Supporting Information

Total Synthesis and Assignment of the Double Bond Position and Absolute Configuration of (–)- Pyrinodemlin A

Yoshiki Morimoto, Satoru Kitao, Tatsuya Okita, and Takamasa Shoji

Organic Letters

THP Ether 7 (n = 6). To a solution of commercially available 6-bromo-1-hexanol (**6**) (n = 6, 3.00 g, 15.7 mmol) and (±)-10-camphorsulfonic acid (183 mg, 0.787 mmol) in dichloromethane (52.5 mL) at 0 °C under a nitrogen atmosphere was added dropwise 3,4-dihydro-2H-pyran (2.22 mL, 23.6 mmol), and the solution was stirred at the same temperature for 2 h. To the solution were added successively a saturated aqueous solution of sodium hydrogen carbonate (3 mL) and water (60 mL), and the aqueous layer was extracted with dichloromethane (60 mL and 15 mL × 2). The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/ethyl acetate = 97:3) on silica gel (100 g) to provide THP ether **7** (n = 6, 4.22 g, 100% yield) as a colorless oil: R_f = 0.39 (hexane/ethyl acetate = 90:10); ^1H NMR (400 MHz, CDCl_3) δ 4.57 (1H, dd, J = 4.4, 2.4 Hz), 3.87 (1H, ddd, J = 11.2, 7.7, 3.4 Hz), 3.74 (1H, dt, J = 9.5, 6.7 Hz), 3.55–3.46 (1H, m), 3.41 (2H, t, J = 6.8 Hz), 3.39 (1H, dt, J = 9.6, 6.5 Hz), 2.00–1.34 (14H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 98.9, 67.4, 62.4, 33.8, 32.7, 30.8, 29.5, 28.0, 25.48, 25.47, 19.7; IR (neat) 2939, 2864, 1352, 1259, 1202, 1136, 1119, 1078, 1065, 1034, 1022, 991, 974, 905, 868, 814 cm^{-1} ; EI-MS m/z (relative intensity) 265 [(M – H) $^+$, 17], 263 [(M – H) $^+$, 18], 101 (11), 85 (100), 83

(72), 57 (26), 56 (59), 55 (58); EI-HRMS calcd for $C_{11}H_{20}O_2^{81}Br$ [(M - H)⁺] 265.0626, found 265.0599; calcd for $C_{11}H_{20}O_2^{79}Br$ [(M - H)⁺] 263.0647, found 263.0630.

Alkyne 8 (n = 6). To a solution of lithium acetylide ethylenediamine complex (6.49 g, 64.1 mmol) and sodium iodide (24.1 g, 0.160 mol) in dimethyl sulfoxide (178 mL) at room temperature under a nitrogen atmosphere was slowly added bromide 7 (n = 6, 14.1 g, 53.4 mmol) dissolved in dimethyl sulfoxide (70 mL), and the solution was stirred at the same temperature for 4 h. To the solution was slowly added water (1 L), and the aqueous layer was extracted with hexane (250 mL × 3). The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate = 98:2) on silica gel (300 g) to give alkyne 8 (n = 6, 9.17 g, 82.1% yield) as a colorless oil; R_f = 0.42 (hexane/ethyl acetate = 90:10); ¹H NMR (400 MHz, CDCl₃) δ 4.57 (1H, dd, J = 4.4, 2.7 Hz), 3.87 (1H, ddd, J = 11.2, 7.6, 3.7 Hz), 3.74 (1H, dt, J = 9.5, 6.8 Hz), 3.55–3.46 (1H, m), 3.39 (1H, dt, J = 9.8, 6.6 Hz), 2.19 (2H, dt, J = 2.6, 7.1 Hz), 1.93 (1H, t, J = 2.7 Hz), 1.91–1.77 (1H, m), 1.76–1.33 (13H, m); ¹³C NMR (100 MHz, CDCl₃) δ 98.9, 84.7, 68.1, 67.5, 62.3, 30.8, 29.6, 28.6, 28.4, 25.8, 25.5, 19.7, 18.3; IR (neat) 3310, 2937, 2860, 1138, 1121, 1078, 1067, 1034, 976, 905, 868, 816 cm⁻¹; CI-MS m/z (relative intensity) 211 [(M + H)⁺, 46], 169 (12), 109 (12), 85 (100); CI-HRMS calcd for $C_{13}H_{23}O_2$ [(M + H)⁺] 211.1698, found 211.1685.

Alkyne 11c. To a solution of diisopropylamine (0.312 mL, 2.20 mmol) in 2.5 mL of tetrahydrofuran at 0 °C under a nitrogen atmosphere was added dropwise 1.38 mL of *n*-butyllithium (1.6 M in hexane, 2.20 mmol), and the solution was stirred at the same temperature for 30 min. After the solution had been cooled to -78 °C, 3-picoline (9) (0.194 mL, 2.00 mmol) was added dropwise to the solution, and the mixture was stirred at -78 °C for additional 20 min. To the solution at -78 °C was added dropwise 1,5-dibromopentane (0.812 mL, 6.00 mmol) dissolved in tetrahydrofuran (0.8 mL), and the solution was allowed to warm to room temperature. After the solution was stirred for 12 h, a

saturated aqueous solution of sodium hydrogen carbonate (20 mL) was added to the solution, and the aqueous layer was extracted with ether (15 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/ethyl acetate = 90:10) on 8 g of silica gel to yield crude bromide **10** ($m = 6$) which was taken to the next step without further purification.

To a solution of alkyne **8** ($n = 6$, 1.04 g, 4.96 mmol) in tetrahydrofuran (3.5 mL) at $-15\text{ }^{\circ}\text{C}$ under a nitrogen atmosphere was added dropwise 3.26 mL of *n*-butyllithium (1.6 M in hexane, 5.22 mmol), and the solution was stirred at the same temperature for 30 min. To the solution at $-15\text{ }^{\circ}\text{C}$ was added dropwise the above crude bromide **10** ($m = 6$) dissolved in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (3.5 mL), and the solution was stirred at the same temperature for additional 30 min. After the solution was stirred at room temperature for 16 h, water (25 mL) was added to the solution, and the aqueous layer was extracted with ether (15 mL $\times$ 3). The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was subjected to flash column chromatography (hexane/ethyl acetate = 80:20) on silica gel (6 g) to give alkyne **11c** (246 mg, 33.1% yield, 2 steps) as a pale yellow oil: $R_f = 0.46$ (hexane/ethyl acetate = 50:50); ^1H NMR (400 MHz, CDCl_3) δ 8.44 (1H, d, $J = 2.2$ Hz), 8.43 (1H, dd, $J = 4.9, 1.5$ Hz), 7.48 (1H, dt, $J = 7.7, 1.9$ Hz), 7.20 (1H, dd, $J = 7.8, 4.9$ Hz), 4.57 (1H, dd, $J = 4.4, 2.7$ Hz), 3.86 (1H, ddd, $J = 11.0, 7.6, 3.4$ Hz), 3.73 (1H, dt, $J = 9.5, 6.8$ Hz), 3.55–3.46 (1H, m), 3.38 (1H, dt, $J = 9.7, 6.6$ Hz), 2.61 (2H, t, $J = 7.7$ Hz), 2.19–2.10 (4H, m), 1.89–1.29 (22H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 150.0, 147.2, 137.8, 135.7, 123.2, 98.9, 80.3, 80.1, 67.6, 62.3, 32.9, 31.0, 30.8, 29.7, 29.1, 29.0, 28.7, 28.64, 28.55, 25.8, 25.5, 19.7, 18.7; IR (neat) 2934, 2858, 1574, 1477, 1464, 1456, 1441, 1423, 1352, 1259, 1200, 1184, 1136, 1121, 1078, 1065, 1034, 978, 905, 868, 814, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 372.3 $[(M + H)^+]$, 70], 288.3 (100), 154.1 (33), 136.1 (24), 85.0 (58); FAB-HRMS calcd for $\text{C}_{24}\text{H}_{38}\text{O}_2\text{N}$ $[(M + H)^+]$ 372.2903,

found 372.2903.

