Supporting Information for:

Selective Preparation of Benzyltitanium Compounds by the Metalative Reppe Reaction. Its Application to the First Synthesis of Alcyopterosin A

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General. ^1H and ^{13}C NMR spectra were taken on a Varian Gemini-300 spectrometer at 300 and 75 MHz, respectively. As the solvent, CDCl_3 was used, unless otherwise specified. ^1H NMR chemical shifts were reported in parts per million shift (δ value) from Me_4Si (δ 0 ppm) in CDCl_3 or the residual proton of the solvent (δ 7.15 ppm) in C_6D_6 as internal standards. ^{13}C NMR chemical shifts were reported in parts per million shift (δ value) from the middle peak of the solvent (δ 77.00 ppm) in CDCl_3 or the solvent peak (δ 128.00 ppm) in C_6D_6 as internal standards. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (J) are given in Hertz. Infrared (IR) spectra were recorded on a JASCO A-100 spectrometer and were reported in wave numbers (cm^{-1}). $\text{Ti}(\text{O-}i\text{-Pr})_4$ was distilled and stocked under argon atmosphere. Isopropylmagnesium chloride was prepared in Et_2O as a 1.3-1.7 M solution from isopropyl chloride and magnesium turnings by the usual procedure, titrated, and stocked under an argon atmosphere. All reactions were carried out under argon. Dry solvents (THF, ethyl ether, CH_2Cl_2) were purchased from Kanto Chemicals Co. (Japan). Chemicals were purified or dried in a standard manner, if necessary.

***tert*-Butyl 5-Hexyl-4-methyl-2-(trimethylsilyl)benzoate (9).** To a stirred solution of *tert*-butyl (trimethylsilyl)propynoate (**2**) (50 mg, 0.252 mmol) and $\text{Ti}(\text{O-}i\text{-Pr})_4$ (0.093

mL, 0.315 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.47 M in Et₂O, 0.429 mL, 0.630 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min, during which period its color turned red. After stirring at -50 °C for an additional 5 h, 1-octyne (**3**) (0.030 mL, 0.202 mmol) was added to the reaction mixture at -50 °C and the solution was stirred for another 3 h. Then, propargyl bromide (**5**) (0.029 mL, 0.378 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil, careful analysis of which by ¹H NMR spectroscopy did not show the presence of any isomeric products. The crude product was separated by preparative TLC (Merck #1.05554, hexane-ether) to afford the title compound (37 mg, 52%) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR, IR, and elemental analyses.

¹H NMR δ 0.31 (s, 9H), 0.90 (t, J = 6.9 Hz, 3H), 1.26-1.42 (m, 8H), 1.59 (s, 9H), 2.33 (s, 3H), 2.60 (t, J = 7.8 Hz, 2H), 7.39 (s, 1H), 7.66 (s, 1H). Irradiation of proton at δ 2.33 ppm (PhMe) showed 3% nOe enhancement to the peak at δ 2.60 ppm (PhCH₂) and 7% nOe enhancement to the peak at δ 7.39 ppm (Ph-H). Irradiation of proton at δ 2.60 ppm (PhCH₂) showed 2% nOe enhancement to the peak at δ 2.33 ppm (PhMe) and 7% nOe enhancement to the peak at δ 7.66 ppm (Ph-H). Thus, the regiochemistry has been confirmed.

¹³C NMR δ 0.29, 13.99, 19.30, 22.56, 28.14 (C(CH₃)₃), 29.30, 30.01, 31.64, 33.09, 80.49, 130.21, 135.72, 137.44, 139.02, 141.71, 167.90.

IR (neat) 2955, 2928, 2857, 1712 (C=O), 1597, 1546, 1457, 1391, 1367, 1290, 1246, 1174, 1129, 1011, 852, 766, 679 cm⁻¹.

Anal. Calcd for C₂₁H₃₆O₂Si: C, 72.36; H, 10.41. Found: C, 72.75; H, 10.67.

Other Possible Reaction Paths from Titanacycle 4 to Benzyltitanium Compound 8. We consider that the mechanism of eq 1 is most likely appropriate for the conversion from **4** to **8** based on the relevant discussion reported in reference 6a. However, at present, as we could not obtain any conclusive evidence such as the detection or isolation of

reaction intermediates even after considerable experimentation, the following reaction path a is also a possible candidate to account for the observation (Scheme 3). However, another path b involving intramolecular carbotitanation may be excluded, because this is not consistent with the outcome shown in Schemes 4 and 5.

Scheme 3. Other Possible Paths from **4** to **8**.

***tert*-Butyl 4-(Deuteriomethyl)-5-hexyl-2-(trimethylsilyl)benzoate (9-*d*₁).**

¹H NMR δ 0.31 (s, 9H), 0.90 (t, J = 6.9 Hz, 3H), 1.26-1.42 (m, 8H), 1.59 (s, 9H), 2.31 (t, J = 2.1 Hz, 2H), 2.60 (t, J = 7.8 Hz, 2H), 7.39 (s, 1H), 7.66 (s, 1H). The peak area at δ 2.31 ppm (PhMe) showed nearly complete deuterium incorporation.

***tert*-Butyl 5-Hexyl-4-(iodomethyl)-2-(trimethylsilyl)benzoate (10).** To a stirred solution of *tert*-butyl (trimethylsilyl)propynoate (**2**) (40 mg, 0.202 mmol) and Ti(O-*i*-Pr)₄ (0.074 mL, 0.252 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.09 M in Et₂O, 0.462 mL, 0.504 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min, during which period its color turned red. After stirring at -50 °C for an additional 5 h, 1-octyne (**3**) (0.024 mL, 0.161 mmol) was added to the reaction mixture at -50 °C and the solution was stirred for another 3 h. Then, propargyl bromide (**5**) (0.023 mL, 0.302 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature to ensure the cyclotrimerization, iodine (130 mg, 1.01 mmol) in 1 mL of ether was added. The reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃ and Na₂S₂O₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil, careful analysis of which by ¹H NMR spectroscopy did not show the presence of any isomeric products. The crude product was separated by preparative TLC (Merck #1.05554, hexane-ether) to afford the title compound (38 mg, 50%) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR and IR analyses.

¹H NMR δ 0.32 (s, 9H), 0.91 (t, J = 6.9 Hz, 3H), 1.26-1.49 (m, 8H), 1.59 (s, 9H), 2.68 (t, J = 7.8 Hz, 2H), 4.48 (s, 2H), 7.54 (s, 1H), 7.65 (s, 1H).

¹³C NMR δ 0.22, 3.24, 13.99, 22.53, 28.09 (C(CH₃)₃), 29.32, 30.09, 31.60, 32.29, 80.98, 130.97, 137.27, 137.77, 139.37, 140.12, 141.68, 167.47.

IR (neat) 2954, 2928, 2857, 1713 (C=O), 1595, 1546, 1456, 1391, 1367, 1293, 1247, 1226, 1173, 1149, 1131, 1081, 993, 914, 845, 793, 766, 746, 680 cm⁻¹.

A correct elemental analysis was hardly obtained owing to the instability of this benzyl iodide.

