Formal Synthesis of (±)-Platensimycin

Yefen Zou, Chun-Hsing Chen, Christopher D. Taylor, Bruce M. Foxman and Barry B. Snider*

Department of Chemistry, MS 015, Brandeis University, Waltham, Massachusetts 02454-9110.

Supporting Material

General Procedures. All reactions were performed under nitrogen atmosphere. All commercially available reagents were used without further purification unless otherwise noted. Dichloromethane was distilled from CaH_2 under nitrogen. Ether and tetrahydrofuran were freshly distilled from benzophenone ketyl radical under nitrogen prior to use. Flash chromatography was performed with silica gel (40-63 μm). NMR spectra were recorded in $CDCl_3$ (unless otherwise noted) on a 400 MHz spectrometer (unless otherwise noted). Chemical shifts are reported in δ and coupling constants (*J* values) in Hz. IR spectra were recorded on an FT-IR spectrometer and are reported in cm^{-1}. Allylic oxidation of **13** was carried out in a sealed vessel in a CEM Discover microwave oven with automatic temperature and pressure display.

(4a*S*,8a*R*)-*rel* and (4a*R*,8a*R*)-*rel*-8a-(2-Bromo-2-propenyl)-2,3,4,4a,8,8a-hexahydro-1,5-naphthalenedione (7 and 8). Ammonia (100 mL) was condensed into an oven dried, three necked flask equipped with dry-ice/acetone condenser at -78 °C under N_2. A solution of 5-methoxy-1-tetralone (**6**) (1.35 g, 7.66 mmol) in Et_2O (10 mL) and *t*-BuOH (0.84 mL, 8.81 mmol) was introduced and potassium was added until the reaction mixture maintained a deep blue color for 15 min. To the suspension, anhydrous LiBr (1.46 g, 16.85 mmol) was added and the mixture was stirred vigorously for 30 min. 2,3-Dibromopropene (95%, 0.75 mL, 7.27 mmol) was added and the reaction was stirred at -78 °C for 1 h. The cold bath and condenser were removed and the ammonia was allowed to evaporate over 1 h. The residue was diluted with THF (30 mL) and treated with conc HCl (20 mL) at 0 °C. The mixture was warmed to 25 °C over 30 min and separated into two layers. The aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to yield 1.9 g of crude product. Flash chromatography on silica gel (9:1 hexanes/EtOAc) gave 0.72 g (35%) of **8** followed by 1.05 g (51%) of **7**.

Data for **7**: ^{1}H NMR 6.95 (ddd, 1, *J* = 10.0, 4.3, 4.3), 6.04 (d, 1, *J* = 10.0), 5.61 (s, 1), 5.58 (s, 1), 3.18 (d, 1, *J* = 14.7), 2.98 (d, 1, *J* = 14.7), 2.93 (dd, 1, *J* = 4.3, 7.3), 2.86 (dd, 1, *J* = 4.3, 18.9), 2.69 (ddd, 1, *J* = 15.9, 7.3, 7.3), 2.45 (ddd, 1, *J* = 15.9, 6.7, 6.7), 2.25-2.17 (m, 2), 2.04-1.85 (m, 3); ^{13}C NMR 210.0, 197.5, 147.6, 128.7, 127.4, 122.2, 53.2, 52.3, 46.5, 38.1, 30.9, 23.6, 22.9; IR

(neat) 2947, 2874, 1708, 1668, 1624, 1451, 1424, 1389, 1253, 1211, 1123, 902, 769, 735; HRMS (CI+) Calcd for $C_{13}H_{16}O_2Br$ (MH^+) 283.0334, found 283.0335.

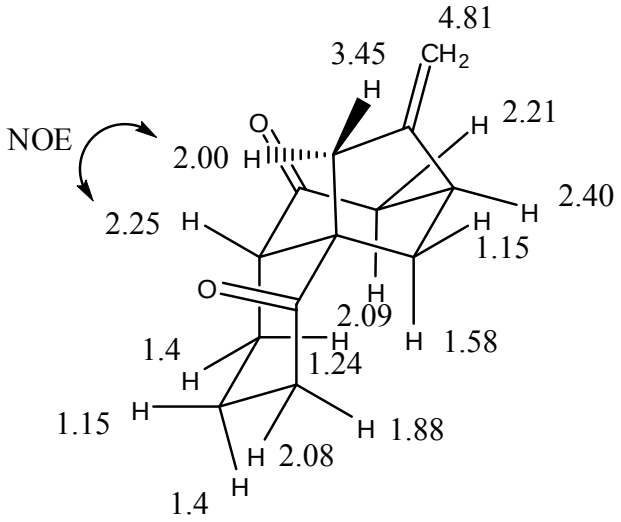
Data for **8**: ^{1}H NMR 6.89 (ddd, 1, *J* = 10.3, 5.1, 4.0), 6.07 (d, 1, *J* = 10.3), 5.52 (s, 1), 5.48 (s, 1), 3.09 (d, 1, *J* = 15.3), 2.88 (ddd, 1, *J* = 13.5, 13.5, 6.1), 2.82 (d, 1, *J* = 15.3), 2.81 (dd, 1, *J* = 19, 4), 2.78 (dd, 1, *J* = 19, 5), 2.65 (dd, 1, *J* = 11.3, 3.3), 2.43 (br d, 1, *J* = 13.5), 2.23-2.17 (m, 2), 1.82-1.60 (m, 2); ^{13}C NMR 211.7, 197.5, 146.6, 128.8, 127.3, 121.4, 56.9, 55.1, 40.5, 38.2, 29.9, 25.7, 19.2; IR (neat) 2944, 2870, 1710, 1661, 1626, 1451, 1426, 1389, 1277, 1218, 1152, 901, 753, 735; HRMS (EI+) Calcd for $C_{13}H_{15}O_2{}^{81}Br$ (M^+) 284.0235, found 284.0237.

Acidic Equilibration of 7 and 8. A solution of **8** (0.72 g, 2.54 mmol) in THF (20 mL) was treated with conc HCl (10 mL) at 0 °C. The mixture was warmed to 25 °C over 30 min and separated into two layers. The aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 0.7 g of crude product. Flash chromatography on silica gel (9:1 hexanes/EtOAc) gave 0.29 g (40%) of **8** and 0.40 g (55%) of **7**. An identical mixture of products was obtained by equilibration of **7**.

(4a*R*,7*S*,9a*S*)-*rel*-Octahydro-6-methylene-4a,7-methano-4a*H*-benzocycloheptene-4,9-dione (5). A solution of **7** (1.0 g, 3.53 mmol), *n*-Bu_3SnH (2.16 mL, 7.76 mmol), and AIBN (50 mg) in benzene (60 mL) was degassed using the freeze-pump-thaw technique (3 cycles) and heated under reflux for 3 h. The reaction was cooled down to 25 °C and the solvent was evaporated. The residue was diluted with Et_2O (20 mL) and treated with aqueous KF solution (10%, 15 mL).[14] The resulting suspension was stirred vigorously at 25 °C overnight. The layers were separated and the aqueous layer was extracted with Et_2O. The combined Et_2O extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 1.2 g of crude product. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 604 mg (84%) of **5**: mp 63-64 °C; ^{1}H NMR ($CDCl_3$) 5.01 (s, 1), 4.96 (s, 1), 3.24 (d, 1, *J* = 17.7), 3.05-3.02 (br, 1), 2.67 (dd, 1, *J* = 16.5, 3.7), 2.57-2.40 (m, 5), 2.19-2.11 (m, 2), 1.99 (dddd, 1, *J* = 12.8, 12.8, 12.8, 3.7), 1.88-1.81 (m, 1), 1.80-1.73 (m, 2); (400 and 800 MHz, C_6D_6) 4.81 (s, 2), 3.45 (d, 1, *J* = 17.6), 2.40 (br, 1), 2.25 (d, 1, *J* = 12.8), 2.21 (d, 1, *J* = 16.0), 2.09 (d, 1, *J* = 16.0), 2.08 (d, 1, *J* = 14.2), 2.00 (d, 1, *J* = 17.6),

1.88 (ddd, 1, *J* = 14.2, 14.2, 6.1), 1.58 (d, 1, *J* = 12.2), 1.45-1.38 (m, 2), 1.24 (dddd, 1, *J* = 13.1, 13.1, 13.1, 2.1), 1.17-1.10 (m, 2); ^{13}C NMR 210.3, 210.0, 150.1, 108.9, 59.8, 56.9, 48.8, 42.6, 39.1, 38.7, 37.4, 26.9, 25.8; IR (neat) 2941, 2874, 1743, 1706, 1660, 1447, 1330, 1220, 1147, 1130, 1006, 884; HRMS (CI+) Calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1150.

The protons were much better resolved in C_6D_6 and were fully assigned from a COSY spectrum as shown below. A 2D NOESY spectrum at 800 MHz showed NOEs from the proton at δ 2.25 to the proton at δ 2.00.



(4a*R*,7*S*,9a*R*)-*rel*-Octahydro-6-methylene-4a,7-methano-4a*H*-benzocycloheptene-4,9-dione (9). A solution of **8** (0.5 g, 1.77 mmol), *n*-Bu_3SnH (1.08 mL, 3.86 mmol), and AIBN (25mg) in benzene (30 mL) was degassed using the freeze-pump-thaw technique (3 cycles) and heated under reflux for 3 h. The reaction was cooled down to 25 °C and the solvent was evaporated. The residue was diluted with Et_2O (10 mL) and treated with aqueous KF solution (10%, 8 mL).[14] The resulting suspension was stirred vigorously at 25 °C overnight. The layers were separated and the aqueous layer was extracted with Et_2O. The combined Et_2O extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 0.6 g of crude product. Flash chromatography on silica gel (7:1 hexanes/EtOAc) gave 292 mg (81%) of **9**: mp 81-82 °C; ^{1}H NMR 4.99 (s, 1), 4.86 (s, 1), 3.05-3.02 (br, 1), 2.70 (d, 1, *J* = 17.1), 2.56-2.52 (m, 3), 2.41-2.37 (m, 2), 2.29 (ddd, 1, *J* = 13.4, 13.4, 5.5), 2.22-2.08 (m, 3), 1.87 (d, 1, *J* = 12.2), 1.77-1.56 (m, 2);

^{13}C NMR 211.1, 208.6, 149.8, 108.4, 58.9, 58.0, 50.0, 42.1, 39.6, 38.6, 37.4, 24.2, 21.4; IR (neat) 2952, 2865, 1709, 1662, 1452, 1342, 1259, 1200, 1180, 886; HRMS (CI+) Calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1154.

Basic Equilibration of 5 and 9. Tricyclic Dione **5** (35 mg, 0.17 mmol) was dissolved in 10% KOH in MeOH (5 mL) at 25 °C. The solution was stirred at 25 °C for 5 h and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to yield 38 mg of crude product. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 7 mg (20%) of **5** followed by 27 mg (78%) of **9**. An identical mixture of products was obtained by equilibration of **9**.

(1*S*,3*S*,4*S*,5a*R*,6*S*,9a*S*)-*rel*- and (1*S*,3*S*,4*S*,5a*R*,6*R*,9a*S*)-*rel*-1,4,5,6,7,8,9,9a-Octahydro-3-methyl-3*H*-1,4:3,5a-dimethano-2-benzoxepin-6-ol (3 and 12). A solution of tricyclic dione **5** (80 mg, 0.39 mmol) in THF (10 mL) was treated with L-Selectride (1 M in THF, 1.6 mL, 1.6 mmol) at -78 °C. The cold bath was removed and the reaction mixture was stirred for 2 h. The reaction was quenched with 3 M NaOH (1 mL) and 30% H_2O_2 (1 mL). The resulting mixture was stirred vigorously at 25 °C overnight. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to yield 78 mg (95%, about 95% pure) of a mixture of diols **4** and **11**.

A mixture of crude diols **4** and **11** (78 mg), CH_2Cl_2 (2 mL), and TFA (3 mL) was stirred at 0 °C for 2 h and concentrated under reduced pressure at 0 °C. The residue was dissolved in MeOH (15 mL) and the resulting solution was treated with K_2CO_3 (30 mg) at 25 °C. The reaction mixture was stirred for 30 min and H_2O (5 mL) and CH_2Cl_2 (20 mL) were added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 72 mg of crude product. Flash chromatography on MeOH-deactivated silica gel (9:1 hexanes/EtOAc) gave 30 mg (42%) of **12** followed by 27 mg (39%) of **3**.

Data for **3**: ^{1}H NMR 4.10 (dd, 1, J = 3.4, 3.4), 3.42-3.41 (m, 1), 2.22 (dd, 1, J = 6.7, 6.7),

2.12 (ddd, 1, *J* = 12.8, 3.7, 3.7), 1.97 (dd, 1, *J* = 11.0, 3.1), 1.90 (d, 1, *J* = 11.6), 1.83-1.55 (m, 6), 1.46 (br d, 1, *J* = 12.2), 1.39 (s, 3), 1.33-1.23 (m, 3); ^{13}C NMR 86.1, 80.2, 73.7, 50.0, 49.3, 45.5, 40.2, 39.4, 38.2, 30.2, 25.2, 23.3, 19.9; IR (neat) 3442, 2936, 2864, 1474, 1448, 1378, 1153, 1035, 820; HRMS (EI+) Calcd for $C_{13}H_{20}O_2$ (M^+) 208.1463, found 208.1460.

Data for **12**: ^{1}H NMR 4.10 (dd, 1, *J* = 3.4, 3.4), 3.51-3.46 (m, 1), 2.24-2.20 (m, 1), 1.90-1.78 (m, 5), 1.70-1.54 (m, 4), 1.41-1.20 (m, 4), 1.38 (s, 3); ^{13}C NMR 85.4, 79.8, 72.5, 50.0, 48.5, 44.8, 44.3, 38.4, 33.3, 32.1, 25.0, 24.0, 23.4; IR (neat) 3426, 2932, 2860, 1704, 1448, 1378, 1060, 940, 820; HRMS (EI+) Calcd for $C_{13}H_{20}O_2$ (M^+) 208.1463, found 208.1460.

(1*S*,3*S*,4*S*,5a*S*,9a*S*)-*rel*-1,4,5,8,9,9a-Hexahydro-3-methyl-3*H*-1,4:3,5a-dimethano-2-benzoxepine (13). To a solution of **3** (25 mg, 0.12 mmol) and pyridine (0.8 mL) in CH_2Cl_2 (8 mL) at -78 °C was added Tf_2O (0.14 mL, 0.48 mmol). The cold bath was removed. The reaction mixture was warmed to -5 °C over 15 min and treated with isopropanol (0.07 mL, 0.48 mmol) to quench the excess Tf_2O. The resulting solution was stirred at 25 °C for 15 min and quenched with saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with Et_2O. The combined Et_2O extracts were washed with saturated $CuSO_4$ solution, H_2O, and brine, dried ($MgSO_4$), and concentrated to yield 30 mg of crude product. Flash chromatography on silica gel (99:1 hexanes/EtOAc) gave 20 mg (90%) of **13**: ^{1}H NMR 5.60 (ddd, 1, *J* = 9.8, 3.7, 3.7), 5.33 (d, 1, *J* = 9.8), 4.14 (dd, 1, *J* = 3.4, 3.4), 2.16-2.09 (m, 3), 1.90-1.72 (m, 4), 1.58-1.42 (m, 5), 1.39 (s, 3); ^{13}C NMR 133.2, 126.8, 86.7, 80.6, 52.7, 45.6, 44.9, 44.6, 43.5, 38.3, 26.2, 23.3, 22.2; IR (neat) 2941, 2865, 1709, 1473, 1447, 1377, 1326, 1090, 1040, 997, 823; HRMS (CI+) Calcd for $C_{13}H_{18}O$ (M^+) 190.1358, found 190.1356.

