Supporting Information

Enantioselective Total Syntheses of Trichodermamides A and B

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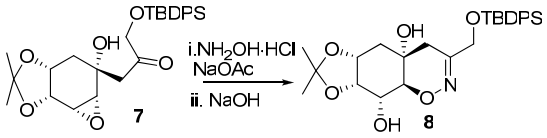
General Procedures.

Solvents. Dry THF and Et_2O were freshly distilled over sodium benzophenone before use. Dry CH_2Cl_2 and benzene were freshly distilled over calcium hydride before use. Anhydrous MeOH, MeCN in AcroSeal bottles were used directly without further purification.

Purification. Flash chromatography were carried out using E. Merck silica gel 60 (240-400 mesh) and the solvent systems listed under individual experiments. Analytical thin-layer chromatography (TLC) was performed on Sorbent silica gel (w/UV-254) plates (0.25 mm). Visualization was effected with ultraviolet light and phosphomolybdic acid (7% w/v) in 95% ethanol.

Characterization. Melting Points (°C) were determined using a Thomas-Hoover melting point apparatus and were uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer 281-B spectrometer. High resolution mass spectra (HRMS) were recorded on Micromass autospec high resolution instrument in either Electro-spray-Ionization (ESI) or Chemical ionization (CI) modes with OPUS software system. Proton magnetic resonance spectra (^{1}H NMR) and carbon magnetic resonance spectra (^{13}C NMR) were recorded on either a Bruker AMX or an Astra 500MHz spectrometers. Rotations of the optical active compounds were recorded on a Jasco P-1010 polarimeter.

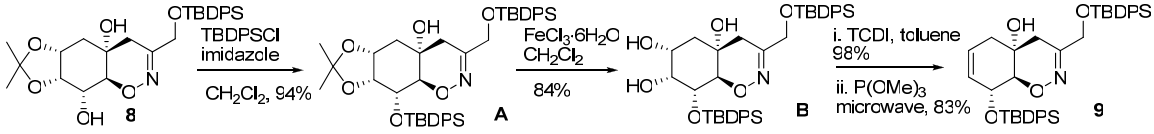
Characterization Data for Key Intermediates.



Compound 8

(4a*S*,6*R*,7*R*,8*R*,8a*S*)-3-((*tert*-Butyldiphenylsilyloxy)methyl)-4a,5,6,7,8,8a-hexahydro-4H-benzo[*e*][1,2]oxazine-6,7-*O*-isopropylidene-4a,8-diol

To a stirred solution containing ketone **7** (1.92 g., 3.89 mmol) in 40 mL of EtOH at rt, was added dropwise an aqueous solution (10 mL) containing $NH_2OH{\cdot}HCl$ (0.81 g , 11.6 mmol) and NaOAc (0.96 g ,11.6 mmol). The reaction mixture was stirred at rt and monitored by TLC until all the starting material was consumed. A NaOH solution (2.96 mL, 2M) was then added dropwise to the reaction mixture and the solution was stirred for 0.5 h. The reaction was then quenched with 50 mL of saturated NH_4Cl solution and the aqueous phase was extracted with 3×50 mL of EtOAc. The organic layers were combined, washed with brine and dried with Na_2SO_4. The crude product was concentrated and purified by column chromatography (50% EtOAc/hexanes) to give 1.20 g oxazine **71** as a colorless oil (2.34 mmol, 60%). EtOAc/hexanes; ^{1}H NMR ($CDCl_3$): δ 7.66-7.64 (4 H, m), 7.47-7.38 (6 H, m), 4.50-4.47 (1 H, m), 4.43 (1 H, dd, *J* = 4.2, 7.2 Hz), 4.34 (1H, d, *J* = 12.6 Hz), 4.28 (1H, d, *J* = 12.6 Hz), 4.09 (1 H, d, *J* = 7.6 Hz, overlapped with a weak broad –OH peak), 3.69 (1 H, dd, J = 4.2, 7.6 Hz), 2.47 (1 H, d, *J* = 15.8 Hz), 2.33 (1 H, d, *J* = 15.8 Hz), 2.12 (1 H, dd, *J* = 2.5, 15.5 Hz), 1. 71 (1 H, dd, *J* = 3.6, 15.5 Hz); 1.56 (3 H, s), 1.37 (3 H, s), 1.07 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 165.5, 135.6, 135.5, 132.6, 132.5, 130.0, 127.9, 109.0, 81.9, 73.2, 72.8, 70.4, 67.2, 64.4, 34.8, 34.4, 26.8, 26.0, 23.5, 19.2; HRMS (ESI) *m/z* calculated for $C_{28}H_{37}NO_6Si$: 511.2390, Found $(M + Na)^+$: 534.2039; $[\alpha]_D^{24}$ -20.0 (c 2.02, $CHCl_3$).



Compound A

(4a*S*,6*R*,7*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-((*tert*-butyldiphenylsilyloxy)-methyl)-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*e*][1,2]oxazine-6,7-*O*-isopropylidene-4a-ol

To a solution containing oxazine **8** (1.96 g, 3.83 mmol) in 50 mL of dry CH_2Cl_2, were added imidazole (0.78 g, 11.5 mmol) and TBDPSCl (1.50 mL ,5.74 mmol) in sequence at 0 °C. The reaction mixture was warmed to rt and stirred until all the starting material was consumed. The reaction was then quenched with 10 mL of saturated NH_4Cl aqueous solution. The organic layer was separated, washed with 10 mL of brine, dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (30% EtOAc/hexanes) to give 2.71 g of compound **72** as a white foam-like solid (3.61 mmol, 94%). ^{1}H NMR ($CDCl_3$): δ 7.83-7.76 (4 H, m), 7.65-7.59 (4 H, m), 7.46- 7.27 (12 H, m), 4.23 (1 H, d, *J* = 12.6 Hz), 4.16 (1 H, d, *J* = 9.0 Hz), 4.07 (2 H, m), 3.64 (1 H, s), 3.55 (1 H, dd, *J* = 3.1, 9.0 Hz), 2.24 (1 H, d, *J* = 15.8 Hz), 2.00 (1 H, d, *J* = 15.8 Hz), 1.89 (1 H, dd, *J* = 3.7, 16.5 Hz), 1.61 (1 H, dd, *J* = 3.7, 16.5 Hz); 1.58 (3 H, s), 1.25 (3 H, s), 1.11 (9 H, s), 1.04 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 165.2, 136.3, 135.9, 125.6, 135.5, 134.3, 132.8, 132.6, 129.9, 129.8, 129.5, 127.8, 127.5, 127.4, 108.6, 82.7, 75.4, 72.5, 71.3, 69.0, 64.5, 36.3, 32.8, 27.1, 26.9, 26.8, 23.7, 19.5, 19.2; HRMS (ESI) *m/z* calculated for $C_{44}H_{55}NO_6Si_2$: 749.3568, Found $(M + Na)^+$: 772.3481.

Compound B

(*4aS*,6*R*,7*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-((*tert*-butyldiphenylsilyloxy)-methyl)-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*e*][1,2]oxazine-4a,6,7-triol

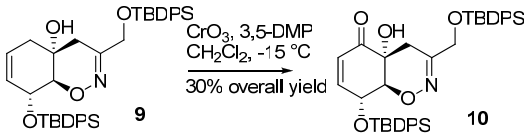
To a solution containing compound **A** (2.71 g, 3.61 mmol) in 40 mL of CH_2Cl_2, was added 3.42 g $FeCl_3{\cdot}6H_2O$ (12.6 mmol) at rt. The mixture was stirred at rt for 20 min. The solid was collected and the filtrate was washed with 20 mL of H_2O. The aqueous phase was extracted with 2×20 mL of EtOAc. The organic layers were combined, washed with 25 mL of 5% HCl solution and 25 mL of brine, then dried with Na_2SO_4. The crude product was purified by column chromatography (30% EtOAc/hexanes) to give 2.19 g of compound **73** as a white foam-like solid (3.08 mmol, 85%). ^{1}H NMR ($CDCl_3$): δ 7.76-7.72 (4 H, m), 7.64-7.60 (4 H, m), 7.45-7.35 (12 H, m), 4.21-4.20 (1 H, m), 4.13 (2 H, s), 4.03-4.02 (1 H, m), 3.77-3.76 (1 H, m), 3.69 (1 H, t, *J* = 3.6 Hz), 2.93-2.63 (2 H, b), 2.35 (1 H, d, *J* = 18.7 Hz), 2.22 (1 H, d, *J* = 18.7 Hz), 2.04-2.00 (1 H, m), 1.74-1.70 (1 H, dd, *J* = 17.6, 3.2 Hz), 1.11 (9H, s), 1.06 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 156.7, 136.3, 136.0, 135.5, 132.70, 132.66, 132.54, 132.50, 130.2, 129.9, 127.9, 127.8, 78.4, 71.7, 70.1, 68.7, 64.8, 36.6, 34.8, 27.0, 26.8, 19.3, 19.2; HRMS (ESI) *m/z* calculated for $C_{41}H_{51}NO_6Si_2$: 709.3225, Found $(M + H)^+$: 710.3344; $[\alpha]_D^{22}$ +16.7 (c 0.97, $CHCl_3$).

Compound 9

(4a*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-((*tert*-butyldiphenylsilyloxy)methyl)-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazin-4a-ol

To a solution containing compound **B** (2.19 g, 3.08 mmol) in 40 mL of dry toluene, was added 1.22 g TCDI (6.16 mmol) at rt. The solution was heated to reflux under argon for 4 h. The solution was then cooled to rt, diluted with 40 mL of EtOAc, washed with 25 mL of H_2O and 25 mL of brine, and dried over Na_2SO_4. The crude product was concentrated and purified by column chromatography (30% EtOAc/hexanes) to give 2.30 g of the corresponding thiocarbonate as a white foam-like solid (3.06 mmol, 99%).

The thiocarbonate (0.121 g, 0.16 mmol) was dissolved in 4 mL of $P(OMe)_3$ in a microwave tube. The tube was sealed and subjected to microwave irradiation to maintain the inner temperature at 150 °C and the inner pressure at 70 psi for 25 min. The solution was then cooled to rt and the solvent was evaporated. The crude product was purified by column chromatography (30% EtOAc/hexanes) to give 88.6 mg of compound **9** as a colorless oil (0.13 mmol, 83%) with the recovery of 14.8 mg of the starting material. (94% yield based on the recovery of starting material). ^{1}H NMR ($CDCl_3$): δ 7.70-7.63 (8 H, m), 7.45-7.36 (10 H, m), 5.68 (1 H, ddd, *J* = 2.6, 5.3, 10.1 Hz), 5.48 (1 H, d, *J* = 10.1 Hz), 4.31 (1 H, s), 4.20 (2 H, s), 4.00 (1 H, s), 3.84 (1 H, d *J* = 2.4 Hz), 2.53 (1 H, d, *J* = 18.4 Hz), 2.42 (1 H, d, *J* = 18.4), 2.27-2.22 (1 H, m), 2.13-2.09 (1 H, m), 1.08 (9H, s), 1.06 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 156.7, 135.81, 135.80, 135.5, 133.0, 132.8, 132.7, 132.4, 130.1, 130.0, 129.9, 127.84, 127.79, 127.74, 126.4, 125.5, 77.7, 67.2, 65.0, 63.9, 35.4, 34.6, 26.9, 26.8, 19.2, 19.1; HRMS (ESI) *m/z* calculated for $C_{41}H_{49}NO_4Si_2$: 675.3200, Found $(M + Na)^+$: 698.3124; $[\alpha]_D^{22}$ -70.4 (c 0.87,$CHCl_3$).

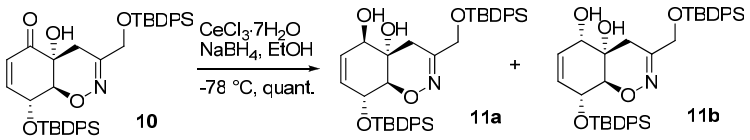


Compound 10

(4a*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-((*tert*-butyldiphenylsilyloxy)methyl)-4a-hydroxy-8,8a-dihydro-4*H*-benzo[*e*][1,2]oxazin-5(4a*H*)-one

To a suspension of 3.70 g CrO_3 (37.0 mmol) in 15 mL of dry CH_2Cl_2 at -15 °C, was added 3.63 g 3,5-dimethylpyrazole (37.0 mmol). The mixture was vigorously stirred at -15 °C for 0.5 h. Oxazine **9** (1.25 g, 1.85 mmol) was dissolved in

1.0 mL of dry CH_2Cl_2 and added dropwise to the mixture. The reaction mixture was stirred for another 0.5 h, then diluted with 30 mL of EtOAc, and quenched with 50 mL of saturated Na_2SO_3 solution. The organic layer was separated, and the aqueous layer was extracted with 2×100 mL of EtOAc. The organic layers were combined, washed with brine and dried with Na_2SO_4. The crude product was concentrated and purified by column chromatography (10% to 30% EtOAc/hexanes) to separate 0.6 g of starting material and 0.23 g of enone **10**. The recycled starting material was re-subjected to the oxidation conditions for two more reaction cycles, and an overall 0.37g of product **10** was obtained (0.54 mmol, 29.0% yield). ^{1}H NMR ($CDCl_3$): δ 7.72-7.62 (5 H, m), 7.60-7.56 (3 H, m), 7.46-7.32 (12 H, m), 6.57 (1 H, dd, *J* = 2.60, 10.4 Hz), 6.00 (1 H, dd, *J* = 1.81, 10.4 Hz), 4.42 (1 H, td, *J* = 2.2, 7.1 Hz), 4.35 (1 H, dd, *J* = 1.4, 7.1 Hz), 4.19 (1 H, d, *J* = 12.2 Hz), 4.08 (1 H, d, *J* = 12.4 Hz), 3.97 (1 H, s), 2.20 (1 H, d, *J* = 18.6 Hz), 2.11 (1 H, dd, *J* = 1.3 Hz, 18.6 Hz), 1.10 (9 H, s), 0.98 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 197.1, 155.3, 149.8, 136.1, 135.8, 133.1, 132.7, 132.6, 131.5, 130.1, 130.0, 125.1, 81.2, 69.4, 68.1, 65.4, 28.2, 26.8, 26.7, 19.3, 19.2; HRMS (ESI) *m/z* calculated for $C_{41}H_{47}NO_5Si_2$: 689.2993, Found $(M + Na)^+$: 712.2882; $[\alpha]_D^{22}$ -40.4 (c 0.77, $CHCl_3$).

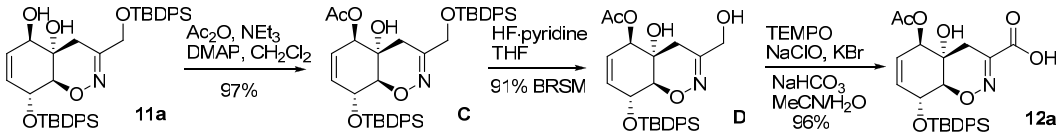


Compound 11a
(4a*S*,5*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-((*tert*-butyldiphenylsilyloxy)-methyl)-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-4a,5-diol
Compound 11b
(4a*S*,5*S*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-((*tert*-butyldiphenylsilyloxy)-methyl)-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-4a,5-diol

To a solution containing enone **10** (0.19 g, 0.275 mmol in 5 mL of EtOH, were added $CeCl_3·7H_2O$ (0.102 g, 0.275 mmol) and 20.8 mg of $NaBH_4$ (0.275 mmol) in sequence at -78 °C. The mixture was stirred at -78 °C for 20 min then quenched with 5 mL of saturated NH_4Cl solution. The mixture was diluted with EtOAc, and washed with water. The aqueous layer was extracted with 2×10 mL of EtOAc. The organic layer was combined, washed with brine and dried with Na_2SO_4. The crude product was concentrated and purified by column chromatography (30% EtOAc/hexanes) to yield two products: 87 mg of compound **11a** and 98 mg of compound **11b** in an overall 97% yield (0.267 mmol).

Compound 11a: R_f 0.20 in 30% EtOAc/hexanes; ^{1}H NMR ($CDCl_3$): δ 7.68-7.62 (8H, m), 7.46-7.34 (12 H, m); 5.79 (1 H, dd, J = 3.0, 10.3 Hz), 5.50 (1 H, dd, J = 3.9, 9.0 Hz), 4.30 (1 H, m), 4.23 (1 H, d, J = 12.4 Hz), 4.18 (1 H, d, J = 12.4 Hz), 4.13 (1 H, m), 3.93 (1 H, s), 3.46 (1 H, s), 2.60 (1 H, d, J = 18.9 Hz), 2.43 (1 H, d, J = 18.9 Hz), 1.62 (1 H, d, J = 9.7 Hz), 1.07 (9 H, s), 1.05 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 159.7, 135.9, 135.8, 135.6, 133.1, 132.8, 132.1, 130.9, 130.2, 130.1, 129.9, 128.7, 127.9, 127.81, 127.78, 127.6, 78.7, 67.4, 67.1, 65.1, 30.7, 26.9, 26.8, 19.23, 19.18; HRMS (ESI) *m/z* calculated for $C_{41}H_{49}NO_5Si_2$: 691.3149, Found $(M + H)^+$: 692.3247; IR (NaCl, cm^{-1}): 3420 (b), 3071 (w), 2957 (m), 2931 (m), 2857 (m), 1472 (m), 1428 (m), 1112 (s), 1060 (s), 1009 (m), 822 (m), 739 (m), 701 (s);$[\alpha]_D^{27}$ -72.1 (c 2.04, $CHCl_3$).

Compound 11b: R_f: 0.34 in 30% EtOAc/hexanes; ^{1}H NMR ($CDCl_3$): δ 7.67-7.63 (8 H, m), 7.49-7.37 (12 H, m), 5.71 (1 H, dd, *J* = 1.9, 10.3 Hz), 5.48 (1 H, dd, *J* = 4.1, 10.2 Hz), 4.30 (1 H, m), 4.23 (2 H, s), 4.09 (1 H, s), 3.91 (1 H, m), 3.81 (1 H, d, *J* = 10.8 Hz), 2.93 (1 H, d, *J* = 18.5 Hz), 2.59 (1 H, d, *J* = 10.9 Hz), 2.33 (1 H, d, *J* = 18.5 Hz), 1.09 (9 H, s), 1.07 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 157.5, 135.8, 135.7, 135.6, 132.8, 132.7, 132.5, 132.0, 130.9, 130.3, 130.2, 129.9, 128.0, 127.9, 127.8, 126.3, 77.1, 67.6, 66.6, 65.8, 65.0, 32.5, 26.9, 26.8, 19.2, 19.1; HRMS (ESI) *m/z* calculated for $C_{41}H_{49}NO_5Si_2$: 691.3149, Found $(M + H^+)$: 692.3247 IR (NaCl, cm^{-1}): 3384 (b), 3071 (w), 2930 (m), 2857 (m), 1589 (w), 1472 (m), 1427 (m), 1112 (s), 1020 (m), 823 (m), 739 (m), 701 (s); $[\alpha]_D^{28}$ -49.4 (c 0.70, $CHCl_3$).



Compound C

(4a*S*,5*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-4a-hydroxy-3-(*tert*-butyldiphenyl-silyloxymethyl)-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazin-5-yl acetate

To a solution containing 98 mg of allylic alcohol **11a** (0.14 mmol) in 1.5 mL of dry CH_2Cl_2, were added 16.0 μL of Ac_2O (0.17 mmol), 38.9 μL of NEt_3 (0.28 mmol) and 1.7 mg of DMAP (0.014 mmol) in sequence at 0 °C. The reaction mixture was warmed to rt and stirred for 2 h. The mixture was then quenched with 5 mL of saturated NH_4Cl solution. The mixture was diluted with 5 mL of EtOAc and washed with 5 mL of H_2O. The aqueous layer was extracted with 2×10 mL of EtOAc. The organic layers were combined, washed with 10 mL of brine and dried with Na_2SO_4. The crude product was concentrated and purified by column chromatography (30% EtOAc/hexanes) to give 99.6 mg of the corresponding acetate **C** (0.0135 mmol, 97% yield). ^{1}H NMR ($CDCl_3$): δ 7.68-7.60 (8 H, m), 7.47-7.35 (12 H, m), 5.53 (2 H, m), 5.47 (1 H, m), 4.24 (1 H, d, *J* = 5.0 Hz), 4.20 (1 H, d, *J* = 12.5 Hz), 4.10 (1 H, d, *J* = 12.5 Hz), 4.06 (1 H, d, *J* = 5.0 Hz), 3.35 (1 H, s), 2.32 (1 H, d, *J* = 18.9 Hz), 2.26 (1 H, d, *J* = 18.9 Hz), 2.00 (3 H, s), 1.07 (9 H, s), 1.04 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 170.5, 156.9, 136.0, 135.8, 135.5, 133.4, 132.8, 132.6, 132.2, 130.0, 129.9, 127.8, 127.7, 124.9, 79.6, 73.8, 67.2, 67.0, 65.1, 28.9, 26.8, 26.7, 20.8, 19.2; HRMS *m/z* (ESI) calculated for $C_{43}H_{51}NO_6Si_2$: 733.3255, Found $(M + H)^+$: 734.3328; $[\alpha]_D^{22}$ -86.3 (c 1.08, $CHCl_3$).

Compound D

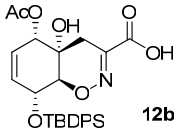
(4a*S*,5*R*,8*R*,8a*S*)-8-(tert-Butyldiphenylsilyloxy)-4a-hydroxy-3-(hydroxymethyl)-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazin-5-yl acetate

To a 0.84 mL of dry THF solution containing compound **C** (74.5 g, 0.101 mmol), was added 0.14 mL of fresh prepared HF·Pyridine/pyridine/THF solution (1 : 2 : 5 v/v) at rt. The reaction was monitored by TLC until most of the starting material was consumed. The reaction was then diluted with 10 mL of THF, quenched with 1.0 mL of 5% HCl. The organic layer was separated, and the aqueous layer was extracted with 2×10 mL of EtOAc. The organic layers were combined, washed with 10 mL of brine and dried with Na_2SO_4. The crude product was concentrated and purified by column chromatography (20% acetone/CH_2Cl_2) to give 27.5 mg compound **D** (0.056 mmol) in 50% yield with the recovery of 30.0 mg of starting material. Yield based on the recovery of starting material: 91% ^{1}H NMR ($CDCl_3$): δ 7.72-7.65 (4 H, m), 7.47-7.36 (6 H, m), 5.57-5.44 (3 H, m), 4.19-4.13 (2 H, m), 4.03 (1 H, d, *J* = 3.9 Hz), 3.97 (1 H, d, *J* = 4.0 Hz), 3.53 (1 H, s), 2.43 (1 H, s), 2.14 (1 H, d, *J* = 19.2 Hz), 2.07 (1 H, d, *J* = 18.9 Hz), 2.06 (3 H, s), 1.08 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 170.8, 156.0, 136.2, 135.9, 132.2, 130.4, 130.0, 129.9, 127.68, 127.66, 125.0, 80.9, 74.9, 67.4, 67.3, 63.9, 27.4, 26.8, 20.9, 19.3; HRMS (ESI) *m/z* calculated for $C_{27}H_{33}NO_6Si$: 495.2077, Found $(M + H)^+$: 496.2169; IR (NaCl, cm^{-1}): 3422 (b), 3071 (w), 2930 (m), 2858 (m), 1743 (s), 1472 (m), 1427 (m), 1372 (m), 1236 (s), 1112 (s), 1072 (m), 1049 (m), 957 (m), 738 (m), 704 (s); $[\alpha]_D^{22}$ -86.3 (c 1.38, $CHCl_3$).

Compound 12a

(4a*S*,5*R*,8*R*,8a*S*)-5-Acetoxy-8-(*tert*-butyldiphenylsilyloxy)-4a-hydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-3-carboxylic acid

To a 2.5 mL of MeCN solution containing compound **D** (27.5 mg, 0.055 mmol), was added 0.10 mL of a TEMPO/MeCN solution (concentration: 0.75 mg/mL, 4.8×10^{-4} mmol), followed by the addition of 1.7 mg of KBr (0.022 mmol). The mixture was cooled to 0 °C. To the stirred reaction mixture, was added dropwise 0.35 mL of 0.3 M NaOCl aqueous solution containing 17.2 mg of $NaHCO_3$ (0.20 mmol). The mixture was warmed to rt and the reaction was monitored by TLC until all the starting material was consumed. The reaction was then quenched with saturated Na_2SO_3 solution and the pH value of the solution was adjusted to 4 with 5% HCl. The solution was then extracted with 2×10 mL of EtOAc, washed with 5 mL of brine and dried with Na_2SO_4. The solution was then concentrated and the residue was dried under reduced pressure to give 27.3 mg of acid **12a** (0.053 mmol) in 96% yield. ^{1}H NMR ($CDCl_3$): δ 7.70-7.62 (4 H, m), 4.48-7.35 (6 H, m), 5.61 (1 H, td, *J* = 2.3, 10.5 Hz); 5.53 (1 H, dd, *J* = 2.3, 4.7 Hz), 5.48 (1 H, td, ddd, *J* = 2.0, 2.3, 10.5 Hz), 4.39 (1 H, dd, *J* = 2.2, 7.3 Hz), 4.03 (1 H, m), 2.44 (1 H, d, *J* = 2.2 Hz), 2.41 (1 H, dd, *J* = 2.2, 19.5 Hz), 2.11 (1 H, *J* = 18.5 Hz), 2.11 (3 H, s), 1.09 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 171.8, 161.7, 147.1, 136.1, 135.9, 133.1, 130.23, 130.16, 130.1, 127.7, 124.9, 83.1, 76.1, 67.6, 67.0, 26.8, 25.4, 20.8, 19.2; HRMS (ESI) *m/z* calculated for $C_{27}H_{31}NO_7Si$: 509.1870, Found $(M + Na)^+$: 532.1785; $[\alpha]_D^{22}$ +6.2° (c 1.36, $CHCl_3$).



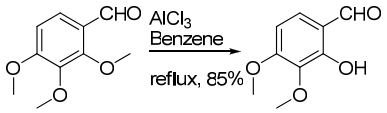
12b

Compound 12b

(4a*S*,5*S*,8*R*,8a*S*)-5-Acetoxy-8-(*tert*-butyldiphenylsilyloxy)-4a-hydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-3-carboxylic acid

Compound **12b** was prepared from compound **11b** following the same procedure as compound **12a**. ^{1}H NMR ($CDCl_3$): δ 7.69-7.63 (4 H, m), 7.48-7.36 (6 H, m), 5.75-5.66 (2 H, m), 5.11 (1 H, d, *J* = 3.0 Hz), 4.31 (1 H, d, *J* = 5.8 Hz), 4.08

(1 H, d, J = 5.7 Hz), 2.41 (1 H, J = 19.0 Hz), 2.20 (1 H, dd, J = 2.3, 19.5 Hz), 2.19 (3 H, s), 1.10 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 170.5, 161.6, 147.2, 136.0, 135.8, 132.9, 132.0, 131.9, 130.3, 130.1, 127.8, 132.9, 81.1, 70.9, 67.8, 64.3, 29.7, 26.9, 21.0, 19.2; HRMS (ESI) calculated for $C_{27}H_{31}NO_7Si$: 509.1870, Found $(M + Na)^+$: 532.1785; $[\alpha]_D^{22}$ +48.1 (c 1.37, $CHCl_3$).

