Electronic Supplementary Material (ESI) for Chemical Communications

Convenient method for the functionalization of the 4- and 6-positions of the androgen skeleton

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Table of Contents

1. Experimental Section

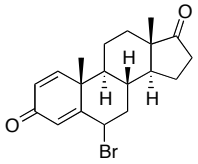
1.1 General Considerations

All reactions were conducted in oven-dried glassware (120 °C, >12 h), under an atmosphere of argon. Commercially available reagents were used as received unless otherwise stated. Solvents were purified by passage through a bed of activated alumina (Grubbs-type solvent purifier). NMR spectra were recorded on Varian INOVA 400 and 600 MHz NMR spectrometers. ^{1}H data is presented as follows: chemical shift (in ppm on the δ scale relative to the residual solvent peaks), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), coupling constant (*J*/Hz), integration, assignment. Coupling constants were taken directly from the spectra. ^{13}C spectra were recorded at 100 MHz and all chemical shift values are reported in ppm on the δ scale relative to the residual solvent peaks. Mass spectrometry was performed on a JEOL JMS-SX102/SX102A/E mass spectrometer using APCI as an ionization method. Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 and reported in units of cm^{-1}. The optical rotation was determined using a Jasco P-2000 polarimeter. Flash chromatography was performed on silica gel 60Å (230-400 mesh).

1.2 Experimental Procedures and Compound Characterisation

Scheme 1 – Int 1

(8*R*,9*S*,10*R*,13*S*,14*S*)-6-bromo-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[α]phenanthrene-3,17(6*H*)-dione

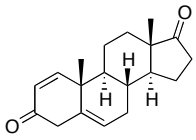


An oven-dried 250 mL round-bottomed flask was charged with steroid (1 eq, 17.6 mmol, 5.00 g), *N*-bromo succinamide (1.1 eq, 19.4 mmol, 3.45 g), and benzoyl peroxide (70% w/w with water, 5 mol%, 0.88 mmol, 213 mg). CCl_4 (50 mL) was added and the reaction stirred rapidly. The reaction was warmed to reflux (80 ^{o}C), and the temperature maintained for 4 h. The reaction was allowed to cool to ambient temperature and a saturated solution of aqueous ammonium chloride (50 mL) was added. The reaction mixture was diluted with CH_2Cl_2 (50 mL). The reaction was separated and organic phase washed with a saturated solution of aqueous ammonium chloride (3 × 50 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic fraction was dried over magnesium sulfate, filtered and concentrated under reduced pressure to afford an orange solid. The bromide was isolated by flash chromatography (eluting with 70:30 hexane/EtOAc), as an off-white solid (4.05 g; 64 %); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.03 (d, 1H, *J* = 10.2 Hz, 1-CH), 6.26 (d, *J* = 1.9 Hz, 1H, 4-CH), 6.23 (app. dt, *J* = 10.2 and 1.9 Hz, 1H, 2-CH), 5.06 (app. t, *J* = 2.1 Hz, 1H, 6-CH), 2.51 (dd, *J* = 19.4 and 9.1 Hz, 1H, 16-CHβ), 2.41 (app. br. d, *J* = 14.8 Hz, 1H, 7-CHβ), 2.32 (ddd, *J* = 21.9, 10.9 and 2.4 Hz, 1H, 7-CHα), 2.11 (ddd, *J* = 18.2, 10.9 and 9.8 Hz, 1H, 16-CHα), 1.97-1.88 (m, 3H), 1.77-1.70 (m, 2H), 1.66 (ddd, *J* = 12.5, 11.2 and 2.1 Hz, 1H, 15-CHβ), 1.59 (s, 3H, 19-CH_3), 1.37-1.27 (m, 2H), 1.18 (ddd, *J* = 15.1, 10.9 and 4.1 Hz, 1H, 9-CH), 1.00 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 164.7, 127.1, 127.0, 53.4, 52.2,

50.6, 47.8, 43.7, 41.1, 37.0, 36.5, 35.9, 34.0, 31.2, 21.8, 20.6, 18.4, 13.9; IR (neat): 2944, 1736, 1660, 1404, 1225, 897; m/z (APCI) 363.1 (40%, M+H), 283.2 (100%, M+H-HBr); HRMS-APCI m/z 363.095 ($C_{19}H_{24}BrO_2$ requires 363.0954); $[\alpha]^{20}_D$ = +99.0 (*c* = 1.0, $CHCl_3$).

Scheme 1 – Int 2

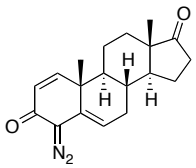
(8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[α]phenanthrene-3,17(4*H*)-dione



A 500 mL beaker was charged with bromide (1.0 eq., 13.8 mmol, 5.00 g). De-ionised water (50 mL) and ethanol (250 mL) were added and the resulting mixture stirred rapidly for 30 minutes. Zinc dust (15 eq., 207 mmol, 6.10 g) was added portion-wise and the resulting slurry was covered and stirred for 72 h at ambient temperature. The reaction was filtered through celite, washing with EtOAc (2 × 50 mL), and concentrated under reduced pressure, affording a white solid. The deconjugated androgen was isolated by flash chromatography (eluting with 80:20 hexane/EtOAc), as a white crystalline solid (2.91 g; 75 %). ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.94 (d, 1H, *J* = 10.2 Hz, C=CH), 5.87 (d, *J* = 10.2 Hz, 1H, C=CH), 5.46-5.44 (m, 1H, C=CH), 3.34 (ddd, *J* = 17.4, 6.3 and 3.6 Hz, 1H, C=C-CH2), 2.91 (d, *J* = 17.4 Hz, 1H), 2.46 (dd, *J* = 19.1 and 8.6 Hz, 1H), 2.20-2.00 (m, 2H), 1.99-1.76 (m, 4H), 1.73-1.49 (m, 4H), 1.38-1.21 (m, 2H), 1.22 (s, 3H, 19-CH3), 0.91 (s, 3H, 18-CH3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 155.6, 136.3, 127.0, 123.0, 51.9, 47.7, 45.9, 45.5, 40.2, 36.0, 31.7, 31.5, 30.2, 22.0, 20.5, 19.5, 13.8; IR (film): 2943, 1720, 1685, 1257, 1087; m/z (APCI) 285.2 (100%, M+H), 283.2 (40%); HRMS-APCI m/z 285.1851 ($C_{19}H_{25}O_2$ requires 285.184); $[\alpha]^{20}_D$ = +120.7 (*c* = 1.0, $CHCl_3$).

