Enantioselective Synthesis of N1999A2

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Supporting Information

Index	
General Experimental Procedures	1
Materials	1
Instrumentation	1
Synthetic Procedures	2–25

General Experimental Procedures. All reactions were performed in oven- or flame-dried round-bottom or modified Schlenk flasks fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Where necessary (so noted), solutions were deoxygenated by alternate freeze (liquid nitrogen)/evacuation/thaw cycles ($\geq$ three iterations). Organic solutions were concentrated by rotary evaporation (house vacuum, $\sim$ 25 Torr) at 23–30 °C. Flash-column chromatography was performed as described by Still et al.,¹ employing silica gel (60-Å pore size, 230–400 mesh, Merck KGA; or 60-Å pore size, 32–63 μ m, standard grade, Sorbent Technologies). Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60-Å pore size, 230–400 mesh, Merck KGA) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) and/or exposure to ceric ammonium molybdate solution (CAM) or an acidic solution of *p*-anisaldehyde (anisaldehyde) followed by brief heating on a hot plate ($\sim$ 200 °C, 10–15 s).

Materials. Commercial reagents and solvents were used as received unless mentioned otherwise. Dichloromethane, ether, tetrahydrofuran, *N,N*-dimethylformamide and toluene were purified by the method of Pangborn et al.² The molarity of solutions of *n*-butyllithium and *t*-butyllithium was determined by titration against a standard solution of 2-butanol in tetrahydrofuran using triphenylmethane as an indicator (average of three determinations).³

Instrumentation. Proton nuclear magnetic resonance (¹H NMR) spectra and carbon nuclear magnetic resonance (¹³C NMR) were recorded with Varian Unity/Inova 600 (600 MHz), Varian Unity/ Inova 500 (500 MHz/125 MHz), or Varian Mercury 400 (400 MHz/100 MHz) NMR spectrometers. Chemical shifts for protons are reported in parts per million scale (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents (CHCl₃: δ 7.26, C₆D₅H: δ 7.15, CD₂HClN: 1.93). Chemical shifts for carbon are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl₃: δ 77.0, C₆D₅H: δ 128.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration,

(1) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

(3) Duhamel, L.; Palquevent, J.-C. *J. Org. Chem.* **1979**, *44*, 3404.

HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{31}O_3Si$, 299.2042; found 299.2046.

tert-Butyldimethylsilyl Ether 7

tert-Butyldimethylsilyl chloride (25.2 g, 0.125 mol, 2.0 equiv) was added to a stirring solution of the alcohol **6** (24.8 g, 0.083 mol, 1.0 equiv) and imidazole (15.0 g, 0.250 mol, 3.0 equiv) in *N,N*-dimethylformamide (200 mL) at 23 °C. After stirring at 23 °C for 17 h, the reaction mixture was partitioned between ether (1 L) and water (500 mL). The organic layer was separated and washed successively with water (500 mL), 1N aqueous hydrochloric acid solution (300 mL), saturated aqueous sodium bicarbonate solution (300 mL), and brine (200 mL). The washed solution was then dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (5% ethyl acetate-hexanes) to give the *tert*-butyldimethylsilyl ether **7** (yellow oil, 32.6 g, 95%, two steps).

R_f = 0.25 (5% ethyl acetate-hexanes). 1H NMR (1:1 mixture of diastereomers, 600 MHz, $CDCl_3$), δ 4.62 (m, br, 1H, C(1')-H), 3.98–3.92 (m, 1H, C(2)-H), 3.88–3.81 (m, 1H, C(5')-H), 3.79 (dd, J_1 = 4.8 Hz, J_2 = 10.2 Hz, 0.5 H, C(1)-H), 3.70 (dd, J_1 = 4.8 Hz, J_2 = 10.2 Hz, 0.5 H, C(1)-H), 3.50–3.47 (m, 1H, C(5')-H), 3.42 (dd, J_1 = 5.4 Hz, J_2 = 10.2 Hz, 0.5 H, C(1)-H), 3.31 (dd, J_1 = 6.6 Hz, J_2 = 9.6 Hz, 0.5 H, C(1)-H), 2.54–2.47 (2 diastereomers, dd (2), J_1 = 6.0 Hz, J_2 = 18.6 Hz, 1H, C(3)-H), 2.42–2.37 (2 diastereomers, dd (2), J_1 = 6.0 Hz, J_2 = 18.6 Hz, 2H, C(3)-H), 1.85–1.79 (m, 1H, C(2')-H), 1.72–1.67 (m, 1H, C(2')-H), 1.62–1.49 (m, 4H, C(3')-H + C(4')-H), 0.97 (t, J = 7.8 Hz, 9H, $Si(CH_2CH_3)_3$), 0.89 (2 diastereomers, s, 9H, $Si(CH_3)_2C(CH_3)_3$), 0.56 (q, J = 7.8 Hz, 6H, $Si(CH_2CH_3)_3$), 0.10 (2 diastereomers, s, 3H, $Si(CH_3)_2C(CH_3)_3$), 0.09 (s, 3H, $Si(CH_3)_2C(CH_3)_3$), 0.07 (s, 3H, $Si(CH_3)_2C(CH_3)_3$). ^{13}C NMR (100 MHz, $CDCl_3$), δ 105.0, 104.9, 99.0, 98.6, 83.4, 83.3, 70.8, 70.6, 70.5, 70.4, 61.8, 61.6, 30.5, 30.4, 26.2, 26.1, 25.8, 25.5, 25.4, 19.2, 19.1, 18.1 (2), 7.4, 4.4, –4.6 (2), –4.7. IR (NaCl, thin film), cm^{-1} 3448, 2954, 2875, 2857, 2176, 1654, 1637, 1463, 1447, 1415, 1361, 1255, 1202, 1125, 1067, 1037, 939, 908, 837, 778, 720. HRMS–CI (m/z) $[M+NH_4]^+$ calcd for $C_{22}H_{48}NO_3Si_2$, 430.3173; found, 430.3170.

Alcohol 8

A solution of dimethylaluminum chloride in hexanes (1.0 M, 125 mL, 125 mmol, 2.5 equiv) was added dropwise via cannula over 20 min to a solution of the *tert*-butyldimethylsilyl ether **7** (20.7 g, 50.1 mmol, 1.0 equiv) in dichloromethane (300 mL) at -78°C . The resulting mixture was allowed to warm to 23°C over 2 h. The reaction mixture was then transferred by cannula into a mixture of saturated aqueous potassium sodium tartrate solution (300 mL) and saturated aqueous sodium bicarbonate solution (300 mL). The resulting biphasic solution was stirred at 23°C for 1 h. The layers were separated. The aqueous layer was extracted with dichloromethane (2×400 mL). The organic extracts were combined and the combined solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (17% ether-hexanes) to provide the alcohol **8** (colorless oil, 15.28 g, 93%).

$R_f = 0.40$ (20% ether-hexanes). ^1H NMR (400 MHz, CDCl_3), δ 3.91–3.86 (m, 1H, C(2)-H), 3.71–3.66 (m, 1H, C(1)-H), 3.63–3.57 (m, 1H, C(1)-H), 2.48 (dd, $J_1 = 7.6$ Hz, $J_2 = 16.8$ Hz, 1H, C(3)-H), 2.41 (dd, $J_1 = 5.2$ Hz, $J_2 = 16.8$ Hz, 1H, C(3)-H), 1.91 (dd, $J_1 = 6.8$ Hz, $J_2 = 7.2$, 1H, C(1)-OH), 0.97 (t, $J = 7.6$ Hz, 9H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.89 (s, 9H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.56 (q, $J = 7.6$ Hz, 6H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.12 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.10 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$). ^{13}C NMR (100 MHz, CDCl_3), δ 104.0, 84.0, 72.8, 71.5, 65.7, 63.8, 44.6, 25.7 (2), 25.6, 25.4, 18.0, 7.4, 4.4, -3.6, -4.6, -4.7, -4.8. IR (NaCl, thin film), cm^{-1} 3421, 2955, 2931, 2876, 2858, 2175, 1472, 1463, 1415, 1389, 1363, 1255, 1115, 1047, 1020, 1005, 975, 938, 854, 838, 808, 778. HRMS-ESI (m/z) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{37}\text{O}_2\text{Si}_2$, 329.2332; found, 329.2331.

Aldehyde 9

A freshly-prepared solution of sulfur trioxide-pyridine complex (7.27 g, 45.7 mmol, 5.0 equiv) in DMSO (50 mL) was added dropwise via cannula over 10 min to a stirring solution of the alcohol **8** (3.00 g, 9.13 mmol, 1 equiv) and triethylamine (12.7 mL, 91.3 mmol, 10 equiv) in dichloromethane (60 mL) at 0°C . After stirring at 0°C for 2 h, the reaction mixture was diluted with a 1:1 mixture of ethyl acetate and hexanes (400 mL). The resulting mixture was washed successively with 1N aqueous hydrochloric acid solution (2×60 mL), saturated aqueous sodium bicarbonate solution (80 mL), and brine (80 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated to give the aldehyde **9** (colorless oil, 2.93 g, 98%), used in the next reaction without purification.

$R_f = 0.43$ (17% ether-hexanes). ^1H NMR (400 MHz, CDCl_3), δ 9.64 (d, $J = 1.2$ Hz, 1H, C(1)-**H**), 4.10 (dt, $J_1 = 1.2$ Hz, $J_2 = 6.2$ Hz, 1H, C(2)-**H**), 2.65 (dd, $J_1 = 5.6$ Hz, $J_2 = 17.2$ Hz, 1H, C(3)-**H**), 2.55 (dd, $J_1 = 7.2$ Hz, $J_2 = 17.2$ Hz, 1H, C(3)-**H**), 0.96 (t, $J = 7.6$ Hz, 9H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.92 (s, 9H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.56 (q, $J = 7.6$ Hz, 6H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.13 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.12 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$). ^{13}C NMR (100 MHz, CDCl_3), δ 202.2, 102.5, 84.8, 76.0, 25.7, 24.6, 18.2, 7.4, 4.3, -4.8 (2). IR (NaCl, thin film), cm^{-1} 2950, 2934, 2876, 2806, 2178, 1742, 1464, 1416, 1377, 1362, 1334, 1255, 1124, 1019, 1006, 972, 937, 839, 780, 738. HRMS- CI (m/z) $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{17}\text{H}_{38}\text{NO}_2\text{Si}_2$, 344.2441; found, 344.2435.

Dibromoolefin **10**

Triphenylphosphine (9.44 g, 36.0 mmol, 4.0 equiv) was added to a solution of carbon tetrabromide (5.97 g, 18.0 mmol, 2.0 equiv) in dichloromethane (60 mL) at 0 °C. After 15 min, a solution of the aldehyde **9** (2.93 g, 9.00 mmol, 1 equiv) in dichloromethane (40 mL) was added dropwise via cannula over 30 min at 0 °C. After stirring at 0 °C for 45 min, the reaction suspension was diluted with a 1:4 mixture of ether and pentane (300 mL). The mixture was filtered through a short plug of silica gel. The filter cake was washed with a 1:4 mixture of ether and pentane (300 mL). The filtrates were combined and the combined solution was concentrated. The residue was purified by flash-column chromatography (100% hexanes) to provide the dibromoolefin **10** (yellow oil, 95% ee, 3.32 g, 77%, 2 steps). The enantiomeric excess of **10** was determined by Mosher ester analysis of a derivative, prepared as shown in the scheme below.

$R_f = 0.26$ (100% hexanes). ^1H NMR (500 MHz, CDCl_3), δ 6.43 (d, $J = 8.0$ Hz, 1H, C(2)-**H**), 4.47 (dt, $J_1 = 6.5$ Hz, $J_2 = 8.0$ Hz, 1H, C(3)-**H**), 2.50 (dd, $J_1 = 6.0$ Hz, $J_2 = 17.0$ Hz, 1H, C(4)-**H**), 2.45 (dd,

$J_1 = 6.0$ Hz, $J_2 = 17.0$ Hz, 1H, C(4)-H), 0.99 (t, $J = 8.0$ Hz, 9H, Si(CH₂CH₃)₃), 0.89 (s, 9H, Si(CH₃)₂C(CH₃)₃), 0.59 (q, $J = 8.0$ Hz, 6H, Si(CH₂CH₃)₃), 0.11 (s, 3H, Si(CH₃)₂C(CH₃)₃), 0.09 (s, 3H, Si(CH₃)₂C(CH₃)₃). ¹³C NMR (100 MHz, CDCl₃), δ 140.4, 102.9, 90.1, 84.3, 72.1, 28.5, 25.7, 18.0, 7.5, 4.4, -4.6, -4.9. IR (NaCl, thin film), cm⁻¹ 3427, 2955, 2931, 2898, 2875, 2858, 2178, 1623, 1472, 1462, 1414, 1362, 1253, 1086, 1018, 931, 836, 778, 726. $[\alpha]_D^{23} -9.6^\circ$ (c 0.57, CHCl₃). HRMS-ESI (m/z) [$M+H$]⁺ calcd for C₁₇H₃₅O₂Si₂, 481.0593; found, 481.0588.

Diyne 11

A solution of sodium bis(trimethylsilyl)amide in tetrahydrofuran (1.0 M, 11.2 mL, 11.2 mmol, 1.2 equiv) was added dropwise via syringe over 10 min to a solution of the dibromoolefin **10** (4.51 g, 9.35 mmol, 1 equiv) in tetrahydrofuran (50 mL) at -78 °C. After 20 min, a solution of *n*-butyllithium in hexanes (2.50 M, 7.48 mL, 18.7 mmol, 2.0 equiv) was added dropwise via syringe over 15 min. The reaction mixture was stirred for an additional 10 min at -78 °C. Saturated aqueous ammonium chloride solution (80 mL) was then added to quench any excess base. The resulting biphasic mixture was partitioned between ether (150 mL) and water (50 mL). The layers were separated, and the aqueous layer was extracted with ether (2 × 80 mL). The organic extracts were combined and the combined solution was washed with brine (80 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (2% ether-hexanes) to provide the diyne **11** (colorless oil, 2.99 g, 99%).

