Synthesis of (±)-Vibralactone

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Supporting Information

Experimental Section

General procedure. NMR spectra were recorded at 400 MHz in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ, coupling constants in Hz, and IR spectra in cm^{-1}.

Methyl 2-Methoxy-1-(3-methyl-2-butenyl)-2,5-cyclohexadiene-1-carboxylate (10). *t*-BuOH (0.44 g, 6.0 mmol) was added to a solution of methyl 2-methoxybenzonate (**8**) (1.0 g, 6.0 mmol) in dry THF (5 mL) and the solution was cooled to -78 °C. Liquid ammonia (60 mL) was condensed into this mixture under nitrogen and potassium was added until the reaction mixture maintained a deep blue coloration for 5 min. 1,3-pentadiene was added dropwise (2-20 drops) until the solution turned yellow-brown. Anhydrous lithium iodide (1.8 g, 13 mmol) was added and the solution was stirred for 1 h at -78 °C. A solution of prenyl bromide (2.69 g, 18 mmol) in dry THF (6 mL) was added. The resulting light yellow solution was stirred for another hour. The reaction was allowed to warm to 25 °C, and the ammonia was removed with a stream of nitrogen. Brine was added and the reaction mixture was extracted with Et_2O. The combined Et_2O extracts were washed with 10% aqueous sodium thiosulfate solution, water, and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to give 2.44 g of crude **10** as a yellow oil. Flash chromatography (20:1 hexanes/EtOAc) gave 1.10 g (77%) of pure **10**: ^{1}H NMR 5.88 (dt, 1, *J* = 9.6, 3.3), 5.42 (br d, 1, *J* = 9.6), 4.94 (t, 1, *J* = 7.6), 4.83 (dd, 1, *J* = 3.7, 3.7), 3.70 (s, 3), 3.52 (s, 3), 2.86 (dddd, 1, *J* = 22.4, 3.7, 3.3, 3.0), 2.77 (dddd, 1, *J* = 22.4, 3.7, 3.3, 3.0); 2.73 (dd, 1, *J* = 14.4, 7.6), 2.43 (dd, 1, *J* = 14.4, 7.6), 1.66 (s, 3), 1.59 (s, 3); ^{13}C NMR 174.1, 152.8, 133.7, 126.9, 126.4, 119.3, 93.3, 54.2, 52.4, 51.8, 33.3, 26.4, 26.0, 17.9; IR (neat) 1735, 1689, 1235; HRMS (EI) calcd for $C_{14}H_{20}O_3$ (M^+) 236.1413, found 236.1415. The 22.4 Hz geminal coupling constant is characteristic of 1,4-cyclohexadienes.[20]

Methyl 1-(3-Methyl-2-butenyl)-6-oxo-2-cyclohexenecarboxylate (9). A solution of diene **10** (800 mg, 3.39 mmol) in MeOH (10 mL) and 5% aqueous hydrochloric acid (5 mL) was stirred at 25 °C for 1 h. The reaction mixture was then neutralized with saturated aqueous sodium carbonate. MeOH was removed under reduced pressure. The residue was extracted three times with EtOAc

(15 mL). The combined extracts were washed with water and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to give 795 mg of crude ketone **9**. Flash chromatography (15:1 hexanes/EtOAc) gave 675 mg (84%) of pure **9**: ^{1}H NMR 6.07 (ddd, 1, *J* = 10.0, 3.8, 3.8), 5.69 (br d, 1, *J* = 10.0), 4.97 (t, 1, *J* = 7.6), 3.69 (s, 3), 2.74 (dd, 1, *J* = 14.4, 7.6), 2.71-2.60 (m, 1), 2.58-2.48 (m, 2), 2.47-2.38 (m, 2), 1.66 (s, 3), 1.60 (s, 3); ^{13}C NMR 207.4, 171.4, 135.5, 129.3, 128.7, 118.0, 60.2, 52.6, 38.0, 33.6, 25.9, 25.4, 17.9; IR (neat) 3032, 1742, 1718, 1228; HRMS (EI) calcd for $C_{13}H_{18}O_3$ (M^+) 222.1256, found 222.1254.

