Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Optimized Quinoline-Based Biofilm Disruptors with Improved Efficacy Against Biofilm Formation in *Vibrio cholerae*

Brian León, F. P. Jake Haeckl, Roger G. Linington*

Department of Chemistry and Biochemistry, University of California, Santa Cruz, 1156 High Street, Santa Cruz, CA 95064, USA.

Table of Contents

Materials and Methods

General Experimental Procedures. All reactions were performed in oven dried glassware under an inert atmosphere of N_2 or Ar. Tetrahydrofuran (THF), toluene (PhMe) and methylene chloride (DCM) were obtained from a Pur-Solv 400 solvent purification system manufactured by Innovative Technology. All reagents were used as purchased without further purification, with the following exceptions: triethylamine was distilled from calcium hydride and stored over sodium hydroxide; oxalyl chloride $(COCl)_2$ was distilled and stored over poly(vinylpyridine). *i*-PrMgCl•LiCl was titrated using I_2 and LiCl.[1] Thin layer chromatography was performed with Merck Silica gel 60 F_{254} and visualized with UV or chemical stain (p-anisaldehyde). Crude reaction mixtures were purified using Silica Gel 60 (230 – 400 mesh ASTM).[2] ^{1}H and ^{13}C NMR spectra were obtained on either 500 or 600 MHz Varian spectrometers equipped with 5 mm broadband and 5 mm HCN triple resonance cryoprobe respectively. ^{1}H and ^{13}C NMR's are referenced to indicated solvent signals. High-resolution mass spectra were obtained on a bench-top Agilent 6230 ESI-TOF-MS. Optical rotation measurements were found on a Jasco P-2000 digital polarimeter. using a 10 mm and 100 mm path length cell at 589 nm. UV Spectra were recorded on a Shimadzu UV-Visible Spectrophotometer (UV-1800) with a path length of 1 cm.

General Suzuki Procedure (GP 1):
To an oven dried 2-neck flask (25 mL) equipped with a stir bar (Ar) was added **SM** (1 eq), $ArB(OH)_2$ (1.3 eq), and Cs_2CO_3 (1.3 eq). A condenser was attached and PhMe (N_2 sparged), EtOH, and H_2O (6.66:1.33:2, 0.025 M) were added. The reaction was degassed using three cycles of the freeze, pump, thaw method. Tetrakis(triphenylphosphine)palladium (0.21 eq) was then added and the biphasic mixture heated to reflux (105 °C) and stirred vigorously for 24 h. Prior to cooling the reaction was a biphasic translucent yellow mixture. Upon cooling to rt the organic layer would turn black. This reaction was partitioned between CH_2Cl_2 (50 mL) and H_2O (50 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried with $MgSO_4$, filtered through a cotton plug, and concentrated *in vacuo*. The crude reaction mixture was next treated with HCl (2M in Et_2O, 23.04 eq). The reaction was then diluted in PhMe and a portion of Et_3N was added slowly and the reaction was concentrated *in vacuo*.

(*R*)-(2-bromoquinolin-4-yl)((*S*)-1-tritylpyrrolidin-2-yl)methanol[3] (7):
To an oven dried vial equipped with a stir bar (N_2) was added 2, 4-dibromoquinoline (5.38 g, 18.74 mmol) which was dissolved in THF (23.5 mL) and taken to –78 °C. Addition of *i*-PrMgCl•LiCl (21.6 mL, 20.62 mmol, 0.96 M in THF) resulted in the formation of a light yellow solution which was allowed to stir at –78 °C for 2 h. Next a solution of **6** (7.68 g, 22.49 mmol) in THF (28.1 mL) was slowly added and the solution was allowed to stir at rt for 12 h. Next the solution was quenched with a saturated NH_4Cl solution and partitioned between CH_2Cl_2 (100 mL) and H_2O (100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried with $MgSO_4$, filtered through a cotton plug, and concentrated *in vacuo*. The residue was purified by flash chromatography (1:9:90, Et_3N:EtOAc:Hex) to afford **11** (4.15 g, 40%) as a white foam. Analytical data matched literature values.

(*R*)-(2-chloroquinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (8):
To a green cap vial equipped with a stir bar (N_2) was added **7** (48.0 mg, 0.087 mmol). This was then dissolved in Et_2O (870 μL) followed by addition of HCl (1.0 mL, 2.01 mmol, 2M in Et_2O). After 12 h the solution was concentrated *in vacuo*. Purification by flash chromatography (Et_3N:MeOH:CH_2Cl_2, 1:5:94) yielded **8** (8.7 mg, 38%) as a colorless film. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.17 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.85 (t, *J* = 7.7 Hz, 1H), 7.77 (s, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 5.91 (d, *J* = 3.0 Hz, 1H), 4.07 (td, *J* = 2.74, 8.2 Hz, 1H), 3.42 – 3.32 (m, 2H), 2.09 – 2.04 (m, 2H), 1.93 – 1.84 (m, 1H), 1.52 – 1.41 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 152.2, 149.1, 132.1, 129.9, 129.0, 125.1, 124.1, 120.6, 111.4, 67.1, 63.8, 47.4, 24.9, 24.0. **HRMS** (ESI): Exact Mass for $C_{14}H_{16}ClN_2O$ [M + H] requires *m/z* 263.0951, found *m/z* 263.0948. **$[\alpha]_D^{26}$:** 61.32 (*c* 0.043, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 236 nm (4.39).

(*R*)-(2-phenylquinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (9):
Prepared according to **GP 1** from **7** (91.5 mg, 0.17 mmol), $ArB(OH)_2$ (26.3 mg, 0.22 mmol), and Cs_2CO_3 (70.3 mg, 0.22 mmol). Next PhMe, EtOH, and H_2O were added (4.4 mL: 880 μL: 1.3 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (404.3 mg, 0.035 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 35:65 to 80:20% MeOH/H_2O + 0.02% formic acid over 14.5 min., 4 mL min^{-1} flow rate). (17.2 mg, 34%) as a colorless film. **^{1}H NMR** (600 MHz, CD_3OD) δ = 8.24 (d, *J*=2.7 Hz, 1H), 8.17 (m, 2H), 8.15 – 8.10 (m, 2H), 7.83 – 7.78 (m, 1H), 7.70 – 7.64 (m, 1H), 7.58 – 7.53 (m, 2H), 7.53 – 7.48 (m, 1H), 5.99 (s, 1H), 4.13 (m, 1H), 3.44 – 3.32 (m, 2H), 2.17 – 2.02 (m, 2H), 1.93 – 1.82 (m, 1H), 1.52 – 1.42 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 158.9, 149.3, 149.1, 149.1, 140.6, 131.1, 130.9, 130.8, 130.0, 128.7, 128.2, 125.3, 123.7, 123.7, 117.5, 67.4, 64.0, 47.3, 24.9, 24.1. **HRMS** (ESI): Exact Mass for $C_{20}H_{21}N_2O$ [M + H]$^+$ requires *m/z* 305.1654, found *m/z* 305.1664. **$[\alpha]_D^{25}$:** -35.59 (*c* 0.094, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 260 nm (4.49).

(*R*)-((*S*)-pyrrolidin-2-yl)(2-(2-(trifluoromethyl)phenyl)quinolin-4-yl)methanol (10)
Prepared according to **GP 1** from **7** (85.4 mg, 0.16 mmol), $ArB(OH)_2$ (39.7 mg, 0.21 mmol), and Cs_2CO_3 (68.1 mg, 0.21 mmol). Next PhMe, EtOH, and H_2O were added (4.1 mL: 830 μL: 1.2 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (37.7 mg, 0.033 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 4.6 mm, 35:65 MeOH/H_2O + 0.02% formic acid over 15 min., 2 mL min^{-1} flow rate). (4.8 mg, 8%) as a colorless film. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.25 – 8.20 (m, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.92 – 7.89 (m, 2H), 7.87 (t, *J* = 7.7 Hz, 1H), 7.82 – 7.73 (m, 2H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 5.99 (s, 1H), 4.08 (t, *J* = 8.3 Hz, 1H), 3.44 – 3.26 (m, 1H), 2.11 – 2.00 (m, 2H), 1.92 – 1.84 (m, 1H), 1.50 – 1.39 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 159.4, 149.1, 148.4, 141.0, 133.3, 132.5, 131.5, 130.5, 130.4, 129.0, 127.5, 127.5, 125.3, 124.7, 123.7, 120.4, 67.1, 64.1, 47.5, 24.9, 24.1. **HRMS** (ESI): Exact Mass for $C_{21}H_{19}F_3N_2O$ [M + H]$^+$ requires *m/z* 373.1527, found *m/z* 373.1540. **$[\alpha]_D^{25}$:** -37.93 (*c* 0.082, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 244 nm (4.63).

(*R*)-((*S*)-pyrrolidin-2-yl)(2-(3-(trifluoromethyl)phenyl)quinolin-4-yl)methanol (11)
Prepared according to **GP 1** from **7** (88.5 mg, 0.16 mmol), $ArB(OH)_2$ (39.8 mg, 0.21 mmol), and Cs_2CO_3 (68.2 mg, 0.21 mmol). Next PhMe, EtOH, and H_2O were added (4.3 mL: 860 μL: 1.3 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (39.1 mg, 0.034 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 4.6 mm, 46:54 MeOH/H_2O + 0.02% formic acid over 15 min., 2 mL min^{-1} flow rate). (4.4 mg, 7%) as a white solid. **^{1}H NMR** (600 MHz,

CD_3OD) δ 8.53 – 8.50 (m, 1H), 8.45 (d, *J* = 7.7 Hz, 1H), 8.31 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.88 – 7.81 (m, 2H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 5.98 (d, *J* = 3.5 Hz, 1H), 4.12 (td, *J* = 3.0, 8.5, 9.2 Hz, 1H), 3.44 – 3.36 (m, 1H), 3.36 – 3.32 (m, 1H), 2.13 – 2.04 (m, 1H), 1.94 – 1.83 (m, 1H), 1.56 – 1.46 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 156.8, 149.6, 149.5, 141.5, 132.3, 132.2, 131.4, 131.4, 130.9, 128.7, 127.2, 125.6, 125.2, 125.2, 123.7, 116.9, 67.6, 64.1, 47.5, 25.0, 24.3. **HRMS** (ESI): Exact Mass for $C_{21}H_{19}F_3N_2O$ $[M + H]^+$ requires *m/z* 373.1527, found *m/z* 373.1539. **$[\alpha]_D^{26}$:** -24.30 (*c* 0.061, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 260 nm (4.45).

(*R*)-(2-(4-nitrophenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (12)
Prepared according to **GP 1** from **7** (101.8 mg, 0.19 mmol), $ArB(OH)_2$ (40.2 mg, 0.24 mmol), and Cs_2CO_3 (78.4 mg, 0.24 mmol). Next PhMe, EtOH, and H_2O were added (4.9 mL: 1.0 mL: 1.5 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (44.9 mg, 0.038 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 60:40 to 95:5% MeOH/H_2O + 0.02% formic acid over 10 min., 4 mL min^{-1} flow rate). (19.1 mg, 30%) as a yellow solid. **^{1}H NMR** (600 MHz, $(CD_3)_2SO$) δ 8.54 (d, *J* = 8.5 Hz, 2H), 8.42 (d, *J* = 8.6 Hz, 2H), 8.36 – 8.29 (m, 2H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 5.72 (s, 1H), 3.86 – 3.74 (m, 1H), 3.12 – 3.05 (m, 1H), 3.05 – 2.97 (m, 1H), 1.98 – 1.88 (m, 1H), 1.88 – 1.79 (m, 1H), 1.72 – 1.62 (m, 1H), 1.50 – 1.39 (m, 1H). **^{13}C NMR** (151 MHz, $(CD_3)_2SO$) δ 153.5, 149.9, 148.0, 147.7, 144.7, 130.2, 130.0, 128.4, 127.3, 124.7, 124.1, 123.8, 116.0, 67.7, 62.5, 45.8, 24.4, 24.3. **HRMS** (ESI): Exact Mass for $C_{20}H_{20}N_3O_3$ $[M + H]^+$ requires *m/z* 350.1504, found *m/z* 350.1513. **$[\alpha]_D^{25}$:** Insufficient Solubility. **UV:** Insufficient Solubility.

(*R*)-((*S*)-pyrrolidin-2-yl)(2-(4-(trifluoromethyl)phenyl)quinolin-4-yl)methanol (4)
Prepared according to **GP 1** from **7** (101.8 mg, 0.19 mmol), $ArB(OH)_2$ (40.2 mg, 0.24 mmol), and Cs_2CO_3 (78.4 mg, 0.24 mmol). Next PhMe, EtOH, and H_2O were added (4.9 mL: 1.0 mL: 1.5 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (44.9 mg, 0.038 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 60:40 to 95:5% MeOH/H_2O + 0.02% formic acid over 10 min., 4 mL min^{-1} flow rate). (19.1 mg, 30%) as a yellow solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.36 (d, J = 8.5 Hz, 2H), 8.29 (s, 1H), 8.23 – 8.16 (m, 2H), 7.85 (d, J = 8.7 Hz, 2H), 7.81 (ddd, J = 1.3, 6.8, 8.2 Hz, 1H), 7.70 – 7.66 (m, 1H), 5.86 (d, J = 3.5 Hz, 1H), 3.90 (td, J = 3.47, 8.1 Hz, 1H), 3.31 – 3.24 (m, 1H), 3.14 (ddd, J = 5.8, 8.1, 11.0 Hz, 1H), 2.07 – 1.94 (m, 3H), 1.85 – 1.76 (m, 1H), 1.50 – 1.42 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 156.9, 150.5, 149.4, 144.3, 131.2, 131.2, 129.3, 129.3, 128.5, 126.8, 126.8, 126.8, 126.8, 125.9, 124.0, 117.2, 68.8, 64.2, 47.6, 25.6, 24.9. **HRMS** (ESI): Exact Mass for $C_{21}H_{20}F_3N_2O$ $[M + H]^+$ requires *m/z* 373.1527, found *m/z* 373.1537. **$[\alpha]_D^{24}$:** -31.192 (*c* 0.075, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 258 nm (4.73).

(*R*)-((*S*)-pyrrolidin-2-yl)(2-(*p*-tolyl)quinolin-4-yl)methanol (13)
Prepared according to **GP 1** from **7** (87.5 mg, 0.16 mmol), $ArB(OH)_2$ (28.1 mg, 0.21 mmol), and Cs_2CO_3 (67.4 mg, 0.21 mmol). Next PhMe, EtOH, and H_2O were added (4.2 mL: 850 μL: 1.4 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (38.6 mg, 0.033 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 4.6 mm, 31:69 MeOH/H_2O + 0.02% formic acid over 15 min., 2 mL min^{-1} flow rate). (8.9 mg, 18%) as a white solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.22 (s, 1H), 8.16 (dd, *J* = 6.9, 8.8 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.80 (t, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 5.94 (d, *J* = 3.2 Hz, 1H), 4.08 (t, *J* = 7.8 Hz, 1H), 3.42 – 3.35 (m, 1H), 3.35 – 3.32 (m, 1H), 2.44 (s, 3H), 2.16 – 2.01 (m, 3H), 1.91 – 1.83 (m, 1H), 1.52 –

1.45 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 158.9, 149.3, 149.1, 141.2, 137.8, 131.1, 130.8, 130.6, 129.3, 128.7, 128.0, 125.3, 123.7, 123.6, 117.3, 67.6, 64.1, 47.4, 25.0, 24.3, 21.4. **HRMS** (ESI): Exact Mass for $C_{21}H_{23}N_2O$ $[M + H]^+$ requires *m/z* 319.1810, found *m/z* 319.1807. **$[\alpha]_D^{24}$:** -41.19 (*c* 0.071, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 268 nm (4.54).

(*R*)-(2-(4-fluorophenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (14)
Prepared according to **GP 1** from **7** (101.9 mg, 0.19 mmol), $ArB(OH)_2$ (33.7 mg, 0.24 mmol), and Cs_2CO_3 (78.5 mg, 0.24 mmol). Next PhMe, EtOH, and H_2O were added (4.9 mL: 980 μL: 1.6 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium (45.0 mg, 0.038 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 60:40 to 95:5% MeOH/H_2O + 0.02% formic acid over 10 min., 4 mL min^{-1} flow rate). (46.9 mg, 79%) as a white solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.58 – 8.52 (m, 1H), 8.48 (s, 1H), 8.44 – 8.38 (m, 1H), 8.27 – 8.20 (m, 2H), 8.15 (t, *J* = 7.5 Hz, 1H), 8.02 – 7.97 (m, 1H), 7.48 (t, *J* = 8.3 Hz, 2H), 6.17 (s, 1H), 4.23 – 4.14 (m, 1H), 3.47 – 3.34 (m, 2H), 2.18 – 2.06 (m, 2H), 1.97 – 1.85 (m, 1H), 1.62 – 1.50 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 167.9, 166.2, 158.5, 155.8, 135.5, 133.1, 133.0, 131.1, 130.2, 125.8, 124.0, 119.7, 118.1, 117.9, 111.4, 67.7, 64.1, 47.5, 24.8, 24.1. **HRMS** (ESI): Exact Mass for $C_{20}H_{20}FN_2O$ $[M + H]^+$ requires *m/z* 323.1559, found *m/z* 323.1559. **$[\alpha]_D^{26}$:** -8.51 (*c* 0.032, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 262 nm (4.05).

(*R*)-(2-(4-(pentafluorosulfanyl)phenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (15)
Prepared according to **GP 1** from **7** (93.8 mg, 0.17 mmol), $ArB(OH)_2$ (55.0 mg, 0.22 mmol), and Cs_2CO_3 (72.3 mg, 0.22 mmol). Next PhMe, EtOH, and H_2O were added (4.6 mL: 910 μL: 1.4 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 40.4 mg, 0.035 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 65:35 to 95:5% MeOH/H_2O + 0.02% formic acid over 10.5 min., 4 mL min^{-1} flow rate). (17.5 mg, 24%) as a white solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.37 (d, *J* = 8.2 Hz, 2H), 8.31 (s, 1H), 8.21 – 8.15 (m, 2H), 8.00 (dd, *J* = 2.50, 8.8 Hz, 2H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 5.97 (d, *J* = 3.2 Hz, 1H), 4.14 – 4.08 (m, 1H), 3.41 – 3.30 (m, 2H), 2.17 – 2.00 (m, 2H), 1.92 – 1.82 (m, 1H), 1.51 – 1.42 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 156.2, 149.6, 149.5, 143.9, 131.4, 131.4, 129.2, 128.9, 127.7, 127.7, 127.6, 127.6, 125.7, 123.7, 117.1, 67.5, 64.0, 47.4, 25.0, 24.2. **HRMS** (ESI): Exact Mass for $C_{20}H_{20}F_5N_2OS$ $[M + H]^+$ requires *m/z* 431.1216, found *m/z* 431.1227. **$[\alpha]_D^{26}$:** -41.47 (*c* 0.044, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 258 nm (4.63).

(*R*)-(2-(4-chlorophenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (16)
Prepared according to **GP 1** from **7** (91.7 mg, 0.17 mmol), $ArB(OH)_2$ (33.9 mg, 0.22 mmol), and Cs_2CO_3 (70.8 mg, 0.22 mmol). Next PhMe, EtOH, and H_2O were added (4.5 mL: 890 μL: 1.3 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 40.5 mg, 0.035 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 60:40 to 95:5% MeOH/H_2O + 0.02% formic acid over 11 min., 4 mL min^{-1} flow rate). (6.4 mg, 12%) as a colorless solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.25 (s, 1H), 8.22 – 8.13 (m, 4H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 2H), 5.95 (s, 1H), 4.08 (t, *J* = 8.1 Hz, 1H), 3.50 – 3.31 (m, 1H), 3.30 – 3.13 (m, 1H), 2.14 – 2.03 (m, 2H), 1.93 – 1.82 (m, 1H), 1.53 – 1.44 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 157.5, 149.4, 139.2, 137.0, 133.1, 133.0, 131.2, 131.1, 130.2, 130.1, 130.1, 128.4, 125.4, 123.6, 117.0, 67.7, 64.1, 47.5, 25.0, 24.3. **HRMS** (ESI): Exact Mass for $C_{20}H_{20}ClN_2O$ [M +

H]$^+$ requires *m/z* 339.1264, found *m/z* 339.1264. **[α]$_D^{25}$:** -31.68 (*c* 0.075, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 266 nm (4.39).

(*R*)-(2-(2,4-bis(trifluoromethyl)phenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (17)
Prepared according to **GP 1** from **7** (103.2 mg, 0.19 mmol), $ArB(OH)_2$ (62.9 mg, 0.24 mmol), and Cs_2CO_3 (79.5 mg, 0.24 mmol). Next PhMe, EtOH, and H_2O were added (5.0 mL: 1.0 mL: 1.5 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 45.1 mg, 0.04 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 70:30 to 95:5% MeOH/H_2O + 0.02% formic acid over 10 min., 4 mL min^{-1} flow rate). (23.4 mg, 28%) as a colorless film. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.27 (d, *J* = 8.4 Hz, 1H), 8.18 (s, 1H), 8.14 (t, *J* = 8.3 Hz, 2H), 7.95 (s, 1H), 7.90 – 7.86 (m, 2H), 7.79 (t, *J* = 7.5 Hz, 1H), 6.05 (s, 1H), 4.16 (t, *J* = 7.8 Hz, 1H), 3.44 – 3.31 (m, 2H), 2.16 – 2.03 (m, 2H), 1.96 – 1.82 (m, 1H), 1.51 – 1.39 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 157.8, 149.5, 148.5, 144.8, 133.9, 131.7, 130.7, 130.5, 130.2, 130.2, 129.3, 125.7, 125.5, 124.6, 123.9, 123.9, 119.9, 66.9, 64.0, 47.3, 24.9, 24.0. **HRMS** (ESI): Exact Mass for $C_{22}H_{19}F_6N_2O$ [M + H]$^+$ requires *m/z* 441.1401, found *m/z* 441.1395. **[α]$_D^{24}$:** -77.56 (*c* 0.03, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 252 nm (4.43).