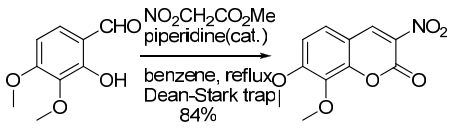


2,3,4-trimethoxy-benzaldehyde 13

Compound 13

2-Hydroxy-3,4-dimethoxybenzaldehyde

2,3,4-Dimethoxybenzaldehyde (10.0 g, 51.0 mmol) was dissolved in 150 mL of dry benzene. To this solution, was added aluminum trichloride (7.40 g, 56.1 mmol) in several batches. The mixture was heated to reflux under argon and monitored by TLC until all the starting material was consumed. The reaction was cooled to rt and quenched with 100 mL of cold water. $NaHSO_4$ solution (100 mL, 1.0 M) was added and the reaction mixture was stirred until all the solid material was dissolved. The aqueous phase was separated and extracted with 2×80 mL of EtOAc. The organic layers were combined, washed with 100 mL of saturated $NaHCO_3$ solution, 80 mL of brine and dried with Na_2SO_4. The crude product was concentrated and recrystallized from EtOAc to give 8.1 g of 2-hydroxy-3,4-dimethoxy-benzaldehyde **13** (43.9 mmol, 85%) as colorless needles. ^{1}H NMR ($CDCl_3$): δ 11.2 (1 H, s), 9.75 (1 H, s), 7.29 (1 H, d, J = 8.7 Hz), 6.61 (1 H, d, J = 8.7 Hz), 3.95 (3 H, s), 3.91 (3 H, s); ^{13}C NMR ($CDCl_3$): δ 194.8, 159.4, 155.7, 130.1, 116.6, 104.4, 60.7, 56.3; HRMS (CI) *m/z* calculated for $C_9H_{10}O_4$: 182.1733, Found $(M+H)^+$: 183.0652; mp 66.0-68.0 °C.

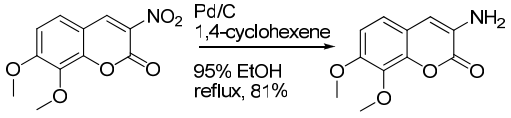


13 14

Compound 14

7,8-Dimethoxy-3-nitro-2*H*-chromen-2-one

2-Hydroxy-3,4-dimethoxybenzaldehyde **13** (1.84 g, 10.0 mmol) was dissolved in 100 mL of dry benzene. To this solution, was added 1.42 g of methyl nitroacetate (12.0 mmol) and 0.2 mL of piperidine (2.0 mmol). The reaction mixture was heated to reflux overnight with a Dean-Stark trap to collect the water. The reaction was then cooled to 0 °C and the yellow precipitate was collected on a sintered glass funnel. The precipitate was dissolved in 70 mL of DMF and cooled to 0 °C. Ice-water (200 mL) was then added to the solution and the bright yellow precipitate was collected, washed with 2×40 mL of cold water and dried under reduced pressure to give 2.12 g of nitrocoumarin **14** (8.4 mmol, 84%). ^{1}H NMR ($CDCl_3$): δ 8.73 (1 H, s), 7.44(1 H, d, J = 8.8 Hz), 6.83 (1 H, d, J = 8.8 Hz), 4.03 (3 H, s), 4.01 (3 H, s); ^{13}C NMR ($CDCl_3$): δ159.6, 151.7, 149.0, 143.1, 136.3, 131.9, 126.5, 110.8, 110.3, 61.6, 56.8; HRMS (ESI) *m/z* calculated for $C_{11}H_9NO_6$: 251.1923, Found $(M+Na)^+$: 274.0321; mp 199.0-200.0 °C.

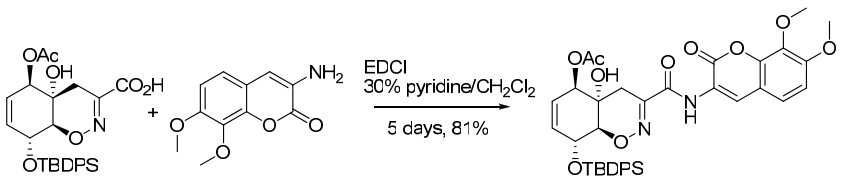


14 4

Compound 4

3-Amino-7,8-dimethoxy-2*H*-chromen-2-one

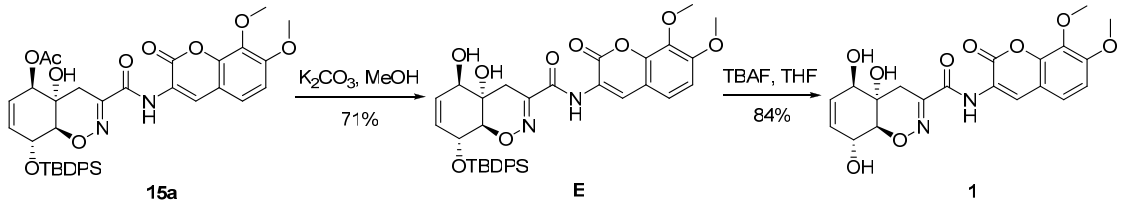
Nitrocoumarin **14** (0.71 g, 2.83 mmol), 0.602 g of Pd/C (0.57 mmol) and 2 mL of cyclohexene were premixed in 10 mL of 95% EtOH and the mixture was heated to reflux. The reaction was monitored by TLC until all the starting material was consumed. The mixture was then cooled to rt and collected through a Celite pad. The Celite pad was washed with 4×40 mL of EtOAc. The filtrate was concentrated and dried under reduced pressure to give 0.510 g of aminocoumarin **4** as a yellow solid (2.29 mmol, 84%). ^{1}H NMR ($CDCl_3$): δ 6.96 (1 H, d, J = 8.8 Hz), 6.83 (1 H, d, J = 8.8 Hz), 4.10 (2 H, s), 3.98 (3 H, s), 3.90 (3 H, s); ^{13}C NMR ($CDCl_3$): δ 159.2, 151.8, 143.1, 136.3, 129.9, 119.4, 115.8, 112.0, 109.3, 61.5, 56.5; HRMS (ESI) *m/z* calculated for $C_{11}H_{11}NO_4$: 221.0688, Found (M^+): 221.0681.



Compound 15a

(4a*S*,5*R*,*8R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-(7,8-dimethoxy-2-oxo-2*H*-chromen-3-ylcarbamoyl)-4a-hydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazin-5-yl acetate

Acid **12a** (21.0 mg, 0.041 mmol), aminocoumarin **4** (11.0 mg, 0.049 mmol) and EDCI (9.5 mg, 0.049 mmol) were dissolved in 0.2 mL of 30% pyridine/CH_2Cl_2 and stirred at rt for 5 days. The solvent was evaporated and the residue was purified by column chromatography (5%-20% acetone/ CH_2Cl_2) to give compound **15a** (23.7 mg, 0.033 mmol, 81% yield). ^{1}H NMR ($CDCl_3$): δ 9.29 (1 H, s), 8.57 (1 H, s), 7.73-7.65 (4 H, m), 7.45-7.35 (6 H, m), 7.18 (1 H, d, *J* = 8.7 Hz), 6.92 (1 H, d, *J* = 8.7 Hz), 5.58-5.47 (3 H, m), 4.35 (1 H, dd, *J* = 2.0, 6.9 Hz), 4.12-4.08 (1 H, m), 4.02 (3 H, s), 3.95 (3 H, s), 3.33 (1 H, s), 2.51 (1 H, dd, *J* = 2.0, 19.4 Hz), 2.18 (1 H, d, *J* = 19.4 Hz), 2.11 (3 H, s), 1.10 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 171.4, 160.9, 157.9, 154.3, 149.0, 144.3, 136.3, 136.1, 135.9, 133.4, 131.8, 130.2, 129.9, 127.9, 127.8, 127.7, 125.0, 124.3, 122.5, 121.1, 114.2, 109.5, 82.4, 75.8, 67.8, 67.1, 61.6, 56.5, 26.9, 25.1, 20.9, 19.2; HRMS (ESI) *m/z* calculated for $C_{38}H_{40}N_2O_{10}Si$: 712.2452, Found (M + Na)$^+$: 735.2452; IR (NaCl, cm^{-1}): 3361(b), 2932 (w), 2857 (w), 1722 (s), 1682 (s), 1608 (s), 1520 (s), 1462 (s), 1428 (m), 1377 (m), 1232 (m), 1169 (w), 1110 (s), 1076 (m), 909 (w), 734 (m), 703 (m); $[\alpha]_D^{22}$ +173.4 (c 0.50, $CHCl_3$).



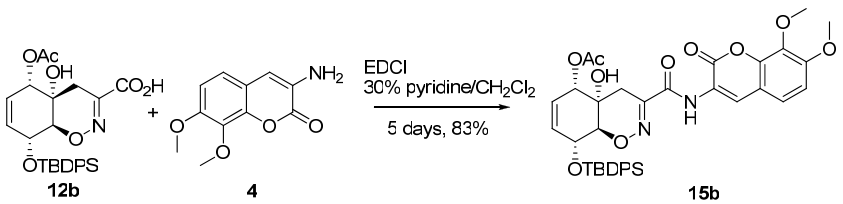
Compound E

(4a*S*,5*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-*N*-(7,8-dimethoxy-2-oxo-2*H*-chromen-3-yl)-4a,5-dihydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-3-carboxamide

To a solution containing amide **15a** (9.8 mg, 0.014 mmol) in 0.2 mL of dry MeOH, was added 2.3 mg of K_2CO_3 at rt. The mixture was monitored by TLC until all the starting material was consumed. The solvent was evaporated and the residue was purified by column chromatography (5%-20% acetone/CH_2Cl_2) to give 6.8 mg of compound **E** (0.010 mmol, 71% yield). R_f: 0.26 in 20% acetone/CH_2Cl_2; ^{1}H NMR ($CDCl_3$): δ 9.25 (1 H, s), 8.56 (1 H, s), 7.71-7.64 (4 H, m), 7.45-7.36 (6 H, m), 7.18 (1 H, d, *J* = 8.7 Hz), 6.92 (1 H, d, *J* = 8.7 Hz), 5.67 (1 H, d, *J* = 10.4 Hz), 5.48 (1 H, td, *J* = 2.4, 10.4 Hz), 4.40 (1 H, m), 4.23 (1 H, dd, *J* = 1.4, 6.0 Hz), 4.17 (1 H, m), 4.01 (3 H, s), 3.95 (3 H, s), 3.00 (1 H, s), 2.62 (1 H, dd, *J* = 1.4, 19.5 Hz), 2.18 (1 H, d, *J* = 19.5 Hz), 2.09 (1 H, m), 1.09 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 160.7, 158.0, 154.2, 150.8, 144.2, 136.2, 136.0, 135.9, 133.2, 131.9, 130.0, 128.6, 127.91, 127.87, 127.7, 125.0, 124.0, 122.6, 121.1, 114.1, 109.5, 82.4, 75.8, 67.8, 67.1, 61.6, 56.5, 26.9, 25.8, 19.2; HRMS (ESI) *m/z* calculated for $C_{36}H_{38}N_2O_9Si$: 670.2347, Found (M + Na)$^+$: 693.2253; $[\alpha]_D^{22}$ +133.4 (c 0.34, $CHCl_3$).

Trichodermamide A (1)

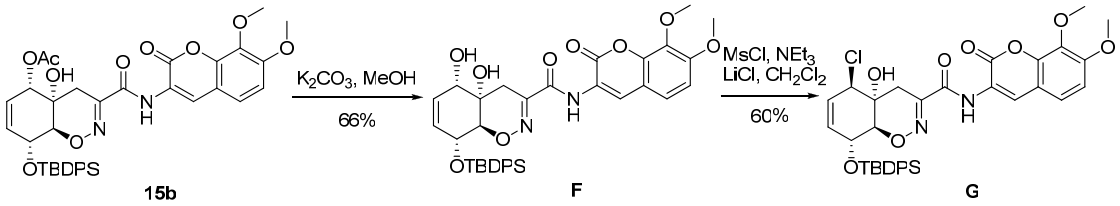
Amide **E** (6.8 mg, 0.010 mmol) was dissolved in 0.3 mL of dry THF and cooled to 0 °C. TBAF (11 μL, 1.0 M in THF) was then added dropwise. The solution was warmed to rt and was monitored by TLC until all the starting material was consumed. The solvent was then evaporated and the residue was purified by column chromatography (20%-50% acetone/ CH_2Cl_2) to give 3.7 mg of trichodermamide A as a white solid (0.0084 mmol, 84% yield). R_f: 0.09 in 20% acetone/ CH_2Cl_2; ^{1}H NMR (10% DMSO-d_6 in $CDCl_3$): δ 9.28 (1 H, s), 8.41 (1 H, s), 7.03 (1 H, d, J = 8.7 Hz), 6.75 (1 H, d, *J* = 8.7 Hz), 5.40 (1 H, d, *J* = 10.6 Hz), 5.37 (1 H, td, *J* = 10.6 Hz), 5.02 (1 H, d, *J* = 5.5 Hz), 4.79 (1 H, s), 4.34 (1 H, d, *J* = 4.3 Hz), 4.02 (1 H, dd, *J* = 2.2, 7.8 Hz), 3.90 (1 H, m); 3.78 (3 H, s), 3.76 (3 H, s), 2.50 (1 H, d, *J* = 19.5 Hz, masked by DMSO peak, deduced); 2.38 (1 H, d, *J* = 19.5 Hz); ^{13}C NMR (10% DMSO-d_6 in $CDCl_3$): δ160.9, 157.7, 153.6, 149.9, 143.5, 135.6, 129.1, 127.4, 123.5, 122.1, 120.7, 113.7, 109.2, 83.3, 73.7, 67.8, 66.1, 60.9, 56.0, 23.7; HRMS (ESI) *m/z* calculated for $C_{20}H_{20}N_2O_9$: 432.1169, Found (M + H)$^+$: 433. 1268; IR (NaCl, cm^{-1}): 3363 (b), 2927 (w), 1713 (s), 1682 (s), 1607 (s), 1524 (s), 1462 (s), 1379 (s), 1286 (s), 1107 (s), 1010 (m), 905 (w), 789 (w); $[\alpha]_D^{23}$ +158.1 (c 0.14, acetone).



Compound 15b

(4a*S*,5*S*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-3-(7,8-dimethoxy-2-oxo-2*H*-chromen-3-ylcarbamoyl)-4a-hydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazin-5-yl acetate

Acid **12b** (27.1 mg, 0.053 mmol), aminocoumarin **4** (14.2 mg, 0.064 mmol) and EDCI (12.3 mg, 0.064 mmol) were dissolved in 0.25 mL of 30% pyridine/CH_2Cl_2 and stirred at rt for 5 days. The solvent was then evaporated and the residue was purified by column chromatography (5%-20% acetone/CH_2Cl_2) to give 31.8 mg of amide **15b** (0.044 mmol, 83% yield). R_f: 0.76 in 20% acetone/CH_2Cl_2; ^{1}H NMR ($CDCl_3$): δ 9.27 (1 H, s), 8.57 (1 H, s), 7.72-7.65 (4 H, m), 7.46-7.36 (6 H, m), 7.18 (1 H, d, *J* = 8.8 Hz), 6.91 (1 H, d, *J* = 8.8 Hz), 5.72 (1 H, m), 5.66 (1 H, dd, *J* = 2.6, 10.3 Hz), 5.15 (1H, d, *J* = 3.5 Hz), 4.29-4.26 (1 H, m), 4.18-4.15 (1 H, m), 4.01 (3 H, s), 3.95 (3 H, s), 3.04 (1 H, s), 2.46 (1 H, dd, *J* = 1.5, 19.0 Hz), 2.34 (1 H, d, *J* = 19.0 Hz), 2.18 (3 H, s), 1.11 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 170.4, 160.5, 157.9, 154.2, 149.0, 144.2, 136.0, 135.8, 133.0, 131.8, 131.6, 130.2, 130.0, 127.9, 127.8, 127.8, 124.33, 124.29, 122.5, 121.1, 114.1, 109.5, 80.5, 70.8, 67.7, 64.5, 61.6, 56.4, 29.7, 26.9, 21.0, 19.2; HRMS (ESI) *m/z* calculated for $C_{38}H_{40}N_2O_{10}Si$: 712.2452, Found $(M + Na)^+$: 735.2333; $[\alpha]_D^{22}$ +14.1 (c 1.71, $CHCl_3$).



Compound F

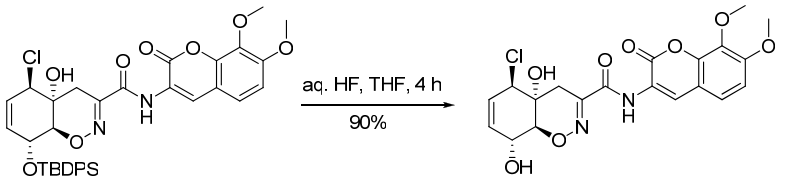
(4a*S*,5*S*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-*N*-(7,8-dimethoxy-2-oxo-2*H*-chromen-3-yl)-4a,5-dihydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-3-carboxamide

To a solution containing amide **15b** (27.5 mg, 0.039 mmol) in 0.2 mL of dry MeOH, was added 6.4 mg of K_2CO_3 (0.046 mmol) at rt. The mixture was monitored by TLC until all the starting material was consumed. The solvent was evaporated and the residue was purified by column chromatography (5%-20% acetone/CH_2Cl_2) to give 17.3 mg of compound **F** (0.030 mmol, 66% yield). ^{1}H NMR ($CDCl_3$): δ 9.29 (1 H, s), 8.59 (1 H, s), 7.69-7.66 (4 H, m), 7.48-7.39 (6 H, m), 7.19 (1 H, d, *J* = 8.7 Hz), 6.91 (1 H, d, *J* = 8.7 Hz), 5.76 (1 H, dd, *J* = 2.5, 10.2 Hz), 5.57 (1 H, dd, *J* = 3.2, 10.2 Hz), 4.27 (1 H, m), 4.13 (1 H, m), 4.00 (3 H, s), 3.95 (3 H, s), 3.85 (1 H, m), 3.80 (1 H, s), 2.81 (1 H, dd, *J* = 1.4, 19.1 Hz), 2.42 (1 H, d, *J* = 19.1 Hz), 2.09 (1 H, m), 1.10 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 160.5, 157.9, 154.3, 150.3, 144.2, 136.2, 135.9, 135.8, 132.7, 131.8, 130.4, 130.2, 129.1, 128.0, 127.8, 124.4, 124.0, 122.5, 121.1, 114.2, 109.5, 79.3, 68.1, 67.0, 65.3, 61.6, 56.4, 29.3, 26.9, 19.1; HRMS (ESI) *m/z* calculated for $C_{36}H_{38}N_2O_9Si$: 670.2347, Found $(M + Na)^+$: 693.2254; $[\alpha]_D^{22}$ +24.7 (c 0.85, $CHCl_3$).

Compound G

(4a*R*,5*R*,8*R*,8a*S*)-8-(*tert*-Butyldiphenylsilyloxy)-5-chloro-*N*-(7,8-dimethoxy-2-oxo-2H-chromen-3-yl)-4a-hydroxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*e*][1,2]oxazine-3-carboxamide

Amide **F** (12.8 mg, 0.019 mmol) was dissolved in 0.5 mL of dry CH_2Cl_2 and cooled to 0 °C. To this solution, was added 4.0 μL of NEt_3 (0.029 mmol) and 1.6 μL of MsCl (0.021 mmol) in sequence. The mixture was warmed to rt and stirred for 2 h. Anhydrous LiCl (4.1 mg, 0.097 mmol) was then added and the mixture was stirred for 2 days. The solvent was evaporated and the residue was purified by column chromatography (30% EtOAc/hexanes) to give 7.9 mg of compound **G** (yield 61%). R_f: 0.33 in 30% EtOAc/hexanes; ^{1}H NMR ($CDCl_3$): δ 9.25 (1 H, s), 8.58 (1 H, s), 7.71-7.64 (4 H, m), 7.45-7.31 (6 H, m), 7.19 (1 H, d, *J* = 8.7 Hz), 6.92 (1 H, d, *J* = 8.7 Hz), 5.62 (1 H, td, *J* = 2.0, 10.4 Hz), 5.57 (1 H, td, *J* = 2.4, 10.4 Hz), 4.84 (1 H, q, *J* = 2.4 Hz), 4.38 (1 H, dd, *J* = 2.2, 7.0 Hz), 4.13-4.08 (1 H, m), 4.03 (3 H, s), 3.96 (3 H, s), 3.46-3.39 (1 H, m), 2.73 (1 H, dd, *J* = 2.2, 19.6 Hz), 2.21 (1 H, d, *J* = 19.6 Hz), 1.10 (9 H, s); ^{13}C NMR ($CDCl_3$): δ 160.5, 157.9, 154.3, 149.3, 144.3, 136.3, 135.9, 133.3, 131.6, 130.1, 130.0, 128.9, 127.7, 124.4, 122.5, 121.1, 114.2, 109.5, 83.0, 68.1, 67.9, 63.5, 61.6, 56.5, 29.7, 26.2, 19.2; HRMS (ESI) *m/z* calculated for $C_{36}H_{37}ClN_2O_9Si$: 688.2008, Found $(M + Na)^+$: 711.1924; $[\alpha]_D^{22}$ +121.1 (c 0.30, $CHCl_3$).



G trichodermamide B (2)

Trichodermamide B (2)

To a solution containing 1.0 mg amide G in 0.2 mL of THF, was added dropwise 0.15 mL of aqeous HF solution (48%). The mixture was stirred at room temperature for 4 h. The reaction was then diluted with 0.5 mL of EtOAc, and quenched with adequate amount of saturated $NaHCO_3$ solution. The organic layer was separated, and the aqueous phase was extracted with 2×2 mL of EtOAc. The organic layers were combined, washed with brine, and dried with Na_2SO_4. The solvent was evaporated and the residue was purified by column chromatography (10% Acetone/CH_2Cl_2) to give 0.6 mg of trichodermamide B as a white solid(yield 90%). ^{1}H NMR (10% DMSO-d_6 in $CDCl_3$): δ 9.41 (1 H, s), 8.56 (1 H, s), 7.16 (1 H, d, *J* = 8.7 Hz), 6.88 (1 H, d, *J* = 8.7 Hz), 5.59 (2 H, m), 4.82 (1 H, m), 4.25 (1 H, dd, *J* = 2.1, 7.5 Hz), 4.11 (1 H, m), 3.92 (3 H, s), 3.89 (3 H, s), 2.82 (1 H, dd, *J* = 2.1, 19.6 Hz), 2.21 (1 H, d, *J* = 19.6 Hz), ^{13}C NMR (10% DMSO-d_6 in $CDCl_3$): δ 160.7, 157.8, 153.8, 149.6, 143.7, 135.7, 129.0, 127.4, 123.9, 122.3, 120.8, 113.8, 109.2, 83.9, 67.3, 65.6, 64.6, 61.2, 56.1, 25.1 (some impurities also showed up around 25.2 ppm); HRMS (ESI) *m/z* calculated for $C_{20}H_{19}ClN_2O_8$: 450.0830, Found $(M + H)^+$: 451.0905; $[\alpha]_D^{29}$ +138.0 (c 0.03, $CHCl_3$).

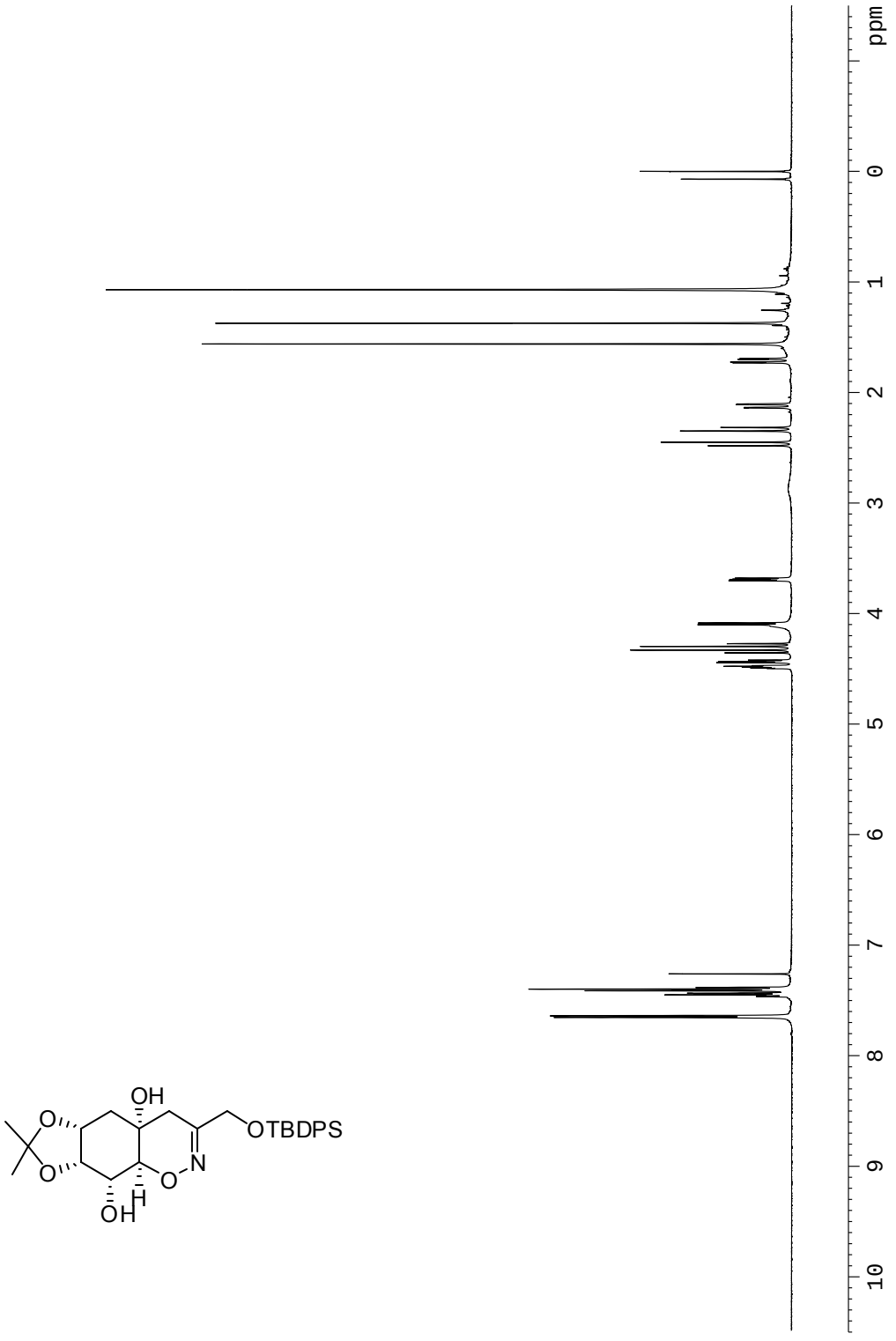


Figure 1. ^{1}H NMR of Compound 8.

