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α,β–Epoxy Vinyl Triflates in Pd-Catalyzed Reactions

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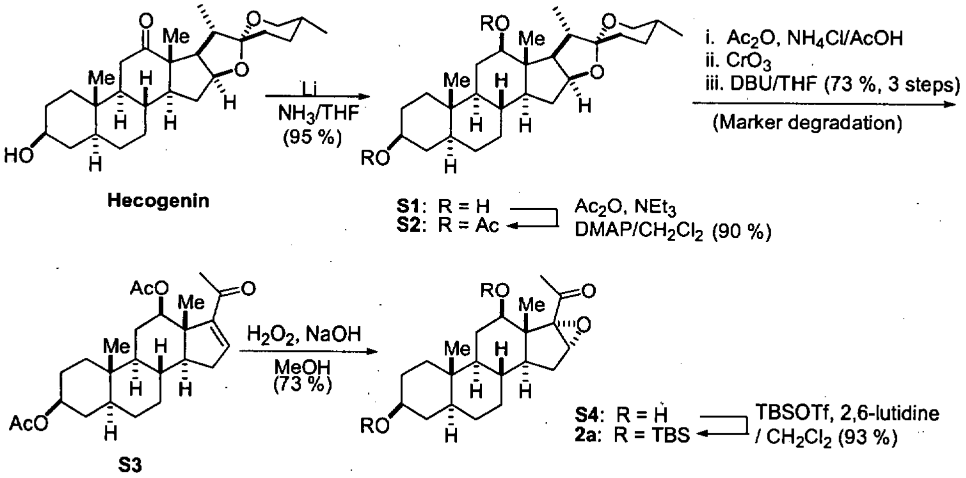
Supporting Information

Experimental procedures for all the new compounds and known compounds without published experimental procedures are described below. Compounds that are not presented in the main text are numbered starting from S1.

Epoxide **2a** was prepared from the commercially available steroid, as shown below. Dissolving metal reduction of hecogenin[1,2] followed by acylation provided rockogenin diacetate (**S2**). This was transformed into enone **S3**[3] by a slight modification[4] of Dauben's procedure[5] ("Marker degradation").[6] Treatment of **S3** with H_2O_2 and NaOH in refluxing MeOH epoxidized the enone and cleaved the acetates, giving diol **S4**. TBS protection of this diol afforded **2a** in 7 steps, 42 % overall yield.



Experimental Section

General. All moisture- or air-sensitive reactions were performed under N_2 or Ar atmosphere in flame-dried glassware. Unless otherwise noted, extracts were dried with anhydrous $MgSO_4$ and concentrated using a rotary evaporator at aspirator pressure.

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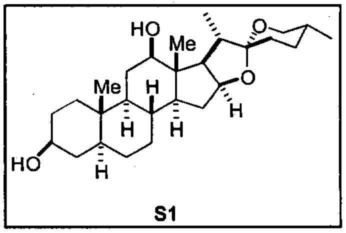
[1] Huffman, J. W.; Alabran, D. M.; Bethea, T. W. *J. Am. Chem. Soc.* **1962**, *27*, 3381.
[2] Isolation of rockogenin by recrystallization removed impurities presented in the starting material. Essentially no C12 α-isomer was seen by this procedure.
[3] This enone was previously made by a similar procedure. Kim, S.; Sutton, S. C.; Guo, C.; LaCour, T. G.; Fuchs, P. L. *J. Am. Chem. Soc.* **1999**, *121*, 2056-2070.
[4] Kemp, S. J. *Ph. D. Thesis, University of California, Berkeley* **1995**.
[5] Dauben, W. G.; Fonken, G. J. *J. Am. Chem. Soc.* **1954**, *76*, 4618.

Purification on silica refers to "flash chromatography" was performed according to the method of Still.[7] Unless other wise noted, Merck silica gel (230-400 mesh) was used as the stationary phase. Fischer basic Al_2O_3 (activity 1, 60-325 mesh) was used where noted. The term "deactivated silica" refers to silica gel, which is pre-treated with 1% NEt_3/hexanes for at least 30 min and washed with hexanes prior to use.

Solvents used in moisture-sensitive reactions were dried using standard methods. THF was degassed when necessary by passing a stream of Ar through it for at least 30 minutes.

Unless otherwise specified, all the reagents and starting materials were used as obtained from commercial suppliers. Bu_3SnH was distilled and stored under either N_2 or Ar. LiCl was dried by keeping at 140 °C under high vacuum (< 0.5 mm Hg) for at least 12 h when needed.

Unless otherwise indicated, IR spectra were recorded on Gemini FTIR instruments from thin films on NaCl plates. ^{1}H NMR spectra were obtained with Bruker spectrometers at 400 or 500 MHz. Spectra chemical shifts are calibrated to the residual protio solvent resonance ($CDCl_3$, δ 7.25). ^{1}H NMR data are described in the following order: chemical shifts, multiplicity [s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad)], integration, and coupling constant(s). ^{13}C spectra were obtained with Bruker instruments at 100 or 125 MHz. Spectra chemical shifts are calibrated to the solvent resonance ($CDCl_3$, δ 77.0). Distortionless enhancement by polarization transfer (DEPT) was routinely conducted to assist with signal assignments. Mass spectra were recorded at U.C. Berkeley using fast atom bombardment (FAB). All the melting points are uncorrected. Elemental analyses were performed at the University of California, Berkeley microanalysis facility.



S1

(25R)-5α-Spirostane-3β,12β-diol (rockogenin)[8] (S1). A solution of hecogenin (21.4 g, 49.5 mmol) in THF (300 mL) was added to a stirring solution of liquid NH_3 (1 L) and THF (500 mL) at –78 °C. Li metal (4.5 g) was added in small pieces and the solution was stirred vigorously until it turned dark blue. Another portion of THF (400 mL) was added and the solution was stirred for 1 h at –78 °C and then for 4 h at –33 °C. The reaction was then quenched with NH_4Cl (10 g) and NH_3 was allowed to evaporate. Water (200 mL) was carefully

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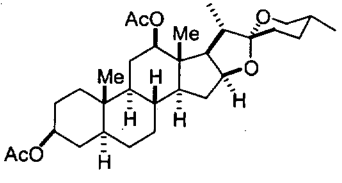
[6] (a) Marker, R. E.; Wagner, R. B.; Ulshafer, P. R.; Wittbecker, E. L.; Goldsmith, D.; Ruof, C. *J. Am. Chem. Soc.* **1947**, *69*, 2167. (b) Cameron, A. F. B.; Evans, R. M.; Hamlet, J. C.; Hunt, J. C.; Jones, P. G. *J. Chem. Soc.* **1955**, 2807.

[7] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[8] Huffman, J. W.; Alabran, D. M.; Bethea, T. W. *J. Am. Chem. Soc.* **1962**, *27*, 3381.

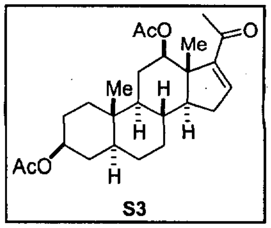
added while cooling in an ice bath, and the solution was concentrated to ~400 mL. To the white suspension was added CH_2Cl_2 (300 mL), and the aqueous layer was extracted with CH_2Cl_2 (100 mL x 3). The combined organic layers were washed with 1 M HCl (200 mL), saturated $NaHCO_3$ (200 mL) and brine (200 mL) to give diol **S1** as a white solid. Recrystallization from EtOAc/hexanes gave white flakes (15.6 g, 35.9 mmol, 73 %). The mother liquor was flash chromatographed (30 % EtOAc/hexanes) to give additional diol **S1** (4.65 g, 10.7 mmol, 22 %): R*f* 0.18 (50% EtOAc/hexanes). mp 202-203 °C. ^{1}H NMR (500 MHz) δ 4.40 (q, 1, *J* = 7.5), 3.57 (sept, 1, *J* = 5.0), 3.46 (m, 1), 3.36 (dd, 1, *J* = 10.9), 3.30 (m, 1), 2.00 (m, 1), 1.9-0.7 (m, 27), 1.02 (d, 3, *J* = 6.81), 0.821(s, 3), 0.779 (d, 3, *J* = 6.34), 0.748 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 109.4 (C), 80.7 (CH), 79.8 (CH), 71.1 (CH), 66.8 (CH_2), 61.7 (CH), 54.7 (CH), 53.3 (CH), 46.0 (CH), 44.8 (C), 42.1 (CH), 38.0 (CH), 31.8 (CH_2), 31.4 (CH_2), 31.2 (CH_2), 30.5 (CH_2), 30.2 (CH), 28.8 (CH_2), 28.5 (CH_2), 17.1 (CH_3), 13.9 (CH_3), 12.3 (CH_3), 10.5 (CH_3). IR (thin film) 3410. $[\alpha]_D$ –55.3 (*c* = 1.29, CH_2Cl_2). Anal. Calcd for $C_{27}H_{45}O_4$: C, 68.69; H, 10.48. Found: C, 68.67; H, 10.53.