^1H NMR δ 0.88 (d, J = 6.6 Hz, 3H), 1.15 (m, 1H), 1.34 (m, 2H), 1.55 (m, 2H), 1.60 (s, 3H), 1.68 (s, 3H), 1.92 (t, J = 2.7 Hz, 1H), 1.97 (m, 2H), 2.20 (m, 2H), 5.09 (t/septet, J = 7.2, 1.5 Hz, 1H).

^{13}C NMR δ 16.02, 17.52, 18.91, 25.31, 25.60, 31.52, 35.48, 36.59, 67.90, 84.85, 124.79, 131.31.

***tert*-Butyl 4-Methyl-5-(3,7-dimethyl-6-octenyl)-2-(trimethylsilyl)benzoate (14).** To a stirred solution of *tert*-butyl (trimethylsilyl)propynoate (**2**) (50 mg, 0.252 mmol) and $\text{Ti}(\text{O-}i\text{-Pr})_4$ (0.093 mL, 0.315 mmol) in 2 mL of Et_2O was added *i*-PrMgCl (1.47 M in Et_2O , 0.429 mL, 0.630 mmol) at -78°C under argon to give a yellow homogeneous solution. The solution was warmed to -50°C over 30 min, during which period its color turned red. After stirring at -50°C for an additional 5 h, 5,9-dimethyl-8-decen-1-yne (**12**) (33 mg, 0.202 mmol) was added to the reaction mixture at -50°C and the solution was stirred for another 3 h. Then propargyl bromide (**5**) (0.029 mL, 0.378 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated *in vacuo* to give a crude oil, careful analysis of which by ^1H NMR spectroscopy did not show the presence of any isomeric products. The crude product was separated by preparative TLC (Merck #1.05554, hexane-ether) to afford the title compound (43 mg, 53%) as a colorless oil, which was fully characterized by ^1H and ^{13}C NMR, IR, and elemental analyses.

^1H NMR δ 0.31 (s, 9H), 0.98 (d, J = 6.6 Hz, 3H), 1.24 (m, 1H), 1.39 (m, 2H), 1.52 (m, 2H), 1.60 (s, 9H), 1.61 (s, 3H), 1.69 (s, 3H), 2.01 (m, 2H), 2.34 (s, 3H), 2.59 (m, 2H), 5.21 (t/septet, J = 6.9, 1.2 Hz, 1H), 7.39 (s, 1H), 7.66 (s, 1H).

^{13}C NMR δ 0.29, 17.54, 19.25, 19.44, 25.46, 25.64, 28.15 ($\text{C}(\text{CH}_3)_3$), 30.71, 32.61, 36.84, 37.30, 80.51, 124.91, 130.19, 131.27, 135.79, 137.49, 138.95, 139.05, 141.94, 167.86.

IR (neat) 2956, 2926, 2855, 1712 ($\text{C}=\text{O}$), 1597, 1547, 1457, 1367, 1289, 1246, 1175, 1128, 1018, 852, 766, 679 cm^{-1} .

Anal. Calcd for $\text{C}_{25}\text{H}_{42}\text{O}_2\text{Si}$: C, 74.57; H, 10.51. Found: C, 74.26; H, 10.13.

5-[2-(Benzyloxy)ethyl]-1-hexyl-3-methylbenzene (20). The whole reaction is shown in Scheme 4 below.

Scheme 4. Generation of **17-19** and Isolation of **20** in Entry 6, Table 1.

To a stirred solution of 1-(trimethylsilyl)-1-octyne (**15**) (50 mg, 0.274 mmol) and $Ti(O-i-Pr)_4$ (0.101 mL, 0.343 mmol) in 2 mL of Et_2O was added $i-PrMgCl$ (1.36 M in Et_2O , 0.504 mL, 0.685 mmol) at $-78\text{ }^\circ C$ under argon to give a yellow homogeneous solution. The solution was warmed to $-50\text{ }^\circ C$ over 30 min, during which period its color turned black. After stirring at $-50\text{ }^\circ C$ for 2 h, 4-(benzyloxy)-1-butyne (**16**) (35 mg, 0.219 mmol) in 1 mL of Et_2O was introduced to

the reaction mixture at -50 °C and the solution was stirred for another 1 h. Then propargyl bromide (**5**) (0.031 mL, 0.411 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil, analysis of which by ¹H NMR spectroscopy showed the presence of 5-[2-(benzyloxy)ethyl]-1-hexyl-3-methyl-2-(trimethylsilyl)benzene (**48**), 5-[2-(benzyloxy)ethyl]-1-hexyl-3-methylbenzene (**20**), and 5-[2-(benzyloxy)ethyl]-1-hexyl-4-methyl-2-(trimethylsilyl)benzene (**49**) in a ratio of 62:32:6. To this crude product in 2 mL of CCl₄ were added CH₃CO₂H (0.062 mL, 1.10 mmol) and CF₃CO₂H (0.042 mL, 0.548 mmol) [Hillard, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, 99, 4058-4069] at room temperature. The solution was stirred for 1 h, during which period major silylarene **48** was selectively desilylated to **20**, while minor silylarene **49** remained unchanged. The reaction mixture was cautiously quenched with an aqueous solution of NaHCO₃ and the organic products were extracted with ether. The combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo* to give a crude oil, chromatography of which (silica gel, hexane-ether) nicely separated **20** from **49**. The title compound (36 mg, 53%) was isolated as a pure colorless oil, which was fully characterized by ¹H and ¹³C NMR, IR, and elemental analyses.

¹H NMR (CDCl₃) δ 0.89 (t, J = 6.6 Hz, 3H), 1.27-1.35 (m, 8H), 2.30 (s, 3H), 2.54 (t, J = 7.8 Hz, 2H), 2.89 (t, J = 7.2 Hz, 2H), 3.69 (t, J = 7.2 Hz, 2H), 4.54 (s, 2H), 6.86 (s, 3H), 7.23-7.35 (m, 5H).

¹H NMR (C₆D₆) δ 0.96 (t, J = 6.9 Hz, 3H), 1.25-1.51 (m, 6H), 1.65 (m, 2H), 2.26 (s, 3H), 2.58 (t, J = 7.8 Hz, 2H), 2.94 (t, J = 7.2 Hz, 2H), 3.63 (t, J = 7.2 Hz, 2H), 4.40 (s, 2H), 6.88 (s, 1H), 6.90 (s, 1H), 6.95 (s, 1H), 7.16 (t, J = 6.9 Hz, 2H), 7.26 (t, J = 6.9 Hz, 2H), 7.34 (d, J = 6.9 Hz, 1H). The three separate aromatic singlet peaks established the regiochemistry of this compound as depicted.

¹³C NMR δ 13.98, 21.20, 22.50, 29.03, 31.46, 31.65, 35.80, 36.17, 71.39, 72.93, 126.19, 127.07, 127.22, 127.58, 127.72, 128.41, 137.81, 138.58, 138.74, 143.09.

IR (neat) 3087, 3063, 3027, 2954, 2927, 2855, 1604, 1496, 1455, 1361, 1249, 1204, 1102, 1029, 850, 734, 697 cm^{-1} .

Anal. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}$: C, 85.11; H, 9.74. Found: C, 85.23; H, 9.60.

5-[2-(Benzyloxy)ethyl]-1-hexyl-3-methyl-2-(trimethylsilyl)benzene (48).