(*R*)-(2-(2,4-dimethylphenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (18)
Prepared according to **GP 1** from **7** (99.2 mg, 0.18 mmol), $ArB(OH)_2$ (35.2 mg, 0.23 mmol), and Cs_2CO_3 (76.5 mg, 0.23 mmol). Next PhMe, EtOH, and H_2O were added (4.8 mL: 970 μL: 1.6 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 43.9 mg, 0.04 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 4.6 mm, 31:69 MeOH/H_2O + 0.02% formic acid over 15 min., 2 mL min^{-1} flow rate). (17.4 mg, 29%) as a white solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.20 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.82 (t, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.34 (dd, *J* = 2.80, 7.7 Hz, 1H), 7.18 (s, 1H), 7.18 – 7.12 (m, 1H), 5.98 (s, 1H), 4.12 (dt, *J* = 4.0, 8.6 Hz, 1H), 3.42 – 3.31 (m, 2H), 2.39 (s, 3H), 2.32 (s, 3H), 2.16 – 2.01 (m, 2H), 1.94 – 1.80 (m, 1H), 1.53 – 1.40 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 161.7, 148.9, 148.7, 140.1, 138.8, 136.9, 132.5, 131.2, 130.5, 130.2, 128.4, 127.8, 124.9, 123.8, 120.9, 67.2, 64.0, 47.3, 25.0, 24.2, 21.3, 20.4. **HRMS** (ESI): Exact Mass for $C_{22}H_{25}N_2O$ [M + H]$^+$ requires *m/z* 333.1967, found *m/z* 333.1976. **[α]$_D^{25}$:** -39.72 (*c* 0.07, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 264 nm (4.16).

(*R*)-(2-(2,4-difluorophenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (19)
Prepared according to **GP 1** from **7** (97.1 mg, 0.18 mmol), $ArB(OH)_2$ (36.3 mg, 0.23 mmol), and Cs_2CO_3 (74.9 mg, 0.23 mmol). Next PhMe, EtOH, and H_2O were added (4.7 mL: 940 μL: 1.6 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 42.9 mg, 0.037 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 60:40 to 95:5% MeOH/H_2O + 0.02% formic acid over 8.5 min., 4 mL min^{-1} flow rate). (18.5 mg, 31%) as a white solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.22 – 8.15 (m, 3H), 8.10 – 8.02 (m, 1H), 7.83 (t, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.22 – 7.13 (m, 2H), 6.00 (s, 1H), 4.12 (t, *J* = 8.7 Hz, 1H), 3.45 – 3.33 (m, 2H), 2.17 – 2.03 (m, 2H), 1.94 – 1.84 (m, 1H), 1.52 – 1.43 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 165.2 (dd, *J* = 12.17, 250.65 Hz), 162.3 (dd, *J* = 12.12, 251.78 Hz), 154.5 (d, *J* = 2.01 Hz), 149.3 , 148.9 , 133.9 (dd, *J* = 4.25, 9.85 Hz), 131.2 , 130.9 , 128.7 , 125.3 , 123.7 , 120.4 (d, *J* = 7.34 Hz), 113.1 (dd, *J* = 3.69, 21.63 Hz), 111.4 , 105.4 (t, *J* = 26.43 Hz), 67.1 , 64.0 , 47.4 , 24.9 , 24.0. **HRMS** (ESI): Exact Mass for $C_{20}H_{19}F_2N_2O$ [M + H]$^+$ requires *m/z* 341.1465, found *m/z* 341.1469. **[α]$_D^{25}$:** -53.44 (*c* 0.09, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 254 nm (4.33).

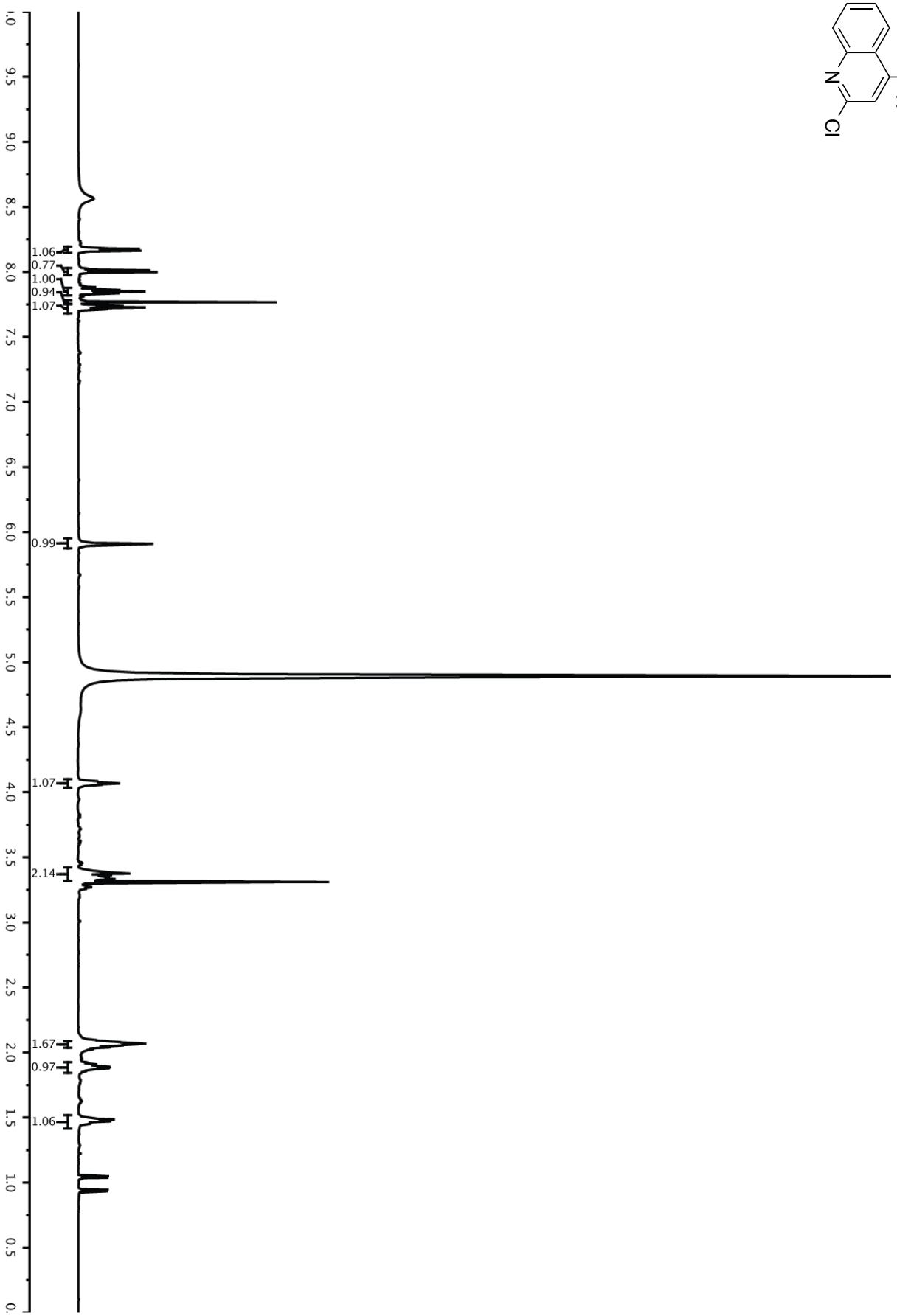
(*R*)-(2-(3-(pentafluorosulfanyl)phenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (20)
Prepared according to **GP 1** from **7** (96.4 mg, 0.18 mmol), $ArB(OH)_2$ (56.5 mg, 0.23 mmol), and Cs_2CO_3 (74.3 mg, 0.23 mmol). Next PhMe, EtOH, and H_2O were added (4.7 mL: 930 μL: 1.4 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 42.5 mg, 0.037 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 65:35 to 95:5% MeOH/H_2O + 0.02% formic acid over 10.5 min., 4 mL min^{-1} flow rate). (14.3 mg, 19%) as a white solid. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.69 (t, *J* = 2.0 Hz, 1H), 8.42 (d, *J* = 7.7 Hz, 1H), 8.31 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.97 (dd, *J* = 2.3, 8.2 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.74 – 7.69 (m, 1H), 6.00 (d, *J* = 3.2 Hz, 1H), 4.15 (td, *J* = 3.1, 8.5, 9.0 Hz, 1H), 3.45 – 3.34 (m, 2H), 2.19 – 2.05 (m, 2H), 1.95 – 1.85 (m, 1H), 1.55 – 1.44 (m, 1H).
^{13}C NMR (151 MHz, CD_3OD) δ 156.2, 149.6, 149.5, 141.7, 131.9, 131.4 (d, *J* = 7.22 Hz), 130.9, 129.3, 128.8, 128.6, 128.0 (m), 126.0 (m), 125.7, 123.7, 116.8, 67.5, 64.0, 47.4, 24.9, 24.2. **HRMS** (ESI): Exact Mass for $C_{20}H_{20}F_5N_2OS$ $[M + H]^+$ requires *m/z* 431.1216, found *m/z* 431.1213. **$[\alpha]_D^{26}$:** -23.38 (*c* 0.06, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 256 nm (4.46).

(*R*)-(2-(2,4-dichlorophenyl)quinolin-4-yl)((*S*)-pyrrolidin-2-yl)methanol (21)
Prepared according to **GP 1** from **7** (92.2 mg, 0.17 mmol), $ArB(OH)_2$ (41.6 mg, 0.22 mmol), and Cs_2CO_3 (71.0 mg, 0.22 mmol). Next PhMe, EtOH, and H_2O were added (4.5 mL: 890 μL: 1.4 mL, 0.025 M) followed by tetrakis(triphenylphosphine) palladium 40.7 mg, 0.035 mmol). **RP-HPLC** (Phenomenex Synergi Fusion-RP 10 micron, 80 Å, 250 x 10 mm, 57:43 to 80:20% MeOH/H_2O + 0.02% formic acid over 14.5 min., 4 mL min^{-1} flow rate). (8.8 mg, 16%) as a colorless film. **^{1}H NMR** (600 MHz, CD_3OD) δ 8.22 (dd, *J* = 1.4, 8.6 Hz, 1H), 8.18 (dd, *J* = 1.2, 8.6 Hz, 1H), 8.08 (d, *J* = 1.0 Hz, 1H), 7.89 (ddd, *J* = 1.3, 6.9, 8.4 Hz, 1H), 7.78 (ddd, *J* = 1.3, 6.9, 8.3 Hz, 1H), 7.70 (d, *J* = 2.0 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 1H), 7.56 (dd, *J* = 2.1, 8.3 Hz, 1H), 6.01 (d, *J* = 2.8 Hz, 1H), 4.15 (ddd, *J* = 3.0, 7.7, 9.3 Hz, 1H), 3.45 – 3.36 (m, 2H), 2.17 – 2.06 (m, 2H), 1.96 – 1.85 (m, 1H), 1.57 – 1.47 (m, 1H). **^{13}C NMR** (151 MHz, CD_3OD) δ 157.5, 148.5, 138.8, 137.0, 134.4, 133.8, 131.8, 130.9, 130.3, 129.3, 128.9, 125.4, 123.7, 121.0, 111.4, 67.0, 64.2, 47.5, 24.8, 24.0. **HRMS** (ESI): Exact Mass for $C_{20}H_{19}Cl_2N_2O$ $[M + H]^+$ requires *m/z* 373.0874, found *m/z* 373.0873. **$[\alpha]_D^{26}$:** -34.91 (*c* 0.05, $CHCl_3$). **UV:** ($CHCl_3$) λ_{max} (log ε) 258 nm (4.16).

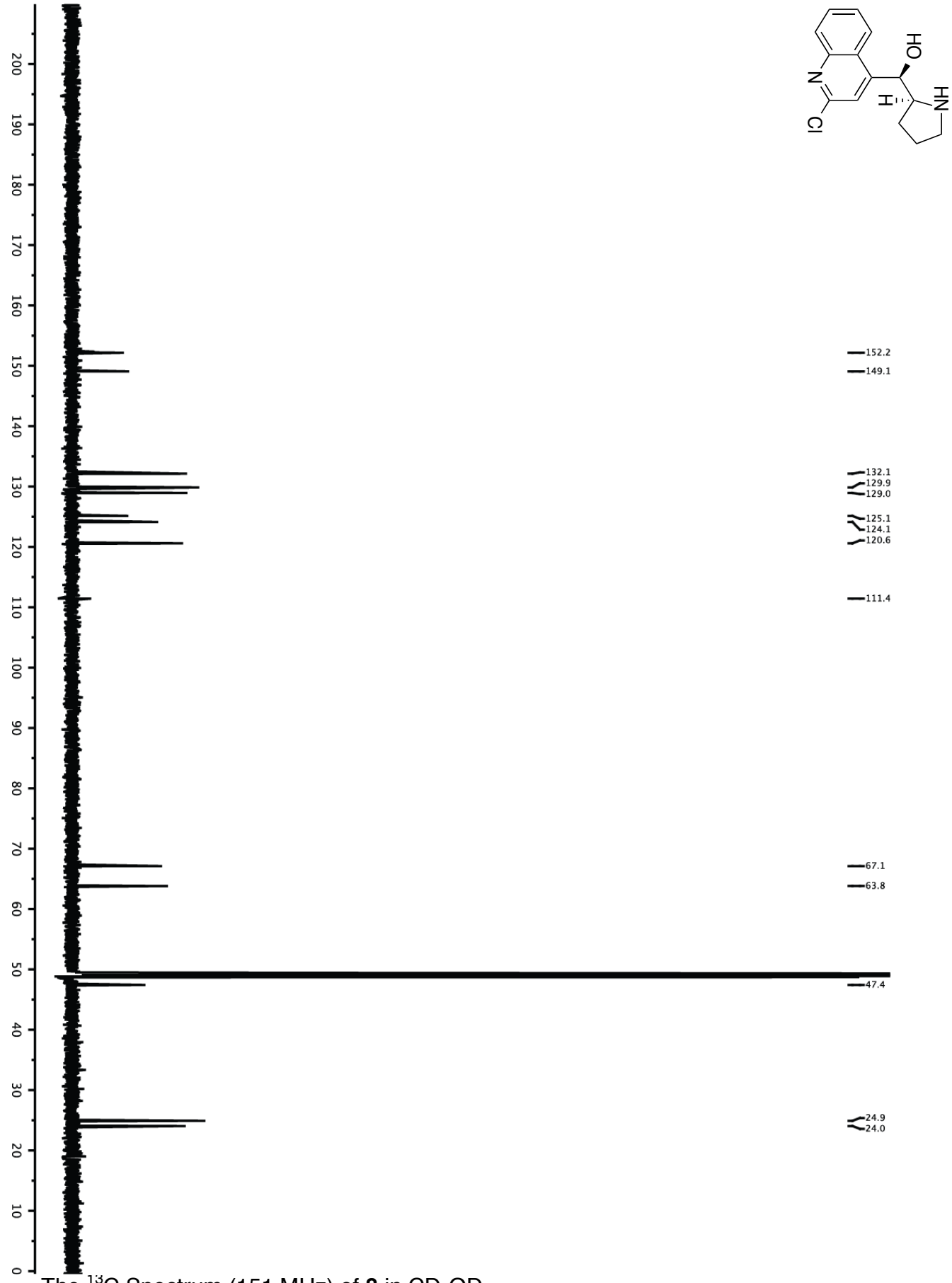
---

[1] A. Krasovskiy and P. Knochel, *Synthesis.,* 2006, **5**, 890 - 891.
[2] C. W. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923-2925.
[3] B. Leon, J. C. N. Fong, K. C. Peach, W. R. Wong, F. H. Yildiz and R. G. Linington, *Org. Lett.*, 2013, ***5***, 2011–2014.

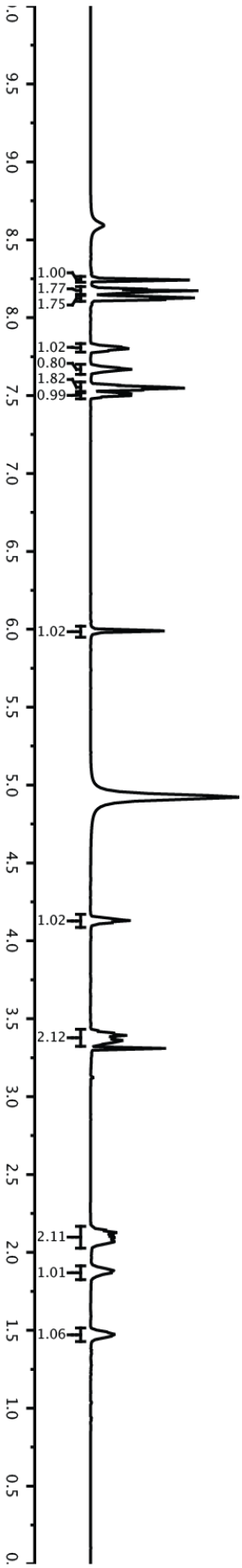
.

