Supporting Information

Overcoming Drug Resistance to Heme-Targeted Antimalarials by Systematic Side Chain Variation of 7-Chloro-4-aminoquinolines

Kim Yearick,[1] Kekeli Ekoue-Kovi,[1] D. Iwaniuk,[1] Jayakumar K. Natarajan,[1,2] John Alumasa,[1] Angel C. de Dios,[1,3] Paul D. Roepe,[1,2,3] * and Christian Wolf,[1,3] *

Dept. of Chemistry[1], Dept. of Biochemistry and Cellular and Molecular Biology[2], and Center for Infectious Diseases[3], Georgetown University

37th and O Streets, Washington, DC

Contents

1) Cell Culture and Antimalarial Activity Measurements

Drug activities were assessed and IC_{50} were quantified essentially as described previously.[22,23] The aminoquinolines were diluted using complete media under sterile conditions and plated in a 96 well plate format. Sorbitol synchronized cultures were utilized with >95% of the parasites at the ring stage. Cultures were diluted to give a working stock of 0.5% parasitemia and 2% hematocrit (final hematocrit 1% & 0.5%Parasitemia). The plates were incubated for 72 h at 37°C. After 72h, 50 µL of 10x SYBR green I dye was added to each well, and the plate was incubated for 1 h at 37°C. Fluorescence was measured at 530 nm (490 nm excitation) using a spectra geminiEM plate reader. Data analysis was performed using sigma plot 9.0 software after downloading data in Excel format. For each assay, each drug dilution was analyzed in triplicate, and the results from at least two separate assays were averaged in each case (S.D. < 10 % in each case). All drugs were all tested against two chloroquine sensitive, and two chloroquine resistant strains of *P. falciparum* (GCO3, HB3 and FCB, Dd2, respectively).

Table 1. Activity versus GCO3 and FCB (results for the two separate assays).

	Strain/Experimental[1] IC_{50} (nM)			
	Assay 1		**Assay 2**	
Compound	**GCO3**	**FCB**	**GCO3**	**FCB**
CQ	**16.6**	**167**	**15.3**	**172**
4a	106	146	130	146
4b	64.0	71.8	65.6	75.6
4c	107	188	172	190
4d	51.7	102	85.6	92.5
4e	112	263	145	168
5a	36.8	45.3	38.6	60.0
5b	22.4	48.3	32.7	49.8
5c	62.8	130	112	181
5d	50.0	65.4	60.3	68.2
5e	150	249	199	277
16a	51.0	128	30.2	97.8
17a	36.8	61.8	27.2	53.3
16b	28.5	118	23.7	101.1
17b	20.4	70.3	18.5	61.7

[1]The experimental IC_{50}´s were obtained from triplicate experiments.

Table 2. Activity versus HB3 and Dd2 (results for the two separate assays).

	Strain/Experimental[1] IC_{50} (nM)			
	Assay 1		Assay 2	
Compound	**HB3**	**Dd2**	**HB3**	**Dd2**
CQ	**13.3**	**128**	**13.6**	**151**
4a	25.7	108	32.6	150
4b	22.2	40.0	32.4	72.6
4c	61.7	137	83.3	202
4d	46.9	86.7	45.1	120
4e	73.7	239	91.9	299
5a	18.1	28.2	36.4	34.2
5b	15.5	27.0	26.8	29.1
5c	24.1	86.9	24.0	82.3
5d	12.3	47.7	19.1	39.1
5e	48.6	270	77.2	278
16a	29.7	73.0	22.9	87.0
17a	24.2	50.9	26.7	52.6
16b	34.5	73.3	21.0	78.9
17b	37.3	66.6	25.3	84.7

[1]The experimental IC_{50}´s were obtained from triplicate experiments.

Table 3. Activity versus HB3, Dd2, GCO3 and FCB (results for the two separate assays).

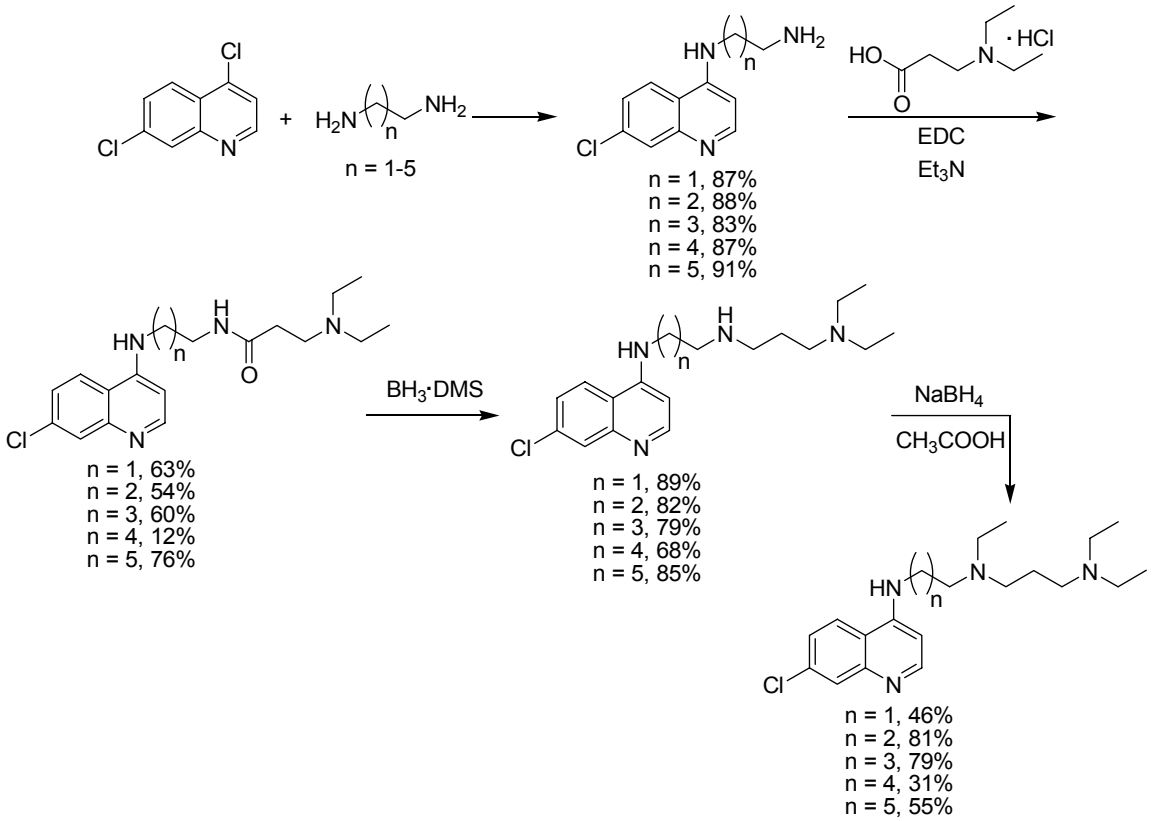
	Strain/Experimental[1] IC_{50} (nM)							
	Assay 1		Assay 2		Assay 1		Assay 2	
Compound	**HB3**	**Dd2**	**HB3**	**Dd2**	**GCO3**	**FCB**	**GCO3**	**FCB**
6a	188	104	185	151	73.2	156	120	216
6b	45.2	95.5	43.0	104	35.1	97.8	49.6	109.5
7a	717	781	714	982	372	805	662	1314
7b	1354	2720	1274	2379	1384	2268	1639	2181

[1]The experimental IC_{50}´s were obtained from triplicate experiments.

2) Synthetic Procedures and Product Characterization

General. All reagents and solvents were commercially available and used without further purification. Flash chromatography was performed on Kieselgel 60, particle size 0.032-0.063 mm. NMR spectra were obtained on a 300 MHz (^{1}H-NMR) and 75 MHz (^{13}C-NMR) Varian FT-NMR spectrometer using $CDCl_3$ as solvent unless indicated otherwise. Electrospray mass spectra (ESI-MS) were collected on a Thermo Finnigan LCQ instrument. Samples were dissolved in acetonitrile/water (1:1 v/v) containing 1% acetic acid (1 mg/mL) for MS analysis.

Scheme 1



Representative procedure for the synthesis of *N*-(7-chloro-4-quinolyl)-1,n-diaminoalkanes. A mixture of 4,7-dichloroquinoline (1.0 g, 5.1 mmol) and ethylenediamine (1.7 mL, 25.3 mmol) was heated to 110 °C for 6 h under inert atmosphere and then cooled to room temperature. Aqueous NaOH (1N, 10 mL) was then added and the mixture was extracted with CH_2Cl_2. The organic layers were washed with water, brine, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. *N*-(7-Chloro-4-quinolyl)-1,2-diaminoethane (1.04 g, 4.4 mmol, 87% yield) was obtained as pale yellow crystals and used without further purification.

***N*-(7-Chloro-4-quinolyl)-1,2-diaminoethane.** ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.26 (bs, 2H), 3.07-3.16 (m, 2H), 3.25-3.36 (m, 2H), 5.60-5.80 (m, 1H), 6.42 (d, J = 5.7 Hz, 1H),

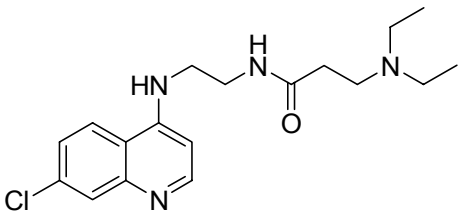
7.37 (dd, *J* = 2.4 Hz, 8.7 Hz, 1H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 2.4 Hz, 1H), 8.54 (d, *J* = 5.7 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 39.2, 44.9, 97.7, 116.6, 122.1, 123.3, 126.8, 133.1, 148.1, 149.5, 150.8.

***N*-(7-Chloro-4-quinolyl)-1,3-diaminopropane.** Employing 1.0 g (5.1 mmol) of 4,7-dichloroquinoline in the procedure described above gave 1.05 g (4.5 mmol, 88% yield) of pale yellow crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.48 (bs, 2H), 1.84-1.96 (m, 2H), 3.00-3.10 (m, 2H), 3.38-3.48 (m, 2H), 6.33 (d, *J* = 5.4 Hz, 1H), 7.30 (dd, *J* = 2.1 Hz, 9.0 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 2.1 Hz, 1H), 8.50 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 29.5, 40.8, 42.8, 97.8, 117.1, 122.0, 124.2, 127.6, 133.9, 148.6, 150.0, 151.5.

***N*-(7-Chloro-4-quinolyl)-1,4-diaminobutane.** Employing 2.0 g (10.1 mmol) of 4,7-dichloroquinoline in the procedure described above gave 2.09 g (8.4 mmol, 83% yield) of pale yellow crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.28 (bs, 2H), 1.56-1.68 (m, 2H), 1.76-1.90 (m, 2H), 2.79 (t, *J* = 6.6 Hz, 2H), 3.22-3.32 (m, 2H), 6.09 (bs, 1H), 6.34 (d, *J* = 5.4 Hz, 1H), 7.29 (dd, *J* = 2.7 Hz, 9.0 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.91 (d, *J* = 2.7 Hz, 1H), 8.49 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 25.9, 30.6, 41.4, 43.0, 98.6, 117.3, 121.6, 124.8, 128.3, 134.5, 149.0, 150.0, 151.9.

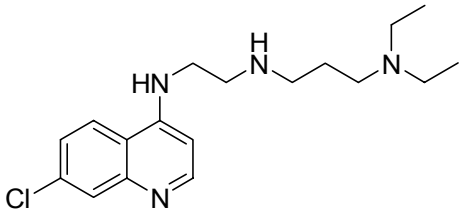
***N*-(7-Chloro-4-quinolyl)-1,5-diaminopentane.** Employing 1.0 g (5.1 mmol) of 4,7-dichloroquinoline in the procedure described above gave 1.16 g (4.4 mmol, 87% yield) of pale yellow crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.15 (bs, 2H), 1.40-1.60 (m, 4H), 1.66-1.86 (m, 2H), 2.71 (t, *J* = 6.6 Hz, 2H), 3.20-3.38 (m, 2H), 5.49 (t, *J* = 4.8 Hz, 1H), 6.36 (d, *J* = 5.4 Hz, 1H), 7.28 (dd, *J* = 2.1, 9.0 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 2.1 Hz, 1H), 8.50 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 24.3, 28.5, 33.1, 41.9, 43.0, 98.9, 117.0, 120.9, 125.0, 128.6, 134.6, 149.0, 149.6, 151.9.

***N*-(7-Chloro-4-quinolyl)-1,6-diaminohexane.** Employing 1.0 g (5.1 mmol) of 4,7-dichloroquinoline in the procedure described above gave 1.28 g (4.6 mmol, 91% yield) of pale yellow crystals. ^{1}H-NMR (300 MHz, DMSO-d_6) δ = 1.30-1.42 (m, 6H), 1.60-1.72 (m, 2H), 2.48-2.56 (m, 2H, overlapping with DMSO signal), 3.20-3.34 (m, 2H, overlapping with water signal), 6.46 (d, *J* = 5.4 Hz, 1H), 7.29 (t, *J* = 4.8 Hz, 1H), 7.44 (dd, *J* = 2.1 Hz, 9.0 Hz, 1H), 7.77 (d, *J* = 2.1 Hz, 1H), 8.27 (d, *J* = 9.0 Hz, 1H), 8.39 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, CD_3OD) δ = 27.7, 28.0, 29.3, 33.5, 42.3, 43.9, 99.5, 118.7, 120.2, 124.3, 125.8, 127.5, 136.2, 149.6, 152.3.

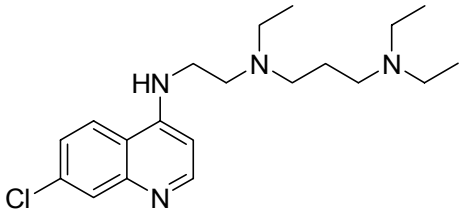


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,2-diaminoethane**. A mixture of *N*-(7-chloro-4-quinolyl)-1,2-diaminoethane (0.1 g, 0.45 mmol), *N,N*-diethylamino-3-propionic acid (0.11 g, 0.6 mmol), EDC (0.11 g, 0.6 mmol) and Et_3N

(0.19 mL, 1.35 mmol) in 4 mL of anhydrous DMF and $CHCl_3$ (1:1 v/v) was stirred at room temperature for 2 days. Saturated $NaHCO_3$ solution was added to the cooled reaction mixture, which was then extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Flash chromatography using EtOH:Et_3N (1:0.05 v/v) as the mobile phase afforded 0.10 g (0.44 mmol, 63% yield) of yellow crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.05 (t, *J* = 7.1 Hz, 6H), 2.48 (t, *J* = 6.1 Hz, 2H), 2.58 (q, *J* = 7.1 Hz, 4H), 2.69 (t, *J* = 6.1 Hz, 2H), 3.30-3.45 (m, 2H), 3.64-3.78 (m, 2H), 6.28 (d, *J* = 5.4 Hz,1H), 7.11 (bs, 1H), 7.40 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.94 (d, *J* = 2.1 Hz, 1H), 8.50 (d, *J* = 5.4 Hz, 1H), 9.51 (bs, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.6, 32.4, 38.4, 46.3, 46.5, 48.9, 98.2, 117.5, 122.7, 125.7, 128.2, 135.2, 148.9, 150.7, 151.8, 176.2; MS (ESI) m/z calcd for $C_{18}H_{25}ClN_4O$ 348.2. Found $(M + H)^+$: 349.1.

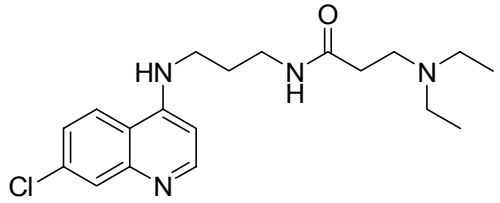


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,2-diaminoethane**. A solution of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,2-diaminoethane (0.08 g, 0.23 mmol) in 2 mL of THF was heated to reflux and borane-dimethyl sulfide complex (0.13 mL, 1.4 mmol) was added. After 14 h, 6M HCl (1 mL) was added and the mixture was heated to 100 ºC for 30 minutes. The clear solution was cooled to room temperature, basified with saturated NaOH and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography using EtOH:Et_3N (1:0.03 v/v) as the mobile phase gave a brown oil (0.07 g, 0.21 mmol, 89% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.03 (t, *J* = 7.1 Hz, 6H), 1.62-1.78 (m, 2H), 2.46-2.60 (m, 6H), 2.74 (t, *J* = 6.6 Hz, 2H), 3.01-3.19 (m, 2H), 3.30-3.41 (m, 2H), 5.98 (bs, 1H), 6.41 (d, *J* = 5.4 Hz, 1H), 7.38 (dd, *J* = 2.2 Hz, *J* = 9.0 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.97 (d, *J* = 2.2 Hz, 1H), 8.54 (d, *J* = 5.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.6, 26.9, 42.1, 47.1, 47.6, 48.5, 51.5, 99.2, 117.7, 122.0, 125.4, 128.7, 135.1, 149.3, 150.1, 152.2; MS (ESI) m/z calcd for $C_{18}H_{27}ClN_4$ 334.2. Found $(M + H)^+$: 335.2.

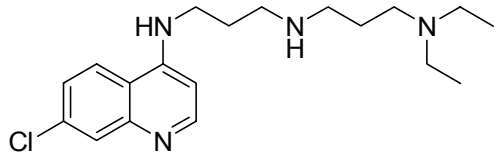


***N*-(7-Chloro-4-quinolyl)-*N′*-ethyl-*N′*-(3-diethylaminopropyl)-1,2-diaminoethane**. To a solution of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,2-diaminoethane (0.06 g, 0.18 mmol) in 1 mL of glacial acetic acid, $NaBH_4$ (0.16 g, 4.3 mmol) was added at 5 ^oC and the reaction temperature was increased to 50 ^oC. After 18 h, the reaction mixture was cooled, basified with saturated NaOH and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated *in vacuo*.

Purification by flash chromatography using EtOH:Et_3N (1:0.03 v/v) as the mobile phase gave a yellow oil (0.03 g, 0.08 mmol, 46% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.03 (t, *J* = 7.1 Hz, 6H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.63-1.82 (m, 2H), 2.43-2.74 (m, 10H), 2.85 (t, *J* = 5.8 Hz, 2H), 3.26-3.39 (m, 2H), 6.11 (bs, 1H), 6.40 (d, *J* = 5.3 Hz, 1H), 7.40 (dd, *J* = 2.1 Hz, *J* = 8.8 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 2.1 Hz, 1H), 8.55 (d, *J* = 5.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.3, 12.1, 24.8, 30.0, 40.0. 46.9, 47.2, 51.3, 51.4, 99.5, 117.7, 121.6, 125.4, 128.9, 135.0, 149.4, 150.2, 152.4; MS (ESI) m/z calcd for $C_{20}H_{31}ClN_4$ 362.2. Found $(M + H)^+$: 363.1.

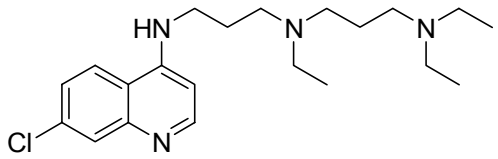


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,3-diaminopropane**. A mixture of *N*-(7-chloro-4-quinolyl)-1,3-diaminopropane (1.0 g, 4.24 mmol), *N,N*-diethylamino-3-propionic acid (0.78 g, 4.3 mmol), EDC (0.98 g, 5.1 mmol) and triethylamine (1.8 mL, 12.9 mmol) in 30 mL of anhydrous DMF and chloroform (1:1 v/v) was stirred at room temperature for 2.5 days. The reaction mixture was concentrated *in vacuo*, then dissolved in dichloromethane and extracted with aqueous NaOH. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography (1:1:0.05 ethanol:hexanes:triethylamine v/v) to give 0.83 g of (2.3 mmol, 54% yield) pale yellow crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.02 (t, *J* = 7.1 Hz, 6H), 1.74-1.83 (m, 2H), 2.41 (t, *J* = 5.7 Hz, 2H) , 2.53 (q, *J* = 7.1 Hz, 4H), 2.67 (t, *J* = 5.9 Hz, 2H), 3.32-3.43 (m, 4H), 6.37 (d, *J* = 5.6 Hz, 1H), 6.76 (t, *J* = 5.7 Hz, 1H), 7.36 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 2.1 Hz, 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 8.45 (d, *J* = 5.6 Hz, 1H), 9.04 (t, *J* = 5.7 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.8, 28.6, 32.7, 35.7, 39.2, 46.5, 49.2, 98.6, 117.9, 122.5, 125.7, 128.5, 135.4, 149.4, 150.5, 151.9, 174.8; MS (ESI) *m*/*z* calcd for $C_{19}H_{27}ClN_4O$ 362.2. Found $(M + H)^+$: 362.9.

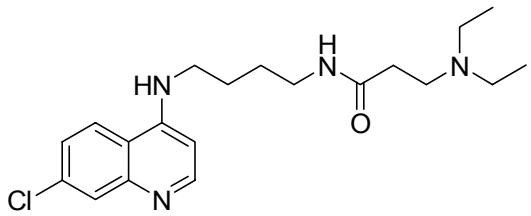


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,3-diaminopropane**. To *N*-(7-chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,3-diaminopropane (0.2 g, 0.55 mmol) in 9 mL of anhydrous DMF, borane-dimethyl sulfide complex (0.35 mL, 3.69 mmol) was added dropwise at 0 °C. The reaction mixture was heated to reflux for 2.5 h and then quenched with 1.6 mL of water. Concentrated HCl (1.0 mL) was added and the reaction was refluxed for another 1.5 h. The reaction mixture was cooled to room temperature, basified (pH > 10) with NaOH and extracted with chloroform. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give a yellow oil (0.16 g, 0.46 mmol, 82% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.01 (t, *J* = 7.1 Hz, 6H), 1.71-1.80 (m, 2H), 1.90-1.97(m, 2H) , 2.48-2.55 (m, 6H), 2.74 (t, *J* = 6.9 Hz, 2H),

2.89-2.93 (m, 2H), 3.37-3.42 (m, 2H), 6.30 (d, J = 5.6 Hz, 1H), 7.29 (dd, J = 2.2 Hz, J = 9.0 Hz, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.92 (d, J = 2.2 Hz, 1H), 8.50 (d, J = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.6, 25.1, 26.4, 42.2, 46.9, 49.6, 52.2, 53.7, 98.4, 117.9, 123.2, 125.2, 128.4, 135.0, 149.3, 150.7, 152.1; MS (ESI) *m*/*z* calcd for $C_{19}H_{29}ClN_4$ 348.2. Found $(M + H)^+$: 349.1.

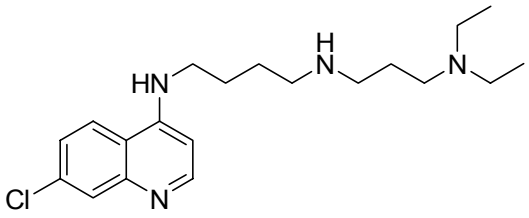


***N*-(7-Chloro-4-quinolyl)-*N′*-ethyl-*N′*-(3-diethylaminopropyl)-1,3-diaminopropane**. To a solution of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,3-diaminopropane (0.09 g, 0.24 mmol) in 4 mL of glacial acetic acid, sodium borohydride (0.24 g, 6.3 mmol) was added at 5 °C. The reaction was warmed to room temperature for 1 h and then heated to 60 °C for 30 h. After cooling to room temperature, the mixture was basified (pH > 10) with NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography (1.0:0.05 ethanol:triethylamine v/v) to give 0.075 g (0.12 mmol, 81% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.94 (t, J = 7.2 Hz, 6H), 1.11 (t, J = 7.2 Hz, 3H), 1.62-1.73 (m, 2H) , 1.88-1.98 (m, 2H), 2.38-2.48 (m, 6H), 2.56 (t, J = 7.7 Hz, 2H), 2.62-2.71 (m, 4H), 3.32-3.42 (m, 2H), 6.31 (d, J = 5.4 Hz, 1H), 7.32 (dd, J = 2.1 Hz, 8.8 Hz, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.86 (bs, 1H), 7.93 (d, J = 2.1 Hz, 1H), 8.50 (d, J = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.8, 24.7, 24.9, 44.9, 47.1, 48.1, 51.4, 52.3, 54.2, 98.6, 117.9, 122.3, 124.9, 128.9, 134.8, 149.5, 150.8, 152.5; MS (ESI) *m*/*z* calcd for $C_{21}H_{33}ClN_4$ 376.2. Found $(M + H)^+$: 376.9.

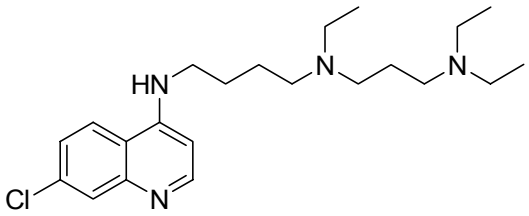


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,4-diaminobutane**. A mixture of *N*-(7-chloro-4-quinolyl)-1,4-diaminobutane (2.0 g, 8.0 mmol), *N,N*-diethylamino-3-propionic acid (1.45 g, 8.0 mmol), EDC (1.84 g, 9.6 mmol), and triethylamine (3.35 mL, 24.0 mmol) in 80 mL of anhydrous DMF and chloroform (1:1 v/v) was stirred at room temperature for 2.5 days. The reaction mixture was concentrated *in vacuo* and partitioned between dichloromethane and 1N NaOH solution. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography (0.5% ammonium hydroxide in MeOH) to give 1.8 g (4.8 mmol, 60% yield) of colorless crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.02 (t, J = 7.2 Hz, 6H), 1.60-1.88 (m, 4H), 2.36 (t, J = 6.0 Hz, 2H), 2.54 (q, J = 7.2 Hz, 4H), 2.65 (t, J = 6.0 Hz, 2H), 3.28-3.42 (m, 4H), 5.71 (bt, 1H), 6.38 (d, J = 5.7 Hz, 1H), 7.35 (dd, J = 2.4 Hz, J = 9.0 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H), 7.93 (d, J = 2.4 Hz, 1H), 8.51 (d, J = 5.7 Hz, 1H), 8.85 (bt, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.3, 25.2, 27.8, 32.3, 38.1, 42.9, 45.8,

48.6, 98.6, 117.3, 121.9, 124.7, 128.0, 134.4, 148.9, 150.0, 151.6, 173.1; MS (ESI) *m*/*z* calcd for $C_{20}H_{29}ClN_4O$ 376.2. Found $(M + H)^+$: 376.9.

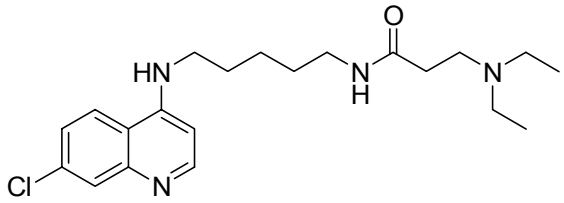


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,4-diaminobutane**. To a solution of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,4-diaminobutane (0.11 g, 0.29 mmol) in anhydrous THF, borane-dimethyl sulfide complex (0.15 mL, 1.59 mmol) was added dropwise at 0 °C. After stirring at 0 °C for 15 minutes, the reaction mixture was heated to reflux for 3 h, cooled to room temperature and carefully quenched with 1.0 mL of water. Concentrated HCl (0.4 mL) and 1.0 mL of water were then added and the mixture was heated to reflux for 1.5 h. After cooling to room temperature, the mixture was basified (pH > 10) with 5N NaOH and extracted with chloroform. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography on basic alumina (2% MeOH in CH_2Cl_2) to afford 0.084 g (0.23 mmol, 79% yield) of a light yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.01 (t, *J* = 7.2 Hz, 6H), 1.66-1.79 (m, 4H), 1.81-1.94 (m, 2H), 2.44-2.59 (m, 6H), 2.68-2.79 (m, 4H), 3.10-3.40 (m, 3H), 6.22 (bs, 1H), 6.36 (d, *J* = 5.4 Hz, 1H), 7.33 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 2.1 Hz, 1H), 8.50 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.6, 26.1, 27.0, 27.7, 43.0, 46.7, 48.9, 49.0, 51.3, 98.6, 98.7, 117.3, 121.5, 124.7, 128.3, 134.5, 149.0, 150.0, 151.8; MS (ESI) *m*/*z* calcd for $C_{20}H_{31}ClN_4$ 362.2. Found $(M + H)^+$: 362.9.

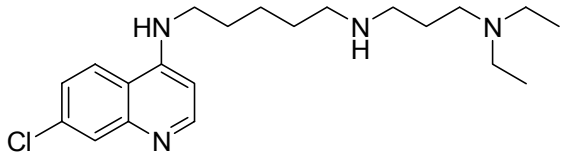


***N*-(7-Chloro-4-quinolyl)-*N′*-ethyl-*N′*-(3-diethylaminopropyl)-1,4-diaminobutane**. To *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,4-diaminobutane (0.14 g, 0.39 mmol) in 5 mL of glacial acetic acid, sodium borohydride (0.3 g, 7.8 mmol) was added portionwise at 0 °C. The reaction was stirred at room temperature for 1 h and then heated at 60 °C for 18 h. The reaction mixture was cooled to room temperature, basified (pH > 10) with 12N NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography on basic alumina (1% MeOH in CH_2Cl_2) to afford 0.12 g (0.31 mmol, 79% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.95-1.08 (m, 9H), 1.55-1.72 (m, 4H), 1.77-1.89 (m, 2H), 2.36-2.63 (m, 12H), 3.25-3.36 (m, 2H), 5.78 (bs, 1H), 6.39 (d, *J* = 5.4 Hz, 1H), 7.34 (dd, *J* = 2.1 Hz, *J* = 8.7 Hz, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.94 (d, *J* = 2.1 Hz, 1H), 8.52 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.1, 11.4, 24.1, 25.1, 26.6, 43.1, 46.7, 47.3, 50.9, 51.4, 52.7, 98.7, 98.8, 117.2,

121.4, 124.7, 128.4, 134.5, 149.0, 149.9, 151.9; MS (ESI) *m*/*z* calcd for $C_{22}H_{35}ClN_4$ 390.3. Found $(M + H)^+$: 391.0.

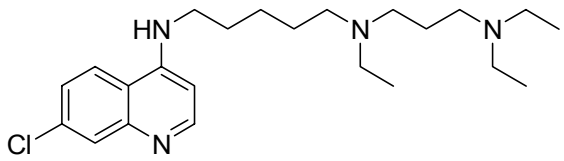


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,5-diaminopentane**. A mixture of *N*-(7-chloro-4-quinolyl)-1,5-diaminopentane (0.25 g, 0.95 mmol), *N,N*-diethylamino-3-propionic acid (0.17 g, 0.93 mmol), EDC (0.22 g, 1.14 mmol), and triethylamine (0.4 mL, 2.9 mmol) in 12 mL of anhydrous DMF and chloroform (1:1 v/v) was stirred at room temperature for 2.5 days. The reaction mixture was concentrated *in vacuo*, then dissolved in dichloromethane and extracted with aqueous NaOH. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography (1.0:0.05 methanol:ammonium hydroxide v/v) to afford 0.045 g (0.11 mmol, 12%) of colorless crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.01 (t, *J* = 7.2 Hz, 6H), 1.49-1.59 (m, 4H), 1.82-1.87 (m, 2H) , 2.53 (t, *J* = 6.0 Hz, 2H), 2.53 (q, *J* = 7.2 Hz, 4H), 2.64 (t, *J* = 6.0 Hz, 2H), 3.26-3.33 (m, 4H), 5.46 (bs, 1H), 6.37 (d, *J* = 5.4 Hz, 1H), 7.35 (dd, *J* = 2.2 Hz, 8.8 Hz, 1H), 7.94 (d, *J* = 2.2 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 8.51 (d, *J* = 5.4 Hz, 1H), 8.80 (bs, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.8, 24.3, 28.0, 30.0, 32.8, 37.9, 43.4, 46.3, 49.2, 100.6, 117.6, 122.0, 128.9, 134.9, 149.5, 150.3, 152.3, 173.7; MS (ESI) *m*/*z* calcd for $C_{21}H_{31}ClN_4O$ 390.2. Found $(M + H)^+$: 391.0.

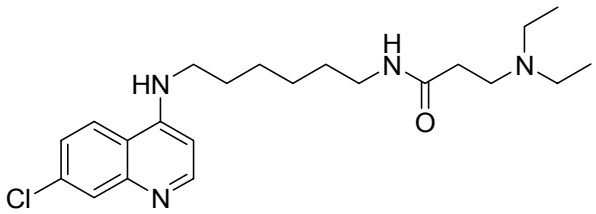


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,5-diaminopentane**. To *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,5-diaminopentane (0.14 g, 0.35 mmol) in 9 mL of anhydrous DMF, borane-dimethyl sulfide complex (0.23 mL, 2.42 mmol) was added dropwise at 0 °C. The reaction mixture was heated to reflux for 2.5 h and then quenched with 1.8 mL of water. Concentrated HCl (0.75 mL) was added and the mixture was refluxed for another 1.5 h. The product mixture was cooled to room temperature, basified (pH > 10) with NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography (1.0:1.0:0.10 ethanol:dichloromethane:triethylamine v/v) to afford 0.09 g (0.24 mmol, 68% yield) as a light yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.99 (t, *J* = 7.1 Hz, 6H), 1.53-1.61 (m, 2H), 1.67-1.83 (m, 6H) , 2.50-2.58 (m, 6H), 2.74 (t, *J* = 6.7 Hz, 2H), 2.84 (t, *J* = 6.4 Hz, 2H), 3.36 (q, *J* = 6.1 Hz, 2H), 5.72 (bs, 1H), 6.28 (d, *J* = 5.4 Hz, 1H), 7.37 (dd, *J* = 2.2 Hz, 9.0 Hz, 1H), 7.93 (d, *J* = 2.2 Hz, 1H), 8.00 (d, *J* = 9.0 Hz, 1H), 8.51 (d, *J* = 5.4 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.8, 24.8, 26.3, 28.5, 29.2, 43.1, 46.9, 49.5, 51.9

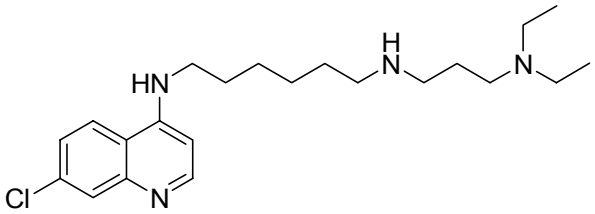
99.2, 117.5, 121.8, 125.4, 128.9, 135.0, 149.4, 150.1, 152.2; MS (ESI) *m*/*z* calcd for $C_{21}H_{33}ClN_4$ 376.2. Found $(M + H)^+$: 377.1.



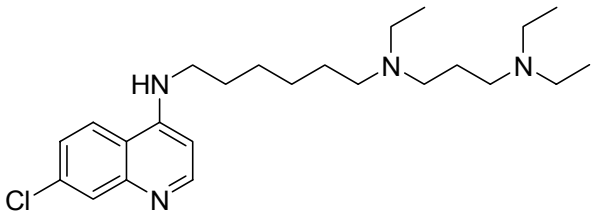
***N*-(7-Chloro-4-quinolyl)-*N′*-ethyl-*N′*-(3-diethylaminopropyl)-1,5-diaminopentane**. To *N*-(7-chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,5-diaminopentane (0.064 g, 0.17 mmol) in 4 mL of glacial acetic acid, sodium borohydride (0.16 g, 4.3 mmol) was added at 5 °C. The reaction was stirred at room temperature for 40 minutes and then heated to 55 °C for 36 h. After cooling to room temperature, the mixture was basified (pH > 10) with NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography (1.0:0.05 ethanol:triethylamine v/v) to afford 0.021 g (0.05 mmol, 31% yield) as colorless crystals. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.02 (t, *J* = 7.2 Hz, 6H), 1.04 (t, *J* = 7.2 Hz, 3H), 1.46-1.55 (m, 6H), 1.74-1.83 (m, 2H) , 2.43-2.59 (m, 12H), 3.29-3.36 (m, 2H), 5.11 (bs, 1H), 6.41 (d, *J* = 5.5 Hz, 1H), 7.37 (dd, *J* = 2.2 Hz, 9.0 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.95 (d, *J* = 2.2 Hz, 1H), 8.54 (d, *J* = 5.5 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.5, 11.8, 24.4, 25.3, 27.0, 28.9, 43.4, 46.3, 47.1, 47.8, 51.2, 51.8, 99.3, 117.4, 121.4, 125.4, 128.5, 135.0, 149.4, 150.0, 152.3; MS (ESI) *m*/*z* calcd for $C_{23}H_{37}ClN_4$ 404.3. Found $(M + H)^+$: 405.1.



***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,6-diaminohexane**. A mixture of *N*-(7-chloro-4-quinolyl)-1,6-diaminohexane (0.1 g, 0.36 mmol), *N,N*-diethylamino-3-propionic acid (0.08 g, 0.43 mmol), EDC (0.08 g, 0.43 mmol) and Et_3N (0.19 mL, 1.35 mmol) was stirred at room temperature in 4 mL of DMF/$CHCl_3$ (1:1 v/v) for 2 days. Saturated $NaHCO_3$ was added to the cooled reaction mixture, which was then extracted with CH_2Cl_2 and dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Purification by flash chromatography using EtOH:Et_3N (1:0.05 v/v) as the mobile phase gave yellow crystals (0.12 g, 0.27 mmol, 76% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ =1.06 (t, *J* = 7.1 Hz, 6H), 1.25-1.62 (m, 6H), 1.63-1.82 (m, 2H), 2.40 (t, *J* = 6.1 Hz, 2H), 2.58 (q, *J* = 7.1 Hz, 4H), 2.69 (t, *J* = 6.1 Hz, 2H), 3.20-3.41 (m, 4H), 5.37 (bs, 1H), 6.41 (d, *J* = 5.4 Hz, 1H), 7.38 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.97 (d, *J* = 2.1 Hz, 1H), 8.53 (d, *J* = 5.4 Hz, 1H), 8.67 (bs, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.7, 26.7, 28.7, 29.8, 32.7, 38.7, 43.1, 46.3, 49.2, 99.1, 117.5, 121.9, 125.3, 128.6, 135.0, 149.2, 150.3, 152.0, 173.2; MS (ESI) m/z calcd for $C_{22}H_{33}ClN_4O$ 404.2. Found $(M + H)^+$: 405.1.

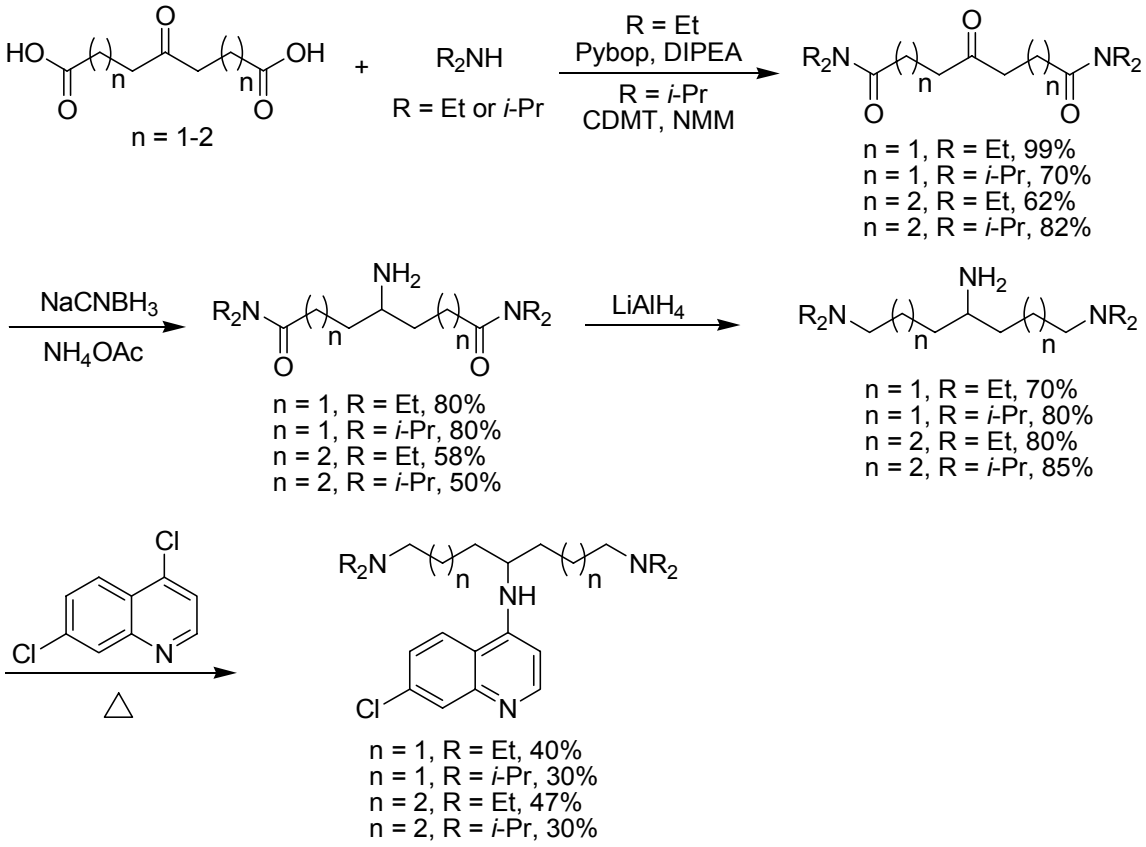


***N*-(7-Chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,6-diaminohexane**. A solution of *N*-(7-chloro-4-quinolyl)-*N′*-(3-diethylaminopropanoyl)-1,6-diaminohexane (0.08 g, 0.18 mmol) in 2 mL of THF was heated to reflux and borane-dimethyl sulfide complex (0.1 mL, 1.1 mmol.) was added. After 14 h, 1 mL of 6M HCl was added and the mixture was heated to 100 ºC for 30 minutes. The clear solution was cooled, basified with saturated NaOH and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Purification by flash chromatography using EtOH:Et_3N (1:0.03 v/v) as the mobile phase gave a brown oil (0.065 g, 0.14 mmol, 85% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ =1.05 (t, *J* = 7.1 Hz, 6H), 1.40-1.61 (m, 4H), 1.62-1.73 (m, 2H), 1.74-1.88 (m, 4H), 2.54-2.68 (m, 6H), 2.72 (t, *J* = 7.1 Hz, 2H), 2.84 (t, *J* = 6.4 Hz, 2H), 3.28-3.42 (m, 2H), 5.50 (bs, 1H), 6.41 (d, *J* = 5.4 Hz, 1H), 7.36 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.95 (d, *J* = 2.1 Hz, 1H), 8.53 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.7, 24.7, 26.7, 26.8, 28.5, 28.6, 43.0, 46.8, 48.7, 49.8, 52.5, 99.1, 117.6, 122.0, 125.4, 128.8, 135.0, 149.4, 150.2, 152.2; MS (ESI) m/z calcd for $C_{22}H_{35}ClN_4$ 390.3. Found $(M + H)^+$: 391.1.



