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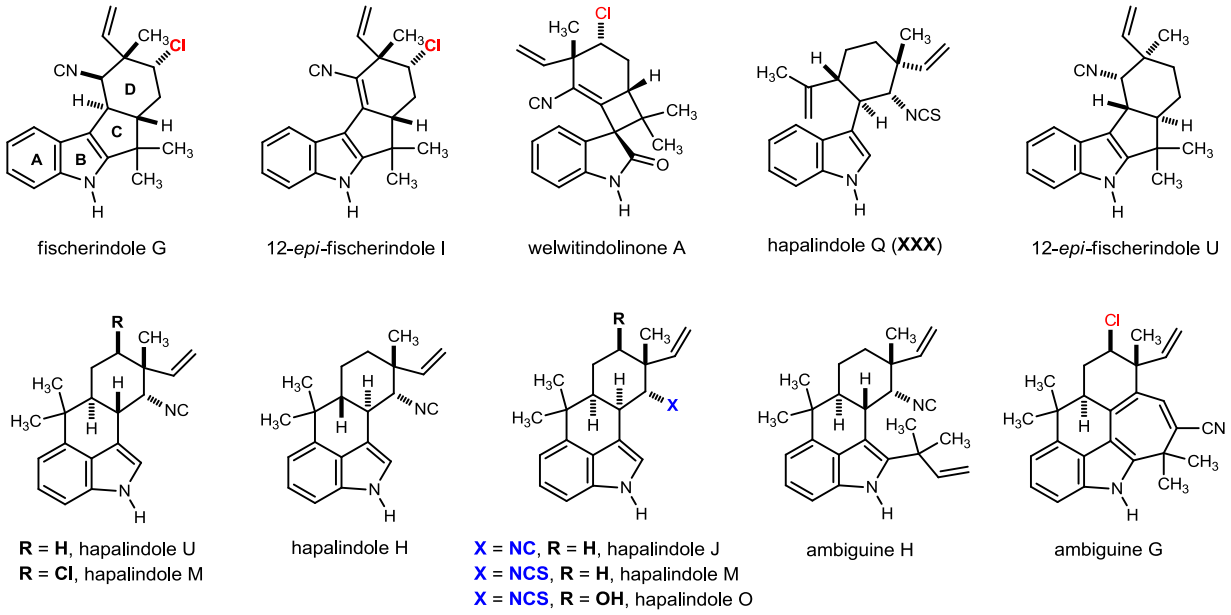
Chart 1. Structural Formulas of Representative Indole Alkaloids Isolated from Terrestrial Blue-Green Algae[1]



[1] Hapalindoles J, M, O, H, U: Muratake, H.; Natsume, M. *Tetrahedron* **1990**, *46*, 6331. Sakagami, M.; Muratake, H.; Natsume, M. *Chem. Pharm. Bull.* **1994**, *42*, 1393. Muratake, H.; Kumagami, H.; Natsume, M. *Tetrahedron* **1990**, *46*, 6351. Hapalindole Q: Vaillancourt, V.; Albizati, K. F. *J. Am. Chem. Soc.* **1993**, *115*, 3499. Kinsman, A. C.; Kerr, M. A. *Org. Lett.* **2001**, *3*, 3189. Kinsman, A. C.; Kerr, M. A. *J. Am. Chem. Soc*. **2003**, *125*, 14120. Hapalindole Q, 12-*epi*-fischerindole: Baran, P. S.; Richter, J. M. *J. Am. Chem. Soc***. 2004**, *126*, 7450. Hapalindole G: Fukuyama, T.; Chen, X. Q. *J. Am. Chem. Soc.* **1994**, *116*, 3125. Welwitindolinone A, fischerindoles I, G: Baran, P. S.; Richter, J. M. *J. Am. Chem. Soc.* **2005**, *127*, 15394. Welwitindolinone A: Reisman, S. E.; Ready, J. M.; Hasuoka, A.; Smith, C. J.; Wood, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 1448. (+)-Ambiguine H, (-)-hapalindole U, (-)-fischerindole I, (+)-welwitindolinone A: Baran, P. S.; Maimone, T. J.; Richter, J. M. *Nature* **2007**, *446*, 404. Richter, J. M.; Ishihara, Y.; Masuda, T.; Whitefield, B. W.; Llamas, T.; Pohjakallio, A.; Baran, P. S. *J. Am. Chem. Soc*. **2008**, *130*, 17938.

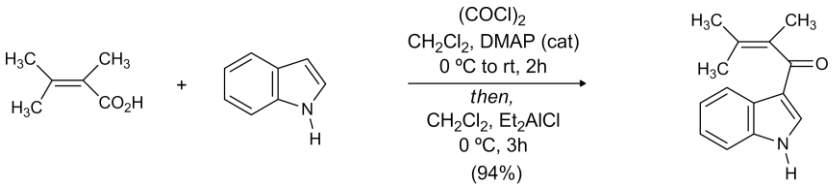
Experimental Section

Unless otherwise noted, all reactions were carried out under argon or nitrogen using flame or oven dried glassware. Tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were dried by passage through a column of activated alumina as described by Grubbs.[2] Molecular sieves (spheres, 4Å) were activated at 400 ºC and then stored at room temperature in an air-tight container.

Flash column chromatography was performed using Sorbent Technologies 40-63 mm, pore size 60 Å silica gel with solvent systems indicated. Analytical thin layer column chromatography was performed using Sorbent Technologies 250 mm glass-backed UV254 silica gel plates that were visualized by fluorescence upon 250 nm radiation and/or the by use of ceric ammonium molybdate or potassium permanganate. Solvent removal was effected by rotary evaporation under vacuum (~ 25-40 mmHg).

IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer and are reported in wavenumbers (cm^{-1}). Liquids and oils were analyzed as neat films on a NaCl plate (transmission), whereas solids were applied to a diamond plate (ATR). Proton nuclear magnetic resonance spectra were recorded on either a Varian INOVA-400 (400 MHz), VXR-400 (400 MHz) or Bruker DRX-500 (500 MHz) spectrometers and are recorded in parts per million from residual undeuterated chloroform and are reported as follows: chemical shift (multiplicity [s=singlet, d=doublet, t=triplet, q=quartet, qu=quintet, m=multiplet], coupling constant(s), integration). ^{13}C NMR data were recorded on a Bruker DRX-500 spectrometer. Ratios of diastereomers and isomeric products were measured directly from integration of ^{1}H NMR absorptions of protons common to the components.

[2] Pangborn, A. B.; Giardello, M.A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.



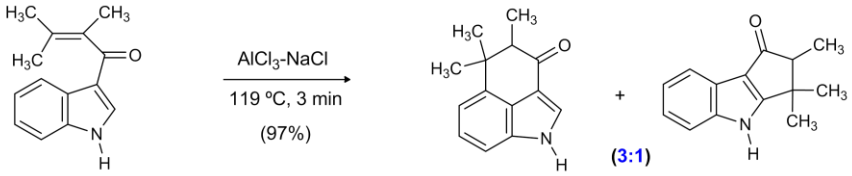
1-(1*H*-Indol-3-yl)-2,3-dimethylbut-2-en-1-one (**4**).

To a 0 °C solution of the acid (12.3 g, 112 mmol) in dichloromethane (240 mL), was added oxalyl chloride (19.6 mL, 224 mmol) over 5 minutes. Dimethyl aminopyridine (12.8 mg, 0.10 mmol) was added and the solution was slowly warmed to room temperature and stirred until complete conversion was achieved, as evidenced by ^{1}H NMR. The solvent was removed *in vacuo* to give the acyl chloride (13.5 g, 91%), which was used without further purification.[3]

To a 0 °C solution of indole (9.24 g, 78.7 mmol) in CH_2Cl_2 (300 mL) was added Et_2AlCl (56.8 mL, 102 mmol, 1.8 M in toluene) dropwise. The reaction was stirred for 30 minutes at 0 °C, and acyl chloride (13.5 g, 102 mmol) in CH_2Cl_2 (50 mL) was added dropwise to the solution. The reaction was stirred for 3 h at 0 °C, with the last 30 min having minimal ice within the ice/water bath. The reaction was quenched by slow dropwise addition of pH=7 buffer solution followed by the addition of satd aq $NaHCO_3$ in the same fashion. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 10-20% ethyl acetate in hexanes) to afford the title product as a yellow solid (15.8 g, 94%). R_f = 0.65 (SiO_2, 50% EtOAc/hexanes); mp = 118-120 °C; IR (film) 3184 (br s), 2983, 2926, 1597 (br s), 1517, 1436, 1376 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.11 (br s, 1H), 8.39 (ddd, *J* = 10.0, 4.0, 3.2 Hz, 1H), 7.73 (d, *J* = 3.2 Hz, 1H), 7.45 (ddd, *J* = 10.0, 4.0, 3.2 Hz, 1H), 7.33-7.26 (m, 2H), 1.96 (br d, *J* = 1.2 Hz, 3H), 1.81 (s, 3H) 1.68 (br d, *J* = 1.2 Hz, 3H); ^{13}C NMR

[3] Due to the low boiling point (~145 °C), the acyl chloride should be put under high vacuum for longer duration of time (~2 minutes).

(100 MHz, $CDCl_3$) ppm 198.0, 137.0, 134.6, 131.5, 130.5, 125.5, 123.6, 122.6, 121.9, 117.0, 111.9, 22.4, 19.8, 17.0; HRMS (EI): Exact mass calcd for $C_{14}H_{16}NO$ $[M+H]^+$ 214.1226, found 214.1220.

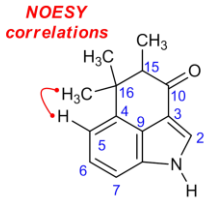


4,5,5-Trimethyl-4,5-dihydrobenzo[cd]indol-3(1*H*)-one (**6**).

The indole (3.00 g, 14.1 mmol) was added in one portion to a melt of $AlCl_3$ (27.1 g, 141 mmol) and NaCl (4.11 g, 70.4 mmol) at 119 °C. After 3 min, the reaction was poured into ice cold water and the solution was made basic by the addition of satd aq $NaHCO_3$. The solution was extracted with CH_2Cl_2 and the combined organic layers were dried, filtered, and concentrated to a brown oil. Column chromatography (SiO_2, 15-20-25-30-35% ethyl acetate in hexanes) provided the desired tricyclic indole as a pale yellow oil (2.17 g, 77%) and its regioisomer as a white solid (710 mg, 23%).

2,3,3-Trimethyl-2,3-dihydrocyclopenta[b]indol-1(4*H*)-one (**5**).

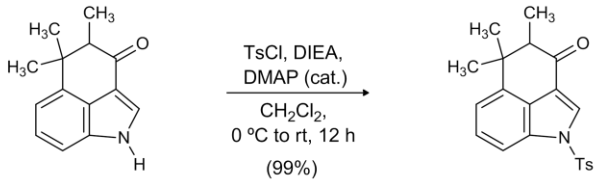
R_f = 0.42 (SiO_2, 50% EtOAc/hexanes); IR (film) 3238 (br), 2967, 2870, 1651, 1607, 1525, 1451, 1338 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.87 (br s, 1H), 7.72 (dd, *J* = 6.6, 3.6 Hz, 1H), 7.30 (s, 1H), 7.29 (dd, *J* = 10.1, 8.2 Hz, 1H), 7.16 (ddd, *J* = 7.8, 4.8, 4.8 Hz, 1H), 2.64 (q, *J* = 7.2 Hz, 1H), 1.38 (s, 6H), 1.14 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 198.3, 138.7, 133.5, 127.0, 124.6, 123.7, 116.7, 113.5, 109.3, 56.8, 41.7, 29.9, 23.8, 13.1; Exact mass calcd for $C_{14}H_{16}NO$ $[M+H]^+$ 214.1226, found 214.1225.



A NOESY crosspeak was observed between the methyl protons and C*5*

aromatic proton. Other key observations, including HMBC correlation between C16 and H5, confirmed the assigned structure of the desired tricyclic indole.

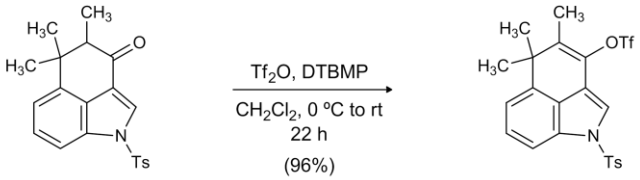
Data for (5): R_f = 0.38 (SiO_2, 50% EtOAc/hexanes); mp = 235-237 °C; IR (film) 3212 (br), 2960, 2834, 1661,1471, 1450 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.16 (br s, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.27-7.19 (m, 2H), 2.87 (q, *J* = 7.6 Hz, 1H), 1.53 (s, 3H), 1.37 (s, 3H), 1.29 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 198.1, 173.8, 142.1, 123.6, 122.3, 121.5, 121.0, 117.1, 112.3, 59.1, 38.8, 27.5, 24.2, 11.3; Exact mass calcd for $C_{14}H_{16}NO$ $[M+H]^+$ 214.1226, found 214.1224.



6,6-Dimethyl-2-tosyl-6,7-dihydrobenzo[cd]indol-8(2*H*)-one (**7**).

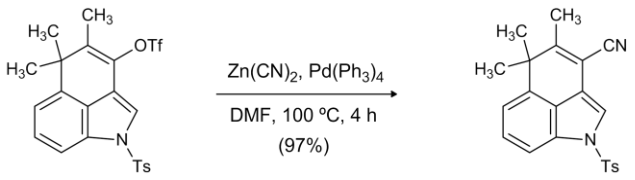
To a solution of the indole (3.05 g, 14.3 mmol) and diisopropyl ethylamine (4.0 mL, 22.9 mmol) in CH_2Cl_2 (90 mL) at 0 °C was added *p*-toluenesulfonyl chloride (3.54 mg, 18.6 mmol) and dimethyl aminopyridine (39.2 mg, 320 µmol). The reaction was stirred for 30 min before being warmed to rt and stirred for 15 h. The reaction was quenched with satd aq NH_4Cl and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated to a yellow oil. Column chromatography (SiO_2, 10-20% ethyl acetate in hexanes) provided the *N*-tosylated indole as a white solid (5.2 g, 99%). R_f = 0.29 (SiO_2, 20% EtOAc/hexanes); mp = 142-144 °C; IR (film) 3127, 2969, 2925, 2870, 1690, 1544, 1434, 1379, 1366 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 2.64 (q, *J* = 7.2 Hz, 1H), 2.38 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.09 (d, *J* = 7.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) ppm

197.7, 145.8, 139.6, 134.8, 133.0, 130.2, 128.2, 127.2, 126.6, 124.3, 119.1, 117.0, 111.4, 56.7, 41.8, 29.3, 24.3, 21.7, 12.0; HRMS (EI): Exact mass calcd for $C_{21}H_{22}NO_3S$ $[M+H]^+$ 368.1315, found 368.1311.



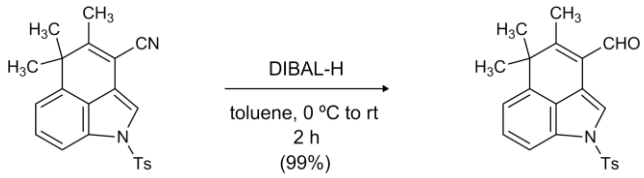
4,5,5-Trimethyl-1-tosyl-1,5-dihydrobenzo[cd]indol-3-yl trifluoromethanesulfonate (**S1**).

To a 0 °C solution of ketone (1.05 g, 2.86 mmol) and 4-methyl-2,6-di-^{t}butylpyridine (1.06 g, 5.15 mmol) in CH_2Cl_2 (5.0 mL) was added trifluoromethanesulfonyl anhydride (0.77 mL, 4.58 mmol) dropwise. The reaction was allowed to warm to room temperature and stirred for 22 h. The reaction was quenched by slow dropwise addition of satd aq $NaHCO_3$ at 0 °C and the solution was stirred for 5 minutes at rt. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 5-10% ethyl acetate in hexanes) to afford the enol triflate as a white solid (1.32 g, 53%). R_f = 0.42 (SiO_2, 20% EtOAc/hexanes); mp = 101-103 °C; IR (film) 2969, 2926, 2855, 1428, 1378, 1246, 1190, 1008 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.32 (s, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 2.35 (s, 3H), 2.03 (s, 3H), 1.49 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 145.1, 138.2, 137.4, 135.4, 135.0, 133.2, 130.0, 127.1, 126.9, 126.6, 119.3, 118.5 (q, $^1J_{CF}$ = 320 Hz), 116.7, 113.7, 111.4, 44.4, 29.9, 21.6, 12.4; HRMS (EI): Exact mass calcd for $C_{22}H_{21}F_3NO_5S_2$ $[M+H]^+$ 500.0808, found 500.0815.



4,5,5-Trimethyl-1-tosyl-1,5-dihydrobenzo[cd]indole-3-carbonitrile (**S2**).

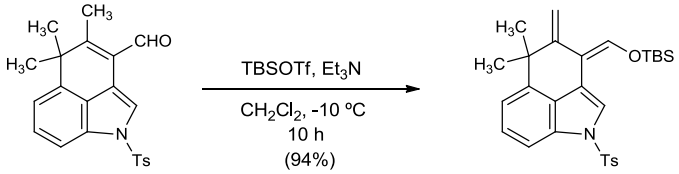
To a degassed solution of enol triflate (3.90 g, 7.82 mmol) and zinc cyanide (1.10 g, 9.38 mmol) in DMF (20 mL) was added $Pd(Ph_3)_4$ (451 mg, 0.39 mmol) and the reaction stirred at 100 °C for 4 h. The reaction was cooled to rt and quenched with H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 10-20% ethyl acetate in hexanes) to afford the nitrile as a white solid (2.79 g, 97%). R_f = 0.29 (SiO_2, 20% EtOAc/hexanes); mp =192 °C; IR (film) 2973, 2927, 2222, 1439, 1369, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.39 (s, 1H), 7.36 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 2.36 (s, 3H), 2.30 (s, 3H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 160.2, 145.1, 137.6, 135.2, 133.1, 130.0, 127.3, 126.9, 125.0, 119.1, 117.7, 116.0, 115.0, 111.4, 102.0, 42.3, 29.9, 21.6, 18.7; HRMS (EI): Exact mass calcd for $C_{22}H_{21}N_2O_2S$ $[M+H]^+$ 377.1318, found 377.1309.



4,5,5-Trimethyl-1-tosyl-1,5-dihydrobenzo[cd]indole-3-carbaldehyde (**8**).

To a 0 °C solution of nitrile (2.45 g, 6.51 mmol) in toluene (30 mL) was added DIBAL-H (4.99 mL, 7.49 mmol, 1.5 M in toluene) and stirred for 1 h at 0 °C. The reaction was quenched by the

stepwise addition of H_2O (30 mL) and 6M HCl (100 mL). The reaction was allowed to warm to room temperature and stirred until the layers became clear (~6 h). The layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 20% ethyl acetate in hexanes) to afford the enal as a white solid (2.45 g, 99%). R_f = 0.16 (SiO_2, 20% EtOAc/hexanes); mp =188 °C; IR (film) 2972, 2925, 2871, 1672, 1438, 1370 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 10.42 (s, 1H), 8.05 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.33 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 1H), 2.44 (s, 3H), 2.33 (s, 3H), 1.52 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 190.2, 161.9, 144.6, 137.8, 135.6, 132.6, 129.8, 126.9, 126.4, 126.3, 126.1, 120.8, 118.7, 113.0, 111.1, 42.9, 29.7, 21.6, 13.9; HRMS (EI): Exact mass calcd for $C_{22}H_{22}NO_3S$ $[M+H]^+$ 380.1320, found 380.1332.

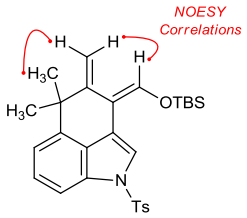


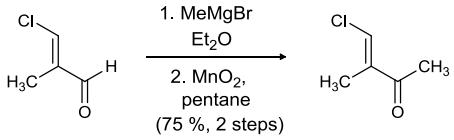
(*Z*)-3-(((*tert*-Butyldimethylsilyl)oxy)methylene)-5,5-dimethyl-4-methylene-1-tosyl-1,3,4,5-tetrahydrobenzo[cd]indole (**9**).

To a -10 °C solution of enal (1.03 g, 2.72 mmol) and triethylamine (833 µL, 5.98 mmol) in CH_2Cl_2 (13 mL) was added TBSOTf (808 µL, 4.62 mmol) and the reaction was stirred for 10 h at -10 °C. The reaction was quenched by slow dropwise addition of satd aq NH_4Cl and the solution was warmed to rt. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 5-10% ethyl acetate in hexanes) to afford the diene as a colorless oil (1.26 g, 94%). R_f = 0.57 (SiO_2, 20%

EtOAc/hexanes); IR (film) 2955, 2927, 2856, 1637, 1375, 1174 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 10.5 Hz, 2H), 7.74 (d, *J* = 10.5 Hz, 1H), 7.66 (s, 1H), 7.28 (dd, *J* = 10.0, 10.0 Hz, 1H), 7.18 (d, *J* = 10.5 Hz, 2H), 7.15 (d, *J* = 9.5 Hz, 1H), 6.83 (s, 1H), 5.06 (d, *J* = 0.5 Hz, 1H), 4.90 (d, *J* = 0.5 Hz, 1H), 2.33 (s, 3H), 1.40 (s, 6H), 1.01 (s, 9H), 0.30 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 151.2, 144.5, 140.3, 137.9, 135.7, 132.9, 129.8, 127.1, 126.8, 125.6, 119.6, 116.8, 116.3, 114.7, 111.1, 106.5, 40.2, 28.4, 25.7, 21.5, 18.3, -5.2; HRMS (EI): Exact mass calcd for $C_{22}H_{21}NO_3S$ $[M-C_6H_{14}Si]^+$ 379.1278, found 379.1278.

A NOESY crosspeak was observed between the methylene proton of the exocyclic alkene and the methine proton, consistent with the diene geometry depicted.



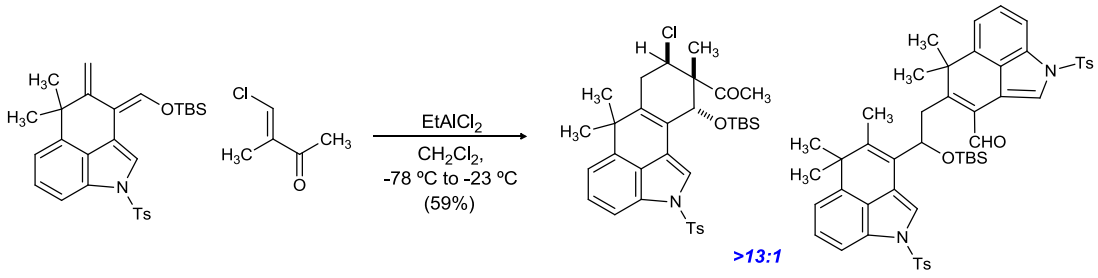


4-Chloro-3-methyl-but-3-en-2-one (**10b**).

A solution of methyl magnesium bromide (33.6 mL, 3.0 M in ether), in ether (70 mL) was cooled to 0 °C and treated with a solution of β-chloro-α-methyl acrolein (10.0g, 95.7 mmol) as a pre-dissolved solution in ether (16 mL). The mixture was warmed to room temperature and quenched with an ether-ice mixture, followed by an aqueous work-up to give the alcohol in sufficient purity for oxidation.

The alcohol (11.53g, 95.7 mmol) was added to a slurry of MnO_2 (83.2 g, 957 mmol) in pentane (300 mL) and stirred vigorously for 22 hours. Additional MnO_2 (8.32 g, 95.7 mmol) was added and the mixture was stirred for an additional 12 h. The mixture was filtered over Celite and concentrated to a yellow oil that was purified by flash chromatography (SiO_2, 8% ether in

hexanes) to furnish the ketone as a light yellow oil (8.5 g, 75%). R_f = 0.10 (6% EtO_2/hexanes); IR (film) 3094, 1678 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 7.26 (q, *J* = 1.6 Hz, 1H), 2.32 (s, 3H), 1.93 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 195.6, 140.2, 133.5, 25.8, 12.0; HRMS (EI): Exact mass calcd for C_5H_7ClO $[M]^+$ 118.0182, found 118.0182.



1-((8*R*,9*S*,10*R*)-10-((*tert*-Butyldimethylsilyl)oxy)-8-chloro-6,6,9-trimethyl-2-tosyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indol-9-yl)ethanone (**11**).

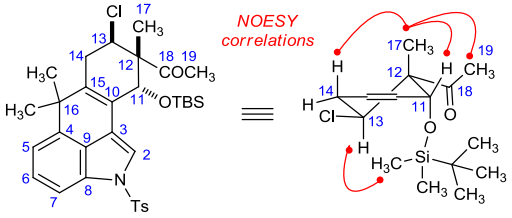
$EtAlCl_2$ (1.79 mL, 3.22 mmol, 1.8 M in toluene) was added dropwise to a -78 °C solution of the diene (1.59 g, 3.22 mmol) and the dienophile (2.66 g, 22.6 mmol) in CH_2Cl_2 (13.0 mL).[4] The reaction was stirred for 30 minutes at -78 °C and 2.5 h at -23 °C. The reaction was quenched by slow dropwise addition of satd aq $NaHCO_3$ and the solution was warmed to rt. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 5-10% ethyl acetate in hexanes) to afford the Diels-Alder adduct (1.16 g, 59%) in addition to the Mukaiyama aldol product (96 mg, 7%).

Diels-Alder adduct (**11**): The adduct was isolated as a single diastereomer (^1H NMR). R_f = 0.36 (SiO_2, 20% EtOAc/hexanes); mp 240-241 °C (decomp); IR (film) 2928, 2887, 2856, 1716, 1367, 1186, 1170, 1117, 1091 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.25 (s, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* =

[4] Rapid addition leads to lower yields.

7.8 Hz, 1H), 5.10 (dd, *J* = 9.6, 7.2 Hz, 1H), 4.76 (s, 1H), 3.15 (dd, *J* = 19.2, 7.2 Hz, 1H), 2.61 (dd, *J* = 18.6, 9.6 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H), 1.48 (s, 3H), 1.42 (s, 3H), 1.11 (s, 3H), 0.71 (s, 9H), -0.08 (s, 3H), -0.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 207.3, 144.9, 142.7, 139.7, 135.8, 133.6, 129.9 (2C), 126.9, 126.4, 121.7, 119.2, 118.9, 116.3, 111.1, 74.5, 56.7, 56.1, 40.8, 34.9, 31.2, 28.8, 26.5, 25.6, 21.5, 18.2, 13.8, -3.7, -4.2; HRMS (EI): Exact mass calcd for $C_{33}H_{42}ClNO_4SSi$ $[M]^+$ 611.2287, found 611.2306.

A complete 2D NMR analysis was carried out to elucidate the structure of Diels-Alder adduct. NOESY correlations from both H11 to H17[5] and H11 to C19, and the absence of NOESY correlations between H11 to either H13 and H14, suggested that the H11 proton is equatorial.



Additionally, a NOESY correlation between TBS-methyl protons and H13α indicated that the -OTBS is in the axial position, thus confirming the stereochemistry at C11. The stereochemistry at C12, which has an axial methyl group, could be relayed to both H14β and H19. These observations support the assignment of the Diels-Alder adduct as depicted.

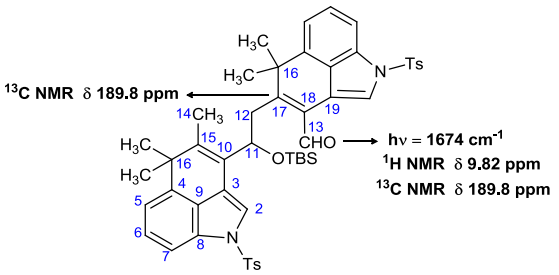
4-(2-((*tert*-Butyldimethylsilyl)oxy)-2-(4,5,5-trimethyl-1-tosyl-1,5-dihydrobenzo[cd]indol-3-yl)ethyl)-5,5-dimethyl-1-tosyl-1,5-dihydrobenzo[cd]indole-3-carbaldehyde (12).

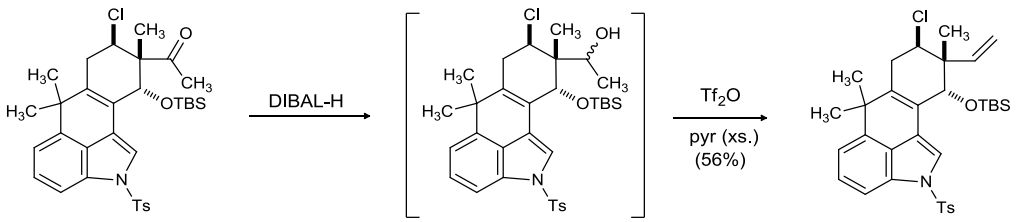
R_f = 0.23 (SiO_2, 20% EtOAc/hexanes); mp 200-202 °C; IR (film) 2962, 2928, 2857, 1674, 1437, 1367, 1187, 1169, 1095 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.07 (s, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.57 (s, 1H), 7.36 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.25 (s, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 4.99 (dd, *J* = 6.5, 6.5 Hz, 1H), 3.28 (br s,

[5] Heterocycle numbering used here throughout instead of IUPAC/CAS numbering.

2H), 2.33 (s, 6H), 1.65 (s, 3H), 1.64 (s, 3H), 1.50 (s, 3H), 1.31 (s, 3H), 1.29 (s, 3H), 0.77 (s, 9H), -0.08 (s, 3H), -0.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 189.7, 159.0, 144.4, 144.3, 139.3, 137.4, 135.5, 135.3, 132.8, 132.4, 129.6, 129.5, 128.4, 126.8, 126.5 (2C), 126.1, 126.0, 121.3, 118.6, 118.3, 115.2, 113.1, 111.0, 110.4, 71.9, 43.1, 41.2, 34.5, 30.7, 27.4, 25.5, 21.3, 17.8, 15.0, -5.0, -5.3; HRMS (EI): Exact mass calcd for $C_{50}H_{56}N_2Na\ O_6S_2Si$ $[M]^+$ 895.3247, found 895.3283.

The ^{1}H NMR analysis showed one well resolved dd pattern at 4.95 in addition to two poorly resolved patterns at 3.30 and 2.25, which are the methine (C11) and methylene (C12) adjacent to each other. A weak IR stretch at 1675 cm^{-1}, and the presence of ^{1}H NMR and ^{13}C NMR NMR peaks at 9.82 and 189.8 ppm indicated the presence of an α,β-unsaturated aldehyde. The presence of enal was confirmed by the downfield shift of C17 in ^{13}C NMR spectrum (159.0 ppm).





(8*R*,9*R*,10*R*)-10-((*tert*-Butyldimethylsilyl)oxy)-8-chloro-6,6,9-trimethyl-2-tosyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indole (**13**).

DIBAL-H (1.70 mL, 2.54 mmol, 1.5 M in toluene) was added to a 0 °C solution of ketone (1.25 g, 2.05 mmol) in toluene (24 mL). The reaction was warmed to rt and stirred for 1 h. After return of the solution to 0 °C, additional DIBAL-H was added (1.70 mL, 2.54 mmol, 1.5 M in toluene). The solution was warmed to rt and stirred for an additional 1 h. After cooling back to 0 °C, Tf_2O

(1.04 mL, 6.15 mmol) and pyridine (590 µL, 8.20 mmol) and the reaction was stirred for 30 minutes at 0 °C. The solution was warmed to rt and more pyridine (2.36 mL, 32.8 mmol) was added. The reaction was stirred for an additional 12 h and quenched by slow dropwise addition of satd aq $NaHCO_3$ at 0 °C. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 5-10% ethyl acetate in hexanes) to afford the desired alkene as a viscous oil (681 mg, 56%) in addition to the tetracycle **15** (42 mg, 6%).

Alkene (**14**): R_f = 0.52 (SiO_2, 20% EtOAc/hexanes); IR (film) 2956, 2926, 2855, 1371, 1171, 1120, 1099 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.35 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.17 (s, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 6.17 (dd, 17.4, 10.8 Hz, 1H), 5.25 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.22 (d, *J* = 18.0 Hz, 1H), 4.77 (dd, *J* = 10.2, 6.6 Hz, 1H), 4.27 (s, 1H), 3.06 (dd, *J* = 18.6, 6.6 Hz, 1H), 2.60 (dd, *J* = 18.6, 10.8 Hz, 1H), 2.35 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H), 1.01 (s, 3H), 0.73 (s, 9H), -0.08 (s, 3H), -0.21 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 144.8, 144.1, 141.3, 139.9, 135.7, 133.4, 129.9, 126.9, 126.6 (2C), 123.6, 119.1, 118.7, 116.0, 114.3, 110.9, 76.5, 61.4, 45.6, 40.7, 34.6, 31.6, 28.3, 25.9, 21.5, 18.4, 13.3, -3.82, -3.92 ; HRMS (EI): Exact mass calcd for $C_{33}H_{42}ClNO_3SSi$ $[M]^+$ 595.2338, found 595.2310.

6,6,9-Trimethyl-2-tosyl-2,6-dihydronaphtho[1,2,3-cd]indole (**S4**).

R_f = 0.44 (SiO_2, 20% EtOAc/hexanes); IR (film) 2966, 2924, 2859, 1369, 1186, 1173, 1123, 1091, 1061 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) 7.81 (d, *J* = 7.8 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.70 (s, 1H), 7.51 (s, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.12 (dd, *J* = 8.4, 1.2 Hz, 1H), 2.38 (s, 3H), 2.33 (s, 3H),

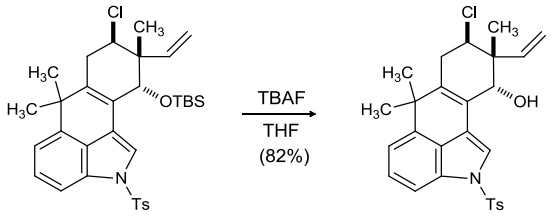
1.62 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 144.7, 142.4, 139.8, 135.9, 135.5, 133.7, 129.9, 129.0, 127.7, 126.8, 126.6, 126.4, 126.1, 124.1, 119.1, 118.6, 116.8, 110.8, 39.1, 33.8, 21.6, 20.9; HRMS (EI): Exact mass calcd for $C_{25}H_{24}NO_2S$ $[M+H]^+$ 402.1522, found 402.1516.

The intermediate alcohol could also be isolated as an inseparable 1:1 mixture of diastereomers.[6]

1-((8*R*,9*R*,10*R*)-10-((*tert*-Butyldimethylsilyl)oxy)-8-chloro-6,6,9-trimethyl-2-tosyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indol-9-yl)ethanol (**S3**).

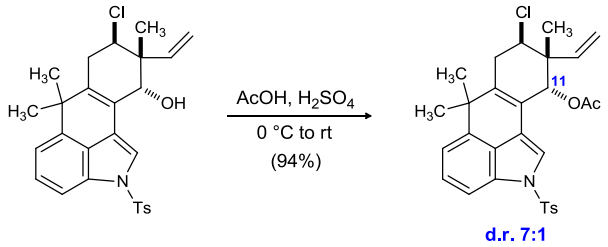
R_f = 0.31 (SiO_2, 20% EtOAc/hexanes); IR (film) 3568, 2928, 2855, 1460, 1437, 1369, 1171, 1095 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, data for both diastereomers) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.38 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.37 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.24 (s, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.22 (s, 1H), 5.07 (dd, *J* = 10.2, 7.2 Hz, 1H), 4.94 (dd, *J* = 9.6, 6.6 Hz, 1H), 4.76 (s, 1H), 4.47 (s, 1H), 4.22 (dd, *J* = 12.6, 6.0 Hz, 1H), 3.96 (ddd, *J* = 16.8, 6.0, 6.0 Hz, 1H), 3.14 (dd, *J* = 18.6, 7.2 Hz, 1H), 3.04 (s, 1H), 3.03 (s, 1H), 3.14 (dd, *J* = 18.6, 7.2 Hz, 1H), 3.14 (dd, *J* = 16.2, 6.0 Hz, 1H), 2.66 (ddd, *J* = 18.6, 9.6, 5.4 Hz, 1H), 2.35 (s, 3H), 2.35 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H), 1.44 (s, 3H), 1.42 (d, *J* = 6.6 Hz, 3H), 1.41 (s, 3H), 1.34 (d, *J* = 7.2 Hz, 3H), 0.86 (s, 3H), 0.80 (s, 9H), 0.80 (s, 9H), 0.73 (s, 3H), 0.25 (s, 3H), -0.02 (s, 3H), -0.33 (s, 3H), -0.42 (s, 3H), –OH protons (2) not observed; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 145.0, 144.9, 143.6, 142.4, 139.7, 135.7, 135.6, 133.5, 129.9, 126.9, 126.8, 126.4, 126.3, 123.1, 122.5, 119.7, 119.4, 119.0, 118.9, 116.1 (2C), 111.0, 75.1, 74.1, 73.3, 71.8, 64.1, 58.9, 45.7, 44.3, 40.8, 40.5, 36.0, 35.0, 30.8, 29.7, 29.3, 28.9, 25.9, 25.7, 21.5, 18.4, 18.3, 17.2, 14.1, 14.0, 9.6, -3.3, -3.6, -3.8, -4.3; HRMS (EI): Exact mass calcd for $C_{33}H_{44}ClNO_4SSi$ $[M]^+$ 611.2443, found 611.2441.

[6] The alcohol is highly sensitive to the base, and should not be stored for an extended period of time.



(8*R*,9*R*,10*R*)-8-Chloro-6,6,9-trimethyl-2-tosyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indol-10-ol (**14**).