(25R)-3β,12β,-Diacetoxy-5α-Spirostane (rockogenin diacetate) (S2).



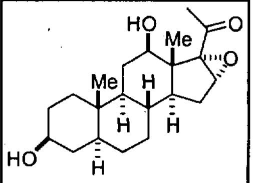
S2

The solution of **S1** (9.02 g, 20.8 mmol), Ac_2O (4.8 mL, 5.1 g, 50 mmol), NEt_3 (14 mL, 10 g, 100 mmol) and DMAP (1 spatula) in CH_2Cl_2 (80 mL) was stirred for 5.5 h. The reaction solution was poured into water (200 mL) and extracted with CH_2Cl_2 (50 mL × 3). The combined layers were washed with saturated $NaHCO_3$ (200 mL), 1M HCl (200 mL), brine (200 mL), dried, and concentrated to give the crude diacetate **S2**. The residue was flash chromatographed (30% EtOAc/hexanes) to give enone **S3** (9.64 g, 18.6 mmol, 90 %) as a white solid. An analytical sample was obtained by recrystallization from MeOH as white needles, mp 207-208 °C (lit.[9] 206-209 °C). R*f* 0.42 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 4.61 (sept, 1, *J* = 5.60), 4.48 (dd, 1, *J* = 4.50, 11.1), 4.34 (q, 1, *J* = 7.20), 3.40 (m, 1), 3.28 (dd, 1, *J* = 10.9), 1.97 (s, 3), 1.95 (s, 3), 1.85-0.8 (m, 28), 0.840 (d, 3, *J* = 6.60), 0.794 (s, 3), 0.787 (s, 3), 0.730 (d, 3, *J* = 6.20). $^{13}C\{^1H\}$ NMR (100 MHz) δ 170.6 (C), 170.4 (C), 109.2 (C), 81.6 (CH), 80.5 (CH), 73.4 (CH), 66,8 (CH_2), 61.2 (CH), 44.5 (C), 42.1 (CH), 36.5 (CH_2), 35.6 (C), 34.1 (CH), 33.8 (CH_2), 31.6 (CH_2), 31.4 (CH_2), 31.1 (CH_2), 30.2 (CH), 28.8 (CH_2), 28.3 (CH_2), 27.3 (CH_2), 21,5 (CH), 21,4 (CH), 17.1 (CH_3), 13.6 (CH_3), 12.1 (CH_3), 11.6 (CH_3). IR (thin film) 1737. $[\alpha]_D$ –48.9 (*c* = 1.07, CH_2Cl_2). Anal. Calcd for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found: C, 72.21; H, 9.50.



S3

3β,12β-Diacetoxy-5α-pregn-14-en-20-one (S3). A mixture of **S2** (10.3 g, 20.0 mmol), Ac_2O (40 mL), pyridine (1.6 mL, 20 mmol) and NH_4Cl (1.04 g, 20 mmol) was heated at 130 °C for 18 h. The reaction was then cooled and concentrated under high vacuum to remove excess of Ac_2O. The brown residue was then dissolved in AcOH (90 mL) and CH_2Cl_2 (50 mL) and cooled to 0°C. To this stirring solution was added CrO_3 solution (1.4 M in 9:1 AcOH/H_2O, 25 mL, 35 mmol) over 10 min. After stirring for 15 min, *i*-PrOH (40 mL) was added and the ice bath was removed. EtOAc (300 mL) and hexanes (150 mL) were added and the organic layer was washed with brine (75 mL), dried and concentrated. The resulting green solid was dissolved in CH_2Cl_2 (100 mL), DBU (6 mL, 40 mmol) was added and heated to reflux for 4 h. The solution was cooled and concentrated to brown viscous oil. This oil was flash chromatographed (20%→30% EtOAc/hexanes) to give enone **S3** (6.10 g, 14.7 mmol, 73 %) as a white solid, mp 136.5-137°C (lit.[10] 138-140 °C). *Rf* 0.36 (30% EtOAc/hexanes). ^1H NMR (400 MHz) δ 6.61 (dd, 1, *J* = 1.78, 3.29), 5.00 (dd, 1, *J* = 5.21, 11.6), 4.66 (sept, 1, *J* = 5.07), 2.29 (ddd, 1, *J* = 3.39, 6.59, 17.1), 2.21 (s, 3), 2.2-0.8 (m, 17), 2.09 (s, 3), 2.00 (s, 3), 1.00 (s, 3), 0.848 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 197.0 (C), 171.1 (C), 170.4 (C), 154.7 (C), 144.1 (CH), 74.6 (CH), 73.2 (CH), 53.7 (CH), 52.9 (CH), 50.8 (C), 44.4 (CH), 36.2 (CH_2), 35.4 (C), 35.1 (C), 33.6 (CH_2), 32.2 (CH), 31.2 (CH_2), 31.0 (CH_2), 28.1 (CH_2), 27.9 (CH_3), 27.8 (CH_2), 27.1 (CH_2), 21.5 (CH_3), 21.2 (CH_3), 12.2 (CH_3), 11.8 (CH_3). IR (thin film) 1736, 1677. $[\alpha]_D$ +33.3 (*c* = 0.93, CH_2Cl_2). Anal. Calcd for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 71.91; H, 8.71.



S4

3β,12β-Dihydroxy-16α,17α-oxido-5α-pregn-20-one (S4). To a solution of **S3** (2.5 g, 6.0 mmol) in MeOH (100 mL) was added a suspension of 10% NaOH in MeOH (7.9 mL, 20 mmol). The solution was cooled to 0 °C and H_2O_2 (30%, 10 mL, 90 mmol) was added dropwise over 10 min. The solution turned bright yellow, which was discharged after stirring at 0 °C for 55 min. The bath was removed and the solution was stirred at reflux for 2 h. After being cooled to rt, the solution was extracted with CH_2Cl_2 (100 mL, 50 mL × 2) and the combined organic layers were washed with 1 M Na_2SO_3 (50 mL) and brine (50 mL). The aqueous layers were combined and back-extracted with CH_2Cl_2 (20 mL × 3). The back-extracts were combined with extracts, dried and concentrated to give a white solid (1.9 g).

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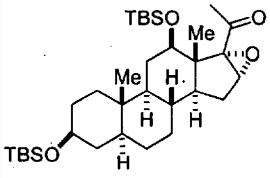
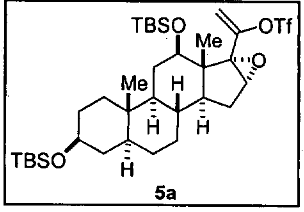
[9] Hirschmann, R.; Snoody Jr., C. S.; Hiskey, C. F.; Wendler, N. L. *J. Am. Chem. Soc.* **1954**, *76*, 4013.

Flash chromatography (30%→40% EtOAc/hexanes) gave epoxide **S4** (1.6 g, 4.58 mmol, 76 %) as a white solid. The analytical sample was obtained by recrystallization from MeOH as white needles: *Rf* 0.17 (50% EtOAc/hexanes). mp 216-217 °C. ^{1}H NMR (500 MHz) δ 4.62 (br s, 1), 3.76 (s, 1), 3.67 (dd, 1, *J* = 5.00, 10.7), 3.57 (sept, 1, *J* = 4.90), 2.11 (s, 3), 1.98 (dd. 1. *J* = 6.43, 13.5), 1.78 (dt, 1, *J* = 3.62, 13.3), 1.2-0.7 (m, 15), 0.92 (s, 3), 0.80 (s, 3). ^{13}C{^{1}H} NMR (100 MHz) δ 207.9(C), 71.2 (CH), 71.1 (C), 70.8 (CH), 60.8 (CH), 52.5 (CH), 46,5 (C), 44.6 (CH), 43. 3 (CH), 37.7 (CH_2), 36.5 (CH_2), 35.3 (C), 31.8 (CH), 31.2 (CH_2), 30.8 (CH_2), 29.4 (CH_2), 28.2 (CH_2), 26.5 (CH_2), 25.3 (CH_3), 12.0 (CH_3), 10.4 (CH_3). IR (thin film) 3450, 3420, 1688. $[\alpha]_D$ +82.5 (*c* = 1.07, CH_2Cl_2). Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.30. Found: C, 72.25; H, 9.70.



