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# Anti-Ebola Activity of Diazachrysene Small Molecules

Života Selaković,[¶] Veronica Soloveva,[#] Dima N. Gharaibeh,[#] Jay Wells,[#] Sandra Šegan, Rekha G. Panchal,[#,*] Bogdan A. Šolaja[¶,*]

[¶] Faculty of Chemistry, University of Belgrade, Studentski trg 16, P.O. Box 51, 11158, Belgrade, Serbia.

[#] United States Army Medical Research Institute of Institute of Infectious Diseases, Fort Detrick, 1425 Porter Street, Frederick, MD 21702, United States.

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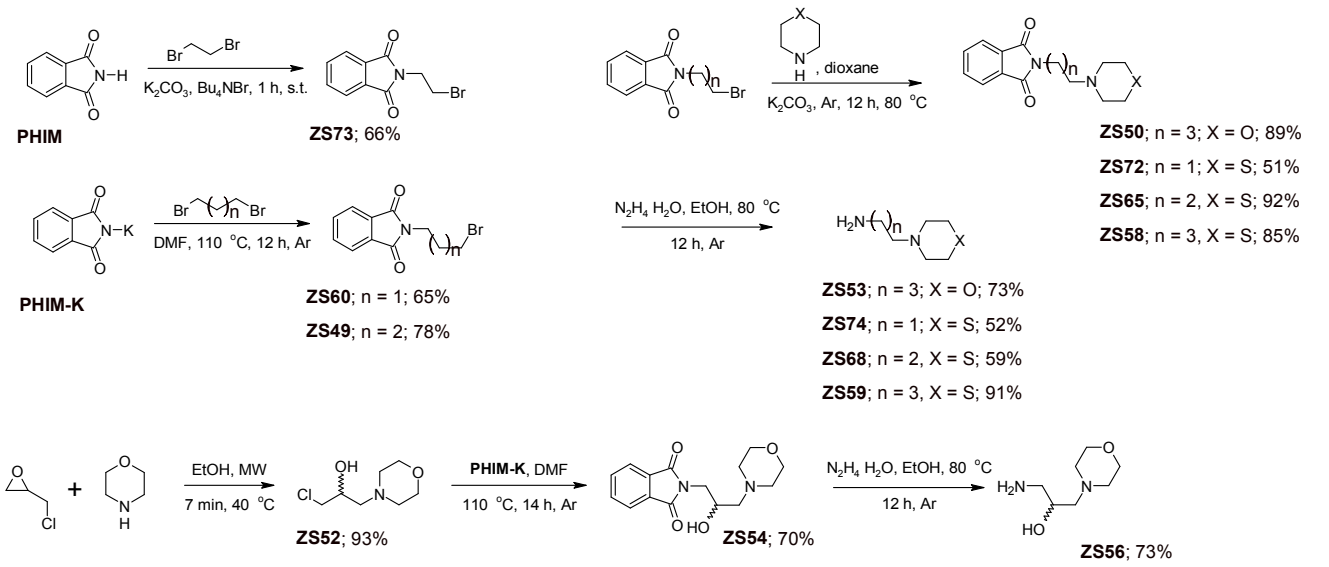
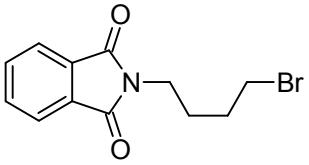



**General procedure for the preparation of α,ω-diaminoalkanes**

A mixture of the appropriate *N*-(ω-aminoalkyl)phtalimide and an excess of hydrazine hydrate in ethanol was stirred at 85 ºC for 12 hours under argon. The mixture was then cooled to room temperature and concentrated hydrochloric acid was added (approximately 1.5 - 2 mL per 100 mg of hydrazine hydrate). The formed precipitate was filtrated and washed with 95% ethanol. The filtrate was then reduced to a minimal volume under reduced pressure and the viscous crude product was dissolved in 50% potassium hydroxide. The product was extracted with dichloromethane and diethyl ether. The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was removed under slightly reduced pressure. The remaining crude diamine was purified by short-path vacuum distillation in a Kugelrohr.

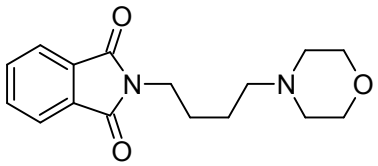
**2-(4-bromobutyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS49).**



A mixture of potassium phtalimide (370.7 mg, 2.001 mmol) and 1,4-dibromobuthane (2.20 g, 10.2 mmol) was stirred in dry DMF (5.0 mL) at 110 ºC for 12 hours. The excess 1,4-dibromobuthane and DMF were removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent Hex/EA gradient 95:5 → 85:15). The yield was 441.1 mg (78%). **ZS49**: white powder, mp = 78 ºC. IR (ATR): 3456w, 3036w, 2972w, 2944m, 2862w, 1767s, 1713s, 1614w, 1557w, 1520w, 1462m, 1433m, 1398s, 1371m, 1336w, 1305w, 1287w, 1258m, 1217w, 1185w, 1154w, 1116w, 1089w, 1022w, 990w, 951w, 916w, 893w, 796w, 743w, 715m $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.87 – 7.83 (m, 2H), 7.74 – 7.70 (m, 2H), 3.73 (t, $J$ = 6.8, 2H), 3.45 (t, $J$ = 6.2, 2H), 1.95 – 1.82 (m, 4H). $^{13}C$ NMR

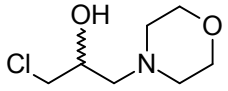
(125 MHz, $CDCl_3$): 168.34, 133.97, 132.02, 123.24, 36.93, 32.75, 29.81, 27.22. HRMS: *m/z* 282.01185 corresponds to molecular formula $C_{12}H_{12}BrNO_2H^+$ (error in ppm -2.01).

**2-(4-morpholin-4-ylbutyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS50).**



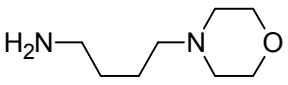
A mixture of **ZS49** (1.53 g, 5.43 mmol), morpholine (947 mg, 10.9 mmol) and potassium carbonate (1.13 g, 8.16 mmol) was stirred in dry dioxane (65 mL) at 85 ºC for 12 hours. The excess morpholine and dioxane were removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent EA/MeOH gradient 98:2 → 8:2). The yield was 1.40 g (89%). **ZS50**: colorless viscous oil. IR (ATR): 3608w, 3466w, 2945m, 2857w, 2809w, 2689w, 1771w, 1711s, 1614w, 1464w, 1440w, 1397m, 1366w, 1334w, 1306w, 1272w, 1187w, 1117m, 1070w, 1044w, 866w, 720m $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.86 – 7.82 (m, 2H), 7.74 – 7.69 (m, 2H), 3.73 – 3.68 (m, 6H), 2.44 (bs, 4H), 2.39 – 2.35 (m, 2H), 1.75 – 1.68 (m, 2H), 1.58 – 1.52 (m, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 168.35, 133.84, 132.06, 123.12, 66.81, 58.27, 53.56, 37.73, 26.44, 23.68. HRMS: *m/z* 289.15430 corresponds to molecular formula $C_{16}H_{20}N_2O_3H^+$ (error in ppm -1.28).

**1-chloro-3-morpholin-4-ylpropan-2-ol (ZS52).**



Racemic epichlorohydrin (1.546 g, 16.71 mmol) and morpholine (1.316 g, 15.10 mmol) were dissolved in ethanol (45 mL) in a MW cuvette under argon. The reaction mixture was subjected to MW irradiation using a *Biotage Initiator 2.5* apparatus for 7 minutes at 40 ºC. The excess epichlorohydrin and ethanol were removed under reduced pressure. The mass of the remaining liquid was monitored during evaporation, to avoid loss of product. The yield was 2.52 g (93%). **ZS52**: colorless viscous liquid. IR (ATR): 3645w, 3345m, 2957m, 2895w, 2858m, 2814m, 2692w, 1647w, 1455w, 1379w, 1297w, 1207w, 1143w, 1118s, 1067w, 1038w, 1010w, 968w, 943w, 914w, 866w, 802w, 739w, 702w, 636w, 579w $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): 4.03 – 3.90 (m, 1H), 3.81 – 3.67 (m, 4H), 3.63 – 3.54 (m, 2H), 3.34 (bs, H-O), 2.74 – 2.59 (m, 2H), 2.56 – 2.41 (m, 4H). $^{13}C$ NMR (50 MHz, $CDCl_3$): 66.84, 66.40, 61.47, 53.71, 46.98. HRMS: *m/z* 180.07774 corresponds to molecular formula $C_7H_{14}ClNO_2H^+$ (error in ppm -4.68).

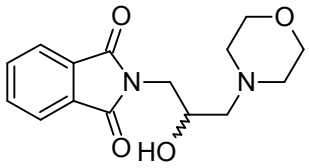
**(4-morpholin-4-ylbutyl)amine (ZS53).**



The general procedure provided above was followed using **ZS50** (2.26 g, 7.84 mmol), hydrazine hydrate (0.70 mL, 14 mmol) and ethanol (100 mL). The yield was 0.90 g (73%). **ZS53**: a

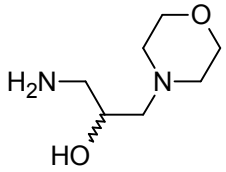
colorless viscous liquid. IR (ATR): 3352w, 2933m, 2857m, 2812m, 1569w, 1462m, 1389w, 1307m, 1114s, 1069w, 1031w, 1006w, 913w, 863w, 794w, 739w, 630w $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CD_3OD$): 3.70 – 3.67 (m, 4H), 2.69 – 2.65 (m, 2H), 2.47 (bs, 4H), 2.39 – 2.34 (m, 2H), 1.58 – 1.49 (m, 4H). $^{13}C$ NMR (125 MHz, $CD_3OD$): 66.19, 58.46, 53.30, 40.80, 29.86, 23.26. HRMS: *m*/*z* 159.14881 corresponds to molecular formula $C_8H_{18}N_2OH^+$ (error in ppm -2.41).

**2-(2-hydroxy-3-morpholin-4-ylpropyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS54).**



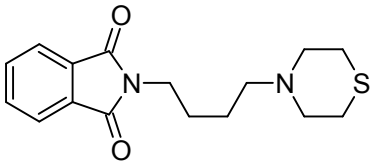
A mixture of potassium phtalimide (1.49 g, 8.07 mmol) and **ZS52** (1.45 g, 8.07 mmol) was stirred in dry DMF (67 mL) at 110 ºC for 14 hours. DMF was removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent EA/MeOH gradient 98:2 → 8:2). The yield was 1.64 g (70%). **ZS54**: white powder, mp = 125 ºC. IR (ATR): 3099w, 3061w, 3042w, 2992w, 2943m, 2917w, 2892w, 2853m, 2816m, 2739w, 2690w, 1766m, 1703s, 1615w, 1460w, 1427m, 1397s, 1323w, 1299w, 1240w, 1139w, 1112m, 1077m, 1014w, 931w, 897w, 858w, 718w $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$ + $CD_3OD$): 7.89 – 7.84 (m, 2H), 7.78 – 7.73 (m, 2H), 4.13 – 4.05 (m, 1H), 3.82 – 3.73 (m, 2H), 3.70 – 3.62 (m, 4H), 2.61 – 2.54 (m, 2H), 2.51 – 2.42 (m, 4H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 168.62, 134.00, 131.74, 123.16, 66.61, 64.79, 62.28, 53.59, 42.00. HRMS: *m/z* 291.13369 corresponds to molecular formula $C_{15}H_{18}N_2O_4H^+$ (error in ppm -0.83).

**1-amino-3-morpholin-4-ylpropan-2-ol (ZS56).**



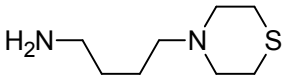
The general procedure provided above was followed using **ZS54** (2.50 g, 8.61 mmol), hydrazine hydrate (1.15 g, 23.0 mmol) and ethanol (80 mL). The yield was 1.10 g (73%). **ZS56**: a colorless viscous liquid. IR (ATR): 3364s, 3298m, 2929m, 2858s, 2814m, 1597w, 1456w, 1297w, 1274w, 1117s, 1070w, 1037w, 1007w, 944w, 916w, 866w $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CD_3OD$): 3.77 – 3.71 (m, 1H), 3.70 – 3.67 (m, 4H), 2.72 (dd, $J_1$ = 13, $J_2$ = 4, 1H), 2.58 – 2.47 (m, 5H), 2.41 – 2.33 (m, 2H). $^{13}C$ NMR (125 MHz, $CD_3OD$): 70.21, 68.00, 64.12, 55.49, 47.22. HRMS: *m/z* 161.12845 corresponds to molecular formula $C_7H_{16}N_2O_2H^+$ (error in ppm -1.52).

**2-(4-thiomorpholin-4-ylbutyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS58).**



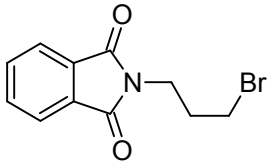
A mixture of **ZS49** (1.00 g, 3.54 mmol), thiomorpholine (0.70 g, 6.8 mmol) and potassium carbonate (0.80 g, 5.8 mmol) was stirred in dry dioxane (20 mL) at 85 ºC for 12 hours. The excess thiomorpholine and dioxane were removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent EA). The yield was 0.92 g (85%). **ZS58**: colorless viscous oil. IR (ATR): 3464w, 2939m, 2866w, 2808m, 2773w, 1771m, 1711s, 1614w, 1465w, 1439m, 1397s, 1368m, 1335w, 1282w, 1188w, 1110w, 1086w, 1050w, 958w, 930w, 864w, 795w, 720m, 530w $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.86 – 7.81 (m, 2H), 7.73 – 7.68 (m, 2H), 3.70 (t, $J$ = 7.2, 2H), 2.70 – 2.62 (m, 8H), 2.40 – 2.35 (m, 2H), 1.72 – 1.65 (m, 2H), 1.55 – 1.48 (m, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 168.42, 133.89, 132.11, 123.16, 58.64, 54.98, 37.80, 27.97, 26.51, 23.80. HRMS: *m/z* 305.13226 corresponds to molecular formula $C_{16}H_{20}N_2O_2SH^+$ (error in ppm +1.42).

**(4-thiomorpholin-4-ylbutyl)amine (ZS59).**



The general procedure provided above was followed using **ZS58** (0.89 g, 2.9 mmol), hydrazine hydrate (0.50 g, 10 mmol) and ethanol (45 mL). The yield was 0.465 g (91%). **ZS59**: a colorless viscous liquid. IR (ATR): 3356s, 2934s, 2865s, 2811s, 1574m, 1467m, 1423w, 1378w, 1322m, 1283w, 1208w, 1115m, 1005w, 955w, 777w, 735w, 705w, 669w, 635w, 612w $cm^{-1}$. $^1H$ NMR (500 MHz, $CD_3OD$): 2.75 – 2.71 (m, 4H), 2.69 – 2.62 (m, 6H), 2.41 – 2.37 (m, 2H), 1.57 – 1.50 (m, 2H), 1.49 – 1.42 (m, 2H). $^{13}C$ NMR (125 MHz, $CD_3OD$): 60.39, 56.30, 42.55, 31.99, 28.38, 24.66. HRMS: *m/z* 175.12690 corresponds to molecular formula $C_8H_{18}N_2SH^+$ (error in ppm +3.17).

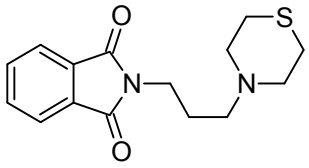
**2-(3-bromopropyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS60).**



A mixture of potassium phtalimide (1.50 g, 8.10 mmol) and 1,3-dibromopropane (8.25 g, 40.9 mmol) was stirred in dry DMF (50 mL) at 110 ºC for 12 hours. The excess 1,3-dibromopropane and DMF were removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent Hex/EA gradient 95:5 → 8:2). The yield was 1.40 g (65%). **ZS60**: white powder, mp = 73 ºC. IR (ATR): 3460w, 3093w, 3062w, 3042w, 2966w, 2943w, 2853w, 1767m, 1714s, 1615w, 1466w, 1434m, 1397s, 1356s, 1311m, 1287w, 1225m, 1188w, 1171w, 1111w, 1085w, 1044w, 1016m, 966w, 916w, 889w, 833w, 803w, 754w,

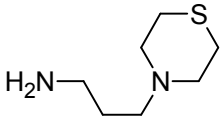
721m, 648w, 605w, 530w $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.88 – 7.83 (m, 2H), 7.75 – 7.70 (m, 2H), 3.84 (t, *J* = 6.9, 2H), 3.42 (t, *J* = 6.8, 2H), 2.27 (quint, *J* = 6.8, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 168.22, 134.03, 131.98, 123.30, 36.70, 31.61, 29.75. HRMS: *m/z* 285.02368 corresponds to molecular formula $C_{11}H_{10}BrNO_2H^+$ (error in ppm +1.29).

**2-(3-thiomorpholin-4-ylpropyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS65).**



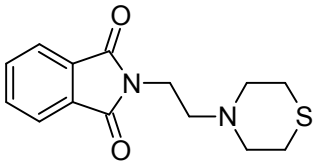

A mixture of **ZS60** (1.00 g, 3.73 mmol), thiomorpholine (0.77 g, 7.5 mmol) and potassium carbonate (2.06 g, 14.9 mmol) was stirred in dry dioxane (50 mL) at 85 ºC for 12 hours. The excess thiomorpholine and dioxane were removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent EA). The yield was 0.99 g (92%). **ZS65**: colourless viscous oil. IR (ATR): 3456w, 3224w, 3103w, 3049w, 3026w, 2942m, 2911m, 2881w, 2804s, 2771m, 2664w, 2416w, 2317w, 2244w, 1999w, 1960w, 1771w, 1699s, 1614w, 1462m, 1442w, 1398s, 1353w, 1333m, 1285m, 1249w, 1220w, 1173w, 1122w, 1074w, 1042w, 1022m, 965w, 930w, 888w, 860w, 841w, 800w, 775w, 718m, 669w, 634w $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.87 – 7.82 (m, 2H), 7.74 – 7.69 (m, 2H), 3.75 (t, *J* = 6.9, 2H), 2.67 – 2.61 (m, 4H), 2.55 – 2.50 (m, 4H), 2.42 (t, *J* = 6.8, 2H), 1.85 (quint, *J* = 6.9, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 168.45, 133.87, 132.25, 123.09, 56.72, 54.98, 36.58, 27.85, 24.89. HRMS: *m/z* 291.11649 corresponds to molecular formula $C_{15}H_{18}N_2O_2SH^+$ (error in ppm +1.07).

**(3-thiomorpholin-4-ylpropyl)amine (ZS68).**



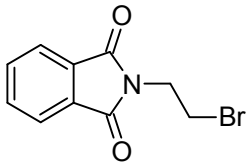

The general procedure provided above was followed using **ZS65** (337.9 mg, 1.164 mmol), hydrazine hydrate (174.5 mg, 3.486 mmol) and ethanol (22 mL). The yield was 110.0 mg (59%). **ZS68**: a colorless viscous liquid. IR (ATR): 3361s, 2944s, 2868s, 2816s, 1589m, 1467m, 1422m, 1378m, 1325m, 1286m, 1211w, 1124m, 1010w, 956m, 782w, 673w $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 2.76 – 2.65 (m, 10H), 2.42 (t, *J* = 7.2, 2H), 1.62 (quint, *J* = 7, 2H), 1.54 (bs, 2H-N, exchangeable with $D_2O$). $^{13}C$ NMR (125 MHz, $CDCl_3$): 57.09, 55.09, 40.69, 30.17, 27.98. HRMS: *m/z* 161.11093 corresponds to molecular formula $C_7H_{16}N_2SH^+$ (error in ppm +1.44).

**2-(2-thiomorpholin-4-ylethyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS72).**



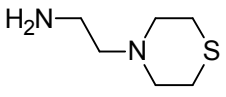
A mixture of **ZS73** (297.9 mg, 1.172 mmol), thiomorpholine (250.0 mg, 2.423 mmol) and potassium carbonate (325.2 mg, 2.353 mmol) was stirred in dry dioxane (10 mL) at 85 ºC for 12 hours. The excess thiomorpholine and dioxane were removed under reduced pressure and the remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent Hex/EA gradient 95:5 → 1:1). The yield was 166.1 mg (51%). **ZS72**: white powder, mp = 115 ºC. IR (ATR): 3456w, 3031w, 3004w, 2954w, 2929m, 2808m, 1767m, 1710s, 1610w, 1469m, 1439m, 1400s, 1328m, 1292m, 1216w, 1190w, 1162w, 1136w, 1108w, 1046w, 1024m, 956w, 874w, 808w, 722m, 631w, 529w $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.87 – 7.82 (m, 2H), 7.74 – 7.70 (m, 2H), 3.80 (t, *J* = 6.5, 2H), 2.80 – 2.75 (m, 4H), 2.65 (t, *J* = 6.5, 2H), 2.61 – 2.56 (m, 4H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 168.33, 133.85, 132.14, 123.16, 56.20, 54.88, 35.08, 27.98. HRMS: *m/z* 277.09985 corresponds to molecular formula $C_{14}H_{16}N_2O_2SH^+$ (error in ppm -2.42).