(4*R*,4a*R*,7S,9a*S*)-*rel*-Octahydro-4-hydroxy-6-methylene-4a,7-methano-4a*H*-benzocyclohepten-9-one (10). A solution of **5** (480 mg, 2.35 mmol) in EtOH (20 mL) was treated with $NaBH_4$ (180 mg, 4.71 mmol) at -78 °C. The mixture was warmed to 0 °C over 20 min. The reaction was quenched with 1 M HCl (5 mL) and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 450 mg of crude product. Flash chromatography on MeOH-deactivated silica gel (9:1

hexanes/EtOAc) gave 420 mg (87%) of **10**: ^{1}H NMR 4.97 (s, 1), 4.88 (s, 1), 3.50-3.43 (m, 1), 2.98-2.93 (m, 1), 2.85 (d, 1, *J* = 17.1), 2.59 (dd, 1, *J* = 15.9, 3.7), 2.33 (d, 1, *J* = 15.9), 2.17 (dd, 1, *J* = 11.0, 6.2), 2.02 (d, 1, *J* = 17.1), 1.96-1.85 (m, 4), 1.64-1.40 (m, 4); ^{13}C NMR 213.1, 151.5, 108.0, 71.6, 59.6, 49.4, 49.1, 42.3, 40.4, 31.9, 29.4, 27.1, 24.2; IR (neat) 3445, 2935, 2862, 1704, 1660, 1448, 1411, 1226, 1047, 882; HRMS (EI+) Calcd for $C_{13}H_{18}O_2$ (M^+) 206.1307, found 206.1311.

(4*R*,4a*R*,7S,9*S*,9a*S*)-*rel*-Octahydro-6-methylene-4a,7-methano-4a*H*-benzocycloheptene-4,9-diol (11). A solution of **10** (356 mg, 1.73 mmol) in THF (20 mL) was treated with L-Selectride (1 M in THF, 6.8 mL, 6.8 mmol) at -78 °C. The cold bath was removed and the reaction mixture was stirred for 2 h. The reaction was quenched by 3 M NaOH (3 mL) and 30% H_2O_2 (3 mL). The resulting mixture was stirred vigorously at 25 °C overnight. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to yield 406 mg of crude product. Flash chromatography on MeOH-deactivated silica gel (7:1 hexanes/EtOAc) gave 298 mg (83%) of a 12:1 inseparable mixture of **11** and the 9*R*-isomer: ^{1}H NMR 5.09 (s, 1), 4.93 (s, 1), 3.64-3.60 (m, 1), 3.53-3.48 (m, 1), 2.83 (d, 1, *J* = 16.7), 2.75-2.72 (m, 1), 2.46 (d, 1, *J* = 16.7), 2.00 (ddd, 1, *J* = 11.6, 4.9, 2.4), 1.87-1.68 (m, 4), 1.62-1.48 (m, 3), 1.47-1.25 (m, 3); ^{13}C NMR 155.6, 106.4, 72.9, 72.8, 50.1, 48.6, 41.8, 40.6, 39.4, 32.1, 29.7, 27.8, 24.1; IR (neat) 3395, 2926, 2860, 1699, 1654, 1448, 1344, 1279, 1085, 1047; HRMS (EI+) Calcd for $C_{13}H_{20}O_2$ (M^+) 208.1463, found 208.1463.

Partial data for the 9*R*-isomer of **11** were determined from the mixture: 4.98 (s, 1), 4.88 (s, 1), 3.77-3.71 (m, 1), 2.97-2.94 (m, 1), 2.66-2.50 (m, 2), 2.33 (d, 1, *J* = 15.9).

Cyclization of 11 to Give 12. A mixture of **11** (201 mg, 0.97 mmol), CH_2Cl_2 (4 mL), and TFA (6 mL) was stirred at 0 °C for 2 h and concentrated under reduced pressure at 0 °C. The residue was dissolved in MeOH (15 mL) and the resulting solution was treated with K_2CO_3 (30 mg) at 25 °C. The reaction mixture was stirred for 30 min and H_2O (5 mL) and CH_2Cl_2 (20 mL) were added. The layers were separated and the aqueous layer was extracted with and CH_2Cl_2.

The combined CH_2Cl_2 extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 220 mg of crude product. Flash chromatography on MeOH-deactivated silica gel (9:1 hexanes/EtOAc) gave 181 mg (90%) of **12**.

Dehydration of 12 to Give 13. To a solution of **12** (176 mg, 0.84 mmol) and pyridine (2.5 mL) in CH_2Cl_2 (25 mL) at -78 °C was added Tf_2O (0.58 mL, 3.38 mmol). The cold bath was removed and the reaction mixture was allowed to warm to -5 °C over 15 min and treated with isopropanol (0.27 mL, 3.38 mmol) to quench the excess Tf_2O. The resulting solution was stirred at 25 °C for 15 min and quenched with saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with Et_2O. The combined Et_2O extracts were shaken with 1 M HCl for a couple of minutes (this effects elimination of the triflate to give the alkene), saturated $CuSO_4$ solution, H_2O, and brine, dried ($MgSO_4$), and concentrated to yield 143 mg of crude product. Flash chromatography on silica gel (99:1 hexanes/EtOAc) gave 135 mg (84%) of **13**.

Oxidation of 13 with CrO_3•dimethylpyrazole. To a suspension of CrO_3 (180 mg, 1.8 mmoL) in CH_2Cl_2 (4 mL) at -25 °C was added 3,5-dimethylpyrazole (173 mg, 1.8 mmoL). The mixture was stirred for 20 min and treated with a solution of **13** (17 mg, 0.09 mmoL) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at -25 °C for 20 h. and aqueous NaOH (6 M, 1 mL) was added. The cold bath was removed and the mixture was stirred for 1 h and diluted with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with 1 M HCl and brine, dried ($MgSO_4$), and concentrated to yield 18 mg of crude product. Flash chromatography on silica gel (99:1 to 4:1 hexanes/EtOAc) gave 2 mg (12%) of recovered **13** followed by 14 mg (75%) of an inseparable 4:1 mixture of **2** and **15**.

Partial data for **15** were determined from the mixture: ^{1}H NMR 6.93 (ddd, 1, J = 9.7, 5.5, 3.1), 6.03 (ddd, 1, J = 9.7, 2.4, 1.2), 4.20 (dd, 1, J = 3.4, 3.4), 2.17 (d, 1, J = 11.6), 1.80 (dd, 1, J = 14.6, 3.7); ^{13}C NMR 200.7, 147.7, 129.3, 86.3, 78.6, 53.7, 47.0, 44.5, 41.6, 41.1, 38.3, 26.4, 23.1.

(1*S*,3*S*,4*S*,5a*S*)-*rel*-4,5-Dihydro-3-methyl-3*H*-1,4:3,5a-Dimethano-2-benzoxepin-8(1*H*)-one (16). A mixture of **13** (21 mg, 0.11 mmol), SeO_2 (98 mg, 0.88 mmol) and dioxane (2 mL)

was heated to 140 °C for 30 min in a sealed vessel (100-130 psi) in a microwave oven. The solution was filtrated through Celite, which was washed with CH_2Cl_2. The combined filtrates were washed with saturated $NaHCO_3$ solution, H_2O, and brine, dried ($MgSO_4$), and concentrated to yield 30 mg of crude product. Flash chromatography on silica gel (8:1 hexanes/EtOAc) gave 13 mg (59%) of dienone **16** followed by 6 mg (27%) of alcohol **17**.

Data for **16**: ^{1}H NMR 6.67 (d, 1, *J* = 10.0), 6.32 (d, 1, *J* = 10.0), 6.13 (s, 1), 4.72 (d, 1, *J* = 4.3), 2.60 (dd, 1, *J* = 6.1, 6.1), 2.78-2.13 (m, 2), 1.99 (d, 1, *J* = 11.6), 1.96 (dd, 1 *J* = 11.6, 3.1, 3.1), 1.79 (d, 1, *J* = 11.6), 1.54 (dd, 1, *J* = 7.9, 3.1), 1.52 (s, 3); ^{13}C NMR 187.1, 160.5, 151.0, 130.0, 121.8, 87.1, 80.0, 54.8, 49.9, 48.6, 44.3, 42.5, 22.2; IR (neat) 2966, 2866, 1720, 1695, 1660, 1631, 1446, 1286, 1246, 1148, 1085, 1034, 1015, 942, 888, 932; HRMS (EI+) Calcd for $C_{13}H_{14}O_2$ (M^+) 202.0994, found 202.0993.

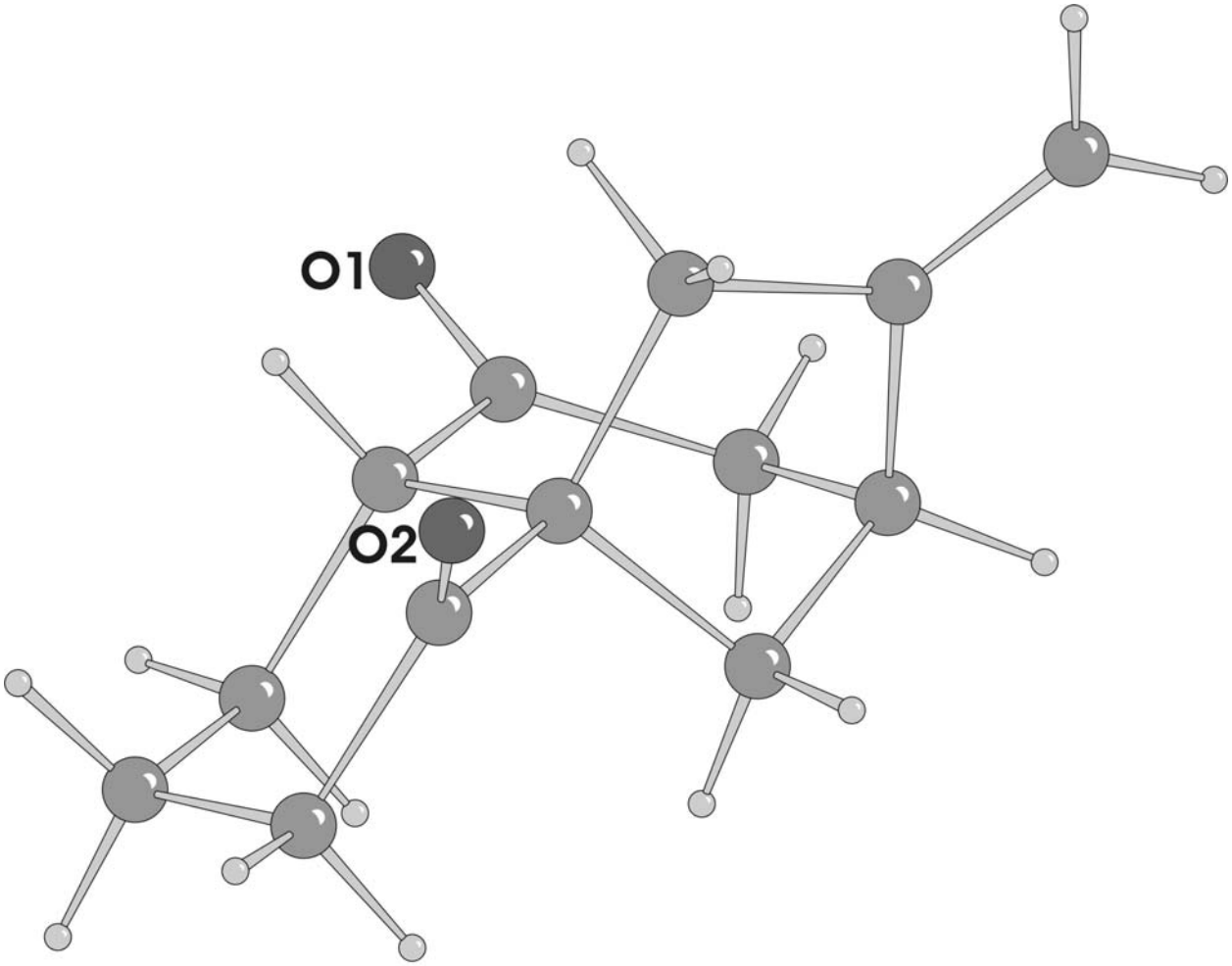
(1*S*,3*S*,4*S*,5a*S*,8*S*,9a*S*)-*rel*-1,4,5,8,9,9a-Hexahydro-3-methyl-3*H*-1,4:3,5a-dimethano-2-benzoxepin-8-ol (17). A mixture of **13** (66 mg, 0.35 mmol), SeO_2 (117 mg, 1.05 mmol) and dioxane (6 mL) was heated to 110 °C for 10 min in a sealed vessel (20 psi) in a microwave oven. The solution was filtrated through Celite, which was washed with CH_2Cl_2. The combined filtrates were washed with saturated $NaHCO_3$ solution, H_2O, and brine, dried ($MgSO_4$), and concentrated to yield 93 mg of crude product. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave 5 mg (7%) of enone **2** followed by 59 mg (83%) of **17**: ^{1}H NMR 5.76 (dd, 1, *J* = 9.8, 4.3), 5.57 (d, 1, *J* = 9.8), 4.19 (dd, 1, *J* = 4.3, 4.3), 4.16 (dd, 1, *J* = 3.4, 3.4), 2.18 (dd, 1, *J* = 6.1, 6.1), 2.12 (ddd, 1, *J* = 12.3, 3.7, 3.7) 1.96-1.60 (m, 6), 1.56-1.50 (m, 2), 1.41 (s, 3); ^{13}C NMR 137.4, 127.5, 86.7, 80.2, 64.3, 52.2, 45.8, 44.2, 42.8, 38.0, 37.7, 31.2, 23.2; IR (neat) 3406, 2946, 2867, 1644, 1473, 1446, 1378, 1327, 1222, 1140, 1007, 981, 823; HRMS (EI+) Calcd for $C_{13}H_{18}O_2$ (M^+) 206.1307, found 206.1309.

(1*S*,3*S*,4*S*,5a*S*,9a*S*)-*rel*-4,5,9,9a-tetrahydro-3-methyl-3*H*-1,4:3,5a-Dimethano-2-benzoxepin-8(1*H*)-one (2). A mixture of alcohol **17** (57 mg, 0.29 mmol) and activated MnO_2 (90%, 190 mg, 1.97 mmol) in CH_2Cl_2 (15 mL) was stirred vigorously at 25 °C for 1 d. The solution was filtrated through Celite, which was washed with CH_2Cl_2. The combined filtrates

were concentrated to gave 53 mg (94%) of pure **2**: ^{1}H NMR 6.62 (d, 1, *J* = 9.8), 5.94 (d, 1, *J* = 9.8), 4.16 (dd, 1, *J* = 3.4, 3.4), 2.43-2.27 (m, 4), 1.95-1.93 (m, 2), 1.89 (d, 1, *J* = 11.6), 1.79-1.74 (m, 2), 1.66 (d, 1, *J* = 11.0), 1.45 (s, 3); ^{13}C NMR 199.1, 155.2, 128.8, 87.0, 78.9, 51.6, 46.2, 44.1, 42.7, 42.2, 37.9, 37.4, 23.1; IR (neat) 2959, 1679, 1448, 1378, 1326, 1281, 1137, 1082, 1037, 993, 820; HRMS (EI+) Calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1154. The data are identical to those previously reported.[2]

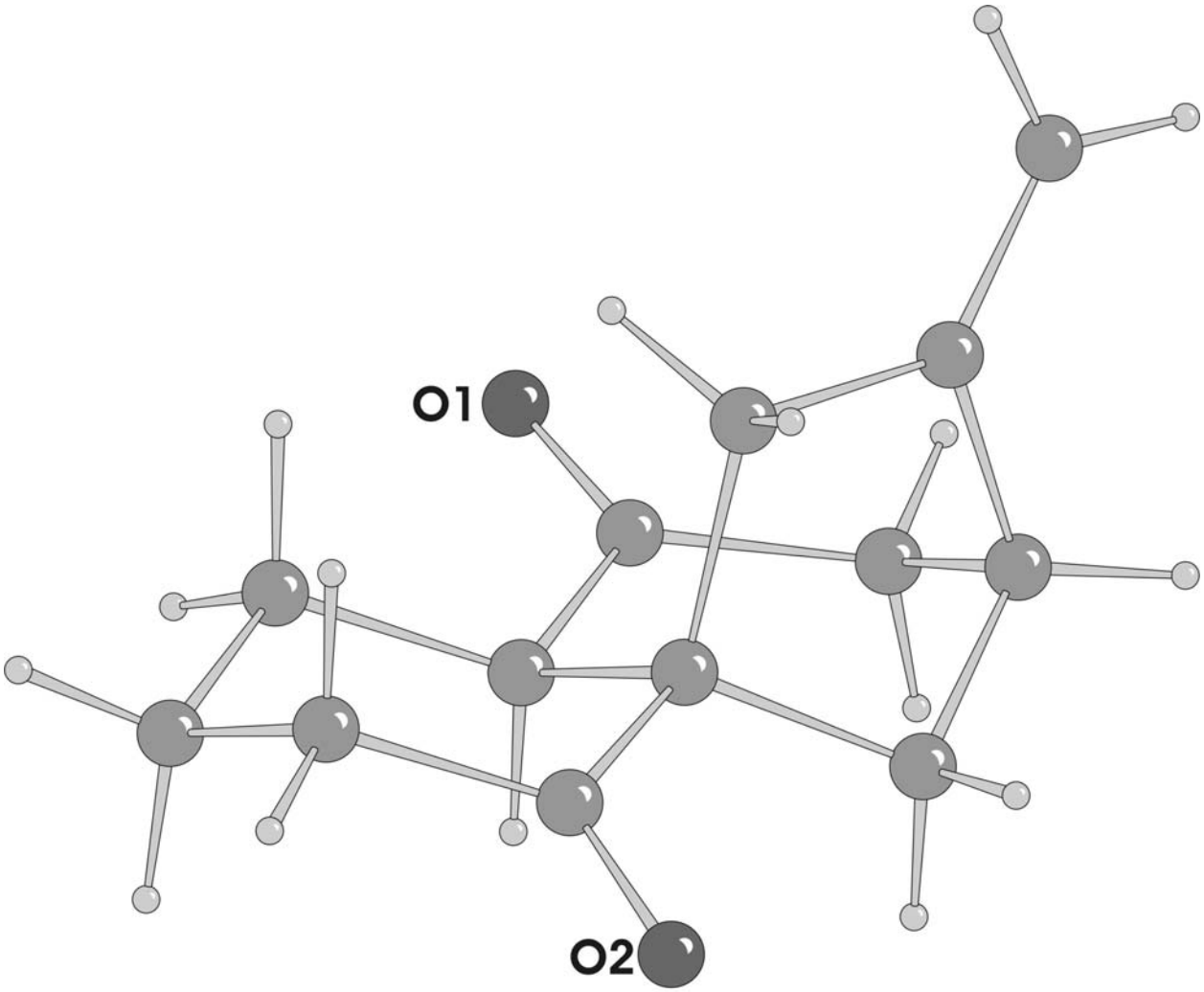
References

14. (a) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636-3638. (b) Leibner, J. E.; Jacobus, J. *J. Org. Chem.* **1979**, *44*, 449-450.