2

(8*R*,9*S*,10*R*,13*S*,14*S*)-4-diazo-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[α]phenanthrene-3,17(4*H*)-dione

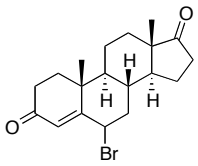


An oven-dried 250 mL round-bottomed flask was charged with deconjugated androgen (1.0 eq., 3.52 mmol, 1.00 g) and diazo transfer reagent (1.2 eq., 4.19 mmol, 951 mg). Anhydrous acetonitrile (100 mL) was added and the reaction was stirred rapidly under an atmosphere of Ar for 20 min at ambient temperature. Diazobicyclo-undecane (1.5 eq., 5.28 mmol, 800 μL) was added drop-wise over 10 minutes. The reaction changed from clear pale yellow to orange and cloudy. The reaction was stirred at ambient temperature for 2 h. The reaction was diluted with Et_2O (50 mL) and quenched with a saturated solution of aqueous ammonium chloride (50 mL). The mixture was separated, extracted with Et_2O (3 × 50 mL) and the combined organic phase washed with brine (2 × 50 mL), dried over magnesium sulfate and concentrated under reduced pressure to afford an orange solid. The steroidal diazo was isolated using the Isolera purification system (SNAP 25 g cartridge, gradient of 90:10 hexane/EtOAc to 5:95 hexane/EtOAc over 10 column

volumes), as an orange solid (720 mg; 67 %). ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.81 (d, 1H, *J* = 10.4 Hz, 1-CH), 5.95 (d, *J* = 10.4 Hz, 1H, 2-CH), 5.36 (dd, *J* = 4.8 and 2.5 Hz, 1H, 6-CH), 2.48 (dd, *J* = 19.2 and 8.9 Hz, 1H, 16-CHα), 2.41-2.31 (m, 1H), 2.11 (dt, *J* = 19.2 and 9.4 Hz, 1H, 16-CHβ), 2.01-1.85 (m, 5H), 1.64-1.50 (m, 2H), 1.46-1.30 (m, 3H), 1.26 (s, 3H, 19-CH_3), 0.92 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 129.0, 126.9, 126.8, 117.9, 51.8, 47.8, 44.7, 39.6, 35.9, 31.8, 31.4, 29.9, 23.7, 21.9, 20.7, 13.9; IR (film): 2944, 2078 (N_2), 1735 (C=O), 1659 (C=O), 1282, 729; m/z (APCI) 311.2 (25%, M+H), 299.2 (100%), 284.2 (39%); HRMS-APCI m/z 311.1757 ($C_{19}H_{23}N_2O_2$ requires 311.1754).

Scheme 1 – Int 3

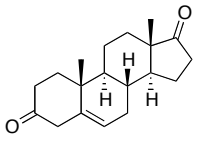
(8*R*,9*S*,10*R*,13*S*,14*S*)-6-bromo-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[α]phenanthrene-3,17(2*H*,6*H*)-dione



An oven-dried 250 mL round-bottomed flask was charged with steroid (1.0 eq., 17.5 mmol, 5.00 g), *N*-bromo succinamide (1.1 eq., 19.2 mmol, 3.42 g), and benzoyl peroxide (70% w/w with water, 5 mol%, 0.88 mmol, 212 mg). CCl_4 (50 mL) was added and the reaction stirred rapidly. The reaction was warmed to reflux (80 °C), and the temperature maintained for 4 h. The reaction was allowed to cool to ambient temperature and a saturated solution of aqueous ammonium chloride (50 mL) was added. The reaction mixture was diluted with CH_2Cl_2 (50 mL). The reaction was separated and organic phase washed with a saturated solution of aqueous ammonium chloride (3 × 50 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic fraction was dried over magnesium sulfate, filtered and concentrated under reduced pressure to afford an orange solid. The bromide was isolated by flash chromatography (eluting with 70:30 hexane/EtOAc), as an off-white solid (3.96 g; 62 %). ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.41 (d, 1H, *J* = 1.9 Hz, 4-CH), 4.88 (ddd, *J* = 13.0, 5.1 and 1.9 Hz, 1H, 6-CH), 2.57 (ddd, *J* = 12.4, 5.1 and 4.8 Hz, 1H), 2.50-2.36 (m, 3H), 2.13-1.93 (m, 2H), 1.88-1.73 (m, 2H), 1.72.164 (m, 2H), 1.64-1.51 (m, 2H), 1.46-1.22 (m, 2H), 1.22 (s, 3H, 19-CH_3), 1.07 (ddd, *J* = 14.0, 10.9 and 4.1, 1H, 9-CH), 0.88 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 164.7, 127.1, 127.0, 53.4, 52.2, 50.6, 47.8, 43.7, 41.1, 37.0, 36.5, 35.9, 34.0, 31.2, 21.8, 20.6, 18.4, 13.9; IR (neat): 2949, 1732, 1668, 1268, 1012; m/z (APCI) 367.1 (15%, M+H), 285.2 (100%); HRMS-APCI m/z 365.1112 ($C_{19}H_{26}O_2Br_1$ requires 365.111); $[\alpha]^{20}_D$ = +12.2 (*c* = 0.5, $CHCl_3$).

Scheme 1 – Int 4

(8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[α]phenanthrene-3,17(2*H*,4*H*)-dione

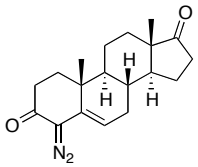


A 500 mL beaker was charged with bromide (1.0 eq., 13.7 mmol, 5.00 g). De-ionised water (50 mL) and ethanol (250 mL) were added and the resulting mixture stirred rapidly for 30 minutes. Zinc dust (15 eq., 206 mmol, 6.20 g) was added portion-wise and the resulting slurry was covered and stirred for 72 h at ambient temperature. The reaction was

filtered through celite, washing with EtOAc (2 × 50 mL), and concentrated under reduced pressure, affording a white solid. The deconjugated androgen was isolated by flash chromatography (eluting with 80:20 hexane/EtOAc), as a white crystalline solid (2.03 g; 52 %). R_f = 0.76 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 5.37 (dd, 1H, *J* = 5.1 and 2.4 Hz, 6-CH), 3.27 (br. d, *J* = 16.5 Hz, 1H, 4-CH_A), 2.84 (d, *J* = 16.5 Hz, 1H, 4-CH_B), 2.51-2.44 (m, 2H), 2.30 (br.d, *J* = 15.2 Hz, 1H), 2.17-2.02 (m, 3H), 1.98-1.93 (m, 1H), 1.87 (br. d, *J* = 12.9 Hz, 1H), 1.75-1.64 (m, 3H), 1.56-1.53 (m, 2H), 1.48 (ddd, *J* = 17.8, 13.4 and 4.5 Hz, 1H, 8-CH), 1.33-1.28 (m, 2H), 1.20 (s, 3H, 19-CH_3), 1.10 (ddd, *J* = 15.3, 11.1 and 3.1 Hz, 1H, 9-CH), 0.91 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 138.9, 124.3, 122.3, 54.1, 51.1, 47.8, 36.9, 36.0, 35.9, 35.4, 34.1, 32.8, 31.7, 30.9, 21.9, 20.8, 19.4, 13.8; IR (film): 2941, 1735, 1708, 1405, 1215, 1013; m/z (APCI) 287.2 (100%, M+H); HRMS-APCI m/z 287.2005 ($C_{19}H_{27}O_2$ requires 287.2006); $[\alpha]^{20}_D$ = +78.9 (*c* = 1.0, $CHCl_3$).