**2-(2-bromoethyl)-1*H*-isoindole-1,3(2*H*)-dione (ZS73).**



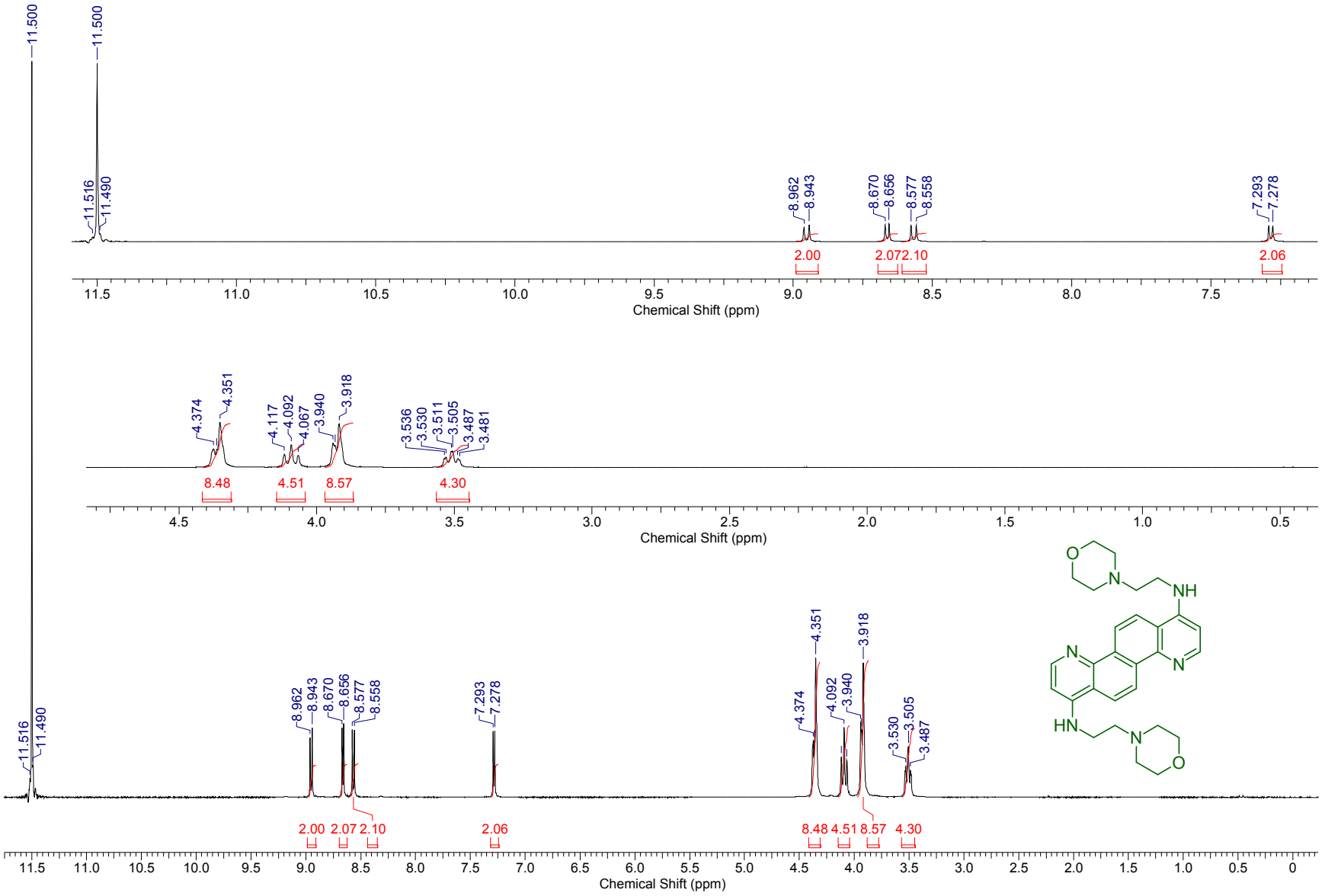
Phtalimide (1.00 g, 6.80 mmol), potassium-carbonate (2.82 g, 20.4 mmol) and tetrabutylammonium bromide (0.22 g, 0.68 mmol) were crushed together in a mortar. The mixture was transferred to a round-bottom flask and 1,2-dibromoethane was added (3.83 g, 20.4 mmol). The mixture was stirred sporadically with a spatula. After one hour, the mixture was dissolved in dichloromethane and the solution was washed with water and dried over anhydrous sodium sulfate. The solvent and excess 1,2-dibromoethane were removed under reduced pressure. The remaining crude product was purified by column chromatography (dry flash, $SiO_2$, eluent Hex/EA gradient 95:5 → 1:1). The yield was 1.15 g (66%). **ZS73**: white powder, mp = 78 ºC. IR (ATR): 3465w, 3094w, 3046w, 2947w, 2915w, 2852w, 1767m, 1712s, 1609w, 1511w, 1469w, 1431m, 1396s, 1360m, 1329m, 1255w, 1230w, 1189w, 1170w, 1088w, 1070m, 1030w, 1008w, 977w, 926w, 866w, 804w, 726m, 716m, 602w, 531w, 510w $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): 7.90 – 7.86 (m, 2H), 7.77 – 7.73 (m, 2H), 4.12 (t, *J* = 6.8, 2H), 3.62 (t, *J* = 6.8, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 167.79, 134.20, 131.82, 123.50, 39.27, 28.11. HRMS: *m/z* 253.98135 corresponds to molecular formula $C_{10}H_8BrNO_2H^+$ (error in ppm +0.91).

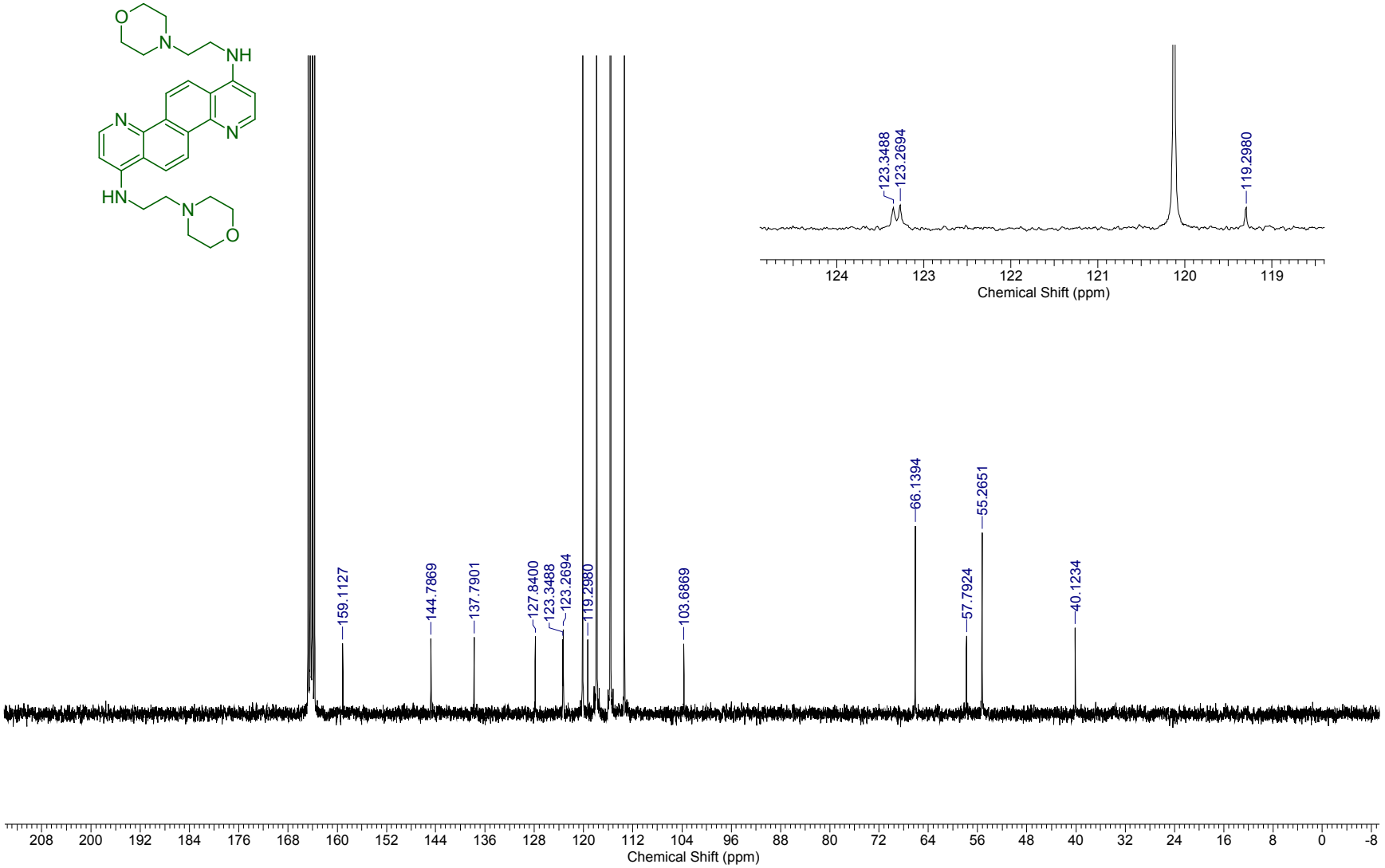
**(2-thiomorpholin-4-ylethyl)amine (ZS74).**



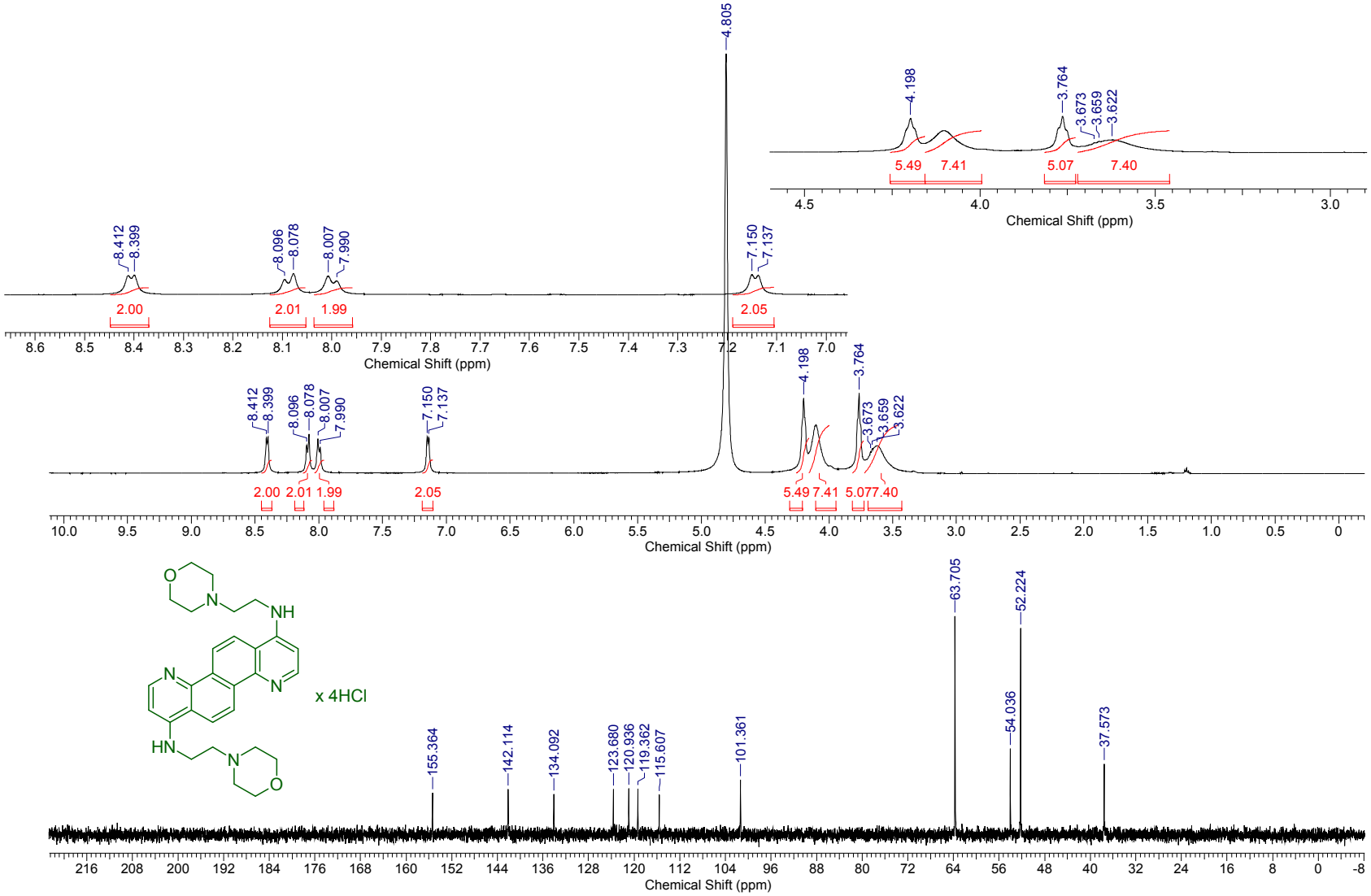
The general procedure provided above was followed using **ZS72** (0.50 g, 1.8 mmol), hydrazine hydrate (0.27 g, 5.4 mmol) and ethanol (27 mL). The yield was 135.3 mg (52%). **ZS74**: a colorless viscous liquid. IR (ATR): 3364s, 2933s, 2874m, 2818s, 1689m, 1570m, 1483s, 1424m, 1366m, 1342m, 1322m, 1302m, 1226w, 1208w, 1169w, 1120m, 1054w, 1011w, 960s, 870w, 813w, 771w, 750w, 670w $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): 2.77 (t, $J$ = 6.2, 2H), 2.75 – 2.70 (m, 4H), 2.70 – 2.65 (m, 4H), 2.43 (t, $J$ = 6, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): 61.72, 55.16, 38.58, 28.01. HRMS: *m/z* 147.09486 corresponds to molecular formula $C_6H_{14}N_2SH^+$ (error in ppm -1.28).

**_N,N′_-bis[2-(morpholin-4-yl)ethyl]quinolino[8,7-_h_]quinoline-1,7-diamine (7): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**

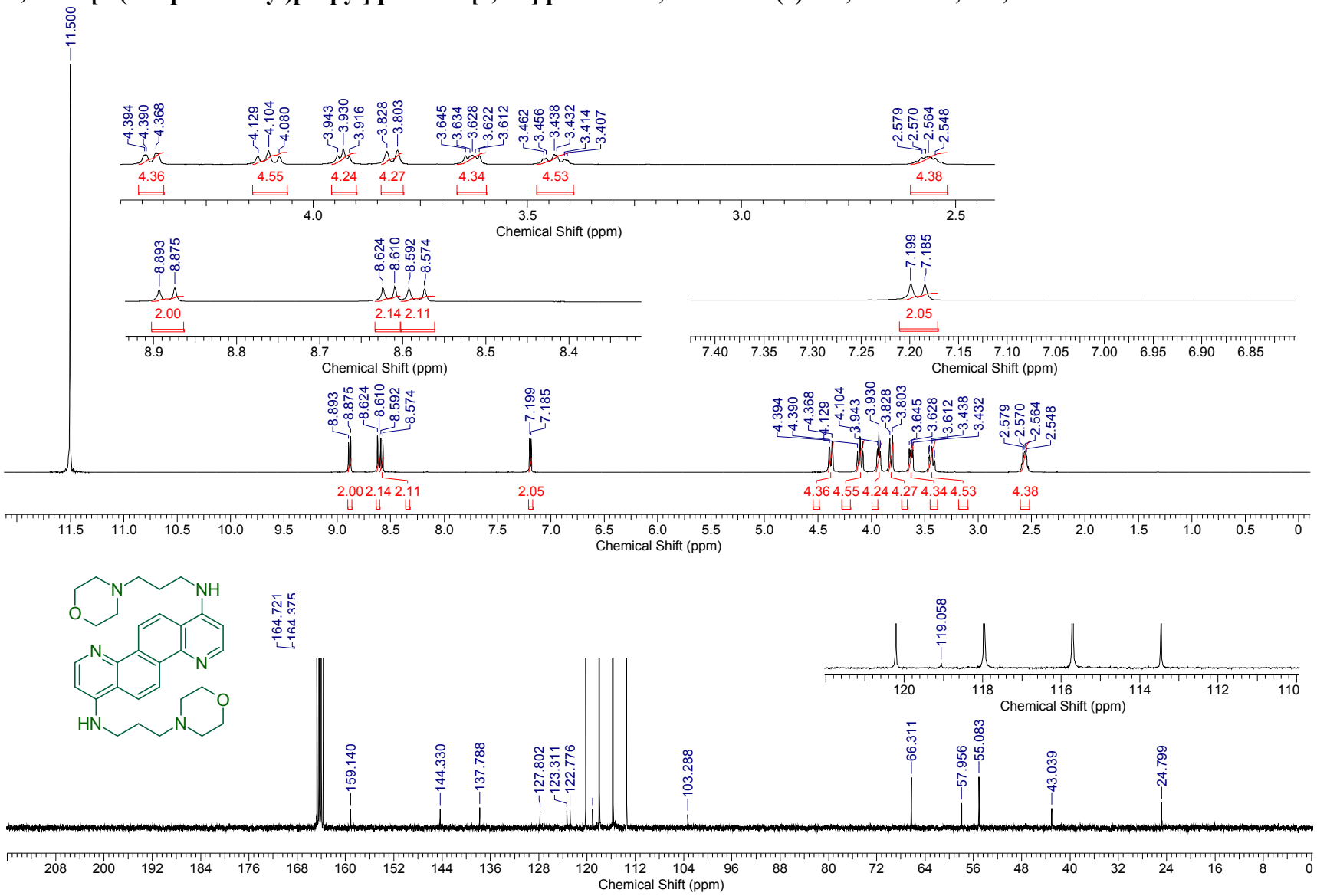



O
N
NH
N
N
HN
N
O
123.3488
123.2694
119.2980
124
123
122
121
120
119
Chemical Shift (ppm)
159.1127
144.7869
137.7901
127.8400
123.3488
123.2694
119.2980
103.6869
66.1394
57.7924
55.2651
40.1234
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)

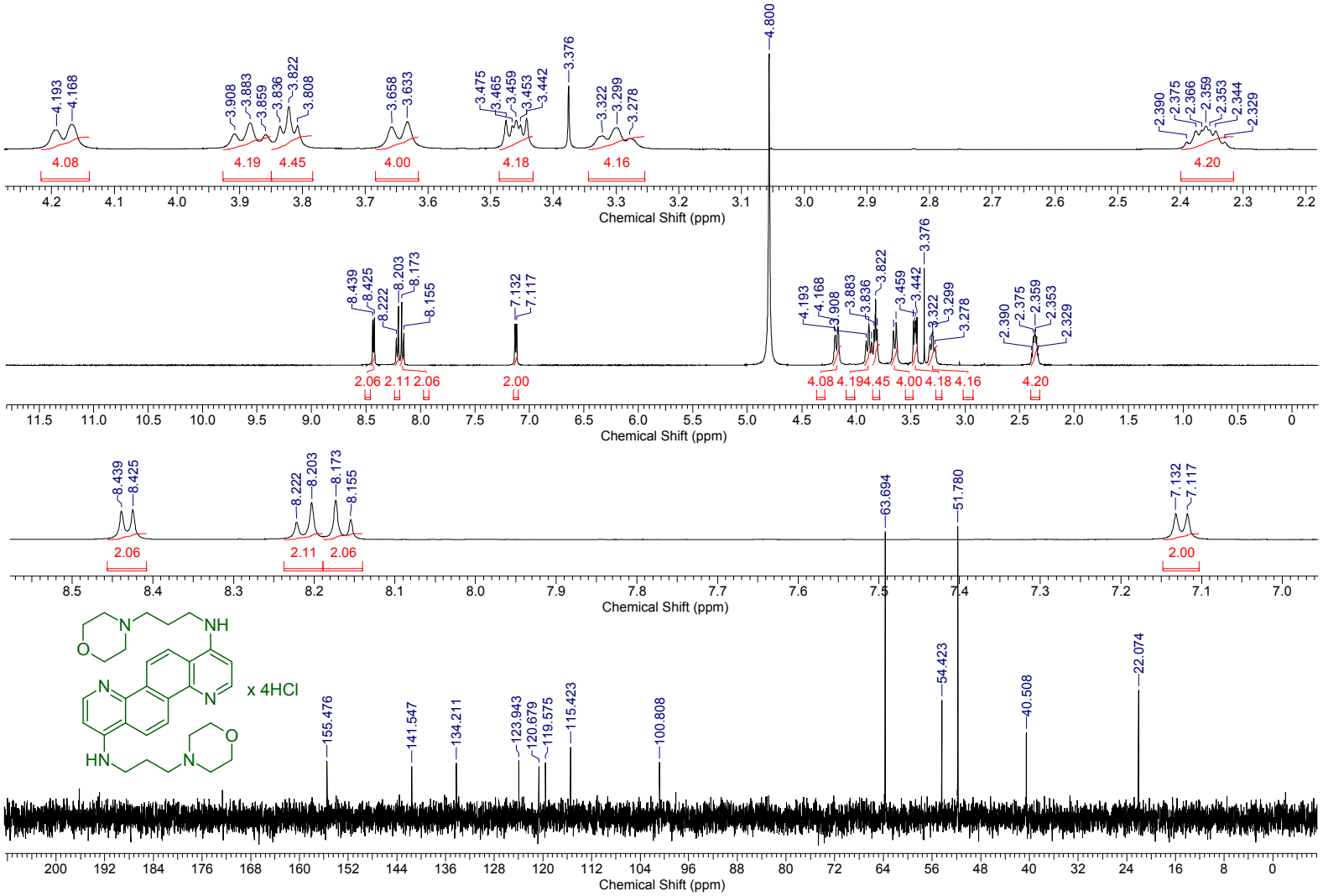
**_N,N′_-bis[2-(morpholin-4-yl)ethyl]quinolino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (5): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**



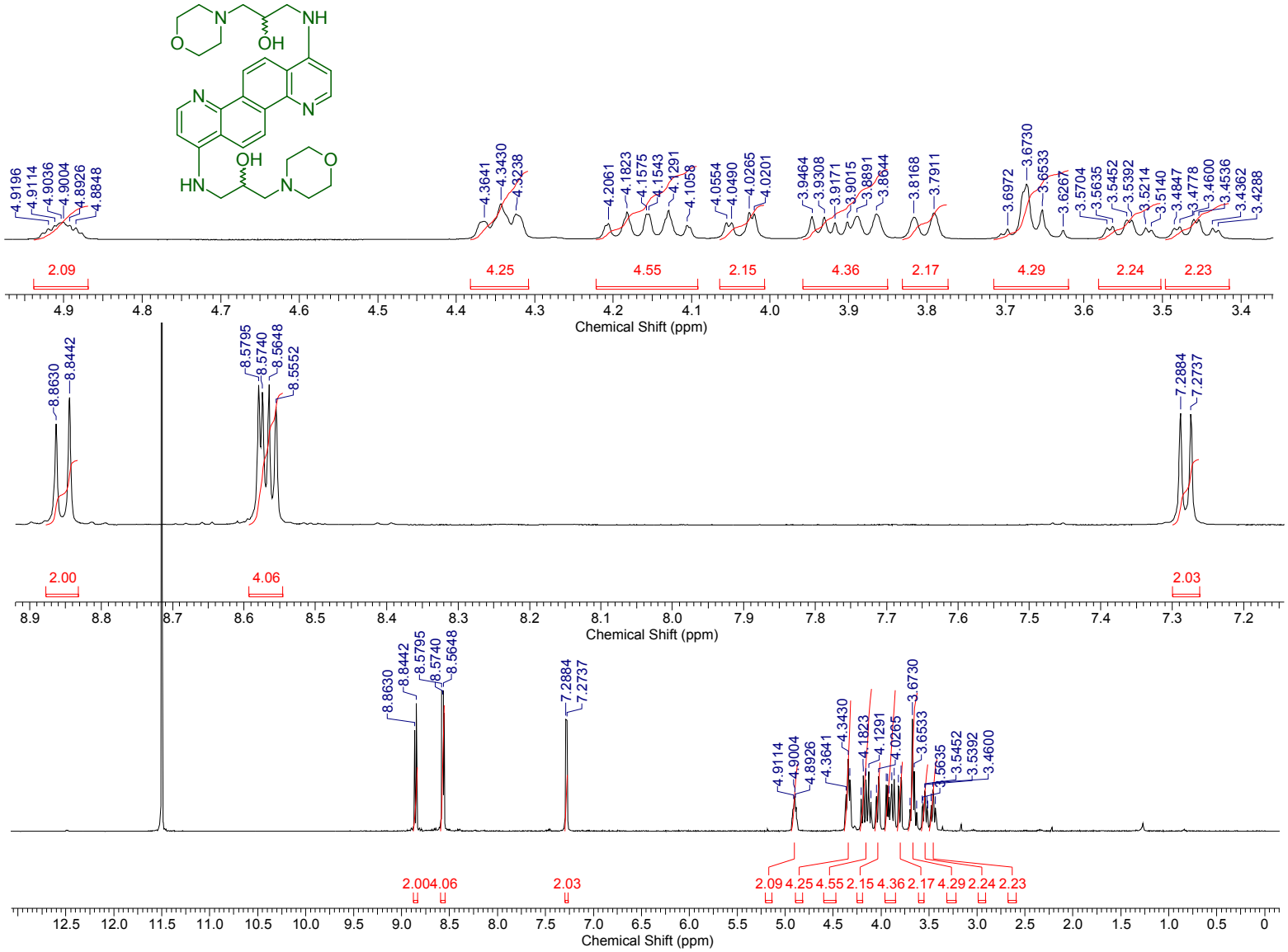
**_N,N′_-bis[3-(morpholin-4-yl)propyl]quinolino[8,7-_h_]quinoline-1,7-diamine (8): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**