Methyl (1*R, 6*R*)-6-Hydroxy-1-(3-methyl-2-butenyl)-2-cyclohexenecarboxylate (6).** Anhydrous $CaCl_2$ (360 mg, 3.24 mmol) was added to a solution of ketone **9** (315 mg, 1.42 mmol) in MeOH (10 mL). The mixture was stirred at 25 °C for 20 min. The reaction was then cooled to 0 °C and sodium borohydride (108 mg, 2.82 mmol) was added portionwise. After a couple of minutes, the reaction turns milky. The reaction was stirred for 30 min and the solvent was removed under reduced pressure. The residue was diluted with EtOAc (50 mL), which was washed with 10% aqueous HCl and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to give 400 mg of crude alcohols **6** and **5**. Flash chromatography (12:1 hexanes/EtOAc) gave 220 mg (69%) of pure **6** followed by 47 mg (15%) of a 1:2 mixture of **6** and **5**.

10 mL of 0.15 M $Zn(BH_4)_2$ solution in Et_2O[11] was added to a solution of ketone **9** (920 mg, 4.14 mmol) in dry Et_2O (10 mL) under nitrogen at -78 °C. The reaction was stirred at -78 °C for 2 h and slowly warmed to 25 °C. The mixture was quenched with H_2O and extracted with 50 mL of Et_2O. The Et_2O extract was washed with 5% hydrochloric acid, H_2O, and brine, dried ($MgSO_4$), and concentrated to give crude **6** containing no **5**. Flash chromatography (12/1 hexanes/EtOAc) gave 668 mg (69%) of pure **6**: ^{1}H NMR 5.755 (br d, 1, *J* = 11.0), 5.745 (d, 1, *J* = 11.0), 5.12 (dd, 1, *J* = 7.3, 7.9), 4.14 (ddd, 1, *J* = 6.7, 6.0, 3.6), 3.70 (s, 3), 2.77 (d, 1, *J* = 3.6, OH), 2.63 (dd, 1, *J* = 14.4, 7.3), 2.33 (dd, 1, *J* = 14.4, 7.9), 2.22-2.04 (m, 2), 1.88-1.76 (m, 2), 1.70 (br s, 3), 1.60 (br s, 3); ^{13}C NMR 176.4, 134.7, 127.45, 127.38, 118.8, 70.0, 52.0, 51.9, 32.9, 26.0, 25.8, 23.1, 17.8; IR 3512, 3026, 1727, 1225; HRMS (EI) calcd for $C_{13}H_{20}O_3$ (M^+) 224.1413, found 224.1413.

Methyl (1*R, 6*S*)-6-Hydroxy-1-(3-methyl-2-butenyl)-2-cyclohexenecarboxylate (5).** Tetramethylammonium borohydride (166 mg, 1.86 mmol) was added to a solution of ketone **9** (207 mg, 0.93 mmol) in MeOH (5 mL) and THF (5 mL) at 0 °C. The ice bath was removed and the reaction was stirred at 25 °C for 12 h. The solvent was removed under reduced pressure. The residue was diluted with EtOAc, and the resulting solution was washed with 10% aqueous HCl, water, and brine. The organic layer was dried ($MgSO_4$) and concentrated to give 220 mg of crude **5** and **6**. Flash chromatography (12:1 hexanes/EtOAc) gave 85 mg (40%) of a 2:1 mixture of **6** and **5** followed by 88 mg (42%) of **5**: ^{1}H NMR 5.78 (ddd, 1, *J* = 9.8, 3.7, 3.7), 5.67 (br d, 1, *J* = 9.8), 5.07 (dd, 1, *J* = 7.2, 7.2), 3.79 (ddd, 1, *J* = 9.2, 9.2, 3.0), 3.71 (s, 3), 3.28 (d, 1, *J* = 9.2, OH), 2.52-2.40 (m, 2), 2.25-2.05 (m, 2), 1.95-1.86 (m, 1), 1.84-1.73 (m, 1), 1.70 (br s, 3), 1.62 (br s, 3); ^{13}C NMR 176.2, 135.2, 128.5, 127.6, 118.3, 71.1, 52.3, 52.0, 35.8, 27.4, 26.0, 23.5, 17.9; IR 3509, 3029, 1728, 1713; HRMS (EI) calcd for $C_{13}H_{20}O_3$ (M^+) 224.1413, found 224.1415.

