Supporting Information

Synthesis and evaluation of 9-aminoacridines with SARS-CoV-2 antiviral activity

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Synthetic Procedures

General procedure for the synthesis of benzoic acids 3a-h

The corresponding amine **2** (2.4 equiv.), potassium carbonate (2 equiv.) and copper (0.4 equiv.) were consistently added to a solution of the corresponding chloro-derivative **1** (1 equiv.) in dry DMF (20 mL). The resulting suspension was stirred at reflux for 8 h and then at room temperature for 16 h. The mixture was poured into hot water (60 mL), stirred for 1 h and filtered. Ethyl acetate (60 mL) was added to the remaining aqueous solution. The aqueous layer was separated, and the organic layer was washed with fresh water (2x20 mL). The combined aqueous fractions were acidified with 2M hydrochloric acid solution to pH 2 and extracted with ethyl acetate (2x40 mL). The combined organic layers were washed with water, dried with Na_2SO_4 and evaporated in vacuo. The residue was treated with *n*-hexane and the precipitate was filtered to afford the corresponding product **3a-h**. These intermediates were used without further purification.

5-Chloro-2-((4-methoxyphenyl)amino)benzoic acid **3a**
Yield 49 %, mp. 198-200 °C. MS (EI): m/z 277.
2-((4-Methoxyphenyl)amino)-5-(trifluoromethyl)benzoic acid **3b**
Yield 41 %, mp. 186-190 °C. MS (EI): m/z 311.
5-Fluoro-2-((4-methoxyphenyl)amino)benzoic acid **3c**
Yield 47 %, mp. 216-218 °C. MS (EI): m/z 261.
4-Chloro-2-((4-methoxyphenyl)amino)benzoic acid **3d**
Yield 50 %, mp. 204-208 °C. MS (EI): m/z 277.
5-Chloro-2-((4-chlorophenyl)amino]benzoic acid **3e**
Yield 56 %, mp. 227-230 °C. MS (EI): m/z 282.
2-((4-Methoxyphenyl)amino)nicotinic acid **3f**
Yield 58 %, mp. 216-218 °C. MS (EI): m/z 244.
5-Chloro-2-((6-methoxypyridin-3-yl)amino)benzoic acid **3g**
Yield 40 %, mp. 182-186 °C. MS (EI): m/z 278.
4-Chloro-2-((4-chlorophenyl)amino)benzoic acid **3h**
Yield 45 %, mp. 224-226 °C. MS (EI): m/z 282.

General procedure for the synthesis of acridines and naphthyridines 4a-h

Triethylamine hydrochloride (0.8 equiv.) was added portion-wise to a suspension of benzoic acid **3** (1 equiv.) in phosphorus oxychloride (3 mL), and the resulting mixture was stirred at reflux for 5-6 h. Then the mixture was cooled and poured on ice. After 30-min stirring ammonia solution was added dropwise to pH 8, the precipitate was filtered, washed with ethanol and *n*-hexane to afford the desired product.

2,9-Dichloro-7-methoxyacridine **4a**
Yield 95 %, mp. 185-186 °C. MS (EI): m/z 278.
9-Chloro-2-methoxy-7-(trifluoromethyl)acridine **4b**
Yield 93%, mp. 196-200 °C. MS (EI): m/z 311.
9-Chloro-2-fluoro-7-methoxyacridine **4c**
Yield 95%, mp. 180-182 °C. MS (EI): m/z 261.
6,9-Dichloro-2-methoxyacridine **4d**
Yield 92%, mp. 184-186 °C. MS (EI): m/z 278.
2,7,9-Trichloroacridine **4e**

Yield 94%, mp. 216-218 °C. MS (EI): m/z 282.
5-Chloro-7-methoxybenzo[*b*]-1,8-naphthyridine **4f**
Yield 88%, mp. $T_{пл}$=188-192 °C. MS (EI): m/z 244.
7,10-Dichloro-2-methoxybenzo[*b*]-1,5-naphthyridine **4g**
Yield 96%, mp. 178-182 °C. MS (EI): m/z 279.
2,6,9-Trichloroacridine **4h**
Yield 93%, mp. 212-214 °C. MS (EI): m/z 282.

General procedure for the synthesis of acridines and naphthyridines 7a-g and 8a-g

4-Amino-2,6-bis(pyrrolidin-1-ylmethyl)phenol (1 equiv., in the case of **7a-g**) or 4-amino-2-(pyrrolidin-1-ylmethyl)phenol (1 equiv., in the case of **8a-g**) was added to a suspension of **4** (1 equiv.) in dry DMF (7 mL), and the reaction mixture was stirred at 100 °C for 1-2 h (TLC control chloroform:methanol 9:1). If a precipitate was observed, it was filtered and washed with DMF, ethyl acetate and ether to afford the desired product. If a solution was observed, it was cooled, poured into water and extracted with ethyl acetate. The separated aqueous fraction was alkalized with an aqueous $NaHCO_3$ solution to pH 2 and extracted with ethyl acetate (2x40 mL). The combined organic layers were washed with water, dried with Na_2SO_4 and not fully evaporated in vacuo. The remaining organic solution was acidified with hydrogen chloride solution 3M in methanol to pH 2 and fully evaporated in vacuo. The residue was recrystallized from a 1:1 mixture of ether:ethyl acetate or other indicated mixture and washed with acetone and ether to afford the desired product.

4-((2-Chloro-7-methoxyacridin-9-yl)amino)-2,6-bis(pyrrolidin-1-ylmethyl)phenol **7a**
Yield 75 %, mp. 207-210 °C (MeOH:ethyl acetate 1:2). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.92 (brs, 8H, $4CH_{2,pyr}$), 3.44 (brs, 8H, $4CH_{2,pyr}$), 3.76 (s, 3H, CH_3), 4.46 (s, 4H, $2CH_2$), 7.64-7.78 (m, 4H, $2CH_{ph}$, HC(6,8)), 7.93 (d, 1H, HC(3), *J* = 9.1), 8.05-8.27 (m, 3H, HC(1,4,9), 10.44 (s, 1H, NH), 10.80 (s, 1H, NH), 11.66 (s, 1H, OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.40, 51.13, 52.39, 56.09, 103.46, 114.05, 115.21, 121.20, 121.66, 121.88, 124.44, 127.97, 128.40, 130.16, 133.43, 134.22, 135.72, 137.74, 152.33, 153.81, 155.73. MS (EI): m/z 517. Anal. calcd for $C_{30}H_{33}ClN_4O_2$: C, 69.69; H, 6.43; N, 10.84. Found: C, 69.73; H, 6.46; N, 10.89.

4-((2-Methoxy-7-(trifluoromethyl)acridin-9-yl)amino)-2,6-bis(pyrrolidin-1-ylmethyl)phenol hydrochloride **7b**
Yield 71 %, mp. 223-225 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.93 (brs, 8H, $4CH_{2,pyr}$), 3.12 (brs, 8H, $4CH_{2,pyr}$), 3.78 (s, 3H, CH_3), 4.46 (s, 4H, $2CH_2$), 7.70-7.89 (m, 4H, HC(3,5,1`,3`)), 8.01-8.25 (m, 2H, HC(4`,6)), 8.31 (d, 1H, HC(5`), *J* = 9.0), 8.54 (s, 1H, HC(8`)), 10.48 (s, 1H, NH), 10.80 (s, 1H, NH), 12.04 (s, 1H,OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.37, 51.14, 52.40, 56.15, 103.93, 112.03, 115.48, 120.91, 121.13, 121.23, 121.98, 122.73, 123.37, 124.26, 124.36, 124.43, 126.32, 128.55, 129.15, 130.25, 133.20, 136.09, 140.60, 154.17, 155.90. MS (EI): m/z 550. Anal. calcd for $C_{31}H_{33}F_3N_4O_2$: C, 67.62; H, 6.04; N, 10.18. Found: C, 67.57; H, 6.07; N, 10.20.

4-((2-Fluoro-7-methoxyacridin-9-yl)amino)-2,6-bis(pyrrolidin-1-ylmethyl)phenol hydrochloride **7c**

Yield 62 %, mp. 240 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 2.00 (brs, 8H, $4CH_{2,pyr}$), 3.74 (s, 3H, CH_3), 4.44 (brs, 4H, $2CH_2$), 7.71 (brs, 4H, HC(3,5,1`,8`), 7.83-8.57 (m, 4H, HC(3`,4`,5`,6`), 10.68 (brs, 2H, NH, H), 11.53 (s, 1H, OH), 15.57 (br s, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.40, 51.29, 52.49, 55.99, 103.02, 103.26, 108.85, 109.34, 113.53, 114.22, 114.36, 121.73, 123.19, 124.17, 128.27, 129.83, 133.15, 135.91, 136.37, 152.28, 153.54, 154.94, 155.57, 159.77, 160.01, 168.16, 169.99. MS (EI): m/z 500. Anal. calcd for $C_{30}H_{33}FN_4O_2$: C, 71.98; H, 6.64; N, 11.19. Found: C, 71.94; H, 6.67; N, 11.17.

4-((2,7-Dichloroacridin-9-yl)amino)-2,6-bis(pyrrolidin-1-ylmethyl)phenol hydrochloride **7d**
Yield 85 %, mp. 238-240 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.94 (br s, 8H, $4CH_{2,pyr}$), 3.25-3.62 (m, 8H, $4CH_{2,pyr}$), 4.49 (s, 4H, $2CH_2$), 7.78 (s, 2H, HC(3, 5)), 8.00 (d, 2H, HC(4`,5`), *J* = 9.1), 8.17 (d, 2H, HC(3`,6`), *J* = 9.2), 8.32 (s, 2H, HC(1`, 8`)),10.47-10.88 (m, 2H, NH), 12.12 (brs, 1H, NH), 15.50 (brs, 1H, OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.42, 51.05, 52.37, 114.57, 121.49, 122.03, 124.85, 128.27, 130.06, 135.27, 138.77, 153.45, 154.25. MS (EI): m/z 521. Anal. calcd for $C_{29}H_{30}Cl_2N_4O$: C, 66.79; H, 5.80; N, 10.74. Found: C, 67.83; H, 5.87; N, 10.79.

4-((2,6-Dichloroacridin-9-yl)amino)-2,6-bis(pyrrolidin-1-ylmethyl)phenol hydrochloride **7e**
Yield 82 %, mp. 240-244 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.95 (brs, 8H, $4CH_{2,pyr}$), 4.45 (s, 8H, $4CH_{2,pyr}$), 7.39 (d, 1H, HC(3`), *J* = 9.2), 7.67 (s, 2H, HC(3,5)), 7.81-8.28 (m, 4H, HC(4`,5`,7,`8`)), 8.44 (brs, 1H, HC(1`)), 9.92-11.36 (brs, 1H, NH, OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.44, 51.44, 52.66, 112.82, 115.54, 116.00, 117.85, 121.20, 122.28, 123.95, 124.91, 128.03, 128.09, 128.67, 129.11, 134.89, 138.96, 139.30, 141.16, 153.80. MS (EI): m/z 521. Anal. calcd for $C_{29}H_{30}Cl_2N_4O$: C, 66.79; H, 5.80; N, 10.74. Found: C, 66.83; H, 5.84; N, 10.76.

4-((7-Methoxybenzo[*b*]-1,8-naphthyridin-5-yl)amino)-2,6-bis(pyrrolidin-1-ylmethyl)phenol hydrochloride **7f**
Yield 62 %, mp. 217-220 °C (decomp.). (EtOH:MeOH 1:1). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.94 (s, 8H, $4CH_{2,pyr}$), 3.24 (s, 8H, $4CH_{2,pyr}$), 3.81 (s, 3H, CH_3), 4.43 (s, 4H, $2CH_2$), 7.30 (s, 1H, HC(1)), 7.60 (s, 3H, $2CH_{ph}$, HC(3)), 7.92 (s, 2H, HC(4,7), 8.34 (brs, 1H, HC(8)), 8.88 (brs, 1H, HC(6)), 11.4-13.3 (brs, 4H, NH, OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.47, 51.65, 52.66, 56.04, 105.39, 117.89, 118.25, 120.51, 122.35, 124.58, 126.48, 126.64, 127.81, 135.60, 136.03, 148.77, 152.66, 153.87, 155.38. MS (EI): m/z 483. Anal. calcd for $C_{29}H_{33}N_5O_2$: C, 72.02; H, 6.88; N, 14.48. Found: C, 72.06; H, 6.92; N, 14.52.

4-((2-Chloro-7-methoxyacridin-9-yl)amino)-2-(pyrrolidin-1-ylmethyl)phenol hydrochloride **8a**
Yield 89 %, mp. 255 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.94 (s, 4H, $2CH_{2,pyr}$), 3.75 (s, 3H, CH_3), 4.28 (s, 2H, CH_2), 7.19 (d, 1H, HC(6), *J* = 8.7), 7.31 (s, 1H, HC(1`)), 7.65 (m, 3H, HC(3,5,8`), 7.88 (d, 1H, HC(5`), *J* = 8.4), 8.11 (m, 3H, HC(3`,4`,6`), 10.0-12.0 (brs , 4H, NH, OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.46, 50.96, 52.50, 55.82, 103.87, 113.94, 114.08, 115.09, 116.94, 118.70, 121.55, 121.94, 124.36, 127.21, 127.63, 128.56, 132.61, 133.80, 136.20, 138.29, 152.01, 155.38, 155.56.

MS (EI): m/z 433. Anal. calcd for $C_{25}H_{24}ClN_3O_2$: C, 69.20; H, 5.58; N, 9.68. Found: C, 69.25; H, 5.62; N, 9.71.