***N*-(7-Chloro-4-quinolyl)-*N′*-ethyl-*N′*-(3-diethylaminopropyl)-1,6-diaminohexane**. To *N*-(7-chloro-4-quinolyl)-*N′*-(3-diethylaminopropyl)-1,6-diaminohexane (0.05 g, 0.13 mmol) in 1 mL of glacial acetic acid, $NaBH_4$ (0.11 g, 2.8 mmol) was added at 5 ^{o}C and the mixture was stirred at 50 °C for 18 h. After cooling to room temperature, the mixture was basified with saturated NaOH and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography using EtOH:Et_3N (1:0.03 v/v) as the mobile phase gave a yellow oil (0.03 g, 0.07 mmol, 55% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.04 (t, *J* = 7.1 Hz, 9H), 1.29-1.58 (m, 6H), 1.58-1.70 (m, 2H), 1.71-1.84 (m, 2H), 2.42 (t, *J* = 7.1 Hz, 6H), 2.45-2.62 (m, 6H), 3.25-3.39 (m, 2H), 5.10 (bs, 1H), 6.41 (d, *J* = 5.4 Hz, 1H), 7.37 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.95 (d, *J* = 2.1 Hz, 1H), 8.54 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.7, 11.8, 24.5, 27.2, 27.3, 27.5, 29.1, 43.4, 47.1, 47.8, 51.3, 51.9, 53.6, 99.3, 117.4, 121.3, 125.4, 129.1, 135.0, 149.4, 150.0, 152.3; MS (ESI) m/z calcd for $C_{24}H_{39}ClN_4$ 418.3. Found $(M + H)^+$: 419.3.

Scheme 2



1,7-Bis(diethylamido)heptan-4-one. To a solution of 4-ketopimelic acid (0.2 g, 1.2 mmol) in CH_3CN was added diisopropylamine (0.5 mL, 2.9 mmol), Pybop (1.19 g, 2.3 mmol) and *N,N*-diisopropylethylamine (0.5 mL, 3.2 mmol). The reaction was refluxed at 80 ^{o}C for 48 h. The solvents were removed *in vacuo* and the residue was dissolved in CH_2Cl_2 and extracted with 2M HCl and water. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give 0.31 g (1.1 mmol, 98% yield) of a brown oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.07 (t, J = 7.2 Hz, 6H), 1.15 (t, J = 7.2 Hz, 6H), 2.56 (t, J = 6.6 Hz, 4H), 2.82 (t, J = 6.6 Hz, 4H), 3.25-3.44 (m, 8H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 13.2, 14.3, 27.1, 37.7, 40.4, 42.0, 171.0, 211.5.

1,7-Bis(diethylamido)-4-aminoheptane. 1,7-Bis(diethylamido)heptan-4-one (0.5 g, 0.7 mmol), ammonium acetate (0.45 g, 4.2 mmol) and sodium cyanoborohydride (0.11 g, 1.8 mmol) were dissolved in 4 mL of MeOH and the solution was stirred at room temperature for 36 h. After removing the solvents *in vacuo*, the residue was dissolved in CH_2Cl_2 and extracted with 4M NaOH. The combined organic layers were concentrated and extracted with 6M HCl. The aqueous layer was basified with concentrated NaOH and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give 0.16 g (0.56 mmol, 80% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.10 (t, J = 6.9 Hz, 6H), 1.16 (t, J = 6.9 Hz, 6H),

1.52-1.70 (m, 2H), 1.72-1.88 (m, 2H), 2.29-2.50 (m, 4H), 2.72-2.86 (m, 3H), 3.18-3.38 (m, 8H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 13.3, 14.6, 29.9, 33.7, 40.3, 42.2, 51.1, 172.3.

1,7-Bis(diethylamino)-4-aminoheptane. 1,7-Bis(diethylamido)-4-aminoheptane (0.1 g, 0.35 mmol) and lithium aluminum hydride in 1M THF (2.1 mL, 2.1 mmol) were mixed in 3 mL of anhydrous toluene and refluxed at 110 ºC for 48 h. The reaction mixture was quenched with 4M NaOH and extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give 0.07 g (0.24 mmol, 70% yield) of a brown oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.03 (t, *J* = 7.2 Hz, 12H), 1.35-1.64 (m, 8H), 2.42 (t, *J* = 7.2 Hz, 4H), 2.54 (q, *J* = 7.2 Hz, 8H), 3.49-3.36 (s, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.6, 23.5, 35.6, 46.8, 50.1 53.1.

***N*-(7-Chloro-4-quinolyl)-1,7-bis(diethylamino)-4-aminoheptane**. 4,7-Dichloroquinoline (0.6 g, 3.0 mmol) and 1,7-bis(diethylamino)-4-aminoheptane (0.06 g, 0.23 mmol) were mixed in a closed vessel and heated to 120 ºC for 3 days. The crude product was treated with 4M NaOH and extracted with $CHCl_3$. The combined organic layers were extracted with brine, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by flash column chromatography using EtOH:CH_2Cl_2:Et_3N (100:50:5 v/v) as the mobile phase to give 0.04 g (0.09 mmol, 40% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.03 (t, *J* = 7.2 Hz, 12H), 1.52-1.80 (m, 8H), 2.47 (t, *J* = 7.2 Hz, 4H), 2.55 (q, *J* = 7.2 Hz, 8H), 3.58-3.72 (m, 1H), 5.62 (bs, 1H), 6.44 (d, *J* = 3.1 Hz, 1H), 7.36 (dd, *J* = 1.8 Hz, 9.0 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 1.8 Hz, 1H), 8.51 (d, *J* = 3.1 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.5, 23.8, 32.3, 47.0, 52.8, 52.9, 99.4, 117.6, 121.8, 125.1, 128.9, 135.0, 149.6, 149.8, 152.2; MS (ESI) *m*/*z* calcd for $C_{24}H_{39}ClN_4$ 418.3. Found: 419.2.

1,7-Bis(diisopropylamido)heptan-4-one. 4-Ketopimelic acid (4.0 g, 23.0 mmol), diethylamine (20.0 mL, 50.0 mmol), and 2-chloro-4,6-dimethoxy-1,3,5-triazine (8.0 g, 46.0 mmol) were dissolved in 70 mL of CH_3CN and *N*-methyl morpholine (12.0 g, 117.0 mmol) was added at once. After 24 h, 2M HCl was added and the solution was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give 6.2 g (18.4 mmol, 80% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.20 (d, *J* = 6.6 Hz, 12H), 1.34 (d, *J* = 6.6 Hz, 12H), 2.59 (t, *J* = 6.6 Hz, 4H), 2.82 (t, *J* = 6.6 Hz, 4H), 3.21-3.42 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 20.9, 21.0, 28.9, 37.7, 45.7, 48.3, 56.1, 170.4, 211.5.

1,7-Bis(diisopropylamido)-4-aminoheptane. 1,7-Bis(diisopropylamido)heptan-4-one (4.5 g, 13.3 mmol), ammonium acetate (13.0 g, 165.0 mmol) and sodium cyanoborohydride (5.0 g, 79.5 mmol) were dissolved in 100 mL of anhydrous MeOH and stirred at room temperature for 48 h. The solvents were removed *in vacuo*. The residue was dissolved in CH_2Cl_2 and extracted with 4M NaOH solution. The combined organic layers were concentrated and extracted with 6M HCl. The aqueous layer was basified and then extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure providing 3.1 g (9.3 mmol, 70% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.20 (d, *J* = 6.9 Hz, 12H), 1.34 (d, *J* = 6.6 Hz, 12H), 1.59-1.85 (m, 4H), 2.27-2.58 (m, 4H), 2.66-3.11 (m, 3H), 3.46 (bs, 2H), 3.82-

4.12 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 20.9, 21.1, 32.1, 33.0, 45.8, 49.1, 51.3, 171.9.

1,7-Bis(diisopropylamino)-4-aminoheptane. A solution of 1,7-Bis(diisopropylamido)-4-aminoheptane (0.15 g, 0.57 mmol) and lithium aluminum hydride in 2M THF (2.1 mL, 4.2 mmol) in 3 mL of anhydrous toluene was refluxed at 110 ºC for 24 h. The reaction mixture was quenched with 4M NaOH and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give 0.14 g (0.46 mmol, 80% yield) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.01 (d, *J* = 6.6 Hz, 24H), 1.15-1.52 (m, 8H), 2.32-2.48 (m, 4H), 2.68-2.82 (m, 1H), 2.92-3.11 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 14.4, 20.8, 28.1, 45.6, 48.6, 51.5.

***N*-(7-Chloro-4-quinolyl)-1,7-bis(diisopropylamino)-4-aminoheptane**. 4,7-Dichloroquinoline (0.6 g, 3.0 mmol) and 1,7-bis(diisopropylamino)-4-aminoheptane (0.06 g, 0.23 mmol) were mixed in a closed vessel and the mixture was heated to 120 ºC for 3 days. The mixture was treated with 4M NaOH and extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by flash column chromatography using EtOH:CH_2Cl_2:Et_3N (100:75:5 v/v) as the mobile phase to give 0.03 g (0.07 mmol, 30%) of a yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.00 (d, *J* = 6.6 Hz, 24H), 1.28-1.75 (m, 8H), 2.43 (t, *J* = 6.6 Hz, 4H), 2.85-3.12 (m, 4H), 3.58-3.74 (m, 1H), 4.77 (d, *J* = 8.2 Hz, 1H), 6.44 (d, *J* = 6.1 Hz, 1H), 7.38 (dd, *J* = 1.8 Hz, 9.0 Hz, 1H), 7.65 (d, *J* = 9.0 Hz, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 8.53 (d, *J* = 6.1 Hz,1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 13.9, 19.0, 20.2, 31.8, 36.7, 52.3, 98.8, 117.0, 124.9, 128.6, 134.6, 149.2, 151.8; MS (ESI) *m*/*z* calcd for $C_{28}H_{47}ClN_4$ 474.4. Found $(M + H)^+$: 475.3.

1,9-Bis(diethylamido)nonan-5-one. To a mixture of 5-oxoazelaic acid (2.5 g, 12.4 mmol) and PyBop (15.4 g, 29.7 mmol) in anhydrous CH_3CN (18.0 mL) under inert atmosphere was added diethylamine (5.11 mL, 49.9 mmol) and *N,N*-diisopropylethylamine (6.0 mL, 34.2 mmol). The reaction proceeded with good stirring at 35 ^{o}C for 64 h and then solvents were removed *in vacuo*. The residue was dissolved in CH_2Cl_2, washed with a 2M HCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to produce a yellow oil (2.39 g, 7.7 mmol, 62% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.08 (t, *J* = 7.1 Hz, 6H), 1.16 (t, *J* = 7.2 Hz, 6H), 1.65-1.90 (m, 4H), 2.33 (t, *J* = 7.5 Hz, 4H), 2.50 (t, *J* = 7.1 Hz, 4H), 3.10-3.30 (m, 8H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 14.9, 14.1, 19.3, 31.8, 40.0, 41.6, 41.9, 171.6, 210.5.

1,9-Bis(diethylamido)-5-aminononane. To a mixture of 1,9-bis(diethylamido)nonan-5-one (2.39 g, 7.7 mmol) in 24 mL of anhydrous MeOH under inert atmosphere was added ammonium acetate (15.4 g, 46.0 mmol) and sodium cyanoborohydride (1.2 g, 19.2 mmol). The reaction mixture was stirred at room temperature for 4 days. The solvents were removed under reduced pressure and the residue was dissolved in CH_2Cl_2 and extracted with 6M HCl. The aqueous layer was basified using a concentrated NaOH solution, extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give 1.39 g of a yellow oil (4.4 mmol, 58% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.97 (t, *J* = 7.2 Hz, 6H), 1.04 (t, *J* = 7.2 Hz, 6H), 1.27-1.64 (m, 8H), 2.21 (t, *J* = 7.2 Hz,

4H), 2.70-2.81 (m, 1H), 3.20-3.51 (m, 8H), 3.83 (bs, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 13.1, 14.3, 21.8, 32.9, 37.4, 40.0, 41.9, 50.8, 171.8.

1,9-Bis(diethylamino)-5-aminononane. To a mixture of 1,9-bis(diethylamido)-5-aminononane (0.2 g, 0.64 mmol) in 1.5 mL of anhydrous toluene under inert atmosphere was added dropwise lithium aluminum hydride as a 2M THF solution (1.4 mL, 3.8 mmol). The reaction mixture was stirred for 24 h at 110 °C. Then, 10 mL of a 4M NaOH was added and the mixture was extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give 0.15 g of a yellow oil (0.51 mmol, 80% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.95 (t, *J* = 7.1 Hz, 12H), 1.17-1.48 (m, 12H), 2.31-2.33 (m, 2H), 2.35 (t, *J* = 7.7 Hz, 4H), 2.45 (q, *J* = 7.1 Hz, 8H), 2.59-2.62 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.9, 24.5, 27.4, 38.36, 47.1, 51.3, 53.1.

***N*-(7-Chloro-4-quinolyl)-1,9-bis(diethylamino)-5-aminononane**. A mixture of 4,7-dichloroquinoline (0.75 g, 3.8 mmol) and 1,9-bis(diethylamino)-5-aminononane (0.07 g, 0.25 mmol) was heated to 120 ^{o}C for 72 h in a closed vessel. Saturated $NaHCO_3$ solution was added to the cooled reaction mixture, which was then extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by flash chromatography using EtOAc:EtOH:Et_3N (1:1:0.01 v/v) as the mobile phase to give a yellow oil (0.05 g, 0.11 mmol, 47% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.99 (t, *J* = 7.2 Hz, 12H), 1.29-1.74 (m, 12H), 2.39 (t, *J* = 7.4 Hz, 4H), 2.48 (q, *J* = 7.2 Hz, 8H), 3.6 (m, 1H), 4.83 (d, *J* = 8.1 Hz, 1H), 6.40 (d, *J* = 5.4 Hz, 1H), 7.34 (dd, *J* = 9.0 Hz, 2.4 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.94 (d, *J* = 2.4 Hz, 1H), 8.49 (d, *J* = 5.4 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 11.8, 24.2, 27.3, 34.8, 47.1, 52.9, 53.0, 99.3, 121.1, 125.3, 129.2, 135.1, 149.6, 149.7, 152.3; MS (ESI) *m*/*z* calcd for $C_{26}H_{43}ClN_4$ 446.3. Found $(M + H)^+$: 447.3.

1,9-Bis(diisopropylamido)nonan-5-one. To a mixture of 5-oxoazelaic acid (1.0 g, 5.0 mmol) and 2-chloro-4,6-dimethoxy-1,3,5-triazine (2.0 g, 11.4 mmol) in anhydrous CH_3CN (18.0 mL) under inert atmosphere was added *N*-methyl morpholine (2.5 g, 24.7 mmol) and diisopropylamine (1.0 g, 9.9 mmol). The mixture was stirred at room temperature for 48 h and then the solvents were removed *in vacuo*. The residue was dissolved in CH_2Cl_2, extracted with 2M HCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a yellow oil (1.5 g, 4.1 mmol, 82% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.17 (d, *J* = 6.6 Hz, 12H), 1.34 (d, *J* = 6.9 Hz, 12H), 1.85 (m, 4H), 2.30 (t, *J* = 7.2 Hz, 4H), 2.48 (t, *J* = 6.9 Hz, 4H), 3.37-3.59 (m, 2H), 3.86-3.95 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 19.7, 20.9, 21.2, 34.5, 42.1, 45.9, 48.6, 171.7, 210.8.

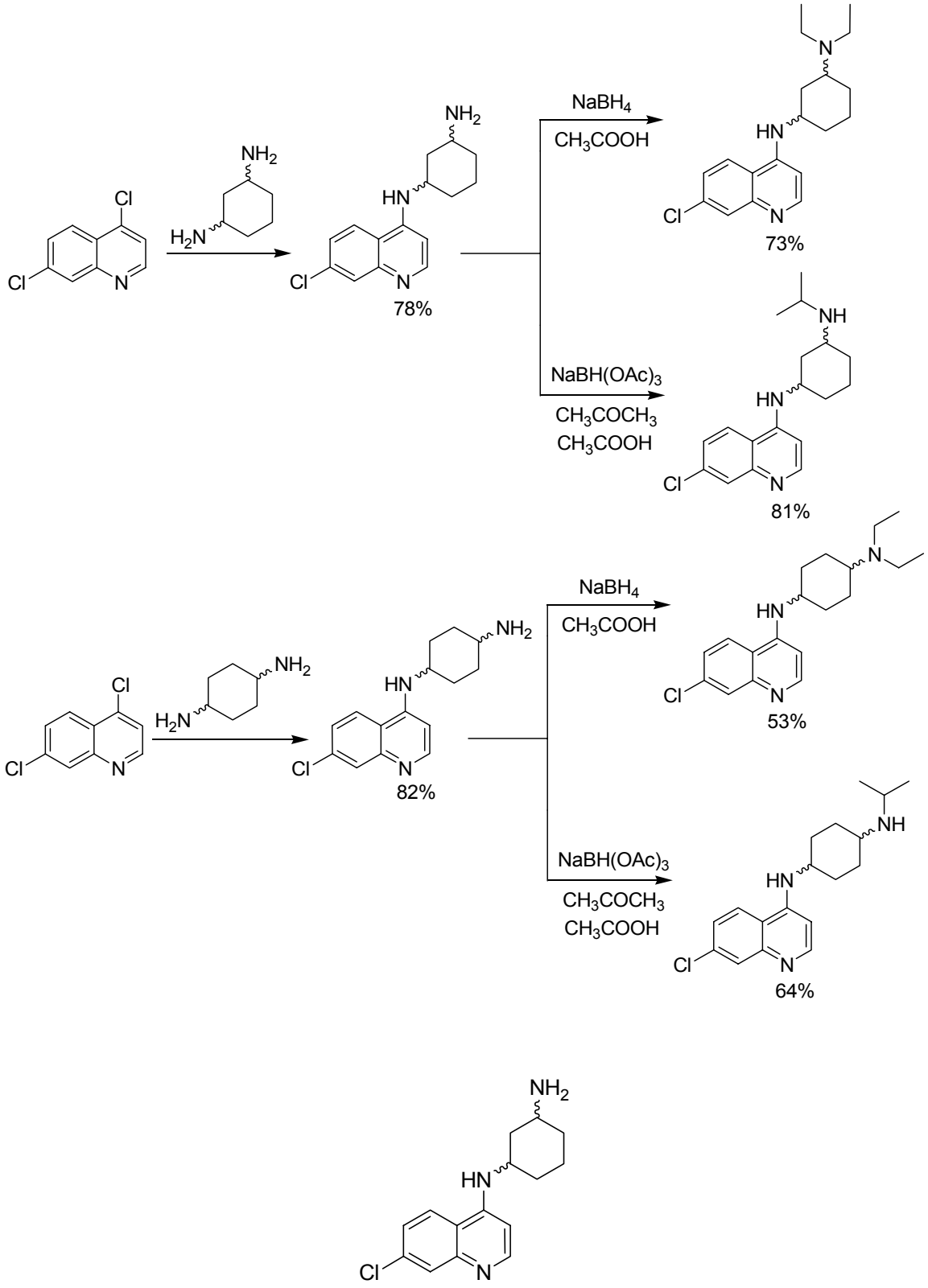
1,9-Bis(diisopropylamido)-5-aminononane. To a mixture of 1,9-bis(diisopropylamido)nonan-5-one (0.73 g, 2.0 mmol) in 4 mL of anhydrous MeOH under inert atmosphere was added ammonium acetate (1.25 g, 16.2 mmol) and sodium cyanoborohydride (0.43 g, 6.8 mmol). The reaction mixture was stirred at room temperature for 3 days. Solvents were removed under reduced pressure and the residue was dissolved in CH_2Cl_2 and extracted with 6M HCl. The aqueous layer was basified using a concentrated NaOH solution, extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to a yellow oil (0.37 g, 1.0 mmol, 50% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.17 (d, *J* = 6.6 Hz, 12H), 1.34 (d, *J* = 6.9 Hz, 12H), 1.40-

1.77 (m, 6H), 2.30 (t, J = 7.2 Hz, 4H), 2.35-2.50 (m, 2H), 2.75-2.82 (m, 1H), 3.40-3.59 (m, 2H), 3.90-4.00 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 20.9, 21.4, 21.6, 34.9, 35.6, 42.6, 46.3, 51.8, 172.3.

1,9-Bis(diisopropylamino)-5-aminononane. To a mixture of 1,9-bis(diisopropylamido)-5-aminononane (0.18 g, 0.5 mmol) in 1.5 mL of anhydrous toluene under inert atmosphere was added dropwise lithium aluminum hydride as a 2M THF solution (1.4 mL, 3.8 mmol). The reaction mixture was stirred for 24 h at 110 °C. Then, 10 mL of 4M NaOH was added and the mixture was extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to a yellow oil (0.15 g, 0.42 mmol, 85% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.02 (d, J = 6.6 Hz, 24H), 1.24-1.46 (m, 12H), 2.40 (t, J = 7.4 Hz, 4H), 2.62-2.69 (m, 1H), 3.02 (sept, J = 6.6 Hz, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 20.9, 24.2, 31.9, 38.3, 45.5, 48.7, 51.5.

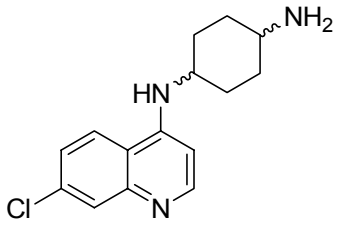
***N*-(7-Chloro-4-quinolyl)-1,9-bis(diisopropylamino)-5-aminononane.** A mixture of 4,7-dichloroquinoline (0.75 g, 3.8 mmol) and 1,9-bis(diisopropylamino)nonan-5-amine (0.07 g, 0.21 mmol) was heated to 120 ^{o}C for 72 h under nitrogen in a closed vessel. After cooling to room temperature, aqueous $NaHCO_3$ was added and the mixture was extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by flash column chromatography using CH_2Cl_2:EtOH:Et_3N (2:1:0.04 v/v) as the mobile phase and a yellow oil (0.03 g, 0.06 mmol, 30% yield) was obtained. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 0.96 (d, J = 6.6 Hz, 24H), 1.25-1.70 (m, 12H), 2.35 (t, J = 7.1 Hz, 4H), 2.97 (sep, J = 6.6 Hz, 4H), 3.50-3.70 (m, 1H), 4.73 (d, J = 8.6 Hz, 1H), 6.41 (d, J = 5.5 Hz, 1H), 7.35 (dd, J = 9.0, 2.0 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.95 (d, J = 2.0 Hz, 1H), 8.50 (d, J = 5.5 Hz, 1H); MS (ESI) m/z calcd for $C_{30}H_{51}ClN_4$ 502.4. Found $(M + H)^+$: 503.3.

Scheme 3

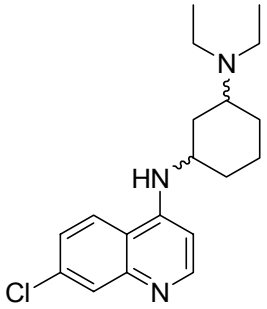


***N*-(7-Chloro-4-quinolyl)-1,3-diaminocyclohexane.** A mixture of 4,7-dichloroquinoline (0.28 g, 1.4 mmol) and 1,3-diaminocyclohexane (*cis*-and *trans*-mixture) (0.5 mL, 4.2

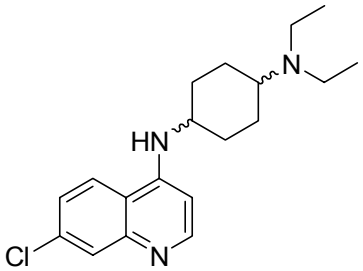
mmol) was heated to 110 °C for 18 h under inert atmosphere and then cooled to room temperature. Aqueous NaOH (1N, 10 mL) was then added and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Purification by flash chromatography using 0.5% Et_3N in MeOH as the mobile phase gave a brown oil (0.31 g, 1.1 mmol, 78% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.24-1.96 (m, 10H, *cis* + *trans*), 2.13 (d, *J* = 7.8 Hz, 1H, *cis* + *trans*), 3.16 (m, 1H, *cis* + *trans*), 3.70 (s, 1H, *cis* or *trans*), 4.01 (s, 1H, *cis* or *trans*), 6.35 (d, *J* = 3.3 Hz, 1H, *cis* or *trans*), 6.44 (d, *J* = 3.0 Hz, 1H, *cis* or *trans*), 7.31 (m, 1H, *cis* + *trans*), 7.63 (d, *J* = 5.1 Hz, 1H, *cis* or *trans*), 7.68 (d, *J* = 5.4 Hz, 1H, *cis* or *trans*), 7.91 (s, 1H, *cis* + *trans*), 7.94 (s, 1H, *cis* + *trans*), 8.47 (d, *J* = 3.0 Hz, 1H, *cis* or *trans*), 8.50 (d, *J* = 3.3 Hz, 1H, *cis* or *trans*); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 19.1, 21.9, 29.2, 30.5, 33.0, 33.7, 37.5, 39.8, 45.5, 46.9, 47.5, 49.9, 98.3, 98.8, 116.9, 121.7, 122.0, 124.6, 124.8, 126.5, 126.7, 134.8, 148.0, 149.2, 149.4, 150.6, 150.7.



***N*-(7-Chloro-4-quinolyl)-1,4-diaminocyclohexane.** A mixture of 4,7-dichloroquinoline (0.28 g, 1.4 mmol) and 1,4-diaminocyclohexane (*cis*-and *trans*-mixture) (0.5 mL, 4.2 mmol) was heated to 110 °C for 18 h under inert atmosphere and then cooled to room temperature. Aqueous NaOH (1N, 10 mL) was then added and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Purification by flash chromatography using 0.5% Et_3N in MeOH as the mobile phase gave a brown oil (0.32 g, 1.16 mmol, 82% yield).^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.22-1.62 (m, 2H, *cis* + *trans*), 1.72-2.12 (m, 8H, *cis* + *trans*), 2.78 (m, 1H, *cis* or *trans*), 3.02 (m, 1H, *cis* or *trans*), 3.71 (m, 1H, *cis* + *trans*), 4.95 (d, *J* = 7.2 Hz, 1H, *cis* or *trans*), 5.14 (d, *J* = 6.3 Hz, 1H, *cis* or *trans*), 6.41 (d, *J* = 5.4 Hz, 1H, *cis* + *trans*), 7.34 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H, *cis* + *trans*), 7.67 (d, *J* = 9.0 Hz, 1H, *cis* + *trans*), 7.94 (d, *J* = 2.1 Hz, 1H, *cis* + *trans*), 8.49 (d, *J* = 5.4 Hz, 1H, *cis* + *trans*); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 27.4, 30.3, 31.2, 33.6, 49.6, 50.5, 51.8, 99.6, 100.0, 118.4, 118.5, 124.0, 124.1, 125.6, 125.7, 127.3, 127.4, 136.0, 136.1, 149.4, 151.1, 151.4, 151.9.

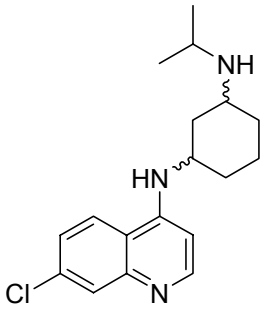


***N*-(7-Chloro-4-quinolyl)-*N'*,*N*'-diethyl-1,3-diaminocyclohexane.** To a solution of *N*-(7-chloro-4-quinolyl)-1,3-diaminocyclohexane (0.1 g, 0.36 mmol) in 4 mL of glacial acetic acid, sodium borohydride (0.53 g, 14.0 mmol) was added portionwise at 0 °C. The reaction was heated at 60 °C for 24 h and then cooled to room temperature, basified (pH > 10) with 12N NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography using 0.5% Et_3N in MeOH as the mobile phase gave yellow crystals (0.09 g, 0.27 mmol, 73% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.03 (m, 6H, *cis* + *trans*), 1.30-2.20 (m, 8H, *cis* + *trans*), 2.61 (m, 4H, *cis* + *trans*), 2.75 (m, 1H, *cis* or *trans*), 2.88 (m, 1H, *cis* or *trans*), 3.61 (m, 1H, *cis* or *trans*), 4.03 (m, 1H, *cis* or *trans*), 5.13 (d, *J* = 6.6 Hz, 1H, *cis* + *trans*), 6.38 (m, 1H, *cis* + *trans*), 7.29 (m, 1H, *cis* + *trans*), 7.68 (m, 1H, *cis* + *trans*), 7.91 (m, 1H, *cis* + *trans*), 8.47 (m, 1H, *cis* + *trans*); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 12.8, 12.9, 20.4, 21.3, 28.0, 28.2, 30.0, 31.4, 33.1, 34.3, 43.1, 47.9, 50.4, 54.4, 56.9, 98.8, 99.3, 117.1, 117.2, 120.6, 121.3, 124.7, 125.0, 128.4, 128.6, 134.5, 134.6, 148.4, 148.7, 149.0, 149.1, 151.7, 151.8; MS (ESI) *m*/*z* calcd for $C_{19}H_{26}ClN_3$ 331.2. Found $(M + H)^+$: 332.2.

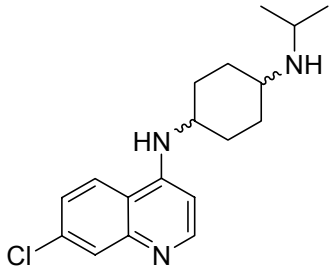


***N*-(7-Chloro-4-quinolyl)-*N'*,*N*'-diethyl-1,4-diaminocyclohexane.** To a solution of *N*-(7-chloro-4-quinolyl)-1,4-diaminocyclohexane (0.11 g, 0.38 mmol) in 4 mL of glacial acetic acid, sodium borohydride (0.43 g, 11.4 mmol) was added portionwise at 0 °C. The reaction was heated at 60 °C for 24 h, cooled to room temperature, basified (pH > 10) with 12N NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography using 0.5% Et_3N in MeOH as the mobile phase gave yellow crystals (0.07 g, 0.2 mmol, 53% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.02 (t, *J* = 7.2 Hz, 6H, *cis* + *trans*), 1.20-2.12 (m, 8H, *cis* + *trans*), 2.50-2.71 (m, 5H, *cis* + *trans*), 3.40 (m, 1H, *cis* or *trans*), 3.78 (m, 1H, *cis* or *trans*), 4.98 (d, *J* = 7.2 Hz, 1H, *cis* or *trans*), 5.11 (d, *J* = 6.6 Hz, 1H, *cis* or *trans*), 6.40 (d, *J* = 5.4 Hz, 1H, *cis* + *trans*), 7.28 (m, 1H, *cis* or *trans*), 7.33 (dd, *J* = 2.1 Hz, *J* = 9.0 Hz, 1H, *cis* or *trans*), 7.64 (m, 1H, *cis* + *trans*), 7.93 (m, 1H, *cis* + *trans*), 8.49 (d, *J* = 5.4 Hz, 1H, *cis* + *trans*); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 12.4,

13.7, 24.6, 27.3, 28.2, 31.9, 42.8, 43.5, 47.3, 51.5, 57.3, 58.7, 99.2, 117.0, 117.1, 120.7, 124.9, 128.5, 134.5, 148.3, 148.6, 149.0, 151.7; MS (ESI) *m*/*z* calcd for $C_{19}H_{26}ClN_3$ 331.2. Found $(M + H)^+$: 331.9.



***N*-(7-Chloro-4-quinolyl)-*N'*-isopropyl-1,3-diaminocyclohexane.** To a solution of *N*-(7-chloro-4-quinolyl)-1,3-diaminocyclohexane (0.1 g, 0.36 mmol), acetone (0.13 mL, 1.8 mmol) and glacial acetic acid (0.04 mL, 0.72 mmol) in anhydrous CH_2Cl_2, sodium triacetoxyborohydride (0.23 g, 1.1 mmol) was added at room temperature and stirred for 2 h. The reaction mixture was quenched with water, basified with 1N NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography using 0.5% Et_3N in MeOH as the mobile phase gave pale yellow crystals (0.09 g, 0.29 mmol, 81% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.04 (m, 2H, *cis* + *trans*), 1.13 (m, 4H, *cis* + *trans*), 1.31-2.12 (m, 10H, *cis* + *trans*), 2.86-3.10 (m, 2H, *cis* + *trans*), 3.75 (m, 1H, *cis* or *trans*), 3.96 (m, 1H, *cis* or *trans*), 6.32 (d, *J* = 5.4 Hz, 1H, *cis* or *trans*), 6.44 (d, *J* = 5.4 Hz, 1H, *cis* or *trans*), 7.29 (m, 1H, *cis* + *trans*), 7.65 (d, *J* = 9.0 Hz, 1H, *cis* or *trans*), 7.74 (d, *J* = 9.0 Hz, 1H, *cis* or *trans*), 7.91 (d, *J* = 2.4 Hz, 1H, *cis* or *trans*), 7.93 (d, *J* = 2.4 Hz, 1H, *cis* or *trans*), 8.45 (d, *J* = 5.4 Hz, 1H, *cis* or *trans*), 8.49 (d, *J* = 5.4 Hz, 1H, *cis* or *trans*); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 19.0, 19.6, 23.1, 23.2, 23.3, 29.8, 30.8, 31.4, 31.9, 36.5, 36.9, 45.0, 45.6, 47.2, 48.8, 49.0, 50.7, 98.3, 99.1, 117.0, 117.3, 120.8, 121.8, 124.4, 124.8, 128.1, 128.4, 134.4, 134.5, 148.4, 148.9, 149.0, 149.1, 151.6; MS (ESI) *m*/*z* calcd for $C_{18}H_{24}ClN_3$ 317.2. Found $(M + H)^+$: 318.2.

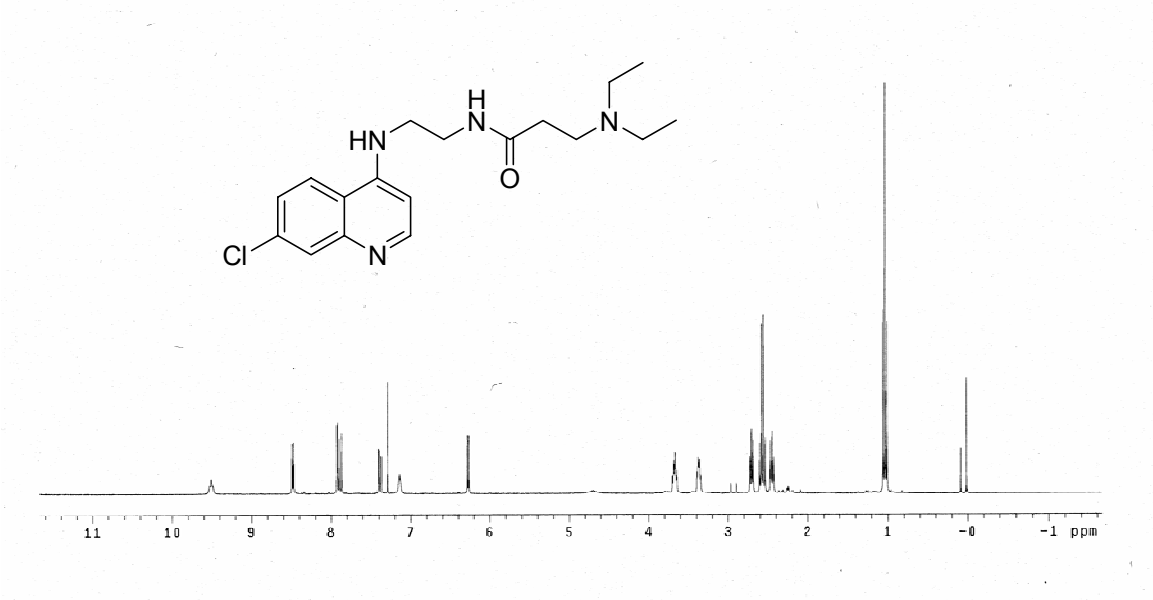


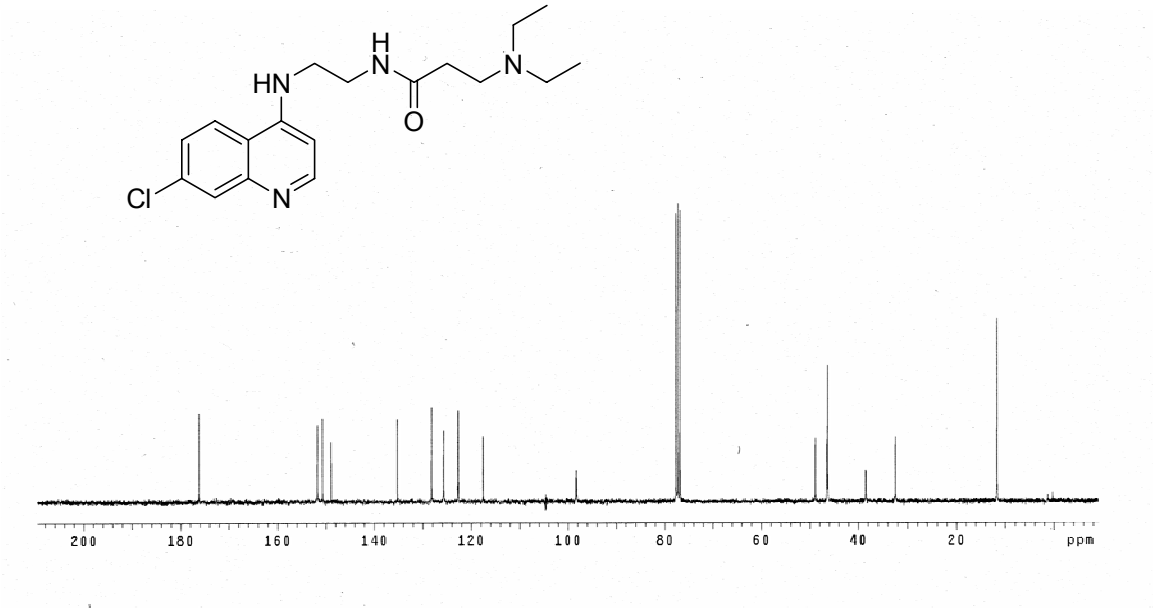
***N*-(7-Chloro-4-quinolyl)-*N'*-isopropyl-1,4-diaminocyclohexane.** To a solution of *N*-(7-chloro-4-quinolyl)-1,4-diaminocyclohexane (0.1 g, 0.36 mmol), acetone (0.13 mL, 1.8 mmol) and glacial acetic acid (0.04 mL, 0.72 mmol) in anhydrous CH_2Cl_2, sodium triacetoxyborohydride (0.23 g, 1.1 mmol) was added at room temperature and stirred for 2 h. The reaction mixture was quenched with water, basified with 1N NaOH and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography using 100% MeOH as the mobile phase gave colorless crystals (0.07 g, 0.22 mmol, 64% yield). ^{1}H-

NMR (300 MHz, $CDCl_3$) δ = 1.05 (m, 6H, *cis* + *trans*), 1.43-1.60 (m, 2H, *cis* + *trans*), 1.67-1.96 (m, 6H, *cis* + *trans*), 2.80 (m, 1H, *cis* + *trans*), 2.90 (m, 1H, *cis* + *trans*), 3.70 (s, 1H, *cis* + *trans*), 5.14 (d, *J* = 6.6 Hz, 1H, *cis* + *trans*), 6.38 (m, 1H, *cis* + *trans*), 7.30 (m, 1H, *cis* + *trans*), 7.64 (dd, *J* = 2.4 Hz, *J* = 9.0 Hz, 1H, *cis* + *trans*), 7.92 (m, 1H, *cis* + *trans*), 8.48 (m, 1H, *cis* + *trans*); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 23.3, 27.5, 28.7, 44.9, 48.1, 50.8, 99.1, 117.0, 120.7, 124.9, 128.6, 134.6, 148.3, 149.1, 151.7; MS (ESI) *m*/*z* calcd for $C_{18}H_{24}ClN_3$ 317.2. Found $(M + H)^+$: 318.1.

