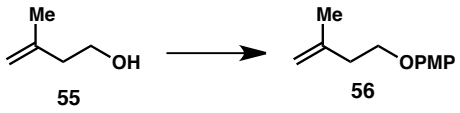
2.5 EXPERIMENTAL SECTION

2.5.1 Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), dimethylformamide (DMF), and toluene (PhMe) were dried by passing through activated alumina columns. Unless otherwise stated, chemicals and reagents were used as received. Triethylamine (Et_3N) was distilled over calcium hydride prior to use. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, or $KMnO_4$ staining. Flash column chromatography was performed either as described by Still et al.[28] using silica gel (particle size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiFlash Rf system (Teledyne ISCO Inc.). Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 400 MR (at 400 MHz and 101 MHz, respectively), a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or a Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal $CHCl_3$ (^{1}H, δ = 7.26), MeCN (^{1}H, δ = 1.94), or DMSO (^{1}H, δ = 2.50), and $CDCl_3$ (^{13}C, δ = 77.0), MeCN (^{13}C, δ = 118.26), or DMSO (^{13}C, δ = 40.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer

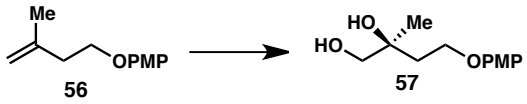
Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode.

2.5.2 Prepartive Procedures and Spectoscopic Data



1-methoxy-4-((3-methylbut-3-en-1-yl)oxy)benzene (56)

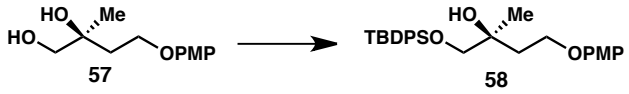
A flask was charged with 4-methoxyphenol (2.54 g, 20.5 mmol) and PPh_3 (2.33 g, 8.87 mmol), and then THF (23 mL) was added. The addition of alcohol **55** (0.588 g, 6.82 mmol) was followed by the addition of diisopropyl azodicarboxylate (1.75 mL, 8.87 mmol), and the reaction was heated to a reflux for 3.5 h. The reaction was cooled to room temperature, and THF was removed under pressure. The resulting residue was loaded unto a column and purified by column chromatography (5% EtOAc/Hex) to produce **56** (1.26 g, 96% yield).



(*S*)-4-(4-methoxyphenoxy)-2-methylbutane-1,2-diol (57)

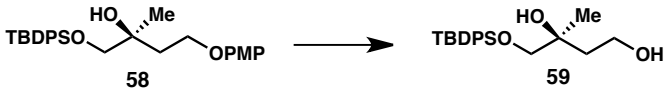
K_2CO_3 (3.49 g, 25.2 mmol), $K_3Fe(CN)_6$ (8.31 g, 25.2 mmol), $K_2OsO_4 \cdot 2H_2O$ (12.4 mg, 0.0336 mmol), and $(DHQ)_2PHAL$ (65.5 mg, 0.0841 mmol) were added all at once to a solution of olefin **56** (1.62 g, 8.41 mmol) in *t*-BuOH (45 mL) and H_2O

(45 mL) at 0 °C. After 5 h at room temperature, Na_2SO_3 (12.7 g, 100 mmol) was added and the mixture was stirred for 5 min. Minimal water was added and the aqueous layer was extracted from EtOAc four times. The combined organics were washed with brine, and dried over $MgSO_4$. The crude was purified by column chromatography (20%→50% EtOAc/Hex) to give **57** (1.68 g, 88% yield).



(*S*)-1-((*tert*-butyldiphenylsilyl)oxy)-4-(4-methoxyphenoxy)-2-methylbutan-2-ol (58)

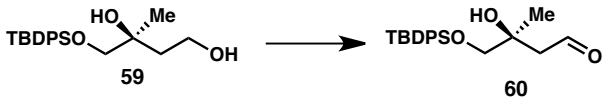
Imidazole (0.247 g, 3.63 mmol), followed by TBDPSCl (0.69 mL, 2.66 mmol), was added to a solution of diol **57** (0.548 g, 2.42 mmol) in DMF (2.7 mL). After stirring overnight at room temperature, the reaction was quenched with sat. NH_4Cl and extracted with ether three times. The combined organic layers were washed with water, then brine, and then dried over $MgSO_4$. The crude product was purified via column chromatography (15%→40% EtOAc/Hex) to give **58** (1.09 g, 97% yield).



(*S*)-4-((*tert*-butyldiphenylsilyl)oxy)-3-methylbutane-1,3-diol (59)

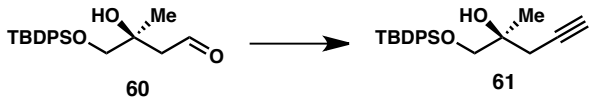
A solution of CAN (2.61 g, 4.76 mmol) in water (11 mL) was added dropwise via an addition funnel to a solution of alcohol **58** (1.09 g, 2.36 mmol) in acetonitrile (9.5 mL) at 0 °C. After 15 min, EtOAc and water was added and the layers were

separated. Aqueous was extracted from EtOAc twice more, and then the combined organics were washed with water, then brine, and then dried over $MgSO_4$. The crude was purified via column chromatography (eluting with CH_2Cl_2 to remove impurities, and then EtOAc to elute product) to give **59** (0.829 g, 98% yield).



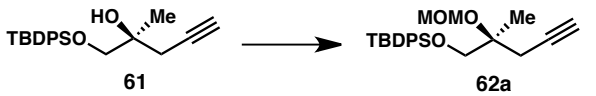
(*S*)-4-((*tert*-butyldiphenylsilyl)oxy)-3-hydroxy-3-methylbutanal (60)

Dess-Martin periodinane (48.8 mg, 0.115 mmol) was added to a solution of diol **59** (27.5 mg, 0.0767 mmol) in dichloromethane (0.5 mL) and this was stirred overnight. The reaction was quenched with a 1:1 mixture of sat. $NaHCO_3$/1.5 M $Na_2S_2O_3$ and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$, and crude aldehyde **60** was used in the next step without purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (t, J = 2.4 Hz, 1H), 7.68 – 7.61 (m, 4H), 7.48 – 7.37 (m, 6H), 3.53 (d, J = 1.3 Hz, 2H), 2.88 (s, 1H), 2.73 (dd, J = 15.6, 2.3 Hz, 1H), 2.49 (dd, J = 15.7, 2.6 Hz, 1H), 1.26 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.1, 135.6, 132.8, 123.0, 127.9, 72.2, 70.9, 51.6, 26.9, 24.3, 19.3; IR (NaCl/thin film): 3453, 3071, 3047, 2959, 2931, 2888, 2858, 2739, 1720, 1472, 1461, 1428, 1391, 1362, 1188, 1155, 1112, 824, 741 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{21}H_{28}O_3Si$ $[M–H]^-$ 355.1735, found 355.1736.