^1H NMR (CDCl_3) δ 0.39 (s, 9H), 0.89 (t, $J = 6.6$ Hz, 3H), 1.27-1.35 (m, 8H), 2.43 (s, 3H), 2.67 (t, $J = 7.8$ Hz, 2H), 2.85 (t, $J = 7.2$ Hz, 2H), 3.69 (t, $J = 7.2$ Hz, 2H), 4.54 (s, 2H), 6.86 (s, 1H), 6.88 (s, 1H), 7.23-7.35 (m, 5H).

^1H NMR (C_6D_6) δ 0.47 (s, 9H), 0.96 (t, $J = 6.9$ Hz, 3H), 1.25-1.51 (m, 6H), 1.65 (m, 2H), 2.44 (s, 3H), 2.81 (t, $J = 7.8$ Hz, 2H), 2.92 (t, $J = 7.2$ Hz, 2H), 3.63 (t, $J = 7.2$ Hz, 2H), 4.40 (s, 2H), 6.90 (s, 1H), 7.00 (s, 1H), 7.16 (t, $J = 6.9$ Hz, 2H), 7.26 (t, $J = 6.9$ Hz, 2H), 7.34 (d, $J = 6.9$ Hz, 1H).

5-[2-(Benzyloxy)ethyl]-1-hexyl-4-methyl-2-(trimethylsilyl)benzene (49).

^1H NMR δ 0.40 (s, 9H), 0.89 (t, $J = 6.6$ Hz, 3H), 1.27-1.35 (m, 8H), 2.27 (s, 3H), 2.64 (t, $J = 7.8$ Hz, 2H), 2.93 (t, $J = 7.2$ Hz, 2H), 3.67 (t, $J = 7.2$ Hz, 2H), 4.54 (s, 2H), 7.02 (s, 1H), 7.22 (s, 1H), 7.23-7.35 (m, 5H).

Proposed Mechanism of the Formation of Bis-titanated Compound 18 and, hence, 20 during the Metalative Reppe Reaction. First, we carried out a few control experiments to disprove the simple desilylation process from **48** to **20** during the metalative Reppe reaction and its workup process. Thus, the mixture of **48** and **20** was treated under the conditions A-D shown below. However, *no desilylation of 48 to 20 was observed*.

Condition A. To a stirred solution of a 61:39 mixture of **48** and **20** (10 mg) and $\text{Ti}(\text{O-}i\text{Pr})_4$ (0.040 mL, 0.136 mmol) in 0.5 mL of ether was added $i\text{-PrMgCl}$ (1.49M in Et_2O , 0.182 mL, 0.271 mmol) at room temperature under argon. After the reaction mixture was stirred for 1 h, the reaction was terminated by the addition of 1N HCl. The organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated to a crude oil, ^1H NMR analysis of which showed the presence of the starting materials in the same original ratio (61:39).

Condition B. To a stirred solution of a 61:39 mixture of **48** and **20** (10 mg) in 0.5 mL of ether was added $i\text{-PrMgCl}$ (1.49M in Et_2O , 0.182 mL, 0.271 mmol) at room temperature under argon. After the reaction mixture was stirred for 1 h, the reaction was terminated by the addition of 1N HCl. The organic products were extracted with ether and the combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated to a crude oil, ^1H NMR analysis of which showed the presence of the starting materials in the same original ratio (61:39).

Condition C. To a stirred solution of a 61:39 mixture of **48** and **20** (10 mg) in 0.5 mL of ether was added 0.7 mL of 1N HCl at room temperature under argon. After the heterogeneous mixture was vigorously stirred for 1 h, the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated to a crude oil, ^1H NMR analysis of which showed the presence of the starting materials in the same original ratio (61:39).

Condition D. To a stirred solution of a 61:39 mixture of **48** and **20** (10 mg) in 0.5 mL of ether was added 0.7 mL of 1N NaOH at room temperature under argon. After the heterogeneous mixture was vigorously stirred for 1 h, the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated to a crude oil, ¹H NMR analysis of which showed the presence of the starting materials in the same original ratio (61:39).

As the formation of **20** does not arise from simple desilylation of **48** under the reaction conditions or at the workup stage as shown above, we concluded that the formation of **20** arose from the bis-titanated species **18**, which, in turn, was generated via the mechanism shown in Scheme 5 below. Thus, the final aromatization takes place either with the migration of the titanium moiety (path a, from **52** to **17**) or desilylation of the silyl group to leave a titanium-carbon bond on the aromatic ring (path b, from **52** to **18**). The presence of these two paths was consistent with the outcome of a deuteration experiment, which actually gave bis-deuterated aromatic compound **20-*d*₂** as well as mono-deuterated **48-*d*₁**. Conversely, this phenomenon strongly supports the proposed mechanism of the present metalative Reppe reaction as shown in eq 1 of the article text.

Scheme 5. Plausible Mechanism for the Generation of Bis-titanated **18** (and, Hence, **20**) in Entry 6, Table 1.

5-[2-(Benzyloxy)ethyl]-2-deuterio-3-(deuteriomethyl)-1-hexylbenzene (20-*d*₂). To a stirred solution of 1-(trimethylsilyl)-1-octyne (**15**) (50 mg, 0.274 mmol) and $\text{Ti}(\text{O-}i\text{-}$

Pr)₄ (0.101 mL, 0.343 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.36 M in Et₂O, 0.504 mL, 0.685 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min, during which period its color turned black. After stirring at -50 °C for 2 h, 4-(benzyloxy)-1-butyne (**16**) (35 mg, 0.219 mmol) in 1 mL of Et₂O was introduced to the reaction mixture at -50 °C and the solution was stirred for another 1 h. Then propargyl bromide (**5**) (0.031 mL, 0.411 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N DCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil, analysis of which by ¹H NMR spectroscopy showed the presence of 5-[2-(benzyloxy)ethyl]-3-(deuteriomethyl)-1-hexyl-2-(trimethylsilyl)benzene (**48-d**₁), the title compound, and 5-[2-(benzyloxy)ethyl]-1-hexyl-4-(deuteriomethyl)-2-(trimethylsilyl)benzene (**49-d**₁).

¹H NMR (C₆D₆) δ 0.96 (t, J = 6.9 Hz, 3H), 1.25-1.51 (m, 6H), 1.65 (m, 2H), 2.24 (t, J = 2.1 Hz, 2H), 2.58 (t, J = 7.8 Hz, 2H), 2.94 (t, J = 7.2 Hz, 2H), 3.63 (t, J = 7.2 Hz, 2H), 4.40 (s, 2H), 6.88 (s, 1H), 6.95 (s, 1H), 7.16 (t, J = 6.9 Hz, 2H), 7.26 (t, J = 6.9 Hz, 2H), 7.34 (d, J = 6.9 Hz, 1H). The peak area at δ 2.24 ppm (PhMe) showed 94% deuterium incorporation. The peak at δ 6.90 ppm (Ph-H) of 5-[2-(benzyloxy)ethyl]-1-hexyl-3-methylbenzene (**20**) disappeared to show nearly complete deuterium incorporation.