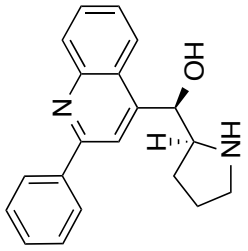


The ^{1}H Spectrum (600 MHz) of **8** in CD_3OD

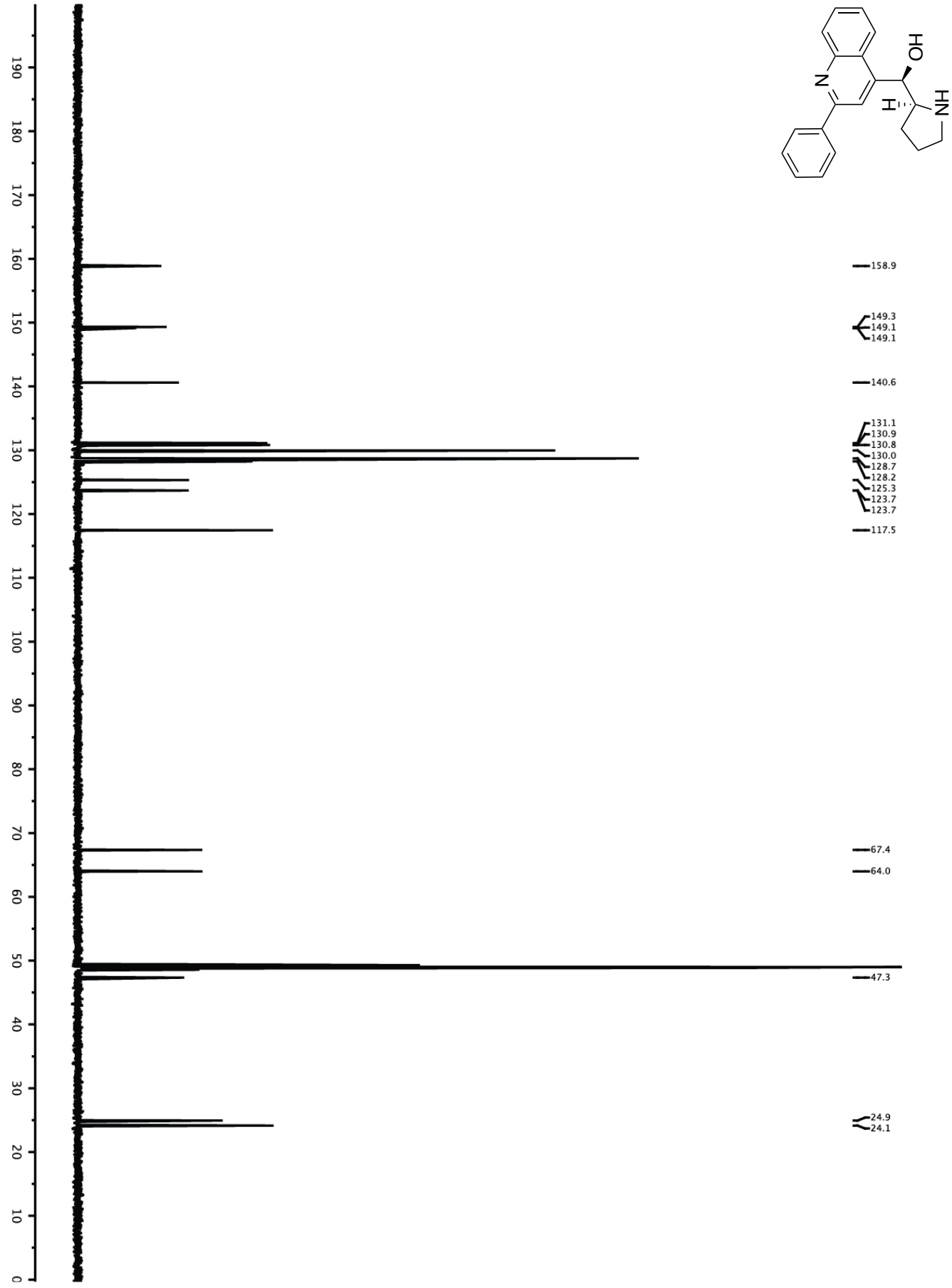


The ^{13}C Spectrum (151 MHz) of **8** in CD_3OD

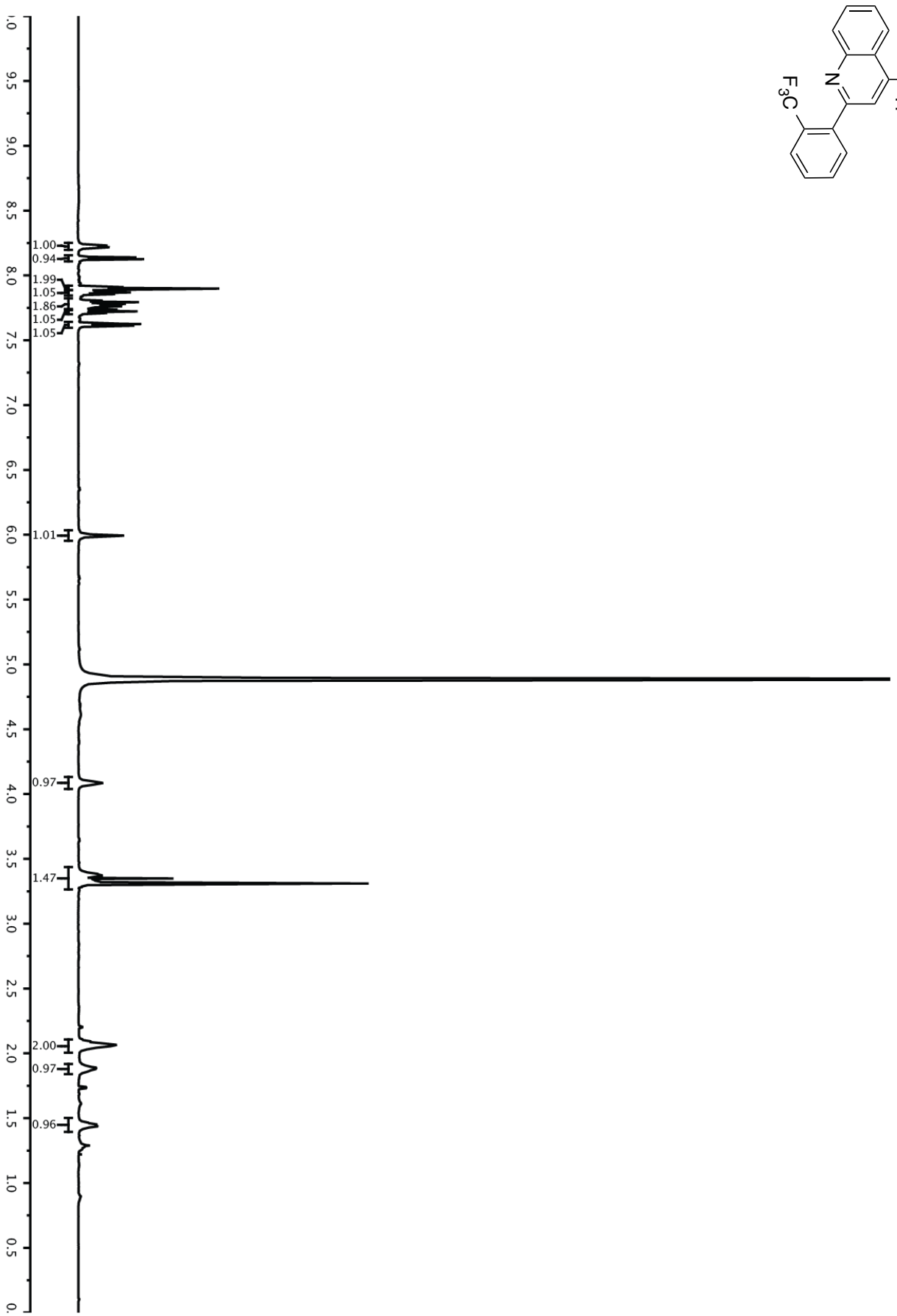




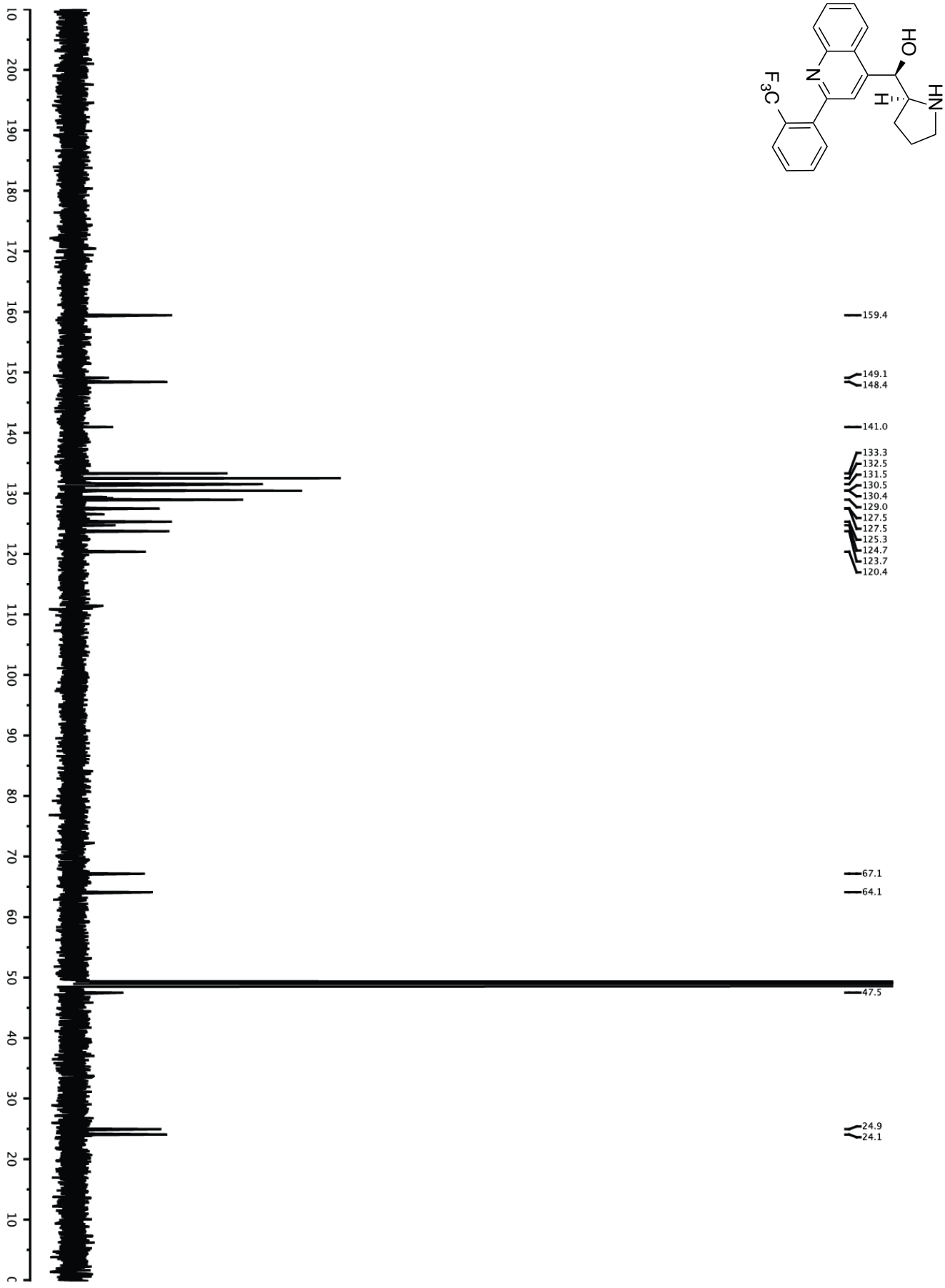
The ^{1}H Spectrum (600 MHz) of **9** in CD_3OD



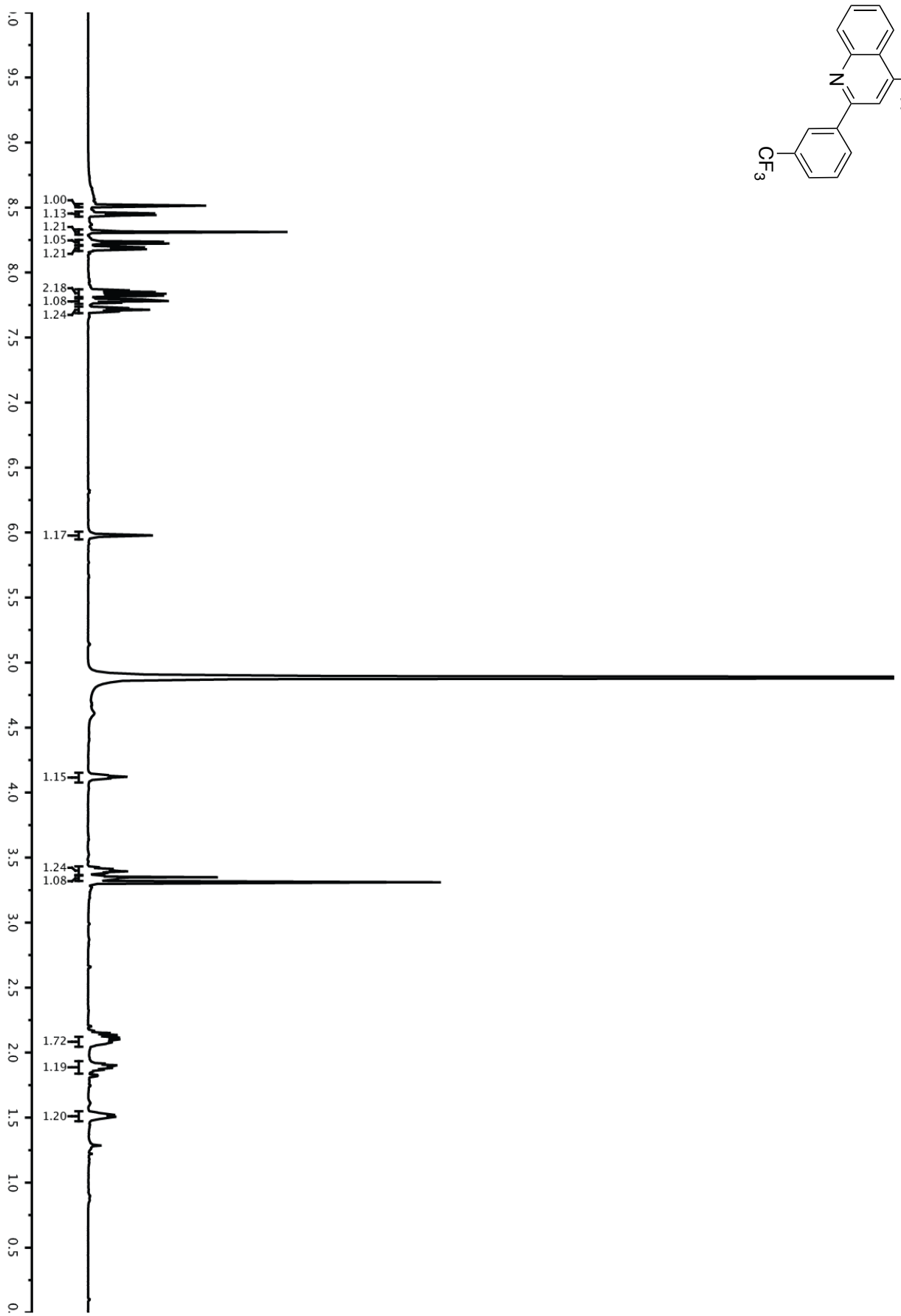
The ^{13}C Spectrum (151 MHz) of **9** in CD_3OD



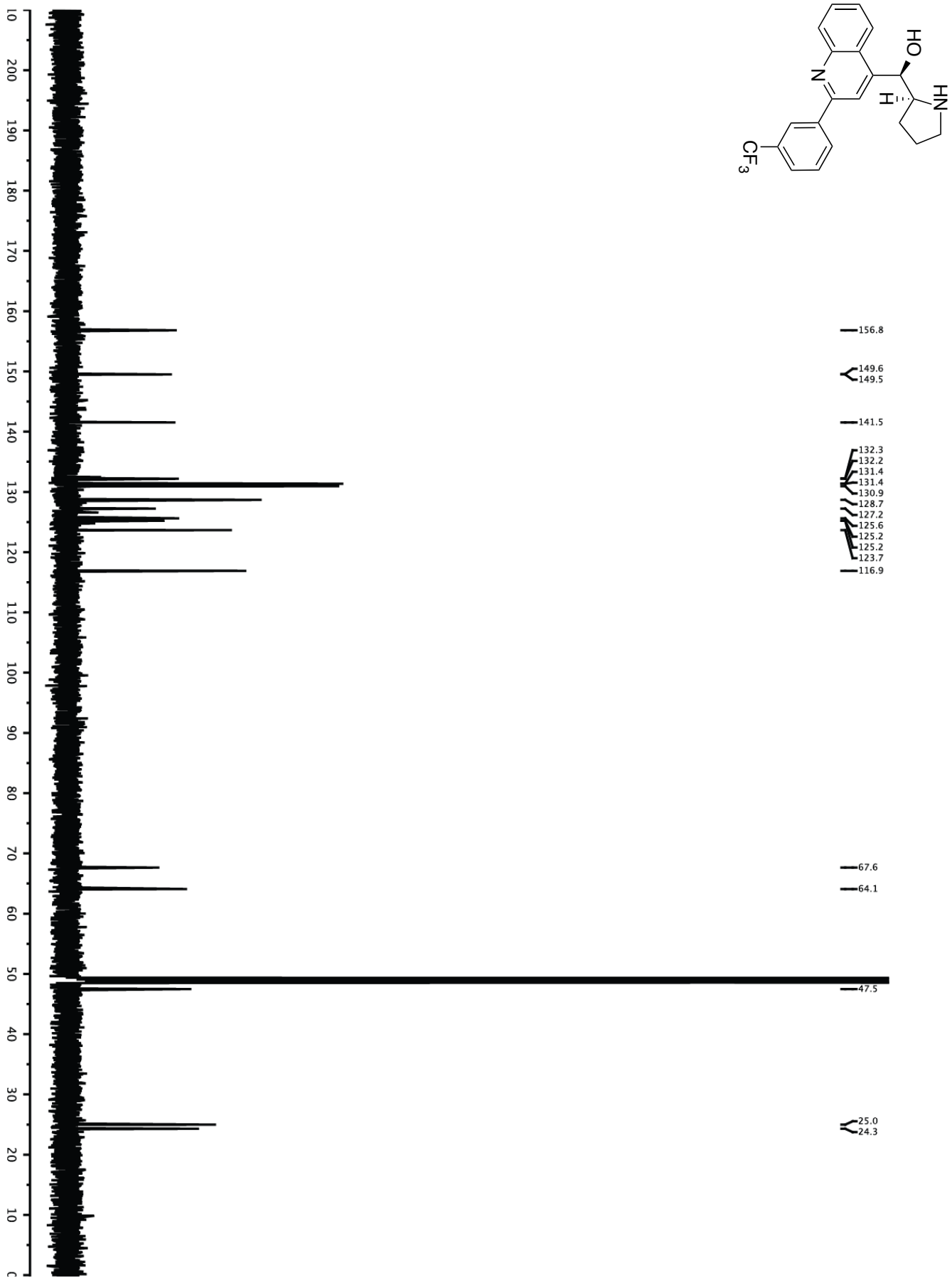
The ^{1}H Spectrum (600 MHz) of **10** in CD_3OD



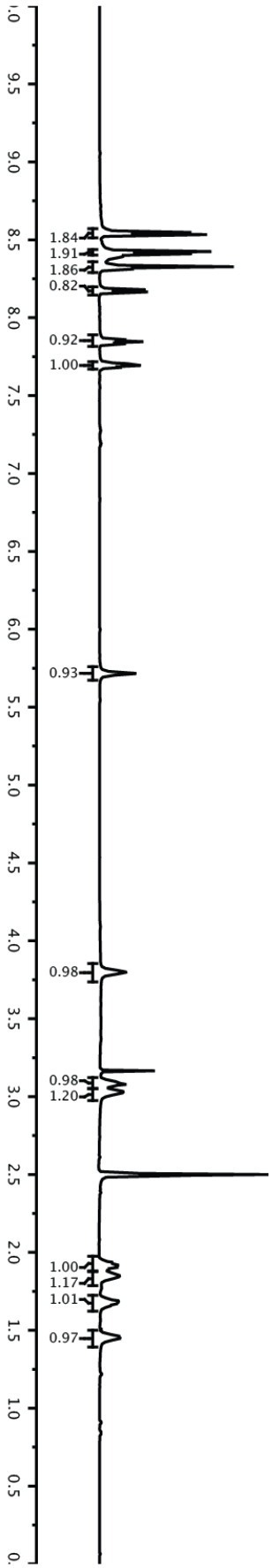
The ^{13}C Spectrum (151 MHz) of **10** in CD_3OD