4

(8*R*,9*S*,10*R*,13*S*,14*S*)-4-diazo-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[α]phenanthrene-3,17(2*H*,4*H*)-dione



An oven-dried 250 mL round-bottomed flask was charged with deconjugated androgen (1.0 eq., 3.50 mmol, 1.00 g) and diazo transfer reagent (1.2 eq., 4.2 mmol, 953 mg). Anhydrous acetonitrile (100 mL) was added and the reaction was stirred rapidly under an atmosphere of Ar for 20 min at ambient temperature. Diazobicyclo-undecane (1.5 eq., 5.25 mmol, 800 μL) was added drop-wise over 10 minutes. The reaction changed from clear pale yellow to orange and cloudy. The reaction was stirred at ambient temperature for 2 h. The reaction was diluted with Et_2O (50 mL) and quenched with a saturated solution of aqueous ammonium chloride (50 mL). The mixture was separated, extracted with Et_2O (3 × 50 mL) and the combined organic phase washed with brine (2 × 50 mL), dried over magnesium sulfate and concentrated under reduced pressure to afford an orange solid. The steroidal diazo was isolated using the Isolera purification system (SNAP 25 g cartridge, gradient of 90:10 hexane/EtOAc to 5:95 hexane/EtOAc over 10 column volumes), as an orange solid (675 mg; 63 %). Compound was unstable and used directly.

General Procedures

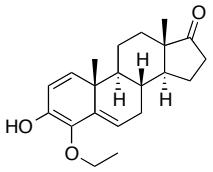
General Procedure for the O-H insertion into alcohols and acids with steroid diazo compounds

An oven dried round-bottomed flask was charged with a solution of ROH (10 eq., 4.0 mmol), in degassed trifluorotoluene (5 mL), to which was added the catalyst (Rh_2(*S*-DOSP)$_4$: 1 mol%, 0.004 mmol; AgOTf: 5 mol%, 0.02 mmol), and the reaction stirred at room temperature for 10 minutes. A solution of steroid diazo (**2** or **6**; 1 eq., 0.4 mmol), in degassed trifluorotoluene (3 mL), was added dropwise over 1 hr. The progress of the reaction was monitored by TLC, and upon consumption of the steroidal diazo starting material (between 2 and 16 hr), the reaction was

concentrated under reduced pressure. Isolation was achieved using flash chromatography (eluting with Hexanes/EtOAc 80:20).

5a

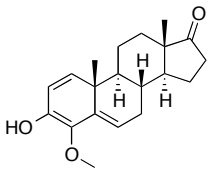
(10*R*,13*S*)-4-ethoxy-3-hydroxy-10,13-dimethyl-9,10,11,12,13,14,15,16-octahydro-7H-cyclopenta[α]phenanthren-17(8H)-one



Isolated as a pale yellow solid (53 mg, 61%). R_f = 0.52 (50:50 Hexane/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 8.08 (br. s, 1H, OH), 7.00 (d, *J* = 10.2 Hz, 1H, 1-CH), 6.23 (d, *J* = 10.2 Hz, 1H, 2-CH), 5.64 (t, *J* = 3.2 Hz, 1H, 6-CH), 4.04 (dq, *J* = 9.4 and 7.0 Hz, 1H, 20-H_A), 3.97 (dq, *J* = 9.4 and 7.0 Hz, 1H, 20-H_B), 2.47 (dd, *J* = 19.0 and 8.9 Hz, 1H, 16β-H), 2.29 (dt, *J* = 14.5 and 2.7 Hz, 1H), 2.85-1.81 (m, 4H), 1.77-1.54 (m, 3H), 1.43 (s, 3H, 19-CH_3), 1.32 (t, *J* = 7 Hz, 3H, 21-CH_3), 1.30-1.19 (m, 3H), 1.16-1.07 (m, 1H), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 156.0, 148.8, 147.5, 127.0, 68.7, 63.9, 51.6, 50.8, 47.9, 44.1, 38.4, 35.9, 31.5, 29.7, 22.2, 22.1, 21.2, 15.7, 14.1; IR (film): 3316, 2941, 1735, 1660, 1628; m/z (APCI) 327.2 (100%, M-H); HRMS-APCI m/z 327.1956 ($C_{21}H_{27}O_3$ requires 327.19547); $[\alpha]^{20}_D$ = +7.4 (*c* = 1.0, $CHCl_3$).

5b

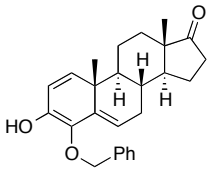
(8R,9S,10R,13S,14S)-4-methoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3H-cyclopenta[α]phenanthrene-3,17(4H)-dione



Isolated as a white solid (44 mg, 49%) R_f = 0.49 (50:50 Hexane/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 10.82 (s, 1H, OH), 6.99 (d, *J* = 10.2 Hz, 1H, 1-CH), 6.29 (d, *J* = 10.2 Hz, 1H, 2-CH), 5.57 (t, *J* = 3 Hz, 1H, 6-CH), 4.87 (m, 1H, 4-CH), 3.40 (s, 3H, OCH_3), 2.51-2.38 (m, 1H), 2.31-2.23 (m, 1H), 2.12-2.03 (m, 1H), 1.98-1.90 (m, 1H), 1.89-1.79 (m, 3H), 1.73-1.52 (m, 2H), 1.33-1.23 (m, 2H), 1.26 (s, 3H, 18-CH_3), 1.15-1.06 (m, 1H), 0.92 (s, 3H, 19-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.3, 182.0, 156.2, 148.7, 127.2, 127.0, 63.8, 63.7, 61.1, 51.7, 50.9, 47.9, 44.2, 38.6, 35.9, 31.5, 29.8, 22.2, 21.2, 14.1; IR (film): 3322, 2941, 1730, 1661, 1629, 1454, 1207; m/z (APCI) 313.22 (10%, M-H), 181.2 (87%), 121.1 (100%); HRMS-APCI m/z 313.1799 ($C_{20}H_{25}O_3$ requires 313.1798); $[\alpha]^{20}_D$ = +12.1 (*c* = 0.5, $CHCl_3$).