5-[2-(Benzyloxy)ethyl]-3-(deuteriomethyl)-1-hexyl-2-(trimethylsilyl)benzene (48-d**₁).**

¹H NMR (C₆D₆) δ 0.39 (s, 9H), 0.89 (t, J = 6.6 Hz, 3H), 1.27-1.35 (m, 8H), 2.43 (t, J = 2.1 Hz, 2H), 2.67 (t, J = 7.8 Hz, 2H), 2.85 (t, J = 7.2 Hz, 2H), 3.69 (t, J = 7.2 Hz, 2H), 4.54 (s, 2H), 6.86 (s, 1H), 6.88 (s, 1H), 7.23-7.35 (m, 5H). The peak area at δ 2.43 ppm (PhMe) showed nearly complete deuterium incorporation.

8-Bromo-4,4-bis[(benzyloxy)methyl]-1,6-octadiyne (22**).** This was prepared as follows. Yields were not optimized.

^1H NMR δ 1.96 (t, J = 2.7 Hz, 1H), 2.41 (d, J = 2.7 Hz, 2H), 2.47 (t, J = 2.7 Hz, 2H), 3.49 (s, 4H), 3.87 (t, J = 2.7 Hz, 2H), 4.52 (s, 4H), 7.24-7.35 (m, 10H).

^{13}C NMR (CDCl_3) δ 15.37, 22.05, 22.46, 42.32, 70.51, 71.12, 73.35, 80.72, 83.62, 127.53 (2 peaks), 128.34, 138.64.

^{13}C NMR (C_6D_6) δ 15.11, 22.27, 22.64, 42.51, 70.91, 71.29, 73.43, 77.90, 80.70, 84.79, 127.76 (2 peaks), 128.49, 138.98.

IR (neat) 3294, 3087, 3063, 3029, 3005, 2907, 2861, 2795, 2717, 2232, 2117, 1496, 1476, 1453, 1427, 1365, 1330, 1309, 1287, 1254, 1208, 1095, 1028, 962, 910, 885, 866, 803, 737, 698 cm^{-1} .

Anal. Calcd for $\text{C}_{24}\text{H}_{25}\text{BrO}_2$: C, 67.77; H, 5.92. Found: C, 67.61; H, 6.26.

Ethyl 2,2-Bis[(benzyloxy)methyl]-4,6-dimethylindan-5-carboxylate (24).

To a stirred solution of ethyl 2-butynoate (**21**) (227 mg, 1.95 mmol) and $\text{Ti}(\text{O}-i\text{-Pr})_4$ (0.719 mL, 2.44 mmol) in 20 mL of Et_2O was added $i\text{-PrMgCl}$ (1.53 M in Et_2O , 3.20 mL, 4.88 mmol) at -78°C under argon to give a yellow homogeneous solution. The solution was warmed to -50°C over 30 min. After stirring at -50°C for an additional 3 h, 4,4-bis[(benzyloxy)methyl]-8-bromo-1,6-octadiyne (**22**) (500 mg, 1.17 mmol) in 2 mL of Et_2O was introduced to the reaction mixture at -50°C . After the solution was stirred for another 3 h, the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated *in vacuo* to give a crude oil. This sample was chromatographed on silica gel to afford the title compound (323 mg, 60%) as a colorless oil, which was fully characterized by ^1H and ^{13}C NMR, IR, and elemental analyses.

^1H NMR δ 1.37 (t, J = 7.2 Hz, 3H), 2.17 (s, 3H), 2.27 (s, 3H), 2.76 (s, 2H), 2.85 (s, 2H), 3.50 (s, 4H), 4.38 (q, J = 7.2 Hz, 2H), 4.51 (s, 4H), 6.85 (s, 1H), 7.24-7.35 (m, 10H).

^{13}C NMR δ 14.42, 16.68, 19.73, 37.93, 39.31, 47.78, 60.85, 73.21, 73.49, 123.90, 127.29 (2 peaks), 128.18, 130.67, 132.09, 133.03, 138.58, 138.90, 143.19, 170.39.

IR (neat) 3087, 3063, 3029, 2925, 2853, 1722 (C=O), 1607, 1584, 1496, 1453, 1363, 1333, 1265, 1173, 1144, 1100, 1042, 903, 853, 735, 697 cm^{-1} .

Anal. Calcd for $\text{C}_{30}\text{H}_{34}\text{O}_4$: C, 78.57; H, 7.47. Found: C, 78.36; H, 7.54.

The regiochemistry was deduced by analogy based on the structure of **43** in Scheme 2.

8-Bromo-1,6-octadiyne (26). This was prepared as follows. Yields were not optimized.

^1H NMR δ 1.74 (quintet, J = 7.2 Hz, 2H), 1.97 (t, J = 2.7 Hz, 1H), 2.30 (d/t, J = 2.7, 7.2 Hz, 2H), 2.38 (t/t, J = 2.4, 7.2 Hz, 2H), 3.92 (t, J = 2.4 Hz, 2H).

^{13}C NMR δ 15.30, 17.38, 17.84, 27.10, 68.95, 76.00, 83.29, 86.83.

IR (neat) 3295, 3003, 2954, 2939, 2908, 2866, 2839, 2234, 2117, 1453, 1431, 1346, 1328, 1311, 1293, 1210, 1148, 1062, 1023, 898, 864, 779 cm^{-1} .

A correct elemental analysis was hardly obtained owing to the instability of this propargyl bromide.

***N,N*-Diethyl-6-hexyl-4-methylindan-5-carboxamide (28).** To a stirred solution of *N,N*-diethyl-2-nonynamide (**25**) (50 mg, 0.239 mmol) and $\text{Ti}(\text{O-}i\text{-Pr})_4$ (0.088 mL, 0.597 mmol) in 2 mL of Et_2O was added *i*-PrMgCl (1.47 M in Et_2O , 0.406 mL, 0.597 mmol) at -78°C under argon to give a yellow homogeneous solution. The solution was warmed to -50°C over 30 min. After stirring at -50°C for an additional 5 h, 8-bromo-1,6-octadiyne (**26**) (35 mg, 0.191 mmol) in 1 mL of Et_2O was introduced to the reaction mixture at -50°C . After the solution was

stirred for another 3 h, the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1*N* HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil, which was separated by preparative TLC (Merck #1.05554, hexane-ethyl acetate) to afford the title compound (44 mg, 73%) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR, IR, and elemental analyses.

¹H NMR δ 0.86 (t, *J* = 6.5 Hz, 3H), 1.02 (t, *J* = 6.9 Hz, 3H), 1.23-1.27 (m, 6H), 1.27 (t, *J* = 6.9 Hz, 3H), 1.52 (m, 1H), 1.64 (m, 1H), 2.04 (quintet, *J* = 7.5 Hz, 2H), 2.13 (s, 3H), 2.44 (m, 2H), 2.78 (t, *J* = 7.5 Hz, 2H), 2.88 (t, *J* = 7.5 Hz, 2H), 3.12 (m, 2H), 3.52 (d/q, *J* = 13.5, 7.2 Hz, 1H), 3.69 (d/q, *J* = 13.5, 7.2 Hz, 1H), 6.93 (s, 1H).

¹³C NMR δ 12.53, 13.66, 13.95, 16.27, 22.47, 24.57, 29.45, 31.08, 31.28, 31.60, 32.97, 33.17, 38.11, 42.38, 122.28, 128.98, 134.38, 136.76, 141.07, 143.88, 171.08.