Alkene 12c. A solution of palladium on calcium carbonate (5%, 65.3 mg) and alkyne 11c (323 mg, 0.870 mmol) in ethyl acetate (2 mL) was vigorously stirred at room temperature under a hydrogen atmosphere for 18 h. The reaction mixture was filtered through a pad of Celite, and the filtrates were concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate = 90:10) on silica gel (15 g) to provide alkene 12c (303 mg, 93.1% yield) as a pale yellow oil: R_f = 0.36 (hexane/ethyl acetate = 70:30); ^1H NMR (400 MHz, CDCl_3) δ 8.49–8.39 (2H, m), 7.48 (1H, br d, J = 7.8 Hz), 7.20 (1H, dd, J = 7.7, 4.8 Hz), 5.40–5.29 (2H, m), 4.57 (1H, dd, J = 4.4, 2.4 Hz), 3.92–3.82 (1H, m), 3.73 (1H, dt, J = 9.6, 6.9 Hz), 3.55–3.45 (1H, m), 3.38 (1H, dt, J = 9.5, 6.7 Hz), 2.60 (2H, t, J = 7.7 Hz), 2.07–1.92 (4H, m), 1.89–1.24 (22H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 150.0, 147.2, 135.7, 129.9, 129.7, 123.2, 98.9, 67.6, 62.3, 33.0, 31.1, 30.8, 29.73, 29.68, 29.60, 29.1, 29.04, 29.02, 27.2, 27.1, 26.1, 25.5, 19.7; IR (neat) 2930, 2854, 1522, 1506, 1456, 1136, 1121, 1078, 1034, 901, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 374.3 [$(\text{M} + \text{H})^+$, 40], 290.3 (100), 272.3 (18), 106.0 (18), 85.0 (41), 55.0 (16); FAB-HRMS calcd for $\text{C}_{24}\text{H}_{40}\text{O}_2\text{N}$ [$(\text{M} + \text{H})^+$] 374.3059, found 374.3052.

Alcohol 13c. To a solution of THP ether 12c (372 mg, 0.998 mmol) in ethanol (10 mL) at room temperature was added a quantity of *p*-toluenesulfonic acid monohydrate (380 mg, 2.00 mmol), and the solution was stirred at the same temperature for 45 min. After the solution was concentrated under reduced pressure, a saturated aqueous solution of sodium hydrogen carbonate (15 mL) was added to the residue, and the aqueous layer was extracted with dichloromethane (10 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate = 50:50) on silica gel (20 g) to afford alcohol 13c (271 mg, 93.9% yield) as a colorless oil: R_f = 0.28 (hexane/ethyl acetate = 50:50); ^1H NMR (400 MHz,

CDCl_3) δ 8.43 (1H, d, $J = 2.0$ Hz), 8.42 (1H, dd, $J = 4.9, 1.7$ Hz), 7.49 (1H, dt, $J = 7.8, 2.0$ Hz), 7.20 (1H, ddd, $J = 7.8, 4.9, 0.7$ Hz), 5.36 (1H, ddd, $J = 10.7, 5.7, 1.6$ Hz), 5.33 (1H, ddd, $J = 10.7, 5.7, 1.6$ Hz), 3.64 (2H, t, $J = 6.6$ Hz), 2.60 (2H, t, $J = 7.7$ Hz), 2.08–1.95 (4H, m), 1.67–1.52 (4H, m), 1.43–1.26 (12H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 147.1, 137.9, 135.8, 129.9, 129.8, 123.2, 62.9, 33.0, 32.8, 31.0, 29.7, 29.5, 29.1, 28.93, 28.90, 27.11, 27.09, 25.6; IR (neat) 3320, 3003, 2928, 2855, 1578, 1456, 1423, 1362, 1340, 1190, 1128, 1059, 1030, 795, 714, 637 cm^{-1} ; FAB-MS m/z (relative intensity) 290.3 $[(\text{M} + \text{H})^+]$, 100, 106.0 (10), 93.0 (8); FAB-HRMS calcd for $\text{C}_{19}\text{H}_{32}\text{ON}$ $[(\text{M} + \text{H})^+]$ 290.2484, found 290.2491.

Aldehyde 14c. To a solution of oxalyl chloride (43.0 μL , 0.495 mmol) in dichloromethane (3 mL) at -78 $^{\circ}\text{C}$ under a nitrogen atmosphere was added dropwise dimethyl sulfoxide (71.0 μL , 0.990 mmol), and the solution was stirred at the same temperature for 10 min. To the solution was added dropwise alcohol 13c (119 mg, 0.413 mmol) dissolved in dichloromethane (1 mL), and the solution was stirred at -78 $^{\circ}\text{C}$ for 30 min. To the solution at -78 $^{\circ}\text{C}$ was added dropwise triethylamine (0.230 mL, 1.65 mmol), and the mixture was allowed to warm to room temperature. After the mixture had been vigorously stirred at room temperature for an additional 1 h, water (10 mL) was added to the mixture, and the aqueous layer was extracted with dichloromethane (10 mL $\times$ 3). The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate = 80:20) on silica gel (5 g) to afford aldehyde 14c (99.8 mg, 84.2% yield) as a pale yellow oil: $R_f = 0.39$ (hexane/ethyl acetate = 50:50); ^1H NMR (400 MHz, CDCl_3) δ 9.76 (1H, t, $J = 1.8$ Hz), 8.44 (1H, d, $J = 2.4$ Hz), 8.43 (1H, dd, $J = 4.6, 1.5$ Hz), 7.49 (1H, ddd, $J = 7.8, 2.2, 1.7$ Hz), 7.21 (1H, ddd, $J = 7.7, 4.8, 0.8$ Hz), 5.41–5.28 (2H, m), 2.60 (2H, t, $J = 7.7$ Hz), 2.42 (2H, dt, $J = 2.0, 7.3$ Hz), 2.10–1.92 (4H, m), 1.72–1.54 (4H, m), 1.45–1.24 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 202.8, 149.8, 147.0, 138.0, 135.9, 130.0, 129.5, 123.3, 43.9,

33.0, 31.1, 29.6, 29.4, 29.0, 28.8, 27.1, 26.9, 22.0; IR (neat) 3003, 2928, 2856, 2718, 1724, 1574, 1477, 1464, 1423, 1190, 1026, 799, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 288.3 $[(M + H)^+]$, 52], 106.0 (32), 93.0 (30); FAB-HRMS calcd for $\text{C}_{19}\text{H}_{30}\text{ON}$ $[(M + H)^+]$ 288.2327, found 288.2334.