5c

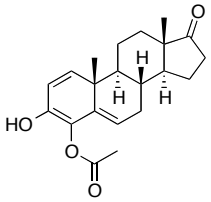
(8*R*,9*S*,10*R*,13*S*,14*S*)-4-(benzyloxy)-3-hydroxy-10,13-dimethyl-9,10,11,12,13,14,15,16-octahydro-7*H*-cyclopenta[α]phenanthren-17(8*H*)-one



Isolated as a white solid (68 mg, 52%) R_f = 0.56 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.82 (br. s, 1H, O-H), 7.42-7.27 (m, 5H, Ar-H), 7.00 (d, *J* = 10.2 Hz, 1H, 1-CH), 6.27 (d, *J* = 10.2 Hz, 1H, 2-CH), 5.40 (t, *J* = 3.1 Hz, 1H, 6-CH), 5.13 (d, *J* = 11.2 Hz, 1H, 20-H_A), 4.92 (d, *J* = 11.2 Hz, 1H, 20-H_B), 2.44 (dd, *J* = 19.6 and 9.1 Hz, 1H, 16-CHβ), 2.11-2.00 (m, 2H), 1.96-1.77 (m, 3H), 1.67 (ddd, *J* = 13.6, 12.4 and 4.6 Hz, 1H, 8-CH), 1.65-1.47 (m, 2H), 1.38 (s, 3H, 19-CH_3), 1.28-1.18 (m, 1H), 1.16-1.05 (m, 1H), 0.97 (ddd, *J* = 12.4, 11.2 and 4.4 Hz, 1H), 0.89 (s, 3H, 18-CH_3), 0.73 (ddd, *J* = 13.0, 127 and 3.8 Hz, 1H, 9-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.8, 156.3, 148.8, 145.9, 137.2, 129.6, 128.7, 128.5, 127.2, 74.4, 51.9, 50.7, 47.8, 44.2, 35.8, 34.1, 31.3, 30.1, 22.2, 22.0, 19.7, 14; IR (film): 3298 (O-H), 2941, 1734 (C=O), 1660 (C=O) , 1157, 1088; m/z (APCI) 389.2 (100%, M-H), 311.2 (60%); HRMS-APCI m/z 389.2109 ($C_{26}H_{29}O_3$ requires 389.2111); $[\alpha]^{20}_D$ = +64.7 (*c* = 0.25, $CHCl_3$).

5d

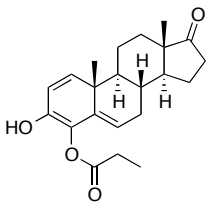
(8*R*,9*S*,10*R*,13*S*,14*S*)-3-hydroxy-10,13-dimethyl-17-oxo-8,9,10,11,12,13,14,15,16,17-decahydro-7H-cyclopenta[α]phenanthren-4-yl acetate



Isolated as a pale yellow solid (54 mg; 68%). R_f = 0.41 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.90 (d, 1H, *J* = 10.2 Hz, 1-CH), 6.05 (app. dd, *J* = 5.9 and 3.3 Hz, 1H, 4-CH), 5.92 (d, *J* = 10.2 Hz, 1H, 2-CH), 5.79-5.75 (m, 1H, 6-CH), 2.47 (dd, *J* = 19.7 and 8.9 Hz, 1H, 16-CHβ), 2.30-2.21 (m, 1H, 7-CHβ), 2.24 (s, 3H, 21-CH_3), 2.18-2.03 (m, 1H, 16-CHα), 2.00-1.76 (m, 4H), 1.75-1.50 (m, 4H), 1.35-1.21 (m, 2H), 1.34 (s, 3H, 19-CH_3), 0.92 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 170.0, 154.6, 134.8, 124.9, 119.0, 74.6, 74.5, 51.8, 47.6, 46.5, 41.9, 35.9, 31.4, 30.9, 29.8, 22.0, 21.0, 20.4, 19.7, 13.8; IR (film): 2937, 1725, 1702, 1373, 1227, 1061, 919; m/z (APCI) 343.2 (81%, M+H), 301.18 (73%), 283.17 (100%); HRMS-APCI m/z 343.1908 ($C_{21}H_{27}O_4$ requires 343.1904); $[\alpha]^{20}_D$ = +39.7 (*c* = 0.5, $CHCl_3$).

5e

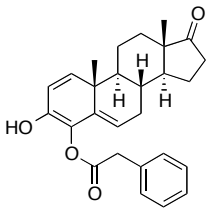
(10*R*,13*S*)-10,13-dimethyl-3,17-dioxo-4,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[α]phenanthren-4-yl propionate



Isolated as a gummy oil (49 mg; 55%). R_f = 0.39 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.95 (d, 1H, *J* = 10.2 Hz, 1-CH), 6.08 (br. s, 1H, H-4), 5.92 (d, *J* = 10.2 Hz, 1H, 2-CH), 5.79-5.76 (m, 1H, H-6), 2.63-2.49 (m, 2H, 21-CH_2), 2.48 (dd, *J* = 19.1 and 8.8 Hz, 1H, 16-CHβ), 2.30-2.23 (m, 1H, 7-CHβ), 2.10 (ddd, *J* = 19.1, 18.0 and 9.1 Hz, 1H, 16-CHβ), 1.99-1.95 (m, 1H, 15-CHα), 1.94-1.84 (m, 2H), 1.84-1.78 (m, 1H), 1.74-1.66 (m, 1H), 1.68-1.59 (m, 1H), 1.58 (ddd, *J* = 14.1, 11.5 and 4.2 Hz, 1H, 15-CHβ), 1.36 (s, 3H, 19-CH_3), 1.35-1.25 (m, 3H), 1.23 (t, *J* = 10.2 Hz, 3H, 22-CH_3), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 173.5, 154.5, 135.0, 124.9, 118.9, 74.3, 51.8, 47.6, 46.5, 41.9, 35.9, 31.4, 30.9, 29.8, 27.6, 21.9, 20.4, 19.7, 13.8, 9.3, 2.0; IR (film): 2942, 1737, 1701, 1373, 1172, 1084, 727; m/z (APCI) 357.2 (45%, M+H), 283.2 (100%); APCI-FTMS m/z 357.2066 ($C_{22}H_{29}O_4$ requires 357.206); $[\alpha]^{20}_D$ = + 43 (*c* = 0.4, $CHCl_3$).

5f

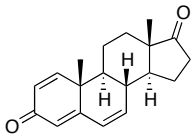
(10*R*,13*S*)-10,13-dimethyl-3,17-dioxo-4,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[α]phenanthren-4-yl 2-phenylacetate



Isolated as a white solid (33 mg; 41%). R_f = 0.39 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.36-7.24 (m, 5H, Ar-H), 6.92 (d, *J* = 10.2 Hz, 1H, 1-CH), 6.05 (br.s, 1H, 4-CH), 5.91 (d, *J* = 10.2 Hz, 1H, 2-CH), 5.57 (app. t, *J* = 2.5 Hz, 1H, 6-CH), 3.84 (s, 2H, 21-CH_2), 2.48 (dd, *J* = 19.4 and 8.6 Hz, 1H, 16-Hβ), 2.21-2.02 (m, 2H), 1.99-1.79 (m, 2H), 1.79-1.69 (m, 1H), 1.69-1.44 (m, 4H), 1.31 (s, 3H, 19-CH_3), 1.31-1.20 (m, 3H), 0.89 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.1, 170.6, 154.6, 134.7, 133.9, 129.7, 128.8, 127.4, 124.8, 119.0, 74.7, 51.7, 47.6, 46.4, 41.9, 41.4, 35.9, 31.4, 30.9, 29.8, 21.9, 20.4, 19.7, 13.8; IR (film): 2945, 1736, 1702, 1454, 1147, 731; m/z (APCI) 419.2 (54%, M+H), 283.2 (100%); HRMS-APCI m/z 419.2224 ($C_{27}H_{31}O_4$ requires 419.2217); $[\alpha]^{20}_D$ = +87.1 (*c* = 0.25, $CHCl_3$).