To a 0 °C solution silyl ether (16.0 mg, 26.9 µmol) in THF (1.0 mL) was added TBAF (80.8 µL, 80.8 µmol, 1.0 M in THF). The solution was warmed to rt and stirred for 1 h. The reaction was quenched with satd aq $NaHCO_3$ and the layers were separated. The aqueous layer was extracted with Et_2O and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 20% ethyl acetate in hexanes) to afford the alcohol as a yellow solid (10.5 mg, 82%). R_f = 0.27 (SiO_2, 20% EtOAc/hexanes); mp 138-140 °C (decomp); IR (film) 3546, 2973, 2925, 1363, 1169, 1117, 1098 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.37 (s, 1H), 7.33 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.11 (dd, *J* = 18.0, 10.8 Hz, 1H), 5.43 (d, *J* = 10.8 Hz, 1H), 5.37 (d, *J* = 18.0 Hz, 1H), 4.52 (dd, *J* = 9.0, 5.4 Hz, 1H), 4.39 (d, *J* = 4.8 Hz, 1H), 3.02 (dd, *J* = 18.6, 5.4 Hz, 1H), 2.66 (dd, *J* = 18.6, 9.0 Hz, 1H), 2.35 (s, 3H), 1.98 (d, *J* = 4.8 Hz, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 144.7, 141.2, 140.8, 139.3, 135.6, 133.2, 126.9 (2C), 126.8, 126.5, 122.2, 118.7, 118.0, 117.3, 117.2, 110.8, 74.5, 61.3, 45.3, 40.7, 33.6, 30.6, 29.4, 21.6, 15.8; HRMS (EI): Exact mass calcd for $C_{27}H_{28}ClNO_3S$ $[M]^+$ 481.1473, found 481.1471.



(8*R*,9*R*,10*R*)-8-Chloro-6,6,9-trimethyl-2-tosyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indol-10-yl acetate (15a).

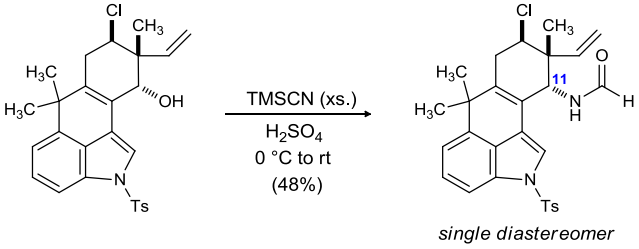
H_2SO_4 (8.0 µL, 0.15 mmol)[7] was added dropwise to a 0 °C solution of alcohol (8.0 mg, 17 µmol) in AcOH (170 µL). The reaction was stirred for 30 min at 0 °C and 30 min at rt. The reaction was cooled to 0 °C and quenched by the sequential addition of satd aq Na_2CO_3 followed by 1.0 M NaOH. The solution was warmed to rt and stirred for 10 min. The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 10% ethyl acetate in hexanes) to afford the acetate as a pale yellow foam (7.7 mg, 94%). The acetate was isolated as a 7:1 ratio of diastereomers (^{1}H NMR). R_f = 0.35 (SiO_2, 20% EtOAc/hexanes); IR (film) 2971, 2927, 1734, 1558, 1506, 1457, 1369 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.23 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 1H), 5.83 (dd, *J* = 17.2, 11.2 Hz, 1H), 5.76 (s, 1H), 5.30 (d, *J* = 10.8 Hz, 1H), 5.29 (d, *J* = 18.0 Hz, 1H), 4.55 (dd, *J* = 10.4, 5.6 Hz, 1H), 3.06 (dd, *J* = 18.4, 6.0 Hz, 1H), 2.58 (dd, *J* = 18.0, 10.8 Hz, 1H), 2.35 (s, 3H), 2.03 (s, 3H), 1.47 (s, 3H), 1.46 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 170.1, 144.7, 143.0, 140.0, 139.0, 135.6, 133.4, 129.8, 127.0, 126.6, 126.5, 119.9, 118.6, 117.7, 117.4, 116.7, 111.0,

[7] 95-98% EMD

74.1, 60.3, 44.0, 40.9, 33.6, 30.8, 29.3, 21.6, 21.0, 14.5; HRMS (EI): Exact mass calcd for $C_{27}H_{27}ClNO_2S$ $[M-C_2H_3O_2]^+$ 464.1451, found 464.1465.[8]

The stereochemistry at C11 was determined by comparing the NMR of **16a** with the acetylated product of the α-alcohol (**16**). The consistency between coupling constants of these two compounds in ^1H NMR analysis suggested similar configuration.

Procedure for alcohol acylation: To a 0 °C solution of α-alcohol (4.0 mg, 8.4 μmol) in THF (200 μL) was added LHMDS (37 μL, 37 μmol, 1.0 M in toluene) dropwise. The reaction was stirred for 1 h at 0 °C, and acetyl bromide (2.5 μL, 34 μmol) was added to the solution. The reaction was stirred for 30 min at 0 °C and 30 min at rt. The reaction was quenched with satd aq NH_4Cl and the layers were separated. The aqueous layer was extracted with Et_2O and the combined organic layers were dried, filtered, and concentrated. The resulting acetate was pure for analytical purposes.



single diastereomer

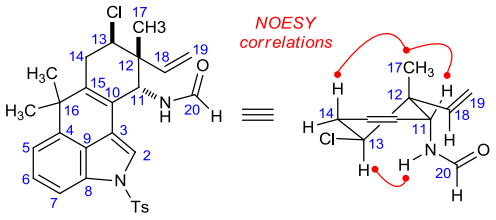
***N*-((8*R*,9*R*,10*R*)-8-Chloro-6,6,9-trimethyl-2-tosyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtha [1,2,3-cd]indol-10-yl)formamide** (**15b**).

H_2SO_4 (225 μL, 4.20 mmol) was added dropwise to a 0 °C solution of alcohol (100 mg, 210 μmol) in TMSCN (420 μL, 3.15 mmol). The reaction was stirred for 30 min at 0 °C and 30 min at rt. The solution was cooled to 0 °C and quenched by the sequential addition of satd aq Na_2CO_3 followed by 1.0 M NaOH. The solution was warmed to rt and stirred for 10 min. The layers were

[8] Elimination of AcOH observed.

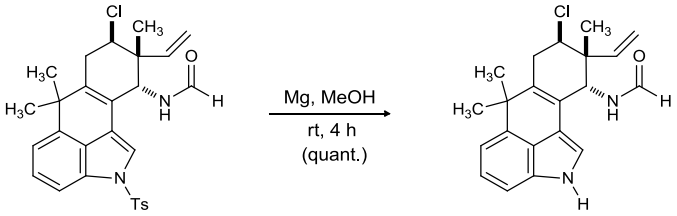
separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 20-30-40% ethyl acetate in hexanes) to afford the formamide as a yellow oil (52 mg, 48%). Only one diastereomer could be detected by NMR analysis. R_f = 0.39 (SiO_2, 50% EtOAc/hexanes); IR (film) 3276, 2962, 2924, 2853, 1663, 1368, 1170, 1119 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 2H), 7.23 (s, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 5.90 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.44 (br d, *J* = 8.8 Hz, 1H), 5.34 (d, *J* = 16.8 Hz, 1H), 5.33 (d, *J* = 11.6 Hz, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 4.23 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.04 (dd, *J* = 18.4, 5.2 Hz, 1H), 2.68 (dd, *J* = 18.4, 9.2 Hz, 1H), 2.35 (s, 3H), 1.45 (s, 3H), 1.44 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 160.5, 144.7, 140.6, 139.9, 138.9, 135.5, 129.9, 129.8, 126.9 (2C), 126.4, 121.1, 118.5, 117.2, 117.1, 116.9, 110.9, 70.5, 61.2, 52.2, 44.0, 40.8, 33.3, 30.6, 29.4, 21.5; HRMS (EI): Exact mass calcd for $C_{28}H_{30}ClN_2O_3S$ $[M+H]^+$ 509.1666 found 509.1664.

A NOESY experiment was carried out to determine the stereochemistry at C11. NOESY correlations from both $H11^5$ to H17 and H11 to H19, and the absence of crosspeaks between H11 to either H13 and H14, suggested that the H11 proton is equatorial. Additionally, a NOESY crosspeak between H13 and N-H was observed which indicated the axial orientation of the formamide functionality. These two observations are consistent with the formation of the α-formamide.



Alternate Procedure for the formation of 15b from 13: H_2SO_4 (45.0 µL, 840 µmol) was added dropwise to a 0 °C solution of silyl ether (20 mg, 42 µmol) in TMSCN (110 µL, 836 µmol). The reaction was stirred for 10 min at 0 °C and 45 min at rt. The solution was cooled to 0

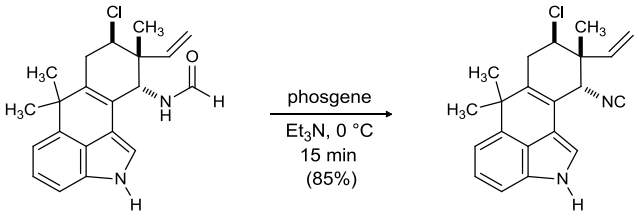
°C and quenched by the sequential addition of satd aq Na_2CO_3 followed by 1.0 M NaOH. The solution was warmed to rt and stirred for 10 min. The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 20-30-40% ethyl acetate in hexanes) to afford the formamide as a yellow oil (8.4 mg, 49%).



***N*-((8*R*,9*R*,10*R*)-8-Chloro-6,6,9-trimethyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd indol-10-yl)formamide (16)**.

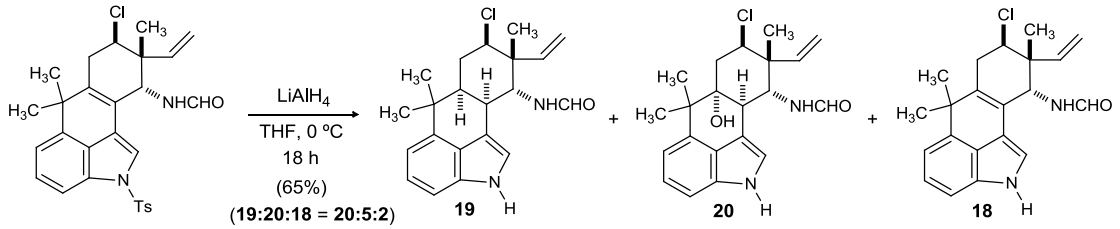
To a solution of formamide (13.0 mg, 25.6 µmol) in MeOH (3.6 mL) was added Mg turnings (56.0 mg, 2.30 mmol) and the reaction and stirred for 4 h at rt. The reaction was quenched with satd aq NH_4Cl and the solution was stirred for 30 min at rt. The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried, filtered, and concentrated. The resulting detosylated product was isolated as a mixture of *cis*- and *trans*-rotamers and found to be pure for all analytical purposes (9.0 mg, 100%). R_f = 0.24 (SiO_2, 50% EtOAc/hexanes); IR (film) 3357, 3278, 2962, 2924, 2850, 1684, 1679, 1669, 1653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, data for the major) δ 8.21 (s, 1H), 7.91 (br s, 1H), 7.23 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 2.1 Hz, 1H), 5.93 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.62 (br d, *J* = 10.4 Hz, 1H), 5.34 (d, *J* = 17.5 Hz, 1H), 5.33 (d, *J* = 11.0 Hz, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 4.30 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.06 (dd, *J* = 18.1, 5.5 Hz, 1H), 2.71 (dd, *J* = 18.1, 10.1 Hz, 1H), 1.51 (s, 3H), 1.48 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, data for both isomers) ppm 164.9, 160.8, 140.7, 140.6, 140.4, 138.8, 138.7, 136.9,

136.1, 133.9, 133.7, 124.7, 124.5, 124.4, 122.3, 118.0, 116.6, 116.4, 114.9 (2C), 114.8, 112.2, 112.1, 111.9, 108.0, 107.9, 62.5, 61.7, 58.4, 53.0, 44.7, 44.0, 41.1, 40.9, 33.3, 31.9, 31.1, 30.7, 30.0, 29.6, 17.2, 15.8; HRMS (EI): Exact mass calcd for $C_{21}H_{24}ClN_2O$ $[M+H]^+$ 355.1577, found 355.1572.



(±)–Hapalindole K (**1**).

To a 0 °C solution of formamide (1.9 mg, 5.4 µmol) and Et_3N (14.4 µL, 107 µmol) in CH_2Cl_2 (0.4 mL) was added phosgene (9.3 µL, 19 µmol, 20% in toluene). The reaction was stirred for 15 min at 0 °C and quenched with satd aq $NaHCO_3$. The solution was warmed to rt and stirred for 10 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 20-30% ethyl acetate in hexanes) to afford hapalindole A (1.6 mg, 85%). R_f = 0.70 (SiO_2, 50% EtOAc/hexanes); IR(film) 3411, 2958, 2920, 2850, 2134 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.93 (br s, 1H), 7.25 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.17 (d, *J* = 1.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.16 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.43 (d, *J* = 10.8 Hz, 1H), 5.38 (d, *J* = 17.4 Hz, 1H), 4.50 (s, 1H), 4.43 (dd, *J* = 7.8, 5.4 Hz, 1H), 3.08 (ddd, *J* = 18.0, 4.8, 0.6 Hz, 1H), 2.68 (br dd, *J* = 18.4, 9.2 Hz, 1H), 1.50 (s, 3H), 1.49 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 158.5, 139.9, 138.6, 136.6, 133.8, 124.7, 124.4, 118.8, 117.6, 116.3, 114.9, 111.5, 108.0, 61.4, 60.3, 43.3, 41.1, 32.9, 30.5, 30.1, 16.7; LRMS (EI): Exact mass calcd for $C_{21}H_{22}ClN_2$ $[M+H]^+$ 357.15, found 357.20.



***N*-((6a*S*,8*R*,9*R*,10*R*,10a*R*)-8-Chloro-6,6,9-trimethyl-9-vinyl-2,6,6a,7,8,9,10,10a-octahydro naphtho[1,2,3-cd]indol-10-yl)formamide (18)**.

$LiAlH_4$ (996 µL, 1.49 mmol, 1.5 M in THF) was added to a 0 °C solution of formamide (25.0 mg, 49.8 µmol) in THF (3.0 mL) and the reaction was stirred for 18 h at 0 °C. The reaction was quenched with sequential addition of H_2O (140 µL) and 0.5 M NaOH and the solution was stirred for 5 min at rt. The layers were separated and the aqueous layer was extracted with Et_2O and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 30-40-50-60-70% ethyl acetate in hexanes) to afford the formamide as a yellow oil in addition to the side products **20** and **18**.

Formamide 18 (isolated as a mixture of *cis*- and *trans*-rotamers):[9] yellow oil (12.0 mg, 48%). R_f = 0.15 (SiO_2, 50% EtOAc/hexanes); IR (film) 3396, 3287, 2961, 2923, 2853, 1679 (br s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, data for the both isomer) δ 8.23 (s, 1H), 8.16 (s, 1H), 8.13 (br s, 1H), 8.08 (br s, 1H), 7.23-7.18 (m, 4H), 7.08 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.97-6.95 (m, 2H), 6.94 (dd, *J* = 6.8, 0.8 Hz, 1H), 6.39 (dd, *J* = 8.8, 8.8 Hz, 1H), 5.91 (br d, *J* = 8.8 Hz, 1H), 5.83 (dd, *J* = 16.6, 11.2 Hz, 1H), 5.84 (dd, *J* = 16.6, 11.2 Hz, 1H), 5.30 (d, *J* = 17.0, 10.8 Hz, 1H), 5.30 (d, *J* = 10.8 Hz, 1H), 5.22 (d, *J* = 16.8 Hz, 1H), 5.21 (d, *J* = 11.6 Hz, 1H), 5.17 (d, *J* = 17.6 Hz, 1H), 4.94 (dd, *J* = 9.2, 1.2 Hz, 1H), 4.19 (dd, *J* = 12.4, 4.4 Hz, 1H), 4.16 (dd, *J* = 10.4, 3.6 Hz, 1H), 3.64 (br s, 1H), 3.63 (br s, 1H), 2.14 (ddd, *J* = 12.8, 7.6, 7.6 Hz, 1H), 2.00-1.96 (m, 2H), 1.94 (ddd, *J* = 13.2, 4.0, 4.0 Hz, 1H), 1.55 (s, 3H), 1.55-1.52 (m, 1H), 1.54 (s, 3H), 1.51 (dd, *J* = 7.6,

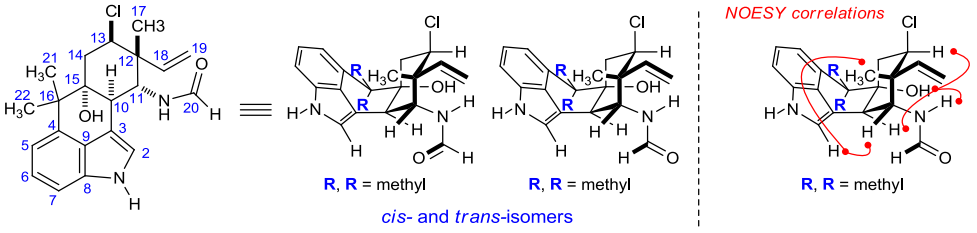
[9] The assigned structure was confirmed after the compound was converted to (±)-hapalindole A

4.0 Hz, 1H), 1.17 (s, 3H), 1.15 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, data for both rotamers) ppm 165.1, 160.1, 144.7, 143.1, 137.7 (2C), 133.6, 133.5, 124.3, 124.0, 123.5, 123.1, 119.5, 118.9, 115.8, 114.8, 113.9, 113.6, 112.0, 111.7, 108.6, 108.5, 64.4, 64.0, 60.9, 55.3, 46.2, 45.8, 45.7, 45.4, 38.1, 38.0, 37.7, 36.4, 32.1, 31.5, 31.1, 24.6 (2C), 22.7, 21.3, 20.0; HRMS (EI): Exact mass calcd for $C_{21}H_{25}ClN_2NaO$ $[M+Na]^+$ 379.1553, found 379.1557.

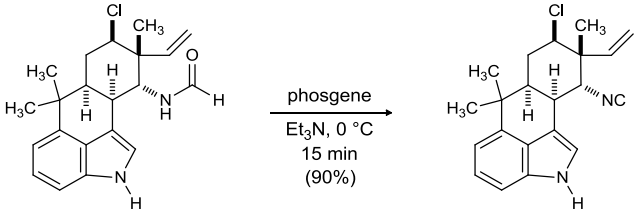
***N*-((6a*R*,8*R*,9*R*,10*R*,10a*R*)-8-chloro-6a-hydroxy-6,6,9-trimethyl-9-vinyl-2,6,6a,7,8,9,10,10a-octahydronaphtho[1,2,3-cd]indol-10-yl)formamide** (**17**).

(isolated as a mixture of *cis*- and *trans*- rotamers): pale yellow oil (3.1 mg, 12%). R_f = 0.07 (SiO_2, 50% EtOAc/hexanes); IR (film) 3356 (br s), 2961, 2923, 2852, 1669 (br s) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, data for the both isomer) δ 8.12 (s, 1H), 8.16 (br s, 1H), 8.02 (s, 1H), 8.00 (s, 1H), 7.42 (br d, *J* = 9.6 Hz, 1H), 7.37 (br d, *J* = 9.6 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.18 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.09 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.97 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 5.86 (dd, *J* = 16.8, 10.8 Hz, 2H), 5.30 (d, *J* = 11.4 Hz, 1H), 5.18 (d, *J* = 10.8 Hz, 1H), 5.17 (d, *J* = 18.6 Hz, 1H), 5.02 (d, *J* = 9.6 Hz, 1H), 4.59 (dd, *J* = 12.6, 4.2 Hz, 1H), 4.54 (dd, *J* = 12.6, 4.2 Hz, 1H), 4.15 (br d, *J* = 7.2 Hz, 1H), 3.58 (br s, 1H), 3.44 (br d, *J* = 0.8 Hz, 1H), 2.13 (ddd, *J* = 13.8, 3.6, 1.2 Hz, 1H), 2.13-2.12 (m, 1H), 2.01 (s, 2H), 1.90 (dd, *J* = 13.8, 12.6 Hz, 1H), 1.86 (dd, *J* = 13.8, 12.6 Hz, 1H), 1.52 (s, 3H), 1.51 (s, 3H), 1.14 (s, 6H), 0.82 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, data for both isomers) ppm 165.0, 159.9, 145.1, 143.0, 138.4, 138.0, 133.4, 133.3, 123.7, 123.5, 123.4 (2C), 119.9, 119.0, 115.9, 114.8, 113.8, 113.6, 111.9, 111.8, 109.0 (2C), 80.6, 80.2, 62.0, 61.6, 61.1, 55.2, 45.6, 43.5, 42.3, 42.1, 37.2, 36.8, 31.9, 26.7, 26.9 (2C), 22.7, 20.3, 19.7, 18.6; HRMS (EI): Exact mass calcd for $C_{21}H_{25}ClN_2NaO_2$ $[M+Na]^+$ 395.1502, found 395.1503.

The ^{1}H NMR analysis indicated a 5:1 mixture of *cis*- and *trans*-rotamers and as a result, the NMR peaks in general were broadened. First, HSQC was used to assign the formamide –NH and –OH protons and then NOESY correlations were used to assign the stereochemistry of newly formed quaternary center (C15). The alcohol proton shows strong correlations to formamide –NH, H13, and H10. As previously elucidated, the formamide functionality is α which indicates that the newly formed quaternary center has α-OH. Additionally, the formamide –NH was observed to shift downfield (δ 7.37 ppm) which also suggests the possibility of hydrogen bonding with α-OH. The presence of NOESY correlation between H2, H11 and H2, H17 also supports the assigned chair conformation of the cyclohexane core.



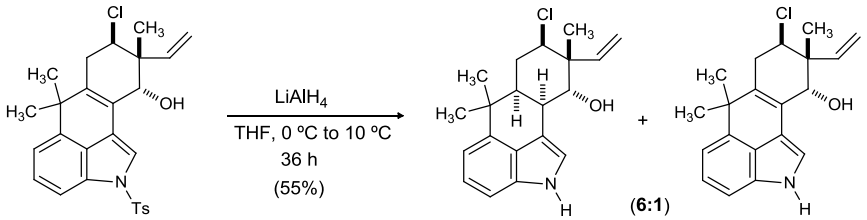
17 (isolated as a mixture of *cis*- and *trans*-isomer): Please see above for characterization data.



(±)–Hapalindole A (**2**).

To a 0 °C solution of the formamide (3.8 mg, 10.7 µmol) and Et_3N (29.8 µL, 214 µmol) in CH_2Cl_2 (0.8 mL) was added phosgene (18.5 µL, 37.5 µmol, 20% in toluene). The reaction was stirred for 15 min at 0 °C and quenched with satd aq $NaHCO_3$. The solution was warmed to rt and stirred for 10 min. The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried, filtered, and concentrated. The resulting residue was

purified by flash column chromatography (SiO_2, 20% ethyl acetate in hexanes) to afford hapalindole A (3.4 mg, 90%) as a oil. R_f = 0.60 (SiO_2, 50% EtOAc/hexanes); IR (film) 3417, 2964, 2924, 2853, 2134, 1439 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.22-7.19 (m, 2H), 6.98 (dd, *J* = 5.4, 2.2 Hz, 1H), 6.89 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.11 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.35 (d, *J* = 11.0 Hz, 1H), 5.24 (d, *J* = 17.5 Hz, 1H), 4.38 (br s, 1H), 4.23 (dd, *J* = 12.5, 4.0 Hz, 1H), 3.88 (br s, 1H), 2.32 (ddd, *J* = 13.4, 4.2, 4.2 Hz, 1H), 2.15 (dddd, *J* = 13.5, 3.5, 3.5, 0.7 Hz, 1H), 1.56 (s, 3H), 1.48 (ddd, *J* = 13.0, 13.0, 13.0 Hz, 1H), 1.20 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 157.9, 143.3, 138.0, 133.5, 124.0, 123.6, 118.7, 116.2, 114.1, 110.7, 108.6, 63.9, 63.2, 44.7, 44.2, 38.1, 37.1, 32.0, 31.1, 24.4, 18.9; HRMS (EI): Exact mass calcd for $C_{21}H_{24}ClN_2$ $[M+H]^+$ 339.1628, found 339.1617.

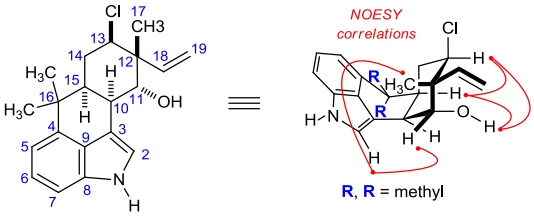


(6a*S*,8R,9*R*,10*R*,10a*R*)-8-Chloro-6,6,9-trimethyl-9-vinyl-2,6,6a,7,8,9,10,10a-octahydro naphtho[1,2,3-cd]indol-10-ol (**19**).

To a 0 °C solution of alcohol (45.0 mg, 94.3 µmol) in THF (6.0 mL) was added $LiAlH_4$ (1.56 mL, 2.37 mmol, 1.5 M in THF) and the reaction was stirred for 36 h at 10 °C. The reaction was quenched with sequential addition of H_2O (500 µL) and 0.5 M NaOH and the solution was stirred for 5 min at rt. The layers were separated and the aqueous layer was extracted with Et_2O and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 10-20-25% ethyl acetate in hexanes) to afford the desired reduced product as a viscous oil (14.3 mg, 47%) in addition to the detosylated side co-product (2.4 mg, 8%). R_f = 0.60 (SiO_2, 50% EtOAc/hexanes); IR (film) 3364 (br), 2959, 2923,

2851, 1457, 1441 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (br s, 1H), 7.20-7.16 (m, 2H), 6.95 (dd, *J* = 6.6, 1.2 Hz, 1H), 6.90 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.98 (dd, 18.0, 10.8 Hz, 1H), 5.40 (dd, *J* = 11.4, 0.6 Hz, 1H), 5.33 (d, *J* = 18.0 Hz, 1H), 4.53 (dd, *J* = 12.0, 4.2 Hz, 1H), 4.43 (br s, 1H), 3.74 (br s, 1H), 2.28 (ddd, *J* = 13.2, 4.2, 4.2 Hz, 1H), 2.18 (br d, *J* = 1.2 Hz, 1H), 2.10 (dddd, *J* = 13.2, 3.6, 3.6, 0.6 Hz, 1H), 1.53 (s, 3H), 1.48 (ddd, *J* = 13.2, 13.2, 13.2 Hz, 1H), 1.20 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 143.9, 138.6, 133.5, 124.5, 123.2, 118.7, 116.3, 113.7, 112.2, 108.3, 64.0, 47.7, 44.5, 37.7, 36.3, 32.1, 31.6, 29.7, 24.6, 20.17; HRMS (EI): Exact mass calcd for $C_{20}H_{25}ClNO$ $[M+H]^+$ 330.1619, found 330.1607.

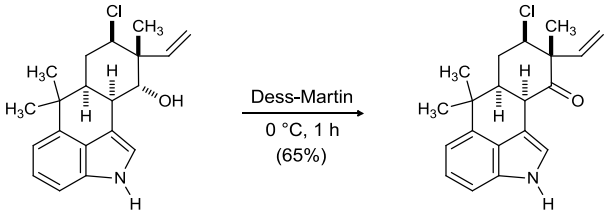
A complete 2D NMR analysis was performed to ascertain the stereochemical outcome of reduction step. First, HSQC was used to assign the –OH proton and also differentiate between H15 and H14α, H14β protons, as the latter is connected to a secondary carbon. Then NOESY correlations were used to assign the stereochemistry of newly formed chiral center (C15 and C10). The alcohol proton shows strong NOESY correlations to H13, and H15. As previously elucidated, the alcohol functionality is α which means that the newly formed chiral centers have α-protons. The presence of NOESY correlations between H2, H11 and H2, H17 also confirms the assigned chair conformation of the cyclohexane core.



(8*R*,9*R*,10*R*)-8-Chloro-6,6,9-trimethyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indol-10-ol (**S5**).

R_f = 0.06 (SiO_2, 20% EtOAc/hexanes); IR (film) 3401 (br), 2963, 2923, 2851, 1460, 1444 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (br s, 1H), 7.23 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz,

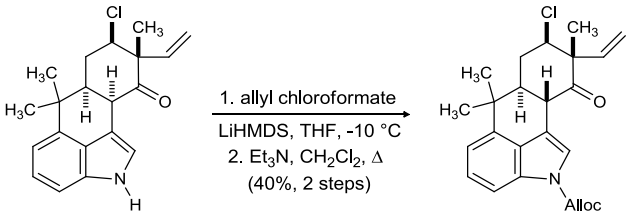
1H), 7.01 (s, 1H), 7.00 (d, *J* = 7.2 Hz, 1H), 6.18 (dd, *J* = 18.0, 11.2 Hz, 1H), 5.40 (d, *J* = 11.2 Hz, 1H), 5.35 (d, *J* = 18.0 Hz, 1H), 4.59 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.42 (s, 1H), 3.05 (dd, *J* = 18.0, 5.6 Hz, 1H), 2.70 (dd, *J* = 18.0, 9.6 Hz, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.20 (s, 3H), (-OH proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 141.9, 139.1, 136.5, 134.0, 124.6, 123.3, 116.4, 115.8, 114.8, 113.1, 107.8, 77.2, 75.2, 61.8, 45.3, 40.7, 33.6, 31.1, 29.6, 15.3; HRMS (EI): Exact mass calcd for $C_{20}H_{23}ClNO$ $[M+H]^+$ 328.1468, found 328.1455.



(6a*S*,8*R*,9*R*,10a*R*)-8-Chloro-6,6,9-trimethyl-9-vinyl-6,6a,7,8,9,10a-hexahydronaphtho[1,2,3-cd]indol-10(2H)-one (**20**).

To a 0 °C solution of alcohol (5.9 mg, 17.9 µmol) in CH_2Cl_2 (600 µL) was added Dess-Martin periodinane (19.0 mg, 44.8 µmol) and the reaction was stirred for 1 h. The reaction was quenched by the addition of an aqueous solution containing 2:1 satd aq $Na_2S_2O_3$:$NaHCO_3$ and was stirred until both layers became clear (~20 min). The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried, filtered, and concentrated. The resulting residue was purified by flash column chromatography (SiO_2, 15% ethyl acetate in hexanes) to afford the enone as a pale yellow foam (3.8 mg, 65%). R_f = 0.60 (SiO_2, 40% EtOAc/hexanes); IR (film) 3399 (br), 2923, 2953, 1698 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.23-7.19 (m, 2H), 6.99 (dd, *J* = 6.6, 1.2 Hz, 1H), 6.76 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.93 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.38 (d, *J* = 10.8 Hz, 1H), 5.23 (d, *J* = 17.4 Hz, 1H), 4.24 (dd, *J* = 12.6, 3.6 Hz, 1H), 4.23 (br s, 1H), 2.27 (dddd, *J* = 13.8, 3.6, 3.6, 1.8 Hz, 1H), 2.18 (ddd, *J* = 13.2, 3.6, 3.6 Hz, 1H), 1.76 (ddd, *J* = 13.2, 13.2, 13.2 Hz, 1H), 1.58 (s, 3H), 1.20 (s,

3H), 1.11 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 211.3, 139.7, 137.3, 133.8, 123.6, 123.5, 120.0, 116.5, 113.9, 108.8, 108.4, 64.9, 57.2, 46.5, 45.8, 37.5, 31.6, 30.7, 24.6, 20.1; HRMS (EI): Exact mass calcd for $C_{20}H_{23}ClNO$ $[M+H]^+$ 328.1468, found 328.1391.



(6a*S*,8*R*,9*R*,10a*S*) Allyl 8-chloro-6,6,9-trimethyl-10-oxo-9-vinyl-6a,7,8,9,10,10a-hexahydro naphtho[1,2,3-cd]indole-2(6*H*)-carboxylate (**22**).

To a -10 °C solution of indole (4.5 mg, 13.7 µmol) in THF (500 µL) was added LiHMDS (34.2 µL, 34.2 µmol, 1.0 M in toluene). The reaction was stirred for 1 h at -10 °C, and allyl chloroformate (3.6 µL, 34 µmol) was added dropwise to the solution. The solution was stirred for 30 min at -10 °C and 30 min at 0 °C. The reaction was quenched with satd aq NH_4Cl and the layers were separated. The aqueous layer was extracted with Et_2O and the combined organic layers were dried, filtered, and concentrated to provide a yellow oil. The crude Alloc protected indole was carried on to the next step without further purification.

To a solution of the crude indole (2.6 mg) in CH_2Cl_2 (300 µL) was added triethyl amine (30.0 µL, 73.5 µmol) and the reaction was stirred for 4 h at 40 °C. The reaction was concentrated and the resulting residue was purified by flash column chromatography (SiO_2, 10% ethyl acetate in hexanes) to afford the desired product as a colorless oil (2.2 mg, 40%). The NMR data matched that in the literature.[10]

[10] Fukuyama, T.; Chen, X. Q. *J. Am. Chem. Soc.* **1994**, *116*, 3125.