(*S*)-1-((*tert*-butyldiphenylsilyl)oxy)-2-methylpent-4-yn-2-ol (61)

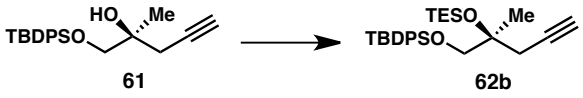
K_2CO_3 (16.6 mg, 0.120 mmol), followed by Ohira–Bestmann reagent (13.8 mg, 0.0719 mmol), was added to a solution of crude aldehyde **60** (25.7 mg, 0.0599 mmol) in MeOH (1 mL), and this was stirred at room temperature overnight. The reaction was quenched with sat. $NaHCO_3$ and diluted with Et_2O. The aqueous layer was extracted from Et_2O three times, and then the combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (5% EtOAc/Hex) to provide alkyne **61** (18.9 mg, 70% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.66 (m, 4H), 7.48 – 7.36 (m, 6H), 3.67 (d, *J* = 9.7 Hz, 1H), 3.54 (d, *J* = 9.8 Hz, 1H), 2.59 (s, 1H), 2.58 – 2.46 (m, 2H), 2.01 (t, *J* = 2.7 Hz, 1H), 1.28 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.6, 129.8, 127.8, 80.8, 72.2, 70.6, 69.5, 29.1, 26.6, 23.0, 19.3; IR (NaCl/thin film): 3561, 3452, 3071, 3050, 2998, 2959, 2931, 2892, 2858, 1590, 1487, 1472, 1464, 1428, 1391, 1362, 1188, 1152, 1113, 1090, 998, 908, 824, 742 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{22}H_{28}O_2Si$ $[M\bullet]^+$ 352.1853, found 352.1832.



(*S*)-5,9,9-trimethyl-8,8-diphenyl-5-(prop-2-yn-1-yl)-2,4,7-trioxa-8-siladecane (62a)

Bu_4NI (3.1 mg, 0.00834 mmol), followed by N,N-diisopropylethylamine (0.02 mL, 0.125 mmol) was added to a solution of alkyne **61** (14.7 mg, 0.0417 mmol) in

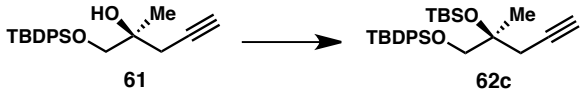
THF (0.5 mL). After dropwise addition of chloromethyl methyl ether (MOMCl, 0.01 mL, 0.167 mmol), the reaction was heated to 80 °C and stirred for 2 h. Upon cooling to room temperature, the reaction was quenched with water and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (5% EtOAc/Hex) to provide **62a** (15.1 mg, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (ddt, *J* = 7.9, 6.2, 1.7 Hz, 4H), 7.46 – 7.35 (m, 6H), 4.81 – 4.76 (m, 2H), 3.73 (d, *J* = 10.2 Hz, 1H), 3.60 (d, *J* = 10.2 Hz, 1H), 3.35 (s, 3H), 2.66 – 2.55 (m, 2H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.35 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.7, 135.5, 129.7, 127.6, 91.6, 81.1, 77.9, 70.2, 68.3, 55.4, 27.4, 26.9, 20.8, 19.3; IR (NaCl/thin film): 3309, 3071, 3050, 2932, 2891, 2858, 1472, 1428, 1390, 1362, 1189, 1144, 1112, 1040, 1007, 996, 918, 824, 739, 702 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{24}H_{32}O_3Si$ $[M+H]^+$ 397.2193, found 397.2182.



(*S*)-8,8-diethyl-2,2,6-trimethyl-3,3-diphenyl-6-(prop-2-yn-1-yl)-4,7-dioxa-3,8-disiladecane (62b)

DMAP (7.6 mg, 0.0618 mmol) and imidazole (16.8 mg, 0.247 mmol) were added to a solution of alkyne **61** (21.8 mg, 0.0618 mmol) in DMF (0.3 mL). Chlorotriethylsilane (TESCl, 0.03 mL, 0.185 mmol) was added and the reaction was heated to 40 °C for 4 h. Upon cooling to room temperature, DMF was extracted from hexanes three times and the combined hexane layers were washed with water, then

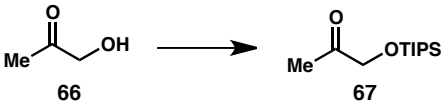
brine, and dried over $MgSO_4$. The crude product was purified by column chromatography (5% EtOAc/Hex) to provide alkyne **62b** (18.2 mg, 63% yield, 85% yield b.r.s.m.). $[\alpha]_D^{25.0}$ = +4 ° (*c* = 0.455, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 4H), 7.45 – 7.35 (m, 6H), 3.58 (d, *J* = 9.6 Hz, 1H), 3.46 (d, *J* = 9.6 Hz, 1H), 2.51 (ddd, *J* = 72.1, 16.4, 2.7 Hz, 2H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.31 (s, 3H), 1.06 (s, 9H), 0.90 (t, *J* = 7.9 Hz, 9H), 0.55 (qd, *J* = 7.9, 1.3 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ135.7, 133.6, 129.6, 127.6, 81.9, 75.3, 70.3, 67.0, 30.0, 26.9, 24.6, 19.3, 6.97, 6.74; IR (NaCl/thin film): 3311, 3071, 3050, 2955, 2932, 2875, 2858, 1472, 1459, 1428, 1239, 1195, 1160, 1112, 1030, 1016, 1009, 821, 740 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{28}H_{42}O_2Si_2$ $[M+H]^+$ 467.2796, found 467.2705.



(*S*)-2,2,3,3,5,9,9-heptamethyl-8,8-diphenyl-5-(prop-2-yn-1-yl)-4,7-dioxa-3,8-disiladecane (62c)

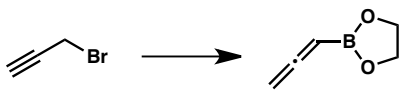
TBSCl (11.5 mg, 0.0766 mmol), imidazole (5.2 mg, 0.0766 mmol) and **61** (13.5 mg, 0.0383 mmol) were heated neat to 120 °C overnight. The reaction was quenched with water and diluted with dichloromethane, and the aqueous layer was extracted from dichloromethane three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by flash chromatography (Hex→5% EtOAc/Hex) to give **62c** (15.9 mg, 89% yield). $[\alpha]_D^{25.0}$ = +2 ° (*c* = 0.795, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.71 (m, 4H), 7.45 – 7.31 (m, 6H), 3.50 (d, *J* = 9.5 Hz, 1H), 3.34 (d, *J* = 9.5 Hz, 1H), 2.45 (dd, *J* = 16.4,

2.7 Hz, 1H), 2.31 (dd, *J* = 16.4, 2.7 Hz, 1H), 1.94 (t, *J* = 2.7 Hz, 1H), 1.11 (s, 3H), 1.03 (s, 9H), 0.85 (s, 9H), -0.03 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.2, 135.6, 129.4, 127.4, 82.0, 69.9, 69.2, 29.7, 27.1, 26.9, 25.9, 24.4, 19.5, 18.3, -5.54, -5.61; IR (NaCl/thin film): 3312, 3071, 3050, 2956, 2930, 2894, 2857, 1472, 1463, 1428, 1390, 1361, 1258, 1193, 1159, 1110, 1103, 1039, 1028, 1006, 851, 837, 822, 777, 741, 703 cm^{-1}; HRMS (ESI) calc'd for $C_{28}H_{42}O_2Si_2$ $[M+H]^+$ 467.2713, found 467.2796.