6

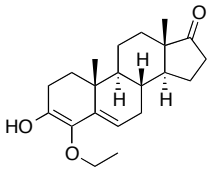
(8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-9,10,11,12,13,14,15,16-octahydro-3*H*-cyclopenta[α]phenanthrene-3,17(8*H*)-dione



Isolated as a clear colourless oil. R_f = 0.49 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.06 (d, 1H, *J* = 10.1 Hz, 1-CH), 6.32 (dd, *J* = 9.9 and 2.9 Hz, 1H, 7-CH), 6.26 (dd, *J* = 10.1 and 1.9 Hz, 1H, 2-CH), 6.11 (dd, *J* = 9.9 and 2.0 Hz, 1H, 6-CH), 6.03 (d, *J* = 1.9 Hz, 1H, 4-CH), 2.59-2.40 (m, 2H), 2.20-2.08 (m, 2H), 1.95-1.89 (m, 2H), 1.78-1.59 (m, 2H), 1.56-1.43 (m, 2H), 1.38-1.28 (m, 1H), 1.22 (s, 3H, 19-CH_3), 0.99 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.4, 161.9, 152.7, 135.9, 128.8, 128.7, 128.6, 128.5, 124.5, 49.1, 48.6, 48.1, 41.3, 37.7, 35.7, 31.4, 21.6, 21.4, 14.1; IR (film): 2938, 1736 (C=O), 1650 (C=O), 1287, 891; m/z (APCI) 283.2 (100%, M+H); HRMS-APCI m/z 283.1693 ($C_{19}H_{23}O_2$ requires 283.1693); $[\alpha]^{20}_D$ = +15.2 (*c* = 0.25, $CHCl_3$).

7a

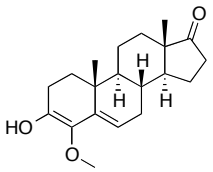
(8*R*,9*S*,10*R*,13*S*,14*S*)-4-ethoxy-3-hydroxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[α]phenanthren-17(2*H*)-one



Isolated as a white powder (46 mg, 53%). R_f = 0.48 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 5.21 (br. s, 1H, 6-CH), 3.97 (dt, *J* = 9.5 and 7.1 Hz, 1H, 20-H_A), 3.73 (dt, *J* = 9.5 and 7.1 Hz, 1H, 20-H_B), 2.61-2.40 (m, 3H), 2.15-2.04 (m, 3H), 2.02-1.93 (m, 2H), 1.86 (dt, *J* = 13.0 and 2.9 Hz, 1H), 1.73-1.56 (m, 4H), 1.46 (ddd, *J* = 13.4, 12.5 and 4.1 Hz, 1H, 8-H), 1.37 (s, 3H, 19-CH_3), 1.33-1.14 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 3H, 21-CH_3), 0.95 (ddd, *J* = 14.5, 9.1 and 4.1 Hz, 1H, 9-H), 0.92 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 151.2, 147.1, 68.9, 63.2, 53.9, 51.3, 47.8, 38.2, 37.1, 36.2, 36.0, 34.5, 31.5, 29.1, 21.9, 20.4, 20.1, 15.6, 13.9; IR (film): 3461 (O-H), 2944, 1735 (C=O), 1681 (C=O), 1196, 1095; m/z (APCI) 330.21 (21%), 329.2 (100%, M-H); HRMS-APCI m/z 329.2116 ($C_{21}H_{29}O_3$ requires 329.2111); $[\alpha]^{20}_D$ = +44.8 (*c* = 0.1. $CHCl_3$).

7b

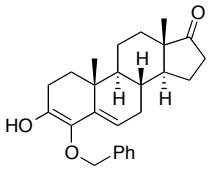
(8*R*,9*S*,10*R*,13*S*,14*S*)-3-hydroxy-4-methoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[α]phenanthren-17(2*H*)-one



Isolated as a clear colourless oil (39 mg, 44 %). R_f = 0.40 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.97 (br. s, 1H, O-H), 5.42 (t, *J* = 2.9 Hz, 1H, 6-CH), 3.66 (s, 3H, 20-CH_3), 2.66-2.40 (m, 4H), 2.26 (dt, *J* = 14.6 and 2.9 Hz, 1H), 2.14-1.18 (m, 4H), 1.75-1.52 (m, 4H), 1.43 (ddd, *J* = 13.5, 12.9, 4.6 Hz, 1H), 1.33 (s, 3H, 19-CH_3), 1.30-1.15 (m, 2H), 0.95 (ddd, *J* = 15.2, 11.4, 5.2 Hz, 1H, 9-H), 0.88 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 124.3, 54.0, 51.0, 47.7, 38.8, 35.9, 35.8, 35.3, 34.1, 32.8, 31.8, 31.5, 30.9, 22.8, 21.9, 20.5, 17.6, 14.3, 13.9; IR (film): 3357, 2944, 1721, 1685, 1208, 1096, 730; m/z (APCI) 315.2 (100%, M-H); HRMS-APCI m/z 315.1959 ($C_{20}H_{27}O_3$ requires 315.1966).

7c

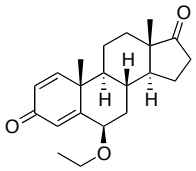
(8*R*,9*S*,10*R*,13*S*,14*S*)-4-(benzyloxy)-3-hydroxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[*a*]phenanthren-17(2*H*)-one



Isolated as a white solid (32 mg, 45%). R_f = 0.50 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.25 (br. s, 1H, O-H), 7.38-7.27 (m, 5H, Ar-H), 5.24 (t, *J* = 3.0 Hz, 1H, 6-CH), 4.94 (d, *J* = 11.1 Hz, 1H, 20-H_A), 4.83 (d, *J* = 11.1 Hz, 1H, 20-H_B), 2.61 (ddd, *J* = 17.1, 15.2 and 4.8 Hz, 1H, 16-Hβ), 2.50-2.39 (m, 3H), 2.12-1.76 (m, 6H), 1.70-1.33 (m, 6H), 1.30 (s, 3H, 19-CH_3), 1.12 (ddd, *J* = 11.3, 10.9 and 5.4 Hz, 1H, 9-H), 0.85 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 148.4, 147.3, 137.1, 130.3, 129.3, 128.6, 128.4, 76.7, 74.4, 54.1, 51.1, 47.7, 38.5, 36.4, 35.9, 34.7, 33.1, 31.4, 29.5, 21.8, 20.2, 18.5, 13.9; IR (film): 3454 (O-H), 2926, 2360, 1734, 1682, 1094; m/z (APCI) 391.2 (100%, M+H), 287.2 (16%); HRMS-APCI m/z 391.2263 ($C_{26}H_{31}O_3$ requires 391.2267); $[\alpha]^{20}_D$ = –96.6 (*c* = 0.2, $CHCl_3$).