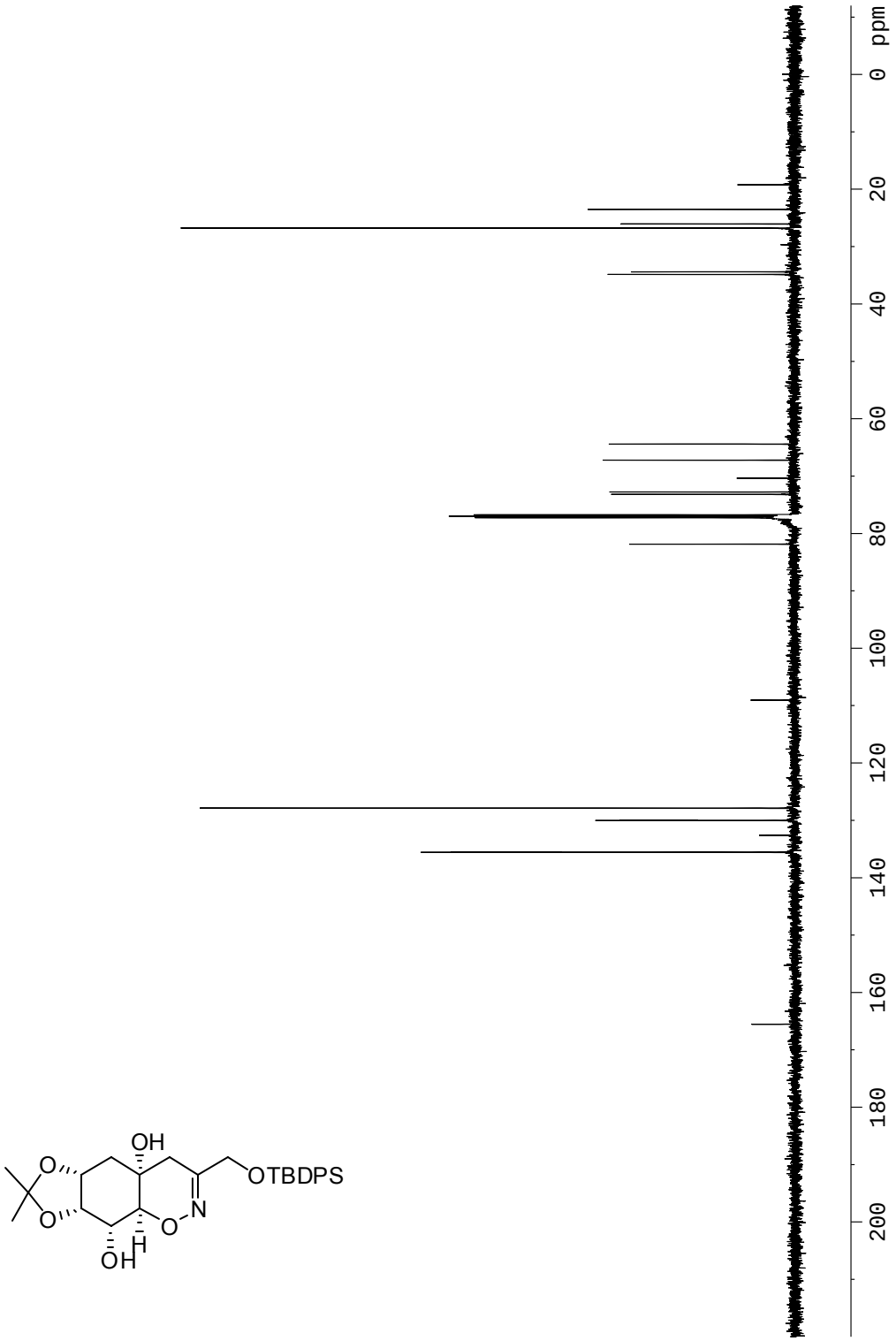


Figure 2. ^{13}C NMR of Compound 8.

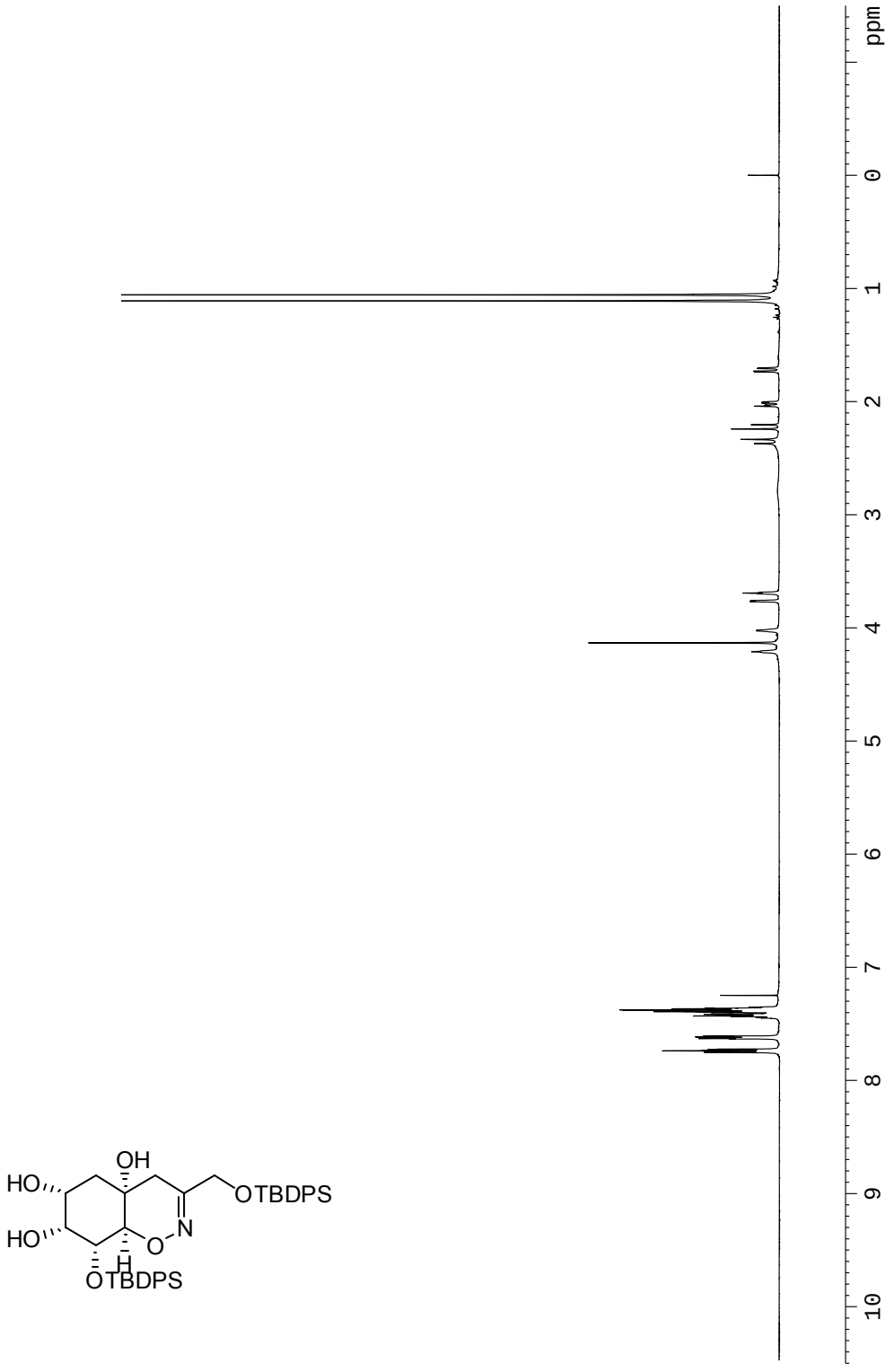


Figure 3. ^{1}H NMR of Compound B.

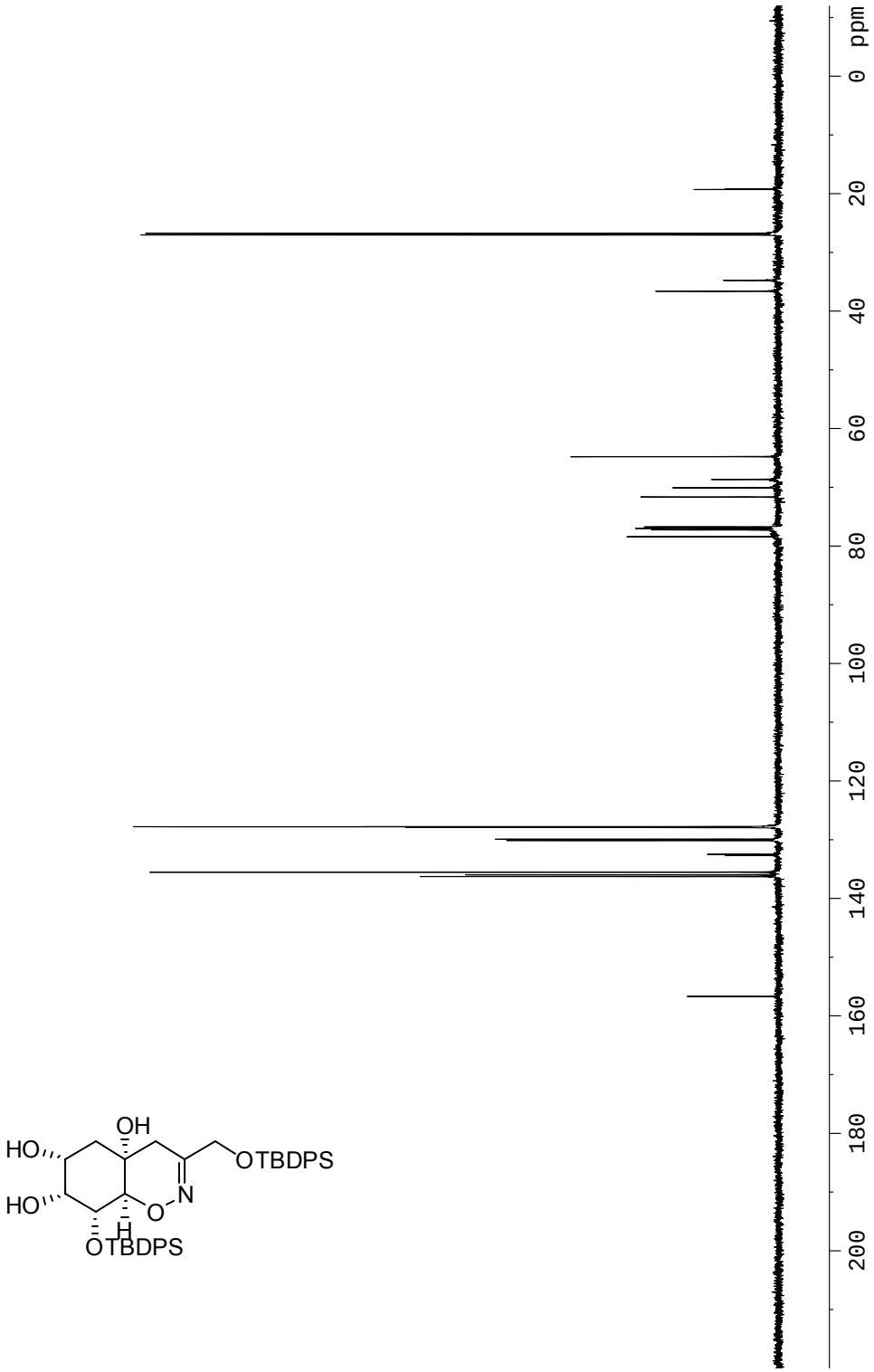


Figure 4. ^{13}C NMR of Compound B.

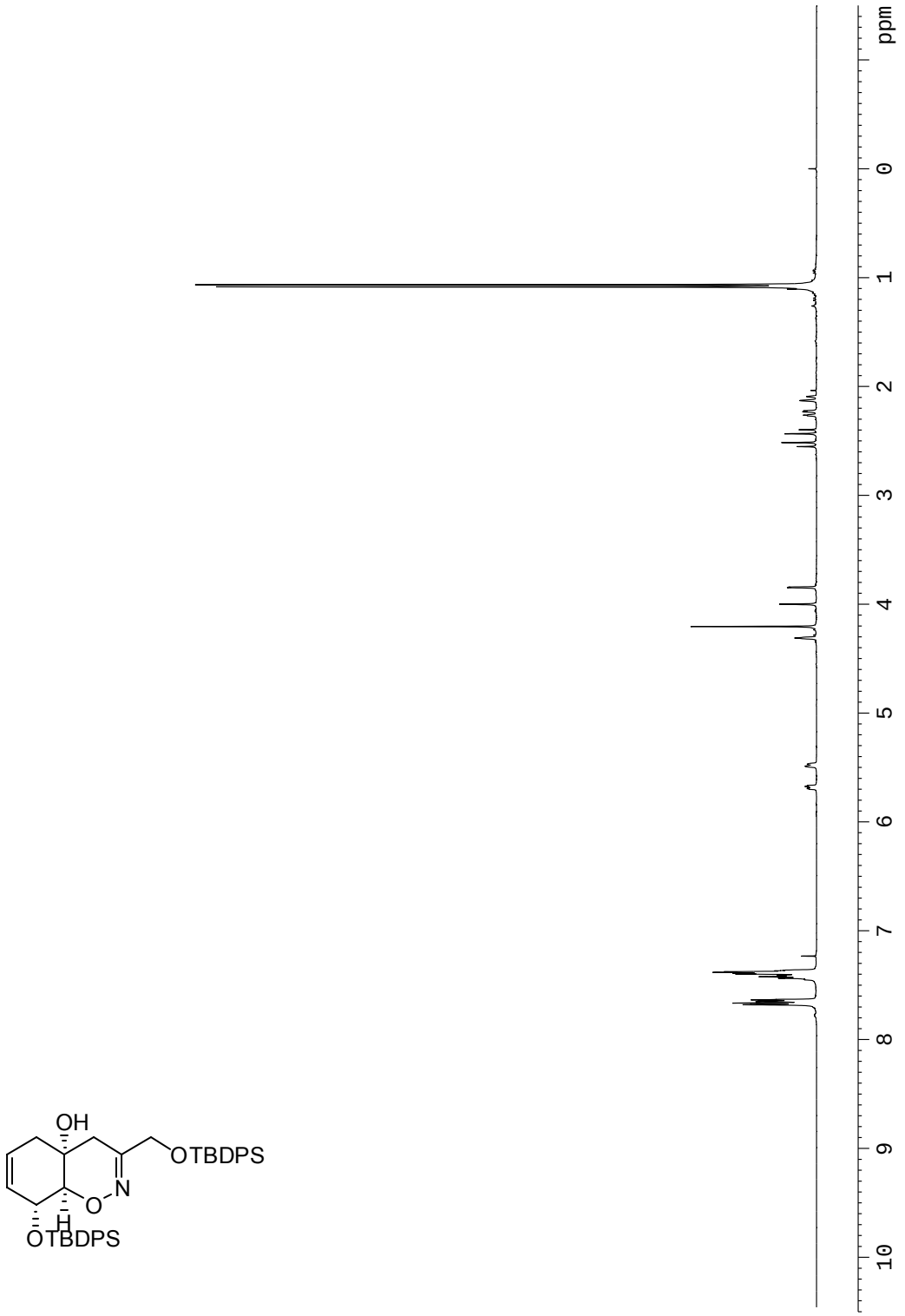


Figure 5. ^{1}H NMR of Compound 9.

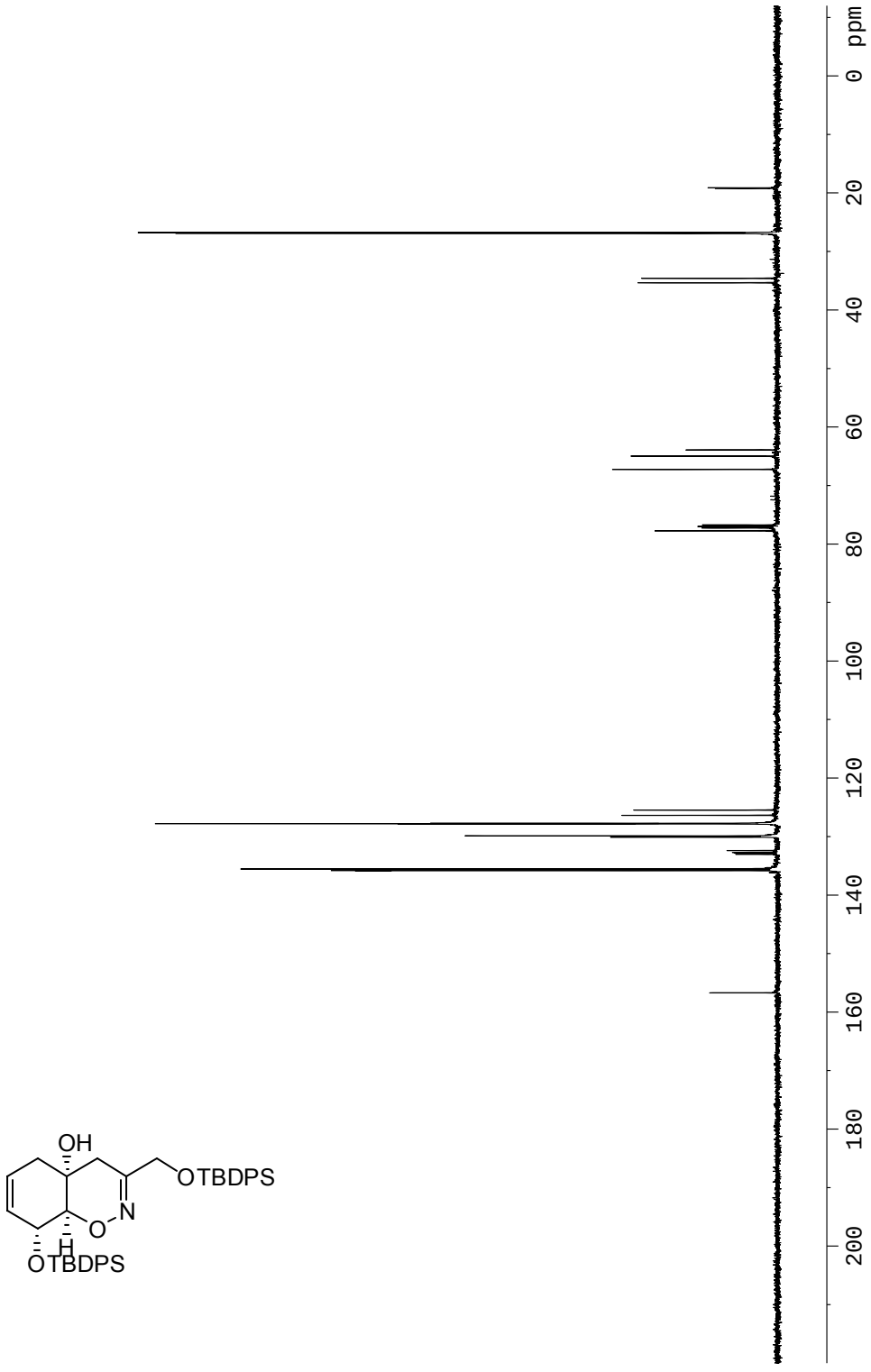


Figure 6. ^{13}C NMR of Compound 9.

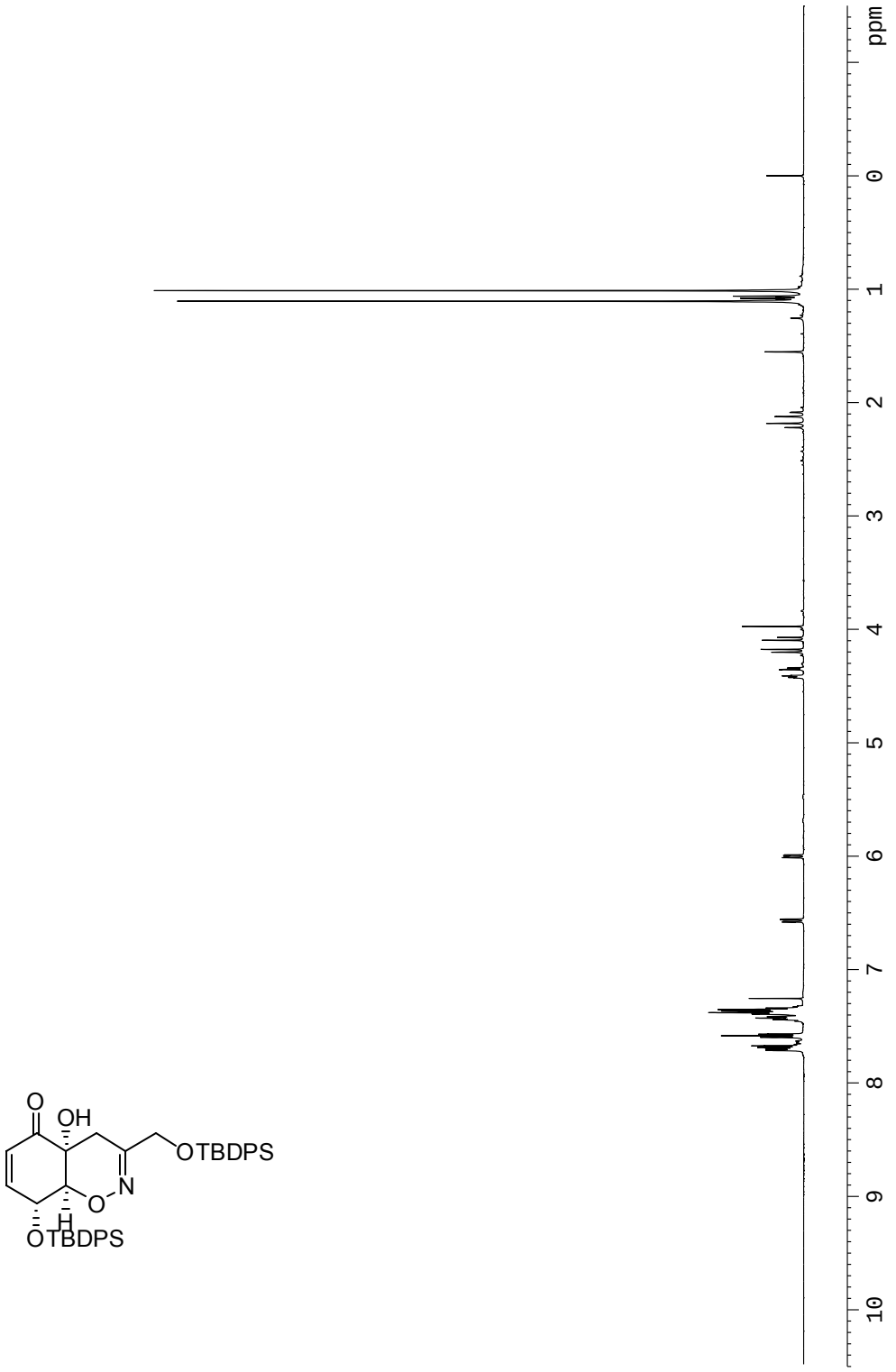


Figure 7. ^{1}H NMR of Compound 10.

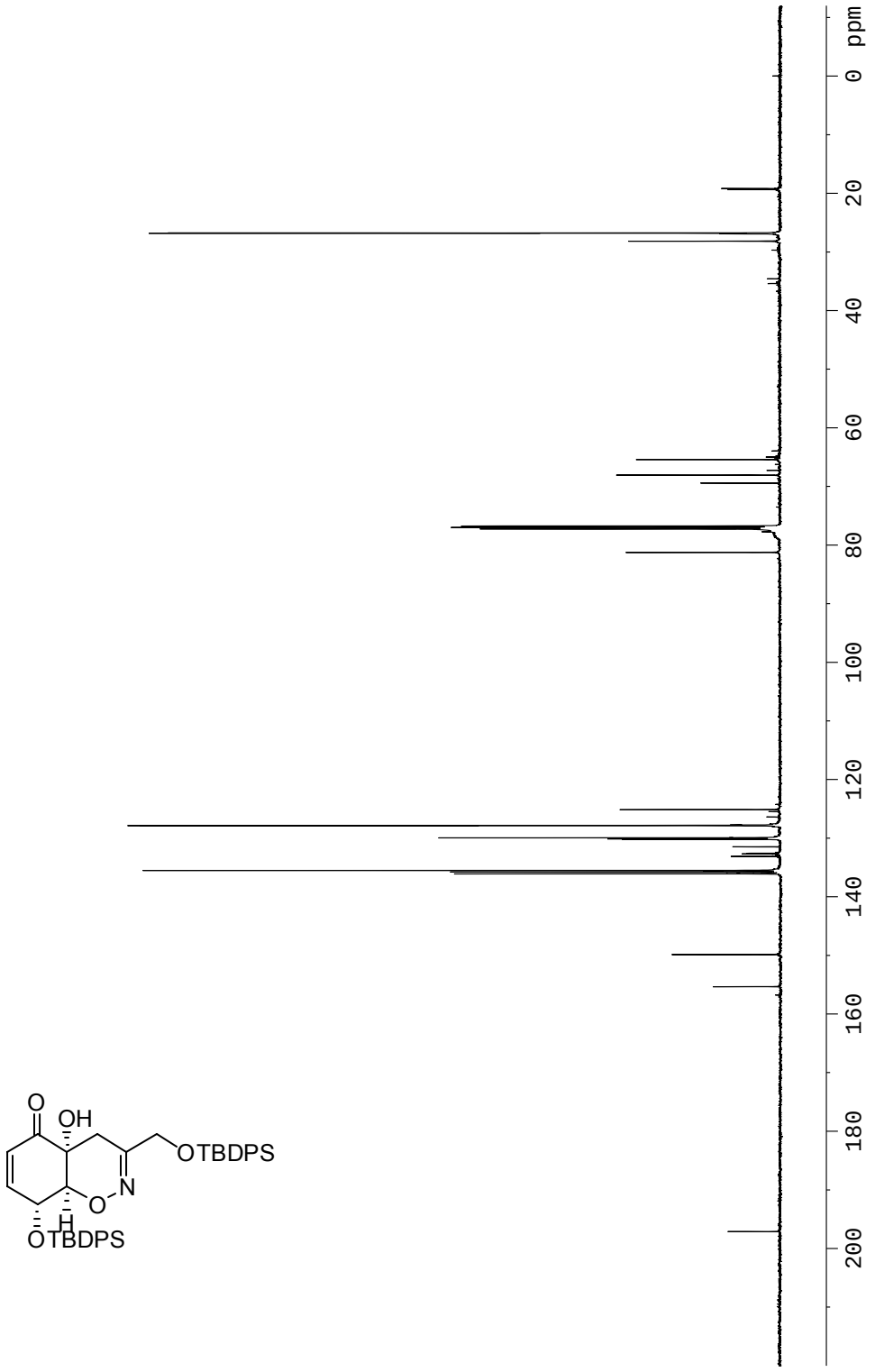


Figure 8. ^{13}C NMR of Compound 10.

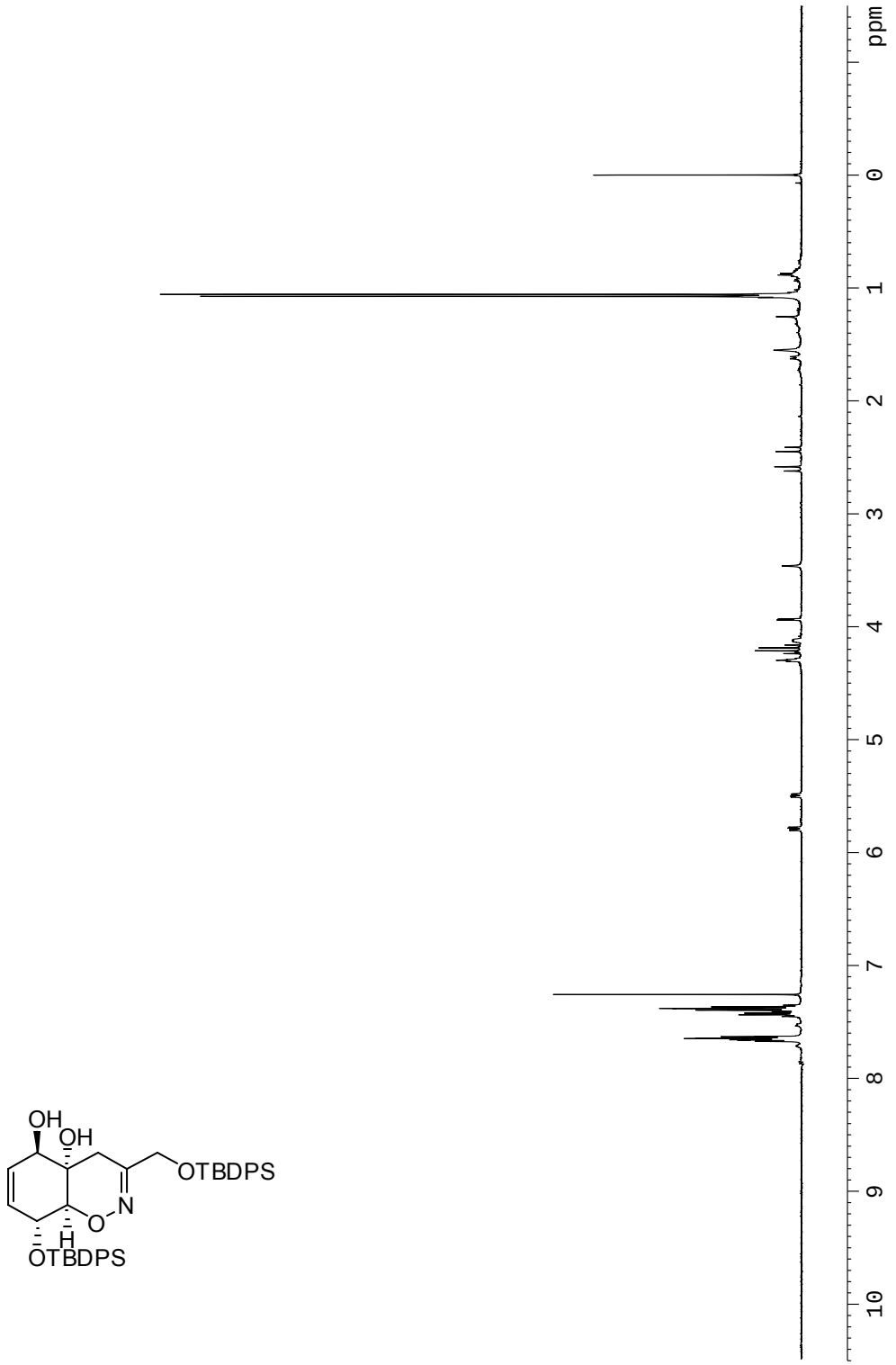


Figure 9. ^{1}H NMR of Compound 11a.

