

rinsed into a separatory funnel containing H₂O (40 mL). The aqueous layer was extracted with EtOAc (2 × 30 mL), concentrated, and chromatographed (silica, hexanes:EtOAc, 15:1 → 4:1) to afford acetonide **106** (2.07 g, 93% yield) as a colorless oil. **106**: R_f = 0.2 (silica, hexanes:EtOAc, 2:1); IR (film): ν_{\max} = 3442 (m), 2947 (m), 1732 (s), 1611 (m), 1460 (m), 1254 (m), 1016 (m), 914 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 6.88 (s, 1 H), 6.61 (s, 1 H), 6.13 (s, 1 H), 4.63–4.56 (m, 1 H), 3.92 (s, 3 H), 3.85 (s, 3 H), 3.19 (d, J = 8.8 Hz, 1 H), 2.55–2.45 (m, 2 H), 2.41 (s, 3 H), 2.10–2.05 (m, 1 H), 1.86–1.80 (m, 1 H), 1.45 (s, 3 H), 1.44 (s, 3 H), 0.37 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 173.5, 157.8, 139.7, 119.6, 118.0, 109.9, 109.1, 86.3, 73.4, 73.1, 55.7, 52.1, 48.0, 30.0, 26.6, 25.2, 21.8, 20.9, 17.5, 14.1; HRMS calcd for C₂₁H₂₈O₆ (M + Na⁺) 399.1778, found 399.1772.

Oxidation of alcohol 106 to ketone 97. Solid Dess–Martin reagent (1.5 g, 3.5 mmol) was added in three portions over 5 min to a vigorously stirred solution of acetonide **106** (620 mg, 1.64 mmol) in CH₂Cl₂ (20 mL) at 0 °C under Ar. The solution was allowed to warm to ambient temperature and stirring was continued for an additional 1 h at which time Et₂O (20 mL) was added to precipitate the reagent followed by sat. aq. Na₂S₂O₃ (30 mL). The heterogeneous mixture was vigorously stirred until the organic phase became clear, at which time it was placed into a separatory funnel. The aqueous layer was separated and extracted with Et₂O (3 × 25 mL) and the combined organics were washed with sat. aq. NaHCO₃ (3 × 20 mL), brine (30 mL), and concentrated. The crude product was dissolved in CH₂Cl₂ (50 mL) and cooled to 0 °C and DBU (200 μ L, 1.3 mmol) was added via syringe. After 10 min the reaction mixture was poured into a separatory funnel containing Et₂O (100 mL). The solution was washed with 0.5 M aq. HCl (80 mL), brine (50 mL), dried over MgSO₄, and concentrated to dryness. Flash chromatography (silica, hexanes:EtOAc, 6:1) provided ketone **97** (580 mg, 93% yield) as a white solid (m.p. 180–182, EtOH). **97**: R_f = 0.3 (silica, hexanes:EtOAc, 1:1); $[\alpha]_D$ = – 67.2 (c = 0.2, CHCl₃); IR (film): ν_{\max} = 2982 (m), 2960 (w), 1738 (s), 1588 (m), 1459 (m), 1091 (w), 917 (m), cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 6.65 (s, 1 H), 6.63 (s, 1 H), 5.84 (s, 1 H), 3.93 (s, 3 H), 3.89 (s, 3 H), 2.98 (s, 1 H), 2.81–1.73 (m, 1 H), 2.43 (s, 3 H), 2.42–2.36 (m, 1 H), 1.81–1.75 (m, 1 H),

1.30 (s, 3 H), 1.10 (s, 3 H), 0.86 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ = 213.1, 172.6, 158.5, 139.5, 130.2, 122.8, 118.8, 111.2, 110.8, 87.8, 74.1, 60.3, 55.9, 52.3, 44.1, 36.0, 30.4, 27.3, 26.7, 21.7, 14.1; HRMS calcd for $\text{C}_{21}\text{H}_{26}\text{O}_6$ ($\text{M} + \text{Na}^+$) 397.1621, found 397.1626. Stereochemistry assigned by nOe experiments

Alkylation of ketone 97 to tertiary alcohol 107. The ketone 97 (540 mg, 1.44 mmol) was alkylated with the cerium Grignard reagent (3 mmol) according to the procedure already described for the preparation of compound (82). Flash chromatography (silica, hexanes:EtOAc, 10:1) yielded the tertiary hydroxy compound **107** (565 mg, 95% yield, colorless oil) as a single diastereoisomer. **107**: R_f = 0.3 (silica, hexanes:EtOAc, 4:1); $[\alpha]_D = -42.2$ (c = 0.104, CHCl_3); IR (film): ν_{max} = 3452 (brw), 2958 (w), 1737 (m), 1460 (m), 1248 (m), 1103 (w), 1024 (w) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 6.64 (s, 1 H), 6.59 (s, 1 H), 5.96 (s, 1 H), 4.24 (s, 1 H), 3.93 (s, 3 H), 3.89 (s, 3 H), 3.02 (s, 1 H), 2.81 (ddd, J = 13.9, 8.2, 8.0 Hz, 1 H), 2.43 (ddd, J = 13.9, 8.2, 5.8 Hz, 1 H), 2.39 (s, 3 H), 2.06 (ddd, J = 13.4, 9.7, 7.5 Hz, 1 H), 1.86 (ddd, J = 13.9, 8.2, 5.8 Hz, 1 H), 1.41 (s, 3 H), 1.41–1.35 (m, 1 H), 1.19 (s, 3 H), 1.18 (d, J = 7.5 Hz, 3 H), 1.15 (d, J = 6.8 Hz, 3 H), 1.09 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ = 173.1, 159.0, 139.1, 134.5, 121.4, 120.0, 110.3, 110.1, 87.2, 85.9, 74.0, 55.9, 55.8, 52.2, 45.9, 34.2, 33.3, 32.8, 27.4, 27.2, 27.2, 21.9, 18.5, 18.0; HRMS calcd for $\text{C}_{24}\text{H}_{34}\text{O}_6$ ($\text{M} + \text{Na}^+$) 441.2247, found 441.2259.