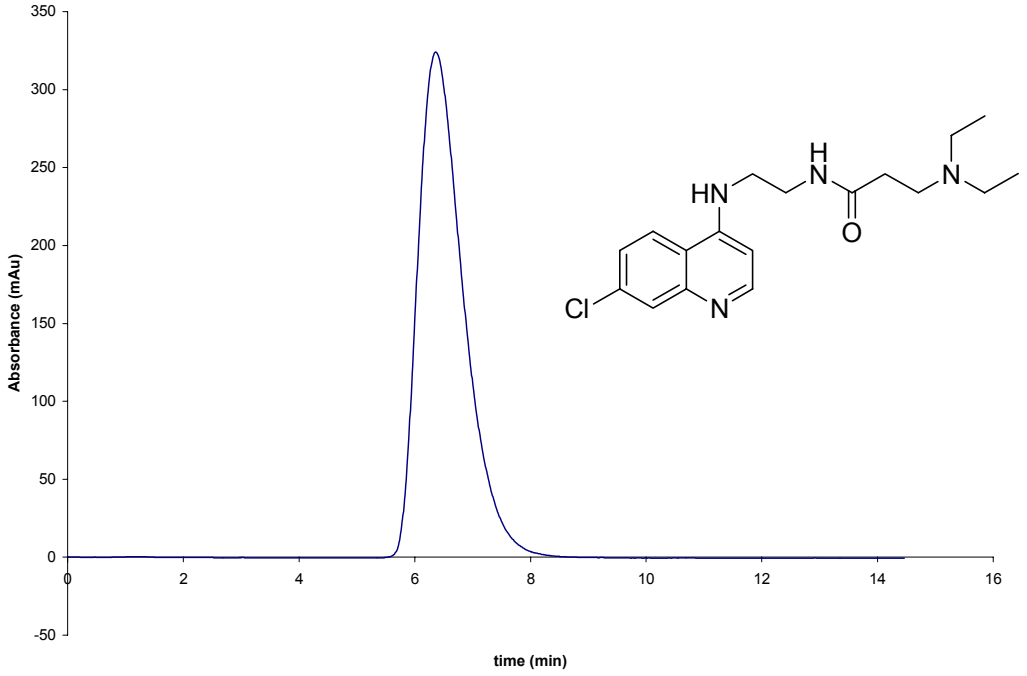
3) NMR Spectra and HPLC Chromatograms

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,2-diaminoethane

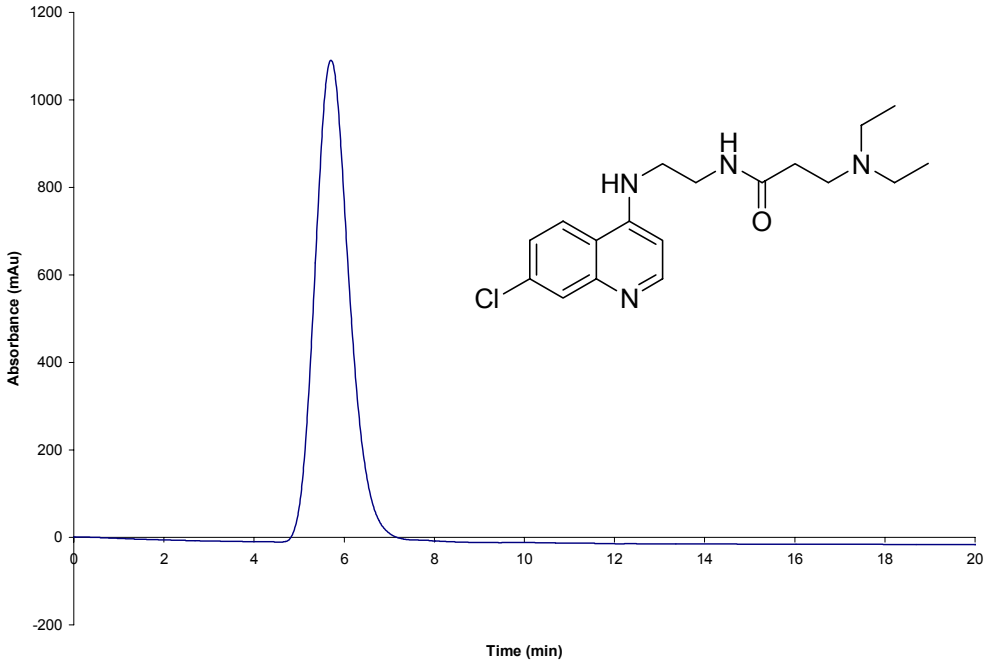




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,2-diaminoethane

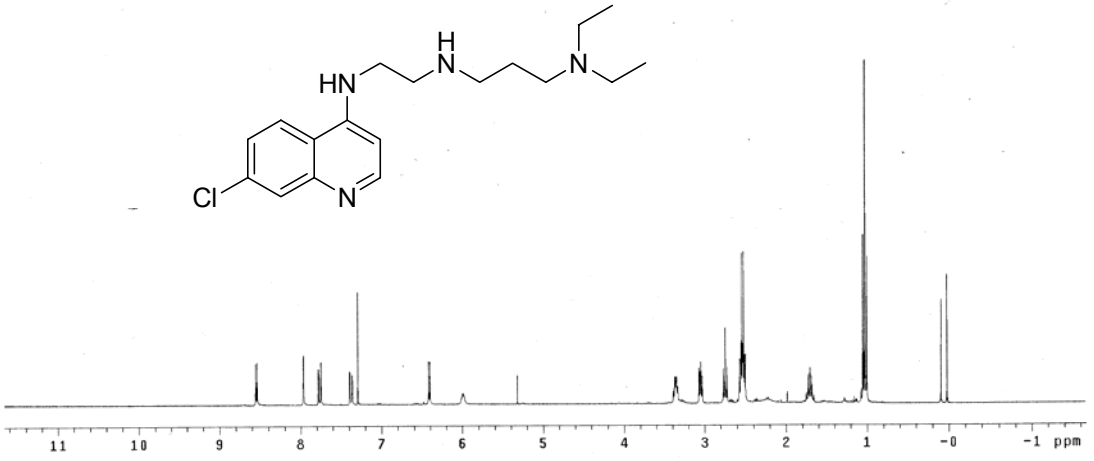


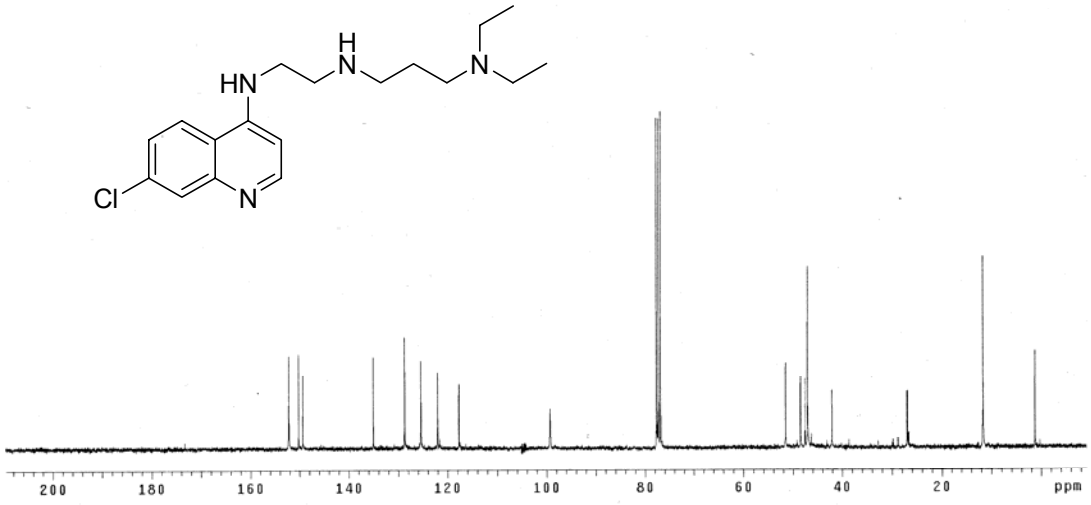
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



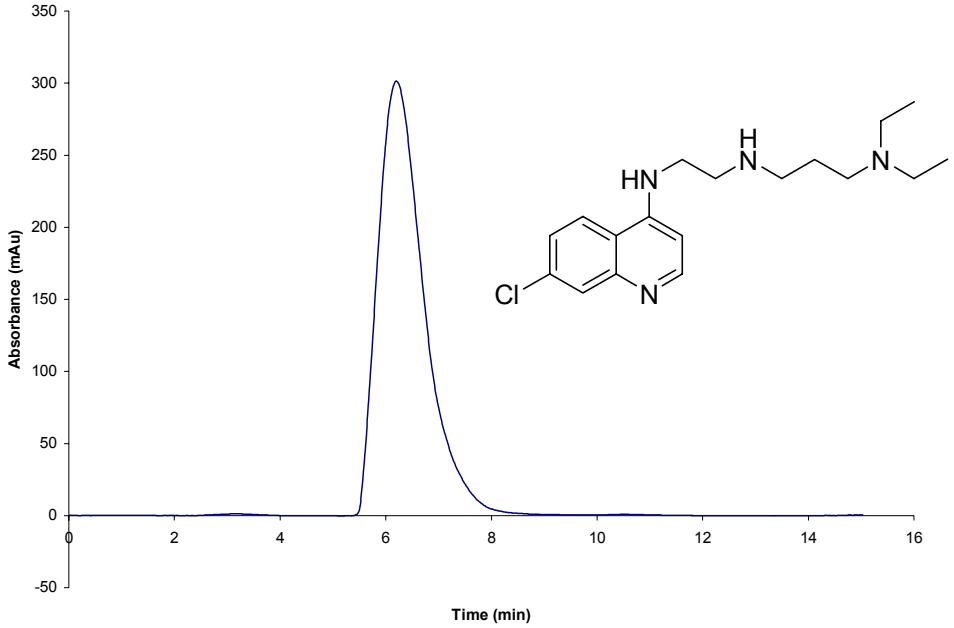
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,2-diaminoethane

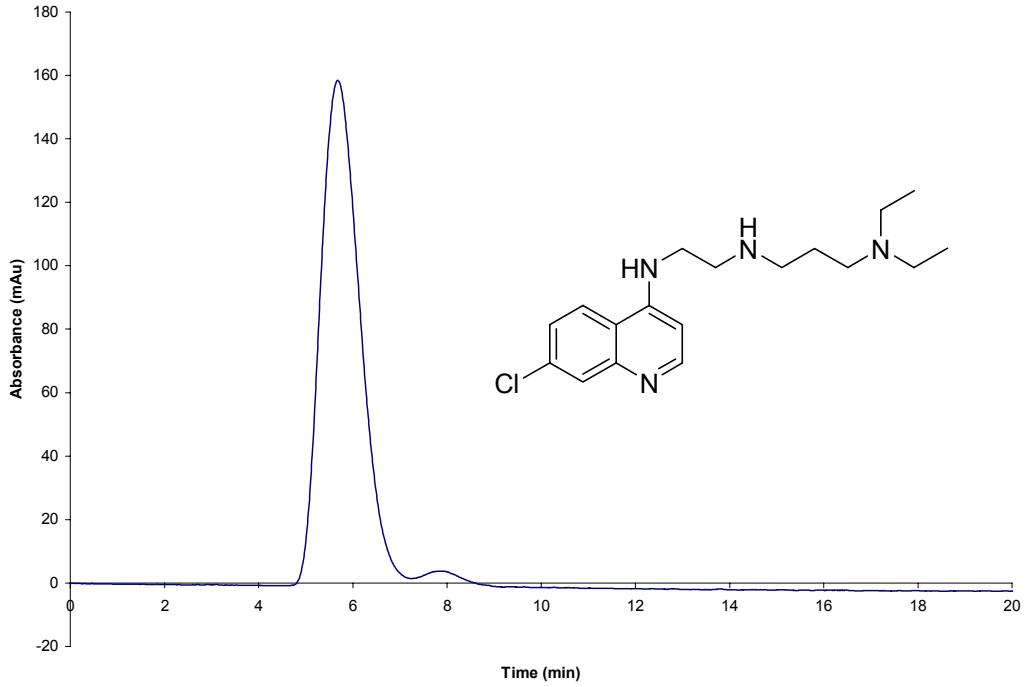




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,2-diaminoethane

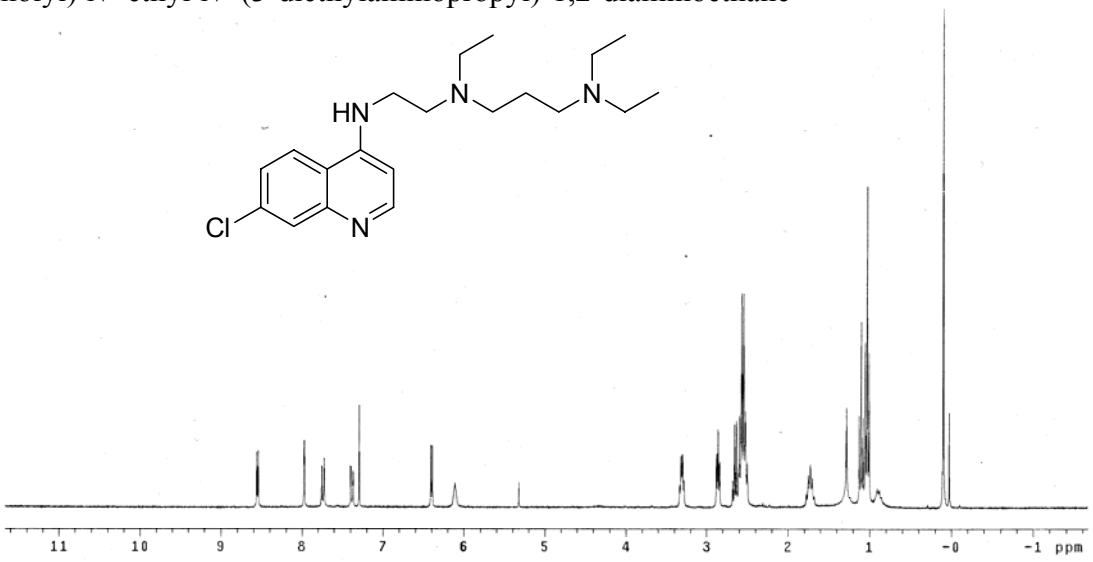


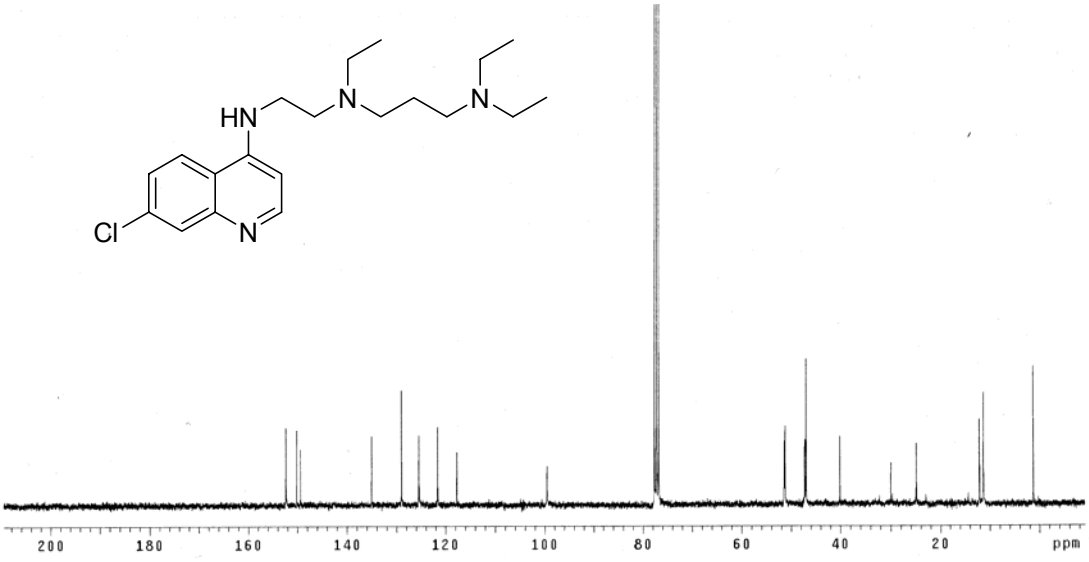
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



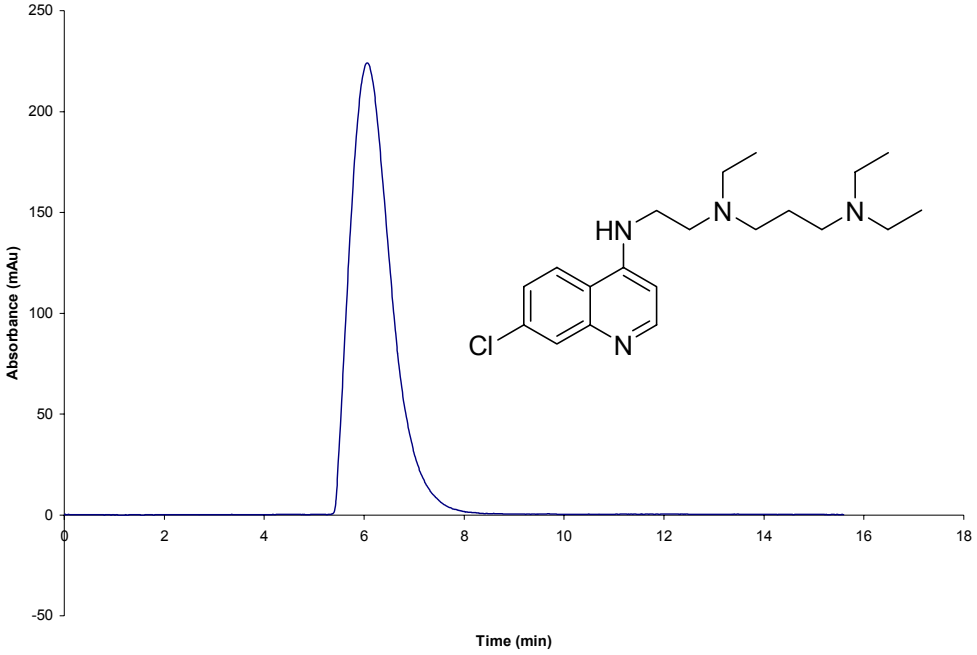
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,2-diaminoethane

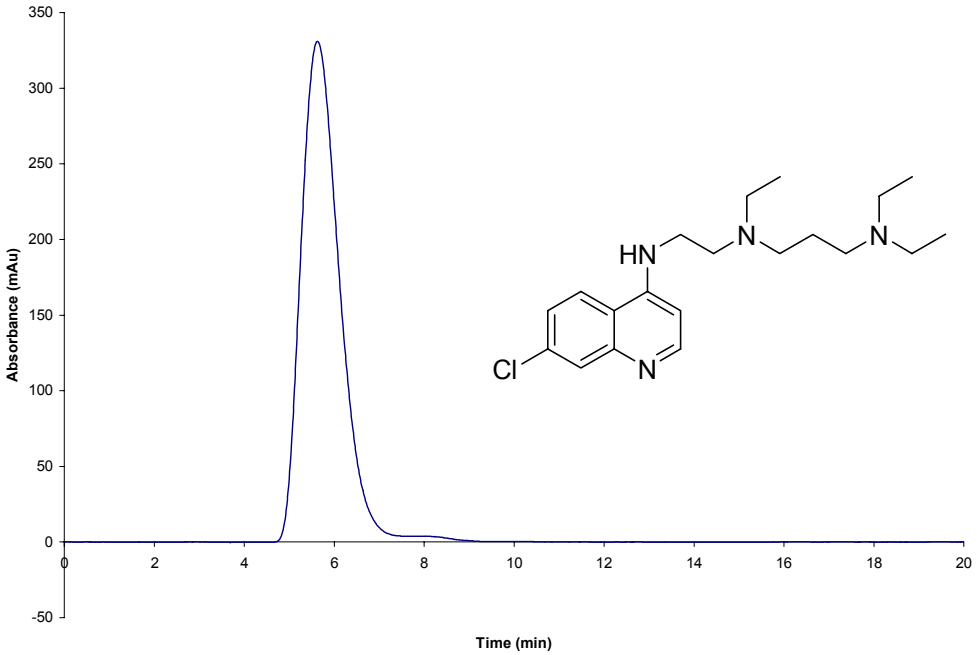




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,2-diaminoethane

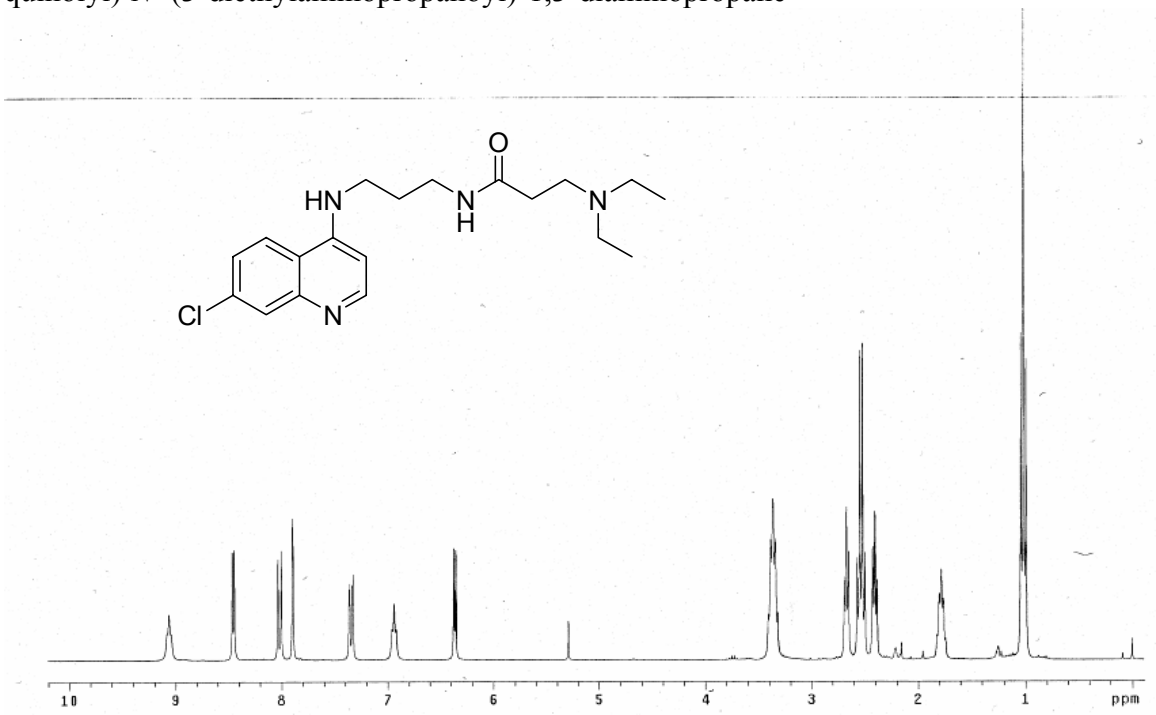


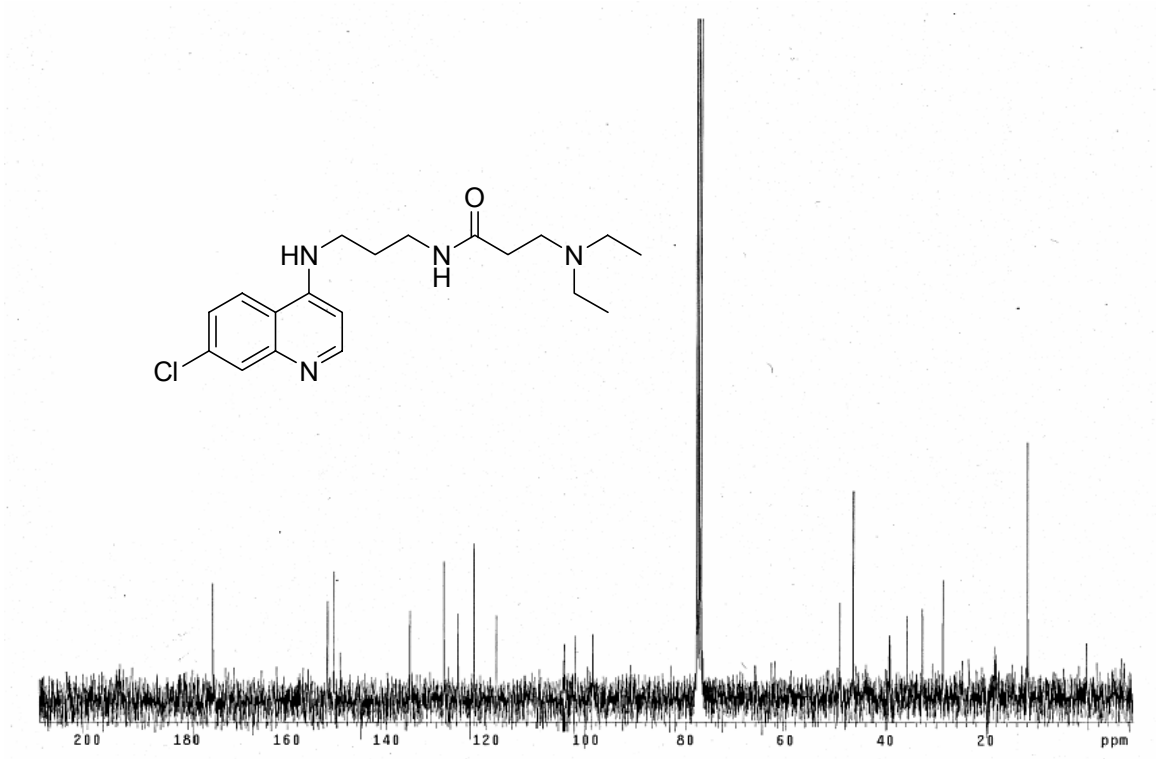
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



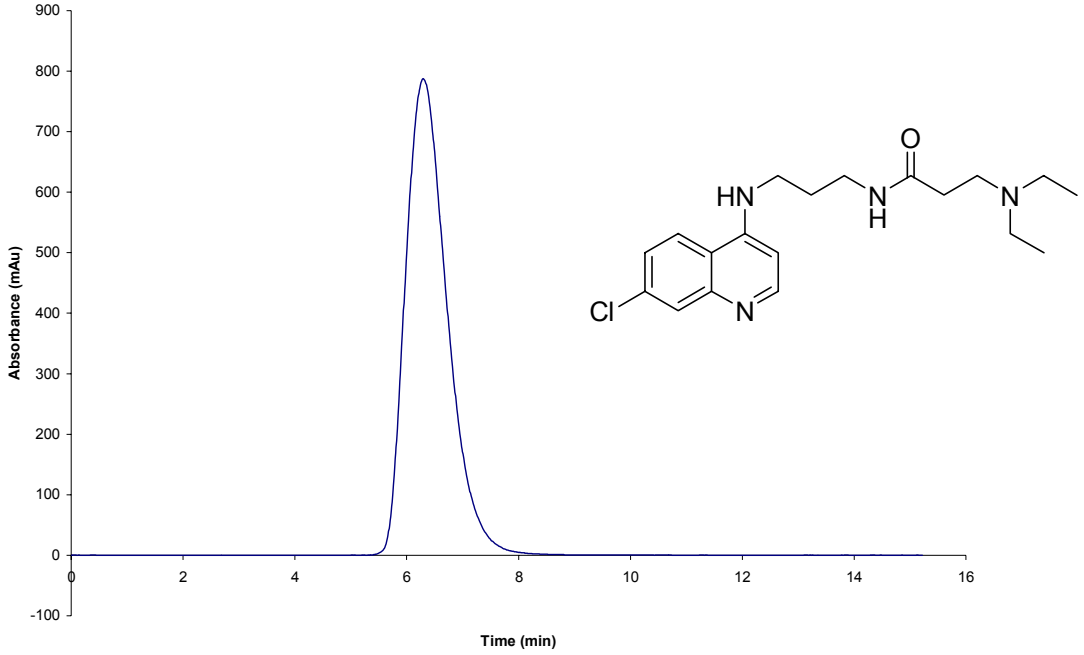
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,3-diaminopropane

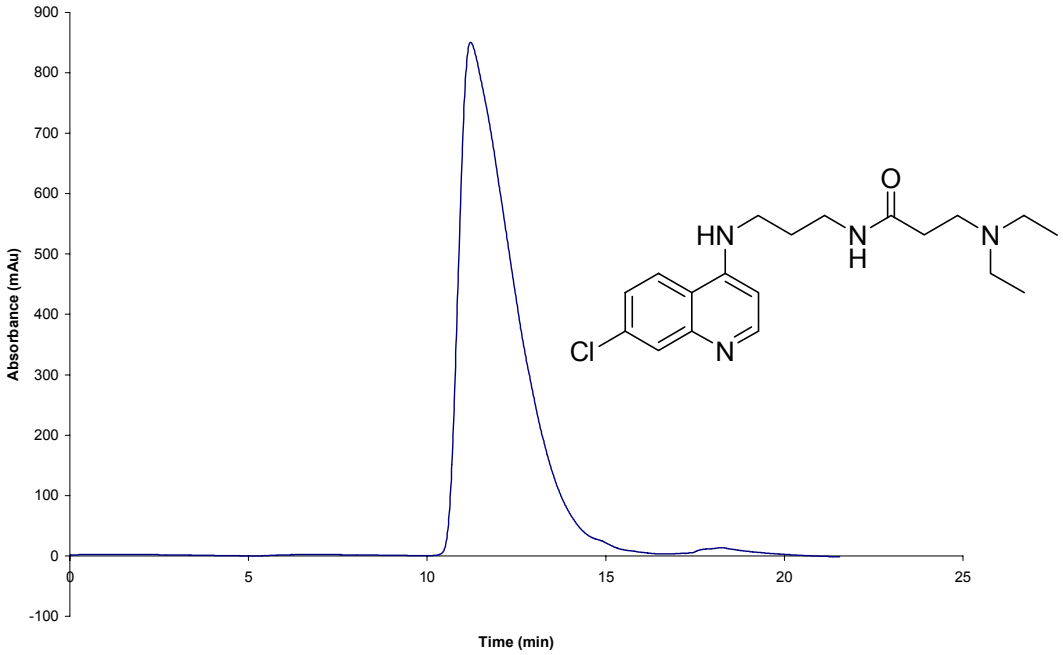




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,3-diaminopropane

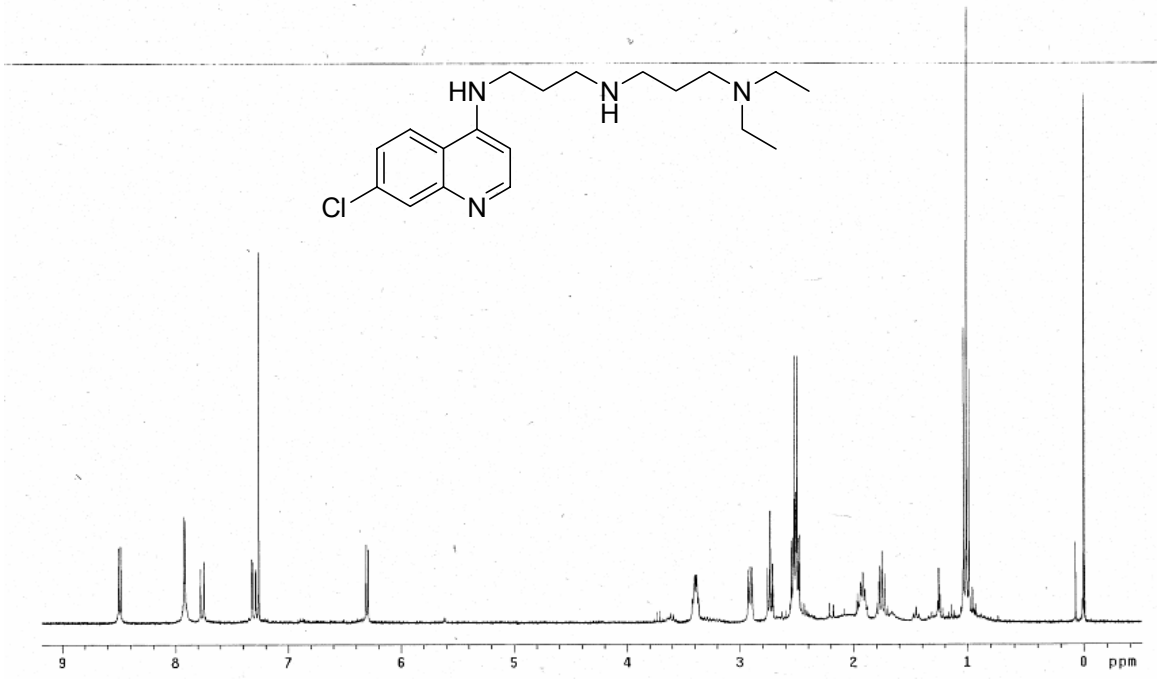


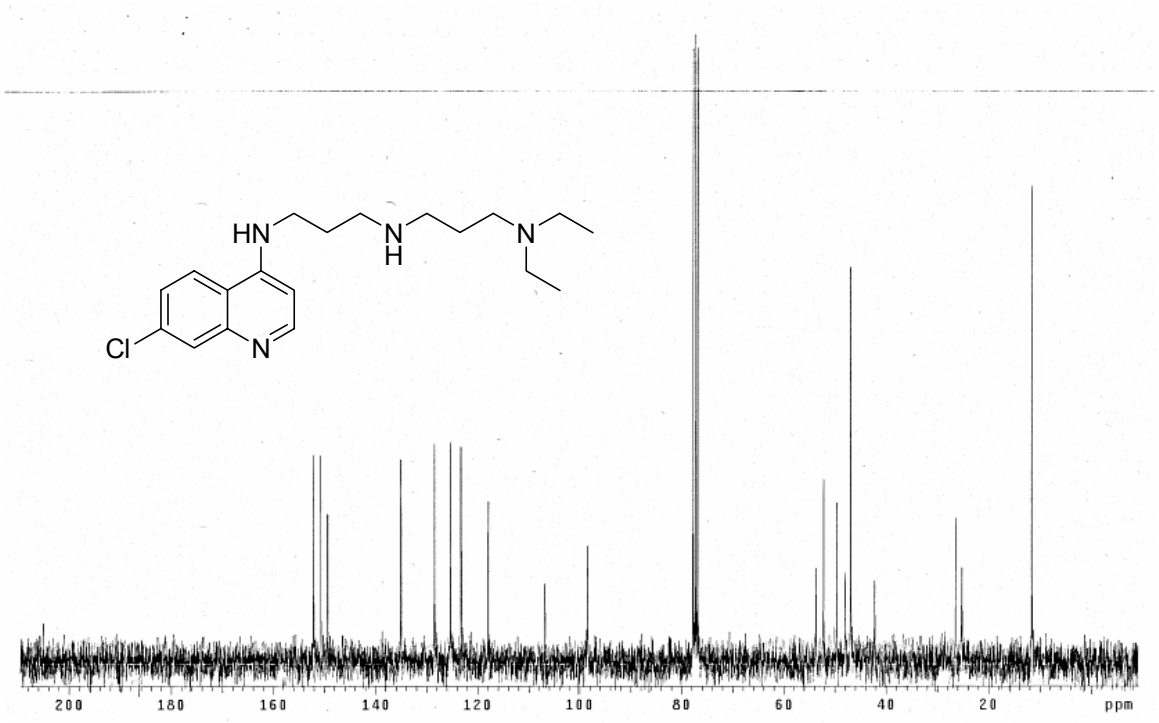
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



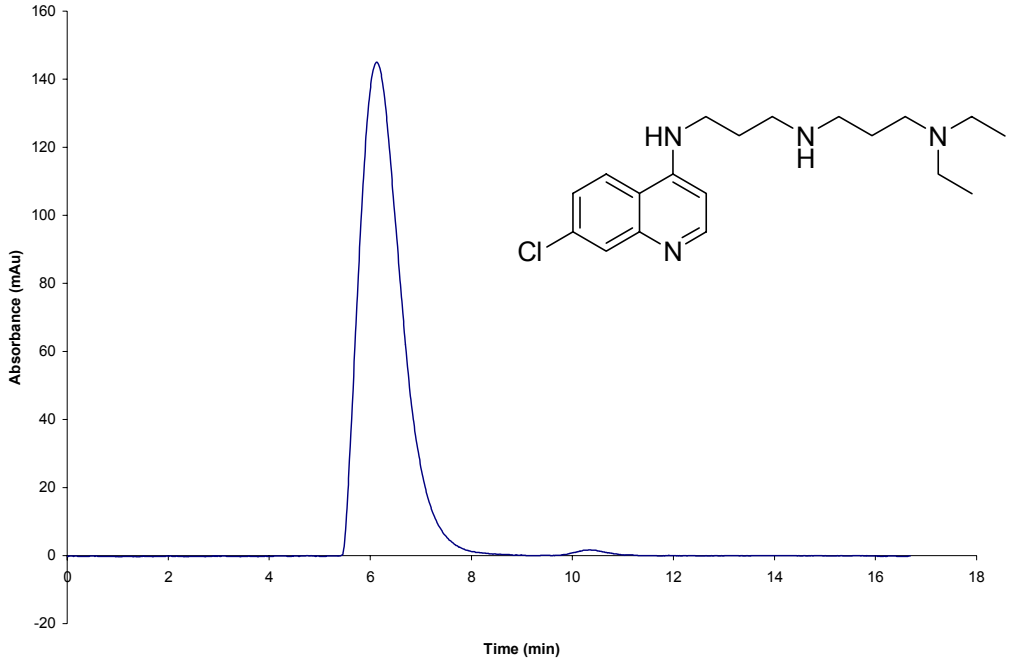
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,3-diaminopropane

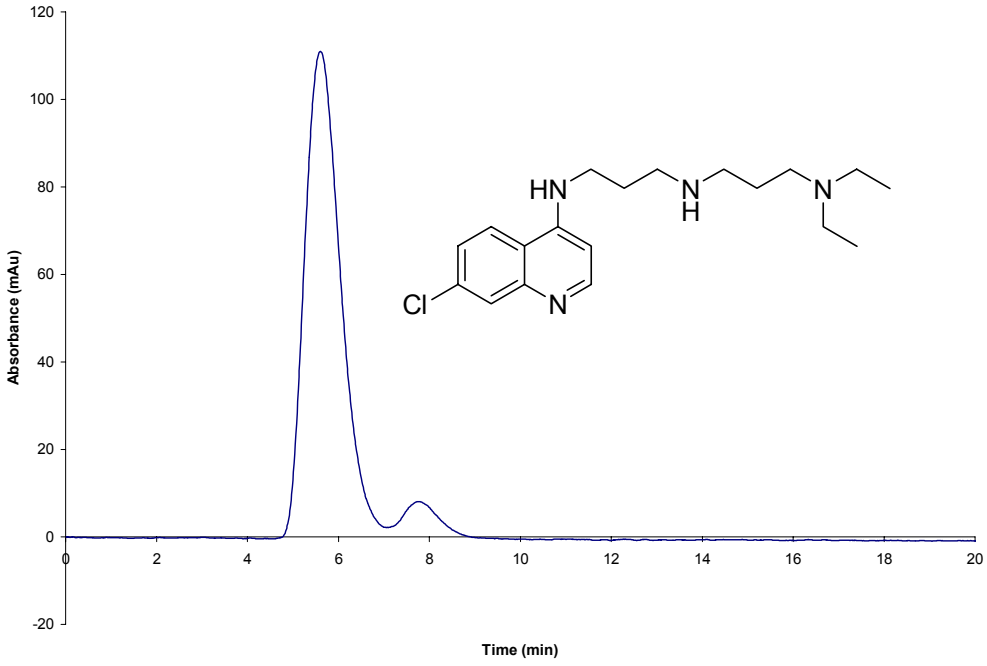




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,3-diaminopropane

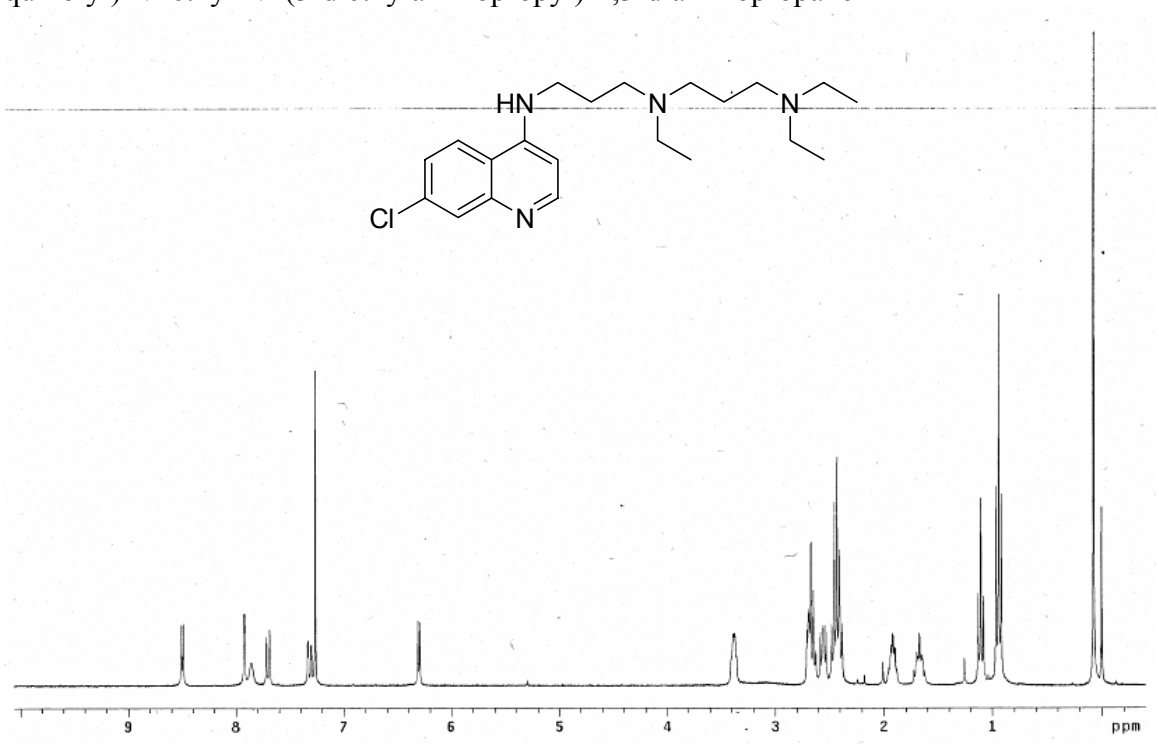


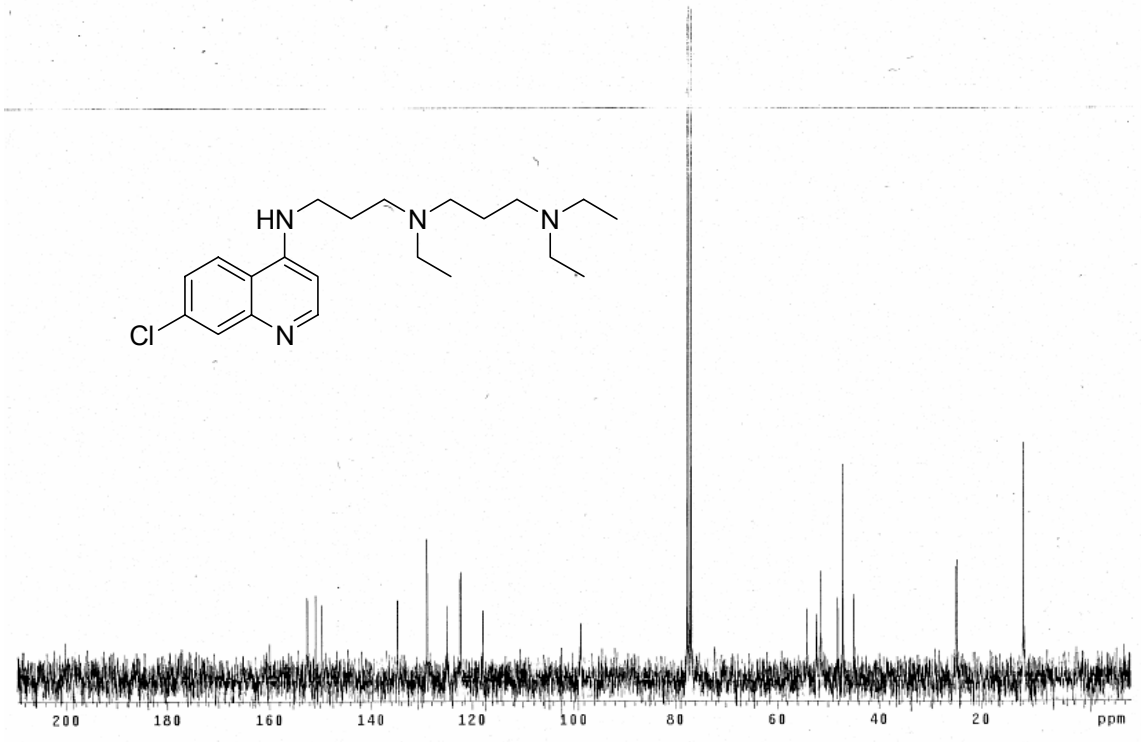
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