$R_f = 0.30$ (100% hexanes). ¹H NMR (400 MHz, CDCl₃), δ 4.48 (dt, $J_1 = 2.4$ Hz, $J_2 = 6.8$ Hz, 1H, C(3)-H), 2.63 (d, $J = 6.8$ Hz, 2H, C(4)-H), 2.40 (d, $J = 2.4$ Hz, 1H, C(1)-H), 0.98 (t, $J = 8.0$ Hz, 9H, Si(CH₂CH₃)₃), 0.91 (s, 9H, Si(CH₃)₂C(CH₃)₃), 0.57 (q, $J = 8.0$ Hz, 6H, Si(CH₂CH₃)₃), 0.15 (s, 3H, Si(CH₃)₂C(CH₃)₃), 0.14 (s, 3H, Si(CH₃)₂C(CH₃)₃). ¹³C NMR (100 MHz, CDCl₃), δ 103.7, 84.3, 84.0, 72.5, 62.1, 30.6, 25.7, 18.2, 7.4, 4.4, -4.7, -5.0. IR (NaCl, thin film), cm⁻¹ 3311, 2956, 2935, 2913, 2876, 2858, 2179, 1644, 1471, 1463, 1415, 1396, 1362, 1345, 1253, 1100, 1013, 950, 930, 839, 779. $[\alpha]_D^{23} -13.9^\circ$ (c 0.61, CHCl₃). HRMS-ESI (m/z) [$M+NH_4$]⁺ calcd for C₁₈H₃₈NOSi₂, 340.2492; found, 340.2495.

Tributylstannanyl Alkyne 27

A solution of *n*-butyllithium in hexanes (2.50 M, 3.22 mL, 8.05 mmol, 1.1 equiv) was

added dropwise via syringe over 15 min to a solution of the diyne **11** (2.36 g, 7.31 mmol, 1 equiv) in tetrahydrofuran (30 mL) at -78°C . After 15 min, tributyltin chloride (2.08 mL, 7.68 mmol, 1.05 equiv) was added via syringe over 2 min. The reaction mixture was allowed to warm to 23°C over 1 h. Water (80 mL) was added and tetrahydrofuran was removed in vacuo. The biphasic residue was extracted with ether (300 mL). The organic layer was separated and washed with water (2×80 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide the tributylstannanyl alkyne **27** (colorless oil, 4.47 g, 100%), used in next reaction without purification.

^1H NMR (500 MHz, CDCl_3), δ 4.48 (t, $J = 6.5$ Hz, 1H, C(3)-**H**), 2.61 (d, $J = 6.5$ Hz, 2H, C(4)-**H**), 1.54 (m, 6H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 1.33 (m, 6H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 0.98 (t, $J = 8.0$ Hz, 9H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.96 (m, 6H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 0.91 (s, 9H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.90 (t, $J = 7.5$ Hz, 9H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 0.57 (q, $J = 8.0$ Hz, 6H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.16 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.14 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$).

(1-Iodovinyl) Stannane 2

A solution of the tributylstannanyl alkyne **27** (4.47 g, 7.31 mmol, 1 equiv) in tetrahydrofuran (50 mL) was added dropwise via cannula over 10 min to a suspension of bis(cyclopentadienyl) zirconium chloride hydride (Schwartz's reagent, Strem Chemicals, 2.64 g, 10.2 mmol, 1.4 equiv) in tetrahydrofuran (60 mL) at 23°C . After stirring at 23°C for 40 min, the reaction solution had become dark-red. A solution of iodine (1.95 g, 7.68 mmol, 1.05 equiv) in tetrahydrofuran (15 mL) was added dropwise via cannula over 5 min. After stirring at 23°C for 20 min, the resulting light-yellow solution was partitioned between ether (300 mL) and water (150 mL). The organic layer was separated and washed with brine (60 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (100% hexanes, silica gel deactivated with Et_3N) to provide the (1-iodovinyl) stannane **2** (yellowish oil, 3.71 g, 69%, 2 steps).

$R_f = 0.25$ (100% hexanes). ^1H NMR (500 MHz, CDCl_3), δ 7.31 (ddt, $J_1 = 2.5$ Hz, $J_2 = 9.0$ Hz, $J_3 = 49.75$ Hz, 1H, C(2)-**H**), 4.04 (dt, $J_1 = 4.5$ Hz, $J_2 = 8.5$ Hz, 1H, C(3)-**H**), 2.45 (dd, $J_1 = 8.0$ Hz, $J_2 = 17.0$ Hz, 1H, C(4)-**H**), 2.33 (dd, $J_1 = 4.5$ Hz, $J_2 = 17.0$ Hz, 1H, C(4)-**H**), 1.57–1.61 (m, 6H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 1.35 (m, 6H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 1.09 (m, 6H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$),

0.98 (t, $J = 8.0$ Hz, 9H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.92 (t, $J = 7.0$ Hz, 9H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 0.88 (s, 9H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.57 (q, $J = 8.0$ Hz, 6H, $\text{Si}(\text{CH}_2\text{CH}_3)_3$), 0.09 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.07 (s, 3H, $\text{Si}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$). ^{13}C NMR (100 MHz, CDCl_3), δ 158.6, 104.2, 103.4, 83.5, 75.6 (t, $J = 11.4$ Hz), 7.5, 4.4, -4.1, -4.4. IR (NaCl, thin film), cm^{-1} 2956, 2930, 2874, 2856, 2176, 1403, 1251, 1098, 837, 777, 738, 726. $[\alpha]_{\text{D}}^{23} -12.1^\circ$ (c 1.2, CHCl_3). HRMS-ESI (m/z) $[\text{M}-\text{C}_4\text{H}_9]^+$ calcd for $\text{C}_{26}\text{H}_{52}\text{IOSi}_2\text{Sn}$, 683.1623; found, 683.1636.

(Z)-Olefin 15

A solution of *n*-butyllithium in hexanes (2.50 M, 9.64 mL, 24.1 mmol, 1.2 equiv) was added dropwise via syringe over 15 min to a thoroughly degassed, stirring suspension of 3-(*tert*-butyldimethylsilyl)propargyltriphenylphosphonium bromide⁵ (**14**, 13.0 g, 26.3 mmol, 1.3 equiv) and lithium iodide (12.1 g, 90.6 mmol, 4.6 equiv) in tetrahydrofuran (250 mL) at -78°C . After the addition was complete, the reaction mixture was warmed to 0°C in an ice-water bath. After stirring at 0°C for 20 min, the reaction mixture was cooled to -78°C . A solution of the propargylic ketone **13**^{5,6} (4.46 g, 19.7 mmol, 1 equiv) in tetrahydrofuran (100 mL) was added dropwise via cannula over 15 min. The reaction mixture was stirred at -78°C for 1 h. Saturated aqueous ammonium chloride solution (150 mL) was added to quench any excess base. The layers were separated and the aqueous layer was extracted successively with pentane (2×150 mL) and ether (2×150 mL). The organic extractions were combined and the combined solution was washed with brine (3×100 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (5% ether-hexanes) to provide the (*Z*)-olefin **15** (yellow oil, 4.45 g, 74%) and, separately, the (*E*)-olefin **28** (yellow oil, 0.92 g, 15%).

R_f (**15**) = 0.53, R_f (**28**) = 0.45 (10% ether-hexanes). ^1H NMR (500 MHz, C_6D_6), δ 6.01 (s, 1H, C(4)-H), 5.49 (t, $J = 7.5$ Hz, 1H, C(7)-H), 4.09 (dd, $J_1 = 7.5$ Hz, $J_2 = 8.0$ Hz, 1H, C(8)-H), 3.96 (t, $J_1 = 7.5$ Hz, $J_2 = 8.0$ Hz, 1H, C(8)-H), 1.57 (s, 3H, C(CH_3)₂), 1.39 (s, 3H, C(CH_3)₂), 0.93 (s, 9H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$), 0.14 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.05 (s, 3H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$), 0.04 (s, 3H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, C_6D_6), δ 136.2, 118.8, 110.4, 105.7, 103.0, 101.9, 101.5, 75.2, 68.4, 26.7, 26.3, 26.1, 16.8, -0.3, -4.8. IR (NaCl, thin film), cm^{-1} 2955, 2930, 2858, 2144,

⁵ (a) Myers, A. G.; Hammond, M.; Wu, Y.; Xiang, J.-N.; Harrington, P. M.; Kuo, E. Y. *J. Am. Chem. Soc.* **1996**, *118*, 10006. (b) Hammond, M., Ph. D. Thesis, California Institute of Technology, 1997.

⁶ For the synthesis of (*S*)-glyceraldehyde acetonide, see: (a) Janson, M.; Kvarnström, I.; Svensson, S. C. T.; Classon, B.; Samuelsson, B. *Synthesis* **1993**, 129. (b) Hubschwerlen, C. *Synthesis* **1986**, 962. (c) Schmid, C. R.; Bradley, D. A. *Synthesis* **1992**, 587.

1472, 1371, 1251, 1067, 841, 776. HRMS–ESI (m/z) [$M+H$] $^+$ calcd for $C_{20}H_{35}O_2Si_2$, 363.2175; found, 363.2167.

Conversion of the (*E*)-Olefin **28 to the (*Z*)-Olefin **15****

A 100-mL, round-bottom flask was charged with the (*E*)-olefin **28** (2.35 g, 6.47 mmol, 1 equiv), benzophenone (226 mg, 1.24 mmol, 0.2 equiv), and ethyl acetate (15 mL). The reaction vessel was irradiated with a Hanovia 450-watt medium-pressure mercury lamp (Pyrex filter) for 4 h. 1H NMR analysis of the reaction mixture at this point showed that a 55:45 mixture of the (*E*)-olefin **28** and the (*Z*)-olefin **15** had formed. The reaction mixture was concentrated and the isomers were separated by flash-column chromatography (5% ether-hexanes) to provide the (*Z*)-olefin **15** (yellow oil, 0.94 g, 40%) and, separately, recovered (*E*)-olefin **28** (yellow oil, 1.37 g, 58%). This process was subject to iteration.

Enediyne **16**

Potassium carbonate (336 mg, 2.43 mmol, 1 equiv) was added to a solution of the (*Z*)-olefin **15** (882 mg, 2.43 mmol, 1 equiv) in methanol (17 mL) at 0 °C. After stirring at 0 °C for 45 min, the reaction mixture was partitioned between pentane (50 mL) and water (15 mL). The aqueous layer was separated and extracted with pentane (2 × 20 mL). The organic extracts were combined and the combined solution was dried over anhydrous sodium sulfate. The dried organic solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (10% ether-hexanes) to give the enediyne **16** (yellow oil, 705 mg, 100%).

R_f = 0.39 (10% ether-hexanes). 1H NMR (500 MHz, C_6D_6), δ 5.96 (s, 1H, C(4)-**H**), 5.45 (t, J = 7.5 Hz, 1H, C(7)-**H**), 4.04 (dd, J_1 = 8.5 Hz, J_2 = 7.5 Hz, 1H, C(8)-**H**), 3.87 (t, J_1 = 8.5 Hz, J_2 = 7.5 Hz, 1H, C(8)-**H**), 2.71 (s, 1H, C(1)-**H**), 1.51 (s, 3H, C(**CH**₃)₂), 1.36 (s, 3H, C(**CH**₃)₂), 0.93 (s, 9H, SiC(**CH**₃)₃(**CH**₃)₂), 0.05 (s, 6H, SiC(**CH**₃)₃(**CH**₃)₂). ^{13}C NMR (100 MHz, C_6D_6), δ 135.2, 119.7, 110.4, 105.6, 101.1, 84.1, 81.1, 74.9, 68.2, 26.6, 26.1, 16.8, –4.8. IR (NaCl, thin film), cm^{-1} 3288, 2987, 2953, 2930, 2884, 2858, 2166, 2122, 2093, 1471, 1372, 1251, 1066, 840. HRMS–ESI (m/z) [$M+H$] $^+$ calcd for $C_{17}H_{27}O_2Si$, 291.1780; found, 291.1789.

1,5-Hexadiyne-3,4-diol **17**

A 100-mL, round-bottom flask was charged with $\text{K}_2\text{OsO}_4 \cdot 2\text{H}_2\text{O}$ (44.2 mg, 0.120 mmol, 0.04 equiv), $(\text{DHQD})_2\text{Pyr}$ (529 mg, 0.600 mmol, 0.20 equiv), $\text{K}_3\text{Fe}(\text{CN})_6$ (4.94 g, 15.0 mmol, 5.0 equiv), K_2CO_3 (2.07 g, 15.0 mmol, 5.0 equiv), *t*-BuOH (5 mL), and H_2O (10 mL). The mixture was stirred at 0 °C for 15 min, and methanesulfonamide (1.14 g, 12.0 mmol, 4.0 equiv) was added. After 5 min, a solution of the enediyne **16** (874 mg, 3.00 mmol, 1.0 equiv) in *t*-BuOH (5 mL) was added, and the reaction mixture was stirred at 0 °C for 16 h. Saturated aqueous sodium bisulfite solution (10 mL) was added, and the resulting biphasic mixture was stirred at 23 °C for 30 min. The mixture was diluted with EtOAc (40 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 40 mL). The organic extracts were combined and the combined solution was washed with brine (30 mL). The washed solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (25% EtOAc-hexanes) to give the 1,5-hexadiyne-3,4-diol **17** (white foam, 518 mg, 53%) and, separately, recovered starting material (**16**, yellow oil, 60.2 mg, 7%).