Reduction of 107 and formation of cyclic ether 108. To a stirred solution of tertiary alcohol **107** (45 mg, 0.11 mmol) in CH_2Cl_2 (3 mL) and Et_3SiH (0.9 mL, 5.5 mmol) was added TFA (170 μL , 2.2 mmol) via syringe. After 1 h, the volatiles were removed under reduced pressure, the residue was azeotroped with toluene (2×10 mL) and the non-volatiles residue purified by flash chromatography (silica, hexanes:EtOAc, 10:1) yielding polycyclic ether **108** (24 mg, 65% yield) as a colorless oil. **108**: R_f = 0.3 (silica, hexanes:EtOAc, 3:1); IR (film): ν_{max} = 2934 (m), 1728 (s), 1585 (m), 1462 (s), 1276 (m), 1131 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 6.54 (s, 1 H), 6.39 (s, 1 H), 3.42 (d, J = 17.5 Hz, 1 H), 3.32 (s, 3 H), 3.25 (s, 3 H), 3.20 (d, J = 17.5 Hz, 1 H), 2.33 (s, 1 H), 2.21 (s, 3 H), 1.93–1.88 (m, 1 H), 1.79 (ddd, J = 12.5, 9.8, 3.3 Hz, 1 H), 1.71 (ddd, J = 13.5, 6.7, 6.7 Hz, 1 H), 1.58 (ddd, J = 12.5, 12.2, 3.4 Hz, 1 H), 1.36–1.30

(m, 2 H), 1.28–1.16 (m, 2 H), 1.14 (s, 3 H), 0.98 (d, $J = 7.0$ Hz, 3 H), 0.80 (d, $J = 6.6$ Hz, 3 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 173.6, 157.2, 136.1, 135.2, 122.2, 119.4, 109.3, 97.4, 86.4, 57.2, 55.1, 51.8, 47.9, 33.6, 31.2, 29.5, 28.5, 21.6, 18.4, 17.7, 15.4$; HRMS calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4$ ($\text{M} + \text{Na}^+$) 367.1880, found 367.1892.

Elimination of tertiary alcohol 107 to form trisubstituted olefin 109. The tertiary hydroxyl group in **107** was eliminated using a modification of the SOCl_2 protocol described for compound **83**. To a cooled ($-60\text{ }^\circ\text{C}$) solution of alcohol **107** (406 mg, 0.97 mmol) in CH_2Cl_2 (5 mL) containing lutidine (5 mL) and pyridine (1 mL) under Ar was added SOCl_2 (550 μL , 7.5 mmol) via syringe. The reaction temperature was maintained for 0.5 h and then allowed to reach $-20\text{ }^\circ\text{C}$ over 2 h, at which time TLC analysis indicated complete conversion. The reaction mixture was quenched with sat. aq. NaHCO_3 (15 mL) at $-20\text{ }^\circ\text{C}$ and the resulting mixture was allowed to reach ambient temperature with stirring. The biphasic mixture was extracted with 1:1 Et_2O :hexanes ($2 \times 25\text{ mL}$), and the combined organic phase was concentrated to dryness and azeotroped with toluene ($3 \times 10\text{ mL}$). The residue was filtered through a plug of silica gel (ether:hexanes, 1:1) to afford a mixture of inseparable elimination products (14:2:1 ratio of **109**:**110**:**111**, 366 mg, 94% total yield) as a clear oil. A small amount of pure **109** for characterization purposes was obtained by repeated PTLC. **109**: $R_f = 0.4$ (silica, hexanes:EtOAc, 3:1); IR (film): $\nu_{\text{max}} = 2957$ (m), 1731 (s), 1462 (m), 1064 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta = 6.78$ (s, 1 H), 6.55 (s, 1 H), 5.26 (s, 1 H), 5.24 (s, 1 H), 3.83 (s, 3 H), 3.70 (s, 3 H), 3.49 (s, 1 H), 2.96 (d, $J = 15.8$ Hz, 1 H), 2.73 (m, 1 H), 2.32 (s, 3 H), 1.92 (dd, $J = 15.8, 2.6$ Hz, 1 H), 1.56 (s, 3 H), 1.52 (s, 3 H), 1.17 (d, $J = 7.0$ Hz, 3 H), 1.12 (d, $J = 6.6$ Hz, 3 H), 1.08 (s, 3 H); ^{13}C NMR (DEPT) (125 MHz, CDCl_3): $\delta = 169.0, 122.8, 120.5, 110.6, 74.3, 56.2, 52.6, 48.5, 31.9, 31.1, 27.7, 24.2, 22.4, 22.2, 21.6$; Unit Mass (ESI) calcd for $\text{C}_{24}\text{H}_{32}\text{O}_5$ ($\text{M} + \text{Na}^+$) 423.2, found 432.2.

Hydrogenation of olefin 109 to compound 112. A 10 mL beaker equipped with a stirbar was charged with compound **109** (10 mg, 0.025 mmol, 14:2:1 mixture of isomers), EtOH or EtOAc (2 mL), and *ca* 5 mg of a hydrogenation catalyst (PtO_2 , Pd/C, $\text{Pd}(\text{OH})_2$,

IrP(cyhex)₃(COD)(py)PF₆, Rh black or Rh/Al₂O₃). The beaker was placed inside a Parr bomb and pressurized with 1–60 atm H₂. The atmosphere within the bomb was pressurized and vented (very slowly!) several times to flush other gases from the system. The solution was stirred from below via a stirplate for the indicated length of time (see Table 5). The isomeric olefins and corresponding reduction products were almost inseparable. A small amount of pure material was obtained by repeated PTLC for initial characterization and stereochemical determination. All product ratios were assigned by characteristic downfield ¹H NMR signals. To monitor reaction progress, the H₂ was slowly vented in a hood and the bomb was re-pressurized with 5 atm Ar before exposing the reaction mixture to the air. Filtration through a pad of Celite afforded clean mixtures of products. **112** (major isomer): *R_f* = 0.35 (silica, hexanes:CH₂Cl₂ with a trace of EtOAc, 1:1, run twice); ¹H NMR (600 MHz, CDCl₃): δ = 6.59 (s, 1 H), 6.50 (s, 1 H), 5.28 (s, 1 H), 3.86 (s, 3 H), 3.77 (s, 3 H), 2.54 (ddd, *J* = 13.2, 9.3, 4.0 Hz, 1 H), 2.46–2.41 (m, 1 H), 2.32 (s, 3 H), 1.89 (ddd, *J* = 12.6, 9.3, 7.0 Hz, 1 H), 1.83 (dddd, *J* = 10.2, 6.9, 6.9, 3.5 Hz, 1 H), 1.49 (ddd, *J* = 12.6, 11.7, 4.2 Hz, 1 H), 1.37 (s, 3 H), 1.36 (s, 3 H), 1.38–1.35 (m, 1 H), 0.93 (d, *J* = 6.9 Hz, 1 H), 0.86 (d, *J* = 6.9 Hz, 1 H), 0.81 (s, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 175.5, 159.3, 140.9, 139.8, 123.3, 118.5, 110.5, 109.8, 88.0, 73.2, 56.7, 56.0, 53.0, 52.1, 49.6, 36.0, 28.7, 27.3, 26.0, 25.9, 25.0, 23.5, 22.7, 16.2; HRMS calcd for C₂₄H₃₄O₅ (M + Na⁺) 425.2298, found 425.2305. Characterization for **113** will be given below (see → **113**)