Oxidation of Alcohols 5 and 6 to Ketone 9. A solution of Dess-Martin periodinane (294 mg, 0.69 mmol) dissolved in CH_2Cl_2 (10 mL) at 0 °C under nitrogen was treated with a solution of 2:1 mixture of alcohol **6** and **5** (73 mg, 0.32 mmol) in CH_2Cl_2 (3 mL). The reaction was stirred for 1 h, and slowly warmed to 25 °C. The solvent was removed under reduced pressure to give 520 mg of crude ketone **9**. Flash chromatography (8:1 hexanes/EtOAc) gave 68 mg (94%) of pure ketone **9**.

2-(3-Methyl-2-butenyl)-1,3-cyclohexadiene (13) and (1*R,6*S*)-1-(3-Methyl-2-butenyl)-7-oxabicyclo[4.2.0]oct-2-ene-8-one (14).** A solution of trans hydroxy ester **6** (159 mg, 0.71 mmol) in MeOH (10 mL) was treated with 3.6 M KOH (5 mL) and heated at 60 °C for 1 h. The solution was cooled and neutralized with 10 % aqueous HCl. MeOH was removed under reduced pressure. The aqueous layer was saturated with NaCl and extracted with EtOAc. The EtOAc extracts were then dried ($MgSO_4$) and concentrated to give 140 mg of crude hydroxy acid **11** that was used without purification.

A solution of crude hydroxy acid **11** in dry CH_2Cl_2 (3 mL) at 0 °C was treated with NEt_3 (271 mg, 2.68 mmol) and MsCl (230 mg, 2.01 mmol) under nitrogen. The mixture was stirred at 0 °C for 30 min. The mixture was allowed to warm to 25 °C, diluted with CH_2Cl_2, and washed with

cold 5% HCl, ice water, and brine. The organic layer was dried ($MgSO_4$) and concentrated to give 275 mg of unstable crude bis mesylate **12**.

A solution of crude bis mesylate **12** in THF (6 mL) and saturated aqueous $NaHCO_3$ (6 mL) was stirred at 25 °C for 20 h. The reaction was diluted with Et_2O, washed with water and brine, and dried ($MgSO_4$). Flash chromatography (pentane to 6:1 pentane/Et_2O) gave 48 mg (46%) of triene **13** followed by 46 mg (33%) of β-lactone **14**.

Data for **13**: ^{1}H NMR 5.83 (dt,1, *J* = 10.0, 3.7), 5.79 (br d, 1, *J* = 10.0), 5.46 (br, 1, $w_{1/2}$ = 8.0), 5.13 (t, 1, *J* = 7.2), 2.71 (d, 2, *J* = 7.2), 2.10 (br, 4), 1.72 (br s, 3), 1.64 (br s, 3); ^{13}C NMR 135.0, 132.7, 127.2, 126.7, 121.9, 119.9, 34.1, 25.8, 22.42, 22.38, 17.7; IR 3033, 1672, 1654; HRMS (EI) calcd for $C_{11}H_{16}$ (M^+) 148.1252, found 148.1250.