2a

3β,12β-Di(*t*-Butyldimethylsilyloxy)-16α,17α-oxido-5α-pregn-20-one (2a). To a solution of **S4** (348 mg, 1.00 mmol) in CH_2Cl_2 (4 mL) was added 2,6-lutidine (321 mg, 349 μL, 3.00 mmol, stored over KOH) and cooled to 0 °C. To this was added TBSOTf (628 mg, 528 μL, 2.30 mmol) dropwise over 10 min and the solution was stirred at 0 °C for 1.5 h and at rt for 20 h. The solution was diluted with CH_2Cl_2 (30 mL), washed with $NaHCO_3$ (20 mL), 0.25 M HCl (20 mL), brine (20 mL), dried, concentrated and flash chromatographed (10% EtOAc/hexanes) to give **2a** (542 mg, 0.929 mmol, 94%) as a white solid. The analytical sample was obtained by recrystallization from MeOH as white needles, mp 123-124 °C. *Rf* 0.65 (30% EtOAc/hexanes). ^{1}H NMR (500 MHz) δ 3.68 (dd, 1, *J* = 4.80, 10.7), 3.52 (sept, 1, *J* = 4.99), 2.07 (s, 3), 1.92 (dd, 1, *J* = 6.3, 13.4), 1.7-0.6 (m, 18), 1.10 (s, 3), 0.86 (s, 9), 0.85 (s, 9), 0.79 (s, 3), 0.02 (s, 6), 0.002 (s, 3), –0.02 (s, 3). ^{13}C{^{1}H} NMR (100 MHz) δ 204.0 (C), 73.5 (CH), 71.7 (CH), 70.4 (C), 60.1 (CH), 53.5 (CH), 49.8 (C), 44.9 (CH), 44.2 (CH), 38.3 (CH_2), 36.7 (CH_2), 35.4 (C), 31.9 (CH), 31.7 (CH_2), 31.4 (CH_2), 30.8 (CH_2), 28.5 (CH_2), 27.8 (CH_3), 27.3 (CH_2), 25.8 (CH_3), 25.6 (C), 18.0 (C), 17.9 (C), 12.1 (CH_3), 10.8 (CH_3), –3.06 (CH_3), –3.85 (CH_3), –4.70 (CH_3). IR (thin film) 1715. $[\alpha]_D$ +38.7 (*c* = 0.95, CH_2Cl_2). Anal. Calcd for $C_{33}H_{60}O_4Si_2$: C, 68.69; H, 10.48. Found: C, 68.87; H, 10.53.



5a

3β,12β-Di(*t*-Butyldimethylsilyloxy)-16α-17α-oxido-20-trifluoromethanesulfonyloxy-5α-pregn-20-ene (5a). To a cold (-78 °C) solution of **2a** (5.1 g, 8.8 mmol)

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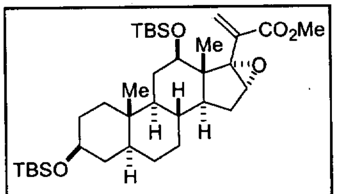
[10] Clegg, A. S.; Denny, W. A.; Jones, s. E. R. H.; Kumar, V.; Meakins, G. D.; Thomas, V. E. *J. Chem. Soc., Perkin. Trans. I* **1972**, 492.

and *N*-(4-chloro-2-pyridyl)triflimide[11] (3.8 g, 11 mmol) in THF (35 mL) was added KHMDS (0.5 M in toluene, 21 mL, 11 mmol) dropwise over 70 min and then stirred for 2 h. This was warmed to rt. after the consumption of the starting material, concentrated and flash chromatographed (2.5%→10% EtOAc/hexanes) to give **5a** (5.8 g, 8.2 mmol, 93%) as a white solid. The analytical sample was obtained by recrystallization from MeOH as white fluffy needles: R*f* 0.66 (30% EtOAc/hexanes). mp 120-121 °C. ^{1}H NMR (500 MHz) δ 5.82 (d, 1, *J* = 3.21), 5.32 (d, 1, *J* = 3.21), 3.80 (dd, 1, *J* = 5.10), 3.53 (sept, 1, *J* = 5.10), 3.53 (s, 1), 1.92 (dd, 1, *J* = 6.22, 13.4), 1.75-0.6 (m, 17), 0.986 (s, 3), 0.870 (s, 3), 0.870 (s, 9), 0.797 (s, 3), 0.0506 (s, 3), 0.0335 (s, 6), 0.0210 (s, 3). ^{13}C{^{1}H} NMR (100 MHz) δ 150.9 (C), 110.4 (CH_2), 73.3 (CH), 71.9 (CH), 66.4 (C), 61.6 (CH), 53.4 (CH), 48.5 (C), 45.0 (CH), 44.5 (CH), 38.4 (CH_2), 36.9 (CH_2), 32.4 (CH), 31.8 (CH_2), 31.4 (CH_2), 31.3 (CH_2), 28.5 (CH_2), 26.6 (CH_2), 26.0 (CH_3), 25.9 (CH_3), 18.2 (C), 18.1 (C), 12.2 (CH_3), 11.4 (CH_3), –3.8 (CH_3), –4.2 (CH_3), –4.6 (CH_3). $[\alpha]_D$ +12.7 (*c* = 1.09, CH_2Cl_2). Anal. Calcd for $C_{33}H_{59}O_6Si_2F_3S$: C, 57.53; H, 8.39. Found: C, 57.90; H, 8.59.



3

3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-20-methoxycarbonyl-5α-pregn-20-ene (3). To a solution of **5a** (5.7 g, 8.0 mmol) in THF (80 mL) was added MeOH (6.5 mL, 320 mmol, freshly distilled from Mg under N_2) and NEt_3 (2.3 mL), then CO was bubbled through the solution for 15 min. To this was added PPh_3 (13 mg, 0.048 mmol) and $Pd(OAc)_2$ (5.4 mg, 0.024 mmol) and CO was again bubbled through for 15 min. The solution was kept under CO (1 atm) for 7.5 h and same amount of the catalyst was added and stirred for additional 12 h. The color of the solution had changed from yellow to pink during this time period. This was diluted with H_2O (20 mL) and extracted with EtOAc (10 mL × 3). Combined organic layers was washed with brine (30 mL), dried, concentrated and flash chromatographed (2.5% EtOAc/hexanes) on basic Al_2O_3 to give **3** (4.1 g, 6.7 mmol, 83%) as a clear, colorless oil: R*f* 0.27 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 6.22 (d, 1, *J* = 1.48), 5.83 (d, 1, *J* = 1.51), 3.94 (dd, 1, *J* = 5.06, 10.5), 3.73 (s, 3), 3.52 (sept, 1, *J* = 5.10), 3.33 (s, 1), 1.89 (dd, 1, *J* = 6.18, 13.0), 1.75-0.93 (m, 18), 0.87 (s, 9), 0.83 (s, 9), 0.78 (s, 3), 0.70-0.057 (m, 2), –0.33 (s, 6), 0.0078 (s, 3), –0.012 (s, 3). ^{13}C{^{1}H} NMR (100 MHz) δ 166.6, 137.5, 128.7, 73.3, 72.0, 67.7, 61.2, 53.6, 51.7, 49.5, 45.0, 43.6, 38.4, 37.0, 35.5, 32.6, 31.9, 31.8,

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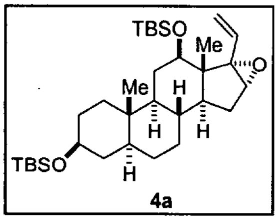
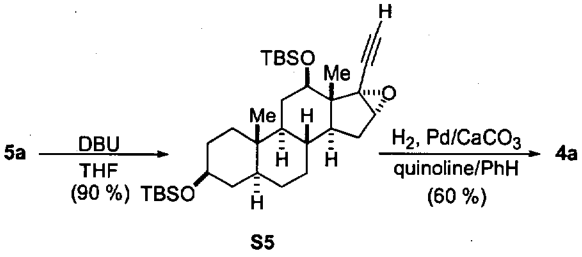
[11] (a) Comins, D. L.; Dehghani, A. *Tetrahedron Lett.*. **1992**, *33*, 6299. (b) Comins, D. L.; Dehghani, A.; Foti, C. J.; Joseph, S. P. *Org. Synth.* **1997**, *74*, 77.