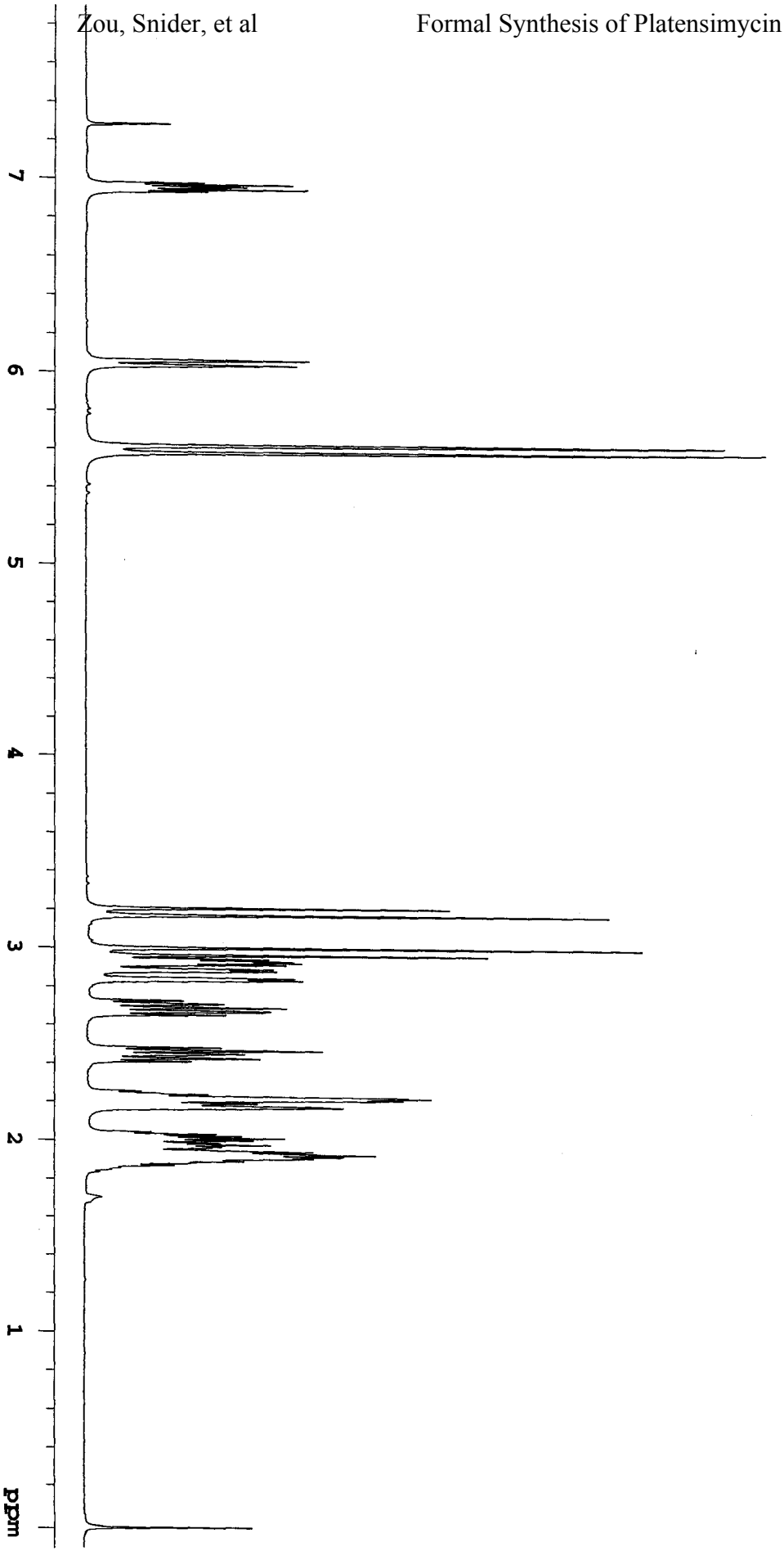
5

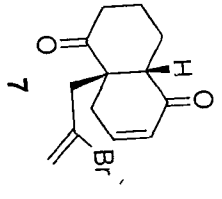
Molecular Structure of **5** Established by X-ray Structure Determination



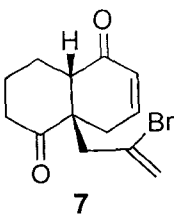
9

Molecular Structure of **9** Established by X-ray Structure Determination

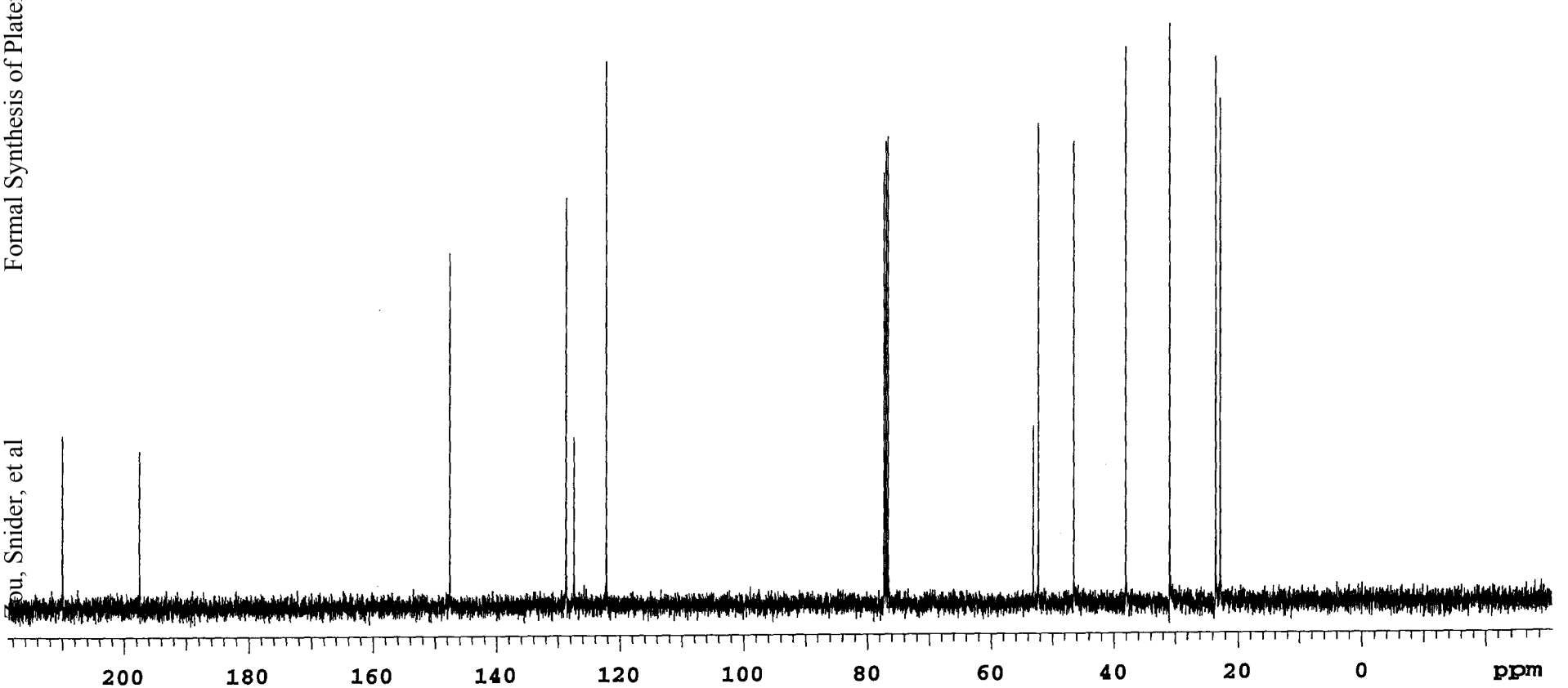

7
6
5
4
3
2
1
ppm

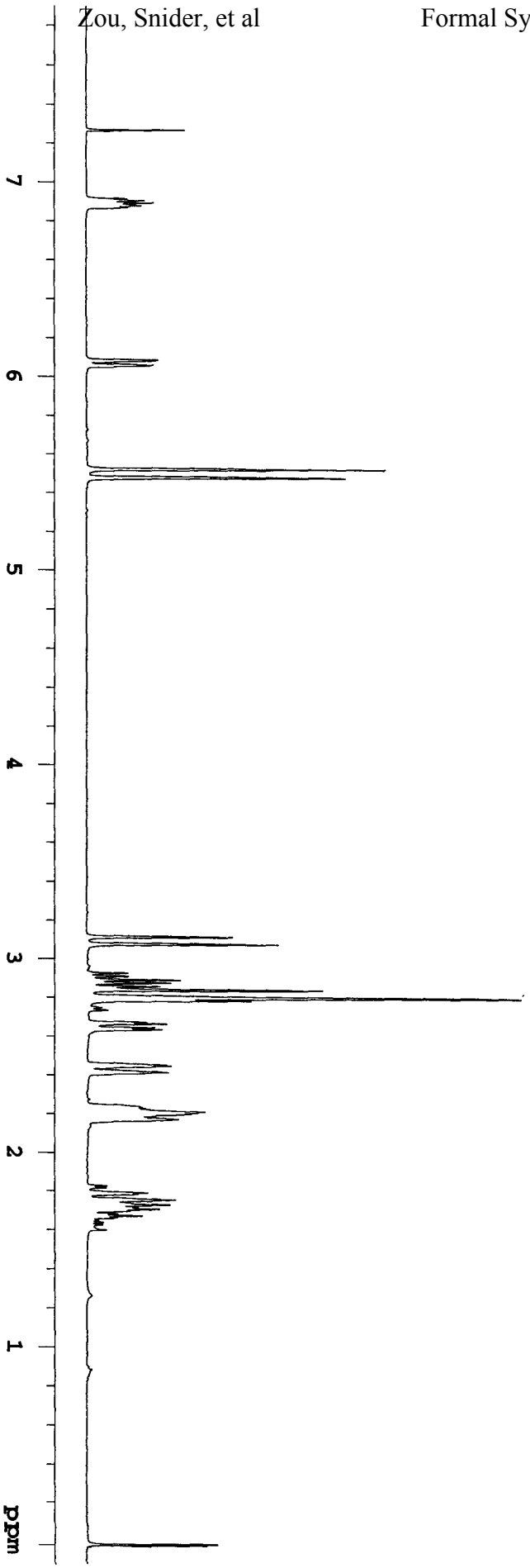

O
H
O
7
Br

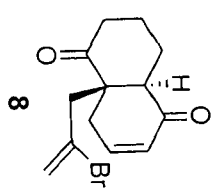
INDEX	FREQUENCY	PPM	HEIGHT
1	21107.351	209.986	27.8
2	19851.553	197.492	25.3
3	14835.226	147.588	57.4
4	12937.032	128.704	66.2
5	12808.859	127.428	27.0
6	12283.193	122.199	88.3
7	7771.932	77.319	69.8
8	7739.889	77.000	75.0
9	7707.845	76.681	75.8
10	5346.548	53.190	28.5
11	5260.336	52.332	77.6
12	4675.161	46.511	74.7
13	3828.298	38.086	90.0
14	3105.032	30.890	93.8
15	2368.795	23.566	88.4
16	2297.079	22.852	81.5