4-((2-Methoxy-7-(trifluoromethyl)acridin-9-yl)amino)-2-(pyrrolidin-1-ylmethyl)phenol hydrochloride **8b**
Yield 77 %, mp. 265 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.69-2.17 (brm, 4H, $2CH_{2,pyr}$), 3.08 (brs, 2H, $CH_{2,pyr}$), 3.77 (s, 3H, CH_3), 4.30 (s, 2H, CH_2), 7.19 (d, 1H, HC(6), *J* = 8.7), 7.38 (d, 1H, HC(3`), *J* = 8.4), 7.71 (brs, 2H, HC(3,5)), 7.84 (s, 1H, HC(1')), 7.99-8.31 (m, 3H, HC(4`,5`,6`), 8.41 (s, 1H, HC(8`)), 10.73 (brs, 1H, NH), 10.96 (brs, 1H, H), 11.87 (brs, 1H, OH), 15.28, (brs, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.43, 50.77, 52.42, 55.95, 103.88, 111.36, 115.00, 116.82, 118.87, 120.89, 121.04, 122.34, 122.97, 124.31, 124.39, 126.31, 127.76, 128.33, 129.00, 129.28, 131.63, 135.77, 140.66, 154.19, 155.78, 155.96. MS (EI): m/z 467. Anal. calcd for $C_{26}H_{24}F_3N_3O_2$: C, 66.80; H, 5.17; N, 8.99. Found: C, 66.83; H, 5.23; N, 9.02.

4-((2-Fluoro-7-methoxyacridin-9-yl)amino)-2-(pyrrolidin-1-ylmethyl)phenol hydrochloride **8c**
Yield 87 %, mp. >270 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.93 (brs, 4H, $2CH_{2,pyr}$), 3.09 (s, 2H, $CH_{2,pyr}$), 3.71 (s, 3H, CH_3), 4.28 (s, 2H, CH_2), 7.18 (d, 1H, HC(6), *J* = 8.7), 7.35 (dd, 1H, HC(5), *J* = 8.7, 2.4), 7.66 (m, 3H, HC(3,1`,8`)) 7.75-7.99 (m, 2H, HC(3',4')), 8.11 (d, 1H, HC(5`), *J* = 9.1), 8.22 (dd, 1H, HC(6`), *J* = 9.2, 5.3), 10.66 (s, 1H, NH), 10.90 (s, 1H, H, NH), 11.37 (s, 1H, OH), 15.36 (br s, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.46, 50.87, 52.48, 55.72, 103.15, 108.78, 109.29, 113.37, 113.55, 114.21, 116.67, 118.58, 121.14, 122.27, 123.98, 124.53, 127.61, 127.97, 129.00, 131.86, 135.67, 136.34, 152.36, 154.62, 155.36, 155.49, 159.45. MS (EI): m/z 417. Anal. calcd for $C_{25}H_{24}FN_3O_2$: C, 71.92; H, 5.79; N, 10.07. Found: C, 71.97; H, 5.84; N, 10.11.

4-((2,7-Dichloroacridin-9-yl)amino)-2-(pyrrolidin-1-ylmethyl)phenol hydrochloride **8d**
Yield 67 %, mp. >270 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 2.01 (brs, 4H, $2CH_{2,pyr}$), 3.09 (brs, 4H, $CH_{2,pyr}$), 4.30 (s, 2H, CH_2), 7.21 (d, 1H, HC(6), *J* = 8.7), 7.37 (dd, 1H, HC(5), *J* = 8.6, 2.3), 7.66 (d, 1H, HC(3), *J* = 2.3), 7.85-8.05 (m, 2H, HC(4`,5`)), 8.14 (d, 2H, HC(3`,6`), *J* = 9.1),8.26 (brs, 2H, HC(1`,8`)), 10.66 (s, 1H, NH), 10.95 (s, 1H, NH), 12.1 (brs, 1H, OH), 15.05 (br s, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.48, 50.77, 52.50, 114.12, 117.03, 118.94, 121.41, 124.77, 127.57, 128.10, 128.92, 131.44, 135.28, 138.71, 153.55, 156.18. MS (EI): m/z 438. Anal. calcd for $C_{24}H_{21}Cl_2N_3O$: C, 65.76; H, 4.83; N, 9.59. Found: C, 65.79; H, 4.85; N, 9.62.

4-((2,6-Dichloroacridin-9-yl)amino)-2-(pyrrolidin-1-ylmethyl)phenol hydrochloride **8e**
Yield 70 %, mp. >270 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 2.02 (brs, 4H, $2CH_{2,pyr}$), 3.05 (brs, 4H, $2CH_{2,pyr}$), 4.28 (s, 2H, CH_2), 7.19 (d, 1H, HC(6), *J* = 8.6), 7.27-7.52 (m, 2H, HC(3`,5)), 7.59 (s, 1H, HC(3)), 7.85-8.27 (m, 4H, HC(1`,3`,7`,8`), 8.40 (s, 1H, HC(5`)), 10.59 (brs, 1H, NH), 10.88 (brs, 1H, NH), 11.95 (brs, 1H, OH), 14.91 (brs, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.42, 50.86, 52.60, 111.94, 114.59, 117.00, 117.79, 118.88, 121.19, 124.08, 124.70, 127.29, 128.10, 128.31, 128.52, 135.33, 138.74, 139.69, 140.90, 154.28, 155.97. MS (EI): m/z 438. Anal. calcd for $C_{24}H_{21}Cl_2N_3O$: C, 65.76; H, 4.83; N, 9.59. Found: C, 65.72; H, 4.79; N, 9.63.

4-((7-Methoxybenzo[*b*]-1,8-naphthyridin-5-yl)amino)-2-(pyrrolidin-1-ylmethyl)phenol hydrochloride **8f**
Yield 75 %, mp. >270 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 2.01 (brs, 4H, $2CH_{2,pyr}$), 3.06 (s, 2H, $CH_{2,pyr}$), 3.84 (s, 3H, CH_3), 4.27 (s, 2H, CH_2), 7.11 (s, 1H, HC(3)), 7.23 (d, 1H, HC(6), *J* = 8.7), 7.40 (m, 3H, HC(5,6',8')), 7.50-7.88 (m, 1H, HC(2`)), 8.07 (m, 2H, HC(5`), NH_{pyr}), 8.40 (d, 1H, HC(3`), *J* = 7.5), 9.01 (d, 1H, HC(1`), *J* = 3.3), 10.85 (brs, 1H, NH), 11.05 (brs, 1H, NH), 12.1 (brs, 1H, OH), 14.44 (brs, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 22.49, 50.70, 52.49, 56.18, 104.03, 107.76, 115.08, 116.96, 118.80, 118.95, 119.49, 120.95, 127.44, 128.36, 128.97, 131.59, 135.71, 147.84, 154.95, 155.84, 155.94, 156.91. MS (EI): m/z 400. Anal. calcd for $C_{24}H_{24}N_4O_2$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.01; H, 6.06; N, 13.97.

General procedure for the synthesis of acridines and naphthyridines 9a-d
N^1,*N*^{1}-Diethylpentane-1,4-diamine (6 equiv.) was added to a suspension of **4** (1 equiv.) in dry DMF (7 mL), and the reaction mixture wascstirred at 100 °C for 6 h. Then the solution was cooled, diluted with waster and extracted with ethyl acetate (3x30 mL). The organic layer was acidified by an aqueous solution of hydrochloric acid to pH 2, and the aqueous layer was separated. The organic layer was additionally washed with water until the aqueous layer became pH 7. The combined aqueous solution was evaporated in vacuo. A mixture of ethyl acetate:isopropanol (5:1) was added to the residue and the resulting mixture was boiled until crystals appeared. The precipitate was filtered, washed with isopropanol, ethyl acetate and ether to afford the desired product.

N^4-(2-Chloro-7-methoxyacridin-9-yl)-*N*^{1},*N*^{1}-diethylpentane-1,4-diamine hydrochloride **9a**
Yield 56 %, mp. 232-236 °C. ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.10 (t, 6H, $2CH_3$, *J* = 6.7), 1.65 (d, 5H, CH_3CHCH_2, *J* = 6.0), 1.88 and 2.11 (s and s, 1H and 1H, CH_2CH_2N), 2.93 (s, 2H, CH_2N), 3.36 (s, 4H, $2CH_2$-CH_3), 4.00 (s, 3H, OCH_3), 4.59 (brs, 1H, CH), 7.71 (d, 1H, HC(6), *J* = 9.2), 8.03 (dt, 4H, HC(3,4,5,8), *J* = 18.0, 9.5), 8.64 (s, 1H, HC(1)), 9.55 (brs, 1H, NH), 10.44 (s, 1H, NH), 14.93 (s, 1H, OH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 8.17, 19.96, 20.77, 33.64, 49.80, 55.30, 56.22, 104.12, 112.79, 113.36, 120.66, 120.98, 124.04, 127.45, 127.62, 134.28, 135.35, 137.54, 155.48. MS (EI): m/z 399. Anal. calcd for $C_{26}H_{30}ClN_3O$: C, 69.07; H, 7.56; N, 10.51. Found: C, 69.11; H, 7.59; N, 10.48.

N^1,*N*^{1}-Diethyl-*N*^{4}-(2-methoxy-7-(trifluoromethyl)acridin-9-yl)pentane-1,4-diamine hydrochloride **9b**
Yield 70 %, mp. 212 °C (decomp.). ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.12 (t, 6H, $2CH_3$, *J* = 6.7), 1.70 (d, 5H, CH_3CHCH_2, *J* = 6.1), 1.93 and 2.14 (s and s, 1H and 1H, CH_2CH_2N), 2.94 (s, 2H, CH_2N), 3.38 (s, 4H, $2CH_2$-CH_3), 4.02 (s, 3H, OCH_3), 4.57 (brs, 1H, CH), 7.87 (dd, 1H, HC(3)), 7.94-8.37 (m, 4H, HC(4,5,6,8)), 8.83 (brs, 1H, HC(1)), 10.08 (s, 1H, NH), 10.49 (s, 1H, NH), 15.03 (s, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 8.12, 8.17, 19.90, 20.58, 33.46, 45.80, 49.72, 55.73, 56.45, 104.48, 110.46, 114.04, 120.33, 120.63, 121.24, 121.68, 122.28, 122.93, 124.17, 126.64, 127.54, 129.36, 132.07, 135.30, 140.72, 155.85, 156.95. MS (EI): m/z 433. Anal. calcd for $C_{24}H_{30}F_3N_3O$: C, 66.49; H, 6.98; N, 9.69. Found: : C, 66.54; H, 7.02; N, 9.73.

N^4-(2,7-Dichloroacridin-9-yl)-N^1,N^1-diethylpentane-1,4-diamine hydrochloride **9c**
Yield 61 %, mp. 256-258 °C. ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 1.15 (t, 6H, $2CH_3$, *J* = 6.7), 1.63 (d, 5H, $C\underline{H_3}CHC\underline{H_2}$, *J* = 5.7), 1.94 and 2.12 (s and s, 1H and 1H, $C\underline{H_2}CH_2N$), 2.98 (s, 2H, $C\underline{H_2}N$), 3.26 (brs, 4H, $N(C\underline{H_2}CH_3)_2$), 4.56 (brs, 1H, CH), 7.84-8.28 (m, 4H, HC(3,4,5,6)), 8.67 (brs, 2H, HC(1,8)), 9.84 (brs, 1H, NH), 10.56 (brs, 1H, NH), 15.02 (brs, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 8.27, 19.92, 20.43, 33.42, 46.11, 50.11, 55.24, 113.25, 121.15, 124.64, 127.97, 135.02, 138.75, 155.77. MS (EI): m/z 404. Anal. calcd for $C_{21}H_{26}Cl_2N_3$: C, 65.35; H, 6.73; N, 10
.39. Found: C, 65.38; H, 6.78; N, 10.34.

N^4-(7-chloro-2-methoxybenzo[*b*][1,5]naphthyridin-10-yl)-N^1,N^1-diethylpentane-1,4-diamine hydrochloride **9d**
Yield 64 %, mp. 160-164 °C. ^{1}H NMR (200 MHz; DMSO-d_6; δ, ppm; *J*, Hz): 0.98-1.34 (m, 6H, $2CH_3$), 1.51 (d, 3H, CH_3, *J* = 6.2), 1.80 (brs, 4H, $2CH_2$), 2.08 (s, 1H, CH), 2.82-3.22 (m, 6H, $3CH_2N$), 4.02 (s, 3H, OCH_3), 6.06 (s, 1H, NH), 7.57 (d, 1H, HC(7), *J* = 9.2), 7.61 (dd, 1H, HC(3), *J* = 1.5, 9.0), 8.06 (d, 1H, HC(4), *J* = 1.5), 8.38 (d, 1H, HC(8), *J* = 9.2), 9.00 (s, 1H, HC(5)), 9.35 (s, 1H, NH), 10.49 (s, 1H, NH), 15.04 (s, 1H, NH). ^{13}C NMR (50 MHz; DMSO-d_6; δ, ppm): 8.23, 20.21, 21.39, 32.84, 45.77, 45.91, 50.23, 52.94, 54.42, 113.52, 117.54, 121.76, 124.33, 124.55, 127.22, 131.06, 135.04, 137.89, 138.72, 152.29, 158.21. MS (EI): m/z 400. Anal. calcd for $C_{22}H_{29}ClN_4O$: C, 65.90; H, 7.29; N, 13.97. Found: C, 65.98; H, 7.36; N, 13.93.