Hydroxylamine 15c. To a solution of aldehyde 14c (52.7 mg, 0.183 mmol) in methanol (5 mL) at room temperature were added consecutively hydroxylamine hydrochloride (17.1 mg, 0.238 mmol) and potassium hydroxide (4.2 mg, 64.2 μmol), and the solution was stirred at the same temperature for 30 min. After the solution was acidified till pH 3 with 2 M aqueous hydrochloric acid, sodium cyanoborohydride (15.8 mg, 0.238 mmol) was added to the solution, and the solution was stirred at room temperature for 2 h with the solution kept at pH 3. After the solution was concentrated under reduced pressure, water (5 mL) was added to the residue, and the solution was adjusted to pH 9 with a 6 M aqueous solution of potassium hydroxide. The aqueous layer was extracted with dichloromethane (5 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by flash column chromatography (chloroform/methanol = 98:2) on silica gel (5 g) to yield hydroxylamine 15c (49.1 mg, 88.0% yield) as a pale yellow oil: R_f = 0.37 (chloroform/methanol = 98:2); ^1H NMR (400 MHz, CDCl_3) δ 8.44 (1H, d, J = 1.7 Hz), 8.42 (1H, dd, J = 4.8, 1.6 Hz), 7.49 (1H, dt, J = 7.8, 1.7 Hz), 7.20 (1H, dd, J = 7.8, 4.9 Hz), 5.40–5.29 (2H, m), 2.93 (2H, t, J = 7.2 Hz), 2.60 (2H, t, J = 7.7 Hz), 2.08–1.92 (4H, m), 1.67–1.48 (4H, m), 1.42–1.24 (12H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 147.1, 137.9, 135.8, 129.9, 129.8, 123.2, 54.0, 33.0, 31.0, 29.6, 29.5, 29.2, 28.9, 27.12, 27.07, 27.05; IR (neat) 3230, 3002, 2927, 2854, 1576, 1457, 1420, 1189, 1027, 754, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 305.2 $[(M + H)^+]$, 100], 304.2 (M^+ , 18), 106.0 (18), 55.0 (16), 43.0 (11); FAB-HRMS calcd for $\text{C}_{19}\text{H}_{33}\text{ON}_2$ $[(M + H)^+]$ 305.2593, found 305.2599.

C13'–C14' Double Bond Positional Isomer 4. A solution of hydroxylamine 15c (34.5 mg, 0.113 mmol) and aldehyde 14a (39.3 mg, 0.136 mmol), which was prepared by the same procedure as that of

14c as shown in Scheme 1, in toluene (5.7 mL) was stirred at room temperature under a nitrogen atmosphere for 40 min and then refluxed for additional 13 h. The solution was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate = 40:60) on silica gel (5 g) to give C13'–C14' double bond positional isomer **4** (59.8 mg, 92.0% yield) as a colorless oil: R_f = 0.25 (chloroform/methanol = 90:10); ^1H NMR (400 MHz, CDCl_3) δ 8.46–8.41 (4H, m), 7.51–7.46 (2H, m), 7.20 (2H, dd, J = 7.8, 4.9 Hz), 5.39–5.29 (2H, m), 4.10–4.00 (1H, m), 3.52–3.42 (1H, m), 2.89–2.78 (2H, m), 2.60 (4H, t, J = 7.7 Hz), 2.64–2.55 (1H, m), 2.06–1.94 (4H, m), 1.84–1.23 (36H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 149.8, 147.1, 137.85, 137.83, 135.7, 129.9, 129.6, 123.1, 77.6 (br), 72.5 (br), 57.1 (br), 49.8, 34.1 (br), 32.9, 31.02, 31.01, 29.65, 29.60, 29.5, 29.3, 29.23, 29.16, 29.0, 28.94, 28.93, 28.7, 27.2, 27.1, 27.04, 26.96, 26.4, 26.2; IR (neat) 2928, 2855, 1574, 1477, 1466, 1421, 1026, 795, 714 cm^{-1} ; EI-MS m/z (relative intensity) 574 [$(\text{M} + \text{H})^+$, 4], 573 (M^+ , 9), 383 (20), 365 (100), 355 (19), 353 (3), 327 (4), 315 (9), 301 (13), 285 (75), 270 (17), 244 (12), 230 (1), 220 (53), 216 (7), 204 (1), 202 (1), 190 (8), 176 (9), 162 (8), 148 (8), 134 (4), 124 (5), 120 (9), 106 (65), 93 (57); EI-HRMS calcd for $\text{C}_{38}\text{H}_{59}\text{ON}_3$ (M^+) 573.4658, found 573.4668.

C15'–C16' Double Bond Positional Isomer 2. This compound was synthesized by the same synthetic methodology as that of **4** as shown in Scheme 1.

C15'–C16' Double Bond Positional Isomer 2: R_f = 0.24 (hexane/ethyl acetate = 50:50); ^1H NMR (400 MHz, CDCl_3) δ 8.46–8.41 (4H, m), 7.48 (2H, d, J = 7.8 Hz), 7.20 (2H, dd, J = 7.7, 4.8 Hz), 5.40–5.29 (2H, m), 4.11–4.00 (1H, m), 3.46 (1H, br s), 2.89–2.78 (2H, m), 2.66–2.56 (1H, m), 2.60 (4H, t, J = 7.7 Hz), 2.08–1.96 (4H, m), 1.77 (1H, br s), 1.72–1.50 (9H, m), 1.51–1.23 (26H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 150.0, 147.2, 137.91, 137.89, 135.7, 130.0, 129.6, 123.2, 77.7 (br), 72.6 (br), 57.1 (br), 49.9, 34.2 (br), 33.0, 31.1, 29.72, 29.69, 29.4, 29.35, 29.31, 29.2, 29.12, 29.09, 28.8,

27.8, 27.5, 27.2, 27.1, 27.0, 26.5, 26.3; IR (neat) 2930, 2853, 1576, 1478, 1465, 1422, 1339, 1188, 1027, 793, 715 cm^{-1} ; EI-MS m/z (relative intensity) 574 $[(M + H)^+]$, 10], 573 (M^+ , 4), 383 (18), 365 (100), 355 (17), 353 (2), 327 (3), 315 (5), 301 (13), 285 (65), 270 (24), 244 (50), 231 (48), 230 (3), 220 (71), 204 (1), 190 (16), 176 (19), 162 (10), 148 (13), 134 (9), 124 (32), 120 (20), 106 (92), 93 (87); EI-HRMS calcd for $C_{38}H_{59}ON_3$ (M^+) 573.4659, found 573.4666.

Phosphonium Bromide 17. A solution of bromide **16** (1.42 g, 5.01 mmol), prepared by the same procedure as that of **10** ($m = 6$) as shown in Scheme 1, in 47% aqueous hydrobromic acid (0.63 mL, 5.51 mmol) was stirred at room temperature for 5 min, and the aqueous layer was azeotropically removed with a small amount of toluene under reduced pressure. After the pyridinium bromide was dissolved in acetonitrile (10 mL) under a nitrogen atmosphere, triphenylphosphine (1.97 g, 7.51 mmol) was added to the solution, and the the solution was refluxed for 29 h with stirring. After the solution had been cooled to room temperature, to the solution was added a saturated aqueous solution of sodium hydrogen carbonate (30 mL), and the aqueous layer was extracted with dichloromethane (30 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by column chromatography (dichloromethane/methanol = 95:5) on silica gel (70 g) to afford phosphonium bromide **17** (2.54 g, 93% yield) as a pale yellow oil: R_f = 0.40 (dichloromethane/methanol = 90:10); ^1H NMR (400 MHz, CDCl_3) δ 8.46–8.37 (2H, m), 7.95–7.76 (9H, m), 7.76–7.67 (6H, m), 7.49 (1H, dt, $J = 7.7, 1.9$ Hz), 7.20 (1H, dd, $J = 7.7, 4.8$ Hz), 3.88–3.68 (2H, m), 2.57 (2H, t, $J = 7.7$ Hz), 1.71–1.50 (6H, m), 1.36–1.14 (8H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 147.0, 137.8, 135.8, 134.93, 134.90, 133.6, 133.5, 130.5, 130.3, 123.2, 118.7, 117.9, 32.8, 30.9, 30.4, 30.2, 29.11, 29.05, 28.96, 28.86, 23.0, 22.6, 22.53, 22.46; IR (nujol) 2924, 2855, 1541, 1489, 1456, 1373, 1339 cm^{-1} ; FAB-MS m/z (relative intensity) 466.2 (M^+ , 100); FAB-HRMS calcd for $C_{32}H_{37}NP$ (M^+) 466.2663, found 466.2668.