7

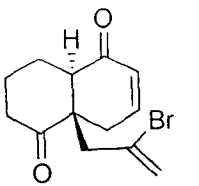




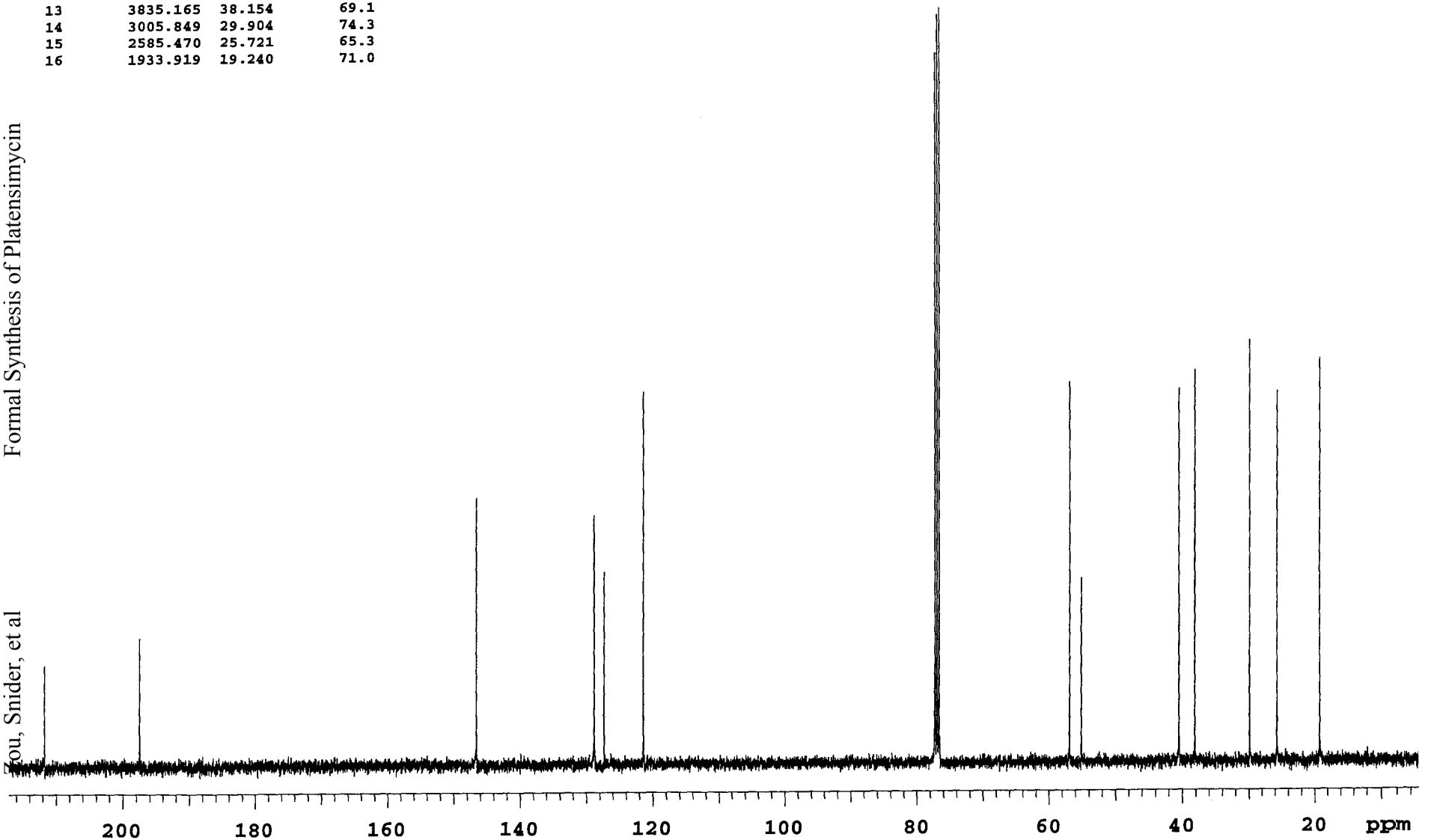


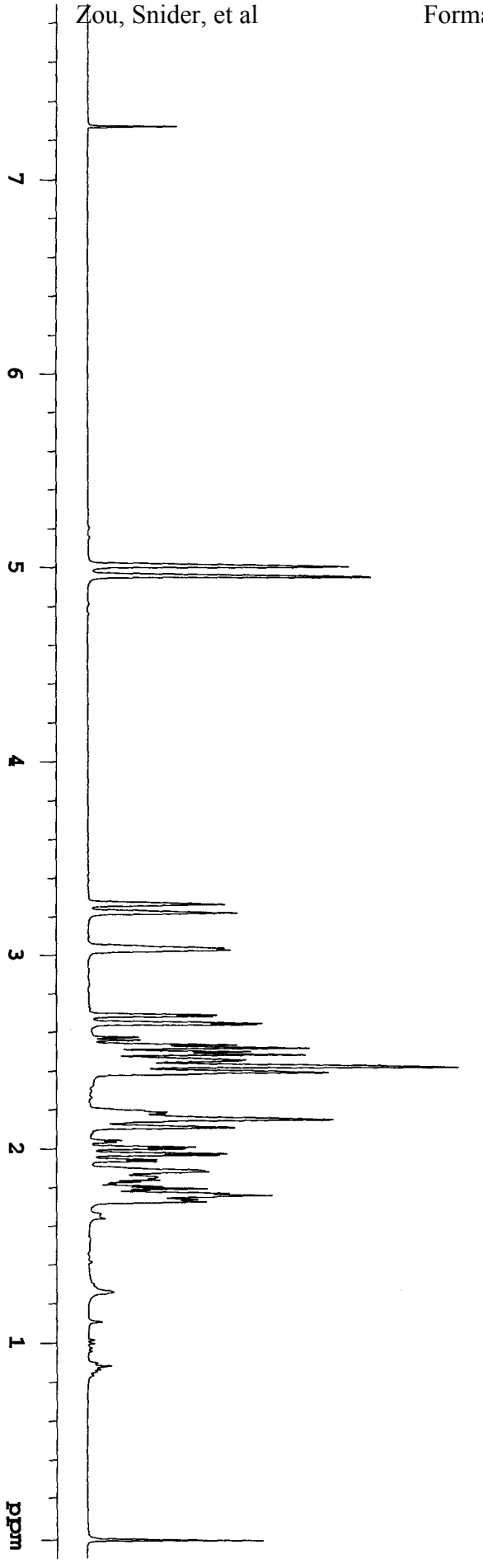
8

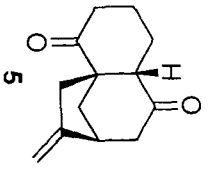
INDEX	FREQUENCY	PPM	HEIGHT
1	21282.827	211.731	17.8
2	19851.552	197.492	22.6
3	14735.280	146.593	47.2
4	12947.713	128.810	44.0
5	12798.940	127.330	33.9
6	12205.373	121.425	65.9
7	7771.932	77.319	126.1
8	7739.889	77.000	132.8
9	7707.845	76.681	134.0
10	5718.862	56.894	67.1
11	5542.623	55.141	32.4
12	4070.913	40.499	65.9
13	3835.165	38.154	69.1
14	3005.849	29.904	74.3
15	2585.470	25.721	65.3
16	1933.919	19.240	71.0



8

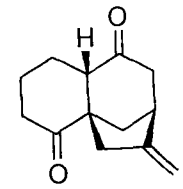



7
6
5
4
3
2
1
ppm


O
H
O
5

400 MHz, C6D6

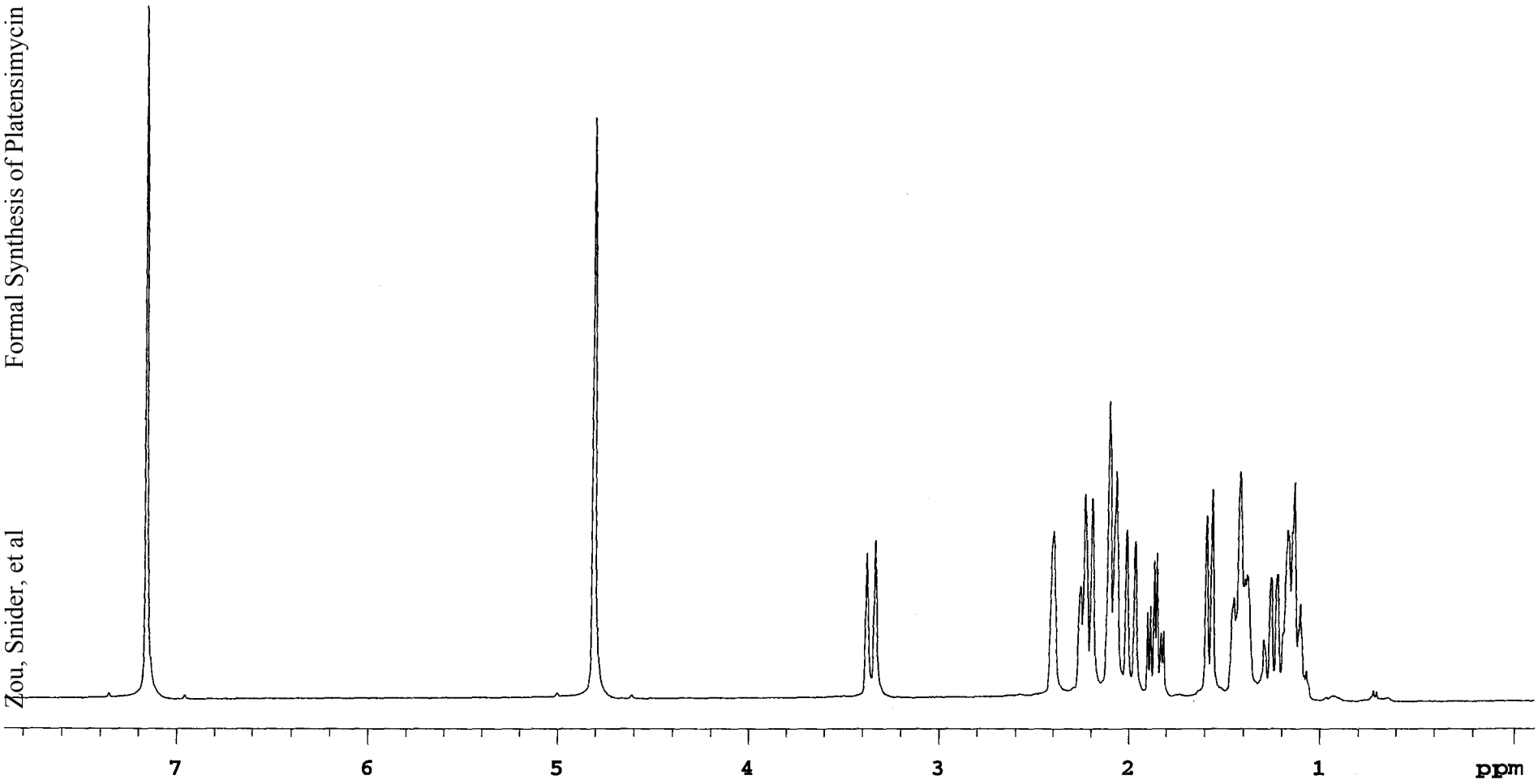
Pulse Sequence: s2pul

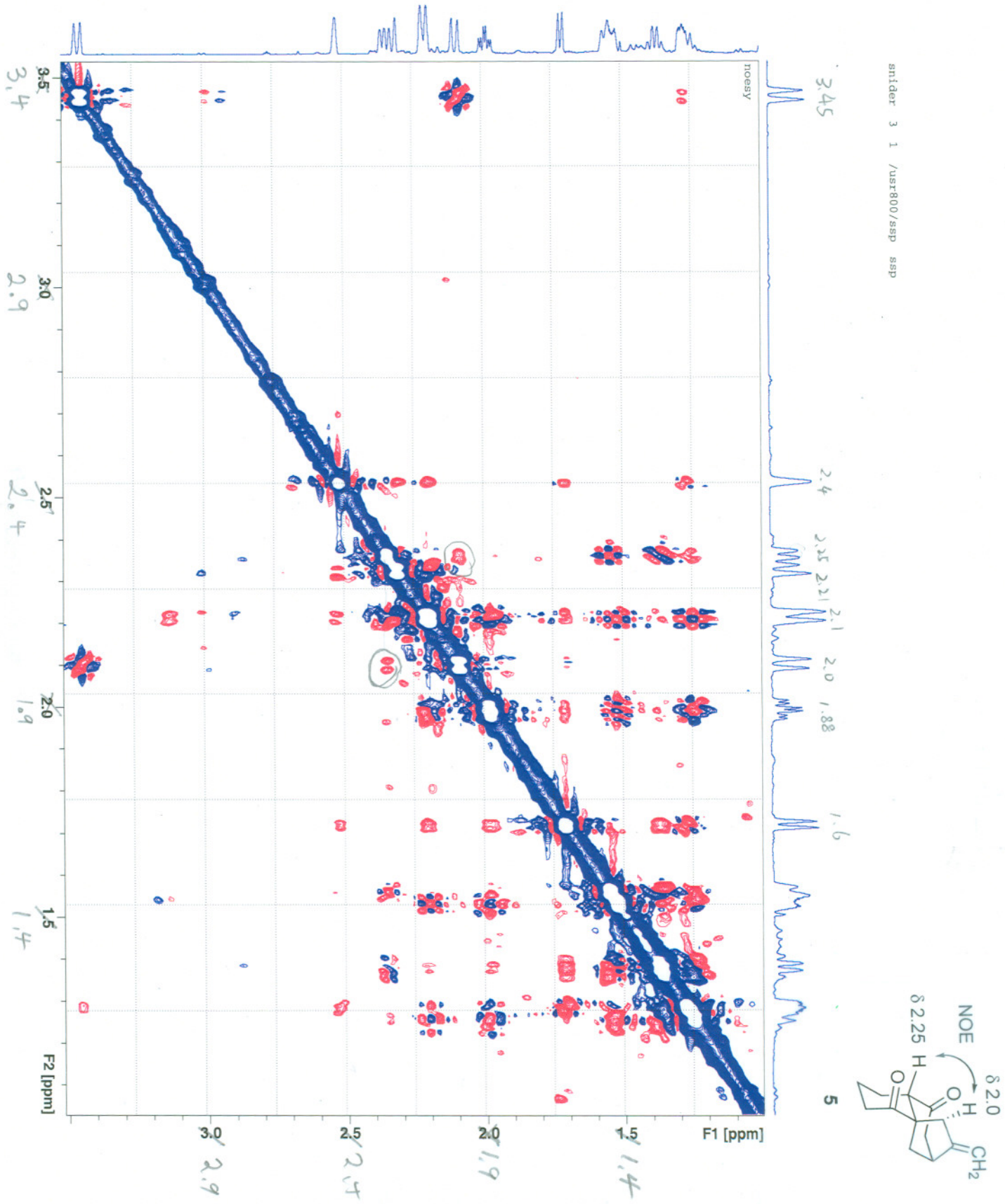


5

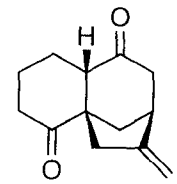
Formal Synthesis of Platensimycin

Zou, Snider, et al

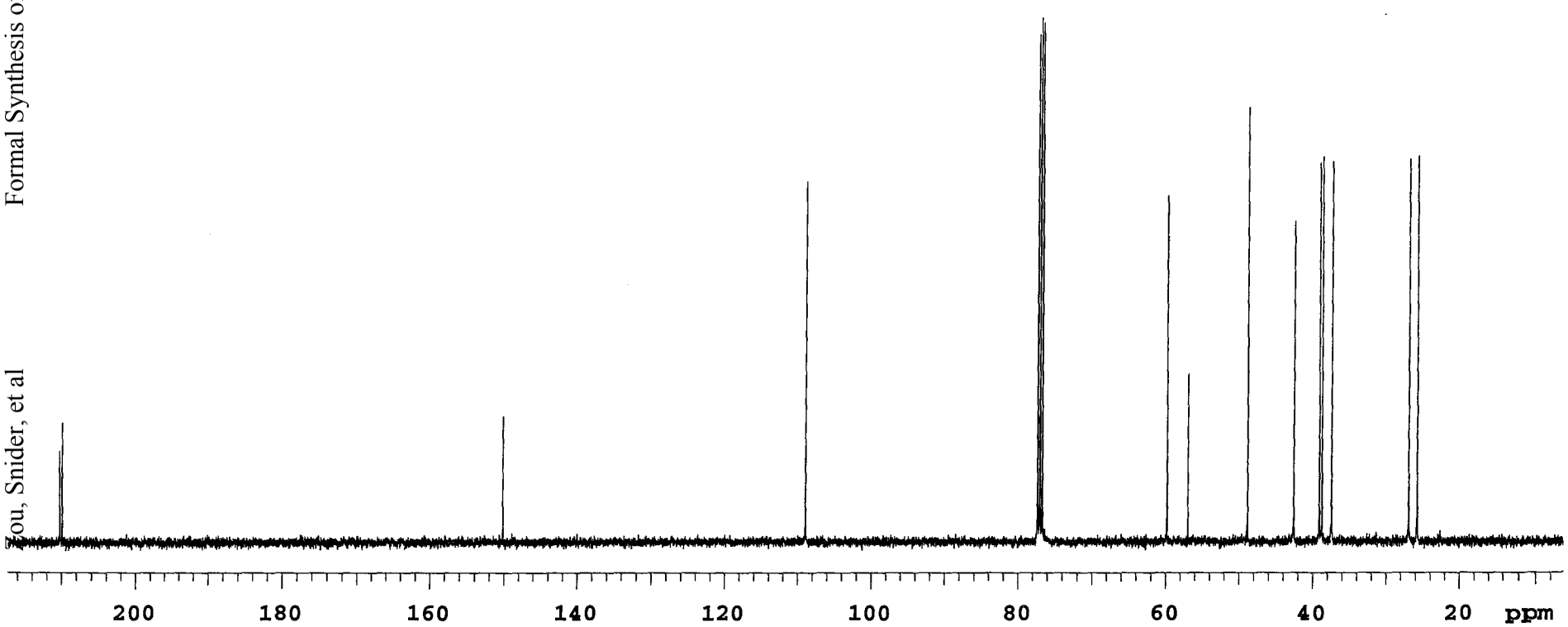


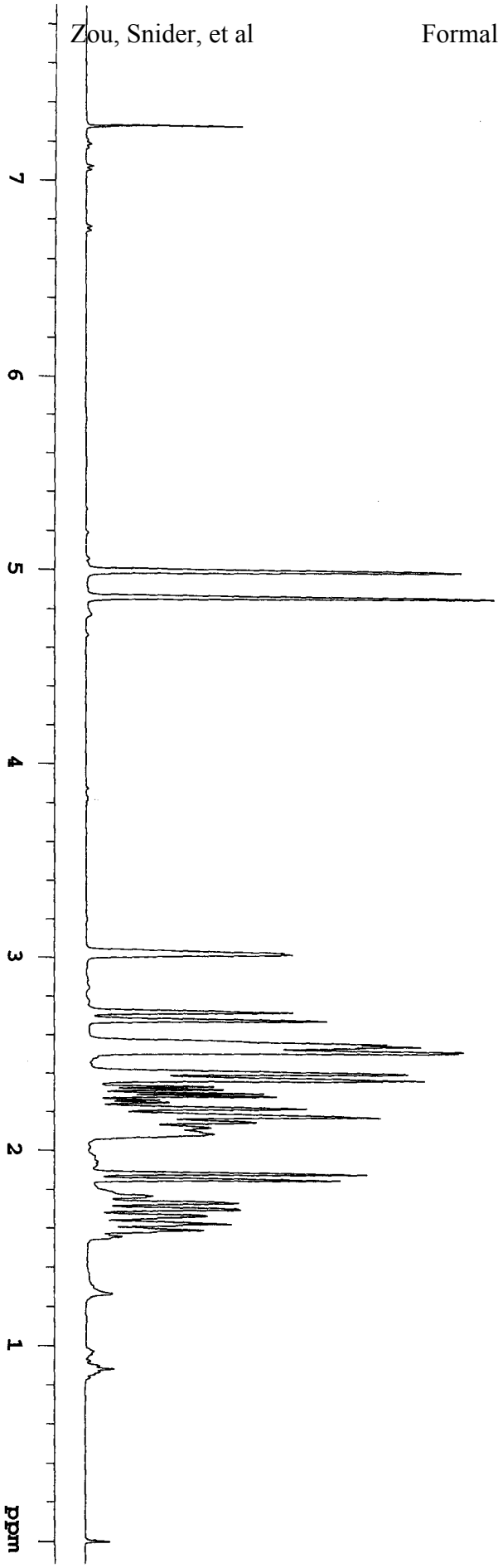

noesy
snider 3 1 /usr800/ssp ssp
F2 [ppm]
F1 [ppm]
3.5
3.0
2.5
2.0
1.5
3.45
2.4
2.25
2.21
2.1
2.0
1.88
1.6
5
δ 2.25 H
NOE
δ 2.0
O
O
H
CH2