1-((triisopropylsilyl)oxy)propan-2-one (67)

Acetol (2.27 g, 30.6 mmol) was added to a solution of imidazole (4.38 g, 64.3 mmol) in DMF (40 mL), followed by the addition of TIPSCl (7.21 mL, 33.7 mmol). After stirring at room temperature for 1.5 h, the reaction was quenched with sat. NH_4Cl, and the aqueous layer was extracted from diethyl ether four times. The combined organic layers were washed with water, then brine, and finally dried over $MgSO_4$. The crude product was purified by column chromatography (5%→20% EtOAc/Hex) to give **67** (6.72 g, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (d, *J* = 1.2 Hz, 2H), 2.22 (s, 3H), 1.18 – 0.99 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.1, 69.9, 26.1, 17.9, 17.7, 12.3, 11.8; IR (NaCl/thin film): 3503, 2944, 2893, 2867, 1720, 1464, 1435, 1417, 1384, 1354, 1248,1231, 1123, 1069, 1014, 996, 919, 882, 838, 799 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{12}H_{26}O_2Si$ $[M+H_3O]^+$ 249.1880, found 249.1871.

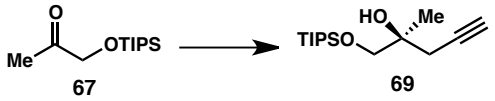


68

2-(propa-1,2-dien-1-yl)-1,3,2-dioxaborolane (68)

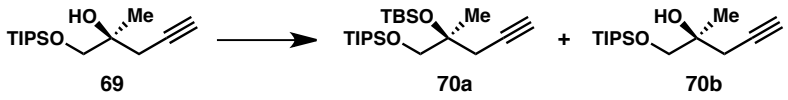
A 2-neck flask was charged with Mg turnings (2.43 g, 100 mmol) and $HgCl_2$ (46.2 mg, 0.170 mmol) and then gently heated while flushing with N_2 to remove excess moisture. Et_2O (15 mL) was added and the reaction flask was fitted with a reflux condenser. Propargyl bromide (10.3 g, 86.8 mmol) in Et_2O (50 mL) was added dropwise, and the reaction was cooled with a salt/ice bath. After stirring for 45 min at room temperature, the Grignard reagent was added dropwise via canula to a solution of trimethyl borate (9.02 g, 86.8 mmol) in Et_2O (100 mL) at –78 °C over about 30 min. The reaction was allowed to warm to room temperature, and then cooled to 0 °C before adding HCl (3M, 100 mL) dropwise using an addition funnel. The mixture was stirred at 0 °C for approximately 25 min and then allowed to warm to room temperature for 5 min. The aqueous layer was extracted from Et_2O (50 mL x 3) and the combined organics were dried over $MgSO_4$. The organic layer was filtered into a flame-dried 500 mL round-bottom flask, and then the solvent was reduced under pressure to leave ~200 mL. Ethylene glycol (8.08 g, 130 mmol) and $MgSO_4$ (100 g) were added and the reaction was stirred using a mechanical stirrer at room temperature for 23 h. The mixture was filtered, washing with Et_2O, and the solvent was reduced under pressure. The crude was dissolved in 150 mL pentane at 0 °C, and excess ethylene glycol as removed as the bottom layer if necessary. If a precipitate

remained, the crude was filtered through oven-dried Celite. The crude product was purified via distillation and stored under inert gas in the fridge.



(*S*)-2-methyl-1-((triisopropylsilyl)oxy)pent-4-yn-2-ol (69)

A mixture of (*S*)-3,3'-Cl-BINOL (35.7 mg, 0.101 mmol) and 2-(propa-1,2-dien-1-yl)-1,3,2-dioxaborolane (0.166 g, 1.501 mmol) was stirred at room temperature for 5 min. To this was added ketone **67** (0.232 g, 1.01 mmol), and the reaction mixture was subjected to microwave irradiation at 10 W for 1.5 h. The next day, the residue was purified via column chromatography (5% EtOAc/Hex) to provide **69** (0.188 g, 69% yield). $[\alpha]_D^{25.0}$ = +2 ° (*c* = 0.435, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (d, *J* = 9.3 Hz, 1H), 3.54 (d, *J* = 9.3 Hz, 1H), 2.62 (s, 1H), 2.50 – 2.37 (m, 2H), 2.01 (t, *J* = 2.7 Hz, 1H), 1.27 (s, 3H), 1.08 (d, *J* = 1.0 Hz, 12H), 1.07 (dd, *J* = 2.3, 1.3 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.0, 81.0, 72.1, 70.4, 69.2, 29.0, 22.9, 18.0, 12.0; IR (NaCl/thin film): 3558, 3454, 3314, 2944, 2888, 2867, 1463, 1422, 1383, 1157, 1100, 1069, 1014, 996, 911, 882, 809, 774 cm^{-1}.



TBSCl (0.120 g, 0.799 mmol), imidazole (0.0544 g, 0.799 mmol) and **69** (0.108 g, 0.399 mmol) were heated neat to 120 °C overnight. The reaction was quenched with water and diluted with dichloromethane, and the aqueous layer was

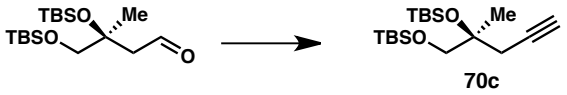
extracted from dichloromethane four times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude mixture was separated using column chromatography (hexanes) to afford **70a** (27.6 g, 18% yield, 41% yield brsm) and **70b** (13.3 mg, 9% yield, 20% yield brsm).

(*S*)-8,8-diisopropyl-2,2,3,3,5,9-hexamethyl-5-(prop-2-yn-1-yl)-4,7-dioxa-3,8-disiladecane (70a)

$[\alpha]_D^{25.0}$ = +3 ° (*c* = 0.735, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 – 3.44 (m, 2H), 2.49 – 2.34 (m, 2H), 1.94 (td, *J* = 2.7, 1.3 Hz, 1H), 1.29 (d, *J* = 1.5 Hz, 3H), 1.07 (d, *J* = 1.2 Hz, 15H), 1.06 – 1.04 (m, 8H), 0.86 (d, *J* = 1.4 Hz, 9H), 0.12 (d, *J* = 1.4 Hz, 3H), 0.09 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.1, 75.5, 70.2, 69.9, 29.9, 25.8, 24.6, 18.2, 18.0, 12.1, -2.09; IR (NaCl/thin film): 3314, 2944, 2893, 2866, 1472, 1458, 1387, 1254, 1197, 1164, 1108, 1066, 1035, 1016, 1004, 882, 835, 806, 774 cm^{-1}.

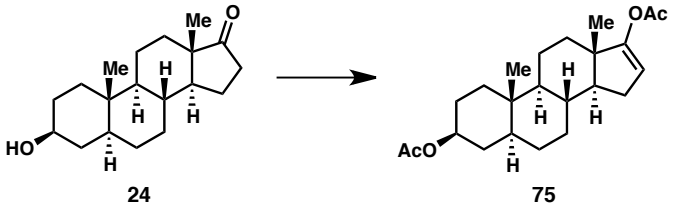
(*S*)-8,8-diisopropyl-2,2,3,3,6,9-hexamethyl-6-(prop-2-yn-1-yl)-4,7-dioxa-3,8-disiladecane (70b)

$[\alpha]_D^{25.0}$ = +3 ° (*c* = 0.460, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.51 (dd, *J* = 61.1, 9.4 Hz, 2H), 2.53 – 2.33 (m, 2H), 1.93 (t, *J* = 2.7 Hz, 1H), 1.28 (s, 3H), 1.05 – 1.04 (m, 21H), 0.90 (s, 9H), 0.06 (d, *J* = 1.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.1, 75.1, 69.9, 69.6, 30.0, 25.9, 24.8, 18.3, 13.5, -5.46, -5.51; IR (NaCl/thin film): 3315, 2929, 2866, 2360, 1653, 1559, 1506, 1472, 1464, 1388, 1257, 1197, 1168, 1144, 1103, 1044, 1006, 882, 851, 837, 776 cm^{-1}.