MOM Ether 19. To a solution of commercially available (*R*)-(+)- α -hydroxy- γ -butyrolactone (**18**) (3.27 g, 32.0 mmol) in dichloromethane (65 mL) at 0 °C under a nitrogen atmosphere were added dropwise *N*-ethyldiisopropylamine (8.21 mL, 48.0 mmol) and chloromethyl methyl ether (3.95 mL, 41.6 mmol), and the solution was stirred at room temperature for 41 h. To the solution was added water (50 mL), and the aqueous layer was extracted with dichloromethane (40 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate = 70:30) on silica gel (150 g) to afford MOM ether **19** (4.11 g, 88% yield) as a colorless oil: R_f = 0.62 (ethyl acetate); $[\alpha]_D^{25}$ +127.6 (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 4.96 (1H, d, *J* = 6.8 Hz), 4.73 (1H, d, *J* = 6.8 Hz), 4.44 (1H, dt, *J* = 3.6, 8.6 Hz), 4.43 (1H, t, *J* = 8.4 Hz), 4.24 (1H, dt, *J* = 6.3, 9.3 Hz), 3.43 (3H, s), 2.58 (1H, dddd, *J* = 12.8, 8.0, 6.4, 3.1 Hz), 2.30 (1H, dq, *J* = 12.8, 8.9 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 174.9, 95.9, 70.3, 65.1, 55.9, 29.9; IR (neat) 2955, 2901, 2829, 1780, 1456, 1387, 1356, 1286, 1221, 1175, 1151, 1132, 1113, 1057, 1028, 1015, 968, 949, 918, 820, 708, 660 cm⁻¹; EI-MS *m/z* (relative intensity) 146 (*M*⁺, 1), 145 [(*M* – *H*)⁺, 6], 131 (9), 115 (48), 87 (27), 86 (100), 85 (42), 57 (22); EI-HRMS calcd for C₆H₉O₄ [(*M* – *H*)⁺] 145.0501, found 145.0484.

Lactol 20. To a solution of MOM ether **19** (3.87 g, 26.5 mmol) in toluene (55 mL) at –78 °C under a nitrogen atmosphere was slowly added diisobutylaluminum hydride (0.95 M in hexane, 30.7 mL, 29.1 mmol), and the solution was stirred at the same temperature for 1 h. Appropriate quantities of methanol and water were each carefully added to the solution at –78 °C, and the mixture was then vigorously stirred at room temperature for 20 min. The resulting mixture was filtered through a pad of Celite, and the filtrates were concentrated under reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate = 70:30) on silica gel (120 g) to give lactol **20** (3.49 g, 89% yield) as a colorless oil: R_f = 0.49 (ethyl acetate); $[\alpha]_D^{25}$ –51.1 (*c* 0.995, CHCl₃); ¹H NMR (400 MHz,

CDCl_3) δ 5.41 (0.8H, br s), 5.32 (0.2H, dd, $J = 7.3, 4.1$ Hz), 4.76 (0.2H, d, $J = 6.8$ Hz), 4.73 (0.2H, d, $J = 6.8$ Hz), 4.70 (0.8H, d, $J = 7.1$ Hz), 4.68 (0.8H, d, $J = 7.1$ Hz), 4.19–4.02 (2.8H, m), 3.86 (0.2H, dt, $J = 5.4, 8.2$ Hz), 3.68 (0.2H, d, $J = 7.6$ Hz), 3.42 (0.6H, s), 3.39 (2.4H, s), 2.94 (0.8H, br s), 2.35–1.88 (2H, m); ^{13}C NMR (100 MHz, CDCl_3), major:minor = 4:1, major: δ 101.1, 95.6, 81.3, 66.9, 55.5, 29.9; minor: δ 96.5, 96.2, 76.5, 64.8, 55.9, 30.0; IR (neat) 3412, 2953, 2897, 2826, 1443, 1354, 1302, 1217, 1151, 1117, 1036, 953, 918 cm^{-1} .

Alcohol 21. To a solution of potassium hydride (30% dispersion in mineral oil, 1.43 g, 10.7 mmol) in tetrahydrofuran (10 mL) at 0 °C under a nitrogen atmosphere was added dropwise HMDS (2.25 mL, 10.7 mmol), and the solution was stirred at the same temperature for 1 h. To a solution of phosphonium salt 17 freshly prepared (5.84 g, 10.7 mmol) in tetrahydrofuran (20 mL) at 0 °C under a nitrogen atmosphere was added dropwise the above solution of KHMDS, and the solution was stirred at the same temperature for 1 h. After the solution had been cooled to –78 °C, to the solution was added dropwise lactol 20 (538 mg, 3.68 mmol) dissolved in tetrahydrofuran (10 mL). The solution was allowed to warm to room temperature and further stirred for additional 30 min. To the solution was added water (150 mL), and the aqueous layer was extracted with dichloromethane (100 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was subjected to flash column chromatography (hexane/ethyl acetate = 50:50) on silica gel (200 g) to yield crude products, which were purified by flash column chromatography (dichloromethane/acetone = 80:20) on silica gel (200 g) to provide alcohol 21 (1.12 g, 91% yield) as a colorless oil: $R_f = 0.44$ (hexane/ethyl acetate = 20:80); $[\alpha]_D^{25} +68.9$ (c 1.03, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.435 (1H, br s), 8.427 (1H, dd, $J = 4.6, 1.7$ Hz), 7.49 (1H, dt, $J = 7.8, 1.7$ Hz), 7.20 (1H, dd, $J = 7.8, 4.9$ Hz), 5.60 (1H, dt, $J = 10.8, 7.3$ Hz), 5.27 (1H, dd, $J = 11.0, 9.3$ Hz), 4.68 (1H, d, $J = 6.6$ Hz), 4.63 (1H, dt, $J = 4.6, 8.8$ Hz), 4.49 (1H, d, $J = 6.8$ Hz), 3.86–3.72 (2H, m), 3.38 (3H, s), 2.60 (2H, t, $J = 7.7$ Hz), 2.54 (1H, br

s), 2.16–1.97 (2H, m), 1.86 (1H, dddd, $J = 13.5, 8.4, 6.9, 4.7$ Hz), 1.81–1.67 (2H, m), 1.67–1.56 (2H, m), 1.43–1.21 (9H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 147.1, 137.9, 135.8, 134.3, 129.0, 123.2, 93.4, 70.1, 60.4, 55.5, 37.9, 32.9, 31.0, 29.6, 29.31, 29.25, 29.1, 29.0, 27.5; IR (neat) 3298, 2926, 2855, 2822, 1576, 1423, 1150, 1097, 1032, 920, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 336.2 $[(\text{M} + \text{H})^+]$, 29], 307.0 (36), 289.0 (26), 274.1 (11), 256.2 (12), 244.2 (7), 154.0 (100), 136.0 (65), 107.0 (21), 89.0 (20); FAB-HRMS calcd for $\text{C}_{20}\text{H}_{34}\text{O}_3\text{N}$ $[(\text{M} + \text{H})^+]$ 336.2539, found 336.2542.