8a

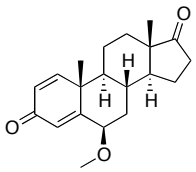
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-ethoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3H-cyclopenta[α]phenanthrene-3,17(6H)-dione



Isolated as a white solid (49 mg, 41%). R_f = 0.54 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 6.99 (d, 1H, *J* = 10.2 Hz, 1-CH), 6.18 (dd, *J* = 10.2 and 1.4 Hz, 1H, 2-CH), 6.13 (d, *J* = 1.4 Hz, 1H, 4-CH), 3.99 (app. t, *J* = 2.9 Hz, 1H, 6-Hα), 3.39 (dq, *J* = 9.2 and 7.0 Hz, 1H, 20-H_A), 3.31 (dq, *J* = 9.2 and 7.0 Hz, 1H, 20-CH_B), 2.43 (dd, *J* = 19.3 and 9.0 Hz, 1H, 16-CHβ), 2.19-2.11 (m, 2H,7-CHβ and 11-CHβ), 2.05 (ddd, *J* = 19.3, 9.6 and 9.0 Hz, 1H, 16-CHα), 1.95-1.90 (m, 1H, 15-CHβ), 1.86-1.79 (m, 2H, 11-CHα and 12-CHβ), 1.70 (dd, *J* = 13.0 and 4.0 Hz, 1H, 8-CHβ), 1.62 (ddd, *J* = 12.4, 9.2 and 3.2 Hz, 1H, 15-CHα), 1.36 (s, 3H, 19-CH_3), 1.30-1.19 (m, 3H, 14-CHα, 12-CHα and 7-CHα), 1.14 (t, *J* = 7 Hz, 3H, 21-CH_3), 1.06 (ddd, *J* = 12.0, 10.9 and 4.0 Hz, 1H, 9-CHα), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 163.7, 156.9, 128.0, 127.9, 127.2, 80.5, 64.3, 52.4, 51.0, 47.9, 43.8, 38.3, 35.9, 31.4, 30.6, 22.1, 22.0, 19.1, 15.2, 14.2; IR (neat): 2941, 1738, 1664, 1403, 1186, 1092, 1010; m/z (APCI) 329.2 (100%, M+H), 283.2 (20%); HRMS-APCI m/z 329.2107 ($C_{21}H_{29}O_3$ requires 329.2111).

8b

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-methoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3H-cyclopenta[α]phenanthrene-3,17(6H)-dione

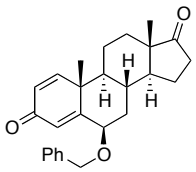


Isolated as an off-white solid (48 mg, 46%). R_f = 0.55 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 7.03 (d, 1H, *J* = 10.1 Hz, 1-CH), 6.2 (dd, *J* = 10.1 and 1.9 Hz, 1H, 2-CH), 6.18 (d, *J* = 1.9 Hz, 1H, 4-CH), 3.89 (app. t, *J* = 2.9 Hz, 1H, 6-CH), 3.23 (s, 3H, OCH_3), 2.45 (dd, *J* = 19.4 and 8.9 Hz, 1H, 16-CHβ), 2.22-2.16 (m, 1H, 7-CHβ), 2.15-2.09 (m, 1H, 7-CHα), 2.10-2.00 (m, 1H, 16-CHα), 1.97-1.89 (m, 1H, 15-CHα), 1.88-1.77 (m, 2H, 11-CHα and 12-CHβ), 1.74 (ddd, *J* = 22.0, 13.1 and 4.1 Hz, 1H, 8-CHβ), 1.66-1.59 (m, 1H, 15-CHβ), 1.38 (s, 3H, 19-CH_3), 1.34-1.20 (m, 3H, 11-CHβ, 12-CHα and 140-CHα), 1.10 (dt, *J* = 12.2 and 4.1 Hz, 1H, 9-CHα), 0.95 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 186.1, 162.9, 156.9, 128.3, 127.2, 82.6, 56.7, 52.1, 50.8, 47.9, 43.9, 38.1, 35.8, 31.4, 30.6, 22.1, 21.9, 19.1, 14.1; IR (film): 902, 1216, 1374, 1661, 1742, 2848, 2916; m/z (ES) 315.2 (45%, M+H), 283.2 (100%), 265.2 (15%); HRMS-ES m/z 315.1955 ($C_{20}H_{27}O_3$ requires 315.1955).

8c

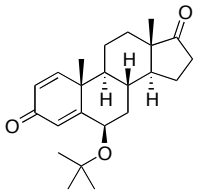
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(benzyloxy)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3H-cyclopenta[α]phenanthrene-3,17(6H)-dione



Isolated as a white solid (26mg, 39%). R_f = 0.56 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 7.37-7.34 (m, 2H, Ar-H), 7.31-7.29 (m, 3H, Ar-H), 7.07 (d, *J* = 10.3 Hz, 1H, 1-CH), 6.25 (d, *J* = 10.3 Hz, 1H, 2-CH), 6.19 (s, 1H, 4-CH), 4.54 (d, *J* = 11.9 Hz, 1H, 20-CH_A), 4.29 (d, *J* = 11.9 Hz, 1H, 20-CH_B), 4.12 (br. s, 1H, 6-CHα), 2.48 (dd, *J* = 19.3 and 8.9 Hz, 1H, 16-CHβ), 2.25-2.18 (m, 2H, 11-CHβ and 7-CHβ), 2.08 (ddd, *J* = 19.3, 18.6 and 9.0 Hz, 1H, 16-CHα), 1.97-1.90 (m, 1H, 15-CHβ), 1.92-1.82 (m, 2H, 12-CHβ and 11-CHα), 1.75 (ddd, *J* = 13.0, 12.6 and 3.2 Hz, 1H, 8-CHβ), 1.68-1.59 (m, 1H, 15-CHα), 1.46 (s, 3H, 19-CH_3), 1.34-1.22 (m, 3H, 14-CHα, 12-CHα and 7-CHα), 1.12 (ddd, *J* = 13.0, 10.8 and 3.9 Hz, 1H, 9-CHα), 0.95 (s, 3H, 18-CH_3); IR (neat): 2942, 1737, 1663, 1453, 1090; m/z (APCI) 391.2 (100%, M+H), 373.2 (6%); HRMS-APCI m/z 391.2267 ($C_{26}H_{30}O_3$ requires 391.2268); $[\alpha]^{20}_D$ = –8.2 (*c* = 0.3, $CHCl_3$);

8d

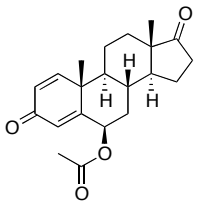
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-tert-butoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3H-cyclopenta[α]phenanthrene-3,17(6H)-dione