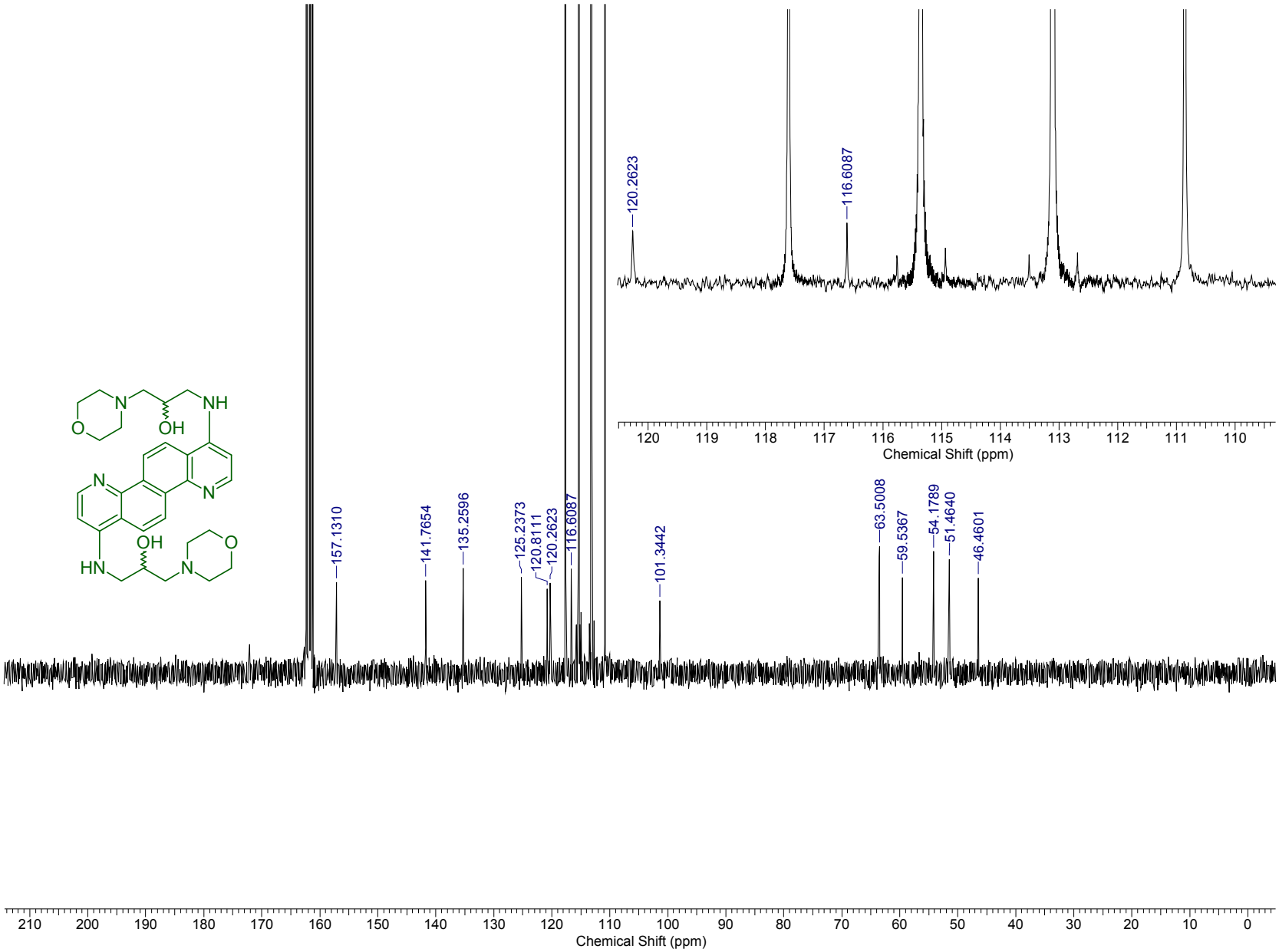


**_N,N′_-bis[3-(morpholin-4-yl)propyl]quinolino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (16): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**

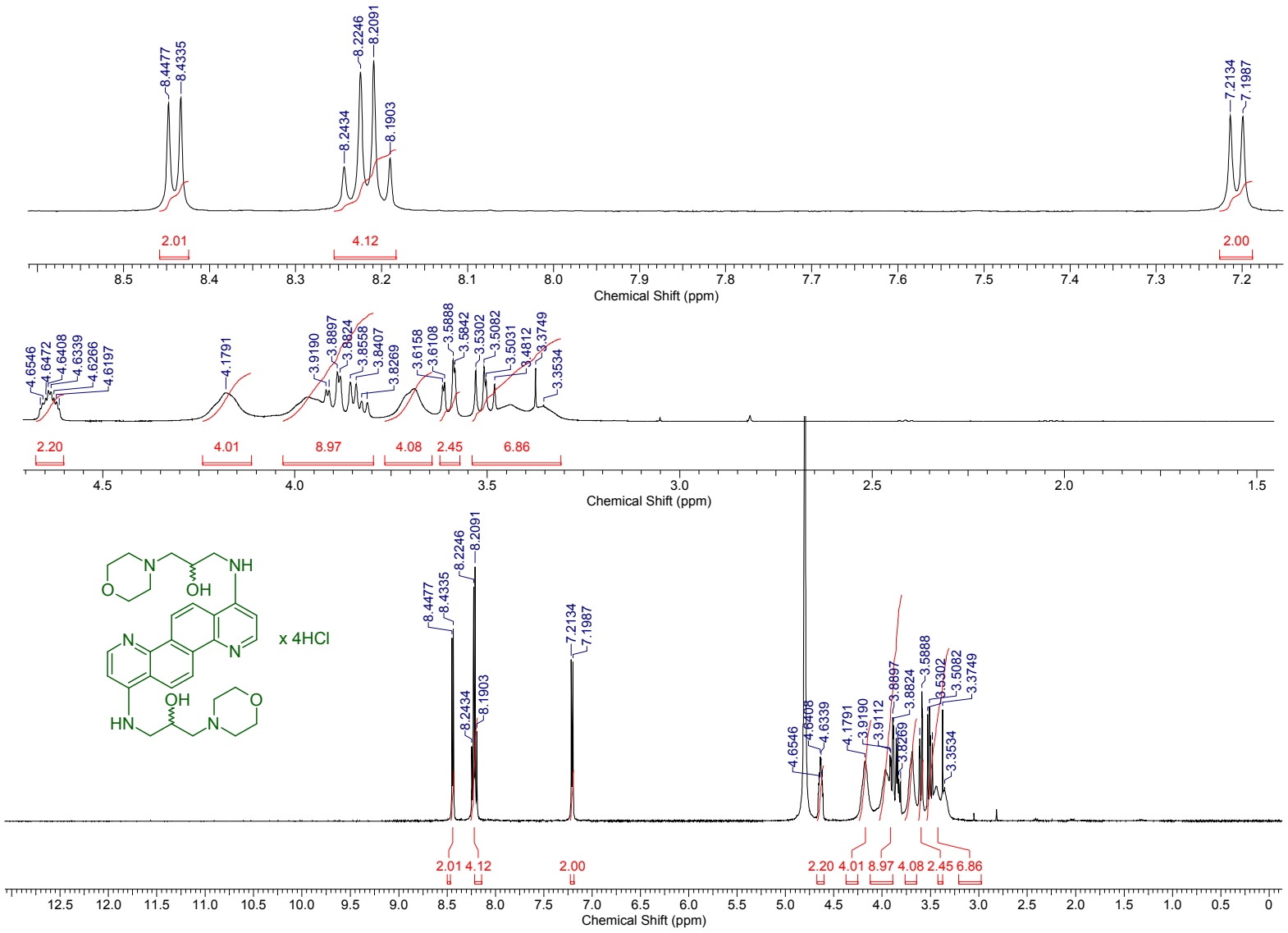


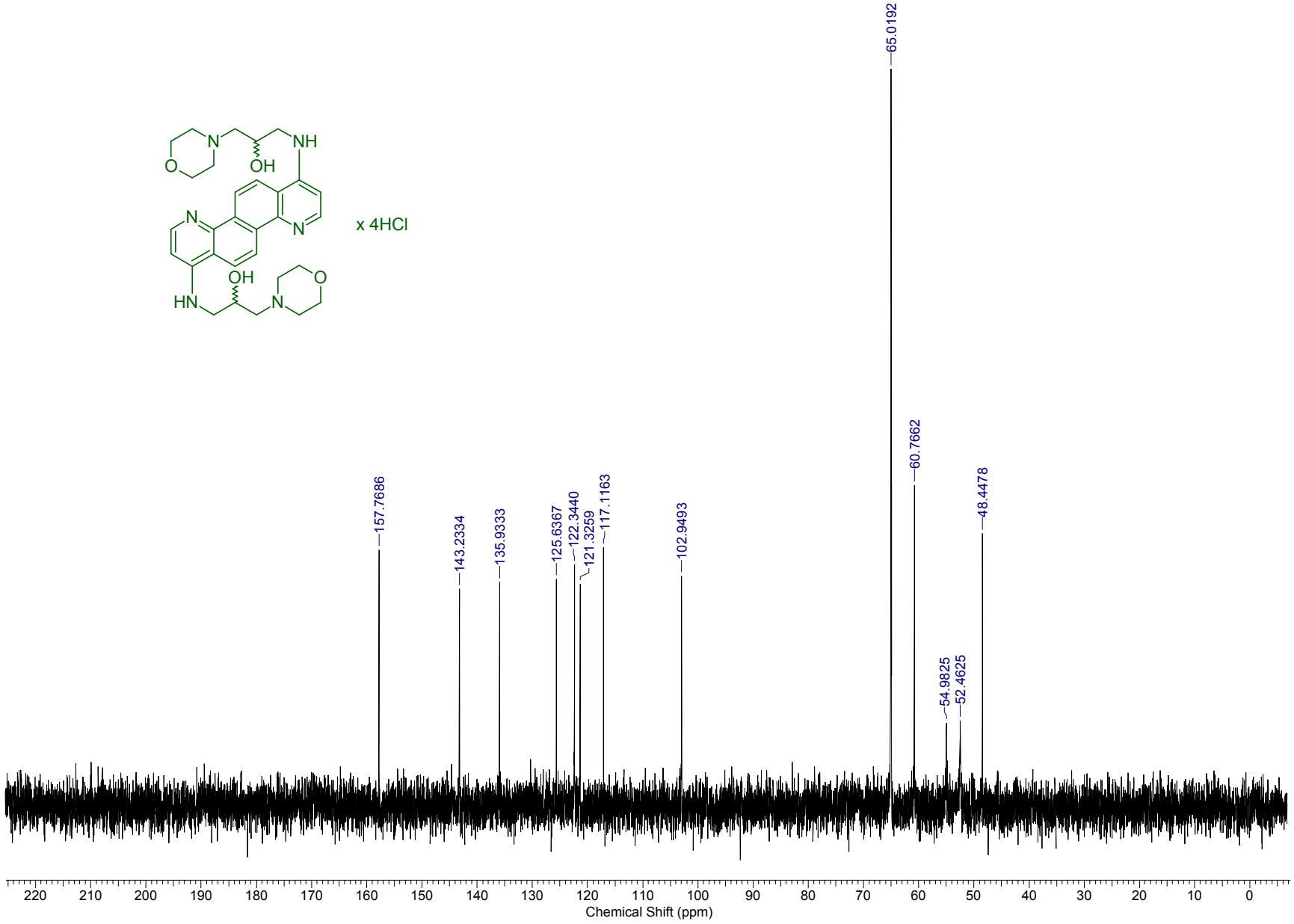
**1,1'-[quino[8,7-*h*]quinoline-1,7-diyldi(imino)]bis(3-morpholin-4-ylpropan-2-ol) (15): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**



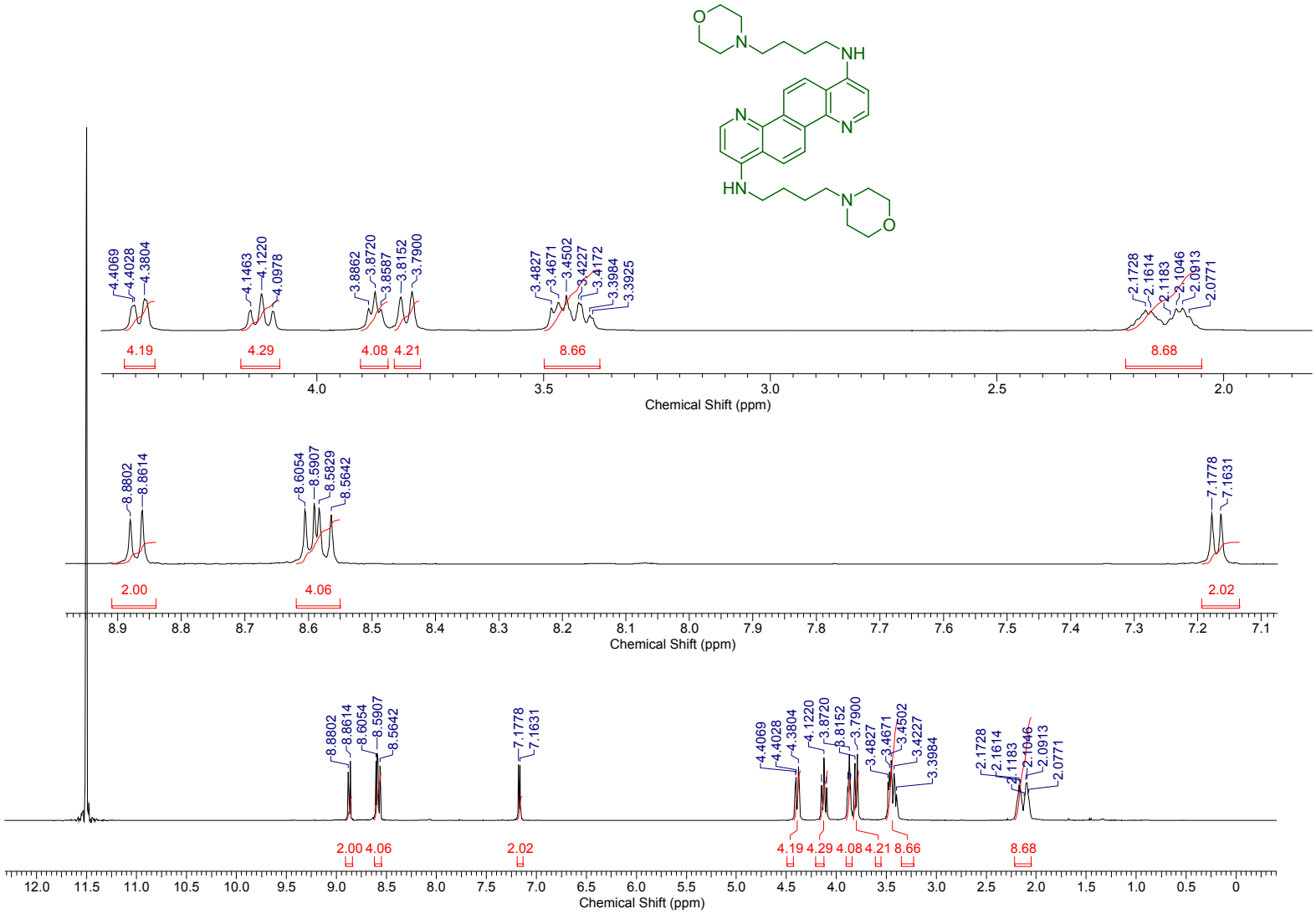

120.2623
116.6087
120
119
118
117
116
115
114
113
112
111
110
Chemical Shift (ppm)
157.1310
141.7654
135.2596
125.2373
120.8111
120.2623
116.6087
101.3442
63.5008
59.5367
54.1789
51.4640
46.4601
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

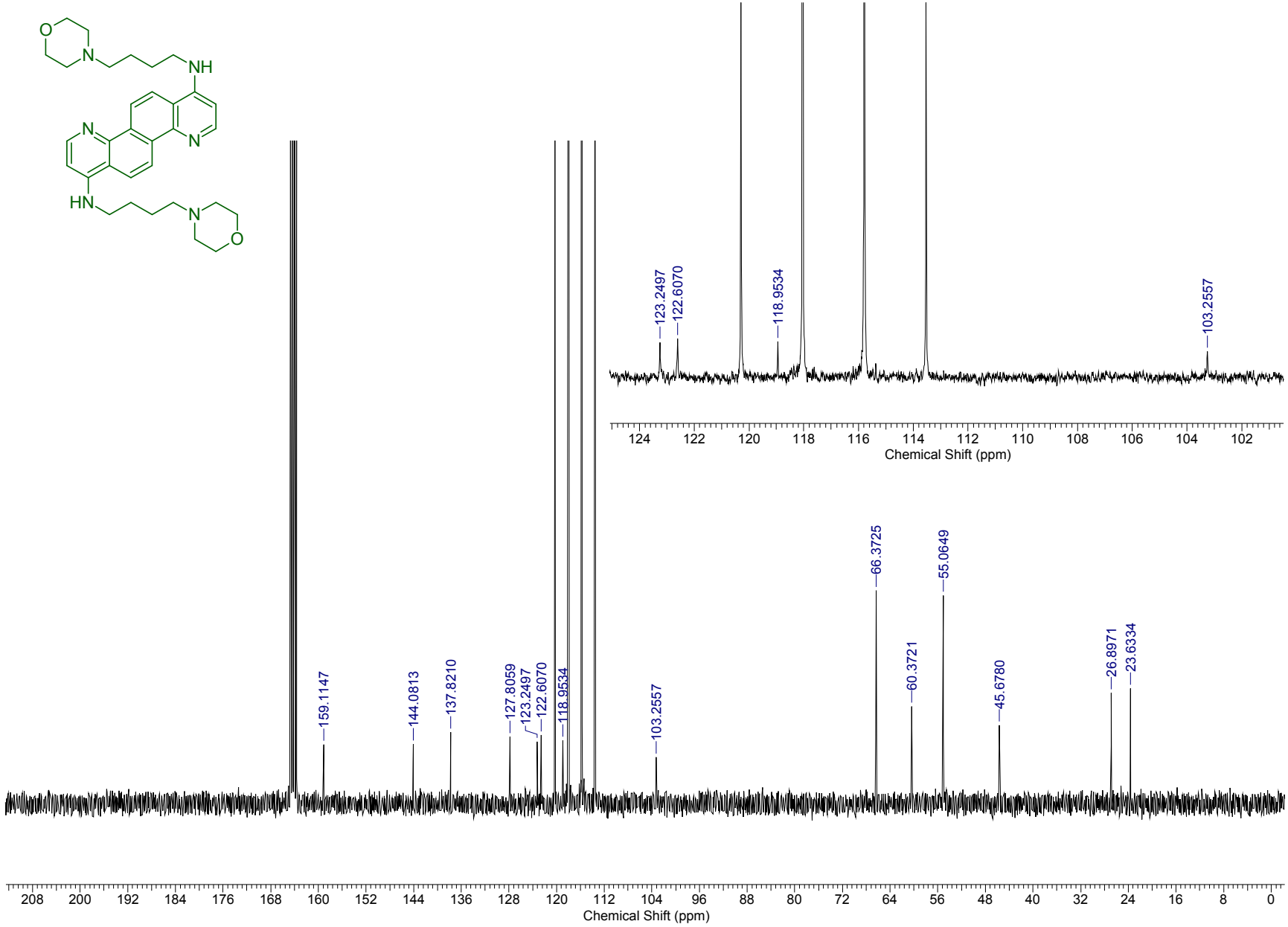
**1,1'-[quino[8,7-*h*]quinoline-1,7-diyldi(imino)]bis(3-morpholin-4-ylpropan-2-ol) tetrahydrochloride (23): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**



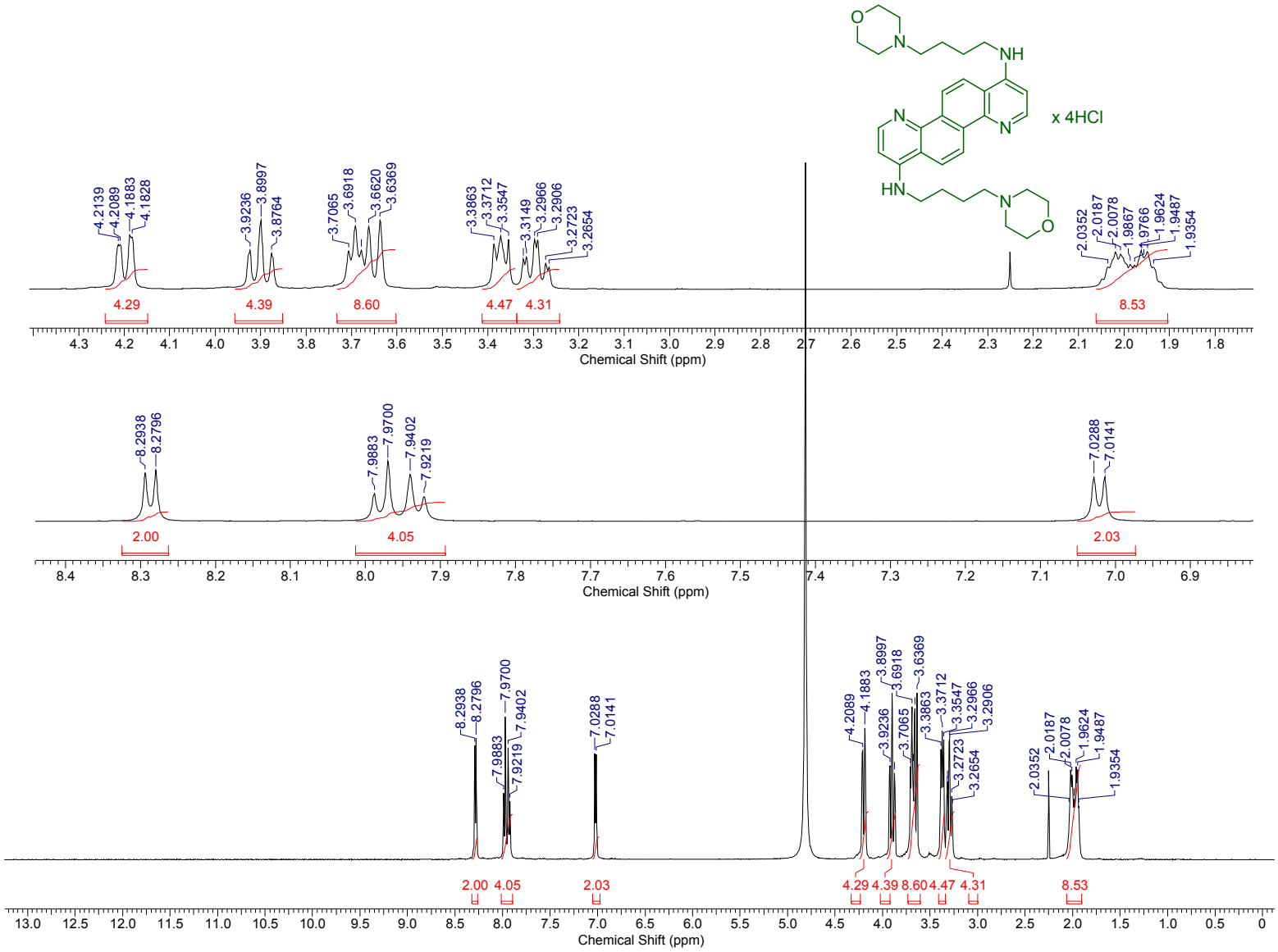

x 4HCl
65.0192
60.7662
54.9825
52.4625
48.4478
157.7686
143.2334
135.9333
125.6367
122.3440
121.3259
117.1163
102.9493
Chemical Shift (ppm)