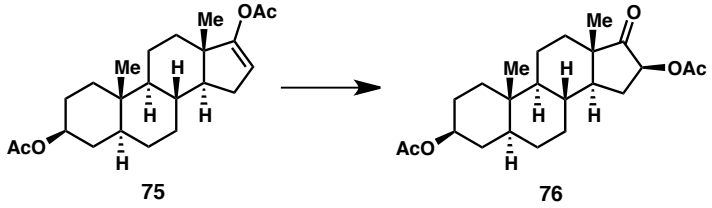
(*S*)-2,2,3,3,5,8,8,9,9-nonamethyl-5-(prop-2-yn-1-yl)-4,7-dioxa-3,8-disiladecane (70c)

K_2CO_3 (78.7 mg, 0.569 mmol), followed by Ohira–Bestmann reagent (65.6 mg, 0.342 mmol), was added to a solution of crude aldehyde (98.7 mg, 0.285 mmol) in MeOH (5 mL), and this was stirred at room temperature overnight. The reaction was quenched with sat. $NaHCO_3$ and diluted with Et_2O. The aqueous layer was extracted from Et_2O three times, and then the combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (hexanes) to provide alkyne **70c** (70.7 mg, 72% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.51 (d, *J* = 9.6 Hz, 1H), 3.41 (d, *J* = 9.5 Hz, 1H), 2.42 (dd, *J* = 16.5, 2.7 Hz, 1H), 2.32 (dd, *J* = 16.5, 2.7 Hz, 1H), 1.94 (t, *J* = 2.7 Hz, 1H), 1.25 (s, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.0, 75.4, 69.8, 69.6, 29.8, 25.9, 25.8, 24.4, 18.3, 18.2, –2.26, –5.50; IR (NaCl/thin film): 3315, 2956, 2930, 2887, 2858, 1472, 1464, 1388, 1362, 1310, 1255, 1197, 1165, 1137, 1104, 1043, 1007, 939, 834, 814, 798, 775 cm^{-1}; HRMS (ESI) calc'd for $C_{18}H_{38}O_2Si_2$ $[M+K]^+$ 381.2042, found 381.2170.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-dimethyl-2,3,4,5,6,7,8,9,10,11,12,13,14,15-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,17-diyl diacetate (75)

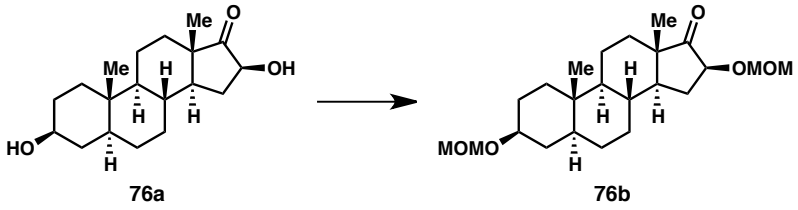
One drop of conc. H_2SO_4 was added to a solution of *trans*-androsterone **24** (0.643 g, 2.21 mmol) in isopropenyl acetate (16 mL) and this was heated to reflux for 4 h. Upon cooling to room temperature, the reaction was quenched with 0.5 M Na_2CO_3 (65 mL). The aqueous layer was extracted from EtOAc (65 mL, then 35 mL) and the combined organics were washed with water (65 mL) and brine (65 mL), and then dried over $MgSO_4$. The crude product was purified via column chromatography (neutral alumina powder, CH_2Cl_2) and then recrystallized from Et_2O to give **75** (0.311 g, 38% yield).



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*)-10,13-dimethyl-17-oxohexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,16-diyl diacetate (76)

Acetic anhydride (0.32 mL, 3.35 mmol) was added to a solution off steroid **75** (0.279 g, 0.745 mmol) and $Pd(OAc)_4$ (0.364 g, 0.820 mmol) in acetic acid (13 mL). After stirring overnight at room temperature, the acetic acid was removed via rotary evaporation. The resulting residue was diluted in Et_2O (20 mL) and water-saturated

Et_2O (20 mL) to decompose the lead complex. The mixture was filtered, and the filtrant was washed with 0.5 M Na_2CO_3 (40 mL), water (40 mL), and brine (40 mL), Upon drying over $MgSO_4$, the crude product was purified via column chromatography (5% EtOAC/95% CH_2Cl_2) to give **76** (0.151 g, 52% yield, 61% b.r.s.m.).

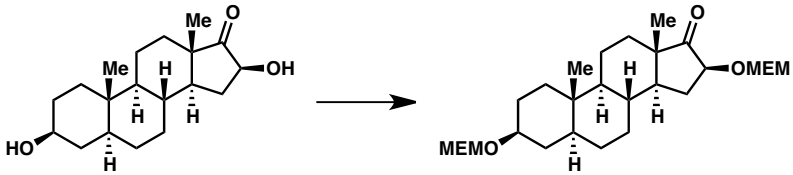


76a **76b**

(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*)-3,16-bis(methoxymethoxy)-10,13-dimethyltetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one (76b)

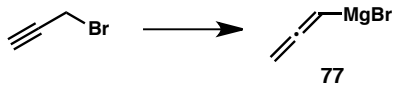
Bu_4NI (35.0 mg, 0.0949 mmol), followed by N,N-diisopropylethylamine (0.33 mL, 1.90 mmol) was added to a solution of steroid **76a** (0.145 g, 0.474 mmol) in THF (4 mL). After dropwise addition of chloromethyl methyl ether (MOMCl, 0.18 mL, 2.37 mmol), the reaction was heated to 50 °C and stirred overnight. Upon cooling to room temperature, the reaction was quenched with water and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (10%→15% EtOAc/Hex) to provide **76b** (0.187 g, 80% yield). $[\alpha]_D^{25.0}$ = –72 ° (*c* = 0.540, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.86 (d, *J* = 6.7 Hz, 1H), 4.73 (d, *J* = 6.7 Hz, 1H), 4.70 – 4.66 (m, 2H), 3.76 (s, 1H), 3.50 (tt, *J* = 11.2, 4.8 Hz, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 2.23 (ddd, *J* = 18.7, 7.7, 1.1 Hz, 1H), 1.96 – 1.90 (m, 1H), 1.91 – 1.69 (m, 3H), 1.64 (ddt, *J* = 16.2, 8.8, 3.4 Hz, 3H), 1.59 – 1.23 (m,

9H), 1.18 – 1.08 (m, 1H), 1.03 – 0.88 (m, 2H), 0.84 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.1, 96.4, 94.6, 89.3, 76.2, 55.5, 55.1, 54.4, 45.3, 44.9, 42.1, 36.9, 36.8, 36.4, 35.9, 35.2, 34.5, 31.8, 28.6, 28.5, 20.5, 12.3, 12.2; IR (NaCl/thin film): 2931, 2849, 1753, 1464, 1449, 1382, 1218, 1146, 1104, 1040, 1009, 916 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{23}H_{38}O_5$ $[M+Na]^+$ 417.2611, found 417.2596.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*)-3,16-bis((2-methoxyethoxy)methoxy)-10,13-dimethyltetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one (76c)