$R_f = 0.25$ (25% ethyl acetate-hexanes). ^1H NMR (500 MHz, CDCl_3), δ 4.62 (d, 1H, C(4)-**H**), 4.33 (t, 1H, $J = 6.5$ Hz, C(7)-**H**), 4.23 (dd, 1H, $J = 6.0$ Hz, C(8)-**H**), 4.16 (dd, 1H, $J = 6.0$ Hz, C(8)-**H**), 2.81 (d, 1H, $J = 5.0$ Hz, C(4)-**OH**), 2.79 (s, 1H, C(3)-**OH**), 2.56 (s, 1H, C(1)-**H**), 1.49 (s, 3H, C(**CH**₃)₂), 1.37 (s, 3H, C(**CH**₃)₂), 0.95 (s, 9H, SiC(**CH**₃)₃(**CH**₃)₂), 0.14 (s, 6H, SiC(**CH**₃)₃(**CH**₃)₂). ^{13}C NMR (100 MHz, CDCl_3), δ 110.4, 101.3, 91.6, 81.2, 78.8, 75.3, 73.6, 68.6, 66.2, 26.2, 26.0, 25.2, 16.5, -4.8. IR (NaCl, thin film), cm^{-1} 3425, 3307, 2980, 2949, 2930, 2886, 2857, 1460, 1372, 1251. HRMS-ESI (m/z) [$\text{M}+\text{H}$]⁺ calcd for $\text{C}_{17}\text{H}_{29}\text{O}_4\text{Si}$, 325.1835; found, 325.1842.

Tetraol **18**

Iron (III) chloride hexahydrate (3.52 g, 13.0 mmol, 3.0 equiv) was added to a stirring solution of the 1,5-hexadiyne-3,4-diol **17** (1.41 g, 4.35 mmol, 1 equiv) in acetonitrile (40 mL) at 23 °C. After stirring at 23 °C for 40 min, the reaction mixture was concentrated to a volume of ca. 15 mL. The concentrate was diluted with ethyl acetate (100 mL). The resulting solution was

washed with water (80 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 80 mL). The organic extracts were combined and the combined solution was washed with brine (2 × 50 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (60% ethyl acetate-hexanes) to provide the tetraol **18** (colorless oil, 1.24 g, 100%).

R_f = 0.20 (60% ethyl acetate-hexanes). ^1H NMR (500 MHz, CDCl_3), δ 4.65 (s, br, 1H, C(4)-H), 3.99–3.92 (m, 3H, C(7)-H + C(8)-H), 3.60 (s, br, 1H, -OH), 3.36 (s, br, 1H, -OH), 3.18 (s, br, 1H, -OH), 2.76 (s, br, 1H, -OH), 2.62 (s, 1H, C(1)-H), 0.95 (s, 9H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$), 0.14 (s, 6H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, CDCl_3), δ 101.9, 91.8, 81.3, 76.2, 74.6, 74.3, 67.2, 62.5, 26.0, 16.5, -4.8. IR (NaCl, thin film), cm^{-1} 3393, 2928, 2857, 2177, 2113, 1467, 1250, 1071. HRMS-ESI (m/z) [$\text{M}+\text{NH}_4$] $^+$ calcd for $\text{C}_{14}\text{H}_{28}\text{NO}_4\text{Si}$, 302.1788; found, 302.1775.

1,5-Hexadiyne-3,4-diol **3**

Camphorsulfonic acid monohydrate (71.8 mg, 0.309 mmol, 0.04 equiv) was added to a solution of the tetraol **18** (2.20 g, 7.73 mmol, 1 equiv) and mesitaldehyde dimethyl acetal (**19**)⁷ (3.01 g, 15.5 mmol, 2.0 equiv) in tetrahydrofuran (300 mL) at 23 °C. After stirring at 23 °C for 5 h, the reaction mixture was partitioned between ethyl acetate (100 mL) and saturated aqueous sodium bicarbonate solution (150 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 100 mL). The organic layers were combined and the combined solution was washed with brine (60 mL). The washed solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (25% ethyl acetate-hexanes) to provide the 1,5-hexadiyne-3,4-diol **3** (colorless oil, 1.76 g, 55%) and, separately, the corresponding minor diastereomer (colorless oil, 0.45 g, 14%).

⁷ Mesitaldehyde dimethyl acetal (**19**) was synthesized as follows: camphorsulfonic acid (10 mg) was added to a solution of mesitaldehyde (3.00 g, 20.2 mmol, 1 equiv) and trimethyl orthoformate (3.22 g, 30.4 mmol, 1.5 equiv) in methanol (30 mL) at 23 °C. After stirring at 23 °C for 12 h, the reaction mixture was partitioned between ether (30 mL) and saturated aqueous sodium bicarbonate solution (30 mL). The aqueous layer was separated and further extracted with ether (30 mL). The organic extracts were combined and the combined solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide mesitaldehyde dimethyl acetal (**19**) (colorless oil, 3.90 g, 99%).

$R_f = 0.25$ (25% ethyl acetate-hexanes). ^1H NMR (500 MHz, CDCl_3), δ 6.82 (s, 2H, Ar-**H**), 6.41 (s, 1H, C(9)-**H**), 4.72 (d, $J = 5.0$ Hz, 1H, C(4)-**H**), 4.53–4.34 (m, 3H, C(7)-**H** + C(8)-**H**), 2.82 (s, 1H, C(3)-OH), 2.81 (d, $J = 4.5$ Hz, 1H, C(4)-OH), 2.66 (s, 1H, C(1)-**H**), 2.37 (s, 6H, Ar-**CH**₃), 2.25 (s, 3H, Ar-**CH**₃), 0.95 (s, 9H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$), 0.14 (s, 3H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$), 0.13 (s, 3H, $\text{SiC}(\text{CH}_3)_3(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, CDCl_3), δ 139.1, 138.1, 130.0, 127.8, 103.3, 101.0, 92.1, 81.6, 77.6, 76.4, 74.4, 69.2, 68.3, 26.0, 20.9, 19.8, 16.5, –4.8 (2). IR (NaCl, thin film), cm^{-1} 3416, 3306, 2928, 2857, 2177, 2116, 1614, 1470, 1251, 1077. $[\alpha]_D^{23} -26.9^\circ$ (c 0.90, CHCl_3). HRMS–ESI (m/z) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{35}\text{O}_4\text{Si}$, 415.2304; found, 415.2313.

Enetriyne Diol **20**

A mixture of the (1-iodovinyl) stannane **2** (2.57 g, 3.47 mmol, 1.8 equiv), the 1,5-hexadiyne-3,4-diol **3** (800 mg, 1.93 mmol, 1 equiv), tetrakis(triphenylphosphine)palladium (669 mg, 0.579 mmol, 0.3 equiv), and copper(I) iodide (221 mg, 1.16 mmol, 0.6 equiv) in benzene (12 mL) was subjected to iterative freeze-pump-thaw cycles (4 $\times$). Triethylamine (807 μL , 5.79 mmol, 3.0 equiv) was then added to the deoxygenated solution at 23 $^\circ\text{C}$. The mixture was stirred at 23 $^\circ\text{C}$ for 21 h, then *N*-acetyl cysteine (5 g) and ether (15 mL) were added, followed by triethylamine (3 mL). After stirring at 23 $^\circ\text{C}$ for 1 h, the mixture obtained was partitioned between ethyl acetate (100 mL) and a 1:1 mixture of saturated aqueous ammonium chloride solution and water (100 mL). The aqueous layer was separated and extracted with ethyl acetate (2 $\times$ 100 mL). The organic extracts were combined and the combined solution was washed with brine (60 mL). The washed solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (8% ethyl acetate-hexanes) to provide the enetriyne diol **20** (colorless oil, 1.03 g, 64%).

$R_f = 0.25$ (17% ether-hexanes). ^1H NMR (600 MHz, CDCl_3), δ 6.81 (s, 2H, Ar-**H**), 6.72 (ddt, $J_1 = 2.4$ Hz, $J_2 = 8.4$ Hz, $J_3 = 50.4$ Hz, 1H, C(12)-**H**), 6.39 (s, 1H, C(15)-**H**), 4.72 (d, $J = 4.8$ Hz, 1H,

C(5)-**H**), 4.52 (m, 2H, C(13)-**H** + C(14)-**H**), 4.34 (t, $J = 7.2$ Hz, 1H, C(14)-**H**), 4.16 (dt, $J_1 = 3.0$ Hz, $J_2 = 8.4$ Hz, 1H, C(11)-**H**), 2.70 (s, 1H, C(4)-OH), 2.61 (d, $J = 4.2$ Hz, 1H, C(5)-OH), 2.47 (dd, $J_1 = 8.4$ Hz, $J_2 = 16.8$ Hz, 1H, C(10)-**H**), 2.37 (s, 6H, Ar-**CH**₃), 2.34 (dd, $J_1 = 3.0$ Hz, $J_2 = 16.8$ Hz, 1H, C(10)-**H**), 2.25 (s, 3H, Ar-**CH**₃), 1.55 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.35 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.11 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 0.99 (t, $J = 7.8$ Hz, Si(CH₂CH₃)₃), 0.95 (s, 9H, Si(CH₃)₂C(CH₃)₃), 0.91 (s, 9H, Si(CH₃)₂C(CH₃)₃), 0.91 (t, $J = 7.2$ Hz, 9H, Sn(CH₂CH₂CH₂CH₃)₃), 0.58 (q, $J = 7.8$ Hz, 6H, Si(CH₂CH₃)₃), 0.14(2) (s, 3H, Si(CH₃)₂C(CH₃)₃), 0.13 (s, 3H, Si(CH₃)₂C(CH₃)₃), 0.08 (s, 3H, Si(CH₃)₂C(CH₃)₃). ¹³C NMR (100 MHz, CDCl₃), δ 156.3, 138.8, 138.0, 130.0, 128.1, 123.3, 104.4, 103.1, 101.7, 91.9, 91.5, 89.4, 83.6, 77.8, 75.4, 74.4, 69.2, 68.5, 30.8, 29.0, 27.3, 26.0, 25.8, 20.9, 20.0, 18.1, 16.5, 13.6, 11.2 (dt, $J_1 = 7.6$ Hz, $J_2 = 166$ Hz), 7.4, 4.4, -4.1, -4.3, -4.8(2). IR (NaCl, thin film), cm⁻¹ 3445, 2952, 2174, 1615, 1464, 1456. $[\alpha]_D^{23}$ -50.3° (c 0.33, CHCl₃). HRMS-ESI (m/z) [M+H]⁺ calcd for C₅₄H₉₅O₅Si₃Sn, 1027.5509; found, 1027.5500.

Enetriyne Triol **29**

A solution of tetrabutylammonium fluoride in tetrahydrofuran (1.0 M, 2.62 mL, 2.62 mmol, 3.05 equiv) was added to a solution of the enetriyne diol **20** (0.88 g, 0.857 mmol, 1 equiv) in tetrahydrofuran (25 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 2.5 h. Saturated aqueous ammonium chloride solution (40 mL) and water (10 mL) were then added and tetrahydrofuran was removed in vacuo. The residual biphasic mixture was extracted with ethyl acetate (2 × 50 mL). The organic extracts were combined and the combined solution was washed with brine (20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (50% ether-hexanes) to provide the enetriyne triol **29** (yellow oil, 534 mg, 91%).

$R_f = 0.32$ (50% ether-hexanes). ¹H NMR (500 MHz, CDCl₃), δ 6.81 (s, 2H, Ar-**H**), 6.78 (ddt, $J_1 = 2.5$ Hz, $J_2 = 7.0$ Hz, $J_3 = 47.5$ Hz, 1H, C(12)-**H**), 6.40 (s, 1H, C(15)-**H**), 4.71 (dd, $J_1 = 2.0$ Hz, $J_2 = 4.5$ Hz, 1H, C(5)-**H**), 4.50 (m, 2H, C(13)-**H** + C(14)-**H**), 4.34 (m, 1H, C(14)-**H**), 4.22 (m, 1H, C(11)-**H**), 2.82 (d, $J = 4.5$ Hz, 1H, C(5)-OH), 2.72 (s, 1H, C(4)-OH), 2.58 (d, $J = 2.0$ Hz, 1H, C(7)-**H**), 2.51 (ddd, $J_1 = 2.5$ Hz, $J_2 = 5.0$ Hz, $J_3 = 16.5$ Hz, 1H, C(10)-**H**), 2.42 (ddd, $J_1 = 2.5$ Hz, J_2

= 7.0 Hz, $J_3 = 16.5$ Hz, 1H, C(10)-H), 2.37 (s, 6H, Ar-CH₃), 2.25 (s, 3H, Ar-CH₃), 2.10 (t, $J = 2.5$ Hz, 1H, C(8)-H), 2.06 (d, $J = 4.5$ Hz, 1H, C(11)-OH), 1.53 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.33 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.08 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 0.90 (t, $J = 7.2$ Hz, 9H, Sn(CH₂CH₂CH₂CH₃)₃). ¹³C NMR (100 MHz, CDCl₃), δ 152.2, 138.9, 138.0, 130.0, 127.9, 127.3, 103.1, 92.3, 90.0, 79.9, 79.6, 77.9, 75.8, 75.2, 71.6, 71.5, 68.9, 68.4, 29.0 (t, $J = 7.8$ Hz), 27.6, 27.3 (t, $J = 24.4$ Hz), 20.9, 20.0, 13.7, 11.9 (dt, $J_1 = 6.1$ Hz, $J_2 = 136$ Hz). IR (NaCl, thin film), cm⁻¹ 3445, 3307, 2955, 2922, 2868, 2858, 2357, 2335, 2190, 2116, 1220, 1155, 1075, 1044, 949, 924, 850. HRMS-ESI (m/z) [M+H]⁺ calcd for C₃₆H₅₃O₅Sn, 685.2915; found, 685.2930.

