Supplementary data

Hydrogen atom transfer methodology for the synthesis of C-22, C-23, and C-25 stereoisomers of cephalostatin north 1 side chain from spirostan sapogenins

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(22*S*,23*R*,25*R*)-3β-Methoxy-26-pivaloyloxy-5α-furostan-23-ol (6-*R*). To a solution of compound **5-*R*** (1.06 g, 2.366 mmol) in CH_2Cl_2 (40 mL) and dry pyridine (40 mL) was added slowly pivaloyl chloride (220 μL, 2.57 mmol) at room temperature under nitrogen and stirred for 24 h. The mixture was poured into an aqueous solution of HCl (10%) and extracted with $CHCl_3$. The combined extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 90:10) to give compound **6-*R*** (1.2 g, 2.255 mmol, 95%): mp 110–110.5 ºC (from *n*-hexane–EtOAc); $[\alpha]_D$ –6 (*c* 0.42); IR 3492, 1728 cm^{-1}; ^1H NMR 0.59 (1H, m), 0.77 (3H, s), 0.78 (3H, s), 0.94 (3H, d, *J* = 6.7 Hz), 1.03 (3H, d, *J* = 6.7 Hz), 1.17 (9H, s), 3.09 (1H, dddd, *J* = 4.6, 4.6, 10.9, 10.9 Hz), 3.30 (3H, s), 3.33 (1H, dd, *J* = 3.7, 8.3 Hz), 3.88 (1H, dd, *J* = 6.6, 10.7 Hz), 3.88 (1H, m), 3.96 (1H, dd, *J* = 5.4, 10.8 Hz), 4.32 (1H, ddd, *J* = 5.1, 7.8, 7.8

Hz); ^{13}C NMR 12.2 (CH_3), 16.1 (CH_3), 16.5 (CH_3), 20.5 (CH_3), 20.8 (CH_2), 27.1 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2), 29.4 (CH), 32.1 (CH_2), 32.2 (CH_2), 32.3 (CH), 34.2 (CH_2), 35.1 (CH), 35.8 (C), 36.3 (CH_2), 36.9 (CH_2), 39.5 (CH_2), 41.4 (C), 44.7 (CH), 54.4 (CH), 55.4 (CH_3), 56.7 (CH), 65.9 (CH), 69.6 (CH), 69.7 (CH_2), 79.7 (CH), 83.3 (CH), 92.9 (CH), 178.5 (C) (one quaternary carbon is missing); MS *m*/*z* (rel intensity) 531 (M^+ – H, <1), 430 (<1), 389 (8), 345 (42), 287 (100); HRMS calcd for $C_{33}H_{55}O_5$ 531.4050; found 531.4098. Anal. Calcd for $C_{33}H_{56}O_5$: C, 74.39; H, 10.59. Found: C, 74.03; H, 10.91.

(22*S*,23*S*,25*R*)-3β-Methoxy-26-pivaloyloxy-5α-furostan-23-ol (6-*S*). To a solution of compound (**5-*S***) (4 g, 8.93 mmol) in CH_2Cl_2 (250 mL) and dry pyridine (250 mL) was added slowly pivaloyl chloride (1.9 mL, 16.0 mmol) at room temperature under nitrogen and stirred for 25 h. The mixture was poured into an aqueous solution of HCl (10%) and extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 80:20) to give compound **6-*S*** (4.6 g, 8.64 mmol, 97%): amorphous; $[\alpha]_D$ –24 (*c* 0.26); IR 3589, 3436, 1728 cm^{-1}; ^{1}H NMR (400 MHz) 0.57 (1H, m), 0.74 (3H, s), 0.76 (3H, s), 0.96 (3H, d, *J* = 7.0 Hz), 0.97 (3H, d, *J* = 7.0 Hz), 1.15 (9H, s), 1.97 (1H, m), 3.07 (1H, m), 3.19 (1H, dd, *J* = 4.5, 8.3 Hz), 3.29 (3H, s), 3.62 (1H, ddd, *J* = 5.3, 10.8, 10.8 Hz), 3.95 (1H, d, *J* = 5.7 Hz), 3.95 (1H, d, *J* = 5.0 Hz), 4.32 (1H, ddd, *J* = 5.0, 7.0, 7.0 Hz); ^{13}C NMR (100.6 MHz) 12.2 (CH_3), 16.4 (CH_3), 18.2 (CH_3), 19.5 (CH_3), 20.7 (CH_2), 27.1 (C), 27.0 (3 × CH_3), 27.7 (CH_2), 28.6 (CH_2), 29.3 (CH), 32.09 (CH_2), 32.14 (CH_2), 33.4 (CH), 34.2 (CH_2), 35.1 (CH), 35.8 (C), 36.8 (CH_2), 37.9 (CH_2), 39.5 (CH_2), 41.2 (C), 44.7 (CH), 54.3 (CH), 55.4 (CH_3), 56.7 (CH), 65.4 (CH), 67.9 (CH_2), 69.7 (CH), 79.7 (CH), 83.4 (CH), 92.9 (CH), 178.4 (C); MS *m*/*z* (rel intensity) 514 (M^+ – H_2O, 7), 412

(4), 287 (100); HRMS calcd for $C_{33}H_{54}O_4$ 514.4022; found 514.4037. Anal. Calcd for $C_{33}H_{56}O_5$: C, 74.39; H, 10.59. Found: C, 74.39; H, 10.64.