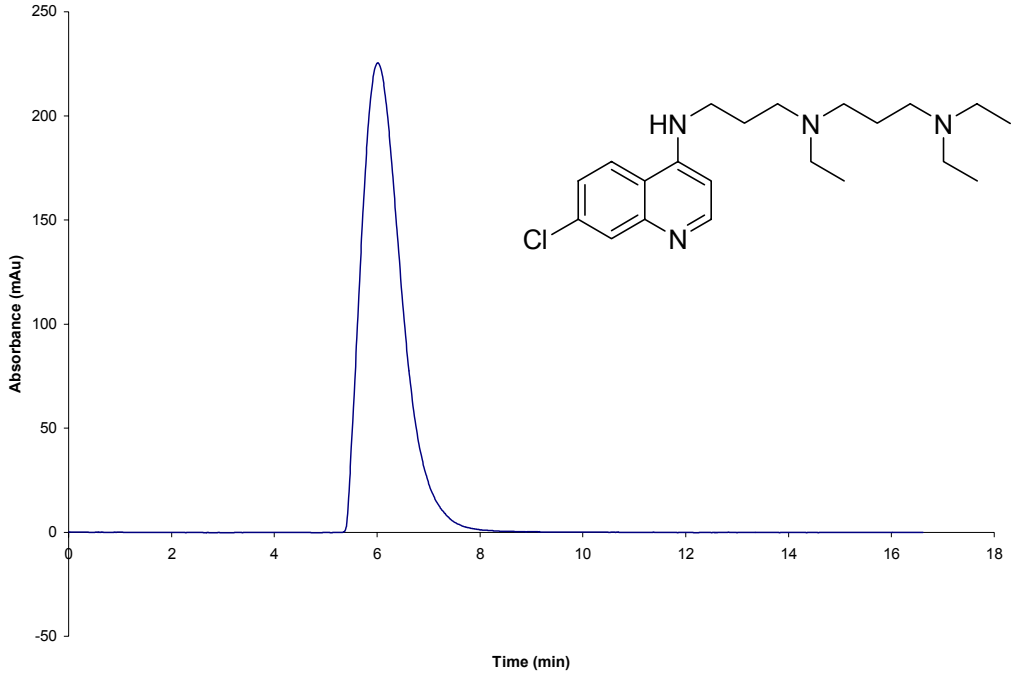
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,3-diaminopropane

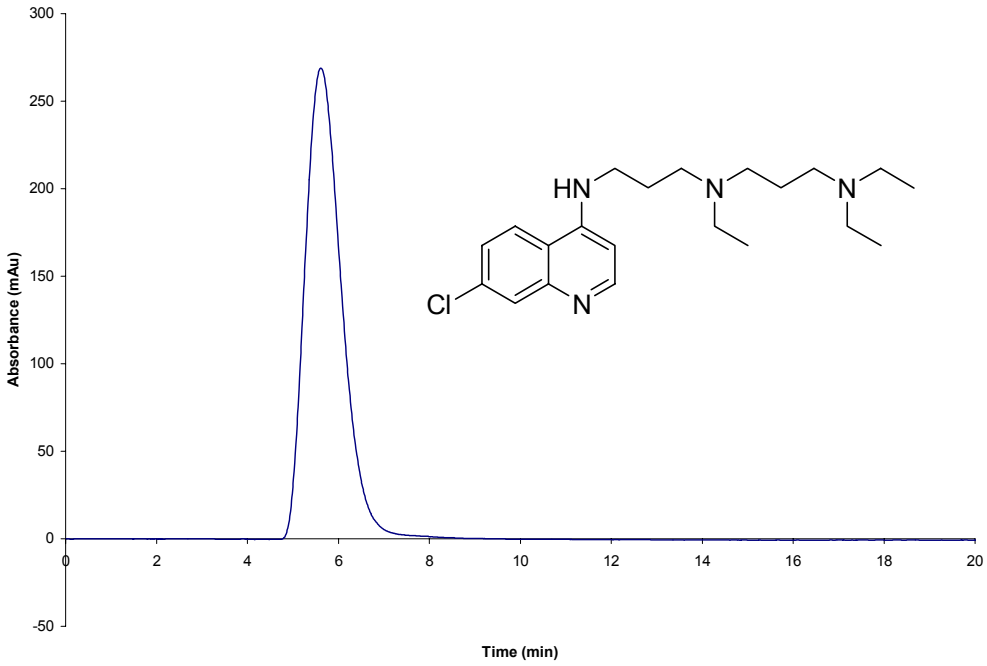




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,3-diaminopropane

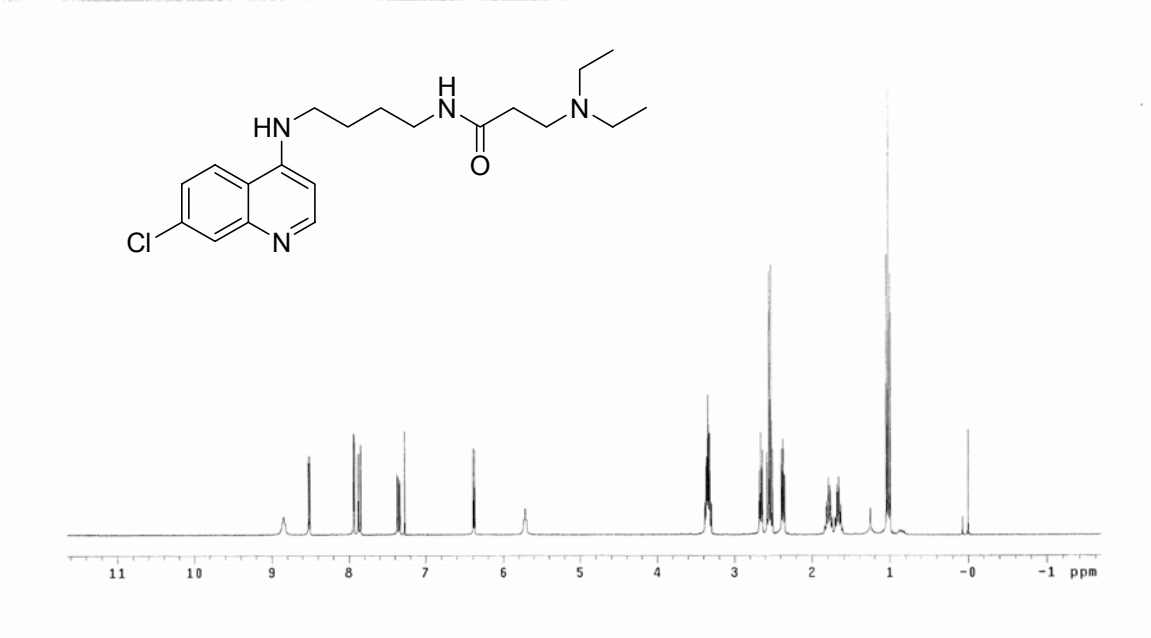


Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

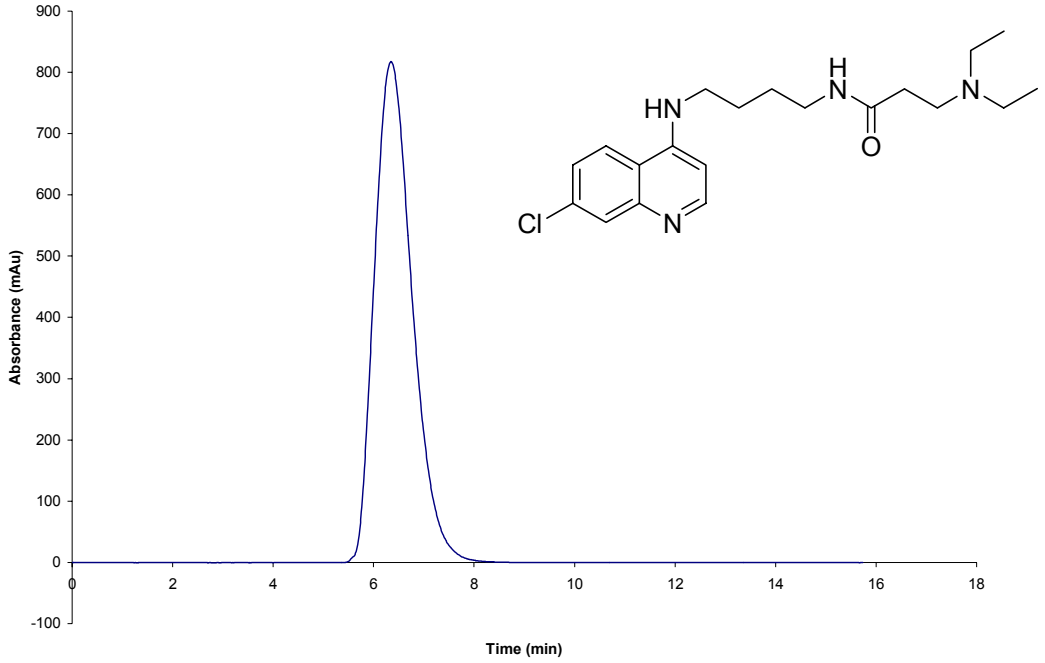


Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

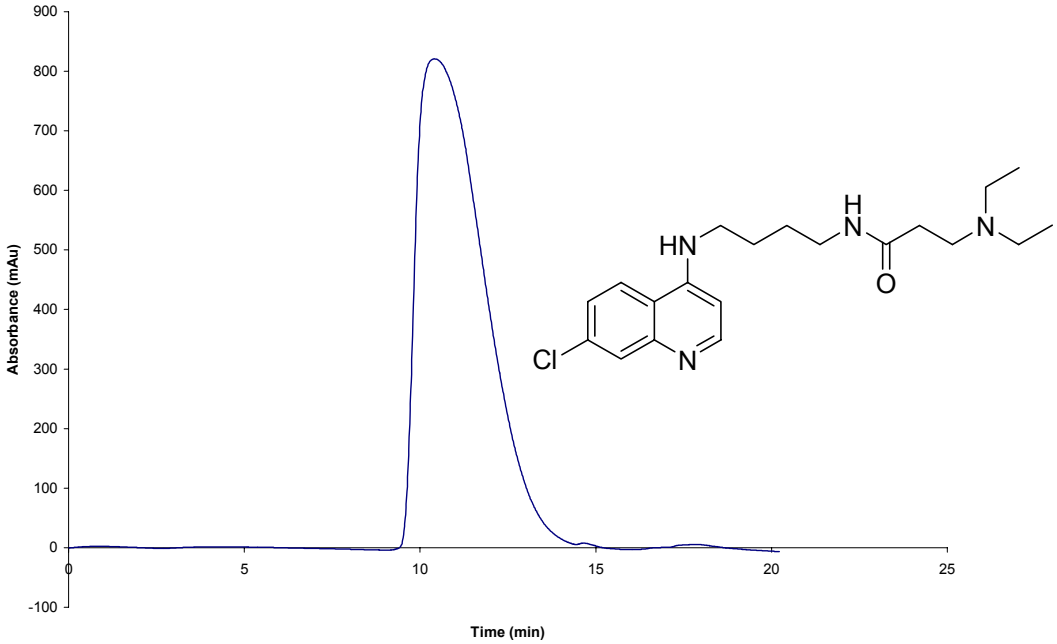
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,4-diaminobutane



HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,4-diaminobutane

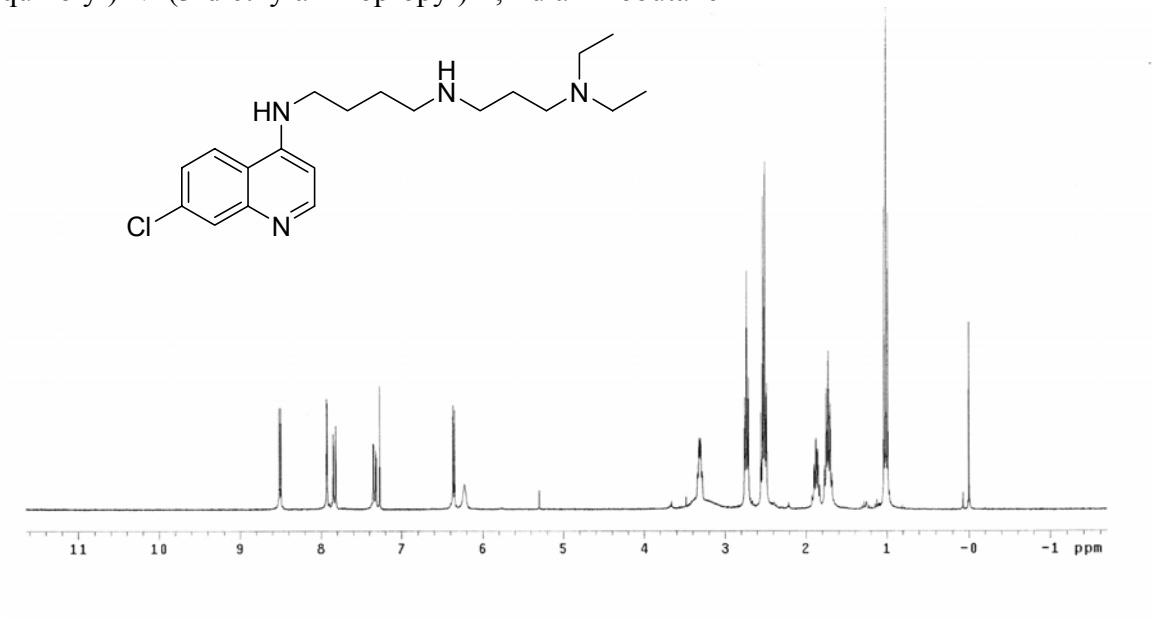


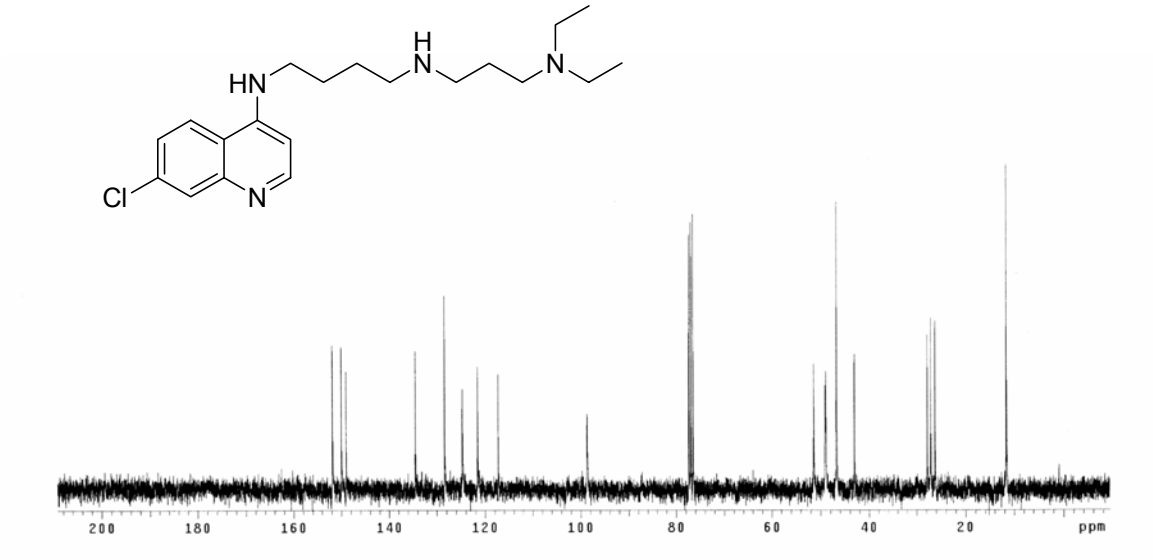
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



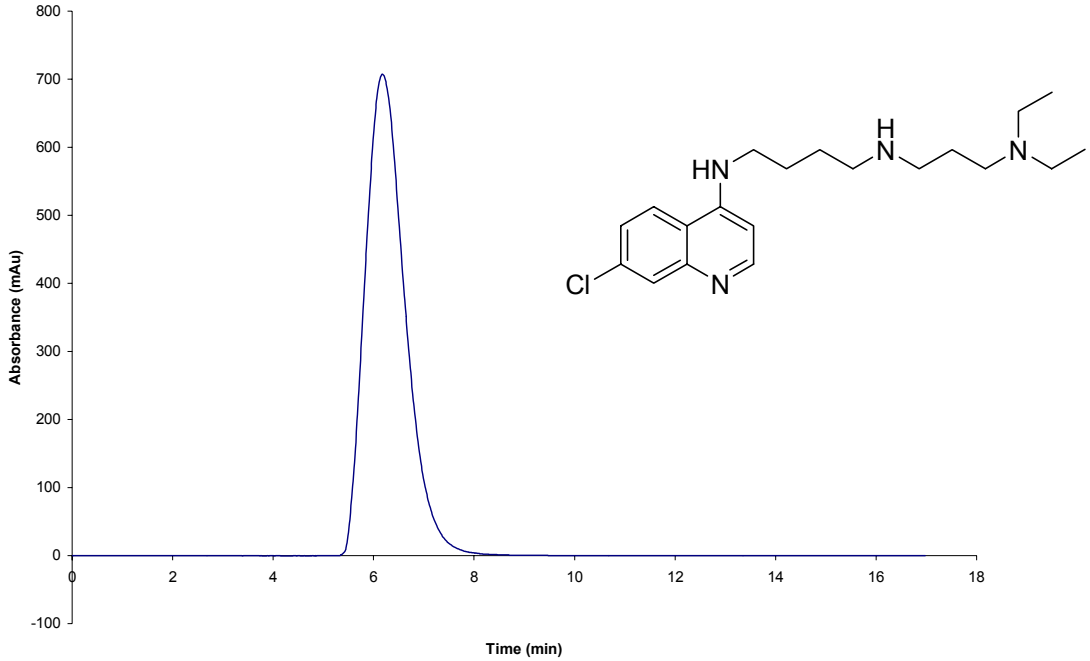
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,4-diaminobutane

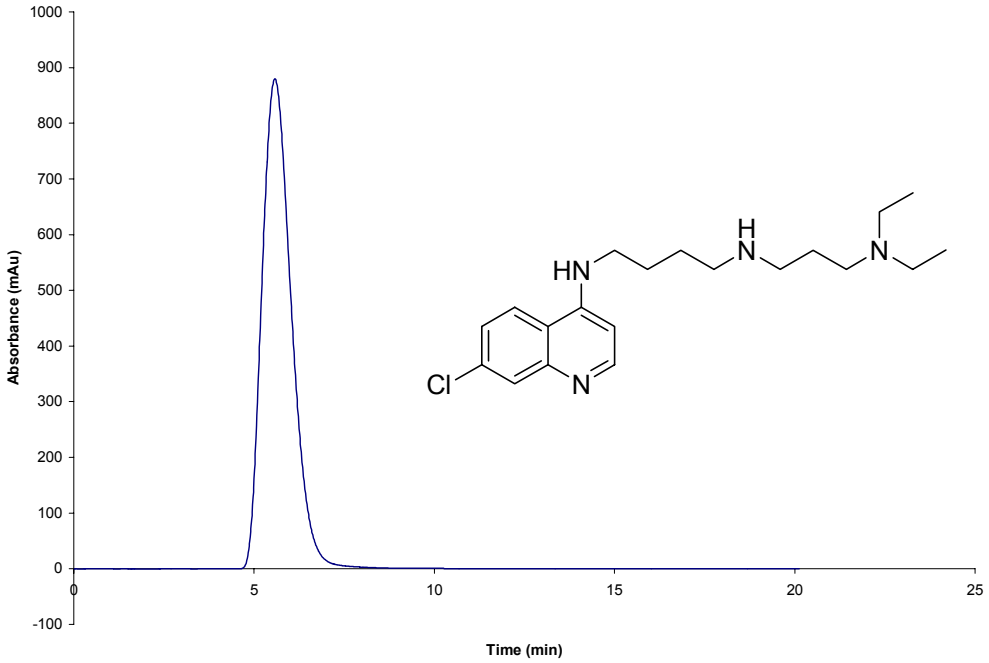




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,4-diaminobutane

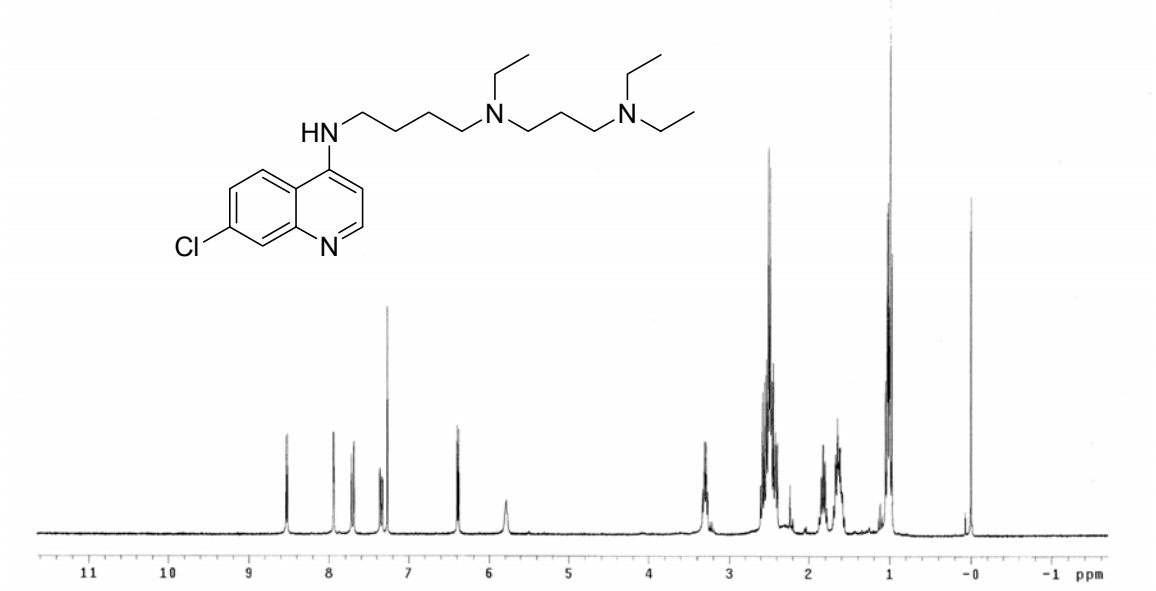


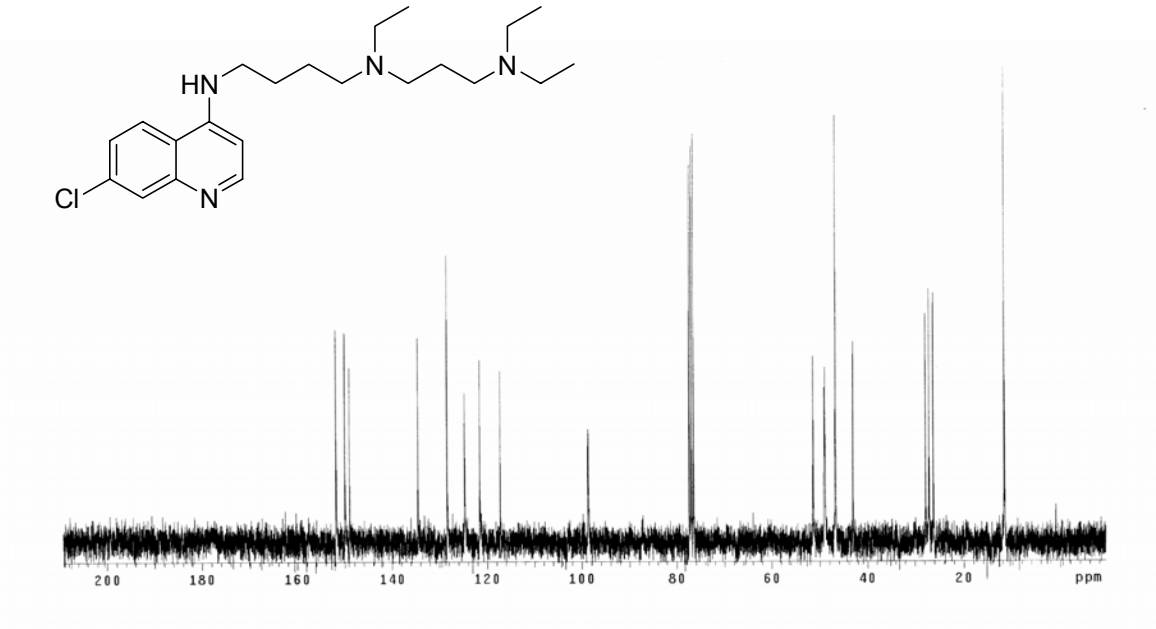
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



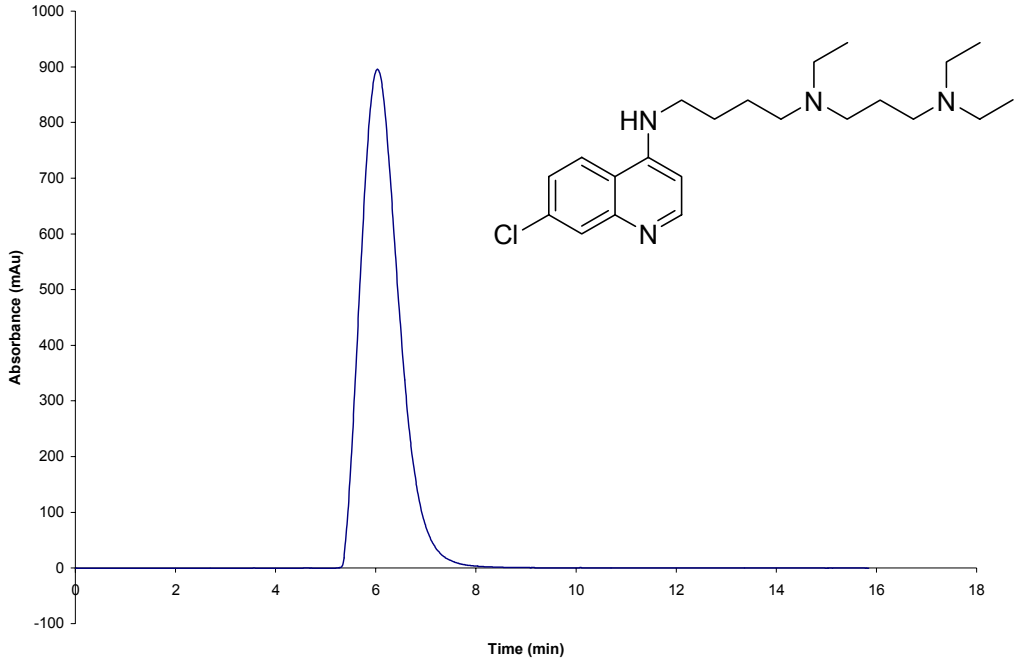
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,4-diaminobutane

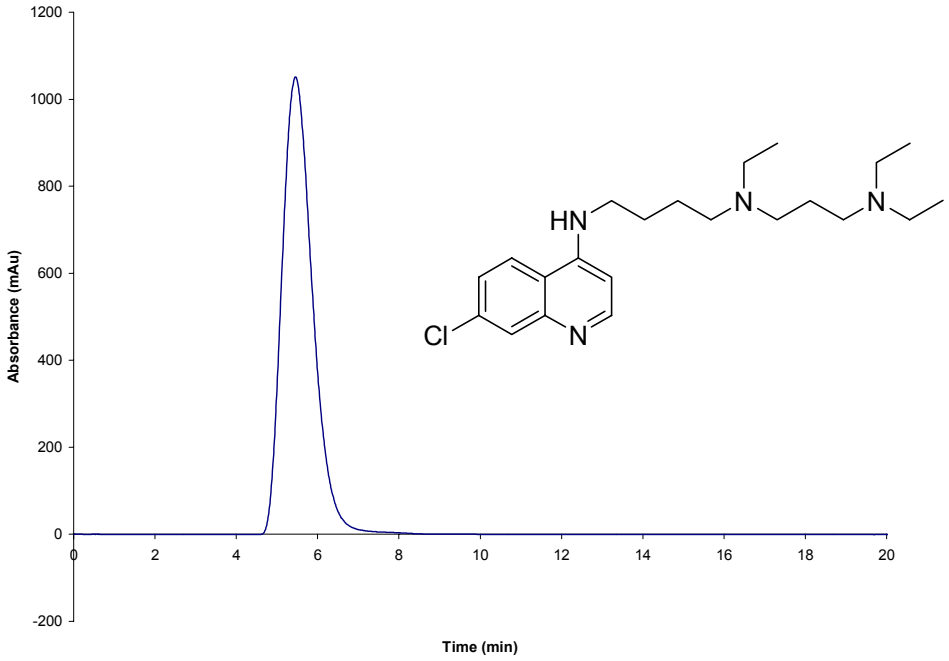




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,4-diaminobutane

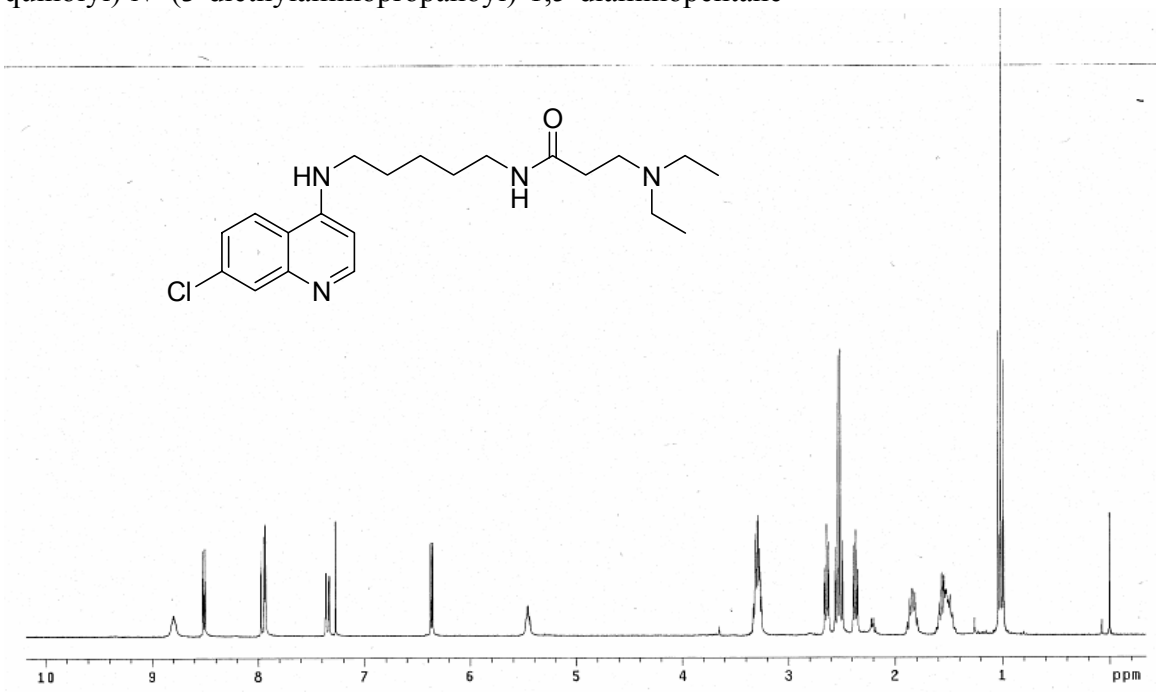


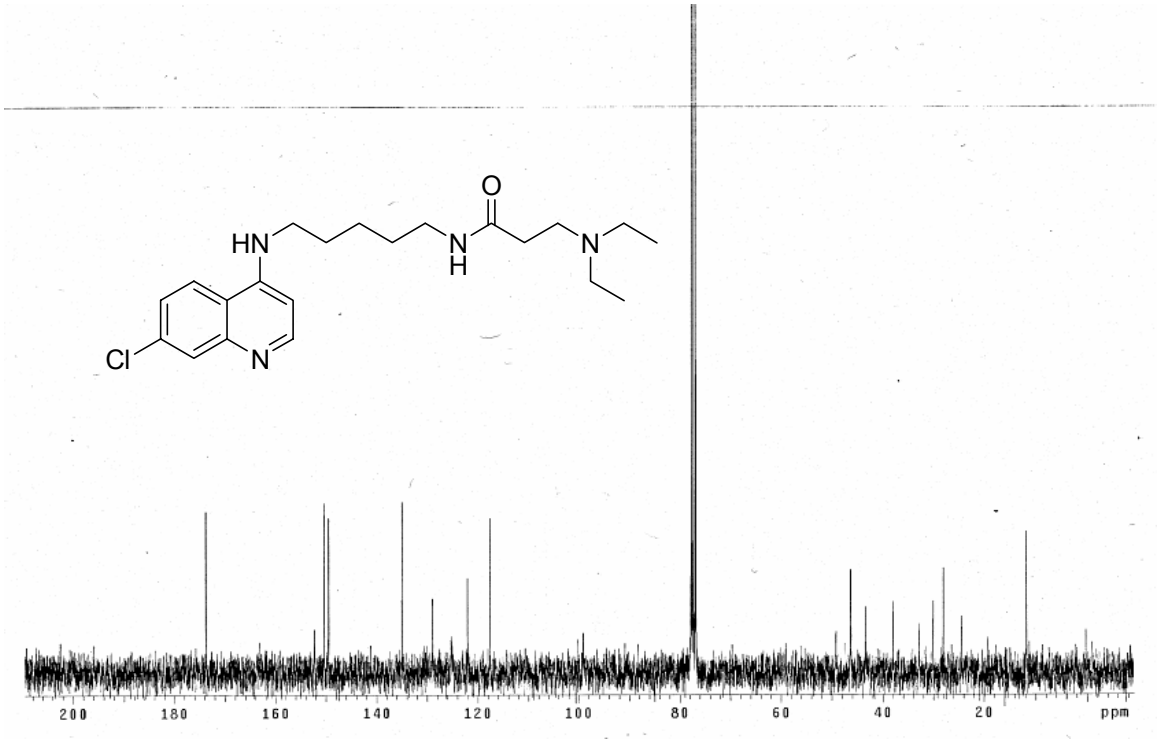
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



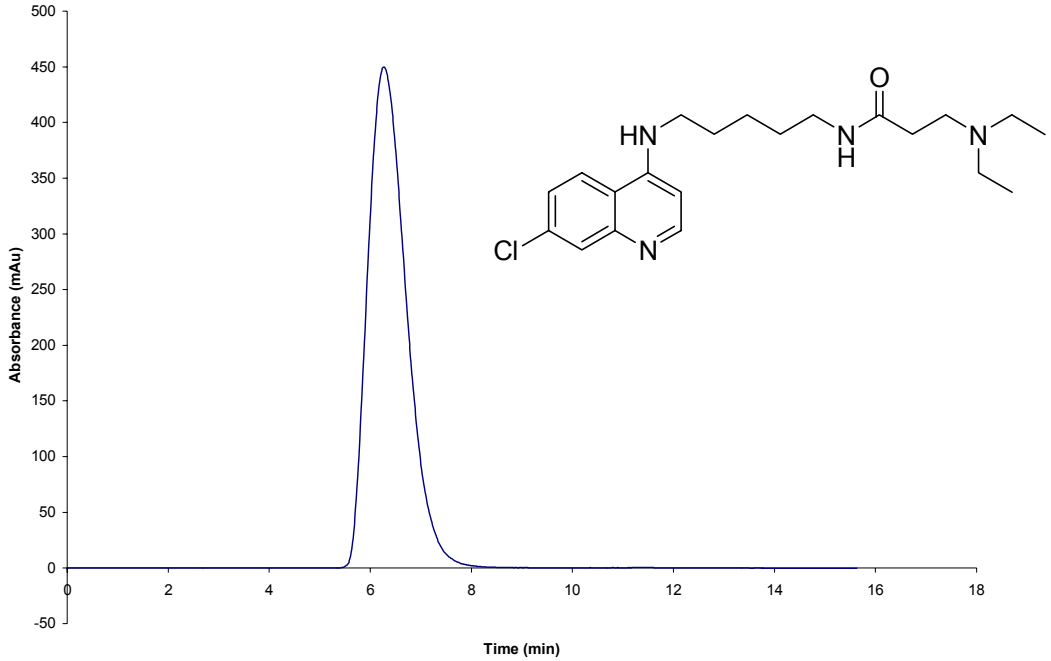
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,5-diaminopentane