Data for **14**: ^{1}H NMR 6.16 (ddd, 1, *J* = 10.0, 7.2, 2.3), 5.57 (dd, 1, *J* = 10.0, 3.0), 5.11 (br t, 1, *J* = 7.6), 4.65-4.62 (m, 1), 2.55 (dd, 1, *J* = 14.4, 7.6), 2.46 (dd, 1, *J* = 14.4, 7.6), 2.31-2.22 (m, 1), 2.22-2.16 (m, 1), 2.15-2.04 (m, 1), 1.73 (br s, 3), 1.65 (br s, 3), 1.40 (dddd, 1, *J* = 14.4, 12.0, 6.0, 3.0); ^{13}C NMR 171.0, 136.4, 132.2, 123.8, 117.1, 76.5, 57.4, 31.3, 25.8, 23.4, 18.6, 18.0; IR 1818, 1672, 1442; HRMS (CI) calcd for $C_{12}H_{17}O_2$ (MH^+) 193.1229, found 193.1227.

Preparation of β-Lactone 14 from Cis Hydroxy Ester 5 A solution of cis hydroxy ester **5** (22 mg, 0.10 mmol) in MeOH (5 mL) was treated with 3.6 M KOH (2 mL) and heated at 60 °C for 1 h. The solution was cooled and neutralized with 10 % aqueous HCl. MeOH was removed under reduced pressure. The aqueous layer was saturated with NaCl and extracted with EtOAc. The EtOAc extracts were then dried ($MgSO_4$) and concentrated to give 20 mg of crude hydroxy acid that was used without purification.

A solution of the crude hydroxy acid in pyridine was cooled to 0 °C and TsCl (38 mg, 0.20 mmol) was added. The mixture was well shaken, sealed and kept in a refrigerator (4 °C) overnight. The mixture was poured onto crushed ice (10 mL) which was extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$) and concentrated. Flash chromatography (6:1 hexanes/Et_2O) gave 16 mg (83%) of pure β-lactone **14**.

(3*S,5*R*,10*S*)-3-(1-Iodo-1-methylethyl)-10-hydroxy-2-oxaspiro[4.5]dec-6-en-1-one (16) and (3*R**,5*R*,10*S*)-3-(1-Iodo-1-methylethyl)-10-hydroxy-2-oxaspiro[4.5]dec-6-en-1-one (17).** A solution of hydroxy ester **5** (316 mg, 1.41 mmol) in MeOH (15 mL) and 6 mL of 3.6 M aqueous KOH solution was heated at 60 °C for 3 h and cooled. The MeOH was removed under reduced pressure. The residue was neutralized with 10% aqueous HCl to pH 1 ~ 2, and then treated with solid sodium bicarbonate until CO_2 evolution ceased. THF (15 mL), KI (468 mg, 2.82 mmol) and I_2 (716 mg, 2.82 mmol) were then added. The mixture was stirred overnight, quenched with 10% aqueous sodium thiosulfate solution, and extracted with EtOAc. The extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to give 645 mg of crude lactones **16** and **17**. Flash chromatography (2:1 hexanes/EtOAc) gave 297 mg (63%) of **16** followed by 153 mg (32%) of **17**. A sample of **17** was recrystallized for X-ray crystal structure determination by dissolution in Et_2O at 25 °C and cooling to 4 °C for 2 d.

Data for **16**: mp 92-93 °C (decomposition); ^{1}H NMR 5.93 (ddd, 1, *J* = 10.0, 3.7, 3.7), 5.58 (br d, 1, *J* = 10.0), 4.17 (dd, 1, *J* = 10.4, 6.4), 3.76 (ddd, 1, *J* = 10.4, 7.6, 2.5), 2.56 (dd, 1, *J* = 12.4, 10.4), 2.46-2.38 (m, 1), 2.35 (d, 1, *J* = 7.6, OH), 2.33-2.26 (m, 1), 2.26 (dd, 1, *J* = 12.4, 6.4), 2.22-2.12 (m, 1), 2.00 (s, 3), 1.98 (s, 3), 1.91-1.83 (m, 1); ^{13}C NMR 177.0, 130.9, 123.7, 84.0, 70.8, 51.4, 46.8, 38.6, 34.1, 31.4, 26.6, 23.9; IR 3444, 1752; HRMS (EI) calcd for $C_{12}H_{17}IO_3$ (M^+) 336.0229, found 336.0223.