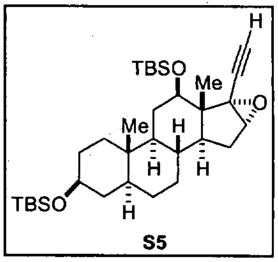
31.4, 29.7, 28.5, 27.1, 26.2, 25.9, 18.3, 12.3, 11.0, –4.6, –4.0, –2.8. IR (thin film) 1721. $[\alpha]_D$ +30.4 (*c* = 0.0048, CH_2Cl_2). Anal. Calcd for $C_{35}H_{62}O_5Si_2$: C, 67.91; H, 10.10. Found: C, 67.85; H, 10.10.



4a

3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-5α-pregn-20-ene (4a) from 3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-20-trifluoromethanesulfonyloxy-5α-pregn-20-ene (5a). The suspension of **5a** (71 mg, 0.1 mmol), LiCl (13 mg, 0.3 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) was in THF (400 μL, degassed) was stirred until becoming yellow and cloudy (~2 min). To this was added Bu_3SnH (32 μL, 35 mg, 0.12 mmol) dropwise over 1 min. The solution became clear during the addition, then again turned cloudy within 30 min. After 9 h of stirring, the solution was diluted with Et_2O (wet, 1 mL), DBU (30 μL) was added, and titrated with 0.1 M I_2/Et_2O until the color remained.[12] The brown suspension was then filtered through a plug of deactivated silica and concentrated to give yellow oil as 1: 0.5: 0.25 mixture of **4a, 5a** and **7a** (α isomer) (ratio determined by ^1H NMR). Flash chromatography (2.5% EtOAc/hexanes) on deactivated silica afforded a 2:1 mixture of **4a** and **5a** (ratio determined by ^1H NMR) both as white solids (46 mg, 0.076 mmol, 76%). Pure sample of **4a** was obtained as shown below.

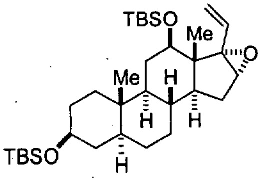




S5

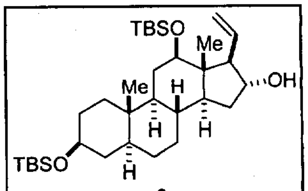
3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-5α-pregn-20-yne (S5). To a stirring solution of **5a** (503 mg, 0.71 mmol) in THF (2.8 mL) was added DBU (117 μL, 130 mg, 0.85 mmol), and the mixture was heated to reflux for 22 hr. After being cooled to rt, the solution was poured into sat. $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (10 mL × 3). Combined extracts were washed with brine (30 mL), dried and concentrated to give a white solid. This was resubjected to the reaction conditions, heated to reflux for additional 22 hr, and worked up as above. Flash chromatography with 2% EtOAc/hexanes afforded **S5** (357 mg, 0.64 mmol, 90 %) as a white solid), mp

63.5-65 °C. R*f* 0.43 (10% EtOAc/hexanes. ^{1}H NMR (400 MHz) δ 3.70 (dd, 1, *J* = 4.84, 10.6), 3.52 (sept, 1, *J* = 5.31), 3.96 (s, 1), 2.27 (s, 1), 1.87 (dd, 1, *J* = 6.43, 13.5), 1.75-1.65 (m, 3), 1.6-1.5 (m, 3), 1.5-1.2 (m, 10), 0.91 (s, 3), 0.90 (s, 3), 0.86 (s, 9), 0.79 (s, 3), 0.70 (m, 1), 0.12 (s, 3), 0.067 (s, 3), 0.022 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 80.8, 72.9, 72.4, 71.9, 62.5, 58.6, 53.6, 48.5, 45.0, 43.3, 38.4, 36.8, 35.5, 32.9, 31.8, 31.4, 31.2, 28.5, 27.0, 26.1, 25.9, 18.2, 12.2, 11.2, –4.26, –4.45, –4.60. IR (thin film) 3310. [α]$_D$ +22.3 (*c* = 0.0118, CH_2Cl_2). Anal. Calcd for $C_{33}H_{58}O_3Si_2$: C, 70.91; H, 10.46. Found: C, 70.54; H, 10.60.



4a

3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-5α-pregn-20-ene (4a) from 3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-5α-pregn-20-yne (S5). The suspension of **S5** (55 mg, 0.098 mmol), Pd/$CaCO_3$ (Lindlar catalyst, 10 mg)[13] and quinoline(10 μL, distilled and stored under nitrogen) in benzene (100 μL) was placed under H_2 (1 atm) for 1.5 h. This was filtered through a plug of celite and concentrated. Purification by flash chromatography (hexanes as eluent) on deactivated silica afforded **4a** (33 mg, 0.059 mmol, 60%) as a white solid, mp 63.5-65 °C. R*f* 0.54 (10% EtOAc/hexanes. ^{1}H NMR (400 MHz) δ 6.32 (dd, 1, *J* = 10.8, 17.1), 5.23 (dd, 1, *J* = 2.01. 17.1), 5.02 (dd, 1, *J* = 2.02, 10.8), 3.66 (dd, 1, *J* = 4.71, 10.6), 3.53 (sept, 1, *J* = 5.35), 3.14 (s, 1), 1.86 (dd, 1, *J* = 6.17, 13.1), 1.8-1.5 (m, 5), 1.45-0.65 (m, 12), 1.24 (s, 3), 0.867 (s, 18), 0.798 (s, 3), 0.032 (s, 6), 0.003 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 133.4 (CH), 114.4 (CH_2), 73.2 (CH), 72.0 (CH), 68.5 (C), 64.7 (CH), 53.6 (CH), 47.7 (C), 45.1 (H), 44.1 (CH), 38.5 (CH_2), 36.9 (CH_2), 35.5 (C), 32.8 (CH), 31.9 (CH_2), 31.5 (CH_2), 31.3 (CH_2), 28.6 (CH_2), 27.4 (CH_2), 26.0 (CH_3), 25.9 (CH_3), 18.3 (C), 18.0 (C), 12.2 (CH_3), 10.9 (CH_3), –3.75 (CH_3), –4.53 (CH_3), –4.59 (CH_3), –4.60 (CH_3). IR (thin film) 1734. [α]$_D$ –20.3 (*c* = 0.0101, CH_2Cl_2). Anal. Calcd for $C_{33}H_{60}O_3Si_2$: C, 70.65; H, 10.78. Found: C, 70.35; H, 11.09.



8a

3β,12β-Di(*t*-butyldimethylsilyloxy)-5α,17β-pregn-20-en-16α-ol (8a) from 3β,12β-Di(*t*-butyldimethylsilyloxy)-16α,17α-oxido-5α-pregn-20-ene (4a). To a yellow, cloudy solution of **4a** (28.1 mg, 0.05 mmol), LiCl (9.2 mg, 0.15 mmol, dried), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and PPh_3 (5.2 mg, 0.02 mmol) in THF (250 μL, degassed) was added Bu_3SnH (16 μL, 18 mg, 0.06 mmol) dropwise. This was stirred for 4 h while the hydride (16 μL) was added during the first 3 h

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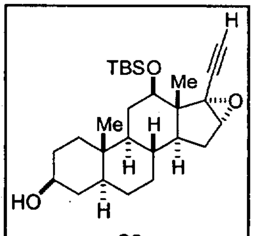
[12] Curran, D. P.; Chang, C. *J. Org. Chem.* **1989**, *54*, 3140.

(48 µl, overall). The solution was diluted with Et_2O (wet, 1 mL), DBU (30 µL) was added, and the solution was titrated with 0.1 M I_2/Et_2O until the color remained.[14] The suspension was then filtered through a plug of deactivated silica and concentrated. Flash chromatography (0%→10% EtOAc/hexanes) gave **4a** (8 mg, 0.014 mmol, 28%) and **8a** (15 mg, 0.026 mmol, 52%) as white solids. Attempts to further purify the homoallyl alcohol **8a** for microanalysis was unsuccessful, due to the presence of a co-polar impurity. The C-3 hydroxy derivative (**S6**) was purified and fully characterized instead.

8a: *Rf* 0.17 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 6.03 (ddd, 1, *J* = 10.4, 17.5), 5.06 (br d, 1, *J* = 17.4), 5.00 (br d, 1, *J* = 11.0), 4.13 (br dd, 1, *J* = 7.11, 7.11), 3.53 (sept, 1, *J* = 5.11), 3.46 (dd, 1, *J* = 4.46, 10.8), 2.00 (br dd, 1, *J* = 6.71, 6.70), 1.8-0.65 (m, 18), 0.849 (s, 3), 0.845 (s, 9), 0.783 (s, 3), 0.673 (s, 3), 0.0343 (s, 6), 0.0306 (s, 6). $^{13}C\{^1H\}$ NMR (100 MHz) δ 138.6 (CH), 114.5 (CH_2), 80.7 (CH), 79.5 (CH), 75.9 (CH), 72.1 (CH), 65.0 (CH), 53.1 (CH), 51.6 (CH), 49.5 (C), 45.0 (CH), 38.5 (CH_2), 37.0 (CH_2), 35.4 (CH_2), 34.1(C), 31.9 (CH_2), 31.7 (CH_2), 30.8 (CH_2), 28.6 (CH_2), 26.1 (CH_3), 25.9 (CH_3), 18.3 (C), 18.1 (C), 12.3 (CH_3), 9.6 (CH_3), –3.5 (CH_3), –4.6 (CH_3), –16.9 (CH_3). IR (thin film) 3391, 1638.