Preparation of hydroxyl keto ester 116 from 112 via 115. The mixture of olefins (**110**:**111**:**112**:**113**, 6:3:71:20 ratio, 27 mg, 0.067 mmol) obtained from the reduction of **109** (H₂, PtO₂) was placed in a 10 mL round-bottom flask fitted with a stirbar and a reflux condenser and dissolved in 1:1 THF: 3 M aq. HCl (2 mL). The biphasic solution was vigorously stirred and heated at 80 °C for 1 h. The resulting solution was cooled and poured into a separation funnel containing H₂O (10 mL) and EtOAc (10 mL). Saturated aq. NaHCO₃ was added until the pH became basic (>7). This mixture was extracted with EtOAc (3 × 10 mL) and concentrated to a gummy residue which appeared clean by TLC (*R_f* = 0.15, silica, hexanes:EtOAc, 4:1), but contained numerous products as determined by ¹H NMR spectroscopic analysis. This crude

mixture was oxidized with $\text{SO}_3 \cdot \text{py}$ -DMSO as previously described (**80** \rightarrow **81**) to afford crude hydroxyl keto ester **116**. Flash chromatography (silica, hexanes:EtOAc, 8:1 \rightarrow 3:1) gave pure **116** (10.5 mg, 45% yield) as an off-white solid. **116**: R_f = 0.1 (silica, hexanes:EtOAc, 3:1); IR (film): ν_{max} = 3435 (m), 2956 (m), 2869 (w), 1736 (s), 1685 (s), 1605 (m) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 6.69 (s, 1 H), 6.56 (s, 1 H), 4.81 (s, 1 H), 3.86 (s, 3 H), 3.57 (s, 3 H), 3.17 (d, J = 5.2 Hz, 1 H), 2.37 (s, 3 H), 1.97–1.93 (m, 1 H), 1.78–1.74 (m, 1 H), 1.64–1.58 (m, 2 H), 1.46–1.42 (m, 1 H), 1.42–1.36 (m, 1 H), 1.26 (s, 3 H), 1.04 (d, J = 6.6 Hz, 3 H), 0.98 (d, J = 6.6 Hz, 3 H), Hz, 1 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 193.4, 171.1, 159.7, 154.2, 148.3, 121.3, 115.4, 110.1, 86.6, 60.1, 56.7, 53.4, 52.1, 49.5, 36.2, 32.4, 25.9, 23.9, 23.4, 22.8, 18.9; HRMS calcd for $\text{C}_{21}\text{H}_{28}\text{O}_5$ ($\text{M} + \text{Na}^+$) 383.1829, found 383.1836.

Preparation of 6-*epi*-debromohamigeran A (117) from 116. To a solution of the ketone **116** (9 mg, 0.025 mmol) in CH_2Cl_2 (3 mL) under Ar at -78°C was added BBr_3 (1 M solution in CH_2Cl_2 , 250 μL , 0.25 mmol). Following the procedure given for (**88** \rightarrow **89**) phenol **117** (8 mg, 93% yield, yellow solid) was obtained after flash column chromatography (silica, hexanes:EtOAc, 15: \rightarrow 5:1). **117**: R_f = 0.6 (silica, hexanes:EtOAc, 6:1); IR (film): ν_{max} = 3464 (m), 2953 (m), 1729 (s), 1632 (s), 1011 (w), 773 (m) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 11.0 (s, 1 H), 6.64 (s, 1 H), 6.58 (s, 1 H), 4.33 (s, 1 H), 3.65 (s, 3 H), 3.32 (d, J = 2.6 Hz, 1 H), 2.34 (s, 3 H), 1.89–1.85 (m, 2 H), 1.77–1.73 (m, 2 H), 1.53–1.50 (m, 3 H), 1.14 (d, J = 6.5 Hz, 3 H), 0.97 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 198.4, 170.7, 161.5, 152.4, 150.7, 120.6, 114.8, 111.8, 84.9, 59.6, 53.5, 51.3, 49.1, 35.7, 34.2, 27.3, 23.9, 23.0, 21.8, 12.2; HRMS calcd for $\text{C}_{20}\text{H}_{26}\text{O}_5$ ($\text{M} + \text{H}^+$) 347.1853, found 347.1861.

Preparation of 6-*epi*-hamigeran A (118) from 117. To a solution of ketone **117** (8 mg, 0.023 mmol) in CH_2Cl_2 (0.5 mL) at 0°C was added a solution of $i\text{Pr}_2\text{NH}$ in CH_2Cl_2 (0.05 M in $i\text{Pr}_2\text{NH}$, 50 μL , 0.002 mmol $i\text{Pr}_2\text{NH}$), followed by slow addition of NBS as a solution in CH_2Cl_2 (0.1 M in NBS, 240 μL , 0.024 mmol NBS). The resulting solution was stirred for 3 h and poured into H_2O (5 mL). The biphasic mixture was extracted with CH_2Cl_2 (2×3 mL), concentrated, and purified by PTLC (silica, hexanes:Et₂O, 10:1) to afford 6-*epi*-hamigeran (**118**) as a yellow solid

(9 mg, 94% yield). **118**: R_f = 0.4 (silica, hexanes:EtOAc, 12:1); IR (film): ν_{\max} = 3495 (s), 1754 (s), 1739 (s), 1639 (m), 1449 (m) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 11.85 (s, 1 H), 6.77 (s, 1 H), 4.26 (s, 1 H), 3.65 (s, 3 H), 3.21 (d, J = 1.9 Hz, 1 H), 2.45 (s, 3 H), 1.86–1.84 (m, 2 H), 1.77–1.74 (m, 1 H), 1.68 (t, J = 7.9 Hz, 1 H), 1.50–1.46 (m, 2 H), 1.12 (s, 3 H), 1.15 (d, J = 6.6 Hz, 3 H), 0.98 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 199.2, 170.8, 158.2, 151.3, 149.7, 122.1, 113.1, 85.4, 60.0, 51.3, 54.1, 49.6, 36.0, 34.6, 29.9, 27.8, 25.3, 24.3, 22.6, 20.6; HRMS calcd for $\text{C}_{20}\text{H}_{25}\text{BrO}_5$ ($\text{M} + \text{Na}^+$) 245.0958, found 245.0955.