Figure 1. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **1**

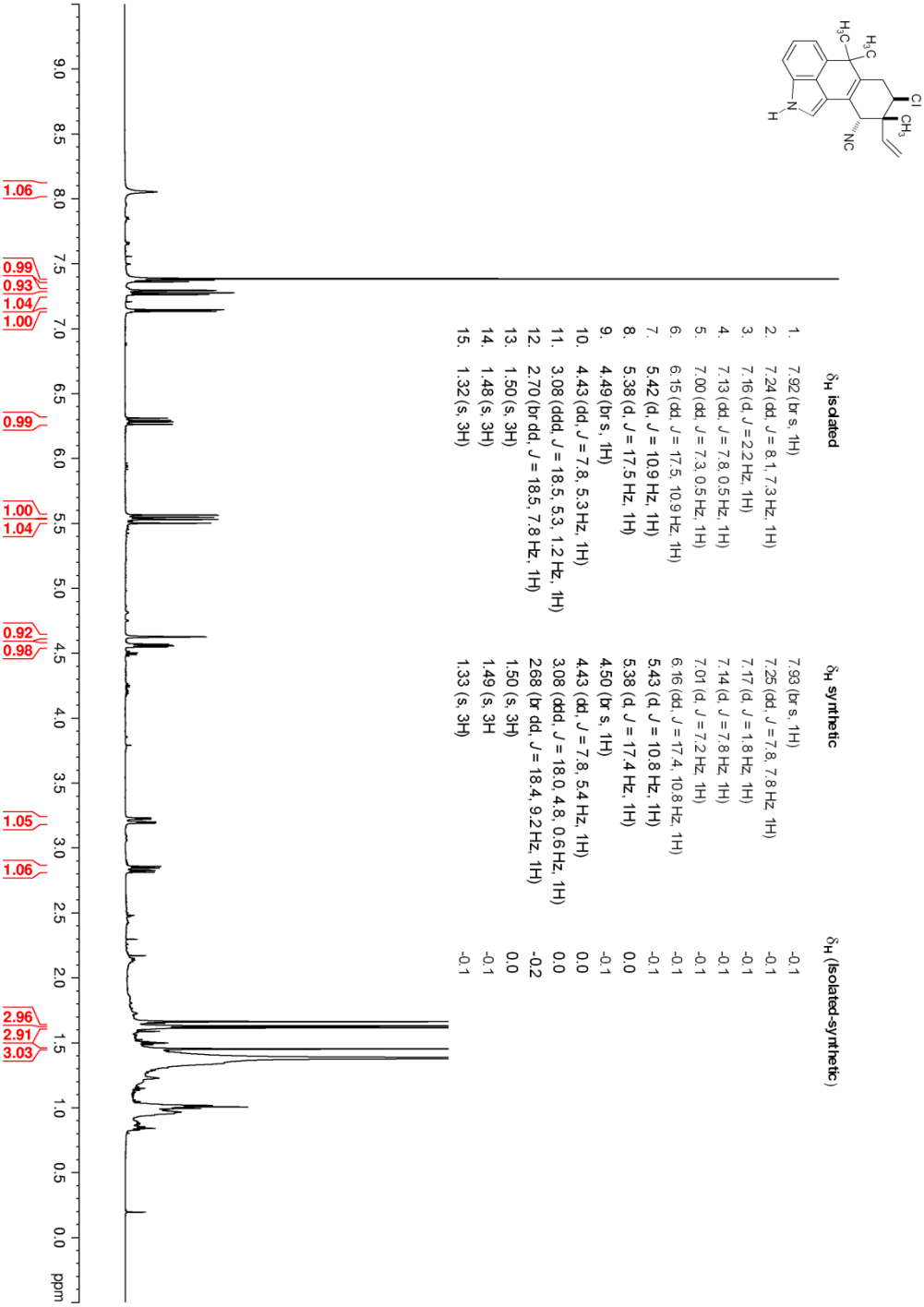


Figure 2. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **1**

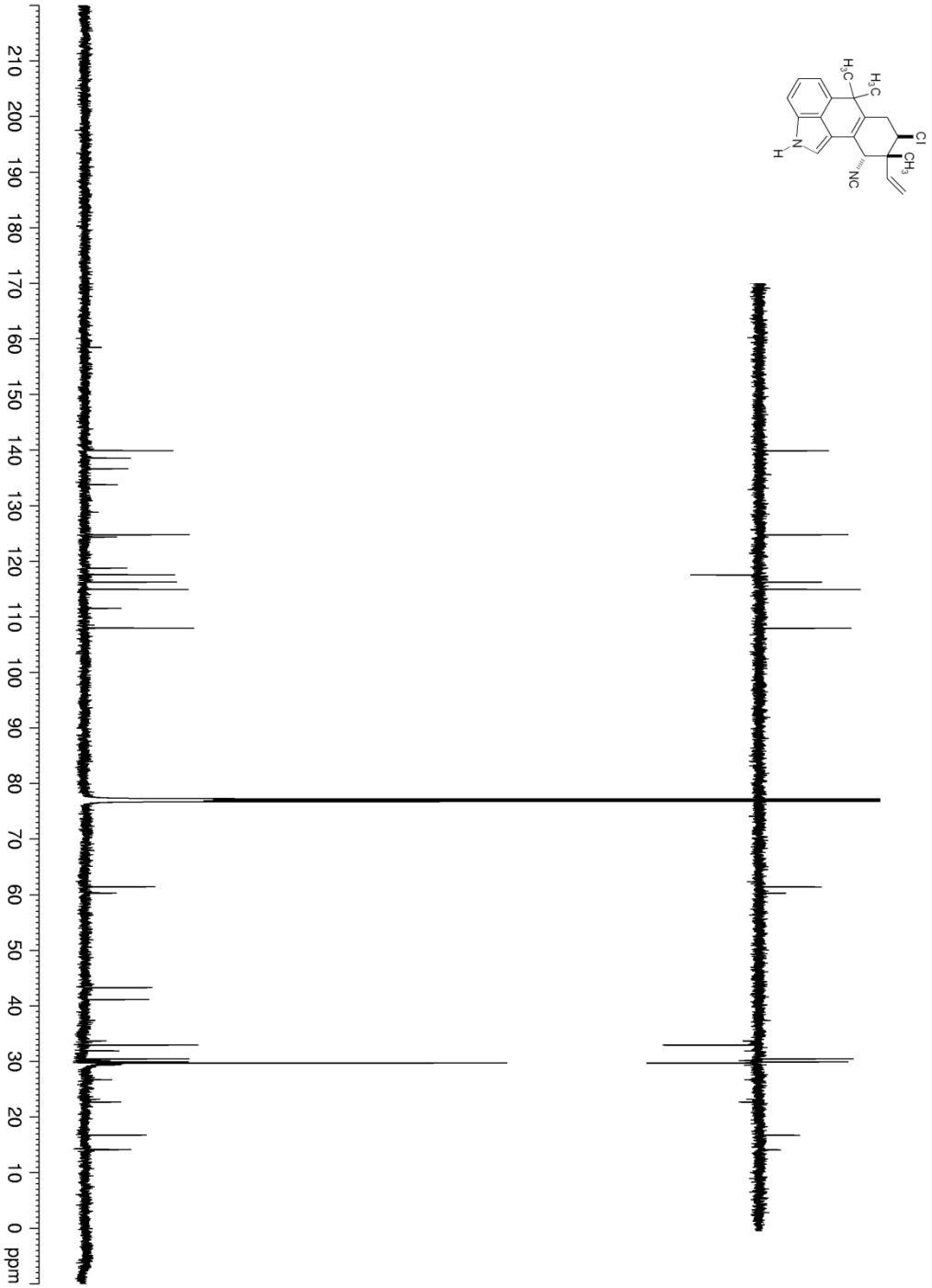


Figure 3. ^{1}H NMR Spectrum (500 MHz, $CDCl_3$) of **2**

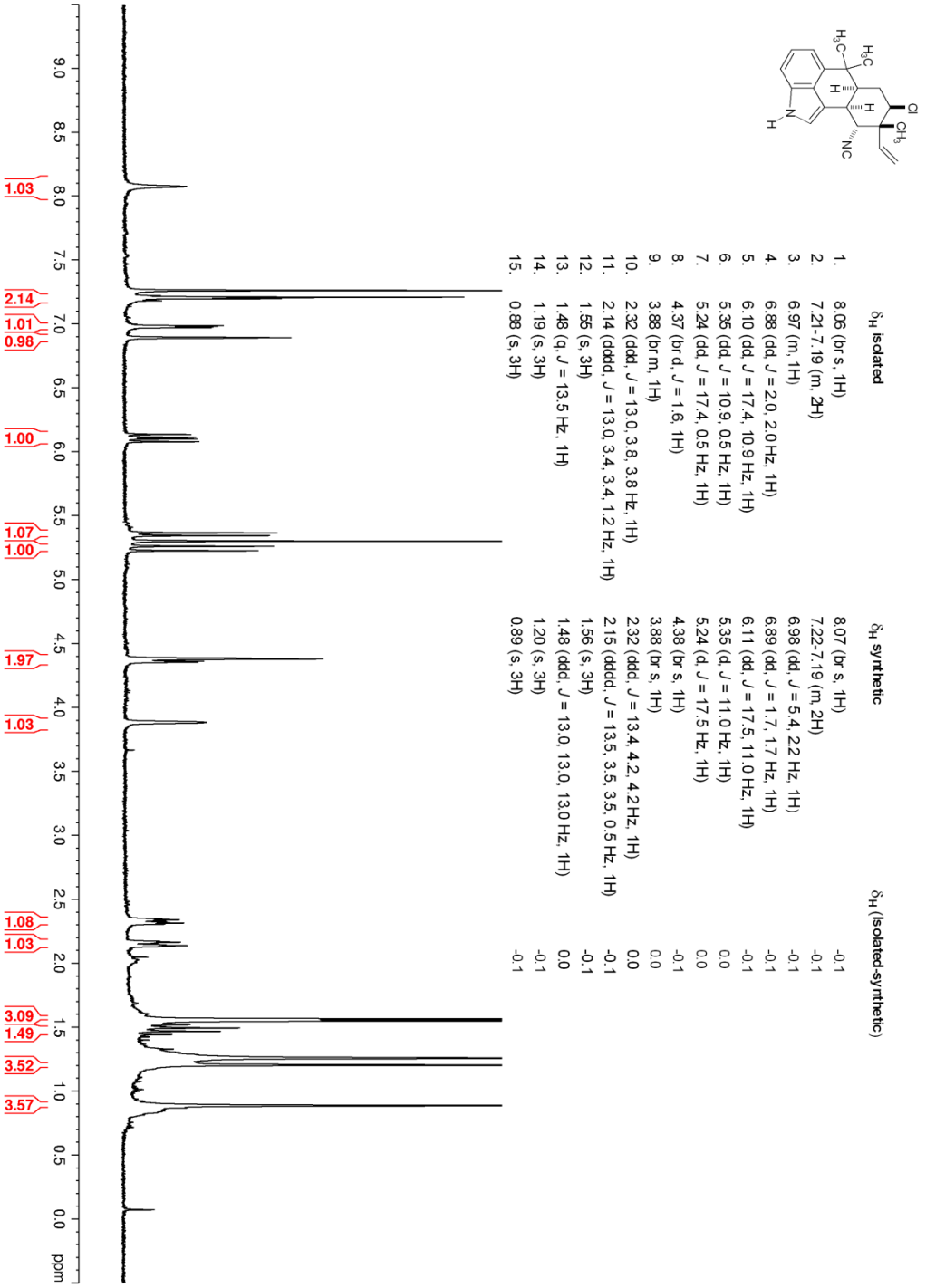


Figure 4. ^{13}C NMR Spectrum (125 MHz, $CDCl_3$) of **2**

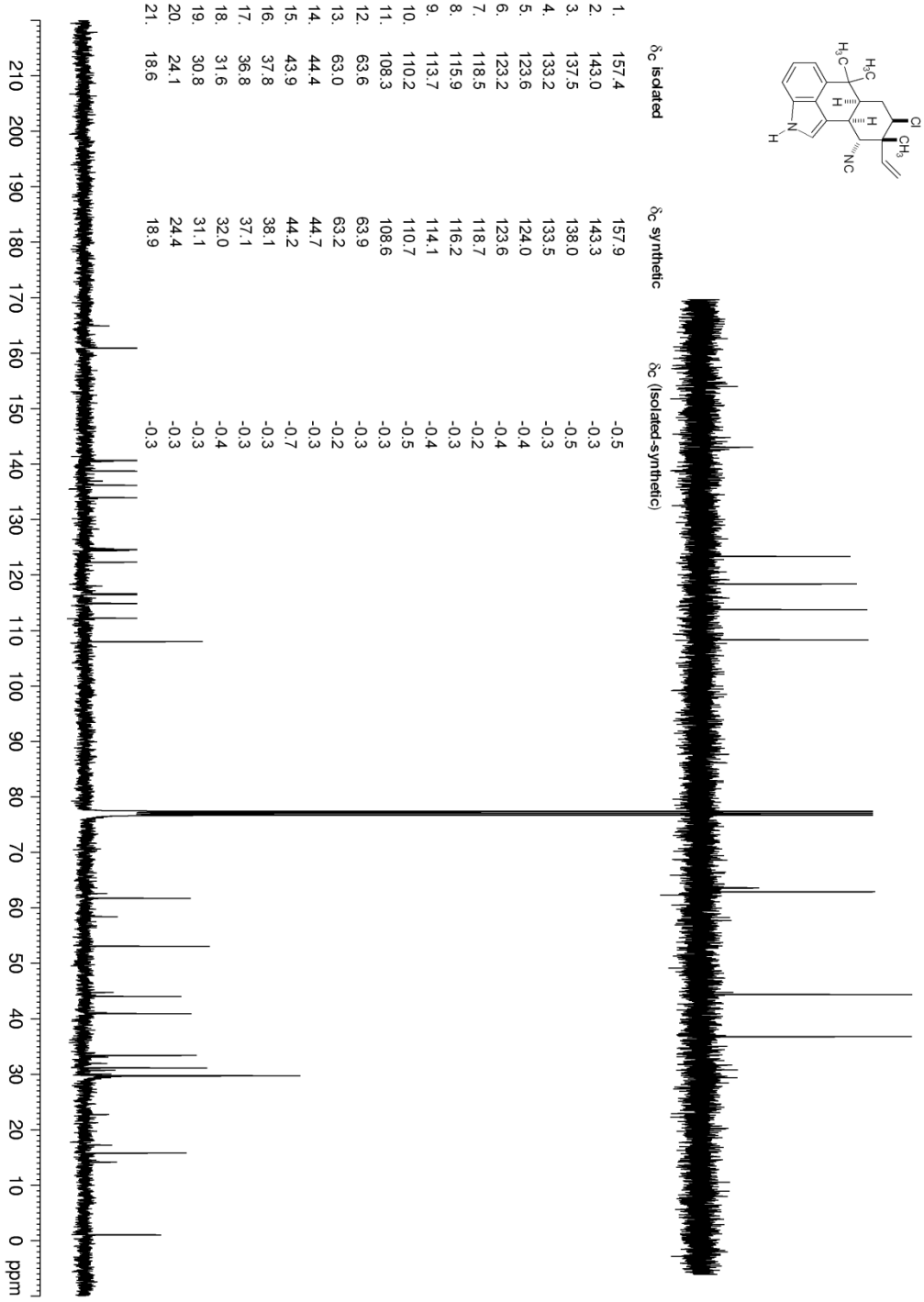


Figure 5. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **4**

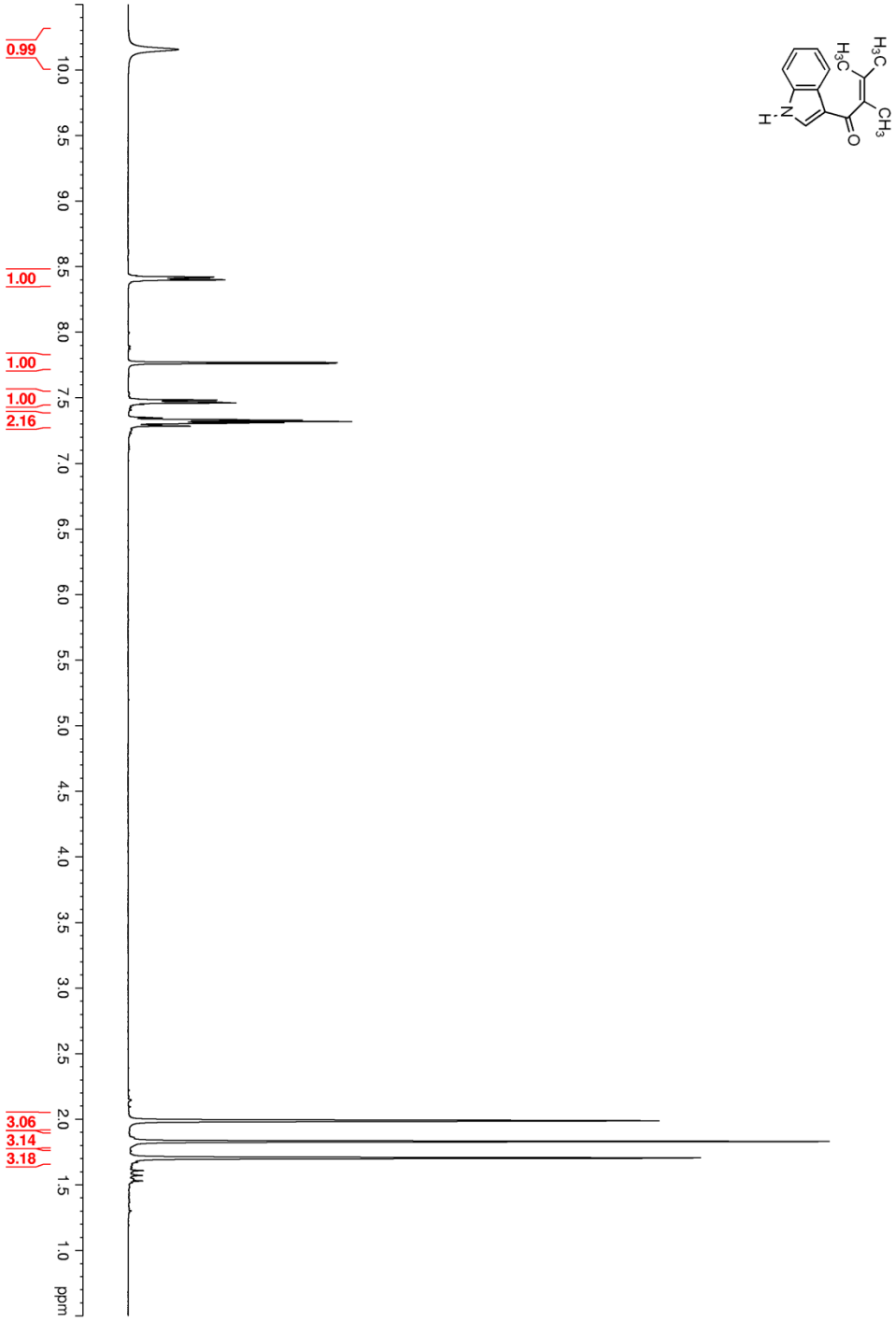


Figure 6. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **4**

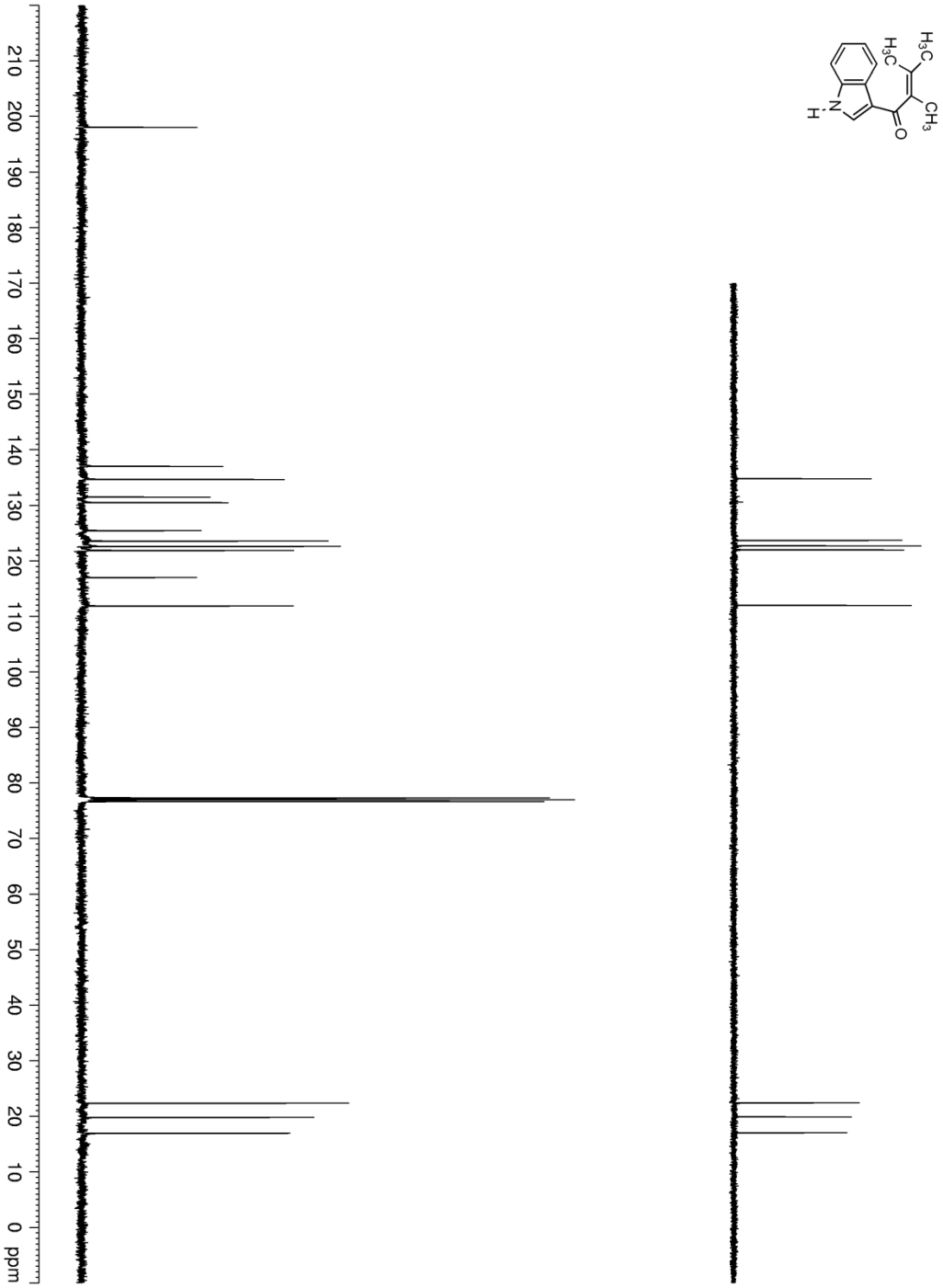


Figure 7. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **5**

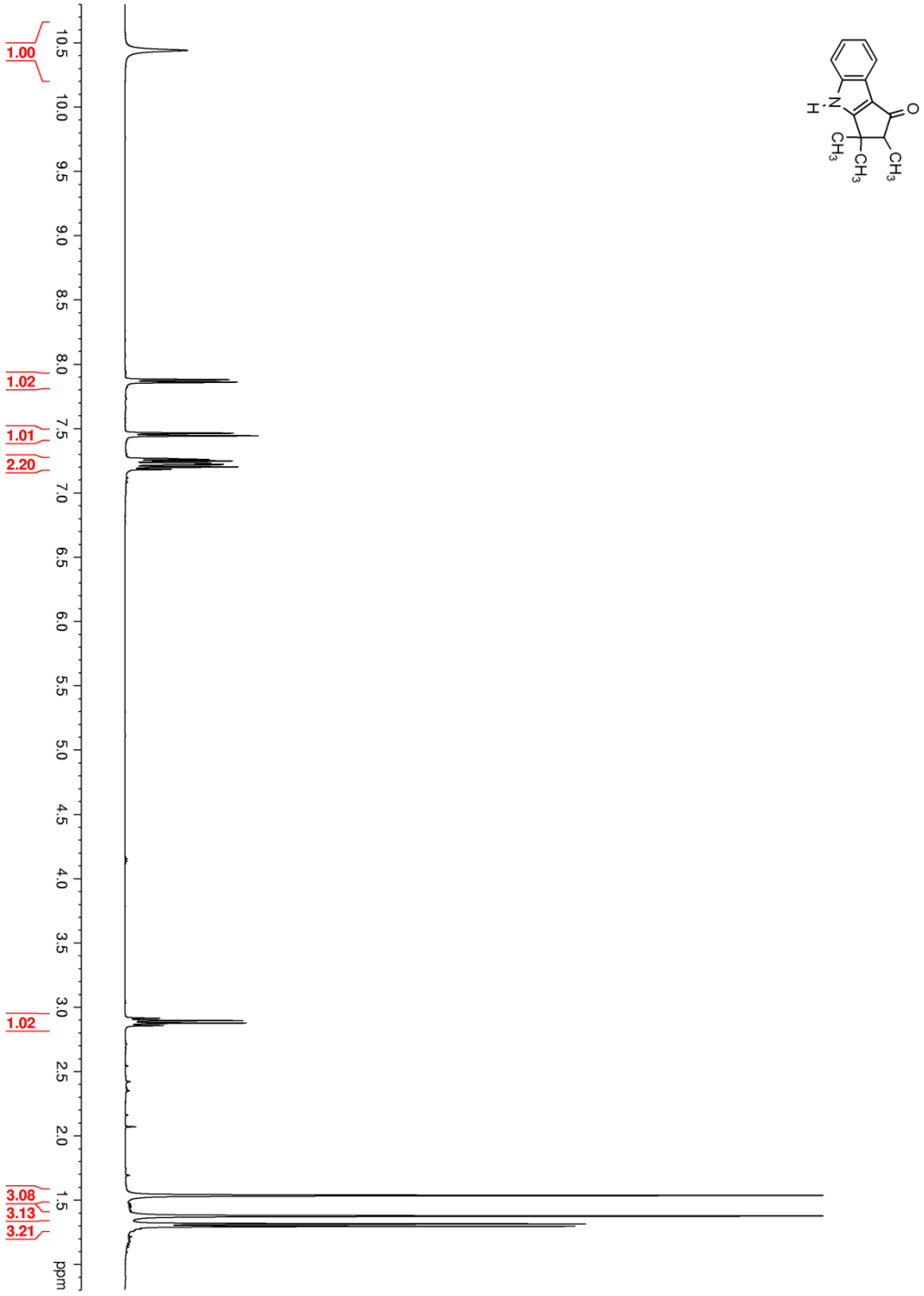


Figure 8. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **5**

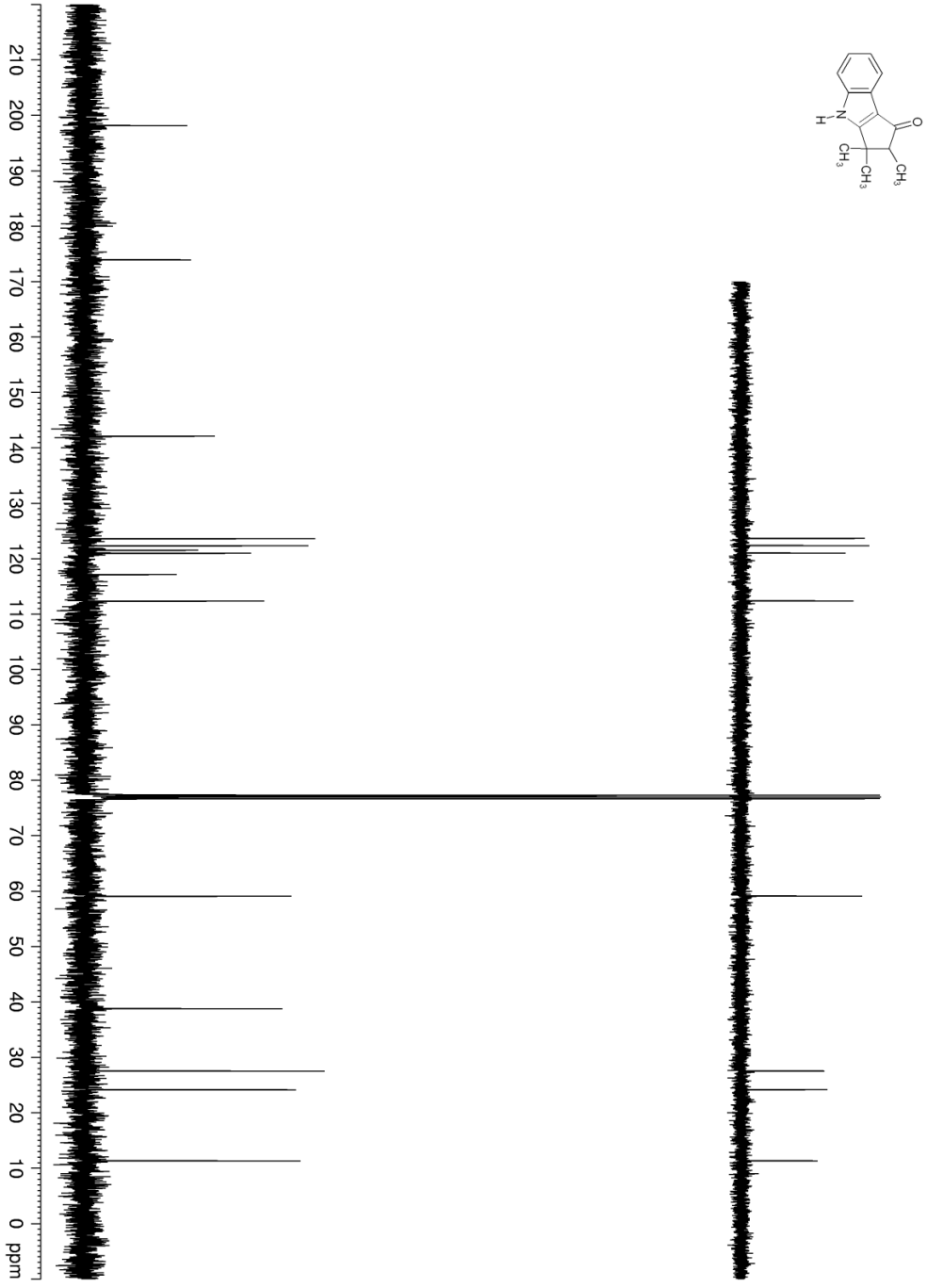


Figure 9. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **6**

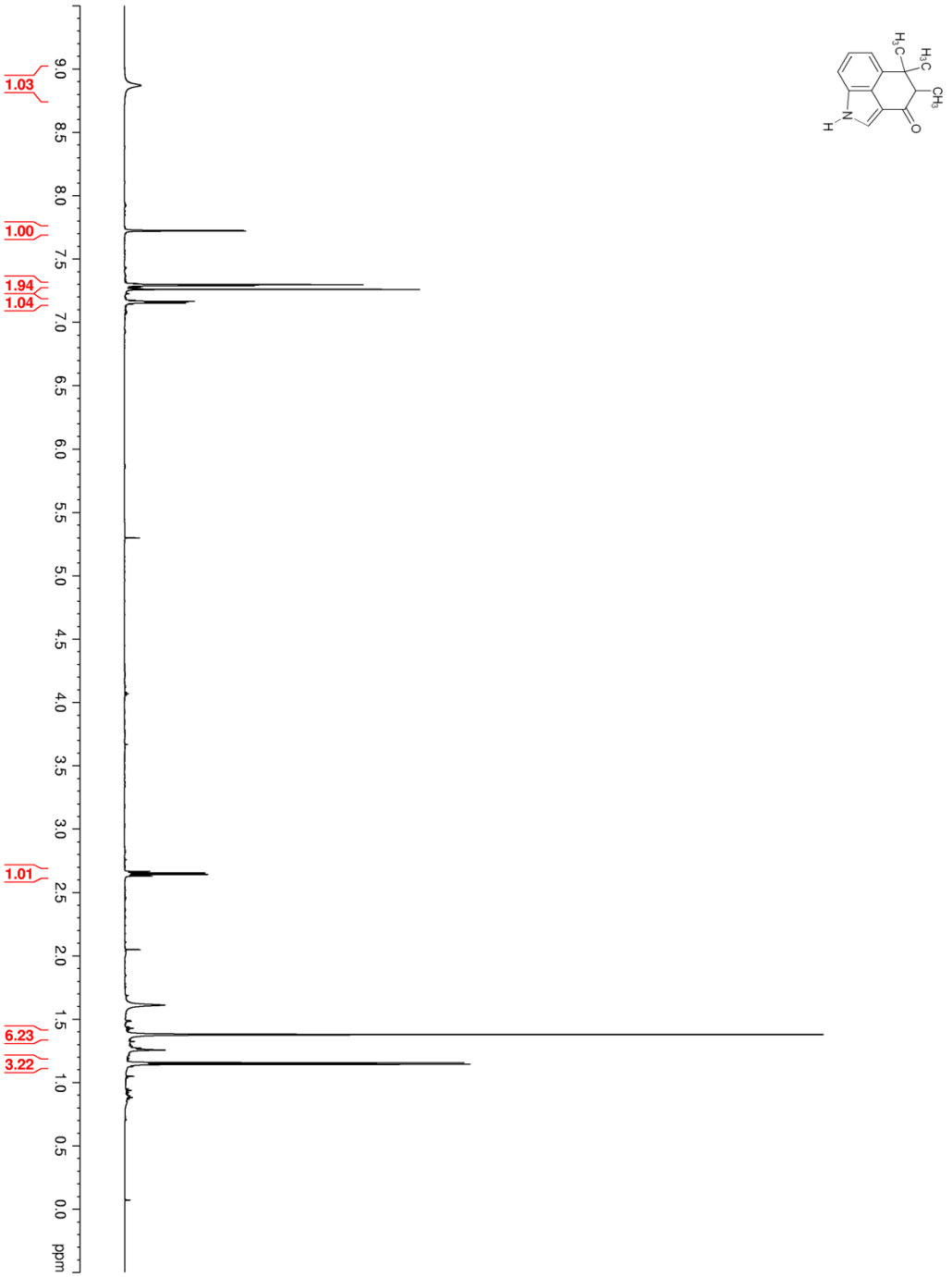


Figure 10. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **6**

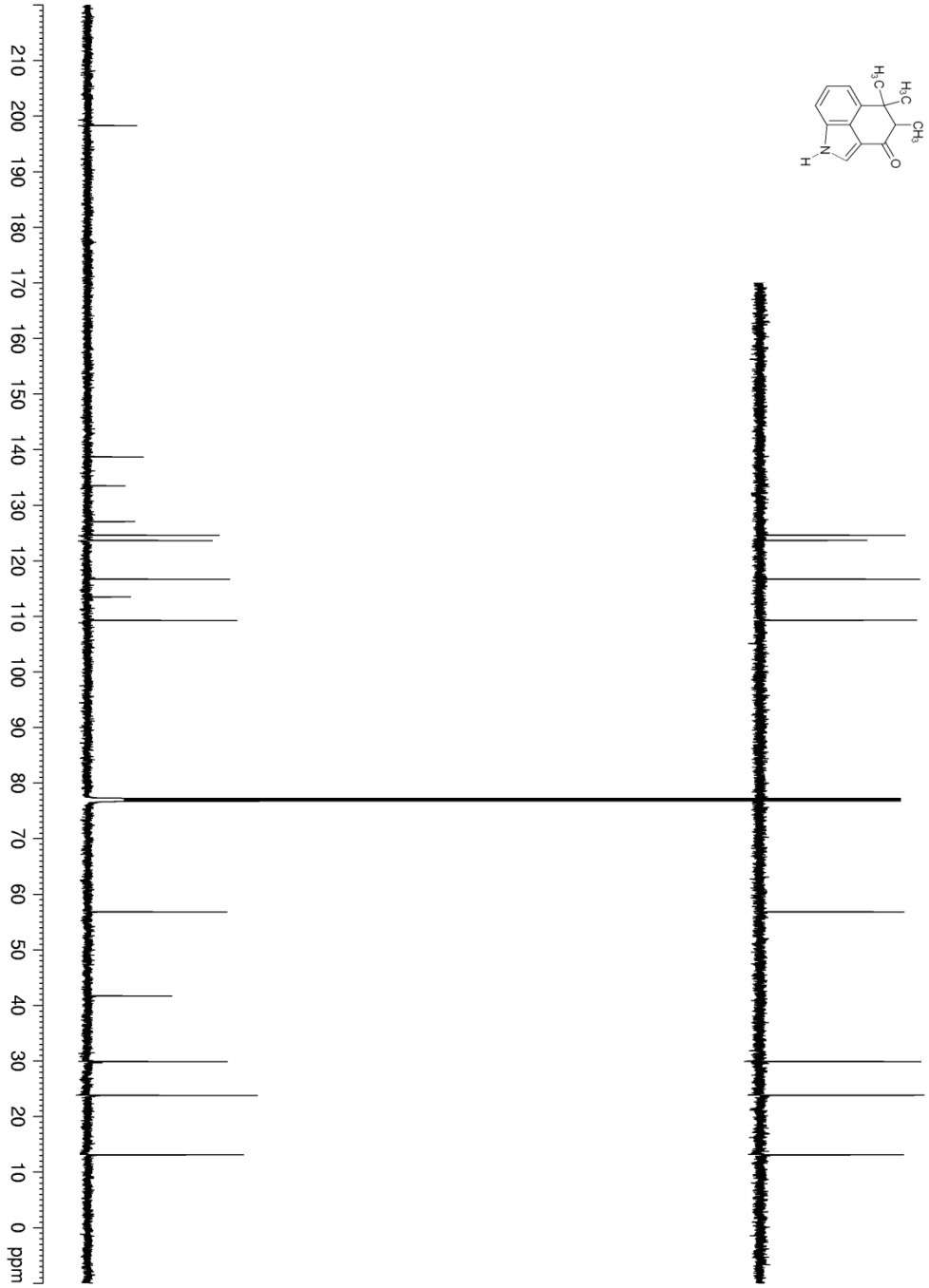