S6

12β-(*t*-butyldimethylsilyloxy)-5α,17β-pregn-20-ene-3β,16α-diol (S6). To a stirring solution of bis-protected alcohol **8a** (140 mg) in THF (400 µL) and H_2O (200 µL) was added AcOH (600 µL) dropwise. This was heated to 60 °C for 24.5 h. After being cooled to rt, H_2O (20 mL) and ether (20 mL) was added and the aqueous layer was extracted with Et_2O (10 mL × 3). A combined layer was washed with brine (30 mL), dried and concentrated. Purification with flash chromatography (20%→100% EtOAc/hexanes) afforded **S6** (58 mg, 0.13 mmol, 43%) as a white solid. Analytical sample was obtained by recrystallization from hexanes as white granules, mp 174-175 °C (46 mg, 0.10 mmol, 34% in 2 steps). *Rf* 0.22 (40% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 6.03 (ddd, 1, *J* = 7.38, 10.5, 17.6), 5.07 (d, 1, *J* = 17.4), 5.01 (d, 1, *J* = 10.5), 4.13 (br dd, 1, *J* = 7.42, 7.40), 3.58 (sept, 1, *J* = 4.89), 3.47 (dd, 1, *J* = 6.96), 1.85-0.65 (m, 19), 0.85 (s, 9), 0.79 (s, 3), 0.68 (s, 3), –0.0013 (s, 3), –0.0097 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 138.6 (CH), 114.5 (CH_2), 79.4 (CH), 75.9 (CH), 71.2 (CH), 65.0 (CH), 53.0 (CH), 51.5 (CH), 49.5 (C), 44.8 (CH), 38.0 (CH_2), 36.7 (CH_2), 35.4 (C), 34.9 (CH_2), 34.1 (CH_2), 34.1 (CH), 31.6 (CH_2), 31.4 (CH_2), 30.8 (CH_2), 28.5

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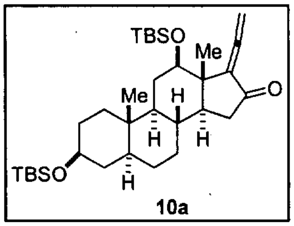
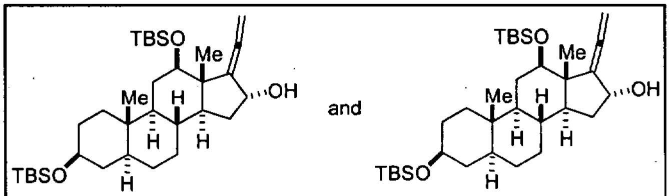
[13] Lindlar, H.; Dubuis, R. *Palladium catalyst for partial reduction of acetylenes*; Wiley, 1973; Collective vol. V: p. 880.

(CH_2), 26.1 (C), 26.0 (CH_3), 18.0 (C), 12.2 (CH_3), 9.58 (CH_3), –3.51 (CH_3), –4.65 (CH_3). IR (thin film) 3380, 1637. $[\alpha]_D$ –21.0 (*c* = 0.0113, CH_2Cl_2). Anal. Calcd for $C_{27}H_{47}O_3Si$: C, 72.43; H, 10.58. Found: C, 72.75; H, 10.82.



10a

3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-dien-16α-ol (7a,α-isomer),3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-dien-16β-ol (7a,β-isomer) and 3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-diene-16-one (10a). To a solution of **5a** (142 mg, 0.2 mmol) in THF (1 mL, degassed) was added $Pd_2(dba)_3\cdot CHCl_3$ (114 mg, 0.11 mmol) and PPh_3 (115 mg, 0.44 mmol), and stirred at rt for 16 h. The solution was diluted with Et_2O (10 mL), filtered through a plug of celite and concentrated. Flash chromatography (2.5%→5% EtOAc/hexanes) afforded **10a** (21 mg, 0.038 mmol, 19%) and an isomeric mixture of **7a** which contained substantial amount of DBA. Attempts to purify this mixture were unsuccessful. The spectral data of **7a** were identical to those obtained from the preparation described below. An analytical sample of **10a** was achieved by Dess-Martin oxidation of **7a**, shown below.



7a(α) **7a(β)**

3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-dien-16α-ol (7a,α-isomer) and 3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-dien-16β-ol (7a,β-isomer) by catalytic Pd reaction. To a suspension of **5a** (142 mg, 0.20 mmol), LiCl (25 mg, 0.6 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and PPh_3 (10.5 mg, 0.04 mmol) in THF (1 mL, degassed) was stirred until becoming yellow and cloudy. To this was added $(Bu_3Sn)_2$ (101 μL, 116 mg, 0.2 mmol) followed by $(Bu_3Sn)_2O$ (102 μL, 119 mg, 0.2 mmol) dropwise. The solution turned clear orange upon addition. After stirring at rt for 4.5 h, this was warmed to 40 °C and stirred for 17 h. The solution was then diluted with Et_2O (10 mL), concentrated, flash chromatographed (10% EtOAc/hexanes) on deactivated silica to give **7a** (α-isomer) (20.8 mg, 0.037 mmol, 19%), 1:1 mixture (ratio determined by ^1H NMR) of α and β isomers (42.5 mg, 0.076 mmol, 38%) and **7a** (β-isomer) (8.4 mg, 0.015 mmol, 8%), both as white solids.

7a (α-isomer): R*f* 0.13 (10% EtOAc/hexanes). mp 70-71.5 °C. ^1H NMR (400 MHz) δ 4.90 (dd, 1, *J* = 10.2, 3.04), 4.87 (dd, 1, *J* = 10.1, 2.98), 4.69(m, 1), 3.74 (s, 1, *J* = 10.7, 4.82), 3.54 (sept, 1, *J* = 4.89), 1.8-1.2 (m, 12),

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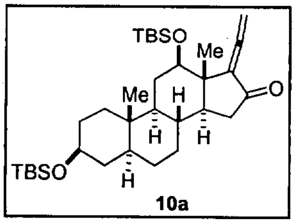
[14] Curran, D. P.; Chang, C. *J. Org. Chem.* **1989**, *54*, 3140.

1.1-0.7 (m, 7), 0.87 (s, 9), 0.86 (s, 9), 0.79 (s, 3), 0.36 (s, 6), 0.27 (s, 3), 0.20 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 201.7 (C), 116.6 (C), 80.1 (CH_2), 76.9 (CH), 72.7 (CH), 72.0 (CH), 53.0 (CH), 50.9 (CH), 45.0 (CH), 38.5 (CH_2), 37.0 (CH_2), 35.5 (CH_2), 34.7 (CH_2), 33.8 (CH), 31.9 (CH_2), 31.5 (CH_2), 28.5 (CH_2), 26.2 (CH_3), 25.9 (CH_3), 18.2 (C), 13.9 (CH_3), 12.3 (CH_3), –2.91 (CH_3), –4.39 (CH_3), –4.58 (CH_3). IR (thin film) 3408, 1958. $[\alpha]_D$ –19.3 ($c = 0.0072$, CH_2Cl_2). Anal. Calcd for $C_{35}H_{60}O_3Si_2$: C, 70.65; H, 10.78. Found: C, 70.47; H, 11.00.

7a (β-isomer): *Rf* 0.10 (10% EtOAc/hexanes). mp 110.5-111.5 °C. ^1H NMR (400 MHz) δ 4.91 (dd, 1, J = 3.41, 10.2), 4.76 (dd, 1, J = 3.19, 10.2), 4.63 (m, 1), 3.62 (dd, 1, J = 4.78, 10.7), 3.53 (sept, 1, J = 5.26), 2.14 (m, 1), 1.78 (d, 1, J = 3.98), 1.7-0.6 (m, 17), 1.05 (s, 3), 0.869 (s, 9), 0.860 (s, 9), 0.801 (s, 3), 0.034 (s, 6), 0.027 (s, 3), 0.0153 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 203.4, 115.3, 74.2, 72.0, 53.1, 50.6, 49.9, 45.0, 38.5, 37.0, 35.5, 34.3, 33.6, 31.9, 31.7, 31.4, 28.5, 26.2, 25.9, 18.2, 14.7, 12.3, –3.03, –4.42, –4.58. IR (thin film) 3418, 1960. $[\alpha]_D$ +41.8 ($c = 0.009$, CH_2Cl_2). Anal. Calcd for $C_{35}H_{60}O_3Si_2$: C, 70.65; H, 10.78. Found: C, 70.47; H, 11.16.