Mesylate 22. To a solution of alcohol **21** (720 mg, 2.15 mmol) and triethylamine (1.20 mL, 8.55 mmol) in dichloromethane (10 mL) at 0 °C under a nitrogen atmosphere was added dropwise methanesulfonyl chloride (0.50 mL, 6.41 mmol), and the mixture was stirred at room temperature for 1 h. Water (20 mL) was added to the solution, and the aqueous layer was extracted with dichloromethane (15 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was subjected to column chromatography (dichloromethane/acetone = 95:5) on silica gel (25 g) to furnish mesylate **22** (718 mg, 81% yield) as a pale yellow oil: $R_f = 0.29$ (dichloromethane/acetone = 70:30); $[\alpha]_D^{26} +55.5$ (c 0.68, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.44 (1H, br s), 8.43 (1H, d, $J = 5.1$ Hz), 7.49 (1H, d, $J = 7.8$ Hz), 7.20 (1H, dd, $J = 7.8, 4.9$ Hz), 5.65 (1H, dt, $J = 10.9, 7.5$ Hz), 5.20 (1H, dd, $J = 11.0, 9.5$ Hz), 4.67 (1H, d, $J = 6.8$ Hz), 4.55 (1H, dt, $J = 5.1, 8.8$ Hz), 4.48 (1H, d, $J = 6.6$ Hz), 4.39 (1H, ddd, $J = 9.8, 7.6, 6.1$ Hz), 4.30 (1H, dt, $J = 9.8, 6.1$ Hz), 3.36 (3H, s), 3.02 (3H, s), 2.60 (2H, t, $J = 7.7$ Hz), 2.17–1.97 (3H, m), 1.97–1.82 (1H, m), 1.61 (2H, quintet, $J = 7.3$ Hz), 1.42–1.22 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 147.1, 137.9, 135.8, 135.3, 128.2, 123.2, 93.4, 66.9, 66.7, 55.5, 37.3, 35.1, 33.0, 31.1, 29.5, 29.33, 29.29, 29.18, 29.08, 27.6; IR (neat) 2928, 2855, 1576, 1466, 1423, 1356, 1175, 1153, 1096, 1036, 972, 920, 841, 791, 716 cm^{-1} ; FAB-MS m/z (relative intensity) 414.2 $[(\text{M} + \text{H})^+, 55]$, 307.1 (27), 256.2 (22), 154.1 (100), 136.0 (68); FAB-HRMS calcd for $\text{C}_{21}\text{H}_{36}\text{O}_5\text{NS}$ $[(\text{M} + \text{H})^+]$ 414.2314, found 414.2328.

Nitrile 23. A solution of mesylate **22** (271 mg, 0.66 mmol), 18-crown-6 (346 mg, 1.31 mmol), and potassium cyanide (85 mg, 1.31 mmol) in acetonitrile (7 mL) was stirred and heated at 50 °C under a nitrogen atmosphere for 20 h. After the solution had been cooled to room temperature, a saturated aqueous solution of sodium hydrogen carbonate (10 mL) was added to the solution, and the aqueous layer was extracted with dichloromethane (10 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate = 70:30) on silica gel (8 g) to provide nitrile **23** (204 mg, 90% yield) as a pale yellow oil: R_f = 0.34 (hexane/ethyl acetate = 50:50); $[\alpha]_D^{25} +75.1$ (c 1.01, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.44 (1H, d, J = 2.4 Hz), 8.43 (1H, dd, J = 4.9, 1.7 Hz), 7.49 (1H, dt, J = 7.8, 1.9 Hz), 7.20 (1H, dd, J = 7.8, 4.9 Hz), 5.68 (1H, dt, J = 10.7, 7.7 Hz), 5.18 (1H, dd, J = 10.9, 9.4 Hz), 4.67 (1H, d, J = 6.6 Hz), 4.50 (1H, dt, J = 5.5, 8.7 Hz), 4.48 (1H, d, J = 6.6 Hz), 3.38 (3H, s), 2.60 (2H, t, J = 7.7 Hz), 2.50 (1H, dt, J = 17.0, 7.6 Hz), 2.44 (1H, ddd, J = 17.0, 7.4, 6.2 Hz), 2.19–2.00 (2H, m), 1.92 (1H, ddt, J = 14.1, 6.3, 7.8 Hz), 1.80 (1H, ddt, J = 13.4, 5.4, 7.8 Hz), 1.61 (2H, quintet, J = 7.4 Hz), 1.42–1.20 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 150.0, 147.2, 137.9, 135.9, 135.8, 127.7, 123.2, 119.6, 93.4, 68.8, 55.6, 33.0, 31.2, 31.1, 29.6, 29.33, 29.30, 29.2, 29.1, 27.7, 13.5; IR (neat) 2928, 2855, 2235, 1576, 1423, 1150, 1096, 1026, 920, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 345.2 $[(\text{M} + \text{H})^+]$, 100], 283.2 (44); FAB-HRMS calcd for $\text{C}_{21}\text{H}_{33}\text{O}_2\text{N}_2$ $[(\text{M} + \text{H})^+]$ 345.2542, found 345.2559.

Aldehyde 24. To a solution of nitrile **23** (343 mg, 1.00 mmol) in toluene (10 mL) at -78 °C under a nitrogen atmosphere was added dropwise diisobutylaluminum hydride (0.95 M in hexane, 3.15 mL, 2.99 mmol), and the solution was stirred at the same temperature for 20 min. Appropriate quantities of methanol and water were each carefully added to the solution at -78 °C, and the mixture was then vigorously stirred at room temperature for 20 min. The resulting mixture was filtered through a pad of Celite, and the filtrates were concentrated under reduced pressure. The residue was purified by column

chromatography (dichloromethane/acetone = 90:10) on silica gel (10 g) to give aldehyde **24** (283 mg, 81% yield) as a colorless oil: R_f = 0.32 (dichloromethane/acetone = 90:10); $[\alpha]_D^{25}$ +70.5 (c 1.03, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 9.78 (1H, t, J = 1.5 Hz), 8.44 (1H, br s), 8.43 (1H, dd, J = 5.1, 1.5 Hz), 7.49 (1H, d, J = 7.8 Hz), 7.20 (1H, dd, J = 7.7, 4.8 Hz), 5.62 (1H, dt, J = 11.1, 7.5 Hz), 5.21 (1H, ddt, J = 10.9, 9.4, 1.2 Hz), 4.65 (1H, d, J = 6.6 Hz), 4.46 (1H, d, J = 6.8 Hz), 4.40 (1H, dt, J = 5.9, 8.3 Hz), 3.35 (3H, s), 2.60 (2H, t, J = 7.7 Hz), 2.53 (2H, dt, J = 1.3, 7.3 Hz), 2.15–1.98 (2H, m), 1.93 (1H, dq, J = 14.5, 7.3 Hz), 1.81 (1H, ddt, J = 14.1, 5.7, 7.0 Hz), 1.61 (2H, quintet, J = 7.1 Hz), 1.41–1.20 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 202.1, 150.0, 147.2, 137.9, 135.8, 134.8, 128.9, 123.2, 93.4, 69.9, 55.5, 40.1, 33.0, 31.1, 29.6, 29.4, 29.3, 29.2, 29.1, 28.1, 27.6; IR (neat) 2928, 2855, 2822, 1724, 1576, 1423, 1150, 1097, 1032, 918, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 348.2 [($\text{M} + \text{H}$) $^+$, 56], 302.2 (100), 286.2 (97), 246.2 (19), 154.0 (81), 136.0 (65), 106.0 (41), 93.0 (32); FAB-HRMS calcd for $\text{C}_{21}\text{H}_{34}\text{O}_3\text{N}$ [($\text{M} + \text{H}$) $^+$] 348.2538, found 348.2539.