Figure 11. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **7**

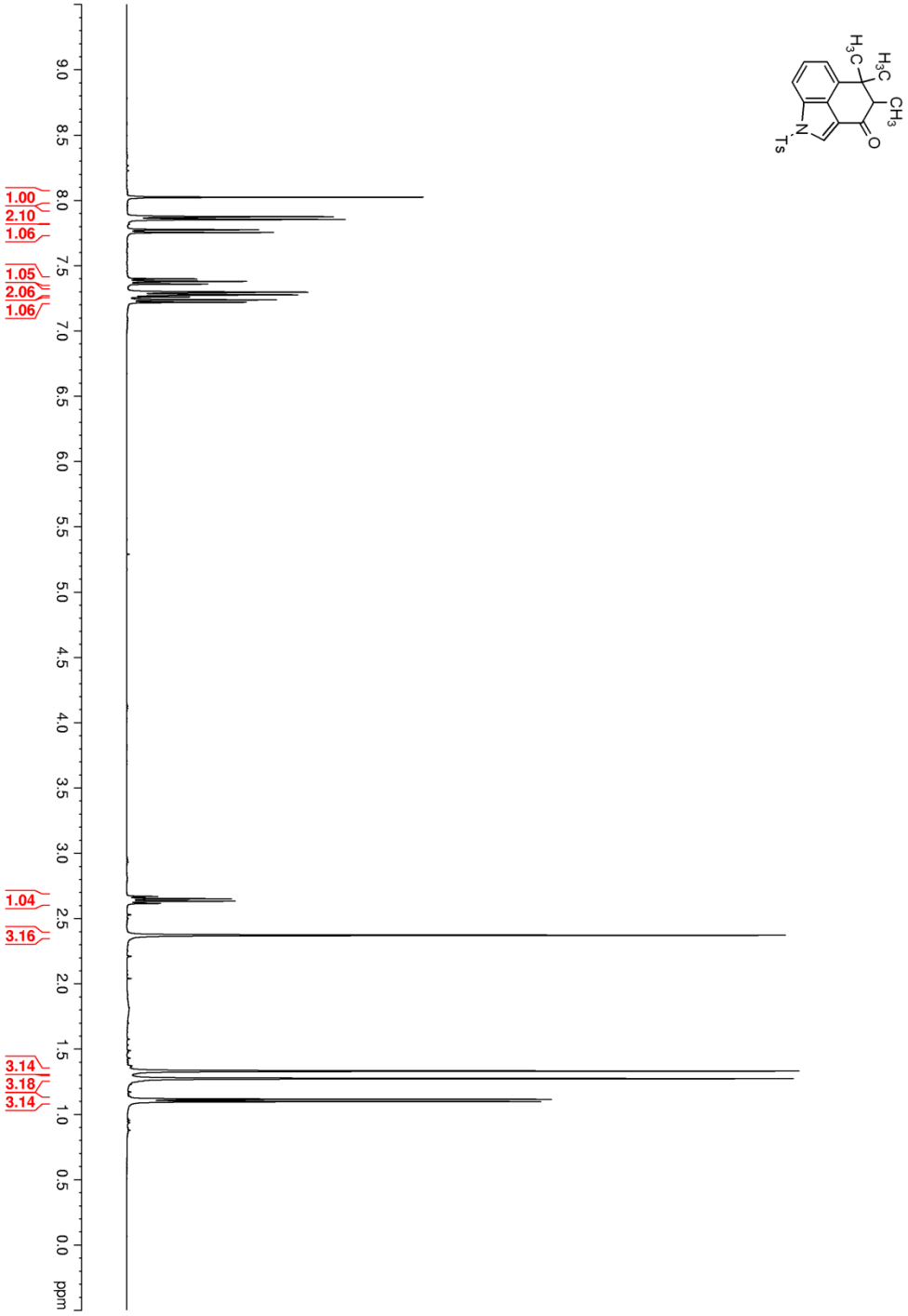


Figure 12. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **7**

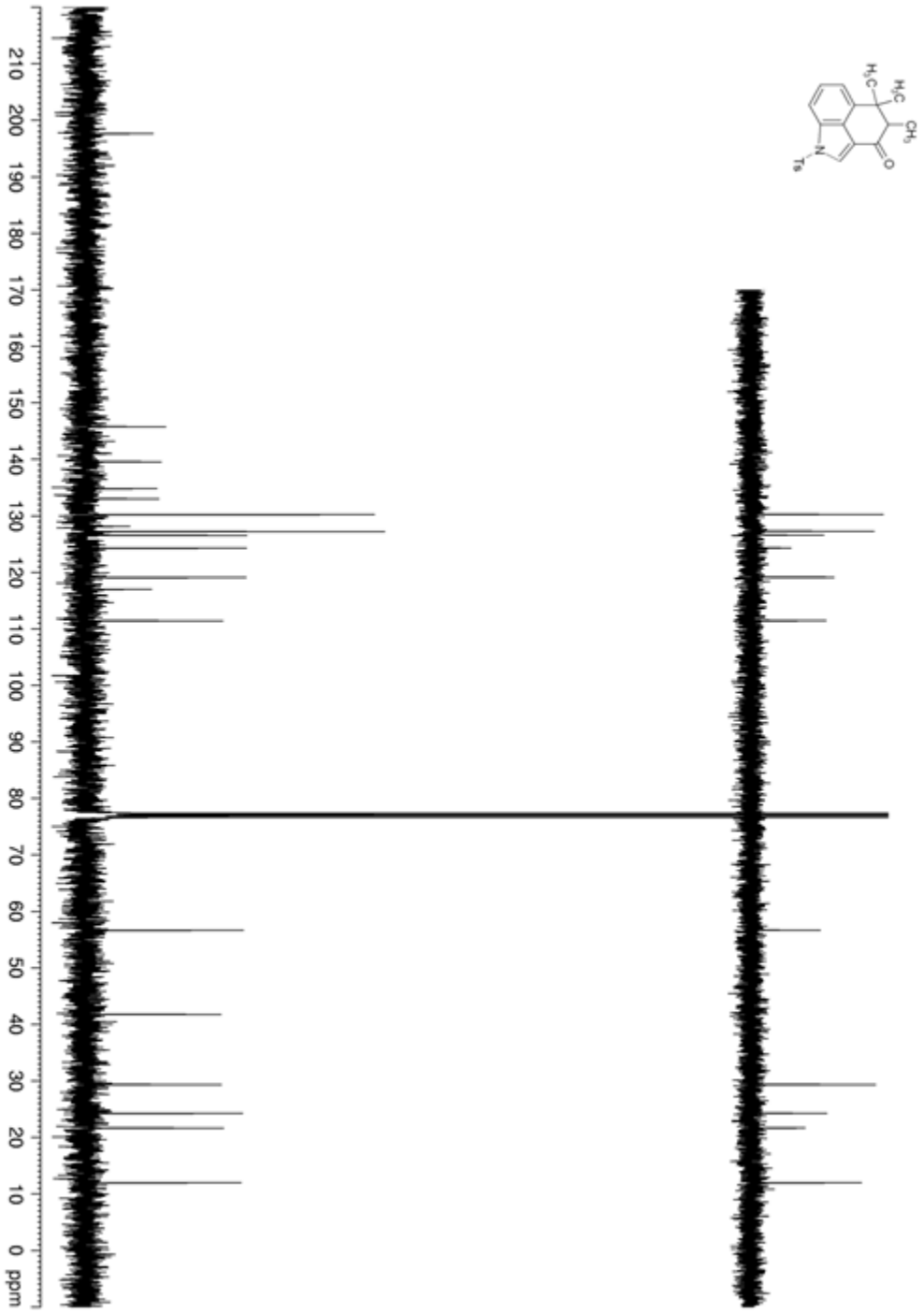


Figure 13. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **8**

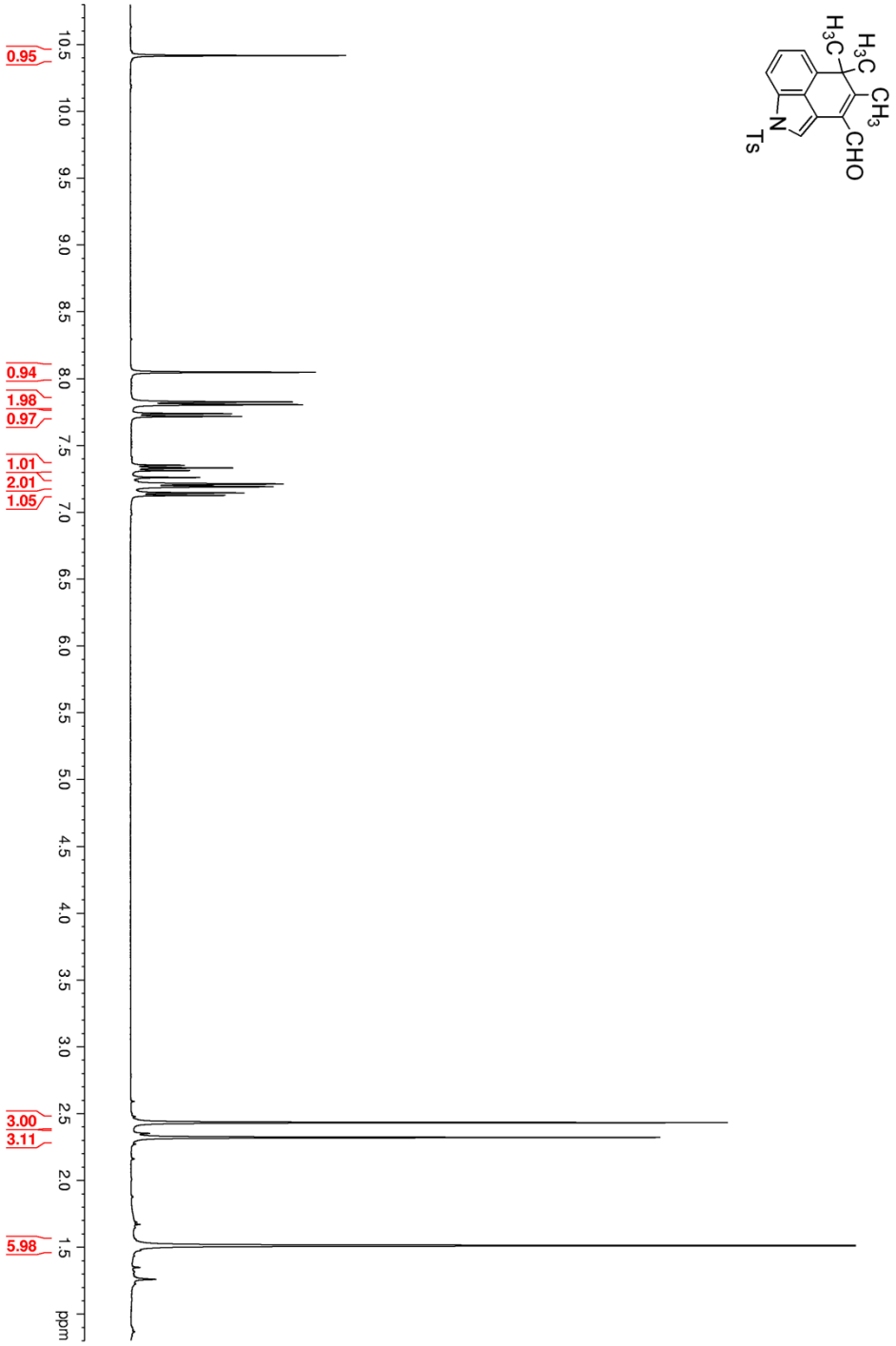


Figure 14. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **8**

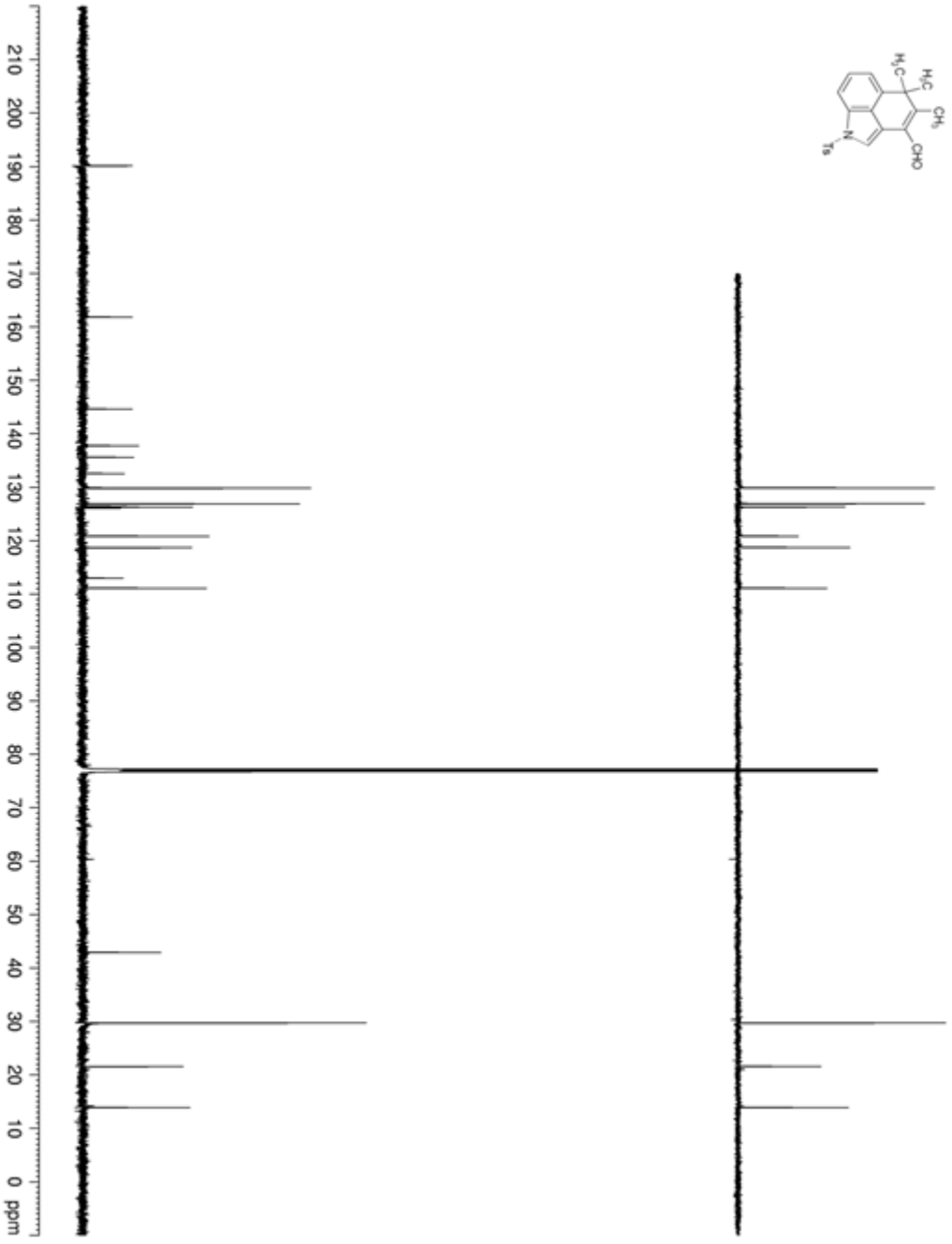


Figure 15. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **9**

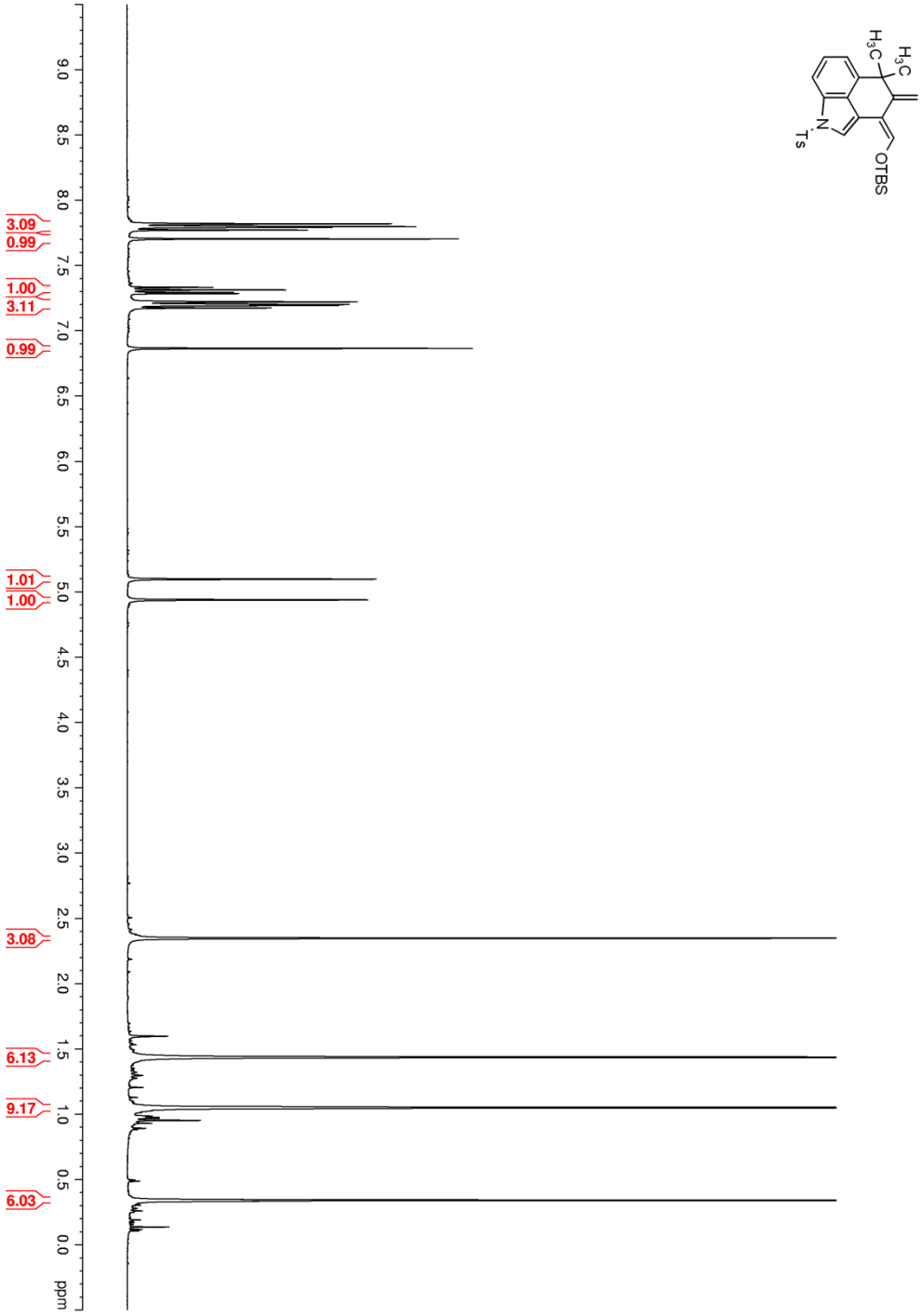


Figure 16. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **9**

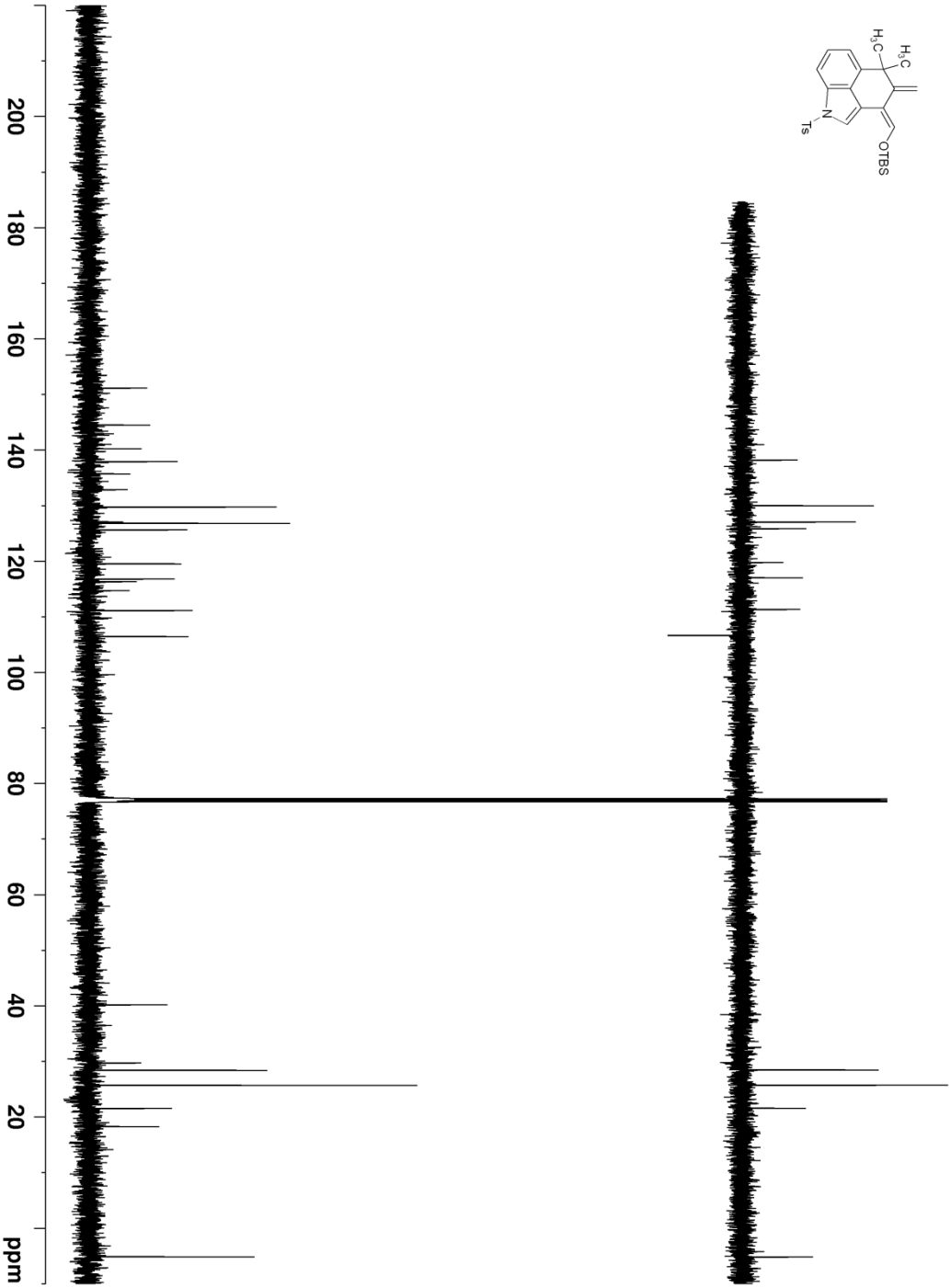


Figure 17. NOESY Spectrum (600 MHz, $CDCl_3$) of **9**

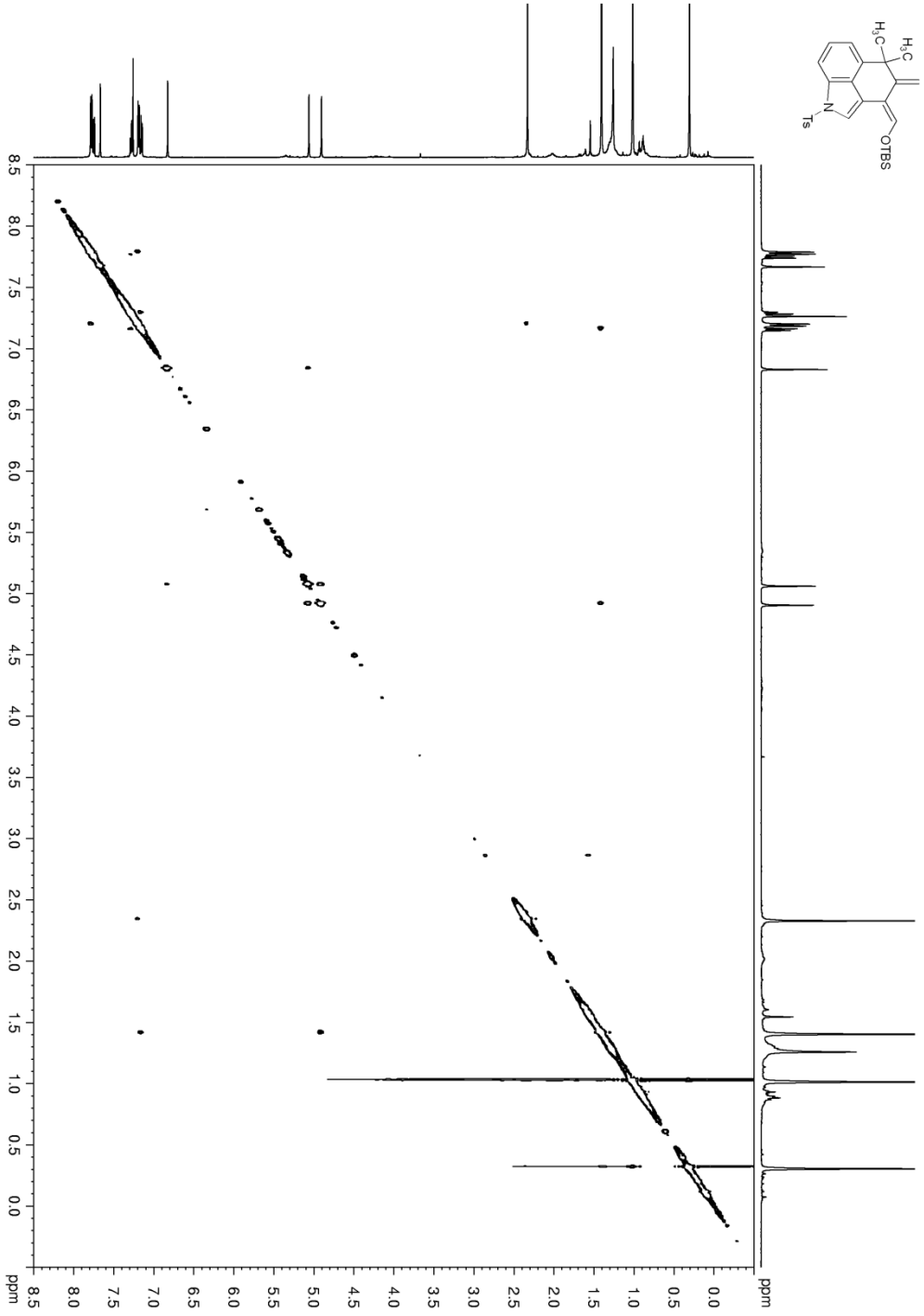


Figure 18. ^{1}H NMR Spectrum (400 MHz, CD_2Cl_2) of **10b**

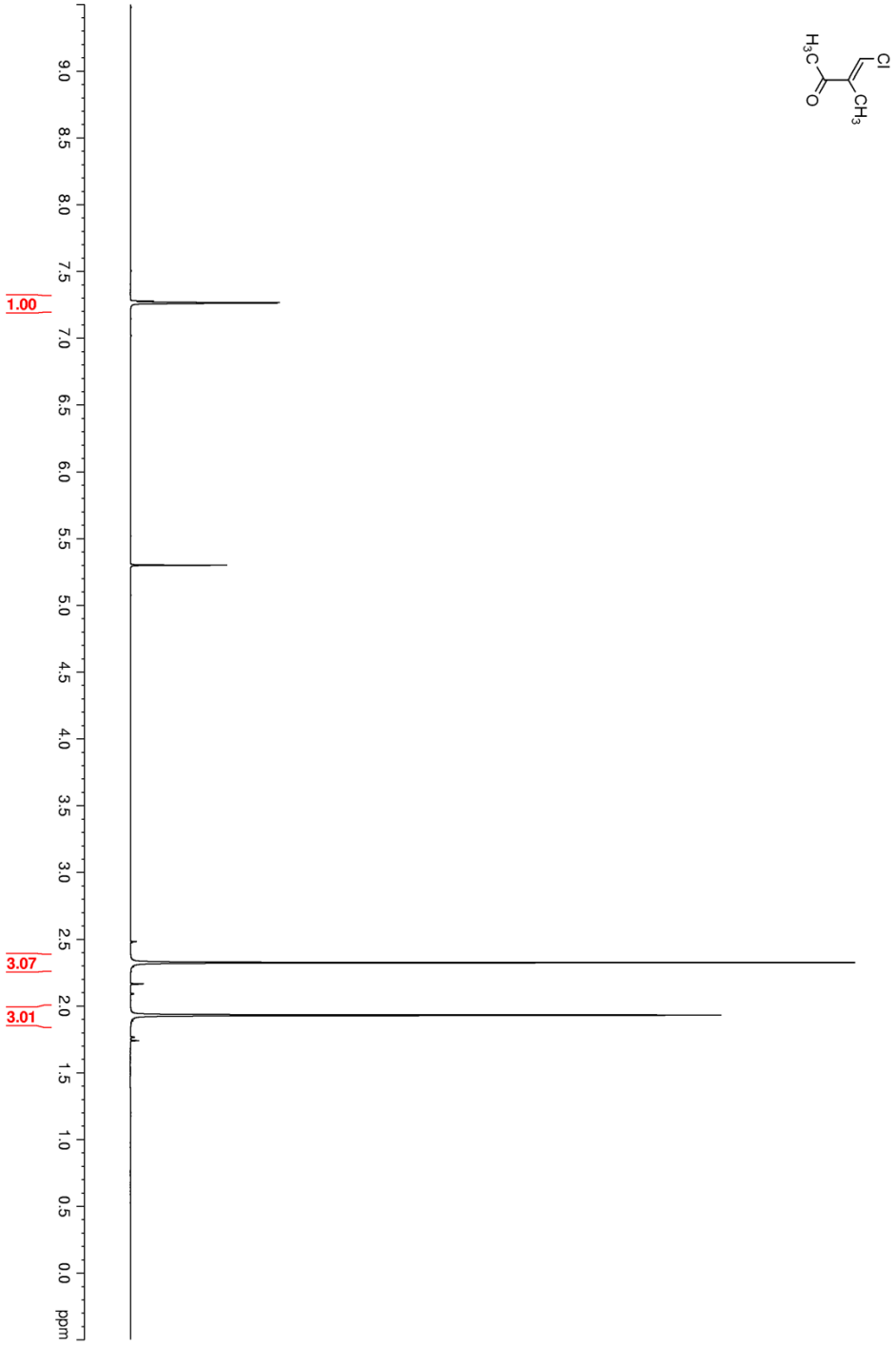


Figure 19. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **10b**

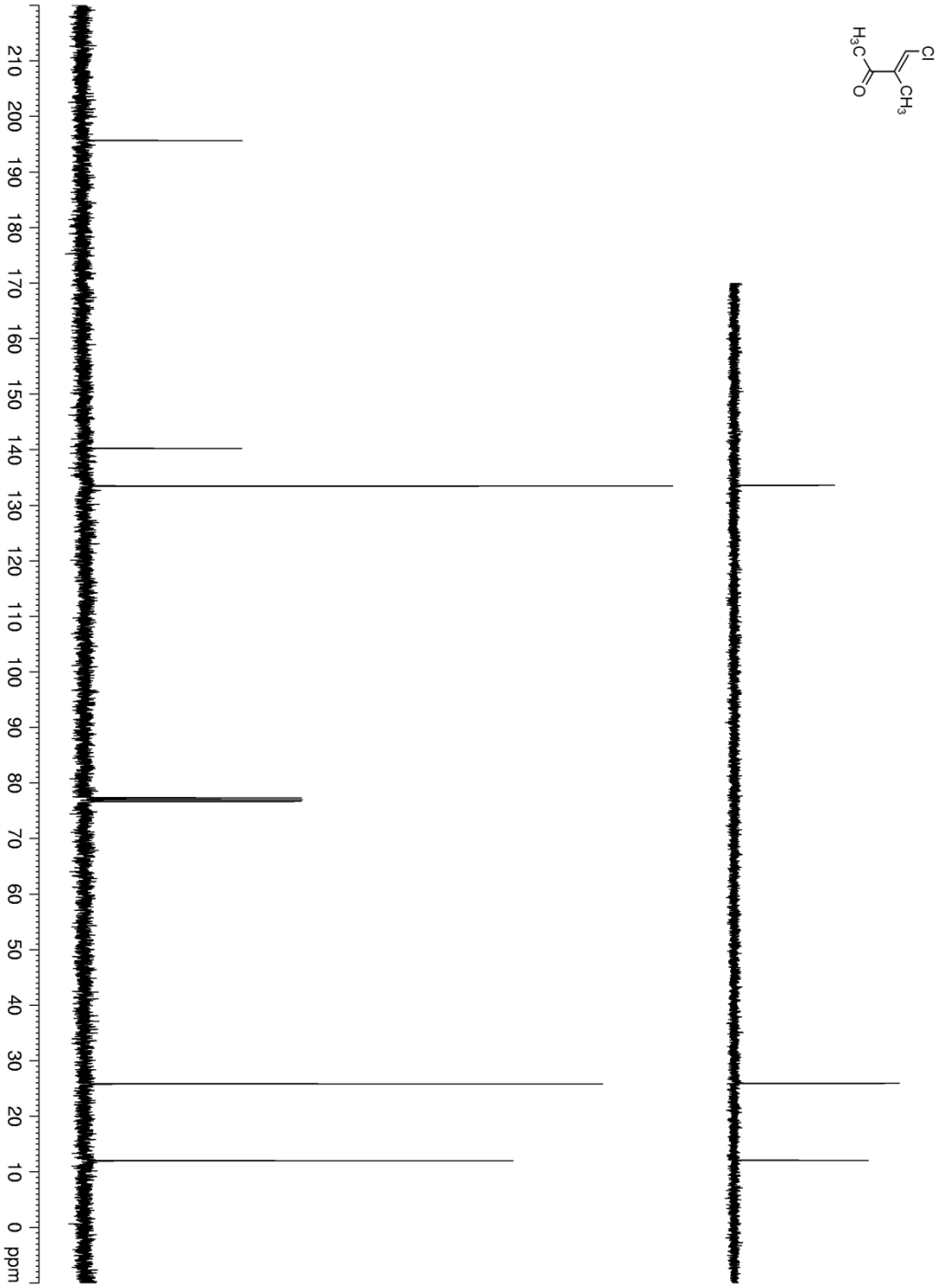


Figure 20. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **11**

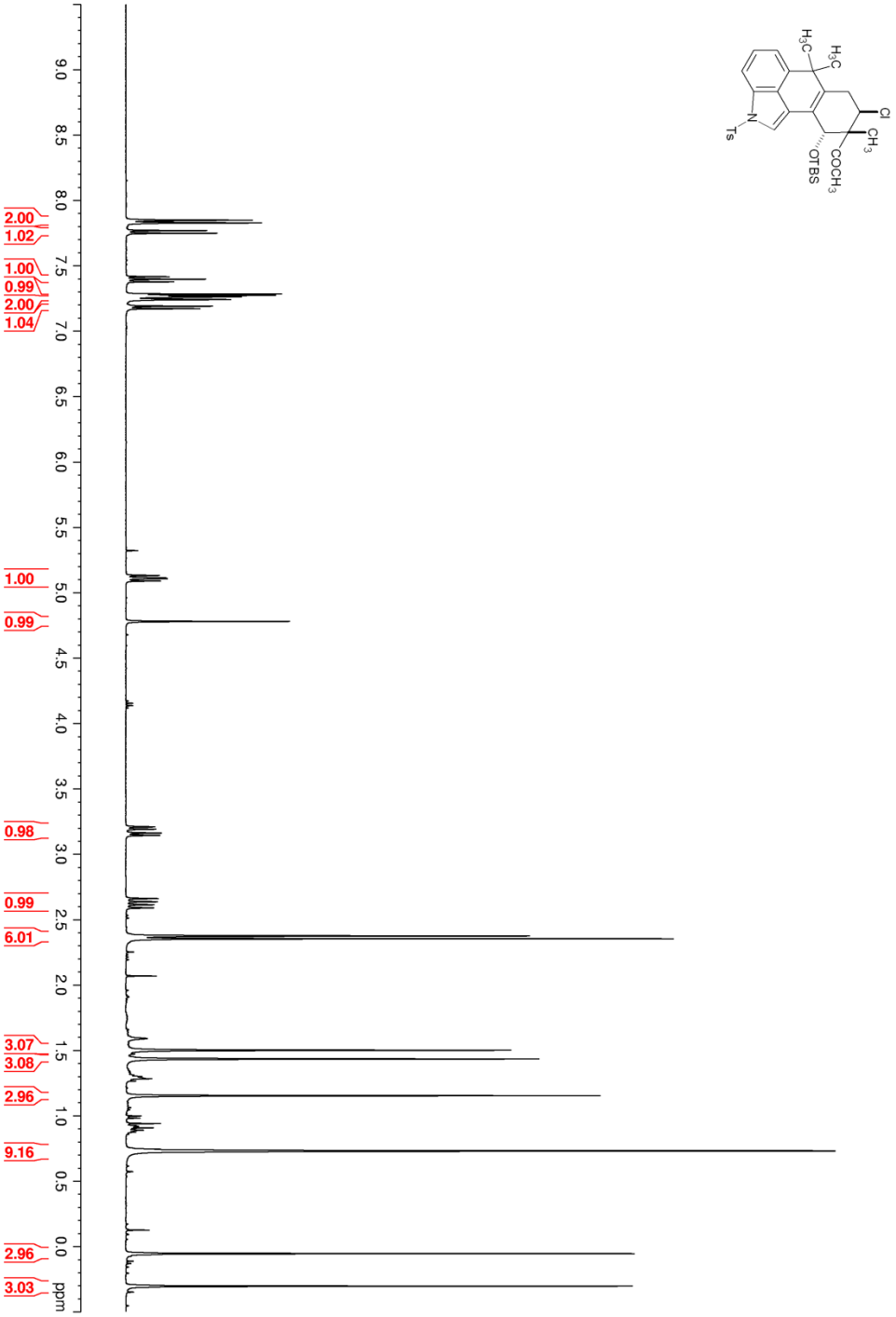