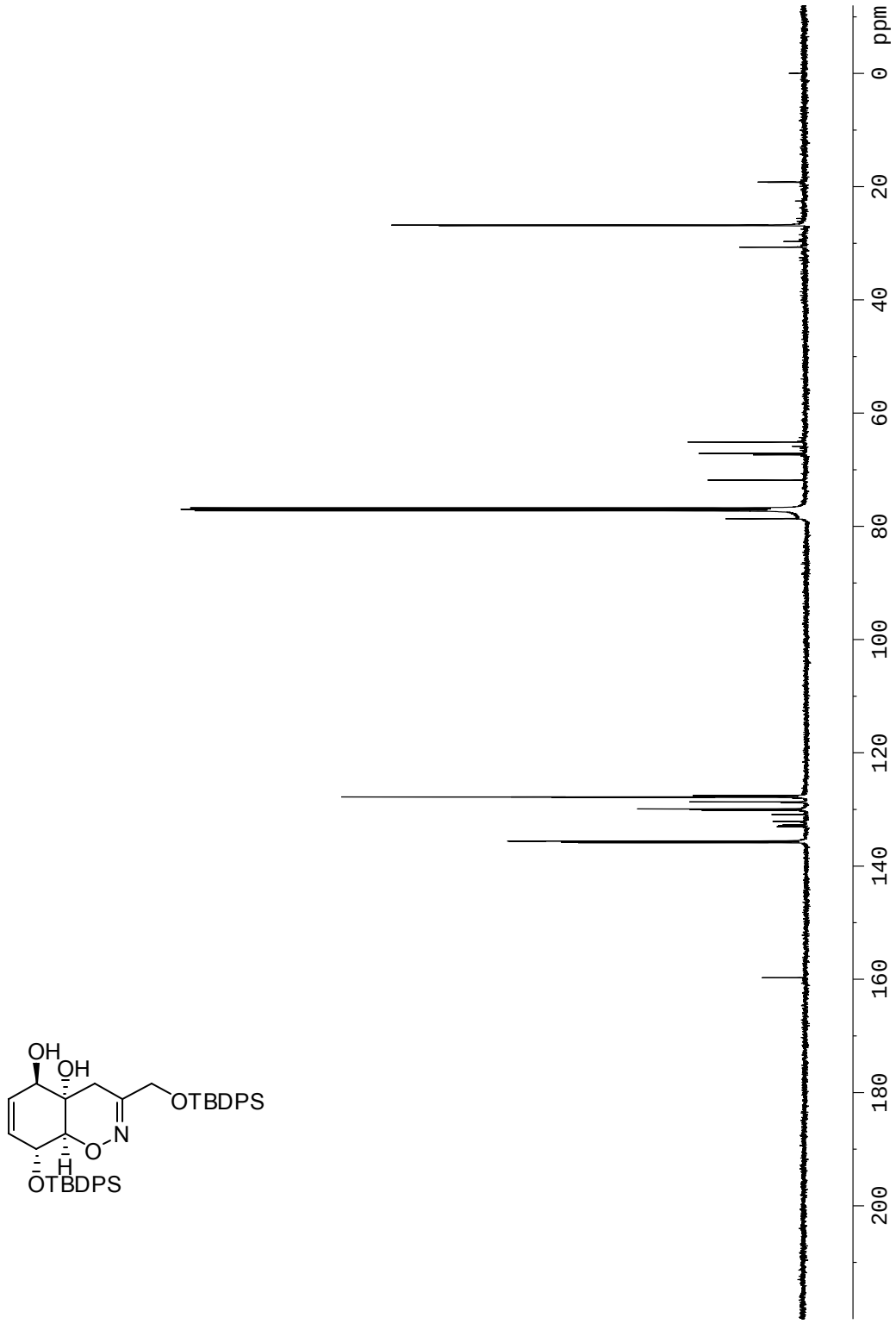


Figure 10. ^{13}C NMR of Compound 11a.

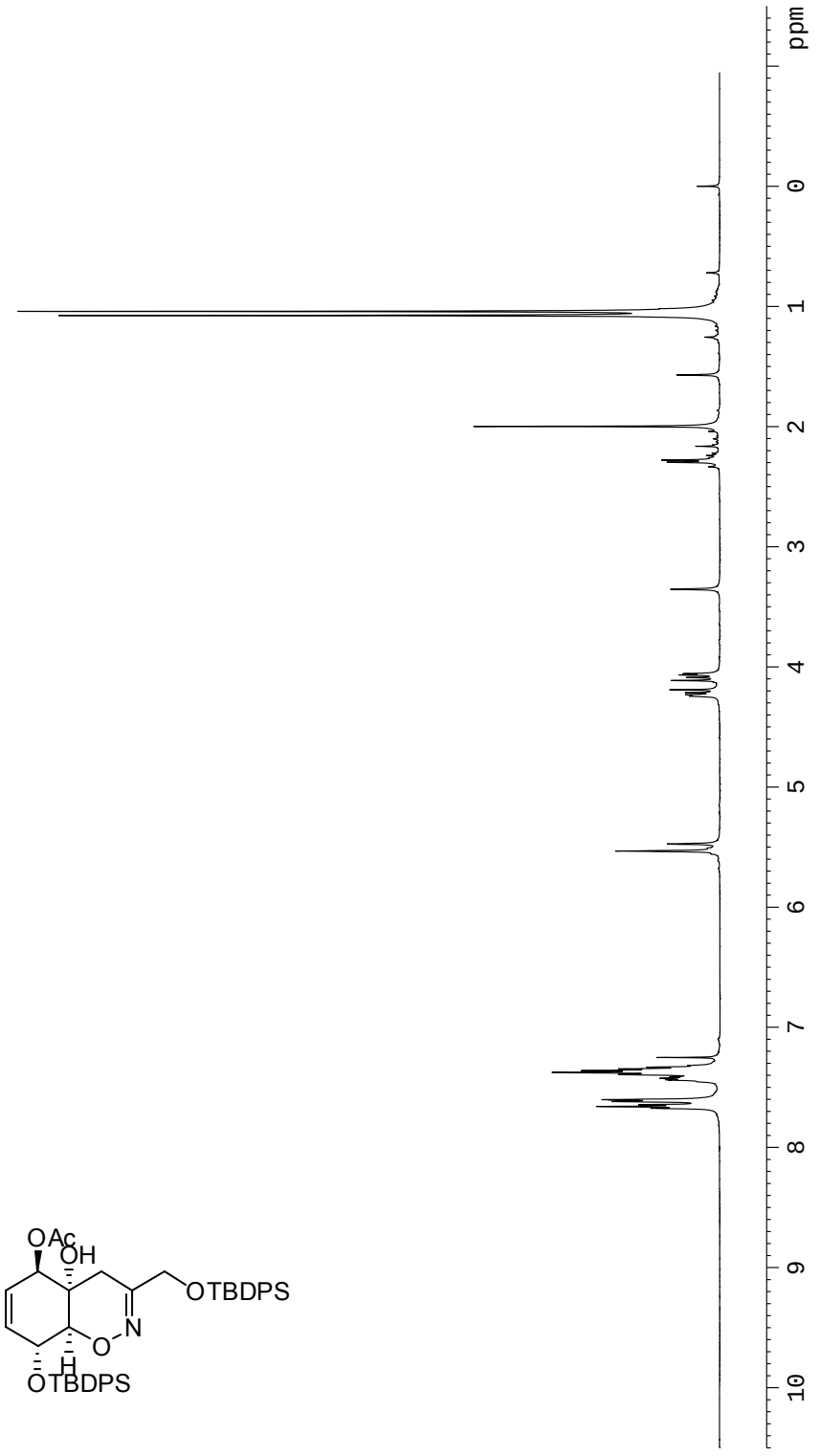


Figure 11. ^{1}H NMR of Compound C.

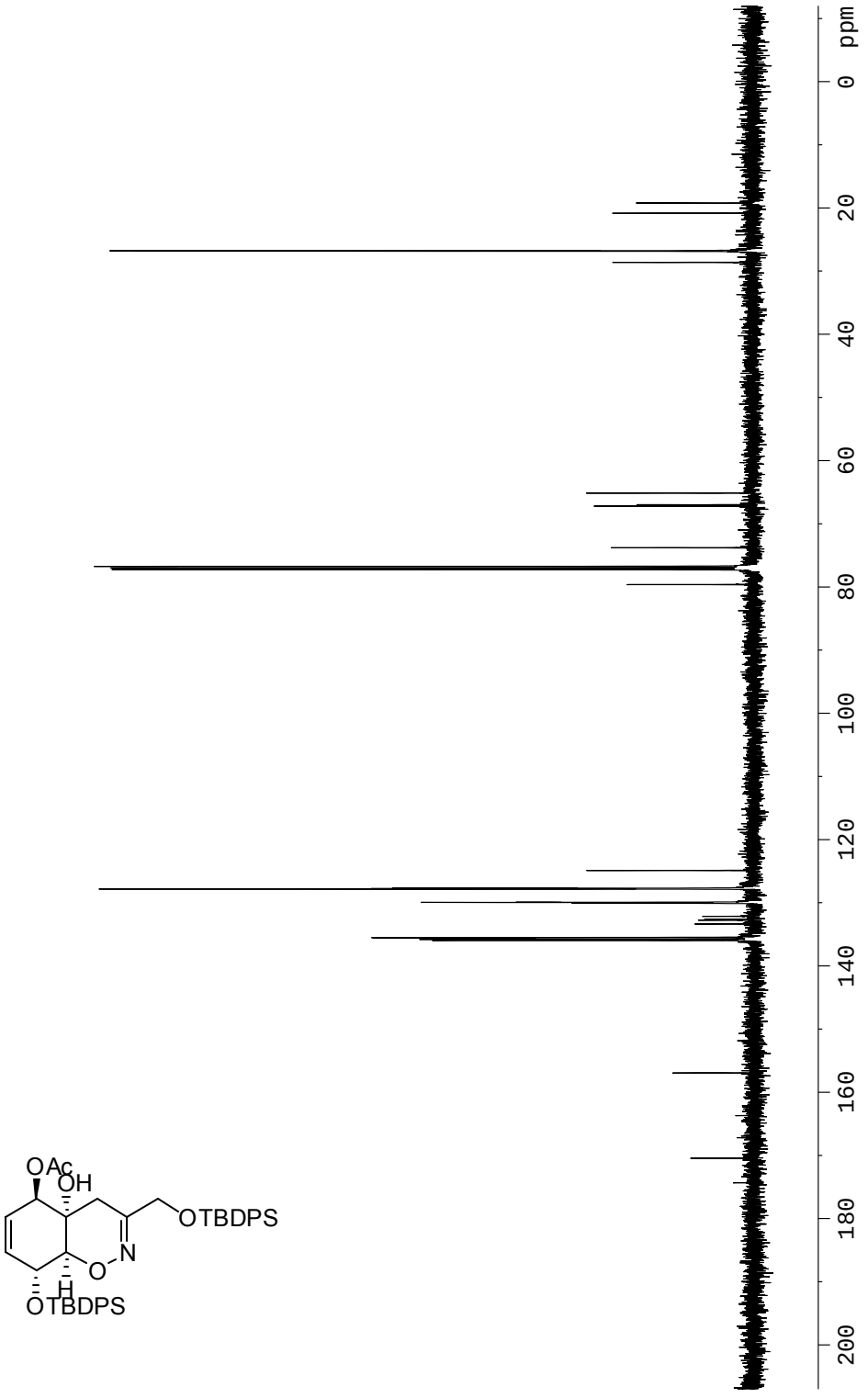


Figure 12. ^{13}C NMR of Compound C.

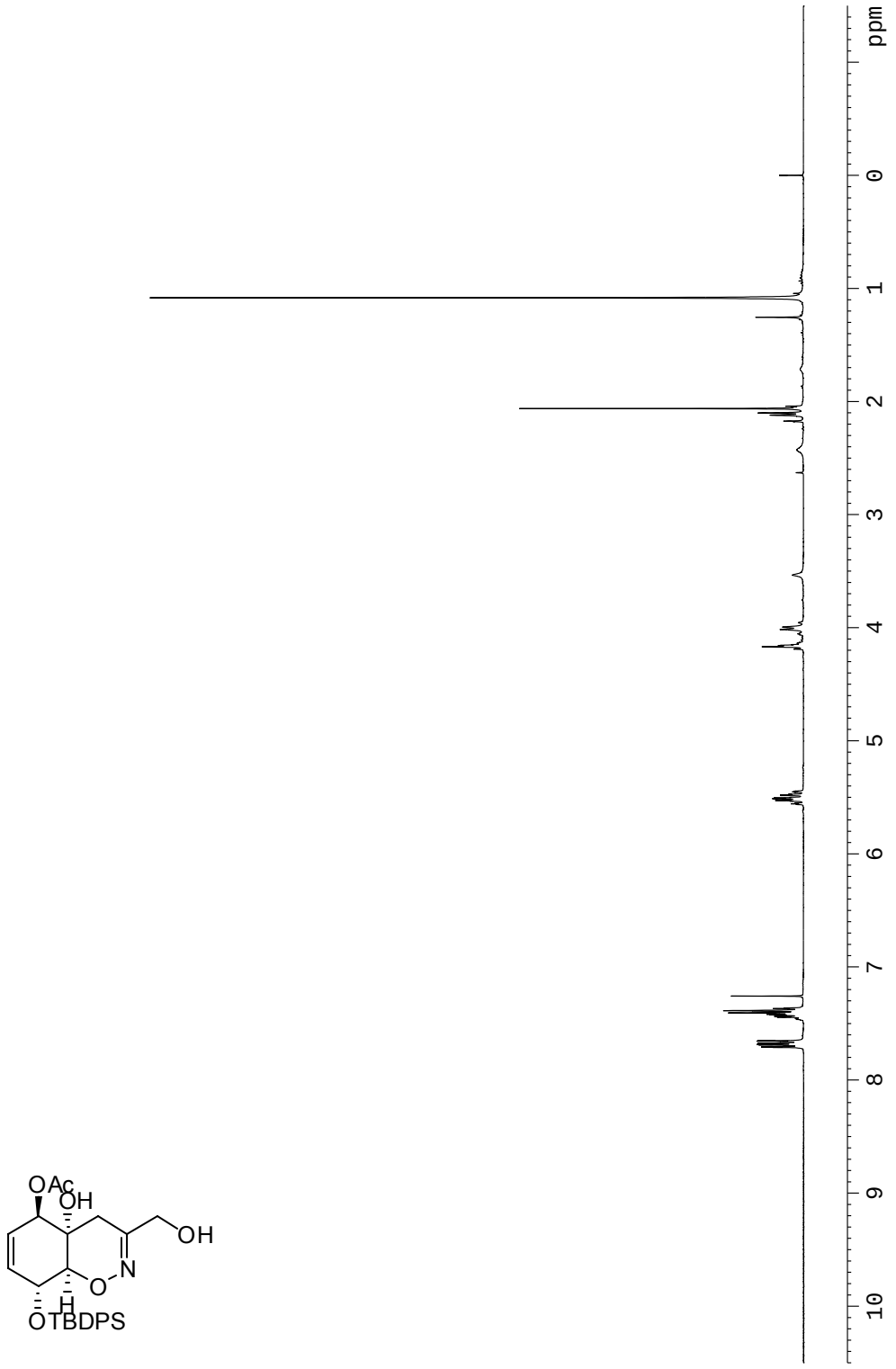


Figure 13. ^{1}H NMR of Compound D.

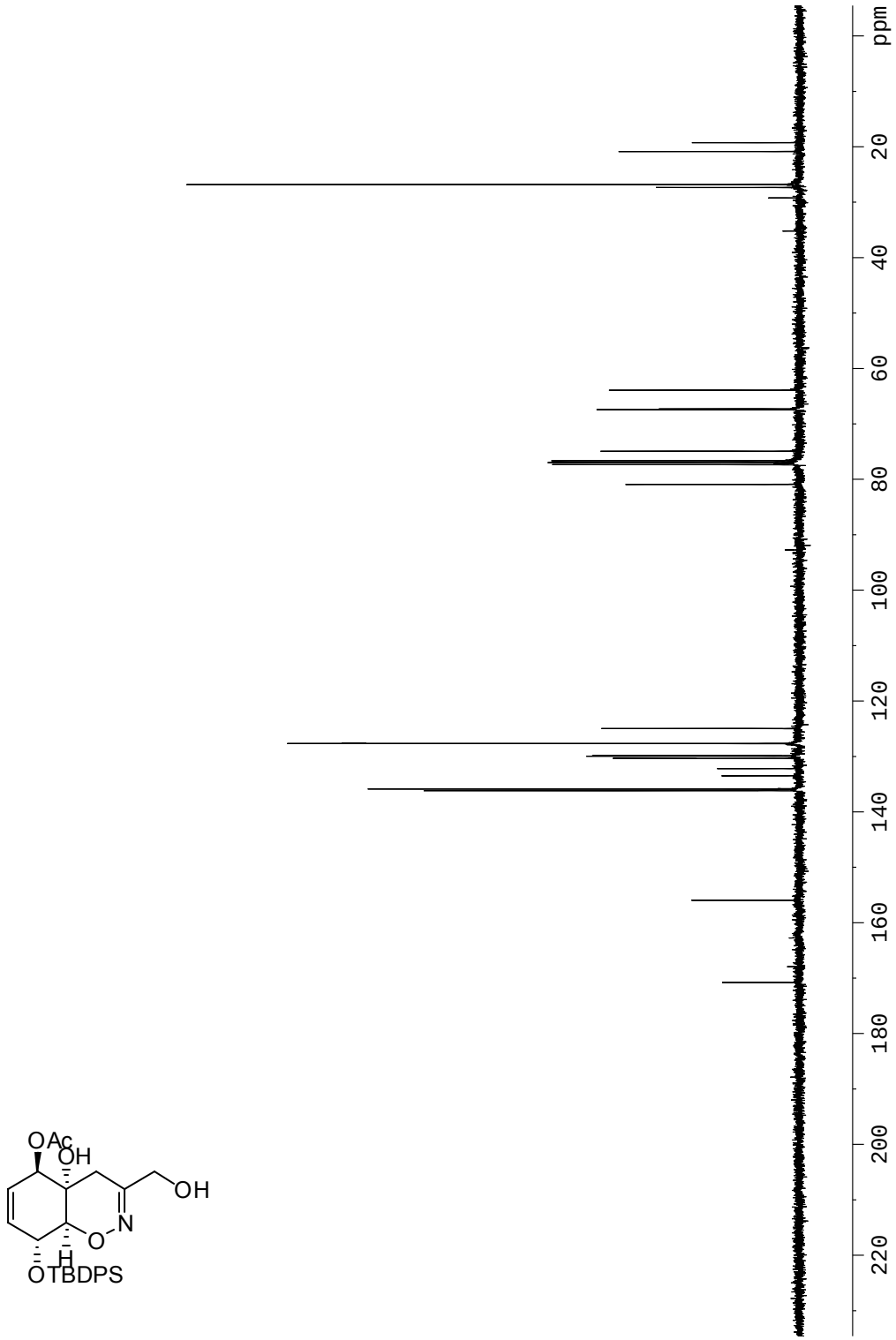


Figure 14. ^{13}C NMR of Compound D.

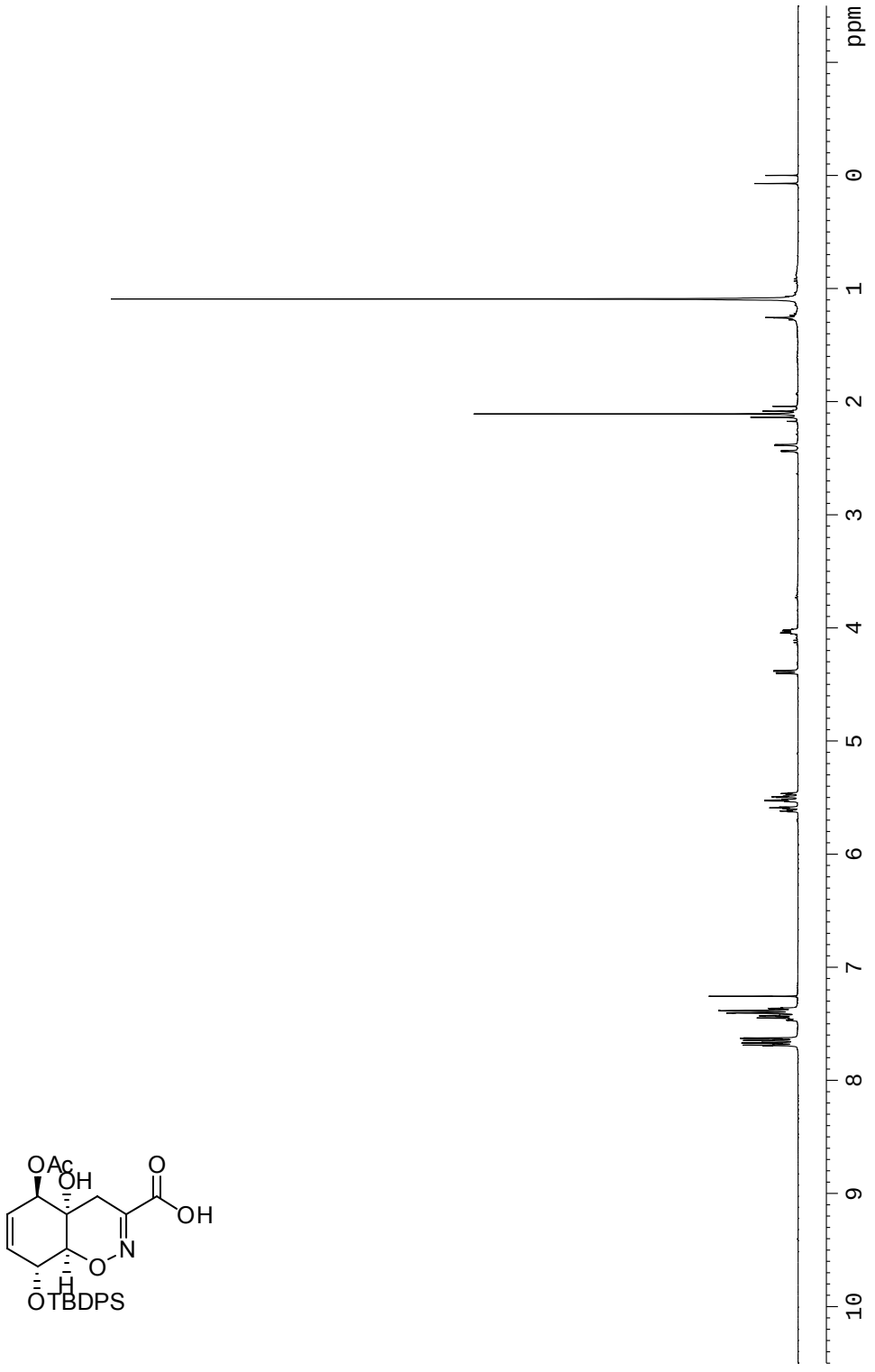


Figure 15. ^{1}H NMR of Compound 12a.

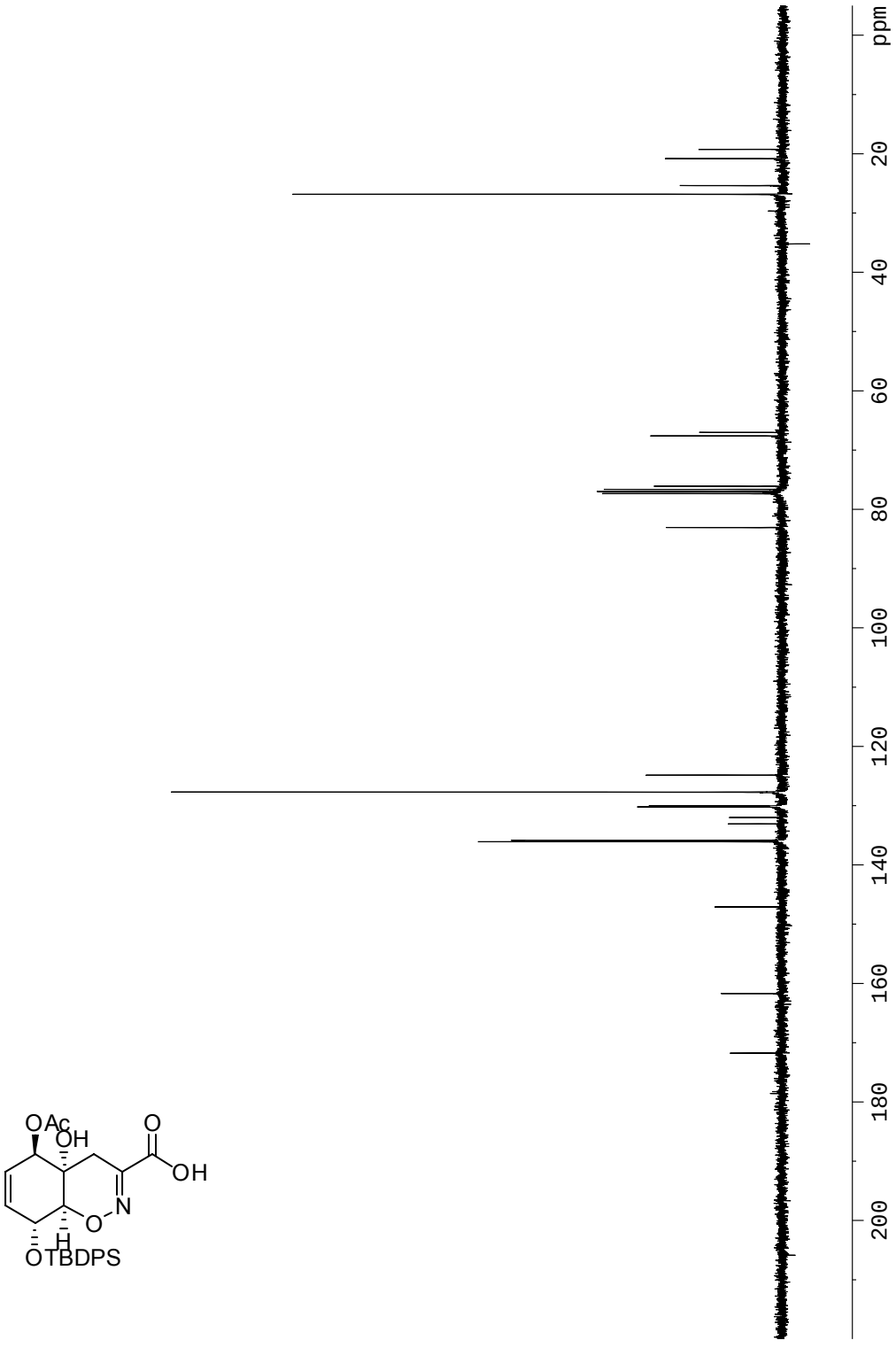


Figure 16. ^{13}C NMR of Compound 12a.