IR (neat) 2929, 2857, 1634 (C=O), 1459, 1434, 1413, 1380, 1315, 1282, 1224, 1126, 1100, 1080, 1047, 866, 783 cm⁻¹.

Anal. Calcd for C₂₁H₃₃NO: C, 79.95; H, 10.54. Found: C, 79.58; H, 10.83.

The regiochemistry was deduced by analogy based on the structure of 7,7-bis[(benzyloxy)methyl]-4-methyl-1,6,7,8-tetrahydroindeno[4,5-*c*]furan-3-one (**31**).

7,7-Bis[(benzyloxy)methyl]-4-methyl-1,6,7,8-tetrahydroindeno[4,5-*c*]furan-3-one (31). To a stirred solution of *N,N*-diethyl-2-butyramide (**29**) (30 mg, 0.216 mmol) and Ti(*O-i*-Pr)₄ (0.080 mL, 0.270 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.47 M in Et₂O, 0.367 mL, 0.539 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min. After stirring at -50 °C for an additional 5 h, 4,4-bis[(benzyloxy)methyl]-8-bromo-1,6-octadiyne (**22**) (74 mg, 0.173 mmol) in 1 mL of Et₂O was introduced to the reaction mixture at -50 °C. After the solution was stirred for another 3 h, the reaction mixture was allowed to warm to room temperature. After the solution was stirred for 4 h at that temperature, the argon atmosphere was replaced by dry oxygen gas, and the stirring was continued overnight. Finally, the reaction was terminated by the addition of 1*N* HCl. The organic

products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil. To this crude product in 2 mL of benzene was added *p*-toluenesulfonic acid monohydrate (39 mg, 0.207 mmol) at room temperature under argon. After being stirred overnight, the reaction was terminated by the addition of aqueous solution of NaHCO₃ and the organic products were extracted with ether. After removal of the solvent, the crude product was separated by preparative TLC (Merck #1.05554, hexane-ethyl acetate) to afford the title compound (40 mg, 54%) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR, IR, and elemental analyses.

¹H NMR δ 2.63 (s, 3H), 2.80 (s, 2H), 2.95 (s, 2H), 3.51 (s, 4H), 4.52 (s, 4H), 5.10 (s, 2H), 7.07 (s, 1H), 7.25-7.35 (m, 10H).

¹³C NMR δ 17.11, 35.73, 39.03, 67.87, 73.25 (3 peaks), 121.51, 127.21, 127.51, 127.62, 128.40, 133.36, 138.08, 138.53, 143.37, 149.92, 171.76.

IR (neat) 3087, 3063, 3030, 2925, 2854, 1760 (C=O), 1624, 1604, 1496, 1482, 1453, 1364, 1332, 1252, 1233, 1207, 1097, 1024, 1005, 903, 785, 737, 698, 682 cm⁻¹.

Anal. Calcd for C₂₈H₂₈O₄: C, 78.48; H, 6.59. Found: C, 78.53; H, 6.41.

The successful lactonization confirmed the regiochemistry of this compound.

6-Hexyl-4-methylindan (34). To a stirred solution of 1-(trimethylsilyl)-1-octyne (**15**) (50 mg, 0.274 mmol) and Ti(O-*i*-Pr)₄ (0.101 mL, 0.343 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.49 M in Et₂O, 0.295 mL, 0.439 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min, during which period its color turned black. After stirring at -50 °C for an additional 2 h, 8-bromo-1,6-octadiyne (**26**) (41 mg, 0.219 mmol) in 1 mL of Et₂O was introduced to the reaction mixture at -50 °C. After the solution was stirred for another 1 h, the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil, which was analyzed by ¹H NMR spectroscopy to be a 57:43 mixture of 6-hexyl-4-methyl-5-(trimethylsilyl)indan and the title compound. The crude sample was

separated by preparative TLC (Merck #1.05554, hexane-ether) to afford a 57:43 mixture of 6-hexyl-4-methyl-5-(trimethylsilyl)indan and the title compound (47 mg, total 88%) as a colorless oil. Then, to this mixture in 2 mL of CCl₄ were added CH₃CO₂H (0.062 mL, 1.10 mmol) and CF₃CO₂H (0.042 mL, 0.548 mmol) at room temperature. After the solution was stirred for 1 h at the same temperature, desilylation was completed. The reaction mixture was cautiously quenched with an aqueous solution of NaHCO₃ and the organic products were extracted with ether. The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure to give a crude oil, which was chromatographed on silica gel (hexane-ether) to afford the pure title compound (24 mg, 51% overall yield from the starting acetylene) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR, IR, and elemental analyses.

¹H NMR δ 0.89 (t, J = 6.9 Hz, 3H), 1.26-1.37 (m, 6H), 1.53 (m, 2H), 2.06 (quintet, J = 7.5 Hz, 2H), 2.24 (s, 3H), 2.58 (t, J = 7.8 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H), 2.90 (t, J = 7.5 Hz, 2H), 6.79 (s, 1H), 6.90 (s, 1H). Two singlet aromatic peaks confirm the regiochemistry of the title compound.

¹³C NMR δ 13.99, 19.08, 22.52, 24.77, 19.10, 30.92, 31.70, 31.89, 32.93, 35.76, 121.76, 127.21, 133.50, 140.34, 141.30, 144.11.

IR (neat) 2955, 2926, 2855, 1596, 1459, 1377, 857, 840 cm⁻¹.

Anal. Calcd for C₁₆H₂₄: C, 88.82; H, 11.18. Found: C, 88.56; H, 10.75.

6-Hexyl-4-methyl-5-(trimethylsilyl)indan.

¹H NMR δ 0.40 (s, 9H), 0.89 (t, J = 6.9 Hz, 3H), 1.26-1.37 (m, 6H), 1.53 (m, 2H), 2.06 (quintet, J = 7.5 Hz, 2H), 2.36 (s, 3H), 2.67 (t, J = 7.8 Hz, 2H), 2.81 (t, J = 7.5 Hz, 2H), 2.90 (t, J = 7.5 Hz, 2H), 6.94 (s, 1H).

2,2-Bis[(benzyloxy)methyl]-5-methyl-4,7-bis(trimethylsilyl)indan (37). To a stirred solution of 4,4-bis[(benzyloxy)methyl]-1,7-bis(trimethylsilyl)-1,6-heptadiyne (**35**) (50 mg, 0.104 mmol) and Ti(O-*i*-Pr)₄ (0.039 mL, 0.131 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.47 M in Et₂O, 0.178 mL, 0.261 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min. After stirring at -50 °C for an

additional 4 h, propargyl bromide (**5**) (0.012 mL, 0.157 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil. The crude product was separated by preparative TLC (Merck #1.05554, hexane-ether) to afford the title compound (40 mg, 73%) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR, IR, and elemental analyses.

¹H NMR δ 0.29 (s, 9H), 0.37 (s, 9H), 2.45 (s, 3H), 2.87 (s, 2H), 2.93 (s, 2H), 3.51(s, 4H), 4.54 (s, 4H), 7.09 (s, 1H), 7.26-7.37(m, 10H).

¹³C NMR δ -0.94, 2.44, 24.07, 39.08 (quaternary carbon), 41.01, 47.61, 73.16, 73.47, 127.42, 127.51, 128.34, 134.25, 135.35, 136.58, 139.01, 140.87, 144.41, 147.49.

