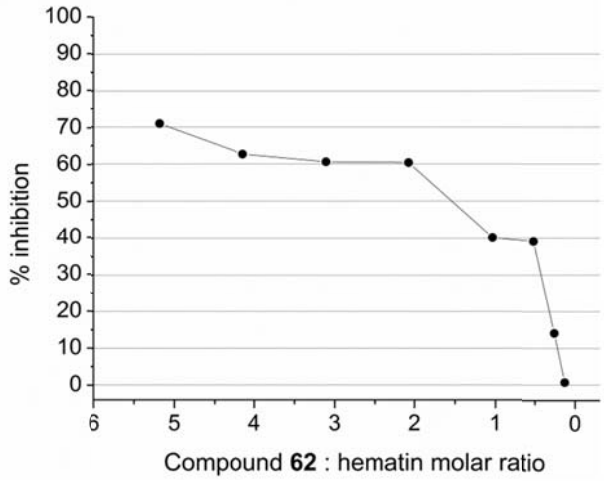


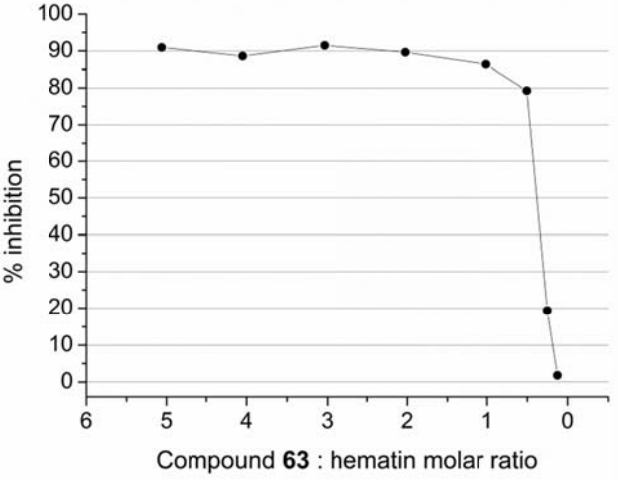

% inhibition
Compound **58** : hematin molar ratio

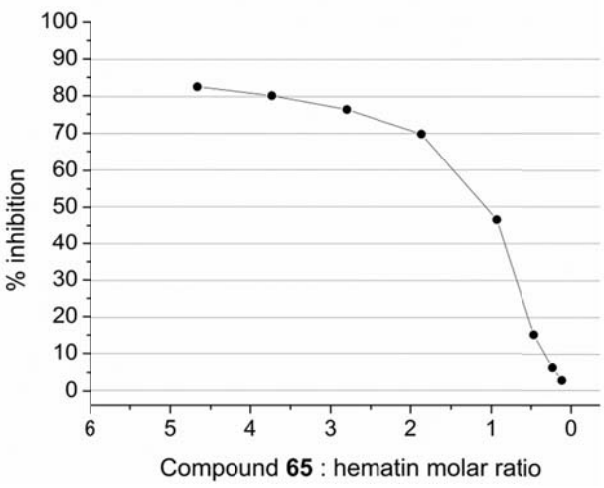

% inhibition
Compound **59** : hematin molar ratio

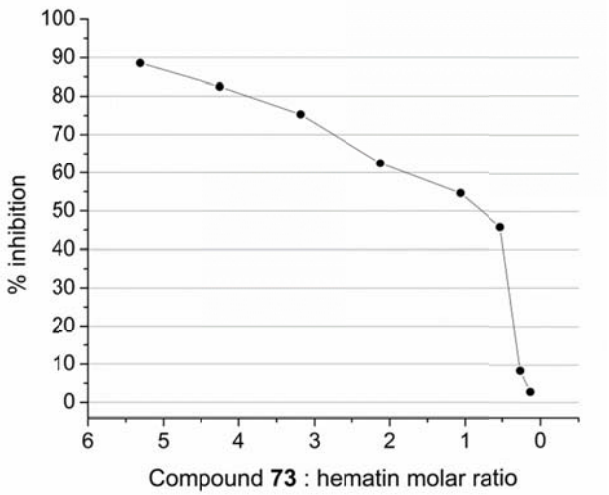

% inhibition
Compound **60** : hematin molar ratio

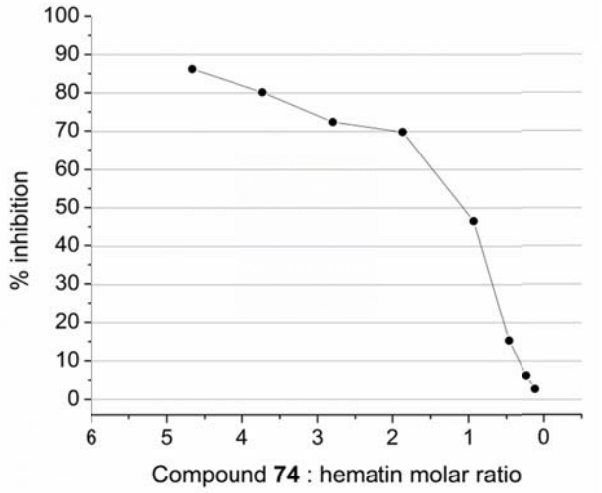

% inhibition
Compound **61** : hematin molar ratio

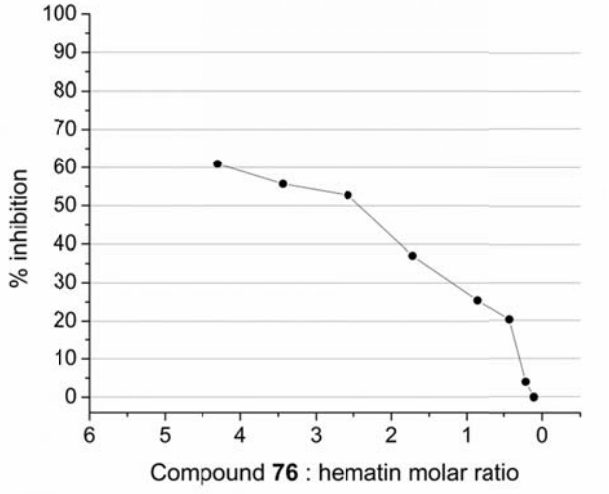

% inhibition
Compound **62** : hematin molar ratio

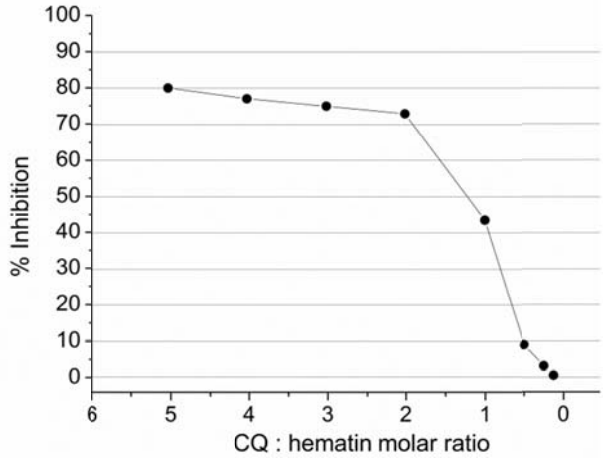

% inhibition
Compound **63** : hematin molar ratio


% inhibition
Compound 65 : hematin molar ratio

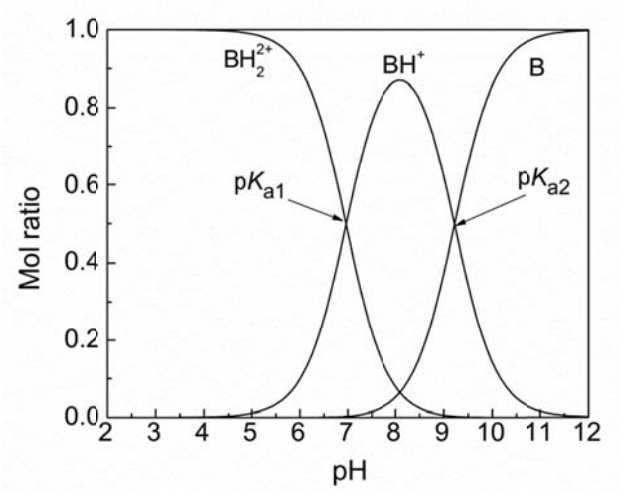

% inhibition
Compound 73 : hematin molar ratio


% inhibition
Compound 74 : hematin molar ratio

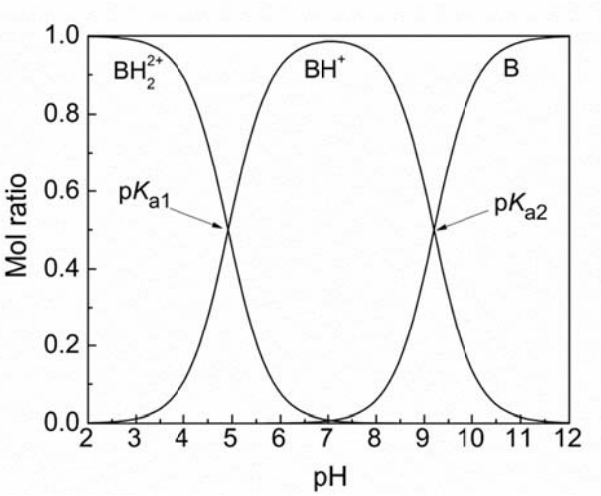

% inhibition
Compound 76 : hematin molar ratio


% Inhibition
CQ : hematin molar ratio

Distribution diagrams



23



25

Chemistry.

Melting points were determined on a Boetius PMHK apparatus and were not corrected. IR spectra were taken on a Thermo-Scientific Nicolet 6700 FT-IR diamond crystal. ^{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. Compounds were analyzed for purity using: Agilent 1200 HPLC system equipped with Quat Pump (G1311B), Injector (G1329B) 1260 ALS, TCC 1260 (G1316A) and Detector 1260 DAD VL+ (G1315C), and Waters 1525 HPLC dual pump system equipped with an Alltech Select degasser system, and a dual k 2487 UV–Vis detector. All compounds were >95% pure. For each compound HPLC analysis was performed in two diverse systems:

Method A: Zorbax Eclipse Plus C18 4.6 × 150 mm, 1.8 µ, 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). Analyses were performed at the UV max of the compounds (at 330 nm for compounds **9**, **10**, **11**, **12**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37**, **38**, **39**, **40**, **41**, **42**, **43**, **44**, **46**, **48**, **49**, **50**, **51**, **52**, **53**, **54**, **55**, **56**, **58**, **59**, **60**, **61**, **62**, **63**, **64**, **65**, **66**, **67**, **70**, **73**, **74**, **75**, **76** and at 254 nm for compounds **45**, **47**, **57**, **68**, **69**, **71**, **72** to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.5 mL/min

Compounds **9**, **10**, **11**, **20**, **21**, **22**, **23**, **25**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **34**, **36**, **40**, **41**, **42**, **43**, **66**, **67**, **68**, **71**, **72**, **73**, **74**, **75** and **76** 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 5%A.

Compounds **26**, **38** and **39** 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 5%A.

Compounds **24**, **35** and **44** were eluted using gradient protocol: 0-3 min 25%A, 3-4 min 25%A→ 5%A, 4-5 min 5%A, 5-7 min 5%A→ 25%A, 7-8 min 25%A.

Compounds **12** and **37** were eluted using gradient protocol 0-3 min 30%A, 3-6 min 30%A→ 5%A, 6-9 min 5%A, 9-10 min 5%A→ 30%A, 10-11 min 30%A.

Compound **45** was eluted using gradient protocol 0-3 min 50%A→ 30%A, 3-6 min 30%A→ 0%A, 6-9 min 0%A→ 50%A, 9-12 min 50%A.

Compounds **47**, **48**, **50**, **51**, **55**, **56**, **57** and **66** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14min 5%A→ 95%A, 14-15 min 95%A.

Compounds **52**, **53**, **54**, **61**, **62** and (**65**) 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.Compounds **46**, **58**, **59**, **63**, **64** and **67** 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, 14-16 min 95%A.

Compounds **49** and **60** 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.

Method B: Zorbax Eclipse Plus C18 4.6 x 150 mm, 1.8 µ, 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). Analyses were performed at the UV max of the compounds (at 330 nm for compounds **9**, **10**, **11**, **12**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **27**, **28**), **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37**, **38**, **39**, **40**, **41**, **42**, **43**, **44**, **46**, **47**, **48**, **50**, **51**, **52**, **53**, **54**,**55**, **56**, **57**, **58**, **61**, **62**, **64**, **66**, **67**, **70**, **73**, **74**, **75**, **76** and at 254 nm for compounds **45**, **59**, **63**, **65**, **68**, **69**, **71**, **72**to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.5 mL/min

Compounds **9**, **10**, **11**, **12**, **20**, **21**, **22**, **23**, **24**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **40**, **41**, **42**, **43**, **44**, **67**, **68**, **71**, **72**, **74**, **73**, **75** and **76** 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 5%A.

Compounds **45**, **25**, **66**,**38**) 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 5%A.

Compound **37** was eluted using gradient protocol 0-2 min 30%A, 2-6 min 30%A→ 5%A, 6-9 min 5%A, 9-10 min 5%A→ 30%A, 10-11 min 30%A.

Compounds **26** and **39** were eluted using gradient protocol 0-1 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 5%A.

Compounds **46**, **52**, **53**, **54**,**58**, **61**, **62**, **64**, **65** and **67** 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.

Compounds **47**, **48**, **50**, **51**, **55**, **56**, **57**, **59**,**63** and **66** 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 C: 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). Analyses were performed at the UV max of the compounds (at 254 nm for compounds **49**, **60**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~ 1mg/mL. Flow rate was 0.5 mL/min

Compounds **49** and **60** 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, 14-17 min 95%A.

N1-(7-Chloroquinolin-4-yl)ethane-1,2-diamine (**AQ2**), N1-(7-chloroquinolin-4-yl)propane-1,3-diamine (**AQ3**), N1-(7-chloroquinolin-4-yl)butane-1,4-diamine (**AQ4**), N1-(7-chloroquinolin-4-yl)-ethane-1,6-hexane (**AQ6**) and *N*-(quinolin-4-yl)propane-1,3-diamine (**AQ7**) and *N*-(quinolin-4-yl)butane-1,4-diamine(**AQ8**) were prepared according to known procedures.[9]

General procedures

Method A: General synthetic procedure for mono-protection of the asymmetrical diamines with Boc.[10]

Tert-butyl phenyl carbonate (2 equiv) was added to a stirred solution of unsymmetrical diamine (1 equiv) in absolute EtOH. The reaction mixture was refluxed overnight (18 h), followed by removal of the volatiles in vacuo. Water was added and 2M HCl was added until pH3, followed by extraction with CH_2Cl_2. The aqueous phase was then made strongly alkaline by addition of aqueous NaOH (2M) and extracted with CH_2Cl_2. The combined organic extracts were dried over anh. Na_2SO_4 and solvent was evaporated under reduced pressure to get the final product.

Method B: General procedure for the synthesis of *N*-Boc protected aminoquinolines[11]

A mixture of 4,7-dichloroquinoline (1 equiv) and monoprotected diaminoalkane (2 equiv) was gradually warmed to 80 °C over 1 h with stirring and the stirring was continued for 6-8 h at 120-130 °C . The reaction mixture was cooled to r.t. and taken up in CH_2Cl_2. The organic layer was washed with $NaHCO_3$, water and brine. The organic layer was dried over anh. Na_2SO_4 and solvent was evaporated under reduced pressure to get final product.

Method C: Removal of the Boc-protecting groups with TFA.

A solution of *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 remaining residue was treated with CH_2Cl_2/2.5M NaOH. The organic layer was dried over anh. $MgSO_4$, and the solvent was evaporated under reduced pressure.

Method D: General procedure for reductive amination.

To a solution of an amine in CH_2Cl_2 were added the appropriate aldehyde (1 equiv) and $NaHB(OAc)_3$ (2 equiv). After stirring the reaction mixture at r.t. for 24 h, aqueous NaOH was added. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2. The organic layer was dried over anh. Na_2SO_4, and the solvent was evaporated under reduced pressure.

Method E: General procedure for reductive amination.

Amine (1.25-1.5 equiv) and appropriate aldehyde (1 equiv) were dissolved in MeOH/CH_2Cl_2 mixture (v:v; 2:1), anh. AcOH (1.25-1.5 equiv) was added, and the mixture was stirred under Ar at r.t. for 3 h. Then, $NaBH_4$ (6 equiv) was added and stirring was continued for another 18 h. The 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 brine, and dried over Na_2SO_4. Finally, the solvent was evaporated under reduced pressure.

Method F: General procedure for the synthesis aminoquinolines.

A mixture of diamine linker (1.2 equiv), 4,7-dichloroquinoline/4-chloroquinoline (1 equiv) and phenol (15 equiv) were heated at 120-130 °C, with stirring for 24 h or the reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*. The reaction mixture was cooled to r.t. and taken up in CH_2Cl_2. The organic layer was successively washed several times with NaOH and finally with brine. The organic layer was dried over anh. Na_2SO_4 and solvent was removed under reduced pressure to get a final product.

Method G: General procedure for reductive amination.[12]

A mixture of appropriate aldehyde/ketone (1 equiv), amine (1.2 equiv) and $Ti(OiPr)_4$ (1.5 equiv) reaction mixture was stirred at r.t. overnight. Following, absolute EtOH and $NaBH_4$ (2 equiv) were added to the mixture and stirring was continued for 24 h. The reaction was quenched with 2M NaOH, and solvent was removed under reduced pressure. Aqueous layer was washed with CH_2Cl_2, and organic layer was dried over anh. Na_2SO_4. The solvent was evaporated, and the residue was purified by chromatography to yield the desired product.

Method H: General procedure for palladium catalyzed amination of quinolines.[13]

Vial was charged with mixture of $Pd(OAc)_2$ (4 mol%) and DPEphos (8 mol%)/SPhos (8 mol%) in dioxane and stirred for a few minutes underAr at r.t. Subsequently, a haloquinoline (1.0 equiv), amine (1.2 equiv) and K_3PO_4 (2.5 equiv) were added to the reaction mixture. Resulting suspension was flushed with argon for several minutes. The vial was quickly capped, heated to 85 ^oC overnight and then cooled down to r.t. The mixture was adsorbed onto silica gel and purified.

Method I: General procedure for protection of amine with Cbz.[14]

Mono-Boc-protected diamine was dissolved in CH_2Cl_2followed by addition of benzylchloroformate (1.95 equiv) and triethylamine (2.05 equiv). The reaction mixture was stirred at r.t. for 3 h and then quenched with aqueous NH_4OH. Aqueous layer was extracted several times with EtOAc. The organic layer was dried over anh. Na_2SO_4, and solvent was evaporated under reduced pressure to give crude product.

Method J: General procedure for removal of the Cbz-protecting group by hydrogenization.

The Cbz-protected amine was hydrogenated using 10% Pd/C as catalyst under 2 atm of hydrogen MeOH. The mixture was stirred at r.t. for 8 h, the catalyst was removed by filtration and the solvent was evaporated under reduced pressure.

Method K: General procedure for N-methylation of aminoquinolines.[15]

To a stirred solution of aminoquinolines (1equiv) in MeOH containing 37% aqueous formaldehyde/acetone (2 equiv) was added mixture of $ZnCl_2$ (2 equiv) and $NaHB_3CN$ (4 equiv) in MeOH. After the reaction mixture was stirred at r.t. for 4 h, the solution was taken up in 0.1M NaOH and most of methanol was evaporated under reduced pressure. Aqueous

solution was extracted with CH_2Cl_2, the combined extracts were washed with water and brine, dried over anh. Na_2SO_4 and the solvent was evaporated under reduced pressure.

Method L: Synthesis of methyl esters.[16]

Difluorobenzaldehyde or bromofluorobenzaldehyde (1 equiv) was dissolved in DMSO, followed by dropwise addition of methyl thioglycolate (1 equiv) and triethylamine (3 equiv). The resulting mixture was stirred under argon atmosphere at 80 °C for 2 h and then allowed to cool to room temperature. The reaction mixture was transferred to a separation funnel, water was added and extracted with EtOAc. 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.

Method M: Preparation of carboxylic acids.[17]

A mixture of the methyl ester (1 equiv), KOH (3 equiv)**,** water and EtOH (1:8, v:v) was stirred at room temperature for 3 h. The mixture was concentrated under reduced pressure, acidified with conc. HCl at 0 °C and transferred to a separation funnel. Product was extracted with EtOAc/THF (4:1, v:v) and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The product was purified using column chromatography.

Method N: Experimental procedure for decarboxylation by microwave heating.[18]

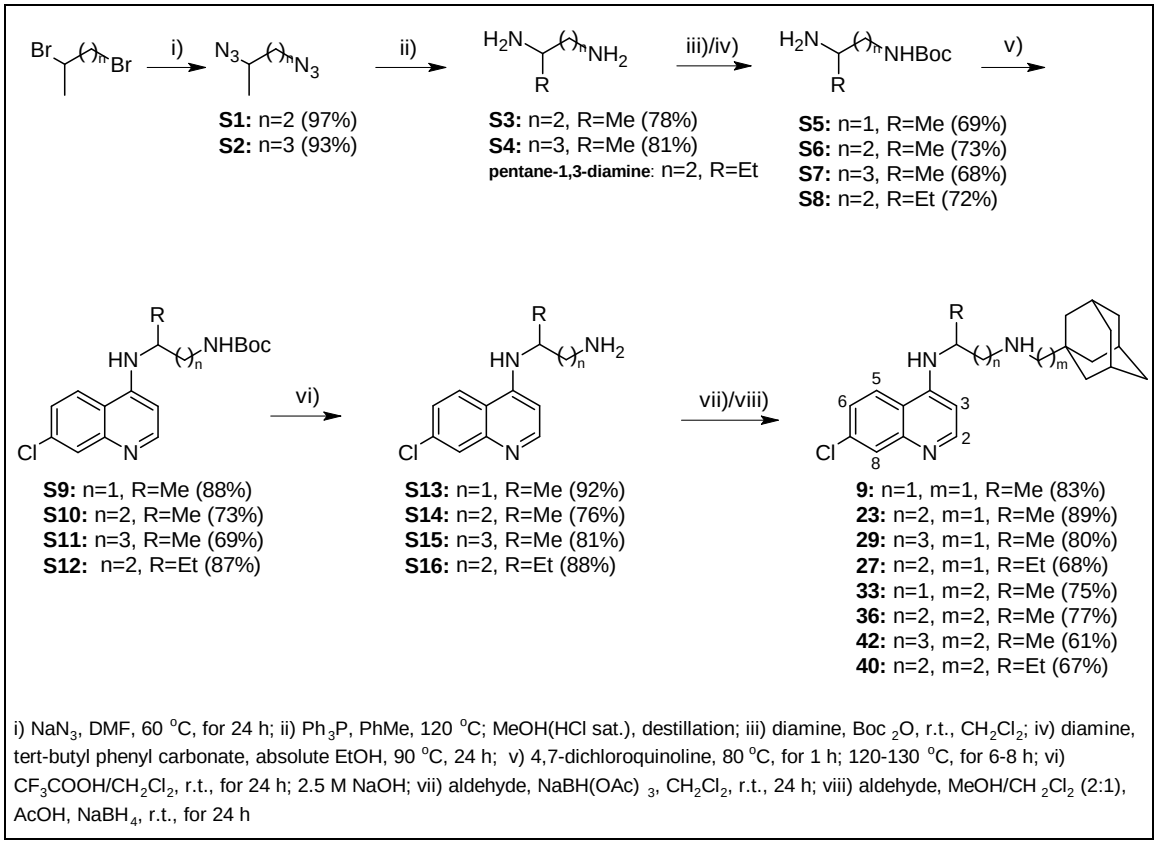
A mixture of the carboxylic acid (1 equiv) and DBU (2.5 equiv) in *N*,*N*-dimethylacetamide was heated in a sealed vessel in microwave reactor at 200 °C for 2 h. The product was purified using column chromatography.

Method O: General experimental procedure for Rieche formylation.[19]

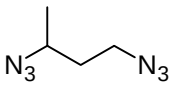
$TiCl_4$ (5 equiv) was dissolved in DCM at -10 °C, and then solution of dichloromethyl methyl ether (10 equiv) in DCM was added dropwise, followed by a solution of substituted benzothiophene(1 equiv) in DCM. After stirring for 1 h, the mixture was warmed to room temperature and then stirred for 24 h. The reaction mixture was poured onto ice-water, and conc. HCl was added. It was stirred for 30 min and then transferred to a separation funnel. Organic layer was washed well with saturated $NaHCO_3$, brine and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The product was purified using column chromatography.

Method P: Sythesis of cyano derivatives.[20]

Bromobenzothiophene (1 equiv) and CuCN (2 equiv) were suspended in NMP and heated for 12 h at 190 °C. The mixture was cooled to 0 °C and 33% aq. ethylendiamine was added. After dilution with ether, the mixture was transferred to a separation funnel. Organic layer was 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.

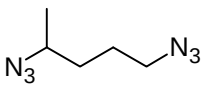


1,3-Diazidobutane (S1).



Sodium azide (15.06 g, 231.58 mmol) was added to a solution of 1,3-dibromobutane (10 g, 46.31 mmol) in DMF (100 mL).Reaction mixture was stirred for 24 h at 60 °C cooled to r.t., and water was added to dissolve excess of NaN_3 and compound was extracted with EtOAc (3× 70 mL). The organic phase was dried over anh. Na_2SO_4, filtered and concentrated under reduced pressure to afford the desired product **S1**as colorless oil (6.30 g, 97%). IR(ATR): 3336w, 2975m, 2934m, 2877w, 2498w, 2099s, 1456m, 1380w, 1355w, 1323w, 1267m, 1134w, 1088w, 1020w, 904w, 869w, 780w, 634w cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$, δ): 3.70-3.50 (m, 1H, $N_3CH(CH_3)$-), 3.50-3.35 (m, 2H, -CH_2N_3), 1.80-1.60 (m, 2H, $N_3CH(CH_3)CH_2$-), 1.32 (d, 3H, J = 6.2, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$, δ): 54.86; 48.05; 35.16; 19.23.

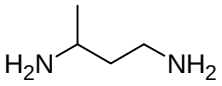
1,4-Diazidopentane (S2).



Sodium azide (14.14 g, 217.44 mmol) was added to a solution of 1,4-dibromopentane (10 g, 43.68 mmol) in DMF (100 mL). The mixture was stirred for 24 h at 60 °C. After cooling to r.t., water was added to dissolve excess of NaN_3 and compound was extracted with EtOAc (3× 70 mL). The organic phase was dried over anh. Na_2SO_4, filtered and concentrated under reduced pressure to afford the desired product **S2** as colorless oil (6.2 g, 93%). IR(ATR): 3336w, 2973m, 2936m, 2874m, 2500w, 2097s, 1456m, 1381w, 1353w, 1258m, 1133w, 971w, 854w, 629w cm^{-1}. ^{1}H-NMR(200 MHz, $CDCl_3$, δ):

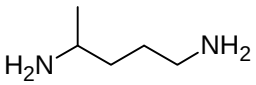
3.60-3.40 (m, 1H, $N_3CH(CH_3)$-), 3.40-3.20 (m, 2H, -CH_2N_3), 1.80-1.40 (m, 4H, $N_3CH(CH_3)CH_2CH_2$-, $N_3CH(CH_3)$-), 1.29 (d, 3H, J = 6.8, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$, δ): 57.32; 50.96; 33.16; 25.38; 19.27.

Butane-1,3-diamine (S3).



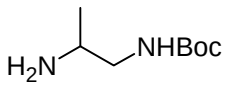
Mixture of 1,3-diazidobutane **S1** (13.50 g, 96.6 mmol) and Ph_3P (50.7 g, 193.2 mmol, 2 equiv) in toluene (150 mL) was stirred at 120 °C for 15 min, and cooled to r.t. Then H_2O (18 mL) was added, and the resulting mixture was stirred overnight at 120 °C. Reaction mixture was transferred into a separation funnel, lower layer was collected and transformed in salt using MeOH(HCl sat.).Solvent was evaporated and dried crystals of 1,3-butanediamine dihydrochloride (11.1 g, 68.9 mmol) were mixed with NaOH powder (18 g, 450 mmol). Distillation afforded colorless oil (4.8 g, 78%, b.p. 138.6 °C/760 Torr).IR(ATR): 3354s, 3281s, 3194m, 2956s, 2922s, 2869m, 2757w, 2664w, 1600s, 1456m, 1376m, 1348w, 1141w, 1091w, 1064w, 881m, 835m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 3.05-2.95 (m, 1H, $NH_2CH(CH_3)$-), 2.85-2.75 (m, 2H, -CH_2NH_2), 1.60-1.40 (m, 2H, -$CH_2CH_2NH_2$), 1.08 (d, 3H, J = 6.3, CH_3). ^{13}C-NMR (125 MHz, D_2O, δ): 44.92; 43.48; 39.44; 24.35. Anal. ($C_4H_{14}Cl_2N_2$) Calcd: C, 29.83; H, 8.76; N, 17.39. Found: C, 29.86; H, 8.91; N, 17.48.

Pentane-1,4-diamine (S4).



Mixture of 1,4-diazidopentane **S2** (16.41 g, 106.3 mmol) and Ph_3P (55.7 g, 212.6 mmol, 2 equiv) in toluene (150 mL) was stirred at 120 °C 15 min, and cooled to r.t.. Then H_2O (23 mL) was added, the resulting mixture was stirred overnight at 120 °C. Reaction mixture was transferred into a separation funnel, lower layer was collected and transformed in salt using MeOH(HCl sat.). Solvent was evaporated and dried crystals of 1,4-pentanediamine dihydrochloride (15.6 g, 89.3 mmol) were mixed with NaOH powder (22 g, 550 mmol). Distillation afforded colorless oil (7.3 g, 81%, b.p. 162.4 °C/760 Torr). IR (ATR): 3427s, 3035s, 2440m, 1994w, 1604m, 1482s, 1469s, 1454s, 1392m, 1334w, 1290w, 1266m, 1201m, 1167m, 1103m, 1044m, 991w, 948m, 946m, 846, 759w, 508m, 437w, 421w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.95-2.70 (m, 1H, $NH_2CH(CH_3)$-), 2.70-2.95 (m, 2H, -CH_2NH_2), 1.60-1.40 (m, 2H, -$CH_2CH_2NH_2$), 1.40-1.25 (m, 2H, $NH_2CH(CH_3)CH_2$-), 1.07 (d, 3H, J = 6.2, -CH_3). ^{13}C-NMR (125 MHz, D_2O): 47.85; 42.85; 37.96; 30.86; 23.35.

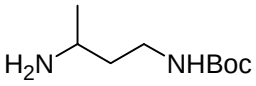
***Tert*-butyl (2-aminopropyl)carbamate (S5).**



Compound **S5** was prepared from 1,2-propanediamine (2 mL, 23.48 mmol) and *tert*-butyl phenyl carbonate (8.7 mL, 46.95 mmol) by method A and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, as colorless solid (2.59 g, 69%); m.p. = 74-76 °C (Hex). IR (ATR): 3371m, 2979m,

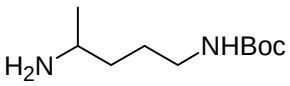
2933m, 1686s, 1528s, 1458w, 1391w, 1367m, 1325w, 1274m, 1250m, 1172s, 1057w, 991w, 909w, 861w, 815w, 783w, 723w, 627m, cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 5.04 (bs, H-N), 3.20-3.10 (m, 1H, -C*H*$_2$NHBoc), 3.05-2.95 (m, 1H, NH_2C*H*(CH_3)-), 2.95-2.85 (m, 1H, -C*H*$_2$NHBoc), 1.44 (s, 9H, -NHCOO-C(C*H*$_3$)$_3$), 1.34 (bs, 2H-N), 1.07 (d, 3H, *J* = 6.2, C*H*$_3$). ^{13}C-NMR(125 MHz, $CDCl_3$, δ): 156.19; 79.06; 48.46; 46.81; 28.33; 21.44. HRMS: *m/z* 175.14451 corresponds to molecular formula $C_8H_{18}N_2O_2H^+$ (error in ppm: + 2.30). Anal.($C_8H_{18}N_2O_2$ × 1/3 CH_2Cl_2) Calcd: C, 49.41; H, 9.29; N, 13.83. Found: C, 49.27; H, 9.09; N, 13.83.

***Tert*-butyl (3-aminobutyl)carbamate (S6).**



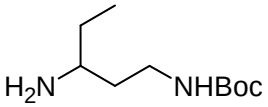
Compound **S6** was prepared by method A from 1,3-butandiamine (1.91 g, 21.55 mmol) and *tert*-butyl phenyl carbonate (8.0 mL, 43.11 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless viscous oil (2.96 g, 73%). IR (ATR): 3344w, 2973m, 2929w, 1686s, 1519m, 1452w, 1390w, 1364m, 1275m, 1249m, 1168s, 1041w, 1015w, 946w, 898w, 868w, 846w, 779w, 758w, 717w, 704w, 6814w, 659w, 644w, 596w, 578w, 566w, 539w, 530w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 5.04 (bs, 1H, -N*H*), 3.35-3.20 (m, 1H, -C*H*$_2$NHBoc), 3.20-3.05 (m, 1H, -C*H*$_2$NHBoc), 3.05-2.90 (m, 1H, NH_2C*H*(CH_3)-), 1.60-1.50 (m, 1H, $NH_2CH(CH_3)CH_2$-), 1.50-1.35 (m, 10H, $NH_2CH(CH_3)CH_2$-, -NHCOO-C(C*H*$_3$)$_3$), 1.31 (bs, 2H, -N*H*$_2$), 1.10 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.04; 78.82; 44.93; 39.33; 37.98; 28.29; 24.24. HRMS: *m/z* 189.15990 corresponds to molecular formula $C_8H_{20}N_2O_2H^+$ (error in ppm: + 0.79).

***Tert*-butyl (4-aminopentyl)carbamate (S7).**



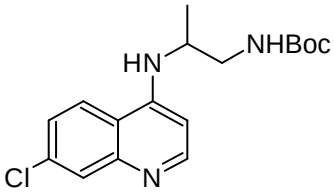
Compound **S7** was prepared by method A from 1,4-pentandiamine (3.00 g, 29.33 mmol) and *tert*-butyl phenyl carbonate (10.88 mL, 58.63 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless viscous oil (4.03 g, 68%). IR(ATR): 3256w, 2897s, 2844m, 1610w, 1571s, 1535s, 1449m, 1376m, 1331m, 1277w, 1263w, 1201w, 1050w, 1119w, 1079w, 904w, 876w, 851w, 806w, 767w, 735m, 703w, 645w, 623w, 597w, 559w, 532w, 510w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 5.00 (bs, H-N), 3.20-3.00 (m, 2H, -C*H*$_2$NHBoc), 3.00-2.85 (m, 1H, NH_2C*H*(CH_3)CH_2-), 2.04 (bs, H-N), 1.60-1.50 (m, 2H, -C*H*$_2$$CH_2$NHBoc 1.50-1.40 (m, 9H, -NHCOO-C(C*H*$_3$)$_3$), 1.40-1.30 (m, 2H, $NH_2CH(CH_3)CH_2$-), 1.08 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.88; 78.68; 46.45; 40.38; 36.69; 28.23; 26.71; 23.59. HRMS: *m/z*203.17601 corresponds to molecular formula $C_{10}H_{22}N_2O_2H^+$ (error in ppm: + 2.97).

***Tert*-butyl (3-aminopentyl)carbamate (S8).**



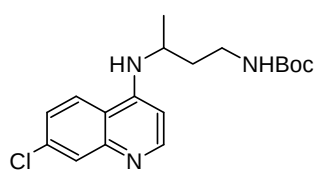
Compound **S8** was prepared by method A from 1,3-diaminopentane (4 mL, 33.47 mmol) and *tert*-butyl phenyl carbonate (12.5 mL, 66.94 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 sat.) = 95/5 as colorless solid (4.87 g, 72%); m.p. = 77-79 °C (Hex). IR (ATR): 3363m, 2966m, 2931m, 2876w, 1683s, 1524m, 1457w, 1389w, 1364m, 1328w, 1272m, 1248m, 1169s, 1042w, 1022w, 953w, 921w, 870w, 816w, 780w, 741w, 509w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 5.21 (bs, H-N), 3.40-3.25 (m, 1H, -C*H*$_2$NHBoc), 3.25-3.15 (m, 1H, -C*H*$_2$NHBoc), 2.75-2.65 (m, 1H, H_2NC*H*(CH_2CH_3)-), 5.34 (bs, 2H-N), 1.70-1.60 (m, 1H, -C*H*$_2$$CH_2$NHBoc), 1.50-1.40 (m, 10H, -C*H*$_2$$CH_3$, -NHCOO-C(C*H*$_3$)$_3$), 1.40-1.30 (m, 2H, -C*H*$_2$$CH_3$, -C*H*$_2$$CH_2$NHBoc), 0.92 (t, 3H, *J* = 7.4, -CH_2C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.04; 78.76; 51.07; 38.16; 36.70; 31.01; 28.33; 10.17. HRMS: *m/z*203.17540 corresponds to molecular formula $C_{10}H_{22}N_2O_2H^+$ (error in ppm: + 4.11). Anal.($C_{10}H_{22}N_2O_2$ × 2/3 H_2O) Calcd: C, 56.05; H, 10.97; N, 13.07. Found: C, 56.12; H, 10.47; N, 12.67.

***Tert*-butyl {2-[(7-chloroquinolin-4-yl)amino]propyl}carbamate (S9).**



Compound **S9** was prepared from 4,7-dichloroquinoline (3.18 g, 16.70 mmol) and mono-*N*-Boc-protected 1,2-diaminopropane **S5** (5.60 g, 32.14 mmol) by method B and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3 sat.) = 95/5 and flash chromatography (Biotage SP1 RP column, gradient: MeOH/H_2O = 6/4→7/3) as colorless solid (4.75 g, 88%); m.p. = 227-229 °C (Hex). IR (ATR): 3372s, 3187s, 2978s, 2933m, 1674s, 1612m, 1578s, 1537m, 1488w, 1452m, 1429w, 1380w, 1366w, 1335w, 1295m, 1252m, 1200w, 1172m, 1154m, 1082w, 1055w, 988w, 957w, 904w, 875w, 855w, 819w, 769w, 648w, 625w, 594w, 511w, 454w, 439w cm^{-1}. ^{1}H-NMR (500 MHz, CD_3OD, δ): 8.29 (d, *J* = 5.5, H-C(2)), 8.01 (d, *J* = 9.0, H-C(5)), 7.72 (d, *J* = 2.0, H-C(8)), 7.30 (dd, J_1 = 1.5, J_2= 9.0, H-C(6)), 6.54 (d, *J* = 5.5, H-C(3)), 3.95-3.80 (m, 1H, ArNHC*H*(CH_3)-), 3.35-3.25 (m, 1H, -C*H*$_2$NHBoc), 3.25-3.10 (m, 1H, -C*H*$_2$NHBoc), 1.36 (s, 9H, -NHCOO-C(C*H*$_3$)$_3$), 1.27 (d, 3H, *J* = 6.5, C*H*$_3$). ^{13}C-NMR (125 MHz, CD_3OD, δ): 159.33; 152.41; 152.13; 149.75; 136.34; 127.65; 125.96; 124.42; 118.76; 100.02; 80.40; 46.25; 28.86; 17.78. HRMS: *m/z* 336.14733 corresponds to molecular formula $C_{17}H_{22}ClN_3O_2H^+$ (error in ppm: - 0.41).Anal.($C_{17}H_{22}ClN_3O_2$) Calcd: C, 60.80; H, 6.60; N, 12.51. Found: C, 60.57; H, 6.70; N, 12.71.

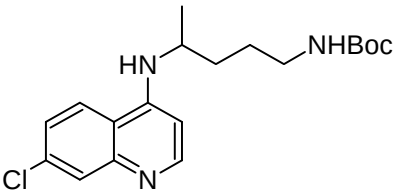
***Tert*-butyl {3-[(7-chloroquinolin-4-yl)amino]butyl}carbamate (S10).**



Compound **S10** was prepared by method Bfrom 4,7-dichloroquinoline (3.33 g, 16.81 mmol) and mono-*N*-Boc-

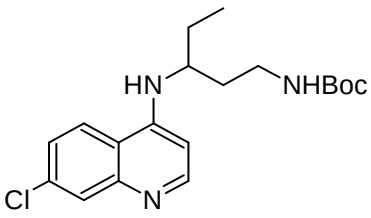
protected butane-1,3-diamine **S6**(3.82 g, 20.18 mmol) and was obtained after dry-flash chromatography SiO_2, gradient: CH_2Cl_2/MeOH(NH_3 sat.) = 95/5→8/2 as colorless solid (4.29 g, 73%); m.p. = 168-171 °C (Hex). IR (ATR): 3342m, 3192m, 2972m, 1677s, 1611m, 1579s, 1538m, 1488w, 1450w, 1434m, 1378w, 1366w, 1334w, 1284m, 1251w, 1228w, 1152m, 1131w, 1088w, 1066w, 1039w, 1017w, 985w, 956w, 930w, 885w, 855w, 808m, 764m, 737m, 645w, 624w, 600w, 576w, 551w, 515w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.4, H-C(2)), 7.94 (d, *J* = 2.1, H-C(8)), 7.78 (d, *J* = 7.6, H-C(5)), 7.35 (dd, J_1 = 2.2, J_2 = 9.0, H-C(6)), 6.39 (d, *J* = 5.4, H-C(3)), 5.36 (bs, H-N), 4.82 (bs, H-N), 3.85-3.75 (m, 1H, ArNHC*H*(CH_3)-), 3.35-3.27 (m, 1H, -C*H*$_2$NHBoc), 3.27-3.15 (m, 1H, -C*H*$_2$NHBoc), 2.00-1.80 (m, 2H, ArNHCH(CH_3)C*H*$_2$-), 1.45 (s, 9H, -NHCOO-C(C*H*$_3$)$_3$), 1.34 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.18; 151.91; 149.33; 148.93; 134.84; 128.74; 125.18; 121.29; 117.33; 99.10; 79.71; 46.46; 37.53; 36.83; 28.39; 20.20.HRMS: *m/z*350.16298 corresponds to molecular formula $C_{18}H_{24}ClN_3O_2H^+$ (error in ppm: + 0.87).Anal.($C_{18}H_{24}ClN_3O_2$× 3/2 H_2O) Calcd: C, 59.74; H, 7.06; N, 11.61. Found: C, 59.66; H, 7.00; N, 11.60.

***Tert*-butyl {4-[(7-chloroquinolin-4-yl)amino]pentyl}carbamate (S11).**



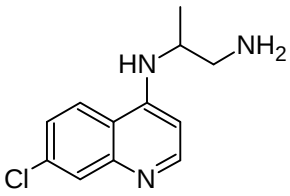
Compound **S11** was prepared by method B from 4,7-dichloroquinoline (881 mg, 4.45 mmol) and mono-*N*-Boc-protected pentane-1,4-diamine **S7** (1.80 g, 8.90 mmol) and was obtained after dry-flash chromatography SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5→8/2, as colorless solid (1.12 g, 69%); m.p. = 137-139 °C (Hex). IR (ATR): 3290w, 3183w, 2967w, 2925w, 2835w, 1677s, 1613w, 1570s, 1541m, 1492w, 1450w, 1438, 1432w, 1383w, 1364w, 1331w, 1294m, 1283m, 1254w, 1212w, 1165w, 1149m, 1105w, 1082w, 1068w, 1056w, 1026w, 978w, 912w, 900w, 878w, 863w, 852w, 819w, 805, 770w, 749w, 719w, 683w, 654w, 635w, 622w, 599w, 550w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.4, H-C(2)), 7.94 (d, *J* = 2.2, H-C(8)), 7.75 (d, *J* = 8.7, H-C(5)), 7.34 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.40 (d, *J* = 5.5, H-C(3)), 5.16 (bs, H-N), 4.66 (bs, H-N), 3.80-3.65 (m, 1H, ArNHC*H*(CH_3)-), 3.25-3.15 (m, 1H, -C*H*$_2$NHBoc), 3.15-3.05 (m, 1H, -C*H*$_2$NHBoc), 1.75-1.65 (m, 1H, ArNHCH(CH_3)C*H*$_2$-), 1.65-1.55 (m, 3H, ArNHCH(CH_3)C*H*$_2$-, -C*H*$_2$CH$_2$NHBoc), 1.45 (s, 9H, -NHCOO-C(C*H*$_3$)$_3$), 1.31 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.26; 151.97; 149.36; 148.92; 134.79; 128.79; 125.12; 121.17; 117.25; 79.41; 99.14; 48.43; 40.24; 33.22; 28.38; 27.28; 20.46. HRMS: *m/z* 364.17863 corresponds to molecular formula $C_{19}H_{26}ClN_3O_2H^+$ (error in ppm: - 2.43). Anal.($C_{19}H_{26}ClN_3O_2$ × 1/2 H_2O) Calcd: C, 61.20; H, 7.30; N, 11.27. Found: C, 60.76; H, 6.88; N, 11.46.