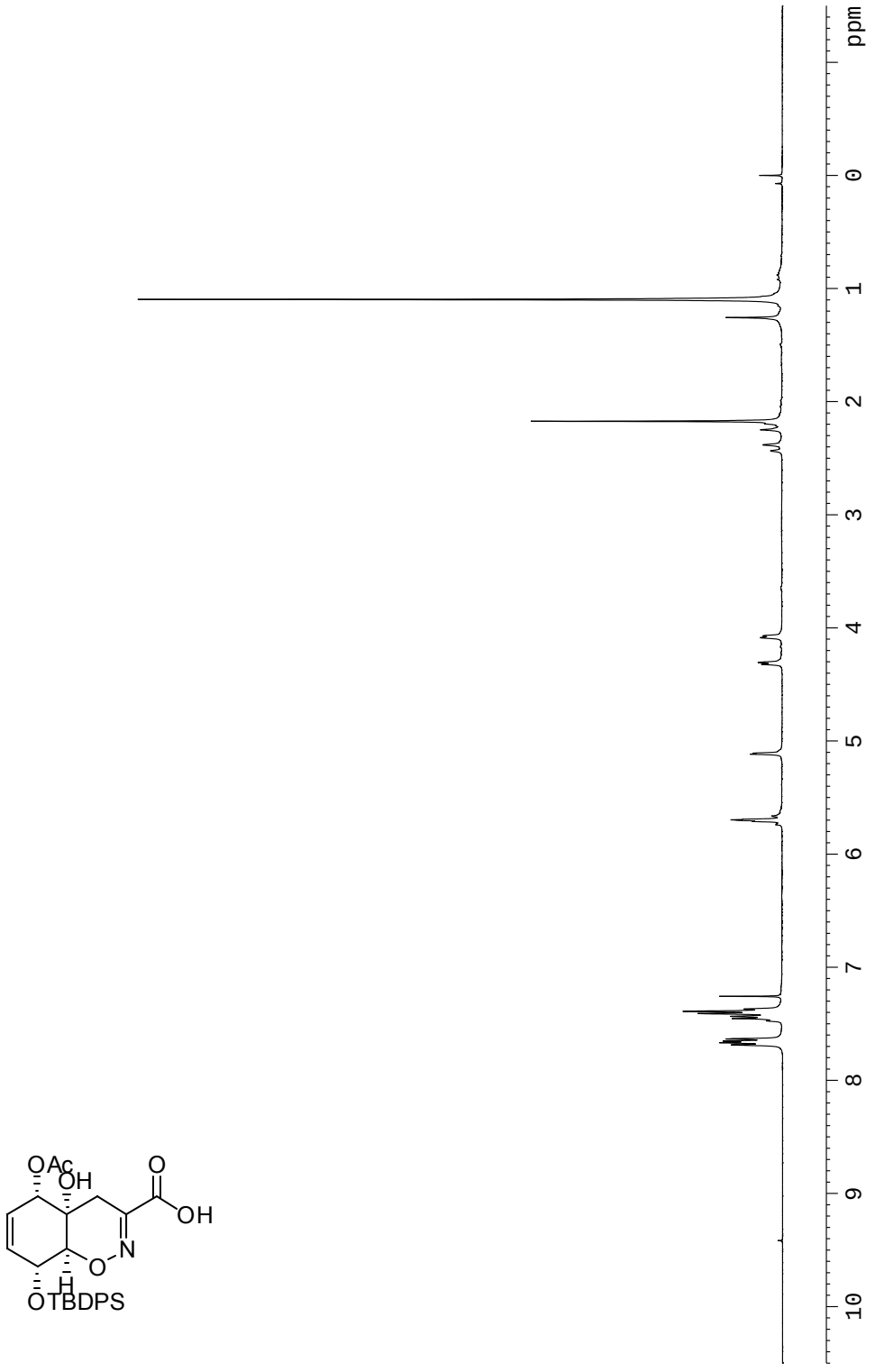


Figure 17. ^{1}H NMR of Compound 12b.

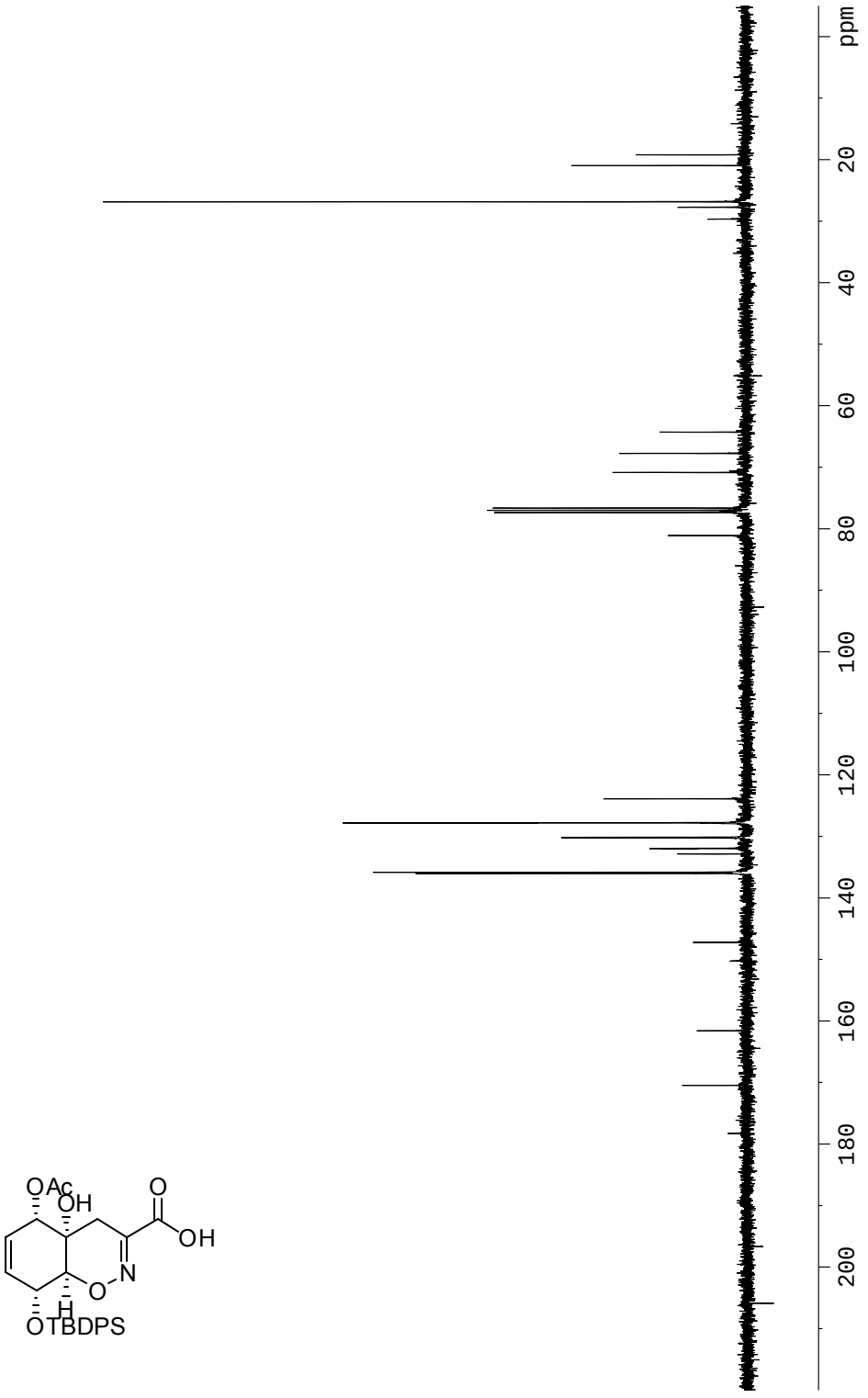


Figure 18. ^{13}C NMR of Compound 12b.

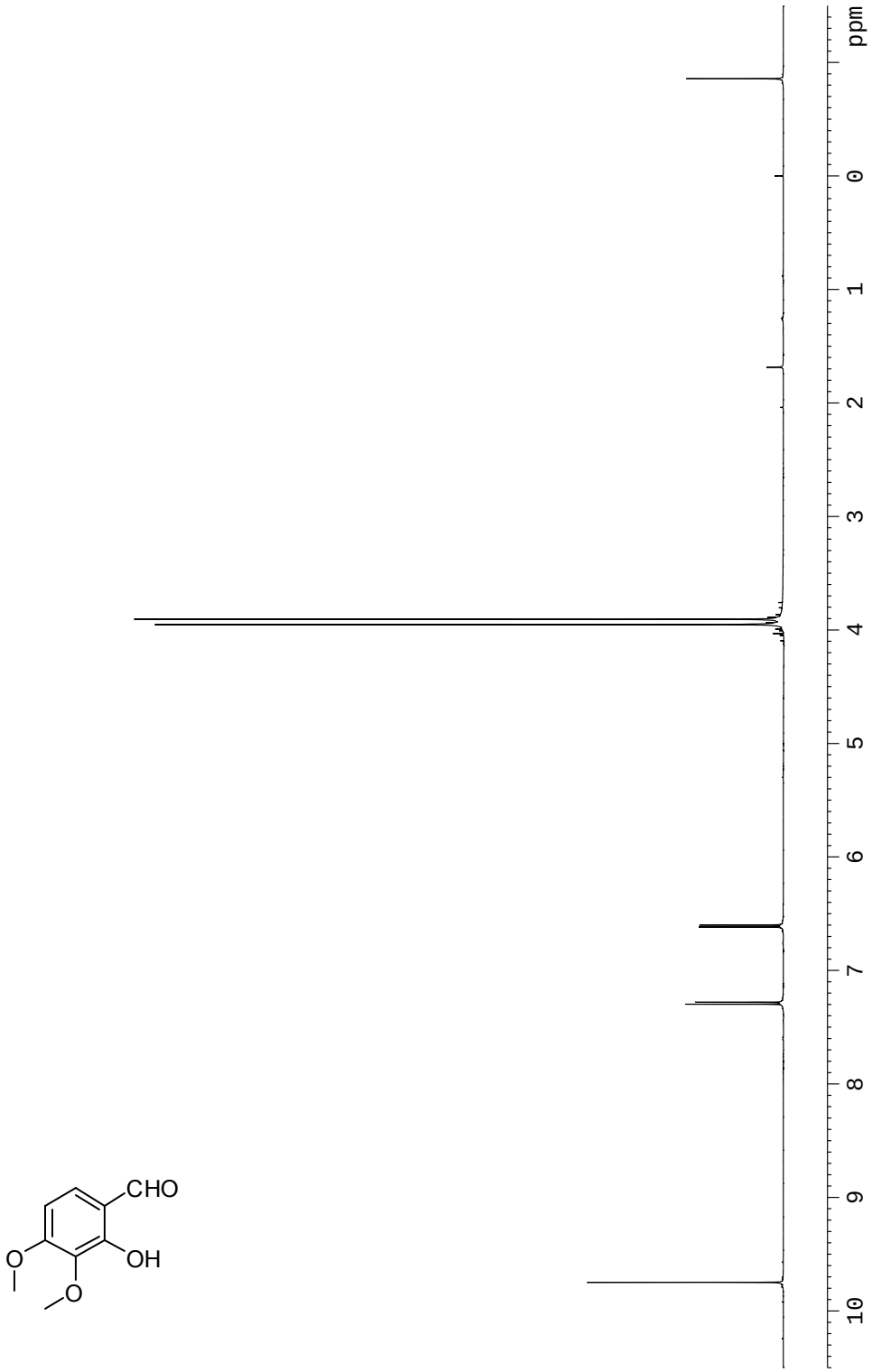


Figure 19. ^{1}H NMR of Compound 13.

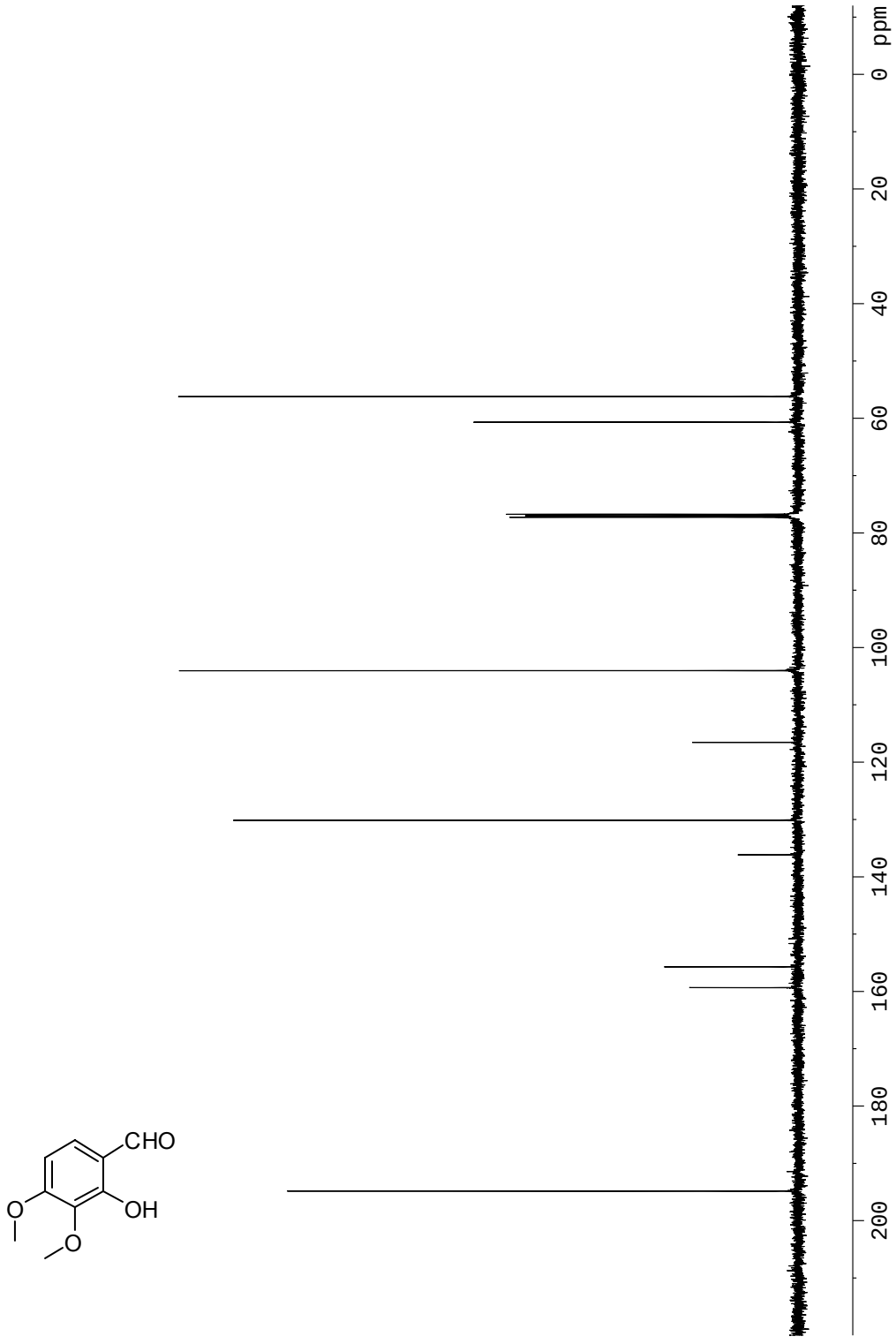


Figure 20. ^{13}**C NMR of Compound 13.**

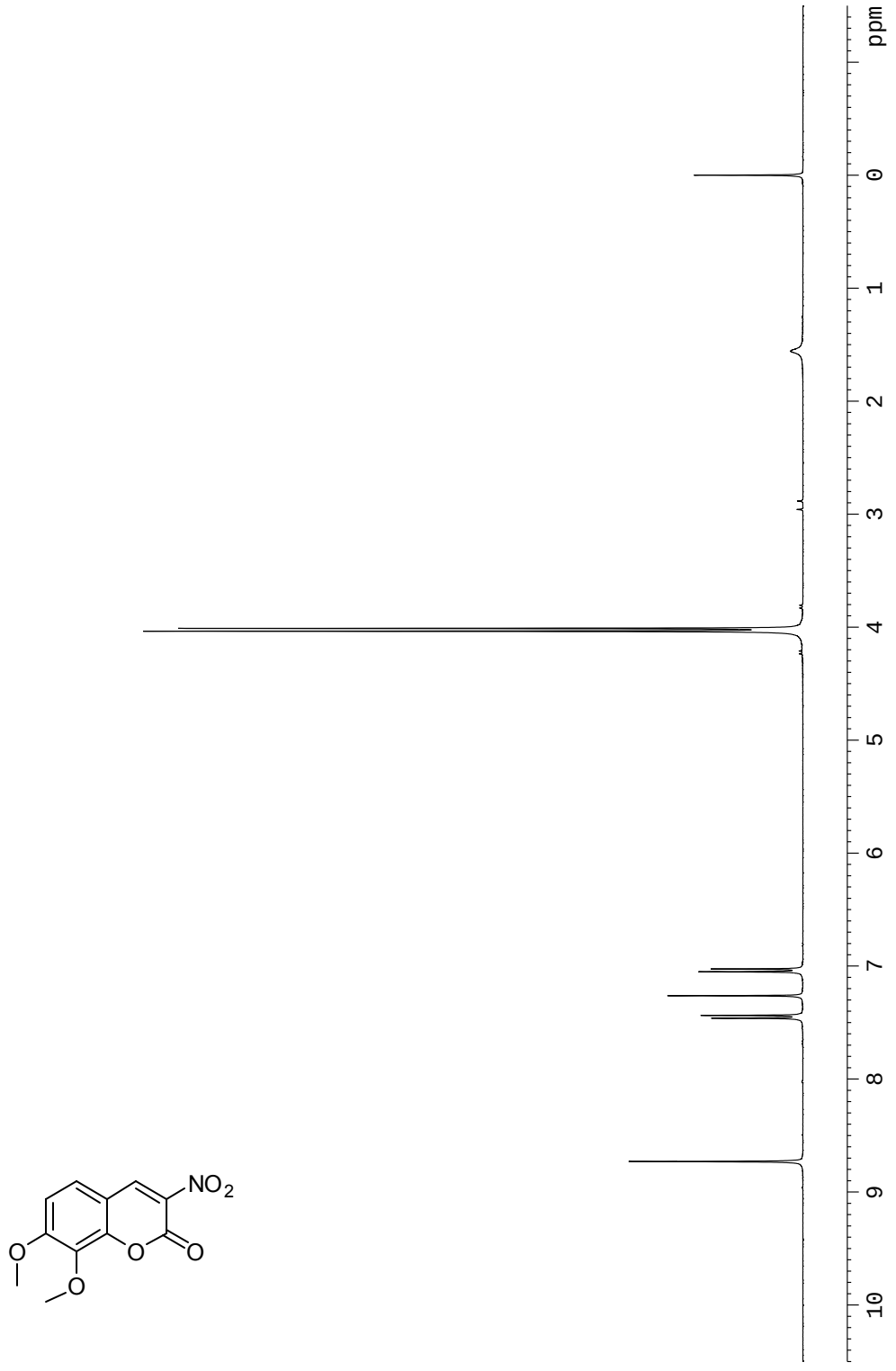


Figure 21. ^{1}H NMR of Compound 14.

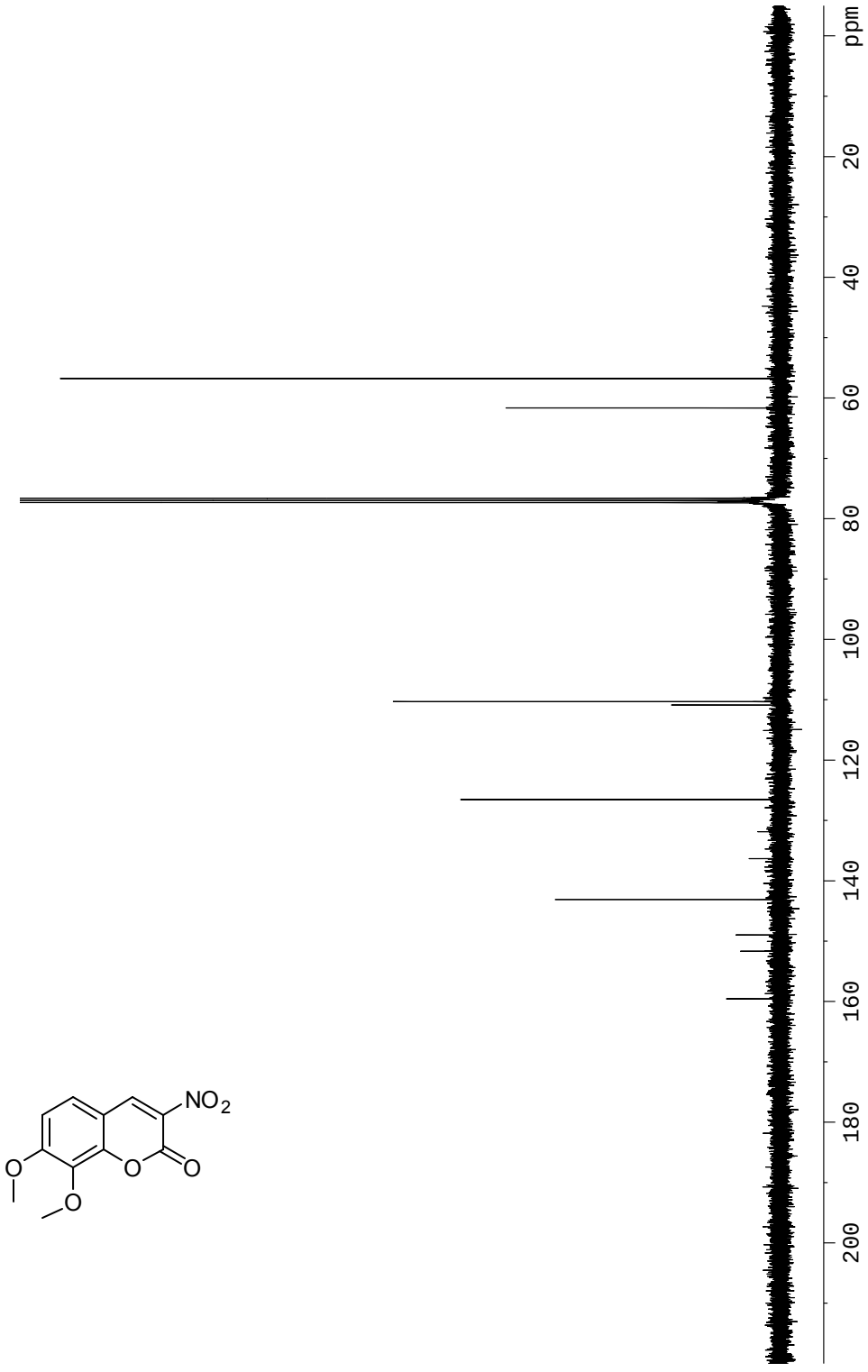


Figure 22. ^{13}**C NMR of Compound 14.**

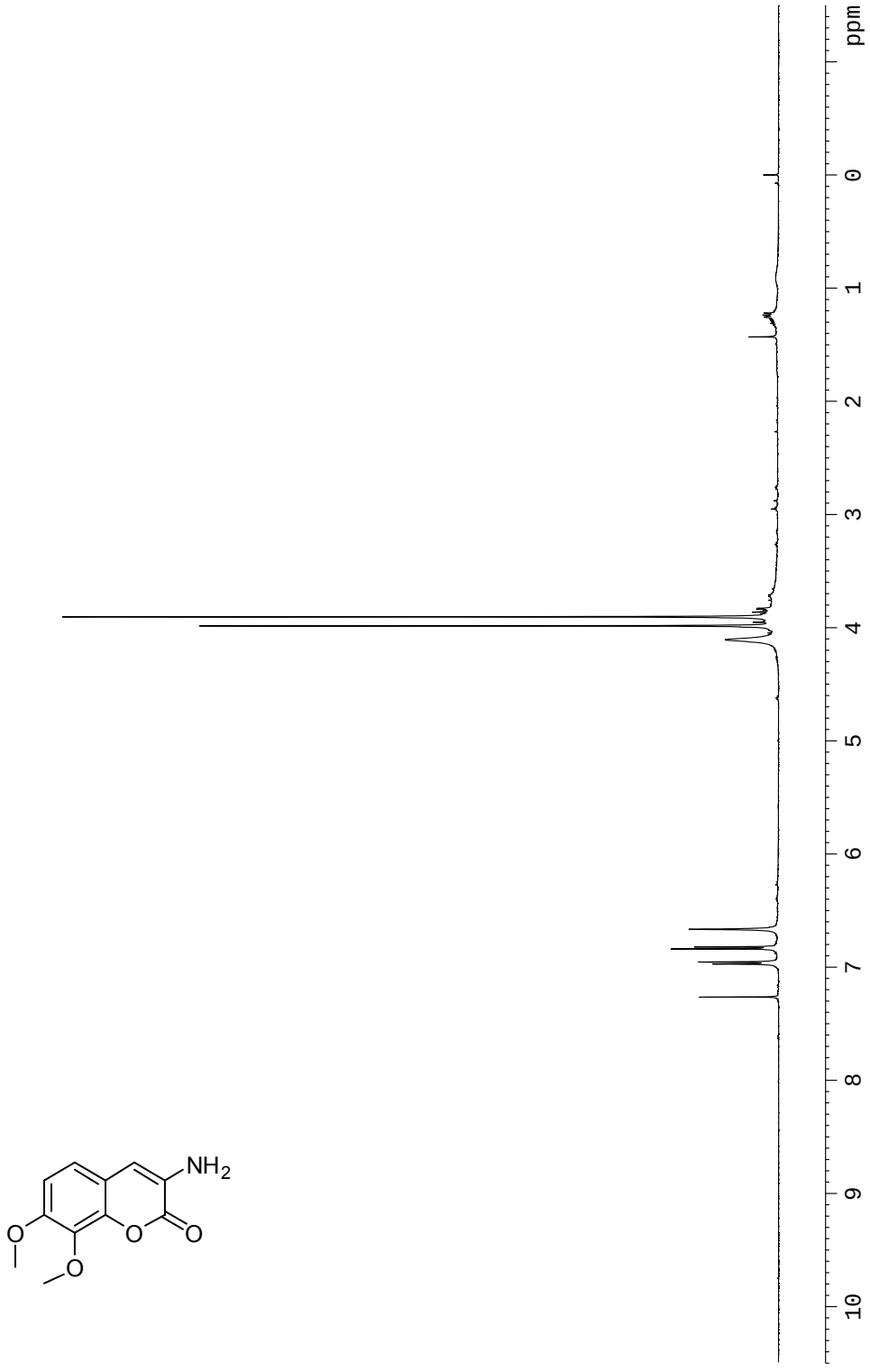


Figure 23. ^{1}H NMR of Compound 4.