Data for **17**: mp 104-107 °C (decomposition); ^{1}H NMR 5.96 (ddd, 1, *J* = 10.0, 4.8, 2.4), 5.45 (br d, 1, *J* = 10.0), 3.87-3.78 (m, 2), 2.54 (dd, 1, *J* = 13.6, 7.2), 2.37-2.13 (m, 3), 2.26 (dd, 1, *J* = 13.6, 9.0), 2.00 (s, 3), 1.92 (s, 3), 1.88 (d, 1, *J* = 5.6, OH), 1.84-1.75 (m, 1); ^{13}C NMR 177.0, 131.2, 126.7, 85.3, 75.2, 52.0, 50.6, 42.6, 33.2, 33.0, 27.4, 24.3; IR 3448, 1749; HRMS (EI) calcd for $C_{12}H_{17}IO_3$ (M^+) 336.0229, found 336.0221.

(3*S,5*R*,9*S*)-3-(1-Iodo-1-methylethyl)-9-hydroxy-1-oxo-2-oxaspiro[4.4]non-6-ene-7-carboxaldehyde (18).** A solution of **16** (170 mg, 0.50 mmol) in a mixture of dry CH_2Cl_2 (10 mL) and MeOH (10 mL) was ozonolyzed at -78 °C until the solution turned light blue and then purged with oxygen until the blue color disappeared. The solution was then treated with PPh_3 (157 mg,

0.60 mmol) and allowed to slowly warm to 25 °C. To this solution was added 40 mL of dry benzene and the solution was then concentrated to 5 mL. Another 10 mL of dry benzene was added and the solution was concentrated to 5 mL again. Finally another 10 mL dry benzene and Bn_2NH•TFA (30 mg, 0.10 mmol) was added and the solution was stirred overnight. The solvent was removed under reduced pressure to give crude **18**. Flash chromatography (2:1 hexanes/EtOAc) gave 140 mg (80%) of pure **18**: ^{1}H NMR 9.73 (s, 1), 6.61 (br s, 1), 4.52 (ddd, 1, *J* = 8.4, 8.4, 8.8), 4.20 (dd, 1, *J* = 9.7, 6.7), 3.01 (dd, 1, *J* = 16.4, 8.4), 2.76 (br dd, 1, *J* = 16.4, 8.4), 2.76 (d, 1, *J* = 8.8, OH), 2.59 (dd, 1, *J* = 13.6, 6.7), 2.52 (dd, 1, *J* = 13.6, 9.7), 2.02 (s, 3), 1.99 (s, 3); ^{13}C NMR 188.8, 174.7, 147.7, 144.8, 85.5, 79.0, 61.7, 45.6, 37.4, 36.2, 34.1, 31.3; IR 3460, 1763, 1683, 1188; HRMS (CI) calcd for $C_{12}H_{16}IO_4$ (MH^+) 351.0094, found 351.0091.