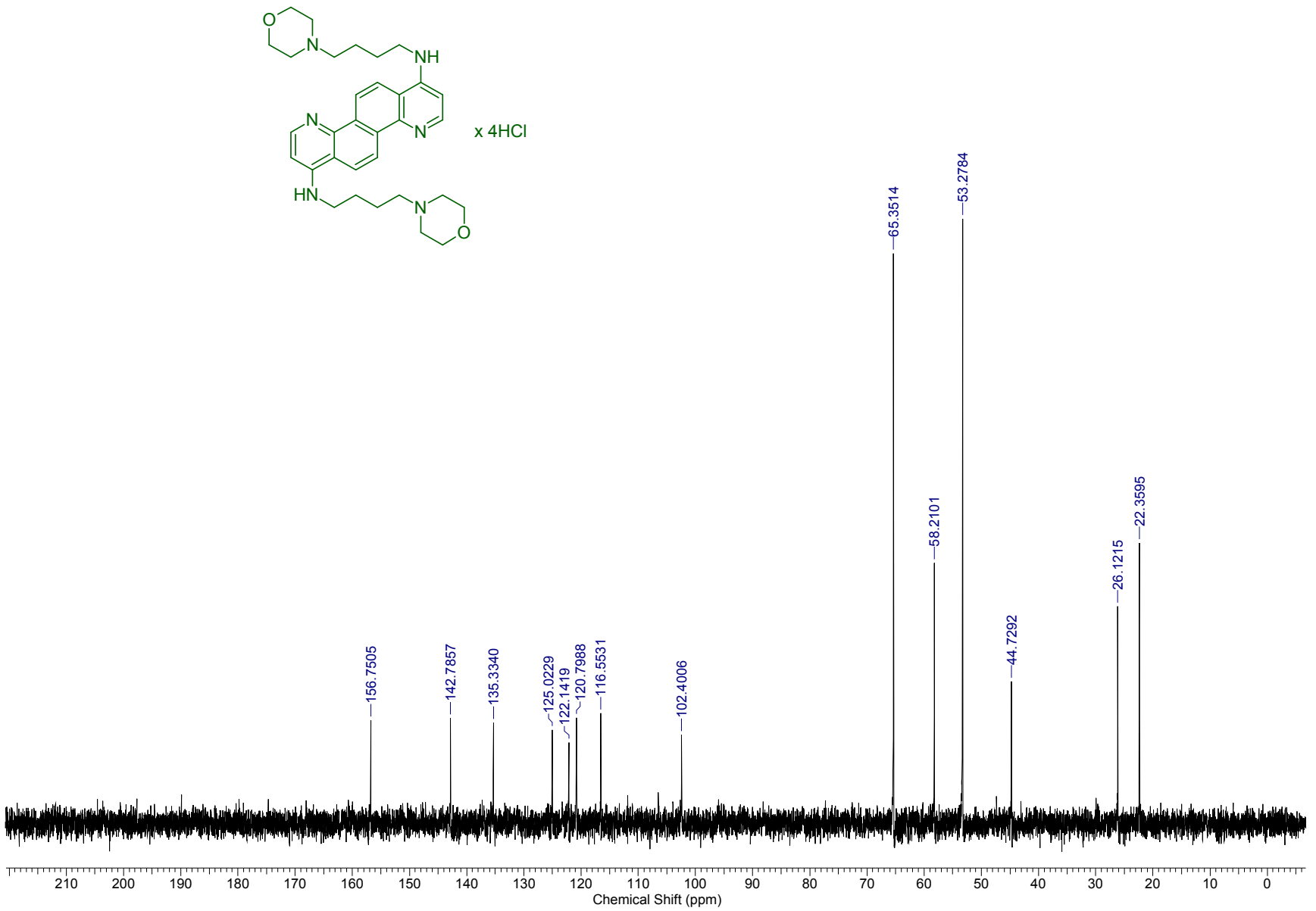
**_N,N′_-bis[4-(morpholin-4-yl)buthyl]quinolino[8,7-_h_]quinoline-1,7-diamine (9): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**



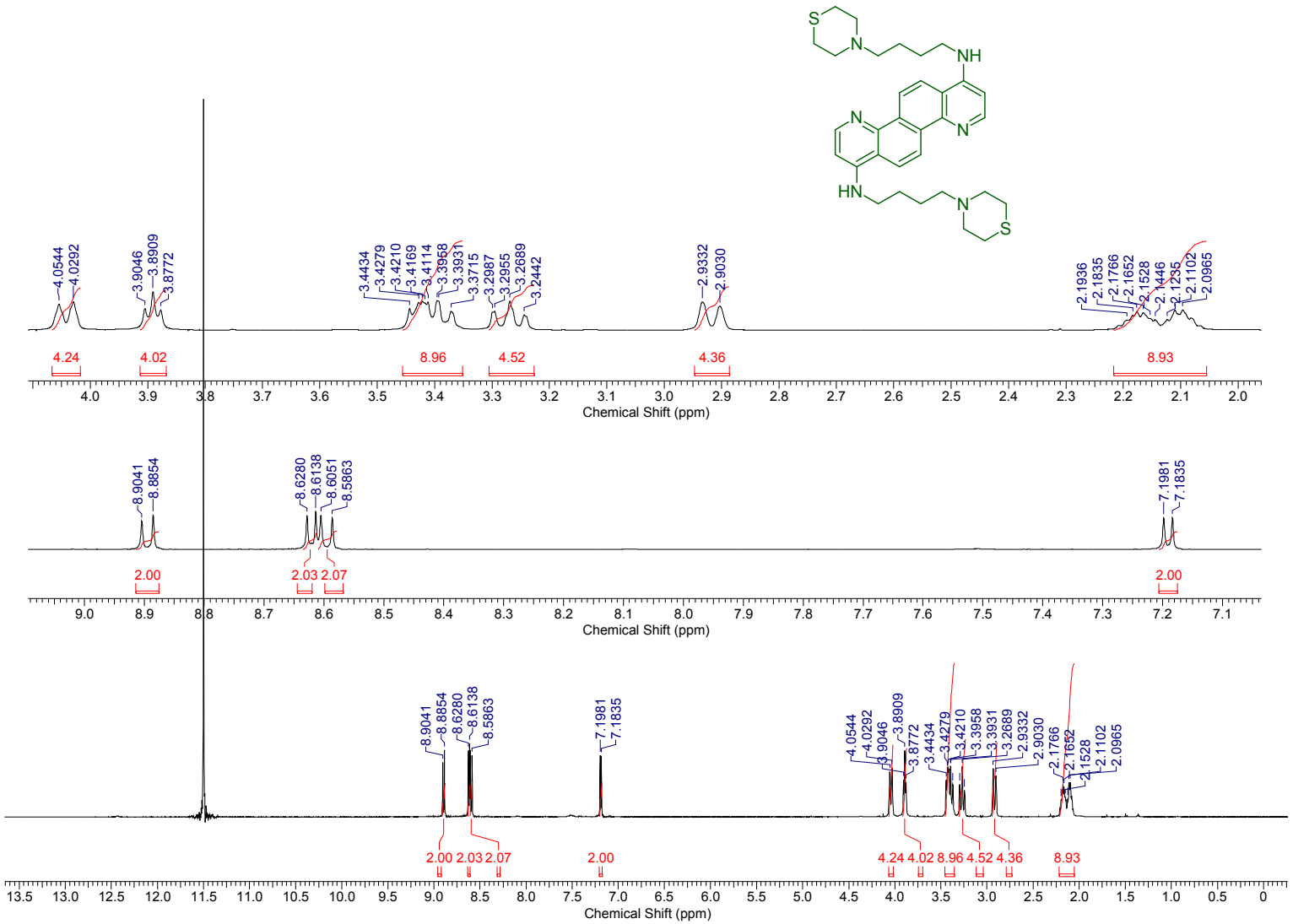

O
N
NH
N
N
HN
N
O
123.2497
122.6070
118.9534
103.2557
124
122
120
118
116
114
112
110
108
106
104
102
Chemical Shift (ppm)
159.1147
144.0813
137.8210
127.8059
123.2497
122.6070
118.9534
103.2557
66.3725
60.3721
55.0649
45.6780
26.8971
23.6334
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

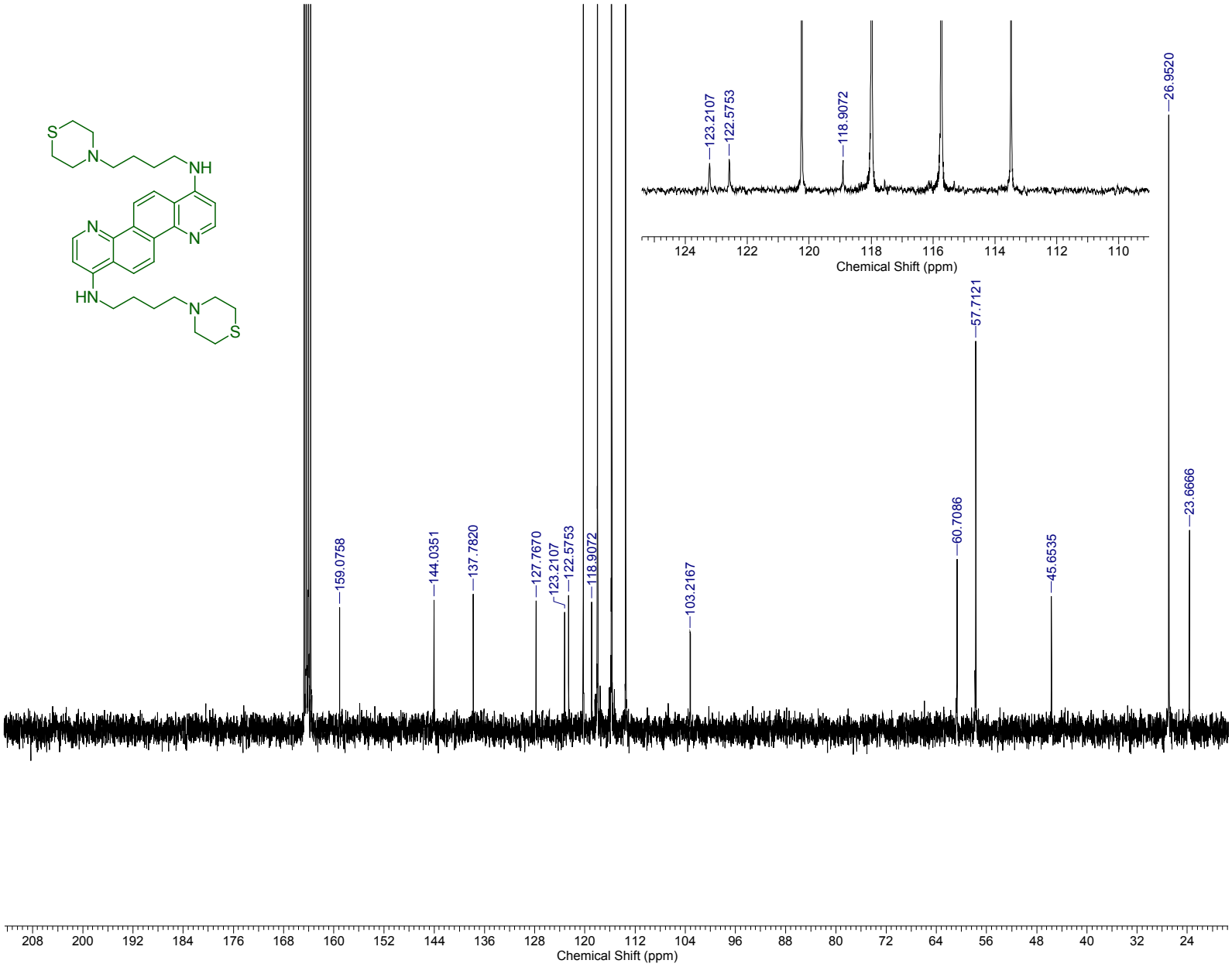
**_N,N′_-bis[4-(morpholin-4-yl)buthyl]quinolino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (17): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**



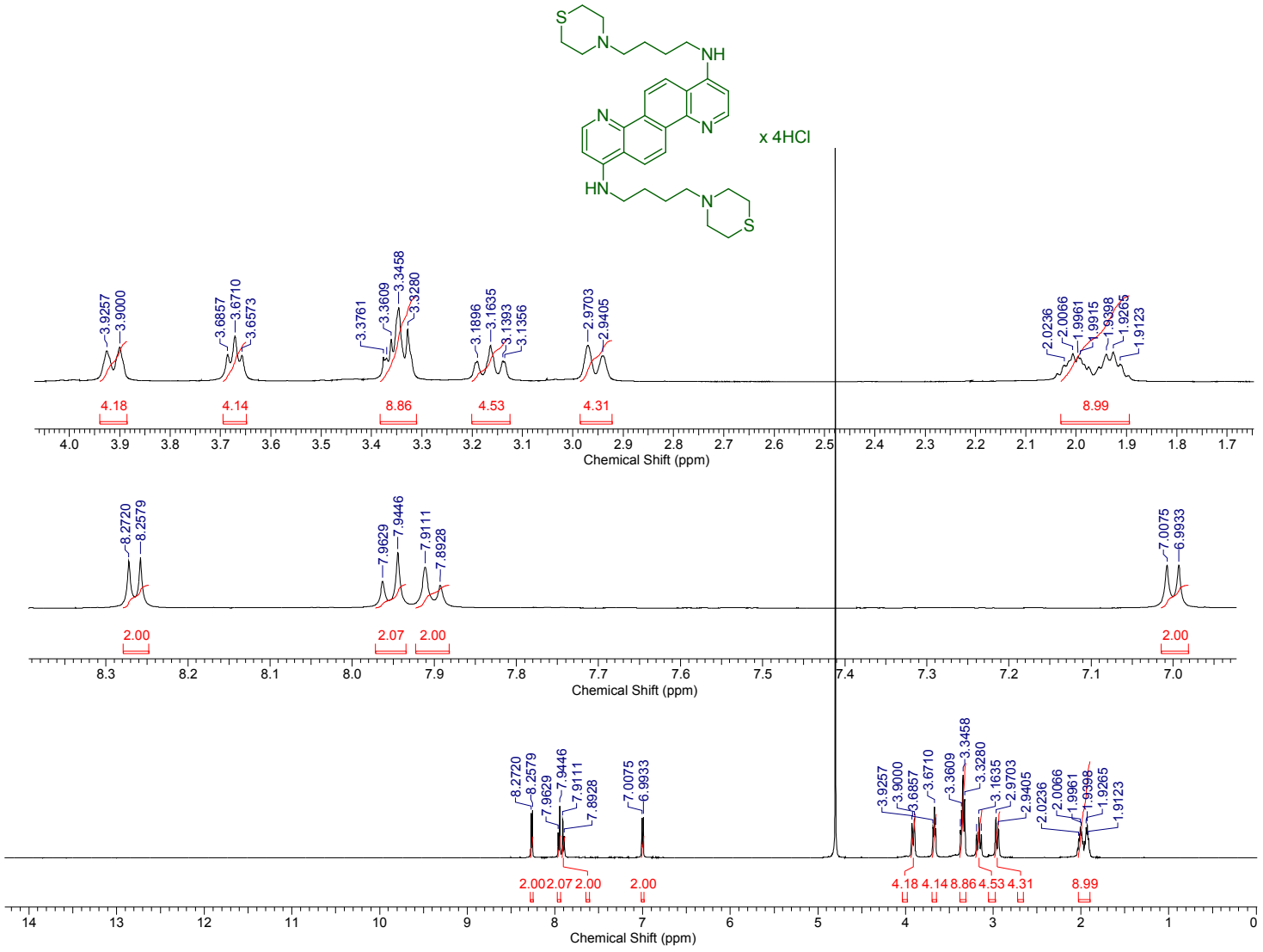

x 4HCl
156.7505
142.7857
135.3340
125.0229
122.1419
120.7988
116.5531
102.4006
65.3514
58.2101
53.2784
44.7292
26.1215
22.3595
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

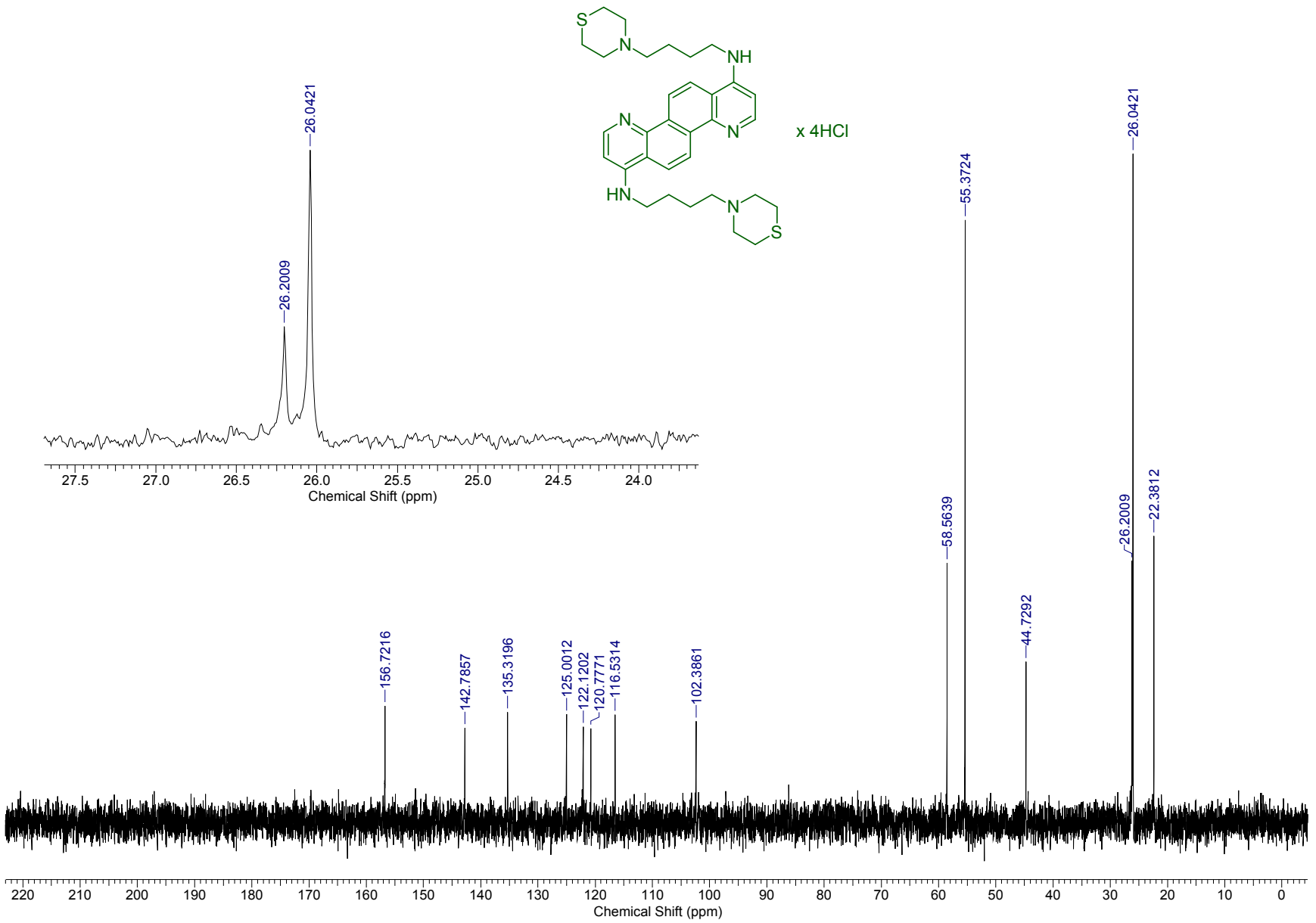
**_N_,_N_'-bis(4-thiomorpholin-4-ylbutyl)quino[8,7-_h_]quinoline-1,7-diamine (12): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**



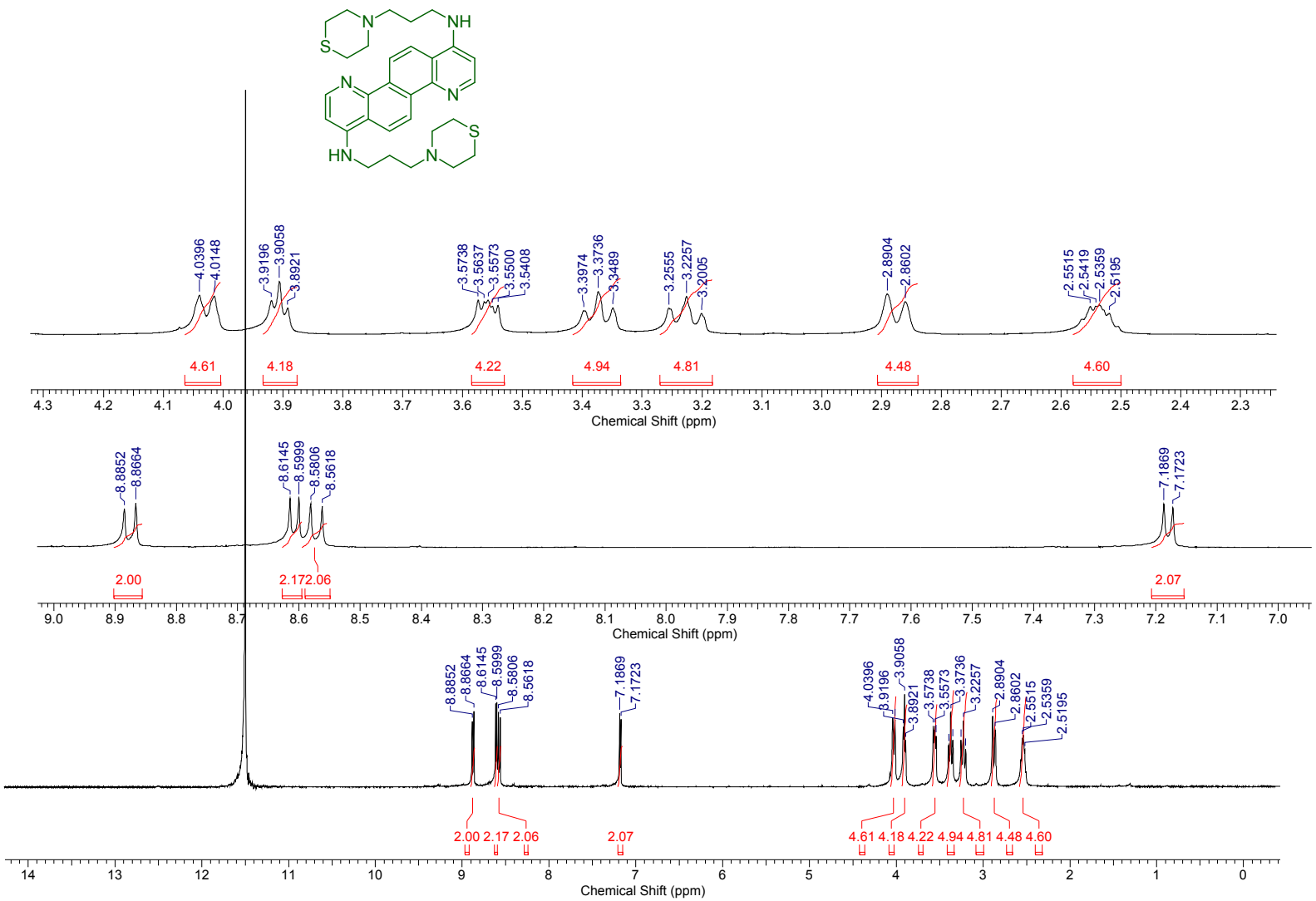

S
N
NH
N
N
HN
N
S
159.0758
144.0351
137.7820
127.7670
123.2107
122.5753
118.9072
103.2167
60.7086
57.7121
45.6535
26.9520
23.6666
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24
Chemical Shift (ppm)
123.2107
122.5753
118.9072
26.9520
124 122 120 118 116 114 112 110
Chemical Shift (ppm)