MOM Ether 25. A solution of hydroxylamine **15b** (301 mg, 0.99 mmol), prepared by the same procedure as that of **15c** as shown in Scheme 1, and aldehyde **24** (283 mg, 0.81 mmol) in toluene (35 mL) was stirred at room temperature under a nitrogen atmosphere for 10 min and then refluxed for additional 13 h. The solution was cooled to room temperature and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/ethyl acetate = 50:50) on silica gel (20 g) to give a diastereomeric mixture (41 mg, 3.1% yield, **25**:the diastereomer = 7.9:1 by integration of the signals in the ^1H NMR spectrum) and MOM ether **25** (453 mg, 92.6% yield) as each pale yellow oil.

MOM Ether 25: R_f = 0.17 (ethyl acetate); $[\alpha]_D^{25}$ -16.7 (c 1.03, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.44 (2H, br s), 8.43 (2H, dd, J = 4.6, 1.7 Hz), 7.48 (2H, d, J = 7.8 Hz), 7.20 (2H, dd, J = 7.6, 4.6 Hz), 5.42–5.28 (2H, m), 4.64 (1H, d, J = 6.8 Hz), 4.59 (1H, d, J = 6.8 Hz), 4.13 (1H, q, J = 3.9 Hz), 4.09 (1H, q, J = 6.2 Hz), 3.59 (1H, br s), 3.35 (3H, s), 2.85 (1H, dt, J = 2.6, 7.4 Hz), 2.87–2.76 (1H, m),

2.60 (4H, t, $J = 7.7$ Hz), 2.65–2.52 (1H, m), 2.10–1.91 (5H, m), 1.91–1.20 (33H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 150.0, 147.2, 137.9, 135.8, 129.9, 129.8, 123.2, 95.0, 78.2, 77.6, 71.1, 56.9, 56.4, 55.4, 33.0, 32.3, 31.1, 29.7, 29.4, 29.33, 29.30, 29.2, 29.1, 28.9, 28.0, 27.21, 27.17, 27.0; IR (neat) 2995, 2928, 2855, 1576, 1477, 1464, 1423, 1373, 1339, 1215, 1148, 1099, 1043, 918, 793, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 634.4 [(M + H) $^+$, 100], 353.3 (21), 220.2 (21), 154.1 (22), 106.0 (20), 93.0 (18); FAB-HRMS calcd for $\text{C}_{40}\text{H}_{64}\text{O}_3\text{N}_3$ [(M + H) $^+$] 634.4948, found 634.4951.

Alcohol 26. To a solution of MOM ether **25** (88 mg, 0.14 mmol) in ethanol (1.5 mL) at room temperature under a nitrogen atmosphere was added dropwise 12 N aqueous hydrochloric acid (0.041 mL, 0.49 mmol), and the solution was stirred at 50 °C for 16 h. After the solution had been cooled to room temperature, to the solution was added a saturated aqueous solution of sodium hydrogen carbonate (10 mL), and the aqueous layer was extracted with dichloromethane (10 mL $\times$ 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by flash column chromatography (dichloromethane/acetone = 60:40) on silica gel (4 g) to furnish alcohol **26** (78 mg, 95% yield) as a pale yellow oil: $R_f = 0.34$ (dichloromethane/acetone = 50:50); $[\alpha]_D^{25} -14.3$ (c 1.00, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.43 (2H, d, $J = 2.2$ Hz), 8.42 (2H, dd, $J = 4.9, 1.5$ Hz), 7.49 (2H, dt, $J = 7.7, 1.9$ Hz), 7.20 (2H, dd, $J = 7.7, 4.8$ Hz), 5.39–5.29 (2H, m), 4.29 (1H, q, $J = 4.2$ Hz), 4.09 (1H, q, $J = 6.8$ Hz), 3.62 (1H, br s), 2.81 (1H, dt, $J = 12.2, 7.4$ Hz), 2.75 (1H, dt, $J = 3.4, 7.5$ Hz), 2.60 (2H, t, $J = 7.7$ Hz), 2.64–2.51 (1H, m), 2.10–1.93 (4H, m), 1.88 (1H, ddt, $J = 12.3, 4.9, 7.4$ Hz), 1.75–1.20 (35H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 147.1, 137.9, 135.83, 135.78, 129.9, 129.8, 123.2, 73.2, 58.3, 35.4, 33.0, 32.9, 31.1, 31.0, 29.69, 29.65, 29.58, 29.30, 29.27, 29.2, 29.1, 28.9, 28.7, 27.9, 27.18, 27.15, 27.13, 27.0; IR (neat) 3281, 3003, 2928, 2855, 1576, 1479, 1464, 1423, 1348, 1188, 1107, 1065, 1045, 1026, 795, 714 cm^{-1} ; FAB-MS m/z (relative intensity) 590.5 [(M + H) $^+$, 100], 286.3 (22), 220.2 (18), 154.1 (35), 136.1 (25), 106.0 (23), 93.0 (12); FAB-HRMS

calcd for $C_{38}H_{60}O_2N_3$ [(M + H)⁺] 590.4686, found 590.4688.

Synthetic (–)-Pyrinodemin A (3). To a solution of alcohol **26** (50 mg, 0.085 mmol) and 4-(*N,N*-dimethylamino)pyridine (29 mg, 0.24 mmol) in acetonitrile (1 mL) at room temperature under a nitrogen atmosphere was added dropwise phenyl chlorothionoformate (0.071 mL, 0.51 mmol), and the solution was stirred at the same temperature for 41 h. Brine (10 mL) was added to the solution, and the aqueous layer was extracted with dichloromethane (10 mL × 3). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was subjected to flash column chromatography (dichloromethane/acetone = 70:30) on silica gel (3 g) to afford the crude thionocarbonate which was taken to the next step without further purification.