(22*S*,23*R*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-pivaloyloxy-5α-furostan (7-*R*). To a solution of compound **6-*R*** (625 mg, 1.14 mmol) in dry CH_2Cl_2 (35 mL) containing TEA (0.98 mL, 7.08 mmol) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.025 mL, 5.3 mmol) and stirred at room temperature for 3 h. The mixture was then poured into a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 97:3) to give compound **7-*R*** (0.6 g, 0.927 mmol, 81%): amorphous; $[\alpha]_D$ –2 (*c* 0.31); IR 1728 cm^{-1}; ^1H NMR 0.03 (3H, s), 0.05 (3H, s), 0.75 (3H, s), 0.77 (3H, s), 0.86 (9H, s), 0.89 (3H, d, *J* = 6.7 Hz), 1.01 (3H, d, *J* = 6.7 Hz), 1.16 (9H, s), 1.55 (1H, dd, *J* = 4.3, 8.1 Hz), 3.1 (1H, dddd, *J* = 6.4, 6.4, 11.1, 11.1, Hz), 3.32 (3H, s), 3.34 (1H, dd, *J* = 4.2, 8.4 Hz), 3.80 (1H, ddd, *J* = 3.9, 3.9, 7.8 Hz), 3.83 (1H, dd, *J* = 6.1, 10.7 Hz), 3.89 (1H, dd, *J* = 5.7, 10.7 Hz), 4.25 (1H, ddd, *J* = 5.3, 5.3, 7.7 Hz); ^{13}C NMR –4.6 (CH_3), –3.8 (CH_3), 12.2 (CH_3), 16.8 (CH_3), 16.9 (CH_3), 18.1 (C), 20.3 (CH_3), 20.8 (CH_2), 26.0 (3 × CH_3), 27.2 (3 × CH_3), 27.9 (CH_2), 28.7 (CH_2), 28.8 (CH), 32.1 (CH_2), 32.2 (CH_2), 33.9 (CH), 34.3 (CH_2), 35.2 (CH), 35.8 (C), 36.9 (CH_2), 37.6 (CH_2), 38.8 (C), 39.7 (CH_2), 41.1 (C), 44.8 (CH), 54.4 (CH), 55.5 (CH_3), 56.7 (CH), 65.5 (CH), 69.6 (CH_2), 71.2 (CH), 79.8 (CH), 83.2 (CH), 92.8 (CH), 178.5 (C); MS *m*/*z* (rel intensity) 645 (M^+ – H, <1), 589 (9), 345 (8), 301 (12), 287 (100); HRMS calcd for $C_{39}H_{69}O_5Si$ 645.4914; found 645.4832. Anal. Calcd for $C_{39}H_{70}O_5Si$: C, 72.39; H, 10.91. Found: C, 72.01; H, 11.23.

(22*S*,23S,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-pivaloyloxy-5α-furostan (7-*S*). To a solution of compound **6-*S*** (4.8 g, 9.02 mmol) in dry CH_2Cl_2 (250

mL) containing TEA (7.5 mL, 54.2 mmol) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (7.9 mL, 40.8 mmol) and stirred at room temperature for 6.5 h. The mixture was then poured into a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 95:5) to give compound **7-*S*** (5.7 g, 8.8 mmol, 98%): amorphous; $[\alpha]_D$ –20 (*c* 0.18); IR 1729 cm^{-1}; ^1H NMR 0.03 (3H, s), 0.04 (3H, s), 0.61 (1H, m), 0.76 (3H, s), 0.78 (3H, s), 0.84 (9H, s), 0.95 (3H, d, *J* = 6.7 Hz), 0.99 (3H, d, *J* = 6.7 Hz), 1.17 (9H, s), 3.06 (1H, dddd, *J* = 4.4, 4.4, 10.6, 10.6 Hz), 3.26 (1H, dd, *J* = 5.0. 8.3 Hz), 3.32 (3H, s), 3.78 (1H, ddd, *J* = 5.0, 5.0, 8.7 Hz), 3.87 (1H, dd, *J* = 6.3, 10.7 Hz), 3.94 (1H, dd, *J* = 4.2, 10.8 Hz), 4.24 (1H, ddd, *J* = 5.5, 7.6, 7.6 Hz); ^{13}C NMR –4.8 (CH_3), –3.8 (CH_3), 12.2 (CH_3), 16.6 (CH_3), 18.1 (CH_3), 18.2 (C), 19.7 (CH_3), 21.2 (CH_2), 26.0 (3 × CH_3), 27.1 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2), 28.9 (CH), 31.9 (CH_2), 32.1 (CH_2), 32.9 (CH), 34.2 (CH_2), 35.1 (CH), 35.8 (C), 36.9 (CH_2), 37.1 (CH_2), 38.7 (C), 39.7 (CH_2), 41.2 (C), 44.7 (CH), 54.4 (CH), 55.4 (CH_3), 56.6 (CH), 65.5 (CH), 68.1 (CH_2), 70.8 (CH), 79.7 (CH), 82.6 (CH), 91.9 (CH), 178.3 (C); MS *m*/*z* (rel intensity) 590 (M^+ – ^{t}Bu, 5), 589 (13), 557 (7), 287 (100); HRMS calcd for $C_{35}H_{61}O_5Si$ 589.4302; found 589.4288. Anal. Calcd for $C_{39}H_{70}O_5Si$: C, 72.39; H, 10.91. Found: C, 72.57; H, 10.90.