IR (neat) 3087, 3063, 3030, 2952, 2895, 2853, 1496, 1453, 1362, 1341, 1249, 1208, 1101, 1028, 839, 752, 735, 696 cm⁻¹.

Anal. Calcd for C₃₂H₄₄O₂Si₂: C, 74.36; H, 8.58. Found: C, 74.26; H, 8.24.

2,2-Bis[(benzyloxy)methyl]-5-(iodomethyl)-4,7-bis(trimethylsilyl)indan

(38). To a stirred solution of 4,4-bis[(benzyloxy)methyl]-1,7-bis(trimethylsilyl)-1,6-heptadiyne (**35**) (50 mg, 0.104 mmol) and Ti(O-*i*-Pr)₄ (0.039 mL, 0.131 mmol) in 2 mL of Et₂O was added *i*-PrMgCl (1.47 M in Et₂O, 0.178 mL, 0.261 mmol) at -78 °C under argon to give a yellow homogeneous solution. The solution was warmed to -50 °C over 30 min. After stirring at -50 °C for an additional 4 h, propargyl bromide (**5**) (0.012 mL, 0.157 mmol) was added and the reaction mixture was allowed to warm to room temperature. After the solution was stirred at that temperature for 4 h to ensure the cyclotrimerization, iodine (40 mg, 0.313 mmol) in 1 mL of Et₂O was added. The reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO₃ and Na₂S₂O₃, dried over Na₂SO₄, and concentrated *in vacuo* to give a crude oil. The crude product was chromatographed on silica gel (hexane-ether) to afford the title compound (44 mg, 72%) as a colorless oil, which was fully characterized by ¹H and ¹³C NMR and IR analyses.

^1H NMR δ 0.27 (s, 9H), 0.45 (s, 9H), 2.81 (s, 2H), 2.91 (s, 2H), 3.47 (s, 4H), 4.51 (s, 4H), 4.69 (s, 2H), 7.24-7.34 (m, 11H).

^{13}C NMR δ 1.02, 2.17, 11.23, 39.28 (quaternary carbon), 40.58, 47.80, 73.18, 73.27, 127.48, 127.53, 127.53, 135.23, 135.29, 137.53, 138.85, 142.16, 147.06, 147.99.

IR (neat) 3087, 3063, 3029, 2952, 2852, 1454, 1361, 1249, 1151, 1100, 838, 751, 696 cm^{-1} .

A correct elemental analysis was hardly obtained owing to the instability of this benzyl iodide.

2,2-Bis[(benzyloxy)methyl]-4,7-bis(trimethylsilyl)indan-5-methanol (39).

To a stirred solution of 4,4-bis[(benzyloxy)methyl]-1,7-bis(trimethylsilyl)-1,6-heptadiyne (**35**) (50 mg, 0.104 mmol) and $\text{Ti}(\text{O-}i\text{-Pr})_4$ (0.039 mL, 0.131 mmol) in 2 mL of Et_2O was added *i*-PrMgCl (1.47 M in Et_2O , 0.178 mL, 0.261 mmol) at -78°C under argon to give a yellow homogeneous solution. The solution was warmed to -50°C over 30 min and was stirred at the same temperature for an additional 4 h. Then propargyl bromide (**5**) (0.012 mL, 0.157 mmol) was added and the reaction mixture was allowed to warm to room temperature. After the solution was stirred for 4 h at that temperature, the argon atmosphere was replaced by dry oxygen gas, and the stirring was continued overnight. Finally, the reaction was terminated by the addition of 1N HCl. The organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated *in vacuo* to give a crude oil. The crude product was chromatographed on silica gel (hexane-ether) to afford the title compound (37 mg, 66%) as a colorless oil, which was fully characterized by ^1H and ^{13}C NMR, IR, and elemental analyses.

^1H NMR δ 0.28 (s, 9H), 0.39 (s, 9H), 1.12 (br s, 1H), 2.88 (s, 2H), 2.94 (s, 2H), 3.49 (s, 4H), 4.51 (s, 4H), 4.70 (s, 2H), 7.24-7.36 (m, 11H).

^{13}C NMR δ -0.98, 2.19, 39.19 (quaternary carbon), 40.84, 47.80, 66.06, 73.20, 73.35, 127.47, 127.54, 128.36, 133.29, 135.95, 137.06, 138.93, 143.58, 147.12, 148.10.

IR (neat) 3316, 3087, 3063, 3030, 2952, 2895, 2854, 1453, 1362, 1248, 1100, 1027, 839, 752, 696 cm^{-1} .

Anal. Calcd for $\text{C}_{32}\text{H}_{44}\text{O}_3\text{Si}_2$: C, 72.13; H, 8.32. Found: C, 72.21; H, 8.63.

2,2-Bis[(benzyloxy)methyl]-5-(buta-2,3-dienyl)-4,7-

bis(trimethylsilyl)indan (40). To a stirred solution of 4,4-bis[(benzyloxy)methyl]-1,7-bis(trimethylsilyl)-1,6-heptadiyne (**35**) (50 mg, 0.104 mmol) and $\text{Ti}(\text{O-}i\text{-Pr})_4$ (0.039 mL, 0.131 mmol) in 2 mL of Et_2O was added $i\text{-PrMgCl}$ (1.47 M in Et_2O , 0.178 mL, 0.261 mmol) at -78°C under argon to give a yellow homogeneous solution. The solution was warmed to -50°C over 30 min. After stirring at -50°C for an additional 4 h, propargyl bromide (**5**) (0.012 mL, 0.157 mmol) was added and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h at that temperature, the reaction mixture was cooled to -50°C . A THF solution of $\text{Li}_2\text{Cu}(\text{CN})\text{Cl}_2$ (0.50 M, 0.209 mL, 0.104 mmol) was added and the mixture was stirred for 1 h at -40°C . Then propargyl bromide (0.016 mL, 0.209 mmol) was added and the reaction mixture was gradually warmed to 0°C over 30 min. After being stirred for 1 h at 0°C , the reaction was terminated by the addition of 1N HCl and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of NaHCO_3 , dried over Na_2SO_4 , and concentrated to give a crude oil. This crude product was separated by preparative TLC (Merck #1.05554, hexane-ether) to afford the title compound (24 mg, 42%) as a colorless oil, which was fully characterized by ^1H and ^{13}C NMR, IR, and elemental analyses.

^1H NMR δ 0.27 (s, 9H), 0.36 (s, 9H), 2.85 (s, 2H), 2.92 (s, 2H), 3.46 (m, 2H), 3.48 (s, 4H), 4.51 (s, 4H), 4.68 (d/t, $J = 6.6, 3.3$ Hz, 2H), 5.24 (quintet, $J = 6.6$ Hz, 1H), 7.19 (s, 1H), 7.18-7.32 (m, 10H).

^{13}C NMR δ 0.77, 2.93, 35.29, 39.27 (quaternary carbon), 41.18, 47.70, 73.16, 73.44, 75.07, 91.10, 127.25, 127.33, 127.69, 128.16, 133.50, 136.49, 138.75, 143.03, 144.69, 147.11, 208.53.

IR (neat) 3087, 3063, 3030, 2952, 2925, 2897, 2853, 1954 ($\text{CH}=\text{C}=\text{CH}_2$), 1496, 1453, 1361, 1249, 1206, 1101, 1028, 839, 752, 696 cm^{-1} .