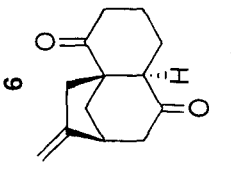
INDEX	FREQUENCY	PPM	HEIGHT
1	21134.054	210.251	14.6
2	21101.247	209.925	19.2
3	15090.047	150.123	20.2
4	10948.049	108.916	57.8
5	7771.932	77.319	81.5
6	7739.889	77.000	84.2
7	7707.845	76.681	83.3
8	6008.779	59.778	55.3
9	5721.151	56.917	26.8
10	4907.857	48.826	69.5
11	4278.432	42.564	51.2
12	3930.532	39.103	60.5
13	3892.385	38.723	61.5
14	3760.397	37.410	60.7
15	2706.014	26.921	61.1
16	2591.573	25.782	61.6



5

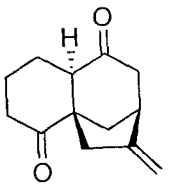




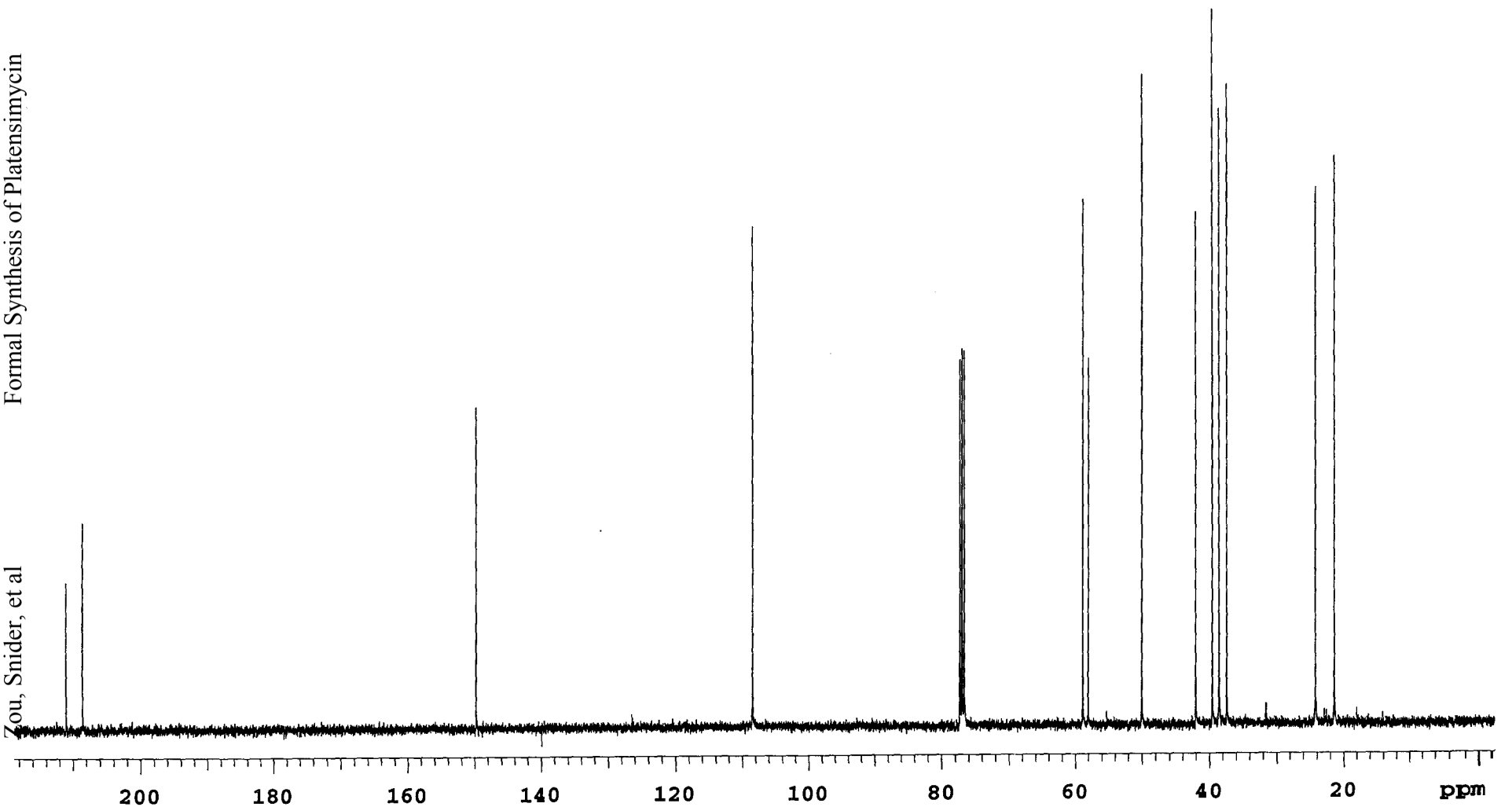


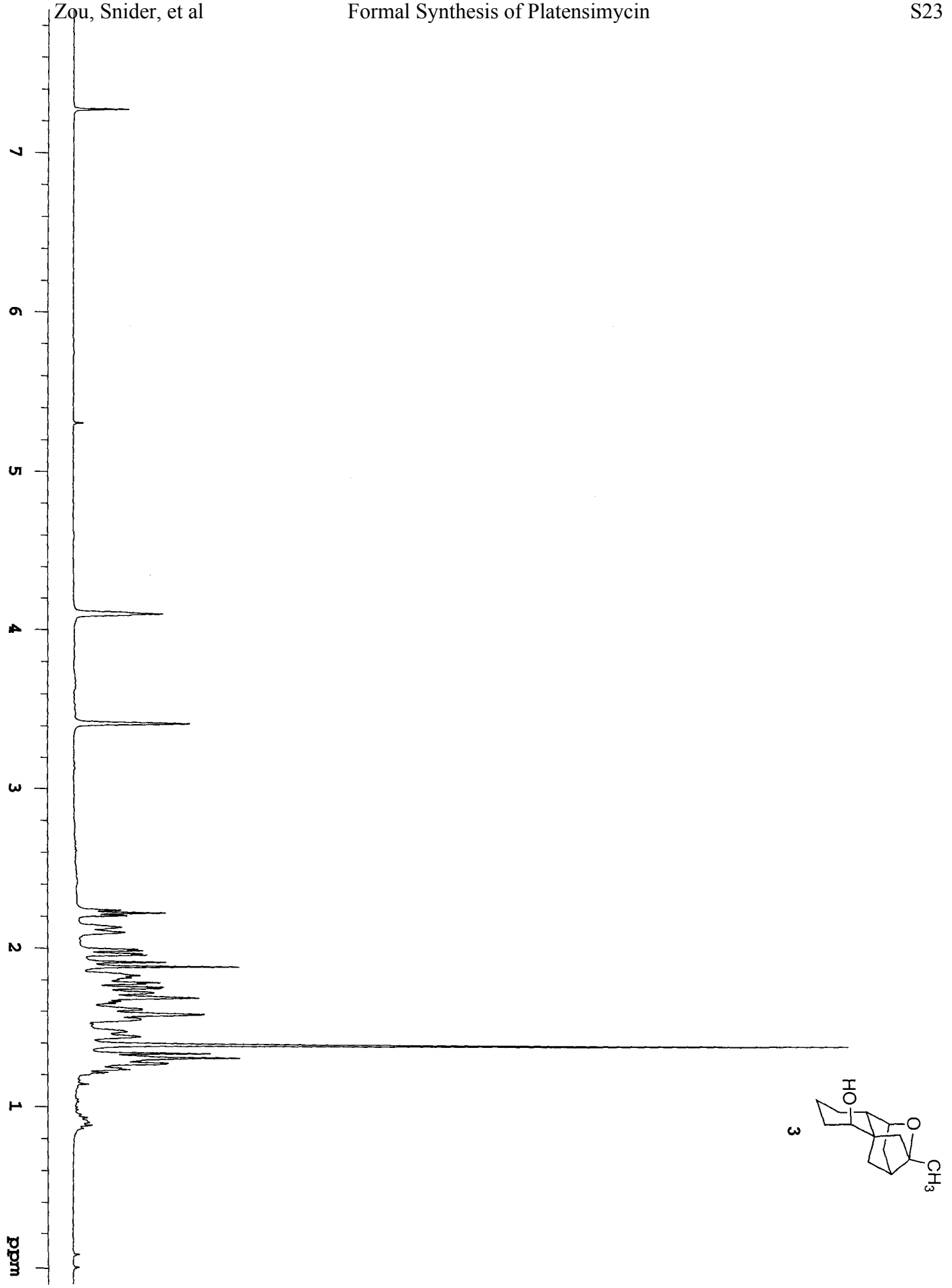
9

INDEX	FREQUENCY	PPM	HEIGHT
1	21216.451	211.071	24.8
2	20968.496	208.604	34.9
3	15058.767	149.812	54.2
4	10900.747	108.446	84.5
5	7771.932	77.319	61.6
6	7739.889	77.000	63.4
7	7707.845	76.681	63.1
8	5917.226	58.867	88.6
9	5834.066	58.040	61.6
10	5029.165	50.032	109.7
11	4228.079	42.063	86.2
12	3977.834	39.573	120.7
13	3877.126	38.571	103.8
14	3761.160	37.418	107.9
15	2436.697	24.241	90.3
16	2152.883	21.418	95.6