(22*S*,23*R*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furostan-26-ol (8-*R*). A solution of compound **7-*R*** (50 mg, 0.077 mmol) in MeOH (15 mL) containing KOH (0.45 g) was heated at 50 ºC for 24 h. The mixture was poured into an aqueous solution of HCl (10%) and extracted with AcOEt. The combined extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 90:10 → 85:15) to give compound **8-*R*** (40 mg, 0.071 mmol, 92%): amorphous; $[\alpha]_D$ –5.4 (*c* 0.24); IR

3639, 3468, cm^{-1}; ^1H NMR 0.07 (3H, s), 0.08 (3H, s), 0.60 (1H, m), 0.77 (3H, s), 0.79 (3H, s), 0.88 (9H, s), 0.90 (3H, d, *J* = 6.8 Hz), 1.03 (3H, d, *J* = 6.7 Hz), 1.55 (1H, dd, *J* = 4.3, 8.1 Hz), 3.1 (1H, dddd, *J* = 6.4, 6.4, 11.1, 11.1 Hz), 3.32 (3H, s), 3.38–3.46 (3H, m), 3.86 (1H, ddd, *J* = 5.5, 5.5, 5.5 Hz), 4.30 (1H, ddd, *J* = 5.0, 8.1, 8.1 Hz); ^{13}C NMR – 4.5 (CH_3), –4.2 (CH_3), 12.3 (CH_3), 16.7 (CH_3), 18.0 (C), 18.1 (CH_3), 20.7 (CH_3), 20.8 (CH_2), 26.0 (3 × CH_3), 27.9 (CH_2), 28.7 (CH_2), 31.4 (CH), 32.2 (CH_2), 32.2 (CH_2), 34.3 (CH_2), 34.9 (CH), 35.2 (CH), 35.9 (C), 36.9 (CH_2), 38.6 (CH_2), 39.6 (CH_2), 41.2 (C), 44.8 (CH), 54.4 (CH), 55.5 (CH_3), 56.8 (CH), 65.6 (CH), 68.9 (CH_2), 72.1 (CH), 79.8 (CH), 83.4 (CH), 92.5 (CH); MS *m*/*z* (rel intensity) 544 (M^+ – H_2O, <1), 505 (9), 487 (3), 287 (100); HRMS calcd for $C_{34}H_{60}O_3Si$ 544.4312; found 544.4292. Anal. Calcd for $C_{34}H_{62}O_4Si$: C, 72.54; H, 11.10. Found: C, 72.71; H, 11.16.

(22*S*,23*S*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furostan-26-ol (8-*S*). A solution of compound **7-*S*** (5.7 g, 8.82 mmol) in MeOH (1.4 L) containing KOH (51 g) was stirred at room temperature for 46 h. The mixture was poured into an aqueous solution of HCl (10%) and extracted with EtOAc. The combined extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 90:10 → 85:15) to give compound **8-*S*** (4.5 g, 8.01 mmol, 91%): amorphous; $[\alpha]_D$ –11.4 (*c* 0.22); IR (neat) 3433 cm^{-1}; ^1H NMR (400 MHz) –0.01 (3H, s), 0.00 (3H, s), 0.53 (1H, m), 0.72 (6H, s), 0.81 (9H, s), 0.82 (3H, d, *J* = 6.9 Hz), 0.94 (3H, d, *J* = 6.7 Hz), 2.70 (1H, br s), 3.03 (1H, dddd, *J* = 4.2, 4.2, 11.0, 11.0 Hz), 3.25 (3H, s), 3.35 (2H, d, *J* = 5.6 Hz), 3.35 (1H, m), 3.75 (1H, ddd, *J* = 5.6, 5.6, 5.6 Hz), 4.18 (1H, ddd, *J* = 5.3, 7.7, 7.7 Hz); ^{13}C NMR (100.6 MHz) –4.8 (CH_3), –4.1 (CH_3), 12.2 (CH_3), 16.6 (CH_3), 18.2 (C), 18.4 (CH_3), 19.6 (CH_3), 20.8 (CH_2), 26.0 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2), 32.0 (CH_2), 32.2 (CH_2), 32.3 (CH), 33.4 (CH), 34.3 (CH_2), 35.2 (CH), 35.8 (C), 36.9

(CH_2), 38.7 (CH_2), 39.7 (CH_2), 41.3 (C), 44.8 (CH), 54.4 (CH), 55.4 (CH_3), 56.7 (CH), 65.7 (CH), 68.0 (CH_2), 71.8 (CH), 79.8 (CH), 82.8 (CH), 91.0 (CH); MS *m*/*z* (rel intensity) 544 (M^+ – H_2O, 1), 505 (2), 287 (100); HRMS calcd for $C_{34}H_{60}O_3Si$ 544.4312; found 544.4300. Anal. Calcd for $C_{34}H_{62}O_4Si$: C, 72.54; H, 11.10. Found: C, 72.65; H, 11.19.

(22*S*,23*R*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-(2-nitrophenylselenenyl)-5α-furostan (9-*R*). To a solution of compound **8-*R*** (140 mg, 0.249 mmol) in dry THF (8 mL) and *o*-nitrophenylselenocyanate (84 mg, 0.374 mmol) at room temperature was added freshly distilled *n*-Bu_3P (95 μL, 77 mg, 0.38 mmol) dropwise under nitrogen. After 0.5 h, the solvent was removed in vacuo and the residue purified by column chromatography (hexanes–EtOAc, 95:5) to give the title compound **9-*R*** (183 mg, 0.245 mmol, 98.5%): mp 140–141 °C (from EtOAc–MeOH); $[\alpha]_D$ +4 (*c* 0.2); IR 3065, 1592, 1591 cm^{-1}; ^1H NMR 0.03 (3H, s), 0.07 (3H, s), 0.61 (1H, m), 0.77 (3H, s), 0.80 (3H, s), 0.84 (9H, s), 1.04 (3H, d, *J* = 6.6 Hz), 1.09 (3H, d, *J* = 6.6 Hz), 2.75 (1H, dd, *J* = 8.2, 11.6 Hz), 2.99 (1H, dd, *J* = 4.9, 11.6 Hz), 3.11 (1H, dddd, *J* = 4.5, 4.5, 10.7, 10.7 Hz), 3.33 (3H, s), 3.35 (1H, dd, *J* = 4.0, 8.4 Hz), 3.84 (1H, ddd, *J* = 3.3, 3.3, 7.6 Hz), 4.28 (1H, m), 7.28 (1H, dd, *J* = 7.9, 8.2 Hz), 7.49 (2H, m), 8.28 (1H, d, *J* = 8.2 Hz); ^{13}C NMR –4.4 (CH_3), –3.7 (CH_3), 12.3 (CH_3), 16.8 (CH_3), 18.0 (C), 20.2 (CH_3), 20.3 (CH_3), 20.8 (CH_2), 25.9 (3 × CH_3), 27.8 (CH_2), 28.6 (CH), 28.7 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.1 (CH), 34.2 (CH_2), 35.2 (CH_2), 35.2 (CH), 35.8 (C), 36.8 (CH_2), 39.6 (CH_2), 41.1 (C), 41.4 (CH_2), 44.7 (CH), 54.3 (CH), 55.5 (CH_3), 56.7 (CH), 65.3 (CH), 71.3 (CH), 79.7 (CH), 83.3 (CH), 92.9 (CH), 125.0 (CH), 126.3 (CH), 129.2 (CH), 131.5 (C), 133.3 (CH), 134.7 (C); MS *m*/*z* (rel intensity) 747 (M^+, <1), 690 (16), 402 (33). Anal. Calcd for $C_{40}H_{65}O_5NSeSi$: C, 64.32; H, 8.77; N, 1.88. Found: C, 64.12; H, 8.97; N, 1.88.