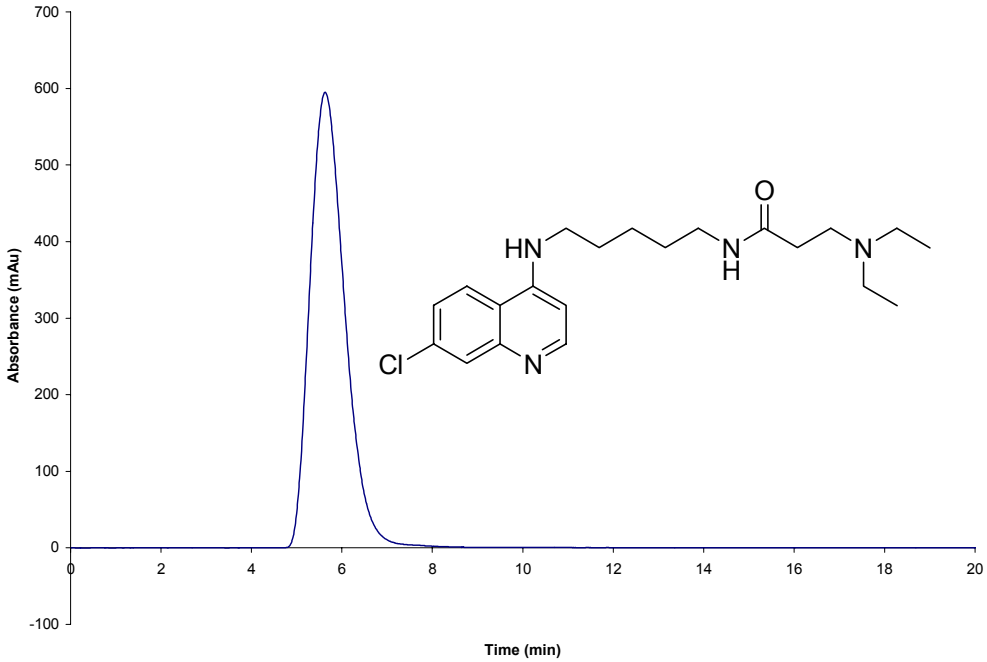




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,5-diaminopentane

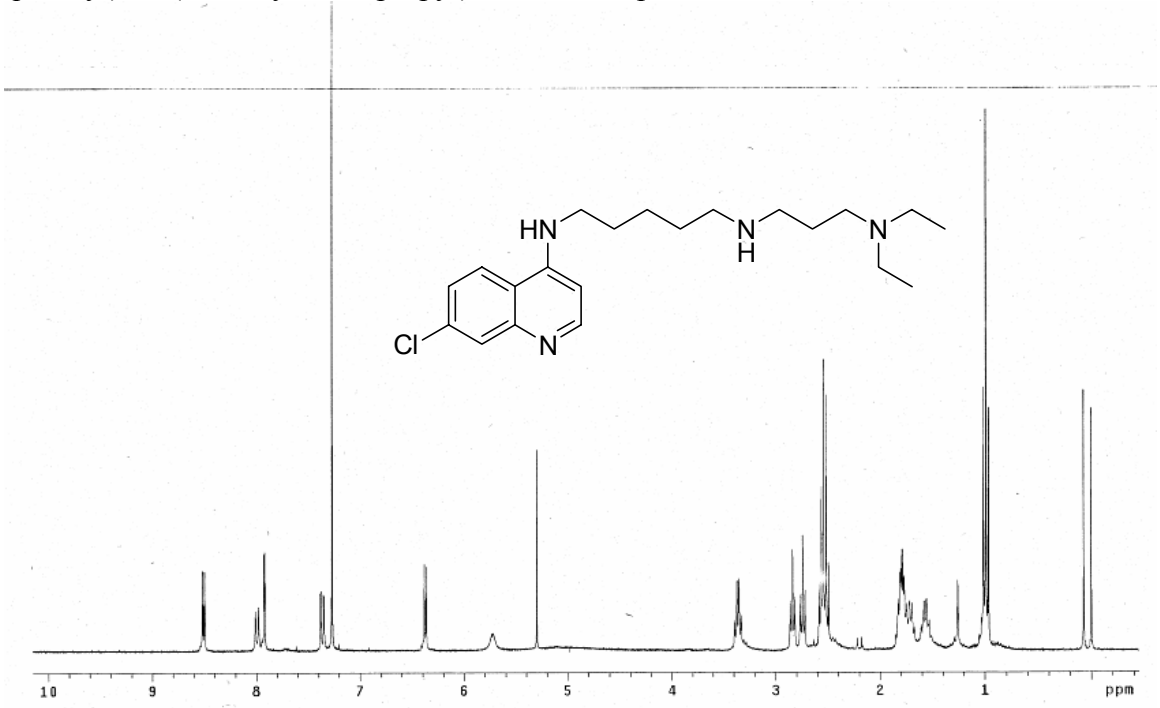


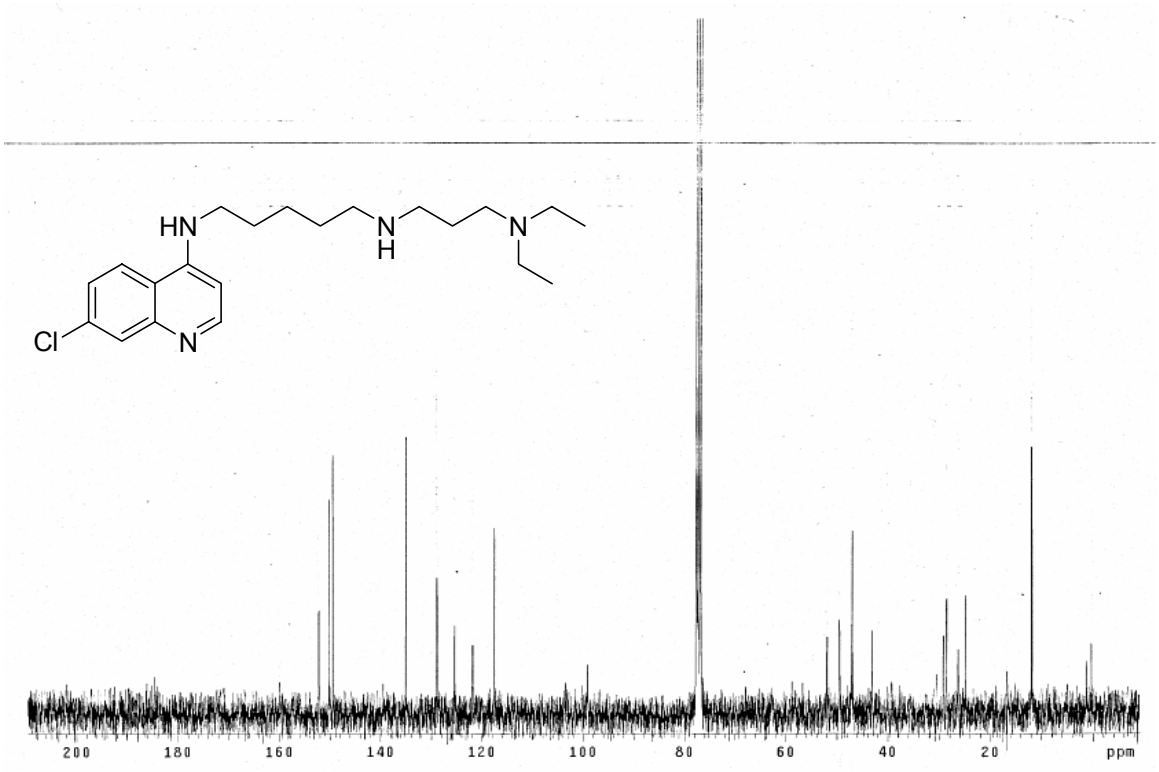
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



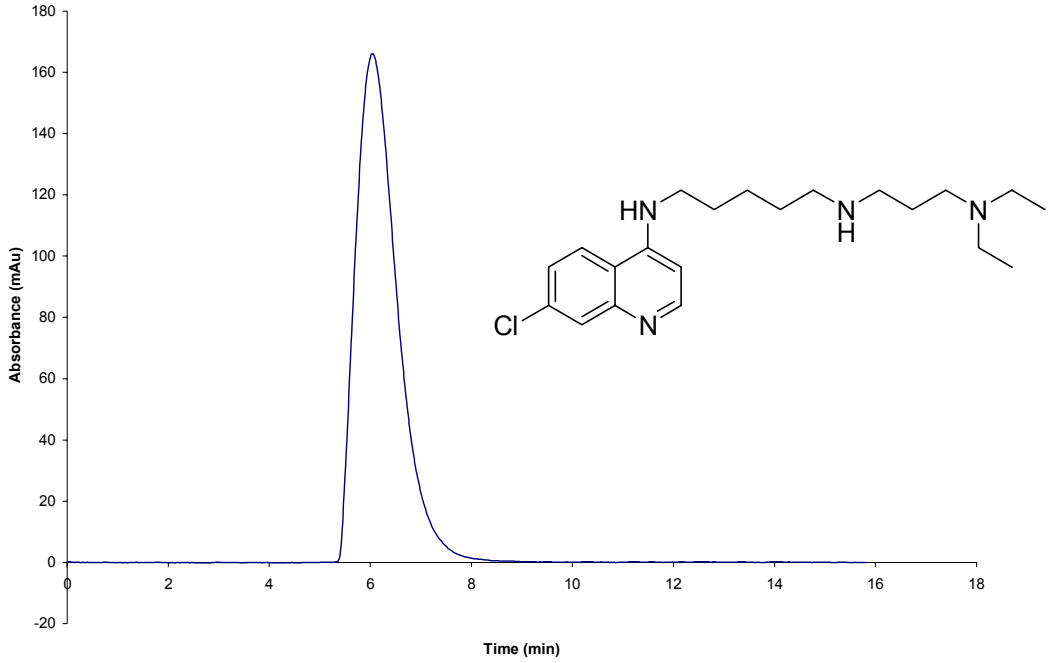
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,5-diaminopentane

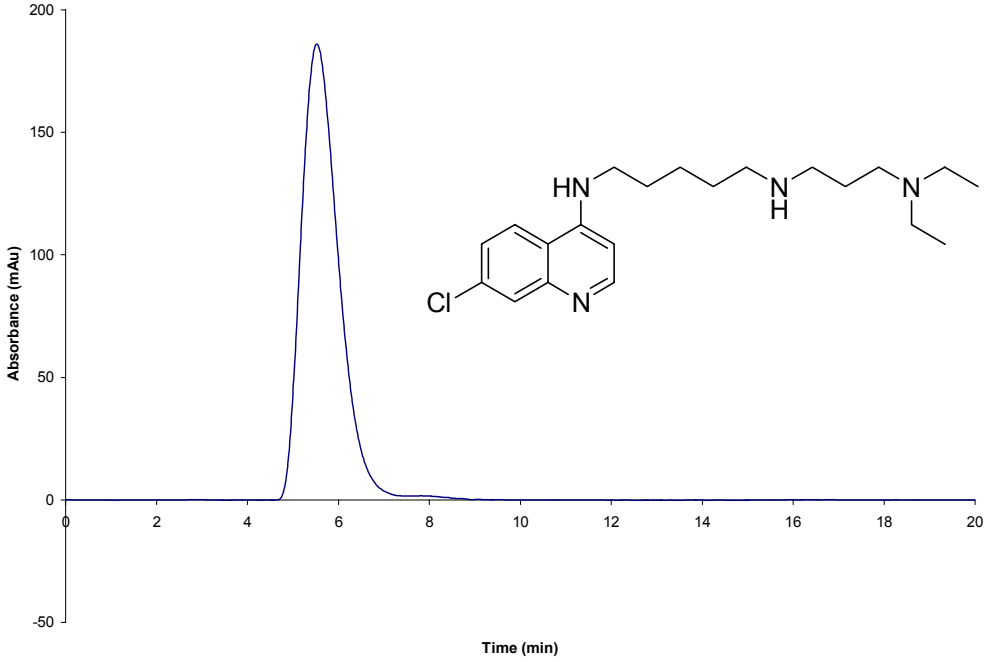




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,5-diaminopentane

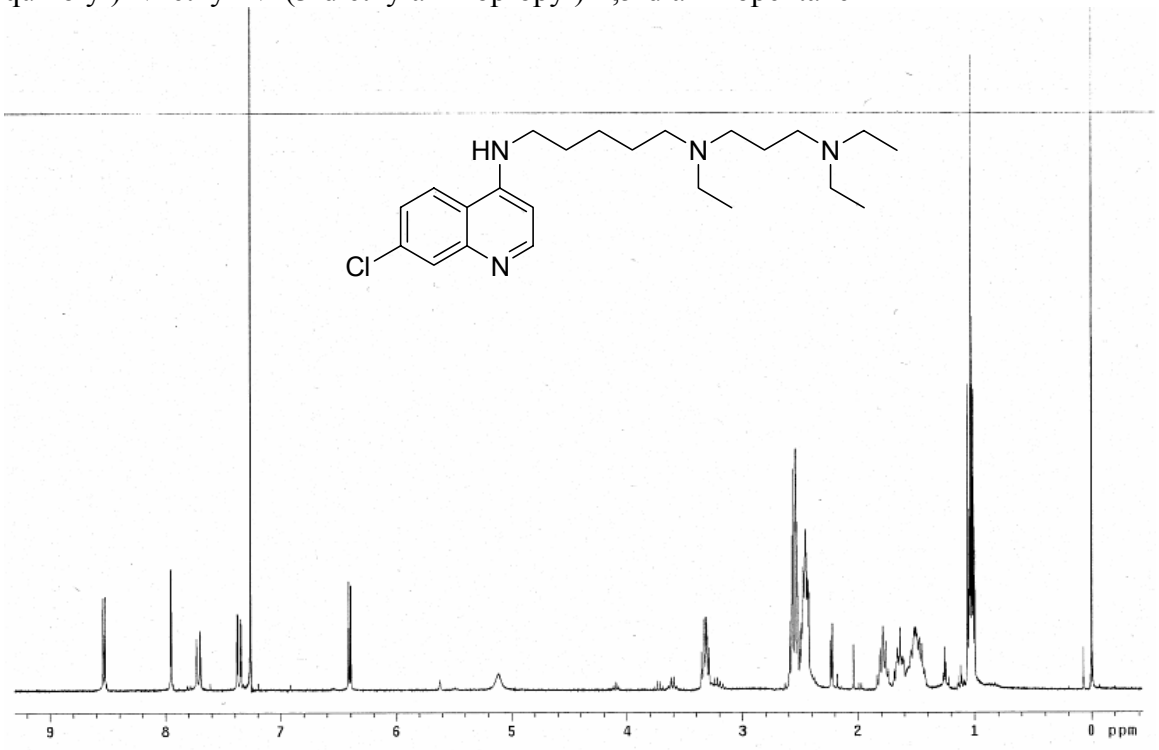


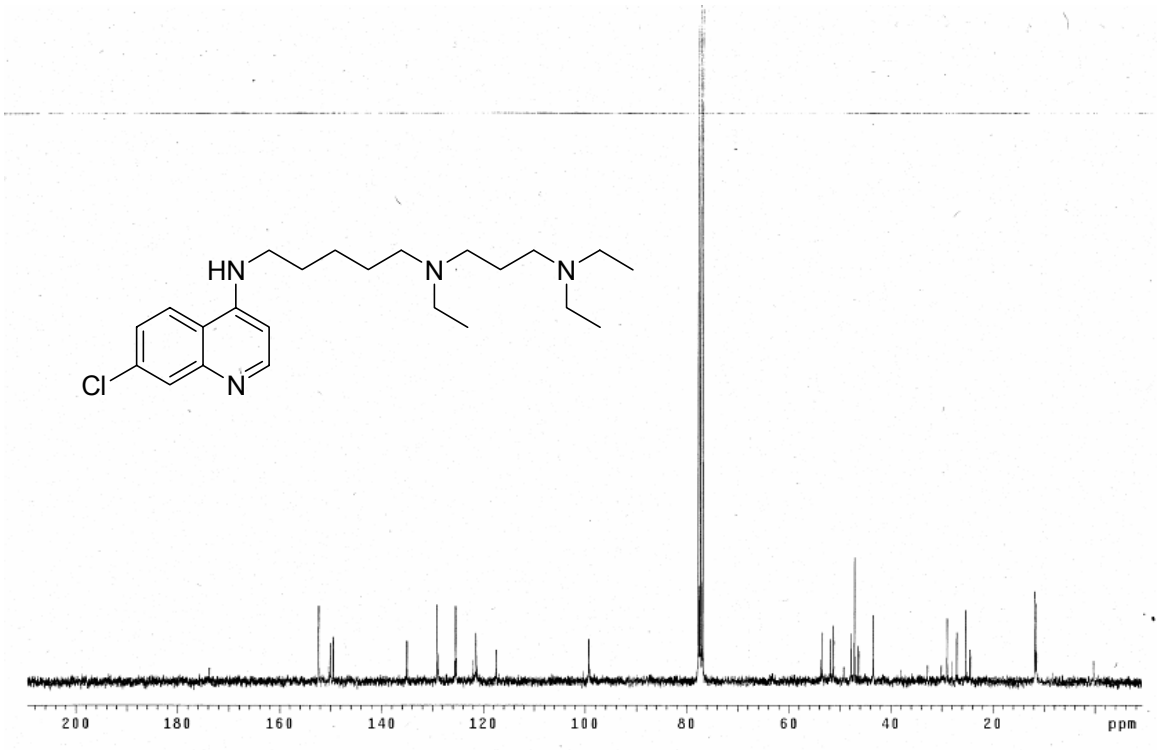
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



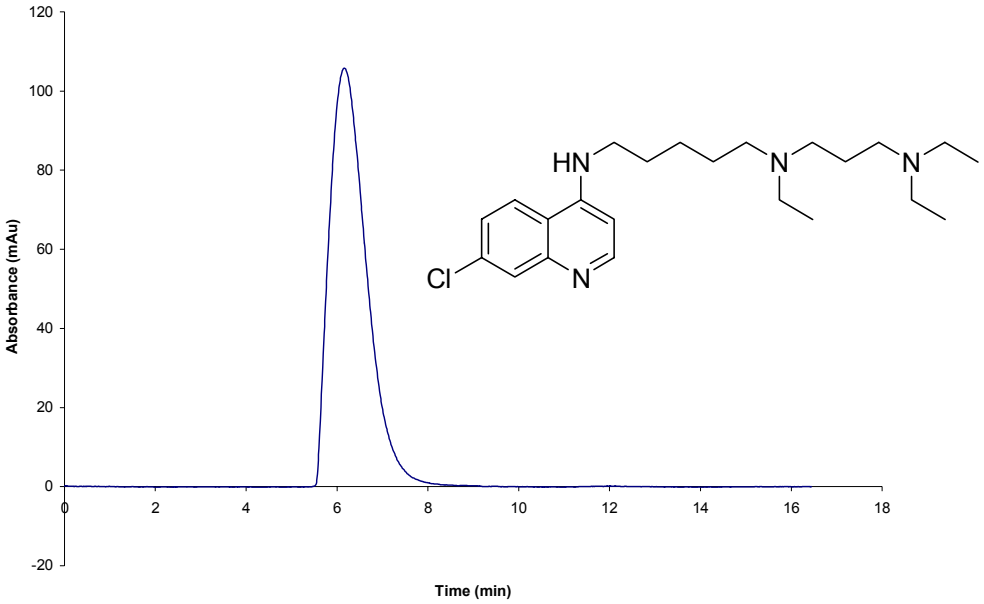
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,5-diaminopentane

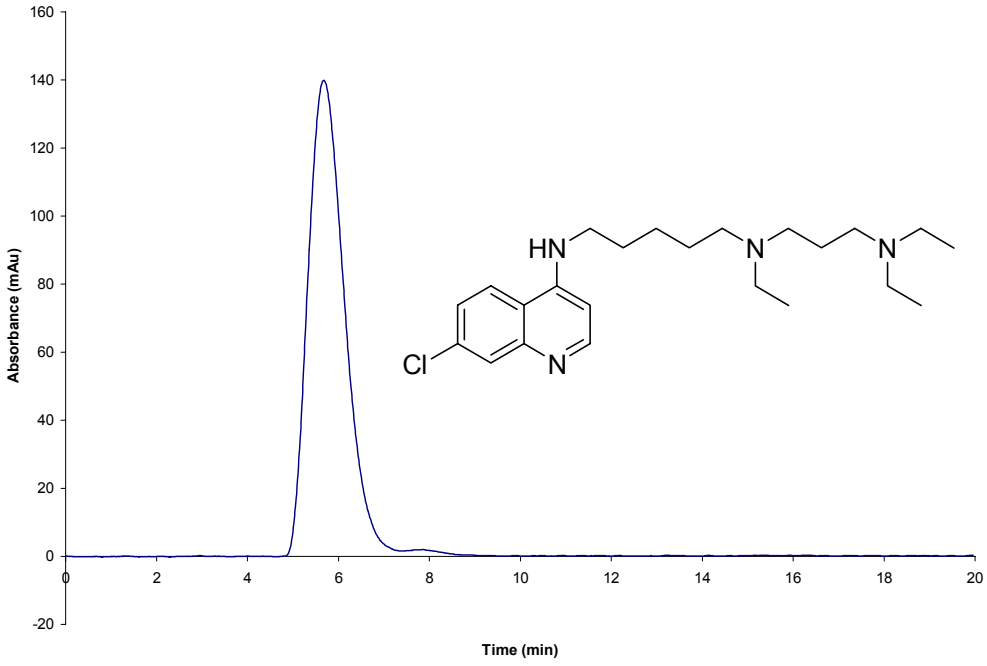




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,5-diaminopentane

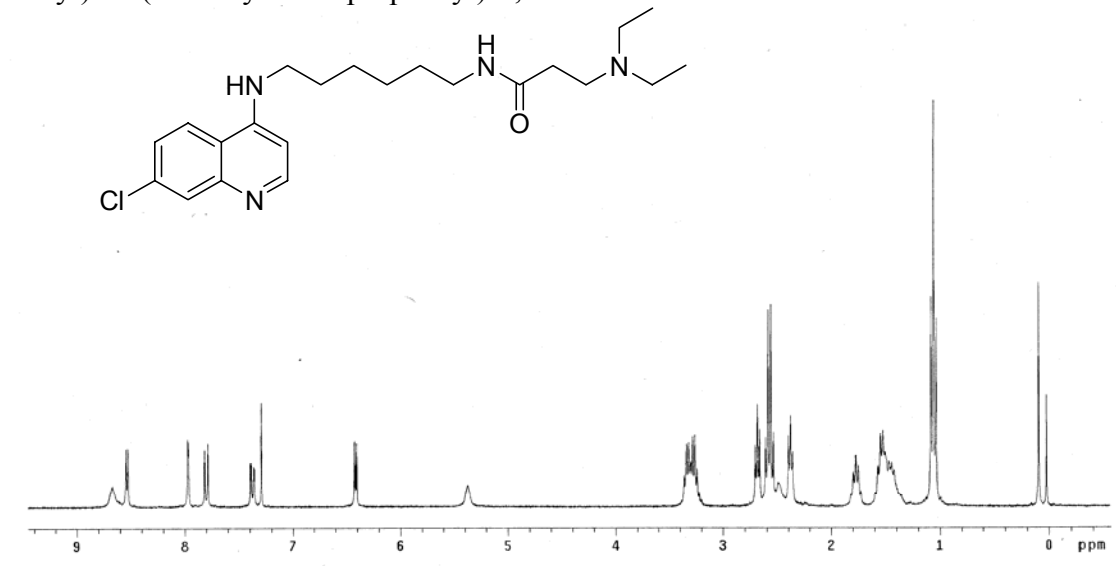


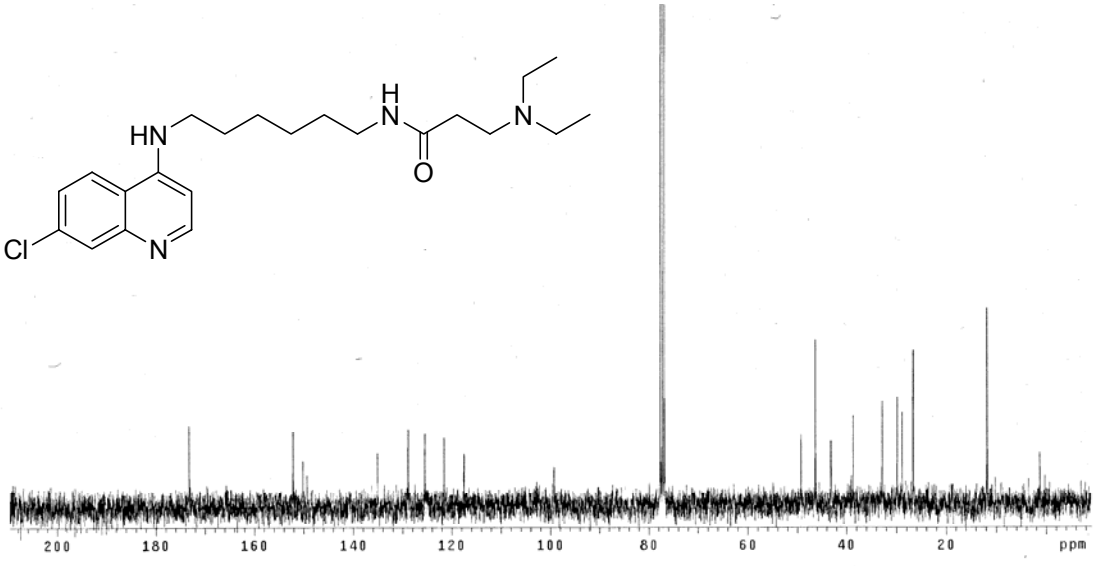
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



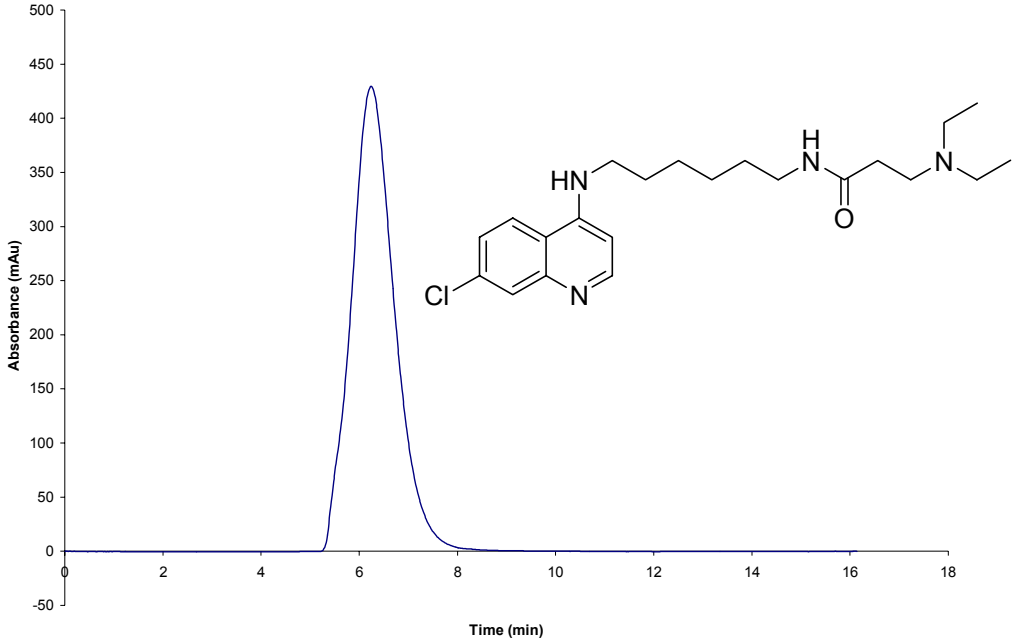
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,6-diaminohexane

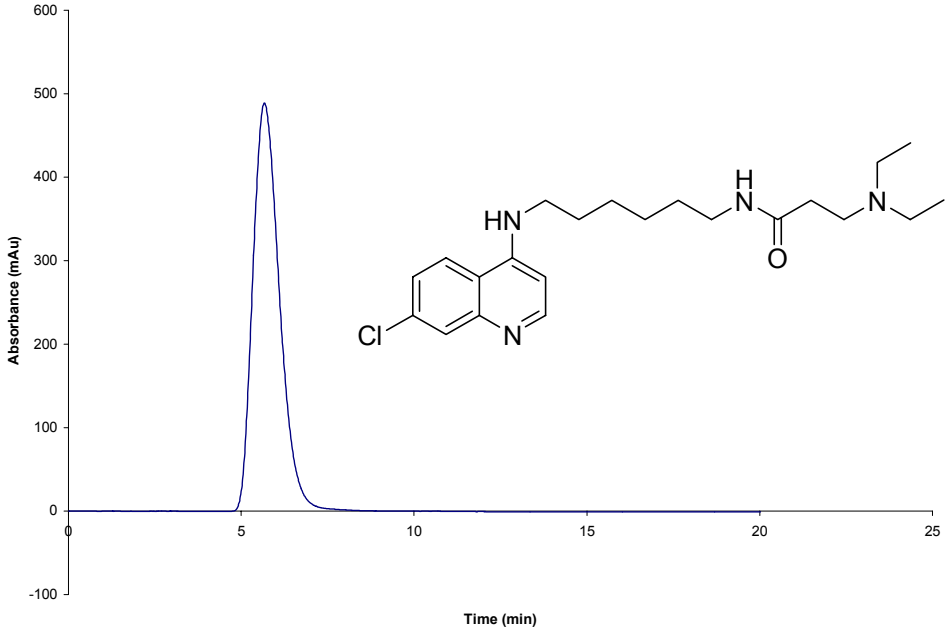




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropanoyl)-1,6-diaminohexane

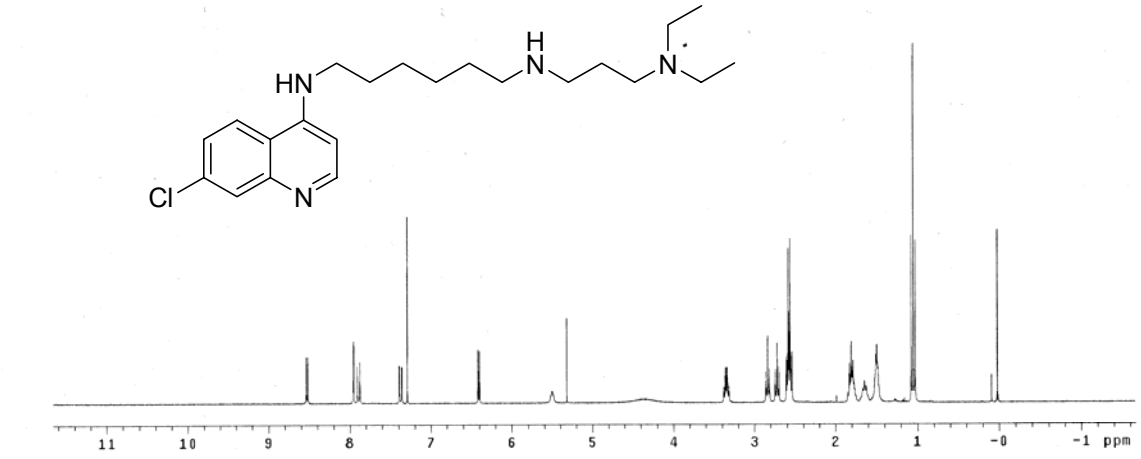


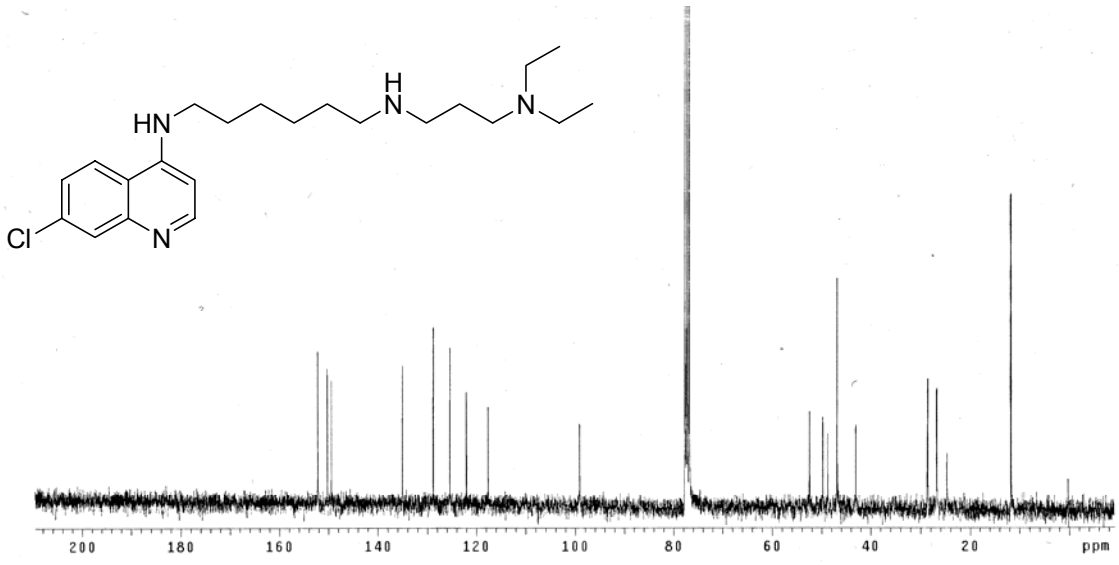
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



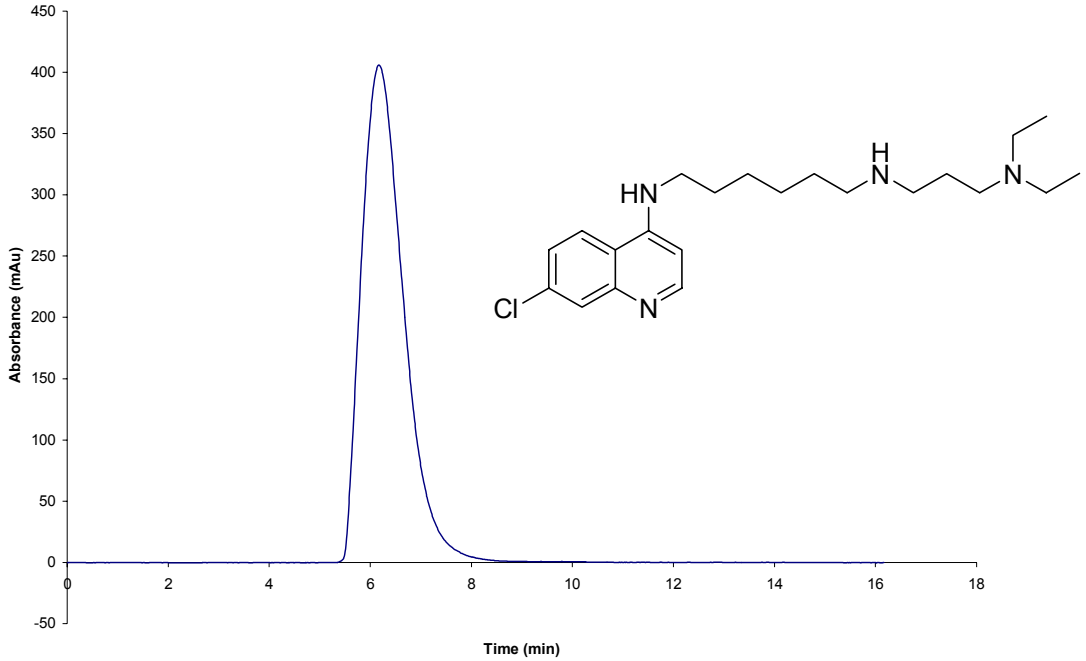
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,6-diaminohexane

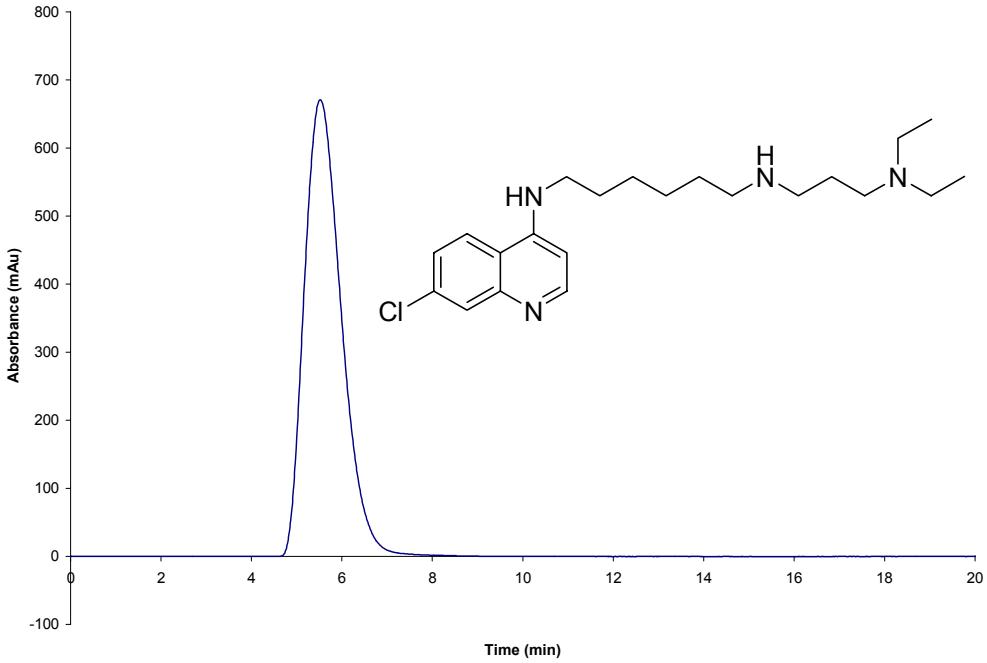




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-(3-diethylaminopropyl)-1,6-diaminohexane

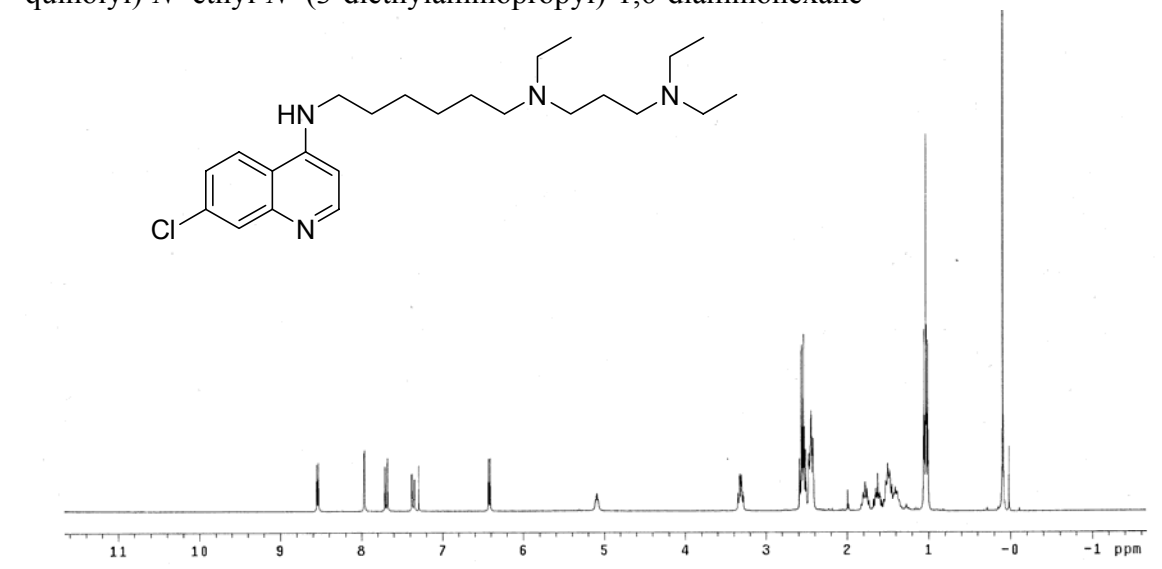


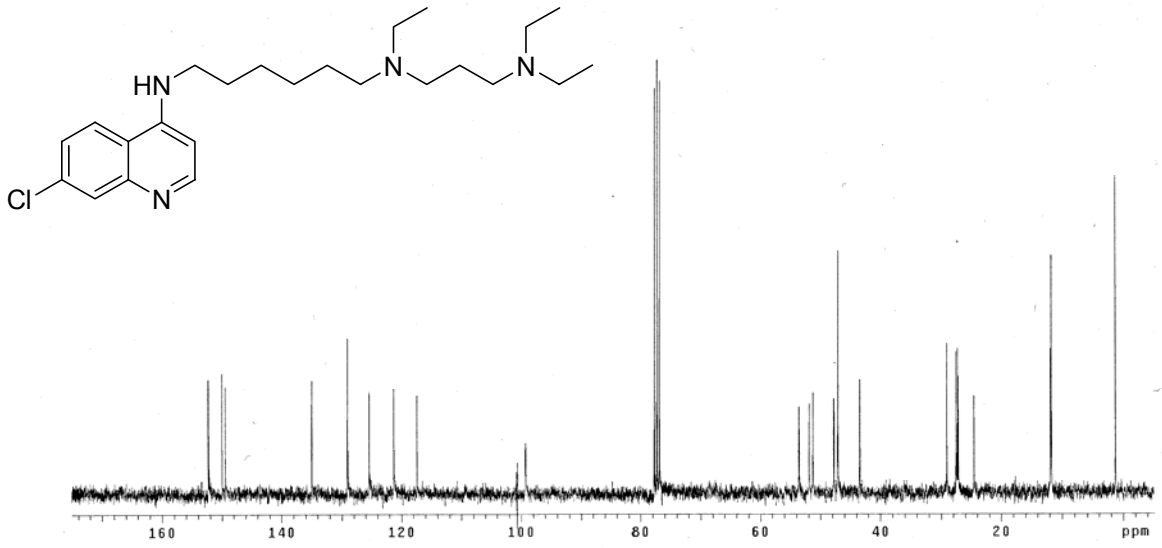
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