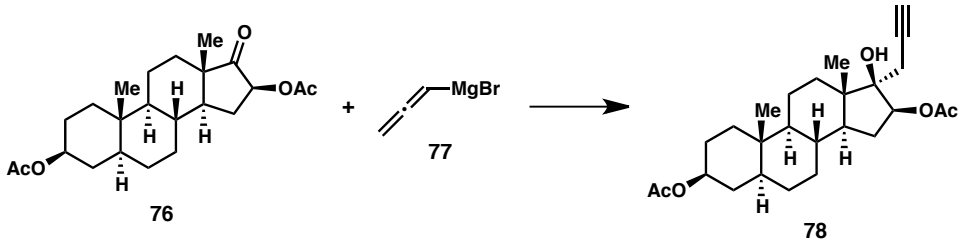
Bu_4NI (8.6 mg, 0.0232 mmol), followed by N,N-diisopropylethylamine (0.08 mL, 0.463 mmol) was added to a solution of steroid **76a** (35.5 mg, 0.116 mmol) in THF (1 mL). After dropwise addition of 2-methoxyethoxymethyl chloride (MEMCl, 0.07 mL, 0.579 mmol), the reaction was heated to 50 °C and stirred overnight. Upon cooling to room temperature, the reaction was quenched with water and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (20%→35% EtOAc/Hex) to provide **76c** (22.7 mg, 41% yield). IR (NaCl/thin film): 3365, 3166, 2930, 2863, 1731, 1451, 1417, 1384, 1298, 1226, 1169, 1132, 1110, 1093, 1046, 930 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{27}H_{46}O_7$ $[M+Na]^+$ 505.3136, found 505.3108.



77

propa-1,2-dien-1-ylmagnesium bromide (77)

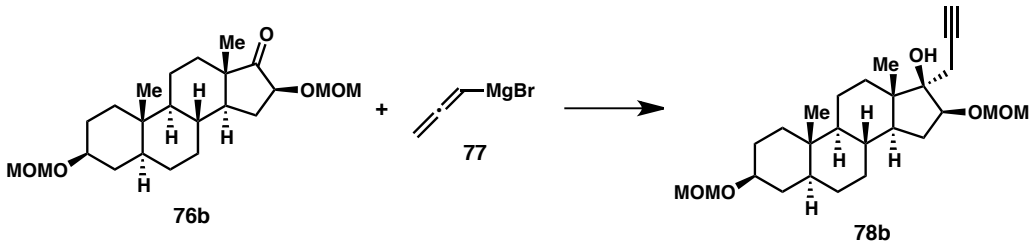
A 2-neck flask was charged with Mg turnings (0.194 g, 7.98 mmol) and $HgCl_2$ (2.2 mg, 0.00798 mmol) and then gently heated while flushing with N_2 to remove excess moisture. Et_2O (2 mL) was added and the reaction flask was fitted with a reflux condenser. Propargyl bromide (0.949 g, 7.98 mmol) was added dropwise while simultaneously adding Et_2O (3 mL) dropwise to maintain reflux. After stirring for 1 h, the reagent was ready to use as is.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*,17*R*)-17-hydroxy-10,13-dimethyl-17-(prop-2-yn-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,16-diyl diacetate (78)

Allenylmagnesium bromide **77** (0.0259 mmol, 0.02 mL of 1.68 M soln. in Et_2O) was added to a solution of steroid **76** (10.1 mg, 0.0259 mmol) in THF (2 mL) at –78 °C. After 1.5 h, another 0.02 mL (0.0259 mmol, 1 equiv) of allenylmagnesium bromide was added, and this was repeated every 30 min until a total of 4 equiv of allenylmagnesium bromide had been added. After a total of 3.5 h, the reaction was quenched with water, and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$, which

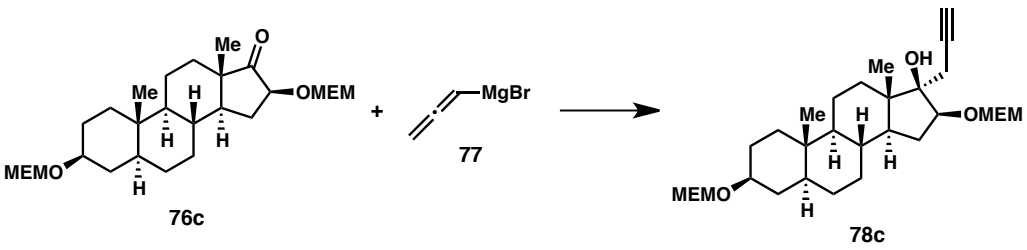
provided pure **78** (8.7 mg, 78% yield) without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (dd, *J* = 8.3, 5.8 Hz, 1H), 4.68 (tt, *J* = 11.4, 4.9 Hz, 1H), 2.61 – 2.49 (m, 2H), 2.41 – 2.26 (m, 2H), 2.10 (s, 3H), 2.02 (s, 3H), 1.86 – 1.78 (m, 1H), 1.73 (dt, *J* = 13.2, 3.6 Hz, 1H), 1.68 – 1.43 (m, 6H), 1.41 – 1.11 (m, 8H), 1.11 – 0.93 (m, 2H), 0.91 (s, 3H), 0.87 (dd, *J* = 12.2, 4.5 Hz, 1H), 0.84 (s, 3H), 0.65 (td, *J* = 11.5, 3.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 169.9, 110.0, 80.7, 80.6, 73.5, 71.2, 54.3, 47.2, 46.0, 44.7, 36.8, 35.8, 35.7, 34.0, 33.2, 32.3, 31.8, 28.4, 27.5, 27.2, 21.4, 21.1, 20.7, 13.8, 12.2; IR (NaCl/thin film): 3305, 3270, 2930, 2853, 1730, 1449, 1377, 1362, 1244, 1155, 1041, 1025 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{26}H_{38}O_5$ $[M–OH]^+$ 413.2692, found 413.2692.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*,17*R*)-3,16-bis(methoxymethoxy)-10,13-dimethyl-17-(prop-2-yn-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-ol (78b)

Allenylmagnesium bromide **77** (0.0467 mmol, 0.03 mL of 1.63 M soln. in Et_2O) was added to a solution of steroid **76b** (9.2 mg, 0.0233 mmol) in toluene (0.5 mL) at –78 °C. After 30 min, another 0.03 mL of allenylmagnesium bromide was added. After a total of 1 h, the reaction was quenched with water, and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$, which provided pure **78b** (7.3 mg, 72% yield)