To a solution of the above crude thionocarbonate and 2,2'-azobisisobutyronitrile (2.9 mg, 0.017 mmol) in toluene (1 mL) at room temperature under a nitrogen atmosphere was added dropwise tributyltin hydride (0.031 mL, 0.117 mmol), and the solution was stirred at 100 °C for 10 min. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate = 70:30) on silica gel (4 g) to provide crude products, which were further purified by flash column chromatography (dichloromethane/acetone = 85:15) on silica gel (2 g) to give the synthetic (–)-pyrinodemin A (**3**) (28.8 mg, 59% yield, 2 steps) as a colorless oil: R_f = 0.56 (dichloromethane/acetone = 50:50); $[\alpha]_D^{26}$ –6.42 (c 0.94, $CHCl_3$); 1H NMR (400 MHz, $CDCl_3$) δ 8.44 (2H, d, J = 2.2 Hz), 8.43 (2H, dd, J = 5.0, 1.6 Hz), 7.48 (2H, d, J = 7.8 Hz), 7.19 (2H, ddd, J = 7.7, 4.8, 0.7 Hz), 5.36–5.32 (2H, m), 4.10–4.01 (1H, m), 3.53–3.41 (1H, m), 2.89–2.78 (2H, m), 2.60 (4H, t, J = 7.7 Hz), 2.64–2.54 (1H, m), 2.07–1.96 (4H, m), 1.82–1.70 (1H, m), 1.74–1.20 (35H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 147.1, 137.9, 135.7, 129.79, 129.77, 123.2, 77.7 (br), 72.6 (br), 57.1 (br), 49.9, 34.1 (br), 33.0, 31.1, 29.7, 29.6, 29.4, 29.3, 29.2, 29.12, 29.07, 28.7, 28.0, 27.1, 27.0, 26.4, 26.3; IR (neat) 2928, 2855, 1575, 1423, 1340, 1188,

1026, 793, 714 cm^{-1} ; EI-MS m/z (relative intensity) 574 $[(M+H)^+, 1]$, 573 (M^+ , 2), 383 (5), 365 (19), 355 (6), 353 (6), 327 (3), 315 (4), 301 (5), 285 (86), 270 (7), 244 (19), 231 (14), 230 (56), 220 (15), 216 (17), 204 (7), 202 (3), 190 (35), 176 (84), 162 (32), 148 (26), 134 (17), 124 (4), 120 (38), 106 (100), 93 (93); EI-HRMS calcd for $\text{C}_{38}\text{H}_{59}\text{ON}_3$ (M^+) 573.4658, found 573.4661.

Table 1. MS Spectral Data for 2–4 and the Natural Product as Provided by Prof. Kobayashi

Baldwin 2 ^a EI	Snider 2 ^b DEI	2 (15'–16') EI	4 (13'–14') EI	3 (14'–15') EI	natural product EI (from Kobayashi)
—	574 (49)	574 (10)	574 (4)	574 (1)	574 (1.7)
—	573 (4)	573 (4)	573 (9)	573 (2)	573 (4.1)
—	383 (8)	383 (18)	383 (20)	383 (5)	383 (11)
365 (55)	365 (29)	365 (100)	365 (100)	365 (19)	365 (60)
355 (10)	355 (18)	355 (17)	355 (19)	355 (6)	355 (12)
—	353 (12)	353 (2)	353 (3)	353 (6)	353 (10)
327 (8)	327 (12)	327 (3)	327 (4)	327 (3)	327 (6)
315 (4)	315 (7)	315 (5)	315 (9)	315 (4)	315 (10)
301 (9)	301 (10)	301 (13)	301 (13)	301 (5)	301 (11)
285 (49)	285 (30)	285 (65)	285 (75)	285 (86)	285 (42)
270 (18)	270 (11)	270 (24)	270 (17)	270 (7)	270 (17)
244 (43)	244 (22)	244 (50)	244 (12)	244 (19)	244 (25)
231 (29)	231 (15)	231 (48)	— ^c	231 (14)	231 (20)
—	230 (8)	230 (3)	230 (1)	230 (56)	230 (6)
220 (38)	220 (31)	220 (71)	220 (53)	220 (15)	220 (39)
—	216 (2)	— ^c	216 (7)	216 (17)	216 (3)
204 (5)	204 (3)	204 (1)	204 (1)	204 (7)	204 (5)
—	202 (2)	— ^c	202 (1)	202 (3)	202 (2)
190 (21)	190 (13)	190 (16)	190 (8)	190 (35)	190 (12)
176 (37)	176 (17)	176 (19)	176 (9)	176 (84)	176 (17)
162 (16)	162 (12)	162 (10)	162 (8)	162 (32)	162 (10)
148 (18)	148 (15)	148 (13)	148 (8)	148 (26)	148 (11)
134 (13)	134 (13)	134 (9)	134 (4)	134 (17)	134 (9)
—	124 (17)	124 (32)	124 (5)	124 (4)	124 (25)
120 (26)	120 (22)	120 (20)	120 (9)	120 (38)	120 (17)
106 (100)	106 (100)	106 (92)	106 (65)	106 (100)	106 (77)
93 (97)	93 (94)	93 (87)	93 (57)	93 (93)	93 (100)

^a Cited from ref 5. ^b Cited from ref 4. ^c Not detected.

Table 2. ^{13}C NMR Data in CDCl_3 for **2–4** and the Natural Product

Baldwin 2 ^a 125.8 MHz	Snider 2 ^b	2 (15'–16') 100 MHz	4 (13'–14') 75 MHz	3 (14'–15') 75 MHz	natural product ^c
149.8 (2C)	150.0 (2C)	150.0	149.8	149.9	150.0 (2C)
147.0 (2C)	147.2 (2C)	147.2	147.1	147.1	146.5 (2C)
137.9 (2C)	137.9 (2C)	137.91 137.89	137.85 137.83	137.9	137.5 (2C)
135.7 (2C)	135.7 (2C)	135.7	135.7	135.7	135.4 (2C)
129.9	130.0	130.0	129.9	129.79	129.3 (2C)
129.5	129.6	129.6	129.6	129.77	
123.1 (2C)	123.2 (2C)	123.2	123.1	123.1	122.5 (2C)
77.6	77.8 (br)	77.7 (br)	77.6 (br)	77.7 (br)	77.2
72.5	72.6 (br)	72.6 (br)	72.5 (br)	72.6 (br)	72.1
56.8	57.2 (br)	57.1 (br)	57.1 (br)	57.1 (br)	57.3
49.8	49.9	49.9	49.8	49.9	49.3
34.1	34.2 (br)	34.2 (br)	34.1 (br)	34.1 (br)	33.6
32.9 (2C)	33.0 (2C)	33.0	32.9	33.0	33.0 (2C)
31.0 (2C)	31.1 (2C)	31.1	31.02 31.01	31.1	31.2 (2C)
[29.6	29.7 (2C)	29.72 29.69	29.65 29.60	29.7	[29.8
29.5	29.4 (2C)	29.4 29.35	29.5	29.6	
29.3	29.33 29.30	29.31	29.3 29.23	29.4	
29.2	29.2	29.2	29.16	29.3	
29.1	29.11	29.12	29.0		29.4] (8C)
29.0] (9C)	29.08	29.09	28.94	29.2	29.2 (2C)
28.6	28.8	28.8	28.93	29.12	
27.7	27.8	27.8	28.7	29.07	28.9 (2C)
27.4	27.5	27.5	27.2	28.7	
27.1	27.18	27.2	27.1	28.0	27.9
27.0	27.12	27.1	27.04	27.1	27.1 (2C)
26.9	27.0	27.0	26.96	27.0	
26.3	26.4	26.5	26.4	26.4	26.5
26.2	26.3	26.3	26.2	26.3	26.3

^a Cited from ref 5. ^b Cited from ref 4. ^c Cited from ref 2.