Bis(diethylisopropylsilyl) Ether 30

Chlorodiethylisopropylsilane (577 μ L, 3.13 mmol, 4.0 equiv) was added via syringe over 2 min to a stirring solution of the enetriyne triol **29** (534 mg, 0.781 mmol, 1 equiv) and imidazole (375 mg, 6.25 mmol, 8.0 equiv) in *N,N*-dimethylformamide (12 mL) at 0 °C. After stirring at 0 °C for 1.5 h, the reaction mixture was partitioned between ethyl acetate (40 mL) and water (40 mL). The aqueous layer was separated and extracted with ethyl acetate (40 mL). The organic extracts were combined and the combined solution was washed with brine (20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (4% ethyl acetate-hexanes) to provide the bis(diethylisopropylsilyl) ether **30** (colorless oil, 653 mg, 89%).

$R_f = 0.60$ (13% ether-hexanes). ¹H NMR (500 MHz, CDCl₃), δ 6.81 (s, 2H, Ar-H), 6.78 (ddt, $J_1 = 2.5$ Hz, $J_2 = 8.5$ Hz, $J_3 = 51.3$ Hz, 1H, C(12)-H), 6.39 (s, 1H, C(15)-H), 4.77 (d, $J = 2.5$ Hz, 1H, C(5)-H), 4.61 (t, $J = 7.0$ Hz, 1H, C(13)-H), 4.51 (dd, $J_1 = 7.0$ Hz, $J_2 = 8.5$ Hz, 1H, C(14)-H), 4.34 (t, $J = 8.5$ Hz, 1H, C(14)-H), 4.17 (m, 1H, C(11)-H), 2.99 (s, 1H, C(4)-OH), 2.51 (d, $J = 2.0$ Hz, 1H, C(7)-H), 2.43 (ddd, $J_1 = 3.0$ Hz, $J_2 = 6.0$ Hz, $J_3 = 16.5$ Hz, 1H, C(10)-H), 2.38 (s, 6H, Ar-CH₃), 2.31 (ddd, $J_1 = 3.0$ Hz, $J_2 = 6.0$ Hz, $J_3 = 16.5$ Hz, 1H, C(10)-H), 2.25 (s, 3H, Ar-CH₃), 1.95 (t, $J = 2.5$ Hz, 1H, C(8)-H), 1.55 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.35 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.11 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.04–0.96 (m, 26H, Si(CH₂CH₃)₂CH(CH₃)₂), 0.91 (t, $J = 7.5$ Hz, 9H, Sn(CH₂CH₂CH₂CH₃)₃), 0.79–0.70 (m, 4H, Si(CH₂CH₃)₂CH(CH₃)₂), 0.69–0.59 (m, 4H, Si(CH₂CH₃)₂CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃), δ 154.4, 138.7, 138.1, 130.0, 128.5, 124.2, 102.9, 91.5, 90.8, 81.0, 80.6, 76.8, 75.8, 75.2, 73.3, 70.3, 68.8, 68.5, 29.1, 27.4, 20.9, 20.0,

17.3, 13.6, 13.1, 12.9, 11.3 (dt, $J_1 = 7.6$ Hz, $J_2 = 166$ Hz), 7.1, 7.0, 4.0, 3.9, 3.6, 3.5. IR (NaCl, thin film), cm^{-1} 3560, 3312, 2957, 2731, 2189, 2122, 1615, 1463, 1080, 1015, 950, 835, 729, 640. $[\alpha]_D^{23} -48.7^\circ$ (c 0.53, CHCl_3). HRMS-ESI (m/z) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{50}\text{H}_{85}\text{O}_5\text{Si}_2\text{Sn}$, 941.4957; found, 941.4928.

Bromoenetriyne 21

N-Bromosuccinimide (161 mg, 0.903 mmol, 1.3 equiv) was added in one portion to a solution of the bis(diethylisopropylsilyl) ether **30** (653 mg, 0.695 mmol, 1 equiv) in dichloromethane (8 mL) at 23 °C. After stirring at 23 °C for 12 h, the reaction mixture was concentrated. The residue was purified by flash chromatography (7% ethyl acetate-hexanes) to provide the bromoenetriyne **21** (colorless oil, 377 mg, 89%).

$R_f = 0.20$ (14% ether-hexanes). ^1H NMR (500 MHz, C_6D_6), δ 6.82(s, 1H, C(15)-H), 6.71 (s, 2H, Ar-H), 6.52 (d, $J = 6.5$ Hz, 1H, C(12)-H), 5.01 (d, $J = 2.0$ Hz, 1H, C(5)-H), 4.89 (t, $J = 6.0$ Hz, 1H, C(13)-H), 4.81 (m, 1H, C(11)-H), 4.59 (t, $J = 7.0$ Hz, 1H, C(14)-H), 4.52 (dd, $J_1 = 5.5$ Hz, $J_2 = 7.5$ Hz, 1H, C(14)-H), 3.15 (s, 1H, C(4)-OH), 2.54 (s, 6H, Ar-CH₃), 2.36 (ddd, $J_1 = 2.0$ Hz, $J_2 = 5.0$ Hz, $J_3 = 13.5$ Hz, 1H, C(10)-H), 2.31 (ddd, $J_1 = 2.5$ Hz, $J_2 = 5.0$ Hz, $J_3 = 14.0$ Hz, 1H, C(10)-H), 2.07 (s, 3H, Ar-CH₃), 2.00 (d, $J = 2.0$ Hz, 1H, C(7)-H), 1.74 (t, $J = 2.5$ Hz, 1H, C(8)-H), 1.09–0.90 (m, 26H, $\text{Si}(\text{CH}_2\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.75–0.69 (m, 8H, $\text{Si}(\text{CH}_2\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, C_6D_6), δ 142.5, 138.6, 138.4, 130.4, 129.3, 104.0, 101.5, 91.6, 84.6, 80.5, 79.7, 77.3, 76.5, 76.1, 71.2, 71.0, 69.0(2), 27.4, 20.9, 20.3, 17.5, 17.4, 13.2(2), 7.3, 7.2(2), 4.0(2), 3.9, 3.7. IR (NaCl, thin film), cm^{-1} 3543, 3311, 2955, 2877, 2359, 2343, 2121, 1615, 1463, 1082. $[\alpha]_D^{23} -101^\circ$ (c 2.0, CHCl_3). HRMS-ESI (m/z) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{38}\text{H}_{58}\text{BrO}_5\text{Si}_2$, 729.3006; found, 729.3002.

Cyclic Bromoenetriyne 22

A 100-mL, round-bottom flask was charged under an argon atmosphere with Cu(OAc)₂ (918 mg, 5.06 mmol, 60 equiv), tetrahydrofuran (15 mL), and pyridine (15 mL), in that order. The mixture was stirred at 23 °C for 5 min, then was warmed to 60 °C. After 10 min, a solution of the bromoenetriyne **21** (61.5 mg, 84.3 μmol, 1 equiv) in a 1:1 mixture of THF and pyridine (30 mL) was added via cannula over 12 min. After 6 min, the reaction mixture was allowed to cool to ambient temperature and the cooled solution was partitioned between a 1:1 mixture of ether and hexanes (120 mL, cooled in an ice-water bath) and 1.0 M aqueous copper (II) sulfate solution (80 mL). The layers were separated and the organic layer was washed with 1.0 M aqueous copper (II) sulfate solution (2 × 80 mL). The aqueous layers were combined and the combined solution was extracted with a 1:1 mixture of ether and hexanes (80 mL). The organic extracts were combined and the combined solution was washed with brine (30 mL). The washed solution was dried over anhydrous sodium sulfate and toluene (3 mL) was added. The dried solution was filtered and the filtrate was concentrated to a volume of ~3 mL. The residue was purified by flash-column chromatography (13% ether-pentane). To determine the yield of the reaction, fractions containing pure **22** were combined and the combined solution (~50 mL) was diluted with C₆D₆ (50 mL). The solution was concentrated to a volume of ca. 1 mL. A ¹H NMR spectrum was taken to confirm purity and that no toluene was present, then an internal standard (toluene, 5.0 μL, 47 μmol) was added. The yield of **22** was determined by comparing integrated peak areas for **22** relative to toluene (calculated: 46.0 mg, 75%).

R_f = 0.47 (20% ether-hexanes). ¹H NMR (500 MHz, C₆D₆), δ 6.68 (s, 1H, C(15)-**H**), 6.58 (s, 2H, Ar-**H**), 6.37 (d, J = 9.0 Hz, 1H, C(12)-**H**), 4.92 (m, 2H, C(13)-**H** and C(11)-**H**), 4.82 (s, 1H, C(5)-**H**), 4.48 (dd, J_1 = 6.6 Hz, J_2 = 9.0 Hz, 1H, C(14)-**H**), 4.48 (t, J = 8.4 Hz, 1H, C(14)-**H**), 2.47 (s, 6H, Ar-CH₃), 2.32 (ddd, J_1 = 0.6 Hz, J_2 = 7.2 Hz, J_3 = 16.8 Hz, 1H, C(10)-**H**), 2.19 (ddd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, J_3 = 16.8 Hz, 1H, C(10)-**H**), 2.07 (s, 3H, Ar-CH₃), 1.98 (s, br, 1H, C(4)-OH), 0.98–0.79 (m, 26H, Si(CH₂CH₃)₂CH(CH₃)₂), 0.59–0.48 (m, 8H, Si(CH₂CH₃)₂CH(CH₃)₂). ¹³C NMR (100 MHz, C₆D₆), δ 142.5, 138.5, 138.3, 130.4, 129.7, 128.3, 128.1, 127.9, 103.4, 103.2, 96.7, 89.8, 89.4, 87.6, 80.0, 77.7, 74.3 (2), 72.2, 67.8, 29.8, 20.6, 20.0, 17.0, 12.7, 12.6, 6.7 (3), 3.5, 3.4, 3.2 (2). IR (NaCl, thin film), cm⁻¹ 3547, 2956, 2877, 1614, 1460, 1107, 1076, 804, 733. HRMS–ESI (m/z) [$M+H$]⁺ calcd for C₃₈H₅₆BrO₅Si₂, 727.2849; found, 727.2827.

Bicyclic Dienediyne **23**

4-Å Molecular sieves (crushed, activated, 2 g) were added to a solution of the cyclic bromoenediyne **22** (21.8 mg, 30.0 μmol , 1 equiv) in a 1:1 mixture of THF and toluene (10 mL). After stirring at 23 °C for 15 min, the mixture was cooled to –78 °C. A solution of lithium hexamethyldisilazide in tetrahydrofuran (1.0 M, 33.0 μL , 33.0 μmol , 1.1 equiv) was added. After 30 sec, a solution of *tert*-butyllithium in pentane (1.7 M, 70.6 μL , 0.120 mmol, 4.0 equiv) was added to the cold (–78 °C) reaction mixture, followed immediately (<3 s) by quenching with a solution of acetic acid in THF (250 μL of a 4:1 mixture of THF and acetic acid, respectively). The reaction mixture was partitioned between a 1:1 mixture of ether and hexanes (30 mL) and saturated aqueous sodium bicarbonate solution (20 mL). The aqueous layer was extracted with ether (20 mL). The organic extracts were combined and the combined solution was washed with brine (10 mL). The washed solution was dried over anhydrous sodium sulfate and toluene (3 mL) was added. The dried solution was filtered and the filtrate was concentrated to a volume of ~3 mL. The residue was purified by flash-column chromatography (13% ether-pentane). To determine the yield of the reaction, fractions containing pure **23** were combined and the combined solution (~50 mL) was diluted with C_6D_6 (50 mL). The solution was concentrated to a volume of ca. 1 mL. A ^1H NMR spectrum was taken to confirm purity and that no toluene was present, then an internal standard (toluene, 5.0 μL , 47 μmol) was added. The yield of **23** was determined by comparing integrated peak areas for **23** relative to toluene (calculated: 5.8 mg, 30%).

R_f = 0.32 (20% ether-hexanes). ^1H NMR (500 MHz, CDCl_3), δ 6.81 (s, 2H, Ar-**H**), 6.33 (s, 1H, C(15)-**H**), 6.24 (s, br, 1H, C(12)-**H**), 5.32 (s, br, 1H, C(8)-**H**), 5.00 (m, 1H, C(11)-**H**), 4.83 (s, 1H, C(5)-**H**), 4.60 (t, J = 6.0 Hz, 1H, C(13)-**H**), 4.33 (dd, J_1 = 7.5 Hz, J_2 = 6.0 Hz, 1H, C(14)-**H**), 4.13 (t, J = 7.0 Hz, 1H, C(14)-**H**), 4.03 (s, 1H, C(4)-OH), 3.01 (dd, J_1 = 5.0 Hz, J_2 = 14.5 Hz, 1H, C(10)-**H**), 2.41 (d, J = 14.5 Hz, 1H, C(10)-**H**), 2.30 (s, 6H, Ar-**CH**₃), 2.22 (s, 3H, Ar-**CH**₃), 1.01–0.92 (m, 26H, $\text{Si}(\text{CH}_2\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.74–0.61 (m, 8H, $\text{Si}(\text{CH}_2\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, C_6D_6), δ 158.3, 143.2, 138.5, 138.4, 130.3, 129.7, 103.6, 102.8, 100.5, 100.3, 92.5, 88.4, 82.3, 78.0, 74.8, 74.1, 67.7, 41.4, 20.9, 20.2, 17.4(2), 13.3, 13.1, 7.2, 7.1, 4.0(2), 3.9. IR (NaCl, thin film), cm^{-1} 2956, 2876, 1462, 1083, 732. HRMS–ESI (m/z) [$\text{M}+\text{H}$] $^+$ calcd for $\text{C}_{38}\text{H}_{57}\text{O}_5\text{Si}_2$, 649.3744; found, 649.3755.