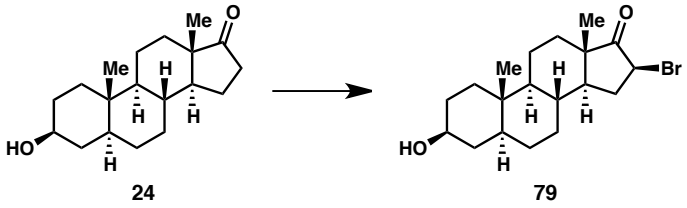
without further purification. $[\alpha]_D^{25.0}$ = –20 ° (*c* = 0.405, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.76 – 4.72 (m, 2H), 4.69 – 4.65 (m, 2H), 3.48 (tt, *J* = 11.1, 4.8 Hz, 1H), 3.42 (s, 3H), 3.36 (s, 3H), 3.28 (s, 1H), 3.19 – 3.16 (m, 1H), 2.46 – 2.34 (m, 2H), 2.02 – 1.95 (m, 2H), 1.83 (tdd, *J* = 12.4, 6.3, 3.4 Hz, 2H), 1.74 – 1.50 (m, 5H), 1.49 – 1.38 (m, 2H), 1.37 – 1.15 (m, 5H), 1.08 (ddt, *J* = 12.2, 8.7, 3.2 Hz, 1H), 1.03 – 0.90 (m, 2H), 0.89 (s, 3H), 0.88 – 0.82 (m, 1H), 0.81 (s, 3H), 0.65 (ddd, *J* = 12.3, 10.5, 4.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 97.7, 94.6, 90.3, 81.4, 76.4, 76.3, 69.5, 56.0, 55.1, 54.6, 48.0, 45.0, 43.8, 39.4, 37.8, 37.0, 35.8, 35.32, 34.8, 32.6, 31.7, 28.7, 28.6, 20.5, 12.4, 12.3; IR (NaCl/thin film): 3528, 3305, 3275, 2931, 2849, 1469, 1449, 1379, 1300, 1215, 1177, 1151, 1103, 1043, 1035, 1009, 927, 917 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{26}H_{42}O_5$ $[M+H]^+$ 435.3105, found 435.3078.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*,17*R*)-3,16-bis((2-methoxyethoxy)methoxy)-10,13-dimethyl-17-(prop-2-yn-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-ol (78c)

Allenylmagnesium bromide **77** (0.0783 mmol, 0.05 mL of 1.62 M soln. in Et_2O) was added to a solution of steroid **76c** (12.6 mg, 0.0261 mmol) in THF (0.5 mL) at –78 °C. After 30 min, another 0.03 mL (0.0522 mmol) of allenylmagnesium bromide was added. After a total of 45 min, the reaction was quenched with water,

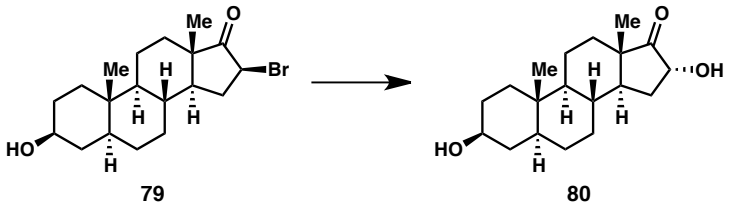
and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$, which provided pure **78c** (8.6 mg, 63% yield) without further purification. $[\alpha]_D^{25.0}$ = –18 ° (*c* = 0.500, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.87 – 4.80 (m, 2H), 4.78 – 4.74 (m, 2H), 3.77 – 3.74 (m, 2H), 3.72 – 3.68 (m, 2H), 3.58 – 3.54 (m, 4H), 3.54 – 3.48 (m, 1H), 3.39 (s, 6H), 3.29 (s, 1H), 3.25 (s, 1H), 2.42 (qd, *J* = 16.4, 2.6 Hz, 2H), 2.00 (dd, *J* = 13.0, 6.7 Hz, 1H), 1.95 (t, *J* = 2.6 Hz, 1H), 1.87 – 1.76 (m, 2H), 1.73 – 1.48 (m, 5H), 1.47 – 1.36 (m, 2H), 1.36 – 1.13 (m, 6H), 1.12 – 1.03 (m, 1H), 1.02 – 0.90 (m, 2H), 0.87 (s, 3H), 0.80 (s, 3H), 0.65 (ddd, *J* = 12.3, 10.5, 4.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 96.8, 93.6, 90.8, 81.5, 76.4, 76.3, 71.9, 71.7, 69.5, 67.9, 66.7, 59.0, 59.0, 54.6, 47.9, 44.9, 43.9, 39.4, 37.8, 37.0, 35.8, 35.2, 34.8, 32.5, 31.7, 28.7, 28.6, 20.5, 12.4, 12.3; IR (NaCl/thin film): 3480, 3305, 3262, 2929, 2849, 1466, 1450, 1378, 1367, 1200, 1170, 1130, 1111, 1090, 1047, 984, 930, 849 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{30}H_{50}O_7$ $[M+Na]^+$ 545.3449, found 545.3474.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*S*)-16-bromo-3-hydroxy-10,13-dimethyltetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one (79)

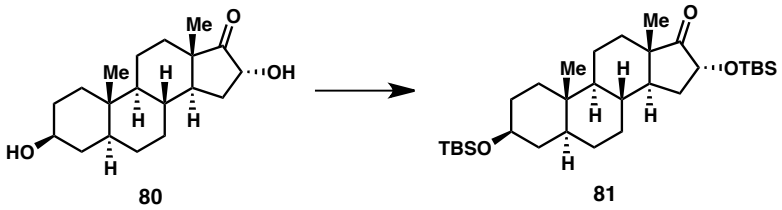
$CuBr_2$ (1.16 g, 5.21 mmol) was added to a solution of *trans*-androsterone **24** (0.505 g, 1.74 mmol) in distilled methanol (20 mL) and this was heated to reflux and stirred overnight. The next day, the reaction was quenched with water, and the

aqueous layer was extracted from chloroform three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude bromide **79** was used in the following step without any further purification.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*)-3,16-dihydroxy-10,13-dimethyltetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one (80)

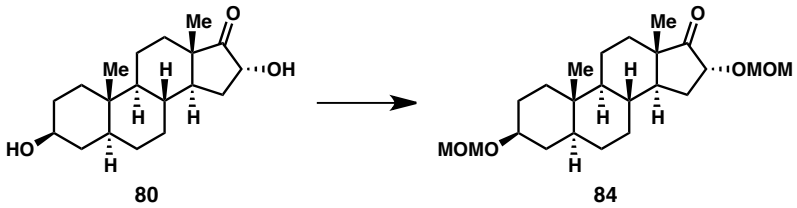
Bromide **79** (0.642 g, 1.74 mmol) was dissolved in 75% aq. DMF (30 mL), and then NaOH (0.0834 g, 2.08 mmol) was added. After 30 min, the reaction was poured into 1% HCl solution and the aqueous was extracted from EtOAc. The organic layer was washed with 5% $NaHCO_3$, then water, and then dried over $MgSO_4$. The crude diol **80** (0.400 g, 75% yield two steps) was clean enough that purification was unnecessary.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*)-3,16-bis((*tert*-butyldimethylsilyl)oxy)-10,13-dimethyltetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one (81)

Imidazole (0.206 g, 3.03 mmol), followed by TBSCl (0.400 g, 2.65 mmol), was added to a solution of **80** (0.387 g, 1.26 mmol) in dichloromethane (10 mL). The