(22*S*,23*S*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-(2-nitrophenylselenenyl)-5α-furostan (9-*S*). To a solution of compound **8-*S*** (609 mg, 1.08 mmol) in dry THF (25 mL) and *o*-nitrophenylselenocyanate (367 mg, 1.62 mmol) at room temperature was added freshly distilled *n*-Bu_3P (403 μL, 327 mg, 1.62 mmol) dropwise under nitrogen. After 0.5 h, the solvent was removed in vacuo and the residue purified by column chromatography (hexanes–EtOAc, 90:10) to give the title compound **9-*S*** (788 mg, 1.05 mmol, 97%): amorphous; $[\alpha]_D$ +8.6 (*c* 0.28); IR 1520, cm^{-1}; ^1H NMR 0.04 (3H, s), 0.05 (3H, s), 0.76 (3H, s), 0.80 (3H, s), 0.87 (9H, s), 0.99 (3H, d, *J* = 6.7 Hz), 1.11 (3H, d, *J* = 6.7 Hz), 2.70 (1H, dd, *J* = 8.8, 11.3 Hz), 3.11 (2H, m), 3.29 (1H, dd, *J* = 4.4, 8.5 Hz), 3.33 (3H, s), 3.85 (1H, ddd, *J* = 6.2, 6.2, 6.2 Hz), 4.22 (1H, ddd, *J* = 5.4, 7.7, 7.7 Hz), 7.28 (1H, dd, *J* = 8.0, 8.0 Hz), 7.49 (1H, dd, *J* = 7.0, 7.0 Hz), 7.53 (1H, d, *J* = 7.8 Hz), 8.25 (1H, d, *J* = 8.0 Hz); ^{13}C NMR (100.6 MHz) –4.7 (CH_3), –3.9 (CH_3), 12.3 (CH_3), 16.8 (CH_3), 18.2 (C), 19.4 (CH_3), 20.8 (CH_2), 21.1 (CH_3), 26.0 (3 × CH_3), 27.9 (CH_2), 28.8 (CH_2), 29.1 (CH), 32.0 (CH_2), 32.2 (CH_2), 32.7 (CH), 34.3 (CH_2), 34.2 (CH_2), 35.2 (CH), 35.9 (C), 36.9 (CH_2), 39.7 (CH_2), 41.2 (C), 41.3 (CH_2), 44.8 (CH), 54.4 (CH), 55.5 (CH_3), 56.7 (CH), 65.4 (CH), 70.6 (CH), 79.8 (CH), 82.9 (CH), 91.3 (CH), 125.1 (CH), 126.3 (CH), 128.8 (CH), 131.6 (C), 133.4 (CH), 133.9 (C); MS *m*/*z* (rel intensity) 690 (M^+ – ^{t}Bu, 6), 689 (1), 287 (100); HRMS calcd for $C_{36}H_{56}NO_5{}^{80}SeSi$ 690.3093; found 690.3048. Anal. Calcd for $C_{40}H_{65}NO_5SeSi$: C, 64.32; H, 8.77; N, 1.88. Found: C, 64.23; H, 8.96; N, 1.93.

(22*S*,23*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furost-25-ene (10-*R*). To a solution of **9-*R*** (450 mg, 0.6 mmol) in THF (45 mL) was added H_2O_2 (0.6 mL, 30% w/w) dropwise at room temperature. The mixture was stirred for 3 h, poured into water and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography