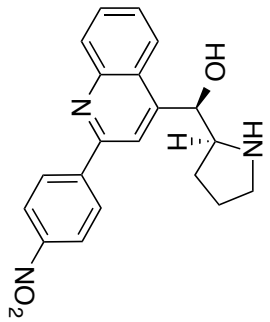


The ^{1}H Spectrum (600 MHz) of **11** in CD_3OD

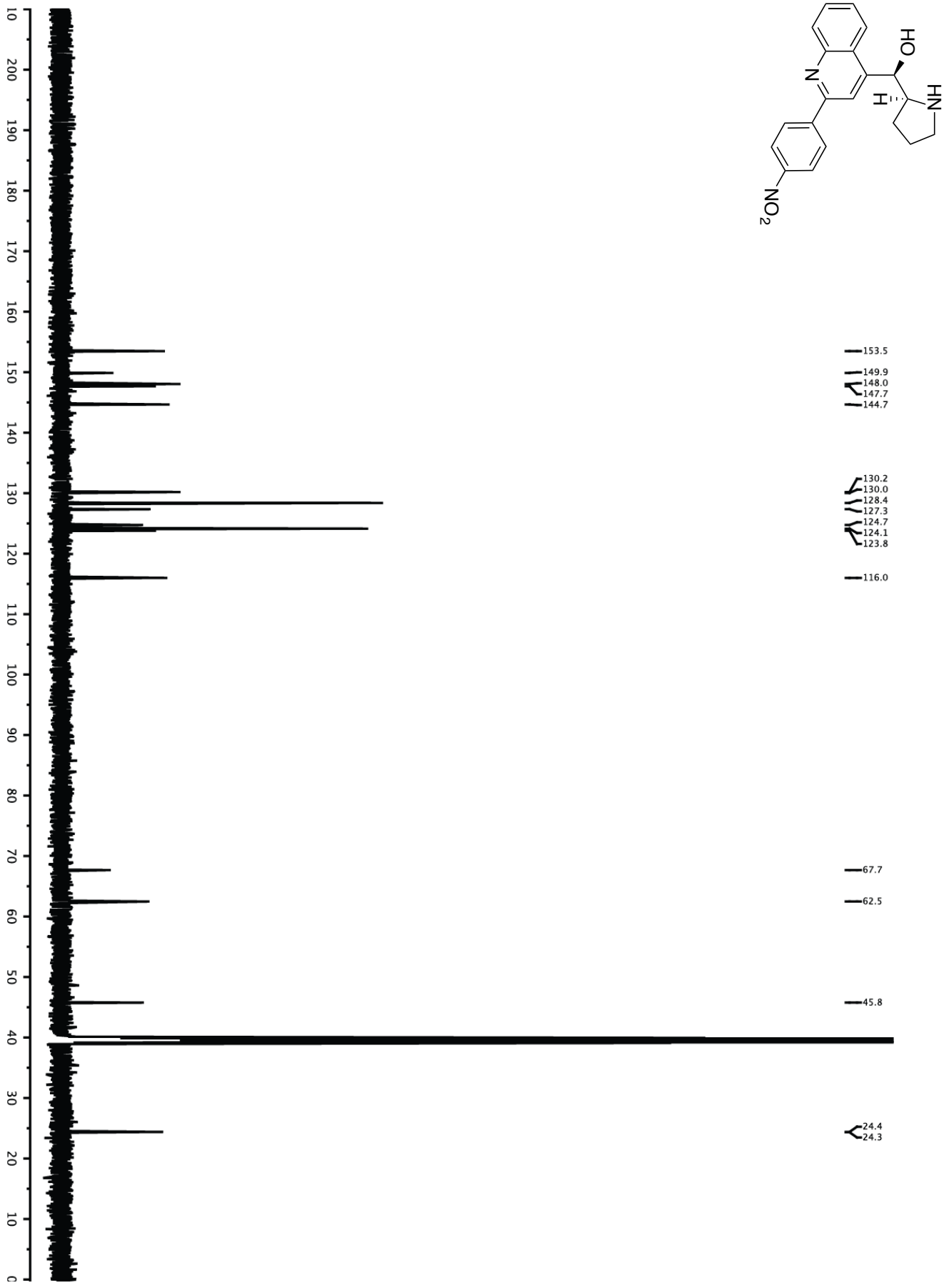


The ^{13}C Spectrum (151 MHz) of **11** in CD_3OD

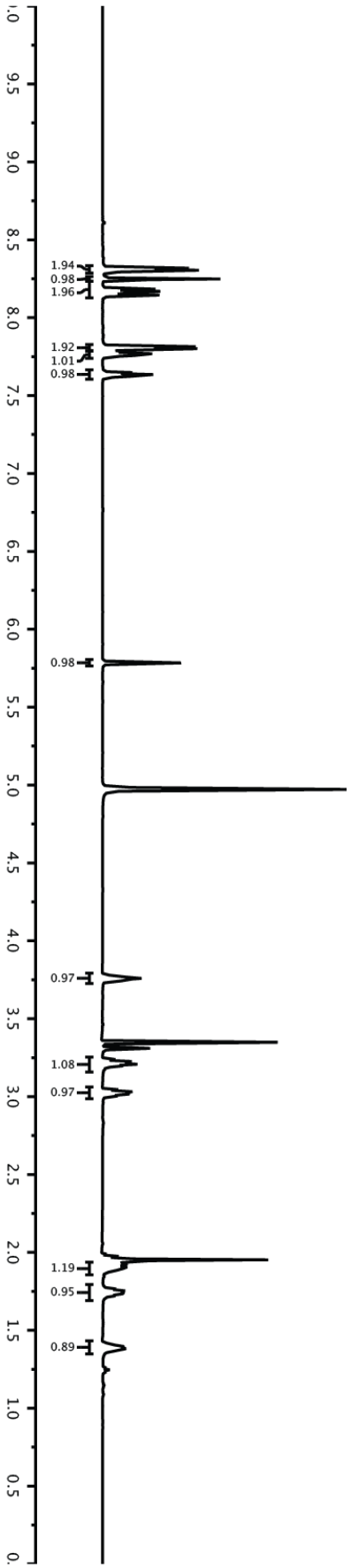


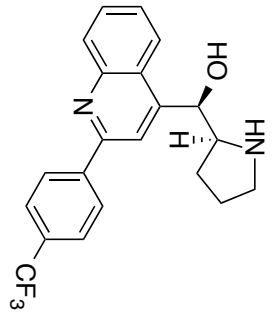


The ^{1}H Spectrum (600 MHz) of **12** in $(CD_3)_2SO$

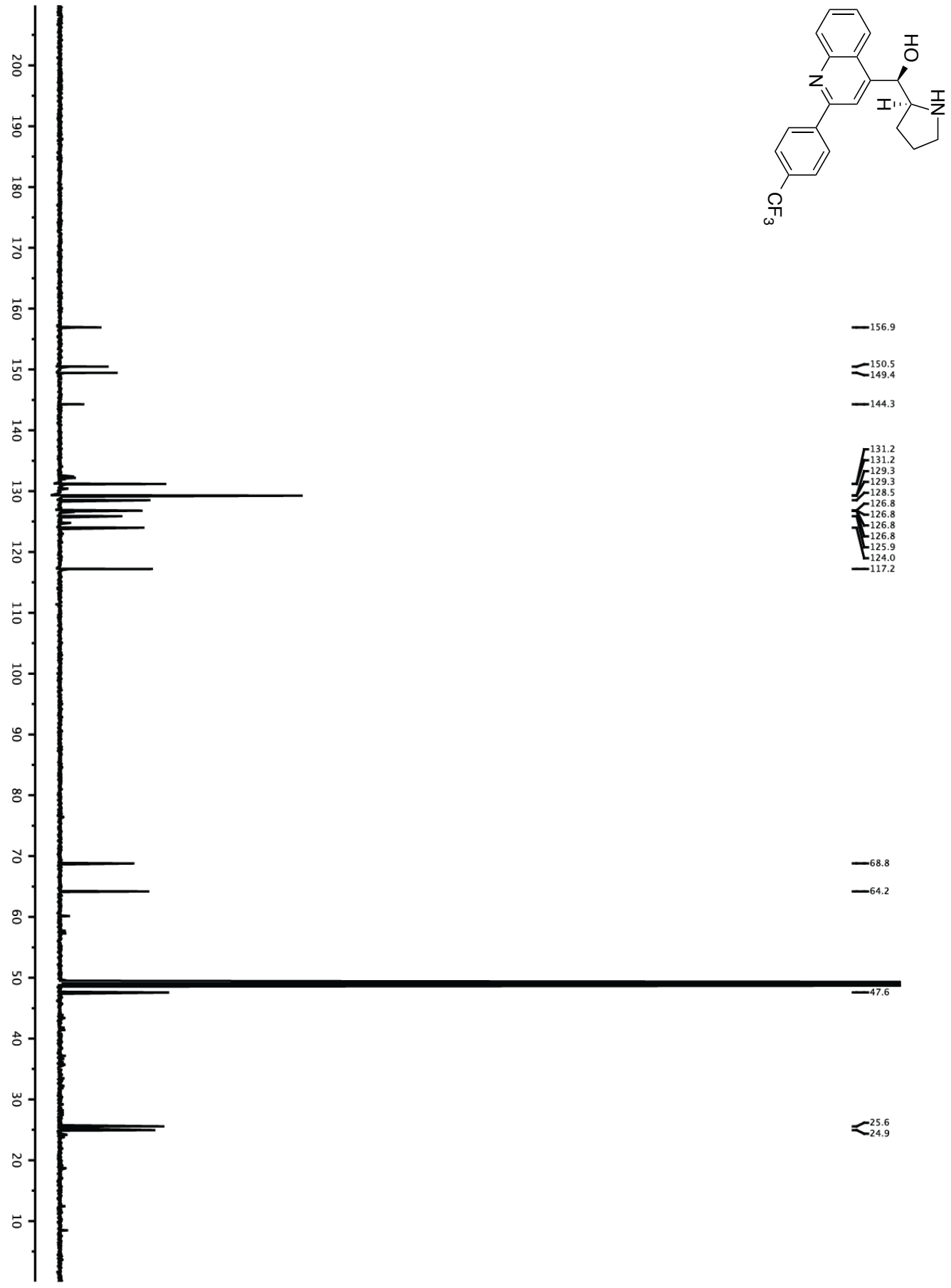


The ^{13}C Spectrum (151 MHz) of **12** in $(CD_3)_2SO$

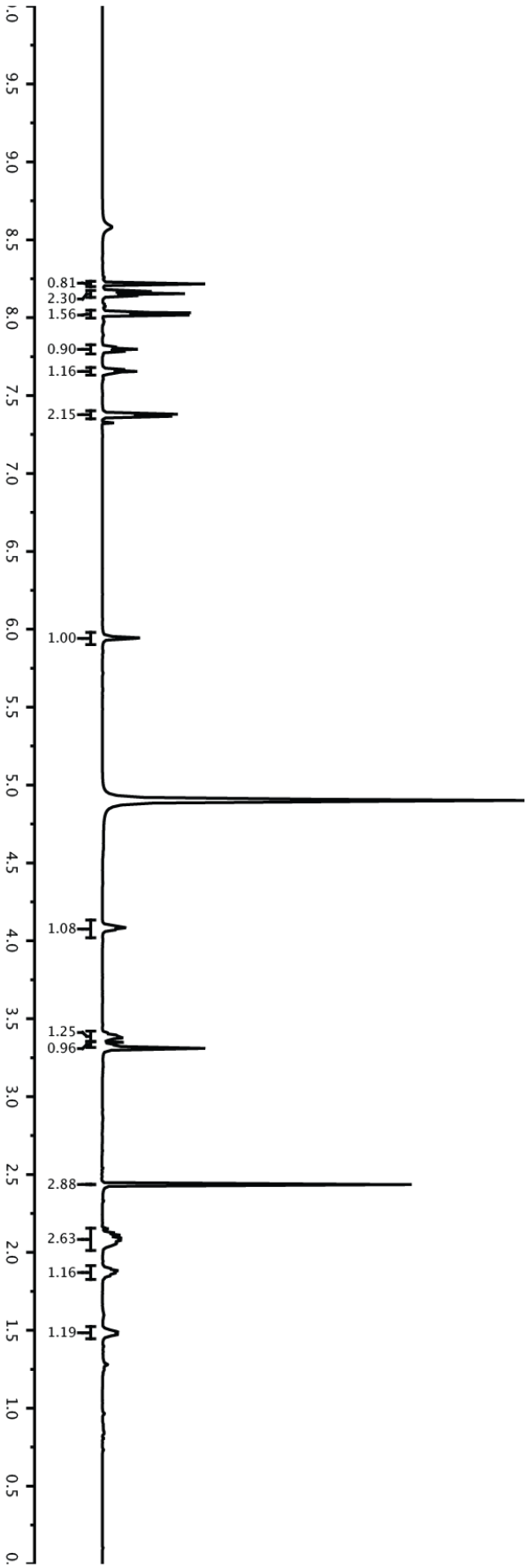


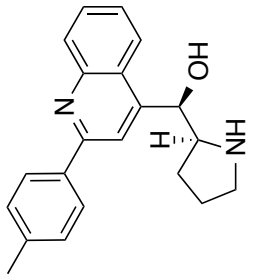


The ^{1}H Spectrum (600 MHz) of **4** in CD_3OD

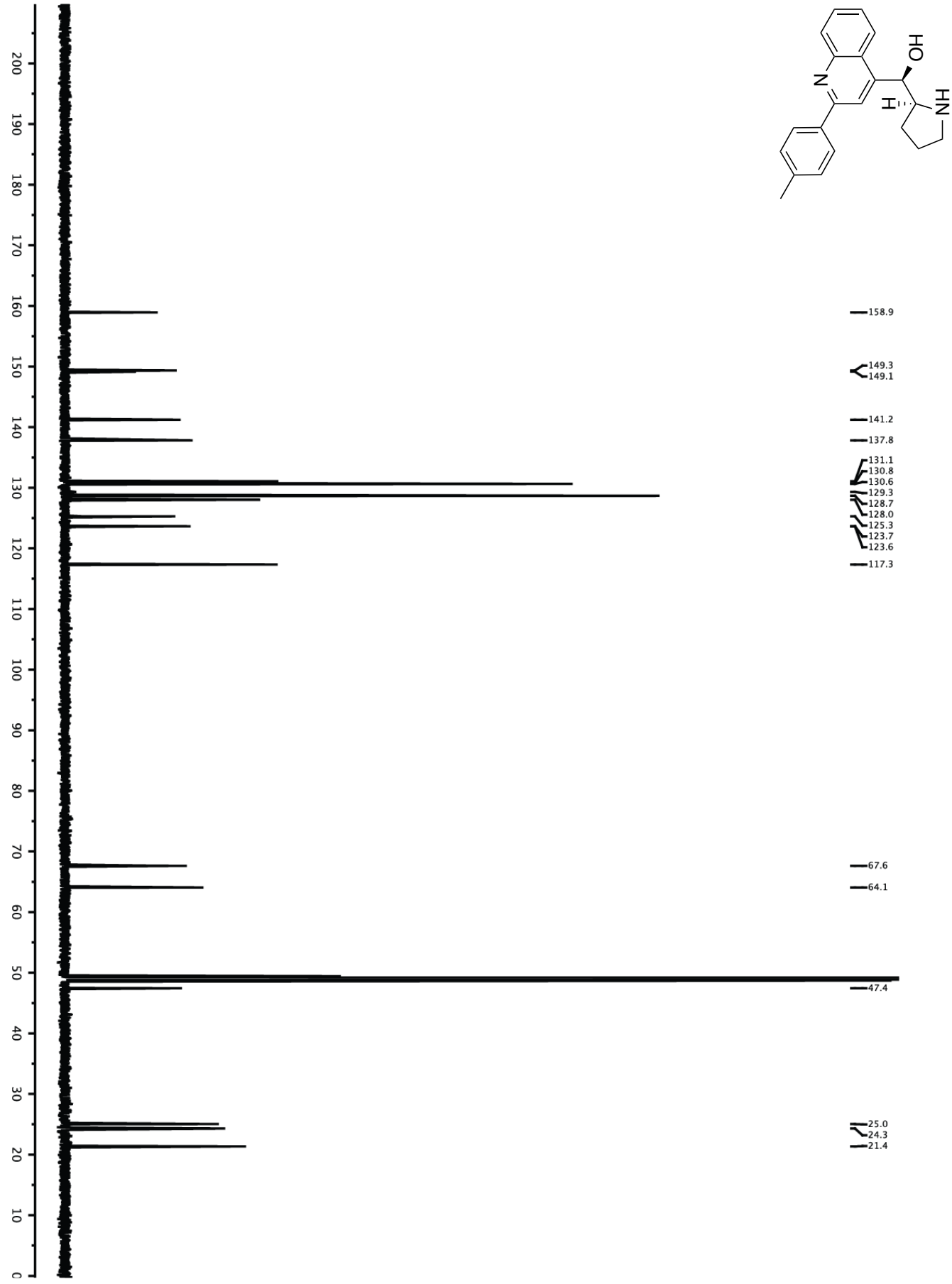


The ^{13}C Spectrum (151 MHz) of **4** in CD_3OD

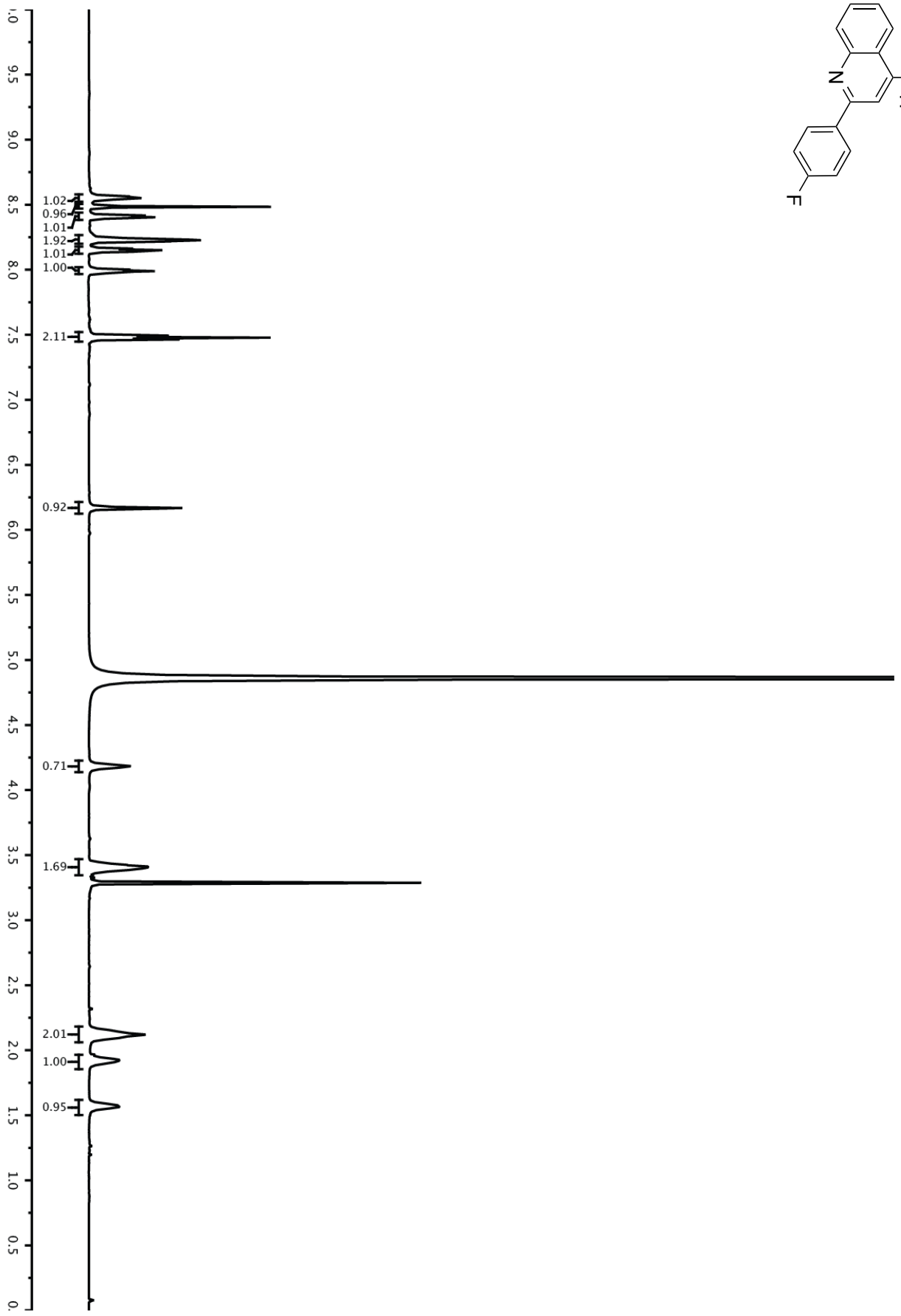




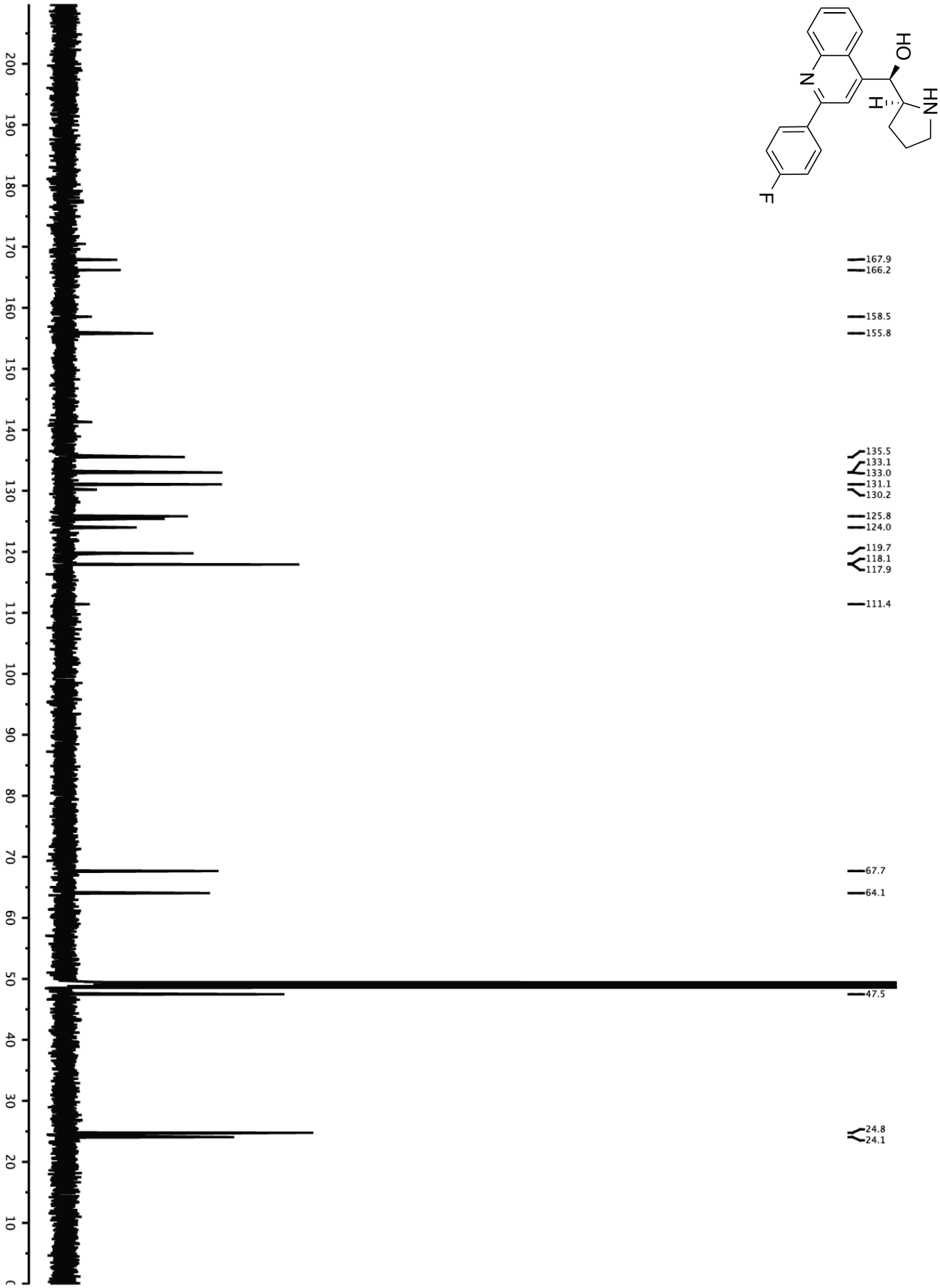
The ^{1}H Spectrum (600 MHz) of **13** in CD_3OD



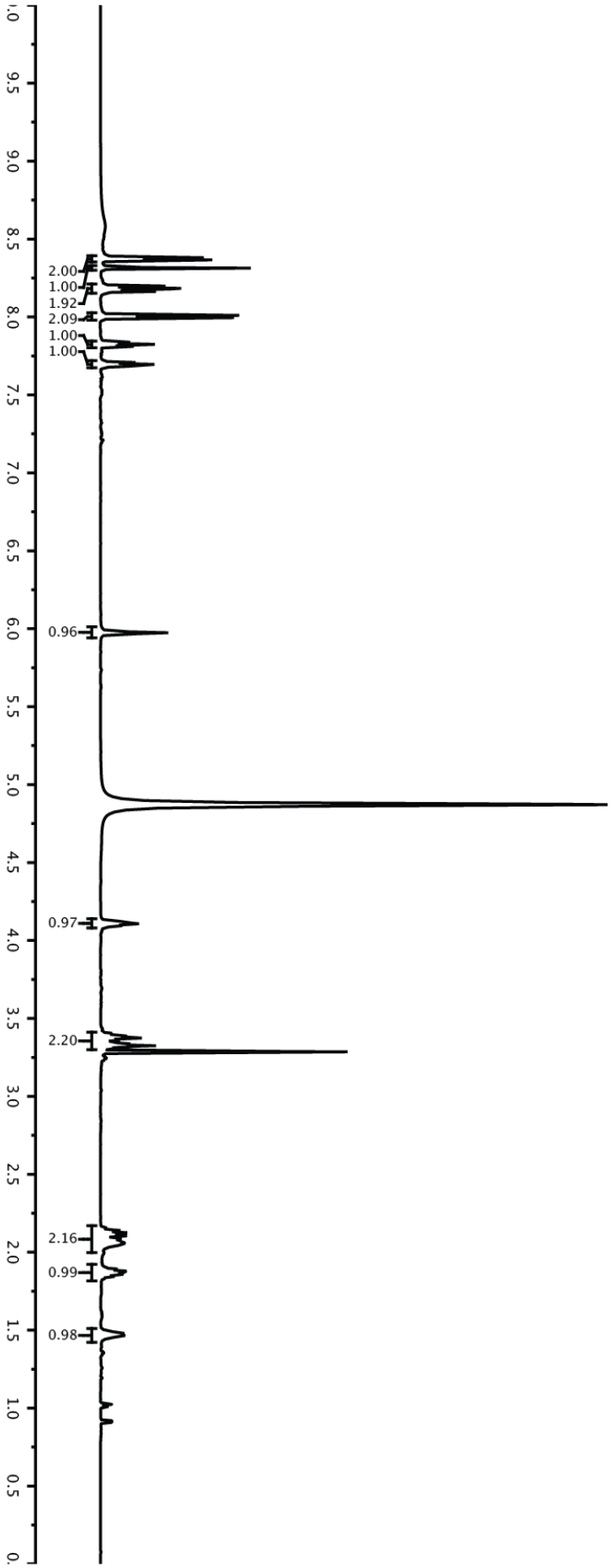
The ^{13}C Spectrum (151 MHz) of **13** in CD_3OD