Figure 21. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **11**

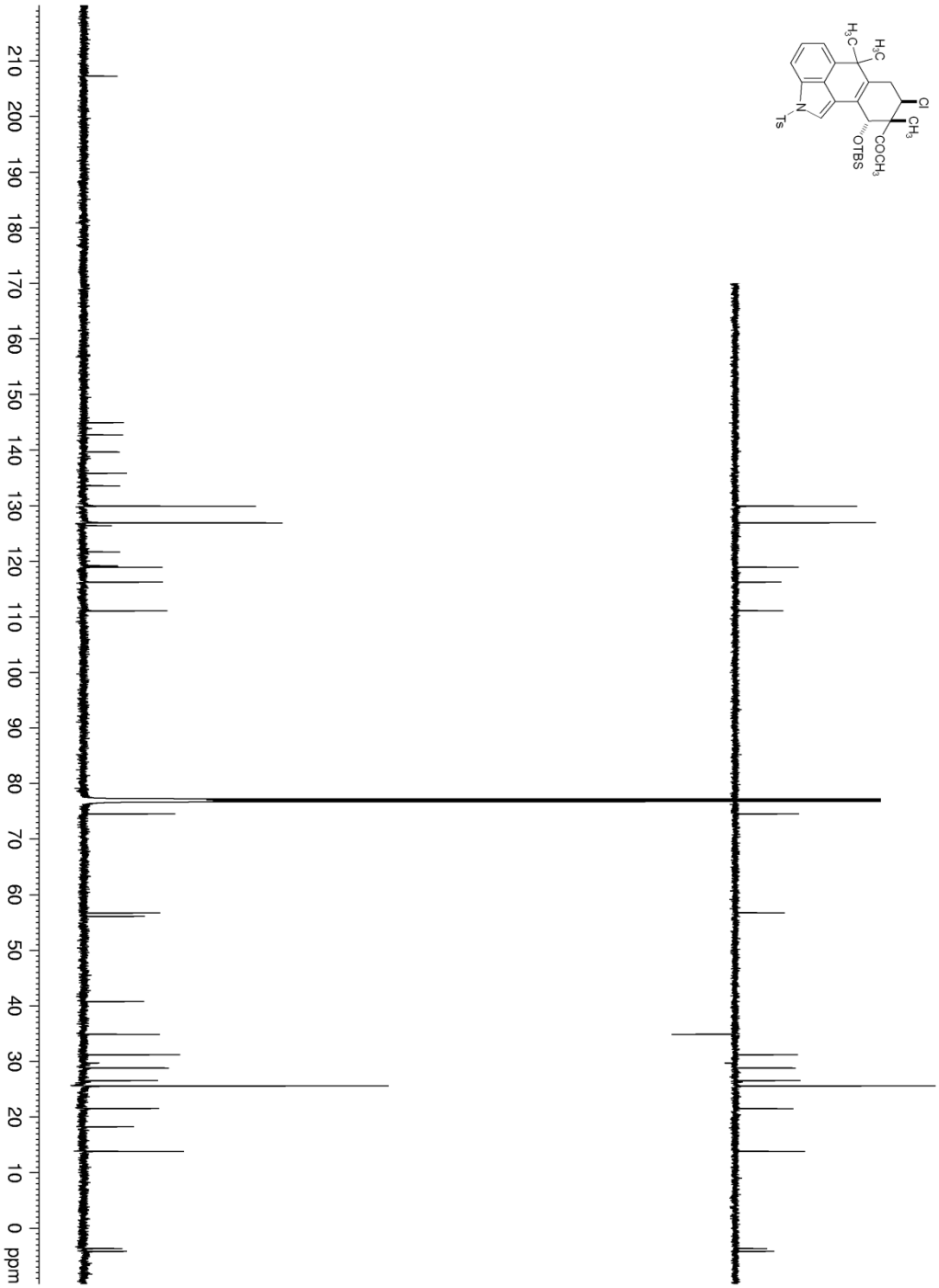


Figure 22. NOESY Spectrum (600 MHz, $CDCl_3$) of **11**

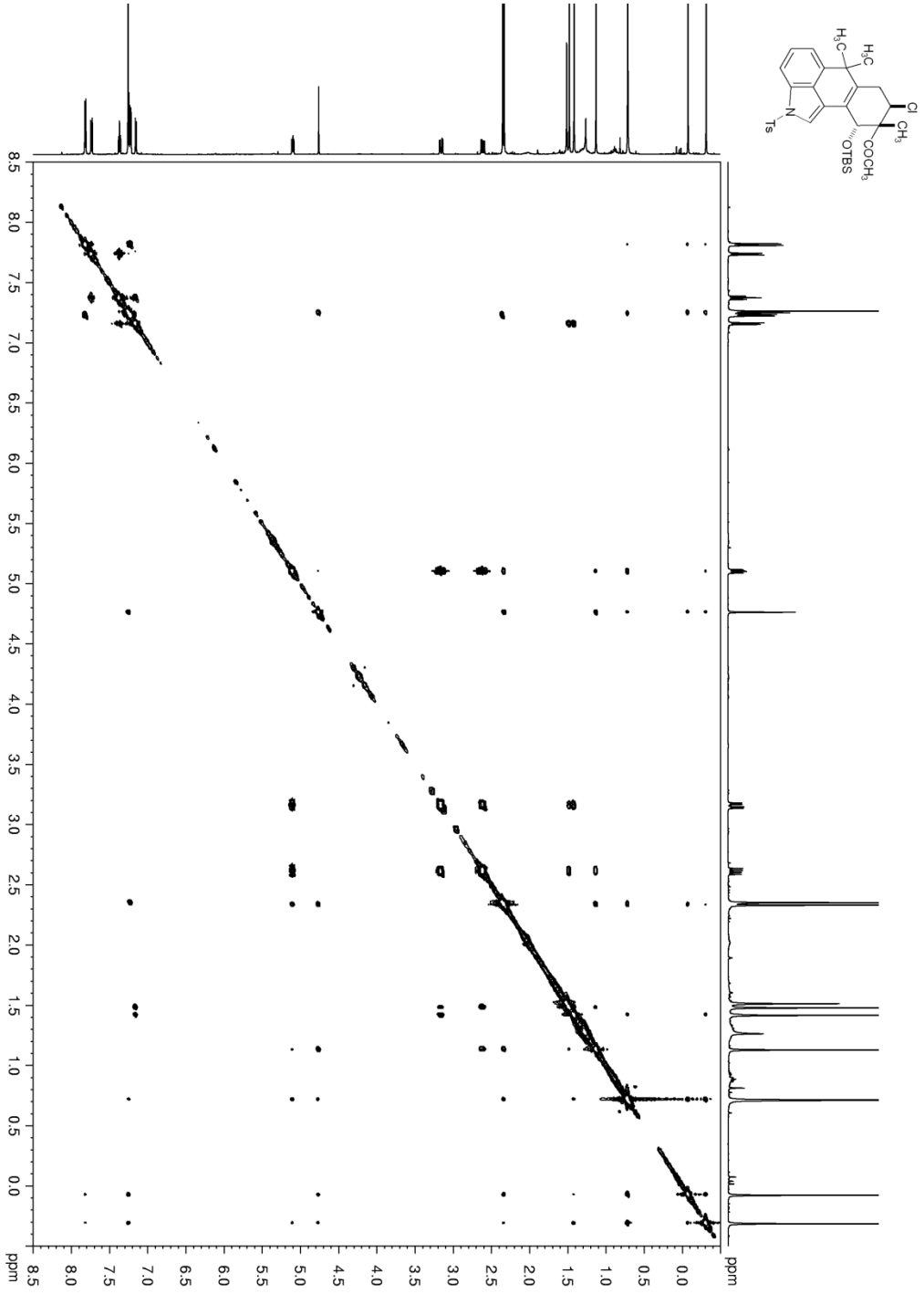


Figure 23. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **12**

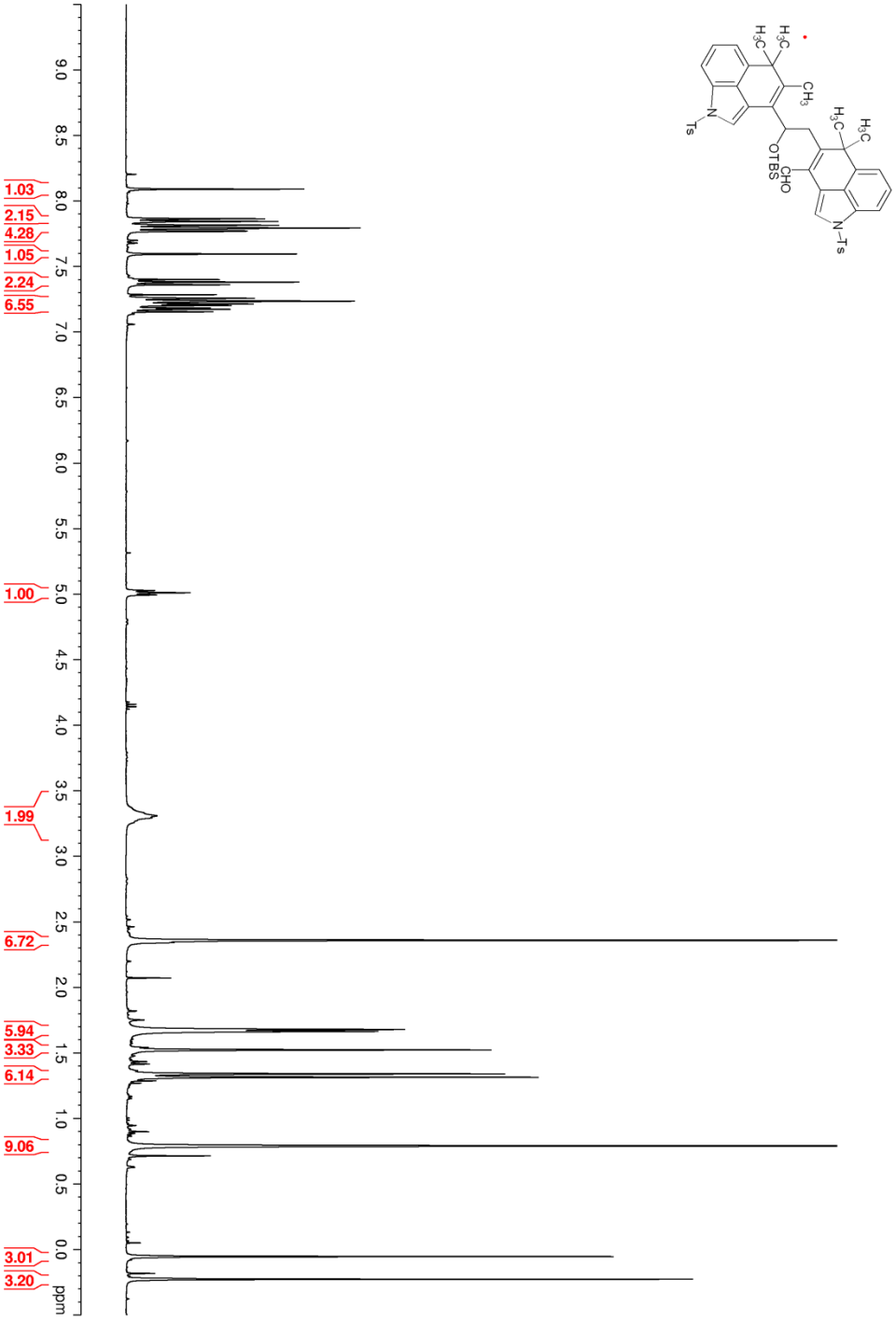


Figure 24. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **12**

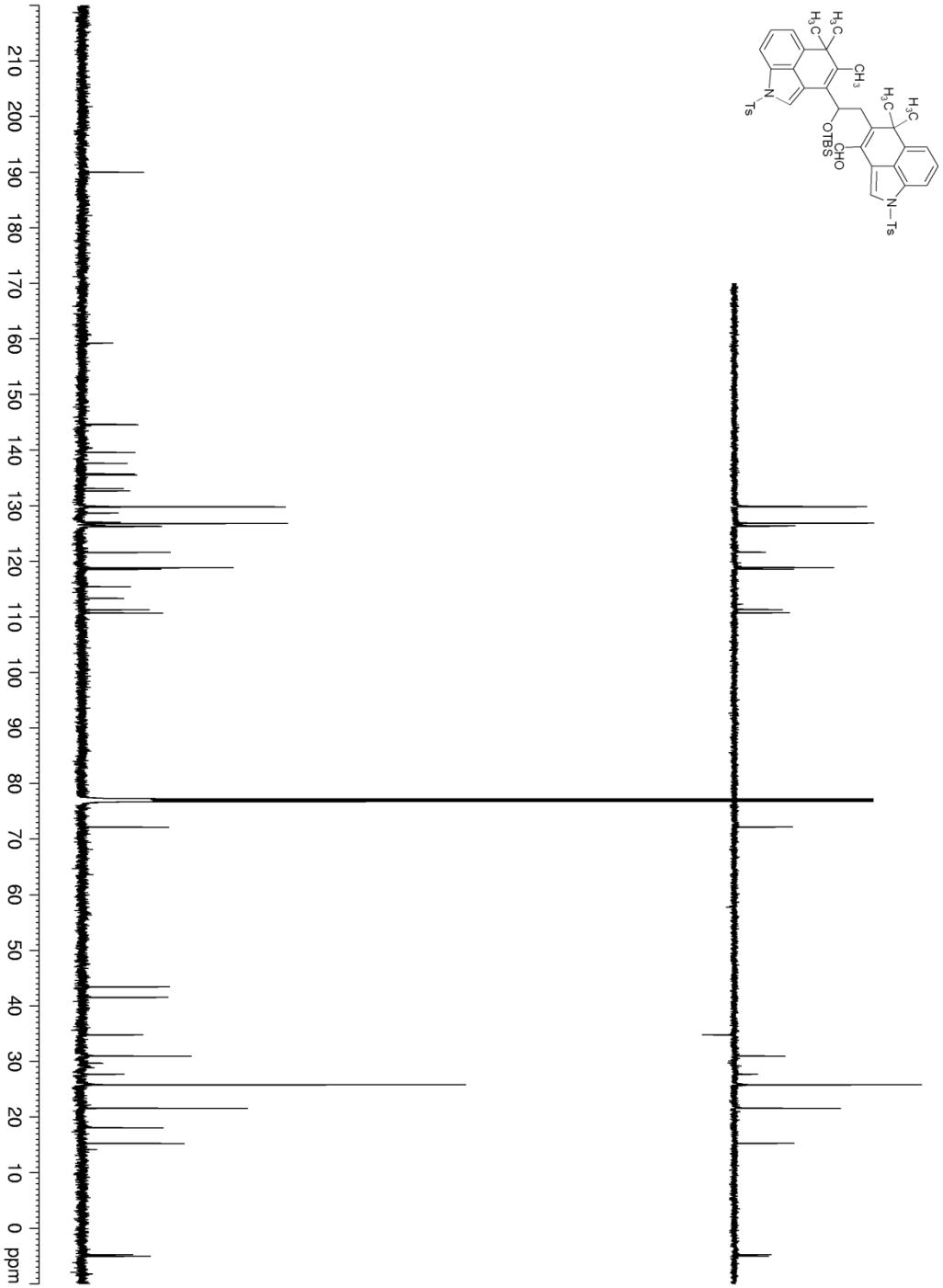


Figure 25. HSQC Spectrum (150 MHz, $CDCl_3$) of **12**

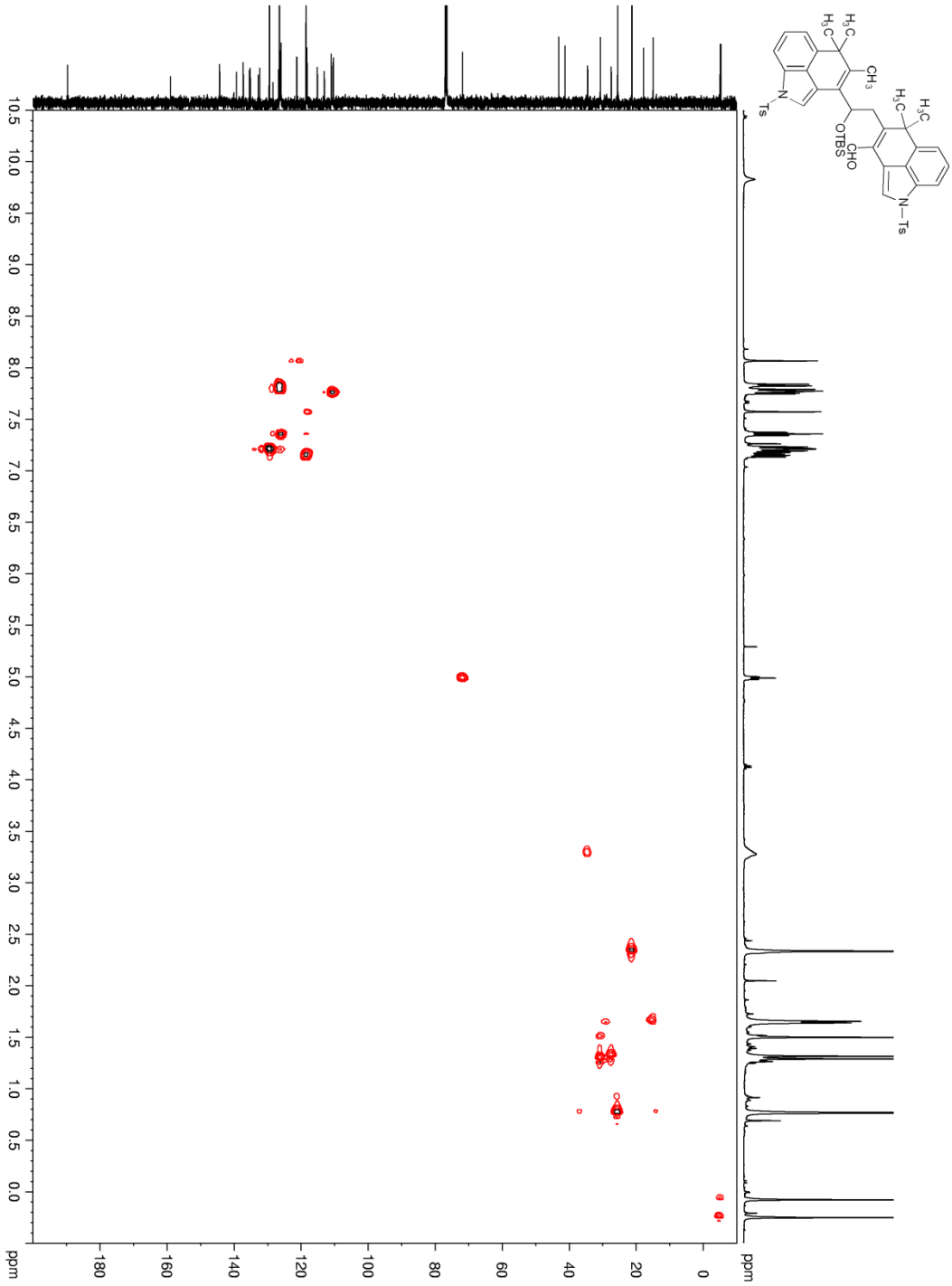


Figure 26. HMBC Spectrum (150 MHz, $CDCl_3$) of **12**

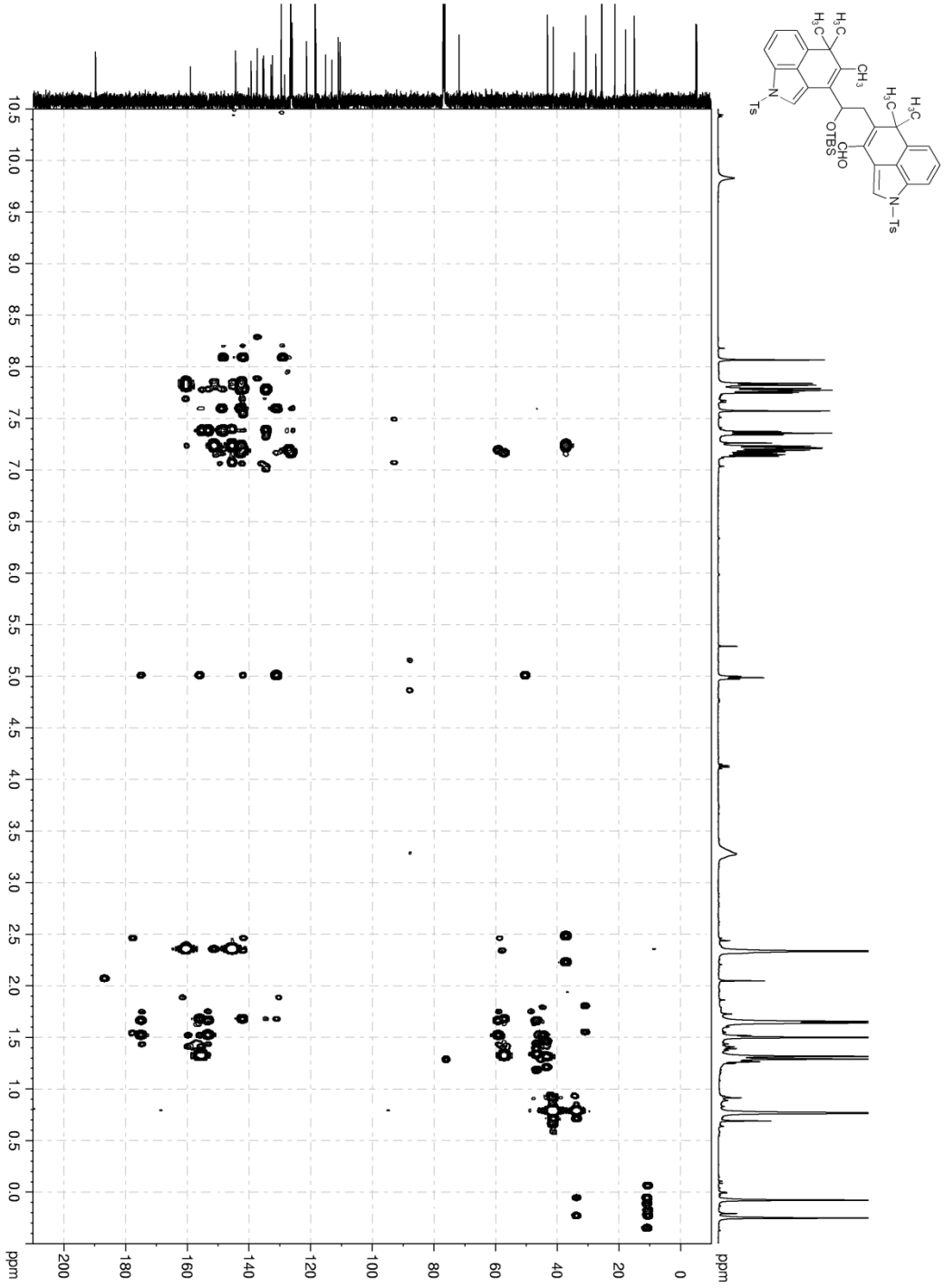


Figure 27. NOESY Spectrum (600 MHz, $CDCl_3$) of **12**

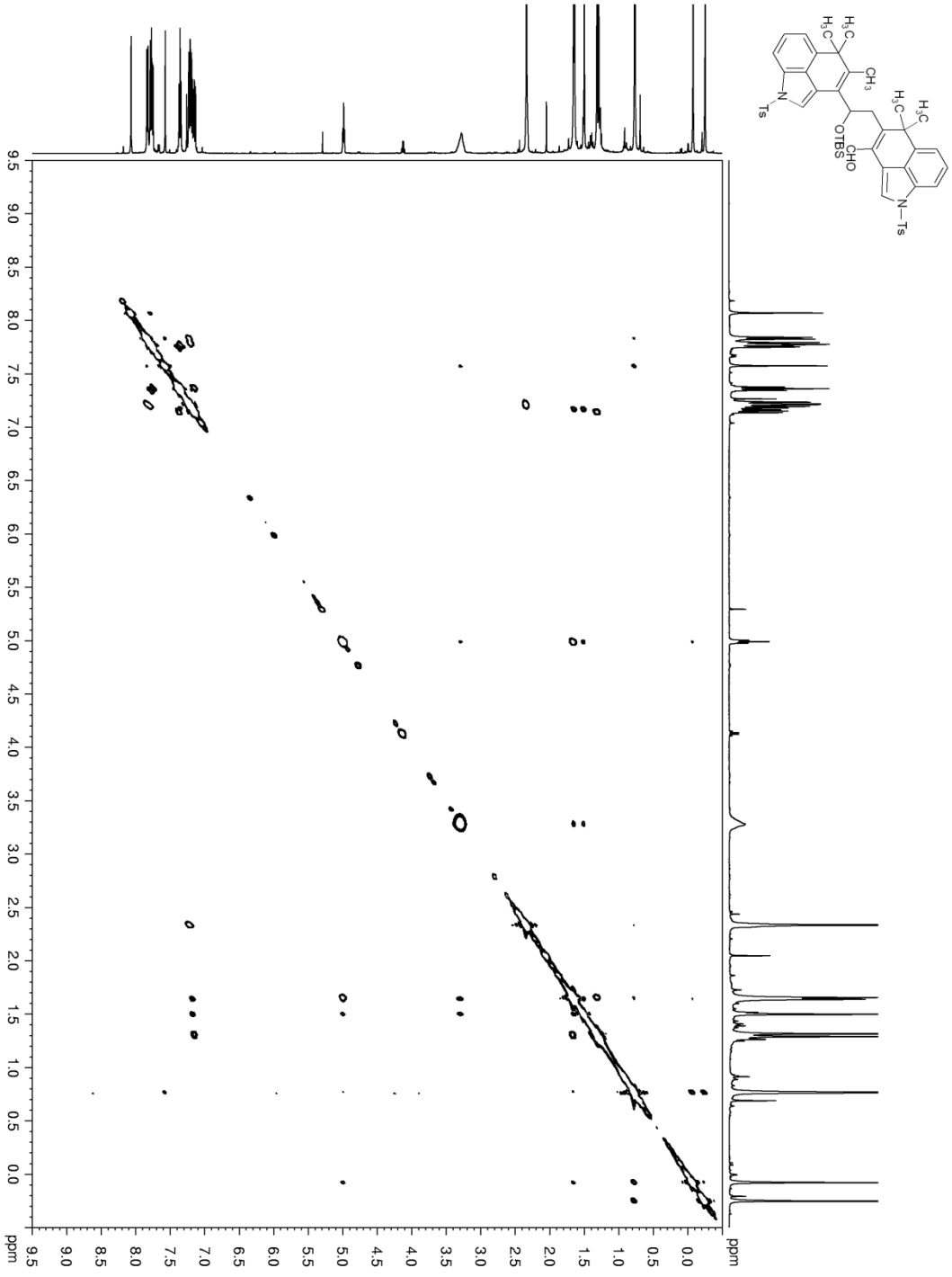


Figure 28. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **13**

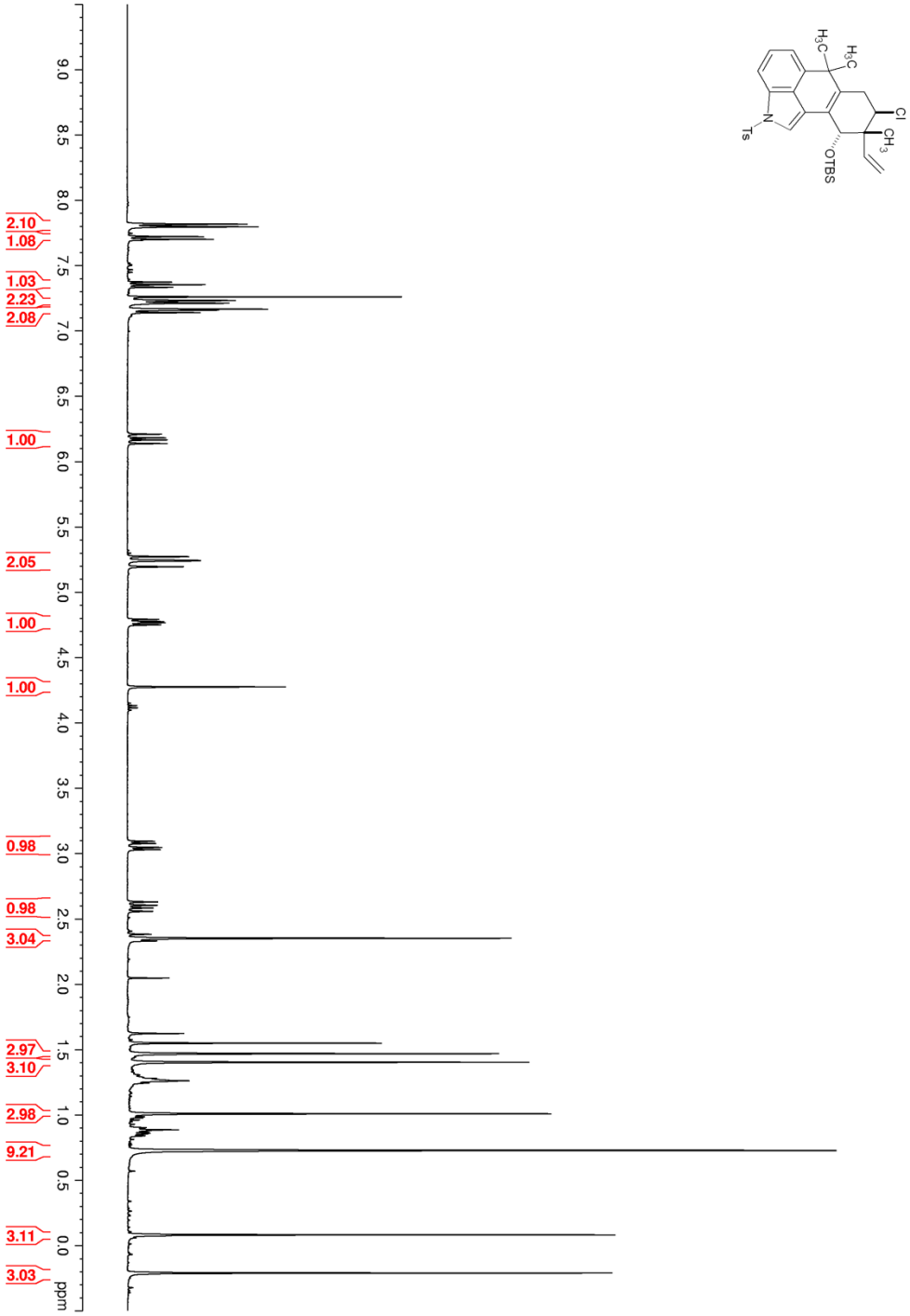


Figure 29. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **13**

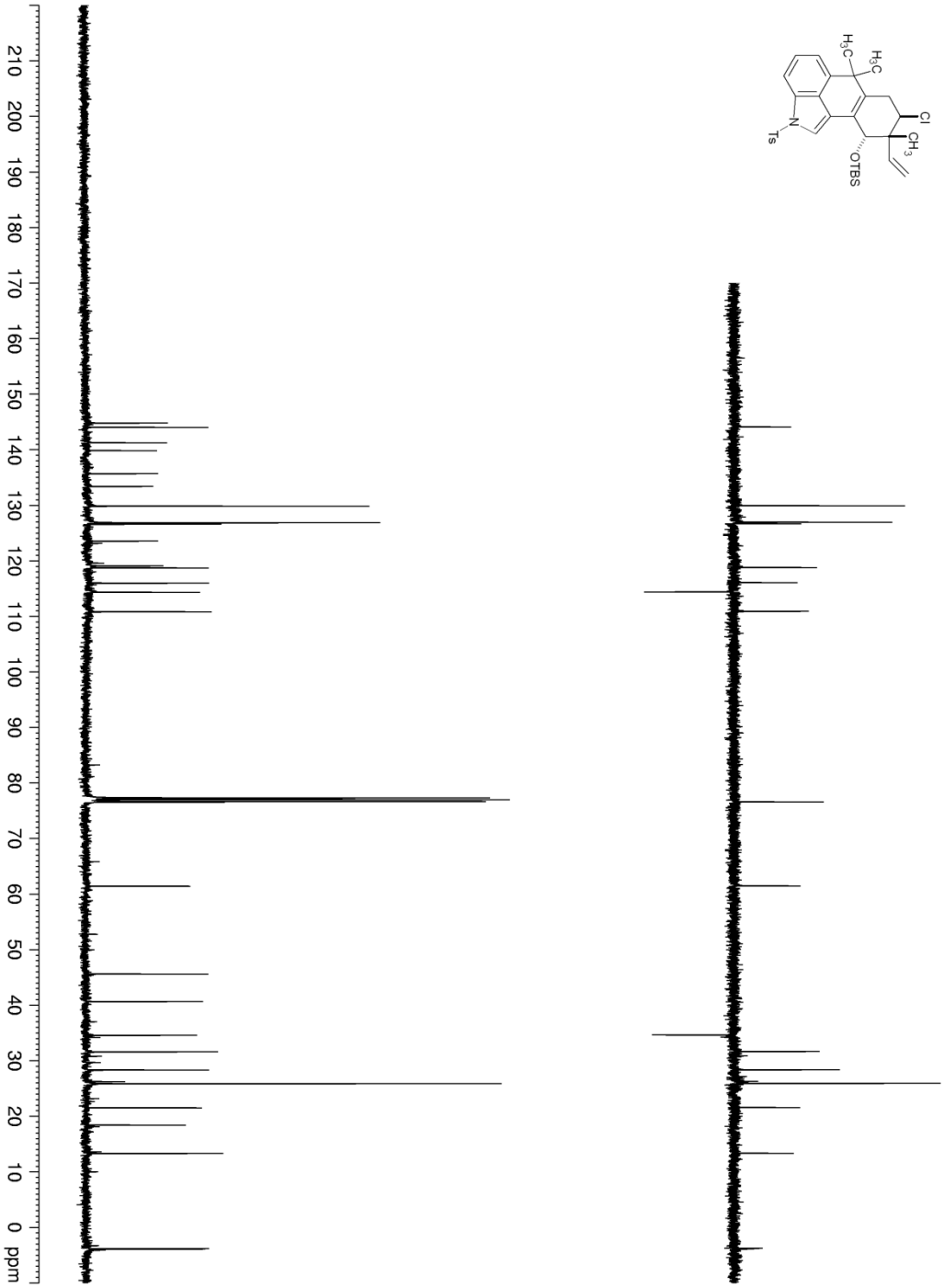


Figure 30. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **14**

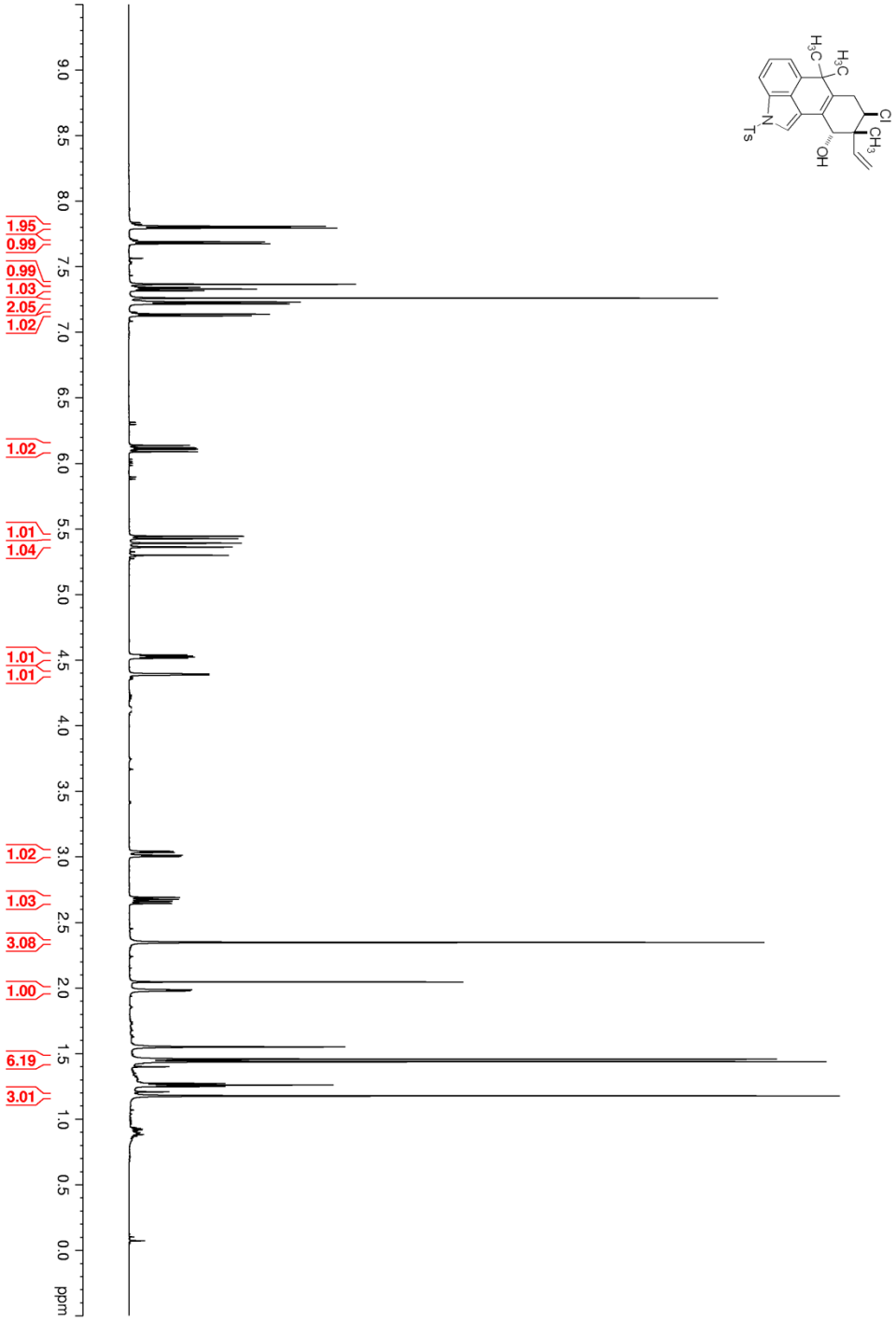


Figure 31. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **14**