***Terc*-butyl 3-{ [(7-chloroquinolin-4-yl)amino]pentyl}carbamate (S12).**



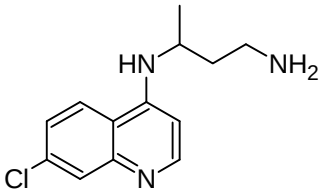
Compound **S12** was prepared by method B from 4,7-dichloroquinoline (4.08 g, 20.60 mmol) and mono-*N*-Boc-protected 1,3-diaminopentane **S8** (5.00 g, 24.72 mmol) and was obtained after dry-flash chromatography SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 and flash chromatography (Biotage SP1 RP column, eluent: MeOH/H_2O = 6/4) as colorless solid (7.82 g, 87%); m.p. = 58-60 °C (Hex). IR (ATR): 3325m, 2971m, 2932m, 2877w, 1687s, 1612w, 1574s, 1538m, 1453m, 1365m, 1332w, 1279m, 1248m, 1165m, 1147m, 1081w, 1042w, 903w, 853m, 805m, 766m, 643w, 599w, 496w cm^{-1}. ^{1}H-NMR (500 MHz, CD_3COOD, δ): 8.47 (d, *J* = 5.5, H-C(2)), 7.94 (d, *J* = 2.0, H-C(8)), 7.80 (d, *J* = 8.5, H-C(5)), 7.34 (dd, J_1 = 2.5, J_2 = 9.0, H-C(6)), 6.36 (d, *J* = 5.5, H-C(3)), 5.37 (bs, H-N), 4.95 (bs, H-N), 3.70-3.50 (m, 1H, ArNHC*H*(CH_2CH_3)-), 3.35-3.25 (m, 1H, -C*H*$_2$NHBoc), 3.25-3.10 (m, 1H, -C*H*$_2$NHBoc), 2.00-1.85 (m, 1H, -C*H*$_2$$CH_2$NHBoc), 1.85-1.70 (m, 1H, -C*H*$_2$$CH_2$NHBoc), 1.75-1.60 (m, 2H, -C*H*$_2$$CH_3$), 1.44 (s, 9H, -NHCOO-C(C*H*$_3$)$_3$), 0.98 (t, 3H, *J* = 7.5, -CH_2C*H*$_3$). ^{13}C-NMR (125 MHz, CD_3COOD, δ): 156.18; 151.85; 149.42; 149.30; 134.82; 128.64; 125.13; 121.29; 117.27; 98.98; 79.59; 52.17; 37.54; 34.18; 28.37; 27.12; 10.22. HRMS: *m/z*364.17865 corresponds to molecular formula $C_{19}H_{26}ClN_3O_2H^+$ (error in ppm: + 0.06). Anal. ($C_{19}H_{26}ClN_3O_2 \times 1/2\ H_2O$) Calcd: C, 61.20; H, 7.30; N, 11.27. Found: C, 61.20; H, 7.22; N, 11.43.

N^2-(7-Chloroquinolin-4-yl)propane-1,2-diamine (S13).



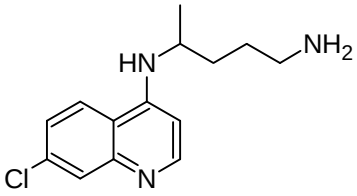
Compound **S13** was prepared by method C from **S9** (1.00 g, 2.98 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1→7/3 and flash chromatography (Biotage SP1 RP column, eluent: MeOH/H_2O = 6/4), asyellow powder softens at 158-159 °C. Yield: 646 mg (92%). IR (ATR): 3312s, 2966s, 2906s, 2157w, 1611m, 1580s, 1541m, 1491w, 1450m, 1426w, 1368w, 1329w, 1283w, 1250w, 1205w, 1171w, 1152w, 1133w, 1050w, 1034w, 1014w, 906w, 872w, 861w, 798m, 762w, 739w, 669w, 645w, 622w, 603w, 567w, 531w, 516w, 491w, 428w cm^{-1}. ^{1}H-NMR(200 MHz, $CDCl_3$/CD_3OD, δ): 8.38 (d, *J* = 5.6, H-C(2)), 7.91 (d, *J* = 9.0, H-C(8)) 7.87 (d, *J* = 2.2, H-C(5)), 7.34 (dd, J_1 = 2.3, J_2 = 8.9, H-C(6)), 6.41 (d, *J* = 5.6, H-C(3)), 3.95-3.85 (m, H, ArNHC*H*(CH_3)-), 3.00-2.90 (m, 2H, -C*H*$_2$$NH_2$), 1.35-1.25 (d, 3H, *J* = 6.0, C*H*$_3$). ^{13}C-NMR (50 MHz, CD_3OD, δ): 151.16; 149.81; 148.46; 134.99; 127.31; 125.03; 121.88; 117.28; 98.83; 45.72; 21.43; 17.17. HRMS: *m/z* 236.09395 corresponds to molecular formula $C_{12}H_{14}ClN_3H^+$ (error in ppm: - 4.03). Anal. ($C_{12}H_{14}ClN_3 \times 1/3\ CH_2Cl_2$) Calcd: C, 56.11; H, 5.60; N, 15.92. Found: C, 55.75; H, 5.60; N, 15.58.

N^3-(7-Chloroquinolin-4-yl)butane-1,3-diamine (S14).



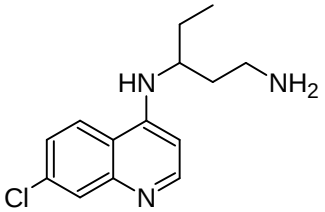
Compound **S14** was prepared by method Cfrom **S10** (650 mg, 1.86 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5→8/2, as colorless powder softens at 106-108 °C. Yield: 353 mg (76%). IR (ATR): 3243m, 2969m, 2927m, 2866w, 1609m, 1569s, 1537m, 1487w, 1448m, 1426m, 1365m, 1329m, 1279w, 1244w, 1198w, 1145m, 1078w, 873w, 854m, 806m, 766w, 731m, 701w, 643w, 622w, 596w, 571w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.4, H-C(2)), 7.91 (d, *J* = 2.1, H-C(8)), 7.72 (d, *J* = 9.0, H-C(5)), 7.30 (dd, *J* = 2.1, *J* = 9.0, H-C(6)), 7.22 (bs, H-N), 6.37 (d, *J* = 5.4, H-C(3)), 3.95-3.80 (m, 1H, ArNHC*H*(CH_3)-), 3.15-3.05 (m, 1H, -C*H*$_2$$NH_2$), 3.05-2.90 (m, 1H, -C*H*$_2$$NH_2$), 1.95-1.80 (m, 1H, -C*H*$_2$$CH_2NH_2$), 1.80-1.70 (m, 1H, -C*H*$_2$$CH_2NH_2$), 1.63 (bs, 2H-N), 1.32 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 151.94; 149.55; 149.33; 134.61; 128.52; 124.84; 121.94; 117.65; 98.58; 48.05; 38.64; 37.65; 19.27. HRMS: *m/z* 250.11106 corresponds to molecular formula $C_{13}H_{16}ClN_3H^+$ (error in ppm: + 2.04). Anal. ($C_{13}H_{16}ClN_3$ × 1/3 CH_2Cl_2) Calcd: C, 61.05; H, 6.57; N, 16.43. Found: C, 61.35; H, 6.34; N, 16.18.

N^4-(7-Chloroquinolin-4-yl)pentane-1,4-diamine (S15).



Compound **S15** was prepared by method Cfrom **S11** (300 mg, 0.86 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5→8/2, as colorless powder softens at132-136 °C. Yield: 176 mg (81%). IR (ATR): 3238m, 3063w, 2968w, 2932m, 2851w, 1568w, 1570s, 1491w, 1452m, 1423m, 1384w, 1363w, 1329w, 1280w, 1251w, 1200w, 1156w, 1128w, 1084w, 941w, 903w, 869w, 842w, 818w, 796m, 771w, 700w, 682w, 643w, 621w, 598w, 561w, 534w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.4, H-C(2)), 7.94 (d, *J* = 2,2, H-C(8)), 7.70 (d, *J* = 9.0, H-C(5)), 7.33 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.45-6.35 (m, H-C(3)), 5.42 (d, *J* = 6.7, H-N), 3.75-3.65 (m, 1H, ArNHC*H*(CH_3)-), 2.80-2.70 (m, 2H, -C*H*$_2$$NH_2$), 1.85-1.65 (m, 2H, -ArNHCH(CH_3)C*H*$_2$-), 1.65-1.50 (m, 2H, -C*H*$_2$$CH_2NH_2$), 1.32 (d, 3H, *J* = 6.2, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.02; 149.41; 149.03; 134.72; 128.85; 125.01; 121.13; 117.34; 99.14; 48.28; 41.80; 33.83; 29.57; 20.21. HRMS: *m/z* 264.12589 corresponds to molecular formula $C_{14}H_{18}ClN_3H^+$ (error in ppm: - 1.19). Anal.($C_{14}H_{18}ClN_3$) Calcd: C, 63.75; H, 6.88; N, 15.93. Found: C, 63.59; H, 6.80; N, 15.96.

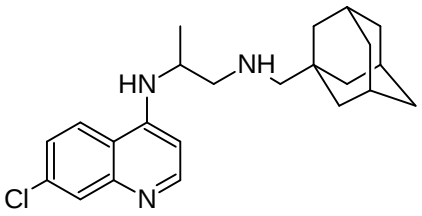
N^3-(7-chloroquinolin-4-yl)pentane-1,3-diamine (S16).



Compound **S16** was prepared by method C from **S12** (540 mg, 1.37 mmol) and was obtained after dry-flash chromatography SiO_2,

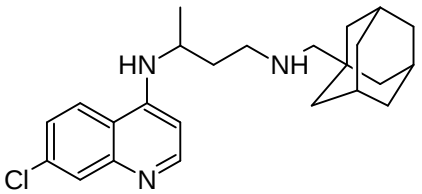
gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1→7/3 and flash chromatography (Biotage SP1 RP column, eluent: MeOH/H_2O = 65/35) asyellow powder softens at 142-144 °C. Yield: 318 mg (88%). IR (ATR): 3265m, 2898s, 2844s, 1610w, 1573s, 1536m, 1486w, 1448m, 1427w, 1366w, 1330w, 1282w, 1263w, 1247w, 1201w, 1136w, 1096w, 1078w, 903w, 876w, 853m, 804m, 763w, 736m, 702w, 644w, 622w, 600w, 539w, 499w, 456w, 429w, 407w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.4, H-C(2)), 7.92 (d, *J* = 2.2, H-C(8)), 7.72 (d, *J* = 8.9, H-C(5)), 7.32 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.92 (d, *J* = 5.4, H-N), 6.36 (d, *J* = 5.5, H-C(3)), 3.75-3.65 (m, 1H, ArNHC*H*-), 3.10-3.00 (m, 1H, -C$H_2$$NH_2$), 3.00-2.90 (m, 1H, -C$H_2$$NH_2$), 1.95-1.85 (m, 1H, -C$H_2$$CH_2NH_2$), 1.85-1.70 (m, 2H, -C$H_2$$CH_2NH_2$, -C$H_2$$CH_3$), 1.70-1.60 (m, 1H, -C$H_2$$CH_3$), 1.41 (s, 2H-N), 0.98 (t, 3H, *J* = 7.4, -CH_2CH_3). ^{13}C-NMR (125 MHz, CD_3OD, δ): 152.03; 149.73; 149.47; 134.61; 128.68; 124.84; 121.75; 117.59; 98.58; 53.75; 38.64; 34.83; 26.16; 10.30. HRMS: *m/z* 264.12636 corresponds to molecular formula $C_{14}H_{18}ClN_3H^+$ (error in ppm: + 0.59). Anal.($C_{14}H_{18}ClN_3$) Calcd: C, 63.75; H, 6.88; N, 15.93. Found: C, 63.46; H, 6.98; N, 15.74.

N^1-(1-Adamantylmethyl)-N^2-(7-chloroquinolin-4-yl)propane-1,2-diamine (9).



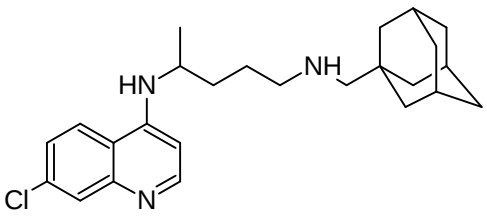
Compound **9** was prepared by method Dfrom amine **S13** (254 mg, 1.08 mmol) and adamantane-1-carboxaldehyde (177 mg, 1.08 mmol) using $NaBH(OAc)_3$ (458 mg, 2.16 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 100/2, as colorless foam (343 mg, 83%)softens at 153-155 °C. IR (ATR): 3230m, 2897m, 9842w, 2804m, 1612w, 1586s, 1541m, 1488w, 1447m, 1370w, 1352w, 1332w, 1308w, 1282w, 1242w, 1198w, 1153m, 1138m, 1110w, 1097w, 1073w, 1029w, 1007w, 986m, 948w, 897w, 874w, 860w, 852w, 835m, 794m, 759m, 718w, 562w, 633w, 610m, 501m, 475w, 443w, 425w, 403w cm^{-1}. λ_{max}(ε) = 330 (10259), 254 (15366), 237 (13922) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.0, H-C(2)), 7.94 (d, *J* = 1.5, H-C(8)), 7.72 (d, *J* = 9.0, H-C(5)), 7.34 (dd, J_1 = 1.8, J_2 = 8.8, H-C(6)), 6.42 (d, *J* = 5.0, H-C(3)), 6.08 (d, *J* = 5.0, H-N), 3.75-3.65 (m, 1H, ArNHC*H*(CH_3)-), 2.90-2.80 (d, 2H, ArNHCH(CH_3)CH_2-), 2.32 (ABq, H_A, *J* = 11.5, -CH_2Ad), 2.24 (ABq, H_B, *J* = 11.5, -CH_2Ad), 1.95 (bs, 3H, -Ad), 1.75-1.55 (m, 6H, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.29 (d, 3H, *J* = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 151.94; 149.41; 149.26; 134.68; 128.64; 125.02; 121.28; 117.70; 99.45; 62.60; 55.14; 47.20; 40.83; 37.14; 33.61; 28.35; 18.07. HRMS: *m/z* 384.21930 corresponds to molecular formula $C_{23}H_{30}ClN_3H^+$(error in ppm: - 2.09). Anal. ($C_{23}H_{30}ClN_3$ ×1/2 H_2O) Calcd: C, 70.30; H, 7.95; N, 10.69. Found: C, 70.62; H, 7.90; N, 10.85. HPLC purity (λ = 330 nm): method A: RT 7.846 min, area 98.53%; method B: RT 9.628 min, area 98.46%.

N^1-(1-Adamantylmethyl)-N^3-(7-chloroquinolin-4-yl)butane-1,3-diamine (23).



Compound **23** was prepared by method E from amine **S14** (430 mg, 1.72 mmol) and adamantane-1-carboxaldehyde (283 mg, 1.72 mmol) using AcOH (141 μL, 2.15 mmol) and $NaBH_4$ (390 mg, 10.32 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, as colorless foam (610 mg, 89%)softens at 135-138 ^oC. IR(ATR): 3250m, 3061w, 2962w, 2897s, 2842m, 1611w, 1570s, 1542m, 1490w, 1450m, 1430m, 1365m, 1345w, 1330m, 1283w, 1253w, 1206w, 1184w, 1136w, 1079w, 928w, 901w, 870m, 850m, 821w, 801m, 770w, 756m, 637w, 612w, 602w, 502w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 326 (10000), 254 (16260) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.49 (d, *J* = 5.4, H-C(2)), 7.92 (d, *J* = 2.0, H-C(8)), 7.80 (d, *J* = 8.9, H-C(5)), 7.35-7.20 (m, H-C(6)), 7.08 (d, *J* = 5.1, H-N), 6.40 (d, *J* = 5.4, H-C(3)), 3.90-3.80 (m, 1H, ArNHC*H*(CH_3)-), 2.95-2.85 (m, 1H, -C*H*$_2$NHCH_2Ad), 2.85-2.70 (m, 1H, -C*H*$_2$NHCH_2Ad), 2.30 (s, 2H, -C*H*$_2$Ad), 2.01 (s, 3H, -Ad), 1.95-1.85 (m, 1H, ArNHCH(CH_3)C*H*$_2$-), 1.85-1.65 (m, 7H, ArNHCH(CH_3)C*H*$_2$-, -Ad), 1.65-1.50 (m, 7H, -Ad, *H*-N-), 1.32 (d, 3H, *J* = 6.3, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.05; 149.61; 149.40; 134.59; 128.60; 124.54; 122.30; 117.67; 98.90; 63.68; 48.32; 47.81; 41.16; 37.17; 35.22; 33.36; 28.43; 19.36. HRMS: *m/z* 398.23673 corresponds to molecular formula $C_{24}H_{32}ClN_3H^+$ (error in ppm: + 2.45). Anal. ($C_{24}H_{32}ClN_3 \times 1/2H_2O$) Calcd: C, 70.83; H, 8.17; N, 10.32. Found: C, 70.71; H, 7.91; N, 10.53. HPLCpurity (λ = 330 nm): method A: RT 7.989 min, area 99.68%; method B: RT 9.636 min, area 99.31%.

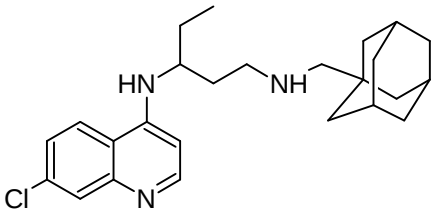
***N*^{1}-(1-Adamantylmethyl)-*N*^{4}-(7-chloroquinolin-4-yl)pentane-1,4-diamine (29).**



Compound **29** was prepared by method E from amine **S15** (75 mg, 0.28 mmol) and adamantane-1-carboxaldehyde (47 mg, 0.28 mmol) using AcOH (120 μL, 0.35 mmol) and $NaBH_4$ (64 mg, 1.68 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3) as colorless foam (94 mg, 80%)softens at 131-132 °C. IR (ATR): 3256w, 2897s, 2844m, 1610w, 1571s, 1535m, 1449m, 1377m, 1331m, 1277w, 1263w, 1201w, 1150m, 1119w, 1079w, 904w, 876w, 851w, 806m, 767w, 735m, 702w, 645w, 623w, 597w, 559w, 532w, 510w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 329 (11176), 255 (16882) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.4, H-C(2)), 7.94 (d, *J* = 2.1, H-C(8)), 7.70 (d, *J* = 9.0, H-C(5)), 7.32 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.41 (d, *J* = 5.5, H-C(3)), 5.29 (d, *J* = 7.0, H-N), 3.80-3.65 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.55 (m, 2H, -C*H*$_2$NHCH_2Ad), 2.24 (s, 2H, -C*H*$_2$Ad), 1.97 (s, 3H, -Ad), 1.85-1.60 (m, 10H, ArNHCH(CH_3)C*H*$_2$-, -C*H*$_2$CH_2NHCH_2Ad, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.32 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ):

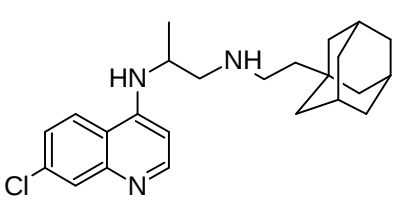
152.02; 151.10; 148.96; 134.35; 128.87; 124.99; 121.13; 117.29; 99.22; 62.69; 50.14; 48.36; 41.00; 37.19; 33.77; 33.37; 28.44; 26.12; 20.25. HRMS: *m/z* 412.25177 corresponds to molecular formula $C_{25}H_{34}ClN_3H^+$ (error in ppm: + 0.89). Anal. ($C_{25}H_{34}ClN \times 1/2H_2O$) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.13; H, 8.11; N, 9.99. HPLC purity (λ = 330 nm): method A: RT 8.010 min, area 97.89%; method B: RT 9.514 min, area 95.43%.

N^1-(1-Adamantylmethyl)-N^3-(7-chloroquinolin-4-yl)pentane-1,3-diamine (27).



Compound **27** was prepared by method D from amine **S16** (51 mg, 0.19 mmol) and 1-adamantylacetaldehyde(32 mg, 0.19 mmol) using $NaBH(OAc)_3$ (80 mg, 0.38 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 100/4, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3) as yellow foam (54 mg, 68%),softens at 121-123 °C. IR (ATR): 3242m, 3063w, 2928m, 2869w, 1661w, 1610w, 1570s, 1541m, 1490w, 1452m, 1426m, 1366m, 1329m, 1283w, 1250m, 1200w, 1143m, 1127m, 1080m, 1005w, 978w, 903w, 874w, 852m, 804m, 869m, 641w, 622w, 599w, 528w, 497m, 447w, 426w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.4, H-C(2)), 7.92 (d, *J* = 2.0, H-C(8)), 7.80 (d, *J* = 9.0, H-C(5)), 7.26 (dd, J_1 = 2.1, J_2 = 8.8, H-C(6)), 6.82 (d, *J* = 6.0, H-N), 6.38 (d, *J* = 5.8, H-C(3)), 3.70-3.60 (m, 1H, ArNHC*H*(CH_2CH_3)-), 2.87-2.78 (m, 1H, -C*H*$_2$NHCH_2Ad), 2.78-2.70 (m, 1H, -C*H*$_2$NHCH_2Ad), 2.30 (ABq, H_A, *J* = 11.6, -C*H*$_2$Ad), 2.24 (ABq, H_B, *J* = 11.6, -C*H*$_2$Ad), 2.00 (m, 3H, -Ad), 1.95-1.85 (m, 1H, -C*H*$_2$CH$_2$NHCH_2Ad), 1.85-1.60 (m, 9H, -Ad, -C*H*$_2$CH$_3$, -C*H*$_2$CH$_2$NHCH_2Ad), 1.60-1.50 (m, 6H, -Ad), 0.97 (t, 3H, *J* = 7.5, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.02; 149.79; 149.42; 134.59; 128.61; 124.55; 122.12; 117.59; 98.84; 63.62; 54.00; 47.75; 41.11; 37.15; 33.33; 32.17; 28.41; 26.15; 10.31. HRMS: *m/z*412.25140 corresponds to molecular formula $C_{25}H_{34}ClN_3H^+$ (error in ppm: - 0.31).Anal.($C_{25}H_{34}ClN_3 \times 1/2H_2O$) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.52; H, 7.88; N, 10.15. HPLC purity (λ = 330 nm): method A: RT 8.009 min, area 98.18%; method B: RT 9.508 min, area 97.79%.

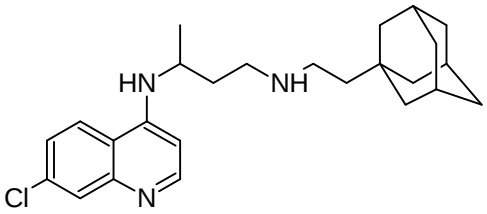
N^1-[2-(1-Adamantyl)ethyl]-N^2-(7-chloroquinolin-4-yl)propane-1,2-diamine (33).



Compound **33** was prepared by method D from amine **S13** (180 mg, 0.76 mmol) and 1-adamantylacetaldehyde(136 mg, 0.76 mmol) using $NaBH(OAc)_3$ (58 mg, 1.52 mmol) and was obtained after dry-flash chromatography: SiO_2 eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 RP column, gradient: MeOH/H_2O = 7/3→9/1) as colorless solid (227 mg, 75%),softens at 46-47 °C. IR (ATR): 3252m, 3063w, 2896s, 2843m, 1610w, 1573s, 1537m, 1447m, 1426w, 1376m, 1330m, 1279w, 1241w, 1205w, 1134m, 1078w, 966w, 901w, 870m, 843w, 805m, 763m,

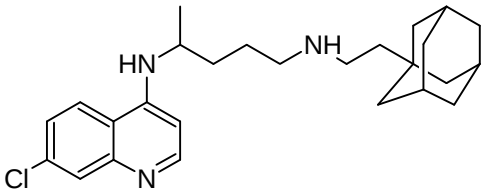
645w, 623w, 600w, 540w, 513w, 490w, 421w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 327 (10189), 253 (16143) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.5, H-C(2)), 7.92 (d, *J* = 1.0, H-C(8)), 7.74 (d, *J* = 9.0, H-C(5)), 7.32 (dd, J_1 = 1.8, J_2 = 8.8, H-C(6)), 6.40 (d, *J* = 5.5, H-C(3)), 5.90 (bs, H-N), 3.75-3.65 (m, 1H, ArNHC*H*(CH_3)-), 2.95-2.85 (m, 2H,ArNHCH(CH_3)CH_2-), 2.70-2.60 (m, 2H, -C$H_2$$CH_2$Ad), 1.92 (bs, 3H, -Ad), 1.75-1.55 (m, 6H, -Ad), 1.48 (bs, 6H, -Ad), 1.35-1.20 (m, 6H, -CH_2Ad, CH_3, *H*-N-). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 151.82; 149.31; 149.13; 134.75; 128.46; 125.04; 121.44; 117.55; 99.31; 54.36, 47.41; 44.59; 44.44; 42.62; 37.03; 31.86; 28.58; 18.11. HRMS: *m/z* 398.23435 corresponds to molecular formula $C_{24}H_{32}ClN_3H^+$ (error in ppm: - 3.51). Anal.($C_{24}H_{32}ClN_3 \times 1/2\ H_2O$) Calcd: C, 70.83; H, 8.17; N, 10.32. Found: C, 70.44; H, 7.91; N, 10.27. HPLC purity (λ = 330 nm): method A: RT 7.891 min, area 97.79%; method B: RT 9.904 min, area 95.06%.

N^1-[2-(1-Adamantyl)ethyl]-N^3-(7-chloroquinolin-4-yl)butane-1,3-diamine (36).



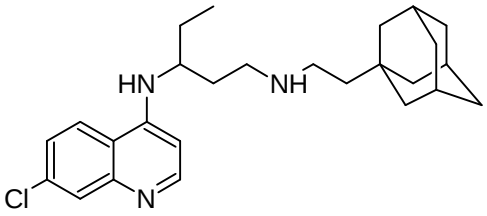
Compound **36** was prepared by method E from amine **S14** (90 mg, 0.36 mmol) and 1-adamantylacetaldehyde (64.3 mg, 0.36 mmol) using AcOH (26 µL, 0.45 mmol) and $NaBH_4$ (82 mg, 2.16 mmol) and was obtained after multiple chromatography: dry-flash: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 6/4) as colorless foam (596 mg, 77%),softens at 62-64 °C. IR (ATR): 3219w, 2897s, 2843m, 1737m, 1610w, 1573s, 1538m, 1448m, 1427w, 1368m, 1330m, 1280w, 1242m, 1199w, 1149m, 1077w, 1046w, 976w, 849m, 804m, 764w, 716w, 644w, 604w, 518w, 505w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 328 (10358), 254 (16434) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.47 (d, *J* = 5.4, H-C(2)), 7.91 (d, *J* = 2.2, H-C(8)), 7.87 (d, *J* = 4.5, H-N), 7.75 (d, *J* = 9.0, H-C(5)), 7.29 (dd, J_1 = 2.2, J_2 = 9.0, H-C(6)), 6.34 (d, *J* = 5.6, H-C(3)), 3.90-3.80 (m, 1H, ArNHC*H*(CH_3)-), 3.05-2.95 (m, 1H, -CH_2NHC$H_2$$CH_2$Ad), 2.85-2.75 (m, 1H, -CH_2NHC$H_2$$CH_2$Ad-), 2.70-2.60 (m, 2H, -C$H_2$$CH_2$Ad), 2.00-1.90 (m, 4H, ArNHCH(CH_3)CH_2-, -Ad), 2.00-1.90 (m, 7H, ArNHCH(CH_3)CH_2-, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.40-1.30 (m, 2H, -CH_2Ad), 1.32 (d, 3H, *J* = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.01; 149.81; 149.40; 134.53; 128.52; 124.54; 122.41; 117.84; 98.51; 48.45; 46.40; 44.98; 44.50; 42.70; 37.09; 34.83; 31.87; 28.62; 19.05. HRMS: *m/z* 398.23435 corresponds to molecular formula $C_{25}H_{34}ClN_3H^+$ (error in ppm: - 1.75). Anal.($C_{25}H_{34}ClN_3 \times 1/2\ H_2O$) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.11; H, 8.07; N, 10.08. HPLC purity (λ = 330 nm):method A: RT 8.535 min, area 98.59%; method B: RT 9.910 min, area 95.42%.

N^1-[2-(1-Adamantyl)ethyl]-N^4-(7-chloroquinolin-4-yl)pentane-1,4-diamine (42).



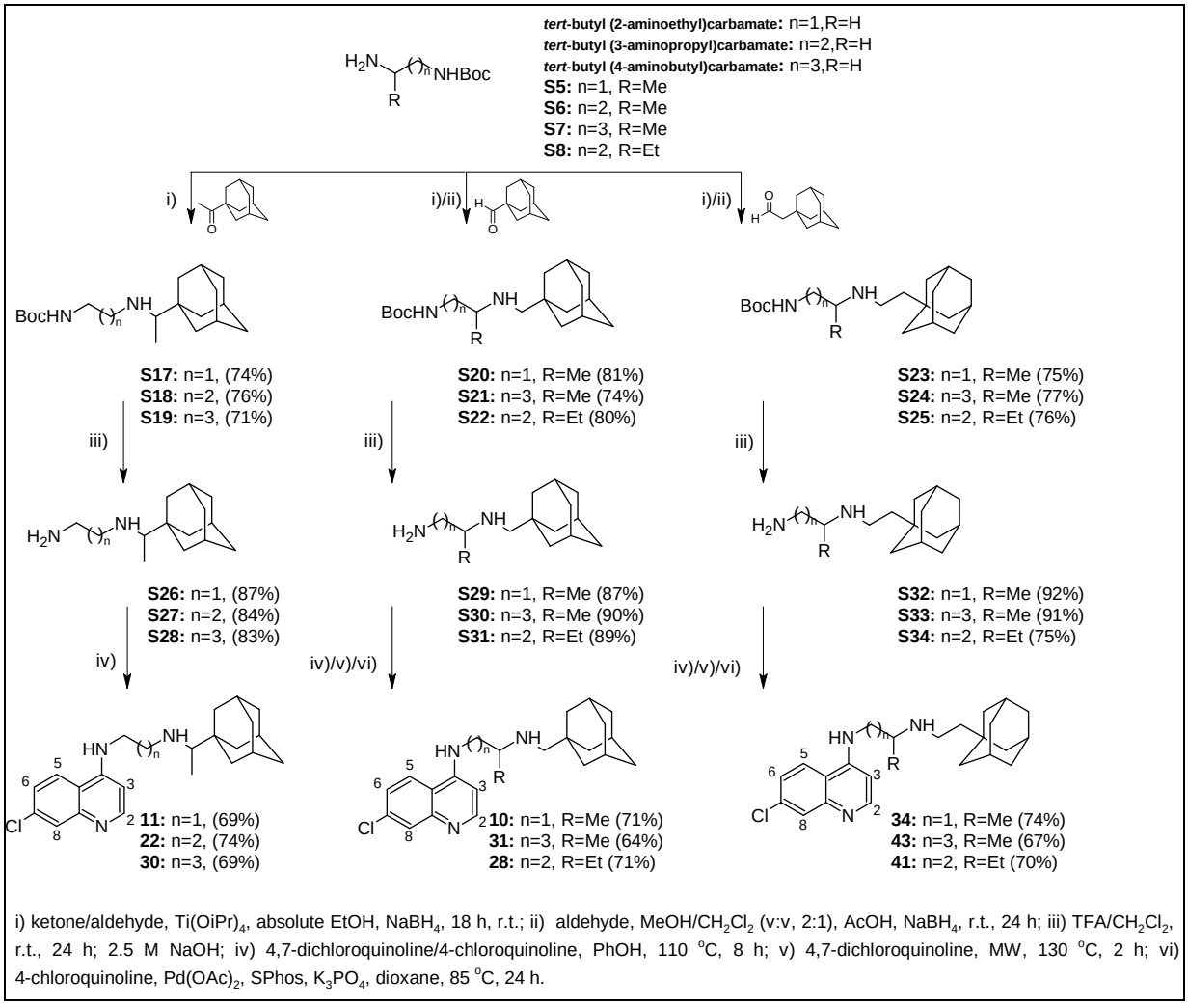
Compound **42** was prepared by method E from amine **S15** (320 mg, 1.21 mmol) and 1-adamantylacetaldehyde (216 mg, 1.21 mmol) using AcOH (86 µL, 1.51 mmol) and $NaBH_4$ (92 mg, 2.42 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1, as colorless foam (314 mg, 61%)softens at 49-51 °C. IR (ATR): 3422m, 2901s, 2845m, 1611w, 1578s, 1540w, 1450m, 1426w, 1379w, 1332w, 1280w, 1253w, 1201w, 1150w, 1081w, 905w, 877w, 854w, 806w, 768w, 646w, 601w, 401w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 328 (11161), 255 (17040) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.4, H-C(2)), 7.93 (d, *J* = 2.1, H-C(8)), 7.73 (d, *J* = 9.0, H-C(5)), 7.33 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.39 (d, *J* = 5.5, H-C(3)), 5.52 (bs, H-N), 3.75-3.60 (m, 1H, ArNHC*H*(CH_3)-), 2.75-2.65 (m, 2H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.65-2.55 (m, 2H, -C*H*$_2$CH$_2$Ad), 1.93 (bs, 3H, -Ad), 1.85-1.75 (m, 1H, ArNHCH(CH_3)C*H*$_2$-), 1.75-1.50 (m, 10H, ArNHCH(CH_3)C*H*$_2$-, -C*H*$_2$CH$_2$NHCH$_2$CH$_2$Ad, -Ad, *H*-N-), 1.45 (m, 6H, -Ad), 1.35-1.25 (m, 5H, C*H*$_3$, -C*H*$_2$Ad). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 151.95; 149.32; 149.11; 134.72; 128.68; 124.96; 121.35; 117.35; 99.12; 49.57; 48.30; 44.48; 44.33; 42.60; 37.08; 34.05; 31.82; 28.61; 26.33; 20.16. HRMS: *m/z* 426.26752 corresponds to molecular formula $C_{26}H_{36}ClN_3H^+$ (error in ppm: + 1.10). Anal.($C_{26}H_{36}ClN_3 \times 3/2\ H_2O$) Calcd: C, 68.93; H, 8.68; N, 9.27. Found: C, 69.08; H, 9.04; N, 9.48. HPLCpurity (λ = 330 nm): method A: RT 8.000 min, area 95.37%; method B: RT 9.821 min, area 95.54%.

***N*^{1}-[2-(1-Adamantyl)ethyl]-*N*^{3}-(7-chloroquinolin-4-yl)pentane-1,3-diamine (40).**

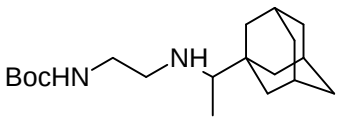


Compound **40** was prepared by method Dfrom amine **S16** (157 mg, 0.60 mmol) and 1-adamantylacetaldehyde(106 mg, 0.60 mmol) using $NaBH(OAc)_3$ (254 mg, 1.20 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 6/4) as colorless foam (171 mg, 67%),softens at 121-123 °C. IR (ATR): 3236m, 2897s, 2843m, 1610w, 1573s, 1538m, 1488w, 1448m, 1428m, 1366m, 1330m, 1281w, 1245w, 1198w, 1166w, 1141m, 1078w, 901w, 876w, 852m, 804m, 763w, 735m, 701w, 643w, 599w, 539w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.45 (d, *J* = 5.4, H-C(2)), 7.91 (d, *J* = 2.2, H-C(8)), 7.67 (d, *J* = 8.9, H-C(5)), 7.76 (d, *J* = 5.6, H-N), 7.29 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.32 (d, *J* = 5.8, H-C(3)), 3.61 (m, 1H, ArNHC*H*(CH_2CH_3)-), 3.00-2.90 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.85-2.75 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.65-2.55 (m, 2H, -C*H*$_2$CH$_2$Ad), 2.00-1.85 (m, 4H, -Ad, -C*H*$_2$CH$_2$NHCH$_2$CH$_2$Ad), 1.85-1.75 (m, 2H, -C*H*$_2$CH$_3$, -C*H*$_2$CH$_2$NHCH$_2$CH$_2$Ad), 1.75-1.55 (m, 7H, -Ad, -C*H*$_2$CH$_3$), 1.40-1.30 (m, 2H, -C*H*$_2$Ad), 0.97

(t, J = 7.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 151.91; 149.97; 149.36; 134.56; 128.43; 124.55; 122.30; 117.74; 98.46; 54.19; 46.53; 44.87; 44.49; 42.65; 37.06; 31.83; 31.62; 28.59; 25.79; 10.33. HRMS: *m/z* 426.26855 corresponds to molecular formula $C_{26}H_{36}ClN_3H^+$ (error in ppm: + 3.51). Anal. ($C_{26}H_{36}ClN_3 \times H_2O$) Calcd: C, 70.32; H, 8.63; N, 9.46. Found: C, 70.71; H, 8.48; N, 9.24. HPLC purity (λ = 330 nm): method A: RT 8.003 min, area 98.19%; method B: RT 9.862 min, area 96.49%.



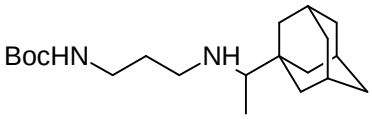
tert-Butyl (2-{[1-(1-adamantyl)ethyl]amino}ethyl)carbamate (S17).



Compound **S17** was prepared by method G from tert-butyl (2-aminoethyl)carbamate(330 mg, 2.06 mmol) and 1-(1-adamantyl)ethanone(306 mg, 1.72 mmol) using $Ti(OiPr)_4$ (610 µL, 2.06 mmol) and $NaBH_4$ (130 mg, 3.44 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent:CH_2Cl_2/MeOH(NH_3sat.) = 95/5, as colorless oil (410 mg, 74%). IR (ATR): 3346m, 2973w, 2899s, 2846s, 1689s, 1518m, 1449m, 1390w, 1364m, 1345w, 1315w, 1271m, 1248m, 1153s, 1040w, 1015w, 991w, 926w, 863w, 812w, 777w, 758w, 736w, 700w, 667w, 637w, 627w, 618w, 600w, 562w, 555w, 541w, 522w, 509w, 503w

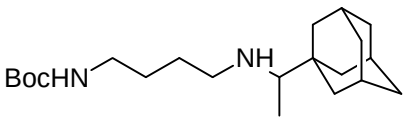
cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 4.96 (bs, H-N), 3.25-3.10 (m, 2H, -C*H*$_2$NHBoc), 2.90-2.80 (m, 1H, -C*H*$_2$CH$_2$NHBoc), 2.65-2.50 (m, 1H, -C*H*$_2$CH$_2$NHBoc), 2.05-2.00 (m, 1H,-C*H*(CH$_3$)Ad), 1.97 (bs, 3H, -Ad), 1.75-1.40 (m, 21H, -Ad, -NHCOO-C(C*H*$_3$)$_3$), 0.94 (d, *J* = 6.5, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.18; 79.02; 62.01; 47.84; 40.61; 38.67; 37.34; 36.14; 28.56; 28.43; 13.55. HRMS: *m/z* 323.26854 corresponds to molecular formula $C_{19}H_{34}N_2O_2H^+$ (error in ppm: - 2.38).

***tert*-Butyl (3-{[1-(1-adamantyl)ethyl]amino}propyl)carbamate (S18).**



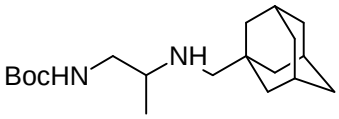
Compound **S18** was prepared by method Gfrom tert-butyl (3-aminopropyl)carbamate (380 mg, 2.18 mmol) and 1-(1-adamantyl)ethanone (325 mg, 1.85 mmol), using Ti(OiPr)$_4$ (645 µL, 2.18 mmol) and $NaBH_4$ (140 mg, 3.70 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (475 mg, 76%). IR(ATR): 3313m, 2903s, 2847s, 2676w, 1574m, 1450m, 1362w, 1344w, 1316w, 1248w, 1103w, 1012w, 974w, 934w, 815w, 735w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 5.88 (bs, H-NBoc), 3.35-2.40 (m, 4H, -C*H*$_2$NHBoc, -C*H*$_2$NHCH(CH$_3$)Ad), 2.10-2.20 (m, 1H,-(CH$_3$)C*H*Ad), 1.98 (m, 3H, -Ad), 1.75-1.40 (m, 23H, -Ad, -NHCOO-C(C*H*$_3$)$_3$, -CH$_2$C*H*$_2$CH$_2$NHBoc), 0.95 (d, *J* = 6.6, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.16, 78.64; 62.61; 47.47; 40.36; 38.69, 37.30; 36.09, 29.56; 28.56; 28.45; 13.19. HRMS: *m/z*337.28334 corresponds to molecular formula $C_{20}H_{36}N_2O_2H^+$ (error in ppm: - 4.79).

***tert*-Butyl (4-{[1-(1-adamantyl)ethyl]amino}butyl)carbamate (S19).**



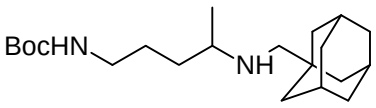
Compound **S19** was prepared by method G from tert-butyl (4-aminobutyl)carbamate(231 mg, 1.23 mmol) and 1-(1-adamantyl)ethanone (110 mg, 0.61 mmol) using Ti(OiPr)$_4$ (364 µL, 2.23 mmol) and $NaBH_4$ (45 mg, 1.22 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (152 mg, 71%). IR (ATR): 3330m, 2971w, 2900s, 2846m, 1692s, 1520m, 1449m, 1389w, 1364m, 1345w, 1315w, 1271w, 1248m, 1171s, 1118w, 1066w, 1039w, 993w, 870w, 781w, 735w, 702w, 670w, 654w, 647w, 640w, 595w, 589w, 561w, 548w, 511w, 503w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 4.99 (bs, H-N), 3.20-2.05 (m, 2H, -C*H*$_2$NHBoc), 2.80-2.65 (m, 1H, -C*H*$_2$NHCH(CH$_3$)Ad), 2.50-2.40 (m, 1H, -C*H*$_2$NHCH(CH$_3$)Ad), 2.10-2.00 (m, 2H, -C*H*(CH$_3$)Ad), 1.97 (m, 3H, -Ad), 1.75-1.40 (m, 25H, -Ad, -C*H*$_2$CH$_2$NHBoc, -C*H*$_2$CH$_2$CH$_2$NHBoc, -NHCOO-C(C*H*$_3$)$_3$), 0.94 (d, 3H, *J* = 6.5, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.98; 78.79; 62.49; 48.34; 40.48; 38.65; 37.30; 35.96; 28.52; 28.39; 27.83; 27.71; 13.40. HRMS: *m/z*351.30112 corresponds to molecular formula $C_{21}H_{38}N_2O_2H^+$ (error in ppm: + 1.48).