Isolated as a colourless crystalline solid (74 mg, 70%). R_f = 0.51 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 7.00 (d, 1H, *J* = 10.1 Hz, 1-CH), 6.18 (dd, *J* = 10.1 and 1.6 Hz, 1H, 2-CH), 6.11 (d, *J* = 1.6 Hz, 1H, 4-CH), 4.29 (app. t, *J* = 2.7 Hz, 1H, 6-CHα), 2.45 (dd, *J* = 19.4 and 9.0 Hz, 1H, 16-CHβ), 2.17 (ddd, *J* = 22.0, 11.4 and 2.7 Hz, 1H, 7-CHβ), 2.10-2.02 (m, 1H, 16-CHα), 1.96-1.89 (m, 2H, 12-CHβ and 15-CHα), 1.85 (dt, *J* = 13.1 and 3.0 Hz, 1H, 11-CHα), 1.72 (ddd, *J* = 22.0, 12.9 and 4.0 Hz, 1H, 8-CHβ), 1.65-1.56 (m, 1H, 15-CHβ), 1.41 (s, 3H, 19-CH_3), 1.30-1.16 (m, 4H, 7-CHα, 11-CHβ, 12-CHα and 14-CHα), 1.16 (s, 9H, t-butyl), 1.01 (dt, *J* = 11.8 and 4.0 Hz, 1H, 9-CHα), 0.96 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 167.1, 157.4, 126.9, 125.5, 125.4, 75.3, 73.1, 73.0, 52.9, 50.8, 48.0, 44.3, 40.4, 35.9, 31.5, 30.4, 28.6, 22.2, 22.1, 20.2, 14.2; IR (film): 961, 1015, 1643, 1783, 2904; m/z (APCI) 357.2 (33%, M+H), 301.2 (65%), 283.2 (100%); HRMS-APCI m/z 357.2423 ($C_{23}H_{33}O_3$ requires 357.2424); $[\alpha]^{20}_D$ = +30.8 (*c* = 1.0, $CHCl_3$).

8e

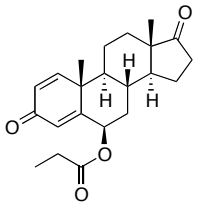
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-3,17-dioxo-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[α]phenanthren-6-yl acetate



Isolated as a white solid (68 mg; 66%). R_f = 0.47 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 7.00 (d, 1H, *J* = 10.2 Hz, 1-CH), 6.30 (d, *J* = 1.9 Hz, 1H, 4-CH), 3.21 (dd, *J* = 10.2 and 1.9 Hz, 1H, 2-CH), 5.52 (t, *J* = 3.2 Hz, 1H, 6-CHα), 2.48 (dd, *J* = 19.4 and 8.9 Hz, 1H, 16-CHβ), 2.16 (dt, *J* = 14.5 and 3.2 Hz, 1H, 7-CHβ), 2.13-2.06 (m, 1H, 16-CHα), 2.10 (s, 3H, 21-CH_3), 1.97-1.92 (m, 1H, 15-CHα), 1.91-1.84 (m, 2H, 12-CHβ and 11-CHβ), 1.71 (dd, *J* = 13.9 and 4.7 Hz, 1H, 8-CHβ), 1.64-1.57 (m, 1H, 15-CHβ), 1.39-1.34 (m, 1H, 7-CHα), 1.34 (s, 3H, 19-CH_3), 1.33-1.20 (m, 3H, 14-CHα, 12-CHα and 11-CHα), 1.14 (ddd, *J* = 13.9, 12.8 and 3.8 Hz, 1H, 9-CHα), 0.97 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 169.9, 159.9, 156.0, 128.8, 128.7, 127.4, 74.6, 51.9, 50.6, 47.9, 43.3, 36.7, 35.8, 31.3, 30.7, 22.1, 22.0, 21.5, 19.7, 14.1; IR (neat): 2943, 1735, 1663, 1372, 1236, 1218, 1021; m/z (APCI) 343.2 (100%, M+H), 283.2 (18%); HRMS-APCI m/z 343.1904 ($C_{21}H_{27}O_4$ requires 343.1904); $[\alpha]^{20}_D$ = +93.8 (*c* = 1.0, $CHCl_3$).

8f

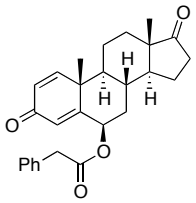
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-3,17-dioxo-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[α]phenanthren-6-yl propionate



Isolated as an off-white solid (81 mg; 71 %). R_f = 0.47 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; CDCl3) δ 7.00 (d, 1H, *J* = 10.2 Hz, 1-CH), 6.30 (d, *J* = 1.9 Hz, 1H, 4-CH), 6.21 (dd, *J* = 10.2 and 1.9 Hz, 1H, 2-CH), 5.54 (t, *J* = 3 Hz, 1H, 6-CHα), 2.48 (dd, *J* = 19.5 and 8.9 Hz, 1H, 16-CHβ), 2.42-2.25 (m, 2H, 21-CH_2), 2.15 (dt, *J* = 14.5 and 3.0 Hz, 1H, 7-CHβ), 2.11-2.02 (m, 1H, 16-CHα), 1.98-1.79 (m, 3H), 1.76-1.65 (m, 1H, 8-CHβ), 1.63-1.52 (m, 1H, 15-CHβ), 1.40-1.31 (m, 1H), 1.33 (s, 3H, 19-CH_3), 1.30-1.16 (m, 4H), 1.13 (t, *J* = 7.6 Hz, 3H, 22-CH_3), 0.85 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 173.3, 160.1, 156.0, 128.7, 127.5, 74.5, 51.9, 50.6, 47.9, 43.3, 36.7, 35.8, 31.8, 31.3, 30.8, 28.0, 22.9, 22.0, 19.8, 14.1, 9.2; IR (film): 2942, 1735, 1680, 1454, 1170, 1011; m/z (APCI) 357.2 (100%, M+H), 283.2 (45%); HRMS-APCI m/z 357.2056 ($C_{22}H_{29}O_4$ requires 357.2060); $[\alpha]^{20}_D$ = +86.2 (*c* = 0.8, $CHCl_3$).

8g

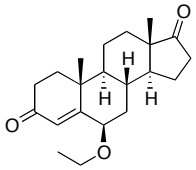
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-3,17-dioxo-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[α]phenanthren-6-yl 2-phenylacetate



Isolated as a white solid (21 mg; 38%). R_f = 0.51 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 7.33-7.12 (m, 5H, Ar-H), 6.94 (d, *J* = 10.2 Hz, 1H, 1-CH), 6.26 (d, *J* = 3.6 Hz, 1H, 4-CH), 6.18 (dd, *J* = 10.2 and 6.8 Hz, 1H, 2-CH), 5.52 (t, *J* = 3.0 Hz, 1H, 6-CHα), 3.63 (s, 2H, 21-CH_2), 2.45 (dd, *J* = 19.6 and 9.4 Hz, 1H, 16-CHβ), 2.15-2.00 (m, 2H), 1.93-1.75 (m, 3H), 1.71-1.53 (m, 2H), 1.42 (ddd, *J* = 18.3, 12.5 and 9.1 Hz, 1H, 15-CHβ), 1.32-1.38 (m, 3H), 1.11-1.01 (m, 1H), 1.07 (s, 3H, 19-CH_3), 0.85 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 170.3, 159.7, 156.1, 134.0, 129.5, 128.9, 128.7, 127.5, 127.3, 75.2, 51.6, 50.3, 47.8, 43.4, 42.2, 36.6, 35.8, 31.2, 31.1, 30.5, 22.0, 21.8, 19.6, 14.1; IR (neat): 2362, 1735, 1665, 1247, 1011; m/z (APCI) 419.2 (100%, M+H), 283.2 (12%); HRMS-APCI m/z 419.2212 ($C_{27}H_{31}O_4$ requires 419.2217); $[\alpha]^{20}_D$ = –2.0 (*c* = 0.1, $CHCl_3$).