Hydroboration of olefin 109 to hydroxy acetone 121. Neat $\text{BH}_3\cdot\text{SMe}_2$ (4 mL, 40 mmol) was added to a mixture of olefins **109–111** (412 mg, 1.03 mmol, 14:2:1 ratio of isomers in favor of **109**) in THF (4 mL). The solution was placed in an ultrasonic bath and sonicated for 8 h while the bath temperature was maintained at 40 °C. The reaction mixture was cooled to 0 °C, diluted with THF (8 mL), and cautiously quenched with 10% aq. NaOH (8 mL). After stirring for 12 h, the biphasic mixture was extracted with Et_2O (3×30 mL) and the combined extracts were dried (MgSO_4) and evaporated to afford a crude mixture of diastomeric alcohols. Flash chromatography (silica, hexanes:EtOAc, 8:1) gave **121** (192 mg, 45% yield) and its diastereoisomer (*ca* 2:1 ratio in favor of **121**). **121**: pale yellow oil; R_f = 0.3 (silica, hexanes:EtOAc, 2:1); IR (film): ν_{\max} = 3440 (m), 2958 (m), 1736 (s), 1611 (m), 1585 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 8.05 (bs, 1 H), 6.82 (s, 1 H), 6.60 (s, 1 H), 5.74 (s, 1 H), 4.40 (ddd, J = 6.7, 3.4, 3.1 Hz, 1 H), 3.93 (s, 3 H), 3.84 (s, 3 H), 3.60 (d, J = 7.3 Hz, 1 H), 2.92 (dd, J = 14.3, 6.6 Hz, 1 H), 2.26–2.20 (m, 2 H), 1.80–1.70 (m, 1 H), 1.48 (s, 3 H), 1.30 (s, 3 H), 1.20 (s, 3 H), 1.03 (d, J = 5.9 Hz, 3 H), 0.94 (d, J = 5.9 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ = 174.3, 159.8, 139.3, 138.6, 122.7, 118.5, 110.0, 109.4, 86.7, 72.9, 68.6, 56.2, 53.5, 52.4, 50.4, 46.9, 28.8, 26.4, 25.7, 24.1, 22.8, 22.4; HRMS calcd for $\text{C}_{24}\text{H}_{34}\text{O}_6$ ($\text{M} + \text{Na}^+$) 441.2247, found 441.2234.

De-oxygenation of alcohol 121 to acetone ester 113. PhOC(S)Cl (125 μL , 0.9 mmol) was added to a solution of **121** (190 mg, 0.45 mmol) in pyridine (3 mL) at room temperature, and the reaction mixture was stirred for 2 h. The reaction mixture was then diluted with Et_2O (10

mL) and poured into a separatory funnel containing 0.5 M aq. HCl (30 mL). The aqueous phase was extracted with Et₂O (2 × 20 mL) and the combined organic extracts were washed with 1 M aq. HCl (10 mL), brine (10 mL), dried over Na₂SO₄ and evaporated. The crude residue was filtered through a short silica column (ether-hexanes) and after concentration it was dissolved in benzene (3 mL) and *n*Bu₃SnH (1 mL, 3.7 mmol), and AIBN (16 mg, 0.1 mmol) were added. This mixture was refluxed for 1 h, cooled to room temperature, concentrated, and chromatographed (silica, hexanes:EtOAc, 15:1) to give compound **113** (115 mg, 64% yield) as a white solid (m.p. 155–157, Et₂O). **113**: *R*_f = 0.7 (silica, hexanes:EtOAc, 2:1); [α]_D = – 12.6 (*c* = 0.085, CHCl₃); IR (film): *v*_{max} = 2955 (m), 1735 (s), 1580 (w), 1376 (m), 911 (m) cm^{–1}; ¹H NMR (600 MHz, CDCl₃): δ = 6.93 (s, 1 H), 6.65 (s, 1 H), 5.3 (s, 1 H), 3.92 (s, 3 H), 3.78 (s, 3 H), 3.18 (d, *J* = 4.8 Hz, 1 H), 2.49–2.43 (m, 1 H), 2.41 (s, 3 H), 2.24–2.16 (m, 2 H), 1.80–1.60 (m, 2 H), 1.61 (s, 3 H), 1.57 (s, 3 H), 1.45–1.40 (m, 1 H), 1.22 (d, *J* = 5.9 Hz, 3 H), 1.20 (s, 3 H), 0.97 (d, *J* = 5.9 Hz, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 173.9, 158.3, 140.2, 139.9, 120.1, 118.5, 110.4, 109.6, 86.8, 73.9, 73.5, 60.8, 56.2, 52.6, 50.7, 49.5, 33.0, 30.4, 27.0, 25.7, 22.3, 21.5, 18.0, 14.6; HRMS calcd for C₂₄H₃₄O₅ (M + Na⁺) 425.2298, found 425.2301.

Hydrolysis of acetonide 113 to diol 128. A solution of acetonide **113** (90 mg, 0.22 mmol) in 1:1 THF:1 M aq. HCl (3 mL) was heated to 80 °C for 1 h and then was worked-up according to the procedure outlined for **116**. Flash chromatography (silica, hexanes:EtOAc, 6:1) gave the corresponding vicinal diol **128** (70 mg, 88% yield) as an off-white solid. **128**: *R*_f = 0.15 (silica, hexanes:EtOAc, 2:1); IR (film): *v*_{max} = 3521 (s), 2956 (m), 1726 (s), 1612 (m), 1578 (s), 1266 (m) cm^{–1}; ¹H NMR (500 MHz, CDCl₃): δ = 6.68 (s, 1 H), 6.55 (s, 1 H), 5.12 (s, 1 H), 4.80 (s, 1 H), 3.84 (s, 3 H), 3.59 (s, 3 H), 3.21 (d, *J* = 4.4 Hz, 1 H), 2.32–2.32 (m, 1 H), 2.32 (s, 3 H), 2.23 (dd, *J* = 12.3, 7.0 Hz, 1 H), 2.02–1.86 (m, 3 H), 1.36–1.30 (m, 1 H), 1.81–1.17 (m, 6 H), 0.77 (d, *J* = 5.5 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 175.2, 159.0, 141.7, 139.5, 122.4, 119.6, 109.7, 79.9, 69.4, 56.3, 53.3, 51.6, 47.7, 44.0, 32.6, 31.1, 23.7, 22.8, 22.7, 16.5, 16.2; HRMS calcd for C₂₁H₃₀O₅ (M + Na⁺) 385.1985, found 385.1977.