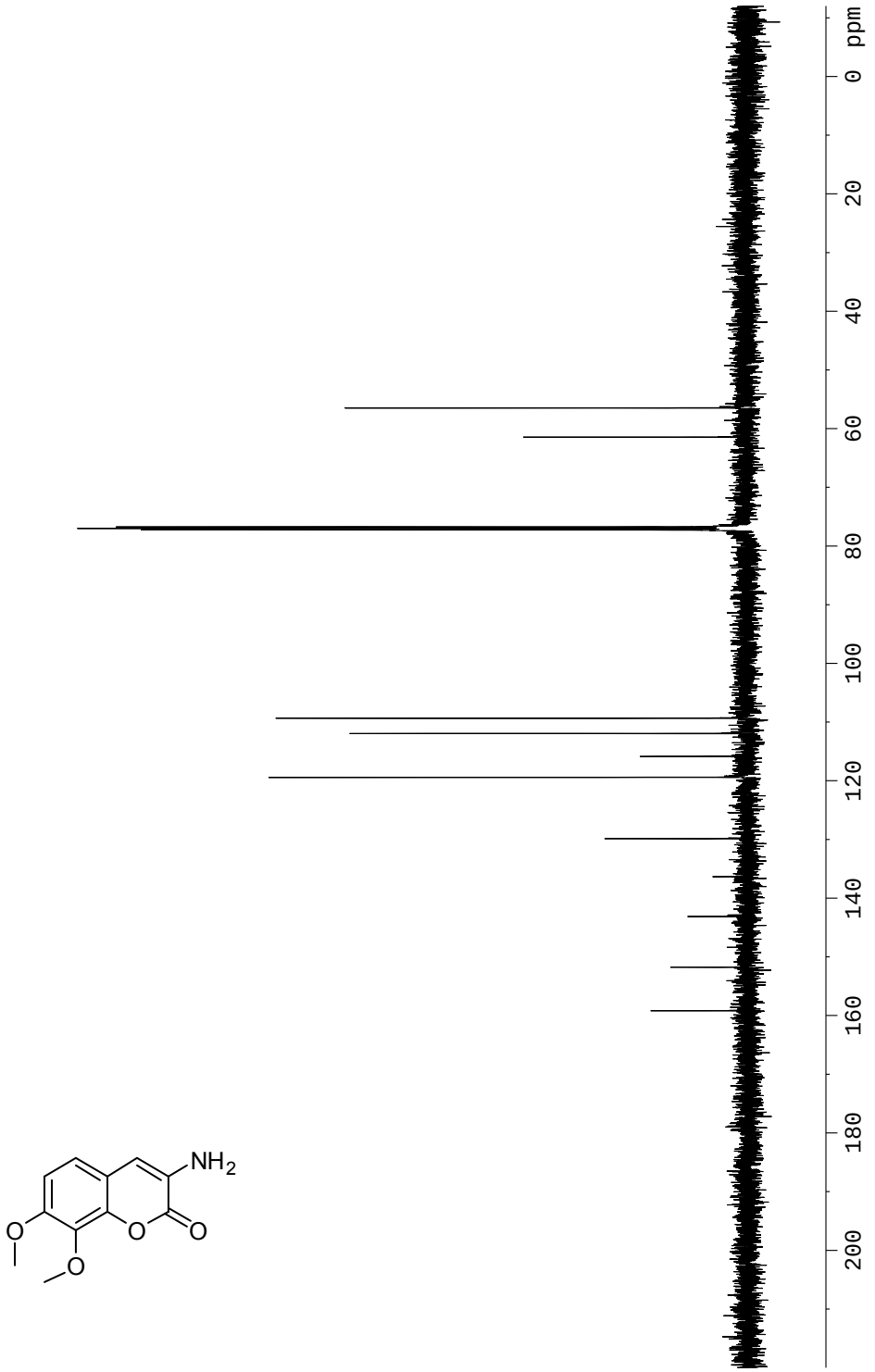


Figure 24. ^{13}C NMR of Compound 4.

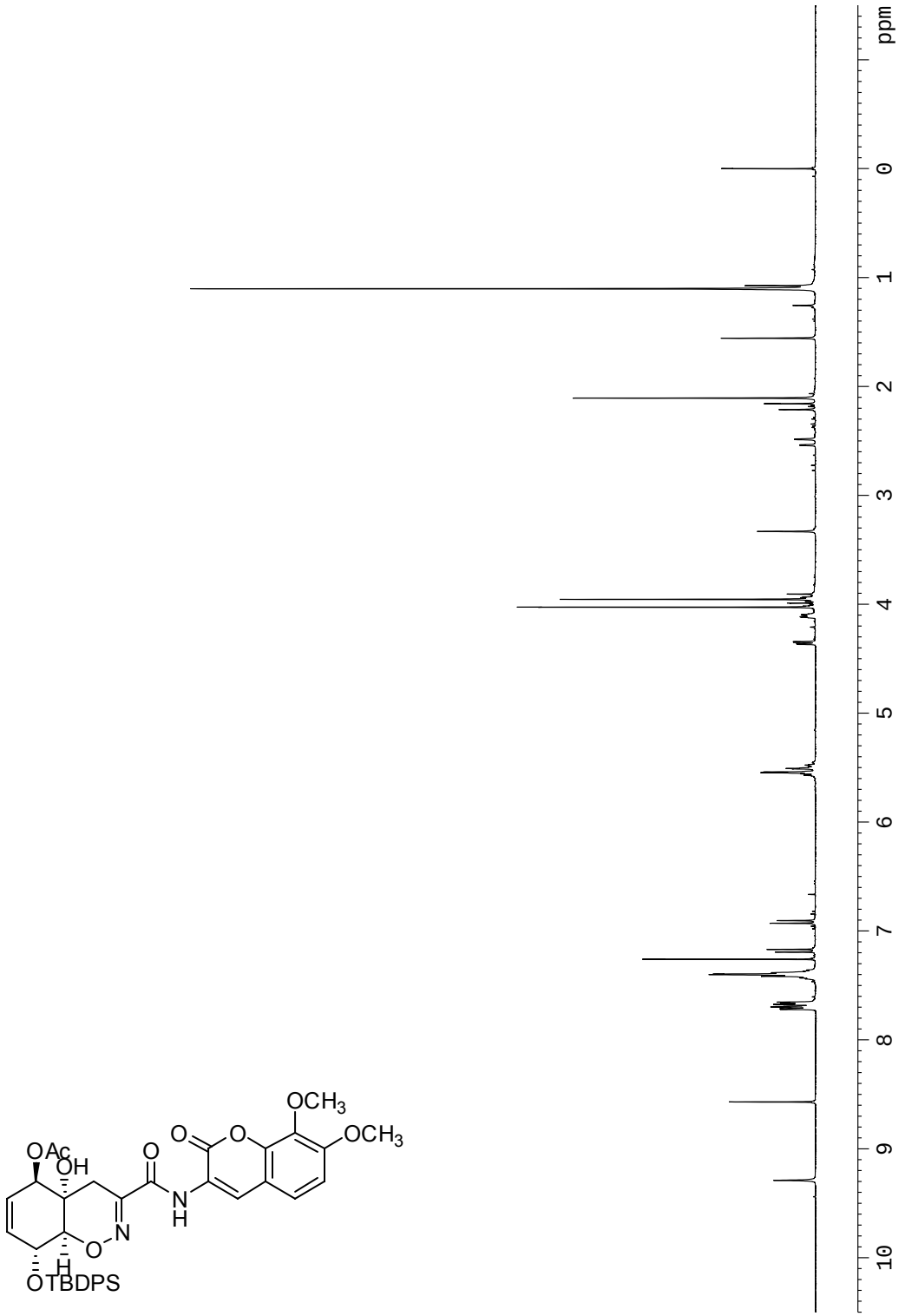


Figure 25. ^{1}H NMR of Compound 15a.

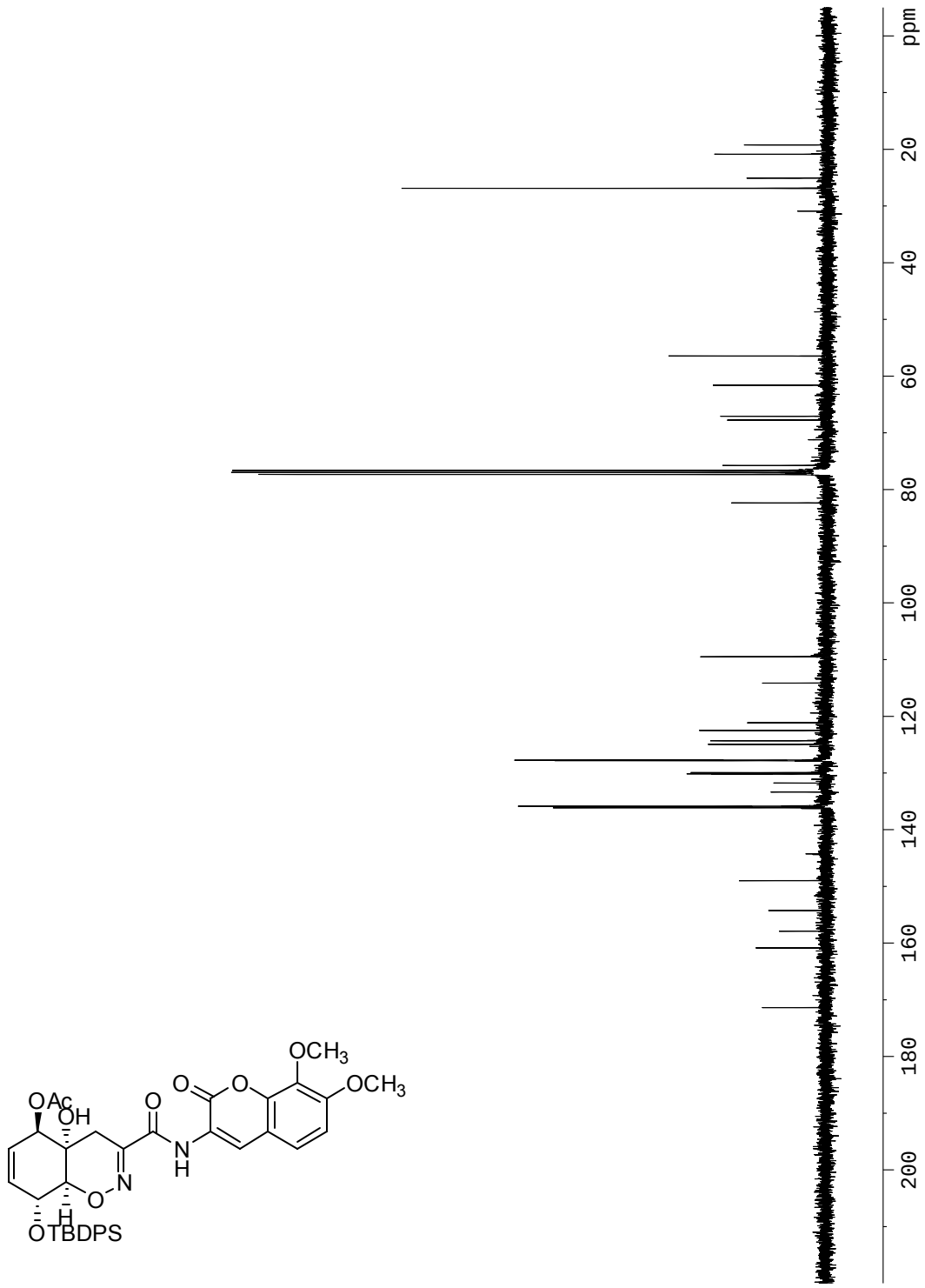


Figure 6. ^{13}C NMR of Compound 15a.

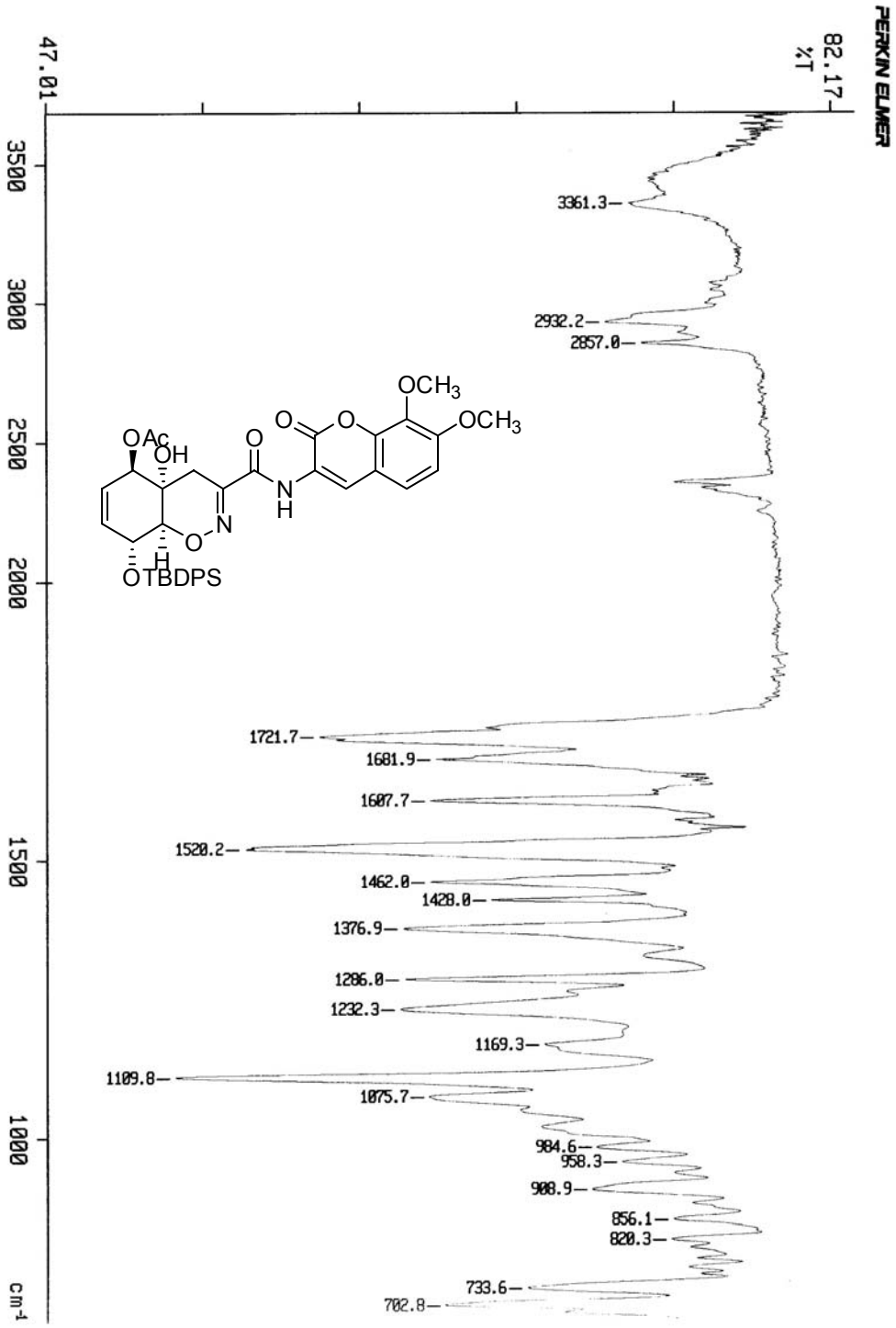


Figure 27. IR Spectrum of Compound 15a.

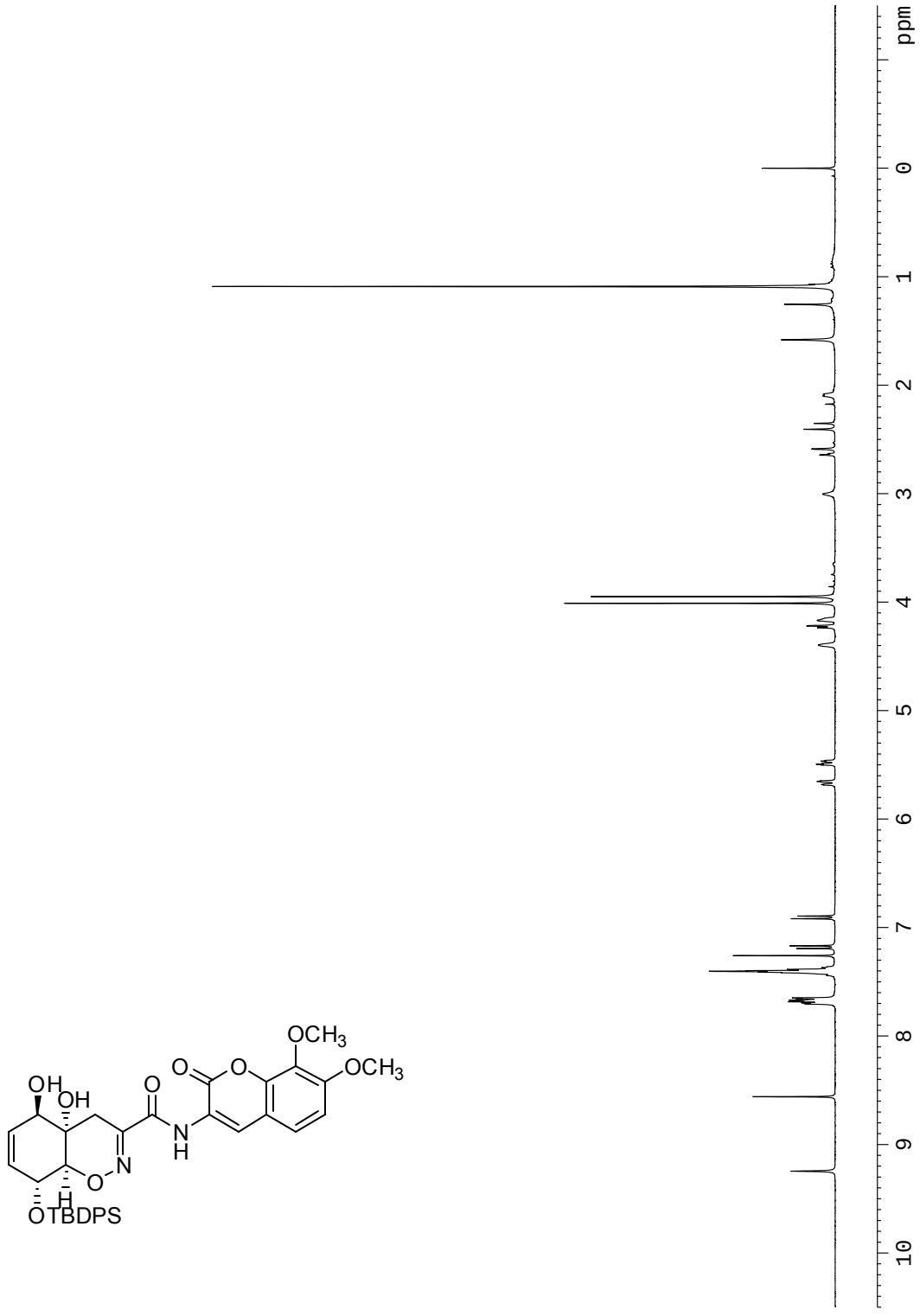


Figure 28. ^{1}H NMR of Compound E.

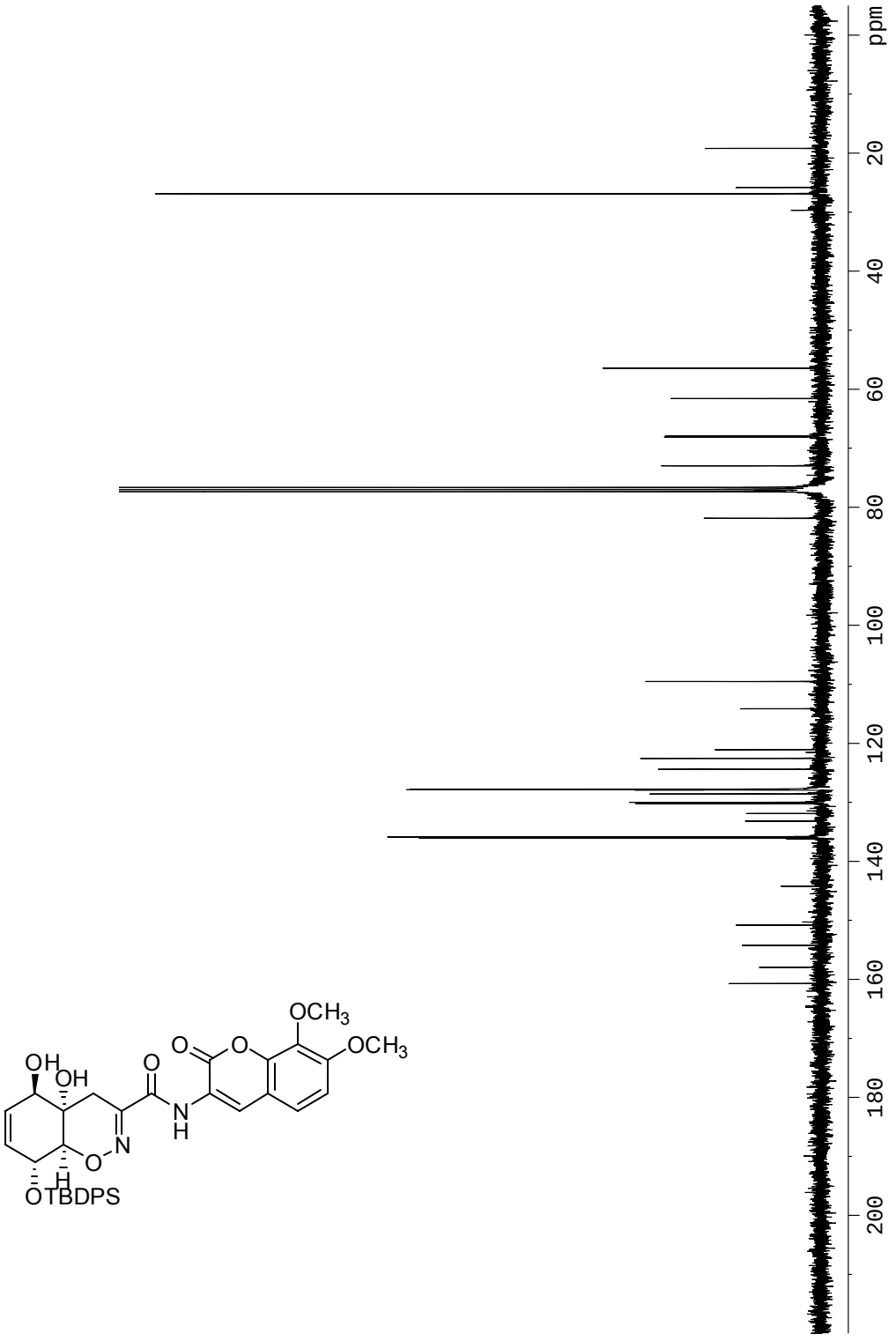


Figure 29. ^{13}C NMR of Compound E.

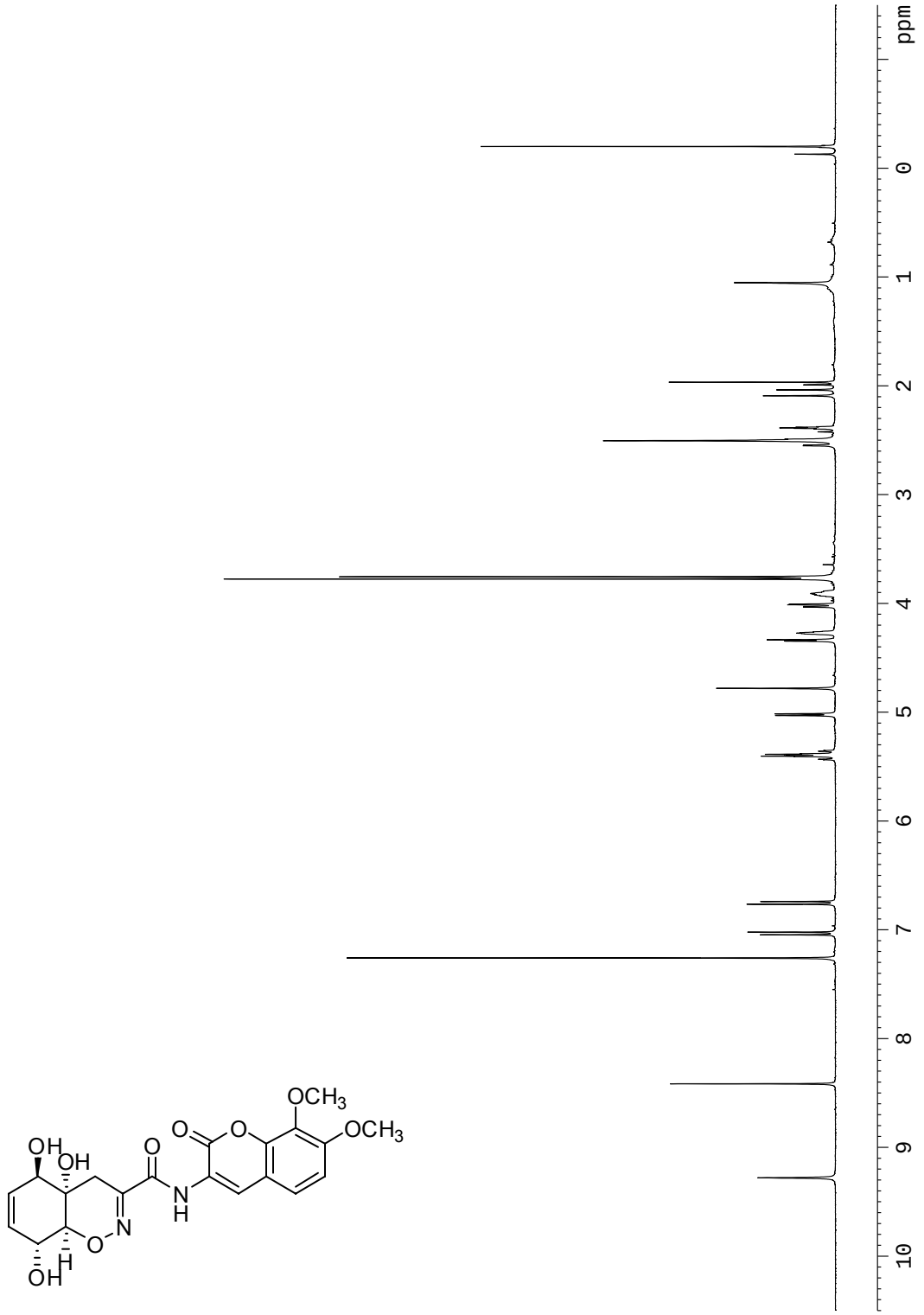


Figure 30. ^{1}H NMR of Trichodermamide A.