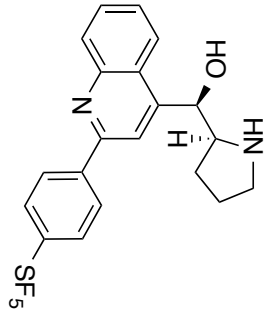


The ^{1}H Spectrum (600 MHz) of **14** in CD_3OD

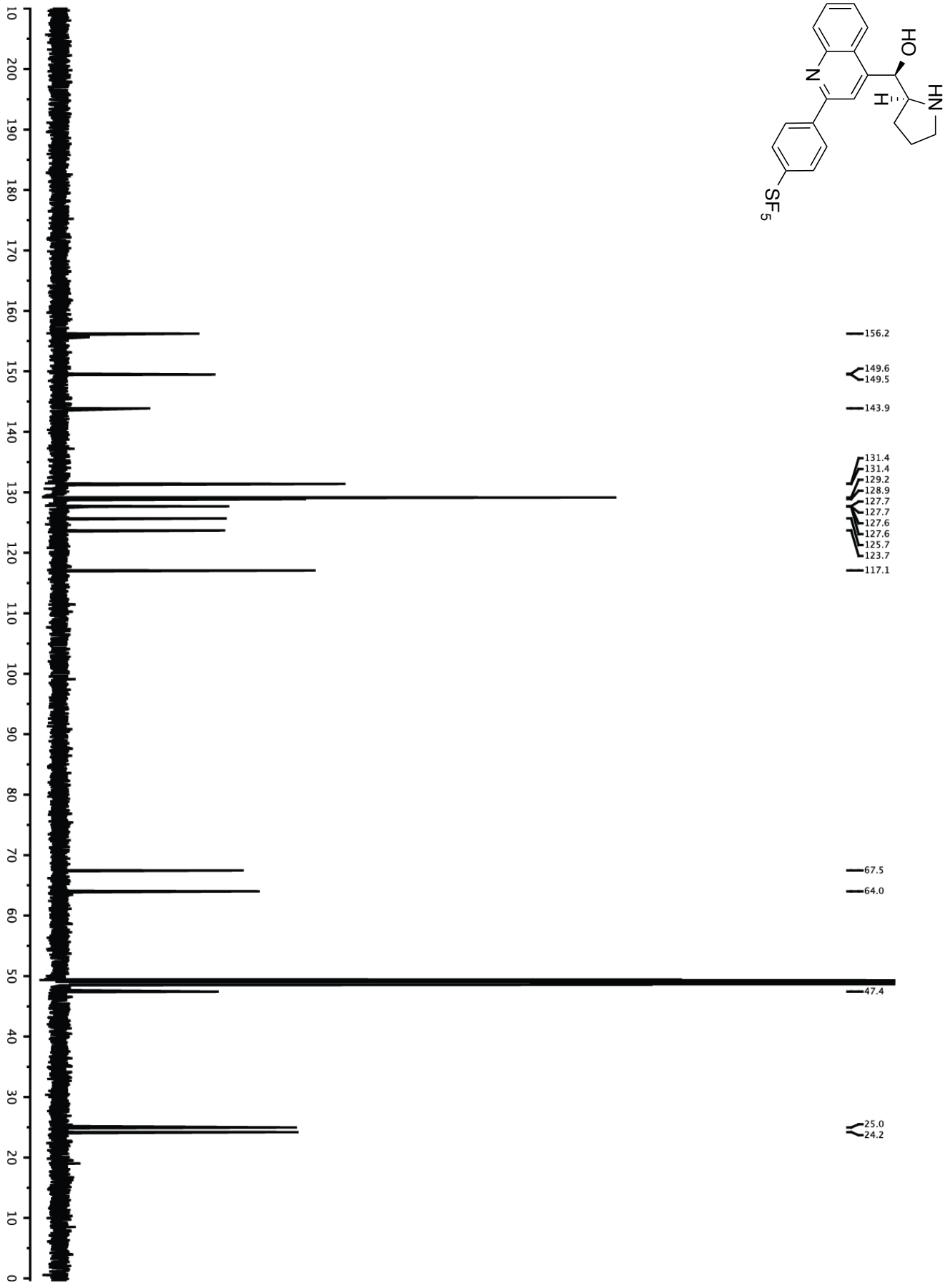


The ^{13}C Spectrum (151 MHz) of **14** in CD_3OD

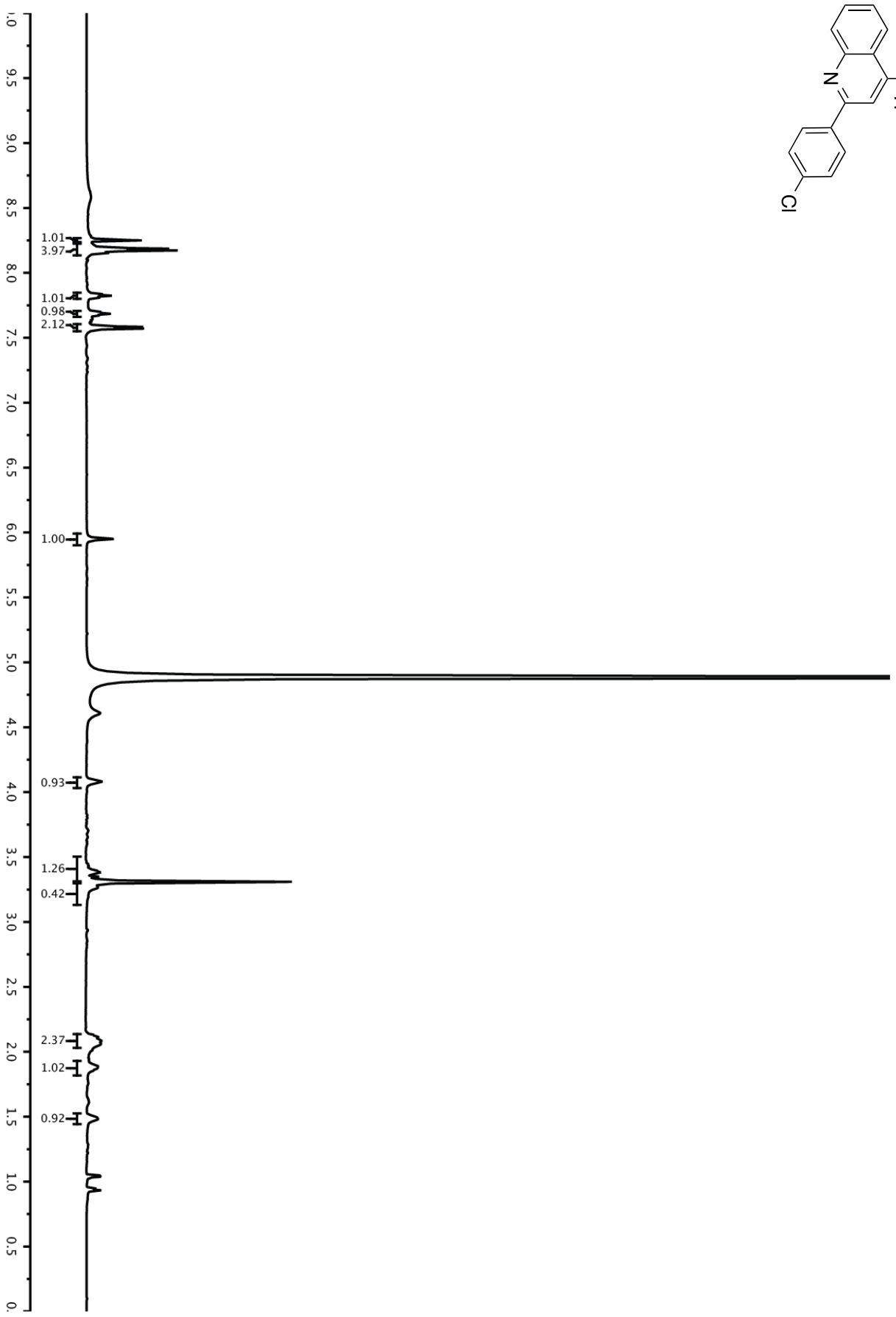




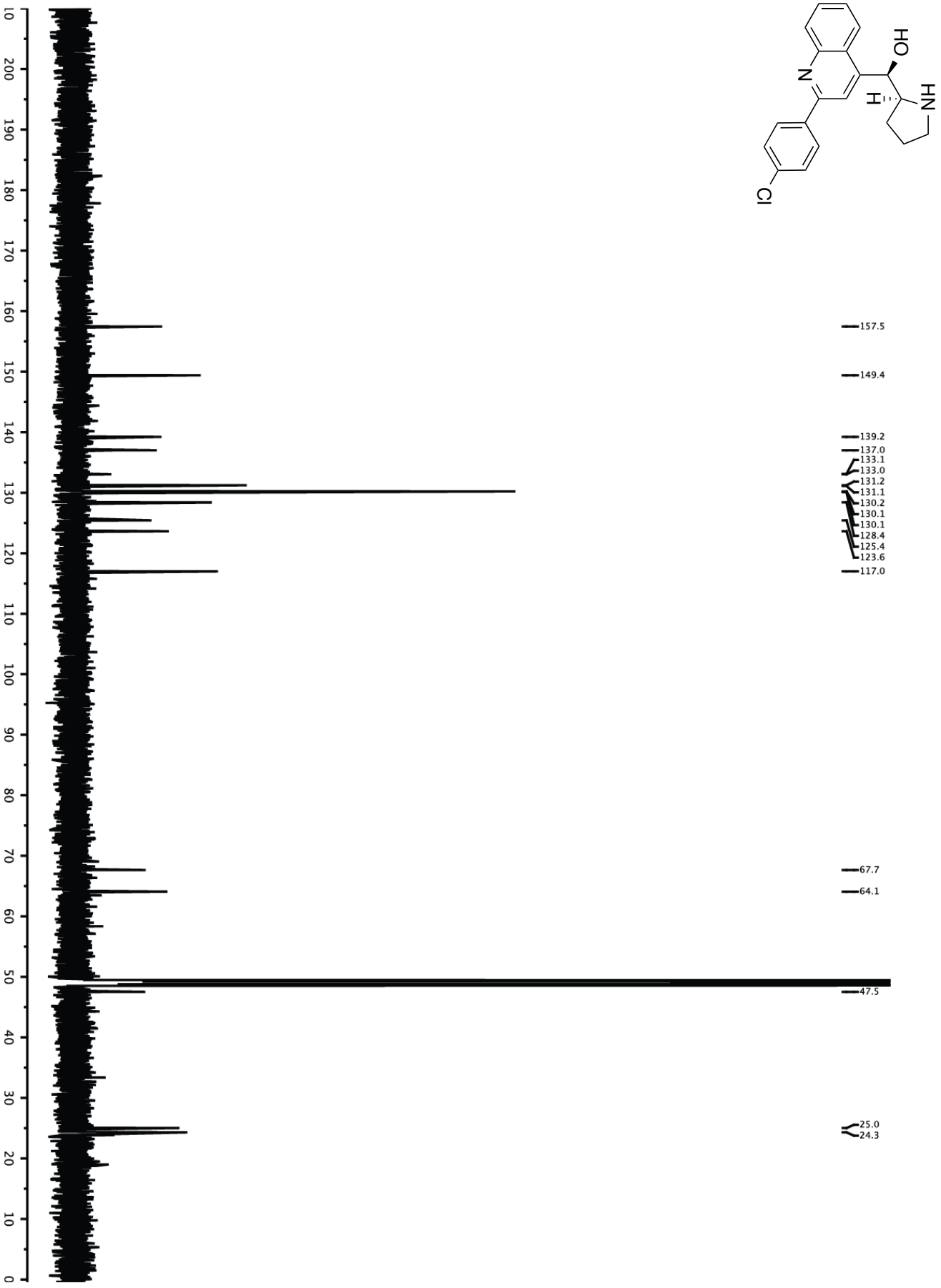
The ^{1}H Spectrum (600 MHz) of **15** in CD_3OD



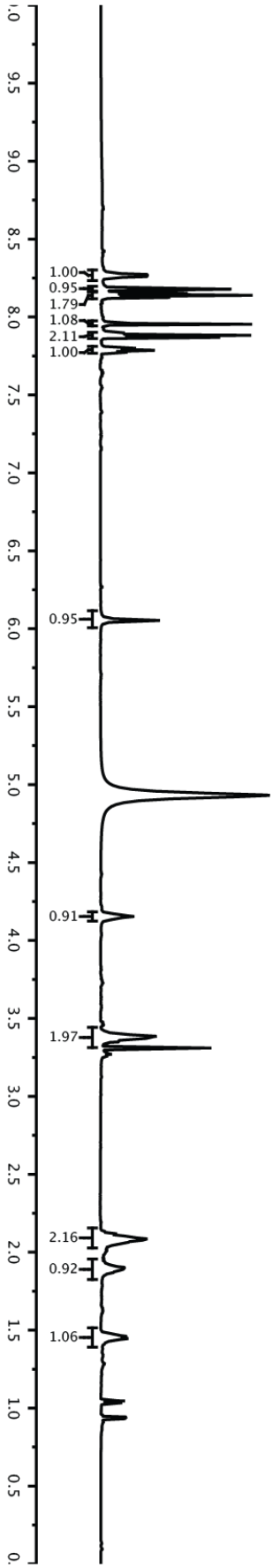
The ^{13}C Spectrum (151 MHz) of **15** in CD_3OD