Oxidation of 128 to hydroxyl keto ester 96. To a solution of diol **128** (55 mg, 0.15 mmol) in CH_2Cl_2 (3 mL) was added first 4Å MS (*ca* 60 mg) and then PDC (140 mg, 0.37 mmol) at ambient temperature. The resulting reddish-brown mixture was stirred at that temperature for 3 h and then Celite (3 g) was added to form a paste which was triturated with Et_2O (10 mL). The latter paste was filtered on a pad of silica gel (Et_2O as eluent) and the obtained solution was evaporated to afford material of reasonable purity which was further purified by PTLC (silica, hexanes:EtOAc, 3:1) to give pure hydroxyl keto ester **96** (44.5 mg, 83% yield) as a light yellow oil. **96**: R_f = 0.3 (silica, hexanes:EtOAc, 3:1); $[\alpha]_D = +38.8$ (c = 0.100, CHCl_3); IR (film): ν_{max} = 3437 (m), 2857 (m), 1738 (s), 1692 (s), 1604 (m), 1460 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 6.72 (s, 1 H), 6.61 (s, 1 H), 4.80 (s, 1 H), 3.86 (s, 3 H), 3.54 (d, J = 5.9 Hz, 1 H), 3.50 (s, 3 H), 2.37 (s, 3 H), 1.95 (m, 1 H), 1.70 (dd, J = 14.8, 8.9 Hz, 1 H), 1.58–1.41 (m, 2 H), 1.39 (s, 3 H), 1.37–1.22 (m, 2 H), 1.16 (d, J = 6.2 Hz, 1 H), 0.72 (d, J = 6.4, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ = 192.1, 169.9, 158.6, 146.1, 145.7, 122.4, 109.7, 84.1, 55.9, 53.1, 52.4, 51.3, 46.7, 34.3, 26.9, 26.8, 24.6, 23.5, 22.6, 21.7; HRMS calcd for $\text{C}_{21}\text{H}_{28}\text{O}_5$ ($M + \text{Na}^+$) 383.1829, found 383.1817.

Preparation of debromohamigeran A (1). A solution of hydroxy keto ester **96** (39 mg, 0.11 mmol) in CH_2Cl_2 (1.5 mL) was deprotected using BBr_3 (1 M solution in CH_2Cl_2 , 1 mL, 1 mmol) at -78°C according to the procedure given previously (**88** \rightarrow **89**). Flash chromatography (silica, hexanes:EtOAc, 10:1) afforded debromohamigeran (**1**) (35 mg, 94% yield) as a yellow solid (m.p. 120–125 $^\circ\text{C}$, Et_2O). **1**: R_f = 0.3 (silica, hexanes:EtOAc, 10:1); $[\alpha]_D = -43.5$ (c = 0.150, CHCl_3); IR (film): ν_{max} = 3459 (m), 2968 (m), 1740 (s), 1640 (s), 1600 (w), 1165 (m) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 10.97 (s, 1 H), 6.66 (s, 1 H), 6.63 (s, 1 H), 4.40 (s, 1 H), 3.59 (s, 3 H), 3.53 (d, J = 5.8 Hz, 1 H), 2.34 (s, 3 H), 2.03–1.99 (m, 1 H), 1.72 (dd, J = 14.4, 11.1 Hz, 1 H), 1.64–1.60 (m, 1 H), 1.60–1.56 (m, 1 H), 1.55–1.53 (m, 1 H), 1.37 (s, 3 H), 1.21 (d, J = 6.5 Hz, 3 H), 0.82 (d, J = 6.5 Hz, 3 H), 0.70–0.67 (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 198.6, 170.7, 162.1, 150.0, 145.0, 122.3, 115.9, 114.7, 84.6, 54.2, 53.8, 51.1, 48.0, 35.0, 28.2, 27.7, 25.2, 24.3, 23.6, 22.8; HRMS calcd for $\text{C}_{20}\text{H}_{26}\text{O}_5$ ($M + \text{Na}^+$) 369.1672, found 369.1681.

Preparation of hamigeran A (2). A solution of debromohamigeran A (1, 9 mg, 0.026 mmol) in CH_2Cl_2 (2 mL) at 0 °C was treated first with a solution of $i\text{Pr}_2\text{NH}$ in CH_2Cl_2 (0.05 M in $i\text{Pr}_2\text{NH}$, 50 μL , 0.002 mmol $i\text{Pr}_2\text{NH}$), followed by slow addition of a dilute NBS solution (0.1 M in CH_2Cl_2 , 260 μL , 0.026 mmol NBS) as described for compound **118**. PTLC (silica, hexanes:EtOAc, 10:1) afforded **2** (10 mg, 95% yield) as a yellow solid (m.p. 200–201 °C, Et_2O). **2**: $R_f = 0.3$ (silica, hexanes:EtOAc, 10:1); $[\alpha]_D = -34.5$ ($c = 0.09$, CHCl_3); IR (film): $\nu_{\text{max}} = 3450$ (s), 1739 (s), 1638 (s), 1607 (m), 1230 (w), 1170 (m) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 11.74$ (s, 1 H), 6.78 (s, 1 H), 4.32 (s, 1 H), 3.61 (s, 3 H), 3.55 (d, $J = 5.6$ Hz, 1 H), 2.47 (s, 3 H), 2.04–2.02 (m, 1 H), 1.72 (dd, $J = 14.6, 11.1$ Hz, 1 H), 1.64–1.60 (m, 1 H), 1.62–1.52 (m, 2 H), 1.36 (s, 3 H), 1.21 (d, $J = 6.6$ Hz, 1 H), 0.82 (d, $J = 6.6$ Hz, 1 H), 0.69 (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 198.9, 170.4, 158.5, 149.2, 143.6, 123.3, 115.6, 111.3, 84.1, 54.2, 54.0, 50.8, 48.0, 34.9, 28.2, 27.7, 25.5, 25.2, 24.2, 22.8$; HRMS calcd for $\text{C}_{20}\text{H}_{25}\text{BrO}_5$ ($M + \text{Na}^+$) 447.0777, found 447.0781.