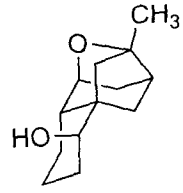


9

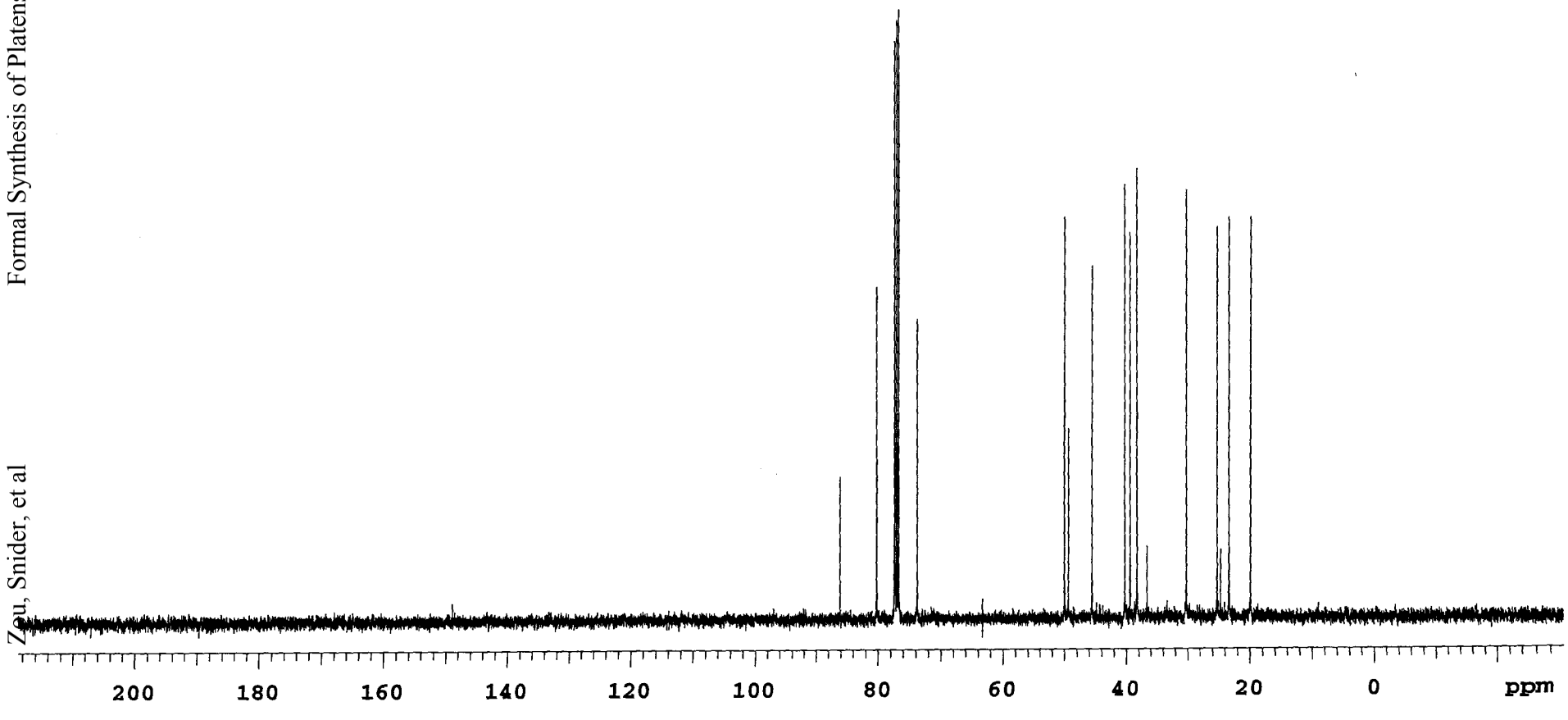


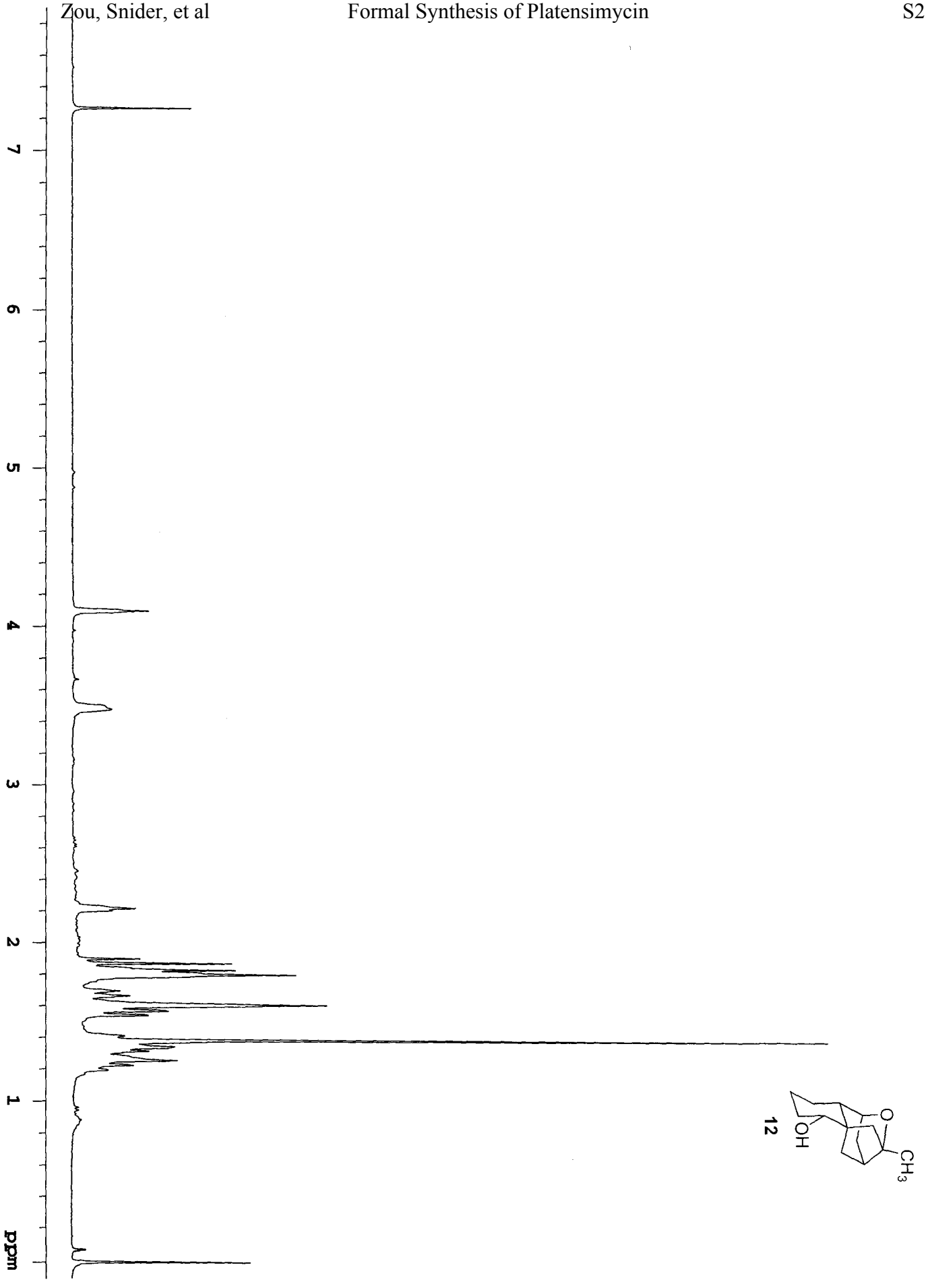

7
6
5
4
3
2
1
ppm
3
HO
O
CH3

INDEX	FREQUENCY	PPM	HEIGHT
1	8653.127	86.085	22.9
2	8058.797	80.173	53.7
3	7771.169	77.311	93.7
4	7739.889	77.000	97.1
5	7707.845	76.681	98.8
6	7408.010	73.698	48.4
7	5021.535	49.957	64.9
8	4956.686	49.311	30.5
9	4574.453	45.509	56.9
10	4044.210	40.234	70.1
11	3956.472	39.361	62.2
12	3844.320	38.245	72.7
13	3032.552	30.169	69.2
14	2532.827	25.198	63.2
15	2343.618	23.315	64.7
16	1997.243	19.870	64.6

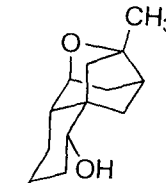


3

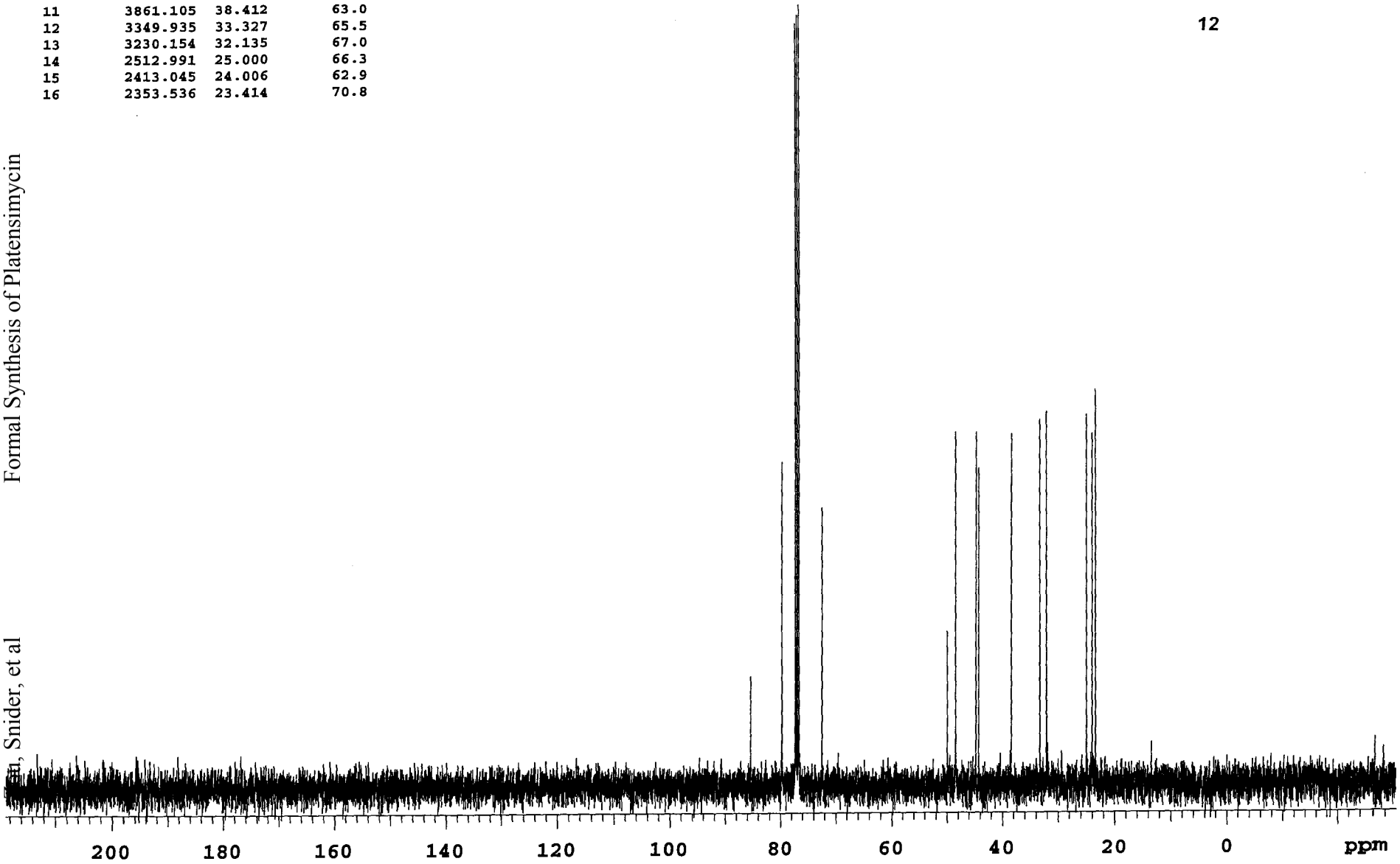


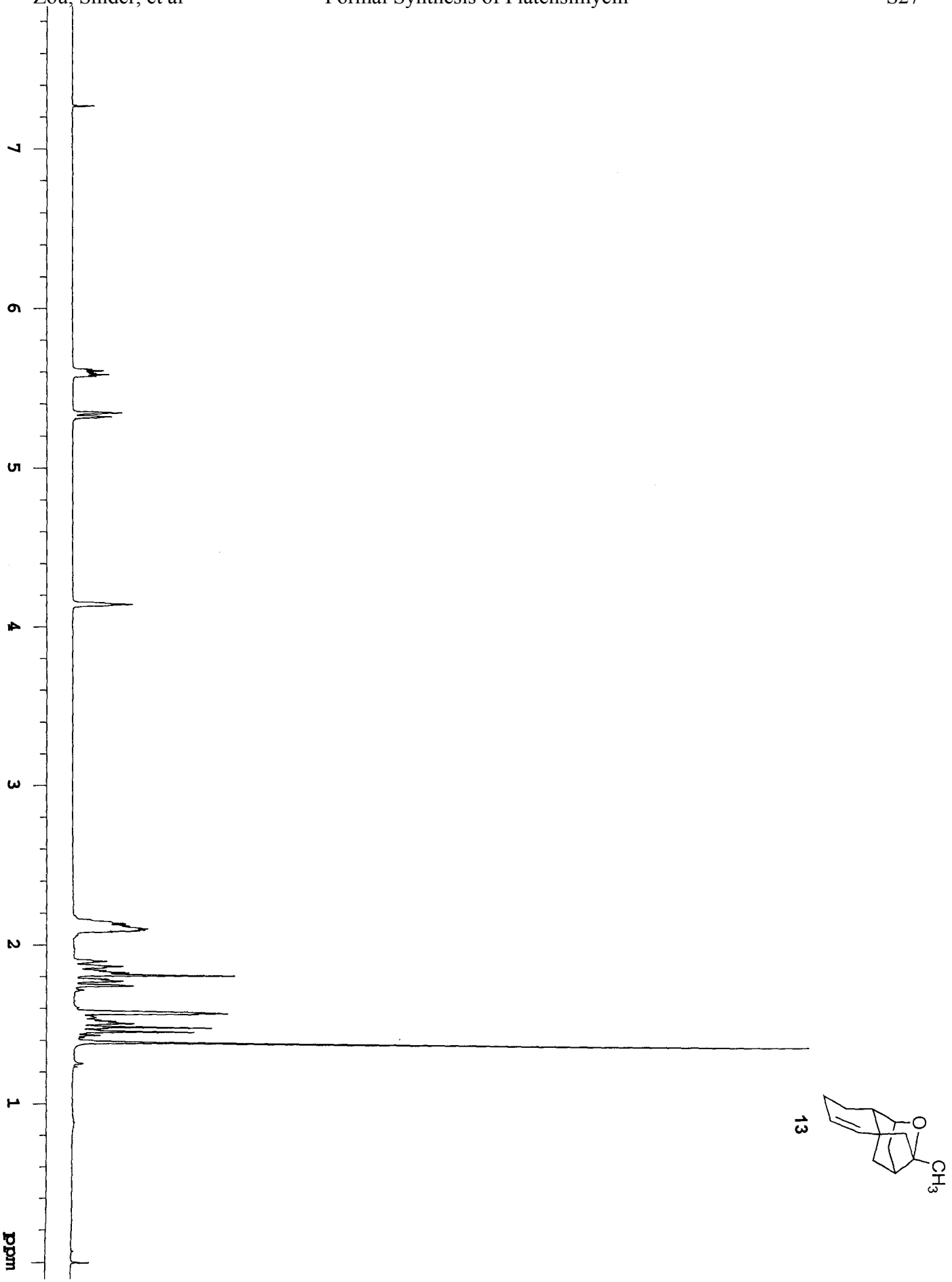

7
6
5
4
3
2
1
ppm
12
OH
O
CH3

INDEX	FREQUENCY	PPM	HEIGHT
1	8587.514	85.433	19.6
2	8017.599	79.763	58.2
3	7771.932	77.319	137.6
4	7739.889	77.000	139.2
5	7707.845	76.681	141.0
6	7288.229	72.507	49.9
7	5024.587	49.987	27.4
8	4871.999	48.469	63.4
9	4501.211	44.780	63.3
10	4450.857	44.279	56.9
11	3861.105	38.412	63.0
12	3349.935	33.327	65.5
13	3230.154	32.135	67.0
14	2512.991	25.000	66.3
15	2413.045	24.006	62.9
16	2353.536	23.414	70.8

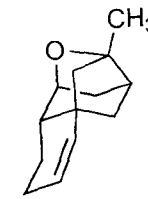


12

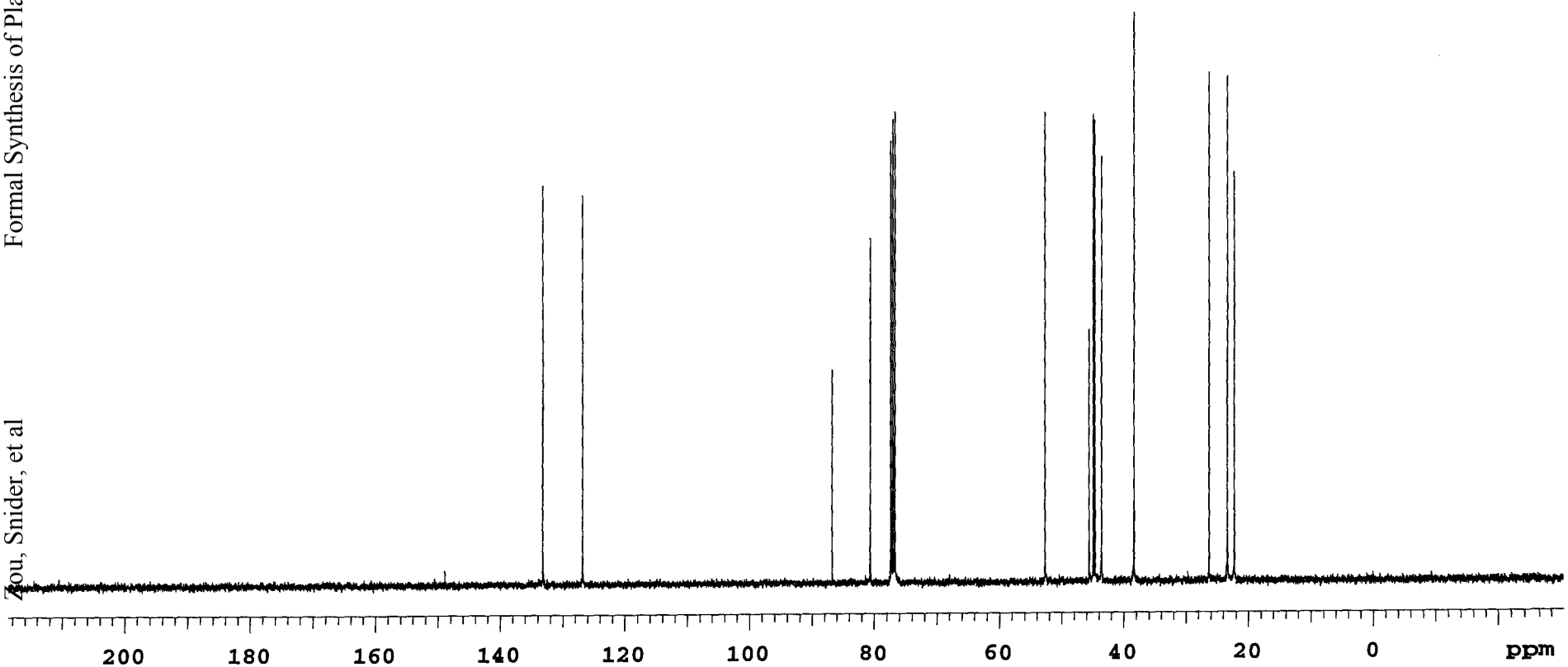


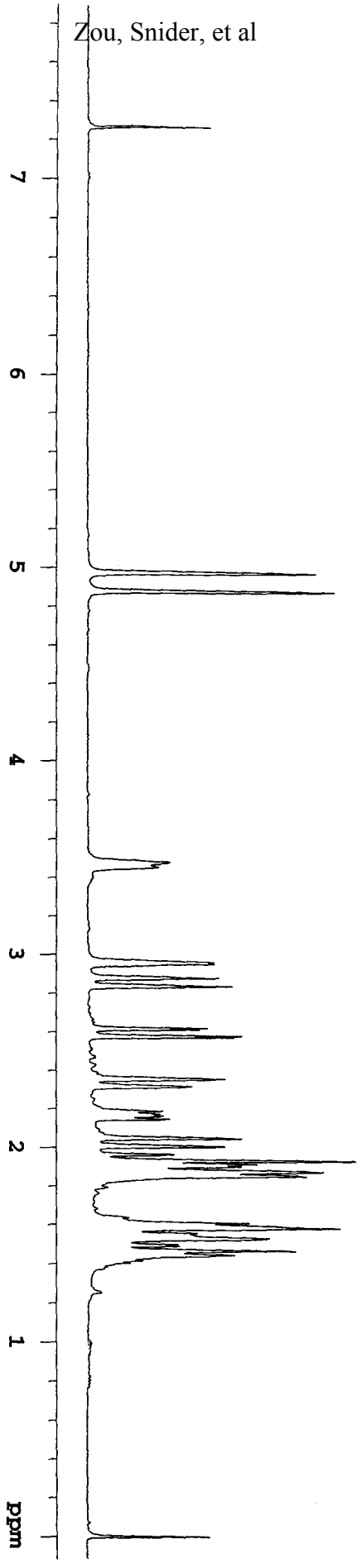

7
6
5
4
3
2
1
ppm
13
O
CH3

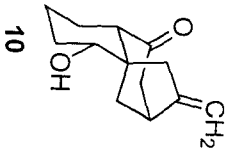
INDEX	FREQUENCY	PPM	HEIGHT
1	13387.929	133.189	64.0
2	12741.720	126.761	62.4
3	8717.977	86.730	34.0
4	8101.522	80.598	55.2
5	7771.932	77.319	70.8
6	7739.889	77.000	74.3
7	7707.845	76.681	75.5
8	5294.668	52.674	75.2
9	4580.556	45.569	40.2
10	4509.603	44.864	74.8
11	4481.374	44.583	74.0
12	4373.800	43.513	68.1
13	3851.186	38.313	91.4
14	2637.350	26.238	81.5
15	2345.144	23.331	80.9
16	2232.992	22.215	65.3