***tert*-Butyl {2-[(1-adamantylmethyl)amino]propyl}carbamate (S20).**



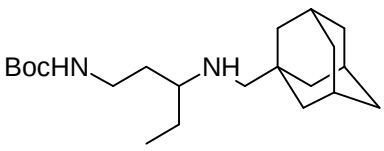
Compound **S20** was prepared by method Efrom mono-*N*-Boc-protected amine **S5** (340 mg, 1.95 mmol) and adamantane-1-carboxaldehyde (320 mg, 1.95 mmol) using AcOH (139 µL, 2.4 mmol) and $NaBH_4$ (443 mg, 11.7 mol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (509 mg, 81%). IR (ATR): 3355m, 2972w, 2897s, 2845m, 1694s, 1500m, 1450m, 1390w, 1364m, 1345w, 1248m, 1165s, 1103w, 986m, 908w, 865w, 777w, 751w, 644w, 620w, 576w, 556w, 545w, 520w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 4.99 (bs, H-N), 3.20-3.10 (m, 1H, -C*H*$_2$NHBoc), 3.05-2.90 (m, 1H, -C*H*$_2$NHBoc), 2.75-2.60 (m, 1H,-C*H*(CH_3)NHCH_2Ad), 2.31 (ABq, H_A, J = 11.5, -C*H*$_2$Ad), 2.12 (ABq, H_B, J = 11.5, -C*H*$_2$Ad), 1.96 (s, 3H, -Ad), 1.75 -1.60 (m, 6H, -Ad), 1.55-1.40 (m, 15H, -Ad, -NHCOO-C(C*H*$_3$)$_3$), 1.03 (d, 3H, J = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 157.06; 77.57; 61.55; 59.68; 53.35; 40.81; 37.24; 33.37; 28.47; 28.469; 18.62. HRMS: *m/z* 323.26937corresponds to molecular formula $C_{19}H_{34}N_2O_2H^+$ (error in ppm: + 0.19).

***tert*-Butyl {4-[(1-adamantylmethyl)amino]pentyl}carbamate (S21).**



Compound **S21** was prepared by method Efrom mono-*N*-Boc-protected amine **S7** (396 mg, 1.96 mmol) and adamantane-1-carboxaldehyde (321 mg, 1.96 mmol) using AcOH (140 µL, 2.4 mmol) and $NaBH_4$ (445 mg, 11.8 mol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (508 mg, 74%). IR (ATR): 3196m, 3004w, 2962w, 2897s, 2846m, 2795w, 1710s, 1566m, 1465m, 1451m, 1383w, 1362m, 1343w, 1319w, 1302w, 1272m, 1245m, 1168m, 1138s, 1097w, 1076w, 1047w, 1036w, 1002w, 979m, 900w, 884w, 866w, 785w, 756m, 715w, 609w, 561w, 503w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 4.87 (bs, H-N), 3.20-3.00 (m, 1H, -C*H*$_2$NHBoc), 2.55-2.45 (m, 1H, -C*H*(CH_3)NHCH_2Ad), 2.74 (ABq, H_A, J = 11.3, -C*H*$_2$Ad), 2.15 (ABq, H_B, J = 11.3, -C*H*$_2$Ad), 1.96 (bs, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.55-1.48 (8H, -Ad, -C*H*$_2$CH$_2$NHBoc), 1.48-1.40 (m, 11H, -C*H*$_2$CH$_2$CH$_2$NHBoc, -NHCOO-C(C*H*$_3$)$_3$), 1.40-1.25 (m, 1H, -C*H*$_2$CH$_2$CH$_2$NHBoc), 1.02 (d, 3H, J = 6.3, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.01; 78.89; 60.18; 53.59; 40.95; 40.82; 37.27; 34.32; 33.30; 28.50; 28.44; 26.43; 20.58. HRMS: *m/z*351.29958 corresponds to molecular formula $C_{21}H_{38}N_2O_2H^+$ (error in ppm: - 2.91).

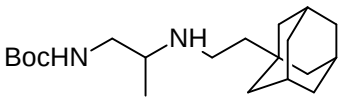
***tert*-Butyl {3-[(1-adamantylmethyl)amino]pentyl}carbamate (S22).**



Compound **S22** was prepared by method Efrom mono-*N*-Boc-protected amine **S8** (370 mg, 1.96 mmol) and adamantane-1-carboxaldehyde (321 mg, 1.96 mmol) using AcOH (139 µL, 2.4 mmol) and $NaBH_4$ (443 mg, 11.7 mol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (549 mg, 80%). IR (ATR):

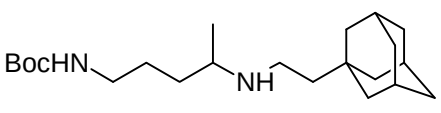
3331m, 2963w, 2898s, 2845m, 1692s, 1504m, 1451m, 1389w, 1363m, 1273w, 1247m, 1170s, 1087w, 1041w, 1022w, 932w, 871w, 808w, 778w, 751w, 623w, 648w, 608w, 588w, 551w, 530w, 521w, 509w, cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 6.64 (bs, H-N), 3.40-3.25 (m, 1H, -C*H*$_2$NHBoc), 3.25-3.05 (m, 1H, -C*H*$_2$NHBoc), 2.55-2.40 (m, 1H, -C*H*(CH_2CH_3)NHCH$_2$Ad), 2.29 (ABq, H_A, J = 11.2, -C*H*$_2$Ad), 2.21 (ABq, H_B, J = 11.2, -C*H*$_2$Ad), 1.97 (s, 3H, -Ad), 1.80-1.60 (m, 7H, -Ad, -C*H*$_2$CH$_2$NHBoc), 1.60-1.50 (m, 7H, -C*H*$_2$CH$_3$, -Ad), 1.50-1.30 (m, 11H, -C*H*$_2$CH$_2$NHBoc, -C*H*$_2$CH$_3$, -NHCOO-C(C*H*$_3$)$_3$), 0.86 (t, 3H, J = 7.5, -CH$_2$C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.21; 78.30; 59.74; 59.48; 40.89; 39.27; 37.21; 33.29; 31.30; 28.48; 26.18; 9.87. HRMS: *m/z*351.30038 corresponds to molecular formula $C_{21}H_{38}N_2O_2H^+$ (error in ppm: - 0.63).

***tert*-Butyl (2-{[2-(1-adamantyl)ethyl]amino}propyl)carbamate (S23).**



Compound **S23** was prepared by method Gfrom mono-*N*-Boc-protected amine **S5** (275 mg, 1.58 mmol) and 1-adamantylacetaldehyde (280 mg, 1.58 mmol) using Ti(OiPr)$_4$ (560 μL, 0.90 mmol) and $NaBH_4$ (120 mg, 3.16 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (398 mg, 75%). IR(ATR): 2972w, 2897s, 2844m, 1698s, 1499m, 1449m, 1390w, 1364m, 1345w, 1315w, 1268w, 1248m, 1166s, 1099w, 1050w, 1038w, 964w, 928w, 902w, 864w, 838w, 812w, 777w, 736m, 704w, 687w, 667w, 503w, 487w, 430w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 4.94 (bs, H-N), 3.20-3.05 (m, 1H, -C*H*$_2$NHBoc), 3.05-3.00 (m, 1H, -C*H*$_2$NHBoc), 2.85-2.75 (m, 1H, -C*H*(CH_3)NHCH$_2$CH$_2$Ad), 2.70-2.60 (m, 1H, -C*H*$_2$CH$_2$Ad), 2.55-2.45 (m, 1H, -C*H*$_2$CH$_2$Ad), 1.94 (bs, 3H, -Ad), 1.75-1.55 (m, 6H, -Ad), 1.53-1.47 (m, 6H, -Ad), 1.47-1.40 (m, 9H, -NHCOO-C(C*H*$_3$)$_3$), 1.30-1.15 (m, 2H, -C*H*$_2$Ad), 1.04 (d, 3H, J = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.24, 79.02; 52.83; 45.54; 45.08; 42.68; 41.47, 37.14; 31.90; 28.67; 28.40; 18.52. HRMS: *m/z*337.28422 corresponds to molecular formula $C_{20}H_{36}N_2O_2H^+$ (error in ppm: - 2.17).

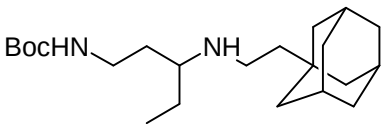
***tert*-Butyl (4-{[2-(1-adamantyl)ethyl]amino}pentyl)carbamate (S24).**



Compound **S24** was prepared by method G from mono-*N*-Boc-protected amine **S7** (360 mg, 1.78 mmol) and 1-adamantylacetaldehyde (317 mg, 1.78 mmol) using Ti(OiPr)$_4$ (632 μL, 2.13 mmol) and $NaBH_4$ (135 mg, 3.56 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (499 mg, 77%). IR (ATR): 3343w, 2967w, 2898s, 2844m, 1690s, 1520m, 1449m, 1389w, 1363m, 1345w, 1269m, 1248m, 1169s, 1041w, 1017w, 989w, 967w, 920w, 867w, 812w, 779w, 523w, 504w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 4.84 (bs, H-N), 3.20-3.05 (m, 2H, -C*H*$_2$NHBoc), 2.70-2.55 (m, 2H, -C*H*(CH_3)NHCH$_2$CH$_2$Ad, -C*H*$_2$CH$_2$Ad), 2.65-2.50 (m, 1H, -

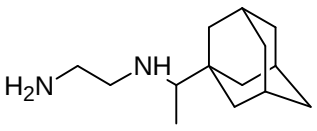
C*H*$_2$CH$_2$Ad), 1.94 (bs, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.30 (m, 18H, -Ad, -C*H*$_2$CH$_2$NHBoc, -C*H*$_2$CH$_2$ CH$_2$NHBoc, -NHCOO-C(C*H*$_3$)$_3$), 1.40-1.30 (m, 1H, -C*H*$_2$CH$_2$ CH$_2$NHBoc), 1.30-1.20 (m, 2H, -C*H*$_2$Ad), 1.04 (d, 3H, *J* = 6.2, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.00; 78.95; 53.12; 44.93; 42.66; 41.52; 40.78; 37.15; 34.31; 31.90; 28.68; 28.43; 26.51; 20.32. HRMS: *m/z* 365.31654 corresponds to molecular formula $C_{22}H_{40}N_2O_2H^+$ (error in ppm: + 0.78).

***tert*-Butyl (3-{[2-(1-adamantyl)ethyl]amino}pentyl)carbamate (S25).**



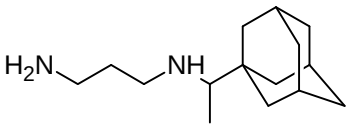
Compound **S25** was prepared by method G from mono-*N*-Boc-protected amine **S8** (350 mg, 1.73 mmol) and 1-adamantylacetaldehyde (308 mg, 1.73 mmol) using $Ti(OiPr)_4$ (616 µL, 2.08 mmol) and $NaBH_4$ (131 mg, 3.46 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5,as colorless oil (479 mg, 76%). IR (ATR): 3330m, 2964m, 2899s, 2845m, 1692s, 1504m, 1449m, 1389w, 1363m, 1315w, 1271m, 1248m, 1170s, 1098w, 1041w, 1022w, 993w, 965w, 918w, 869w, 812w, 780w, 758w, 691w, 681w, 667w, 654w, 618w, 600w, 579w, 557w, 548w, 540w, 503w, 520w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 5.74 (bs, H-NBoc), 3.30-3.20 (m, 1H, -C*H*$_2$NHBoc), 3.20-3.10 (m, 1H, -C*H*$_2$NHBoc), 2.65-2.55 (m, 1H, -C*H*$_2$CH$_2$Ad), 2.55-2.45 (m, 2H, -C*H*$_2$CH$_2$Ad, -C*H*(CH$_2$CH$_3$)NHCH$_2$CH$_2$Ad), 1.94 (s, 3H, -Ad), 1.75-1.60 (m, 7H, -Ad, -C*H*$_2$CH$_2$NHBoc), 1.60-1.35 (m, 18H, -Ad, -C*H*$_2$CH$_2$NHBoc, -C*H*$_2$CH$_3$, -NHCOO-C(C*H*$_3$)$_3$), 1.30-1.20 (m, 2H, -CH$_2$C*H*$_2$Ad), 0.88 (t, 3H, *J* = 7.5, -CH$_2$C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.16; 78.69; 58.14; 45.02; 42.68; 40.97; 38.39; 37.16; 32.36; 31.90; 28.68; 28.47; 26.30; 10.00. HRMS: *m/z* 365.31603 corresponds to molecular formula $C_{22}H_{40}N_2O_2H^+$ (error in ppm: - 0.61).

***N*-[1-(1-Adamantyl)ethyl]ethane-1,2-diamine (S26).**



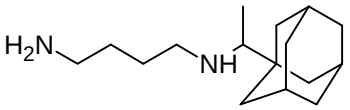
Compound **S26** was prepared using method C from **S17** (400 mg, 1.24 mmol) and was obtainedafter dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as a light yellow viscous oil (239 mg, 87%). IR(ATR): 3238m, 3063w, 2968w, 2932m, 2851m, 1608w, 1570s, 1491w, 1452m, 1423m, 1384w, 1363m, 1329w, 1280w, 1251m, 1200w, 1156w, 1128w, 1084w, 941w, 903w, 869w, 842w, 818w, 796m, 770m, 700m, 682w, 643m, 621w, 598w, 561w, 534w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.85-2.75 (m, 2H, -C*H*$_2$NH$_2$, -C*H*$_2$CH$_2$NH$_2$), 2.75-2.65 (m, 1H, -C*H*$_2$CH$_2$NH$_2$), 2.55-2.45 (m, 1H, -C*H*$_2$NH$_2$), 2.05-2.00 (m, 1H, -C*H*(CH$_3$)Ad), 1.97 (s, 3H, -Ad), 1.75-1.45 (m, 12H, -Ad), 1.31 (bs, 2H-N), 0.95 (d, 3H, *J* = 6.5, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 62.31; 51.41; 42.07; 38.73; 37.37; 36.17; 28.59; 13.62. HRMS: *m/z*223.21613 corresponds to molecular formula $C_{14}H_{26}N_2H^+$ (error in ppm: - 3.34).

***N*-[1-(1-Adamantyl)ethyl]propane-1,3-diamine (S27).**



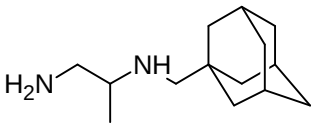
Compound **S27**was prepared using method C from **S18**(450 mg, 1.34 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as light yellow viscous oil (266 mg, 84%). IR (ATR): 3322w, 2896s, 2844s, 2675w, 1636w, 1564m, 1444s, 1403w, 1372w, 1355m, 1345w, 1330w, 1298w, 1251w, 1149w, 1119w, 1100w, 1086w, 1064w, 1012w, 916w, 890w, 814w, 781w, 728w, 704w, 617w, 602m, 572w, 522w, 508w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.85-2.70 (m, 3H, -C$H_2$$NH_2$, -C$H_2$NHCH($CH_3$)Ad), 2.55-2.40 (m, 1H, -CH_2NHCH(CH_3)Ad), 2.10-2.00 (m, 2H,-CH(CH_3)Ad), 1.97 (bs, 3H, -Ad), 1.75-1.40 (m, 14H, -C$H_2$$CH_2$$NH_2$, -Ad), 1.14 (bs, 2H-N and H-N), 0.94 (d, 3H, J = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 62.64; 46.92; 40.76; 38.72; 37.37; 36.04; 34.18; 28.58; 13.50. HRMS: *m/z* 237.23171 corresponds to molecular formula $C_{15}H_{28}N_2H^+$ (error in ppm: -3.44).

***N*-[1-(1-Adamantyl)ethyl]butane-1,4-diamine (S28).**



Compound **S28**was prepared using method C from **S19**(280 mg, 0.80 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as light yellow viscous oil (166 mg, 83%). IR (ATR): 2897s, 2844s, 1572m, 1447s, 1374m, 1358w, 1344w, 1313m, 1248w, 1188w, 1146w, 1116m, 1104m, 1064w, 1045w, 1016w, 813w, 776w, 737w, 698w, 628w, 598w, 586w, 546w, 533w, 512w, 501w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.80-2.65 (m, 3H, -C$H_2$$NH_2$, -C$H_2$NHCH($CH_3$)Ad), 2.50-2.35 (m, 1H, -CH_2NHCH(CH_3)Ad), 2.10-2.00 (m, 1H, -CH(CH_3)Ad), 1.97 (bs, 3H, -Ad), 1.75-1.45 (m, 16H, -Ad, -C$H_2$$CH_2$$NH_2$, -C$H_2$$CH_2$$CH_2$$NH_2$), 1.42 (bs, H-N and 2H-N), 0.94 (d, 3H, J = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 62.41; 48.71; 42.03; 38.59; 37.24; 35.88; 31.51; 28.46; 27.59; 13.41. HRMS: *m/z*251.24786 corresponds to molecular formula $C_{16}H_{30}N_2H^+$ (error in ppm: - 1.24).

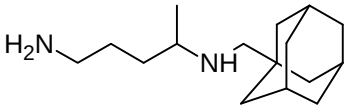
***N*^{2}-(1-Adamantylmethyl)propane-1,2-diamine (S29).**



Compound **S29** was prepared using method C from **S20** (500 mg, 1.55 mmol) and was obtained afterdry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as light yellow viscous oil (299 mg, 87%). IR (ATR): 2895s, 2844s, 1449m, 1370w, 1344w, 1315w, 1222w, 1152w, 1087w, 1052w, 998w, 987w, 951w, 932w, 853w, 813w, 778w, 734m, 625w, 600w, 586w, 542w, 521w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.75-2.65 (m, 1H, -C$H_2$$NH_2$), 2.55-2.45 (m, 2H, -C$H_2$$NH_2$, NH_2CH(CH_3)-), 2.34 (ABq, H_A, J = 11.4, -CH_2Ad), 2.12 (ABq, H_B, J = 11.4, -CH_2Ad), 1.96 (s, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.00 (d, 3H, J = 6.2, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 60.16; 56.12; 47.41; 40.94; 37.30; 33.45;

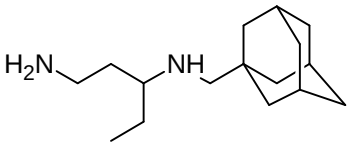
28.52; 18.50.HRMS: *m/z* 223.21628 corresponds to molecular formula $C_{14}H_{26}N_2H^+$ (error in ppm: - 2.65).

N^4-(1-Adamantylmethyl)pentane-1,4-diamine (S30).



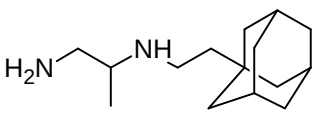
Compound **S30** was prepared by method C from **S21** (300 mg, 0.85 mmol) and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as light yellow viscous oil (214 mg, 90%). IR (ATR): 3280w, 2895s, 2843s, 2675w, 2150w, 1577m, 1447m, 1369w, 1339w, 1311m, 1220w, 1150m, 1085m, 993w, 950w, 808m, 719m, 610w, 549w, 523w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.75-2.65 (m, 2H, -C*H*$_2$NH$_2$), 2.60-2.55 (m, 1H, -C*H*(CH$_3$)NHCH$_2$Ad), 2.28 (ABq, H_A, J = 11.4, -C*H*$_2$Ad), 2.17 (ABq, H_B, J = 11.4, -C*H*$_2$Ad), 1.96 (bs, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.55-1.50 (m, 6H, -Ad), 1.50-1.40 (m, 3H, -C*H*$_2$CH$_2$NH$_2$, -C*H*$_2$CH$_2$CH$_2$NH$_2$), 1.35-1.25 (m, 1H, -C*H*$_2$CH$_2$CH$_2$NH$_2$), 1.02 (d, 3H, J = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 60.29; 54.00; 42.53; 40.96; 37.27; 34.33; 33.29; 30.45; 28.50; 20.58. HRMS: *m/z*251.24818 corresponds to molecular formula $C_{16}H_{30}N_2H^+$ (error in ppm: - 4.72).

N^3-(1-Adamantylmethyl)pentane-1,3-diamine (S31).



Compound **S31** was prepared from **S22** (350 mg, 1.00 mmol) by method Cand was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1as a yellow viscous oil (223 mg, 89%). IR (ATR): 3311m, 2903s, 2847s, 2678w, 2235w, 1644m, 1559m, 1448m, 1402w, 1367m, 1306w, 1223w, 1169w, 1134w, 1099w, 993w, 813w, 727w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.85-2.70 (m, 2H, -C*H*$_2$NH$_2$), 2.50-2.35 (m, 1H, -C*H*(CH$_2$CH$_3$)NHCH$_2$Ad), 2.25 (ABq, H_A, J = 11.3, -C*H*$_2$Ad), 2.15 (ABq, H_B, J = 11.3, -C*H*$_2$Ad), 1.95 (s, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.45 (m, 8H, -C*H*$_2$CH$_2$NH$_2$, -Ad), 1.45-1.35 (m, 2H, -C*H*$_2$CH$_3$), 0.87 (t, 3H, J = 7.5, -CH$_2$C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 59.65; 58.25; 40.93; 39.77; 37.29; 33.44; 28.51; 26.66; 9.92. HRMS: *m/z* 251.24754 corresponds to molecular formula $C_{16}H_{30}N_2H^+$ (error in ppm: - 2.51).

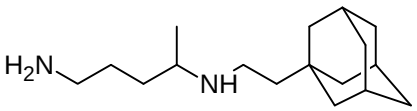
N^2-[2-(1-adamantyl)ethyl]propane-1,2-diamine (S32).



Compound **S32** was prepared from **S23** (350 mg, 1.04 mmol) by method C and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as a yellow viscous oil (226 mg, 92%). IR (ATR): 2897s, 2844s, 1495w, 1449m, 1370w, 1345w, 1316w, 1265w, 1183w, 1150w, 1099m, 812w, 728s, 695m, 631w, 617w, 600w, 590w, 530w, 522w, 506w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.75-2.67 (m, 2H, -C*H*$_2$NH$_2$, -C*H*$_2$CH$_2$Ad), 2.67-2.57 (m, 1H, -C*H*(CH$_3$)NHCH$_2$CH$_2$Ad), 2.57-2.45 (m, 2H, -C*H*$_2$NH$_2$, -C*H*$_2$CH$_2$Ad), 1.94 (bs, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.35-1.15 (m, 2H, -C*H*$_2$Ad), 1.03 (d, 3H, J =

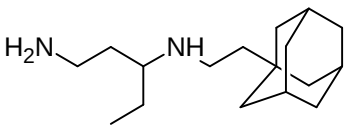
6.2, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 55.56; 47.61; 45.13; 42.70; 41.66; 37.17; 31.90; 28.70; 18.31. HRMS: *m/z* 237.23151 corresponds to molecular formula $C_{15}H_{28}N_2H^+$ (error in ppm: - 4.29).

N^4-[2-(1-Adamantyl)ethyl]pentane-1,4-diamine (S33).



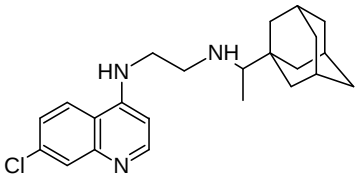
Compound **S33** was prepared from **S24** (300 mg, 0.82 mmol) by method C and was obtained after dry-flash chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 as a yellow viscous oil (198 mg, 91%). IR (ATR): 2896s, 2843s, 2656w, 1572m, 1448m, 1372w, 1314m, 1141w, 1098w, 988w, 967w, 922w, 879w, 812w, 703w, 619w, 591w, 572w, 533w, 512w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.75-2.65 (m, 2H, -C*H*$_2$NH$_2$), 2.65-2.60 (m, 2H, -C*H*(CH$_3$)NHCH$_2$CH$_2$Ad, -C*H*$_2$CH$_2$Ad), 2.60-2.50 (m, 1H, -C*H*$_2$CH$_2$Ad), 1.94 (bs, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.55-1.40 (m, 9H, -C*H*$_2$CH$_2$NH$_2$, -C*H*$_2$CH$_2$CH$_2$NH$_2$, -Ad), 1.35-1.25 (m, 1H, -C*H*$_2$CH$_2$CH$_2$NH$_2$), 1.25-1.20 (m, 2H, -C*H*$_2$Ad), 1.05 (d, 3H, *J* = 6.2, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 53.37; 45.07; 42.67; 42.50; 41.58; 37.16; 34.45; 31.89; 30.37; 28.68; 20.40. HRMS: *m/z*256.26328 corresponds to molecular formula $C_{17}H_{32}N_2H^+$ (error in ppm: - 2.05).

N^3-[2-(1-Adamantyl)ethyl]pentane-1,3-diamine(S34).



Compound **S34** was prepared from **S25** (250 mg, 0.74 mmol) by method C and was obtained after dry-flash chromatography (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 9/1) as a yellow viscous oil (147 mg, 75%). IR (ATR): 2957w, 2905s, 2844s, 1574m, 1448s, 1379w, 1344w, 1314m, 1099m, 812m, 775w, 722w, 700w, 680w, 620w, 608w, 599w, 590w, 582w, 501w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.85-2.70 (m, 2H, -C*H*$_2$NH$_2$), 2.70-2.50 (m, 3H, -C*H*(CH$_2$CH$_3$)NHCH$_2$CH$_2$Ad, -C*H*$_2$CH$_2$Ad), 1.94 (s, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.50 (m, 8H, -C*H*$_2$CH$_2$NH$_2$, -Ad), 1.50-1.40 (m, 2H, -C*H*$_2$CH$_3$), 1.30-1.20 (m, 2H, -C*H*$_2$Ad), 0.87 (t, 3H, *J* = 7.5, -CH$_2$C*H*$_3$,). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 57.63; 45.08; 42.68; 41.31; 39.52; 37.42; 37.17; 31.91; 28.69; 26.48; 9.87. HRMS: *m/z* 265.26347 corresponds to molecular formula $C_{17}H_{32}N_2H^+$ (error in ppm: - 1.33).

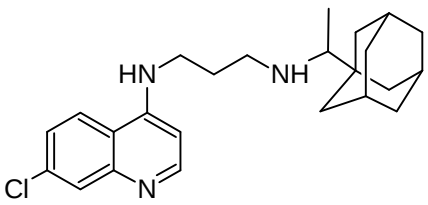
***N*-[1-(1-Adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)ethane-1,2-diamine (11).**



Amine **S26** (180 mg, 0.81 mmol) and 4,7-dichloroquinoline (481 mg, 2.43 mmol) were mixed in a MW cuvette under Ar. Reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*, 4h, 130 ^{o}C. Compound **11** was obtained after multiple chromatographydry-flash (SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5), and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3) as colorless powder,softens at 96-98 °C. Yield: 214 mg (69%). IR (ATR): 3254w, 2898s, 2844m, 1610w,

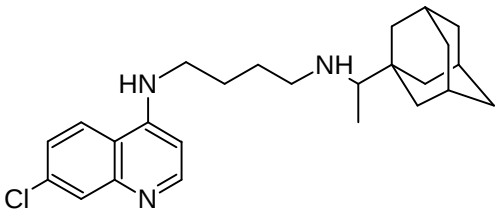
1577s, 1524m, 1446m, 1367m, 1327m, 1281w, 1240w, 1197w, 1159w, 1136m, 1101m, 1077m, 1014w, 968w, 921w, 876m, 846w, 804m, 761w, 736m, 702w, 643w, 623w, 600w, 542w, 527w, 506w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.53 (d, *J* = 5.0, H-C(2)), 7.95 (d, *J* = 2.0, H-C(8)), 7.72 (d, *J* = 8.5, H-C(5)), 7.35 (dd, J_1 = 2.0, J_2 = 9.0, H-C(6)), 6.38 (d, *J* = 5.5, H-C(3)), 6.17 (bs, H-N), 3.35-3.25 (m, 1H, ArNHCH_2-), 3.25-3.15 (m, 2H, ArNHCH_2-, ArNHCH$_2$CH_2-), 2.90-2.80 (m, 1H, ArNHCH$_2$CH_2-), 2.15-2.05 (m, 1H, -C*H*(CH_3)Ad), 1.98 (m, 3H, -Ad), 1.80-1.45 (m, 12H, -Ad), 1.03 (d, 3H, *J* = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.11; 150.00; 149.15; 134.73; 128.73; 125.13; 121.19; 117.46; 99.26; 61.64; 45.96; 42.14; 38.89; 37.31; 36.32; 28.52; 13.62. HRMS: *m/z*384.22025 corresponds to molecular formula $C_{23}H_{30}ClN_3H^+$ (error in ppm: + 0.39). Anal.($C_{23}H_{30}ClN_3$) Calcd: C, 71.95; H, 7.88; N, 10.94. Found: C, 71.76; H, 8.15; N, 10.88. HPLC purity (λ = 330 nm): method A: RT 7.986 min, area 99.01%; method B: RT 9.475 min, area 98.26%.

N-[1-(1-Adamantyl)ethyl]-N'-(7-chloroquinolin-4-yl)propane-1,3-diamine (22).



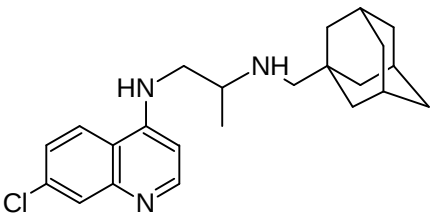
Amine **S27** (230 mg, 0.97 mmol) and 4,7-dichloroquinoline (385 mg, 1.95 mmol) were mixed in a MW cuvette under Ar. The reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*, 4h, 130 ^{o}C. Compound **22** was obtained after multiple chromatography: dry-flash(SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5) and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 75/25) as colorless powder,softens at 90-92 °C. Yield: 174 mg (74%). IR(ATR): 3243m, 3067w, 2897s, 2844m, 1610w, 1583s, 1534m, 1447m, 1427m, 1365m, 1344m, 1328m, 1281w, 1241w, 1211w, 1158w, 1137m, 1097w, 1075m, 1042w, 1015w, 995w, 970w, 899m, 876m, 852m, 801m, 763m, 703w, 673w, 642w, 631w, 620w, 598w, 570w, 554w, 542w, 532w, 515w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.4, H-C(2)), 7.92 (d, *J* = 2.2, H-C(8)), 7.81 (d, *J* = 8.9, H-C(5)), 7.40 (bs, H-N), 7.26 (dd, J_1 = 2.2, J_2 = 8.8, H-C(6)), 6.32 (d, *J* = 5.4, H-C(3)), 3.50-3.40 (m, 1H, ArNHCH_2-), 3.35-3.25 (m, 1H, ArNHCH_2-), 2.95-2.85 (m, 1H, ArNHCH$_2$CH$_2$CH_2-), 2.85-2.80 (m, 1H, ArNHCH$_2$CH$_2$CH_2-), 2.10-2.05 (m, 1H, -C*H*(CH_3)Ad), 2.03 (m, 3H, -Ad), 2.00-1.85 (m, 2H, ArNHCH$_2$CH_2-), 1.80-1.55 (m, 12H, -Ad), 0.98 (d, 3H, *J* = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.19; 150.42; 149.19; 134.57; 128.59; 124.52; 122.38; 117.49; 98.41; 63.84; 48.97; 44.22; 38.88; 37.23; 36.00; 28.51; 28.24; 13.74. HRMS: *m/z* 398.23424corresponds to molecular formula $C_{24}H_{32}ClN_3H^+$ (error in ppm: - 3.80). Anal. ($C_{24}H_{32}ClN_3$) Calcd: C, 72.43; H, 8.10; N, 10.56. Found: C, 72.14; H, 8.27; N, 10.42. HPLC purity (λ = 330 nm): method A: RT 8.586 min, area 99.59%; method B: RT 9.697 min, area 98.93%.

***N*-[1-(1-Adamantyl)ethyl]-*N*'-(7-chloroquinolin-4-yl)butane-1,4-diamine (30).**



Amine **S28** (263 mg, 1.05 mmol) and 4,7-dichloroquinoline (624 mg, 3.15 mmol) were mixed in a MW cuvette under Ar. The reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*, 4h, 130 °C. Compound **30** was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 55/45) as colorless powder,softens at 146-148 °C. Yield: 298 mg (69%). IR (ATR): 3254m, 2900m, 2844m, 2755w, 1609w, 1569s, 1536m, 1475w, 1448m, 1367m, 1344w, 1325m, 1285w, 1252w, 1228w, 1196w, 1161w, 1134m, 1116w, 1076m, 1019w, 978w, 902m, 875m, 850m, 825m, 804m, 763m, 741w, 645w, 621w, 598m, 553w, 516m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.53 (d, J = 5.0, H-C(2)), 7.95 (d, J = 2.0, H-C(8)), 7.71 (d, J = 9.0, H-C(5)), 7.34 (dd, J_1 = 2.0, J_2 = 9.0, H-C(6)), 6.40 (d, J = 5.5, H-C(3)), 5.41 (bs, H-N), 3.40-3.25 (m, 2H, ArNHCH_2-), 2.85-2.75 (m, 1H, -CH_2NHCH(CH_3)Ad), 2.60-2.50 (m, 1H, -CH_2NHCH(CH_3)Ad), 2.15-2.05 (m, 1H, -CH_2NHCH(CH_3)Ad), 1.98 (m, 3H, -Ad), 1.90-1.80 (m, 2H, ArNHCH_2CH_2-), 1.75-1.45 (m, 14H, -Ad, ArNHCH_2CH_2CH_2-), 0.96 (d, 3H, J = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.10; 149.75; 149.21; 134.73; 128.86; 125.05; 121.13; 117.19; 99.01; 62.28; 47.85; 43.20; 38.82; 37.33; 36.10; 28.56; 27.83; 26.34; 13.43. HRMS: *m/z* 412.24953corresponds to molecular formula $C_{25}H_{34}ClN_3H^+$ (error in ppm: -4.55). Anal.($C_{25}H_{34}ClN_3 \times 1/2\ H_2O$) Calcd: C, 71.32; H, 8.38; N, 9.98. Found: C, 71.16; H, 7.88; N, 10.16. HPLCpurity (λ = 330 nm): method A: RT 7.952 min, area 96.65%; method B: RT 9.593 min, area 97.85%.

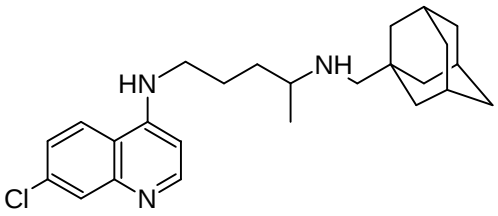
***N*^{2}-(1-Adamantylmethyl)-*N*^{1}-(7-chloroquinolin-4-yl)propane-1,2-diamine (10).**



Compound **10** was prepared from amine **S29**(150 mg, 0.67 mmol) and 4,7-dichloroquinoline (111 mg, 0.56 mmol) in phenol (790 mg, 8.40 mmol) by method Fand was obtained after multiple chromatography: dry-flash: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3) as colorless foam,softens at 148-150 °C. Yield: 149 mg (71%). IR (ATR): 3362w, 3335w, 3032w, 2958w, 2905s, 2842m, 1605w, 1578s, 1562s, 1520m, 1472m, 1444m, 1361w, 1345w, 1333w, 1295w, 1273w, 1246w, 1207w, 1183w, 1155m, 1136w, 1098w, 1083m, 1018w, 998w, 986w, 964w, 940w, 929w, 899m, 848m, 806m, 762m, 748m, 672w, 647w, 560m, 546w, 523m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.52 (d, J = 5.0, H-C(2)), 7.95 (d, J = 2.0, H-C(8)), 7.72 (d, J = 9.0, H-C(5)), 7.35 (dd, J_1 = 2.0, J_2 = 9.0, H-C(6)), 6.34 (d, J = 5.5, H-C(3)), 6.25 (bs, H-NAr), 3.35-3.25 (m, 1H, ArNHCH_2-), 3.05-2.95 (m, 1H, ArNHCH_2CH(CH_3)-), 2.95-2.85 (m, 1H,

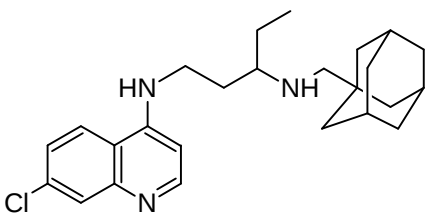
ArNHCH_2-), 2.43 (ABq, H_A, J = 11.5, -CH_2Ad), 2.14 (ABq, H_B, J = 11.5, -CH_2Ad), 1.99 (s, 3H, -Ad), 1.80-1.45 (m, 12H, -Ad), 1.22 (d, 3H, J = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.14; 150.02; 149.18; 134.70; 128.74; 125.06; 121.24; 117.51; 99.20; 59.07; 52.16; 46.73; 40.94; 37.21; 33.47; 28.42; 19.54. HRMS: *m/z* 384.21824 corresponds to molecular formula $C_{23}H_{30}ClN_3H^+$ (error in ppm: - 4.85). Anal.($C_{23}H_{30}ClN_3$) Calcd: C, 71.95; H, 7.88; N, 10.94. Found: C, 71.76; H, 8.12; N, 11.12. HPLC purity (λ = 330 nm): method A: RT 8.000 min, area 99.64%; method B: RT 9.433 min, area 99.22%.

N^4-(1-Adamantylmethyl)-N^1-(7-chloroquinolin-4-yl)pentane-1,4-diamine (31).



Compound **31** was prepared from amine **S30** (239 mg, 0.95 mmol) and 4,7-dichloroquinoline (157 mg, 0.79 mmol) in phenol (1115 mg, 11.85 mmol) by method F and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 75/25) as colorless foam softens at 148-150 °C. Yield: 250 mg (64%). IR (ATR): 3200w, 3061w, 3007w, 2896s, 2841s, 2003w, 1609w, 1576s, 1548m, 1488w, 1449m, 1430m, 1366m, 1333w, 1302w, 1280w, 1250w, 1213m, 1150w, 1135m, 1098w, 1078w, 1018w, 979w, 951w, 897w, 882w, 868w, 848w, 816w, 800w, 764w, 748w, 724w, 714w, 667w, 643w, 620w, 599w, 573w, 557w, 505w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.52 (d, J = 5.5, H-C(2)), 7.93 (d, J = 2.0, H-C(8)), 7.72 (d, J = 8.5, H-C(5)), 7.34 (dd, J_1 = 2.5, J_2 = 9.0, H-C(6)), 6.39 (d, J = 5.5, H-C(3)), 5.66 (bs, H-NAr), 3.40-3.30 (m, 1H, ArNHCH_2-), 3.30-3.20 (m, 1H, ArNHCH_2-), 2.75-2.65 (m, 1H, -CH(CH_3)NHCH_2Ad), 2.29 (ABq, H_A, J = 11.3, -CH_2Ad), 2.20 (ABq, H_B, J = 11.3, -CH_2Ad), 1.97 (m, 3H, -Ad), 1.90-1.75 (m, 16H, ArNHCH$_2$CH_2-), 1.75-1.60 (m, 6H, -Ad), 1.60-1.45 (m, 8H, ArNHCH$_2$CH$_2$CH_2-, -Ad), 1.07 (d, 3H, J = 6.0, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.13; 149.83; 149.24; 134.70; 128.86; 125.01; 121.24; 117.28; 98.97; 59.40; 52.98; 43.50; 41.04; 37.23; 34.23; 33.34; 28.46; 24.90; 20.71. HRMS: *m/z*412.24972 corresponds to molecular formula $C_{25}H_{34}ClN_3H^+$ (error in ppm: - 4.08). Anal. ($C_{25}H_{34}ClN_3$) Calcd: C, 72.88; H, 8.32; N, 10.20. Found: C, 72.68; H, 8.53; N, 9.95. HPLC purity (λ = 330 nm): method A: RT 8.054 min, area 97.97%; method B: RT 9.525 min, area 99.50%.

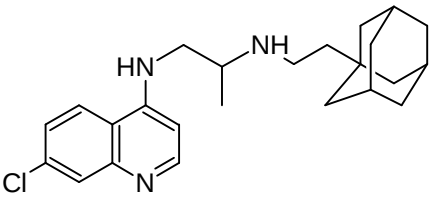
N^3-(1-Adamantylmethyl)-N^1-(7-chloroquinolin-4-yl)pentane-1,3-diamine (28).



Compound **28** was prepared from amine **S28** (350 mg, 1.40 mmol) and 4,7-dichloroquinoline (231 mg, 1.17 mmol) in phenol (165 mg, 17.55 mmol) by method F and was

obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 65/35) as colorless foam,softens at 121-123 °C. Yield 409 mg (71%). IR(ATR): 3254m, 2897s, 2844m, 1610w, 1584s, 1537m, 1449m, 1428w, 1366m, 1329m, 1281w, 1243w, 1168w, 1140m, 1103w, 1077m, 902w, 876w, 849m, 805m, 765w, 737m, 701w, 644w, 623w, 606w, 687w, 673w, 643w, 514w, 506w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.2, H-C(2)), 7.93 (bs, H-C(8)), 7.91 (d, *J* = 8.9, H-C(5)), 7.54 (bs, H-NA*r*), 7.30-7.20 (m, H-C(6)), 6.33 (d, *J* = 5.4, H-C(3)), 3.45-3.38 (m, 1H, ArNHCH_2-), 3.38-3.30 (m, 1H, ArNHCH_2-), 2.70-2.60 (m, 1H, ArNHCH$_2$CH$_2$C*H*(CH_2CH_3)-), 2.41 (ABq, H_A, *J* = 11.4, -CH_2Ad), 2.39 (ABq, H_B, *J* = 11.4, -CH_2Ad), 2.05-1.95 (m, 8H, -Ad, ArNHCH$_2$CH_2-), 1.85-1.45 (m, 16H, -Ad, ArNHCH$_2$CH_2-, -CH_2CH$_3$), 0.94 (t, 3H, *J* = 7.4, -CH$_2$CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.17, 150.49, 149.17, 134.56, 128.54, 124.50, 122.42, 117.53, 98.48, 60.67; 60.32; 41.79; 41.22; 37.17; 33.38; 29.65; 28.43; 25.84; 10.38. HRMS: *m/z*412.25061 corresponds to molecular formula $C_{25}H_{34}ClN_3H^+$ (error in ppm: -1.92). Anal. ($C_{25}H_{34}ClN_3$) Calcd: C, 72.88; H, 8.32; N, 10.20. Found: C, 72.50; H, 7.97; N, 10.06. HPLC purity (λ = 330 nm): method A: RT 9.632 min, area 96.33%; method B: RT 9.550 min, area 95.41%;

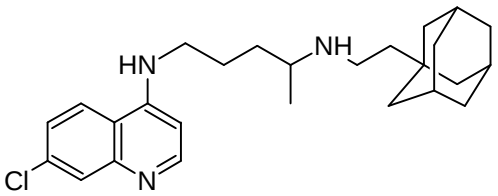
N^2-[2-(1-Adamantyl)ethyl]-N^1-(7-chloroquinolin-4-yl)propane-1,2-diamine (34).