(3*R,5*R*,9*S*)-3-(1-Iodo-1-methylethyl)-9-hydroxy-1-oxo-2-oxaspiro[4.4]non-6-ene-7-carboxaldehyde (19).** A solution of **17** (173 mg, 0.51 mmol) in a mixture of dry CH_2Cl_2 (10 mL) and MeOH (10 mL) was ozonolyzed at -78 °C until the solution turned light blue and then purged with oxygen until the blue color disappeared. The solution was then treated with PPh_3 (160 mg, 0.61 mmol), and allowed to slowly warm to 25 °C. To this solution was added 40 mL of dry benzene and the solution was then concentrated to 5 mL. Another 10 mL of dry benzene was added and the solution was concentrated to 5 mL again. Finally another 10 mL dry benzene and Bn_2NH•TFA (30 mg, 0.10 mmol) was added and the solution was stirred overnight. The solvent was removed under reduced pressure to give crude **19**. Flash chromatography (2:1 hexanes/EtOAc to 1:1 hexanes/EtOAc) gave 163 mg (90%) of pure **19**: ^{1}H NMR 9.76 (s, 1), 6.59 (br s, 1), 4.56 (ddd, 1, *J* = 7.2, 7.2, 7), 3.85 (dd, 1, *J* = 8.0, 8.0), 3.03 (dd, 1, *J* = 16.0, 7.2), 2.67 (dd, 1, *J* = 16.0, 7.2), 2.65 (br d, 1, *J* = 7, OH), 2.525 (dd, 1, *J* = 13.0, 6.5), 2.51 (dd, 1, *J* = 13.0, 8.5), 2.03 (s, 3), 1.95 (s, 3); ^{13}C NMR 189.0, 173.8, 147.8, 146.9, 85.3, 81.8, 62.6, 49.1, 39.9, 36.9, 33.2, 33.1; IR 3446, 1757, 1682, 1175; HRMS (CI) calcd for $C_{12}H_{16}IO_4$ (MH^+) 351.0094, found 351.0093.

(1*R,5*S*)-1-(3-methyl-2-buten-1-yl)-7-oxo-6-oxabicyclo[3.2.0]hept-2-ene-3-carboxaldehdye (21).** A slurry of iodolactone **19** (128 mg, 0.36 mmol) in THF (6 mL) and activated Zn (351 mg, 5.4 mmol) was treated with AcOH (1.5 mL). The mixture was stirred at 0 °C

for 15 min, diluted with EtOAc, and filtered through a pad of silica gel. The combined filtrates were concentrated under reduced pressure to about 5 mL volume. 20 mL of heptane was added and the resulting solution was again concentrated under reduced pressure to give 126 mg of crude hydroxy acid **2**. Addition of heptane and reconcentration aided in the removal of acetic acid.

A solution of crude hydroxy acid **2** in dry pyridine (6 mL) was cooled at 0 °C and TsCl (103 mg, 0.54 mmol) was added. The mixture was stirred at 0 °C for 1 h, and then sealed and placed in a refrigerator (4 °C) overnight. The mixture was poured onto crushed ice and extracted with EtOAc. The combined extracts were washed with saturated $NaHCO_3$, water, and brine, dried ($MgSO_4$) and concentrated to give 51 mg of crude **21**. Flash chromatography on MeOH-deactivated silica gel (4:1 hexanes/EtOAc) gave 40 mg (53%) of **21**: ^{1}H NMR 9.84 (s, 1), 6.67 (s, 1), 5.12 (br t, 1, *J* = 7.2), 4.90 (d, 1, *J* = 6.1), 3.06 (d, 1, *J* = 19.6), 2.90 (dd, 1, *J* = 19.6, 6.1), 2.75 (dd, 1, *J* = 15.2, 7.6), 2.59 (dd, 1, *J* = 15.2, 7.6), 1.74 (br s, 3), 1.66 (br s, 3); ^{13}C NMR 188.9, 170.0, 146.8, 144.6, 137.2, 116.2, 78.0, 76.6, 34.2, 27.3, 25.8, 18.0; IR 1819, 1684, 1612, 1106; HRMS (EI) calcd for $C_{12}H_{14}O_3$ (M^+) 206.0943, found 206.0942.