Figure S1. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **7a.**

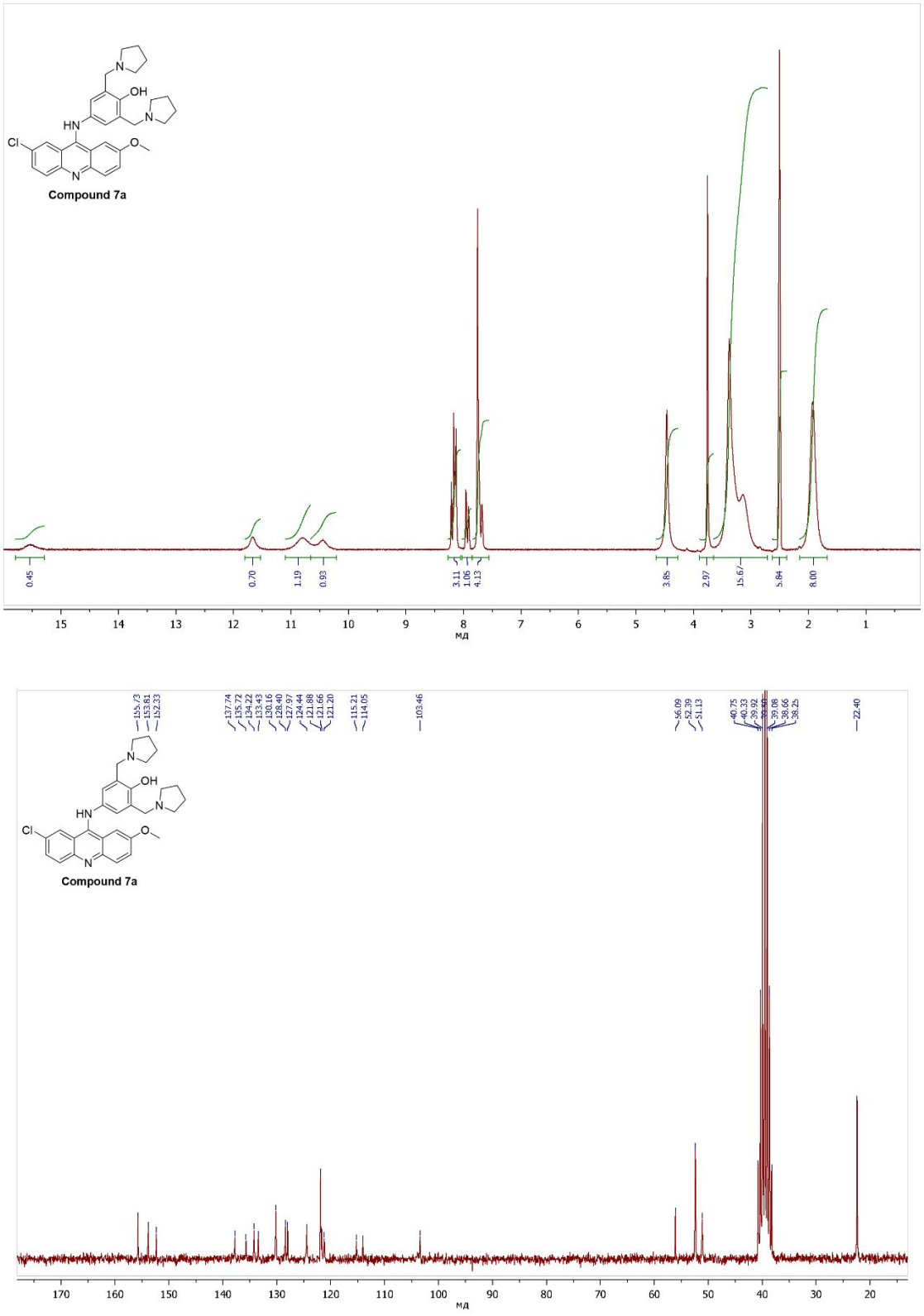


Figure S2. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **7b.**

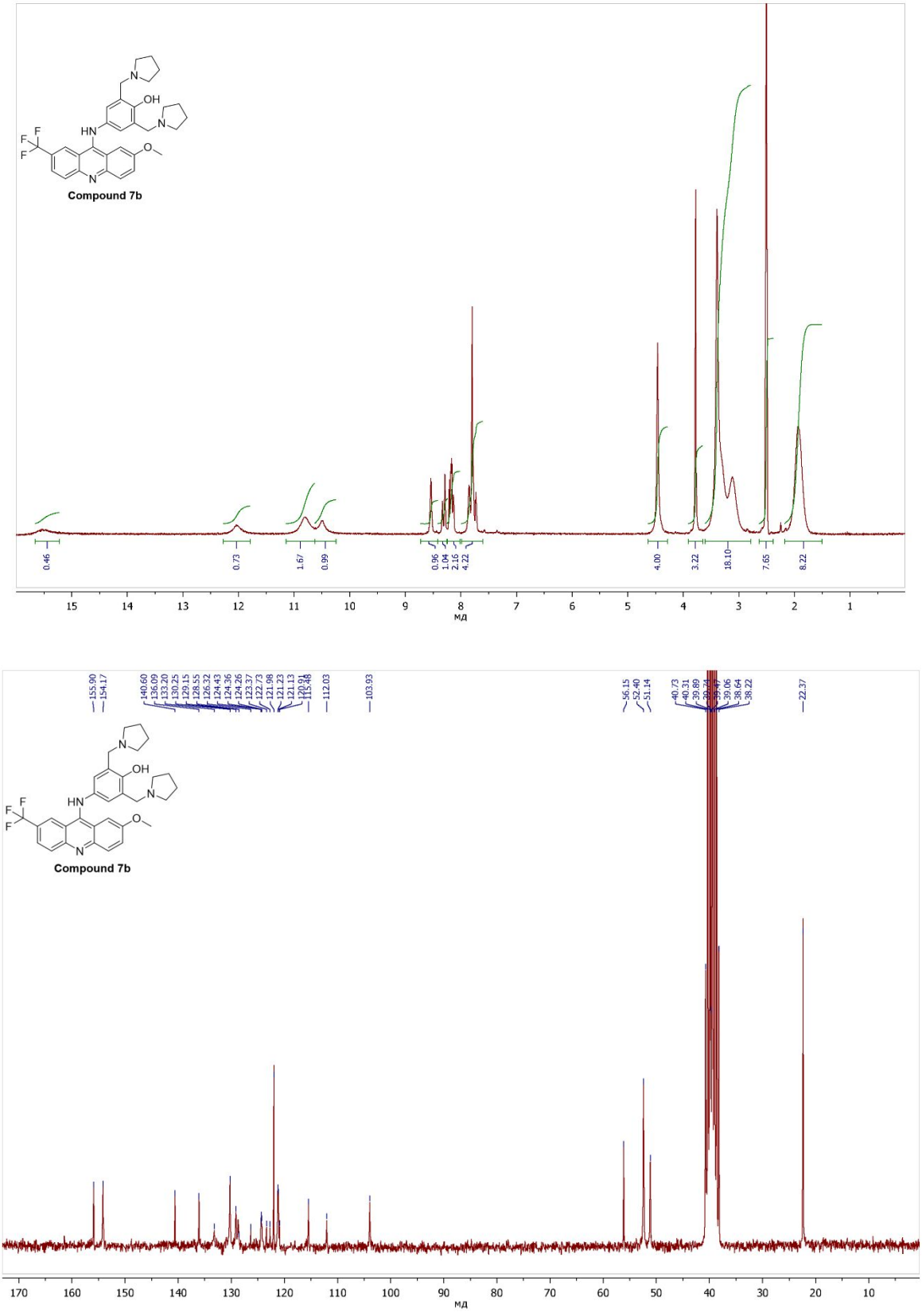


Figure S3. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **7c**.

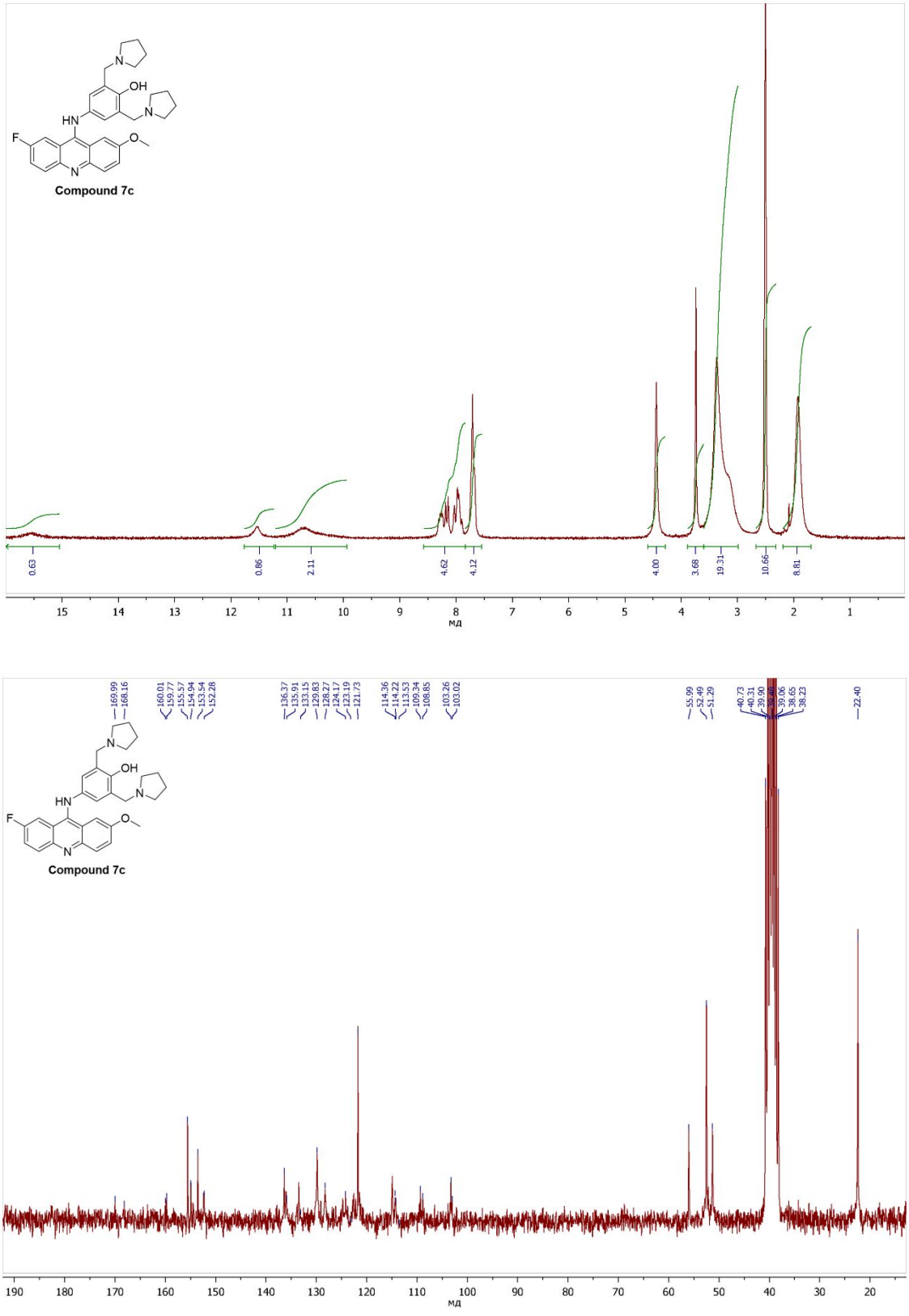
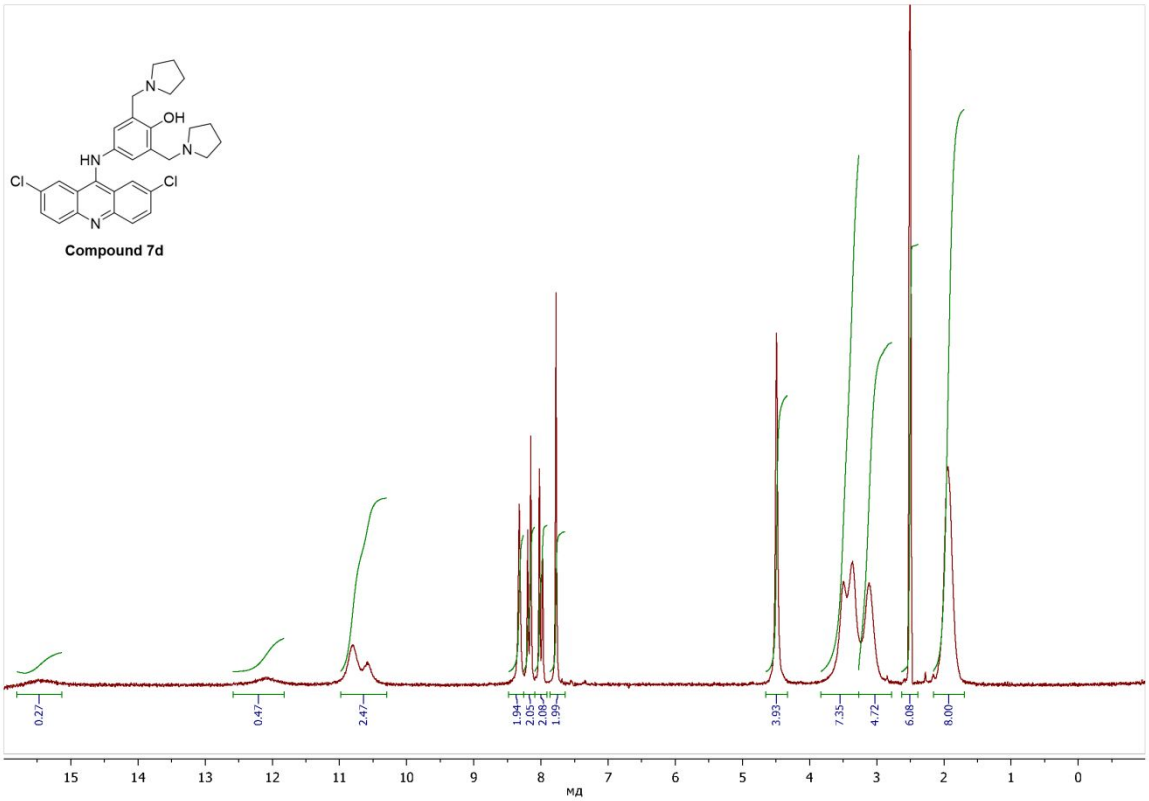


Figure S4. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **7d**.