Compound **34**was prepared from amine **S32**(140 mg, 0.59 mmol) and 4,7-dichloroquinoline (97 mg, 0.49 mmol) in phenol (692 mg, 7.35 mmol) by method F and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 1/1) as colorless powder,softens at 134-136 °C. Yield: 174 mg (74%). IR (ATR): 3245w, 2895s, 2842m, 1737m, 1670w, 1566s, 1489w, 1449m, 1427m, 1367m, 1331w, 1304w, 1284w, 1238m, 1202w, 1156w, 1136m, 1076m, 1046m, 989w, 966w, 897w, 869w, 843m, 804m, 769m, 704w, 646w, 622w, 594w, 570w, 544w, 524w, 517w, 509w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.52 (d, *J* = 5.3, H-C(2)), 7.95 (d, *J* = 2.1, H-C(8)), 7.70 (d, *J* = 8.9, H-C(5)), 7.36 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.36 (d, *J* = 5.4, H-C(3)), 6.01 (bs, H-NAr), 3.35-3.25 (m, 1H, ArNHCH_2CH(CH_3)-), 3.15-3.05 (m, 1H, ArNHCH$_2$C*H*(CH_3)-), 3.05-2.95 (m, 1H, ArNHCH_2CH(CH_3)-), 2.80-2.70 (m, 1H, -NHCH_2CH$_2$Ad), 2.65-2.55 (m, 1H, -NHCH_2CH$_2$Ad), 1.94 (bs, 3H, -Ad), 1.75-1.55 (m, 6H, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.35-1.25 (m, 3H, -NHCH$_2$CH_2Ad, *H*-N-), 1.22 (d, 3H, *J* = 6.0, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.12; 150.01; 149.19; 134.75; 128.76; 125.14; 121.25; 117.47; 99.20; 51.74; 47.22; 45.24; 42.77; 41.27; 37.10; 32.00; 28.64; 19.30. HRMS: *m/z* 398.23395 corresponds to molecular formula $C_{24}H_{32}ClN_3H^+$ (error in ppm: - 4.53). Anal.($C_{24}H_{32}ClN_3$) Calcd: C, 72.43;

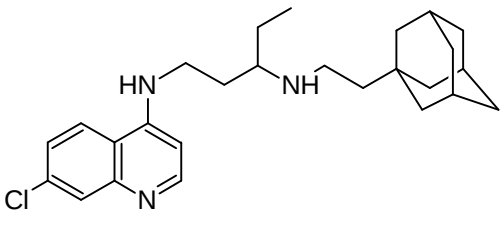
H, 8.10; N, 10.56. Found: C, 71.98; H, 8.49; N, 10.59. HPLC purity (λ = 330 nm): method A: RT 8.017 min, area 99.00%; method B: RT 9.696 min, area 98.87%.

N^4-[2-(1-Adamantyl)ethyl]-N^1-(7-chloroquinolin-4-yl)pentane-1,4-diamine (43).



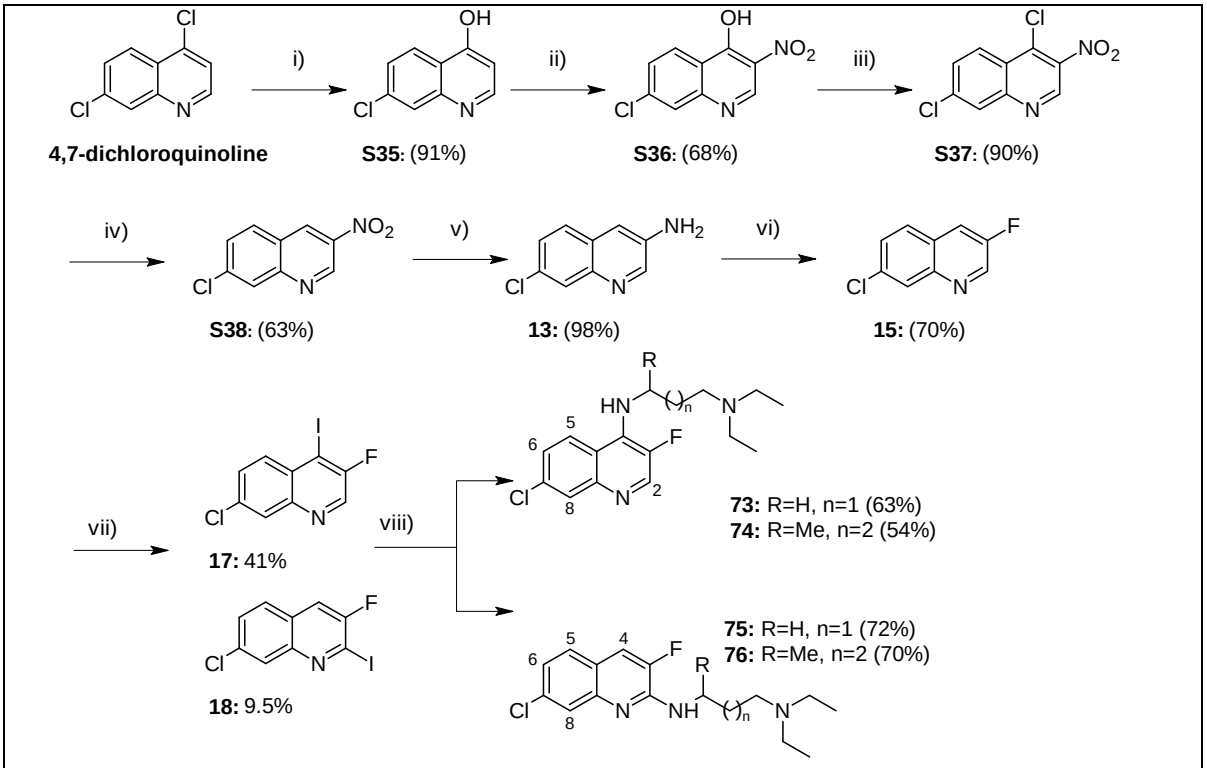
Compound **43** was prepared from amine **S33**(145 mg, 0.55 mmol) and 4,7-dichloroquinoline (91 mg, 0.46 mmol) in phenol (649 mg, 6.90 mmol) by method F was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3) as colorless powder,softens at 140-143 °C. Yield: 157 mg, (67%). IR (ATR): 3252m, 3063w, 2898s, 2844s, 2017s, 1610w, 1587s, 1539m, 1449m, 1429w, 1367m, 1330m, 1279w, 1248w, 1204w, 1135m, 1098w, 1078w, 890w, 877w, 853w, 804w, 764w, 737w, 701w, 692w, 668w, 659w, 643w, 619w, 602w, 582w, 563w, 552w, 542w, 529w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.52 (d, *J* = 5.4, H-C(2)), 7.94 (d, *J* = 2.2, H-C(8)), 7.70 (d, *J* = 9.0, H-C(5)), 7.34 (dd, J_1 = 2.2, J_2 = 8.9, H-C(6)), 6.38 (d, *J* = 5.4, H-C(3)), 5.87 (bs, H-NAr), 3.40-3.20 (m, 2H, ArNHCH_2-), 2.80-2.70 (m, 1H, -C*H*(CH_3)NHCH_2CH_2Ad), 2.70-2.60 (m, 1H, -CH_2CH_2Ad), 2.60-2.50 (m, 1H, -CH_2CH_2Ad), 1.93 (m, 3H, -Ad), 1.90-1.75 (m, 2H, ArNHCH_2CH_2-), 1.75-1.52 (m, 8H, ArNHCH_2CH_2CH_2-, -Ad), 1.48 (m, 6H, -Ad), 1.35-1.20 (m, 2H, -CH_2Ad), 1.25 (d, 3H, *J* = 5.0, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 152.12; 149.93; 149.25; 134.69; 128.81; 125.01; 121.34; 117.33; 98.93; 52.84; 45.09; 43.56; 42.68; 41.35; 37.12; 34.70; 31.90; 28.65; 24.93; 20.50. HRMS: *m/z*426.26530 corresponds to molecular formula $C_{26}H_{36}ClN_3H^+$ (error in ppm: - 4.11).Anal. ($C_{26}H_{36}ClN_3 \times 1/3\ H_2O$) Calcd: C, 72.28; H, 8.55; N, 9.73. Found: C, 72.02; H, 8.86; N, 9.40. HPLC purity (λ = 330 nm): method A: RT 8.089 min, area 99.50%; method B: RT 9.746 min, area 96.70%.

N^3-[2-(1-Adamantyl)ethyl]-N^1-(7-chloroquinolin-4-yl)butane-1,3-diamine (41).



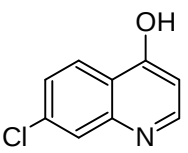
Compound **41** was prepared from amine linker **S34**(123 mg, 0.47 mmol) and 4,7-dichloroquinoline (77 mg, 0.39 mmol) in phenol (550 mg, 5.85 mmol) by method F and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 65/35) as colorless foam,softens at 131-134 °C. Yield: 139 mg (70%). IR (ATR): 3213w, 2897s, 2843m, 1738w, 1610w, 1578s, 1537m, 1448m, 1429w, 1365m, 1329m, 1282w, 1240w, 1218w, 1168w, 1140m, 1098w, 1077w, 1047w, 990w, 972w, 906w, 876w, 850w, 801m, 765w, 735w, 641w, 582w, 538w, 513w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.4, H-C(2)), 8.42 (bs, H-N), 7.95-7.90 (m, H-C(8)), 7.73 (d, *J* = 8.9,

H-C(5)), 7.28 (dd, J_1 = 8.9, J_2 = 2.2, H-C(6)), 6.27 (d, J = 5.4, H-C(3)), 3.50-3.35 (m, 1H, ArNHCH_2-), 3.35-3.25 (m, 1H, ArNHCH_2-), 2.80-2.70 (m, 2H, -(CH_2CH_3)CH-, -C$H_2$$CH_2$Ad), 2.70-2.60 (m, 1H, -C$H_2$$CH_2$Ad), 2.00-1.90 (m, 4H, -Ad, ArCH_2CH_2-), 1.75-1.55 (m, 8H, -Ad, -C$H_2$$CH_3$, Ar$CH_2CH_2$-), 1.55-1.14 (m, 7H, -C$H_2$$CH_3$, -Ad), 1.45-1.35 (m, 1H, -CH_2Ad), 1.35-1.20 (m, 1H, -CH_2Ad), 0.94 (t, 3H, J = 7.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 151.99; 150.72; 148.96; 134.57; 128.26; 124.50; 122.55; 117.63; 98.03; 59.81; 45.37; 42.68; 42.08; 41.21; 37.04; 31.88; 29.29; 28.57; 25.96; 10.14. HRMS: *m/z* 426.26759 corresponds to molecular formula $C_{26}H_{36}ClN_3H^+$ (error in ppm: - 1.26).Anal.($C_{26}H_{36}ClN_3$ × 1/3 H_2O) Calcd: C, 72.28; H, 8.55; N, 9.73. Found: C, 72.76; H, 8.48; N, 9.70. HPLC purity (λ = 330 nm): method A: RT 7.869 min, area 95.47%; method B: RT 10.335 min, area95.39%.



i) glac. CH_3COOH, 125 °C, 1 h; NaOH, CH_3COOH; ii) HNO_3, CH_3CH_2COOH, 125 °C, 24 h; iii) $POCl_3$, 115 °C, 18 h; iv) *p*-toluenesulfonylhydrazine, $CHCl_3$, 24 h, r.t.; 0.5 M NaOH, 80 °C, 1 h; v) $SnCl_2$ x $2H_2O$, MeOH, 80 °C; vi) 48% aq HBF_4, $NaNO_2$; 1,2-dichlorbenzen, 2 h, 110 °C vii) LDA, THF, 4 h, -85 °C; I_2, THF, 2 h, -78 °C viii) amine, $Pd(OAc)_2$, DPEphos, K_3PO_4, dioxane, 85 °C, 24 h.

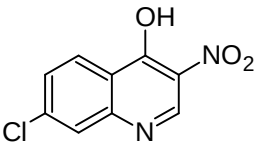
7-Chloroquinolin-4-ol (S35).[21]



A mixture of 4,7-dichloroquinoline (10 g, 50 mmol) and 6.5 equiv of glacial acetic acid (18.8 mL, 325 mmol) was refluxed at 125 °C for one hour. Dry ether was added to the cooled reaction mixture and the colorless solid was filtered off. Obtained crude product was dissolved in conc. NaOH, reaction mixture was filtered and acidified with acetic acid. Formedprecipitate was collected by filtration, washed with water and dried. 7-Chloroquinolin-4-ol (**S35**) was obtained as colorless solid (9.07 g,

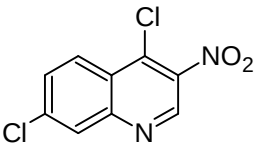
91%); m.p. = 276-279 °C (Et_2O). IR (ATR): 3228w, 3116w, 3057m, 2945m, 2877m, 2799m, 2635w, 1629m, 1599s, 1558s, 1507s, 1455s, 1414m, 1356m, 1300w, 1244w, 1206m, 1143w, 1080w, 1056w, 904w, 862m, 822m, 796s, 572m, 479m cm^{-1}. ^{1}H-NMR (200 MHz, DMSO, δ): 8.07 (d, *J* = 8.6, H-C(5)), 7.93 (d, *J* = 7.4, H-C(2)), 7.61 (d, *J* = 2.0, H-C(8)), 7.30 (dd, J_1 = 2.0, J_2 = 7.4, H-C(6)), 6.05 (d, *J* = 7.4, H-C(3)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 176.17; 141.19; 140.39; 136.04; 127.24; 124.44; 123.29; 117.73; 109.21. HRMS: *m/z*180.02100 corresponds to molecular formula $C_9H_6ClNOH^+$ (error in ppm: - 0.40).

7-Chloro-3-nitroquinolin-4-ol (S36).[22]



A mixture of 7-chloroquinolin-4-ol **S35** (2.00 g, 11.13 mmol) in propionic acid (20 mL) was heated to 125 °C with stirring. Nitric acid (65%, 964 µL, 13.92 mmol) was added dropwise to a stirred solution while maintaining the reaction mixture temperature at 125 °C. Upon completedaddition the mixture was stirred for 18h and cooled to ambient temperature. The mixture was diluted with ethanol, and the solid was collected by filtration. 7-Chloro-3-nitroquinolin-4-olwas obtained after chromatography: SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 8/2 as light-yellow solid,softens at 199-202 °C (Hex). Yield: 1.95 g (79%). IR(ATR): 3442m, 3194w, 3156w, 3071w, 3039w, 2919m, 2852m, 1628s, 1557w, 1533m, 1499m, 1460w, 1404w, 1336s, 1267w, 1234w, 1198w, 1158w, 1113w, 1078w, 879w, 831w, 781m, 673w, 618m, 516w, 441w, 420w cm^{-1}. ^{1}H-NMR (500 MHz, MeOD, δ): 10.03 (s, H-C(2)), 9.03 (d, *J* = 8.4, H-C(5)), 8.55 (s, H-C(8)), 8.33 (d, *J* = 8.2, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 176.73; 152.97; 149.19; 147.29; 140.99; 137.80; 136.52; 135.63; 128.64. HRMS: *m/z*225.00527 corresponds to molecular formula $C_9H_5ClN_2O_2H^+$ (error in ppm: - 3.89).

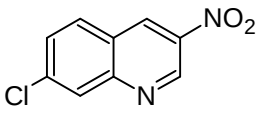
4,7-Dichloro-3-nitroquinoline (S37).



The mixture of 7-chloro-3-nitroquinolin-4-ol **S36** (1.00 g, 4.45 mmol) and $POCl_3$ (4 mL) was heated to 115 °C overnight. The resulting solution was cooled to ambient temperature and poured into an ice/water mixture (50 mL). A solid was collected by vacuum filtration, washed with water and dried. 4,7-Dichloro-3-nitroquinolin was obtained after dry-flash chromatography: SiO_2, eluent: Hex/EtOAc = 9/1 as light-yellow solid,softens at 153-155 °C (hexane). Yield: 974 mg, (90%). IR (ATR): 3064m, 1604m, 1581s, 1556s, 1531s, 1479m, 1438w, 1397w, 1373w, 1355s, 1333s, 1294m, 1253m, 1207m, 1168m, 1144w, 1080s, 1021m, 973w, 962w, 926m, 898m, 875m, 818s, 810s, 772m, 740w, 700m, 650w, 605m, 562w, 540m, 486w, 466w, 444m, 422m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 9.27 (s, H-C(2)), 8.38 (d, *J* = 9.0, H-C(5)), 8.22 (d, *J* = 2.0, H-C(8)), 7.77 (dd, J_1 = 2.0, J_2 = 9.0, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 149.51; 145.68; 141.12; 139.80; 136.68; 130.76; 129.23; 127.27; 124.07. HRMS: *m/z*242.97178

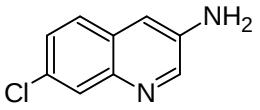
corresponds to molecular formula $C_9H_4Cl_2N_2O_2H^+$ (error in ppm: - 0.38).Anal.($C_9H_4Cl_2N_2O_2$) Calcd: C, 44.48; H, 1.66; N, 11.53. Found: C, 44.57; H, 1.36; N, 11.06.

7-Chloro-3-nitroquinoline (S38).[23]



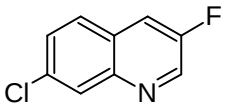
A solution of 4,7-dichloro-3-nitroquinoline **S37** (1.65 g, 6.79 mmol) and *p*-toluenesulfonylhydrazine (1.39 g, 7.47 mmol) in 60 mL of $CHCl_3$ was stirred at r.t. for 24 h and filtered to collect the cream-colored hydrazino intermediate. The precipitate was washed with cold $CHCl_3$ and air dried. The intermediate was dissolved in 0.5N NaOH (150 mL) andheated to 80 ^oC for 1h. The dark-red mixture was cooled to r.t., filtered, and the brown solid was washed thoroughly with water. Crude product was further purified by dry-flash chromatography: SiO_2, eluent: Hex/EtOAc = 8/2 as light-yellow solid,softens at 136-138 °C (Hex). Yield: 892 mg (63%). IR (ATR): 3085m, 2960w, 2928w, 2857w, 2762w, 1606s, 1563m, 1539m, 1479m, 1437w, 1411w, 1380w, 1351s, 1320s, 1256w, 1219w, 1170m, 1142w, 1094w, 1064m, 975w, 933m, 914w, 875w, 831s, 787w, 770w, 740w, 677w, 633w, 544w, 521w, 470w, 446w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 9.65 (d, *J* = 2.4, H-C(2)), 9.02 (d, *J* = 2.4, H-C(4) or H-C(8)), 8.24 (d, *J* = 1.2, H-C(8) or H-C(4)), 8.00 (d, *J* = 8.7, H-C(5)), 7.70-7.60 (m, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 150.34; 145.11; 140.96; 139.82; 132.02; 130.75; 130.04; 128.98; 124.38. HRMS: *m/z*209.01116 corresponds to molecular formula $C_9H_5ClN_2O_2H^+$ (error in ppm: - 0.32).

7-Chloroquinolin-3-amine (13).



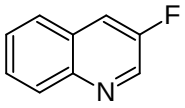
A solution of 7-chloro-3-nitroquinoline **S38** (200 mg, 0.96 mmol) and $SnCl_2$ (910 mg, 4.80 mmol) in MeOH was heated toreflux for 1 h under Ar atmosphere. Thereafter the excess MeOH was evaporated and the residue was dissolved in EtOAc and sat. $NaHCO_3$ solution was added. The resulting mixture was filtered through a celite followed by separation of organic layer via partitioning. Organic layer was collected, dried over anh.Na_2SO_4 and concentrated under reduced pressure to obtain the crude product which was purifiedby dry-flash chromatography: SiO_2, eluent: Hex/EtOAc = 1/1 as yellow solid softens at 126-129 °C (Hex). Yield: 168 mg (98%). IR (ATR): 3315s, 3171s, 1637m, 1607s, 1566m, 1510w, 1489s, 1458m, 1364m, 1341m, 1282m, 1206s, 1135m, 1068m, 986m, 917m, 884m, 862m, 829m, 801m, 763m, 647m, 544w, 521w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 2.8, H-C(2)), 7.95 (d, *J* = 2.0, H-C(8)), 7.52 (d, *J* = 8.9, H-C(5)), 7.40-7.35 (m, H-C(6)), 7.20 (d, *J* = 2.6, H-C(4)), 3.96 (bs, 2H-N). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 143.94; 142.92; 139.90; 130.99; 128.08; 127.89; 127.55; 127.02; 114.64. HRMS: *m/z*179.03700 corresponds to molecular formula $C_9H_7ClN_2H^+$ (error in ppm: - 0.26).

7-Chloro-3-fluoro-quinoline (15).



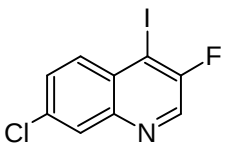
The mixture of amine **13** (500 mg, 2.80 mmol) and48% tetrafluoroboric acid (730 µL, 5.60 mmol) was stirred on ice bath. Solution of sodium nitrite (193 mg, 2.80 mmoL) in water (1 mL) was added dropwise after 15 min. The reaction mixture was stirred as the temperature rose to r.t. Thendiazonium tetrafluoroborate precipitate was filteredoff,washed with cold EtOH and Et_2O then dried under reduced pressure. Diazonium salt was suspendedin 1,2-dichlorobenzene and the mixture was stirred for2 h at 110 ^oC. 7-Chloro-3-fluoroquinoline**15**was obtained after dry-flash chromatography SiO_2, eluent: Hex/EtOAc = 9/1, as light-yellow solid,softens at 76-80 °C (Hex). Yield: 356 mg (70%). IR (ATR): 3076m, 3053m, 2957w, 2857w, 1615m, 1596s, 1565m, 1485m, 1443m, 1414w, 1359w, 1333s, 1263m, 1184s, 1149w, 1129w, 1094w, 1071m, 988m, 961w, 935w, 913m, 891s, 812m, 776m, 645m, 537m, 512m, 477m, 461m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.81 (d, *J* = 2.8, H-C(2)), 8.11 (d, *J* = 1.8, H-C(8)), 7.80-7.70 (m, 2H, H-C(4) and H-C(5)), 7.55-7.50 (m, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.25 (d, *J* = 257.0, C(3)); 145.60 (C(8a)); 142.52 (d, *J* = 27.2, C(2)); 134.41 (C(7)); 128.73 (C(6)); 128.53 (C(5)); 129.20 (C(4a)); 128.35 (d, *J* = 5.1, C(8)); 118.31 (d, *J* = 17.3, C(4)). HRMS: *m/z*182.01646 corresponds to molecular formula $C_9H_5ClFNH^+$ (error in ppm: - 1.49).

3-Fluoro-quinoline (16).



Amixture of 3-aminoquinoline **14**(3.00 g, 20.96 mmol) and48% tetrafluoroboric acid (30 mL, 41.93 mmol) was stirred on ice bath. Solution of sodium nitrite (1.44 g, 20.96 mmol) in water (6 mL) was added dropwise after 15 min. The reaction mixture was stirred as the temperature rose to r.t. Then diazonium tetrafluoroborate precipitate was filtered off, washed with cold EtOH and Et_2O then dried under reduced pressure. Diazonium salt was suspendedin toluene and the mixture was warmed 1 h at the 110 ^oC. 3-Fluoroquinoline **16**was obtained after chromatography SiO_2, eluent: Hex/EtOAc = 9/1,as light-yellow solid (4.9 g, 97%). IR (ATR): 3414w, 3064m, 2927w, 1652w, 1612s, 1560w, 1498s, 1463s, 1426m, 1371w, 1339s, 1213s, 1155s, 984m, 957w, 894m, 859w, 782m, 735m, 710w, 611w, 472w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.82 (d, *J* = 2.8, H-C(2)), 8.13 (d, *J* = 8.5, H-C(8)), 7.85-7.75 (m, 2H, H-C(4) and H-C(5)), 7.75-7.65 (m, H-C(7)), 7.65-7.55 (m, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.25 (d, *J* = 255.0, C(3)); 145.40 (C(8a)); 141.54 (d, *J* = 27.6, C(2)); 129.49 (C(8)); 128.54 (C(7)); 128.42 (d, *J* = 5.7, C(4a)); 127.67 (C(6)); 127.27 (d, *J* = 4.6, C(5)); 118.32 (d, *J* = 17.2, C(4)). HRMS: *m/z*148.05503 corresponds to molecular formula $C_9H_6FNH^+$ (error in ppm: - 4.52).

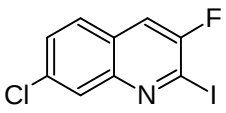
7-Chloro-3-fluoro-4-iodoquinoline (17).



Diisopropylamine (1.8 mL, 12.89 mmol) was added to n-butyllithium/hexane (4.9 mL, 12.28 mmol) in THF (6.5 mL) at -78°C. After 30 min a solution 3-fluoro-7-chloroquinoline (2.23 g, 12.28 mmol) in 5.5 mL of THF was slowly added to solution of the formed LDA at -85 °C. The resulting solution was stirred for 4h at -78 °C, and iodine (3.4 g, 13.51 mmol) in 6 mL THF was slowly added at -85 °C. Stirring was continued for 2h at -78 °C before the reaction was quenched by THF/H_2O = 9/1 (10 mL). Extraction with EtOAc, drying over anh.Na_2SO_4, filtration and solvent removal afforded crude product which was purified by multiple chromatography: dry-flash SiO_2, gradient: Hex/EtOAc = 95/5→9/1,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 9/1). Yield: 1.53 g (41%) of **17**. IR (ATR): 3080m, 3031w, 2959w, 2925w, 1837w, 1738w, 1602m, 1585s, 1551s, 1481s, 1441s, 1384w, 1357s, 1317s, 1307s, 1254m, 1210m, 1179m, 1139m, 1075m, 1018w, 949w, 925s, 895w, 870m, 851w, 814m, 755m, 642w, 576w, 536m, 509m, 429w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.60 (s, H-C(2)), 8.11 (d, *J* = 2.0, H-C(8)), 7.97 (d, *J* = 8.9, H-C(5)), 7.65-7.60 (m, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 157.11 (d, *J* = 255.3, C(3)); 145.36 (C(8a)); 140.80 (d, *J* = 30.0, C(2)); 135.37 (C(7)); 132.16 (C(5)); 129.93 (C(6)); 129.20 (C(4a)); 128.63 (C(8)); 94.90 (d, *J* = 23.0, C(4)). HRMS: *m/z*307.91326 corresponds to molecular formula $C_9H_4ClFINH^+$ (error in ppm: - 0.36).

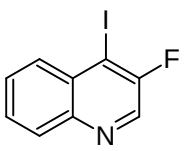
The compound **18** was also isolated as side product (359 mg, 9.5%).

7-Chloro-3-fluoro-2-iodoquinoline (18).



IR (ATR): 3171w, 3071w, 3037s, 2923s, 2853m, 1729w, 1689w, 1603m, 1481m, 1404m, 1373w, 1330s, 1297w, 1255w, 1191s, 1135w, 1071w, 1016m, 918m, 866w, 815wcm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.08 (d, *J* = 1.8, H-C(8)), 7.72 (d, *J* = 8.7, H-C(5)), 7.64 (d, *J* = 7.1, H-C(4)), 7.55 (dd, J_1= 2.0, J_2 = 8.8, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 154.77 (d, *J* = 256.0, C(3)); 146.73 (C(8a)); 135.35 (C(7)); 129.27 (C(6)); 128.21 (d, *J* = 20.0, C(5)); 127.94 (C(8)); 126.36 (C(4a)); 117.50 (d, *J* = 85.2, C(4)); 111.95 (d, *J* = 120.1, C(2)). HRMS: *m/z*307.91325 corresponds to molecular formula $C_9H_4ClFINH^+$ (error in ppm: - 0.40).

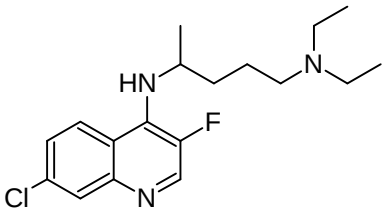
3-Fluoro-4-iodoquinoline (19).[24]



Diisopropylamine (1 mL, 7.14 mmol) was added to n-butyllithium/hexane (2.7 mL, 6.80 mmol) in THF (25 mL) at -78 °C. After 30 min a solution 3-fluoroquinoline (1.00 g, 6.80 mmol) in 5.5 mL of THF was slowly added to the solution of the formed LDA at -85 °C. The resulting solution was stirred for 4h at -78 °C, and iodine (1.90 g, 7.14 mmol) in 7 mL THF was slowly added at -85 °C. Stirring was continued for 2h at -78 °C before the reaction was quenched THF/H_2O = 9/1 (10 mL). Extraction with EtOAc, drying over anh. Na_2SO_4, filtration and solvent removal afforded

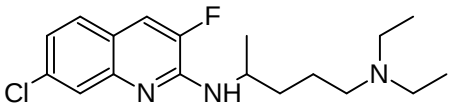
crude product which was purified by dry-flash chromatography SiO_2, gradient: Hex/EtOAc = 95/5 → 9/1. Yield: 1.30 g (70%)of **19**.IR (ATR): 3069m, 2924m, 2854w, 1586s, 1558s, 1491s, 1455s, 1414m, 1382w, 1339s, 1306s, 1262m, 1213s, 1141s, 1011w, 959w, 920m, 797w, 754s, 723m, 630w, 506w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.61 (s, H-C(2)), 8.09 (dd, J_1 = 0.6, J_2 = 8.1, H-C(8)), 8.02 (dd, J_1 = 1.5, J_2 = 8.4, H-C(5)), 7.75-7.70 (m, H-C(7)), 7.70-7.62 (m, H-C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 157.02 (d, J = 252.7, C(3)); 145.33 (d, J = 1.8, C(8a)); 139.85 (d, J = 30.7, C(2)); 130.87 (d, J = 5.4, C(5)); 130.62 (C(4a)); 129.86 (C(8)); 129.15 (d, J = 2.7, C(7)); 129.07 (C(6)); 95.19 (d, J = 21.7, C(4)). HRMS: *m/z*273.95195 corresponds to molecular formula $C_9H_5FINH^+$ (error in ppm: - 1.46).

N^4-(7-Chloro-3-fluoroquinolin-4-yl)-N^1,N^1-diethylpentane-1,4-diamine (74).



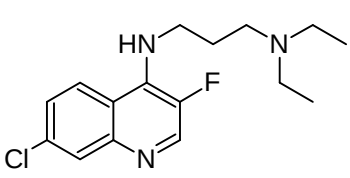
Compound **74** was prepared from 7-chloro-3-fluoro-4-iodoquinoline (300 mg, 0.98 mmol) and 2-amino-5-diethylaminopentane (378 µL, 1.95 mmol) using $Pd(OAc)_2$ (8.8 mg, 0.039 mmol), DPEphos (42 mg, 0.078 mmol) and K_3PO_4 (518 mg, 2.44 mmol) by method Hand was and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2 and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 8/2) as colorless foam (329 mg, 54%),softens at 48-50 °C. IR(ATR): 3304m, 3069w, 2970s, 2936m, 2871w, 2810w, 1595s, 1574s, 1536m, 1488w, 1452m, 1418m, 1380m, 1351m, 1294w, 1265m, 1221w, 1197w, 1140m, 1078m, 929w, 906w, 877w, 815m, 764w, 735w, 656w, 540w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 336 (11554), 252 (16869) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.52 (d, J = 5.5, H-C(2)), 7.96 (d, J = 2.2, H-C(8)), 7.75 (d, J = 9.1, H-C(5)), 7.42-7.36 (m, H-C(6)), 4.73 (d, J = 7.7, -N*H*), 4.20-4.05 (m, 1H, ArNHC*H*(CH_3)-), 2.54 (q, 4H, J = 7.2, -NH(C$H_2$$CH_3$)$_2$), 2.50-2.43 (m, 2H, -C$H_2$NH($CH_2CH_3$)$_2$), , 1.75-1.55 (m, 4H, ArNHCH(CH_3)CH_2-, ArNHCH(CH_3)CH_2CH_2-), 1.29 (dd, 3H, J_1 = 0.9, J_2 = 6.3, ArNHCH(CH_3)-), 1.01 (t, 6H, J = 7.0, -NH(CH_2CH_3)$_2$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.62 (C(8a)); 143.42 (d, J = 240.1, C(3)); 142.45 (d, J = 27.3, C(2)); 135.77 (d, J = 6.3, C(4)); 133.97 (C(7)); 128.96 (C(8)); 125.95 (C(6)); 121.89 (d, J = 5.4, C(5)); 119.45 (d, J = 4.5, C(4a)); 52.54; 51.34 (d, J = 8.1, ArNH*C*H(CH_3)-); 46.78; 36.12; 23.70; 22.30; 11.26. HRMS: *m/z*338.18020 corresponds to molecular formula $C_{18}H_{25}ClFN_3H^+$ (error in ppm: + 2.43. Anal. ($C_{18}H_{25}ClFN_3$ × 1/2 H_2O) Calcd: C, 62.33; H, 7.56; N, 12.11. Found: C, 62.00; H, 7.32; N, 11.85. HPLCpurity (λ = 330 nm) method A: RT 7.677min, area 98.24%; method B: RT 9.229 min, area 98.45%.

N^4-(7-Chloro-3-fluoroquinolin-2-yl)-N^1,N^1-diethylpentane-1,4-diamine (76).



Compound **76** was prepared from 7-chloro-3-fluoro-2-iodoquinoline (100 mg, 0.33 mmol) and 2-amino-5-diethylaminopentane (126 µL, 0.65 mmol) using $Pd(OAc)_2$ (2.9 mg, 0.013 mmol), DPEphos (14 mg, 0.026 mmol) and K_3PO_4 (173 mg, 0.81 mmol) by method Hand was and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,and flash chromatography (Biotage SP1 RP column, eluent: MeOH/H_2O = 8/2) as yellow viscous oil (76 mg, 70%). IR(ATR): 3440m, 3288m, 2968s, 2932m, 2871w, 2806w, 1637s, 1609m, 1568m, 1532s, 1492w, 1463m, 1416m, 1377w, 1345w, 1286w, 1261m, 1190m, 1145m, 1120m, 1098m, 1070m, 969w, 948w, 883m, 800w, 761w, 721w, 602w, 513w, 475w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 346 (8397), 333 (8354), 243 (37616) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.68 (d, *J* = 2.0, H-C(8)), 7.43 (d, *J* = 8.4, H-C(5)), 7.37 (d, *J* = 11.3, H-C(4)), 7.16 (dd, J_1 = 1.6, *J* = 8.5, H-C(6)), 5.21 (d, *J* = 6.5, H-N), 4.45-4.35 (m, 1H, ArNHC*H*(CH_3)-), 2.58 (q, 4H, *J* = 7.2, -NH(C$H_2$$CH_3$)$_2$), 2.55-2.50 (m, 2H, -C$H_2$NH($CH_2CH_3$)$_2$), 1.75-1.55 (m, 4H, ArNHCH(CH_3)CH_2-, ArNHCH(CH_3)CH_2CH_2-), 1.29 (d, *J* = 1.3, ArNHCH(CH_3)-), 1.04 (t, *J* = 7.2, -NH(CH_2CH_3)$_2$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 148.41 (d, *J* = 13.6, C(8a)); 147.15 (d, *J* = 258.1, C(3)); 143.86 (d, *J* = 2.7, C(2)); 133.87 (C(7)); 127.78 (d, *J* = 5.0, C(5)); 125.25 (C(8)); 123.08 (C(6)); 121.32 (d, *J* = 4.1, C(4a)); 115.90 (d, *J* = 15.3, C(4)); 52.63; 46.73 (d, *J* = 5.4, ArNH*C*H(CH_3)-); 45.84; 34.81; 23.15; 20.84; 11.06. HRMS: *m/z*338.17891 corresponds to molecular formula $C_{18}H_{25}ClFN_3H^+$ (error in ppm: - 1.40).Anal. ($C_{18}H_{25}ClFN_3 \times 1/2\ H_2O$) Calcd: C, 62.33; H, 7.56; N, 12.11. Found: C, 62.28; H, 7.69; N, 11.94. HPLCpurity (λ = 330 nm) method A: RT 8.042 min, area 96.24%; method B: RT 10.764 min, area 96.01%.

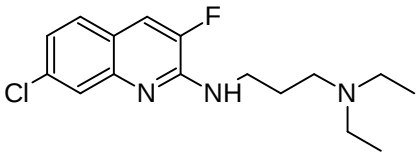
***N*'-(7-Chloro-3-fluoroquinolin-4-yl)-*N*,*N*-diethylpropane-1,3-diamine (73).**



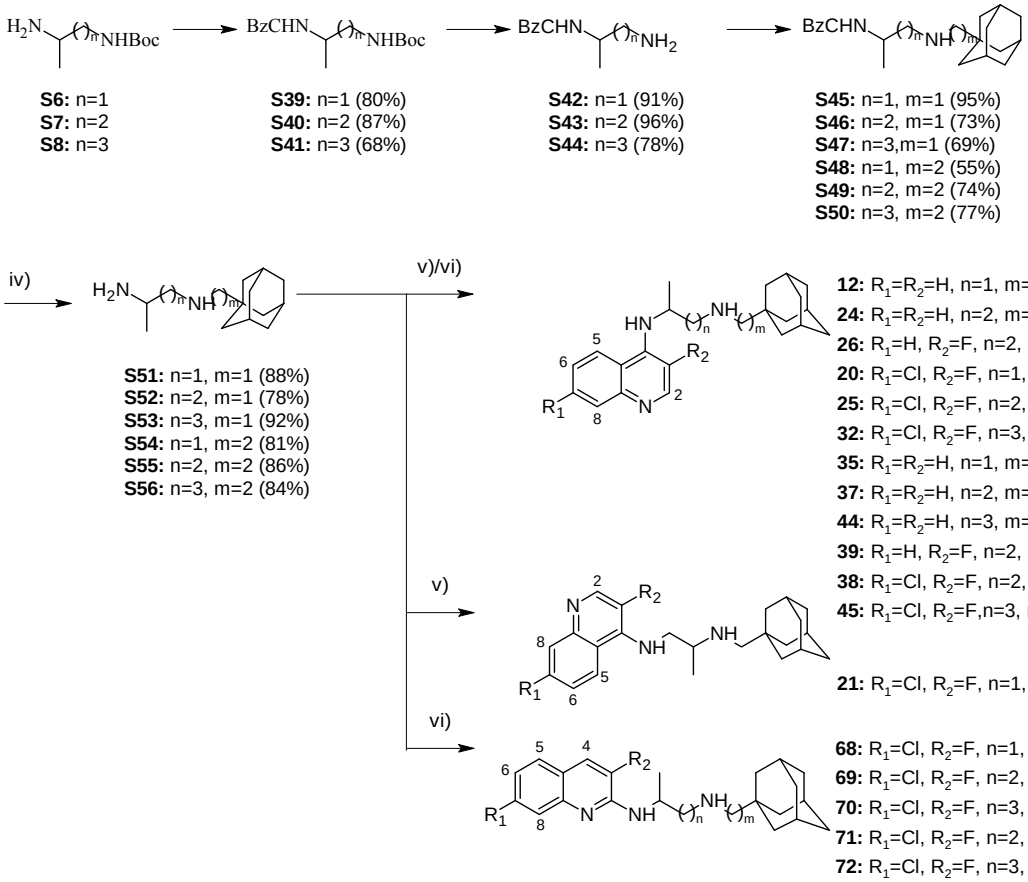
Compound **73** was prepared from7-chloro-3-fluoro-4-iodoquinoline (100 mg, 0.32 mmol) and 3-diethylamino-1-propilamine (105 µL, 0.65 mmol) using $Pd(OAc)_2$ (2.9 mg, 0.013 mmol), SPhos (10.7 mg, 0.026 mmol) and K_3PO_4 (178 mg, 0.81 mmol) by method H and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 85/15) as colorless foam (64 mg, 63%)softens at 47-48°C. IR(ATR): 3234m, 3065w, 2970s, 2934m, 2872w, 2822m, 1640w, 1597s, 1574s, 1540m, 1489w, 1470w, 1454w, 1429m, 1380m, 1360m, 1294w, 1268w, 1246w, 1195m, 1166w, 1138m, 1077m, 934m, 892m, 812m, 762m, 737w, 654w, 622w, 540w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 337 (9690), 252 (15073) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.45 (d, *J* = 6.0, H-C(2)), 7.91 (d, *J* = 2.2, H-C(8)), 7.75 (d, *J* = 9.0, H-C(5)), 7.32 (dd, J_1 = 1.6, J_2 = 9.0, H-C(6)), 3.90-3.80 (m,

2H, ArNHC*H*$_2$-), 2.72-2.68 (m, 2H, -C*H*$_2$NH(CH$_2$CH$_3$)$_2$), 2.65 (q, 4H, *J* = 7.1, -NH(C*H*$_2$CH$_3$)$_2$), 2.04 (bs, H-N), 1.90-1.80 (m, 2H, ArNHCH$_2$C*H*$_2$-), 1.10 (t, 6H, *J* = 7.1, -NH(CH$_2$C*H*$_3$)$_2$). ^{13}C-NMR (125 MHz, $CDCl_3$): 146.60 (C(8a)); 143.50 (d, *J* = 226.3, C(3)); 142.45 (d, *J* = 27.2, C(2)); 137.28 (d, *J* = 5.9, C(4)); 133.72 (d, *J* = 7.2, C(7)); 128.65 (C(8)); 125.23 (C(6)); 122.74 (d, *J* = 5.0, C(5)); 119.28 (d, *J* = 5.9, C(4a)); 53.50; 47.44 (d, *J* = 9.9, ArNH*C*H$_2$-); 47.03; 25.31; 11.28. HRMS: *m/z*310.14830 corresponds to molecular formula $C_{16}H_{21}ClFN_3H^+$ (error in ppm: + 0.71).(+)ESI-HRMS (*m/z* (%)): 310.14830 ([M+H]$^+$, 100); calculated 310.14808 (error in ppm: 0.71). Anal**.** ($C_{16}H_{21}ClFN_3 \times 1/2\ H_2O$) Calcd: C, 60.28; H, 6.96; N, 13.18. Found: C, 60.65; H, 7.07; N, 12.79. HPLCpurity (λ = 330 nm) method A: RT 7.585min, area 99.71%; method B: RT 8.693 min, area 95.30%.

***N*'-(7-Chloro-3-fluoroquinolin-2-yl)-*N*,*N*-diethylpropane-1,3-diamine (75).**

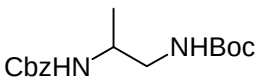


Compound **75** was prepared from 7-chloro-3-fluoro-2-iodoquinoline (100mg, 0.32 mmol) and 3-diethylamino-1-propilamine (74 µL, 0.46 mmol) using $Pd(OAc)_2$ (2.0 mg, 0.009 mmol), SPhos (7.5 mg, 0.018 mmol) and K_3PO_4(124 mg, 0.57 mmol) by method H and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,and flash chromatography (Biotage SP1 RP column, eluent; MeOH/H_2O = 8/2) as yellow viscous oil (51 mg, 72%). IR(ATR): 3450w, 3241m, 2970m, 2931m, 2873w, 2815m, 1639m, 1610w, 1563w, 1537s, 1497w, 1459m, 1416m, 1378w, 1338m, 1292m, 1256m, 1193m, 1146m, 1124m, 1098w, 1070m, 1032w, 979w, 921w, 885m, 800w, 761w, 739w, 604w, 514w, 476w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 343 (8682), 332 (8760), 242 (35685) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.69 (d, *J* = 2.0, H-C(8)), 7.50-7.40 (bs, 1H, *H*-N-), 7.41 (d, *J* = 8.5, H-C(5)), 7.33 (d, *J* = 11.2, H-C(4)), 7.14 (dd, J_1 = 2.0, J_2 = 8.4, H-C(6)), 3.75-3.60 (m, 2H, ArNHC*H*$_2$-), 2.64 (t, 2H, *J* = 6.0, -C*H*$_2$NH(CH$_2$CH$_3$)$_2$), 2.57 (q, 4H, *J* = 7.1, -NH(C*H*$_2$CH$_3$)$_2$), 1.90-1.75 (m, 2H, ArNHCH$_2$C*H*$_2$-), 1.07 (t, 6H, *J* = 7.2, -NH(CH$_2$C*H*$_3$)$_2$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 149.16 (d, *J* = 14.0, C(8a)); 147.58 (d, *J* = 259.0, C(3)); 145.54 (d, *J* = 2.7, C(2)); 133.77 (d, *J* = 7.2, C(7)); 127.77 (d, *J* = 5.0, C(5)); 125.03 (C(8)); 122.80 (C(6)); 121.26 (d, *J* = 4.5, C(4a)); 115.56 (d, *J* = 15.4, C(4)); 53.00; 46.83; 41.57; 25.11; 11.53. HRMS: *m/z*310.14742 corresponds to molecular formula $C_{16}H_{21}ClFN_3H^+$ (error in ppm: - 2.14).Anal. ($C_{16}H_{21}ClFN_3 \times 1/4\ H_2O$) Calcd: C, 61.14; H, 6.89; N, 13.37. Found: C, 61.33; H, 6.96; N, 13.40. HPLCpurity (λ = 330 nm) method A: RT 7.559 min, area 99.45%; method B: RT 8.647 min, area 99.28%.