Anal. Calcd for $\text{C}_{35}\text{H}_{46}\text{O}_2\text{Si}_2$: C, 75.76; H, 8.35. Found: C, 75.40; H, 8.24.

8-Bromo-4,4-dimethyl-1,6-octadiyne (42). To a stirred solution of 1-(dimethylphenylsilyl)-4,4-dimethyl-1,6-heptadiyne (5.1 g, 20.02 mmol) [Fleming, I.; de Marigorta, E. M. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 889-900] in 90 mL of THF was added

n-BuLi (1.55 M in hexane, 16.8 mL, 26.07 mmol) at -78 °C under argon. The reaction mixture was stirred for 15 min and was allowed to warm to 0 °C. Then powdered paraformaldehyde ((HCHO)_n, 1.32 g, 44.1 mmol) was added. After stirring for additional 3 h at room temperature, the reaction was terminated by the addition of an aqueous NH₄Cl solution. The organic products were extracted with ether, and the combined organic layers were dried over Na₂SO₄ and concentrated to an oil, which was chromatographed on silica gel to afford 5,5-dimethyl-8-(dimethylphenylsilyl)-2,7-octadiyn-1-ol (4.3 g, 75 %) as a colorless oil. To a solution of the above 5,5-dimethyl-8-(dimethylphenylsilyl)-2,7-octadiyn-1-ol (4.3 g, 15.12 mmol) in 16 mL of THF was added 1 M-Bu₄NF in THF (30.24 mL, 30.24 mmol) at 0 °C under argon. After the reaction mixture was stirred for 2 h at room temperature, aqueous NH₄Cl solution was added. The organic layer was extracted with ether. Combined organic extracts were dried over MgSO₄ and concentrated to an oil, which was chromatographed on silica gel to afford 5,5-dimethyl-2,7-octadiyn-1-ol (1.69 g, 74 %) as a colorless oil. To a solution of this 5,5-dimethyl-2,7-octadiyn-1-ol (1.29 g, 8.2 mmol) and pyridine (0.066 mL, 0.82 mmol) in 12.2 mL of Et₂O was added PBr₃ (0.39 mL, 4.1 mmol) at -30 °C under argon. The reaction mixture was allowed to warm to room temperature and was stirred for 5 h. The reaction was terminated by the addition of ice, water, and ether. The organic layer was extracted with pentane. The combined organic layers were dried over Na₂SO₄ and concentrated to an oil, which was chromatographed on silica gel to afford the title compound (1.16 g, 67 %) as a colorless oil.

¹H NMR δ 1.06 (s, 6H), 2.01 (t, J = 2.4 Hz, 1H), 2.19 (d, J = 2.4 Hz, 2H), 2.26 (t, J = 2.4 Hz, 2H), 3.94 (t, J = 2.4 Hz, 2H).

¹³C NMR δ 16.38, 26.23, 30.89, 31.24, 33.98 (quaternary carbon), 70.32, 77.35, 81.80, 85.66.

IR (neat) 3298, 2962, 2929, 2900, 2874, 2833, 2232, 2120, 1388, 1369, 1210 cm⁻¹.

Anal. Calcd for C₁₀H₁₃Br: C, 56.36; H, 6.15. Found: C, 56.05; H, 6.40.

Ethyl 2,2,4,6-Tetramethylindan-5-carboxylate (43). To a stirred solution of ethyl 2-butyrate (**21**) (0.080 mL, 0.686 mmol) and Ti(O-*i*-Pr)₄ (0.253 mL, 0.86 mmol) in 6.86 mL of Et₂O was added *i*-PrMgCl (1.40 M in Et₂O, 1.27 mL, 1.78 mmol) at -78 °C under argon.

The solution was allowed to warm to -50 °C over 30 min and was kept at this temperature for 3.5 h. After 8-bromo-4,4-dimethyl-1,6-octadiyne (**42**) (88 mg, 0.412 mmol) was introduced and the solution was stirred for another 3 h at -50 °C, the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h, the reaction was terminated with water (0.4 mL). The heterogeneous mixture was filtered through a short pad of Celite with the aid of ether. The filtrate was concentrated to an oil, which was chromatographed on preparative TLC (Merck# 1.05554, hexane-ethyl acetate) to afford the title compound (74 mg, 73 %) as a colorless oil.

¹H NMR δ 1.13 (s, 6H), 1.38 (t, J = 7.2 Hz, 3H), 2.17 (s, 3H), 2.27 (s, 3H), 2.62 (s, 2H), 2.69 (s, 2H), 4.38 (q, J = 7.2 Hz, 2H), 6.85 (s, 1H).

Irradiation of proton at δ 6.85 ppm (aryl H) showed 4% nOe enhancement to the peak at δ 2.27 ppm (benzyl Me) and 3% nOe enhancement to the peak at δ 2.69 ppm (benzyl H). Irradiation of proton at δ 2.17 ppm (benzyl Me) showed 2% nOe enhancement to the peak at δ 2.62 ppm (benzyl H). Irradiation of proton at δ 2.62 ppm (benzyl H) showed 2% nOe enhancement to the peak at δ 2.17 ppm (benzyl Me). Thus, the regiochemistry has been confirmed.

¹³C NMR δ 14.19, 16.45, 19.52, 28.94, 39.41 (quaternary carbon), 46.25, 47.87, 60.72, 123.96, 130.63, 132.08, 132.91, 140.31, 144.72, 170.84.

IR (neat) 2953, 2926, 2866, 2836, 1725 (C=O), 1609, 1581, 1465, 1419, 1383, 1364, 1328, 1264, 1245, 1226, 1176, 1144, 1096, 1042, 860 cm⁻¹.

Anal. Calcd for C₁₆H₂₂O₂: C, 78.01; H, 9.00. Found: C, 78.06; H, 8.88.

2,2,4,6-Tetramethylindan-5-methanol (44). To a stirred suspension of LiAlH₄ (196 mg, 5.17 mmol) in 1.5 mL of Et₂O was added ethyl 2,2,4,6-tetramethylindan-5-carboxylate (**43**) (254 mg, 1.03 mmol) in 1.0 mL of Et₂O under argon. After stirring for 1.5 h, the reaction was terminated by the dropwise addition of an aqueous 1N HCl at 0 °C. The organic layer was extracted with ether. The combined ethereal layers were washed with an aqueous NaHCO₃ solution, dried over Na₂SO₄, and concentrated to an oil, which was chromatographed on silica gel to afford the title compound (193 mg, 91 %) as a colorless oil.

¹H NMR δ 1.15 (s, 6H), 1.59 (br s, 1H), 2.30 (s, 3H), 2.40 (s, 3H), 2.66 (s, 2H), 2.70 (s, 2H), 4.73 (s, 2H), 6.88 (s, 1H).

^{13}C NMR δ 15.50, 19.57, 29.10, 39.25 (quaternary carbon), 46.85, 47.93, 59.36, 124.46, 133.52, 134.31, 135.38, 140.95, 143.34.

IR (neat) 3360, 3007, 2951, 2920, 2835, 1609, 1581, 1456, 1435, 1381, 1363, 1288, 1272, 1248, 1211, 1174, 1031, 993, 859 cm^{-1} .

Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}$: C, 82.30; H, 9.87. Found: C, 81.75; H, 10.17.

2,2,4,6-Tetramethylindan-5-carbaldehyde. To a suspension of PCC (57 mg, 0.263 mmol) in 1.0 mL of CH_2Cl_2 was added 2,2,4,6-tetramethylindan-5-methanol (**44**) (29.9 mg, 0.146 mmol) prepared above in 1 mL of CH_2Cl_2 under argon. After being stirred for 3 h at room temperature, the reaction mixture was diluted with dry ether and filtered through a short pad of silica gel with the aid of ether. The filtrate was concentrated to an oil, which was chromatographed on silica gel to afford the title compound (28.4 mg, 96 %) as a colorless oil.

^1H NMR δ 1.15 (s, 6H), 2.48 (s, 3H), 2.57 (s, 3H), 2.69 (s, 2H), 2.73 (s, 2H), 6.91 (s, 1H), 10.59 (s, 1H).

^{13}C NMR δ 16.35, 20.57, 28.88 (CMe_2), 39.33 (quaternary carbon), 46.17, 48.26, 125.76, 130.88, 137.21, 140.15, 141.93, 149.46, 193.84.

IR (neat) 2953, 2924, 2867, 2818, 1685 ($\text{C}=\text{O}$), 1603, 1465, 1430, 1380, 1365, 1328, 1245, 1216, 1174, 1078, 861, 767 cm^{-1} .

Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}$: C, 83.12; H, 8.97. Found: C, 83.51; H, 9.08.

2,2,4,6-Tetramethyl-5-vinylindan (45). To a suspension of $\text{Ph}_3\text{PCH}_3(\text{Br})$ (123.6 mg, 0.346 mmol) in 1.6 mL of Et_2O was added *n*-BuLi (1.57 M in hexane, 0.22 mL, 0.346 mmol) at 0 °C under argon. After stirring for 1 h at room temperature, the yellow solution was cooled to 0 °C and 2,2,4,6-tetramethylindan-5-carbaldehyde prepared above (25 mg, 0.124 mmol) was added. After the reaction mixture was heated at reflux for 3 h, it was filtered through a short pad of Celite with the aid of ether. The filtrate was concentrated to an oil, which was chromatographed on silica gel to afford the title compound (21 mg, 86%) as a colorless oil.

^1H NMR δ 1.16 (s, 6H), 2.19 (s, 3H), 2.27 (s, 3H), 2.67 (s, 2H), 2.72 (s, 2H), 5.22 (dd, J = 2.1, 18 Hz, 1H), 5.52 (dd, J = 2.1 Hz, 11.4 Hz, 1H), 6.69 (dd, J = 11.4, 18 Hz, 1H), 6.88 (s, 1H).

^{13}C NMR δ 16.99, 20.94, 29.20, 39.17 (quaternary carbon), 46.94, 47.93, 119.05, 123.78, 131.72, 133.88, 135.66, 135.73, 140.30, 141.77.

IR (neat) 3081, 2952, 2920, 2865, 2836, 1629, 1465, 1381, 1364, 993, 918, 860 cm^{-1} .

Anal. Calcd for $\text{C}_{15}\text{H}_{20}$: C, 89.94; H, 10.06. Found: C, 89.45; H, 10.07.

2-[2,2,4,6-Tetramethylindan-5-yl]ethanol (46). To a solution of 2,2,4,6-tetramethyl-5-vinylindan (**45**) (10 mg, 0.05 mmol) prepared above in 0.5 mL of THF was added $\text{BH}_3\cdot\text{THF}$ (1.0 M in THF, 0.25 mL, 0.25 mmol) at $-30\text{ }^\circ\text{C}$ under argon. After the reaction mixture was stirred at room temperature for 15 min and at $35\text{ }^\circ\text{C}$ for 3 h, the reaction was terminated by the slow and successive addition of 0.36 mL of water, 0.72 mL of an aqueous 3N NaOH solution, and 3.18 mL of 35% aqueous H_2O_2 solution. The heterogeneous solution was stirred at room temperature for 3 h and the organic products were extracted with ether. The combined organic layers were washed with an aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$, dried over MgSO_4 , and concentrated to an oil, which was separated on silica gel to afford the title compound (7.3 mg, 67 %) and its regioisomer, 1-[2,2,4,6-tetramethylindan-5-yl]ethanol, (3.3 mg, 31 %) as colorless oils.

^1H NMR δ 1.15 (s, 6H), 1.49 (br s, 1H), 2.22 (s, 3H), 2.33 (s, 3H), 2.66 (s, 2H), 2.70 (s, 2H), 2.96 (t, J = 7.5 Hz, 2H), 3.75 (t, J = 7.5 Hz, 2H), 6.86 (s, 1H).

^{13}C NMR δ 16.20, 20.49, 29.38, 32.86, 39.26 (quaternary carbon), 47.20, 47.94, 62.00, 124.12, 131.68, 132.78, 134.70, 140.53, 141.09.

IR (neat) 3397, 2954, 2920, 1653, 1041 cm^{-1} .

Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}$: C, 82.52; H, 10.16. Found: C, 82.27; H, 10.56.

A By-product of 46. 1-[2,2,4,6-Tetramethylindan-5-yl]ethanol.

^1H NMR δ 1.14 (s, 3H), 1.16 (s, 3H), 1.54 (d, J = 6.9 Hz, 3H), 1.69 (br s, 1H), 2.34 (s, 3H), 2.39 (s, 3H), 2.65 (s, 2H), 2.69 (s, 2H), 5.40 (q, J = 6.9 Hz, 1H), 6.82 (s, 1H).

Alcyopterosin A (41). To a solution of 2-[2,2,4,6-tetramethylindan-5-yl]ethanol (**46**) (13 mg, 0.06 mmol) in 0.1 mL of pyridine was added SOCl₂ (0.007 mL, 0.096 mmol) at 60 °C under argon. Then the reaction mixture was cooled to 40 °C and LiCl (6 mg, 0.12 mmol) was added. After stirring for 6 h at that temperature, 3 mL of pentane was added, and the reaction was terminated by the addition of brine. The organic products were extracted with pentane. The combined pentane extracts were washed successively with aqueous 1N HCl and NaHCO₃ solutions, dried over Na₂SO₄, and concentrated to an oil, which was chromatographed on silica gel to afford the title compound (9.8 mg, 70 %) as a colorless oil.

¹H NMR δ 1.14 (s, 6H), 2.21 (s, 3H), 2.32 (s, 3H), 2.65 (s, 2H), 2.69 (s, 2H), 3.11 (t, J = 8.1 Hz, 2H), 3.53 (t, J = 8.1 Hz, 2H), 6.85 (s, 1H).

¹³C NMR δ 15.81, 20.03, 29.16, 33.37, 39.19 (quaternary carbon), 42.41, 47.03, 47.85, 124.42, 132.03, 132.71, 134.65, 140.92, 141.95.

IR (neat) 2953, 2924, 2867, 2837, 1465, 1381, 1364, 1320, 1245, 701 cm⁻¹.

These physical properties were in good agreement with those reported in the literature [Palermo, J. A.; Brasco, M. F. R.; Spagnuolo, C.; Seldes, A. M. *J. Org. Chem.* **2000**, 65, 4482-4486].