10a

3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-diene-16-one (10a) from 3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-dien-16α-ol (7a,α-isomer) and 3β,12β-Di(*t*-butyldimethylsilyloxy)-5α-pregna-17(20),20-dien-16β-ol (7a,β-isomer). To a solution of isomers **7a** (24.8 mg, 0.044 mmol) in CH_2Cl_2 (300 μL) was added Dess-Martin periodinane[15] (25 mg, 0.05 mmol) The resulting mixture was stirred for 1.5 h, diluted with CH_2Cl_2 (10 mL), poured into saturated $NaHCO_3$ (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine (20 mL), dried, concentrated and flash chromatographed (2% EtOAc/hexanes) to give **10a** (22.7 mg, 0.041 mmol, 92%) as a white solid, mp 66.5-67.5 °C. *Rf* 0.18 (20% EtOAc/hexanes). ^1H NMR (400 MHz) δ 5.24 (d, 1, J = 14.4), 5.15 (d, 1, J = 14.4), 3.83 (dd, 1, J = 4.83, 10.7), 3.54 (sept, 1, J = 5.04), 2.28 (dd, 1, J = 6.83, 17.3), 2.16 (dd, 1, J = 13.3, 17.0), 1.75 (ddd, 1, J = 4.48, 8.97, 13.2), 1.75-0.8 (m, 15), 1.07 (s, 3), 0.872 (s, 9), 0.861 (s, 9), 0.830 (s, 3), 0.0386 (s, 9), 0.0234 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 206.4 (C), 206.3 (C), 113.7 (C), 81.5 (CH_2), 76.4 (CH), 72.0 (CH), 52.7 (CH), 49.7 (CH), 48.9 (C), 44.9 (CH), 38.7 (CH_2), 38.4 (CH_2), 36.8 (CH_2), 35.6 (C), 33.4 (CH), 31.8 (CH_2), 31.7 (CH_2), 31.3 (CH_2), 28.4 (CH_2), 26.1 (CH_3), 25.9 (CH_3), 18.3 (C), 18.2 (C), 14.4 (CH_3), 12.3 (CH_3), –2.90 (CH_3), –4.42 (CH_3), –4.58 (CH_3). IR (thin film) 1965,

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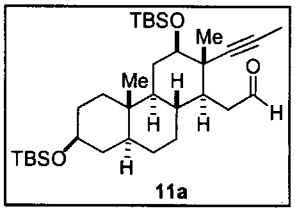
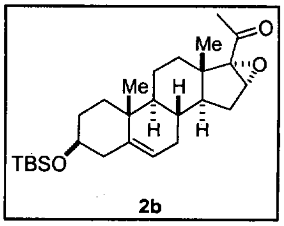
[15] (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.

1935, 1717. $[\alpha]_D$ –71.6 (c = 0.019, CH_2Cl_2). Anal. Calcd for $C_{33}H_{58}O_3Si_2$: C, 70.91; H, 10.46. Found: C, 71.14; H, 10.69.



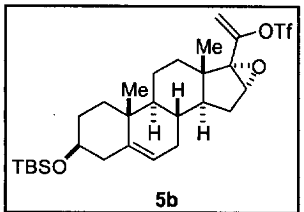
11a

3β,12β-Di(*t*-butyldimethylsilyloxy)-16,17-seco-5α-pregn-17(20)-yn-16-al (11a). To a solution of **5a** (142 mg, 0.20 mmol) in THF (800 μL, degassed) was added $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and PPh_3 (5.2 mg, 0.02 mmol). The mixture was stirred under Ar until becoming yellow and clear and Bu_3SnH (59 μL, 64 mg, 0.22 mmol) was then dropwise, whereupon the solution turned orange. Stirring was continued for 1.5 h while being monitored by TLC. Additional hydride was added in portions during this time period (60 μL each, 4 times total). This was then diluted with Et_2O (10 mL), concentrated and flash chromatographed (0.25%→5% EtOAc/hexanes) on deactivated silica to give aldehyde **11a** (63 mg, 0.11 mmol, 56%) of about 95% purity as a clear light yellow oil: R_f 0.40 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 9.76 (d, 1, J = 2.60), 3.62 (dd, 1, J = 4.29, 11.4), 3.52 (sept, 1, J = 5.20), 2.78 (dd, 1, J = 2.85, 17.3), 2.34 (ddd, 1, J = 2.90, 7.43, 17.2), 1.88 (ddd, 1, J = 3.06, 7.44, 10.7), 1.70 (s, 3), 1.66-0.76 (m, 15), 0.968 (s, 3), 0.885 (s, 9), 0.862 (s, 9), 0.734 (s, 3). $^{13}C\{^1H\}$ NMR (100 MHz) δ 202.8 (C), 86.7 (C), 77.2 (C), 76.8(CH), 71.9 (CH), 50.8 (CH), 45.9 (CH_2), 45.3 (CH), 44.4 (CH), 42.8 (C), 38.3 (CH_2), 36.8 (CH_2), 36.0 (CH_2), 35.4 (CH), 32.0 (CH_2), 31.7 (CH_2), 29.7 (CH_2), 28.5 (CH_2), 25.9 (CH_3), 25.8 (CH_3), 18.2 (C), 18.1 (C), 13.8 (CH_3), 12.2 (CH_3), 3.5 (CH_3), –4.3 (CH_3), –4.6 (CH_3), –4.9 (CH_3). IR (thin film) 2736, 1725. $[\alpha]_D$ –34.8 (c = 0.0029, CH_2CH_2). Attempts to further purify this compound for microanalysis were unsuccessful, due to the instability of this compound.



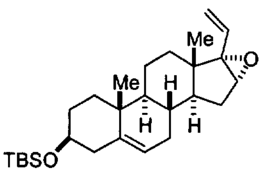
2b

3β-(*t*-butyldimethylsilyloxy)-16α,17α-oxidopregn-5-ene-20-one (2b). To a stirring solution of epoxy alcohol **6** (2.49 g, 7.59 mmol) in CH_2Cl_2 (30 mL) was added NEt_3 (1.25 mL, 901 mg, 9.00 mmol), TBSCl (1.26 g, 8.35 mmol) and DMAP (one spatulas). After stirring for 23 h, the solution was poured into H_2O (50 mL) and extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers was washed with 1 M HCl (70 mL), saturated $NaHCO_3$ (70 mL), brine (70 mL), dried, concentrated and flash chromatographed (2.5% EtOAc/hexanes) to give ketone **2b** (2.67 g, 6.03 mmol, 80 %). R_f 0.51 (20% EtOAc/hexanes). mp 118-119 °C. ^{1}H NMR (400 MHz) δ 5.28 (d, 1, J = 5.37), 3.66 (s, 1), 3.45 (sept, 1, J = 4.72), 2.24 (m, 1), 2.14 (ddd, 1, j = 2.22, 5.08, 13.4), 2.01 (s, 3), 1.94 (dd, 1, J = 6.15, 19.5), 1.9-0.8 (m, 14), 1.02 (s, 3), 0.99 (s, 3), 0.867 (s, 9), 0.0369 (s, 6). $^{13}C\{^1H\}$ NMR (100 MHz) δ 204.8 (C), 141.8 (CH), 120.4 (CH), 72.4 (CH), 70.9 (C), 60.4 (CH), 50.3 (CH), 45.5 (CH), 42.7 (CH_2), 41.4 (C), 37.2 (CH_2), 36.7 (C), 31.9(CH_2), 31.4 (CH_2), 31.3 (CH_2), 29.7 (CH), 27.5 (CH_2), 25.9 (CH), 25.9 (CH_3), 20.4 (CH_2), 19.3 (CH_3), 18.2 (C), 15.1 (CH_3). IR (thin film) 1703. $[\alpha]_D$ –8.75 (*c* = 0.0088, CH_2CH_2). Anal. Calcd for $C_{27}H_{44}O_3Si$: C, 72.92; H, 9.97. Found: C, 72.86; H, 10.18.