Preparation of debromohamigeran B methyl ether (122). A solution of hydroxy keto ester **96** (21 mg, 0.06 mmol) in MeOH (1 mL) and 2 M aq KOH (0.5 mL) was heated to 70 °C for 2 h. The reaction mixture was cooled to ambient temperature, acidified with 0.1 M aq. HCl (11 mL), and extracted with EtOAc (2×8 mL). The combined organic phase was washed with brine (10 mL), dried over MgSO_4 , and concentrated to afford a crude oil which was dissolved in dioxane (3 mL). Tetrabutylammonium periodate (53 mg, 0.13 mmol) was added in 1 portion, the flask was fitted with a micro-condenser, and the temperature was raised to 100 °C (oil bath). After stirring for 1 h at this temperature, the reaction mixture was poured onto H_2O (10 mL), extracted with EtOAc (2×10 mL), dried over Na_2SO_4 , and concentrated to give a yellowish solid which was purified by rapid flash chromatography (silica, hexanes:EtOAc, 10:1) to afford **122** in varying yields (11.5 mg, up to 65% yield). **122**: $R_f = 0.7$ (silica, hexanes:EtOAc, 4:1); IR (film): $\nu_{\text{max}} = 3444$ (w), 2965 (m), 2879 (m), 1730 (m), 1681 (m), 1604 (w) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta = 6.73$ (s, 1 H), 6.68 (s, 1 H), 3.93 (s, 3 H), 3.11 (d, $J = 10.3$ Hz, 1 H), 2.50–2.46 (m, 2 H), 2.43 (s, 3 H), 2.08 (ddd, $J = 6.7, 6.7, 4.1$ Hz, 1 H), 1.97–1.90 (m, 1 H), 1.86–1.80 (m, 2

H), 1.76–1.72 (m, 1 H), 1.06 (d, $J = 7.0$ Hz, 3 H), 0.93 (s, 3 H), 0.86 (d, $J = 7.0$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 198.2, 181.8, 161.4, 147.4, 146.4, 128.6, 128.5, 118.6, 111.3, 56.8, 56.0, 48.3, 42.0, 31.5, 29.7, 29.5, 22.7, 17.6, 16.0$; HRMS calcd for $\text{C}_{19}\text{H}_{24}\text{O}_3$ ($\text{M} + \text{Na}^+$) 303.1955, found 303.1959.

Preparation of debromohamigeran B (124). A solution of methoxy diketone **122** (10 mg, 0.033 mmol) in CH_2Cl_2 (1 mL) was treated with BBr_3 (1 M solution in CH_2Cl_2 , 0.3 mL, 0.3 mmol) at -78°C according to the previously described procedure (**88** \rightarrow **89**). Preparative TLC (silica, hexanes:EtOAc, 6:1) provided pure debromohamigeran B (**124**) (9 mg, 95% yield) as a light yellow oil. **124**: $R_f = 0.7$ (silica, hexanes:EtOAc, 6:1); IR (film): $\nu_{\text{max}} = 3740$ (m), 2959 (m), 1720 (s), 1632 (s), 1565 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta = 11.92$ (s, 1 H), 6.73 (s, 1 H), 6.69 (s, 1 H), 3.49 (s, 3 H), 3.39 (d, $J = 9.5$ Hz, 1 H), 2.64–2.62 (m, 1 H), 2.38 (s, 3 H), 2.38–2.26 (m, 1 H), 1.84–1.80 (m, 1 H), 1.70–1.50 (m, 2 H), 1.30 (s, 3 H), 0.54 (d, $J = 6.6$ Hz, 3 H), 0.42 (d, $J = 6.6$ Hz, 3 H); HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_3$ ($\text{M} + \text{H}^+$) 287.1642, found 287.1640.

Conversion of hamigeran A (2) to hamigeran B (3). Hamigeran A (**2**, 8 mg, 0.019 mmol) was dissolved in MeOH (2 mL) and H_2O (1 mL) at room temperature. Vigorous stirring was initiated and solid $\text{Ba}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$ (100 mg, 0.32 mmol) was added. After 2 h, the reaction mixture was poured onto H_2O (3 mL) and extracted with 1:1 hexanes:Et₂O (3 \times 3 mL). The combined organic extract was dried over Na_2SO_4 , the solvents evaporated under reduced pressure and the solid residue obtained was purified by PTLC (silica, hexanes:EtOAc, 10:1) providing pure hamigeran B (**3**) (6.0 mg, 87% yield) as a yellowish-orange solid (m.p. 154–156 $^\circ\text{C}$, CH_2Cl_2). **3**: $R_f = 0.6$ (silica, hexanes:EtOAc, 6:1); $[\alpha]_D = -168^\circ$ ($c = 0.112$, CHCl_3); IR (film): $\nu_{\text{max}} = 3715$ (m), 2950 (m), 1725 (s), 1635 (m), 1608 (m), 1280 (m), 889 (m) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 12.64$ (s, 1 H), 6.82 (s, 1 H), 3.38 (d, $J = 9.5$ Hz, 1 H), 2.63 (ddd, $J = 13.1, 7.6, 5.4$ Hz, 1 H), 2.50 (s, 3 H), 2.32–2.29 (m, 1 H), 1.82–1.80 (m, 1 H), 1.71–1.67 (m, 1 H), 1.58–1.54 (m, 1 H), 1.29 (s, 3 H), 1.22–1.20 (m, 1 H), 0.53 (d, $J = 6.6$ Hz, 1 H), 0.45 (d, $J = 6.6$ Hz, 1 H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 199.9, 185.3, 161.7, 151.1, 143.6, 125.1, 118.1,$

112.4, 57.8, 57.0, 52.1, 34.7, 29.0, 27.6, 25.3, 25.3, 25.2, 24.2, 20.6; HRMS calcd for $C_{18}H_{21}BrO_3$ ($M + Na^+$) 387.0566, found 387.0572.

Preparation of 4-bromohamigeran B (4). Debromohamigeran B (**3**, 7 mg, 0.025 mmol) was dissolved in DMF (500 μ L). A 20 mg/mL solution of NBS in CH_2Cl_2 was prepared and a portion of this solution (1 mL) was added to the stirred solution of **3**. After 3 h at room temperature, the solution was poured onto H_2O (10 mL). Extraction (Et_2O , 2×10 mL) and concentration gave a deep yellow residue which was purified by PTLC (silica, hexanes:EtOAc, 8:1) to give the targeted natural product 4-bromohamigeran B (**4**, 10 mg, 94% yield) as a yellow solid (m.p. 140–145 $^{\circ}C$, CH_2Cl_2). **4**: R_f = 0.6 (silica, hexanes:EtOAc, 6:1); $[\alpha]_D = -80.0$ ($c = 0.112$, $CHCl_3$); IR (film): $\nu_{max} = 3715$ (m), 2950 (m), 1722 (s), 1640 (s), 1277 (s), 1056 (m) cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$): $\delta = 12.94$ (s, 1 H), 3.71 (d, $J = 10.2$ Hz, 1 H), 2.29 (s, 3 H), 2.79–2.75 (m, 1 H), 2.69–2.66 (m, 1 H), 1.85–1.83 (m, 1 H), 1.69–1.65 (m, 1 H), 1.54–1.50 (m, 1 H), 1.28 (s, 3 H), 1.23–1.19 (m, 1 H), 0.52 (d, $J = 6.7$ Hz, 3 H), 0.46 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 197.3$, 185.9, 161.2, 151.2, 141.7, 119.5, 114.8, 114.4, 58.3, 53.0, 41.5, 32.1, 30.3, 27.7, 22.6, 21.6, 19.6, 15.0; HRMS calcd for $C_{18}H_{20}Br_2O_3$ ($M + Na^+$) 464.9671, found 464.9660.