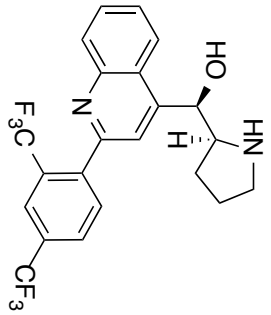


The ^{1}H Spectrum (600 MHz) of **16** in CD_3OD

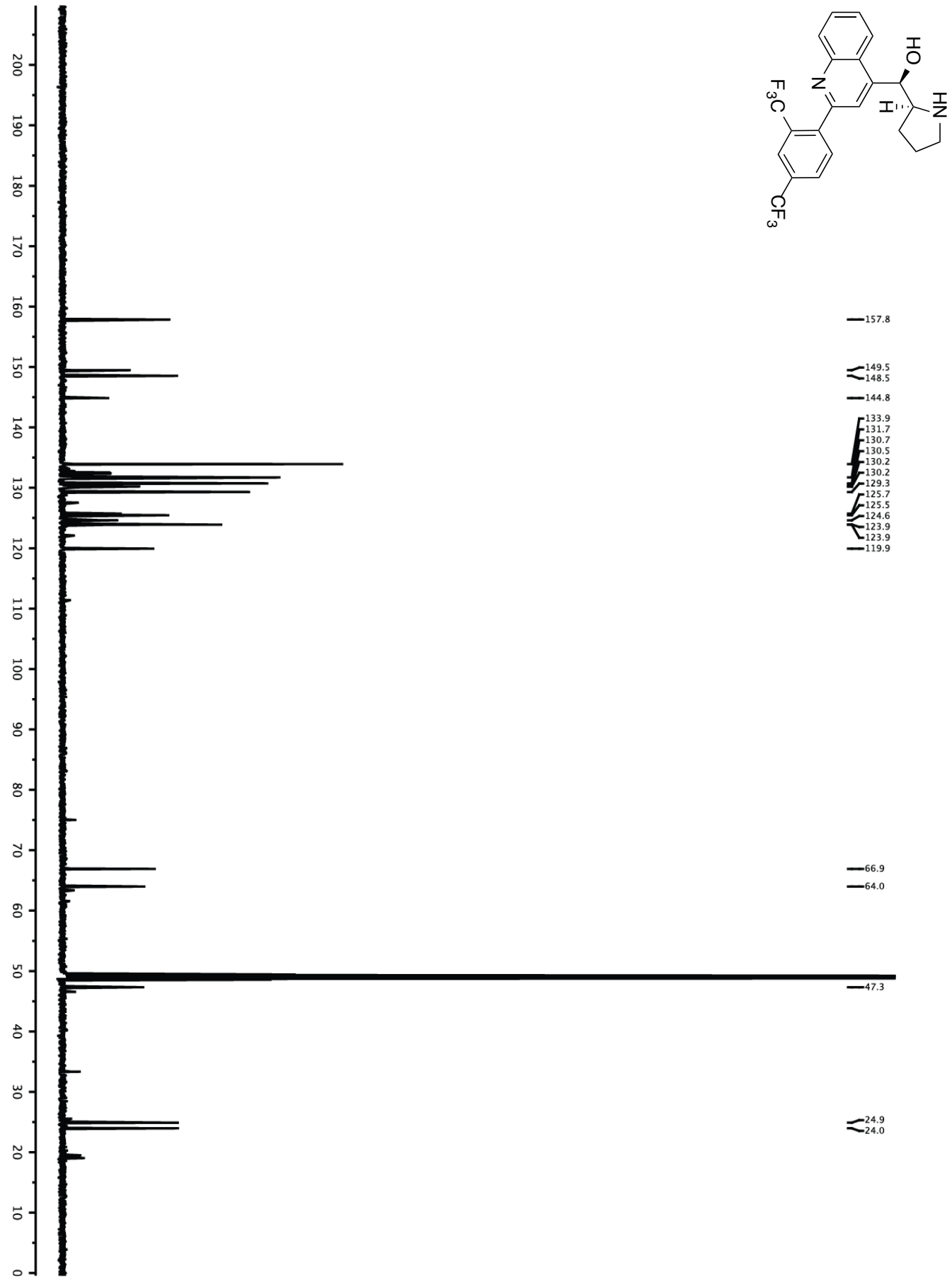


The ^{13}C Spectrum (151 MHz) of **16** in CD_3OD

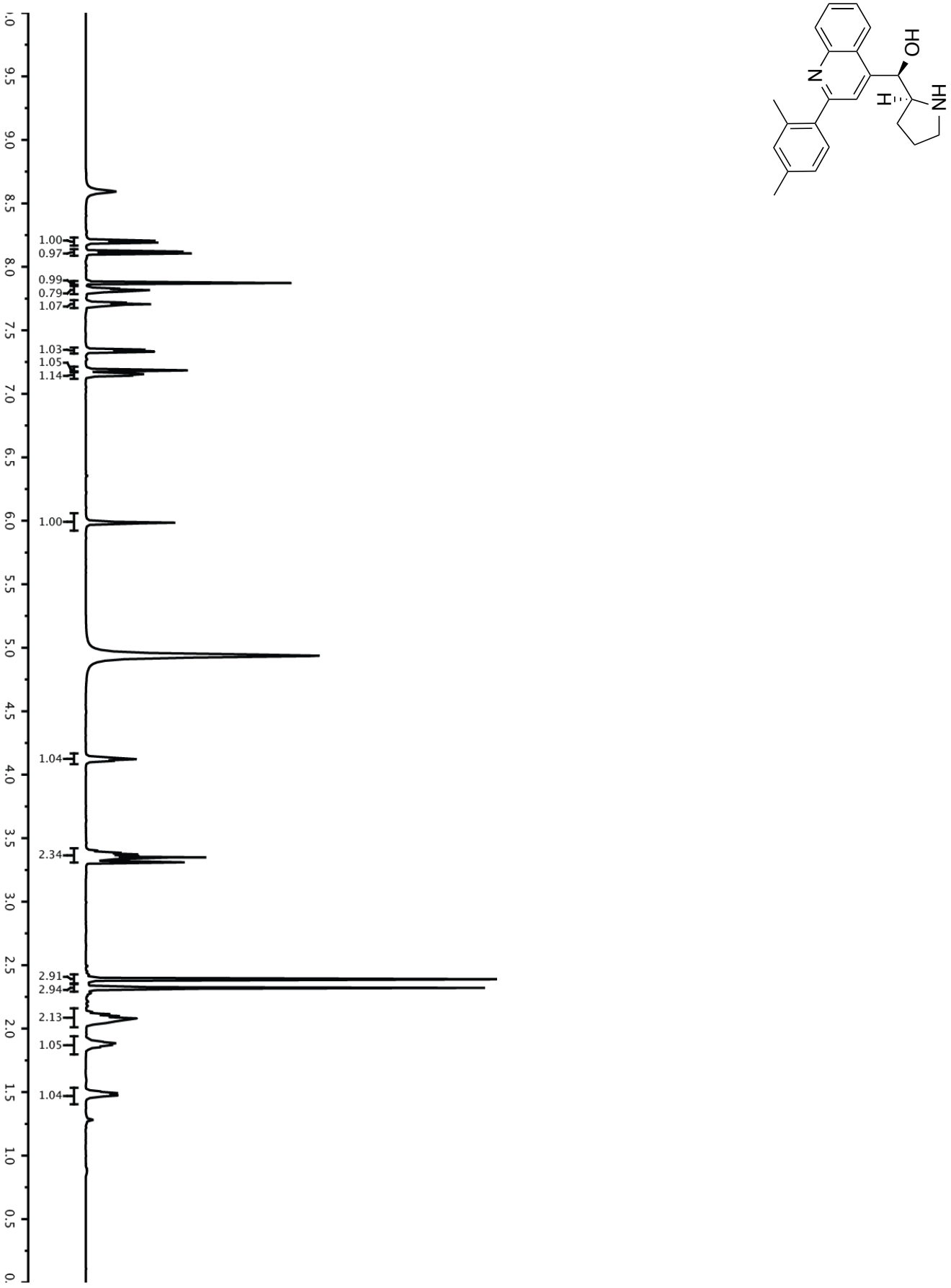




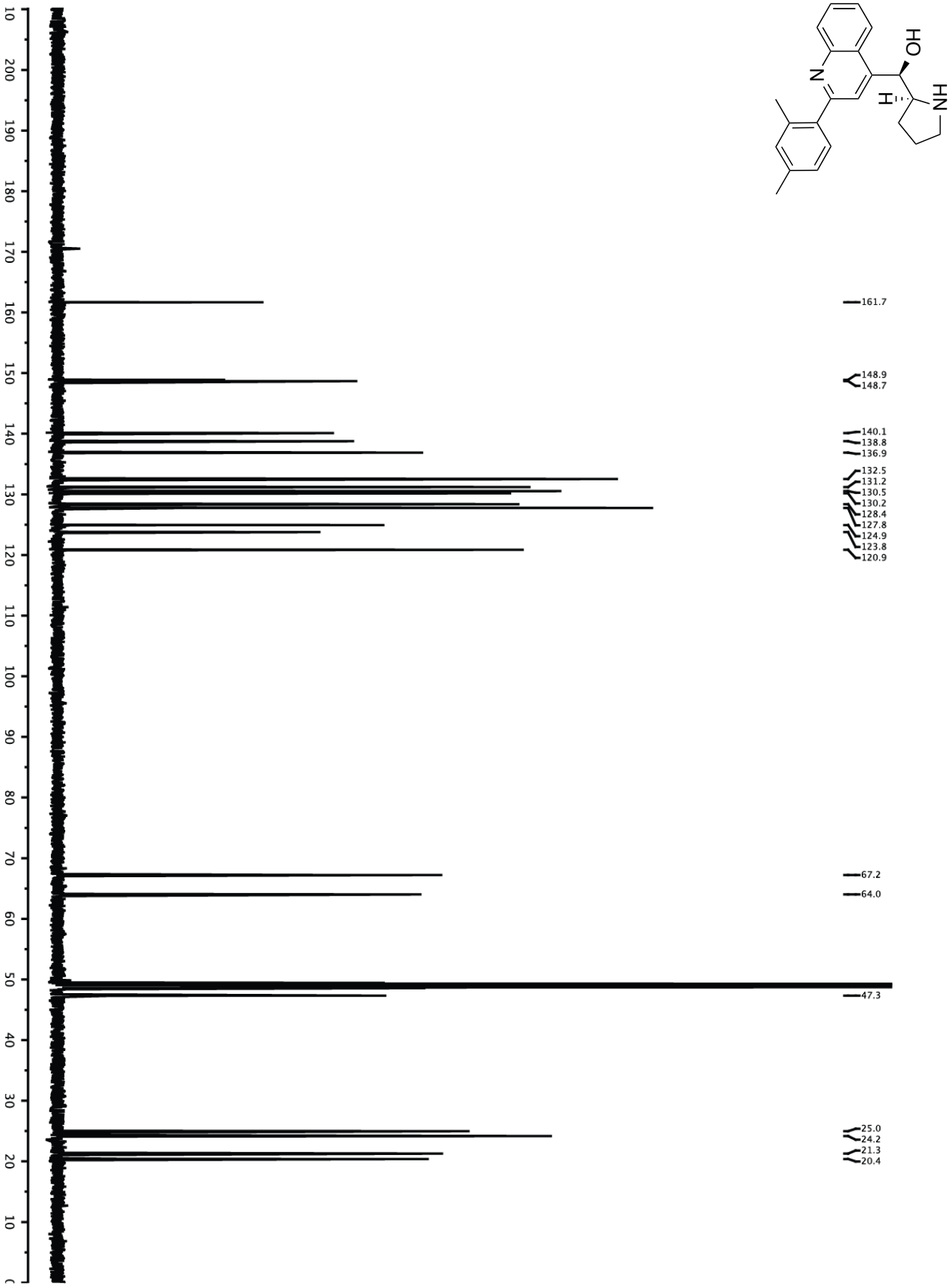
The ^{1}H Spectrum (600 MHz) of **17** in CD_3OD



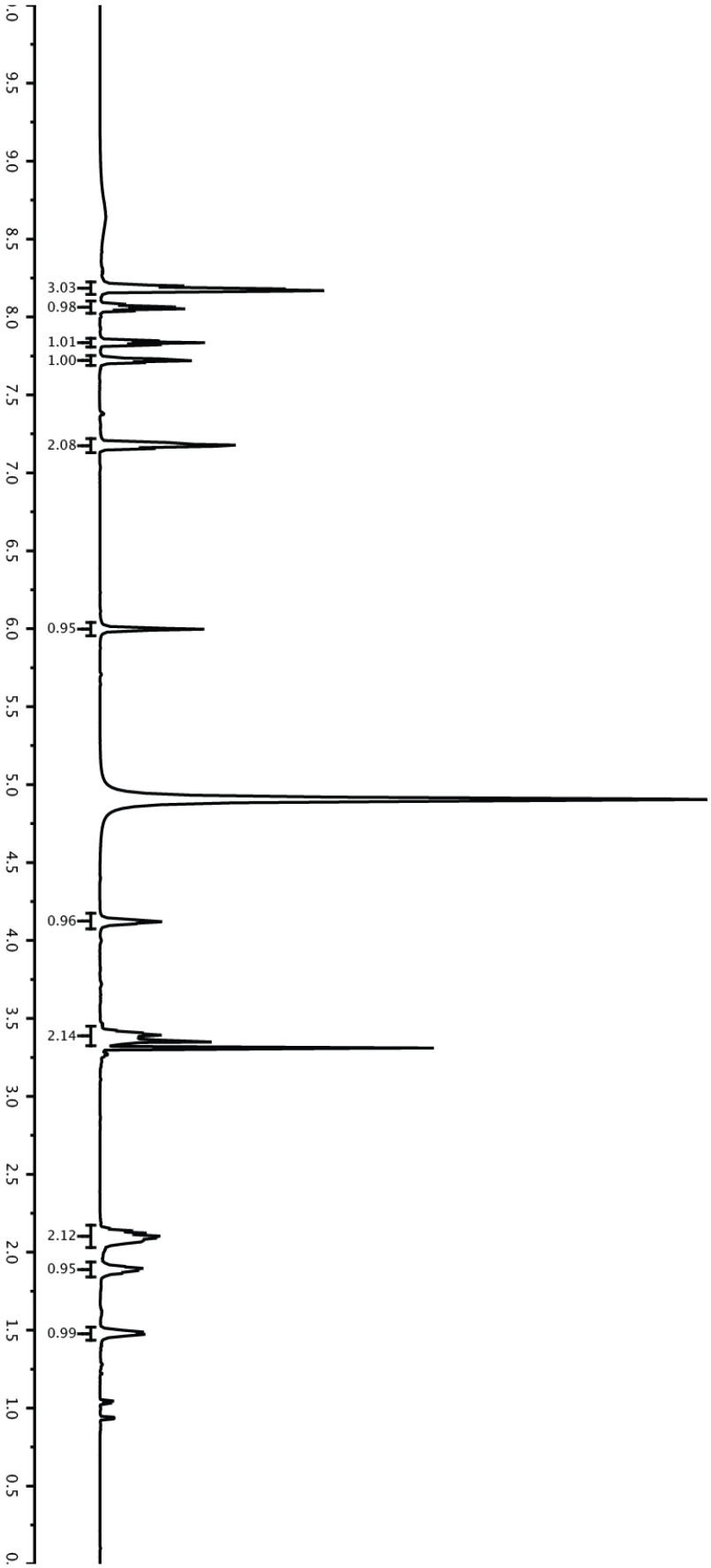
The ^{13}C Spectrum (151 MHz) of **17** in CD_3OD