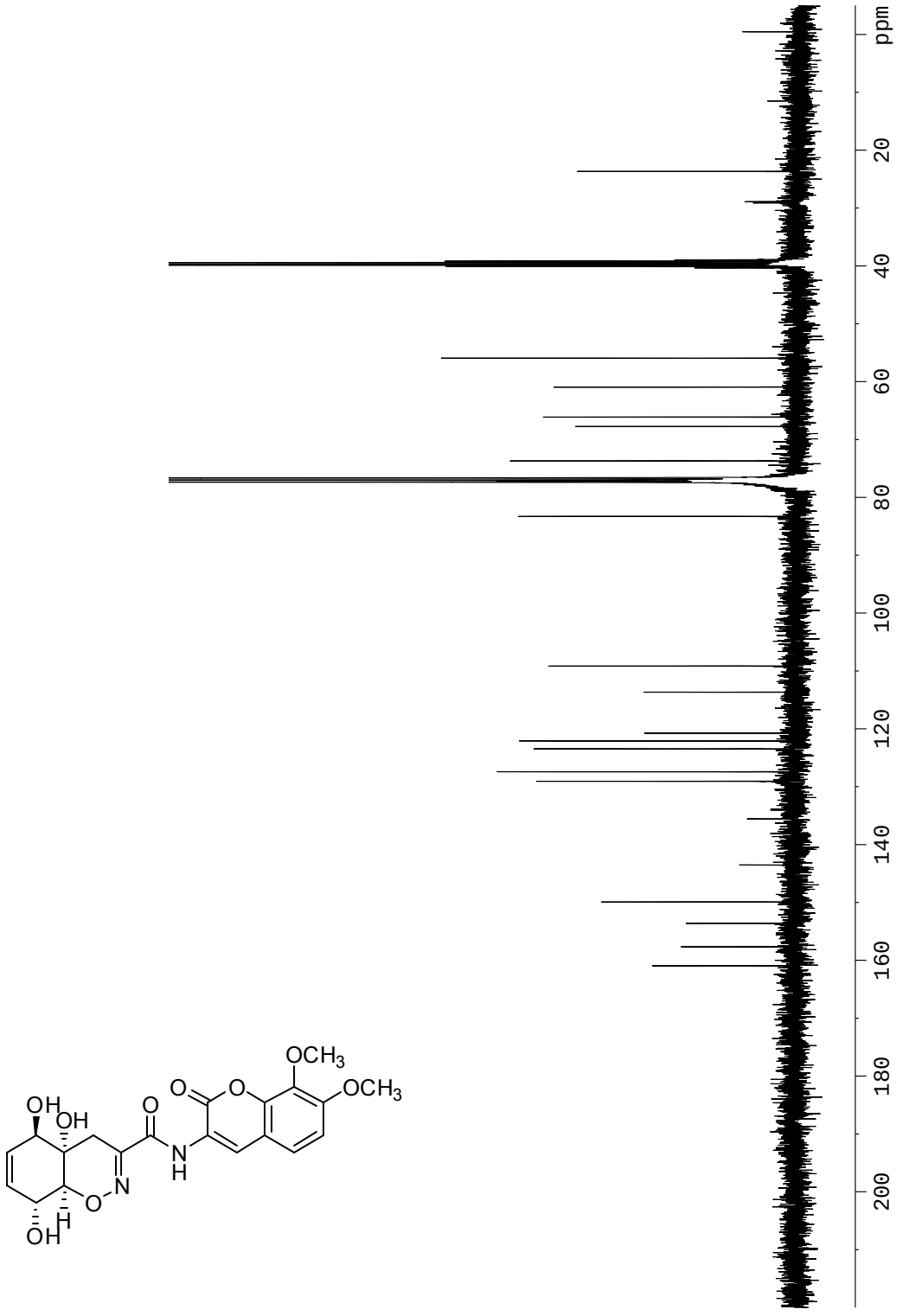


Figure 31. ^{13}C NMR of Trichodermamide A.

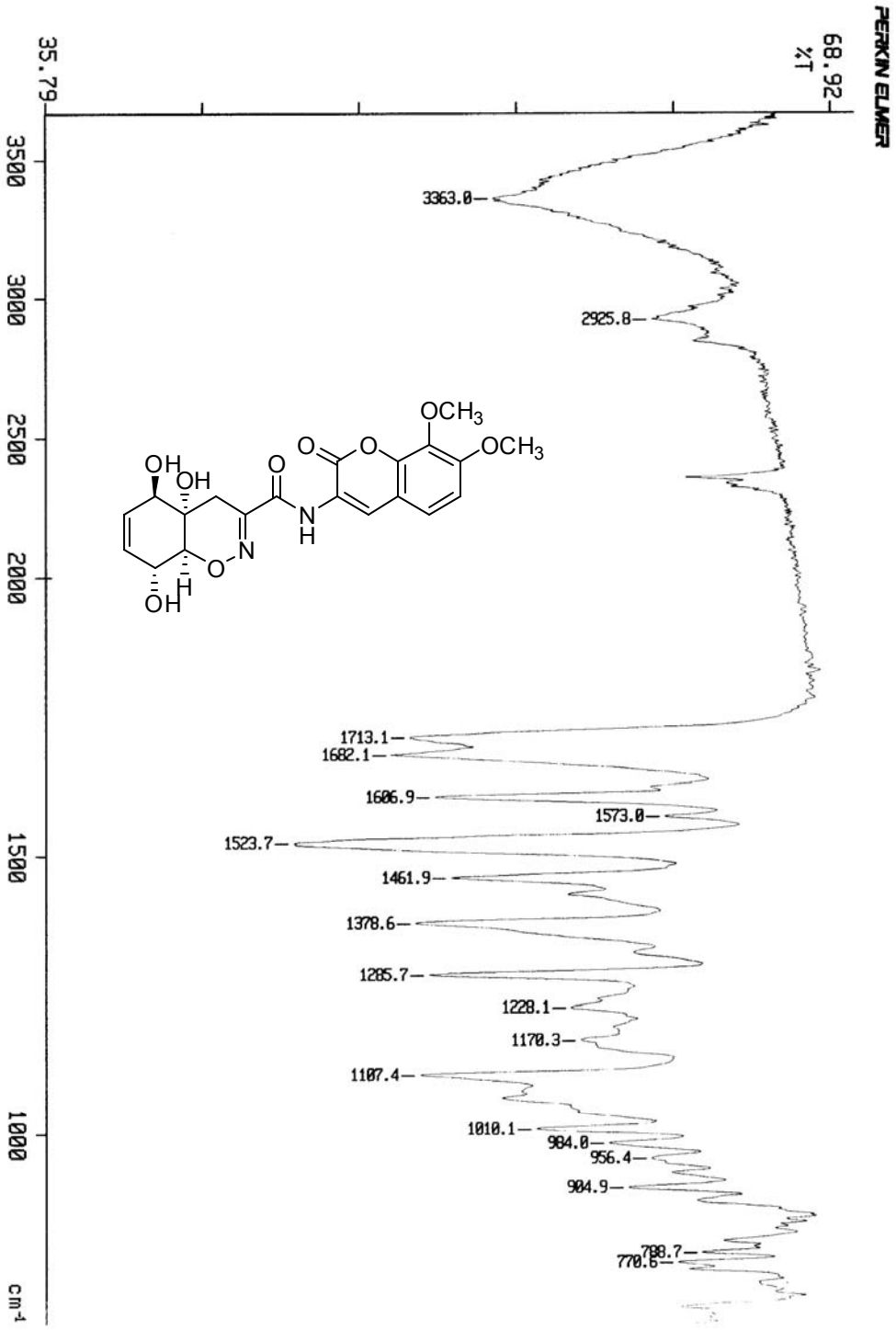


Figure 32. IR Spectrum of Trichodermamide A.

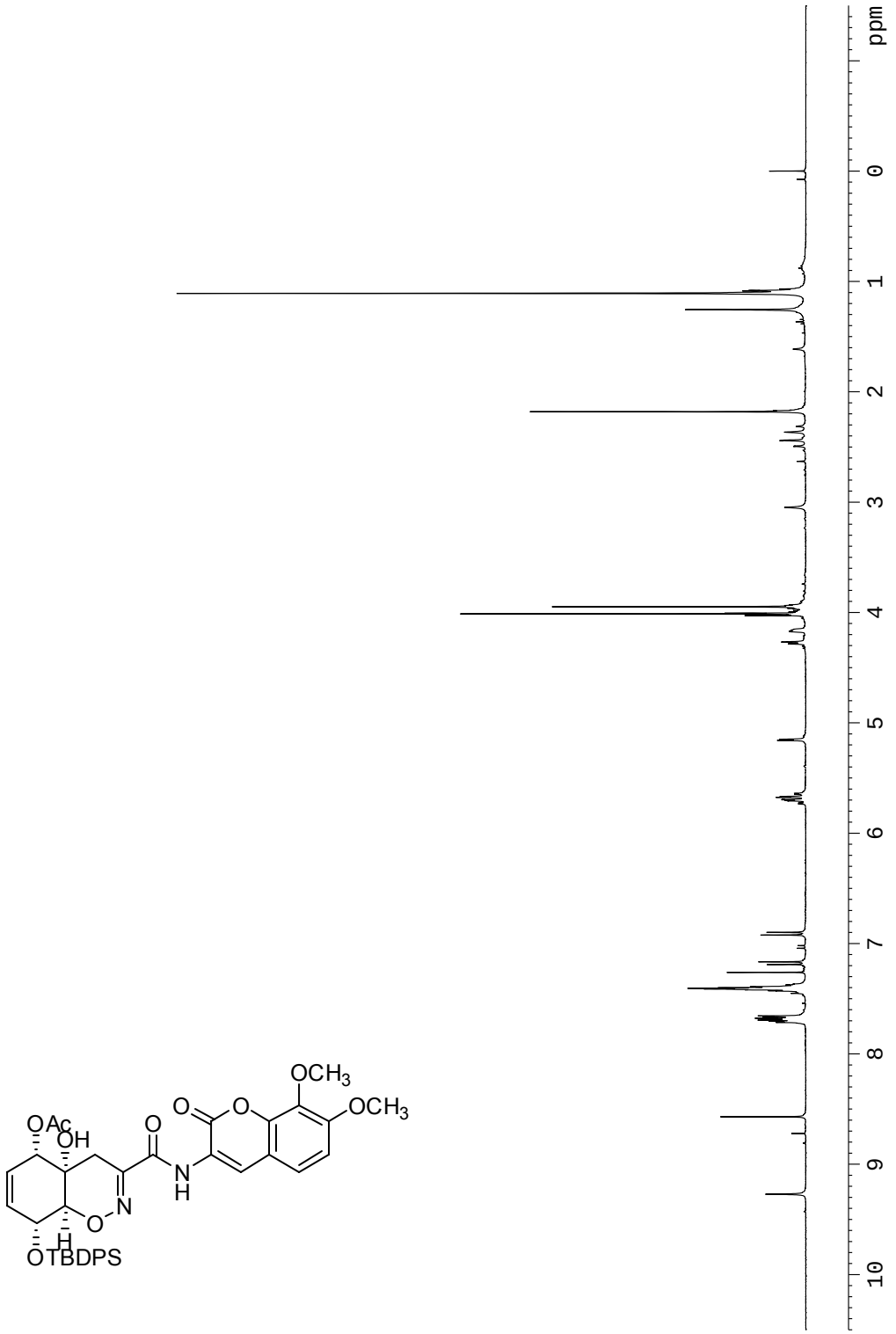


Figure 33. ^{1}H NMR of Compound 15b.

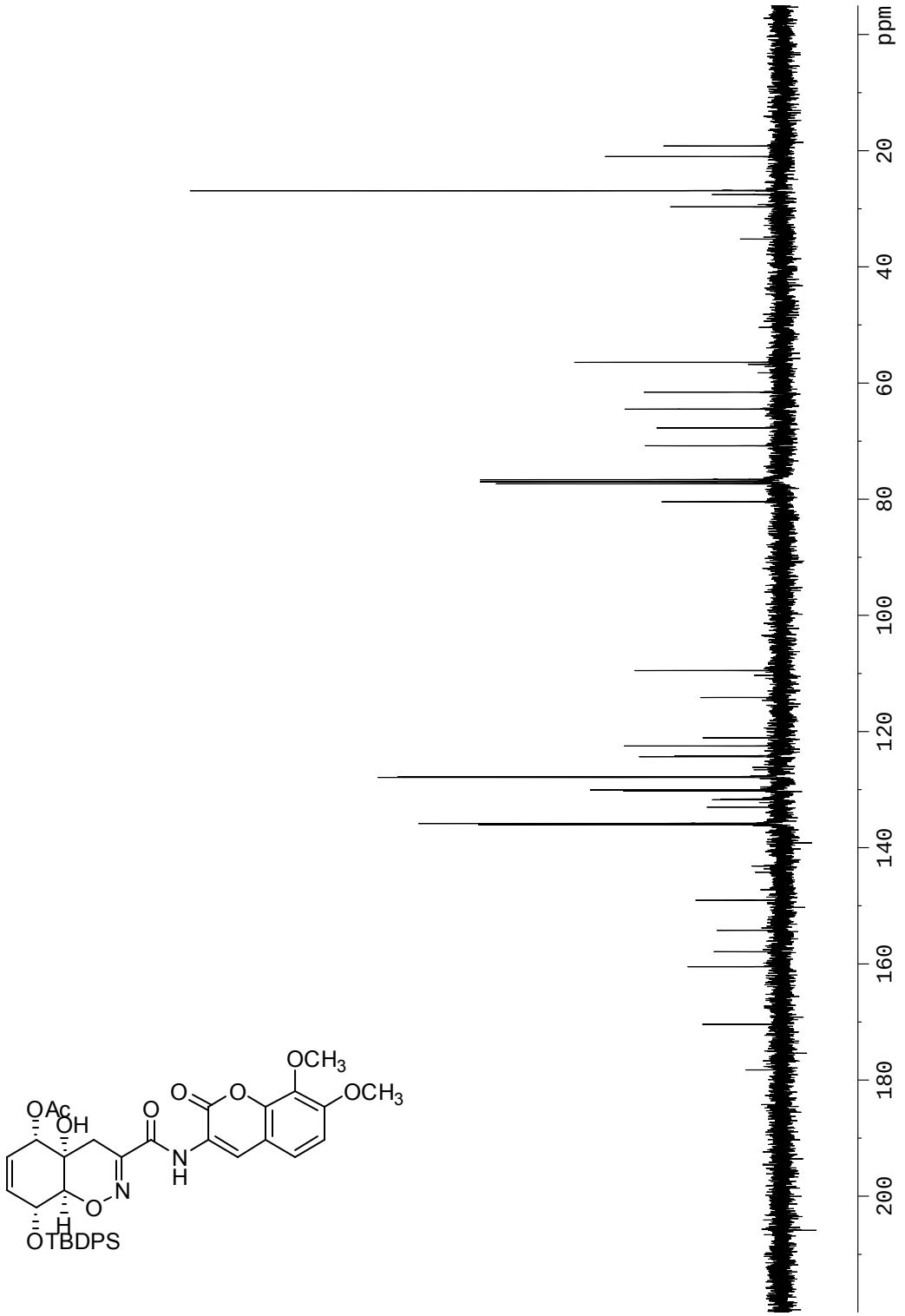


Figure 34. ^{13}C NMR of Compound 15b.

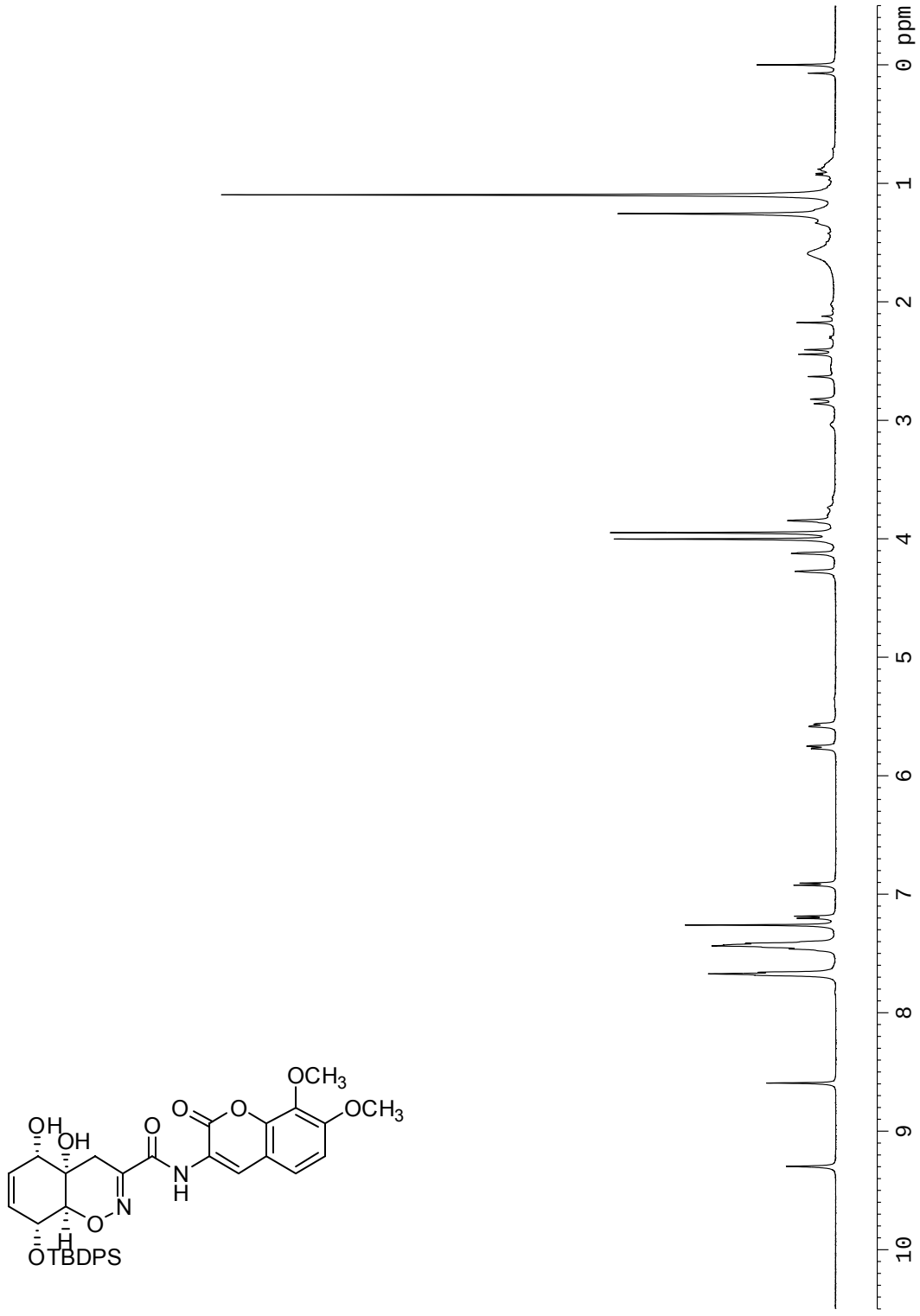


Figure 35. ^{1}H NMR of Compound F.

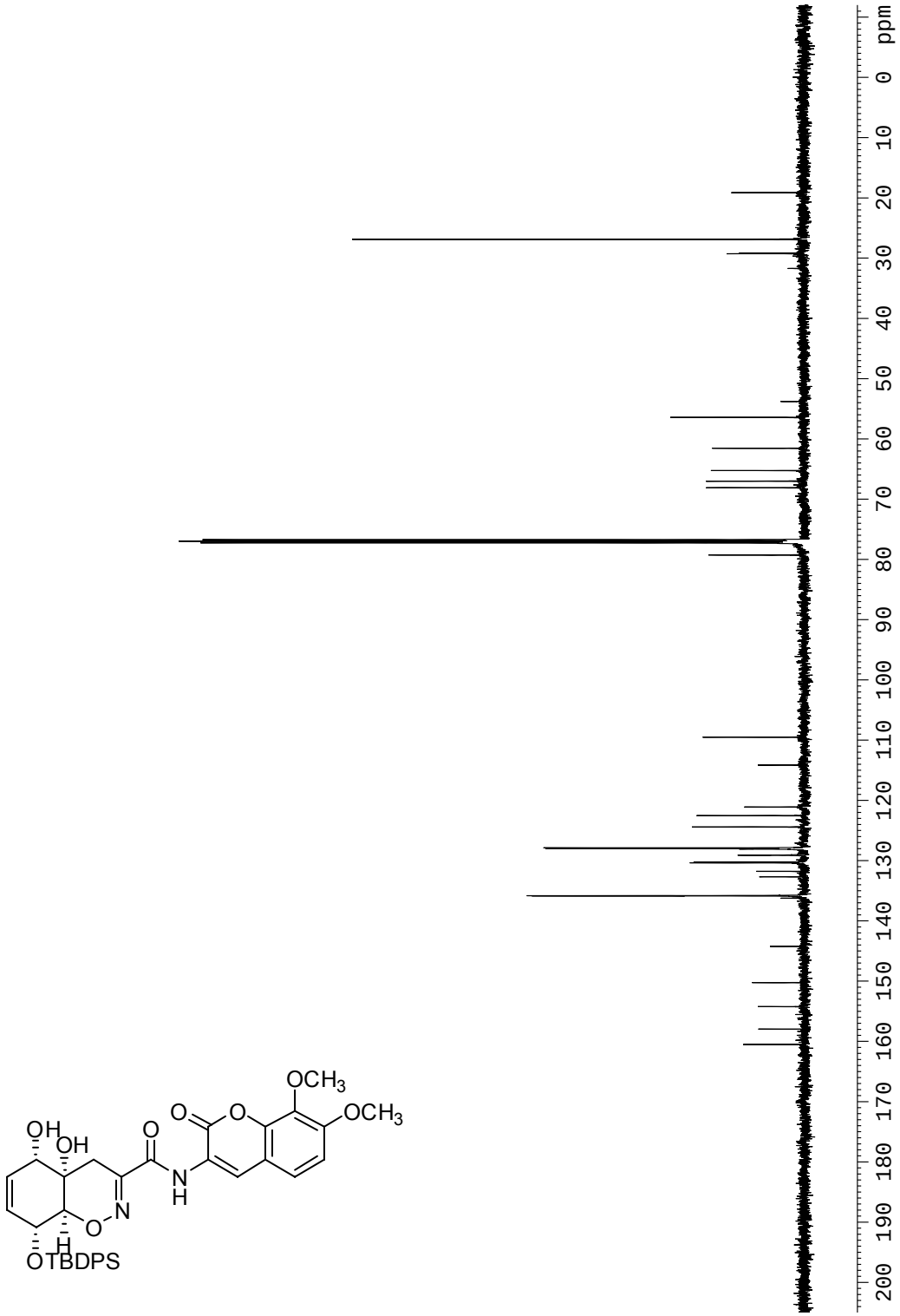


Figure 36. ^{13}**C NMR of Compound F.**

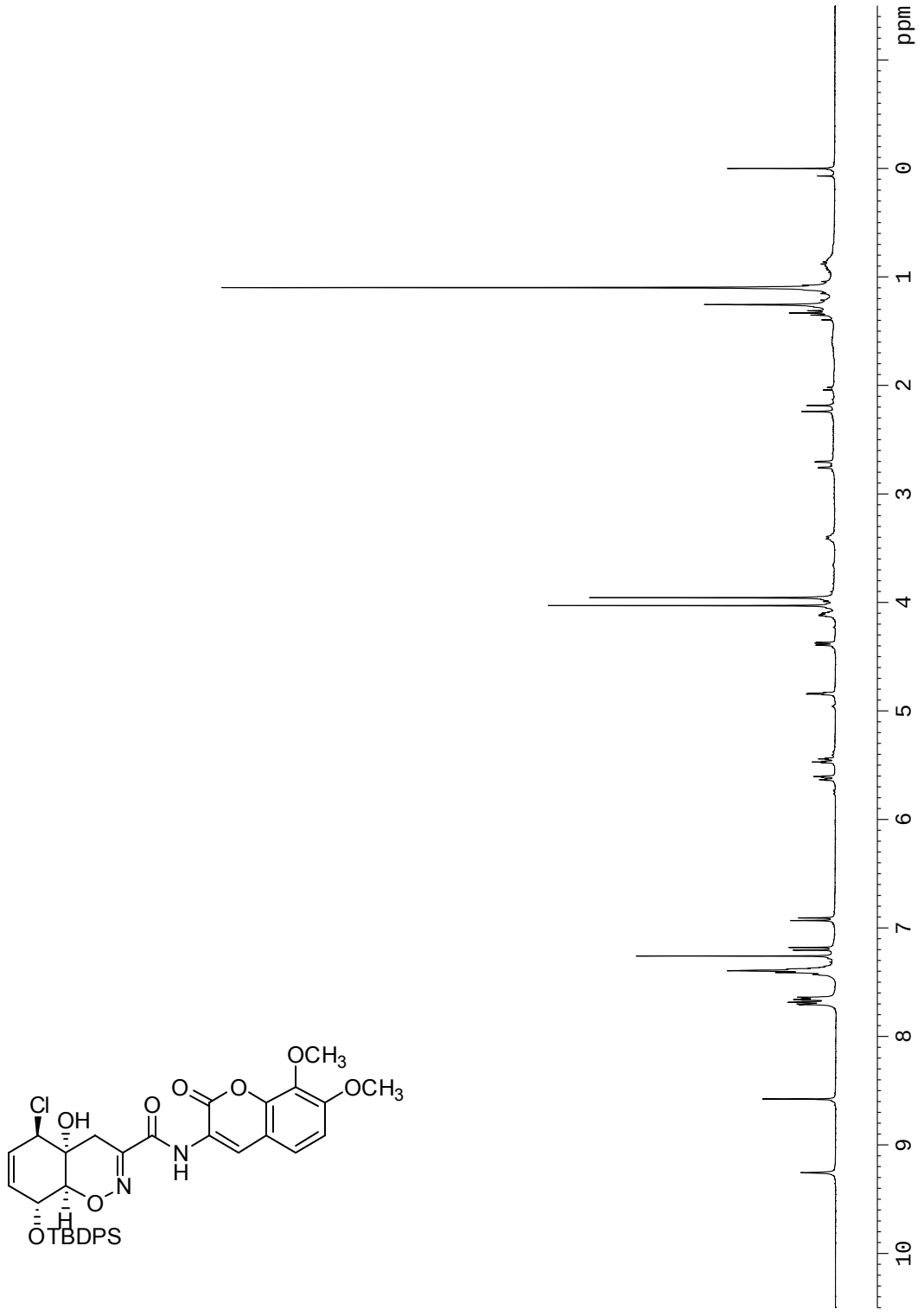


Figure 37. ^{1}H NMR of Compound G.

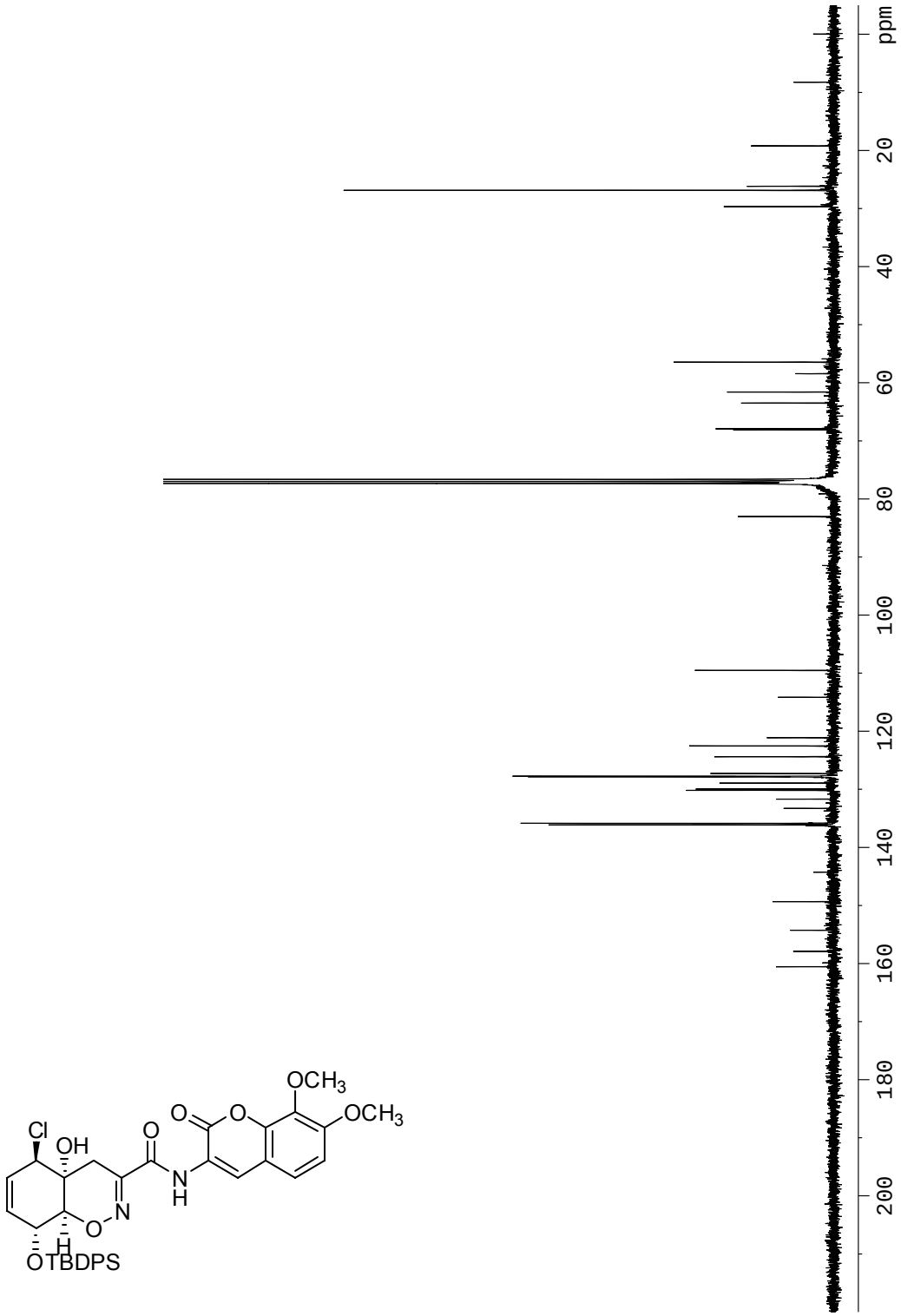


Figure 38. ^{13}C NMR of Compound G.