Photochemical ring-contraction of diketone 122 to indanone derivative 123. A solution of diketone **122** (8 mg, 0.026 mmol) in benzene (2 mL) was placed in a 15 mL quartz test tube equipped with a stirbar. The tube was placed 20 cm from a 450 W Hanovia lamp (Kimax filter) and irradiated while vigorously stirred and monitored (TLC) for disappearance of starting material. Upon completion of the reaction (1 h), the solvent was removed and the residue was purified by PTLC (silica, hexanes:EtOAc, 10:1, run twice) furnishing indanone **123** (6 mg, 87% yield as a white solid). **123**: R_f = 0.5 (silica, hexanes:EtOAc, 10:1); IR (film): $\nu_{max} = 2925$ (m), 2862 (w), 1702 (s), 1600 (w), 1462 (m) cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$): $\delta = 6.95$ (s, 1 H), 6.68 (s, 1 H), 4.00 (s, 3 H), 3.35 (d, $J = 7.7$ Hz, 1 H), 2.50 (s, 3 H), 2.18 (dd, $J = 12.8, 6.2$ Hz, 1 H), 1.90–1.84 (m, 1 H), 1.84–1.76 (m, 1 H), 1.76–1.71 (m, 1 H), 1.65 (ddd, $J = 11.8, 5.8, 5.8$ Hz, 1 H), 1.47 (ddd, $J = 13.0, 12.8, 6.0$ Hz, 1 H), 1.34 (s, 3 H), 1.30 (d, $J = 6.2$ Hz, 3 H), 0.91 (d,

$J = 6.2$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 209.6, 157.7, 156.6, 147.3, 124.0, 120.3, 110.0, 57.2, 55.6, 52.7, 52.3, 38.1, 28.6, 27.7, 23.5, 23.2, 22.7, 21.9$; HRMS calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$ ($\text{M} + \text{H}^+$) 273.1849, found 273.1845.

Demethylation of 123 to phenol 125. A solution of methoxy ketone **123** (11 mg, 0.038 mmol) in CH_2Cl_2 (2 mL) was treated with BBr_3 (1 M solution in CH_2Cl_2 , 0.4 mL, 0.4 mmol) at -78°C according to the previously described procedure (**88** \rightarrow **89**). PTLC (silica, hexanes:EtOAc, 8:1) provided compound **125** (11 mg, 95% yield) as a light yellow oil. **125**: $R_f = 0.5$ (silica, hexanes:EtOAc, 4:1); IR (film): $\nu_{\text{max}} = 3475$ (w), 2933 (m), 2857 (w), 1691 (m), 1599 (m), 1454 (w) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 9.26$ (s, 1 H), 6.77 (s, 1 H), 6.59 (s, 1 H), 3.31 (d, $J = 7.7$ Hz, 1 H), 2.37 (s, 3 H), 2.28–2.25 (m, 1 H), 2.06 (dd, $J = 13.1, 6.6$ Hz, 1 H), 1.77–1.74 (m, 1 H), 1.65–1.60 (m, 1 H), 1.44 (dq, $J = 6.6, 6.4$ Hz, 1 H), 1.29 (s, 3 H), 1.22 (d, $J = 6.6$ Hz, 3 H), 0.87 (d, $J = 6.6$ Hz, 3 H); HRMS calcd for $\text{C}_{17}\text{H}_{22}\text{O}_2$ ($\text{M} + \text{H}^+$) 311.1618, found 311.1616.

Oxidative cleavage of diol 128 to α -keto ester aldehyde 129. Solid activated MnO_2 (20 mg) was added to a solution of diol **128** (3 mg, 0.08 mmol) in CH_2Cl_2 (2 mL). The resulting suspension was stirred for 1 h, filtered, and concentrated to afford the title compound (**128**). This compound gave poorly resolved NMR spectra due to rotational isomers and it was found that D_2O addition to the CDCl_3 solution sharpened the peaks (at 40°C). **128**: $R_f = 0.3$ (silica, hexanes:EtOAc, 4:1); IR (film): $\nu_{\text{max}} = 2947$ (m), 2925 (m), 2859 (m), 1734 (s), 1696 (s) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 10.50$ (s, 1 H), 6.61 (s, 1 H), 6.37 (s, 1 H), 4.92 (d, $J = 7.0$ Hz, 1 H), 3.84 (s, 3 H), 3.52 (s, 3 H), 2.73–2.71 (m, 1 H), 2.31 (s, 3 H), 2.09–2.06 (m, 1 H), 0.77 (d, $J = 6.6$ Hz, 3 H), 0.74 (d, $J = 6.6$ Hz, 3 H); HRMS calcd for $\text{C}_{20}\text{H}_{28}\text{O}_5$ ($\text{M} + \text{Na}^+$) 383.1829, found 383.1846.

Preparation of MOM-hamigeran B (130). To a solution of hamigeran B (**3**, 5 mg, 0.0125 mmol) in CH_2Cl_2 (0.7 mL) at 0°C was added $i\text{Pr}_2\text{NEt}$ (30 μL) and MOMCl (15 μL). The initially deep-red solution changed to a faint yellow over 30 min, at which time the reaction mixture was quenched with water (5 mL) and extracted into Et_2O (2×5 mL). Concentration and flash column chromatography (silica, hexanes:EtOAc, 6:1) gave MOM derivative **130** (4 mg,

76% yield) as a light yellow oil. **130**: $R_f = 0.5$ (silica, hexanes:EtOAc, 1:1); IR (film): $\nu_{\max} = 2946$ (m), 1720 (s), 1628 (m), 1442 (m), 1279 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta = 7.19$ (s, 1 H), 5.64 (d, $J = 6.0$ Hz, 1 H), 5.54 (d, $J = 6.0$ Hz, 1 H), 4.31 (s, 3 H), 4.09 (d, $J = 9.4$ Hz, 1 H), 3.38 (s, 3 H), 3.30–3.16 (m, 1 H), 2.82–2.37 (m, 1 H), 2.63–2.56 (m, 3 H), 3.35 (s, 3 H), 2.28–2.24 (m, 1 H), 1.77 (d, $J = 6.7$ Hz, 3 H), 1.68 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 201.0, 180.7, 156.3, 147.7, 144.4, 129.7, 126.1, 121.2, 102.3, 58.8, 56.2, 55.7, 52.1, 35.7, 28.9, 28.1, 24.9, 24.4, 23.5, 20.5$; HRMS calcd for $\text{C}_{21}\text{H}_{27}\text{BrO}_4$ ($M + \text{Na}^+$) 432.0828, found 431.0823.