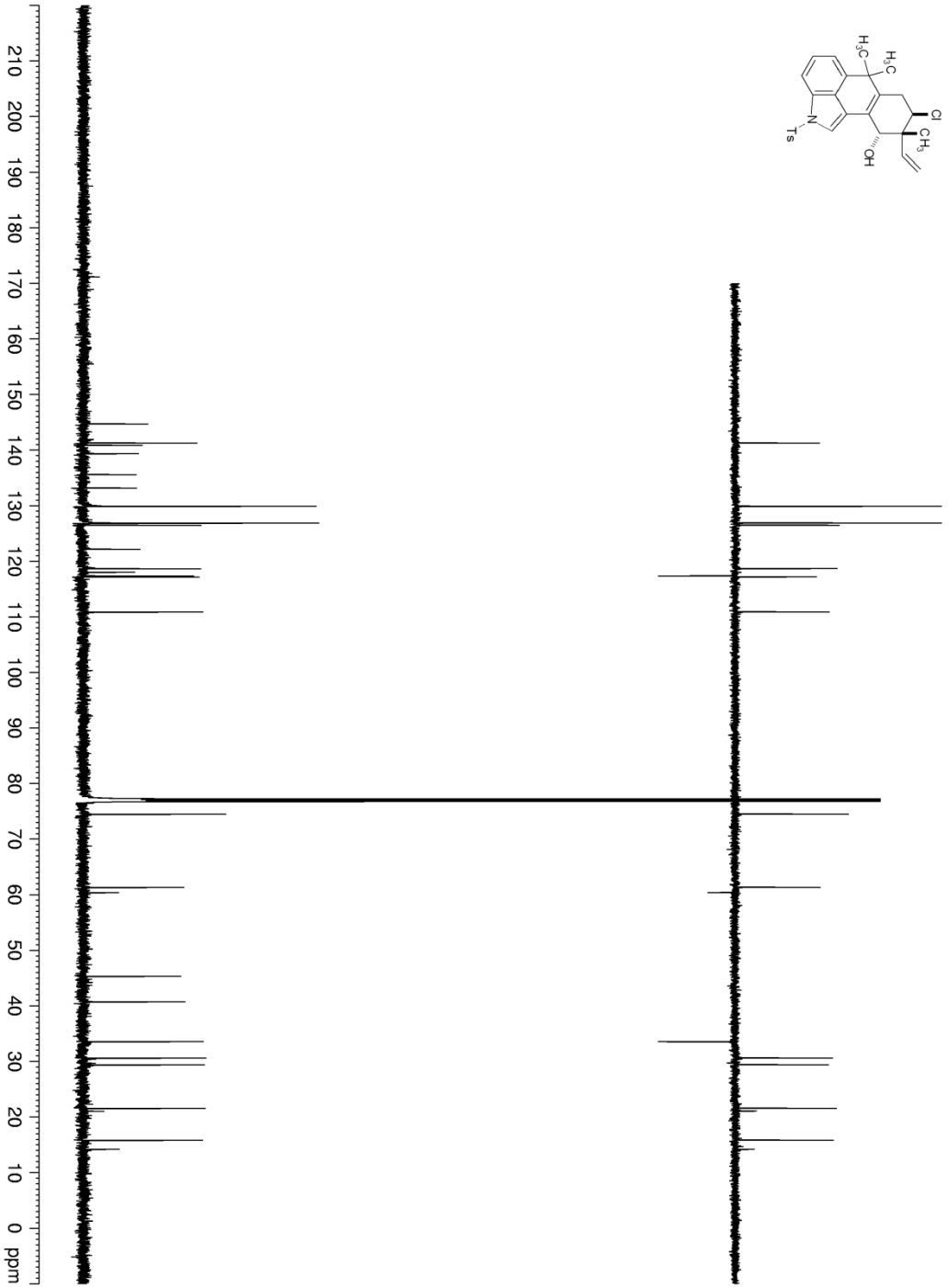


Figure 32. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **15a**

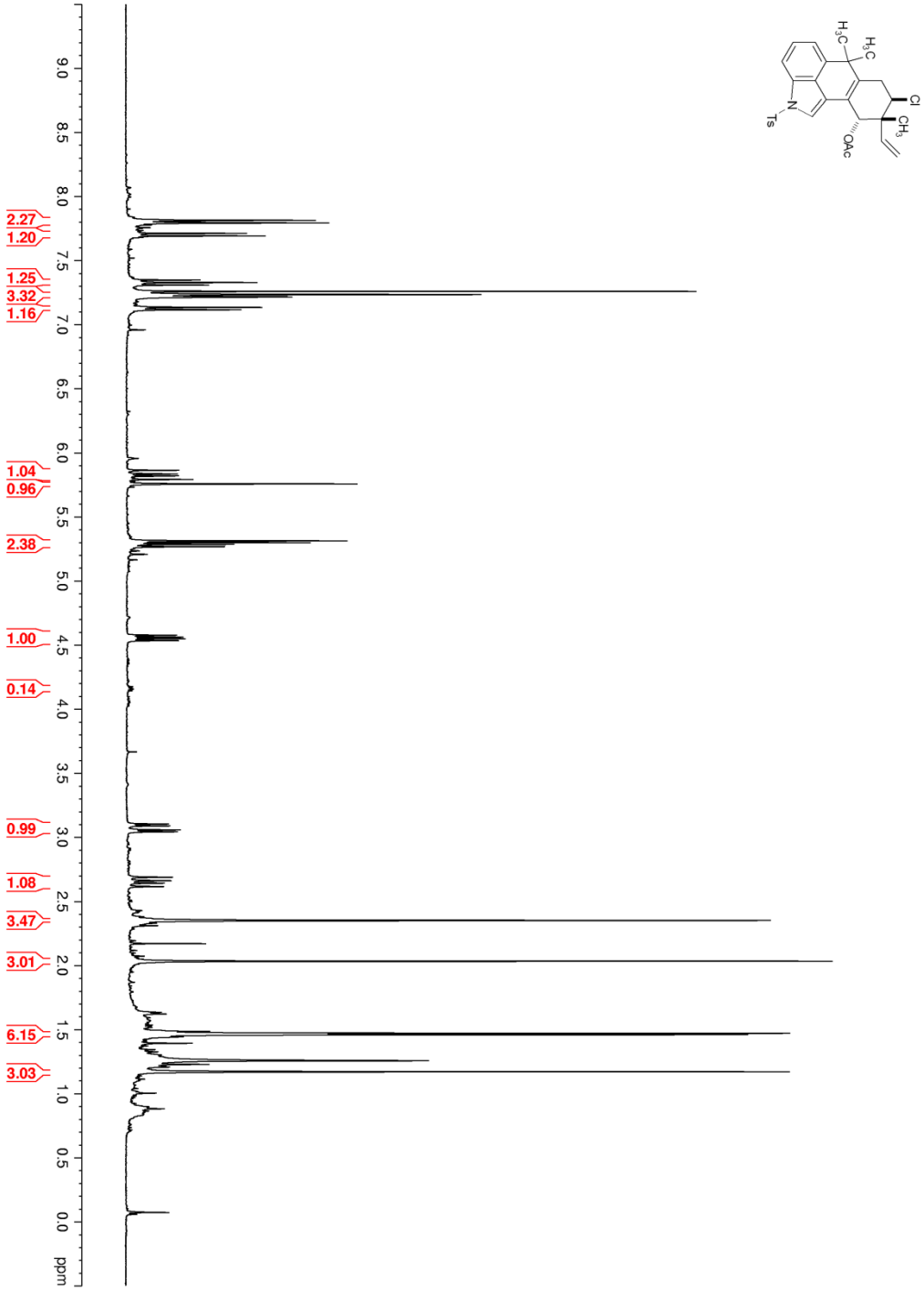


Figure 33. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **15a**

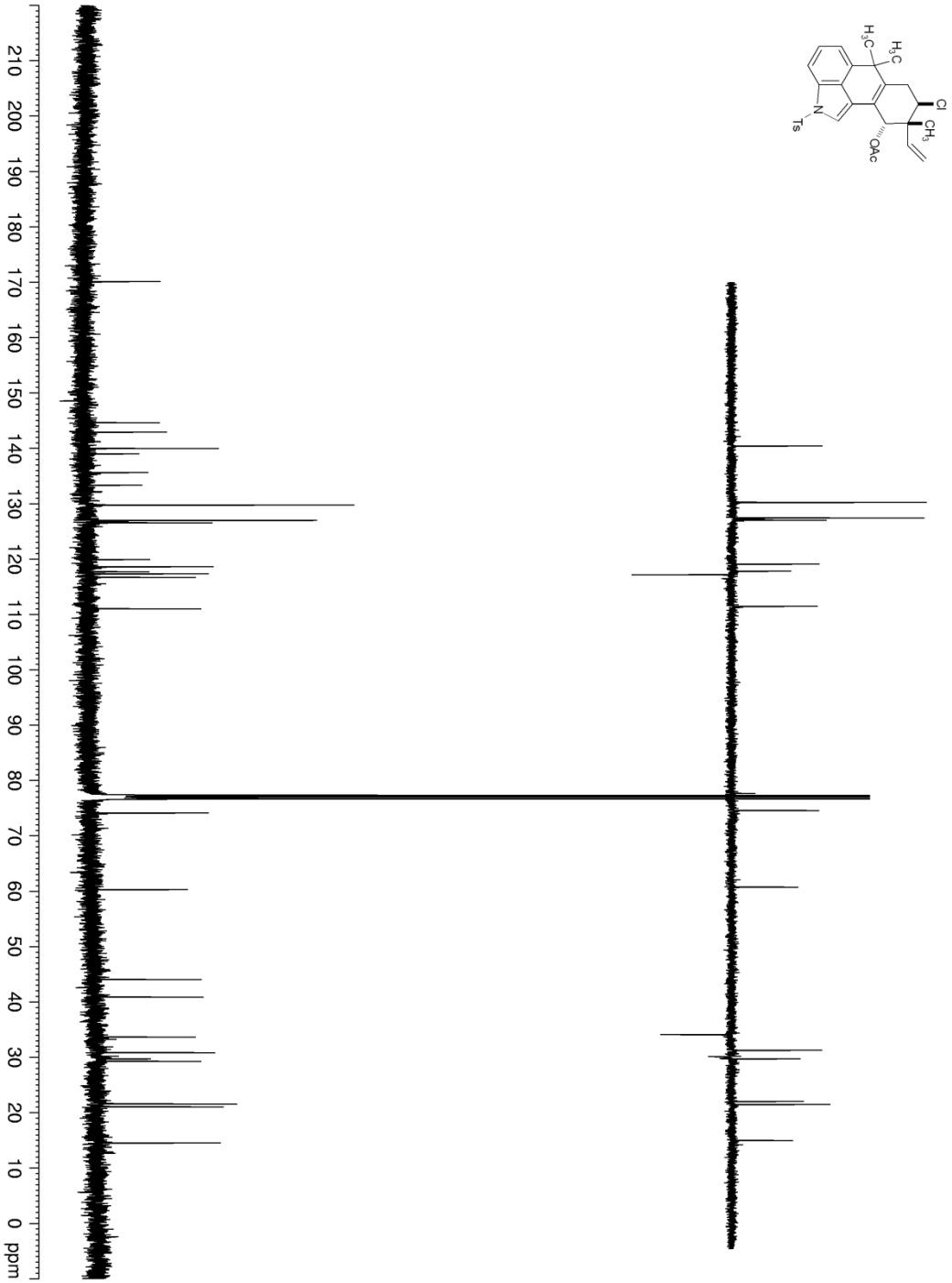


Figure 34. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **15b**

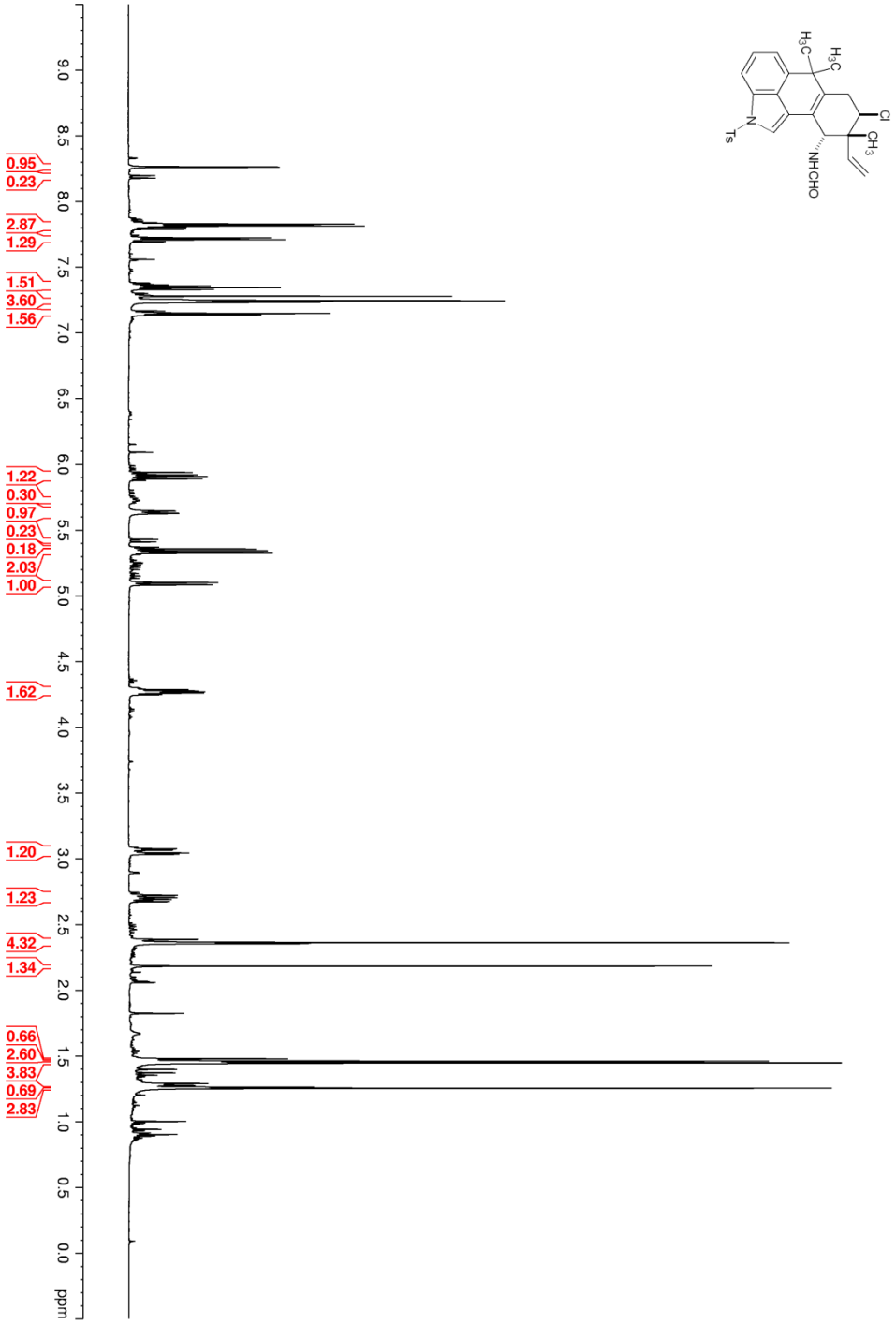


Figure 35. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **15b**

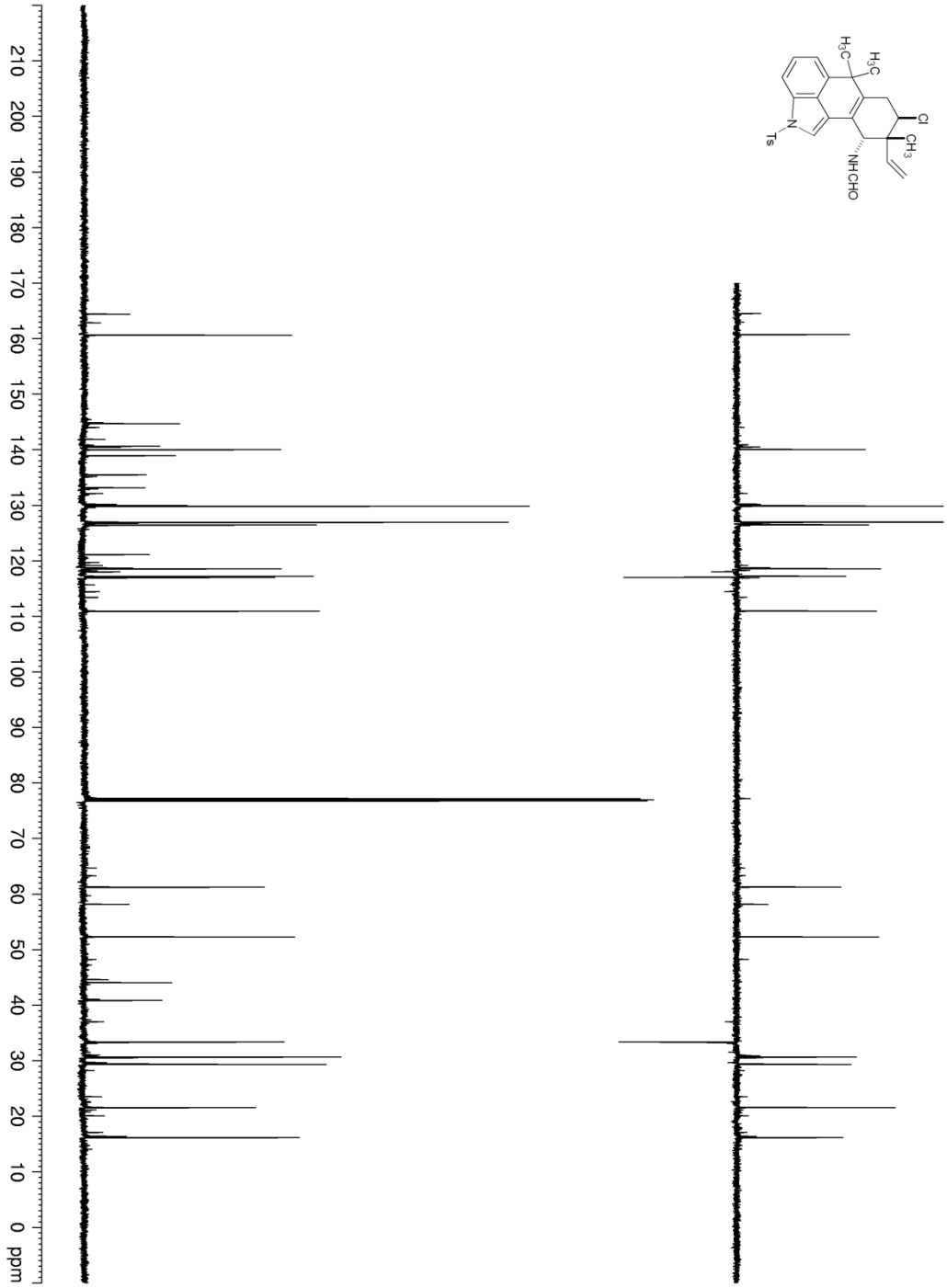


Figure 36. HSQC Spectrum (150 MHz, $CDCl_3$) of **15b**

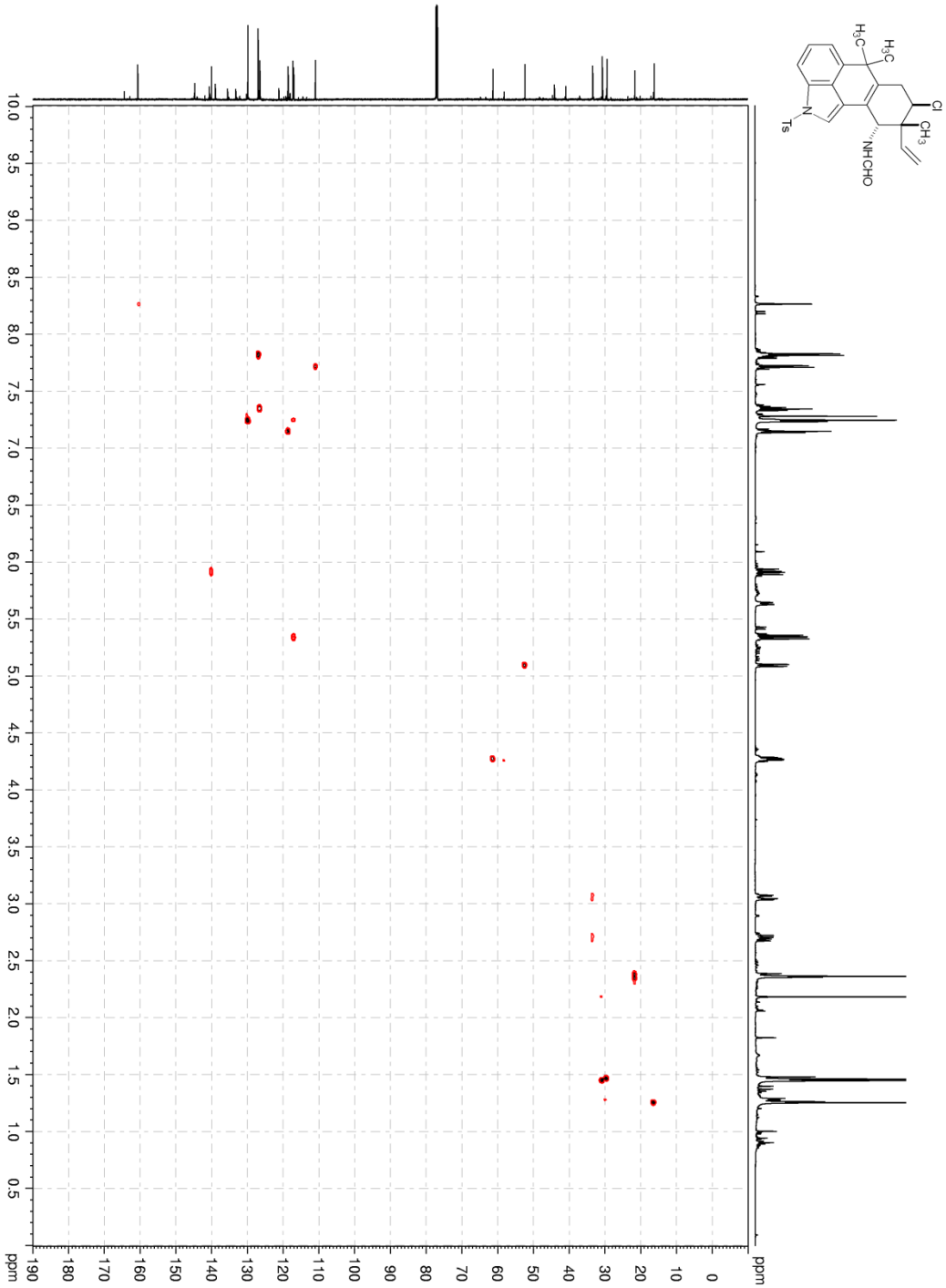


Figure 37. HMBC Spectrum (150 MHz, $CDCl_3$) of **15b**

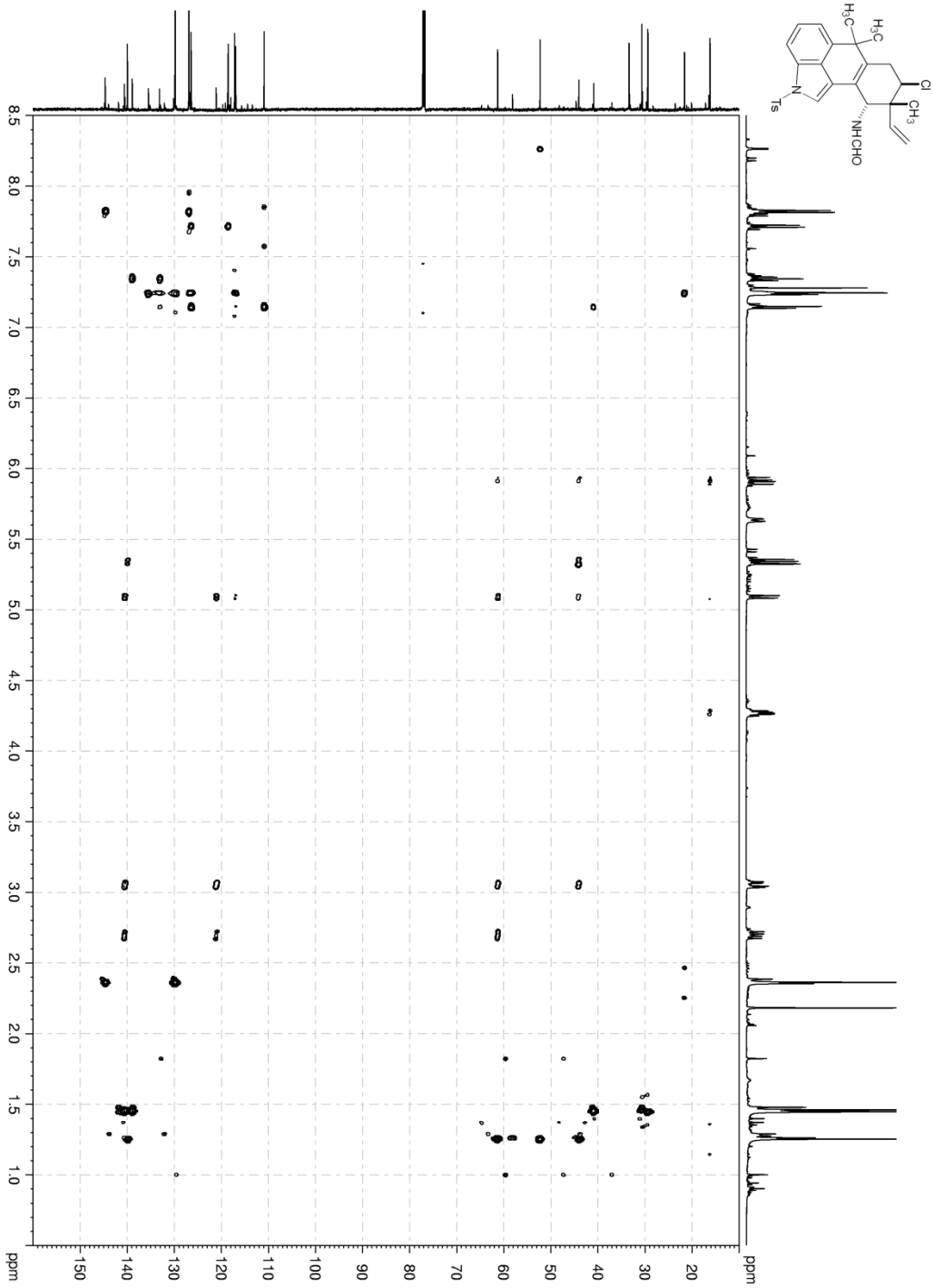


Figure 38. NOESY Spectrum (600 MHz, $CDCl_3$) of **15b**

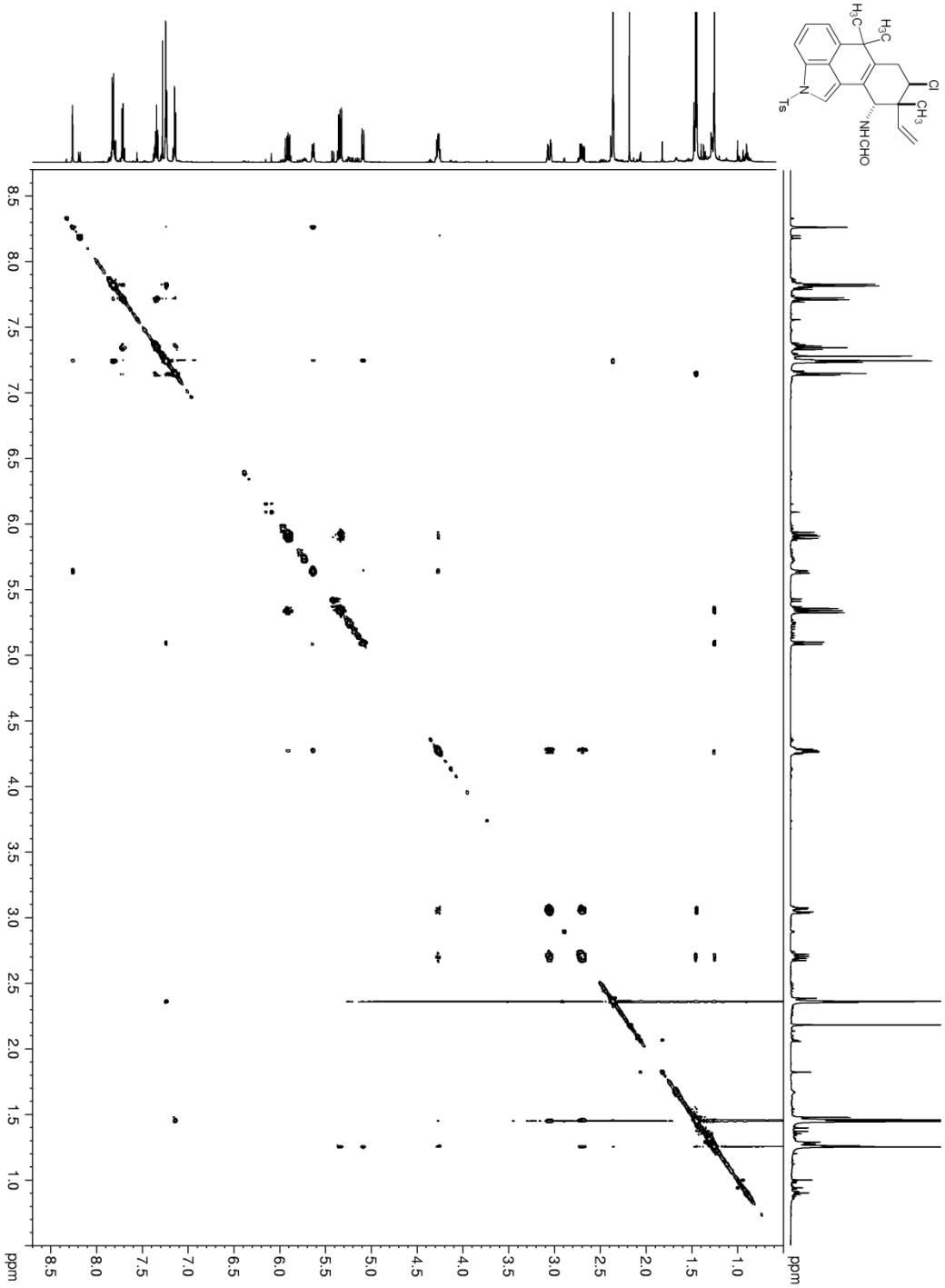


Figure 39. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **16**

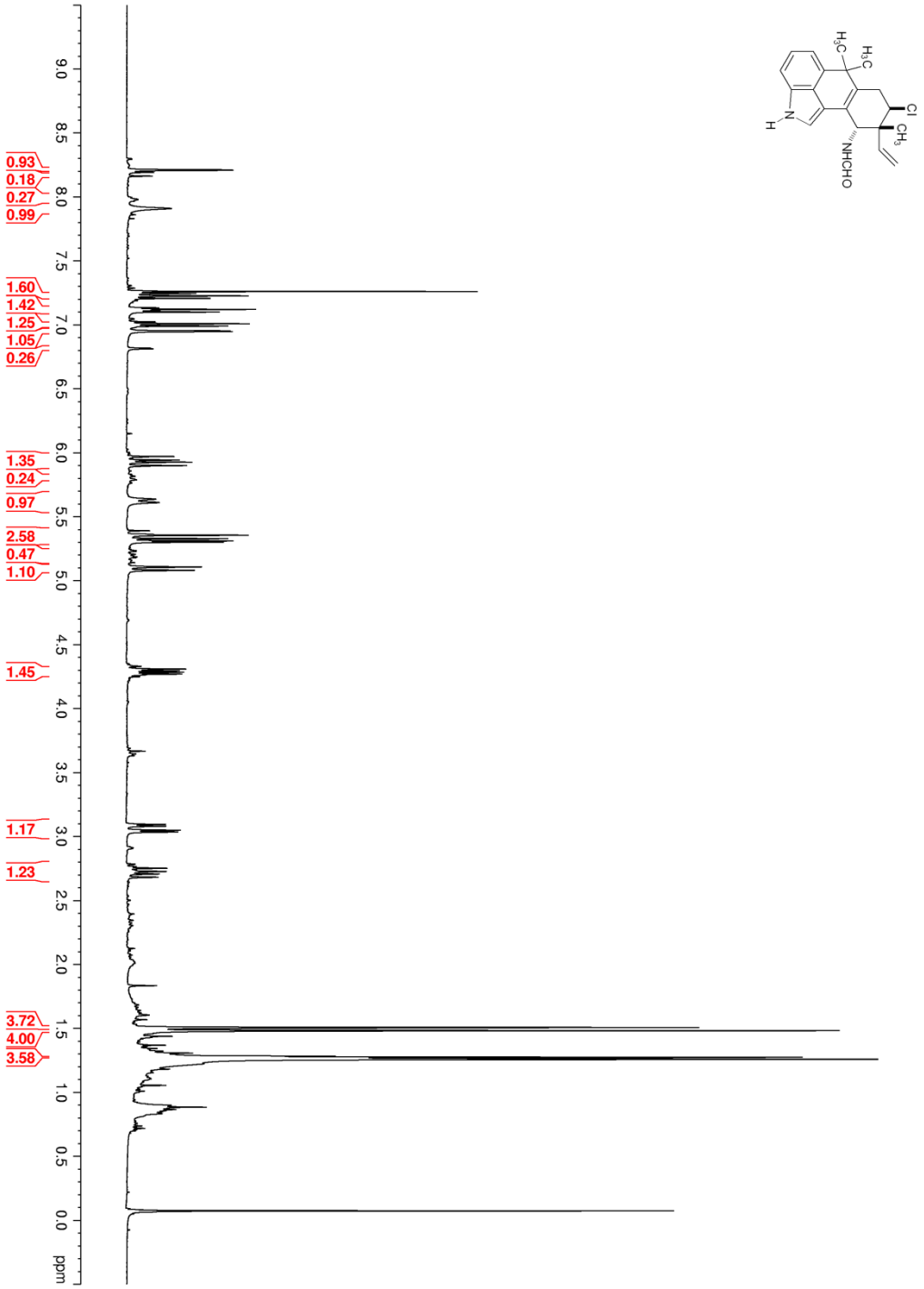


Figure 40. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **16**

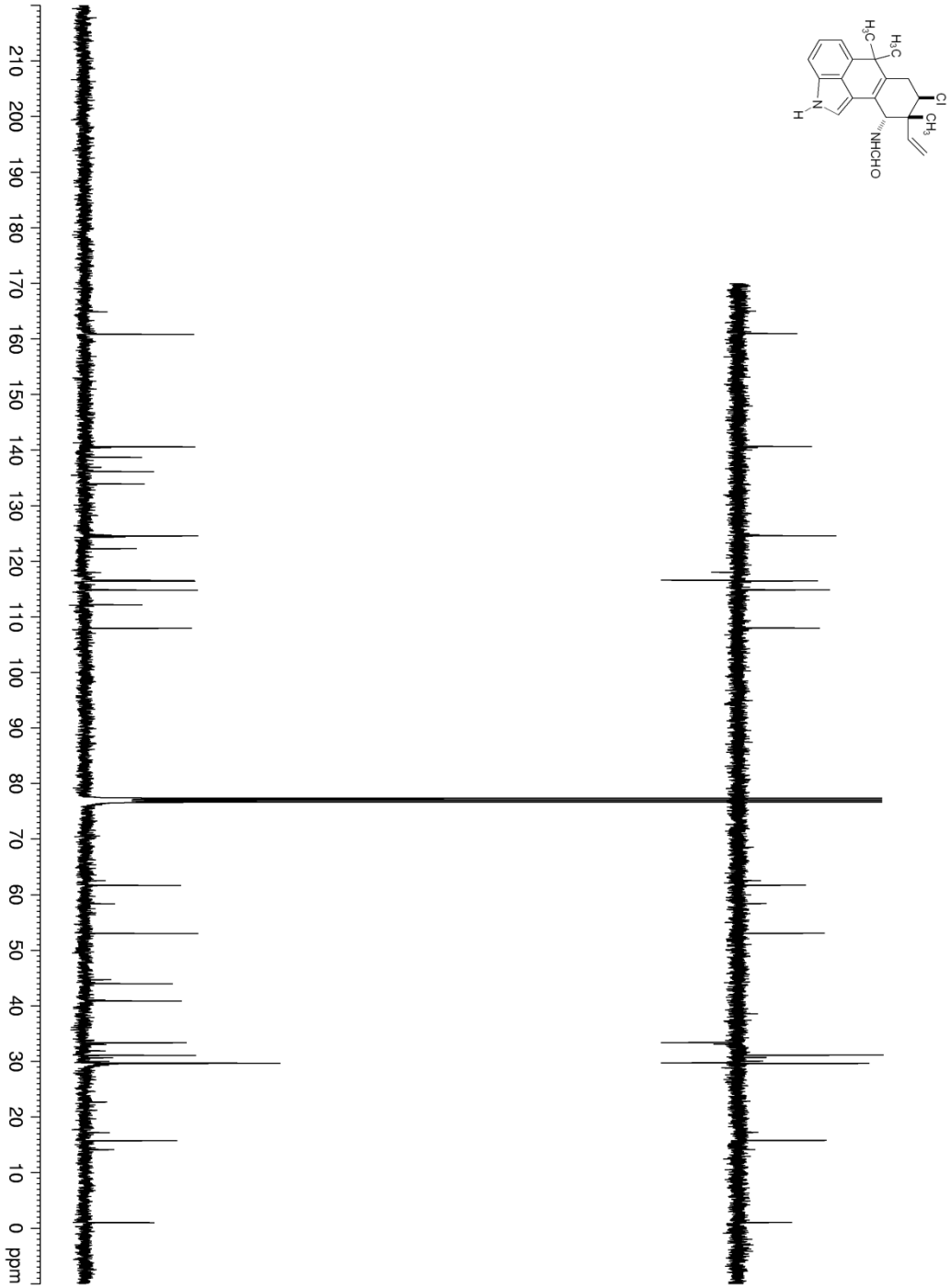


Figure 41. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **17**