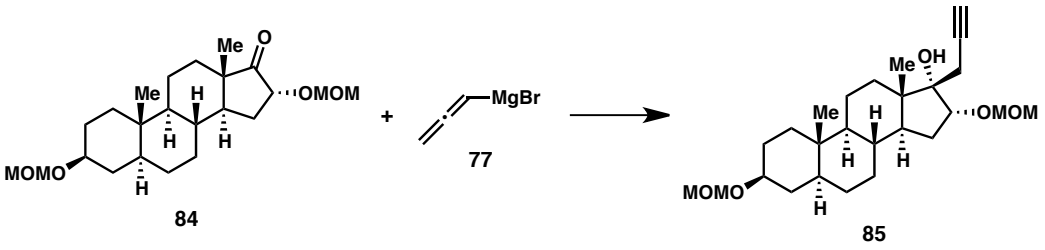
reaction was heated to 50 °C overnight and then quenched water and diluted with dichloromethane. The aqueous layer was extracted from dichloromethane three times, and then the combined organics were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (hexanes) to give **81** (0.539 g, 80% yield). $[\alpha]_D^{25.0}$ = +9 ° (*c* = 0.740, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.31 (d, *J* = 8.1 Hz, 1H), 3.54 (dd, *J* = 11.3, 6.5 Hz, 1H), 1.95 – 1.02 (m, 20H), 0.94 (d, *J* = 8.1 Hz, 2H), 0.92 (s, 1H), 0.89 (d, *J* = 4.9 Hz, 15H), 0.81 (s, 1H), 0.77 (d, *J* = 2.1 Hz, 1H), 0.28 – 0.19 (m, 1H), 0.11 (s, 3H), 0.10 (s, 3H), 0.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.6, 72.3, 72.0, 54.5, 48.4, 47.4, 45.1, 38.7, 37.1, 35.7, 35.6, 35.0, 32.8, 31.9, 30.7, 28.5, 25.9, 25.8, 25.7, 25.6, 25.6, 20.2, 14.6, 12.3, -4.53; IR (NaCl/thin film): 2929, 2856, 1754, 1723, 1711, 1693, 1470, 1461, 1454, 1446, 1385, 1360, 1253, 1179, 1150, 1095, 1071, 1004, 870,835, 776 cm^{-1}.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*)-3,16-bis(methoxymethoxy)-10,13-dimethyltetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one (84)

Bu_4NI (14.6 mg, 0.0396 mmol), followed by N,N-diisopropylethylamine (0.14 mL, 0.792 mmol) was added to a solution of steroid **80** (60.7 mg, 0.198 mmol) in THF (1.6 mL). After dropwise addition of chloromethyl methyl ether (MOMCl, 0.08 mL, 0.990 mmol), the reaction was heated to 50 °C and stirred overnight. Upon cooling to room temperature, the reaction was quenched with water and the aqueous

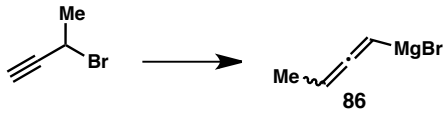
layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography (20% EtOAc/Hex) to provide **84** (76.4 mg, 98% yield). $[\alpha]_D^{25.0}$ = +86 ° (*c* = 0.255, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.87 (d, *J* = 6.7 Hz, 1H), 4.70 – 4.65 (m, 3H), 4.32 (dd, *J* = 7.1, 2.5 Hz, 1H), 3.49 (tt, *J* = 11.2, 4.8 Hz, 1H), 3.40 (s, 3H), 3.36 (s, 3H), 1.92 – 1.68 (m, 5H), 1.68 – 1.60 (m, 2H), 1.59 – 1.38 (m, 4H), 1.38 – 1.23 (m, 5H), 1.11 (ddt, *J* = 15.7, 12.5, 3.4 Hz, 1H), 1.04 – 0.92 (m, 2H), 0.90 (s, 3H), 0.83 (s, 3H), 0.70 (ddd, *J* = 13.7, 7.5, 4.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 217.3, 96.1, 94.6, 76.2, 74.4, 55.6, 55.1, 54.4, 48.8, 47.7, 44.9, 36.9, 35.8, 35.3, 35.0, 31.6, 30.7, 29.7, 28.7, 28.4, 20.2, 14.4, 12.2; IR (NaCl/thin film): 2930, 2856, 1751, 1464, 1449, 1375, 1215, 1146, 1102, 1066, 1043, 1012, 917 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{23}H_{38}O_5$ $[M+H]^+$ 395.2792, found 395.2767.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*,17*S*)-3,16-bis(methoxymethoxy)-10,13-dimethyl-17-(prop-2-yn-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-ol (85)

$TiCl_4$ (0.01 mL, 0.0471 mmol) was added to a solution of steroid **84** (9.3 mg, 0.0236 mmol) in THF (0.5 mL) at –78 °C, followed by the addition of allenylmagnesium bromide **77** (0.0707 mmol, 0.04 mL of 1.63 M soln. in Et_2O). After 30 min, the reaction was quenched with water and diluted with Et_2O, and the

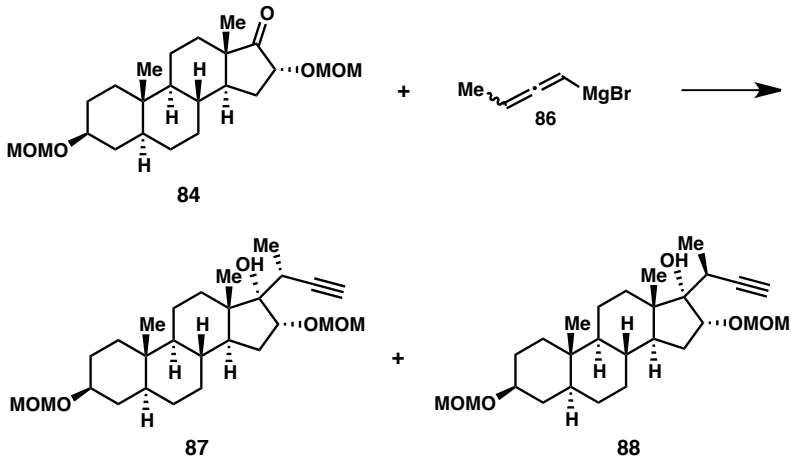
aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$ to give pure **85** (7.9 mg, 77% yield) without further purification. $[\alpha]_D^{25.0}$ = –30 ° (*c* = 0.455, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.72 (q, *J* = 6.8 Hz, 2H), 4.67 (d, *J* = 1.2 Hz, 2H), 4.03 (dd, *J* = 8.0, 3.1 Hz, 1H), 3.48 (tt, *J* = 11.2, 4.7 Hz, 1H), 3.40 (s, 3H), 3.36 (s, 3H), 3.21 (s, 1H), 2.49 – 2.39 (m, 2H), 1.87 – 1.80 (m, 1H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.92 (td, *J* = 11.4, 9.0 Hz, 2H), 1.78 – 1.68 (m, 2H), 1.65 – 1.53 (m, 8H), 1.48 – 1.38 (m, 2H), 1.36 – 1.19 (m, 7H), 1.13 – 1.05 (m, 2H), 1.00 – 0.82 (m, 3H), 0.80 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 96.5, 94.6, 81.6, 81.5, 80.2, 76.3, 70.2, 56.0, 55.1, 54.1, 48.4, 47.2, 45.0, 37.0, 35.7, 35.4, 35.3, 32.4, 32.1, 30.5, 28.8, 28.7, 25.8, 20.2, 15.5, 12.3; IR (NaCl/thin film): 3478, 3311, 3264, 2941, 2923, 2898, 2848, 1468, 1450, 1384, 1353, 1219, 1150, 1104, 1076, 1040, 1026, 1013, 989, 960, 916 cm^{-1}; HRMS (Multimode-ESI/APCI) calc'd for $C_{26}H_{42}O_5$ $[M+Na]^+$ 457.2924, found 457.2914.



86

buta-1,2-dien-1-ylmagnesium bromide (86)

86 was prepared from 3-bromobut-1-yne using the same procedure as allenylmagnesium bromide **77**.