Preparation of hamigeran E (7). MOM-protected diketone **130** (4 mg, 0.01 mmol) was dissolved in dioxane (1 mL) and 2 N aq. NaOH (0.3 mL) was added at 0 °C with stirring. A 30% aq. solution of H_2O_2 (0.15 mL) was added dropwise and the reaction mixture was stirred at that temperature for 10 min when TLC analysis indicated complete consumption of the starting material. The reaction mixture was diluted with H_2O (2 mL) and 2 M aq. HCl (0.5 mL), and the product was extracted out of the aq. phase with EtOAc (7×3 mL). The combined organic phase was concentrated to a reddish-brown residue which was dissolved in THF (3 mL) and 3 M aq. HCl (3 mL). Con. H_2SO_4 (1 drop) was added and the biphasic mixture was vigorously stirred at room temperature for 30 min. The resulting mixture was diluted with H_2O (3 mL) and the somewhat water-soluble product was extracted with EtOAc (8×5 mL). Concentration and flash chromatography (silica, pre-washed with 2% AcOH solution in CHCl_3 , 2 \rightarrow 6% MeOH in CHCl_3 with 0.5% AcOH) gave hamigeran E (**7**, 2 mg, 49% yield) as a colorless, amorphous solid (from benzene). **7**: $R_f = 0.1$ (silica plates pre-treated with AcOH, 6% MeOH in CHCl_3 with 0.5% AcOH); IR (film): $\nu_{\max} = 2400\text{--}3600$ (brm), 2955 (m), 1712 (s), 1554 (m), 1381 (m), 1250 (m) cm^{-1} ; The ^1H NMR spectrum of hamigeran E was complicated by rotational isomers which made all of the signals broad: ^1H NMR (500 MHz, CDCl_3 , 40 °C): $\delta = 6.57$ (s, 1 H), 3.80–3.76 (brm, 1 H), 2.39 (s, 3 H), 2.23–2.10 (brm, 2 H), 1.84–1.70 (brm, 2 H), 1.51 (s, 3 H), 1.30–1.27 (brm, 1 H), 1.18–1.08 (brm, 1 H), 0.82 (d, $J = 6.0$ Hz, 1 H), 0.60 (brs, 3 H). It was possible to resolve the ^1H NMR peaks by using wet CD_3CN at 70 °C: ^1H NMR (500 MHz, wet CD_3CN , 70 °C): $\delta =$

6.67 (s, 1 H), 3.89 (d, $J = 7.0$ Hz, 1 H), 2.65–2.60 (m, 1 H), 2.18 (s, 3 H), 2.19–2.10 (m, 2 H), 1.81–1.73 (m, 2 H), 1.49 (s, 3 H), 1.23–1.19 (m, 1 H), 0.84 (d, $J = 6.6$ Hz, 3 H), 0.61 (d, $J = 6.6$ Hz, 3 H); ^{13}C NMR (125 MHz, wet CD_3CN , 70 °C): $\delta = 179.9, 163.2, 155.1, 142.0, 140.9, 130.1, 122.4, 57.6, 33.6, 30.0, 28.6, 28.3, 23.2, 21.4, 21.2$; HRMS calcd for $\text{C}_{19}\text{H}_{25}\text{BrO}_5$ ($\text{M} + \text{Na}^+$) 421.0621, found 421.0631.

Preparation of 5-*epi*-dibromo hamigeran E (132). Diketone **93** (8 mg, 0.02 mmol) was dissolved in CH_2Cl_2 (1.5 mL) at 0 °C and $i\text{Pr}_2\text{NEt}$ (50 μL) and MOMCl (25 μL) were added according to the procedure given for the preparation of **130** above. This MOM ether was dissolved in dioxane (2 mL) and 2 N aq. NaOH (0.6 mL) at 0 °C and a 30% aq. solution of H_2O_2 (0.3 mL) was added according to the procedure given for the preparation of **7**. Work-up and treatment with acid (as before, see **130** \rightarrow **7**) led to a solid residue which was purified by flash chromatography (silica pre-washed with 2% AcOH solution in CHCl_3 , 2 \rightarrow 6% MeOH in CHCl_3 with 0.5% AcOH) gave 5-*epi*-dibromohamigeran E (**132**, 5 mg, 60% yield) as a yellow solid. **132**: $R_f = 0.1$ (silica plates pre-treated with AcOH, 6% MeOH in CHCl_3 with 0.5% AcOH); IR (film): $\nu_{\text{max}} = 2400\text{--}3600$ (brm), 1716 (s), 1499 (m), 1386 (m) cm^{-1} ; The NMR spectrum of hamigeran E was complicated by rotational isomers which make all of the peaks broad. ^1H NMR (500 MHz, CDCl_3 , 40 °C): $\delta = 5.16$ (d, $J = 4.0$ Hz, 1 H), 3.30–3.25 (brm, 1 H), 2.70 (brs, 3H), 2.39–2.33 (brm, 1 H), 2.22–2.12 (brm, 1 H), 2.11–2.04 (brm, 1 H), 1.61–1.55 (brm, 2 H), 0.88–0.83 (brm, 1H), 0.83 (brs, 3 H), 0.65–0.59 (brd, $J = 6.0$ Hz, 3 H), 0.82 (d, $J = 5.4$ Hz, 1 H).

References

- (1) Charlton, J.; Plourde, G.; Koh, K. *Can. J. Chem.* **1989**, *67*, 574–579.
- (2) For a recent review of the Diels–Alder reaction in total synthesis, see Nicolaou, K. C.; Snyder, S.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668–1698.

(3) For an early example of photo-enolization/Diels–Alder reactions with benzaldehydes, see: Arnold, B.; Mellows, S.; Sammes, P.; Wallace, T. *J. Chem. Soc., Perkin Trans. 1* **1974**, 3, 401–409.