2-Hydroxy-1-naphthoic Acid 32

Hydrogen fluoride-pyridine complex (2.0 mL) was added to a solution of the naphthoic acid derivative **31**⁸ (300 mg, 0.683 mmol, 1 equiv) in tetrahydrofuran (4 mL) at 23 °C. After stirring at 23 °C for 21 h, the mixture was partitioned between ethyl acetate (40 mL) and saturated aqueous sodium bicarbonate solution (40 mL). The aqueous layer was separated and extracted with ethyl acetate (40 mL). The combined organic layers were washed successively with 2N aqueous hydrochloric acid solution (20 mL), water (20 mL), and brine (20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was washed with hexanes (10 mL) to give the acid **32** (white solid, 192 mg, 99%).

¹H NMR (500 MHz, CD₃OD), δ 8.39 (s, 1H, C(8)-H), 8.18 (d, J = 9.5 Hz, 1H, C(4)-H), 7.00 (d, J = 9.0 Hz, 1H, C(3)-H), 5.11 (s, 2H, C(5)-CH₂OH), 3.93 (s, 3H, C(7)-OCH₃). ¹³C NMR (100 MHz, CD₃OD), δ 174.8, 165.3, 155.5, 136.3, 134.1, 133.5, 124.1, 122.9, 118.3, 107.2, 106.0, 59.0, 56.3. IR (NaCl, thin film), cm⁻¹ 3446, 2954, 1631, 1610, 1416, 1228, 1111, 1005. HRMS-ESI (*m/z*) [M-H]⁻ calcd for C₁₃H₁₀ClO₅Si, 281.0217; found, 281.0230.

Diethylisopropylsilyl-protected Naphthoic Acid 4

Diethylisopropylsilyl chloride (0.252 mL, 1.53 mmol, 4.0 equiv) was added to a solution of the naphthoic acid **32** (108 mg, 0.382 mmol, 1 equiv) and imidazole (156 mg, 2.29 mmol, 6.0 equiv) in *N,N*-dimethylformamide (4 mL) at 23 °C. After stirring at 23 °C for 17 h, the mixture was partitioned between ethyl acetate (40 mL) and saturated aqueous sodium bicarbonate solution (40 mL). The aqueous layer was separated and extracted with ethyl acetate (40 mL). The combined organic layers were washed successively with 0.25N aqueous hydrochloric acid solution (40 mL), water (2 × 15 mL), and brine (15 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was warmed to 40 °C under high vacuum (~0.1 Torr) for 2 h to remove all traces of diethylisopropyl silanol. After cooling, the diethylisopropylsilyl-protected naphthoic acid **4** was

⁸ Ji, N.; Rosen, B. M.; Myers, A. G. *Org. Lett.* **2003**, *6*, 4551.

obtained as a white solid (155 mg, 99%).

^1H NMR (400 MHz, CD_3OD), δ 8.40 (s, 1H, C(8)-**H**), 8.17 (d, J = 9.6 Hz, 1H, C(4)-**H**), 6.97 (d, J = 9.2 Hz, 1H, C(3)-**H**), 5.16 (s, 2H, C(5)-**CH**₂ODEIPS), 3.93 (s, 3H, C(7)-**OCH**₃), 0.99-0.91 (m, 11H, C(5)-**CH**₂OSi(**CH**(**CH**₃)₂)(**CH**₂**CH**₃)₂), 0.67 (t, J = 8.0 Hz, 6H, C(5)-**CH**₂OSi(**CH**(**CH**₃)₂)(**CH**₂**CH**₃)₂). ^{13}C NMR (100 MHz, CDCl_3), δ 174.9, 165.4, 155.4, 136.3, 134.1 (2), 124.4, 122.1, 118.1, 107.2, 105.9, 60.7, 56.4, 17.7, 14.0, 7.3, 4.3. IR (NaCl, thin film), cm^{-1} 2955, 2876, 1633, 1419, 1216, 1062, 725. HRMS-ESI (m/z) [$\text{M}-\text{H}$][−] calcd for $\text{C}_{20}\text{H}_{27}\text{ClO}_5\text{Si}$, 409.1238; found, 409.1222.

Ester 24

Triethylamine trihydrofluoride (616 μL , 3.78 mmol, 60 equiv) was added to a solution of the bicyclic dienediynes **23** (40.9 mg, 63.0 μmol , 1 equiv) in CH_3CN (15 mL) at -25°C . After stirring at -25°C for 13 h, the reaction mixture was partitioned between a 1:1 mixture of ether and hexanes (80 mL) and saturated aqueous sodium bicarbonate solution (60 mL). The aqueous layer

was separated and extracted with a 1:1 mixture of ether and hexanes (60 mL). The organic extracts were combined and the combined solution was washed with brine (20 mL). The washed organic solution was dried over anhydrous sodium sulfate and toluene (3 mL) was added. The solution was filtered and the filtrate was concentrated to a volume of ~3 mL. The residue was purified by flash-column chromatography (67% ether-pentane). Fractions containing **33** were combined and the combined solution was diluted with anhydrous tetrahydrofuran (100 mL).⁹ The resulting solution was concentrated to a volume of ~10 mL and the concentrate was cooled in ice.

The naphthoic acid **4** (54.4 mg, 0.132 mmol, 2.1 equiv) and *N,N'*-dicyclohexylcarbodiimide (72.7 mg, 0.378 mmol, 6 equiv) were added in sequence to the ice-cold solution of the allylic alcohol **33** in tetrahydrofuran (~10 mL). After stirring at 0 °C for 2.5 h, the reaction mixture was filtered through a plug of Celite®, and the filtrate was diluted with a 1:1 mixture of ether and hexanes (40 mL). The resulting solution was washed with water (20 mL). The aqueous layer was separated and extracted with a 1:1 mixture of ether and hexanes (40 mL). The organic layers were combined and the combined solution was washed with brine (15 mL). The washed organic solution was dried over anhydrous sodium sulfate and toluene (3 mL) was added. The residue was purified by flash-column chromatography (33% ether-pentane). To determine the yield of the reaction, fractions containing pure **24** were combined (~50 mL) and the combined solution was diluted with C₆D₆ (50 mL). The solution was concentrated to a volume of ca. 1 mL. A ¹H NMR spectrum was taken to confirm purity and that no toluene was present, then an internal standard (toluene, 5.0 µL, 47 µmol) was added. The yield of **24** was determined by comparing integrated peak areas for **24** relative to toluene (calculated: 25.4 mg, 44%, 2 steps).

$R_f = 0.27$ (66% ether-hexanes). ¹H NMR (500 MHz, C₆D₆), δ 6.69 (s, 2H, Ar-**H**), 6.66 (s, 1H, C(15)-**H**), 5.82 (m, br, 1H, C(12)-**H**), 5.00 (s, br, 1H, C(8)-**H**), 5.00 (t, $J = 9.0$ Hz, 1H, C(13)-**H**), 4.91 (s, 1H, C(5)-**H**), 4.57 (dd, $J_1 = 9.0$ Hz, $J_2 = 6.5$ Hz, 1H, C(14)-**H**), 4.46 (t, $J = 8.0$ Hz, 1H, C(14)-**H**), 4.25 (m, 1H, C(11)-**H**), 2.46 (s, 6H, Ar-CH₃), 2.36 (dd, $J_1 = 8.0$ Hz, $J_2 = 20.0$ Hz, 1H, C(10)-**H**), 2.35 (s, br, 1H, C(4)-OH), 2.07 (s, 3H, Ar-CH₃), 1.98 (d, $J = 20.0$ Hz, 1H, C(10)-**H**), 1.06–0.96 (m, 13H, Si(CH₂CH₃)₂CH(CH₃)₂), 0.76–0.59 (m, 4H, Si(CH₂CH₃)₂CH(CH₃)₂). HRMS–ESI (m/z) [$M+H$]⁺ calcd for C₃₁H₄₁O₅Si, 521.2723; found, 521.2737.

⁹ For analytical purposes, in a separate experiment pooled column fractions of pure intermediate **33** were diluted with C₆D₆ (~50 mL), the resulting solution was partially concentrated (~1 mL), and a ¹H NMR spectrum was recorded, providing the data tabulated below and reproduced as part of this Supporting Information.

$R_f = 0.25$ (33% ether-hexanes). ^1H NMR (500 MHz, C_6D_6), δ 12.72 (s, 1H, C(2')-OH), 8.43 (d, $J = 9.5$ Hz, 1H, C(4')-H), 8.06 (s, 1H, C(8')-H), 7.19 (d, $J = 9.5$ Hz, 1H, C(3')-H), 6.70 (s, 2H, Ar-H), 6.57 (s, 1H, C(15)-H), 5.88 (s, br, 1H, C(12)-H), 5.50 (m, 1H, C(11)-H), 5.24 (d, $J = 2.5$ Hz, 2H, C(9')-H), 4.98 (s, br, 1H, C(8)-H), 4.90 (t, $J = 6.5$ Hz, 1H, C(13)-H), 4.85 (s, 1H, C(5)-H), 4.54 (dd, $J_1 = 9.0$ Hz, $J_2 = 6.5$ Hz, 1H, C(14)-H), 4.38 (d, $J = 9.0$ Hz, 1H, C(14)-H), 3.55 (s, 3H, C(7')-OCH₃), 2.47 (m, 1H, C(10)-H), 2.42 (s, 6H, Ar-CH₃), 2.27 (s, 1H, C(4)-OH), 2.13 (d, $J = 15.0$ Hz, 1H, C(10)-H), 2.09 (s, 3H, Ar-CH₃), 1.03–0.95 (m, 26H, Si(CH₂CH₃)₂CH(CH₃)₂), 0.72–0.57 (m, 8H, Si(CH₂CH₃)₂CH(CH₃)₂). ^{13}C NMR (100 MHz, C_6D_6), δ 171.8, 165.8, 156.5, 154.9, 138.6, 138.3, 136.5, 136.3, 134.9, 132.8, 131.8, 130.4, 129.4, 128.5, 123.9, 121.6, 117.7, 106.5, 104.7, 104.4, 103.6, 102.5, 101.5, 91.7, 86.7, 82.2, 78.1, 77.2, 74.4, 67.4, 60.1, 55.6, 37.4, 20.9, 20.1, 17.4(2), 13.2, 13.1, 7.2(2), 3.9(2), 3.8. IR (NaCl, thin film), cm^{-1} 2956, 2877, 1646, 1613, 1464, 1420, 1203, 1113, 816. HRMS-ESI (m/z) [$\text{M}+\text{H}$]⁺ calcd for $\text{C}_{51}\text{H}_{66}\text{ClO}_9\text{Si}_2$, 913.3934; found, 913.3900.

Epoxide **26**

A solution of tetrabutylammonium fluoride in tetrahydrofuran (1.0 M, 432 μL , 0.432 mmol, 6.0 equiv) was added to a solution of the ester **24** (65.7 mg, 72.0 μmol , 1 equiv) and *o*-nitrophenol (60.1 mg, 0.432 mmol, 6.0 equiv) in THF (25 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 90 min, then was diluted with a 1:1 mixture of ether and hexanes (80 mL). The mixture was washed with saturated aqueous ammonium chloride solution (60 mL). The aqueous layer was separated and extracted with a 1:1 mixture of ether and hexanes (80 mL). The organic extracts were combined and the combined solution was washed with brine (30 mL). The washed solution was dried over sodium sulfate and toluene (3 mL) was added. The dried solution was filtered and the filtrate was concentrated to a volume of ~3 mL. The residue was purified by flash-column chromatography (50% ether–pentane, grading to 67% ether–pentane). Fractions containing pure **34** were combined and the combined solution was diluted with anhydrous dichloromethane (200 mL).¹⁰ The resulting solution was concentrated to a volume of ~15 mL and the concentrate was cooled to –78 °C.

¹⁰For analytical purposes, in a separate experiment pooled column fractions of pure intermediate **34** were diluted with C_6D_6 (~50 mL), the resulting solution was partially concentrated (~1 mL), and a ^1H NMR spectrum was recorded, providing the data tabulated below and reproduced as part of this Supporting Information.

Triethylamine (113 μ L, 0.810 mmol, 11 equiv) and chlorotriethylsilane (54.3 μ L, 0.324 mmol, 4.5 equiv) were added in sequence to the cold (-78 $^{\circ}$ C) solution of the triol **34** in dichloromethane ($\sim$ 15 mL). After stirring at -78 $^{\circ}$ C for 40 min, the reaction mixture was partitioned between a 1:1 mixture of ether and hexanes (80 mL) and brine (40 mL). The layers were separated and the aqueous layer was extracted with a 1:1 mixture of ether and hexanes (40 mL). The organic extracts were combined and the combined solution was dried over anhydrous sodium sulfate. Toluene (3 mL) was added. The dried solution was filtered and the filtrate was concentrated to a volume of $\sim$ 3 mL. The residue was purified by flash-column chromatography (67% ether-pentane). Fractions containing the diol **25** were combined and the combined solution was diluted with anhydrous dichloromethane (200 mL).¹¹ The resulting solution was concentrated to a volume of $\sim$ 12 mL.