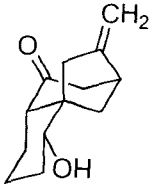
13



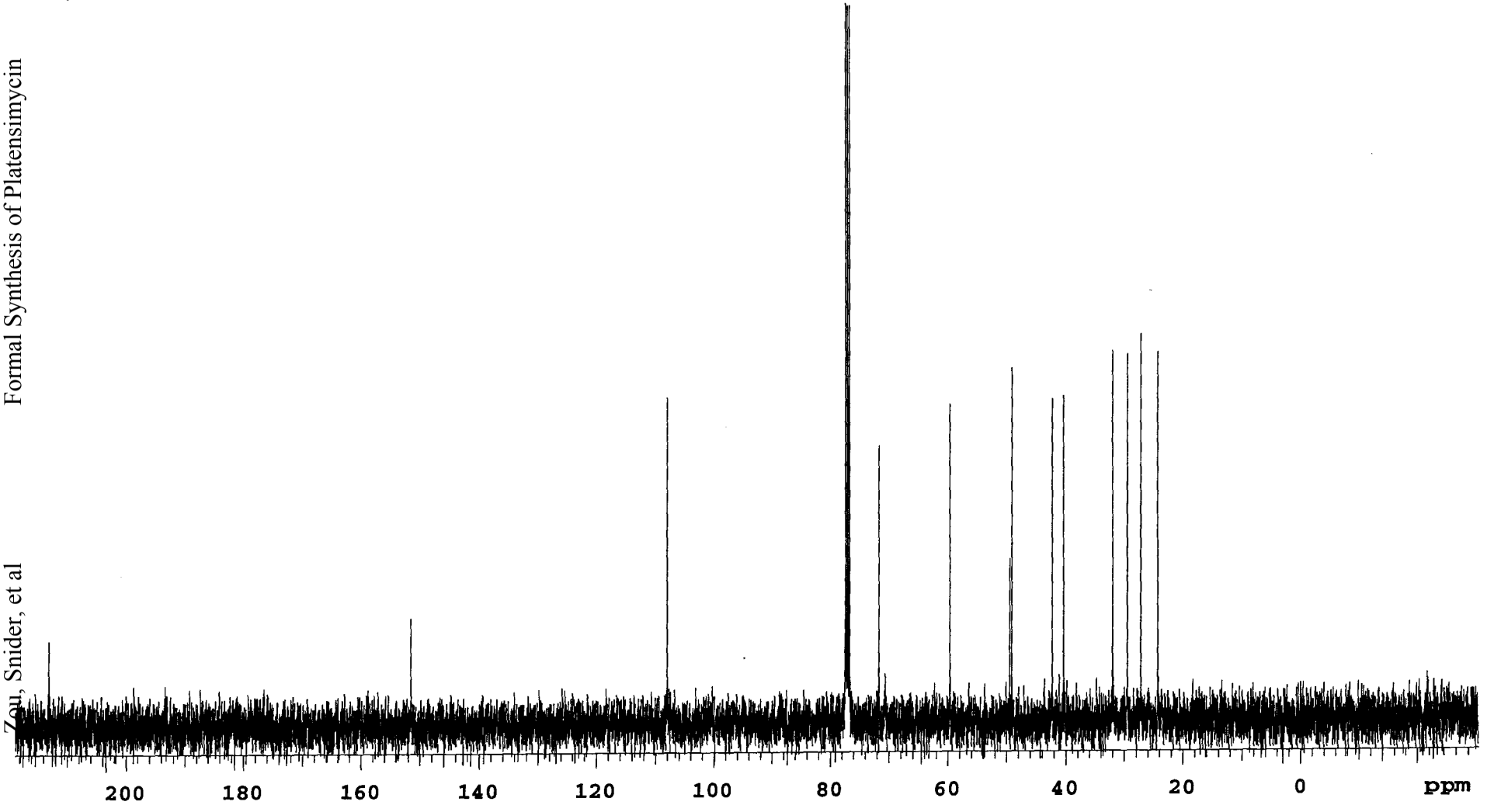

7
6
5
4
3
2
1
ppm

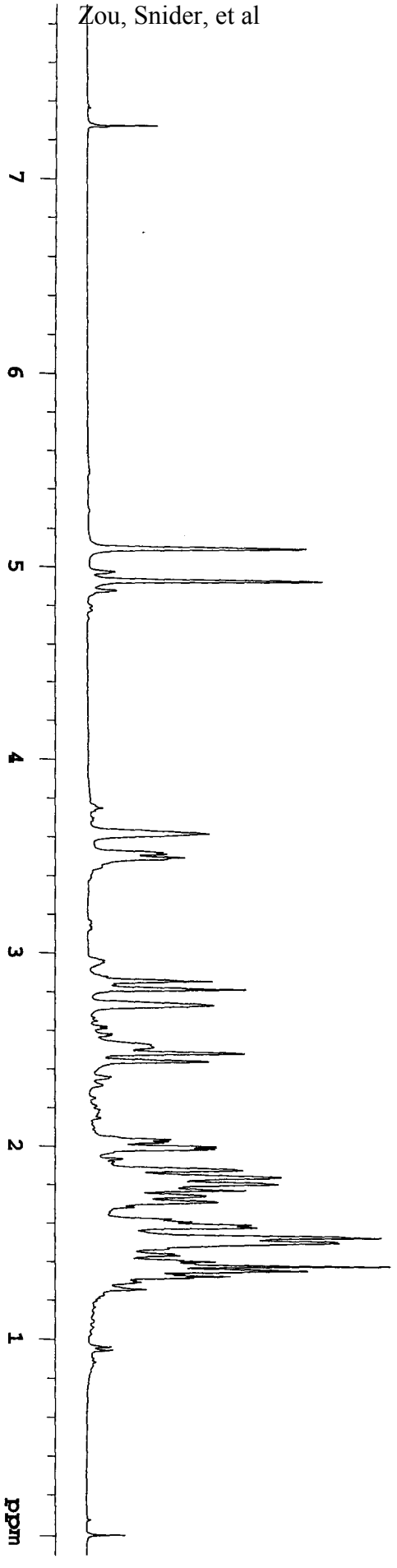

10
OH
O
CH2

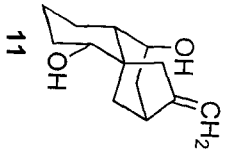
INDEX	FREQUENCY	PPM	HEIGHT
1	21416.341	213.060	14.5
2	15232.717	151.542	18.2
3	10855.733	107.998	55.7
4	7771.932	77.319	123.3
5	7739.889	77.000	122.7
6	7708.608	76.689	122.9
7	7202.016	71.649	47.2
8	5990.468	59.596	54.3
9	4970.418	49.448	27.8
10	4933.797	49.084	60.3
11	4249.441	42.275	55.0
12	4057.943	40.370	55.5
13	3208.791	31.923	63.1
14	2955.495	29.403	62.5
15	2726.613	27.126	66.0
16	2435.171	24.226	62.9



10

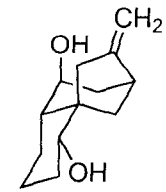




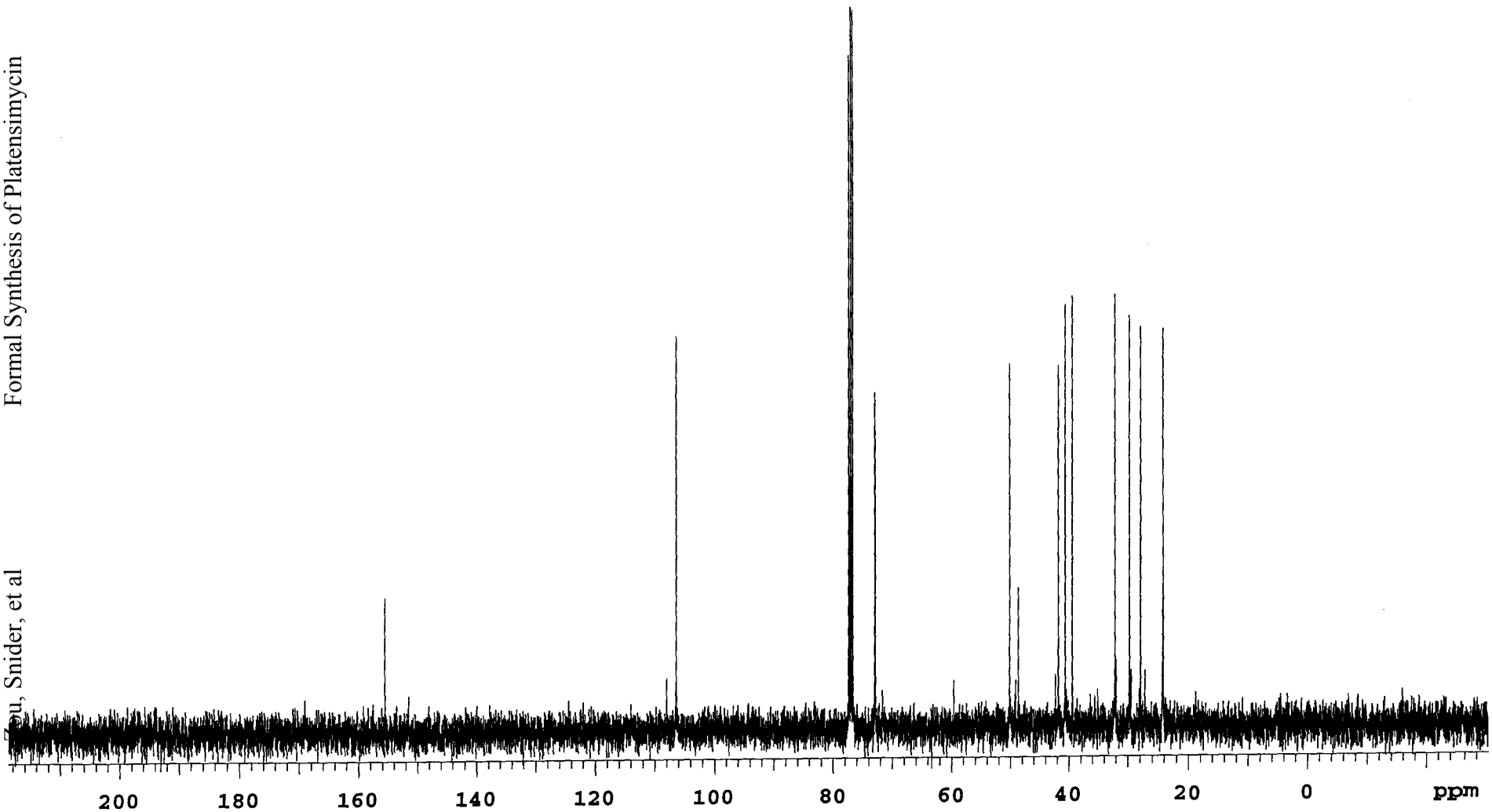


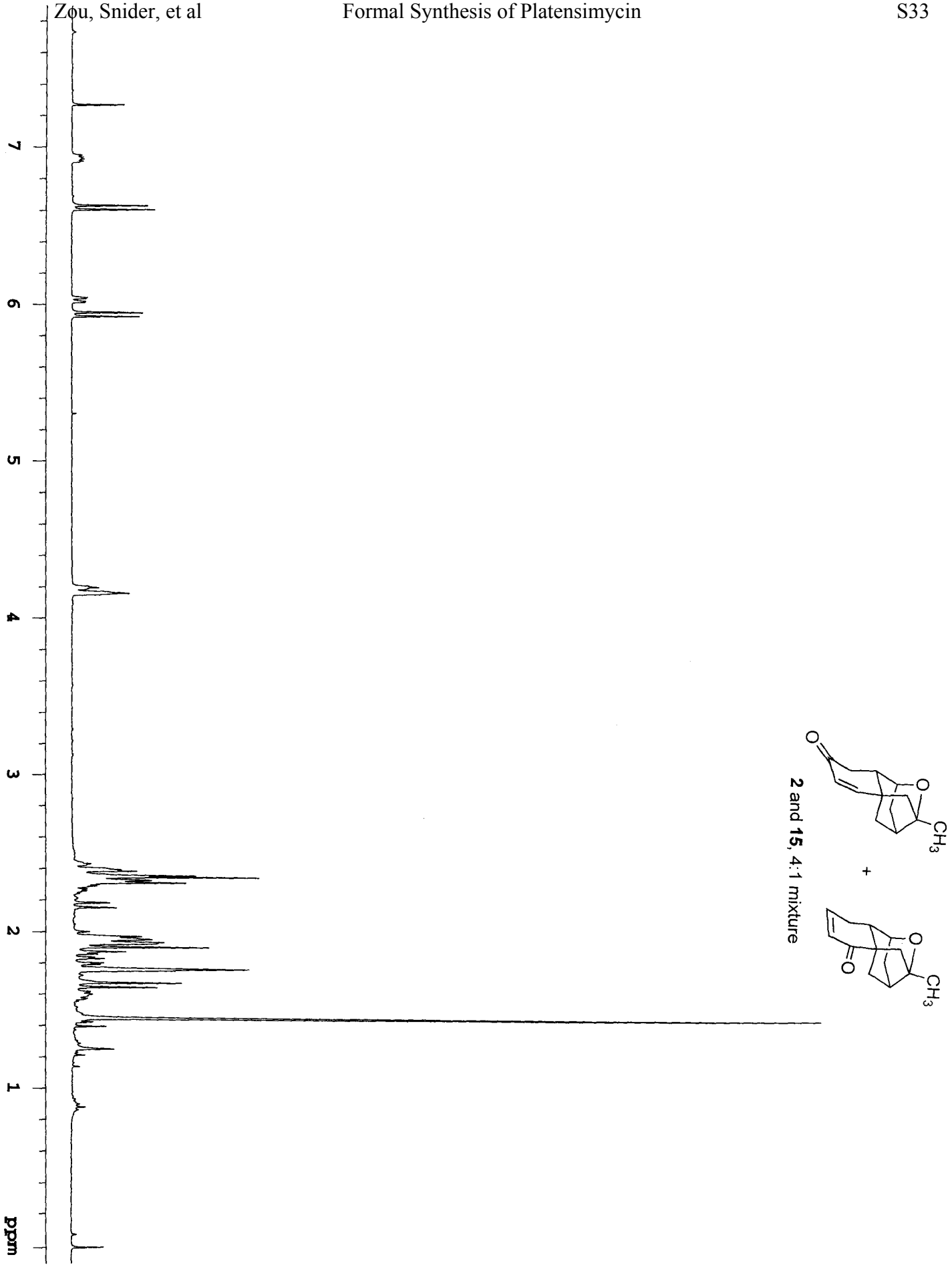
11

INDEX	FREQUENCY	PPM	HEIGHT
1	15639.364	155.588	22.4
2	10691.701	106.366	66.3
3	7771.932	77.319	113.8
4	7739.889	77.000	122.1
5	7707.845	76.681	121.6
6	7327.139	72.894	56.4
7	7320.272	72.825	50.0
8	5032.980	50.070	61.1
9	4882.681	48.575	23.4
10	4199.087	41.774	60.7
11	4080.831	40.598	71.2
12	3957.998	39.376	72.5
13	3224.050	32.074	72.8
14	2981.435	29.661	69.2
15	2797.567	27.831	67.3
16	2423.727	24.112	66.9