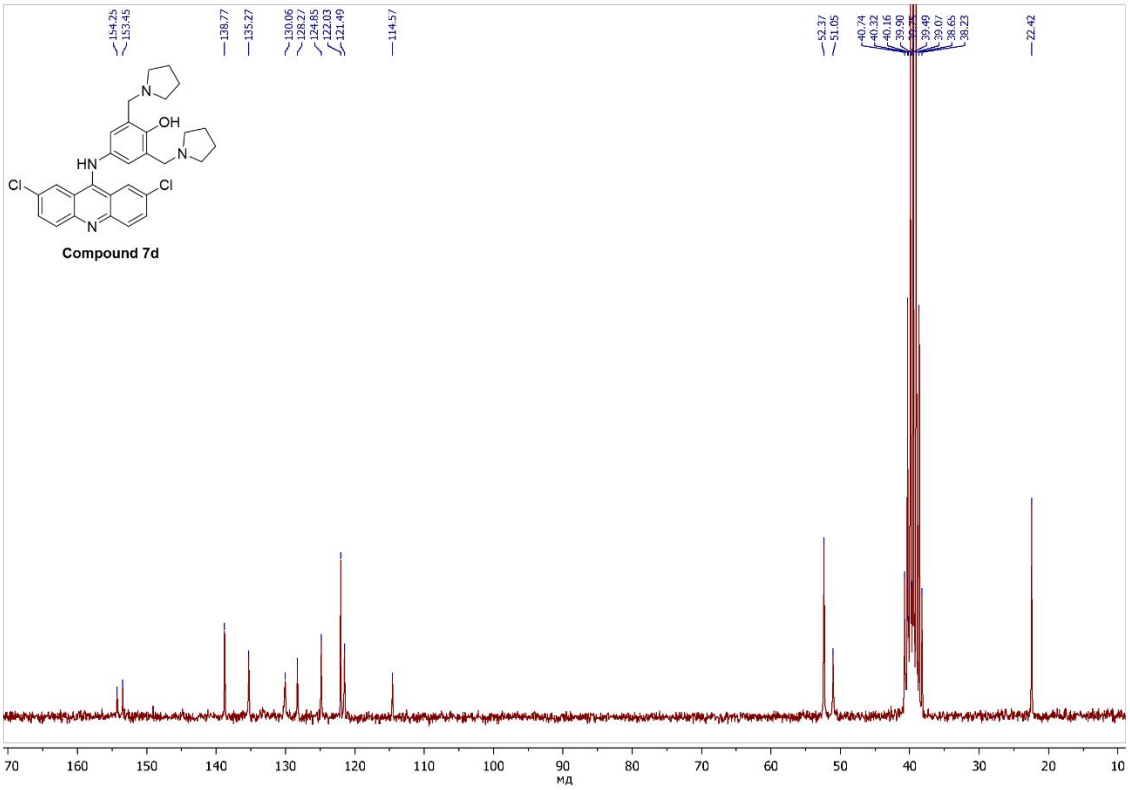
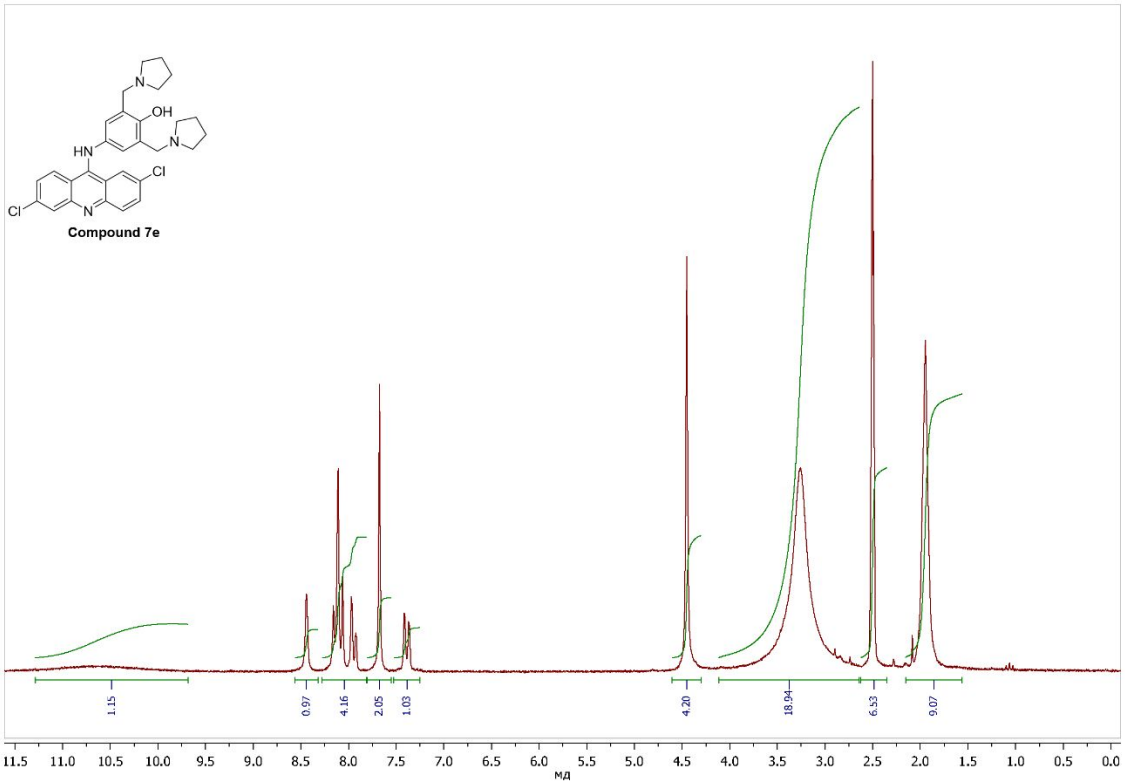


Figure S5. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **7e**.



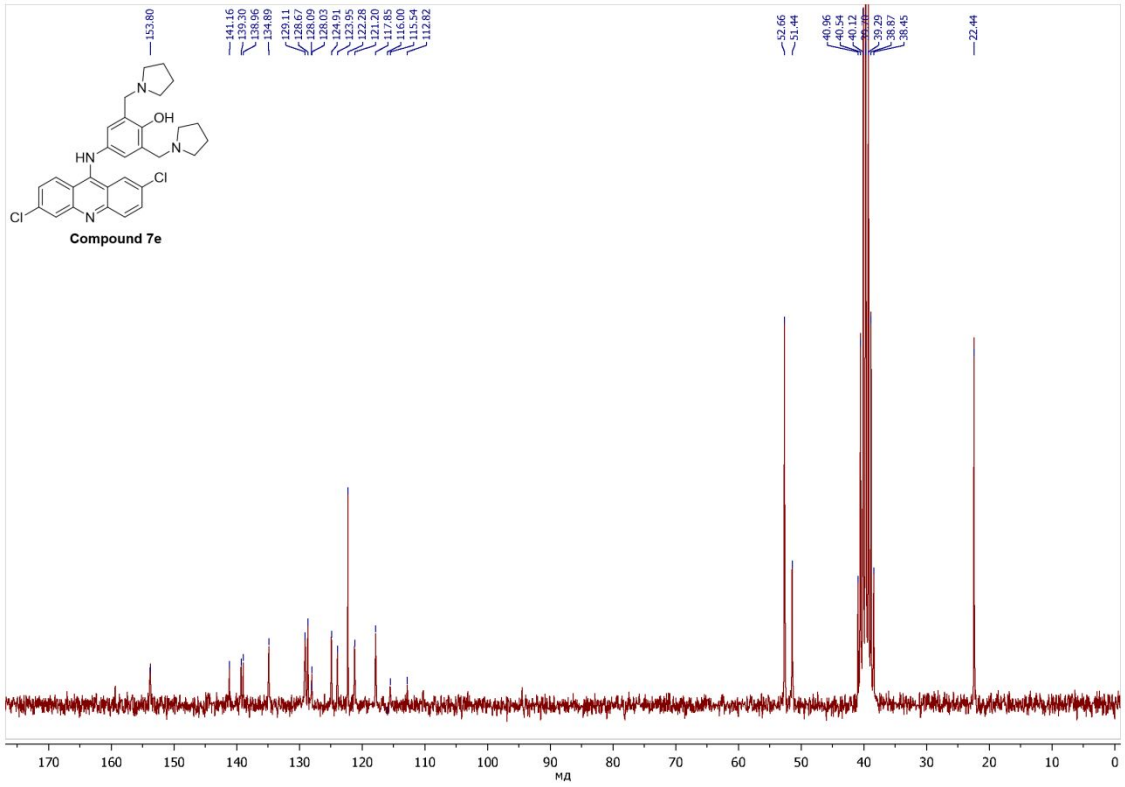
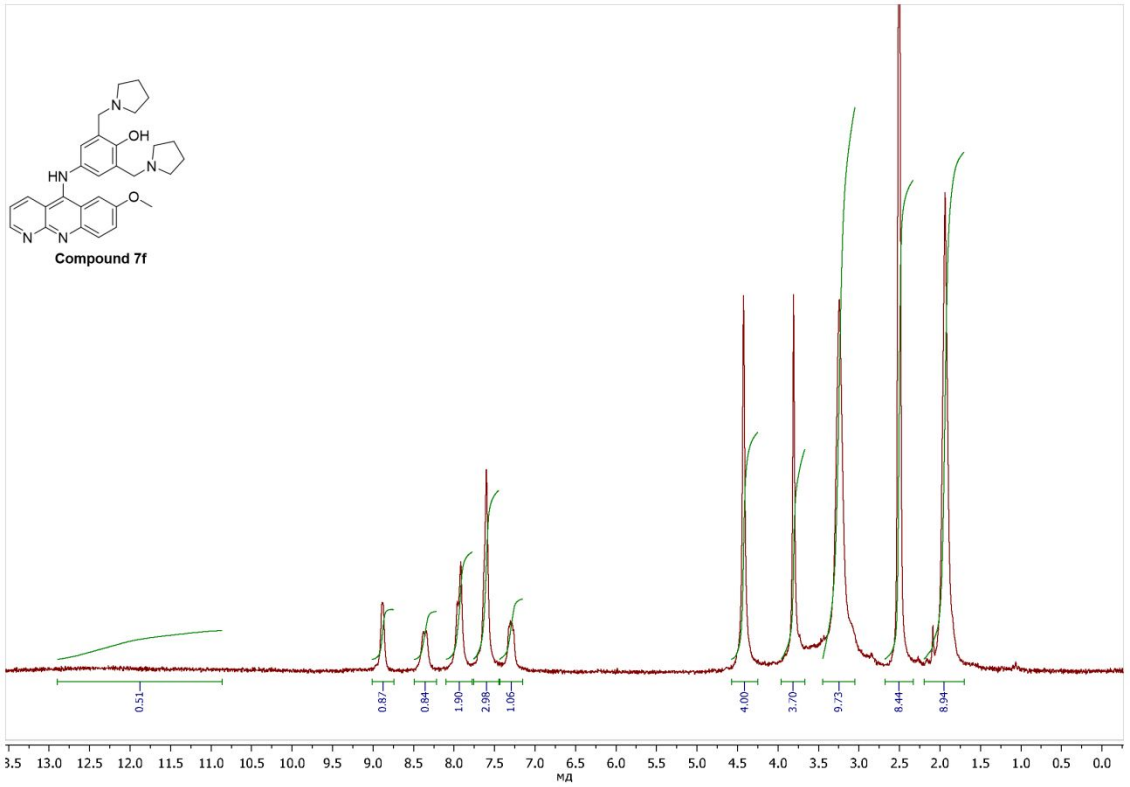


Figure S6. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **7f**.



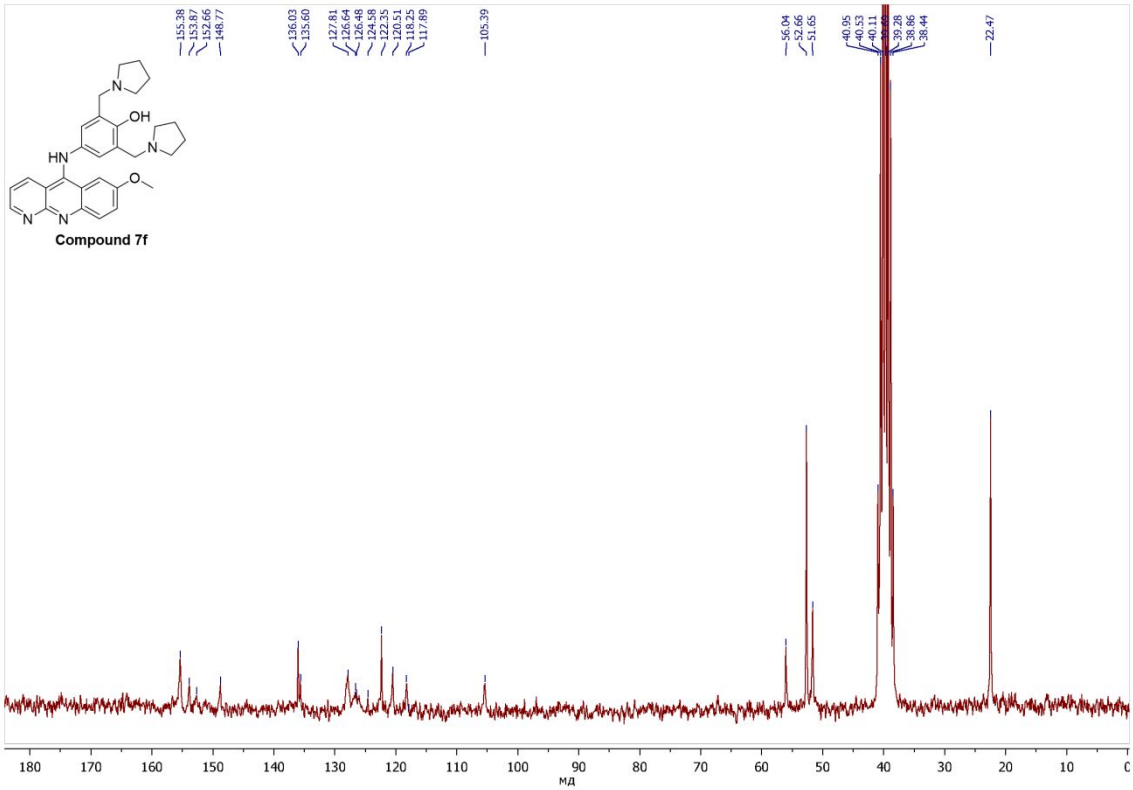


Figure S7. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **8a**.