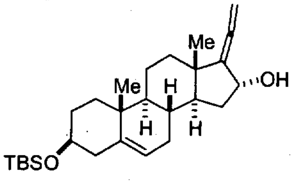
5b

3β-(*t*-butyldimethylsilyloxy)-16α,17α-oxido-20-(trifluoromethanesulfonyloxy) pregna-5,20-diene (5b). To a cold (–78 °C) solution of **2b** (2.95 g, 6.67 mmol) and $PhNTf_2$ (2.88 g, 8.00 mmol) in THF (33 mL) was added KHMDS (0.5 M in toluene, 16 mL, 8.00 mmol) dropwise over 45 min with cannula. The stirring was continued at this temperature for 2 h after the completion of the addition. The solution was warmed to rt, concentrated, and the brown residue was flash chromatographed (1%→5% EtOAc/hexanes) to give triflate **5b** (3.25 g, 5.66 mmol, 85 %) as a white solid, mp 77-79 °C. *Rf* 0.53 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 5.44 (d, 1, *J* = 3.88), 5.36 (d, 1, *J* = 3.86), 5.29 (br d, 1, *J* = 5.00), 3.64 (s, 1), 3.47 (sept, 1, *J* = 4.75), 2.0-0.8 (m, 16), 2.27-2.14 (m, 2), 1.00 (s, 3), 0.928 (s, 3), 0.873 (s, 9), 0.0431 (s, 6). $^{13}C\{^1H\}$ NMR (100 MHz) δ 150.7 (C), 141.6 (C), 120.4 (CH), 109.3 (CH_2), 72.3 (CH), 67.7 (C), 60.6 (CH), 50.2 (CH), 45.7 (CH), 42.7 (CH_2), 41,7 (C), 37.1 (CH_2), 36.6 (C), 31.9 (CH_2), 31.6 (CH_2), 31.3 (CH_2), 30.1 (CH), 26.7 (CH_2), 25.8 (CH_3), 20.4 (CH_2), 19.2 (CH_3), 18.1 (C), 15.4 (C), –4.7 (CH_3). IR (thin film); $[\alpha]_D$ –74.83 (*c* = 0.0101, CH_2CH_2). Anal. Calcd for $C_{28}H_{44}O_5SiSF$: C, 58.21; H, 7.68. Found: C, 58.39; H, 7.85.



4b

and

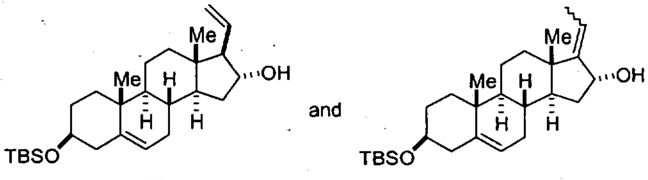


7b(α)

3β-(*t*-Butyldimethylsilyloxy)-16α,17α-oxidopregna-5,20-diene (4b) and 3β-(*t*-Butyldimethylsilyloxy)pregna-5,17(20),20-triene-16α-ol (7b,α-isomer). To a stirring yellow and cloudy solution of **5b** (402 mg, 0.7 mmol), $Pd(OAc)_2$ (15 mg, 0.07 mmol), PPh_3 (37 mg, 0.14 mmol) and LiCl (89 mg, 2.1 mmol) in THF (2.6 mL, degassed) was added Bu_3SnH (226 μL, 244 mg, 0.84 mmol) dropwise over 5 min. The stirring was continued for 14.5 h. The solution was diluted with Et_2O (2 mL), DBU (227 μL, 252 mg, 1.6 mmol) was added and the solution was titrated with 1 M I_2/Et_2O solution until the color remained,[14] and was then filtered through a plug of deactivated silica and concentrated. Flash chromatography (0%→20% EtOAc/hexanes) on deactivated silica gave allyl epoxide **4b** (70.7 mg, 0.17 mmol, 24%) and allenic alcohol **7b** (α-isomer) (112 mg, 0.272 mmol, 39%) as a white solid.

Allyl epoxide **4b**: R*f* 0.63 (20% EtOAc/hexanes). mp 134-135 °C. ^{1}H NMR (400 MHz) δ 6.12 (dd, 1, *J* = 10.8, 17.1), 5.38 (dd, 1, *J* = 1.99, 17.1), 5.29 (m, 1), 5.21 (dd, 1, *J* = 1.98, 10.8), 3.46 (sept, 1, *J* = 4.87), 3.27 (s, 1), 2.25-2.17 (m, 2), 1.9-0.8 (m, 15), 0.88 (s, 3), 0.87 (s, 12), 0.041 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 141.7(C), 131.0 (CH), 120.7 (CH), 117.5 (CH_2), 72.5 (CH), 69.5 (C), 63.2 (CH), 50.5 (CH), 45.6 (CH), 42.8 (CH_2), 41.8 (C), 37.3 (CH_2), 36.8 (C), 32.0 (CH_2), 31.6 (CH_2), 30.4 (CH), 27.7 (CH_2), 25.9 (CH_3), 20.5 (CH_2), 19.4 (CH_3), 18.2 (C), 15.6 (CH_3), –4.62 (CH_3). IR (thin film) 1667, 1637. $[\alpha]_D$ –63.36 (*c* = 0.0119, CH_2CH_2). Anal. Calcd for $C_{27}H_{44}O_2Si$: C, 75.64; H, 10.34. Found: C, 75.27; H, 10.50.

7b (α-isomer): R*f* 0.19 (30% EtOAc/hexanes). mp 153.5-154.5 °C. ^{1}H NMR (500 MHz) δ 5.31 (m, 1), 4.99 (dd, 1, *J* = 3.21, 9.97), 4.89 (dd, 1, *J* = 3.15, 9.96), 4.83 (m, 1), 3.48 (sept, 1, *J* = 4.77), 2.26 (m, 1), 2.17 (ddd, 1, *J* = 2.16, 4.92, 13.5), 1.99 (m, 1), 1.8-0.8 (m, 18), 1.00 (s, 3), 0.88 (s, 9), 0.87 (s, 3), 0.05 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 201.0 (C), 141.6 (C), 120.8 (CH), 118.4 (C), 80.1 (CH_2), 72.4 (CH), 72.4 (CH), 52.7 (CH), 50.3 (CH), 44.7 (C), 42.7 (CH_2), 37.3 (CH_2), 36.7 (C), 36.1 (CH_2), 35.6 (CH_2), 32.0 (CH_2), 31.6 (CH_2), 31.4 (CH), 25.9 (CH_3), 20.7 (CH_2), 19.4 (CH_3), 18.8 (CH_3), 18.2 (C), –4.62 (CH_3). IR (thin film) 3446, 1960. $[\alpha]_D$ –74.83 (*c* = 0.0101, CH_2CH_2). Anal. Calcd for $C_{27}H_{44}O_2Si$: C, 75.64; H, 10.34. Found: C, 75.55; H, 10.14.



8b

9b(*E* or *Z*)

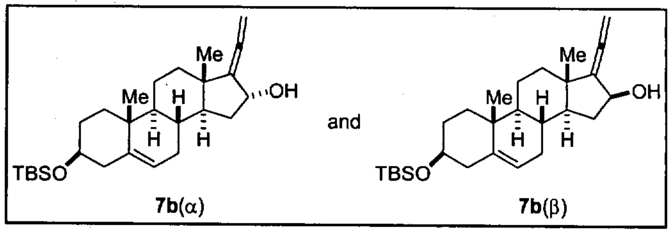
[17(20)*Z*] and [17(20)*E*]-3β-(*t*-butyldimethylsilyloxy)pregna-5,17(20)-diene-16α-ol (9b,*Z* and *E*),3β-(*t*-butyldimethylsilyloxy)pregna-5,20-diene-16α-ol (8b). To a stirring orange-yellow solution of **4b** (71.1 mg, 0.166 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol) and LiCl (24.7 mg, 0.583 mmol) in THF (650 μL, degassed) was added Bu_3SnH (49 μL, 53 mg, 0.183 mmol). The orange color turned light yellow upon addition of the reagent and stirring was continued for 1 h. The solution was diluted with Et_2O (2 mL), DBU (55 μL, 61 mg, 0.4 mmol) was added, and the solution was titrated with 1 M I_2 in Et_2O s until the color remained.[14] This was filtered through a plug of silica and concentrated. Flash chromatography with deactivated silica (0.5%→2% EtOAc/hexanes) afforded **9b** (*Z* isomer) (3.2 mg, 0.0074 mmol, 5%), allyl alcohol **9b** (*E*-isomer) (20.1 mg, 0.047 mmol, 28%) and a mixture of allyl alcohol **9b** (*Z*-isomer) and homoallyl alcohol **8b** (8.3 mg, 0.033 mmol, 21%), all as white solids. An analytical sample of **9b** (*E*-isomer) (7.4

mg, 0.017 mmol, 10%) was obtained by further purification of this mixture by chromatography on deactivated silica (1.5% EtOAc/hexanes).