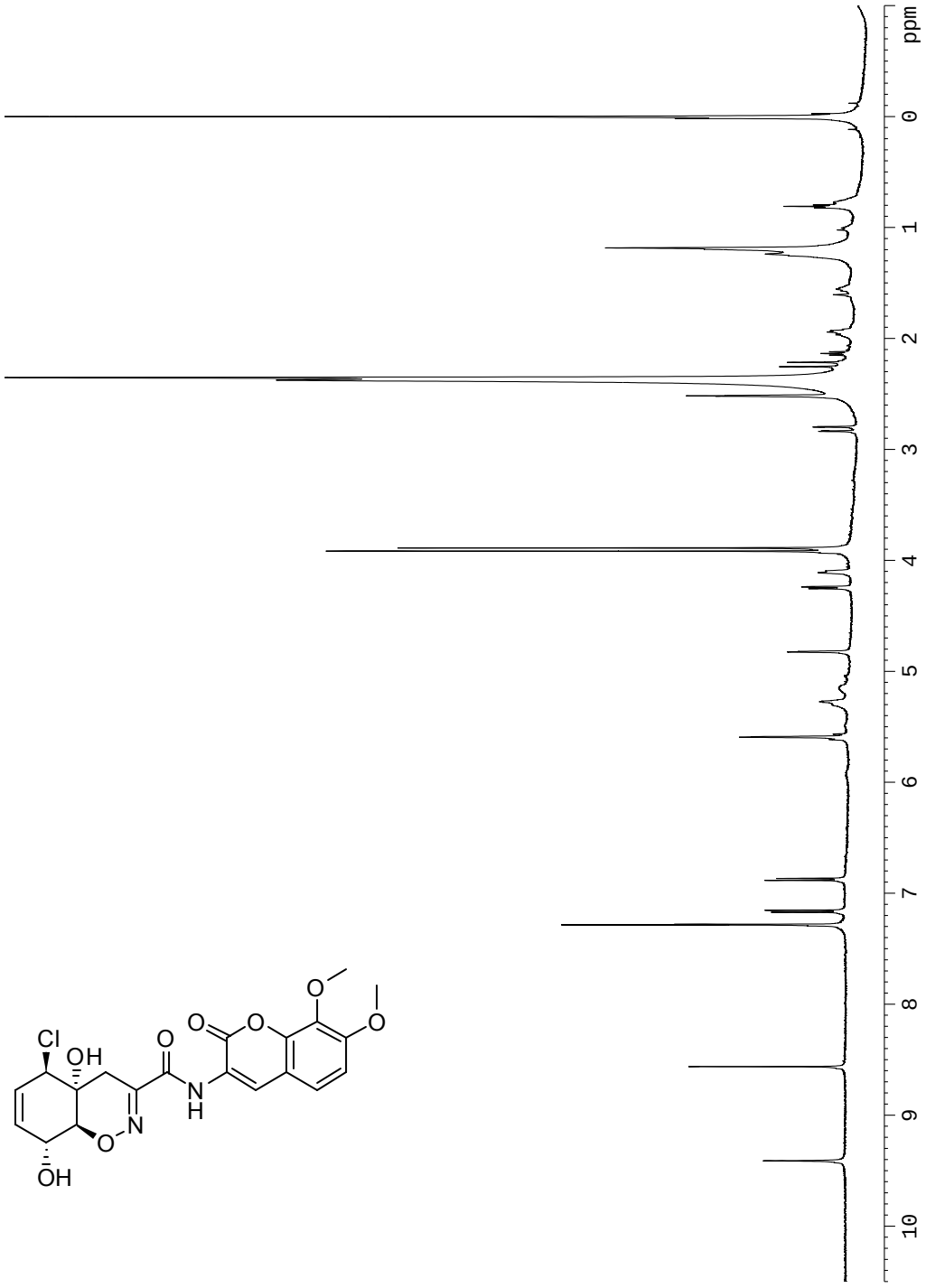


Figure 39. ^{1}H-NMR of trichodermamide B

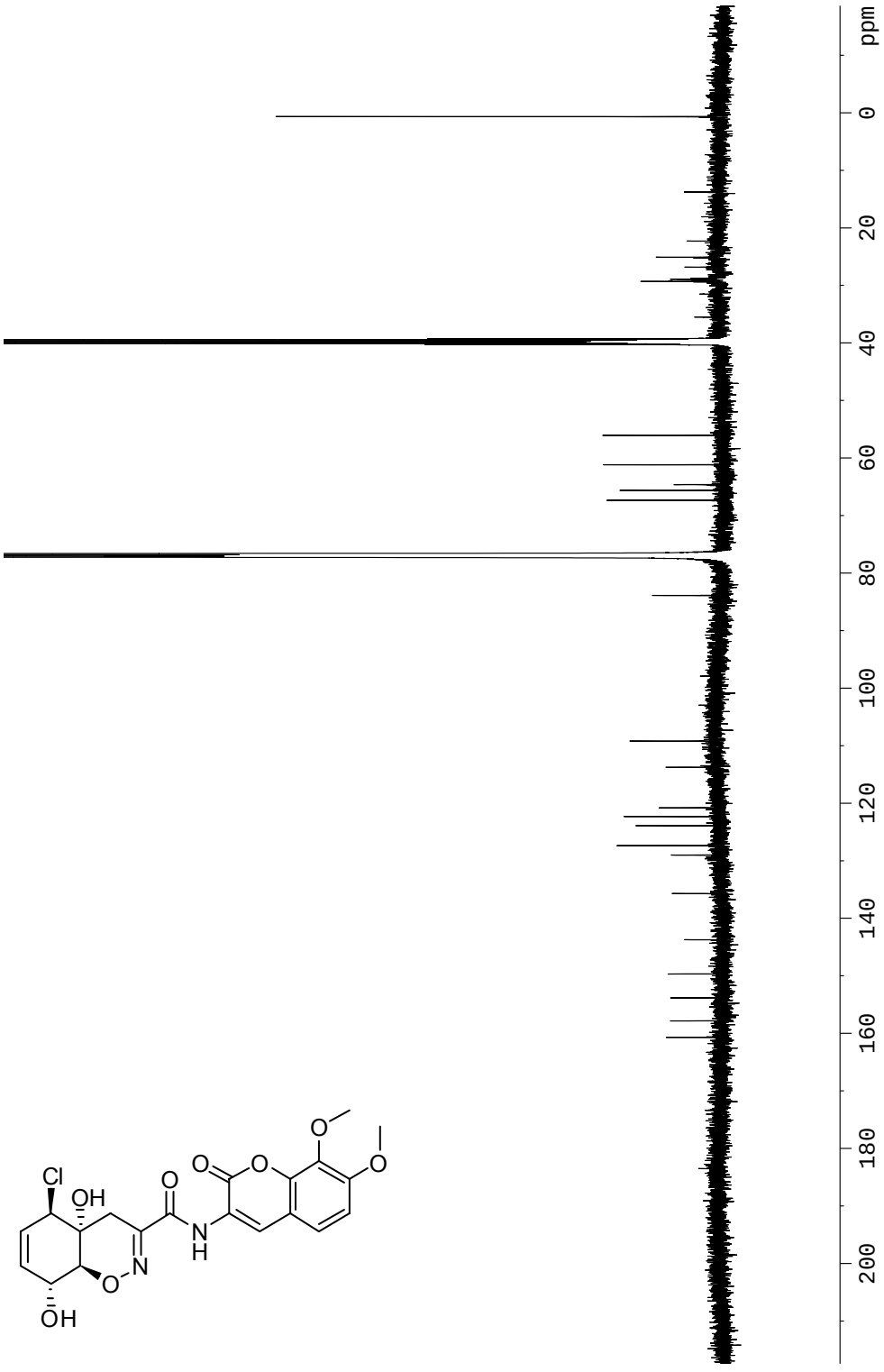
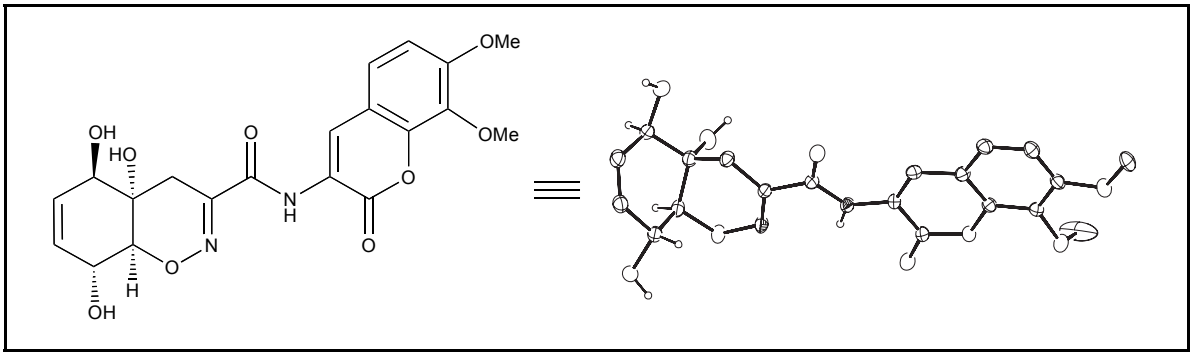


Figure 40. ^{13}C-NMR of trichodermamide B

X-ray Structure Determination of Trichodermamide A



Trichodermamide A, $C_{20}H_{20}N_2O_9$, crystallizes in the orthorhombic space group I222 (systematic absences hkl: h+k+l=odd) with a=10.9542(12)Å, b=13.687(2)Å, c=32.040(4)Å, V=4803.6(10)Å^3, Z=8 and d_{calc}=1.196 g/cm^3. X-ray intensity data were collected on a Rigaku Mercury CCD area detector employing graphite-monochromated Mo-K_α radiation (λ=0.71073 Å) at a temperature of 143K. Preliminary indexing was performed from a series of twelve 0.5° rotation images with exposures of 45 seconds. A total of 660 rotation images were collected with a crystal to detector distance of 35 mm, a 2θ swing angle of -10°, rotation widths of 0.5° and exposures of 30 seconds: scan no. 1 was a ϕ-scan from 157.5° to 367.5° at ω = 10° and χ = 20°; scan no. 2 was an ω-scan from -20° to 5° at χ = -90° and ϕ = 135°; scan no. 3 was an ω-scan from -20° to 4° at χ = -90° and ϕ = 315°; scan no. 4 was an ω-scan from -20° to 11° at χ = -90° and ϕ = 0°; scan no. 5 was an ω-scan from -20° to 20° at χ = -90° and ϕ = 225°. Rotation images were processed using CrystalClear[i], producing a listing of unaveraged F^2 and $\sigma(F^2)$ values which were then passed to the CrystalStructure[ii] program package for further processing and structure solution on a Dell Pentium III computer. A total of 21165 reflections were measured over the ranges $5.08 \le 2\theta \le 50.06$ °, $-13 \le h \le 13$, $-16 \le k \le 15$, $-38 \le l \le 38$ yielding 4253 unique reflections (R_{int} = 0.0396). The intensity data

were corrected for Lorentz and polarization effects and for absorption using REQAB[iii] (minimum and maximum transmission 0.773, 1.000).

The structure was solved by direct methods (SIR97[iv]). Refinement was by full-matrix least squares based on F^2 using SHELXL-97[v]. All reflections were used during refinement (F^2's that were experimentally negative were replaced by $F^2 = 0$). The weighting scheme used was $w=1/[\sigma^2(F_o^2)+ 0.0821P^2 + 1.9748P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a "riding" model. Refinement converged to R_1=0.0531 and wR_2=0.1357 for 3751 reflections for which $F > 4\sigma(F)$ and R_1=0.0593, wR_2=0.1417 and GOF = 1.090 for all 4253 unique, non-zero reflections and 287 variables[vi]. The maximum Δ/σ in the final cycle of least squares was 0.000 and the two most prominent peaks in the final difference Fourier were +0.379 and -0.301 e/Å^3.

Table 1. lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Table 2. Anisotropic thermal parameters are in Table 3. Tables 4. and 5. list bond distances and bond angles. Figure 1. is an ORTEP[vii] representation of the molecule with 30% probability thermal ellipsoids displayed.

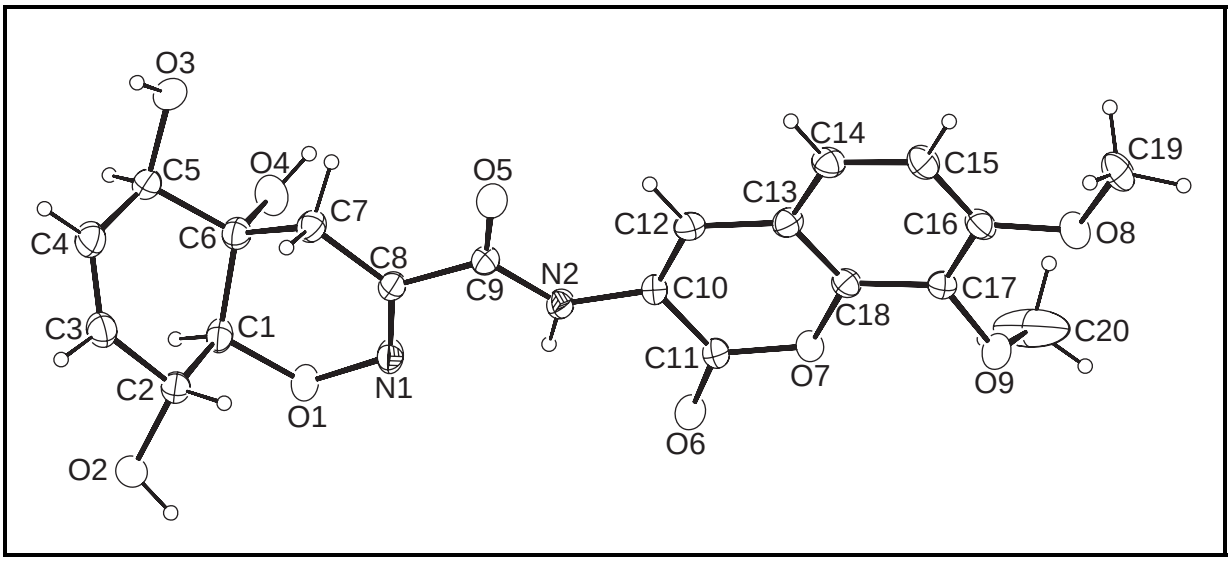


Figure 1. ORTEP drawing of the title compound with 30% probability thermal ellipsoids.

Table 1. Summary of Structure Determination of Trichodermamide A

Formula:	$C_{20}H_{20}N_2O_9$
Formula weight:	432.38
Crystal class:	orthorhombic
Space group:	I222 (#23)
Z	8
Cell constants:	
a	10.9542(12)Å
b	13.687(2)Å
c	32.040(4)Å
V	4803.6(10)Å^3
μ	0.96 cm^{-1}
crystal size, mm	0.38 x 0.18 x 0.03
D_{calc}	1.196 g/cm^3
F(000)	1808
Radiation:	Mo-K_α (λ=0.71073Å)
2θ range	5.08 – 50.06 °
hkl collected:	-13≤ h ≤13; -16≤ k ≤15; -38≤ l ≤38
No. reflections measured:	21165
No. unique reflections:	4253 (R_{int}=0.0396)
No. observed reflections	3751 (F>4σ)
No. reflections used in refinement	4253
No. parameters	287
R indices (F>4σ)	R_1=0.0531
	wR_2=0.1357
R indices (all data)	R_1=0.0593
	wR_2=0.1417
GOF:	1.090
Final Difference Peaks, e/Å^3	+0.379, -0.301

Table 2. Refined Positional Parameters for Trichodermamide A

Atom	x	y	z	U_{eq}, Å^2
C1	0.8892(2)	0.3824(2)	0.12857(7)	0.0348(6)
H1	0.9691	0.4140	0.1263	0.046
C2	0.8997(2)	0.2831(2)	0.10748(8)	0.0382(6)
H2	0.8323	0.2412	0.1167	0.051
C3	0.8963(3)	0.2927(2)	0.06083(8)	0.0427(7)
H3	0.9203	0.2391	0.0450	0.057
C4	0.8616(3)	0.3722(2)	0.04092(8)	0.0451(7)
H4	0.8586	0.3704	0.0119	0.060
C5	0.8270(3)	0.4645(2)	0.06222(8)	0.0405(7)
H5	0.8966	0.5093	0.0604	0.054
C6	0.7976(2)	0.4494(2)	0.10821(8)	0.0351(6)
C7	0.6705(2)	0.4053(2)	0.11457(8)	0.0357(6)
H7a	0.6083	0.4515	0.1059	0.048
H7b	0.6619	0.3464	0.0980	0.048
C8	0.6560(2)	0.3820(2)	0.15989(7)	0.0314(6)
C9	0.5292(2)	0.3796(2)	0.17666(8)	0.0331(6)
C10	0.4081(2)	0.3755(2)	0.24166(8)	0.0324(6)
C11	0.4284(2)	0.3631(2)	0.28621(8)	0.0352(6)
C12	0.2944(2)	0.3852(2)	0.22672(8)	0.0346(6)
H12	0.2826	0.3959	0.1983	0.046
C13	0.1906(2)	0.3794(2)	0.25394(8)	0.0336(6)
C14	0.0706(2)	0.3836(2)	0.24051(8)	0.0372(6)
H14	0.0546	0.3912	0.2122	0.049
C15	-0.0256(2)	0.3768(2)	0.26799(8)	0.0389(6)
H15	-0.1056	0.3795	0.2583	0.052
C16	-0.0019(2)	0.3659(2)	0.31089(8)	0.0367(6)
C17	0.1170(2)	0.3618(2)	0.32540(8)	0.0333(6)
C18	0.2116(2)	0.3690(2)	0.29675(8)	0.0316(5)
C19	-0.2152(2)	0.3578(3)	0.32738(10)	0.0482(7)
H19a	-0.2343	0.4195	0.3147	0.072
H19b	-0.2675	0.3475	0.3510	0.072
H19c	-0.2274	0.3063	0.3075	0.072
C20	0.1620(7)	0.4248(4)	0.39294(13)	0.137(3)
H20a	0.2451	0.4460	0.3900	0.205
H20b	0.1468	0.4070	0.4215	0.205
H20c	0.1080	0.4768	0.3850	0.205
N1	0.7419(2)	0.3666(2)	0.18653(7)	0.0374(5)
N2	0.5175(2)	0.3762(2)	0.21897(6)	0.0347(5)
H2a	0.5841	0.3744	0.2332	0.046
O1	0.8637(2)	0.3699(2)	0.17298(5)	0.0407(5)
O2	1.0134(2)	0.2375(2)	0.11778(6)	0.0516(6)
H2b	1.0076	0.2106	0.1405	0.077
O3	0.7249(2)	0.5105(2)	0.04277(6)	0.0528(6)
H3a	0.7130	0.4857	0.0198	0.079

O4	0.8068(2)	0.5405(2)	0.13026(7)	0.0473(5)
H4a	0.7395	0.5667	0.1312	0.071
O5	0.4421(2)	0.3840(2)	0.15279(6)	0.0420(5)
O6	0.5280(2)	0.3543(2)	0.30235(6)	0.0456(5)
O7	0.32962(14)	0.36248(14)	0.31210(5)	0.0343(4)
O8	-0.0901(2)	0.3580(2)	0.34077(6)	0.0457(5)
O9	0.1415(2)	0.3429(2)	0.36689(6)	0.0444(5)

$U_{eq}=1/3[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*cos\gamma+2U_{13}aa^*cc^*cos\beta+2U_{23}bb^*cc^*cos\alpha]$

Table 3. Refined Thermal Parameters (U's) for Trichodermamide A

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0281(13)	0.049(2)	0.0276(12)	-0.0001(12)	0.0030(10)	-0.0032(12)
C2	0.0334(14)	0.048(2)	0.0332(12)	0.0050(12)	0.0027(11)	0.0041(12)
C3	0.039(2)	0.052(2)	0.0368(13)	-0.0033(13)	0.0032(12)	0.0067(13)
C4	0.042(2)	0.062(2)	0.0311(13)	0.0009(13)	0.0020(12)	0.006(2)
C5	0.036(2)	0.049(2)	0.0368(14)	0.0125(12)	0.0057(11)	0.0049(12)
C6	0.0332(14)	0.0387(14)	0.0333(13)	0.0016(11)	0.0027(11)	-0.0016(12)
C7	0.0325(14)	0.045(2)	0.0296(13)	0.0037(11)	-0.0011(11)	-0.0019(11)
C8	0.0305(13)	0.0359(13)	0.0278(12)	0.0038(10)	0.0016(10)	0.0007(11)
C9	0.0354(14)	0.0307(13)	0.0332(12)	0.0042(11)	0.0055(11)	0.0014(11)
C10	0.0295(13)	0.0365(13)	0.0313(12)	0.0032(11)	0.0065(10)	0.0032(12)
C11	0.0283(13)	0.043(2)	0.0348(13)	0.0060(12)	0.0054(11)	0.0043(12)
C12	0.0366(14)	0.0364(14)	0.0307(12)	0.0038(11)	-0.0029(11)	0.0039(12)
C13	0.0342(13)	0.0351(13)	0.0316(12)	0.0035(11)	-0.0018(11)	-0.0008(12)
C14	0.0323(13)	0.041(2)	0.0381(13)	0.0015(12)	-0.0060(12)	0.0022(12)
C15	0.0279(13)	0.043(2)	0.046(2)	-0.0016(12)	-0.0007(11)	-0.0006(12)
C16	0.0274(12)	0.0380(14)	0.0449(14)	0.0011(12)	0.0020(11)	0.0057(12)
C17	0.0315(13)	0.0386(14)	0.0299(12)	0.0033(11)	-0.0002(10)	0.0068(12)
C18	0.0248(12)	0.0357(13)	0.0343(12)	0.0020(11)	-0.0021(10)	0.0005(12)
C19	0.0251(13)	0.057(2)	0.063(2)	-0.004(2)	0.0054(13)	0.0015(14)
C20	0.261(8)	0.092(3)	0.058(2)	-0.037(2)	-0.068(4)	0.095(4)
N1	0.0301(11)	0.0507(14)	0.0314(11)	0.0018(10)	0.0061(9)	-0.0013(11)
N2	0.0247(10)	0.0473(13)	0.0321(10)	0.0090(10)	0.0014(9)	0.0011(10)
O1	0.0275(9)	0.0657(13)	0.0287(9)	0.0025(9)	0.0009(7)	-0.0012(10)

O2	0.0395(11)	0.0678(14)	0.0476(11)	0.0179(10)	0.0075(9)	0.0175(10)
O3	0.0584(13)	0.069(2)	0.0303(9)	0.0128(10)	0.0017(9)	0.0191(12)
O4	0.0457(11)	0.0440(11)	0.0523(12)	-0.0084(9)	0.0099(10)	-0.0031(9)
O5	0.0321(10)	0.0586(13)	0.0354(9)	0.0054(9)	-0.0002(8)	0.0008(9)
O6	0.0300(10)	0.0697(14)	0.0372(9)	0.0116(10)	0.0007(8)	0.0019(10)
O7	0.0244(9)	0.0459(10)	0.0325(9)	0.0034(8)	0.0010(7)	0.0018(8)
O8	0.0262(9)	0.0636(13)	0.0474(11)	0.0033(10)	0.0037(8)	0.0025(10)
O9	0.0348(10)	0.0650(14)	0.0335(9)	0.0067(9)	0.0035(8)	0.0012(10)

The form of the anisotropic displacement parameter is:

$\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+ 2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$.

Table 4. Bond Distances in Trichodermamide A, Å

C1-O1	1.460(3)	C1-C6	1.508(4)	C1-C2	1.522(4)
C2-O2	1.432(3)	C2-C3	1.501(4)	C3-C4	1.317(4)
C4-C5	1.485(4)	C5-O3	1.427(3)	C5-C6	1.523(3)
C6-O4	1.436(3)	C6-C7	1.531(4)	C7-C8	1.495(3)
C8-N1	1.287(3)	C8-C9	1.490(3)	C9-O5	1.224(3)
C9-N2	1.362(3)	C10-C12	1.342(4)	C10-N2	1.402(3)
C10-C11	1.454(4)	C11-O6	1.213(3)	C11-O7	1.364(3)
C12-C13	1.435(4)	C13-C14	1.384(4)	C13-C18	1.398(3)
C14-C15	1.377(4)	C15-C16	1.407(4)	C16-O8	1.365(3)
C16-C17	1.384(4)	C17-O9	1.381(3)	C17-C18	1.388(4)
C18-O7	1.386(3)	C19-O8	1.436(3)	C20-O9	1.414(5)
N1-O1	1.404(3)				

Table 5. Bond Angles in Trichodermamide A, °

O1-C1-C6	111.4(2)	O1-C1-C2	110.0(2)	C6-C1-C2	113.7(2)
O2-C2-C3	106.8(2)	O2-C2-C1	110.6(2)	C3-C2-C1	111.2(2)
C4-C3-C2	124.2(3)	C3-C4-C5	123.6(2)	O3-C5-C4	112.0(2)
O3-C5-C6	108.4(2)	C4-C5-C6	112.6(2)	O4-C6-C1	105.6(2)
O4-C6-C5	110.1(2)	C1-C6-C5	111.1(2)	O4-C6-C7	109.9(2)
C1-C6-C7	107.9(2)	C5-C6-C7	112.0(2)	C8-C7-C6	108.1(2)
N1-C8-C9	116.0(2)	N1-C8-C7	127.0(2)	C9-C8-C7	117.0(2)
O5-C9-N2	123.4(2)	O5-C9-C8	120.0(2)	N2-C9-C8	116.5(2)
C12-C10-N2	127.5(2)	C12-C10-C11	120.2(2)	N2-C10-C11	112.3(2)
O6-C11-O7	117.0(2)	O6-C11-C10	124.6(2)	O7-C11-C10	118.4(2)
C10-C12-C13	120.9(2)	C14-C13-C18	117.7(2)	C14-C13-C12	124.1(2)
C18-C13-C12	118.1(2)	C15-C14-C13	121.7(2)	C14-C15-C16	119.3(2)
O8-C16-C17	115.3(2)	O8-C16-C15	124.2(2)	C17-C16-C15	120.5(2)
O9-C17-C16	120.9(2)	O9-C17-C18	120.3(2)	C16-C17-C18	118.5(2)
O7-C18-C17	117.2(2)	O7-C18-C13	120.5(2)	C17-C18-C13	122.2(2)
C8-N1-O1	119.0(2)	C9-N2-C10	126.6(2)	N1-O1-C1	119.1(2)
C11-O7-C18	121.6(2)	C16-O8-C19	117.8(2)	C17-O9-C20	116.8(3)

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[vi]. $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$

$wR_2 = \{ \sum w (F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2 \}^{1/2}$

$GOF = \{ \sum w (F_o^2 - F_c^2)^2 / (n - p) \}^{1/2}$

where n = the number of reflections and p = the number of parameters refined.

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