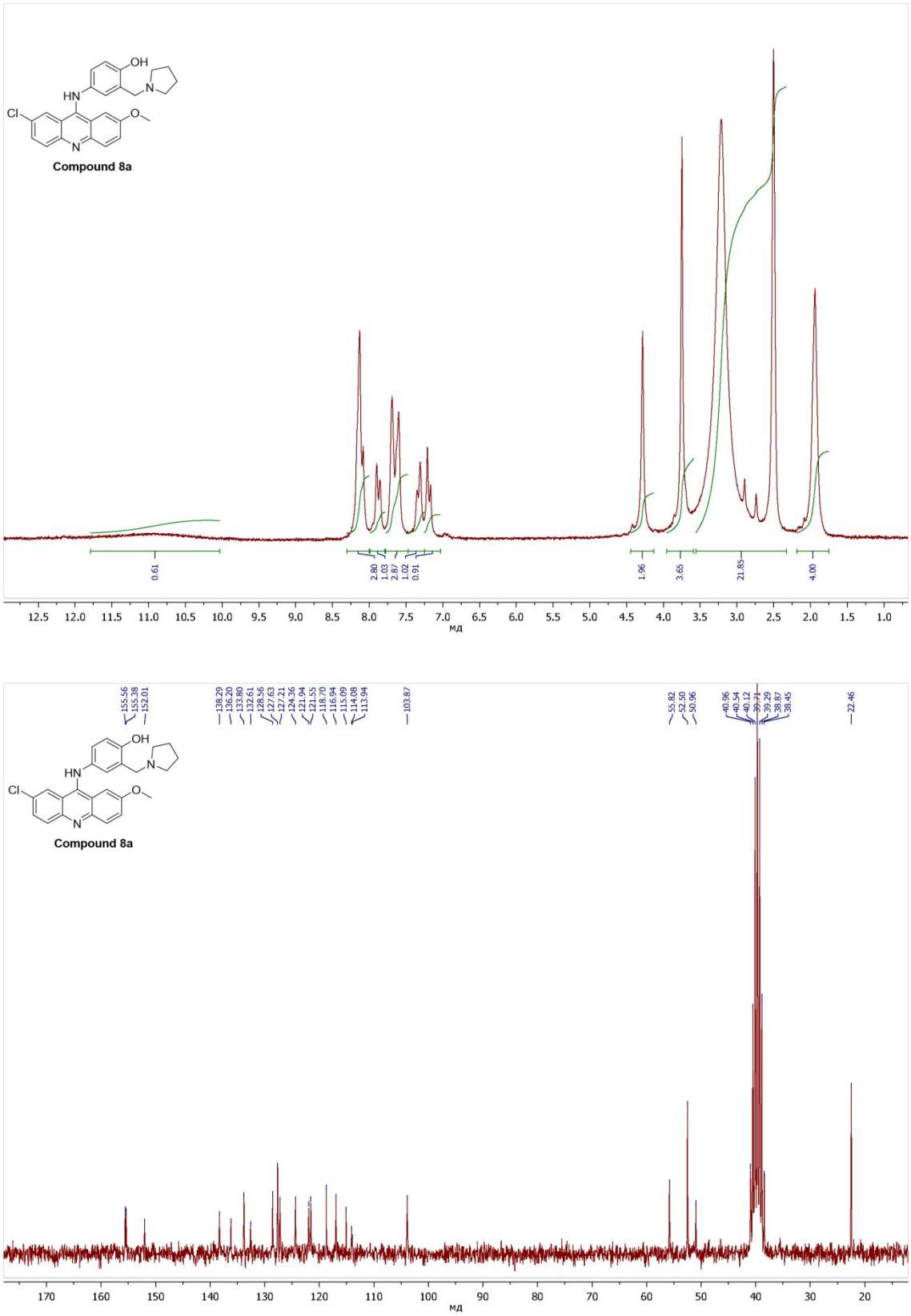
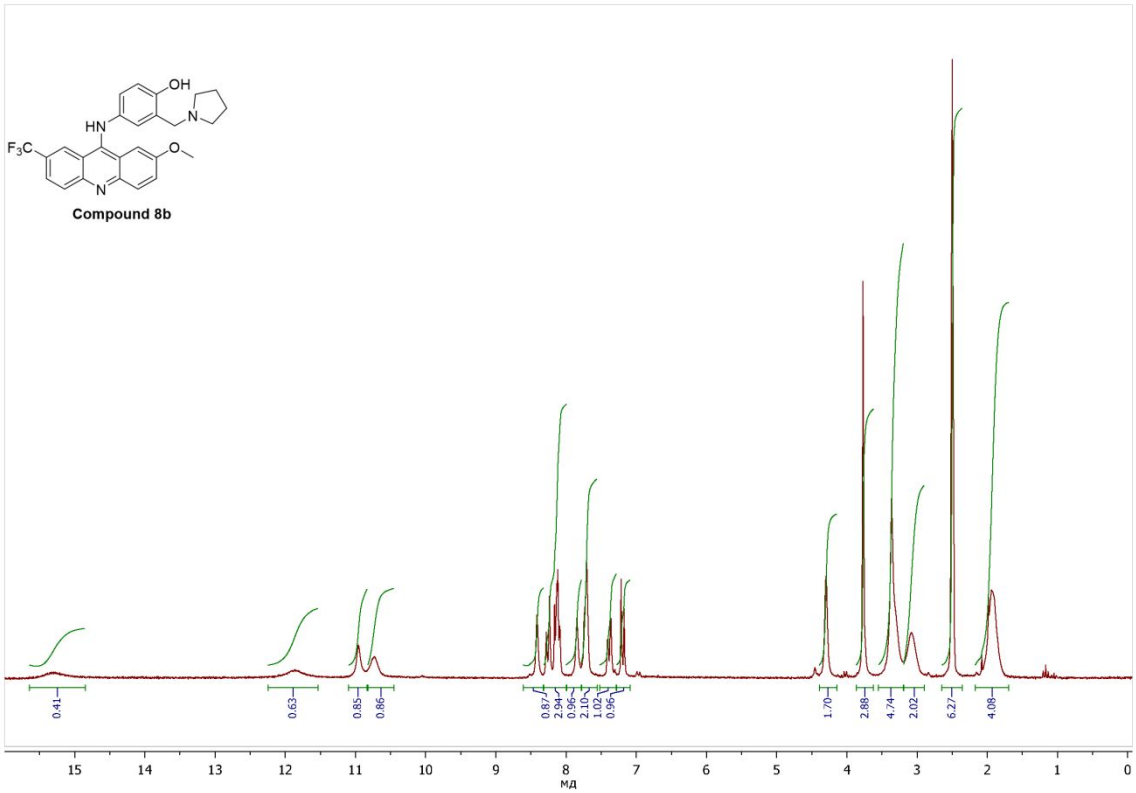


Figure S8. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **8b**.



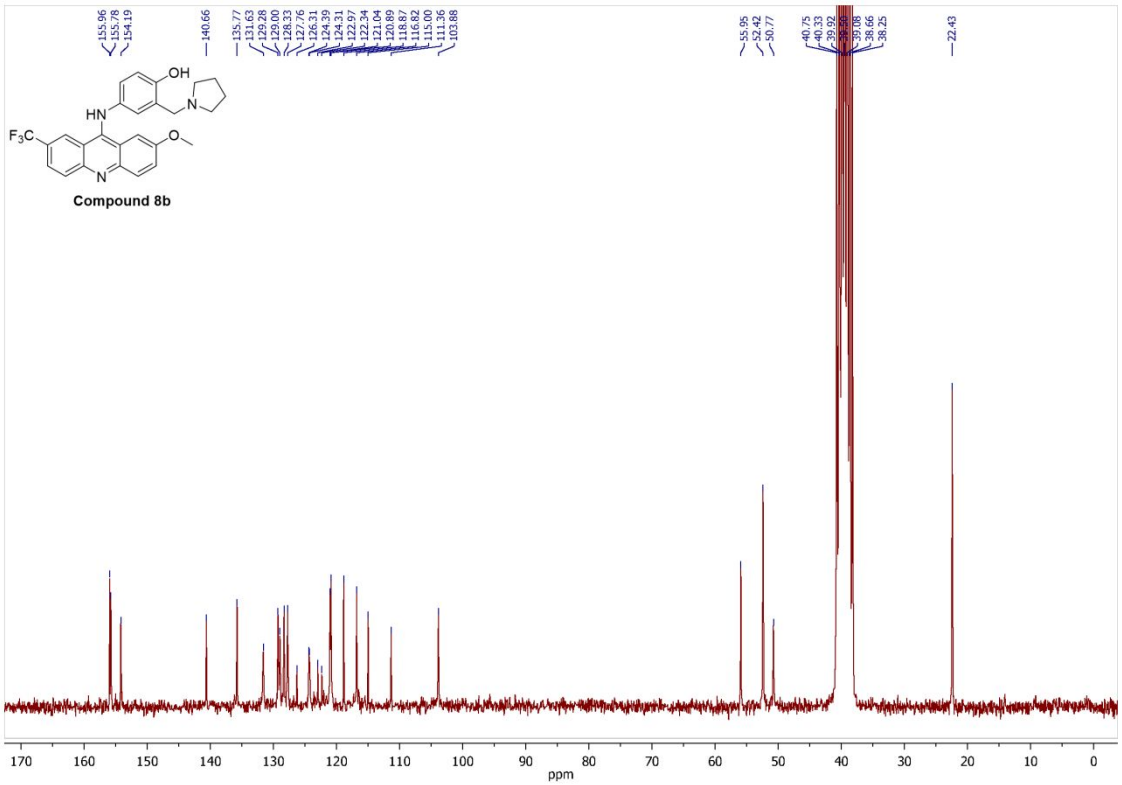


Figure S9. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **8c**.

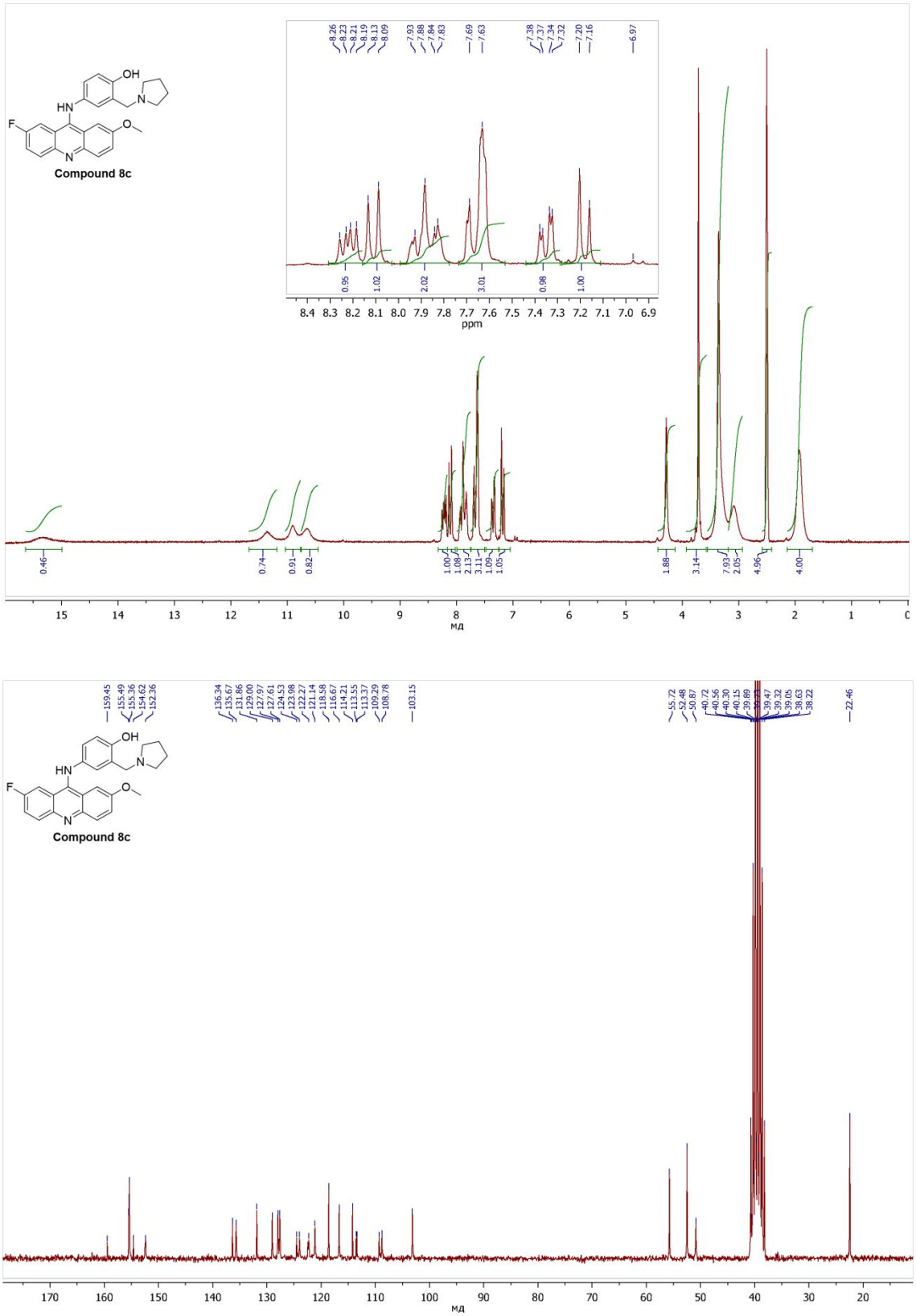
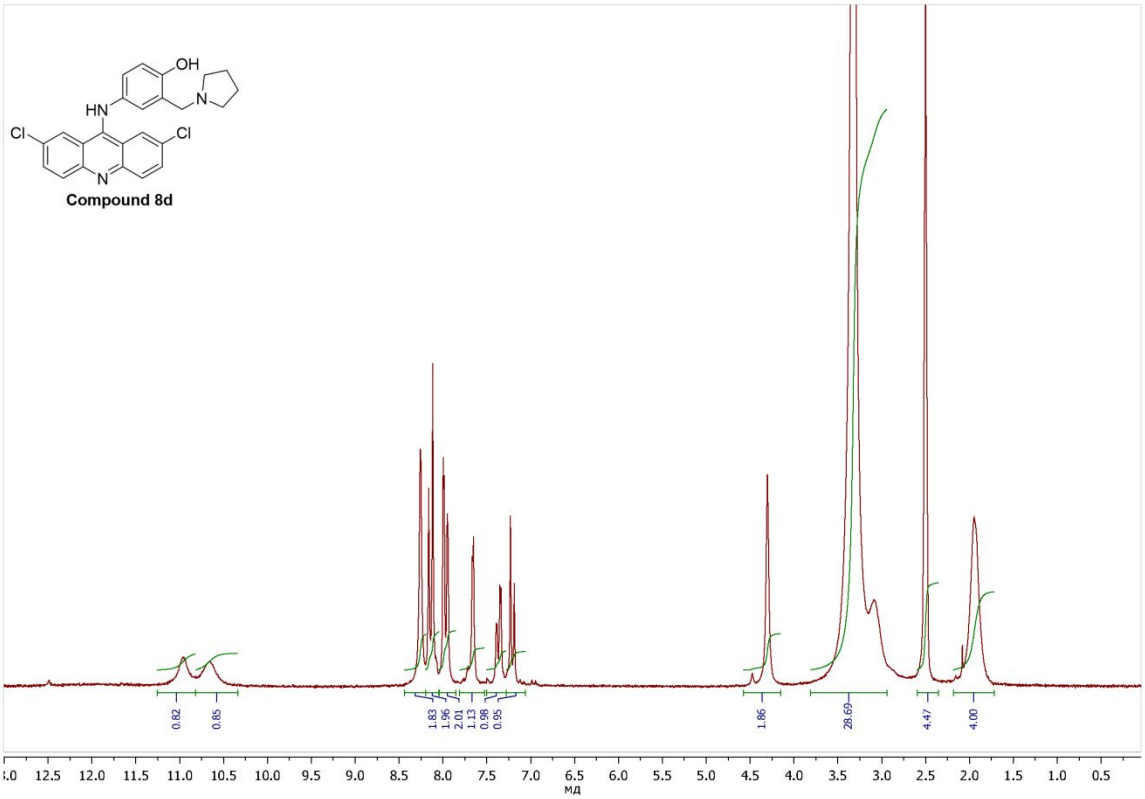