9b (*Z*-isomer): R*f* 0.46 (20% EtOAc/hexanes). mp 91.5-92.5 °C. ^{1}H NMR (400 MHz) δ 5.33 (m, 2), 4.79 (m, 1), 3.48 (sept, 1, *J* = 4.92), 2.26 (m, 1), 2.17 (br dd, 1, *J* = 3.02, 13.4), 2.5-0.7 (m, 18), 1.56 (s, 3), 1.00 (s, 3), 0.877 (s, 9), 0.735 (s, 3), 0.0473 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 156.1, 141.6, 120.9, 117.7, 72.5, 71.2, 52.0, 50.6, 43.9, 42.8, 37.3, 36.8, 36.6, 36.0, 32.1, 31.8, 31.1, 25.9, 21.0, 20.3, 19.4, 18.3, 14.6, –4.58. IR (thin film) 3602, 3152, 1725, 1602. $[\alpha]_D$ –35.56 (*c* = 0.0009, CH_2CH_2).

9b (*E*-isomer): R*f* 0.42 (20% EtOAc/hexanes). mp 96.5-97 °C. ^{1}H NMR (400 MHz) δ 5.58 (q, 1, *J* = 7.19), 5.31 (m, 1), 4.43 (br s, 1), 3.47 (sept, 1, *J* = 5.00), 2.26 (m, 2), 2.16 (m, 1), 1.98 (br d, 1, *J* = 17.0), 1.8-0.7 (m, 16), 1.73 (d, 3, *J* = 7.17), 1.00 (s, 3), 0.876 (s, 9), 0.868 (s, 3), 0.0462 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 155.4 (C), 141.5 (C), 120.9 (CH), 119.6 (CH), 78.9 (CH), 74.4 (CH), 72.5 (CH), 52.8 (CH), 50.2 (CH), 44.2 (C), 42.8 (C), 37.3 (CH_2), 37.2 (CH_2), 36.7 (C), 35.1 (CH_2), 32.0 (CH_3), 31.6 (CH_2), 30.8 (CH), 25.9 (CH_3), 21.1 (CH_2), 19.4 (CH), 18.2 (C), 17.3 (CH), 13.2 (CH), –4.60 (CH_3). IR (thin film) 3601, 1448, 1721, 1669. $[\alpha]_D$ –47.27 (*c* = 0.0033, CH_2CH_2). Anal. Calcd for $C_{27}H_{48}O_2Si$: C, 74.94; H, 11.18. Found: C, 74.58; H, 10.99.

8b: R*f* 0.42 (20% EtOAc/hexanes). mp 120-121 °C. ^{1}H NMR (400 MHz) δ 5.80 (ddd, 1, *J* = 8.63, 9.27, 17.9), 5.31 (m, 1), 5.14 (br d, 1, *J* = 4.67), 5.10 (br s, 1), 4.24 (br t, 1, *J* = 7.17), 3.48 (sept, 1, *J* = 4.83), 2.26 (m, 1), 2.16 (br dd, 1, *J* = 3.10, 13.2), 2.0-0.7 (m, 18), 1.90 (t, 1, *J* = 7.55), 0.989 (s, 3), 0.878 (s, 9), 0.656 (s, 3), 0.0469 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 141.7, 136.9, 117.0, 76.6, 72.5, 66.2, 53.6, 50.4, 44.6, 42.8, 37.3, 36.7, 35.7, 32.1, 31.8, 31.5, 29.7, 25.9, 20.2, 19.5, 18.3, 14.1, –4.59. IR (thin film) 3401, 1660, 1638. $[\alpha]_D$ –55.38 (*c* = 0.0013, CH_2CH_2).



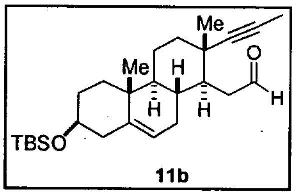
7b(α)

7b(β)

3β-(*t*-butyldimethylsilyloxy)pregna-5,17(20),20-triene-16α-ol (7b,α-isomer) and 3β-(*t*-butyldimethylsilyloxy)pregna-5,17(20),20-triene-16β-ol (7b,β-isomer). Triflate **5b** (192 mg, 0.33 mmol), $Pd(OAc)_2$ (75 mg, 0.33 mol) and PPh_3 (438 mg, 1.67 mmol) was dissolved in THF (1 mL, degassed) and stirred at rt for 46 h and then at 40 °C for 19 h. After being cooled to rt, the solution was filtered through a plug of silica and concentrated. Flash chromatography (100% CH_2Cl_2) on basic Al_2O_3 gave **7b** (α-isomer) (54.3 mg, 0.13 mmol, 38%), a mixture of α and β-isomers (25.1 mg, 0.059 mmol, 18%) and **7b** (β-isomer) (35.1 mg, 0.082 mmol, 25%). The spectral data of **7b** (α-isomer) were identical to those obtained from catalytic Pd-reduction.

7b (β-isomer): R*f* 0.39 (20% EtOAc/hexanes). mp 159.5-160.5 °C. ^{1}H NMR (500 MHz) δ 5.30 (m, 1), 4.90 (dd, 1, *J* = 10.0, 3.16), 4.86 (dd, 1, *J* = 10.0, 2.85), 4.77 (m, 1), 3.47 (sept, 1, *J* = 4.80), 2.28-2.16 (m, 2), 2.03 (m, 1), 1.85-0.8 (m, 15), 1.05 (s, 3), 1.01 (s, 3), 0.88 (s, 9), 0.04 (s, 3). ^{13}C{^{1}H} NMR (100 MHz) δ 202.6, 141.7, 120.6, 116.7, 79.2, 74.1, 72.5, 52.8, 50.3, 43.6, 42.8, 37.3, 36.7, 36.2, 35.0, 32.0, 31.8, 31.3, 25.9, 20.7, 19.4, 19.4, 18,2, –4.60. IR (thin film) 3599, 3446, 1958, 1602. $[\alpha]_D$ +1.538 (*c* = 0.0013, CHCl$_3$).

3β-(*t*-butyldimethylsilyloxy)-16,17-secopregn-5en-20-yn-16α-al (11b).



11b

Triflate **5b** (50 mg, 0.087 mol) was dissolved in THF (450 μL) and degassed by passing Ar through for 5 min. To this was added Pd(OAc)$_2$ (2.2 mg, 0.01 mmol) and PPh$_3$ (5.2 mg, 0.02 mmol) and stirred until the solution becomes yellow and cloudy (~5 min). Bu$_3$SnH (24 μL, 26 mg, 0.09 mmol) was then added dropwise and stirring was continued for 5 min. The solution was diluted with Et$_2$O (10 mL) and concentrated. The crude ^{1}H NMR showed **5b** and the aldehyde, with trace of α-allenic alcohol **7b** (α-isomer). Flash chromatography (1% EtOAc/hexanes, 1% NEt$_3$) of the crude products on deactivated silica gave aldehyde **11b** (24 mg, 0.043 mmol, 49%) and **7b** (α-isomer) (8 mg, 0.018 mmol, 21 %). The spectral data of α-allenic alcohol was identical to those obtained previously. Attempts to further purify the aldehyde **11b** for microanalysis was unsuccessful.

Aldehyde **11b**: R*f* 0.36 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz) δ 9.77 (dd, 1, *J* = 1.90, 2.70), 5.28 (br s, 1), 5.24 (m, 1), 3.45 (sept, 1, *J* = 5.02), 2.68 (ddd, 1, *J* = 1.75, 4.59, 16.8), 2.32 (ddd, 1, *J* = 2.88, 6.41, 16.8), 2.25-0.8 (m, 17), 1.06 (s, 3), 0.936 (s, 3), 0.866 (s, 9), 0.0361 (s, 6). ^{13}C{^{1}H} NMR (100 MHz) δ 202.9 (CH), 141.1 (C), 120.2 (CH), 87.6 (C), 76.8 (C), 72.4 (CH), 49.2 (CH), 46.7 (CH$_2$), 42.4 (CH$_2$), 39.5 (CH$_2$), 37.0 (CH$_2$), 36.8 (C), 35.0 (C), 33.2 (CH), 32.3 (CH$_2$), 32.0 (CH$_2$), 31.9 (C), 25.9 (CH$_3$), 1.8 (CH$_2$), 19.5 (CH3), 19.3 (CH$_3$), 18.2 (C), 3.4 (CH$_3$), –4.6 (CH$_3$). IR (thin film) 1718, 1672.