DABCO (48.5 mg, 0.432 mmol, 6.0 equiv) and *p*-toluenesulfonyl chloride (41.2 mg, 0.216 mmol, 3.0 equiv) were added in sequence to the solution of the diol **25** in dichloromethane ($\sim$ 12 mL) at 23 $^{\circ}$ C. After stirring at 23 $^{\circ}$ C for 110 min, the reaction mixture was diluted with a 1:1 mixture of ether and hexanes (80 mL). The resulting mixture was washed with brine (40 mL) and the layers were separated. The aqueous layer was extracted with a 1:1 mixture of ether and hexanes (80 mL). The organic extracts were combined and the combined solution was dried over anhydrous sodium sulfate. Toluene (4 mL) was added to the dried solution, and the resulting solution was concentrated to a volume of $\sim$ 4 mL. The residue was purified by flash chromatography (17% ether-pentane, grading to 25% ether-pentane). To determine the yield of the reaction, fractions containing pure **26** were combined and the combined solution ($\sim$ 50 mL) was diluted with C_6D_6 (50 mL). The solution was concentrated to a volume of ca. 1 mL. A 1H NMR spectrum was taken to confirm purity and that no toluene was present, then an internal standard (toluene, 5.0 μ L, 47 μ mol) was added. The yield of **26** was determined by comparing integrated peak areas for **26** relative to toluene (calculated: 20.8 mg, 33% over 3 steps).

R_f = 0.33 (66% ether-hexanes). 1H NMR (500 MHz, C_6D_6), δ 12.64 (s, br, 1H, C(2')-OH), 8.43 (d, J = 9.0 Hz, 1H, C(4')-H), 8.07 (s, 1H, C(8')-H), 7.19 (d, J = 9.5 Hz, 1H, C(3')-H), 6.68 (s, 2H, Ar-H), 6.55 (s, 1H, C(15)-H), 5.95 (t, J = 2.0 Hz, 1H, C(12)-H), 5.53 (m, 1H, C(11)-H), 5.23 (s, 2H, C(9')-H), 4.98 (s, br, 1H, C(8)-H), 4.56 (dd, J_1 = 8.0 Hz, J_2 = 7.0 Hz, 1H, C(13)-H), 4.38 (s, 1H, C(5)-H), 4.34 (dd, J_1 = 9.0 Hz, J_2 = 6.5 Hz, 1H, C(14)-H), 4.18 (d, J = 8.5 Hz, 1H, C(14)-H), 3.57 (s, 3H, C(7')-OCH₃), 2.46 (ddd, J_1 = 18.5 Hz, J_2 = 8.5 Hz, J_3 = 2.0 Hz, 1H, C(10)-H), 2.36 (s, 6H, Ar-CH₃), 2.16 (d, J = 18.0 Hz, 1H, C(10)-H), 2.07 (s, 3H, Ar-CH₃), 1.01–0.89 (m, 13H, Si(CH₂CH₃)₂CH(CH₃)₂), 0.70–0.59 (m, 4H, Si(CH₂CH₃)₂CH(CH₃)₂). HRMS-ESI (m/z) [$M+H$]⁺ calcd for C₄₄H₄₉ClO₉Si, 785.2912; found, 785.2947.

¹¹ For analytical purposes, in a separate experiment pooled column fractions of pure intermediate **25** were diluted with C_6D_6 ($\sim$ 50 mL), the resulting solution was partially concentrated ($\sim$ 1 mL), and a 1H NMR spectrum was recorded, providing the data tabulated below and reproduced as part of this Supporting Information.

$R_f = 0.37$ (66% ether-hexanes). $^1\text{H NMR}$ (500 MHz, C_6D_6), δ 8.36 (d, $J = 9.5$ Hz, 1H, C(4')-H), 7.18 (s, 1H, C(8')-H), 7.01 (d, $J = 9.5$ Hz, 1H, C(3')-H), 6.68 (s, 2H, Ar-H), 6.56 (s, 1H, C(15)-H), 6.47 (t, $J = 2.5$ Hz, 1H, C(12)-H), 5.88 (m, 1H, C(11)-H), 5.28 (s, 2H, C(9')-H), 5.02 (t, $J = 2.0$ Hz, 1H, C(8)-H), 4.55 (dd, $J_1 = 7.5$ Hz, $J_2 = 6.0$ Hz, 1H, C(13)-H), 4.40 (s, br, 1H, C(5)-H), 4.34 (dd, $J_1 = 8.5$ Hz, $J_2 = 7.0$ Hz, 1H, C(14)-H), 4.18 (t, $J = 8.5$ Hz, 1H, C(14)-H), 3.46 (s, 3H, C(7')-OCH₃), 2.66 (ddd, $J_1 = 20.5$ Hz, $J_2 = 7.0$ Hz, $J_3 = 2.0$ Hz, 1H, C(10)-H), 2.54 (d, $J = 18.5$ Hz, 1H, C(10)-H), 2.37 (s, 6H, Ar-CH₃), 2.07 (s, 3H, Ar-CH₃), 1.05–0.75 (m, 26H, Si(CH₂CH₃)₂(CH(CH₃)₂) and Si(CH₂CH₃)₃), 0.72 (q, $J = 8.0$ Hz, 4H, Si(CH₂CH₃)₂). HRMS–ESI (m/z) [$\text{M}+\text{H}$]⁺ calcd for C₅₀H₆₄ClO₉Si₂, 899.3777; found, 899.3773.

$R_f = 0.25$ (25% ether-hexanes). $^1\text{H NMR}$ (500 MHz, CD₃CN), δ 8.19 (d, $J = 9.0$ Hz, 1H, C(4')-H), 7.10 (d, $J = 9.5$ Hz, 1H, C(3')-H), 7.05 (s, 1H, C(8')-H), 6.83 (s, 2H, Ar-H), 6.77 (s, br, 1H, C(12)-H), 6.28 (s, 1H, C(15)-H), 5.50 (d, $J = 7.0$ Hz, br, 1H, C(11)-H), 5.54 (s, br, 1H, C(8)-H), 5.29 (s, 2H, C(9')-H), 4.49 (dd, $J_1 = 7.0$ Hz, $J_2 = 8.5$ Hz, 1H, C(13)-H), 4.36 (t, $J = 7.0$ Hz, 1H, C(14)-H), 3.96 (s, 1H, C(5)-H), 3.96 (m, 1H, C(14)-H), 3.91 (s, 3H, C(7')-OCH₃), 3.30 (dd, br, $J_1 = 13.5$ Hz, $J_2 = 7.0$ Hz, 1H, C(10)-H), 2.85 (d, $J = 13.5$ Hz, 1H, C(10)-H), 2.33 (s, 6H, Ar-CH₃), 2.33 (s, 3H, Ar-CH₃), 1.00–0.64 (m, 26H, Si(CH₂CH₃)₂(CH(CH₃)₂) and Si(CH₂CH₃)₃), 0.52 (q, $J = 8.0$ Hz, 4H, Si(CH₂CH₃)₂). IR (NaCl, thin film), cm⁻¹ 3631, 3539, 2954, 2882, 1728, 1613, 1272, 1210, 1113, 858, 735. HRMS–ESI (m/z) [$\text{M}+\text{H}$]⁺ calcd for C₅₀H₆₂ClO₈Si₂, 881.3672; found, 881.3677.

N1999A2 (1)

Cold, dry trifluoroacetic acid (180 μL , cooled in an ice-water bath for at least 30 min prior to use) was added dropwise over 2 min to an ice-cold solution of the epoxide **26** (10.4 mg, 11.8 μmol , 1 equiv) in tetrahydrofuran (2.6 mL) and water (0.9 mL). After stirring at 0 °C for 5 h, the reaction mixture was partitioned between pH 7 aqueous phosphate buffer (30 mL) and ether (30 mL). The layers were separated and the aqueous layer was extracted with ether (30 mL). The

organic layers were combined and the combined solution was dried over anhydrous sodium sulfate. The dried solution was concentrated to a volume of ca. 8 mL and pentane (5 mL) was added, leading to precipitation of N1999A2 as a yellowish solid. The solid was filtered and washed with 80% ether-pentane (3×10 mL) to provide pure N1999A2 (**1**) (4.7 mg, 76%).

R_f = 0.20 (100% ether). ^1H NMR (500 MHz, 50% CD_3CN - $\text{DMSO}-d_6$), δ 10.82 (s, 1H, C(2')-OH), 8.22 (d, J = 9.5 Hz, 1H, C(4')-H), 7.43 (s, 1H, C(8')-H), 7.13 (d, J = 9.5 Hz, 1H, C(3')-H), 6.81 (s, br, 1H, C(12)-H), 6.12 (d, J = 7.0 Hz, br, 1H, C(11)-H), 5.59 (s, br, 1H, C(8)-H), 5.31 (d, J = 4.5 Hz, 1H, C(13)-OH), 5.15 (t, J = 5.0 Hz, C(9')-OH), 5.06 (d, J = 5.0 Hz, 2H, C(9')-H), 4.63 (s, br, 1H, C(14)-OH), 3.94 (s, 1H, C(5)-H), 3.93 (s, 3H, C(7')-OH), 3.63–3.55 (m, 3H, C(13)-H + C(14)-H), 3.29 (ddd, J_1 = 18 Hz, J_2 = 7.0 Hz, J_3 = 2.0 Hz, 1H, C(10)-H), 2.94 (d, J = 18.5 Hz, 1H, C(10)-H). IR (NaCl, thin film), cm^{-1} 3628, 3539, 2964, 2934, 2872, 1723, 1638, 1205, 1119. HRMS-ESI (m/z) $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{27}\text{H}_{25}\text{ClO}_8$, 526.1269; found, 526.1286.

STANDARD 1H OBSERVE

exp3 std1h

SAMPLE DEC. & VT
date Aug 1 2004 dfrq 400.025
solvent CDCl3 dn H1
file exp dpwr 40
ACQUISITION dof 0
sfrq 400.025 dm nnn
tn H1 dmm c
at 2.733 dar 7500
np 32768 temp 20.0
sw 5995.2 PROCESSING
fb not used lb wtfile 0.10
bs 8
ss 2 proc ft
tpwr 60 fn not used
pw 10.0
dl 0 werr
tof 0 wexp
nt 16 wbs
ct 16 wmt
alock n
gain not used
FLAGS
il n
jn n
dp y
DISPLAY
sp -211.5
wp 4000.8
vs 60
sc 0
wc 250
hzmm 16.00
ls 146.79
rfl 3879.3
rfp 2904.2
th 20
ins 100.000
nm cdc ph

13C OBSERVE

exp3 std13c

SAMPLE		DEC. & VT	
date	Aug 1 2004	dfrq	400.025
solvent	CDCl3	dn	H1
file	exp	dpwr	48
ACQUISITION		dot	0
sfrs	100.595	dm	yyy
tn	C13	dmm	w
at	1.311	daf	16900
np	65536	temp	22.0
sw	25000.0	PROCESSING	
fb	13800	lb	1.00
bs	16	wtfile	
tpwr	61	proc	ft
pw	5.0	fn	not used
d1	0		
tor	0	werr	
nt	2000	wexp	
ct	928	wbs	
clock	n	wnt	
gain	not used		
FLAGS			
fl	n		
in	n		
dp	y		
DISPLAY			
sp	-3000.5		
wp	25000.0		
vs	55		
sc	0		
wc	250		
hzm	100.00		
ls	500.00		
rf1	10745.6		
rfp	7745.1		
th	21		
ins	100.000		
nm	ph

P-E

STANDARD PROTON PARAMETERS

exp3 PROTON

SAMPLE SPECIAL 20.0
 date Jul 15 2004 temp gain not used
 solvent CDC13 exp spin 0
 file ACQUISITION hst 0.000
 sw 9596.9 pw90 6.250
 at 2.040 alfa 0
 np 39310 FLAGS
 fb 5000 il n
 bs 5 in n
 ss 2 dp y
 dl 1.000 hs nn
 nt 16 PROCESSING
 ct 16 lb 0.10
 TRANSMITTER fn not used
 tn H1 DISPLAY
 sfrq 599.780 sp -576.8
 tof 576.5 wp 6865.2
 tpwr 60 rfl 5576.9
 pw 3.125 rfp 4354.4
 DECOUPLER rp -17.1
 dn C13 lp -12.8
 dorf 0 PLOT
 dm nnn wc 250
 decwave sc 0
 dprv 49 vs 96
 dmf 14800 th 7
 nm cdc ph

SAMPLE DEC. & VT 400.025
 date Jul 15 2004 dfrq H1
 solvent CDC13 dn 40
 file ACQUISITION exp dprv 0
 sfrq 100.595 dm yyy
 tn C13 dmm w
 at 1.311 dmf 16900
 np 65536 temp 22.0
 sw 25000.0 PROCESSING
 fb 13800 lb 1.00
 bs 16 wfile
 tpwr 61 proc ft
 pw 5.0 fn not used
 dl 0
 tof 0 werr
 nt 2000 wexp
 ct 560 wbs
 alock n wnt
 gain not used
 FLAGS
 il n
 in n
 dp y
 DISPLAY
 sp -1222.0
 wp 14055.3
 vs 39
 sc 0
 wc 250
 hzmm 56.22
 ls 500.00
 rfl 10744.8
 rfp 7745.1
 th 4
 ins 100.000
 nm ph

P-E

STANDARD 1H OBSERVE

```

expl stdih
SAMPLE
date Jul 25 2001 dfrq 400.068
solvent CDCl3 dn H1
file exp dpr 40
ACQUISITION
sfrq 400.068 dm nnn
tn H1 dnm c
at 2.731 def 8000
sw 5998.8 lb PROCESSING 20.0
fb 3400 lb 0.10
bs 8 wfile
ss 2 proc ft
tpwr 60 fn not used
pw 10.0
d1 0.120 werr
tof 0 wexp
nt 16 wbs
ct 0 wnt
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -980.8
wp 5998.8
vs 151
sc 0
wc 250
hzmm 24.00
ls 289.57
rfl 3685.3
rfp 2904.5
th 20
ins 100.000
nm cdc ph
  