(benzene) to give compound **10-*R*** (300 mg, 0.551 mmol, 92%): amorphous; $[\alpha]_D$ –15 (*c* 0.254); IR 3076, 1646, 1462 cm^{-1}; ^1H NMR 0.05 (3H, s), 0.06 (3H, s), 0.61 (1H, m), 0.80 (6H, s), 0.88 (9H, s), 1.03 (3H, d, *J* = 6.7 Hz), 1.73 (3H, s), 1.97 (1H, ddd, *J* = 6.6, 6.6, 12.8 Hz), 2.08 (1H, m), 2.26 (2H, d, *J* = 6 Hz), 3.11 (1H, dddd, *J* = 4.6, 4.6, 10.7, 10.7 Hz), 3.33 (3H, s), 3.39 (1H, dd, *J* = 8.4, 3.8 Hz), 3.94 (1H, ddd, *J* = 5.9, 5.9, 5.9 Hz), 4.28 (1H, ddd, *J* = 5.3, 5.3, 7.8 Hz), 4.75 (1H, brs), 4.78 (1H, brs); ^{13}C NMR –4.7 (CH_3), –4.2 (CH_3), 12.3 (CH_3), 16.9 (CH_3), 18.2 (C), 20.3 (CH_3), 20.8 (CH_2), 23.1 (CH_3), 26.0 (3 × CH_3), 27.9 (CH_2), 28.7 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 33.3 (CH), 34.3 (CH_2), 35.2 (CH), 35.9 (C), 36.9 (CH_2), 39.8 (CH_2), 41.2 (C), 42.6 (CH_2), 44.8 (CH), 54.4 (CH), 55.5 (CH_3), 56.7 (CH), 65.7 (CH), 71.7 (CH), 79.8 (CH), 83.0 (CH), 92.0 (CH), 113.2 (CH_2), 142.5 (C); MS *m*/*z* (rel intensity) 543 (M^+ – H, <1), 529 (<1), 489 (40), 345 (10), 287 (100); HRMS calcd for $C_{34}H_{59}O_3Si$ 543.4234; found 543.4233. Anal. Calcd for $C_{34}H_{60}O_3Si$: C, 74.94; H, 11.10. Found: C, 75.00; H, 11.05.

(22*S*,23*S*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furost-25-ene (10-*S*). To a solution of compound **9-*S*** (376 mg, 0.5 mmol) in THF (37 mL) was added H_2O_2 (0.5 mL, 30% w/w) dropwise at room temperature. The mixture was stirred for 4 h, poured into water and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 97:3) to give compound **10-*S*** (223 mg, 0.41 mmol, 82%): mp 116.3–116.6 °C (from EtOAc); $[\alpha]_D$ –9 (*c* 0.22); IR 3080, 1450 cm^{-1}; ^1H NMR (400 MHz) –0.01 (3H, s), 0.00 (3H, s), 0.76 (6H, s), 0.82 (9H, s), 0.96 (3H, d, *J* = 6.7 Hz), 1.68 (3H, s), 3.06 (1H, m), 3.27 (1H, dd, *J* = 4.3, 8.6 Hz), 3.28 (3H, s), 3.81 (1H, ddd, *J* = 4.2, 4.2, 8.0 Hz), 4.21 (1H, ddd, *J* = 0.0, 4.1, 7.9 Hz), 4.72 (1H, br s), 4.73 (1H, br s); ^{13}C NMR (100.6 MHz) –4.8 (CH_3), –4.1 (CH_3), 12.2 (CH_3), 16.8 (CH_3), 18.2 (C), 19.4 (CH_3), 20.8 (CH_2), 22.7 (CH_3), 26.0 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2),

32.0 (CH_2), 32.2 (CH_2), 32.6 (CH), 34.3 (CH_2), 35.1 (CH), 35.8 (C), 36.9 (CH_2), 39.8 (CH_2), 41.3 (C), 42.1 (CH_2), 44.7 (CH), 54.4 (CH), 55.4 (CH_3), 56.7 (CH), 65.4 (CH), 70.9 (CH), 79.7 (CH), 82.7 (CH), 91.3 (CH), 113.2 (CH_2), 142.3 (C); MS *m*/*z* (rel intensity) 487 (M^+ – ^{t}Bu, 19), 457 (13), 255 (100); HRMS calcd for $C_{30}H_{51}O_3Si$ 487.3607; found 487.3581. Anal. Calcd for $C_{34}H_{60}O_3Si$: C, 74.94; H, 11.10. Found: C, 74.94; H, 10.96.

(22*S*,23*R*,25*S*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-acetoxy-5α-furostan-25-ol (12-*R*) and (22*S*,23*R*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-acetoxy-5α-furostan-25-ol (14-*R*). To a solution of compound **10-*R*** (180 mg, 0.33 mmol) in dry CH_2Cl_2 was added pyridine (58 mL, 0.7 mmol) and OsO_4 (92 mg, 0.36 mmol). After 1.5 h, the solvent was removed in vacuo, and the residue dissolved in THF (4 mL) and treated with aqueous saturated solution of Na_2SO_3 (4 mL). The mixture was refluxed for 2 h, poured into an aqueous saturated solution of $NaHCO_3$ and extracted with EtOAc. The crude residue of the inseparable mixture of diols **11-*R*** and **13-*R***, was acetylated with Ac_2O and pyridine to give after carefully chromatography (hexanes–EtOAc, 93:7) compound **12-*R*** (66 mg, 0.106 mmol, 32%) and compound **14-*R*** (137 mg, 0.221 mmol, 67%). Compound **12-*R***: amorphous; $[\alpha]_D$ –5 (*c* 0.55); IR 3405, 1743 cm^{-1}; ^{1}H NMR – 0.09 (3H, s), 0.10 (3H, s), 0.61 (1H, m), 0.77 (3H, s), 0.79 (3H, s), 0.89 (9H, s), 1.05 (3H, d, *J* = 6.7 Hz), 1.19 (3H, s), 1.55 (1H, dd, *J* = 3.8, 7.8 Hz), 2.09 (3H, s), 3.11 (1H, dddd, *J* = 4.6, 4.6, 10.8, 10.8 Hz), 3.33 (3H, s), 3.41 (1H, dd, *J* = 7.2, 7.2 Hz), 3.89 (1H, ddd, *J* = 5.0, 7.0, 7.0 Hz), 3.95 (1H, d, *J* = 10.9 Hz), 3.96 (1H, d, *J* = 10.9), 4.37 (1H, ddd, *J* = 4.7, 7.5, 7.5 Hz); ^{13}C NMR –4.5 (CH_3), –4.3 (CH_3), 12.2 (CH_3), 16.4 (CH_3), 17.9 (C), 20.7 (CH_2), 21.0 (2 × CH_3), 25.8 (3 × CH_3), 26.2 (CH_3), 27.9 (CH_2), 28.6 (CH_2), 32.17 (CH_2), 32.21 (CH_2), 34.3 (CH_2), 35.2 (CH), 35.9 (C), 35.9 (CH), 36.9 (CH_2), 39.3 (CH_2), 41.2 (C), 44.8