Figure S10. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **8d**.



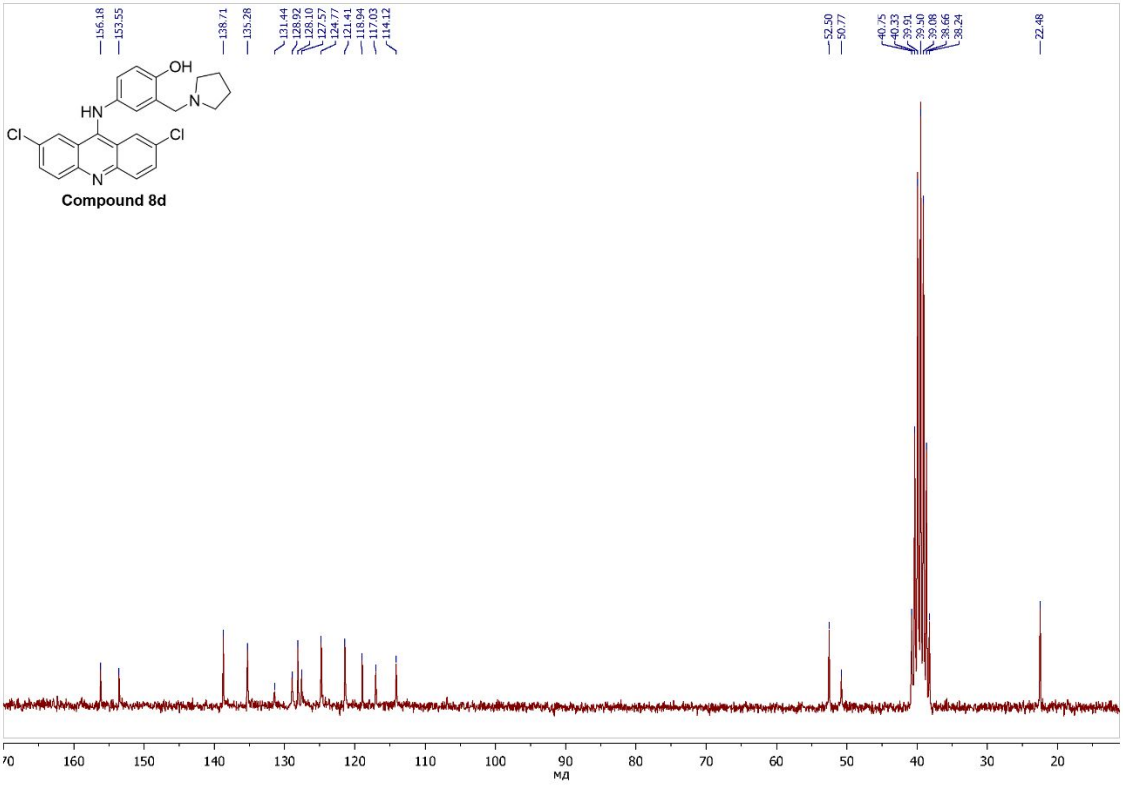


Figure S11. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **8e**.

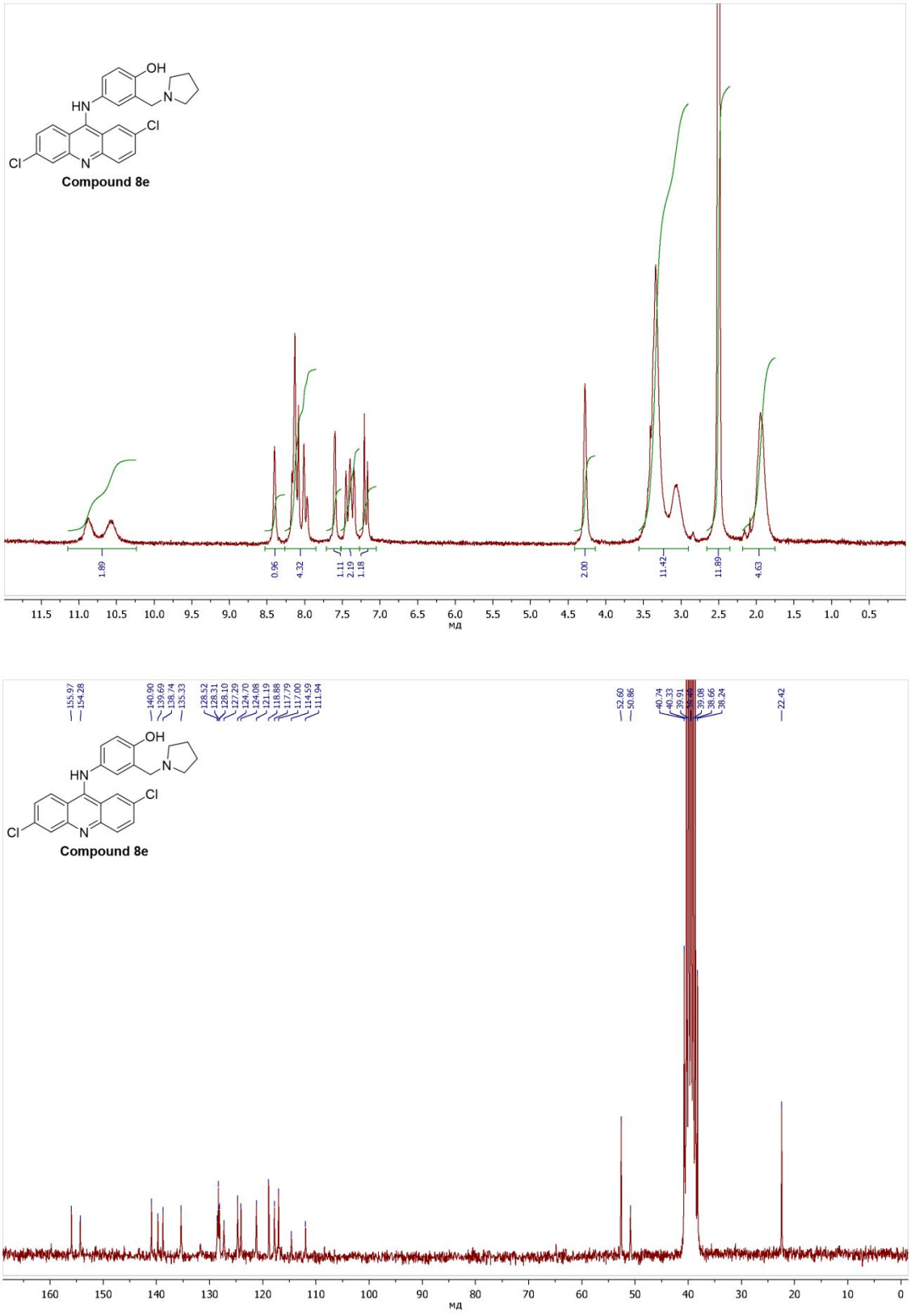
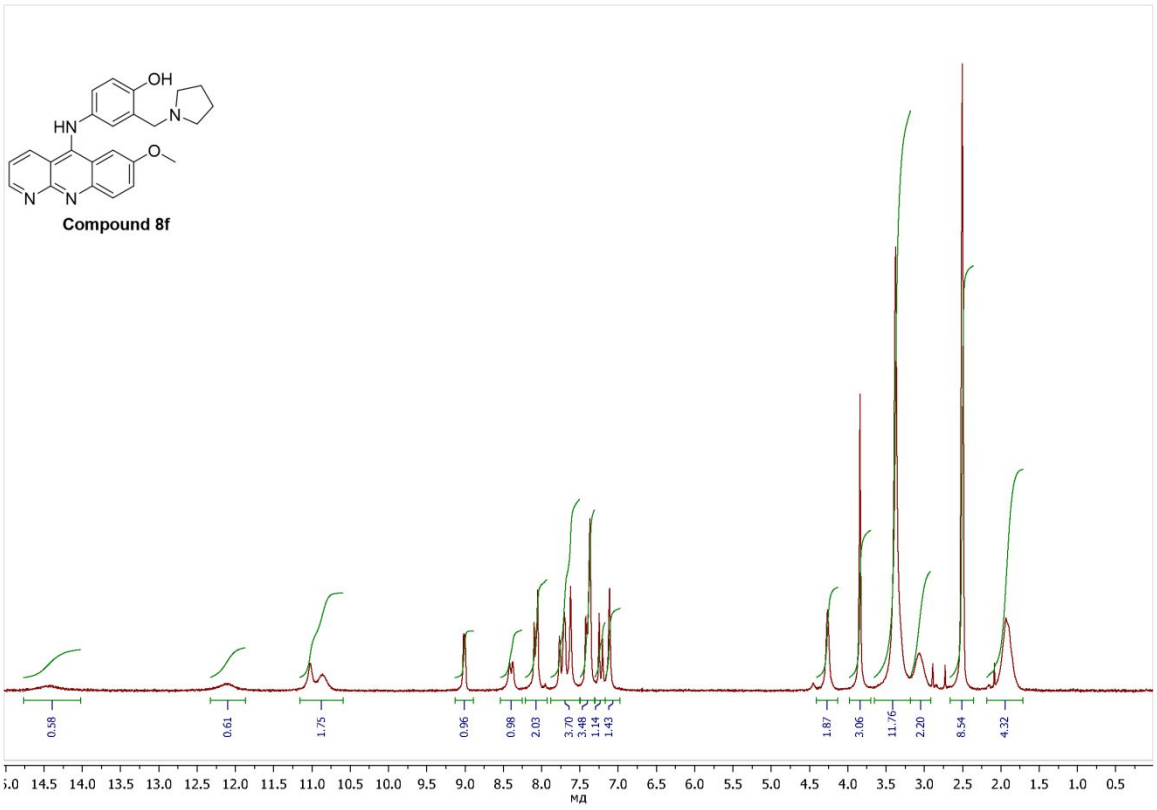


Figure S12. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **8f**.