$TiCl_4$ (0.01 mL, 0.0542 mmol) was added to a solution of steroid **84** (10.7 mg, 0.0271 mmol) in THF (0.5 mL) at –78 °C, followed by the addition of buta-1,2-dienyl-magnesium bromide **86** (0.0814 mmol, 0.05 mL of 1.50 M soln. in Et_2O). After 30 min, the reaction was quenched with water and diluted with Et_2O, and the aqueous layer was extracted from Et_2O three times. The combined organic layers were washed with brine and dried over $MgSO_4$ to give a mixture of **87** and **88**. The two products were separated by column chromatography (15% EtOAc/Hex) to afford **87** (5.7 mg, 47% yield) and **88** (2.8 mg, 23% yield).

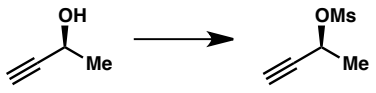
(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*,17*S*)-17-((*S*)-but-3-yn-2-yl)-3,16-bis(methoxymethoxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-ol (87)

$[\alpha]_D^{25.0}$ = +5 ° (*c* = 0.240, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.83 (d, *J* = 6.7 Hz, 1H), 4.71 – 4.65 (m, 3H), 3.96 (dd, *J* = 7.6, 2.5 Hz, 1H), 3.49 (tt, *J* = 11.2, 4.8 Hz, 1H), 3.41 (s, 3H), 3.36 (s, 3H), 3.21 (s, 1H), 2.73 (qd, *J* = 6.9, 2.5 Hz, 1H), 2.01 (d, *J* = 2.4 Hz, 1H), 1.91 – 1.76 (m, 3H), 1.70 (dt, *J* = 13.3, 3.6 Hz, 1H), 1.59 (tddd, *J* = 20.4, 12.4, 9.0, 5.5 Hz, 7H), 1.48 – 1.37 (m, 1H), 1.36 – 1.29 (m, 2H), 1.28 (d, *J* = 6.9

Hz, 3H), 1.25 (t, *J* = 1.3 Hz, 2H), 1.12 – 1.04 (m, 1H), 0.95 (tdd, *J* = 13.0, 8.3, 4.6 Hz, 2H), 0.79 (s, 3H), 0.75 (s, 3H), 0.69 (ddd, *J* = 12.5, 10.4, 3.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 97.9, 94.6, 87.6, 83.2, 82.1, 76.3, 69.5, 56.3, 55.1, 53.8, 49.0, 47.4, 44.9, 37.0, 35.6, 35.3, 35.3, 33.7, 33.3, 32.1, 32.0, 28.7, 28.7, 20.5, 16.7, 15.0, 12.2; IR (NaCl/thin film): 3520, 3306, 3270, 2928, 2849, 1461, 1450, 1383, 1352, 1340, 1296, 1218, 1151, 1104, 1070, 1044, 989, 917 cm^{-1}.

(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*,17*S*)-17-((*R*)-but-3-yn-2-yl)-3,16-bis(methoxymethoxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-ol (88)

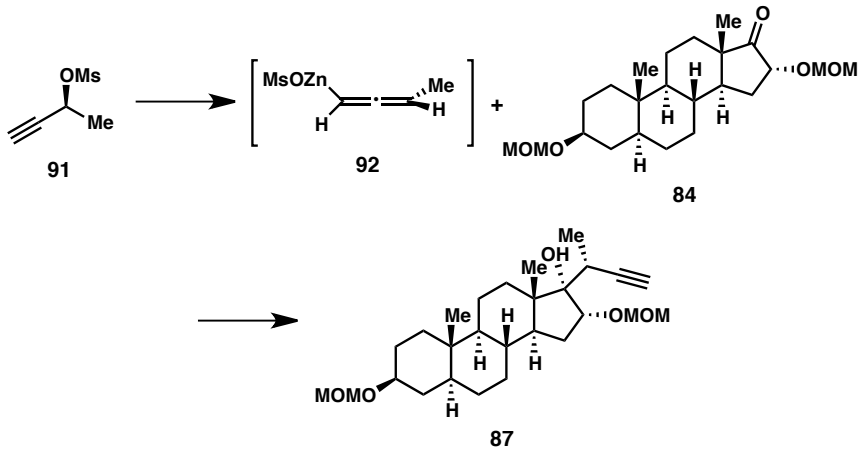
$[\alpha]_D^{25.0}$ = –24 ° (*c* = 0.125, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.75 (d, *J* = 6.8 Hz, 1H), 4.70 – 4.64 (m, 3H), 4.01 (dd, *J* = 8.1, 2.0 Hz, 1H), 3.49 (tt, *J* = 11.2, 4.7 Hz, 1H), 3.40 (s, 3H), 3.36 (s, 3H), 3.13 (s, 1H), 2.68 (qd, *J* = 7.0, 2.5 Hz, 1H), 2.11 (d, *J* = 2.5 Hz, 1H), 2.06 – 2.00 (m, 1H), 1.91 – 1.68 (m, 5H), 1.68 – 1.02 (m, 12H), 1.01 – 0.85 (m, 3H), 0.84 (s, 3H), 0.81 (d, *J* = 0.6 Hz, 3H), 0.74 – 0.65 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 96.1, 94.6, 87.0, 82.3, 80.8, 76.4, 70.7, 56.6, 55.1, 53.9, 49.0, 45.0, 37.0, 35.7, 35.3, 35.3, 32.5, 32.1, 31.9, 31.7, 29.7, 28.8, 28.8, 20.4, 16.3, 15.1, 12.2; IR (NaCl/thin film): 3538, 3231, 2930, 2848, 2819, 1459, 1449, 1377, 1355, 1261, 1219, 1150, 1135, 1103, 1041, 987, 917, 908, 796 cm^{-1}.



89 **91**

(*S*)-but-3-yn-2-yl methanesulfonate (91)

Et_3N (0.09 mL, 0.673 mmol) was added to a solution of alcohol **89** (23.6 mg, 0.337 mmol) in dichloromethane (1.7 mL) at –78 °C, followed by the addition of mesyl chloride (0.04 mL, 0.505 mmol). After 1.25 h at –78 °C, the reaction was quenched with sat. $NaHCO_3$ and allowed to warm to room temperature. The organic layer was separated, washed with brine, and concentrated. The resulting reside was diluted with ether, which was washed twice with water, and then once with brine. The combined aqueous layers were washed with ether twice. The combined organic layers were then dried over $MgSO_4$. The crude mesylate **91** (34.3 mg, 69% yield) was used without further purification.



(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,16*R*,17*S*)-17-((*S*)-but-3-yn-2-yl)-3,16-bis(methoxymethoxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-ol (87)

Triphenyl phosphine (3.5 mg, 0.0134 mmol), followed by mesylate **91** (0.119 g, 0.804 mmol), was added to a solution of $Pd(OAc)_2$ (9.0 mg, 0.0134 mmol) in THF (0.9 mL) at –78 °C. In a separate flask with stir bar, $TiCl_4$ (0.07 mL, 0.536 mmol) was added to a solution of steroid **84** (0.106 g, 0.268 mmol) in THF (0.9 mL) at –78

°C. After stirring for 5 min, the steroid solution was added dropwise to the mesylate solution at –78 °C. Following the dropwise addition of Et_2Zn (1.6 mL, 1.0 M in hexanes, 1.61 mmol), the reaction was warmed to –20 °C and stirred overnight. The reaction was quenched at –20 °C with 10% HCl (caution: evolution of gaseous ethane), and then diluted with ether and warmed to room temperature. Aqueous was extracted from ether twice, and the combined organics were washed with brine and dried over $MgSO_4$. The crude product was purified via flash chromatography (15% EtOAc/Hex) to afford alcohol **87** (18.1 mg, 15% yield, 22% b.r.s.m.). See above for characterization data.