(CH), 45.1 (CH_2), 54.4 (CH), 55.5 (CH_3), 56.8 (CH), 65.2 (CH), 69.8 (C), 70.5 (CH_2), 71.3 (CH), 79.8 (CH), 84.1 (CH), 93.2 (CH), 170.8 (C); MS *m*/*z* (rel intensity) 619 (M^+ – H, 2), 545 (5), 489 (58), 287 (100); HRMS calcd for $C_{36}H_{63}O_6Si$ 619.4394; found 619.4329. Anal. Calcd for $C_{36}H_{64}O_6Si$: C, 69.63; H, 10.39. Found: C, 69.52; H, 10.44. Compound **14-*R***: amorphous; $[\alpha]_D$ –10 (*c* 0.76); IR 3424, 1742 cm^{-1}; ^1H NMR 0.09 (3H, s), 0.10 (3H, s), 0.61 (1H, m), 0.79 (3H, s), 0.80 (3H, s), 0.88 (9H, s), 1.06 (3H, d, *J* = 6.7 Hz), 1.22 (3H, s), 1.58 (1H, dd, *J* = 3.6, 7.7 Hz), 2.08 (3H, s), 3.10 (1H, dddd, *J* = 4.6, 4.6, 10.9, 10.9 Hz), 3.32 (3H, s), 3.37 (1H, dd, *J* = 7.3, 7.3 Hz), 3.90 (1H, d, *J* = 10.8 Hz), 3.93 (1H, m), 3.93 (1H, d, *J* = 10.8 Hz), 4.36 (1H, ddd, *J* = 4.5, 7.5, 7.5 Hz); ^{13}C NMR –4.5 (CH_3), –4.3 (CH_3), 12.2 (CH_3), 16.3 (CH_3), 17.9 (C), 20.7 (CH_2), 20.9 (CH_3), 21.2 (CH_3), 24.6 (CH_3), 25.8 (3 × CH_3), 27.8 (CH_2), 28.6 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.2 (CH_2), 35.2 (CH), 35.8 (C), 36.0 (CH), 36.9 (CH_2), 39.2 (CH_2), 41.2 (C), 44.7 (CH), 45.4 (CH_2), 54.3 (CH), 55.5 (CH_3), 56.7 (CH), 65.4 (CH), 69.6 (C), 71.2 (CH), 71.9 (CH_2), 79.7 (CH), 84.0 (CH), 93.5 (CH), 170.9 (C); MS *m*/*z* (rel intensity) 619 (M^+ – H, < 1), 545 (2), 489 (20), 471 (5), 287 (100); HRMS calcd for $C_{36}H_{63}O_6Si$ 619.4394; found 619.4329. Anal. Calcd for $C_{36}H_{64}O_6Si$: C, 69.63; H, 10.39. Found: C, 69.75; H, 10.51.

Asymmetric Dihydroxylation of (22*S*,23*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furost-25-ene (10-*R*). To a solution of OsO_4 (11 mg, 0.04 mmol) in CH_2Cl_2 (0.65 mL) was added (1*S*,2*S*)-N^1,N^2-bis(mesitylmethyl)-1,2-diphenyl-1,2-ethanediamine (25 mg, 0.053 mmol) at rt. The mixture was then cooled to –90 °C and **10-*R*** (20 mg, 0.036 mmol) in CH_2Cl_2 (0.6 mL) was added slowly under N_2. The reaction was stirred at this temperature for 4.5 h. The solvent was removed in vacuo, a solution of saturated aqueous sodium bisulfite and THF (1:1, 4 mL) was added, and the mixture heated at reflux for 2 h. The THF layer was separated and the aqueous solution

was basified with $NaHCO_3$ and extracted with EtOAc. Concentration of the combined THF and EtOAc solutions in vacuo afforded a residue which was purified by column chromatography (hexanes–EtOAc, 80:20) to give the inseparable mixture of **11-*R*** and **13-*R*** (20 mg, 0.035 mmol, 97%). After acetylation (Ac_2O/pyridine) the acetates could be separated by Chromatotron chromatography (hexanes–EtOAc, 93:7) to give **12-*R*** (7 mg, 0.011 mmol) and **14-*R*** (14 mg, 0.022 mmol).

(22*S*,23*S*,25*S*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furostan-25,26-diol (11-*S*) and (22*S*,23*S*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-5α-furostan-25,26-diol (13-*S*). To a solution of compound **10-*S*** (593 mg, 1.09 mmol) in dry CH_2Cl_2 (32 mL) was added pyridine (202 μL, 2.5 mmol) and OsO_4 (283 mg, 1.11 mmol). After 1.5 h, the solvent was removed in vacuo, and the residue dissolved in THF (10 mL) and treated with aqueous saturated solution of Na_2SO_3 (10 mL). The mixture was refluxed for 1.5 h, poured into an aqueous saturated solution of $NaHCO_3$ and extracted with EtOAc. The combined extracts were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (toluene–EtOAc, 85:15) to give compound **11-*S*** (374 mg, 0.65 mmol, 60%) and compound **13-*S*** (249 mg, 0.43 mmol, 40%). Compound **11-*S***: mp 63.2–63.7 ºC (from EtOAc); $[\alpha]_D$ –21.0 (*c* 0.11); IR 3427 cm^{-1}; ^1H NMR (400 MHz) 0.08 (3H, s), 0.09 (3H, s), 0.62 (1H, m), 0.78 (3H, s), 0.80 (3H, s), 0.88 (9H, s), 1.03 (3H, d, *J* = 6.6 Hz), 1.16 (3H, s), 2.10 (1H, m), 3.10 (1H, dddd, *J* = 4.5, 4.5, 10.8, 10.8 Hz), 3.32 (3H, s), 3.39 (1H, d, *J* = 10.8 Hz), 3.42 (1H, dd, *J* = 4.3, 8.8 Hz), 3.45 (1H, d, *J* = 10.9 Hz), 4.12 (1H, ddd, *J* = 5.8, 5.8, 5.8 Hz), 4.29 (1H, ddd, *J* = 5.6, 7.7, 7.7 Hz); ^{13}C NMR (100.6 MHz) –4.6 (CH_3), –4.0 (CH_3), 12.2 (CH_3), 16.8 (CH_3), 18.1 (C), 19.4 (CH_3), 20.8 (CH_2), 25.1 (CH_3), 26.0 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2), 31.7 (CH_2), 32.2 (CH_2), 32.9 (CH), 34.3 (CH_2), 35.1 (CH), 35.9 (C), 36.9 (CH_2), 39.8 (CH_2), 41.4 (C), 42.5 (CH_2), 44.8 (CH), 54.4 (CH), 55.5 (CH_3), 56.6