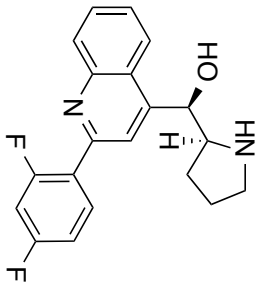


The ^{1}H Spectrum (600 MHz) of **18** in CD_3OD

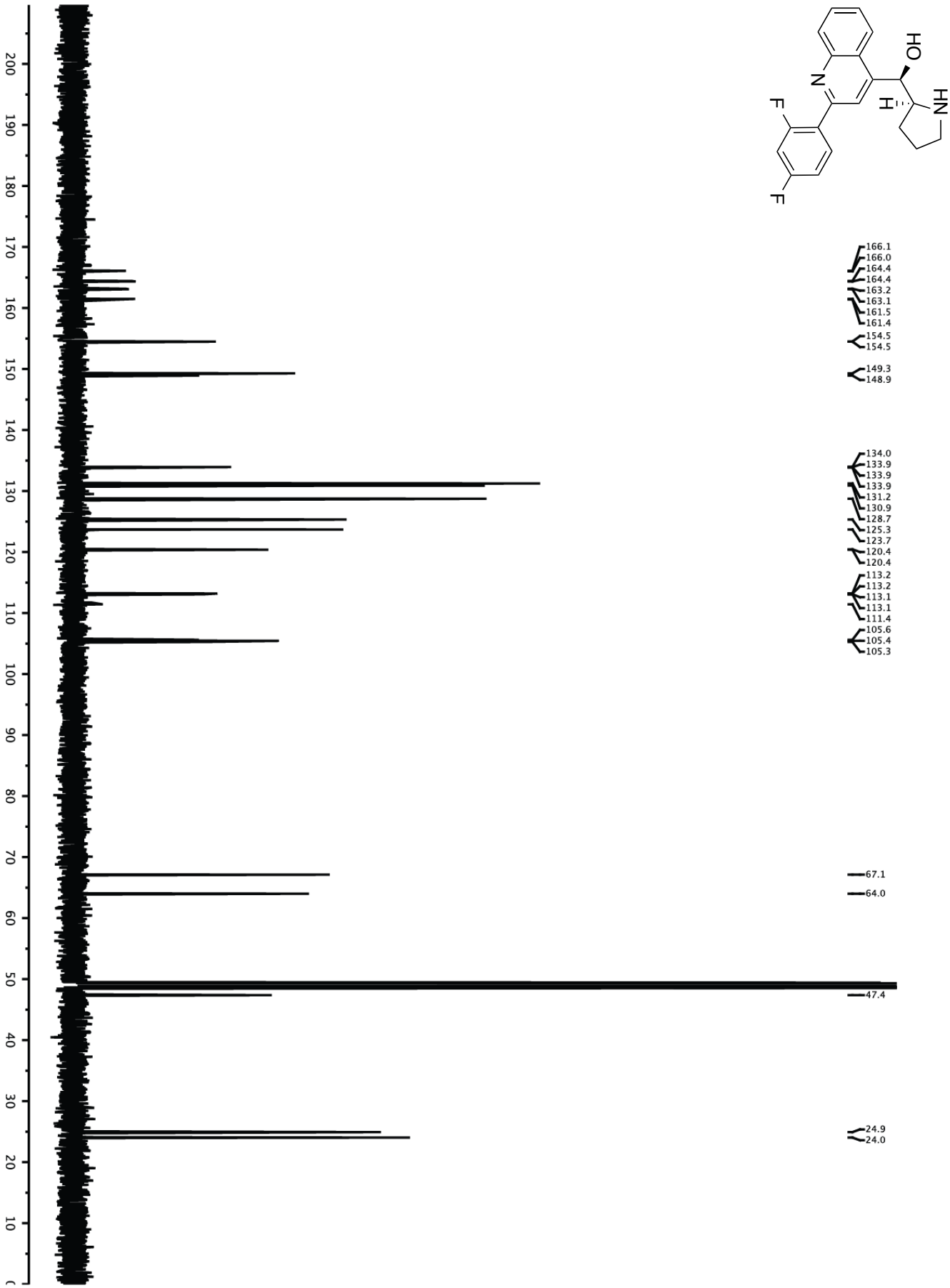


The ^{13}C Spectrum (151 MHz) of **18** in CD_3OD

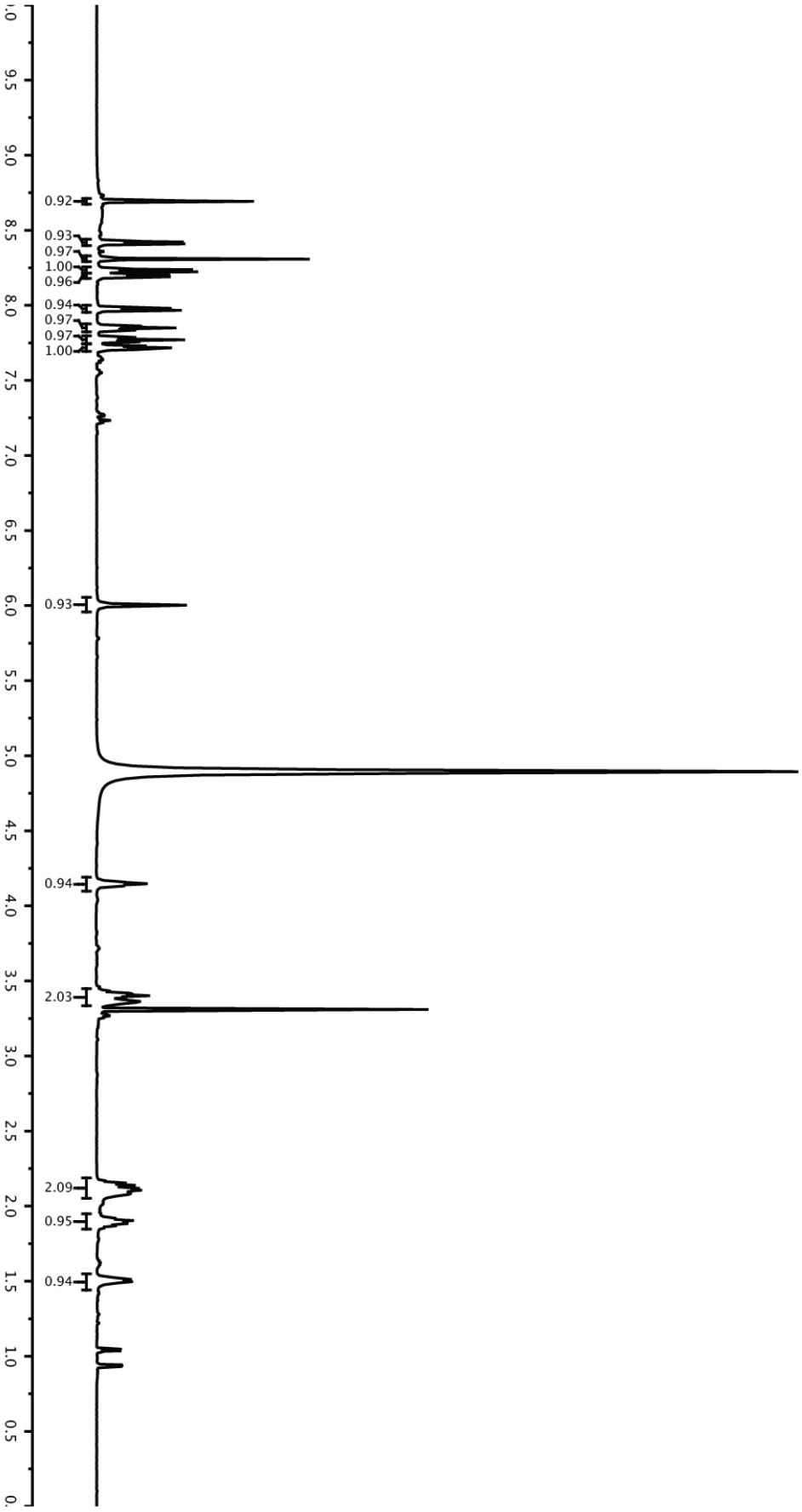


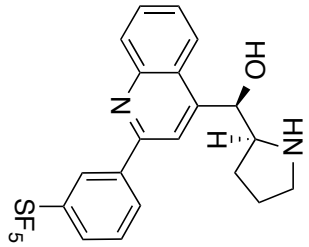


The ^{1}H Spectrum (600 MHz) of **19** in CD_3OD

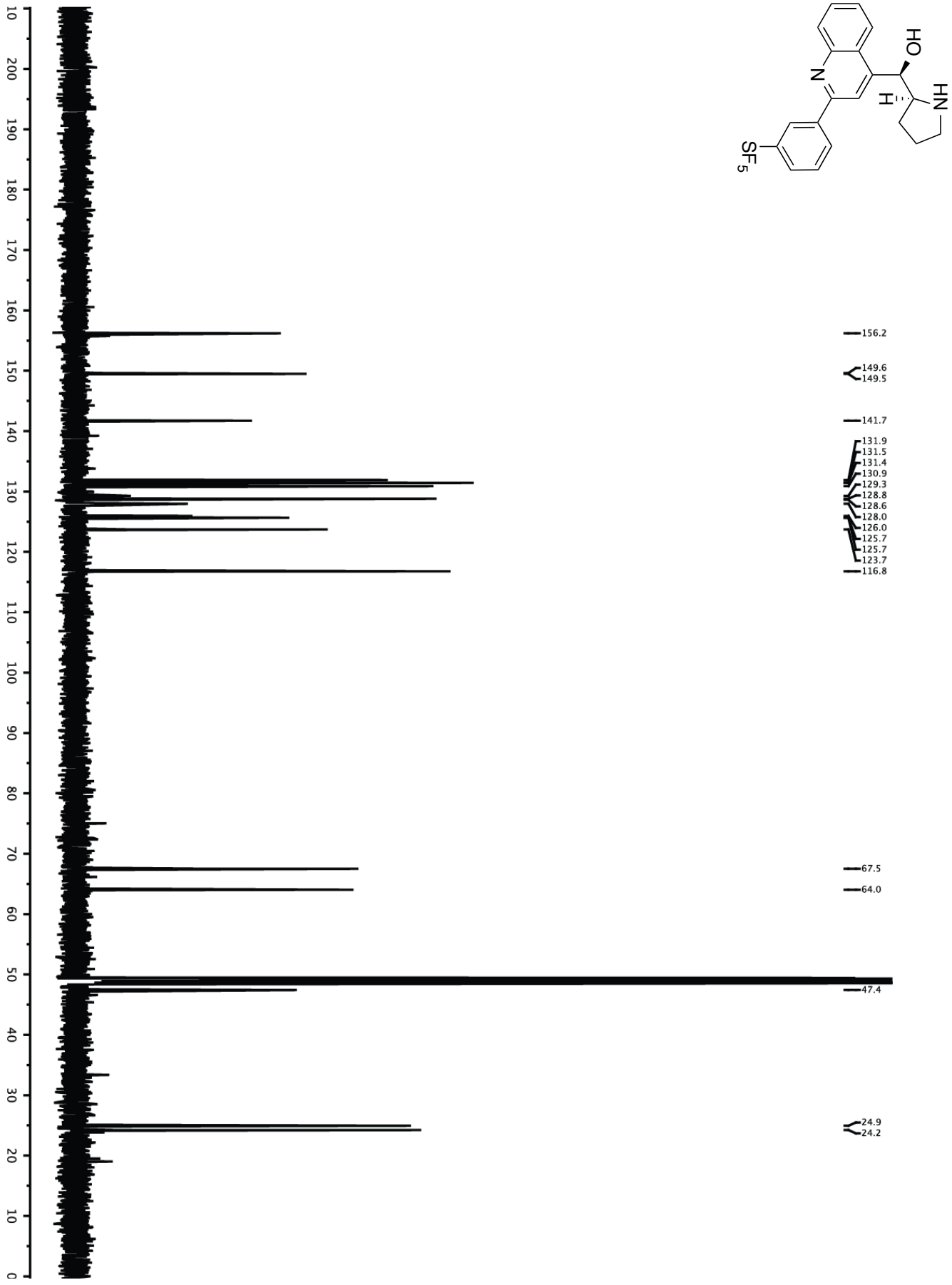


The ^{13}C Spectrum (151 MHz) of **19** in CD_3OD

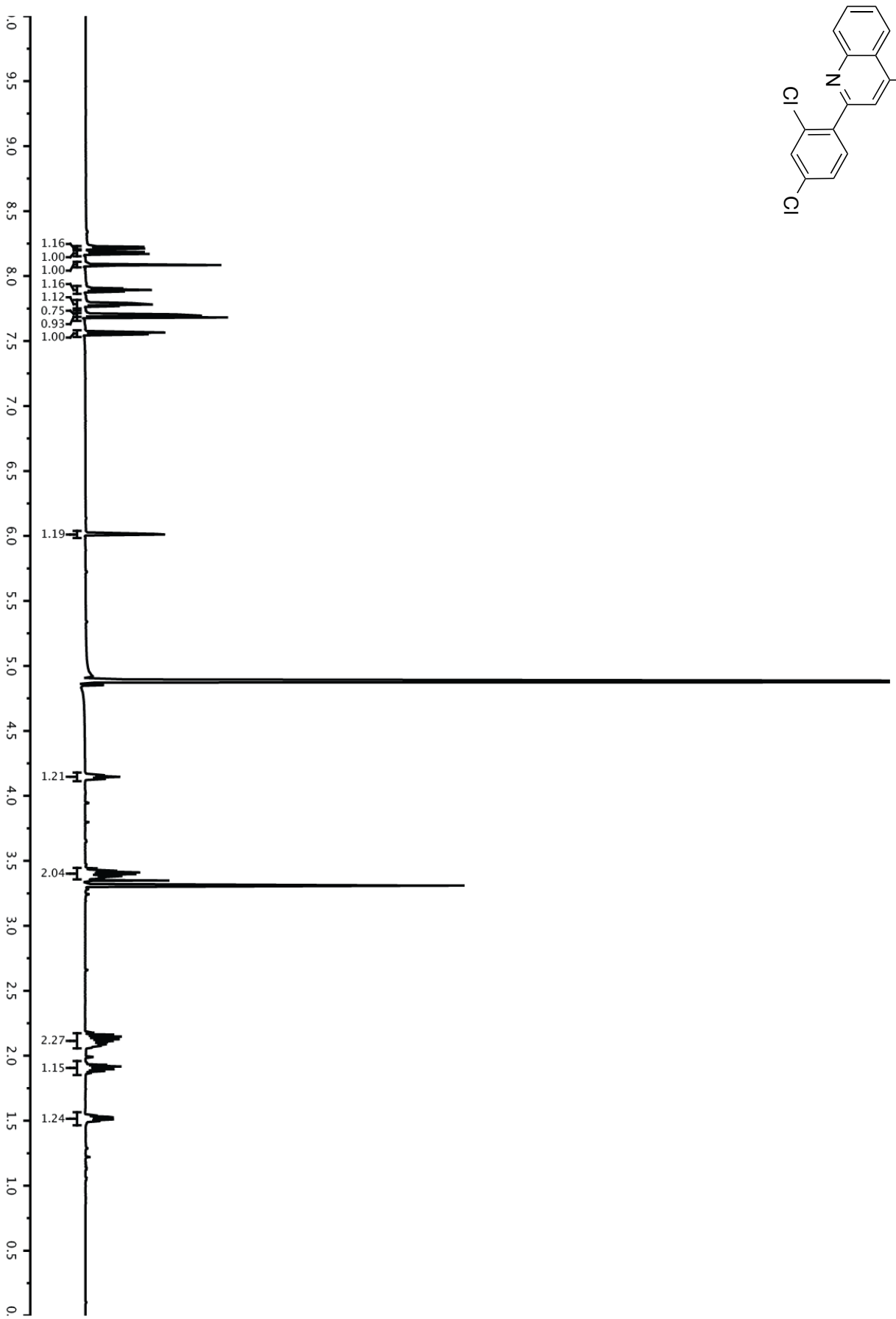




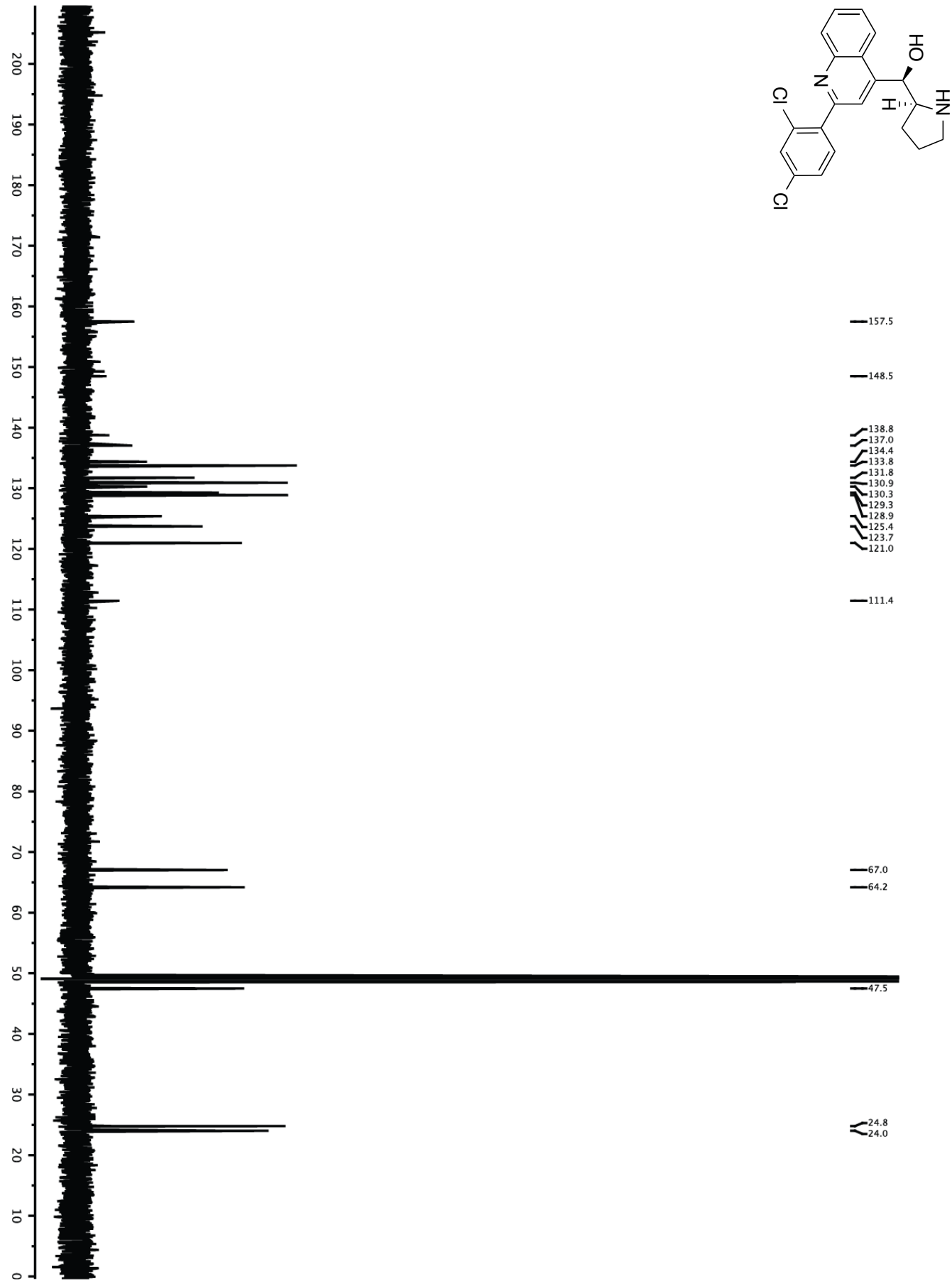
The ^{1}H Spectrum (600 MHz) of **20** in CD_3OD



The ^{13}C Spectrum (151 MHz) of **20** in CD_3OD



The ^{1}H Spectrum (600 MHz) of **21** in CD_3OD



The ^{13}C Spectrum (151 MHz) of **21** in CD_3OD

Inhibition and Detachment Assay Protocol

Experimental Procedure:

Both the inhibition assay and dispersal assay follow the general procedure developed and utilized in our laboratory previously.[4, 5, 6] In general, a GFP-expressing rugose variant and a GFP-expressing biofilm-deficient knockout Δ*vpsI*Δ*vpsII* of *V. cholerae* O1 El Tor are dispensed into 384-well screening plates from a diluted overnight culture. After dispensing DMSO control, inhibitor chemical control taurochenodeoxycholic acid (TCDCA), or antibiotic chemical control (doxycycline) in DMSO are pinned into the screening plate. Test compounds solutions in DMSO are present in columns 3-12 in each screening plate (Figure S1), allowing for both inhibition and dispersal assays to take place in the same assay plate. For the inhibition assay, compounds are pinned into the bacterial plate at t_0 and OD_{600} readings are taken immediately. After 2 hours of incubation (t_{2h}), the plate is reversed (rotated 180°) and the same compounds are pinned into the same plate in lanes 13-22 and OD_{600} readings are taken again for dispersal initial readings, followed by an additional 2.5 hours of incubation. After a total of 4.5 hours of incubation, OD_{600} readings are acquired and the differences can then be used to determine cellular viability. Immediately following absorbance readings, plates are washed, PBS buffer is added, and each well is imaged in 8 contiguous sites within each well.[4, 5, 6] Data is representative of three biological replicates and two technical replicates for each biological replicate, totaling six technical replicates.

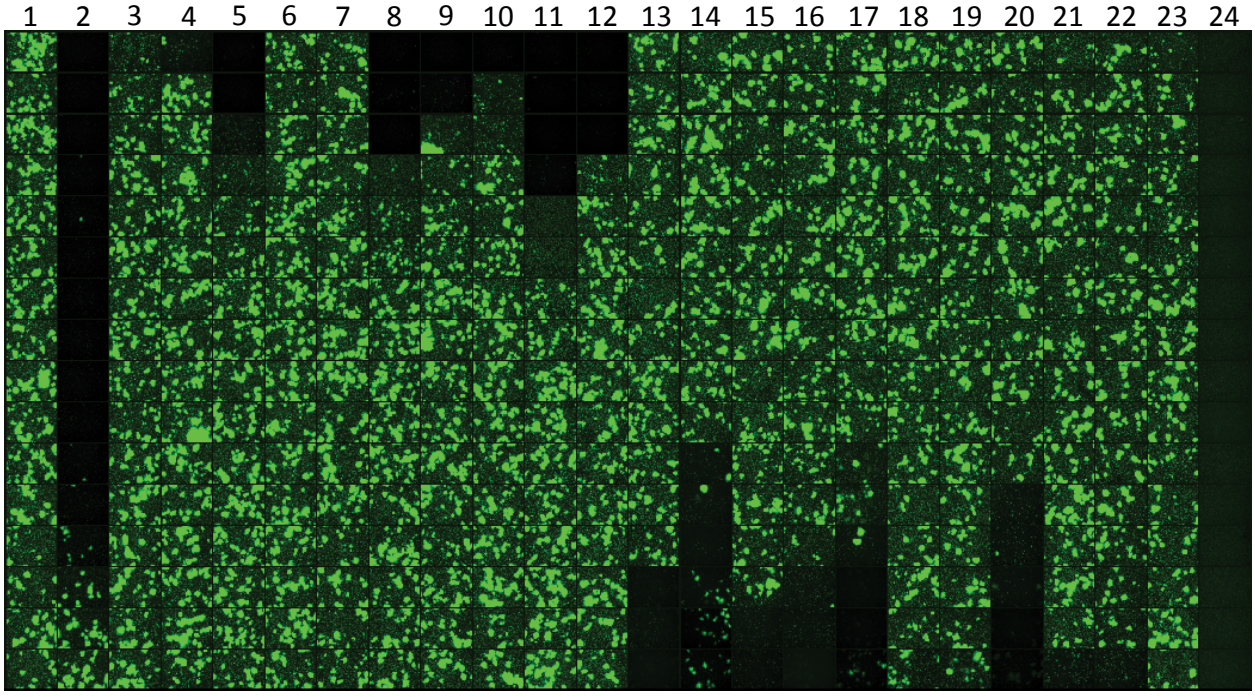


Figure S1. Lane 1 contains the DMSO vehicle control, lane 2 contains doxycycline (100μM in the top 4 wells, 50μM in the next 4 wells and a two-fold dilution in the bottom 8 wells), lane 23 contains TCDCA in a two-fold dilution from 100μM, and lane 24 contains the knockout ΔvpsIΔvpsII. Lanes 3-12 contain compound in two-fold dilutions. Lanes 13-22 contain the same compounds in the dispersal assay (dilutions starting from the bottom based on pinning geometry) within the same plate.

Data Acquisition and Processing:

Imaging data was processed as previously reported.[4] Briefly, an automated pipeline for measuring intensity and surface coverage of GFP signals was created using MetaXpress software (Molecular Devices). This creates a comma-separated output which is normalized with the OD_{600} data with a custom script in Matlab (MathWorks). The combined normalized output is analyzed using JMP (SAS) and Prism (GraphPad). BIC_{50} and BDC_{50} curves were generated in Prism using two subsequent analyses that are present in the Prism package. First, Transform was applied such that X = log (X) to obtain the log of the concentration of compound in each well on the X-axis. Second, a Non-linear fit of the transformed data was applied using the setting "log(inhibitor) vs. response -- Variable slope (four parameters)" which is under the Dose-response – Inhibition tab. No other statistical methods were applied. Some dose-response curves did not converge or produce fit lines.

Data Interpretation:

For each assay, four compound designations are possible for any well, following the analysis outlined above. In the case of strong antibiotic activity, both biofilm-associated and planktonic cells are eliminated, resulting in blank wells and normalized OD_{600} readings near zero (Figure S2A). In the case of elimination of only planktonic cells, lower OD_{600} readings would be associated with the presence of some biofilm coverage (Figure S2B). For compounds with strong inhibition of biofilm coverage, but non-bactericidal activity, high OD_{600} readings will be associated with low biofilm coverage and only evidence of planktonic cells without large biofilm colonies (Figure S3C). Finally, compounds with no effect will show large mature biofilms and planktonic cells with high OD_{600} readings, following similar appearance and characteristics to the DMSO vehicle control (Figure S2D). Compounds capable of dispersing biofilms will display the same characteristics of those of the inhibitors, but have been added after the formation of biofilms (after 2 hours).

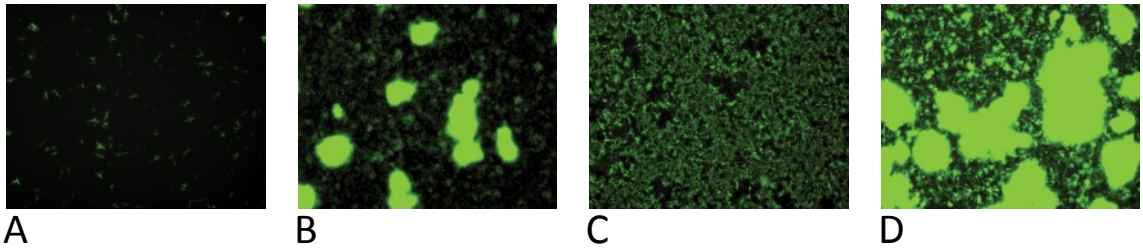


Figure S2. Percent biofilm coverage (BC). A) Strong antibiotic activity ($OD_{600} < 0.5$, BC < 0.2); B) Weak antibiotic activity ($OD_{600} < 0.5$, BC >0.2); C) Strong inhibitor activity ($OD_{600} > 0.7$, BC < 0.2); D) No activity ($OD_{600} > 0.7$, BC > 0.2).

Screening Montage:

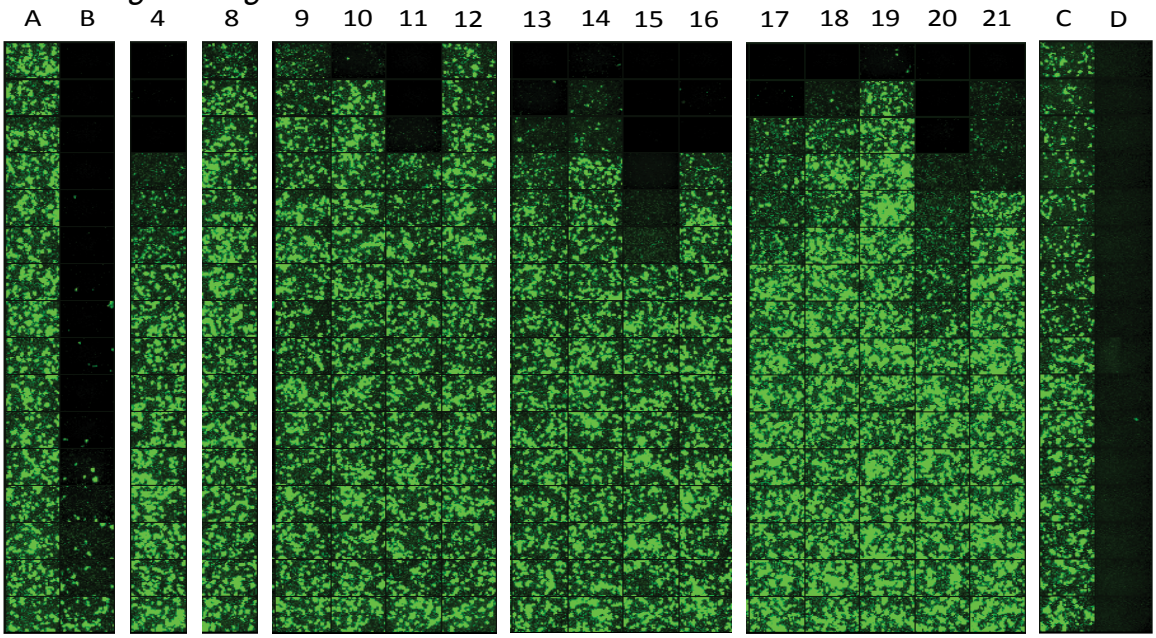


Figure S3. Representative dilution montage of compounds 4,8-21 inhibition activity. A) DMSO vehicle control lane. B) Doxycycline antibiotic control lane. C) TCDCA inhibitor control lane. D) Δ*vps*-IΔ*vps*-II control lane. Spaces between columns indicate compounds were not run in adjacent lanes. No space indicates compounds were adjacent to one another.

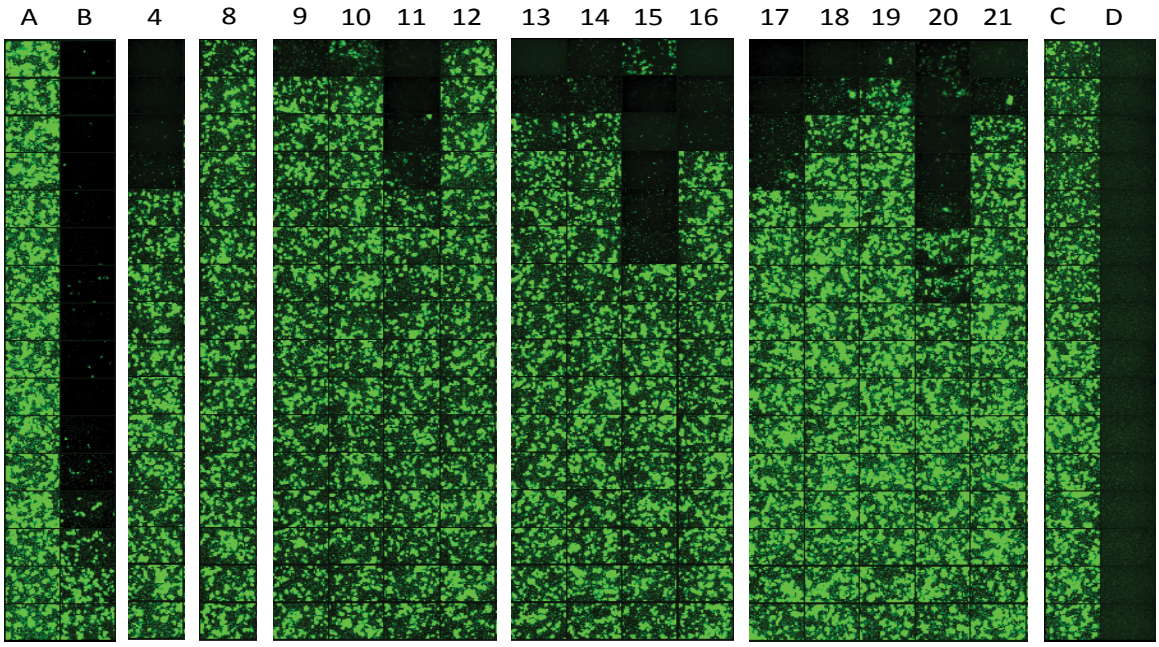


Figure S4. Representative dilution montage of compounds 4,8-21 dispersal activity. A) DMSO vehicle control lane. B) Doxycycline antibiotic control lane. C) TCDCA inhibitor control lane. D) Δ*vps*-IΔ*vps*-II control lane. Spaces between columns indicate compounds were not run in adjacent lanes. No space indicates compounds were adjacent to one another.

Minimum Inhibitory Concentration Protocol

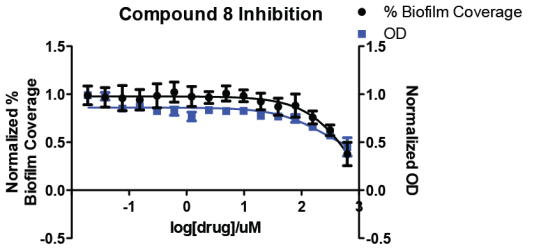
Experimental Procedure:

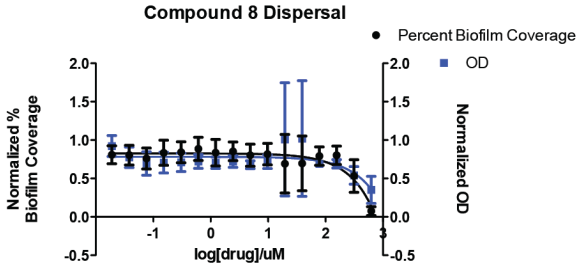
MIC values were obtained as previously reported.[3] Briefly, overnight saturated cultures of *V. cholerae* were diluted 1:1000 with fresh LB media and 40 μL of culture was dispensed into each well of sterile, clear 384-well plates. 300 nL of DMSO stock of each compound in the synthetic library using a Perkin Elmer Janus MDT robot pinning tool. After inoculation, screening plates were stacked into a Perkin Elmer EnVision plate reader/shaker and OD_{600} readings were taken once every hour for 18 hours with shaking. Computer generated growth curves for serially diluted compounds were used to determine MIC values by correlation of the OD_{600} readings at the pre-exponential phase of bacteria to the concentrations of the individual wells. Values were reported in Figure S5.