Table 3. ¹H NMR Data in CDCl₃ for 2–4 and the Natural Product

Baldwin 2 ^a 500 MHz	Snider 2 ^b	2 (15'–16') 400 MHz	4 (13'–14') 400 MHz	3 (14'–15') 400 MHz	natural product ^c
8.49–8.36 (4, br s)	8.46–8.41 (4, m)	8.46–8.41 (4, m)	8.46–8.41 (4, m)	8.44 (2, d, 2.2)	8.44 (2, m)
				8.43 (2, dd, 5.0, 1.6)	8.42 (2, br s)
7.50–7.43 (2, m)	7.48 (2, br d, 7.9)	7.48 (2, d, 7.8)	7.51–7.46 (2, m)	7.48 (2, d, 7.8)	7.48 (2, d, 7.5)
7.21–7.14 (2, m)	7.20 (2, dd, 7.9, 4.9)	7.20 (2, dd, 7.7, 4.8)	7.20 (2, dd, 7.8, 4.9)	7.19 (2, ddd, 7.7, 4.8, 0.7)	7.19 (2, br t, 7.0)
5.38–5.28 (2, m)	5.39–5.30 (2, m)	5.40–5.29 (2, m)	5.39–5.29 (2, m)	5.36–5.32 (2, m)	5.34 (2, m)
4.08–4.00 (1, m)	4.05 (1, ddd, 6, 6, 6)	4.11–4.00 (1, m)	4.10–4.00 (1, m)	4.10–4.01 (1, m)	4.05 (1, m)
3.51–3.40 (1, m)	3.50–3.42 (1, br)	3.46 (1, br s)	3.52–3.42 (1, m)	3.53–3.41 (1, m)	3.46 (1, m)
2.89–2.78 (2, m)	2.89–2.78 (2, m)	2.89–2.78 (2, m)	2.89–2.78 (2, m)	2.89–2.78 (2, m)	2.84 (1, m)
					2.82 (1, m)
2.72–2.60 (1, m)	2.64–2.60 (1, m)	2.66–2.56 (1, m)	2.60 (4, t, 7.7)	2.60 (4, t, 7.7)	2.60 (4, t, 7.6)
2.60 (4, t, 7.7)	2.60 (4, t, 7.6)	2.60 (4, t, 7.7)	2.64–2.55 (1, m)	2.64–2.54 (1, m)	2.59 (1, m)
2.07 (2, m)	2.07–1.96 (4, m)	2.08–1.96 (4, m)	2.06–1.94 (4, m)	2.07–1.96 (4, m)	2.03 (4, m)
2.04 (2, m)	1.82–1.72 (1, br)	1.77 (1, br s)	1.84–1.23 (36, m)	1.82–1.70 (1, m)	1.76 (1, m)
1.80 (1, m)	1.71–1.50 (9, m)	1.72–1.50 (9, m)		1.74–1.20 (35, m)	1.66 (1, m)
1.72 (1, m)					1.65 (1, m)
1.70 (1, m)					1.64 (1, m)
1.69 (1, m)					1.60 (4, m)
1.64 (4, m)					1.55 (1, m)
1.59 (1, m)	1.50–1.36 (6, m)	1.51–1.23 (26, m)			1.53 (2, m)
1.59 (2, m)					1.44 (1, m)
1.49 (1, m)					1.42 (1, m)
1.49 (1, m)					1.40 (1, m)
1.47 (1, m)					1.33 (4, m)
1.46 (1, m)					
1.44 (2, m)					
1.34 (1, m)	1.36–1.24 (20, m)				
1.42–1.28 (18, m)					1.3–1.2 (18)

^a Cited from ref 5. ^b Cited from ref 4. ^c Cited from ref 2.

Kobayashi's EI-MS spectrum of natural product

MS5 SPECTRUM
Sample: 441-10
RT 3.45 EI (Pos.) GC 342.9c BP: m/z 93.8000 Int. 490.3416 Lv 1.00
Scan# (4E) 13-JAN-97 15:31

75 MHz (CDCl₃) ¹³C NMR spectrum of synthetic (-)-3

Date : Fri Jul 5 06:46:44 2002
 File Name : auto_13c.nmdata
 Comment :
 Slice History :
 EXMODE : bcm

POINT : 32768 point
 SAMP : 32768 point
 FREQU : 20366.6 Hz
 FILTR : 10200 Hz
 DELAY : 19.6 usec
 DEATH : 27.3 usec
 INTVL : 49.1 usec
 TIMES : 10000 times
 DUMMY : 1 times
 PD : 1.3911 sec
 ACQTM : 1608.9088 msec
 PREDL : 10.0000 msec
 INJMT : 10.0000 msec
 RESOL : 0.62 Hz
 PW1 : 4.30 usec
 13C : 13C
 DBNUC : 75.45 MHz
 DBFRQ : 125840.00 Hz
 DBSET : 30
 RGAIN : 30
 TRNUC : 300.40 MHz
 TRFRQ : 131150.00 Hz
 TRSET : 50.0 usec
 TRPW : 0
 TRNS : 0

SCANS : 10000 times
 SLVNT : CDCl₃
 SPINNING : 13 Hz
 TEMP : 25.9 C

Date : Wed Jul 3 17:42:16 2002
 File Name : LoadingF10.nm
 Comment :
 Slice History : non
 EXMODE :
 POINT 32768 points
 SAMPO 32768 points
 FREQU 7993.6 Hz
 FILTR 4000 Hz
 DELAY 50.0 usec
 DEAUT 72.2 usec
 INTVL 125.1 usec
 TIMES 8 times
 DUMMY 0 times
 PD 2.9007 sec
 ACQTM 4099.2769 msec
 PREDL 10.0000 msec
 INIWT 0.5000 msec
 RESOL 0.24 Hz
 PW1 5.70 usec
 OBNUC 1H
 OBFRQ 399.65 MHz
 OBSET 134300.00 Hz
 RGAIN 23
 SCANS 8 times
 SLVNT CDCL3
 SPINNING 12 Hz
 TEMP 25.5 C

EL-MS spectrum of synthetic 2

S25

100 MHz (CDCl₃) ¹³C NMR spectrum of synthetic 2

Date : Tue Oct 22 17:01:45 2002

File Name : .LoadingFID.nmdata
 Comment : 13C NMR
 Slice History :
 EXNO : bcn

Parameter	Value
POINT	32768 points
SAMPO	32768 points
FREQ	27100.3 Hz
FILTR	13550 Hz
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DEADT	19.6 usec
INTVL	35.9 usec
TIMES	400 times
DUMMY	1 times
PD	1.7909 sec
ACQTM	1209.1393 msec
PREDL	10.0000 msec
INTWT	1000.0000 msec
RESOL	0.83 Hz
PW1	5.15 usec
OBNUC	13C
OBFRQ	100.40 MHz
OBSET	135500.00 Hz
RGAIN	29
IRNUC	1H
IRFRQ	399.65 MHz
IRSET	134500.00 Hz
IRPW	50.0 usec
IRNS	0
SCANS	400 times
SLVNT	CDCl3
SPINNING	13 Hz
TEMP	26.6 C

EL-MS spectrum of synthetic 4

75 MHz (CDCl₃) ¹³C NMR spectrum of synthetic 4

Date : Thu Jun 27 11:10:35 2002

FileName : auto_1h.nmdata

Comment :
SliceHistory :
EXMODE : non

POINT 32768 points
SAMPD 32768 points
FREQU 7993.6 Hz
FILTR 4000 Hz
DELAY 50.0 usec
DEADT 72.2 usec
INTVL 125.1 usec
TIMES 8 times
DUMMY 0 times
PD 2.9007 sec
ACQTM 4099.2769 msec
PREDL 10.00000 msec
ININT 0.5000 msec
RESOL 0.24 Hz
PW1 5.70 usec
OBNUC 1H
OBFRQ 399.65 MHz
OBSET 134300.00 Hz
RGAIN 22
SCANS 8 times
SLVNT CDCL3
SPINNING 11 Hz
TEMP 23.7 C