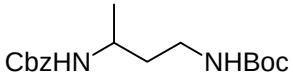
i) benzyl-chloroformate (1.2 equiv), Et_3N (3.0 equiv), CH_2Cl_2, 3 h, r.t.; ii) TFA/CH_2Cl_2, 2 h, r.t., 2.5 NaOH, r.t.; iii) aldehyde (1 equiv), $Ti(OiPr)_4$ (1.2 ekv), $NaBH_4$, absolute EtOH, 24 h; iv) H_2, Pd(C) (10%), MeOH, 20 psi, r.t., 6 h; v) MW, 4-chloroquinoline/4-quinoline (1 equiv), NMP, 180 ^oC, 1 h; vi) $Pd(OAc)_2$ (4 mol%), SPhos (8 mol%), 4-chloroqunoline (1 equiv), K_3PO_4 (2.5 equiv), dioxane.

Benzyl *tert*-butyl propane-1,2-diylbiscarbamate (S39).



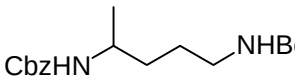
Compound **S39** was prepared from mono-Boc-protected 1,2-propanediamine (3.30 g, 18.94 mmol) using benzyl-chloroformate (3.2 mL, 22.72 mmol) and Et_3N (5.1 mL, 36.93 mmol) by method Iand was obtained after dry-flash chromatography: SiO_2, gradient: Hex/EtOAc = 9/1 → 1/1,as colorless oil (4.67 g, 80%). IR(ATR): 3356s, 2981m, 2932w, 2880w, 1688s, 1537s, 1453w, 1389w, 1368w, 1318m, 1271m, 1230m, 1172m, 1065m, 998w, 915w, 865w, 779w, 730w, 695w, 666w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.40-7.28 (m, 5H, -*Ph*), 5.20-5.00 (m, 3H, -C*H*$_2$Ph, H-N), 4.95-4.70 (bs, H-N), 3.85-3.70 (m, 1H, CbzNHC*H*(CH_3)-), 3.25-3.10 (m, 2H, -C*H*$_2$NHBoc), 1.42 (s, 9 H, -NHCOO-C(C*H*$_3$)$_3$), 1.15 (d, 3H, *J* = 6.7, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.64; 156.20; 136.51; 128.48; 128.06; 79.54; 66.58; 48.14; 45.78; 28.31; 18.54. HRMS: *m/z*309.18088 corresponds to molecular formula $C_{16}H_{24}N_2O_4H^+$ (error in ppm: - 2.11).

Benzyl *tert*-butyl butane-1,3-diylbiscarbamate (S40).



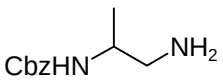
Compound **S40** was prepared from mono-Boc-protected 1,3-butanediamine (488 mg, 2.6 mmol) using benzyl-chloroformate (513 µL, 5.70 mmol) and Et_3N (1.08 mL, 7.8 mmol) by method Iand was obtained after dry-flash chromatography: SiO_2, gradient: Hex/EtOAc = 9/1 → 1/1,as colorless oil (728 mg, 87%). IR(ATR): 3354m, 3040w, 2976m, 2938w, 1745m, 1688s, 1597m, 1533s, 1475m, 1388w, 1368w, 1331w, 1257s, 1173m, 1113w, 1080w, 1006w, 947w, 875w, 814w, 783w, 756m, 697w, 647w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.40-7.30 (m, 5H, -*Ph*), 5.09 (s, 2H, -C*H*$_2$Ph), 4.66 (bs, H-N), 3.90-3.75 (m, 1H, CbzNHC*H*(CH_3)-), 3.40-3.25 (m, 1H, -C*H*$_2$NHBoc 3.05-2.90 (m, 1H, -C*H*$_2$NHBoc), 1.75-1.60 (m, 1H), 1.55-1.35 (m, 10 H, -C*H*$_2$C*H*$_2$NHBoc,-NHCOO-C(C*H*$_3$)$_3$), 1.18 (d, 3H, *J* = 6.7, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.17; 156.01; 136.45; 128.52; 128.01; 79.04; 66.64; 44.61; 37.63; 37.15; 28.40; 21.40. HRMS: *m/z*323.19590 corresponds to molecular formula $C_{17}H_{26}N_2O_4H^+$ (error in ppm: - 1.95).

Benzyl *tert*-butyl pentane-1,4-diylbiscarbamate (S41).



Compound **S41** was prepared from mono-Boc-protected 1,4-pentanediamine (2.02 g, 10 mmol) using benzyl-chloroformate (3.12 mL, 22 mmol) and Et_3N (4.16 mL, 30 mmol) by method I and was obtained by dry-flash chromatography: SiO_2, gradient: Hex/EtOAc = 9/1 → 1/1,as colorless oil (2.3 g, 68%). IR(ATR): 3320s, 2975m, 2942m, 2868w, 1684s, 1541s, 1454m, 1368w, 1341w, 1277s, 1257s, 1170m, 1108w, 1085w, 993w, 859w, 754w, 730w, 695w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.35-7.20 (m, 5H, -*Ph*), 5.01 (s, 1H, -C*H*$_2$Ph), 4.51 (bs, H-N), 3.70-3.55 (m, 1H, CbzNHC*H*(CH_3)-), 3.10-2.90 (m, 2H, -C*H*$_2$NHBoc), 1.50-1.30 (m, 13H, CbzNHCH(CH_3)C*H*$_2$-, CbzNHCH(CH_3)CH$_2$C*H*$_2$-, -NHCOO-C(C*H*$_3$)$_3$), 1.07 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.98; 155.72; 136.59; 128.50; 128.07; 126.96; 66.52; 46.92; 40.37; 34.32; 28.39; 26.68; 21.24. HRMS: *m/z*337.21241 corresponds to molecular formula $C_{18}H_{28}N_2O_4H^+$ (error in ppm: + 0.68).

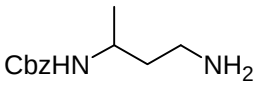
Benzyl (2-amino-1-methylethyl)carbamate (S42).



Compound **S42** was prepared from **S36** (1.80 g, 5.82 mmol) using methodCand was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,as colorless oil (1.10 g, 91%). IR(ATR): 3312m, 3033w, 2968m, 1703s, 1534s, 1454m, 1377w, 1337w, 1253s, 1095m, 1049m, 914w, 747m, 699m cm^{-1}. **1**H-NMR (500 MHz, $CDCl_3$, δ): 7.45-7.25 (m, 5H, -*Ph*), 5.20-5.05 (m, 2H, -C*H*$_2$Ph), 4.97 (bs, H-N), 3.80-3.65 (m, 1H, CbzNHC*H*(CH_3)-), 2.80-2.70 (m, 1H, -C*H*$_2$NH$_2$), 2.70-2.60 (m, 1H, -C*H*$_2$NH$_2$), 1.28 (s, 2H-N), 1.13 (d, 3H, *J* = 6.9, C*H*$_3$).

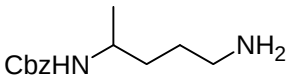
^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.12; 136.56; 128.48; 128.04; 66.54; 49.13; 47.26; 18.40. HRMS: *m/z*209.12811 corresponds to molecular formula $C_{11}H_{16}N_2O_2H^+$ (error in ppm: -1.63).

Benzyl (3-amino-1-methylpropyl)carbamate (S43).



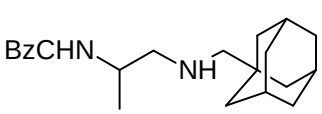
Compound **S43** was prepared from **S40** (6.6 g, 20.6 mmol) using method C and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2, as colorless oil (4.40 g, 96%)softens at 88-90 °C.IR (ATR): 3329m, 3034w, 2967m, 2936m, 1537s, 1454m, 1338w, 1260s, 1098m, 1056m, 910w, 744w, 698w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.40-7.25 (m, 5H, -*Ph*), 5.15-5.05 (m, 3H, -C*H*$_2$Ph, -N*H*), 3.95-3.80 (m, 1H, CbzNHC*H*(CH_3)-), 2.85-2.70 (m, 2H, -C*H*$_2$$NH_2$), 1.65-1.55 (m, 1H, -C*H*$_2$$CH_2NH_2$), 1.55-1.45 (m, 1H, -C*H*$_2$$CH_2NH_2$), 1.26 (s, 2H-N), 1.17 (d, 3H, *J* = 6.6, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.95; 136.65; 128.46; 128.01; 66.44; 45.14; 40.39; 38.70; 21.33. HRMS: *m/z*223.14348 corresponds to molecular formula $C_{12}H_{18}N_2O_2H^+$ (error in ppm: - 2.82).

Benzyl (4-amino-1-methylbutyl)carbamate (S44).



Compound **S44** was prepared from **S41** (2.20 g, 6.5 mmol) using method C and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,as colorless oil (1.21 g, 78%). IR (ATR): 3335s, 3058w, 3035w, 2986w, 2934m, 2164w, 1690s, 1566m, 1537s, 1463m, 1426w, 1386w, 1326m, 1261s, 1120w, 1076m, 1024w, 970w, 912w, 876w, 844w, 822w, 781w, 751w, 732w, 698w, 643w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.45-7.20 (m, 5H, -*Ph*), 5.08 (s, 1H, -C*H*$_2$Ph), 4.72 (bs, H-N), 3.80-3.65 (m, 1H, CbzNHC*H*(CH_3)-), 2.80-2.60 (m, 2H, -C*H*$_2$$NH_2$), 1.60-1.35 (m, 6H, CbzNHCH(CH_3)C*H*$_2$-, CbzNHCH(CH_3)CH_2C*H*$_2$-, 2H-N), 1.15 (d, 3H, *J* = 6.7, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.78; 136.65; 128.49; 128.05; 66.47; 46.97; 41.92; 34.42; 29.88; 21.18. HRMS: *m/z*237.15860 corresponds to molecular formula $C_{13}H_{20}N_2O_2H^+$ (error in ppm: - 4.87).

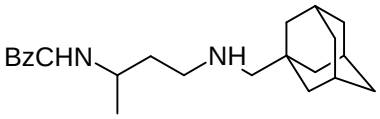
Benzyl {2-[(1-adamantylmethyl)amino]-1-methylethyl}carbamate (S45).



Compound**S45** was prepared from mono-*N*-Cbz-protected 1,2-propanediamine diamine **S42** (2.80 g, 13.4 mmol) and adamantane-1-carboxaldehyde (2.00 g, 12.18 mmol) using $Ti(OiPr)_4$ (5.4 mL, 18.12 mmol) and $NaBH_4$ (685 mg, 18.12 mmol) using method G and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 → 7/3,as colorless oil (4.1 g, 95%). IR (ATR): 3332m, 3089w, 3063w, 3033w, 2965w, 2901s, 2845s, 2676w, 1703s, 1532m, 1501m, 1452m, 1403w, 1372w, 1341w, 1311w, 1241m, 1156w, 1069m, 1026w, 774w, 737w, 698w, 646w, 604w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.40-7.25 (m, 5H, -*Ph*), 5.15-5.05 (s, 2H, -C*H*$_2$Ph), 3.85-3.70 (m, 1H, CbzNHC*H*(CH_3)-), 2.65-2.55 (m, 2H, -

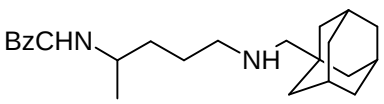
CH_2NHCH_2Ad), 2.30-2.15 (m, 2H, -CH_2Ad), 1.95 (s, 3H, -Ad), 1.75-1.55 (m, 6H, -Ad), 1.54-1.40 (m, 6H, -Ad), 1.15 (d, 3H, J = 6.6, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.15; 136.76; 128.48; 128.00; 66.43; 62.68; 55.63; 46.52; 40.80; 37.22; 35.56; 28.45; 19.13. HRMS: *m/z*357.25278 corresponds to molecular formula $C_{22}H_{32}N_2O_2H^+$ (error in ppm: -2.44).

Benzyl {3-[(1-adamantylmethyl)amino]-1-methylpropyl}carbamate (S46).



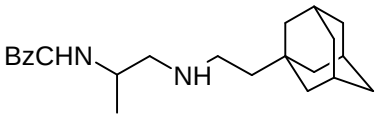
Compound **S46** was prepared by method G from mono-*N*-Cbz-protected 1,3-butanediamine **S43** (1.54 g, 6.9 mmol) and adamantane-1-carboxaldehyde (948 mg, 5.8 mmol) using $Ti(OiPr)_4$ (2.6 mL, 8.66 mmol) and $NaBH_4$ (327 mg, 8.66 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 → 7/3,as colorless oil (1.51 g, 73%). IR (ATR): 3319w, 3063w, 3032w, 2901s, 2845s, 2677w, 1707s, 1528m, 1451m, 1375w, 1343w, 1254m, 1154w, 1088m, 1030w, 979w, 775w, 736w, 697w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.40-7.25 (m, 5H, -*Ph*), 6.44 (bs, 1H, -N*H*), 5.15-5.00 (m, 2H, -CH_2Ph), 3.90-3.75 (m, 1H, CbzNHC*H*(CH_3)-), 2.80-2.70 (m, 1H, -CH_2NHCH_2Ad), 2.70-2.60 (m, 1H, -CH_2NHCH_2Ad), 2.23 (ABq, H_A, J = 11.3, -CH_2Ad), 2.20 (ABq, H_B, J = 11.3, -CH_2Ad), 1.92 (s, 3H, -Ad), 1.80-1.55 (m, 7H, -CH_2CH$_2$NHCH$_2$Ad,-Ad), 1.55-1.40 (m, 7H, -CH_2CH$_2$NHCH$_2$Ad, -Ad), 1.19 (d, 3H, J = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.05; 136.89; 128.37; 127.81; 66.20; 62.90; 47.23; 46.56; 40.87; 37.16; 35.36; 33.25; 28.41; 20.82. HRMS: *m/z*371.26950 corresponds to molecular formula $C_{23}H_{34}N_2O_2H^+$ (error in ppm: + 0.52).

Benzyl {4-[(1-adamantylmethyl)amino]-1-methylbutyl}carbamate (S47).



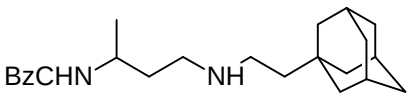
Compound **S47** was prepared by method G from mono-*N*-Cbz-protected 1,4-pentanediamine **S44** (1.28 g, 5.42 mmol) and adamantane-1-carboxaldehyde (780 mg, 4.75 mmol) using $Ti(OiPr)_4$ (2.1 mL, 7.12 mmol) and $NaBH_4$ (269 mg, 7.12 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 → 7/3) as colorless oil (1.26 g, 69%). IR(ATR): 3320w, 3033w, 2902s, 2846s, 1703s, 1533m, 1452m, 1342w, 1252m, 1090m, 911w, 733m, 697w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.40-7.20 (m, 5H, -*Ph*), 5.08 (s, 1H, -CH_2Ph), 3.80-3.60 (m, 1H, CbzNHC*H*(CH_3)-), 2.65-2.50 (m, 2H, -CH_2NHCH_2Ad), 2.21 (s, 2H, -CH_2Ad), 1.94 (s, 3H, -Ad), 1.78-1.58 (m, 6H, -Ad), 1.58-1.40 (m, 10H, CbzNHCH(CH_3)CH_2-, CbzNHCH(CH_3)CH$_2$CH_2-, -Ad), 1.14 (d, 3H, J = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.84; 136.72; 128.44; 128.06; 127.96; 66.38; 62.87; 50.58; 47.02; 40.89; 37.18; 34.54; 33.28; 28.43; 26.09; 21.12. HRMS: *m/z*385.28474 corresponds to molecular formula $C_{24}H_{36}N_2O_2H^+$ (error in ppm: - 0.56).

Benzyl (2-{[2-(1-adamantyl)ethyl]amino}-1-methylethyl)carbamate (S48).



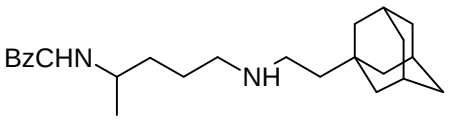
Compound **S48** was prepared by method G from mono-**N**-Cbz-protected 1,2-propanediamine **S42** (1.20 g, 5.76 mmol) and 1-adamantylacetaldehyde (890 mg, 5.00 mmol) using $Ti(OiPr)_4$ (2.6 mL, 8.64 mmol) and $NaBH_4$ (327 mg, 8.64 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 → 7/3,as colorless oil (1.38 g, 55%). IR (ATR): 3325m, 2903s, 2846s, 1716s, 1535m, 1453m, 1348w, 1254m, 1084w, 736w, 692w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.40-7.25 (m, 5H, -*Ph*), 5.22-5.05 (m, 3H, H-N, -C*H*$_2$Ph), 3.90-3.75 (m, 1H, CbzNHC*H*(CH_3)-), 2.70-2.64 (m, 2H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.64-2.50 (m, 2H, -C*H*$_2$CH$_2$Ad), 1.93 (s, 3H, -Ad), 1.75-1.55 (m, 6H, -Ad), 1.53-1.42 (m, 6H, -Ad), 1.30-1.20 (m, 2H, -C*H*$_2$Ad), 1.16 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 156.08; 136.62; 128.46; 127.99; 66.49; 54.80; 46.55; 44.39; 44.20; 42.58; 37.09; 31.81; 28.62; 19.08. HRMS: *m/z*371.26930 corresponds to molecular formula $C_{23}H_{34}N_2O_2H^+$ (error in ppm: - 0.91).

Benzyl (3-{[2-(1-adamantyl)ethyl]amino}-1-methylpropyl)carbamate (S49).



Compound **S49** was prepared by method G from mono-*N*-Cbz-protected 1,3-butanediamine **S43** (1.47 g, 6.63 mmol) and 1-adamantylacetaldehyde (1.07 mg, 6.05 mmol) using $Ti(OiPr)_4$ (2.7 mL, 9.03 mmol) and $NaBH_4$ (343 mg, 9.03 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 → 7/3,as colorless oil (1.71 g, 74%). IR (ATR): 3181w, 2964w, 2902s, 2846s, 1712s, 1559m, 1449m, 1370w, 1260m, 1095m, 1055w, 1024w, 839w, 768w, 737w, 695w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.45-7.25 (m, 5H, -*Ph*), 5.46 (bs, H-N) 5.15-5.05 (m, 2H, -C*H*$_2$Ph), 3.90-3.75 (m, 1H, CbzNHC*H*(CH_3)-), 2.76-2.67 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.67-2.60 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.60-2.50 (m, 2H, -C*H*$_2$CH$_2$Ad), 1.93 (s, 3H, -Ad), 1.75-1.57 (m, 6H, -Ad), 1.58-1.30 (m, 8H, CbzNHCH(CH_3)C*H*$_2$-, -Ad), 1.30-1.20 (m, 2H, -C*H*$_2$Ad), 1.18 (d, 3H, *J* = 6.6, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 155.94; 136.77; 128.43; 127.93; 66.32; 46.61; 45.96; 44.65; 44.28; 42.59; 37.11; 36.67; 31.80; 28.64; 21.20. HRMS: *m/z*385.28474 corresponds to molecular formula $C_{24}H_{36}N_2O_2H^+$ (error in ppm: - 0.56).

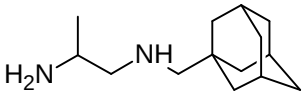
Benzyl (4-{[2-(1-adamantyl)ethyl]amino}-1-methylbutyl)carbamate (S50).



Compound **S50** was prepared by method Gfrom mono-*N*-Cbz-protected1,4-pentanediamine **S44** (1.58 g, 6.68 mmol) and 1-adamantylacetaldehyde (993 mg, 5.57 mmol) using $Ti(OiPr)_4$ (2.5 mL, 8.35 mmol) and $NaBH_4$ (316 mg, 8.35 mmol) and was obtained after dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 9/1 → 7/3,as colorless oil (1.70 g, 77%). IR (ATR): 3312w, 3031w, 2898s, 2844s, 1696s, 1530s,

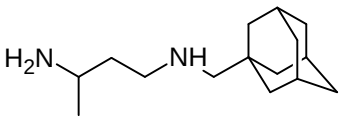
1449s, 1376w, 1344w, 1249s, 1182s, 1087m, 1063m, 1028w, 813w, 774w, 735m, 696s, 679w, 621w, 596w, 541w, 532w, 525w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.45-7.20 (m, 5H, -*Ph*), 5.20-5.05 (s, 1H, -C*H*$_2$Ph), 5.05-4.95 (bs, 1H, -N*H*), 3.80-3.65 (m, 1H, CbzNHC*H*(CH_3)-), 2.65-2.50 (m, 4H, -C*H*$_2$NHCH$_2$CH$_2$Ad, -C*H*$_2$CH$_2$Ad), 2.00-1.85 (m, 3H, -Ad), 1.75-1.65 (m, 6H, -Ad), 1.55-1.40 (m, 10H, CbzNHCH(CH_3)C*H*$_2$-, CbzNHCH(CH_3)CH$_2$C*H*$_2$-, -Ad), 1.35-1.20 (m, 2H, -C*H*$_2$Ad), 1.14 (d, 3H, *J* = 6.7, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 136.69; 128.46; 127.99; 66.40; 49.78; 46.92; 44.44; 44.22; 42.59; 37.12; 34.77; 31.81; 28.64; 26.19; 21.09. HRMS: *m/z*399.29961 corresponds to molecular formula $C_{25}H_{38}N_2O_2H^+$ (error in ppm: - 2.49).

***N*^{1}-(1-Adamantylmethyl)propane-1,2-diamine (S51).**



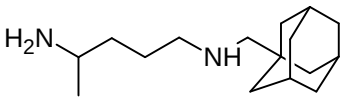
Compound **S51** was prepared by method Jfrom **S45** (1.50 g, 4.2 mmol) using Pd/C 10% (150 mg) and was obtained by dry-flash chromatography: SiO_2, gradient: EtOAc/[MeOH/(NH_3 aq) = 9/1] = 9/1 → 8/2,as colorless oil (823 mg, 88%). IR (ATR): 3346w, 2901s, 2845s, 2676w, 1583w, 1451m, 1368w, 1345w, 1312w, 1153w, 1100w, 1052w, 883w, 829w, 768w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 3.05-2.90 (m, 1H, NH_2C*H*(CH_3)-), 2.65-2.50 (m, 1H, -C*H*$_2$NHCH$_2$Ad), 2.40-2.15 (m, 3H, -C*H*$_2$NHCH$_2$Ad, -C*H*$_2$Ad), 1.96 (s, 3H, -Ad), 1.75-1.60 (m, 8H, 2H-N, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.05 (d, 3H, *J* = 6.2, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 62.79; 59.06; 46.25; 40.86; 37.22; 33.49; 28.44; 21.71. HRMS: *m/z*223.21688 corresponds to molecular formula $C_{14}H_{26}N_2H^+$ (error in ppm: - 4.11).

***N*^{1}-(1-Adamantylmethyl)butane-1,3-diamine (S52).**



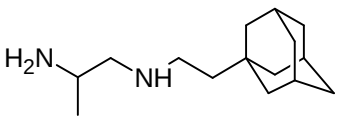
Compound **S52** was prepared by method Jfrom **S46** (1.40 g, 3.9 mmol) using Pd/C10% (140 mg) and was obtained by dry-flash chromatography: SiO_2, gradient: EtOAc/[MeOH/(NH_3 aq) = 9/1] = 9/1 → 8/2,as colorless powder softness at 108-110 ^{o}C. Yield: 724 mg (78%). IR (ATR): 3284w, 2902s, 2845s, 2659w, 2574w, 1663w, 1633w, 1520m, 1470m, 1452w, 1425w, 1405m, 1366w, 1344w, 1311m, 1268w, 1152w, 1101w, 1033w, 948w, 878w, 810w, 764w, 641w, 593w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 3.05-2.95 (m, 1H, NH_2C*H*(CH_3)-), 2.75-2.60 (m, 2H, -C*H*$_2$NHCH$_2$Ad), 2.25 (ABq, H_A, *J* = 11.4, -C*H*$_2$Ad), 2.23 (ABq, H_B, *J* = 11.4, -C*H*$_2$Ad), 1.96 (s, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.40 (m, 10H, NH_2CH(CH_3)C*H*$_2$-, -N*H*$_2$, -Ad), 1.08 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 63.17; 48.77; 46.07; 40.95; 39.70; 37.23; 33.32; 28.47; 24.48. HRMS: *m/z*237.23236 corresponds to molecular formula $C_{15}H_{28}N_2H^+$ (error in ppm: - 0.71).

***N*[1]-(1-Adamantylmethyl)pentane-1,4-diamine (S53).**



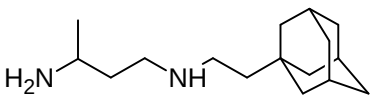
Compound **S53** was prepared by method J from **S47** (650 mg, 1.69 mmol) using 10%Pd/C (65 mg) and was obtained by dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,as colorless oil (389 mg, 92%). IR(ATR): 2902s, 2846s, 1582w, 1452m, 1367w, 1315w, 1154w, 1118w, 810w, 753m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.95-2.80 (m, 1H, $NH_2CH(CH_3)$-), 2.65-2.50 (m, 2H, -CH_2NHCH_2Ad), 2.24 (s, 2H, -NHCH_2Ad), 1.96 (s, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.40 (m, 8H, $NH_2CH(CH_3)CH_2CH_2$-, -Ad), 1.40-1.25 (m, 2H, $NH_2CH(CH_3)CH_2$-), 1.07 (d, 3H, J = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 62.95; 51.11; 46.92; 40.95; 37.86; 37.21; 33.31; 28.46; 26.82; 24.00. HRMS: *m/z*251.24854corresponds to molecular formula $C_{16}H_{30}N_2H^+$ (error in ppm: + 1.45).

***N*[1]-[2-(1-Adamantyl)ethyl]propane-1,2-diamine (S54).**



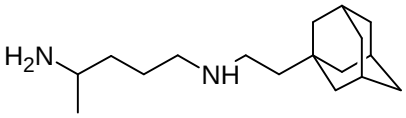
Compound **S54** was prepared by method J from **S48** (1.15 g, 3.1 mmol) using 10%Pd/C (115 mg) and was obtained by dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,as colorless oil (594 mg, 81%). IR (ATR): 3286w, 2902s, 2845s, 1575w, 1450m, 1374w, 1318w, 1105w, 814w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 3.00-2.90 (m, 1H, $NH_2CH(CH_3)$-), 2.70-2.50 (m, 3H, -$CH_2NHCH_2CH_2$Ad, -CH_2CH_2Ad), 2.45-2.30 (m, 1H, -$CH_2NHCH_2CH_2$Ad), 1.93 (s, 3H, -Ad), 1.80-1.60 (m, 6H, -Ad), 1.60-1.40 (m, 8H, 2H-N, -Ad), 1.35-1.20 (m, 2H, -CH_2Ad), 1.06 (d, 3H, J = 6.3, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 58.56; 46.56; 44.68; 44.38; 42.64; 37.14; 31.84; 28.66; 22.12. HRMS: *m/z*237.23155 corresponds to molecular formula $C_{15}H_{28}N_2H^+$ (error in ppm: - 4.09).

***N*[1]-[2-(1-Adamantyl)ethyl]butane-1,3-diamine (S55).**



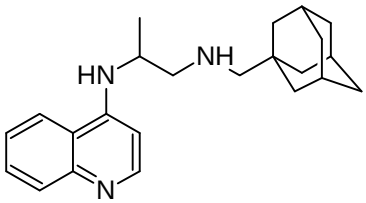
Compound **S55** was prepared by method J from **S49** (1.30 g, 3.4 mmol) using 10%Pd/C (130 mg) and was obtained by dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,as colorless oil (728 mg, 86%); m.p. = 55-57 ^{o}C. IR(ATR): 3334m, 3307m, 3275m, 3190m, 2966w, 2902s, 2845s, 2657w, 1609w, 1449m, 1385w, 1343w, 1316w, 1155w, 1119m, 1021w, 985w, 945w, 878w, 812w, 775w, 687w, 477w, 440w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 3.05-2.90 (m, 1H, $NH_2CH(CH_3)$-), 2.70-2.64 (m, 2H, $NH_2CH(CH_3)CH_2CH_2$-), 2.63-2.55 (m, 2H, -NHCH_2CH_2Ad), 1.93 (m, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.40 (m, 8H, $NH_2CH(CH_3)CH_2$-, -Ad), 1.40-1.30 (m, 2H-N), 1.30-1.20 (m, 2H, -CH_2Ad), 1.08 (d, 3H, J = 6.2, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 47.73; 45.71; 44.76; 44.47; 42.63; 40.21; 37.14; 31.83; 28.65; 24.50. HRMS: *m/z*251.24756 corresponds to molecular formula $C_{16}H_{30}N_2H^+$ (error in ppm: - 2.46).

***N*^{1}-[2-(1-Adamantyl)ethyl]pentane-1,4-diamine (S56).**



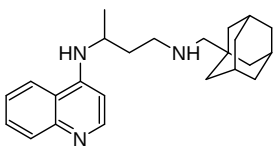
Compound **S56** was prepared by method J from **S50** (1.2 g, 3.0 mmol) using 10%Pd/C (120 mg) and was obtained by dry-flash chromatography: SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,as colorless powder softness at 80-81 °C. Yield: 669 mg (84%). IR(ATR): 3280w, 2902s, 2845s, 2675w, 1639w, 1572w, 1450m, 1374w, 1316w, 1295w, 1118w, 815w, 744 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 2.95-2.85 (m, 1H, $NH_2CH(CH_3)$-), 2.70-2.60 (m, 4H, -CH_2NHCH_2CH_2Ad, -NHCH_2CH_2Ad), 1.93 (m, 3H, -Ad), 1.75-1.60 (m, 6H, -Ad), 1.60-1.30 (m, 10H, $NH_2CH(CH_3)CH_2$-, $NH_2CH(CH_3)CH_2CH_2$-, -Ad), 1.30-1.20 (m, 2H, -CH_2CH_2Ad), 1.15 (d, 3H, *J* = 6.7, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 50.31; 46.88; 44.73; 44.30; 42.64; 37.94; 37.15; 31.84; 28.67; 27.10; 24.01. HRMS: *m/z*265.26374 corresponds to molecular formula $C_{17}H_{32}N_2H^+$ (error in ppm: - 0.33).

***N*^{1}-(1-Adamantylmethyl)-*N*^{2}-quinolin-4-ylpropane-1,2-diamine (12).**



4-Chloroquinoline (405 mg, 1.82 mmol) and amine linker **S51** (298 mg, 1.82 mmol) were mixed in NMP (1.5 mL) in MW cuvette under Ar. The reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*, 1h, 180 °C. Compound **12** was obtained after multiple chromatography: dry-flashSiO_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),as colorless foam. Yield: 458 mg, (72%). IR(ATR): 3318m, 3069m, 2965m, 2901s, 2845s, 2676s, 1676m, 1617m, 1579s, 1532s, 1451s, 1394s, 1371s, 1340m, 1248w, 1223w, 1185m, 1152m, 1126w, 1048w, 885m, 810m, 762m, 737w, 702w, 651w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.53 (d, *J* = 5.3, H-C(2)), 7.97 (d, *J* = 8.3, H-C(8)), 7.79 (m, *J* = 8.2, H-C(5)), 7.70-7.55 (m, H-C(7)), 7.47-7.37 (m, H-C(6)), 6.45 (d, *J* = 5.5, H-C(3)), 6.01 (bs, H-N), 3.80-3.67 (m, 1H, ArNHCH(CH_3)-), 2.85 (d, 2H, *J* = 5.5, -CH_2NHCH_2Ad), 2.40-2.33 (m, 2H, -CH_2Ad), 2.05-1.90 (m, 3H, -Ad), 1.85-1.55 (m, 12H, -Ad), 1.30 (d, 3H, *J* = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 150.79; 149.47; 148.36; 129.67; 128.96; 124.45; 119.64; 119.21 99.16; 62.69; 55.34; 47.30; 40.85; 37.17; 33.65; 28.39; 18.17. HRMS: *m/z*350.25887 corresponds to molecular formula $C_{23}H_{31}N_3H^+$ (error in ppm: - 0.59).Anal. ($C_{23}H_{31}N_3 \times H_2O$) Calcd: C, 75.16; H, 9.05; N, 11.43. Found: C, 75.64; H, 8.98; N, 11.23. HPLCpurity (λ = 330 nm) method A: RT 0.977 min, area 95.50%; method B: RT 9.286 min, area 95.16%.

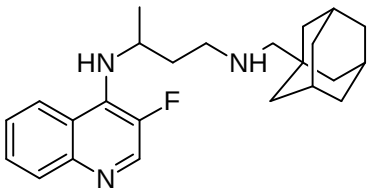
***N*^{1}-(1-Adamantylmethyl)-*N*^{3}-quinolin-4-ylbutane-1,3-diamine (24).**



Compound **24** was prepared by method Hfrom amine linker **S52** (120 mg, 0.64 mmol) and 4-chloroquinoline (70 mg, 0.43 mmol) using

$Pd(OAc)_2$ (3.79 mg 0.017 mmol), SPhos (13.88 mg, 0.036 mmol) and K_3PO_4 (224mg, 1.08 mmol) and was obtained after dry-flash chromatography:SiO_2, gradient:EtOAc/[MeOH/(NH_3 aq) = 9/1] = 9/1 → 7/3,as alight yellow foam softens at 160-161 °C. Yield: 114 mg (73%). IR (ATR): 3270m, 3070m, 2965m, 2902s, 2846s, 1618s, 1580w, 1539s, 1451s, 1396m, 1395m, 1373w, 1340m, 1264m, 1151m, 1126m, 1103w, 809m, 763 m, 738m, 703w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.3, H-C(2)), 7.95 (dd, J_1 = 0.8, J_2 = 8.4, H-C(8)), 7.88 (dd, J_1 = 0.8, J_2 = 8.4, H-C(5)), 7.65-7.55 (m, H-C(7)), 7.40-7.30 (m, H-C(6)), 6.87 (bs, H-N), 6.42 (d, *J* = 5.6, H-C(3)), 3.95-3.80 (m, 1H, ArNHC*H*(CH_3)-), 2.95-2.85 (m, 1H, -CH_2NHCH_2Ad), 2.80-2.70 (m, 1H, -CH_2NHCH_2Ad), 2.29 (s, 2H, -NHCH_2Ad), 2.05-1.95 (m, 3H, -Ad), 1.95-1.85 (m, 1H, ArNHCH(CH_3)CH_2-), 1.84-1.60 (m, 8H, ArNHCH(CH_3)CH_2-, -Ad, *H*-N-), 1.58 (m, 6H, -Ad), 1.32 (d, 3H, *J* = 6.3, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 150.88; 149.60; 148.43; 129.56; 128.87; 124.00; 120.55; 119.14; 98.58; 63.65; 48.12; 47.83; 41.10; 37.17; 35.46; 33.44; 28.44; 19.15. HRMS: *m/z*364.27556 corresponds to molecular formula $C_{24}H_{33}N_3H^+$ (error in ppm: + 2.30).Anal. ($C_{24}H_{33}N_3 \times 1/2H_2O$) Calcd: C, 77.37; H, 9.20; N, 11.28. Found: C, 77.37; H, 9.03; N, 11.18. HPLC purity (λ = 330 nm) method A: RT 0.953 min, area 99.05%; method B: RT 9.386 min, area 97.27%.

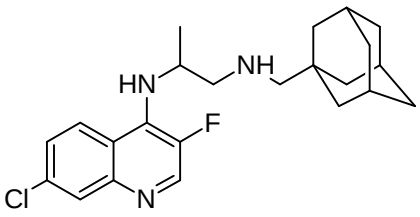
N^1-(1-Adamantylmethyl)-N^3-(3-fluoroquinolin-4-yl)butane-1,3-diamine (26).



Compound **26** was prepared by method Hfrom amine linker **S52** (880 mg, 3.72 mmol) and 3-fluoro-4-iodoquinoline **19** (1.00 g, 3.72 mmol) using $Pd(OAc)_2$ (33.4 mg, 0.15 mmol), DPEphos (160 mg, 0.30 mmol) and K_3PO_4 (1.97 g, 9.14 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient:CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 7/3 and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, gradient: MeOH/H_2O = 8/2 → 9/1,as colorless oil (572 mg, 49%). IR (ATR):3265m, 2902s, 2845m, 1601s, 1574s, 1540s, 1496w, 1451m, 1398m, 1366w, 1345w, 1270w, 1202w, 1148w, 759m cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.7, H-C(2)), 8.00-7.88 (m, H-C(8) and H-C(5)), 7.60-7.54 (m, H-C(7)), 7.41-7.35 (m, H-C(6)), , 6.31 (s, H-N), 4.37-4.27 (m, 1H, ArNHC*H*(CH_3)-), 2.95-2.85 (m, 1H, -CH_2NHCH_2Ad), 2.85-2.75 (m, 1H, -CH_2NHCH_2Ad), 2.30 (s, 2H, -CH_2Ad), 2.01-1.96 (m, 3H, -Ad), 1.80-1.60 (m, 9H, ArNHCH(CH_3)CH_2-, -Ad, *H*-N-), 1.60-1.50 (m, 6H, -Ad), 1.30 (dd, J_1 = 0.9, J_2 = 6.42, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.01 (C(8a)); 143.22 (d, *J* = 238.3, C(3)); 141.60 (d, *J* = 27.1, C(2)); 135.80 (d, *J* = 5.4, C(4)); 129.85 (C(8)); 127.90 (C(7)); 124.83 (C(6)); 124.68 (C(4a)); 121.27 (d, *J* = 5.4, C(5)); 63.70; 50.44 (d, *J* = 8.1, CH); 41.06; 37.15; 36.21; 33.33; 28.42; 21.71 (d, *J* = 2.7, CH_3). HRMS: *m/z*382.26498 corresponds to molecular formula $C_{24}H_{32}FN_3H^+$ (error in ppm: -

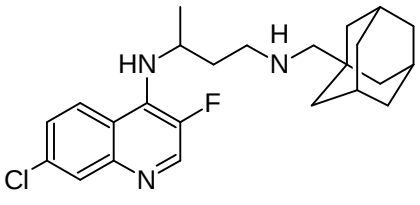
0.83).HPLCpurity (λ = 330 nm) method A: RT 7.545 min, area 99.28%; method B: RT 8.251 min, area 99.45%.

***N*^{1}-(1-Adamantylmethyl)-*N*^{2}-(7-chloro-3-fluoroquinolin-4-yl)propane-1,2-diamine (20).**



Compound **20** was prepared from amine linker **S51** (120 mg, 0.51 mmol) and 7-chloro-3-fluoro-4-iodoquinoline **17** (148 mg, 0.48 mmol) in MW (*Biotage Initiator 2.5* apparatus, PrOH, 4h, 180 °C) and was obtained after dry-flash chromatography SiO_2 eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 85/15),as colorless viscous oil (13 mg, 6.7%). IR(ATR): 3331m, 3070w, 2903s, 2846s, 2675w, 1736w, 1598s, 1572s, 1521m, 1477w, 1449m, 1417m, 1380m, 1344m, 1315w, 1260m, 1192w, 1146w, 1078m, 1001w, 927m, 901w, 879w, 811m, 761m, 738w, 539w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 334 (7180) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.5, H-C(2)), 7.95 (d, *J* = 2.0, H-C(8)), 7.79 (d, *J* = 9.0, H-C(5)), 7.38 (dd, J_1 = 2.0, J_2= 9.0, H-C(6)), 5.83 (d, *J* = 6.5, H-N), 4.25-4.05 (m, 1H, ArNHC*H*(CH_3)-), 2.90-2.75 (m, 1H, -CH_2NHCH_2Ad), 2.39 (ABq, H_A, *J* = 11.5, -CH_2Ad), 2.26 (ABq, H_B, *J* = 11.5, -CH_2Ad), 1.99 (s, 3H, -Ad), 1.80-1.60 (m, 6H, -Ad), 1.60-1.50 (m, 6H, -Ad), 1.28 (d, 3H, *J* = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.62 (C(8a)); 143.46 (d, *J* = 239.1, C(3)); 142.40 (d, *J* = 27.1, C(2)); 135.93 (d, *J* = 5.9, C(4)); 133.92 (d, *J* = 2.3, C(7)); 128.88 (C(8)); 125.88 (C(6)); 121.95 (d, *J* = 5.4, C(5)); 119.71 (d, *J* = 5.4, C(4a)); 62.98; 55.68; 49.81 (d, ArNH*C*H(CH_3)-, *J* = 7.7); 40.94; 37.21; 33.72; 28.43; 20.15 (d, ArNHCH(*C*H_3)-, *J* = 3.6). HRMS: *m/z*402.21082 corresponds to molecular formula $C_{23}H_{29}ClFN_3H^+$ (error in ppm: + 0.35).Anal. ($C_{23}H_{29}ClFN_3$) Calcd: C, 68.73; H, 7.27; N, 10.45. Found: C, 68.39; H, 7.23; N, 10.44. HPLCpurity (λ = 330 nm) method A: RT 8.000 min, area 97.70%; method B: RT 10.703 min, area 95.31%.

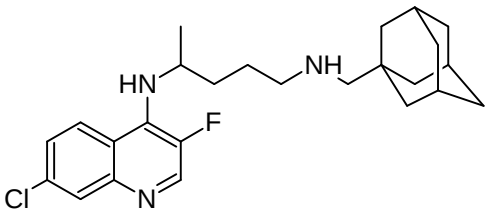
***N*^{1}-(1-Adamantylmethyl)-*N*^{3}-(7-chloro-3-fluoroquinolin-4-yl)butane-1,3-diamine (25).**



Compound **25** was prepared by method H from amine linker **S52** (135 mg, 0.57 mmol) and 7-chloro-3-fluoro-4-iodoquinoline **17** (159.6 mg, 0.52 mmol) using $Pd(OAc)_2$ (5.2 mg, 0.023 mmol), SPhos (18.88 mg, 0.046 mmol) and K_3PO_4 (303 mg, 1.43 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 8/2) as colorless viscous oil (101.7 mg, 47%). IR (ATR): 3280m, 3070w, 2902s, 2846s, 2674w, 1596s, 1572s, 1540m, 1486w, 1450m, 1422m, 1380m, 1346m, 1295w, 1262m, 1191m, 1148m, 1115m, 1078m, 983w, 927m, 902w, 879m, 813m,

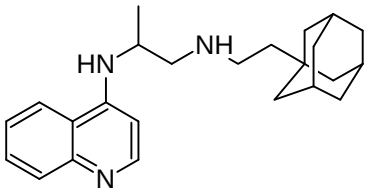
761w, 737m, 656w, 539w, 426w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 250 (15462), 337 (9685) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.8, H-C(2)), 7.92 (d, *J* = 1.6, H-C(8)), 7.86 (d, *J* = 9.0, H-C(5)), 7.35-7.20 (m, H-C(6)), 6.63 (d, *J* = 4.6, H-N), 4.40-4.25 (m, 1H, ArNHC*H*(CH_3)-), 3.00-2.85 (m, 1H, -C*H*$_2$NHCH_2Ad), 2.85-2.70 (m, 1H, -C*H*$_2$NHCH_2Ad), 2.30 (s, 2H, -C*H*$_2$Ad), 2.05-1.90 (m, 4H, -Ad, ArNHCH(CH_3)C*H*$_2$-), 1.90-1.60 (m, 8H, ArNHCH(CH_3)C*H*$_2$-, -Ad, *H*-N-), 1.60-1.50 (m, 6H, -Ad), 1.30 (d, 3H, *J* = 6.2, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.60 (C(8a)); 143.19 (d, *J* = 239.1, C(3)); 142.46 (d, *J* = 27.5, C(2)); 136.12 (d, *J* = 5.4, C(4)); 133.76 (d, *J* = 7.2, C(7)); 128.63 (C(8)); 125.37 (C(6)); 122.94 (d, *J* = 5.0, C(5)); 119.64 (d, *J* = 5.4, C(4a)); 50.58 (d, *J* = 8.6, ArNH*C*H(CH_3)-); 47.52; 41.05; 37.08; 35.75; 33.30; 28.36; 21.60. HRMS: *m/z*416.22602 corresponds to molecular formula $C_{24}H_{31}ClFN_3H^+$ (error in ppm: - 0.75).Anal. ($C_{24}H_{31}ClFN_3 \times 2/3\ H_2O$) Calcd: C, 67.35; H, 7.61; N, 9.82. Found: C, 67.17; H, 7.47; N, 9.74. HPLCpurity (λ = 330 nm) method A: RT 8.589min, area 97.89%; method B: RT 11.009 min, area 97.73%.