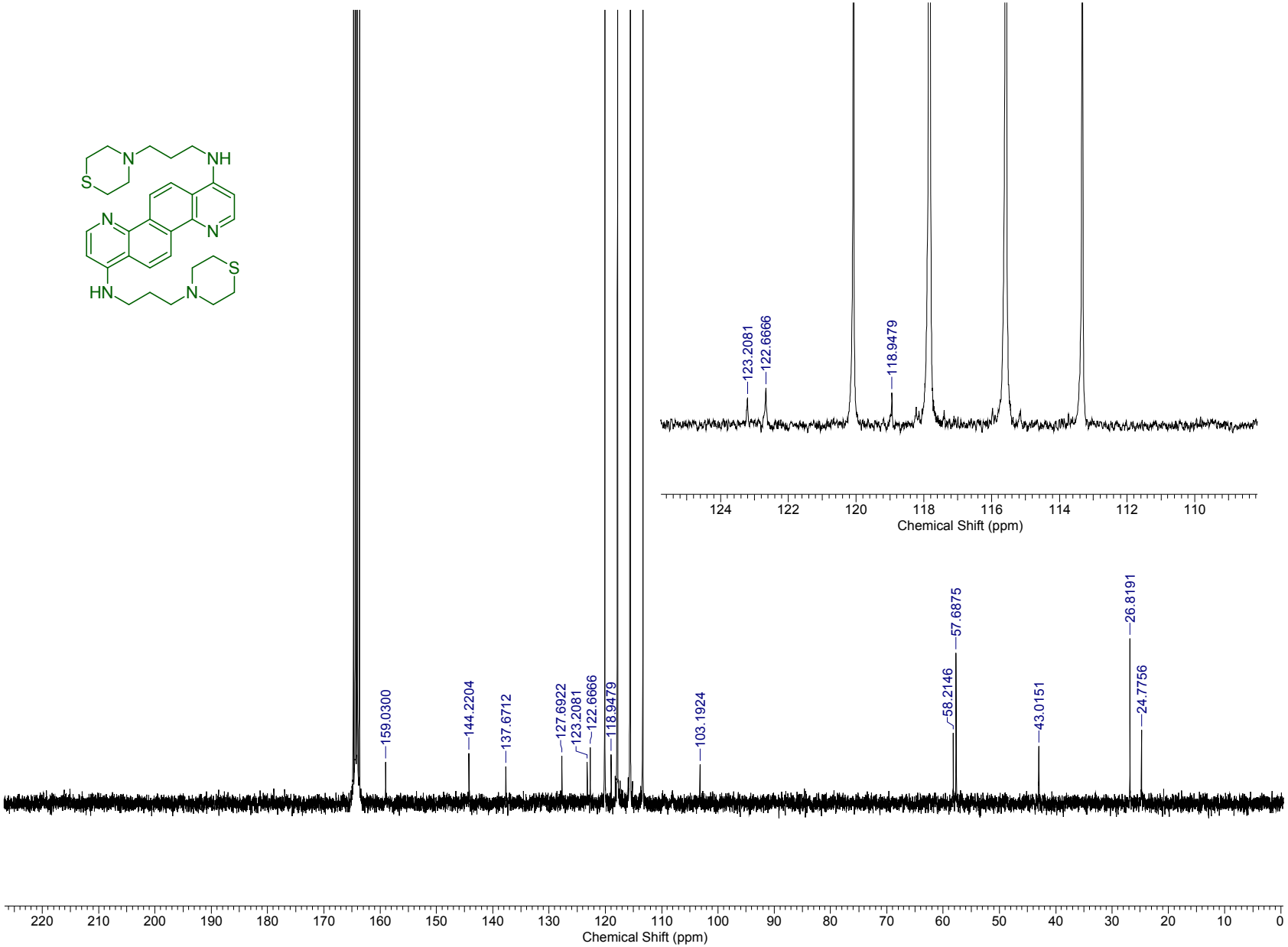
**_N_,_N_'-bis(4-thiomorpholin-4-ylbutyl)quino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (20): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**



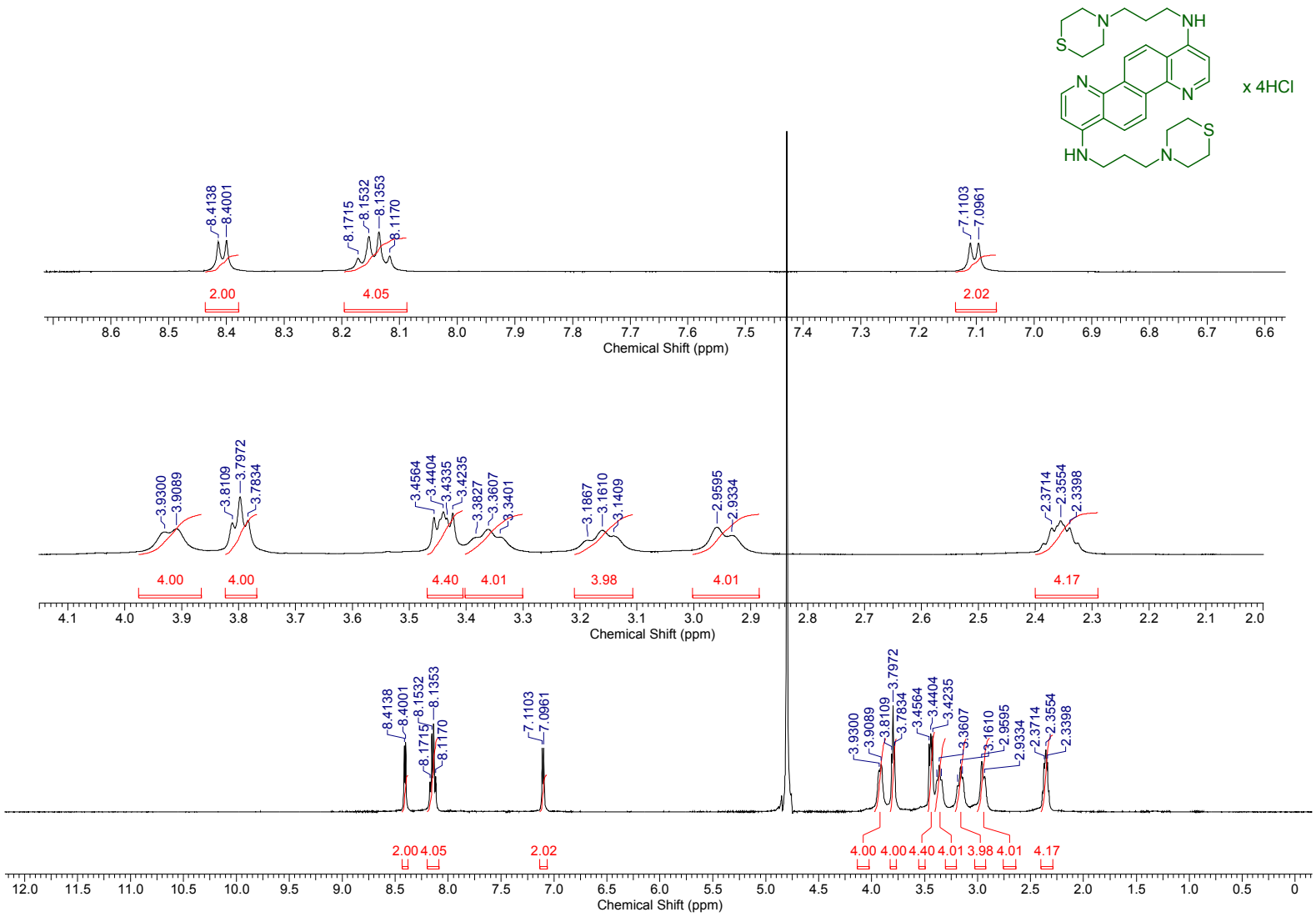

S
N
NH
N
N
HN
N
S
x 4HCl
26.0421
26.2009
27.5
27.0
26.5
26.0
25.5
25.0
24.5
24.0
Chemical Shift (ppm)
55.3724
26.0421
58.5639
26.2009
22.3812
44.7292
156.7216
142.7857
135.3196
125.0012
122.1202
120.7771
116.5314
102.3861
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

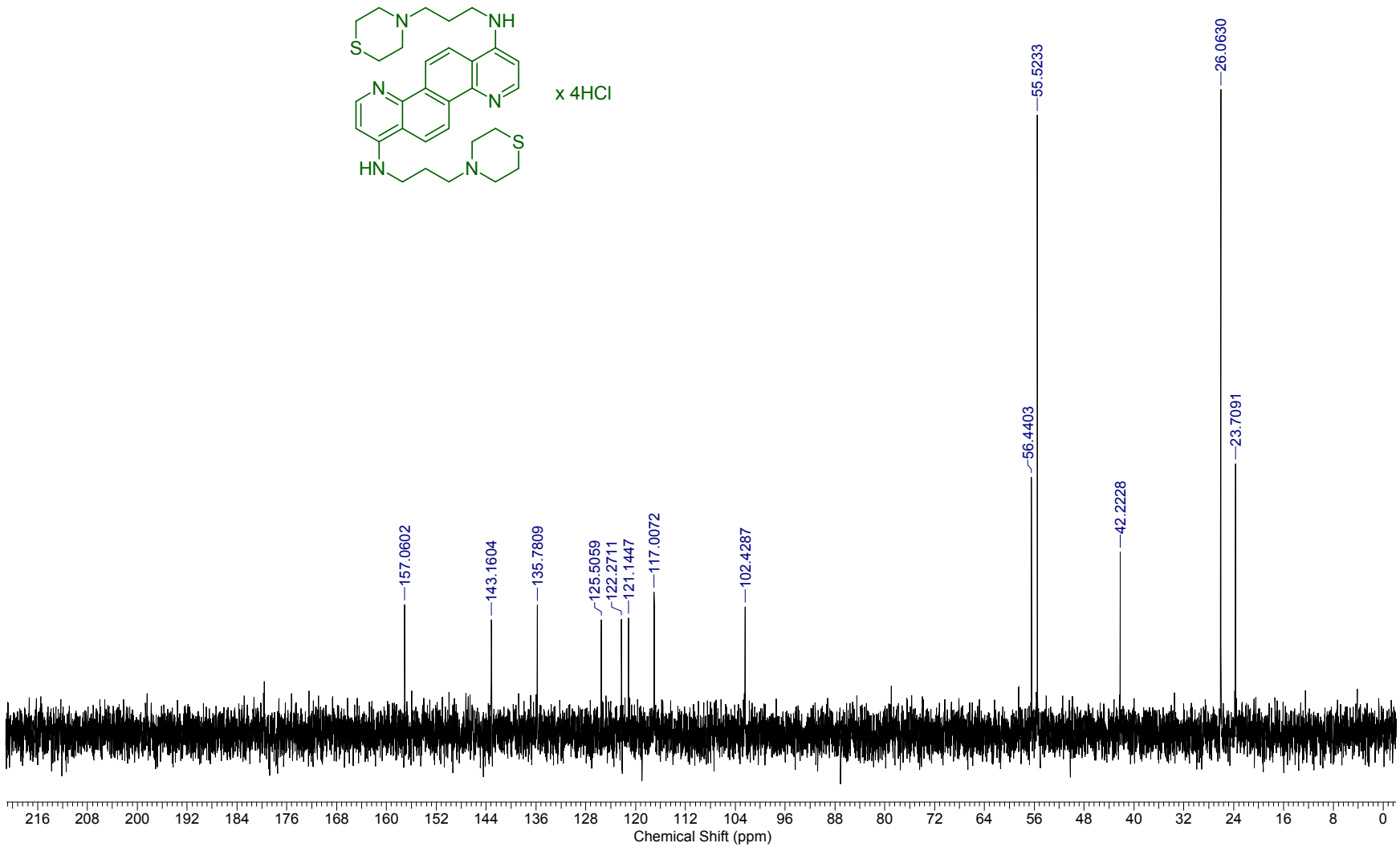
**_N_,_N_'-bis(3-thiomorpholin-4-ylpropyl)quino[8,7-_h_]quinoline-1,7-diamine (11): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**



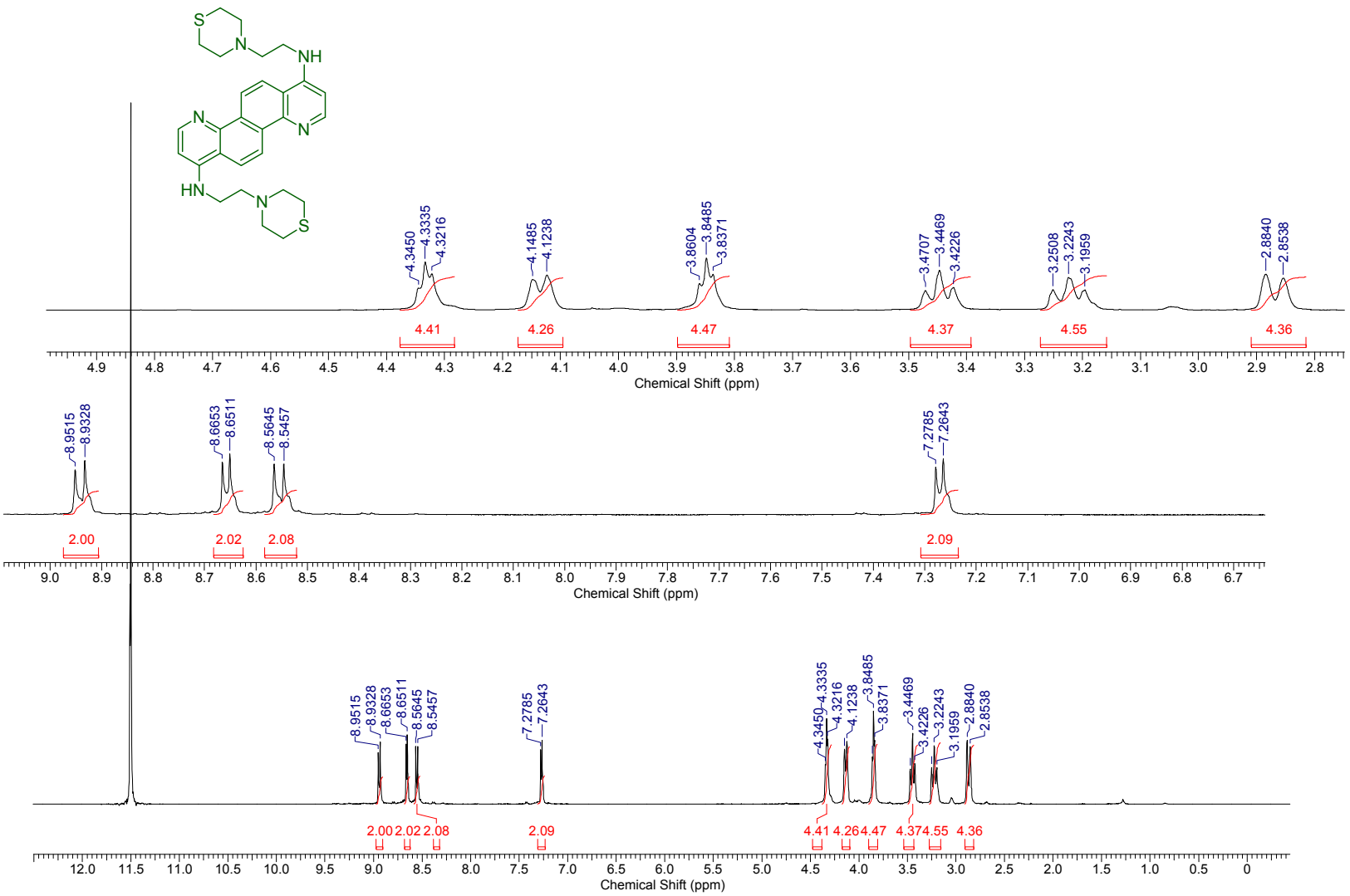

N
NH
S
N
N
HN
N
S
123.2081
122.6666
118.9479
124
122
120
118
116
114
112
110
Chemical Shift (ppm)
159.0300
144.2204
137.6712
127.6922
123.2081
122.6666
118.9479
103.1924
58.2146
57.6875
43.0151
26.8191
24.7756
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

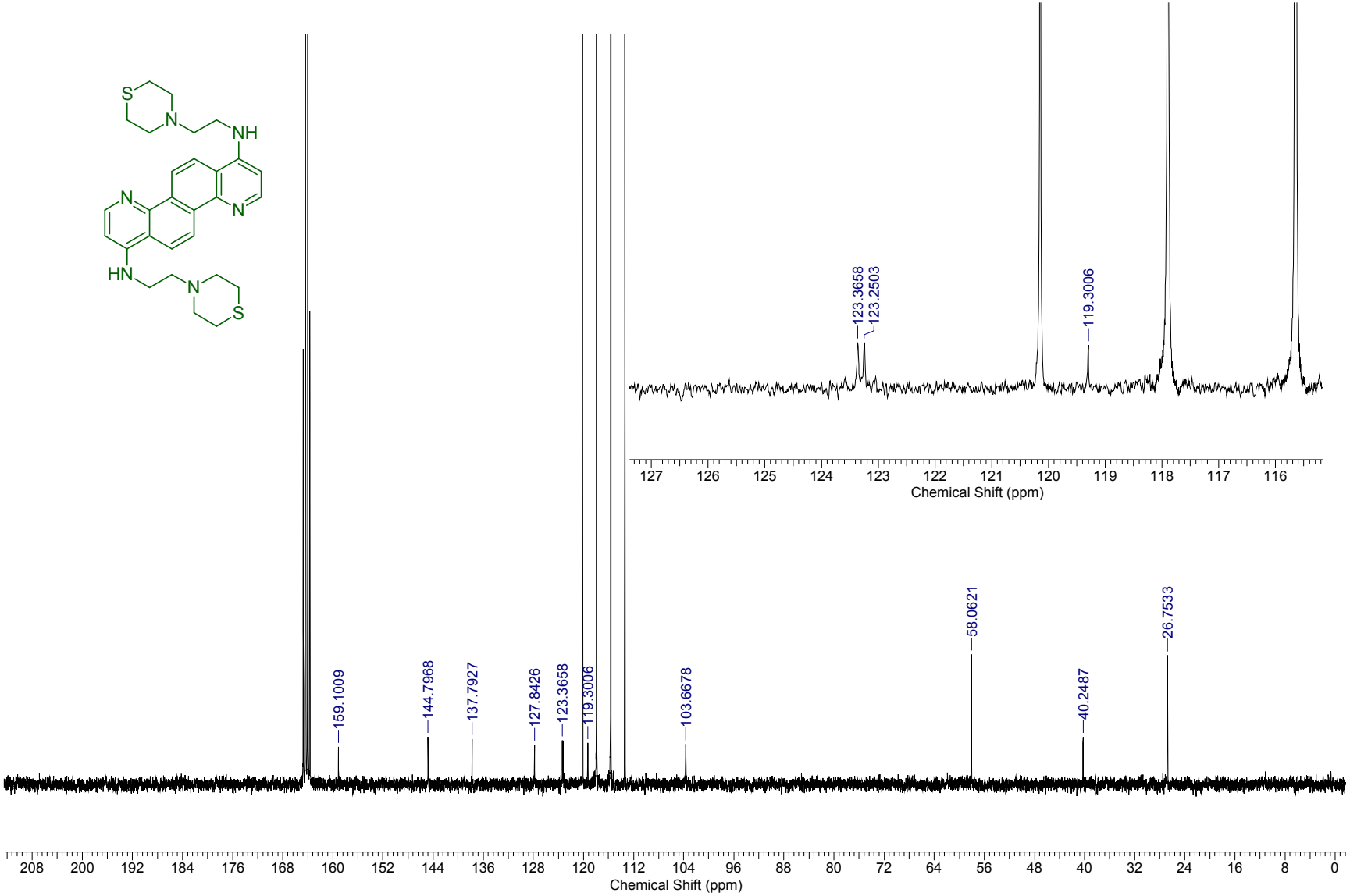
**_N_,_N_'-bis(3-thiomorpholin-4-ylpropyl)quino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (19): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**



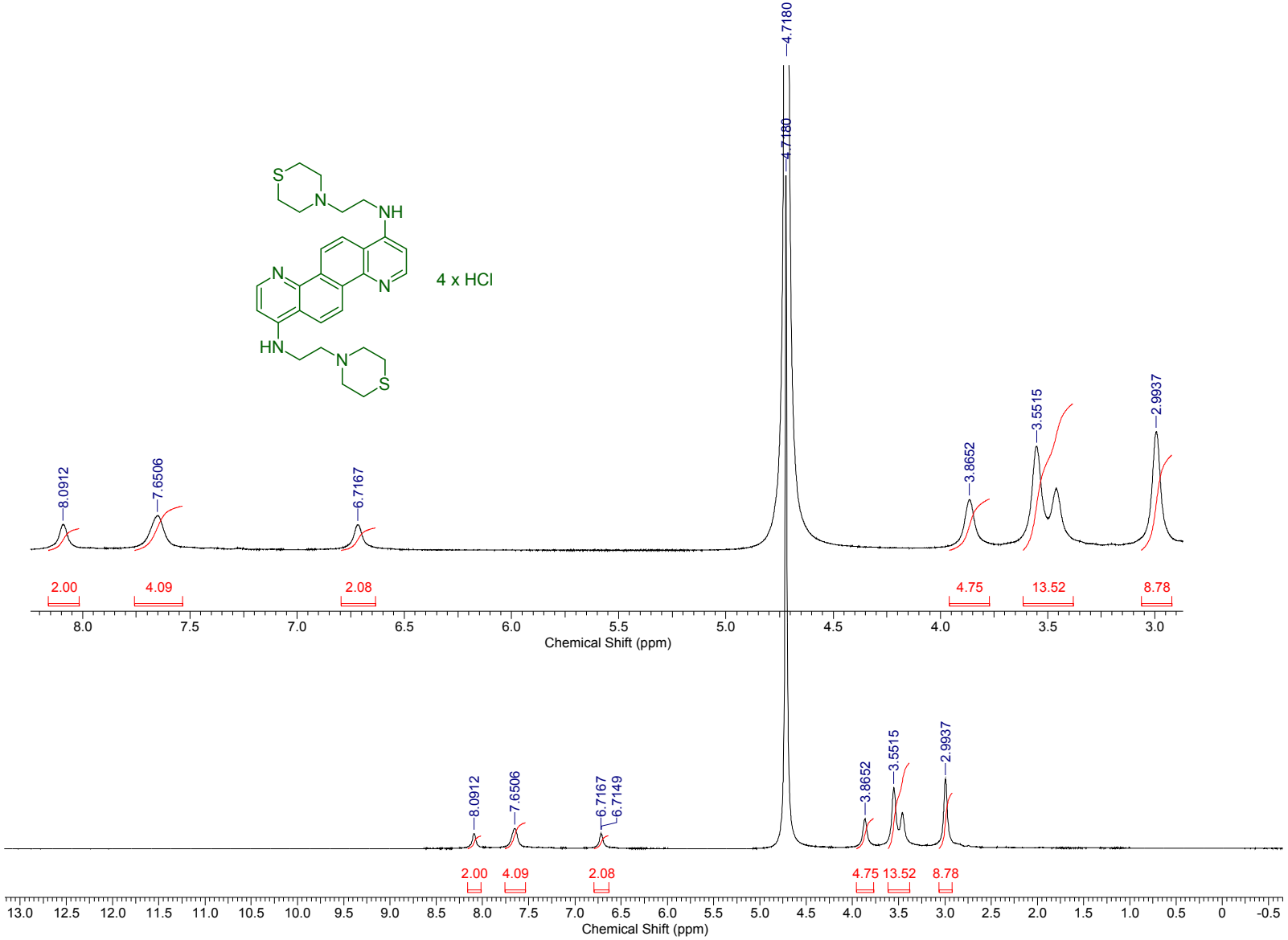

x 4HCl
157.0602
143.1604
135.7809
125.5059
122.2711
121.1447
117.0072
102.4287
56.4403
55.5233
42.2228
26.0630
23.7091
216 208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

**_N_,_N_'-bis(2-thiomorpholin-4-ylethyl)quino[8,7-_h_]quinoline-1,7-diamine (10): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**