```

13C OBSERVE

exp2 std13c

SAMPLE DEC. & VT
 date Jul 20 2004 dfrq 400.025
 solvent CDCl3 dn H1
 file exp dpwr 48
 ACQUISITION dof 0
 sfrq 100.595 dm yyy
 tn C13 dm w
 at 1.311 dar 16900
 np 65536 temp 22.0
 sw 25000.0 PROCESSING
 fb 13800 lb 1.00
 bs 16 wtfile
 tpwr 61 proc
 pw 5.0 fo not used
 dl 0
 tof 0 werr
 nt 2000 wexp
 ct 352 wbs
 alock n wnt
 gain not used
 FLAGS
 il n
 in n
 dp y
 DISPLAY
 sp -3000.5
 vp 25000.0
 vs 98
 sc 0
 wc 250
 hzmm 100.00
 is 500.00
 rfl 10745.6
 rfp 7745.1
 th 6
 ins 100.000
 nm ph

P-E

STANDARD 1H OBSERVE

```

expl std1h
SAMPLE
date Jul 26 2004 dfrq DEC. & VT 400.025
solvent CDCl3 dn H1
file exp dpwr 40
ACQUISITION exp dof 0
sfrq 400.025 dm nnn
tn H1 dmm c
at 2.733 dmf 7500
np 32768 temp 20.0
sw 5385.2 PROCESSING
fb not used lb 0.10
bs 8 wtf file
ss 2 proc ft
tpwr 10.0 fn not used
d1 0.120 werr
tof 0 wexp
nt 16 wbs
ct 16 wnt
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -457.7
vp 4821.3
vs 98
sc 0
wc 250
hzmm 19.29
ls 144.79
rfi 3878.3
rfp 2904.2
th 20
ins 100.000
nm cdc ph

```

13C OBSERVE

```

expl std13c
SAMPLE
date Jul 26 2004 dfrq DEC. & VT 400.025
solvent CDCl3 dn H1
file exp dpwr 48
ACQUISITION exp dof 0
sfrq 100.595 dm yyy
tn C13 dmm w
at 1.311 dmf 16900
np 65536 temp 22.0
sw 25000.0 PROCESSING
fb 13800 lb 1.00
bs 16 wtf file
tpwr 61 proc ft
pw 5.0 fn not used
d1 1.000
tof 0 werr
nt 10000 wexp
ct 344 wbs
alock n wnt
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -2998.2
vp 25000.0
vs 83
sc 0
wc 250
hzmm 100.00
ls 500.00
rfi 10743.3
rfp 7745.1
th 11
ins 100.000
nm ph

```

P-E

STANDARD PROTON PARAMETERS

```

exp1 szpul
SAMPLE
date Feb 4 2003 dfrq DEC. & VT 499.750
solvent CDC13 dn H1
file exp dpr 34
ACQUISITION
sfrq 499.750 dm nnn
tn H1 dm C
at 2.048 dmf 14300
np 32768 dseq 1.0
sw 8000.0 dres 23.0
fb 4000 homo n
ss 8 temp PROCESSING
tpwr 54 lb 0.10
pw 6.0 wfile
d1 0.200 proc ft
tof 0 fn not used
nt 16 math f
ct 16
alock n verr
gain not used wexp
FLAGS n wbs
il n wnt wft
in n
dp y
hs nn
DISPLAY
sp -250.2
vp 5497.1
vs 93
sc 0
wc 250
hzmm 21.89
ls 262.83
rfl 5130.3
rfp 3628.2
th 2
ins 1.000
nm ph
  
```

13C OBSERVE

exp2 std13c

SAMPLE DEC. & VT 400.025
 date Jul 22 2004 dfrq dn H1
 solvent CDC13 exp dpr 48
 file exp dof 0
 ACQUISITION
 sfrq 100.595 dm yyy
 tn C13 dmm w
 at 1.311 dmf 16900
 np 65536 temp 22.0
 sv 25000.0 PROCESSING
 fb 13800 lb 1.00
 bs 16 wfile
 tpr 61 proc ft
 pw 5.0 fn not used
 d1 0
 tof 0 werr
 nt 1500 wexp
 ct 272 wbs
 alock n wnt
 gain not used
 FLAGS
 il n
 in n
 dp y
 DISPLAY
 sp -2999.7
 wp 25000.0
 vs 58
 sc 0
 wc 250
 hzmm 100.00
 ls 500.00
 rfl 10744.8
 rfp 7745.1
 th 11
 ins 100.000
 nm ph

P-E

STANDARD 1H OBSERVE

```

exp3 std1h
SAMPLE DEC. & VT
date Jan 7 2002 dfrq 400.068
solvent CDCl3 dn H1
file exp dpwr 40
ACQUISITION dof 0
sfrq 400.068 dm nnn
tn H1 dmm C
at 2.731 dmf 7500
np 32768 temp 20.0
sw 5999.6 PROCESSING
fb 3400 lb 0.10
bs 8 wtfile
ss 2 proc ft
tpwr 60 fn not used
pw 10.0
d1 0.120 werr
tof 0 wexp
nt 16 wbs
ct 16 wnt
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -200.2
wp 4400.5
vs 100
sc 0
wc 250
hzmm 17.60
is 374.35
rfi 3885.0
rpf 2304.5
th 20
ins 100.000
nm cdc ph

```

13C OBSERVE

```

exp3 std13c
SAMPLE DEC. & VT
date Jan 7 2002 dfrq 400.068
solvent CDCl3 dn H1
file exp dpwr 40
ACQUISITION dof 0
sfrq 100.606 dm VVV
tn C13 dmm W
at 1.280 dmf 8000
np 64000 temp 22.0
sw 25000.0 PROCESSING
fb 13800 lb 1.00
bs 16 wtfile
ss 2 proc ft
tpwr 91 fn not used
pw 3.0
d1 0 werr
tof 0 wexp
nt 10000 wbs
ct 1744 wnt
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -2999.6
wp 25000.0
vs 57
sc 0
wc 250
hzmm 100.00
is 500.00
rfi 10745.6
rpf 7745.9
th 5
ins 100.000
nm ph

```

P-E

STANDARD PROTON PARAMETERS

```

expl s2pul

SAMPLE
date Dec 19 2001 dfrq 499.750
solvent CDC13 dn H1
file exp dpr 34
ACQUISITION
sfrq 499.750 dm nnn
tn H1 dnm c
at 2.048 def 14300
np 32768 dseq 1.0
sw 8000.0 dres n
fb 4000 homo n
bs 8 temp 22.0
ss 2
PROCESSING
tpwr 54 lb 0.10
pv 6.0 wfile ft
d1 0 proc ft
tof 0 fn not used
nt 16 math f
ct 16
alock n werr
g4in not used wexp
FLAGS n wbs
il n wnt wft
in n
dp y
hs nn
DISPLAY
sp -250.0
wp 5496.9
vs 133
sc 0
wc 250
hzmm 21.99
ls 33.57
rf1 5141.9
rfp 3628.2
th 7
ins 100.000
nm ph
  
```

STANDARD CARBON PARAMETERS

exp3 s2pu1

SAMPLE DEC. & VT
date Oct 28 2005 dfrq 500.211
solvent CDCl3 dn H1
file exp dpwr 38
ACQUISITION dof 9
sfrq 125.789 dm yyy
tn C13 dmm w
at 1.170 dmf 15970
np 65536 dseq
sw 28001.4 dres 1.0
fb 15000 homo n
bs 16 temp 22.0
tpwr 57
pw 8.0 lb PROCESSING 1.00
d1 0.100 wfile
tof 0 proc ft
nt 100000 fn not used
ct 24400 math f
a1ock n
gain 56 weff
FLAGS n wexp
in n vbs
dp y wnt
hs nn
DISPLAY
sp -2080.4
wp 28000.5
vs 61
sc 0
wc 250
h2mm 112.00
is 500.00
rfl 11766.1
rfp 9684.9
th 88
ins 100.000
nm cdc ph

P-E

STANDARD PROTON PARAMETERS

```

exp2 s2pu1
SAMPLE
date Nov 6 2001 dfrq 499.750
solvent Benzene dn H1
file exp dpwr 34
ACQUISITION
sfrq 499.750 dm nnn
in H1 dmm c
at 2.048 dmf 14300
np 32768 dseq
sw 8000.0 dres 1.0
fb 4000 homo n
bs 8 temp 22.0
ss 2 PROCESSING
tpwr 54 lb 0.10
pw 6.0 wfile
d1 0 proc ft
tof 0 fn not used
nt 16 math f
ct 16
alock n verr
gain not used wexp
flags n vbs
in n vft
dp y
hs nm
DISPLAY
sp -250.3
wp 5486.9
vs 139
sc 0
wc 250
hzmm 21.88
is 33.57
rfl 5079.6
rfp 3373.2
th 7
ins 100.000
nm ph

```

exp2 std13c

```

SAMPLE
date Jun 19 2003 dfrq 400.046
solvent Benzene dn H1
file exp dpwr 46
ACQUISITION
sfrq 100.601 dm yyy
in C13 dmm w
at 1.280 dmf 11000
np 64000 temp 22.0
sw 25000.0 PROCESSING
fb 13800 lb 1.00
bs 16 wfile
ss 2 proc ft
tpwr 61 fn not used
pw 9.0
d1 1.000 verr
tof 10000 wexp
nt 288 vbs
ct 288 vnt
alock n
gain not used
flags n
in n
dp y
DISPLAY
sp -2985.7
wp 25000.0
vs 133
sc 0
wc 250
hzmm 100.00
is 1500.00
rfl 15841.4
rfp 12875.2
th 11
ins 100.000
nm ph

```

STANDARD PROTON PARAMETERS

exp4 s2pu1

SAMPLE		DEC. & VT	
date	Nov 11 2001	dfrq	499.750
solvent	Benzene	dn	H1
file	exp	dpr	34
ACQUISITION		dof	0
sfrq	499.750	dm	nnn
tn	H1	dmm	c
at	2.048	def	14300
np	32768	dseq	
sw	8000.0	dres	1.0
fb	4000	homo	n
bs	8	temp	22.0
ss	2	PROCESSING	
tpwr	54	lb	0.10
pw	6.0	wtfile	
d1	0	proc	ft
tof	0	fn	not used
nt	16	math	f
ct	16		
elock	n	werr	
gain	not used	wexp	
flags	n	wbs	
il	n	wnt	wft
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.3		
wp	5486.9		
vs	116		
sc	0		
wc	250		
h2am	21.99		
ls	33.57		
rf1	5070.6		
rfp	3573.2		
th	7		
lms	100.000		
nm	ph

exp1 std13c

SAMPLE				DEC. & VT	
date	Jun 19 2003	dfrq		400.046	
acquisition	Benzena	dn		116	
	exp	dpr		46	
		fls		0	
sfrf	100.601	dm		0	
tn	C130	dmp		11080	
np	1.200	inf		22.0	
bs	250.000	PROCESSING			
fb	13800	lb		1.00	
bs	16	wrtite		1.00	
ts	2	proc			
tpwr	61	fn		not used	
ts	3				
d1	1.000	werr			
dof		exp			
nt	10000	wbs			
ct		480			
a:lock		wnt			
gain		not used			
	FLAGS				
il		n			
in		n			
dp		n			
sp	DISPLAY				
rs	-2865.7				
wp	25000.0				
vc	56				
sc	0				
wc	250				
hzmm	100.00				
ls	500.000				
rfl	15841.4				
rfs	12875.7				
th					
inp	100.000				
ph

expl s2pul

```

SAMPLE      DEC. & VT
date Oct 8 2001 dfrq 500.211
solvent CDC13 dn H1
file exp dpwr 32
ACQUISITION dof 0
sfrq 500.211 dm nnn
tn H1 dnm c
at 2.048 dmf 8770
np 32768 dseq 1.0
sw 8000.0 dres n
fb 4000 homo n
bs 8 temp 22.0
ss 2 PROCESSING
tpwr 56 lb 0.10
pw 5.0 wfile
d1 0 proc ft
tof 0 fn not used
nt 16 math f
ct 16
alock n werr
gain not used wexp
flags n wnt wft
il n
in n
dp y
hs nn
DISPLAY
sp -250.6
wp 5502.3
vs 191
sc 0
wc 250
hzmm 22.01
is 758.76
rfl 5130.2
rfp 3631.5
th
ins
nm cdc ph

```

expl std13c

```

SAMPLE      DEC. & VT
date Jun 24 2003 dfrq 400.846
solvent Benzene dn H1
file exp dpwr 46
ACQUISITION dof 0
sfrq 100.601 dm yyy
tn C13 dnm w
at 1.280 dmf 11000
np 64000 temp 22.0
sw 25000.0 PROCESSING
fb 13800 lb 1.00
bs 16 wfile
ss 2 proc ft
tpwr 61 fn not used
d1 1.000 werr
tof 0 wexp
nt 10000 wbs
ct 544 wnt
alock n
gain not used
flags n
il n
in n
dp y
DISPLAY
sp -2985.7
wp 25000.0
vs 118
sc 0
wc 250
hzmm 100.00
is 500.00
rfl 15841.4
rfp 12875.7
th 2
ins
nm ph 100.000