***N*^{1}-(1-Adamantylmethyl)-*N*^{4}-(7-chloro-3-fluoroquinolin-4-yl)pentane-1,4-diamine (32).**



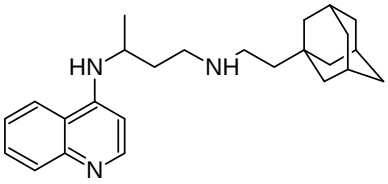
Compound **32** was prepared by method H from 7-chloro-3-fluoro-4-iodoquinoline **17** (105 mg, 0.34 mmol) and amine linker **S53** (94 mg, 0.38 mmol) using $Pd(OAc)_2$ (3.0 mg, 0.014 mmol), DPEphos (14.65 mg, 0.027 mmol) and K_3PO_4 (180 mg, 0.85 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 7/3, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, gradient: MeOH/H_2O = 8/2 → 9/1),as colorless foam (74 mg, 49%). IR(ATR): 3301m, 2902s, 2846s, 1596m, 1573s, 1536w, 1450m, 1418m, 1381m, 1351m, 1296w, 1264m, 1202w, 1147m, 928w, 878w, 814m, 761w, 738m, 657w, 541w cm^{-1}.$\lambda_{max}(\varepsilon)$ = 252 (18402), 335 (11598) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.5, H-C(2)), 7.95 (d, *J* = 2.0, H-C(8)), 7.74 (d, *J* = 9.0, H-C(5)), 7.36 (dd, J_1 = 1.5, J_2 = 9.0, H-C(6)), 4.59 (d, *J* = 8.0, H-N), 4.20-4.05 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.55 (m, 2H, -C*H*$_2$NHCH_2Ad), 2.21 (s, 2H, -C*H*$_2$Ad), 1.96 (s, 3H, -Ad), 1.80-1.55 (m, 10H, -Ad, ArNHCH(CH_3)C*H*$_2$-, ArNHCH(CH_3) CH_2C*H*$_2$-), 1.55-1.45 (m, 6H, -Ad), 1.30 (d, 3H, *J* = 6.5, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.51 (C(8a)); 143.23 (d, *J* = 242.8, C(3)); 142.37 (d, *J* = 27.5, C(2)); 135.65 (d, *J* = 5.4, C(4)); 133.90 (d, *J* = 2.3, (C(7)); 128.88 (C(8)); 125.87 (C(6)); 121.75 (d, *J* = 4.9, C(5)); 119.26 (d, *J* = 5.0, C(4a)); 62.72; 51.27 (d, *J* = 9.0, ArNH*C*H(CH_3)-,); 50.35; 40.90; 37.13; 35.53; 33.27; 28.37; 26.19; 22.19. HRMS: *m/z*430.24165 corresponds to molecular formula $C_{25}H_{33}ClFN_3H^+$ (error in ppm: -0.76).HPLCpurity (λ = 330 nm) method A: RT 8.579 min, area 98.70%; method B: RT 9.680 min, area 98.15%.

N^1-[2-(1-Adamantyl)ethyl]-N^2-quinolin-4-ylpropane-1,2-diamine (35).



Amine linker **S54** (260 mg, 1.10 mmol) and 4-chloroquinoline (180 mg, 1.10 mmol) and were mixed in NMP (1.5 mL) in MW cuvette under Ar. The reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5 apparatus*, 1h, 180 °C. Compound **35** 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),as light yellow foam softens at 112-113 °C. Yield: 253 mg (63%). IR (ATR): 3251m, 3059m, 2962m, 2902s, 2844s, 1708w, 1618w, 1578s, 1543s, 1451s, 1396s, 1374m, 1343m, 1280w, 1258w, 1159w, 1130w, 1108w, 909w, 807w, 763m, 733w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.53 (d, *J* = 5.3, H-C(2)), 7.97 (d, *J* = 8.0, H-C(8)), 7.81-7.76 (m, H-C(5)), 7.65-7.59 (m, H-C(7)), 7.46-7.37 (m, H-C(6)), 6.45 (d, *J* = 5.4, H-C(3)), 5.69 (bs, H-N), 3.87-3.73 (m, 1H, ArNHC*H*(CH_3)-), 2.91-2.81 (m, 2H, ArNHC*H*(CH_3)CH_2-), 2.70-2.61 (m, 2H, -C$H_2$$CH_2$Ad), 1.92 (s, 3H, -Ad), 1.73-1.57 (m, 7H, -N*H*,-Ad), 1.55-1.44 (m, 6H, -Ad), 1.35-1.24 (m, 5H, CH_3, -CH_2Ad). ^{13}C-NMR (125 MHz. $CDCl_3$, δ): 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. HRMS: *m/z*364.27554 corresponds to molecular formula $C_{24}H_{33}N_3H^+$ (error in ppm: - 1.37).Anal. ($C_{24}H_{33}N_3 \times H_2O$) Calcd: 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 0.998 min,area 99.11%; method B: RT 9.586 min, area 95.01%.

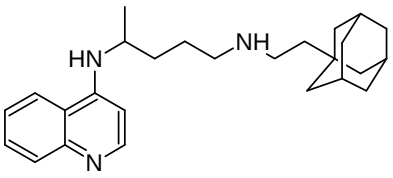
N^1-[2-(1-Adamantyl)ethyl]-N^3-quinolin-4-ylbutane-1,3-diamine (37).



Compound **37** was prepared by method Hfrom amine linker **S55** (150 mg, 0.60 mmol) and 4-chloroquinoline (82 mg, 0.50 mmol) using $Pd(OAc)_2$ (4.48 mg, 0.02 mmol), SPhos (16.38 mg, 0.04 mmol) and K_3PO_4 (265 mg, 1.25 mmol) and was obtained after dry-flash chromatography:SiO_2, gradient: EtOAc/[MeOH/(NH_3 aq) = 9/1] = 9/1 → 7/3,as colorless foam softens at 64-66 °C. Yield: 146 mg (77%). IR (ATR): 3250m, 3069m, 2962m, 2902s, 2844s, 1654w, 1618w, 1543s, 1448m, 1397m, 1373m, 1340m, 1281w, 1263m, 1182w, 1148m, 1051w, 1025w, 960w, 810m, 764m, 737m, 702w, 651w, 633w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.49 (d, *J* = 5.4, H-C(2)), 7.94 (d, *J* = 8.3, H-C(8)), 7.84 (d, *J* = 8.2, H-C(5)), 7.70-7.50 (m, H-Nand H-C(7)), 7.40-7.35 (m, H-C(6)), 6.37 (d, *J* = 5.5, H-C(3)), 3.95-3.80 (m, 1H, ArNHC*H*(CH_3)-), 3.15-2.90 (m, 1H, -CH_2NHC$H_2$$CH_2$Ad), 2.85-2.75 (m, 1H, -CH_2NHC$H_2$$CH_2$Ad), 2.70-2.60 (m, 2H, -C$H_2$$CH_2$Ad), 2.00-1.85 (m, 4H, -Ad, -ArNHCH(CH_3)CH_2-), 1.80-1.55 (m, 7H, ArNHCH(CH_3)CH_2-, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.40-1.35 (m, 2H, -CH_2Ad), 1.32 (d, 3H, *J* = 6.3, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ):

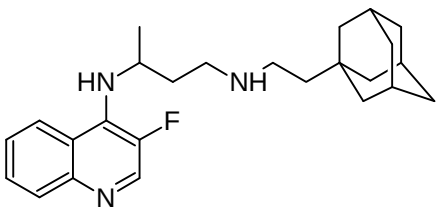
150.76; 149.81; 148.35; 129.39; 128.83; 123.99; 120.69; 119.27; 98.21; 48.19; 46.60; 44.79; 44.45; 42.65; 37.07; 35.05; 31.83; 28.60; 19.21. HRMS: *m/z*378.29070 corresponds to molecular formula $C_{25}H_{35}N_3H^+$ (error in ppm: + 0.85).HPLC purity (λ = 330 nm) method A: RT 0.999 min, area 97.38%; method B: RT 2.506 min, area 99.48%.

***N*^{1}-[2-(1-Adamantyl)ethyl]-*N*^{4}-quinolin-4-ylpentane-1,4-diamine (44).**



Compound**44** was prepared by method H from amine linker **S56** (242 mg, 0.73 mmol) and 4-chloroquinoline (100 mg, 0.61 mmol) and using $Pd(OAc)_2$ (5.47 mg, 0.024 mmol), SPhos (20 mg, 0.049 mmol) and K_3PO_4 (324mg, 1.53 mmol) and was obtained after dry-flash chromatography:SiO_2, gradient: EtOAc/[MeOH/(NH_3 aq) = 9/1] = 9/1 → 7/3,as yellow foam softens at 64-65 °C. Yield: 203 mg (85%). IR (ATR): 3651w, 3287m, 3067s, 2902s, 2845s, 1618w, 1580s, 1541s, 1450m, 1396m, 1342m, 1261w, 1225w, 1139w, 808w, 766m, 736w, 652w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.52 (d, *J* = 5.4, H-C(2)), 7.96 (d, *J* = 8.5, H-C(8)), 7.78 (d, *J* = 8.4, H-C(5)), 7.65-7.55 (m, H-C(7)), 7.45-7.35 (m, H-C(6)), 6.41 (d, *J* = 5.3, H-C(3)), 5.39 (d, *J* = 6.1, H-N), 3.80-3.65 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.63 (m, 2H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.63-2.55 (m, 2H, -C*H*$_2$CH$_2$Ad), 1.97-1.87 (m, 3H, -Ad), 1.85-1.55 (m, 10H, ArNHCH(CH_3)C*H*$_2$-, ArNHCH(CH_3)CH$_2$C*H*$_2$-, -Ad), 1.50-1.40 (m, 6H, -Ad), 1.35-1.20 (m, 5H, C*H*$_3$, -C*H*$_2$Ad). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 150.88; 148.99; 148.51; 129.78; 128.86; 124.30; 119.54; 118.84; 98.79; 49.67; 48.16; 44.51; 44.29; 42.57; 37.06; 34.12; 31.78; 28.59; 26.40; 20.20. HRMS: *m/z*392.30696 corresponds to molecular formula $C_{26}H_{37}N_3H^+$ (error in ppm: + 2.38).Anal.($C_{26}H_{37}N_3 \times H_2O$) Calcd: C, 76.24; H, 9.60; N, 10.26; Found: C, 76.28; H, 9.30; N, 10.19. HPLC purity (λ = 330 nm) method A: RT 1.000 min, area 98.19%; method B: RT 9.653 min, area 95.14%.

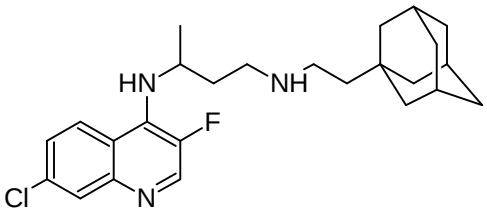
***N*^{1}-[2-(1-Adamantyl)ethyl]-*N*^{3}-(3-fluoroquinolin-4-yl)butane-1,3-diamine (39).**



Compound **39** was prepared by method Efrom aminoquinoline **S56** (245 mg, 1.05 mmol) and 1-adamantylacetaldehyde(156 mg, 0.88 mmol) using AcOH (121 μL, 1.32 mmol) and $NaBH_4$ (200 mg, 5.28 mmol) and was obtained after obtained after flash chromatography SiO_2, gradient: Hex/EtOAc = 7/3 → 8/2,as colorless viscous oil (167 mg, 48%). IR(ATR): 3302m, 2904s, 2845s, 1680w, 1600m, 1577m, 1540m, 1449w, 1398m, 1364w, 1270w, 1200w, 1143w, 762w, 736w cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.5, H-C(2)), 8.05 (d, *J* = 8.2, H-C(8)), 7.95 (d, *J* = 8.2, H-C(5)), 7.63-7.56 (m, H-C(7)), 7.48-7.42 (m, H-C(6)), 6.21 (bs, H-N), 4.25 (s, 1H, ArNHC*H*(CH_3)-), 3.10-3.03 (m, 2H, ArNHCH(CH_3)C*H*$_2$-), 2.85-2.73 (m, 2H, -C*H*$_2$CH$_2$Ad), 2.11-2.02 (m, 1H, ArNHCH(CH_3)CH$_2$C*H*$_2$-), 2.02-1.94(m, 1H, ArNHCH(CH_3)CH$_2$C*H*$_2$-), 1.90 (s, 3H, -Ad),

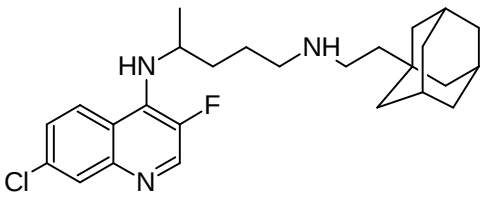
1.75-1.53 (m, 6H, -Ad), 1.53-1.38 (m, 8H, -C*H*$_2$Ad, -Ad), 1.30 (d, 3H, *J* = 6.4, C*H*$_3$). ^{13}C-NMR(125 MHz, $CDCl_3$, δ): 145.93 (C(8a)); 142.76 (d, *J* = 238.3, C(3)); 141.47 (d, *J* = 27.1, C(2)); 135.88 (d, *J* = 5.4, C(4)); 129.67 (C(8)); 127.72 (C(7)); 124.55 (C(6)); 121.35 (d, *J* = 5.4, C(4a)); 121.15 (d, *J* = 5.4, C(5)); 50.24 (d, *J* = 9.0, CH); 46.16; 44.69; 44.46; 42.55; 36.98; 35.44; 31.72; 28.52; 21.31 (d, *J* = 3.6, CH_3).HRMS: *m/z*396.28038 corresponds to molecular formula $C_{25}H_{34}FN_3H^+$ (error in ppm: -1.45).HPLCpurity (λ = 330 nm) method A: RT 8.269 min, area 98.81%; method B: RT 8.721 min, area 99.15%.

***N*^{1}-[2-(1-Adamantyl)ethyl]-*N*^{3}-(7-chloro-3-fluoroquinolin-4-yl)butane-1,3-diamine (38).**



Compound **38** was prepared by method H from amine linker **S55** (123 mg, 0.49 mmol) and 7-chloro-3-fluoro-4-iodoquinoline **17**(137 mg, 0.45 mmol) using $Pd(OAc)_2$ (4.0 mg, 0.018 mmol), DPEphos (19.39 mg, 0.036 mmol) and K_3PO_4 (239 mg, 1.13 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 8/2),as colorless viscous oil (46 mg, 24%). IR(ATR): 3283m, 2974w, 2906s, 2848s, 2779w, 2696w, 2448w, 1570s, 1493w, 1451w, 1416w, 1380m, 1346m, 1265w, 1194w, 1131m, 1075w, 1014w, 937m, 817m, 767m, 727m, 638w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 250 (13796), 331 (8004) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.46 (d, *J* = 6.0, H-C(2)), 7.91 (d, *J* = 2.0, H-C(8)), 7.84 (d, *J* = 9.5, H-C(5)), 7.48 (bs, H-N), 7.31 (dd, J_1 = 1.5, J_2 = 9.0, H-C(6)), 4.35 (bs, 1H, ArNHC*H*(CH_3)-), 3.05-2.95 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.95-2.85 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.75-2.60 (m, 2H, -C*H*$_2$CH$_2$Ad), 2.05-1.90 (m, 4H, -Ad, ArNHCH(CH_3)C*H*$_2$-), 1.75-1.60 (m, 7H, -Ad, ArNHCH(CH_3)C*H*$_2$-), 1.55-1.45 (m, 6H, -Ad), 1.45-1.30 (m, 2H, -C*H*$_2$Ad), 1.32 (d, 3H, *J* = 7.0, C*H*$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.10 (C(8a)); 143.22 (d, *J* = 204.5, C(3)); 142.04 (d, *J* = 28.5, C(2)); 136.18 (d, *J* = 4.5, C(4)); 134.52 (d, *J* = 1.8, C(7)); 128.21 (C(8)); 126.50 (C(6)); 122.92 (d, *J* = 5.0, C(5)); 119.70 (d, *J* = 5.0, C(4a)); 50.06 (d, *J* = 10.5, ArNH*C*H(CH_3)-); 45.40; 43.08; 41.99; 39.72; 36.66; 33.32; 31.61; 28.25; 22.77. HRMS: *m/z*430.24104 corresponds to molecular formula $C_{25}H_{33}ClFN_3H^+$ (error in ppm: - 2.19). HPLCpurity (λ = 330 nm) method A: RT 5.879 min, area 96.49%; method B: RT 11.796 min, area 97.32%.

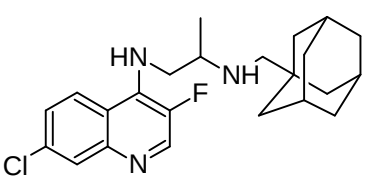
***N*^{1}-[2-(1-adamantyl)ethyl]-*N*^{4}-(7-chloro-3-fluoroquinolin-4-yl)pentane-1,4-diamine (45).**



Compound **45** was prepared by method H from amine linker **56**(73 mg, 0.24 mmol) and 7-chloro-3-fluoro-4-iodoquinoline **17**(66 mg, 0.22 mmol) using $Pd(OAc)_2$

(2.1 mg, 0.009 mmol), DPEphos (4.7 mg, 0.019 mmol) and K_3PO_4 (117 mg, 0.6 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 7/3,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, gradient: MeOH/H_2O = 8/2 → 9/1) as yellow foam (39 mg, 41%).IR(ATR): 3294m, 3069w, 2903s, 2846j, 2676w, 1734w, 1595m, 1574s, 1539m, 1487w, 1450m, 1419m, 1381m, 1350m, 1294w, 1265m, 1199w, 1142m, 1105m, 1078w, 928w, 877w, 815m, 763w, 738w, 656w, 540w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 237 (10560), 251 (10259), 331 (6457), 338(6502) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.6, H-C(2)), 7.93 (d, *J* = 2.0, H-C(8)), 7.76 (d, *J* = 9.0, H-C(5)), 7.36 (dd, J_1 = 2.0, J_2 = 9.0, H-C(6)), 4.86 (d, *J* = 7.8, H-N), 4.20-4.05 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.60 (m, 2H, -CH_2NHCH_2CH_2Ad), 2.70-2.60 (m, 2H, -CH_2CH_2Ad), 1.91 (s, 3H, Ad), 1.75-1.55 (m, 10H, Ad, ArNHCH(CH_3)CH_2-, ArNHCH(CH_3)CH_2CH_2-), 1.50-1.40 (m, 6H, Ad), 1.27 (d, 3H, *J* = 6.3, CH_3), 1.30-1.20 (m, 2H, -CH_2Ad). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.56 (C(8a)); 143.24 (d, *J* = 240.0, C(3)); 142.43 (d, *J* = 27.5, C(2)); 135.76 (d, *J* = 5.9, C(4)); 133.95 (C(7)); 128.87 (C(8)); 125.93 (C(6)); 121.19 (d, *J* = 5.0, C(5)); 119.37 (d, *J* = 5.0, C(4a)); 51.25 (d, *J* = 8.6, ArNH*C*H(CH_3)-); 49.57; 44.30; 44.20; 42.56; 37.06; 35.64; 31.78; 28.59; 26.26; 22.27. HRMS: *m/z*444.25601 corresponds to molecular formula $C_{26}H_{35}ClFN_3H^+$ (error in ppm: - 3.64). HPLCpurity (λ = 254 nm) method A: RT 4.409 min, area 95.01%; method B: RT 9.856 min, area 95.13%.

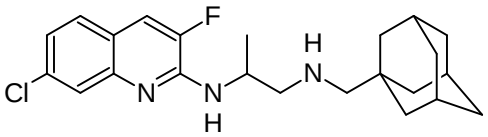
N^2-(1-adamantylmethyl)-N^1-(7-chloro-3-fluoroquinolin-4-yl)propane-1,2-diamine (21).



Compound **21** was prepared from amine linker **S20** (122 mg, 0.55 mmol) and 7-chloro-3-fluoro-4-iodoquinoline **17**(160 mg, 0.52 mmol) in MW (*Biotage Initiator 2.5 apparatus*, PrOH, 4h, 180 °C) and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 RP column, eluent: MeOH/H_2O = 9/1) as colorless viscous oil (127 mg, 61%). IR (ATR): 3322s, 2964w, 2910s, 2845s, 2659w, 1614m, 1598m, 1570m, 1519m, 1476m, 1454m, 1419w, 1377w, 1354w, 1310m, 1256m, 1211w, 1192w, 1159m, 1135w, 1097m, 1072w, 1054w, 953w, 922w, 897w, 875w, 809m, 759m, 656w, 577w, 538m, 495w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 237 (14605), 250 (15056), 336 (9232) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 8.51 (d, *J* = 5.5, H-C(2)), 7.93 (d, *J* = 2.0, H-C(8)), 7.76 (d, *J* = 9.0, H-C(5)), 7.34 (dd, J_1= 2.0, J_2= 9.0, H-C(6)), 6.06 (s, H-N), 3.80-3.70 (m, 1H, ArNHCH_2-), 3.35-3.25 (m, 1H, ArNHCH_2-), 2.95-2.85 (m, 1H, -C*H*(CH_3)NHCH_2Ad), 2.43 (ABq, H_A, *J* = 11.4, -CH_2Ad), 2.13 (ABq, H_B, *J* = 11.4, -CH_2Ad), 1.99 (s, 3H, -Ad), 1.80-1.64 (m, 6H, -Ad), 1.64-1.45 (m, 6H, -Ad), 1.18 (d, 3H, *J* = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 146.49 (C(8a)); 143.51 (d, *J* = 239.1, C(3)); 142.22 (d, *J* = 26.6, C(2)); 136.88 (d, *J* = 5.9, C(4)); 133.80 (C(7)); 128.78 (C(8)); 125.62

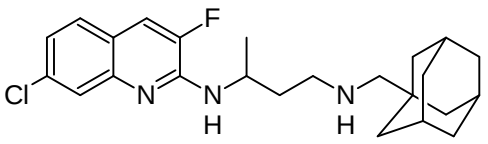
(C(6)); 121.91 (d, *J* = 5.4, C(5)); 119.19 (d, *J* = 5.0, C(4a)); 59.14; 53.12; 49.15 (d, *J* = 8.1, ArNH*C*H(CH$_3$)-); 40.92; 37.16; 33.38; 29.64; 19.06. HRMS: *m/z*402.21027 corresponds to molecular formula $C_{23}H_{29}ClFN_3H^+$ (error in ppm: - 1.03).Anal. ($C_{23}H_{29}ClFN_3$) Calcd: C, 68.73; H, 7.27; N, 10.45. Found: C, 67.06; H, 6.98; N, 10.18. HPLC purity (λ = 254 nm) method A: RT 7.970 min, area 97.00%; method B: RT 9.932 min, area 99.14%.

N^1-(1-Adamantylmethyl)-N^2-(7-chloro-3-fluoroquinolin-2-yl)propane-1,2-diamine (68).



Compound **68** was prepared from amine linker **S51** (166 mg, 0.75 mmol) and 7-chloro-3-fluoro-2-iodoquinoline **18** (153 mg, 0.50 mmol) in MW (*Biotage Initiator 2.5 apparatus*, PrOH, 4h, 180 ^oC) and was obtained after multiple chromatography: dry-flash SiO_2, eluent: CH_2Cl_2/MeOH(NH_3sat.) = 95/5, and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 85/15),as colorless viscous oil (18.3 mg, 9.1%). IR(ATR): 3362m, 2902s, 2846s, 2675w, 1717w, 1637m, 1608m, 1566w, 1528s, 1492w, 1453m, 1451m, 1368w, 1344m, 1316w, 1260m, 1188m, 1148m, 1118m, 1073w, 976w, 929w, 880m, 801m, 760m, 602w, 513w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 241 (32222), 331 (7158), 343 (6902) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.71 (d, *J* = 1.8, H-C(8)), 7.43 (d, *J* = 8.5, H-C(5)), 7.38 (d, *J* = 11.2, H-C(4)), 7.17 (dd, J_1 = 1.8, J_2= 8.4, H-C(6)), 5.68 (d, *J* = 5.4, H-N), 4.45-4.35 (m, 1H, ArNHC*H*(CH$_3$)CH$_2$-), 2.85-2.75 (m, 1H, -C*H*$_2$NHCH$_2$Ad), 2.34 (ABq, H_A, *J* = 11.7, -C*H*$_2$Ad), 2.32 (ABq, H_B, *J* = 11.7, -C*H*$_2$Ad), 1.93 (s, 3H, -Ad), 1.80-1.55 (m, 6H, -Ad), 1.55-1.40 (m, 6H, -Ad), 1.33 (d, 3H, *J* = 6.6, CH$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 148.87 (d, *J* = 13.5, C(8a)); 147.30 (d, *J* = 258.6, C(3)); 145.20 (d, *J* = 2.7, C(2)); 133.90 (d, *J* = 2.3, C(7)); 127.79 (C(5)); 125.26 (C(8)); 123.23 (C(6)); 121.48 (d, *J* = 4.1, C(4a)); 116.01 (d, *J* = 15.4, C(4)); 62.27; 55.65; 45.61; 40.66; 37.08; 33.48; 28.34; 18.93. HRMS: *m/z*402.21021 corresponds to molecular formula $C_{23}H_{29}ClFN_3H^+$ (error in ppm: - 1.16).Anal. ($C_{23}H_{29}ClFN_3 \times 1/3\ H_2O$) Calcd: C, 67.72; H, 7.33; N, 10.30. Found: C, 67.72; H, 6.99; N, 10.28. HPLCpurity (λ = 254 nm) method A: RT 8.772 min, area 95.58%; method B: RT 10.676 min, area 95.05%.

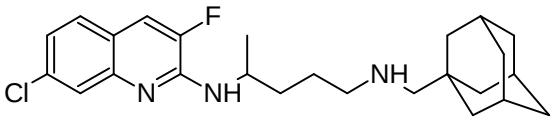
N^1-(1-Adamantylmethyl)-N^3-(7-chloro-3-fluoroquinolin-2-yl)butane-1,3-diamine (69).



Compound **69** was prepared by method H from amine linker **S52** (78 mg, 0.33 mmol) and 7-chloro-3-fluoro-2-iodoquinoline **18** (93 mg, 0.30 mmol) using $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), SPhos (9.85 mg, 0.024 mmol) and K_3PO_4 (159 mg, 0.75 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 8/2,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 8/2),as colorless viscous oil (66 mg, 53%). IR(ATR): 3439w, 3262m, 3085w,

3040w, 2901s, 2845s, 2675w, 1637m, 1606w, 1568m, 1531s, 1492w, 1457m, 1416m, 1376w, 1345m, 1316w, 1289w, 1258m, 1189m, 1147m, 1119m, 1074w, 1005w, 970w, 930w, 882m, 799m, 760m, 739w, 601w, 512w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 242 (32836), 330 (8319), 341 (7836) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.68 (d, *J* = 1.7, H-C(8)), 7.41 (d, *J* = 8.5, H-C(5)), 7.35 (d, *J* = 11.3, H-C(4)), 7.14 (dd, J_1 = 1.7, J_2 = 8.4, H-C(6)), 6.30 (d, *J* = 6.4, H-N), 4.55-4.45 (m, 1H, ArNHC*H*(CH_3)-), 2.85-2.75 (m, 1H, -CH_2NHCH$_2$CH$_2$Ad), 2.75-2.65 (m, 1H, -CH_2NHCH$_2$CH$_2$Ad), 2.27 (ABq, H_A, *J* = 11.4, -CH_2Ad), 2.19 (ABq, H_B, *J* = 11.4, -CH_2Ad), 2.00-1.90 (m, 3H, Ad), 1.90-1.80 (m, 1H, ArNHCH(CH_3)CH_2-), 1.75-1.60 (m, 6H, Ad), 1.57-1.47 (m, 6H, Ad), 1.32 (d, 3H, *J* = 6.4, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 148.59 (d, *J* = 13.1, C(8a)); 147.31 (d, *J* = 259.0, C(3)); 145.44 (d, *J* = 2.7, C(2)); 133.78 (d, *J* = 2.7, C(7)); 127.71 (d, *J* = 5.0, C(5)); 125.23 (C(8)); 122.88 (C(6)); 121.27 (d, *J* = 4.0, C(4a)); 115.76 (d, *J* = 13.33, C(4)); 63.19; 47.52; 45.26; 40.89; 37.20; 35.87; 33.26; 28.47; 20.55. HRMS: *m/z*416.22589 corresponds to molecular formula $C_{24}H_{31}ClFN_3H^+$ (error in ppm: -1.07).HPLCpurity (λ = 254 nm) method A: RT 8.726min, area 95.12%; method B: RT 11.064 min, area 95.72%.

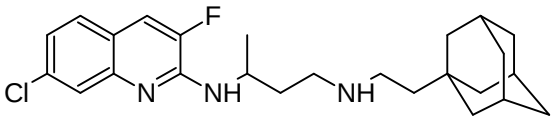
N^1-(1-Adamantylmethyl)-N4-(7-chloro-3-fluoroquinolin-2-yl)pentane-1,4-diamine (70).



Compound **70** was prepared by method H from amine linker **S53** (67 mg, 0.27 mmol) and 7-chloro-3-fluoro-2-iodoquinoline **18**(75 mg, 0.24 mmol) using $Pd(OAc)_2$ (2.2 mg, 0.009 mmol), DPEphos (10.34 mg, 0.019 mmol) and K_3PO_4 (127 mg, 0.6 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 7/3,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 8/2 → 9/1),as colorless viscous oil (55 mg, 51%). IR(ATR): 3442m, 3323w, 2902s, 2846m, 1637m, 1609w, 1568w, 1530s, 1492w, 1458m, 1415m, 1345w, 1262w, 1188w, 1146w, 1119w, 1069w, 883w, 799w, 760w, 733w, 602w, 514w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 242 (35870), 332 (7652), 345 (7674) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.69 (d, *J* = 1.5, H-C(8)), 7.42 (d, *J* = 9.0, H-C(5)), 7.36 (d, *J* = 11.5, H-C(4)), 7.16 (dd, J_1 = 2.0, J_2 = 8.5, H-C(6)), 5.11 (d, *J* = 6.5, H-N), 4.50-4.30 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.55 (m, 2H, -CH_2NHCH$_2$Ad), 2.22 (s, 2H, -CH_2Ad), 1.94 (s, 3H, -Ad), 1.75-1.55 (m, 10H, -Ad, ArNHCH(CH_3)CH_2-, ArNHCH(CH_3)CH$_2$CH_2-), 1.55-1.45 (m, 6H, -Ad), 1.29 (d, 3H, *J* = 6.5, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 148.36 (d, *J* = 13.5, C(8a)); 147.14 (d, *J* = 258.1, C(3)); 145.37 (d, *J* = 2.2, C(2)); 133.86 (d, *J* = 2.2, C(7)); 127.74 (d, *J* = 5.0, (C(5)); 125.32 (C(8)); 123.06 (C(6)); 121.29 (d, *J* = 4.0, C(5)); 115.84 (d, *J* = 15.2, C(4a)); 62.81; 50.62; 45.94; 40.90; 37.18; 34.36; 33.28; 28.44; 26.15; 20.79. HRMS: *m/z*430.24169 corresponds to molecular formula $C_{25}H_{33}ClFN_3H^+$ (error in ppm: -

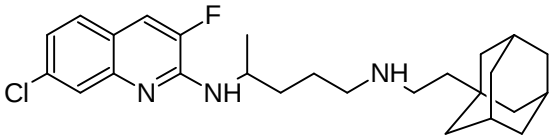
0.67).HPLCpurity (λ = 330 nm) method A: RT 9.631min, area 95.45%; method B: RT 10.444 min, area 98.16%.

N^1-[2-(1-Adamantyl)ethyl]-N^3-(7-chloro-3-fluoroquinolin-2-yl)butane-1,3-diamine (71).



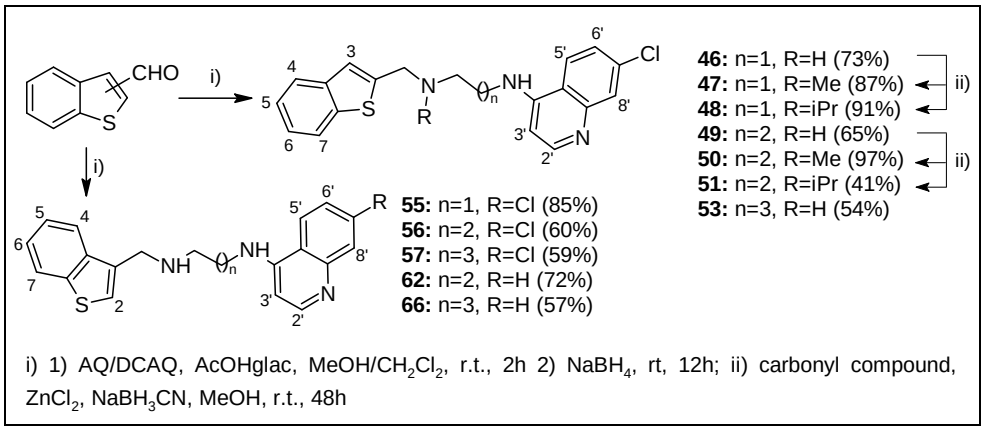
Compound **71** was prepared by method H from amine linker **S55**(89 mg, 0.36 mmol) and7-chloro-3-fluoro-2-iodoquinoline **18**(99 mg, 0.32 mmol) using $Pd(OAc)_2$ (2.9 mg, 0.013 mmol), DPEphos (13.79 mg, 0.026 mmol) and K_3PO_4 (169 mg, 0.8 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 7/3,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, eluent: MeOH/H_2O = 8/2 → 9/1),as colorless viscous oil (73 mg, 53%). IR(ATR): 3340m, 3233m, 2903s, 2845s, 2676w, 1637m, 1609w, 1567w, 1533s, 1492w, 1456m, 1415m, 1372w, 1344w, 1258w, 1189m, 1146m, 1119m, 1073w, 968w, 908w, 882m, 800w, 760w, 733m, 602w, 513w, 476w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 252 (28029), 347 (8156) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.67 (d, *J* = 2.0, H-C(8)), 7.43 (d, *J* = 8.5, H-C(5)), 7.37 (d, *J* = 11.0, H-C(4)), 7.16 (dd, J_1 = 1.5, J_2 = 8.5, H-C(6)), 5.94 (d, *J* = 6.5, H-N), 4.55-4.45 (m, 1H, ArNHC*H*(CH_3)-), 2.83-2.73 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.73-2.65 (m, 1H, -C*H*$_2$NHCH$_2$CH$_2$Ad), 2.60-2.53 (m, 1H, -C*H*$_2$CH$_2$Ad), 2.53-2.45 (m, 1H, -C*H*$_2$CH$_2$Ad), 1.95-1.80 (m, 4H, ArNHCH(CH_3)C*H*$_2$-,-Ad), 1.75-1.55 (m, 7H, -Ad, ArNHCH(CH_3)C*H*$_2$-), 1.47-1.43 (m, 6H, -Ad), 1.33 (d, 3H, *J* = 6.5, C*H*$_3$), 1.20-1.30 (-C*H*$_2$Ad). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 148.64 (d, *J* = 13.5, C(8a)); 147.22 (d, *J* = 258.6, C(3)); 145.32 (d, *J* = 2.8, C(2)); 133.91 (d, *J* = 2.2, C(7)); 127.81(d, *J* = 4.9, (C(5)); 125.19 (C(8)); 123.06 (C(6)); 121.30 (d, *J* = 4.6, C(5)); 115.89 (d, *J* = 15.4, C(4a)); 46.69; 44.88; 44.76; 44.36; 42.57; 37.14; 36.81; 31.78; 28.67; 21.07. HRMS: *m/z*430.24162 corresponds to molecular formula $C_{25}H_{33}ClFN_3H^+$ (error in ppm: - 0.84).HPLCpurity (λ = 254 nm) method A: RT 9.012min, area 95.42%; method B: RT 11.228 min, area 96.01%.

N^1-[2-(1-Adamantyl)ethyl]-N^4-(7-chloro-3-fluoroquinolin-2-yl)pentane-1,4-diamine (72).



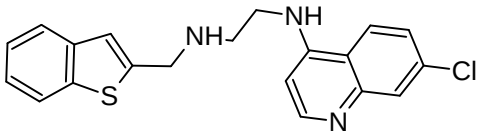
Compound **72** was prepared by method H from amine linker **S56** (89 mg, 0.34 mmol) and 7-chloro-3-fluoro-2-iodoquinoline **18** (94 mg, 0.30 mmol) using $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), DPEphos (12.9 mg, 0.024 mmol) and K_3PO_4 (159 mg, 0.75 mmol) and was obtained after multiple chromatography: dry-flash SiO_2, gradient: CH_2Cl_2/MeOH(NH_3sat.) = 95/5 → 7/3,and flash chromatography (Biotage SP1 NH column, eluent: Hex/EtOAc = 7/3 and RP column, gradient: MeOH/H_2O = 8/2 → 9/1),as colorless viscous oil (74 mg, 56%). IR(ATR): 2903s, 2846s, 2676w, 1628m, 1592w, 1514s, 1463m, 1425m, 1379m, 1331w, 1252m, 1216w, 1196w, 1146m, 1119m, 1070m, 976w, 930m, 887m, 800m, 738m, 648w, 600w, 519w, 474w, 409w cm^{-1}. $\lambda_{max}(\varepsilon)$ = 253(26082), 349

(7096) nm. ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 7.69 (d, *J* = 2.0, H-C(8)), 7.34 (d, *J* = 8.5, H-C(5)), 7.38 (d, *J* = 11.0, H-C(4)), 7.12 (dd, J_1 = 2.0, J_2 = 8.5, H-C(6)), 5.14 (d, *J* = 6.5, H-N), 4.50-4.30 (m, 1H, ArNHC*H*(CH_3)-), 2.70-2.60 (m, 2H, -C*H*$_2$NHCH_2Ad), 2.60-2.50 (m, 2H, -C*H*$_2$CH_2Ad), 1.92 (s, 3H, -Ad), 1.75-1.55 (m, 10H, ArNHCH(CH_3)C*H*$_2$-, ArNHCH(CH_3)CH_2C*H*$_2$, -Ad), 1.55-1.45 (m, 6H, -Ad), 1.29 (d, 3H, *J* = 6.5, C*H*$_3$), 1.27-1.229 (d, 2H, -C*H*$_2$Ad). ^{13}C-NMR (125 MHz, $CDCl_3$, δ): 148.42 (d, *J* = 13.0, C(8a)); 147.17 (d, *J* = 250.0, C(3)); 145.39 (d, *J* = 2.2, C(2)); 133.65 (d, *J* = 2.2, C(7)); 127.80 (d, *J* = 4.5, (C(5)); 125.30 (C(8)); 123.14 (C(6)); 121.35 (d, *J* = 4.1, C(5)); 115.92 (d, *J* = 15.2, C(4a)); 49.84; 45.83; 44.62; 44.24; 42.61; 37.15; 34.58; 31.83; 28.67; 26.36; 20.82. HRMS: *m/z*444.25698 corresponds to molecular formula $C_{26}H_{35}ClFN_3H^+$ (error in ppm: - 1.46).HPLCpurity (λ = 254 nm) method A: RT 9.784 min, area 96.93%; method B: RT 12.131 min, area 96.48%.



i) 1) AQ/DCAQ, AcOHglac, MeOH/CH_2Cl_2, r.t., 2h 2) $NaBH_4$, rt, 12h; ii) carbonyl compound, $ZnCl_2$, $NaBH_3CN$, MeOH, r.t., 48h

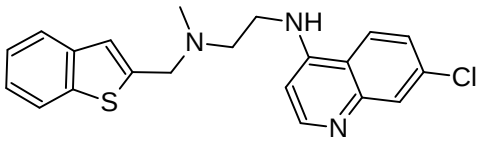
***N*-(1-benzothiophen-2-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)ethane-1,2-diamine(46).**



Compound **46** was prepared by method E from1-benzothiophene-2-carbaldehyde (240 mg, 1.48 mmol), using amine **AQ2** (489 mg, 2.21 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 9/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 6/4 and flash chromatography, Biotage SP1, RP column, eluent MeOH/H_2O gradient 65/35 → MeOH). Final product **46** was obtained as a pale yellow powder (396 mg, 73%). M.p. = 135 – 139 ºC. IR (ATR): 3226m, 3063m, 2946w, 2836w, 1578s, 1452m, 1374m, 1330w, 1285w, 1254w, 1210w, 1137m, 1080w, 1023w, 965w, 930w, 895w, 850w, 813w, 778m, 742w, 643w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.49 (d, *J* = 5.3, H-C(2')), 7.95 (d, *J* = 2.1, H-C(8')), 7.82-7.79 (m, H-C(7)), 7.76 (d, *J* = 8.9, H-C(5')), 7.70-7.67 (m, H-C(4)), 7.37 (dd, J_1 = 8.9, J_2 = 2.3, H-C(6')), 7.35-7.28 (m, H-C(5) and H-C(6)), 7.16-7.15 (m, H-C(3)), 6.34 (d, *J* = 5.5, H-C(3')), 5.87 (bs, H-N exchangeable with D_2O), 4.15-4.13 (m, 2H, -C*H*$_2$NHCH_2CH_2NH-), 3.34-3.29 (m, 2H, -CH_2NHCH_2C*H*$_2$NH-), 3.09-3.06 (m, 2H, -CH_2NHC*H*$_2$CH_2NH-), 1.86 (s, H-N exchangeable with D_2O).^{13}C NMR

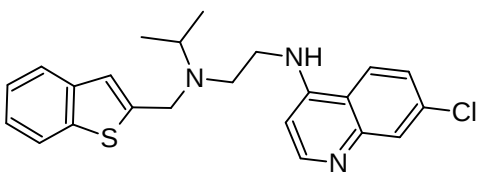
(125 MHz, $CDCl_3$, δ): 152.01, 149.78, 149.11, 144.98, 139.65, 139.45, 134.74, 128.65, 125.18, 124.32, 124.11, 123.16, 122.34, 121.56, 121.38, 117.34, 99.12, 48.56, 46.44, 42.09. HRMS: *m/z* 368.09836 corresponds to molecular formula $C_{20}H_{18}ClN_3SH^+$ (error in ppm -0.02). Anal. ($C_{20}H_{18}ClN_3S \times 0.25H_2O$) Calcd: C, 64.50; H, 5.01; N, 11.28; S, 8.61. Found: C, 64.67; H, 4.95; N, 11.31; S 8.53. HPLC purity (λ = 330 nm): method A: RT 8.938 min, area 98.51%; method B: RT 8.116 min, area 98.14%.