Following the procedure for conversion of **19** to **21**, a slurry of iodolactone **18** (89 mg, 0.25 mmol) in THF (6 mL) and activated Zn (330 mg, 5.0 mmol) was treated with AcOH (1.5 mL) to give 91 mg of crude hydroxy acid **2**. A solution of crude hydroxy acid **2** in dry pyridine (6 mL) was cooled at 0 °C and treated with TsCl (96 mg, 0.50 mmol) to give 53 mg of crude **21**. Flash chromatography on MeOH-deactivated silica gel (4:1 hexanes/EtOAc) gave 26 mg (50%) of **21**.

(1*R,5*S*)-3-(Hydroxymethyl)-1-(3-methyl-2-buten-1-yl)-6-oxabicyclo[3.2.0]hept-2-en-7-one (Vibralactone, 1).** Sodium borohydride (8 mg, 0.2 mmol) was added to a stirred solution of aldehyde **21** (20 mg, 0.1 mmol) in DME (5 mL) and H_2O (two drops of water) at 0 °C. The solution was stirred for 10 min and allowed to warm to 25 °C over 30 min. The solvent was removed under reduced pressure. The residue was taken up in EtOAc and the solution was washed with water and brine, dried ($MgSO_4$), and concentrated to give 22 mg of crude **1**. Flash chromatography (2:1 hexanes/EtOAc) gave 15.6 mg (78%) of pure vibralactone (**1**): ^{1}H NMR 5.62 (br s, 1), 5.13 (br dd, 1, *J* = 7.6, 7.6), 4.81 (d, 1, *J* = 4.4), 4.25 (br d, 2, *J* = 4.8), 2.77 (dd, 1, *J* = 19, 4.4), 2.75 (d, 1, *J* =

19), 2.62 (dd, 1, *J* = 15.2, 7.6), 2.43 (dd, 1, *J* = 15.2, 7.6), 1.72 (br s, 3), 1.64 (br s, 3), 1.65-1.63 (1, OH, partially obscured by Me group); ^{13}C NMR 172.9, 146.5, 136.0, 122.5, 117.2, 78.4, 75.1, 61.4, 37.3, 27.6, 25.8, 18.0; IR 3407, 1815, 1110; HRMS (CI) calcd for $C_{12}H_{17}O_3$ (MH^+) 209.1178, found 209.1176.

References and Notes

20. Rabideau, P. W.; Wetzel, D. M.; Paschal, J. W. *J. Org. Chem.* **1982**, *47*, 3993-3994.

Table 1. NMR Spectral Data for Natural[1] and Synthetic Vibralactone (1) in $CDCl_3$

	^{13}C natural[1]	^{13}C synthetic	^{1}H natural[1]	^{1}H synthetic
1	75.1	75.1		
2	122.4	122.5	5.60 (1, s)	5.62 (1, s)
3	146.6	146.5		
4	37.3	37.3	2.77 (1, dd, 18.8, 4.3)	2.77 (1, dd, 19, 4.4)
			2.71 (1, d, 18.8)	2.75 (1, d, 19)
5	78.5	78.4	4.79 (1, d, 4.3)	4.81 (1, d, 4.4)
7	173.0	172.9		
8	27.6	27.6	2.60 (1 , dd, 15.1, 7.3)	2.62 (1, dd, 15.2, 7.6)
			2.41 (1, dd, 15.1, 7.3)	2.43 (1, dd, 15.2, 7.6)
9	117.2	117.2	5.11 (1, t, 7.3)	5.13 (1, t, 7.6)
10	136.0	136.0		
11	18.0	18.0	1.62 (3, s)	1.64 (3, s)
12	25.8	25.8	1.71 (3, s)	1.72 (3, s)
13	61.3	61.4	4.22 (2, s)	4.25 (2, d, 4.8 coupling to OH)

The proton spectra differ systematically by δ 0.02 as a result of referencing differences. The apparent chemical shifts for H-4 differ because those for synthetic **1** were calculated using the proper formula for AB patterns rather than taking the midpoints of the doublets. There is no difference in the appearance of the spectra.