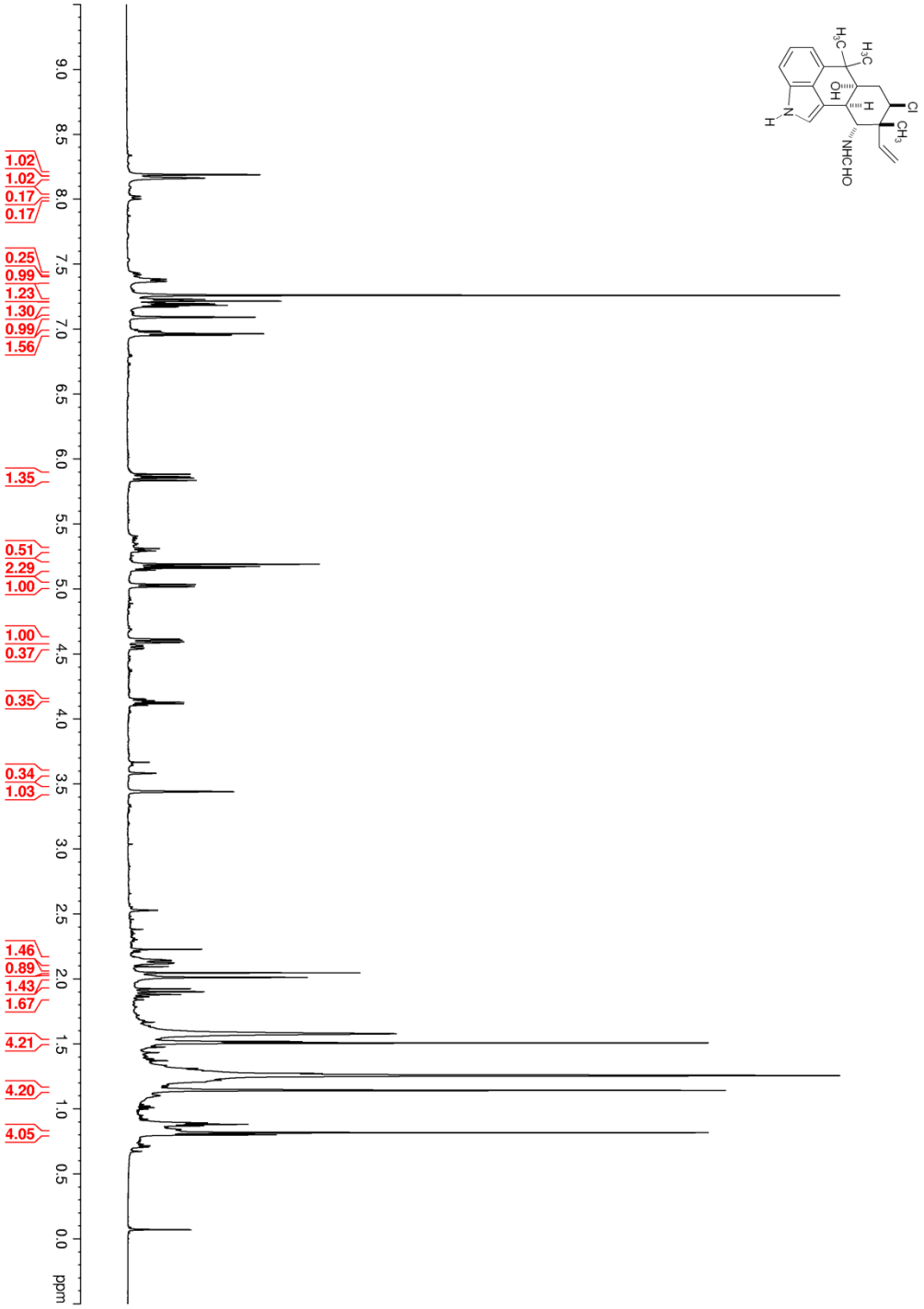


Figure 42. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **17**

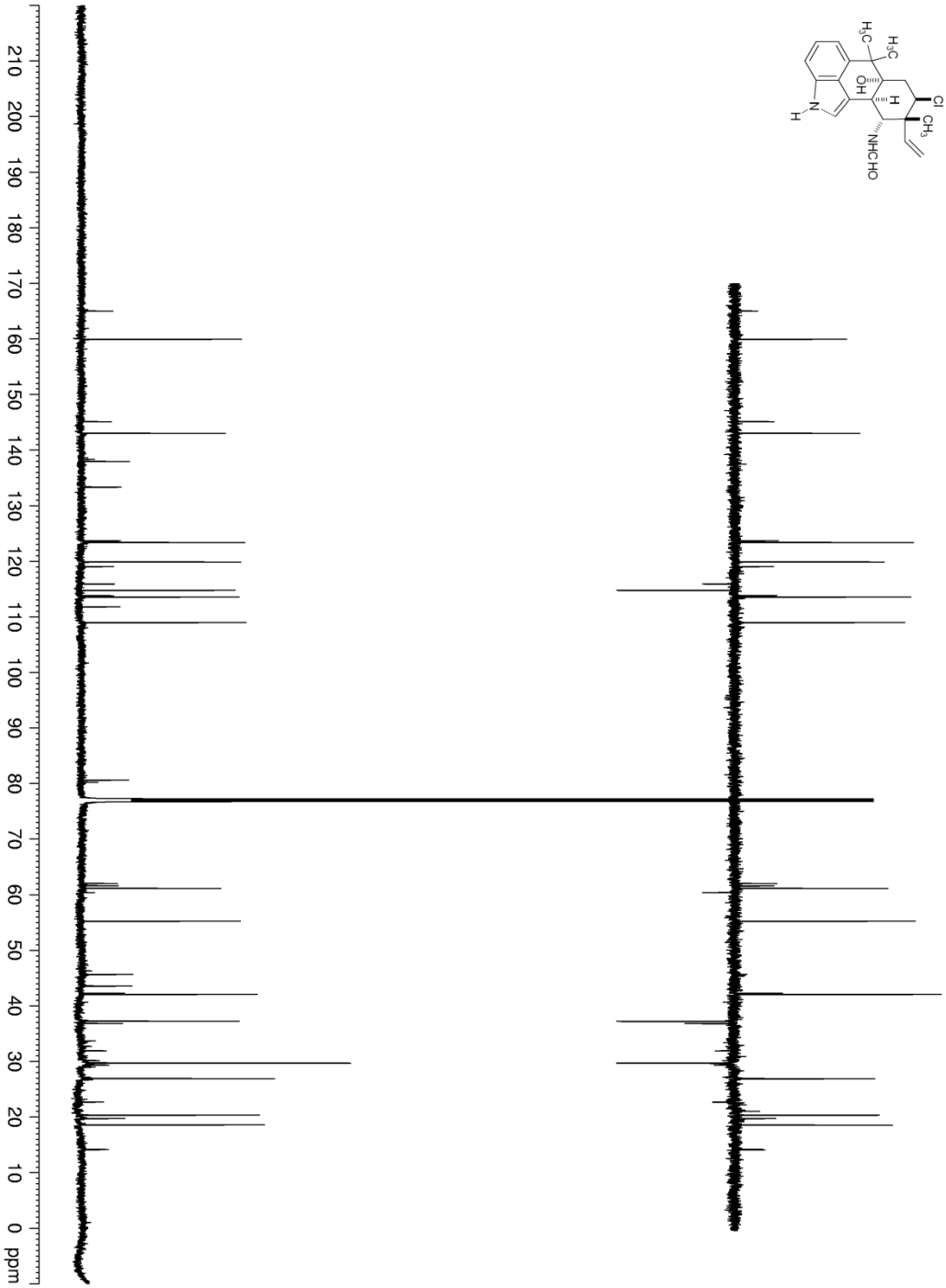


Figure 43. HSQC Spectrum (150 MHz, $CDCl_3$) of **17**

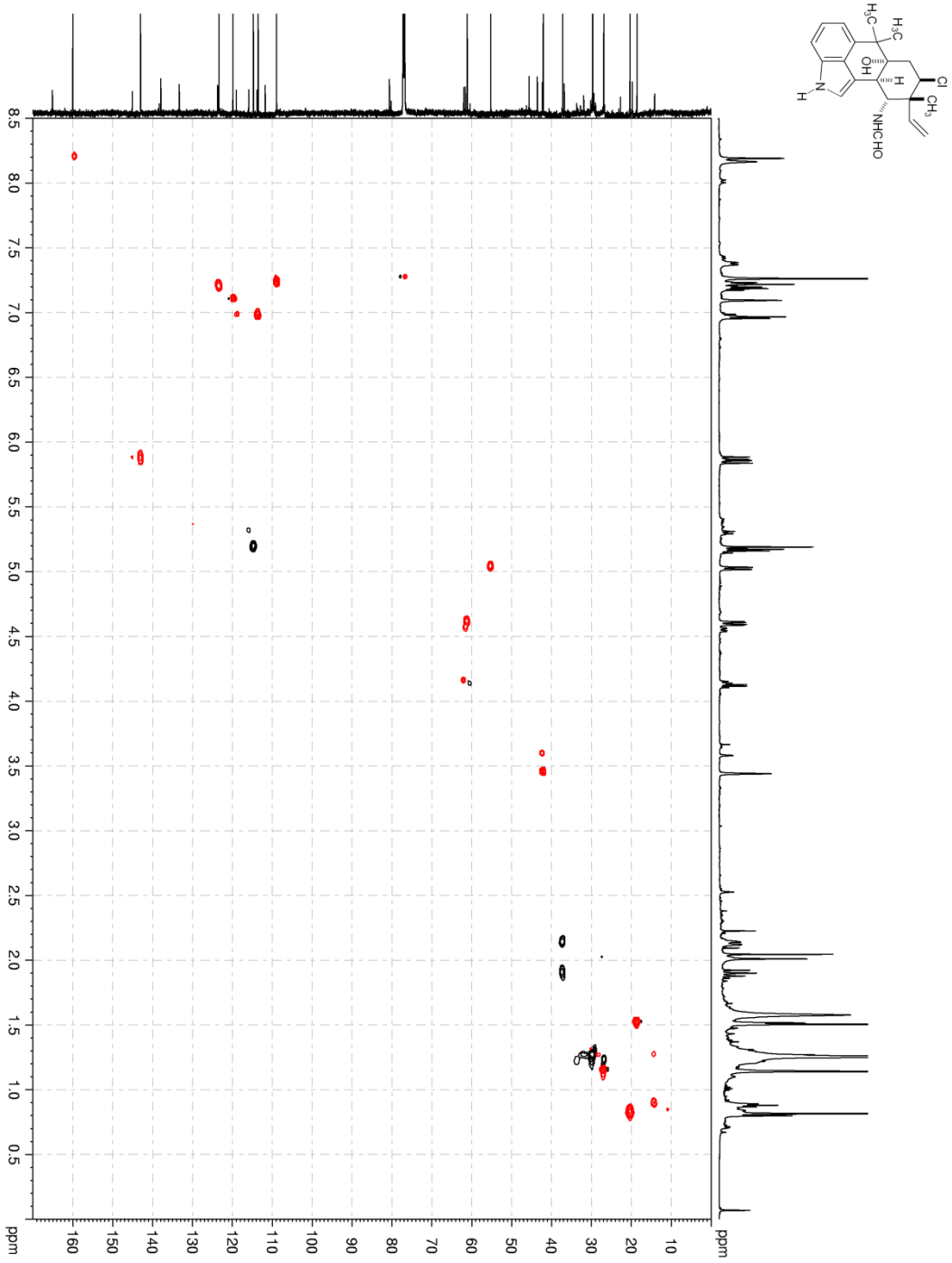


Figure 44. NOESY Spectrum (600 MHz, $CDCl_3$) of **17**

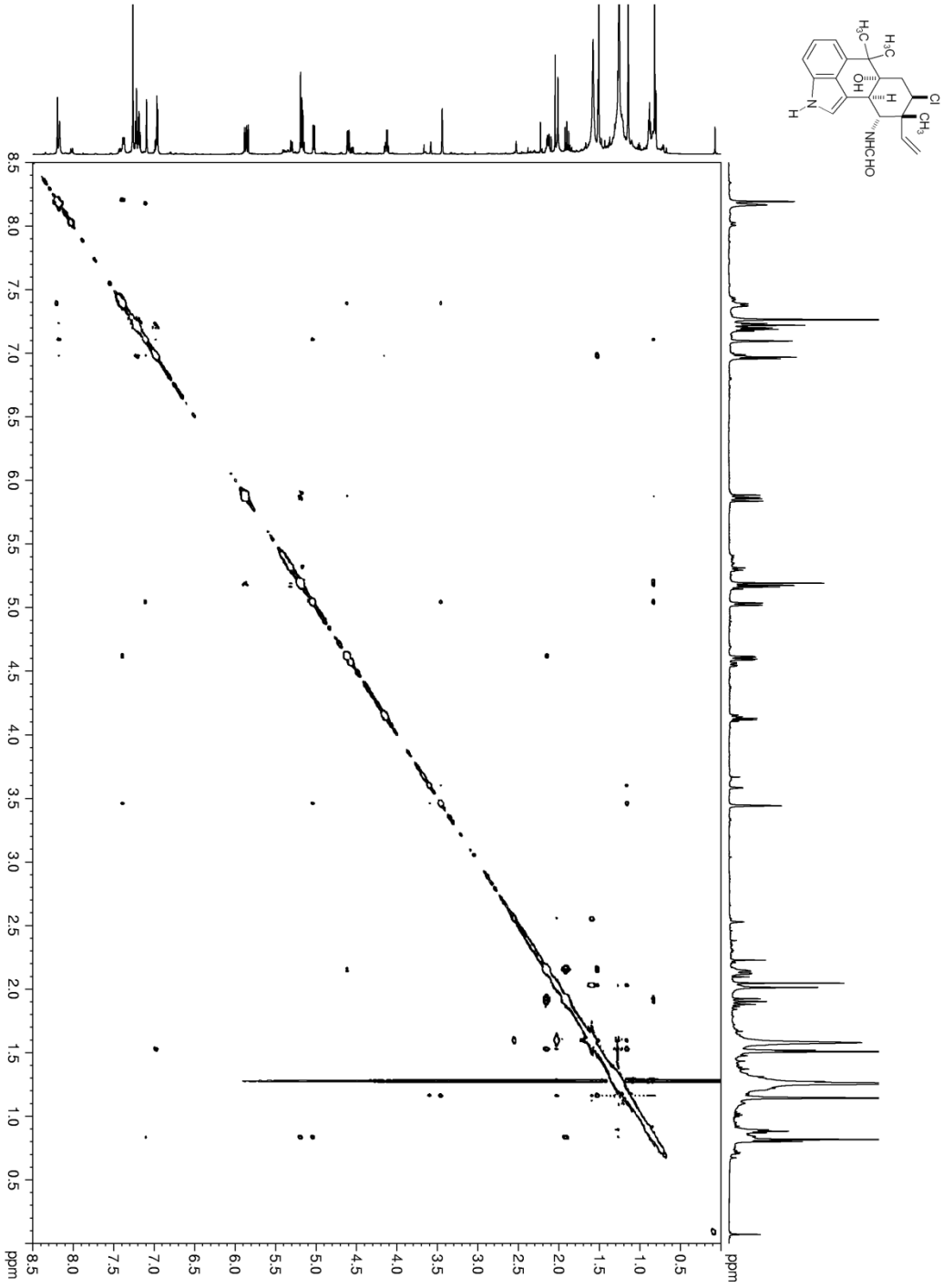


Figure 45. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **18**

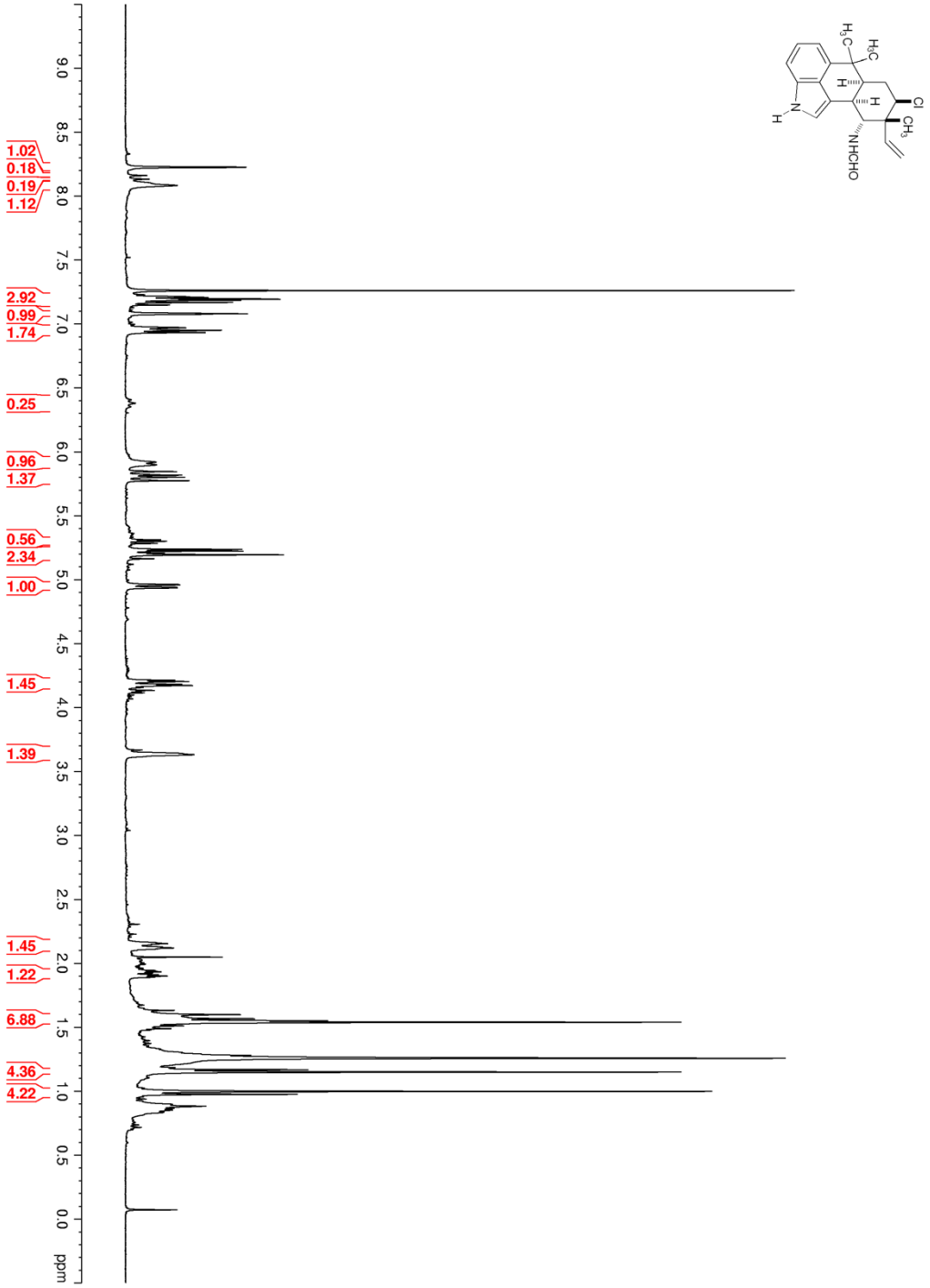


Figure 46. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **18**

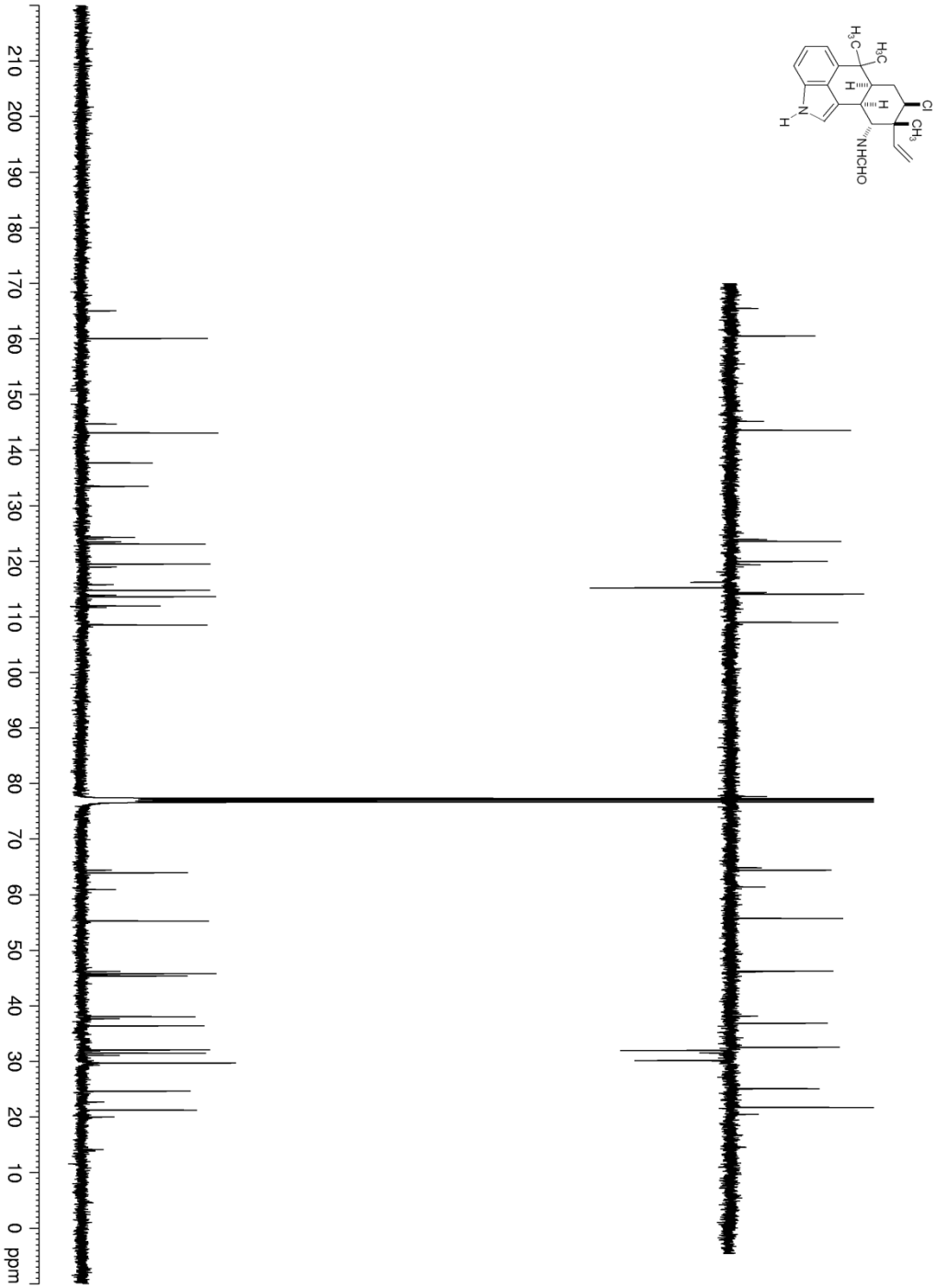


Figure 47. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **19**

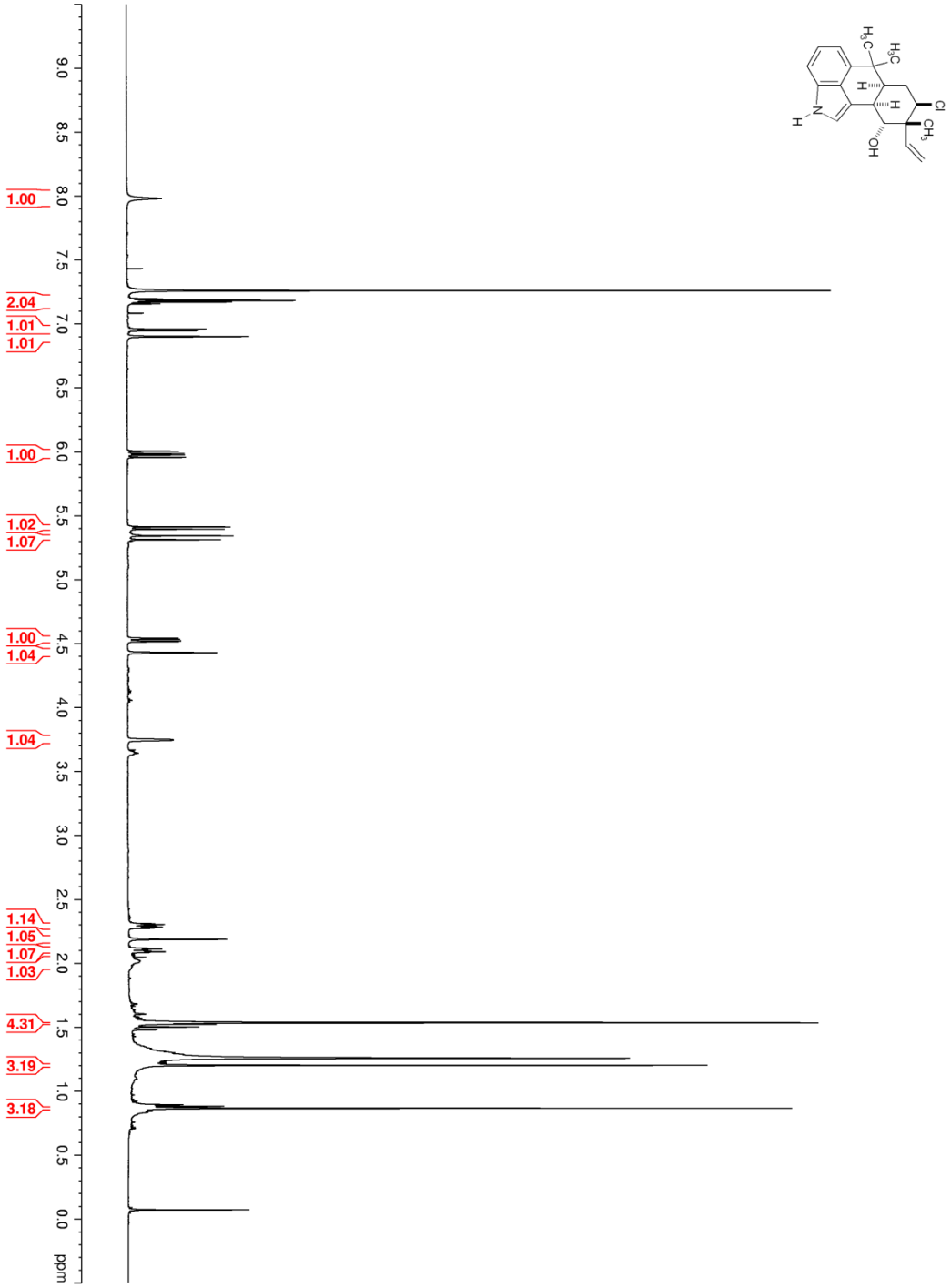


Figure 48. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **19**

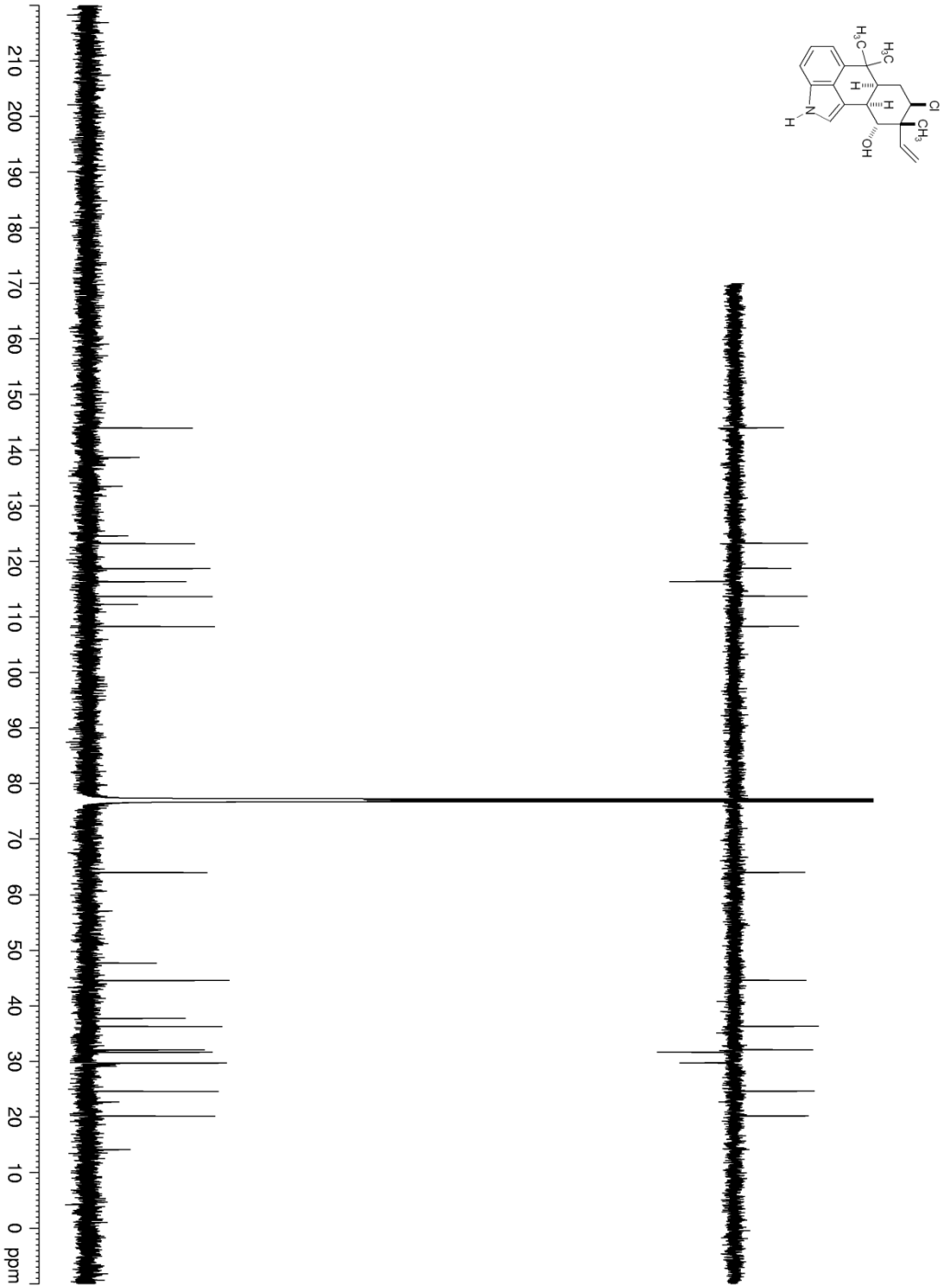


Figure 49. HSQC Spectrum (150 MHz, $CDCl_3$) of **19**

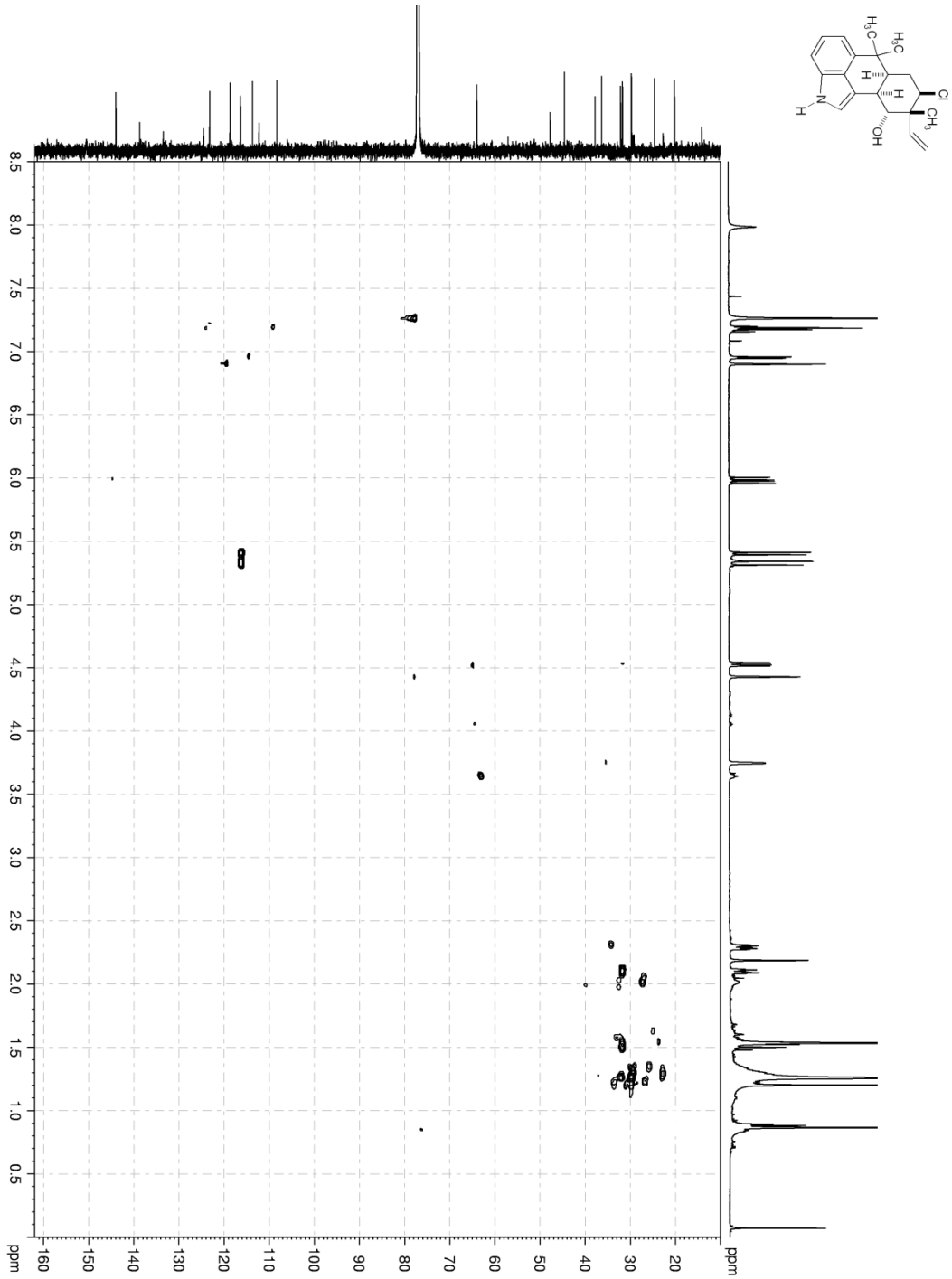


Figure 50. NOESY Spectrum (600 MHz, $CDCl_3$) of **19**

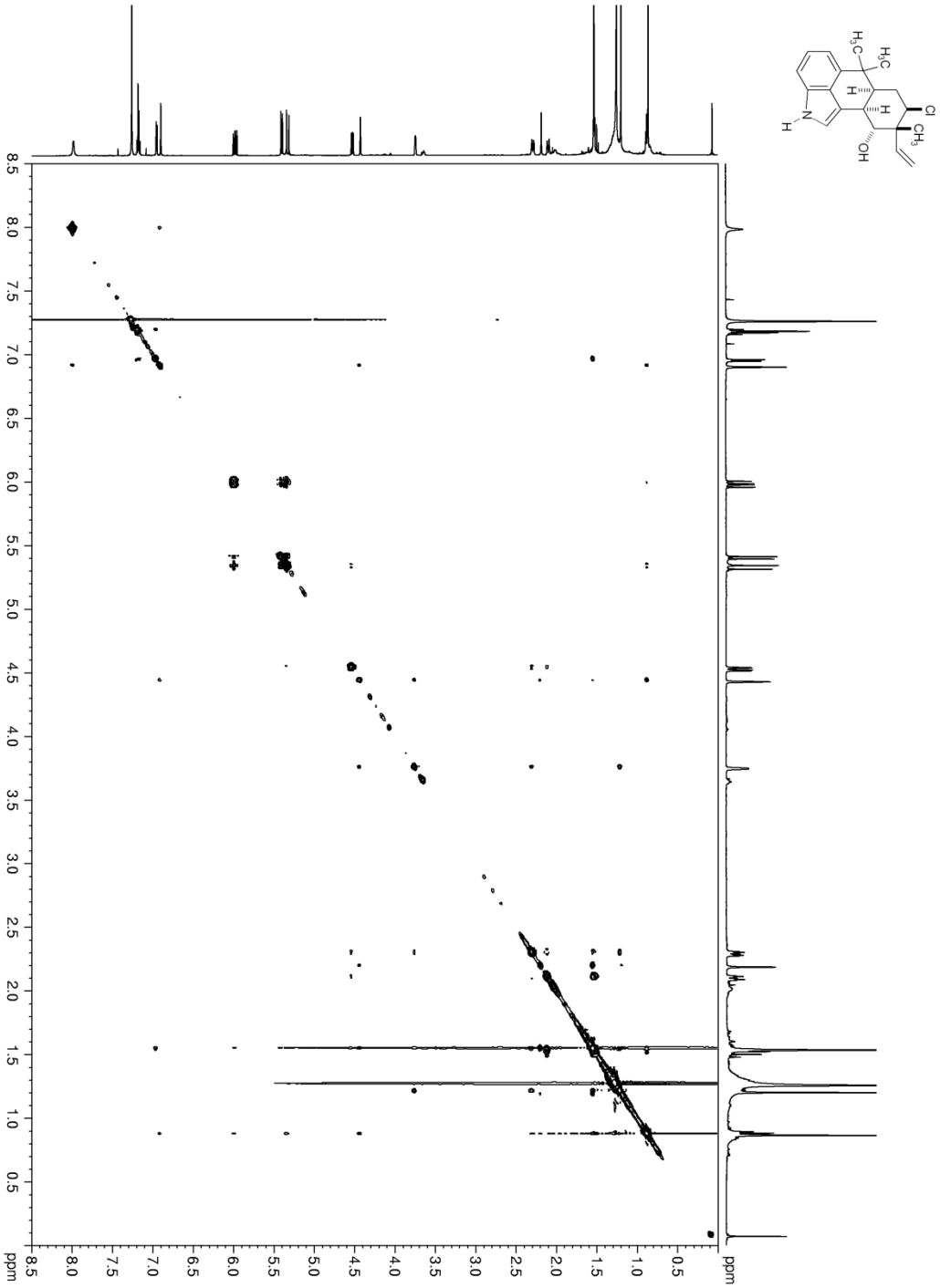


Figure 51. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **20**