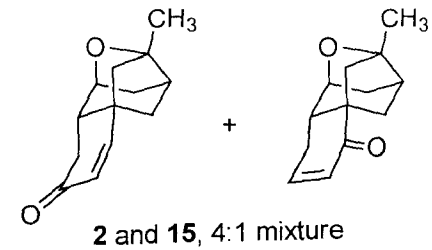


11

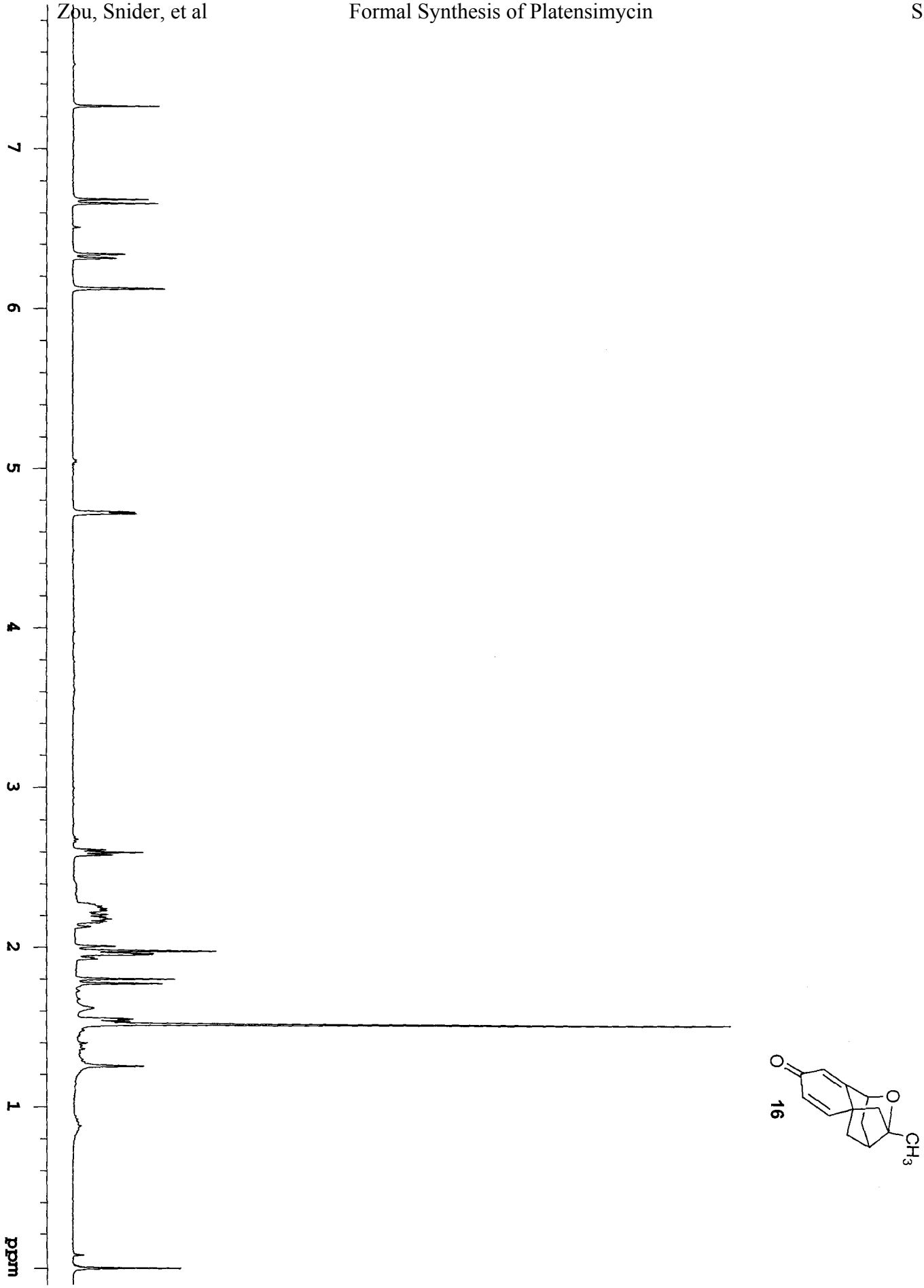



7
6
5
4
3
2
1
ppm
O
O
CH3
+
O
O
CH3
2 and 15, 4:1 mixture

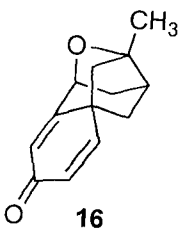
INDEX	FREQUENCY	PPM	HEIGHT
1	20172.750	200.688	8.9
2	20014.059	199.109	31.9
3	15599.691	155.193	68.6
4	14845.144	147.686	28.0
5	12996.542	129.296	33.1
6	12950.002	128.833	77.5
7	8746.206	87.011	45.3
8	8676.778	86.321	21.6
9	7936.727	78.958	69.6
10	7892.477	78.518	33.8
11	7771.932	77.319	284.8
12	7739.889	77.000	284.0
13	7708.608	76.689	280.5
14	5403.005	53.752	22.2
15	5190.145	51.634	81.6
16	4727.041	47.027	37.7
17	4641.592	46.177	53.8
18	4469.167	44.461	35.3
19	4434.072	44.112	102.2
20	4289.114	42.670	87.0
21	4241.811	42.200	95.9
22	4180.013	41.585	43.8
23	4132.711	41.114	43.4
24	3851.949	38.321	44.6
25	3809.988	37.904	92.7
26	3761.922	37.425	104.2
27	2982.198	29.668	8.3
28	2652.608	26.389	46.0
29	2321.493	23.095	102.0
30	2316.915	23.050	42.0



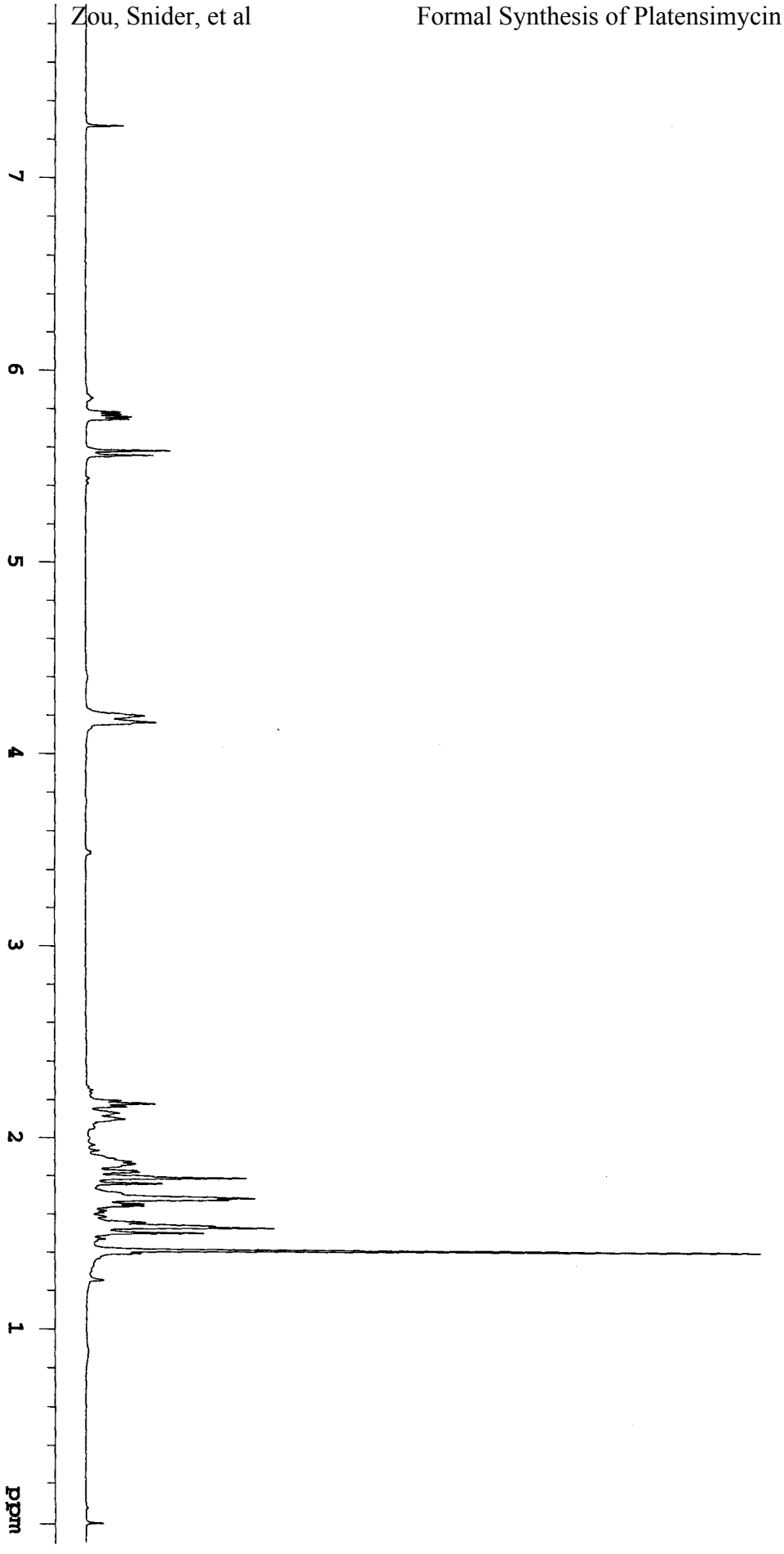
2 and **15**, 4:1 mixture

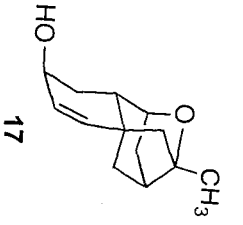

7
6
5
4
3
2
1
ppm
O
O
CH3
16

INDEX	FREQUENCY	PPM	HEIGHT
1	18808.614	187.117	16.6
2	16129.934	160.468	13.8
3	15174.734	150.965	51.0
4	13067.495	130.001	49.7
5	12246.572	121.835	48.7
6	8754.598	87.095	31.2
7	8038.961	79.975	53.8
8	7771.932	77.319	166.2
9	7739.889	77.000	172.9
10	7707.845	76.681	171.1
11	5507.528	54.791	62.2
12	5014.669	49.888	21.3
13	4886.495	48.613	61.1
14	4457.723	44.347	58.6
15	4273.855	42.518	62.5
16	2232.229	22.207	61.3



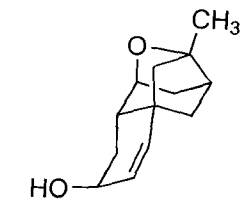
16



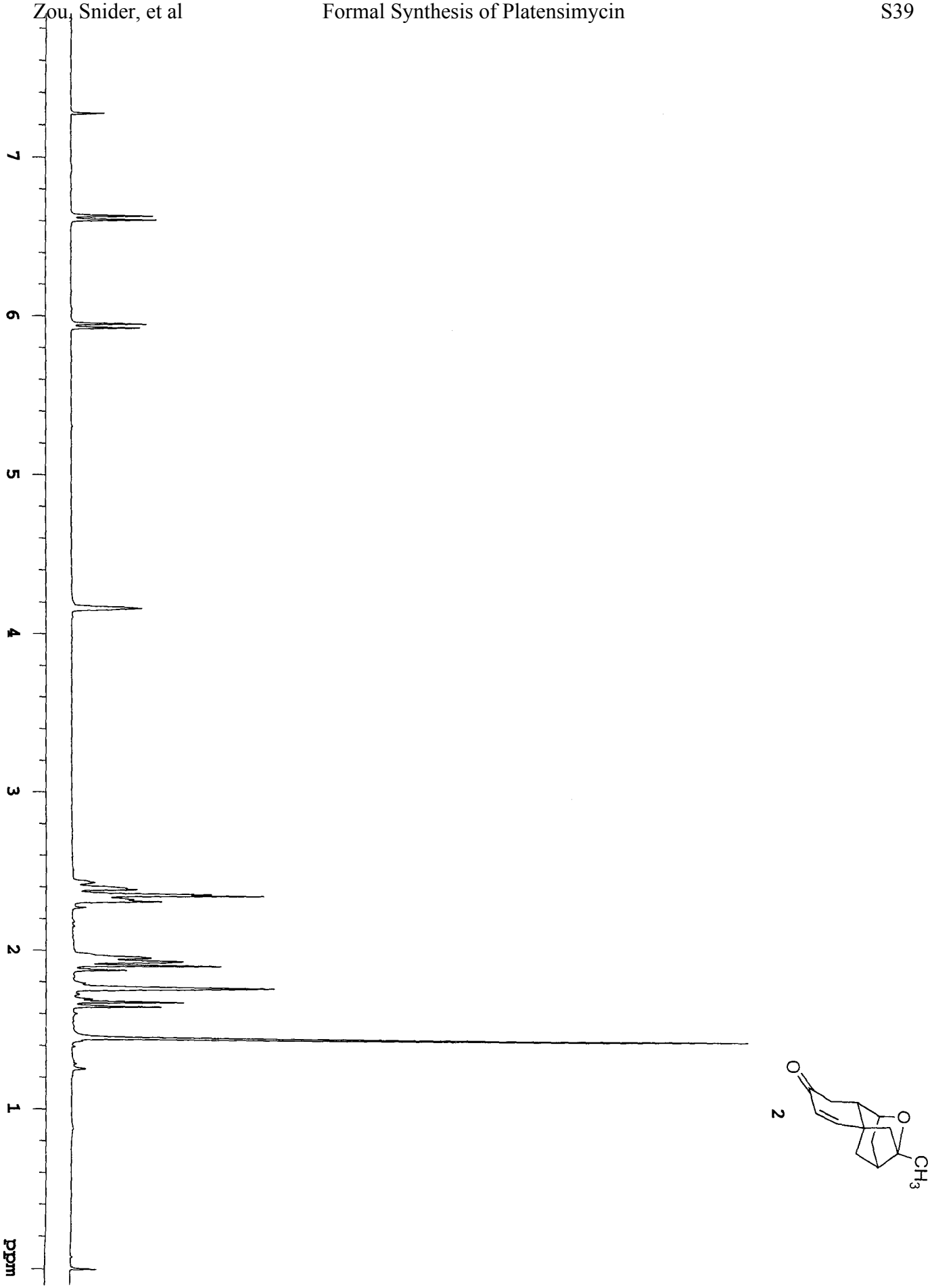


17

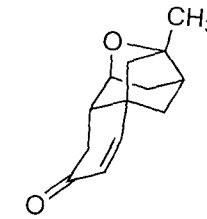
INDEX	FREQUENCY	PPM	HEIGHT
1	13815.938	137.447	66.2
2	12818.014	127.520	62.4
3	8717.214	86.723	26.4
4	8064.138	80.226	70.7
5	7771.932	77.319	165.4
6	7739.889	77.000	171.5
7	7707.845	76.681	167.5
8	6461.965	64.287	74.1
9	5245.077	52.180	72.6
10	4601.919	45.782	31.9
11	4447.805	44.249	78.4
12	4297.506	42.754	82.5
13	3818.380	37.987	82.5
14	3792.440	37.729	74.3
15	3140.890	31.247	83.7
16	2334.463	23.224	77.6



17


7
6
5
4
3
2
1
ppm
O
O
CH3
2

INDEX	FREQUENCY	PPM	HEIGHT
1	20011.770	199.086	19.8
2	15598.165	155.178	49.4
3	12949.239	128.825	52.6
4	8744.680	86.996	22.3
5	7935.201	78.943	55.1
6	7771.932	77.319	106.9
7	7739.889	77.000	112.8
8	7707.845	76.681	112.9
9	5189.382	51.626	59.4
10	4640.829	46.169	28.9
11	4433.309	44.105	64.7
12	4288.351	42.662	63.5
13	4241.048	42.192	66.2
14	3809.225	37.896	72.7
15	3761.160	37.418	67.3
16	2320.730	23.088	67.8



2