9a

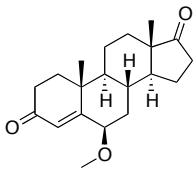
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-ethoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[α]phenanthrene-3,17(2*H*,6*H*)-dione



Isolated as a clear colourless oil (25 mg, 42%). R_f = 0.42 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 5.76 (s, 1H, 4-CH), 3.80 (t, *J* = 2.8 Hz, 1H, 6-CH), 3.38 (dt, *J* = 9.3 and 7.1 Hz, 1H, 20-CH_A), 3.23 (dt, *J* = 9.3 and 7.1 Hz, 1H, 20-CH_B), 2.53-2.45 (m, 1H), 2.45 (dd, *J* = 19.3 and 9.1 Hz, 1H, 16-CHβ), 2.39-2.35 (m, 1H), 2.14-2.05 (m, 3H), 2.02 (ddd, *J* = 13.3, 4.9 and 2.8 Hz, 1H), 1.98-1.94 (m, 1H), 1.87-1.84 (m, 1H), 1.74-1.59 (m, 4H), 1.47 (ddd, *J* = 16.7, 13.2 and 4.1 Hz, 1H), 1.31-1.23 (m, 2H), 1.29 (s, 3H, 19-CH_3), 1.15 (t, *J* = 7.1 Hz, 3H, 21-CH_3), 0.96-0.91 (m, 1H, 9-CH), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 164.5, 128.0, 79.6, 63.7, 54.2, 51.3, 47.8, 38.4, 37.3, 37.2, 36.0, 34.4, 31.5, 30.2, 21.9, 20.4, 18.1, 15.2, 14.0; IR (film): 2943, 2859, 1736, 1678, 1227, 1079; m/z (APCI) 331.2 (100%, M+H); HRMS-APCI m/z 331.2268 ($C_{21}H_{31}O_3$ requires 331.2268).

9b

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-methoxy-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1H-cyclopenta[α]phenanthrene-3,17(2H,6H)-dione

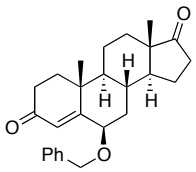


Isolated as a clear colourless oil (21 mg, 39%). R_f = 0.42 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 5.79 (s, 1H, 4-CH), 3.69 (t, *J* = 3.0 Hz, 1H, 6-CHα), 3.19 (s, 3H, OCH_3), 2.57-2.35 (m, 3H), 2.18-1.91 (m, 5H), 1.86 (dt, *J* =

13.0 and 3.8 Hz, 1H, 7-CHβ), 1.76-1.54 (m, 4H), 1.48 (dd, *J* = 13.0 and 4.2 Hz, 1H, 8-CHβ), 1.33-1.19 (m, 2H), 1.28 (s, 3H, 19-CH_3), 0.95 (dd, *J* = 10.8 and 4.2 Hz, 1H, 9-CHα), 0.91 (s, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 163.6, 128.4, 81.8, 56.3, 54.1, 51.2, 47.8, 38.5, 37.3, 37.0, 36.0, 34.4, 31.5, 30.3, 21.9, 20.4, 18.2, 18.1, 14.0; IR (film): 2942, 1736, 1680, 1227, 1085, 729; m/z (APCI) 317.2 (100% M+H); HRMS-APCI m/z 317.2116 ($C_{20}H_{29}O_3$ requires 317.2111).

9c

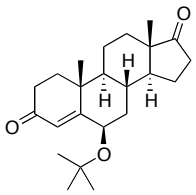
(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(benzyloxy)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[*a*]phenanthrene-3,17(2*H*,6*H*)-dione



Isolated as a white solid (82 mg, 61%). R_f = 0.56 (50:50 Hexanes/EtOAc); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.38-7.24 (m, 5H, Ar-H), 5.79 (s, 1H, 4-CH), 4.50 (d, *J* = 12.0 Hz, 1H, 20-CH_A), 4.22 (d, *J* = 12.0 Hz, 1H, 20-CH_B), 3.90 (t, *J* = 3.0 Hz, 1H, 6-CH), 2.60-2.37 (m, 4H), 2.20-2.01 (m, 4H), 2.00-1.80 (m, 2H), 1.78-1.43 (m, 4H), 1.34 (s, 3H, 19-CH_3), 1.00-0.94 (m, 1H, 9-H), 0.91 (2, 3H, 18-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 138.1, 130.4, 128.8, 128.5, 127.9, 79.0, 70.2, 54.1, 51.2, 47.9, 38.6, 37.4, 37.0, 36.1, 34.7, 31.6, 30.5, 21.9, 20.4, 18.4, 14.2; IR (film): 2944, 2359, 1717, 1679, 1454, 1053; m/z (APCI) 393.2 (100%, M+H), 375.23 (81%), 285.2 (25%); HRMS-APCI m/z 393.2426 ($C_{26}H_{33}O_3$ requires 393.2424); $[\alpha]^{20}_D$ = −12.7 (*c* = 0.5, $CHCl_3$).

9d

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(*tert*-butoxy)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-1*H*-cyclopenta[*α*]phenanthrene-3,17(2*H*,6*H*)-dione



Isolated as a clear colourless oil (31 mg; 46%). R_f = 0.53 (50:50 Hexanes/EtOAc); ^{1}H NMR (600 MHz; $CDCl_3$) δ 5.76 (s, 1H, 4-CH), 4.14 (t, *J* = 2.9 Hz, 1H, 6-CHα), 2.53-2.42 (m, 2H), 2.32 (dt, *J* = 16.7 and 4.2 Hz, 1H), 2.15-2.03 (m, 2H), 2.02-1.91 (m, 2H), 1.90-1.87 (m, 2H), 1.72-1.59 (m, 2H), 1.54-1.43 (m, 2H), 1.34 (s, 3H, 19-CH_3), 1.29-1.18 (m, 3H), 1.15 (s, 9H, *t*-butyl), 0.94 (s, 3H, 18-CH_3), 0.92-0.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 168.7, 125.8, 75.3, 72.3, 54.5, 51.2, 47.9, 39.0, 38.9, 37.6, 36.0, 34.3, 31.6, 30.1, 28.7, 21.9, 20.5, 19.3, 14.1; IR (neat): 2942, 1738, 1677, 1365, 1188, 1042; m/z (APCI) 359 (25%, M+H), 303.2 (100%); HRMS-APCI m/z 359.2577 ($C_{23}H_{35}O_3$ requires 359.2581).