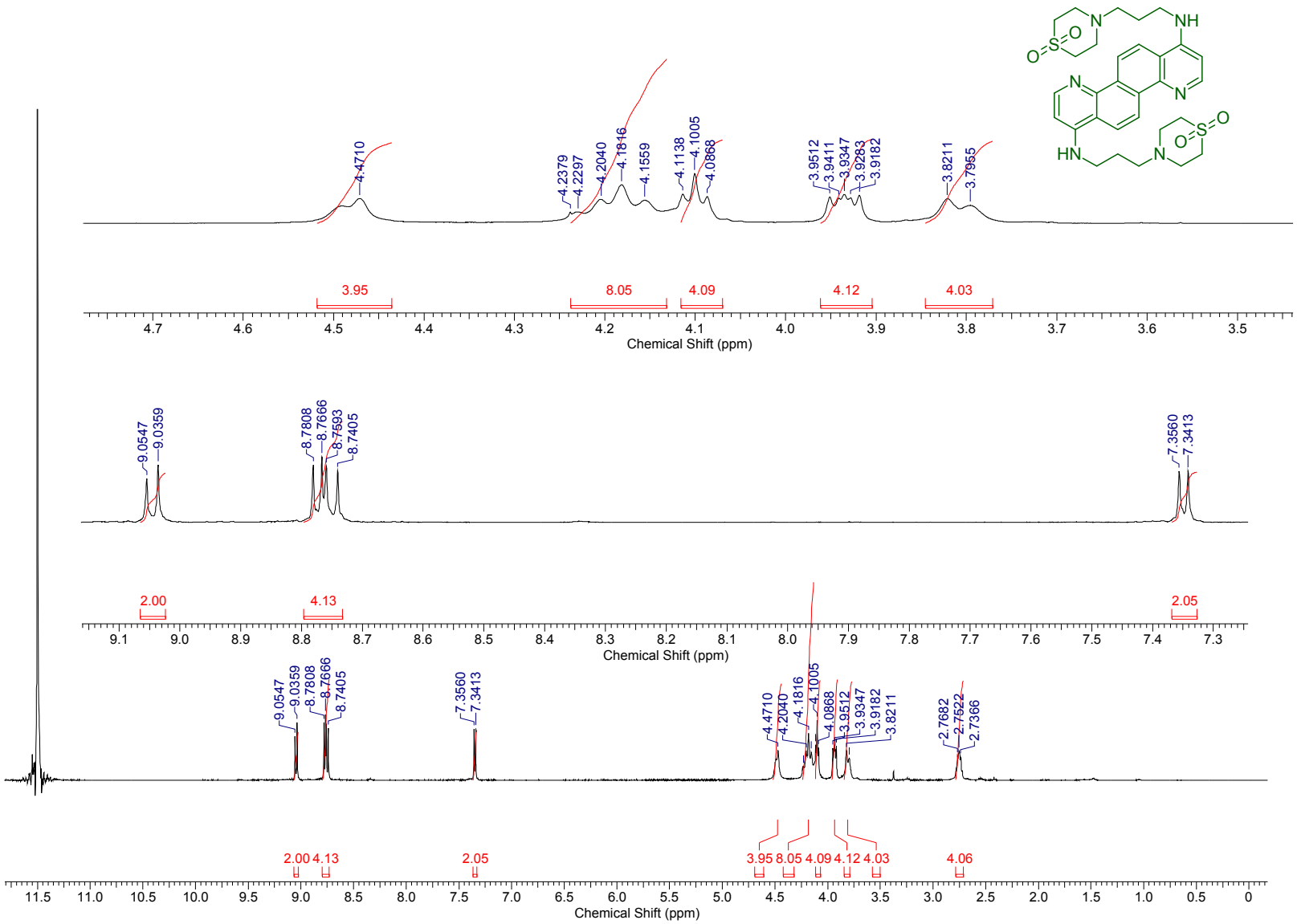


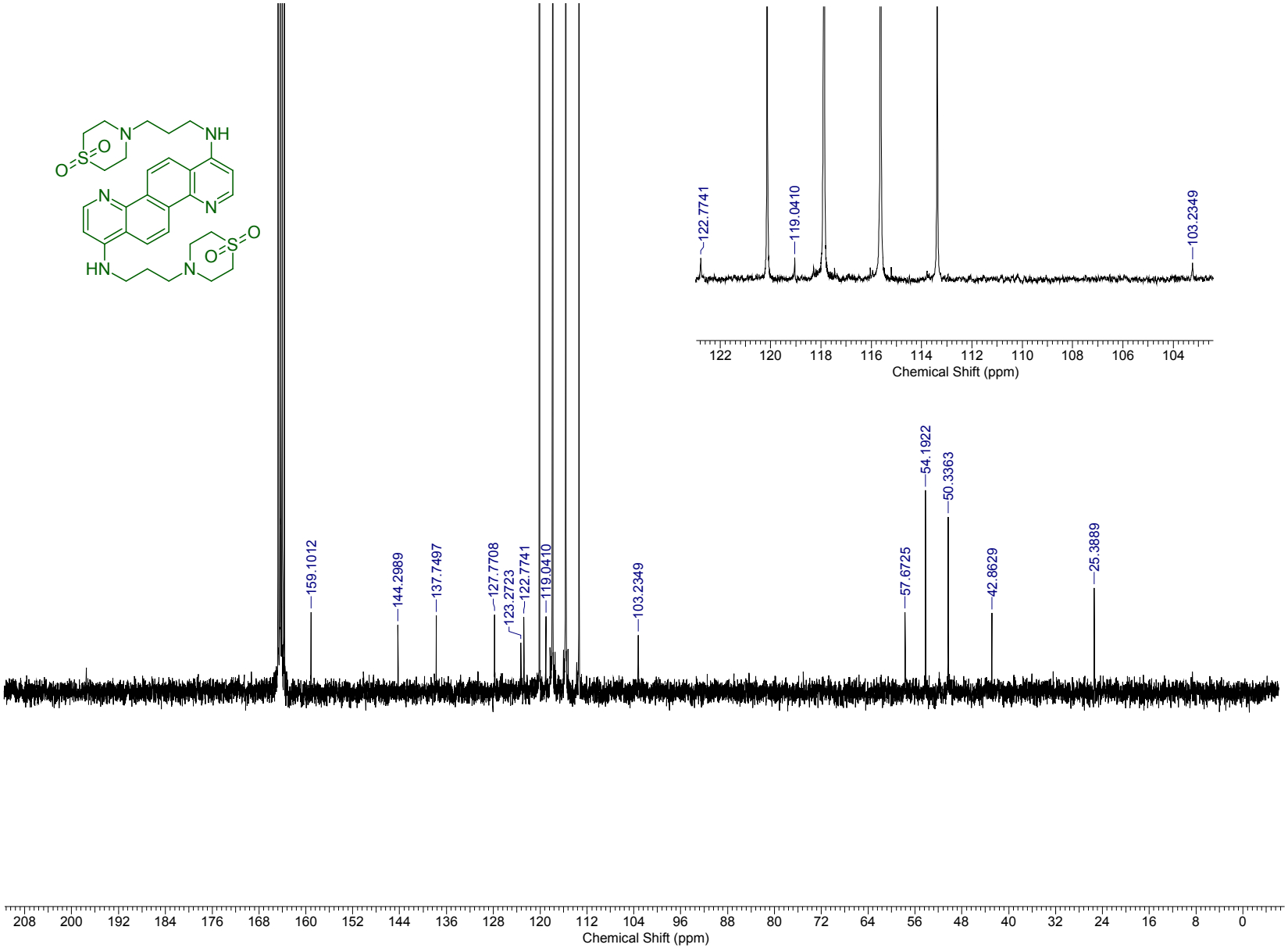

S
N
NH
N
N
HN
N
S
123.3658
123.2503
119.3006
127 126 125 124 123 122 121 120 119 118 117 116
Chemical Shift (ppm)
159.1009
144.7968
137.7927
127.8426
123.3658
119.3006
103.6678
58.0621
40.2487
26.7533
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

**_N_,_N_'-bis(2-thiomorpholin-4-ylethyl)quino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (18): 500 MHz $^{1}$H; solvent $D_2O$**

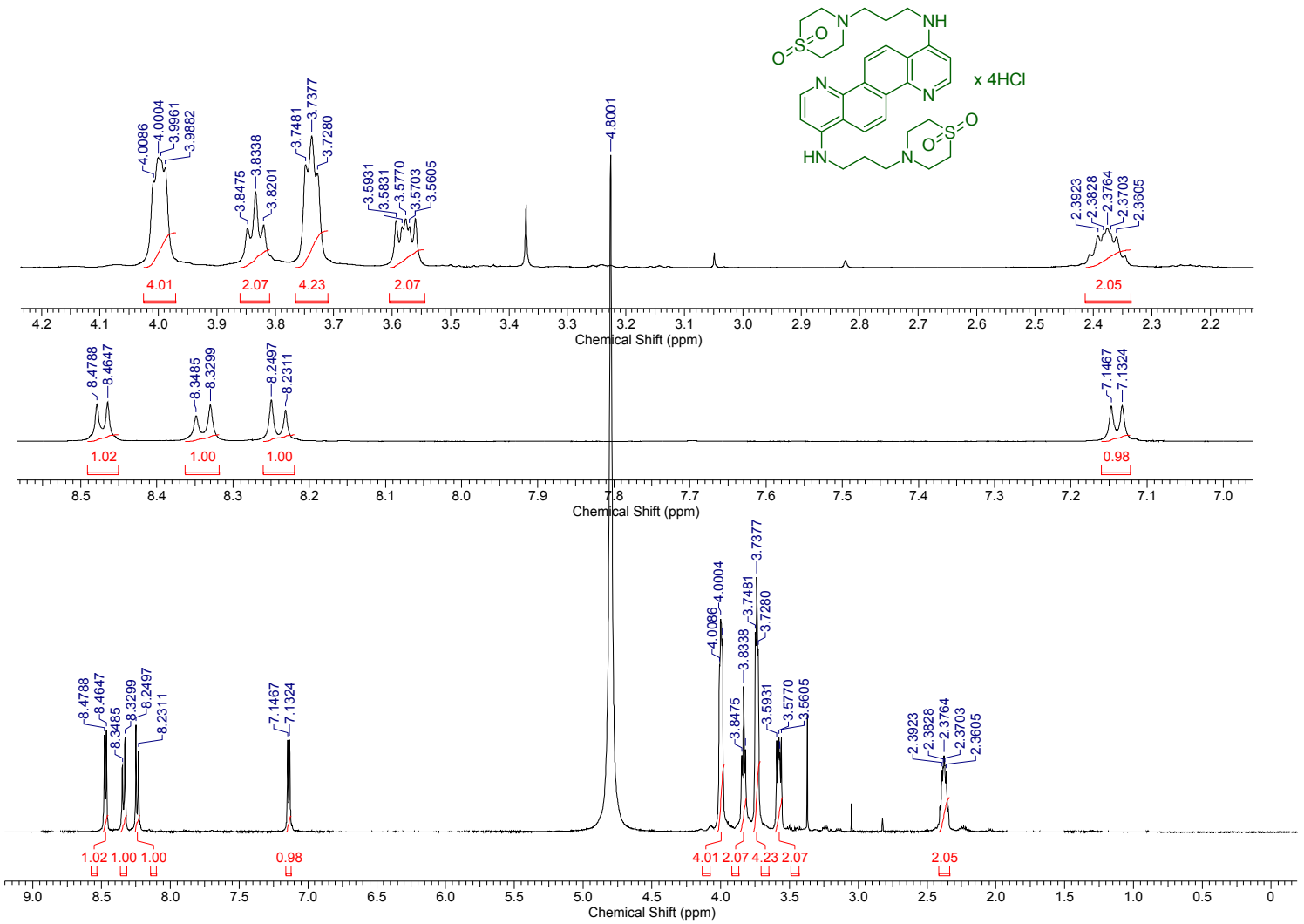


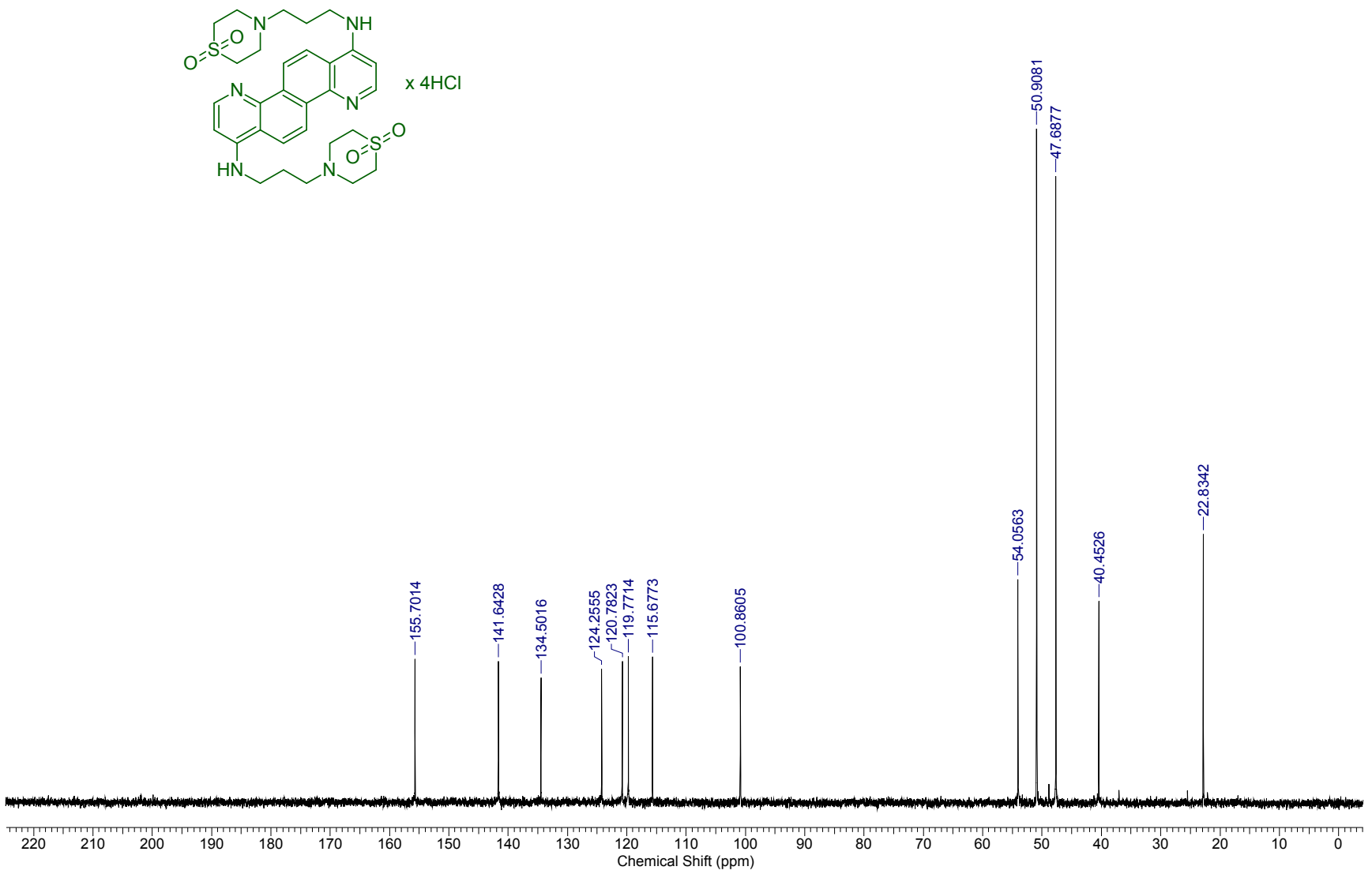
**_N_,_N_'-bis[3-(1,1-dioxidothiomorpholin-4-yl)propyl]quino[8,7-_h_]quinoline-1,7-diamine (14): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**



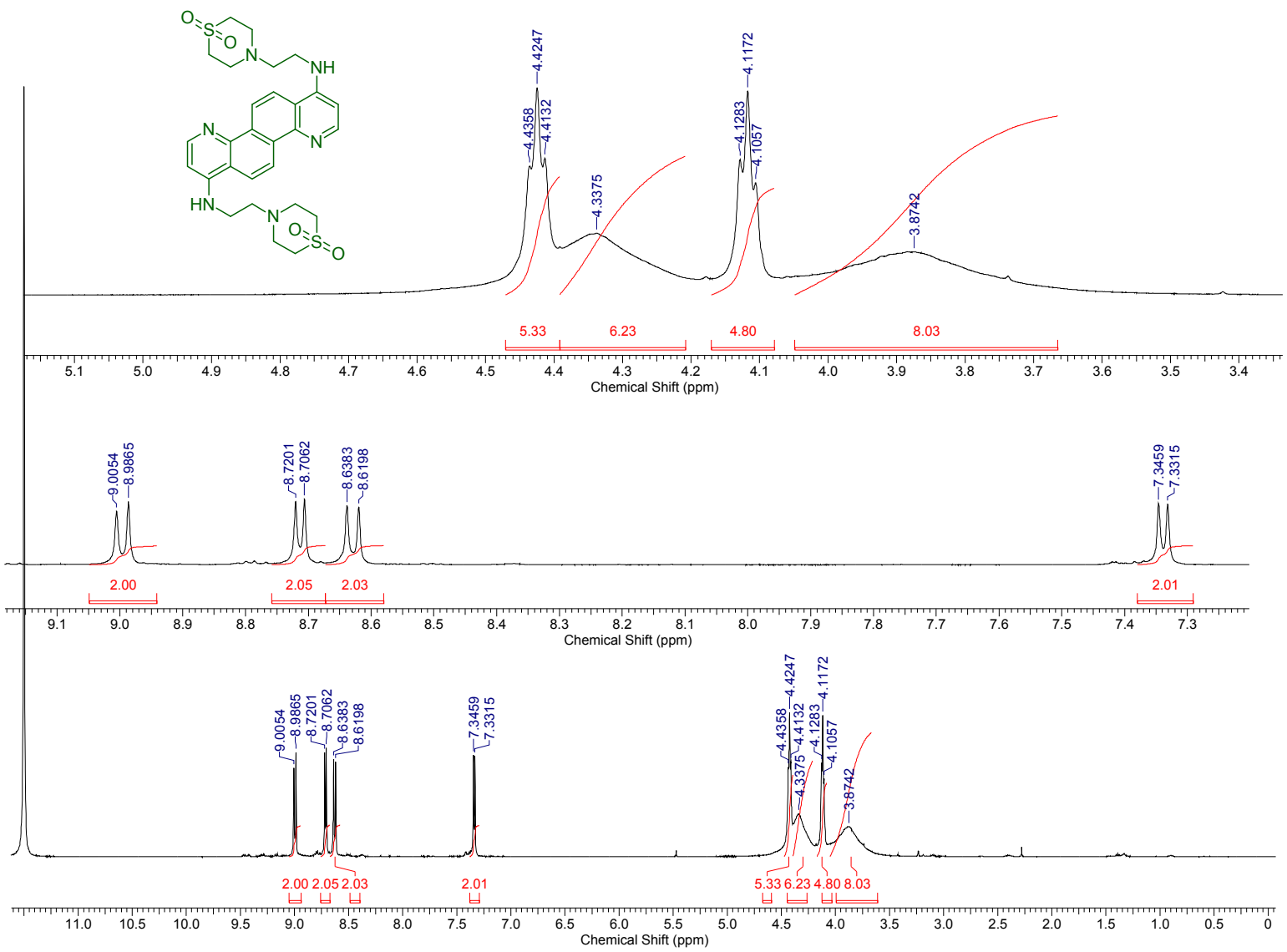

122.7741
119.0410
103.2349
122 120 118 116 114 112 110 108 106 104
Chemical Shift (ppm)
159.1012
144.2989
137.7497
127.7708
123.2723
122.7741
119.0410
103.2349
57.6725
54.1922
50.3363
42.8629
25.3889
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

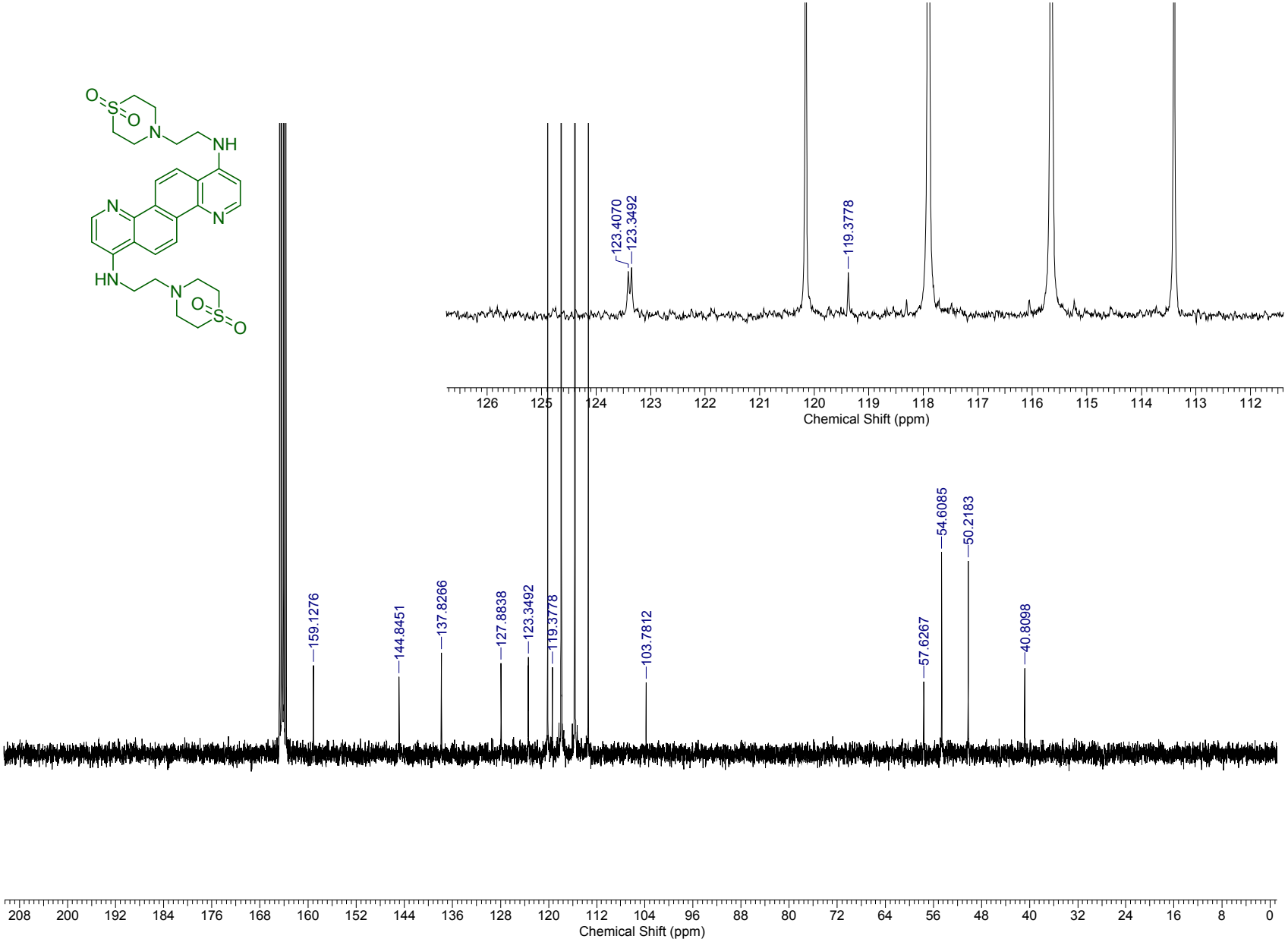
**_N_,_N_'-bis[3-(1,1-dioxidothiomorpholin-4-yl)propyl]quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (22): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**