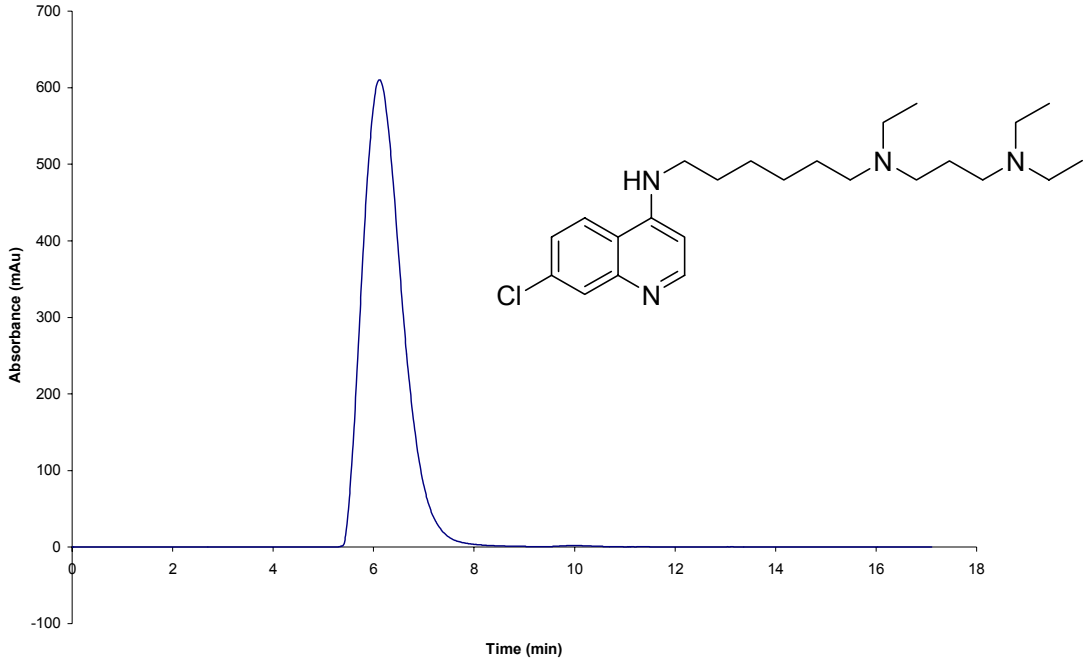
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,6-diaminohexane

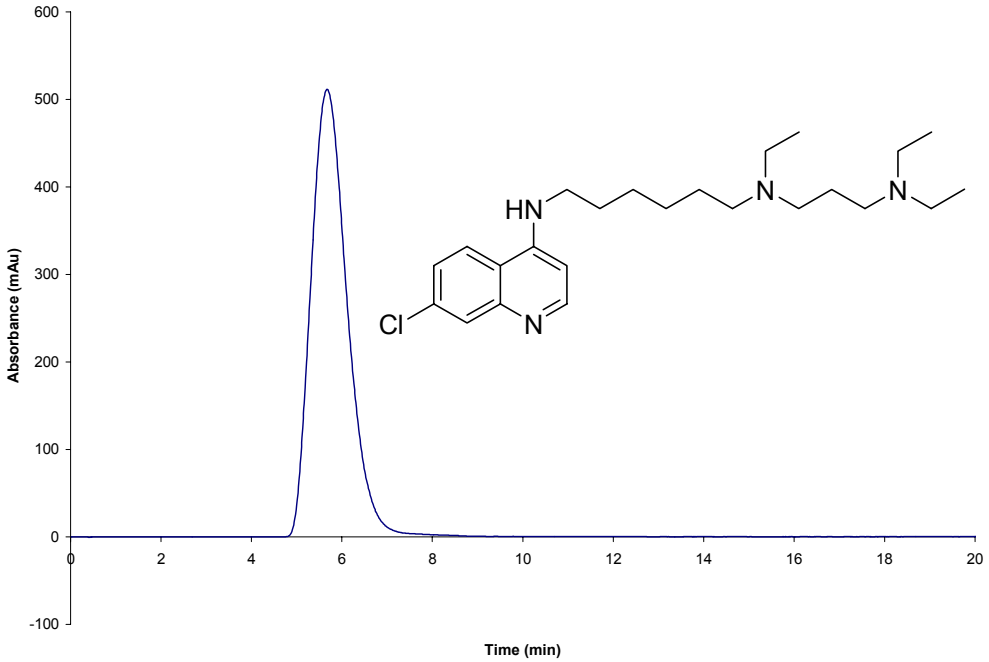




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N*′-ethyl-*N*′-(3-diethylaminopropyl)-1,6-diaminohexane

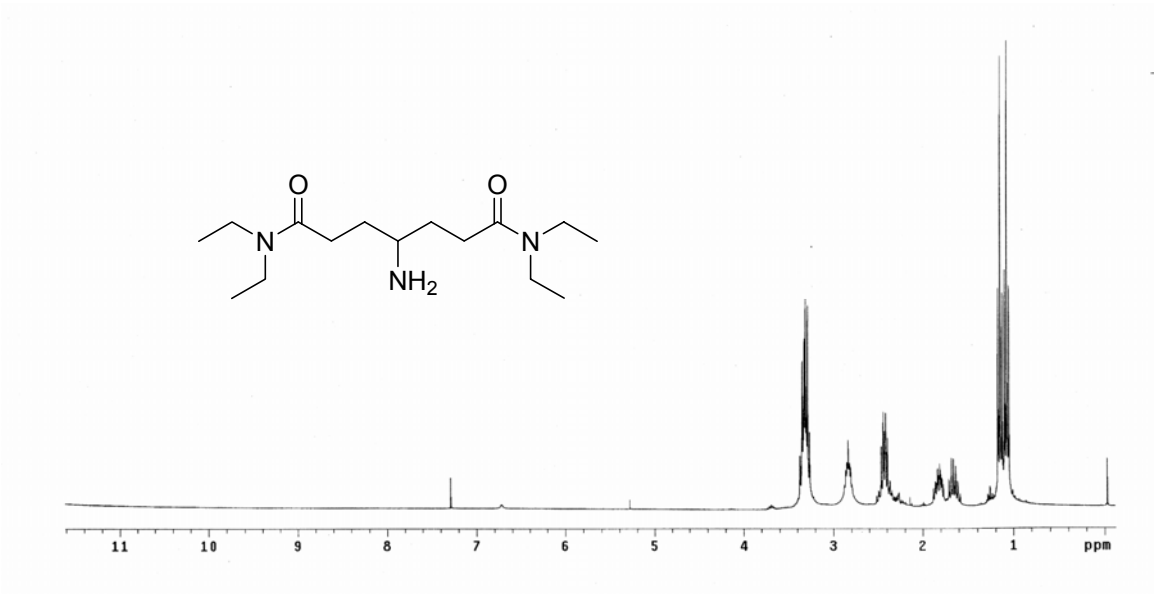


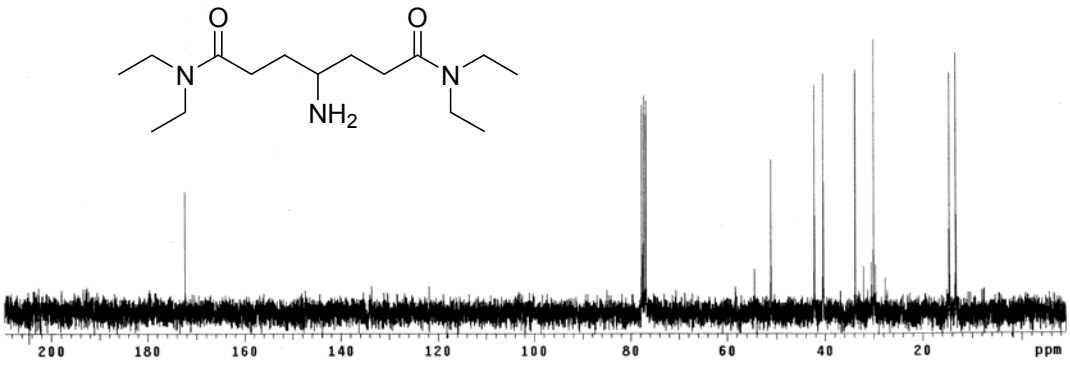
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



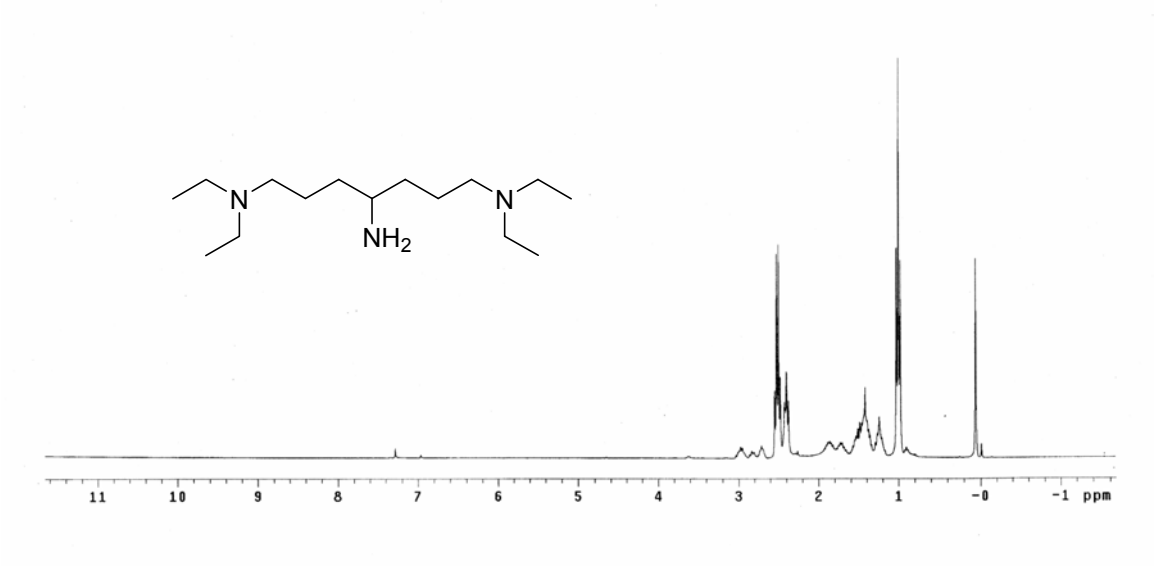
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

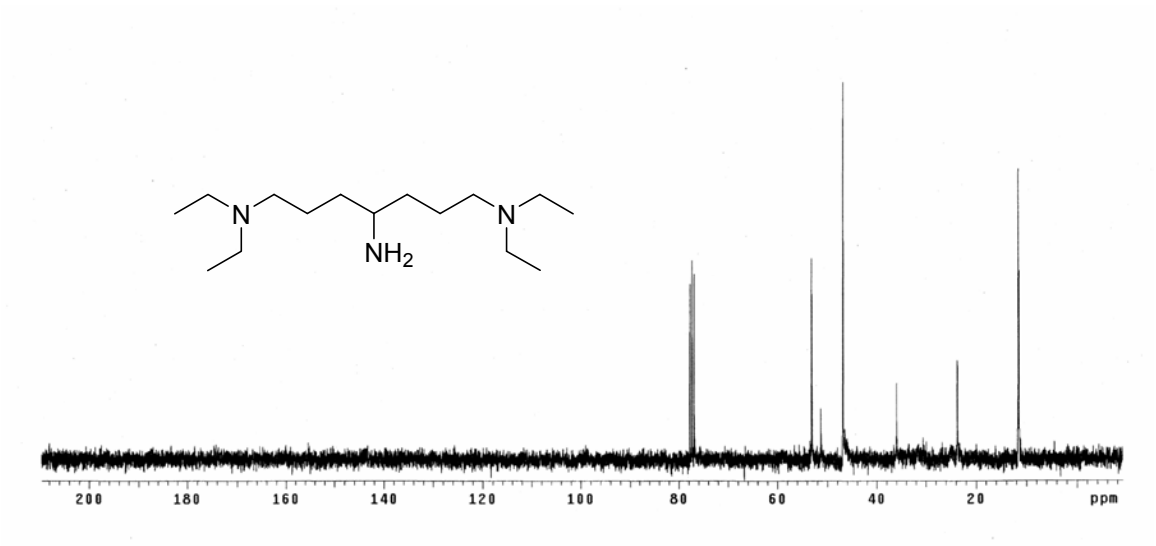
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,7-bis(diethylamido)-4-aminoheptane



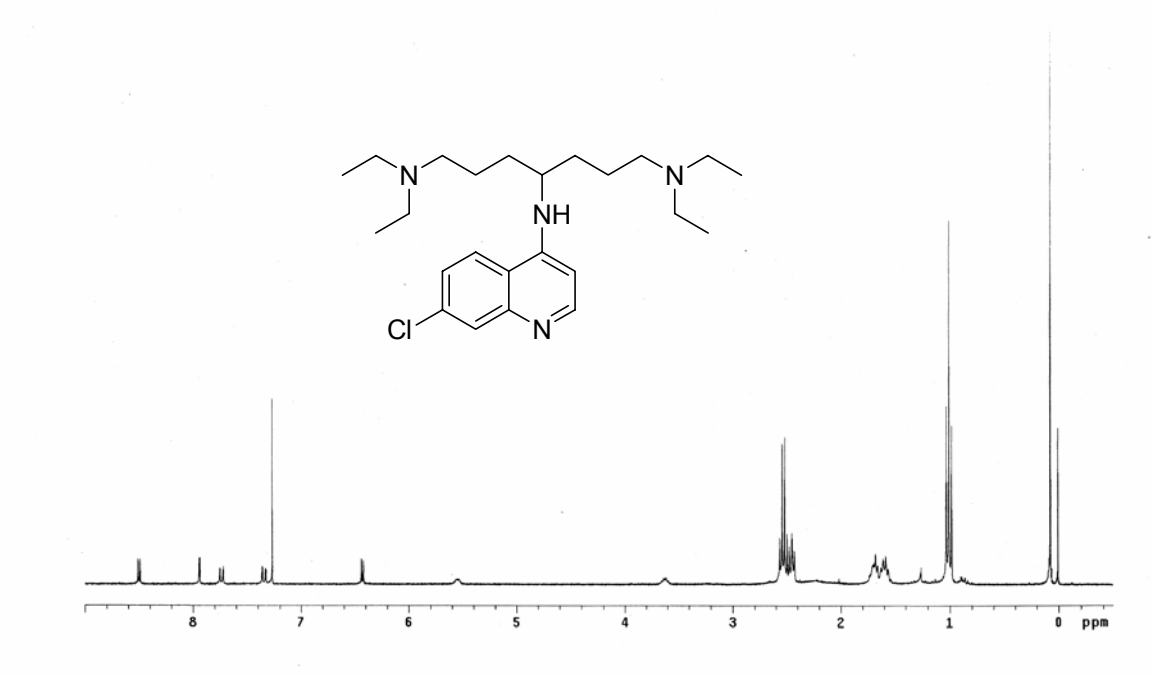


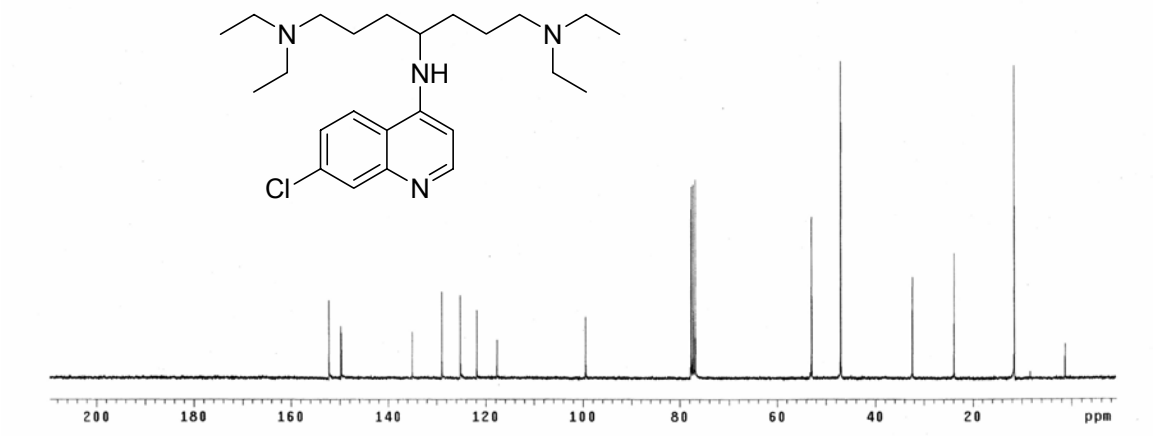
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,7-bis(diethylamino)-4-aminoheptane



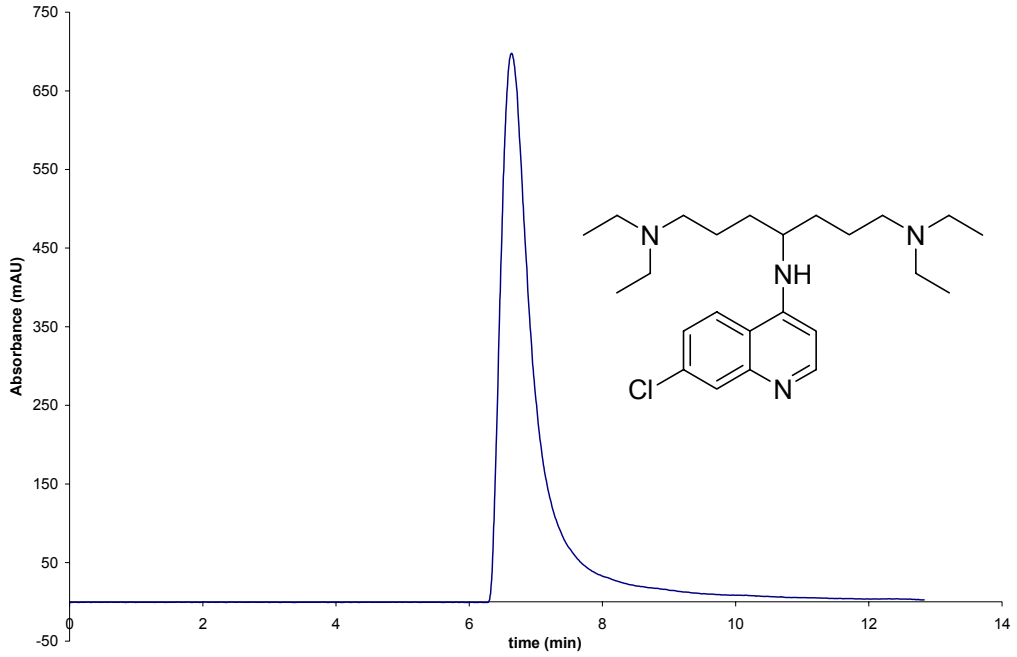


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-1,7-bis(diethylamino)-4-aminoheptane

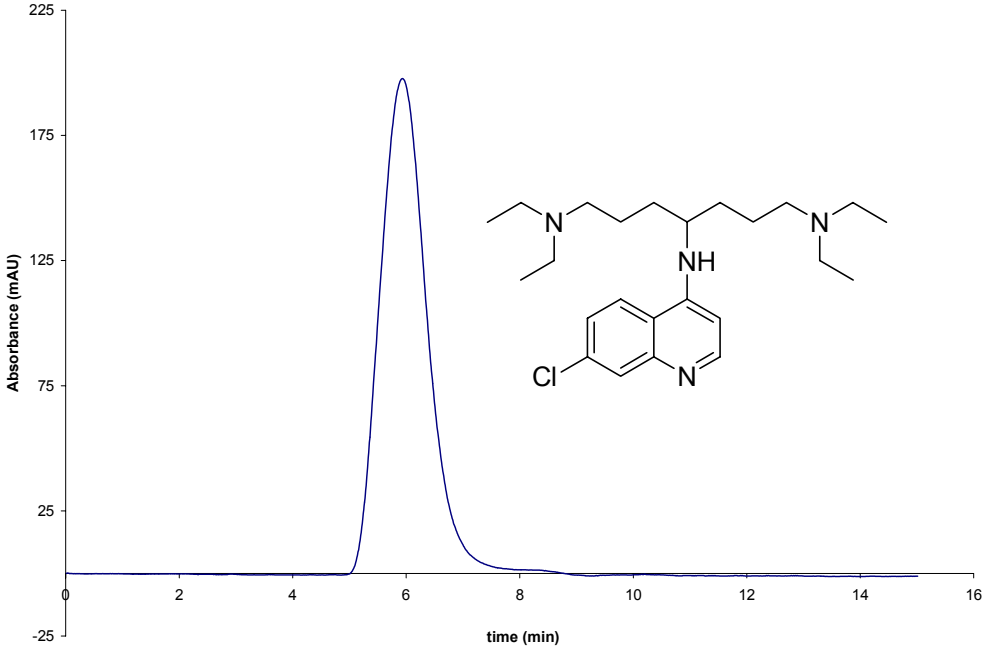




HPLC analysis of *N*-(7-chloro-4-quinolyl)-1,7-bis(diethylamino)-4-aminoheptane

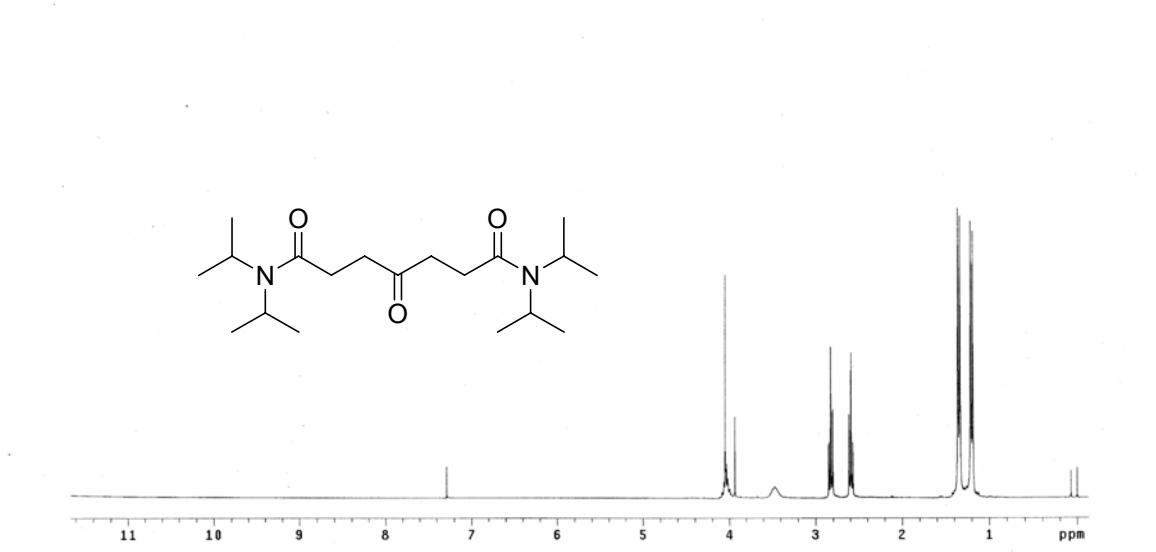


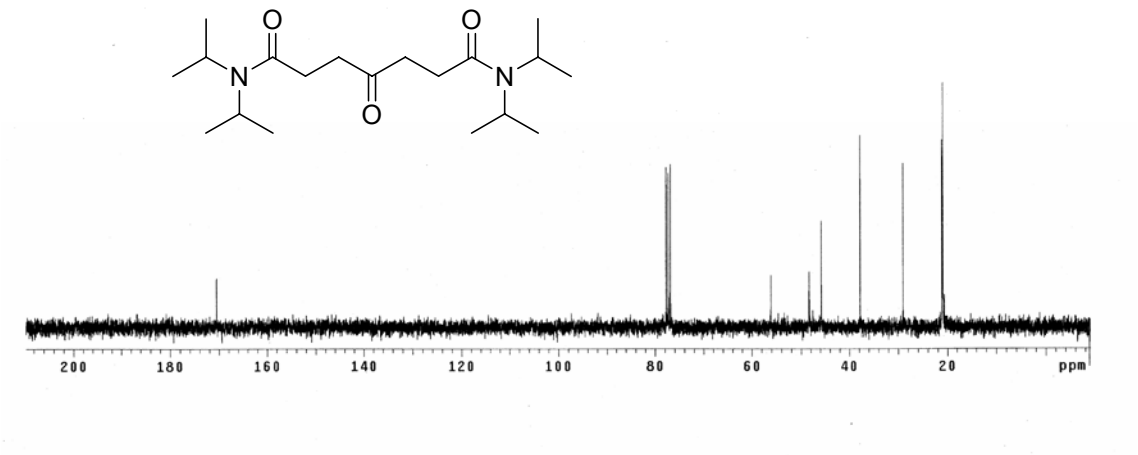
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



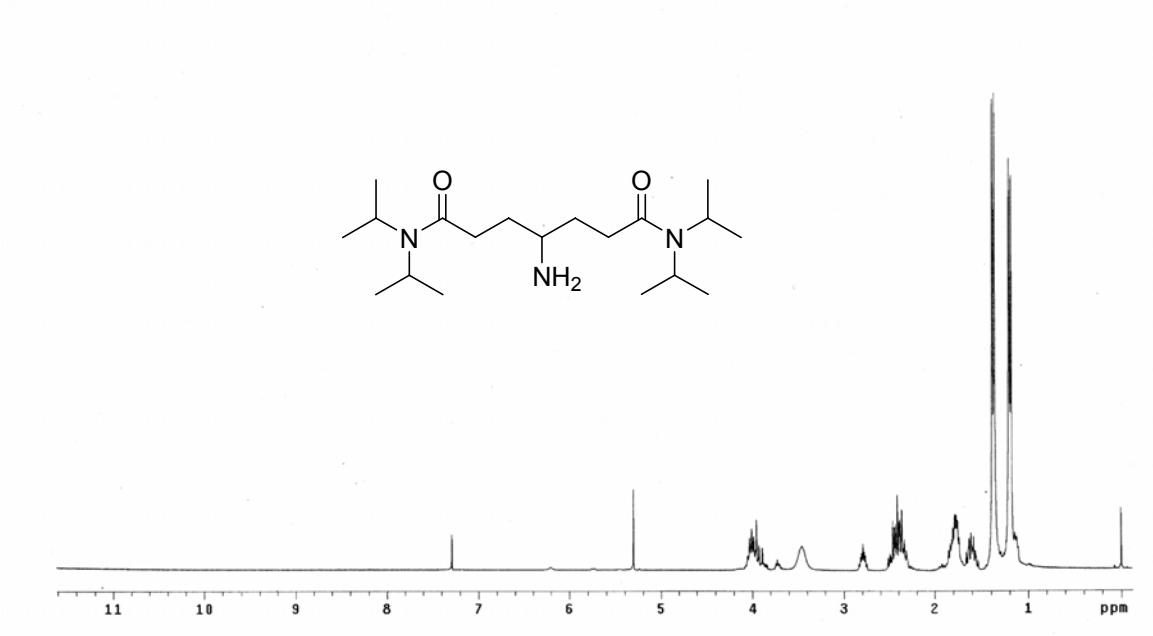
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 20 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,7-bis(diisopropylamido)heptan-4-one

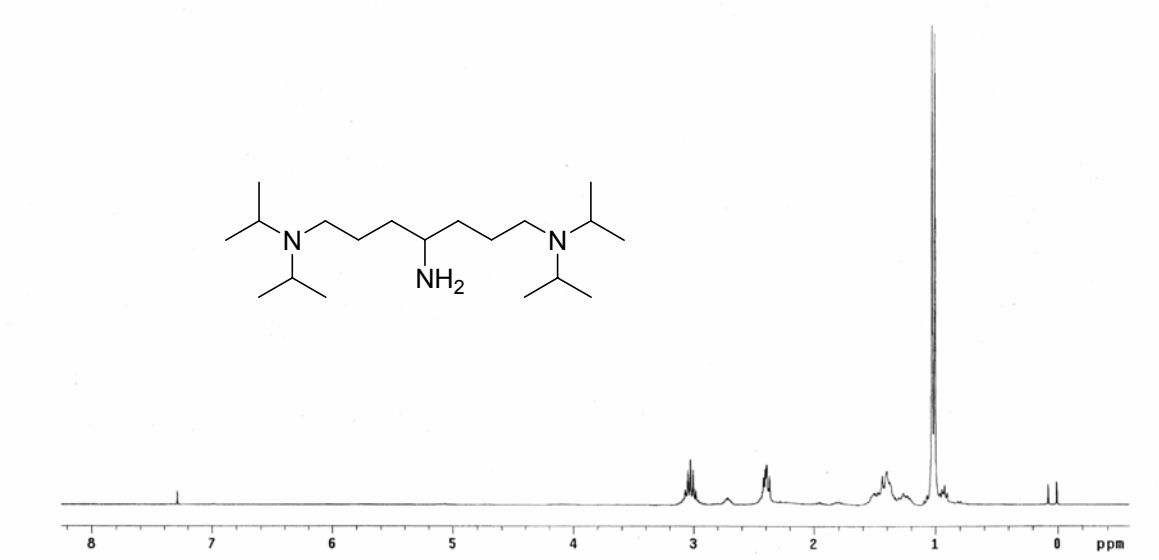


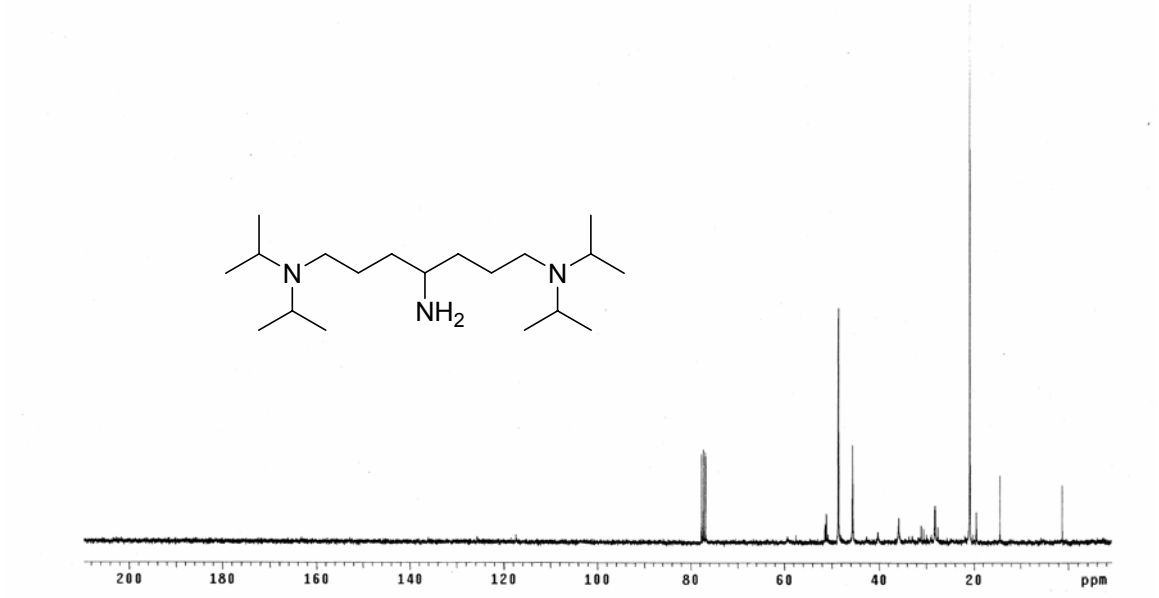


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,7-bis(diisopropylamido)-4-aminoheptane

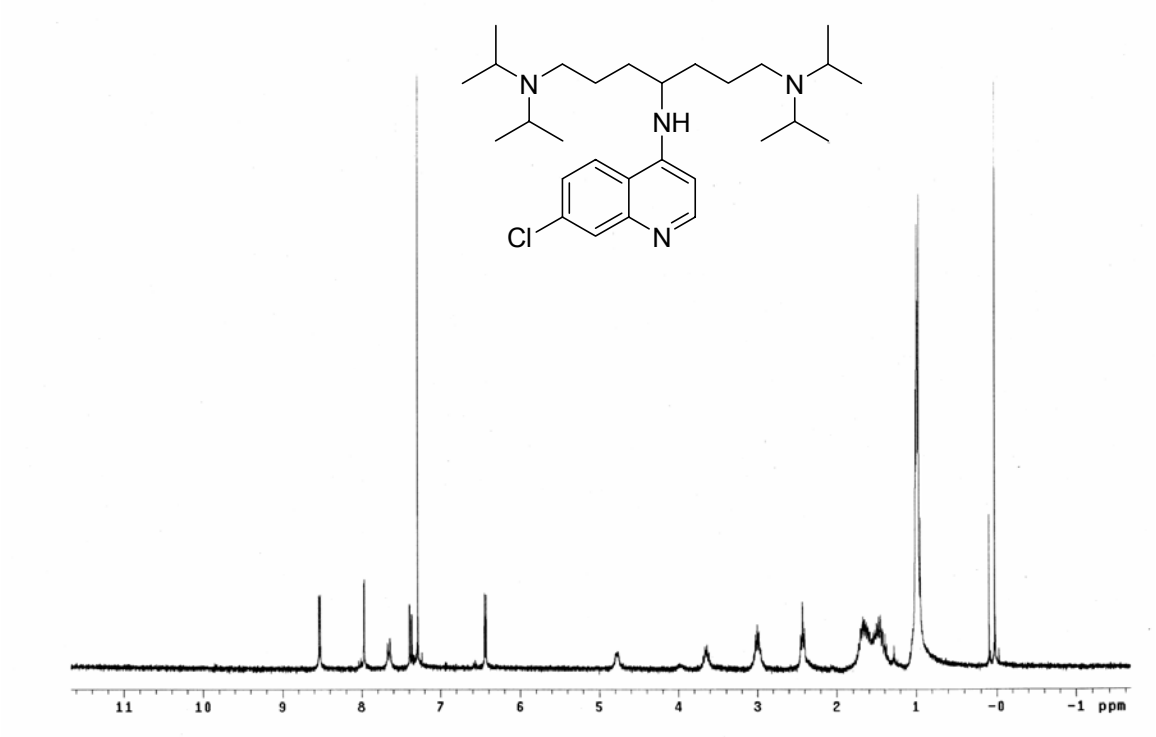


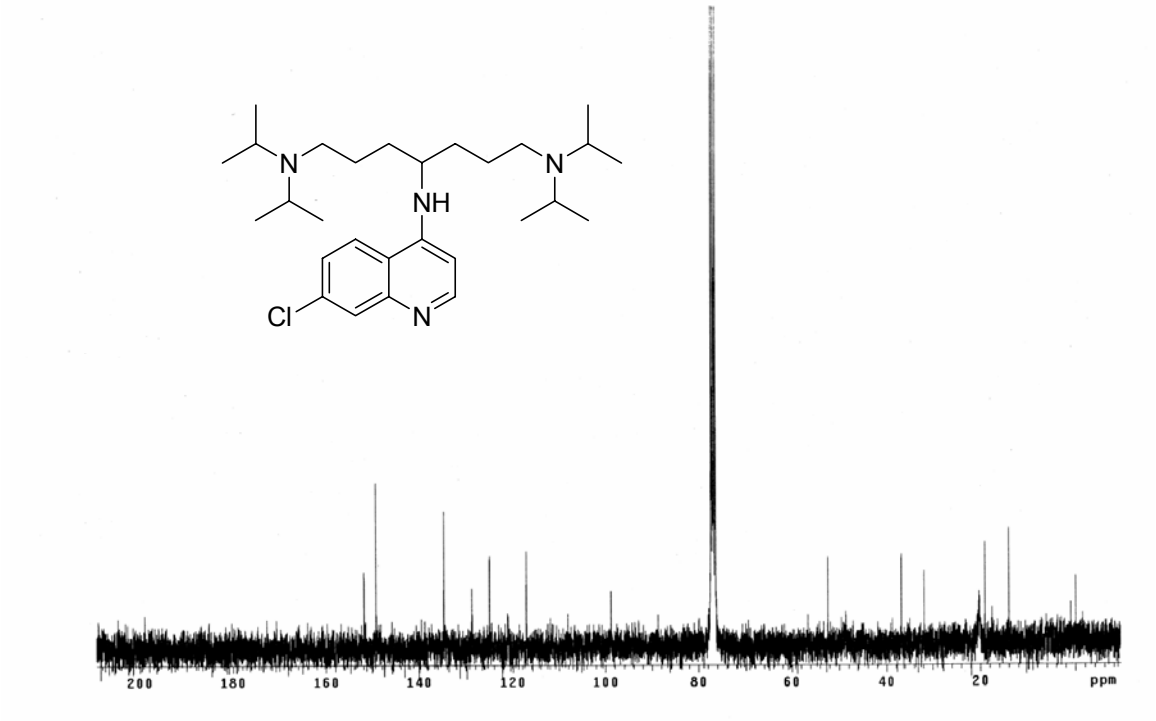
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,7-bis(diisopropylamino)-4-aminoheptane



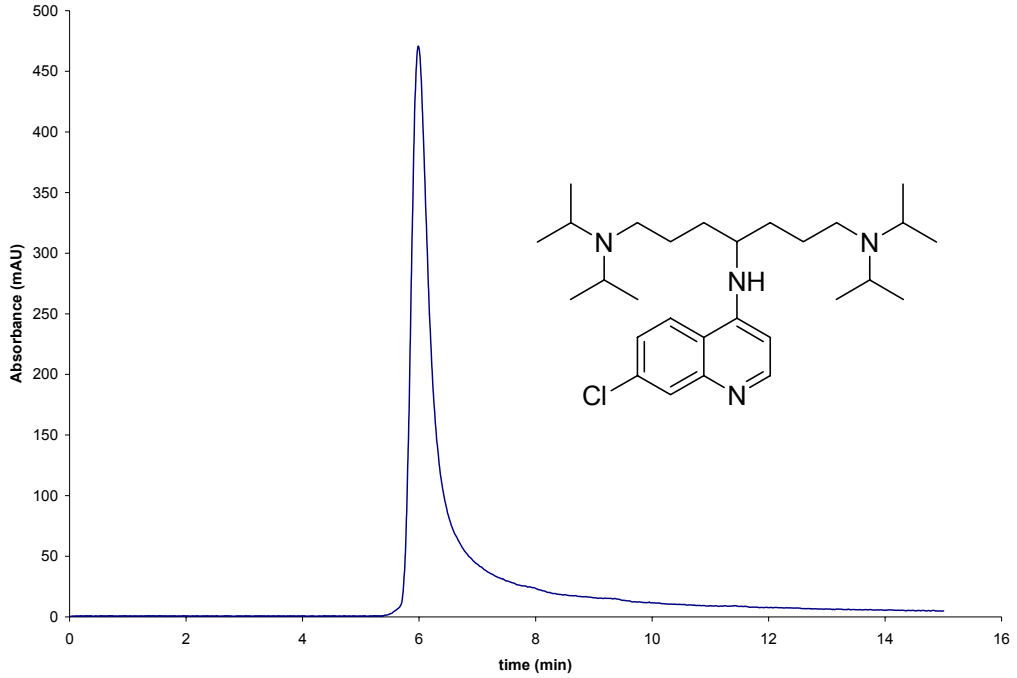


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-1,7-bis(diisopropylamino)-4-aminoheptane

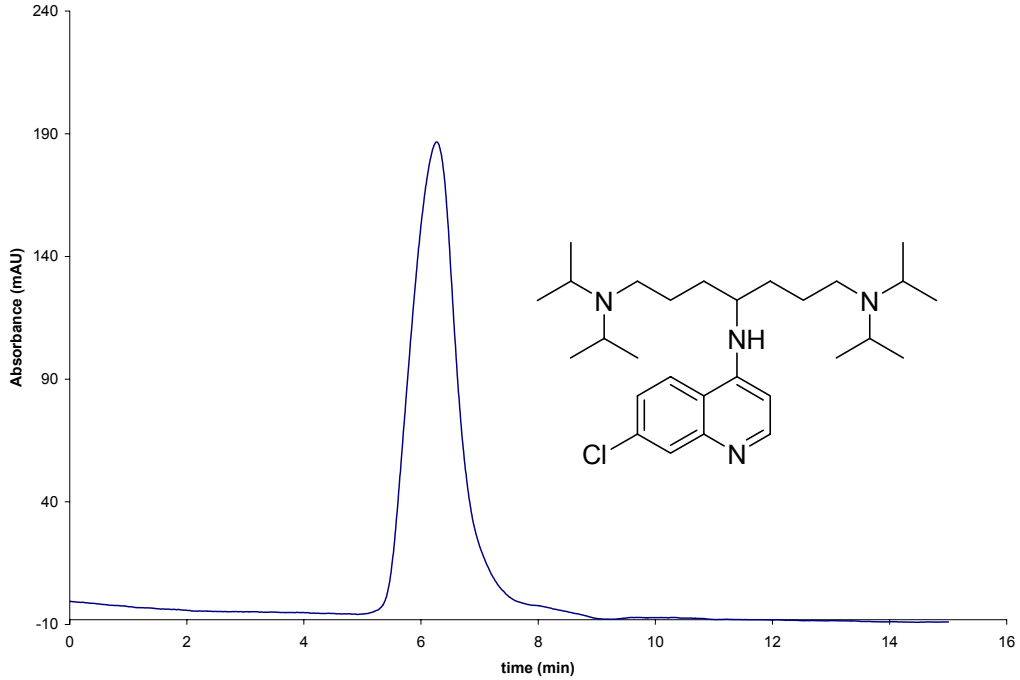




HPLC analysis of *N*-(7-chloro-4-quinolyl)-1,7-bis(diisopropylamino)-4-aminoheptane