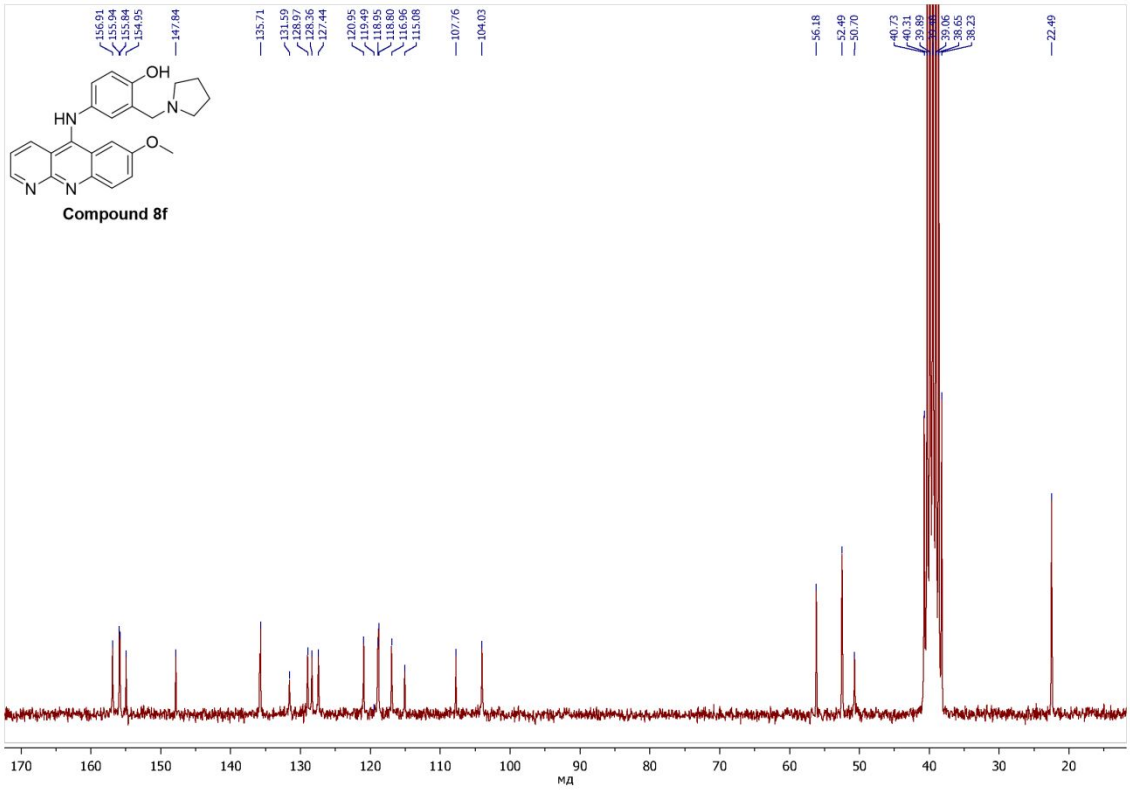


Figure S13. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **9a**.

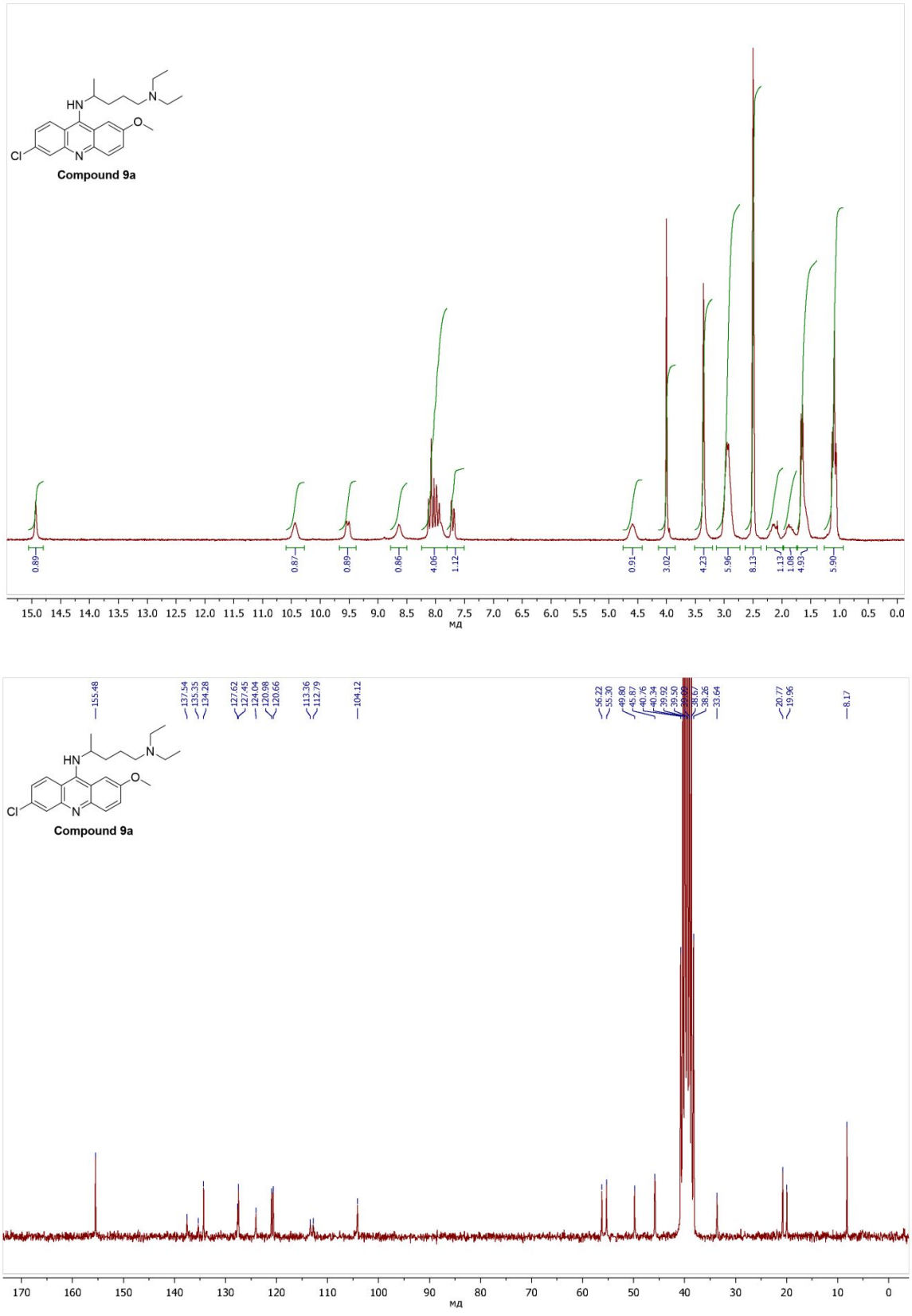


Figure S14. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **9b**.

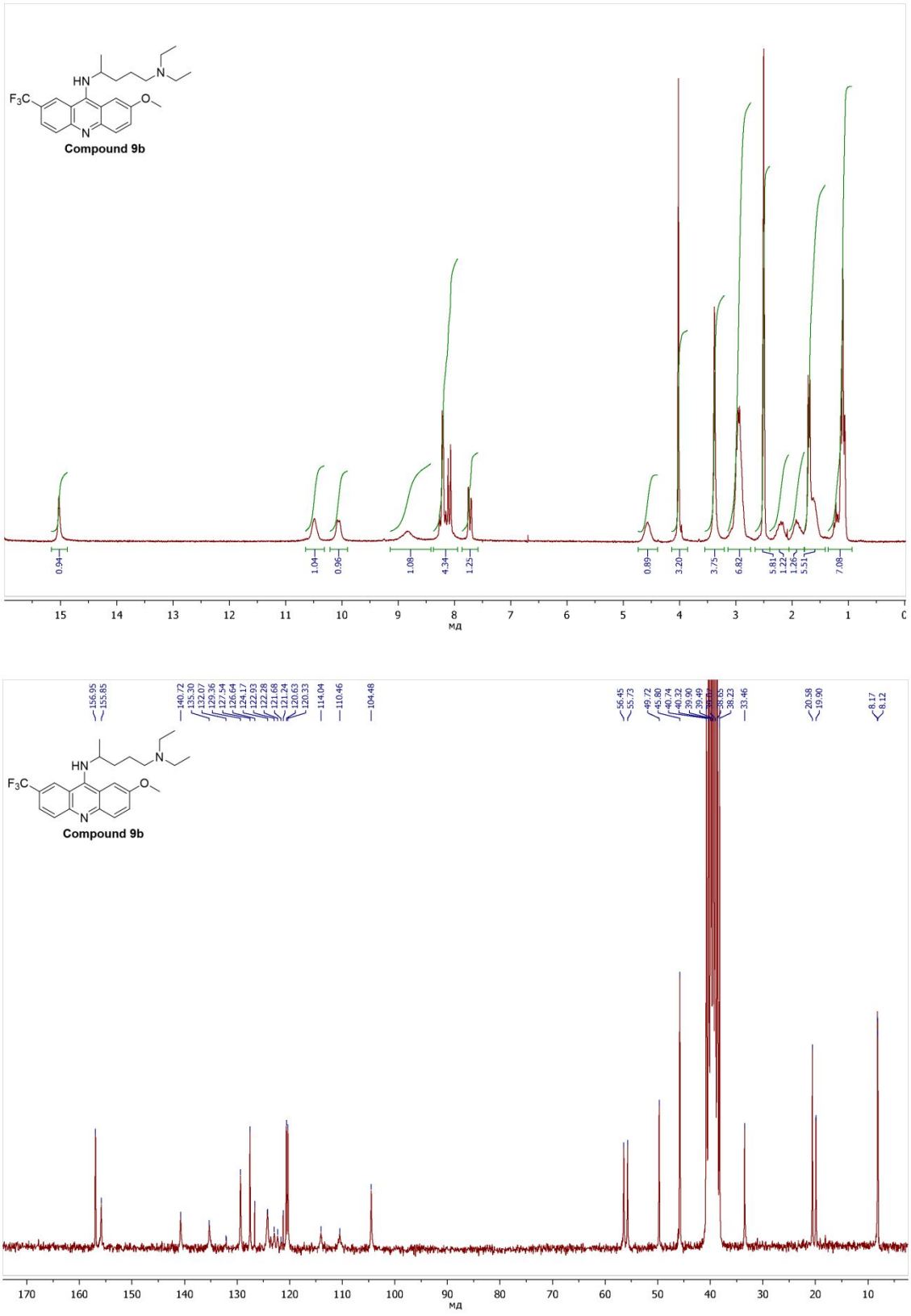


Figure S15. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **9c**.

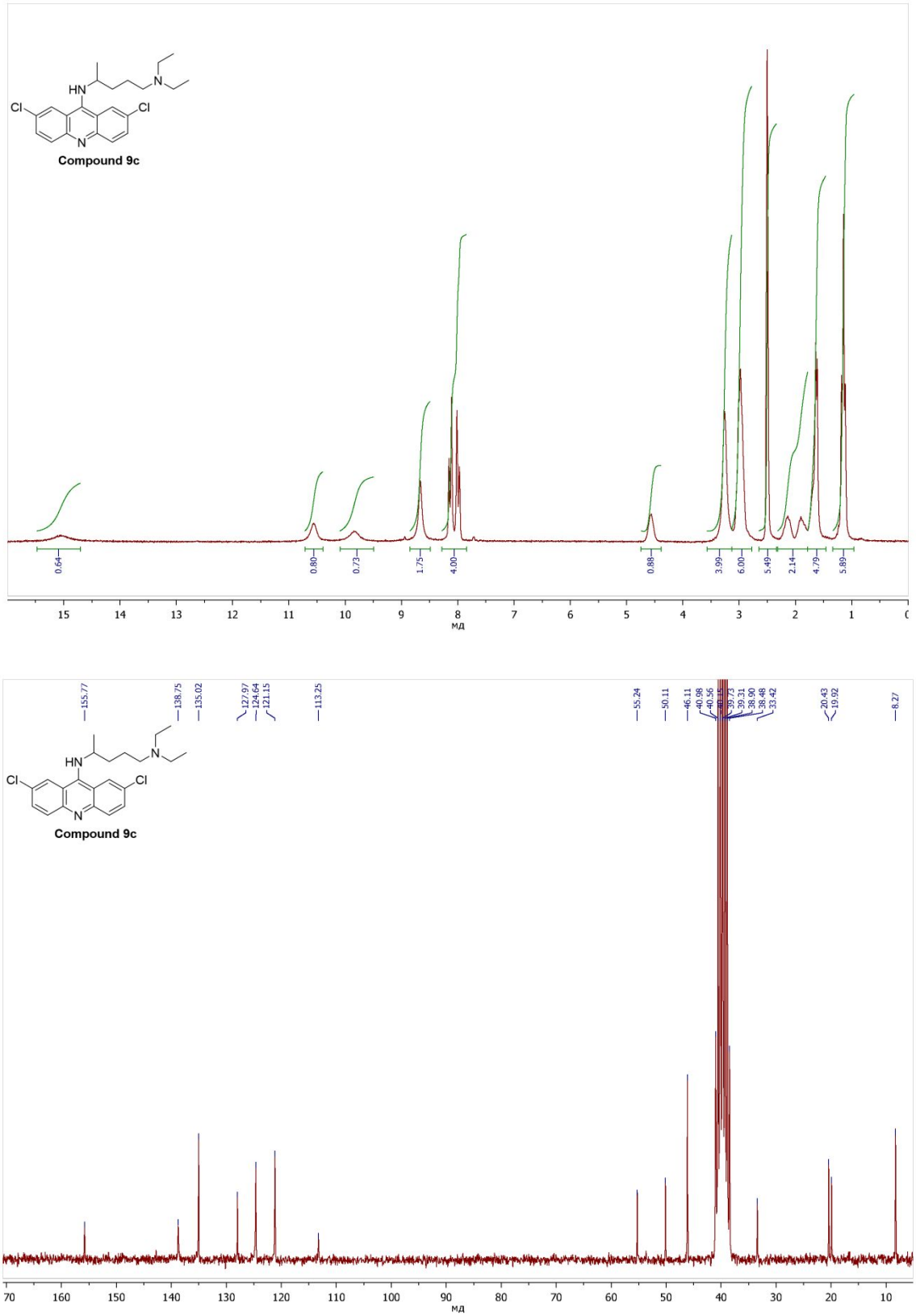
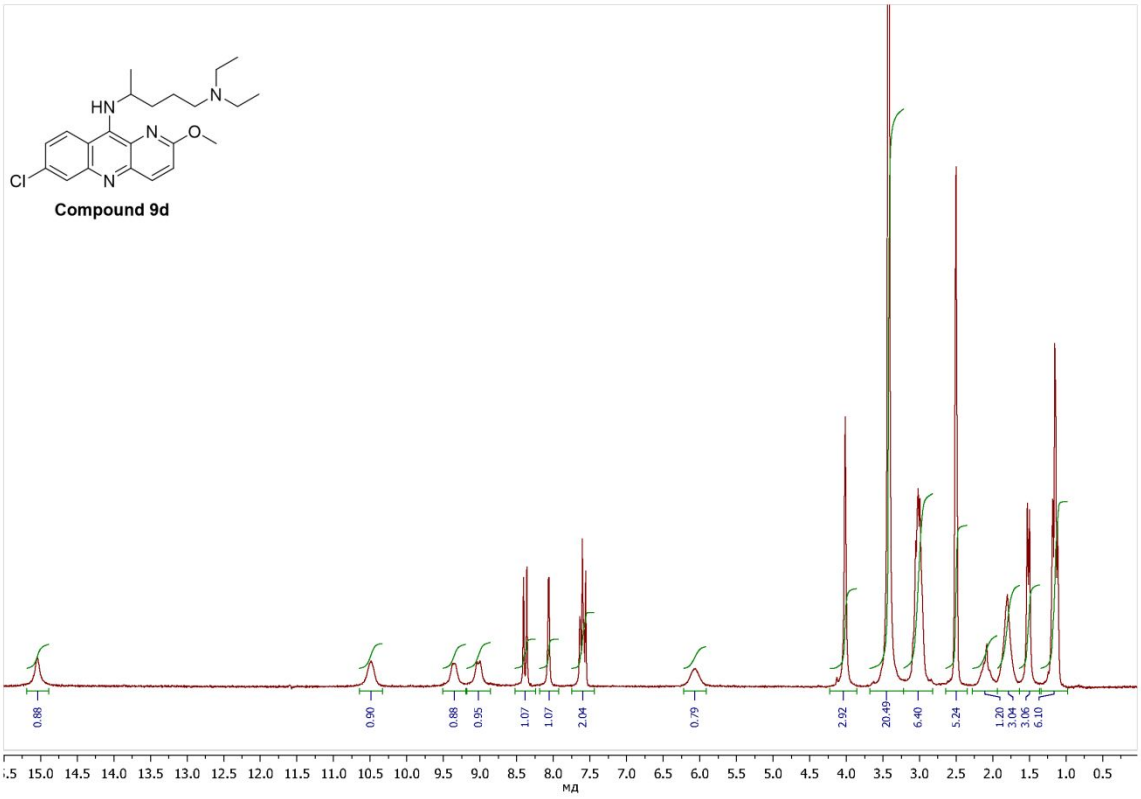