_N_-(1-benzothien-2-ylmethyl)-_N'_-(7-chloroquinolin-4-yl)-_N_-methylethane-1,2-diamine(47).



Compound **47** was prepared by method K from **46** (199 mg, 0.543 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 1/1). Final product **47** was obtained as yellow oil (180 mg, 87%). IR (ATR): 3395w, 3060w, 2950w, 2846w, 2801w, 1609m, 1581s, 1527m, 1452m, 1366m, 1330m, 1275w, 1241w, 1206w, 1130w, 1076w, 1032w, 879w, 809w, 747w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.49 (d, *J* = 5.3, H-C(2')), 7.95 (d, *J* = 2.1, H-C(5')), 7.86 (d, *J* = 8.9, H-C(8')), 7.82-7.79 (m, H-C(7)), 7.70-7.67 (m, H-C(4)), 7.41 (dd, J_1 = 8.9, J_2 = 2.2, H-C(6')), 7.35-7.28 (m, H-C(5) and H-C(6)), 7.16 (s, H-C(3)), 6.31 (d, *J* = 5.4, H-C(3')), 5.94 (bs, H-N exchangeable with D_2O), 3.89 (s, 2H, -C*H*$_2$N(CH$_3$)CH$_2$CH$_2$NH-), 3.29 (q, 2H, *J* = 4.6, -CH$_2$N(CH$_3$)CH$_2$C*H*$_2$NH-), 2.83 (t, 2H, *J* = 5.8, -CH$_2$N(CH$_3$)C*H*$_2$CH$_2$NH-), 2.40 (s, 3H, C*H*$_3$-N). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.94, 149.79, 149.00, 143.64, 139.66, 139.51, 134.78, 128.54, 125.14, 124.38, 124.28, 123.23, 122.47, 122.34, 121.62, 117.33, 99.08, 57.52, 53.92, 41.73, 39.63.HRMS: *m/z* 382.11463 corresponds to molecular formula $C_{21}H_{20}ClN_3SH^+$ (error in ppm 1.86). Anal. ($C_{21}H_{20}ClN_3S \times 0.5H_2O$) Calcd: C, 64.52; H, 5.41; N, 10.75; S, 8.20. Found: C, 64.82; H, 5.05; N, 10.88; S, 8.56. HPLC purity (λ = 254 nm) method A: RT 8.685 min, area 95.12%; (λ = 330 nm) method B: RT 7.428 min, area 95.57%.

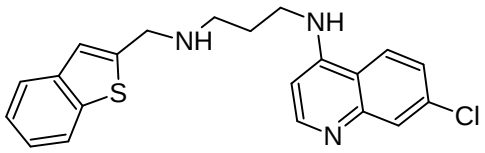
_N_-(1-benzothien-2-ylmethyl)-_N'_-(7-chloroquinolin-4-yl)-_N_-isopropylethane-1,2-diamine(48).



Compound **48** was prepared by method K from **46** (184 mg, 0.500 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/hexane gradient 1/1 → EtOAc, EtOAc/MeOH gradient 9/1 → 7/3). Final product **48** was obtained as pale yellow powder (187 mg, 91%). M.p. = 127 ºC. IR (ATR): 3388s, 2960m, 2869w, 2829m, 1608m, 1583s, 1523m, 1477m, 1363w, 1328m, 1265w, 1237w, 1173w, 1122w, 1077w, 882w, 841w, 794w, 748m cm^{-1}. ^1H

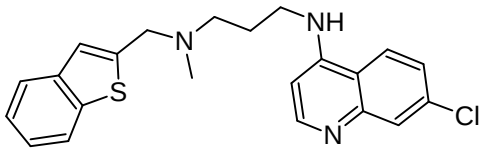
NMR (500 MHz, $CDCl_3$, δ): 8.47 (d, *J* = 5.3, H-C(2')), 7.93 (d, *J* = 2.2, H-C(5')), 7.77-7.73 (m, H-C(8') and H-C(7)), 7.65-7.62 (m, H-C(4)), 7.34 (dd, J_1 = 8.9, J_2 = 2.2, H-C(6')), 7.32-7.25 (m, H-C(6) and H-C(5)), 7.15-7.13 (m, H-C(3)), 6.29 (d, *J* = 5.4, H-C(3')), 5.94 (bs, H-N exchangeable with D_2O), 3.88 (d, 2H, *J* = 0.8, -C*H*$_2$N(iPr)CH_2CH_2NH-), 3.25 (q, 2H, *J* = 5.0, -CH_2N(iPr)CH_2C*H*$_2$NH-), 3.13 (sept, 1H, *J* = 6.6, $(CH_3)_2$C*H*-N), 2.91 (t, 2H, *J* = 5.8, -CH_2N(iPr)C*H*$_2CH_2$NH-), 1.13 (d, 6H, *J* = 6.6, (C*H*$_3)_2$CH-N). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.97, 149.84, 149.09, 146.11, 139.75, 139.44, 134.71, 128.60, 125.12, 124.36, 124.14, 123.07, 122.34, 121.77, 121.59, 117.44, 99.15, 49.10, 48.89, 46.95, 39.87, 17.90. HRMS: *m/z* 410.14550 corresponds to molecular formula $C_{23}H_{24}ClN_3SH^+$ (error in ppm 0.67). Anal. ($C_{23}H_{24}ClN_3S$) Calcd: C, 67.38; H, 5.90; N, 10.25; S, 7.82. Found: C, 67.09; H, 6.28; N, 10.16; S, 8.09. HPLC purity (λ = 330 nm): method A: RT 9.325 min, area 98.75%; method B: RT 7.604 min, area 97.41%.

***N*-(1-benzothiophen-2-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)propane-1,3-diamine (49).**



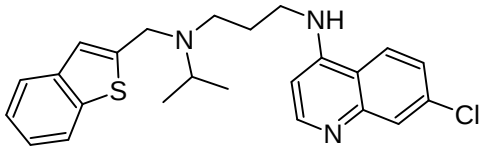
Compound **49** was prepared by method E from1-benzothiophene-2-carbaldehyde (314 mg, 1.93 mmol), using amine **AQ3** (682 mg, 2.89 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 9/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 6/4 and flashchromatography, Biotage SP1, RP column, eluent MeOH/H_2O gradient 75/25 → MeOH). Final product **49** was obtained as a pale yellow powder (480 mg, 65%). M.p. = 120 – 122 ºC. IR (ATR): 3648w, 3266m, 3058w, 2924w, 2843w, 1609w, 1581s, 1537w, 1453w, 1366w, 1331w, 1281w, 1241w, 1204w, 1138w, 1077w, 878w, 853w, 808w, 748w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.3, H-C(2')), 7.91-7.89 (m, H-C(8')), 7.79 (d, *J* = 7.8, H-C(7)), 7.70 (d, *J* = 7.3, H-C(4)), 7.57 (d, *J* = 10.2, H-C(5')), 7.39-7.30 (m, H-C(5) and H-C(6)), 7.16 (bs, H-C(3)), 7.13-7.08 (m, H-N exchangeable with D_2O), 7.05-7.01 (m, H-C(6')), 6.31 (d, *J* = 5.3, H-C(3')), 4.12 (s, 2H, -C*H*$_2$NH$CH_2CH_2CH_2$NH-), 3.43-3.38 (m, 2H, -CH_2NHCH_2CH_2C*H*$_2$NH-), 2.98-2.94 (m, 2H, -CH_2NHC*H*$_2CH_2CH_2$NH-), 1.96-1.80 (m, 2H, -CH_2NHCH_2C*H*$_2CH_2$NH- and H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.02, 150.25, 149.09, 144.04, 139.62, 139.54, 134.58, 128.41, 124.87, 124.44, 124.24, 123.25, 122.40, 122.02, 121.98, 117.43, 98.38, 49.34, 48.51, 43.36, 27.54. HRMS: *m/z* 382.11399 corresponds to molecular formula $C_{21}H_{20}ClN_3SH^+$ (error in ppm 0.29). Anal. ($C_{21}H_{20}ClN_3S\times0.25H_2O$) Calcd: C, 65.27; H, 5.35; N, 10.87; S, 8.30. Found: C, 65.31; H, 5.30; N, 10.93; S, 8.18. HPLC purity (λ = 330 nm) method A: RT 7.941 min, area 98.67%; (λ = 254 nm) method C: RT 5.254 min, area 98.63%.

***N*-(1-benzothien-2-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)-*N*-methylpropane-1,3-diamine (50).**



Compound **50** was prepared by method K from **49** (201 mg, 0.524 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 1/1). Final product **50** was obtained as yellow oil (202 mg, 97%). IR (ATR): 3270m, 3060w, 2949m, 2845w, 2804w, 1610m, 1582s, 1539w, 1456w, 1368w, 1333w, 1138w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.4, H-C(2')), 7.91 (d, *J* = 2.2, H-C(5')), 7.75-7.72 (m, H-C(7)), 7.69-7.66 (m, H-C(4)), 7.40 (d, *J* = 8.9, H-C(8')), 7.37-7.29 (m, H-C(5) and H-C(6)), 7.16-7.14 (m,H-C(3)), 7.03 (dd, J_1 = 8.9, J_2 = 2.2, H-C(6')), 6.72 (bs, H-N exchangeable with D_2O), 6.35 (d, *J* = 5.4, H-C(3')), 3.85 (d, 2H, *J* = 0.6, -C*H*$_2$N(CH_3)$CH_2CH_2CH_2$NH-), 3.45-3.41 (m, 2H, -CH_2N(CH_3)CH_2CH_2C*H*$_2$NH-), 2.65 (t, 2H, *J* = 5.7, -CH_2N(CH_3)C*H*$_2CH_2CH_2$NH-), 2.43 (s, 3H, C*H*$_3$-N), 1.92 (quin, 2H, *J* = 5.8, -CH_2N(CH_3)CH_2C*H*$_2CH_2$NH-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.00, 150.21, 149.15, 143.00, 139.84, 139.51, 134.59, 128.47, 124.94, 124.39, 124.29, 123.27, 122.95, 122.39, 121.65, 117.45, 98.57, 58.17, 55.84, 42.74, 42.26, 24.83. HRMS: *m/z* 396.13031 corresponds to molecular formula $C_{22}H_{22}ClN_3SH^+$ (error in ppm 1.87). Anal. ($C_{22}H_{22}ClN_3S\times0.5H_2O$) Calcd: C, 65.25; H, 5.72; N, 10.38; S, 7.92. Found: C, 65.73; H, 5.91; N, 10.66; S, 7.75. HPLC purity (λ = 330 nm): method A: RT 8.443 min, area 95.02%; method B: RT 7.444 min, area 96.11%.

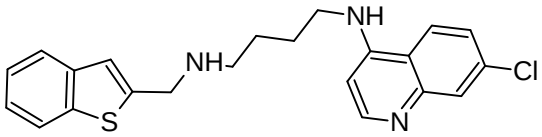
***N*-(1-benzothien-2-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)-*N*-isopropylpropane-1,3-diamine (51).**



Compound **51** was prepared by method K from **49** (249 mg, 0.652 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH, EtOAc/MeOH/NH_3 gradient 18/1/1 → 9/1/1). Final product **51** was obtained as pale yellow powder (115 mg, 41%). M.p. = 86 – 88 ºC. IR (ATR): 3240w, 3060w, 2964m, 1610m, 1580s, 1534m, 1455m, 1366m, 1330w, 1280w, 1221w, 1169w, 1135w, 1079w, 1022w, 879w, 853w, 810w, 744m cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.45 (d, *J* = 5.4, H-C(2')), 7.86 (d, *J* = 2.2, H-C(5')), 7.77-7.74 (m, H-C(7)), 7.69-7.65 (m, H-C(4)), 7.39-7.30 (m, H-C(5) and H-C(6)), 7.17-7.14 (d, *J* = 9.0, H-C(8') and H-C(3)), 6.87 (dd, J_1 = 8.9, J_2 = 2.2, H-C(6')), 6.32 (d, *J* = 5.4, H-C(3')), 5.96 (bs, H-N exchangeable with D_2O), 3.85 (s, 2H,-C*H*$_2$N(iPr)$CH_2CH_2CH_2$NH-), 3.42 (q, 2H, *J* = 5.7, -CH_2N(iPr)CH_2CH_2C*H*$_2$NH-), 3.21-3.12 (m, 1H, (CH_3)$_2$C*H*-N), 2.67 (t, 2H, *J* = 5.8, -CH_2N(iPr)C*H*$_2CH_2CH_2$NH-), 2.01 (bs, H-N

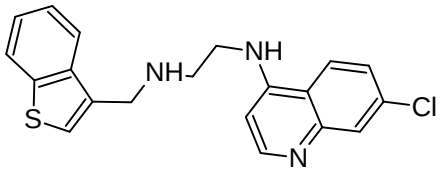
exchangeable with D_2O), 1.89-1.82 (m, 2H, -CH_2N(iPr)$CH_2C\mathit{H}_2CH_2$NH-), 1.08 (d, 6H, *J* = 6.6, ($C\mathit{H}_3$)$_2$CH-N). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.89, 149.82, 149.07, 146.12, 139.79, 139.59, 134.53, 128.42, 124.77, 124.40, 124.18, 123.14, 122.41, 122.10, 121.39, 117.19, 98.64, 49.40, 49.15, 47.51, 41.74, 25.45, 17.57. HRMS: *m/z* 424.16183 corresponds to molecular formula $C_{24}H_{26}ClN_3SH^+$ (error in ppm 2.25). Anal. ($C_{24}H_{26}ClN_3S\times0.5H_2O$) Calcd: C, 66.57; H, 6.28; N, 9.70; S, 7.41. Found: C, 66.94; H, 6.44; N, 9.54; S, 6.95. HPLC purity (λ = 330 nm): method A: RT 8.478 min, area 95.72%; method B: RT 7.472 min, area 95.45%.

***N*-(1-benzothiophen-2-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)butane-1,4-diamine (53).**



Compound **53** was prepared by method E from1-benzothiophene-2-carbaldehyde (162 mg, 0.999 mmol), using amine **AQ4** (375 mg, 1.52 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 9/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 6/4 and flashchromatography, Biotage SP1, RP column, eluent MeOH/H_2O gradient 85/15 → MeOH). Final product **53** was obtained as pale yellow powder (320 mg, 54%). M.p. = 101 – 104 ºC. IR (ATR): 3436w, 3283m, 3137w, 3105w, 3062w, 2935m, 2858w, 2180w, 1610w, 1580s, 1537w, 1453m, 1366w, 1332w, 1136w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.5, H-C(2')), 7.94-7.92 (m, H-C(8')), 7.78 (d, *J* = 8.0, H-C(5')), 7.70-7.64 (m, 2H-Ar), 7.35-7.21 (m, 3H-Ar), 7.14 (s, H-C(3)), 6.36 (d, *J* = 5.3, H-C(3')), 5.72-5.66 (m, H-N exchangeable with D_2O), 4.09 (s, 2H, -$C\mathit{H}_2$NH$CH_2CH_2CH_2CH_2$NH-), 3.32-3.27 (m, 2H, -CH_2NH$CH_2CH_2CH_2C\mathit{H}_2$NH-), 2.78 (t, 2H, *J* = 6.6, -CH_2NH$C\mathit{H}_2CH_2CH_2CH_2$NH-), 1.86 (quin, 2H, *J* = 6.8, -CH_2NH$CH_2CH_2C\mathit{H}_2CH_2$NH-), 1.73-1.45 (m, 2H, -CH_2NH$CH_2C\mathit{H}_2CH_2CH_2$NH- and H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.06, 149.82, 149.16, 144.90, 139.70, 139.53, 134.68, 128.73, 125.05, 124.25, 123.98, 123.11, 122.34, 121.38, 121.18, 117.22, 98.91, 49.11, 48.35, 43.17, 27.64, 26.25. HRMS: *m/z* 396.12788 corresponds to molecular formula $C_{22}H_{22}ClN_3SH^+$ (error in ppm 0.73). Anal. ($C_{22}H_{22}ClN_3S\times0.25H_2O$) Calcd: C, 65.74; H, 5.68; N, 10.45; S, 7.98. Found: C, 65.60; H, 5.61; N, 10.36; S, 7.83. HPLC purity (λ = 330 nm): method A: RT 11.020 min, area 98.99%; method B: RT 8.229 min, area 97.99%.

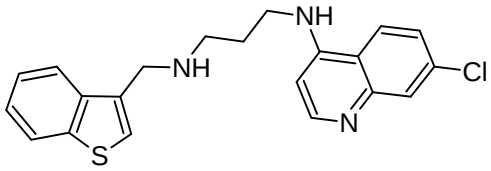
***N*-(1-benzothiophen-3-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)ethane-1,2-diamine(55).**



Compound **55** was prepared by method E from1-benzothiophene-3-carbaldehyde (70.0 mg, 0.432 mmol), using amine **AQ2** (144 mg, 0.648 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → 7/3 and flashchromatography, Biotage SP1, RP column, eluent MeOH/H_2O gradient 8/2 → MeOH).

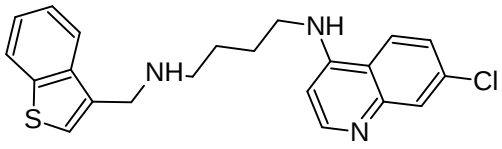
Final product **55** was obtained as pale yellow powder (135 mg, 85%). M.p. = 104 – 108 ºC. IR (ATR): 3324w, 3219m, 3036m, 2967m, 1583s, 1490w, 1454m, 1427m, 1372m, 1334w, 1281m, 1242w, 1211w, 1167w, 1136m, 1078w, 898w, 850m, 797w, 761m, 731m, 641w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.48 (d, *J* = 5.3, H-C(2')), 7.92 (d, *J* = 2.2, H-C(8')), 7.91-7.85 (m, 2H-Ar), 7.40-7.34 (m, 3H-Ar), 7.30 (s, H-C(2)), 7.24 (dd, J_1 = 2.3, J_2 = 9.1, H-C(6')), 6.30 (d, *J* = 5.4, H-C(3')), 5.76 (bs, H-N exchangeable with D_2O), 4.10 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$NH-), 3.30-3.26 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$NH-), 3.10-3.06 (m, 2H, -CH$_2$NHC*H*$_2$CH$_2$NH-), 1.74 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.99, 149.71, 149.03, 140.86, 138.21, 134.69, 134.60, 128.58, 125.10, 124.51, 124.09, 123.68, 123.07, 121.89, 121.23, 117.24, 99.11, 47.16, 46.79, 41.95. HRMS: *m/z* 368.09643 corresponds to molecular formula $C_{20}H_{18}ClN_3SH^+$ (error in ppm -5.00). HPLC purity (λ = 330 nm): method A: RT 8.402 min, area 98.48%; method B: RT 7.404 min, area 98.45%.

***N*-(1-benzothiophen-3-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)propane-1,3-diamine (56).**



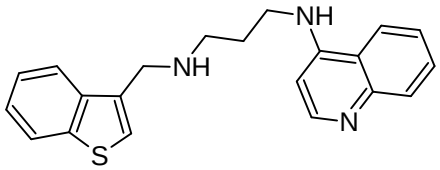
Compound **56** was prepared by method E from1-benzothiophene-3-carbaldehyde (90.0 mg, 0.555 mmol), using amine **AQ3** (196 mg, 0.832 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2, flashchromatography, Biotage SP1, NH column, eluent EtOAc/Hex gradient 7/3 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH, Biotage SP1, SiO_2 column, eluent EtOAc/MeOH+NH_3(9/1) gradient 95/5 → 7/3). Final product **56** was obtained as pale yellow powder (127 mg, 60%). M.p. = 122 – 123 ºC. IR (ATR): 3298w, 3214m, 3059w, 2952m, 2888w, 2827w, 1611w, 1581s, 1539m, 1456m, 1426m, 1358w, 1327m, 1277w, 1224w, 1168w, 1139w, 1112w, 1082w, 893w, 848w, 811w, 764m, 731m, 636w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.46 (d, *J* = 5.4, H-C(2')), 7.91 (d, *J* = 8.0, H-C(4)), 7.87 (d, *J* = 2.0, H-C(8'), 7.79 (d, *J* = 8.1, H-C(5')), 7.44-7.27 (m, 4H-Ar and H-N exchangeable with D_2O), 6.91 (dd, J_1 = 2.0, J_2 = 8.8, H-C(6')), 6.27 (d, *J* = 5.4, H-C(3')), 4.09 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$NH-), 3.43-3.38 (m, 2H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$NH-), 3.04 (t, 2H, *J* = 5.5, 2H, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$NH-), 2.05-1.93 (m, 2H, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$NH- and H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.85, 150.37, 148.84, 140.67, 138.12, 134.56, 134.45, 128.17, 124.79, 124.62, 124.27, 123.49, 123.04, 121.88, 121.42, 117.33, 98.23, 49.41, 47.59, 43.81, 27.38. HRMS: *m/z* 382.11218 corresponds to molecular formula $C_{21}H_{20}ClN_3SH^+$ (error in ppm -4.57). Anal. ($C_{21}H_{20}ClN_3S$) Calcd: C, 66.04; H, 5.28; N, 11.00; S, 8.40. Found: C, 65.69; H, 5.54; N, 10.84; S, 8.00. HPLC purity (λ = 330 nm): method A: RT 8.487 min, area 99.20%; method B: RT 7.438 min, area 99.18%.

***N*-(1-benzothiophen-3-ylmethyl)-*N*'-(7-chloroquinolin-4-yl)butane-1,4-diamine (57).**



Compound **57** was prepared by method E from1-benzothiophene-3-carbaldehyde (80.0 mg, 0.493 mmol), using amine **AQ4** (185 mg, 0.740 mmol). The product was purified using column chromatography (flash, Biotage SP1, SiO_2 column, eluent EtOAc/MeOH+NH_3(9/1) gradient 95/5 → 7/3). Final product **57** was obtained as pale yellow powder (115 mg, 59%). M.p. = 82 – 85 ºC. IR (ATR): 3304w, 3220m, 3056w, 2927m, 2851w, 2817w, 1582s, 1540m, 1459m, 1427m, 1365w, 1327m, 1276w, 1255w, 1228w, 1164w, 1136m, 1079w, 898w, 864w, 835w, 749w, 724w, 638w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.49 (d, *J* = 5.4, H-C(2')), 7.92 (d, *J* = 2.0, H-C(8')), 7.89-7.85 (m, H-C(4)), 7.81-7.78 (m, H-C(7)), 7.58 (d, *J* = 8.9, H-C(5')), 7.40-7.33 (m, 2H-Ar), 7.30 (s, H-C(2)), 7.12 (dd, J_1 = 2.0, J_2 = 8.9, H-C(6')), 6.34 (d, *J* = 5.4, H-C(3')), 5.83 (bs, H-N exchangeable with D_2O), 4.06 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.32-3.26 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$C*H*$_2$NH-), 2.81 (t, 2H, *J* = 6.6, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$CH$_2$NH-), 1.88 (quin, 2H, *J* = 6.8, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$CH$_2$NH-), 1.80 (bs, H-N exchangeable with D_2O), 1.72 (quin, 2H, *J* = 6.8, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$CH$_2$NH-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.98, 149.96, 149.02, 140.73, 138.22, 134.86, 134.74, 128.58, 125.01, 124.50, 124.11, 123.04, 122.99, 121.57, 121.23, 117.22, 98.87, 48.91, 47.62, 43.16, 27.70, 26.34. HRMS: *m/z* 396.12784 corresponds to molecular formula $C_{22}H_{22}ClN_3SH^+$ (error in ppm -4.38). HPLC purity (λ = 254 nm) method A: RT 8.153 min, area 97.42%; (λ = 330 nm) method B: RT 7.519 min, area 97.71%.

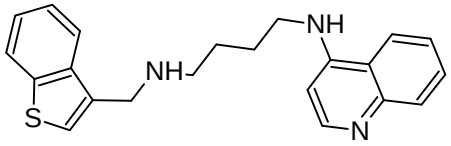
***N*-(1-benzothiophen-3-ylmethyl)-*N*'-(quinolin-4-yl)propane-1,3-diamine(62).**



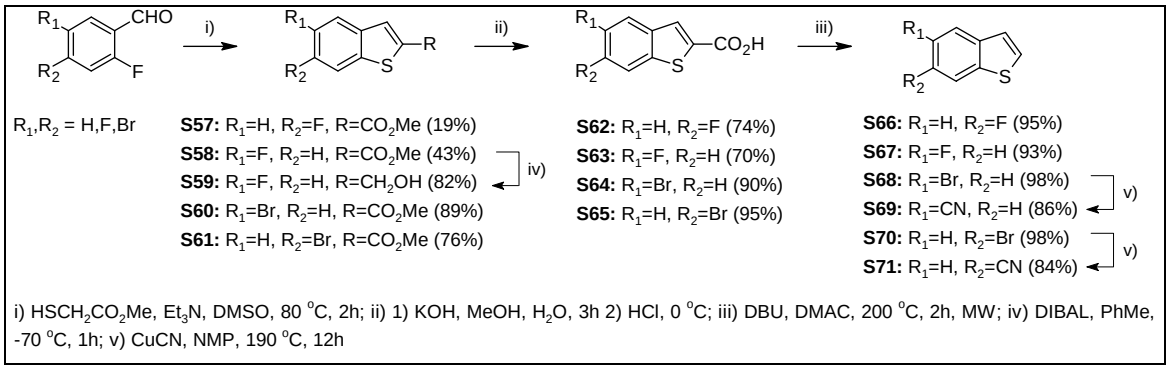
Compound **62** was prepared by method E from1-benzothiophene-3-carbaldehyde (115 mg, 0.709 mmol), using amine **AQ7** (214 mg, 1.06 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 7/3). Final product **62** was obtained as pale yellow oil (177 mg, 72%). IR (film): 3750w, 3673w, 3648w, 3447s, 2917w, 2845w, 1650w, 1576w, 1557w, 1541w, 1458w, 1433w, 1397w, 1370w, 1338w, 1132w, 763w, 732w, 617w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$-exchange with D_2O, δ): 8.50 (d, *J* = 5.5, H-C(2')), 7.94-7.89 (m, 2H-Ar), 7.83-7.80 (m, H-C(8')), 7.56-7.49 (m, 2H-Ar), 7.38-7.31 (m, 3H-Ar), 7.14-7.09 (m, H-C(6)), 6.33 (d, *J* = 5.2, H-C(3')), 4.10 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$NH-), 3.42 (t, 2H, *J* = 6.0, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$NH-), 3.02 (t, 2H, *J* = 5.6, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$NH-), 2.00-1.94 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$NH-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 150.66, 150.26, 147.46, 140.68, 138.17, 134.49, 129.07, 128.85, 124.56, 124.41, 124.24, 123.47, 123.02, 121.47, 120.28, 118.77, 97.92, 49.20, 47.64, 43.65, 27.57.

HRMS: *m/z* 348.15179 corresponds to molecular formula $C_{21}H_{21}N_3SH^+$ (error in ppm -3.18). HPLC purity (λ = 330 nm): method A: RT 8.708 min, area 97.43%; method B: RT 7.815 min, area 97.16%.

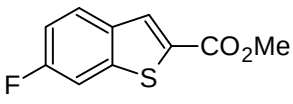
***N*-(1-benzothiophen-3-ylmethyl)-*N*'-(quinolin-4-yl)butane-1,4-diamine (66).**



Compound **66** was prepared by method E from1-benzothiophene-3-carbaldehyde (80.0 mg, 0.493 mmol), using amine **AQ8** (159 mg, 0.739 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 2/8 → EtOAc, EtOAc/MeOH gradient 95/5 → 1/9, and flash, Biotage SP1, NH column, eluent EtOAc/Hex gradient 7/3 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH). Final product **66** was obtained as pale yellow oil (101 mg, 57%). IR (ATR): 3307m, 3077m, 2935m, 2859m, 2818m, 1585s, 1547m, 1500s, 1442m, 1401w, 1376w, 1343w, 1283w, 1257w, 1226w, 1130w, 1035m, 809w, 766m, 733w, 652w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.31 (d, *J* = 5.4, H-C(2')), 8.08-8.04 (m, H-C(8')), 7.86-7.83 (m, H-C(4)), 7.82-7.76 (m, 2H-Ar), 7.62-7.58 (m, H-C(7')), 7.42 (bs, H-C(2)), 7.41-7.30 (m, 3H-Ar), 6.46 (d, *J* = 5.7, H-C(3')), 4.00 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.36 (t, 2H, *J* = 6.9, -CH$_2$NHCH$_2$CH$_2$CH$_2$C*H*$_2$NH-), 2.73 (t, 2H, *J* = 7.2, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$CH$_2$NH-), 1.81-1.74 (m, 2H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$CH$_2$NH-), 1.73-1.65 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$CH$_2$NH-). ^{13}C NMR (125 MHz, CD_3OD, δ): 152.69, 151.12, 148.80, 141.93, 139.68, 135.53, 130.46, 128.69, 125.55, 125.46, 125.13, 124.54, 123.76, 122.57, 122.20, 120.26, 99.14, 49.96, 47.56, 43.76, 28.02, 27.21. HRMS: *m/z* 362.16853 corresponds to molecular formula $C_{22}H_{23}N_3SH^+$ (error in ppm -0.08). HPLC purity (λ = 330 nm): method A: RT 8.366 min, area 97.01%; method B: RT 7.416 min, area 96.78%.



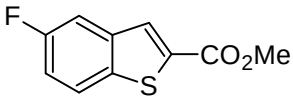
Methyl 6-fluoro-1-benzothiophene-2-carboxylate (S57).



Compound **S57**was prepared from2,4-difluorobenzaldehyde (7.91 g, 55.6 mmol) by method L. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 95/5. Final product **S57**was obtained as colorless crystals (2.22 g, 19%). M.p. = 86 – 89 ºC (Hex/EtOAc=95/5); lit.[25] m.p. 85.5-86 ºC (MeOH). IR (ATR): 3413w, 3106w, 3065w,

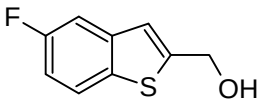
2960w, 2847w, 1726s, 1609w, 1567w, 1527m, 1465w, 1434w, 1338w, 1308w, 1250s, 1193m, 1068w, 1045w, 960w, 908w, 884w, 849w, 803w, 777w, 751w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.02 (s, H-C(3)), 7.85-7.80 (m, H-C(4)), 7.55-7.51 (m, H-C(7)), 7.16 (td, J_1 = 2.3, J_2 = 9.0, H-C(5)), 3.94 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 162.95 (d, J = 16.2), 161.03, 143.36 (d, J = 10.8), 135.23, 133.18 (d, J = 3.6), 130.08, 126.89 (d, J = 9.0), 114.48 (d, J = 25.4), 108.69 (d, J = 25.3), 52.52. HRMS: *m/z* 211.02230 corresponds to molecular formula $C_{10}H_7FO_2SH^+$ (error in ppm -0.27).

Methyl 5-fluoro-1-benzothiophene-2-carboxylate (S58).



Compound **S58** was prepared from2,5-difluorobenzaldehyde (5.00 g, 35.2 mmol) by method L. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 95/5). Final product **S58** was obtained as colorless crystals (3.18 g, 43%). M.p. = 68 – 71 ºC (Hex/EtOAc=95/5); lit.[26] m.p. 75-76 ºC. IR (ATR): 3409w, 3240w, 3087w, 2961w, 2846w, 2772w, 1717s, 1607w, 1574w, 1527s, 1497w, 1430m, 1327w, 1295w, 1253s, 1204s, 1144w, 1078w, 1057w, 944w, 876w, 809w, 770w, 750w, 708w, 651w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.00 (s, H-C(3)), 7.80 (dd, J_1 = 4.7, J_2 = 8.8, H-C(7)), 7.53 (dd, J_1 = 2.5, J_2 = 9.0, H-C(4)), 7.23 (td, J_1 = 2.5, J_2 = 8.9, H-C(6)), 3.95 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 162.38 (d, J = 128.2), 159.93, 139.54 (d, J = 9.9), 137.65, 135.73, 129.98 (d, J = 4.5), 124.08 (d, J = 9.0), 116.19 (d, J = 25.3), 110.56 (d, J = 22.6), 52.6. GC/MS (*m/z,%)*: 210.0 ([M^+], 64), 179.0 (100), 151.0 (20), 107.0 (45).

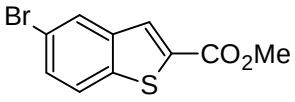
(5-fluoro-1-benzothiophen-2-yl)methanol(S59).



Compound**S58** (590mg, 2.8 mmol) was dissolved with stirring in dry PhMe (15 mL) under Ar at -70 °C, followed by slow addition of 0.6 M DIBAL (19 mL, 11 mmol). Reaction was quenched after 1 h with MeOH/H_2O (4/1) and the solvent was removed under reduced pressure. The crude mixture was dissolved in DCM (40 mL), transferred to a separation funnel, washed with water (2 × 30 mL) and brine (30 mL), and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 7/3). Final product **S59**was obtained as a white powder (420mg, 82%). M.p. = 89 – 90 ºC (lit.[27] m.p. 94 ºC (*i*Pr_2O-hexane). IR (ATR): 3249s, 2932m, 2352w, 1750w, 1601m, 1576w, 1538m, 1442s, 1362w, 1297w, 1251w, 1192w, 1143s, 1014s, 947w, 876s, 839w, 812s, 779w, 721w, 693w, 664, 641w, 588w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 7.72 (dd, J_1 = 4.8, J_2 = 8.7, H-C(7)), 7.38 (dd, J_1 = 2.5, J_2 = 9.4, H-C(4)), 7.16 (s, H-C(3)), 7.07 (td, J_1 = 2.5, J_2 = 8.9, H-C(6)), 4.92 (d, 2H, J = 5.2, -CH_2OH), 2.02 (t, J = 5.8, H-O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.85 (d, J = 239.2), 147.48, 140.51 (d, J = 9.9),

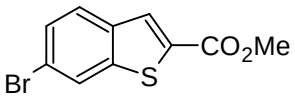
135.21, 123.54 (d, J = 9.0), 121.51 (d, J = 4.5), 113.08 (d, J = 25.3), 108.98 (d, J = 23.5), 60.82.GC/MS (*m/z,%)*: 182.0 ([M^+], 95), 165. 0 (90), 153.0 (100), 109.0 (53).

Methyl 5-bromo-1-benzothiophene-2-carboxylate(S60).



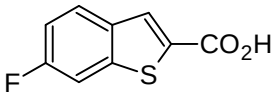
Compound **S60** was prepared from5-bromo-2-fluorobenzaldehyde (1.00 g, 4.92 mmol) by method L. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 95/5). Final product **S60** was obtained as pale yellow powder (1.19 g, 89%). M.p. = 110 ºC. IR (ATR): 3083w, 2999w, 2956w, 1720s, 1554m, 1517s, 1435m, 1310w, 1285m, 1251s, 1196m, 1168m, 1062m, 949w, 882m, 796m, 750m, 711w, 542w, 479w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.02-8.00 (m, H-C(4)), 7.97-7.96 (m, H-C(3)), 7.74-7.71 (m, H-C(7)), 7.54 (dd, J_1 = 1.9, J_2 = 8.6, H-C(6)), 3.95 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 162.76, 140.64, 140.17, 135.12, 130.02, 129.43, 127.96, 124.10, 118.91, 52.64. HRMS: *m/z* 270.9422 corresponds to molecular formula$C_{10}H_7BrO_2SH^+$ (error in ppm -0.32).

Methyl 6-bromo-1-benzothiophene-2-carboxylate(S61).



Compound **S61** was prepared from4-bromo-2-fluorobenzaldehyde (5.00 g, 24.6 mmol) by method L. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 9/1). Final product **S61** was obtained as pale yellow powder (5.10 g, 76%). M.p. = 114 ºC (lit.[28] m.p. 113-115 ºC). IR (ATR): 3405w, 3068w, 2956w, 2842w, 1805w, 1710s, 1580m, 1503m, 1429m, 1380m, 1329w, 1307m, 1283s, 1192m, 1169s, 1136m, 1086s, 1062s, 956w, 917m, 865s, 809s, 751s, 719m, 700w, 641w, 565m, 490w, 456w, 429m, 403w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.02-7.99 (m, H-C(7) and H-C(2)), 7.72 (d, J = 8.4, H-C(4)), 7.51 (dd, J_1 = 1.7, J_2 = 8.6, H-C(5)), 3.94 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 162.84, 143.47, 137.34, 133.90, 130.09, 128.58, 126.54, 125.28, 121.26, 52.60. GC/MS (*m/z,%)*: 271.9 ([M^+], 87), 269.9 (89), 240.9 (100), 210.9 (22), 168.9 (20), 131.9 (41).

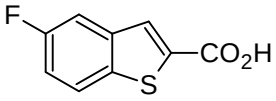
6-fluoro-1-benzothiophene-2-carboxylic acid (S62).[29]



Compound **S62** was prepared frommethyl ester **S57** (247 mg, 1.18 mmol) by method M. The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM → DCM/MeOH = 9/1). Final product **S62** was obtained as white powder (171 mg, 74%). M.p. = 182 – 186 °C. IR (ATR): 2811w, 2575w, 1665s, 1604m, 1566w, 1523s, 1468w, 1438m, 1341w, 1319m, 1279w, 1255m, 1196m, 1177m, 1062w, 921m, 870w, 845w, 806w, 759w cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD, δ): 8.04 (s, H-C(3)), 7.94 (dd, J_1 = 5.2, J_2 = 8.7, H-C(4)), 7.68 (dd, J_1 = 2.4, J_2 = 9.0, H-C(7)), 7.22 (td, J_1 = 2.4, J_2 = 9.0, H-C(5)). ^{13}C NMR (125 MHz, CD_3OD, δ): 165.38, 163.45 (d, J = 244.6), 144.88 (d, J = 10.8), 137.06, 135.81 (d, J = 3.6), 131.13, 128.29 (d, J =

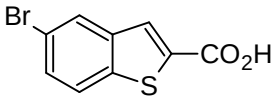
9.9), 115.29 (d, J = 24.4), 109.55 (d, J = 25.3). HRMS: *m/z* 194.99178 corresponds to molecular formula $[C_9H_5SFO_2\text{-}H]^-$ (error in ppm -1.91).

5-fluoro-1-benzothiophene-2-carboxylic acid(S63).



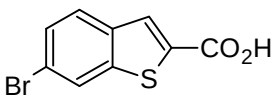
Compound **S63** was prepared frommethyl ester **S58** (1.30 g, 6.2 mmol) by method M. The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM → DCM/MeOH = 7/3). Final product **S63** was obtained as white powder (850mg, 70%). M.p. = 220-224 °C. IR (ATR): 2966m, 2848m, 2803m, 2633m, 2565m, 2524m, 1677s, 1603w, 1571w, 1525s, 1446w, 1409m, 1332w, 1305s, 1271s, 1242w, 1209s, 1147w, 1130w, 1079w, 1055w, 954w, 930w, 882w, 809w, 760w, 711w, 655w, 598w, 509w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.00 (s, H-C(3)), 7.91 (dd, J_1 = 4.8, J_2 = 8.9, H-C(7)), 7.64 (dd, J_1 = 2.5, J_2 = 9.2, H-C(4)), 7.27 (td, J_1 = 2.8, J_2 = 8.9, H-C(6)). ^{13}C NMR (125 MHz, CD_3OD, δ): 166.55, 162.33 (d, J = 240.1), 141.31 (d, J = 9.9), 139.21, 131.34, 131.06 (d, J = 12.6), 125.39 (d, J = 9.0), 116.94 (d, J = 25.3), 111.42 (d, J = 22.6). HRMS: *m/z* 194.99273 corresponds to molecular formula $[C_9H_5SFO_2\text{-}H]^-$ (error in ppm 2.98).

5-bromo-1-benzothiophene-2-carboxylic acid(S64).



Compound **S64** was prepared frommethyl ester **S60** (1.19 g, 4.39 mmol) by method M. The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM → DCM/MeOH = 9/1). Final product **S64** was obtained as white powder (1.01 g, 90%). M.p. = 234 – 236 °C (lit.[30] m.p. 235 °C (H_2O/EtOH)). IR (ATR): 2977m, 2828m, 2662m, 2557m, 1667s, 1551s, 1517s, 1439m, 1401w, 1302s, 1265m, 1178s, 1072w, 1042w, 936w, 886m, 799m, 759m, 711w, 600w, 507w, 473w, 424w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.11-8.09 (m, H-C(4)), 8.00-7.97 (m, H-C(3)), 7.84-7.81 (m, H-C(7)), 7.22 (dd, J_1 = 1.8, J_2 = 8.7, H-C(6)). ^{13}C NMR (125 MHz, CD_3OD, δ): 165.24, 142.17, 141.96, 137.87, 130.95, 130.54, 129.05, 125.41, 119.80. HRMS: *m/z* 254.91145 corresponds to molecular formula $[C_9H_5BrO_2S\text{-}H]^-$ (error in ppm 4.69).

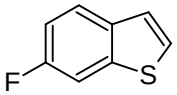
6-bromo-1-benzothiophene-2-carboxylic acid(S65).



Compound **S65** was prepared frommethyl ester **S61** (2.00 g, 7.38 mmol) by method M. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 1/1). Final product **S65** was obtained as white powder (1.80 g, 95%). M.p. = 260 – 265 °C. IR (ATR): 3082m, 2982m, 2839m, 2690m, 2579m, 1664s, 1586m, 1552w, 1513m, 1425m, 1383w, 1333w, 1316m, 1276w, 1244w, 1181w, 1139w, 1090w, 1051w, 918w, 871w, 803w, 754w, 564w, 514w cm^{-1}. ^1H NMR (500 MHz, CD_3OD+$CDCl_3$, δ): 8.08-8.05 (m, H-C(7)), 7.98 (bs, H-C(3)), 7.78 (d, J = 8.5, H-C(4)), 7.51 (dd, J_1 = 1.7, J_2 = 8.6, H-C(5)). ^{13}C NMR

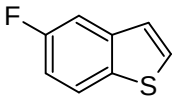
(125 MHz, CD_3OD+$CDCl_3$, δ): 165.42, 144.71, 138.91, 130.78, 129.35, 127.61, 126.12, 121.83. HRMS: *m/z* 254.91154 corresponds to molecular formula $[C_9H_5BrO_2S\text{-}H]^-$ (error in ppm -2.13).

6-fluoro-1-benzothiophene(S66).



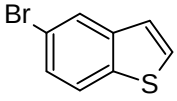
Compound **S66** was prepared fromcarboxylic acid **S62** (163 mg, 0.831 mmol) by method N. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex). Final product **S66** was obtained as colorless liquid (121 mg, 95%). IR (film): 3106w, 3073w, 2927w, 1879w, 1754w, 1697w, 1625w, 1606m, 1565m, 1530w, 1496w, 1467s, 1392w, 1342w, 1310w, 1251s, 1218s, 1184w, 1118w, 1081w, 1040w, 912s, 884w, 844m, 811s, 783w, 745w, 689m, 649w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.75 (dd, J_1 = 5.3, J_2 = 8.7, H-C(4)), 7.55 (dd, J_1 = 2.2, J_2 = 9.0, H-C(7)), 7.38, 7.30 (ABq, J_{AB} = 14.1, H-C(2) and H-C(3)), 7.12 (td, J_1 = 2.4, J_2 = 8.8, H-C(5)). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 172.86, 162.94, 125.98 (d, J = 3.6), 124.48 (d, J = 9.1), 123.35, 113.49, 113.25 (d, J = 23.7), 108.43 (d, J = 24.6). GC/MS (*m/z,%)*: 152.0 ($[M^+]$, 100).

5-fluoro-1-benzothiophene(S67).