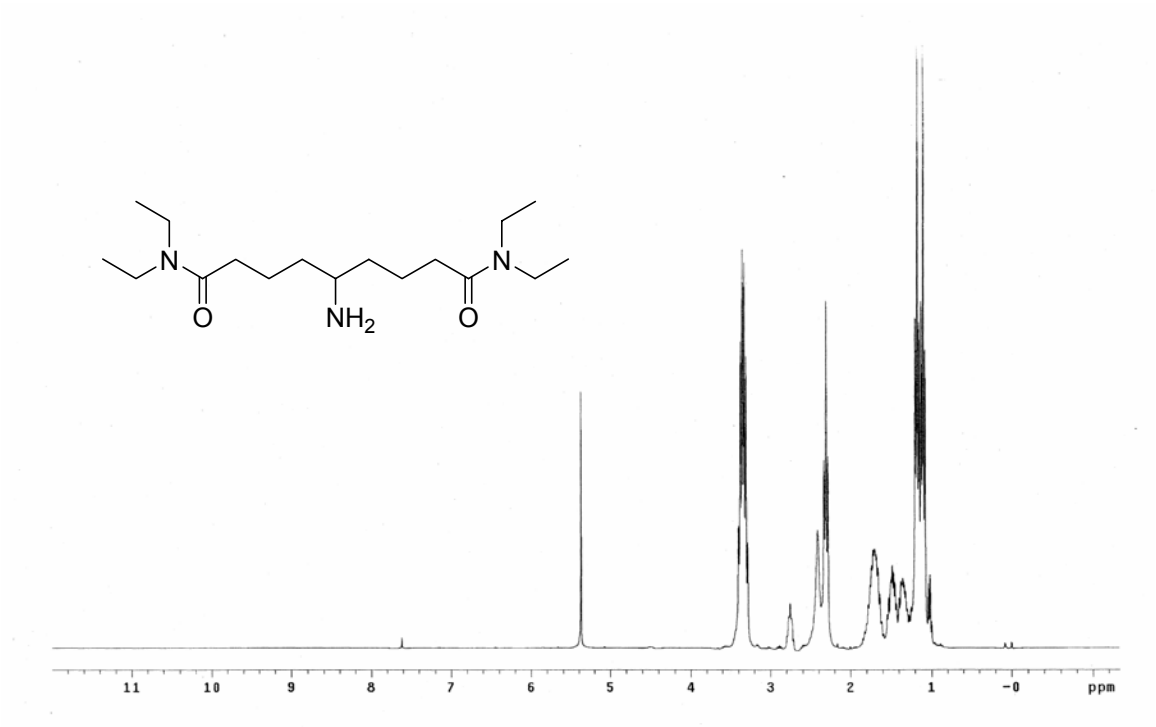


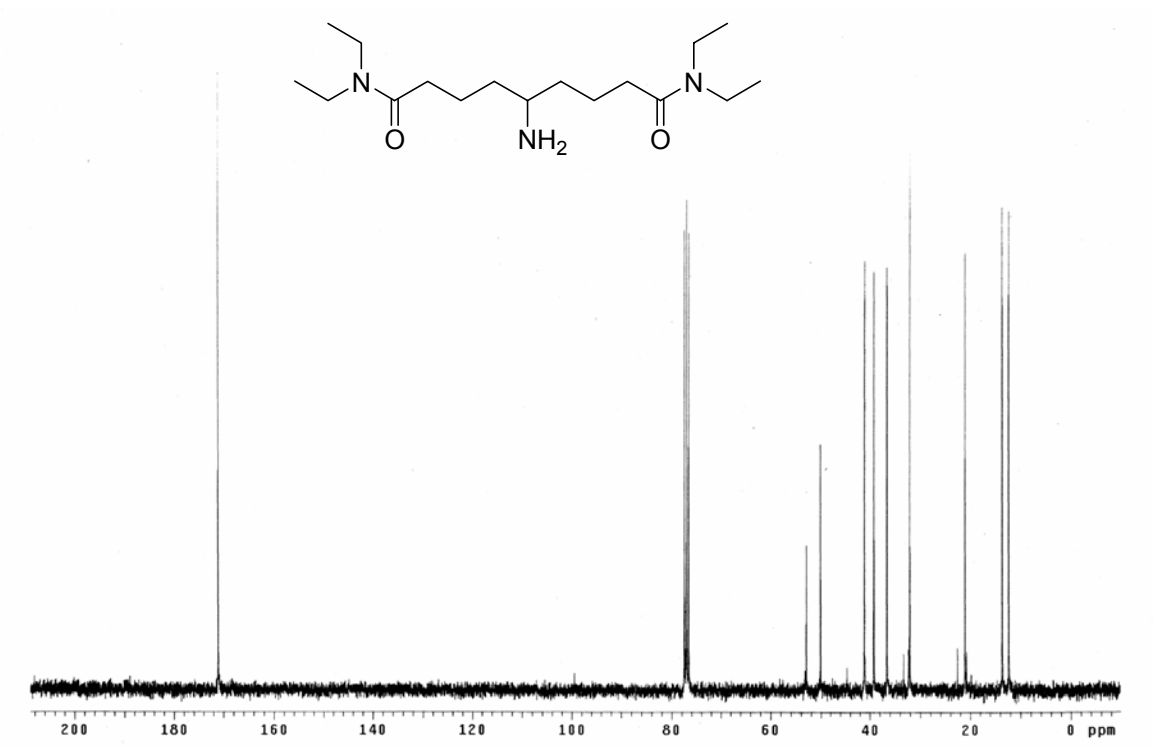
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



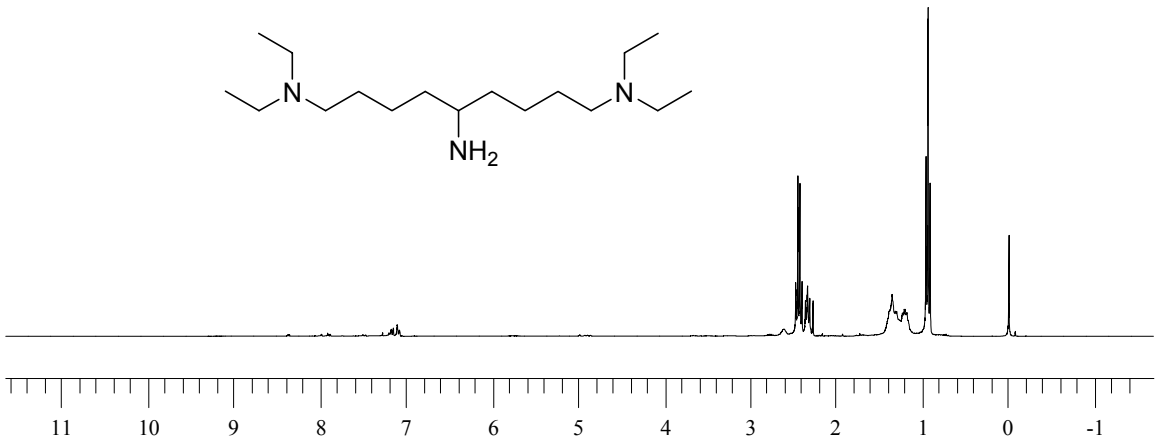
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 20 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

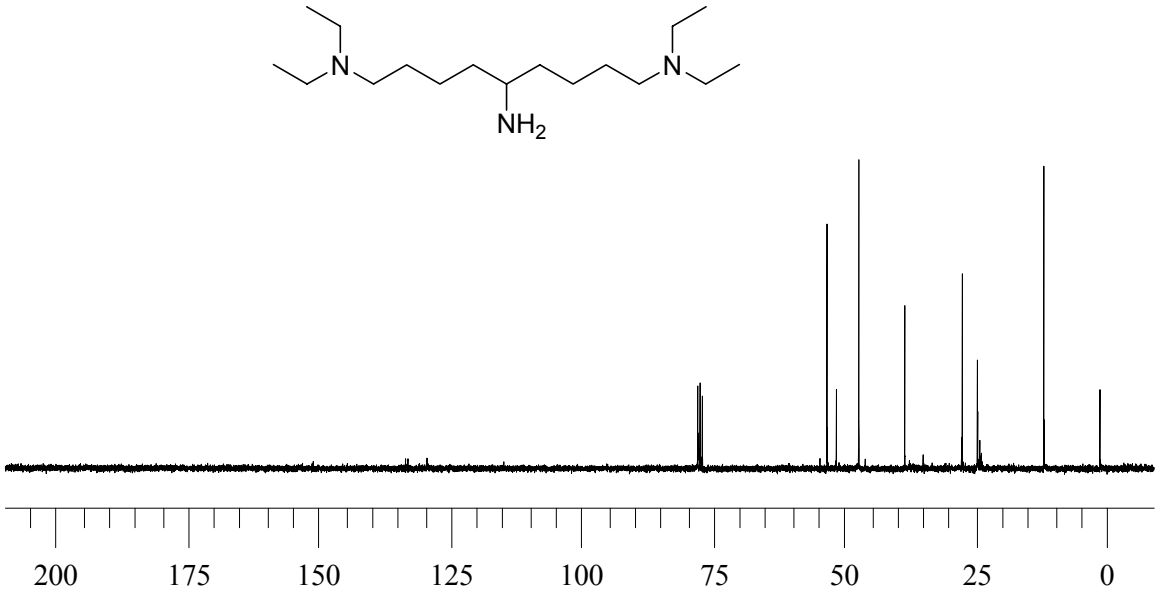
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,9-bis(diethylamido)-5-aminononane



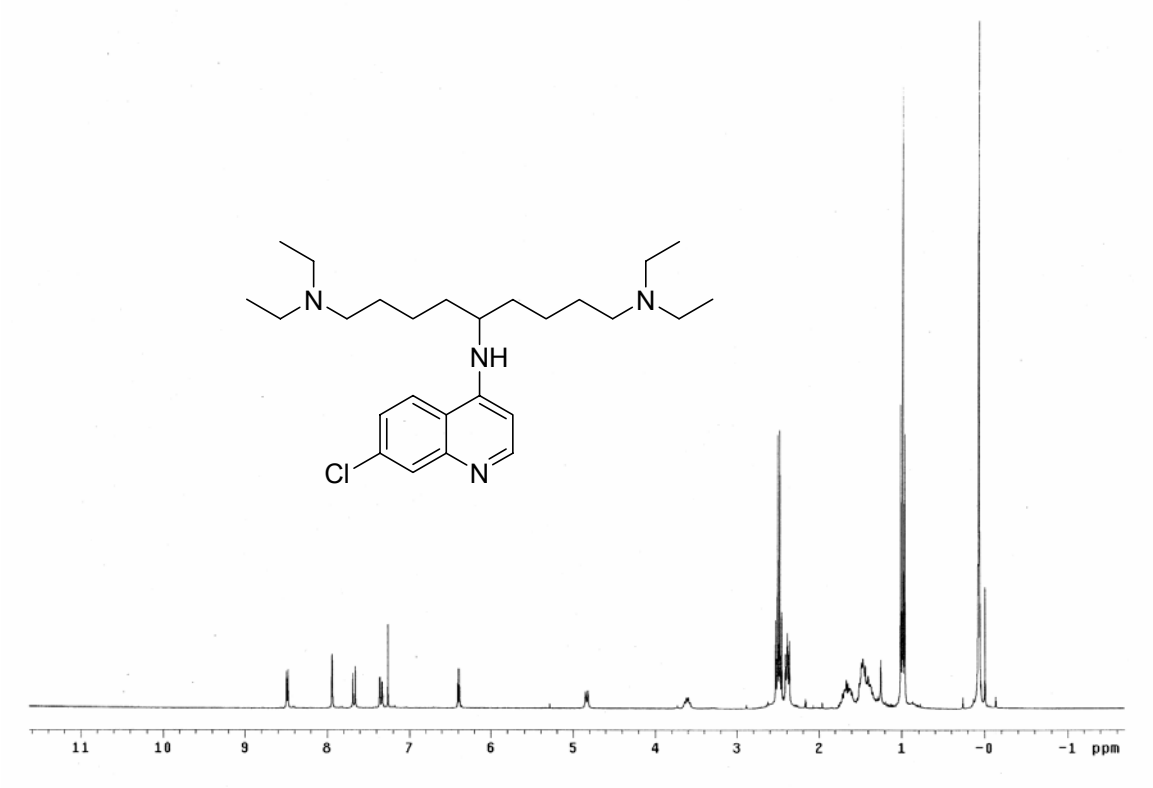


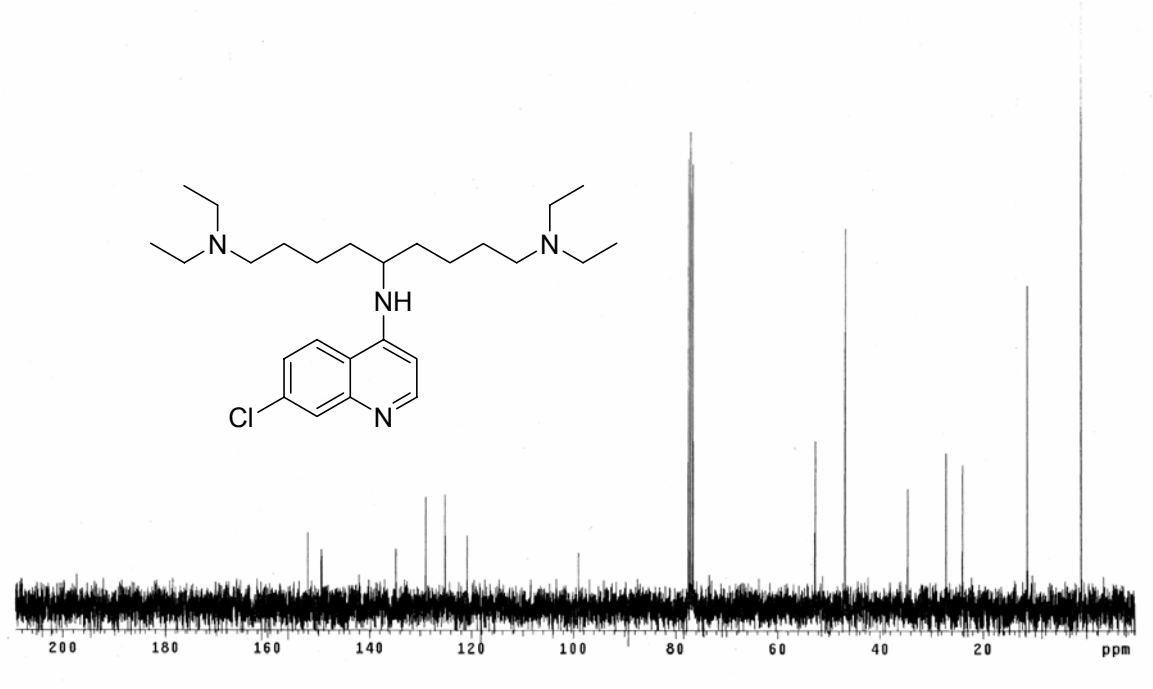
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,9-bis(diethylamino)-5-aminononane



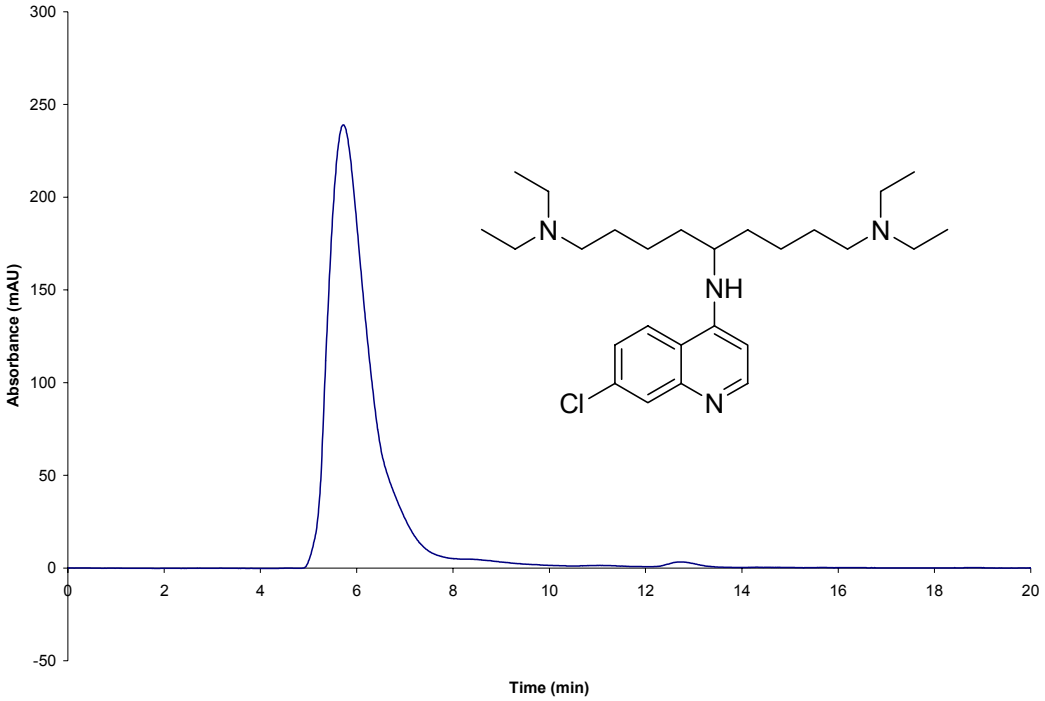


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-1,9-bis(diethylamino)-5-aminononane

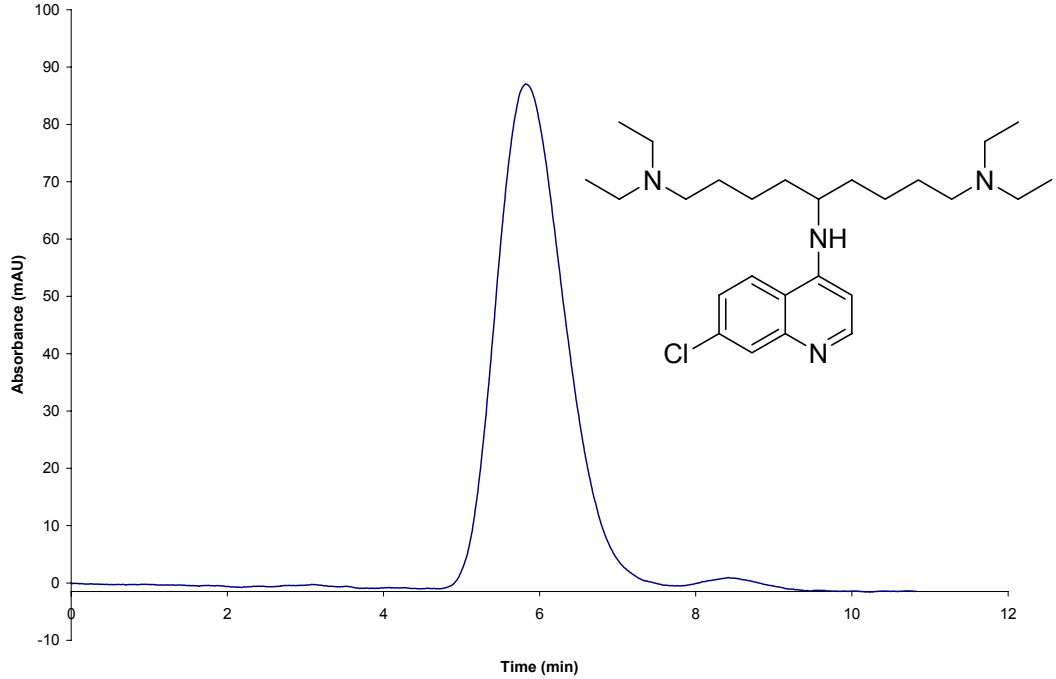




HPLC analysis of *N*-(7-chloro-4-quinolyl)-1,9-bis(diethylamino)-5-aminononane

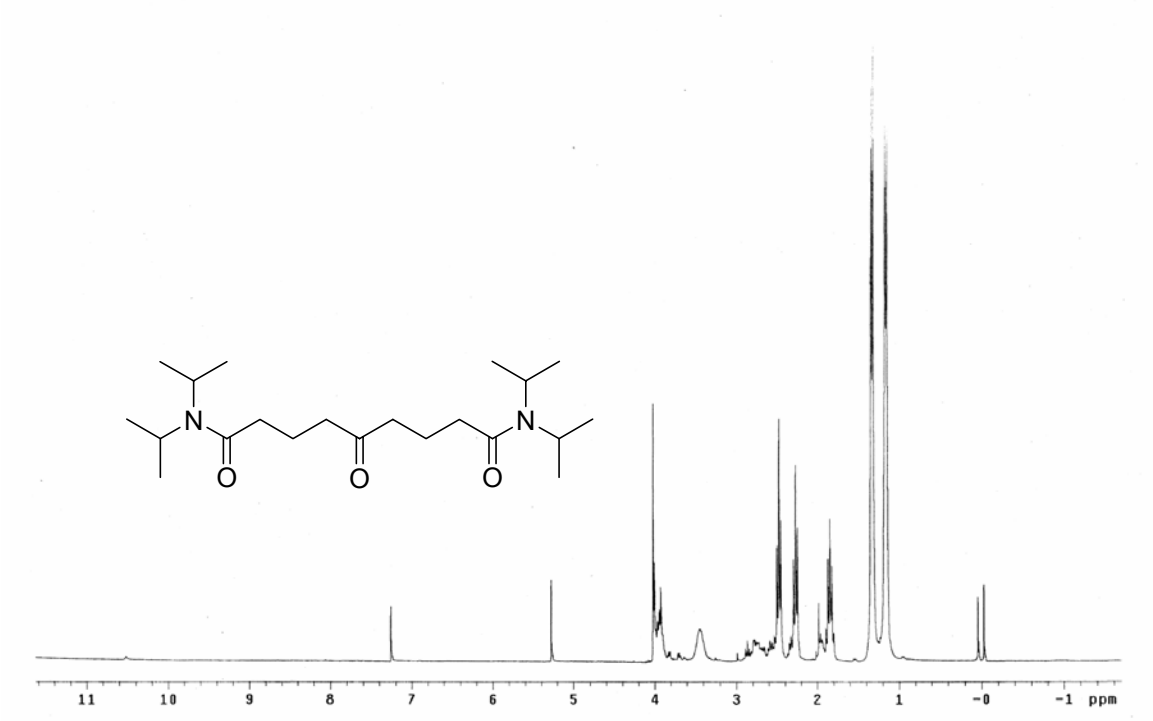


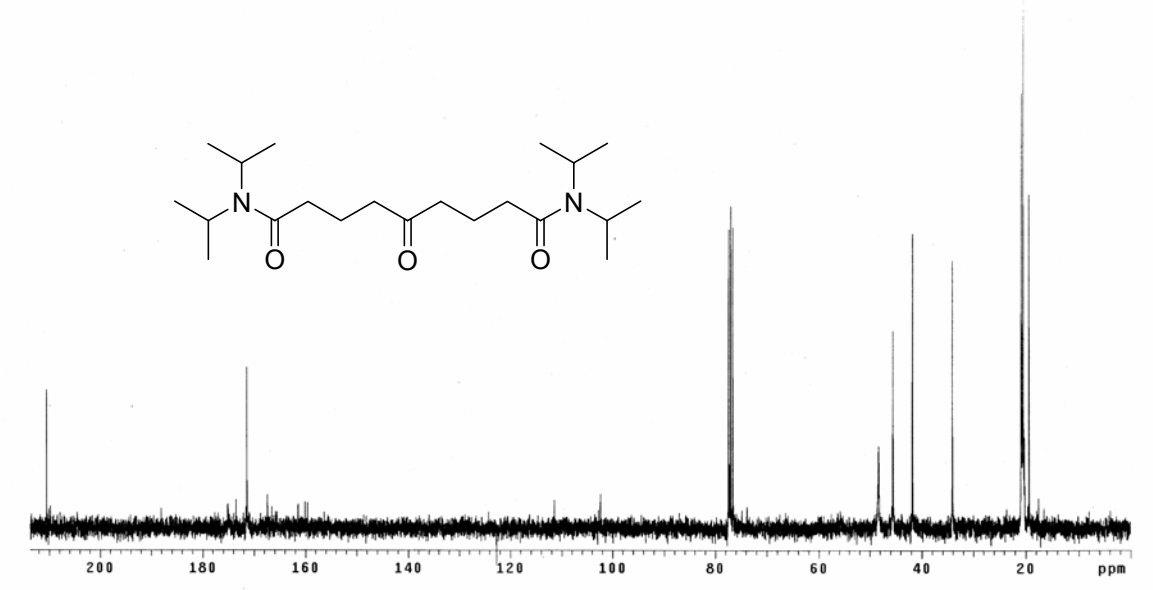
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 20% acetonitrile, 80% water containing 0.1% trifluoroacetic acid, injection volume: 5 μL, concentration: 2 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



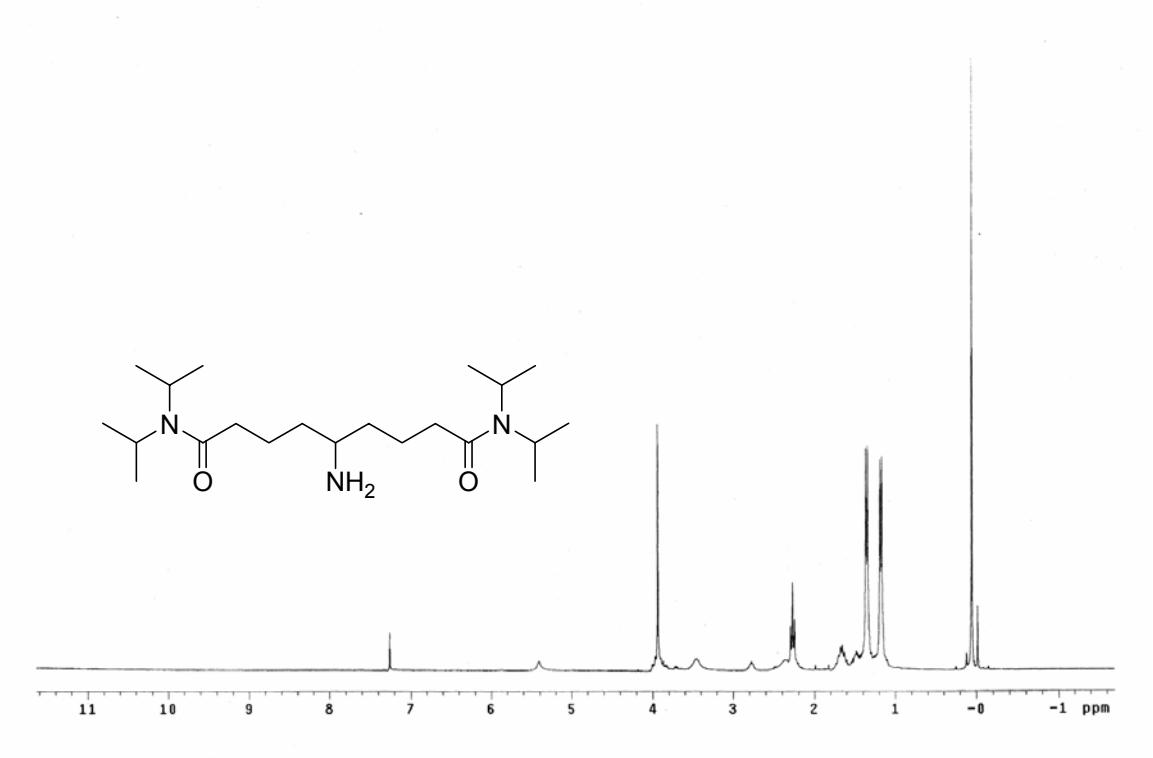
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 2 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

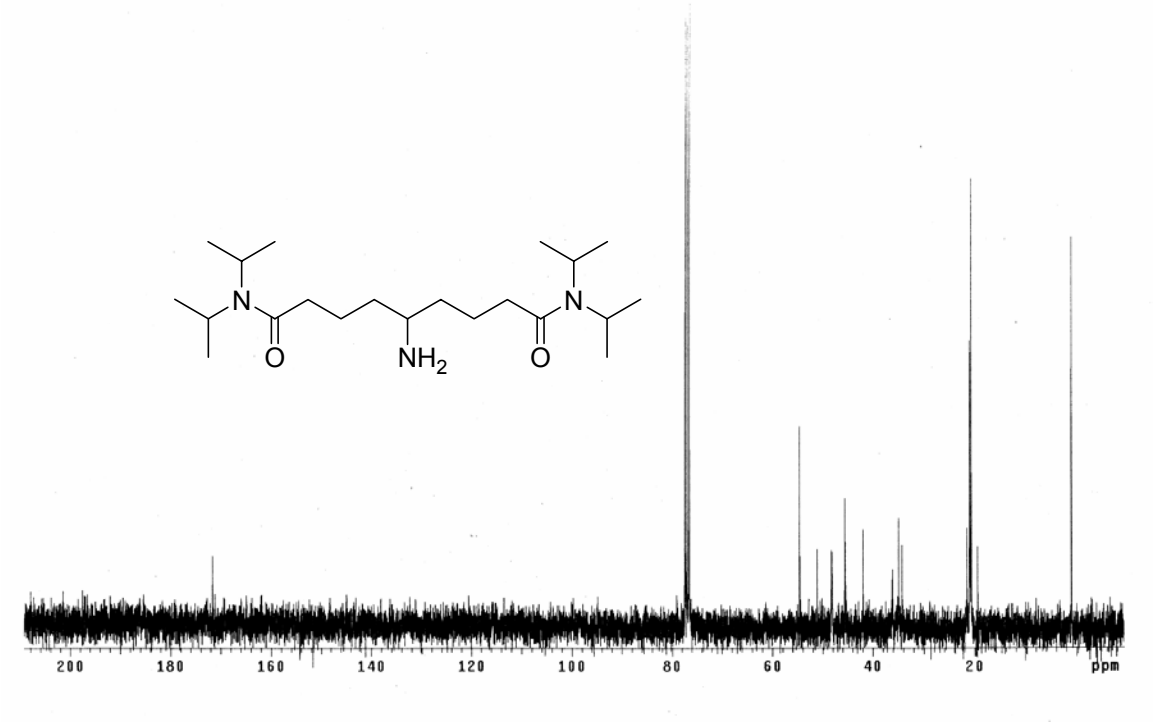
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,9-bis(diisopropylamido)nonan-5-one



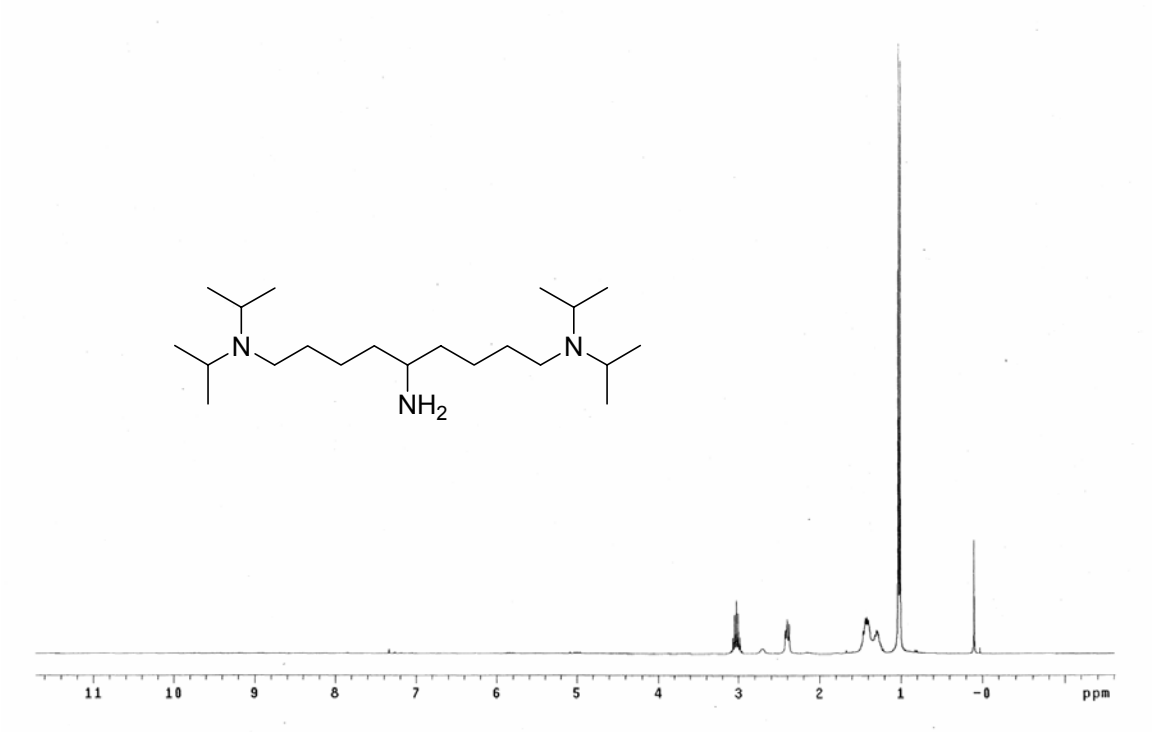


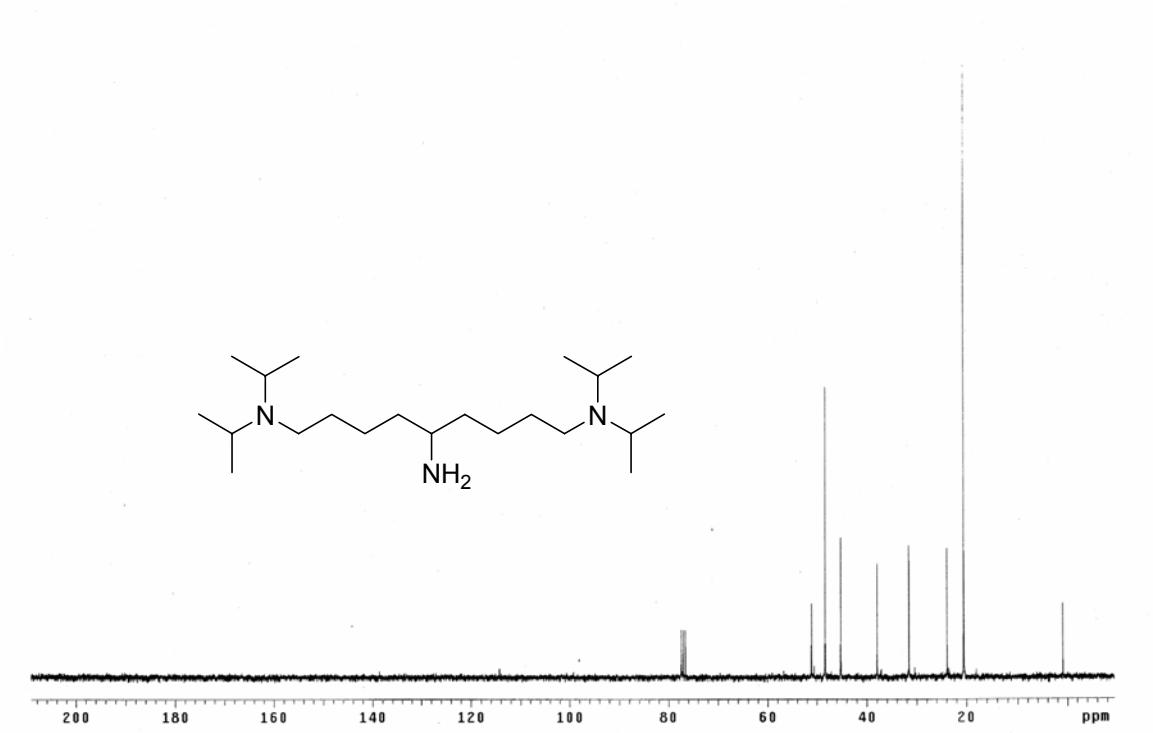
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,9-bis(diisopropylamido)-5-aminononane



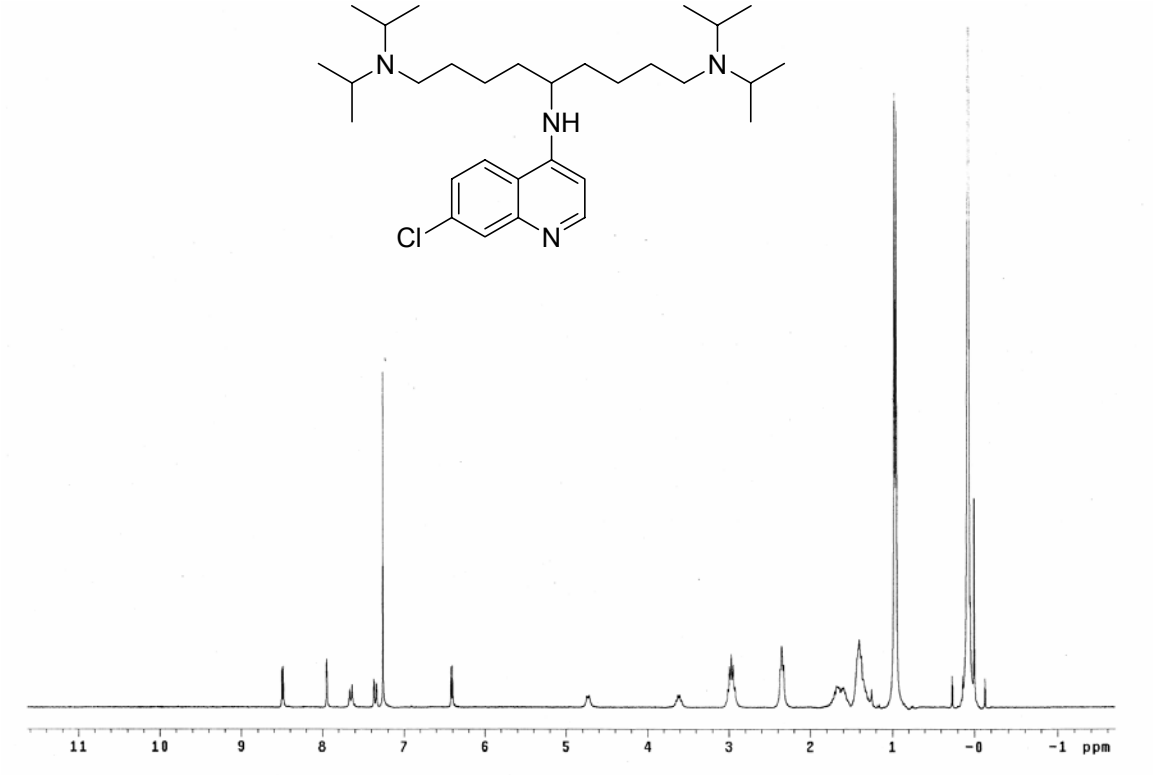


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of 1,9-bis(diisopropylamino)-5-aminononane

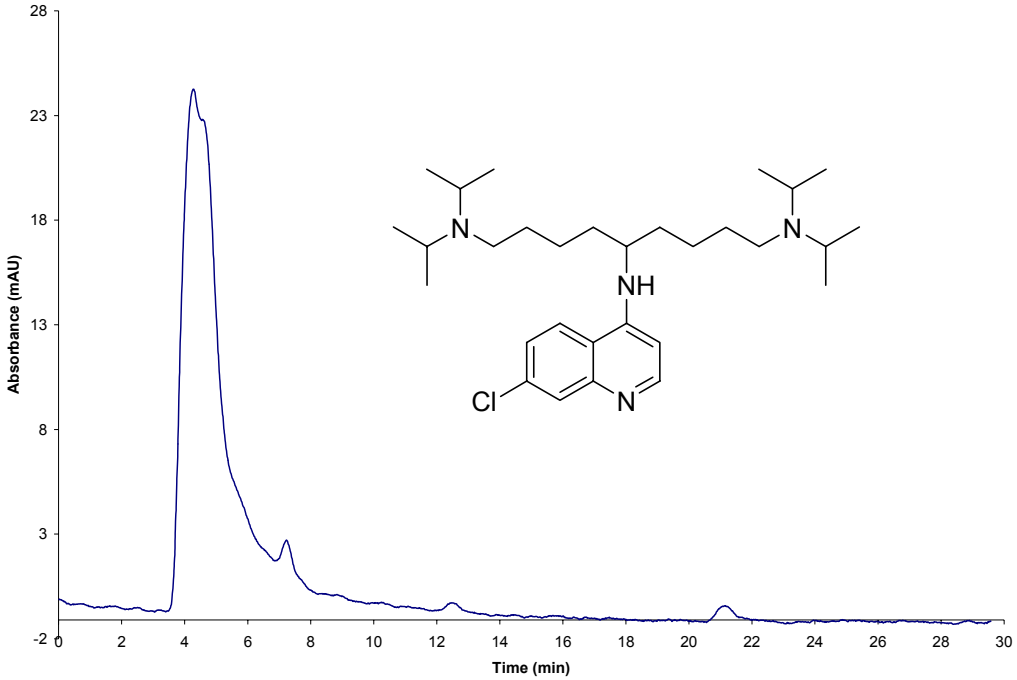




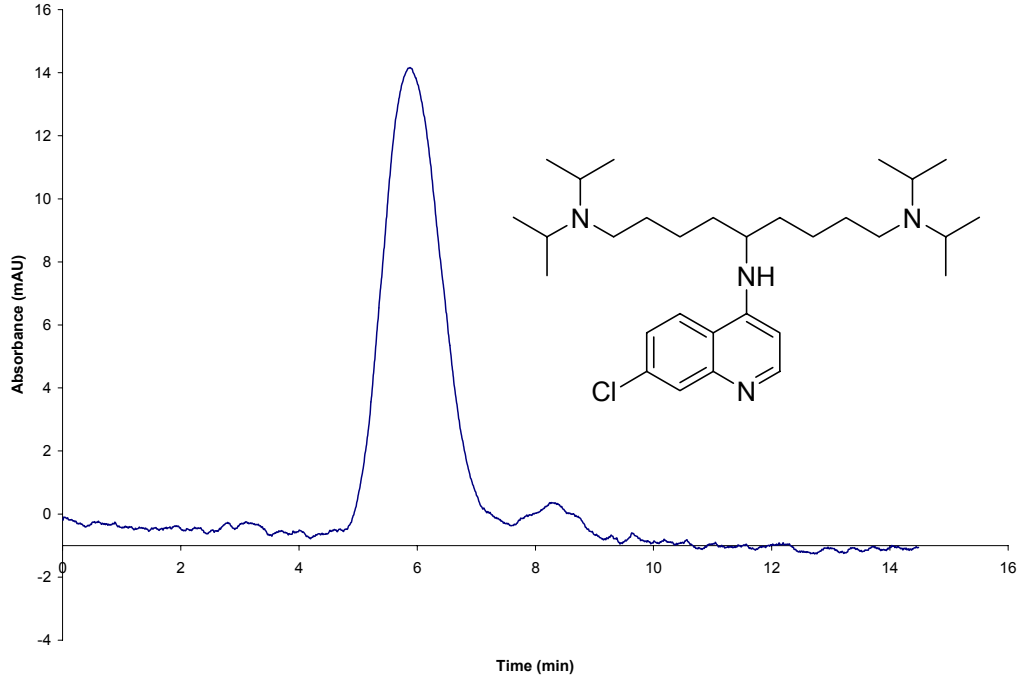
^{1}H-NMR (300 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-1,9-bis(diisopropylamino)-5-aminononane