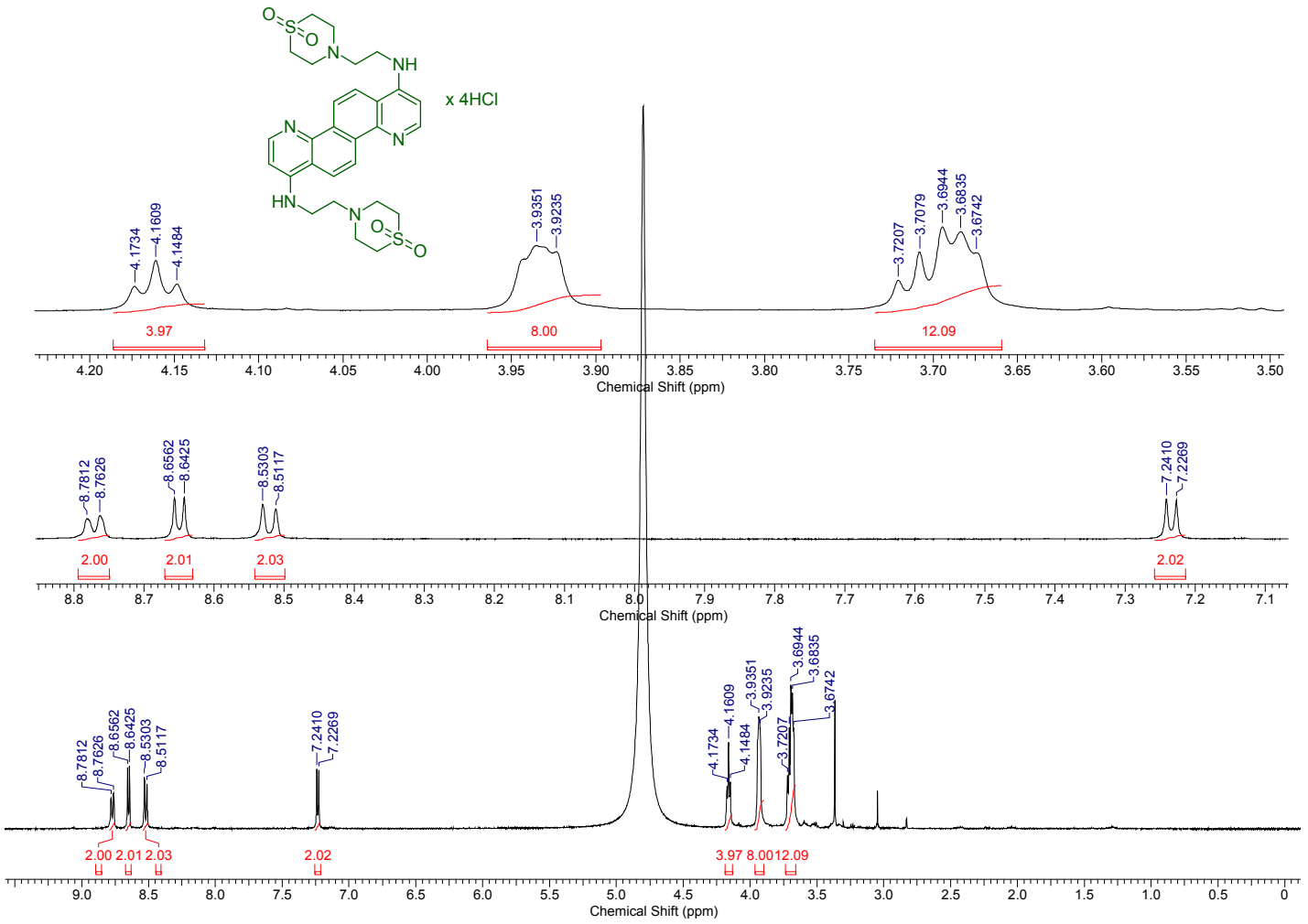

x 4HCl
155.7014
141.6428
134.5016
124.2555
120.7823
119.7714
115.6773
100.8605
54.0563
50.9081
47.6877
40.4526
22.8342
Chemical Shift (ppm)

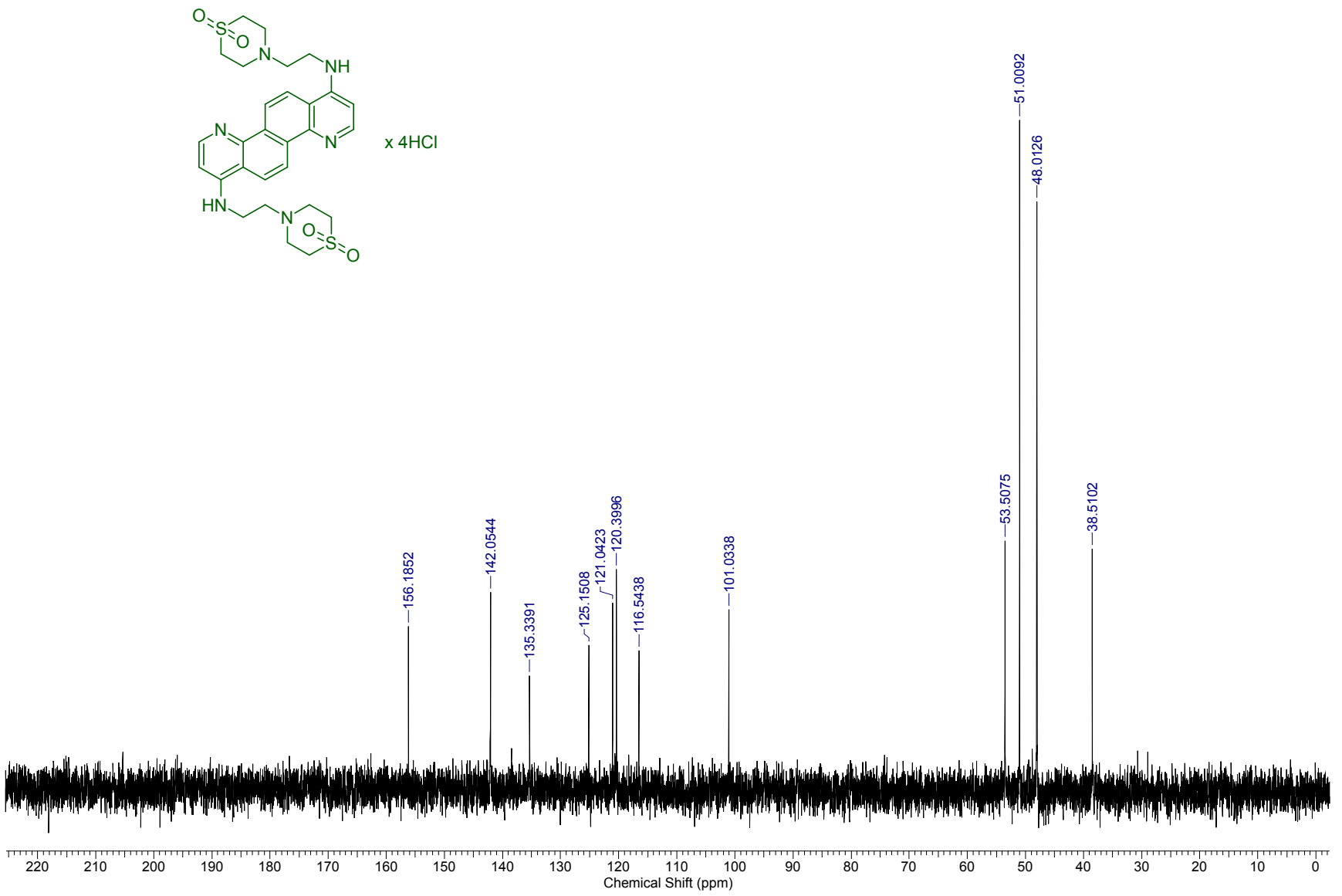
**_N_,_N_'-bis[2-(1,1-dioxidothiomorpholin-4-yl)ethyl]quino[8,7-*h*]quinoline-1,7-diamine (13): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent TFA-d.**




O
S
O
N
NH
N
N
HN
N
O
S
O
123.4070
123.3492
119.3778
126
125
124
123
122
121
120
119
118
117
116
115
114
113
112
Chemical Shift (ppm)
159.1276
144.8451
137.8266
127.8838
123.3492
119.3778
103.7812
57.6267
54.6085
50.2183
40.8098
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

**_N_,_N_'-bis[2-(1,1-dioxidothiomorpholin-4-yl)ethyl]quino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (21): $^{1}$H, 500 MHz; $^{13}$C, 125 MHz. Solvent $D_2O$.**




x 4HCl
156.1852
142.0544
135.3391
125.1508
121.0423
120.3996
116.5438
101.0338
53.5075
51.0092
48.0126
38.5102
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

**HPLC purity determination**

*Methods:*

*Method A*: Octadecylsilica was used as the stationary phase (Symmetry C18 analytical column, 4.6 mm × 150 mm, 5 μm, series no. 021336278136 37). Compounds were dissolved in water. The final concentrations were 0.1 - 0.5 mg/mL, and the injection volume was 10 μL for compound **5**. The eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). Wavelength = 254 nm.

*Method B*: Octadecylsilica was used as the stationary phase (Nucleosil C18 analytical column, 4 mm × 150 mm, 5 μm). Compounds were dissolved in water. The final concentrations were 0.1 - 0.5 mg/mL, and the injection volume was 10 μL for compound **5**. The eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). Wavelength = 254 nm.

*Method C*: Octadecylsilica was used as the stationary phase (Zorbax Eclipse Plus C18 4.6 x 150 mm, 1.8 μm, S.N. USWKY01594). Compounds were dissolved in water. The final concentrations were ~ 1 mg/mL, and the injection volume was 2.5 μL for compounds **16** and **21** and 5 μL for compounds **17, 18, 19, 20, 22** and **22**. The eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). Wavelength = 254 nm.

*Method D*: Octadecylsilica was used as the stationary phase (Zorbax Eclipse Plus C18 4.6 x 150 mm, 1.8 μm, S.N. USWKY01594). Compounds were dissolved in water. The final concentrations were ~ 1 mg/mL, and the injection volume was 2.5 μL for compounds **16** and **21** and 5 μL for compounds **17, 18, 19, 20, 22** and **22**. The eluent was made from the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). Wavelength = 254 nm.

*Chromatografy protocols:*

***N,N′*-bis[2-(morpholin-4-yl)ethyl]quinolino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (5).**
HPLC purity: method A, using gradient protocol 0 – 2 min 44% A → 42% A, 2 - 6 min 42% → 40% A, 6 - 8 min 40% → 30% A, 8 - 9 min 30% A → 44% A, flow 0.5 mL/min, RT 2.084, area 96.93 %; method B, using gradient protocol 0 - 2 min 70% → 68% A, 2 - 6 min 68% → 64% A, 6 - 8 min 64 % A, 8 - 10 min 64% → 50% A, 10 - 11 min 50% → 70% A, flow 0.5 mL/min, RT 2.069, area 96.66 %.

***N,N′*-bis[3-(morpholin-4-yl)propyl]quinolino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (16).**
HPLC purity: method C, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 3.518, area 96.97 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.193, area 98.82 %.

***N,N'*-bis[4-(morpholin-4-yl)buthyl]quinolino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (17).**
HPLC purity: method C, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.194, area 95.14 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.165, area 98.81 %.

***N,N'*-bis(2-thiomorpholin-4-ylethyl)quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (18).**
HPLC purity: method C, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.262, area 98.07 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.192, area 97.41 %.

***N,N'*-bis(3-thiomorpholin-4-ylpropyl)quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (19).**
HPLC purity: method C, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A→ 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 3.345, area 96.59 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.199, area 98.24 %.

***N,N'*-bis(4-thiomorpholin-4-ylbutyl)quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (20).**
HPLC purity: method C, using gradient protocol 0 - 3 min 40% A, 3 - 6 min 40% A → 0% A, 6 - 9 min 0% A, 9 - 10 min 0% A → 40% A, 10 – 11 min 40% A, flow rate 0.5 mL/min, RT 3.265, area 96.04 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.195, area 97.80 %.

***N,N'*-bis[2-(1,1-dioxidothiomorpholin-4-yl)ethyl]quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (21).**
HPLC purity: method C, using gradient protocol 0 - 3 min 75% A → 20% A, 3 - 6 min 20% A → 0% A, 6 - 8 min 75% A, flow rate 0.5 mL/min, RT 2.525, area 95.18 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.173, area 99.05 %.

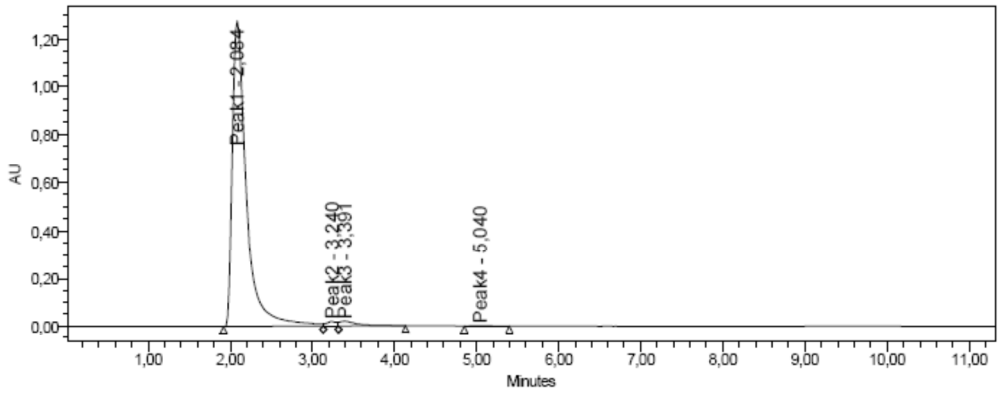
***N,N'*-bis[3-(1,1-dioxidothiomorpholin-4-yl)propyl]quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (22).**
HPLC purity: method C, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.270, area 95.95 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.238, area 95.18 %.

**1,1'-[quino[8,7-*h*]quinoline-1,7-diyldi(imino)]bis(3-morpholin-4-ylpropan-2-ol) tetrahydrochloride (23).**

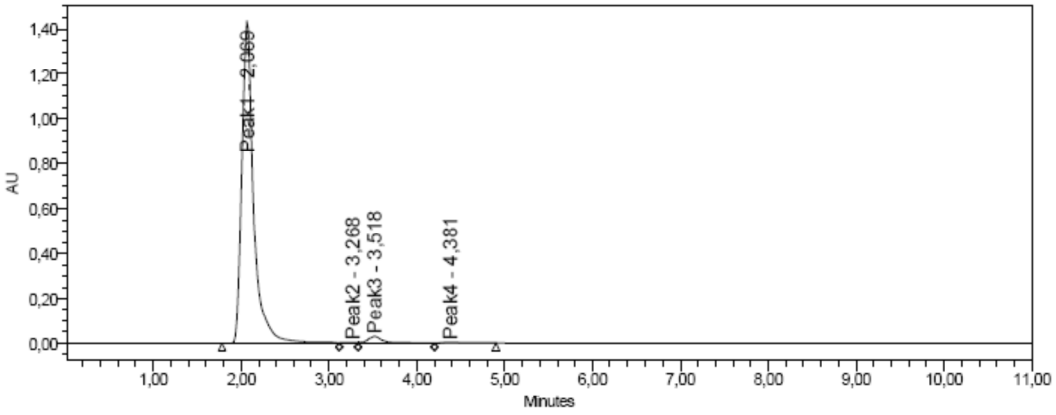
HPLC purity: method C, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 3.445, area 97.64 %; method D, using gradient protocol 0 - 3 min 50% A → 30% A, 3 - 6 min 30% A → 0% A, 6 - 9 min 0% A → 50% A, 9 - 12 min 50% A, flow rate 0.5 mL/min, RT 2.204, area 98.39 %.

*Chromatograms:*

**_N,N′_-bis[2-(morpholin-4-yl)ethyl]quinolino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (5).**

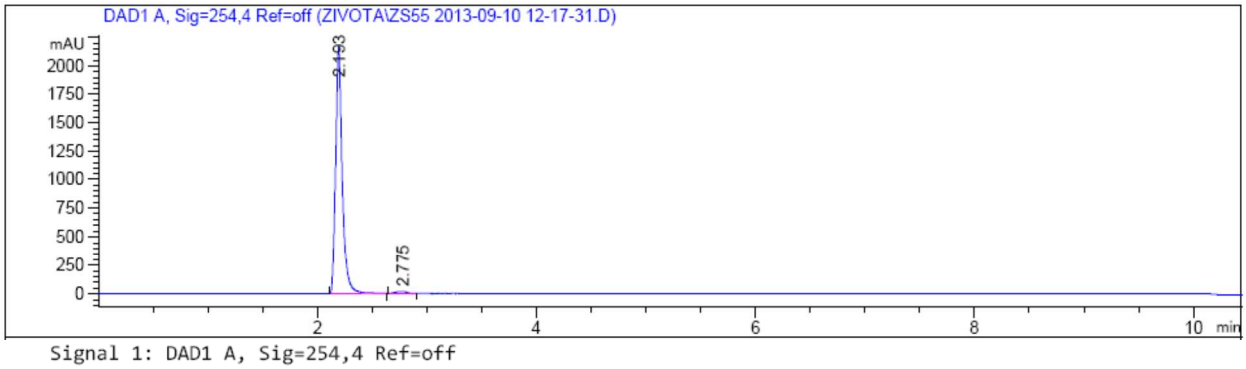



| | Peak Name | RT | Area | % Area | Height |
|---|---|---|---|---|---|
| 1 | Peak1 | 2,084 | 15137224 | 96,93 | 1271419 |
| 2 | Peak2 | 3,240 | 164248 | 1,05 | 18052 |
| 3 | Peak3 | 3,391 | 300620 | 1,92 | 19580 |
| 4 | Peak4 | 5,040 | 15328 | 0,10 | 1013 |



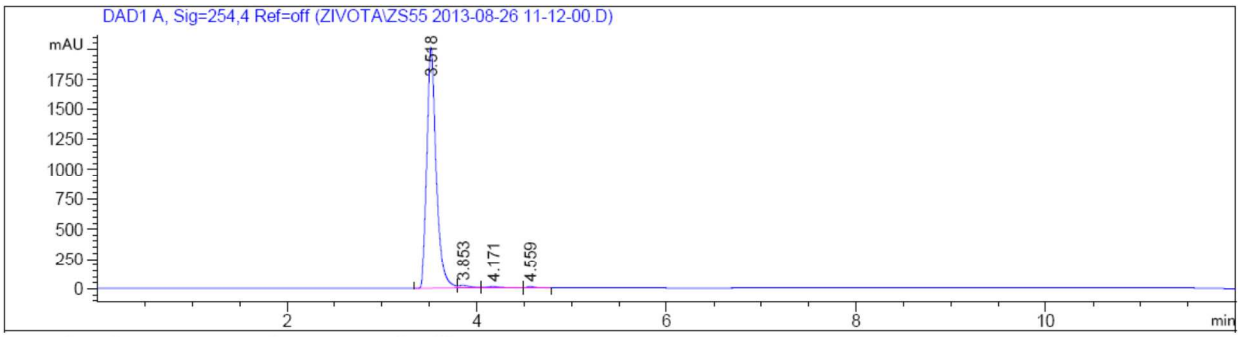

| | Peak Name | RT | Area | % Area | Height |
|---|---|---|---|---|---|
| 1 | Peak1 | 2,069 | 13463005 | 96,66 | 1432099 |
| 2 | Peak2 | 3,268 | 45774 | 0,33 | 3984 |
| 3 | Peak3 | 3,518 | 371287 | 2,67 | 30557 |
| 4 | Peak4 | 4,381 | 48792 | 0,35 | 2290 |

**_N,N′_-bis[3-(morpholin-4-yl)propyl]quinolino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (16).**




Signal 1: DAD1 A, Sig=254,4 Ref=off

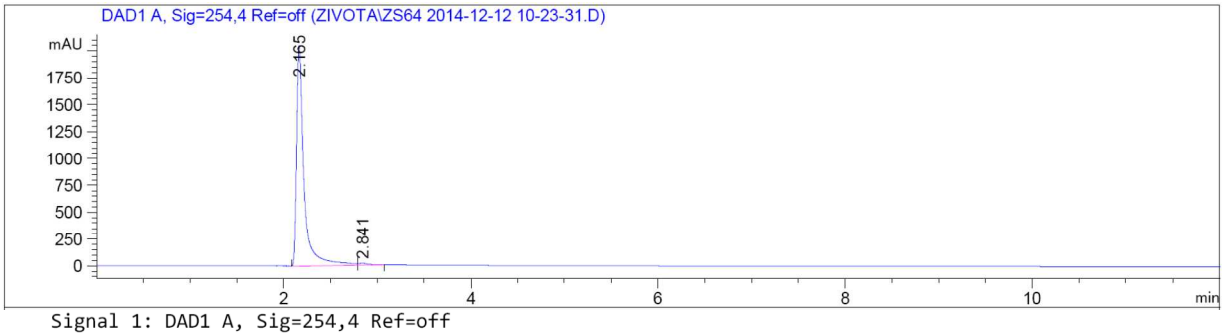
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.193 | BB | 0.0599 | 9061.44922 | 2160.32202 | 98.8233 |
| 2 | 2.775 | BB | 0.0945 | 107.89571 | 16.13487 | 1.1767 |




Signal 1: DAD1 A, Sig=254,4 Ref=off

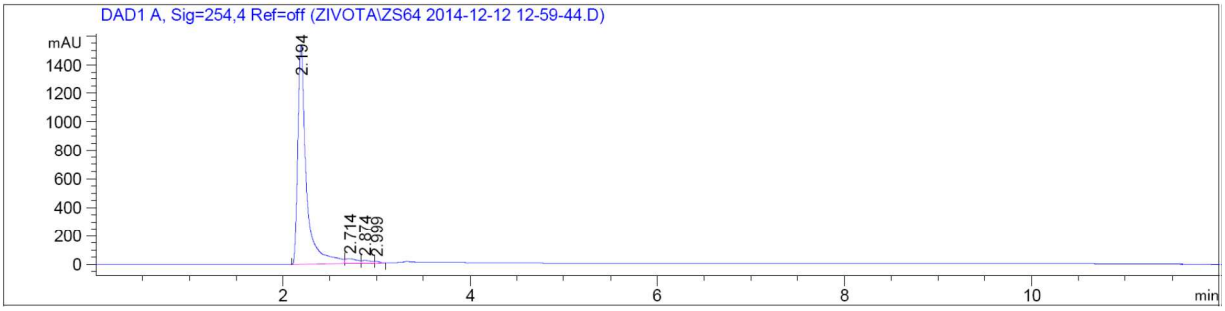
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 3.518 | BV | 0.1004 | 1.38660e4 | 2011.21167 | 96.9766 |
| 2 | 3.853 | VV | 0.1268 | 212.32091 | 22.98375 | 1.4849 |
| 3 | 4.171 | VB | 0.1428 | 147.53647 | 14.13038 | 1.0318 |
| 4 | 4.559 | BB | 0.0711 | 72.43646 | 15.90922 | 0.5066 |

**_N,N′_-bis[4-(morpholin-4-yl)buthyl]quinolino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (17).**



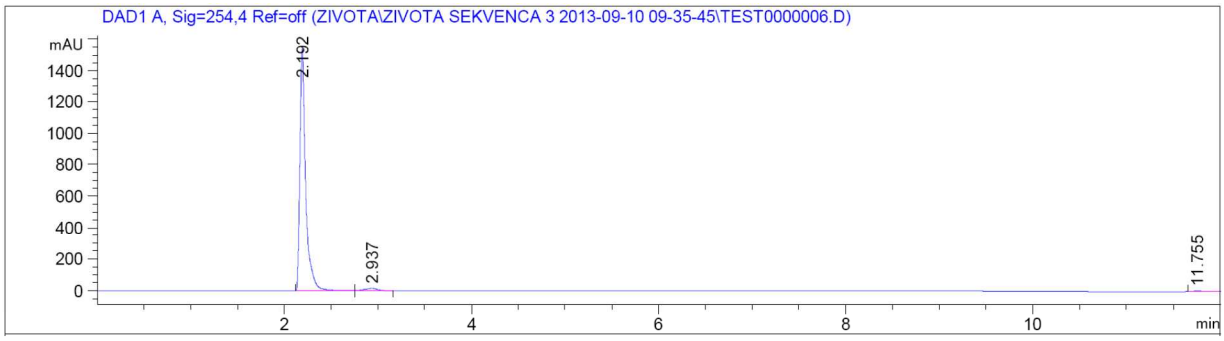

Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.165 | BV | 0.0798 | 1.12701e4 | 2045.38208 | 98.8086 |
| 2 | 2.841 | VB | 0.0986 | 135.89500 | 18.97442 | 1.1914 |