```

```

exp3 s2pu1
SAMPLE
date Apr 1 2006 dfrq DEC. & VT 499.618
solvent CDCl3 dn H1
file exp dper 3d
ACQUISITION dof 0
sfrq 499.618 dm nm
tn H1 dm c
at 2.048 dmf 14300
np 32768 dseq 1.0
sw 8000.0 dres 1.0
fb 4000 homo n
bs 8 temp 23.0
ss 2 PROCESSING 0.10
tpwr 54 lb
pw 6.0 wtfile
d1 0.200 proc ft
tof 0 fn not used
nt 32 math f
ct 32
a1ock n werr
gain not used wexp
FLAGS n wbs
in n wft
dp y
hs nn
DISPLAY
sp -250.2
wp 5495.6
vs 95
sc 0
wc 250
h2mm 21.38
is 262.83
rf1 5121.6
rfp 3627.2
th 3
ins 1.000
nm ph
  
```

exp3 s2pu1

SAMPLE				DEC. & VT	
date	Apr	1	2006	dfrs	499.618
solvent			CDC13	df	H1
exp			flp	tpwr	34
ACQUISITION				dn	0
sfra		125.640	dm	dm	yyy
cn			C13	dms	14200
at		1.092	dmf		
bs		655	dscq		
sw		29995.3	dres		
fb		17000	homo		1.0
tpwr		16	temp		2.0
		57			
			lb		1.00
d1		1.000	wtfile		
tof		0	proc		ft
nt		1000	fn		not used
ct		3520	math		
atlock		50			
gain			werr		
fl	FLAGS		wexp		
in			wnt		
dp		y			
hs					
DISPLAY					
sp		-3990.2			
wp		29995.3			
vc		35			
sc		0			
ws		28			
h2nm		119.95			
rfl		12700.5			
rfp		8673.4			
th		6			
ins		100.00			
nm	cdc	ph

06/04/02 23: 35
X: 16 scans, 4.0cm-1

STANDARD PROTON PARAMETERS

exp2 s2pu1

SAMPLE DEC. & VT
 date Jan 11 2006 dfrq 500.211
 solvent CDC13 dn H1
 file exp dpr 32
 ACQUISITION exp dpr 0
 sfrq 500.211 dm nnn
 tn H1 dm c
 at 2.048 dmf 8770
 np 32768 dseq
 sw 8000.0 dres 1.0
 fb 4000 homo n
 bs 5 temp 22.0
 ss 2 PROCESSING
 tpwr 58 lb 0.10
 pw 5.0 wfile
 d1 0 proc ft
 tof 0 fn not used
 nt 16 math f
 ct 0
 alock n verr
 gain not used wexp
 flags n wnt wft
 il n
 in n
 dp y
 hs nn
 DISPLAY
 sp -253.3
 wp 5502.0
 vs 73
 sc 0
 wc 250
 hzmm 22.01
 ls 758.76
 rfl 5153.3
 rfp 3831.5
 th 7
 ins 100.000
 nm cdc ph

STANDARD CARBON PARAMETERS

exp2 s2pu1

SAMPLE DEC. & VT
 date Jan 11 2006 dfrq 500.211
 solvent CDC13 dn H1
 file exp dpr 38
 ACQUISITION exp dpr 0
 sfrq 125.769 dm yvy
 tn C13 dm w
 at 1.170 dmf 15970
 np 65536 dseq
 sw 28001.4 dres 1.0
 fb 15000 homo n
 bs 16 temp 22.0
 tpwr 57 PROCESSING
 pw 8.0 lb 1.00
 d1 0.100 wfile
 tof 0 proc ft
 nt 10000 fn not used
 ct 0 math f
 alock n verr
 gain 56 wexp
 flags n wnt
 il n
 in n
 dp y
 hs nn
 DISPLAY
 sp -2081.2
 wp 28000.5
 vs 51
 sc 0
 wc 250
 hzmm 112.00
 ls 500.00
 rfl 11766.9
 rfp 9684.9
 th 6
 ins 100.000
 nm cdc ph

```

expt1 std13c
SAMPLE
date Jul 27 2005 dfrq 400.025
solvent CDCl3 dn H1
file ACQUISITION exp dpwr 51
sfrq 100.595 dm 0
tn C13 dmm w
at 1.311 dmf 10000
np 65536 temp 22.0
sw 25000.0 PROCESSING
fb 13800 lb 1.00
bs 16 wtfile
tpwr 61 proc ft
pw 3.2 fn not used
d1 1.000
tof 0 werr
nt 10000 wexp svf(n1)
ct 2824 vbs
alock n wnt
gain not used
FLAGS
il n
in n
dp Y
DISPLAY
sp -3000.9
wp 24999.2
vs 78
sc 0
wc 250
h2mm 100.00
is 500.00
rfl 10746.8
rpf 7745.1
th 11
ins ph 100.000
nm

```

SAMPLE				SPECIAL	
date	May 11	2005	temp		20.0
acq	CDC13	exp	gain	0	0.00
solvent			ppm		0.00
sw	ACQUISITION		hst	9556.9	0.008
ns			psd		8.250
nt	2.048		altra		
ap	39310			FLAGS	
bs	5000				
bs	2	in			
bs	8	dp			y
nt	1.000	hs			ns
nt	16			PROCESSING	10
nt	16	fb			18
nt					used
to	TRANSMITTER				
tn				DISPLAY	
tn	599.7	h6	sp		-323.1
tn	571.6	wp			6597.3
tn		rfl			9.7
tpw	3.125	rp			4354.4
tpw		rfp			110.5
de	DECOUPLER				-19.0
de					
do	C13	0		PLOT	
do					
decw		nc			250
decw		cc			98.7
dpr	49	vs			0.00
dpr	14800	ch			
		ns	cdc	ph

```

expl std13c
-
SAMPLE          DEC. & VT
date Jul 29 2005 drrq 400.025
solvent CDCl3   dn      H1
file           exp      51
ACQUISITION     dof      0
sfrq 100.595    dm      yyy
tn C13          dmm      v
at 1.311        dmf      10000
np 65536        temp     22.0
sv 25000.0      PROCESSING
fb 13800        lb      1.00
bs 16          wtfile
tpwr 61        proc     ft
pw 3.2         fn      not used
dl 1.000
tof 0          verr     svf(n1)
nt 10000       wexp
ct 4448        vbs
atock n        vnt
gain not used
-
FLAGS
il n
in n
dp y
DISPLAY
sp -3000.9
wp 24999.2
vs 63
sc 0
wc 250
hzm 100.00
ls 500.00
rf1 10746.8
rfp 7745.1
th
ins ph 100.000
nm

```

exp1 PROTON

SAMPLE SPECIAL 20.0
 date Apr 24 2005 temp gain not used
 solvent Benzene exp spin 0
 file ACQUISITION hst 0.000
 sw 9596.9 pw90 6.250
 at 2.048 alfa 0
 np 39310 FLAGS
 fb 5000 l1 n
 bs 8 l2 n
 ss 1.000 dp y
 nt 16 hs mn
 ct 16 lb not used
 tn H1
 sfrq 599.700 sp
 tof 576.6 wp 5597.3
 tpwr 60 rfl 5475.9
 pw 3.125 rfp 4286.4
 DECOUPLER rp 104.0
 dn C13 lp -10.5
 d0f 0
 de nnn wc 250
 decwave 49 vs 175
 dpwr 14800 th
 dmf nm cdc ph 7

exp2 std13c

SAMPLE DEC. & VT 400.025
 date Jul 31 2005 dfrq dn H1
 solvent Benzene exp dpwr 51
 file ACQUISITION d0f 0
 sfrq 100.595 dm yyy
 tn C13 dm w
 at 1.311 dmf 10000
 np 65536 temp 22.0
 sw 25000.0 PROCESSING 1.00
 fb 13800 lb
 bs 16 wtf file
 tpwr 61 proc ft
 pw 3.2 fn not used
 d1 1.000
 tof 0 werr
 nt 10000 wexp svf(n1)
 ct 3888 vds
 alock n wnt
 gain not used
 FLAGS
 l1 n
 l2 n
 dp y
 DISPLAY
 sp -2964.4
 vp 24999.2
 vs 282
 sc 0
 wc 250
 hznm 100.00
 is 500.00
 rfl 15840.1
 rfp 12875.0
 th 6
 ins 100.000
 nm ph

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 .

STANDARD PROTON PARAMETERS

exp1 PROTON

SAMPLE		SPECIAL	
date	Aug 16 2005	temp	20.0
solvent	Benzene	nals	not used
file	exp	spin	0
ACQUISITION		hst	9.000
sw	9586.9	pu99	7.400
at	2.048	alfa	0
np	59310	FLAGS	
fb	5000	ll	n
bs	8	in	n
ss	2	dp	y
d1	10.000	hs	nn
nt	32	PROCESSING	
ct	32	lb	0.10
TRANSMITTER		fn	not used
tn	598.780	sp	-300.1
tof	576.6	wp	6597.5
tpwr	60	rfl	1187.8
pw	3.700	rfp	0
DECOUPLER		rp	141.8
dn	0	lp	-9.5
dot	0	PLOT	
dm	nnn	wc	250
decwave	49	sc	0
dpr	14800	vs	57
dnt		th	7
		nm	cdc ph

The ^{13}C NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 .

The infrared spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 (pure C_6D_6 was used for the background spectrum).

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in CD_3CN .

The ^{13}C NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 .

The infrared spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in CD₃CN (pure CD₃CN was used for background spectrum).

STANDARD PROTON PARAMETERS

exp4 s2pu1

date Oct 25 2005 dfrq 500.213 DEC. & VT
 solvent CD300 dn H1
 file exp dpwr 32
 ACQUISITION exp dpr 0
 sfrq 500.213 dm nnn
 tn H1 dm c
 at 2.048 dmf 6264
 np 32786 dseq 1.0
 sv 8000.0 dres n
 fb 4000 homo 22.0
 bs 8 temp
 ss 2 PROCESSING
 tpwr 58 lb 0.10
 pw 5.0 wfile
 d1 0 proc
 tof 0 fn not used
 nt 16 math f
 ct 16
 a lock n werr
 gain not used wexp
 flags n wnt wft
 in n
 dp y
 hs nn
 DISPLAY
 sp -250.2
 wp 5502.0
 vs 58
 sc 0
 wc 250
 hzmm 22.01
 is 758.76
 rfl 3153.3
 rfp 1650.7
 th 2
 ins 100.000
 nm cdc ph

13C OBSERVE

exp1 std13c

SAMPLE DEC. & VT
date Oct 25 2005 dfrq 400.027
solvent CD3OD dn H1
file exp dpr 51
ACQUISITION exp dof 0
sfrq 100.596 dm yvy
tn 013 dmm w
at 1.311 dmf 10000
np 65536 temp 22.0
sw 25000.0 PROCESSING
fb 13800 lb 1.00
bs 16 wfile ft
tpr 81 proc not used
pw 3.2 fn
dl 1.000
tof 0 werr
nt 10000 wexp svf(n1)
ct 2400 vbs
alock n wnt
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -2857.8
wp 24999.2
vs 238
sc 0
wc 250
hzm 100.00
ls 500.00
rf1 7787.3
rfp 4926.7
th 11
ins 100.000
nm ph

STANDARD PROTON PARAMETERS

exp2 s2pu1

SAMPLE DEC. & VT
 date Oct 26 2005 dfrq 500.211
 solvent CDC13 dn H1
 file exp dpwr 32
 ACQUISITION dof 0
 sfrq 500.211 dm nmh
 tn H1 dm C
 at 2.048 daf 8770
 np 32758 dseq
 sw 8000.0 dres 1.0
 fb 4000 homo n
 bs 8 temp 22.0
 ss 2 PROCESSING
 tpwr 58 lb 0.10
 pw 5.0 wtfile
 d1 0 proc ft
 tof 0 fn not used
 nt 32 math f
 ct 32
 alock n werr
 gain not used wexp
 FLAGS n wbs
 il n wnt
 in n
 dp y
 hs m
 DISPLAY
 sp -252.3
 wp 6752.4
 vs 112
 sc 0
 wc 250
 hzmm 27.01
 is 758.76
 rfl 5131.3
 rfp 3831.5
 th 7
 ins 100.000
 nm cdc ph

exp1 std13c

SAMPLE DEC. & VT
 date Oct 26 2005 dfrq 400.025
 solvent CDC13 dn H1
 file exp dpwr 51
 ACQUISITION dof 0
 sfrq 100.595 dm yyy
 tn C13 dm w
 at 1.311 daf 10000
 np 65536 temp 22.0
 sw 25000.0 PROCESSING
 fb 13800 lb 1.00
 bs 16 wtfile
 tpwr 51 proc ft
 pw 3.2 fn not used
 d1 1.000
 tof 0 werr
 nt 10000 wexp svf(n1)
 ct 6688 wbs
 alock n wnt
 gain not used
 FLAGS
 il n
 in n
 dp y
 DISPLAY
 sp -2399.4
 wp 24999.2
 vs 115
 sc 0
 wc 250
 hzmm 100.00
 is 500.00
 rfl 10745.2
 rfp 7745.1
 th 11
 ins 100.000
 nm ph

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 .

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of

the compound (structure shown) in C₆D₆.

The ¹³C NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C₆D₆.

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 .

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in C_6D_6 .

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in CD_3CN .

The ^1H NMR spectrum reproduced below was recorded from a partially-concentrated solution of the compound (structure shown) in a 1:1 mixture of $\text{DMSO}-d_6$ and CD_3CN .

The ^1H NMR spectrum below was reproduced from Supporting Information, The First Total

Synthesis of N1999A2: Absolute Stereochemistry and Stereochemical Implications into DNA Cleavage, *J. Am. Chem. Soc.* **2001**, 123, 11294.

The ultraviolet spectrum below (right) was reproduced from Supporting Information, The First Total Synthesis of N1999A2: Absolute Stereochemistry and Stereochemical Implications into DNA Cleavage, *J. Am. Chem. Soc.* **2001**, 123, 11294.

UV spectra of synthetic N1999A2 (**1**, left) and natural N1999A2 (right).