HPLC analysis of *N*-(7-chloro-4-quinolyl)-1,9-bis(diisopropylamino)-5-amininonane

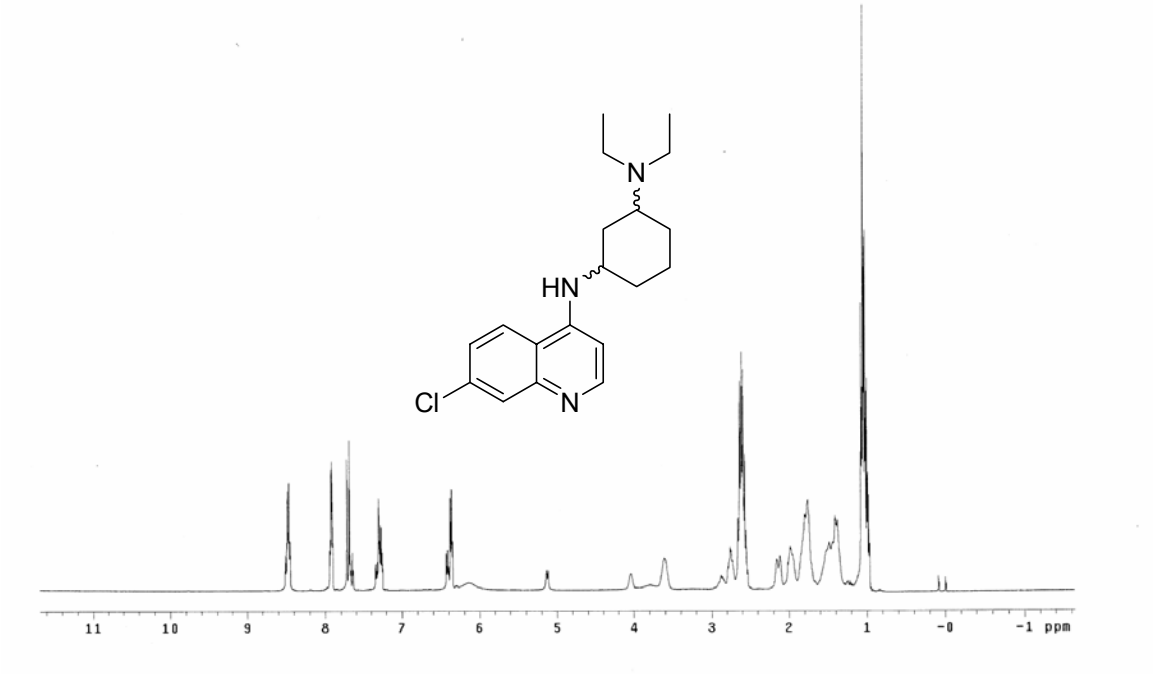


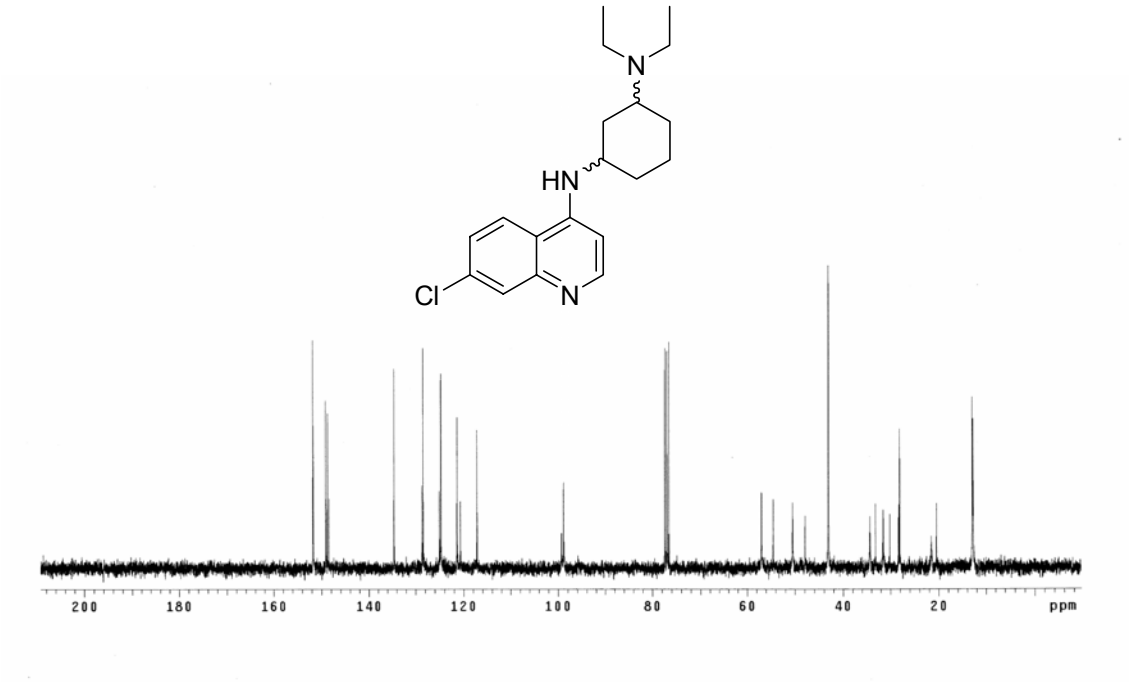
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 20% acetonitrile, 80% water containing 0.1% trifluoroacetic acid, injection volume: 5 μL, concentration: 0.5 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



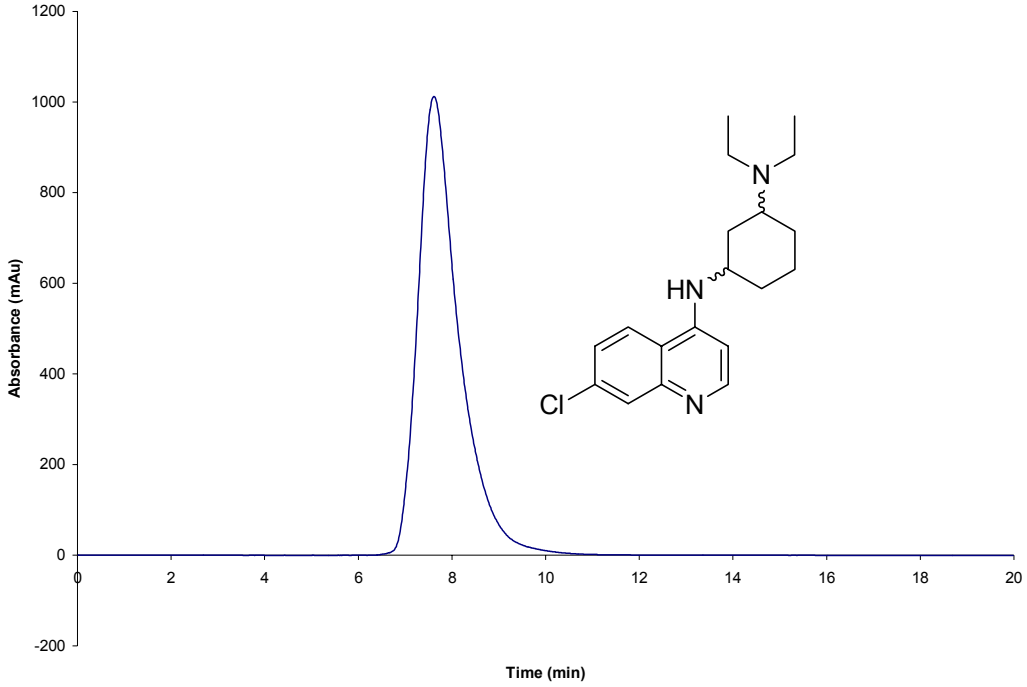
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 7 μL, concentration: 0.5 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N',N*'-diethyl-1,3-diaminocyclohexane

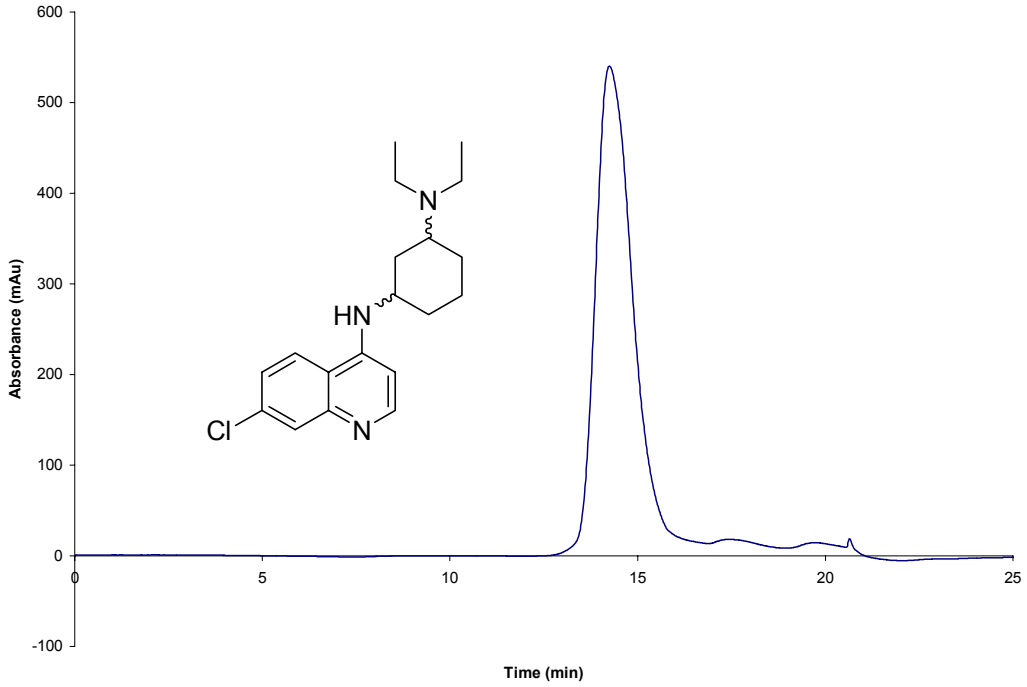




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N'*,*N*'-diethyl-1,3-diaminocyclohexane

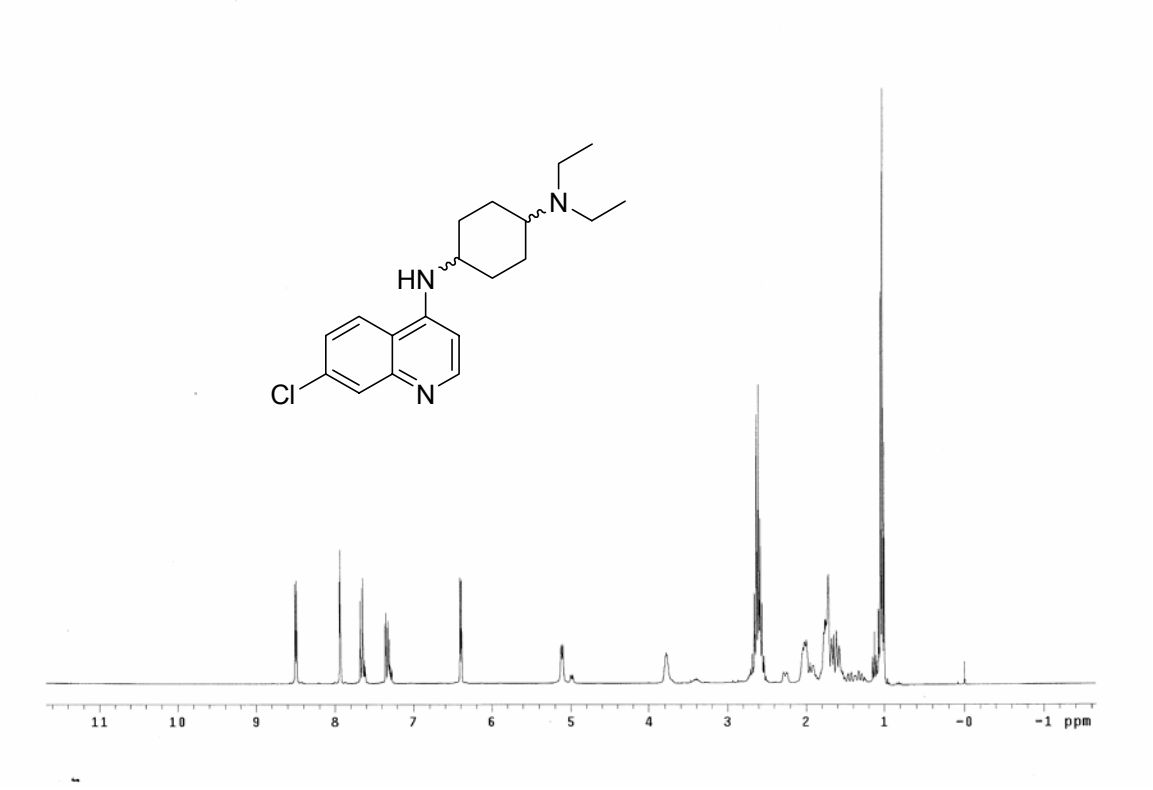


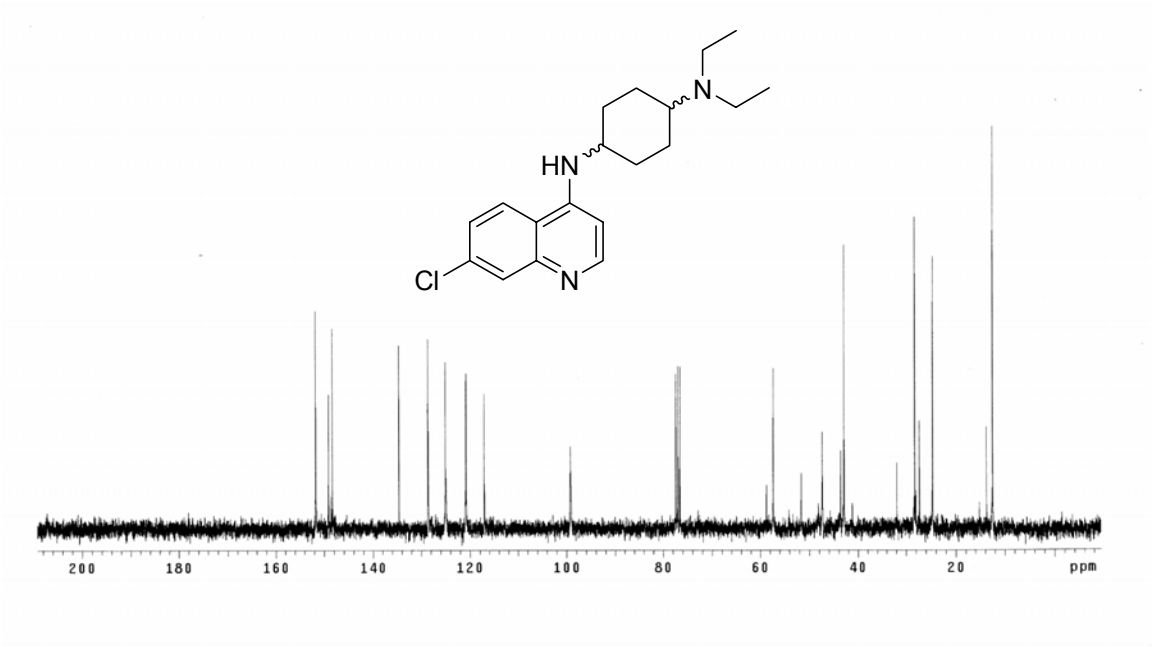
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 20% acetonitrile, 80% water containing 0.1% trifluoroacetic acid, injection volume: 20 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



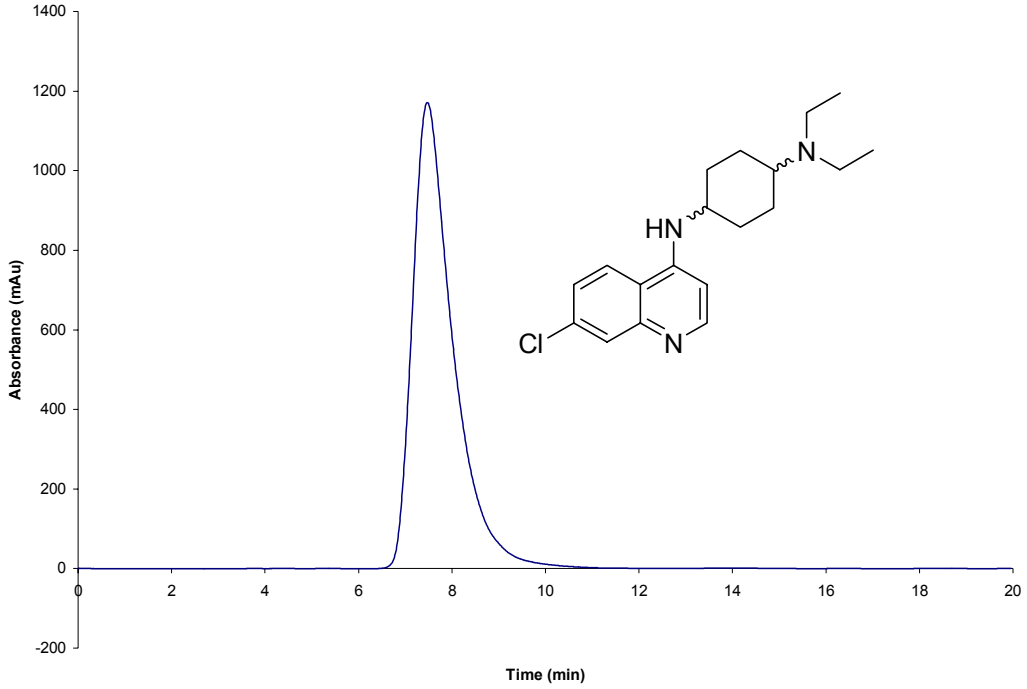
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N',N*'-diethyl-1,4-diaminocyclohexane

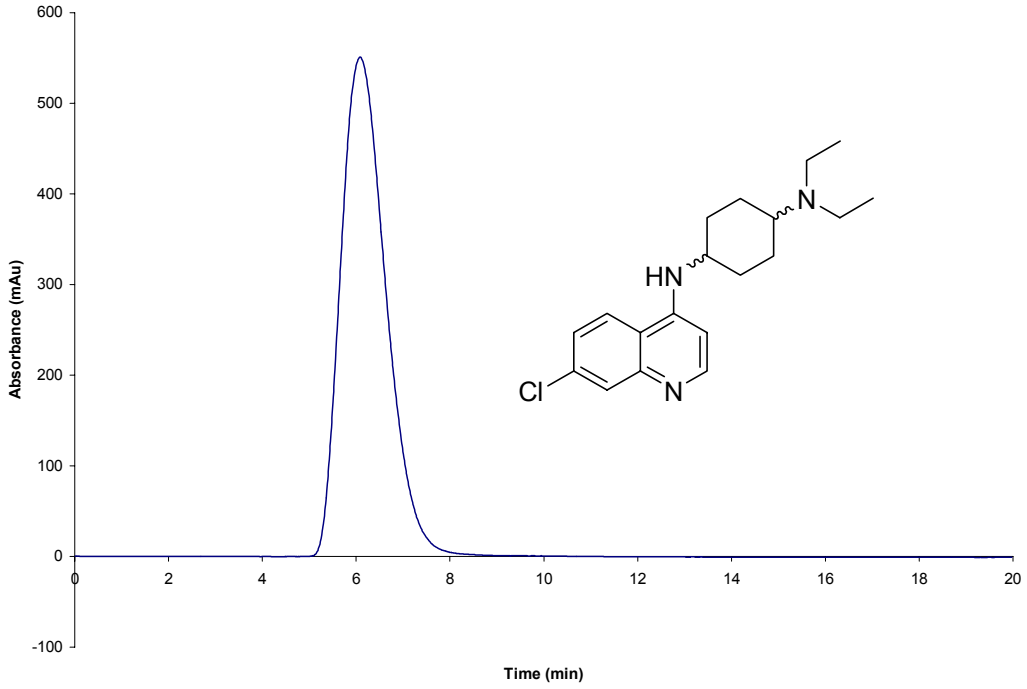




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N'*,*N*'-diethyl-1,4-diaminocyclohexane

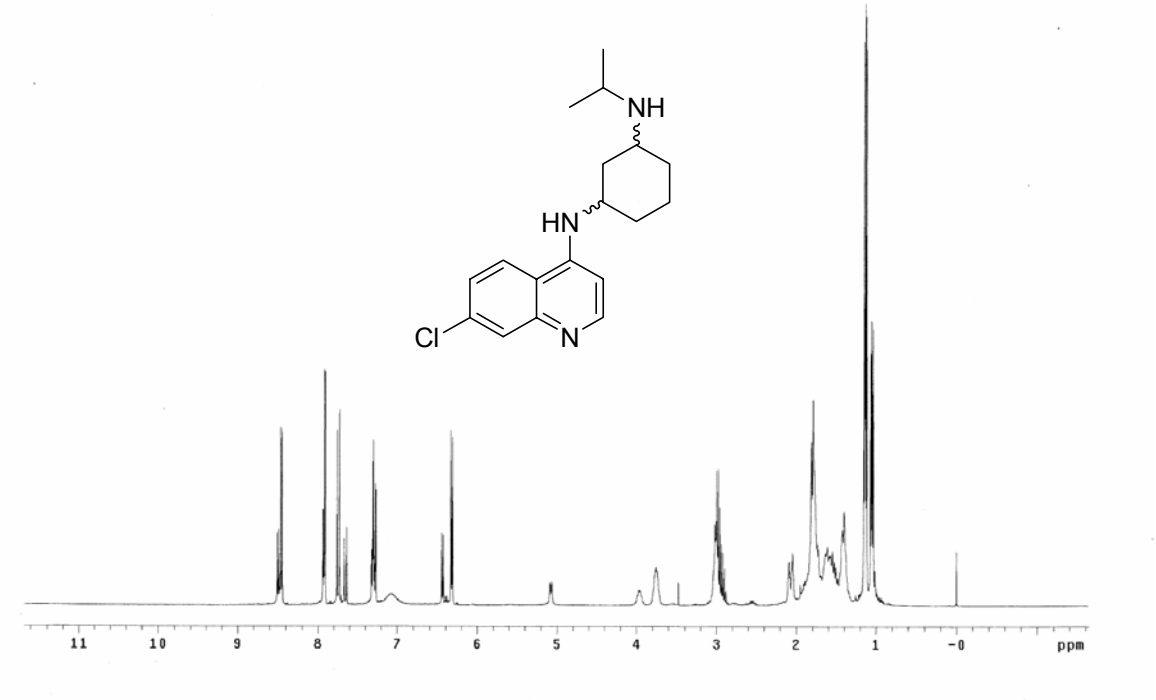


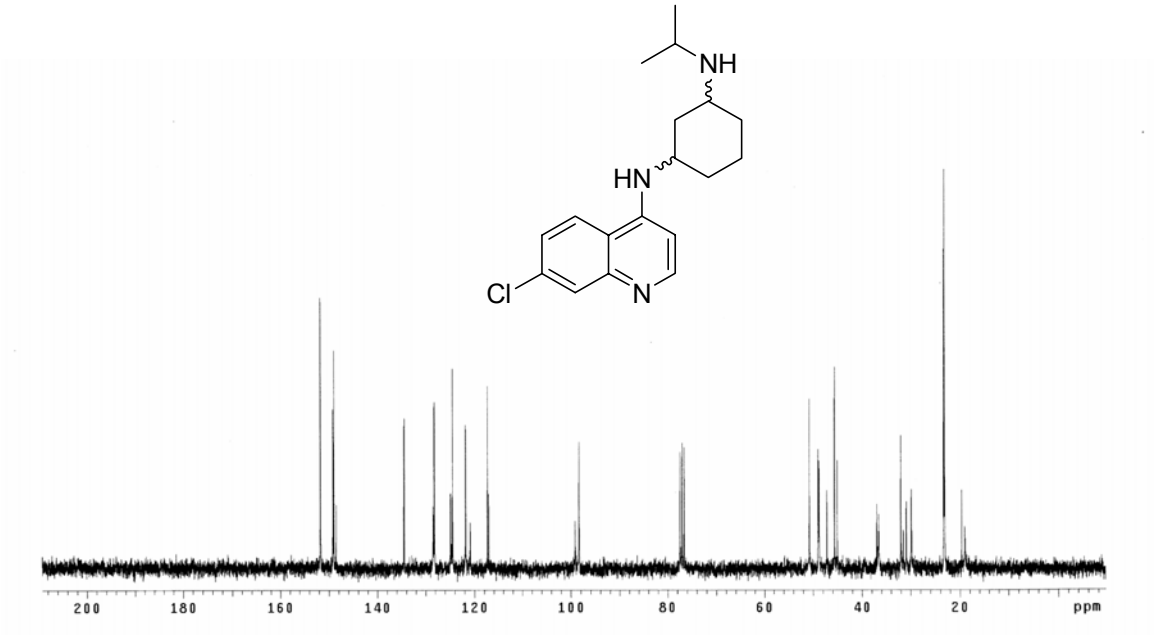
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 20% acetonitrile, 80% water containing 0.1% trifluoroacetic acid, injection volume: 20 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



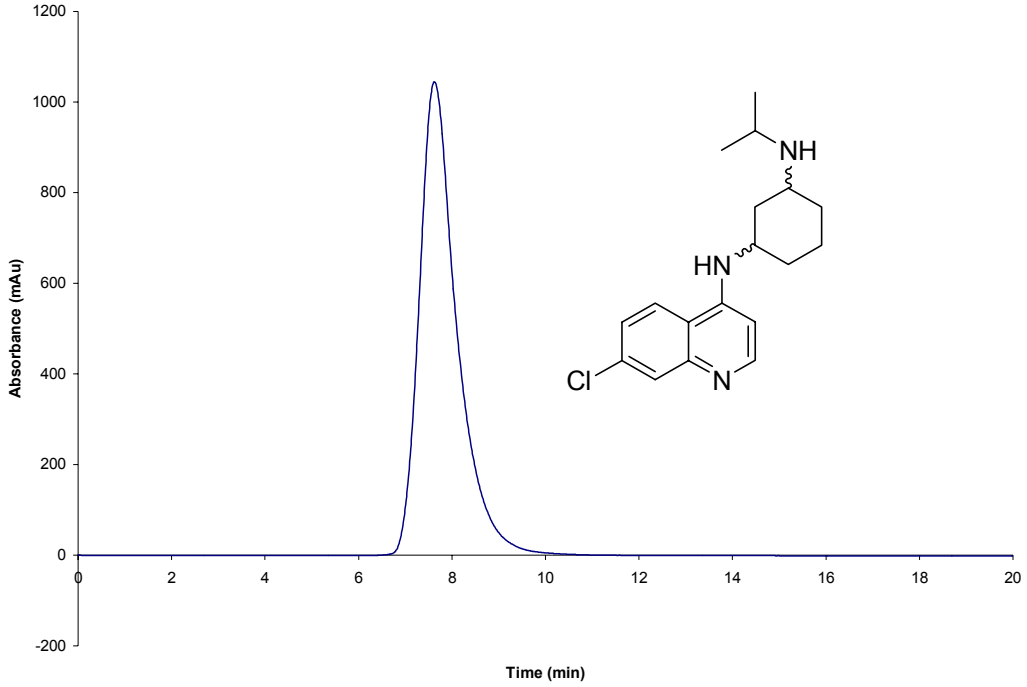
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 75% acetonitrile, 25% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N'*-isopropyl-1,3-diaminocyclohexane

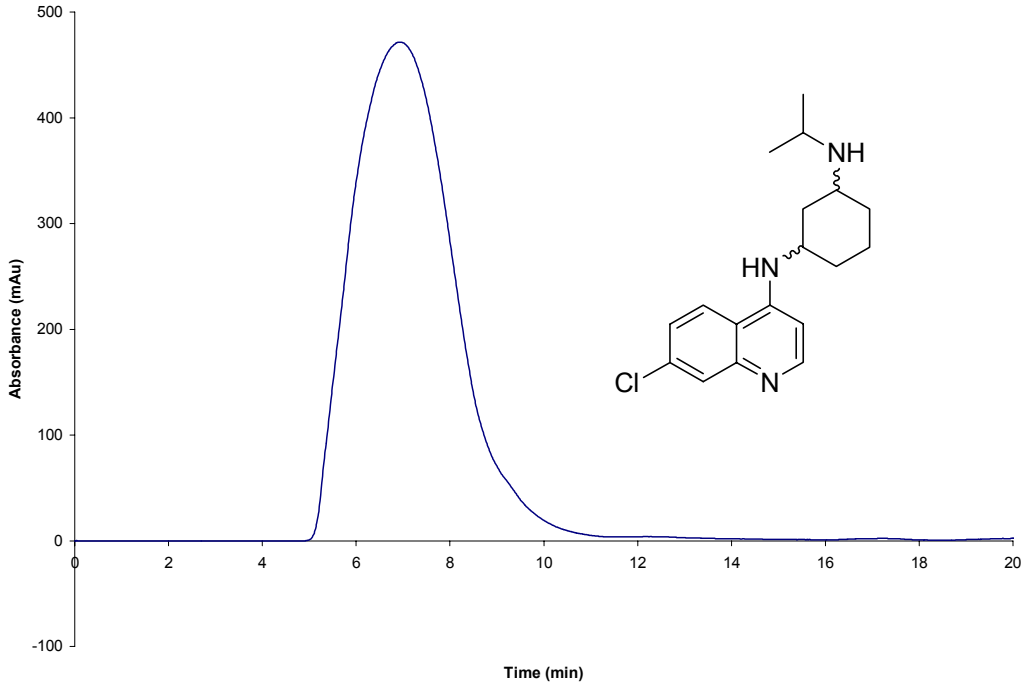




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N'*-isopropyl-1,3-diaminocyclohexane

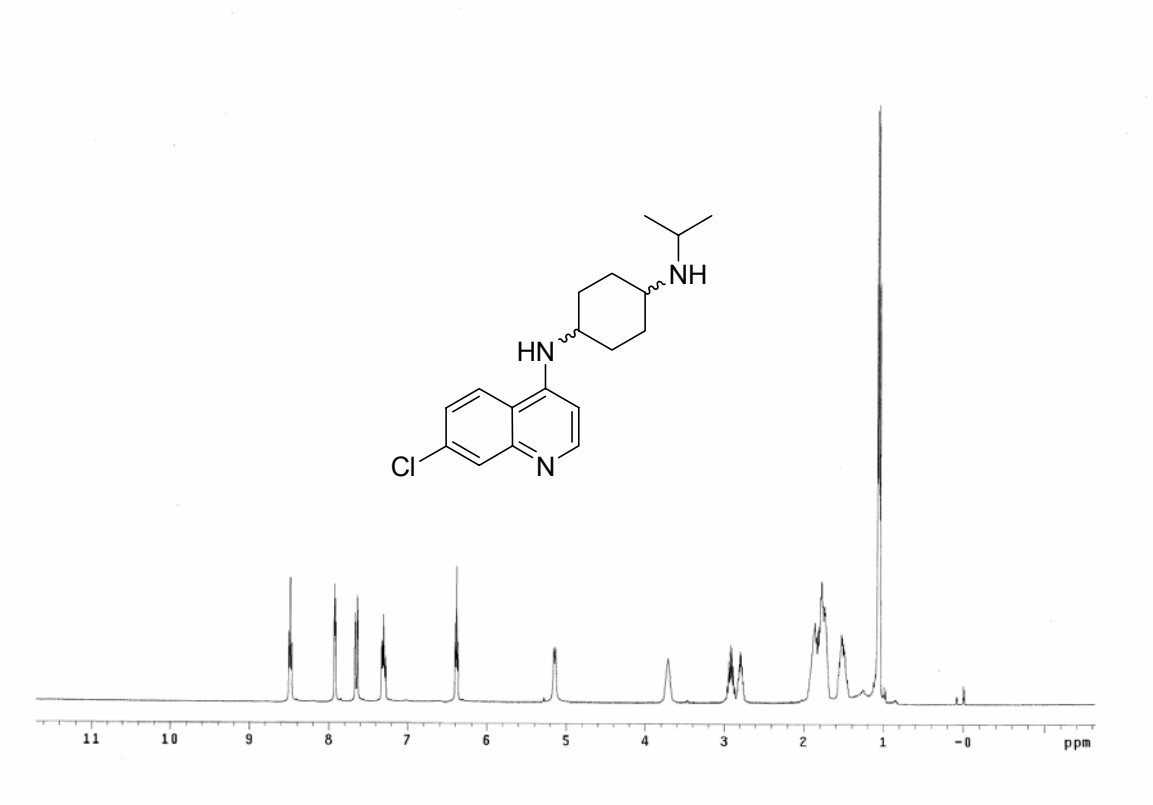


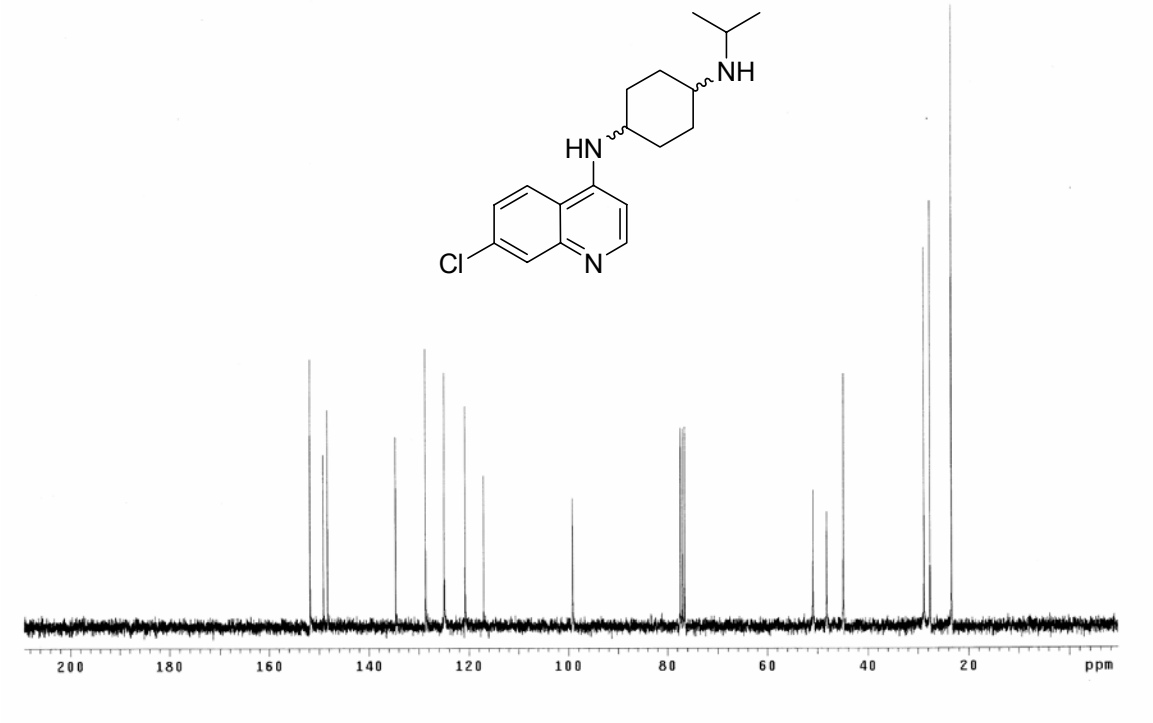
Conditions: C18 column (YMC-ODS-AQ), mobile phase: 20% acetonitrile, 80% water containing 0.1% trifluoroacetic acid, injection volume: 20 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



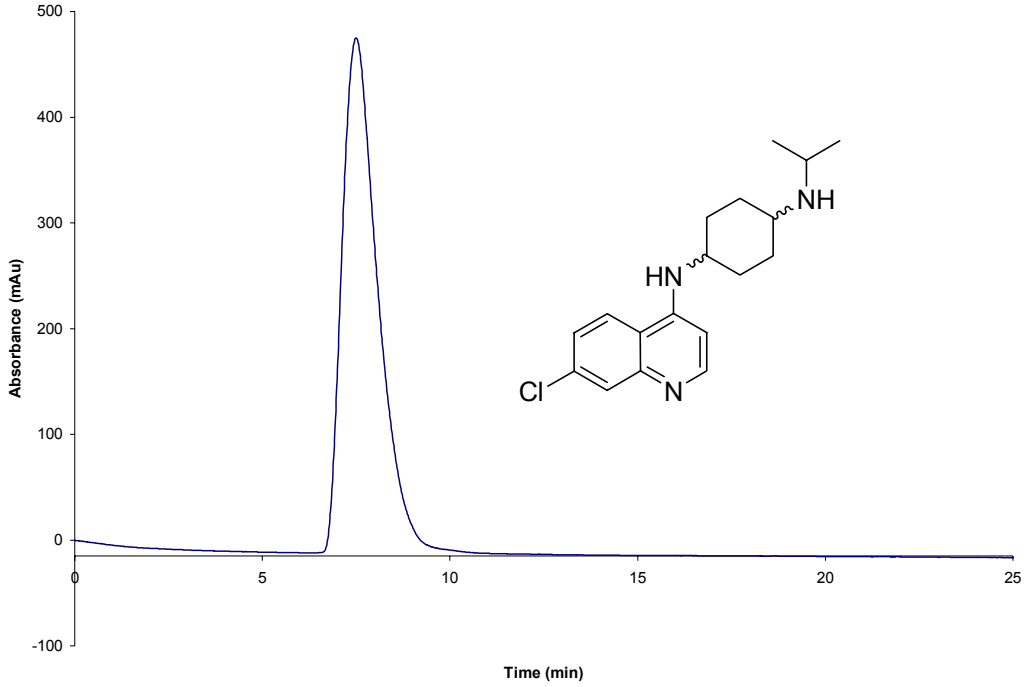
Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) of *N*-(7-chloro-4-quinolyl)-*N'*-isopropyl-1,4-diaminocyclohexane

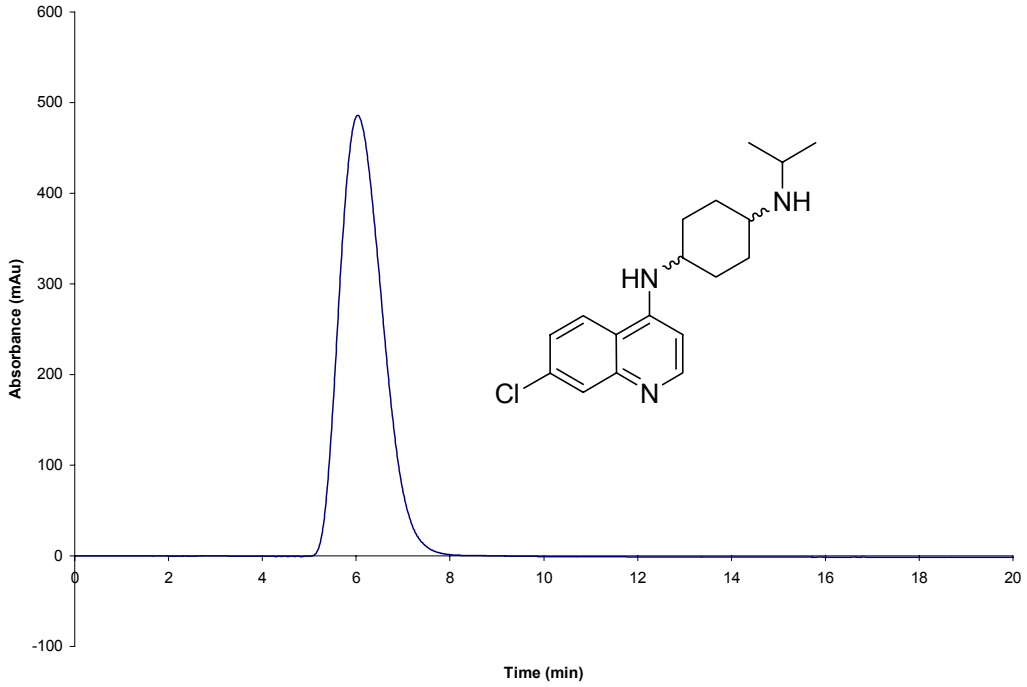




HPLC analysis of *N*-(7-chloro-4-quinolyl)-*N'*-isopropyl-1,4-diaminocyclohexane



Conditions: C18 column (YMC-ODS-AQ), mobile phase: 20% acetonitrile, 80% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min



Conditions: Nucleosil NH2 column (Alltech applied science), mobile phase: 80% acetonitrile, 20% water containing 0.1% trifluoroacetic acid, injection volume: 10 μL, concentration: 1 mg/mL, UV detection: 254 nm, flow rate: 1 mL/min