(CH), 64.9 (CH), 70.0 (CH), 70.4 (CH_2), 71.3 (C), 79.8 (CH), 83.1 (CH), 91.5 (CH); MS *m*/*z* (rel intensity) 547 (M^+ – OMe, <1), 503 (17), 287 (100); HRMS calcd for $C_{33}H_{59}O_4Si$ 547.4183; found 547.4174. Anal. Calcd for $C_{34}H_{62}O_5Si$: C, 70.54; H, 10.79. Found: C, 70.68; H, 10.52. Compound **13-*S***: mp 119.2–120.3 ºC (from EtOAc); $[\alpha]_D$ –10 (*c* 0.16); IR 3482 cm^{-1}; ^1H NMR (400 MHz) 0.08 (3H, s), 0.11 (3H, s), 0.76 (6H, s), 0.85 (9H, s), 1.00 (3H, d, *J* = 6.6 Hz), 1.18 (3H, s), 3.07 (1H, dddd, *J* = 4.7, 4.7, 9.4, 9.4 Hz), 3.29 (3H, s), 3.30 (1H, m), 3.24 (1H, d, *J* = 11.5 Hz), 3.27 (1H, d, *J* = 11.1 Hz), 4.13 (1H, ddd, *J* = 4.2, 5.8, 9.5 Hz), 4.23 (1H, ddd, *J* = 5.0, 7.7, 7.7 Hz); ^{13}C NMR (100.6 MHz) –4.6 (CH_3), –3.5 (CH_3), 12.2 (CH_3), 16.4 (CH_3), 18.2 (C), 20.1 (CH_3), 20.7 (CH_2), 23.6 (CH_3), 26.1 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2), 31.8 (CH_2), 32.1 (CH_2), 33.5 (CH), 34.2 (CH_2), 35.1 (CH), 35.8 (C), 36.9 (CH_2), 39.5 (CH_2), 40.0 (CH_2), 41.3 (C), 44.7 (CH), 54.3 (CH), 55.4 (CH_3), 56.7 (CH), 65.5 (CH), 71.0 (CH_2), 72.1 (C), 72.2 (CH), 79.7 (CH), 82.8 (CH), 92.3 (CH); MS *m*/*z* (rel intensity) 547 (M^+ – OMe, 2), 503 (27), 287 (100); HRMS calcd for $C_{33}H_{59}O_4Si$ 547.4183; found 547.4185. Anal. Calcd for $C_{34}H_{62}O_5Si$: C, 70.54; H, 10.79. Found: C, 70.68; H, 10.52.

(22*S*,23*S*,25*S*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-acetoxy-5α-furostan-25-ol (12-*S*). The compound **11-*S*** (672 mg, 1.16 mmol) was acetylated with Ac_2O and pyridine to give after chromatography (hexanes–EtOAc, 85:15) compound **12-*S*** (567 mg, 0.91 mmol, 79%): amorphous; $[\alpha]_D$ –24.4 (*c* 0.09); IR 3478, 1742 cm^{-1}; ^1H NMR (400 MHz) 0.06 (3H, s), 0.09 (3H, s), 0.766 (3H, s), 0.771 (3H, s), 0.85 (9H, s), 1.01 (3H, d, *J* = 6.9 Hz), 1.18 (3H, s), 2.05 (3H, s), 3.08 (1H, dddd, *J* = 4.5, 4.5, 10.8, 10.8 Hz), 3.29 (3H, s), 3.36 (1H, dd, *J* = 5.2, 8.6 Hz), 3.92 (1H, d, *J* = 11.1 Hz), 4.02 (1H, d, *J* = 10.8 Hz), 4.08 (1H, ddd, *J* = 7.2, 7.2, 7.2 Hz), 4.25 (1H, ddd, *J* = 5.5, 7.7, 7.7 Hz); ^{13}C NMR (100.6 MHz) –4.6 (CH_3), –3.8 (CH_3), 12.2 (CH_3), 16.5 (CH_3), 18.1 (C), 19.9 (CH_3), 20.7 (CH_2), 20.9 (CH_3), 25.3 (CH_3), 26.0 (3 × CH_3), 27.8 (CH_2),

28.7 (CH_2), 31.8 (CH_2), 32.1 (CH_2), 33.1 (CH), 34.2 (CH_2), 35.1 (CH), 35.8 (C), 36.9 (CH_2), 39.7 (CH_2), 41.3 (CH_2), 41.3 (C), 44.7 (CH), 54.3 (CH), 55.4 (CH), 56.7 (CH_3), 65.2 (CH), 70.2 (C), 70.7 (CH_2), 71.0 (CH), 79.7 (CH), 83.0 (CH), 91.7 (CH), 170.8 (C); MS *m*/*z* (rel intensity) 503 ($M^+ - C_6H_{13}O_2$, 7), 489 (4), 287 (100); HRMS calcd for $C_{30}H_{51}O_4Si$, 503.3557; found 503.3586. Anal. Calcd for $C_{36}H_{64}O_6Si$: C, 69.63; H, 10.39. Found: C, 69.71; H, 10.36.