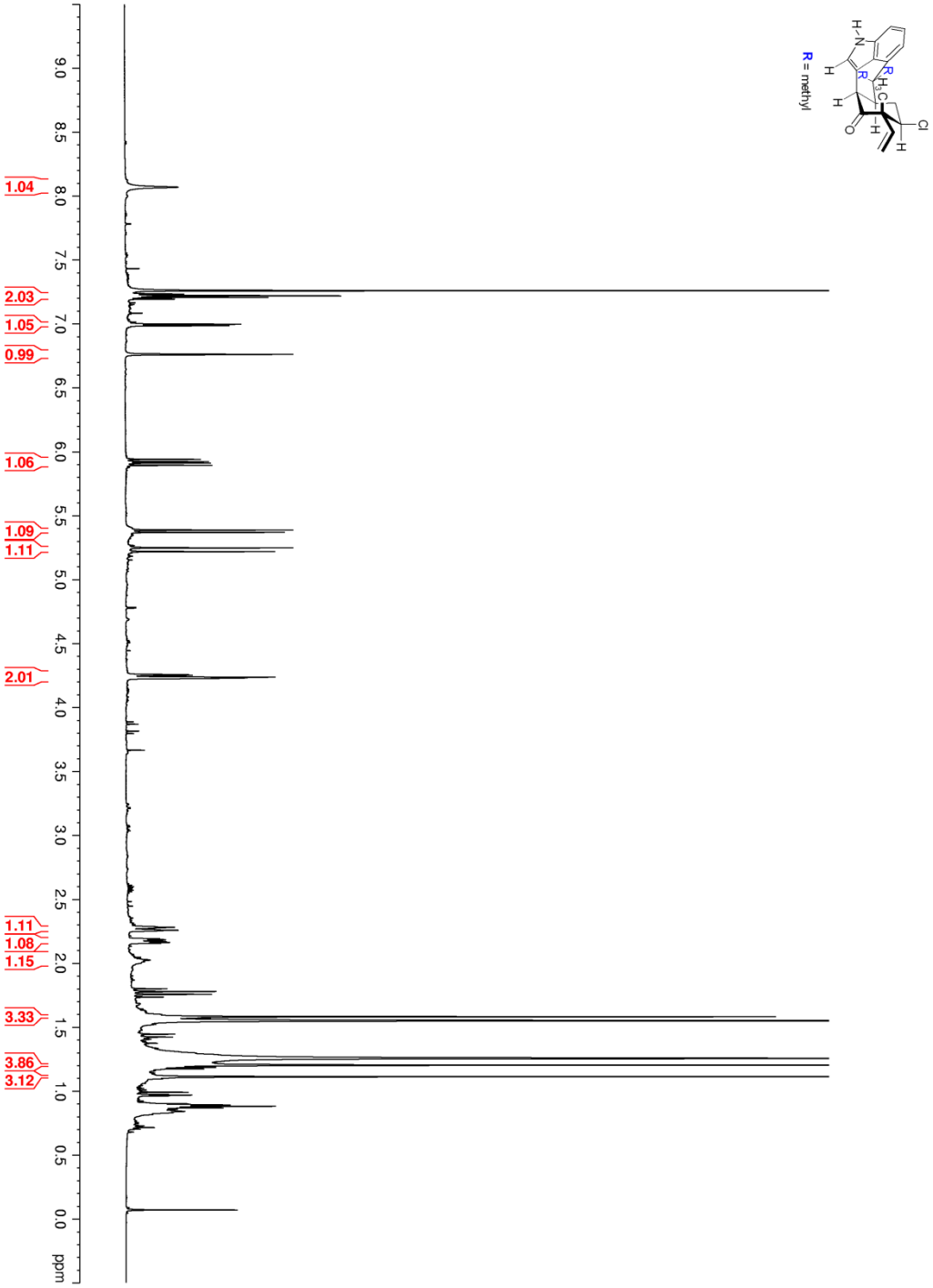


Figure 52. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **20**

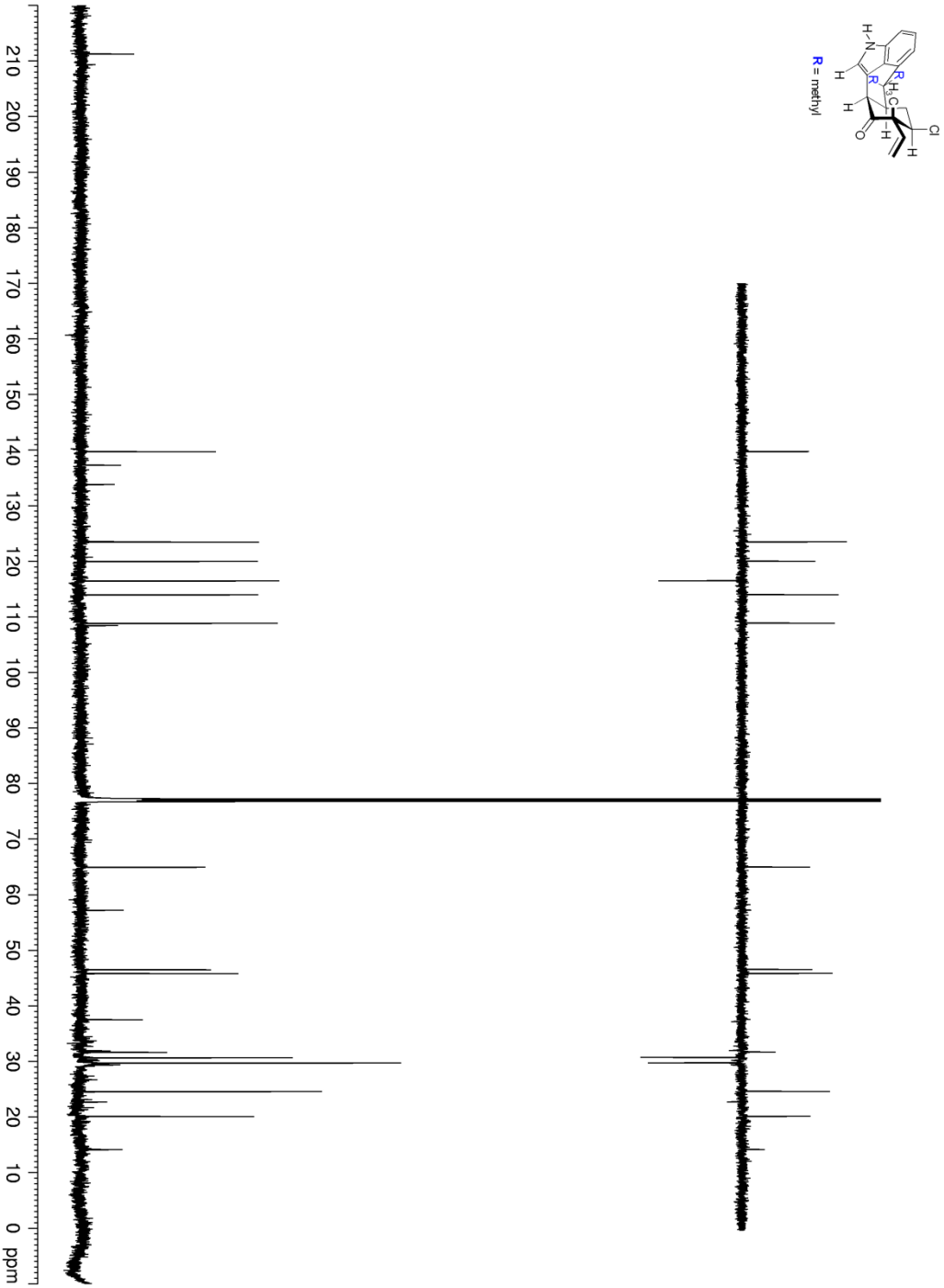


Figure 53. ^{1}H NMR Spectrum (500 MHz, $CDCl_3$) of **22**

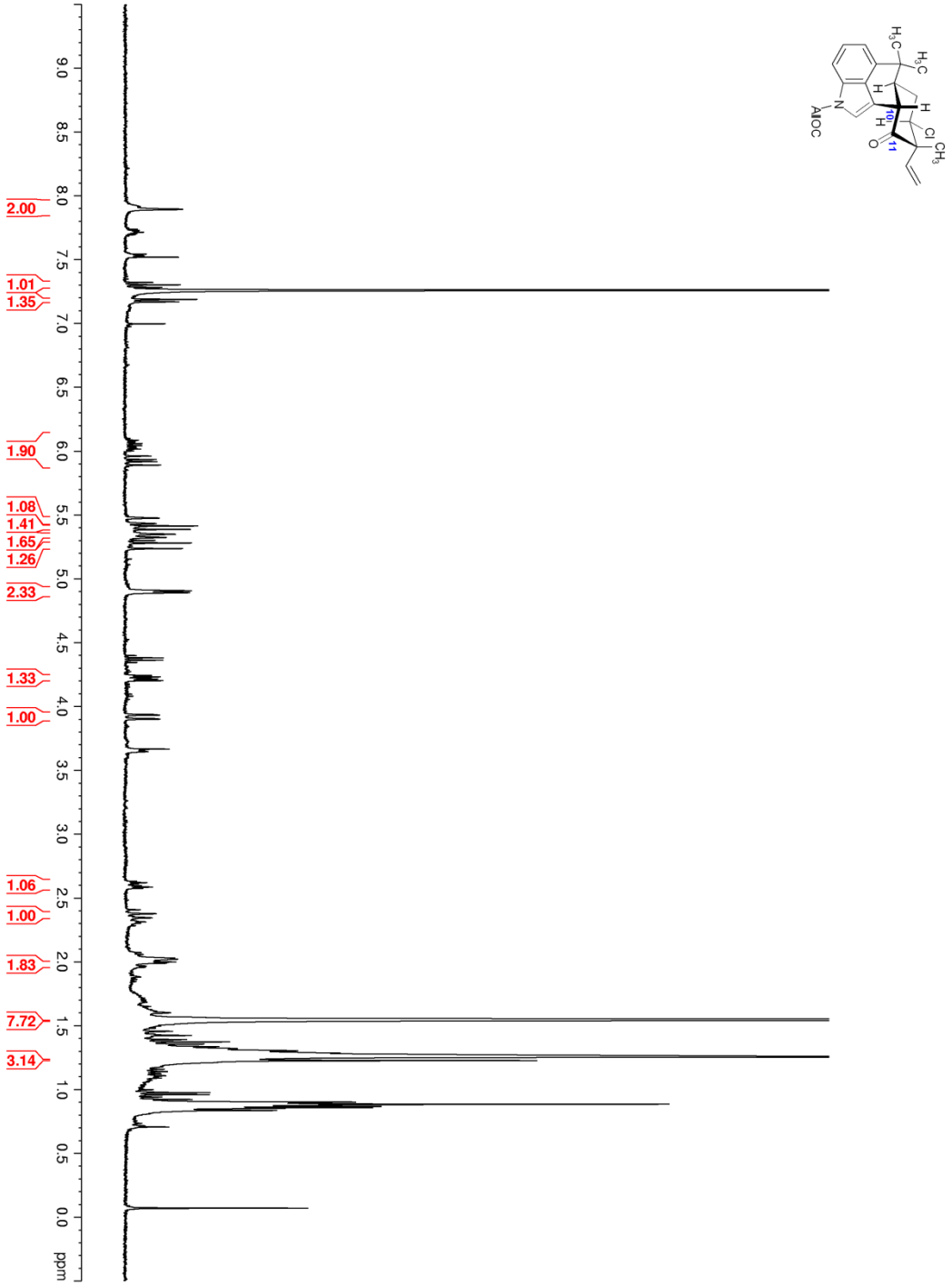


Figure 54. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **S1**

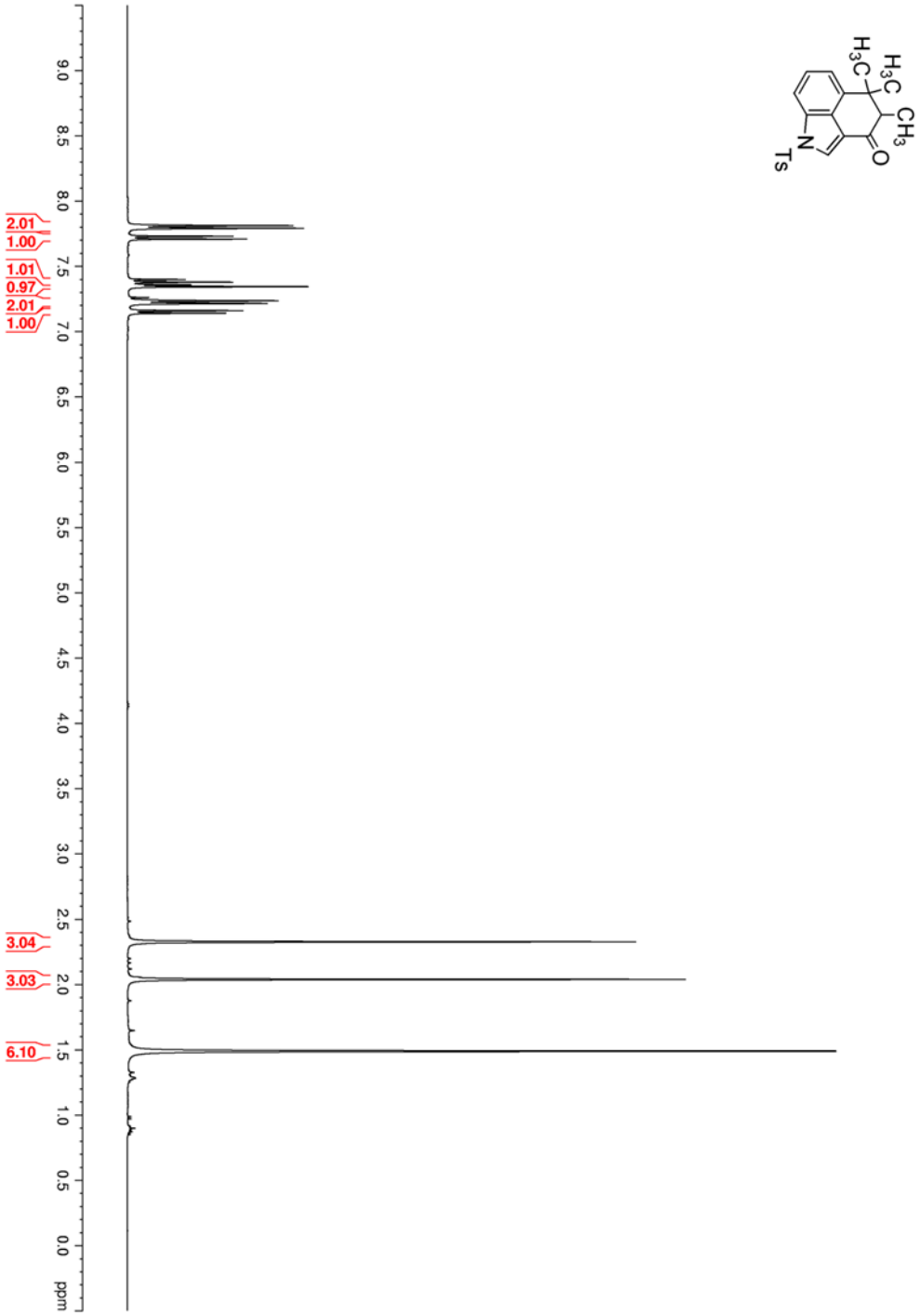


Figure 55. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **S1**

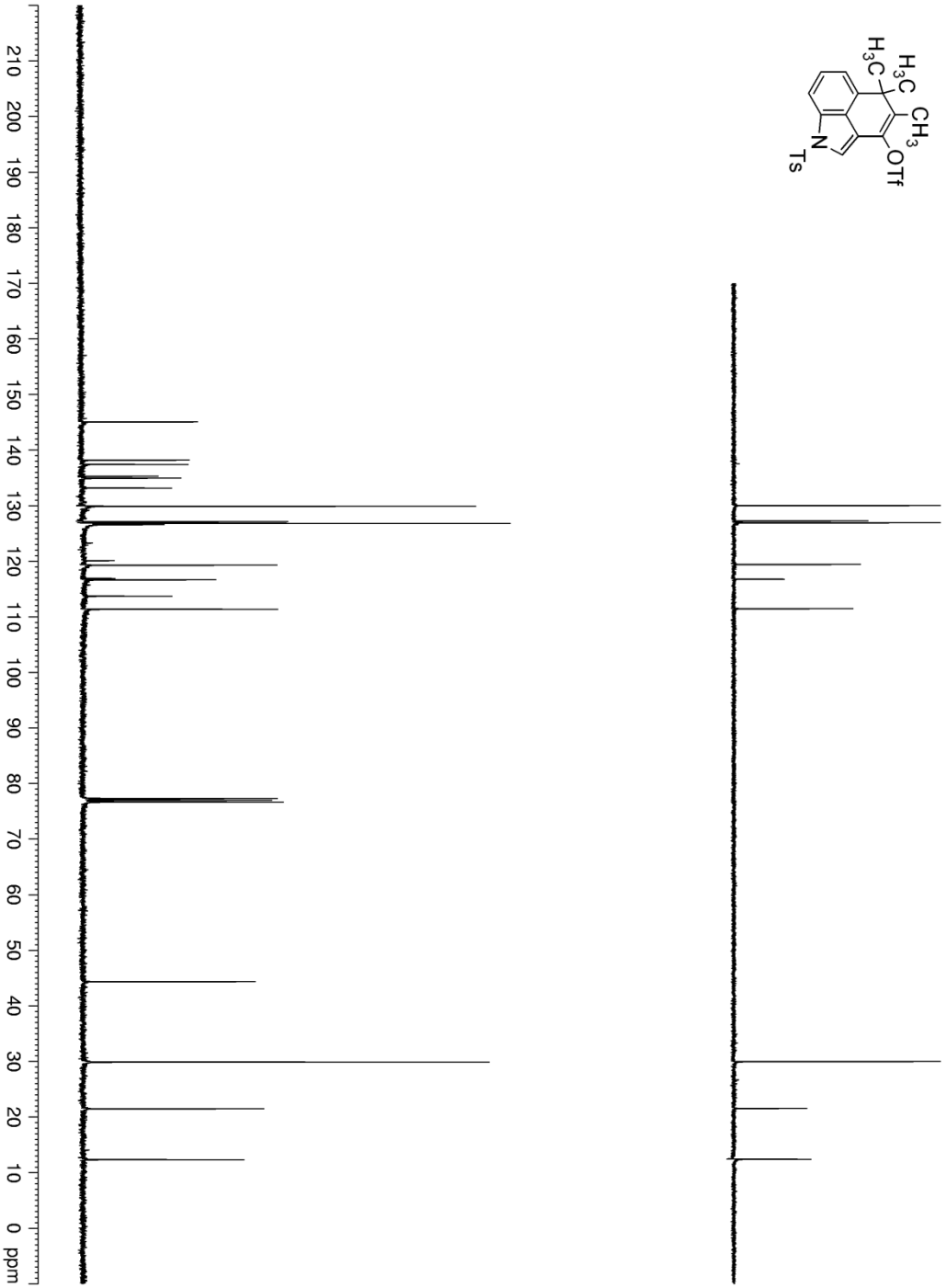


Figure 56. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **S2**

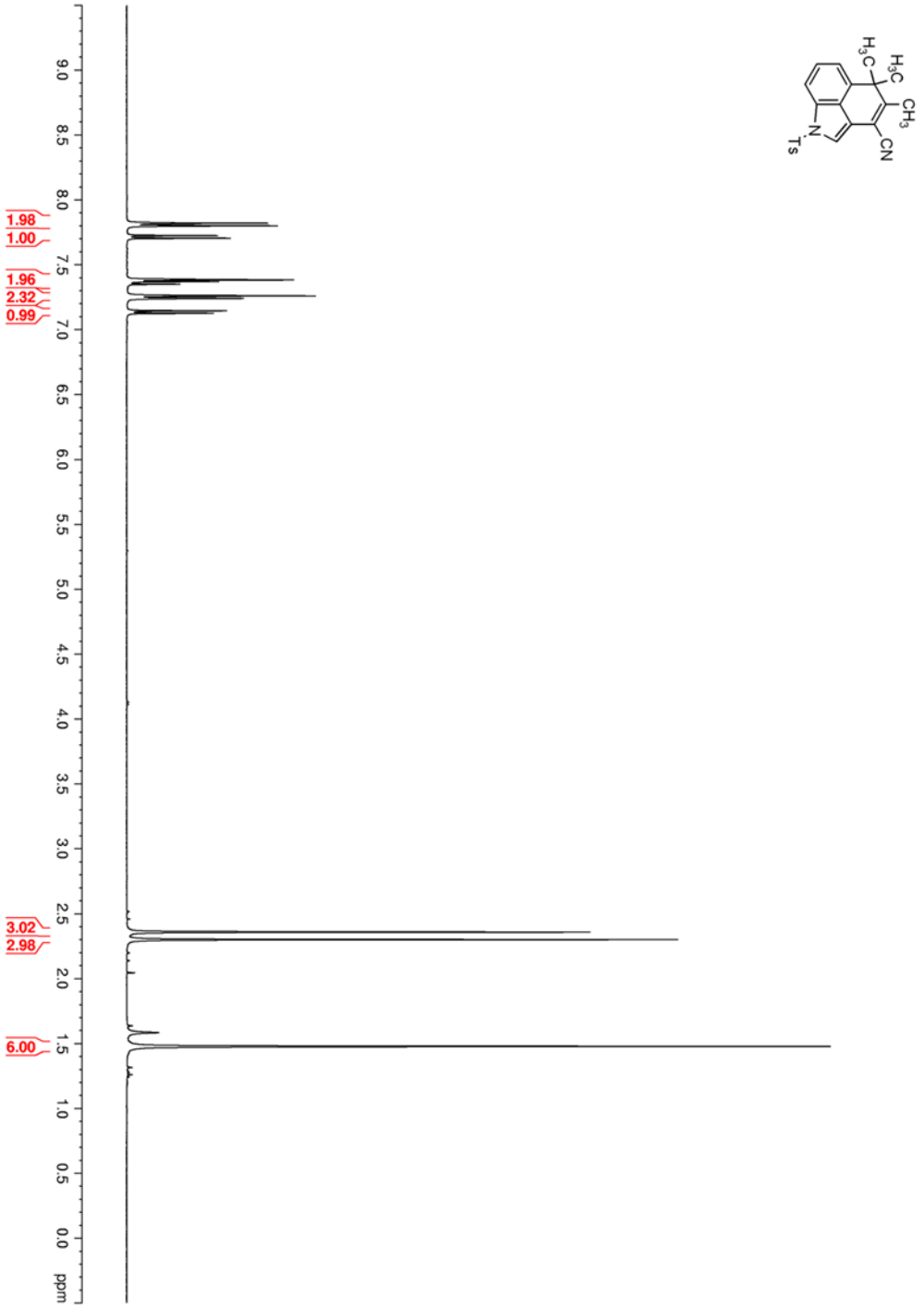


Figure 57. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **S2**

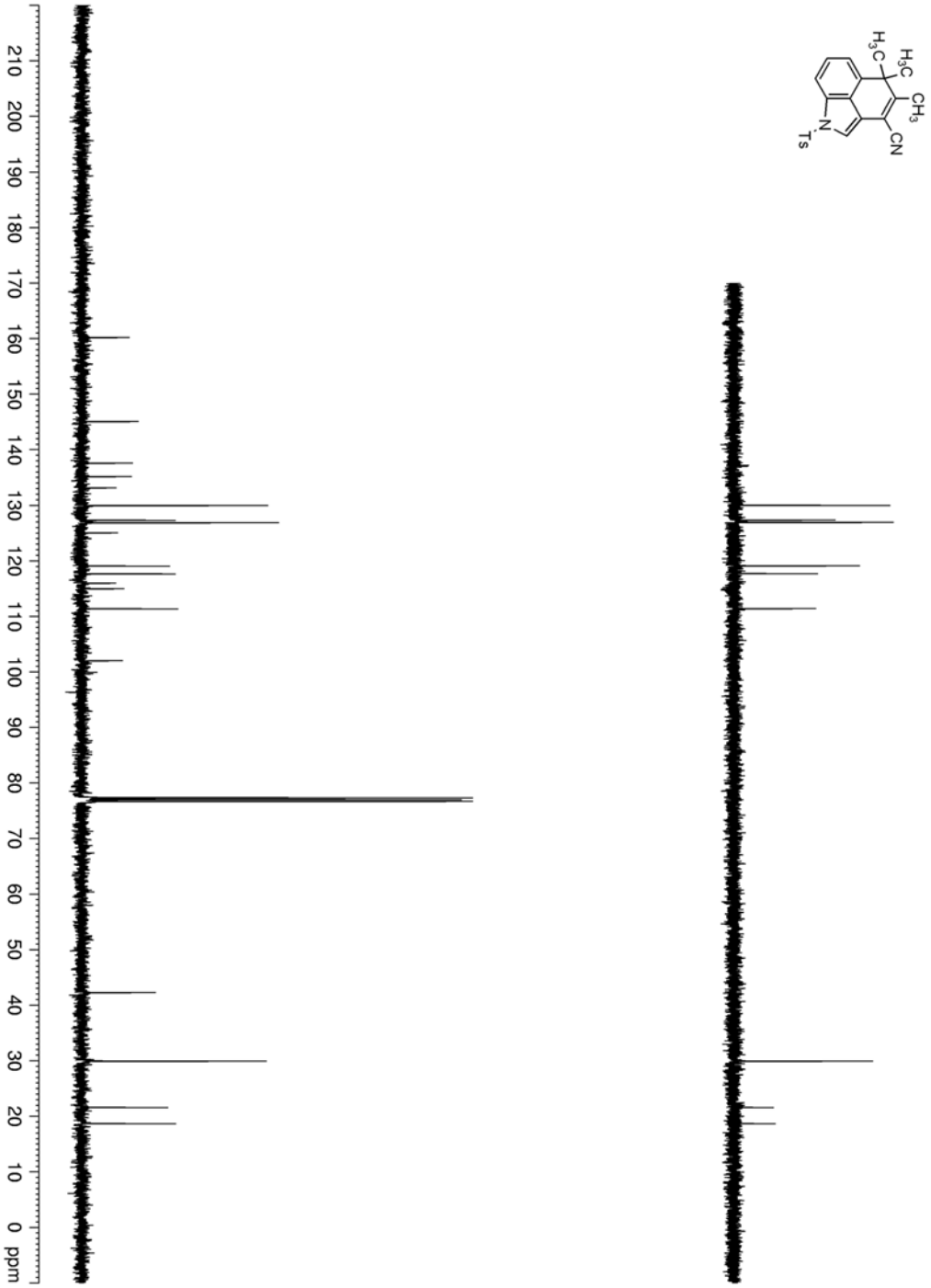


Figure 58. ^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of **S3**

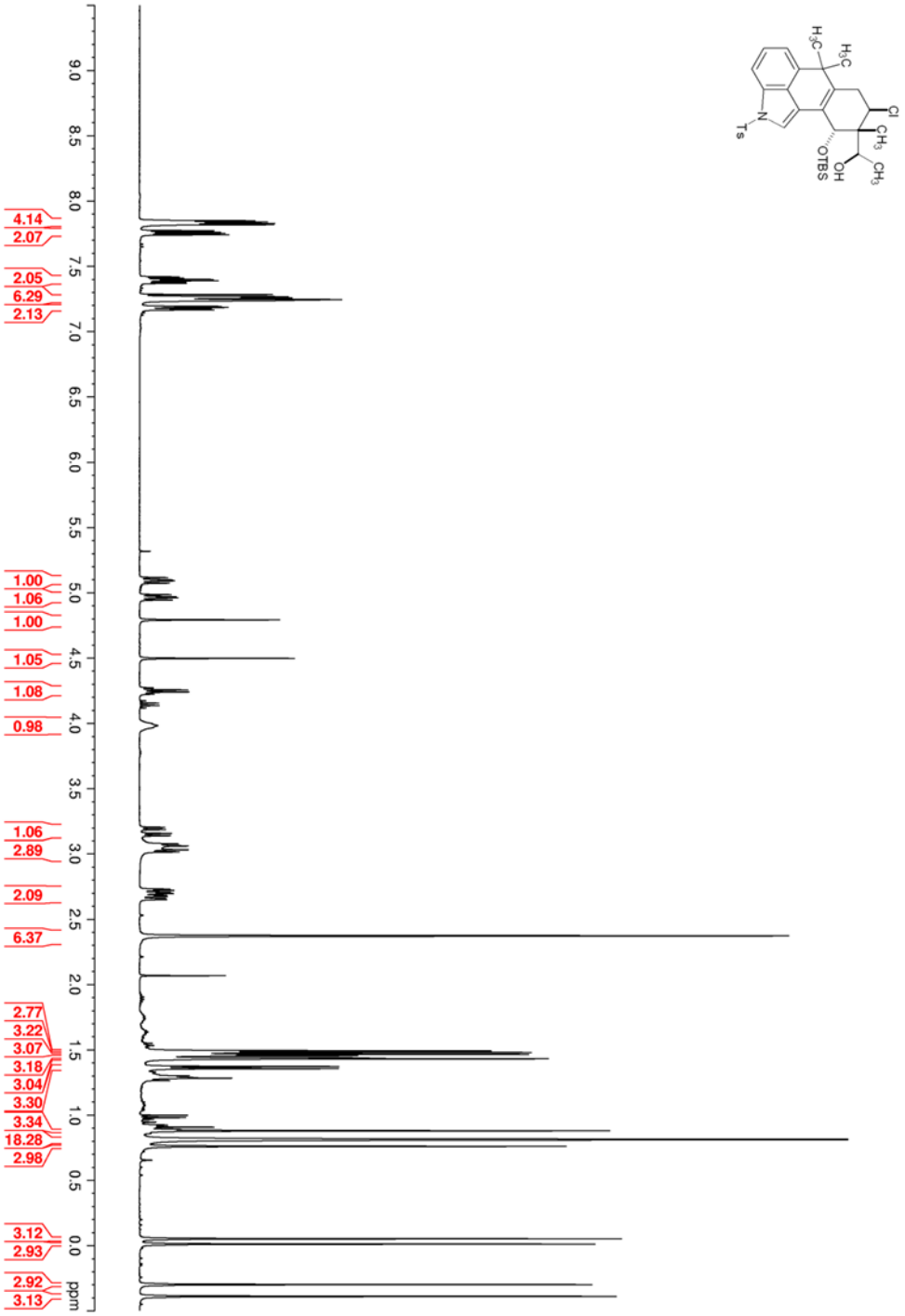


Figure 59. ^{13}C NMR Spectrum (150 MHz, $CDCl_3$) of **S3**

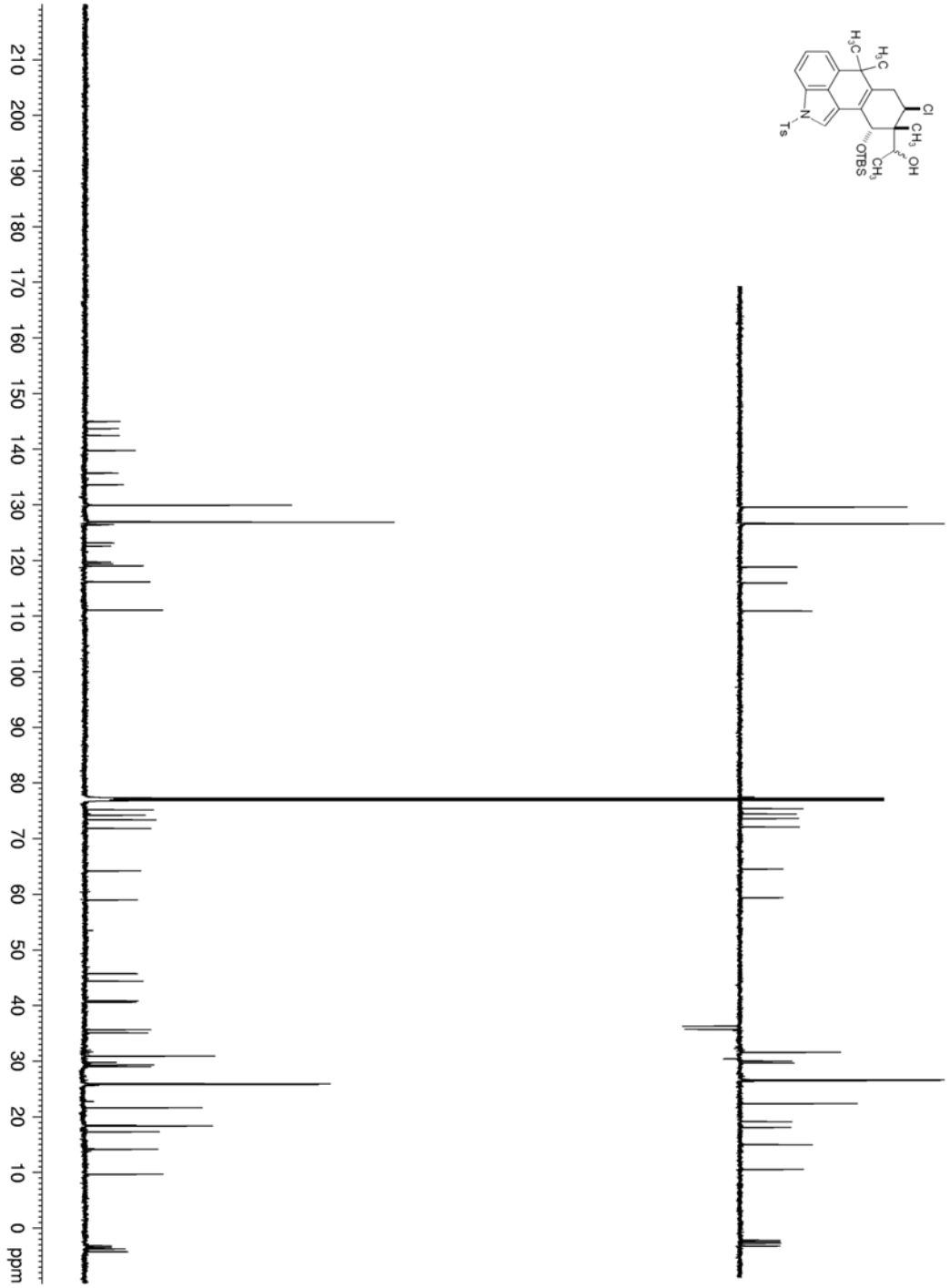


Figure 60. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **S4**

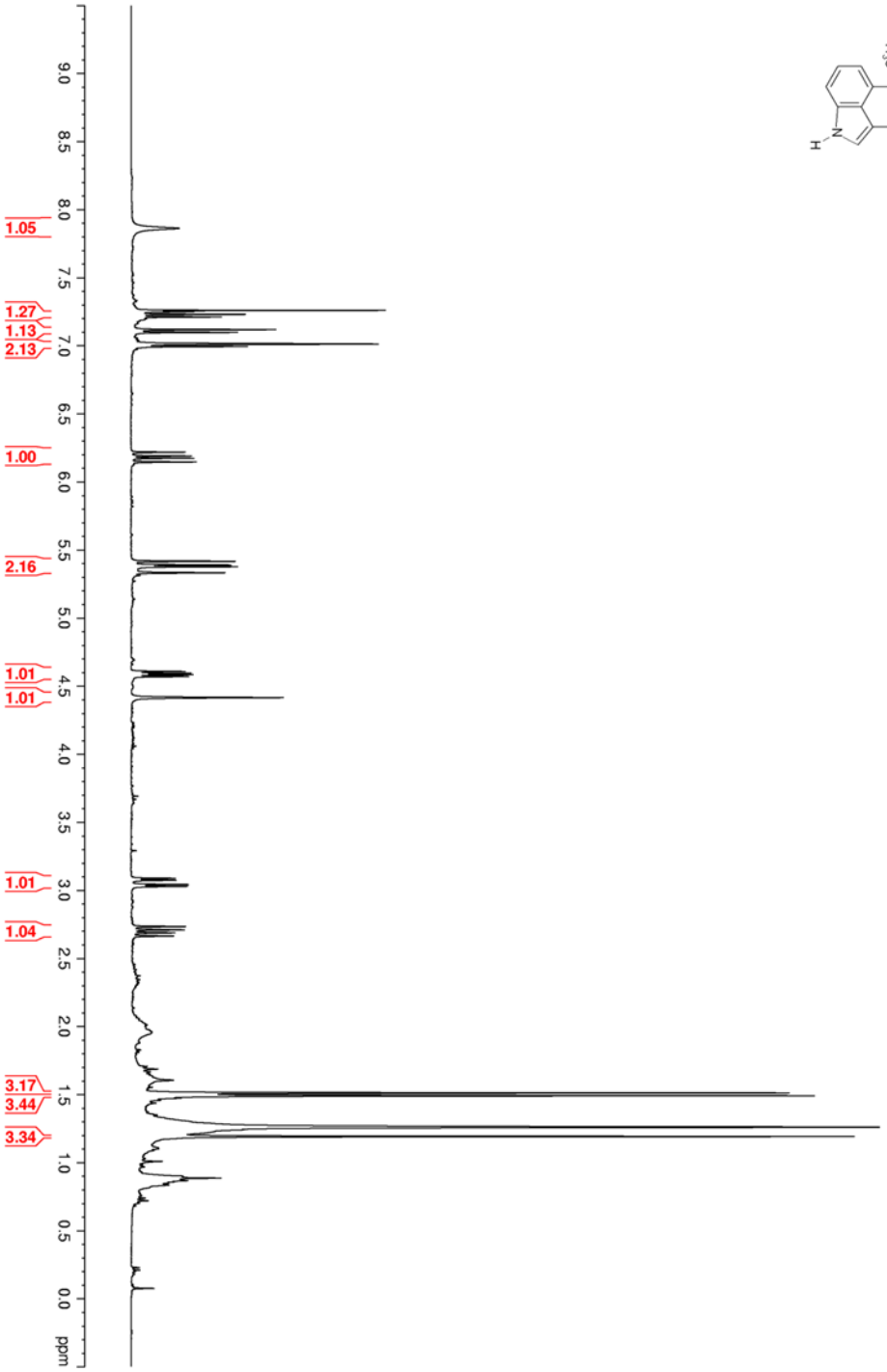


Figure 61. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **S4**