Compound **S67** was prepared fromcarboxylic acid **S63** (1.40 g, 7.1 mmol) by method N. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex). Final product **S67** was obtained as colorless liquid (1.00 g, 93%). IR (film): 3907w, 3084w, 3012w, 2927w, 2372w, 2175w, 1879w, 1781w, 1725w, 1618w, 1582w, 1563m, 1525w, 1501w, 1455w, 1421m, 1319w, 1422m, 1319w, 1267w, 1248m, 1232w, 1139m, 1092w, 1051w, 942w, 891m, 862s, 833m, 808s, 750s, 694s, 632w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 7.79 (dd, J_1 = 4.9, J_2 = 8.8, H-C(7)), 7.52 (d, J = 5.2, H-C(3)), 7.47 (dd, J_1 = 2.5, J_2 = 9.4, H-C(4)), 7.29 (d, J = 5.2, H-C(2)), 7.13-7.07 (m, H-C(6)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.8 (d, J = 240.0), 140.58 (d, J = 8.8), 135.12, 128.78, 123.56 (d, J = 5.0), 123.46, 113.12 (d, J = 23.8), 108.98 (d, J = 22.5). GC/MS (*m/z*,%): 152.0 ($[M^+]$, 100).

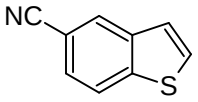
5-bromo-1-benzothiophene(S68).



Compound **S68** was prepared fromcarboxylic acid **S64** (1.00 g, 3.89 mmol) by method N. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex). Final product **S68** was obtained as white powder (814 mg, 98%). M.p. = 43 – 44 °C (lit.[31] m.p. 47 °C). IR (ATR): 3102m, 2924m, 2850w, 2176w, 2004w, 1874w, 1775w, 1730w, 1579s, 1545m, 1491m, 1431s, 1404s, 1310m, 1272w, 1250m, 1223m, 1191s, 1151m, 1090m, 1061s, 940w, 887m, 866m, 811s, 798s, 751s, 727s, 691s, 546w, 475m, 412w, 402w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 7.97-7.95 (m, H-C(4)), 7.75-7.71 (m, H-C(7)), 7.48-7.46 (m, H-C(2)), 7.45-7.41 (m, H-C(6)), 7.28-7.26 (m, H-C(3)).

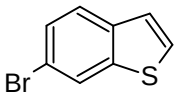
^{13}C NMR (125 MHz, $CDCl_3$, δ): 141.22, 138.34, 128.14, 127.26, 126.23, 123.76, 123.10, 118.22. GC/MS (*m/z,%)*: 213.9 ([M^+], 100), 133.0 (55), 89.0 (45).

1-benzothiophene-5-carbonitrile(S69).



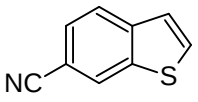
Compound **S69** was prepared fromcompound **S68** (735 mg, 3.45 mmol) by method P. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 9/1). Final product **S69** was obtained as colorlesscrystals (472 mg, 86%). M.p. = 67 – 69 °C (Hex/EtOAc=9/1); lit.[32] m.p. 63 °C. IR (ATR): 3107s, 3087m, 2223s, 1777w, 1594w, 1540w, 1429m, 1320m, 1257m, 1225w, 1134w, 1090m, 1050w, 907m, 823s, 758m, 704s, 623w, 598w, 574w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.15 (s, H-C(4)), 7.97 (d, J = 8.4, H-C(7)), 7.61 (d, J = 5.5, H-C(2)), 7.57-7.54 (m, H-C(6)), 7.41 (d, J = 5.5, H-C(3)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 143.80, 139.31, 129.05, 128.16, 126.14, 123.68, 123.44, 119.36, 107.96. GC/MS (*m/z,%)*: 159.0 ([M^+], 100).

6-bromo-1-benzothiophene(S70).

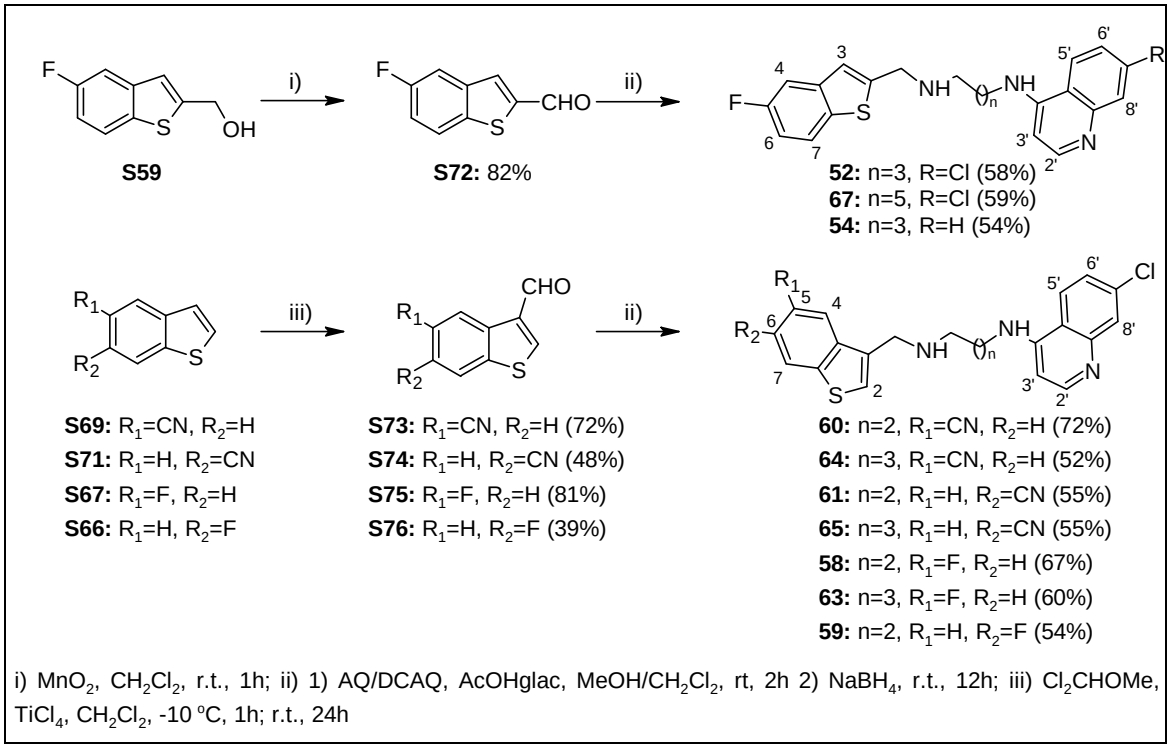


Compound **S70** was prepared fromcarboxylic acid **S65** (1.00 g, 3.89 mmol) by method N. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex). Final product **S70** was obtained as white powder (811 mg, 98%). M.p. = 53 – 54 °C (lit.[30] m.p. 56°C).IR (ATR): 3105w, 3076w, 1576m, 1541w, 1482w, 1439m, 1377m, 1336m, 1300w, 1246w, 1200w, 1061m, 950w, 866m, 816s, 744m, 689m, 566m, 427w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.01 (s, H-C(7)), 7.66 (d, J = 8.5, H-C(4)), 7.48-7.44 (m, H-C(5)), 7.41, 7.29 (AMq, J_{AM} = 5.5, H-C(2) and H-C(3)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 141.26, 138.32, 127.62, 126.90, 124.96, 124.65, 123.54, 118.14. GC/MS (*m/z,%)*: 213.9 ([M^+], 100), 211.9 (99), 133.0 (48), 89.0 (38).

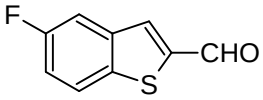
1-benzothiophene-6-carbonitrile(S71).



Compound **S71** was prepared fromcompound **S70** (600mg, 2.8 mmol) by method P. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 9/1). Final product **S71** was obtained as pale yellow powder (380mg, 84%). M.p. = 41 – 42 °C (lit.[33] m.p. 41.5-42 °C (acetone/ligroin)). IR (ATR): 3818w, 3541w, 3415w, 3102m, 2971w, 2782w, 2621w, 2275w, 2225s, 2173w, 1907w, 1774w, 1647w, 1594m, 1550w, 1484w, 1454m, 1391m, 1344m, 1311m, 1259m, 1192m, 1137w, 1084m, 1049w, 959w, 893m, 825s, 777m, 760m, 702m, 633w, 604m, 510w, 485w, 455, 406w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.22-8.20 (m, H-C(7)), 7.90 (d, J = 7.9, H-C(4)), 7.72 (d, J = 5.5, H-C(3)), 7.59 (dd, J_1 = 1.2, J_2 = 8.2, H-C(5)), 7.43-7.41 (m, H-C(2)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 142.40, 139.58, 131.20, 127.27, 126.81, 124.30, 123.94, 119.27, 107.56. GC/MS (*m/z,%)*: 159.0 ([M^+], 100).

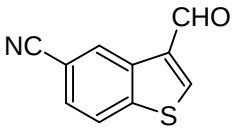


5-fluoro-1-benzothiophene-2-carbaldehyde(S72).



Alcohol**S59** (300 mg, 1.6 mmol) was dissolved in DCM (30 mL) and MnO_2 (1.40 g, 16 mmol) was added. Resulting mixture was stirred at room temperature for 1 h. The mixture was filtrated through Celite, solvent was removed under reduced pressure and product **S72** was used in the next step without further purification. **S72** was obtained as white powder (240mg, 82%). M.p. = 117 – 119 ºC (lit.[27] m.p. 122 ºC (EtOH)). IR (ATR): 3449s, 3101w, 3065w, 2921w, 2850w, 2793w, 1886w, 1671s, 1566w, 1518w, 1440w, 1383w, 1330w, 1282w, 1247w, 1167m, 1115w, 952w, 868w, 808w, 718w, 657w, 597w, 489w, 418w, 403w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 10.11 (s, 1H, C*H*O), 7.99 (s, H-C(3)), 7.85 (dd, J_1 = 4.8, J_2 = 9.0, H-C(7)), 7.60 (dd, J_1 = 2.5, J_2 = 8.9, H-C(4)), 7.28 (td, J_1= 2.5, J_2 = 8.7, H-C(6)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 184.46, 161.01 (d, J = 242.5), 145.52, 139.41, 138.16, 133.47 (d, J = 5.0), 124. 68 (d, J = 8.8), 117.40 (d, J = 25.0), 111.20 (d, J = 22.5). GC/MS (*m/z,%)*: 180.0 ([M^+], 100), 179 (91), 151 (20), 107 (48).

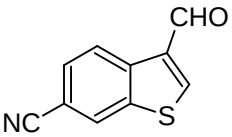
3-formyl-1-benzothiophene-5-carbonitrile(S73).



Compound **S73** was prepared fromcompound **S69** (393 mg, 2.47 mmol) by method O. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 3/7). Final product **S73** was obtained as white powder (331 mg, 72%). M.p. = 107–108 °C. IR (ATR): 3824w, 3317w, 3084s, 2931w, 2838m, 2744w, 2358w, 2228s, 1907w, 1810w, 1676s, 1597w, 1545w, 1507m, 1437s, 1387w, 1352w, 1305w, 1259w, 1168m, 1099m, 1041m, 906w, 885w, 861w, 812m, 736w, 715w, 695w, 637w, 512w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 10.16 (s, 1H, C*H*O),

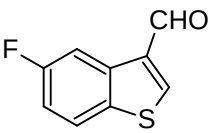
9.05 (s, H-C(2)), 8.47 (s, H-C(4)), 8.00 (d, J = 8.5, H-C(7)), 7.70-7.67 (m, H-C(6)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 184.86, 144.65, 144.14, 135.91, 135.11, 129.62, 128.27, 123.43, 118.74, 110.18. GC/MS (*m/z,%)*: 187.0 ([M^+], 76), 186.0 (100), 158.0 (20), 114.0 (40).

3-formyl-1-benzothiophene-6-carbonitrile(S74).



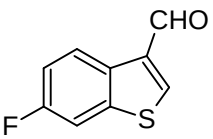
Compound **S74** was prepared from compound **S71** (120mg, 0.75 mmol) by method O. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 3/7). Final product **S74** was obtained as a white powder (68 mg, 48%). M.p. = 129 – 132 °C. IR (ATR): 3821w, 3417w, 3325w, 3096m, 3066m, 2838w, 2750w, 2222m, 1932w, 1797w, 1666s, 1595w, 1494m, 1458w, 1396m, 1263w, 1191w, 1142m, 1098m, 1044w, 1007w, 902w, 839m, 719w, 650w, 614w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$+CD_3OD, δ): 10.00 (s, 1H, C*H*O), 8.63 (d, J = 8.4, H-C(4)), 7.56 (s, H-C(2)), 8.14-8.13 (m, H-C(7)), 7.61 (dd, J_1 = 1.4, J_2 = 8.4, H-C(5)). ^{13}C NMR (125 MHz, $CDCl_3$+CD_3OD, δ): 185.36, 147.02, 140.15, 137.98, 135.66, 128.50, 126.99, 125.31, 118.30, 109.13. GC/MS (*m/z,%)*: 187.0 ([M^+], 76), 186.0 (100), 158.0 (20), 114.0 (40).

5-fluoro-1-benzothiophene-3-carbaldehyde(S75).



Compound **S75** was prepared from compound **S67** (300mg, 2.0 mmol) by method O. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 9/1). Final product **S75**was obtained as white powder (290 mg, 81%). M.p. = 111 – 112 °C (lit.[34] m.p. 111-113 °C (50 % EtOH)). IR (ATR): 3324w, 3168w, 3089m, 2954w, 2888w, 2832w, 2806w, 2740w, 1670s, 1628w, 1600m, 1568m, 1502m, 1449m, 1433m, 1385m, 1348w, 1312w, 1286w, 1250m, 1196m, 1144m, 1090w, 1040w, 912m, 866m, 798m, 737w, 716w, 641w, 626w, 535w, 472w cm^{-1}. $^{1\,h}$ NMR (500 MHz, $CDCl_3$, δ): 10.11 (s, 1 h, C*H*O), 8.41-8.36 (m, H-C(2) and H-C(4)), 7.82 (dd, J_1 = 4.8, J_2 = 9.0, H-C(7)), 7.23 (td, J_1 = 2.3, J_2 = 8.5, H-C(6)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 185.06, 161.60 (d, J = 242.5), 144.89, 136.38 (d, J = 10.0), 136.14 (d, J = 5.0), 135.72, 123.48 (d, J = 123.48), 115.14 (d, J = 26.2), 110.80 (d, J = 23.8). GC/MS (*m/z,%)*: 180.0 ([M^+], 96), 180.0 (100), 151.0 (21), 107.0 (49).

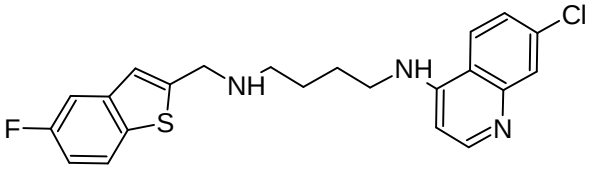
6-fluoro-1-benzothiophene-3-carbaldehyde (S76). Compound **S76** was prepared from



compound **S66** (350mg, 2.3 mmol) by method O. The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex → Hex/EtOAc = 95/5. Final product **S76** was obtained as white powder (160mg, 39%). M.p. = 92 – 96 °C. IR (ATR): 3319w, 3110m, 3073w, 2991w, 2843w, 2745w, 1667s, 1622m, 1601m, 1570m, 1498m, 1470m, 1388m, 1323w, 1242m, 1207m, 1152w, 1129m, 1085w, 1039w, 896m, 858m, 827m, 715m, 676w, 445w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 10.11 (s, 1H, C*H*O), 8.68-8.63 (m, H-C(4)), 8.28 (s, H-C(2)), 7.58-7.55 (m, H-C(7)), 7.27 (td, J_1 =

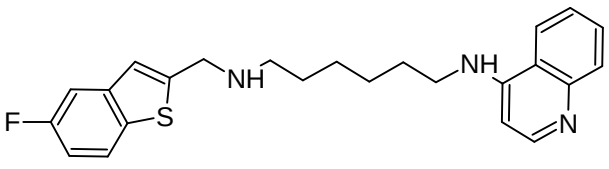
2.5, J_2 = 8.9, H-C(5)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 185.15, 161.24 (d, J = 245.0), 142.73, 141.37 (d, J = 10.0), 135.95, 131.64, 126.08 (d, J = 8.8), 115.11 (d, J = 22.5), 108.57 (d, J = 25.0). GC/MS (*m/z,%)*: 180.0 ([M^+], 96), 180.0 (100), 151.0 (24), 107.0 (48).

_N_-(7-chloroquinolin-4-yl)-_N_'-[(5-fluoro-1-benzothiophen-2-yl)methyl]butane-1,4-diamine(52).



Compound **52**was prepared fromaldehyde **S72** (97.4 mg, 0.540 mmol) by method E, using amine **AQ4** (202 mg, 0.811 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2). Final product **52** was obtained as pale yellow powder (128 mg, 58%). M.p. = 105 – 106 ºC. IR (ATR): 3232m, 3062m, 2934m, 2862m, 1582s, 1545m, 1448m, 1366m, 1332w, 1279w, 1250w, 1204w, 1137w, 1083w, 952w, 900w, 864m, 802m, 765w, 675w, 639w cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD, δ): 8.30 (d, J = 5.7, H-C(2')), 8.07 (d, J = 9.2, H-C(5')), 7.77-7.72 (m, 2H-Ar), 7.40-7.34 (m, 2H-Ar), 7.18 (s, H-C(3)), 7.05 (td, J_1 = 2.5, J_2 = 8.9, H-C(6)), 6.48 (d, J = 5.7, H-C(3')), 4.05-4.03 (m, 2H, -CH_2NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.38-3.34 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$CH_2NH-), 2.71 (t, 2H, J = 7.2, -CH$_2$NHCH_2CH$_2$CH$_2$CH$_2$NH-), 1.79 (quin, 2H, J = 7.3, -CH$_2$NHCH$_2$CH$_2$CH_2CH$_2$NH-), 1.72-1.65 (m, 2H, -CH$_2$NHCH$_2$CH_2CH$_2$CH$_2$NH-). ^{13}C NMR (125 MHz, CD_3OD, δ): 152.50 (d, J = 91.2), 152.14, 149.39, 148.07, 142.35, 136.52 (d, J = 25.3), 136.42, 127.35, 125.99, 124.58 (d, J = 10.0), 124.35, 123.10 (d, J = 3.8), 118.72, 113.54 (d, J = 26.2), 109.51 (d, J = 23.8), 99.63, 43.81, 27.96, 27.07. HRMS: *m/z* 414.12065 corresponds to molecular formula $C_{22}H_{21}ClN_3SFH^+$ (error in ppm 1.20). HPLC purity (λ = 330 nm): method A: RT 7.750 min, area 96.09%; method B: RT 7.897 min, area 96.80%.

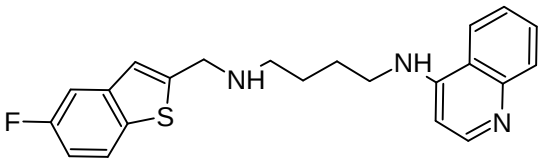
_N_-(7-chloroquinolin-4-yl)-_N_'-[(5-fluoro-1-benzothien-2-yl)methyl]hexane-1,6-diamine(67).



Compound **67** was prepared fromaldehyde **S72** (73.5 mg, 0.408 mmol) by method E, using amine **AQ6** (169 mg, 0.608 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2 and flash, Biotage SP1, NH column, eluent EtOAc/Hex gradient 8/2 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH). Final product **67** was obtained as white powder (106 mg, 59%). M.p. = 71–74 ºC. IR (ATR): 3226m, 3108m, 3066m, 3011m, 2929m, 2888m, 2855m, 2832m, 2774w, 1733w, 1700w, 1652w, 1581s, 1546m, 1492w, 1472m, 1443s, 1370m, 1331w, 1298w, 1255w, 1208m, 1166w, 1130m, 1085w, 1028w, 974w, 952w,

906w, 884w, 863m, 808m, 777w, 757w, 736w, 680w, 647w, 600w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.54-8.51 (m, H-C(2')), 7.97-7.95 (m, H-C(8')), 7.71-7.66 (m, H-C(7)), 7.65-7.62 (m, H-C(5')), 7.36-7.31 (m, H-C(4) and H-C(6')), 7.09 (s, H-C(3)), 7.03 (td, J_1 = 2.4, J_2 = 8.8, H-C(6)), 6.40 (d, J = 5.5, H-C(3')), 4.98 (bs, H-N exchangeable with D_2O), 4.06 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.33-3.26 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$NH-), 2.70 (t, 2H, J = 7.0, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH-), 1.80-1.65 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$NH- and H-N exchangeable with D_2O), 1.60-1.52 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH-), 1.50-1.40 (m, 4H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$C*H*$_2$CH$_2$CH$_2$NH-). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.78 (d, J = 239.2), 152.02, 149.66, 149.07, 148.46, 140.74 (d, J = 9.0), 134.87, 134.84, 128.81, 125.26, 123.36 (d, J = 9.9), 120.72 (d, J = 9.0), 117.06, 112.50 (d, J = 25.3), 108.54 (d, J = 23.5), 99.05, 49.20, 49.02, 43.17, 29.91, 28.81, 26.96. HRMS: *m/z* 442.15060 corresponds to molecular formula $C_{24}H_{25}ClN_3SFH^+$ (error in ppm -1.93). HPLC purity (λ = 330 nm): method A: RT 9.345 min, area 99.36%; method B: RT 8.823 min, area 99.17%.

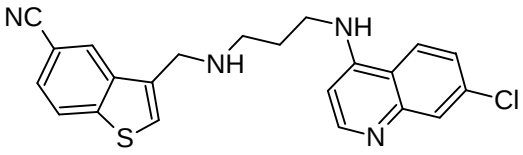
***N*-[(5-fluoro-1-benzothiophen-2-yl)methyl]-*N*'-(quinolin-4-yl)butane-1,4-diamine (54).**



Compound **54**was prepared fromaldehyde **S72** (90.0 mg, 0.499 mmol) by method E, using amine **AQ8** (161 mg, 0.749 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2 and flash, Biotage SP1, SiO_2 column, eluent EtOAc/MeOH+NH_3(9/1) gradient 95/5 → 3/7). Final product **54** was obtained as pale yellow oil (101 mg, 54%). IR (ATR): 3435w, 3266m, 3117w, 3063m, 3012w, 2933m, 2858m, 1580s, 1541m, 1495w, 1443m, 1396w, 1374w, 1341m, 1282w, 1255w, 1223w, 1206w, 1152w, 1128m, 952w, 864w, 803w, 764w, 737w, 689w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.54 (d, J = 5.5, H-C(2')), 7.97 (d, J = 8.5, H-C(8')), 7.74 (d, J = 8.5, H-C(5')), 7.69 (dd, J_1 = 4.8, J_2 = 8.8, H-C(7)), 7.63-7.57 (m, H-C(7')), 7.37-7.33 (m, H-C(4) and H-C(6')), 7.10 (s, H-C(3)), 7.04 (td, J_1 = 2.5, J_2 = 8.8, H-C(6)), 6.40 (d, J = 5.5, H-C(3')), 5.48 (bs, H-N exchangeable with D_2O), 4.09 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.36-3.31 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$C*H*$_2$NH-), 2.78 (t, 2H, J = 6.8, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$CH$_2$NH-), 1.91-1.67 (m, 4H, -CH$_2$NHCH$_2$C*H*$_2$C*H*$_2$CH$_2$NH- and H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.82 (d, J = 239.2), 151.03, 149.74, 148.38, 147.99, 140.71 (d, J = 9.9), 134.87, 129.89, 128.92, 124.46, 123.41 (d, J = 9.0), 120.91 (d, J = 4.5), 119.38, 118.75, 112.62 (d, J = 25.3), 108.61 (d, J = 22.6), 98.67, 49.16, 48.51, 43.15, 27.66, 26.38. HRMS: *m/z* 380.15894 corresponds to molecular formula

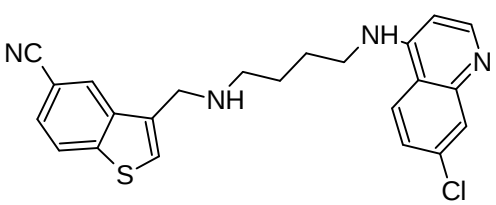
$C_{22}H_{22}N_3SFH^+$ (error in ppm -0.48). HPLC purity (λ = 330 nm): method A: RT 8.950 min, area 97.85%; method B: RT 7.746 min, area 97.41%.

3-[({3-[(7-chloroquinolin-4-yl)amino]propyl}amino)methyl]-1-benzothiophene-5-carbonitrile(60).



Compound **60** was prepared fromaldehyde **s73** (79.6 mg, 0.425 mmol) by method E, using amine **AQ3** (151 mg, 0.630 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2). Final product **59** was obtained as white powder (124 mg, 72%). M.p. = 129 – 130 ºC. IR (ATR): 3215m, 3061m, 3013m, 2965m, 2838m, 2225m, 1581s, 1439m, 1367m, 1282w, 1261w, 1235w, 1137m, 1079w, 897w, 851w, 801w, 768w, 735w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.49 (d, *J* = 5.2, H-C(2')), 8.14-8.12 (m, H-C(4)), 7.95 (d, *J* = 8.2, H-C(7)), 7.88 (d, *J* = 2.2, H-C(8')), 7.53 (dd, J_1 = 1.6, J_2 = 8.2, H-C(6)), 7.49 (s, H-C(2)), 7.35 (d, *J* = 8.8, H-C(5')), 7.00 (dd, J_1 = 2.2, J_2 = 8.8, H-C(6')), 6.82 (s, H-N exchangeable with D_2O), 6.32 (d, *J* = 5.2, H-C(3')), 4.10 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$NH-), 3.45-3.39 (m, 2H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$NH-), 3.05-3.01 (m, 2H, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$NH-), 2.02-1.95 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$NH-), 1.82 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.07, 150.04, 149.03, 144.77, 138.13, 134.84, 134.50, 128.56, 126.43, 126.36, 125.80, 124.74, 123.90, 121.38, 119.19, 117.28, 107.95, 98.55, 49.06, 47.41, 43.26, 27.79. HRMS: *m/z* 407.10826 corresponds to molecular formula $C_{22}H_{19}ClN_4SH^+$ (error in ppm -2.23). HPLC purity (λ = 330 nm) method A: RT 8.036 min, area 98.36%; (λ = 254 nm) method C: RT 5.223 min, area 97.09%.

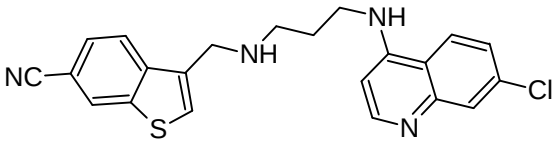
3-[({4-[(7-chloroquinolin-4-yl)amino]butyl}amino)methyl]-1-benzothiophene-5-carbonitrile(64).



Compound **64** was prepared fromaldehyde **S73** (118 mg, 0.630 mmol) by method E, using amine **AQ4** (236 mg, 0.945 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2 and flash, Biotage SP1, NH column, eluent EtOAc/Hex gradient 8/2 → EtOAc, EtOAc/MeOH gradient 95/5 → MeOH). Final product **64** was obtained as white powder (137 mg, 52%). M.p. = 112 – 113 ºC. IR (ATR): 3309m, 3270w, 3106w, 3054w, 3005m, 2972w, 2944m, 2875m, 2840w, 2227m, 1613w, 1579s, 1545m, 1455w, 1432w, 1367w, 1332w, 1308w, 1277w, 1240w, 1203w, 1140w, 1108w, 1085w, 1047w, 925w, 895w, 865w, 846w, 803m, 761w, 743w, 677w, 627w, 602w, 567w, 542w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$ + CD_3OD, δ): 8.54-8.50 (m, H-

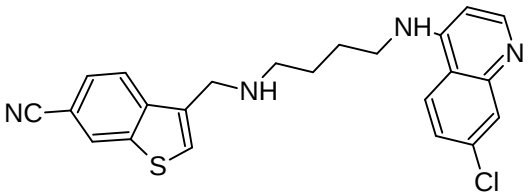
C(2')), 8.22 (s, H-C(8')), 7.95-7.91 (m, H-C(7) and H-C(5')), 7.62-7.58 (m, H-C(4)), 7.56-7.52 (m, H-C(6')), 7.45 (bs, H-C(2)), 7.25-7.20 (m, H-C(5)), 6.38 (d, *J* = 5.4, H-C(3')), 5.44 (bs, H-N exchangeable with D_2O), 4.07 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.35-3.30 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$C*H*$_2$NH-), 2.82 (t, 2H, *J* = 6.8, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$CH$_2$NH-), 1.89 (quin, 2H, *J* = 6.8, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$CH$_2$NH-), 1.74 (quin, 2H, *J* = 6.9, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$CH$_2$NH-), 1.60 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD, δ): 151.14, 150.49, 148.18, 144.82, 138.05, 135.08, 134.46, 127.20, 126.38, 126.20, 125.83, 125.06, 123.78, 121.68, 119.28, 117.05, 107.41, 98.48, 46.91, 42.72, 27.18, 26.01. HRMS: *m/z* 421.12435 corresponds to molecular formula $C_{23}H_{21}ClN_4SH^+$ (error in ppm -1.11). HPLC purity (λ = 330 nm): method A: RT 8.920 min, area 99.20%; method B: RT 8.539 min, area 96.73%.

3-[({3-[(7-chloroquinolin-4-yl)amino]propyl}amino)methyl]-1-benzothiophene-6-carbonitrile(61).



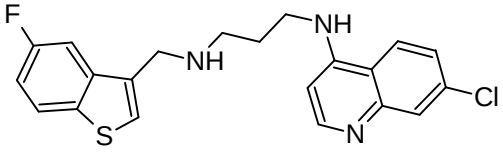
Compound **61** was prepared fromaldehyde **S74** (58.5 mg, 0.312 mmol) by method E, using amine **AQ3** (111 mg, 0.469 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 75/25, flash, Biotage SP1, NH column, eluent EtOAc/Hex 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 → 1/1). Final product **61** was obtained as white powder (70.3 mg, 55%). M.p. = 48 – 50 ºC. IR (film): 3256m, 3058m, 2945m, 2849m, 2226s, 1916w, 1610s, 1581s, 1537s, 1454s, 1367, 1331m, 1281m, 1264m, 1242m, 1199m, 1169w, 1139m, 1078w, 1052w, 899m, 878m, 851m, 818s, 766m, 736s, 702m, 646w, 606w, 503w, 458w, 432w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.51-8.48 (m, H-C(2')), 8.22-8.19 (m, H-C(8')), 7.92-7.89 (m, H-C(7)), 7.86 (d, *J* = 8.4, H-C(5')), 7.61 (s, H-C(2)), 7.51-7.47 (m, H-C(6')), 7.36-7.32 (m, H-C(4)), 7.00-6.90 (m, H-C(5) and H-N exchangeable with D_2O), 6.32 (d, *J* = 5.5, H-C(3')), 4.12 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$NH-), 3.45-3.40 (m, 2H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$NH-), 3.05-3.02 (m, 2H, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$NH-), 2.02-1.96 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$NH-), 1.77 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.04, 141.01, 140.55, 134.97, 128.07, 127.62, 126.84, 124.79, 122.37, 121.46, 118.98, 117.26, 107.98, 98.48, 49.22, 47.42, 43.50, 27.70. HRMS: *m/z* 407.10922 corresponds to molecular formula $C_{22}H_{19}ClN_4SH^+$ (error in ppm 0.13). HPLC purity (λ = 330 nm): method A: RT 8.763 min, area 96.57%; method B: RT 7.719 min, area 97.71%.

3-[({4-[(7-chloroquinolin-4-yl)amino]butyl}amino)methyl]-1-benzothiophene-6-carbonitrile(65).



Compound **65** was prepared fromaldehyde **S74** (62.7 mg, 0.335 mmol) by method E, using amine **AQ4** (125 mg, 0.502 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent Hex/EtOAc gradient 1/1 → EtOAc, EtOAc/MeOH gradient 95/5 → 8/2). Final product **65** was obtained as white powder (88.2 mg, 65%). M.p. = 62 – 65 ºC. IR (ATR): 3296m, 3125m, 3052m, 2938s, 2863m, 2821m, 2222m, 1611m, 1580s, 1538m, 1455m, 1371m, 1326m, 1282w, 1256w, 1199w, 1139w, 1080w, 1022m, 907w, 874w, 855w, 823m, 800m, 606w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.53-8.50 (m, H-C(2')), 8.19-8.17 (m, H-C(7)), 7.95-7.89 (m, H-C(7) and H-C(5')), 7.61-7.56 (m, H-C(2) and H-C(6') and H-C(4)), 7.22-7.19 (m, H-C(5)), 6.38 (d, J = 5.5, H-C(3')), 5.48 (bs, H-N exchangeable with D_2O), 4.09-4.06 (m, 2H, -CH_2NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.35-3.30 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$CH_2NH-), 2.81 (t, 2H, J = 6.8, -CH$_2$NHCH_2CH$_2$CH$_2$CH$_2$NH-), 1.88 (quin, 2H, J = 6.8, -CH$_2$NHCH$_2$CH$_2$CH_2CH$_2$NH-), 1.73 (quin, 2H, J = 6.9, -CH$_2$NHCH$_2$CH_2CH$_2$CH$_2$NH-), 1.64 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 152.03, 141.16, 140.60, 135.44, 134.81, 128.79, 127.72, 127.57, 126.71, 125.12, 122.63, 120.89, 119.18, 117.13, 107.79, 98.97, 49.14, 47.53, 43.14, 27.70, 26.45. HRMS: *m/z* 421.12558 corresponds to molecular formula $C_{23}H_{21}ClN_4SH^+$ (error in ppm 1.81). HPLC purity (λ = 330 nm) method A: RT 10.621 min, area 98.74%; (λ = 254 nm) method B: RT 7.777 min, area 95.86%.

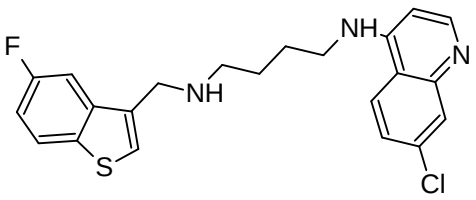
***N*-(7-chloroquinolin-4-yl)-*N*'-[(5-fluoro-1-benzothiophen-3-yl)methyl]propane-1,3-diamine(58).**



Compound **58** was prepared fromaldehyde **S75** (181 mg, 1.00 mmol) by method E, using amine **AQ3** (353 mg, 1.50mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → 4/6, flash, Biotage SP1, NH column, eluent EtOAc/Hex 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 → 7/3). Final product **58** was obtained as a white powder (269 mg, 67%). M.p. = 133 – 134 ºC. IR (ATR): 3240m, 3060w, 2953w, 2852w, 1607m, 1579s, 1535m, 1435m, 1360w, 1329m, 1279w, 1251w, 1230w, 1205w, 1137w, 1104w, 1082w, 913w, 850w, 800w, 761w, 718w, 665w, 642w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.50-8.47 (m, H-C(2')), 7.90-7.88 (m, H-C(8')), 7.83 (dd, J_1 = 4.8, J_2 = 8.9, H-C(7)), 7.46 (dd, J_1 = 2.4, J_2 = 9.5, H-C(4)), 7.43

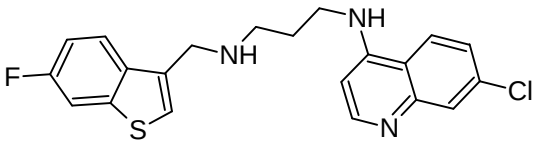
(s, H-C(2)), 7.35 (d, *J* = 9.0, H-C(5')), 7.17-7.09 (m, H-C(6) and H-N exchangeable with D_2O), 7.01-6.97 (m, H-C(6')), 6.32 (d, *J* = 5.5, H-C(3')), 4.06 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$NH-), 3.45-3.40 (m, 2H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$NH-), 3.06-3.02 (m, 2H, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$NH-), 2.01-1.94 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$NH-), 1.69 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.88 (d, *J* = 240.1), 152.04, 150.24, 149.05, 139.37 (d, *J* = 9.0), 135.98, 134.48 (d, *J* = 22.5), 128.48, 125.89, 124.81, 124.17 (d, *J* = 9.9), 121.61, 117.36, 113.51 (d, *J* = 25.3), 107.28 (d, *J* = 22.5), 98.39, 49.36, 47.64, 43.68, 27.60. HRMS: *m/z* 400.10388 corresponds corresponds to molecular formula $C_{21}H_{19}ClFN_3SH^+$ (error in ppm -1.56). Anal. ($C_{21}H_{19}ClFN_3S$) Calcd: C, 63.07; H, 4.79; N, 10.51; S, 8.02. Found: C, 63.09; H, 4.77; N, 10.30; S, 7.72. HPLC purity (λ = 330 nm): method A: RT 8.998 min, area 98.73%; method B: RT 8.544 min, area 99.17%.

_N_-(7-chloroquinolin-4-yl)-_N'_-[(5-fluoro-1-benzothiophen-3-yl)methyl]butane-1,4-diamine(63).



Compound **63** was prepared fromaldehyde **S75** (181 mg, 1.00 mmol) by method E, using amine **AQ4** (376 mg, 1.51 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → 1/1, flash, Biotage SP1, NH column, eluent EtOAc/Hex 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 → 1/1). Final product **63** was obtained as a white powder (251 mg, 60%). M.p. = 110 – 113 ºC. IR (ATR): 3228m, 3063w, 2945w, 2855w, 2810w, 1579s, 1543m, 1490w, 1433m, 1366w, 1330w, 1279w, 1245w, 1225w, 1196w, 1161w, 1134w, 1078w, 954w, 898w, 854w, 806w, 782w, 640w, 619w, 543w, 483w, 452w, 423w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.50 (d, *J* = 5.2, H-C(2')), 7.94-7.91 (m, H-C(8')), 7.77 (dd, J_1 = 4.8, J_2 = 8.7, H-C(7)), 7.59 (d, *J* = 8.9, H-C(5')), 7.51-7.46 (m, H-C(4)), 7.38 (s, H-C(2)), 7.18-7.14 (m, H-C(6')), 7.10 (td, J_1 = 2.4, J_2 = 8.8, H-C(6)), 6.36 (d, *J* = 5.3, H-C(3')), 5.65 (bs, H-N exchangeable with D_2O), 4.00 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$CH$_2$NH-), 3.32-3.27 (m, 2H, -CH$_2$NHCH$_2$CH$_2$CH$_2$C*H*$_2$NH-), 2.80 (t, *J* = 6.6, 2H, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$CH$_2$NH-), 1.88 (quin, 2H, *J* = 6.8, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$CH$_2$NH-), 1.75-1.55 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$CH$_2$NH- and H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.74 (d, *J* = 240.1), 152.01, 149.82, 149.08, 139.46 (d, *J* = 9.0), 135.97, 134.81, 134.74 (d, J = 9.0), 128.68, 125.43, 125.02, 123.98 (d, *J* = 9.0), 121.05, 117.18, 113.29 (d, *J* = 24.4), 107.47 (d, *J* = 22.6), 98.91, 48.99, 47.67, 43.14, 27.69, 26.40. HRMS: *m/z* 414.11939 corresponds to molecular formula $C_{22}H_{21}ClFN_3SH^+$ (error in ppm -1.85). HPLC purity (λ = 330 nm) method A: RT 9.136 min, area 99.72%; (λ = 254 nm) method B: RT 7.522 min, area 95.22%.

***N*-(7-chloroquinolin-4-yl)-*N*'-[(6-fluoro-1-benzothiophen-3-yl)methyl]propane-1,3-diamine(59).**



Compound **59** was prepared fromaldehyde **S76** (161 mg, 0.888 mmol) by method E, using amine **AQ3** (314 mg, 1.33 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/Hex gradient 1/9 → EtOAc, EtOAc/MeOH gradient 95/5 → 4/6, flash, Biotage SP1, NH column, eluent EtOAc/Hex 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 → 3/7). Final product **59** was obtained as a white powder (194 mg, 54%). M.p. = 149 – 150 ºC. IR (ATR): 3433w, 3294m, 3210m, 3067m, 3015m, 2927m, 2853m, 1606m, 1581s, 1539m, 1466m, 1430w, 1369w, 1330w, 1282w, 1251w, 1208w, 1168w, 1139w, 1109w, 1080w, 896w, 854w, 807w, 761w, 737w, 683w, 646w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.50-8.47 (m, H-C(2')), 7.90 (bs, H-C(8')), 7.74-7.70 (m, H-C(4)), 7.60-7.56 (m, H-C(7)), 7.37-7.33 (m, H-C(5')), 7.30 (s, H-C(2)), 7.22 (bs, H-N exchangeable with D_2O), 7.07-7.01 (m, H-C(5)), 7.00-6.96 (m, H-C(6')), 6.31 (d, *J* = 5.2, H-C(3')), 4.08 (s, 2H, -C*H*$_2$NHCH$_2$CH$_2$CH$_2$NH-), 3.45-3.40 (m, 2H, -CH$_2$NHCH$_2$CH$_2$C*H*$_2$NH-), 3.06-3.03 (m, 2H, -CH$_2$NHC*H*$_2$CH$_2$CH$_2$NH-), 2.01-1.95 (m, 2H, -CH$_2$NHCH$_2$C*H*$_2$CH$_2$NH-), 1.76 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 160.70 (d, *J* = 243.7), 151.97, 150.31, 141.61 (d, *J* = 9.9), 134.71, 134.12, 128.39, 124.83, 122.98, 122.46 (d, *J* = 10.0), 121.70, 117.33, 113.28 (d, *J* = 23.5), 109.07 (d, *J* = 25.3), 98.36, 49.37, 47.69, 43.75, 27.52. HRMS: *m/z* 400.10427 corresponds to molecular formula $C_{21}H_{19}ClFN_3SH^+$ (error in ppm -0.56). HPLC purity (λ = 330 nm) method A: RT 9.049 min, area 95.99%; (λ = 254 nm) method B: RT 7.455 min, area 97.07%.

***N*-(quinolin-4-yl)propane-1,3-diamine (AQ7).**

^1H NMR (500 MHz, CD_3OD, δ): 8.35 (d, *J* = 5.7, H-C(2)), 8.09-8.06 (m, H-C(8)), 7.77 (d,*J* = 8.0, H-C(5)), 7.64-7.60 (m, H-C(6)), 7.45-7.40 (m, H-C(5)), 6.52 (d, *J* = 5.5, H-C(3)), 3.43 (t, 2H, *J* = 7.1, ArNHC*H*$_2$-), 2.80 (t, 2H, *J* = 6.9, ArNHCH$_2$CH$_2$C*H*$_2$-), 1.90 (quin, 2H, *J* = 7.1, ArNHCH$_2$C*H*$_2$-).^{13}C NMR (125 MHz, CD_3OD, δ): 152.77, 151.41, 149.07, 130.57, 128.98, 125.72, 122.28, 120.46, 99.32, 41.81, 40.48, 32.40. HRMS: *m/z* 202.13373 corresponds to molecular formula $C_{12}H_{15}N_3H^+$ (error in ppm -0.73).

***N*-(quinolin-4-yl)butane-1,4-diamine (AQ8).**

^1H NMR (200 MHz, CD_3OD, δ): 8.31 (d, *J* = 14.0, H-C(2)),8.11-8.04 (m, H-C(8)),7.82-7.75 (m, H-C(5)),7.63-7.53 (m, H-C(6)),7.44-7.34 (m, H-C(5)),6.42 (d, *J* = 14.0, H-C(3)), 3.30 (t, 2H, *J* = 18.5, ArNHC*H*$_2$-), 2.65 (t, 2H, *J* = 16.8, ArNHCH$_2$CH$_2$CH$_2$C*H*$_2$-), 1.80-1.47 (m, 4H, ArNHCH$_2$C*H*$_2$C*H*$_2$-). ^{13}C NMR (50 MHz, CD_3OD, δ): 152.65, 151.30, 148.97, 130.46,

128.87, 125.56, 122.26, 120.33, 99.16, 43.81, 42.32, 31.39, 26.88.HRMS: *m/z* 216.14910 corresponds to molecular formula $C_{13}H_{17}N_3H^+$ (error in ppm -1.94).

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