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.194 | BV | 0.0906 | 9701.94238 | 1537.26025 | 95.1387 |
| 2 | 2.714 | VV | 0.1237 | 307.27243 | 33.61236 | 3.0132 |
| 3 | 2.874 | VV | 0.0868 | 142.72745 | 21.13876 | 1.3996 |
| 4 | 2.999 | VB | 0.0561 | 45.73892 | 12.52812 | 0.4485 |

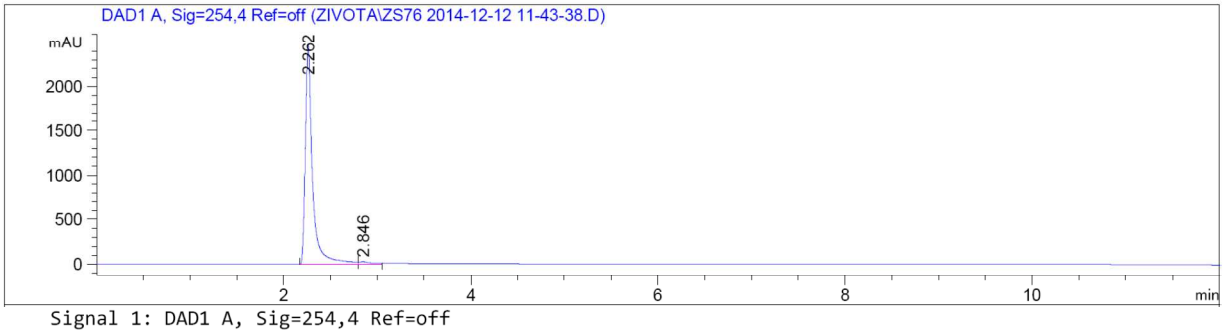
**_N_,_N_'-bis(2-thiomorpholin-4-ylethyl)quino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (18).**




Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.192 | BV | 0.0613 | 6587.48291 | 1543.39941 | 97.4159 |
| 2 | 2.937 | VB | 0.1319 | 143.28293 | 15.34592 | 2.1189 |

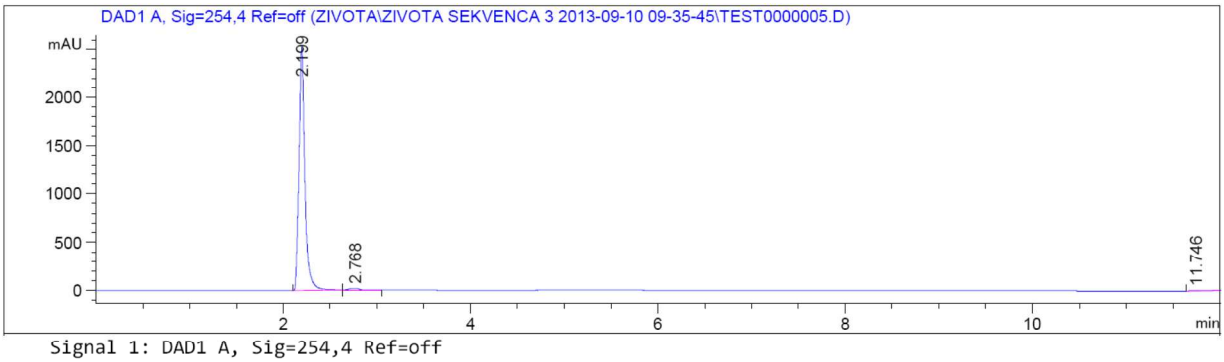
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 3 | 11.755 | BBA | 0.0995 | 31.46000 | 4.10192 | 0.4652 |




Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.262 | BV | 0.0749 | 1.30371e4 | 2476.25024 | 98.0720 |
| 2 | 2.846 | VV | 0.1227 | 256.30182 | 27.64402 | 1.9280 |

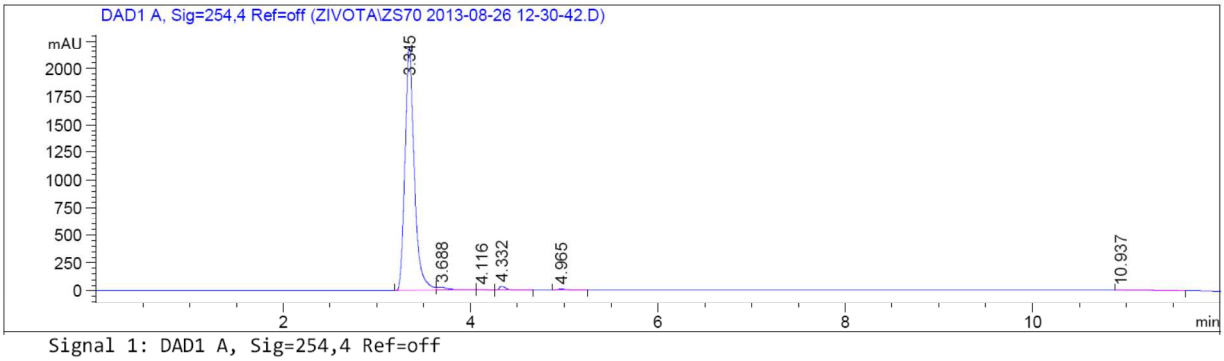
**_N_,_N_'-bis(3-thiomorpholin-4-ylpropyl)quino[8,7-_h_]quinoline-1,7-diamine tetrahydrochloride (19).**




Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.199 | BV | 0.0627 | 1.10606e4 | 2521.31909 | 98.2394 |
| 2 | 2.768 | VB | 0.1113 | 165.88248 | 20.73806 | 1.4733 |

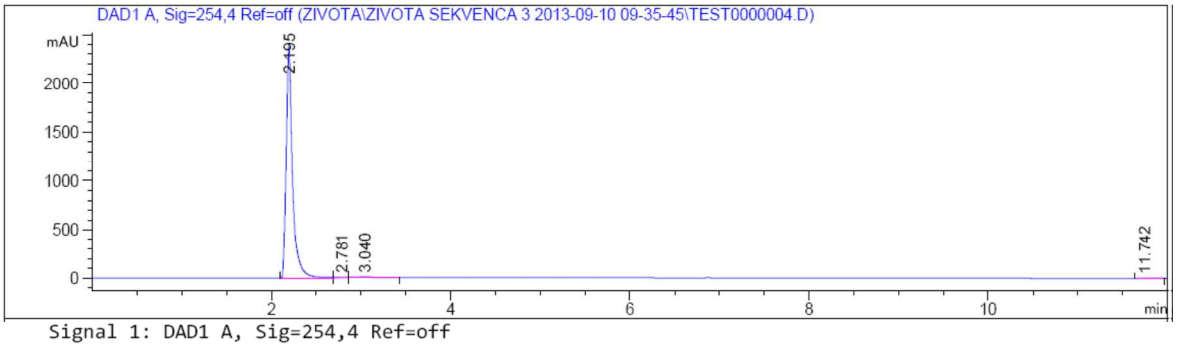
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 3 | 11.746 | BBA | 0.1025 | 32.33705 | 4.14508 | 0.2872 |




Signal 1: DAD1 A, Sig=254,4 Ref=off

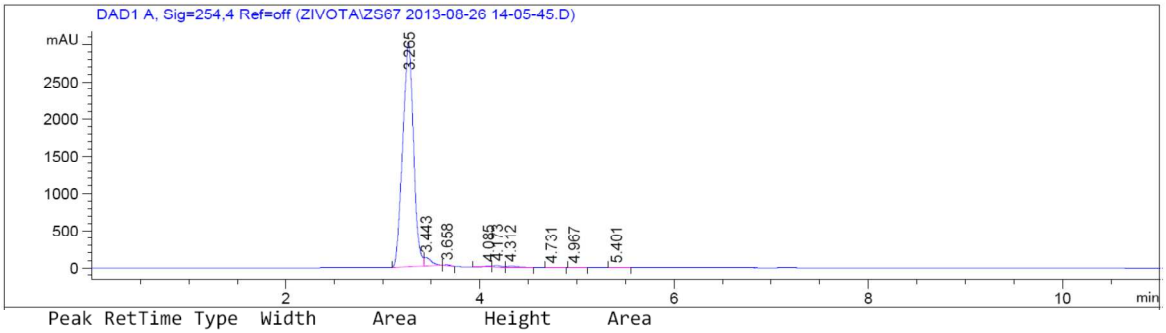
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 3.345 | BV | 0.0991 | 1.51614e4 | 2195.51611 | 96.5897 |
| 2 | 3.688 | VV | 0.1371 | 249.15981 | 24.20363 | 1.5873 |
| 3 | 4.116 | VB | 0.1081 | 21.61705 | 2.41142 | 0.1377 |
| 4 | 4.332 | BB | 0.0720 | 156.26575 | 33.43215 | 0.9955 |
| 5 | 4.965 | BB | 0.0977 | 67.06100 | 9.81786 | 0.4272 |
| 6 | 10.937 | BB | 0.3849 | 41.19987 | 1.27707 | 0.2625 |

**_N_,_N_'-bis(4-thiomorpholin-4-ylbutyl)quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (20).**



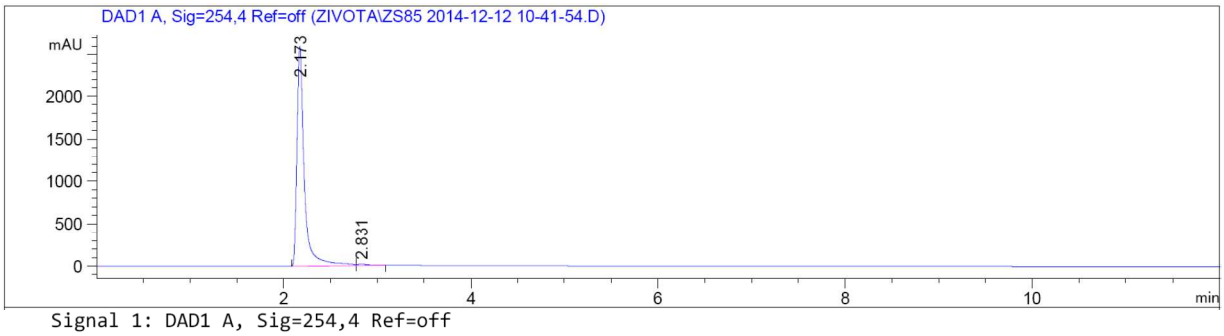

Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.195 | BV | 0.0698 | 1.17624e4 | 2395.91382 | 97.8033 |
| 2 | 2.781 | VV | 0.1192 | 63.79713 | 6.97420 | 0.5305 |
| 3 | 3.040 | VB | 0.1485 | 168.25615 | 14.75438 | 1.3990 |
| 4 | 11.742 | BB | 0.0978 | 32.12887 | 4.29398 | 0.2671 |



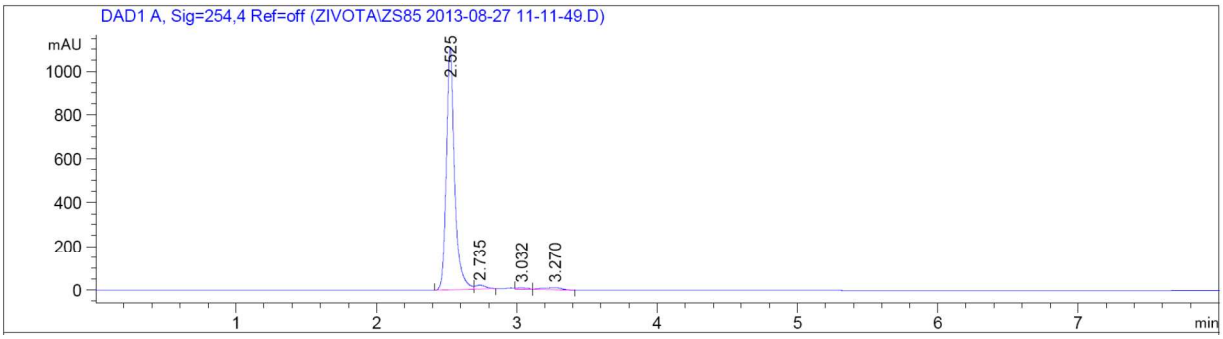

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 3.265 | BV | 0.0979 | 2.32766e4 | 3004.96655 | 96.0366 |
| 2 | 3.443 | VB | 0.0741 | 549.13635 | 110.26232 | 2.2657 |
| 3 | 3.658 | BB | 0.0655 | 37.27638 | 9.05340 | 0.1538 |
| 4 | 4.085 | BV | 0.0760 | 82.98620 | 15.62592 | 0.3424 |
| 5 | 4.173 | VV | 0.0872 | 134.56548 | 22.50902 | 0.5552 |
| 6 | 4.312 | VB | 0.1059 | 127.31277 | 16.16335 | 0.5253 |
| 7 | 4.731 | BB | 0.0548 | 5.69620 | 1.42036 | 0.0235 |
| 8 | 4.967 | BB | 0.0653 | 9.26454 | 2.08620 | 0.0382 |
| 9 | 5.401 | BB | 0.0671 | 14.38406 | 3.10299 | 0.0593 |

**_N_,_N_'-bis[2-(1,1-dioxidothiomorpholin-4-yl)ethyl]quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (21).**




Signal 1: DAD1 A, Sig=254,4 Ref=off

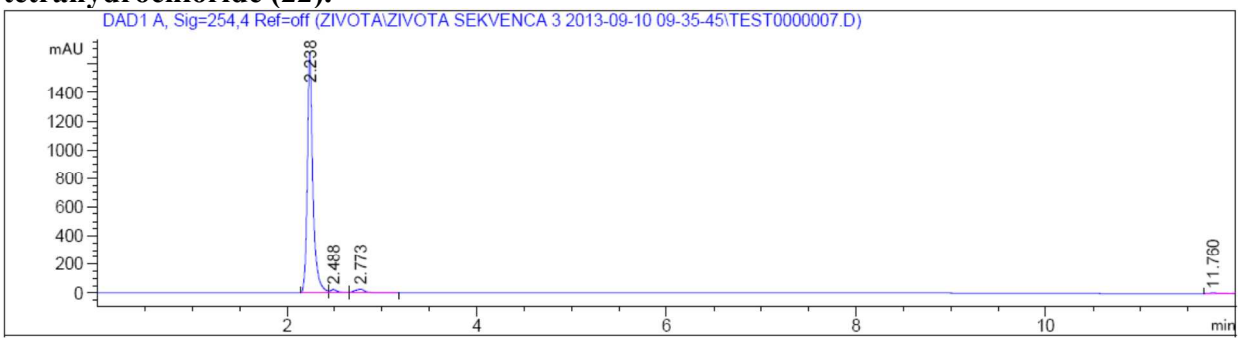
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.173 | BV | 0.0790 | 1.41265e4 | 2596.45435 | 99.0528 |
| 2 | 2.831 | VB | 0.0993 | 135.09166 | 18.57555 | 0.9472 |




Signal 1: DAD1 A, Sig=254,4 Ref=off

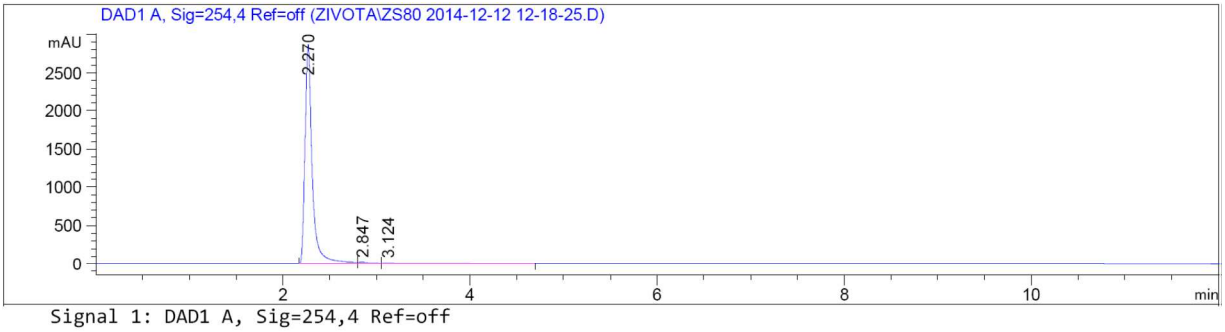
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.525 | BV | 0.0594 | 4503.33643 | 1107.98633 | 95.1794 |
| 2 | 2.735 | VB | 0.0818 | 95.00602 | 17.79110 | 2.0080 |
| 3 | 3.032 | VV | 0.0771 | 39.50109 | 6.21815 | 0.8349 |
| 4 | 3.270 | VB | 0.1352 | 93.57801 | 9.51661 | 1.9778 |

**_N_,_N_'-bis[3-(1,1-dioxidothiomorpholin-4-yl)propyl]quino[8,7-*h*]quinoline-1,7-diamine tetrahydrochloride (22).**



Signal 1: DAD1 A, Sig=254,4 Ref=off

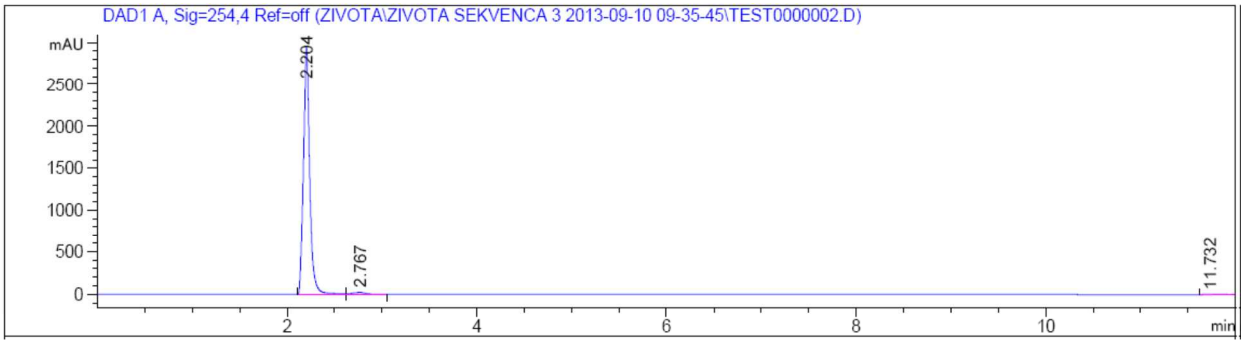
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.238 | BV | 0.0583 | 6811.22119 | 1678.83447 | 95.1831 |
| 2 | 2.488 | VV | 0.0786 | 129.50829 | 23.39858 | 1.8098 |
| 3 | 2.773 | VB | 0.1057 | 185.25792 | 24.77897 | 2.5889 |
| 4 | 11.760 | BBA | 0.1003 | 29.92380 | 3.93200 | 0.4182 |




Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.270 | BV | 0.0787 | 1.55423e4 | 2868.60010 | 95.9505 |
| 2 | 2.847 | VV | 0.1238 | 256.15170 | 27.84160 | 1.5814 |
| 3 | 3.124 | VB | 0.4041 | 399.79041 | 11.89528 | 2.4681 |

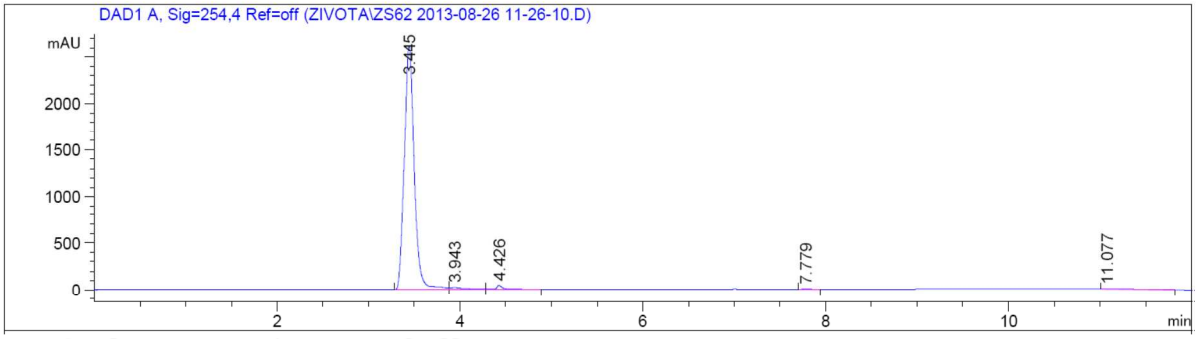
**1,1'-[quino[8,7-*h*]quinoline-1,7-diyldi(imino)]bis(3-morpholin-4-ylpropan-2-ol) tetrahydrochloride (23).**




Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.204 | BV | 0.0660 | 1.34486e4 | 2934.71289 | 98.3895 |
| 2 | 2.767 | VB | 0.1114 | 183.10385 | 22.75548 | 1.3396 |

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 3 | 11.732 | BBA | 0.1051 | 37.03384 | 4.54206 | 0.2709 |




Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 3.445 | BV | 0.1122 | 1.95633e4 | 2616.44165 | 97.6410 |
| 2 | 3.943 | VV | 0.1451 | 215.16223 | 19.44633 | 1.0739 |
| 3 | 4.426 | VB | 0.0663 | 198.70300 | 42.28283 | 0.9917 |
| 4 | 7.779 | BB | 0.0617 | 6.52556 | 1.39160 | 0.0326 |
| 5 | 11.077 | BBA | 0.5612 | 52.25087 | 1.08912 | 0.2608 |

## Log $P_{OW}$ determination

The partition coefficients of the investigated compounds were determined using reversed-phase thin-layer chromatography. An HPTLC vertical developing chamber (Camag, Muttenz, Switzerland) in the tank configuration was used for this purpose. Standard and investigated substances were simultaneously chromatographed using commercially available sorbent RP-18 W F254s (Art. 13124, Merck, Darmstadt, Germany) and mobile phase containing THF/ $NH_3$/ $H_2O$ (65/5/30).

The investigated and standard substances were dissolved in water, and the plates were spotted with 0.5 mL aliquots of freshly prepared solutions (C ~1 mg/mL). Before development, the spotted plates were equilibrated for 15 min in the chromatographic chamber with vapours of the corresponding mobile phase. Detection of individual zones was performed using UV lamp (254nm).

All solvents used throughout the present study were of analytical-grade purity. Water was purified using a water purification system Millipore Simplicity 185 S.A., 67120 (Molshem, France).

All experiments were performed at ambient temperature (22±2°C).

The log $P_{OW}$ of the investigated compounds was experimentally determined by simultaneous chromatographing with standards. Standard compounds were chosen based on their structural similarity to the investigated derivatives, as it was described previously (Ref. 1). $logP_{ow}$ values of standard compounds (Ref. 1): 7 (0.41), 8 (0.29), 10 (0.27), 11 (0.21), 1 (0.14), 4 (0.27), 3 (0.12) and AQ2 (-0.29) were correlated with corresponding $R_M$ values. Linear regression of the calibration data gives:
$R_M = -0.512 + 0.158 logPow$
$R^2 = 0.982$, N = 8, SD =0.030 , $P < 0.0001$
Log $P_{OW}$ values of the investigated substances were calculated by substituting the $R_M$ values into the equation.

1. Šegan S. et al. *Journal of Pharmaceutical and Biomedical Analysis*, **2013**, *72*, 231-239,