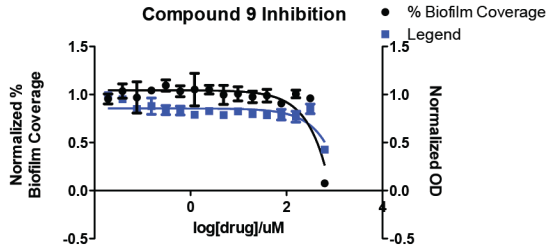
Compound	Substitution	BIC_{50}	BDC_{50}	MIC	HeLa LD_{50}
4	4-CF_3	25.3	62.6	312.5	24.3
8	Cl	>625	>625	>625	569.8
9	Ph	77.8	>250	>625	127
10	Ortho-CF_3	>250	>250	156.3	625
11	Meta-CF_3	56.5	151.5	156.3	35.5
12	4-NO_2	>625	>625	N/A	218
13	4-Me	75.8	148.3	78.1	34.5
14	4-F	123.9	>250	312.5	104.2
15	4-SF_5	12.9	15.6	78.1	23.4
16	4-Cl	79.2	119.3	78.1	65.9
17	2,4-CF_3	29.4	49.1	156.3	27.3
18	2,4-Me	169.5	175.9	312.5	108.7
19	2,4-F	>250	>250	312.5	67.2
20	3-SF_5	4.4	7.4	78.1	7.27
21	2,4-Cl	52.5	153.3	>625	N/A

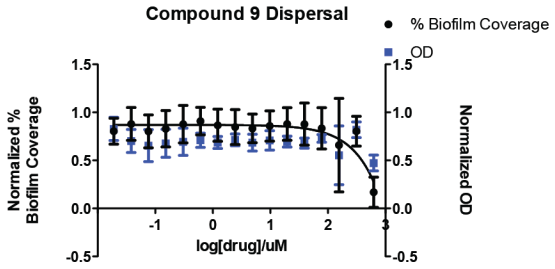
Table S1. Biological Activity of Second Generation Library. BIC: Biofilm Inhibitory Concentration, BDC: Biofilm Dispersal Concentration. Minimum Inhibitory Concentration (MIC), Screening data from Cytological Profiling assay (HeLa LD_{50}) Activities in μM.

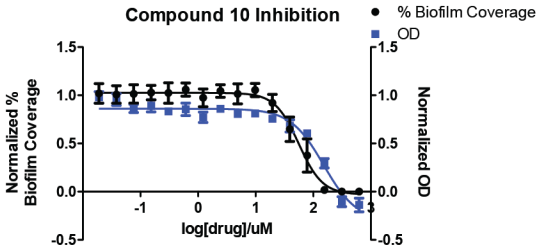
Inhibition and Dispersal Activity Curves:

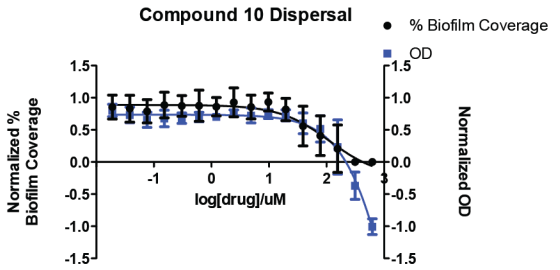


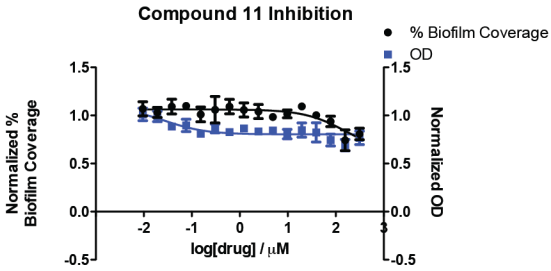


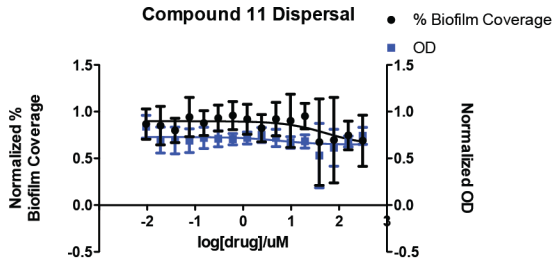


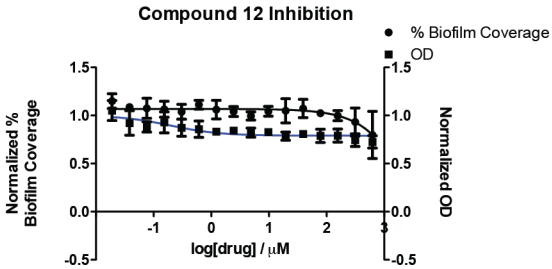


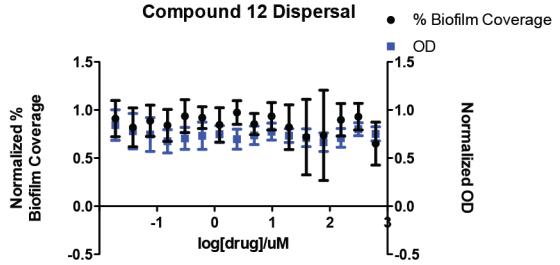


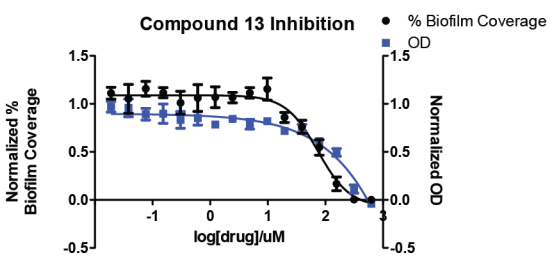


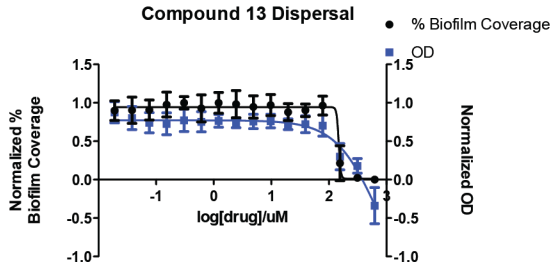


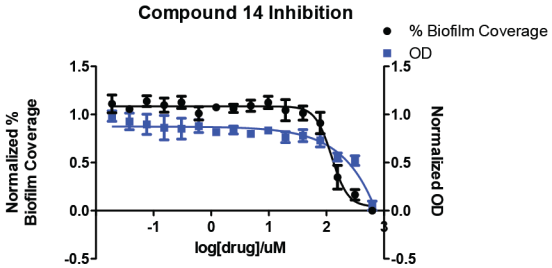


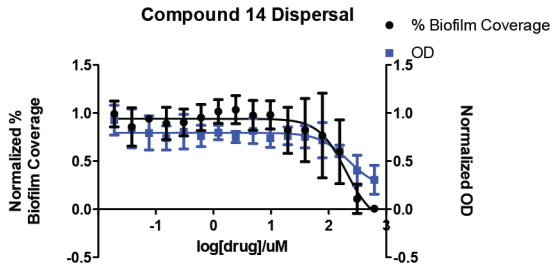


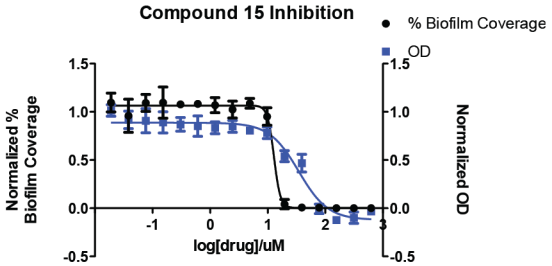


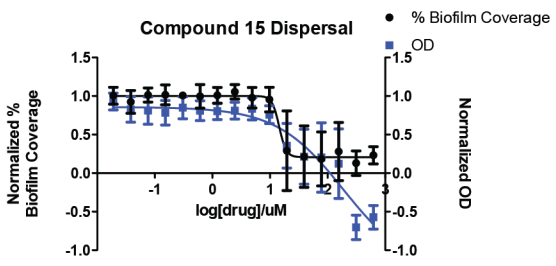

Compound 13 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

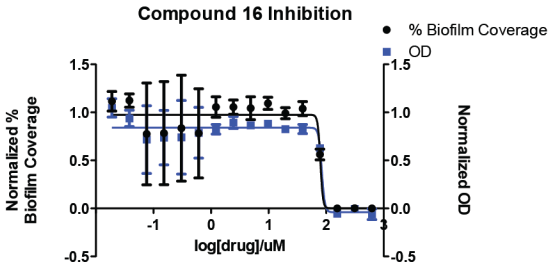

Compound 13 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

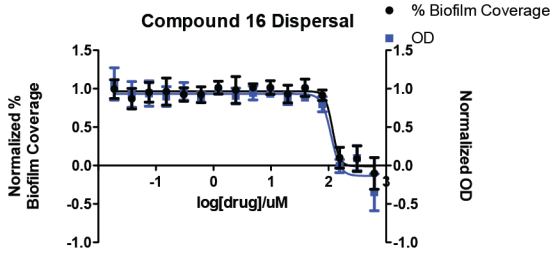

Compound 14 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

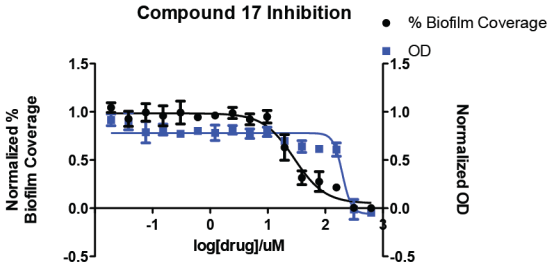

Compound 14 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

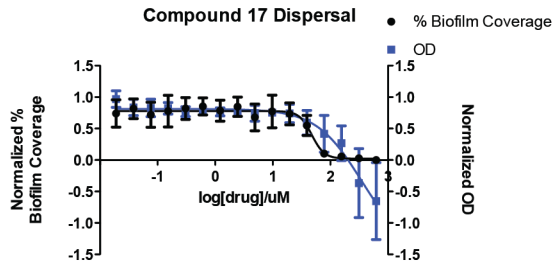

Compound 15 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

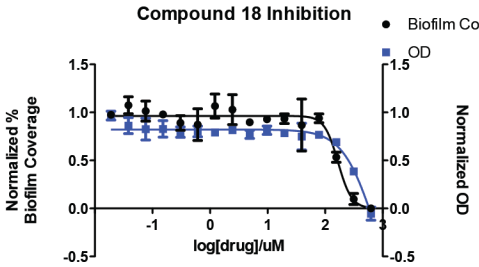

Compound 15 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

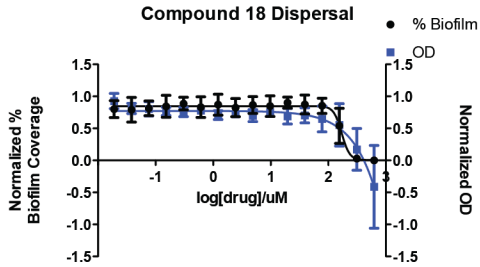

Compound 16 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

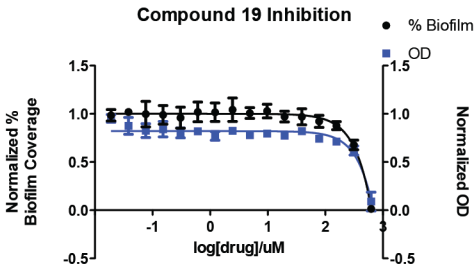

Compound 16 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

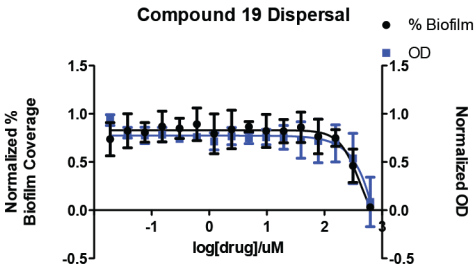

Compound 17 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

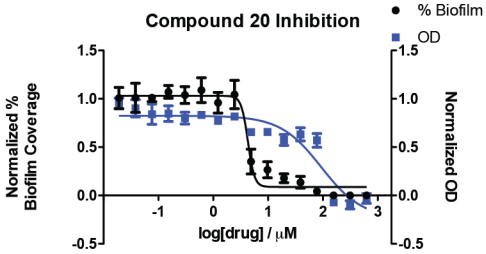

Compound 17 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

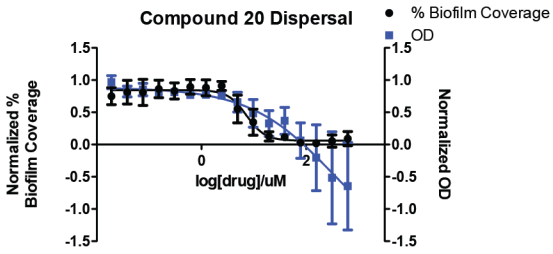

Compound 18 Inhibition
Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

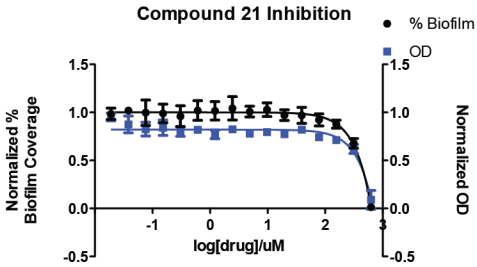

Compound 18 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

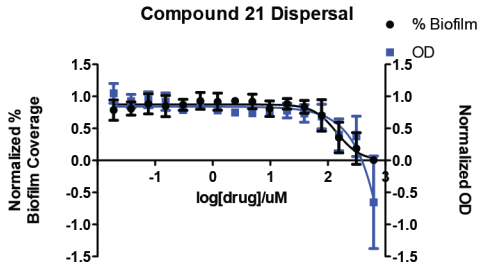

Compound 19 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM


Compound 19 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

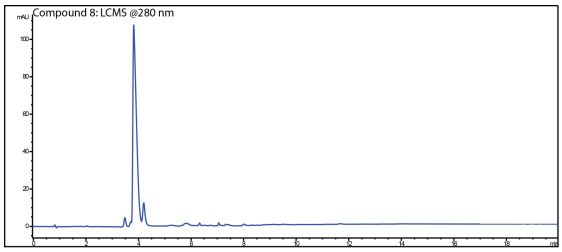

Compound 20 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug] / μM

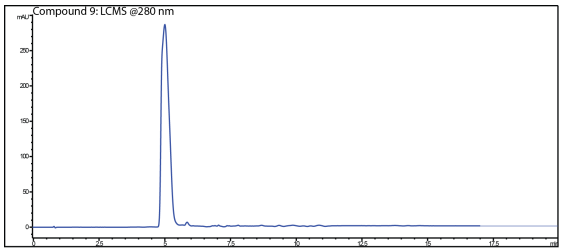

Compound 20 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

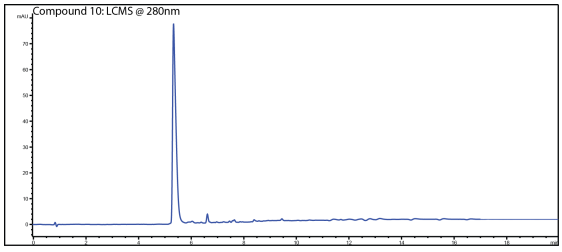

Compound 21 Inhibition
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

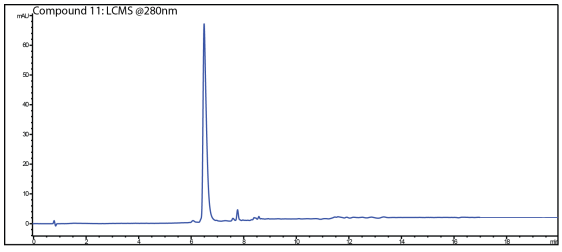

Compound 21 Dispersal
% Biofilm Coverage
OD
Normalized % Biofilm Coverage
Normalized OD
log[drug]/uM

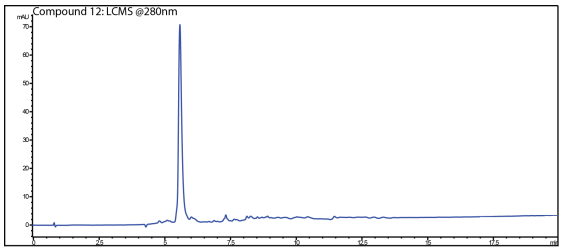
Analytical Quality Control Liquid Chromatograms*:*

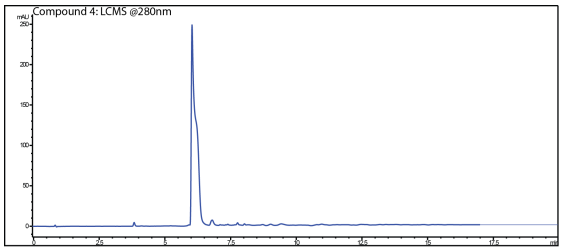


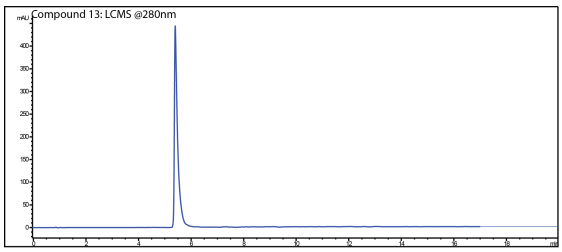


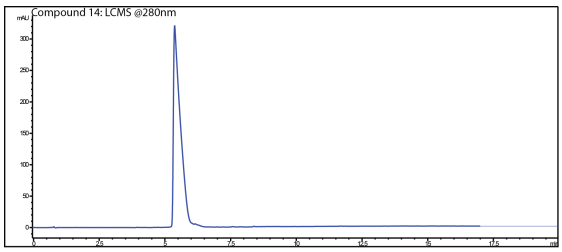


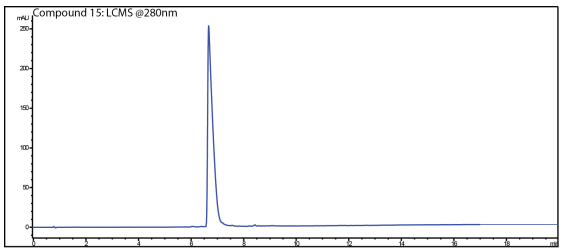


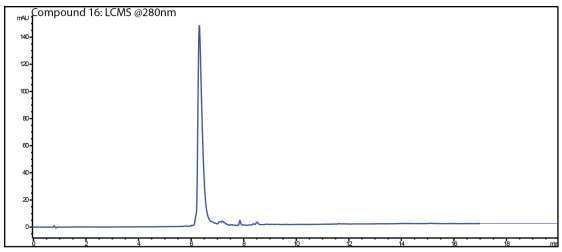


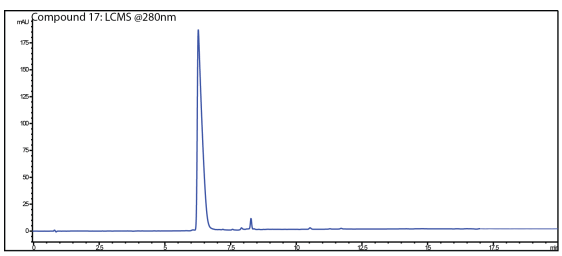


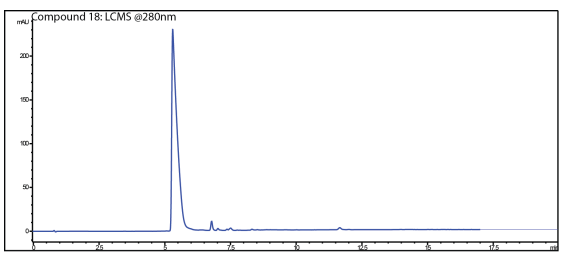


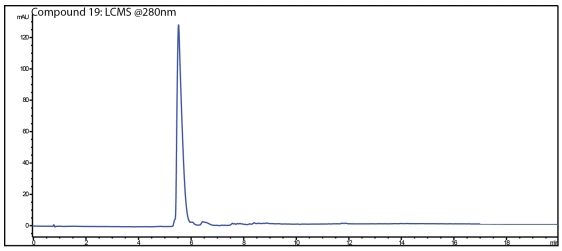


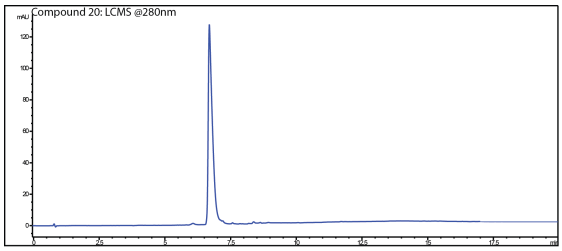


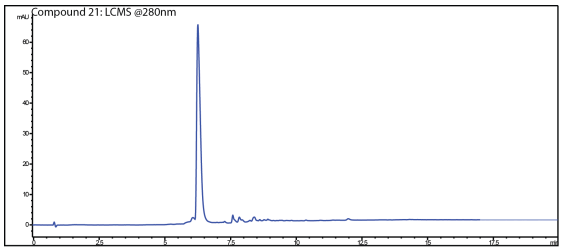












Liquid Chromatogram conditions: 10% MeOH/H_2O to 90 %MeOH/H_2O over 15 min and holding at same conditions for remaining 5 minutes.

[4] K. C. Peach, W. M. Bray, N. J. Shikuma, N. C. Gassner, R. S. Lokey, F. H. Yildiz and R. G. Linington, *Mol. Biosyst.*, 2011, **7**, 1176-1184.
[5] G. Navarro, A. T. Cheng, K. C. Peach, W. M. Bray, V. S. Bernan, F. H. Yildiz and R. G. Linington, *Antimicrob. Agents Chemother.*, 2014, **58**, 1092–1099.
[6] C. J. A. Warner, A. T. Cheng, F. H. Yildiz and R. G. Linington, *Chem. Commun.*, 2014, **51**, 1305–1308.