Figure S16. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) and ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of compound **9d**.



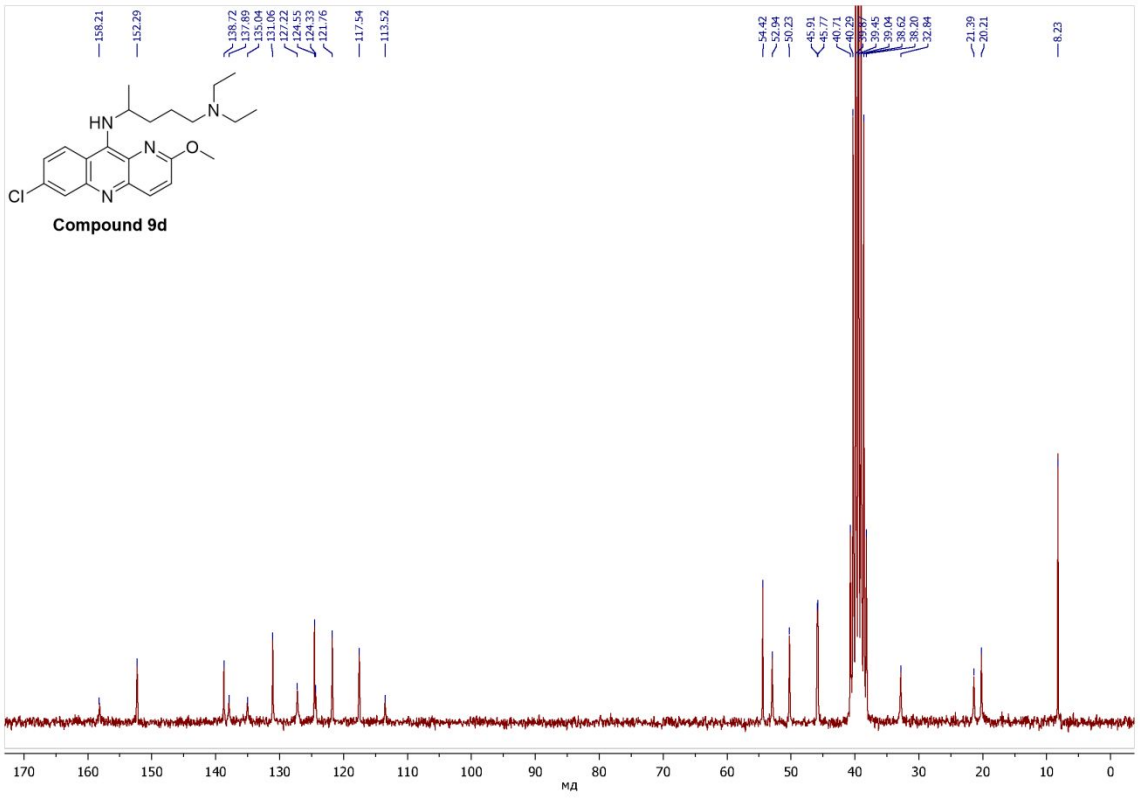
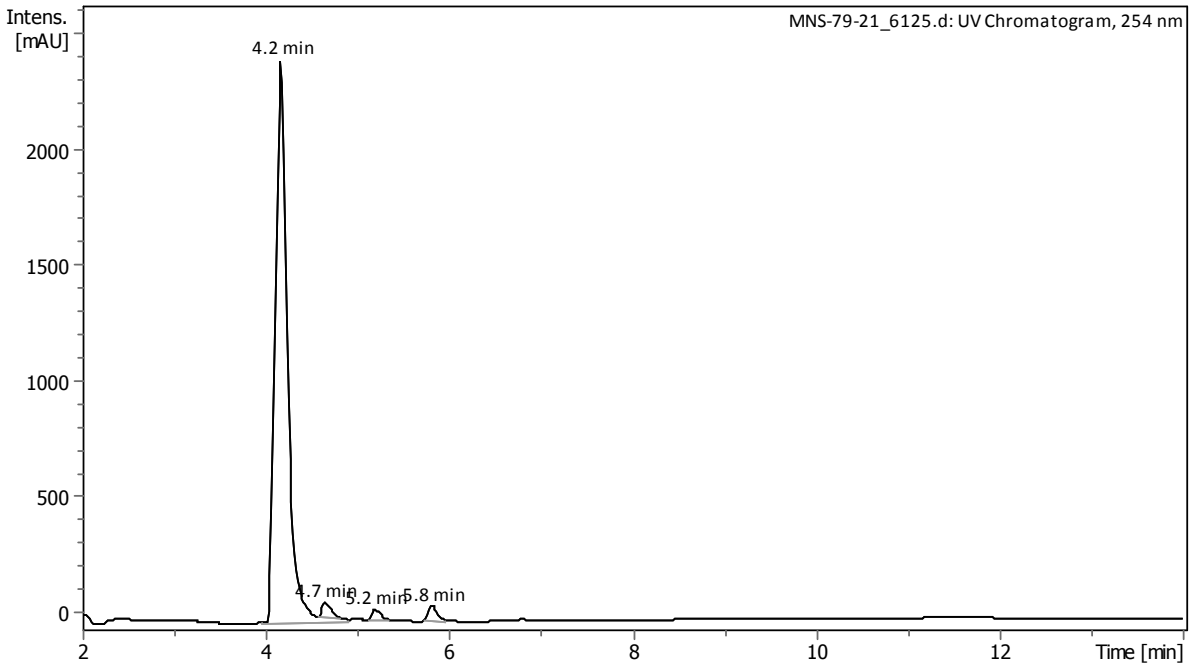
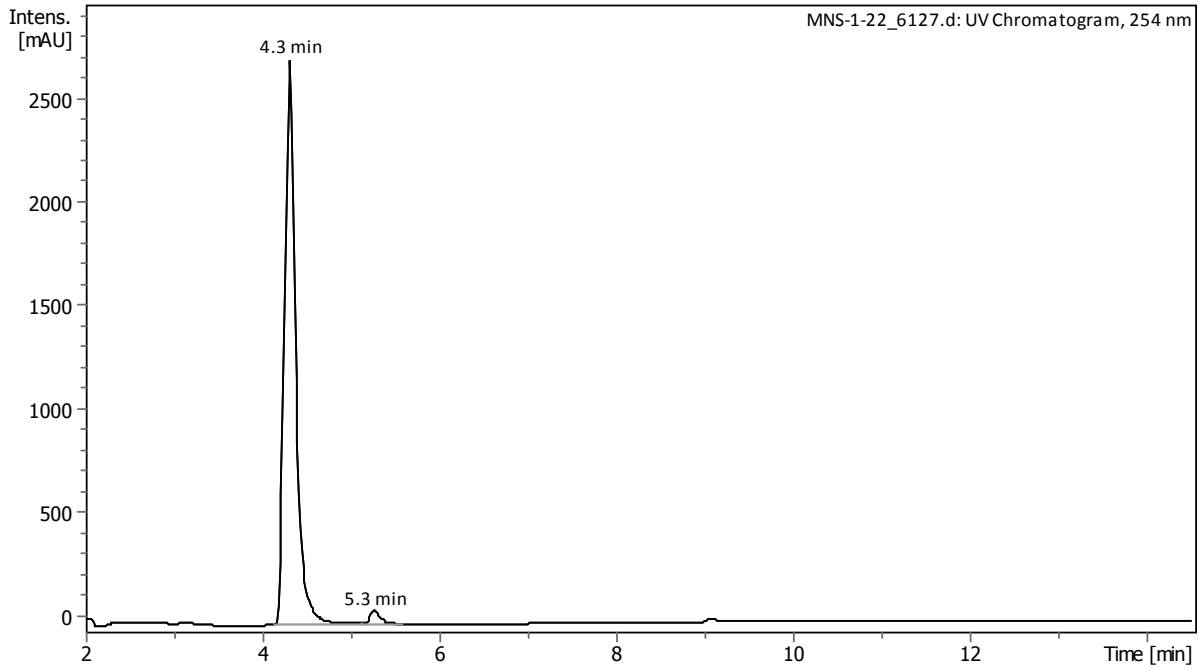


Figure S17. HPLC trace of compound **7a.**



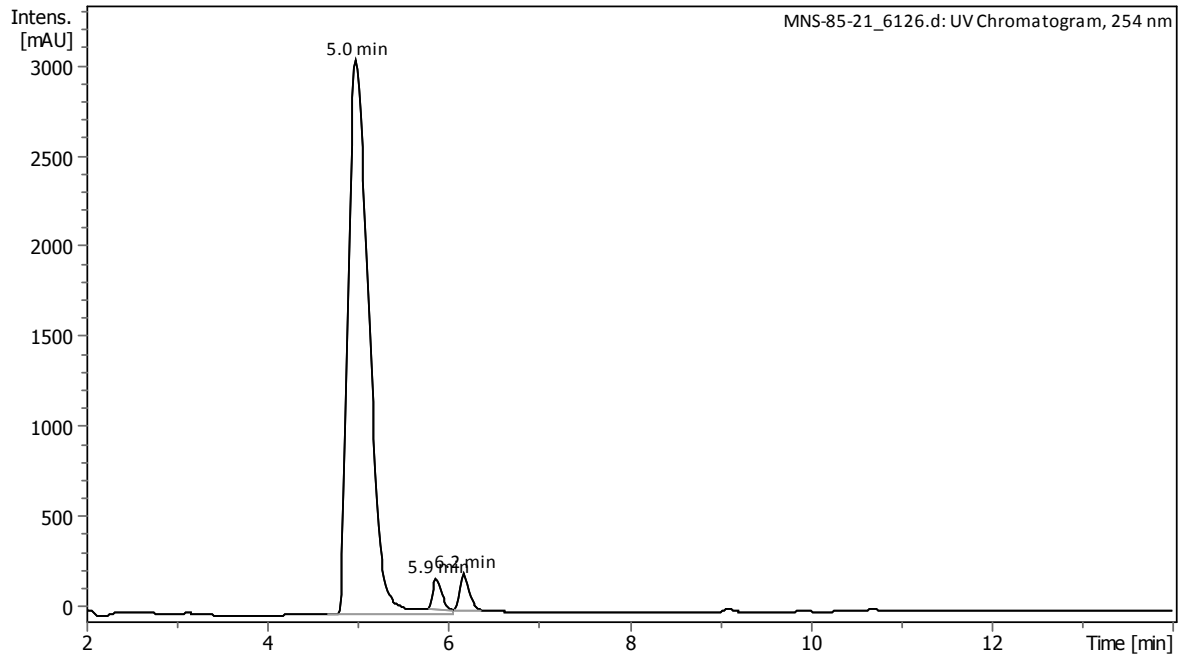
#	RT, min	Area	S/N	Area Total, %
1	4.2	23192.87	45113.7	95.00
2	4.7	420.97	1151.1	1.72
3	5.2	321.76	844.6	1.32
4	5.8	478.45	1235.6	1.96

Figure S18. HPLC trace of compound **7e.**



#	RT, min	Area	S/N	Area Total, %
1	4.3	24151.42	62175.4	97.81
2	5.3	540.97	1491.8	97.81

Figure S19. HPLC trace of compound **9c.**



#	RT, min	Area	S/N	Area Total, %
1	5.0	49913.9	22289.3	95.10
2	5.9	1128.2	1200.8	2.15
3	6.2	1445.8	1491.8	2.75