(22*S*,23*S*,25*R*)-3β-Methoxy-23-*tert*-butyldimethylsilyloxy-26-acetoxy-5α-furostan-25-ol (14-*S*). The compound **13-*S*** (469 mg, 0.81 mmol) was acetylated with Ac_2O and pyridine to give after chromatography (hexanes–EtOAc, 85:15) compound **14-*S*** (392 mg, 0.63 mmol, 78%): amorphous; $[\alpha]_D$ –36.7 (*c* 0.06); IR 3417, 1741 cm^{-1}; ^1H NMR (400 MHz) 0.08 (3H, s), 0.12 (3H, s), 0.59 (1H, m), 0.77 (3H, s), 0.78 (3H, s), 0.86 (9H, s), 1.00 (3H, d, *J* = 6.6 Hz), 1.23 (3H, s), 2.07 (3H, s), 3.08 (1H, dddd, *J* = 4.5, 4.5, 10.8, 10.8 Hz), 3.30 (3H, s), 3.34 (1H, dd, *J* = 5.3, 8.5 Hz), 3.89 (1H, d, *J* = 11.1 Hz), 3.93 (1H, d, *J* = 11.1 Hz), 4.12 (1H, ddd, *J* = 5.6, 5.6, 5.6 Hz), 4.25 (1H, ddd, *J* = 5.0, 7.7, 7.7 Hz), 4.42 (1H, br s); ^{13}C NMR (100.6 MHz) –4.6 (CH_3), –3.6 (CH_3), 12.2 (CH_3), 16.5 (CH_3), 18.2 (C), 19.8 (CH_3), 20.8 (CH_2), 20.9 (CH_3), 24.4 (CH_3), 26.1 (3 × CH_3), 27.8 (CH_2), 28.7 (CH_2), 31.8 (CH_2), 32.2 (CH_2), 33.3 (CH), 34.3 (CH_2), 35.1 (CH), 35.8 (C), 36.9 (CH_2), 39.7 (CH_2), 40.7 (CH_2), 41.3 (C), 44.7 (CH), 54.3 (CH), 55.5 (CH_3), 56.7 (CH), 65.2 (CH), 70.5 (C), 71.3 (CH), 71.4 (CH_2), 79.7 (CH), 82.9 (CH), 92.0 (CH), 170.9 (C); MS *m*/*z* (rel intensity) 602 ($M^+ - H_2O$, <1), 545 (3), 503 (3), 287 (100); HRMS calcd for $C_{36}H_{62}O_5Si$; 602.4367 found 602.4316. Anal. Calcd for $C_{36}H_{64}O_6Si$: C, 69.63; H, 10.39. Found: C, 69.51; H, 10.37.

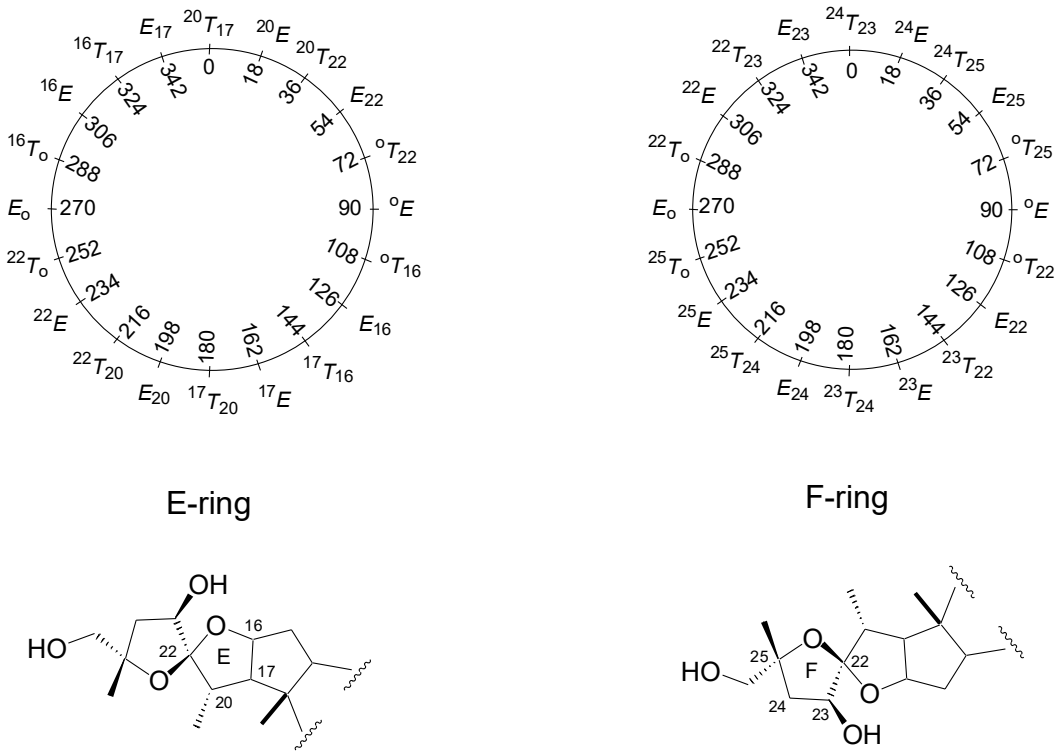

FIGURE 1. Pseudorotational wheels for E and F-rings (steroid numbering is used).